Synthesis of a Versatile Neuraminic Acid "*C*"-Disaccharide Precursor for the Synthesis of *C*-Glycoside Analogues of Gangliosides

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Gangliosides are cell-surface sialic acid containing glycolipids. They are found in high concentration on the surface of central nervous system cells. Gangliosides are believed to play a role in important biological events such as cell growth regulation, cell−cell adhesion, and malignancy.[1−3] GM4 (**1**, Scheme 1) is structurally the simplest ganglioside and has been isolated as a minor component from brain, rat kidney, mouse erythrocytes, and chicken egg yolk.[4−6] GM4 is an important cell adhesion molecule in cell growth and tissue regeneration and promotes neuron adhesion through its interaction with myelin-associated glycoprotein.[7] GM3 (**2**, Scheme 1) was first isolated from equine erythrocytes[8] and is known to modulate the epidermal growth factor (EGF) and the platelet-derived growth factor (PDGF) receptors.[9,10] Tumors, such as those involved in brain cancer, overexpress EGF receptor. GM4 and GM3 are also found in high concentration in tumor cells.[11]

N-Acetylneuraminic acid is often found at the nonreducing end of the oligosaccharide component of these gangliosides. *N*-Acetylneuraminic acid is involved in a number of important biological events, including intracellular interactions such as adhesion, aggregation and agglutination; masking antigenic oligosaccharides and suppression of undesired immune reactions; influence on the cell membrane permeability for ions, amino acids, and proteins; and protection of glycoproteins against proteolysis.[12−15] Terminal *N*-acetylneuraminic acid is an attachment site of pathogens to the cells, and often, the removal of this carbohydrate initiates catabolic and inflammatory processes.[16,17]

In vivo, sialic acid containing glycoconjugates are catabolized by the removal of the terminal sialic acid residue through the action of hydrolase-type enzymes called neuraminidases that cleave the glycosidic bond of *N*-acetylneuraminic acid.[18] The design of nonhydrolyzable analogues of *N*-acetylneuraminic acid glycosides is an attractive approach to control, at the molecular level, events of crucial importance to glycobiology and immunology. Thus, the replacement of the interglycosidic oxygen atom by a hydroxymethylene group generates a new class of hydrolytically and metabolically inert "*C*"-glycosides.

We are interested in the synthesis of the *C*-glycoside analogues of GM4 and GM3 (**3** and **4**, Scheme 1) because such glycoconjugates are expected to be resistant to catabolism and to have increased biological half-lives, leading to derivatives with significant therapeutic potential. For example, the *C*-glycoside of GM4 is expected to demonstrate stable cell adhesion over a prolonged period of time,[7] while the *C*-analogue of GM3 (**4**, Scheme 1) is expected to inhibit EGF receptor mediated signal transduction.[9] Both analogues **3** and **4** are also potential candidates as cancer vaccines.

Recently, our laboratory developed a method for the synthesis of *C*-glycosides of *N*-acetyneuraminic acid using samarium iodide.[19] We now report the use of this method for the synthesis of a common *C*-glycoside precursor of GM4 and GM3 (**22**(*S*), (Scheme 3), this precursor being also versatile for the synthesis of *C*-glycoside analogues of other related gangliosides such as GM2 or GM1. This *C*-glycoside precursor was obtained through samarium(II) iodide coupling of the 3-formyl derivative **15** (Scheme 2) with the *N*-acetyneuraminic acid phenyl sulfone derivative **17** (Scheme 3).

Results and Discussion

In a previous paper,[19] our laboratory described the synthesis of methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(R)-hydroxy[3-(methyl 2,4,6-tri-*O*-benzyl-3-deoxy-α-D-galactopyranosidyl)]methyl]-D-erythro-L-*manno*-nonate. Attempts to use this *C*-disaccharide as a building block for the synthesis of **3** and **4**, using previously described chemistry to convert the anomeric methyl group into thiophenyl[20] or acetate, failed. This led us to design the 3-formyl synthon **15** in which the anomeric position was protected as a *p*-methoxyphenyl

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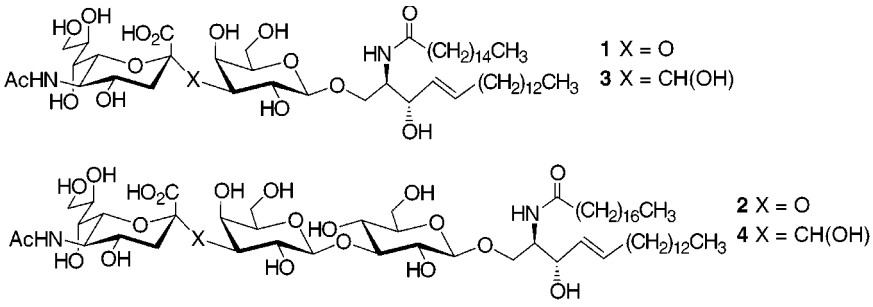
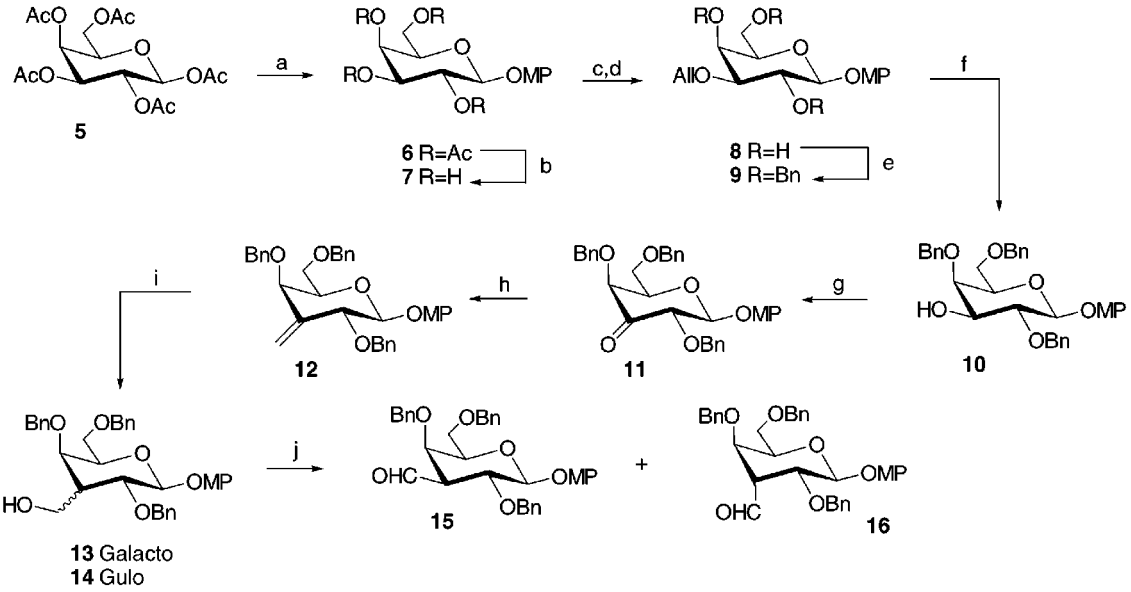
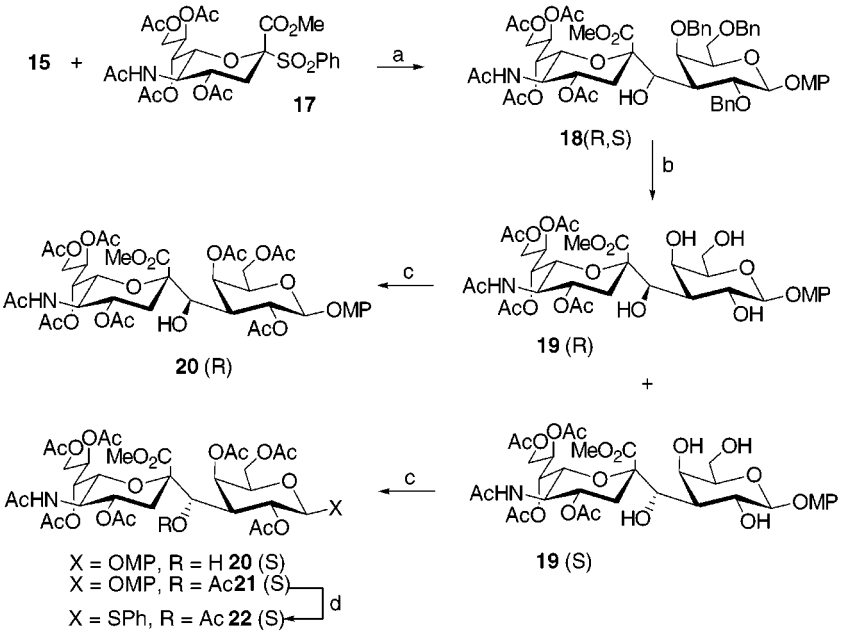
Scheme 1



Scheme 2



Scheme 3



ether, a protecting group known to be readily converted into the corresponding hydroxyl,[21] halogen, or thiophenyl.[22]

The 3-formyl galactoside key intermediate **15** was synthesized, following the procedure described by Kong et al.[23] and Schmidt et al.[24] (Scheme 2). Glycosidation of β-D-galactose pentaacetate **5** with *p*-methoxyphenol and trifluoromethanesulfonate as promoter[25] afforded the

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corresponding *p*-methoxyphenyl glycoside **6** in 92% yield. Deacetylation of **6**, followed by regioselective allylation of the dibutyltin complex of **7**, gave the corresponding 3-*O*-allyl galactopyranoside **8** in 85% yield. Benzylation of **8** under standard conditions (91%), followed by selective deallylation using palladium(II) chloride, afforded the 3-hydroxyl derivative **10** in 94% yield. Oxidation of **10** using DMSO−acetic anhydride[26] led to the corresponding 3-ketopyranoside **11** in 84% yield. Methylenation of **11** using Tebbe's reagent[27] afforded the 3-methylene derivative **12** in 84% yield. Hydroboration of **12** using 9-BBN[28] led to a mixture of the corresponding 3-hydroxymethylene galactopyranoside **13** and gulopyranoside **14**, which were not separable by chromatography on silica gel. These two epimers were obtained in a ratio *galacto*-**13**: *gulo*-**14** of 1.5:1.0, as determined by ^{1}H NMR spectroscopy. The configuration at C-3 was deduced from the large $J_{2,3}$ vicinal coupling constant (11.1 Hz) for the galacto epimer **13** and from the smaller $J_{2,3}$ vicinal coupling constant (5.5 Hz) for the gulo epimer **14**. Oxidation of the mixture **13**−**14** with the system DMSO−oxalyl chloride−triethylamine[29] afforded the 3-formyl galactopyranoside **15** and the 3-formyl gulopyranoside **16** in 60% and 13% yield, respectively. The two epimers **15** and **16** were easily separable by chromatography on silica gel, and their configuration at C-3 was determined by ^{1}H NMR spectroscopy. The high $J_{2,3}$ vicinal coupling constant of 11.1 Hz observed for **15** and the smaller $J_{2,3}$ vicinal coupling constant of 6.6 Hz observed for **16** allowed the unambiguous assignment of the galacto configuration in **15** and gulo configuration in **16**. The ratio of the 3-formyl galacto and gulo derivatives **15** and **16** obtained upon oxidation of **13**−**14** ranged from 4.6:1.0 to 1.0:1.0. These variations in the ratio could be the result of a partial in situ epimerization of the 3-formyl group in the presence of triethylamine.

Reaction of the 3-formyl galactoside **15** with the neuraminic acid sulfone **17** in the presence of freshly prepared samarium(II) iodide afforded the corresponding *C*-disaccharides **18**(*R*) and **18**(*S*) (Scheme 3) in 85% yield. TLC of the reaction mixture indicated a diastereoisomeric ratio of approximately 4:1. However, the first minor isomer (*R*) was difficult to resolve from the second major isomer (*S*), decreasing its isolated yield and leading to an *R*/*S* ratio of 1.0:1.5. Standard debenzylation of the diastereoisomeric mixture **18**(*R*)−**18**(*S*) afforded the corresponding disaccharides **19**(*R*) and **19**(*S*) in 90% yield, separable by chromatography on silica gel. Although both (*R*) and (*S*) isomers could be isolated pure at this stage, the chirality of the hydroxymethylene bridge in each isomer could not be assigned from their ^{1}H NMR spectra because of overlapping signals. Acetylation of the first isomer (**19**(*R*)) quantitatively afforded the corresponding acetylated derivative **20**(*R*) having the free bridge hydroxyl, while acetylation of the second isomer (**19**(*S*)) under the same conditions quantitatively afforded the corresponding acetylated derivative **20**(*S*) having the free bridge hydroxyl, together with some peracetylated derivative **21**(*S*), the ratio **20**(*S*)/**21**(*S*) being 1.6:1.0. At this step, ^{1}H NMR and 2D NOESY spectroscopy and molecular modeling were carried out to assign the hydroxymethylene stereochemistry for **20**(*R*) and **20**(*S*). The ^{1}H NMR spectrum of the first isomer (**20**(*R*)) displayed a coupling constant between the bridge proton and the proton H-3′ of the galactose moiety ($J_{Hb,3'}$) of 2.7 Hz, while in the second isomer (**20**(*S*)), the same coupling was 5.2 Hz. Molecular modeling of the two diastereoisomers **20**(*R*) and **20**(*S*) used the package SYBYL (ver. 6.3) from Tripos Inc., St. Louis, MO. All energy calculations were performed with parameters from the Tripos force field. Charges were assigned according to the Gasteiger−Huckel protocol. A distance-dependent dielectric ($\epsilon = 4$) was used for chloroform as solvent. After energy minimization of both isomers, the torsion angles between the bridge carbon (Cb)−bridge hydrogen (Hb) bond and the carbon 3 (C-3′)−proton 3 (H-3′) bond of the galactose residue were determined. In the (*R*) isomer, this torsion angle was approximately 60°, while in the (*S*) isomer it was 180°. These two torsion angles correspond to a smaller $J_{Hb,3'}$ coupling constant in the (*R*) isomer than in the (S) isomer; the chirality of the bridge carbon was assigned as (*R*) in the first isomer and as (*S*) in the second isomer. This assignment was further confirmed by the following observation. The molecular model of the (*R*)-isomer indicated that the equatorial proton H-3e of the neuraminic acid moiety pointed toward the bridge hydroxyl, implying that this equatorial proton should be downfield shifted in the ^{1}H NMR spectrum of the (*R*) isomer. In the (*S*) isomer, molecular modeling indicated that the axial proton H-3a of the neuraminic acid moiety pointed toward the bridge hydroxyl, implying a downfield shift of this proton in the ^{1}H NMR spectrum of the (*S*) isomer. The two chemical shifts expected for H-3e and H-3a of the neuraminic acid residue were in accordance with the experimental ^{1}H NMR spectra of **20**(*R*) and **20**(*S*). The assigned stereochemistry was also confirmed by 2D NOESY spectroscopy of **20**(*R*) and **20**(*S*). As expected, a strong NOE between bridge H/Gal H-3 for **20**(*R*) and bridge H/Gal H-2 for **20**(*S*) were observed. Differences are observed in the H-4′ (Gal) chemical shifts of **20**(*R*) and **20**(*S*), 5.26 and 4.60 ppm, respectively. The signal at 1.78 ppm demonstrates a second shielded acetate in **20**(*S*). These observations suggest the possible presence of an orthoacetate involving the bridge hydroxyl and the 4-hydroxyl group of the neuraminic acid residue.

Removal of the *p*-methoxyphenyl glycoside in **20**(*R*) was next attempted by selective oxidation using ceric ammonium nitrate (CAN) for 50 min at 0 °C.[21] FABMS spectroscopy of the resulting compound indicated the presence of two different molecular peaks, the first one at 793 ($[M + NH_4]^+$ 811, $[M + Na]^+$ 816, and $[M + K]^+$ 832), corresponding to the expecting molecular weight after *p*-methoxyphenyl removal, and the second one at 775 ($[M + H]^+$ 776), corresponding to an unsaturated derivative resulting from an elimination of *p*-methoxyphenol. ^{1}H NMR spectroscopy of the same sample showed the presence of three anomeric protons between 6.2 and 6.4 ppm. One of these signals was consistent with the presence of a C1−C2 double bond in the galactose moiety. The large downfield chemical shifts observed for the two other anomeric protons indicated a possible acetyl migration to the anomeric position after *p*-methoxyphenyl removal. These two anomeric acetates could not be separated from the unsaturated derivative. The *p*-methoxyphenyl glycoside of the peracetylated derivative **21**(*S*)

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was converted directly to the corresponding thiophenyl glycoside **22**(*S*) in 73% yield by reaction of **21**(*S*) with thiophenol and trifluoroboron etherate.[22] *C*-Disaccharide **22**(*S*) is the common key intermediate for the full elaboration of the *C*-glycoside analogues of GM4 and GM3 or other related gangliosides.

Conclusion

A common versatile *N*-acetylneuraminic acid *C*-disaccharide precursor of the *C*-glycoside analogues of gangliosides GM4 and GM3 has been synthesized. Samarium(II) iodide coupling of *N*-acetylneuraminic acid sulfone with a 3-formyl galactopyranoside derivative afforded the corresponding *C*-disaccharide as a mixture of (*R*) and (*S*) isomers at the newly formed hydroxymethylene bridge. This diastereoisomeric mixture was resolved after debenzylation of the galactoside residue, and the chirality of each isomer assigned after acetylation. After 48 h acetylation, the bridge hydroxyl in the (*R*) isomer could not be acetylated, while this hydroxyl was partially acetylated in the (*S*) isomer. Conversion of the *p*-methoxyphenyl group in the peracetylated (*S*) isomer into the corresponding thiophenyl glycoside was accomplished, affording the key intermediate for the synthesis of *C*-glycoside analogues of GM4, GM3, and other related gangliosides.

Experimental Section

Nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 25 °C, in deuterated chloroform or methanol. Chemical shifts were recorded in ppm (δ) and coupling constants in Hz, relative to tetramethylsilane as the internal standard. The ^{1}H NMR spectra were fully assigned using single frequency decoupling, 2D COSY, and 2D NOESY NMR spectroscopy. Melting points are uncorrected. Thin-layer chromatography (TLC) was performed using E. Merck plates of silica gel 60 with fluorescent indicator. Visualization was effected by spraying plates with Von's reagent (1.0 g of ceric ammonium sulfate and 24.1 g of ammonium molybdate in 31 mL of sulfuric acid and 470 mL of water) followed by heating at 140 °C. Flash chromatography was conducted with silica gel (230−430 mesh, E. Merck).

***p*-Methoxyphenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (6).** *p*-Methoxyphenol (20.5 mmol, 2.5 g) and trimethylsilyl trifluoromethanesulfonate (0.25 mL) were added to a solution of β-D-galactose pentaacetate (5.0 g, 12.8 mmol) in anhydrous CH_2Cl_2 at 0 °C under nitrogen. After 4 h at 0 °C, the reaction mixture was neutralized by addition of triethylamine (1 mL) and concentrated under reduced pressure. Purification by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:3 → 1.5:1) afforded **6** as an amorphous white solid in 92% yield (5.35 g): $[\alpha]^{23}_D = +3°$ (*c* 1, $CHCl_3$) [lit.[22] $[\alpha]_D = +9.6°$ (*c* 0.54, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.01, 2.06, 2.08 and 2.19 (4 s, 3 H each, 4 OAc), 3.78 (s, 3 H, OMe), 4.01 (m, 1 H, H-5), 4.16 (dd, 1 H, $J_{5,6b}$ 6.5 Hz, $J_{6a,6b}$ 11.3 Hz, H-6b), 4.23 (dd, 1 H, $J_{5,6a}$ 6.9 Hz, H-6a), 4.92 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 5.09 (dd, 1H, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 3.3 Hz, H-3), 5.5.44−5.48 (m, 2 H, H-2 and H-4), 6.80 and 6.96 (2 d, 2 H each, Ph).

***p*-Methoxyphenyl 3-*O*-allyl-β-D-galactopyranoside (8)**. To a solution of **6** (5.25 g, 11.57 mmol) in anhydrous methanol (50 mL) and under nitrogen was added a catalytic amount of sodium methoxide. After 5 h at room temperature, the reaction mixture was neutralized with resin IR 120 (H^+) and filtered, and the solvent was evaporated. The resulting *p*-methoxyphenyl β-D-galactopyranoside **7** was used without any further purification and characterization. Compound **7** (3.24 g, 11.34 mmol) in solution in anhydrous methanol (50 mL) and under nitrogen was reacted with dibutyltin oxide (3.11 g, 12.48 mmol). After 4 h at reflux, the reaction mixture was concentrated under vacuum. The dried residue was suspended in toluene (80 mL) and treated with allyl bromide (1.17 mL, 13.61 mmol) and tetrabutylammonium iodide (4.17 g, 11.34 mmol). The suspension was stirred under nitrogen at 60 °C for 18 h. TLC of the resulting brownish solution showed the presence of 50% of unreacted starting material. This solution was reacted with additional allyl bromide (0.58 mL, 6.80 mmol). After 18 h at 60 °C, the solvent was evaporated, and the residue was purified by chromatography on silica gel (ethyl acetate) to afford **8** in 85% yield (3.16 g), isolated as yellowish crystals. Recrystallization of **8** in ethyl acetate afforded white crystals: mp = 140−141 °C; $[\alpha]^{23}_D = -8°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, CD_3OD) δ 3.32 (m, 1 H, H-5), 3.39 (dd, 1H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 3.2 Hz, H-3), 3.58 (t, 1 H, $J_{5,6b}$ 6.1 Hz, $J_{6a,6b}$ 6.0 Hz, H-6b), 3.75 (s, 3 H, OMe), 3.78 (dd, 1 H, $J_{5,6a}$ 4.8 Hz, H-6a), 3.86 (dd, 1H, $J_{1,2}$ 7.9 Hz, H-2), 4.07 (d, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.17 and 4.26 (2 dd, 1 H each, OCH_2), 4.74 (d, 1H, H-1), 5.18 and 5.34 (2 dd, 1 H each, CH=CH_2), 6.00 (m, 1 H, CH=CH_2), 6.80 and 7.08 (2 d, 2 H each, Ph). Anal. Calcd for $C_{16}H_{22}O_7$ (326.3): C, 58.89; H, 6.79. Found: C, 59.18; H, 6.91.

***p*-Methoxyphenyl 3-*O*-Allyl-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (9).** To a solution of **8** (1.21 g, 3.71 mmol) in anhydrous DMF (15 mL), under nitrogen and cooled at 0 °C, was added NaH (116 mg, 4.83 mmol). The reaction mixture was stirred for 15 min at 0 °C and treated with benzyl bromide (0.66 mL, 5.57 mmol). After 12 h at room temperature, the reaction mixture was cooled at 0 °C, quenched by slow addition of water, and extracted with chloroform. The combined organic layers were washed with H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvents were evaporated. Purification by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:3) afforded **9** as white crystals in 91% yield (2.01 g): mp = 59−61 °C; $[\alpha]^{24}_D = -23°$(*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.48 (dd, 1H, $J_{2,3}$ 9.6 Hz, $J_{3,4}$ 2.8 Hz, H-3), 3.63 (bs, 3 H, H-5, H-6a and H-6b), 3.75 (s, 3 H, OMe), 3.90 (d, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.01 (dd, 1H, $J_{1,2}$ 7.8 Hz, H-2), 4.22 (m, 2 H, OCH_2), 4.40, 4.45, 4.64, 4.84, 4.96 and 4.97 (6 d, 1 H each, $J_{A,B}$ 11.7 Hz, CH_2Ph), 4.83 (d, 1H, H-1), 5.19 and 5.33 (2 dd, 1 H each, CH=CH_2), 5.95 (m, 1 H, CH=CH_2), 6.78 and 7.02 (2 d, 2 H each, C_6H_4), 7.22−7.40 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{37}H_{40}O_7$ (596.7): C, 74.48; H, 6.76. Found: C, 74.32; H, 6.75.

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-β-D-galactopyranoside (10).** Compound **9** (2.67 g, 4.49 mmol) was dissolved in a mixture of anhydrous methanol and toluene (21 mL, v/v 3:1) and reacted with $PdCl_2$ (~100 mg) under nitrogen and at room temperature. After 4 h of reaction, the reaction mixture was filtrated over a pad of Celite, and the solvents were evaporated. Purification of the residue by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:4) afforded **10** as white crystals in 94% yield (2.35 g): mp = 84−86 °C; $[\alpha]^{24}_D = -11°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66−3.73 (m, 3 H, H-5, H-6a and H-6b), 3.74 (t, 1H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 2.9 Hz, H-3), 3.76 (s, 3 H, OMe), 3.83 (dd, 1H, $J_{1,2}$ 7.7 Hz, H-2), 3.90 (d, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.44, 4.49, 4.66, 4.78, 4.81 and 5.05 (6 d, 1 H each, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.84 (d, 1H, H-1), 6.78 and 7.02 (2 d, 2 H each, C_6H_4), 7.22−7.40 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{34}H_{36}O_7$ (556.7): C, 73.36; H, 6.52. Found: C, 72.96; H, 6.63.

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-β-D-*xylo*-hex-3-ulopyranoside (11).** Compound **10** (2.93 g, 5.27 mmol) in solution in anhydrous DMSO (18 mL) was reacted with Ac_2O (15 mL) under nitrogen and at room temperature. After 12 h, Ac_2O was evaporated and the remaining solution diluted with H_2O and extracted with $CHCl_3$. The combined organic layers were washed with H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvent was evaporated. The residue was purified by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:3) to give **11** as a light yellow solid in 84% yield (2.45 g): mp = 85−87 °C; $[\alpha]^{23}_D = -52°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.76 (s, 3 H, OMe), 3.66−3.73 (bs, 3 H, H-5, H-6a and H-6b), 3.92 (s, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.34, 4.42, 4.45, 4.51, 4.59 and 4.94 (6 d, 1 H each, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.76 (bd, 2 H, H-1 and H-2), 6.78 and 7.08 (2 d, 2 H each, C_6H_4), 7.22−7.40 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{34}H_{34}O_7$ (554.6): C, 73.63; H, 6.18. Found: C, 73.76; H, 6.35.

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-3-deoxy-3-*C*-(methylene)-β-D-*xylo*-hex-3-ulopyranoside (12).** To a solution of **11** (2.36 g, 4.26 mmol) in anhydrous THF (60 mL) under nitrogen and cooled at −40 °C was added dropwise within 20 min Tebbe's reagent (17 mL). After 1 h at − 40 °C, the reaction mixture was allowed to warm at 0 °C. After 50 min at 0 °C was added very

slowly a 10% aqueous NaOH solution (10 mL), and the reaction mixture was stirred for 30 min at 0 °C. The reaction mixture was filtered through a pad of Celite and the solid washed several times with ethyl acetate. The combined organic extracts were evaporated, and the residue was purified by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:5) to afford **12** as white crystals in 84% yield (1.98 g): mp = 74−76 °C; $[\alpha]^{23}_D$ = −9° (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74−3.81 (m, 3 H, H-5, H-6a and H-6b), 3.76 (s, 3 H, OMe), 3.98 (s, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.30 (dt, 1H, $J_{1,2}$ 7.6 Hz, H-2), 4.24, 4.48, 4.52, 4.54, 4.79 and 4.99 (6 d, 1 H each, $J_{A,B}$ 11.7 Hz, CH_2Ph), 4.81 (d, 1H, H-1), 5.17 and 5.56 (2 t, 1 H each, C=CH_2), 6.79 and 7.03 (2 d, 2 H each, C_6H_4), 7.22−7.42 (m, 15 H, 3 C_6H_5). Anal. Calcd for $C_{35}H_{36}O_6$ (552.6): C, 76.06; H, 6.57. Found: C, 76.16; H, 6.70.

***p*-Methoxyphenyl 2,4,6-tri-*O*-benzyl-3-deoxy-3-*C*-(hydroxymethyl)-*β*-D-*galacto*-hexopyranoside (13) and *p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-3-deoxy-3-*C*-(hydroxymethyl)-*β*-D-*gulo*-hexopyranoside (14).** Compound **12** (1.89 g, 3.42 mmol) in solution in anhydrous THF (80 mL) was reacted with 9-BBN (0.5 M in THF, 43 mL, 21.6 mmol) at reflux and under nitrogen. After 5 h of reaction, the reaction mixture was cooled at 0 °C, and a 10% aqueous solution of NaOH (34 mL) was slowly added followed by a 30% aqueous solution of H_2O_2 (34 mL). The reaction mixture was stirred for 30 min and extracted with $CHCl_3$. The combined organic extracts were washed with a 20% aqueous solution of sodium hydrogen sulfite and with H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvent was evaporated. The residue was purified by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:5) to give **13** and **14** as a colorless oil in 91% yield (2.452 g), in a ratio of **13**:**14** = 1.5:1.0. **13**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90 (m, 1 H, $J_{2,3}$ 11.1 Hz, $J_{3,4}$ < 1.5 Hz, H-3), 3.65−3.87 (m, 5 H, H-5, H-6a, H-6b, CH_2), 3.77 (s, 3 H, OMe), 3.85 (dd, 1 H, $J_{1,2}$ 7.7 Hz, H-2), 3.95 (d, 1 H, H-4), 4.35−5.03 (m, 3 CH_2Ph), 4.92 (d, 1 H, H-1), 6.80 and 7.04 (2 d, 2 H each, C_6H_4), 7.20−7.40 (m, 15 H, 3 C_6H_5). **14**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.61 (bq, 1 H, $J_{2,3}$ 5.5 Hz, $J_{3,4}$ <1.5 Hz, H-3), 3.65−3.87 (m, 4 H, H-6a, H-6b, CH_2), 3.76 (s, 3 H, OMe), 3.95 (d, 1 H, H-4), 4.02 (bt, 2 H, H-2, H-5) 4.35−5.03 (m, 3 CH_2Ph), 5.27 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1), 6.80 and 7.04 (2 d, 2 H each, C_6H_4), 7.20−7.40 (m, 15 H, 3 C_6H_5).

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-3-deoxy-3-*C*-(formyl)-*β*-D-*galacto*-hexopyranoside (15) and *p*-Methoxyphenyl 2,4,6-Tri-*O*-benzyl-3-deoxy-3-*C*-(formyl)-*β*-D-*gulo*-hexopyranoside (16).** Anhydrous DMSO (1.30 *μ*L) was carefully added to a 2.0 M solution of oxalyl chloride in CH_2Cl_2 (3.86 mL, 7.71 mmol) under nitrogen and cooled at −78 °C. After 10 min, a solution of **12**−**13** (1.76 g, 3.08 mmol) in anhydrous CH_2Cl_2 (10 mL) was added dropwise and the reaction mixture stirred 1 h at −78 °C. The reaction mixture was treated with triethylamine (4.3 mL, 30.9 mmol) for 45 min at −78 °C, allowed to warm at 0 °C, quenched by addition of H_2O, and extracted with $CHCl_3$. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica gel (ethyl acetate−petroleum ether, v/v 1:5) to give **16** as a colorless oil in 13% yield (0.22 g) and **15** as white needles in 60% yield (1.05 g): **16** $[\alpha]^{23}_D$ = −32° (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.56 (bd, 1 H, $J_{1,2}$ 7.2 Hz, $J_{2,3}$ 6.6 Hz, H-3), 3.67 (m, 2 H, H-6a and H-6b), 4.05 (m, 1 H, H-5), 3.76 (s, 3 H, OMe), 4.07 (m, 1 H, H-4), 5.16 (dd, 1H, H-2), 4.41, 4.45, 4.47, 4.48, 4.71 and 4.95 (6 d, 1 H each, $J_{A,B}$ 11.7 Hz, CH_2Ph), 5.10 (d, 1H, H-1), 6.78 and 7.00 (2 d, 2 H each, C_6H_4), 7.20−7.38 (m, 15 H, 3 C_6H_5), 9.89 (s, 1 H, CHO). Anal. Calcd for $C_{35}H_{36}O_7$ (568.7): C, 73.92; H, 6.38. Found: C, 72.98; H, 7.08. **15**: mp = 114−116 °C; $[\alpha]^{23}_D$ = +1° (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.56 (bd, 1 H, $J_{1,2}$ 7.7 Hz, $J_{2,3}$ 11.1 Hz. H-3), 3.64 (dd, 1 H, $J_{5,6b}$ 9.3 Hz, $J_{6a,6b}$ 9.3 Hz, H-6b), 3.69 (t, 1 H, H-6a), 3.76 (m, 1 H, H-5), 3.76 (s, 3 H, OMe), 4.22 (d, 1 H, $J_{4,5}$ < 1.5 Hz, H-4), 4.34 (dd, 1H, H-2), 4.47, 4.48, 4.49, 4.52, 4.82 and 5.05 (6 d, 1 H each, $J_{A,B}$ 11.7 Hz, CH_2Ph), 4.94 (d, 1H, H-1), 6.80 and 7.08 (2 d, 2 H each, C_6H_4), 7.20−7.38 (m, 15 H, 3 C_6H_5), 9.55 (s, 1 H, CHO). Anal. Calcd for $C_{35}H_{36}O_7$ (568.7): C, 73.92; H, 6.38. Found: C, 73.39; H, 6.36.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-hydroxy-[3-(*p*-methoxyphenyl 2,4,6-tri-*O*-benzyl-3-deoxy-*β*-D-galactopyranosidyl)]-methyl]-D-*erythro*-L-*manno*-nonate (18(*R*)) and Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-hydroxy-[3-(*p*-methoxyphenyl 2,4,6-tri-*O*-benzyl-3-deoxy-*β*-D-galactopyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (18(*S*)). A solution of compounds **15** (111 mg, 0.19 mmol) and **17** (100 mg, 0.16 mmol) in $CHCl_3$ (2 mL) was evaporated to dryness and the resulting residue dried for 1 h under high vacuum. To the dried residue placed under nitrogen was added a solution of freshly prepared SmI_2 (∼0.1 M, 15 mL), and the reaction mixture was stirred at room temperature for 15 min. The reaction mixture was then diluted with ether, washed successively with 1 N HCl, saturated aqueous $Na_2S_2O_3$ and H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica gel ($CHCl_3$−CH_3OH, v/v 40:1) to give **18**(*R*) and **18**(*S*) as a white solid in 85% yield (142 mg). **18**(*R*): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77 (t, 1 H, $J_{3a,4}$, $J_{3a,3e}$ 12.4 Hz, H-3a), 1.89, 1.96, 2.00, 2.02 and 2.17 (5 s, 3 H each, 5 OAc), 2.15 (ovl with OAc, 1 H, H-3′), 2.54 (dd, 1 H, $J_{3e,4}$ 4.4 Hz, H-3e), 3.68 (dd, 1 H, $J_{5',6'b}$ 6.7 Hz, $J_{6'a,6'b}$ 9.3 Hz, H-6′b), 3.73 (s, 3 H, CO_2CH_3), 3.77 (s, 3 H, PhOC*H*$_3$), 3.79 (dd, 1 H, $J_{5',6'a}$ < 1.5 Hz, H-6′a), 3.90 (t, 1 H, H-5′), 3.97 (dd, 1 H, $J_{4,5}$, $J_{5,6}$ 10.4 Hz, $J_{5,NH}$ 10.2 Hz, H-5), 4.00 (m ovl with H-9b, 1 H, $J_{1',2'}$ 7.5 Hz, H-2′), 4.01 (dd ovl with H-2′, 1 H, $J_{9a,9b}$ 12.5 Hz, H-9b), 4.11 (m, 2 H, H-6 and Hb), 4.23 (dd, 1 H, $J_{8,9a}$ 2.2 Hz, H-9a), 4.35 (bs, 1 H, H-4′), 4.52, 4.58, 4.61, 4.67, 4.76 and 5.06 (6 d, 1 H each, 3 C*H*$_2$Ph), 4.80 (m, 1 H, H-4), 5.01 (d, 1 H, H-1′), 5.14 (d, 1 H, NH), 5.28 (dd, 1 H, $J_{6,7}$ < 1.5 Hz, $J_{7,8}$ 9.4 Hz, H-7), 5.44 (m, 1 H, H-8), 6.60 and 7.10 (2d, 2 H each, *Ph*OCH$_3$), 7.20−7.40 (m, 15 H, 3 CH_2*Ph*). **18**(*S*): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82, 1.84, 1.94, 2.00 and 2.16 (5 s, 3 H each, 5 OAc), 2.21 (dd, 1 H, $J_{3e,4}$ 5.1 Hz, H-3e), 2.27 (t, 1 H, $J_{3a,4}$, $J_{3a,3e}$ 13.0 Hz, H-3a), 2.38 (m, 1 H, $J_{2',3'}$ 11.2 Hz, H-3′), 3.17 (d, 1 H, $J_{Hb,OH}$ 1.5 Hz, OH), 3.64 (m, 2 H, Hb and H-5′), 3.73 (m, 1 H, $J_{5',6'b}$ 2.9 Hz, H-6′b), 3.76 (s, 3 H, CO_2CH_3), 3.77 (s, 3 H, PhOC*H*$_3$), 3.82 (m, 2 H, $J_{8,9b}$ 5.0 Hz, H-9b and H-6′a), 3.90 (m, 2 H, H-5 and H-4′), 3.93 (dd, 1 H, $J_{5,6}$ 10.4 Hz, $J_{6,7}$ 2.0 Hz, H-6), 4.07 (dd, 1 H, $J_{1',2'}$ 7.4 Hz, H-2′), 4.14 (dd, 1 H, $J_{8,9a}$ 1.5 Hz, $J_{9a,9b}$ 12.0 Hz, H-9a), 4.47, 4.48, 4.54, 4.62, 4.66 and 5.18 (6 d, 1 H each, 3 C*H*$_2$-Ph), 4.76 (m, 1 H, H-4), 5.02 (d, 1 H, $J_{5,NH}$ 9.7 Hz, NH), 5.20 (dd, 1 H, $J_{7,8}$ 8.9 Hz, H-7), 5.29 (d, 1 H, H-1′), 5.43 (m, 1 H, H-8), 6.80 and 7.00 (2d, 2 H each, *Ph*OCH$_3$), 7.20−7.40 (m, 15 H, 3 CH_2*Ph*).

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-hydroxy-[3-(*p*-methoxyphenyl 3-deoxy-*β*-D-galactopyranosidyl)]-methyl]-D-*erythro*-L-*manno*-nonate (19(*R*)) and Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-hydroxy-[3-(*p*-methoxyphenyl 3-deoxy-*β*-D-galactopyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (19(*S*)). A solution of compounds **18**(*R*)−**18**(*S*) (558 mg, 0.53 mmol) in EtOAc/CH_3OH/H_2O/80% aqueous AcOH (20 mL/20 mL/10 mL/1 drop) was stirred at room temperature under an atmosphere of H_2. After 15 h, the reaction mixture was filtered over a pad of Celite and the filtrate evaporated under vacuum. The residue was purified by chromatography on silica gel ($CHCl_3$−CH_3OH, v/v 35:1) to give **19**(*R*) and **19**(*S*) as white solids in 54% (223 mg) and 36% (149 mg) yields, respectively. **19**(*R*): mp = 146−149 °C; $[\alpha]^{23}_D$ = +4° (*c* 1, $CHCl_3$); HRFABMS (+ve) calcd for $C_{34}H_{47}NO_{19}$ $[M + Na]^+$ 796.2640, found 796.2628; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88, 2.01, 2.02, 2.15 and 2.17 (5 s, 3 H each, 5 OAc), 1.86 (t, 1 H, $J_{3a,4}$, $J_{3a,3e}$ 13.0 Hz, H-3a), 1.99 (ovl with OAc, 1 H, H-3′), 2.54 (dd, 1 H, $J_{3e,4}$ 4.4 Hz, H-3e), 3.63 (t, 1 H, $J_{5',6'b}$ 5.5 Hz, $J_{6'a,6'b}$ 10.7 Hz, H-6′b), 3.77 (s, 6 H, PhOC*H*$_3$ and CO_2CH_3), 3.83 (dd, 1 H, $J_{5',6'a}$ < 1.5 Hz, H-6′a), 3.89 (m, 1 H, H-5′), 3.94 (dd, 1 H, $J_{8,9b}$ 8.1 Hz, $J_{9a,9b}$ 12.3 Hz, H-9b), 4.08 (dd, 1 H, $J_{4,5}$, $J_{5,6}$ 10.2 Hz, $J_{5,NH}$ 9.5 Hz, H-5), 4.22 (bt, 1 H, $J_{1',2'}$ 7.6 Hz, $J_{2',3'}$ 9.4 Hz, H-2′), 4.30 (bd ovl with H-9a, 1 H, $J_{6,7}$ 2.0 Hz, H-6), 4.33 (dd, 1 H, $J_{8,9a}$ < 1.5 Hz, H-9a), 4.37 and 4.75 (2 bs, 1 H each, Hb and H-4′), 4.79 (m, 1 H, H-4), 4.85 (d, 1 H, H-1′), 5.22 (dd, 1 H, $J_{7,8}$ 9.2 Hz, H-7), 5.28 (bd, 1 H, NH), 5.56 (bt, 1 H, H-8), 6.80 and 7.10 (2 d, 2 H each, *Ph*OCH$_3$). **19**(*S*): mp = 138−141 °C; $[\alpha]^{23}_D$ = −12.5° (*c* 1, $CHCl_3$); HRFABMS (+ve) calcd for $C_{34}H_{47}NO_{19}$ $[M + Na]^+$ 796.2640, found 796.2629; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.86, 1.88, 2.04, 2.12 and 2.15 (5 s, 3 H each, 5 OAc), 2.16 (bd ovl with OAc, 1 H, H-3′), 2.31 (t, 1 H, $J_{3a,4}$ 12.6 Hz, $J_{3a,3e}$ 13.1 Hz, H-3a), 2.46 (dd, 1 H, $J_{3e,4}$ 4.6 Hz, H-3e), 3.66 (bt, 1 H, H-6′b), 3.85 (bs, 2 H, H-5′ and H-6′a), 3.94 (dd, 1 H, $J_{8,9b}$ 7.1 Hz, $J_{9a,9b}$

12.0 Hz, H-9b), 3.95 (dd, 1 H, $J_{5,6}$ 10.5 Hz, $J_{6,7}$ 1.9 Hz, H-6), 4.03 (dd, 1 H, $J_{4,5}$ 10.5 Hz, $J_{5,NH}$ 10.0 Hz, H-5), 4.14 (bt, 1 H, $J_{1',2'}$ 7.7 Hz, H-2′), 4.28 (bs, 2 H, Hb and H-4′), 4.29 (dd, 1 H, $J_{8,9a}$ 2.5 Hz, H-9a), 4.92 (m, 1 H, H-4), 5.03 (d, 1 H, H-1′), 5.21 (dd, 1 H, $J_{7,8}$ 8.8 Hz, H-7), 5.02 (b, 1 H, NH), 5.51 (m, 1 H, H-8), 6.80 and 7.00 (2d, 2 H each, *Ph*OCH_3).

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(R)-hydroxy-[3-(*p*-methoxyphenyl 2,4,6-tri-*O*-acetyl-3-deoxy-*β*-D-galactopyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (20(*R*)). A solution of **19**(*R*) (52 mg, 0.067 mmol) in anhydrous pyridine (5 mL) was reacted with Ac_2O (0.1 mL) under nitrogen. After 48 h at room temperature, the reaction mixture was quenched with CH_3OH and evaporated under vacuum. The residue was dried by coevaporation with toluene and purified by chromatography on silica gel ($CHCl_3$−CH_3OH, v/v 45:1) to afford **20**(*R*) as a white solid in quantitative yield (60 mg): mp = 120−122 °C; $[\alpha]^{23}_D = +12°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.83 (t, 1 H, $J_{3a,4}$ 12.2 Hz, $J_{3a,3e}$ 12.7 Hz, H-3a), 1.90, 2.02, 2.04, 2.06, 2.10, 2.11, 2.15 and 2.16 (8 s, 3 H each, 8 OAc), 2.35 (bd, 1 H, $J_{2',3'}$ 11.4 Hz, $J_{3',4'}$, $J_{3',Hb}$ 2.7 Hz H-3′), 2.60 (dd, 1 H, $J_{3e,4}$ 4.4 Hz, H-3e), 2.92 (d, 1 H, $J_{OH,Hb}$ 2.9 Hz, OH), 3.74 (s, 3 H, CO_2CH_3), 3.77 (s, 3 H, PhOCH_3), 3.88 (m, 1 H, H-5′), 4.05 (m, 2 H, $J_{6,7}$ < 1.5 Hz, H-5 and H-6), 4.10 (dd, 1 H, $J_{8,9b}$ 5.4 Hz, $J_{9a,9b}$ 12.5 Hz, H-9b), 4.30 (dd, 1 H, $J_{8,9a}$ 2.9 Hz, H-9a), 4.37−4.40 (m, 2 H, H-6′a and H-6′b), 4.41 (bs, 1 H, Hb), 4.83 (m, 1 H, H-4), 4.88 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′), 5.16 (bd, 1 H, $J_{5,NH}$ 9.4 Hz, NH), 5.26 (d, 1 H, H-4′), 5.33 (bd, 1 H, $J_{7,8}$ 10.0 Hz, H-7), 5.39 (m, 1 H, H-8), 5.43 (dd, 1 H, H-2′), 6.80 and 7.10 (2 d, 2 H each, *Ph*OCH_3). Anal. Calcd for $C_{40}H_{53}NO_{22}$ (899.9): C, 53.39; H, 5.94. Found: C, 53.13; H, 6.11.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-*O*-acetyl-[3-(*p*-methoxyphenyl 2,4,6-tri-*O*-acetyl-3-deoxy-*β*-D-galactopyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (21(*S*)) and Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-hydroxy-[3-(*p*-methoxyphenyl 2,4,6-tri-*O*-acetyl-3-deoxy-*β*-D-galactopyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (20(*S*)). A solution of **19**(*S*) (50 mg, 0.065 mmol) in anhydrous pyridine (5 mL) was reacted with Ac_2O (0.1 mL) under nitrogen. After 48 h at room temperature, the reaction mixture was quenched with CH_3OH and evaporated under vacuum. The residue was dried by coevaporation with toluene and purified by chromatography on silica gel ($CHCl_3$−CH_3OH, v/v 45:1) to afford **21**(*S*) and **20**(*S*) as white solids in 38% (23 mg) and 61% (35 mg) yields, respectively. **21**(*S*); mp = 127−130 °C; $[\alpha]^{22}_D = -1°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (t, 1 H, $J_{3a,4}$ 12.3 $J_{3a,3e}$ 12.7 Hz, H-3a), 1.78, 1.88, 2.01, 2.04, 2.07, 2.11, 2.14, 2.18 and 2.21 (9 s, 3 H each, 9 OAc), 2.30 (dd, 1 H, $J_{3e,4}$ 4.4 Hz, H-3e), 3.05 (m, 1 H, $J_{2',3'}$ 11.4 Hz, $J_{3',Hb}$ 4.5 Hz, $J_{3',4'}$ 3.2 Hz, H-3′), 3.75 (s, 4 H, H-5′ and CO_2CH_3), 3.87 (s, 3 H, PhOCH_3), 3.98 (dd, 1 H, $J_{8,9b}$ 6.7 Hz, $J_{9a,9b}$ 12.3 Hz, H-9b), 3.89 (dd, 1 H, $J_{5,6}$ 10.8 Hz, $J_{6,7}$ 2.4 Hz, H-6), 4.03−4.06 (m, 2 H, H-6′a and H-6′b), 4.09 (dd, 1 H, $J_{4,5}$ 10.5 Hz, $J_{5,NH}$ 10.0 Hz, H-5), 4.29 (dd, 1 H, $J_{8,9a}$ 2.6 Hz, H-9a), 4.64 (d, 1 H, H-4′), 4.78 (m, 1 H, H-4), 5.08−5.13 (m, 3 H, H-2′, Hb and NH), 5.25 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 5.31 (dd, 1 H, $J_{7,8}$ 10.2 Hz, H-7), 5.78 (m, 1 H, H-8), 6.80 and 7.00 (2 d, 2 H each, *Ph*OCH_3). Anal. Calcd for $C_{42}H_{55}NO_{23}$ (941.9): C, 53.56; H, 5.89. Found: C, 53.54; H, 5.81. **20**(*S*). The purity of **20**(*S*) was confirmed on TLC using both silica and aluminum oxide developed with $CHCl_3/CH_3OH$, 9:1: mp = 132−134 °C; $[\alpha]^{22}_D = -9°$ (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80, 1.88, 2.03, 2.04, 2.10, 2.15, 2.18 and 2.20 (8 s, 3 H each, 8 OAc), 2.30 (t, 1 H, $J_{3a,4}$ 12.5 Hz, $J_{3a,3e}$ 13.2 Hz, H-3a), 2.40 (dd, 1 H, $J_{3e,4}$ 4.7 Hz, H-3e), 2.49 (bd, 1 H, $J_{OH,Hb}$ 5.2 Hz, OH), 2.82 (bd, 1 H, $J_{2',3'}$ 11.4 Hz, $J_{3',Hb}$ 5.2 Hz, $J_{3',4'}$ 2.7 Hz, H-3′), 3.61 (m, 1 H, H-5′), 3.76 (s, 3 H, CO_2CH_3), 3.82 (s, 3 H, PhOCH_3), 3.89 (dd, 1 H, $J_{8,9b}$ 6.9 Hz, $J_{9a,9b}$ 12.4 Hz, H-9b), 3.97−4.08 (m, 5 H, H-5, H-6, Hb, H-6′a and H-6′b), 4.30 (dd, 1 H, $J_{8,9a}$ 2.6 Hz, H-9a), 4.60 (d, 1 H, H-4′), 4.83 (m, 1 H, H-4), 5.11 (bd, 1 H, $J_{5,NH}$ 9.6 Hz, NH), 5.18 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1′), 5.27 (bd, 1 H, $J_{6,7}$ < 1.9 Hz, $J_{7,8}$ 10.2 Hz, H-7), 5.44 (dd, 1 H, H-2′), 5.68 (m, 1 H, H-8), 6.80 and 7.00 (2 d, 2 H each, *Ph*OCH_3); HRMS calcd for $C_{40}H_{53}NO_{22}$ $[M + Na^+]^+$ 922.2942, found 922.2954. Anal. Calcd for $C_{40}H_{53}NO_{22}$ (899.9): C, 53.39; H, 6.11. Found: C, 52.91; H, 6.11.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-2-*C*-[(*R*)-*O*-acetyl-[3-(phenyl 2,4,6-tri-*O*-acetyl-3-deoxythio-*β*-D-*galacto*-pyranosidyl)]methyl]-D-*erythro*-L-*manno*-nonate (22(*S*)). To a solution of **22**(*S*) (27 mg, 0.029 mmol) in anhydrous toluene (3 mL) and under nitrogen were added thiophenol (15 μL, 0.143 mmol) and $BF_3{\cdot}OEt_2$ (3.6 μL, 0.029 mmol). After 48 h at 60 °C, the reaction mixture was successively washed with saturated aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica gel ($CHCl_3$−CH_3OH, v/v 40:1) to afford **22**(*S*) as a yellowish solid in 73% yield (19 mg): FABMS (+ve) $[M + Na]^+$ 950, $[M + NH_4]^+$ 945; ^{1}H NMR (500 MHz, $CDCl_3$) δ ∼1.70 (ovl with OAc, H-3a), 1.79, 1.88, 2.01, 2.02, 2.07, 2.09, 2.10, 2.18 and 2.20 (9 s, 3 H each, 9 OAc), 2.28 (dd, 1 H, $J_{3e,4}$ 4.4 Hz, $J_{3a,3e}$ 12.8 Hz, H-3e), 3.05 (m, 1 H, $J_{2',3'}$ 10.5 Hz, $J_{3',Hb}$ 4.7 Hz, $J_{3',4'}$ 2.9 Hz, H-3′), 3.76 (s, 4 H, H-5′ and CO_2CH_3), 3.93 (dd, 1 H, $J_{8,9b}$ 6.1 Hz, $J_{9a,9b}$ 12.3 Hz, H-9b), 3.97 (dd, 1 H, $J_{5,6}$ 10.2 Hz, $J_{6,7}$ 2.3 Hz, H-6), 4.03−4.06 (m, 2 H, H-6′a and H-6′b), 4.07 (dd, 1 H, $J_{4,5}$ 10.8 Hz, $J_{5,NH}$ 10.3 Hz, H-5), 4.29 (dd, 1 H, $J_{8,9a}$ 2.6 Hz, H-9a), 4.66 (d, 1 H, H-4′), 4.77 (m, 1 H, H-4), 4.96 (dd, 1 H, $J_{1',2'}$ 9.7 Hz, H-2′), 5.12 (bd, 1 H, NH), 5.17 (d, 1 H, H-1′), 5.32 (dd, 1 H, $J_{7,8}$ 10.0 Hz, H-7), 5.75 (m, 1 H, H-8), 7.40−7.50 (m, 5 H, SPh).

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Supporting Information Available: NMR spectra for compounds **20**(*S*) and **20**(*R*). This material is available free of charge via the Internet at http://pubs.acs.org.

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