Carbohydrate Research, 233 (1992) 87–99
Elsevier Science Publishers B.V., Amsterdam

Synthesis of disialoganglioside GD1α and its positional isomer *

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(Received September 11th, 1991; accepted January 22nd, 1992)

ABSTRACT

The first total syntheses of disialoganglioside GD1α and its α2-6 positional isomer are described. Suitably protected pentasaccharide derivatives, derived from known pentasaccharide precursors, were selected as the glycosyl acceptors. Using our facile method of stereoselective α-glycosidation of sialic acid, these acceptors were coupled with methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate in acetonitrile medium in the presence of dimethyl(methylthio)sulfonium triflate (DMTST) to get the desired di-α-sialyl hexasaccharide derivatives in moderate yields. The hexasaccharide trichloroacetimidates upon coupling with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol gave the corresponding β-linked sphingosine glycosides in high yields. These were subjected in sequence to selective reduction of the azido group and coupling of the thus formed amino group with octadecanoic acid, *O*-deacylation, and saponification of the methyl ester groups to obtain ganglioside GD1α and its positional isomer having the main-chain residue 2-6 linked.

INTRODUCTION

Studies[2,3] on rat ascites and adult bovine brains have revealed that these cells express some gangliosides specifically related to cell–cell adhesion and malignancy. These are also the major gangliosides expressed in mammalian brain in the developmental stage[4]. In the studies cited GM1b and GD1α, among the several gangliosides present, were isolated in extremely minute quantities and well characterized. Earlier, ganglioside GM1b was contemplated as a product of the degradation of GD1α and now, in the recent studies[2,3], the structural similarities of these gangliosides and their association in specific functions have lead to the speculation that their syntheses in vivo are interdependent, and that asialo-GM1 is the precursor in this process.

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* Synthetic Studies on Sialoglycoconjugates, Part 34. For part 33, see ref. 1.

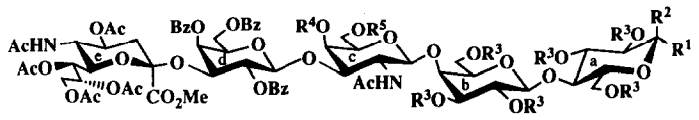
With our interest focussed on the preparation and biological evaluation of native gangliosides and their analogs, we have accomplished the synthesis of several of these compounds[5]. We also developed a facile method of stereoselective α-glycosidation[6] of sialic acid with suitably protected galactose and lactose acceptors, employing dimethyl(methylthio)sulfonium triflate (DMTST)[7] as the glycosidation promoter in acetonitrile. Using this method we have achieved the stereoselective α-glycosidation of sialic acid in moderate yields even with bulky pentasaccharide acceptors. Here we report the first total syntheses of ganglioside GD1α and its α2-6 positional isomer.

RESULTS AND DISCUSSION

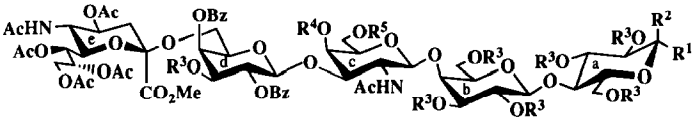
The synthetic strategy devised for the synthesis of the core α-disialyl oligosaccharides was such that the suitably protected pentasaccharide acceptor derivatives **2** and **5** were first prepared, and then a sialyl unit was introduced at the C-6 position of the GalNAc residue as the last step. The acceptors were obtained in good yields by treating the precursors **1** and **3** with aqueous 80% acetic acid, which removed the benzylidene group to make a primary hydroxyl group available for further glycosylation. The preparation of the precursors **1** and **4**, intermediates in the total synthesis of ganglioside GM1b, has already been reported[8].

The individual glycosylations of **2** and **5** with methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)-onate[6b] **7** in the presence of DMTST were performed for 9–10 h at 0–10°. The molar ratio of glycosyl acceptor to donor was approximately 1:3. The choice of acetonitrile as the reaction medium was obvious for the reasons that α glycosides of sialic acid are obtained stereoselectively by using this solvent[5]. It has also been established that the solvent molecules participate in the formation of a transient intermediate involving the anomeric carbon, and this in turn directs the nucleophilic attack by the acceptor. In the case of sialyl glycosylations, this mechanism is believed[6c] to favor the formation of α glyclosides. Thus, the glycosylations of **2** and **5** with **7** in the presence of DMTST in acetonitrile gave mixtures of hexasaccharides in which the α anomers were predominant. Although the percentage yields of the α glycosides **9** (41%) and **13** (40%) were good, the yields of the β glycosides **3** (12%) and **6** (12%) were a little higher than expected on the basis of earlier reports[5,6]. This is attributed to the bulk of the acceptor molecules, resulting in steric hindrance to glycosylation at C-6 of the GalNAc residue. In accord with this reasoning significant amounts of unreacted acceptors were recovered.

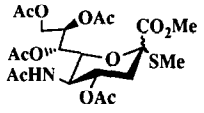
The stereochemistry of the hexasaccharide derivatives was established by their ^{1}H NMR data, particularly the chemical shifts of the equatorial H-3 protons of the respective sialyl residues. Thus, compound **9** showed a one-proton doublet of doublets at δ 2.42 due to H-3*eq* of the α2-3-linked sialyl residue (e), and another one-proton doublet of doublets at δ 2.56 due to H-3*eq* of the newly introduced α2-6 sialyl residue (f). Similarly, compound **13** had two partially overlapped



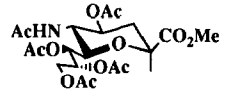
	R^1	R^2	R^3	R^4	R^5
1	OSE	H	Bn	benzylidene	
2	OSE	H	Bn	H	H
3	OSE	H	Bn	H	β-sialyl unit (X)



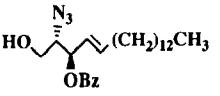
	R^1	R^2	R^3	R^4	R^5
4	OSE	H	Bn	benzylidene	
5	OSE	H	Bn	H	H
6	OSE	H	Bn	H	β-sialyl unit (X)



7 (α: β = 1:1)

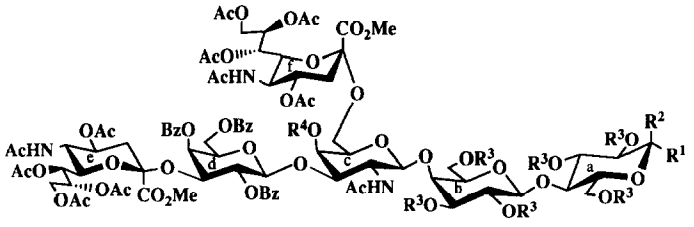
X = 

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

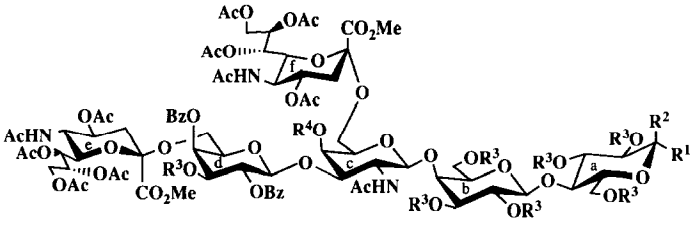


8

one-proton doublets of doublets at δ 2.54 and 2.59, showing the presence of two α2-6 sialyl residues. These assignments are based on the fact that H-3*eq* in the terminal sialyl residues of **2** and **5** appears at δ 2.40 (α2-3) and 2.53 (α2-6), respectively, and they were confirmed by the immunological reactions of the synthetic gangliosides with a specific monoclonal antibody[10] (KA-17) against natural GD1α. On the other hand, in the ^{1}H NMR spectra of the corresponding β glycosides **3** and **6**, H-3*eq* of the newly introduced sialyl residues (f) appeared at δ 2.37 and δ 2.51, respectively. Earlier studies[11] on the ^{1}H NMR of sialyl glycosides have shown that the equatorial H-3 proton of an α glycoside appears at lower field in the spectrum than that of a β glycoside. Based on this finding, the stereochemistry of the newly introduced sialyl residues in compounds **9** and **13** was assigned as α and that in compounds **3** and **6** as β. In addition, the spectra of all these compounds contained eleven three-proton singlets (3 NCOCH_3, 8 OCOCH_3), a further two three-proton singlets (2 CH_3O), and a fortyfive-proton multiplet (9 Ph), as required for products having two sialyl residues.



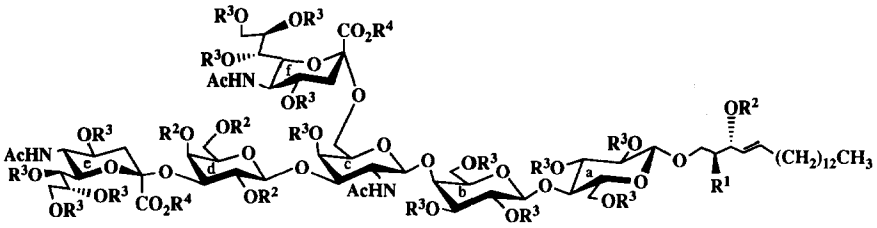
	R^1	R^2	R^3	R^4
9	OSE	H	Bn	H
10	OSE	H	Ac	Ac
11	—H, OH—		Ac	Ac
12	H	$OC(=NH)CCl_3$	Ac	Ac



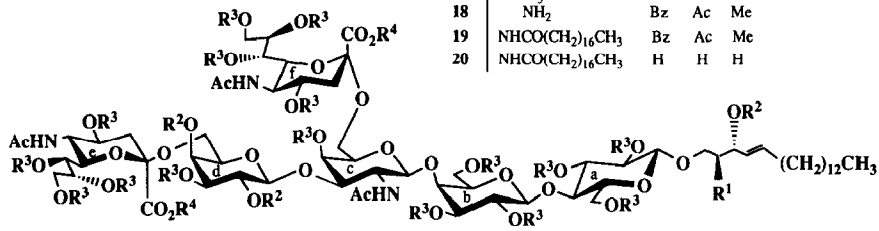
	R^1	R^2	R^3	R^4
13	OSE	H	Bn	H
14	OSE	H	Ac	Ac
15	—H, OH—		Ac	Ac
16	H	$OC(=NH)CCl_3$	Ac	Ac

The benzyl groups in **9** and **13** were removed by hydrogenation in the presence of 10% Pd–C in 8:1 ethanol–acetic acid, and this followed by acetylation gave the respective oligosaccharide derivatives **10** and **14** in high yields. Selective removal of the 2-(trimethylsilyl)ethyl group by treatment with trifluoroacetic acid for 2 h at room temperature in dichloromethane afforded the respective 1-hydroxy compounds **11** and **15**, and these on reatment[12] with trichloroacetonitrile, in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichoromethane for 4 h at 0° gave the trichloroacetimidates **12** and **16** in high yields. The stereochemistry of these compounds was established as α by their ^{1}H NMR spectra, which showed a doublet at δ 6.5 ($J_{1,2}$ 3.6 Hz, H-1a) and a singlet at δ 8.7 (C=N*H*).

The glycosylation[12a,13] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[13,14] (**8**) with the α-trichloroacetimidates was accomplished by using boron trifluoride etherate as promoter, to get the β-linked sphingosine derivatives **17** and **21** in 63 and 53% yields, respectively. The azido groups were then selectively reduced[15] by continuously bubbling hydrogen sulfide into solutions of **17** and **21** in aqueous 83% pyridine for 48 h at 0–15°, leading to the amines **18** and **22**. These were subsequently condensed with octadecanoic acid, in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane,



	R^1	R^2	R^3	R^4
17	N_3	Bz	Ac	Me
18	NH_2	Bz	Ac	Me
19	$NHCO(CH_2)_{16}CH_3$	Bz	Ac	Me
20	$NHCO(CH_2)_{16}CH_3$	H	H	H



	R^1	R^2	R^3	R^4
21	N_3	Bz	Ac	Me
22	NH_2	Bz	Ac	Me
23	$NHCO(CH_2)_{16}CH_3$	Bz	Ac	Me
24	$NHCO(CH_2)_{16}CH_3$	H	H	H

to afford the corresponding fully protected gangliosides **19** and **23** in 83 and 81% yields, respectively.

Finally, *O*-deacylation with sodium methoxide in methanol and subsequent saponification of the methyl ester groups in **19** and **23** afforded ganglioside GD1α (**20**) and its analog **24** in high yields. The ^{1}H NMR spectrum of **20** at 400 MHz was in good agreement with the spectrum reported by Hirabayashi et al.[3], and only **20** reacted with a specific monoclonal antibody[10] (KA-17) prepared by using natural GD1α as an antigen.

In conclusion, the glycosylation of bulky pentasaccharide acceptors with the methyl 2-thioglycoside of neuraminic acid was effectively accomplished by the use of DMTST in acetonitrile to get moderate yields of the desired α-glycosides.

EXPERIMENTAL

General methods.—Specific rotations were determined with a Union PM-201 polarimeter at 25° and IR spectra were recorded with a Jasco IRA-100 spectrophotometer. ^{1}H NMR spectra were recorded with JEOL JNM-GX270 and GX400 spectrometers. Preparative chromatography was performed on silica gel (Wako Co., 200 mesh) with the solvents specified. Concentrations were conducted in vacuo.

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-2-deoxy*-β-D-*galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*benzyl*-β-D-*galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**2**).—A mixture of **1** (ref. 8, 1.15 g, 0.52 mmol) and aq 80% acetic acid (125 mL) was heated for 24 h at 60°, and concentrated to dryness. Column chromatography (100:3 CH_2Cl_2–MeOH) of the residue on silica gel (50 g) gave amorphous **2** (808 mg, 73.5%); $[\alpha]_D$ +38.6° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.97 (m, 2 H, Me_3SiCH_2), 1.51, 1.72 (2 s, 6 H, 2 $NCOCH_3$), 1.60 (t, 1 H, $J_{gem} = J_{3ax,5}$ 12.8 Hz, H-3e-*ax*), 1.86, 1.88, 2.05, 2.19 (4 s, 12 H, 3 $OCOCH_3$), 2.40 (dd, 1 H, $J_{3eq,4}$ 4.5 Hz, H-3e-*eq*), 3.81 (s, 3 H, OCH_3), 4.83 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1d), 5.06 (d, 1 H, $J_{NH,5}$ 9.8 Hz, N*H*-e), 5.18 (dd, 1 H, H-7e) 5.33 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4d), 5.42 (dd, 1 H, $J_{1,2} = J_{2,3}$ 7.9 Hz, H-2d), 5.57 (m, 1 H, H-8e), and 7.18–8.17 (m, 45 H, 9 Ph).

Anal. Calcd for $C_{114}H_{132}N_2O_{36}Si$ (2134.4): C, 64.15; H, 6.23; N, 1.31. Found: C, 64.08; H, 6.29; N, 1.35.

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 → 6)*-O-*(2,4-di*-O-*benzoyl-3*-O-*benzyl*-β-D-*galactopyranosyl)-(1 → 3)*-O-*(2-acetamido-2-deoxy*-β-D-*galactopyrano*-*syl)-(1 → 4)*-O-*(2,3,6-tri*-O-*benzyl*-β-D-*galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**5**).—Treatment of **4** (ref. 8, 1.4 g, 0.6 mmol) with aq 80% acetic acid (175 mL), as just described for **2**, afforded amorphous **5** (1.05 g, 75%), $[\alpha]_D$ +37.7° (*c* 0.52, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.98 (m, 2 H, Me_3SiCH_2), 1.84, 1.94 (2 s, 6 H, 2 $NCOCH_3$), 1.60 (t, 1 H, $J_{gem} = J_{3ax,4} = 12.8$ Hz, H-3e-*ax*), 1.99, 2.01, 2.10, 2.12 (4 s, 12 H, 4 $OCOCH_3$), 2.53 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3e-*eq*), 3.33 (s, 3 H, OCH_3), 5.09 (d, 1 H, NH-e), 5.50 (dd, 1 H, H-2d), 5.87 (d, 1 H, H-4d), and 7.17–8.22 (m, 45 H, 9 Ph).

Anal. Calcd for $C_{114}H_{134}N_2O_{35}Si$ (2120.4): C, 64.58; H, 6.37; N, 1.32. Found: C, 64.21; H, 6.29; N, 1.35.

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-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dide*-*oxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-2-de*-*oxy*-β-D-*galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*benzyl*-β-D-*galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzyl*-β-D-*glucopyranoside* (**9**).—A mixture of **2** (620 mg, 0.29 mmol), **7** (ref. 6b, 506 mg, 0.96 mmol) and molecular sieves 3A in acetonitrile (15mL) was stirred for 5 h at room temperature, then cooled to 0°. A mixture of DMTST (730 mg, 2.8 mmol) and molecular sieves 3A (300 mg) was added and the reaction was monitored by TLC while the mixture was stirred at 0–10°. After 9 h the solids were filtered off and washed with CH_2Cl_2, and the combined filtrate and washings was washed with M $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. Column chromatography of the residue on silica gel (50 g) using 50:1 CH_2Cl_2–MeOH as eluent gave unreacted acceptor (292 mg), and then

elution with 25:1 CH_2Cl_2–MeOH gave amorphous **3** (90 mg, 12%) and **9** (308 mg, 41%). ^1H NMR ($CDCl_3$) for **3**: δ 1.0 (m, 2 H, Me_3SiCH_2), 1.50, 1.61, 1.78, 1.84, 1.85, 1.88, 1.95, 2.05, 2.10 (6 H), 2.21 (10 s, 33 H, $NCOCH_3$, $OCOCH_3$), 2.37 (dd, 1 H, H-3*eq* of the β2-6 sialyl residue), 2.42 (dd, 1 H, H-3*eq* of the α2-3 sialyl residue), and 7.1–8.2 (m, 45 H, 9 PhH). The desired compound **9** had $[\alpha]_D$ +17.3° (*c* 1.7, $CHCl_3$); ν_{max} 3400 (NH), 1740 and 1230 (ester), 1680 and 1540 (amide), 860 and 840 (Me_3Si), and 740 and 720 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.0 (m, 2 H, Me_3SiCH_2), 2.42 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3e-*eq*), 2.56 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3f-*eq*), 3.69 (s, 3 H, CH_3O-f), 3.79 (s, 3 H, CH_3O-e), 5.33 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4d), 5.44 (dd, 1 H, $J_{1,2} = J_{2,3} = 7.7$ Hz, H-2d), and 7.18–8.17 (m, 45 H, 9 Ph).

Anal. Calcd for $C_{134}H_{159}N_3O_{48}Si$ (2607.8): C, 61.71; H, 6.15; N, 1.61. Found: C, 61.53; H, 6.11; N, 1.61.

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-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranoside* (**10**).—Compound **9** (312 mg, 0.12 mmol) was dissolved in 7:1 EtOH–acetic acid (125 mL). The solution was subjected to hydrogenolysis in the presence of 10% Pd–C (412 mg) for 48 h at 45°, then the insolubles were filtered off and washed with EtOH. The combined filtrate and washings was concentrated to dryness and the residue was acetylated with acetic anhydride (2 mL) and pyridine (3 mL) for 72 h at 45°. Methanol was added and the mixture was concentrated. Column chromatography (20:1 CH_2Cl_2–MeOH) of the residue on silica gel (40 g) gave amorphous **10** (214 mg, 76%), $[\alpha]_D$ +6.0° (*c* 0.40, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (m, 2 H, Me_3SiCH_2), 1.53–2.19 (18 s, 54 H, 3 $NCOCH_3$ and 15 $OCOCH_3$), 2.39 (dd, 1 H, H-3e-*eq*), 2.53 (dd, 1 H, H-3f-*eq*), 2.74 (m, 1 H, H-2c), 3.74 (s, 3 H, CH_3O-f), 3.79 (s, 3 H, CH_3O-e), 5.44 (dd, 1 H, $J_{1,2} = J_{2,3} = 7.7$ Hz, H-2d), 5.46 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4c), 5.80 (d, 1 H, NH-c), and 7.40–8.19 (m, 15 H, 3 Ph).

Anal. Calcd for $C_{106}H_{137}N_3O_{55}Si$ (2361.4): C, 53.92; H, 5.85; N, 1.78. Found: C, 53.89; H, 5.82; N, 1.77.

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-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranose* (**11**).—A solution of **10** (218 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) and trifluoroacetic acid (1.5 mL) was stirred for 2 h at room temperature. The mixture was then concentrated. Column chromatography (20:1 CH_2Cl_2–MeOH) of the residue on silica gel (30 g) gave amorphous **11** (181 mg, 91%); $[\alpha]_D$ +19.3° (*c* 0.60, $CHCl_3$); ν_{max} 3400 (NH, OH), 1740 and 1230 (ester), 1670 and 1540 (amide), and 720 cm^{-1} (Ph).

Anal. Calcd for $C_{101}H_{125}N_3O_{55}$ (2261.1): C, 53.65; H, 5.57; N, 1.86. Found: C, 53.53; H, 5.55; N, 1.89.

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-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galacto-pyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β-D-glucopyranosyl trichloroacetimidate* (**12**).—To a solution of **11** (208 mg, 0.092 mmol) in CH_2Cl_2 (2 mL) and trichloroacetonitrile (0.5 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.05 mL) at 0°, and the mixture was stirred for 4 h at 0°, then concentrated. Column chromatography (20:1 CH_2Cl_2–MeOH) of the residue on silica gel (30 g) gave amorphous **12** (199 mg, 90%); $[\alpha]_D$ +22.9° (*c* 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.52–2.19 (18 s, 54 H, 3 NCOCH_3 and 15 OCOCH_3), 2.40 (dd, 1 H, H-3e-*eq*), 2.51 (dd, 1 H, H-3f-*eq*), 2.98 (m, 1 H, H-2c), 3.77 (s, 3 H, CH_3O-f), 3.80 (s, 3 H, CH_3O-e), 5.44 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4c), 6.11 (d, 1 H, N*H*-c), 6.51 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1a), 7.45–8.23 (m, 15 H, 3 Ph), and 8.73 (s, 1 H, C=N*H*).

Anal. Calcd for $C_{103}H_{125}Cl_3N_4O_{55}$ (2405.5): C, 51.42; H, 5.24; N, 1.86. Found: C, 51.49; H, 5.21; N, 1.89.

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 → 6)*-O-*(2,4-di*-O-*benzoyl-3*-O-*benzyl-β-D-galactopyranosyl)-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*benzyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*benzyl-β-D-glucopyranoside* (**13**).—Glycosylation of **5** (400 mg, 0.19 mmol) with **7** (275 mg, 0.52 mmol), in a fashion similar to that described for **9**, afforded amorphous **6** (62.4 mg, 12%) and **13** (208 mg, 40%). ^{1}H NMR ($CDCl_3$) for **6**: δ 1.0 (m, 2 H, Me_3SiCH_2), 2.51, 2.55 (2 dd, 2 H, H-3*eq* of the sialyl residues), and 7.0–8.2 (m, 45 H, 9 Ph). The desired compound **13** had $[\alpha]_D$ +22.7° (*c* 0.44, $CHCl_3$); ν_{max} 3400 (NH), 1740 and 1230 (ester), 1680 and 1540 (amide), 860 and 840 (Me_3Si), and 740 and 720 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 1.0 (m, 2 H, Me_3SiCH_2), 1.56–2.09 (11 s, 33 H, 3 NCOCH_3 and 8 OCOCH_3), 2.54 (dd, 1 H, H-3e-*eq*), 2.59 (dd, 1 H, H-3f-*eq*), 3.40 (s, 3 H, CH_3O-e), 3.68 (s, 3 H, CH_3O-f), 5.89 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4d), and 7.18–8.14 (m, 45 H, 9 Ph).

Anal. Calcd for $C_{134}H_{161}N_3O_{47}Si$ (2593.8): C, 62.05; H, 6.26; N, 1.62. Found: C, 62.40; H, 6.00; N, 1.62.

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 → 6)*-O-*(3*-O-*acetyl-2,4-di*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β-D-glucopyranoside* (**14**).—The benzyl groups in **13** (401 mg, 0.15 mmol), dissolved in 6:1 EtOH–acetic acid (100 mL),

were removed by hydrogenolytic cleavage over 10% Pd–C (584 mg). The debenzylated product was acetylated as described for **10**, to get amorphous **14** (282 mg, 79%); $[\alpha]_D$ −2.2° (*c* 0.54, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (m, 2 H, Me_3SiCH_2), 1.56–2.20 (19 s, 57 H, 3 $NCOCH_3$ and 16 $OCOCH_3$) 2.44 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3e-*eq*), 2.53 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3f-*eq*), 2.92 (m, 1 H, H-2c), 3.43 (s, 3 H, CH_3O-e), 3.70 (s, 3 H, CH_3O-f), 5.74 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4d), 5.80 (d, 1 H, NH-c), and 7.30–8.18 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{101}H_{135}N_3O_{55}Si$ (2299.2): C, 52.76; H, 5.92; N, 1.82. Found: C, 52.97; H, 5.69; N, 1.76.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)-O-(3*-O-*acetyl-2,4-di*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β-D-glucopyranose* (**15**).—The 2-(trimethylsilyl)ethyl group in **14** (275 mg, 0.12 mmol) was removed in a fashion similar to that described for **11**, to get amorphous 1-hydroxy compound **15** (233 mg, 89%); $[\alpha]_D$ +10.0° (*c* 0.34, $CHCl_3$); ν_{max} 3400 (NH, OH), 1740 and 1230 (ester), 1670 and 1540 (amide), and 720 cm^{-1} (Ph).

Anal. Calcd for $C_{96}H_{123}N_3O_{55}$ (2199.0): C, 52.43; H, 5.64; N, 1.91. Found: C, 52.33; H, 5.69; N, 1.96.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)*-O-*(3*-O-*acetyl-2,4-di*-O-*benzoyl-β-D-galactopyranosyl(-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri*-O-*acetyl-β-D-glucopyranosyl trichloroacetimidate* (**16**).—A solution of **15** (225 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) was treated with trichloroacetonitrile (0.5 mL) as just described for **12**, to afford amorphous **16** (209 mg, 89%); $[\alpha]_D$ +16.9° (*c* 0.34, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.57–2.22 (19 s, 57 H, 3 $NCOCH_3$ and 16 $OCOCH_3$), 2.44 (dd, 1 H, $J_{3eq,4}$ 4.7 Hz, H-3e-*eq*), 2.53 (dd, 1 H, $J_{3eq,4}$ 4.7 Hz, H-3f-*eq*), 2.92 (m, 1 H, H-2c), 3.45 (s, 3 H, CH_3O-e), 3.74 (s, 3 H, CH_3O-f), 5.78 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4d), 6.11 (d, 1 H, NH-c), 6.49 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1a), 7.41–8.24 (m, 10 H, 2 Ph), and 8.69 (s, 1 H, C=NH).

Anal. Calcd for $C_{98}H_{123}Cl_3N_4O_{55}$ (2343.4): C, 50.23; H, 5.29; N, 2.39. Found: C, 50.21; H, 5.22; N, 2.35.

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-*[(methyl 5-acetamido-4,6,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-glucopyranosyl)-(1 → 1)-(2S,3R,4E)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**17**).—To a solution of **12** (195 mg, 0.081 mmol) in CH_2Cl_2 (2 mL)

were added (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[13,14b] (**8**, 68 mg, 0.16 mmol) and molecular sieves 4A (AW-300, 1.4 g). The mixture was stirred for 12 h at room temperature, then cooled to 0°. Boron trifluoride etherate (0.05 mL) was added, the mixture was stirred at 0° for 12 h, and CH_2Cl_2 (25 mL) was added. The insolubles were filtered off and washed with CH_2Cl_2. The combined filtrate and washings was washed with M Na_2CO_3 and water, dried (Na_2SO_4), and concentrated. Column chromatography (20:1 CH_2Cl_2–MeOH) of the residue on silica gel (40 g) gave amorphous **17** (137 mg, 63%); $[\alpha]_D$ +2.9° (*c* 0.28, $CHCl_3$); ν_{max} 3400 (NH), 2100 (N_3), 1740 and 1230 (ester), 1680 and 1540 (amide), and 720 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): (aglycon) δ 0.87 (s, 3 H, C*H*$_3$), 1.24 (s, 22 H, 11 C*H*$_2$), 5.87 (m, 1 H, $J_{4,5}$ 14.2, $J_{5,6} = J_{5,6'} = 7.7$ Hz, H-5); (pentasaccharide) δ 1.53–2.15 (18 s, 54 H, 3 NCOC*H*$_3$ and 15 OCOC*H*$_3$), 2.38 (dd, 1 H, H-3e-*eq*), 2.47 (dd, 1 H, H-3f-*eq*), 2.92 (m, 1 H, H-2c), 3.77 (s, 3 H, C*H*$_3$O-f), 3.80 (s, 3 H, C*H*$_3$O-e), 6.26 (d, 1 H, N*H*-c), and 7.41–8.31 (m, 20 H, 4 Ph).

Anal. Calcd for $C_{126}H_{162}N_6O_{57}$ (2672.7): C, 56.62; H, 6.10; N, 3.14. Found: C, 56.32; H, 6.21; N, 3.20.

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-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β*-D-*galacto-pyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-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* (**19**).—Compound **17** (127 mg, 0.048 mmol) was dissolved in aq 83% pyridine (15 mL) and cooled to 0°. Hydrogen sulfide gas was bubbled through the solution for 48 h at 0–15°, then it was concentrated. A solution of the residue (**18**) in CH_2Cl_2 was treated with octadecanoic acid (41 mg, 0.14 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC, 28 mg, 0.18 mmol) for 24 h at room temperature. The mixture was partioned between CH_2Cl_2 and water. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (20:1 CH_2Cl_2–MeOH) of the residue on silica gel (30 g) gave amorphous **19** (114 mg, 83%); $[\alpha]_D$ +43.8° (*c* 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$): (aglycon) δ 0.88 (s, 6 H, 2 C*H*$_3$), 1.25 (s, 50 H, 25 C*H*$_2$), 5.86 (m, 1 H, $J_{4,5}$ 14.2, $J_{5,6} = J_{5,6'} = 7.3$ Hz, H-5); (pentasaccharide) δ 1.53–2.15 (18 s, 54 H, 3 NCOC*H*$_3$ and 15 OCOC*H*$_3$), 2.43 (dd, 1 H, H-3e-*eq*), 2.52 (dd, 1 H, H-3f-*eq*), 2.92 (m, 1 H, H-2c), 3.74 (s, 3 H, C*H*$_3$O-f), 3.81 (s, 3 H, C*H*$_3$O-e), 6.26 (d, 1 H, N*H*-c), and 7.41–8.25 (m, 20 H, 4 Ph).

Anal. Calcd for $C_{144}H_{198}N_4O_{58}$ (2913.1): C, 59.37; H, 6.85; N, 1.92. Found: C, 59.09; H, 6.73; N, 1.99.

Ganglioside GC1α (**20**).—To a solution of **19** (100 mg, 0.034 mmol) in MeOH (5 mL) was added NaOMe (20 mg), and the mixture was stirred for 40 h at 45°. Water (0.5 mL) was added and the mixture was stirred for a further 16 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with 5:4:1 $CHCl_3$–MeOH–H_2O and the combined filtrate and

washings was concentrated. Column chromatography (5:4:1 $CHCl_3$–MeOH–H_2O) of the residue on silica gel (30 g) gave amorphous **20** (52.5 mg, 83%); $[\alpha]_D$ +3.4° (*c* 0.32, 5:4:1 $CHCl_3$–MeOH–H_2O); ν_{max} 3500–3300 (NH, OH), 2950 and 2840 (methyl, methylene), 1720 (COOH), and 1680 and 1540 cm^{-1} (amide); ^1H NMR [$(CD_3)_2SO$–D_2O]: (aglycon) δ 0.84 (s, 6 H, 2 CH_3), 1.23 (s, 50 H, 25 CH_2), 1.46 (br m, 2 H, $COCH_2CH_2$), 1.93 (q, 2 H, CH=CHCH_2), 2.01 (t, 2 H, $COCH_2$), 5.32 (dd, 1 H, $J_{3,4}$ 6.6, $J_{4,5}$ 15.4 Hz, H-4), 5.51 (m, 1 H, $J_{5,6(6')}$ 6.6 Hz, H-5); (pentasaccharide) δ 1.82, 1.87, 1.88 (3 s, 9 H, 3 $NCOCH_3$), 2.64 (dd, 1H, $J_{3eq,4}$ 4.4 Hz, H-3f-*eq*), 2.74 (dd, 1H $J_{3eq,4}$ 4.4 Hz, H-3e-*eq*), 3.03 (t, 1 H, H-2a), 3.84 (br d, 1 H, H-4b), 4.15 (d, 1 H, $J_{1,2}$ 8.01 Hz, H-1a), 4.20 (d, 1 H, $J_{1,2}$ 8.07 Hz, H-1b), 4.23 (d, 1 H, $J_{1,2}$ 7.33 Hz, H-1d), 4.50 (d, 1 H, $J_{1,2}$ 8.8 H-1c).

Anal. Calcd for $C_{84}H_{148}N_4O_{39}$ (1838.1): C, 54.88; H, 8.11; N, 3.04. Found: C, 54.61; H, 8.22; N, 3.05.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)*-O-*(3*-O-*acetyl-2,4-di*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-glucopyranosyl)-(1 → 1)-(2S,3R,4E)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**21**).—Coupling of **16** (190 mg, 0.081 mmol) with **8** (67 mg, 0.16 mmol), as described for **17**, yielded amorphous **21** (112 mg, 53%); $[\alpha]_D$ +0.7° (*c* 0.59, $CHCl_3$); ν_{max} 3400 (NH), 2100 (N_3), 1740 and 1230 (ester), 1680 and 1540 (amide), and 720 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): (aglycon) δ 0.85 (s, 3 H, CH_3), 1.21 (s, 22 H, 11 CH_2), 5.84 (m, 1 H, $J_{4,5}$ 14.6, $J_{5,6} = J_{5,6'} = 7.8$ Hz, H-5); (pentasaccharide) δ 1.54–2.18 (19 s, 57 H, 3 $NCOCH_3$ and 16 $OCOCH_3$), 2.42 (dd, 1 H, $J_{3eq,4}$ 4.7 Hz, H-3e-*eq*), 2.52 (dd, 1 H, $J_{3eq,4}$ 4.4 Hz, H-3f-*eq*), 2.88 (m, 1 H, H-2c), 3.40 (s, 3 H, CH_3O-e), 3.77 (s, 3 H, CH_3O-f), 5.84 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4d), 6.11 (d, 1 H, N*H*-c), and 7.33–8.15 (m, 15 H, 3 Ph).

Anal. Calcd for $C_{121}H_{160}N_6O_{57}$ (2578.6): C, 56.36; H, 6.25; N, 3.26. Found: C, 56.25; H, 6.29; N, 3.30.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)*-O-*(3*-O-*acetyl-2,4-di*-O-*benzoyl-β-D-galactopyranosyl)-(1 → 3)*-O-*[(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)]*-O-*(2-acetamido-4*-O-*acetyl-2-deoxy-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-galactopyranosyl)-(1 → 4)*-O-*(2,3,6-tri*-O-*acetyl-β-D-glucopyranosyl)-(1 → 1)-(2S,3R,4E)-3*-O-*benzoyl-2-octadeca-namido-4-octadecene-1,3-diol* (**23**).—Selective reduction of the azido group in **21** (107 mg, 0.041 mmol), and subsequent coupling of the product (**22**) with octadecanoic acid (35 mg, 0.12 mmol) as described for **19**, gave amorphous **23** (96 mg, 81%); $[\alpha]_D$ +3.8° (*c* 0.80, $CHCl_3$); ^1H NMR ($CDCl_3$): (aglycon) δ 0.87 (s, 3 H, CH_3), 1.25 (s, 50 H, 25 CH_2), 5.85 (m, 1 H, $J_{4,5}$ 14.6, $J_{5,6} = J_{5,6'} = 6.9$ Hz, H-5); (pentasaccharide) δ 1.55–2.20 (19 s, 57 H, 3 $NCOCH_3$ and 16 $OCOCH_3$), 2.44 (dd, 1 H, $J_{3eq,4}$ 4.6 Hz, H-3e-*eq*), 2.53 (dd, 1 H, $J_{3eq,4}$ 4.2 Hz, H-3f-*eq*), 2.80 (m, 1 H,

H-2c), 3.46 (s, 3 H, CH_3O-e), 3.80 (s, 3 H, CH_3O-f), 5.74 (d, 1 H, H-4d), 6.31 (d, 1 H, N*H*-c), and 7.33–8.15 (m, 15 H, 3 Ph).

Anal. Calcd for $C_{139}H_{196}N_4O_{58}$ (2851.1): C, 58.56; H, 6.93; N, 1.97. Found: C, 58.31; H, 6.99; N, 2.01.

O-*(5-Acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 6)*-O-β-D-*galactopyranosyl-(1 → 3)*-O-*[5-acetamido-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 6)]*-O-*(2-acetamido-2-deoxy*-β-D-*galacto-pyranosyl)-(1 → 4)*-O-β-D-*galactopyranosyl-(1 → 4)*-O-β-D-*glucopryanosyl(1 → 1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol (ganglioside GD1α positional isomer)* (**24**).—*O*-Deacylation and saponification of **23** (76 mg, 0.026 mmol), as described for **20**, yielded amorphous **24** (46 mg, 94%); $[\alpha]_D$ +1.2° (*c* 0.80, 5:4:1 $CHCl_3$–MeOH–H_2O); ν_{max} 3500–3300 (NH, OH), 2950 and 2840 (methyl, methylene), 1720 (COOH), and 1680 and 1540 cm^{-1} (amide); ^1H NMR [$(CD_3)_2SO$–D_2O]: (aglycon) δ 0.88 (s, 6 H, 2 CH_3), 1.25 (s, 50 H, 25 CH_2), 1.46 (br m, 2 H, $COCH_2CH_2$), 1.93 (q, 2 H, CH=CHCH_2), 2.01 (t, 2 H, COCH_2), 5.33 (dd, 1 H, $J_{3,4}$ 6.3, $J_{4,5}$ 14.6 Hz, H-4), 5.53 (m, 1 H, $J_{5,6(6')}$ 7.1 Hz, H-5); (pentasaccharide) δ 1.37 (t, 1 H, $J_{gem} = J_{3ax,4} = 12$ Hz, H-3e-*ax*), 1.82, 1.87, 1.88 (3 s, 9 H, 3 NCOCH_3), 2.64 (2 dd, 2 H, H-3e-*eq* and H-3f-*eq*), 3.03 (t, 1 H, H-2a), 3.84 (br d, 1 H, H-4b), 4.16 (d, 1 H, $J_{1,2}$ 7.33 Hz, H-1a), 4.18 (d, 1 H, $J_{1,2}$ 7.51 Hz, H-1b), 4.21 (d, 1 H, $J_{1,2}$ 8.06 Hz, H-1d), 4.56 (d, 1 H, $J_{1,2}$ 8.23 Hz, H-1c).

Anal. Calcd for $C_{84}H_{148}N_4O_{39}$ (1838.1): C, 54.88; H, 8.11; N, 3.04. Found: C, 54.66; H, 8.28; N, 3.00.

ACKNOWLEDGMENT

This work was supported in part by Grants-in-Aid No. 03255207 and 03660133, respectively for Research on Priority Areas and for Scientific Research, from the Japanese Ministry of Education, Science and Culture.

REFERENCES

1 H. Prabhanjan, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 222 (1991) c1–c4.
2 T. Taki, Y. Hirabayashi, H. Ishikawa, S. Ando, K. Kon, Y. Tanaka, and M. Matsumoto, *J. Biol. Chem.*, 261 (1986) 3075–3078.
3 Y. Hirabayashi, A. Hyogo, T. Nakao, K. Tsuchiya, Y. Suzuki, M. Matsumoto, K. Kon, and S. Ando, *J. Biol. Chem.*, 265 (1990) 8144–8151.
4 M. Ohashi, in T. Yamakawa, T. Osawa, and S. Handa (Eds.), *Glycoconjugates: Proceedings of the VIth International Symposium on Glycoconjugates*, Japan Scientific Societies Press, Tokyo, 1981, pp. 33–34.
5 (a) K.P.R. Kartha, A. Kameyama, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 145–158; (b) T. Murase, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 188 (1989) 71–80; (c) T. Murase, A. Kameyama, K.P.R. Kartha, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 265–283; (d) A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 193 (1989) c1–c5; (e) A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 799–804; (f) A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 200 (1990) 269–285; (g) A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 209 (1991)

c1–c4; (h) A. Hasegawa, T. Murase, K. Adachi, M. Morita, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 9 (1990) 181–199; (i) A. Hasegawa, T. Murase, M. Morita, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 9 (1990) 201–214; (j) A. Hasegawa, K. Hotta, A. Kameyama, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 10 (1991) 439–459.

6 (a) T. Murase, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 184 (1988) c1–c4.; (b) A. Hasegawa, H. Ohki, T. Nagahama, H. Ishida, and M. Kiso, *Carbohydr. Res.*, 212 (1991) 277–281; (c) A. Hasegawa, T. Nagahama, H. Ohki, K. Hotta, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 10 (1991) 493–498.

7 (a) P. Fügedi and P.J. Garegg, *Carbohydr. Res.*, 149 (1986) c9–c12; (b) O. Kanie, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 7 (1988) 501–506.

8 (a) H. Prabhanjan, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 211 (1991) c1–c5; (b) H. Prabhanjan, A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 220 (1991) 127–143.

9 R.R. Schmidt, M. Behrendt, and A. Toepfer, *Synlett*, (1990) 694–697; (b) A.J. Ratcliffe and B. Fraser-Reid, *J. Chem. Soc., Perkin Trans. 1*, (1990) 747–750.

10 Y. Hirabayashi, unpublished.

11 U. Dabrowski, H. Friebolin, R. Brossmer, and M. Supp, *Tetrahedron Lett.*, 48 (1979) 4637–4640.

12 (a) R.R. Schmidt and G. Grundler, *Synthesis*, (1981) 885–887; (b) M. Numata, M. Sugimoto, K. Koike, and T. Ogawa, *Carbohydr. Res.*, 163 (1987) 209–225.

13 Y. Ito, M. Kiso and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 285–294.

14 (a) M. Kiso, A. Nakamura, T. Tomita, and A. Hasegawa, *Carbohydr. Res.*, 158 (1986) 101–111; (b) R.R. Schmidt and P. Zimmermann, *Angew. Chem. Int. Ed. Engl.*, 25 (1986) 725–726.

15 T. Adachi, Y. Yamada, I. Inoue, and M. Saneyoshi, *Synthesis*, (1977) 45–46.