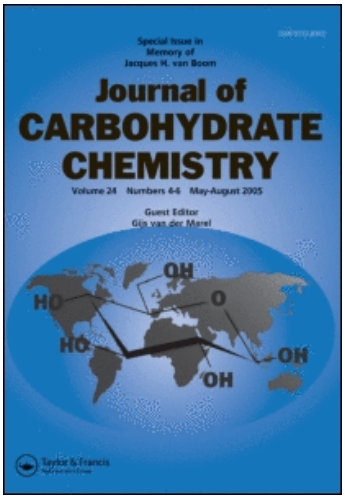

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 48: TOTAL SYNTHESIS OF GANGLIOSIDES GM_1 AND GD_{1a}

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ABSTRACT

A stereocontrolled, facile total synthesis of gangliosides GM_1 and GD_{1a}, in connection with systematic synthesis of ganglio-series of ganglioside, is described. Glycosylation of 2-(trimethylsilyl)ethyl *O*-(2-acetamido-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**), with methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**8**) or 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 (**9**) by use of *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH) or dimethyl(methylthio)sulfonium triflate (DMTST) as a promoter, gave the corresponding β-glycoside **10** and **18** in 66 and 62% yields, which were converted, *via* reductive removal of the benzyl groups, *O*-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, and subsequent imidate formation, into the α-trichloroacetimidates **13** and **21**. Glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**14**) with **13** or **21** by use of trimethylsilyl trifluoromethanesulfonate gave the corresponding β-glycoside **15** and **22**, which on channeling through selective reduction of the azido group, coupling of the thus formed amino group with octadecanoic acid, *O*-deacylation, and saponification of the methyl ester group, gave the title gangliosides GM_1 and GD_{1a}.

INTRODUCTION

Mammals, birds, amphibians and fishes have similar brain gangliosides. These gangliosides are of the ganglio-series with predominantly, gangliotetraose, β-D-Gal-(1→3)-β-D-GalNAc-(1→4)-β-D-Gal-(1→4)-D-Glc, as a neutral oligosaccharide, though

with a varying degree of sialylation. The concentration of complex gangliosides in membrane elements of the brain is suggestive of a functional role in the nervous system. Recently, the biological importance of the gangliosides in nervous system has been well documented.[1-6] As biologically derived gangliosides are polymorphous molecule and available in very limited quantity, a facile, chemical synthesis of a variety of gangliosides and their analogs is required, in order to elucidate of their functions at the molecular level.

We have reported[7-10] the successful syntheses of several series of gangliosides and their analogs based on dimethyl(methylthio)sulfonium triflate[11,12] (DMTST) or *N*-iodosuccinimide(NIS)-trifluoromethanesulfonic acid[13] (TfOH) promoted, stereoselective α-glycosylation of sialic acid with suitably protected sugar residues in acetonitrile medium. We describe herein a facile, total synthesis of gangliosides GM_1 and GD_{1a}, in connection with developement of the systematic synthesis of ganglio-series of ganglioside. Ganglioside GM_1 was first synthesized by Ogawa et al.[14] after multiple steps in very low yield.

RESULTS AND DISCUSSION

For the synthesis of the both gangliosides GM_1 and GD_{1a}, the core oligosaccharide **4**, having a sialyl α(2→3)Gal unit already linked and providing free hydroxyl groups at C-3 and C-4 of the GalNAc residue for further, regioselective glycosylation at C-3, with methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**8**) or 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[15] (**9**) as the donor, was selected as the glycosyl acceptor.

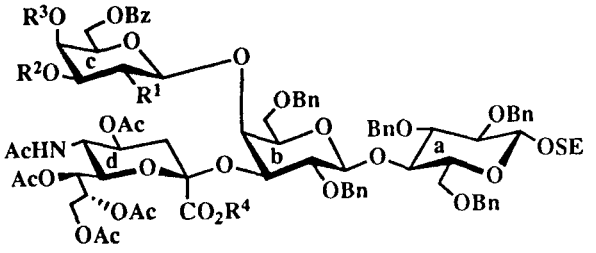
The glycosyl acceptor **4** was obtained from a known tetrasaccharide derivative[16] **1**, an intermediate prepared in the total synthesis of ganglioside GM_2. Treatment[14,16] of **1** with lithium iodide in pyridine for 6 h under reflux to remove the methyl ester group gave the carboxyl group free derivative **2** in 95% yield, which was converted, *via* treatment with hydrazine monohydrate in aqueous 95% ethanol, *N*-acetylation and subsequent *O*-de-isopropylidenation with aqueous 80% acetic acid at 50 °C, into 2-(trimethylsilyl)ethyl *O*-(2-acetamido-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**) in 88% yield. The glycosyl donor **8** was prepared from 2-(trimethylsilyl)ethyl 3-*O*-benzyl-β-D-galactopyranoside[17] (**5**). *O*-Benzoylation

of **5** with benzoyl chloride in pyridine gave **6**, which on treatment [18,19] with boron trifluoride etherate and acetic anhydride in toluene, afforded the 1-*O*-acetyl derivative **7** quantitatively. Replacement of the anomeric acetoxy group of **7** with the methylthio group by use of (methylthio)trimethylsilane in the presence of trimethylsilyl trifluoromethanesulfonate in dichloromethane gave **8** in 70% yield.

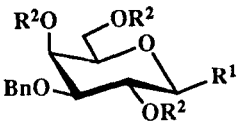
The glycosylation of **4** with **8** in dichloromethane for 26 h at room temperature in the presence of NIS-TfOH and powdered 4Å molecular sieves (MS-4Å) gave the desired β-glycoside **10** in 66% yield. Catalytic hydrogenolysis (10% Pd-C) in ethanol-acetic acid of the benzyl groups in **10** and subsequent *O*-acetylation gave compound **11** in 78% yield. Significant signals in the ^{1}H NMR spectrum of **11** were at δ 5.04 (d, $J_{1,2}$ = 7.9 Hz, H-1d) and at δ 5.70 (d, $J_{3,4}$ = 3.3 Hz, H-4c), indicating the newly formed glycosidic configuration to be β and the linkage position of **8** to the C-3 of GalNAc residue in **4**.

On the other hand, glycosylation of **4** with **9** in dichloromethane for 25 h at room temperature in the presence of DMTST (4.0 equiv. relative to the donor) and MS-4Å, gave the expected hexasaccharide **18** in 62% yield, which was converted, *via* catalytic hydrogenolysis of the benzyl group and subsequent *O*-acetylation, into the oligosaccharide **19**. The ^{1}H NMR spectrum of **19** showed the presence of seventeen, three-proton singlets at δ 1.37-2.20 (3 AcN and 14 AcO), two three-proton singlets at δ 3.63 and 3.80 (2 MeO), a one-proton doublet at δ 5.64 ($J_{3,4}$ = 3.1 Hz, H-4c), and multiplets at δ 7.26-8.21 due to twenty aromatic protons, indicating the structure assigned. Treatment[9,20] of compound **11** or **19** with trifluoroacetic acid in dichloromethane for 2 h at room temperature gave the corresponding 1-hydroxy compounds **12** and **20** in high yields, respectively. Treatment of **12** or **20** with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 4 h at 0 °C gave the corresponding α-trichloroacetimidates **13** and **21** in quantitative and 85% yields. Significant signals in the ^{1}H NMR spectra of **13** and **21** were at δ 6.55 ($J_{1,2}$ = 3.5 Hz, H-1a) and 8.73 (s, C=NH) for **13**, and at δ 6.47 ($J_{1,2}$ = 4.0 Hz, H-1a) and 8.64 (s, C=NH) for **21**, indicating the configuration of the imidates to be α.

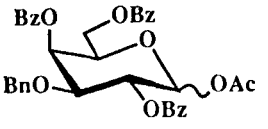
Glycosylation[7,21] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[22] by **13** or **21** in the presence of trimethylsilyl trifluoromethanesulfonate (TMS·OTf) and MS-4Å (AW-300) at 0 °C, yielded only the corresponding β-glycosides **15** and **22** in 48 and 63% yields, respectively. The observed chemical shifts and coupling constants due to the newly formed glycosidic linkage in the ^{1}H NMR spectra of **15** and **22** were at δ 4.58 ($J_{1,2}$ = 7.5 Hz, H-1a) for **15** and at δ 4.59 ($J_{1,2}$ = 8.2 Hz, H-1a) for **22**, showing both of



	R^1	R^2	R^3	R^4
1	NPhth	-Ipd-		Me
2	NPhth	-Ipd-		H
3	NHAc	-Ipd-		Me
4	NHAc	H	H	Me



	R^1	R^2
5	OSE	H
6	OSE	Bz
8	SMe	Bz



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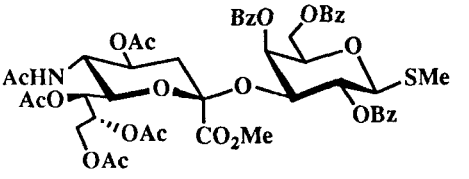
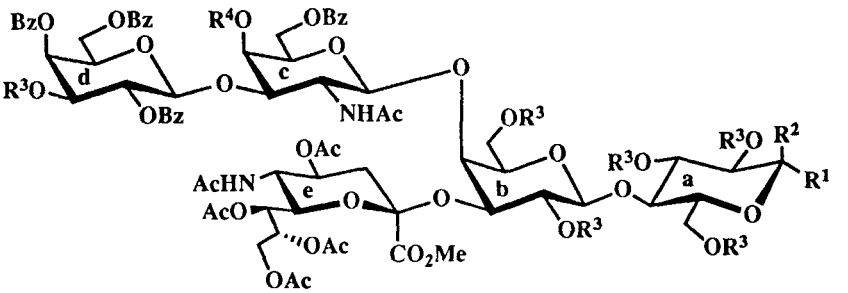
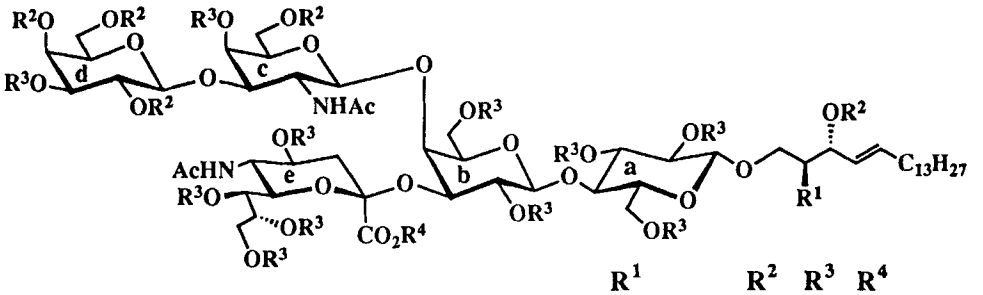


9

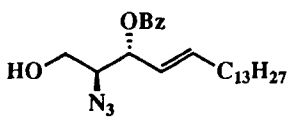
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
Phth = phthaloyl
Bz = benzoyl
Ipd = isopropylidene



	R^1	R^2	R^3	R^4
10	OSE	H	Bn	H
11	OSE	H	Ac	Ac
12	H , OH		Ac	Ac
13	H	$OC(=NH)CCl_3$	Ac	Ac



	R^1	R^2	R^3	R^4
15	N_3	Bz	Ac	Me
16	$NHCO(CH_2)_{16}Me$	Bz	Ac	Me
17	$NHCO(CH_2)_{16}Me$	H	H	H



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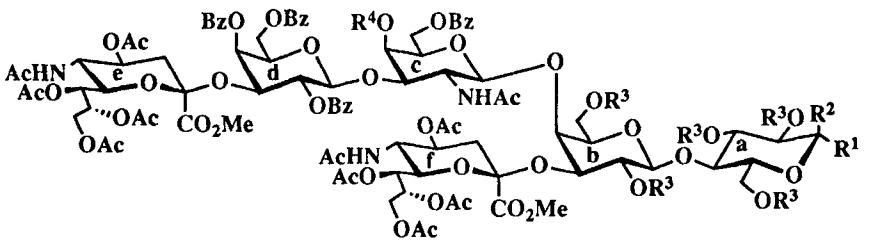
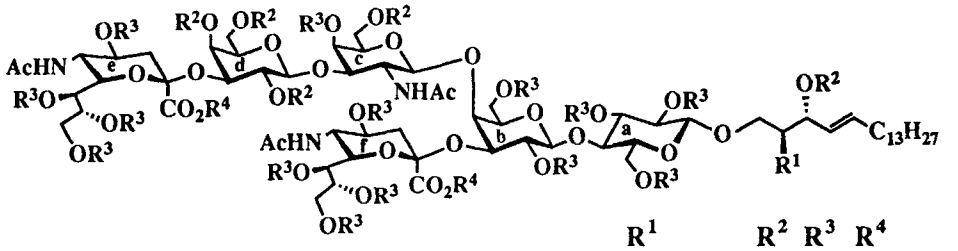


	R^1	R^2	R^3	R^4
18	OSE	H	Bn	H
19	OSE	H	Ac	Ac
20	H , OH		Ac	Ac
21	H	$OC(=NH)CCl_3$	Ac	Ac



	R^1	R^2	R^3	R^4
22	N_3	Bz	Ac	Me
23	$NHCO(CH_2)_{16}Me$	Bz	Ac	Me
24	$NHCO(CH_2)_{16}Me$	H	H	H

the anomeric configuration to be β. Other ^1H NMR data are consistent with the structures assigned. Selective reduction[22a,23] of the azido group in **15** or **22** with H_2S gas in 5:1 pyridine-water gave the amine, which on condensation with octadecanoic acid by use of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane, gave gangliosides GM_1 and GD_{1a} derivatives **16** and **23** in 72 and 76% yields, respectively. Finally, *O*-deacylation of **16** or **23** with sodium methoxide in methanol, and subsequent saponification of the methyl ester group, yielded GM_1 (**17**) and GD_{1a} (**24**) in 89% and quantitative yields after chromatography on a column of Sephadex LH-20.

In conclusion, a facile and stereocontrolled total synthesis of GM_1 and GD_{1a} was achieved by use of the key glycosyl acceptor **4** and the thioglycoside donors **8** and **9**, promising a further developement of the systematic synthesis of ganglio-series of gangliosides.

EXPERIMENTAL

General Procedures. Specific rotations were determined with a Union PM-201 polarimeter at 25 °C, and IR spectra were recorded with a Jasco A-100 spectrophotometer. ^1H NMR spectra were recorded at 270 and 400 MHz with JEOL JNM-GX spectrometers. 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*-(6-*O*-Benzoyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-β-D-galactopyranosyl)-(1→4)-*O*-[(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*--2-nonulopyranosylonic acid)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (2). To a solution of **1**[16] (2.17 g, 1.2 mmol) in pyridine (45 mL) was added lithium iodide (1.86 g), and the mixture was refluxed for 6 h, with stirring, under nitrogen in the dark and then concentrated. Dichloromethane (200 mL) was added, and the mixture was washed with 2M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (20:1 dichloromethane-methanol) of the residue on silica gel (200 g) gave **2** (2.05 g, 95%) as an amorphous mass: $[\alpha]_D$ +20.0° (*c* 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2O$), 1.32, 1.50 (2s, 6H, Me_2C), 1.83 (6H), 1.93 (9H) (2s, 15H, AcN, 4AcO), and 7.11-8.20 (m, 34H, 7Ph).

Anal. Calcd for $C_{95}H_{110}N_2O_{30}Si$ (1788.0): C, 63.81; H, 6.20; N, 1.57. Found: C, 63.88; H, 6.21; N, 1.63.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (3). A solution of **2** (1.95 g, 1.1 mmol) in aqueous 95% ethanol (50 mL) was treated with hydrazine monohydrate (0.85 mL) for 6 h under reflux. The precipitate was collected and washed with ethanol, and the combined filtrate and washings were concentrated. The residue was acetylated with acetic anhydride (10 mL)-pyridine (10 mL), and the product in methanol (20 mL) was treated with large excess of diazomethane in ether. After decomposition of the excess diazomethane by addition of acetic acid, the mixture was concentrated. Column chromatography (30:1 toluene-methanol) of the residue on silica gel (150 g) afforded **3** (1.16 g, 62%) as an amorphous mass: $[\alpha]_D$ +19.0° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2O$), 1.36, 1.57 (2s, 6H, Me_2C), 1.77, 1.87 (2s, 6H, 2AcN), 1.91, 1.92, 1.97, 2.04 (4s, 12H, 4AcO), 3.80 (s, 3H, MeO), and 7.14-7.99 (m, 30H, 6Ph).

Anal. Calcd for $C_{90}H_{112}N_2O_{29}Si$ (1714.0): C, 63.05; H, 6.59; N, 1.63. Found: C, 63.11; H, 6.64; N, 1.59.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl-(1→4)-*O*-[(methyl 5 - acetamido - 4,7,8,9 - tetra-*O*-acetyl - 3,5 - dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (4). A solution of **3** (1.1 g, 0.64 mmol) in aqueous 80% acetic acid (10 mL) was heated, with stirring, at 50 °C overnight and concentrated. Column chromatography (50:1 dichloromethane-methanol) of the residue on silica gel (100 g) gave **4** (937 mg, 88%) as an amorphous mass: $[\alpha]_D$ -1.8° (*c* 0.66, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.02 (m, 2H, Me_3SiCH_2 CH_2O), 1.83, 1.89, 1.91, 1.99, 2.08, 2.18 (6s, 18H, 2AcN, 4AcO), 3.90 (s, 3H, MeO), and 7.18-7.98 (m, 30H, 6Ph),

Anal. Calcd for $C_{87}H_{108}N_2O_{29}Si$ (1673.9): C, 62.42; H, 6.50; N, 1.67. Found: C, 62.41; H, 6.58; N, 1.66.

2-(Trimethylsilyl)ethyl 2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranoside (6). To a solution of **5**[17] (2.0 g, 5.4 mmol) in dichloromethane (4 mL) and pyridine (3.9 mL) cooled to 0 °C was gradually added benzoyl chloride (2.8 mL, 24.3 mmol), and the mixture was stirred for 1 h at room temperature, concentrated, and then extracted with dichloromethane. The extract was successively washed with 2M HCl and water, dried

(Na_2SO_4) and concentrated. Column chromatography (1:6 ethyl acetate-hexane) of the residue on silica gel (100 g) gave **6** (3.52 g, quantitative) as an amorphous mass: $[\alpha]_D$ +76.0° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2O$), 3.90 (dd, 1H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.18 (t, 1H, $J_{5,6}$ = 6.0 Hz, $J_{5,6'}$ = 8.1 Hz, H-5), 4.54 (dd, 1H, Jgem = 11.5 Hz, H-6), 4.73 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 5.64 (dd, 1H, H-2), 6.01 (d, 1H, H-4), and 7.13-8.29 (m, 20H, 4Ph).

Anal. Calcd for $C_{39}H_{42}O_9Si$ (682.8): C, 68.60; H, 6.20. Found: C, 68.41; H, 6.38.

1-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-D-galactopyranose (7). To a solution of **6** (1.0 g, 1.46 mmol) in toluene (8 mL) were added boron trifluoride etherate (0.16 mL) and acetic anhydride (2.5 mL), and the mixture was stirred overnight at room temperature and concentrated. Column chromatography (1:4 ethyl acetate-hexane) of the residue on silica gel (60 g) gave **7** (900 mg, quantitative) as an amorphous mass: ^1H NMR ($CDCl_3$) δ 3.88 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.4 Hz, H-3 for the α-anomer), 4.21 (dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.3 H, H-3 for the β-anomer), 5.67 (dd, $J_{1,2}$ = 3.9 Hz, H-2 for the α), 5.69 (t, $J_{1,2}$ = 8.5 Hz, H-2 for the β), 5.89 (d, H-1β), 5.96 (d, H-4 for the β), 6.06 (d, H-4 for the α), and 6.63 (d, H-1α).

Anal. Calcd for $C_{36}H_{32}O_{10}$ (624.6): C, 69.22; H, 5.16. Found: C, 69.05; H, 5.34.

Methyl 2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (8). To a solution of **7** (900 mg, 1.44 mmol) in dichloromethane (9 mL) were added methylthio trimethylsilane (433 mg, 3.6 mmol) and boron trifluoride etherate (0.18 mL, 1.44 mmol) and the mixture was stirred overnight at room temperature. Dichloromethane (100 mL) was added to the mixture, and the mixture was successively washed with M sodium carbonate and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:6 ethyl acetate-hexane) of the residue on silica gel (100 g) gave **8** (620 mg, 70%) as an amorphous mass: $[\alpha]_D$ +92.5° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.29 (s, 3H, MeS), 3.87 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 4.15 (t, 1H, $J_{5,6}$ = $J_{5,6'}$ = 6.6 Hz, H-5), 4.42 (dd, 1H, Jgem = 11.4 Hz, H-6), 4.56 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.61 (dd, 1H, H-6'), and 5.67 (t, 1H, H-2).

Anal. Calcd for $C_{35}H_{32}O_8S$ (612.7): C, 68.61; H, 5.26. Found: C, 68.43; H, 5.31.

2-(Trimethylsilyl)ethyl *O*-(2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2, 3,6-tri-*O*-benzyl-β-D-glucopyranoside (10). To a solution of **4** (50 mg, 0.03 mmol) and **8** (28 mg, 0.05 mmol) in dichloromethane (1 mL) were added molecular sieves 4Å

(MS-4Å; 200 mg), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. *N*-Iodosuccinimide (NIS; 20 mg, 0.09 mmol) and trifluoromethanesulfonic acid (TfOH; 16 μL) were added, and the mixture was stirred for 20 h at 0 °C while the progress of reaction was monitored by TLC. The precipitate was collected and washed with dichloromethane, and the combined filtrate and washings were successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (80:1 dichloromethane-methanol) gave **10** (44 mg, 66%) as an amorphous mass: $[\alpha]_D$ +37.5° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2O$), 1.67, 1.70, 1.83, 1.91, 1.97, 2.01 (6s, 18H, 2AcN, 4AcO), 2.50 (dd, 1H, Jgem = 13.2 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e-*eq*), 3.49 (s, 3H, MeO), 5.29 (m, 1H, H-8e), 5.89 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-4d), and 7.01-8.18 (m, 50H, 10Ph).

Anal. Calcd for $C_{121}H_{136}N_2O_{37}Si$ (2238.5): C, 64.92; H, 6.12; N, 1.25. Found: C, 64.90; H, 6.23; N, 1.24.

2-(Trimethylsilyl)ethyl *O*-(3-*O*-Acetyl-2,4,6 - tri - *O*-benzoyl - β- D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (11). A solution of **10** (151 mg, 0.067 mmol) in ethanol (25 mL) and acetic acid (5 mL) was hydrogenolyzed in the presence of 10% Pd-C (150 mg) for 2 days at 40 °C, then filtered and concentrated. The residue was treated with acetic anhydride (2 mL) and pyridine (3 mL) for 2 days at room temperature and concentrated. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel (50 g) gave **11** (105 mg, 78%) as an amorphous mass: $[\alpha]_D$ -4.8° (*c* 0.7, $CHCl_3$); IR (KBr) 3350 (NH), 1780 and 1210 (ester), 1660 and 1540 (amide), 860 and 840 (TMS), and 740 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2O$), 1.83-2.23 (13s, 39H, 2AcN, 11AcO), 3.66 (s, 3H, MeO), 5.04 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1d), 5.27 (dd, 1H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, H-3d), 5.35 (dd, 1H, $J_{6,7}$ = 2.4 Hz, $J_{7,8}$ = 9.4 Hz, H-7e), 5.52 (dd, 1H, H-2d), 5.70 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4c), 5.77 (d, 1H, H-4d), and 7.28-8.20 (m, 20H, 4Ph).

Anal. Calcd for $C_{93}H_{114}N_2O_{44}Si$ (1992.0): C, 56.07; H, 5.77; N, 1.41. Found: C, 55.91; H, 5.74; N, 1.53.

***O*-(3-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranose (12).** To a solution of **11** (135 mg, 0.068 mmol) in

dichloromethane (0.7 mL) was added trifluoroacetic acid (0.3 mL), and the mixture was stirred for 2 h at room temperature then concentrated. Column chromatography (35:1 dichloromethane-methanol) of the residue on silica gel (30 g) gave **12** (125 mg, quantitative) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 1.52-2.22 (m, 39H, 2AcN, 11AcO), 3.66 (s, 3H, MeO), 5.05 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1d), 5.28 (dd, 1H, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.2 Hz, H-3d), 5.69 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4c), 5.76 (d, 1H, H-4d), and 7.26-8.20 (m, 20H, 4Ph).

Anal. Calcd for $C_{88}H_{102}N_2O_{44}$ (1891.8): C, 55.87; H, 5.43; N, 1.48. Found: C, 55.99; H, 5.46; N, 1.45.

***O*-(3-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (13).** To a solution of **12** (104 mg, 0.055 mmol) in dichloromethane (1 mL) and trichloroacetonitrile (0.17 mL) cooled to -5 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 10 mg), and the mixture was stirred for 3 h at 0 °C. Column chromatography (40:1 chloroform-methanol) of the mixture on silica gel (30 g) gave **13** (110 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +19.5° (*c* 2.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.59-2.30 (13s, 39H, 2AcN, 11AcO), 3.73 (s, 3H, MeO), 5.13 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1d), 5.36 (dd, 1H, $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 2.9 Hz, H-3d), 5.85 (d, 1H, H-4d), 6.55 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1a), 7.36-8.27 (m, 20H, 4Ph), and 8.73 (s, 1H, C=NH).

Anal. Calcd for $C_{90}H_{102}N_3O_{44}Cl_3$(2036.2): C, 53.08; H, 5.05; N, 2.06. Found: C, 53.00; H, 5.14; N, 2.05.

***O*-(3-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (15).** To a solution of **13** (110 mg, 0.054 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[22] (**14**; 93 mg, 0.21 mmol) in dichloromethane (1.5 mL) were added molecular sieves 4Å (AW-300, 900 mg) and the mixture was stirred for 3 h at room temperature and then cooled to 0 °C. Trimethylsilyl trifluoromethanesulfonate (21 μL, 0.1 mmol) was added, and the mixture was stirred for 24 h at 0 °C then filtered. The insoluble material was washed with dichloromethane, and the combined filtrate and washings were washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated.

Column chromatography (65:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave **15** (60.5 mg, 48%) as an amorphous mass: $[\alpha]_D$ +1.0° (*c* 1.0, $CHCl_3$); IR (KBr) 3300 (NH), 2100 (N_3), 1760 and 1220 (ester), 1660 and 1540 (amide), and 740 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, *Me*CH_2), 1.25 (s, 22H, 11CH_2), 1.83-2.22 (13s, 39H, 2AcN, 11AcO), 3.66 (s, 3H, MeO), 4.58 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1a), 5.69 (d, 1H, $J_{3,4}$= 3.0 Hz, H-4c), 5.76 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4d), and 7.26-8.20 (m, 25H, 5Ph).

Anal. Calcd for $C_{113}H_{139}N_5O_{46}$ (2303.3): C, 58.92; H, 6.08; N, 3.04. Found: C, 58.84; H, 6.19; N, 3.13.

***O*-(3-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(2→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (16)**. Hydrogen sulfide was bubbled through a stirred solution of **15** (50 mg, 0.022 mmol) in aqueous 83% pyridine (10 mL) for 3 days at 0 °C. The reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated, and the residue was stirred with octadecanoic acid (12.4 mg, 0.044 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC; 12.5 mg, 0.065 mmol) in dichloromethane (0.5 mL) for 20 h at room temperature. Column chromatography (50:1 chloroform-methanol) of the mixture on silica gel (20 g) gave **16** (42 mg, 72%) as an amorphous mass: $[\alpha]_D$ +7.8° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 1.51-2.22 (13s, 39H, 2AcN, 11AcO), 2.82 (dd, 1H, Jgem = 12.1 Hz, $J_{3e,4}$ = 5.5 Hz, H-3e-*eq*), 3.68 (s, 3H, MeO), 5.68 (m, 1H, H-8e), and 7.26-8.20 (m, 25H, 5Ph).

Anal. Calcd for $C_{131}H_{175}N_3O_{56}$ (2543.8): C, 61.85; H, 6.93; N, 1.65. Found: C, 61.70; H, 6.89; N, 1.83.

Ganglioside GM_1 (17). To a solution of **16** (27 mg, 0.01 mmol) in methanol (3 mL) was added sodium methoxide (10 mg), the mixture was stirred for 24 h at 45 °C. Water (0.5 mL) was added and the mixture was stirred for a further 24 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with 5:4:1 chloroform-methanol-water, and the combined filtrate and washings were concentrated. Column chromatography (5:4:1 chloroform-methanol-water) of the residue on Sephadex LH-20 (30 g) gave **17** (15 mg, 89%) as an amorphous mass: $[\alpha]_D$ +7.2° (*c* 0.5, 5:4:1 $CHCl_3$-MeOH-H_2O); ^1H NMR [98:2 $(CD_3)_2SO$-D_2O] δ 0.90 (t, 6H, 2*Me*CH_2), 1.25 (s, 50H, 25CH_2), 1.47 (br. m, 2H, $COCH_2CH_2$), 1.85, 1.90 (2s, 6H, 2AcN).

Anal. Calcd for $C_{73}H_{131}N_3O_{31}$ (1546.9): C, 56.68; H, 8.53; N, 2.71. Found: C, 56.65; H, 8.69; 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→3)-O-(2-acetamido-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (18). To a solution of **4** (40 mg, 0.024 mmol) and **9**[15] (50 mg, 0.048 mmol) in dichloromethane (1 mL) were added MS-4Å (250 mg), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. A mixture of DMTST (39 mg, 0.14 mmol) and MS-4Å (200 mg) was added and the reaction was monitored by TLC, while the mixture was stirred at 0 °C. After 25 h the precipitate was filtered off and washed with dichloromethane, and the combined filtrate and washings were washed with M Na_2CO_3 and water, dried (Na_2SO_4), and concentrated. Column chromatography (30:1 toluene-methanol) of the residue on silica gel (20 g) gave **18** (40 mg, 62%) as an amorphous mass: $[\alpha]_D$ +29.5° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.02 (m, 2H, $Me_3SiCH_2CH_2O$), 1.53-2.18 (11s, 33H, 3AcN, 8AcO), 2.43 (dd, 1H, Jgem = 12.9 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e-*eq*), 2.57 (dd, 1H, Jgem = 13.4 Hz, $J_{3e,4}$ = 4.5 Hz, H-3f-*eq*), 3.63, 3.80 (2s, 6H, 2MeO), 4.55 (d, 1H, $J_{1,2}$ = 7.4 Hz, H-1a), 5.04 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1d), 5.35 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4d), 5.50 (dd, 1H, $J_{2,3}$ = 10.2 Hz, H-2d), and 7.15-8.17 (m, 45H, 9Ph).

Anal. Calcd for $C_{134}H_{157}N_3O_{49}Si$ (2621.8): C, 61.39; H, 6.04; N, 1.60. Found: C, 61.47; H, 5.91; N, 1.59.

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→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (19). As described for **11**, a suspension of **18** (52 mg, 0.02 mmol) in ethanol (10 mL)-acetic acid (4 mL) in the presence of 10% Pd-C (60 mg) was hydrogenolyzed and acetylated, to give **19** (43 mg, 90%) as an amorphous mass: $[\alpha]_D$ +8.2° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (m, 2H, $Me_3SiCH_2CH_2O$), 1.37-2.20 (17s, 51H, 3AcN, 14AcO), 2.46 (dd, 1H, Jgem = 12.4 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e-*eq*), 2.80 (dd, 1H, Jgem = 12.5 Hz, $J_{3e,4}$ = 4.4 Hz, H-3f-*eq*), 3.05 (dt, 1H, $J_{1,2}$ = 8.2 Hz, $J_{2,NH}$ = 7.2 Hz, $J_{2,3}$ = 10.9 Hz, H-2c), 3.63, 3.80 (2s, 6H, 2MeO), 4.40 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), 4.90 (near t, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 9.9 Hz,

H-3a), 5.14 (d, 1H, H-1c), 5.64 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4c), and 7.26-8.21 (m, 20H, 4Ph).

Anal. Calcd for $C_{111}H_{139}N_3O_{55}Si$ (2423.4): C, 55.01; H, 5.78; N, 1.73. Found: C, 54.81; H, 5.55; N, 1.90.

***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→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranose (20).** To a solution of **19** (105 mg, 0.043 mmol) in dichloromethane (0.5 mL) was added trifluoroacetic acid (0.2 mL), and the mixture was stirred for 2 h at room temperature then concentrated. Column chromatography (30:1 chloroform-methanol) of the residue on silica gel (30 g) gave **20** (91 mg, 90%) as an amorphous mass: IR (KBr) 3500-3300 (OH, NH), 1750 and 1220 (ester), 1650 and 1550 (amide), and 740 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.54-2.17 (17s, 51H, 3AcN, 14AcO), 2.45 (dd, 1H, Jgem = 12.9 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e-*eq*), 2.86 (dd, 1H, Jgem = 12.5 Hz, $J_{3e,4}$ = 4.6 Hz, H-3f-*eq*), 3.64, 3.80 (2s, 6H, 2MeO), and 7.28-8.19 (m, 20H, 4Ph).

Anal. Calcd for $C_{106}H_{127}N_3O_{55}$ (2323.2): C, 54.80; H, 5.51; N, 1.81. Found: C, 54.81; H, 5.70; N, 1.75.

***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→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (21).** To a solution of **20** (70 mg, 0.03 mmol) in dichloromethane (0.7 mL) and trichloroacetonitrile (0.15 mL) cooled to -5 °C was added DBU (8 mg), and the mixture was stirred for 5 h at 0 °C and concentrated. Column chromatography (35:1 chloroform-methanol) of the residue on silica gel (20 g) gave **21** (64 mg, 85%) as an amorphous mass: $[\alpha]_D$ +23.5° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.56-2.18 (17s, 51H, 3AcN, 14AcO), 2.45 (dd, 1H, Jgem = 12.8 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e-*eq*), 2.86 (dd, 1H, Jgem = 12.7 Hz, $J_{3e,4}$ = 4.5 Hz, H-3f-*eq*), 3.64, 3.80 (2s, 6H, 2MeO), 6.47 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1a), 7.27-8.19 (m, 20H, 4Ph), and 8.64 (s, 1H, C=NH).

Anal. Calcd for $C_{108}H_{127}N_4O_{55}$ (2467.6): C, 52.57; H, 5.19; N, 2.27. Found: C, 52.72; H, 5.30; N, 2.27.

***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→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (22).** Condensation of **21** (64 mg, 0.023 mmol) with **14** (32 mg, 0.07 mmol), as described for **15**, gave **22** (45 mg, 63%) as an amorphous mass: $[\alpha]_D$ +8.1° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, *Me*CH_2), 1.25 (s, 22H, 11CH_2), 1.53-2.18 (17s, 51H, 3AcN, 14AcO), 2.45 (dd, 1H, Jgem = 12.4 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e-*eq*), 2.80 (dd, 1H, Jgem = 12.6 Hz, $J_{3e,4}$ = 4.5 Hz, H-3f-*eq*), 3.63, 3.80 (2s, 6H, 2MeO), 4.58 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1a), and 7.27-8.19 (m, 25H, 5Ph).

Anal. Calcd for $C_{131}H_{164}N_6O_{57}$ (2734.7): C, 57.54; H, 6.06; N, 3.07. Found: C, 57.44; H, 6.20; N, 3.08.

***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→3)-*O*-(2-acetamido-4-*O*-acetyl-6-*O*-benzoyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (23).** Selective reduction of the azido group in **22** (30 mg, 0.011 mmol) with hydrogen sulfide, and subsequent condensation with octadecanoic acid (6.3 mg, 0.033 mmol) using WSC (6.3 mg, 0.033 mmol), as described for **16**, yielded **23** (26 mg, 76%) as an amorphous mass: $[\alpha]_D$ +13.5° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 1.53-2.09 (17s, 51H, 3AcN, 14AcO), 3.63, 3.80 (2s, 6H, 2MeO), 5.87 (dt, 1H, $J_{4,5}$ = 14.5 Hz, $J_{5,6'}$ = 7.0 Hz, H-5 for Cer unit), and 7.24-8.19 (m, 25H, 5Ph).

Anal. Calcd for $C_{149}H_{200}N_4O_{58}$ (2975.2): C, 60.15; H, 6.78; N, 1.88. Found: C, 60.09; H, 6.83; N, 1.86.

Ganglioside GD1a (24). *O*-Deacylation and subsequent saponification of the methyl ester group of **23** (30 mg, 0.01 mmol), as described for **17**, gave **24** (20 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -20.0° (*c* 0.1, 5:5:1 $CHCl_3$-MeOH-H_2O) ; IR (KBr) 3700-2800 (OH, NH), 2940 and 2850 (Me, methylene), 1700 (C=O), and 1650 and 1550 cm^{-1} (amide); ^1H NMR [49:1 $(CD_3)_2SO$-D_2O] δ 0.85 (t, 6H, 2*Me*CH_2), 1.23 (s, 52H, 26CH_2), 1.76, 1.88, 1.89 (3s, 9H, 3AcN), 2.60, 2.68 (2dd, 2H, Jgem = 12.5 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3e,f-*eq*), 4.18 (d, $J_{1,2}$ = 8.0 Hz, H-1b), 4.28, 4.30 (2d, 2H, $J_{1,2}$ = 7.7

Hz, H-1c,d), 4.80 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), and 5.36, 5.58 (2m, 2H, H-4.5 for Cer unit).

Anal. Calcd for $C_{84}H_{148}N_4O_{39}$ (1838.1): C, 54.89; H, 8.12; N, 3.05. Found: C, 54.71; H, 8.30; N, 3.05.

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