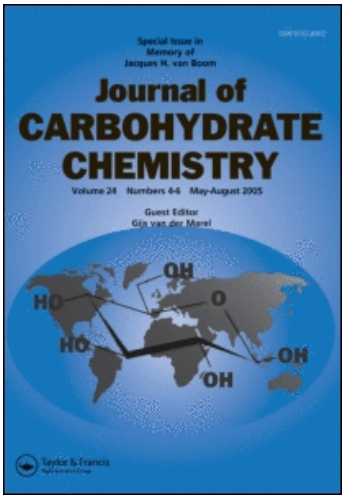

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Tomohiro Terada[a]; Tsuyoshi Toyoda[a]; Hideharu Ishida[a]; Makoto Kiso[a]; Akira Hasegawa[a]
[a] Department of Applied Bioorganic Chemistry, Gifu University, Gifu, Japan

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 74: SYNTHESIS OF KDN-GANGLIOSIDES GM_1, GM_2, AND GD_{1a}

Tomohiro Terada, Tsuyoshi Toyoda, Hideharu Ishida, Makoto Kiso and Akira Hasegawa*

Department of Applied Bioorganic Chemistry, Gifu University, Gifu 501-11, Japan

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ABSTRACT

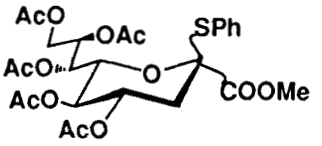
KDN-containing gangliosides GM_1, GM_2, and GD_{1a} have been synthesized. Glycosylation of 2-(trimethylsilyl)ethyl *O*-(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**3**) with methyl 6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-1-thio-β-D-galactopyranoside (**5**) gave the tetrasaccharide (**6**), which was converted, *via* de-esterification, removal of the phthaloyl group, *N*-acetylation, and *O*-deisopropylidenation, into the tetrasaccharide acceptor (**9**). Reductive removal of the benzyl groups in **9**, *O*-acetylation and subsequent removal of the 2-(trimethylsilyl)ethyl group followed by imidate formation, gave the KDN-GM_2 oligosaccharide glycosyl donor **12**. Glycosylation of **9** with methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**13**) and methyl (methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (**18**), using dimethyl(methylthio)sulfonium triflate (DMTST), gave the penta- and hexasaccharides **14** and **19**, which were converted *via* reductive removal of their benzyl groups, *O*-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, and reaction with trichloroacetonitrile, into the corresponding α-trichloroacetimidates **17** and **22**. Glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol with **12**, **17**, and **22** in the presence of boron trifluoride etherate afforded the expected β-glycosides, which were transformed in good yields, *via* selective reduction of the azido group, coupling with octadecanoic acid, *O*-deacylation, and de-esterification, into the target gangliosides **26** **29**, and **32**.

INTRODUCTION

Gangliosides are a type of glycosphingolipid that are distinguished from other glycosphingolipids because their containing sialic acid is α-linked at definite positions of the oligosaccharide residues. Recently, gangliosides have received much attention owing to their important biological functions.[1-6] In addition, KDN, a novel type of sialic acid, 3-deoxy-D-*glycero*-D-*galacto*-2-nonulopyranosylonic acid, in which the acetamido group at C-5 of *N*-acetylneuraminic acid is replaced by a hydroxyl, was isolated[7] from rainbow trout eggs. Now a number of KDN-glycoconjugates have been reported to occur in various living organisms ranging from bacterial to mammalian species. Nevertheless, the biological function of KDN-glycoconjugates has not been established, because only a limited amount of these materials has been available for testing. We have a synthetic program in this area, and our efforts have resulted in the development[8,9] of a facile procedure for the α-stereoselective coupling of sialic acid using the protected methyl or phenyl 2-thioglycoside as the glycosyl donor and the suitably protected sugar acceptors, with DMTST or *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH) as the promoter in acetonitrile solution. We have synthesized[9c,10,11] various types of gangliosides for elucidating their biological functions at the molecular level. As a continuation of our synthetic efforts toward the goal of elucidating the functions of sialoglycoconjugates, we describe herein the synthesis of KDN-gangliosides GM_2, GM_1, and GD_{1a}.

RESULTS AND DISCUSSION

For the synthesis of the desired KDN-gangliosides GM_1, GM_2, and GD_{1a} we employed the methyl 1-thioglycosides **5**, **13**, and **18** of the galactosamine,[12] galactose,[13] and KDN-α(2→3)-galactose[14] as the glycosyl donors and 2-(trimethylsilyl)ethyl *O*-(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**3**) as a suitably protected glycosyl acceptor. The acceptor **3** was coupled with the donor **5** using NIS-TMS•OTf as a



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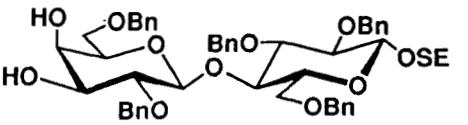

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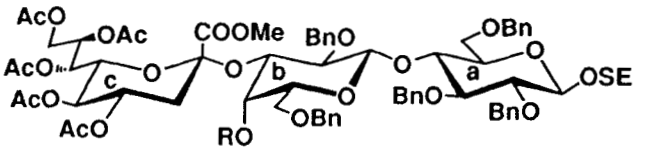

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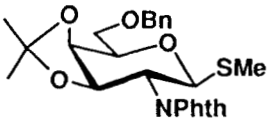
4 R = Ac



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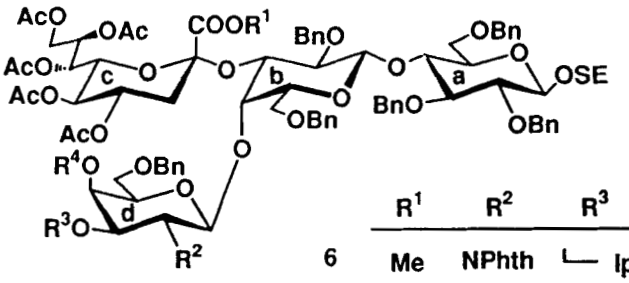
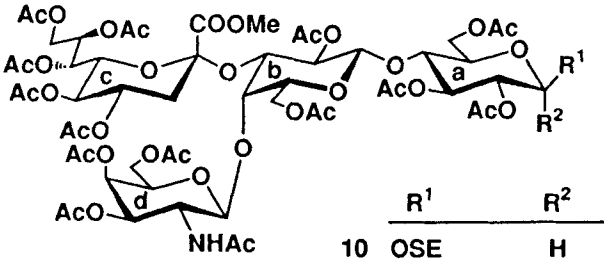
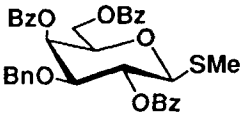


	R^1	R^2	R^3	R^4
6	Me	NPhth	lpd	
7	H	NPhth	lpd	
8	Me	NHAc	lpd	
9	Me	NHAc	H	H

SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
lpd = isopropylidene
Phth = phthaloyl



	R^1	R^2
10	OSE	H
11	H, OH	
12	H	$OC(=NH)CCl_3$



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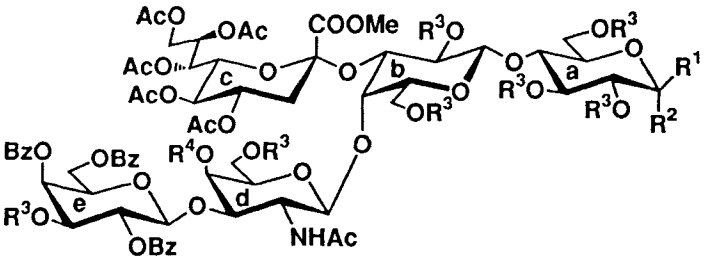
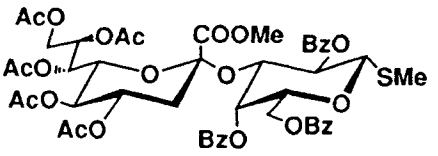


	R^1	R^2	R^3	R^4
14	OSE	H	Bn	H
15	OSE	H	Ac	Ac
16	H, OH		Ac	Ac
17	H	$OC(=NH)CCl_3$	Ac	Ac



18

promoter, to afford the tetrasaccharide **6**. The tetrasaccharide acceptor was then glycosylated with **13** or **18**. By further processing, according to our usual procedures,[16] the resulting tetra-, penta-, and hexasaccharide intermediates could be transformed into the end product by introduction of a ceramide moiety.

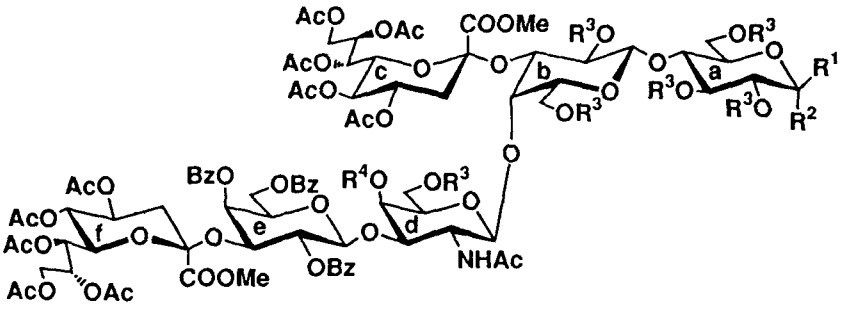
Glycosylation of 2-(trimethylsilyl)ethyl *O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[17] (**2**) with methyl (phenyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate[18] (**1**), in dry acetonitrile in the presence of NIS-trimethylsilyl trifluoromethanesulfonate (TMS•OTf) and molecular sieves 3Å (MS-3Å) for 2 h at -40 °C, gave exclusively the α-glycoside **3** in 54% yield; significant signals of the KDN residue in the ^{1}H NMR spectrum were a one-proton doublet of doublets at δ 2.62 (J_{gem} = 12.0, $J_{3eq,4}$ = 4.7 Hz, H-3*eq*), a one-proton multiplet at δ 4.79 ($J_{3ax,4}$ = 11.5, $J_{4,5}$ = 10.7 Hz, H-4), and a one-proton doublet of doublets at δ 5.32 ($J_{6,7}$ = 2.1, $J_{7,8}$ = 8.8 Hz, H-7), indicating the anomeric configuration[18] to be α. Acetylation of **3** gave the acetate **4** quantitatively; the observed chemical shift and coupling constants for H-4 of the Gal residue (δ 5.43, br d, $J_{3,4}$ = 3.2 Hz) indicated the glycosylated position to be the 3-OH. Coupling of **3** with methyl 6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-1-thio-β-D-galactopyranoside[12] (**5**) in dichloromethane, in the presence of NIS-TfOH and molecular sieves 4Å, gave the tetrasaccharide **6** in 71% yield, which on reaction with lithium iodide in pyridine for 12 h under reflux afforded **7** in 90% yield. Treatment of **7** with hydrazine monohydrate in aq 95% ethanol followed by *N*- and *O*-acetylation, and then methyl esterification of the carboxyl group with diazomethane, afforded compound **8** in good yield. Hydrolysis of the isopropylidene group in **8** with aq 80% acetic acid overnight at 50 °C gave in 94% yield the key glycosyl acceptor **9** for the synthesis of KDN-GM_1 and KDN-GD_{1a}. Catalytic hydrogenolysis (10% Pd-C) of the benzyl groups of **9** in ethanol-acetic acid for 48 h at 45 °C, and subsequent *O*-acetylation gave the per-*O*-acetyl-KDN-ganglioside GM_2 oligosaccharide **10** in 85% yield.

Treatment[19] of **10** with trifluoroacetic acid in dichloromethane for 30 min at room temperature gave the 1-hydroxy compound **11**. When treated[20] with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicy-

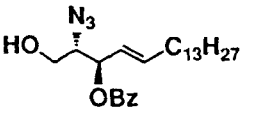
clo[5.4.0]undec-7-ene (DBU) for 30 min at 0 °C, compound **11** gave the α-trichloroacetimidate **12** in 91% yield; significant signals of the Glc residue in the ^{1}H NMR spectrum were a one-proton doublet at δ 6.50 ($J_{1,2}$ = 3.8 Hz, H-1) and a one-proton singlet at δ 8.64 (C = NH), indicating the anomeric configuration of the imidate to be α.

Glycosylation of **9** with **13** or **18**, in dichloromethane in the presence of DMTST[21,22] as a promoter and MS-4Å, gave the corresponding pentasaccharide **14** (61%) and hexasaccharide **19** (65%), respectively. The ^{1}H NMR data for the Gal unit in **14** [δ 4.93 (d, $J_{1,2}$ = 7.6 Hz, H-1e) and 5.45 (dd, $J_{2,3}$ = 10.0 Hz, H-2e)] and for the KDN-Gal unit in **19** [δ 4.87 (d, $J_{1,2}$ = 7.5 Hz, H-1e) and 5.49 (dd, $J_{2,3}$ = 7.9 Hz, H-2e)] indicated the newly formed glycosidic linkage to be β. Catalytic hydrogenolysis of the benzyl groups in **14** and **19** in ethanol-acetic acid and subsequent *O*-acetylation gave the per-*O*-acyl compounds **15** and **20** in 73 and 90% yields, which on selective removal of the 2-(trimethylsilyl)ethyl group and subsequent treatment with trichloroacetonitrile as described for the preparation of **12**, afforded the corresponding penta- and hexasaccharide glycosyl donors **17** and **22** in good yields. The ^{1}H NMR data for the Glc unit in **17** [δ 6.49 ($J_{1,2}$ = 3.1 Hz, H-1), 8.65 (C = NH)] and in **22** [δ 6.49 ($J_{1,2}$ = 3.7 Hz, H-1), 8.37 (C = NH)] established the anomeric configuration of the imidates.

Final glycosylation[23] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[24] (**23**) with **12**, **17**, and **22** in dichloromethane in the presence of boron trifluoride etherate and molecular sieves 4Å (AW-300) for 3 h at 0 °C gave the corresponding β-glycosides **24** (76%), **27** (66%), and **30** (69%), respectively; the ^{1}H NMR data for the Glc unit [δ 4.50~4.51 (d, $J_{1,2}$ = 7.6~7.9 Hz, H-1a)] indicated the glycosidic linkage to be β. Selective reduction[16,25] of the azido group in **24**, **27**, and **30** with hydrogen sulfide in aq 83% pyridine and subsequent condensation with octadecanoic acid, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane, gave the corresponding acylated KDN-gangliosides **25** (69%), **28** (60%), and **31** (55%), respectively. Finally, *O*-deacylations of **25**, **28**, and **31** with sodium methoxide in methanol, with subsequent saponification of the sialate methyl ester group, furnished the desired KDN-gangliosides GM_2 (**26**), GM_1



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



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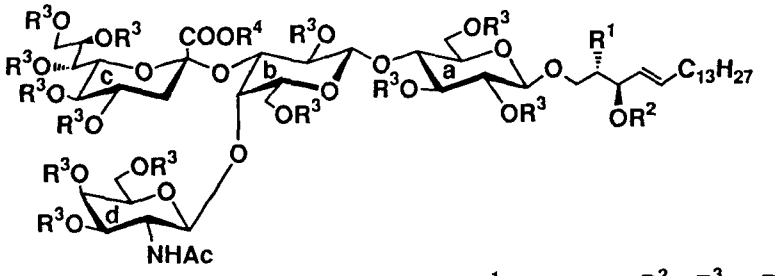
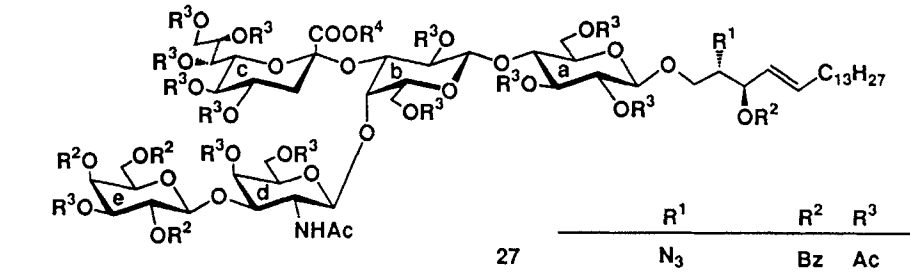
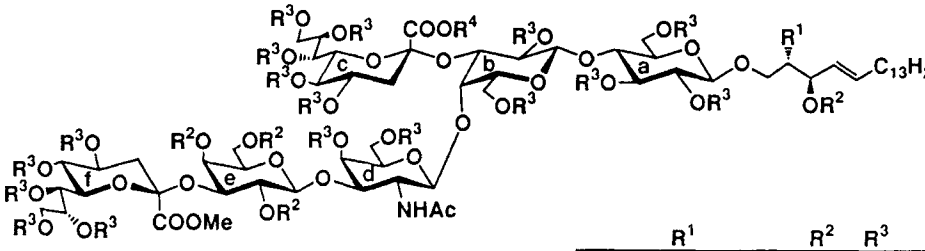


	R^1	R^2	R^3	R^4
24	N_3	Bz	Ac	Me
25	$NHCO(CH_2)_{16}Me$	Bz	Ac	Me
26	$NHCO(CH_2)_{16}Me$	H	H	H



	R^1	R^2	R^3	R^4
27	N_3	Bz	Ac	Me
28	$NHCO(CH_2)_{16}Me$	Bz	Ac	Me
29	$NHCO(CH_2)_{16}Me$	H	H	H



	R^1	R^2	R^3	R^4
30	N_3	Bz	Ac	Me
31	$NHCO(CH_2)_{16}Me$	Bz	Ac	Me
32	$NHCO(CH_2)_{16}Me$	H	H	H

(**29**), and GD_{1a} (**32**) in high yields. The ^1H NMR data of the products thus obtained are consistent with the structures assigned.

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. ^1H NMR spectra were recorded at 270 MHz with a Jeol JNM-GX 270 spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,6-di-

O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (3). To a solution of 2-(trimethylsilyl)ethyl *O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[17] (**2**, 7.0 g, 7.8 mmol) and methyl (phenyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate[18] (**1**, 5.5 g, 9.4 mmol) in MeCN (30 mL) were added molecular sieves 3Å (MS-3Å, 10 g), and the mixture was stirred for 5 h at room temperature then cooled to -40 °C. To the cooled mixture were added, with stirring, *N*-iodosuccinimide (NIS, 3.45 g, 14 mmol) and trimethylsilyl trifluoromethanesulfonate (TMS•OTf, 0.36 mL), and the stirring was continued for 2 h at -40 °C. The precipitate was filtered off and washed thoroughly with CH_2Cl_2. The combined filtrate and washings 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 EtOAc-hexane) of the residue on silica gel (300 g) gave **3** (5.75 g, 54%) as an amorphous mass; $[\alpha]_D$ +7.7° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.15 (m, 2H, $Me_3SiCH_2CH_2$), 1.83, 1.99, 2.00, 2.11, 2.15 (5s, 15H, 5AcO), 2.62 (dd, 1H, J_{gem} = 12.0 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3c*eq*), 3.91 (s, 3H, MeO), 4.79 (m, 1H, $J_{3ax,4}$ = 11.5 Hz, $J_{4,5}$ = 10.7 Hz, H-4c), 4.98 (t, 1H, $J_{5,6}$ = 10.7 Hz, H-5c), 5.32 (dd, 1H, $J_{6,7}$ = 2.1 Hz, $J_{7,8}$ = 8.8 Hz, H-7c), 5.45 (m, 1H, H-8c), and 7.21-7.40 (m, 25H, 5Ph).

Anal. Calcd for $C_{72}H_{90}O_{24}Si$ (1367.6): C, 63.24; H, 6.63. Found: C, 63.15; H, 6.58.

A sample (40 mg) of **3** was acetylated with Ac_2O (1 mL) in pyridine (2 mL) overnight at room temperature to give **4** (42 mg, quantitative) as an amorphous mass; $[\alpha]_D$ +6.7° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.10 (m, 2H, $Me_3SiCH_2CH_2$), 1.80-2.20 (6s, 18H, 6AcO), 2.58 (dd, 1H, J_{gem} = 13.2 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c*eq*), 3.88 (s, 3H, MeO), 4.83 (m, 1H, H-4c), 5.01 (t, 1H, $J_{5,6}$ = 11.0 Hz, H-5c), 5.39 (m, 1H, H-8c), 5.43 (br d, 1H, $J_{3,4}$ = 3.2 Hz, H-4b), and 7.20-7.40 (m, 25H, 5Ph).

Anal. Calcd for $C_{74}H_{84}O_{26}Si$ (1417.5): C, 62.70; H, 5.97. Found: C, 62.53; H, 6.12.

2-(Trimethylsilyl)ethyl O-(Methyl 4,5,7,8,9-Penta-O-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-O-[(6-O-

benzyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (6). To a solution of methyl 6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-1-thio-β-D-galactopyranoside[12] (**5**, 3.48 g, 7.4 mmol) and **3** (7.24 g, 5.3 mmol) in CH_2Cl_2 (60 mL) were added MS-4Å (6 g), and the mixture was stirred for 12 h at room temperature then cooled to -10 °C. NIS (3.63 g, 14.8 mmol) and trifluoromethanesulfonic acid (TfOH, 0.13 mL) were added and the mixture was stirred for 2 h at -10 °C while the progress of the reaction was monitored by TLC. Processing as described for **3** gave **6** (6.52 g, 71%) as an amorphous mass; $[\alpha]_D$ +23.0° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.04 (m, 2H, $Me_3SiCH_2CH_2$), 1.34, 1.51 (2s, 6H, Me_2C), 1.67, 1.92, 1.97, 2.01, 2.07 (5s, 15H, 5AcO), 2.81 (dd, 1H, J_{gem} = 11.3 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3c*eq*), 3.79 (s, 3H, MeO), 4.45 (d, 1H, 7.3 Hz, H-1b), 4.90 (m, 1H, H-4c), 5.28 (dd, 1H, $J_{6,7}$ = 2.3 Hz, $J_{7,8}$ = 9.2 Hz, H-7c), 5.44 (m, 1H, H-8c), and 7.14-7.85 (m, 34H, 6Ph, NPhth).

Anal. Calcd for $C_{96}H_{113}NO_{30}Si$ (1789.0): C, 64.45; H, 6.37; N, 0.78. Found: C, 64.40; H, 6.23; N, 0.69.

2-(Trimethylsilyl)ethyl *O*-(4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-*O*-[(6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (7). To a solution of **6** (6.5 g, 3.6 mmol) in pyridine (100 mL) was added LiI (1.92 g, 14.4 mmol) and the mixture was refluxed for 12 h, with stirring, under N_2 gas in the dark then concentrated. Dichloromethane (200 mL) was added and the mixture was washed with 2M HCl, and water, dried (Na_2SO_4) and concentrated. Column chromatography of the residue on silica gel (200 g) gave **7** (5.82 g, 90%) as an amorphous mass; $[\alpha]_D$ +12.5° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.31, 1.56 (2s, 6H, Me_2C), 1.73-2.09 (5s, 15H, 5AcO), 2.91 (dd, 1H, J_{gem} = 13.2 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3c*eq*), 4.30 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1a), 4.49 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1b), 5.05 (m, 1H, H-4c), 5.31 (dd, 1H, $J_{6,7}$ = 2.4 Hz, $J_{7,8}$ = 9.4 Hz, H-7c), 5.41 (m, 1H, H-8c), and 7.06-7.78 (m, 34H, 6Ph, NPhth).

Anal. Calcd for $C_{95}H_{111}NO_{30}Si$ (1774.9): C, 64.28; H, 6.30; N, 0.79. Found: C, 64.33; H, 6.18; N, 0.81.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (8). A solution of **7** (5.7 g, 3.2 mmol) in aq 95% EtOH (100 mL) was treated with hydrazine monohydrate (3.2 mL) for 8 h under reflux. The precipitate was collected and washed with EtOH, and the combined filtrate and washings was concentrated. The residue was acetylated with Ac_2O (5 mL) in pyridine (10 mL), and the product in MeOH (20 mL) was treated with large excess of diazomethane in ether. After decomposition of the excess diazomethane by addition of AcOH, the mixture was concentrated. Column chromatography (2:1 EtOAc-hexane) of the residue on silica gel (150 g) afforded **8** (3.83 g, 71%) as an amorphous mass; $[\alpha]_D$ +18.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.10 (m, 2H, $Me_3SiCH_2CH_2$), 1.34, 1.67 (2s, 6H, Me_2C), 1.88-2.04 (6s, 18H, 5AcO, AcN), 2.40 (dd, 1H, J_{gem} = 14.0 Hz, $J_{3eq,4}$ = 4.4 Hz, H-3c*eq*), 3.81 (s, 3H, MeO), 4.41 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1a), 4.51 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.80 (ddd, $J_{3ax,4}$ = 13.8 Hz, $J_{4,5}$ = 9.7 Hz, H-4c), 5.22 (m, 2H, H-7c,8c), 7.20-7.41 (m, 30H, 6Ph).

Anal. Calcd for $C_{90}H_{113}NO_{29}Si$ (1701.0): C, 63.55; H, 6.70; N, 0.82. Found: C, 63.37; H, 6.59; N, 0.62.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (9). A solution of **8** (500 mg, 0.29 mmol) in aq 80% AcOH (10 mL) was heated, with stirring, overnight at 50 °C and concentrated. Column chromatography (80:1 CH_2Cl_2-MeOH) of the residue on silica gel (100g) gave **9** (460 mg, 94%) as an amorphous mass; $[\alpha]_D$ +0.4° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.13 (m, 2H, $Me_3SiCH_2CH_2$), 1.78, 1.95, 1.97, 2.00, 2.04, 2.09 (6s, 18H, 5AcO, AcN), 2.33 (dd, 1H, J_{gem} = 14.3 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c*eq*), 3.85 (s, 3H, MeO), 4.39 (d,

1H, $J_{1,2}$ = 7.7 Hz, H-1a), 4.51 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.81 (ddd, $J_{3ax,4}$ = 13.5 Hz, $J_{4,5}$ = 10.3 Hz, H-4c), 5.24 (m, 2H, H-7c, 8c), and 7.13-7.45 (m, 30H, 6Ph).

Anal. Calcd for $C_{87}H_{109}NO_{29}Si$ (1660.9): C, 62.92; H, 6.62; N, 0.84. Found: C, 62.80; H, 6.49; N, 0.76.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (10). A solution of **9** (340 mg, 0.2 mmol) in EtOH (45 mL) and AcOH (8 mL) was hydrogenolyzed in the presence of 10% Pd-C (400 mg) for 48 h at 45 °C. The solids were filtered off and washed with MeOH. The combined filtrate and washings was concentrated, and the residue was acetylated with Ac_2O (2 mL) in pyridine (5 mL) for 24 h at 40 °C. Column chromatography (60:1 CH_2Cl_2-MeOH) of the product on silica gel (30 g) gave **10** (252 mg, 85%) as an amorphous mass; $[\alpha]_D$ -24.5° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.96 (m, 2H, $Me_3SiCH_2CH_2$), 1.96-2.19 (14s, 52H, 13AcO, AcN), 2.86 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 4.3 Hz, H-3c*eq*), 3.70 (s, 3H, MeO), 4.47 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1a), 4.60 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1b), 4.86 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H-3a), 4.93 (ddd, 1H, $J_{3ax,4}$ = 13.0 Hz, $J_{4,5}$ = 10.0 Hz, H-4c), 4.97 (dd, 1H, H-2a), 5.14 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1d), 5.16 (t, 1H, $J_{2,3}$ = 7.9 Hz, H-2b), 5.36 (br d, 1H, $J_{3,4}$ = 3.2 Hz, H-4d), 5.40 (dd, 1H, $J_{6,7}$ = 2.9 Hz, $J_{7,8}$ = 9.8 Hz, H-7c), 5.57 (m, 1H, H-8c), 5.83 (dd, 1H, $J_{2,3}$ = 11.1 Hz, H-3d), and 5.96 (d, 1H, NH).

Anal. Calcd for $C_{61}H_{89}NO_{37}Si$ (1456.4): C, 50.31; H, 6.16; N, 0.96. Found: C, 50.22; H, 6.13; N, 0.79.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (12).** To a solution of **10** (160 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) was added CF_3CO_2H (3 mL), and the mixture was stirred for 30 min at room

temperature then concentrated. Column chromatography (20:1 CH_2Cl_2-MeOH) of the residue on silica gel (20 g) gave **11** (140 mg, quantitative). To a solution of **11** obtained in CH_2Cl_2 (2 mL) and trichloroacetonitrile (0.5 mL), cooled to -5 °C, was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 19 μL), and the mixture was stirred for 30 min at 0 °C. Column chromatography (50:1 CH_2Cl_2-MeOH) of the mixture on silica gel (30 g) afforded **12** (150 mg, 91%) as an amorphous mass; $[\alpha]_D$ +9.1° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.97-2.15 (14s, 42H, 13AcO, AcN), 2.88 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 4.3 Hz, H-3c*eq*), 3.81 (s, 3H, MeO), 4.60 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1b), 4.62 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.8 Hz, H-3a), 5.08 (dd, 1H, $J_{1,2}$ = 3.8 Hz, H-2a), 5.15 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1d), 5.36 (br d, 1H, $J_{3,4}$ = 3.7 Hz, H-4d), 5.42 (dd, 1H, $J_{6,7}$ = 2.7 Hz, $J_{7,8}$ = 9.8 Hz, H-7c), 5.51 (t, 1H, H-2b), 5.87 (dd, 1H, $J_{2,3}$ = 11.1 Hz, H-3d), 6.07 (d, 1H, NH), 6.50 (d, 1H, H-1a), and 8.64 (s, 1H, C = NH).

Anal. Calcd for $C_{58}H_{77}N_2O_{37}Cl_3$ (1500.6): C, 46.42; H, 5.17; N, 1.85. Found: C, 46.41; H, 5.15; N, 1.75.

2-(Trimethylsilyl)ethyl *O*-(2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (14). To a solution of **9** (500 mg, 0.3 mmol) and methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside[13] (**13**, 274 mg, 0.45 mmol) in CH_2Cl_2 (10 mL) were added MS-4Å (1 g) and the mixture was stirred for 5 h at room temperature then cooled to -20 °C. DMTST (230 mg, 0.9 mmol) was added and the mixture was stirred for 20 h at -20 °C. The solids were collected and washed with CH_2Cl_2, and the combined filtrate and washings was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:1 EtOAc-hexane) of the residue on silica gel (40 g) gave **14** (410 mg, 61%) as an amorphous mass; $[\alpha]_D$ +3.5° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.18 (m, 2H, $Me_3SiCH_2CH_2$), 1.67 (s, 3H, AcN), 1.96, 1.98, 1.99, 2.04, 2.06 (5s, 15H, 5AcO), 2.55 (dd, 1H, J_{gem} = 13.5 Hz, $J_{3eq,4}$ = 5.1 Hz, H-3c*eq*), 4.93 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1e), 5.25 (dd, 1H, $J_{6,7}$ =

1.7 Hz, $J_{7,8}$ = 9.6 Hz, H-7c), 5.45 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-2e), and 7.30-8.10 (m, 50H, 10Ph).

Anal. Calcd for $C_{121}H_{137}NO_{37}Si$ (2225.5): C, 65.30; H, 6.21; N, 0.63. Found: C, 65.12; H, 6.12; N, 0.59.

2-(Trimethylsilyl)ethyl *O*-(3-*O*-Acetyl-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (15). Hydrogenolysis of **14** (380 mg, 0.17 mmol) in EtOH (50 mL) and AcOH (9 mL) in the presence of 10% Pd-C (500 mg) for 48 h at 40 °C, and subsequent acetylation with Ac_2O (2 mL) in pyridine (5 mL) for 24 h at 40 °C gave the product, which was purified by column chromatography (100:1 CH_2Cl_2-MeOH) on silica gel (50 g) to give **15** (242 mg, 73%) as an amorphous mass; $[\alpha]_D$ -5.6° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.05 (m, 2H, $Me_3SiCH_2CH_2$), 1.68 (s, 3H, AcN), 1.90-2.19 (13s, 39H, 13AcO), 2.58 (dd, 1H, J_{gem} = 12.9 Hz, $J_{3eq,4}$ = 6.0 Hz, H-3c*eq*), 3.82 (s, 3H, MeO), 4.93 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1e), 5.02 (m, 1H, H-4c), 5.21 (br d, 1H, $J_{3,4}$ = 3.2 Hz, H-4e), 5.25 (dd, 1H, $J_{6,7}$ = 2.7 Hz, $J_{7,8}$ = 9.9 Hz, H-7c), 5.38 (m, 1H, H-8c), 5.46 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-2e), 5.62 (dd, 1H, H-3e), 5.87 (br d, 1H, $J_{3,4}$ = 3.2 Hz, H-4d), 6.11 (d, 1H, NH), and 7.03-8.28 (m, 15H, 3Ph).

Anal. Calcd for $C_{88}H_{111}NO_{45}Si$ (1930.9): C, 54.74; H, 5.79; N, 0.73. Found: C, 54.54; H, 5.69; N, 0.66.

***O*-(3-*O*-Acetyl-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl trichloroacetimidate (17).** Selective removal of the 2-(trimethylsilyl)ethyl group in **15** (224 mg, 0.12 mmol) with CF_3CO_2H (5 mL) in CH_2Cl_2 (6 mL) for 2 h at room temperature, and subsequent treatment with trichloroacetonitrile (0.54 mL) in CH_2Cl_2 (2 mL) in the presence of DBU (19 mg) for 3 h at 0 °C as described for **12** gave **17** (215 mg, 94%)

as an amorphous mass; $[\alpha]_D$ +24.0° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.78-2.18 (14s, 42H, 13AcO, AcN), 2.35 (dd, 1H, J_{gem} = 13.8 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3c*eq*), 3.75 (s, 3H, MeO), 4.56 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 5.18 (t, 1H, $J_{2,3}$ = 7.5 Hz, H-2b), 5.39 (dd, 1H, $J_{1,2}$ = 3.1 Hz, $J_{2,3}$ = 7.8 Hz, H-2a), 5.80 (br d, 1H, $J_{3,4}$ = 3.4 Hz, H-4d), 6.49 (d, 1H, H-1a), 7.24-8.18 (m, 15H, 3Ph), and 8.65 (s, 1H, C = NH).

Anal. Calcd for $C_{85}H_{99}N_2O_{25}Cl_3$ (1975.1): C, 51.69; H, 5.05; N, 1.42. Found: C, 51.55; H, 4.95; N, 1.33.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (19). Glycosylation of **9** (400 mg, 0.24 mmol) with **18**[14] (476 mg, 0.48 mmol) in CH_2Cl_2 (4.8 mL) in the presence of DMTST (370 mg, 1.4 mmol) and MS-4Å (650 mg) for 24 h at -10 °C, then workup as described for the preparation of **14** gave **19** (410 mg, 65%) as an amorphous mass; $[\alpha]_D$ +3.3° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.04 (m, 2H, $Me_3SiCH_2CH_2$), 1.86-2.20 (11s, 33H, 10AcO, AcN), 2.49 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3c*eq*), 2.76 (dd, 1H, J_{gem} = 11.6 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3f*eq*), 3.37 (dt, 1H, $J_{1,2} = J_{2,3} = J_{2,NH}$ = 7.6 Hz, H-2d), 3.61, 3.86 (2s, 6H, 2MeO), 4.87 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1e), 5.04 (d, 1H, H-1d), 5.28 (dd, 1H, $J_{6,7}$ = 2.1 Hz, $J_{7,8}$ = 9.6 Hz, H-7c), 5.38 (br d, 1H, $J_{3,4}$ = 3.0 Hz, H-4e), 5.44 (m, 1H, H-8c), 5.49 (dd, 1H, $J_{2,3}$ = 7.9 Hz, H-2e), 5.53 (d, 1H, NH), 5.63 (m, 1H, H-8f), and 7.09-8.17 (m, 45H, 9Ph).

Anal. Calcd for $C_{134}H_{157}NO_{50}Si$ (2609.8): C, 61.67; H, 6.06; N, 0.54. Found: C, 61.50; H, 6.06; N, 0.44.

2-(Trimethylsilyl)ethyl *O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-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→4)-*O*-[(methyl 4,5,7,8,9-

penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (20). Hydrogenolysis of **19** (380 mg, 0.15 mmol) in EtOH (50 mL) and AcOH (8.7 mL) in the presence of 10% Pd-C (500 mg) for 48 h at 45 °C, and subsequent acetylation with Ac_2O (2 mL) in pyridine (5 mL) for 24 h at 40 °C, then conventional workup gave **20** (310 mg, 90%) as an amorphous mass; $[\alpha]_D$ +6.1° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.05 (m, 2H, $Me_3SiCH_2CH_2$), 1.84-2.13 (18s, 54H, 17AcO, AcN), 2.51 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3c*eq*), 2.57 (dd, 1H, J_{gem} = 12.3 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3f*eq*), 3.37 (dt, 1H, $J_{1,2} = J_{2,3} = J_{2,NH}$ = 7.7 Hz, H-2d), 3.58, 3.81 (2s, 6H, 2MeO), 4.57 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.79 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1e), 5.04 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1d), 5.37 (t, 1H, H-2b), 5.38 (br d, 1H, $J_{3,4}$ = 3.3 Hz, H-4e), 5.43 (m, 1H, H-8c), 5.55 (br d, 1H, $J_{3,4}$ = 3.1 Hz, H-4d), 5.71 (d, 1H, NH), and 7.12-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{106}H_{135}NO_{57}Si$ (2363.3): C, 53.87; H, 5.76; N, 0.59. Found: C, 53.69; H, 5.61; N, 0.63.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (22).** Selective removal of the 2-(trimethylsilyl)ethyl group in **20** (360 mg, 0.15 mmol) with CF_3CO_2H (2 mL) in CH_2Cl_2 (3 mL) for 2 h at room temperature, and subsequent treatment with trichloroacetonitrile (0.7 mL) in CH_2Cl_2 (3 mL) in the presence of DBU (25 mg) for 30 min at 0 °C as described for **17** gave **22** (313 mg, 85%) as an amorphous mass; $[\alpha]_D$ +30.0° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.86-2.19 (18s, 54H, 17AcO, AcN), 2.51 (dd, 1H, J_{gem} = 12.3 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3c*eq*), 2.93 (dd, 1H, J_{gem} = 12.3 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3f*eq*), 3.51, 3.80 (2s, 6H, 2MeO), 4.55 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1b), 4.91 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1e), 4.97 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1d), 5.27 (dd, 1H, $J_{1,2}$ = 3.7

Hz, $J_{2,3}$ = 7.6 Hz, H-2a), 5.35 (t, 1H, H-2b), 5.49 (t, 1H, H-2e), 5.63 (m, 1H, H-8f), 6.15 (d, 1H, NH), 6.49 (d, 1H, H-1a), 7.17-8.11 (m, 15H, 3Ph), and 8.37 (s, 1H, C = NH).

Anal. Calcd for $C_{103}H_{123}N_2O_{57}Cl_3$ (2407.4): C, 51.39; H, 5.15; N, 1.16. Found: C, 51.28; H, 5.03; N, 1.01.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (24).** To a solution of **12** (154 mg, 0.1 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[24] (**23**, 127 mg, 0.3 mmol) in CH_2Cl_2 (1.5 mL) were added MS-4Å (AW-300, 500 mg) and the mixture was stirred for 6 h at room temperature then cooled to 0 °C. BF_3•OEt_2 (36 μL, 0.3 mmol) was added and the mixture was stirred for 3 h at 0 °C. The solids were filtered off and washed with CH_2Cl_2, and the combined filtrate and washings were concentrated. Column chromatography (60:1 CH_2Cl_2-MeOH) of the residue on silica gel (50 g) gave **24** (138 mg, 76%) as an amorphous mass; $[\alpha]_D$ -27.2° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3H, CH_3CH_2), 1.24 (s, 22H, $11CH_2$), 1.96-2.16 (14s, 42H, 13AcO, AcN), 2.86 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.3 Hz, H-3c*eq*), 3.83 (s, 3H, MeO), 4.50 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1a), 4.60 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1b), 4.82 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.8 Hz, H-4a), 4.94 (m, 1H, H-4c), 4.97 (dd, 1H, H-2a), 5.13 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1d), 5.17 (t, 1H, $J_{2,3}$ = 7.7 Hz, H-2b), 5.36 (br d, $J_{3,4}$ = 3.0 Hz, H-4d), 5.41 (dd, 1H, $J_{6,7}$ = 2.6 Hz, $J_{7,8}$ = 9.8 Hz, H-7c), 5.50 (m, 1H, H-8c), 5.84 (dd, 1H, $J_{2,3}$ = 11.3 Hz, H-3d), 5.92 (dt, 1H, $J_{4,5}$ = 14.1 Hz, $J_{5,6} = J_{5,6'}$ = 7.1 Hz, H-5 of sphingosine), 5.97 (d, 1H, NH), and 7.14-8.21 (m, 5H, Ph).

Anal. Calcd for $C_{81}H_{114}N_4O_{39}$ (1767.8): C, 55.03; H, 6.50; N, 3.17. Found: C, 54.89; H, 6.38; N, 3.15.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-[(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)]-*O*-(2,6-di-*O*-acetyl-β-D-**

galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (25). Hydrogen sulfide was bubbled through a stirred solution of **24** (125 mg, 0.07 mmol) in aq 83% pyridine (18 mL) for 2 days at 0 °C, with the progress of the reaction monitored by TLC. The mixture was concentrated and the residue was stirred with octadecanoic acid (58.3 mg, 0.21 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC, 39 mg, 0.21 mmol) in dry CH_2Cl_2 (3 mL) for 12 h at room temperature. After completion of the reaction, CH_2Cl_2 (50 mL) was added and the solution was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (60:1 CH_2Cl_2-MeOH) of the residue on silica gel (20 g) gave **25** (98 mg, 69%) as an amorphous mass; $[\alpha]_D$ -10.0° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, $2CH_3CH_2$), 1.25 (s, 52H, $26CH_2$), 1.92-2.19 (14s, 42H, 13AcO, AcN), 2.87 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 3.9 Hz, H-3c*eq*), 3.85 (s, 3H, MeO), 4.43 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1a), 4.55 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1b), 4.90 (t, 1H, $J_{2,3}$ = 7.8 Hz, H-2a), 5.13 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1d), 5.15 (t, 1H, $J_{2,3}$ = 8.7 Hz, H-2b), 5.41 (dd, 1H, $J_{6,7}$ = 2.6 Hz, $J_{7,8}$ = 9.6 Hz, H-7c), 5.52 (m, 1H, H-8c), 5.92 (dt, 1H, $J_{4,5}$ = 14.3 Hz, $J_{5,6}$ = $J_{5,6'}$ = 7.1 Hz, H-5 of sphingosine), 6.18 (d, 1H, NH), and 7.08-8.20 (m, 5H, Ph).

Anal. Calcd for $C_{99}H_{150}N_2O_{40}$ (2008.3): C, 59.21; H, 7.53; N, 1.39. Found: C, 59.00; H, 7.43; N, 1.35.

KDN-Ganglioside GM2 (26). To a solution of **25** (60 mg, 0.03 mmol) in MeOH (3 mL) was added NaOMe (10 mg) and the mixture was stirred for 24 h at room temperature. 0.2 M Potassium hydroxide (0.7 mL) was added and the solution was stirred for 12 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with 1:1 $CHCl_3$-MeOH, and the combined filtrate and washings were concentrated. Column chromatography (1:1 $CHCl_3$-MeOH) of the residue on Sephadex LH-20 (20 g) gave **26** (33 mg, 82%) as an amorphous mass; $[\alpha]_D$ +8.2° (*c* 0.22, 5:5:1 $CHCl_3$-MeOH-H_2O); ^1H NMR [49:1 $(CD_3)_2SO$-D_2O, at 55 °C]: δ 0.85 (t, 6H, $2CH_3CH_2$), 1.24 (s, 52H, $26CH_2$), 1.86 (s, 3H, AcN), 2.50 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3c*eq*), 4.21, 4.31 (2d, 2H, $J_{1,2}$ = 7.6 Hz, H-1a and H-1b), 4.81 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1d), and 5.34, 5.58 (m, 2H, H-4,5 of sphingosine).

Anal. Calcd for $C_{65}H_{118}N_2O_{26}$ (1343.7): C, 58.10; H, 8.85; N, 2.08. Found: C, 57.97; H, 8.61; N, 2.07.

***O*-(3-*O*-Acetyl-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (27).** Coupling of **17** (197 mg, 0.1 mmol) with **23** (127 mg, 0.29 mmol) as described for **24** gave **27** (149 mg, 66%) as an amorphous mass; $[\alpha]_D$ +2.3° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.89 (t, 3H, CH_3CH_2), 1.24 (s, 22H, $11CH_2$), 1.80-2.22 (14s, 42H, 13AcO, AcN), 2.36 (dd, 1H, J_{gem} = 14.0 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3c*eq*), 3.80 (s, 3H, MeO), 4.51 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1a), 4.53 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 5.03 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1e), 5.14 (t, 1H, $J_{2,3}$ = 7.6 Hz, H-2a), 5.27 (br d, 1H, $J_{3,4}$ = 3.3 Hz, H-4d), 5.30 (t, 1H, $J_{2,3}$ = 7.5 Hz, H-2b), 5.40 (dd, 1H, $J_{6,7}$ = 3.1 Hz, $J_{7,8}$ = 9.0 Hz, H-7c), 5.52 (t, 1H, $J_{3,4}$ = 7.6 Hz, H-2e), 5.93 (dt, 1H, $J_{4,5}$ = 14.3 Hz, $J_{5,6}$ = $J_{5,6'}$ = 6.7 Hz, H-5 of sphingosine), and 7.34-8.09 (m, 20H, 4Ph).

Anal. Calcd for $C_{108}H_{136}N_4O_{47}$ (2242.3): C, 57.85; H, 6.11; N, 2.50. Found: C, 57.65; H, 6.06; N, 2.40.

***O*-(3-*O*-Acetyl-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (28).** Selective reduction of the azido group in **27** (60 mg, 0.059 mmol) with H_2S in aq 83% pyridine (18 mL), and subsequent coupling with octadecanoic acid (22 mg, 0.078 mmol) in the presence of WSC (15 mg) in CH_2Cl_2 (3 mL) as described for **25** gave **28** (40.1 mg, 60%) as an amorphous mass; $[\alpha]_D$ -0.8° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, $2CH_3CH_2$), 1.24 (s, 52H, $26CH_2$), 1.75-2.18 (14s, 42H,

13AcO, AcN), 2.86 (dd, 1H, J_{gem} = 13.1 Hz, $J_{3eq,4}$ = 4.1 Hz, H-3c*eq*), 3.81 (s, 3H, MeO), 4.47 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1a), 4.57 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1b), 4.93 (t, 1H, H-2a), 5.01 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1e), 5.15 (t, 1H, $J_{2,3}$ = 7.6 Hz, H-2b), 5.40 (dd, 1H, $J_{6,7}$ = 3.0 Hz, $J_{7,8}$ = 9.0 Hz, H-7c), 5.41 (t, 1H, $J_{2,3}$ = 7.9 Hz, H-2e), 5.78 (br d, $J_{3,4}$ = 2.3 Hz, H-4d), 5.87 (d, 1H, NH), 5.98 (dt, 1H, $J_{4,5}$ = 13.9 Hz, $J_{5,6}$ = $J_{5,6'}$ = 7.3 Hz, H-5 of sphingosine), and 7.23-8.11 (m, 20H, 4Ph).

Anal. Calcd for $C_{126}H_{172}N_2O_{48}$ (2482.7): C, 60.96; H, 6.85; N, 1.13. Found: C, 60.95; H, 6.85; N, 1.06.

KDN-Ganglioside GM1 (29). Deacylation and saponification of **28** (27 mg, 0.01 mmol) as described for **26** gave **29** (15 mg, 89%) as an amorphous mass; $[\alpha]_D$ +3.5° (*c* 0.5, 5:4:1 $CHCl_3$-MeOH-H_2O); ^1H NMR [49:1 $(CD_3)_2SO$-D_2O]: δ 0.90 (t, 6H, 2C*H*$_3$CH$_2$), 1.25 (s, 52H, 26CH$_2$), 1.90 (s, 3H, AcN), 2.45 (br dd, 1H, H-3c*eq*), and 5.45, 5.65 (2m, 2H, H-4,5 of sphingosine).

Anal. Calcd for $C_{71}H_{128}N_2O_{31}$ (1505.8): C, 56.63; H, 8.57; N, 1.86. Found: C, 56.47; H, 8.28; N, 1.65.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-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→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (30).** Coupling of **22** (314 mg, 0.14 mmol) with **23** (164 mg, 0.38 mmol) as described for **24** gave **30** (252 mg, 69%) as an amorphous mass; $[\alpha]_D$ +16.5° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.89 (t, 3H, C*H*$_3$CH$_2$), 1.25 (s, 22H, 11CH$_2$), 1.71-2.19 (18s, 54H, 17AcO, AcN), 2.36, 2.58 (2br dd, 2H, H-3c*eq*, H-3f*eq*), 5.68 (m, 1H, H-5 of sphingosine), and 7.30-8.10 (m, 20H, 4Ph).

Anal. Calcd for $C_{126}H_{160}N_4O_{59}$ (2674.6): C, 56.58; H, 6.03; N, 2.09. Found: C, 56.53; H, 5.88; N, 2.00.

***O*-(Methyl 4,5,7,8,9-Penta-*O*-acetyl-3-deoxy-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-ga-**

lactopyranosyl)-(1→4)-*O*-[(methyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-*O*-(2,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (31). Selective reduction of the azido group in **30** (229 mg, 0.085 mmol) with H_2S in aq 83% pyridine (10 mL) and subsequent coupling with octadecanoic acid (71 mg, 0.25 mmol) in the presence of WSC (48 mg, 0.25 mmol) as described for **25** gave **31** (137 mg, 55%) as an amorphous mass; $[\alpha]_D$ +9.4° (*c* 2.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, 2C*H*$_3$CH$_2$), 1.24 (s, 52H, 26CH_2), 1.85-2.15 (18s, 54H, 17AcO, AcN), 2.50, 2.60 (br dd, 2H, H-3c*eq*, H-3f*eq*), 3.60, 3.81 (2s, 6H, 2MeO), 5.70 (m, 1H, H-5 of sphingosine), and 7.26-8.07 (m, 20H, 4Ph).

Anal. Calcd for $C_{144}H_{196}N_2O_{60}$ (2915.1): C, 59.33; H, 6.78; N, 0.96. Found: C, 59.13; H, 6.68; N, 0.89.

KDN-Ganglioside GD_{1a} (32). Deacylation and saponification of **31** (100 mg, 0.034 mmol) as described for **26** yielded **32** (52 mg, 86%) as an amorphous mass; $[\alpha]_D$ -3.4° (*c* 0.5, 1:1 $CHCl_3$-MeOH); ^1H NMR [49:1 $(CD_3)_2SO$-D_2O, at 55 °C]: δ 0.88 (t, 6H, 2C*H*$_3$CH$_2$), 1.25 (s, 52H, 26CH_2), 1.92 (s, 3H, AcN), 2.43 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3c*eq*), 2.61 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3f*eq*), 4.22, 4.27, 4.31 (3d, 3H, $J_{1,2}$ = 7.5-7.6 Hz, H-1a,b,e), 4.73 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1d), 5.31, 5.53 (2m, 2H, H-4,5 of sphingosine).

Anal. Calcd for $C_{80}H_{142}N_2O_{39}$ (1756.0): C, 54.72; H, 8.15; N, 1.60. Found: C, 54.66; H, 8.02; N, 1.51.

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