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Synthesis of L-*glycero*-D-*manno*-heptopyranose-containing oligosaccharide structures found in lipopolysaccharides from *Haemophilus influenzae*

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Abstract

Syntheses are described of the tetrasaccharide 2-(4-trifluoroacetamidophenyl)ethyl *O*-(β-D-galactopyranosyl)-(1 → 2)-*O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1 → 2)-*O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1 → 3)-L-*glycero*-α-D-*manno*-heptopyranoside (**20**) and the three trisaccharides 2-(4-trifluoroacetamidophenyl)ethyl *O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1 → 2)-*O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1 → 3)-L-*glycero*-α-D-*manno*-heptopyranoside (**17**), 2-(4-trifluoroacetamidophenyl)ethyl *O*-(β-D-glucopyranosyl)-(1 → 4)-*O*-(β-D-glucopyranosyl)-(1 → 4)-L-*glycero*-α-D-*manno*-heptopyranoside (**5**), and 2-(4-trifluoroacetamidophenyl)ethyl *O*-(β-D-galactopyranosyl)-(1 → 4)-*O*-(β-D-glucopyranosyl)-(1 → 4)-L-*glycero*-α-D-*manno*-heptopyranoside (**8**), corresponding to structures found in the lipooligosaccharides of *Haemophilus influenzae*. © 1997 Elsevier Science Ltd.

Keywords: Carbohydrates; Oligosaccharide synthesis; Bacterial antigens; Lipopolysaccharide; Heptopyranose

1. Introduction

The major virulence factor in *H. influenzae* infections is normally a capsular polysaccharide. However, it has been found that bacterial outer-membrane components modulate the pathogenicity [1], and that non-capsulated bacteria also give not severe but frequent respiratory infections. The lipopolysaccharide of *H. influenzae* lacks the O-antigen with its repeating units and is a lipooligosaccharide (LOS), which consists of hexoses (mainly D-glucose and D-galactose), L-*glycero*-D-*manno*-heptose, and Kdo linked to a lipid A moiety. Due to the lack of repeating units and also to a severe micro-heterogeneity especially in the hexose parts, structural elucidation of the LOS has been troublesome. Gene manipulation and better separation and spectrometric techniques have made analysis possible; suggested structures have recently been published (Fig. 1) [2–6].

In this paper, syntheses of a number of parts of the suggested structures are described. As a primary synthetic target, the triheptoside backbone **17** (Scheme 3) was chosen. Elongation of this at the non-reducing

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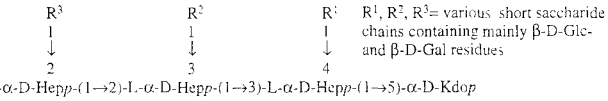


Fig. 1. Generalised structure of the dephosphorylated LOS of *H. influenzae* without the lipid A moiety.

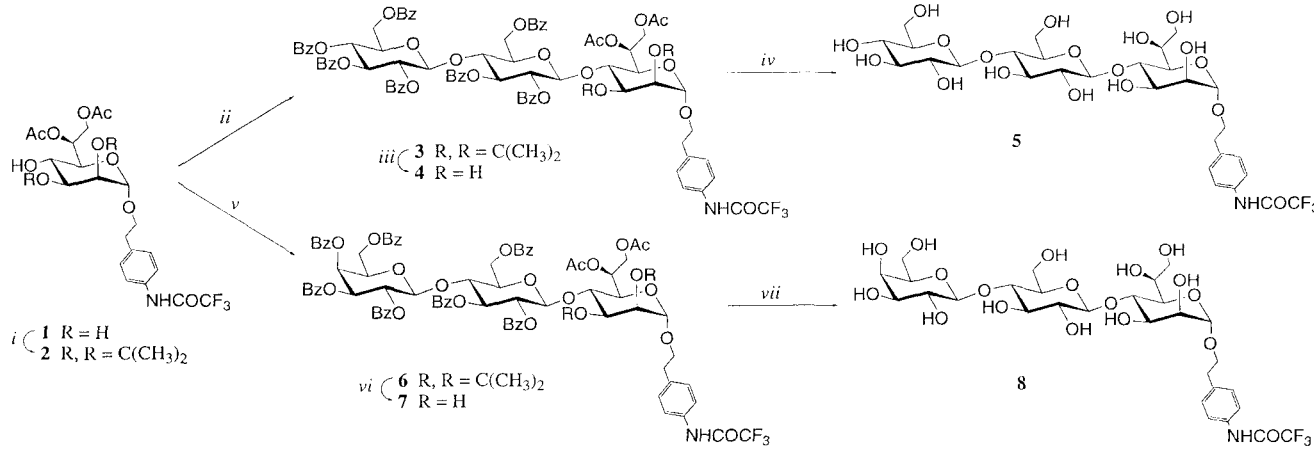
end with a β-D-galactopyranosyl residue to give the linear tetrasaccharide **20** (Scheme 3) was also performed, as well as syntheses of derivatives **5** and **8** with cellobiose or lactose β-linked to the 4-position of a heptose moiety (Scheme 1), all structures found in the LOS of *Haemophilus influenzae*. The synthetic oligosaccharides will be used as model compounds to verify and simplify structural studies, and in the production and characterisation of monoclonal antibodies. All oligosaccharides were synthesised as spacer glycosides using 2-(4-trifluoroacetamidophenyl)ethanol as linking arm to enable the formation of glycoconjugates to be used in various biological experiments.

2. Results and discussion

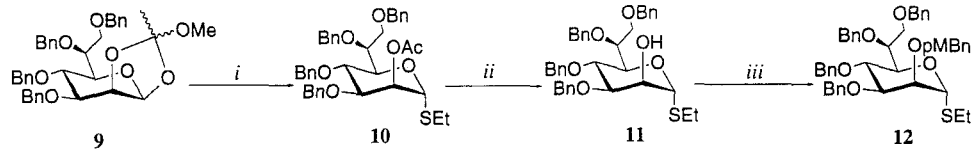
From our earlier syntheses of heptose-containing oligosaccharides corresponding to structures found in the *Salmonella* Ra core [7–9], two precursors suitable for the present synthesis, the spacer heptopyranoside derivatives **1** and **13** (Schemes 1 and 3), were available. However, since (1 → 2)- and (1 → 4)-substituted heptose residues are absent in the *Salmonella* structure, new protecting group schemes had to be elaborated for the *Haemophilus* cell wall structures.

Treatment of **1** [8] with neat dimethoxypropane in the presence of *p*-toluenesulfonic acid gave the 2,3-*O*-isopropylidene derivative **2**, with a free 4-hydroxyl group, in almost quantitative yield (96%) (Scheme 1). Glycosylation of this position with either hepta-*O*-benzoyl-α-cellobiosyl bromide or hepta-*O*-benzoyl-α-lactosyl bromide using silver trifluoromethanesulfonate (silver triflate) [10] as promoter yielded the β-(1 → 4)-linked trisaccharides **3** (80%) and **6** (81%), respectively. A similar derivative with lactose β-linked to the 4-position of a heptopyranoside has been synthesised previously by van Boom et al. [11]. Removal of the isopropylidene acetal by aqueous acetic acid gave derivatives **4** (84%) and **7** (75%), which were initially designed to allow synthesis of branched 3,4-linked *Haemophilus* structures. However, all couplings using, i.a., **4** or its 2-*O*-acetyl or 2-*O*-benzyl analogue as acceptor together with various heptosyl donors and promoters failed and these branched structures seem to have to be constructed *via* an alternative pathway. Deacylation of **4** and **7**, using sodium methoxide in MeOH, produced the first two target compounds **5** (98%) and **8** (86%), respectively.

To construct the triheptoside backbone **17**, a heptosyl donor with a temporary 2-*O*-protecting group allowing later elongation at this position was needed. Therefore, attempts were made to synthesise the ethyl 1,2-thioorthoacetate from the known 2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranosyl bromide [12] by treatment with ethyl mercaptan and collidine [13]. Exchange of the acetyl groups with benzyl groups followed by rearrangement of the thioorthoester would give compound **10** (Scheme 2), which could be processed to give the desired thioglycoside donor. The formation of the thioorthoester, however, proved difficult. With ethyl mercaptan, almost no orthoester was formed. The addition of small



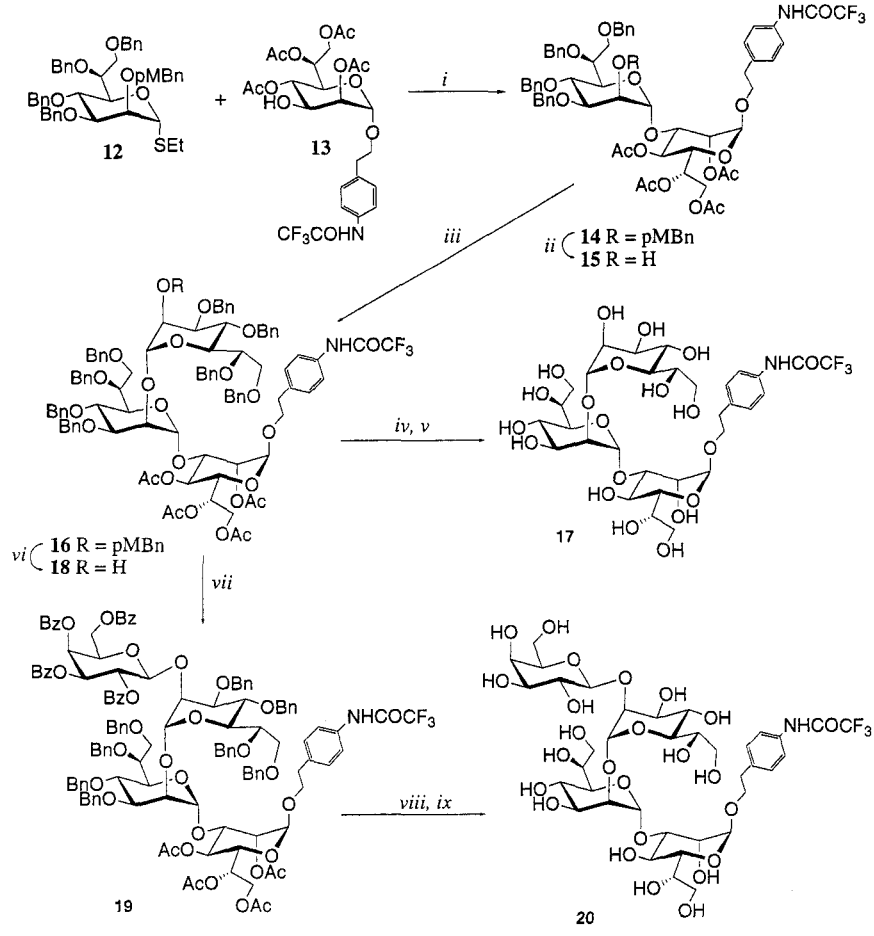
Scheme 1. (*i*) $Me_2C(OMe)_2$, *p*-TsOH, (*ii*) hepta-*O*-benzoyl-cellobiosyl bromide, AgOTf, (*iii*) aq AcOH, (*iv*) MeO^-, MeOH, (*v*) hepta-*O*-benzoyl-lactosyl bromide, AgOTf, (*vi*) aq AcOH, (*vii*) MeO^-, MeOH.



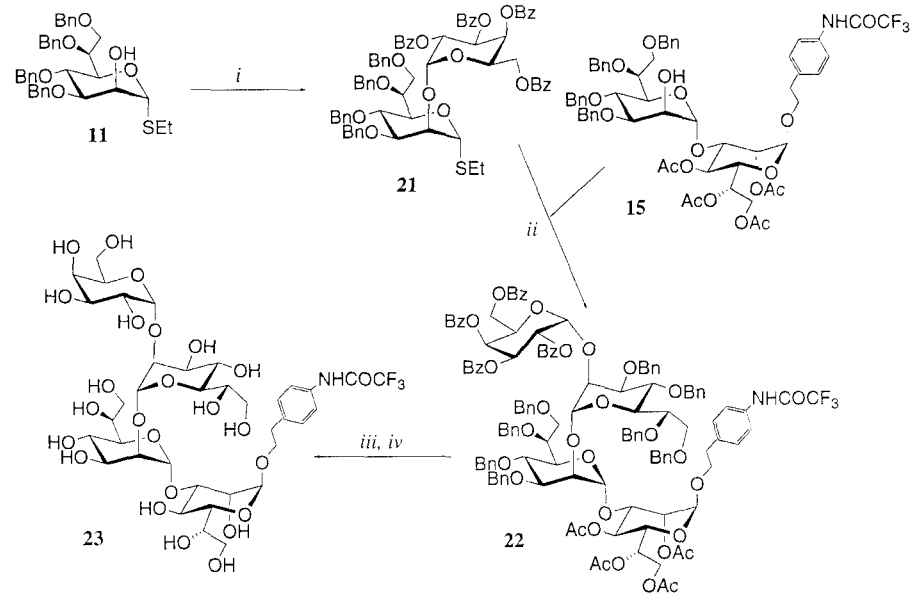
Scheme 2. (*i*) EtSH, TMSOTf, CH_2Cl_2, (*ii*) NaOMe, MeOH, (*iii*) *p*-MBnBr, NaH, DMF.

amounts of methanol, on the other hand, produced the methyl orthoester smoothly, although the mercaptan was present in large amounts. Therefore, the known methyl orthoester **9** [12] was chosen as precursor and was rearranged in the presence of a large excess of ethyl mercaptan, with trimethylsilyl trifluoromethanesulfonate, to give the 2-*O*-acetyl thioglycoside **10** in 76% yield (Scheme 2). Since acetyl groups were present in the acceptor molecule, the 2-*O*-acetyl group in **10** was changed into an orthogonal *p*-methoxybenzyl protecting group via deacetylation (→ **11**, 90%) and *p*-methoxybenzylation to give the desired glycosyl donor **12** (99%).

Coupling of donor **12** with acceptor **13** [9] using dimethyl(methylthio)sulfonium triflate (DMTST) [14] as promoter gave the α-(1 → 3)-linked disaccharide **14** (89%), which, after removal of the *p*-methoxybenzyl group with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (→ **15**, 84%), could again be used as acceptor in a similar coupling with, once more, **12** as donor and DMTST as promoter to form the protected triheptoside backbone **16** (89%) of the *Haemophilus* LOS (Scheme 3). In both these couplings, the *manno*-configuration of the heptose donor as earlier observed [8,9] ensured the exclusive formation of an α-*trans*-glycosidic linkage, although a



Scheme 3. (*i*) DMTST, CH_2Cl_2, (*ii*) DDQ, CH_2Cl_2, H_2O, (*iii*) **12**, DMTST, CH_2Cl_2, (*iv*) H_2, Pd/C, (*v*) NaOMe, MeOH, (*vi*) DDQ, CH_2Cl_2, H_2O, (*vii*) tetra-*O*-benzoyl-D-galactopyranosyl bromide, AgTf, CH_2Cl_2, (*viii*) H_2, Pd/C, (*ix*) NaOMe, MeOH.



Scheme 4. (*i*) Tetra-*O*-benzoyl-D-galactopyranosyl bromide, AgOTF, CH_2Cl_2 ii) DMTST, CH_2Cl_2, (*iii*) NaOMe, MeOH, (*iv*) H_2, Pd/C.

non-participating group was used at O-2 of the donor. Deprotection of derivative **16** through catalytic hydrogenolysis, followed by Zemplén deacylation, gave the target trisaccharide **17** (94%).

Synthesis of the tetrasaccharide **20**, elongated with a β-galactosyl residue at the 2″-position of **17**, was originally planned to be accomplished through a convergent approach using disaccharide **15** as acceptor and a disaccharide donor constructed by the coupling of thioglycoside **11** with an acylated galactosyl donor. However, when the formation of this disaccharide donor was tried, using tetra-*O*-benzoyl-α-D-galactopyranosyl bromide as donor in a silver triflate-promoted coupling, a 67% yield of the pure α-linked disaccharide **21** was obtained (Scheme 4). Although acylated galactosyl donors, in spite of the presence of a 2-*O*-participating group, are known sometimes to give partly the α-*cis*-linkage (see e.g. [15–17]), this exclusive formation of the α-product in good yield was not expected, especially not since benzoyl groups, considered to be the preferred participating group in silver triflate promoted reactions, were used [18]. Attempts to form the β-linked disaccharide donor using other galactosyl donors, promoters, and solvents were severely hampered by the high reactivity of the thioglycoside acceptor **11**, causing i.a. transglycosylation [19,20] and decomposition of the acceptor and low yields in the various couplings [21]. Since this problem would be avoided with the use of an *O*-glycoside acceptor and since trisaccharide **16** was already in our hands, the block synthesis approach was abandoned and the *p*-methoxybenzyl group was removed from compound **16** by DDQ-treatment to give the suitable trisaccharide acceptor **18** (Scheme 3). Now with this acceptor, using exactly the same coupling conditions as earlier with acceptor **11**, i.e. tetra-O-benzoyl-α-D-galactopyranosyl bromide as donor and silver triflate as promoter, a 74% yield (86% counted on consumed aglycone) of the exclusively β-linked tetrasaccharide **19** was obtained. An investigation of the causes behind this extraordinary difference in the stereochemical outcome of the two couplings, using either acceptor **11** or **18**, is presently under way. Deprotection of **19** gave the target compound **20** (82%), a native part of the *Haemophilus* LOS.

In a DMTST-promoted glycosylation, the α-linked disaccharide donor **21** was coupled to acceptor **15** to give the tetrasaccharide **22** (73%), which after deprotection afforded the unnatural tetrasaccharide analogue **23** (69%) (Scheme 4).

3. Experimental

General methods.—These were as described [7]. NMR spectra in D_2O were recorded at 25 °C (unless otherwise stated) using acetone ($\delta = 31.0$, ^{13}C) or sodium [$^2H_4$]-3-trimethylsilyl-propanoate (TSP) ($\delta = 0.00$, ^1H) as references.

*2-(4-Trifluoroacetamidophenyl)ethyl 6,7-di-O-acetyl-2,3-O-isopropylidene-*L*-glycero-α-*D*-manno-heptopyranoside* (**2**).—A mixture of 2-(4-trifluoroacet-amidophenyl)ethyl 6,7-di-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranoside (**1**) [8] (817 mg, 1.60 mmol), *p*-toluenesulfonic acid (25 mg, 0.145 mmol), and 2,2-dimethoxypropane (10 mL) was stirred at room temperature for 25 min, then diluted with CH_2Cl_2, washed with $NaHCO_3$ (aq, satd) and water, dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (1.6% → 8% MeOH–$CHCl_3$) followed by recrystallisation from EtOAc–light petroleum ether (bp 40–60 °C) gave **2** (847 mg, 1.54 mmol, 96%); mp 174 °C; $[\alpha]_D$ −9.2° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$ with about 10% CD_3OD): δ 20.7, 20.8 (*Me*CO), 26.3, 28.1 (Me_2CO_2), 35.6 (CH_2CH_2Ph), 63.2, 68.1, 68.6, 68.8, 69.1, 75.7, 78.5 (C-2-7, CH_2CH_2O), 97.5 (C-1), 109.8 (Me_2CO_2), 121.4, 129.7, 134.8, 136.6 (aromatic C), 171.8, 171.4 (Me*C*O). Anal. Calcd for $C_{24}H_{30}O_{10}NF_3$: C, 52.5; H, 5.5. Found: C, 52.5; H, 5.5.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranosyl)-(1 → 4)-6,7-di-*O*-acetyl-2,3-*O*-isopropylidene-*L*-glycero-α-*D*-manno-heptopyranoside* (**3**).—2,3,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-cellobiosyl bromide (311 mg, 0.274 mmol) and **2** (75 mg, 0.136 mmol) were dissolved in CH_2Cl_2 (10 mL) under argon. *Sym*-collidine (29 μL, 0.219 mmol) and powdered molecular sieves (4 Å) were added and the mixture was stirred at 0 °C for 20 min, whereafter a solution of silver trifluoromethanesulfonate (71 mg) in dry toluene was added. After 15 min, the reaction was quenched with triethylamine (0.5 mL). The reaction mixture was centrifuged and the supernatant concentrated in vacuo. Silica gel column purification (7 → 33% EtOAc–toluene) of the residue gave unreacted **2** (9 mg, 12%) and **3** (174 mg, 0.109 mmol, 80%); $[\alpha]_D$ +31.1° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.3, 20.4 (*Me*CO), 25.9, 27.9 (Me_2CO_2), 35.2 (CH_2CH_2Ph), 61.9, 62.5, 66.4, 68.0, 68.3, 69.3, 72.0, 72.2, 72.3, 72.9, 73.2, 74.6, 76.6, 76.8, (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 96.8 (C-1), 100.4, 101.2 (C-1′,1″), 109.2 (Me_2CO_2), 121.2–137.0 (aromatic C), 155.0 (CF_3CO), 164.8, 165.0, 165.3, 165.4, 165.6, 165.8 ($PhCO_2$), 171.8, 171.4 (Me*C*O). Anal. Calcd for $C_{85}H_{78}O_{27}NF_3$: C, 63.7; H, 4.9. Found: C, 63.5; H, 4.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranosyl)-(1 → 4)-6,7-di-*O*-acetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**4**).—Compound **3** (89 mg, 55 μmol) in aq AcOH (70%, 5 mL) was heated to 50–55 °C and stirred overnight. The mixture was concentrated and coevaporated twice with dry toluene. The residue was purified on a silica gel column (10 → 60% EtOAc–toluene) to yield **4** (73 mg, 47 μmol, 84%); $[\alpha]_D$ +48.5° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.3, 21.0 (*Me*CO), 35.1 (CH_2CH_2Ph), 61.7, 62.1, 62.5, 67.3, 67.5, 68.1, 69.2, 69.3, 71.9, 72.0, 72.4, 72.5, 72.8, 73.4, 76.5, 78.8 (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 97.9 (C-1), 100.6, 101.1 (C-1′,1″), 121.8–137.4 (aromatic carbons), 155.1 (CF_3CO), 164.7, 165.0, 165.0, 165.6, 165.7, 165.8, 165.9 ($PhCO_2$), 169.8, 170.4 (Me*C*O). Anal. Calcd for $C_{82}H_{74}O_{27}NF_3$: C, 63.0; H, 4.8. Found: C, 62.8; H, 4.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(β-*D*-glucopyranosyl)-(1 → 4)-*O*-(β-*D*-glucopyranosyl)-(1 → 4)-*L*-glycero-α-*D*-manno-heptopyranoside* (**5**).—1 M sodium methoxide in MeOH (0.4 mL) was added to a soln of **4** (125 mg, 80 μmol) in MeOH (5 mL), and the soln was stirred at room temperature for 5 h. The mixture was neutralised by the addition of Dowex H^+ ion exchange resin, decanted, concentrated, dissolved in water (6 mL, containing 1% *n*-BuOH), and washed once with diethyl ether (4 mL). Purification by gel permeation chromatography (Sephadex G-50 column, eluent H_2O containing 1% *n*-BuOH) followed by lyophilisation gave **5** (59 mg, 79 μmol, 98%); $[\alpha]_D$ +20.3° (*c* 1.0 H_2O); ^{13}C NMR (D_2O): δ 35.3 (CH_2CH_2Ph), 60.7, 61.3, 63.8, 68.7, 68.9, 70.2, 70.4, 70.8, 73.7, 73.9, 74.9, 75.6, 76.2, 76.8, 76.8, 79.2 (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 99.9 ($J_{C\text{-}1,H\text{-}1}$ 172 Hz, C-1), 103.2 ($J_{C\text{-}1,H\text{-}1}$ 163 Hz), 103.3 ($J_{C\text{-}1,H\text{-}1}$ 163 Hz) (C-1′,1″), 123.0, 130.7, 134.0, 138.8 (aromatic C); ^1H NMR (D_2O, assorted peaks): δ 4.59 ($J_{1,2}$ 7.7 Hz), 4.61 ($J_{1,2}$ 8.1 Hz) (H-1′,1″), 4.89 ($J_{1,2}$ 2 Hz, H-1). Anal. Calcd for $C_{29}H_{42}O_{18}NF_3 \cdot 2H_2O$: C, 44.3; H, 5.9. Found: C, 43.8; H, 5.3.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranosyl)-(1 → 4)-6,7-di-*O*-acetyl-2,3-*O*-isopropylidene-*L*-glycero-α-*D*-manno-heptopyranoside* (**6**).—2,3,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-lactosyl bromide (310 mg, 0.273 mmol) and **2** (75 mg, 0.136 mmol) were coupled as described for hepta-*O*-benzoyl-cellobiosyl bromide and **2** above, to give **6** (178 mg, 0.111 mmol, 81%); $[\alpha]_D$ +51.2° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.4 (*Me*CO), 26.0, 27.9 (Me_2CO_2), 35.2 (CH_2CH_2Ph), 60.9, 61.8, 62.6, 66.5, 67.5, 68.1, 68.4, 70.0, 71.4, 71.8, 72.1, 73.2, 73.3, 74.6, 76.3 (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 96.9 (C-1), 100.6, 101.2 (C-1′,1″), 109.2

(Me_2CO_2), 121.3–137.0 (aromatic C), 155.0 (CF_3CO), 164.9, 165.3, 165.3, 165,4, 165.5, 165.6, 165.9 ($PhCO_2$), 169.7, 170.0 (MeCO). Anal. Calcd for $C_{85}H_{78}O_{27}NF_3$: C, 63.7; H, 4.9. Found: C, 62.7; H, 4.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri-O-benzoyl-β-D-glucopyranosyl)-(1 → 4)-6,7-di-O-acetyl*-L-glycero-α-D-manno-*heptopyranoside* (**7**).—Compound **6** (107 mg, 67 μmol) was dissolved in a small amount of MeCN and concentrated. The residue was treated with 70% HOAc (5 mL) and stirred for 30 h at 40 °C, then concentrated and coevaporated twice with toluene. Purification on a silica gel column (10 → 60% EtOAc–toluene) gave 78 mg (50 μmol, 75%) of **7**; $[\alpha]_D$ +56.2° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.3, 21.0 (*Me*CO), 35.1 (CH_2CH_2Ph), 60.7, 61.7, 62.0, 67.3, 67.5, 68.0, 69.2, 69.3, 69.9, 71.4, 71.7, 71.8, 72.6, 73.4, 76.0, 78.8 (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 98.0 (C-1), 100.7, 101.2 (C-1′,1″), 121.7–137.3 (aromatic C), 155.1 (CF_3CO), 164.7, 165.0, 165.2, 165.4, 165.5, 165.8 (PhCO), 169.8, 170.4 (MeCO). Anal. Calcd for $C_{82}H_{74}O_{27}NF_3$: C, 63.0; H, 4.8. Found: C, 63.1; H, 5.0.

2-(4-Trifluoroacetamidophenyl)ethyl O-β-D-*galactopyranosyl-(1 → 4)*-O-β-D-*glucopyranosyl-(1 → 4)*-L-glycero-α-D-manno-*heptopyranoside* (**8**).—Using the same protocol as for **4** above, Zemplén deacylation of **7** (114 mg, 73 μmol) gave 47 mg (63 μmol, 86%) of **8**; $[\alpha]_D$ +32.3° (*c* 1.0, H_2O); ^{13}C NMR (D_2O): δ 35.3 (CH_2CH_2Ph), 60.8, 61.8, 63.8, 68.7, 68.9, 69.3, 70.2, 70.4, 70.8, 71.7, 73.3, 73.7, 75.0, 75.6, 76.1, 76.9, 79.0 (C-2-7, C-2′-6′, C-2″-6″, CH_2CH_2O), 99.9 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz, C-1), 103.3 ($J_{C\text{-}1,H\text{-}1}$ 161 Hz), 103.7 ($J_{C\text{-}1,H\text{-}1}$ 163 Hz) (C-1′,1″), 122.9, 130.6, 133.9, 138.7 (aromatic C); ^1H NMR (D_2O, assorted peaks): δ 4.53 ($J_{1,2}$ 7.7 Hz), 4.62 ($J_{1,2}$ 8.1 Hz) (H-1′,1″), 4.90 ($J_{1,2}$ 2 Hz, H-1). Anal. Calcd for $C_{29}H_{42}O_{18}NF_3 \cdot 2H_2O$: C, 44.3; H, 5.9. Found: C, 43.5; H, 5.3.

Ethyl 2-O-acetyl-3,4,6,7-tetra-O-benzyl-1-thio-L-glycero-α-D-manno-*heptopyranoside* (**10**).—A mixture of 1,2-*O*-(1-methoxy)-ethylidene-3,4,6,7-tetra-*O*-benzyl-L-*glycero*-β-D-*manno*-heptopyranose [11] (**9** (*R*)- and (*S*)-stereoisomers, 593 mg, 0.946 mmol) and ethanethiol (2.8 mL, 37.8 mmol) in nitromethane (15 mL) containing powdered molecular sieves (4 Å),was cooled to 0 °C under an argon atmosphere. After stirring for 1 h, trimethylsilyl trifluoromethanesulfonate (36 μL, 0.186 mmol) was added and stirring was continued for an additional 1.5 h. The mixture was then concentrated, diluted with diethyl ether, and filtered through Celite. The filtrate was washed with $NaHCO_3$ (aq, satd) and water, dried (Na_2SO_4) and concentrated. Purification by silica gel column chromatography (4:1 light petroleum bp 40–60 °C–EtOAc) gave **10** (474 mg, 0.721 mmol, 76%); $[\alpha]_D$ +58.8° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 14.6 (*Me*CH_2S), 21.2 (*Me*CO), 25.2 (MeCH_2S), 70.3, 70.6, 71.7, 72.0, 73.1, 73.5, 74.0, 74.7, 75.1, 79.0 (C-2-7, PhCH_2O), 82.3 (C-1), 127.5–138.6 (aromatic C), 170.4 (MeCO). Anal. Calcd for $C_{39}H_{44}O_7S$: C, 71.3; H, 6.8. Found: C, 71.3; H, 6.8.

Ethyl 3,4,6,7-tetra-O-*benzyl-1-thio*-L-glycero-α-D-manno-*heptopyranoside* (**11**).—To a solution of **10** (474 mg, 0.721 mmol) in MeOH (5 mL) was added 10 drops of 1 M NaOMe in MeOH. After stirring at room temperature for 1.5 h, Dowex H^+ ion exchange resin was added, and the mixture was stirred for an additional 10 min. The solution was decanted, concentrated, and subjected to silica gel column chromatography (2:1 light petroleum bp 40–60 °C–EtOAc) yielding **11** (401 mg, 0.652 mmol, 90%); $[\alpha]_D$ +111.8° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 14.6 (*Me*CH_2S), 24.7 (MeCH_2S), 69.6, 70.6, 71.6, 71.7, 72.8, 73.4, 73.9, 74.6, 75.0, 80.9 (C-2-7, PhCH_2O), 83.6 (C-1), 127.5–138.6 (aromatic C). Anal. Calcd for $C_{37}H_{42}O_6S$: C, 72.3; H, 6.9. Found: C, 72.3; H, 6.9.

Ethyl 3,4,6,7-tetra-O-*benzyl-2*-O-p-*methoxybenzyl-1-thio*-L-glycero-α-D-manno-*heptopyranoside* (**12**).—Sodium hydride (78 mg, 55–65% dispersed in oil, 1.8–2.1 mmol) was washed with light petroleum, then slurried in a small portion of dry DMF and transferred to a stirred solution of **11** (401 mg, 0.652 mmol) in dry DMF (5 mL) at 0 °C. Freshly distilled *p*-methoxybenzyl bromide (182 μL, 1.3 mmol) in 1.5 mL DMF was added dropwise to the mixture during 5 min. After 80 min the reaction was quenched by adding MeOH (0.5 mL) carefully. The mixture was diluted with toluene, washed three times with water and concentrated. Purification by silica gel chromatography (4 → 30% EtOAc–light petroleum bp 40–60 °C) yielded 476 mg (0.648 mmol, 99%) of **12**; $[\alpha]_D$ +48.0° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 14.7 (*Me*CH_2S), 25.0 (MeCH_2S), 55.3 (PhO*Me*), 70.8, 71.3, 71.8, 72.1, 72.9, 73.4, 74.4, 74.6, 75.2, 75.4, 80.7 (C-2-7, PhCH_2O), 81.7 (C-1), 113.7, 127.4–138.8, 159.2 (aromatic C). Anal. Calcd for $C_{45}H_{50}O_7S$: C, 73.5; H, 6.9. Found: C, 73.0; H, 6.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(3,4,6,7-tetra*-O-*benzyl-2*-O-p-*methoxybenzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)-2,4,6,7-tetra*-O-*acetyl-*

L-glycero-α-D-manno-*heptopyranoside* (**14**).—2-(4-Trifluoroacetamidophenyl)ethyl 2,4,6,7-tetra-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranoside (**13**) [9] (180 mg, 0.303 mmol) and **12** (305 mg, 0.415 mmol) were dissolved in dry diethyl ether (10 mL). Powdered molecular sieves (4 Å) were added and the mixture was stirred under argon for 1 h. The mixture was cooled to 0 °C and dimethyl(methylthio)sulfonium triflate (DMTST) (243 mg, 0.941 mmol) was added. After 10 min, the mixture was allowed to attain room temperature and was then stirred for an additional 30 min. After the addition of triethylamine (0.5 mL), the reaction mixture was filtered through Celite and concentrated. Purification by silica gel chromatography (two columns; 7 → 35% EtOAc–toluene and 18:1 $CHCl_3$–acetone) gave **14** (340 mg, 0.268 mmol, 89%); $[\alpha]_D$ +12.6° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.6, 20.8, 21.0 (*Me*CO), 35.5 (CH_2CH_2Ph), 55.3 (*Me*OPh), 62.9, 66.8, 68.7, 68.9, 71.3, 71.7, 71.9, 72.3, 72.8, 72.9, 73.0, 73.2, 73.8, 74.2, 74.4, 75.2, 79.3 (C-2-7, C-2′-7′, $PhCH_2O$, CH_2CH_2O), 97.2 (C-1), 100.4 (C-1′), 113.7, 121.4–138.8, 159.2 (aromatic C), 169.4, 170.0, 170.3, 170.9 (Me*C*O). Anal. Calcd for $C_{68}H_{74}O_{19}NF_3$: C, 64.5; H, 5.9. Found: C, 64.9; H, 6.0.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)-2,4,6,7-tetra*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranoside* (**15**).—2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 30 mg, 0.132 mmol) was added to a solution of **14** (107 mg, 85 mmol) in water-saturated CH_2Cl_2 (10 mL). The solution was stirred overnight at room temperature, then concentrated and subjected to silica gel chromatography (13 → 65% EtOAc–toluene) to give **15** (81 mg, 71 μmol, 84%); $[\alpha]_D$ +26.3° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.6, 20.7, 21.0 (*Me*CO), 35.4 (CH_2CH_2Ph), 62.7, 66.8, 66.9, 68.2, 68.5, 68.9, 70.9, 71.6, 71.7, 71.9, 72.9, 73.1, 73.3, 73.5, 74.2, 74.8, 79.7 (C-2-7, C-2′-7′, $PhCH_2O$, CH_2CH_2O), 97.2 (C-1), 101.5 (C-1′), 121.4–138.6 (aromatic C), 154.8 (CF_3CO), 169.7, 170.0, 170.3, 170.8 (Me*C*O). Anal. Calcd for $C_{60}H_{66}O_{18}NF_3$: C, 62.9; H, 5.8. Found: C, 62.8; H, 5.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(3,4,6,7-tetra*-O-*benzyl-2*-O-p-*methoxybenzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 2)*-O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)-2,4,6,7-tetra*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranoside* (**16**).—A solution of **12** (61 mg, 83 μmol) and **15** (76 mg, 66 μmol) in dry diethyl ether (8 mL) containing powdered molecular sieves (4 Å) was stirred in an argon atmosphere for 1.5 h. To the mixture was added DMTST (58 mg, 0.225 mmol) and the stirring was continued for 3 h. After the addition of triethylamine (0.25 mL) followed by further stirring for 30 min, the mixture was centrifuged and the supernatant concentrated. The residue was purified on a silica gel column (4:1 toluene–EtOAc) to yield **16** (107 mg, 59 μmol, 89%); $[\alpha]_D$ +13.4° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.7, 20.9, 21.0 (*Me*CO), 35.2 (CH_2CH_2Ph), 55.1 (*Me*OPh), 62.5, 66.5, 66.9, 68.9, 68.9, 71.7, 71.4, 71.7, 71.8, 72.0, 72.4, 72.8, 72.9, 73.1, 73.8, 74.0, 74.1, 74.4, 74.9, 80.1 (C-2-7, C-2′-7′, C-2″-7″, $PhCH_2O$, CH_2CH_2O), 97.2, 99.5, 100.9 (C-1,1′,1″), 113.6, 121.2–138.9 (aromatic C), 154.8 (CF_3CO), 159.0 (aromatic C), 169.5, 170.2, 170.7 (Me*C*O). Anal. Calcd for $C_{103}H_{110}O_{25}NF_3$: C, 68.0; H, 6.1. Found: C, 68.0; H, 6.2.

2-(4-Trifluoroacetamidophenyl)ethyl O-(L-glycero-α-D-manno-*heptopyranosyl)-(1 → 2)*-O-(L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)*-L-glycero-α-D-manno-*heptopyranoside* (**17**).—Compound **16** (119 mg, 65 μmol), dissolved in absolute EtOH/water (100:1, 20 mL), was hydrogenolysed over Pd/C at 6.8 atm for 24 h. The catalyst was filtered off and the soln was concentrated. The residue was dissolved in MeOH (5 mL) and made alkaline by adding NaOMe (1 M in MeOH) while stirring. After 50 min Dowex 50 H^+ ion exchange resin was added. After 10 min, the soln was decanted and concentrated. The remaining syrup was dissolved in water containing 1% of *n*-BuOH (6 mL), washed with diethyl ether (3 mL) and desalted by size exclusion chromatography on a Sephadex G50 column eluted with water + 1% *n*-BuOH. Concentration and lyophilisation yielded **17** (50 mg, 62 μmol, 94%); $[\alpha]_D$ +69.4° (*c* 1.0, H_2O); ^{13}C NMR (D_2O): δ 35.5 (CH_2CH_2Ph), 63.6, 63.7, 64.0, 66.2, 66.9, 67.0, 68.6, 69.3, 69.7, 70.7, 70.8, 71.0, 71.2, 72.3, 72.4, 72.7, 78.7, 79.0 (C-2-7, C-2′-7′, C-2″-7″, CH_2CH_2O), 100.0 ($J_{C\text{-}1,H\text{-}1}$ 171 Hz), 101.4 ($J_{C\text{-}1,H\text{-}1}$ 174 Hz), 102.8 ($J_{C\text{-}1,H\text{-}1}$ 172 Hz) (C-1,1′,1″), 123.0, 130.6, 133.8, 139.2 (aromatic C); ^1H NMR (D_2O, assorted peaks): δ 4.85 ($J_{1,2}$ 2 Hz), 5.15 ($J_{1,2}$ 1.8 Hz), 5.36 ($J_{1,2}$ 2 Hz) (H-1,1′,1″). Anal. Calcd for $C_{31}H_{46}O_{20}NF_3 \cdot 2.5H_2O$: C, 43.6; H, 6.0. Found: C, 43.3; H, 5.6.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 2)*-O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)-2,4,6,7-tetra*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranoside* (**18**).—Freshly

recrystallised DDQ (85 mg, 0.374 mmol) was added to a soln of **16** (589 mg, 0.324 mmol) in water-saturated CH_2Cl_2. The soln was stirred overnight at room temperature. The solvent was evaporated by a stream of air and the crude product was purified on silica gel columns (two columns: 10 → 50% EtOAc–toluene and 1:1 light petroleum bp 40–60 °C–EtOAc). Concentration of the product-containing fractions gave 372 mg (0.219 mmol, 68%) of **18**; $[\alpha]_D$ +26.3° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.7, 20.9, 21.0 (*Me*CO), 35.3 (CH_2CH_2Ph), 62.5, 66.7, 66.9, 68.2, 68.7, 68.9, 71.2, 71.5, 71.6, 71.7, 71.8, 72.1, 72.6, 72.8, 73.1, 73.7, 73.9, 74.5, 74.9, 80.2 (C-2-7, C-2′-7′, C-2″-7″, PhCH_2O, CH_2CH_2O), 97.2, 100.5 (C-1,1′,1″), 121.2–138.8 (aromatic C), 154.8 (CF_3CO), 169.5, 170.1, 170.2, 170.7 (Me*C*O). Anal. Calcd for $C_{95}H_{102}O_{24}NF_3$: C, 67.2; H, 6.1. Found: C, 67.1; H, 6.1.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galactopyranosyl)-(1 → 2)-*O*-(3,4,6,7-tetra-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranosyl)-(1 → 2)-*O*-(3,4,6,7-tetra-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranosyl)-(1 → 3)-2,4,6,7-tetra-*O*-acetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**19**).—To a soln of **18** (94 mg, 55 μmol) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (73 mg, 0.111 mmol) in dry CH_2Cl_2 (7 mL) was added a *sym*-collidine soln in dry toluene (10% v/v, 67 μL, 51 μmol) and powdered molecular sieves (4 Å). The mixture was stirred for 70 min at room temperature in an argon atmosphere. The flask was cooled to −20 °C and silver triflate (28 mg, 0.109 mmol) dissolved in dry toluene (0.3 mL) was added. After 60 min, at which point the temperature had reached −5 °C, triethylamine (0.25 mL) was added and the mixture was stirred for an additional 10 min. Centrifugation and washing of the nascent pellet, followed by concentration of the supernatants, yielded a crude product which was purified on a silica gel column (0 → 60% EtOAc–toluene) to give recovered **18** (13 mg, 7.7 μmol, 14%) and **19** (93 mg, 41 μmol, 74%); $[\alpha]_D$ +7.9° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.6, 20.7, 21.0 (*Me*CO), 35.2 (CH_2CH_2Ph), 61.5, 62.5, 66.4, 66.9, 68.0, 68.9, 69.7, 71.0, 71.1, 71.1, 71.3, 71.6, 72.0, 72.3, 72.3, 72.6, 72.8, 73.0, 73.1, 74.1, 74.2, 74.4, 74.9, 75.3, 75.4, 78.8, 79.3 (C-2-7, C-2′-7′, C-2″-7″, C-2‴-6‴, PhCH_2O, CH_2CH_2O), 97.3 ($J_{C\text{-}1,H\text{-}1}$ 174 Hz), 99.7 ($J_{C\text{-}1,H\text{-}1}$ 159 Hz), 100.1 ($J_{C\text{-}1,H\text{-}1}$ 171 Hz), 101.0 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz) (C-1,1′,1″,1‴), 121.1–138.9 (aromatic C), 164.9, 165.5, 165.7, 165.8 (PhCO_2), 169.4, 170.1, 170.2, 170.7 (Me*C*O). Anal. Calcd for $C_{129}H_{128}O_{33}NF_3$: C, 68.0; H, 5.7. Found: C, 68.2; H, 5.9.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(β-D-galactopyranosyl)-(1 → 2)-*O*-(L-glycero-α-D-manno-heptopyranosyl)-(1 → 2)-*O*-(L-glycero-α-D-manno-heptopyranosyl)-(1 → 3)-L-glycero-α-D-manno-heptopyranoside* (**20**).—To a soln of **19** (91 mg, 40 μmol) in absolute EtOH (15 mL) was added 2 mL of aq AcOH (60%) and palladium on activated carbon. The mixture was put in a Parr apparatus and hydrogenolysed at 8.2 atm for 40 h. The catalyst was removed by filtration through Celite. The concentrated residue was dissolved in absolute MeOH and adjusted to pH 10 by adding 10 droplets of a NaOMe soln (1 M in MeOH). After 30 min, Dowex H^+ ion exchange resin was added and stirring was continued for 30 min. The organic phase was decanted off and concentrated. Traces of AcOH were removed by coevaporation with 1:1 toluene–EtOH (2 × 6 mL). The residue was dissolved in distilled water containing 1% of *n*-BuOH and washed twice with 2 mL portions of diethyl ether. The crude product was purified on a Bio-Gel P2-gel column, eluted with 1% *n*-BuOH in water and freeze-dried yielding **20** (32 mg, 33 μmol, 82%); $[\alpha]_D$ +50.3° (*c* 1.0, H_2O); ^{13}C NMR (D_2O): δ 35.5 (CH_2CH_2Ph), 62.0, 63.5, 63.8, 64.0, 66.2, 67.0, 67.2, 68.7, 69.3, 69.3, 69.4, 69.6, 70.4, 70.7, 71.0, 71.3, 72.3, 72.5, 72.7, 73.2, 76.0, 77.9, 78.7, 79.1 (C-2-7, C-2′-7′, C-2″-7″, C-2‴-6‴, CH_2CH_2O), 100.0 ($J_{C\text{-}1,H\text{-}1}$ 172 Hz), 100.9 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz), 101.3 ($J_{C\text{-}1,H\text{-}1}$ 176 Hz) (C-1,1′,1″), 102.9 ($J_{C\text{-}1,H\text{-}1}$ 160 Hz) (C-1‴), 123.1, 130.7, 134.1, 139.2 (aromatic C); ^1H NMR (D_2O, assorted peaks): δ 4.54 ($J_{1,2}$ 7.3 Hz, H-1‴), 4.86 ($J_{1,2}$ < 2 Hz), 5.26 ($J_{1,2}$ < 2 Hz), 5.37 ($J_{1,2}$ < 2 Hz) (H-1,1′,1″). Anal. Calcd for $C_{37}H_{56}O_{25}NF_3 \cdot 1.5H_2O$: C, 44.5; H, 6.0. Found: C, 44.4; H, 5.6.

Ethyl O-*(2,3,4,6-tetra-*O*-benzoyl-α-D-galacto-pyranosyl)-(1 → 2)-3,4,6,7-tetra-*O*-benzyl-1-thio-*L*-glycero-α-D-manno-heptopyranoside* (**21**).—Compound **11** (30 mg, 49 μmol) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactosyl bromide (39 mg, 59 μmol) were dissolved in dry CH_2Cl_2 (4 mL) containing powdered molecular sieves under an argon atmosphere. The mixture was stirred at room temperature for 1 h and then cooled to −20 °C. A soln of silver triflate (16 mg, 62 μmol) in dry toluene was added. Stirring was continued until the temperature reached −10 °C (20 min). Triethylamine (0.2 mL) was then added and the mixture was concentrated and purified by silica gel chromatography (0 → 8% acetone–CH_2Cl_2) to give 40 mg (34 μmol, 67%) of **21**; $[\alpha]_D$ +116.6° (*c*

1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 14.5 (*Me*CH_2S), 25.2 (Me*C*H_2S), 62.8, 67.3, 68.2, 69.4, 70.7, 72.3, 72.6, 73.4, 74.2, 74.3, 75.4, 79.9 (C-2-7, C-2′-6′, Ph*C*H_2O), 83.9 ($J_{C\text{-}1,H\text{-}1}$ 167 Hz, C-1), 97.8 ($J_{C\text{-}1,H\text{-}1}$ 174 Hz, C-1′), 127.1–139.0 (aromatic C), 165.2, 165.6, 165.9, 166.1 (Ph*C*O). Anal. Calcd for $C_{71}H_{68}O_{15}S$: C, 71.5; H, 5.7. Found: C, 71.6; H, 5.8.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6-tetra*-O-*benzoyl*-α-D-*galactopyranosyl)-(1 → 2)*-O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 2)*-O-*(3,4,6,7-tetra*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)-2,4,6,7-tetra*-O-*acetyl*-L-glycero-α-D-manno-*heptopyranoside* (**22**).—Compound **15** (63 mg, 55 μmol) and **21** (72 mg, 60 μmol) were dissolved in dry diethyl ether (10 mL). Powdered molecular sieves were added and the mixture was stirred under an argon atmosphere for 80 min. The flask was cooled in an ice bath and DMTST (47 mg, 0.182 mmol) was added. After 20 min the ice bath was removed, and the mixture was stirred overnight. After the addition of triethylamine (0.25 mL) and 30 min continued stirring, the mixture was centrifuged and the supernatant concentrated. Silica gel chromatography of the residue (24:1 $CHCl_3$–acetone) gave 91 mg (40 μmol, 73%) of **22**; $[\alpha]_D$ +54.4° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 20.7, 20.8, 21.0 (*Me*CO), 35.3 (CH_2CH_2Ph), 61.6, 62.5, 66.4, 66.7, 66.9, 68.2, 68.9, 69.2, 71.0, 71.7, 72.0, 72.5, 72.9, 73.1, 73.3, 74.0, 74.2, 74.3, 74.8, 75.5, 75.6, 79.4 (C-2-7, C-2′-7′, C-2″-7″, C-2‴-6‴, Ph*C*H_2O, CH_2CH_2O), 97.2, 97.5, 99.7, 100.6 (C-1,1′,1″,1‴), 121.2–139.0 (aromatic C), 154.8 (CF_3CO), 165.3, 165.6, 165.9 (Ph*C*O), 169.5, 170.1, 170.2, 170.7 (Me*C*O). Anal. Calcd for $C_{129}H_{128}O_{33}NF_3$: C, 68.0; H, 5.7. Found: C, 68.0; H, 5.6.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(*α-D-*galactopyranosyl)-(1 → 2)*-O-*(*L-glycero-α-D-manno-*heptopyranosyl)-(1 → 2)*-O-*(*L-glycero-α-D-manno-*heptopyranosyl)-(1 → 3)*-L-glycero-α-D-manno-*heptopyranoside* (**23**).—Compound **22** (71 mg, 31 μmol) was dissolved in absolute EtOH (15 mL). Palladium on activated carbon and a small portion of water (0.25 mL) was added. The mixture was hydrogenolysed at 5.8 atm overnight and then centrifuged, decanted, and concentrated. The residue was dissolved in MeOH (3 mL). Under stirring, 10 droplets of NaOMe (1 M in MeOH) were added and the soln was stirred continuously for 20 min and then neutralised by adding Dowex 50 H^+ ion exchange resin. After an additional 10 min of stirring, the methanolic phase was decanted off, concentrated, dissolved in water containing 1% of *n*-BuOH (6 mL) and washed once with diethyl ether (3 mL). The aqueous phase was desalted on a size exclusion chromatography column (Sephadex G 50, eluent water + 1% *n*-BuOH) which, after concentration and lyophilisation of product-containing fractions, gave **23** (21 mg, 22 μmol, 69%); $[\alpha]_D$ +76.7° (*c* 1.0, H_2O); ^{13}C NMR (D_2O): δ 35.5 (CH_2CH_2Ph), 62.2, 63.5, 63.8, 64.0, 66.2, 67.0, 67.2, 68.7, 69.3, 69.6, 69.7, 70.1, 70.7, 71.0, 71.2, 72.2, 72.3, 72.8, 78.7, 79.5, 80.1 (C-2-7, C-2′-7′, C-2″-7″, C-2‴-6‴, CH_2CH_2O), 100.0 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz), 101.2, 101.3, 101.7 ($J_{C\text{-}1,H\text{-}1}$ 169 Hz) (C-1,1′,1″,1‴), 123.1, 130.7, 133.8, 139.4 (arom.); ^1H NMR (D_2O, assorted peaks): δ 4.85 ($J_{1,2}$ 2 Hz), 5.25 ($J_{1,2}$ 4 Hz), 5.38 ($J_{1,2}$ 2 Hz), 5.42 ($J_{1,2}$ 2 Hz) (H-1,1′,1″,1‴). HRMS Calcd for $C_{37}H_{55}O_{25}NF_3$ [M − H]: 970.3016. Found: 970.3057.

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