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Synthesis of C-linked analogues of β-D-galactopyranosyl-(1→3)-D-galactopyranosides and of β-D-galactopyranosyl-(1→3)-D-galactal

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Received 17 August 2004; accepted 30 September 2004
Available online 22 October 2004

Abstract—C-linked disaccharide derivatives mimicking *O*-β-D-galactopyranosyl-(1→3)-D-galactopyranosides (end groups in Core-B structures of biologically important proteoglycans) have been obtained from isolevoglucosenone and β-D-galactopyranosylcarbaldehyde derivatives. The β-D-galactopyranosyl-(1→3)-CH(OH)-D-galactal derivatives **3a** (4,6-di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptito1-1-*C*-yl]-3-deoxy-D-galactal), **3b** (4,6-di-*O*-benzyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-benzyl-D-*glycero*-L-manno-heptitol-1-*C*-yl]-3-deoxy-D-galactal) and the β-D-galactopyranosyl-(1→3)-CH_2-D-galactal **3c** (4,6-*O*-diacetyl-3-*C*-) [6-*O*-acetyl-2,3,4-tri-*O*-(*tert*-butyl)dimethylsilyl-β-D-*galacto*pyranosylmethyl]-3-deoxy-D-galactal have been prepared. One of them, **3a**, has been shown to be a suitable agent for the *O*-glycosidation and the construction of glycoconjugates bearing the β-D-Gal*p*-(1→3)-CH(OH)-D-Gal*p*-*O* moiety.

1. Introduction

Carbohydrates regulate the cell/cell[1] and cell/invader[2] interactions, and play a crucial role in the construction of multicellular organs and organisms. With a growing understanding of the precise function that cell-surface carbohydrates play in disorders such as inflammation, viral and bacterial infections, to cancer, numerous carbohydrate analogues have now been developed and entered into clinical studies.[3] Disaccharide mimetics such as C-linked disaccharides and oligosaccharides containing them offer the advantage of being resistant to acidic and enzymatic hydrolysis.[4,5] They are potential inhibitors of glycosidases and glycosyltransferases.[6] The disaccharide *O*-β-D-galactopyranosyl-(1→3)-*O*-β-D-galactopyranosyl **1** is found as an end group in Core-B structures of a large number of proteoglycans[7] and has been isolated from a variety of other sources.[8] We report herein efficient syntheses of protected forms **2** of C-linked analogues of **1**, including the β-D-galactopyranosyl-(1→3)-D-galactal derivatives **3**, compounds suitable for *O*-glycosidation[9] and for the preparation of *C*-glycosides.[10,11] An isomer of **2** (α-methyl α-galactopyranosyl, (*S*)-hydroxymethylene linker) had been prepared already in 1992 by Schmidt and Beyerbach.[12] Their method involved the direct lithiation of 3,4,6-*O*-tribenzyl 2-phenylsulfinyl-D-galactal with methyl 2,4,6-*O*-tribenzyl-3-deoxy-α-D-*galacto*pyranosyl bearing a β-carbaldehyde group at C(3). We had applied the Oshima–Nozaki coupling reaction of enones and aldehydes[13] to a 2,3,4,6-*O*-tetrabenzyl-β-D-*gluco*pyranosylcarbaldehyde and isolevoglucosenone **4**[14] and obtained 2,3-anhydro-3-*C*-[(l*S*)-2,6-anhydro-D-*glycero*-D-*gulo*-heptitol-l-*C*-yl]-β-D-*gulo*pyranose[15] and a fluorinated derivative.[16] We will show now that 2,3,4,6-*O*-tetrabenzyl-**5a** and 2,3,4,6-*O*-tetra [(*tert*-butyl)dimethylsilyl]-β-D-*galacto*pyranosylcarbaldehyde **5b**[17,18] can be condensed with isolevoglucosenone **4** (Scheme 1) to produce enones **6a** and **6b**, respectively (Baylis–Hillmann type of products) which can be readily converted into C-linked analogues of β-D-*galacto*pyranosyl-(1→3)-D-galactal derivatives **3a**–**3c**. The carbon linker is a hydroxymethylene group in **3a** and **3b**, and a methylene group in **3c**. Galactal **3b** was converted into β-D-*galacto*pyranosyl-(1→3)-CH(OH)-D-*galacto*pyranosides **2** and **17** and into β-D-*galacto*pyranosyl-(1→3)-CH(OH)-D-*talo*pyranosides **16**. Galactal **3a** was converted into β-D-*galacto*pyranosyl-(1→3)-CH(OH)-2-deoxy-D-*lyxo* pyranoside α-*O*-conjugated with L-serine **21**.

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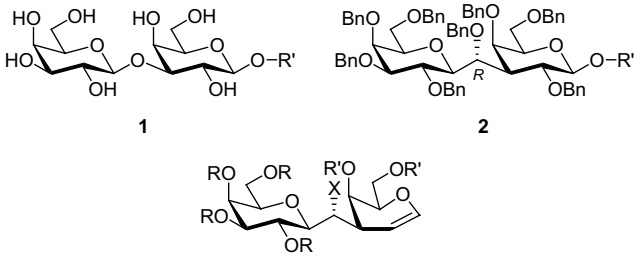
doi:10.1016/j.tetasy.2004.09.029



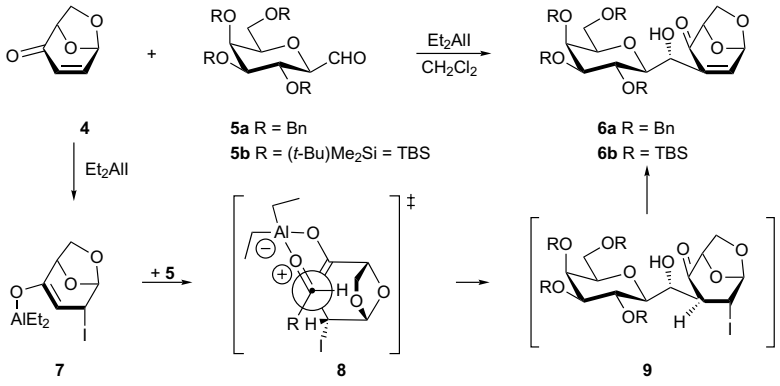
2. Results and discussion

Slow addition of Et_2AlI in solution in toluene to a mixture of **4** and aldehydes **5a** and **5b** in CH_2Cl_2 (−80 °C) led to the formation of enones **6a** and **6b** in 73% and 95% yield, respectively. These reactions imply the formation of aluminum enolate **7**, which adds to aldehydes **5a** and **5b** following the Zimmerman–Traxler model **8**[19] (steric factors control the diastereoselectivity) giving iodo-aldols **9** which are unstable and eliminate HI during aqueous work-up (Scheme 1).

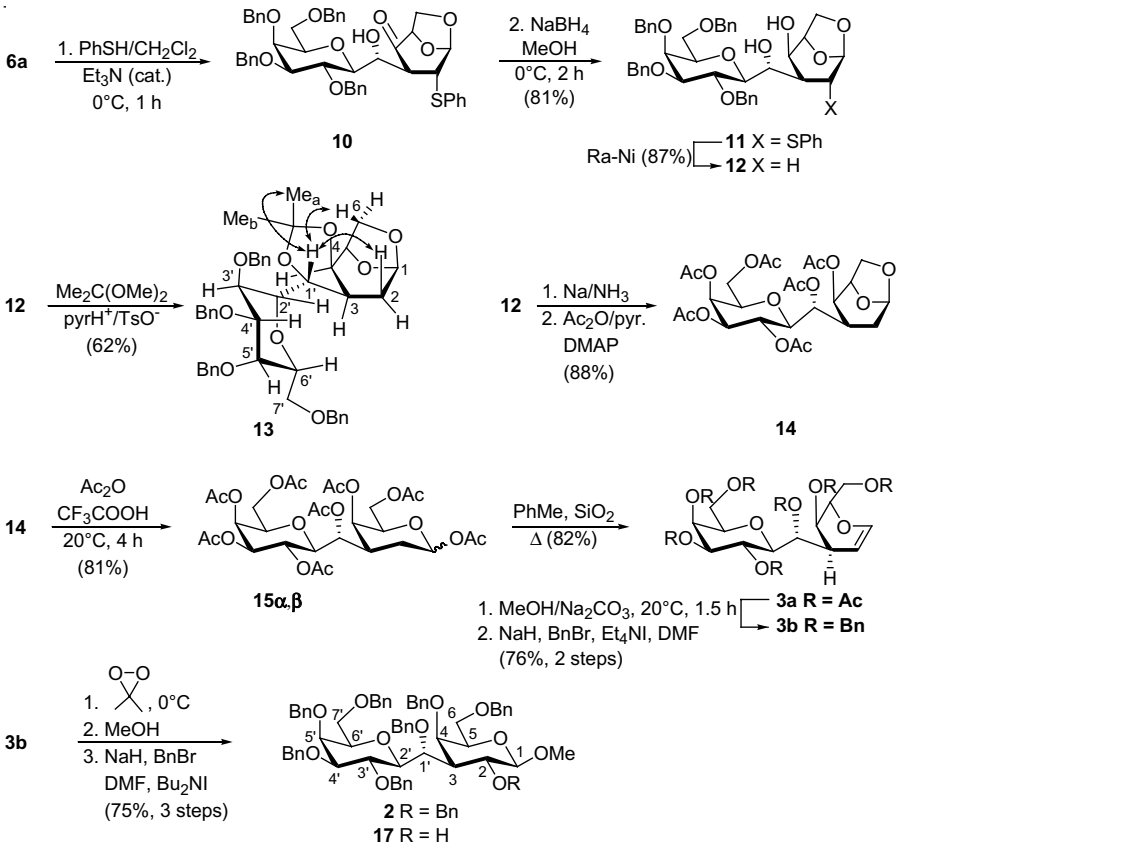
Attempts to reduce both the C=C and C=O double bonds of enones **6a** and **6b** by direct methods [$NaBH_4$, $LiAlH(t\text{-BuS})_3$, cat. hydrogenation followed by hydride reduction] led to mixtures of diastereomeric products. Addition of thiophenol to **6a** catalyzed by Et_3N generated a single adduct **10** that could not be isolated because the thiophenol was eliminated readily at 20 °C. Thus the crude adduct **10** was treated directly with $NaBH_4$ at 0 °C to produce a single diol **11** that was isolated in 81% yield.[15] Desulfurization of **11** with Raney nickel in THF gave diol **12** (87% yield). It was converted into its acetonide **13** (62%) under standard conditions. The 2-D-NOESY ^1H NMR spectrum of **13** confirmed its structure and of its precursor ($^3J_{3,4} = 8.2$ Hz). Moreover, its ^{13}C NMR spectrum showed $\delta_C(Me) = 25.5$, 27.5 ppm, typical for a 1,4-*anti*-disubstitution of the 1,3-dioxane moiety.[20] A Birch reduction of the benzyl ethers of **12**, followed by acetylation provided hexaacetate **14** in 88% yield. Treatment of **14** with Ac_2O and CF_3COOH gave a 1:0.3 mixture of α/β pyranosides **15α** and **15β**. When this mixture was heated under reflux in toluene containing silica gel, a smooth elimination of acetic acid occurred with the formation of galactal **3a** isolated in 82% yield after flash chromatography. Exchange of the acetyl groups for benzyl groups was done by treating **3a** with $MeOH/Na_2CO_3$ at 20 °C for 90 min, followed by solvent removal and reaction of the polyol with NaH in DMF and then with benzyl bromide and Bu_4Nl. This gave **3b** in 76% yield for the two steps.

Galactal **3b** reacted with dimethyldioxirane in acetone at 0 °C. The unstable intermediate epoxide (*Brigl* anhydride) reacted with MeOH to give semi-protected [free at OH at C(2)] methyl β-D-*galacto*pyranoside, which was not isolated but benzylated under standard conditions to furnish the perbenzylated *C*-disaccharide **2** (Scheme 2) in 71% yield (three steps). The ^1H NMR spectrum of **2** (vicinal H/H coupling constants) proved its structure. Interestingly, when **3b** was epoxidized with *meta*-chloroperbenzoic acid (Scheme 3), the intermediate epoxide reacted with MeOH to give the semi-protected *C*-disaccharide **16** in 52% yield together with 20% of **17** (Scheme 2). This is a C-linked analogue of (β-D-*galacto*pyranosyl) (1→3)-(methyl α-D-*talo*pyranoside). The preferred α-face epoxidation of galactal **3b** with dimethyldioxirane is to be expected for steric reasons. The preferred β-face epoxidation of **3b** with *m*-CPBA can be attributed to hydrogen bridging of the peracid with the 4- or 6-benzyloxy group. To further test the usefulness of our *C*-*galacto*pyranosyl(1→3)galactal derivatives, we reacted peracetate **3a** with *Z*-Ser-OBn and Fmoc-Ser-OBn (semiprotected forms of L-serine) in the presence of I(*sym*-collidine)$_2$$ClO_4$(Lemieux's,[21] Thiem's[22] haloglycosidations). This produced iodo-talopyranosides **18** (72%) and **19** (70%), respectively. Attempts to displace the iodide of **18** and **19** by all kinds of azides (NaN_3/DMF, LiN_3/DMF, tetramethylguadinium azide/DMF, Me_3SiN_3/Bu_4NF/THF, azidoadamantane/DMF) led to products of decomposition and/or to the α-D-*threo*-hex-2-enopyranoside **20**.[23] Radical dehalogenation[24] of **18** with Bu_3SnH/AlBN generated the 2-deoxy-α-*galacto*pyranoside **21** in 72% yield (Scheme 3).[25]

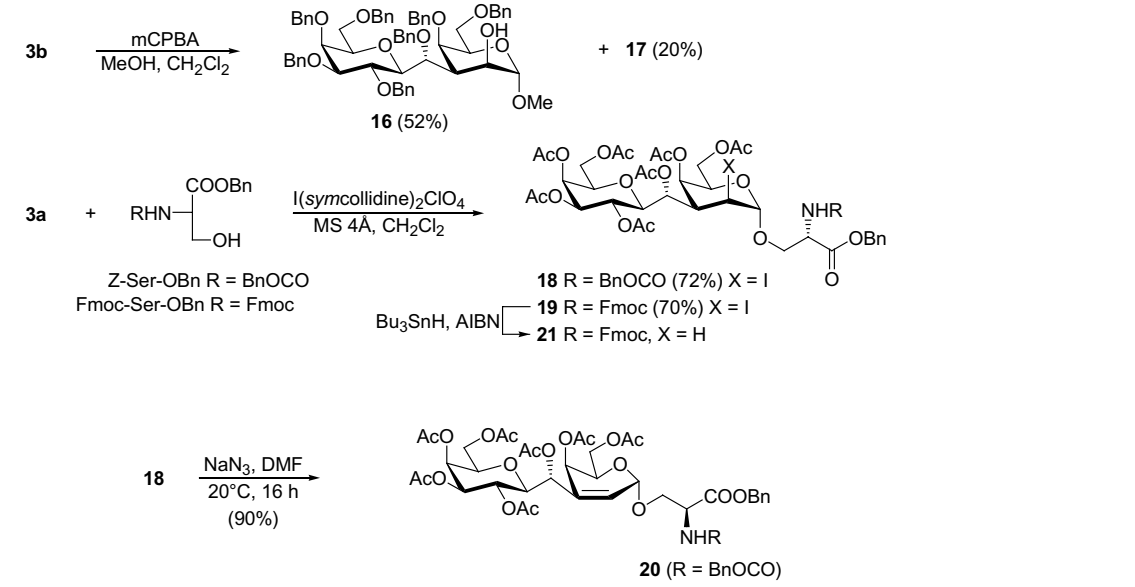
We have also explored the possibility of generating β-D-*galacto*pyranosyl-*C*(1→3)galactal, in which there is a carbon linker in a methylene rather than a hydroxymethylene group. In the presence of Raney nickel in



Scheme 1.

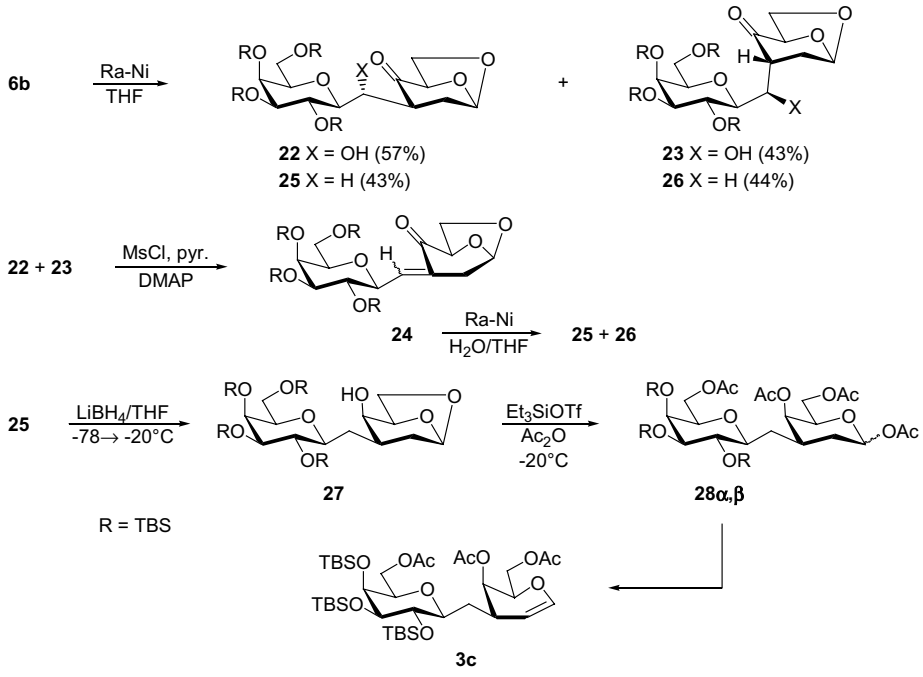


Scheme 2.



Scheme 3.

THF, the TBS-protected C-galactoside **6b** was reduced quantitatively into a mixture of aldols from which **22** and **23** were isolated (flash chromatography) in 57% and 43% yield, respectively. The crude mixture of **22** and **23** was treated with CH_3SO_2Cl/pyridine and a catalytical amount of DMAP. This led to the formation of a mixture of unstable enones **24** that were not isolated but treated with Raney nickel in aqueous THF at 20 °C. This produced a mixture of ketones from which pure **25** and **26** were isolated in 43% and 44% yield, respectively. Reduction of **25** with $LiBH_4$ in THF gave alcohol **27** in 79% yield, the structure of which (1,6-anhydro-2-deoxy-D-*lyxo* configuration) was given by its ^1H NMR spectrum. Treatment of **27** with triethylsilyl



Scheme 4.

trifluoromethanesulfonate and acetic anhydride ring-opened the 1,6-anhydro moiety and acetylated the D-lyxose derivative without formation of furanosides. The mixture of α- and β-pyranosides **28α,β** thus obtained, was not purified but directly treated with silica gel in benzene heated under reflux. This produced the C-linked analogue of β-D-*galacto*pyranosyl-(1→3)-D-galactal **3c** in 60% yield (Scheme 4).

3. Conclusion

The Oshima–Nozaki condensation of β-D-*galacto*pyranosylcarbaldehyde derivatives with isolevoglucosenone has allowed the efficient and highly stereoselective synthesis of C-linked disaccharides mimicking β-D-Gal*p*(1→3)-D-Gal*p*. Useful β-D-*galacto*pyranosyl(1→3)-CH(OH)-galactal and β-D-*galacto*pyranosyl-(1→3)-CH_2-D-galactal derivatives have been prepared and shown to be suitable for further derivatization and *O*-glycosidations.

4. Experimental

4.1. General

See Ref. 25; THF and Et_2O were distilled from sodium and benzophenone; toluene from CaH_2; MeOH from magnesium. Electrospray mass analyses were recorded on a Finnigan MAT.SSQ710C spectrometer in the positive ionization mode. High resolution FAB mass spectra were recorded on a FAB-LSIMS (University of Seville, Spain). Elemental analyses were performed by the Ilse Beetz Laboratory, Kronach, Germany. Signal assignments in ^{1}H NMR spectra are confirmed by 2D-COSY and NOESY spectra.

4.2. 1,6-Anhydro-3-*C*-[(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-β-D-*glycero*-hex-2-en-4-ulopyranose 6a

A solution of Et_2AlI (1 M) in toluene (8.5 mL, 8.5 mmol) was added dropwise in 90 min to a stirred solution of aldehyde **5**[17] (3.53 g, 6.4 mmol) and isolevoglucosenone **4** (1.21 g, 9.5 mmol) in anhydrous CH_2Cl_2 (24 mL) cooled to −80 °C under an Ar atmosphere. After stirring at −80 °C for 19 h, the cooling bath was removed and Et_2O (80 mL) and then 1 M aq HCl (60 mL) added under vigorous stirring (red mixture becomes yellowish). After the addition of H_2O (50 mL), the aqueous phase was extracted with Et_2O (3 × 50 mL). The combined organic phases were washed with brine (100 mL) and dried over $MgSO_4$. Solvent evaporation, FC (8:2 then 7:3 light petroleum/EtOAc) afforded 3.17 g (73%) of a white solid; mp 46–48 °C. $[\alpha]_{589}^{25} = +78$, $[\alpha]_{546}^{25} = +52$, $[\alpha]_{435}^{25} = +225$, $[\alpha]_{405}^{25} = +573$ (*c* 0.12, $CHCl_3$). UV (MeCN) 243 (6000), 213 (18500). IR (KBr) 3420, 3030, 2870, 1695, 1455, 1365, 1095, 910, 735, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.25 (m, 20H, ArH), 7.04 (dd, $^3J_{1,2} = 3.4$, $^4J_{1',2} = 1.4$, H-2), 5.75 (d, $^3J_{1,2} = 3.4$, H-1), 4.98–4.35 (m, 9H, 4 O–CH_2–Ph, H-1′), 4.66 (dd, $^3J_{5,6exo} = 6.1$, $^3J_{5,6endo} = 1.1$, H-5), 4.15 (dd, $^3J_{3',4'} = 9.5$, $^3J_{2',3'} = 9.5$, H-3′), 3.92–3.88 (m, 2H, H-5′, H_{exo}-6), 3.64 (dd, $^3J_{3',4'} = 9.5$, $^3J_{4',5'} = 2.7$, H-4′), 3.58 (dd, $^3J_{2',3'} = 9.5$, $^3J_{1',2'} = 1.5$, H-2′), 3.51 (dd, $^2J = 8.2$, $^3J_{5,6endo} = 1.1$, H_{endo}-6), 3.48–3.45 (m, 3H, H-6′, H_2-7′). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 194.5 (s, C-4), 142.1 (d, 165, C-2), 138.5, 138.4, 138.2, 137.8, 137.8 (5s, 4C_{arom}, C-3), 128.4–127.5 (20d, CH_{arom}), 96.8 (d, 177, C-1), 84.6 (d, 138, C-4′), 79.2 (d, 160, C-5), 79.0 (d, 141, C-2′), 77.3 (d, 143, C-6′), 75.1 (t, 142, O–CH_2–Ph), 74.5 (t, 143, O–CH_2–Ph), 74.5 (d, 142, C-3′), 74.0 (d, 144, C-5′), 73.4 (t, 141, O–CH_2–Ph), 72.4 (t, 142, O–CH_2–Ph), 69.3 (t, 142, C-7′),

66.0 (d, 147, C-1′), 62.2 (t, 154, C-6). CI-MS (NH_3) *m/z* 697 (1, $[M+18]^+$), 570 (1), 451 (1), 181 (4), 91 (71), 83 (100). Anal. Calcd for $C_{41}H_{42}O_9$: C, 72.55; H, 6.24. Found: C, 72.50; H 6.28.

4.3. 1,6-Anhydro-3-*C*-[(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-2-phenylthio-β-D-*galacto*-pyranose 11

Triethylamine (61 μL, 0.43 mmol) was added to a solution of enone **6** (1.42 g, 2.1 mmol) and thiophenol (0.24 mL, 2.3 mmol) in 9 mL of CH_2Cl_2 cooled to 0 °C. The reaction mixture was stirred at 0 °C for 1 h at which point 9 mL of MeOH and 164 mg of $NaBH_4$ (4.3 mmol) were added and the reaction mixture stirred for 2 h at 0 °C. Then, CH_2Cl_2 (30 mL) and 1 M aq HCl (6 mL) were added under stirring. After the addition of H_2O (30 mL), the aqueous phase was extracted with CH_2Cl_2 (3×20 mL). The combined organic phases were washed with a satd aq soln of $NaHCO_3$ (40 mL), brine (40 mL) and dried over $MgSO_4$. Solvent evaporation, FC (7:3 light petroleum ether/EtOAc) afforded 1.33 g (81%) of **11**, colorless oil. $[\alpha]_{589}^{25} = -15$, $[\alpha]_{546}^{25} = -19$, $[\alpha]_{435}^{25} = -34$, $[\alpha]_{405}^{25} = -42$ (*c* 0.27, $CHCl_3$). UV (MeCN) 255 (8300), 216 (18600). IR (film) 3375, 3030, 2870, 1455, 1365, 1210, 1115, 910, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.18 (m, 25H, ArH), 5.60 (s, H-1), 4.95–4.39 (m, 8H, 4 OCH_2Ph), 4.57–4.52 (m, 2H, H-1′, H–C4), 4.36 (dd, $^3J_{5,6exo} = 5.3$, $^3J_{4,5} = 5.3$, H-5), 4.17 (d, $^2J = 7.7$, H_{endo}-6), 4.03 (dd, $^3J_{3',4'} = 9.4$, $^3J_{2',3'} = 9.4$, H-3′), 3.87 (d, $^3J_{4',5'} = 2.5$, H-5′), 3.53 (dd, $^2J = 7.7$, $^3J_{5,6exo} = 5.3$, H_{exo}-6), 3.51 (dd, $^3J_{3',4'} = 9.4$, $^3J_{4',5'} = 2.5$, H-4′), 3.38–3.36 (m, 2H, H_2-7′), 3.29–3.27 (m, 2H, H-2, H-6′), 3.07 (d, $^3J_{2',3'} = 9.4$, H-2′), 2.20–2.15 (m, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.4, 138.2, 137.9, 137.5, 134.6 (5s, 5 C_{arom}), 132.3–127.4 (25d, CH_{arom}), 102.9 (d, 177, C-1), 84.6 (d, 137, C-4′), 79.2 (d, 141, C-2′), 76.6 (d, 145, C-6′), 75.7 (t, 142, OCH_2Ph), 74.8 (d, 158, C-5), 74.4 (t, 145, OCH_2Ph), 74.2 (d, 142, C-3′), 73.6 (t, 141, OCH_2Ph), 73.2 (d, 143, C-5′), 72.4 (t, 142, OCH_2Ph), 69.9, 67.2 (2d, 147, 149, C-1′, C-4), 68.5 (t, 144, C-7′), 62.9 (t, 152, C-6), 50.8 (d, 144, C-2), 41.4 (d, 131, C-3). CI-MS (NH_3) *m/z* 792 (4, $[M+1]^+$), 682 (4), 593 (3), 399 (3), 253 (4), 181 (8), 91 (100). Anal. Calcd for $C_{47}H_{50}O_9S$: C, 71.37; H, 6.37. Found: C, 71.38; H, 6.42.

4.4. 1,6-Anhydro-3-*C*-[(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-β-D-*lyxo*-hexopyranose 12

A solution of **11** (935 mg, 1.18 mmol) in THF (70 mL) was treated with Raney nickel (~7 g) and the suspension stirred for 1 h at 20 °C. When the reaction was complete (TLC 1:1 light petroleum ether/EtOAc), the solid was filtered off and washed with EtOAc. The filtrate and the washing were combined and dried over $MgSO_4$. Solvent evaporation, FC (3:2 light petroleum ether/EtOAc) afforded 701 mg (87%) of **12**, colorless oil. $[\alpha]_{589}^{25} = +3$, $[\alpha]_{546}^{25} = -7$, $[\alpha]_{435}^{25} = -9$, $[\alpha]_{405}^{25} = -12$ (*c* 0.15, $CHCl_3$). UV (MeCN) 210 (15300). IR (film) 3390, 3030, 2870, 1455, 1360, 1210, 1105, 865, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 20H, ArH), 5.43 (br s, H-1), 4.92–4.42 (m, 8H, 4OCH_2Ph), 4.40 (br dd, $^3J_{4,5} = 5.2$, $^3J_{5,6exo} = 4.8$, H-5), 4.35 (d, $^3J_{1',3} = 10.1$, H-1′), 4.28 (br dd, $^3J_{3,4} = 6.2$, $^3J_{4,5} = 5.2$, H-4), 4.18 (d, $^2J = 7.9$, H_{endo}-6), 4.08 (dd, $^3J_{3',4'} = 9.4$, $^3J_{2',3'} = 9.4$, H-3′), 3.94 (d, $^3J_{4',5'} = 2.3$, H-5′), 3.64–3.50 (m, 5H, H-4′, H-6′, H_{exo}-6, H_2-7′), 3.35 (d, $^3J_{2',3'} = 9.4$, H-2′), 2.31 (dddd, $^3J_{1',3} = 10.1$, $^3J_{2endo,3} = 7.2$, $^3J_{3,4} = 6.2$, $^3J_{2exo,3} = 3.6$, H-3), 1.81 (ddd, $^2J = 14.7$, $^3J_{2endo,3} = 7.2$, $^3J_{1,2endo} = 2.4$, H_{endo}-2), 1.66 (br dd, $^2J = 14.7$, $^3J_{2exo,3} = 3.6$, H_{exo}-2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.5, 138.2, 138.1, 137.7 (4s, 4C_{arom}), 128.5–127.5 (20d, CH_{arom}), 99.9 (d, 169, C-1), 84.6 (d, 137, C-4′), 78.4 (d, 142, C-2′), 77.0 (d, 143, C-6′), 75.5 (t, 145, OCH_2Ph), 75.3 (d, 157, C-5), 74.4 (t, 144, OCH_2Ph), 74.1 (d, 147, C-3′), 73.6 (t, 142, OCH_2Ph), 73.5 (d, 142, C-5′), 72.4 (t, 141, OCH_2Ph), 71.2 (d, 148, C-1′), 69.3 (d, 147, C-4), 68.9 (t, 144, C-7′), 63.9 (t, 151, C-6), 35.1 (d, 132, C-3), 32.2 (t, 128, C-2). CI-MS (NH_3) *m/z* 701 (3, $[M+18]^+$), 684 (2, $[M+1]^+$), 633 (2), 581 (1), 485 (1), 181 (8), 91 (100). Anal. Calcd for $C_{41}H_{46}O_9$: C, 72.11; H, 6.79. Found: C, 72.16; H, 6.77.

4.5. 1,6-Anhydro-3-*C*-[(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-β-D-*lyxo*-hexopyranose-1′,4-acetonide 13

A mixture of **12** (47 mg, 0.07 mmol), 2,2-dimethoxypropane (1.3 mL), dry acetone (1.3 mL) and PPTS (13 mg) was stirred at 20 °C for 2 h. After the addition of CH_2Cl_2 (10 mL) and H_2O (20 mL), the aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were washed with a satd aq soln of $NaHCO_3$ (20 mL), brine (20 mL) and dried over $MgSO_4$. Solvent evaporation, FC (8:2 light petroleum ether/EtOAc) afforded 31 mg (62%) of **13**, colorless oil. $[\alpha]_{589}^{25} = +1$, $[\alpha]_{546}^{25} = +3$, $[\alpha]_{435}^{25} = +5$, $[\alpha]_{405}^{25} = +8$ (*c* 0.24, $CHCl_3$). UV (MeCN) 212 (15400). IR (film) 3030, 2865, 1495, 1455, 1365, 1210, 1135, 1100, 1030, 910, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 20H, ArH), 5.48 (d, $^3J_{1,2exo} = 4.0$, H-1), 5.03–4.44 (m, 8H, 4OCH_2Ph), 4.51 (br dd, $^3J_{4,5} = 6.4$, $^3J_{5,6exo} = 5.7$, H-5), 4.43 (br dd, $^3J_{3,4} = 8.2$, $^3J_{4,5} = 6.4$, H-4), 4.29 (d, $^2J = 7.7$, H_{endo}-6), 4.14 (dd, $^3J_{3',4'} = 9.4$, $^3J_{2',3'} = 9.4$, H-3′), 4.11 (dd, $^3J_{1',3} = 11.2$, $^3J_{1',2'} = 2.1$, H-1′), 3.97 (d, $^3J_{4',5'} = 2.2$, H-5′), 3.63–3.57 (m, 4H, H-4′, H_{exo}-6, H_2-7′), 3.26 (m, H-6′), 3.25 (dd, $^3J_{2',3'} = 9.4$, $^3J_{1',2'} = 2.1$, H-2′), 2.58 (dddd, $^3J_{1',3} = 11.2$, $^3J_{2exo,3} = 9.6$, $^3J_{3,4} = 8.2$, $^3J_{2endo,3} = 5.0$, H-3), 1.90 (ddd, $^2J = 14.8$, $^3J_{2exo,3} = 9.6$, $^3J_{1,2exo} = 4.0$, H_{exo}-2), 1.44 (dd, $^2J = 14.8$, $^3J_{2endo,3} = 5.0$, H_{endo}-2), 1.41 (s, 3H, H_b-3), 1.31 (s, 3H, H_a-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.9, 138.9, 138.3, 138.0 (4s, 4C_{arom}), 128.4–127.3 (20d, CH_{arom}), 100.6 (s, Cacetonide), 99.9 (d, 170, C-1), 85.5 (d, 137, C-4′), 77.7, 77.7 (2d, 140, 140, C-2′, C-6′), 74.8 (t, 145, OCH_2Ph), 74.2 (d, 147, C-3′), 74.1 (t, 146, OCH_2Ph), 73.6 (d, 150, C-5′), 73.5 (t, 141, OCH_2Ph), 72.2 (t, 141, OCH_2Ph), 72.0 (d, 155, C-5), 69.8 (d, 145, C-1′), 69.1 (t, 145, C-7′), 65.2 (d, 148, C-4), 62.9 (t, 150, C-6), 30.7 (t, 127, C-2), 28.4 (d, 134, C-3), 27.5 (q, 129, Me(b)acetonide), 25.5 (q, 126, Me(a)acetonide). CI-MS (NH_3) *m/z* 741 (28, $[M+18]^+$), 573 (7), 181 (7), 91 (100). Anal. Calcd for $C_{44}H_{50}O_9$: C, 73.11; H, 6.97. Found: C, 73.09; H, 7.04.

4.6. 4-*O*-Acetyl-1,6-anhydro-3-*C*-[(1*R*)-1,3,4,5,7-penta-O-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-β-D-*lyxo*-hexopyranose 14

Metallic Na (530 mg, 23 mmol) was added to liquid NH_3 (30 mL, condensed at −78 °C). A solution of **12** (642 mg, 0.94 mmol) in anhydrous THF (8 mL) was added dropwise under stirring. After stirring at −78 °C for 40 min, solid NH_4Cl (1.3 g) was added and the cooling bath removed. Once at 20 °C, the residue was taken in MeOH and purified by FC (2:1 CH_2Cl_2/MeOH) affording an oil that was mixed with Ac_2O (6 mL), pyridine (9 mL), 4-dimethylaminopyridine (0.5 mg) and stirred at 20 °C for 15 h. Solvent evaporation in vacuo gave a residue, which was taken in toluene (10 mL) and the solvent evaporated to dryness in vacuo. The latter operation was repeated and the residue purified by FC (1:1 light petroleum ether/EtOAc) affording 475 mg (88%, two steps), white solid, mp 84–86 °C. $[\alpha]_{589}^{25} = +24$, $[\alpha]_{546}^{25} = +28$, $[\alpha]_{435}^{25} = +46$, $[\alpha]_{405}^{25} = +57$ (*c* 0.28, $CHCl_3$). UV (MeCN) final absorbance: 194 (ε = 1500). IR (KBr) 3470, 2975, 1750, 1375, 1245, 1120, 1085, 1050, 1030, 945, 910, 595 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.58 (d, $^3J_{1,2endo} = 5.7$, H-1), 5.41 (d, $^3J_{4',5'} = 3.4$, H-5′), 5.27 (dd, $^3J_{1',3} = 10.6$, $^3J_{1',2'} = 2.2$, H-1′), 5.14 (dd, $^3J_{3',4'} = 10.0$, $^3J_{2',3'} = 9.9$, H-3′), 5.11 (m, H-4), 5.01 (dd, $^3J_{3',4'} = 10.0$, $^3J_{4',5'} = 3.4$, H-4′), 4.80 (dd, $^3J_{4,5} = 7.8$, $^3J_{5,6exo} = 4.7$, H-5), 4.21 (dd, $^2J = 11.4$, $^3J_{6',7'a} = 7.5$, H_a-7′), 4.08 (dd, $^2J = 11.4$, $^3J_{6',7'b} = 5.7$, H_b-7′), 3.85 (m, H-6′), 3.84 (d, $^2J = 7.7$, H_{endo}-6), 3.52 (dd, $^3J_{2',3'} = 9.9$, $^3J_{1',2'} = 2.2$, H-2′), 3.43 (dd, $^2J = 7.7$, $^3J_{5,6exo} = 4.7$, H_{exo}-6), 2.49 (dddd, $^3J_{2,3endo} = 11.7$, $^3J_{1',3} = 10.6$, $^3J = 6.5$, $^3J = 5.2$, H-3), 2.18–1.97 (19H, H_{exo}-2, 6 MeCOO), 1.53 (dd, $^2J = 13.2$, $^3J_{2endo,3} = 11.7$, H_{endo}-2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.8, 170.2, 170.1, 170.0, 169.6, 169.5 (6s,-COO), 98.3 (d, 174, C-1), 76.9 (d, 142, C-2′), 75.3 (d, 141, C-6′), 72.6 (d, 148, C-4′), 72.2 (d, 158, C-5), 68.4 (d, 154, C-4), 68.0 (d, 149, C-1′), 67.4 (d, 153, C-5′), 64.6 (d, 156, C-3′), 62.7 (t, 152, C-6), 61.6 (t, 149, C-7′), 30.9 (t, 129, C-2), 30.5 (d, 133, C-3), 20.7–20.5 (6q, 130, *C*H_3COO). CI-MS (NH_3) *m/z* 592 (100, $[M+18]^+$), 515 (35). Anal. Calcd for $C_{25}H_{34}O_{15}$: C, 52.26; H, 5.96. Found: C, 52.19; H, 6.00.

4.7. 1,4,6-Tri-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-α-D-*lyxo*-hexopyranose 15α,β

A mixture of **14** (445 mg, 0.77 mmol), Ac_2O (16 mL) and CF_3COOH (3.8 mL) was stirred at 20 °C for 4 h. This was poured onto ice (20 mL) and neutralized with a satd aq soln of $NaHCO_3$ (pH 8). The mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (50 mL) and dried over $MgSO_4$. Solvent evaporation, FC (1:2 light petroleum ether/EtOAc) afforded 422 mg (81%) of a colorless oil, a 1:0.3 mixture of **15α/15β**. $[\alpha]_{589}^{25} = +51$, $[\alpha]_{546}^{25} = +59$, $[\alpha]_{435}^{25} = +98$, $[\alpha]_{405}^{25} = +118$ (*c* 0.26, $CHCl_3$). UV (MeCN) final absorbance: 194 (ε = 1800). IR (film) 2970, 1750, 1435, 1370, 1235, 1115, 1055, 940, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) data for the anomer **15α**: δ 6.27 (d, $^3J_{1,2ax} = 1.8$, H-1), 5.44 (d, $^3J_{4',5'} = 3.1$, H-5′), 5.17 (dd, $^3J_{3',4'} = 9.9$, $^3J_{2',3'} = 9.9$, H-3′), 5.15–4.97 (m, 3H, H-1′, H-4, H-4′), 4.26–3.80 (m, 6H, H-5, H-6′, H_2-6, H_2-7′), 3.59 (dd, $^3J_{2',3'} = 9.9$, $^3J_{1',2'} = 2.4$, H-2′), 2.79 (m, H-3), 2.17–1.97 (25H, H_{ax}-2, 8 MeCOO), 1.69 (dd, $^2J = 13.0$, $^3J_{2eq,3} = 3.3$, H_{eq}-2). For the anomer **15β**: δ 5.76 (dd, $^3J_{1,2ax} = 9.8$, $^3J_{1,2eq} = 2.5$, H-1), 5.41 (d, $^3J_{4',5'} = 3.2$, H-5′), 2.58 (m, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) data for the anomer **15α**: δ 170.5–168.8 (8s, –COO), 91.1 (d, 174, C-1), 76.2 (d, 138, C-2′), 75.1 (d, 141, C-6′), 72.6 (d, 148, C-4′), 70.5 (d, 144, C-5), 67.8, 64.1 (2d, 147, 157, C-1′, C-4), 67.1 (d, 154, C-5′), 64.5 (d, 156, C-3′), 63.2, 60.7 (2t, 150, 153, C-6, C-7′), 33.3 (d, 134, C-3), 26.0 (t, 130, C-2), 20.9–20.5 (8q, 130, *C*H_3COO). For the anomer **15β**: δ 93.1 (d, 165, C-1), 37.9 (d, 128, C-3), 27.5 (t, 130, C-2). CI-MS (NH_3) *m/z* 695 (76, $[M+18]^+$), 634 (65), 617 (100), 556 (10), 496 (20). Anal. Calcd for $C_{29}H_{40}O_{18}$: C, 51.48; H, 5.96. Found: C, 51.47; H, 6.08.

4.8. 4,6-Di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-3-deoxy-D-galactal 3a

A mixture of **15α,β** (354 mg, 0.52 mmol) and silica gel (1.2 g) in toluene (13 mL) was heated under reflux for 6 h in a flask equipped with a Dean–Stark apparatus. After cooling to 20 °C and evaporation of the solvent, a FC (1:1 light petroleum ether/EtOAc) afforded 263 mg (82%) of **3a**, white solid, mp 83–85 °C. $[\alpha]_{589}^{25} = +17$, $[\alpha]_{546}^{25} = +21$, $[\alpha]_{435}^{25} = +30$, $[\alpha]_{405}^{25} = +32$ (*c* 0.25, $CHCl_3$). UV (MeCN) final absorbance: 204 (ε = 8800). IR (KBr) 1750, 1650, 1435, 1370, 1240, 1055 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.51 (dd, $^3J_{1,2} = 6.3$, $^4J_{1,3} = 2.5$, H-1), 5.43 (d, $^3J_{4',5'} = 3.3$, H-5′), 5.29 (d, $^3J_{3,4} = 3.1$, H-4), 5.13 (dd, $^3J_{3',4'} = 9.6$, $^3J_{2',3'} = 9.6$, H-3′), 5.12 (m, H-1′), 5.03 (dd, $^3J_{3',4'} = 9.6$, $^3J_{4',5'} = 3.3$, H-4′), 4.49 (br d, $^3J_{1,2} = 6.3$, H-2), 4.24–4.07 (m, 4H, H-5, H_a-6, H_2-7′), 3.99 (dd, $^2J = 10.3$, $^3J_{5,6b} = 6.2$, H_b-6), 3.89 (dd, $^3J_{6',7'a} = 7.0$, $^3J_{6',7'b} = 6.2$, H-6′), 3.71 (dd, $^3J_{2',3'} = 9.6$, $^3J_{1',2'} = 2.4$, H-2′), 3.19 (br d, $^3J_{1',3} = 10.7$, H-3), 2.18, 2.08, 2.06, 2.05, 2.04, 1.99, 1.97 (7s, 21H, 7 MeCOO). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.0–169.5 (7s, –COO), 145.0 (d, 190, C-1), 96.5 (d, 165, C-2), 76.4 (d, 146, C-2′), 75.4 (d, 143, C-6′), 74.7 (d, 146, C-5), 72.8 (d, 148, C-4′), 67.7, 64.7 (2d, 150, 155, C-1′, C-3′), 67.5 (d, 153, C-5′), 63.4 (t, 148, C-6), 63.2 (d, 152, C-4), 62.5 (t, 150, C-7′), 36.0 (d, 130, C-3), 20.9–20.5 (7q, 130, 7 MeCOO). CI-MS (NH_3) *m/z* 634 (100, $[M+18]^+$), 617 (43, $[M+1]^+$), 557 (18), 496 (34). Anal. Calcd for $C_{27}H_{36}O_{16}$: C, 52.60; H, 5.89. Found: C, 52.53; H, 5.92.

4.9. 4,6-Di-*O*-benzyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-benzyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-3-deoxy-D-galactal 3b

To a solution of **3a** (850 mg, 1.37 mmol) in MeOH (35 mL) was added Na_2CO_3 (830 mg, 7.8 mmol). The reaction mixture was stirred at 20 °C for 1.5 h, filtrated, and the solvent evaporated. The crude polyol dissolved in anhyd DMF (12 mL) was added dropwise at 0 °C to a suspension of NaH (0.7 g, 15 mmol, 55% dispersion in paraffin) in DMF (5 mL). After 20 min, benzyl bro-

mide (1.5 mL, 13 mmol) in DMF (2.5 mL) and tetrabutylammonium iodide (30 mg) were added. The reaction mixture was brought to 20 °C and stirred for 15 h. After completion of the reaction, the mixture was cooled to 0 °C, quenched with H_2O (50 mL) and extracted with Et_2O (3 × 50 mL). The combined organic phases were washed with brine (3 × 50 mL) and dried over $MgSO_4$. Solvent evaporation, FC (9:1 then 8.5:1.5 light petroleum/EtOAc) afforded 994 mg (76%, 2 steps) of **3b**, colorless oil. $[\alpha]_{589}^{25} = -2.0$, $[\alpha]_{546}^{25} = -3.5$, $[\alpha]_{435}^{25} = -12$, $[\alpha]_{405}^{25} = -19$ (*c* 0.26, $CHCl_3$). UV (MeCN) 258 (2000), 217 (16700). IR (film) 3065, 3030, 2865, 1650, 1495, 1455, 1360, 1250, 1095, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.02 (m, 35H, ArH), 6.39 (dd, $^3J_{1,2} = 6.2$, $^4J_{1,3} = 2.5$, H-1), 4.97–4.31 (m, 14H, 7 OCH_2Ph), 4.45 (d, $^3J_{1,2} = 6.2$, H-2), 4.29 (dd, $^3J_{1',3} = 10.3$, $^3J_{1',2'} = 2.3$, H-1′), 4.22 (dd, $^3J_{3',4'} = 9.5$, $^3J_{2',3'} = 9.5$, H-3′), 4.04 (br t, $^3J_{5,6a} = 6.4$, $^3J_{5,6b} = 6.4$, H-5), 4.00 (d, $^3J = 2.2$, H-5′), 3.96 (br s, H-4), 3.67–3.50 (m, 6H, H-4′, H_2-7′, H-2′, H_a-6, H-6′), 3.38 (dd, $^2J = 9.5$, $^3J_{5,6b} = 6.4$, H_b-6), 3.26 (br d, $^3J_{1',3} = 10.3$, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 144.1 (d, 188, C-1), 139.2, 139.0, 138.6, 138.5, 138.4, 137.9, 137.9 (7s, $7C_{arom}$), 128.4–127.0 (35d, CH_{arom}), 98.3 (d, 162, C-2), 84.8 (d, 138, C-4′), 79.1 (d, 138, C-2′), 77.2 (d, 141, C-6′), 76.9 (d, 144, C-5), 75.2 (d, 147, C-3′), 75.2 (t, 144, OCH_2Ph), 74.6 (t, 139, OCH_2Ph), 74.3 (t, 144, OCH_2Ph), 74.1 (d, 143, C-5′), 73.5 (t, 137, OCH_2Ph), 73.5 (d, 147, C-1′), 73.3 (t, 141, OCH_2Ph), 72.3 (t, 137, OCH_2Ph), 70.4 (d, 145, C-4), 69.5 (t, 142, C-6), 69.0 (t, 143, C-7′), 67.1 (t, 143, OCH_2Ph), 35.0 (d, 127, C-3). CI-MS (NH_3) *m/z* 971 (3, $[M+18]^+$), 861 (5), 723 (7), 616 (4), 445 (3), 181 (7), 91 (100). Anal. Calcd for $C_{62}H_{64}O_9$: C, 78.13; H, 6.77. Found: C, 78.15; H, 6.84.

4.10. Methyl 2,4,6-tri-*O*-benzyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-benzyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-3-deoxy-β-D-*galacto*-pyranoside 2

Galactal **3a** (90 mg, 0.09 mmol) was dissolved in 1.8 mL of CH_2Cl_2, and the resulting solution was cooled to 0 °C. A solution of dimethyldioxirane (~0.05 M in acetone, 3.5 mL, 0.17 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h, until TLC indicated complete consumption of the glycal. The solution was evaporated with a stream of dry N_2 and the residue dried in vacuo to afford the 1,2-anhydro sugar. The 1,2-anhydro sugar was dissolved in 2.0 mL of anhydrous MeOH, and 300 μL of CH_2Cl_2 and the solution stirred at 20 °C for 4.5 h. The MeOH was removed in vacuo to afford methyl glycoside **17**. A part of the crude methyl glycoside (33 mg, 0.03 mmol) dissolved in anhydrous DMF (0.3 mL) was added dropwise at 0 °C to a suspension of NaH (9 mg, 0.2 mmol, 55% dispersion in paraffin) in DMF (0.2 mL). After 20 min, benzyl bromide (16 μL, 0.14 mmol) in DMF (0.1 mL) and tetrabutylammonium iodide (2 mg) were added. The reaction mixture was brought to 20 °C and stirred for 15 h. After completion of the reaction, the mixture was cooled to 0 °C, quenched with H_2O (10 mL), and extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with brine (3 × 10 mL) and dried over $MgSO_4$. Solvent evaporation, FC (8:2 light petroleum/EtOAc) afforded 26 mg (71%, 3 steps) of **2**, colorless oil. $[\alpha]_{589}^{25} = +24$, $[\alpha]_{546}^{25} = +28$, $[\alpha]_{435}^{25} = +51$, $[\alpha]_{405}^{25} = +60$ (*c* 0.25, $CHCl_3$). UV (MeCN) 254 (2000), 216 (22000). IR (film) 3090, 3065, 3030, 2920, 2860, 1495, 1455, 1360, 1210, 1095, 990, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.08 (m, 40H, ArH), 5.00–4.32 (m, 16H, 8OCH_2Ph), 4.42 (m, H-1′), 4.32 (d, $^3J_{1,2} = 9.5$, H-1), 4.21 (dd, $^3J_{3',4'} = 9.5$, $^3J_{2',3'} = 9.5$, H-3′), 4.09 (d, $^3J_{3,4} = 1.8$, H-4), 3.89 (d, $^3J_{4',5'} = 2.3$, H-5′), 3.71–3.67 (m, 2H, H-2, H-5′), 3.66 (dd, $^3J_{2',3'} = 9.5$, $^3J_{1',2'} = 2.1$, H-2′), 3.59–3.57 (m, 3H, H_2-6, H_a-7′), 3.53 (s, 3H, OCH_3), 3.52 (m, H_b-7′), 3.42 (dd, $^3J_{3',4'} = 9.5$, $^3J_{4',5'} = 2.3$, H-4′), 3.08 (dd, $^3J_{6',7'a} = 7.4$, $^3J_{6',7'b} = 5.8$, H-6′), 2.41 (dt, $^3J_{2,3} = 9.5$, $^3J_{1',3} = 9.5$, $^3J_{3,4} = 1.8$, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 139.2, 139.2, 139.1, 138.8, 138.8, 138.5, 138.2, 138.1 (8s, $8C_{arom}$), 128.4–126.8 (40d, CH_{arom}), 106.8 (d, 161, C-1), 84.9 (d, 135, C-4′), 81.1 (d, 141, C-2′), 77.2 (d, C-2), 76.6 (d, C-5), 76.1 (d, C-6′), 75.8 (d, C-3′), 74.9, 74.4, 74.2 (3t, 3 OCH_2Ph), 74.1, 74.05, 73.9 (3d, C-1′, C-4, C-5′), 74.0, 73.3, 73.2, 71.9, 69.7 (5t, 5 OCH_2Ph), 69.2 (t, C-6), 68.9 (t, C-7′), 56.8 (q, 142, OCH_3), 44.5 (d, 122, C-3). Electrospray-MS (+, 50:50:1 MeCN/H_2O/AcOH) *m/z* 1113.8 (17, $[M+Na]^+$), 1108.3 (53, $[M+18]^+$), 1059.4 (35).

4.11. Methyl 4,6-di-*O*-benzyl-1,3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-benzyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-3-deoxy-α-D-*talo*-pyranoside 16

Galactal **3b** (104 mg, 0.11 mmol) was dissolved in anhydrous MeOH (1 mL) and CH_2Cl_2 (30 μL) and the resulting solution cooled to 0 °C. *m*CPBA (32 mg, 0.13 mmol) was added and the reaction mixture stirred at 0 °C for 1.5 h, until TLC indicated complete consumption of the glycal. After the addition of CH_2Cl_2 (15 mL), H_2O (10 mL), and $NaHCO_3$ (10 mL), the aqueous phase was extracted with CH_2Cl_2 (15 mL, three times). The combined organic extracts were washed with brine (20 mL) and dried over $MgSO_4$. Solvent evaporation afforded a mixture of methyl glycosides. The major product **16** (52%) being the one for which epoxidation occurred on the β face was contaminated with a mixture of **17** (mixture of anomers) (20%) for which epoxidation occurred on the α face. FC (7.5:2.5 light petroleum/EtOAc) afforded 55 mg (52%) of pure **16**, colorless oil. $[\alpha]_{589}^{25} = +29$, $[\alpha]_{546}^{25} = +40$, $[\alpha]_{435}^{25} = +65$, $[\alpha]_{405}^{25} = +79$ (*c* 0.11, $CHCl_3$). UV (MeCN) 251 (2300), 215 (25400). IR (film) 3500, 3030, 2910, 2865, 1495, 1455, 1360, 1210, 1095, 1060, 910, 735, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.11 (m, 35H, ArH), 5.05–4.73 (m, 7H, OCH_2Ph), 4.69 (s, H-1), 4.68 (dd, $^3J_{1',3} = 11.1$, $^3J_{1',2'} = 2.6$, H-1′), 4.60–4.45 (m, 7H, OCH_2Ph), 4.30 (dd, $^3J_{3',4'} = 9.5$, $^3J_{2',3'} = 9.6$, H-3′), 4.05–4.02 (m, 3H, H-5′, H-5, H-4), 3.77 (dd, $^3J_{2',3'} = 9.6$, $^3J_{1',2'} = 2.6$, H-2′), 3.74–3.58 (m, 7H, H-4′, H-2, H-6′, H_2-6, H_2-7′), 3.33 (s, 3H, OCH_3), 2.82 (dt, $^3J_{1',3} = 11.1$, $^3J_{2,3} = 2.0$, $^3J_{3,4} = 2.0$, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 139.2, 139.0, 138.9, 138.4, 138.1, 138.0, 137.7 (7s, $7C_{arom}$), 128.4–127.0 (35d, CH_{arom}), 101.7 (d, 169, C-1), 84.9 (d, 139, C-4′), 78.6 (d, 141, C-2′), 77.4 (d, 144, C-6′), 75.3 (t, 143, OCH_2Ph), 75.2 (d, 141, C-3′), 74.9 (t, 142, OCH_2Ph), 74.6 (t, 141, OCH_2Ph), 74.5 (d, 142,

C-5′), 73.5, 69.9 (2d, 145, 147, C-4, C-5), 73.4 (t, 141, OCH_2Ph), 73.3 (t, 139, OCH_2Ph), 72.4 (t, 144, OCH_2Ph), 71.2 (d, 143, C-1′), 69.3, 69.2 (2t, 143, 143, C-6, C-7′), 67.9 (d, 149, C-2), 66.9 (t, 146, OCH_2Ph), 54.9 (q, 139, OCH_3), 35.0 (d, 125, C-3). CI-MS (NH_3) *m/z* 1018 (1, $[M+17]^+$), 909 (1), 723 (1), 181 (7), 91 (100).

4.12. *N*-[(Benzyloxy)carbonyl]-*O*-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-2-iodo-α-D-*talo*-pyranosyl}-L-serine phenylmethyl ester 18

A solution of galactal **3a** (44 mg, 0.071 mmol) and *Z*-Ser-OBn (30 mg, 0.091 mmol) in CH_2Cl_2 (2 mL) was stirred for 30 min at 20 °C in the presence of powdered 4 Å molecular sieves (20 mg). I(*sym*-collidine)$_2ClO_4$ (176 mg, 0.375 mmol) was added, the reaction stirred for 2 h at 20 °C and then filtered. The filtrate was washed with 10% aq soln of $Na_2S_2O_3$ (5 mL), brine (10 mL), and dried over $MgSO_4$. Solvent evaporation, FC (6:4 light petroleum/EtOAc) afforded 55 mg (72%) of **18**, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.32 (m, 10H, ArH), 5.91 (d, $^3J_{N,C^*} = 7.9$, H–N), 5.36 (dd, $^3J_{4',5'} = 2.2$, $^3J_{5',6'} = 0.9$, H-5′), 5.31–5.08 (m, 4H, 2 OCH_2Ph), 5.25 (dd, $^3J_{1',3} = 10.2$, $^3J_{1',2'} = 2.3$, H-1′), 5.20 (s, H-1), 5.07 (dd, $^3J_{3',4'} = 9.6$, $^3J_{2',3'} = 9.6$, H-3′), 5.01 (dd, $^3J_{3',4'} = 9.6$, $^3J_{4',5'} = 2.2$, H-4′), 5.00 (m, H-4), 4.59 (dt, $^3J_{C^*,N} = 7.9$, $^3J_{C^*,H2\text{-}Ser} = 2.8$, H–C*), 4.19 (dd, $^2J = 11.2$, $^3J_{6',7'a} = 8.7$, H_a-7′), 4.12 (dd, $^2J = 11.5$, $^3J_{5,6a} = 3.3$, H_a-6), 4.02–3.96 (m, 4H, H-5, H_b-7′, H_2-Ser), 3.87 (dd, $^2J = 11.5$, $^3J_{5,6b} = 8.3$, H_b-6), 3.67 (d, $^3J_{2,3} = 3.7$, H-2), 3.57–3.53 (m, 2H, H-2′, H-6′), 2.39 (ddd, $^3J_{1',3} = 10.2$, $^3J_{2,3} = 3.7$, $^3J_{3,4} = 3.0$, H-3), 2.15–1.97 (7s, 21H, 7 MeCOO). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.6, 170.5, 170.2, 170.2, 170.1, 170.1, 169.6, 169.4 (8s, –COO), 155.7 (s, HN–COO), 136.1, 135.5 (2s, $2C_{arom}$), 128.7–128.1 (10d, CH_{arom}), 102.0 (d, C-1), 75.3, 74.8 (2d, C-2′, C-6′), 72.6 (d, C-4′), 69.8 (d, C-1′), 68.3 (d, C-5), 68.2 (t, CH_2-Ser), 67.2, 67.1 (2t, $2OCH_2Ph$), 67.0 (d, C-5′), 64.4 (d, C-3′), 63.0 (t, C-6), 62.5 (d, C-4), 60.1 (t, C-7′), 54.3 (d, C*), 35.3 (d, C-3), 20.8–20.3 (7q, 1d, *C*H_3COO, C-2). Electrospray-MS (+, 50:50:1 MeCN/H_2O/AcOH) *m/z* 1089.5 (40, $[M+18]^+$), 1072.1 (100, $[M]^+$), 743.4 (15).

4.13. *N*-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-*O*-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-2-iodo-α-D-*talo*-pyranosyl}-L-serine phenylmethyl ester 19

A solution of galactal **3a** (94 mg, 0.15 mmol) and Fmoc-Ser-OBn (81 mg, 0.19 mmol) in CH_2Cl_2 (4.3 mL) was stirred for 30 min at 20 °C in the presence of powdered 4 Å molecular sieves (30 mg). I(*sym*-collidine)$_2ClO_4$ (350 mg, 0.75 mmol) was added, the reaction stirred 2 h at 20 °C and then filtered. The filtrate was washed with a 10% aq soln of $Na_2S_2O_3$ (10 mL), brine (20 mL) and dried over $MgSO_4$. Solvent evaporation, FC (5:5 light petroleum/EtOAc) afforded 120 mg (70%) of **19**, white solid, mp 87–90 °C. $[\alpha]_{589}^{25} = +45$, $[\alpha]_{546}^{25} = +54$, $[\alpha]_{435}^{25} = +92$, $[\alpha]_{405}^{25} = +109$ (*c* 0.19, $CHCl_3$). UV (MeCN) 299 (7500), 288 (6600), 265 (22400), 209 (49200). IR (KBr) 3400, 2965, 1750, 1520, 1370, 1235, 1055, 740, 595 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.31 (m, 13H, ArH), 6.05 (d, $^3J_{N,C^*} = 7.7$, H–N), 5.38 (dd, $^3J_{4',5'} = 3.2$, $^3J_{5',6'} = 1.0$, H-5′), 5.32–5.16 (m, 2H, OCH_2Ph), 5.27 (dd, $^3J_{1',3} = 12.0$, $^3J_{1',2'} = 1.9$, H-1′), 5.23 (s, H-1), 5.10 (dd, $^3J_{3',4'} = 9.7$, $^3J_{2',3'} = 9.7$, H-3′), 5.03 (dd, $^3J_{3',4'} = 9.7$, $^3J_{4',5'} = 3.2$, H-4′), 5.02 (d, $^3J_{3,4} = 2.8$, H-4), 4.61 (dt, $^3J_{C^*,N} = 7.7$, $^3J_{C^*,H2\text{-}Ser} = 2.8$, H–C*), 4.41–4.38 (m, 2H, H_2-Fmoc), 4.26–4.23 (m, 2H, H-Fmoc), H_a-7′, 4.10–3.95 (m, 5H, H_a-6, H_b-7′, H_2-Ser, H-5), 3.88 (dd, $^2J = 11.4$, $^3J_{5,6b} = 8.2$, H_b-6), 3.68 (d, $^3J_{2,3} = 3.9$, H-2), 3.56 (dd, $^3J_{2',3'} = 9.7$, $^3J_{1',2'} = 1.9$, H-2′), 3.55 (m, H-6′), 2.44 (ddd, $^3J_{1',3} = 12.0$, $^3J_{2,3} = 3.9$, $^3J_{3,4} = 2.8$, H-3), 2.15, 2.07, 2.06, 2.03, 1.99, 1.98, 1.97 (7s, 21H, 7 MeCOO). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.6–169.4 (8s, –COO), 155.8 (s, HN–COO), 143.8, 143.8, 141.3, 141.3, 135.4 (5s, $5C_{arom}$), 128.7–120.0 (13d, CH_{arom}), 102.2 (d, 175, C-1), 75.3 (d, 140, C-2′), 74.9 (d, 141, C-6′), 72.6 (d, 148, C-4′), 69.9 (d, 152, C-1′), 68.4 (d, 146, C-5), 68.4 (t, 148, CH_2-Ser), 67.3, 67.3 (2t, 149, OCH_2Ph, CH_2-Fmoc), 67.1 (d, 152, C-5′), 64.5 (d, 155, C-3′), 63.0 (t, 150, C-6), 62.5 (d, 150, C-4), 60.2 (t, 149, C-7′), 54.4 (d, 140, C*), 47.0 (d, 133, CH-Fmoc), 35.4 (d, 128, C-3), 20.8–20.4 (7q, 1d, 130, *C*H_3COO, C-2). Electrospray-MS (+, 50:50:1 MeCN/H_2O/AcOH) *m/z* 1182 (20, $[M+Na]^+$), 1159 (100, $[M]^+$). Anal. Calcd for $C_{52}H_{58}O_{21}NI$: C, 53.85; H, 5.04. Found: C, 53.93; H, 5.02.

4.14. *N*-[(Benzyloxy)carbonyl]-*O*-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-α-D-*threo*-hex-2-eno-pyranosyl}-L-serine phenylmethyl ester 20

Glycoconjugate **18** (7.5 mg, 0.007 mmol) was dissolved in DMF_{d7} (350 μL, reaction followed by ^{1}H NMR) and NaN_3 (1.6 mg, 0.025 mmol) then added. After 16 h at 20 °C, only one product formed cleanly (by ^{1}H NMR). Evaporation and FC (5:5 light petroleum/EtOAc) afforded 7 mg (90%) of **20**, white solid, mp 52–55 °C. $[\alpha]_{589}^{25} = -42$, $[\alpha]_{546}^{25} = -43$, $[\alpha]_{435}^{25} = -81$, $[\alpha]_{405}^{25} = -104$ (*c* 0.094, $CHCl_3$). UV (MeCN) 262 (9000), 197 (17200). IR (KBr) 2975, 1750, 1370, 1230, 1050, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (m, 10H, ArH), 5.84 (d, $^3J_{N,C^*} = 8.8$, H–N), 5.80 (d, $^3J_{1,2} = 2.4$, H-2), 5.45 (d, $^3J_{4,5} = 1.1$, H-4), 5.41 (d, $^3J_{4',5'} = 3.0$, H-5′), 5.30–5.25 (m, 2H, H-1′, H-3′), 5.24–5.12 (m, 4H, OCH_2Ph), 5.02–4.99 (m, 2H, H-1, H-4′), 4.60 (dt, $^3J_{C^*,N} = 8.8$, $^3J_{C^*,H2\text{-}Ser} = 2.8$, H–C*), 4.18–3.95 (m, 7H, H-5, H_2-7′, H_2-Ser, H_2-6), 3.76 (br t, $^3J_{6',H2-7'} = 6.3$, H-6′), 3.43 (dd, $^3J_{2',3'} = 9.8$, $^3J_{1',2'} = 2.3$, H-2′), 2.19, 2.09, 2.08, 2.03, 1.99, 1.99, 1.97 (7s, 21H, 7 MeCOO). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.5, 170.3, 170.2, 170.1, 169.9, 169.9, 169.8, 169.5 (8s, –COO), 155.9 (s, HN–COO), 136.0, 135.3, 133.8 (3s, $2C_{arom}$, C-3), 128.6–128.1 (11d, $10CH_{arom}$, C-2), 94.8 (d, 169, C-1), 79.2 (d, 144, C-2′), 75.1 (d, 143, C-6′), 72.1 (d, 146, C-4′), 69.5, 65.1 (2d, 150, 154, C-1′, C-3′), 69.4 (t, 147, CH_2-Ser), 68.0 (d, 146, C-5), 67.4 (d, 153, C-5′), 67.3 (t, 145, OCH_2Ph), 67.1 (t, 148, OCH_2Ph), 63.0 (d, 149, C-4), 62.3 (t, 150, C-6), 61.6 (t, 147, C-7′), 54.5 (d, 140, C*), 20.7–20.5 (7q, 130, *C*H_3COO). CI-MS (NH_3) *m/z* 961 (62,

$[M+18]^+$), 615 (90), 337 (100), 91 (92). Anal. Calcd for $C_{45}H_{53}O_{21}N$: C, 57.26; H, 5.66. Found: C, 57.27; H, 5.70.

4.15. *N*-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-*O*-[4,6-di-*O*-acetyl-3-*C*-[(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2,3-dideoxy-α-D-*lyxo*-hexopyranosyl]-L-serine phenylmethyl ester 21

To a solution of **19** (58 mg, 0.05 mmol) in dry benzene (250 μL) under an argon atmosphere was added Bu_3SnH (30 μL, 0.113 mmol) and AIBN (3 mg). The solution was stirred for 45 min at 55 °C and then, concentrated in vacuo to afford a residue which was purified by FC (5:5 light petroleum/EtOAc) to provide 37 mg (72%) of **21**, white solid, mp 84–86 °C. $[\alpha]_{589}^{25} = +31$, $[\alpha]_{546}^{25} = +39$, $[\alpha]_{435}^{25} = +64$, $[\alpha]_{405}^{25} = +76$ (*c* 0.18, $CHCl_3$). UV (MeCN) 299 (8100), 288 (7000), 264 (24400), 211 (35700). IR (KBr) 3450, 2965, 1750, 1520, 1370, 1240, 1055, 805, 745, 595 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79–7.30 (m, 13H, ArH), 6.04 (d, $^3J_{N,C^*} = 8.1$, H–N), 5.38 (d, $^3J_{4',5'} = 3.1$, H-5′), 5.32–5.14 (m, 2H, OCH_2Ph), 5.16 (dd, $^3J_{3',4'} = 9.8$, $^3J_{2',3'} = 9.8$, H-3′), 4.98 (dd, $^3J_{3',4'} = 9.8$, $^3J_{4',5'} = 3.1$, H-4′), 4.96 (dd, $^3J_{1',3} = 10.6$, $^3J_{1',2'} = 2.1$, H-1′), 4.90 (s, H-4), 4.84 (d, $^3J_{1,2ax} = 3.5$, H-1), 4.61 (dt, $^3J_{C^*,N} = 8.1$, $^3J_{C^*,H2\text{-}Ser} = 2.7$, H–C*), 4.40–4.37 (m, 2H, H_2-Fmoc), 4.26–4.22 (m, 2H, H-Fmoc, H_a-7′), 4.14 (dd, $^2J = 11.1$, $^3J_{6',7'b} = 5.3$, H_b-7′), 4.05 (dd, $^2J = 11.2$, $^3J_{5,6a} = 3.4$, H_a-6), 3.98–3.92 (m, 3H, H_2-Ser, H-5), 3.85 (dd, $^2J = 11.2$, $^3J_{5,6b} = 8.1$, H_b-6), 3.63 (dd, $^3J_{6',7'a} = 7.8$, $^3J_{6',7'b} = 5.3$, H-6′), 3.45 (dd, $^3J_{2',3'} = 9.8$, $^3J_{1',2'} = 2.1$, H-2′), 2.73 (ddd, $^3J_{2ax,3} = 12.8$, $^3J_{1',3} = 10.6$, $^3J_{2eq,3} = 3.6$, H-3), 2.16, 2.06, 2.04, 2.00, 1.99, 1.98, 1.97 (7s, 21H, CH_3COO), 1.76 (ddd, $^2J = 12.8$, $^3J_{2ax,3} = 12.8$, $^3J_{1,2ax} = 3.5$, H_{ax}-2), 1.35 (dd, $^2J = 12.8$, $^3J_{2eq,3} = 3.6$, H_{eq}-2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.7–169.6 (8s, –COO), 155.8 (s, HN–COO), 143.8, 143.8, 141.2, 141.2, 135.5 (5s, $5C_{arom}$), 128.6–120.0 (13d, CH_{arom}), 96.7 (d, 167, C-1), 76.3 (d, 144, C-2′), 74.9 (d, 141, C-6′), 72.7 (d, 148, C-4′), 68.8 (d, 148, C-5), 68.0 (d, 142, C-1′), 68.0 (t, 146, CH_2-Ser), 67.3 (t, 148, CH_2-Fmoc), 67.1 (d, 150, C-5′), 67.1 (t, 146, OCH_2Ph), 64.7 (d, 157, C-3′), 64.5 (d, 153, C-4), 63.6 (t, 147, C-6), 60.4 (t, 149, C-7′), 54.5 (d, 141, C*), 47.0 (d, 135, CH-Fmoc), 33.2 (d, 129, C-3), 27.0 (t, 131, C-2), 20.8–20.6 (7q, 130, CH_3COO). Electrospray-MS (+, 50:50:1 MeCN/H_2O/AcOH) *m/z* 1156.4 (18, $[M+Na]^+$), 1034.3 (100, $[M+1]^+$). Anal. Calcd for $C_{52}H_{59}O_{21}N$: C, 60.40, H, 5.75. Found: C, 60.42; H, 5.91.

4.16. 1,6-Anhydro-3-*C*-{(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*glycero*-hex-2-enopyran-4-ulose 6b

A 1 M solution of Et_2AlI in toluene (12 mL, 12 mmol) was added dropwise to a mixture of **5b**[15] (6 g, 9.40 mmol) and **4** (2 mg, 15.9 mmol) in CH_2Cl_2 (100 mL) at −78 °C. The solution was stirred at this temperature for 12 h and diluted with Et_2O (10 mL). Two molar aq HCl (0.5 mL) was added and the phases separated. The aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic phases were washed sequentially with 2 M aq HCl (5 mL), H_2O (5 mL), and brine (5 mL), dried over $MgSO_4$, and concentrated in vacuo. FC (9:1, light petroleum ether/EtOAc) 6.9 g (95%), colorless oil.[17] R_f = 0.38 (light petroleum ether/EtOAc). $[\alpha]_{589}^{25} = +79$, $[\alpha]_{546}^{25} = +85$, $[\alpha]_{435}^{25} = +330$, $[\alpha]_{405}^{25} = +710$ (*c* 0.24, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, $^3J_{1,2} = 3.5$, $^4J_{1',2} = 1.0$, H-2), 5.83 (d, $^3J_{1,2} = 3.5$, H-1), 4.75 (dd, $^3J_{5,6} = 6.4$, $^3J_{5,6} = 1.3$, H-5), 4.45 (dd, $^3J_{3',4'} = 8.6$, $^3J_{2',3'} = 7.0$, H-3′), 4.26 (d, $^2J = 12.4$, H_a-7′), 4.23 (ddd, $^3J_{1',2'} = 7.0$, $^3J_{1',OH} = 6.7$, $^4J_{1',2} = 1.0$, H-1′), 4.06 (dd, $^2J = 8.3$, $^3J_{5,6exo} = 6.4$, H_{exo}-6), 3.99 (d, $^3J_{3',4'} = 8.6$, H-4′), 3.96 (d, $^3J_{5',6'} = 4.1$, H-5′), 3.91 (t, $^3J_{1',2'} = {}^3J_{2',3'} = 7.0$, H-2′), 3.80 (dd, $^3J_{5',6'} = 4.1$, $^3J_{6',7'b} = 1.9$, H-6′), 3.75 (dd, $^2J = 12.4$, $^3J_{6',7'b} = 1.9$, H_b-7′), 3.81 (dd, $^2J = 10.2$, $^3J_{6',7'a} = 12.7$, H_a-7′), 3.65 (dd, $^2J = 8.3$, $^3J_{5,6endo} = 1.3$, H_{endo}-6), 2.94 (d, $^3J_{1',OH} = 6.7$, OH), 0.94, 0.93, 0.90, 0.90 (4s, 36H, 4 *t*-Bu), 0.14, 0.12, 0.10, 0.09, 0.08, 0.07, 0.06, 0.05 (8s, 24H, $4Me_2Si$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 194.5 (s, C-4), 143.5 (s, 165, C-2), 137.0 (s, C-3), 96.9 (d, 177, C-1), 79.7 (d, 141, C-2′), 79.1 (d, 160, C-5), 73.1 (d, 143, C-6′), 70.5 (d, 144, C-5′), 67.3 (d, 142, C-3′), 67.1 (d, 147, C-1′), 66.9 (d, 138, C-4′), 62.3 (t, 154, C-6), 58.2 (t, 142, C-7′), 25.9, 25.89, 25.85, 25.7 (4q, 125, $(CH_3)_3CSi$), 18.2, 18.1, 17.9, 17.0 (4s, $(CH_3)_3CSi$), −4.4, −4.6, −4.7, −4.9, −5.0, −5.1, −5.3, −5.5 (8q, 118, CH_3Si). CIMSHR *m/z* found 797.43190 (calcd for $C_{37}H_{74}O_9Si_4$ + Na: 797.4307). Anal. Calcd for $C_{37}H_{74}O_9Si_4$: C, 57.32; H, 9.62. Found: C, 57.24; H, 9.56.

4.17. 1,6-Anhydro-3-{(1*S*)-2,6-anhydro-3,4,5,7-tetra-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*glycero*-hexopyranos-4-ulose 22 and 1,6-anhydro-3-{(1*R*)-2,6-anhydro-3,4,5,7-tetra-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*erythro*-hexopyran-4-ulose 23

One hundred and three milligrams of an aqueous suspension of Raney Nickel was added to a stirred solution of compound **10** (103 mg, 0.129 mmol) in tetrahydrofuran (1.11 mL) and the mixture was further stirred at 20 °C until complete conversion of the starting material (TLC control). The mixture diluted with Et_2O (200 mL) and filtrated through a pad of silica gel. FC (9.5:0.5, light petroleum ether/EtOAc), afforded 59 mg (57%) of **22** and 45 mg (43%) of **23**, both as colorless oil. Data of **22**: R_f = 0.16, (9.5:0.5, light petroleum ether/EtOAc). $[\alpha]_{589}^{25} = +4$, $[\alpha]_{546}^{25} = +3$, $[\alpha]_{435}^{25} = -1$, $[\alpha]_{405}^{25} = -10$ (*c* 0.42, $CHCl_3$). IR (film) 3405, 2955, 2860, 1715, 1460, 1360, 1265, 1095, 835, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, H-1), 4.50 (dd, $^3J_{5',6'} = 2.2$, $^3J_{6',7'} = 9.7$, H-6′), 4.42 (d, $^3J_{5,6} = 5.4$, H-5), 4.22 (dd, $^3J_{6',7'} = 2.7$, $^2J = 11.8$, H-7a′), 4.20 (dd, $^3J_{3',4'} = 2.7$, $^3J_{2',3'} = 2.7$, H-3), 4.0 (d, $^2J = 8.9$, H_{exo}-6), 3.85 (m, 3H, H_{endo}-6, H-4′, H-1′), 3.75 (t, $^3J_{2',3'} = 2.7$, $^3J_{1',2'} = 3.2$, H-2′), 3.70 (dd, $^3J_{6',7'} = 1.61$, $^2J = 11.8$, H-7′), 3.55 (d, $^3J_{5',6'} = 9.7$, H-5′), 3.07 (m, H-3), 2.51 (m, H_{endo}-2), 2.13 (m, H_{exo}-2), 0.97, 0.97, 0.91, 0.88 (4s, 36H, 4 *t*-Bu), 0.15, 0.14, 0.14, 0.12, 0.08, 0.07, 0.01, 0.01 (8s, 24H, $4Me_2Si$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206.0 (s, C-4), 102.0 (d, 173, C-1), 79.5 (d, 141, C-2′), 79.5 (d, 163, C-5), 73.2 (d, 147, C-1′), 70.2 (d, 146, C-4′), 67.3 (d, 141, C-3′), 66.8 (t, 106, C-6), 65.2 (d,

146, C-6′), 64.7 (d, 140, C-5′), 58.5 (t, 145, C-7′), 44.4 (d, 125, C-3), 32.2 (t, 128, C-2, *t*-Bu), 18.4, 18.3, 18.1, 18.0 (4s, *t*-Bu), −4.4, −4.6, −4.8, −4.9, −5.0, −5.0, −5.3, −5.3, −5.5 (8q, 118, 4Me_2Si). CIMSHR *m/z* found 799.4464 (calcd for $C_{37}H_{76}O_9Si_4$ + Na: 799.4442).

Data of **23**: R_f = 0.16 (9.5:0.5, light petroleum ether/EtOAc). $[\alpha]_{589}^{25} = +10$, $[\alpha]_{546}^{25} = +9$, $[\alpha]_{435}^{25} = +14$, $[\alpha]_{405}^{25} = +16$ (*c* 0.44, $CHCl_3$). IR (film) 3405, 2955, 2860, 1715, 1460, 1360, 1265, 1095, 835, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, H-1), 4.50 (dd, $^3J_{5',6'}$ = 2.2, $^3J_{6',7'}$ = 9.7, H-6′), 4.42 (d, $^3J_{5,6}$ = 5.4, H-5), 4.22 (dd, $^3J_{6',7'}$ = 2.7, ^2J = 11.8, H_a-7′), 4.20 (dd, $^3J_{3',4'}$ = 2.7, $^3J_{2',3'}$ = 2.7, H-3), 4.0 (d, ^2J = 8.9, H_{exo}-6), 3.85 (m, 3H, H_{endo}-6, H-4′, H-1′), 3.75 (t, $^3J_{2',3'}$ = 2.7, $^3J_{1',2'}$ = 3.2, H-2′), 3.70 (dd, $^3J_{6',7'}$ = 1.6, ^2J = 11.8, H-7′), 3.55 (d, $^3J_{5',6'}$ = 9.7, H-5′), 3.07 (m, H-3), 2.51 (m, H_{endo}-2), 2.13 (m, H_{exo}-2), 0.97, 0.97, 0.91, 0.88 (4s, 36H, 4 *t*-Bu), 0.15, 0.14, 0.14, 0.12, 0.08, 0.07, 0.01, 0.01 (8s, 24H, 4 Me_2Si). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206 (s, C-4), 102 (d, 173, C-1), 79.5 (d, 141, C-2′), 79.5 (d, 163, C-5), 73.2 (d, 147, C-1′), 70.2 (d,146, C-4′), 67.3 (d, 141, C-3′), 66.8 (t, 106, C-6), 65.2 (d, 146, C-6′), 64.7 (d, 140, C-5′), 58.5 (t, 144.6, C-7′), 44.4 (d, 125, C-3), 32.2 (t, 128, C-2), 18.4, 18.3, 18.1, 18.0 (4s, 4 Me_3CSi), −4.4, −4.6, −4.8, −4.9, −5.0, −5.0, −5.3, −5.3, −5.5 (8q, 118, 4 Me_2Si). CIMSHR *m/z* found 799.4464 (calcd for $C_{37}H_{76}O_9Si_4$ + Na: 799.4442).

4.18. 1,6-Anhydro-3-*C*-{2,6-anhydro-3,4,5,7-1-deoxy-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-ylidene}-2,3-dideoxy-β-D-*glycero*-hexopyran-4-ulose 24

Methanesulfonyl chloride (98%, 0.370 mL, 4.76 mmol) was added to a stirred solution of **22** and **23** (0.74 g, 0.959 mmol) in dry pyridine (15 mL) containing DMAP (50 mg) under an Ar atmosphere. The mixture was stirred for 14 h and then quenched by the addition of 20% aq soln of $CuSO_4{\cdot}5H_2O$ solution (30 mL). The solution was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic phases washed with 2 M aq HCl (3 × 30 mL), dried over $MgSO_4$, and then concentrated in vacuo to yield **24** as an unstable colorless oil, which was used without further purification in the next step.

4.19. 1,6-Anhydro-3-{2,6-anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*threo*-hexopyran-4-ulose 25 and 1,6-anhydro-3-{2,6-anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*erythro*-hexopyran-4-ulose 26

Raney Nickel (1 g) in aqueous suspension was added to a stirred solution of **24** (0.9 g, 1.19 mmol) in THF (5 mL). The mixture was stirred at 20 °C until complete conversion of **24** (TLC control). The mixture was diluted with Et_2O (200 mL) and filtrated through a pad of Celite. FC (9:0.5:0.5 light petroleum ether/Et_2O/CH_2Cl_2): 390 mg (43%) of **25**, and 400 mg (44%) of **26**.

Data of **25**: colorless oil. $[\alpha]_{589}^{25} = -10$, $[\alpha]_{546}^{25} = -13$, $[\alpha]_{435}^{25} = -44$, $[\alpha]_{405}^{25} = -73$ (*c* 0.21, $CHCl_3$). IR (film): 2955, 2895, 2855, 1730, 1470, 1255, 1095, 835, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.70 (d, ^3J = 5.4, H-1), 4.53 (dd, $^3J_{5,6exo}$ = 5.4, $^3J_{5,6endo}$ = 0.5, H-5), 4.19 (dd, $^3J_{5',6'}$ = 2.7, $^3J_{4',5'}$ = 6.5, H-5′), 4.15 (dd, $^3J_{6',7'}$ = 9.7, ^2J = 11.8, H_a-7′), 4.00 (d, $^3J_{1',2'}$ = 10.5, H-2′), 3.88 (t, $^3J_{6',7'}$ = 7.5, H-6′), 3.77 (dd, ^2J = 7.3, ^3J = 0.5, H_{endo}-6), 3.72 (dd, ^3J = 3.2, H-4′), 3.72 (m, H_{exo}-6), 3.65 (m, H-7′), 3.49 (d, ^3J = 3.5, H-3′), 2.92 (m, H-3), 2.68 (m, H_{exo}-2), 1.67 (dd, ^2J = 12.9, ^3J = 8.06, H_b-1′), 1.46 (m, H_a-1′), 1.30 (m, H_{endo}-2), 0.97, 0.97, 0.91, 0.88 (4s, 36H 4 *t*-Bu), 0.15, 0.14, 0.14, 0.12, 0.08, 0.07, 0.01, 0.01 (8s, 24H, 4Me_2Si). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 213 (s, C-4), 100.1 (d, 173, C-1), 79 (d, 141, C-6′), 79 (d, 163, C-5), 74 (d, 147, C-3′), 74 (d, 146, C-4′), 67 (d, 141, C-5′), 67 (t, 106, C-6), 65 (d, 146, C-2′), 58 (d, 145, C-7′), 39 (d, 125, C-3), 36 (t, 128, C-2), 30 (t, 128, C-1′), 18.4, 18.3, 18.1, 18.0 (4s, 4 *t*-BuSi), −4.4, −4.6, −4.8, −4.9, −5.0, −5.0, −5.3, −5.3, −5.5 (8q, 118, 4Me_2Si). CIMSHR *m/z* found 783.4542 (calcd for $C_{37}H_{76}O_8Si_4$ + Na: 783.4515).

Data of **26**: colorless oil. IR (film) 2955, 2895, 2855, 1730, 1470, 1255, 1095, 835, 775 cm^{-1}. CIMSHR *m/z* found 783.4521 (calcd for $C_{37}H_{76}O_8Si_4$ + Na: 783.4515).

4.20. 1,6-Anhydro-3-*C*-{2,6-anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*lyxo*-hexopyranose 27

A THF solution of $LiBH_4$ (0.56 mL, 1.13 mmol) was added dropwise to a solution of **25** (0.140 mg, 0.188 mmol) in THF (5 mL) at −78 °C. The mixture was stirred for 4 h, from −78 to 15 °C. A satd aq soln of NH_4Cl (25 mL) was then added. The reaction mixture was warmed to 20 °C at which point a satd soln of sodium potassium tartarate (25 mL) was added. The aqueous phase was then extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were dried and concentrated in vacuo. FC (light petroleum ether/Et_2O 9:1) 110 mg (79%), colorless oil. $[\alpha]_{589}^{25} = +4$, $[\alpha]_{546}^{25} = +7$, $[\alpha]_{435}^{25} = +9$, $[\alpha]_{405}^{25} = +11$ (*c* 0.08, $CHCl_3$). IR (film) 3425, 2955, 2855, 1620, 1470, 1360, 1130, 865, 835, 775, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (s, H-1), 4.48 (m, H_{exo}-6), 4.54 (m, H-2′), 4.42 (t, $^3J_{6',7'}$ = 4.6, H-6′), 4.29 (m, H-4′), 4.26 (m, H-4), 4.24 (m, H_a-7′), 3.95 (d, $^3J_{5,6endo}$ = 2.5, $^3J_{3,5}$ = 6.8, $^3J_{5,6exo}$ = 9.6, H-5), 3.88 (t, $^3J_{5',6'}$ = 3.1, H-5′), 3.73 (dd, ^2J = 12.3, $^3J_{5,6endo}$ = 2.5, H_{endo}-6), 3.70 (ddd, ^3J = 2.5, $^3J_{6',7'}$ = 1.6, H_b-7′), 3.46 (d, $^3J_{3',4'}$ = 3.7, H-3′), 2.99 (ddd, ^3J = 6.8, ^3J = 12.3, ^3J = 18.5, H-3), 2.03 (m, H_a-1′), 1.99 (m, H_{endo}-2), 1.83 (m, H_b-1′), 1.66 (m, H_{endo}-2), 0.97, 0.97, 0.91, 0.88 (4s, 36H, 4 *t*-Bu), 0.15, 0.14, 0.14, 0.12, 0.08, 0.07, 0.01, 0.01 (8s, 24H, 4Me_2Si). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 101.5 (d, 173, C-1), 78.1 (d, 163, C-5), 75.6 (d, 141, C-6′), 74.4 (d, 147, C-3′), 73.8 (d, 141, C-5′), 69.2 (d, 146, C-4′), 67.5 (d, 141, C-4), 64.8 (d, 144.6, C-7′), 64.5 (d, 146, C-2′), 58.6 (t, 106, C-6), 36.5 (t, 128, C-2), 34.6 (t, 128, C-1′), 30.8 (d, 125, C-3), 18.4, 18.3, 18.1, 18.0 (4s, 4 *t*-BuSi), −4.4, −4.6, −4.8, −4.9, −5.0, −5.0, −5.3, −5.3, −5.5 (8q, 118, 4Me_2Si). CIMSHR *m/z* found 785.4662 (calcd for $C_{37}H_{78}O_8Si_4$ + Na: 785.4671).

4.21. 4,6-Di-*O*-acetyl-3-*C*-{7-*O*-acetyl-2,6-anhydro-1-deoxy-3,4,5-tri-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-α,β-D-*lyxo*-hexopyranosyl acetate 28α,β

A catalytic amount of triethylsilyl triflate (1.3 μL) was added dropwise via a syringe to a solution of compound **27** (0.12 g, 0.157 mmol) in acetic anhydride (2 mL) cooled at 0 °C. The mixture was stirred at 0 °C for 30 min, and then a satd aq soln of $NaHCO_3$ added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were dried over $MgSO_4$, concentrated in vacuo and coevaporated with toluene in vacuo. The oily product obtained was used directly in the next step. $[\alpha]^{25}_{589} = +50$, $[\alpha]^{25}_{546} = +51$, $[\alpha]^{25}_{435} = +99$, $[\alpha]^{25}_{405} = +118$ (*c* 0.21, $CHCl_3$). CIMSHR *m/z* found 857.4334 (calcd for $C_{39}H_{74}O_{13}Si_3$ + Na: 857.4309).

4.22. 4,6-Di-*O*-acetyl-3-*C*-{7-*O*-acetyl-2,6-anhydro-1-deoxy-3,4,5-tri-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-3-deoxy-D-galactal 3c

Silica gel (870 mg) was added to a solution of **28α,β** (0.286 g, 0.315 mmol) in toluene (10 mL) and the mixture heated under reflux for 3 h. Filtration, washing with CH_2Cl_2 (100 mL), concentration in vacuo, FC (9:0.5:0.5, light petroleum ether/Et_2O/CH_2Cl_2) gave 160 mg (60%) of yellowish oil. $[\alpha]^{25}_{589} = -7$, $[\alpha]^{25}_{546} = -10$, $[\alpha]^{25}_{435} = -27$, $[\alpha]^{25}_{405} = -40$ (*c* 0.09, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (dd, $^3J_{1,2} = 6.2$, $^4J_{1,3} = 2.7$, H-1), 5.49 (d, $^3J_{3,4} = 3.4$ H-4), 5.16 (dd, $^3J_{6exo,6endo} = 12.6$, $^3J_{5,6exo} = 9.9$, H_{exo}-6), 4.72 (dt, $^3J_{1,2} = 6.2$, $^3J_{2,3} = 3.9$, $^4J = 1.6$, C–H_2), 4.30–3.94 (m, 7H, H-5, H_{endo}-6, H-2′, H-5′, H-6′, H_a-7′, H_b-7′), 3.72 (t, $^3J_{3',4'} = 4.0$, H-4′), 3.40 (d, $^3J_{3',4'} = 4.0$, H-3′), 2.70 (br s, C-3), 2.10 (s, 6H, 2 Ac), 2.06 (s, 3H, Ac), 1.58 (m, H_a-1′), 1.25 (m, H_b-1′), 0.95, 0.94, 0.93 (3s, 27H, 3 *t*-Bu), 0.12, 0.12, 0.12, 0.10, 0.09, 0.06 (8s, 6H, 3Me_2Si). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.0, 170.7, 170.3 (3 Ac), 142.2 (d, 148, C-1), 104 (d, 146, C-2), 75.8 (d, 142, C-5′), 74.4 (d, 146, C-4′), 74.1 (d, 147, C-2′), 73.5 (d, 147, C-3′), 67.1 (d, 163, C-5), 65.6 (d, 142, C-6′), 65.0 (d, 142, −4), 63.4 (d, 145, C-7′), 60.2 (t, 106, C-6), 32.9 (d, 125, C-3), 32.3 (t, 128, C-1′), 26.1, 25.8, 25.6, (3s, 3 Me(Ac)), 21.1, 20.8, 20.7, (3s, 3 *t*-BuSi), −4.4, −4.5, −4.7, −4.72, −5.0, −5.1 (6q, 118, 3 Me_2Si). CIMSHR *m/z* found 797.4151 (calcd for $C_{37}H_{70}O_{11}Si_3$ + Na: 797.4123).

Acknowledgements

We are grateful to the Swiss National Science Foundation (Grant No. 200020-100002), and the 'Office Fédéral de l'Education et de la Science' (Bern, COST D13/0001/99) for generous support. We thank the University of Lausanne and Mrs. Antoinette Charon for a *Peace* grant in favor of L.A. We thank also Prof. I. Robina, Universidad de Sevilla, Spain, for discussions and help with the HRMS. We thank also Mr. M. Rey, F. Sepúlveda and Miss C. Bühlmann for technical help.

References

1. Rademacher, T. W.; Parekh, R. B.; Dwek, R. A. *Annu. Rev. Biochem.* **1988**, *57*, 785–838; Lis, H.; Sharon, N. *Eur. J. Biochem.* **1993**, *218*, 1–27; Hart, G. W. *Curr. Opin. Cell. Biol.* **1992**, *4*, 1017–1023; Varki, A.; Freeze, H. H. In *Subcellular Biochemistry*; Maddy, A. H., Harris, J. R., Eds., Plenum: New York, 1994; p 71; Sears, P.; Wong, C.-H. *Angew. Chem., Int. Ed.* **1999**, *38*, 2301–2324.
2. Bertozzi, C. R.; Kiessling, L. L. *Science (Washington, DC)* **2001**, *291*, 2357–2364; Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. *Science (Washington, DC)* **2001**, *291*, 2370–2376; *Glycosciences: Status and Perspectives*; Gabius, H.-J., Gabius, S., Eds.; Chapmann & Hall: London, U.K., 1997; Sears, P.; Wong, C.-H. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 12086–12093; Kiessling, L. L.; Pohl, N. L. *Chem. Biol.* **1996**, *3*, 71–77; Beuth, J.; Ko, H. L.; Pulverer, G.; Uhlenbruck, H.; Pichlmaier, H. *Glycoconjugate J.* **1995**, *12*, 1–6; Lasky, L. A. *Annu. Rev. Biochem.* **1995**, *64*, 113–139; Toyokuni, T.; Singhal, A. K. *Chem. Soc. Rev.* **1995**, *24*, 231–242; Varki, A. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 7390–7397; Feizi, T. *Curr. Opin. Struct. Biol.* **1993**, *3*, 701–710; Hakkomori, S. *Curr. Opin. Immun.* **1991**, *3*, 646–653; Wharton, S. A.; Weis, W.; Skehel, J. J., ; Wiley, D. C. *The Influenza Virus*; Plenum: New York, 1989.
3. Alper, J. *Science (Washington, DC)* **2001**, *291*, 2338–2343; Bols, M. *Acc. Chem. Res.* **1998**, *31*, 1–8; Barchi, J. J. *Curr. Pharm. Des.* **2000**, *6*, 485–501; Musser, J. H.; Anderson, M. B.; Fugedi, P. *Pharm. News* **1996**, *3*, 11–17; Mulligan, M. S.; Paulson, J. C.; DeFrees, S.; Zheng, Z. L.; Lowe, J. B.; Ward, P. A. *Nature (London)* **1993**, *364*, 149–151; Ragupathi, G.; Howard, L.; Cappello, S.; Koganty, R. R.; Qiu, D.; Longenecker, B. M.; Reddish, M. A.; Lloyd, K. O.; Livingston, P. O. *Cancer Immunol. Immunother.* **1999**, *48*, 1–8; MacLean, G. D.; Longenecker, B. M. *Can. J. Oncol.* **1994**, *4*, 249–254; MacLean, G. D.; Reddish, M.; Koganty, R. R.; Wong, T.; Gandhi, S.; Smolenski, M.; Samuel, J.; Nabholtz, N. M.; Longenecker, B. M. *Cancer Immunol. Immunother.* **1993**, *36*, 215–222; Platt, F. M.; Neises, G. R.; Reinkensmeier, G.; Townsend, M. J.; Perry, V. H.; Proia, R. L.; Winchester, B.; Dwek, R. A.; Butters, T. D. *Science (Washington, DC)* **1997**, *276*, 428–431.
4. Levy, D. E.; Tang, C. Tetrahedron Organic Chemistry Series. In *The Chemistry of C-Glycosides*; Baldwin, J. E., Magnus, P. D., Eds.; Pergamon–Elsevier Science: Oxford, 1995; Postma, M. H. D. *C-Glycoside Synthesis*; Boca Raton, FL: CRC, 1995; Du, Y.; Linhardt, R. J.; Vlahov, I. R. *Tetrahedron* **1998**, *54*, 9913–9959.
5. Springer, G. F. *Science (Washington, DC)* **1984**, *224*, 1198–1206; Jennings, H. J.; Ashton, F. E.; Gamian, A.; Michon, F.; Roy, R. *Can. Prog. Biotechnol.* **1987**, *3*, 149–156; Taylor-Papadimitriou, J.; Epenetos, A. A. *Trends Biotechnol.* **1994**, *12*, 227–233; MacLean, G. D.; Reddish, M. A.; Bowen-Yacyshyn, M. B.; Poppema, S.; Longeneeker, B. M. *Cancer Invest.* **1994**, *12*, 46–56; Rye, P. D.; Bovin, N. V.; Vlasova, E. V.; Walker, R. A. *Glycobiology* **1995**, *5*, 385–389; Springer, G. F. *Crit. Rev. Oncol.* **1995**, *6*, 57–85; Ragupathi, G. *Cancer Immunol. Immunother.* **1996**, *43*, 152–157; Cooper, D. K. C.; Oriol, R. Glycobiology in Xenontransplantation research. In *Glycosciences*; Gabius, S., Ed.; Chapman & Hall: Weinheim, 1997; p 531; Kim, Y. J.; Varki, A. *Glycoconjugate J.* **1997**, *14*, 569–576; Hakomori, S.; Zhang, Y. *Chem. Biol.* **1997**, *4*, 97–104; Hallberg, E. C.; Strokan, V.; Cairns, T. D. H.; Breimer, M. E.; Samuelsson, B. E. *Xenotransplantation* **1998**, *5*, 246–256;

Hakomori, S. *Acta Anat.* **1998**, *161*, 79–90; Kuduk, S. D.; Schwarz, J. B.; Chen, X.-T.; Glunz, P. W.; Sames, D.; Ragupathi, G.; Livingston, P. O.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 12474–12485; Orntoft, T. F.; Vestergaard, E. M. *Electrophoresis* **1999**, *20*, 362–371; Lo-Man, R.; Bay, S.; Vichier-Guerre, S.; Deriaud, E.; Cantacuzene, D.; Leclerc, C. *Cancer Res.* **1999**, *59*, 1520–1524; Allen, J. R.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 10875–10882; Kuberan, B.; Linhardt, R. J. *Curr. Org. Chem.* **2000**, *4*, 653–677; Bousquet, E.; Spadaro, A.; Pappalardo, M. S.; Bernardini, R.; Romeo, R.; Panza, L.; Ronsisvalle, G. *J. Carbohydr. Chem.* **2000**, *19*, 527–541.

6. Pasquarello, C.; Demange, R.; Vogel, P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 793–796; Pasquarello, C.; Picasso, S.; Demange, R.; Malissard, M.; Berger, E. G.; Vogel, P. *J. Org. Chem.* **2000**, *65*, 4251–4260.
7. Rodén, L. Metabolic Conjugation and Metabolic Hydrolysis; Fishman, W. E., Ed.; Academic, 1970; Vol. 2, pp 245–442; Stern, E. L.; Lindahl, B.; Rodén, L. *J. Biol. Chem.* **1971**, *246*, 5707–5715; Montreuil, J. *Adv. Carbohydr. Chem. Biochem.* **1980**, *37*, 157–223.
8. Hirst, E. L.; Perlin, A. S. *J. Chem. Soc.* **1954**, 2622–2627; Bailey, R. W. *Oligosaccharides*; Pergamon: Oxford, 1965, p 48; Aspinall, G. O.; Young, R. *J. Chem. Soc.* **1965**, 3003–3004; Hirst, E. L.; Mackie, W.; Percival, E. *J. Chem. Soc.* **1965**, 2958–2967; Parikh, V. M.; Jones, J. K. N. *Can. J. Chem.* **1966**, *44*, 1531–1539; Rodén, L.; Smith, R. *J. Biol. Chem.* **1966**, *241*, 5949–5954; Lindberg, B.; Rodén, L.; Silvander, B. G. *Carbohydr. Res.* **1966**, *2*, 413–417; Michalski, J.-C.; Bouquelet, S.; Montreuil, J.; Strecker, G.; Dulac, O.; Munnich, A. *Clin. Chim. Acta* **1984**, *137*, 43–51.
9. Fritzsimmons, B. J.; Leblanc, Y.; Chan, N.; Rokach, J. *J. Am. Chem. Soc.* **1988**, *110*, 5229–5231; Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661–6666; Sebesta, D. P.; Roush, W. R. *J. Org. Chem.* **1992**, *57*, 4799–4802; Liu, K. K. C.; Danishefsky, S. J.; McCluse, K. F.; Randolph, J. T.; Ruggeri, R. B. *Science* **1993**, *260*, 1307–1309; Wang, J.; Wurster, J. A.; Wilson, L. J.; Liotta, D. *Tetrahedron Lett.* **1993**, *34*, 4881–4884; Liu, K. K.-C.; Danishefsky, S. L. *J. Org. Chem.* **1994**, *59*, 1892–1894; Randolph, J. T.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1995**, *117*, 5693–5700; Danishefsky, S. J.; Behar, W.; Randolph, J. I.; Llod, K. O. *J. Am. Chem. Soc.* **1995**, *117*, 5701–5711; Kim, H.; Men, H.; Lee, C. *J. Am. Chem. Soc.* **2004**, *126*, 1336–1337; Geiger, J.; Barroca, N.; Schmidt, R. R. *Synthesis* **2004**, 836–840.
10. Marouka, K.; Nonoshita, K.; Itoh, T.; Yamamoto, H. *Chem. Lett.* **1987**, 2215–2216; Casiraghi, G.; Cornia, M.; Rassu, G.; Zetta, L.; Gasparri Fava, G.; Ferrari Belicchi, M. *Carbohydr. Res.* **1989**, *191*, 243–251; Daves, G. D., Jr. *Acc. Chem. Res.* **1990**, *23*, 201–206; Dubois, E.; Beau, J.-M. *Carbohydr. Res.* **1992**, *228*, 103–120; Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M. *Tetrahedron Lett.* **1994**, *35*, 5673–5676; Lopez, J. C.; Gomez, A. M.; Fraser-Reid, B. *J. Org. Chem.* **1995**, *60*, 3871–3878; Thorn, S. N.; Gallagher, T. *Synlett* **1996**, 185–187; Williams, L. J.; Garbaccio, R. M.; Danishefsky, S. J. *Carbohydr. Chem. Biol.* **2000**, *1*, 61–92; Berber, H.; Brigaud, T.; Lefebvre, O.; Plantier-Royan, R.; Portella, C. *Chemistry (Weinheim)* **2001**, *7*, 903–909; Ramnauth, J.; Poulin, P.; Rakhit, S.; Maddaford, S. P. *Org. Lett.* **2001**, *3*, 2013–2015; Yadav, J. S.; Reddy, B. V.; Chandraiah, L.; Reddy, K. S. *Carbohydr. Res.* **2001**, 221–224; Hayashi, M. *Recent Res. Develop. Org. Bioorg. Chem.* **2001**, *4*, 63–87; Parrish, J. D.; Little, R. D. *Org. Lett.* **2002**, *4*, 1439–1442; Hayashi, M.; Kawabata, W.; Nakayama, S.-Z. *Chirality* **2003**, *15*, 10–16; Seeberger, P. H. *Chem. Commun.* **2003**, 1115–1121; Geiger, J.; Barroca, N.; Schmidt, R. R. *Synlett* **2004**, 836–840; Kim, H.; Men, H.; Lee, C. *J. Am. Chem. Soc.* **2004**, *126*, 1336–1337.
11. For other methods of synthesis of C(1→3)-disaccharides, see for example: Miller, W. H.; Ryckman, D. M.; Goekjian, P. G.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 5580–5582; Wang, Y.; Goekjian, P. G.; Ryckman, D. M.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 4151–4153; Paton, R. M. In *Carbohydrate Mimics*; Chapleur, Y., Ed.; Wiley-VCH, Verlag GmbH: Germany, 1998; pp 49–66, and references cited therein; Vogel, P.; Ferritto, R.; Kraehenbuehl, A. K.; Baudat, A. In *Carbohydrate Mimics*; Chapleur, Y., Ed.; Wiley-VCH Verlag GmbH: Weinheim, Germany, 1998; pp 19–46, and references cited therein; Krintel, S. L.; Jimenez-Barbero, J.; Skrydstrup, T. *Tetrahedron Lett.* **1999**, *40*, 7565–7568; Gerber, P.; Vogel, P. *Tetrahedron Lett.* **1999**, *40*, 3165–3168; Skrydstrup, T.; Vauzeilles, B.; Beau, J.-M. Carbohydrates in Chemistry and Biology; Ernst, B., Hart, G. W., Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 1, pp 495–530; Liu, L.; Postema, M. H. D. *J. Am. Chem. Soc.* **2001**, *123*, 8602–8603; Liu, L.; McKee, M.; Postema, M. H. D. *Curr. Org. Chem.* **2001**, *5*, 1133; Vauzeilles, B.; Sinaÿ, P. *Tetrahedron Lett.* **2001**, *42*, 7269–7272; Munch-Mikkelsen, L.; Krintel, S. L.; Jimenez-Barbero, J.; Skrydstrup, T. *J. Org. Chem.* **2002**, *67*, 6297–6308; Postema, M. H. D.; Piper, J. L.; Liu, L.; Shen, J.; Faust, M.; Andreana, P. *J. Org. Chem.* **2003**, *68*, 4748–4754; Stepànek, P.; Kniezo, L.; Dvoràkova, H.; Vojlisek, P. *Synlett* **2003**, 963–966; Cardona, F.; Goti, A.; Brandi, A. *Org. Lett.* **2003**, *5*, 1475–1478; Stephànek, P.; Vich, O.; Kniezo, L.; Dvoràkova, H.; Vojlisek, P. *Tetrahedron: Asymmetry* **2004**, *15*, 1033–1041; Dondoni, A.; Marra, A. *Chem. Rev.* **2004**, *104*, 2557–2599.
12. Schmidt, R. R.; Beyerbach, A. *Liebigs Ann. Chem.* **1992**, 983–986.
13. Itoh, A.; Ozawa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1980**, *21*, 361–364; Itoh, A.; Ozawa, S.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 274–278.
14. Horton, D.; Roski, J. P.; Norris, P. *J. Org. Chem.* **1996**, *61*, 3783–3793; Witczak, Z. J. *Levoglucosenone and Levoglucosans; Chemistry and Applications*; ATL: Science Publishers: Mount Prospect, IL, USA, 1994.
15. Zhu, Y.-H.; Demange, R.; Vogel, P. *Tetrahedron: Asymmetry* **2000**, *11*, 263–282, When isolevoglucosenone **4** and aldehyde **5a** were treated with Me_2AlSPh, a product of condensation was obtained at −78 °C. Its direct reduction with various hydride reagents [$LiBH_4$, $(i\text{-Bu})_2AlH$, $Na(CN)BH_3$] also furnished **11**, but with a yield never surpassing 20% as several other undefined products were formed concurrently.
16. Jiménez-Barbero, J.; Demange, P.; Schenk, K.; Vogel, P. *J. Org. Chem.* **2001**, *66*, 5132–5138.
17. Kobertz, N. R.; Bertozzi, C. R.; Bednarski, M. D. *Tetrahedron Lett.* **1992**, 737–740; Kobertz, W. R.; Bertozzi, C. R.; Bednarski, M. D. *J. Org. Chem.* **1996**, *61*, 1894–1897.
18. For alternative synthesis of **5**, see: Dondoni, A.; Boscarato, A.; Zuurmond, H. *Tetrahedron Lett.* **1996**, *37*, 7587–7590; Dondoni, A.; Scherrmann, M.-C. *J. Org. Chem.* **1994**, *59*, 6404–6412; Dondoni, A. *Synthesis* **1998**, 1681–1706; Dondoni, A.; Giovannini, P. P. *Synthesis* **2000**, *22*, 1701–1706; Dondoni, A. *Pure Appl. Chem.* **2000**, *72*, 1577–1588.
19. Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920–1923.
20. Rychnovsky, S. D.; Rogers, B. N.; Richardson, T. *Acc. Chem. Res.* **1998**, *31*, 9.

21. Lemieux, R. U.; Levine, S. *Can. J. Chem.* **1964**, *42*, 1417–1480; Lemieux, R. U.; Fraser-Reid, B. *Can. J. Chem.* **1965**, *43*, 1468–1473.
22. Thiem, J.; Karl, H.; Schwenter, J. *Synthesis* **1978**, 696–698; Thiem, J.; Ossowski, P. *J. Carbohydr. Chem.* **1984**, *3*, 287–313.
23. For similar difficulties, see for example: Friesen, R. W.; Danishefsky, S. J. *Tetrahedron* **1990**, *46*, 103–112; Kottenhahn, M.; Kessler, H. *Liebigs Ann. Chem.* **1991**, *22*, 727–744.
24. Tatsuta, K.; Fujimoto, F.; Kinoshita, M. *Carbohydr. Res.* **1977**, *54*, 85–104; Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656–6660.
25. Moreno-Vargas, A. J.; Vogel, P. *Tetrahedron: Asymmetry* **2003**, *14*, 3173–3176.