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Systematic synthesis of α-sialyl-(2 → 3)- and -(2 → 6)-isoglobopentaosylceramides (V^3Neu5AciGb$_5$Cer and V^6Neu5AciGb$_5$Cer) [1]

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Abstract

Systematic syntheses of the isoglobo-series gangliosides, α-sialyl-(2 → 3)- and -(2 → 6)-isoglobopentaosyl ceramides (**21** and **24**, V^3Neu5AciGb$_5$Cer and V^6Neu5AciGb$_5$Cer) are described. 2-(Trimethylsilyl)ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**), the core structure of the isoglobo-series gangliosides was prepared by the glycosylation of 2-(trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**2**) with methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**1**), and subsequent *O*-deacetylation. Coupling of **4** and methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside gave an isoglobotetraoside derivative **6**, from which the phthaloyl and *O*-acetyl groups were removed. *N*-Acetylation then gave a tetrasaccharide acceptor **7**. Dimethyl(methylthio)sulfonium triflate-promoted coupling of **7** with methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*)-(2 → 3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside or -(2 → 6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside gave the pentasaccharide derivative **9** and **14** in good yields. Compounds **9** and **14** were converted into the corresponding α-trichloroimidates **12** and **17** which, on coupling with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**18**), gave the β-glycoside **19** and **22**, respectively. Finally, **19** and **22** were transformed, via selective reduction of azide group, condensation with octadecanoic acid, *O*-deacylation, and hydrolysis of the methyl ester group into **21** and **24**, respectively. © 1996 Elsevier Science Ltd.

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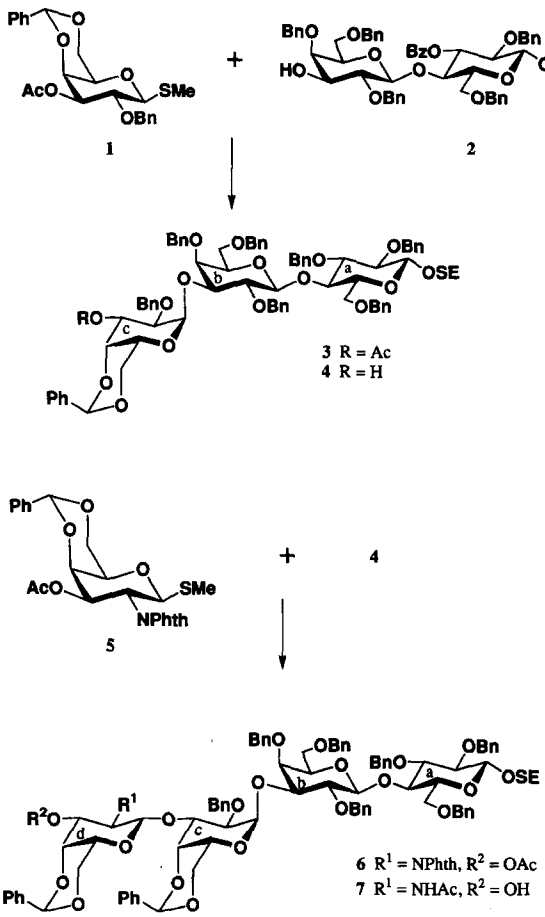
1. Introduction

Glycosphingolipids are covalent conjugates of hydrophilic oligosaccharide and hydrophobic ceramide moieties and are present in the plasma membranes of all mammalian cell walls [2]. Isoglobo-series glycosphingolipids are distinguished from other glycosphingolipids in that they contain galactosyl α-(1 → 3) galactose moieties in their structure and are known to be recognized by bacterial adhesins [3], as well as globo-series glycosphingolipids, because of their unique moleclar surface topology. Isoglobopentaosyl ceramide, termed also as extended isoglobo-series glycosphingolipids, was first found in rat gastric mucosa [4] as a fucosylated derivative, and recently in rat kidney [5] as a sulfated derivative.

In order to investigate the function of glycosphingolipids at the molecular level we have synthesized a series of gangliosides, such as ganglio- [6], lacto- [7], neolacto- [8] and globo-series [9] ganglides, including their analogues and derivatives [10]. By using the compounds synthesized by our group, some biologically important results have been obtained: sialyl Le^x is epitope is one the ligands recognized by selectins [11] and ganglioside GM3 and its related compounds possess potential immunosupressive activity [12]. We describe herein the systematic synthesis of isoglobo-series gangliosides, α-sialyl-(2 → 3)- and -(2 → 6)-isoglobopentaosylceramides as a part of our continuing research.

2. Results and discussion

2-(Trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside [13] (**2**) was selected as the glycosyl acceptor, and methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside [9] (**1**), methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside [14] (**5**), methyl (methyl 5-acetamide-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside [13] (**8**), and methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside [15] (**13**) as the glycosyl donors in the synthesis of sialyl isoglobopentaosyl ceramide **21** and its positional isomer **24**. Glycosylation of **2** with **1** at −50 °C in the presence of *N*-iodosuccinimide (NIS)-trifluoromethanesulfonic acid (TfOH) [16,17] gave the desired α-glycoside **3** (91%). A significant signal of the terminal Gal unit in the ^{1}H NMR spectrum of **3** is δ 5.21 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), indicating the newly formed glycosidic linkage to be α. *O*-Deacetylation of **3** with sodium methoxide afforded **4** in a quantitative yield, which was used as the glycosyl acceptor for the next glycosylation. Condensation of **4** with **5** under similar conditions as described for the glycosylation of **2** with **1**, except that the reaction was performed at −10 °C, gave an isoglobotetraoside derivative **6** in 84% yield (see Scheme 1).

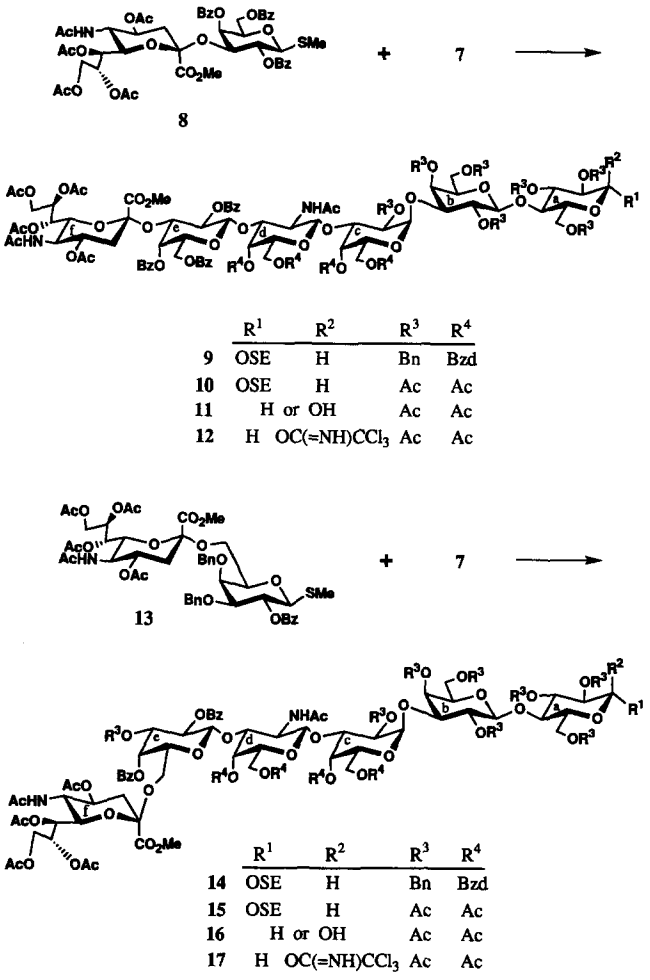


Scheme 1.

O-Deacetylation and conversion of the phthalimide **6** to the amine by heating with hydrazine hydrate in aq 95% ethanol, followed by *N*-acetylation with acetic anhydride, afforded the isoglobotetraose acceptor **7**.

Glycosylation of **7** with 1.5 equiv of **8** in dichloromethane for 8 h at 0 °C in the presence of dimethyl(methylthio)sulfonium triflate (DMTST) and powdered molecular sieves 4A gave the expected hexasaccharide derivative **9** (54%) (Scheme 2). In the same way, coupling of **7** and **13** gave the corresponding hexasaccharide **14**, which is the positional isomer of **9**.

Catalytic hydrogenolysis (Pd–C) in ethanol of the benzyl and benzylidene groups in **9** and **14** and subsequent *O*-acetylation gave the hexasaccharide derivatives **10** and **15**. Treatment [18] of **10** and **15** with trifluoroacetic acid in dichloromethane at 0 °C gave the 1-hydroxy compounds **11** and **16**, which were treated with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to afford



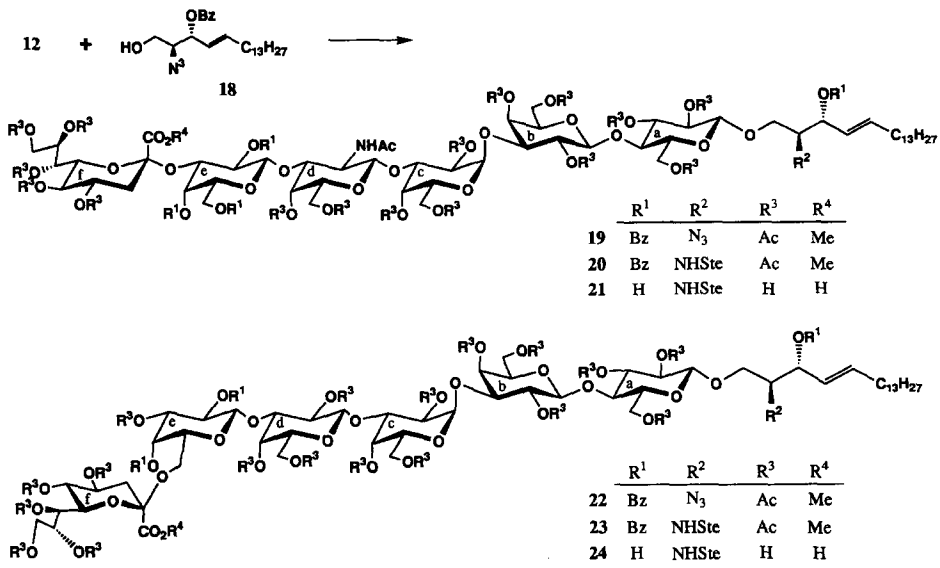
	R^1	R^2	R^3	R^4
9	OSE	H	Bn	Bzd
10	OSE	H	Ac	Ac
11	H or OH		Ac	Ac
12	H	$OC(=NH)CCl_3$	Ac	Ac

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

Scheme 2.

the trichloroacetimidates **12** and **17**. The ^{1}H NMR spectra of these compounds showed signals at δ 6.45 (d, 1 H, $J_{1,2} \sim 3.7$ Hz, H-1a), signifying that the trichloroacetimidates were α anomers.

The glycosylation [19,20] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol [20,21] (**18**) with **12** and **17** in the presence of boron trifluoride etherate as promotor gave the corresponding β glycosides **19** and **22** in 65 and 58% yields, respectively (Scheme 3). The aq 83% pyridine solutions of these compounds were submitted to hydrogen sulfide bubbling for 3 h at 0 °C for selective reduction [22] of the azido group to give the corresponding amines, which were subsequently condensed with octadecanoic acid, in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC) in dichloromethane, to give the fully protected gangliosides **20** and **23** in high yields.



Scheme 3.

O-Deacylation with sodium methoxide in methanol and subsequent saponification of the methyl ester group in **20** and **23** afforded α-sialyl-(2 → 3)-isoglobopentaosylceramide (**21**) and α-sialyl-(2 → 6)-isoglobopentaosylceramide (**24**) in quantitative yields after chromatography on a column of Sephadex LH-20.

In conclusion, the first total synthesis of sialyl-isoglobopentaosylceramide (**21**) was aceived by successive and stereoselective gycosylations of the lactose derivative **2** with the thioglycosides **1**, **5**, and **8**. This procedure was efficiently applied to the synthesis of the positional isomer **24**.

3. Experimental

General methods.—Optical rotations were determined with a Union PM-201 polarimeter at 25 °C, and ^{1}H NMR spectra were recorded at 270 MHz using the 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 3-O-acetyl-2-O-benzyl-4,6-O-benzylidene-α-D-glucopyranosyl-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**3**).—To a solution of methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**1**, 2.5 g, 5.9 mmol) and 2-(trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**2**, 4 g, 4.0 mmol) in dry dichloromethane (50 mL) were added powdered molecular sieves 4A

(MS-4A, 4 g), and the mixture was stirred for 6 h at room temperature, then cooled to −50 °C. To the cooled mixture were added, with stirring, *N*-iodosuccinimide (NIS, 2.9 g, 12 mmol) and trifluoromethanesulfonic acid (TfOH, 107 μL, 1.2 mmol), and the stirring was continued for 8 h at −50 °C. The precipitates were removed by filtration and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3, M $Na_2S_2O_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 ethyl acetate–hexane) of the residue on silica gel gave **3** (4.9 g, 91%): $[\alpha]_D$ +75° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.03 (m, 2 H, $Me_3SiCH_2CH_2O$), 2.03 (s, 3 H, AcO), 3.40 and 3.60 (m, 2 H, $Me_3SiCH_2CH_2O$), 5.21 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1c), 5.34 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.5 Hz, H-3c), and 7.03–7.42 (m, 40 H, Ph-H). Anal. Calcd for $C_{81}H_{92}O_{17}Si$ (1365.7): C, 71.23; H, 6.79. Found: C, 70.98; H, 6.75.

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene-α-D-galactopyranosyl-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**4**).—To a solution of **3** (3.7 g, 2.7 mmol) in methanol (20 mL) was added sodium methoxide until pH 9, and the mixture was stirred for 2 h at room temperature. The solution was treated with Amberlite IR-120 (H^+) resin, and the resin was removed by filtration. The resin was washed with methanol, and the combined filtrate and washings was concentrated. Column chromatography (1:4 ethyl acetate–hexane) of the residue on silica gel gave **4** (3.6 g, quant.) as an amorphous mass: $[\alpha]_D$ +41° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.03 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.92 (br s, 1 H, OH), 3.40 and 3.60 (m, 2 H, $Me_3SiCH_2CH_2O$), 5.24 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1c), 5.27 (s, 1 H, CHPh), and 7.04–7.43 (m, 40 H, Ph-H). Anal. Calcd for $C_{79}H_{90}O_{16}Si$ (1323.66): C, 71.68; H, 6.85. Found: C, 71.48; H, 6.57.

2-(Trimethylsilyl)ethyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranosyl-(1 → 3)-2-O-benzyl-4,6-O-benzylidene-α-D-galactopyranosyl-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**6**).—To a solution of **4** (3.14 g, 2.3 mmol) and methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (**5**, 1.67 g, 3.5 mmol) in dichloromethane (15 mL) was added powdered MS-4A (4 g), and the mixture was stirred for 6 h at room temperature, then cooled to −10 °C. To the cooled mixture were added, with stirring, NIS (1.7 g, 6.9 mmol) and TfOH (62.7 μL, 0.69 mmol), and the stirring was continued for 8 h at −10 °C. The precipitates were removed by filtration and washed thoroughly with dichloromethane. The filtrate and washings were combined and washed with M Na_2CO_3, M $Na_2S_2O_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:2 ethyl acetate–hexane) of the residue on silica gel gave **6** (3.5 g, 84%) as an amorphous mass: $[\alpha]_D$ +33° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.90 (s, 3 H, AcO), 3.40 and 3.60 (m, 2 H, $Me_3SiCH_2CH_2O$), 5.27 and 5.50 (2 s, 2 H, 2 CHPh), 5.58 (dd, 1 H, $J_{2,3}$ 11.2, $J_{3,4}$ 3.7 Hz, H-3d), 6.80–7.64 (m, 49 H, Ph-H). Anal. Calcd for $C_{102}H_{109}NO_{23}Si$ (1745.0): C, 70.20; H, 6.29; N, 0.80. Found: C, 70.29; H, 6.16; N, 0.79.

2-(Trimethylsilyl)ethyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranosyl-(1 → 3)-2-O-benzyl-4,6-O-benzylidene-α-D-galactopyranosyl-(1 → 3)-2,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**7**).—A solution of **6** (3.4 g, 1.9 mmol) in aq 95% ethanol (20 mL) was treated with hydrazine

hydrate (1.1 mL) for 8 h under reflux. The precipitate was collected and washed with ethanol, and the combined filtrate and washings were concentrated. The residue was treated with acetic anhydride (5 mL) in methanol (20 mL) for 2 h at room temperature, pyridine (3 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2 M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:1 ethyl acetate–hexane) of the residue on silica gel afforded **7** (2.3 g, 80%) as an amorphous mass: $[\alpha]_D$ +53° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.45 (s, 3 H, AcN), 3.40 and 3.60 (m, 2 H, $Me_3SiCH_2CH_2O$), 5.21 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1c), 7.06–7.45 (m, 45 H, Ph-H). Anal. Calcd for $C_{94}H_{107}NO_{21}Si$ (1572.92): C, 70.25; H, 6.72; N, 0.89. Found: C, 70.26; H, 6.83; N, 0.78.

2-(Trimethylsilyl)ethyl (methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri*-O-*benzoyl-β*-D-*galacto-pyranosyl-(1 → 3)-2-acetamido-4,6*-O-*benzylidene-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-2*-O-*benzyl-4,6*-O-*benzylidene-α*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*benzyl-β*-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**9**).—To a solution of methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (**8**, 159 mg, 0.15 mmol) and **7** (181 mg, 0.1 mmol) in dry dichloromethane (5 mL) was added powdered MS-4A (500 mg), and the mixture was stirred for 6 h at room temperature, then cooled to 0 °C. To the mixture was added, with stirring, dimethyl(methylthio)sulfonium triflate (DMTST, 183 mg, 0.70 mmol), and the stirring was continued for 8 h at 0 °C. The precipitates were removed by filtration and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (2:1 ethyl acetate–hexane) of the residue on silica gel gave **9** (143 mg, 54%) as an amorphous mass: $[\alpha]_D$ +18° (*c* 2.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.57 and 1.66 (2 s, 6 H, 2 AcN), 1.75, 1.88, 2.00, 2.17 (4 s, 12 H, 4 AcO), 2.39 (dd, 1 H, J_{gem} 12.0, $J_{3eq,4}$ 3.5 Hz, H-3f*eq*), 3.81 (s, 3 H, MeO), 5.27 and 5.30 (2 s, 2 H, 2 C*H*Ph), 5.50 (m, 1 H, H-8f), 6.98–8.10 (m, 60 H, Ph-H). Anal. Calcd for $C_{141}H_{156}N_2O_{41}Si$ (2962.86): C, 66.08; H, 6.13; N, 1.09. Found: C, 65.94; H, 6.30; N, 0.91.

2-(Trimethylsilyl)ethyl (methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri*-O-*benzoyl-β*-D-*galacto-pyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyrano-syl-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranoside* (**10**).—A solution of **9** (408 mg, 0.14 mmol) in ethanol (10 mL) was hydrogenated in the presence of 10% Pd–C (200 mg) for 6 h at room temperature, then the catalyst was removed by filtration, and the solution was concentrated. The residue was acetylated with acetic anhydride (2 mL) and pyridine (3 mL) for 6 h at room temperature. The product was purified by chromatography on a column of silica gel with 20:1 CH_2Cl_2–MeOH to give **10** (212 mg, 80%) as an amorphous mass: $[\alpha]_D$ +38° (*c* 2.9, $CHCl_3$); ^1H NMR: δ 0.92 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.39 and 1.54 (2 s, 6 H, 2 AcN), 1.75, 1.80, 1.99, 2.00, 2.01, 2.02, 2.04, 2.05, 2.07, 2.08, 2.09, 2.10 (15 s, 45 H, 15 AcO), 2.47 (dd, 1 H, J_{gem} 12.5, $J_{3eq,4}$

4.2 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 5.50 (dd, 1 H, $J_{6,7}$ 3.4, $J_{7,8}$ 10.4 Hz, H-7f), 5.60 (m, 1 H, H-8f), 7.28–8.20 (m, 15 H, Ph-H). Anal. Calcd for $C_{100}H_{128}O_{52}N_2Si$ (2218.17): C, 54.14; H, 5.81; N, 1.26. Found: C, 54.11; H, 5.51; N, 1.18.

(Methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl*-α-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*acetyl*-D-*glucopyranose* (**11**).—To a solution of **10** (233 mg, 0.10 mmol) in dichloromethane (1 mL) was added trifluoroacetic acid (2.5 mL) at 0 °C, and the mixture was stirred for 6 h at room temperature and concentrated. Column chromatography (10:1 CH_2Cl_2–MeOH) of the residue on silica gel gave **11** (190 mg, 90%) as an amorphous mass: ^{1}H NMR: δ 1.32 and 1.38 (2 s, 6 H, 2 AcN), 1.77–2.09 (15 s, 45 H, 15 AcO), 2.44 (dd, 1 H, J_{gem} 12.9, $J_{3eq,4}$ 4.6 Hz, H-3f*eq*), 3.81 (s, 3 H, MeO), 7.23–8.19 (m, 15 H, Ph-H). Anal. Calcd for $C_{95}H_{116}N_2O_{52}$ (2117.93): C, 53.87; H, 5.52; N, 1.32. Found: C, 53.73; H, 5.69; N, 1.14.

(Methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl-2-deoxy*-β-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl*-α-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl trichloroacetimidate* (**12**).—To a solution of **11** (264 mg, 0.12 mmol) in dichloromethane (1 mL) and trichloroacetonitrile (0.37 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 22.3 μL) at 0 °C, and the mixture was stirred for 3 h at 0 °C, then concentrated. Column chromatography (30:1 CH_2Cl_2–MeOH) of the residue on silica gel gave **13** (241 mg, 85%) as an amorphous mass: $[\alpha]_D$ +55° (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 1.25 and 1.39 (2 s, 6 H, 2 AcN), 1.90–2.18 (15 s, 45 H, 15 AcO), 2.44 (dd, 1 H, J_{gem} 13.0, $J_{3eq,4}$ 4.6 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 6.80 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1a), 7.20–8.80 (m, 15 H, Ph-H). Anal. Calcd for $C_{98}H_{116}N_3O_{52}Cl_3$ (2274.35): C, 51.75; H, 5.14; N, 1.84. Found: C, 51.72; H, 4.84; N, 1.76.

2-(Trimethylsilyl)ethyl (methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)-2,4-di*-O-*benzoyl-3*-O-*benzyl*-β-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6*-O-*benzylidene-2-deoxy*-β-D-*galactopyranosyl-(1 → 3)-2*-O-*benzyl-4,6*-O-*benzylidene*-α-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*benzyl*-β-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**14**).—Glycosylation of **7** (972 mg, 0.60 mmol) with methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2 → 6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**13**, 900 mg, 0.91 mmol) in a fashion similar to that described for **9** afforded amorphous **14** (939 mg, 61%): $[\alpha]_D$ +40° (*c* 1.3, $CHCl_3$); ^{1}H NMR: δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.57 and 1.65 (2 s, 6 H, 2 AcN), 1.77, 1.89, 2.07, 2.18 (4 s, 12 H, 4 AcO), 2.35 (dd, 1 H, J_{gem} 12.1, $J_{3eq,4}$ 3.5 Hz, H-3f*eq*), 3.82 (s, 3 H, MeO), 5.30 and 5.35 (2 s, 6 H, 2 C*H*Ph), 6.97–8.10 (m, 60 H, Ph-H). Anal. Calcd for $C_{148}H_{158}N_2O_{40}Si$ (2632.95): C, 67.51; H, 6.05; N, 1.06. Found: C, 67.23; H, 6.05; N, 0.85.

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

*→ 3)-2,4,6-tri-*O*-acetyl-α-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-acetyl-β-*D*-glucopyranoside* (**15**).—The benzyl and benzylidene group of **14** (842 mg, 0.33 mmol) were removed by hydrogenolytic cleavage over 10% Pd–C (1 g) in 10 mL of EtOH. The deprotected product was acetylated as described for **10** to get amorphous **15** (383 mg, 63%): $[\alpha]_D$ +33° (*c* 2.4, $CHCl_3$); ^1H NMR: δ 0.85 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.39 and 1.54 (2 s, 6 H, 2 AcN), 1.76 1.88, 1.99, 2.01, 2.02, 2.05, 2.06, 2.07, 2.09, 2.13, 2.14, 2.15 (16 s, 48 H, 16 AcO), 2.50 (dd, 1 H, J_{gem} 12.0, $J_{3eq,4}$ 4.1 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 5.54 (m, 1 H, H-7f), 5.60 (m, 1 H, H-8f), 7.30–8.20 (m, 10 H, Ph-H). Anal. Calcd for $C_{95}H_{126}N_2O_{52}Si$ (2156.10): C, 52.92; H, 5.89; N, 1.30. Found: C, 52.65; H, 5.84; N, 1.29.

*(Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-α-*D*-galacto-2-nonulopyranosylonate)-(2 → 6)-3-*O*-acetyl-2,4-di-*O*-benzoyl-β-*D*-galactopyranosyl-(1 → 3)-2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-α-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-acetyl-*D*-glucopyranose* (**16**).—The 2-(trimethylsilyl)ethyl group in **15** (604 mg, 0.28 mmol) was removed in a fashion similar to that described for **11** to get amorphous 1-hydroxy compound **16** (541 mg, 95%); ^1H NMR: δ 1.32 and 1.38 (2 s, 6 H, 2 AcN), 1.67, 1.85, 1.98, 2.00, 2.02, 2.05, 2.06, 2.07, 2.08, 2.09, 2.10 (16 s, 48 H, 16 AcO), 2.50 (dd, 1 H, J_{gem} 13.0, $J_{3eq,4}$ 4.6 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 5.60 (m, 1 H, H-8f), 7.21–8.25 (m, 10 H, Ph-H). Anal. Calcd for $C_{90}H_{114}N_2O_{52}$ (2055.86): C, 52.58; H, 5.59; N, 1.36. Found: C, 52.53; H, 5.45; N, 1.09.

*(Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-α-*D*-galacto-2-nonulopyranosylonate)-(2 → 6)-3-*O*-acetyl-2,4-di-*O*-benzoyl-β-*D*-galactopyranosyl-(1 → 3)-2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-α-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-acetyl-α-*D*-glucopyranosyl trichloroacetimidate* (**17**).—A solution of **16** (541 mg, 0.26 mmol) in dichloromethane (2 mL) was treated with trichloroacetonitrile (0.94 mL) as described for **12** to afford **17** (573 mg, 98%): $[\alpha]_D$ +53° (*c* 1.2 $CHCl_3$); ^1H NMR: δ 1.25 and 1.40 (2 s, 6 H, 2 AcN), 1.85–2.20 (16 s, 48 H, 16 AcO), 2.50 (dd, 1 H, J_{gem} 12.0, $J_{3eq,4}$ 4.5 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 6.45 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1a), 7.20–8.70 (m, 10 H, Ph-H). Anal. Calcd for $C_{93}H_{114}Cl_3N_3O_{52}$ (2212.26): C, 50.49; H, 5.19; N, 1.90. Found: C, 50.20; H, 5.16; N, 1.81.

*(Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-α-*D*-galacto-2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl-(1 → 3)-2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-α-*D*-galactopyranosyl-(1 → 3)-2,4,6-tri-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-acetyl-β-*D*-glucopyranosyl-(1 → 1)-(2S,3R,4E)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol* (**19**).—To a solution of **12** (241 mg, 0.10 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**18**, 226 mg, 0.50 mmol) in dichloromethane (1 mL) was added MS-4A (AW-300, 1 g), and the mixture was stirred for 6 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (26 μL) was added, and the mixture was stirred for 8 h at 0 °C and then filtered. The filtrate was washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (50:1 CH_2Cl_2–MeOH) of the residue on silica gel gave **19** (174 mg, 65%): $[\alpha]_D$ +22° (*c* 0.5, $CHCl_3$); ^1H NMR: δ 0.80 (t, 3 H, J_{Me,CH_2} 6.6 Hz, *Me*CH_2), 1.25 (s, 22 H, 11 CH_2), 1.41 and

1.52 (2 s, 6 H, 2 AcN), 1.78–2.15 (15 s, 48 H, 15 AcO), 2.50 (dd, 1 H, J_{gem} 12.1, $J_{3eq,4}$ 3.9 Hz, H-3f*eq*), 3.80 (s, 3 H, MeO), 7.20–8.30 (m, 20 H, Ph-H). Anal. Calcd for $C_{120}H_{153}N_5O_{54}$ (2529.52): C, 56.97; H, 6.09; N, 2.76. Found: C, 56.72; H, 6.05; N, 3.05.

(Methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranosyl-(1 → 1)-(2S,3R,4E)-3*-O-*benzoyl-2-octadecanamido-4-octadecene-1,3-diol* (**20**).—Hydrogen sulfide was bubbled through a stirred solution of **19** (240 mg, 0.04 mmol) in aq 83% pyridine (3 mL) for 3 h at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (56 mg, 0.19 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (56 mg, 0.28 mmol) in dichloromethane (3 mL) for 8 h at room temperature. Dichloromethane (60 mL) was added, and the mixture was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (30:1 CH_2Cl_2–MeOH) of the residue on silica gel gave **20** (184 mg, 58%): $[\alpha]_D$ +25° (*c* 0.4, $CHCl_3$); ^{1}H NMR: δ 0.85 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 *Me*CH_2), 1.24 (s, 52 H, 26 CH_2), 1.89–2.78 (17 s, 51 H, 15 AcO and 2 AcN), 2.45 (m, 1 H, H-3f*eq*), 3.80 (s, 3 H, MeO), 5.82 (m, 1 H, H-5 of ceramide), 7.20–8.20 (m, 20 H, Ph-H). Anal. Calcd for $C_{148}H_{189}N_3O_{55}$ (2890.11): C, 61.50; H, 6.59; N, 1.45. Found C, 61.30; H, 6.31; N, 1.49.

(5-Acetamido-3,5-dideoxy-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 3)-β*-D-*galactopyranosyl-(1 → 3)-2-acetamido-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-α*-D-*galactopyranosyl-(1 → 3)-β*-D-*galactopyranosyl-(1 → 4)-β*-D-*glucopyranosyl-(1 → 1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol* (**21**).—To a solution of **20** (184 mg, 0.063 mmol) in methanol (8 mL) was added a catalytic amount of sodium methoxide, and the mixture was stirred for 12 h at 40 °C. Water (1 mL) was added, and the mixture was stirred for additional 8 h at 40 °C, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with methanol, and the filtrate and washings were concentrated. Column chromatography (5:4:0.7 $CHCl_3$–MeOH–H_2O) of the residue on Sephadex LH-20 gave **21** (107 mg, quant.) as an amorphous mass: $[\alpha]_D$ −1° (*c* 1.2, 5:4:0.7 CH_3Cl_3–MeOH–H_2O); ^{1}H NMR (1:1 Me_2SO-d_6–D_2O): δ 0.85 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 *Me*CH_2), 1.24 (s, 52 H, 26 CH_2), 1.46 (m, 2 H, C$H_2$$CH_2$CO), 1.80 and 1.92 (2 s, 6 H, 2 AcN), 2.80 (m, 1 H, H-3f*eq*), 5.56 (m, 1 H, H-5 of ceramide). Anal. Calcd for $C_{104}H_{153}N_3O_{41}$ (2101.35): C, 59.43; H, 7.30; N, 1.97. Found: C, 59.53; H, 7.20; N, 1.98.

(Methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)-3*-O-*acetyl-2,4-di*-O-*benzoyl-β*-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranosyl-(1 → 1)-(2S,3R,4E)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**22**).—Coupling of **17** (573 mg, 0.26 mmol) and **18** (553 mg, 1.3 mmol), as described for **19**, yielded amorphous **22** (358 mg, 56%): $[\alpha]_D$ +25° (*c* 1.2, $CHCl_3$); ^{1}H NMR: δ 0.95 (t, 3 H, J_{Me,CH_2} 6.6 Hz, *Me*CH_2), 1.25 (s, 22 H, 11 CH_2), 1.43 and 1.50 (2 s, 6 H, 2 AcN), 1.78–2.20 (16 s, 48 H, 16 AcO), 2.50 (dd, 1 H, J_{gem}

12.1, $J_{3eq,4}$ 3.9 Hz, H-3f*eq*), 3.81 (s, 3 H, MeO), 7.20–8.30 (m, 15 H, Ph-H). Anal. Calcd for $C_{115}H_{151}N_5O_{54}$ (2467.45): C, 55.98; H, 6.17; N, 2.84. Found: C, 55.80; H, 6.04; N, 2.58.

(Methyl 5-acetamido-4,7,8,9-tetra-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2 → 6)-3*-O-*acetyl-2,4-di*-O-*benzoyl-β*-D-*galactopyranosyl-(1 → 3)-2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-α*-D-*galactopyranosyl-(1 → 3)-2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl-(1 → 4)-2,3,6-tri*-O-*acetyl-β*-D-*galactopyranosyl-(1 → 1)-(2S,3R,4E)-3*-O-*benzoyl-2-octadecanamido-4-octadecene-1,3-diol* (**23**).—Selective reduction of the azido group in **22** (226 mg, 0.09 mmol), and subsequent coupling of the product with octadecanoic acid (52 mg, 0.18 mmol) as described for **20**, gave amorphous **23** (150 mg, 58%): $[\alpha]_D$ +35° (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 0.85 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 *Me*CH_2), 1.25 (s, 52 H, 26 CH_2), 1.77 and 1.89 (2 s, 6 H, 2 AcN), 2.01–2.78 (16 s, 48 H, 16 AcO), 2.50 (m, 1 H, H-3f*eq*), 3.80 (s, 3 H, MeO), 5.82 (m, 1 H, H-5 of ceramide), 7.18–8.19 (m, 15 H, Ph-H). Anal. Calcd for $C_{143}H_{187}N_3O_{55}$ (2828.04): C, 60.73; H, 6.67; N, 1.49. Found: C, 60.61; H, 6.44; N, 1.36.

(5-Acetamido-3,5-dideoxy-D-glycero-α-D-galacto-*2-nonulopyranosylonic acid)-(2 → 6)-β*-D-*galactopyranosyl-(1 → 3)-2-acetamido-2-deoxy-β*-D-*galactopyranosyl-(1 → 3)-α*-D-*galactopyranosyl-(1 → 3)-β*-D-*galactopyranosyl-(1 → 4)-β*-D-*glucopyranosyl-(1 → 1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol* (**24**).—*O*-Deacylation and saponification of **23** (85 mg, 0.029 mmol), as described for **21**, yielded amorphous **24** (63 mg, quant.): $[\alpha]_D$ −2.0° (*c* 1.2, 5:4:0.7 $CHCl_3$–MeOH–H_2O); ^{1}H NMR (1:1 Me_2SO-d_6–D_2O): δ 0.85 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 *Me*CH_2), 1.24 (s, 52 H, 26 CH_2), 1.47 (m, 2 H, C$H_2$$CH_2$CO), 2.80 (m, 1 H, H-3f*eq*), 5.56 (m, 1 H, H-5 of ceramide). Anal. Calcd for $C_{104}H_{153}N_3O_{41}$ (2101.35): C, 59.43; H, 7.30; N, 1.97. Found: C, 59.53; H, 7.20; N, 1.98.

References

[1] A. Kameyama, T. Ehara, Y. Yamada, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 14 (1995) 507–523.

[2] H. Wiegandt (Ed.), *Glycolipids, New Comprehensive Biochemistry*, Vol. 10, Elsevier, Amsterdam, 1985, pp 199–260.

[3] K.-A. Karlsson, *Annu. Rev. Biochem.*, 58 (1989) 309–350.

[4] G.C. Hannson, J.-F. Bouhouns, and J. Ångström, *J. Biol. Chem.*, 262 (1987) 13135–13141.

[5] K. Tadano-Aritomi, M. Okuda, I. Ishizuka, H. Kubo, and P. Ireland, *Carbohydr. Res.*, 265 (1994) 49–59.

[6] (a) H.-K. Ishida, H. Ishida, M. Kiso, and A. Hasegawa, *Tetrahedron Asymm.*, 5 (1994) 2493–2512; (b) K. Hotta, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 14 (1995) 491–506, and references therein.

[7] A. Kameyama, T. Ehara, Y. Yamada, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 13 (1994) 641–654, and references therein.

[8] T. Ehara, A. Kameyama, Y. Yamada, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 281 (1996) 237–252, and references therein.

[9] H. Ishida, R. Miyawaki, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, accepted for publication.

[10] M. Kiso, K. Ando, H. Inagaki, H. Ishida, and A. Hasegawa, *Carbohydr. Res.*, 272 (1995) 159–178, and references therein.

[11] (a) D. Tyrell, P. James, N. Rao, C. Foxall, S. Abbas, F. Dasgupta, M. Nashed, A. Hasegawa, M. Miso, D.

Asa, J. Kidd, and B.K. Brandley, *Proc. Natl. Acad. Sci. USA*, 88 (1991) 10372–10376; (b) M.J. Polley, M.L. Phillips, E. Wayner, E. Nudelman, A.K. Singhal, S. Hakomori, and J.C. Paulson, *Proc. Natl. Acad. Sci. USA*, 88 (1991) 6224–6228.

[12] (a) S. Ladisch, A. Hasegawa, R. Li, and M. Kiso, *Biochemistry*, 34 (1995) 1197–1202; (b) S. Ladisch, A. Hasegawa, R. Li, and M. Kiso, *Biochem. Biophys. Res. Commun.*, 203 (1994) 1102–1109.

[13] A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 20 (1990) 269–285.

[14] K. Hotta, S. Komba, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 13 (1994) 665–677.

[15] A. Hasegawa, K. Hotta, A. Kameyama, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 10 (1991) 439–459.

[16] G.H. Veeneman, S.H. van Leeuwen, and J.H. van Boom, *Tetrahedron Lett.*, 31 (1990) 1331–1334.

[17] A. Hasegawa, T. Nagahama, H. Ohki, K. Hotta, H. Ishida, and M. Kiso, *J. Carbohydr. Chem.*, 10 (1991) 493–498.

[18] K. Jansson, S. Ahlfors, T. Frejd, J. Kihlberg, and G. Magnusson, *J. Org. Chem.*, 53 (1988) 5629–5647.

[19] R.R. Schmidt and G. Grundler, *Synthesis*, (1981) 885.

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

[21] R.R. Schmidt and P. Zimmermann, *Angew. Chem., Int. Ed. Engl.*, 25 (1986) 725–726.

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