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Carbohydrate Research 274 (1995) 165–181

CARBOHYDRATE RESEARCH

Synthesis of sialyl Lewis X ganglioside analogues containing modified L-fucose residues ☆

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Received 5 December 1994; accepted 3 February 1995

Abstract

Sialyl Le^x ganglioside analogues containing 2-*epi*-, 2,3-di-*epi*-, 4-*epi*-, and 2-*O*-methyl-L-fucose in place of the L-fucose residue 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 fucose analogues, using dimethyl(methylthio)sulfonium triflate (DMTST) as a promoter, gave the corresponding protected 2-(trimethylsilyl)ethyl deoxy-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. Dimethyl(methylthio)sulfonium triflate-promoted glycosylation of these compounds 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. Glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol these 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 gangliosides. The 2-(trimethylsilyl)ethyl glycosides of sialyl Le^x oligosaccharides containing modified fucose were also prepared from the intermediates of the ganglioside synthesis.

Keywords: Ganglioside, Lewis X, sialyl; L-Fucose; Selectin recognition

☆ Synthetic Studies on Sialoglycoconjugates, Part 69. For Part 68, see ref. [1].

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SSDI 0008-6215(95)00135-2

1. Introduction

In a previous paper [1] we described the importance of synthetic studies [2–9] on sialyl Le^x, sialyl Le^a and various types of analogues for progress toward the goal of elucidating the structural features of carbohydrate ligands required for selectin [10–16] recognition. As a part of our continuing efforts, we describe herein the synthesis of the four sialyl Le^x ganglioside analogues containing modified fucose residues for clarifying the role of fucose structure in selectin recognition.

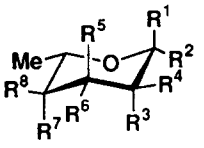
2. Results and discussion

For synthesis of the desired sialyl Le^x gangliosides analogues, we employed the methyl 1-thioglycosides **1–5** [1] of the stereoisomers, the 2-*O*-methyl derivative of L-fucose 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 [3] (**6**) as a suitably protected glycosyl acceptor. The acceptor **6** was coupled with the donors using dimethyl(methylthio)sulfonium triflate [17] (DMTST) as a promoter to afford the corresponding trisaccharides **7**, **9**, **11**, **13**, and **15**. The trisaccharide acceptors were then glycosylated with the α-sialyl-(2 → 3)-galactose donor **17** [18]. By further processing according to our usual procedures [19], the resulting pentasaccharide intermediates could be transformed into the end products by introduction of a ceramide moiety.

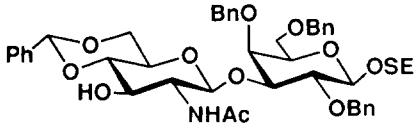
Glycosylation of **6** with methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-α-L-talopyranoside (**1**) [1] in dry benzene in the presence of DMTST and 4 Å molecular sieves gave exclusively the α-glycoside **7** in 86% yield. A significant signal of the talose residue in the ^{1}H NMR spectrum was a one-proton doublet at δ 4.98 ($J_{1,2}$ 1.5 Hz), indicating the newly formed glycosidic linkage to be α. Reductive ring-opening of the benzylidene acetal in **7** with sodium cyanoborohydride–hydrogen chloride according to the method of Garegg et al. [20] afforded the trisaccharide glycosyl acceptor **8** in 78% yield.

In essentially the same way, reaction of **6** with methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-β-L-gulopyranoside (**2**) [1], methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-6-deoxy-1-thio-β-L-glucopyranoside (**3**) [1], methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-α-L-rhamnopyranoside (**4**) [1], or methyl 3,4-di-*O*-acetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (**5**) [1] furnished the corresponding trisaccharides **9** (60%), **11** (70%), **13** (92%), and **15** (79%), respectively. These were converted into the glycosyl acceptors **10**, **12**, **14**, and **16** in good yields by reductive ring-opening of the benzylidene group.

Glycosylation of **8** 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 (**17**) [18] in dry CH_2Cl_2 in the presence of DMTST and powdered 4 Å molecular sieves gave the expected pentasaccharide **18** in 53% yield. A one-proton doublet of doublets at δ 5.47 ($J_{1,2}$ 8.4, $J_{2,3}$ 9.5 Hz, H-2d) in the ^{1}H NMR spectrum indicated 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 **18** in ethanol–acetic acid and subsequent *O*-acetylation gave the per-*O*-acyl



	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
1	SMe	H	OBn	H	H	OBn	OBn	H
2	H	SMe	H	OBn	OBn	H	OBn	H
3	H	SMe	H	OBn	H	OBn	H	OAc
4	SMe	H	OBn	H	H	OBn	H	OBn
5	H	SMe	H	OMe	H	OAc	OAc	H



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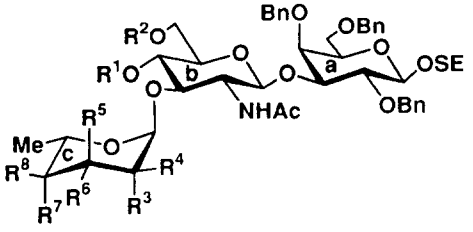
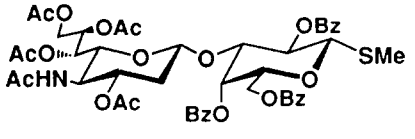


	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
7	benzylidene		OBn	H	H	OBn	OBn	H
8	H	Bn	OBn	H	H	OBn	OBn	H
9	benzylidene		H	OBn	OBn	H	OBn	H
10	H	Bn	H	OBn	OBn	H	OBn	H
11	benzylidene		H	OBn	H	OBn	H	OAc
12	H	Bn	H	OBn	H	OBn	H	OAc
13	benzylidene		OBn	H	H	OBn	H	OBn
14	H	Bn	OBn	H	H	OBn	H	OBn
15	benzylidene		H	OMe	H	OAc	OAc	H
16	H	Bn	H	OMe	H	OAc	OAc	H

Bn = benzyl
SE = 2-(trimethylsilyl)ethyl

compound **19** in 70% yield, which on *O*-deacylation and subsequent saponification of the methyl ester group gave the 2-*epi*-fucose-containing sialyl Le^x oligosaccharide **21** in quantitative yield.

Treatment [21] of **19** with trifluoroacetic acid in CH_2Cl_2 gave the 1-hydroxy compound, which was reacted [19,22] with trichloroacetonitrile in CH_2Cl_2 in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the α-trichloroacetimidate **20** in 84% yield. The ^{1}H NMR data for the D-Gal unit in **20** [δ 6.49 ($J_{1,2}$ 3.5 Hz, H-1a), 8.62 (C=NH)] established the anomeric configuration of the imidate. In a similar way, glycosylation of **10**, **12**, **14**, or **16** with **17** gave the corresponding pentasaccharides **22** (14%), **23** (41%), **27** (44%), and **31** (45%), respectively. Compounds **23**, **27**, and **31** were converted to their per-*O*-acyl derivatives **24**, **28** and **32** by reductive removal of the benzyl groups, followed by *O*-acetylation. *O*-Deacylation of **24**, **28** and **32** and subsequent saponification of the methyl ester groups yielded the desired 4-*epi*-, 2,4-di-*epi*-, and 2-*O*-methyl-L-fucose-containing sialyl Le^x oligosaccharide analogues **26**, **30** and **34** in quantitative yield.



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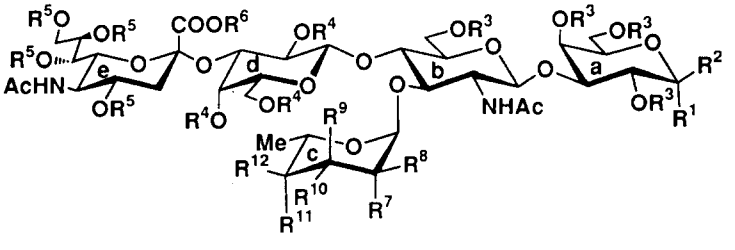
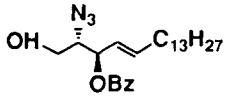


	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9	R^{10}	R^{11}	R^{12}
18	H	SE	Bn	Bz	Ac	Me	OBn	H	H	OBn	OBn	H
19	H	SE	Ac	Bz	Ac	Me	OAc	H	H	OAc	OAc	H
20	OC(=NH)CCl_3,H		Ac	Bz	Ac	Me	OAc	H	H	OAc	OAc	H
21	H	SE	H	H	H	H	OH	H	H	OH	OH	H
22	H	SE	Bn	Bz	Ac	Me	OBn	H	OBn	H	OBn	H
23	H	SE	Bn	Bz	Ac	Me	H	OBn	H	OBn	H	OAc
24	H	SE	Ac	Bz	Ac	Me	H	OAc	H	OAc	H	OAc
25	OC(=NH)CCl_3,H		Ac	Bz	Ac	Me	H	OAc	H	OAc	H	OAc
26	H	SE	H	H	H	H	H	OH	H	OH	H	OH
27	H	SE	Bn	Bz	Ac	Me	OBn	H	H	OBn	H	OBn
28	H	SE	Ac	Bz	Ac	Me	OAc	H	H	OAc	H	OAc
29	OC(=NH)CCl_3,H		Ac	Bz	Ac	Me	OAc	H	H	OAc	H	OAc
30	H	SE	H	H	H	H	OH	H	H	OH	H	OH
31	H	SE	Bn	Bz	Ac	Me	H	OMe	H	OAc	OAc	H
32	H	SE	Ac	Bz	Ac	Me	H	OMe	H	OAc	OAc	H
33	OC(=NH)CCl_3,H		Ac	Bz	Ac	Me	H	OMe	H	OAc	OAc	H
34	H	SE	H	H	H	H	H	OMe	H	OH	OH	H

Compounds **24**, **28**, and **32** were converted via selective removal of the 2-(trimethylsilyl)ethyl group and subsequent α-imidate formation, as described for the preparation of **20**, into the corresponding pentasaccharide glycosyl donors **25**, **29**, and **33**, respectively, in good yields.

The final glycosylation [23] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**35**) [24] with **20**, **25**, **29** or **33** thus obtained, in CH_2Cl_2 in the presence of boron trifluoride etherate and 4 Å molecular sieves, gave the desired β-glycosides **36**, **38**, **40** and **42**, in 65, 85, 64, and 60% yields, respectively.

Selective reduction [19,25] of the azido group in **36**, **38**, **40**, and **42** with hydrogen sulfide in aqueous pyridine, and subsequent condensation with octadecanoic acid, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (WSC) in CH_2Cl_2 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 methyl ester group, into the target, modified L-fucose-containing sialyl Le^x ganglioside analogues **37**, **39**, **41**, and **43** in good yields. These gangliosides were evaluated by Dr B.K. Brandley of Glycomed, Inc., Alameda, CA, USA, according to his published method [16]. In this system, the new gangliosides were not recognized at all by three selectins, indicating the critical importance for selectin recognition of the presence and definite configuration of the hydroxyl groups of the fucose residue in the sialyl Le^x structure.



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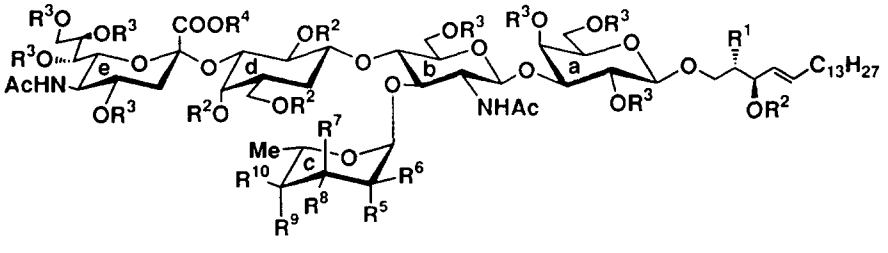

	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9	R^{10}
36	N_3	Bz	Ac	Me	OBn	H	H	OBn	OBn	H
37	$NHCOC_{17}H_{35}$	H	H	H	H	H	H	OH	OH	H
38	N_3	Bz	Ac	Me	H	OBn	H	OBn	H	OAc
39	$NHCOC_{17}H_{35}$	H	H	H	H	OH	H	OH	H	OH
40	N_3	Bz	Ac	Me	OBn	H	H	OBn	H	OBn
41	$NHCOC_{17}H_{35}$	H	H	H	OH	H	H	OH	H	OH
42	N_3	Bz	Ac	Me	H	OMe	H	OAc	OAc	H
43	$NHCOC_{17}H_{35}$	H	H	H	H	OMe	H	OH	OH	H

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. ^{1}H NMR spectra were recorded at 270 MHz with a Jeol JNM-GX 270 spectrometer. Preparative 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-(2,3,4-tri-O-benzyl-6-deoxy-α-L-talopyranosyl)-(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**).—To a solution of methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-α-L-talopyranoside (**1**, 187 mg, 0.4 mmol) [1] 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 (**6**, 282 mg, 0.33 mmol) [3] in dry benzene (4 mL) were added powdered 4 Å molecular sieves (MS-4A, 1.12 g), and the mixture was stirred for 4 h at room temperature, then cooled to 5°C. Dimethyl(methylthio)sulfonium triflate (DMTST, 200 mg, 0.6 mmol) [17] was added to the mixture, and it was stirred for 10 h at 5°C while 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 was washed with water, dried (Na_2SO_4) and concentraded. Column chromatography (1:3 EtOAc–hexane) of the residue on silica gel (40 g) gave **7** (365 mg, 86%) as an amorphous mass: $[\alpha]_D$ −37.5° (*c* 1.4, $CHCl_3$); IR: ν 3400 (NH), 1660 and 1550 (amide), 860 and 840 (Me_3Si), and 740 and 700 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 0.91 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.53 (s, 3 H, AcN), 4.98 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1c), 5.47 (s, 1 H, C*H*Ph), and 7.19–7.45 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{87}NO_{15}Si$ (1258.6): C, 70.62; H, 6.97; N, 1.11. Found: C, 70.36; H, 6.77; N, 0.88.

2-(Trimethylsilyl)ethyl O-(2,3,4-tri-O-benzyl-6-deoxy-α-L-talopyranosyl)-(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**).—To a solution of **7** (280 mg, 0.22 mmol) in dry THF (4.6 mL) was added MS-3A (800 mg), the mixture was stirred for 3 h at room temperature, and sodium cyanoborohydride ($NaBH_3CN$, 230 mg, 3.3 mmol) 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 was concentrated, then extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (200:1 CH_2Cl_2–MeOH) of the residue on silica gel (50 g) afforded **8** (218 mg, 78%) as an amorphous mass: $[\alpha]_D$ −19.6° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$); δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.38 (d, 3 H, $J_{5,6}$ 6.8 Hz, H-6c), 1.43 (s, 3 H, AcN), 4.14 (m, 1 H, H-5c), and 7.21–7.37 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{89}NO_{15}Si$ (1260.6): C, 70.51; H, 7.12; N, 1.11. Found: C, 70.42; H, 7.04; N, 1.09.

2-(Trimethylsilyl)ethyl O-(2,3,4-tri-O-benzyl-6-deoxy-α-L-gulopyranosyl)-(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 **6** (670 mg, 0.8 mmol) with methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-β-L-gulopyranoside (**2**, 443 mg, 0.95 mmol) [1] in

benzene (10 mL) in the presence of DMTST (956 mg, 2.38 mmol) and MS-4A (1.3 g) for 3 h at 5°C, then workup as described for **7**, gave **9** (590 mg, 60%) as an amorphous mass: $[\alpha]_D$ −51.2° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.71 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6c), 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.47 (s, 3 H, AcN), 3.16 (s, 1 H, H-4c), 3.89 (br s, 1 H, H-4a), 4.99 (s, 1 H, H-1c), 5.49 (s, 1 H, C*H*Ph), and 7.14–7.47 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{87}NO_{15}Si$ (1258.6): C, 70.62; H, 6.97; N, 1.11. Found: C, 70.59; H, 6.80; N, 0.97.

2-(Trimethylsilyl)ethyl O-*(2,3,4-tri*-O-*benzyl-6-deoxy-α*-L-*gulopyranosyl)-(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** (787 mg, 0.63 mmol) with $NaBH_3CN$ (600 mg, 9.45 mmol) in THF (8.7 mL), as described for the preparation of **8**, gave **10** (538 mg, 68%) as an amorphous mass: $[\alpha]_D$ −26.6° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.96 (m, 2 H, $Me_3SiCH_2CH_2$), 1.16 (d, 3 H, $J_{5,6}$ 6.8 Hz, H-6c), 1.40 (s, 3 H, AcN), 4.99 (br s, 1 H, H-1c), and 7.19–7.33 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{89}NO_{15}Si$ (1260.6): C, 70.51; H, 7.12; N, 1.11. Found: C, 70.40; H, 7.03; N, 1.07.

2-(Trimethylsilyl)ethyl O-*(4*-O-*acetyl-2,3-di*-O-*benzyl-6-deoxy-α*-L-*glucopyranosyl)-(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* (**11**).—Glycosylation of **6** (674 mg, 0.8 mmol) with methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-6-deoxy-1-thio-β-L-glucopyranoside (**3**, 400 mg 0.96 mmol) [1] in benzene (10 mL) in the presence of DMTST (1.0 g, 2.88 mmol) and MS-4A (2.8 g) for 3 h at 5°C, then workup as described for the preparation of **7**, gave **11** (682 mg, 70%) as an amorphous mass: $[\alpha]_D$ −52.2° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.78 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.51 (s, 3 H, AcN), 1.88 (s, 3 H, AcO), 4.99 (d, 1 H, $J_{1,2}$ 2.7 Hz, H-1c), 5.56 (s, 1 H, C*H*Ph), and 7.27–7.49 (m, 30 H, 6 Ph). Anal. Calcd for $C_{69}H_{83}NO_{16}Si$ (1210.5): C, 68.46; H, 6.91; N, 1.16. Found: C, 68.27; H, 6.73; N, 1.15.

2-(Trimethylsilyl)ethyl O-*(4*-O-*acetyl-2,3-di*-O-*benzyl-6-deoxy-α*-L-*glucopyranosyl)-(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**).—Reductive ring-opening of the benzylidene acetal group in **11** (1.07 g, 0.88 mmol) with $NaBH_3CN$ (830 mg, 13.2 mmol) in THF (18 mL), as described for **8**, gave **12** (910 mg, 85%) as an amorphous mass: $[\alpha]_D$ −21.5° (*c* 1.0, $CHCl_3$); IR: ν 3425 (NH, OH), 1750 and 1240 (ester), 1670 and 1530 (amide), 860 and 840 (Me_3Si), and 740 and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.13 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.45 (s, 3 H, AcN), 1.89 (s, 3 H, AcO), 5.03 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1c), and 7.27–7.39 (m, 30 H, 6 Ph). Anal. Calcd for $C_{69}H_{85}NO_{16}Si$ (1212.5): C, 68.35; H, 7.07; N, 1.16. Found: C, 68.19; H, 6.81; N, 1.08.

2-(Trimethylsilyl)ethyl O-*(2,3,4-tri*-O-*benzyl-α*-L-*rhamnopyranosyl)-(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* (**13**).—Glycosylation of **6** (51 mg, 0.18 mmol) with methyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-α-L-rhamnopyranoside (**4**, 100 mg, 0.22 mmol) [1] in benzene (3 mL) in the presence of DMTST (95 mg, 0.27 mmol) and MS-4A (600 mg) for 10 h at 5°C, then workup as described for **7**, gave **13** (208 mg, 92%) as an amorphous mass: $[\alpha]_D$ −20.5° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.33 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.47 (s, 3 H, AcN), 4.76 (d, 1 H, $J_{1,2}$

1.8 Hz, H-1c), 5.50 (s, 1 H, C*H*Ph), and 7.28–7.32 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{87}NO_{15}Si$ (1258.6): C, 70.62; H, 6.97; N, 1.11. Found: C, 70.36; H, 6.78; N, 1.10.

2-(Trimethylsilyl)ethyl O-*(2,3,4-tri*-O-*benzyl-α*-L-*rhamnopyranosyl)-(1 → 3)*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**14**).—Reductive ring-opening of the benzylidene acetal group in **13** (370 mg, 0.29 mmol) with $NaBH_3CN$ (300 mg, 4.35 mmol) in THF (4 mL), as described for **8**, gave **14** (315 mg, 85%) as an amorphous mass: $[\alpha]_D$ −12.2° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.96 (m, 2 H, $Me_3SiCH_2CH_2$), 1.33 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.42 (s, 3 H, AcN), 4.75 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1c), and 7.25–7.54 (m, 35 H, 7 Ph). Anal. Calcd for $C_{74}H_{89}NO_{15}Si$ (1260.6): C, 70.51; H, 7.12; N, 1.11. Found: C, 70.42; H, 6.98; N, 1.10.

2-(Trimethylsilyl)ethyl O-*(3,4-di*-O-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(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* (**15**).—Glycosylation of **6** (161 mg, 0.19 mmol) with methyl 3,4-di-*O*-acetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (**5**, 67 mg 0.23 mmol) [1] in benzene (1.7 mL) in the presence of DMTST (200 mg, 0.48 mmol) and MS-4A (500 mg) for 10 h at 5°C, then workup as described for **7**, gave **15** (165 mg, 79%) as an amorphous mass: $[\alpha]_D$ −78.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.54 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.57 (s, 3 H, AcN), 2.00, 2.10 (2 s, 6 H, 2 AcO), 3.40 (s, 3 H, MeO), 4.97 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1c), 5.10 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-4c), 5.34 (d, 1 H, NH), 5.53 (s, 1 H, C*H*Ph), and 7.29–7.51 (m, 20 H, 4 Ph). Anal. Calcd for $C_{58}H_{75}NO_{17}Si$ (1086.3): C, 64.13; H, 6.96; N, 1.29. Found: C, 63.98; H, 6.81; N, 1.27.

2-(Trimethylsilyl)ethyl O-*(3,4-di*-O-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(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**).—Reductive ring-opening of the benzylidene acetal group in **15** (414 mg, 0.38 mmol) with $NaBH_3CN$ (360 mg, 5.7 mmol) in THF (7 mL), then workup as described for the preparation of **8**, gave **16** (320 mg, 76%) as an amorphous mass: $[\alpha]_D$ −43.0° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.14 (d, 3 H, $J_{5,6}$ 6.7 Hz, H-6c), 1.60 (s, 3 H, AcN), 2.03 2.18 (2 s, 6 H, 2 AcO), 3.38 (s, 3 H, MeO), 3.84 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4a), 5.08 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1c), 5.17 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1b), 5.22 (dd, 1 H, $J_{2,3}$ 10.7, $J_{3,4}$ 3.4 Hz, H-3c), 5.28 (br d, 1 H, H-4c), 5.37 (d, 1 H, NH), and 7.27–7.42 (m, 20 H, 4 Ph). Anal. Calcd for $C_{58}H_{77}NO_{17}Si$ (1088.3): C, 64.01; H, 7.13; N, 1.29. Found: C, 63.96; H, 6.93; N, 1.18.

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-*[(2,3,4-tri*-O-*benzyl-6-deoxy-α*-L-*talopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**18**).—To a solution of **8** (138 mg, 0.11 mmol) and **17** (218 mg, 0.22 mmol) in CH_2Cl_2 (0.7 mL) was added MS-4A (600 mg), and the mixture was stirred for 4 h at room temperature, then cooled to 0°C. DMTST (439 mg, 1.1 mmol) was added. The mixture was stirred for 2 days at 5°C, neutralized with Et_3N and filtered, and the residue was washed with CH_2Cl_2. The combined filtrate and washings was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (3:1 EtOAc–hexane) of the residue on silica gel (50 g) gave **18** (128 mg, 53%) as an amorphous mass: $[\alpha]_D$

+1.0° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.96 (m, 2 H, $Me_3SiCH_2CH_2$), 1.44 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.56, 1.60 (2 s, 6 H, 2 AcN), 1.80, 1.93, 1.99, 2.14 (4 s, 12 H, 4 AcO), 2.42 (dd, 1 H, H-3e*eq*), 3.76 (s, 3 H, MeO), 5.27 (dd, 1 H, $J_{6,7}$ 2.1, $J_{7,8}$ 8.5 Hz, H-7e), 5.74 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 9.5 Hz, H-2d), 5.65 (m, 1 H, H-8e), and 7.18–8.23 (m, 50 H, 10 Ph). Anal. Calcd for $C_{121}H_{138}N_2O_{35}Si$ (2208.5): C, 65.81; H, 6.30; N, 1.27. Found: C, 65.61; H, 6.06; N, 1.20.

2-(Trimethylsily)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-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*talopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**19**).—A solution of **18** (297 mg, 0.13 mmol) in EtOH (20 mL) and AcOH (8 mL) was hydrogenolysed in the presence of 10% Pd–C (300 mg) for 48 h at 45°C, then filtered and concentrated. The residue was acetylated with Ac_2O (1 mL) in pyridine (5 mL) for 20 h at 40°C. The product was purified by chromatography on a column of silica gel (30 g) with 2:1 EtOAc–hexane, affording **19** (176 mg, 70%) as an amorphous mass: $[\alpha]_D$ −1.7° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.90 (m, 2 H, $Me_3SiCH_2CH_2$), 1.22 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.54, 1.77 (2 s, 6 H, 2 AcN), 1.84–2.14 (11 s, 33 H, 11 AcO), 2.40 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.80 (s, 3 H, MeO), 5.28 (dd, 1 H, $J_{6,7}$ 2.5, $J_{7,8}$ 8.5 Hz, H-7e), 5.41 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.1 Hz, H-2d), 5.65 (m, 1 H, H-8e), and 7.43–8.17 (m, 15 H, 3 Ph). Anal. Calcd for $C_{86}H_{110}N_2O_{42}Si$ (1871.9): C, 55.18; H, 5.92; N, 1.50. Found: C, 55.07; H, 5.73; N, 1.41.

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-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*talopyranosyl)-(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* (**20**).—To a solution of **19** (127 mg, 0.068 mmol) in CH_2Cl_2 (9 mL) was added CF_3CO_2H (1.3 mL), and the mixture was stirred for 10 min at room temperature and concentrated. The product was purified by chromatography on a column of silica gel (20 g) with 4:1 EtOAc–hexane to give the 1-hydroxy compound. To a solution of this in CH_2Cl_2 (1.4 mL), cooled to −5°C, were added trichloroacetonitrile (0.2 mL, 2 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 12 μL, 0.08 mmol), the mixture was stirred for 45 min at 0°C, and the progress of the reaction was monitored by TLC. The mixture was chromatographed on a column of silica gel (15 g) with 30:1 CH_2Cl_2–MeOH to give **20** (110 mg, 84%) as an amorphous mass: $[\alpha]_D$ +21.0° (*c* 2.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.22 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6c), 1.56, 1.76 (2 s, 6 H, 2 AcN), 1.82–2.13 (11 s, 33 H, 11 AcO), 2.41 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.69 (s, 3 H, MeO), 5.65 (m, 1 H, H-8e), 6.49 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1a), 7.46–8.17 (m, 15 H, 3 Ph), and 8.62 (s, 1 H, C=NH). Anal. Calcd for $C_{83}H_{98}Cl_3N_3O_{42}$ (1916.0): C, 52.03; H, 5.16; N, 2.19. Found: C, 51.89; H, 5.09; N, 2.02.

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-*(6-deoxy-α*-L-*talopyranosyl)-(1 → 3)*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**21**).—To a solution of **19** (30 mg, 0.016 mmol) in MeOH (1.6 mL) was

added NaOMe (10 mg), and the mixture was stirred for 12 h at 40°C. Water (0.5 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 was concentrated. Column chromatography (MeOH) of the residue on Sephadex LH-20 (30 g) gave **21** (17 mg, quant) as an amorphous mass: $[\alpha]_D$ −30° (*c* 0.5, MeOH); ^{1}H NMR (CD_3OD): δ 0.95 (m, 2 H, $Me_3SiCH_2CH_2$), 1.16 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.97 (2 s, 6 H, 2 AcN), 2.84 (br dd, 1 H, H-3e*eq*), 4.20 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1a), 4.48 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1d), 4.64 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1b), and 5.04 (br s, 1 H, H-1c). Anal. Calcd for $C_{42}H_{75}N_2O_{28}Si$ (1084.1): C, 46.53; H, 6.97; N, 2.58. Found: C, 46.50; H, 6.94; N, 2.57.

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-*[(2,3,4-tri*-O-*benzyl-6-deoxy-α*-L-*gulopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**22**).—Glycosylation of **10** (178 mg, 0.14 mmol) with **17** (239 mg, 0.24 mmol) in dry CH_2Cl_2 (0.9 mL) in the presence of DMTST (481 mg, 1.2 mmol) and MS-4A (800 mg) for 5 days at 5°C and workup as described for **18** gave **22** (42 mg, 14%) as an amorphous mass: $[\alpha]_D$ −22.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.91 (d, 3 H, $J_{5,6}$ 6.7 Hz, H-6c), 1.01 (m, 2 H, $Me_3SiCH_2CH_2$), 1.23, 1.64 (2 s, 6 H, 2 AcN), 1.76, 1.80, 1.91, 2.16 (4 s, 12 H, 4 AcO), 2.47 (dd, 1 H, J_{gem} 12.8, $J_{3eq,4}$ 4.9 Hz, H-3e*eq*), 3.84 (s, 3 H, MeO), 5.44 (t, 1 H, $J_{1,2} = J_{2,3} = 8.5$ Hz, H-2d), 5.66 (m, 1 H, H-8e), and 7.07–8.20 (m, 50 H, 10 Ph). Anal. Calcd for $C_{121}H_{138}N_2O_{35}Si$ (2208.5): C, 65.81; H, 6.30; N, 1.27. Found: C, 65.70; H, 6.20; N, 1.25.

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-*[(4*-O-*acetyl-2,3-di*-O-*benzyl-6-deoxy-α*-L-*glucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**23**).—Glycosylation of **12** (300 mg, 0.25 mmol) with **17** (419 mg, 0.42 mmol) in dry CH_2Cl_2 (1.4 mL) in the presence of DMTST (800 mg) and MS-4A (1.2 g) for 3 days at 5°C and workup as described for **18** gave **23** (444 mg, 41%) as an amorphous mass: $[\alpha]_D$ −21.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.97 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.61, 1.73 (2 s, 6 H, 2 AcN), 1.76, 1.78, 1.90, 1.94, 2.15 (5 s, 15 H, 5 AcO), 2.43 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.81 (s, 3 H, MeO), 5.26 (dd, 1 H, $J_{6,7}$ 2.6, $J_{7,8}$ 9.7 Hz, H-7e), 5.44 (t, 1 H, $J_{1,2} = J_{2,3} = 8.1$ Hz, H-1d), 5.66 (m, 1 H, H-8e), and 6.99–8.30 (m, 45 H, 9 Ph). Anal. Calcd for $C_{116}H_{134}N_2O_{36}Si$ (2160.4): C, 64.49; H, 6.25; N, 1.30. Found: C, 64.37; H, 6.04; 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-*nonulopyranosylonate)-(2 → 3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1 → 4)*-O-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*glucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**24**).—Hydrogenolysis of **23** (431 mg, 0.2 mmol) in EtOH (72 mL) and AcOH (12 mL) in the presence of 10% Pd–C (500 mg) for 48 h at 45°C, and subsequent acetylation with Ac_2O (5 mL) in pyridine (9 mL) as described for the preparation of **19**, gave **24** (300 mg, 80%) as an amorphous mass: $[\alpha]_D$ −30.5° (*c* 0.9,

$CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.18 (d, 3 H, $J_{5,6}$ 5.9 Hz, H-6c), 1.48, 1.69 (2 s, 6 H, 2 AcO), 1.78–2.15 (11 s, 33 H, 11 AcO), 2.32 (dd, 1 H, J_{gem} 12.3, $J_{3eeq,4}$ 4.4 Hz, H-3e*eq*), 3.73 (s, 3 H, MeO), 5.42 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4d), 5.64 (m, 1 H, H-8e), and 7.44–8.22 (m, 15 H, 3 Ph). Anal. Calcd for $C_{86}H_{110}N_2O_{42}Si$ (1871.9): C, 55.18; H, 5.92; N, 1.50. Found: C, 54.97; H, 5.74; N, 1.51.

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-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*glucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl trichloroacetimidate* (**25**).—Selective removal of the 2-(trimethylsily) ethyl group in **24** (250 mg, 0.13 mmol) with CF_3CO_2H (1.8 mL) in CH_2Cl_2 (0.9 mL) for 10 min at room temperature, and subsequent reaction of the product with trichloroacetonitrile (0.38 mL, 3.9 mmol) in CH_2Cl_2 (2.6 mL) in the presence of DBU (20 μL) for 45 min at 0°C as described for **20** gave **25** (228 mg, 89%) as an amorphous mass: $[\alpha]_D$ +0.7° (*c* 2.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.17 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.45, 1.67 (2 s, 6 H, 2 AcN), 1.78–2.17 (11 s, 33 H, 11 AcO), 2.33 (dd, 1 H, J_{gem} 12.3, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.72 (s, 3 H, MeO), 5.23 (dd, 1 H, $J_{6,7}$ 2.1, $J_{7,8}$ 9.3 Hz, H-7e), 5.64 (m, 1 H, H-8e), 6.49 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1a), 7.46–8.21 (m, 15 H, 3 Ph), and 8.63 (s, 1 H, C=NH).

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-*[(6-deoxy-α*-L-*glucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**26**).—Deacylation and saponification of **25** (45 mg, 0.024 mmol) as described for **21** yielded **26** (21 mg, quant) as an amorphous mass: $[\alpha]_D$ −27.5° (*c* 0.5, MeOH); ^1H NMR (CD_3OD): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.17 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.95, 1.98 (2 s, 6 H, 2 AcN), 2.84 (br dd, 1 H, H-3e*eq*), 4.21 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1a), 4.50 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1d), 4.66 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1b), and 5.03 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1c). Anal. Calcd for $C_{42}H_{75}N_2O_{28}Si$ (1084.1): C, 46.53; H, 6.97; N, 2.58. Found: C, 46.41; H, 6.94; N, 2.52.

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-*[(2,3,4-tri*-O-*benzyl-α*-L-*rhamnopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**27**).—Glycosylation of **14** (314 mg, 0.25 mmol) with **17** (422 mg, 0.43 mmol) in CH_2Cl_2 (1.5 mL) in the presence of DMTST (850 mg, 2.13 mmol) and MS-4A (1.2 g) for 3 days at 5°C and workup as described for **18** gave **27** (248 mg, 44%) as an amorphous mass: $[\alpha]_D$ +7.2° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2$), 1.19 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6c), 1.68, 1.78 (2 s, 6 H, 2 AcN), 1.80, 1.90, 1.94, 2.16 (4 s, 12 H, 4 AcO), 2.43 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.82 (s, 3 H, MeO), 5.25 (dd, 1 H, $J_{6,7}$ 1.8, $J_{7,8}$ 8.6 Hz, H-7e), 5.43 (t, 1 H, $J_{1,2} = J_{2,3} = 7.8$ Hz, H-2d), 5.66 (m, 1 H, H-8e), and 7.04–8.17 (m, 50 H, 10 Ph). Anal. Calcd for $C_{121}H_{138}N_2O_{35}Si$ (2208.5): C, 65.81; H, 6.30; N, 1.27. Found: C, 65.64; H, 6.20; N, 1.17.

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-*gal-*

actopyranosyl)-(1 → 4)-O-*[(2,3,4-tri*-O-*acetyl-α*-L-*rhamnopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**28**).—Hydrogenolysis of **27** (180 mg, 0.082 mmol) in EtOH (24 mL) and AcOH (5 mL) in the presence of 10% Pd–C (180 mg) for 48 h at 45°C, and subsequent acetylation of the product with Ac_2O (1 mL) in pyridine (3 mL) for 48 h at 40°C as described for **19** gave **28** (127 mg, 83%) as an amorphous mass: $[\alpha]_D$ +5.7° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.91 (m, 2 H, $Me_3SiCH_2CH_2$), 1.15 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.61, 1.78 (2 s, 6 H, 2 AcN), 1.87–2.18 (11 s, 33 H, 11 AcO), 2.35 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.75 (s, 3 H, MeO), 5.27, 5.39 (2 br d, 2 H, $J_{3,4}$ 3.0 Hz, H-4a,-4d), 5.33 (dd, 1 H, $J_{6,7}$ 2.8, $J_{7,8}$ 6.7 Hz, H-7e), 5.50 (dd, 1 H, $J_{1,2}$ 8.6, $J_{2,3}$ 8.9 Hz, H-2d), 5.56 (m, 1 H, H-8e), and 7.43–8.18 (m, 15 H, 3 Ph). Anal. Calcd for $C_{86}H_{110}N_2O_{42}Si$ (1871.9): C, 55.18; H, 5.92; N, 1.50. Found: C, 55.17; H, 5.81; N, 1.43.

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-*[(2,3,4-tri*-O-*acetyl-α*-L-*rhamnopyranosyl)-(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* (**29**).—Selective removal of the 2-(trimethylsilyl)ethyl group in **28** (96 mg, 0.05 mmol) with CF_3CO_2H (1 mL) in CH_2Cl_2 (5 mL) for 10 min at 0°C, followed by treatment of the product with trichloroacetonitrile (0.15 mL) in CH_2Cl_2 (1 mL) in the presence of DBU (8.5 μL, 0.06 mmol) for 45 min at 0°C and *w*orkup as described for **20**, gave **29** (82 mg, 84%) as an amorphous mass: $[\alpha]_D$ +26.5° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.15 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.66, 1.77 (2 s, 6 H, 2 AcN), 1.87–2.18 (11 s, 33 H, 11 AcO), 2.35 (dd, 1 H, J_{gem} 12.2, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.70 (s, 3 H, MeO), 5.68 (m, 1 H, H-8e), 6.50 (d, 1 H, $J_{1,2}$ 3.8, H-1a), 7.44–8.19 (m, 15 H, 3 Ph), and 8.62 (s, 1 H, C=NH). Anal. Calcd for $C_{83}H_{98}Cl_3N_3O_{42}$ (1916.0): C, 52.03; H, 5.16; N, 2.19. Found: C, 51.94; H, 4.92; N, 2.01.

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-*[(α*-L-*rhamnopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**30**).—Deacylation and saponification of **28** (29 mg, 0.015 mmol) as described for **21** yielded **30** (17 mg, quant) as an amorphous mass: $[\alpha]_D$ −20.0° (*c* 0.3, MeOH); ^1H NMR (CD_3OD): δ 0.96 (m, 2 H, $Me_3SiCH_2CH_2$), 1.20 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.96, 1.98 (2 s, 6 H, 2 AcN), 2.85 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*, 4.21 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1a), 4.49 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1d), 4.64 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1b), and 4.96 (br s, 1 H, H-1c). Anal. Calcd for $C_{42}H_{75}N_2O_{28}Si$ (1084.1): C, 46.53; H, 6.97; N, 2.58. Found: C, 46.50; H, 7.15; N, 2.49.

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-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*benzyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranoside* (**31**).—Glycosylation of **16** (508 mg, 0.47 mmol) with **17** (790 mg, 0.8 mmol) in CH_2Cl_2 (2.5 mL) in the presence of DMTST (1.5 g, 4 mmol) and MS-4A (2.1 g) for 48 h at 5°C and workup as described for **18** gave **31** (430 mg, 45%) as an amorphous mass: $[\alpha]_D$ −26.5° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.82 (d, 3 H, $J_{5,6}$

6.6 Hz, H-6c), 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.61, 1.73 (2 s, 6 H, 2 AcN), 1.79–2.15 (6 s, 18 H, 6 AcO), 2.44 (dd, 1 H, J_{gem} 12.3, $J_{3eq,4}$4.4 Hz, H-3e*eq*), 3.24 (MeO), 3.83 (MeOCO), 5.25 (dd, 1 H, $J_{6,7}$2.6, $J_{7,8}$ 9.5 Hz, H-7e), 5.40 (t, 1 H, $J_{1,2} = J_{2,3} = 9.0$ Hz, H-2d), 5.65 (m, 1 H, H-8e), 6.10 (d, 1 H, NH), and 7.16–8.17 (m, 35 H, 7 Ph). Anal. Calcd for $C_{105}H_{126}N_2O_{37}Si$ (2036.2): C, 61.94; H, 6.24; N, 1.38. Found: C, 61.87; H, 6.10; N, 1.17.

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-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-6*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranoside* (**32**).—Hydrogenolysis of **31** (380 mg, 0.19 mmol) in EtOH (30 mL) and AcOH (4.5 mL) in the presence of 10% Pd–C (380 mg) for 48 h at 45°C, and subsequent acetylation with Ac_2O (1.0 mL) in pyridine (5 mL) for 48 h at 40°C as described for **19** gave **32** (290 mg, 84%) as an amorphous mass: $[\alpha]_D$ −20.0° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2$), 1.08 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.55, 1.78 (2 s, 6 H, 2 AcN), 1.91–2.12 (10 s, 30 H, 10 AcO), 2.42 (dd, 1 H, J_{gem}12.6, $J_{3eq,4}$ 4.6 Hz, H-3e*eq*), 3.44 (MeO),3.81 (MeOCO), 5.65 (m, 1 H, H-8e), 5.97 (d, 1 H, NH), and 7.42–8.18 (m, 15 H, 3 Ph). Anal. Calcd for $C_{85}H_{110}N_2O_{41}Si$ (1843.9): C, 55.37; H, 6.01; N, 1.52. Found: C, 55.25; H, 6.00; N, 1.27.

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-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(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* (**33**).—Selective removal of the 2-(trimethylsilyl)ethyl group in **32** (235 mg, 0.13 mmol) with CF_3CO_2H (1.8 mL) in CH_2Cl_2 (2 mL) for 10 min at room temperature, followed by treatment of the product with trichloroacetonitrile (0.3 mL, 3.3 mmol) in CH_2Cl_2 (2.7 mL) in the presence of DBU (20 μL, 0.13 mmol) for 45 min at 0°C and workup as described for **20**, gave **33** (207 mg, 87%) as an amorphous mass: $[\alpha]_D$ +7.0° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.08 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6c), 1.55, 1.78 (2 s, 6 H, 2 AcN), 1.90–2.13 (10 s, 30 H, 10 AcO), 2.42 (dd, 1 H, J_{gem} 12.8, $J_{3eq,4}$ 4.4 Hz, H-3e*eq*), 3.44 (s, 3 H, MeO), 3.81 (s, 3 H, MeOCO), 5.64 (m, 1 H, H-8e), 6.01 (d, 1 H, NH), 6.49 (d, 1 H, $J_{1,2}$ 3.7, H-1a), 7.42–8.17 (m, 15 H, 3 Ph), and 8.61 (s, 1 H, C=NH). Anal. Calcd for $C_{82}H_{98}Cl_3N_3O_{41}$ (1888.0): C, 52.17; H, 5.23; N, 2.23. Found: C, 51.96; H, 5.21; N, 2.18.

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*-O-*methyl-α*-L-*fucopyranosyl)-(1 → 3)]*-O-*(2-acetamido-2-deoxy-β*-D-*glucopyranosyl)-(1 → 3)-β*-D-*galactopyranoside* (**34**).—Deacylation and subsequent saponification of **32** (83 mg, 0.045 mmol) as described for **21** yielded **34** (49 mg, quantitative) as an amorphous mass; $[\alpha]_D$ −38.0° (*c* 1.2, MeOH); ^{1}H NMR (CD_3OD): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2$), 1.13 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.96, 1.99 (2 s, 6 H, 2 AcN), 2.82 (br dd, 1 H, H-3e*eq*), 3.41 (MeO), 4.19 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1a), 4.46 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1d), 4.61 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1b), and 5.26 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1c). Anal. Calcd for $C_{43}H_{76}N_2O_{28}Si$ (1097.2): C, 47.07; H, 6.98; N, 2.55. Found: C, 46.94; H, 6.98; N, 2.36.

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-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*talopyranosyl)-(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*)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**36**).—To a solution of **20** (115 mg, 0.06 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol [24] (**35**, 64 mg, 0.15 mmol) in CH_2Cl_2 (1.2 mL) was added MS-4A (AW-300, 1.2 g), and the mixture was stirred for 6 h at room temperature, then cooled to 0°C. $BF_3 \cdot OEt_2$ (31 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. The combined filtrate and washings were washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (30:1 CH_2Cl_2–MeOH) of the residue on silica gel (20 g) gave **36** (85 mg, 65%) as an amorphous mass: $[\alpha]_D$ −1.5° (*c* 1.6, $CHCl_3$); IR: ν 3350 (NH), 2950 and 2850 (Me, methylene), 2100 (N_3), 1740 and 1230 (ester), 1650 and 1540 (amide), and 760 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J_{Me,CH_2} 6.2 Hz, CH_3CH_2), 1.24 (m, 25 H, 11 CH_2, H-6c), 1.55, 1.77 (2 s, 6 H, 2 AcN), 1.85–2.14 (11 s, 33 H, 11 AcO), 3.80 (s, 3 H, MeO), 5.64 (m, 1 H, H-8e), and 7.42–8.17 (m, 20 H, 4 Ph). Anal. Calcd for $C_{106}H_{135}N_5O_{44}$ (2183.2): C, 58.32; H, 6.23; N, 3.21. Found: C, 58.23; H, 6.20; N, 3.19.

O-*(Methyl 5-acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-*β*-D-*galactopyranosyl-(1 → 4)*-O-*[(6-deoxy-α*-L-*talopyranosyl)-(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* (**37**).—Hydrogen sulfide was bubbled through a stirred solution of **36** (78 mg, 0.036 mmol) in aq 83% pyridine (7.8 mL) for 3 days at 0°C, with the progress of the reaction being monitored by TLC. The mixture was concentrated, and the residue was stirred with octadecanoic acid (21 mg, 0.072 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC, 21 mg, 0.108 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 (20 g) with 30:1 CH_2Cl_2–MeOH to give the protected ganglioside [63 mg, 72%, $[\alpha]_D$ +6.2° (*c*, 1.1, $CHCl_3$)]. O-Deacylation and subsequent saponification of the product (55 mg, 0.023 mmol) as described for **21** yielded **37** (35 mg, quant) as an amorphous mass: $[\alpha]_D$ −12.0° (*c* 0.9, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^1H NMR [49:1 $(CD_3)_2SO$–D_2O]: δ 0.85 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 CH_3CH_2), 1.03 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.24 (s, 52 H, 26 CH_2), 1.81 (2 s, 6 H, 2 AcN), 2.03 (t, 2 H, $COCH_2CH_2$), 2.77 (dd, 1 H, H-3e*eq*), 4.28 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1a), 4.91 (br s, 1 H, H-1c), 5.36 (dd, 1 H, $J_{3,4}$ 6.8, $J_{4,5}$ 15.2 Hz, H-4 of sphingosine), and 5.55 (dt, 1 H, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{30}$ (1530.8): C, 57.28; H, 8.63; N, 2.74. Found: C,57.30; H, 8.90; N, 2.71.

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-*[(2,3,4-tri*-O-*acetyl-6-deoxy-α*-L-*glucopyranosyl)-(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*)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**38**).—Coupling of **25** (227 mg, 0.12 mmol) with **35** (127 mg, 0.3 mmol) in CH_2Cl_2 (2.3 mL) in the presence

of $BF_3 \cdot OEt_2$ (64 μL, 0.24 mmol) and MS-4A (AW-300, 2 g) as described for **36** gave **38** (220 mg, 85%) as an amorphous mass: $[\alpha]_D$ −21.6° (*c* 2.2, $CHCl_3$); IR: ν 3375 (NH), 2940 and 2850 (Me, methylene), 2100 (N_3), 1740 and 1230 (ester), 1670 and 1540 (amide), and 750 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J_{Me,CH_2} 6.2 Hz, CH_3CH_2), 1.19 (d, 3 H, $J_{5,6}$ 5.7 Hz, H-6c), 1.25 (s, 22 H, 11 CH_2), 1.48, 1.69 (2 s, 6 H, 2 AcN), 1.78–2.18 (11 s, 33 H, 11 AcO), 2.31 (dd, 1 H, J_{gem} 11.9, $J_{3eq,4}$ 3.7 Hz, H-3e*eq*), 3.73 (s, 3 H, MeO), 5.66 (m, 1 H, H-8e), 5.93 (m, 1 H, H-5 of sphingosine), and 7.42–8.22 (m, 20 H, 4 Ph). Anal. Calcd for $C_{106}H_{135}N_5O_{44}$ (2183.2): C, 58.32; H, 6.23; N, 3.21. Found: C, 58.30; H, 5.99; N, 3.21.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-*[(6-deoxy*-α-L-*glucopyranosyl)-(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* (**39**).—Selective reduction of the azido group in **38** (220 mg, 0.1 mmol) with H_2S in aq 83% pyridine (24 mL), followed by coupling the product with octadecanoic acid (56 mg, 0.2 mmol) in the presence of WSC (57 mg, 0.3 mmol) and workup as described for **37**, gave the protected ganglioside [165 mg, 67%; $[\alpha]_D$ −13.5° (*c* 1.3, $CHCl_3$)] as an amorphous mass. *O*-Deacylation and subsequent saponification of the product (160 mg, 0.067 mmol) as described for **21** yielded **39** (102 mg, quant) as an amorphous mass: $[\alpha]_D$ −18.2° (*c* 0.3, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^1H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.86 (t, 6 H, J_{Me,CH_2} 6.4 Hz, 2 CH_3CH_2). 1.07 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6c), 1.24 (s, 52 H, 26 CH_2), 1.82, 1.90 (2 s, 6 H, 2 AcN), 2.01 (t, 2 H, $COCH_2CH_2$), 2.73 (br dd, 1 H, H-3e*eq*), 4.89 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1c), 5.33 (dd, 1 H, $J_{3,4}$7.0, $J_{4,5}$15.2 Hz, H-4 of sphingosine), and 5.54 (m, 1 H, $J_{5,6} = J_{5,6'} = 7.7$ Hz, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{30}$ (1530.8): C, 57.28; H, 8.63; N, 2.74. Found: C, 57.26; H, 8.52; N, 2.62.

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-*[(2,3,4-tri*-O-*acetyl-α-L-rhamnopyranosyl)-(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* (**40**).—Coupling of **29** (85 mg, 0.044 mmol) with **35** (47 mg, 0.11 mmol) as described for **36** gave **40** (63 mg, 64%) as an amorphous mass: $[\alpha]_D$ +5.3° (*c* 1.1, $CHCl_3$); IR: ν 3150 (NH), 2950 and 2850 (Me, methylene), 2100 (N_3), 1740 and 1220 (ester), 1660 and 1540 (amide), and 740 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.89 (t, 3 H, J_{Me,CH_2} 6.6 Hz, CH_3CH_2), 1.16 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.25 (s, 22 H, 11 CH_2), 1.62, 1.78 (2 s, 6 H, 2 AcN), 1.89–2.18 (11 s, 33 H, 11 AcO), 2.33 (br dd, 1 H, H-3e*eq*), 3.76 (s, 3 H, MeO), and 7.45–8.19 (m, 20 H, 4 Ph). Anal. Calcd for $C_{106}H_{135}N_5O_{44}$ (2183.2): C, 58.32; H, 6.23; N, 3.21. Found: C, 58.14; H, 6.21; N, 3.09.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-*[*α-L-*rhamnopyranosyl-(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* (**41**).—Selective reduction of the azido group in **40** (55 mg, 0.025 mmol) with H_2S in aq 83% pyridine (10 mL), followed by coupling with octadecanoic acid (15 mg, 0.05 mmol) in the presence of WSC (15 mg, 0.075 mmol) and workup as described for **37**, gave the protected ganglioside [43 mg,

70%; $[\alpha]_D$ +10.5° (*c* 0.8, $CHCl_3$] as an amorphous mass. *O*-Deacylation and subsequent saponification of the product (40 mg) as described for **21** yielded **41** (25 mg, quantitative) as an amorphous mass: $[\alpha]_D$ −6.0° (*c* 0.6, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^{1}H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.85 (t, 6 H, J_{Me,CH_2} 6.4 Hz, 2 CH_3CH$_2$), 1.08 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6c), 1.24 (s, 52 H, 26 CH_2, 1.81, 1.87 (2 s, 6 H, 2 AcN), 2.03 (t, 2 H, COCH_2CH$_2$), 2.77 (br dd, 1 H, H-3e*eq*), 4.30 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1a), 4.62 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1b), 4.83 (br s, 1 H, H-1c), 5.36 (dd, 1 H, $J_{4,5}$ 15.6 Hz, H-4 of sphingosine), and 5.55 (dt, 1 H, $J_{5,6} = J_{5,6'} = 7.1$ Hz, H-5 of sphingosine). Anal. Calcd for $C_{73}H_{131}N_3O_{30}$ (1530.8): C, 57.28; H, 8.63; N, 2.74. Found: C, 57.02; H, 8.60; N, 2.62.

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-*acetyl-2*-O-*methyl-α*-L-*fucopyranosyl)-(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*)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**42**).—Coupling of **33** (53 mg, 0.03 mmol) with **35** (30 mg, 0.075 mmol) as described for **36** gave **42** (36 mg, 60%) as an amorphous mass: $[\alpha]_D$ −15.6° (*c* 1.7, $CHCl_3$); IR: ν 3350 (NH), 2950 and 2850 (Me, methylene), 2100 (N_3), 1740 and 1220 (ester), 1660 and 1540 (amide), and 750 and 710 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J_{Me,CH_2} 6.2 Hz, CH_3CH$_2$), 1.08 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.24 (s, 22 H, 11 CH_2), 1.56, 1.77 (2 s, 6 H, 2 AcN), 1.91–2.12 (10 s, 30 H, 10 AcO), 2.42 (br dd, 1 H, H-3e*eq*), 3.45 (s, 3 H, MeO), 3.70 (s, 3 H, MeOCO), 5.64 (m, 1 H, H-8e), 5.92 (m, 1 H, H-5 of sphingosine), 6.09 (d, 1 H, NH), and 7.42–8.18 (m, 20 H, 4 Ph). Anal. Calcd for $C_{105}H_{135}N_5O_{43}$ (2155.2): C, 58.52; H, 6.31; N, 3.25. Found: C, 58.41; H, 6.28; N, 3.13.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-*[(2*-O-*methyl-α*-L-*fucopyranosyl)-(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* (**43**).—Selective reduction of the azido group in **42** (122 mg, 0.60 mmol) with H_2S in aq 83% pyridine (10 mL), followed by coupling of the product with octadecanoic acid (32 mg, 0.12 mmol) in the presence of WSC (33 mg, 0.18 mmol) and workup as described for **37**, gave the protected ganglioside [108 mg, 79%; $[\alpha]_D$ −7.8° (*c* 1.2, $CHCl_3$)] as an amorphous mass. *O*-Deacylation and subsequent saponification of the product (78 mg) as described for **21** yielded **43** (46 mg, 92%) as an amorphous mass: $[\alpha]_D$ −23.5° (*c* 0.9, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^{1}H NMR [49:1 $(CD_3)_2SO$–D_2O)]: δ 0.86 (t, 6 H, 2 CH_3CH$_2$), 0.99 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6c), 1.24 (s, 52 H, 26 CH_2), 1.81, 1.90 (2 s, 6 H, 2 AcN), 2.08 (t, 2 H, COCH_2CH$_2$), 2.84 (br dd, 1 H, H-3e*eq*), 4.37 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1a), 4.76 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1b), 5.15 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1c), 5.35 (dd, 1 H, $J_{3,4}$ 6.8, $J_{4,5}$ 15.2 Hz, H-4 of sphingosine), and 5.60 (m, 1 H, H-5 of sphingosine). Anal. Calcd for $C_{74}H_{133}N_3O_{30}$ (1544.9): C, 57.53; H, 8.68; N, 2.72. Found: C, 57.37; H, 8.59; N, 2.64.

Acknowledgements

This work was supported in part by Grant-in-Aid (no. 06281227 and no. 05274102) for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture of Japan.

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