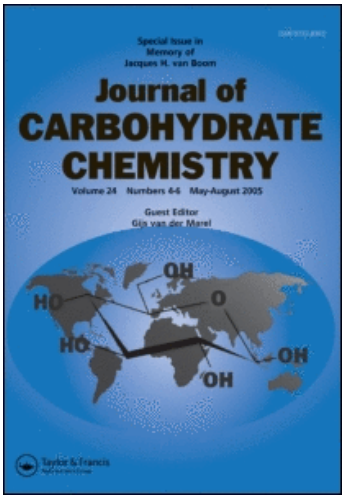

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Synthetic Studies on Sialoglycoconjugates 54: Synthesis of I-Active Ganglioside Analog

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 54: SYNTHESIS OF I-ACTIVE GANGLIOSIDE ANALOG

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ABSTRACT

A stereocontrolled synthesis of I-active ganglioside analog is described. Glycosylation of 2-(trimethylsilyl)ethyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**5**) with methyl 4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**10**) by use of *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH) gave the desired trisaccharide **11**, which was transformed into trisaccharide acceptor **14** *via* removal of the phthaloyl group followed by *N*-acetylation, and debenzylidenation. Glycosylation of **14** with methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**8**) gave the biantennary compound **15**, which was transformed into the acceptor **16**. Dimethyl(methylthio)sulfonium triflate (DMTST)-promoted coupling of **16** with methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (**17**) afforded the desired hexasaccharide **19**. Coupling of the hexasaccharide acceptor **20**, prepared from **19** by reductive ring-opening of benzylidene acetal, with **17** gave octasaccharide derivative **21**. Compound **21** was transformed, *via* removal of the benzyl group followed by *O*-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group and subsequent imidate formation, into the final glycosyl donor **24**. Condensation of **24** with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**18**) gave the β-glycoside **25**, which on channeling through selective reduction of azido group, coupling of the amino group with octadecanoic acid, *O*-deacylation and saponification of the methyl ester group, gave the title compound **28**.

INTRODUCTION

Numerous glycosphingolipids are found as constituents of the outer surface of cell membranes.[1,2] These compounds have important biological roles in such as cell growth, differentiation, adhesion, oncogenesis, receptor functions for viruses and bacterial toxins, and ligand activities for E-, P-, and L-selectins.[2] In order to investigate the functions of sialoglycoconjugates at the molecular level, we have synthesized a series of gangliosides and their analogs,[3] by using our newly developed methods for ganglioside synthesis.[4-6]

In the studies on the isolation and characterization of various glycoconjugates from human lung, I- and sialyl I-antigen **1** have been recognized as specific markers for differentiated type cells in the developing lung of human embryos and in lung cancers.[7] In order to elucidate the role of the biantennary structure in the function of the sialyl I-antigen, here we describe the synthesis of I-active ganglioside analog, VI^3 Neu5Ac α, IV^3 Neu5Ac α, II^6 klado Lc$_6$ Cer, in which the lactotriose residue in crude sialyl I-antigen **1** is replaced by D-glucopyranose.

RESULTS AND DISCUSSION

For the synthesis of desired I-active ganglioside analog, we have selected 2-(trimethylsilyl)ethyl *O*-(2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-[(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)]-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**16**) as a key glycosyl acceptor, which has the biantennary structure obtained by coupling of the glucosamine derivative **8** and the lactotriose acceptor **14** constructed from the lactose unit **5** and the glucosamine unit **10**. We have employed 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[8] (**17**) as the glycosyl donor.

2-(Trimethylsilyl)ethyl *O*-(2-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**5**) was obtained in good yield from 2-(trimethylsilyl)ethyl *O*-[3-*O*-(4-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-β-D-glucopyranoside[8] (**2**) *via* 4,6-*O*-benzylidenation, *O*-benzylation, and oxidative removal of the 4-methoxybenzyl group with 2,3-dichloro-5,6-dicyanobenzoquinone[9]. One of the glucosamine donors, methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**8**), was prepared from methyl 2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[10] (**6**) by 4,6-*O*-benzylidenation and 3-*O*-benzylation. The glycosyl

donor **10** was obtained from **8** by the reductive ring-opening[11] of benzylidene acetal with sodium cyanoborohydride-hydrogen chloride according to the method of Garegg *et al.* and subsequent acetylation. The glycosylation of **5** with **10** in dichloromethane for 2 h at 0 °C in the presence of *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH) and powdered molecular sieves 4Å (MS-4Å) afforded the desired β-glycoside **11** in 94% yield. The observed chemical shifts and coupling constants of the glucosamine unit for H-1 (δ 5.06, $J_{1,2}$ = 11.2 Hz) and H-4 (δ 5.12, $J_{3,4} = J_{4,5}$ = 9.7 Hz) indicated the structure assigned. *O*-Deacetylation and conversion from the phthalimide to the acetamide by heating with hydrazine hydrate in aqueous 95% ethanol, *N*-acetylation, and *O*-acetylation of **11** afforded the lactotriose derivative **13.** The hydrolysis of the benzylidene group in **13** gave the lactotriose acceptor **14.**

The condensation of **14** with **8** in a similar condition as described for the glycosylation of **5** with **10** gave the biantennary compound **15** in 61% yield. Significant signals of the glucosamine unit in the ^{1}H NMR spectrum of **15** were a one-proton doublet at δ 5.45 ($J_{1,2}$ = 10.8 Hz, H-1), a one-proton singlet at 5.60 (PhC*H*), and forty-four aromatic protons at δ 7.17-7.67 (9 Ph), indicating the newly formed glycosidic linkage to be β. By removal of the phthaloyl, followed by *N*-acetylation, the branching tetrasaccharide acceptor **16** was formed from **15** in 89% yield.

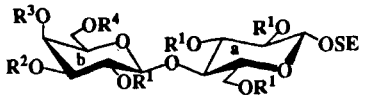
The glycosylation of **16** with **17** in the presence of dimethyl(methylthio)sulfonium triflate[4] (DMTST) as the glycosyl promoter and powdered MS-4Å in dichloromethane for 16 h at 0~6 °C gave the hexasaccharide **19** in 74% yield, which had the expected stereochemistry. The ^{1}H NMR spectrum of **19** showed the presence of seven three-proton singlets at δ 1.49, 1.78, 1.92-2.15 (*O*-acetyl and *N*-acetyl), a three-proton singlet at δ 3.83 (*O*-methyl), fifty-five aromatic protons (11Ph) at δ 7.13-8.30, and a one-proton doublet of doublets at δ 5.51 ($J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 12.6 Hz, H-2d), and those data are consistent with the structure assigned. The reductive ring-opening of the benzylidene acetal in **19** afforded the hexasaccharide acceptor **20** in 80% yield.

The glycosylation of **20** with **17** by use of DMTST in the presence of powdered MS-4Å in dichloromethane for 16 h at 0~6 °C gave expected octasaccharide derivative **21** in 28% yield; significant signals of **21** in ^{1}H NMR spectrum were a two-proton multiplet at δ 2.45 (H-3e-*eq* and H-3h-*eq*), two three-proton singlets at δ 3.78, 3.82 (*O*-methyl), seventy aromatic protons (14Ph) at δ 7.03-8.31, and a two-proton doublet of doublets at δ 5.52 ($J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 13.3 Hz, H-2d and H-2g), indicating the structure assigned.

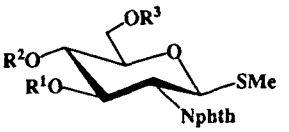
Catalytic hydrogenolysis (10% Pd-C) of the benzyl group in **21** in ethanol-acetic acid for 48 h at 45 °C and subsequent *O*-acetylation gave the per-*O*-acyl compound **22** in 31% yield. Treatment[12] of **22** with trifluoroacetic acid in dichloromethane for 30 min at

Neu5Acα(2→3)Galβ(1→4)GlcNAcβ(1→6)
Galβ(1→4)GlcNAcβ(1→3)Galβ(1→4)Glcβ(1→1)Cer
Neu5Acα(2→3)Galβ(1→4)GlcNAcβ(1→3)

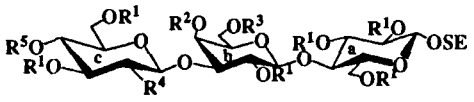
1



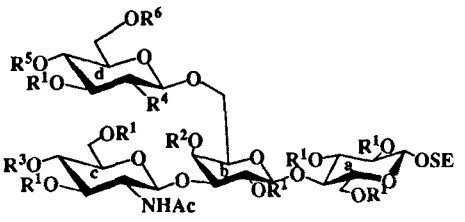
	R^1	R^2	R^3	R^4
2	H	MPM	H	H
3	H	MPM	benzylidene	
4	Bn	MPM	benzylidene	
5	Bn	H	benzylidene	



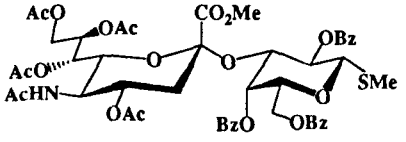
	R^1	R^2	R^3
6	H	H	H
7	H	benzylidene	
8	Bn	benzylidene	
9	Bn	H	Bn
10	Bn	Ac	Bn



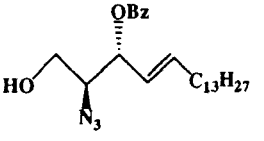
	R^1	R^2	R^3	R^4	R^5
11	Bn	benzylidene		Nphth	Ac
12	Bn	benzylidene		NHAc	H
13	Bn	benzylidene		NHAc	Ac
14	Bn	H	H	NHAc	Ac



	R^1	R^2	R^3	R^4	R^5	R^6
15	Bn	H	Ac	Nphth	benzylidene	
16	Bn	H	H	NHAc	benzylidene	

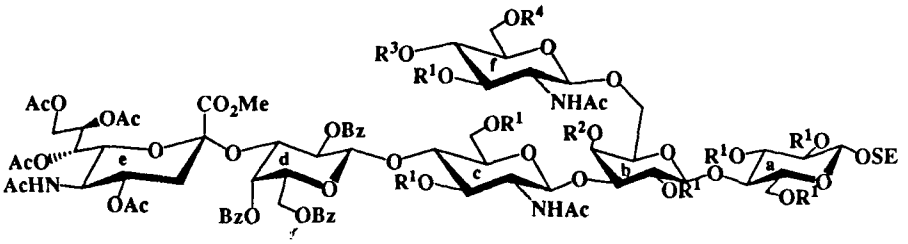


17

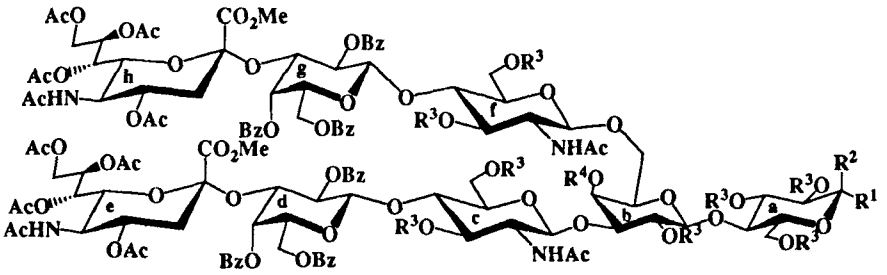


18

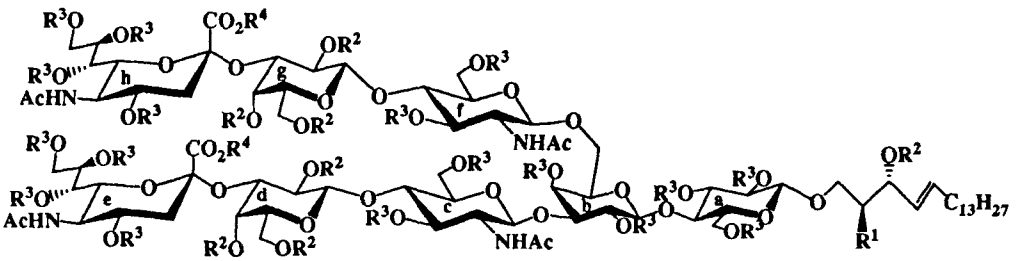
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
Bz = benzoyl
MPM = *p*-methoxybenzyl



	R^1	R^2	R^3	R^4
19	Bn	H	benzylidene	
20	Bn	H	H	Bn



	R^1	R^2	R^3	R^4
21	OSE	H	Bn	H
22	OSE	H	Ac	Ac
23	H , OH		Ac	Ac
24	H	$OC(=NH)CCl_3$	Ac	Ac



	R^1	R^2	R^3	R^4
25	N_3	Bz	Ac	Me
26	NH_2	Bz	Ac	Me
27	$NHCO(CH_2)_{16}CH_3$	Bz	Ac	Me
28	$NHCO(CH_2)_{16}CH_3$	H	H	H

0 °C gave the 1-hydroxy compound **23**. 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, **23** gave the trichloroacetimidate **24** in 59% yield. The ^{1}H NMR data for Gal unit in **24** [δ 6.44 ($J_{1,2}$ = 3.8 Hz, H-1a), 8.61 (C=NH)] indicated the trichloroacetimidate to be α.

The final glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[13] (**18**) with **24** in dichloromethane in the presence of boron trifluoride etherate[13b,14] for 8 h at 0 °C afforded the desired β-glycoside **25** in 46% yield. Selective reduction[15] of azido group in **25** with hydrogen sulfide in aq 83% pyridine for 3 days at 0 °C gave the amine, which, on condensation with octadecanoic acid, using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) in dichloromethane gave the acylated sialyl I-antigen analog **27** in 62% yield, after chromatography.

Finally, *O*-deacylation of **27** with sodium methoxide in methanol, with subsequent saponification of the methyl ester group, yielded the desired sialyl I-antigen analog **28**, α-Neu5Ac-(2→3)-β-D-Gal-(1→4)-β-D-GlcNAc-(1→6)-[α-Neu5Ac-(2→3)-β-D-Gal-(1→4)-β-D-GlcNAc-(1→3)-]β-D-Gal-(1→4)-β-D-Glc-(1→1)-Cer, in quantitative yield after chromatography on a column of Sephadex LH-20.

EXPERIMENTAL

General Procedures. Specific rotations were determined with a Union PM-201 polarimeter at 25 °C. ^{1}H NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

2-(Trimethylsilyl)ethyl *O*-[4,6-*O*-Benzylidene-3-*O*-(4-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-β-D-glucopyranoside (3). To a solution of 2-(trimethylsilyl)ethyl *O*-[3-*O*-(4-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-β-D-glucopyranoside[8] (**2**; 3.5 g, 6.20 mmol) in DMF (50 mL) was added Drierite (5.0 g), and the mixture was stirred for 2 h at room temperature. Benzaldehyde dimethyl acetal (1.9 mL, 12.40 mmol) and *p*-toluenesulfonic acid monohydrate (50 mg) were added, and the mixture was stirred for 16 h at room temperature, then neutralised with Amberlite IR-410 (HO^-) resin and concentrated. Column chromatography (3:1 AcOEt-hexane) of the residue on silica gel (100 g) afforded **3** (2.9 g, 72%) as an amorphous mass: $[\alpha]_D$ +16.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.98 (m, 2H, $Me_3SiCH_2CH_2$), 3.76 (s, 3H, $CH_3OC_6H_4CH_2$), 4.19, 4.63 (2d, 2H, J_{gem} = 12.3 Hz, $CH_3OC_6H_4CH_2$), 4.28, 4.43

(2d, 2H, J ▫ 8.3 Hz, 8.1 Hz, H-1a, 1b), 5.32 (s, 1H, PhC*H*), and 6.82-7.48 (m, 9H, 2Ph).

Anal. Calcd for $C_{32}H_{46}O_{12}Si$ (650.8): C, 59.06; H, 7.12. Found: C, 58.92; H, 7.29

2-(Trimethylsilyl)ethyl *O*-[2-*O*-Benzyl-4,6-*O*-benzylidene-3-*O*-(4-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-2, 3, 6-tri-*O*-benzyl-β-D-glucopyranoside (4). To a solution of **3** (2.9 g, 4.46 mmol) in *N,N*-dimethylformamide (DMF, 25 mL) was added a suspension of sodium hydride in oil (1.1 g, 60% of sodium hydride by weight). The mixture was stirred for 30 min at 0 °C, benzyl bromide (3.2 mL, 26.8 mmol) was added dropwise, and stirring was continued for 3 h at room temperature. The reaction was monitored by TLC and, when complete, methanol (5 mL) was added, and the mixture was concentrated and extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:1 AcOEt-hexane) of the residue on silica gel (100 g) gave **4** (4.1 g, 88%) as a syrup: $[\alpha]_D$ +14.9° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 3.76 (s, 3H, $CH_3OC_6H_4CH_2$), 4.32, 4.51 (2d, 2H, J_{gem} = 12.3 Hz , $CH_3OC_6H_4CH_2$), 4.37, 4.43 (2d, 2H, J = 7.9 Hz , H-1a, 1b), 5.42 (s, 1H, PhC*H*), and 6.80-7.51 (m, 29H, 6Ph).

Anal. Calcd for $C_{60}H_{70}O_{12}Si$ (1011.3): C, 71.26; H, 6.98. Found: C, 71.23; H, 6.68.

2-(Trimethylsilyl)ethyl *O*-(2-*O*-Benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (5). To a stirred solution of **4** (7.6 g, 7.48 mmol) in dichloromethane (90 mL) were added 2,3-dichloro-5,6-dicyanobenzoquinone (2.6 g, 11.2 mmol) and water (3 mL), and stirring was continued for 1 h at room temperature. The precipitate was collected and washed with dichloromethane, and the combined filtrate and washings were washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:5 AcOEt-hexane) of the residue on silica gel (300 g) gave **5** (5.4 g, 82%) as an amorphous mass: $[\alpha]_D$ -4.1° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 2.41 (broad d, 1H, OH), 5.50 (s, 1H, PhC*H*), and 7.15-7.48 (m, 25H, 5Ph).

Anal. Calcd for $C_{52}H_{62}O_{11}Si$ (891.1): C, 70.09; H, 7.01. Found: C, 69.83; H, 6.97.

Methyl 4,6-O-Benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (7). To a solution of methyl 2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**6**; 10.4 g, 31 mmol) in DMF (100 mL) was added Drierite (10 g), and the mixture was stirred for 2 h at room temperature. Benzaldehyde dimethyl acetal (9.2

mL, 61 mmol) and *p*-toluenesulfonic acid monohydrate (90 mg) were added, and the mixture was stirred for 48 h at room temperature, then neutralised with Amberlite IR-410 (HO^-) resin and concentrated. Column chromatography (3:2 AcOEt-hexane) of the residue on silica gel (300 g) afforded **7** (8.9 g, 68%) as an amorphous mass: $[\alpha]_D$ +48.2° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.18 (s, 3H, S*Me*), 3.62 (t, 1H, Jgem = $J_{5,6'}$ = 8.8 Hz, H-6'), 3.73 (dt, 1H, $J_{4,5}$ = 8.8 Hz, $J_{5,6}$ = 4.2 Hz, H-5), 3.82 (t, 1H, H-6), 4.36 (t, 1H, $J_{1,2}$ = $J_{2,3}$ =10.3 Hz, H-2), 4.42 (dd, 1H, $J_{3,4}$ = 9.7 Hz, H-4), 4.70 (dd, 1H, H-3) 5.31 (d, 1H, H-1), 5.58 (s, 1H, PhC*H*), and 7.25-8.04 (m, 9H, 2Ph).

Anal. Calcd for $C_{22}H_{21}NO_6S$ (427.5): C, 61.81; H, 4.95; N, 3.28. Found: C, 61.61; H, 4.67; N, 3.30.

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (8). To a solution of **7** (8.93 g, 20.9 mmol) in *N,N*-dimethylformamide (DMF, 25 mL) was added a suspension of sodium hydride in oil (1.25 g, 60% of sodium hydride by weight). The mixture was stirred for 30 min at 0 °C, benzyl bromide (3.2 mL, 31.3 mmol) was added dropwise, and stirring was continued for 16 h at room temperature. The reaction was monitored by TLC and, when complete, methanol (5 mL) was added, and the mixture was worked up as described for **4**. Column chromatography (1:1 AcOEt-hexane) of the residue on silica gel (100 g) gave **8** (7.6 g, 88%) as a syrup: $[\alpha]_D$ +54.1° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.14 (s, 3H, S*Me*), 3.71 (m, 1H, H-5), 3.77 (dd, 1H, Jgem = $J_{5,6'}$ = 8.8 Hz, H-6'),3.85 (dd, 1H, $J_{5,6}$ = 5.7 Hz, H-6), 4.33 (t, 1H, $J_{1,2}$ = $J_{2,3}$ =10.1 Hz, H-2), 4.44 (dd, 1H, $J_{3,4}$ = 10.3 Hz, H-4), 4.49 (dd, 1H, H-3) 5.24 (d, 1H, H-1), 5.64 (s, 1H, PhC*H*), and 6.85-7.85 (m, 14H, 3Ph).

Anal. Calcd for $C_{29}H_{27}NO_6S$(517.6): C, 67.29; H, 5.26; N, 2.71. Found: C, 67.38; H, 5.13; N, 2.70

Methyl 3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (9). To a solution of **8** (4.0 g, 7.73 mmol) in dry tetrahydrofuran (120 mL) were added molecular sieves 3Å (MS-3Å; 20 g), and the mixture was stirred for 1 h at room temperature, and sodium cyanoborohydride (7.3 g) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. TLC indicated that the reaction was complete after 5 min. The mixture was neutralized with triethylamine and filtered, the residue was washed with methanol and the combined filtrate and washings were concentrated then extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 AcOEt-hexane) of the residue on silica gel (100 g) afforded **9** (3.78 g, 94%) as an amorphous mass: $[\alpha]_D$

+47.9° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.10(s, 3H, S*Me*), 4.26 (t, 1H, $J_{1,2} = J_{2,3}$ =9.9 Hz, H-2), 4.29 (dd, 1H, $J_{3,4}$ = 7.4 Hz, $J_{4,5}$ = 4.5 Hz, H-4), 5.17 (d, 1H, H-1), and 6.85-7.85 (m, 14H, 3Ph).

Anal. Calcd for $C_{29}H_{29}NO_6S$(519.6): C, 67.03; H, 5.63; N, 2.70. Found: C, 67.04; H, 5.74; N, 2.59.

Methyl 4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (10). A solution of **9** (4.17 g, 8.0 mmol) in acetic anhydride (25 mL) and pyridine (40 mL) was stirred for 3 h at room temperature, and methanol (30 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. Column chromatography (1:3 AcOEt-hexane) of the residue on silica gel (200 g) gave **10** (4.50 g, quantitative) as an amorphous mass: $[\alpha]_D$ +112.4° (*c* 0.17, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.93,2.10(2s, 6H, AcO and MeS), 4.37 (t, 1H, $J_{1,2} = J_{2,3}$ =10.7 Hz, H-2), 4.51 (dd, 1H, $J_{3,4}$ = 9.0 Hz, H-3), 5.18 (dd, 1H, $J_{4,5}$ = 10.4 Hz, H-4), 5.20 (d, 1H, H-1), and 6.87-7.75 (m, 14H, 3Ph).

Anal. Calcd for $C_{31}H_{31}NO_7S$(561.7): C, 66.29; H, 5.56; N, 2.49. Found: C, 66.44; H, 5.67; N, 2.49

2-(Trimethylsilyl)ethyl *O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (11). To a solution of **5** (200 mg, 0.22 mmol) and **10** (214 mg, 0.38 mmol) in dry dichloromethane (5 mL) was added MS-4Å (0.5 g), and the mixture was stirred for 5 h at room temperature then cooled to 0 °C. To the cooled mixture were added, with stirring, *N*-iodosuccinimide (NIS; 172 mg, 0.76 mmol) and trifluoromethanesulfonic acid (TfOH; 17 μL, 0.08 mmol), and the stirring was continued for 2 h at 0 °C. The precipitate was filtered off, 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 (1:3 AcOEt-hexane) of the residue on silica gel (20 g) gave **11** (296 mg, 94%) as an amorphous mass: $[\alpha]_D$ +120.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.96 (m, 2H, $Me_3SiCH_2CH_2$), 2.01 (s, 3H, AcO), 5.06 (d, 1H, $J_{1,2}$ = 11.2 Hz, H-1c), 5.12 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.7 Hz, H-4c), 5.41 (s, 1H, PhC*H*), and 6.78-7.51 (m, 39H, 8Ph)

Anal. Calcd for $C_{82}H_{89}NO_{18}Si$ (1404.7): C, 70.12; H, 6.39; N, 1.00. Found: C, 70.02; H, 6.55; N, 1.01.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-β-

D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (13). A solution of **11** (1.82 g, 1.30 mmol) in aqueous 95% ethanol (50 mL) was treated with hydrazine hydrate (0.6 mL) for 12 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 (1 mL) and pyridine (2 mL) for 2 h at room temperature, and methanol (2 mL) was added. The mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2 M hydrochloric acid, water, and M sodium carbonate, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 AcOEt-hexane) of the residue on silica gel (100 g) afforded **7** (1.58 g, 92%) as an amorphous mass: $[\alpha]_D$ +128.1° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.40, 2.01 (2s, 6H, AcO and AcN), 5.13 (t, 1H, $J_{3,4} = J_{4,5}$ = 8.2 Hz, H-4c), 5.42 (s, 1H, PhC*H*), and 7.16-7.55 (m, 35H, 7Ph)

Anal. Calcd for $C_{68}H_{85}NO_{17}Si$ (1216.5): C, 67.14; H, 7.04; N, 1.15. Found: C, 67.38; H, 7.10; N, 1.11.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (14). A solution of **13** (1.58 g, 1.20 mmol) in aqueous 80% acetic acid (30 mL) was heated for 24 h at 60 °C and concentrated. Column chromatography (1:1 AcOEt-hexane) of the residue on silica gel (100 g) gave **14** (1.35 g, 92%) as an amorphous mass: $[\alpha]_D$ +174.0° (*c* 0.80, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.42, 1.89 (2s, 6H, AcO and AcN), 5.08 (d, $J_{1,2}$ = 8.3 Hz, H-1c), 5.13 (t, 1H, $J_{3,4} = J_{4,5}$ = 8.2 Hz, H-4c), and 7.16-7.55 (m, 30H, 6Ph).

Anal. Calcd for $C_{61}H_{81}NO_{17}Si$ (1128.4): C, 64.93; H, 7.24; N, 1.24. Found: C, 64.79; H, 7.41; N, 1.06.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 6)]-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (15). To a solution of **14** (1.05 g, 0.85 mmol) and **8** (0.75 g, 1.45 mmol) in dry dichloromethane (20 mL) was added MS-4Å (3.0 g), and the mixture was stirred for 5 h at room temperature then cooled to 0 °C. To the cooled mixture were added, with stirring, NIS (654 mg, 2.91 mmol) and TfOH (66 μL, 0.34 mmol), and the stirring was continued for 2 h at 0 °C, and then worked-up, as described for **11**. Column chromatography (1:3 AcOEt-hexane) of the residue on silica gel (20 g) gave **15** (890 mg, 61%) as an amorphous mass: $[\alpha]_D$ +42.0° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.03 (m,

2H, $Me_3SiCH_2CH_2$), 1.70, 1.85 (2s, 6H, AcO and AcN), 5.11 (t, 1H, $J_{3,4} = J_{4,5}$ = 8.6 Hz, H-4c) 5.16 (d, 1H, $J_{1,2}$ = 10.8 Hz, H-1c), 5.45 (d, 1H, $J_{1,2}$ = 10.8 Hz, H-1d), 5.60 (s, 1H, PhC*H*) and 7.17-7.67 (m, 44H, 9Ph)

Anal. Calcd for $C_{99}H_{112}N_2O_{24}Si$ (1742.1): C, 68.26; H, 6.48; N, 1.61. Found: C, 68.23; H, 6.18; N, 1.52.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1 → 6)]-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (16). A solution of **15** (810 mg, 0.47 mmol) in aqueous 95% ethanol (20 mL) was treated with hydrazine hydrate (1.0 mL) for 72 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 (1 mL) in methanol (10 mL) for 2 h at room temperature, pyridine (2 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2 M hydrochloric acid, water, and M sodium carbonate, dried (Na_2SO_4) and concentrated. Column chromatography (2:1 AcOEt-hexane) of the residue on silica gel (100 g) afforded **16** (664 mg, 89%) as an amorphous mass: $[\alpha]_D$ +11.9° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.92, 1.95 (2s, 6H, 2AcN), 5.18(d, 1H, $J_{1,2}$ = 9.2 Hz, H-1c), 5.32(d, 1H, $J_{1,2}$ = 8.1 Hz, H-1d), 5.56 (s, 1H, PhC*H*) and 7.01-7.04 (m, 40H, 8Ph)

Anal. Calcd for $C_{93}H_{112}N_2O_{23}Si$ (1654.0): C, 67.53; H, 6.83; N, 1.69. Found: C, 67.28; H, 6.79; 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→ 3)-*O*-(2, 4, 6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3, 6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-[*O*-(2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (19). To a solution of **16** (410 mg, 0.262 mmol) and 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[8] (**17**; 521 mg,0.523 mmol) in dry dichloromethane (25 mL) was added MS-4Å (7.5 g), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. Dimethyl(methylthio)sulfonium triflate (DMTST; 540 mg, 2.09 mmol) was added to the mixture, and the mixture was stirred for 16 h at 6 °C, filtered, washed with

dichloromethane. The combined filtrate and washings were washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (4:1 AcOEt-hexane) of the residue on silica gel (10 g) gave **19** (490 mg, 74%) as an amorphous mass: $[\alpha]_D$ +5.28° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.99 (m, 2H, $Me_3SiCH_2CH_2$), 1.49, 1.78, 1.92, 1.98, 2.15 (5s, 21H, 4AcO and 3AcN), 2.47 (dd, 1H, Jgem = 13.1 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3e-*eq*), 3.83 (s, 3H, MeO), 5.10 (d, 1H, $J_{1,2}$ = 12.9 Hz, H-1c), 5.21 (d, 1H, $J_{1,2}$ = 12.5 Hz, H-1f), 5.51 (dd, 1H, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 12.6 Hz, H-2d), 5.57 (s, 1H, PhC*H*), 5.71 (m, 1H, H-8e), and 7.13-8.30 (m, 55H, 11Ph).

Anal. Calcd for $C_{136}H_{169}N_3O_{41}Si$ (2529.9): C, 64.57; H, 6.73, N, 1.66. Found: C, 64.37; H, 6.45; N, 1.68.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4, 7, 8, 9-tetra-*O*-acetyl-3, 5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-*O*-(2, 4, 6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3, 6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-[*O*-(2-acetamido-3, 6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1 → 4)-2, 3, 6-tri-*O*-benzyl-β-D-glucopyranoside (20). To a solution of **19** (92 mg, 0.037 mmol) in dry tetrahydrofuran (3 mL) were added MS-3Å (0.8 g), and the mixture was stirred for 1 h at room temperature, and sodium cyanoborohydride (35 mg) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. TLC indicated that the reaction was complete after 5 min, and then worked-up, as described for **9**. Column chromatography (3:1 AcOEt-hexane) of the residue on silica gel (10 g) afforded **20** (74 mg, 80%) as an amorphous mass: $[\alpha]_D$ +3.0° (*c* 2.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.96 (m, 2H, $Me_3SiCH_2CH_2$), 1.49, 1.78-2.00 (7s, 21H, 4AcO and 3AcN), 2.47 (m, 1H, H-3e-*eq*), 3.83 (s, 3H, MeO), 5.70 (m, 1H, H-8e), and 7.14-8.26 (m, 55H,11Ph)

Anal. Calcd for $C_{136}H_{171}N_3O_{41}Si$ (2531.9): C, 64.52; H, 6.81, N, 1.66. Found: C, 64.53; H, 6.92; N, 1.55.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4, 7, 8, 9-tetra-*O*-acetyl-3, 5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-*O*-(2, 4, 6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2, 4, 6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-

benzyl-β-D-glucopyranoside (21). To a solution of **20** (73 mg, 0.029 mmol) and **17** (58 mg, 0.058 mmol) in dry dichloromethane (0.8 mL) was added MS-4Å (1.2 g), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. DMTST (60 mg, 0.232 mmol) was added to the mixture, the mixture was stirred for 16 h at 6 °C, and then worked-up, as described for **19**, affording **21** (28 mg, 28%) as an amorphous mass: $[\alpha]_D$ +14.0° (*c* 2.26, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.50, 1.79-2.19 (9s, 36H, 8AcO and 4AcN), 2.45 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.78, 3.82 (2s, 6H, 2MeO), 5.07 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1c), 5.24 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1f), 5.52 (dd, 2H, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 13.3 Hz, H-2d and H-2g), and 7.03-8.31 (m, 70H, 14Ph).

Anal. Calcd for $C_{183}H_{204}N_4O_{60}Si$ (3447.7): C, 63.75; H, 5.96, N, 1.63. Found: C, 63.90; H, 6.07; N, 1.63.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4, 7, 8, 9-tetra-*O*-acetyl-3, 5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-*O*-(2, 4, 6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3, 6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (22). A solution of **21** (226 mg, 0.065 mmol) in ethanol (42 mL) and acetic acid (5.7 mL) was hydrogenated in the presence of 10% Pd-C (300 mg) for 48 h at 45 °C, then filtered and concentrated. The residue was acetylated with acetic anhydride (0.3 mL)-pyridine (1.2 mL) for 16 h at room temperature. The product was purified by chromatography on a column of silica gel (20 g) with 4:1 AcOEt-hexane afforded **22** (64 mg, 31%) as an amorphous mass: $[\alpha]_D$ +3.47° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.94 (m, 2H, $Me_3SiCH_2CH_2$), 1.55, 1.57, 1.68-2.19 (14s, 63H, 17AcO and 4AcN), 2.49 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.82, 3.84 (2s, 6H, 2MeO), 5.64 (m, 2H, H-8e and H-8h), and 7.21-8.22 (m, 30H, 6Ph).

Anal. Calcd for $C_{145}H_{174}N_4O_{69}Si$ (3105.0): C, 56.09; H, 5.65, N, 1.80. Found: C, 55.95; H, 5.82; N, 1.62.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-**

(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranose (23). To a solution of **22** (52 mg, 0.017 mmol) in dichloromethane (1 mL) was added trifluoroacetic acid (3 mL) at 0 °C, and the mixture was stirred for 30 min at 0 °C and concentrated. Column chromatography (20:1 CH_2Cl_2-MeOH) of the residue on silica gel (10 g) gave **23** (41 mg, 82%) as an amorphous mass: $[\alpha]_D$ +9.3° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.56, 1.59, 1.78-2.19 (9s, 63H, 17AcO and 4AcN), 2.44 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.78, 3.81 (2s, 6H, 2MeO), 5.62 (m, 2H, H-8e and H-8h), and 7.19-8.19 (m, 30H, 6Ph)

Anal. Calcd for $C_{140}H_{162}N_4O_{69}$ (3004.8): C, 55.96; H, 5.43, N, 1.86. Found: C, 55.82; H, 5.60; N, 1.68

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→ 3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl Trichloroacetimidate (24).** To a solution of **23** (40 mg, 0.013 mmol) in dichloromethane (1.0 mL) and trichloroacetonitrile (0.05 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 5.0 mg) at -5 °C, and the mixture was stirred for 3 h at 0 °C, then concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **24** (24 mg, 59%) as an amorphous mass: $[\alpha]_D$ +11.4° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.53, 1.54, 1.78-2.21 (15s, 63H, 17AcO and 4AcN), 2.46 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.79, 3.81 (2s, 6H, 2MeO), 5.62 (m, 2H, H-8e and H-8h), 6.44 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1a), 7.04-8.19 (m, 30H, 6Ph), and 8.61 (s, 1H, C=NH).

Anal. Calcd for $C_{142}H_{162}N_5O_{69}Cl_3$ (3149.2): C, 54.16; H, 5.19, N, 2.22. Found: C, 54.13; H, 4.89; N, 2.14.

***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→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-**

(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2,4-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 (25). To a solution of **24** (24 mg, 0.008 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[13] (**18**; 20 mg, 0.046 mmol) in dichloromethane (0.5 mL) were added MS-4Å (AW-300, 0.7 g) and the mixture was stirred for 5 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (5 μL) was added, and the mixture was stirred for 8 h at 0 °C and then filtered. The insoluble material was washed with dichloromethane, and the combined filtrate and washings were washed with M sodium hydrogen carbonate and water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **25** (10 mg, 46%) as an amorphous mass: $[\alpha]_D$ -12.0° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.87 (t, 3H, $J_{Me,CH2}$ = 6.6 Hz, *Me*CH_2), 1.26 (s, 22H, 11CH_2), 1.54, 1.67, 1.78-2.18 (12s, 63H, 17AcO and 4AcN), 2.48 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.79, 3.81 (2s, 6H, 2MeO), 5.60 (m, 2H, H-8e and H-8h), 5.92 (m, 1H, H-5 for sphingosine), and 7.33-8.19 (m, 30H, 6Ph).

Anal. Calcd for $C_{165}H_{199}N_7O_{71}$ (3416.4): C, 58.01; H, 5.87, N, 2.87. Found: C, 57.76; H, 5.83; N, 3.16.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-[(methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(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 (27).** Hydrogen sulfide was bubbled through a stirred solution of **26** (20 mg, 0.006 mmol) in aqueous 83% pyridine (3 mL) for 3 days at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (10 mg, 0.035 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride(10 mg, 0.053 mmol) in dry dichloromethane (2.0 mL) for 24 h at room temperature. Dichloromethane (50 mL) was added, and the mixture was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 CH_2Cl_2-MeOH) of the residue on silica gel (10 g) gave **27** (13.2 mg, 62%) as an amorphous mass: $[\alpha]_D$ +9.84° (*c* 0.26, $CHCl_3$); ^1H NMR

($CDCl_3$) δ 0.89 (t, 6H, 2*Me*CH_2), 1.26 (s, 50H, 25CH_2), 1.54-2.21 (20s, 63H, 17AcO and 4AcN), 2.49 (m, 2H, H-3e-*eq* and H-3h-*eq*), 3.79 , 3.81 (2s, 6H, 2MeO), 5.62 (m, 2H, H-8e and H-8h), and 7.22-8.27 (m, 30H, 6Ph).

Anal. Calcd for $C_{183}H_{235}N_5O_{72}$ (3656.9): C, 60.11; H, 6.48; N, 1.92. Found: C, 59.91; H, 6.20; N, 1.94

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→ 3)-*O*-[(5-acetamido-3, 5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→ 4)-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→6)]-*O*-(β-D-galactopyranosyl)-(1→4)-(β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol (28).** To a solution of **27** (13 mg, 0.035 mmol) in methanol (1 mL) was added sodium methoxide (5 mg), and the mixture was stirred for 24 h at 40 °C, and water (0.1 mL) was added. The solution was stirred for 10 h at room temperature, then treated with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with methanol, and the combined filtrate and washings were concentrated. Column chromatography (7:40:50 H_2O-MeOH-$CHCl_3$) of the residue on Sephadex LH-20 (10 g) gave **27** (7.9 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +3.8° (*c* 0.16, 7:40:50 H_2O-MeOH-$CHCl_3$); ^1H NMR [98:2 $(CD_3)_2SO$-D_2O] δ 1.01 (t, 6H, 2*Me*CH_2), 1.21 (s, 50H, 25CH_2), and 1.77, 1.81, 1.86, 1.87 (4s, 12H, 4AcN),

Anal. Calcd for $C_{98}H_{174}N_5O_{49}$ (2206.5): C, 53.35; H, 7.95, N, 3.17. Found: C, 53.44; H, 7.82; N, 3.16.

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