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1,6-ANHYDRO-4-*O*-BENZYL-β-D-GLUCOPYRANOSE

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ABSTRACT

Benzylation of phenyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside (**1**) with benzyl bromide and silver oxide in *N*,*N*-dimethylformamide gave 57% of phenyl 2,3,6-tri-*O*-acetyl-4-*O*-benzyl-β-D-glucopyranoside (**2**). Deacetylation of **2** and treatment with hot alkali converted **2** into crystalline 1,6-anhydro-4-*O*-benzyl-β-D-glucopyranose (**3**) in high yield. Methylation or acetylation of **3** followed in each case by hydrogenation over palladium gave 1,6-anhydro-2,3-di-*O*-methyl- and 2,3-di-*O*-acetyl-β-D-glucopyranose (**4** and **8**), respectively. Hydrolysis of **4** and treatment of the product with aniline gave the known 2,3-di-*O*-methyl-*N*-phenyl-D-glucosylamine. Methylation of **8** with diazomethane followed by deacetylation yielded 1,6-anhydro-4-*O*-methyl-β-D-glucopyranose (**11**).

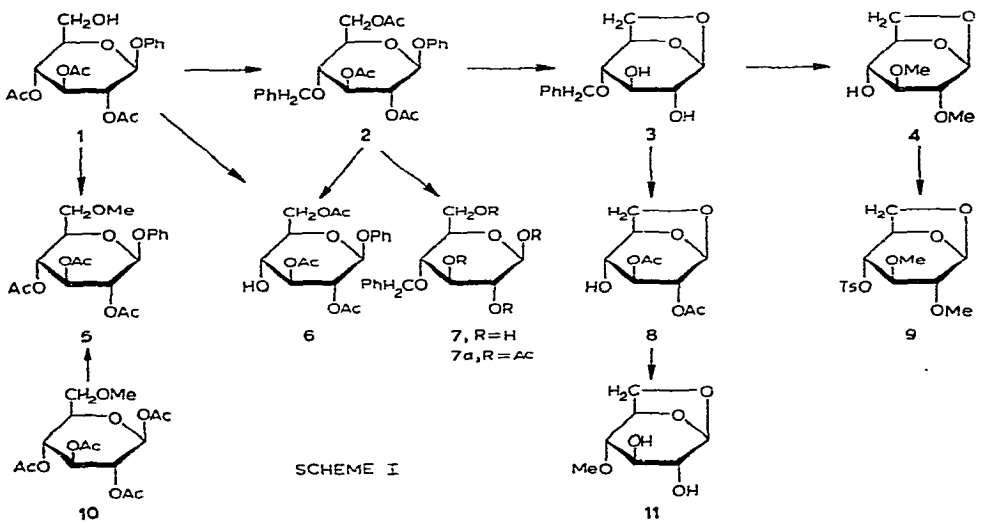
INTRODUCTION

In our investigation of the mechanism of acid-catalyzed polymerization of 1,6-anhydro-β-D-glucopyranose (levoglucosan), we had need for 1,6-anhydrokojibiose and 1,6-anhydrosophorose. For this purpose, we have prepared and characterized 1,6-anhydro-4-*O*-benzyl-β-D-glucopyranose (**3**). Treatment of **3** under Koenigs–Knorr conditions would be expected to produce principally (1→2)-linked 1,6-anhydrodisaccharides, since the hydroxyl group on C-3 of levoglucosan is much less reactive[1–4] than the hydroxyl group on C-2 or C-4. Compound **3** is also of interest, as it could probably be used to prepare D-glucans that are less highly branched than those obtained from levoglucosan.

The sequence of reactions used to synthesize and identify compound **3** is shown in Scheme I.

Treatment of phenyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-D-glucopyranoside with hydrogen bromide in acetic acid gave compound **1**, which crystallized in dimorphic states, one shaped as prisms having m.p. 137–138°, the other as fine needles having m.p. 143–144°. Apparently, neither of these forms corresponds to the one (m.p. 114°) previously reported[5], and furthermore, the measured specific rotation $[\alpha]_D^{25}$ −18.9 ±0.5° (*c* 2.1, chloroform) differed from the reported value $[\alpha]_D^{20}$ −28.3° (*c* 7.2, chloroform). Because of these discrepancies, and because acetyl migration could lead

to one of four different phenyl β-D-glucopyranoside triacetates, the structure of **1** was examined, and firmly established, by n.m.r. studies and by methylation. In methyl sulfoxide-d_6, the n.m.r. signal for the hydroxyl proton of **6** was a triplet at τ 5.20, which is consistent only with the presence of a primary carbinol group[6]. Methylation of **6**, under conditions where acetyl migration does not occur[7], gave phenyl 2,3,4-tri-*O*-acetyl-6-*O*-methyl-β-D-glucopyranoside (**5**). Compound **5** was identical with that prepared by standard methods from the known[7] 1,2,3,4-tetra-*O*-acetyl-6-*O*-methyl-β-D-glucopyranose (**10**).



SCHEME I

Benzylation[8] of **1** with benzyl bromide and silver oxide in *N*,*N*-dimethylformamide gave, in 57% yield, a crystalline product whose n.m.r. spectrum was consistent with a phenyl monobenzylglucoside triacetate (**2**). Preliminary results indicated that **2** was the 4-benzyl ether, as it was readily degraded in alkali to an anhydro sugar and was different from phenyl 2,3,6-tri-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranoside. Hydrogenolysis of **2** over palladium gave phenyl 2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**6**), whose structure was determined by applying the methods used to determine the constitution of **1**. In this case, the n.m.r. spectrum of **6** in methyl sulfoxide-d_6 showed a doublet at τ 4.31, which confirmed the presence of a secondary hydroxyl group, and methylation of **6** with diazomethane gave[9] phenyl 2,3,6-tri-*O*-acetyl-4-*O*-methyl-β-D-glucopyranoside.

Deacetylation of **2** followed by hydrolysis in acid gave 4-*O*-benzyl-D-glucose (**7**), m.p. 138–139°, $[\alpha]_D^{22}$ +65→+53 ±1° (*c* 0.94, water). Croon and Lindberg[8] reported that the α-D anomer of this derivative has m.p. 178–179°, $[\alpha]_D^{20}$ +96→+52° (*c* 2.0, water). The n.m.r. spectrum of **7** in dry methyl sulfoxide-d_6 shows a poorly resolved doublet of doublets centered at τ 3.82 ($J_{1-OH,H-1}$ 4.5 Hz and $J_{1-OH,H-2}$ ~0.5 Hz) and a doublet at τ 3.44 ($J_{1-OH,H-1}$ 6.4 Hz). These signals were assigned[10] to the anomeric hydroxyl protons of the α- and β-D-pyranose forms, respectively, and, from their

integrated intensities, it was determined that the lower-melting form of 4-*O*-benzyl-D-glucopyranose is a mixture of 47% of the α-D and 53% of the β-D anomer. Compound **7** has infrared absorption bands at 841 and 885 cm^{-1}, which is additional evidence[11] for an anomeric mixture of glycopyranoses. Kim *et al.*[12] recently reported g.l.c. evidence for the presence of two anomeric forms in crystalline 2- and 4-*O*-benzyl-D-glucose*. The n.m.r. signal intensities for the anomeric protons of **7** were used for determining the equilibrium concentration of anomers in water at 60° (72% of the β-D). Assuming that the entropy difference between anomers of 4-*O*-benzyl-D-glucopyranose is equal to the difference of 0.87 cal/mole·degree found[13] for α- and β-D-glucopyranose, the composition of anomers of **7** in equilibrium at 25° was estimated to be 26% α-D and 74% β-D. By using the initial and equilibrium compositions and the corresponding specific rotations of the solutions, and assuming that the rotational contributions of anomers do not change with concentration, the specific rotation of the pure α-D anomer was calculated to be +95°. This value is in good agreement with the reported value, +96°. Acetylation of **7** with acetic anhydride and pyridine yielded 30% of crystalline 1,2,3,6-tetra-*O*-acetyl-4-*O*-benzyl-β-D-glucopyranose (**7a**).

Deacetylation of **2** gave phenyl 4-*O*-benzyl-β-D-glucopyranoside, which was smoothly converted in 82% yield into 1,6-anhydro-4-*O*-benzyl-β-D-glucopyranose (**3**) by heating it for 32 h at 105° in 1:2 (v/v) 2-methoxyethanol–2.6M aqueous potassium hydroxide. Methylation of **3**, followed by hydrogenation over palladium, gave crystalline 1,6-anhydro-2,3-di-*O*-methyl-β-D-glucopyranose (**4**), previously reported[14] as a syrup. Hydrolysis of **4** gave 2,3-di-*O*-methyl-D-glucose, identified by its conversion into 2,3-di-*O*-methyl-*N*-phenyl-D-glucosylamine. Also, compound **4** reacted with *p*-toluenesulfonyl chloride in pyridine to give the known[14] 1,6-anhydro-2,3-di-*O*-methyl 4-*O*-*p*-tolylsulfonyl-β-D-glucopyranose (**9**).

1,6-Anhydro-4-*O*-benzyl-β-D-glucopyranose (**3**) was acetylated and the product hydrogenated, to give 2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (**8**), which resisted all attempts at crystallization. G.l.c. and t.l.c. indicated that **8** was homogeneous, and its n.m.r. spectrum showed only two signals for acetyl protons, at τ 7.90 and 7.88. The spectrum of 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose shows three signals for acetyl, at τ 7.90, 7.88, and 7.84, and, therefore, the signal at 7.84 probably arises from the acetoxy group on C-4 (and not[15] that on C-2). The diacetate **8** was methylated with diazomethane, and the product deacetylated to give, in good yield, 1,6-anhydro-4-*O*-methyl-β-D-glucopyranose (**11**), which has been prepared in this laboratory by another route and fully characterized[9].

EXPERIMENTAL

General. — Melting points were determined on a Thomas–Hoover, "Unimelt",

*Unfortunately, these authors did not give the physical constants they observed for these benzyl ethers. They also reported that 3-*O*-benzyl-D-glucopyranose consists solely of the β-D form; this was confirmed by the n.m.r. spectrum of 3-*O*-benzyl-D-glucose in methyl sulfoxide-d_6, since only one signal (doublet at τ 3.43, $J_{1-OH,H-1}$ 6.2 Hz) was observed for the proton of the anomeric hydroxyl group.

melting-point apparatus, and are uncorrected. Solutions were evaporated under diminished pressure below 50°. Thin-layer chromatograms were obtained on microscope slides coated with silica gel G (Brinkmann Instruments, Inc., Great Neck, N. Y.) and, after being developed with appropriate solvents, the components were visualized by spraying the plate with a 5% solution of sulfuric acid in methanol and charring the zones on a hot plate. Column chromatography was performed with silica gel (Davison, grade 950, 60–200 mesh) as adsorbent, with 1–2% loading. Fractions were collected at 5-min intervals, at a flow-rate of 1–2 ml/min. I.r. spectra of solids were obtained with a Perkin–Elmer Model 21 recording i.r. spectrophotometer. N.m.r. spectra of protons (^{1}H) were recorded at 25° with a Varian A-60 n.m.r. spectrometer. Chemical shifts are reported as τ values in p.p.m. from the reference signal of either tetramethylsilane (TMS) in chloroform-*d* and methyl sulfoxide-d_6, or of sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) in deuterium oxide. In parentheses after the chemical shift are given the integrated intensities of the signal and an abbreviation for singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Specific optical rotations were determined with a Zeiss–Winkel polarimeter.

Phenyl 2,3,4-tri-O-acetyl-β-D-glucopyranoside (**1**). — Phenyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-D-glucopyranoside (9.8 g, 15.7 mmoles) was dissolved in warm glacial acetic acid (25 ml), and the mixture was cooled to 5° in an ice–water bath. Cold, 32% hydrogen bromide in acetic acid (2.9 ml) was added, the mixture was shaken for 2–3 min, and the insoluble bromotriphenylmethane was removed by filtration through a coarse, sintered-glass funnel. After the precipitate had been washed with cold acetic acid, the filtrate was poured onto ice–water (50 g), and the aqueous phase was extracted three times with chloroform. The chloroform layer was successively washed with water, aqueous sodium hydrogen carbonate solution, and water, and dried (anhydrous sodium sulfate). The chloroform was evaporated, and the residue was crystallized from isopropyl alcohol to give 4.6 g of **1** (77%) having m.p. 135–138°. One recrystallization from the same solvent gave **1** having a constant m.p. (137–138°), $[\alpha]_D^{25}$ −19° (*c* 2.1, chloroform) [lit.[5] m.p. 114°, $[\alpha]_D^{20}$ −28.3° (*c* 7.2, chloroform)]. After melting at 137–138°, **1** frequently resolidified. The higher-melting, dimorphic form was isolated by crystallization of **1** from the melt; it had a sharp melting-point at 143–144°, and m.p. 137–138° mixed with the other form. The form melting at 143–144° was reconverted into the other form by crystallization from isopropyl alcohol. Both forms gave identical n.m.r. spectra in chloroform-*d*: 7.97, 7.95, 7.94 (each 3 protons, s, acetyl); 7.79 (1 proton, t, OH); 6.55–6.09 (3 protons, m); 5.00–4.60 (4 protons, m); 3.13–2.50 (5 protons, m, aromatic).

Anal. Calc. for $C_{18}H_{22}O_9$: C, 56.54; H, 5.80. Found: C, 56.42; H, 5.72.

Phenyl 2,3,4-tri-O-acetyl-6-O-methyl-β-D-glucopyranoside (**5**). — *a.* To 2.0 g of 1,2,3,4-tetra-*O*-acetyl-6-*O*-methyl-β-D-glucopyranose[7] were added 2.0 g of phenol and 0.02 g of *p*-toluenesulfonic acid monohydrate[16]. The mixture was heated under diminished pressure for 1 h on a steam bath, cooled, and dissolved in benzene. The benzene layer was successively washed with water, four times with M aqueous sodium hydroxide, and water, dried (anhydrous sodium sulfate), and evaporated, to give 1.53 g

(70%) of a syrup that contained no starting material but was a mixture of α-D- and β-D-glycosides, as evidenced by t.l.c. with 1:1 petroleum ether (b.p. 60–110°)–isopropyl ether as developer. The β-D-glucoside crystallized at −5° from absolute ethanol to give 1.0 g (46%) of crude material. Two recrystallizations from absolute ethanol gave pure material, m.p. 92–93°.

b. Compound **1** (1.0 g, 2.62 mmoles) was dissolved in dichloromethane (15 ml), and the solution was cooled to −5°. After boron trifluoride etherate (0.04 ml) had been added, a solution of diazomethane in dichloromethane[17], predried with potassium hydroxide pellets and cooled to 0°, was added slowly, with stirring, until a yellow-green color persisted in the reaction mixture. Polymethylene was removed by filtration, and the filtrate was washed with aqueous sodium hydrogen carbonate solution and water, dried (sodium sulfate), and evaporated, and the residue was crystallized from ethanol at −5°. The first crop of crystals weighed 0.83 g (80%) and had m.p. 90–93°. Recrystallization from ethanol gave pure **5**, m.p. 92–93°, mixed m.p. with a sample prepared by procedure *a*, 92–93°; $[\alpha]_D^{23}$ −15° (*c* 0.8, chloroform). The compounds had identical n.m.r. spectra in chloroform-*d*; 7.98 (9 protons, s, acetyl); 6.64 (3 protons, s, methoxyl); 6.53–6.10 (3 protons, m); 5.00–5.40 (4 protons, m); and 6.87–7.50 (5 protons, m, aromatic).

Anal. Calc. for $C_{19}H_{24}O_9$: C, 57.58; H, 6.11. Found: C, 57.34; H, 6.02.

Phenyl 2,3,6-tri-O-acetyl-4-O-benzyl-β-D-glucopyranoside (**2**). — Compound **1** (20 g, 57.5 mmoles) was dissolved in a mixture of dry *N,N*-dimethylformamide (150 ml) and benzyl bromide (60 ml). The mixture was stirred vigorously while silver oxide (60 g) was added portionwise during 1 h, and stirring was continued for an additional 4 h at room temperature. The silver salts were removed by filtration, and the salts were washed with *N,N*-dimethylformamide (50 ml) and chloroform (100 ml). The filtrate was added to 2 liters of 2% aqueous potassium cyanide solution, and this mixture was extracted three times with a total of a liter of chloroform. The extract was washed three times with water, dried (anhydrous sodium sulfate), and evaporated to a thin syrup. Benzyl bromide and benzyl alcohol were removed by evaporation at 70–75°/0.4–0.7 mm. The crystalline residue was dissolved in hot abs. ethanol (100 ml), and the solution was filtered through a bed of charcoal. Examination of the reaction products by t.l.c., with pure isopropyl ether as developer, showed one major (R_F 0.4) and one minor product (R_F 0.6), and no starting-material. The major product crystallized at 5° to give 14.1 g (57%) of crude material, m.p. 106–112°. Two recrystallizations from ethanol gave 11.0 g of pure **2**, m.p. 114–115°, $[\alpha]_D^{26}$ −31° (*c* 2.0, chloroform); n.m.r. data (chloroform-*d*): 8.01 (3 protons, s, acetyl); 7.97 (6 protons,s, acetyl); 6.31–6.15 (2 protons, m); 5.76–5.60 (2 protons, m); 5.38 (2 protons, s,benzylic); 5.00–4.50 (3 protons, m); 3.18–2.55 (10 protons, m, aromatic).

Anal. Calc. for $C_{25}H_{28}O_9$: C, 63.55; H, 5.97. Found: C, 63.50; H, 6.02.

Phenyl 2,4,6-tri-O-acetyl-3-O-benzyl-α- and -β-D-glucopyranoside. — Benzylation[8] of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3.0 g) with benzyl bromide and silver oxide in *N,N*-dimethylformamide, followed by hydrolysis, gave 3-*O*-benzyl-D-glucose, 1.3 g (44%). The product crystallized from acetone at 5° as needles having

a constant m.p. (125–126°), $[\alpha]_D^{25}$ +26→+43 ±1° (*c* 1.2, water) [lit.[18] 127–128°, $[\alpha]_D$ +29.1° (*c* 7.8, water)]. Apparently, 3-*O*-benzyl-β-D-glucopyranose solidifies in different crystalline forms, since other workers[8,19] have found that this derivative has m.p. 137–138°, $[\alpha]_D^{25}$ +16.1→+41.8° (water). 1,2,4,6-Tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose (530 mg, 1.21 mmoles), prepared[20] by acetylation of 3-*O*-benzyl-β-D-glucopyranose, was fused with 1 g of phenol and 0.02 g of zinc chloride under diminished pressure. The reaction mixture was processed in the usual way, to give 0.28 g of the syrupy phenyl α-D- and β-D-glycoside acetates, which were separated by preparative t.l.c. with isopropyl ether as developer. The faster-moving component was the α-D anomer, which crystallized from absolute ethanol; yield 0.08 g (22%), m.p. 121–122°, $[\alpha]_D^{27}$ +109° (*c* 1.0, chloroform). The slower-moving component was crystallized from ethanol to give 0.134 g (34%) of pure phenyl 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranoside; m.p. 114–115°, mixed m.p. with compound **2**, 82–93°; $[\alpha]_D^{27}$ −31° (*c* 1.9, chloroform).

Anal. Calc. for $C_{25}H_{28}O_9$: C, 63.55; H, 5.97. Found for the α-D anomer: C, 63.49; H, 5.97. Found for the β-D-anomer: C, 63.34; H, 5.97.

*Phenyl 2,3,6-tri-*O*-acetyl-β-D-glucopyranoside* (**6**). — Compound **2** (1 g, 2.12 mmoles) was hydrogenated in 10 ml of glacial acetic acid over 1.0 g of 5% palladium-on-charcoal. The mixture was stirred for 24 h at room temperature under hydrogen (1 atm.), and the catalyst was removed by filtration. The filtrate was freeze-dried, and the residue was crystallized from absolute ethanol at −10°. The total yield (first two crops of crystals) was 0.56 g (69%), m.p. 132–134°. Two recrystallizations from ethanol gave **6** having a constant m.p. of 134.5–135.5°, $[\alpha]_D^{24}$ −56° (*c* 3.7, chloroform); lit.[5] m.p. 130°, $[\alpha]_D^{18}$ −52.2° (*c* 4.0, chloroform).

Anal. Calc. for $C_{18}H_{22}O_9$: C, 56.54; H, 5.80. Found: C, 56.54; H, 5.80.

Compound **6** was identical in all respects with the product obtained by the alkali-catalyzed rearrangement of phenyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside (**1**). Methylation of **6** with diazomethane–boron trifluoride gave phenyl 2,3,6-tri-*O*-acetyl-4-*O*-methyl-β-D-glucopyranoside, which was also prepared from the known 1,2,3,6-tetra-*O*-acetyl-4-*O*-methyl-β-D-glucopyranose[9].

*Phenyl 4-*O*-benzyl-β-D-glucopyranoside, 4-*O*-benzyl-D-glucopyranose* (**7**), *and 1,2,3,6-tetra-*O*-acetyl-4-*O*-benzyl-β-D-glucopyranose* (**7a**). — Compound **2** (1.5 g, 31.8 mmoles) was deacetylated in the usual way with sodium methoxide in methanol. The product was crystallized from abs. ethanol at −10° to give 1.05 g (91%) of material having m.p. 117–119°, $[\alpha]_D^{26}$ −16° (*c* 3.2, acetone).

To a solution of phenyl 4-*O*-benzyl-β-D-glucopyranoside (0.73 g, 2.12 mmoles) in *p*-dioxane (20 ml) was added 4.0% aqueous sulfuric acid solution (40 ml), and the mixture was heated for 4 h on a steam bath. The solution was cooled, the acid was neutralized with barium carbonate, and the salts were removed by filtration. The filtrate was evaporated to dryness, the residue was extracted with hot, absolute ethanol, and the extract was evaporated to a syrup (0.77 g), which was purified by column chromatography on 70 g of silica gel, with 15:1 (v/v) ethyl acetate–methanol as eluant. Two fractions were obtained; the first was an oil containing mainly phenol, whereas

the second was a crystalline solid, yield 0.51 g (89%). The crystals were dissolved in hot acetone, and the solution was filtered through a bed of charcoal; on cooling at −10°, 4-*O*-benzyl-D-glucose (7) crystallized as short needles, m.p. 138–139°, $[\alpha]_D^{22}$ +65→+53 ±1° (*c* 0.94, water); n.m.r. data (methyl sulfoxide-d_6): 6.9–6.2 (6 protons, m), 5.80–5.45 (2 protons, m), 5.34, 5.17 (each 1 proton, s, benzylic), 5.30–4.95 (2 protons, m), 3.82 (0.47 proton, doublet of doublets, anomeric hydroxylproton of α-D anomer), 3.44 (0.53 proton, d, anomeric hydroxyl proton of β-D-form), 2.68 (5 protons, s, aromatic); at equilibrium in D_2O at 60°: 6.80–6.00 (6 protons, m), 5.40 (0.72 proton, d, anomeric hydrogen atom of β-D form, $J_{1,2}$ 7.8 Hz), 5.28, 5.22 (each 1 proton,s, benzylic), 4.78 (0.28 proton,d, anomeric hydrogen atom of α-form, $J_{1,2}$ 3.2 Hz), 2.58 (5 protons, s, aromatic).

Anal. Calc. for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.56; H, 6.71.

Compound 7 was acetylated with acetic anhydride and pyridine in the usual way. Crystallization of the product from ethanol gave 30% of 1,2,3,6-tetra-*O*-acetyl-4-*O*-benzyl-β-D-glucopyranose (7a), m.p. 108–109°, $[\alpha]_D^{22}$ 0 ±1° (*c* 0.9, chloroform). The n.m.r. (chloroform-*d*) signal of H-1 was at τ 4.29, $J_{1,2}$ 7.6 Hz, consistent[21] with the assigned β-D anomeric configuration.

Anal. Calc. for $C_{21}H_{26}O_{10}$: C, 57.53; H, 5.98. Found: C, 57.54; H, 5.88.

1,6-Anhydro-4-O-benzyl-β-D-glucopyranose (3). — To 3.2 g (9.25 mmoles) of phenyl 4-*O*-benzyl-β-D-glucopyranoside in a Teflon-lined, bomb calorimeter (Parr Instrument Co.) were added 17 ml of 2-methoxyethanol and 33 ml of 2.6M aqueous potassium hydroxide solution. The mixture was heated for 32 h at 105°, whereupon, the phenyl glycoside (R_F 0.62) was converted into a single new compound (R_F 0.37), as indicated by t.l.c. with 1:1 isopropyl ether–ethyl acetate as irrigant. The cooled solution was rendered neutral with 1.3M aqueous sulfuric acid, and evaporated to dryness, and the residue was extracted three times with hot abs. ethanol. The ethanolic extract was evaporated to dryness, the residue was dissolved in 110 ml of 50% aqueous ethanol, and the solution was passed through 50 ml of Amberlite MB-3 (H^+,OH^-) resin. The resin was washed with 125 ml of 50% aqueous ethanol, and the total effluent was evaporated to a colorless syrup (2.4 g). A small portion of the syrup was distilled at 130–135°/0.15–0.2 mm in a micro-sublimation apparatus. The distillate crystallized. The compound was crystallized from ethyl ether, and gave 1.55 g (65%) of material having m.p. 53–55°. A second crop (0.4 g) brought the total yield of 3 to 1.95 g (82%). One recrystallization from ethyl ether gave pure 3, m.p. 53–54°, $[\alpha]_D^{23}$ −43° (*c* 1.15, ethanol).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 62.03; H, 6.33.

1,6-Anhydro-2,3-di-O-methyl-β-D-glucopyranose (4). — A solution of compound 3 (0.47 g, 1.86 mmoles) in *N*,*N*-dimethylformamide (15 ml) and methyl iodide (5 ml) was stirred at room temperature while silver oxide (3.5 g) was added portionwise during 8 h. Stirring was continued for 26 h, and the reaction was processed in the usual way to give 0.48 g of a syrup that was chromatographically pure, as indicated by t.l.c. The product resisted attempts at crystallization, and column chromatography on 25 g of silica gel, with 4:1 chloroform–ethyl acetate as the devel-

oper, again yielded a syrup (0.34 g). This syrup was hydrogenated (1 atm) at room temperature in 3 ml of ethyl acetate over 0.3 g of 10% palladium-on-charcoal. After 24 h, the catalyst was removed by filtration, and the filtrate was evaporated to a syrup, yield 0.23 g (100%), which was purified by column chromatography on silica gel with ethyl acetate as the developer. The eluate containing **4** was evaporated to a syrup that crystallized spontaneously, yield 0.15 g (66%). The crystals were dissolved in ethyl ether, the solution was filtered through a bed of charcoal, and ligroine was added to faint turbidity. The solution was nucleated, and kept at −10°, to give pure **4** (0.10 g), m.p. 43–45°, $[\alpha]_D^{23}$ −87° (*c* 0.9, chloroform).

Anal. Calc. for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.55; H, 7.49.

Compound **4** (36 mg, 0.19 mmole) was heated for 2 h in a sealed tube at 100° with 4.0 ml of 2M aqueous hydrochloric acid. The mixture was evaporated to dryness at 35°, to give an acid-free residue (41 mg). The hydrolyzate was examined by paper chromatography, with water-saturated butanone as irrigant; the only product detectable with *p*-anisidine–hydrogen chloride spray[22] had R_F 0.2, and was indistinguishable from authentic 2,3-di-*O*-methyl-D-glucose. The hydrolyzate was subjected to preparative paper-chromatography in the same solvent system, and 25 mg (63%) of pure 2,3-di-*O*-methyl-D-glucose was isolated. This D-glucose derivative was refluxed for 5 h with freshly distilled aniline (0.3 ml) in methanol (2.5 ml). After being kept overnight, the solution was concentrated, the last traces of aniline were removed by co-evaporation with methanol and toluene, and the orange-colored syrup (37 mg) was crystallized from methanol–ether–petroleum ether (b.p. 30–60°). One recrystallization gave 13 mg (24%) of pure 2,3-di-*O*-methyl-*N*-phenyl-D-glucosylamine, m.p. and mixed m.p. with an authentic sample, 134°; lit.[23] m.p. 134°.

*1,6-Anhydro-2,3-di-*O*-methyl-4-*O*-p-tolylsulfonyl-β-*D*-glucopyranose* (**9**). — 1,6-Anhydro-2,3-di-*O*-methyl-β-D-glucopyranose (20 mg, 0.10 mmole) was added to 40 mg of *p*-toluenesulfonyl chloride in 0.75 ml of pyridine. The reaction mixture was kept overnight at room temperature, and 0.1 ml of water was added. After 1 h, the product was dissolved in chloroform, and the solution was processed in the usual way. Crystallization at −10° from acetone–ether–petroleum ether (b.p. 30–60°) gave 25 mg of **9**, m.p. 71–73°. One recrystallization gave pure **9**, m.p. 73–75°, $[\alpha]_D^{26}$ −58° (*c* 0.9, chloroform); lit.[14] m.p. 74–77°, $[\alpha]_D^{22}$ −45 ±1° (*c* 0.92, methanol).

*2,3-Di-*O*-acetyl-1,6-anhydro-β-*D*-glucopyranose* (**8**) *and 1,6-anhydro-4-*O*-methyl-β-*D*-glucopyranose* (**11**). — Compound **3** (300 mg, 1.19 mmoles) was acetylated overnight with acetic anhydride and pyridine. The reaction mixture was processed in the usual way, and the product (372 mg) was hydrogenated over 0.4 g of 10% palladium-on-charcoal in 4 ml of ethyl acetate. After 24 h, the mixture was filtered, and the filtrate was evaporated to give **8**, yield 270 mg (91%). Compound **8** could not be induced to crystallize under a variety of conditions. Chromatography on 25 g of silica gel (4:1 ethyl acetate–chloroform as developer) yielded 250 mg of syrupy **8**. The purity of **8** was shown in the following way. T.l.c. with 10:3 isopropyl ether–ethyl acetate as irrigant showed a single component having R_F 0.17 (2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose had R_F 0.44), and g.l.c. (injection port 200°, column

152°) with 5% SE-30 on DMCS Chromosorb W (5 ft × 1/8 in i.d.) showed one peak. The n.m.r. data for **8** in chloroform-*d* were: 7.90, 7.88 (each 3 protons, s, acetyl), 7.10–6.80 (1 proton, m, hydroxyl), 6.51–5.82 (3 protons, m), 5.50–5.14 (3 protons, m), 4.62–4.52 (1 proton, m, anomeric proton). An analytical sample of **8**, distilled at 90–100°/0.15–0.20 mm, had $[\alpha]_D^{27}$ −45° (*c* 4.9, chloroform).

Anal. Calc. for $C_{10}H_{14}O_7$: C, 48.78; H, 5.73. Found: C, 49.03; H, 5.97.

Syrupy 2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (180 mg, 0.73 mmole) was methylated[7] with diazomethane–boron trifluoride reagent. The product, yield 184 mg (90%), was deacetylated in the normal way with sodium methoxide in methanol, to produce 100 mg (78%) of a chromatographically pure (R_F 0.35, t.l.c., 9:1 ethyl acetate–methanol) 4-methyl ether (**11**), which crystallized slowly from a mixture of acetone and petroleum ether (30–60°). A total of two crops of crystals gave 65 mg (51%) of crude material, which was recrystallized once to a constant m.p. of 67–68°; $[\alpha]_D^{25}$ −64° (*c* 3.0, acetone). The mixed m.p. with a sample of **11** prepared by a different procedure[9] was 67–68°.

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