C-Linked Disaccharide Analogue of the Thomsen–Friedenreich (T)-Epitope α-O-Conjugated to L-Serine

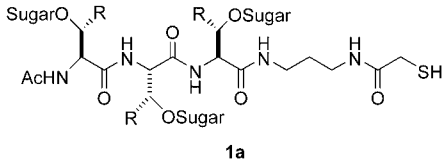
Loay Awad, Jens Riedner, and Pierre Vogel*[a]

Abstract: Condensation of a silylated β-D-galactopyranosylaldehyde (**3**) with isolevoglucosenone (**4**) in the presence of Et_2AlI provided bicyclic enone **5**. Subsequent addition of BnNHOMe gave adduct **6**, which was converted into 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-azido-2,3-dideoxy-β-D-*galacto*-hexopyranose after liberation of the 2-amino group, its transformation into a 2-azido moiety, desilylation, and peracetylation. Ring-opening of the 1,6-anhydro galactopyranosyl unit and *O*-glycosidation with Fmoc-Ser-O-*t*Bu afforded a 5:1 mixture of α- and β-galactosides. Treatment with CH_3COSH gave pure *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro 1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-[(*N*-acetyl)-amino]-2,3-dideoxy-α-D-galactopyranosyl}-L-serine *tert*-butyl ester (**2**), a protected form of a C-disaccharide analogue of the Thomsen–Friedenreich (or T) epitope (β-D-Gal*p*-(1→3)-α-D-GalNAc*p*) α-O-conjugated to L-serine.

Keywords: antitumor agents · C-glycosides · disaccharides · glycosidation · Oshima–Nozaki condensation · sugar epitope

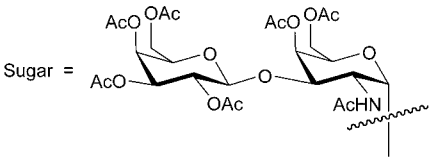
Introduction

The Thomsen–Friedenreich or T epitope (β-D-Gal*p*-(1→3)-α-D-GalNAc*p*)-α-O has been known for a long time as a tumor-associated antigen.[1] The presence of T antigen during an early fetal phase, its absence in noncarcinomatous post-fetal tissues, and its association with carcinomas suggest that T antigen is a stage-specific oncofetal carbohydrate antigen. The T antigen is also related to blood group antigens.[2] In epithelial cells, the T epitope is carried by mucin (MUC1), which belongs to a family of highly glycosylated proteins present on the apical surfaces of many epithelial cells. On tumor cells MUC1 is post-translationally modified, resulting in incomplete *O*-glycosylation and exposing the T epitope.[3] Everyone has "preexisting" anticarcinoma anti-T antibodies, induced predominantly by the intestinal flora, while cellular immune responses to T epitopes are evoked only by carcinomas and some lymphomas.[4] The T antigens have been prepared and their immunogenicity in conjugate vaccines has been confirmed.[4,5] The clustered antigen motifs such as **1a** prepared by Danishefsky and co-workers[6] have demonstrated the potential for antitumor vaccines[7] based on T antigen conjugates.



1a

R = H, Me



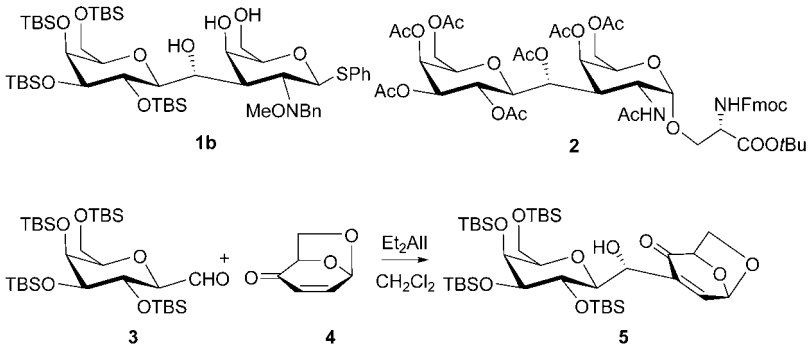
Disaccharide conjugates are relatively short-lived in the blood stream, because of their hydrolysis catalyzed by ubiquitous glycosidases. Disaccharide mimetics such as C-linked disaccharide analogues offer improved stability towards hydrolysis, as required for a disaccharide-based vaccine. In a preliminary communication we proposed a first approach to

[a] L. Awad, Dr. J. Riedner, Prof. Dr. P. Vogel
Laboratory of Glycochemistry and Asymmetric Synthesis
Ecole Polytechnique Federale de Lausanne (EPFL), BCH
1015 Lausanne (Switzerland)
Fax: (+41) 21-693-9355
E-mail: pierre.vogel@epfl.ch

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

 DOI: 10.1002/chem.200401301

the synthesis of a C-glycoside analogue of epitope T disaccharide **1b**.[8] As the O-glycosidation of semiprotected forms of L-serine with **1b** (and derivatives of **1b**) failed to generate the desired α-galactopyranosides as required for T epitope, we were forced to explore other synthetic routes.[9] We describe one of them here and show that the protected form of a C-linked disaccharide analogue of T epitope has been obtained. It was necessary to use a 2-azido-2-deoxygalactopyranosyl intermediate for the α-galactosylation of L-serine, and the construction of this has not been straightforward, since the chemistry known for simpler galactosyl derivatives and O-linked disaccharides did not apply to our C-linked disaccharide analogues.[9] Our studies use enones **5**, which are obtained in good yield by the Oshima–Nozaki condensation[10] between the D-galactopyranosylcarbaldehyde **3** and the readily available isolevoglucosenone (**4**) (Scheme 1).



Scheme 1. Synthesis of C(1→3)-disaccharide precursors.

Results and Discussion

For the synthesis of this compound, we envisaged the application of the chemistry developed from isolevoglucosenone (**4**) and aldehyde **3**. Under our previous conditions[8] (0.1 mmol of **3**, −78 °C) the yield of the condensation[10] of aldehyde **3** and isolevoglucosenone (**4**) had been 61 %. With use of large amounts of **3** (10 mmol) and **4** (15 mmol), high concentrations, and slow addition of Et_2AlI at −90 °C, the yield of isolated enone **5** climbed to 95 % (Scheme 1).

For the conjugate addition to enone **5**, we chose hydroxylamine derivatives as nitrogen nucleophiles. Because of the α-effect, their nucleophilicities are much higher than those of other amines.[11] Initially a Lewis acid such as Me_2AlCl was used to activate the enone, but unfortunately no reaction occurred when MeONHBn was added to a mixture of **5** and Me_2AlCl between −78 °C and 0 °C. In fact, we found that use of a Lewis acid was not necessary for this addition. The best results were obtained with use of no solvent and no catalyst (Table 1).

MeONHBn and enone **5** give a 1:1 mixture of stereomeric adducts **6** and **6′**, which are isomerized during slow chromatography on silica gel at room temperature. Thanks to this, conditions were found under which adduct **6** could be obtained pure in 82 % yield (Scheme 2).

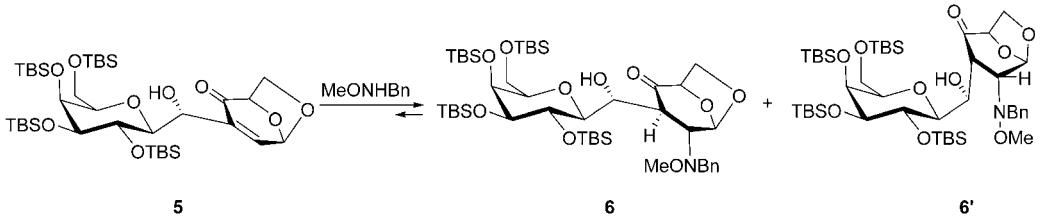
When pure **6** was dissolved in THF with MeONHBn, a mixture of **6** and **6′** was obtained upon standing at 25 °C for 2–3 h. Fast column chromatography on silica gave a first fraction containing of mixture of **6** and **6′** (major), and a second fraction of pure **6** (minor). Slow elution led to a smaller fraction of **6** and **6′** and increased amounts of pure **6** (second fraction), indicating that **6** and **6′** exist in equilibrium in the presence of an amine and that the equilibrium shifts in favor of **6** when the mixture is adsorbed on silica gel. Slower elution thus allows the conversion of absorbed **6′** into absorbed **6**, which is finally recovered pure from the column.

It is proposed that the mechanism of the isomerization **6**⇄**6′** involves reversible E_{1cb}-like eliminations (**6**⇄**5**+MeONHBn and **6′**⇄**5**+MeONHBn), both catalyzed by MeONHBn.

Table 1. Conjugate addition of methoxybenzylamine to enone **5**.

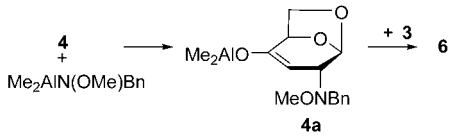
Entry	Catalyst	Solvent	*T* [°C]	Yield [%]
1	Me_2AlCl	CH_2Cl_2	−78→0	no reaction
2	Me_2AlCl	CH_2Cl_2	25	20
3	–	CH_2Cl_2	25	18
4	–	no solvent	25	82

In a preliminary work[8] we showed that treatment of isolevoglucosenone (**4**) with Me_2AlNBn_2 gave an aluminum enolate that could be treated directly with sugar-derived aldehydes to give the corresponding 2-amino-2-deoxy-3-C-linked disaccharide derivatives in a one-pot fashion. We



Scheme 2. Reversible addition of methoxybenzylamine to enone **5**.

thus attempted to obtain **6** in a similar way by treatment of isolevoglucosenone (**4**) with $Me_2AlN(OMe)Bn$, followed by addition of aldehyde **3**. From related Oshima–Nozaki reactions with **4**, we expected (Zimmerman–Traxler[12] steric factors) that the double adduct preferred under kinetic control conditions should be **6** (Scheme 3). After several unfruitful



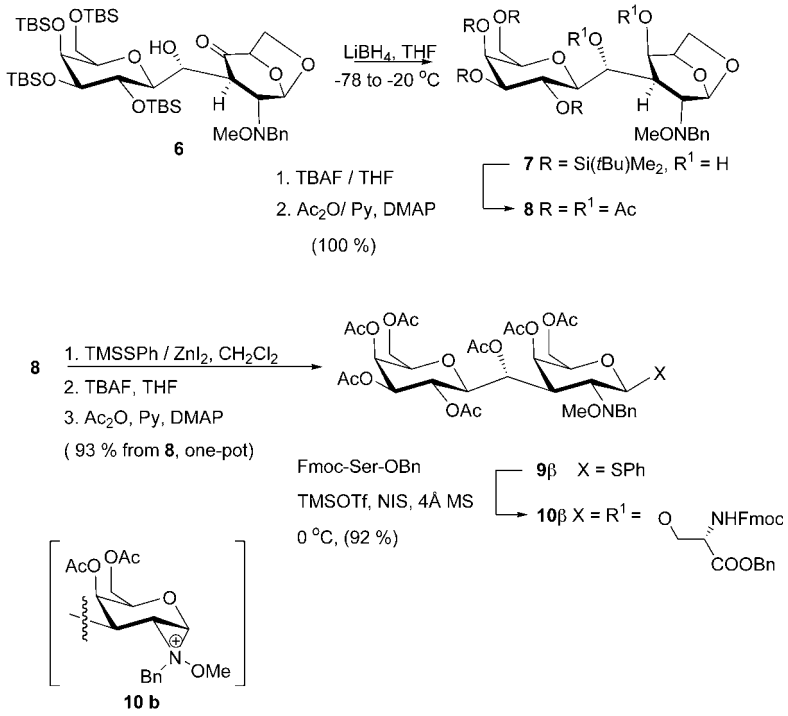
Scheme 3. One-pot double addition.

assays we found that the reaction between **4** and $Me_2AlN(OMe)Bn$ in THF at −78 °C gave the expected enolate **4a**. After the addition of **3** to this solution, a slow reaction occurred at −78 °C. Subsequent aqueous workup and purification by chromatography on silica gel gave **6** in only 19% yield (Scheme 3). Attempts to run the reaction at higher temperatures and/or for longer times led to decomposition only.

Reduction of ketone **6** with $LiBH_4$ furnished diol **7** in 90% yield; hydride addition to the *exo* face of the bicyclo[3.2.1]octanone system is preferred for steric reasons. Treatment of **7** with Bu_4NF (TBAF) in THF (20 °C, 3 h) and then with Ac_2O/pyridine and a catalytic amount of 4-dimethylaminopyridine (DMAP) provided peracetate **8** quantitatively (Scheme 4).

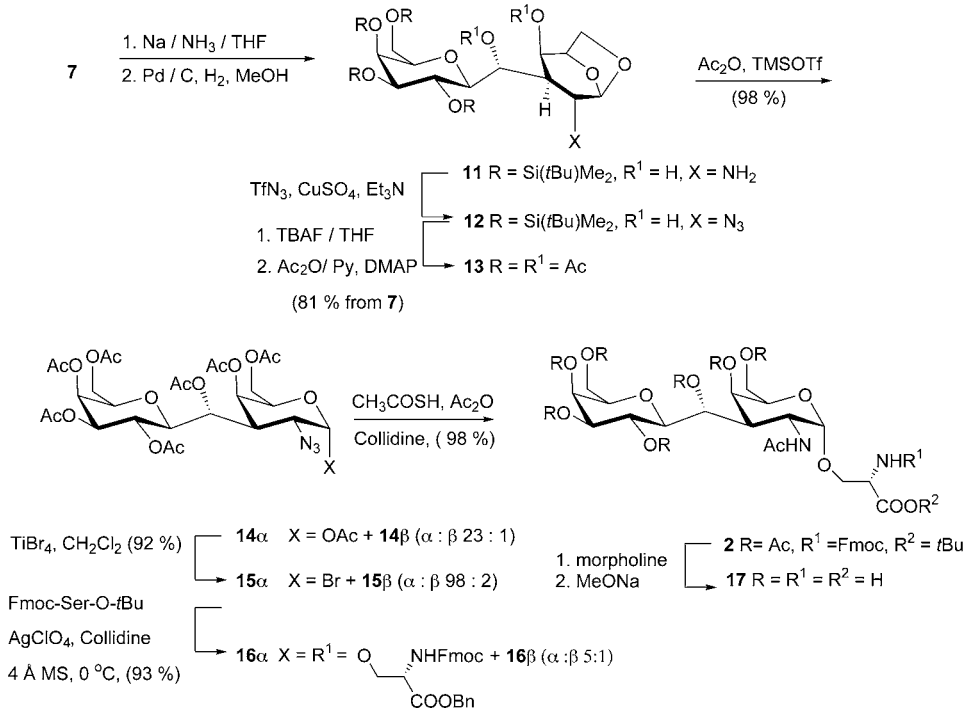
Ring-opening of the 1,6-anhydrogalactose moiety of **8** with ZnI_2 in CH_2Cl_2 required suitable conditions that would avoid the easy formation of furanoside rather than pyranoside derivatives.[13] The crude product obtained was therefore not isolated but was immediately desilylated (TBAF, THF) and peracetylated under standard conditions to produce thiogalactoside **9** in 93% yield (Scheme 4). Glycosidation of Fmoc-Ser-OBn with **9** under the conditions of Imamura et al.[14] led exclusively to the β-D-galactoside **10** (92% yield). The structure of **10β** was deduced from its ^1H NMR spectrum, which showed ^3J(H-1, H-2) = 7.4 Hz, and ^3J(H-2,H-3) = 12.3 Hz. Thus, participation of the 2-(*N*-benzyl-*N*-methoxy)amino group cannot be avoided (Scheme 4; formation of intermediate **10b**).

It was thought that it may be the bulk of the 2-BnNOMe substituent that does not allow α-glycosidations, so a nonbulky and nonparticipating group that was readily convertible into a 2-acetamido moiety was desired at C-2. Inspired by the work of Wong and co-workers,[15] we converted the *N*-benzyl-*N*-methoxyamino group of **7** into the corresponding primary amine **11** under Birch's conditions[16] with subsequent catalytic (Pd/C, H_2) hydrogenation (Scheme 5).[17] The obtained amine **11** was not isolated but was directly treated with trifluoromethanesulfonyl azide, cupric sulfate, and triethylamine in a H_2O/MeOH/CH_2Cl_2 mixture. Azide **12** was thus obtained in 81% yield (based on **7**). Smooth ring-opening of the 1,6-anhydrogalactose moiety of **12** involved initial peracetylation (Ac_2O/pyridine/DMAP) and then treatment with $Me_3SiOSO_2CF_3$ in Ac_2O to give **14** in 98% yield. Conversion of galactosyl acetate **14** into the corresponding bromide **15** (92%) was done with $TiBr_4$ in CH_2Cl_2 (20 °C, 12 h). Königs–Knorr glycosidation ($AgClO_4$/CH_2Cl_2, 2,4,6-collidine, 4 Å molecular sieves)[18] of *N*-Fmoc-serine *tert*-butyl ester gave a 5:1 mixture of α- (**16α**) and β-galactoside (**16β**) in 93% yield. Flash chromatography provided pure **16α**. The preferred formation of the α-galactoside is ascribed to a kinetic anomeric effect (no participating group at C-2; Scheme 5).[19]



Scheme 4. β-O-Galactosidation: participation by the 2-methoxy (benzyl)-amino group.

Treatment of **16α** with ethanethioic acid, collidine, and Ac_2O[20] furnished **2**—a protected form of a C-linked analogue of epitope T α-O-conjugated to L-serine—in 89% yield. This form should be suitable for the construction of clusters through peptide synthesis and further conjugation to immunogenic proteins, as demonstrated by Danishefsky and co-workers[6] for an O-linked analogue of **2**



Scheme 5. Synthesis of C-linked disaccharide α-O-conjugated to L-serine.

that was converted into cluster **1**. We have verified that the disaccharide **2** protected as a peracetate can be deprotected. When **2** was treated with morpholine in DMF, followed by MeONa/MeOH, disaccharide **17** was obtained in 52% yield after HPLC purification.

Conclusion

The C-linked disaccharide α-O-conjugated with L-serine (**16α**) mimicking epitope T has been obtained for the first time. The method relies on the Oshima–Nozaki condensation of silylated β-D-galactopyranosylcarbaldehyde derivative **3** with isolevoglucosenone (**4**) to give enone **5**. Stereoselective 1,4-addition of MeONHBn to enone **5** generated a 1,6-anhydro-2-(*N*-benzyl-*N*-methyl)-2-deoxygalactose intermediate **6**, which was converted into the corresponding peracetylated β-galactosyl-β(1-CH(OH)-3)-2-azido-2-deoxygalactopyranosyl bromide **15**. Königs–Knorr glycosidation of Fmoc-Ser-O-*t*Bu with **15** afforded a 5:1 mixture of α- and β-galactosides. The α-galactoside **16α** can be obtained pure and can be converted into **2**. The mimic of epitope T thus obtained is protected in a form suitable for clustering and further conjugation.

Experimental Section

General remarks: Reagents were purchased from Acros, Fluka, Senn, Aldrich, or Merck and were used without further purification. All solvents for extraction and chromatography were distilled prior to use. Anhydrous THF, Et_2O, and toluene were distilled from sodium benzophenone, CH_2Cl_2 from CaH_2, and methanol from magnesium. Reactions were monitored by TLC (Merck Kieselgel 60F 254 silica gel plates; detection with UV (254 nm) light or molybdate reagent (21 g of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1 g $Ce(SO_4)_2$, 31 mL H_2SO_4, and 470 mL H_2O). Flash chromatography (FC) was performed over 230–400 mesh silica gel (Merck No. 9385). Melting points were measured with a Mettler FP52 instrument and were uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. UV spectra were recorded on a Kontron Uvikon 810 CW spectrophotometer. IR spectra were recorded on Perkin–Elmer Paragon 1000 FT-IR spectrometer. Mass spectra were recorded on a Nermag R 10–10 C instrument in chemical ionization mode. Electron spray mass analyses were recorded on a Finnigan MAT SSQ 710C spectrometer in positive ionization mode. ^{1}H NMR spectra were recorded on Bruker DPX 400 FT, Bruker ARX 400 FT, or AMX 600 spectrometers; all ^{1}H signal assignments were confirmed by COSY spectra. ^{13}C NMR spectra were recorded on Bruker DPX 400 FT (100.61 MHz) or Bruker ARX 400 FT (100.61 MHz) machines; all ^{13}C signal assignments were confirmed by HMQC spectra. Chemical shifts are in ppm, relative to internal standards, such as residual signals of solvents, and coupling constants are in Hertz. High-resolution FAB mass spectra were recorded on a FAB-LSIMS device (Universidad de Sevilla, Spain). Microanalyses were performed by the Ilse Beetz Laboratory, Kronach (Germany).

1,6-Anhydro-3-{(1*R*)-2,6-anhydro-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2,3-dideoxy-β-D-*glycero*-hex-2-enopyran-4-ulose (5): A solution of Et_2AlI (1 M in toluene, 12 mL, 12.0 mmol) was added dropwise at −78 °C to a mixture of aldehyde **3** (6.0 g, 9.4 mmol) and **4** (2.0 g, 15.9 mmol) in CH_2Cl_2 (100 mL). The solution was stirred at this temperature for 2 h and was diluted with Et_2O (500 mL). Aqueous HCl (2 M, 50 mL) was added, and the aqueous phase was extracted with Et_2O (2×200 mL). The combined organic phases were washed sequentially with aqueous HCl (2 M, 50 mL), H_2O (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated. FC (light petroleum ether/EtOAc 9:1) afforded **5** (6.89 g, 96%) as a colorless oil; R_f=0.37 (petroleum ether (PE)/diethyl ether 4:1); $[\alpha]_D^{25}$=+79 (c=0.243 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.39 (dd, ^3J(H−C(1),H−C(2))=3.5, ^4J(H−C(2),H−C(1′))=1.0 Hz; H−C(2)), 5.83 (d, ^3J(H-1,H−C(2))=3.5 Hz; H−C(1)), 4.75 (dd, ^3J(H−C(5),H−C(6))=6.4, ^3J(H−C(5),H−C(6))=1.3 Hz; H−C(5)), 4.45 (dd, ^3J(H−C(3′),H−C(4′))=8.6, ^3J(H−C(2′),H−C(3′))=7.0 Hz; H−C(3′)), 4.26 (d, ^2J=12.4 Hz; H_a−C(7′)), 4.23 (ddd, ^3J(H−C(1′),H−C(2′))=7.0, ^3J(H−C(1′),OH−C(1′))=6.7, ^4J(H−C(2),H−C(1′))=1.0 Hz; H−C(1′)), 4.06 (dd, ^2J=8.3, ^3J(H−C(5),H_{exo}−C(6))=6.4 Hz; H_{exo}-6), 3.99 (d, ^3J(H−C(3′),H−C(4′))=8.6 Hz; H−C(4′)), 3.96 (d, ^3J(H−C(5′),H−C(6′))=4.1 Hz; H−C(5′)), 3.91 (t, ^3J(H−C(1′),H−C(2′))=^3J(H-2′, H-3′)=7.0 Hz; H−C(2′)), 3.80 (dd, ^3J(H−C(5′),H−C(6′))=4.1, ^3J(H−C(6′),H_b-(7′))=1.9 Hz; H−C(6′)), 3.75 (dd, ^2J=12.7, ^3J(H−C(6′),H_b−C(7′))=1.9 Hz; H_b-(7′)), 3.65 (dd, ^2J=8.3, ^3J(H−C(5),H_{endo}−C(6))=1.3 Hz; H_{endo}−C(6)), 2.94 (d, ^3J(H−C(1′),OH−C(1′))=6.7 Hz; OH−C(1′)), 0.94, 0.93, 0.90, 0.90 (4×s, 4×9H; 4×*t*Bu), 0.14, 0.12, 0.10, 0.09, 0.08, 0.07, 0.06, 0.05 ppm (8×s, 8×3H; 8×$SiCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=194.5 (s; C(4)), 143.6 (d, ^1J(C,H)=165 Hz; C(2)), 137.0 (s; C(3)), 96.9 (d, ^1J(C,H)=177 Hz; C(1)), 79.7 (d, ^1J(C,H)=141 Hz; C(2′)), 79.1 (d, ^1J(C,H)=160 Hz; C(5)), 73.1 (d, ^1J(C,H)=

143 Hz; C(6′)), 70.5 (d, ^1J(C,H) = 144 Hz; C(5′)), 67.3 (d, ^1J(C,H) = 142 Hz; C(3′)), 67.1 (d, ^1J(C,H) = 147 Hz; C(1′)), 66.9 (d, ^1J(C,H) = 138 Hz; C(4′)), 62.3 (t, ^1J(C,H) = 154 Hz; C(6)), 58.2 (t, ^1J(C,H) = 142 Hz; C(7′)), 25.9, 25.89, 25.85, 25.7 (4 × q, ^1J(C,H) = 125 Hz; $(CH_3)_3$CSi), 18.2, 18.1, 17.9, 17.0 (4 × s; $(CH_3)_3C$Si), −4.4, −4.6, −4.7, −4.9, −5.0, −5.1, −5.3, −5.5 ppm (8 × q, ^1J(C,H) = 118 Hz; CH_3Si); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{37}H_{74}O_9Si_4Na^+$: 797.4307; found: 797.4310; elemental analysis calcd (%) for $C_{37}H_{74}O_9Si_4$ (775.32): C 57.32, H 9.62; found: C 57.24, H 9.56.

1,6-Anhydro-3-{(1*R*)-2,6-anhydro-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2-[(*N*-benzyl-*N*-methoxy)amino]-2,3-dideoxy-β-D-*xylo*-hexopyran-4-ulose (6): A solution of **5** (200 mg, 0.258 mmol) in CH_2Cl_2 (1 mL) was stirred at RT, and BnNHOMe (120 mg, 0.876 mmol) was added. The mixture was allowed to stir at ambient temperature for 12 h. Slow chromatography on silica gel (light petroleum ether/diethyl ether 9:1) afforded **6** (193 mg, 82 %) as a colorless oil; R_f = 0.61 (PE/diethyl ether 4:1); $[\alpha]_D^{25} = -1.7$ (*c* = 0.40 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.43 (m, 2H; ArH), 7.38–7.26 (m, 3H; ArH), 6.07 (s; H−C(1)), 4.50 (dd, ^3J(H-5,H_{exo}−C(6)) = 5.8, ^3J(H-5,H_{endo}−C(6)) = 0.9 Hz; H-5), 4.27 (dd, ^3J(H−C(1′),H−C(2′)) = 6.6, ^3J(H−C(1′),H−C(3)) = 2.6 Hz; H−C(1′)), 4.23 (d, ^2J = 13.0 Hz; H_a−C(NCH_2Ph)), 4.19–4.10(m, 3H; H−C(6′), H_a−C(7′), H−C(5′)), 3.95 (d, ^3J(H−C(3′),H−C(4′)) = 4.2 Hz; H−C(3′)), 3.87 (d, ^2J = 13.0 Hz; H_b−C(NCH_2Ph)), 3.84 (d, ^2J = 7.6 Hz; H_{endo}−C(6)), 3.85–3.80 (m, 2H; H−C(4′), H−C(2′)), 3.74 (dd, ^2J = 7.6, ^3J(H_{exo}−C(6),H−C(5)) = 5.8 Hz; H_{exo}−C(6)), 3.70 (dd, ^2J = 12.9, ^3J(H_b−C(7′),H−C(6′)) = 1.2 Hz; H_b−C(7′)), 3.45 (d, ^3J(H−C(2),H−C(3)) = 9.83 Hz; H−C(2)), 3.25 (m, 4H; H−C(3),3H−C(OCH_3)), 0.96, 0.93, 0.92, 0.87 (4 × s, 36H; 36 × H−C(SiC(CH_3)$_3$)), 0.14, 0.13, 0.13, 0.12, 0.11, 0.10, 0.10, 0.09 ppm (8 × s, 24H; 24 × H−C(SiCH_3)); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 214.0 (s; C(4)), 137.0 (s; C(arom)), 129.8 (d, ^1J(C,H) = 159 Hz; C(arom)), 128.1 (d, ^1J(C,H) = 156 Hz; C(arom)), 127.3 (d, ^1J(C,H) = 159 Hz; C(arom)), 100.3 (d, ^1J(C,H) = 179 Hz; C(1)), 79.5 (d, ^1J(C,H) = 146 Hz; C(2′)), 78.4 (d, ^1J(C,H) = 159 Hz; C(5)), 73.3 (d, ^1J(C,H) = 154, C4′), 70.2 (d, ^1J(C,H) = 141 Hz; C(3′)), 67.4 (d, ^1J(C,H) = 144 Hz; C(1′)), 70.4 (d, ^1J(C,H) = 146 Hz; C(5′)), 67.0 (t, ^1J(C,H) = 154 Hz; C(6)), 66.7 (d, ^1J(C,H) = 147 Hz; C(6′)), 64.9 (d, ^1J(C,H) = 126 Hz; C(2)), 62.0 (q, ^1J(C,H) = 125 Hz; C(OCH_3)), 58.5 (t, ^1J(C,H) = 143 Hz; C(7′)), 46.3 (d, ^1J(C,H) = 143 Hz; C(3)), 25.9, 25.89, 25.85, 25.7 (4 × q, ^1J(C,H) = 125 Hz; $(CH_3)_3$CSi), 18.2, 18.1, 17.9, 17.0 (4 × s; $(CH_3)_3C$Si), −4.4, −4.6, −4.7, −4.9, −5.0, −5.1, −5.3, −5.5 ppm (8 × q, ^1J(C,H) = 118 Hz, CH_3Si); IR (film): $\tilde{\nu}$ = 3550, 2954, 2857, 1718, 1471, 1263, 1129, 880, 777, 741 cm^{-1}; HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{45}H_{85}NO_{10}Si_4Na^+$: 934.5148; found: 934.5134; elemental analysis calcd (%) for $C_{45}H_{85}NO_{10}Si_4$ (912.50): C 59.23, H 9.39, N 1.53; found: C 59.33, H 9.33, N 1.55.

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-[(*N*-benzyl-*N*-methoxy)amino]-2,3-dideoxy-β-D-*galacto*-hexopyranose (7): A solution of $LiBH_4$ in THF (7.0 mL, 14.0 mmol) was added dropwise at −78 °C to a solution of **6** (3.50 mg, 3.84 mmol) in THF (50 mL). The mixture was stirred at −78 °C to 15 °C for 4 h. An aqueous NH_4Cl solution (25 mL) was added. The reaction mixture was warmed to 20 °C. An aqueous solution of sodium potassium tartrate (25 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (100 mL; three times). The combined organic phases were dried and concentrated in vacuo. FC (4:1, light petroleum ether/Et_2O) gave **7** (3.22 g, 92 %) as a colorless oil; R_f = 0.32 (PE/diethyl ether 7:3); $[\alpha]_D^{25} = +26$ (*c* = 0.275 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.39 (m, 2H; ArH); 7.38–7.27 (m, 3H; ArH), 5.84 (s; H−C(1)), 4.84 (m; H−C(4)), 4.54 (dd, ^3J(H-5,H−C(4)) = 7.0, ^3J(H−C(5),H_{exo}−C(6)) = 5.4 Hz; H−C(5)), 4.43 (dd, ^2J = 11.5, ^3J(H_a−C(7′),H−C(6′)) = 9.9 Hz; H_a−C(7′)), 4.37–4.30 (m, 2H; H_{endo}−C(6), H−C(1′)), 4.27 (dd, ^3J(H−C(5′),H−C(6′)) = 6.4, ^3J(H−C(5′),HC-(4′)) = 2.6 Hz; H−C(5′)), 4.13 (d, ^3J(H−C(2′),H-(1′)) = 9.3 Hz; H−C(2′)), 3.64 (d, ^2J = 13.1 Hz; H_a−C(NCH_2Ph)), 3.98–3.89 (m, 3H; H−C(3′), H−C(6′), H_b−C(NCH_2Ph)), 3.72 (dd, ^3J(H−C(4′),H−C(3′)) = 3.5, ^3J(H−C(4′),H−C(5′)) = 2.6 Hz; H−C(4′)), 3.80 (dd, ^2J = 11.5, ^3J(H_b−C(7′),H−C(6′)) = 1.9 Hz; H_b−C(7′)), 3.51 (dd, ^2J = 7.4, ^3J(H-5,H_{exo}−C(6)) = 5.4 Hz; H_{exo}−C(6)), 3.3 (s, 3H; H−C(OCH_3)), 4.24 (d, ^3J(H−C(2),H−C(3)) = 9.6 Hz; H−C(2)), 2.64 (ddd, ^3J(H-3,H-2) = 9.6, ^3J(H-3,H-4) = 6.7, ^3J(H−C(3), H−C(1′)) = 2.6 Hz; H−C(3)), 0.98, 0.95, 0.94, 0.93 (4 × s, 36H; 36 × H−C(SiC(CH_3)$_3$)), 0.16, 0.15, 0.14, 0.13, 0.120, 0.12, 0.11, 0.10 ppm (8 × s, 24H; 24 × H−C(SiCH_3)); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 137.6 (s; C(arom)), 129.6 (d, ^1J(C,H) = 159 Hz; C(arom)), 128.3 (d, ^1J(C,H) = 156 Hz; C(arom)), 127.3 (d, ^1J(C,H) = 156 Hz; C(arom)), 99.6 (d, ^1J(C,H) = 179 Hz; C(1)), 79.1 (d, ^1J(C,H) = 147 Hz; C(6′)), 73.6 (d, ^1J(C,H) = 159 Hz; C(5)), 73.4 (d, ^1J(C,H) = 154 Hz; C4′), 70.7 (d, ^1J(C,H) = 141 Hz; C(3′)), 69.0 (d, ^1J(C,H) = 144 Hz; C(1′)), 67.4 (d, ^1J(C,H) = 146 Hz; C(2′)), 67.3 (d, ^1J(C,H) = 146 Hz; C(5′)), 66.3 (t, ^1J(C,H) = 144 Hz; C(4)), 64.2 (d, ^1J(C,H) = 143 Hz; C(2)), 61.6 (t, ^1J(C,H) = 154 Hz; C(6)), 61.6 (q, ^1J(C,H) = 122 Hz; C(OCH_3)), 58.5 (t, ^1J(C,H) = 143 Hz; C(7′)), 58.5 (t, ^1J(C,H) = 145 Hz; C(NCH_2Ph)), 34.9 (d, ^1J(C,H) = 126 Hz; C(3)), 26.0, 25.9, 25.8, 25.7(4×q, ^1J(C,H) = 125 Hz; $(CH_3)_3$CSi), 18.3, 18.0, 17.9, 17.8 (4 × s; $(CH_3)_3C$Si), −4.4, −4.6, −4.8, −4.9, −5.0, −5.1, −5.3, −5.5 ppm (8 × q, ^1J(C,H) = 118 Hz; CH_3Si); IR (film): $\tilde{\nu}$ = 3477, 2953, 2856, 1714, 1633, 1471, 1256, 1099, 836, 778, 739 cm^{-1}; HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{45}H_{87}NO_{10}Si_4Na^+$: 936.5304; found: 936.5304; elemental analysis calcd for $C_{45}H_{87}NO_{10}Si_4$ (914.52): C 59.10, H 9.59, N 1.53; found: C 59.15, H 9.50, N 1.62.

4-*O*-Acetyl-1,6-anhydro-3-{(1*R*)-1,3,4,5,7-penta-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2-[(*N*-benzyl-*N*-methoxy)amino]-2,3-dideoxy-β-D-*galacto*-hexopyranose (8): Compound **7** (1.12 g, 1.22 mmol) was dissolved in THF (3 mL), a solution of TBAF in THF (8 mL g, 9.76 mmol) was added, and the resulting solution was stirred for 3 h at 20 °C. The mixture was evaporated to dryness, and the residue was then dissolved in pyridine (5 mL). A catalytic amount of DMAP was added, followed by acetic anhydride (3 mL), and the solution was stirred for 2 days at 20 °C. MeOH (5 mL) was added, and the mixture was evaporated to dryness and then dissolved in EtOAc (25 mL). The solution was quenched with aqueous HCl (10 mL), washed with a sat. aqueous solution of $NaHCO_3$ (5 mL), water, and brine, and dried ($MgSO_4$). Evaporation of the filtrate and FC gave **8** (870 mg, 100 %) as a colorless oil; R_f = 0.6 (PE/EtOAc 1:1); $[\alpha]_{589}^{25} = +73$ (*c* = 0.183 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.42 (m, 2H; H−C(arom)), 7.33–7.22 (m, 6H; H−C(arom)), 5.87–5.77 (m, 3H; H−C(1′), H−C(1), H−C(4)), 5.33 (dd, ^3J(H−C(6′),H−C(5′)) = 6.2, ^3J(H−C(6′),H_a−C(7′)) = 3.1 Hz; H−C(6′)), 5.25 (dd, ^3J(H−C(3′),H−C(4′)) = 4.0, ^3J(H−C(3′),H−C(2′)) = 3.7 Hz; H−C(3′)), 4.84 (dd, ^3J(H−C(4′),H−C(3′)) = 4.0, ^3J(H−C(4′),H−C(5′)) = 1.2 Hz; H−C(4′)), 4.72 (dd, ^3J(H−C(5),H−C(4)) = 7.7, ^3J(H−C(5),H_{exo}−C(6)) = 4.6 Hz; H−C(5)), 4.68 (d, ^2J = 12.9 Hz; H_a−C(7′)), 4.29–4.20 (m, 3H; H_b−C(7′), H−C(2′), H−C(5′)), 4.02 (d, ^2J = 12.9 Hz; H_a−C(NCH_2Ph); 3.95 (d, ^2J = 7.4 Hz; H_{endo}−C(6)), 3.79 (d, ^2J = 12.9 Hz; H_b−C(NCH_2Ph); 3.42 (dd, ^2J = 7.4, ^3J(H_{exo}−C(6),H−C(5)) = 4.6 Hz; H_{exo}−C(6)), 3.20 (s, 3H; H−C(OCH_3)), 2.72 (m; H−C(2)), 5.31 (ddd, ^3J(H−C(3),H−C(2)) = 10.8, ^3J(H−C(3),H−C(4)) = 5.5, ^3J(H−C(3),H−C(1′)) = 2.6 Hz; H−C(3)), 2.13–1.87 ppm (6 × s, 18H; H−C(CH_3COO)); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 170.7, 170.1, 169.8, 169.4, 169.2, 168.8 (6 × s; C(CH_3COO)), 137.3 (s; C(arom)), 129.9 (d, ^1J(C,H) = 159 Hz; C(arom)), 128.0 (d, ^1J(C,H) = 156 Hz; C(arom)), 127.2 (d, ^1J(C,H) = 156 Hz; C(arom)), 99.3 (d, ^1J(C,H) = 179 Hz; C(1)), 71.9 (d, ^1J(C,H) = 159 Hz; C(5)), 71.7 (d, ^1J(C,H) = 146 Hz; C(2′)), 67.3 (d, ^1J(C,H) = 144 Hz; C(1′)), 67.1 (d, ^1J(C,H) = 154 Hz; C(4′)), 66.6 (d, ^1J(C,H) = 141 Hz; C(3′)), 66.3 (d, ^1J(C,H) = 144 Hz; C(4)), 65.5 (d, ^1J(C,H) = 147 Hz; C(6′)), 65.4 (d, ^1J(C,H) = 146 Hz; C(5′)), 64.5 (d, ^1J(C,H) = 143 Hz; C(2)), 62.6 (t, ^1J(C,H) = 154 Hz; C(6)), 62.3 (q, ^1J(C,H) = 122 Hz; OCH$_3$), 59.2 (t, ^1J-(C,H) = 143 Hz; C(7′)), 59.2 (t, ^1J(C,H) = 145 Hz; C(NCH_2Ph)), 33.0 (d, ^1J(C,H) = 126 Hz; C(3)), 21.0–20.5 ppm (6 × q, ^1J(C,H) = 130 Hz; H−C-(CH_3COO)); IR (film): $\tilde{\nu}$ = 2058, 2983, 2897, 1751, 1665, 1431, 1370, 735, 701 cm^{-1}; HRMS (MALDI-TOF): calcd for $C_{33}H_{43}NO_{16}Na^+$: 732.2479; found: 732.2469.

4,6-Di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-[(*N*-benzyl-*N*-methoxy)amino]-2,3-dideoxy-β-D-*galacto*-hexopyranosyl phenylsulfide (9β): A mixture of **8** (0.316 g, 0.450 mmol), (phenylthio)trimethylsilane (0.254 mL, 1.345 mmol), and ZnI_2 (0.42 g, 1.333 mmol) in dry CH_2Cl_2 (7 mL) was stirred at 20 °C for 2 h. The mixture was diluted with CH_2Cl_2 (50 mL) and washed successively with sat. aqueous $NaHCO_3$ (30 mL), water (20 mL, three times), and brine (20 mL), dried ($MgSO_4$), and evaporated. The residue was dissolved in THF (10 mL), TBAF (0.450 mL, 0.450 mmol) was added, and the mixture was stirred at 20 °C for 1 h. The solvent was

evaporated, the residue was dissolved in pyridine (10 mL), and then DMAP (40 mg) and Ac_2O (4 mL) were added. The mixture was stirred at 20 °C for 18 h. The solvent was evaporated, and FC gave **9β** (370 mg, 96 %) as a colorless oil; $R_f = 0.64$ (PE/EtOAc 1:1); $[\alpha]_D^{25} = +24$ ($c = 0.206$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$; data for the β anomer): $\delta = 7.65$–7.55 (m, 4H; H–C(arom)), 7.35–7.25 (m, 6H; H–C(arom)), 6.10 (dd, ^3J(H–C(1′),H–C(3)) = 9.9, ^3J(H–C(1′),H–C(2′)) = 1.5 Hz; H–C(1′)), 5.61 (s; H–C(4)), 6.34 (d, ^3J(H–C(1),H–C(2)) = 8.6 Hz; H–C(1)), 5.31 (dd, ^3J(H–C(5′),H–C(6′)) = 6.5, ^3J(H–C(5′),H–C(4′)) = 3.1 Hz; H–C(5′)), 5.173 (t, ^3J(H–C(4′),H–C(3′)) = 3.4 Hz; H–C(4′)), 4.86 (d, ^3J(H–C(3′),H–C(4′)) = 3.4 Hz; H–C(3′)), 4.75 (dd, ^2J = 12.9, ^3J(H_a–C(7′),H–C(6′)) = 9.9 Hz; H_a–C(7′)), 4.59 (d, ^2J = 12.6 Hz; H_a–C(NCH_2Ph)), 4.50 (d, ^3J(H–C(2′),H–C(1′)) = 10.2 Hz; H–C(2′)), 4.38 (dd, ^2J = 12.9, ^3J(H_a–C(7′),H–C(6′)) = 1.8 Hz; H_b–C(7′)), 4.30–4.18 (m, 2H; H_{endo}–C(6), H–C(6′)), 4.08 (dd, ^2J = 11.4, ^3J(H_{exo}–C(6),H–C(5)) = 7.4 Hz; H_{exo}–C(6)), 3.90 (t, ^3J(H–C(5),H_{exo}–C(6)) = 6.8 Hz; H–C(5)), 3.75 (d, ^2J = 12.6 Hz; H_a–C-(NCH_2Ph)), 3.11–3.08 (m, 4H; H–C(OCH_3), H–C(2)), 2.57 (d, ^3J(H–C(3),H–C(2)) = 12.3 Hz; H–C(3)), 2.27–1.83 ppm (7 × s, 21H; CH_3COO); ^{13}C NMR (100.6 MHz, $CDCl_3$; data for the β anomer): $\delta = 170.6$, 170.5, 170.3, 169.8, 169.6, 169.1, 169.0 (7 × s; −COO), 138.7 (s; C(arom)), 134.0 (s; C(arom)), 131.9 (d, ^1J(C,H) = 162 Hz; C(arom)), 130.0 (d, ^1J(C,H) = 158 Hz; C(arom)), 128.7 (d, ^1J(C,H) = 159 Hz; C(arom)), 128.0 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.4 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.3 (d, ^1J(C,H) = 159 Hz; C(arom)), 83.4 (d, ^1J(C,H) = 159 Hz; C(1)), 76.2 (d, ^1J(C,H) = 139 Hz; C(5)), 72.9 (d, ^1J(C,H) = 150 Hz; C(6′)), 67.6 (d, ^1J(C,H) = 155 Hz; C(1′)), 67.1 (d, ^1J(C,H) = 155 Hz; C(3′)), 66.7 (d, ^1J(C,H) = 157 Hz; C(4′)), 65.6 (d, ^1J(C,H) = 149 Hz; C(5′)), 65.4 (d, ^1J(C,H) = 150 Hz; C(4)), 64.9 (d, ^1J(C,H) = 144 Hz; C(2′)), 63.2 (q, ^1J(C,H) = 130 Hz; OCH_3), 62.5 (t, ^1J(C,H) = 149 Hz; C(6)), 60.8 (d, ^1J(C,H) = 139 Hz; C(2)), 59.5 (t, ^1J(C,H) = 148 Hz; C(7′)), 41.4 (d, ^1J(C,H) = 127 Hz; C(3)), 21.3–20.7 ppm (7 × q, ^1J(C,H) = 130 Hz; CH_3COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{41}H_{51}NO_{17}SNa^+$: 884.2775; found: 884.2776.

***N*-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-[(*N*-benzyl-*N*-methoxy)amino]-2,3-dideoxy-β-D-galactopyranosyl}-L-serine benzyl ester (10β)**: A mixture of preactivated molecular sieves (4 Å, 200 mg), **9β** (167 mg, 0.194 mmol), and *N*-Fmoc-threonine-OBn (170 mg, 0.407 mmol) were dissolved in dry CH_2Cl_2. NIS (44 mg, 0.194 mmol) and TMSOTf (70 μL, 0.388 mmol) were added at 0 °C. The reaction mixture was continuously stirred at 0 °C until **9β** was completely consumed (TLC analysis). The mixture was filtered through a pad of Celite and washed with CH_2Cl_2 (50 mL), and the combined filtrate and washings were washed with sat. aqueous $NaHCO_3$ (10 mL), sat. aqueous $Na_2S_2O_3$ (10 mL), and brine, dried over Na_2SO_4, and concentrated in vacuo. FC (hexanes/EtOAc 4:1→3:1) gave **10β** only (205 mg, 92 %), as a white foam; $R_f = 0.64$ (PE/EtOAc 1:1); $[\alpha]_D^{25} = +31$ ($c = 0.211$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$; data for the β anomer): $\delta = 7.81$–7.10 (m, 18H; H–C(arom)), 6.84 (d, ^3J(H–N,H–C*(Ser)) = 9.2 Hz; H–N); 6.12 (dd, ^3J(H–C(1′),H–C(3)) = 9.9, ^3J(H–C(1′),H–C(2′)) = 1.2 Hz; H–C(1′)), 5.56 (s; H–C(4)), 5.34 (dd, ^3J(H–C(5′),H–C(6′)) = 6.5, ^3J(H–C(5′),H–C(4′)) = 3.1 Hz; H–C(5′)), 5.29 (t, ^3J(H–C(4′),H–C(3′)) = 3.1 Hz; H–C(4′)), 5.23 (t, ^2J = 12.9 Hz, 2H; H–C(CH_2Ph), 6.34 (d, ^3J(H–C(1),H–C(2)) = 7.7 Hz; H–C(1)), 4.81 (m, 1H; H–C(3′)), 4.78 (dd, ^2J = 12.5, ^3J(H_a–C(7′),H–C(6′)) = 9.9 Hz; H_a–C(7′)), 4.67 (dt, ^3J(H–C*(Ser), H–N) = 9.2, ^3J(H–C*(Ser) H_2–C(Ser) = 3.1 Hz; H–C*(Ser)), 4.63 (d, ^2J = 11.7 Hz; H_2–C(Ser)), 4.53–4.39 (m, 4H; H_2–C(Fmoc), H_b–C(7′), H–C(6′)), 4.36 (d, ^2J = 12.9 Hz; H_a–C(NCH_2Ph), 4.30–4.15 (m, 3H; H–C(2′), H_{endo}–C(6), H–C(Fmoc)), 4.03 (dd, ^2J = 11.4, ^3J(H_{exo}–C(6),H–C(5)) = 7.1 Hz; H_{exo}–C(6)), 4.63 (dd, ^2J = 11.7, ^3J(H_2–C(Ser),H–C*(Ser) = 3.1 Hz; H_2–C(Ser)), 3.88 (t, ^3J(H–C(5),H_{exo}–C(6)) = 6.47 Hz; H–C(5)), 3.6 (d, ^2J = 12.6 Hz; H_a–C(NCH_2Ph)), 3.08 (s, 3H; H–C(OCH_3)), 2.84 (dd, ^3J(H–C(2),H–C(3)) = 12.3, ^3J(H–C(2),H–C(1)) = 7.7 Hz; H–C(2)), 2.57 (br dd, ^3J(H–C(3),H–C(2)) = 12.3 Hz; H–C(3)), 2.25–1.89 ppm (7 × s, 21H; CH_3COO); ^{13}C NMR (100.6 MHz, $CDCl_3$; data for the β anomer): $\delta = 170.5$, 170.4, 170.2, 170.1, 169.8, 168.9, 168.7 (7 × s; −COO), 156.3 (s; C(carbamate)), 143.7 (s; C(arom)), 143.6 (s; C(arom)), 141.2 (s; C(arom)), 141.0 (s; C(arom)), 138.1 (s; C(arom)), 135.1 (s; C(arom)), 130.4 (d, ^1J(C,H) = 162 Hz; C(arom)), 128.4 (d, ^1J(C,H) = 158 Hz; C(arom)), 128.2 (d, ^1J(C,H) = 158 Hz; C(arom)), 128.1 (d, ^1J(C,H) = 158 Hz; C(arom)), 128.0 (d, ^1J(C,H) = 159 Hz; C(arom)), 128.0 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.9 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.6 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.5 (d, ^1J(C,H) = 159 Hz; C(arom)), 127.1 (d, ^1J(C,H) = 159 Hz; C(arom)), 126.9 (d, ^1J(C,H) = 159 Hz; C(arom)), 124.9 (d, ^1J(C,H) = 159 Hz; C(arom)), 119.8 (d, ^1J(C,H) = 159 Hz; C(arom)), 103.9 (d, ^1J(C,H) = 159 Hz; C(1)), 74.3 (d, ^1J(C,H) = 139 Hz; C(5)), 72.9 (d, ^1J(C,H) = 144 Hz; C(2′)), 70.4 (t, ^1J(C,H) = 153 Hz; CH_2(Ser)), 67.4 (t, ^1J(C,H) = 149 Hz; CH_2(Bn)), 67.3 (t, ^1J(C,H) = 150 Hz; CH_2(Fmoc)), 67.3 (d, ^1J(C,H) = 139 Hz; C(1′)), 67.0 (d, ^1J(C,H) = 155 Hz; C(3′)), 66.5 (d, ^1J(C,H) = 157 Hz; C(4′)), 65.6 (d, ^1J(C,H) = 150 Hz; C(4)), 65.4 (d, ^1J(C,H) = 149 Hz; C(5′)), 64.9 (d, ^1J(C,H) = 150 Hz; C(6′)), 63.4 (q, ^1J(C,H) = 130 Hz; OCH_3), 62.5 (t, ^1J(C,H) = 149 Hz; C(NCH_2Ph)), 61.7 (t, ^1J(C,H) = 148 Hz; C(7′)), 61.0 (d, ^1J(C,H) = 139 Hz; C(2)), 59.5 (t, ^1J(C,H) = 149 Hz; C(6)), 54.5 (d, ^1J(C,H) = 138 Hz; C*(Ser)), 47.1 (d, ^1J(C,H) = 130 Hz; C(Fmoc)), 41.1 (d, ^1J(C,H) = 127 Hz; C(3)), 21.1–20.5 ppm (7 × q, ^1J(C,H) = 130 Hz; CH_3COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{60}H_{68}N_2O_{22}Na^+$: 1191.416; found: 1191.416.

1,6-Anhydro-3-*C*-{(1*R*)-2,6-anhydro-3,4,5,7-tetrakis-*O*-[(*tert*-butyl)dimethylsilyl]-D-*glycero*-L-*manno*-heptitol-1-*C*-yl}-2-azido-2,3-dideoxy-β-D-*galacto*-hexopyranose (12): A solution of **7** (300 mg, 0.329 mmol) in dry THF (5 mL) was added at −78 °C to a stirred mixture of metallic sodium (184 mg, 8.0 mmol, 24 equiv) in liquid NH_3 (10 mL). After the system had been stirred for 30 min at −78 °C, NH_4Cl (540 mg, 10 mmol, 30 equiv) was added and the ammonia was allowed to evaporate at 20 °C. After the addition of H_2O (20 mL), the aqueous phase was extracted with CH_2Cl_2 (20 mL, three times). The combined organic phases were dried and concentrated in vacuo. The residue was dissolved in MeOH (10 mL), and 10 % Pd on charcoal (35 mg) was added. The degassed mixture was stirred under H_2 at 20 °C for 12 h. The catalyst was filtered off, the solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (1 mL). $CuSO_4$ in H_2O (1 mg in 2 mL) was added, then triethylamine (131 μl, 0.987 mmol), followed by MeOH (7 mL). The freshly prepared solution of trifluoromethanesulfonyl azide in dichloromethane (1 mL, 0.6 M, 0.6 mmol) was added at once. The reaction was stirred until TLC showed reaction to be complete, and the mixture was extracted with CH_2Cl_2 (15 mL, three times). These combined organic phases were dried and concentrated in vacuo. FC (light petroleum ether/diethyl ether 7:3) afforded **12** (220 mg, 81 %, three steps) as a colorless oil; $R_f = 0.62$ (PE/diethyl ether 7:3); $[\alpha]_D^{25} = +28$ ($c = 0.296$ in $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 5.43$ (s; H–C(1)), 4.81 (t, ^3J(H–C(4),H–C(3)) = 7.4 Hz; H–C(4)), 4.72 (dd, ^2J = 12.3, ^3J(H_a–C(7′),H–C(6′)) = 10.5 Hz; H_a–C(7′)), 4.47 (dd, ^3J(H–C(5′),H–C(6′)) = 6.2, ^3J(H–C(5′),HC-(4′)) = 2.5 Hz; H–C(5′)), 4.38–4.28 (m, 3H; H–C(5),H–C(1′), H–C(2′)), 3.25 (d, ^2J = 7.4 Hz; H_{endo}–C(6)), 4.20 (d, ^3J(H–C(3′),H-(4′)) = 4.3 Hz; H–C(3′)), 4.13 (dt, ^3J(H_a–C(7′),H–C(6′)) = 10.5, ^3J(H–C(6′),H–C(5′)) = 6.2, ^3J(H–C(6′),(H_b–C(7′)) = 2.5 Hz; H–C(6′)), 3.99 (dd, ^3J(H–C(4′),H–C(3′)) = 4.3, ^3J(H–C(4′),H–C(5′)) = 2.5 Hz; H–C(4′)), 3.96 (dd, ^2J = 12.3, ^3J(H_b–C(7′),H–C(6′)) = 2.5 Hz; H_b–C(7′)), 3.63 (d, ^3J(H–C(2),H–C(3)) = 6.2 Hz; H–C(2)), 3.63–3.50 (br s, 2H; 2 × H–C(OH)), 3.27 (dd, ^2J = 6.8, ^3J(H-5,H_{exo}–C(6)) = 4.9 Hz; H_{exo}–C(6)), 2.64 (ddd, ^3J(H-3,H-2) = 9.9, ^3J(H-3,H-4) = 7.4, ^3J(H–C(3), H–C(1′)) = 3.1 Hz; H–C(3)), 1.05, 1.01, 0.99, 0.96 (4 × s, 36H; 36 × H–C(SiC(CH_3)$_3$)), 0.28, 0.21, 0.19, 0.17, 0.16, 0.15, 0.11, 0.06 ppm (8 × s, 24H; 24 × H–C(SiCH_3)); ^{13}C NMR (100.6 MHz, C_6D_6): $\delta = 102.5$ (d, ^1J(C,H) = 179 Hz; C(1)), 78.9 (d, ^1J(C,H) = 147 Hz; C(6′)), 74.2 (d, ^1J(C,H) = 159 Hz; C(5)), 74.1 (d, ^1J(C,H) = 154 Hz; C4′), 71.5 (d, ^1J(C,H) = 141 Hz; C(3′)), 70.6 (d, ^1J(C,H) = 144 Hz; C(1′)), 68.8 (d, ^1J(C,H) = 146 Hz; C(2′)), 67.9 (d, ^1J(C,H) = 146 Hz; C(5′)), 66.8 (t, ^1J(C,H) = 144 Hz; C(4)), 63.5 (d, ^1J(C,H) = 143 Hz; C(2)), 62.7 (t, ^1J(C,H) = 154 Hz; C(6)), 59.1 (t, ^1J(C,H) = 143 Hz; C(7′)), 40.4 (d, ^1J(C,H) = 126 Hz; C(3)), 26.3, 26.1, 26.0, 25.9 (4 × q, ^1J(C,H) = 125 Hz; (CH_3)$_3$CSi), 18.5, 18.2, 18.1, 18.0 (4 × s; (CH_3)$_3$CSi), −4.3, −4.4, −4.4, −4.6, −4.8, −4.9, −5.0, −5.1 ppm (8 × q, ^1J(C,H) = 118 Hz; CH_3Si); IR (film): $\tilde{\nu} = 3477$, 2953, 2856, 1714, 1633, 1471, 1256, 1099, 836, 778, 739 cm^{-1}; HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{37}H_{77}N_3O_9Si_4Na^+$: 842.4634; found: 842.4631; elemental analysis calcd (%) for $C_{37}H_{77}N_3O_9Si_4$ (920.36): C 54.17, H 9.46, N 5.12; found: C 54.19, H 9.38, N 5.12.

4-*O*-Acetyl-1,6-anhydro-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-azido-2,3-dideoxy-β-D-*galacto*-hexopyranose (13): The *tert*-butyldimethylsilyl-protected **12** (600 mg, 0.733 mmol) was dissolved in THF (4 mL), a solution of TBAF in THF (4 mL, 4.0 mmol) was added, and the resulting solution was stirred for 3 h at room temperature. The mixture was evaporated to dryness and was then dissolved in pyridine (5 mL). A catalytic amount of DMAP (10 mg, 0.08 mmol) was added, followed by acetic anhydride (3 mL, 31.80 mmol), and the solution was stirred for 2 days at 20 °C. MeOH (5 mL) was added, the mixture was evaporated to dryness and then dissolved in ethyl acetate (25 mL), and the solution was quenched with aqueous HCl (10 mL), washed successively with saturated aqueous $NaHCO_3$ (5 mL), water, and brine, and dried ($MgSO_4$). Evaporation of the filtrate and FC (light petroleum ether/EtOAc 1:1) gave **13** (355 mg, 89 %) as a white solid. m.p. 46–47 °C; $R_f = 0.57$ (PE/EtOAc 1:1); $[\alpha]_D^{25} = +51$ ($c = 0.124$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.74$ (dd, ^3J(H–C(4),H–C(5)) = 8.0, ^3J(H–C(4),H–C(3)) = 5.9 Hz; H–C(4)), 5.52 (s; H–C(1)), 5.43–5.36 (m, 2H; H–C(5′), H–C(1′)), 5.22 (t, ^3J(H–C(4′),H–C(5′)) = 4.0 Hz; H–C(4′)), 5.03 (dd, ^3J(H–C(3′),H–C(4′)) = 4.3, ^3J(H–C(3′),H–C(2′)) = 1.8 Hz; H–C(3′)), 4.82–4.74 (m, 2H; H_a–C(7′), H–C(5)), 4.39–4.27 (m, 2H; H–C(6′),H–C(2′)), 4.19 (dd, $^2J = 12.6$, ^3J(H_b–C(7′),H–C(6′)) = 2.5 Hz; H_b–C(7′)), 3.97 (d, $^2J = 7.4$ Hz; H_{endo}–C(6)), 3.43 (dd, $^2J = 7.4$, ^3J(H_{exo}–C(6),H–C(5)) = 4.3 Hz; H_{exo}–C(6)), 3.25 (d, ^3J(H–C(2),H–C(3)) = 10.2 Hz; H–C(2)), 2.18–2.00 ppm (7×s, 22H; H–C(3), CH_3COO); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 167.0$, 169.9, 169.8, 169.7, 169.7, 169.4, 168.9 (7×s, −COO), 102.9 (d, ^1J(C,H) = 175 Hz; C(1)), 72.3 (d, ^1J(C,H) = 149 Hz; C(6′)), 72.1 (d, ^1J(C,H) = 146 Hz; C(5)), 67.5 (d, ^1J(C,H) = 149 Hz; C(5′)), 67.2 (d, ^1J(C,H) = 148 Hz; C(4′)), 66.9 (d, ^1J(C,H) = 149 Hz; C(3′)), 65.6 (d, ^1J(C,H) = 156 Hz; C(1′)), 65.5 (d, ^1J(C,H) = 144 Hz; C(2′)), 65.0 (d, ^1J(C,H) = 151 Hz; C(4)), 63.2 (t, ^1J(C,H) = 149 Hz; C(6)), 62.1 (d, ^1J(C,H) = 129 Hz; C(2)), 59.3 (t, ^1J(C,H) = 147 Hz; C(7′)), 36.4 (d, ^1J(C,H) = 127 Hz; C(3)), 21.0–20.6 ppm (7×q, ^1J(C,H) = 130 Hz; *C*H_3COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{25}H_{33}N_3O_{15}Na^+$: 638.1809; found: 638.1801; elemental analysis calcd (%) for $C_{25}H_{33}N_3O_{15}$ (615.54): C 48.78, H 5.40, N 6.83; found: C 48.82, H 5.46, N 6.83.

4,6-Di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-azido-2,3-dideoxy-α-D-*galacto*-hexopyranosyl acetate (14α): Compound **13** (0.35 g, 0.57 mmol) was dissolved in Ac_2O (10 mL). After the mixture had been cooled to −40 °C, $Me_3SiOSO_2CF_3$ (0.123 mL, 0.683 mmol) was added (syringe) and the mixture was stirred for 1 h. CH_2Cl_2 (30 mL) was added and the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL). The organic phase was collected and extracted with H_2O and then with brine and dried ($MgSO_4$). Solvent evaporation and FC (hexanes/EtOAc 2:1→1:3) gave **14α** (400 mg, 98 %) as a white foam; $R_f = 0.50$ (PE/EtOAc 1:1); $[\alpha]_D^{25} = +89$ ($c = 0.3775$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$; data for the α anomer): $\delta = 6.34$ (d, ^3J(H–C(1),H–C(2)) = 3.4 Hz; H–C(1)), 5.58 (s; H–C(4)), 5.38 (dd, ^3J(H–C(1′),H–C(3)) = 10.2, ^3J(H–C(1′),H–C(2′)) = 2.5 Hz; H–C(1′)), 5.31 (dd, ^3J(H–C(5′),H–C(6′)) = 6.5, ^3J(H–C(5′),H–C(4′)) = 3.1 Hz; H–C(5′)), 5.17 (t, ^3J(H–C(4′),H–C(5′)) = 3.1 Hz; H–C(4′)), 4.86 (dd, ^3J(H–C(3′),H–C(4′)) = 4.5, ^3J(H–C(3′),H–C(2′)) = 1.5 Hz; H–C(3′)), 4.77 (dd, $^2J = 12.9$, ^3J(H_a–C(7′),H–C(6′)) = 10.2 Hz; H_a–C(7′)), 4.50 (dd, ^3J(H–C(2′),H–C(1′)) = 10.2, ^3J(H–C(2′),H–C(3′)) = 1.5 Hz; H–C(2′)), 4.33–4.25 (m, 2H; H_b–C(7′),H–C(6′)), 4.14 (t, ^3J(H–C(5),H_{exo}–C(6)) = 6.5 Hz; H–C(5)), 4.08 (d, $^2J = 11.1$ Hz; H_{endo}–C(6)), 3.91 (dd, $^2J = 11.1$, ^3J(H_{exo}–C(6),H–C(5)) = 6.5 Hz; H_{exo}–C(6)), 3.61 (dd, ^3J(H–C(2),H–C(3)) = 12.3, ^3J(H–C(2),H–C(1)) = 3.4 Hz; H–C(2)), 2.45 (dt, ^3J(H–C(3),H–C(2)) = 12.3, ^3J(H–C(3),H–C(1′)) = 2.5 Hz; H–C(3)), 2.08–1.99 ppm (8×s, 24H; CH_3COO); ^{13}C NMR (100.6 MHz, $CDCl_3$; data for the α anomer): $\delta = 170.3$, 170.2, 169.8, 169.7, 169.3, 168.8, 168.7, 168.6 (8×s, −COO), 90.1 (d, ^1J(C,H) = 175 Hz; C(1)), 72.7 (d, ^1J(C,H) = 149 Hz; C(6′)), 69.9 (d, ^1J(C,H) = 146 Hz; C(5)), 66.6 (d, ^1J(C,H) = 156 Hz; C(1′)), 66.6 (d, ^1J(C,H) = 148 Hz; C(4′)), 66.5 (d, ^1J(C,H) = 149 Hz; C(3′)), 65.3 (d, ^1J(C,H) = 149 Hz; C(5′)), 64.8 (d, ^1J(C,H) = 151 Hz; C(4)), 64.6 (d, ^1J(C,H) = 144 Hz; C(2′)), 61.3 (t, ^1J(C,H) = 149 Hz; C(6)), 59.3 (t, ^1J(C,H) = 147 Hz; C(7′)), 54.8 (d, ^1J(C,H) = 129 Hz; C(2)), 37.1 (d, ^1J(C,H) = 127 Hz; C(3)), 20.8–20.4 ppm (8×q, ^1J(C,H) = 130 Hz; *C*H_3COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{25}H_{33}N_3O_{15}Na^+$: 740.2126; found: 740.2128; elemental analysis calcd for $C_{29}H_{39}N_3O_{18}$ (717.63): C 48.54, H 5.48, N 6.86; found: C 48.59, H 5.50, N 5.78.

4,6-Di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-azido-2,3-dideoxy-α-D-*galacto*-hexopyranosyl bromide (15α): A solution of **14** (0.50 g, 0.697 mmol) and anhydrous $TiBr_4$ (0.99 mg, 1.35 mmol) in anhydrous CH_2Cl_2 (14 mL) was stirred at 20 °C for 12 h. After addition of CH_2Cl_2 (150 mL), the solution was washed with ice-cold H_2O (50 mL, twice) and dried ($MgSO_4$). Solvent evaporation in vacuo and quick FC (hexane/EtOAc 1:1) gave **15α** (472 mg, 92 %) as a yellow foam, which was dried and stored at −20 °C until use; $R_f = 0.50$ (PE/EtOAc 1:1); $[\alpha]_D^{25} = +116$ ($c = 0.243$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.69$ (d, ^3J(H–C(1),H–C(2)) = 3.7 Hz; H–C(1)), 5.69 (s; H–C(4)), 5.413 (dd, ^3J(H–C(1′),H–C(3)) = 9.6, ^3J(H–C(1′),H–C(2′)) = 1.8 Hz; H–C(1′)), 5.36 (dd, ^3J(H–C(5′),H–C(6′)) = 6.5, ^3J(H–C(5′),H–C(4′)) = 3.1 Hz; H–C(5′)), 5.22 (t, ^3J(H–C(4′),H–C(5′)) = 3.7 Hz; H–C(4′)), 4.97–4.89 (m, 2H; H_{exo}–C(6), H–C(3′)), 4.53 (dd, ^3J(H–C(2′),H–C(1′)) = 9.9, ^3J(H–C(2′),H–C(3′)) = 1.5 Hz; H–C(2′)), 4.40 (t, ^3J(H–C(5),H_{exo}–C(6)) = 6.5 Hz; H–C(5)), 4.24–4.16 (m, 2H; H_{endo}–C(6),H_a–C(7′)), 4.02 (dd, $^2J = 11.7$, ^3J(H_a–C(7′),H–C(6′)) = 7.4 Hz; H_b–C(7′)), 3.70 (dd, ^3J(H–C(2),H–C(3)) = 12.0, ^3J(H–C(2),H–C(1)) = 3.7 Hz; H–C(2)), 2.59 (dt, ^3J(H–C(3),H–C(2)) = 12.0, ^3J(H–C(3),H–C(1′)) = 1.8 Hz; H–C(3)), 2.19–2.00 ppm (8×s, 24H; CH_3COO); ^{13}C NMR (100.6 MHz, $CDCl_3$; data for the α anomer): $\delta = 170.7$, 170.3, 169.8, 169.6, 169.3, 168.9, 168.8 (7×s; −COO), 92.8 (d, ^1J(C,H) = 184 Hz; C(1)), 72.9 (d, ^1J(C,H) = 153 Hz; C(6′)), 72.6 (d, ^1J(C,H) = 146 Hz; C(5)), 66.8 (d, ^1J(C,H) = 149 Hz; C(5′)), 66.7 (d, ^1J(C,H) = 148 Hz; C(4′)), 66.6 (d, ^1J(C,H) = 149 Hz; C(3′)), 65.4 (d, ^1J(C,H) = 139 Hz; C(1′)), 64.7 (d, ^1J(C,H) = 151 Hz; C(4)), 64.6 (d, ^1J(C,H) = 143 Hz; C(2′)), 61.1 (t, ^1J(C,H) = 151 Hz; C(7′)), 59.2 (t, ^1J(C,H) = 155 Hz; C(6)), 57.6 (d, ^1J(C,H) = 142 Hz; C(2)), 38.0 (d, ^1J(C,H) = 129 Hz; C(3)), 20.9–20.5 ppm (7×q, ^1J(C,H) = 130 Hz; *C*H_3COO); elemental analysis calcd (%) for $C_{27}H_{36}BrN_3O_{16}$ (738.49): C 43.91, H 4.91, Br 10.82, N 5.69; found: C 43.81, H 5.05, Br 10.73, N 5.65.

Mixture (5:1) of *N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-azido-2,3-dideoxy-α- and -β-D-galactopyranosyl}-L-serine *tert*-butyl ester (16α, 16β): A mixture of *N*-Fmoc-Serine-O*t*Bu (408 mg, 1.03 mmol), anhydrous CH_2Cl_2 (10 mL), $AgClO_4$ (370 mg, 1.73 mmol), 2,4,6-collidine (240 μL, 1.73 mmol), and molecular sieves (4 Å, dried under vacuum at 200 °C, 1 g) was stirred at 20 °C for 10 min. A solution of bromide **15α** (834 mg, 1.129 mmol) in anhydrous CH_2Cl_2 (10 mL) was added slowly (syringe) to the stirred mixture over 30 min. After the system had been stirred at 20 °C for 5 h, CH_2Cl_2 (100 mL) was added and the mixture was filtered through a pad of Celite (washing with CH_2Cl_2). Solvent evaporation and FC (hexanes/EtOAc 4:1→3:1) gave **16α/16β** (5:1, 1.1 g, 93 %) as a white foam; $R_f = 0.48$ (PE/EtOAc 1:1); $[\alpha]_{589}^{25} = +91$ ($c = 0.375$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$; data for the α anomer): $\delta = 7.80$–7.26 (4×m, 8H; ArH); 6.04 (d, ^3J(H–N,H–C*) = 8.0 Hz; H–N), 5.56 (s; H–C(4)), 5.38 (dd, ^3J(H–C(1′),H–C(3)) = 9.6, ^3J(H–C(1′),H–C(2′)) = 2.6 Hz; H–C(1′)), 5.32 (dd, ^3J(H–C(5′),H–C(6′)) = 6.7, ^3J(H–C(5′),H–C(4′)) = 3.2 Hz; H–C(5′)), 5.22 (t, ^3J(H–C(4′),H–C(3′)) = 3.5 Hz; H–C(4′)), 4.96 (d, ^3J(H–C(1),H–C(2)) = 2.9 Hz; H–C(1)), 4.83 (d, ^3J(H–C(4′),H–C(3′)) = 3.5 Hz; H–C(3′)), 4.75 (dd, $^2J = 12.8$, ^3J(H–C(6_{exo}),H–C(5)) = 9.9 Hz; H–C(6_{exo})), 4.54–4.44 (m, 2H; H–C(2′), H–C*(Ser)), 4.43–4.31 (m, 3H; H_{endo}–C(6), H_2–C(Fmoc)), 4.30–4.11 (m, 5H; H_a–C(7′), H–C(6′), H–C(5), H–C(Fmoc), H_2–C(Ser)), 4.30–4.11 (m, 2H; H_b–C(7′), H_2–C(Ser)), 3.33 (dd, ^3J(H–C(2),H–C(3)) = 12.2, ^3J(H–C(2),H–C(1)) = 2.9 Hz; H–C(2)), 2.59 (d, ^3J(H–C(3),H–C(2)) = 12.2 Hz; H–C(3)), 2.25–1.94 (7×s, 21H; CH_3COO), 1.48 ppm (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100.6 MHz, $CDCl_3$; data for the α anomer): $\delta = 170.7$, 170.4, 170.3, 169.9, 169.8, 168.9, 168.7, 168.4 (8×s, −COO), 155.8 (s; C(carbamate)), 143.6 (s; C(Fmoc)), 141.2 (s; C(Fmoc)), 127.6 (d, ^1J(C,H) = 159 Hz; C(Fmoc)), 126.9 (d, ^1J(C,H) = 159 Hz; C(Fmoc)), 125.1 (d, ^1J(C,H) = 158 Hz; C(Fmoc)), 119.8 (d, ^1J(C,H) = 158 Hz; C(Fmoc)), 99.3 (d, ^1J(C,H) = 184 Hz; C(1)), 82.8 (s; $C(CH_3)_3$), 72.9 (d, ^1J(C,H) = 153 Hz; C(6′)), 70.7 (t, ^1J(C,H) = 153 Hz; *C*H_2(Ser)), 68.8 (d, ^1J(C,H) = 146 Hz; C(5)), 66.8 (t, ^1J(C,H) = 150 Hz; *C*H_2(Fmoc)), 66.6 (d, ^1J(C,H) = 148 Hz; C(4′)), 66.6 (d, ^1J(C,H) = 139 Hz; C(1′)), 66.4 (d,

^1J(C,H) = 149 Hz; C(3′)), 65.8 (d, ^1J(C,H) = 151 Hz; C(4)), 65.4 (d, ^1J(C,H) = 149 Hz; C(5′)), 64.6 (d, ^1J(C,H) = 143 Hz; C(2′)), 62.1 (t, ^1J(C,H) = 151 Hz; C(7′)), 59.4 (t, ^1J(C,H) = 155 Hz; C(6)), 55.0 (d, ^1J(C,H) = 138, C*(Ser)), 54.9 (d, ^1J(C,H) = 142 Hz; C(2)), 47.0 (d, ^1J(C,H) = 130 Hz; C(Fmoc)), 37.0 (d, ^1J(C,H) = 129 Hz; C(3)), 27.7 (q, ^1J(C,H) = 128 Hz, 3C; (*C*H$_3$)CO), 20.9–20.5 ppm (7×q, ^1J(C,H) = 130 Hz; *C*H$_3$COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{49}H_{60}N_4O_{21}Na^+$: 1063.3647; found: 1063.3612; elemental analysis calcd (%) for $C_{49}H_{60}N_4O_{21}$ (1041.02): C 56.53, H 5.81, N 5.38; found: C 56.56, H 5.79, N 5.36.

***N*-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-{4,6-di-*O*-acetyl-3-*C*-[(1*R*)-2,6-anhydro-1,3,4,5,7-penta-*O*-acetyl-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-[(*N*-acetyl)amino]-2,3-dideoxy-α-D-galactopyranosyl}-L-serine *tert*-butyl ester (2)**: Compound **16α** (120 mg, 0.115 mmol) was dissolved in a collidine/CH$_3$COSH/Ac$_2$O mixture (4:4:1, 6 mL). After stirring at 20 °C for 18 h the mixture was co-evaporated with toluene under vacuum (10^{-3} Torr). FC (hexanes/EtOAc 4:1→1:2) gave **2** (107 mg, 89 %) as a white foam; R_f = 0.25 (PE/EtOAc 1:1); $[\alpha]_{589}^{25}$ = +65 (*c* = 0.21 in CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.74–7.23 (4×m, 8H; ArH), 5.89 (d, ^3J(H–N,H–C*) = 8.3 Hz; H–N), 5.52 (s; H–C(4)), 5.49 (d, ^3J(H-(NAc),H–C(2)) = 8.7 Hz; H–N), 5.33–5.27 (m, 2H; H–C(1′), H–C(5′)), 5.23 (t, ^3J(H–C(4′),H–C(5′)) = 3.4 Hz; H–C(4′)), 4.75–4.65 (m, 3H; H–C(1), H_{exo}–C(6), H–C(5′)), 4.60 (td, ^3J(H–C(2),H–C(3)) = 12.9, ^3J(H–C(2),H-(NAc)) = 10.0, ^3J(H–C(2),H–C(1)) = 3.4 Hz; H–C(2)), 4.52–4.35 (m, 5H; H$_2$–C(Fmoc), H–C(Ser), H–C(2′), H–C(3′), H_{endo}–C(6)), 4.26–4.17 (m, 3H; H–C(Fmoc), H–C(6′), H_a–C(7′)), 4.14–4.06 (m, 1H; H–C(5)), 3.97–3.87 (m, 3H; H$_2$–C(Ser), H_b–C(7′)), 2.53 (d, ^3J(H–C(2),H–C(3)) = 12.9 Hz; H–C(2)), 2.22–1.87 (8×s, 24H; CH$_3$COO), 1.47 ppm (s, 9H; (CH$_3$)$_3$C); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 170.7, 170.3, 170.0, 169.7, 169.5, 169.4, 169.1, 169.0, 168.9 (9×s, –COO), 155.9 (s; C(carbamate)), 143.6 (s; C(Fmoc)), 141.3 (s; C(Fmoc)), 127.7 (d, ^1J(C,H) = 159 Hz; C(Fmoc)), 127.0 (d, ^1J(C,H) = 159 Hz; C(Fmoc)), 124.9 (d, ^1J(C,H) = 158 Hz; C(Fmoc)), 120.0 (d, ^1J(C,H) = 158 Hz; C(Fmoc)), 98.8 (d, ^1J(C,H) = 169 Hz; C(1)), 82.8 (s; C(CH$_3$)$_3$); 72.9 (d, ^1J(C,H) = 149 Hz; C(6′)), 69.8 (t, ^1J(C,H) = 153, *C*H$_2$(Ser)), 68.9 (d, ^1J(C,H) = 140 Hz; C(5)), 67.0 (t, ^1J(C,H) = 150 Hz; *C*H$_2$(Fmoc)), 67.0 (d, ^1J(C,H) = 149 Hz; C(3′)), 66.4 (d, ^1J(C,H) = 149 Hz; C(4′)), 65.8 (d, ^1J(C,H) = 160 Hz; C(4)), 65.5 (d, ^1J(C,H) = 159 Hz; C(5′)), 65.2 (d, ^1J(C,H) = 148 Hz; C(1′)), 64.8 (d, ^1J(C,H) = 139 Hz; C(2′)), 62.4 (t, ^1J(C,H) = 163 Hz; C(7′)), 59.7 (t, ^1J(C,H) = 151 Hz; C(6)), 55.0 (d, ^1J(C,H) = 138 Hz; C*(Ser)), 47.1 (d, ^1J(C,H) = 130 Hz; C(Fmoc)), 43.5 (d, ^1J(C,H) = 130 Hz; C(Ser)), 38.0 (d, ^1J(C,H) = 128 Hz; C(3)), 28.6 (q, ^1J(C,H) = 128 Hz, 3C; (*C*H$_3$)CO), 23.4 (q, ^1J(C,H) = 129 Hz; *C*H$_3$CON), 21.1–20.6 ppm (7×q, ^1J(C,H) = 130 Hz; *C*H$_3$COO); HRMS (MALDI-TOF): *m*/*z*: calcd for $C_{51}H_{64}N_2O_{22}Na^+$: 1079.3848; found: 1079.3843; elemental analysis calcd for $C_{51}H_{64}N_2O_{22}$ (1057.05): C 57.95, H 6.10, N 2.65; found: C 57.88, H 6.11, N 2.59.

3-*C*-[(1*R*)-2,6-Anhydro-D-*glycero*-L-*manno*-heptitol-1-*C*-yl]-2-[(*N*-acetyl)amino]-2,3-dideoxy-α-D-galactopyranosyl-L-serine (17): Product **2** (60 mg, 0.058 mmol) was dissolved in a DMF/morpholine mixture (1:1, 5 mL). After stirring at 20 °C for 2 h, the mixture was coevaporated with toluene under vacuum, the residue was subjected to FC (CH$_2$Cl$_2$, MeOH 9:1), the solvent was evaporated, the residue was dissolved in MeOH, and NaOMe solution (1 M, 2 drops) was added. After 1 h the mixture was neutralized by addition of Dowex 50WX8–100, stirred for 5 min, filtered, and evaporated. HPLC gave **17** (15 mg, 55 %) as a yellow foam; ^{1}H NMR (400 MHz, D$_2$O): δ = 5.62 (s; H–C(1)), 5.20 (d, ^3J(H–C(2), H–C(3)) = 12.4 Hz; H–C(2)), 5.06 (s; H–C(1′)), 4.87–4.33 (m, 15H), 5.20 (td, ^3J(H–C(3), H–C(2)) = 12.4 Hz; H–C(3)), 2.70 ppm (s, 3H; CH$_3$CON); ^{13}C NMR (100.6 MHz, D$_2$O): δ = 177.8, 173.7, 99.8, 80.9, 78.9, 74.8, 72.6, 70.9, 69.8, 68.8, 68.6, 68.4, 64.3, 60.5, 56.8, 46.8, 39.1, 24.3; HRMS: *m*/*z*: calcd for $C_{18}H_{33}N_2O_{13}$: 485.198; found: 485.200.

Acknowledgements

We thank the Swiss National Science Foundation and the OFES (Bern, European COST D13/0001/99 and FP6-TRIoH projects) for financial support. We also thank the University of Lausanne (Mrs. A. Charon) for a Peace Grant in favor of L.A. We are also grateful to Prof. I. Robina (Univ. of Seville, Spain) for discussions and help with the HRMS spectra, to Mr. R. Mimna for discussions, and to Messrs. R. Rey Sepulveda and S. R. Dubbaka for technical help. The work was supported by the Swiss National Science Foundation and the OFES (Bern, European COST D13/0001/99 and FP6-TRIoH projects).

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Received: December 17, 2004
Published online: April 8, 2005

