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#### ABSTRACT

The methyl glucoside tetranitrates reacted vigorously at room temperature with an excess of hydroxylamine base dissolved in anhydrous pyridine. Gas consisting of 91% nitrogen and amounting to 1.25 to 1.3 moles per mole was evolved within 20 min. and only a little more during the next 12 hr. Approximately 1.35 moles of nitrate groups in the original tetranitrate had been replaced by hydroxyl groups, for the most part at least without Walden inversions or other change, because hydrogenation of the sirupy product reduced it in more than 80% yield to crystalline methyl glucoside. The product from methyl- $\beta$ -glucoside tetranitrate consisted of the 2,3,6-trinitrate (28%), the 3,6-dinitrate (17%), and an unidentified trinitrate (8%) which might have been a mixture.

The structures of the first two compounds were confirmed by preparing the fully methylated derivatives, denitrating the latter, and identifying the resulting known, partly methylated methyl- $\beta$ -glucosides. New syntheses of methyl- $\beta$ -glucoside-3,6-dinitrate, methyl 2,4-dimethyl- $\beta$ -glucoside, and methyl-4-methyl- $\beta$ -glucoside were found.

### INTRODUCTION

Segall and Purves (38) found that 1 mole of nitrogen per glucose unit was evolved when cellulose trinitrate was dissolved in anhydrous pyridine containing an excess of hydroxylamine base, and approximately one mole of nitrate group was removed from the nitrocellulose. Apart from a small substitution (0.08) of oxime, the nitrate was replaced by a hydroxyl group which was probably of a secondary rather than a primary nature. Severe technical difficulties, however, caused further attempts to determine the structure of the partly denitrated cellulose to be deferred. It therefore became desirable to apply the hydroxylamine-pyridine reaction to the fully nitrated derivative of a simpler carbohydrate related to cellulose, and to locate the nitrate group or groups removed by the reagent. The present research employed the tetranitrates of methyl  $\alpha$ - and  $\beta$ -glucopyranoside for this purpose, because data were available concerning their well-characterized, partly denitrated derivatives (13, 14, 15, 16, 35) which could also be converted, by methylation and subsequent denitration, to one or other of the known methyl ethers of methyl  $\alpha$ - or  $\beta$ -glucoside (7, 13, 14, 15). Gladding and Purves (16) and Ansell, Honeyman, and Williams (4, 5) described the action of aqueous and alcoholic alkali on monosaccharide nitrates, but reports concerning organic bases seemed to be restricted to one by Wigner (40), who found in 1903 that pyridine alone removed one nitrate group selectively from mannitol hexanitrate. Hayward (18) recently showed that the group removed was in the third (or fourth) position.

Preliminary experiments on the stability of the methyl glucoside tetranitrates to anhydrous pyridine showed that, although highly colored substances

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were formed, no gas was evolved at room temperature. About 60% of the unchanged tetranitrates could be recovered after 16 hr. by pouring the solutions into water. In a similar experiment with an alcohol solution of hydroxylamine, at least 75% of the  $\beta$ -tetranitrate could be recovered after 12 hr. Although gas was steadily evolved from the colorless solution, a blank containing no tetranitrate behaved in the same way and the observation was attributed to a slow decomposition of the base. The conjunction of either  $\alpha$ - or  $\beta$ -tetranitrate with free hydroxylamine plus pyridine almost immediately produced a vigorous exothermic reaction; large volumes of a colorless gas were evolved, no unchanged tetranitrate could be isolated after 10 min., and the solution became only slightly yellow after 14 days.

Pure methyl- $\alpha$ -glucoside tetranitrate, which was more readily available than the  $\beta$ -isomer, was used to prepare a series of eight partly denitrated products isolated after reaction times extending from 10 min. to 12 hr. All these products proved to have refractive indices, methoxyl contents, and nitrogen contents that were practically the same. The partial denitration was therefore rapid, and the resulting pale yellow glass was stable or nearly so to the reagent. The fact that analyses for nitrate nitrogen were about 0.7% less than those for total nitrogen suggested that not all of the nitrogen was present as nitrate groups. By analogy with the behavior of cellulose trinitrate, the difference was tentatively attributed to an oxime substitution of about 0.18. On this basis the calculated average substitutions were methoxyl 0.85, nitrate 2.34, and oxime 0.18 moles per methyl glucoside unit, and the yield was about 80% of theory. Since the methoxyl substitution should obviously be unity, the above assumption was unsatisfactory, although no better one was found.

The partly denitrated methyl glucoside tetranitrate was submitted to catalytic hydrogenolysis over a palladized charcoal catalyst by Kuhn's method (26), and pure crystalline methyl- $\alpha$ -glucoside was recovered in a yield of only 82% of theory, whereas the recoveries from the original  $\alpha$ - and  $\beta$ -tetranitrates were 95% to 96%. This decrease in yield provided another reason for the view that perhaps 15% of the product from the partial denitration had failed to retain the basic methyl glucoside structure. All attempts to isolate crystalline di- or tri-nitrates from the product failed, and the same lack of success was encountered when the methylated, benzoylated, or acetylated derivatives were examined, either before or after the removal of the remaining nitrate groups by hydrogenolysis. The  $\alpha$ -series of products was therefore abandoned in favor of the  $\beta$ -series derived from methyl- $\beta$ -glucoside. derivatives of which were often more readily crystallized (34). After two hours in the pyridine-hydroxylamine, the  $\beta$ -tetranitrate gave an 84% yield of a golden-yellow, extremely viscous sirup from which 90% of pure methyl- $\beta$ -glucoside was recovered by hydrogenolysis.

The volume of gas evolved from the  $\beta$ -tetranitrate during the above reaction was measured at intervals, and was corrected for a rapid initial increase in temperature to about 70°C. The latter, nearly linear portion of the rate plot (Fig. 1), when extrapolated to zero time, corresponded to a production of





about 1.25 moles per mole of tetranitrate in the initial rapid reaction. No good explanation was found for the slower reaction represented by the linear portion of the plot, because neither the yield nor the analyses of the partly denitrated product varied substantially with the reaction time, and because no gas was evolved in blank determinations with the pyridine-hydroxylamine reagent. Hydroxylamine, however, was known not to be stable in alkaline solution (30), and its breakdown might have been catalyzed by the sugar nitrate or its decomposition products, as well as by silver, mercury, and other ions (23, 33). The gas evolved during 12 hr. was shown by analysis in an Orsat apparatus and by its density to be nitrogen of 91.4% purity. An absorption of 8.6% in acid cuprous sulphate- $\beta$ -naphthol solution was attributed to the pyridine vapor known to be present, rather than to carbon monoxide. and the solubility of nitrous oxide in pyridine made it possible that small amounts were formed but escaped detection. The presence of nitrous oxide was associated with oxime formation in the parallel research with cellulose trinitrate (38).

Five-gram portions of methyl- $\beta$ -glucoside tetranitrate were then partially denitrated in pyridine-hydroxylamine for two hours with control of temperature (25° to 35°C.), and the products were combined, dried to constant weight, and identified as Sirup 1. If it was assumed that one-half of the gas evolved, in this case 1.3 moles per mole of tetranitrate, came from the hydroxylamine, the loss of the other half from the tetranitrate indicated that Sirup 1 should contain 12.0% of nitrogen and 9.84% of methoxyl groups. The values found were N, 11.8; OCH<sub>3</sub>, 9.1%, the methoxyl content again being definitely low. Efforts were then directed to separating and identifying

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the chemical constituents of the sirup by chromatographic methods, but the methods tried proved unsatisfactory because the literature yielded no information as to suitable conditions, and because reference compounds were inaccessible. Sirup 1 was then subjected to the series of reactions summarized in Table I.





<sup>a</sup> Five grams of the tetranitrate, 50 ml. of pyridine, and 6.25 gm. of hydroxylamine near 30°C. for two hours.

<sup>b</sup> Substitutions per glucose unit; nitrate substitution might include a little oxime.

Substitutions per glucose unit.
 Calc. from yields and substitutions of the three components (next line of table).

Methylation with silver oxide and methyl iodide gave Sirup 2 in practically quantitative yield and with little loss of nitrate groups. When these groups were removed by hydrogenolysis, the yield was again close to theory (Sirup 3) but was only 74% when this mixture of partly methylated methyl glucosides was acetylated with pyridine and acetic anhydride. The product, Sirup 4, crystallized in part, and systematic fractional recrystallization separated

crude methyl-4-methyl- $\beta$ -glucopyranoside triacetate (48%), an isomeric triacetate (11%), and a very viscous, uncrystallized residue (Sirup 5). After purification, the identity of the 4-methyl glucopyranoside triacetate was unequivocally established by means of its melting point and specific rotation (8, 27, 31) and by de-acetylation to methyl 4-methyl- $\beta$ -glucoside. This glucoside was obtained in the crystalline state, m.p. 101°C., in agreement with the recent independent work of McGilvray (29). The substance had the expected behavior toward aqueous sodium periodate, reducing 0.99 mole without the liberation of formic acid or formaldehyde. Acid hydrolysis yielded 4-methyl glucose (32) and its crystalline phenylosazone (13).

The melting point, 76° to 78°C., and the specific levorotation of -38° in chloroform found for the isomeric methyl monomethyl- $\beta$ -glucoside triacetate did not agree with the values recorded for the 2-methyl (9), the 3-methyl (21), or the 6-methyl (19, 20) derivatives. De-acetylation resulted in a glass that could not be crystallized, either as such or as the benzoate. The glass had the methoxyl content of a methyl monomethyl hexoside, but when oxidized with aqueous sodium periodate consumed only 0.6 mole with the liberation of a little formic acid and no formaldehyde. These fractional amounts suggested that the glass was a mixture of various methyl monomethyl glucosides and that the homogeneity observed in the crystalline triacetate was spurious.

The residual Sirup 5 (Table I) was first de-acetylated with methanolic barium methylate, and the uncrystallized product did not change in specific rotation when dissolved for 48 hr. at 0°C. in anhydrous methanol-chloroform containing sodium methylate. Although de-acetylation appeared to be complete, a portion of the product could not be methylated with silver oxide and methyl iodide beyond OCH<sub>3</sub>, 50.1, 49.6%, and no methyl tetramethyl  $\beta$ -glucoside (OCH<sub>3</sub>, 62%) was recovered by fractional distillation of the methylated sample. It was assumed that Sirup 5 contained an acetyl group resistant to saponification by sodium or barium methylate, or of the type encountered by Helferich and Lang (21) and Dewar and Fort (13). The remainder of Sirup 5 was again submitted to de-acetylation, this time with aqueous sodium hydroxide (21), and 55% was recovered as crystalline methyl 2,4-dimethyl- $\beta$ -glucoside with the correct melting point and rotation (13). The structure of this substance was confirmed by its failure to react with aqueous sodium periodate, by its hydrolysis to 2,4-dimethyl glucose, and by the capacity of the latter to yield the crystalline 4-methyl glucose phenylosazone (1,13) with elimination of a methyl group.

The above results clearly showed that the partial denitration of methyl- $\beta$ -glucoside tetranitrate led to a mixture of nitrates which included the 2,3,6and 3,6-derivatives. After standing for two months in a desiccator over phosphorus pentoxide, a sample of Sirup 1 (Table I) deposited in 5% yield the crystalline 3,6-dinitrate, which was identified by its rotation and melting point. This identity was confirmed by a quantitative methylation to the uncrystallized methyl 2,4-dimethyl- $\beta$ -glucoside-3,6-dinitrate (13), and by hydrogenolysis of the latter in 93% yield to crystalline methyl 2,4-dimethyl $\beta$ -glucoside (1, 13). Methyl- $\beta$ -glucoside-3,6-dinitrate was more conveniently isolated by extracting a chloroform solution of Sirup 1 with water, in which the dinitrate was rather soluble (15). The yield was 11.9% by weight, but the extract also contained 20% of a yellow sirup that could not be crystallized. Evaporation of the chloroform solution left a sirup which on methylation yielded another with the approximate composition of a methyl monomethyl glucoside trinitrate. Found: OCH<sub>3</sub>, 17.1, 17.5%. Calc. OCH<sub>3</sub>, 18.1%. A series of experiments, analogous to those already described, recovered the 4-methyl, and the acetylated, unidentified monomethyl, derivatives of methyl glucoside from this trinitrate, but no other substances were identified. Sirup 1, after the partial removal of the 3,6-dinitrate by crystallization, was also acetylated, but fractional crystallization of the mixed acetate nitrates did not yield chemical individuals. These two series of experiments have not been described in detail because they merely confirmed, but did not extend, the results already reported.

Throughout the work noted in Table I and supported by other results, there was no indication that methylation produced an additional substitution of more than two in Sirup I. The partial denitration of the methyl glucoside tetranitrate therefore appeared to remove only one or two nitrate groups from each molecule, and to give a mixture consisting exclusively of di- and tri-nitrates, perhaps contaminated with minor amounts of oximes and other substances. When this possibility was neglected, the production of tri- and di-nitrates was in a molar ratio of about 70:30 from the amount of gas evolved (Fig. 1), about 62:38 from the substitution of nitrate groups in Sirup 1 (Table I), and about 64:36 from the separation effected by extracting a chloroform solution of Sirup 1 with water. The 2,3,6-trinitrate and the 3,6dinitrate preponderated, because about 28% of the original tetranitrate was recovered as crude methyl-4-methyl- $\beta$ -glucoside triacetate, and about 18% as methyl-2,4-dimethyl  $\beta$ -glucoside, from Sirup 4. These yields might actually be greater, because losses of an undetermined nature reduced the yield of Sirup 4 to about 68% of theory.

The isolation of the unidentified methyl monomethyl glucoside triacetate, and of numerous intractable sirups with reasonable analyses, showed that the removal of nitrate groups from the tetranitrate by hydroxylamine in pyridine was to some extent of a random nature. Methyl- $\beta$ -glucoside tetranitrate, moreover, failed to serve as a model of cellulose trinitrate, because the group most affected was in the fourth position of the former substance, and the fourth positions of the glucose residues of the latter were not nitrated. In both cases the partial denitration probably depended upon the superior reactivity of some nitrate groups, whose elimination stabilized the remainder. The elimination might involve the formation of nitrohydroxamic acid, NO<sub>2</sub>NHOH, and its decomposition to nitrogen when in the presence of excess hydroxylamine (3), as previously discussed (38).

## EXPERIMENTAL

### Materials and Methods

Pure methyl- $\beta$ -D-glucoside hemihydrate (24, 25, 28, or 36), when nitrated with acetic anhydride-acetic acid-100% nitric acid as described by Brissaud

(10), gave an 80 to 85% yield of the crystalline 2, 3, 4, 6-tetranitrate with the correct physical constants (6). Pure methyl- $\alpha$ -D-glucoside was nitrated with a phosphoric anhydride – 100% nitric acid mixture (38). The 2,3,4,6 tetranitrate, isolated in 86% yield, showed a marked tendency to remain as a supercooled liquid, but was recrystallized repeatedly by the slow cooling of its solution in ethanol. The analyses and physical constants (10, 26) of the product showed it to be quite pure. Since the two tetranitrates and also their partially nitrated derivatives were explosives, the scale of the preparations was restricted to 5 gm. or less, and all evaporations were under reduced pressure with bath temperatures below 50°C. Samples for analysis were dried to constant weight *in vacuo*. Vacuum distillation of the nitrates was not attempted.

Free crystalline hydroxylamine, prepared as required by a published method (38), was sensitive to moisture, heat, metals, and traces of alkali. The substance was immediately dissolved in pyridine which had been dried over barium oxide and which boiled at 115° to 115.5°C. The solution was stored at 0°C. for not more than 48 hr. before use.

Commercial electrolytic hydrogen and an Adams Low Pressure apparatus were employed in the hydrogenolyses. The palladized charcoal catalyst was prepared by the method of Hartung (17) and when thoroughly dry was pyrophoric. Two-gram-samples of methyl  $\alpha$ - or  $\beta$ -glucoside tetranitrate, when hydrogenated in dioxane-ethanol at 30 to 40 p.s.i. and room temperature for 30 min. over 2 gm. of the catalyst, absorbed 7.6 and 7.8 moles of hydrogen per mole. Theory, 8 moles. The crystalline methyl glucosides were recovered from the filtered hydrogenated liquors in 96 to 98% yield, as Kuhn reported (26). Other hydrogenolyses of nitrate groups were carried out in the same manner.

Total nitrogen, nitrate nitrogen, and methoxyl groups were determined by methods previously indicated (38), and acetyl groups by saponification with alcoholic sodium hydroxide (11). In the oxidations with aqueous sodium periodate, the procedures described by several authors (2,22,37) were adapted and combined so that a single 100 mgm. to 200 mgm. sample revealed the change in optical rotation, the moles of periodate consumed, and of formic acid and formaldehyde produced.

Degrees of substitution were calculated by solving simultaneous equations of the type, % OCH<sub>3</sub> = 3100 x/(180 + 14x + 45y + 13z + 42w), where x, y, z, and w were the molar substitutions of methoxyl, nitrate, oxime, and acetyl groups, respectively. One or more of the unknowns was usually zero in practice, and the small, doubtful oxime substitution z was usually ignored.

## Action of Hydroxylamine-Pyridine on Methyl Glucoside Tetranitrates (Sirup 1)

In a typical experiment, 5 gm. of the  $\beta$ -tetranitrate was mixed with 50 ml. of an ice-cold 12.5% solution of pure hydroxylamine in pyridine contained in a flask fitted with a thermometer and calcium chloride drying tube. The nitrate dissolved readily to give a clear, colorless solution which almost immediately commenced to evolve gas, and to become hot. The final temperature was restricted to 25° to 35°C. by external cooling. After two hours, the solution, now pale yellow and still evolving gas, was poured into 500 ml. of water, the aqueous mixture was rendered just acid to Congo red by adding 4 N sulphuric acid and was extracted with one 200 ml. and four 100 ml. volumes of ether. Continuous extraction of the aqueous residue with ether for seven days removed only 0.17 gm. of a brown liquid that soon changed to a black tar. The washed and dried ether extracts on evaporation gave the golden yellow glass denoted as Sirup 1 (Table I), which was very soluble in acetone, ether, and chloroform, and soluble in methanol, ethanol, and benzene. Found: OCH<sub>3</sub>, 9.11, 9.19; total N (micro-Kjeldahl), 11.7, 11.9%. Calc. for glucose substituted with 0.92 methoxyl and 2.62 nitrate groups (mol. wt. 311): OCH<sub>3</sub>, 9.18; total N, 11.8%. The average yield of 3.5 gm. was 84% of theory according to these substitutions.

One-gram samples of methyl- $\alpha$ -glucoside tetranitrate were separately dissolved in 10 ml. volumes of the pyridine-hydroxylamine reagent, but the solutions were precipitated into water after 10, 20, 30, 60, 120, 240, 360, and 720 min. at room temperature. The aqueous mixtures when extracted with chloroform gave uniform yields of pale yellow glasses with refractive indices within the range  $n_{\rm D}^{20}$ , 1.4925  $\pm$  0.0015, and of constant composition. Found for all samples: OCH<sub>3</sub>, 8.72  $\pm$  0.07; total N (micro-Kjeldahl) 11.65  $\pm$  0.25%; for samples after 10 min. and 120 min., nitrate N (nitrometer) 10.93, 10.95%. Calc. for glucose substituted by 0.846 methoxyl, 2.34 nitrate, and 0.18 oxime groups (mol. wt. 300); OCH<sub>3</sub>, 8.7; total N, 11.7; nitrate N, 10.09%. The yields, 0.65 gm., were about 80% of theory.

# Gas Evolved from Methyl-β-glucoside Tetranitrate-Hydroxylamine-Pyridine

The tetranitrate, 1.00 gm., was placed in a 125 ml. round-bottomed flask fitted with a thermometer and dropping funnel, and connected to two 100 ml. gas burettes by a 3-way stopcock, substantially as described by SegalI and Purves (38). A 12.5% solution of hydroxylamine in pyridine (10 ml.), was run into the flask and the volume and temperature of the gas evolved was noted at two to four minute intervals. The results (Fig. 1) were closely reproducible and were corrected for the vapor pressure of pyridine (31).

To determine the nature of the gas, samples were collected in the absence of air by carrying out the partial denitration for 12 hr. in the Toricellian vacuum of a Lunge nitrometer (38). The samples were then analyzed in an Orsat apparatus fitted with pipettes containing potassium hydroxide, potassium pyrogallate, and acidified cuprous sulphate- $\beta$ -naphthol reagents (39) for the absorption of carbon dioxide, oxygen, and carbon monoxide, respectively. Found: CO<sub>2</sub>, 0.0, 0.0; O<sub>2</sub>, 0.0, 0.0; CO (apparent), 8.6, 8.6; residual gas, 91.4, 91.4%. The residual gas, when dried with anhydrous calcium chloride, was found to have a molecular weight of 28.8 by the method of Daniels, Mathews, and Williams (12). A control determination with commercial nitrogen of 98.4% purity gave the correct molecular weight of 28.02.

# Methylation, Denitration, and Acetylation of Sirup 1 (Table I)

In a typical experiment, Sirup 1, 3 gm., dissolved in 75 ml. of methyl iodide, was heated under reflux with 10 gm. of silver oxide and 4 gm. of powdered Drierite for eight hours. Filtration and evaporation yielded 3.38 gm. of

Sirup 2, which gave a positive diphenylamine test for nitrate groups. Found: OCH<sub>3</sub>, 21.8, 21.5; N, 10.7, 10.7%. Calc. for glucose substituted with 2.26 methoxyl and 2.46 nitrate groups (mol. wt. 322): OCH<sub>3</sub>, 21.75; N, 10.7%. Remethylation did not alter the methoxyl content.

Hydrogenolysis of 6.78 gm. of Sirup 2 yielded 4.41 gm. (98%) of Sirup 3, a colorless, nitrate-free glass. Found: OCH<sub>3</sub>, 32.5, 32.7%. Calc. for glucose substituted with 2.22 methoxyl groups (mol. wt. 211): OCH<sub>3</sub>, 32.6%. A 7.15 gm. sample of Sirup 3 was acetylated overnight at room temperature with pyridine (196 ml.) and acetic anhydride (19.6 ml.) and 8.0 gm. (72%) of the acetate was recovered in a clear, colorless state (Sirup 4).

A solution of all of this product in 55 ml. of anhydrous ether was cooled to 0°C. and was diluted until just turbid with about 5 ml. of pentane. The long needles that separated were removed, and six further crops of crystals were recovered from the mother liquors over a period of four weeks. Evaporation of the mother liquors yielded 3.86 gm. of a tough, viscous sirup which was retained as Sirup 5. The first three crops of crystals, 3.06 gm., all melting between 105° and 108°C., and also the fourth, 0.17 gm., m.p. 96° to 99°C., were crude methyl-4-methyl- $\beta$ -glucoside triacetate. The remaining three fractions, 0.88 gm., each melting rather sharply between 76° and 81°C., contained the crystalline isomer.

### Methyl-4-methyl- $\beta$ -glucopyranoside and its Triacetate

After recrystallization from ether, the crude triacetate, 3.23 gm., yielded 2.51 gm. of pure material as long, colorless needles, with the proper methoxyl content. The melting point,  $107.5^{\circ}$  to  $108.5^{\circ}$ C., and the specific rotation in chloroform,  $-34.8^{\circ}$ , agreed closely with the published values (8,27,32).

A solution of 2.11 gm. in 50 ml. of anhydrous methanol was deacetylated according to Levene and Tipson (28) by adding 2.7 ml. of 0.2 N barium methylate in methanol. After standing overnight at 0°C., barium was removed as the carbonate, and the filtrate yielded 1.3 gm. of long needles. Repeated crystallization from ethyl acetate established the melting point of methyl-4-methyl- $\beta$ -glucoside at 101° to 101.5°C., and the compound had specific levorotations of  $[\alpha]_{D}^{20} - 21.0^{\circ}$  in water (c, 2),  $-17.4^{\circ}$  in methanol (c, 3.44). McGilvray (29) found m.p. 102° to 103°C., and  $[\alpha]_{D}^{20} - 17.6^{\circ}$  in water.

A 200 mgm. sample of the glucoside was dissolved at 20°C. in water, 15 ml. of 0.1458 M sodium metaperiodate, NaIO<sub>4</sub>, was added and the final volume was adjusted to 25 ml. The specific rotation changed from  $-21^{\circ}$  to  $-126^{\circ}$  in 80 min.; no formic acid or formaldehyde was formed and 0.99 moles of periodate per mole of glucoside was consumed.

Hydrolysis of the glucoside, 1.105 gm., with N sulphuric acid near 100°C. caused the specific rotation to assume the constant value of  $51.0^{\circ}$  in 11 hr., and 1.04 gm. of 4-methyl glucose was isolated as a colorless, copper reducing glass with the correct methoxyl content. A 3.846% solution of the sugar in water mutarotated from  $[\alpha]_{D}^{20} + 62.1^{\circ}$  (19 min.) to a constant value of  $+ 56.2^{\circ}$  (330 min.). Munro and Percival (32) reported the final value as  $+ 53^{\circ}$  (c, 2.1). The phenylosazone of the sugar was prepared in 58% yield, and after recrystal-

lization from aqueous acetone the fine yellow needles melted at  $157.5^{\circ}$  to  $159^{\circ}$ C., in agreement with the published value (32).

## Methyl-monomethyl-hexoside Triacetate

Fractions 5 to 7 of Sirup 4, 0.88 gm., were recrystallized from alcohol*n*-pentane until the melting point became constant at 76° to 77.5°C. and the rotation in chloroform was  $-34.6^{\circ}$  (*c*, 16.4). Found: OCH<sub>3</sub>, 18.7, 18.5; acetyl, 36.7, 37.7; N, 0.0, 0.0%. Calc. for C<sub>6</sub>H<sub>7</sub>O<sub>4</sub>(OCH<sub>3</sub>)<sub>2</sub>(CH<sub>3</sub>CO)<sub>3</sub>: OCH<sub>3</sub>, 18.6; acetyl, 38.6%.

An accumulation of 1.64 gm. of the triacetate was dissolved in 10.0 ml. of chloroform and was de-acetylated by adding 0.0165 gm. of sodium dissolved in 16.0 ml. of methanol to the solution. The observed rotation was  $[\alpha]_{D}^{20} - 3.36^{\circ}$  after four minutes and attained constancy at  $-1.96^{\circ}$  after 96 min. The product, 1.025 gm. (101%) could not be crystallized, and 4% solutions in water and methanol at 20°C. had specific rotations (D line) of  $-22.1^{\circ}$  and  $-22.9^{\circ}$ , respectively. Found: OCH<sub>3</sub>, 28.3, 28.4%. Calc. for C<sub>8</sub>H<sub>16</sub>O<sub>6</sub>: OCH<sub>3</sub>: 29.8%.

A solution of 0.933 millimoles (0.194 gm.) of the monomethyl methyl hexoside in 25 ml. of 0.15 M sodium periodate changed in rotation from  $-0.54^{\circ}$  (3 min.) to constancy at  $-1.14^{\circ}$  (60 min.). No formaldehyde was detected in the liquor, but 0.012 millimoles of formic acid was produced and 0.556 millimoles (60%) of periodate was consumed.

# Methyl-2,4-dimethyl- $\beta$ -glucopyranoside and 2,4-Dimethyl Glucose

Sirup 5 (Table I), 3.725 gm., was de-acetylated with alcoholic barium methylate at 0°C. (28), and the uncrystallized product (Sirup 6), 2.95 gm., was dissolved in 40 ml. of water. When this solution was shaken with three 10 ml. volumes of chloroform, the portion extracted and the portion remaining in the aqueous residue had the same properties. Found in each: OCH<sub>3</sub>, 32.9, 32.7%;  $n_p1.4668$ ;  $[\alpha]_p^{20} - 19.7^\circ$  in water.

A second sample of Sirup 6, 0.55 gm., was again de-acetylated by solution for 20 hr. at room temperature in 15 ml. of 0.05 N sodium hydroxide (21). The alkali was exactly neutralized with sulphuric acid and the crystalline residue from the evaporation of the liquor was extracted with boiling acetone. The colorless crystals, 0.55 gm., recovered from the acetone melted at 99° to 113°C., and recrystallization from alcohol-petroleum ether gave 0.22 gm. of Sirup 9, which was not further examined, and 0.28 gm. of pure methyl-2,4dimethyl- $\beta$ -glucoside. Yield, 55% of theory from Sirup 5.

Pure methyl-2,4-dimethyl- $\beta$ -glucoside, which could also be recrystallized from carbon tetrachloride, melted at 123.5° to 124°C. and had specific rotations of  $[\alpha]_{p}^{20} - 17.7°$  in acetone (c, 3.3), and -26.5° in water (c, 3.26). Dewar and Fort (13) found m.p. 124°C. and a rotation of -16.3° in acetone; while the values quoted by Adams, Reeves, and Goebel (1) were m.p. 122° to 124°C. and  $[\alpha]_{p}^{29} - 18.6°$ . A second m.p. of 107° to 108°C. was found for the freshly remelted substance, as Adams and his co-workers reported. No change in rotation or pH occurred when the glucoside was dissolved in aqueous sodium periodate at 20°C. for four hours. No periodate was consumed and no formaldehyde could be detected in the final solution.

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A 0.81 gm. sample of the pure glucoside, when hydrolyzed with boiling N sulphuric acid, gave 0.77 gm. of 2,4-dimethyl glucose as a sirup that did not crystallize. Found: OCH<sub>3</sub>, 29.3, 29.0%. Calc. for C<sub>6</sub>H<sub>10</sub>O<sub>6</sub>(OCH<sub>3</sub>)<sub>2</sub>: OCH<sub>3</sub>, 29.8%. The product readily reduced Fehling's solution, and its specific rotation in water changed from  $[\alpha]_{D}^{20} + 59.2^{\circ}$  (c, 2.88) after 11 min. to a constant value of 62.2° after two hours. When heated near 100°C. for 2.5 hr. with 10 ml. of water, 3 gm. of sodium acetate, 2 gm. of phenylhydrazine, and 3 drops of saturated sodium bisulphite solution, 0.72 gm. of the dimethyl glucose yielded a red oil that was extracted with ether. After being washed with 4 N acetic acid, cooling of the ether solution and the addition of n-pentane caused the crystallization of 0.05 gm. of 4-methyl glucose phenylosazone. Recrystallization from aqueous acetone caused the product to melt correctly at 157° to 158°C., and a mixed m.p. with an authentic sample was not depressed.

### $Methyl-\beta$ -glucopyranoside-3,6-dinitrate

This dinitrate was conveniently isolated by dissolving 26.5 gm. of Sirup 1 (Table I) in 500 ml. of chloroform and extracting the solution four times with 200 ml. volumes of water. The combined aqueous extracts were then continuously re-extracted with ether for 24 hr., or until a fresh ether extract gave no color in the diphenylamine test for the nitrate group. Evaporation of the ether then left 8.56 gm. of a semicrystalline mass which on recrystallization from chloroform gave 3.14 gm. (11.9%) by weight) of the dinitrate.

The large colorless prisms of methyl- $\beta$ -glucoside-3,6-dinitrate when recrystallized from cold chloroform melted at 144° to 145°C. and had a specific rotation of  $[\alpha]_{p}^{20} - 7.2^{\circ}$  in acetone (c, 1.52), in agreement with the observations of Dewar and Fort (13). Found: OCH<sub>3</sub>, 10.9, 10.3; N, 9.85, 9.84%. Calc. for C<sub>6</sub>H<sub>9</sub>O<sub>5</sub>(OCH<sub>3</sub>)(NO<sub>2</sub>)<sub>2</sub>: OCH<sub>3</sub>, 10.9; N, 9.86%.

Two grams of the pure dinitrate, when twice methylated with silver oxide and methyl iodide, yielded 2.15 gm. of an uncrystallized product with the methoxyl and nitrogen contents of methyl-2,4-dimethyl-β-glucoside-3,6dinitrate. The refractive index,  $n_{\rm D}^{20}$ , 1.4623, and the specific rotation in chloroform,  $\left[\alpha\right]_{p}^{20} - 7.9^{\circ}$ , (c, 5.36) were close to those reported (13). A 1.34 gm. sample of this methylated dinitrate on hydrogenolysis gave 0.89 gm. (93%)of crystalline, nitrate-free methyl-2,4-dimethyl- $\beta$ -glucoside with the proper rotation, m.p., and mixed m.p. (13).

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