Syntheses with Partially Benzylated Sugars. VIII.[1] Substitution at C-5 in an Aldose. The Synthesis of 5-*O*-Methyl-D-glucofuranose Derivatives

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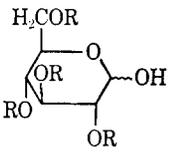
A synthetic route of possibly general applicability for the preparation of C-5-substituted aldoses has been explored. 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (1) was oxidized with dimethyl sulfoxide–acetic anhydride at room temperature to 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (2); with dimethylamine, this lactone gave 2,3,4,6-tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (3). The C-5 position thus exposed was methylated and the methyl ether (4) converted into 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-D-glucono-1,4-lactone (9); reduction of 9 with bis(3-methyl-2-butyl)borane gave 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (11) which was further benzoylated to 1,2,3,6-tetra-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (12).

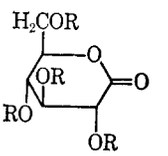
Since the great majority of aldoses and their derivatives exist in the pyranose ring form which engages C-5, the preparation of C-5-substituted aldoses presents a special problem which has been met by many ingenious and effective solutions based in great measure on the specific properties of individual sugars. In this article we shall describe a sequence of reactions which, in principle, should serve for the synthesis of a variety of 5-substituted aldoses.

Aldoses which are fully benzylated except at C-1 and -4 (furanoses) or C-5 (pyranoses) are readily accessible through the benzylation and subsequent hydrolysis of alkyl glycosides. These partially benzylated aldoses need only be converted to some type of acyclic derivative in order to expose C-4 or -5 for further substitution. One might choose a dithioacetal for this purpose and, indeed, an earlier paper in this series[3] described the use of the diethyl dithioacetal from 2,3,5-tri-*O*-benzyl-D-arabinofuranose as an intermediate in the synthesis of 4-*O*-methyl-D-arabinopyranose. However, this type of acyclic derivative suffers from serious limitations; dithioacetals are not always readily preparable from partially benzylated sugars of the type under discussion,[4] they give rise to undesirable side reactions (presumably quaternization of the sulfur) under alkylating conditions, and they make hydrogenation over noble metal catalysts difficult if not impossible. The latter two difficulties were circumvented in the synthesis of 4-*O*-methyl-D-arabinopyranose[3] through conversion of the dithioacetal into a dibenzyl acetal, but this stratagem is cumbersome inasmuch as the C-5 (or C-4) hydroxyl group must be temporarily masked.

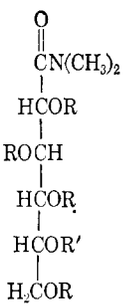
An alternative method for freeing the ring-bound carbon atom in partially benzylated sugars is through the preparation of acyclic aldonic acid derivatives. Here, after making the desired transformation at C-5, one is ultimately confronted with the problem of reducing an aldonic acid to an aldose in high yield. Since certain marked improvements have recently been made in the conversion of acid derivatives to aldehydes,[5,6] we have undertaken the exploration of this alternative pathway. Owing to the ready availability of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (1),[1] we chose the D-glucopyranose series for this investigation and, as a further matter of convenience, elected to methylate C-5.



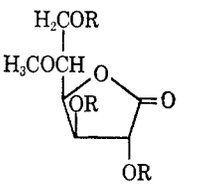
1, R = $C_6H_5CH_2$



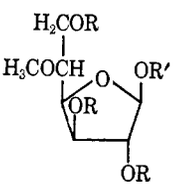
2, R = $C_6H_5CH_2$



3, R = $C_6H_5CH_2$, R′ = H
4, R = $C_6H_5CH_2$, R′ = CH_3
5, R = R′ = H
6, R = R′ = CH_3CO
7, R = H, R′ = CH_3



8, R = H
9, R = C_6H_5CO
10, R = CH_3CO



11, R = C_6H_5CO, R′ = H
12, R = R′ = C_6H_5CO

The first step in the synthesis—the oxidation of 2,3,-4,6-tetra-*O*-benzyl-D-glucopyranose (1) to the corresponding lactone (2)—initially presented some experimental difficulties. While Kiss[7] recommended *N*-bromocarbamide for the oxidation of partially benzylated aldoses, in our hands this reagent failed to oxidize 1. Similarly unsatisfactory results were obtained with chromic anhydride–pyridine and with oxygen in the presence of a platinum catalyst. However, a mixture of dimethyl sulfoxide and acetic anhy-

(1) Paper VII of this series: T. D. Perrine, C. P. J. Glaudemans, R. K. Ness, J. Kyle, and H. G. Fletcher, Jr., *J. Org. Chem.*, **32**, 664 (1967).

(2) Fellow in the Visiting Program of the National Institutes of Health, 1965–1967.

(3) H. G. Fletcher, Jr., and H. W. Diehl, *ibid.*, **30**, 2321 (1965).

(4) For example, all attempts by Dr. J. R. Plimmer in this laboratory to prepare a diethyl dithioacetal from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose have thus far yielded only a mixture of the anomeric forms of the ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-D-glucopyranosides.

(5) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **86**, 1089 (1964).

(6) P. Kohn, R. H. Samaritano, and L. M. Lerner, *ibid.*, **87**, 5475 (1965).

(7) J. Kiss, *Chem. Ind.* (London), 73 (1964). While this author did not specify the substrates which he had used, B. P. Vaterlaus, J. Kiss, and H. Spiegelberg [*Helv. Chim. Acta*, **47**, 381 (1964)] described the oxidation of 3,5,6-tri-*O*-benzyl-2-*O*-methyl-D-glucofuranose to the corresponding aldonolactone using *N*-bromoacetamide. It is possible that furanoses are more readily oxidized by *N*-bromoamides than are pyranoses.

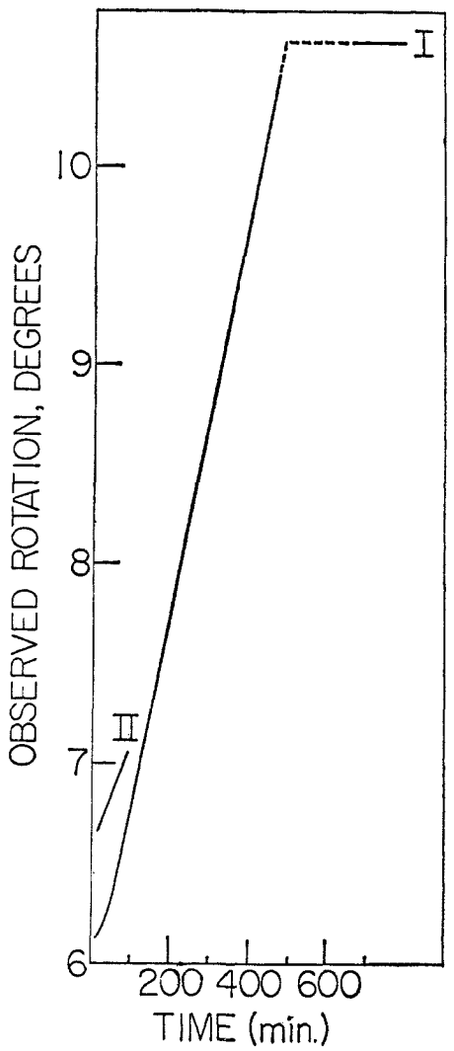
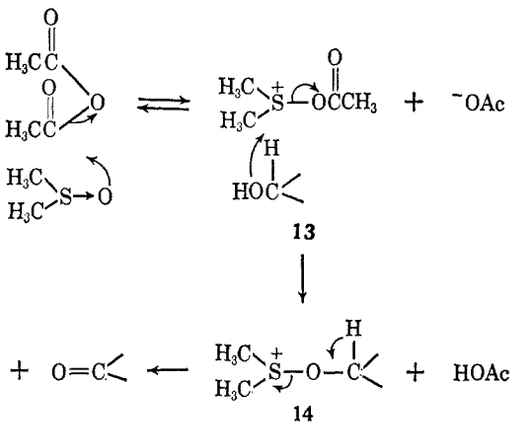


Figure 1.—Plot of rotation against time in oxidation of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) by dimethyl sulfoxide–acetic anhydride: I, all three components mixed simultaneously; II, dimethyl sulfoxide and acetic anhydride mixed 44 hr before addition of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose.

dride[8-11] was found to oxidize **1** to **2** at room temperature in high yield.[12] The reaction could readily be followed polarimetrically and some data, obtained thus in two experiments (I and II), are plotted in Figure 1. Inasmuch as both reagents were present in large excess (42 and 21 molar equiv for dimethyl sulfoxide and acetic anhydride, respectively, in experiment I), it might be expected, *a priori*, that first-order kinetics would be observed. However, as the plot of rotation against time gives virtually straight lines, the reaction is zero order, clearly indicating its multistep character. Albright and Goldman[8] suggested a mechanism for the oxidation of secondary alcohols by dimethyl sulfoxide–acetic anhydride; with some minor elaborations, it serves to rationalize the kinetics observed here. One

(8) J. D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 4214 (1965).
(9) W. Sowa and G. H. S. Thomas, *Can. J. Chem.*, **44**, 836 (1966).
(10) B. Lindberg and K. N. Slessor, *Carbohydrate Res.*, **1**, 492 (1966).
(11) D. Horton and J. S. Jewell, *ibid.*, **2**, 251 (1966).
(12) A related reaction was reported by K. Onodera, S. Hirano, and N. Kashimura [*J. Am. Chem. Soc.*, **87**, 4651 (1965)], who heated 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose with methyl sulfoxide and phosphorus pentaoxide. These workers extracted their product with chloroform and then obtained, *from methanolic solution, methyl 2,3,4,6-tetra-O-acetyl-D-gluconate.* It is highly probable that 2,3,4,6-tetra-*O*-acetyl-D-glucono-1,5-lactone was the immediate product of this oxidation and that the ester isolated arose through solvolysis of this lactone by methanol.

SCHEME I



may envisage the first and rate-determining step as the reversible formation of the acyloxysulfonium salt **13** which then attacks the 2,3,4,6-tetra-*O*-benzyl-D-gluco-

pyranose (represented as HOC< in Scheme I) to give the alkoxysulfonium salt **14**. This intermediate then decomposes to dimethyl sulfide and 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**, represented as O=C< in Scheme I). Since but a minor fraction of the reagents is consumed by the over-all reaction, the rate of formation of **13** is constant throughout the course of the oxidation; if the second and third steps are fast compared with the first step, they will also take place at a constant rate as, in fact, is observed. It will be noted that the plot (Figure 1) of the initial data from experiment I reveals a slight acceleration of the rate. The dimethyl sulfoxide used was not especially dried and it seems probable that **13** would react with water much more rapidly than with **1**. In experiment II, the dimethyl sulfoxide and acetic anhydride were mixed nearly 2 days prior to the addition of **1**; as may be seen in Figure 1, the rate of the reaction was then constant from the earliest observation.[13]

Although **1** is a superbly crystalline substance, all attempts to crystallize 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**) were unsuccessful. However, treatment of **2** with dimethylamine afforded 2,3,4,-6-tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (**3**) in crystalline form and in high yield. That **3** was indeed a D-gluconic acid derivative was demonstrated through the preparation of two derivatives: first, the benzyl groups were removed by catalytic hydrogenolysis to give *N*,*N*-dimethyl-D-gluconamide (**5**) and, second, this substance was acetylated to yield the pentaacetate **6**. Both **5** and **6** were obtained in crystalline form independently from authentic D-glucono-1,5-lactone.

The single hydroxyl group (at C-5) in the acyclic gluconic acid derivative **3** was methylated and then attention turned to the problem of reducing the etherified D-gluconic acid derivative (**4**) to a D-glucose derivative. Brown and Tsukamoto[5] have described the reduction of *N*,*N*-dimethylamides of carboxylic acids to aldehydes in high yield through the use of lithium di- and triethoxyaluminohydrides and we initially explored the use of these reagents for the re-

(13) *Polarimetric observations of the oxidation of (−)-menthol by dimethyl sulfoxide–acetic anhydride have, in one experiment, revealed an "induction period" of approximately 14 min. It is possible that this effect may be ascribed to the initial presence of water.*

duction of **4**. In our hands, the results obtained were erratic; moreover, the product obtained proved markedly unstable, evolving benzaldehyde spontaneously. It is possible that the free aldehydo group of 2,3,4,6-tetra-*O*-benzyl-5-*O*-methyl-*aldehydo*-D-glucose readily forms a peroxide in the presence of oxygen and that this peroxide attacks a sterically accessible benzyl group, liberating it as benzaldehyde.[14]

In passing, it may be noted that 2 molar equiv of lithium aluminum hydride readily reduces 2,3,4,6-tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (**3**) to 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**).

In view of the unstable nature of the product obtained from **4** by reduction with lithium ethoxyaluminohydrides, we turned to the elegant procedure which Kohn, Samaritano, and Lerner[6] devised for the reduction of acylated aldono-1,4-lactones to partially acylated aldofuranoses through the use of bis(3-methyl-2-butyl)-borane. The benzyl groups were removed from 2,3,4,6-tetra-*O*-benzyl-5-*O*-methyl-*N*,*N*-dimethyl-D-gluconamide (**4**) by catalytic hydrogenolysis over a palladium catalyst and the resulting amorphous 5-*O*-methyl-*N*,*N*-dimethyl-D-gluconamide (**7**) was converted, through the action of Amberlite IR-120 (H^+), into 5-*O*-methyl-D-glucono-1,4-lactone (**8**). Although this lactone was also amorphous, it gave a crystalline tetrabenzoate (**9**) and a crystalline tetraacetate (**10**).

The reduction of the tetrabenzoate (**9**) with bis(3-methyl-2-butyl)borane proceeded smoothly to give 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (**11**) in high yield; the introduction of a fourth benzoyl group into **11** afforded 1,2,3,6-tetra-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (**12**). In aqueous dioxane solution, **11** showed a dextrorotation while the H_1 signal in the nmr spectra of both **11** and **12** appeared as a sharp singlet; this evidence may be regarded as showing that both **11** and **12** are β anomers.

In conclusion, it may be noted that the excellent crystallinity and high melting points of **9** and **12** suggest that these new substances may constitute the best derivatives currently available for the identification of 5-*O*-methyl-D-glucofuranose.

Experimental Section[15]

Oxidation of 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (1).—A solution of **1**[1] (3.7 g, 6.8 mmoles) in dimethyl sulfoxide (21 ml, 300 mmoles) was diluted with acetic anhydride (14 ml, 150 mmoles) and left at room temperature overnight. The reaction mixture was cooled, water was added, and the syrup which precipitated was centrifuged, the aqueous layer being discarded. The syrup was washed thoroughly with fresh water and centrifuged; the washings were discarded; this washing was repeated a total of ten times and the syrup was then dissolved in chloroform (200 ml). After a further washing with water, the chloroform solution was dried with sodium sulfate and concentrated *in vacuo* to give crude 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**2**) as a pale yellow syrup, 3.1 g (84%). On tlc (benzene–ether, 7:1, v/v), the product gave but a single spot, though with considerable tailing, when sprayed with dilute sulfuric acid and heated; when sprayed with the hydroxylamine–ferric chloride reagents,[16] only a single component (without tailing) was visible. Since pure **2**, prepared from 2,3,4,6-tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (**3**) as described later in this paper, behaved in a similar fashion on tlc, it seems likely that the tailing represents 2,3,4,6-tetra-*O*-benzyl-D-gluconic acid. The syrupy **2** showed infrared absorption (neat) at 1750 ± 5 cm^{-1} (C=O, δ-lactone) but none in the hydroxyl absorption region.

Since the oxidation of **1** takes place in solution at room temperature, the rate of the reaction was measured polarimetrically. In experiment I a sample of **1** (3.7770 g, 6.99 mmoles) was dissolved in dimethyl sulfoxide (21.0 ml, 296 mmoles) and the solution, in a 1.5-dm polarimeter tube, diluted with acetic anhydride (14.0 ml, 148 mmoles). In experiment II a mixture of dimethyl sulfoxide (42.0 ml, 592 mmoles) and acetic anhyride (28.0 ml, 297 mmoles) was stored at 20° for 44 hr; 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**, 5.0759 g, 9.39 mmoles) was then dissolved in the mixture and the reaction observed polarimetrically in a 1.5-dm tube at 21.5°. Rotational data from both experiments are plotted against time in Figure 1.

2,3,4,6-Tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (3).—A solution of **2** (12.8 g) in anhydrous ether (60 ml) was cooled and treated with dimethylamine (10 ml) and stored in a closed container at room temperature for 3 hr. The solvent was evaporated *in vacuo* from the crystalline mass and the residue was recrystallized twice from cyclohexane: 11.7 g (85%); mp 103–105°; $[\alpha]^{20}D$ +35.1° (*c* 2.93, $CHCl_3$); infrared absorption (Nujol) at 3500 ± 5 (OH) and 1640 ± 5 cm^{-1} (C=O, amide).

Anal. Calcd for $C_{36}H_{41}NO_6$ (583.74): C, 74.07; H, 7.08; N, 2.40. Found: C, 74.08; H, 7.04; N, 2.35.

2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (2) from 2,3,4,6-Tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (3).—To a solution of **3** (500 mg) in dioxane (10 ml) was added dry Amberlite IR-120 (H^+) (2 g) and the resulting suspension was boiled and stirred under reflux for 4 hr. The resin was removed from the cooled solution by filtration and the filtrate was concentrated *in vacuo* to a syrup which was chromatographed on silica gel (25 g) using benzene–ether (1:1, v/v) as eluent. Removal of the solvent from the eluate afforded a colorless syrup: *ca.* 200 mg (43%); $[\alpha]^{20}D$ +79.9° (*c* 4.54 $CHCl_3$).

Anal. Calcd for $C_{34}H_{34}O_6$ (538.64): C, 75.81; H, 6.36; Found: C, 75.81; H, 6.43.

***N*,*N*-Dimethyl-D-gluconamide (5) from D-Glucono-1,5-lactone.**—To a suspension of D-glucono-1,5-lactone (2 g) in methanol (20 ml) was added anhydrous dimethylamine (5 ml); the lactone dissolved immediately with the evolution of heat. After storage at room temperature for 2 hr, the solution was concentrated *in vacuo* to give a white powder (2.4 g) which was recrystallized from a mixture of methanol (50 ml) and pentane (50 ml): 2 g (80%); mp 140–141°; $[\alpha]^{20}D$ −30.9° (*c* 2.13, H_2O).

Anal. Calcd for $C_8H_{17}NO_6$ (223.23): C, 43.04; H, 7.68; N, 6.28. Found: C, 43.05; H, 7.55; N, 6.24.

2,3,4,5,6-Penta-*O*-acetyl-*N*,*N*-dimethyl-D-gluconamide (6).

A. From *N*,*N*-Dimethyl-D-gluconamide (5).—A sample of **5** (500 mg) was treated with pyridine (5 ml) and acetic anhydride (2 ml) and the solution was stored at room temperature overnight. The reaction mixture was worked up in conventional fashion to yield a syrup which crystallized spontaneously. Recrystallization from ethyl acetate–pentane gave pure **6**: 600 mg (62%); mp 108–109°; $[\alpha]^{20}D$ +52.8° (*c* 2.64, $CHCl_3$); infrared absorption (Nujol) at 1750 ± 5 (C=O, ester) and 1655 ± 5 cm^{-1} (NH).

Anal. Calcd for $C_{18}H_{27}NO_{11}$ (433.42): C, 49.88; H, 6.28; N, 3.23. Found: C, 49.99; H, 6.30; N, 3.14.

B. From 2,3,4,6-Tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (3).—A solution of **3** (1.4 g) in methanol (20 ml) was shaken with hydrogen in the presence of palladium black until absorption of the gas had ceased. After removal of the catalyst and solvent, the product was obtained as a syrup (400 mg) which crystallized on seeding with authentic **5**; it was recrystallized from methanol–pentane, mp 142° dec. Its infrared absorption spectrum and behavior on tlc (2-propanol–water, 1:1, v/v) were indistinguishable from those of an authentic sample of **5**. Acetylation in conventional fashion gave **6**, mp and mmp with **6** made from D-glucono-1,5-lactone 108–109°. The infrared absorption spectrum

(14) R. Gigg and C. D. Warren [*J. Chem. Soc., Sect. C*, 1879 (1966)] reported 2,3,4,5-tetra-*O*-benzyl-*aldehydo*-L-lyxose "as a syrup which was dried under high vacuum and used as soon as possible in the subsequent reaction," suggesting that this substance may also be unstable. Partially benzylated sugars such as 2,3,5-tri-*O*-benzyl-D-arabinose often evolve traces of benzaldehyde on prolonged storage, but the stability of such hemiacetals is fully adequate for the synthetic purposes described in this series of papers.

(15) Melting points are corrected. Thin layer chromatography was conducted on silica gel G (E. Merck AG, Darmstadt) using the solvent systems specified, compounds being detected by spraying with 10% sulfuric acid and heating at 100°. Column chromatography was carried out using silica gel (0.05–0.20 mm) of E. Merck AG. Nmr spectra were obtained in $CDCl_3$ solution using a Varian A-60 spectrometer and tetramethylsilane as an internal standard.

(16) M. Abdel-Akher and F. Smith, *J. Am. Chem. Soc.*, **73**, 5859 (1951).

and tlc behavior (benzene–ether, 1:2, v/v) were identical with those of authentic material as prepared in A.

2,3,4,6-Tetra-*O*-benzyl-5-*O*-methyl-*N*,*N*-dimethyl-D-gluconamide (4).—To a solution of **3** (3.5 g) in *N*,*N*-dimethylformamide (20 ml) were added methyl iodide (3 ml), barium oxide (2.5 g, freshly powdered lumps), and barium hydroxide octahydrate (1 g) and the suspension was stirred under a reflux condenser at 30–35° (bath) overnight. Water was added and the mixture was extracted with three 100-ml portions of ether; the combined extracts were washed with water.[17] Moisture was removed with sodium sulfate and the solution was concentrated *in vacuo* to yield **4** as a syrup (3.2 g, 89%) which was chromatographically homogeneous on tlc (benzene–ether, 1:1, v/v). Prior to analysis, the product was chromatographed on a column of silica gel using benzene–ether (5:4, v/v), $[\alpha]^{20}D$ +16.1° (*c* 3.22, $CHCl_3$).

Anal. Calcd for $C_{37}H_{43}NO_6$ (579.76): C, 74.35; H; 7.25; N, 2.34. Found: C, 74.54; H, 7.52; N, 2.32.

2,3,6-Tri-*O*-benzoyl-5-*O*-methyl-D-glucono-1,4-lactone (8).—Palladium chloride (1 g) was suspended in methanol and the solution was shaken with hydrogen until the palladium was fully reduced. The methanol was decanted and the catalyst repeatedly washed by decantation with fresh methanol. A solution of **4** (11.5 g) in methanol (200 ml) was added to the catalyst and the suspension was shaken with hydrogen until absorption of the gas had ceased (3 hr); removal of the catalyst and the solvent then gave syrupy 5-*O*-methyl-*N*,*N*-dimethyl-D-gluconamide (**7**) which was chromatographically homogeneous (tlc, dioxane–ether, 2:1, v/v): 4.5 g (99%), infrared absorption (neat) at 3450 ± 5 (OH) and 1630 ± 5 cm^{-1} (C=O, amide).

To a solution of **7** (3.3 g) in dioxane (60 ml) was added dry Amberlite IR-120 (H^+) (8 g) and the suspension was stirred and boiled under reflux for 1.5 hr; removal of the resin and the solvent gave crude 5-*O*-methyl-D-glucono-1,4-lactone (**8**) as a yellow syrup (2.4 g) which was chromatographed on a column of silica gel (150 g) using dioxane–ether (2:1, v/v) as eluent[18] to yield 5-*O*-methyl-D-glucono-1,4-lactone (**8**) as a syrup (1.9 g 72%), infrared absorption (neat) at 1780 ± 5 cm^{-1} (C=O of γ-lactone).

To a cooled solution of **8** (2.85 g) in dry pyridine (65 ml) was added benzoyl chloride (7.5 ml) and the resulting mixture was left at room temperature overnight. A few drops of water were added and, after storage at room temperature for 1 hr, the reaction mixture was poured into ice water. The precipitate which formed was removed by filtration, washed with water, and dried, 6.8 g. After two recrystallizations from absolute ethanol, the 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-D-glucono-1,4-lactone (**9**) was chromatographically homogeneous (tlc, benzene–ether, 7:1, v/v): 5.7 g (76%); mp 156–158°; $[\alpha]^{20}D$ +105° (*c* 1.01, $CHCl_3$); infrared absorption (Nujol) at 1820 ± 5 (C=O, γ-lactone) and 1740–1700 cm^{-1} (ester C=O).

Anal. Calcd for $C_{28}H_{24}O_9$ (504.50): C, 66.66; H, 4.80. Found: C, 66.54; H, 4.94.

2,3,6-Tri-*O*-acetyl-5-*O*-methyl-D-glucono-1,4-lactone (10).—A solution of chromatographed **8** (1.4 g) in dry pyridine (10 ml) was treated with acetic anhydride (5 ml) and stored at room temperature overnight. The reaction mixture was worked up in conventional fashion to yield a syrup (2.0 g, 86%) which was chromatographically homogeneous (tlc, benzene–ether, 1:1, v/v). A little ether was added to the syrup which was then scratched to initiate crystallization. After two recrystallizations from ether, **10** was obtained in pure form: mp 61–62°; $[\alpha]^{20}D$ +54.5° (*c* 4.00, $CHCl_3$); infrared absorption at 1800 ± 5 (C=O, γ-lactone) and 1740 ± 5 cm^{-1} (C=O, ester).

Anal. Calcd for $C_{13}H_{18}O_9$ (318.28): C, 49.06; H, 5.70. Found: C, 49.30; H, 5.78.

2,3,6-Tri-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (11).—The procedure of Kohn, Samaritano, and Lerner[6] was used. Bis(3-methyl-2-butyl)borane was prepared from 2-methyl-2-butene (16.4 ml) and a 1.37 *N* solution of diborane in tetrahydrofuran (60 ml). To this solution was added dropwise, under nitrogen and at room temperature, a solution of **9** (5 g) in tetrahydrofuran (40 ml, freshly distilled from lithium aluminum hydride). The reaction mixture was stirred at room temperature for 5 hr and then stored overnight under nitrogen at room temperature. Water (10 ml) was added dropwise and the mixture boiled under reflux for 30 min. The solution was then cooled to 0° and 30% hydrogen peroxide (15 ml) added slowly while the pH was maintained between 6.5 and 7.5 through the addition of 3 *N* sodium hydroxide (*ca.* 18 ml). The white precipitate which formed was removed by filtration and washed thoroughly with tetrahydrofuran. The major part of the solvent was removed *in vacuo* (25–30° bath) from the combined filtrate and washings and the residual solution extracted with chloroform (200 ml). The extract was washed successively with aqueous ferrous sulfate solution and with water; it was then dried with magnesium sulfate. Concentration *in vacuo* of the solution afforded a syrup (4.5 g, 90%) which strongly reduced hot Fehling solution and, except for some tailing, was homogeneous on chromatography (tlc, benzene–ether, 7:1, v/v). The syrup crystallized spontaneously and the 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (**11**) was then recrystallized successively from ethyl acetate–pentane (1:1, v/v) and from a small volume of methanol: mp 147–148°; $[\alpha]^{20}D$ +42.6° (*c* 1.36, $CHCl_3$, 5 min); $[\alpha]^{20}D$ +31.9° (10 min) → +55.8° (1240 min, constant, *c* 1.49, dioxane–water, 18:7, v/v); infrared absorption (Nujol) at 3450 ± 5 (OH), 1710 and 1690 ± 5 cm^{-1} (C=O, ester); nmr signals at τ 6.53 (singlet, 1 H, H_1) and 6.75 (singlet; 3 H, CH_3).

Anal. Calcd for $C_{28}H_{26}O_9$ (506.52): C; 66.39; H, 5.17. Found: C, 66.41; H, 5.33.

1,2,3,6-Tetra-*O*-benzoyl-5-*O*-methyl-β-D-glucofuranose (12).—To a cooled solution of **11** (1.5 g) in pyridine (4 ml) was added benzoyl chloride (800 mg) and the reaction mixture was stored at 0° for 2 hr and then at room temperature overnight. Several drops of water were added and, 1 hr later, the reaction mixture was poured into ice water (60 ml). On scratching, the gum that separated solidified completely; it was removed by filtration, washed with aqueous sodium bicarbonate solution and with water, and then dried, 2 g. The product appeared to be chromatographically homogeneous in benzene–ether (7:1, v/v). It was recrystallized from methanol (250 ml): 1.5 g (83%); mp 141–143° (a further recrystallization from absolute ethanol raised this to mp 144–147°); $[\alpha]^{20}D$ +29.2 (*c* 2.05, $CHCl_3$); infrared absorption (Nujol) at 1710 ± 5 cm^{-1} (C=O, ester); nmr signals at τ 3.31 (singlet, H_1), 4.23 (singlet, H_2), and 6.68 (singlet, CH_3).

Anal. Calcd for $C_{35}H_{30}O_{10}$ (610.63): C, 68.84; H, 4.95. Found: C, 68.58; H, 4.89.

Reduction of 2,3,4,6-Tetra-*O*-benzyl-*N*,*N*-dimethyl-D-gluconamide (3) to 2,3,4,6-Tetra-*O*-benzyl-D-glucose (1) with Lithium Aluminum Hydride.—To a mixture of lithium aluminum hydride (64 mg, 1.69 mmoles) and ether (10 ml) which was cooled to 0–4° was added a solution of **3** (1.0 g, 1.71 mmoles) in tetrahydrofuran (20 ml) and the mixture was stirred at 0° overnight. Examination by tlc[19] then showed that about half of the starting material was still present. A second quantity (64 mg) of lithium aluminum hydride, dissolved in ether (20 ml), was added to the reaction mixture which was then held at 0° for an additional 3 hr. With stirring, 5 *N* sulfuric acid (20 ml) was added and, after 10 min, the mixture was extracted with two 250-ml portions of ether. The extract was washed successively with aqueous sodium bicarbonate solution and water. After drying with sodium sulfate, it was concentrated *in vacuo* to give a white solid (700 mg) which was recrystallized from cyclohexane: 500 mg (54%); mp 152–154°; infrared spectrum and tlc behavior identical with those of authentic 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose.

Registry No.—**1**, 4132-28-9; **2**, 13096-62-3; **3**, 13096-63-4; **4**, 13096-64-5; **5**, 13096-65-6; **6**, 13096-66-7; **7**, 13096-67-8; **8**, 13096-68-9; **9**, 13096-69-0; **10**, 13096-70-3; **11**, 13096-71-4; **12**, 13096-72-5.

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(17) A yellow color in the extract was usually discharged at this stage; when it persisted, it was removed by washing the solution with aqueous sodium thiosulfate solution.

(18) As will be noted, chromatography on **8** on silica gel entails considerable loss and, indeed, when a higher proportion of silica gel is used, the loss becomes substantial. It is probable that the conversion of **8** to the corresponding free acid (with a much slower rate of migration) is responsible for this loss; in any event, the excellent crystallizing properties of 2,3,6-tri-*O*-benzoyl-5-*O*-methyl-D-glucono-1,4-lactone (**9**) suggest that higher yields of this substance might be obtained through the direct benzoylation of crude, unchromatographed **8**.

(19) For this purpose, a small sample of the reaction mixture was treated with dilute sulfuric acid and the upper layer which separated was examined using benzene–ether (7:1, v/v).