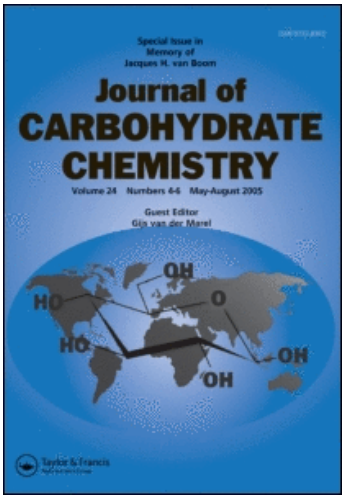

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Total Synthesis of Glycohexa- and Nonaosyl Ceramide with a Sialyl Le^a and Sialyl Dimeric Le^a Sequence

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TOTAL SYNTHESIS OF GLYCOHEXA- AND NONAOSYL CERAMIDE WITH A SIALYL Le^a AND SIALYL DIMERIC Le^a SEQUENCE[1]

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ABSTRACT

A total synthesis of tumor-associated glycolipid antigen sialyl Le^a, and a first total synthesis of glycononaosyl ceramide with a dimeric Le^a sequence are described. Regio- and stereoselective coupling of sialyl donor **12** with suitably protected Le^a trisaccharide fluoride **17** was performed by orthogonal glycosylation to give the expected tetrasaccharide **18** in good yield. Glycosylation of its acetate **19** with lactose derivative **8** by use of Cp_2HfCl_2-AgOTf as a promoter, gave the desired hexasaccharide **20**. On the other hand, glycosylation between sialyl Le^a tetrasaccharide donor **34** and Le^a pentasaccharide acceptor **35** under the agency of PhSeOTf afforded the desired nonasaccharide **36**. After replacement of the benzyl groups in **20** and **36** by acetyl groups, the anomeric acetate was transformed into the α-trichloroacetoimidates **23**, **39** and the fluoride derivative **40**. The crucial couplings of **23**, **39** and **40** with azidosphingosine derivative **3** or ceramide derivative **4** were executed to afford β-glycosides **24** and **41**. Compound **24** was converted to **26** *via* reduction of the azide group followed by *N*-acylation. The target gangliosides **1** and **2** were obtained from **26**

and **41**, respectively, by selective cleavage of the methyl ester, conversion of the *N*-phthalimido group to the *N*-acetamido group, and *O*-deprotection.

INTRODUCTION

Sialyl Le^a ganglioside has been isolated[2] from human adenocarcinoma cell line SW1116, and found[3] to be widespread as the tumor-associated glycolipid antigen of digestive organs. Recently it was reported that MUC1 and CD43 mucins, which have a sialyl Le^a epitope, can inhibit leukocyte adhesion to E-selectin.[4] In 1993, Kitagawa reported the isolation and characterization of hybrid-type sialyl Le^a-Le^x glycosphingolipid, but sialyl dimeric Le^a glycosphingolipid has not been isolated from nature so far.

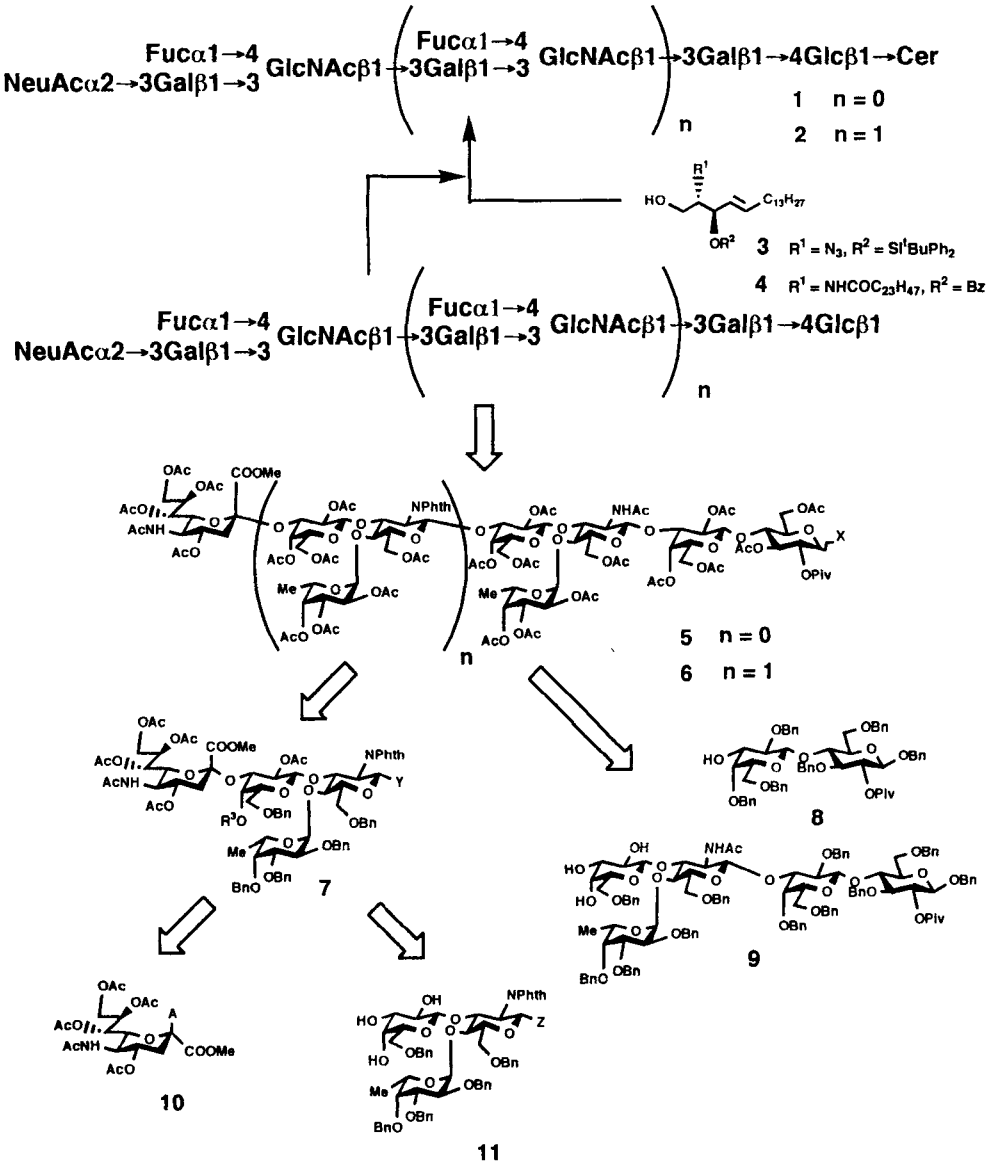
In order to facilitate further biochemical studies of **1** and **2**, an achievement of their efficient synthesis is a challenging task. As part of our current investigation[5-7] on the synthesis of glycosphingolipid with biological importance, we report herein a stereo-controlled synthesis of sialyl Le^a ganglioside **1** which is carried out by taking a different and efficient strategy from that reported by Hasegawa[8] as well as a first total synthesis of sialyl dimeric Le^a glycononaosyl ceramide **2**.

RESULTS AND DISCUSSION

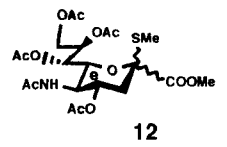
A retrosynthetic analysis of the targets **1**, **2** (Scheme 1) led us to design the putative glycosyl donors **5**, **6** that could be coupled with azidosphingoshine derivative **3**[9] or ceramide derivative **4**.[10] The glycosyl donors **5**, **6** were expected to be constructed from the coupling between tetrasaccharide donor **7** and lactose acceptor **8**[11] or pentasaccharide acceptor **9**.[5] The efficiency of the pivaloyl auxiliary group at *O*-2a of **9** was established in previous studies.[12] Putative donor **7** was further dissected into sialic acid donor **10** and Le^a trisaccharide acceptor **11**.

1 Synthesis of SLe^a-Lac-Cer

In order to construct donor **18**, triol **17**, which was designed to afford a better coupling yield for the next α-sialylation, was selected as the glycosyl acceptor. Le^a trisaccharide **13**[5] was converted into compound **17** as follows. Deallylation of **13** with 1) $[Ir(COD)(PMeph_2)_2]PF_6$[13] in THF and 2) I_2 in aq. THF afforded hemiacetal **14** in 97%



Scheme 1



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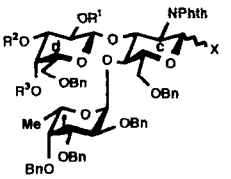
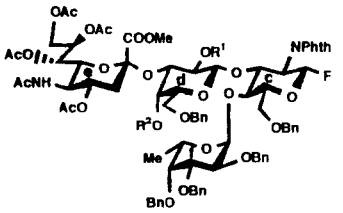
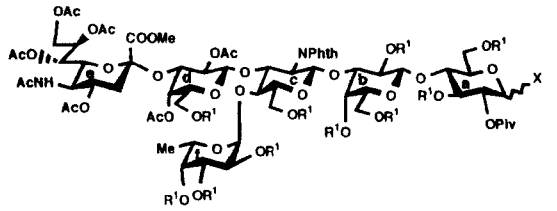


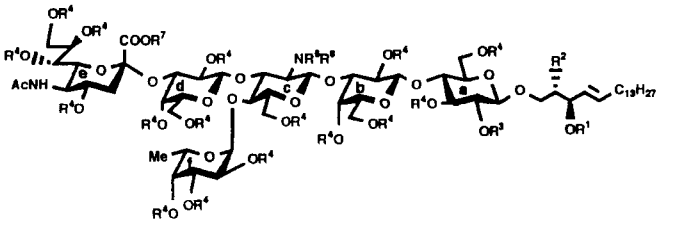
	R^1	R^2	R^3	X
13	Ac	Ac	Ac	OAll (β)
14	Ac	Ac	Ac	OH (β)
15	Ac	Ac	Ac	F (αβ)
16	H	H	H	F (α)
17	H	H	H	F (β)



	R^1	R^2
18	H	H
19	Ac	Ac



	R^1	X
20	Bn	OBn (β)
21	Ac	OAc
22	Ac	OH
23	Ac	$OCNHCCl_3$ (α)



	R^1	R^2	R^3	R^4	R^5	R^6	R^7
24	TBDPS	N_3	Piv	Ac	Phth		Me
25	TBDPS	NH_2	Piv	Ac	Phth		Me
26	TBDPS	$NHCOC_{23}H_{47}$	Piv	Ac	Phth		Me
27	TBDPS	$NHCOC_{23}H_{47}$	Piv	Ac	H	Ac	Li
1	H	$NHCOC_{23}H_{47}$	H	H	H	Ac	Na

Scheme 2

yield. Hemiacetal **14** was treated with DAST (diethylaminosulfur trifluoride)[14] at -15 °C to give compound **15** in 90% yield (α : β = 1 : 4). Zemplén *O*-deacetylation of **15** and silica gel separation afforded triol **16** (16%), **17** (71%). To our delight, glycosylation between trisaccharide fluoride **17** and thioglycoside **12**[15] smoothly proceeded under the agency of PhSeOTf[16] in CH_3CN at -40 °C to give the desired tetrasaccharide **18** and corresponding β epimer in 46% and 14%, respectively, without affecting the anomeric fluoride according to the concept of orthogonal glycosylation strategy.[17] No self-condensed product was detected.

The regiochemistry of newly introduced glycosidic linkage of **18** was deduced by converting **18** into its acetate **19**, which showed in the Homonuclear Hartmann-Hahn (HOHAHA) NMR spectra newly deshielded signals for H-2d at δ 4.539 and H-4d at δ 5.142, respectively, confirmig that sialyl residue was unambiguously introduced at C-3d of the galactose residue.

The configuration at C-2e in **19** was assigned as α, based on the ^1H NMR data. The signal for H-4e in **19** was observed at δ 4.85, and the $J_{7e,8e}$ value was observed to be 8.4 Hz, consistent with previous observations.[18] Having the designed tetrasaccharide donor **19** in hand, crucial glycosylation was examined. The glycosylation of **19** with lactose derivative **8**[11] was performed in CH_3CN for 4.5 h at -15 °C in the presence of CP_2HfCl_2 - AgOTf[19] and molecular sieves 3A, to give the desired hexasaccharide **20** in 65% yield. The configuration of C-1c was expected to be β, due to the presence of the *N*-2 phthaloyl group in **19**, which favors the formation of 1,2-*trans* stereochemistry. Indeed, the ^1H NMR spectrum showed a signal for the anomeric proton of H-1c at δ 5.152, thus confirming the β configuration.

The transformation of **20** into glycosyl donor **23** was performed as follows. Catalytic hydrogenolysis of **20** by Perlman's catalyst in MeOH-H_2O (4 : 1) for 17 h, and subsequent acetylation afforded **21** in 99% yield. Chemoselective cleavage of the anomeric acetate of **21** with hydrazinium acetate[20] in DMF afforded hemiacetal **22** in 94% yield. Treatment of **22** with trichloroacetonitrile[21] in the presence of 1,8-diaza-bicyclo[5.4.0]undec-7-ene (DBU) gave α-trichloroacetimidate **23** in 91% yield. Significant signals in the ^1H NMR spectrum of **23** were a one-proton doublet at δ 5.217 (J 3.3Hz) and a one-proton singlet at δ 8.613 (C = NH), indicating the α-configuration. The final glycosylation between **23** and **3** was achieved in CH_2Cl_2 in the presence of boron trifluoride etherate[22] at -15 °C to afford the desired **24** in 86% yield.

The newly introduced glycosidic linkage of **24** was rigorously confirmed to be β (δH 4.172, d, J = 8.1Hz), as revealed in the HOHAHA experiment.

Selective reduction of the azide group in **24** with Ph_3P in toluene-H_2O = 2 : 1,[23] and subsequent condensation with tetracosanoic acid, using 2-chloro-1-methylpyridinium iodide and Bu_3N in CH_2Cl_2,[24] gave the acylated sialyl Le^a ganglioside **26** in 88% yield.

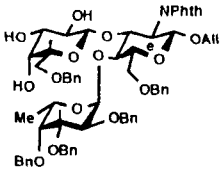
Further conversion into the target glycolipid **1** was executed as follows. Compound **26** was refluxed for 1 day with a large excess of LiI in pyridine[25] to give a 79% yield of the lithium salt **27**. Subsequent treatment of **27** with i) NH_2NHMe in refluxing EtOH[26] ii) Ac_2O in MeOH iii) aq. NaOH in 1 : 1 MeOH-THF iv) Bu_4NF in THF, afforded the target compound **1** in 59% yield, after gel filtration through Sephadex LH-20 using 5 : 5 : 1 $CHCl_3$-MeOH-H_2O. The ^1H NMR data of **1** was consistent with the structure assigned. (Figure 1)

2 Synthesis of SdLe^a-Lac-Cer

Glycosylation between three molar equivalent **29**[27] with Le^a trisaccharide acceptor **28** in CH_3CN was performed by the action of $HgBr_2$-$Hg(CN)_2$ at room temperature[28] to afford the desired α-(2→3)-linked tetrasaccharide **30** in 71% yield based on acceptor, accompanied by a 20% yield of its β-lactone compound. The structure of **31** was confirmed as follows. Acetylation of **30** with acetic anhydride in pyridine at room temperature for 5 h gave only 2-*O*-acetylated **31** in 94% yield. It is worthy of mention that H-4f was not acetylated, presumably due to steric hindrance. HOHAHA NMR spectra showed that H-2f in **31** was deshielded to δ 4.861. The configuration at C-2g in compound **31** was assigned as α,[29] based on the ^1H NMR data. The signal for H-4g in **31** was observed at δ 4.74 , and the $J_{7g,8g}$ value was obseved to be 8.8 Hz,[18] consistent with previous observations.

Compound **31** was converted into thioglycoside **34** as follows. Deallylation of **31** was performed as described for **13** to give hemiacetal **32** in quantitive yield. **32** was transformed into β-trichloroacetimidate **33** in 89% yield in the presence of CCl_3CN and 1,8-diaza-bicyclo[5.4.0]undec-7-one (DBU).[21] The imidate **33** was treated with Bu_3SnSMe and boron trifluoride etherate at -10 °C to give thioglycoside **34** in 96% yield.

Having prepared the designed tetrasaccharide donor **34**, and the pentasaccharide acceptor **35**, crucial glycosylation was examined. PhSeOTf-promoted[16] glycosylation between **34** and **35** in CH_3CN at -10 °C was performed in a regio- and



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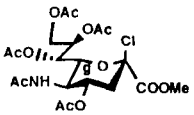

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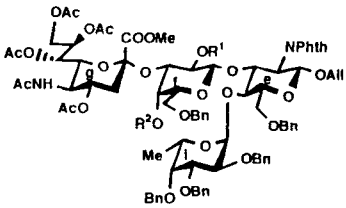
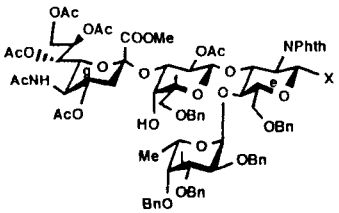
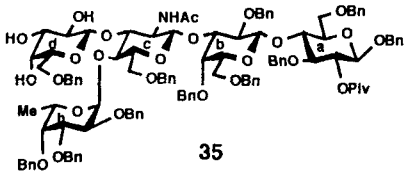


	R^1	R^2
30	H	H
31	Ac	H



	X
32	OH
33	$OCNHCCl_3$
34	SMe



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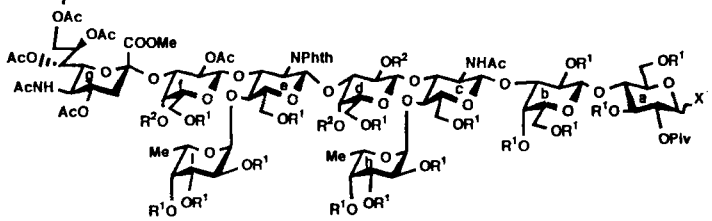
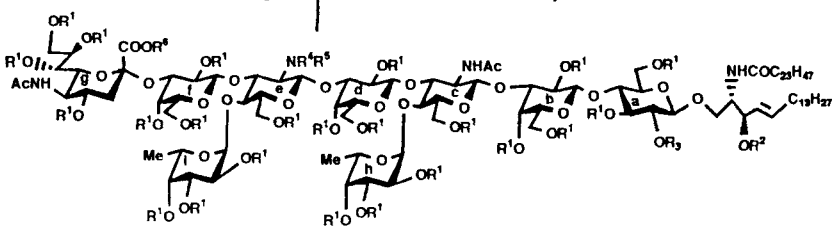


	R^1	R^2	X
36	Bn	H	OBn (β)
37	Ac	Ac	OAc
38	Ac	Ac	OH
39	Ac	Ac	$OCNHCCl_3$ (α)
40	Ac	Ac	F



	R^1	R^2	R^3	R^4 R^5	R^6
41	Ac	Bz	Piv	Phth	Me
42	Ac	Bz	Piv	Phth	Li
2	H	H	H	H Ac	Na

Scheme 3

stereo-controlled manner to afford nonasaccharide **36** in 47% yield. (Glycosylation of **33** with **35** in the presence of boron trifluoride etherate at -15 °C afforded a 15% yield of **36**). In the ^{1}H NMR spectrum of **36**, the anomeric proton of H-1e appeared as a one-proton doublet (J = 7.7Hz) at δ 5.234, showing the newly formed glycosidic linkage to be β.

The transformation of **36** into glycosyl donors **39** and **40** was performed as follows. Hydrogenolysis of **36**, subsequent acetylation, and chemoselective cleavage of the anomeric acetate,[20] afforded α-trichloroacetimidate **39** in 62% yield. The final coupling between **39** and ceramide derivative **4**[9] was achieved in freshly distilled $CHCl_3$ in the presence of boron trifluoride etherate[22] at -15 °C to afford a 34% yield of the desired **41** accompanied by recovered hemiacetal **38**. The HOHAHA NMR spectral data showed the signals for H-2f and H-4f at δ 4.804, δ 4.948 and, H-2d and H-4d at δ 4.966, δ 5.246 respectively, indicating the internal dimeric Le^a linkages. The newly introduced glycosidic linkage of **41** was rigorously confirmed to be β (δH, 4.406, d, J = 8.1Hz). Next aiming at increasing the coupling yield, compound **38** was converted into fluoride **40**. Glycosylation of **40** with ceramide derivative **4** in the presence of $SnCl_2$-AgOTf[30] at -15 °C afforded a 40% yield of **41**.

Further conversion into the target glycolipid **2** was executed as follows. Compound **41** was refluxed for 1 day with a large excess LiI in pyridine[25] to give an 88% yield of the lithium salt **42**. Subsequent treatment of **42** with i)NH_2NHMe in refluxing EtOH[26] ii)Ac_2O in 2 : 2 : 1 MeOH-THF-CH_2Cl_2 iii)aq. NaOH in 1 : 1 MeOH-THF, afforded the target compound **2** in 74% yield, after gel filtration through Sephadex LH-20 using 5 : 5 : 1 $CHCl_3$-MeOH-H_2O. The structure of **2** was confirmed by ^{1}H NMR as shown in Figure 1.

In conclusion, the total synthesis of sialyl monomeric Le^a and the first total synthesis of sialyl dimeric Le^a ganglioside were achieved by employing the trichloroacetimidate donors **33** and **39** and thioglycoside **34** as key glycosyl donors, and the suitably protected lactose and Le^a derivatives **8** and **35** as glycosyl acceptors.

EXPERIMENTAL

General methods. Optical rotations were determined for solutions in $CHCl_3$ at 22 ± 3 °C with a JASCO Model DIP-370 polarimeter, unless otherwise stated. All

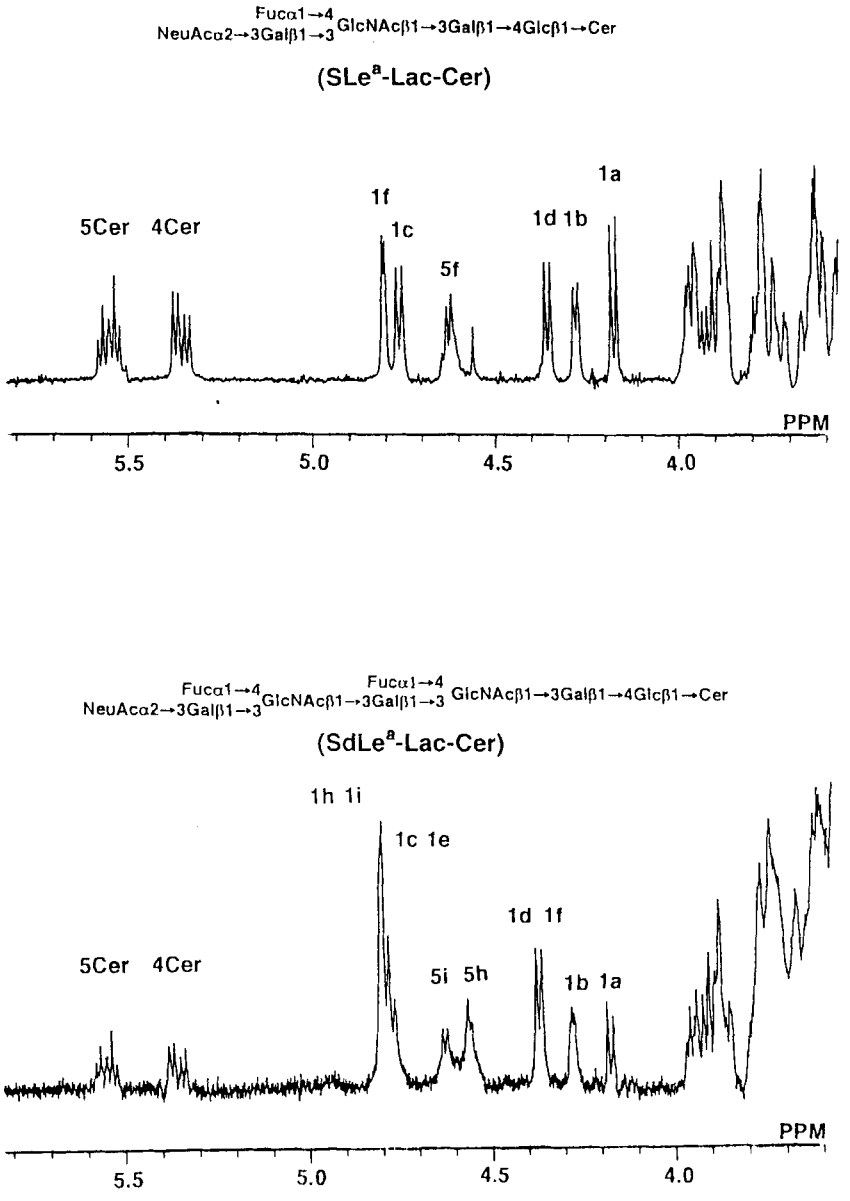


Figure 1. Expansions of 500MHz ^{1}H NMR spectrum of ganglioside **1**, **2**.

reactions were monitored by high-performance thin-layer chromatography on Kieselgel 60 F_{254} (Merck) with detection by UV light and/or by charring with 5% sulfuric acid in ethanol. Flash chromatography was performed on columns of Wakogel C-300 (200~300 mesh). ^{1}H NMR spectra were recorded with a JNM-GX 500 Fourier-transform instrument. The values of δH are expressed in ppm. downfield from internal Me_4Si, for solutions in $CDCl_3$ at 25 °C unless otherwise noted. Fast atom bombardment (FAB) and electrospray ionization (ESI) mass spectroscopy were recorded on a Finnigan MAT TSQ 700 triple stage quadrupole mass spectrometer equipped with an Ion Tech FAB gun or electrospray ion source. Powdered molecular sieves (3A or 4A; GL Sciences Inc. Japan) and lithium iodide were heated to 250 °C under vacuum overnight. All reactions except hydrogenation were performed under atmospheres of dry nitrogen. $(ClCH_2)_2$, CH_2Cl_2, CH_3CN, EtCN, $CHCl_3$, were distilled from CaH_2.

***O*-(2,3,4-Tri-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose (14).** To a solution of (1,5-cyclooctadiene) bis(methyldiphenylphosphine) iridium hexafluorophosphate (57 mg, 48 μmol) which was activated by H_2 in THF (25 mL) was added a solution of **13** (595 mg, 0.48 mmol) in THF (10 mL). The mixture was stirred for 2 h at room temperature, then I_2 (730 mg, 2.88 mmol) and H_2O (13 mL) was added. This was stirred for 1 h at room temperature. The mixture was diluted with $CHCl_3$, washed successively with aq. sodium thiosulfate, aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on SiO_2 with 5 : 1 toluene-EtOAc to afford **14** (232 mg, 97%): $[\alpha]_D$ -19.8° (*c* 1.0); R_f 0.14 (3 : 1 toluene-EtOAc); ^{1}H NMR ($CDCl_3$) δ 5.346 (d, 1H, J = 3.3 Hz, h-4d), 5.087 (d, 1H, J = 4.0 Hz, H-1f), 4.970 (dd, 1H, J = 8.1, 9.9 Hz, H-2d), 4.837 (dd, 1H, J = 9.2, 10.6 Hz, H-2c), 4.436 (dd, 1H, J = 3.6, 9.5 Hz, H-3d), 4.201 (d, 1H, J = 8.5 Hz, H-1d), 3.986 (t, 1H, J = 9.5 Hz, H-3c), 1.962, 1.841, 1.661 (3s, 9H, 3Ac), 1.274 (d, 3H, J = 6.6 Hz, H-6f).

Anal. Calcd for $C_{67}H_{71}N_1O_{19}$: C, 67.38; H, 5.99; N, 1.17. Found: C, 67.10; H, 6.02; N, 1.23.

***O*-(2,3,4-Tri-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-D-glucopyranosyl Fluoride (15).** To a solution of **14** (120 mg, 0.10 mmol) in $(ClCH_2)_2$ (1 mL) was added diethylaminosulfur trifluoride (54 μL, 0.40

mmol) at -15 °C. The mixture was diluted with EtOAc, and washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on SiO_2 with 3 : 1 toluene-EtOAc afforded **15** (108 mg, 90%) as a 4 : 1 mixture of β and α anomers: R_f 0.55 (2 : 1 toluene-EtOAc); ^1H NMR ($CDCl_3$) δ 5.687 (dd, 0.8H, J = 7.5, 54 Hz, H-1c(β)), 5.341 (d, 0.8H, J = 3.0 Hz, H-4d(β)), 5.132 (d, 0.8H, J = 3.5 Hz, H-1f(β)), 4.171 (d, 0.8H, J = 8.5 Hz, H-1d(β)), 3.894 (dd, 1.6H, J = 2.5, 10.0 Hz, H-2f(β) and H-3f(β)), 1.981, 1.840, 1.667 (3s, 9H, 3Ac), 1.275 (d, 2.4H, J = 6.5 Hz, H-6f(β)).

Anal. Calcd for $C_{67}H_{70}F_1N_1O_{18}$: C, 67.27; H, 5.90; N, 1.17. Found: C, 67.07; H, 5.94; N, 1.22.

***O*-(6-*O*-Benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-α-D-glucopyranosyl Fluoride (16), and *O*-(6-*O*-Benzyl-β-D-galacto-pyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Fluoride (17).** To a solution of **15** (97 mg, 81 μmol) in 7 : 2 MeOH-$(ClCH_2)_2$ (9 mL) was added 0.1N MeONa (400 μL), and the mixture was stirred for 2 h at room temperature, neutralized with Amberlyst 15E (H^+) resin, and filtered. The filtrate was concentrated in vacuo. Chromatography of the residue on SiO_2 with 1 : 1 toluene-EtOAc afforded **16** (14 mg, 16%), **17** (53 mg, 61%).

Compound **16** had: $[\alpha]_D$ +3.98° (*c* 1.0); R_f 0.21 (1 : 2 toluene-EtOAc); ^1H NMR ($CDCl_3$) δ 5.881 (dd, 1H, J = 2.2, 53.5 Hz, H-1c), 5.110 (d, 1H, J = 3.3 Hz, H-1f), 4.533 (d, 1H, J = 7.3 Hz, H-1d), 3.869 (s, 3H, OMe), 1.173 (d, 3H, J = 6.2 Hz, H-6f).

Anal. Calcd for $C_{61}H_{64}F_1N_1O_{15} \cdot 3H_2O$: C, 65.17; H, 6.28; N, 1.25. Found: C, 65.19; H, 6.24; N, 1.22.

Compound **17** had: $[\alpha]_D$ -20.5° (*c* 1.0); R_f 0.22 (1 : 2 toluene-EtOAc); ^1H NMR ($CDCl_3$) δ 5.776 (dd, 1H, J = 7.7, 53.9 Hz, H-1c), 5.112 (d, 1H, J = 3.7 Hz, H-1f), 4.833 (dd, 1H, J = 9.2, 11.0 Hz, H-2c), 4.018 (d, 1H, J = 7.7 Hz, H-1d), 1.097 (d, 3H, J = 6.6 Hz, H-6f).

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→**

4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Fluoride (18). A mixture of **12** (64 mg, 123 μmol), **17** (49 mg, 46 μmol) and 3A molecular sieves (300 mg) in 2 : 1 MeCN-EtCN (1.5 mL) was stirred for 9 h at 20 °C under argon. After cooling to -40 °C, a solution of AgOTf (42 mg, 179 μmol) and PhSeCl (31 mg, 179 μmol) in MeCN (1 mL) were added. After stirring for 3 h at -40 °C, the reaction mixture was quenched with Et_3N, diluted with EtOAc and filtered through a Celite bed. The filtrate was washed with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed firstly on Bio-Beads SX-4 in toluene and then purified on SiO_2 with 2 : 1 EtOAc-toluene afforded **18** (33 mg, 46%) and corresponding β epimer (10 mg, 14%).

Compound **18** had: R_f 0.26 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 7.812 (m, 4H, Phth), 5.786 (dd, 1H, J = 7.7, 53.9 Hz, H-1c), 5.236 (dd, 1H, J = 1.8, 8.1 Hz, H-7e), 5.099 (d, 1H, J = 4.0 Hz, H-1f), 5.056 (m, 1H, H-4e), 4.842 (t, 1H, J = 9.9 Hz, H-2c), 4.086 (d, 1H, J = 9.2 Hz, H-1d), 3.733 (s, 3H, OMe), 2.442 (d, 1H, J = 4.8, 12.8 Hz, H-3e*eq*), 2.052, 2.047, 2.017, 1.997, 1.878 (5s, 15H, 5Ac), 1.120 (d, 3H. J = 6.6 Hz, H-6f).

Anal. Calcd for $C_{81}H_{91}F_1N_2O_{27}$: C, 63.03; H, 5.94; N, 1.81. Found: C, 63.13; H, 5.91; N, 1.77.

Compound β epimer had: $[\alpha]_D$ -23.6° (*c* 1.0); R_f 0.28 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 7.811 (m, 4H, Phth), 5.794 (dd, 1H, J = 7.7, 54.0 Hz, H-1c), 5.142 (m, 1H, H-4e), 5.096 (d, 1H, J = 4.0 Hz, H-1f), 4.081 (d, 1H, J = 9.2 Hz, H-1d), 2.405 (d, 1H, J = 4.6, 12.8 Hz, H-3e eq), 1.122 (d, 3H, J = 6.6 Hz, H-6f).

***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-di-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-gluco-pyranosyl Fluoride (19).** To a solution of **18** (173 mg, 112 μmol) in pyridine (5 mL) was added acetic anhydride (5 mL), and the mixture was stirred for 5 days at room temperature. Catalytic amount of DMAP was added, and the reaction mixture was stirred for another 5 days at room temperature, and coevaporated with toluene. Chromatography of the residue on SiO_2 with 8 : 1 toluene-MeOH afforded **19** (152 mg, 83%): R_f 0.50 (5 : 1 toluene-MeOH); ^1H NMR ($CDCl_3$) δ 7.807 (m, 4H, Phth), 5.590 (dd, 1H, J = 7.7, 54.6 Hz, H-1c), 5.278 (dd, 1H, J = 2.6, 8.4 Hz, H-7e), 5.142 (d, 1H, J = 3.7 Hz, H-4d or

H-1f), 4.539 (t, 1H, J = 8.1 Hz, H-2d), 3.774 (s, 3H, OMe), 2.452 (dd, 1H, J = 4.8, 12.5 Hz, H-3e*eq*), 2.133, 2.060, 2.049, 1.979, 1.915, 1.818, 1.699 (7s, 21H, 7Ac), 1.321 (d, 3H, J = 6.6 Hz, H-6f).

Anal. Calcd for $C_{85}H_{95}F_1N_2O_{29}$: C, 62.72; H, 5.88; N, 1.72. Found: C, 62.55; H, 5.92; N, 1.75.

Benzyl *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-di-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside (20). To a stirred mixture of Cp_2HfCl_2 (57 mg, 145 μmol), AgOTf (77 mg, 290 μmol) and 3A molecular sieves (1.4 g) was added a solution of **19** (135 mg, 83 μmol) and **8** (120 mg, 124 μmol) in CH_3CN (1.5 mL) at -15 °C. The mixture was gradually warmed over a period of 4.5 h to room temperature, quenched with Et_3N, diluted with EtOAc, and filtered through a Celite bed. The filtrate was washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by successive chromatography, firstly on Bio-Beads SX-3 with toluene and then on SiO_2 with 5 : 1 $CHCl_3$-acetone to afford **20** (138 mg, 65%): $[\alpha]_D$ - 16.2 ° (*c* 1.0); R_f 0.43 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 7.617 (m, 4H, Phth), 5.223 (dd, 1H, J = 2.6, 8.8 Hz, H-7e), 5.152 (d, 1H, J = 8.4 Hz, H-1c), 5.037 (d, 1H, J = 3.7 Hz, H-1f), 4.954 (d, 1H, J = 4.0 Hz, H-4d), 3.758 (s, 3H, OMe), 2.084, 2.030, 2.006, 1.969, 1.874, 1.804, 1.677 (7s, 21H, 7Ac). 1.086 (s, 9H, *tert*-Bu).

Anal. Calcd for $C_{144}H_{160}N_2O_{41}$: C, 67.17; H, 6.26; N, 1.09. Found: C, 66.88; H, 6.27; N, 1.15.

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,3,6-tri-*O*-acetyl-2-*O*-pivaloyl-D-glucopyranose (21).** A mixture of **20** (119 mg, 46 μmol) and $Pd(OH)_2$-C (119 mg) in 4 : 1 MeOH-H_2O (8 mL) was stirred under H_2 for 19 h at room temperature, diluted with 4 : 1 MeOH-H_2O and filtered through a Celite

bed. The filtrate was coevaporated with toluene. To a solution of the residue in pyridine (3 mL) was added acetic anhydride (3 mL) and DMAP. The mixture was stirred for 5 days at room temperature and then coevaporated with toluene in vacuo. Chromatography of the residue on SiO_2 with 20 : 1 $CHCl_3$-MeOH afforded **21** (75 mg, 99%) as a 1 : 1 mixture of α and β anomers: R_f 0.27 (20 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 7.795 (m, 4H, Phth), 6.237 (d, 0.5H, J = 3.7 Hz, H-1a(α)), 5.613 (d, 0.5H, J = 8.4 Hz, H-1a(β)), 1.274 (d, 3H, J = 6.2 Hz, H-6f), 1.091, 1.104 (2s, 9H, *tert*-Bu).

Anal. Calcd for $C_{89}H_{116}N_2O_{52} \cdot 2H_2O$: C, 51.34; H, 5.81; N, 1.35. Found: C, 51.06; H, 5.50; N, 1.41.

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-D-glucopyranose (22).** A mixture of **21** (98 mg, 48 μmol) and H_2NNH_2-AcOH (9 mg, 96 μmol) in DMF (1 mL) was stirred for 1 h at room temperature. The mixture was diluted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), and concentrated in vacuo. Chromatography of the residue on Sephadex LH-20 with 1 : 1 $CHCl_3$-MeOH afforded **22** (90 mg, 94%): R_f 0.44 (10 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 3.783 (s, 3H, OMe), 2.18-1.81 (br, 54H, 18Ac), 1.149 (s, 9H, *ter-t*Bu).

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-α-D-glucopyranosyl Trichloroacetimidate (23).** A solution of **22** (90 mg, 45 μmol), CCl_3CN (70 μL, 676 μmol), and DBU (15 μL, 95 μmol), in $(ClCH_2)_2$ (1 mL) was stirred for 45 min at 0 °C. The reaction mixture was directly chromatographed on SiO_2 with 30 : 1 $CHCl_3$-MeOH to afford **23** (89 mg, 91%): $[\alpha]_D$ -3.8 ° (*c* 1.0); R_f 0.45 (15 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 8.613 (s, 1H, C = NH), 7.783 (m, 4H, Phth), 6.452 (d, 1H, J = 3.7 Hz, H-1a), 5.245 (d, 1H, J = 2.6 Hz, H-4b), 5.217 (d, 1H, J = 3.3 Hz, H-4d), 5.200 (d, 1H, J = 3.7 Hz, H-1f),

5.098 (d, 1H, J = 10.3 Hz, NH), 5.001 (d, 1H, J = 7.3 Hz, H-1d), 4.754 (t, 1H, J = 9.6 Hz, H-2d), 4.658 (dd, J = 8.1, 9.9 Hz, H-2b), 4.470 (d, 1H, J = 8.1 Hz, H-1c), 4.229 (d, 1H, J = 8.1 Hz, H-1b), 3.782 (s, 3H, OMe), 2.462 (dd, 1H, J = 4.8, 12.5 Hz, H-3e *eq*), 2.166, 2.160, 2.118, 2.103, 2.093, 2.079, 2.077, 2.074, 2.047, 2.001, 1.967, 1.842, 1.832, 1.810, (14s, 51H, 17Ac), 1.274 (d, 3H, J = 6.6 Hz, H-6f), 1.099 (s, 9H, *tert*-Bu).

Anal. Calcd for $C_{89}H_{114}Cl_3N_3O_{51}$: C, 49.76; H, 5.35; N, 1.96. Found: C, 49.98; H, 5.27; N, 2.01.

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fuco-pyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-gluco-pyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*, 3*R*, 4*E*)-2-azido-3-*O*-*tert*-butyldiphenylsilyl-4-octadecene-1,3-diol (24).** To a stirred mixture of **23** (49 mg, 23 μmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-*tert*-butyldiphenylsilyl-4-octadecene-1,3-diol (**3**, 26 mg, 46 μmol) and 4A molecular sieves (500 mg) in $CHCl_3$ (1 mL) was added $BF_3 \cdot Et_2O$ (4 μL, 46 μmol) at -15 °C. The mixture was stirred for 30 minutes and gradually warmed to room temperature, diluted with $CHCl_3$, and filtered through a Celite bed. The filtrate was washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue over SiO_2 with 2 : 1 toluene-acetone afforded **24** (50 mg, 86%): $[\alpha]_D$ -25.7° (*c* 0.8); R_f 0.61 (1 : 1 toluene-acetone); ^1H NMR ($CDCl_3$) δ 5.262 (d, 1H, J = 2.6 Hz, H-4b), 5.010 (d, 1H, J = 8.4 Hz, H-1d), 4.809 (dd, 1H, J = 7.7, 9.5 Hz, H-2d), 4.630 (dd, 1H, J = 8.1, 9.9 Hz, H-2b), 4.467 (d, 1H, J = 7.7 Hz, H-1c), 4.282 (d, 1H, J = 8.1 Hz, H-1b), 4.172 (d, 1H, J = 8.1 Hz, H-1a), 3.783 (s, 3H, OMe), 2.461 (dd, 1H, J = 4.8, 12.8 Hz, H-3e*eq*), 2.161, 2.159, 2.105, 2.099, 2.079, 2.072, 2.060, 2.047, 1.999, 1.967, 1.957, 1.941, 1.961, 1.824, 1.810 (15s, 51H, 17Ac), 1.067 (s, 9H, *tert*-Bu), 0.883 (t, 3H, J = 7.0 Hz, CH_2Me).

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fuco-pyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-gluco-**

pyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*, 3*R*, 4*E*)-3-*O*-*tert*-butyldiphenylsilyl-2-tetracosanoylamino-4-octadecene-1,3-diol (26). To a solution of **24** (35 mg, 14 μmol) in toluene (2 mL) and H_2O (1 mL) were added triphenylphosphine (7 mg, 28 μmol). After heating under reflux for 19 h, the solvent was evaporated in vacuo, the residue was applied to a column of Sephadex LH-20 and was eluted with 1 : 1 MeOH-$CHCl_3$ to afford the amino derivative **25** (28 mg, 82%). A mixture of thus obtained **25** (28 mg, 11 μmol), tetracosanoic acid (9 mg, 262 μmol), 2-chloro-1-methylpyridinium iodide (7 mg, 26 μmol) and Bu_3N (11 μL, 52 μmol) in $(ClCH_2)_2$ (1 mL) was stirred for 1 h at room temperature. The mixture was diluted with AcOEt, washed with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by successive chromatography on Sephadex LH-20 with 1 : 1 MeOH-$CHCl_3$ and on SiO_2 with 3 : 1 toluene-acetone to give **26** (28 mg, 88%): $[\alpha]_D$ -18.5° (*c* 1.0); R_f 0.38 (25 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 5.408 (d, 1H, J = 8.8 Hz, NH), 5.013 (d, 1H, J = 8.4 Hz, H-1d), 4.816 (dd, 1H, J = 8.1, 9.9 Hz, H-2d), 4.629 (dd, 1H, J = 8.1, 9.5 Hz, H-2b), 4.471 (d, 1H, J = 8.1 Hz, H-1c), 4.337 (d, 1H, J = 7.7 Hz, H-1b), 3.783 (s, 3H, OMe), 2.463 (dd, 1H, J = 4.4, 12.8 Hz, H-3e*eq*), 2.164, 2.160, 2.115, 2.106, 2.080, 2.074, 2.050, 2.002, 1.967, 1.942, 1.929, 1.830, 1.811 (13s, 51H, 17Ac). 1.092 (s, 9H, *tert*-Bu), 0.880 (t, 6H, J = 7.0 Hz, $2CH_2Me$).

***O*-(Lithium 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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*, 3*R*, 4*E*)-3-*O*-*tert*-butyldiphenylsilyl-2-tetracosanoylamino-4-octadecene-1,3-diol (27).** A solution of **26** (28 mg, 10 μmol) in pyridine (1.5 mL) was added dropwise onto LiI (30 mg, 226 μmol, dried at 200 °C for 12 h in vacuo), and the mixture was heated for 12.5 h at reflux under argon. The reaction mixture was chromatographed over Sephadex LX-20 with 1 : 1 $CHCl_3$-MeOH to afford **27** (22 mg, 79%): R_f 0.65 (5 : 1 $CHCl_3$-MeOH); ^1H NMR (CD_3OD) δ 5.075 (d, 1H, J = 8.4 Hz, H-1d), 4.815 (dd, 1H, J = 8.1, 9.5 Hz, H-2d), 4.773 (t, 1H, J = 9.2 Hz, H-2a), 4.641 (dd, 1H, J = 8.1, 9.9 Hz, H-2b), 4.548 (d, 1H, J = 8.1 Hz, H-1c), 2.486 (dd, 1H, J = 4.3, 12.8 Hz, H-3e*eq*),

2.185, 2.181, 2.134, 2.129, 2.110, 2.105, 2.072, 2.063, 2.028, 1.966, 1.961, 1.956, 1.823, 1.801 (14s, 51H, 17Ac), 1.099 (s, 9H, *tert*-Bu), 0.891 (t, 6H, J = 7.0 Hz, $2CH_2Me$).

***O*-(Sodium 5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-β-D-galactopyranosyl-(1→3)-*O*-[α-L-fucopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→1)-(2*S*,3*R*,4*E*)-2-tetracosanoylamino-4-octadecene-1,3-diol. (1) (Sialyl monomeric Le^a ganglioside)** To a solution of **27** (22 mg, 7.8 μmol) in EtOH (5 mL) was added $MeNHNH_2$ (2.5 mL), and the mixture was stirred for 18 h at 80 °C, and then concentrated in vacuo. The residue was purified over Sephadex LH-20 with MeOH to afford the amino derivative. To the solution of amino derivative in MeOH (2 mL) was added acetic anhydride (70 μL), and the mixture was stirred for 1 h at room temperature and concentrated in vacuo. The residue in 1 : 1 MeOH-THF (0.6 mL) was treated with 1N-NaOH (0.3 mL) for 1 day at room temperature, and the mixture was chromatographed on a sephadex LH-20 with 60 : 30 : 5 $CHCl_3$-MeOH-H_2O and then concentrated. THF (200 μL) and Bu_4NF (528 μL) were added to the residue, and the mixture was stirred for 14 h at 60 °C and then concentrated in vacuo. The residue was purified over Sephadex LH-20 with 60 : 30 : 5 $CHCl_3$-MeOH-H_2O to give **1** (8 mg, 59%): R_f 0.25 (60 : 30 : 5 $CHCl_3$-MeOH-H_2O); ^1H NMR (50 : 1 $(CD_3)_2SO$-D_2O) δ 5.562 (dt, 1H, J = 7.0, 15.0 Hz, H-5Cer), 5.366 (dd, 1H, J = 7.0, 15.4 Hz, H-4Cer), 4.813 (d, 1H, J = 3.7 Hz, H-1f), 4.771 (d, 1H, J = 8.1 Hz, H-1c), 4.366 (d, 1H, J = 7.7 Hz, H-1d), 4.289 (d, 1H, J = 6.6 Hz, H-1b), 4.185 (d, 1H, J = 8.1 Hz, H-1a), 2.773 (dd, 1H, J = 4.8, 12.1 Hz, H-3e*eq*), 1.850, 1.899 (2s, 6H, 2NAc), 1.023 (d, 3H, J = 6.6 Hz, H-6f), 0.853 (t, 6H, J = 7.0 Hz, $2CH_2Me$); FABMS (TEA matrix): *m/z* $(M-Na)^-$ 1775.

Allyl *O*-(Methyl-5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (30). To a stirred mixture of 1 : 1 $HgBr_2$-$Hg(CN)_2$ (161 mg), and 1 : 2 mixture of 3A-4A molecular sieves (3.6 g) was added a solution of **28** (466 mg, 0.42 mmol) in CH_3CN (2 mL), and the mixture was stirred for 1 h at room temperature. A solution of **29** (661 mg, 1.26 mmol) in CH_3CN (2 mL) was added, and this was stirred for 1 day at room

temperature. The mixture was quenched with Et_3N, diluted with EtOAc, and filtered through a Celite bed. The filtrate was washed with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by successive chromatography, first on Bio-Beads SX-3 with toluene and then on SiO_2 with 1 : 2 toluene-EtOAc, to give **30** (472 mg, 71%): $[\alpha]_D$ +25.6° (*c* 1.0); R_f 0.25 (1 : 2 toluene-AcOEt); ^1H NMR ($CDCl_3$) δ 5.666 (m, 1H, $-CH_2-CH = CH_2$), 5.120 (d, 1H, J = 3.7 Hz, H-1i), 4.348 (dd, 1H, J = 8.4, 10.6 Hz, H-2e), 3.739 (s, 3H, OMe), 2.425 (dd, 1H, J = 4.8, 13.2 Hz, H-3g*eq*), 2.049, 2.044, 2.027, 1.986, 1.872 (5s, 15H, 5Ac), 1.124 (d, 3H, J = 6.6 Hz, H-6i).

Anal. Calcd for $C_{84}H_{96}N_2O_{28}$: C, 63.79; H, 6.12; N, 1.77. Found: C, 63.68; H, 6.10; N, 1.74.

Allyl *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-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (31). To a solution of **30** (507 mg, 0.321 mmol) in pyridine (15 mL) was added acetic anhydride (15 mL), and the mixture was stirred for 1 day at room temperature, and coevaporated with toluene. Chromatography of the residue over SiO_2 with 3 : 1 toluene-acetone afforded **31** (490 mg, 94%): $[\alpha]_D$ -28.8° (*c* 1.0); R_f 0.39 (5 : 1 toluene-MeOH); ^1H NMR ($CDCl_3$) δ 5.593 (m, 1H, $-CH_2-CH = CH_2$), 5.119 (d, 1H, J = 3.3 Hz, H-1i), 4.861 (t, 1H, J = 9.5 Hz, H-2f), 4.378 (d, 1H, J = 7.7 Hz, H-1f), 4.288 (t, 1H, J = 10.6 Hz, H-2e), 3.969 (t, 1H, J = 9.5 Hz, H-3e), 3.664 (s, 3H, OMe), 2.519 (dd, 1H, J = 4.4, 12.8 Hz, H-3g*eq*), 2.091, 2.044, 2.031, 1.993, 1.975, 1.824 (6s, 18H, 6Ac), 1.740 (t, 1H, J = 12.8 Hz, H-3g*ax*), 1.291 (d, 3H, J = 6.6 Hz, H-6i).

Anal. Calcd for $C_{88}H_{100}N_2O_{30} \cdot H_2O$: C, 63.45; H, 6.05; N, 1.68. Found: C, 63.55; H, 6.05; 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-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose (32).** To a solution of (1,5-cyclooctadiene)bis(methylphenylphosphine) iridium hexafluoro-phosphate (27 mg, 22.7 μmol), which was activated by H_2 in THF (5 mL), was added a solution of **31** (361 mg, 227 μmol) in THF (5 mL). The mixture was stirred for 4 h at room temperature, then I_2 (341 mg, 1.34 mmol) and H_2O (6 mL) were

added. Stirring was continued for 0.5 h at room temperature. The mixture was diluted with $CHCl_3$, washed successively with aq. sodium thiosulfate, aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on SiO_2 with 2 : 1 $CHCl_3$-acetone to afford **32** (360 mg, qu.): $[\alpha]_D$ -24.8° (*c* 1.0); R_f 0.17 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 5.276 (dd, 1H, J = 1.8, 8.8 Hz, H-7g), 5.141 (t, 1H, J = 8.8 Hz, H-2f), 5.050 (d, 1H, J = 3.3 Hz, H-1i), 4.147 (dd, 1H, J = 8.4, 10.6 Hz, H-2e), 3.968 (t, 1H, J = 9.5 Hz, H-3e), 3.814 (t, 1H, J = 8.8 Hz, H-4e), 3.660 (s, 3H, OMe), 2.516 (dd, 1H, J = 4.4, 12.8 Hz, H-3g*eq*), 2.056, 2.025, 2.002, 1.962, 1.840 (5s, 18H, 6Ac).

Anal. Calcd for $C_{83}H_{94}N_2O_{29}$: C, 62.95; H, 5.98; N, 1.77. Found: C, 62.85; H, 6.05; N, 1.75.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Trichloroacetimidate (33).** A mixture of **32** (49 mg, 31 μmol), CCl_3CN (46 μL, 0.46 mmol), and DBU (3 μL, 22 μmol) in CH_2Cl_2 (1.0 mL) was stirred for 1 h at 0 °C. The reaction mixture was directly chromatographed on SiO_2 with 3 : 1 $CHCl_3$-acetone to afford **33** (47 mg, 89%): $[\alpha]_D$ -17.5° (*c* 1.0); R_f 0.32 (3 : 1 $CHCl_3$- acetone); ^1H NMR ($CDCl_3$) δ 8.459 (s, 1H, C = NH), 6.215 (d, 1H, J = 8.8 Hz, H-1e), 5.138 (d, 1H, J = 3.7 Hz, H-1i), 4.927 (1H, J = 10.9 Hz, H-2f), 4.562 (t, 1H, J = 10.6 Hz, H-2e), 4.396 (d, 1H, J = 7.7 Hz, H-1f), 4.086 (t, 1H, J = 9.5 Hz, H-3e), 3.659 (s, 3H, OMe), 3.540 (br-d, 1H, H-4f), 2.525 (dd, 1H, J = 4.4, 13.2 Hz, H-3g*eq*), 2.091, 2.048, 2.026, 2.003, 1.954, 1.840 (6s, 18H, 6Ac), 1.288 (d, 3H, J = 6.2 Hz, H-6i).

Methyl *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-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (34). To a stirred mixture of **33** (233 mg, 135 μmol) and powdered molecular sieves (4A, 0.3 g) in dry CH_2Cl_2 (1.5 mL) was added Bu_3SnSMe (69 μL, 0.20 mmol) at -10 °C. After stirring for 10 min at -10 °C, boron trifluoride etherate (24 μL, 18 μmol) was added, and the mixture was stirred for 2 h. The mixture was diluted with EtOAc, filtered through Celite and the filtrate was washed successively with aq. KF, aq.

$NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on SiO_2 with 6 : 1 $CHCl_3$-acetone and gel filtration over Bio-Beads S-X1 with toluene afforded **34** (209 mg, 96%): $[\alpha]_D$ +25.6° (*c* 1.0); R_f 0.32 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 5.139 (d, 1H, J = 3.7 Hz, H-1i), 4.364 (d, 1H, J = 7.3 Hz, H-1f), 3.973 (t, 1H, J = 9.2 Hz, H-3e), 3.826 (t, 1H, J = 8.8 Hz, H-4e), 3.555 (br-d, 1H, H-4f), 2.514 (dd, 1H, J = 4.8, 12.5 Hz, H-3g*eq*), 2.093, 2.080, 2.051, 2.036, 2.003, 1.970, 1.838 (7s, 21H, 6Ac and 1SMe), 1.740 (t, 1H, J = 12.5 Hz, H-3g*ax*), 1.284 (d, 3H, J = 6.6 Hz, H-6i).

Anal. Calcd for $C_{84}H_{96}N_2O_{28}S_1 \cdot 2H_2O$: C, 61.16; H, 6.11; N, 1.70. Found: C, 61.01; H, 6.13; N, 1.74.

Benzyl *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-di-*O*-acetyl-6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(6-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside (36). (Method A) To a stirred mixture of **35** (27 mg, 14 μmol) and powdered molecular sieves (3A, 0.3 g) in dry CH_3CN (3 mL) was added a solution of **33** (39 mg, 22 μmol) in dry CH_3CN (1.5 mL) at -40 °C. After stirring for 10 min at -40 °C, boron trifluoride etherate (2.9 μL, 44 μmol) was added, and the mixture was stirred for 2 h. The mixture was diluted with EtOAc, filtered through Celite and the filtrate was washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on SiO_2 with 6 : 1 $CHCl_3$-acetone and gel filtration over Bio-Beads SX-1 with toluene afforded **36** (8 mg, 15%). (Method B) To a stirred mixture of **35** (40 mg, 20 μmol) and powdered molecular sieves (3A, 0.3 g) in dry CH_3CN (3 mL) was added a solution of **34** (23 mg, 14 μmol) in dry CH_3CN (1.5 mL) at -20 °C. After stirring for 10 min at -10 °C, AgOTf (13 mg, 55 μmol) and PhSeCl (10 mg, 55 μmol) were added, and the mixture was stirred for 2 h, and worked up as described in Method A. Chromatography of the residue on SiO_2 with 6 : 1 $CHCl_3$-acetone and gel filtration over Bio-Beads SX-1 with toluene afforded **36** (23 mg, 47%): $[\alpha]_D$ -25.8° (*c* 1.0); R_f 0.53 (3 : 1 $CHCl_3$-acetone); ^1H NMR ($CDCl_3$) δ 5.234 (d, 1H, J = 7.7 Hz, H-1e), 3.662 (s,

3H, OMe), 1.279 (d, 3H, J = 6.2 Hz, H-6h), 1.121 (s, 9H, *tert*-Bu), 0.798 (d, 3H, J = 6.2 Hz, H-6i).

Anal. Calcd for $C_{197}H_{221}N_3O_{54} \cdot 3H_2O$: C, 66.70; H, 6.45; N, 1.18. Found: C, 66.40; H, 6.23; 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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,3,6-tri-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranose (37).** A mixture of **36** (81 mg, 23 μmol) and 20% $Pd(OH)_2$-C (81 mg) in 4 : 1 MeOH-H_2O (8 mL) was stirred under H_2 for 19 h at room temperature, diluted with 4 : 1 MeOH-H_2O and filtered through a Celite bed. The filtrate was coevaporated with toluene. To a solution of the residue in pyridine (3 mL) was added acetic anhydride (2 mL) and a catalytic amount of DMAP. The mixture was stirred for 1 day at room temperature and then coevaporated with toluene in vacuo. Chromatography of the residue on sephadex LH-20 with 1 : 1 $CHCl_3$-MeOH afforded **37** (56 mg, 85%) as a 1 : 1 mixture of α and β anomers: R_f 0.21 (20 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 6.289 (d, 0.5H, J = 4.0 Hz, H-1a(α)), 5.692 (d, 0.5H, J = 8.1 Hz, H-1a(β)), 3.785 (s, 3H, OMe), 1.272 (d, 3H, J = 6.2 Hz, H-6h), 1.134, 1.121 (2S, 9H, *tert*-Bu), 0.830 (d, 3H, J = 6.2 Hz, H-6i).

Anal. Calcd for $C_{123}H_{163}N_3O_{73} \cdot H_2O$: C, 51.48; H, 5.80; N, 1.46. Found: C, 51.41; H, 5.44; N, 1.48.

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranose (38).** A mixture of **37** (56 mg, 20 μmol) and H_2NNH_2-AcOH (5 mg, 60 μmol) in DMF (1 mL)

was stirred for 1.5 h at room temperature. The mixture was chromatographed on Sephadex LH-20 with MeOH to afford **38** (52 mg, 94%): R_f 0.14 (20 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 3.784 (s, 3H, OMe), 1.133, 1.120 (2s, 9H, *tert*-Bu).

Anal. Calcd for $C_{121}H_{161}N_3O_{72} \cdot H_2O$: C, 51.40; H, 5.74; N, 1.49. Found: C, 51.28; H, 5.79; N, 1.61.

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-α-D-glucopyranosyl Trichloroacetimidate (39).** A solution of **38** (52 mg, 18 μmol), CCl_3CN (29 μL, 260 μmol), and DBU (6 μL, 38 μmol) in $(ClCH_2)_2$ (1 mL) was stirred for 2 h at 0 °C. The reaction mixture was directly chromatographed on SiO_2 with 35 : 1 $CHCl_3$-MeOH to afford **39** (34 mg, 62%): $[\alpha]_D$ -24.5° (*c* 1.0); R_f 0.61 (20 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 8.660 (s, 1H, C = NH), 6.505 (d, 1H, J = 3.6 Hz, H-1a), 5.568 (t, 1H, J = 9.5 Hz, H-3a), 5.359 (br-s, 1H, H-1h or 1i), 5.307 (d, 1H, J = 4.0 Hz, H-4b or 4d), 5.269 (d, 2H, J = 3.3 Hz, H-4d or 4b and H-1i or 1h), 5.181 (br-s, 1H, H-4h or 4i), 5.047 (d, 1H, J = 9.3 Hz, H-1e), 5.007 (br-s, 1H, H-4i or 4h), 4.975 (d, 1H, J = 8.1 Hz, H-1c), 4.955 (d, 1H, J = 4.0 Hz, H-4f), 4.927 (t, 1H, J = 9.2 Hz, H-2d or 2b), 4.814 (t, 1H, J = 9.9 Hz, H-2c or 2f), 4.595 (d, 1H, J = 8.0 Hz, H-1f), 4.479 (t, 1H, J = 9.5 Hz, H-2b or 2d), 4.377 (d, 1H, J = 8.4 Hz, H-1b or 1d), 4.361 (d, 1H, J = 7.7 Hz, H-1d or 1b), 4.298 (br-dd, 1H, H-3f), 3.785 (s, 3H, OMe), 1.272 (d, 3H, J = 6.2 Hz, H-6h), 1.130 (s, 9H, *tert*-Bu), 0.832 (d, 3H, J = 6.6 Hz, H-6i).

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galacto-**

pyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl Fluoride (40). A mixture of **38** (10 mg, 4 μmol) and DAST (2 μL, 14 μmol) in $(ClCH_2)_2$ (1 mL) was stirred for 2 h at -15 °C. The mixture was diluted with EtOAc, filtered through Celite and the filtrate was washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on SiO_2 with 35 : 1 $CHCl_3$-MeOH afforded **40** (9 mg, qu.): R_f 0.24 (20 : 1 $CHCl_3$-MeOH); ^1H NMR ($CDCl_3$) δ 5.353 (br-s, H-1h or H-1i), 5.304 (br-s, H-4b or H4d), 5.181 (br-s, H-4h or H-4i), 4.502 (d, 1H, J = 9.0 Hz, H-1f), 4.471 (t, 1H, J = 9.2 Hz, H-2d or H-2b), 4.375 (br-d, H-1b or H-1d), 4.362 (d, 1H, J = 7.3 Hz, H-1d or H-1b), 3.786 (s, 3H, OMe), 1.190 (s, 9H, *tert*-Bu).

***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*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(6-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→4)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-tetracosanoylamino-4-octadecene-1,3-diol (41).** (Method A) To a stirred mixture of **39** (34 mg, 11 μmol) and **4** (17 mg, 22 μmol) and 4A molecular sieves (500 mg) in $CHCl_3$ (1 mL) was added boron trifluoride etherate (8 μL, 44 μmol) at -10 °C. The mixture was stirred for 1 h. The mixture was quenched with Et_3N, diluted with $CHCl_3$ and filtered through a Celite bed. The filtrate was washed successively with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue over SiO_2 with 2 : 1 toluene-acetone afforded **41** (14 mg, 34%). (Method B) To a stirred mixture of **40** (16 mg, 6 μmol), **4** (8 mg, 11 μmol) and 4A molecular sieves (500 mg) in $CHCl_3$ (1 mL) were added $SnCl_2$ (5 mg, 33 μmol) and AgOTf (17 mg, 86 μmol) at -10 °C. The mixture was stirred for 1 h, and worked up as described in Method A. Chromatography of the residue over SiO_2 with 2 : 1 toluene-acetone afforded **41** (8 mg, 40%): $[\alpha]_D$ -36.9° (*c* 1.0); R_f 0.44 (1 : 1 toluene-acetone); ^1H NMR ($CDCl_3$) δ 5.869 (dt, 1H, J = 7.3, 14.7 Hz, 5-Cer), 5.714 (d, 1H, J = 9.5 Hz, NH), 5.532 (t, 1H, J = 7.7 Hz, 3-Cer), 5.451 (dd, 1H, J = 7.7, 15.0 Hz, H-4Cer), 5.355 (d, 1H, J = 2.2 Hz, H-4h or 4i), 5.305 (d, 1H, J = 3.3 Hz, H-4b or

4d), 5.255 (br-s, 1H, H-4i or 4h), 5.246 (br-s, 1H, H-4d or 4b), 5.215 (br-s, 1H, H-1h or 1i), 5.497 (br-s, 1H, H-1i or 1h), 4.969 (d, 2H, J = 8.1 Hz, H-1c and 1e), 4.948 (d, 1H, J = 2.9 Hz, H-4f), 4.870 (t, 1H, J = 8.1 Hz, H-2b or H-2d), 4.804 (t, 1H, J = 7.3 Hz, H-2f), 4.504 (d, 1H, J = 7.7 Hz, H-1f), 4.466 (t, 1H, J = 8.8 Hz, H-2d or 2b), 4.406 (d, 1H, J = 8.1 Hz, H-1a), 4.369 (d, 1H, J = 7.7 Hz, H-1b or 1d), 4.262 (d, 1H, J = 8.1 Hz, H-1d or 1b), 3.785 (s, 3H, OMe), 1.142 (s, 9H, *tert*-Bu), 0.849 (d, 3H, J = 6.2 Hz, H-6i).

***O*-(Sodium 5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-β-D-galactopyranosyl-(1→3)-*O*-[α-L-fucopyranosyl-(1→4)]-*O*-acetamido-2-deoxy-2-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→3)-*O*-[α-L-fucopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranosyl)-(1→1)-(2*S*, 3*R*, 4*E*)-2-tetracosanoylamino-4-octadecene-1,3-diol (2). (Sialyl dimeric Le^a ganglioside).** A solution of **41** (8 mg, 2.3 μmol) in pyridine (1 mL) was added dropwise onto LiI (8.1 mg, 60.5 μmol, dried at 200 °C for 1 day in vacuo), and the mixture was heated for 7 h at reflux under argon. The reaction mixture was chromatographed first on Sephadex LH-20 with 1 : 2 $CHCl_3$-MeOH and then on SiO_2 with 10 : 1 $CHCl_3$-MeOH to afford **42** (7 mg, 88%). A solution of **42** (7 mg, 2.0 μmol) in EtOH (5 mL) was added $MeNHNH_2$ (2.5 mL), and the mixture was stirred for 18 h at 80 °C, and then concentrated in vacuo. The residue was purified over Sephadex LH-20 with 5 : 5 : 1 $CHCl_3$-MeOH-H_2O to afford the amino derivative. To the solution of amino derivative in 2 : 2 : 1 MeOH-THF-CH_2Cl_2 (2.5 mL) was added acetic anhydride (100 μL), and the mixture was stirred for 3 h at room temperature and concentrated in vacuo. The residue in 1 : 1 MeOH-THF (0.6 mL) was stirred with 1N NaOH (0.3 mL) for 1 day at room temperature, and the mixture was chromatographed on a Sephadex LH-20 with 5 : 5 : 1 $CHCl_3$-MeOH-H_2O to give **2** (3.4 mg, 74%): ^{1}H NMR (50 : 1 $(CD_3)_2SO$-D_2O) δ 5.542 (dt, 1H, J = 7.0, 15.0 Hz, H-5Cer), 5.354 (dd, 1H, J = 7.0, 15.4 Hz, H-4Cer), 4.792 (br-d, 2H, H-1h and H-i), 4.782 (d, 1H, J = 8.1 Hz, H-1c), 4.764 (d, 1H, J = 8.0 Hz, H-1e), 4.621, 4.555 (2q, 2H, H-5h and H-5i), 4.362 (d, 2H, J = 8.0 Hz, H-1d and H-1f), 4.270 (br-d, 1H, H-1b), 4.167 (d, 1H, J = 8.1 Hz, H-1a), 2.754 (dd, 1H, J = 4.9, 12.1 Hz, H-3e*eq*), 1.879, 1.831, 1.819 (3s, 9H, 3NAc), 0.840 (t, 6H, J = 7.0 Hz, $2CH_2Me$); FABMS (TEA matrix): *m/z* $(M-Na)^-$ 2287.

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