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Note

Synthesis of *N*-acetyl-4,8-dideoxyneuraminic acid-containing ganglioside GM_3 [1]

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Ganglioside GM_3, as well as other gangliosides, offers a variety of modifications in its sialic acid and ceramide moieties GM_3 exhibits various types of important biological activities such as an influenza A virus receptor [2,3], an inducer [4] of monocytic differentiation of human myeloid, an enhancer or inhibitor of protein kinase activity [5], an immunosuppressant [6,7], and a substrate for *Trypanosoma cruzi trans*-sialidase [8]. In view of these facts, it is of interest to clarify the functions of GM_3 at the molecular level. Previously [9], we have synthesized GM_3, analogues containing a variety of lipophilic parts in place of ceramide, as well as analogues with modified sialic acids, in order to elucidate the role of the ceramide and sialic acid parts in the function of GM_3. In continuing to investigate the structure–activity relationships of gangliosides, we describe herein the synthesis of *N*-acetyl-4,8-dideoxyneuraminic acid-containing GM_3.

Treatment of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-9-*O*-*tert*-butyldimethylsilyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosid]onate (**1**) [10]

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[1] Synthetic studies on Sialoglycoconjugates, Part 77. For Part 76, see ref. [1].

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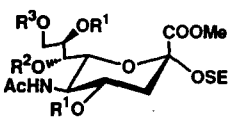
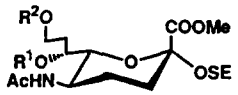
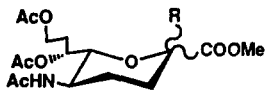


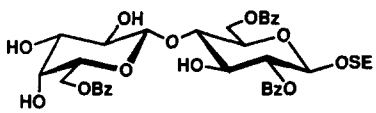
1 $R^1 = R^2 = H$, $R^3 = TBDMS$
2 $R^1 = C(S)OPh$, $R^2 = H$, $R^3 = TBDMS$



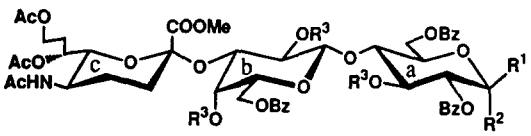
3 $R^1 = H$, $R^2 = TBDMS$
4 $R^1 = R^2 = Ac$



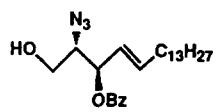
5 R = OAc (β)
6 R = SPh



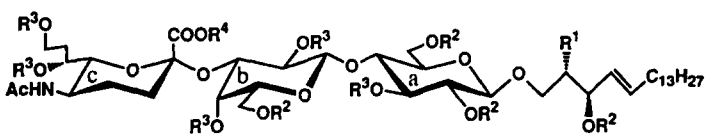
7



8 $R^1 = OSE$, $R^2 = R^3 = H$
9 $R^1 = OSE$, $R^2 = H$, $R^3 = Ac$
10 R^1, $R^2 = H$, OH, $R^3 = Ac$
11 $R^1 = H$, $R^2 = OC(=NH)CCl_3$, $R^3 = Ac$



12



13 $R^1 = N_3$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
14 $R^1 = NHCOC_{17}H_{35}$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
15 $R^1 = NHCOC_{17}H_{35}$, $R^2 = R^3 = R^4 = H$

with phenyl chlorothionoformate [11] in pyridine–dichloromethane gave the 4,8-di-*O*-(phenoxy)thiocarbonyl derivative (**2**) in 85% yield. The latter compound was reduced with tributyltin hydride in the presence of α,α'-azobis-isobutyronitrile (AIBN) to give the 4,8-dideoxy compound (**3**) in 68% yield. Hydrolysis of the *tert*-butyldimethylsilyl

group in **3** with 80% aq acetic acid and subsequent *O*-acetylation gave **4**. Compound **4** on treatment [12] with trifluoroacetic acid in dichloromethane for 2 h at room temperature and subsequent *O*-acetylation afforded methyl 5-acetamido-2,7,9-tri-*O*-acetyl-3,4,5,8-tetradeoxy-D-*lyxo*-2-nonulopyranosylonate (**5**) in 66% yield. The replacement [13] of the anomeric acetoxy group in **5** with a phenylthio group by stirring for 17 h at room temperature with thiophenol in dichloromethane in the presence of boron trifluoride etherate gave the phenyl 2-thioglycoside (**6**) of 4,8-dideoxy-Neu5Ac in 89% yield as an anomeric mixture with $\alpha:\beta = 1:2$. The glycosylation of 2-(trimethylsilyl)ethyl 6-*O*-benzoyl-β-D-galactopyranosyl-(1 → 4)-2,6-di-*O*-benzoyl-β-D-glucopyranoside (**7**) 9a,[14] with **6** in acetonitrile for 10 h at −40 °C in the presence of *N*-iodosuccinimide (NIS)–trifluoromethanesulfonic acid (TfOH) gave exclusively the α-glycoside **8** in 42% yield. Acetylation of **8** with acetic anhydride in pyridine gave **9**. The observed chemical shift and coupling constant for H-7c (δ 5.07, $J_{6,7}$ 2.3 Hz) are characteristic of α-glycosidically linked [9g] sialic acid analogues, and the values for H-2b (δ 5.17, $J_{1,2}$ 8.2, $J_{2,3}$ 10.1 Hz), H-3b (δ 4.63, $J_{3,4}$ 3.5 Hz), and H-4b (δ 5.24) indicate the position of glycosylation to be C-3b. Other ^{1}H NMR data are given in the Experimental section and are consistent with the structure assigned.

Selective removal of the 2-(trimethylsilyl)ethyl group of **9** was achieved by treatment with trifluoroacetic acid in dichloromethane for 1 h at room temperature to give the 1-hydroxy derivative **10**. Treatment [9,15] of **10** with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 2 h at 0 °C gave the trichloroacetimidate **11** as the α anomer in 86% yield.

The glycosylation [9,16] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**12**) [17,18] with **11** in dichloromethane for 2 h at 0 °C in the presence of boron trifluoride etherate and 4A molecular sieves gave only the β glycoside **13** in 62% yield. Selective reduction [9,19] of the azido group in **13** with hydrogen sulfide in 83% aq pyridine and subsequent condensation with octadecanoic acid using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane furnished the acylated GM_3 analogue **14**. *O*-Deacylation of **14** with sodium methoxide in methanol, with subsequent saponification of the sialate methyl ester group, yielded the desired product **15** in good yield.

1. 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.

*Methyl [2-(trimethylsilyl)ethyl 5-acetamido-9-*O*-tert-butyldimethylsilyl-3,5-dideoxy-4,8-di-*O*-(phenoxy)thiocarbonyl-*D*-glycero-α-*D*-galacto-2-nonulopyranosid]onate* (**2**).—To a solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-9-*O*-*tert*-butyldimethylsilyl-D-*glycero*-α-D-*galacto*-2-nonulopyranosid]onate (**1**, 5.8 g, 10.8 mmol) [10] in pyridine (180 mL) and CH_2Cl_2 (80 mL) was added, with stirring, phenyl chlorothionoformate

(11.5 mL) at 0 °C, and the mixture was stirred for 2 h at room temperature. Methanol (2 mL) was added to the mixture, and it was concentrated and extracted with CH_2Cl_2. The extract was successively washed with M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 EtOAc–hexane) of the residue on silica gel (200 g) gave **2** (7.5 g, 85%) as an amorphous mass: $[\alpha]_D$ −46.0° (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.94 (m, 2 H, $Me_3SiCH_2CH_2$), 0.95 (s, 9 H, Me_3Si), 2.05 (s, 3 H, AcN), 2.15 (t, 1 H, $J_{gem} = J_{3ax,4} = 12.5$ Hz, H-3*ax*), 2.95 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3*eq*), 3.36 (m, 1 H, Me_3SiCH_2CH), 3.88 (s, 3 H, MeO), 3.89 (dd, 1 H, $J_{5,6}$ 10.5, $J_{6,7}$ 1.5 Hz, H-6), 4.04 (m, 1 H, Me_3SiCH_2CH), 4.16 and 4.18 (m, 2 H, H-9), 4.37 (q, 1 H, $J_{4,5} = J_{5,NH} = 10.4$ Hz, H-5), 4.66 (m, 1 H, H-7), 5.59 (m, 1 H, H-8), 5.66 (ddd, 1 H, H-4), 6.14 (d, 1 H, NH), and 7.08–7.49 (m, 10 H, 2 Ph). Anal. Calcd for $C_{37}H_{55}NO_{11}S_2Si_2$ (810.2): C, 54.86; H, 6.84; N, 1.73. Found: C, 54.72; H, 6.81; N, 1.69.

*Methyl [2-(trimethylsilyl)ethyl 5-acetamido-9-*O*-tert-butyldimethylsilyl-3,4,5,8-tetradeoxy-α-*D*-lyxo-2-nonulopyranosid]onate* (**3**).—To a solution of **2** (7.4 g, 9.1 mmol) in toluene (300 mL) were added tributyltin hydride (25 mL) and α,α′-azobis-isobutyronitrile (AIBN, 1.3 g), and the mixture was stirred for 1 h at 100 °C then concentrated. Column chromatography (1:1 EtOAc–hexane) of the residue on silica gel (200 g) gave **3** (3.2 g, 68%) as an amorphous mass: $[\alpha]_D$ −5.7° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.90 (s, 9 H, Me_3Si), 0.91 (m, 2 H, $Me_3SiCH_2CH_2$), 1.60–2.10 (m, 5 H, H-3*ax*, H-4, H-8), 1.99 (s, 3 H, AcN), 2.37 (br dt, 1 H, J_{gem} 13.4, $J_{3eq,4ax} = J_{3eq,4eq} = 3.5$ Hz, H-3*eq*), 3.35 (dd, 1 H, $J_{5,6}$ 10.2, $J_{6,7}$ 1.9 Hz, H-6), 3.40 and 3.93 (m, 2 H, $Me_3SiCH_2CH_2$), 3.79 (s, 3 H, MeO), 3.81 and 3.83 (m, 2 H, H-9), 3.87 (m, 1 H, H-5), 4.06 (m, 1 H, H-7), and 5.60 (d, 1 H, $J_{5,NH}$ 8.2 Hz, NH). Anal. Calcd for $C_{23}H_{47}NO_7Si_2$ (505.8): C, 54.62; H, 9.37; N, 2.77. Found: C, 54.57; H, 9.35; N, 2.66.

*Methyl [2-(trimethylsilyl)ethyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-α-*D*-lyxo-2-nonulopyranosid]onate* (**4**).—A solution of **3** (2.0 g, 4.0 mmol) in 80% aq AcOH (40 mL) was heated for 10 h at 40 °C then concentrated. To a solution of the residue in pyridine (20 mL) was added Ac_2O (15 mL), and the mixture was stirred for 10 h at room temperature, then concentrated. Column chromatography (1:1 EtOAc–hexane) of the residue on silica gel (80 g) gave **4** (1.4 g, 74%) as an amorphous mass: $[\alpha]_D$ +9.5° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.89 (m, 2 H, $Me_3SiCH_2CH_2$), 1.32 (m, 1 H, H-4*ax*), 1.79 (ddd, 1 H, $J_{gem} = J_{3ax,4ax} = 13.7$, $J_{3ax,4eq}$ 4.0 Hz, H-3*ax*), 1.90 (s, 3 H, AcN), 1.99–2.22 (m, 3 H, H-4*eq*, H-8), 2.04, 2.07 (2 s, 6 H, 2 AcO), 2.22 (m, 1 H, H-3*eq*), 3.40 and 3.95 (m, 2 H, $Me_3SiCH_2CH_2$), 3.78 (s, 3 H, MeO), 3.81 (m, 1 H, H-6), 3.90 (m, 1 H, H-5), 4.14 and 4.22 (m, 2 H, H-9), 5.09 (m, 1 H, H-7), and 5.64 (d, 1 H, $J_{5,NH}$ 9.2 Hz, NH). Anal. Calcd for $C_{21}H_{37}NO_9Si$ (475.6): C, 53.03; H, 7.84; N, 2.95. Found: C, 53.00; H, 7.76; N, 2.91.

*Methyl 5-acetamido-2,7,9-tri-*O*-acetyl-3,4,5,8-tetradeoxy-β-*D*-lyxo-2-nonulopyranosonate* (**5**).—To a solution of **4** (2.1 g, 4.4 mmol) in CH_2Cl_2 (36 mL) was added trifluoroacetic acid (18 mL) at 0 °C, and the mixture was stirred for 2 h at room temperature then concentrated. To a solution of the residue in pyridine (20 mL) was added Ac_2O (15 mL), and the mixture was stirred for 15 h at room temperature and concentrated, then extracted with CH_2Cl_2. The extract was successively washed with M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (5:4

EtOAc–hexane) of the residue on silica gel (100 g) gave **5** (1.2 g, 66%) as an amorphous mass: $[\alpha]_D$ −27.0° (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.86–2.22 (m, 6 H, H-3, H-4, H-8), 1.94 (s, 3 H, AcN), 2.05, 2.10, 2.14 (3 s, 9 H, 3 AcO), 3.79 (s, 3 H, MeO), 3.82 (dd, 1 H, $J_{5,6}$ 9.2, $J_{6,7}$ 2.2 Hz, H-6), 3.98–4.14 (m, 3 H, H-5, H-9), 5.16 (m, 1 H, $J_{7,8} = J_{7,8'} = 7.7$ Hz, H-7), 5.80 (d, 1 H, $J_{5,NH}$ 9.2 Hz, NH). Anal. Calcd for $C_{18}H_{27}NO_{10}$ (417.4): C, 51.79; H, 6.52; N, 3.36. Found: C, 51.55; H, 6.58; N, 3.25.

*Methyl (phenyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-2-thio-*D*-lyxo-2-nonulopyranosid)onate* (**6**).—To a solution of **5** (800 mg, 1.9 mmol) in CH_2Cl_2 (8.5 mL) were added thiophenol (0.2 mL) and $BF_3 \cdot OEt_2$ (1.2 mL) at 0 °C, and the mixture was stirred for 17 h at room temperature. Dichloromethane (100 mL) was added, and the mixture was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (3:2 EtOAc–hexane) of the residue on silica gel (60 g) gave **6** (800 mg, 89%) as an amorphous mass: $[\alpha]_D$ +230.6° (*c* 1.3, $CHCl_3$); ν 3300 (NH), 1730 and 1250 (ester), 1660 and 1550 (amide), and 750 and 690 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 1.79–2.18 (m, 5 H, H-3*ax*-α, H-3*ax*-β, H-4α, H-4β, H-8α, H-8β), 1.89, 1.96, 2.03, 2.04, 2.07, 2.12 (6 s, 9 H, 2 Ac, AcN), 2.37 (dt, 1 H, H-3*eq*-β), 2.56 (dt, 1 H, H-3*eq*-α), 3.70 (s, 3 H, MeO-β), 3.79 (s, 3 H, MeO-α), 3.93–4.20 (m, 3 H, H-5α, H-5β, H-9α, H-9β), 5.07 (dt, 1 H, H-7α), 5.20 (m, 1 H, H-7β), 5.57 (d, 1 H, NH-α), 5.87 (d, 1 H, NH-β), and 7.28–7.56 (m, 5 H, Ph); the anomeric ratio (α:β) was estimated as ~1:2 from the ratio of intensities of the $CH_3C(=O)O$–signals. Anal. Calcd for $C_{22}H_{29}NO_8S$ (467.5): C, 56.52; H, 6.25; N, 3.00. Found: C, 56.30; H, 6.13; N, 2.90.

*2-(Trimethylsilyl)ethyl (methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-α-*D*-lyxo-2-nonulopyranosylonate)-(2 → 3)-6-*O*-benzoyl-β-*D*-galactopyranosyl-(1 → 4)-2,6-di-*O*-benzoyl-β-*D*-glucopyranoside* (**8**).—To a solution of **6** (230 mg, 0.49 mmol) and 2-(trimethylsilyl)ethyl 6-*O*-benzoyl-β-D-galactopyranosyl-(1 → 4)-2,6-di-*O*-benzoyl-β-D-glucopyranoside [9a,14] (**7**; 217 mg, 0.29 mmol) in MeCN (4 mL) and CH_2Cl_2 (0.6 mL) was added 3 Å molecular sieves (3A-MS, 700 mg), and the mixture was stirred for 7 h at room temperature, then cooled to −40 °C. *N*-Iodosuccinimide (100 mg) and trifluoromethanesulfonic acid (10 μL) were added, and the mixture was stirred for 10 h at −40 °C. The solids were filtered off and washed thoroughly with CH_2Cl_2. 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 (3:1 EtOAc–hexane) of the residue on silica gel (50 g) gave **8** (134 mg, 42%) as an amorphous mass: $[\alpha]_D$ +7.2° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.03 (m, 2 H, $Me_3SiCH_2CH_2$), 1.35–2.22 (m, 5 H, H-3c-*ax*, H-4c, H-8c), 2.14, 2.20, 2.22 (3 s, 9 H, 2 AcO, AcN), 2.55 (m, 1 H, H-3c-*eq*), 3.48 (dd, 1 H, $J_{5,6}$ 10.1, $J_{6,7}$ 2.2 Hz, H-6c), 3.90 (s, 3 H, MeO), 4.54 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1b), 4.76 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1a), 5.06 (m, 1 H, H-7c), 5.38 (t, 1 H, $J_{2,3}$ 8.0 Hz, H-2a), 5.70 (d, 1 H, $J_{5,NH}$ 8.4 Hz, NH), and 7.30–8.21 (m, 15 H, 3 Ph). Anal. Calcd for $C_{54}H_{69}NO_{22}Si$ (1112.2): C, 58.32; H, 6.25; N, 1.26. Found: C, 58.05; H, 5.98; N, 1.15.

*2-(Trimethylsilyl)ethyl (methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-α-*D*-lyxo-2-nonulopyranosylonate)-(2 → 3)-2,4-di-*O*-acetyl-6-*O*-benzoyl-β-*D*-galactopyranosyl-(1 → 4)-3-*O*-acetyl-2,6-di-*O*-benzoyl-β-*D*-glucopyranoside* (**9**).—Acetylation of **8** (180 mg, 0.16 mmol) with Ac_2O (3 mL) in pyridine (4 mL) for 15 h at room

temperature and a usual work-up gave **9** (176 mg, 88%) as an amorphous mass: $[\alpha]_D$ +12.5° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.98 (m, 2 H, $Me_3SiCH_2CH_2$), 1.47 (m, 1 H, H-4c-*ax*), 1.69 (m, 1 H, H-3c-*ax*), 1.99–2.39 (m, 4 H, H-3c-*eq*, H-4c-*eq*, H-8c), 1.99–2.30 (6 s, 18 H, 5 AcO, AcN), 3.48 (br dd, 1 H, $J_{5,6}$ 10.4, $J_{6,7}$ 2.3 Hz, H-6c), 3.85 (s, 3 H, MeO), 4.63 (dd, 1H, $J_{2,3}$ 10.1, $J_{3,4}$ 3.5 Hz, H-3b), 4.78 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1a), 4.82 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1b), 5.07 (m, 1 H, $J_{6,7}$ 2.3 Hz, H-7c), 5.17 (dd, 1 H, H-2b), 5.24 (br d, 1 H, H-4b), 5.33 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2a), 5.39 (d, 1 H, $J_{5,NH}$ 9.4 Hz, NH), 5.59 (t, 1 H, H-3a), and 7.43–8.17 (m, 15 H, 3 Ph). Anal. Calcd for $C_{60}H_{75}NO_{25}Si$ (1238.3): C, 58.20; H, 6.11; N, 1.13. Found: C, 58.09; H, 5.83; N, 0.98.

*Methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-*α*-*D*-*lyxo*-2-nonulopyranosylonate-(2 → 3)-2,4-di-*O*-acetyl-6-*O*-benzoyl-*β*-*D*-galactopyranosyl-(1 → 4)-3-*O*-acetyl-2,6-di-*O*-benzoyl-*D*-glucopyranose* (**10**).—A solution of **9** (100 mg, 0.08 mmol) in trifluoroacetic acid (1.2 mL) and CH_2Cl_2 (1.2 mL) was stirred for 1 h at room temperature and concentrated. Column chromatography (3:1 EtOAc–hexane) of the residue on silica gel (50 g) gave **10** (91 mg, quant) as an amorphous mass: $[\alpha]_D$ +40.0° (*c* 1.9, $CHCl_3$, after 10 h); ν 3400 (NH, OH), 1730 and 1240 (ester), 1650 and 1550 (amide), and 750 and 710 cm^{-1} (Ph). Anal. Calcd for $C_{55}H_{63}NO_{25}$ (1138.1): C, 58.05; H, 5.58; N, 1.23. Found: C, 57.94; H, 5.54; N, 1.01.

*Methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-*α*-*D*-*lyxo*-2-nonulopyranosylonate-(2 → 3)-2,4-di-*O*-acetyl-6-*O*-benzoyl-*β*-*D*-galactopyranosyl-(1 → 4)-3-*O*-acetyl-2,6-di-*O*-benzoyl-*α*-*D*-glucopyranosyl trichloroacetimidate* (**11**).—To a stirred solution of **10** (91 mg, 0.08 mmol) in CH_2Cl_2 (1.4 mL), cooled to 0 °C, were added trichloroacetonitrile (0.3 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 13 mg), and the mixture was stirred for 2 h at 0 °C, then directly applied to a column of silica gel (40 g) eluted with 30:1 CH_2Cl_2–MeOH. Concentration of the eluate gave **11** (89 mg, 86%) as an amorphous mass: $[\alpha]_D$ +41.5° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.23–2.29 (m, 5 H, H-3c-*eq*, H-4c, H-8c), 1.57 (m, 1 H, H-3c-*ax*) 1.87, 1.96, 1.99, 2.05, 2.14, 2.20 (6 s, 18 H, 5 AcO, AcN), 3.36 (dd, 1 H, $J_{5,6}$ 10.4, $J_{6,7}$ 1.5 Hz, H-6c), 3.73 (s, 3 H, MeO), 4.78 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1b), 5.09 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2b), 5.16 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4b), 5.28 (dd, 1 H, $J_{1,2}$ 3.9, $J_{2,3}$ 9.8 Hz, H-2a), 5.43 (d, 1 H, $J_{5,NH}$ 9.5 Hz, NH), 5.85 (t, 1 H, H-3a), 6.67 (d, 1 H, H-1a), 7.32–8.04 (m, 15 H, 3 Ph), and 8.58 (s, 1 H, C=NH). Anal. Calcd for $C_{57}H_{63}Cl_3N_2O_{25}$ (1282.5): C, 53.38; H, 4.95; N, 2.18. Found: C, 53.19; H, 5.08; N, 2.15.

*Methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-*α*-*D*-*lyxo*-2-nonulopyranosylonate-(2 → 3)-2,4-di-*O*-acetyl-6-*O*-benzoyl-*β*-*D*-galactopyranosyl-(1 → 4)-3-*O*-acetyl-2,6-di-*O*-benzoyl-*β*-*D*-glucopyranosyl)-(1 → 1)-(2S,3R,4E)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol* (**13**).—To a solution of **11** (89 mg, 0.07 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol [13] (**12**; 60 mg, 0.14 mmol) in CH_2Cl_2 (2.6 mL) was added 4A-MS (AW 300, 1.9 g), and the mixture was stirred for 2 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (56 μL) was added to the mixture, and this was stirred for 2 h at 0 °C. The precipitate was filtered off and washed with CH_2Cl_2. The filtrate and washings were combined, and the solution was washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (3:1 EtOAc–hexane) of the residue on silica gel (30 g) gave **13** (67 mg, 62%) as an amorphous mass: $[\alpha]_D$ −4.6° (*c* 1.3, $CHCl_3$); ν 3400 (NH), 2950 and 2850 (Me,

methylene), 2100 (azide), 1720 and 1250 (ester), 1660 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.80 (t, 3 H, *Me*CH_2), 1.18 (s, 22 H, 11 CH_2), 1.49 (m, 1 H, H-3c-*ax*), 1.80, 1.88, 1.92, 1.93, 2.05, 2.10 (6 s, 18 H, 5 AcO, AcN), 3.28 (dd, 1 H, $J_{5,6}$ 10.3, $J_{6,7}$ 2.0 Hz, H-6c), 3.65 (s, 3 H, MeO), 4.44 (d, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 3.5 Hz, H-3b), 4.61 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1a), 4.64 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1b), 4.97 (dd, 1 H, H-2b), 5.05 (d, H-4b), 5.17 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2a), 5.40 (t, 1 H, H-3a), 5.42 (m, 1 H, H-4 of sphingosine), 5.61 (dt, 1 H, H-5 of sphingosine), and 7.22–8.03 (m, 20 H, 4 Ph). Anal. Calcd for $C_{80}H_{100}N_4O_{27}$ (1549.7): C, 62.01; H, 6.50; N, 3.62. Found: C, 61.96; H, 6.33; N, 3.49.

*Methyl 5-acetamido-7,9-di-*O*-acetyl-3,4,5,8-tetradeoxy-*α*-*D*-lyxo-2-nonulopyranosylonate-(2 → 3)-2,4-di-*O*-acetyl-6-*O*-benzoyl-*β*-*D*-galactopyranosyl-(1 → 4)-3-*O*-acetyl-2,6-di-*O*-benzoyl-*β*-*D*-glucopyranosyl-(1 → 1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol* (**14**).—Hydrogen sulfide was bubbled through a solution of **13** (67 mg, 0.04 mmol) in 83% aq pyridine (6 mL) for 72 h while the solution was stirred at 0 °C. The course of the reaction was monitored by TLC. The mixture was concentrated to a syrup, which was dissolved in CH_2Cl_2 (4 mL). Octadecanoic acid (40 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC, 40 mg) were added to the solution, and the mixture was stirred for 11 h at room temperature. Dichloromethane (30 mL) was added, and the solution was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (4:1 EtOAc–hexane) of the residue on silica gel (50 g) gave **14** (45 mg, 58%) as an amorphous mass: $[\alpha]_D$ +14.0° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6 H, 2 *Me*CH_2), 1.26 (s, 52 H, 26 CH_2), 1.88–2.17 (6 s, 18 H, 5 AcO, AcN), 3.36 (dd, 1 H, $J_{5,6}$ 10.4, $J_{6,7}$ 2.4 Hz, H-6c), 3.73 (s, 3 H, MeO), 4.49 (t, 1 H, $J_{2,3}$ 10.1, $J_{3,4}$ 3.3 Hz, H-3b), 4.60 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1a), 4.66 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1b), 5.38 (m, 1 H, H-7c), 5.76 (dt, 1 H, H-5 of sphingosine), and 7.26–8.10 (m, 20 H, 4 Ph). Anal. Calcd for $C_{98}H_{136}N_2O_{28}$ (1790.2): C, 65.75; H, 7.66; N, 1.56. Found: C, 65.52; H, 7.56; N, 1.52.

*5-Acetamido-3,4,5,8-tetradeoxy-*α*-*D*-lyxo-2-nonulopyranosylonic acid-(2 → 3)-*β*-*D*-galactopyranosyl-(1 → 4)-*β*-*D*-glucopyranosyl-(1 → 1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol* (**15**).—To a solution of **14** (45 mg, 0.03 mmol) in MeOH (3 mL) was added NaOMe (20 mg), and the mixture was stirred for 19 h at 40 °C. The course of the reaction was monitored by TLC (4:2:1 BuOH–EtOH–H_2O). Water (1 mL) was added to the mixture, and this was stirred for 24 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with 1:1 MeOH–H_2O, and the combined filtrate and washings was concentrated to a syrup that was chromatographed on a column of Sephadex LH-20 (40 g) with 1:1 $CHCl_3$–MeOH to give **15** (18 mg, 60%) as an amorphous mass: $[\alpha]_D$ −3.2° (*c* 0.6, 1:1 $CHCl_3$–MeOH); ^1H NMR ($CDCl_3$–CD_3OD): δ 0.89 (t, 6 H, 2 *Me*CH_2), 1.27 (s, 52 H, 26 CH_2), 1.67–2.21 (m, 5 H, H-3c-*ax*, H-4, H-8), 1.99 (s, 3 H, AcN), 2.45 (m, 1 H, H-3c-*eq*), 4.30 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1a), 4.42 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1b), 5.45 (dd, 1 H, $J_{3,4}$ 7.4, $J_{4,5}$ 15.4 Hz, H-4 of sphingosine), and 5.70 (dt, 1 H, $J_{5,6} = J_{5,6'} = 6.6$ Hz, H-5 of sphingosine). Anal. Calcd for $C_{57}H_{108}N_2O_{19}$ (1149.5): C, 61.65; H, 9.45; N, 2.44. Found: C, 61.57; H, 9.60; N, 2.28.

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