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Synthesis of 2-(4-trifluoroacetamidophenyl)ethyl *O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→7)-*O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→3)-L-*glycero*-α-D-*manno*-heptopyranoside, corresponding to the heptose region of the *Salmonella* Ra core structure*

Per J. Garegg, Stefan Oscarson, Helena Ritzén, and Maria Szönyi
Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm (Sweden)

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ABSTRACT

The title trisaccharide was synthesized from methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside by acetolysis, followed by conversion into ethyl thioglycosides and also glycosyl bromides, which were both used in glycosylation reactions. In glycosylations using thioglycosides as glycosyl donors, *N*-iodosuccinimide–silver triflate and dimethyl(methylthio)sulfonium triflate were used as promoters, and in glycosylations with glycosyl bromides silver triflate was used. The protecting groups introduced into intermediates during the synthesis of the title trisaccharide were designed to allow later glycosylation at O-3′ to give larger oligosaccharide fragments of the *Salmonella* LPS core region, and also to allow the introduction of phosphate groups at O-4 and O-4′, a structural element that is suggested to be present in the Ra core.

INTRODUCTION

Several syntheses of oligosaccharides corresponding to fragments of core regions of lipopolysaccharides from the cell walls of *Salmonella* bacteria have been communicated from this laboratory[1]. We now describe the synthesis of the heptose region of the Ra core[2], *i.e.*, the trisaccharide, *O*-(L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→7)-*O*-(-L-*glycero*-α-D-*manno*-heptopyranosyl)-(1→3)-L-*glycero*-α-D-*manno*-heptopyranose. The 2-(4-trifluoroacetamidophenyl)ethyl glycoside (**15**) was synthesized to make it possible to attach it to proteins, solid phases, fatty chains, *etc.*, and be used *i.a.* as an immunogen, for affinity chromatography, and for formation of liposomes and membranes. The title compound **15** will also be used in inhibition tests to investigate the specificity of monoclonal antibodies raised against rough mutants of *Salmonella*, and also to investigate the receptor site of phage G 13.

The number and positions of phosphate groups in core structures are not very well established. Neither are their biological importance and significance. Synthetic oligosaccharides containing phosphate groups can be used as model compounds in

* Dedicated to Professor Serge David on the occasion of his 70th birthday.

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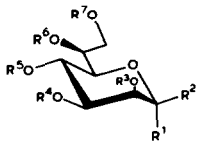
n.m.r. and m.s. analysis and, thereby, simplify the determination of these structural element in the native core. They will also be important in immunological work. In the synthesis of **15**, the pattern of protective group of intermediates has been designed to allow later introduction of phosphate groups at O-4 and O-4', suggested to be the place of phosphate groups in the native core[2], and also to allow glycosylation at O-3' to make larger fragments corresponding to core structures. In the synthesis, thioglycosides of the heptopyranose have been synthesized and used as glycosyl donors with different promoters [dimethyl(methylthio)sulfonium triflate (DMTST)[3,4], *N*-iodosuccinimide (NIS)–silver triflate[5], and methyl triflate[6]]. The reducing triheptosaccharide has earlier been obtained by an alternative route by Diziewiszek *et al.*[7].

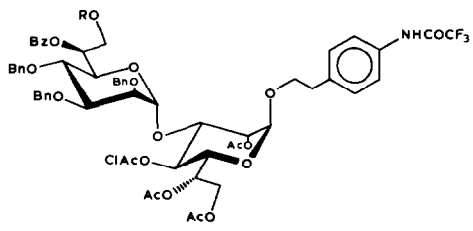
RESULTS AND DISCUSSION

Methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside[8] (**1**) was used as the precursor for all three heptose units of **15**. In order to convert **1** into a glycosyl donor, it was first acetylated to give **2**, and the methyl glycoside was then subjected to mild acetolysis to give **3**. An attempt to introduce the spacer arm was first made by a silver triflate-promoted[9,10] coupling between 2-(4-trifluoroacetamidophenyl)ethanol and the bromide derivative of **3**, obtained from **3** by treatment with hydrogen bromide–acetic acid. The reaction was rapid and high-yielding, but the stereoselectivity was low. An α:β ratio of ~ 1:1 was obtained both with dichloromethane or toluene as solvent. The thioglycoside **4** was synthesized by reaction of **3** with ethanethiol and zinc chloride in dichloromethane to give the α-thioglycoside **4** (78%). The reaction between **4** and 2-(4-trifluoroacetamidophenyl)ethanol, in the presence of methyl triflate[6] as promoter and diethyl ether as solvent to improve the selectivity for the α anomer, proceeded with better stereoselectivity, giving an α:β ratio of ~ 5:1, and the desired α-glycoside **5** in 55% yield. Changing the promoter to NIS–silver triflate[5] once more gave a good yield but low stereoselectivity. Finally, the best yield of the α-glycoside **5** (70%) was obtained by treatment of the α,β mixture, obtained in the NIS–silver triflate- or in the silver triflate-promoted couplings, with BF_3-etherate in acetonitrile to anomerize the β compound[12]. Catalytic hydrogenolysis of **5** gave the 2,3,4-triol derivative **6** (98%), which was treated with trimethylorthoacetate and 4-toluenesulfonic acid to give the 2,3-orthoester. To make, later, selective deblocking of OH-4 of the reducing end unit possible, this position was now acylated with chloroacetyl chloride and pyridine in dichloromethane. The orthoester was then opened[13] by treatment with aqueous trifluoroacetic acid to give the OH-3 derivative **7** (78% overall).

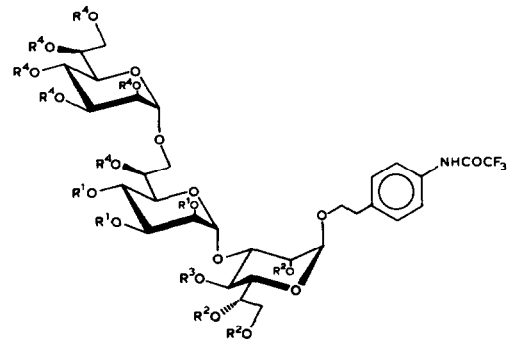
The intermediate heptose unit was synthesized from the thioglycoside **4**. Zemplén deacetylation gave the 6,7-diol **8**, which was selectively silylated in the primary position with *tert*-butylchlorodimethylsilane in pyridine, and then benzoylated to yield the suitably protected glycosyl donor **9** (80%). The glycosylation reaction between **9** and **7** in the presence of DMTST[3,4] as promoter gave the α-disaccharide **11** (73%). The problem with the low reactivity of acylated heptose glycosyl donors, as found and discussed by us[1], and Paulsen and Heitmann[14], was not encountered with this 2,3,4-tri-



1 R^1 = OMe, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = H
2 R^1 = OMe, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = Ac
3 R^1 = OAc, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = Ac
4 R^1 = SEt, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = Ac
5 R^1 = $O(CH_2)_2PhNHCOCF_3$ (4), R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = Ac
6 R^1 = $O(CH_2)_2PhNHCOCF_3$ (4), R^2 = R^3 = R^4 = R^5 = H, R^6 = R^7 = Ac
7 R^1 = $O(CH_2)_2PhNHCOCF_3$ (4), R^2 = H R^3 = R^6 = R^7 = Ac, R^4 = H, R^5 = ClAc
8 R^1 = SEt, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = R^7 = H
9 R^1 = SEt, R^2 = H, R^3 = R^4 = R^5 = Bn, R^6 = Bz, R^7 = $Si(CH_3)_2Bu^t$
10 R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = Bz, R^7 = H



11 R = $Si(CH_3)_2Bu^t$
12 R = H



13 R^1 = Bn, R^2 = Ac, R^3 = ClAc, R^4 = Bz
14 R^1 = H, R^2 = Ac, R^3 = ClAc, R^4 = Bz
15 R^1 = R^2 = R^3 = R^4 = H

O-benzyl derivate, owing probably to the higher reactivity of benzylated glycosyl donors. Paulsen and Heitmann[14] used the 3,4,6,7-tetra-*O*-benzyl derivative with the same result. Diethyl ether was once more used as solvent to obtain α selectivity. DMTST is not very soluble in diethyl ether but sufficiently so for this type of coupling reactions. No β product was found in this coupling reaction.

To introduce the last heptose unit, the silyl group was removed from **11** by treatment with aqueous acetic acid at room temperature to give the OH-7′ derivative **12**. Glycosylation of **12** with known 2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranosyl bromide[14] in the presence of silver triflate as promoter[8,9] gave complex mixtures of products. The problems with orthoester formation during this reaction, as discussed in our earlier publication[1], was found also here, but this time even more severe. Experiments with different amounts of 1,3,5-trimethylpyridine and with the acetylated thioglycoside as donor, instead of the glycosyl bromide, all gave mainly the orthoester. Finally, exchange of the acetyl by benzoyl groups gave the benzoylated glycosyl bromide, which in a silver triflate-promoted reaction with **12** yielded the trisaccharide **13** (68%).

Compound **13** was debenzylated by catalytic hydrogenolysis to give the 2',3',4'-triol derivate **14** (64%), which can be protected, as described above for compound **6**, to give a suitable derivate for the intended reactions, glycosylation at OH-3' and phosphorylation at OH-4 and -4'. Compound **14** was then deprotected by Zemplén deacetylation to give the title compound **15** (91%).

EXPERIMENTAL

General methods. — These methods were the same as described earlier[1].

*Methyl 6,7-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**2**). — A solution of methyl 2,3,4-tri-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside[8] (**1**, 1.72 g) and a small amount of 4-dimethylaminopyridine in 2:1 pyridine–acetic anhydride (9 mL) was stirred at room temperature for 2 h, after which the mixture was concentrated. Toluene was added to and evaporated twice from the residue, which then was subjected to silica gel column chromatography (9:1 toluene–ethyl acetate) to give **2** (1.81 g, 90%), $[\alpha]_D$ + 3° (*c* 1, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 21.0 (CH_3CO), 54.8 (OCH_3), 62.4 (C-7), 68.2, 69.8, 72.0, 72.5, 73.6, 73.8, 75.3, 80.4 (C-2,3,4,5,6,3 CH_2Ph), 99.1 (C-1), 127.7–138.2 (arom.), 170.3, and 170.5 (CH_3CO).

Anal. Calc. for $C_{33}H_{38}O_9$: C, 68.5; H, 6.6. Found: C, 68.2; H, 6.7.

*1,6,7-Tri-*O*-acetyl-2,3,4-tri-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranose* (**3**). — Conc. H_2SO_4 (0.34 mL) was added dropwise at − 20° to a solution of **2** (1.81 g) in 2:1 acetic anhydride–acetic acid (30 mL). After 10 min, sodium acetate (3.5 g) was added, and the mixture was concentrated and partitioned between water and ethyl acetate. The organic layer was separated, washed with aq. $NaHCO_3$ and water, dried ($MgSO_4$), filtered, concentrated, and purified by silica gel column chromatography (9:1 toluene–ethyl acetate) to give an α,β mixture (1.75 g, 92%). The α anomer **3** crystallized from diethyl ether–light petroleum (b.p. 40–60°), m.p. 82°, $[\alpha]_D$ − 1° (*c* 1.5, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 20.9, 20.9 (CH_3CO), 62.7 (C-7), 68.0, 72.0, 72.2, 72.3, 72.7, 73.1, 75.4, 79.3 (C-2,3,4,5,6,3 CH_2Ph), 91.2 ($J_{C\text{-}1,H\text{-}1}$ 175 Hz, C-1), 127.8–137.8 (arom.), 168.5, 170.3, and 170.4 (CH_3CO). The β anomer showed $[\alpha]_D$ − 27° (*c* 1.3, chloroform); ^{13}C-N.m.r. ($CDCl_3$): δ 20.7, 21.0 (CH_3CO), 62.4 (C-7), 67.9, 72.1, 72.9, 73.1, 74.1, 74.4, 75.4, 82.6 (C-2,3,4,5,6,3 CH_2Ph), 93.3 ($J_{C\text{-}1,H\text{-}1}$ 161 Hz, C-1), 127.7–138.1 (arom.), 168.9, 170.4, and 170.5 (CH_3CO).

Anal. Calc. for $C_{34}H_{38}O_{10}$: C, 67.3; H, 6.3. Found (α anomer): C, 67.3; H, 6.2.

*Ethyl 6,7-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-*L*-glycero-α-*D*-manno-heptopyranoside* (**4**). — To a stirred solution of **3** (1.80 g) and ethanethiol (320 μL) in dichloromethane (50 mL) was added $ZnCl_2$ (1.1 g). After 3 h, the mixture was diluted with dichloromethane, washed with saturated aq. $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Silica gel column chromatography (9:1 toluene–ethyl acetate) of the residue gave **4** (1.40 g, 78%) which crystallized from ether–light petroleum (b.p. 40–60°), m.p. 68–70°, $[\alpha]_D$ + 43° (*c* 1.6, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 14.8 (SCH_2CH_3), 20.7, 21.0 (CH_3CO), 25.3 (SCH_2CH_3), 62.4 (C-7), 68.3, 70.3, 71.9, 72.0, 73.8, 75.4, 75.7, 80.5 (C-2,3,4,5,6, 3 CH_2Ph), 82.0 (C-1), 127.8–138.0 (arom.), 170.3, and 170.5 (CH_3CO).

Anal. Calc. for $C_{34}H_{39}O_8S$: C, 67.2; H, 6.5. Found: C, 67.4; H, 6.7.

*2-(4-Trifluoroacetamidophenyl)ethyl 6,7-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**5**). — A catalytic amount of silver triflate was added to a stirred mixture of **4** (100 mg), 2-(4-trifluoroacetamidophenyl)ethanol (46 mg), and *N*-iodosuccinimide (44 mg) in 5:1 dichloromethane–acetonitrile (2,4 mL). After 10 min, the mixture was filtered through silica and concentrated. The α,β mixture obtained was dissolved in acetonitrile (2 mL) and treated with BF_3- etherate (150 μL). After 3 h, triethylamine (1 mL) was added and the solution was concentrated. Silica gel column chromatography (9:1 toluene–ethyl acetate) of the residue gave **5** (90 mg, 70%), $[\alpha]_D$ + 13° (*c* 1, chloroform) and 35 mg of an α,β mixture; ^{13}C-n.m.r. ($CDCl_3$) for **5**: δ 20.8, 20.9 (CH_3CO), 35.5 (CH_2CH_2Ph), 63.0 (C-7), 68.3 (×2), 70.2, 72.0, 72.5, 73.6, 74.0, 75.2, 79.9 (C-2,3,4,5,6, CH_2CH_2O, 3 CH_2Ph), 97.8 (C-1), 113.7, 117.9 (CF_3), 121.2–138.2 (arom.), 154.6, 155.2 (CF_3CO), 170.5, and 170.8 (CH_3CO).

Anal. Calc. for $C_{42}H_{44}F_3NO_{10}$: C, 64.7; H, 5.7. Found: C, 64.5; H, 5.5.

*2-(4-Trifluoroacetamidophenyl)ethyl 6,7-di-*O*-acetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**6**). — A solution of **5** (700 mg) in ethyl acetate (5 mL) was hydrogenolyzed over 10% Pd–C at 400 kPa for 16 h. The solution was filtered, concentrated, and subjected to silica gel column chromatography (19:1 dichloromethane–methanol) to give **6** (450 mg, 98%), $[\alpha]_D$ + 19° (*c* 0.8, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 20.9 (CH_3CO), 35.4 (CH_2CH_2Ph), 63.3 (C-7), 66.7, 68.4, 69.5, 70.3, 70.8, 71.0 (C-2,3,4,5,6, CH_2CH_2O), 99.7 (C-1), 113.7, 118.0 (CF_3), 121.2–137.3 (arom.), 154.9, 155.4 (CF_3CO), 171.0, and 172.6 (CH_3CO).

Anal. Calc. for $C_{21}H_{26}F_3NO_{10}$: C, 49.5; H, 5.7. Found: C, 49.6; H, 5.8.

*2-(4-Trifluoroacetamidophenyl)ethyl 2,6,7-tri-*O*-acetyl-4-*O*-chloroacetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**7**). — Trimethyl orthoacetate (84 μL) was added to a solution of **6** (170 mg) and 4-toluenesulfonic acid (60 μL, 5% in acetonitrile) in dry acetonitrile (17 mL), and the mixture was stirred at room temperature for 30 min. Pyridine (0.5 mL) was added and the solution was diluted with toluene, concentrated, and toluene was evaporated twice from the residue. 15:1 Dichloromethane–pyridine (16 mL), chloroacetyl chloride (53 μL), and 4-dimethylaminopyridine (a few crystals) were added to the residue with stirring which was continued for 2 h. The solution was diluted with dichloromethane and washed with water. The organic phase was dried ($MgSO_4$) and concentrated. Aqueous trifluoroacetic acid (90%, 0.1 mL) was added to a solution of the residue in acetonitrile (15 mL). After 30 min, the solution was concentrated and purified by silica gel column chromatography (1:1 toluene–ethyl acetate) to give **7** (164 mg, 78%), $[\alpha]_D$ − 18° (*c* 0.84, chloroform); n.m.r. ($CDCl_3$): ^{13}C, δ 20.6, 20.7, 21.0, ($COCH_3$), 35.4 (CH_2CH_2Ph), 40.6 ($COCH_2Cl$), 62.8, 67.1, 68.2, 68.3, 68.8, 69.6, 72.4 (C-2,3,4,5,6,7,OCH_2CH_2), 97.1 (C-1), 117.1 (CF_3), 121.4–137.1, 154.6, 155.2 (CF_3CO), 167.6 ($COCH_2Cl$), 170.5, 170.6, and 171.0 (CH_3CO); ^{1}H, δ 4.86 (1 H, H-1), 4.97 (1 H, H-4), 5.03 (1 H, H-2), and 5.13 (1 H, H-6).

Anal. Calc. for $C_{25}H_{29}ClF_3NO_{12}$: C, 47.7; H, 4.6. Found: C, 47.7; H, 4.7.

*Ethyl 2,3,4-tri-*O*-benzyl-1-thio-*L*-glycero-α-*D*-manno-heptopyranoside* (**8**). — A solution of **4** (300 mg) in methanol (5 mL) was treated with methanolic M sodium

methoxide (0.1 mL) for 2 h, neutralized with Dowex 50 (H^+) cation-exchange resin, filtered, and concentrated. The residue was purified by silica gel column chromatography (3:1 toluene–ethyl acetate) to give **8** (223 mg, 92%), $[\alpha]_D$ + 63° (*c* 0.9, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 14.8 (SCH_2CH_3), 25.4 (SCH_2CH_3), 65.1 (C-7), 69.5 (C-6), 72.2, 72.5, 73.0, 74.4, 75.3, 76.4, 80.2 (C-2,3,4,5, 3 CH_2Ph), 82.5 (C-1), and 127.7–138.3 (arom.).

Anal. Calc. for $C_{30}H_{36}O_6S$: C, 68.7; H, 6.9. Found: C, 68.5; H, 7.0.

*Ethyl 6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-7-*O*-(*tert*-butyldimethylsilyl)-1-thio-*L*-glycero-α-*D*-manno-heptopyranoside* (**9**). — *Tert*-butylchlorodimethylsilane (38 mg, 1.1 equiv.) was added to a solution of **8** (118 mg) in anhydrous pyridine (5 mL) at 0°. The mixture was allowed to attain room temperature and kept overnight. Benzoyl chloride (107 μL) and 4-dimethylaminopyridine (a few crystals) were added, and the reaction mixture was stirred for another 30 min. The mixture was diluted with toluene, washed with water, dried ($MgSO_4$), concentrated, and purified by silica gel column chromatography (toluene) to give **9** (134 mg, 80%), $[\alpha]_D$ + 65° (*c* 1.3, chloroform); n.m.r. ($CDCl_3$): ^{13}C, δ − 5.4, − 5.2 [$Si(CH_3)_2$], 14.6 (SCH_2CH_3), 18.2 [$C(CH_3)_3$], 24.9 (SCH_2CH_3) 25.8 [$C(CH_3)_3$], 60.0 (C-7), 69.3 (C-6), 71.8, 72.1, 72.3, 74.2, 75.4, 76.6, 81.0 (C-2,3,4,5, 3 CH_2Ph), 81.4 (C-1), 127.6–138.2 (arom.), and 166.5 (C_6H_5CO); ^{1}H, δ 5.50 (1 H, H-1), and 5.56 (1 H, H-6).

Anal. Calc. for $C_{43}H_{54}O_7SSi$: C, 69.5; H, 7.3. Found: C, 69.5; H, 7.3.

2-(4-Trifluoroacetamidophenyl)ethyl O-[*6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-7-*O*-(tert*butyldimethylsilyl)*-*L*-glycero-α-*D*-manno-heptopyranosyl]-(1→3)-2,6,7-tri-*O*-acetyl-4-*O*-chloroacetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**11**). — DMTST (100 mg) was added at 0° to a stirred solution of **9** (80 mg) and **7** (70 mg) in dry diethyl ether (25 mL) containing molecular sieves (4A). The mixture was stirred for 2 h at room temperature, triethylamine was added, and stirring was continued for 30 min. The mixture was concentrated and purified by chromatography on two silica gel columns (9:1 toluene–ethyl acetate and 6:1 toluene–ethyl acetate without applied pressure) to give **11** (106 mg, 73%), $[\alpha]_D$ + 24° (*c* 1.7, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ − 5.4, − 5.2 [$Si(CH_3)_2$], 18.2 [$C(CH_3)_3$], 20.7, 20.9 ($COCH_3$), 25.8 [$C(CH_3)_3$], 35.4 (CH_2CH_2Ph), 40.4 ($COCH_2Cl$), 61.9, 62.9, 66.7, 68.5, 68.7, 68.8, 71.3, 71.7, 72.1, 72.2, 73.2, 73.5, 74.0, 74.7, 75.3, 79.4 (C-2,3,4,5,6,7,2′,3′,4′,5′,6′,7′, 3 CH_2Ph, OCH_2CH_2), 97.0 ($J_{C\text{-}1,H\text{-}1}$ 174 Hz, C-1), 100.7 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz, C-1′), 121.6–138.5 (arom.), 166.1 (×2) (C_6H_5CO, $COClCH_2$), 169.8, 170.4, and 170.9 (CH_3CO).

Anal. Calc. for $C_{66}H_{77}ClF_3NO_{19}Si$: C, 60.5; H, 5.9. Found: C, 60.7; H, 5.8.

2-(4-Trifluoroacetamidophenyl)ethyl O-(*6-*O*-benzoyl-2,3,4-tri-*O*-benzyl-*L*-glycero-α-*D*-manno-heptopyranosyl)-(1→3)-2,6,7-tri-*O*-acetyl-4-*O*-chloroacetyl-*L*-glycero-α-*D*-manno-heptopyranoside* (**12**). — A solution of **11** (100 mg) in 70% aqueous acetic acid (10 mL) was stirred overnight at room temperature, and then diluted with toluene and concentrated. Toluene was twice evaporated from the residue, which was purified by silica gel column chromatography (1:1 toluene–ethyl acetate) to afford **12** (83 mg, 91%), $[\alpha]_D$ + 36° (*c* 1.7, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 20.9 ($COCH_3$), 35.1 (CH_2CH_2Ph), 40.4 ($COCH_2Cl$), 62.6, 62.7, 63.8, 66.8, 68.4, 68.6 (×2), 71.6, 71.9, 72.4,

73.2, 73.4, 74.5, 74.8, 75.1, 79.4 (C-2,3,4,5,6,7,2′,3′,4′,5′,6′,7′, 3 CH_2Ph, OCH_2CH_2), 97.1 (C-1), 101.4 (C-1′), 121.7–138.3 (arom.), 166.2, 167.1 (C_6H_5CO, $COCH_2Cl$), 170.3, 170.5, and 170.8 (CH_3CO).

1,2,3,4,6,7-Hexa-O-*benzoyl*-L-glycero-α-D-manno-*heptopyranose* (**10**). — A solution of 1,2,3,4,6,7-hexa-*O*-acetyl-L-*glycero*-α-D-*manno*-heptopyranose[14] in methanol was treated with methanolic M sodium methoxide for 2 h, neutralized with Dowex 50 (H^+) cation-exchange resin, filtered, and concentrated. The residue was dissolved in pyridine, treated with benzoyl chloride, and kept overnight. Concentration and purification on a silica gel column (9:1 toluene–ethyl acetate) gave **10**, which crystallized from diethyl ether–light petroleum (b.p. 40–60°), m.p. 102°, $[\alpha]_D$ −30° (*c* 1.0, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 61.9 (C-7), 65.1, 67.5, 69.5, 70.1, 71.2 (C-2,3,4,5,6), 91.2 (C-1), 128.2–134.0 (arom.), 163.6, 165.2, 165.3, 165.6, and 165.7 (C_6H_5CO).

Anal. Calc. for $C_{49}H_{38}O_{13}$: C, 70.5; H, 4.6. Found: C, 70.5; H, 4.8.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6,7-penta*-O-*benzoyl*-L-glycero-α-D-manno-*heptopyranosyl*-*(1→7)*-O-(6-O-*benzoyl*-*2,3,4-tri*-O-*benzyl*-L-glycero-α-D-manno-*heptopyranosyl*)-*(1→3)*-*2,6,7-tri*-O-*acetyl*-*4*-O-*chloroacetyl*-L-glycero-α-D-manno-*heptopyranoside* (**13**). — Silver trifluoromethanesulfonate (50 mg) in dry toluene (0.5 mL) was added to a stirred mixture of **12** (93 mg), 2,3,4,6,7-penta-*O*-benzoyl-L-*glycero*-α-D-*manno*-heptopyranosyl bromide [obtained from 1,2,3,4,6,7-hexa-*O*-benzoyl-L-*glycero*-α-D-*manno*-heptopyranose (124 mg) by treatment with HBr–acetic acid[15]] and molecular sieves (4A) in dichloromethane (2 mL). The mixture was stirred at room temperature for 5 h, concentrated, and purified by silica gel column chromatography (9:1 toluene–ethyl acetate) to give **13** (101 mg, 68%), $[\alpha]_D$ −10° (*c* 0.9, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 20.9 ($COCH_3$), 35.5 (CH_2CH_2Ph), 40.4 ($COCH_2Cl$), 62.8, 64.0, 65.8, 66.0, 66.9, 68.2, 68.4, 68.5, 68.7, 69.3, 70.0, 70.6, 71.3, 71.5, 72.0, 73.1, 73.5, 74.7, 74.8, 75.0, 79.6 (C-2,3,4,5,6,7,2′,3′,4′,5′,6′,7′,2″,3″,4″,5″,6″,7″, 3 CH_2Ph, OCH_2CH_2, one overlap), 97.4, 97.5 (C-1, 1″), 101.1 (C-1′), 121.4–138.4 (arom.), 165.2, 165.2, 165.6, 166.0, 166.1, 166.1 (C_6H_5CO, $COCH_2Cl$), 170.0, 170.5, and 170.8 (CH_3CO).

Anal. Calc. for $C_{102}H_{95}ClF_3NO_{30}$: C, 64.2; H, 5.0. Found: C, 64.2; H, 5.2.

2-(4-Trifluoroacetamidophenyl)ethyl O-*(2,3,4,6,7-penta*-O-*benzoyl*-L-glycero-α-D-manno-*heptopyranosyl*)-*(1→7)*-O-(6-O-*benzoyl*-L-glycero-α-D-manno-*heptopyranosyl*)-*(1→3)*-*2,6,7-tri*-O-*acetyl*-*4*-O-*chloroacetyl*-L-glycero-α-D-manno-*heptopyranoside* (**14**). — A solution of **13** (30 mg) in ethyl acetate (5 mL) was hydrogenolyzed over 10% Pd–C (50 mg) at 400 kPa for 24 h. The solution was applied to a silica gel column and eluted (9:1 chloroform–methanol) to give **14** (16.5 mg, 64%), $[\alpha]_D$ −3° (*c* 0.7, chloroform); ^{13}C-n.m.r. ($CDCl_3$): δ 20.7, 20.9 ($COCH_3$), 35.5 (CH_2CH_2Ph), 40.3 ($COCH_2Cl$), 62.5, 63.9 (C-7,7″), 65.6, 66.9 (×2), 67.4, 68.3, 68.4, 68.6, 68.8, 69.9 (×2), 70.0, 70.4, 70.5, 70.8, 71.1, 71.8 (C-2,4,5,6,2′,3′,4′,5′,6′,7′,2″,3″,4″,5″,6″, OCH_2CH_2), 74.4 (C-3), 97.8, 98.1 (C-1,1″), 102.3 (C-1′), 121.3–136.7 (arom.), 165.1, 165.4, 165.5, 166.2, 167.9 (C_6H_5CO, $COCH_2Cl$), 170.3, 170.4, and 170.7 (CH_3CO).

Anal. Calc. for $C_{81}H_{77}ClF_3NO_{30}$: C, 59.4; H, 4.7. Found: C, 59.3; H, 4.9.

2-(4-Trifluoroacetamidophenyl) ethyl O-(L-glycero-α-D-manno-*heptopyranosyl*)-

(1→7)-O-(L-glycero-α-D-manno-*heptopyranosyl)-(1→3)*-L-glycero-α-D-manno-*heptopyranoside* (**15**). — A solution of **14** (30 mg) in methanol (2 mL) was treated with methanolic M sodium methoxide (0.2 mL). When t.l.c. (12:3:3:2 ethyl acetate–methanol–acetic acid–water) indicated complete deacylation (3 h), the base was neutralized with Dowex 50 (H^+) cation-exchange resin. After filtration and concentration, the residue was purified by gel filtration on a column of Bio-Gel P-2 eluted with water to give **15** (13.5 mg, 91%), $[\alpha]_D$ +86° (*c* 0.5, water); ^{13}C-n.m.r. (D_2O): δ 35.6 (CH_2CH_2Ph), 63.9, 64.1 (C-7,7″), 66.5, 66.9, 67.0, 68.0, 68.4, 69.5, 69.6, 69.9, 70.8 (×2), 71.1, 71.4, 71.7, 72.3, 72.7, 73.0 (C-2,4,5,6,2′,3′,4′,5′,6′,7′,2″,3″,4″,5″,6″, OCH_2CH_2), 78.6 (C-3), 99.9, 100.1 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz, C-1; $J_{C\text{-}1,H\text{-}1}$ 170 HZ, C-1″), 103.2 ($J_{C\text{-}1,H\text{-}1}$ 172 Hz, C-1′), 123.0, 130.7, 133.8, and 139.3 (arom.).

Anal. Calc. for $C_{31}H_{46}F_3NO_{20}\cdot 4\,H_2O$: C, 42.2; H, 6.2. Found: C, 42.2; H, 5.9.

Methylation analysis[16,17] of **15** showed the presence of 1,5,7-tri-*O*-acetyl-2,3,4,6-tetra-*O*-methylheptitol, 1,3,5-tri-*O*-acetyl-2,4,6,7-tetra-*O*-methylheptitol, and 1,5-di-*O*-acetyl-2,3,4,6,7-penta-*O*-methylheptitol.

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