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Synthesis of deoxy-L-fucose-containing sialyl Lewis X ganglioside analogues †

Akira Hasegawa *, Takashi Ando, Mitsutoshi Kato, Hideharu Ishida, Makoto Kiso

Department of Applied Bioorganic Chemistry, Gifu University, Gifu 501-11, Japan

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Abstract

Sialyl Le^x ganglioside analogs containing 2-, 3-, and 4-deoxyfucose in the place of L-fucose have been synthesized. Glycosylation of 2-(trimethylsilyl)ethyl *O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri*O*-benzyl-β-D-galactopyranoside with the methyl 1-thioglycoside derivatives of the respective deoxyfucoses, using dimethyl(methylthio)sulfonium triflate (DMTST) as a promoter, gave the corresponding three protected 2-(trimethylsilyl)ethyl dideoxy-α-L-hexopyranosyl-(1 → 3)-*O*-2(-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-β-D-galactopyranosides. These were transformed by reductive ring-opening of their benzylidene acetal groups into the glycosyl acceptors **6**, **8**, and **10**. Dimethyl(methylthio)sulfonium triflate promoted glycosylation of **6**, **8**, and **10** with methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside afforded the desired pentasaccharides, which were converted via reductive removal of their benzyl groups, *O*-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, and reaction with trichloroacetonitrile, into the corresponding α-trichloroacetimidates **14**, **18**, and **22**. Glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol with **14**, **18**, and **22** in the presence of boron trifluoride etherate afforded the expected β-glycosides, which were transformed in good yields, via selective reduction of the azido group, coupling with octadecanoic acid, *O*-deacylation, and deesterification, into the target compounds.

1. Introduction

In the immediately preceding paper [1] we discussed the importance of synthetic studies [2–7] on sialyl Le^x and various types of analogues for progress toward the

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* Corresponding author.

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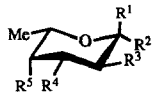
goal of elucidating the structural features of this carbohydrate ligand required for selectin [8–10] recognition. As a part of our continuing efforts along these lines, we describe here the synthesis of sialyl Le^x ganglioside (pentasaccharide) analogues containing the three possible pyranose-forming deoxy-L-fucoses.

2. Results and discussion

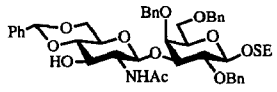
For the synthesis of the desired sialyl Le^x ganglioside analogues we employed the methyl 1-thioglycosides **1–3** of the deoxy-L-fucoses [1] as the glycosyl donors and 2-(trimethylsilyl)ethyl *O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside [4] (**4**) as a suitably protected glycosyl acceptor. The acceptor **4** was coupled with the donors using dimethyl(methylthio)sulfonium triflate [12] (DMTST) as a promoter, to afford the corresponding trisaccharides **5**, **7**, and **9**. The trisaccharide acceptors were then glycosylated with the α-sialyl-(2 → 3)-galactose donor [13] **11**. By further processing according to our usual procedures [14] the resulting pentasaccharide intermediates could be converted into the end products by introduction of a ceramide moiety.

The glycosylation of **4** with methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-1-*thio*-α,β-L-*lyxo*-hexopyranoside [1] (**1**), in dry benzene in the presence of DMTST and 3A molecular sieves, gave exclusively the α-glycoside **5** in 86% yield; significant signals of the 2-deoxy-L-fucose residue in the ^1H NMR spectrum were a three-proton doublet at δ 0.68 ($J_{5,6}$ 6.4 Hz, H-6), a one-proton multiplet at δ 2.01 (H-2c*ax*), a one-proton multiplet at δ 2.17 (J_{gem} 12.5, $J_{1,2eq} = J_{2eq,3} = 3.5$ Hz, H-2c*eq*) and a one-proton broad doublet at δ 5.04 (H-1c), indicating the structure assigned. Reductive ring-opening of the benzylidene acetal in **5** with sodium cyanoborohydride–hydrogen chloride according to the method of Garegg et al. [15] afforded the trisaccharide glycosyl acceptor **6** in 61% yield. In essentially the same way, reaction of **4** with methyl 2,4-di-*O*-benzyl-3,6-dideoxy-1-thio-β-L-*xylo*-hexopyranoside [1] (**2**) or methyl 2,3-di-*O*-benzyl-4,6-dideoxy-β-L-*xylo*-hexopyranoside [1] (**3**) furnished the corresponding deoxy-α-L-fucosyl-(1 → 3)-*N*-acetyl-β-D-glucosaminyl-(1 → 3)-β-D-galactopyranosides **7** and **9** in good yields, respectively. These were converted into the glycosyl acceptors **8** and **10** by reductive ring-opening of the benzylidene group.

Glycosylation of **6** with **11** in dry dichloromethane in the presence of DMTST and powdered 4A molecular sieves gave the expected pentasaccharide **12** in 42% yield. In the ^1H NMR spectrum were a one-proton doublet at δ 5.08 ($J_{1,2}$ 8.0 Hz, H-1d) and a one-proton doublet of doublets at δ 5.44 ($J_{2,3}$ 10.0 Hz, H-2d), indicating the newly formed glycosidic linkage to be β, as anticipated. Deprotection was then undertaken in order to obtain the unsubstituted oligosaccharide for structural assignment and biological study. Catalytic hydrogenolysis of the benzyl groups of **12** in ethanol–acetic acid and subsequent *O*-acetylation gave the per-*O*-acyl compound **13** in 73% yield, which on *O*-deacylation and subsequent saponification of the methyl ester group furnished the 2-deoxyfucose-containing sialyl Le^x oligosaccharide **15** in quantitative yield. Treatment [16] of **13** with trifluoroacetic



	R^1	R^2	R^3	R^4	R^5
1	H , SMe		H	OBz	OBz
2	H	SMe	OBn	H	OBn
3	H	SMe	OBn	OBn	H



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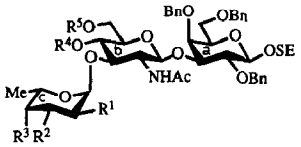
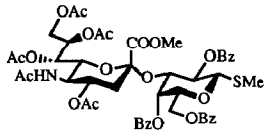


	R^1	R^2	R^3	R^4	R^5
5	H	OBz	OBz	benzylidene	
6	H	OBz	OBz	H	Bn
7	OBn	H	OBn	benzylidene	
8	OBn	H	OBn	H	Bn
9	OBn	OBn	H	benzylidene	
10	OBn	OBn	H	H	Bn



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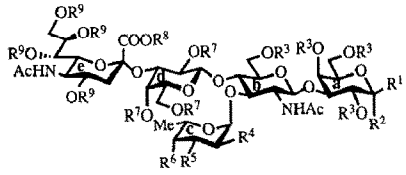
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
Bz = benzoyl

Scheme 1.

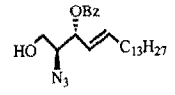
acid in dichloromethane gave the 1-hydroxy compound, which was reacted with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the α-trichloroacetimidate **14** in 85% yield. The ^{1}H NMR data for the Gal unit in **14** [δ 6.50 ($J_{1,2}$ 2.9 Hz, H-1), 8.65 (C=NH)] established the anomeric configuration of the imidate.

In a similar way, glycosylation of **8** or **10** with **11** gave the corresponding pentasaccharides **16** and **20** in 44 and 38% yields, respectively, and these were converted to the per-*O*-acyl compounds **17** and **21** by reductive removal of the benzyl groups followed by *O*-acetylation. *O*-Deacylation of **17** and **21** and subsequent saponification of the methyl ester groups yielded the desired 3- and 4-deoxy-L-fucose-containing sialyl Le^x oligosaccharide analogues **19** and **23**.

Compounds **17** and **21** were converted via selective removal of the 2-(trimethylsilyl)ethyl group and subsequent α-imidate formation, as described for the preparation of **14**, into the corresponding pentasaccharide glycosyl donors **18** and **22**, respectively, in good yields.



	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9
12	OSE	H	Bn	H	OBz	OBz	Bz	Me	Ac
13	OSE	H	Ac	H	OBz	OBz	Bz	Me	Ac
14	H	$OC(=NH)CCl_3$	Ac	H	OBz	OBz	Bz	Me	Ac
15	OSE	H	H	H	OH	OH	H	H	H
16	OSE	H	Bn	OBn	H	OBn	Bz	Me	Ac
17	OSE	H	Ac	OAc	H	OAc	Bz	Me	Ac
18	H	$OC(=NH)CCl_3$	Ac	OAc	H	OAc	Bz	Me	Ac
19	OSE	H	H	OH	H	OH	H	H	H
20	OSE	H	Bn	OBn	OBn	H	Bz	Me	Ac
21	OSE	H	Ac	OAc	OAc	H	Bz	Me	Ac
22	H	$OC(=NH)CCl_3$	Ac	OAc	OAc	H	Bz	Me	Ac
23	OSE	H	H	OH	OH	H	H	H	H



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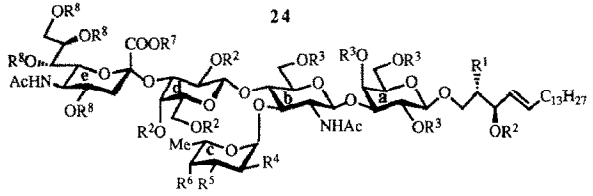

	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
25	N_3	Bz	Ac	H	OBz	OBz	Me	Ac
26	$NHCOC_{17}H_{35}$	H	H	H	OH	OH	H	H
27	N_3	Bz	Ac	OAc	H	OAc	Me	Ac
28	$NHCOC_{17}H_{35}$	H	H	OH	H	OH	H	H
29	N_3	Bz	Ac	OAc	OAc	H	Me	Ac
30	$NHCOC_{17}H_{35}$	H	H	OH	OH	H	H	H

Scheme 2.

The final glycosylation [17] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol [18] (**24**) with **14**, **18** or **22** thus obtained, in dichloromethane in the presence of boron trifluoride etherate and 4A molecular sieves, gave the desired β-glycosides **25**, **27** and **29**, in 59, 64, and 60% yields, respectively.

Selective reduction [14,19] of the azido group in **25**, **27**, and **29** with hydrogen sulfide in aqueous pyridine, and subsequent condensation with octadecanoic acid, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (WSC) in dichloromethane furnished good yields of the corresponding acylated ganglioside analogues, which were transformed via *O*-deacylation with sodium methoxide in methanol, with subsequent saponification of the sialate methyl ester group, into the desired

deoxy-L-fucose-containing sialyl Le^x ganglioside analogues **26**, **28**, and **30** in good yields.

These gangliosides were tested by Dr. B.K. Brandley of Glycomed, Inc., Alameda, CA, USA, according to his published method [20]. In this system, the new gangliosides were not recognized at all by either E- or L-selectin. On the other hand, the 2- and 4-deoxyfucose-containing sialyl Le^x ganglioside analogues **26** and **30** adhered to P-selectin about as strongly as sialyl Le^x ganglioside, while the 3-deoxyfucose analog **28** was not bound at all. These results show that for E- and L-selectin, hydroxyls on C-2, -3, and -4 of the fucose residue are required for recognition, but that P-selectin requires only the C-3 hydroxyl group, indicating the critical importance of the hydroxyl groups of the fucose residue in sialyl Le^x structure for selectivity in selectin recognition.

3. Experimental

General methods.—Optical rotations were determined with a Union PM-201 Polarimeter at 25°C and IR spectra were recorded with a Jasco IRA-100 spectrophotometer. ^1H NMR spectra were recorded at 270 MHz with a Jeol JNM-GX 270 spectrometer. Preparative column chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted in vacuo.

2-(Trimethylsilyl)ethyl O-*(3,4-di-*O*-benzoyl-2,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 3)-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**5**).—To a solution of methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-1-thio-L-*lyxo*-hexopyranoside [1] (**1**, 123 mg, 0.32 mmol) and 2-(trimethylsilyl)ethyl *O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside [4] (**4**, 224 mg, 0.27 mmol) in dry benzene (3 mL) were added powdered 4A molecular sieves (MS-4A, 0.4 g) and the mixture was stirred for 8 h at room temperature then cooled to 7°C. Dimethyl(methylthio)sulfonium triflate [12] (DMTST, 248 mg, 0.81 mmol) and MS-3A (82 mg) were added to the mixture and it was stirred for 10 h at 5–10°C; the course of the reaction was monitored by TLC. After dilution with CH_2Cl_2 (50 mL) the solids were collected and washed with CH_2Cl_2, and the combined filtrate and washings were washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (1:2 EtOAc–hexane) of the residue on silica gel (50 g) gave **5** (278 mg, 86%) as an amorphous mass; $[\alpha]_D$ −95.3° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.68 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.01 (m, 2 H, $Me_3SiCH_2CH_2$), 1.58 (s, 3 H, AcN), 2.01 (m, 1 H, H-2c*ax*), 2.17 (dt, 1 H, J_{gem} 12.5, $J_{1,2eq} = J_{2eq,3} = 3.5$ Hz, H-2c*eq*), 5.04 (br d, 1 H, H-1c), 5.38 (d, 1 H, $J_{3,4}$ 1.8 Hz, H-4c), 5.56 (s, 1 H, PhC*H*), 5.59 (m, 1 H, H-3c), and 7.25–8.04 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{77}NO_{16}Si$ (1180.4): C, 68.17; H, 6.58; N, 1.19. Found: C, 68.30; H, 6.53; N, 1.09.

2-(Trimethylsilyl)ethyl O-*(3,4-di-*O*-benzoyl-2,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*

O-benzyl-β-D-galactopyranoside (**6**).—To a solution of **5** (310 mg, 0.26 mmol) in dry THF (3.5 mL) were added MS-3A (0.4 g), the mixture was stirred for 1 h at room temperature, and sodium cyanoborohydride ($NaBH_3CN$, 250 mg) was gradually added. After the reagent had dissolved HCl in ether was added dropwise at room temperature until the evolution of gas ceased. TLC indicated that the reaction was complete after 5 min. The mixture was neutralized with Et_3N and filtered, the residue was washed with MeOH, and the combined filtrate and washings were concentrated then extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (1 : 1 EtOAc–hexane) of the residue on silica gel (50 g) afforded **6** (300 mg, 97%) as an amorphous mass; $[\alpha]_D$ −61.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.31 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.72 (s, 3 H, AcN), 2.03 (m, 1 H, H-2c*ax*), 2.34 (dt, 1 H, J_{gem} 12.1, $J_{1,2eq} = J_{2eq,3} = 4.4$ Hz, H-2c*eq*), 5.05 (m, 1 H, H-3c), 5.18 (br d, 1 H, H-1c), 5.20 (d, 1 H, N*H*), 5.58 (br d, 1 H, H-4c), and 7.23-8.10 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{79}NO_{16}Si$ (1182.5): C, 68.06; H, 6.73; N, 1.18. Found: C, 68.27; H, 6.61; N, 1.36.

2-(Trimethylsilyl)ethyl O-*(2,4-di-O-benzyl-3,6-dideoxy-α-L-xylo-hexopyranosyl)-(1 → 3)*-O-*(2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranoside* (**7**).—Glycosylation of **4** (381 mg, 1.06 mmol) with methyl 2,4-di-*O*-benzyl-3,6-dideoxy-1-thio-β-L-*xylo*-hexopyranoside [1] (**2**, 1.1 g, 1.31 mmol) in benzene (11 mL) in the presence of DMTST (0.8 g) and MS-3A (0.4 g) for 12 h at 7°C, then workup as described for **5**, gave **7** (980 mg, 82%) as an amorphous mass; $[\alpha]_D$ −9.8° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.55 (s, 3 H, AcN), 1.77 (m, 1 H, H-3c*ax*), 1.96 (m, 1 H, H-3c*eq*), 4.97 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1c), 5.24 (d, 1 H, N*H*), 5.54 (s, 1 H, PhC*H*), and 7.23–7.51 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{80}NO_{14}Si$ (1151.5): C, 69.89; H, 7.00; N, 1.22. Found: C, 69.98; H, 6.87; N, 1.21.

2-(Trimethylsilyl)ethyl O-*(2,4-di-O-benzyl-3,6-dideoxy-α-L-xylo-hexopyranosyl)-(1 → 3)*-O-*(2-acetamido-6-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranoside* (**8**).—Reductive ring-opening of the benzylidene acetal group in **7** (970 mg, 0.84 mmol) with $NaBH_3CN$ (0.8 g) in THF (10 mL), as described for the preparation of **6**, gave **8** (777 mg, 80%) as an amorphous mass; $[\alpha]_D$ −5.9° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2$), 1.20 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6c), 1.85 (ddd, 1 H, J_{gem} 13.4, $J_{2,3ax}$ 10.3, $J_{3ax,4}$ 2.8 Hz, H-3c*ax*), 2.12 (m, 1 H, H-3c*eq*), 4.97 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1c), and 7.07–7.67 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{82}NO_{14}Si$ (1153.5): C, 69.77; H, 7.17; N, 1.21. Found: C, 69.74; H, 6.97; N, 1.13.

2-(Trimethylsilyl)ethyl O-*(2,3-di-O-benzyl-4,6-dideoxy-α-L-xylo-hexopyranosyl)-(1 → 3)*-O-*(2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranoside* (**9**).—Glycosylation of **4** (1.8 g, 2.14 mmol) with methyl 2,3-di-*O*-benzyl-4,6-dideoxy-1-thio-β-L-*xylo*-hexopyranoside [1] (**3**, 642 mg, 1.79 mmol) in benzene (18 mL) in the presence of DMTST (1.4 g) and MS-3A (0.5 g) for 12 h at 7°C, then workup as described for the preparation of **5**, gave **9** (1.2 g, 57%) as an amorphous mass; $[\alpha]_D$ −22.1° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.87 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 0.97 (m, 2 H, $Me_3SiCH_2CH_2$), 1.48 (s, 3 H, AcN),

1.98 (m, 1 H, H-4c*eq*), 4.90 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1c), 5.55 (s, 1 H, PhC*H*), and 7.24–7.67 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{80}NO_{14}Si$ (1151.5): C, 69.89; H, 7.00; N, 1.22. Found: C, 69.77; H, 6.94; N, 1.04.

2-(Trimethylsilyl)ethyl O-*(2,3-di-*O*-benzyl-4,6-dideoxy-α-*L*-*xylo*-hexopyranosyl)-(1 → 3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**10**).—Reductive ring-opening of the benzylidene acetal group in **9** (1.2 g, 1.04 mmol) with $NaBH_3CN$ (1.0 g) in THF (13 mL), as described for the preparation of **6**, gave **10** (1.0 g, 87%) as an amorphous mass; $[\alpha]_D$ −26.1° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.19 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.41 (s, 3 H, AcN), 2.07 (m, 1 H, H-4c), 5.01 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1c), and 7.24–7.67 (m, 30 H, 6 Ph). Anal. Calcd for $C_{67}H_{82}NO_{14}Si$ (1153.5): C, 69.77; H, 7.17; N, 1.21. Found: C, 69.49; H, 7.06; N, 0.99.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate)-(2 → 3)-*O*-(2,4,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-[(3,4-di-*O*-benzoyl-2,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**12**).—To a solution of **6** (182 mg, 0.15 mmol) and **11** (427 mg, 0.43 mmol) in dry CH_2Cl_2 (2.6 mL) was added MS-4A (1.4 g), and the mixture was stirred for 8 h at room temperature then cooled to 0°C. DMTST (443 mg, 1.72 mmol) and MS-3A (200 mg) were added the mixture was stirred for 2 days at 7°C then filtered, and the solids were washed with CH_2Cl_2. The combined filtrate and washings were washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (60:1 CH_2Cl_2–MeOH) of the residue on silica gel (100 g) gave **12** (138 mg, 42%) as an amorphous mass; $[\alpha]_D$ −36.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.98 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.62, 1.80 (2 s, 6 H, 2 AcN), 1.82, 1.91, 1.98, 2.16 (4 s, 12 H, 4 AcO), 2.45 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.84 (s, 3 H, MeO), 5.22 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1c), 5.27 (d, 1 H, $J_{6,7}$ 2.6, $J_{7,8}$ 9.5 Hz, H-7e), 5.43 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4d), 5.44 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2d), 5.69 (m, 1 H, H-8e), 6.14 (d, 1 H, N*H*), and 6.99–8.17 (m, 45 H, 9 Ph). Anal. Calcd for $C_{114}H_{128}N_2O_{36}Si$ (2130.3): C, 64.27; H, 6.06; N, 1.31. Found: C, 64.00; H, 5.76; N, 1.27.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate)-(2 → 3)-*O*-(2,4,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-[(3,4-di-*O*-benzoyl-2,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-galactopyranoside* (**13**).—A solution of **12** (137 mg, 0.064 mmol) in EtOH (24 mL) and AcOH (4 mL) was hydrogenolyzed in the presence of 10% Pd–C (140 mg) for 48 h at 40°C, then filtered and concentrated. The residue was acetylated with Ac_2O (1 mL) in pyridine (2 mL) for 20 h at 40°C. The product was purified by chromatography on a column of silica gel (15 g) with 40:1 CH_2Cl_2–MeOH, affording **13** (91 mg, 73%) as an amorphous mass; $[\alpha]_D$ −26.9° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.12 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.59, 1.78 (2 s, 6 H, 2 AcN), 1.90–2.17 (8 s, 24 H, 8 AcO), 2.44 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.84 (s, 3 H, MeO), 5.23 (d, 1 H, $J_{1,2ax}$ 3.1 Hz, H-1c), 5.28 (dd, 1 H, $J_{6,7}$ 2.5, $J_{7,8}$ 9.8 Hz, H-7e), 5.47 (dd, 1 H, $J_{1,2}$ 8.2, $J_{2,3}$ 9.9 Hz,

H-1c), 5.28 (dd, 1 H, $J_{6,7}$ 2.5, $J_{7,8}$ 9.8 Hz, H-7e), 5.47 (dd, 1 H, $J_{1,2}$ 8.2, $J_{2,3}$ 9.9 Hz, H-2d), 5.70 (m, 1 H, H-8e), and 7.22–8.21 (m, 25 H, 5 Ph). Anal. Calcd for $C_{94}H_{112}N_2O_{40}Si$ (1938.0): C, 58.26; H, 5.83; N, 1.45. Found: C, 58.24; H, 5.92; N, 1.29.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 4)*-O-*[(3,4-di*-O-*benzoyl-2,6-dideoxy-α-L-lyxo-hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-α-D-galactopyranosyl trichloroacetimidate* (**14**).—To a solution of **13** (79 mg, 0.041 mmol) in CH_2Cl_2 (0.3 mL) at 0°C was added CF_3CO_2H (0.6 mL), and the mixture was stirred for 30 min at 0°C and concentrated. The product was purified by chromatography on a column of silica gel (15 g) with 20:1 CH_2Cl_2–MeOH to give the 1-hydroxy compound. To this, in solution in dry CH_2Cl_2 (0.7 mL) cooled to −5°C, were added trichloroacetonitrile (0.1 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 4.4 mg) and the mixture was stirred for 2 h at 0°C, and the progress of the reaction was monitored by TLC. The mixture was chromatographed on a column of silica gel (10 g) with 30:1 CH_2Cl_2–MeOH to give **14** (68 mg, 85%) as an amorphous mass; $[\alpha]_D$ +11.0° (*c* 0.2, $CHCl_3$); *ν* 3300 (NH), 1750 and 1230 (ester), 1660 and 1550 (amide), and 720 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.14 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.54, 1.75 (2 s, 6 H, 2 AcN), 1.85–2.15 (8 s, 24 H, 8 AcO), 2.46 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.82 (s, 3 H, MeO), 5.25 (d, 1 H, $J_{1,2ax}$ 2.7 Hz, H-1c), 5.65 (m, 1 H, H-8e), 6.50 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1a), 7.41–8.46 (m, 25 H, 5 Ph), and 8.65 (s, 1 H, C=N*H*). Anal. Calcd for $C_{91}H_{100}Cl_3N_3O_{40}$ (1982.2): C, 55.14; H, 5.09; N, 2.12. Found: C, 55.33; H, 4.93; N, 1.98.

2-(Trimethylsilyl)ethyl O-*(5-acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-*β-D-galactopyranosyl-(1 → 4)*-O-*[(2,6-dideoxy-α-L-lyxo-hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-β-D-galactopyranoside* (**15**).—To a solution of **13** (11 mg, 0.006 mmol) in MeOH (2 mL) was added NaOMe (5 mg), and the mixture was stirred for 12 h at 40°C. Water (0.1 mL) was added and the solution was stirred for 10 h at 40°C, then treated with Amberlite IR-120 (H^+) resin and filtered. The resin was washed with MeOH, and the combined filtrate and washings were concentrated. Column chromatography (MeOH) of the residue on Sephadex LH-20 (30 g) gave **15** (5 mg, quantitative) as an amorphous mass; $[\alpha]_D$ −29.5° (c 0.2, CH_3OH); ^1H NMR (CD_3OD): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.13 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.67 (br ddd, 1 H, J_{gem} 12.3 Hz, H-2c*ax*), 1.81 (br ddd, 1 H, H-2c*eq*), 1.94, 1.98 (2 s, 6 H, 2 AcN), 2.85 (br dd, 1 H, H-3e*eq*), 4.20 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1a), 4.47 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1d), 4.63 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1b), and 5.10 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1c). Anal. Calcd for $C_{42}H_{74}N_2O_{27}Si$ (1067.1): C, 47.27; H, 6.99; N, 2.63. Found: C, 47.37; H, 7.26; N, 2.65.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 4)*-O-*[(2,4-di*-O-*benzyl-3,6-dideoxy-α-L-xylo-hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β-D-galactopyranoside* (**16**).—Glycosylation of **8** (500 mg, 0.043 mmol)

with **11** (734 mg, 0.074 mmol) in dry CH_2Cl_2 (2.5 mL) in the presence of DMTST (1.3 g) and MS-4A (2.1 g) for 48 h at 7°C and workup as described for **12** gave **16** (412 mg, 44%) as an amorphous mass; $[\alpha]_D$ −13.0° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.17 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.57, 1.64 (2 s, 6 H, 2 AcN), 1.81–2.16 (4 s, 12 H, 4 AcO), 2.44 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.80 (s, 3 H, MeO), 5.26 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1c), 5.29 (dd, 1 H, $J_{6,7}$ 2.7, $J_{7,8}$ 8.9 Hz, H-7e), 5.35 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4d), 5.46 (t, 1 H, $J_{1,2} = J_{2,3} = 8.1$ Hz, H-2d), 5.68 (m, 1 H, H-8e), and 7.10–8.23 (m, 45 H, 9 Ph). Anal. Calcd for $C_{114}H_{132}N_2O_{34}Si$ (2102.4): C, 65.12; H, 6.29; N, 1.33. Found: C, 65.17; H, 6.39; N, 1.22.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,4-di*-O-*acetyl-3,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**17**).—Hydrogenolysis of **16** (206 mg, 0.098 mmol) in EtOH (36 mL) and AcOH (6 mL) in the presence of 10% Pd–C (210 mg) for 24 h at 40°C, and subsequent acetylation with Ac_2O (2 mL) in pyridine (9 mL) as described for the preparation of **13** gave **17** (116 mg, 65%) as an amorphous mass; $[\alpha]_D$ −17.5° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.16 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.60, 1.79 (2 s, 6 H, 2 AcN), 1.90–2.16 (10 s, 30 H, 10 AcO), 2.41 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.81 (s, 3 H, MeO), 5.25 (2 d, 2 H, $J_{3,4}$ 2.6 Hz, H-4a, H-1c), 5.28 (dd, 1 H, $J_{6,7}$ 2.1, $J_{7,8}$ 8.5 Hz, H-7e), 5.36 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4d), 5.44 (t, 1 H, $J_{1,2} = J_{2,3} = 8.1$ Hz, H-2d), 5.66 (m, 1 H, H-8e), and 7.46–8.20 (m, 15 H, 3 Ph). Anal. Calcd for $C_{84}H_{108}N_2O_{40}Si$ (1812.8): C, 55.65; H, 5.95; N, 1.55. Found: C, 55.80; H, 6.06; N, 1.55.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,4-di*-O-*acetyl-3,6-dideoxy-α*-D-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galacto-pyranosyl trichloroacetimidate* (**18**).—Selective removal of the 2-(trimethylsilyl)ethyl group in **17** (94 mg, 0.052 mmol) with CF_3CO_2H (0.7 mL) in CH_2Cl_2 (0.4 mL) for 20 min at 0°C, and subsequent reaction with trichloroacetonitrile (0.2 mL) in CH_2Cl_2 (1 mL) in the presence of DBU (8.7 mg) for 4 h at 0°C as described for **14** gave **18** (84 mg, 86%) as an amorphous mass; $[\alpha]_D$ +8.8° (*c* 1.1, $CHCl_3$); ν 3280 (NH), 1750 and 1240 (ester), 1680 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.17 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6c), 1.60, 1.78 (2 s, 6 H, 2 AcN), 1.88–2.16 (10 s, 30 H, 10 AcO), 2.40 (dd, 1 H, J_{gem} 13.0, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.81 (s, 3 H, MeO), 5.67 (m, 1 H, H-8e), 6.49 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1a), 7.46–8.18 (m, 15 H, 3 Ph), and 8.62 (s, 1 H, C=N*H*). Anal. Calcd for $C_{81}H_{96}Cl_3N_3O_{40}$ (1857.0): C, 52.40; H, 5.16; N, 2.26. Found: C, 52.52; H, 5.11; N, 2.16.

2-(Trimethylsilyl)ethyl O-*(5-acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-*β*-D-*galactopyranosyl-(1 → 4)*-O-*[(3,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**19**).—Deacylation and saponification of **17** (20 mg, 0.011 mmol) as described for **15** yielded **19** (12 mg, quantitative) as an amorphous mass;

$[\alpha]_D$ −18.0° (*c* 0.5, MeOH); ^{1}H NMR (CD_3OD): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.07 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.73 (br ddd, 1 H, H-3c*ax*), 1.94, 1.98 (2 s, 6 H, 2 AcN), 2.10 (br ddd, 1 H, H-3c*eq*), 2.85 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 3.9 Hz, H-3e*eq*), 4.20 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1a), 4.49 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1d), 4.61 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1b), and 5.05 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1c). Anal. Calcd for $C_{42}H_{74}N_2O_{27}Si$ (1067.1): C, 47.27; H, 6.99; N, 2.63. Found: C, 47.05; H, 6.91; N, 2.40.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,3-di*-O-*benzyl-4,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**20**).—Glycosylation of **10** (600 mg, 0.052 mmol) with **11** (880 mg, 0.088 mmol) in CH_2Cl_2 (3 mL) in the presence of DMTST (1.5 g) and MS-4A (2.5 g) for 48 h at 7°C and workup as described for **12** gave **20** (410 mg, 38%) as an amorphous mass; $[\alpha]_D$ −22.2° (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.02 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.59, 1.70 (2 s, 6 H, 2 AcN), 1.80, 1.92, 1.97, 2.15 (4 s, 12 H, 4 AcO), 2.45 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.9 Hz, H-3e*eq*), 3.83 (s, 3 H, MeO), 5.27 (dd, 1 H, $J_{6,7}$ 2.7, $J_{7,8}$ 9.6 Hz, H-7e), 5.33 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1c), 5.40 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4d), 5.43 (near t, 1 H, $J_{1,2} = J_{2,3} = 7.9$ Hz, H-2d), 5.67 (m, 1 H, H-8e), and 7.11–8.20 (m, 45 H, 9 Ph). Anal. Calcd for $C_{114}H_{132}N_2O_{34}Si$ (2102.4): C, 65.12; H, 6.29; N, 1.33. Found: C, 64.94; H, 6.29; N, 1.23.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,3-di*-O-*acetyl-4,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**21**).—Hydrogenolysis of **20** (116 mg, 0.055 mmol) in EtOH (20 mL) and AcOH (3 mL) in the presence of 10% Pd–C (120 mg) for 48 h at 40°C, and subsequent acetylation with Ac_2O (0.6 mL) in pyridine (1.2 mL) as described for **13** gave **21** (87 mg, 87%) as an amorphous mass; $[\alpha]_D$ −17.2° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.22 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.55, 1.79 (2 s, 6 H, 2 AcN), 1.84–2.15 (10 s, 30 H, 10 AcO), 2.43 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.79 (s, 3 H, MeO), 5.67 (m, 1 H, H-8e), and 7.43–8.20 (m, 15 H, 3 Ph). Anal. Calcd for $C_{84}H_{108}N_2O_{40}Si$ (1812.8): C, 55.65; H, 5.95; N, 1.55. Found: C, 55.54; H, 5.86; N, 1.30.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,3-di*-O-*acetyl-4,6-dideoxy-α*-D-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galactopyranosyl trichloroacetimidate* (**22**).—Selective removal of the 2-(trimethylsilyl)ethyl group in **21** (81 mg, 0.045 mmol) with CF_3CO_2H (0.6 mL) in CH_2Cl_2 (0.4 mL) for 20 min at 0°C, and subsequent treatment with trichloroacetonitrile (0.2 mL) in CH_2Cl_2 (1 mL) in the presence of DBU (7.5 mg) for 2 h at 0°C as described for **14** gave **21** (72 mg, 86%) as amorphous mass; $[\alpha]_D$ +11.0° (*c* 1.4, $CHCl_3$); ν 3380 (NH), 1740 and 1240 (ester), 1680 and 1540 (amide), and 710 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 1.23 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.54, 1.78 (2 s, 6 H, 2 AcN), 1.83–2.15

(10 s, 30 H, 10 AcO), 2.43 (dd, 1 H, J_{gem} 12.6, $J_{3eq,4}$ 4.5 Hz, H-3e*eq*), 3.78 (s, 3 H, MeO), 5.66 (m, 1 H, H-8e), 6.48 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1a), 7.16–8.19 (m, 15 H, 3 Ph), and 8.62 (s, 1 H, C=N*H*). Anal. Calcd for $C_{81}H_{96}Cl_3N_3O_{40}$ (1857.0): C, 52.40; H, 5.16; N, 2.26. Found: C, 52.21; H, 5.03; N, 2.08.

2-(Trimethylsilyl)ethyl O-*(5-acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-*[(4,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**23**).—Deacylation and subsequent saponification of **21** (90 mg, 0.05 mmol) as described for **15** yielded **23** (43 mg, 82%) as an amorphous mass; $[\alpha]_D$ −34.0° (*c* 0.9, MeOH); ^{1}H NMR (CD_3OD): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.07 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.95, 1.98 (2 s, 6 H, 2 AcN), 2.85 (dd, 1 H, J_{gem} 9.7, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 4.20 (d, 1 H, $J_{1,2}$ 6.9 Hz, H-1a), 4.48 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1d), 4.67 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1b), and 5.05 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1c). Anal. Calcd for $C_{42}H_{74}N_2O_{27}Si$ (1067.1): C, 47.27; H, 6.99; N, 2.63. Found: C, 47.25; H, 6.70; N, 2.39.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(3,4-di*-O-*benzoyl-2,6-dideoxy-α*-L-lyxo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1 → 1)-(2*S,*3*R,*4*E)UD*)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**25**).—To a solution of **14** (41 mg, 0.021 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol [18] (**24**, 44 mg, 0.11 mmol) in CH_2Cl_2 (0.5 mL) were added MS-4A (AW-300, 0.5 g), and the mixture was stirred for 6 h at room temperature then cooled to 0°C. Boron trifluoride etherate (11 μL) was added and the mixture was stirred for a further 3 h at 0°C. The solids were filtered off and washed with CH_2Cl_2, and the combined filtrate and washings were concentrated. Column chromatography (30:1 CH_2Cl_2–MeOH) of the residue on silica gel (10 g) gave **25** (27 mg, 59%) as an amorphous mass; $[\alpha]_D$ +16.1° (*c* 0.6, $CHCl_3$); ν 3300 (NH), 2940 and 2870 (methyl, methylene), 2100 (N_3), 1740 and 1230 (ester), 1670 and 1550 (amide), and 710 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3 H, J_{vic} 6.2 Hz, CH_3CH_2), 1.24 (s, 22 H, 11 CH_2), 1.50, 1.77 (2 s, 6 H, 2 AcN), 1.87–2.17 (8 s, 24 H, 8 AcO), 2.44 (dd, 1 H, J_{gem} 12.7, $J_{3eq,4}$ 4.5 Hz, H-3e*eq*), 3.83 (s, 3 H, MeO), 5.92 (m, 1 H, H-5 of sphingosine), and 7.41–8.19 (m, 30 H, 6 Ph). Anal. Calcd for $C_{114}H_{137}N_5O_{42}$ (2249.3): C, 60.87; H, 6.14; N, 3.11. Found: C, 60.81; H, 6.16; N, 3.23.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-*[(2,6-dideoxy-α*-L-lyxo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)*-O-β-D-*galactopyranosyl-(1 → 1)-(2*S,*3*R,*4*E)-2-octadecanamido-4-octadecene-1,3-diol* (**26**).—Hydrogen sulfide was bubbled through a stirred solution of **25** (27 mg, 0.012 mmol) in aq 83% pyridine (3 mL) for 2 days at 0°C, with the progress of the reaction monitored by TLC. The mixture was concentrated and the residue was stirred with octadecanoic acid (7 mg, 0.024 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC, 7 mg, 0.036 mmol) in dry CH_2Cl_2 (0.7 mL) for 12 h at room

temperature. After completion of the reaction, CH_2Cl_2 (50 mL) was added to the mixture, and the solution was washed with water, dried (Na_2SO_4), and concentrated to a syrup that was chromatographed on a column of silica gel (10 g) with 30:1 CH_2Cl_2–MeOH to give the protected ganglioside analogue. *O*-Deacylation and subsequent saponification of the product as described for **15** yielded **26** (10 mg, 55%) as an amorphous mass; $[\alpha]_D$ −5.3° (*c* 0.4, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^{1}H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.92 (t, 6 H, J_{vic} 6.7 Hz, 2 CH_3CH$_2$), 1.09 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.30 (s, 52 H, 26 CH_2), 1.87, 1.96 (2 s, 6 H, 2 AcN), 2.07 (t, 2 H, COCH_2CH$_2$), 2.83 (dd, 1 H, H-3e*eq*), 4.26 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1a), 5.40 (dd, 1 H, $J_{3,4}$ 7.0, $J_{4,5}$ 15.1 Hz, H-4 of sphingosine), and 5.60 (dt, 1 H, $J_{5,6} = J_{5,6'}$ = 7.6 Hz, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{29}$ (1514.8): C, 57.88; H, 8.72; N, 2.77. Found: C, 57.79; H, 8.82; N, 2.69.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 4)*-O-*[(2,4-di*-O-*acetyl-3,6-dideoxy*-α-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)*-O-*(2,4,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 1)-(2S,3R,4E)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**27**). —Coupling of **18** (84 mg, 0.045 mmol) with **24** (50 mg, 0.113 mmol) as described for **25** gave **27** (61 mg, 64%) as an amorphous mass; $[\alpha]_D$ −10.0° (*c* 0.4, $CHCl_3$); ν 3150 (NH), 2100 (N_3), 1740 and 1260 (ester), 1680 and 1550 (amide), and 700 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J_{vic} 6.7 Hz, CH_3CH$_2$), 1.26 (s, 22 H, 11 CH_2), 1.60, 1.79 (2 s, 6 H, 2 AcN), 1.90-2.16 (10 s, 30 H, 10 AcO), 2.42 (dd, 1 H, J_{gem} 12.7, $J_{3eq,4}$ 4.5 Hz, H-3e*eq*), 3.81 (s, 3 H, MeO), 5.65 (m, 1 H, H-8e), 5.93 (m, 1 H, H-5 of sphingosine), and 7.42–8.19 (m, 20 H, 4 Ph). Anal. Calcd for $C_{104}H_{133}N_5O_{42}$ (2124.2): C, 58.81; H, 6.26; N, 3.30. Found: C, 59.04; H, 6.32; N, 3.26.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-*β-D-galactopyranosyl-(1 → 4)*-O-*[(3,6-dideoxy*-α-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)*-O-*β-D-galactopyranosyl-(1 → 1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol* (**28**).—Selective reduction of the azido group in **27** (61 mg, 0.029 mmol) with H_2S in aq 83% pyridine (5 mL), subsequent coupling with octadecanoic acid (16 mg, 0.058 mmol) in the presence of WSC (17 mg), and then deacylation and saponification, as described for **26** gave **28** (42 mg, 97%) as an amorphous mass; $[\alpha]_D$ −5.4° (*c* 0.4, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^{1}H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.90 (t, 6 H, 2 CH_3CH$_2$), 1.06 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.28 (s, 52 H, 26 CH_2), 1.95, 2.04 (2 s, 6 H, 2 AcN), 2.16 (t, 2 H, COCH_2CH$_2$), 2.91 (br dd, 1 H, H-3e*eq*), 4.94 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1c), 5.49 (br dd, 1 H, H-4 of sphingosine), and 5.67 (dt, 1 H, $J_{5,6} = J_{5,6'}$ = 7.0 Hz, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{29}$ (1514.8): C, 57.88; H, 8.72; N, 2.77. Found: C, 57.61; H, 8.42; N, 2.73.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 4)*-O-*[(2,3-di*-O-*acetyl-4,6-dideoxy*-α-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)*-O-*(2,4,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 1)-(2S,3R,4E)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**29**).

—Coupling of **22** (213 mg, 0.115 mmol) with **24** (245 mg, 0.575 mmol) as described for **25** gave **29** (147 mg, 60%) as an amorphous mass; $[\alpha]_D$ −10.6° (*c* 0.8, $CHCl_3$); ν 3250 (NH), 2100 (N_3), 1740 and 1230 (ester), 1670 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J_{vic} 6.4 Hz, CH_3CH_2), 1.25 (s, 22 H, 11 CH_2), 1.55, 1.78 (2 s, 6 H, 2 AcN), 1.84–2.14 (10 s, 30 H, 10 AcO), 2.44 (br dd, 1 H, H-3e*eq*), 3.78 (s, 3 H, MeO), 5.88 (m, 1 H, H-5 of sphingosine), and 7.16–8.19 (m, 20 H, 4 Ph). Anal. Calcd for $C_{104}H_{133}N_5O_{42}$ (2124.2): C, 58.81; H, 6.26; N, 3.30. Found: C, 58.77; H, 6.07; N, 3.19.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-*β*-D-*galactopyranosyl-(1 → 4)*-O-*[(4,6-dideoxy-α*-L-xylo-*hexopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)*-O-*β*-D-*galactopyranosyl-(1 → 1)-(2*S,*3*R,*4*E*)-2-octadecanamido-4-octadecene-1,3-diol* (**30**).—Selective reduction of the azido group in **29** (147 mg, 0.069 mmol) with H_2S in aq 83% pyridine (10 mL), subsequent coupling with octadecanoic acid (39 mg, 0.138 mmol) in the presence of WSC (40 mg), and then deacylation and saponification as described for **26** gave **30** (86 mg, 82%) as an amorphous mass; $[\alpha]_D$ −13.5° (*c* 0.4, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^1H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.90 (t, 6 H, 2 CH_3CH_2), 1.01 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.28 (s, 52 H, 26 CH_2), 1.86, 1.94 (2 s, 6 H, 2 AcN), 2.06 (t, 2 H, $COCH_2CH_2$), 2.80 (br dd, 1 H, H-3e*eq*), 5.38 (dd, 1 H, $J_{3,4}$ 7.3, $J_{4,5}$ 15.2 Hz, H-4 of sphingosine), and 5.58 (dt, 1 H, $J_{5,6} = J_{5,6'} = 7.3$ Hz, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{29}$ (1514.8): C, 57.88; H, 8.72; N, 2.77. Found: C, 57.85; H, 8.66; N, 2.58.

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