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# Synthesis of methyl 3-*O*-(α-D-glucopyranosyl)-7-*O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-L-*glycero*-α-D-*manno*-heptopyranoside*

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ABSTRACT

The title trisaccharide glycoside, which is related to part of the core region of the lipopolysaccharide from *Salmonella*, and the disaccharide glycosides methyl 3-*O*-α-D-glucopyranosyl-L-*glycero*-α-D-*manno*-heptopyranoside and methyl 7-*O*-L-*glycero*-α-D-*manno*-heptopyranosyl-L-*glycero*-α-D-*manno*-heptopyranoside have been synthesised. Methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside, obtained *via* a one-carbon elongation at C-6 of methyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside, was used as precursor both for the heptosyl donor and acceptor.

## INTRODUCTION

The core region of the lipopolysaccharides of *Salmonella* bacteria has the structure[1] shown in Fig. 1. Monoclonal antibodies raised against mutant *Salmonella* bacteria that lack the O-antigen side chain and sometimes also parts of the core region will be directed towards various parts of the core region. In order to investigate the specificity of these antibodies, synthetic oligosaccharides of parts of the core are necessary. Oligosaccharides from the hexose region[2,3] and structures related to the Kdo[4] and heptose[5] regions have been synthesised. We now describe the synthesis of the title trisaccharide glycoside that corresponds to the part that links the hexose and the heptose regions. This is probably a receptor for a phage (G13)[6].

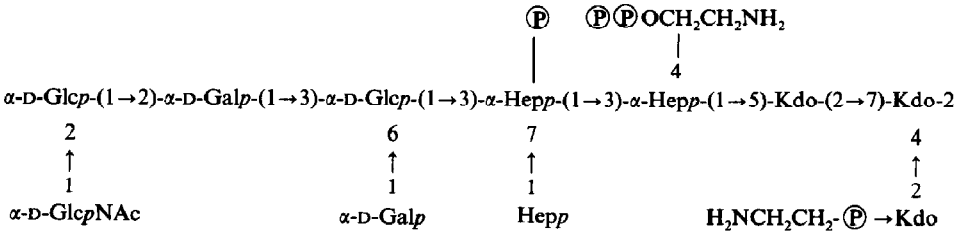


Fig. 1 The core region of the lipopolysaccharides of *Salmonella* bacteria.

* Dedicated to Professor Leslie Hough in the year of his 65th birthday.
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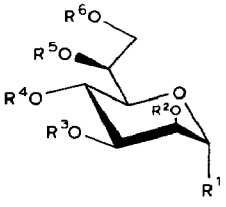
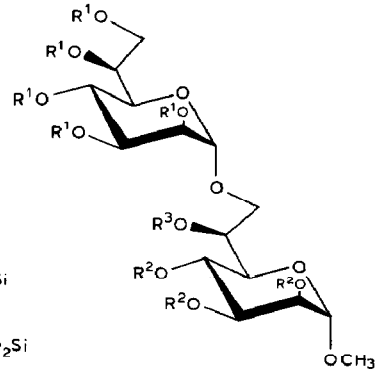
## RESULTS AND DISCUSSION

The heptose precursor used, namely, methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside (**1**), was synthesised by the reaction of methyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside and the Grignard complex of isopropoxydimethylsilylmethyl chloride, followed by oxidative cleavage of the carbon–silicon bond as described by Fleming and Sanderson[7], and by van Boom and co-workers[8]. This synthesis was preferred to that described by Dziewiszek and Zamojski[9], which used the Grignard reagent of benzyl chloromethyl ether, since we found it difficult, as did van Boom and co-workers[8], to obtain good reproducibility, due to the instability of the Grignard reagent. van Boom and co-workers[8] did not publish any data on **1**, so that a comparison could not be made. Therefore, the stereochemistry was determined by conversion of **1** into the penta- (**6**) and hexa-acetate (**7**) and comparison with data published for these derivatives[10,11].





**1** $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = Bn, $R^5$ = $R^6$ = H
**2** $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = Bn, $R^5$ = Bz, $R^6$ = $Bu^tMe_2Si$
**3** $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = H, $R^5$ = Bz, $R^6$ = $Bu^tMe_2Si$
**4** $R^1$ = OMe, $R^2$ = $R^3$ = Ac, $R^4$ = H, $R^5$ = Bz, $R^6$ = $Bu^tMe_2Si$
**5** $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = Bn, $R^5$ = Bz, $R^6$ = H
**6** $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = $R^5$ = $R^6$ = Ac
**7** $R^1$ = OAc, $R^2$ = $R^3$ = $R^4$ = $R^5$ = $R^6$ = Ac
**8** $R^1$ = Br, $R^2$ = $R^3$ = $R^4$ = $R^5$ = $R^6$ = Ac

**9** $R^1$ = Ac, $R^2$ = Bn, $R^3$ = Bz
**10** $R^1$ = $R^2$ = $R^3$ = H

In order to synthesise the heptose glycosyl acceptors, **1** was regioselectively silylated at O-7 with *tert*-butyldimethylsilyl chloride in pyridine and the product was benzoylated to give **2**. Hydrogenolysis of **2** removed the benzyl groups and yielded **3**, which was treated in sequence with trimethyl orthoacetate, acetic anhydride, and acid to open the cyclic 2,3-orthoester[12] and afford the 3-hydroxy derivative **4**. Treatment of **2** with aqueous acetic acid removed the silyl group and yielded the 7-hydroxy derivative **5**.

The heptosyl donor was obtained by hydrogenolysis of **1** followed by acetylation to give **6**, and then acetolysis to afford the crystalline hexa-acetate **7**. Treatment of **7** with hydrogen bromide in glacial acetic acid then gave the glycosyl bromide **8**.

Silver triflate-promoted coupling[13] of **8** and **5** in the presence of collidine (2,4,6-trimethylpyridine, 0.8 equiv.) gave the (1→7)-linked disaccharide derivative **9**. In the absence of collidine, mainly decomposition products were obtained, whereas, with 1 equiv. of collidine, the orthoester was the main product[14]. The reactivity of **8** was low, as described by Paulsen *et al.*[10], and prolonged reaction was necessary in order to obtain a

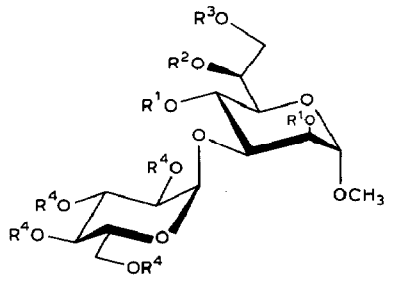
good yield of the product. In a model experiment, where the methyl thioglycoside of **7** reacted with methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside in the presence of methyl triflate[15], no disaccharide derivative was formed. Only the 6-*O*-methyl ether of the aglycon was obtained, thereby providing further evidence of the low reactivity of the acylated heptose derivatives as glycosyl donors.

Zemplén *O*-deacylation of **9** followed by hydrogenolysis gave the first target compound **10**.

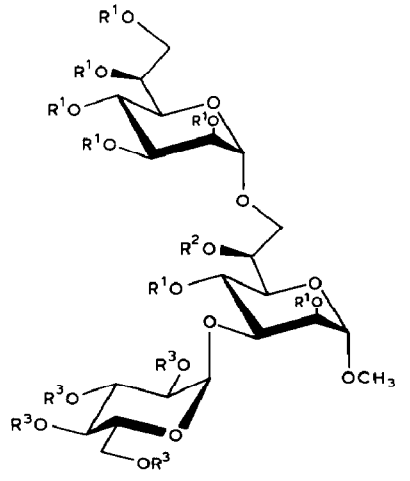
In order to obtain the (1→3)-linked disaccharide derivative, methyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside[3] was treated with **4** in ether in the presence of methyl triflate[15] to yield the α-linked product **11** together with the β anomer. Halide-assisted glycosylation[16] of **4** with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl bromide gave only the α-linked disaccharide derivative **11**, but in a lower yield and after a much longer reaction time. Furthermore, since the two anomers are easy to separate on silica gel, the methyl triflate-catalysed coupling is more advantageous. The $^{13}$C-n.m.r. resonances of the anomeric carbons in the glucopyranosyl moiety of the α- and the β-linked disaccharide derivatives have about the same chemical shift, which was expected considering glycosylation shifts found for aldopyranoses (1→3)-linked to mannopyranoses in unprotected sugars[17], but the $J_{C\text{-}1',H\text{-}1'}$ and $J_{H\text{-}1',H\text{-}2'}$ values identified **11** as the α product.

Desilylation of **11** with aqueous acetic acid gave the 7-hydroxy derivative **12**, Zemplén *O*-deacylation of which followed by hydrogenolysis gave the other disaccharide target compound **13**.

Glycosylation at O-7 of **12**, with **8** in the presence of silver triflate and collidine, gave the trisaccharide derivative **14**. Once again the reaction was rather slow and an excess of collidine gave the orthoester as the main product. Deprotection of **14** as described above for **9** and **12** then gave the title trisaccharide methyl glycoside **15**.



**11** $R^1$ = Ac, $R^2$ = Bz, $R^3$ = $Bu^tMe_2Si$, $R^4$ = Bn
**12** $R^1$ = Ac, $R^2$ = Bz, $R^3$ = H, $R^4$ = Bn
**13** $R^1$ = $R^2$ = $R^3$ = $R^4$ = H



**14** $R^1$ = Ac, $R^2$ = Bz, $R^3$ = Bn
**15** $R^1$ = $R^2$ = $R^3$ = H

EXPERIMENTAL

*General methods.* — Melting points are corrected. Concentrations were performed under reduced pressure. Optical rotations were measured at room temperature with a Perkin–Elmer 241 polarimeter. N.m.r. spectra were recorded on a JEOL GX-270 instrument at 25°, using internal $Me_4Si$ as standard for solutions in $CDCl_3$, and at 70°, using internal acetone ($\delta_C$ 31.0, $\delta_H$ 2.225) for solutions in $D_2O$. All $^1H$ assignments were based on 2D experiments. T.l.c. was performed on Silica Gel $F_{254}$ (Merck) with detection by u.v. light and/or by charring with sulfuric acid. Column chromatography was performed on silica gel (Matrex Silica Si 60A, 35–70$\mu$, Amicon) in the flash mode unless otherwise stated. Molecular sieves (3 or 4 Å, Fluka) were desiccated at 300° overnight. Solvents were dried by distillation from phosphorus pentaoxide (dichloromethane), sodium wire (toluene), or molecular sieves (acetonitrile).

*Methyl 2,3,4-tri-*O*-benzyl-*L-glycero-α-D-manno-*heptopyranoside*[11] (**1**). — A few drops of isopropoxydimethylsilylmethyl chloride were added under dry nitrogen to a stirred suspension of dry magnesium turnings (0.62 g) and dibromomethane (0.10 mL) in tetrahydrofuran (25 mL) that was boiling gently under reflux. When the formation of the Grignard reagent had started, isopropoxydimethylsilylmethyl chloride (4.7 mL) was added dropwise and boiling under reflux was continued until almost all of the magnesium was consumed. The Grignard reagent was cooled to 0° and a solution of dry methyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside[18] [prepared by Swern oxidation[9] of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (6.0 g)] in tetrahydrofuran (25 mL) was added slowly. After 2 h at 0°, no Grignard reagent remained (test with Michler's ketone[19]). The mixture was washed with saturated aqueous $NH_4Cl$ at 0°, diluted with ether, dried ($MgSO_4$), filtered, and concentrated at 0°. Aqueous 30% hydrogen peroxide (11.5 mL) was added immediately to a mixture of the residue in methanol–tetrahydrofuran (1:1, 64 mL) and $NaHCO_3$ (1.0 g). After boiling under refluxing for 15 h, the mixture was cooled, treated with aqueous 10% $NaHSO_3$, and extracted with ether (5 × 40 mL), and the combined extracts were washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (1:1 toluene–ethyl acetate) of the residue gave **1** (3.7 g, 56%), $[\alpha]_D$ +23° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): $^{13}C$, $\delta$ 54.8 ($OCH_3$), 64.9, 69.5, 72.3, 72.4, 73.1, 74.4, 74.7, 75.3, 80.1 (C-2, 3, 4, 5, 6, 7 and 3 Ph$CH_2$), 99.5 (C-1), 126.1–138.4 (aromatic C); $^1H$, $\delta$ 3.60 (H-5), 3.65 (H-7b), 3.77 (H-7a), 3.88 (H-3), 3.98 (H-6), 4.14 (H-4), 6.91 (H-1).

*Anal.* Calc. for $C_{29}H_{34}O_7$: C, 70.5; H, 6.9. Found: C, 70.4; H, 7.2.

*Methyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-7-*O*-(*tert*-butyldimethylsilyl)-*L-glycero-α-D-manno-*heptopyranoside* (**2**). — *tert*-Butyldimethylsilyl chloride (1.3 equiv., 0.17 g) was added to a solution of **1** (0.42 g) in anhydrous pyridine at 0°. The mixture was allowed to attain room temperature and then left overnight. Benzoyl chloride (0.1 mL) and 4-dimethylaminopyridine (a few crystals) were added, and the mixture was stirred for 30 min, diluted with toluene, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (toluene, without pressure) of the residue gave **2** (0.41 g, 67%), $[\alpha]_D$ +28° (*c* 2, chloroform). $^{13}C$-N.m.r. data ($CDCl_3$): $\delta$ −5.4, −5.2

[$Si(CH_3)_2$], 18.2 [$C(CH_3)_3$], 25.8 [$C(CH_3)_3$], 54.7 ($OCH_3$), 59.9, 68.8, 71.6, 72.2, 72.7, 74.0, 74.9, 75.3, 80.7 (C-2, 3, 4, 5, 6, 7 and 3 Ph$CH_2$), 98.8 (C-1), 126.8–138.6 (aromatic C), 166.1 (benzoyl C=O).

*Anal.* Calc. for $C_{42}H_{52}O_8Si$: C, 70.8; H, 7.4. Found: C, 70.5; H, 7.4.

*Methyl 6-O-benzoyl-7-O-(*tert*-butyldimethylsilyl)-*L*-glycero-α-*D*-manno-heptopyranoside* (**3**). — A solution of **2** (0.67 g) in ethyl acetate (20 mL) was hydrogenolysed over 10% Pd–C (0.12 g) at 400 kPa for 24 h, then filtered, and concentrated. Crystallisation of the residue from ether–light petroleum gave **3** (0.34 g, 82%), m.p. 127–128°, $[\alpha]_D$ +23° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): $^{13}C$, δ −5.5, −5.3 [$Si(CH_3)_2$], 18.1 [$C(CH_3)_3$], 25.8 [$C(CH_3)_3$], 54.8 ($OCH_3$), 61.1 (C-7), 66.9 (C-6), 69.9, 70.1, 71.1, 73.0 (C-2, 3, 4, 5), 100.9 (C-1), 128.2–133.2 (aromatic C), 167.5 (C=O); $^1H$, δ 4.63 (1 H, H-1), 5.32 (1 H, H-6).

*Anal.* Calc. for $C_{21}H_{34}O_8Si$: C, 57.0; H, 7.7. Found: C, 56.3; H, 7.7.

*Methyl 2,4-di-O-acetyl-6-O-benzoyl-7-O-(*tert*-butyldimethylsilyl)-*L*-glycero-α-*D*-manno-heptopyranoside* (**4**). — A solution of **3** (0.54 g), trimethyl orthoacetate (0.55 mL), and *p*-toluenesulfonic acid (0.1 mL, 5% in acetonitrile) in dry acetonitrile (50 mL) was stirred at room temperature for 30 min. Pyridine (4 mL), acetic anhydride (4 mL), and 4-dimethylaminopyridine (a few crystals) were added, stirring was continued for 1 h, the solution was diluted with toluene and concentrated, and toluene was evaporated from the residue. Aqueous 90% trifluoroacetic acid (0.30 mL) was added to a solution of the residue in acetonitrile (30 mL) and, after 30 min, the solution was concentrated. Column chromatography (1:1 toluene–ethyl acetate) of the residue gave **4** (0.58 g, 90%), $[\alpha]_D$ +16° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): $^{13}C$, δ −5.4, −5.3 [$Si(CH_3)_2$], 18.1 [$C(CH_3)_3$], 20.8 ($CH_3CO$), 25.8 [$C(CH_3)_3$], 55.3 ($OCH_3$), 59.8, 67.1, 68.8(×2), 70.6, 72.4 (C-2, 3, 4, 5, 6, 7), 98.2 (C-1), 125.3–133.2 (aromatic C), 165.8 (benzoyl C=O), 170.4, 171.3 (acetyl C=O); $^1H$, δ 3.81 (H-7,7), 4.07 (H-3,5), 4.78 (H-1), 4.99 (H-2,4), 5.21 (H-6).

*Anal.* Calc. for $C_{25}H_{38}O_{10}Si$: C, 57.0; H, 7.3. Found: C, 56.5; H, 7.7.

*Methyl 6-O-benzoyl-2,3,4-tri-O-benzyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**5**). — A solution of **2** (166 mg) in aqueous 70% acetic acid (10 mL) was stirred overnight at room temperature, then diluted with toluene, and concentrated, and toluene was evaporated twice from the residue. Column chromatography (3:1 toluene–ethyl acetate) then afforded **5** (96 mg, 69%), $[\alpha]_D$ +47° (*c* 1, chloroform). $^{13}C$-N.m.r. data ($CDCl_3$): δ 54.9 ($OCH_3$), 62.9 (C-7), 71.6, 72.1, 72.6, 72.8, 73.8, 74.8, 75.3, 80.3 (C-2, 3, 4, 5, 6 and 3 Ph$CH_2$), 99.0 (C-1), 127.5–133.1 (aromatic C), 166.8 (benzoyl C=O).

The $^1H$-n.m.r. spectrum showed a downfield signal at δ 5.52 (1 H) corresponding to H-6.

*Anal.* Calc. for $C_{36}H_{38}O_8$: C, 72.2; H, 6.4. Found: C, 72.0; H, 6.4.

*Methyl 2,3,4,6,7-penta-O-acetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**6**). — A solution of **1** (2.0 g) in ethyl acetate–ethanol (1:1, 40 mL) was hydrogenolysed over 10% Pd–C (0.1 g) at 400 kPa for 24 h, then filtered, and concentrated. The residue was treated with acetic anhydride (10 mL), 4-dimethylaminopyridine (a few crystals), and pyridine (20 mL). After 2 h, the mixture was diluted with toluene and concentrated, and toluene

was evaporated twice from the residue. Column chromatography (3:1 toluene–ethyl acetate) then afforded **6** (1.14 g, 67%), $[\alpha]_D$ +22° (*c* 1, chloroform); lit.[11] $[\alpha]_D$ +20° (chloroform). $^{13}$C-N.m.r. data ($CDCl_3$): $\delta$ 20.6, 20.7 ($CH_3CO$), 55.0 ($CH_3O$), 61.8, 64.8, 66.9, 68.3, 69.3, 69.5 (C-2, 3, 4, 5, 6, 7), 99.0 (C-1), 169.6, 169.8, 170.0, 170.2, 170.4 (C=O).

*1,2,3,4,6,7-Hexa*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranose* (**7**). — Conc. sulfuric acid (0.4 mL) was added dropwise with stirring to an ice-cold solution of **6** (0.98 g) in acetic acid–acetic anhydride (30 mL, 1:2). Stirring was continued for 2 h at 0–5°, then for 24 h at room temperature. The solution was diluted with dichloromethane, neutralised with aqueous sodium hydrogencarbonate, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:1 toluene–ethyl acetate) of the residue gave **7** (0.94 g, 90%), m.p. 127–129° (from ether–hexane), $[\alpha]_D$ +27° (*c* 1, chloroform); lit.[10] m.p. 125–127°, $[\alpha]_D$ +27° (chloroform). $^{13}$C-N.m.r. data ($CDCl_3$): $\delta$ 20.6, 20.7, 20.8 ($CH_3CO$), 62.1, 64.3, 66.8, 68.4, 68.9, 70.8 (C-2, 3, 4, 5, 6, 7), 90.6 (C-1), 166.8, 169.4, 169.7, 169.9, 170.2, 170.5 (C=O).

*Methyl 6*-O-*benzoyl-2,3,4-tri*-O-*benzyl-7*-O-*(2,3,4,6,7-penta*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranosyl)*-L-glycero-α-D-manno-*heptopyranoside* (**9**). — A saturated solution of hydrogen bromide in glacial acetic acid (1 mL) was added to a solution of **7** (0.15 g) in glacial acetic acid at +5°. After stirring for 4 h, t.l.c. showed complete conversion into the glycosyl bromide **8**. The solution was diluted with toluene and co-concentrated twice with toluene to give **8**, which was used without further purification.

Silver trifluoromethanesulfonate (0.92 g) in toluene (0.5 mL) was added to a stirred solution of **8**, **5** (0.13 g), and 2,4,6-trimethylpyridine (0.8 equiv., 23 μL) in dichloromethane containing 4 Å molecular sieves. The mixture was stirred at room temperature overnight, then concentrated. Column chromatography (6:1 toluene–ethyl acetate) of the residue gave **9** (0.18 g, 82%), m.p. 80–83° (from ethanol), $[\alpha]_D$ +27° (*c* 1, chloroform). $^{13}$C-N.m.r. data ($CDCl_3$): $\delta$ 20.6, 20.7, 20.8 ($CH_3CO$), 55.0 ($OCH_3$), 61.7, 65.0. 66.9(×2), 68.6, 69.1(×2), 69.3, 69.7, 72.2, 72.9, 73.7, 74.9, 75.3 (C-2, 3, 4, 5, 6, 7, C-2′, 3′, 4′, 5′, 6′, 7′, and 3 Ph$CH_2$), 98.3, 99.1 (C-1, 1′), 125.3–138.6 (aromatic C), 165.8 (benzoyl C=O), 169.5 (×2), 169.6, 170.2, 170.3 (acetyl C=O).

*Anal.* Calc. for $C_{53}H_{60}O_{19}$: C, 63.6; H, 6.0. Found: C, 62.9; H, 6.0.

*Methyl 7*-O-L-glycero-α-D-manno-*heptopyranosyl*-L-glycero-α-D-manno-*heptopyranoside* (**10**). — A solution of **9** (105 mg) in methanol (2 mL) was treated with methanolic M sodium methoxide (0.5 mL). When t.l.c. indicated complete deacylation (2 h), the solution was neutralised with Dowex-50 ($H^+$) resin, filtered, and concentrated. A solution of the residue in ethyl acetate–ethanol (4 mL; 1:1) was hydrogenolysed over 10% Pd–C (50 mg) at 400 kPa for 24 h, then filtered, and concentrated. A solution of the residue in water was washed with ethyl acetate and passed through a column of Bio-Gel P-2 to give **10** (38 mg, 86%), $[\alpha]_D$ +65° (*c* 1, water). N.m.r. data ($D_2O$): $^{13}$C, $\delta$ 55.6 ($OCH_3$), 64.0, 67.0(×2), 68.2, 69.8(×2), 70.7, 70.8, 71.7(×2), 72.2, 72.3, (C-2, 3, 4, 5, 6, 7, 2′, 3′, 4′, 5′, 6′, 7′), 101.4, 101.9, (C-1, 1′); $^1$H, $\delta$ 4.77 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.92 (d, 1 H, $J_{1',2'}$ 1.5 Hz, H-1′).

*Anal.* Calc. for $C_{15}H_{26}O_{13}\cdot 1.5\ H_2O$: C, 40.7; H, 6.6. Found: C, 40.5; H, 6.6.

*Methyl 2,4-di-O-acetyl-6-O-benzoyl-7-O-*(tert-*butyldimethylsilyl)-3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-*L-glycero-α-D-manno-*heptopyranoside* (**11**). — Methyl triflate (0.30 mL) was added to a stirred mixture of **4** (0.19 g) and methyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside[3] (0.31 g) in ether containing 4 Å molecular sieves. After 1 h, triethylamine (1 mL) was added, stirring was continued for 30 min, and the mixture was diluted with dichloromethane, filtered, and concentrated. Column chromatography (19:1 toluene–ethyl acetate, first flash and then without pressure) of the residue gave **11** (0.27 g, 70%), $[\alpha]_D$ +23° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): $^{13}C$, δ −5.4, −5.3 [$Si(CH_3)_2$], 18.1 [$C(CH_3)_3$], 20.5, 21.1 ($CH_3CO$), 25.8 [$C(CH_3)_3$], 55.3 ($OCH_3$) 59.3 (C-7), 65.6, 67.3, 68.1, 70.6, 71.6(×2), 73.5, 74.9, 75.5, 76.5, 77.4, 80.0, 81.4 (C-2, 3, 4, 5, 6, C-2′, 3′, 4′, 5′, 6′, and 4 Ph$CH_2$, one overlap), 98.0 $J_{C\text{-}1,H\text{-}1}$ 174 Hz, C-1), 99.9 ($J_{C\text{-}1',H\text{-}1'}$ 167 Hz, C-1′), 127.5–138.8 (aromatic C), 165.8 (benzoyl C=O), 169.4, 170.3 (acetyl C=O); $^1H$, δ 3.43 (H-2′), 3.50 (H-6′), 3.60 (H-4′), 3.66 (H-5′), 3.86 (H-7), 3.87 (H-3′), 4.05 (H-3), 4.17 (H-5), 4.85 (H-1), 4.89 (H-1′), 5.07 (H-6), 5.18 (H-2), 5.42 (H-4).

Eluted second was the β anomer (32 mg, 10%). $^{13}C$-N.m.r. data: 98.2 ($J_{C\text{-}1',H\text{-}1'}$ 172 Hz, C-1), 100.0 ($J_{C\text{-}1',H\text{-}1'}$ 160 Hz, C-1′).

*Methyl 2,4-di-O-acetyl-6-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-*L-glycero-α-D-manno-*heptopyranoside* (**12**). — A mixture of **11** (166 mg) and aqueous 70% acetic acid (50 mL) was stirred for 36 h at room temperature, then diluted with toluene, and concentrated, and toluene was evaporated twice from the residue. Column chromatography (3:1 toluene–ethyl acetate) then afforded **12** (136 mg, 92%), $[\alpha]_D$ +23° (*c* 1, chloroform). $^{13}C$-N.m.r. data ($CDCl_3$): δ 20.5, 21.1 ($CH_3CO$), 55.5 ($OCH_3$), 62.0, 65.7, 68.1, 69.5, 71.5, 71.6, 71.8, 73.4, 73.5, 75.0, 75.6, 77.4(×2), 80.0, 81.4 (C-2, 3, 4, 5, 6, 7, C-2′, 3′, 4′, 5′, 6′, and 4 Ph$CH_2$), 98.1 (C-1), 100.0 (C-1′), 127.5–138.8 (aromatic C), 166.7 (benzoyl C=O), 169.4, 170.3 (acetyl C=O).

*Anal.* Calc. for $C_{53}H_{58}O_{16}$: C, 66.9; H, 6.2. Found: C, 66.5; H, 6.1.

*Methyl 3-O-α-D-glucopyranosyl-*L-glycero-α-D-manno-*heptopyranoside* (**13**). — Compound **12** (55 mg) was deprotected, as described for **9**, to give **13** (19 mg, 82%), $[\alpha]_D$ +98° (*c* 1, water). N.m.r. data ($D_2O$): $^{13}C$, δ 55.5 ($OCH_3$), 61.6, 63.8, 66.3, 69.7, 70.6(×2), 72.2, 72.6, 73.2, 73.8 (C-2, 4, 5, 6, 7 and C-2′, 3′, 4′, 5′, 6′), 79.8 (C-3), 101.2, 101.7 (C-1, 1′); $^1H$, δ 4.75 (H-1), 5.24 (d, $J_{1',2'}$ 4.0 Hz, H-1′).

*Anal.* Calc. for $C_{14}H_{26}O_{13}$: C, 41.8; H, 6.5. Found: C, 41.9; H, 6.7.

*Methyl 2,4-di-O-acetyl-6-O-benzoyl-7-O-(2,3,4,6,7-penta-O-acetyl-*L-glycero-α-D-manno-*heptopyranosyl)-3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-*L-glycero-α-D-manno-*heptopyranoside* (**14**). — A solution of silver trifluoromethanesulfonate (41 mg) in toluene (2 mL) was added to a stirred mixture of **8** [prepared as described above from **7** (75 mg)], **12** (85 mg), and 2,4,6-trimethylpyridine (0.5 equiv., 6 μL) in dichloromethane containing 4 Å molecular sieves. The mixture was stirred at room temperature overnight, then concentrated. Column chromatography (3:1 toluene–ethyl acetate) of the residue gave **14** (84 mg, 70%), $[\alpha]_D$ +22° (*c* 0.8 chloroform). $^{13}C$-N.m.r. data ($CDCl_3$): δ 20.6, 20.9, 21.1 ($CH_3CO$), 55.6 ($OCH_3$), 62.0, 64.2, 64.8, 65.3, 66.9, 67.9, 68.1, 68.4, 68.9, 69.0, 69.2, 71.4, 71.6, 73.3, 73.5, 74.9, 75.5, 77.4(×2), 79.9, 81.4

(C-2,3,4,5,6,7, C-2′,3′,4′,5′,6′, C-2″,3″,4″,5″,6″,7″, and 4 $PhCH_2$), 98.1, 98.3 (C-1,1″), 100.0 (C-1′), 127.5–138.8 (aromatic C), 165.6 (benzoyl C=O), 169.5, 169.6, 169.8, 169.9, 170.3(×2), 170.4 (acetyl C=O).

*Anal.* Calc. for $C_{70}H_{80}O_{26}$: C, 62.9; H, 6.0. Found: C, 62.9; H, 6.2.

*Methyl 3-O-(α-D-glucopyranosyl)-7-O-(L-glycero-α-D-manno-heptopyranosyl)-L-glycero-α-D-manno-heptopyranoside* (**15**). — Compound **14** (75 mg) was deprotected, as described for **9**, to give **15** (23 mg, 70%), $[\alpha]_D$ +94° (*c* 0.5, water). N.m.r. data ($D_2O$): $^{13}C$, $\delta$ 55.6 ($OCH_3$), 61.6, 64.0, 66.3, 67.0, 68.1, 69.8(×2), 70.6, 70.8, 71.7, 72.4(×2), 72.6, 73.2(×2), 73.8 (C-2,4,5,6,7, C-2′,3′,4′,5′,6′, and C-2″,3″,4″,5″,6″,7″), 79.8 (C-3), 101.3, 101.5, 101.8 (C-1,1′,1″, $J_{C\text{-}1,H\text{-}1} = J_{C\text{-}1',H\text{-}1'} = J_{C\text{-}1'',H\text{-}1''}$ = 172 Hz); $^1H$, $\delta$ 4.75 (H-1), 4.92 (H-1″), 5.24 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1′).

*Anal.* Calc. for $C_{21}H_{37}O_{18}\cdot H_2O$: C, 42.4; H, 6.6. Found: C, 42.4; H, 6.5.

Sugar[20] and methylation[21,22] analysis ($NaBD_4$) showed the correct L-*glycero*-D-*manno* configuration and the expected substitution pattern.

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