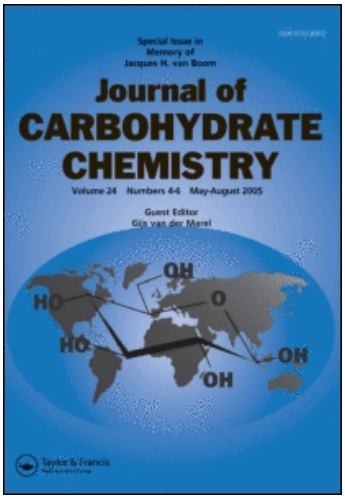

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Synthetic Studies on Sialoglycoconjugates 82: First Total Synthesis of Sialyl Globopentaosyl Ceramide (V^{3}Neu5AcGb5Cer) and its Positional Isomer (V^{6}Neu5AcGb5Cer)^{1,2}

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 82: FIRST TOTAL SYNTHESIS OF SIALYL GLOBOPENTAOSYL CERAMIDE (V^3Neu5AcGb5Cer) AND ITS POSITIONAL ISOMER (V^6Neu5AcGb5Cer)[1,2]

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ABSTRACT

The first, total synthesis of sialyl globopentaosyl ceramide (V^3Neu5AcGb5Cer) and its positional isomer (V^6Neu5AcGb5Cer) are described. α-Selective glycosylation of 2-(trimethylsilyl)ethyl *O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**7**) with the suitably protected galactose donor, methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside gave the desired trisaccharide, which was transformed into the trisaccharide acceptor, by removal of the *O*-acetyl group. Glycosylation of this acceptor with methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside gave the globotetraose derivative, which was transformed into the acceptor **12** by removal of the phthaloyl and *O*-acetyl groups followed by *N*-acetylation. DMTST promoted coupling of this acceptor 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 sialyl globopentaoside derivative in good yield, which was transformed, by removal of the benzyl and benzylidene groups followed by *O*-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group and subsequent imidate formation, into the final glycosyl donor **17**. Condensation of this imidate derivative with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**18**)

gave the β-glycoside, which on channeling through selective reduction of the azido group, coupling of the amino group with octadecanoic acid, *O*-deacylation and saponification of the methyl ester group, gave the title compound, sialyl globopentaosyl ceramide. The positional isomer was also obtained by coupling of the globotetraose acceptor with methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside, followed by essentially the same procedure employed for the synthesis of sialyl globopentaosyl ceramide.

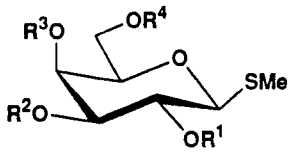
INTRODUCTION

The globo-series gangliosides have a unique molecule surface topology, and are involved in the process of embryogenesis and/or differentiation of cultured teratocarcinoma cells as developmentally regulated antigens.[3,4] Sialyl globopentaosyl ceramide ($V^3Neu5AcGb_5Cer$), one of the extended globo-series gangliosides, was first isolated from adult leghorn chicken pectoral muscle,[5] and almost stimultaneously from a human teratocarcinoma cell line.[6] This ganglioside is defined also as the antigen which is recognized by a monoclonal antibody against stage-specific embryonic antigen (SSEA)-4.[7]

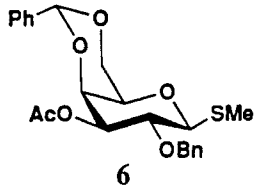
In previous papers, we have reported[8,9,10] the total synthesis of ganglio-, lacto-, neolacto-, and polysialo-series gangliosides during the course of the structure function relationship study of gangliosides at the molecular level. We describe herein a first total synthesis of sialyl globopentaosyl ceramide and its positional isomer, as a part of our continuing study described above.

RESULTS AND DISCUSSION

For the synthesis of the desired globo-series gangliosides **22** and **31**, we have selected methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**6**) as a key glycosyl donor, which is suitable for α-galactosylation of the lactoside derivative to prepare the globotriose derivative. The appropriately protected galactose donor **6** was obtained in good yield from methyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside[11] (**1**) by 6-*O*-*t*-butyldimethylsilylation,



	R^1	R^2	R^3	R^4
1	H	isopropylidene		H
2	H	isopropylidene		TBDMS
3	Bn	isopropylidene		TBDMS
4	Bn	H	H	H
5	Bn	H	benzylidene	
6	Bn	Ac	benzylidene	



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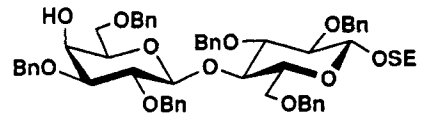

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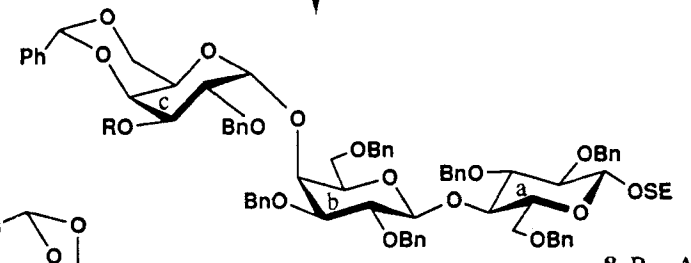
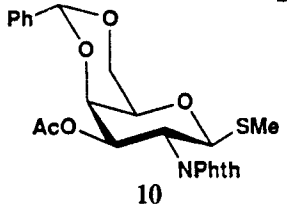


8 R = Ac
9 R = H



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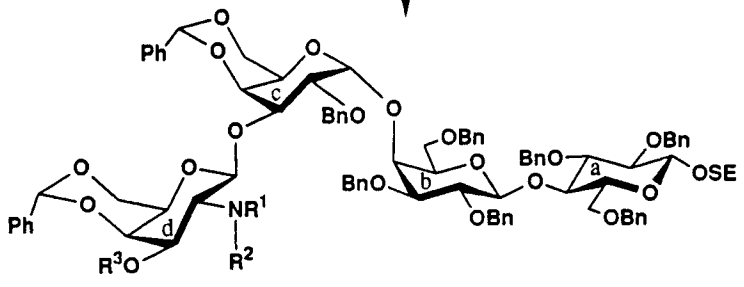
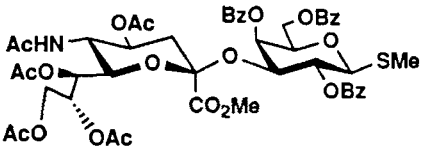


11 R^1 : R^2 = Phth, R^3 = Ac
12 R^1 = H, R^2 = Ac, R^3 = H

TBDMS = *tert*-butyldimethylsilyl
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
phth = phthaloyl



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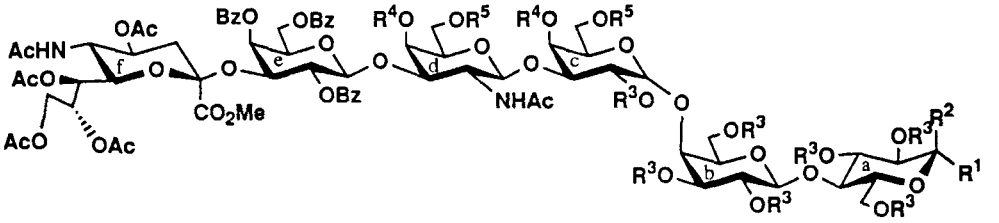
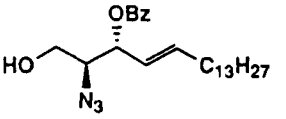


	R^1	R^2	R^3	R^4	R^5
14	OSE	H	Bn	benzylidene	
15	OSE	H	Ac	Ac	Ac
16	H , OH		Ac	Ac	Ac
17	H	$OC(=NH)CCl_3$	Ac	Ac	Ac



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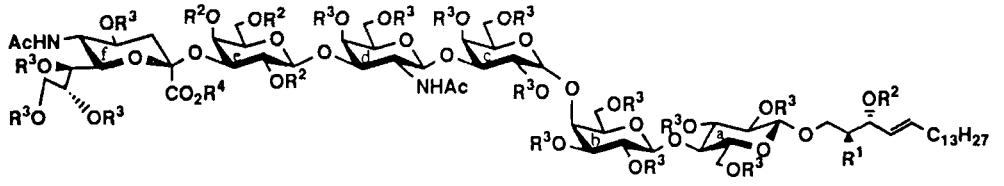


	R^1	R^2	R^3	R^4
19	N_3	Bz	Ac	Me
20	NH_2	Bz	Ac	Me
21	$CO(CH_2)_{16}CH_3$	Bz	Ac	Me
22	$NHCO(CH_2)_{16}CH_3$	H	H	H

Bz = benzoyl

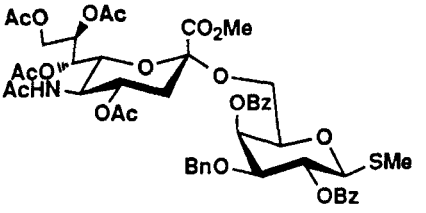
2-*O*-benzylation, acidic hydrolysis of the isopropylidene and silyl groups, 4,6-*O*-benzylidenation and 3-*O*-acetylation. The glycosylation of 2-(trimethylsilyl)ethyl *O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[12] (**7**) with **1** in dichloromethane for 6 h at -40 °C in the presence of *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH)[13,14] and powdered molecular sieves 4Å (MS-4Å) afforded the desired α-glycoside **8** in 84% yield. The observed chemical shift and coupling constant of the introduced galactose residue for H-1 (δ 5.15, $J_{1,2}$ = 3.3 Hz) indicated the newly formed glycosidic linkage to be α. *O*-Deacetylation of **8** afforded the globotriose acceptor **9**.

Condensation of **9** with methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside[15] (**10**) at room temperature in a similar procedure as described for the glycosylation of **6** with **7** gave a globotetraose derivative **11** in 64% yield. *O*-Deacetylation of **11** and conversion of the phthalimide to the acetamide by heating with hydrazine hydrate in aqueous 95% ethanol followed by *N*-acetylation with acetic anhydride afforded the desired globotetraose acceptor **12**.

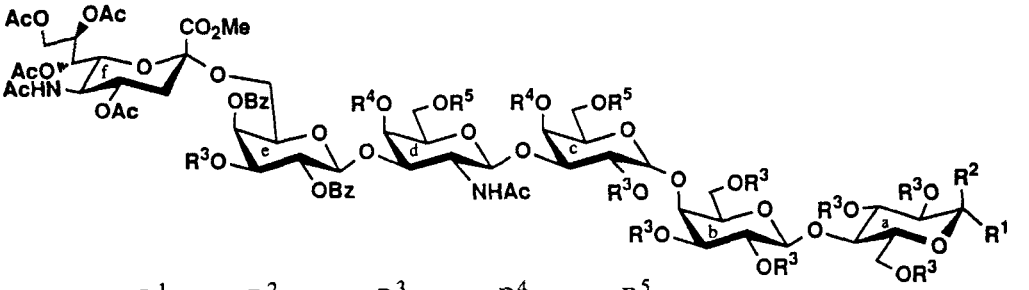
Glycosylation of **12** with sialyl α(2→3) galactose donor **13**[16] (2.0 equiv to the acceptor) in dichloromethane for 24 h at 0 °C in the presence of dimethyl-(methylthio)sulfonium triflate (DMTST, 4.0 equiv to the acceptor) and powdered MS 4Å gave the expected hexasaccharide derivative **14** in 56% yield.

Catalytic hydrogenolysis over 10% Pd-C in ethanol-acetic acid of the benzyl and benzylidene groups in **14** and subsequent *O*-acetylation gave the hexasaccharide derivative **15** in 70% yield. Treatment[12] of **15** with trifluoroacetic acid in dichloromethane for 30 min at room temperature gave the 1-hydroxy compound **16**. When treated with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 3 h at 0 °C, **16** gave the α-trichloroacetimidate **17** in 80% yield.

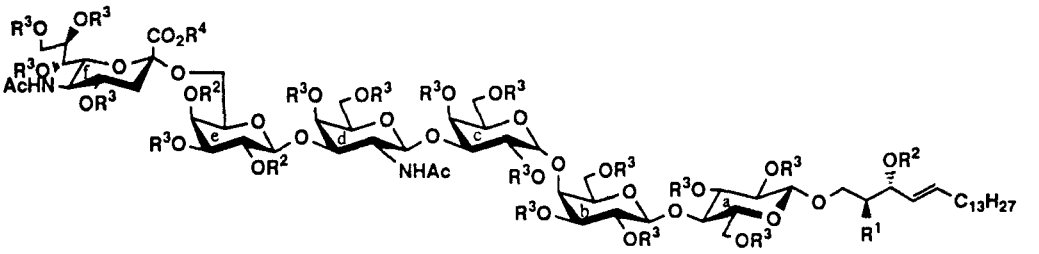
The final glycosylation[17] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[17b,18] (**18**) with **17** in dichloromethane in the presence of boron trifluoride etherate for 8 h at room temperature afforded the desired β-glycoside **19** in 52% yield. Selective reduction[19] of the azido group in **19** with hydrogen sulfide in aqueous 83%



23 + 12 ⟶



	R^1	R^2	R^3	R^4	R^5
24	OSE	H	Bn	benzylidene	
25	OSE	H	Ac	Ac	Ac
26	H , OH		Ac	Ac	Ac
27	H	$OC(=NH)CCl_3$	Ac	Ac	Ac



	R^1	R^2	R^3	R^4
28	N_3	Bz	Ac	Me
29	NH_2	Bz	Ac	Me
30	$CO(CH_2)_{16}CH_3$	Bz	Ac	Me
31	$NHCO(CH_2)_{16}CH_3$	H	H	H

pyridine for 7 days at 0 °C gave the amine, and this on condensation with octadecanoic acid, using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) in dichloromethane gave the acylated sialyl globopentaosyl ceramide **21** in 80% yield, after chromatography.

Finally, *O*-deacylation of **21** with sodium methoxide in methanol, and subsequent saponification of the methyl ester group, yielded the desired sialyl globopentaosyl ceramide **22**, α-Neu5Ac-(2→3)-β-D-Gal-(1→3)-β-D-GalNAc-(1→3)-α-D-Gal-(1→4)-β-D-Gal-(1→4)-β-D-Glc-(1→1)-Cer, in a quantitative yield after chromatography on a column of Sephadex LH-20.

A positional isomer of sialyl globopentaosyl ceramide in regard to Neu5Ac, α-Neu5Ac-(2→6)-β-D-Gal-(1→3)-β-D-GalNAc-(1→3)-α-D-Gal-(1→4)-β-D-Gal-(1→4)-β-D-Glc-(1→1)-Cer was synthesized by coupling of the globotetraose acceptor **12** and sialyl α(2→6)galactose donor **23**,[16] followed by the manipulation of the protecting groups and introduction of the ceramide moiety in essentially the same way as described for the synthesis of sialyl globopentaosyl ceramide **22**.

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*.

Methyl 6-*O*-*tert*-Butyldimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (2). To a stirred solution of methyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**1**, 1.9 g, 7.5 mmol) was added *tert*-butyldimethylsilyl chloride (1.75 g, 11.25 mmol) at 0 °C; stirring was continued at room temperature for 2 h. After addition of methanol, the solution was concentrated to a syrup, which was extracted with dichloromethane. The extract was successively washed with 2 M

hydrochloric acid and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:6 AcOEt-hexane) of the residue on silica gel gave **2** (2.5 g, 90%): mp 90-92 °C: $[\alpha]_D$ +7° (*c* 0.4, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.81 (s, 9H, Me_3C), 1.26 and 1.44 (2s, 6H, Me_2C), 2.12 (s, 3H, MeS), 2.76 (s, 1H, OH), 3.48 (dd, 1H, $J_{1,2}$ = 10.0 Hz, $J_{2,3}$ = 7.1 Hz, H-2), 4.01 (d, 1H, H-1), 4.17 (dd, 1H, $J_{3,4}$ = 1.8 Hz, H-3).

Anal. Calcd for $C_{16}H_{32}O_5SSi$ (364.5): C, 52.71; H, 8.84. Found: C, 52.57; H, 9.01.

Methyl 2-*O*-Benzyl-6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (3). To a solution of **2** (3.05 g, 8.0 mmol) in *N,N*-dimethylformamide (DMF; 20 mL) was added a suspension of sodium hydride in oil (481 mg, 11.0 mmol; 60% of sodium hydride by weight) at 0 °C, and the mixture was stirred for 30 min at 0 °C. Benzyl bromide (1.4 mL, 12 mmol) was added dropwise, and the mixture was stirred for 3 h at room temperature. After addition of methanol, the mixture was concentrated to a syrup, which was extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:6 AcOEt-hexane) of the residue on silica gel gave **3** (3.76 g, quant.) as a syrup: $[\alpha]_D$ +20° (*c* 0.8, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.80 (s, 9H, Me_3C), 1.25 and 1.44 (2s, 6H, Me_2C), 2.10 (s, 3H, MeS), 3.36 (dd, 1H, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 6.2 Hz, H-2), 3.68 (m. 1H, H-5), 3.76 (near s, 1H, H-4), 3.78 (dd, 1H, $J_{3,4}$ = 1.3 Hz, H-3), 4.16 (m, 2H, H-6,6'), 4.22 (d, 1H, H-1), and 4.76 and 4.93 (2d, 2H, J_{gem} = 10.6 Hz, CH_2Ph).

Anal. Calcd for $C_{23}H_{38}O_5SSi$ (454.7): C, 60.75; H, 8.42. Found: C, 60.72; H, 8.12.

Methyl 2-*O*-Benzyl-1-thio-β-D-galactopyranoside (4). A solution of **3** (2.0 g, 4.2 mmol) in aqueous 80% acetic acid (10 mL) was heated for 6 h at 60 °C and concentrated. Recrystallization of the residue from ether gave **4** (1.2 g, 100%) as crystals: mp 161-162 °C: $[\alpha]_D$ +17° (*c* 0.4, CH_2Cl_2).

Anal. Calcd for $C_{14}H_{20}O_5S$ (300.4.): C, 55.98; H, 6.71. Found: C, 55.78; H, 6.59.

Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (5). To a solution of **4** (1.2 g, 3.9 mmol) in DMF (10 mL) was added Drierite (1 g) and the mixture was stirred for 2 h at room temperature. Benzaldehyde dimethyl acetal (1.2 mL, 7.8 mmol) and *p*-toluenesulfonic acid (6 mg) were added, and the mixture was stirred for 24 h at room temperature, then neutralized with $NaHCO_3$ and concentrated. Column chromatography (1:2 AcOEt-hexane) of the residue on silica gel afforded **5** (1.2 g, 85%) as an amorphous mass: $[\alpha]_D$ -6° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.27 (s, 3H, MeS), 3.45 (d, 1H, H-4), 3.65 (t, 1H, $J_{1,2}$ = 9.4 Hz, $J_{2,3}$ = 9.2 Hz, H-2), 4.01 (dd, 1H, J_{gem} = 12.6 Hz, H-6), 4.32 (dd, 1H, H-6'), 4.35 (d, 1H, H-1), 4.78 and 4.93 (2d, 2H, J_{gem} = 11.5 Hz, CH_2Ph), 7.25-7.52 (m, 5H, Ph).

Anal. Calcd for $C_{21}H_{24}O_5S$ (388.5): C, 64.93; H, 6.23. Found: C, 64.66; H, 6.18.

Methyl 3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside (6). A solution of **5** (2.5 g, 6.4 mmol) in acetic anhydride (5 mL) and pyridine (10 mL) was stirred for 2 h at room temperature, and methanol (5 mL) was added. The solution was concentrated to a syrup, which was extracted with dichloromethane. The extract was successively washed with 2 M hydrochloric acid and water, dried (Na_2SO_4) and concentrated. Recrystallization of the residue from AcOEt-hexane gave **6** (2.6 g, 100%): mp 167-168 °C, $[\alpha]_D$ +71° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.04 (s, 3H, AcO), 2.28 (s, 3H, MeS), 3.53 (d, 1H, $J_{4,5}$ = 1.0 Hz, H-4), 3.92 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 9.6 Hz, H-2), 3.97 (dd, 1H, $J_{5,6}$ = 2.0 Hz, J_{gem} = 12.5 Hz, H-6), 4.32 (dd, 1H, $J_{5,6'}$ = 1.7 Hz, H-6'), 4.65 and 4.93 (2d, 2H, J_{gem} = 11.0 Hz, CH_2Ph), 4.94 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-3), 5.48 (s, 1H, PhC*H*), 7.22-7.57 (m, 10H, 2Ph).

Anal. Calcd for $C_{23}H_{26}O_6S$ (430.52): C, 64.17; H, 6.09. Found: C, 64.11; H, 5.88.

2-(Trimethylsilyl)ethyl *O*-(3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-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 (8).

To a solution of **6** (235 mg, 0.76 mmol) and 2-(trimethylsilyl)ethyl *O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[12] (**7**, 500 mg, 0.50 mmol) in dry dichloromethane (5 mL) were added powdered molecular sieves 4Å (MS-4Å, 800 mg), and the mixture was stirred for 6 h at room temperature then cooled to -40 °C. To the cooled mixture were added, with stirring, *N*-iodosuccinimide (NIS, 374 mg, 1.5 mmol) and trifluoromethanesulfonic acid (TfOH, 13.5 μL, 0.15 mmol), and the stirring was continued for 6 h at -40 °C. The precipitate was removed by filtration and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3, M $Na_2S_2O_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:4 AcOEt-hexane) of the residue on silica gel gave **8** (531 mg, 84%) as an amorphous mass: $[\alpha]_D$ +60° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.87 (s, 3H, AcO), 3.40 and 3.60 (m, 2H, $Me_3SiCH_2CH_2$), 5.15 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1c), 5.24 (dd, 1H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 3.4 Hz, H-3c), 5.29 (s, 1H, PhC*H*), and 7.14-7.37 (m, 40H, 8Ph).

Anal. Calcd for $C_{81}H_{92}O_{17}Si$ (1365.7): C, 71.23; H, 6.79. Found: C, 70.98; H, 6.75.

2-(Trimethylsilyl)ethyl *O*-(2-*O*-Benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (9). To a solution of **8** (500 mg, 0.40 mmol) in methanol (1 mL) was added sodium methoxide (20 mg), and the mixture was stirred for 2 h at room temperature. The solution was treated with Amberlite IR-120 (H^+) resin, and the resin was removed by filtration. The resin was washed with methanol, and the combined filtrate and washings were concentrated. Column chromatography (1:4 AcOEt-hexane) of the residue on silica gel gave **9** (483 mg, 99%) as an amorphous mass: $[\alpha]_D$ +53° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 3.40 and 3.60 (m, 2H, $Me_3SiCH_2CH_2$), 5.15 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1c), and 7.12-7.39 (m, 40H, 8Ph).

Anal. Calcd for $C_{79}H_{90}O_{16}Si$ (1323.6): C, 71.63; H, 6.85. Found: C, 71.48; H, 6.57.

2-(Trimethylsilyl)ethyl *O*-(3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-(1→3)-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-α-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 (11). To a solution of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (**10**, 190 mg, 0.61 mmol) and **9** (495 mg, 0.41 mmol) in dry dichloromethane (5 mL) were added powdered MS-4Å (600 mg), and the mixture was stirred for 6 h at room temperature then cooled to 0 °C. To the cooled mixture were added, with stirring, NIS (303 mg, 1.2 mmol) and TfOH (10.9 μL, 0.12 mmol), and the stirring was continued for 6 h at room temperature. The precipitate was removed by filtration and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3, M $Na_2S_2O_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:4 AcOEt-hexane) of the residue on silica gel gave **11** (382 mg, 64%) as an amorphous mass: $[\alpha]_D$ +32° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.84 (s, 3H, AcO), 3.40 and 3.60 (m, 2H, $Me_3SiCH_2CH_2$), 5.42 and 5.43 (2s, 2H, 2PhC*H*), 5.59 (dd, 1H, $J_{2,3}$ = 11.5 Hz, $J_{3,4}$ = 3.7 Hz, H-3d), and 6.89-7.64 (m, 49H, phenyl).

Anal. Calcd for $C_{102}H_{109}NO_{23}Si$ (1745.06): C, 70.20; H, 6.29; N, 0.80. Found: C, 70.29; H, 6.16; N, 0.79.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-α-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 (12). A solution of **11** (1.1 g, 0.63 mmol) in aq 95% ethanol (20 mL) was treated with hydrazine hydrate (0.36 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 treated with acetic anhydride (2 mL) in methanol (10 mL) for 2 h at room temperature, pyridine (3 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2M HCl and water, dried (Na_2SO_4),

and concentrated. Column chromatography (1:1 AcOEt-hexane) of the residue on silica gel afforded **12** (793 mg, 80%) as an amorphous mass: $[\alpha]_D$ +48° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.46 (s, 3H, AcN), 3.40 and 3.60 (m, 2H, $Me_3SiCH_2CH_2$), 5.19 (d, 1H, $J_{1,2}$ = 10.2 Hz, H-1d), 5.38 and 5.44 (2s, 2H, 2PhC*H*), 5.70 (d, 1H, NH), and 7.08-7.47 (m, 45H, 9Ph).

Anal. Calcd for $C_{94}H_{107}NO_{21}Si$ (1572.9): C, 70.25; H, 6.72; N, 0.89. Found: C, 70.26; H, 6.83; N, 0.78.

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-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-α-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 (14). To a solution of 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 (**13**, 272 mg, 0.27 mmol) and **12** (220 mg, 0.13 mmol) in CH_2Cl_2 (5 mL) was added MS-4Å (200 mg), and the mixture was stirred for 6 h at room temperature then cooled to 0 °C. To the mixture was added, with stirring, dimethyl(methylthio)sulfonium triflate (282 mg, 1.08 mmol), and the stirring was continued for 24 h at 0 °C. The precipitates were removed by filtration, and washed thoroughly with CH_2Cl_2. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (50:1 CH_2Cl_2-MeOH) of the residue on silica gel gave **14** (187 mg, 56%) as an amorphous mass: $[\alpha]_D$ +30° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.57 and 1.65 (2s, 6H, 2AcN), 1.77, 1.89, 2.07, 2.18 (4s, 12H, 4AcN), 2.39 (dd, 1H, J_{gem} = 12.1 Hz, $J_{3eq,4}$ = 3.5 Hz, H-3f*eq*), 3.81 (s, 3H, MeO), 5.29 and 5.33 (2s, 2H, 2PhC*H*), 5.50 (m, 1H, H-8f), and 6.97-8.10 (m, 60H, 12Ph).

Anal. Calcd for $C_{141}H_{156}N_2O_{41}Si$ (2562.86): C, 66.08; H, 6.13; N, 1.09. Found: C, 65.94; H, 6.30; N, 0.91.

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-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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 (15). A solution of **14** (218 mg, 0.09 mmol) in EtOH (10 mL) and acetic acid (2 mL) was hydrogenated in the presence of 10% Pd-C (200 mg) for 24 h at 40 °C, the catalyst removed by filtration and the solution concentrated. The residue was acetylated with acetic anhydride (2 mL) and pyridine (3 mL) for 6 h at room temperature. The product was purified by chromatography on a column of silica gel with 50:1 CH_2Cl_2-MeOH to give **15** (132 mg, 70%) as an amorphous mass: $[\alpha]_D$ +19° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.92 (m, 2H, $Me_3SiCH_2CH_2$), 1.39 and 1.54 (2s, 6H, 2AcN), 1.76-2.13 (15s, 45H, 15AcO), 2.46 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3f*eq*), 3.80 (s, 3H, MeO), 5.53 (dd, 1H, $J_{6,7}$ = 3.4 Hz, $J_{7,8}$ = 10.4 Hz, H-7f), 5.60 (m, 1H, H-8f), and 7.29-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{100}H_{128}N_2O_{52}Si$ (2218.17): C, 54.14; H, 5.81; N, 1.26. Found: C, 54.11; H, 5.51; N, 1.18.

***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-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranose (16).** To a solution of **15** (117.7 mg, 0.053 mmol) in CH_2Cl_2 (1 mL) was added trifluoroacetic acid (1 mL) at 0 °C, and the mixture was stirred for 30 min at room temperature and concentrated. Column chromatography (30:1 CH_2Cl_2-MeOH) of the residue on silica gel gave **16** (98.8 mg, 88%) as an amorphous mass: ^1H NMR ($CDCl_3$) δ 1.32 and 1.39 (2s, 6H, 2AcN), 1.77-2.09 (15s, 45H, 15AcO), 2.44 (dd, 1H, J_{gem} = 12.9 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3f*eq*), 3.81 (s, 3H, MeO), and 7.23-8.19 (m, 15H, 3Ph).

Anal. Calcd for $C_{95}H_{116}N_2O_{52}$ (2117.93): C, 53.87; H, 5.52; N, 1.32. Found: C, 53.73; H, 5.69; N, 1.14.

***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-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (17).** To a solution of **16** (71 mg, 0.029 mmol) in CH_2Cl_2 (1 mL) and trichloroacetonitrile (87.6 μL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 4.3 μL) at 0 °C, and the mixture was stirred for 3 h at 0 °C, then concentrated. Column chromatography (20:1 CH_2Cl_2-MeOH) of the residue on silica gel gave **17** (59.9 mg, 80%) as an amorphous mass: $[\alpha]_D$ +47° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.25 and 1.39 (2s, 6H, 2AcN), 1.90-2.18 (15s, 45H, 15AcO), 2.44 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3f*eq*), 3.81 (s, 3H, MeO), 6.41 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1a), and 7.16-8.72 (m, 15H, 3Ph).

Anal. Calcd for $C_{98}H_{116}N_3O_{52}Cl_3$ (2274.35): C, 51.75; H, 5.14; N, 1.84. Found: C, 51.72; H, 4.84; 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→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (19).** To a solution of **17** (48.3 mg, 0.021 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[18] (**18**, 36.3 mg, 0.084 mmol) in CH_2Cl_2 (2 mL) were added 4Å molecular sieves (AW-300, 0.5 g) and the mixture was stirred for 3 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (5.2 μL) was added, and the mixture was stirred for 8 h at room temperature and then filtered. The insoluble materials were washed with CH_2Cl_2, and

the combined filtrate and washings were washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (20:1 CH_2Cl_2-MeOH) of the residue on silica gel gave **19** (27.6 mg, 52%) as an amorphous mass: $[\alpha]_D$ +59° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J_{Me, CH_2} = 6.6 Hz, *Me*CH_2), 1.25 (s, 22H, 11CH_2), 1.42 and 1.53 (2s, 6H, 2AcN), 1.77-2.15 (15s, 45H, 15AcO), 2.45 (dd, 1H, J_{gem} = 12.9 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3*eq*), 3.82 (s, 3H, MeO), and 7.16-8.19 (m, 20H, 4Ph).

Anal. Calcd for $C_{120}H_{153}N_5O_{54}$ (2529.52): C, 56.97; H, 6.09; N, 2.76. Found: C, 56.72; H, 6.05; 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→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (21).** Hydrogen sulfide was bubbled through a stirred solution of **19** (15.1 mg, 5.9 μmol) in aq 83% pyridine (10 mL) for 7 days at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (3.4 mg, 11.8 μmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (3.4 mg, 17.7 μmol) in CH_2Cl_2 (1 mL) for 8 h at room temperature. Dichloromethane (20 mL) was added, and the mixture was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (15:1 CH_2Cl_2-MeOH) of the residue on silica gel gave **21** (13.6 mg, 80%) as an amorphous mass: $[\alpha]_D$ +35° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (t, 6H, J_{Me, CH_2} = 7.0 Hz, 2*Me*CH_2), 1.25 (s, 52H, 26CH_2), 1.43 and 1.52 (2s, 6H, 2AcN), 1.77-2.15 (15s, 45H, 15AcO), 2.45 (dd, 1H, J_{gem} = 12.7 Hz, $J_{3eq,4}$ = 4.3 Hz, H-3*eq*), 3.82 (s, 3H, MeO), 5.00 (m, 1H, H-8f), 5.42 (m, 1H, H-7f), 5.83 (m, 1H, H-5 of ceramide), and 7.26-8.20 (m, 20H, 4Ph).

Anal. Calcd for $C_{148}H_{189}N_3O_{55}$ (2890.11): C, 61.51; H, 6.59; N, 1.45. Found: C, 61.30; H, 6.31; N, 1.47.

O-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-O-β-D-galactopyranosyl-(1→3)-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→3)-O-α-D-galactopyranosyl-(1→4)-O-(β-D-galactopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol (22). To a solution of **21** (8.3 mg, 2.8 μmol) in MeOH (1 mL) was added a catalytic amount of NaOMe, and the mixture was stirred for 6 h at 40 °C. Water (0.5 mL) was added and the mixture was stirred for additional 6 h at 40 °C, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with methanol, and the filtrate and washings were combined and concentrated. Column chromatography (5:4:0.7 $CHCl_3$-MeOH-H_2O) of the residue on Sephadex LH-20 gave **17** (5.8 mg, quant.). $[\alpha]_D$ -3.0° (*c* 0.6, 5:4:0.7 $CHCl_3$-MeOH-H_2O); ^1H NMR (1:1 DMSO-d6-D_2O) δ 0.86 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 1.48 (m, 2H, COC*H*$_2$$CH_2$), 1.82 and 1.89 (2s, 6H, 2AcN), 2.50 (dd, 1H, H-3f*eq*).

Anal. Calcd for $C_{104}H_{153}N_3O_{41}$ (2101.35): C, 59.44; H, 7.33; N, 1.99. Found: C, 59.53; H, 7.20; N, 1.98.

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-4,6-O-benzylidene-2-deoxy-β-D-galactopyranosyl)-(1→3)-O-(2-O-benzyl-4,6-O-benzylidene-α-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 (24). Glycosylation of **12** (973 mg, 0.60 mmol) 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-di-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**23**, 900 mg, 0.91 mmol) in a fashion similar to that described for **14**, afforded amorphous **24** (874 mg, 57%): $[\alpha]_D$ +42° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.98 (m, 2H, $Me_3SiCH_2CH_2$), 1.82 (s, 6H, 2AcN), 1.97-2.10 (4s, 12H, 4AcO), 2.54 (dd, J_{gem} = 12.6 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3f*eq*), 3.45 (s, 3H, MeO), 5.02 (d, 1H, $J_{1,2}$ = 3.48 Hz, H-1c), 5.37, 5.64 (2s, 6H, 2PhC*H*), and 7.00-8.11 (m, 60H, 12Ph).

Anal. Calcd for $C_{148}H_{158}N_2O_{40}Si$ (2632.95): C, 67.51; H, 6.05; N, 1.06. Found: C, 67.23; H, 6.05; N, 0.85.

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*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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 (25). The benzyl and benzylidene groups in **24** (842 mg, 0.33 mmol), dissolved in 5:1 EtOH-acetic acid (6 mL), were removed by hydrogenolytic cleavage over 10% Pd-C (584 mg). The deprotected product was acetylated as described for **15**, to give amorphous **25** (383 mg, 63%): $[\alpha]_D$ +43° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.73 (m, 2H, $Me_3SiCH_2CH_2$), 1.84 and 1.88 (2s, 6H, 2AcN), 1.91-2.24 (16s, 48H, 16AcO), 2.48 (dd, J_{gem} = 12.5 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3*eq*), 3.47 (s, 3H, MeO), 4.88 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1c), 5.58 (d, 1H, $J_{3,4}$ = 2.2 Hz, H-3 for Gal), and 7.27-8.14 (m, 10H, 2Ph).

Anal. Calcd for $C_{95}H_{126}N_2O_{52}Si$ (2156.10): C, 52.92; H, 5.89; N, 1.30. Found: C, 52.65; H, 5.84; N, 1.29.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-*O*-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranose (26).** The 2-(trimethylsilyl)ethyl group in **25** (383 mg, 0.17 mmol) was removed in a fashion similar to that described for **11**, to give amorphous 1-hydroxy compound **26** (326 mg, 90%): ^1H NMR ($CDCl_3$) δ 1.85 and 1.86 (2s, 6H, 2AcN), 1.88-2.23 (16s, 48H, 16AcO), 2.50 (dd, J_{gem} = 12.0 Hz, $J_{3eq,4}$ = 4.3 Hz, H-3*eq*), 3.50 (s, 3H, MeO), and 7.30-8.15 (m, 10H, 2Ph).

Anal. Calcd for $C_{90}H_{114}N_2O_{52}$ (2055.86): C, 52.58; H, 5.59; N, 1.36. Found: C, 52.53; H, 5.45; N, 1.09.

***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*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (27).** A solution of **26** (191 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) was treated with trichloroacetonitrile (0.33 mL) as just described for **17**, to afford amorphous **27** (161 mg, 80%): $[\alpha]_D$ +56° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.84 and 1.87 (2s, 6H, 2AcN), 1.96-2.24 (16s, 48H, 16AcO), 2.50 (dd, J_{gem} = 11.9 Hz, $J_{3eq,4}$ = 4.1 Hz, H-3f*eq*), 3.60 (s, 3H, MeO), 6.50 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1a), and 7.29-8.69 (m, 10H, 2Ph).

Anal. Calcd for $C_{93}H_{114}N_3O_{52}Cl_3$ (2212.26): C, 50.49; H, 5.19; N, 1.90. Found: C, 50.20; H, 5.16; N, 1.81.

***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*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (28).** Coupling of **27** (161 mg, 0.07 mmol) with **18** (155 mg, 0.36 mmol), as described for **19**, yielded amorphous **28** (99 mg, 55%): $[\alpha]_D$ +30° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.87 (t, 3H, J_{Me,CH_2} = 6.6 Hz, *Me*CH_2), 1.24 (s, 22H, 11CH_2), 1.84 and 1.86 (2s, 6H, 2AcN), 1.97-2.17 (16s, 48H, 16AcO), 2.48 (dd, J_{gem} = 12.9 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3f*eq*), 3.47 (s, 1H, MeO), 5.76 (d, 1H, $J_{3,4}$ = 3.2 Hz, H-4e), 5.90 (m, 1H, H-8f), and 7.26-8.13 (m, 15H, 3Ph).

Anal. Calcd for $C_{115}H_{151}N_5O_{54}$ (2467.45): C, 55.98; H, 6.17; N, 2.84. Found: C, 55.81; H, 6.05; N, 2.59.

***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*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-α-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)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (30). Selective reduction of the azido group in **28** (42 mg, 16 μmol), and subsequent coupling of the product (**29**) with octadecanoic acid (9.6 mg, 33 μmol) as described for **21**, gave amorphous **30** (35 mg, 78%). $[\alpha]_D$ +36° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (t, 6H, J_{Me, CH_2} = 7.0 Hz, 2*Me*CH_2), 1.25 (s, 52H, 26CH_2), 1.42 and 1.53 (2s, 6H, 2AcN), 1.77-2.18 (16s, 48H, 16AcO), 2.43 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3f*eq*), 3.83 (s, 3H, MeO), 5.01 (m, 1H, H-8f), 5.44 (m, 1H, H-7f), 5.84 (m, 1H, H-5 of ceramide), and 7.26-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{143}H_{187}N_3O_{55}$ (2828.04): C, 60.73; H, 6.67; N, 1.49. Found: C, 60.63; H, 6.40; N, 1.32.

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→6)-*O*-β-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→3)-*O*-α-D-galactopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol (31).** *O*-Deacylation and saponification of **30** (80 mg, 28 μmol), as described for **22**, yielded amorphous **31** (59 mg, 99%): $[\alpha]_D$ -2° (*c* 0.85, 5:4:1 $CHCl_3$:CH_3OH); ^1H NMR (1:1 DMSO-d6-D_2O) δ 0.84 (t, 6H, 2*Me*CH_2), 1.25 (s, 52H, 26CH_2), 1.47 (m, 2H, COC*H*$_2$$CH_2$), 1.80 and 1.86 (2s, 6H, 2AcN), 2.50 (dd, 1H, H-3f*eq*).

Anal. Calcd for $C_{104}H_{153}N_3O_{41}$ (2101.35): C, 59.44; H, 7.33; N, 1.99. Found: C, 59.53; H, 7.20; N, 1.98.

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