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PREPARATION OF OLIGOSACCHARIDES WITH β-D-MANNOPYRANOSYL AND 2-AZIDO-2-DEOXY-β-D-MANNOPYRANOSYL RESIDUES BY INVERSION AT C-2 AFTER COUPLING*

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ABSTRACT

Di- and tri-saccharides with a 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranosyl unit were prepared by coupling 1,2,4,6-tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose (**1**) to suitably, partially benzylated, acceptor sugar derivatives. Deacetylation followed by acetalation gave 3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl derivatives which were treated with *N,N'*-sulfuryldi-imidazole. The resulting 2-imidazylate group was displaced easily with inversion by benzoate or azide, leading to β-D-mannopyranosyl or 2-azido-2-deoxy-β-D-mannopyranosyl derivatives, respectively. Protected derivatives of β-D-Man*p*-(1→4)-D-Glc, β-D-Man*p*-(1→4)-D-Man, β-D-Man*p*-(1→4)-β-D-Man*p*-(1→4)-D-Glc, 2-azido-2-deoxy-β-D-Man*p*-(1→4)-D-Glc, and 2-azido-2-deoxy-β-D-Man*p*-(1→6)-D-Glc were prepared thus.

INTRODUCTION

β-D-Mannopyranosyl and 2-acetamido-2-deoxy-β-D-mannopyranosyl residues occur frequently in bacterial polysaccharides and glycoproteins[1]. The synthesis of the 1,2-*cis* glycosidic bond in these units is difficult. The use of a mannopyranosyl halide without a participating group at position 2 and silver silicate as promoter requires that the hydroxyl group of the substrate be reactive[2]. The introduction of a 2-acetamido-2-deoxy-β-D-mannopyranosyl residue required first the synthesis of an activated derivative of 2-azido-2-deoxy-D-mannopyranose[3]. These methods are useful when the substrate is a protected oligosaccharide and the number of chemical steps should be kept to a minimum. The use of activated D-glucopyranosyl derivatives can introduce β-D-glucopyranosyl units, and conversion into the β-D-*manno* structure can be achieved by oxidation of HO-2 to a ketone

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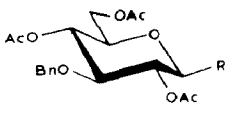
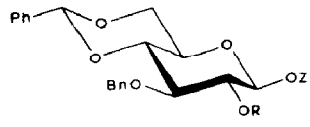
followed by reduction[4], or oximation and reduction[5]. This route was designed because S_N2 substitution reactions at position 2 are often impossible. However, the introduction of such new leaving groups as imidazylate[6] has changed the situation. Compared to the popular triflic anhydride, the *N,N'*-sulfuryldi-imidazole reagent is a cheap crystalline solid which can be stored easily at room temperature and tolerates the acetamido group. We now report the use of this reagent in the syntheses of protected derivatives of β-D-Man*p*-(1→4)-D-Glc, β-D-Man*p*-(1→4)-D-Man, β-D-Man*p*-(1→4)-β-D-Man*p*-(1→4)-D-Glc, 2-azido-2-deoxy-β-D-Man*p*-(1→4)-D-Glc, and 2-azido-2-deoxy-β-D-Man*p*-(1→6)-D-Glc.

RESULTS AND DISCUSSION

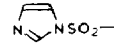
As precursor of the β-D-*manno* residue, 1,2,4,6-tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose (**1**) was used. Compound **1** was prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose by the sequence benzylation, hydrolysis with acid, and treatment with acetic anhydride–sodium acetate.

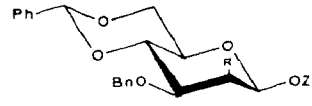


1 R = OAc
2 R = OZ



3 R = H

4 R = 

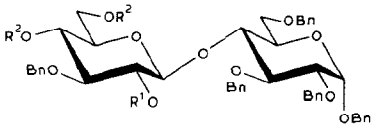


5 R = OBz
6 R = N_3

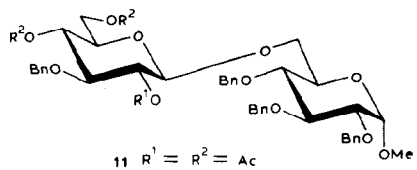
Condensation of **1** with a sugar derivative (Z-OH) partially protected with benzyl groups, in the presence of trimethylsilyl triflate as promoter[7], gave the β-D-glucopyranoside **2**, deacetylation of which followed by acetalation gave **3** with HO-2 unsubstituted. Derivatization with *N,N'*-sulfuryldi-imidazole gave the imidazylate **4** which, on treatment with tetrabutylammonium benzoate or azide in toluene at 80°, afforded the D-*manno* benzoate **5** or the 2-azido-2-deoxy-D-*manno* derivative **6**, respectively, in near quantitative yields. In this way, benzyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside gave the disaccharide derivatives **19** and **20**, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside gave **24**, and methyl 2,3,6-tri-*O*-benzyl-α-D-mannopyranoside[8] gave **25**. The overall yields for the five steps were in the range 35–67% and depend upon the yield of the glycosidation step.

The preparations can be scaled-up easily, since **1** can be converted into more reactive derivatives after selective hydrolysis[9] of AcO-1 and inexpensive coupling procedures can be used. Furthermore, the β-D-*manno* unit introduced in this way is amenable to consecutive glycosidations on positions 2, 4, and 6 after standard transformations.

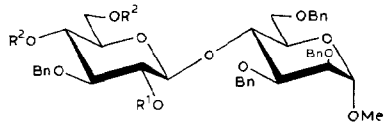
Starting with the β-D-*manno* disaccharide derivative **19**, the benzyl group was replaced by a benzyl ether function and the acetal group was converted[10] into a



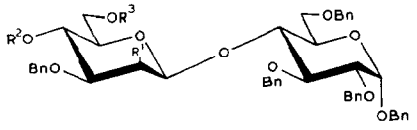
7 $R^1 = R^2 = Ac$
8 $R^1 = R^2 = H$
9 $R^1 = H, R^2, R^2 = PhCH$
10 $R^1 = Ims, R^2, R^2 = PhCH$



11 $R^1 = R^2 = Ac$
12 $R^1 = R^2 = H$
13 $R^1 = H, R^2, R^2 = PhCH$
14 $R^1 = Ims, R^2, R^2 = PhCH$



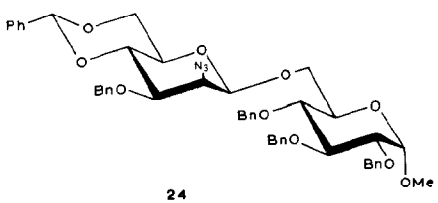
15 $R^1 = R^2 = Ac$
16 $R^1 = R^2 = H$
17 $R^1 = H, R^2, R^2 = PhCH$
18 $R^1 = Ims, R^2, R^2 = PhCH$



19 $R^1 = OBz, R^2, R^3 = PhCH$
20 $R^1 = N_3, R^2, R^3 = PhCH$
21 $R^1 = OH, R^2, R^3 = PhCH$
22 $R^1 = OBn, R^2, R^3 = PhCH$
23 $R^1 = OBn, R^2 = H, R^3 = Bn$

6-benzyl ether to give **23**. The low yield (~30%) in the conversion **23** → **26** reflected the difficulty in the separation of the products. Glycosidation of a similar unit in methyl 2,3,6-tri-*O*-benzyl-α-D-mannopyranoside proceeded in 87% yield. However, the following steps, from **26** to **29**, proceeded smoothly. The synthesis of the trisaccharide derivative **29** is the first involving consecutive β-D-mannopyranosylations. A β-D-Man*p*-(1→4)-β-D-Man*p*-(1→4)-D-Glc sequence is present[11] in the main chain of the capsular polysaccharide of *Klebsiella* K69, the repeating unit of which is: -4)-β-D-Glc*p*-(1→4)-β-D-Man*p*-(1→4)-β-D-Man*p*-(1-

Kunz and Günther[12] have developed an approach to the synthesis of the β-D-mannopyranosyl unit which looks well adapted to chain-elongation on C-3.



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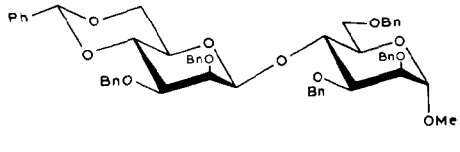
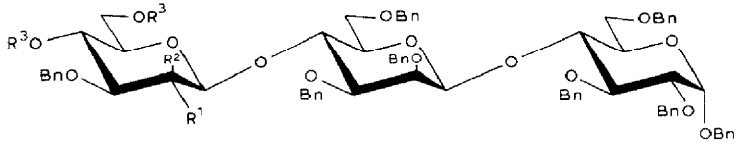


25

EXPERIMENTAL

General methods. — Reactions were monitored by t.l.c. on silica gel, using hexane–ethyl acetate (2:1). ^{1}H-N.m.r. spectra at 250 MHz were recorded for solutions in $CDCl_3$ (internal Me_4Si). The signals of aromatic and benzylic protons are not reported. Optical rotations were obtained for solutions in CH_2Cl_2.



26 R^1 = OAc, R^2 = H, R^3 = Ac
27 R^1 = OH, R^2 = R^3 = H
28 R^1 = OH, R^2 = H, R^3, R^3 = PhCH
29 R^1 = H, R^2 = OBzn, R^3, R^3 = PhCH

*1,2,4,6-Tetra-*O*-acetyl-3-*O*-benzyl-β-*D*-glucopyranose* (**1**). — A mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (5.2 g), benzyl bromide (4.7 mL), and sodium hydride (1.6 g of a 60% suspension in oil) in *N,N*-dimethylformamide (26 mL) was heated at 90° for 2 h, methanol (5 mL) was added, and heating at 90° was continued for 10 min. The cooled solution was poured into water and extracted with ether. The extract was washed to neutrality and concentrated, and a solution of the residue in aqueous 60% acetic acid was heated for 2 h at 90°, then concentrated to dryness. The residue was treated with 0.1M sulfuric acid (50 mL) at 90° for 2 h. The solution was cooled to room temperature, diluted with water (50 mL), extracted twice with CH_2Cl_2, and passed through a column of Dowex-1 (HCO_2^-) (40 mL), which was rinsed with water (400 mL). The combined aqueous solutions were concentrated to dryness (5.4 g).

A solution of the combined residues (10.8 g) from two preparations and anhydrous sodium acetate (1.8 g) in acetic anhydride (20 mL) was heated at 110° for 4 h and then poured into a mixture of ice and water, the solid was collected, and a solution in ether was washed with water and concentrated to dryness. The residue crystallized from hexane–ether to give **1** (12.5 g, 71%), m.p. 104° (from ethanol), $[\alpha]_D$ ~0° (*c* 1.7, dichloromethane); lit.[13] m.p. 107°, $[\alpha]_D$ −1.3° (chloroform). N.m..r. data: δ 3.74 (ddd, H-5), 3.76 (dd, H-3), 4.10 (dd, $J_{5,6a}$ 3, $J_{6a,6b}$ 12 Hz, H-6a), 4.24 (dd, $J_{5,6b}$ 5 Hz, H-6b), 4.62 (PhCH_2), 5.17 (dd, $J_{3,4} = J_{4,5}$ = 10 Hz, H-4), 5.18 (dd, $J_{2,3}$ 10 Hz, H-2), 5.66 (d, $J_{1,2}$ 8 Hz, H-1), 7.30 (Ph).

Anal. Calc. for $C_{23}H_{28}O_{11}$: C, 57.50; H, 5.83; O, 36.67. Found: C, 57.57; H, 5.86; O, 36.94.

General procedure for glycosidation with **1**. — A solution of the acceptor (1 mmol) and **1** (1.2 mmol) in anhydrous CH_2Cl_2 (10 mL) was stirred for 0.5 h at room temperature in the presence of crushed molecular sieves (4 Å), then cooled to −20°. Trimethylsilyl trifluoromethanesulfonate (0.167 mL) was added, and the mixture was allowed to attain room temperature, stirred until the reaction was complete, then neutralized (10% NEt_3 in CH_2Cl_2), filtered, and concentrated to dryness. In this way, the following compounds were obtained.

*Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-benzyl-β-*D*-glucopyranosyl)-α-*D*-glucopyranoside* (**7**). — Glycosidation of benzyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside gave **7** (3.18 g, 69.3%), isolated by chromatography (hexane–ethyl

acetate, 2:1); m.p. 122° (from ethanol), $[\alpha]_D$ +36° (*c* 1.8). N.m.r. data: δ 1.88, 1.95 (3 Ac), 3.25 (ddd, *J* 3, 4 and 10 Hz, H-5′), 3.40 (dd, *J* 9.5 and 9.5 Hz, H-3′), 3.46 (H-6a,6b), 3.64 (m, H-5), 3.72 (dd, *J* 3 and 12 Hz, H-6′a), 4.11 (dd, *J* 4 and 12 Hz, H-6′b), 4.45 (d, *J* 10 Hz, H-1′), 4.81 (d, *J* 3 Hz, H-1), 4.96 (dd, *J* 9.5 and 10 Hz, H-2′), 5.09 (dd, *J* 9.5 and 10 Hz, H-4′).

Anal. Calc. for $C_{53}H_{58}O_{14}$: C, 69.27; H, 6.36; O, 24.37. Found: C, 69.20; H, 6.28; O, 24.11.

*Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-benzyl-β-*D*-glucopyranosyl)-α-*D*-glucopyranoside* (**11**). — Glycosidation of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside gave **11** (0.94 g, 74%), isolated by chromatography (toluene–acetone, 95:5) as a second fraction, m.p. 128° (from methanol), $[\alpha]_D$ +19° (*c* 1.5). N.m.r. data: δ 1.90, 1.95, 2.04 (3 Ac), 3.34 (MeO), 3.43 (dd, *J* 9.5 and 9.5 Hz, H-3), ~3.55 (m, H-2,5′), 3.66 (dd, *J* 9.5 and 9.5 Hz, H-4), 3.76 (ddd, *J* 1, 4 and 10 Hz, H-5), 3.97 (dd, *J* 9 and 9 Hz, H-3′), ~4.1 (m, H-6b,6′a,6′b), 4.44 (d, *J* 8 Hz, H-1′), 4.57 (s, H-1), 5.12 (dd, *J* 8 and 9 Hz, H-2′), 5.13 (dd, *J* 9 and 9 Hz, H-4′).

Anal. Calc. for $C_{47}H_{54}O_{14}$: C, 66.97; H, 6.46; O, 26.57. Found: C, 66.68; H, 6.31; O, 26.73.

The first fraction contained methyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (148 mg, 25%).

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-acetyl-3-*O*-benzyl-β-*D*-glucopyranosyl)-α-*D*-mannopyranoside* (**15**). — Glycosidation of methyl 2,3,6-tri-*O*-benzyl-α-D-mannopyranoside, followed by chromatography (hexane–ethyl acetate, 4:1), gave **15** (3.66 g, 87%), m.p. 132° (from ethanol), $[\alpha]_D$ +9° (*c* 1.3). N.m.r. data: δ 3.25–3.35 (m, MeO, H-5′), 3.50 (dd, *J* 9 and 10 Hz, H-3′), 4.97 (dd, *J* 7.5 and 9 Hz, H-2), 5.07 (dd, *J* 9 and 9 Hz, H-4′).

Anal. Calc. for $C_{47}H_{54}O_{14}$: C, 66.97; H, 6.46; O, 26.57. Found: C, 66.81; H, 6.44; O, 26.37.

Methanolysis and acetalation. — A solution of the triacetate (1 mmol) in methanol or 1:1 methanol–1,4-dioxane, containing methanolic 1% NaOMe (5.20 mL), was kept at room temperature until the starting material disappeared (t.l.c.), then neutalized with Dowex-50 (H^+) resin, filtered, and concentrated to dryness. A suspension of the residue in benzaldehyde (2.5 mL) was stirred overnight with zinc chloride (0.5 g) at room temperature and then treated in the usual way. Alternatively, a solution of the crude triol (1 mmol), α,α-dimethoxytoluene (760 mg), and toluene-*p*-sulfonic acid (35 mg) in acetonitrile (35 mL) was stirred for 1 h at room temperature, then neutralized with triethylamine and concentrated to dryness. The following compounds were obtained in this manner.

Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-glucopyranoside (**9**; 2.17 g, 70%), m.p. 132° (from ether–hexane), $[\alpha]_D$ −26° (*c* 1). N.m.r. data: δ 5.46 (s, PhC*H*).

Anal. Calc. for $C_{54}H_{56}O_{11}$: C, 73.61; H, 6.41; O, 19.98. Found: C, 73.67; H, 6.47; O, 19.89.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-gluco-

pyranosyl)-α-D-glucopyranoside (**13**; 317 mg, 84%); m.p. 156° (from methanol), $[\alpha]_D$ +16° (*c* 1).

Anal. Calc. for $C_{48}H_{52}O_{11}$: C, 71.62; H, 6.51; O, 21.87. Found: C, 70.91; H, 6.44; O, 21.89.

Methyl 2,3,6-tri-O-benzyl-4-O-(3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyl)-α-D-mannopyranoside (**17**). — Alkaline methanolysis of **15** gave the crude triol **16**, which was converted into the benzylidene acetal **17**, isolated by chromatography (hexane–ethyl acetate, 4:1) as a gum (186 mg, 64%), $[\alpha]_D$ +10.4° (*c* 1.3).

Anal. Calc. for $C_{48}H_{52}O_{11}$: C, 71.62; H, 6.51. Found: C, 71.01; H, 6.55.

Nucleophilic substitution. — Sodium hydride (60% dispersion in oil; 65 mg) was added to a solution of the alcohol (1 mmol) in *N,N*-dimethylformamide (10 mL). The mixture was kept for 0.5 h at room temperature and then cooled to −40°, sulfuryldi-imidazole (300 mg) was added, and the solution was stirred at −30° until t.l.c. (hexane–ethyl acetate, 2:1) indicated the end of the reaction (1–3 h). The solution was cooled to −40°, methanol (0.2 mL) was added, the mixture was allowed to attain room temperature, and the imidazyl derivative was separated by ether–water partition.

The crude imidazyl derivatives **10, 14**, and **18**, obtained as low-melting solids in quantitative yields, were pure enough for the next step. They could be characterized by the three downfield singlets for the imidazole protons, in the n.m.r. spectrum, *e.g.*, δ 6.95, 7.18, and 7.90 for **10**.

A solution of the imidazole derivative (1 mmol) and either tetrabutylammonium benzoate (726 mg) or azide (648 mg) in toluene (10 mL) was boiled under reflux until t.l.c. (hexane–ethyl acetate, 2:1) indicated the disappearance of starting material (1–2 h). The solution was cooled, washed with water, and concentrated to dryness. The disaccharide derivatives **19, 20, 24**, and **25** were obtained in this way and yields were calculated from the starting alcohols.

Benzyl 4-O-(2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-β-D-mannopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**19**). — Chromatography (hexane–ethyl acetate, 3:1) gave the pure product as a syrup (317 mg, 90%), $[\alpha]_D$ −20° (*c* 1). N.m.r. data: δ 3.46 (dd, *J* 3 and 10 Hz, H-3′), 3.48 (dd, 3.5 and 9 Hz, H-2), 3.54 (dd, *J* 1.5 and 11 Hz, H-6′a), 3.70 (H-6,5′), 3.75 (H-3,6a), 3.98 (dd, *J* 10 and 10 Hz, H-4,4′ superimposed), 4.16 (dd, *J* 5, 10 Hz, H-6b), 4.57 (d, *J* 1 Hz, H-1′), 4.78 (d, *J* 4 Hz, H-1), 5.57 (s, PhC*H*), 5.60 (dd, *J* 1 and 3.5 Hz, H-2′).

Anal. Calc. for $C_{61}H_{60}O_{12}$: C, 74.37; H, 6.14; O, 19.49. Found: C, 74.56; H, 6.35; O, 19.52.

Benzyl 4-O-(2-azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-β-D-mannopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**20**). — The crude product was crystallized from ethanol to give **20** (484 mg, 95%), m.p. 121°, $[\alpha]_D$ +15.5° (*c* 1.1); ν_{max} 2105 cm^{-1} (N_3). N.m.r. data: δ 2.97 (ddd, *J* 5, 9.5, and 9.5 Hz, H-5), 3.41 (dd, *J* 3.5 and 9.5 Hz, H-2), 3.70 (dd, *J* 1 and 3.5 Hz, H-2′), 4.65 (H-1′), 4.85 (d, *J* 3.5 Hz, H-1), 5.51 (s, PhC*H*).

Anal. Calc. for $C_{54}H_{55}N_3O_{10}$: C, 71.58; H, 6.12; O, 17.66. Found: C, 71.67; H, 6.12; O, 17.45.

Methyl 6-O-(2-azido-3-O-benzyl-4,6-O-benzylidene-2-deoxy-β-D-mannopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**24**). — Crystallization of the crude product from methanol gave **24** (230 mg; 96%), m.p. 137°, $[\alpha]_D$ +5° (*c* 0.8); ν_{max} 2100 cm^{-1} (N_3). N.m.r. data: δ 3.19 (ddd, *J* 5, 10, and 10 Hz, H-5), 3.34 (MeO), 3.42 (dd, *J* 10 and 10 Hz, H-3), 3.49 (dd, *J* 3.5 and 9.5 Hz, H-2), 3.59 (dd, *J* 3.5 and 10 Hz, H-3'), 3.71 (dd, *J* 0.5 Hz and 3.5 Hz, H-2'), 3.75 (H-5'), 3.84 (dd, *J* 10 and 10 Hz, H-4), 3.96 (dd, *J* 10 and 10 Hz, H-4'), 4.19 (d, *J* 0.5 Hz, H-1'), 4.25 (dd, *J* 5 and 10 Hz, H-6a), 4.55 (d, *J* 3.5 Hz, H-1), 5.56 (s, PhC*H*).

Anal. Calc. for $C_{48}H_{51}N_3O_{10}$: C, 69.46; H, 6.20; N, 5.06; O, 19.28. Found: C, 69.24; H, 6.49; N, 4.80; O, 19.21.

Methyl 4-O-(2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-β-D-mannopyranosyl)-2,3,6-tri-O-benzyl-α-D-mannopyranoside (**25**). — Chromatography (hexane–ethyl acetate, 4:1) of the product gave **25** as a syrup (0.35 g, 77%), $[\alpha]_D$ −43° (*c* 2). N.m.r. data: δ 3.15 (m, H-5'), 3.25 (MeO), 3.54 (dd, *J* 3 and 9 Hz, H-3'), 3.58–3.83 (m, 6 H), 3.97 (dd, *J* 9 and 9 Hz, H-4'), 4.07–4.18 (m, H-1',6'a), 4.32 (dd, *J* 9 and 9 Hz, H-4), 5.55 (Ph*H*), 5.05 (dd, *J* 1 and 3 Hz, H-2').

Anal. Calc. for $C_{55}H_{56}O_{12}$: C, 72.67; H, 6.21; O, 21.12. Found: C, 72.81; H, 6.24; O, 20.83.

Benzyl 2,3,6-tri-O-benzyl-4-O-(3-O-benzyl-4,6-O-benzylidene-β-D-mannopyranosyl)-α-D-glucopyranoside (**21**). — Sodium (120 mg) was added to a solution of **19** (1.7 g) in methanol (12.5 mL) and 1,4-dioxane (12.5 mL). The mixture was kept at room temperature until methanolysis was complete (t.l.c.), then neutralized with Dowex-50 (H^+) resin, filtered, and concentrated to dryness. Chromatography (hexane–ethyl acetate, 3:1 and 2:1) gave **21** (1.436 g, 95%), m.p. 142° (from methanol), $[\alpha]_D$ +37° (*c* 1).

Anal. Calc. for $C_{54}H_{56}O_{11}$: C, 73.61; H, 6.41; O, 19.98. Found: C, 73.84; H, 6.60; O, 19.94.

Benzyl 2,3,6-tri-O-benzyl-4-O-(2,3-di-O-benzyl-4,6-O-benzylidene-β-D-mannopyranosyl)-α-D-glucopyranoside (**22**). — A solution of **21** (1.4 g) and benzyl bromide (0.2 mL) in *N,N*-dimethylformamide (15 mL) was stirred for 1 h at room temperature in the presence of sodium hydride (60% dispersion in oil, 95 mg). After the usual treatment, the product was isolated by chromatography (hexane–ethyl acetate, 3:1) as a syrup (1.461 g, 94%), $[\alpha]_D$ +8.4° (*c* 2.6).

Anal. Calc. for $C_{61}H_{62}O_{11}$: C, 75.44; H, 6.44; O, 18.12. Found: C, 75.20; H, 6.23; O, 18.29.

Benzyl 2,3,6-tri-O-benzyl-4-O-(2,3,6-tri-O-benzyl-β-D-mannopyranosyl)-α-D-glucopyranoside (**23**). — To a solution of **22** (1.377 g) and sodium cyanoborohydride (1 g) in oxolane (30 mL) in the presence of crushed 4 Å molecular sieves (6 g) at 0° was added saturated ethereal hydrogen chloride (5 mL) dropwise. The mixture was stirred for 0.5 h, then diluted with dichloromethane, washed with cold water, cold saturated aqueous $NaHCO_3$, and water, and concentrated to dryness.

To a solution of the residue in dichloromethane was added silica gel, which caused evolution of gas, and **23** was isolated by chromatography (hexane–ethyl acetate, 3:1) as a syrup (855 mg, 62%), $[\alpha]_D$ −12° (*c* 4.3).

Anal. Calc. for $C_{61}H_{64}O_{11}$: C, 75.28; H, 6.63; O, 18.09. Found: C, 75.48; H, 6.61; O, 18.37.

Benzyl O-(3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**28**). — Glycosylation of **23** with **1** gave a crude syrup which was submitted to alkaline methanolysis. T.l.c. (hexane–ethyl acetate, 2:1, then 1:1) gave the triol **27** (232 mg, 22%), $[\alpha]_D$ +71° (*c* 2.25). Acetalation and chromatography (hexane–ethyl acetate, 2:1) then gave **28** (168 mg, 87%), $[\alpha]_D$ +2.2° (*c* 3.2). N.m.r. data: δ 5.43 (PhC*H*O_2).

Anal. Calc. for $C_{81}H_{84}O_{16}$: C, 74.06; H, 6.45; O, 19.49. Found: C, 73.83; H, 6.67; O, 19.72.

Benzyl O-(2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-β-D-mannopyranosyl)-(1→4)-O-(2,3,6-tri-O-benzyl-β-D-mannopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**29**). — Prepared from **28** *via* the imidazylate, and purified by chromatography (hexane–ethyl acetate, 2:1), **29** (74 mg, 44%) had $[\alpha]_D$ −27° (*c* 1.5). N.m.r. data: δ 3.52 (dd, *J* 3 and 10 Hz, H-3″), 4.74 (s, H-1″), 5.55 (PhC*H*), 5.66 (d, *J* 3 Hz, H-2″).

Anal. Calc. for $C_{88}H_{88}O_{16}$: C, 74.55; H, 6.26; O, 19.19. Found: C, 74.41; H, 6.49; O, 19.36.

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