Carbohydrate Research, 252 (1994) 283–290
Elsevier Science B.V., Amsterdam

Note

A facile total synthesis of ganglioside GD2 †

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(Received April 19th, 1993; accepted June 17th, 1993)

Recently, as more and more biological functions[2–9] of gangliosides are being revealed, their stereocontrolled synthesis is urgently required to aid the elucidation of their functions at the molecular level. In particular, a facile systematic synthesis of polysialogangliosides containing the α-sialyl-(2 → 8)-sialic acid unit in their molecules is of interest in connection with the important biological roles of these glycolipids[10,11].

We have developed[12–15] an α-stereoselective procedure for glycosylation with sialic acid, α-sialyl-(2 → 8)-sialic acid and α-sialyl-(2 → 8)-α-sialyl-(2 → 8)-sialic acid employing their 2-thioglycosides as glycosyl donors and suitably protected acceptors, with dimethyl(methylthio)sulfonium triflate (DMTST) or *N*-iodosuccinimide (NIS)–trifluoromethanesulfonic acid (or TMS triflate) as glycosylation promoters in acetonitrile, and have synthesized a variety of gangliosides[16] and their analogues[17]. In previous reports[14], we described the synthesis of ganglioside GD3, in which α-sialyl-(2 → 8)-sialic acid is linked as the α-glycoside at C-3′ of the lactose moiety in the molecule, in a connection with a novel approach to the systematic synthesis of polysialoglycoconjugates.

As a part of our continuing studies on the systematic synthesis and elucidation of the functions of gangliosides, we describe here a facile total synthesis of gangliosides GD2. This ganglioside, which was first isolated from human brain by Kuhn and Wiegandt[18], is well known as a human melanoma-associated antigen[11,19].

RESULTS AND DISCUSSION

Methyl 6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-1-thio-β-D-galactopyranoside[20] (**2**) was selected as the glycosyl donor, and compound **1** (ref 14) as the acceptor in the synthesis of GD2.

† Synthetic Studies on Sialoglycoconjugates, Part 51. For Part 50, see ref 1.
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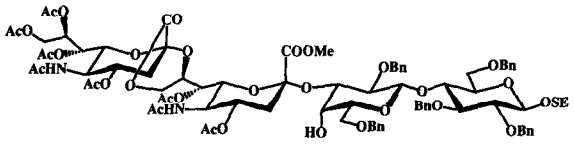
SSDI 0008-6215(93)E0260-8



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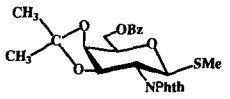
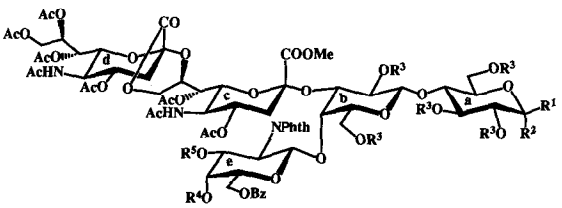


2

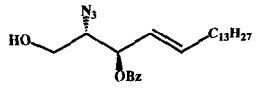
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
Bz = benzoyl
Phth = phthaloyl



	R^1	R^2	R^3	R^4	R^5
3	OSE	H	Bn	- Ipd -	
4	OSE	H	Bn	H	H
5	OSE	H	Ac	Ac	Ac
6	H , OH		Ac	Ac	Ac
7	H	$OC(=NH)CCl_3$	Ac	Ac	Ac

The glycosylation of **1** with **2** in dichloromethane for 12 h at room temperature in the presence of 1.7 equiv of *N*-iodosuccinimide (NIS), 0.2 equiv of trifluoromethanesulfonic acid, and powdered 4A molecular sieves gave the expected β-glycoside **3** in 84% yield. The structure of **3** was unambiguously proved by 270 MHz ^{1}H NMR spectroscopy. Significant signals were a one-proton doublet of doublets of δ 3.37 ($J_{1,2}$ 7.7, $J_{2,3}$ 9.0 Hz, H-2e) and a one-proton doublet at δ 4.34 (H-1e), indicating the newly formed glycosidic linkage to be β. Other ^{1}H NMR data, given in the Experimental, are consistent with the structure **3**.

Removal of the isopropylidene group from **3** with aqueous 80% acetic acid for 5 h at 60°C gave **4** in 80% yield, and this on catalytic hydrogenolysis (10% Pd–C) in ethanol–acetic acid of the benzyl group and subsequent *O*-acetylation gave compound **5** in 85% yield. Treatment[21] of **5** with trifluoroacetic acid in dichloromethane for 2 h at room temperature gave the 1-hydroxy compound **6** in 94% yield. Reaction[22] of **6** with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 2 h at 0°C gave the α-trichloroacetimidate **7** in 76% yield after column chromatography. Significant signals in the ^{1}H NMR spectrum were at δ 6.49 (d, $J_{1,2}$ 3.8 Hz, H-1a) and 8.66 (C=NH), indicating the imidate to be α.



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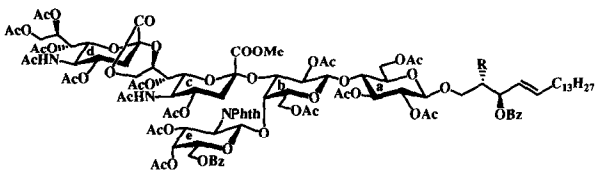
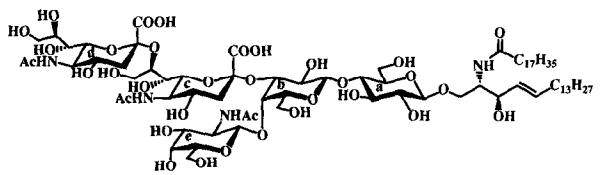


9 R = N_3
10 R = $NHCOC_{17}H_{35}$



11 Ganglioside GD2

Glycosylation[22,23] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[23,24] (**8**) with **7** in dichloromethane in the presence of TMS triflate for 10 h at 0°C afforded the desired β-glycoside **9** in 44% yield. Selective reduction[23,25] of the azido group in **9** with hydrogen sulfide in aqueous 83% pyridine for 3 days at 0°C gave the amine which, on condensation with octadecanoic acid, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane, gave the acylated ganglioside **10** in 85% yield after chromatography.

Finally, *O*-deacylation of **10** with sodium methoxide in methanol, subsequent hydrolysis of the methyl ester and lactone functions, and treatment with ethylenediamine in *n*-butanol for 1 h at 70°C, followed by *N*-acetylation, gave ganglioside GD2 in 72% yield after Sephadex LH-20 column chromatography.

In summary, a facile, stereocontrolled, first total synthesis of GD2 was accomplished. The work shows that the glycosyl acceptor **1** and the disialyl pentasaccharide **4** described herein could be used as the intermediates suitable for systematic syntheses of polysialoglycoconjugates.

EXPERIMENTAL

General methods.—Optical rotations were determined with a Union PM-201 polarimeter at 25°C and IR spectra were recorded with a Jasco IRA-100 spectrophotometer. ^{1}H NMR spectra were recorded at 270 MHz with a Jeol JNM-GX

270 spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted in vacuo.

2-(Trimethylsilyl)ethyl O-*[methyl 5-acetamido-8-*O-*(5-acetamido-4,7,8,9-tetra-*O-*acetyl-3,5-dideoxy-*D-glycero-α-D-galacto-*2-nonulopyranosylono-1',9-lactone)-4,7-di-*O-*acetyl-3,5-dideoxy-*D-glycero-α-D-galacto-*2-nonulopyranosylonate]-(2 → 3)-*O-*[(6-*O-*benzoyl-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* (**3**).—To a solution of 2-(trimethylsilyl)ethyl *O*-[methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-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] (**1**; 100 mg, 0.06 mmol) and methyl 6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-2-phthalimido-1-thio-β-D-galactopyranoside[12] (**2**; 45 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) were added 4A molecular sieves (180 mg), and the suspension was stirred for 5 h at room temperature. To the mixture were then added, with stirring, *N*-iodosuccinimide (NIS; 40 mg, 0.15 mmol) and trifluoromethanesulfonic acid (TfOH; 2 μL, 0.02 mmol), and the stirring was continued for 12 h at room temperature; the progress of the reaction was monitored by TLC. The solids were filtered off and washed thoroughly with CH_2Cl_2. The combined filtrate and washings was washed with M Na_2CO_3 and M $Na_2S_2O_3$, dried (Na_2SO_4), and concentrated. Column chromatography (40:1 CH_2Cl_2–MeOH) of the residue on silica gel (25 g) gave **3** (106 mg, 85%) as an amorphous mass, $[\alpha]_D$ + 10.3° (*c* 1.0, $CHCl_3$); ν 3300 (NH), 1740 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), 860 and 840 (TMS), and 710 and 700 cm^{-1}) (Ph); ^1H NMR ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.36 and 1.56 (2 s, 6 H, Me_2C), 1.82–2.08 (8 s, 24 H, 2 AcN and 6 AcO), 2.47 (dd, 1 H, $J_{3ax,3eq}$ 15.0, $J_{3eq,4}$ 4.1 Hz, H-3d*eq*), 2.60 (dd, 1 H, $J_{3ax,3eq}$ 15.0, $J_{3eq,4}$ 4.8 Hz, H-3c*eq*), 2.75 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.1 Hz, H-2b), 3.37 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.0 Hz, H-2e), 3.51 (br d, 1 H, $J_{2,3}$ 9.0 Hz, H-3e), 3.84 (d, 1 H, $J_{2,3}$ 9.1 Hz, H-3b), 3.95 (s, 3 H, MeO), 4.23 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1b), 4.34 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1e), 4.85 (m, 1 H, H-4c), 5.19 (m, 1 H, H-4d), 5.28 (d, 1 H, $J_{7,8}$ 9.5 Hz, H-7c), 5.38 (d, 1 H, $J_{7,8}$ 8.6 Hz, H-7d), and 6.92–8.05 (m, 34 H, 7 Ph). Anal. Calcd for $C_{111}H_{131}N_3O_{39}Si$ (2159.3): C, 61.74; H, 6.12; N, 1.95. Found: C, 61.49; H, 6.36; N, 1.76.

2-(Trimethylsilyl)ethyl O-*[methyl 5-acetamido-8-*O-*(5-acetamido-4,7,8,9-tetra-*O-*acetyl-3,5-dideoxy-*D-glycero-α-D-galacto-*2-nonulopyranosylono-1',9-lactone)-4,7-di-*O-*acetyl-3,5-dideoxy-*D-glycero-α-D-galacto-*2-nonulopyranosylonate]-(2 → 3)-*O-*[(6-*O-*benzoyl-2-deoxy-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* (**4**).—A solution of compound **3** (190 mg, 0.88 mmol) in aq 80% AcOH (5.0 mL) was stirred for 6 h at 60°C and concentrated. Column chromatograpy (30:1 CH_2Cl_2–MeOH) of the residue on silica gel (30 g) gave **4** (140 mg, 80%) as an amorphous mass; $[\alpha]_D$ + 6.8° (*c* 1.2, $CHCl_3$); ν 3600–3100 (OH, NH), 1730 and 1220 (ester), 1700

(imide), 1650 and 1540 (amide), 860 and 840 (TMS), and 710 and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.82–2.07 (8 s, 24 H, 2 AcN and 6 AcO), 2.47 (dd, 1 H, $J_{3ax,3eq}$ 14.1, $J_{3eq,4}$ 6.2 Hz, H-3d*eq*), 2.54 (dd, 1 H, $J_{3ax,3eq}$ 12.8 $J_{3eq,4}$ 6.2 Hz, H-3c*eq*), 2.80 (dd, 1 H, $J_{1,2}$ 7.4, $J_{2,3}$ 8.9 Hz, H-2b), 3.93 (s, 3 H, MeO), 5.29 (dd, 1 H, $J_{6,7}$ 2.2, $J_{7,8}$ 8.6 Hz, H-7c), 5.41 (d, 1 H, $J_{7,8}$ 8.3 Hz, H-7d), and 6.91–8.05 (m, 34 H, 7 Ph). Anal. Calcd for $C_{108}H_{127}N_3O_{39}Si$ (2119.3): C, 61.21; H, 6.04; N, 1.98. Found: C, 61.09; H, 6.03; N, 1.72.

2-(Trimethylsilyl)ethyl O-*[methyl-5-acetamido-8-*O-*(5-acetamido-4,7,8,9-tetra-*O-*acetyl-3,5-dideoxy-*D-glycero-*α*-D-*galacto-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O-*acetyl-3,5,-dideoxy-*D-glycero-*α*-D-galacto-2-nonulopyranosylonate-(2 → 3)-*O-*[(3,4-di-*O-*acetyl-6-*O-*benzoyl-2-deoxy-2-phthalimido-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* (**5**).—A solution of **4** (240 mg, 0.11 mmol) in EtOH (15 mL) and AcOH (15 mL) was hydrogenolyzed in the presence of 10% Pd–C (240 mg) for 3 days at 45°C; the progress of the reaction was monitored by TLC. The precipitate was filtered off and washed with EtOH. The combined filtrate and washings were concentrated. The residue was acetylated with Ac_2O (2 mL) and pyridine (4 mL) overnight at 45°C. Methanol (2 mL) was added to the mixture, and it was concentrated then extracted with CH_2Cl_2. The extract was washed with 2 M HCl and M Na_2CO_3, dried (Na_2SO_4), and concentrated. Column chromatography (25 : 1 CH_2Cl_2–MeOH) of the residue on silica gel (30 g) gave **5** (190 mg, 85%) as an amorphous mass; $[\alpha]_D$-1.2° (*c* 0.9, $CHCl_3$); ν 3300 (NH), 1740 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), 860 and 840 (TMS), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2$), 1.85–2.23 (15 s, 45 H, 2 AcN and 13 AcO), 2.51 (dd, 1 H, $J_{3ax,3eq}$ 12.6, $J_{3eq,4}$ 4.2 Hz, H-3d*eq*), 2.90 (dd, 1 H, $J_{3ax,3eq}$ 14.0 $J_{3eq,4}$ 4.3 Hz, H-3c*eq*), 3.85 (s, 3 H, MeO), 4.85 (dd, 1 H, $J_{1,2}$ 8.1, $J_{2,3}$ 9.4 Hz, H-2a), 4.91 (m, 1 H, H-4c), 5.60 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4e), 5.68 (m, 1 H, H-4d), 6.01 (dd, 1 H, $J_{2,3}$ 11.5, $J_{3,4}$ 2.9 Hz, H-3e), and 7.43–8.12 (m, 9 H, 2 Ph). Anal. Calcd for $C_{87}H_{111}N_3O_{46}Si$ (1962.9): C, 53.24; H, 5.70; N, 2.14. Found: C, 53.11; H, 5.43; N, 1.98.

O-*[Methyl 5-acetamido-8-*O-*(5-acetamido-4,7,8,9-tetra-*O-*acetyl-3,5-dideoxy-*D-glycero-*α*-D-galacto-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O-*acetyl-3,5-dideoxy-*D-glycero-*α*-D-galacto-2-nonulopyranosylonate]-(2 → 3)-*O-*[(3,4-di-*O-*acetyl-6-*O-*benzoyl-2-deoxy-2-phthalimido-β-*D-*galactopyranosyl)-(1 → 4)]-*O-*(2,6-di-*O-*acetyl-β-*D-*galactopyranosyl)-(1 → 4)-2,3,6-tri-*O-*acetyl-*D-*glucopyranose* (**6**).—A solution of **5** (190 mg, 0.1 mmol) in CH_2Cl_2 (1.2 mL) and CF_3CO_2H (2.6 mL) was stirred for 2 h at room temperature; the progress of the reaction was monitored by TLC. Ethyl acetate (2.5 mL) was added, and the mixture was concentrated to a syrup which was chromatographed on a column of silica gel (10 g) with 60 : 1 CH_2Cl_2–MeOH to give **6** (170 mg, 94%) as an amorphous mass; ν 3600–3100 (OH, NH), 1730 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), and 710 cm^{-1} (Ph). Anal. Calcd for $C_{82}H_{99}N_3O_{46}$ (1862.7): C, 52.88; H, 5.36; N, 2.26. Found: C, 52.67; H, 5.14; N, 2.06.

O-[*Methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate]-(2 → 3)-*O*-[(2,4-di-*O*-acetyl-6-*O*-benzoyl-2-deoxy-2-phthalimido-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* (**7**).—To a solution of **6** (170 mg, 0.09 mmol) in CH_2Cl_2 (2.2 mL) and trichloroacetonitrile (0.5 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (25 μL, 0.1 mmol), and the mixture was stirred for 2 h at 0°C. Column chromatography (30:1 CH_2Cl_2–MeOH) of the mixture on silica gel (10 g) gave **7** (160 mg, 76%) as an amorphous mass; $[\alpha]_D$ + 14.0° (*c* 1.0, $CHCl_3$); ν 3300 (NH), 1730 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.85–2.20 (15 s, 45 H, 2 AcN and 13 AcO), 2.51 (dd, 1 H, $J_{3ax,3eq}$ 13.5, $J_{3eq,4}$ 6.0 Hz, H-3d*eq*), 2.93 (dd, 1 H, $J_{3ax,3eq}$ 14.3, $J_{3eq,4}$ 4.0 Hz, H-3c*eq*), 3.86 (s, 3 H, MeO), 4.92 (m, 1 H, H-4c), 5.05 (dd, 1 H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.9 Hz, H-2a), 5.17 (m, 1 H, H-8d), 5.61 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4e), 5.78 (m, 1 H, H-4d), 6.01 (dd, 1 H, $J_{2,3}$ 11.3, $J_{3,4}$ 3.1 Hz, H-3e), 6.49 (d, 1 H, $J_{1,2}$, 3.8 Hz, H-1a), 7.16–8.02 (m, 9 H, 2 Ph), and 8.66 (s, 1 H, C=NH). Anal. Calcd for $C_{84}H_{99}Cl_3N_4O_{46}$ (2007.1): C, 50.27; H, 4.97; N, 2.79. Found; C, 50.28; H, 4.91; N, 2.68.

O-*[Methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate]-(2 → 3)-*O*-[(3,4-di-*O*-acetyl-6-*O*-benzoyl-2-deoxy-2-phthalimido-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*,3R,4E)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol* (**9**).—To a solution of **7** (50 mg, 0.025 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[24b] (**8**; 25 mg, 0.05 mmol) in CH_2Cl_2 (0.3 mL) were added 4A molecular sieves (AW-300, 500 mg), and the mixture was stirred for 5 h at room temperature, then cooled to 0°C. Under continued stirring TMS triflate (10 μL, 0.05 mmol) was added, and the stirring was continued for 10 h at 0°C. The solids were filtered off and washed with CH_2Cl_2. The combined filtrate and washings was successively washed with M Na_2CO_3 and H_2O, dried (Na_2SO_4), and concentrated. Column chromatography (30:1 CH_2Cl_2–MeOH) of the residue on silica gel (5 g) gave **9** (25 mg, 44%) as an amorphous mass; $[\alpha]_D$-5.8° (*c* 1.1, $CHCl_3$); ν 3300 (NH), 2940 and 2850 (Me), 2100 (N_3), 1740 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.87 (t, 3 H, J_{Me,CH_2} 7.0 Hz, *Me*CH_2), 1.24 (s, 22 H, 11 CH_2), 1.85–2.23 (15 s, 45 H, 2 AcN and 13 AcO), 2.51 (m, 1 H, H-3d*eq*), 2.87 (m, 1 H, H-3c*eq*), 3.84 (s, 3 H, MeO), 5.92 (dt, 1 H, $J_{4,5}$ 14.1, $J_{5,6} = J_{5,6'}$ = 6.4 Hz, H-5 of sphingosine), 6.00 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 2.7 Hz, H-3e), and 7.28–8.05 (m, 14 H, 3 Ph). Anal. Calcd for $C_{107}H_{136}N_6O_{48}$ (2274.3): C, 56.51; H, 6.03; N, 3.70. Found: C, 56.37; H, 5.91; N, 3.41.

O-[*Methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylono-1',9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate]-(2 → 3)-*O*-[(3,4-di-*O*-acetyl-6-*O*-

benzoyl-2-deoxy-2-phthalimido-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)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (**10**).—Hydrogen sulfide gas was bubbled through a solution of **9** (53 mg, 0.023 mmol) in aq 83% pyridine (3.6 mL) for 3 days while the solution was stirred at 0°C. The mixture was concentrated to a syrup, which was used without purification. A solution of the residue in dry CH_2Cl_2 (1.5 mL) was treated with octadecanoic acid (20 mg, 0.07 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC; 15 mg, 0.07 mmol), and the mixture was stirred for 12 h at room temperature. 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 (5 g) gave **10** (50 mg, 85%) as an amorphous mass; $[\alpha]_D$ + 1.2° (*c* 1.0, $CHCl_3$); ν 3300 (NH), 1730 and 1220 (ester), 1700 (imide), 1650 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6 H, J_{Me,CH_2} 6.8 Hz, 2 *Me*CH_2), 1.25 (s, 52 H, 26 CH_2), 2.50 (dd, 1 H, $J_{3ax,3eq}$ 13.3, $J_{3eq,4}$ 5.3 Hz, H-3d*eq*), 2.89 (dd, 1 H, $J_{3ax,3eq}$ 13.2, $J_{3eq,4}$ 4.5 Hz, H-3c*eq*), 3.85 (s, 3 H, MeO), 5.86 (m, 1 H, H-5 of ceramide), 6.01 (dd, 1 H, $J_{2,3}$ 10.7, $J_{3,4}$ 3.5 Hz, H-3e), and 7.40–8.01 (m, 14 H, 3 Ph). Anal. Calcd for $C_{125}H_{172}N_4O_{49}$ (2514.7): C, 59.70; H, 6.89; N, 2.23. Found: C, 59.41; H, 6.63; N, 2.06.

Ganglioside GD2 (**11**).—To a solution of **10** (50 mg, 0.02 mmol) in MeOH (1 mL) was added sodium NaOMe, and the mixture was stirred for 12 h at room temperature. Potassium hydroxide (0.2 M) was added and the mixture was stirred an additional 6 h at room temperature, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 $CHCl_3$–MeOH. The filtrate and washings were combined and concentrated, then to a solution of the residue in *n*-BuOH (0.3 mL) was added ethylenediamine (80 μL), and the mixture was stirred for 1 h at 70°C. Acetic anhydride (25 μL) and MeOH (0.5 mL) were added to the mixture at 0°C, and the solution was stirred for 3 h at room temperature and concentrated. Column chromatography (5:5:1 $CHCl_3$–MeOH–H_2O) of the residue on Sephadex LH-20 gave GD2 (**11**; 24 mg, 72%) as an amorphous mass; $[\alpha]_D$-7.1° (*c* 0.3, 5:5:1 $CHCl_3$–MeOH–H_2O); ^1H NMR (Me_2SO-d_6): δ 0.94 (t, 6 H, J_{Me,CH_2} 6.6 Hz, 2 *Me*CH_2), 1.32 (s, 52 H, 26 CH_2), 1.87–1.96 (3 s, 9 H, 3 AcN), 2.26 (t, 2 H, COC$H_2$$CH_2$), and 5.41 (m, 1 H, H-5 of ceramide). Anal. Calcd. for $C_{78}H_{138}N_4O_{34}$ (1676.0): C, 55.90; H, 8.30; N, 3.34. Found: C, 55.89; H, 8.09; N, 3.24.

ACKNOWLEDGMENT

This work was supported in part by Grants-in-Aid (no. 04250102 and no. 03660132) for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture of Japan.

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