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A CONVENIENT SYNTHESIS OF 6′-*C*-SUBSTITUTED β-MALTOSE HEPTAACETATES AND OF PANOSE

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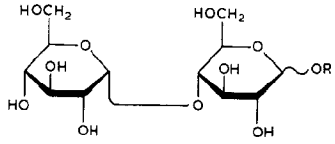
ABSTRACT

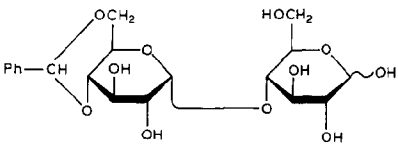
Benzylidenation of β-maltose monohydrate with α,α-dimethoxytoluene in *N,N*-dimethylformamide in the presence of *p*-toluenesulfonic acid gave, in 70% yield, 4′,6′-*O*-benzylidenemaltose, which was acetylated to afford 1,2,3,6,2′,3′-hexa-*O*-acetyl-4′,6′-*O*-benzylidene-β-maltose (**4**). Removal of the benzylidene group of **4** gave 1,2,3,6,2′,3′-hexa-*O*-acetyl-β-maltose (**5**), which was transformed into 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-6′-*O*-*p*-tolylsulfonyl-β-maltose (**8**). Several 6′-substituted β-maltose heptaacetates were synthesized by displacement reactions of **8** with various nucleophiles. Condensation of **5** with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide, under catalysis by halide ion, followed by removal of protecting groups, furnished panose in good yield.

INTRODUCTION

The hepta-*O*-acetyl derivatives of maltose (**1**), modified at specific positions, have been shown[1,2] to be useful intermediates for the preparation of derivatives of phenyl α-maltoside which serve as substrates in mechanistic studies[2,3] of Taka-amylase A. The preparation of the hepta-*O*-acetyl derivatives of **1**, specifically substituted at C-6′, was first reported in 1966 by Dutton and Slessor[4], who obtained 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-6′-deoxy-β- (**12**) and 6′-*S*-acetyl-6′-thio-α-maltose in low yields from 1,6-anhydro-β-maltose by a long sequence of reactions. Using an essentially similar reaction-sequence, Arita *et al.*[1] synthesized hepta-*O*-acetyl-6′-*O*-



1 R = H
2 R = H · H_2O (β anomer)



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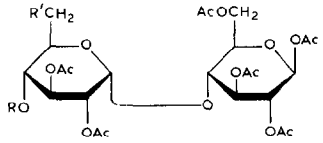
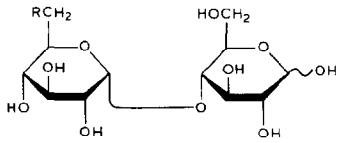
p-tolylsulfonyl, -6′-deoxy-6′-iodo, -6′-chloro-6′-deoxy, -6′-deoxy, and -6′-*O*-methyl derivatives of **1**, but these compounds were obtained as a mixture of the anomers. Acetolysis of 2,3,2′,3′,4′-penta-*O*-acetyl-1,6-anhydro-6′-deoxy-6′-iodo-β-maltose has been reported[5] to give 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-6′-deoxy-6′-iodo-β-maltose (**11**). 1,2,3.6,2′,3′,4′-Hepta-*O*-acetyl-6′-*O*-trityl-β-maltose[6] (**6**) and its α anomer[7] have been synthesized by selective tritylation of β-maltose monohydrate (**2**), and subsequent acetylation. A relatively simple method for the preparation of 6′-substituted derivatives of **1** through the action of *Aspergillus oryzae* amylase on 6-monosubstituted cyclomaltohexaoses has been developed[8].

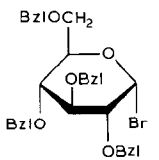




4 R,R′ = PhCHO
5 R = H, R′ = OH
6 R = Ac, R′ = OTr
7 R = Ac, R′ = OH
8 R = Ac, R′ = OTs
9 R = Ac, R′ = Br
Tr = Ph_3C
Ts = $SO_2C_6H_4Me$-*p*

10 R = Ac, R′ = Cl
11 R = Ac, R′ = I
12 R = Ac, R′ = H
13 α anomer (at C-1) of **11**
14 R = Ac, R′ = N_3
15 R = Bz, R′ = Br

16 R = Br
17 R = Cl
18 R = H
19 R = N_3
20 R = NH_2



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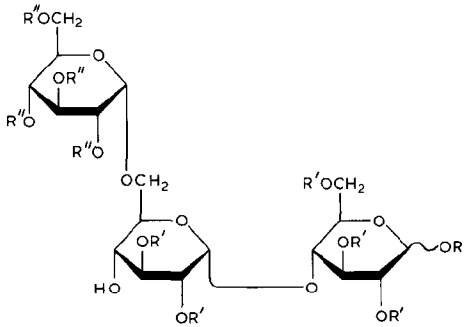
Bzl = $PhCH_2$



22 R = Ac(β anomer), R′ = Ac, R″ = Bzl
23 R = H(α anomer), R′ = R″ = H

We report here a convenient synthesis of several 6′-*C*-substituted β-maltose heptaacetates, as well as the corresponding free disaccharides, starting from **2**, and a simple, preparative approach to *O*-α-D-glucopyranosyl-(1→6)-*O*-α-D-glucopyranosyl-(1→4)-α-D-glucose (panose, **23**). Compound **23** has been isolated[9] from acid hydrolyzates of amylopectin, glycogen, and pullulan, and prepared enzymically[9–11]. It has also been synthesized chemically by condensation[6] of 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride with **6** or with 1,2,3,6,2′,3′,4′-

hepta-*O*-acetyl-β-maltose (**7**), by coupling[12] of benzyl 2,3,6,2′,3′,4′-hexa-*O*-acetyl-β-maltoside with 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride, and by reaction of benzyl 2,3,6,2′,3′,4′-hexa-*O*-benzyl-α-maltoside with 2,3,4-tri-*O*-benzyl-6-*O*-(*p*-nitrobenzoyl)-α-D-glucopyranosyl bromide[13] or 2,3,4,6-tetra-*O*-benzyl-D-glucose[14].

RESULTS AND DISCUSSION

Recently, a number of the cyclic acetal derivatives of reducing disaccharides were synthesized by using various combinations of the reagents[15]. We applied to **2** the method of benzylidene acetal formation with α,α-dimethoxytoluene and *p*-toluenesulfonic acid in *N,N*-dimethylformamide that had been successfully employed for the benzylidenation of the glycosides of mono-[16] and di-saccharides[17]. Treatment of **2** with 2.4 mol. equiv. of α,α-dimethoxytoluene in *N,N*-dimethylformamide in the presence of *p*-toluenesulfonic acid, with continuous removal[16,17] of the resulting methanol by evaporation under diminished pressure, gave a mixture that was fractionated by chromatography on a column of silica gel, to afford 4′,6′-*O*-benzylidenemaltose (**3**) as an amorphous powder in 70% yield. Methylation[18] of **3**, followed by hydrolysis, reduction with sodium borohydride, and acetylation, gave a 1:1 mixture of the peracetates of 2,3- and 2,3,6-tri-*O*-methyl-D-glucitol (g.l.c.), proving the structure of **3**. Acetylation[19] of **3** with acetic anhydride and sodium acetate afforded crystalline 1,2,3,6,2′,3′-hexa-*O*-acetyl-4′,6′-*O*-benzylidene-β-maltose (**4**) in 86% yield. The n.m.r. spectrum of **4** in chloroform-*d* showed the H-1 resonance at δ 5.75 as a doublet, $J_{1,2}$ 7.9 Hz, consistent with the β configuration of C-1. Subsequently, it was found that the isolation of **3** is unnecessary for large-scale preparation of **4**. The product mixture obtained by the benzylidenation of **2** was acetylated, as for **3**, to give a mixture from which **4** was directly obtained pure, in 47% yield, by fractional recrystallization.

Removal of the benzylidene group from **4** with aqueous acetic acid gave crystalline 1,2,3,6,2′,3′-hexa-*O*-acetyl-β-maltose (**5**) in 84% yield. That no migration of the acetyl groups had occurred during the debenzylidenation was confirmed by reconversion of **5** into **4** by treatment with α,α-dimethoxytoluene in acetonitrile in the presence of *p*-toluenesulfonic acid. Tritylation of **5** with 1.5 mol. equiv. of trityl chloride in pyridine, followed by acetylation, and purification of the product by column chromatography, gave, in 88% yield, the known[6] **6** which, on *O*-detritylation with aqueous acetic acid followed by column chromatography, produced, in 83% yield, the hepta-*O*-acetyl derivative[6] (**7**) having HO-6′ free. *p*-Toluenesulfonylation of **7** gave crystalline 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-6′-*O*-*p*-tolylsulfonyl-β-maltose (**8**) in 90% yield. The overall yield of **8** was 66%, based on **5**. Alternatively, the preparation of **8** was achieved more conveniently, without the need for chromatography, than by this reaction-sequence; treatment of **5** with 2 mol. equiv. of *p*-toluenesulfonyl chloride in pyridine, and subsequent acetylation, afforded **8** in 65% yield. The compounds obtained by the two routes were identical in all respects.

The sulfonyloxy group in **8** underwent ready nucleophilic displacement with bromide, chloride, and iodide ions in *N,N*-dimethylformamide at 80°, to give high yields of the 6′-bromo-6′-deoxy (**9**), 6′-chloro-6′-deoxy (**10**), and 6′-deoxy-6′-iodo (**11**) derivatives, respectively, of β-maltose heptaacetate, all of the compounds being obtained in crystalline form. Reductive dehalogenation of **11** in methanol and 1,4-dioxane, in the presence of palladium-on-charcoal and triethylamine, provided the known[4] **12**. The physical constants (m.p. 174–175°, $[\alpha]_D$ +64.1°) of **11** were very different from those (m.p. 86–87°, $[\alpha]_D$ +82.4°) reported by Guerrera and Weill[5] for this compound, suggesting that their substance may have been the corresponding α anomer **13**, in light of its mode of synthesis[1,5]. Reaction of **8** with sodium azide in *N,N*-dimethylformamide at 100° proceeded with considerable *O*-deacetylation, so that re-acetylation with acetic anhydride and sodium acetate was necessary in order to obtain the 6′-azido-6′-deoxy derivative **14**. Under milder reaction-conditions, the displacement reaction did not proceed to completion. Oxidative removal of the benzylidene group of **4** with *N*-bromosuccinimide[20] yielded the 1,2,3,6,2′,3′-hexa-*O*-acetyl-4′-*O*-benzoyl-6′-bromo-6′-deoxy derivative **15**.

O-Deacetylation of **9, 10, 12,** and **14** with sodium methoxide in methanol furnished 6′-bromo-6′-deoxymaltose[8] (**16**), 6′-chloro-6′-deoxymaltose[8] (**17**), 6′-deoxymaltose[4,8] (**18**), and 6′-azido-6′-deoxymaltose[8] (**19**), respectively. Compound **16** was also obtained by *O*-deacylation of **15**. Catalytic hydrogenation of **19** in the presence of palladium-on-charcoal afforded 6′-amino-6′-deoxymaltose[8] (**20**).

Condensation of **5** with 1.6 mol. equiv. of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide[21] (**21**), in dichloromethane and *N,N*-dimethylformamide in the presence of tetraethylammonium bromide and molecular sieve[22], gave, after chromatographic fractionation, crystalline *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→6)-*O*-(2,3-di-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose (**22**) in 71% yield. The α configuration at the newly formed, interglucosidic linkage in **22** was indicated[23] by the ^{13}C-n.m.r. spectrum, which showed a signal for C-1″ at δ 98.1 with $^1J_{CH}$ 168.3 Hz. Catalytic hydrogenolysis of **22** in acetic acid in the presence of palladium-on-charcoal, followed by *O*-deacetylation, furnished, in 82% yield, compound **23**, which was identified by comparison with an authentic specimen[10], and characterized further as panitol dodecaacetate (**24**). The two-step procedure **5** + **21**→**22**→**23**, giving **23** in an overall yield of 58% (based on **5**), is considered to offer advantages of improved yield, procedural convenience, and lower cost, in comparison with the existing synthetic method[6,12–14], as the disaccharide glycosyl acceptor **5** was readily prepared from commercially available **2** in 39% yield without recourse to chromatography.

EXPERIMENTAL

General methods. — Organic solutions were dried with anhydrous sodium sulfate. Solutions were evaporated, at a temperature <50°, under diminished pressure. Melting points were determined with a Yanagimoto micro melting-point

apparatus and are uncorrected. Optical rotations were determined with an Applied Electronic automatic polarimeter, and i.r. spectra were recorded with a Shimadzu IR-2C spectrometer for potassium bromide pellets. ^{1}H-N.m.r. spectra were recorded with a Hitachi R-90H spectrometer; tetramethylsilane (in chloroform-*d*) and sodium 4,4-dimethyl-4-silapentanoate-d_4 (in deuterium oxide) were the internal standards. The ^{13}C-n.m.r. spectrum of **22** was recorded with a Bruker WH 400 spectrometer operated at 100.6 MHz, and with tetramethylsilane as the internal standard. Gas–liquid chromatography was performed with a Hitachi gas chromatograph 063, using 3% of ECNSS-M on Gas-Chrom Q (80–100 mesh) at 180°, with nitrogen as the carrier gas, and a flame-ionization detector. Retention times are given, relative to that of 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-glucitol as unity. T.l.c. was performed on Silica gel No. 7731 (Merck); spots were made visible by spraying the plates with 5% sulfuric acid, followed by heating. Column chromatography was performed on Silica gel No. 7734 (Merck). All proportions for the solvent systems used for elution of t.l. and column chromatograms were v/v. Descending, paper chromatography (p.c.) was performed on Toyo No. 50 filter-paper in 6:4:3 1-butanol–pyridine–water, with detection with the alkaline silver nitrate reagent[24].

4-O-(4,6-O-Benzylidene-α-D-glucopyranosyl)-D-glucopyranose (**3**). — A mixture of **2** (5.0 g, 13.9 mmol), α,α-dimethoxytoluene (5.0 g, 32.9 mmol), and *p*-toluenesulfonic acid monohydrate (0.25 g) in dry *N,N*-dimethylformamide (38 mL) was rotated for 2 h in a rotary evaporator at a bath temperature of <50°, under a pressure of ~4 kPa; t.l.c. in 3:1 chloroform–methanol then showed the presence of one major (**3**, R_F 0.32) and several faster-moving, minor products, in addition to a small amount of unreacted **2** (R_F 0.01). The mixture was cooled, the acid neutralized with triethylamine, and the solution evaporated; this was followed by a few additions and evaporations of toluene. The resulting syrup was fractionated on a column of silica gel with 4:1 chloroform–methanol, to give **3** (4.20 g, 70%), which failed to crystallize; $[\alpha]_D^{20}$ +81.1° (*c* 1.4, water); n.m.r. data (deuterium oxide): δ 7.90–7.49 (m, 5 H, Ph), 5.66 (s, 1 H, benzylic-H), 5.39 (d, 1 H, $J_{1',2'}$ 3.7 Hz, H-1′), and 5.24 (d, 0.4 H, $J_{1,2}$ 3.6 Hz, H-1-α); the H-1-β signal was obscured by overlapping with the HOD signal. The compound reduced boiling Fehling solution.

Anal. Calc. for $C_{19}H_{26}O_{11}$: C, 53.02; H, 6.09. Found: C, 52.89; H, 6.21.

Successive methylation[18] of a portion of **3**, hydrolysis with 0.5M sulfuric acid for 10 h at 100°, reduction with sodium borohydride, acetylation, and g.l.c. of the resulting products gave peaks corresponding to the peracetates of 2,3,6-tri-*O*-methylglucitol (*T* 2.49, 50%) and 2,3-di-*O*-acetylglucitol (*T* 5.37, 50%).

1,2,3,6-Tetra-O-acetyl-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranose (**4**). — (*a*) Compound **3** (3.30 g) was acetylated[19] with acetic anhydride (35 mL) and sodium acetate (3 g) under reflux for 20 min. The mixture was cooled, and poured onto crushed ice, and the precipitate formed was filtered off, and washed with water. A solution of the solid in chloroform was

successively washed with aqueous sodium hydrogencarbonate and water, dried, and evaporated. Recrystallization of the solid residue from ethanol gave **4** (4.50 g, 86%); m.p. 219–220°, $[\alpha]_D^{20}$ + 35.5° (*c* 1.6, chloroform); n.m.r. data (chloroform-*d*): δ 7.47–7.31 (m, 5 H, Ph), 5.75 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 5.47 (s, 1 H, benzylic-H), and 2.10, 2.08, 2.06, 2.03, 2.02, and 2.00 (6 s, each 3 H, 6 AcO).

Anal. Calc. for $C_{31}H_{38}O_{17}$: C, 54.54; H, 5.61. Found: C, 54.51; H, 5.62.

(*b*) Treatment of **2** (30.0 g) in *N,N*-dimethylformamide (220 mL) with α,α-dimethoxytoluene (30 g) and *p*-toluenesulfonic acid monohydrate (1.5 g), as described for the preparation of **3**, followed by acetylation of the product with acetic anhydride (250 mL) and sodium acetate (30 g) as just described, afforded a mixture that was recrystallized thrice from ethanol, to give **4** (26.7 g, 47%); m.p. and mixed m.p. 220–221°, $[\alpha]_D^{20}$ +36.0° (*c* 1.5, chloroform); the n.m.r. spectrum was identical with that of the compound prepared by method *a*.

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3-di-*O*-acetyl-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**5**). — A solution of **4** (10.36 g) in acetic acid (93 mL) was heated to 95°, water (60 mL) was added in small portions, and the mixture was stirred for 10 min, cooled, and evaporated; the last traces of the solvents were removed by repeated addition and evaporation of toluene. The residue was recrystallized twice from ethanol, to give **5** (7.58 g, 84%); m.p. 205–206° $[\alpha]_D^{20}$ + 53.1° (*c* 2.1, chloroform).

Anal. Calc. for $C_{24}H_{34}O_{17}$: C, 48.49; H, 5.76. Found: C, 48.56; H, 5.87.

A solution of **5** (0.45 g), α,α-dimethoxytoluene (0.3 g), and *p*-toluenesulfonic acid monohydrate (20 mg) in acetonitrile (5 mL) was stirred for 1 h at room temperature, made neutral with triethylamine, and evaporated. A solution of the residue in chloroform was washed successively with aqueous sodium hydrogencarbonate and water, dried, and evaporated. The solid was recrystallized from ethanol, to give **4** (0.47 g, 90%); m.p. and mixed m.p. 218–219°, $[\alpha]_D^{20}$ +35.0° (*c* 1.1, chloroform).

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**6**). — A solution of **5** (1.02 g) and chlorotriphenylmethane (0.72 g, 1.5 mol. equiv.) in pyridine (5 mL) was stirred for 2 days at room temperature, cooled to 0°, treated with acetic anhydride (2 mL), and then kept for 5 h at room temperature. The solution was poured into ice–water, and the precipitate that separated was filtered off, washed with water, and dried. The major product was isolated by chromatography on a column of silica gel with 4:1 benzene–ethyl acetate, to give **6** (1.33 g, 88%): double m.p. 128–130° and 164–165° (from ethanol), $[\alpha]_D^{20}$ +94.8° (*c* 2.4, chloroform); lit.[6] m.p. 164–164.5°, $[\alpha]_D^{20}$ +96° (*c* 2.165, chloroform); the authentic sample of **6**, provided by Drs. Koizumi and Utamura[7], showed a similar, double m.p. of 128–131° and 165–166°, and the n.m.r. spectrum of our compound was identical with that of theirs.

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**7**). — Treatment of **6** (1.04 g) with 80% acetic acid (20 mL) for 30 min at 95°, as described earlier[6], followed by purification of the product by elution from a column of silica gel with 2:1 benzene–ethyl acetate, gave **7** (0.62 g, 83%);

m.p. 179–180° (methanol), $[\alpha]_D^{20}$ +63.6° (*c* 1.7, chloroform); lit.[6] m.p. 177–178°, $[\alpha]_D^{19}$ +65° (*c* 1.58, chloroform).

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-p-tolylsulfonyl-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**8**). — (*a*) A solution of **7** (0.50 g) in anhydrous pyridine (3 mL) was cooled to −10°, treated with *p*-toluenesulfonyl chloride (0.22 g), and kept overnight at 5°. The precipitate that separated on addition of water was filtered off, washed with water, dried, and recrystallized from ethanol, to give **8** (0.56 g, 90%); m.p. 157–158°, $[\alpha]_D^{20}$ +67.5° (*c* 1.0, chloroform); n.m.r. data (chloroform-*d*): δ 7.84–7.72 (m, 4 H, aryl-H), 5.73 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 2.46 (s, 3 H, aryl-CH_3), 2.11 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.01 (s, 6 H, 2 AcO), 1.97 (s, 3 H, OAc), and 1.94 (s, 3 H, OAc).

Anal. Calc. for $C_{33}H_{42}O_{20}S$: C, 50.13; H, 5.35; S, 4.05. Found: C, 50.20; H, 5.46; S, 3.92.

(*b*) To a stirred solution of **5** (16.61 g, 27.9 mmol) in dry pyridine (170 mL), maintained at −20°, was added portionwise *p*-toluenesulfonyl chloride (10.65 g, 55.9 mmol) during 90 min. The mixture was further stirred for 2 h at −20°, kept overnight at 0°, treated with acetic anhydride (70 mL), and then kept for 5 h at room temperature. The solution was processed as described for the preparation of **6**, and the residue was recrystallized thrice from ethanol, to give **8** (14.36 g, 65%); m.p. and mixed m.p. 157–158°, $[\alpha]_D^{20}$ +68.1° (*c* 1.2, chloroform); the n.m.r. spectrum was identical with that of the compound obtained in method *a*.

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-bromo-6-deoxy-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**9**). — A solution of **8** (2.49 g) in *N,N*-dimethylformamide (50 mL) containing sodium bromide (4 g) was stirred for 5 h at 80°. The mixture was cooled, and evaporated to dryness, and the residue was partitioned between chloroform and water. The organic layer was washed with water, dried, and evaporated. Crystallization from ethanol gave **9** (1.85 g, 84%); m.p. 171–172° (from ethanol), $[\alpha]_D^{20}$ +66.7° (*c* 1.7, chloroform).

Anal. Calc. for $C_{26}H_{35}BrO_{17}$: C, 44.65; H, 5.04; Br, 11.42. Found: C, 44.50; H, 4.95; Br, 11.30.

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-chloro-6-deoxy-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**10**). — Compound **8** (1.86 g) in *N,N*-dimethylformamide (35 mL) was stirred with lithium chloride (3 g) for 4 h at 80°. The mixture was processed as just described, to give **10** (1.26 g, 82%); m.p. 185–186° (ethanol), $[\alpha]_D^{20}$ +68.6° (*c* 1.4, chloroform).

Anal. Calc. for $C_{26}H_{35}ClO_{17}$: C, 47.68; H, 5.39; Cl, 5.41. Found: C, 47.79; H, 5.49; Cl, 5.29.

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**11**). — A solution of **8** (3.65 g) in *N,N*-dimethylformamide (75 mL) was stirred with sodium iodide (5 g) for 4 h at 80°. Processing of the mixture, as described for the preparation of **9**, gave **11** (2.96 g, 86%); m.p. 174–175° (from ethanol), $[\alpha]_D^{20}$ +64.1° (*c* 1.3, chloroform); lit.[5] m.p. 86–87° (from ethyl acetate–hexane), $[\alpha]_D^{24}$ +82.4° (*c* 0.73, methanol).

Anal. Calc. for $C_{26}H_{35}IO_{17}$: C, 41.84; H, 4.73; I, 17.00. Found: C, 41.70; H, 4.70; I, 16.88.

1,2,3,6-Tetra-O-acetyl-4-O-(2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranosyl)-β-D-glucopyranose (**12**). — A solution of **11** (1.67 g) in 1:1 (v/v) methanol–1,4-dioxane (100 mL) containing triethylamine (1 mL) was hydrogenated in the presence of 10% palladium-on-charcoal (1.5 g) at atmospheric pressure for 1 day at room temperature. The catalyst was filtered off through a Celite pad, and washed with methanol. The filtrate and washings were combined, and evaporated to a syrup, which was dissolved in chloroform. The solution was washed with water, dried, and evaporated, to give a mass which, on recrystallization from ethanol, afforded **12** (1.18 g, 85%); m.p. 188–189°, $[\alpha]_D^{20}$ +67.9° (*c* 1.6, chloroform); lit.[4] m.p. 183–185°, $[\alpha]_D$ +64° (*c* 0.68, chloroform); n.m.r. data (chloroform-*d*): δ 5.75 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 2.13 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.03 (s, 6 H, 2 AcO), 2.01 (s, 3 H, OAc), 2.00 (s, 3 H, OAc), 1.99 (s, 3 H, OAc), and 1.15 (d, 3 H, $J_{1,2}$ 6.2 Hz, CH_3-5′).

1,2,3,6-Tetra-O-acetyl-4-O-(2,3,4-tri-O-acetyl-6-azido-6-deoxy-α-D-glucopyranosyl)-β-D-glucopyranose (**14**). — A solution of **8** (4.82 g) and sodium azide (7 g) in *N,N*-dimethylformamide (100 mL) was stirred for 2 h at 100°. The mixture was processed as described for the preparation of **9**, and the residual syrup was acetylated with acetic anhydride (50 mL) and sodium acetate (3 g), as described for the preparation of **4**. Crystallization from ethanol gave **14** (3.06 g, 76%); m.p. 167–168°, $[\alpha]_D^{20}$ +77.9° (*c* 1.7, chloroform); ν_{max} 2100 cm^{-1} (N_3).

Anal. Calc. for $C_{26}H_{35}N_3O_{17}$: C, 47.20; H, 5.33; N, 6.35. Found: C, 47.30; H, 5.24; N, 6.22.

1,2,3,6-Tetra-O-acetyl-4-O-(2,3-di-O-acetyl-4-O-benzoyl-6-bromo-6-deoxy-α-D-glucopyranosyl)-β-D-glucopyranose (**15**). — A mixture of **4** (2.50 g), *N*-bromosuccinimide (0.78 g), and barium carbonate (5 g) in anhydrous carbon tetrachloride (60 mL) and 1,1,2,2-tetrachloroethane (40 mL) was boiled and stirred for 1 h under reflux. The mixture was filtered through a layer of Celite, and the inorganic solid was washed with chloroform. The filtrate and washings were combined and evaporated. A solution of the residue in chloroform was washed with water, dried, and evaporated to a syrup, which was eluted from a column of silica gel with 4:1 benzene–ethyl acetate, to give **15** (2.55 g, 91%) as a white powder; $[\alpha]_D^{20}$ +32.9° (*c* 1.2, chloroform); n.m.r. data (chloroform-*d*): δ 8.04–7.34 (m, 5 H, Ph), 5.78 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), and 2.14, 2.10, 2.07, 2.05, 2.02, and 1.89 (6 s, each 3 H, 6 AcO).

Anal. Calc for $C_{31}H_{37}BrO_{17}$: C, 48.89; H, 4.90; Br, 10.49. Found: C, 48.98; H, 4.75; Br, 10.60.

4-O-(6-Bromo-6-deoxy-α-D-glucopyranosyl)-D-glucose (**16**), *4-O-(6-chloro-6-deoxy-α-D-glucopyranosyl)-D-glucose* (**17**), *4-O-(6-deoxy-α-D-glucopyranosyl)-D-glucose* (**18**), *and 4-O-(6-azido-6-deoxy-α-D-glucopyranosyl)-D-glucose* (**19**). — *O*-Deacetylation of **9** (1.02 g), **10** (0.84 g), **12** (0.85 g), and **14** (2.84 g) in anhydrous

methanol with a catalytic amount of sodium methoxide overnight at room temperature, followed by neutralization of the base with Amberlite IR-120 (H^+) ion-exchange resin, and purification of each product by elution from a column of silica gel with 40:25:4 chloroform–methanol–water, gave the corresponding free sugars **16, 17, 18,** and **19**, respectively, as chromatographically homogeneous powders.

Compound **16** (0.53 g, 90%): $[\alpha]_D^{20}$ +103.6° (*c* 2.3, water); lit.[8] $[\alpha]_D^{22}$ +105° (*c* 1.0, water). Compound **16** (0.66 g, 81%) was also obtained from **15** (1.52 g) by a similar *O*-deacylation; $[\alpha]_D^{20}$ +102.1° (*c* 1.8 water).

Compound **17** (0.42 g, 86%) as the monohydrate[8]: $[\alpha]_D^{20}$ +114.2° (*c* 1.2, water); lit.[8] $[\alpha]_D^{22}$ +116° (*c* 1.1, water).

Compound **18** (0.42 g, 89%) as the monohydrate[4,8]: $[\alpha]_D^{20}$ +130.5° (*c* 2.0, water); lit.[4] $[\alpha]_D$ +112.7° (*c* 2.27, water); $[\alpha]_D^{22}$ +134° (*c* 1.04, water)[8].

Compound **19** (1.45 g, 88%) as the monohydrate[8]: $[\alpha]_D^{20}$ +105.2° (*c* 1.4, water); lit.[8] $[\alpha]_D^{22}$ +103° (*c* 1.1, water).

*4-O-(6-Amino-6-deoxy-α-*D*-glucopyranosyl)-*D*-glucose* (**20**). — Compound **19** (1.22 g) was dissolved in 95% methanol (80 mL) and hydrogenated in the presence of palladium-on-charcoal (1.1 g) for 2 h at room temperature and pressure. The catalyst was filtered off through a Celite pad, and washed with methanol. The filtrate and washings were combined and evaporated, to give a syrup which was purified by precipitation from methanol, to afford **20** (0.89 g, 74%) as the monohydrate[8]; $[\alpha]_D^{20}$ +114.0° (*c* 1.9, water); t.l.c. (3:1:1 2-butanone–methanol-M acetic acid): R_F 0.31 (ninhydrin-positive); lit.[8] $[\alpha]_D^{22}$ +111° (*c* 0.64, water); D-glucose was not reduced under identical conditions.

*O-(2,3,4,6-Tetra-O-benzyl-α-*D*-glucopyranosyl)-(1→6)-O-(2,3-di-O-acetyl-α-*D*-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-β-*D*-glucopyranose* (**22**). — A solution of **5** (6.10 g, 10.3 mmol) in dry dichloromethane (110 mL) and *N,N*-dimethylformamide (30 mL) was stirred for 2 h at room temperature in the presence of tetraethylammonium bromide (3.47 g, 16.5 mmol) and molecular sieve 4A (20 g). A solution of freshly prepared[21] **21** (9.97 g, 16.5 mmol) in dichloromethane (40 mL) was added, and the mixture was stirred for 2 days at room temperature. The solids were removed by filtration, and washed thoroughly with dichloromethane. The filtrate and washings were combined, washed successively with aqueous sodium hydrogencarbonate and water, dried, and evaporated to a syrup which was fractionated on a column of silica gel, eluting first with 2:1 hexane–ethyl acetate and then with 1:1 hexane–ethyl acetate, to give **22** (8.14 g, 71%); m.p. 152–153° (ethanol–2-propanol), $[\alpha]_D^{20}$ +51.3° (*c* 2.0, chloroform); n.m.r. data (chloroform-*d*): δ_H 7.24–7.12 (m, 20 H, arom. H), 5.73 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), and 2.06–2.00 (singlets, 18 H, 6 AcO); δ_C 98.13 (C-1″, $^1J_{CH}$ 168.3 Hz), 96.08 (C-1′, $^1J_{CH}$ 173.5 Hz), and 91.45 (C-1, $^1J_{CH}$ 162.1 Hz).

Anal. Calc. for $C_{58}H_{68}O_{22}$: C, 62.36; H, 6.14. Found: C, 62.46; H, 6.13.

*O-α-*D*-Glucopyranosyl-(1→6)-O-α-*D*-glucopyranosyl-(1→4)-α-*D*-glucose* (**23**). — Hydrogenolysis of **22** (5.75 g) in acetic acid (60 mL) in the presence of 10% palladium-on-charcoal (3 g) overnight at atmospheric pressure and room tempera-

ture, followed by processing of the mixture as described for the preparation of **12**, and *O*-deacetylation of the product, as described previously, gave **23** (2.13 g, 82%); m.p. 219–220° (dec.) (from aqueous methanol), unchanged on admixture with an authentic specimen[10] provided by Dr. T. Watanabe, $[\alpha]_D^{20}$ +162.1 (2 min) → +151.4° (3 h, constant; *c* 2.0, water); lit.[6] m.p. 221° (dec.), $[\alpha]_D^{20}$ +161 → +151° (*c* 0.3, water); m.p. 220° (dec.), $[\alpha]_D^{25}$ +160 → +151° (*c* 2.8, water)[11]; the compound showed in p.c. a single spot, having an R_F value identical with that of the authentic sample.

Reduction of **23** (0.26 g) with sodium borohydride, followed by acetylation[11], gave **24** (0.38 g, 73%); m.p. 149.5–150.5° (from ethanol), $[\alpha]_D^{20}$ +119.4° (*c* 1.1, chloroform); lit.[11] m.p. 148.5–150°, $[\alpha]_D^{27}$ +120° (*c* 4.0, chloroform).

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