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A TOTAL SYNTHESIS OF HEMATOSIDE, α-NeuGc-(2→3)-β-Gal-(1→4)-β-Glc-(1→1)-Cer*†

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ABSTRACT

Methyl (5 - acetoxyacetamido - 4,7,8,9 - tetra - *O* - acetyl - 3,5 - dideoxy - D - *glycero*-β-D-*galacto*-2-nonulopyranosyl chloride)onate, prepared from *N*-glycolylneuraminic acid, was used for the glycosylation of benzyl *O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside to give benzyl *O*-[methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α- (**9**) and β-D-*galacto*-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**13**), and a regioisomer (**17**). Compounds **9** and **13** were converted into the corresponding glycotriaosyl glycosyl donors which, upon coupling with (2*S*,3*R*,4*E*)-3-*O*-*tert*-butyldiphenylsilyl-2-*N*-tetracosanoylsphingenine, afforded completely protected hematoside (**22**) and a stereoisomer **26**, respectively. Deprotection of **22** and **26** completed the first total synthesis of both hematoside and a stereoisomer, β-NeuGc-(2→3)-β-Gal-(1→4)-β-Glc-(1→1)-Cer.

INTRODUCTION

Sialosyl-lactosylceramide[2] (**1**, hematoside) has been isolated from equine, bovine, and canine erythrocytes, and the structure assigned on the basis of enzymic and chemical analysis. Recently, **1** and related *N*-glycolylneuraminyl-lactogangliosides have been identified as the antigens for human Hanganutziu-Deicher (H-D) heterophile antibodies[3] which are frequently detected in sera from patients with various cancers as well as in the Marek's disease lymphoma-derived chicken cell line[4].

As part of a project on the synthesis of glycosphingolipids, we now describe the first total synthesis of **1**. Based on retrosynthetic considerations (see **1**–**5**), a ceramide derivative **3**, the *N*-glycolylneuraminic acid derivative **4**, and a known[5] hexabenzyl-lactose **5** were designed.

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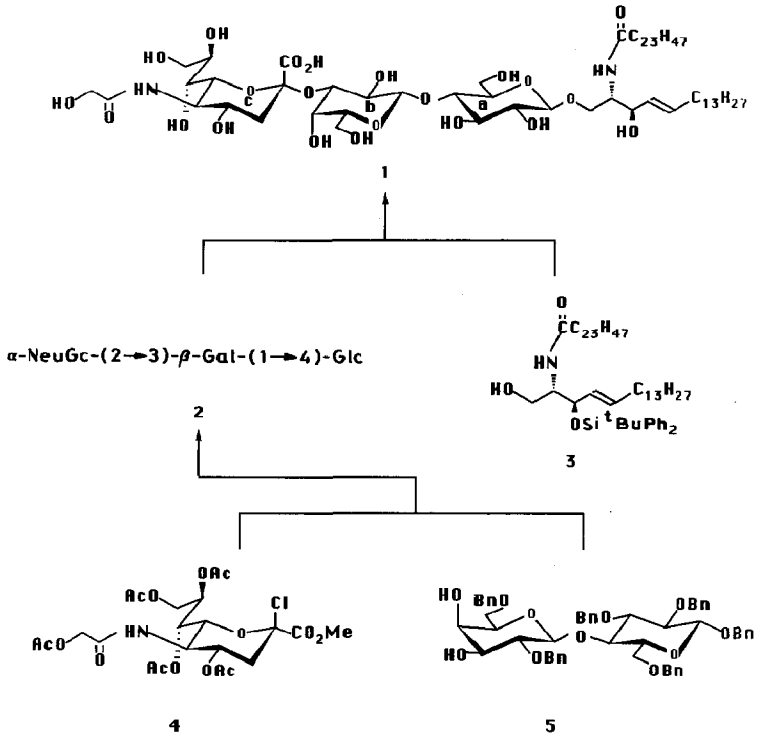
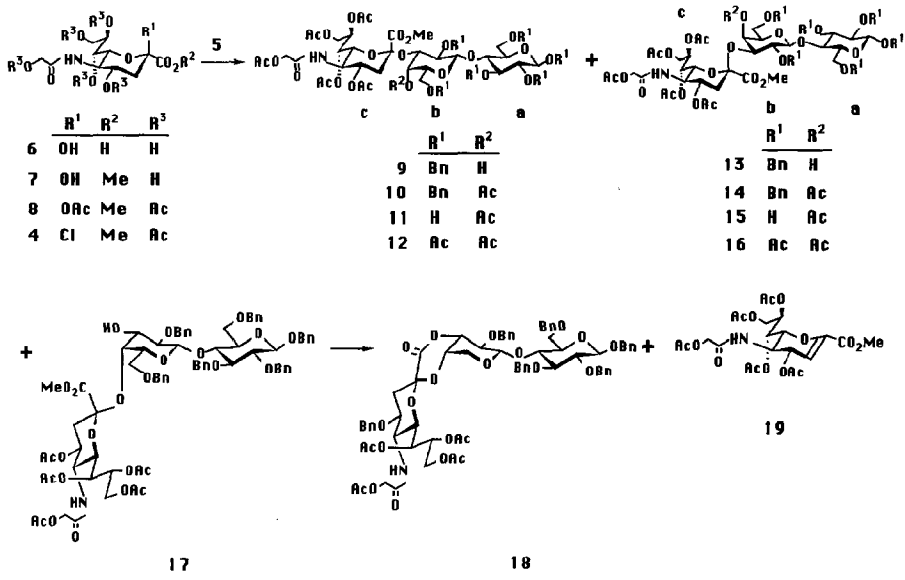
RESULTS AND DISCUSSION

The protected ceramide **3**, was prepared from synthetic (2*S*,3*R*,4*E*)-2-*N*-tetracosanoyl-1-*O*-tritylsphingenine[6] in 2 steps (*tert*-butylchlorodiphenylsilane and imidazole in *N*,*N*-dimethylformamide; toluene-*p*-sulfonic acid in methanol) in 83% overall yield.



N-Glycolylneuraminic acid (**6**) was converted into the chloride **4** in 3 steps (Dowex 50W-X8 in methanol at 20°; acetic anhydride in pyridine; hydrogen chloride in acetyl chloride). The β configuration at C-2 was assigned on the basis of ^{1}H-n.m.r. data; H-4 was deshielded and gave a signal at δ 5.469 (dt, *J* 4.9 and 11.0 Hz).

Mercuric cyanide–mercuric bromide-promoted glycosylation of the diol **5** with **4** in dichloroethane in the presence of powdered molecular sieves 4A proceeded as reported[7] for the glycosylation of **5** with the 5-acetamido analogue of **4**. Chromatography of the products afforded the trisaccharide derivatives **9**, **13**, and a 1:1 mixture of **17** and **18**, in yields of 7.3, 18.1, and 8.5%, respectively, as well as 60% of the 2,3-alkene **19**. The structures of the glycosylation products were determined as follows. Acetylation of **9** and **13** gave the hexa-acetates **10** and **14**, respectively, for which the ^{1}H-n.m.r. data showed that H-4b in **10** and **14** were deshielded and gave

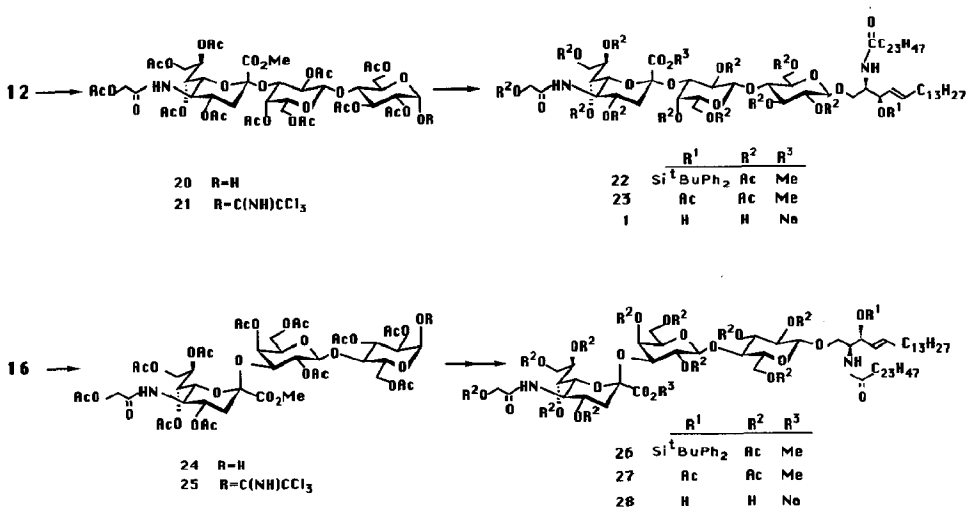


signals at δ 5.049 and 5.378, respectively, thus showing that, in **9** and **13**, the new glycosidic linkage had been introduced at C-3b of the lactose residue. The configurations at C-2c for **9** and **13** were assigned as α and β, respectively, according to the ^{1}H-n.m.r. data. The signal for H-4c in **9** appeared at δ 4.920, whereas that in **13** appeared at δ 5.333, and the respective $J_{7c,8c}$ values of 8.0 and 2.4 Hz accorded with previous observations[8].

Another trisaccharide-containing fraction was found to be a 1:1 mixture of **17** and **18**, which, on storage at room temperature, was gradually converted into the lactone **18**. The configuration at C-2c in **17** was deduced from the ^{1}H-n.m.r. data for **18**, which showed that H-4c was deshielded (δ 5.272) and that the signal for H-7c with $J_{7,8}$ 1.9 Hz was characteristic[8] for acetylated β-D-sialic acids. Lactonisation of **17** to give **18** was deduced from the disappearance of a methyl signal and the appearance of a characteristic triplet[9] for H-3c*e* at δ 2.516. A similar facile lactonisation had been reported[9] for benzyl *O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-β-D-*galacto*-2-nonulopyranosyl)onate]-(2→4)-2,6-di-*O*-benzyl-β-D-galactopyranoside.

The transformation of **9** and **13** into such glycosyl donors as **2** was investigated next. The hexa-acetate **10** was hydrogenolysed to give the hexaol **11** which, in turn, was acetylated to give the peracetate **12** as a 1:1 $\alpha\beta$-mixture in 95% overall yield.

Regioselective deacetylation[10] of **12** with hydrazinium acetate in *N*,*N*-dimethylformamide afforded 97% of the hemiacetal **20**, which was treated with trichloroacetonitrile[11] in the presence of 1,8-diazabicylo[5.4.0]undec-7-ene to give 92% of the α-imidate **21**, a synthetic equivalent of **2**. Following essentially the same reaction sequence, **14** was converted into the glycosyl donor **25** in 4 steps in 43%



overall yield.

Boron trifluoride etherate-catalysed coupling[11] of the ceramide derivative **3** and the glycosyl donor **21** was performed in the presence of powdered molecular sieves AW-300 in 1,2-dichloroethane to give 52% of the hematoside derivative **22**. In a similar manner, the glycosyl donor **25** was transformed into 58% of the protected glycolipid **26**. Both **22** and **26** were deprotected *via* **23** and **27** to give, respectively, hematoside (**1**) and the stereoisomer **28** in good yields. The ^{1}H-n.m.r. data for **1** and **28** proved the configuration at C-1a to be β-D for each compound since the signals for H-1a and H-1b of **1** at δ 4.159 and 4.200 were doublets with J 7.8 Hz, and those for H-1a and H-1b of **28** at δ 4.176 and 4.193 were doublets with $J \sim 7$ Hz.

EXPERIMENTAL

General. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter, for solutions in $CHCl_3$ at 25°, unless noted otherwise. Column chromatography was performed on Silica Gel (Merck 70–230 mesh). Flash chromatography was performed on columns of Wako gel C-300 (200–300 mesh) T.l.c. and high-performance (h.p.) t.l.c. was performed on Silica Gel 60 F_{254} (Merck). Molecular sieves were purchased from Nakarai Chemicals. I.r. spectra were recorded with an EPI-G2 Hitachi spectrophotometer, using KBr pellets for the crystalline samples, and films for the liquid samples. N.m.r. spectra were recorded with either a JEOL GX400 [^{1}H (400 MHz)] or FX90Q [^{13}C (22.50 MHz)] spectrometer. The values of δ_C and δ_H are expressed in p.p.m. downward from the signal for internal Me_4Si, for solutions in $CDCl_3$, unless noted otherwise. Values of δ_H (D_2O) and δ_C (D_2O) are expressed in p.p.m. downward from the signal for Me_4Si, by reference to internal Me_2CO (2.225) or Me_3COH (1.230),

and 1,4-dioxane (67.4) or MeOH (49.8), respectively.

(2S,3R,4E)-3-O-tert-Butyldiphenylsilyl-2-N-tetracosanoylsphingenine (**3**). — A mixture of *(2S,3R,4E)*-2-*N*-tetracosanoyl-1-*O*-tritylsphingenine[6] (800 mg, 0.9 mmol), ^{t}BuPh$_2$SiCl (370 mg, 1.4 mmol), and imidazole (183 mg, 2.7 mmol) in *N,N*-dimethylformamide (15 mL) was stirred for 16 h at 20°, then diluted with Et_2O, washed with H_2O and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (10:1 hexane–EtOAc containing 1% of Et_3N) of the residue gave *(2S,3R,4E)*-3-*O*-*tert*-butyldiphenylsilyl-2-*N*-tetracosanoyl-1-*O*-tritylsphingenine (1.01 g), $[\alpha]_D$ −8° (*c* 1.6, ethyl acetate), R_F 0.57 (5:1 hexane–EtOAc). ^{1}H-N.m.r. data: δ 5.18–5.10 (m, 3 H, H-4,5 and NH), 4.386 (t, 1 H, *J* 4.8 Hz, H-3), 4.270 (td, 1 H, *J* 9.1 and 4.4 Hz, H-2), 3.298 (dd, 1 H, *J* 9.2 and 5.8 Hz, H-1), 3.146 (dd, 1 H, *J* 9.2 and 5.3 Hz, H-1), 1.884 (t, 2 H, *J* 7.2 Hz, H-2′), 1.749 (td, 2 H, *J* 6.3 and 4.7 Hz, H-6), 1.472 (bt, 2 H, *J* 6.1 Hz, H-3′), 0.949 (s, 9 H, 3 CMe), and 0.880 (t, 6 H, *J* 5.8 Hz, CH_2CH_3).

Anal. Calc. for $C_{77}H_{116}NO_3Si$: C, 81.7; H, 10.3; N, 1.2. Found: C, 81.7; H, 10.3; N, 1.2.

A mixture of the foregoing product (1.0 g, 883 μmol) and toluene-*p*-sulfonic acid (67 mg, 352 μmol) in 20:1 $Cl(CH_2)_2Cl$–MeOH (21 mL) was stirred for 1 h at 20°, then neutralised with aq. $NaHCO_3$, and extracted with $CHCl_3$. The organic layer was washed with H_2O and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (5:1 hexane–EtOAc) of the residue gave **3** (650 mg, 83%), $[\alpha]_D$ +14° (*c* 0.4, ethyl acetate), R_F 0.11 (5:1 hexane–EtOAc). N.m.r. data: ^{1}H, δ 7.7–7.3 (m, 10 H, aromatic), 5.942 (d, 1 H, *J* 7.6 Hz, CONH), 5.45–5.35 (m, 2 H, H-4,5), 4.335 (dd, 1 H, *J* 5.9 and 3.7 Hz, H-3), 3.887 (ddd, 1 H, *J* 11.1, 4.4, and 2.6 Hz, H-1), 3.831 (m, 1 H, H-2), 3.600 (ddd, 1 H, *J* 11.0, 7.2, and 2.9 Hz, H-1), 3.169 (dd, 1 H, *J* 9.0 and 3.0 Hz, HO-1), 1.962 (m, 2 H, H-2′), 1.869 (m, 2 H, H-6), 1.574 (m, 2 H, H-3′), 1.066 (s, 9 H, CMe), and 0.879 (t, 6 H, CH_2CH_3); ^{13}C, δ 173.5 (C=O), 76.0 (C-3), 62.6 (C-1), and 56.0 (C-2).

Anal. Calc. for $C_{58}H_{101}NO_3Si$: C, 78.4; H, 11.5; N, 1.6. Found: C, 78.7; H, 11.6; N, 1.6.

Methyl (3,5-dideoxy-5-hydroxyacetamido)-D-glycero-D-galacto-*2-nonulopyranosyl)onate* (**7**). — A mixture of **6** (1.12 g, 3.4 mmol) and Dowex 50W-X8 (H^+) resin (3.1 g) in MeOH (225 mL) was stirred for 24 h at 20°, then filtered through Celite, and concentrated *in vacuo* to give crude **7** (1.08 g, 92%), which was used directly for conversion into **8**. Crystallisation from MeOH gave material with m.p. 182–183° (dec.), $[\alpha]_D$ −30° (*c* 1, water), R_F 0.48 (2:1:1 PrOH–BuOH–0.1M HCl); ν_{max} 1745, 1645, and 1550 cm^{-1}. ^{1}H-N.m.r. data [99:1 $(CD_3)_2SO$–D_2O]: δ 7.813 (d, 1 H, *J* 8.8 Hz, NH), 4.034 (ddd, 1 H, *J* 11.7, 10.7, and 4.9 Hz, H-4), 3.911 (d, 1 H, *J* 16.1 Hz, $COCH_2OH$, 3.865 (d, 1 H, *J* 16.1 Hz, $COCH_2OH$), 3.93–3.84 (dd, overlapped, H-6), 3.714 (s, 3 H, OMe), 3.597 (dd, 1 H, *J* 11.2 and 2.4 Hz, H-9), 3.574 (q, 1 H, *J* 10.3 Hz, H-5), 3.502 (ddd, 1 H, *J* 9.3, 6.4, and 2.5 Hz, H-8), 3.312 (dd, 1 H, *J* 11.2 and 6.8 Hz, H-9), 3.217 (dd, 1 H, *J* 9.3 and 1.0 Hz, H-7), 2.050 (dd, 1 H, *J* 12.7 and 4.9 Hz, H-3*e*), and 1.721 (t, 1 H, *J* 12.7 Hz, H-3*a*).

Anal. Calc. for $C_{12}H_{21}NO_{10}\cdot 0.7H_2O$: C, 41.0; H, 6.4; N, 4.0. Found: C, 40.9; H, 6.3; N, 3.9.

*Methyl (5-acetoxyacetamido-2,4,7,8,9-penta-*O*-acetyl-3,5-dideoxy-*D*-glycero-α- and -β-*D*-galacto-2-nonulopyranosyl)onate* (**8**). — A solution of **7** (1.05 g, 3.1 mmol) in pyridine (15 mL)–Ac_2O (10 mL) was stirred for 42 h at 20° and then co-concentrated with toluene *in vacuo*. Column chromatography (50:1 $CHCl_3$–MeOH) of the residue gave α-**8** (445 mg), αβ-**8** (688 mg), and β-**8** (518 mg) (total yield, 1.65 g, 90%).

Compound α-**8** had $[\alpha]_D$ +4° (*c* 1), R_F 0.23 (50:1 $CHCl_3$–MeOH); ν_{max} 1750, 1690, and 1540 cm^{-1}. N.m.r. data: ^1H, δ 6.197 (d, 1 H, *J* 10.0 Hz, NH), 5.334 (dd, 1 H, *J* 6.4 and 2.3 Hz, H-7), 5.204 (dd, 1 H, *J* 6.4, 6.0, and 2.5 Hz, H-8), 5.076 (ddd, 1 H, *J* 11.8, 10.4, and 4.8 Hz, H-4), 4.787 (dd, 1 H, *J* 10.6 and 2.3 Hz, H-6), 4.588 (d, 1 H, *J* 15.2 Hz, $COCH_2OAc$), 4.370 (dd, 1 H, *J* 12.3 and 2.5 Hz, H-9), 4.320 (d, 1 H, *J* 15.2 Hz, $COCH_2OAc$), 4.175 (q, 1 H, *J* 10.4 Hz, H-5), 4.063 (dd, 1 H, *J* 12.3 and 6.0 Hz, H-9), 3.768 (s, 3 H, OMe), 2.571 (dd, 1 H, *J* 13.0 and 4.8 Hz, H-3*e*), 2.078 (t, 1 H, *J* 13.0 Hz, H-3*a*), 2.182, 2.130, 2.111, 2.109, 2.039, and 2.024 (6 s, 18 H, 6 OAc); ^{13}C, δ 95.5 (C-2), 52.9 (OMe), 49.0 (C-5), and 37.1 (C-3).

Anal. Calc. for $C_{24}H_{33}NO_{16}\cdot 0.4H_2O$: C, 48.1; H, 5.7; N, 2.3. Found: C, 48.1; H, 5.6; N, 2.4.

Compound β-**8** had $[\alpha]_D$ −35° (*c* 1), R_F 0.16 (50:1 $CHCl_3$–MeOH); ν_{max} 1750, 1700, and 1530 cm^{-1}. N.m.r. data: ^1H, δ 5.981 (d, 1 H, *J* 9.5 Hz, NH), 5.332 (ddd, 1 H, *J* 11.4, 10.2, and 4.7 Hz, H-4), 5.316 (dd, 1 H, *J* 5.1 and 2.2 Hz, H-7), 5.080 (ddd, 1 H, *J* 6.7, 5.1, and 2.5 Hz, H-8), 4.614 (d, 1 H, *J* 15.3 Hz, $COCH_2OAc$), 4.490 (dd, 1 H, *J* 12.3 and 2.5 Hz, H-9), 4.302 (d, 1 H, *J* 15.3 Hz, $COCH_2OAc$), 4.188 (dd, 1 H, *J* 10.8 and 2.2 Hz, H-6), 4.125 (dd, 1 H, *J* 12.3 and 6.7 Hz, H-9), 4.103 (q, 1 H, *J* 10.2 Hz, H-5), 3.799 (s, 3 H, OMe), 2.558 (dd, 1 H, *J* 13.4 and 4.7 Hz, H-3*e*), 2.102 (dd, 1 H, *J* 13.4 and 11.4 Hz, H-3*a*), 2.201, 2.168, 2.145, 2.072, 2.043, and 2.023 (6 s, 18 H, 6 OAc); ^{13}C, δ 97.6 (C-2), 53.1 (OMe), 49.5 (C-5), and 36.1 (C-3).

Anal. Calc. for $C_{24}H_{33}NO_{16}\cdot 0.7H_2O$: C, 47.7; H, 5.7; N, 2.3. Found: C, 47.7; H, 5.4; N, 2.4.

Conversion of **8** *into the chloride* **4**. — A solution of **8** (120 mg, 200 μmol) in AcCl saturated with HCl at 0° was stirred for 24 h at 20°, and then co-concentrated with benzene *in vacuo* to give methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-β-*D*-*galacto*-2-nonulopyranosyl chloride)onate (**4**) quantitatively; $[\alpha]_D$ −57° (*c* 0.8), R_F 0.46 (1:2 toluene–EtOAc). N.m.r. data: ^1H, δ 6.068 (d, 1 H, *J* 10.0 Hz, NH), 5.469 (dt, 1 H, *J* 11.0 and 4.9 Hz, H-4), 5.431 (dd, 1 H, *J* 6.8 and 2.2 Hz, H-7), 5.182 (ddd, 1 H, *J* 10.0, 2.4, and 2.4 Hz, H-8), 4.629 (d, 1 H, *J* 15.3 Hz, $COCH_2OAc$), 4.434 (dd, 1 H, *J* 12.7 and 2.7 Hz, H-9), 4.423 (dd, 1 H, *J* 10.3 and 2.2 Hz, H-6), 4.312 (d, 1 H, *J* 15.3 Hz, $COCH_2OAc$), 4.213 (td, 1 H, *J* 10.2 and 10.5 Hz, H-5), 4.074 (dd, 1 H, *J* 12.5 and 5.9 Hz, H-9), 3.888 (s, 3 H, OMe), 2.796 (dd, 1 H, *J* 13.9 and 4.6 Hz, H-3*e*), 2.295 (dd, 1 H, *J* 13.9 and 11.2 Hz, H-3*a*), 2.210, 2.123, 2.095, 2.062 and 2.039 (5 s, 15 H, 5 OAc); ^{13}C, δ 96.7 (C-2), 74.0 (C-8),

70.3 (C-6), 68.0 (C-7), 67.1 (C-4), 62.8 (C-9), 62.1 ($COCH_2$), 53.7 (OCH_3), 48.8 (C-5), 40.9 (C-3), 20.9 (2 $COCH_3$), and 20.6 (3 $COCH_3$).

Benzyl O-*[methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α- (**9**) *and* -β-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,6-di*-O-*benzyl*-β-D-*galactopyranosyl)-(1→4)*-*2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**13**), *benzyl* O-*[methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-β-D-galacto-*2-nonulopyranosyl)onate]-(2→4)*-O-*(2,6-di*-O-*benzyl*-β-D-*galactopyranosyl)-(1→4)*-*2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**17**), *lactone* **18**, *and methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-2,3-dehydro-3,5-dideoxy*-D-glycero-D-galacto-*2-nonulopyranosyl)onate* (**19**). — To a stirred mixture of **5** (3.0 g, 3.4 mmol), $HgBr_2$ (1.08 g, 3.0 mmol), $Hg(CN)_2$ (750 mg, 3.0 mmol), and powdered molecular sieves 4A (3.0 g) in $Cl(CH_2)_2Cl$ (5 mL) was added dropwise a solution of **4** (1.0 g, 1.6 mmol) in $Cl(CH_2)_2Cl$ (7 mL) at −10 to −5°. The mixture was stirred for 16 h at 20°, then for 24 h at 70°, filtered through Celite, and diluted with EtOAc, the organic layer was washed with aq. $NaHCO_3$, H_2O, and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (2:1 then 1:2 toluene–EtOAc) of the residue gave **9** (165 mg, 7.3%), **13** (408 mg, 18.1%), a mixture (1:1, 192 mg, 8.5%) of **17** and **18**, and **19** (500 mg, 60%). Upon standing for 4 weeks at 20°, the mixture of **17** and **18** gradually changed into **18**.

Compound **9** had $[\alpha]_D$ −7° (*c* 1.3), R_F 0.48 (1:2 toluene–EtOAc). N.m.r. data: ^1H, δ 5.808 (d, 1 H, *J* 9.7 Hz, NH), 5.416 (ddd, 1 H, *J* 8.5, 6.1, and 3.0 Hz, H-8c), 5.261 (dd, 1 H, *J* 8.0 and 1.7 Hz, H-7c), 4.920 (m, 1 H, H-4c), 3.774 (s, 3 H, OMe), 2.521 (dd, 1 H, *J* 13.1 and 4.6 Hz, H-3c*e*), 2.189, 2.100, 2.001, 1.984, and 1.883 (5 s, 15 H, 5 OAc); ^{13}C, δ 102.5, 102.3 (C-1a,1b), 98.5 (C-2c), 53.0 (OCH_3), 49.4 (C-5c), and 36.7 (C-3c).

Anal. Calc. for $C_{76}H_{87}NO_{25}$: C, 64.5; H, 6.2; N, 1.0. Found: C, 64.2; H, 6.3; N, 1.0.

Compound **13** had $[\alpha]_D$ −4° (*c* 1.1), R_F 0.57. N.m.r. data: ^1H, δ 5.585 (d, 1 H, *J* 10.2 Hz, NH), 5.333 (td, 1 H, *J* 10.9, and 4.6 Hz, H-4c), 5.297 (t, 1 H, *J* 2.4 Hz, H-7c), 5.259 (td, 1 H, *J* 2.4 and 8.7 Hz, H-8c), 3.618 (s, 3 H, OMe), 2.555 (dd, 1 H, *J* 13.4 and 4.6 Hz, H-3c), 2.183, 2.103, 2.044, 1.996, and 1.913 (5 s, 15 H, 5 OAc); ^{13}C, δ 102.4, 102.3 (C-1a,1b), 99.7 (C-2c), 62.6 (C-9c and $COCH_2OAc$), 52.5 (OCH_3), 49.1 (C-5c), and 37.3 (C-3c).

Anal. Found: C, 64.5; H, 6.1; N, 0.7.

A 1:1 mixture of **17** and **18** had R_F 0.66. ^1H-N.m.r. data for **17** (extracted from the data for the mixture): δ 5.385 (ddd, 1 H, *J* 8.5, 3.8, and 2.8 Hz, H-8c), 3.695 (s, 3 H, OMe), 2.455 (dd, 1 H, *J* 11.9 and 4.2 Hz, H-3c*e*), 2.106, 2.048, 2.046, 2.030, and 2.021 (5 s, 15 H, 5 OAc).

Compound **18** had $[\alpha]_D$ −1.4° (*c* 1), R_F 0.66. N.m.r. data: ^1H, δ 5.227 (d, 1 H, *J* 10.0 Hz, NH), 5.272 (td, 1 H, *J* 11.0 and 5.0 Hz, H-4c), 5.268 (t, 1 H, *J* 1.9 Hz, H-7c), 5.195 (td, 1 H, *J* 9.7 and 2.1 Hz, H-8c), 2.516 (t, 1 H, *J* 12.6 Hz, H-3c*e*), 2.161, 2.142, 2.029, 2.010, and 1.999 (5 s, 15 H, 5 OAc); ^{13}C, δ 102.5, 101.9 (C-1a, 1b), 96.9 (C-2c), and 49.7 (C-5c).

Anal. Calc. for $C_{77}H_{85}NO_{26}$: C, 64.9; H, 6.0; N, 1.0. Found: C, 65.2; H, 6.1; N, 0.9.

Compound **19** had $[\alpha]_D$ +56° (*c* 0.5), R_F 0.32. N.m.r. data: ^{1}H, δ 6.299 (d, 1 H, *J* 9.2 Hz, NH), 5.992 (d, 1 H, *J* 2.9 Hz, H-3), 5.656 (dd, 1 H, *J* 7.8 and 2.9 Hz, H-4), 5.447 (dd, 1 H, *J* 4.6 and 3.1 Hz, H-7), 5.350 (ddd, 1 H, *J* 7.0, 5.2, and 3.5 Hz, H-8), 4.638 (dd, 1 H, *J* 12.2 and 2.9 Hz, H-9), 4.570 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 4.463 (dd, 1 H, *J* 8.2 and 3.1 Hz, H-6), 4.385 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 4.368 (td, 1 H, *J* 9.5 and 7.8 Hz, H-5), 4.197 (dd, 1 H, *J* 12.2 and 6.8 Hz, H-9), 3.811 (s, 3 H, OMe), 2.173, 2.130, 2.080, and 2.062 (4 s, 1:1:2:1, 5 OAc); ^{13}C, δ 145.1 (C-2), 108.1 (C-3), 52.3 (OCH_3), and 46.6 (C-5).

Anal. Calc. for $C_{22}H_{29}NO_{14}$: C, 49.7; H, 5.5; N, 2.6. Found: C, 49.3; H, 5.5; N, 2.6.

Benzyl O-*[methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(4*-O-*acetyl-2,6-di*-O-*benzyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**10**). — A solution of **9** (81 mg, 57 μmol) in 1:1 pyridine–Ac_2O (10 mL) was stirred for 16 h at 60° and then concentrated *in vacuo*. Column chromatography (1:1 toluene–EtOAc) of the residue gave **10** quantitatively, $[\alpha]_D$ −13° (*c* 0.5), R_F 0.27 (1:1 toluene–EtOAc). N.m.r. data: ^{1}H, δ 5.779 (d, 1 H, *J* 10.2 Hz, NH), 5.598 (ddd, 1 H, *J* 8.6, 4.9, and 2.4 Hz, H-8c), 5.282 (dd, 1 H, *J* 8.5 and 2.7 Hz, H-7c), 5.049 (d, 1 H, *J* 2.9 Hz, H-4b), 4.103 (q, 1 H, *J* 10.5 Hz, H-5c), 2.616 (dd, 1 H, *J* 12.7 and 4.6 Hz, H-3c*e*), 1.851 (t, 1 H, *J* 12.4 Hz, H-3c*a*), 2.185, 2.123, 2.000, 1.997, 1.971, and 1.749 (6 s, 18 H, 6 OAc); ^{13}C, δ 102.3, 102.0 (C-1a,1b), and 97.5 (C-2c).

Anal. Calc. for $C_{78}O_{89}NO_{26}$: C, 64.3; H, 6.2; N, 1.0. Found: C, 64.0; H, 6.0; N, 1.1.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(4*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)*-D-*glucopyranose* (**11**). — A mixture of **10** (232 mg, 159 μmol) and 10% Pd–C (150 mg) in MeOH (50 mL) was stirred for 16 h at 20° under H_2, then filtered through Celite, and concentrated *in vacuo* to give **11**, which was used directly for the next step. Compound **11** had $[\alpha]_D$ +24.5° (*c* 0.5, methanol), R_F 0.63 (2:1:1 BuOH–EtOH–H_2O). N.m.r. data (CD_3OD): ^{1}H, δ 5.541 (ddd, 1 H, *J* 8.8, 5.4, and 2.9 Hz, H-8c), 5.314 (dd, 1 H, *J* 8.8 and 1.7 Hz, H-7c), 5.095 (d, 0.5 H, *J* 3.9 Hz, H-1aα), 5.036 (bs, 1 H, H-4b), 4.945 (ddd, 1 H, *J* 12.1, 8.0, and 4.4 Hz, H-4c), 4.591 (d, 1 H, *J* 7.8 Hz, H-1b), 4.501 (d, 0.5 H, *J* 7.8 Hz, H-1a*β*), 4.435 (d, 1 H, *J* 15.1 Hz, COC*H*$_2$OAc), 4.321 (d, 1 H, *J* 14.9 Hz, COC*H*$_2$OAc), 3.847 (s, 3 H, OMe), 2.608 (dd, 1 H, *J* 12.5 and 4.9 Hz, H-3c*e*), 2.151, 2.119, 2.083, 2.020, 1.983 (5 s, 15 H, 5 OAc), 2.062 and 2.058 (2 s, 3 H, OAc), and 1.947 (t, 1 H, *J* 12.0 Hz, H-3c*a*); ^{13}C, δ 105.2 (C-1b), 99.0 (C-2c), 98.1 (C-1a*β*), and 93.9 (C-1aα).

Anal. Calc. for $C_{36}H_{33}NO_{26}$: C, 46.3; H, 5.9; N, 1.5. Found: C, 46.5; H, 5.8; N, 1.9.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galacto*-

pyranosyl)-(1→4)-2,3,6-tri-O-*acetyl*-α- *and*-β-D-*glucopyranosyl acetate* (**12**). — A solution of **11** (130 mg, 142 μmol) in 1:1 pyridine–Ac_2O (16 mL) was stirred for 3 days at 20° and then concentrated *in vacuo*. Column chromatography (1:5 toluene–EtOAc) of the residue gave **12** (151 mg, 95%) as a 1:1 αβ-mixture, $[\alpha]_D$ +11° (*c* 0.6), R_F 0.74 (20:1 $CHCl_3$–MeOH). ^{1}H-N.m.r. data: δ 6.258 (d, 0.5 H, *J* 3.7 Hz, H-1aα), 5.782 (d, 1 H, *J* 10.0 Hz, NH), 5.682 (d, 0.5 H, H-1aβ), 4.648 (d, 1 H, *J* 8.0 Hz, H-1b), 4.570 (d, 1 H, *J* 15.4 Hz, $COCH_2OAc$), 4.276 (d, 1 H, *J* 15.4 Hz, $COCH_2OAc$), 3.869 (s, 15 H, OMe), 3.866 (s, 1.5 H, OMe), 2.60 (m, 1 H, H-3c*e*), and 1.679 (t, 1 H, *J* 12.5 Hz, H-3c*a*).

Anal. Calc. for $C_{48}H_{65}NO_{32}$: C, 49.4; H, 5.6; N, 1.2. Found: C, 49.2; H, 5.6; N, 1.5.

Benzyl O-*[methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-β-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(4*-O-*acetyl-2,6-di*-O-*benzyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**14**). — Acetylation of **13** (144 mg, 102 μmol), as for **10**, gave a quantitative yield of **14**, $[\alpha]_D$ −13° (*c* 1), R_F 0.40 (1:1 toluene–EtOAc). N.m.r. data: ^{1}H, δ 6.454 (d, 1 H, *J* 10.3 Hz, NH), 5.378 (d, 1 H, *J* 3.2 Hz, H-4b), 5.37–5.30 (m, 2 H, H-7c,8c), 5.101 (ddd, 1 H, *J* 12.2, 8.5, and 4.1 Hz, H-4c), 4.095 (q, 1 H, *J* 10.5 Hz, H-5c), 3.444 (s, 3 H, OMe), 2.571 (dd, 1 H, *J* 13.1 and 4.6 Hz, H-3c*e*), 2.169, 2.143, 2.106, 2.034, 1.952, and 1.819 (6 s, 18 H, 6 OAc); ^{13}C, δ 102.3, 101.9 (C-1a,1b), and 99.3 (C-2c).

Anal. Calc. for $C_{78}H_{89}NO_{26}$: C, 64.3; H, 6.2; N, 1.0. Found: C, 64.7; H, 6.2; N, 1.1.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-β-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(4*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)*-D-*glucopyranose* (**15**). — Hydrogenolysis of **14** (390 mg, 268 μmol), as described for **10**, gave **15** as a 1:1 αβ-mixture (232 mg, 94%), $[\alpha]_D$ +20° (*c* 1.1, methanol), R_F 0.63 (2:1:1 BuOH–EtOH–H_2O). N.m.r. data: ^{1}H, δ 2.680 (dd, 0.5 H, *J* 13.4 and 4.9 Hz, H-3c*e*), 2.546 (dd, 0.5 H, *J* 13.4 and 4.9 Hz, H-3c*e*), 1.843 (t, 0.5 H, *J* 12.0 Hz, H-3c*a*), and 1.774 (t, 0.5 H, *J* 11.7 Hz, H-3c*a*); ^{13}C (CD_3OD), δ 105.1 (C-1b), 100.6 (C-2c), 98.1 (C-1aβ), and 93.8 (C-1aα).

Anal. Calc. for $C_{36}H_{53}NO_{26}$: C, 47.2; H, 5.8; N, 1.5. Found: C, 47.3; H, 5.8; N, 1.8.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-β-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galacto-pyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-D-*glucopyranosyl acetate* (**16**). — Acetylation of **15** (220 mg, 240 μmol), as described for **12**, gave **16** (247 mg, 88%), R_F 0.83 (20:1 $CHCl_3$–MeOH). ^{1}H-N.m.r. data: δ 6.316 (d, 1 H, *J* 10.5 Hz, NH), 6.254 (d, 0.5 H, *J* 3.7 Hz, H-1aα), 5.675 (d, 0.5 H, *J* 8.3 Hz, H-1aβ), 3.847 (s, 1.5 H, OMe), 3.841 (s, 1.5 H, OMe), 2.436 (dd, 1 H, *J* 13.2 and 4.4 Hz, H-3c*e*), and 1.776 (t, 1 H, *J* 13.4 Hz, H-3c*a*).

Anal. Calc. for $C_{48}H_{65}NO_{32}$: C, 49.6; H, 5.6; N, 1.2. Found: C, 49.9; H, 5.6; N, 1.2.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-

α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,4,6-tri*-O-*acetyl*-β-D-*galacto-pyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-D-*glucopyranose* (**20**). — A solution of **12** (140 mg, 120 μmol) and NH_2NH_2·AcOH (15 mg, 160 μmol) in *N,N*-dimethylformamide (2 mL) was stirred for 25 min at 60°, cooled to 20°, and diluted with EtOAc (20 mL). The organic layer was washed with H_2O and aq. NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (1:2 acetone–CCl_4) of the residue gave **20** (133 mg, 97%), $[\alpha]_D$ +14° (*c* 0.7), R_F 0.55 (1:1 acetone–CCl_4). ^{1}H-N.m.r. data: δ 5.832 (d, 1 H, *J* 10.0 Hz, NH), 4.654 (d, 1 H, *J* 8.1 Hz, H-1b), 4.565 (d, 1 H, *J* 15.1 Hz, COC*H*$_2$OAc), 4.278 (d, 1 H, *J* 15.4 Hz, COC*H*$_2$OAc), 3.864 (s, 3 H, OMe), 2.602 (dd, 1 H, *J* 12.7 and 4.4 Hz, H-3c*e*), 2.181, 2.176, 2.082, 2.081, 2.078, 2.073, 2.067, 1.992 (8 s, 24 H, 8 OAc), 2.106, 2.102, 2.096, 2.093, 2.049, and 2.045 (6 s, 9 H, 3 OAc of α- and β-D-glucose residue).

Anal. Calc. for $C_{46}H_{63}NO_{31}$: C, 49.1; H, 5.6; N, 1.2. Found: C, 48.8; H, 5.7; N, 1.7.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,4,6-tri*-O-*acetyl*-β-D-*galactopy-ranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl trichloroacetimidate* (**21**). — To a solution of **20** (116 mg, 103 μmol) in CH_2Cl_2 (1 mL) was added Cl_3CCN (358 μL, 3.57 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (15 μL, 110 μmol) at 0°. The mixture was stirred for 4 h at 0° and directly subjected to column chromatography (1:2 acetone–CCl_4) to give **21** (121 mg, 92%), $[\alpha]_D$ +34° (*c* 0.3), R_F 0.28. N.m.r. data: ^{1}H, δ 8.649 (s, 1 H, C=NH), 6.492 (d, 1 H, *J* 3.6 Hz, H-1a), 5.779 (d, 1 H, *J* 10.0 Hz, CONH), 5.553 (t, 1 H, *J* 9.7 Hz, H-3a), 5.496 (ddd, 1 H, *J* 9.3, 4.4, and 2.7 Hz, H-8c), 5.373 (dd, 1 H, *J* 9.2 and 2.6 Hz, H-7c), 4.899 (d, 1 H, *J* 2.6 Hz, H-4b), 4.664 (d, 1 H, *J* 8.0 Hz, H-1b), 4.571 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 4.274 (d, 1 H, *J* 15.1 Hz, COC*H*$_2$OAc), 3.869 (s, 3 H, OMe), 2.604 (dd, 1 H, *J* 12.7 and 4.6 Hz, H-3c*e*), 1.683 (t, 1 H, *J* 12.4 Hz, H-3c*a*), 2.206, 2.186, 2.180, 2.100, 2.084, 2.075 (6 H), 2.073, 2.054, 2.012, and 1.992 (10 s, 33 H, 11 OAc): ^{13}C, δ 101.2 (C-1b) and 97.0 (C-2c).

Anal. Calc. for $C_{48}H_{64}Cl_3N_2O_{31}$·1.5$H_2O$: C, 44.4; H, 5.2; N, 2.2. Found: C, 44.1; H, 4.8; N, 2.5.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosyl)onate]-(2→3)*-O-*(2,4,6-tri*-O-*acetyl*-β-D-*galacto-pyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)-(1→1)-(2*S,*3*R,*4*E)-*3*-O-tert-*butyldiphenylsilyl-2*-N-*tetracosanoylsphingenine* (**22**). — To a mixture of **21** (80 mg, 63 μmol), **3** (70 mg, 79 μmol), and powdered molecular sieves AW-300 (1.5 g) in $Cl(CH_2)_2Cl$ (3 mL) was added BF_3·ether (15 μL, 124 μmol) at −10 to −5°. The mixture was stirred for 16 h at 0–10°, diluted with $Cl(CH_2)_2Cl$, and filtered through Celite, washed with aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (1:1 toluene–EtOAc) of the residue gave **22** (66 mg, 52%), $[\alpha]_D$ −11° (*c* 0.4), R_F 0.13. N.m.r. data: ^{1}H, δ 7.70–7.30 (m, 10 H, aromatic), 5.773 (d, 1 H, *J* 10.0 Hz, CON*H*cer), 5.520 (m, 1 H, H-8c), 5.407 (d, 1 H, *J* 8.3 Hz, CONH), 5.367 (dd, 1 H, *J* 9.3 and 2.7 Hz, H-7c), 5.266 (dd, 1 H, *J* 14.8 and 7.2 Hz,

H-4cer), 5.175 (t, 1 H, *J* 9.5 Hz, H-3a), 5.105 (dt, 1 H, *J* 14.8 and 7.2 Hz, H-5cer), 4.959 (m, 1 H, H-4c), 4.894 (d, 1 H, *J* 2.9 Hz, H-4b), 4.640 (d, 1 H, *J* 8.0 Hz, H-1b), 4.570 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 4.428 (d, 1 H, *J* 8.0 Hz, H-1a), 4.275 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 3.867 (s, 3 H, OMe), 2.601 (dd, 1 H, *J* 12.9 and 4.6 Hz, H-3c*e*), 2.245, 2.183, 2.175, 2.095, 2.083, 2.075, 2.073, 2.043, 2.013, 1.992, 1.961 (11 s, 33 H, 11 OAc), 0.993 (s, 9 H, 3 CMe), and 0.881 (t, 6 H, *J* 5.6 Hz, CH$_2$C*H*$_3$); ^{13}C, δ 101.0, 100.8 (C-1a,1b), and 96.9 (C-2c).

Anal. Calc. for $C_{104}H_{163}N_2O_{33}Si$: C, 62.5; H, 8.2; N, 1.4. Found: C, 62.5; H, 8.2; N, 1.6.

*O-[Methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-*α*-*D*-galacto-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,4,6-tri-*O*-acetyl-*β*-*D*-galacto-pyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-*β*-*D*-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-O-acetyl-2-N-tetracosanoylsphingenine* (**23**). — A mixture of solutions of **22** (24 mg, 12 *μ*mol) in tetrahydrofuran (2 mL) and M Bu_4NF in tetrahydrofuran (60 *μ*L, 60 *μ*mol) was stirred for 16 h at 20° and then concentrated *in vacuo*. A solution of the residue in 1:1 pyridine–Ac_2O (2 mL) was stirred for 16 h at 40° and then concentrated *in vacuo*. Column chromatography (50:1 $CHCl_3$–MeOH) of the residue gave **23** (14 mg, 64%), $[\alpha]_D$ −9° (*c* 0.7), R_F 0.48 (40:1 $CHCl_3$–MeOH). ^{1}H-N.m.r. data: δ 5.772 (d, 1 H, *J* 10.3 Hz, NH), 5.764 (td, 1 H, *J* 14.8 and 7.2 Hz, H-5cer), 5.660 (d, 1 H, *J* 9.3 Hz, NH), 5.520 (ddd, 1 H, *J* 9.3, 5.6, and 3.1 Hz, H-8c), 5.356 (dd, 1 H, *J* 9.3 and 3.3 Hz, H-7c), 5.347 (dd, 1 H, *J* 14.8 and 7.4 Hz, H-4cer), 5.238 (t, 1 H, *J* 7.3 Hz, H-3cer), 5.176 (t, 1 H, *J* 9.3 Hz, H-3a), 4.947 (td, 1 H, *J* 10.5 and 5.2 Hz, H-4c), 4.660 (d, 1 H, *J* 8.0 Hz, H-1b), 4.570 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 4.425 (d, 1 H, *J* 8.0 Hz, H-1a), 4.274 (d, 1 H, *J* 15.3 Hz, COC*H*$_2$OAc), 3.866 (s, 3 H, OMe), 2.599 (dd, 1 H, *J* 12.6 and 4.6 Hz, H-3c*e*), 2.239, 2.184, 2.179, 2.108, 2.090, 2.081, 2.076 (6 H), 2.041, 2.037, 2.006, 1.991 (11 s, 36 H, 12 OAc), 1.682 (t, 1 H, *J* 12.4 Hz, H-3c*a*), and 0.880 (t, 6 H, *J* 7.0 Hz, CH$_2$C*H*$_3$).

Anal. Calc. for $C_{90}H_{146}N_2O_{34}\cdot C_6H_5CH_3$: C, 61.6; H, 8.2; N, 1.5. Found: C, 61.4; H, 8.3; N, 1.3.

Deacylation and saponification of **23**. — A solution of **23** (12 mg, 6.6 *μ*mol) in 0.05M NaOMe–MeOH (3 mL) was stirred for 16 h at 20° and then concentrated *in vacuo*. A solution of the residue in 2:2:1 MeOH–tetrahydrofuran–H_2O (2.5 mL) was stirred for 16 h at 20°, then neutralised with Amberlite IRC-50 (H^+) resin, filtered, and concentrated *in vacuo*. Column chromatography (10:6:1 $CHCl_3$–MeOH–H_2O) of the residue on Sephadex LH-20 gave **1** (8.5 mg, 97%), $[\alpha]_D$ −8.5° (*c* 0.1, pyridine) {lit.[12] $[\alpha]_D$ −11.9° (pyridine)}, R_F 0.25 (2:1:1 BuOH–EtOH–H_2O). ^{1}H-N.m.r. data [49:1 $(CD_3)_2SO$–D_2O, 65°]: δ 5.534 (td, 1 H, *J* 14.9 and 6.8 Hz, H-5cer), 5.343 (dd, 1 H, *J* 15.3 and 7.3 Hz, H-4cer), 4.200 (d, 1 H, *J* 7.8 Hz, H-1b), 4.159 (d, 1 H, *J* 7.8 Hz, H-1a), 3.041 (t, 1 H, *J* 8.5 Hz, H-2a), 2.757 (dd, 1 H, *J* 11.9 and 5.1 Hz, H-3c*e*), 2.026 (t, 2 H, *J* 7.3 Hz, H-2′cer), 1.930 (m, 2 H, H-6cer), and 0.852 (t, 6 H, *J* 6.3 Hz, CH$_2$C*H*$_3$).

*O-[Methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-*β*-*D*-galacto-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,4,6-tri-*O*-acetyl-*β*-*D*-galacto-*

*pyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-*D*-glucopyranose* (**24**). — Treatment of **16** (220 mg, 188 μmol), as described above for **20**, gave **24** (144 mg, 68%), $[\alpha]_D$ +17° (*c* 0.5), R_F 0.58 (1:1 acetone–CCl_4). ^{1}H-N.m.r. data: δ 4.597 (d, 1 H, *J* 15.6 Hz, COCH_2OAc), 4.351 (d, 1 H, *J* 15.4 Hz, COCH_2OAc), 3.849 (s, 3 H, OMe), 2.435 (dd, 1 H, *J* 13.2 and 4.6 Hz, H-3c*e*), and 1.772 (t, 1 H, *J* 12.6 Hz, H-3c*a*).

Anal. Calc. for $C_{46}H_{64}NO_{31}$: C, 49.1; H, 5.6; N, 1.2. Found: C, 48.9; H, 5.7; N, 1.4.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-β-*D*-galacto-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,4,6-tri-*O*-acetyl-β-*D*-galacto-pyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-*D*-glucopyranosyl trichloroacetimidate* (**25**). — Treatment of **24** (140 mg, 124 μmol), as described above for **21**, gave **25** (120 mg, 76%), $[\alpha]_D$ +27° (*c* 0.8), R_F 0.37 (1:2 acetone–CCl_4). N.m.r. data: ^{1}H, δ 8.667 (s, 1 H, C=NH), 6.474 (d, 1 H, *J* 3.7 Hz, H-1a), 6.314 (d, 1 H, *J* 10.3 Hz, NH), 5.533 (t, 1 H, *J* 9.7 Hz, H-3a), 5.297 (d, 1 H, *J* 2.9 Hz, H-4b), 5.043 (m, 1 H, H-4c), 4.601 (d, 1 H, *J* 15.3 Hz, COCH_2OAc), 4.433 (d, 1 H, *J* 8.0 Hz, H-1b), 4.349 (d, 1 H, *J* 15.6 Hz, COCH_2OAc), 3.840 (s, 3 H, OMe), 2.436 (dd, 1 H, *J* 13.4 and 4.6 Hz, H-3c*e*), 1.777 (t, 1 H, *J* 12.2 Hz, H-3c*a*), 2.304, 2.185, 2.152, 2.117, 2.083, 2.069, 2.062, 2.061, 2.043, 2.017, and 1.982 (11 s, 33 H, 11 OAc); ^{13}C, δ 101.2 (C-1b), 99.6 (C-2c), and 93.2 (C-1a).

Anal. Calc. for $C_{48}H_{64}Cl_3N_2O_{31}$: C, 45.4; H, 5.1; N, 2.2. Found: C, 45.6; H, 5.0; N, 2.3.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-β-*D*-galacto-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,4,6-tri-*O*-acetyl-β-*D*-galacto-pyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-*D*-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-tert-butyldiphenylsilyl-2-*N*-tetracosanoylsphingenine* (**26**). — Reaction of **25** (100 mg, 79 μmol) and **3** (70 mg, 79 μmol), as described above for **22**, gave **26** (91 mg, 58%), $[\alpha]_D$ −12° (*c* 0.4), R_F 0.23 (1:1 toluene–EtOAc). N.m.r. data: ^{1}H, δ 7.7–7.3 (m, 10 H, aromatic), 5.041 (m, 1 H, H-4c), 4.598 (d, 1 H, *J* 15.3 Hz, COCH_2OAc), 4.426 (d, 1 H, *J* 7.8 Hz, H-1b), 4.378 (d, 1 H, *J* 7.1 Hz, H-1a), 4.350 (d, 1 H, *J* 15.3 Hz, COCH_2OAc), 3.841 (s, 3 H, OMe), 2.434 (dd, 1 H, *J* 13.4 and 4.6 Hz, H-3c*e*), 2.302, 2.181, 2.150, 2.088, 2.070, 2.060, 2.052, 2.042, 2.032, 1.981, 1.960 (11 s, 33 H, 11 OAc), 1.772 (t, 1 H, *J* 12.4 Hz, H-3c*a*), 1.690 (q, 2 H, *J* 7.3 Hz, H-6), 1.473 (t, 2 H, *J* 6.0 Hz, H-3′), 0.997 (s, 9 H, 3 CMe), and 0.880 (t, 2 H, *J* 5.6 Hz, CH_2CH_3).

Anal. Calc. for $C_{104}H_{163}N_2O_{33}Si\cdot 2H_2O$: C, 61.4; H, 8.3; N, 1.4. Found: C, 61.1; H, 8.0; N, 1.4.

O-*[Methyl (5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero-β-*D*-galacto-2-nonulopyranosyl)onate]-(2→3)-*O*-(2,4,6-tri-*O*-acetyl-β-*D*-galacto-pyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-*D*-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-acetyl-2-*N*-tetracosanoylsphingenine* (**27**). — Treatment of **26** (20 mg, 10 μmol), as described above for **23**, gave **27** (17 mg, 94%), $[\alpha]_D$ −5° (*c* 0.9), R_F 0.70 (40:1 $CHCl_3$–MeOH). N.m.r. data: ^{1}H, δ 6.317 (d, 1 H, *J* 10.0 Hz, NH), 5.768 (dt, 1 H, *J* 15.0 and 6.4 Hz, H-5cer), 5.630 (d, 1 H, *J* 9.3 Hz, NH), 5.038 (ddd, 1 H, *J* 12.0, 10.0, and 4.4 Hz, H-4c), 4.597 (d, 1 H, *J* 15.4 Hz, COCH_2OAc), 4.433 (d, 1 H, *J* 7.8 Hz,

H-1b), 4.405 (d, 1 H, *J* 8.0 Hz, H-1a), 4.349 (d, 1 H, *J* 15.6 Hz, $COCH_2OAc$), 3.841 (s, 3 H, OMe), 2.428 (dd, 1 H, *J* 12.1 and 4.6 Hz, H-3c*e*), 2.295, 2.222, 2.159, 2.150, 2.086, 2.066, 2.060, 2.053, 2.042, 2.040, 2.004, 1.981 (12 s, 36 H, 12 OAc), 1.771 (t, 1 H, *J* 12.2 Hz, H-3c*a*), and 0.880 (t, 6 H, *J* 6.5 Hz, CH_2CH_3).

Anal. Calc. for $C_{90}H_{146}N_2O_{34}\cdot H_2O$: C, 59.5; H, 8.2; N, 1.5. Found: C, 59.1; H, 8.0; N, 1.7.

Deacylation and saponification of **27**. — Treatment of **27** (16 mg, 8.3 μmol), as described above for **23**, gave *O*-[(3,5-dideoxy-5-hydroxyacetamido-D-*glycero*-β-D-*galacto*-2-nonulopyranosyl)onate]-(2→3)-*O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→1)-(2*S*,3*R*,4*E*)-2-*N*-tetracosanoylsphingenine (**28**; 11 mg, 94%), $[\alpha]_D$ −20° (*c* 0.1, pyridene), R_F 0.25 (2:1:1 BuOH-EtOH-H_2O). ^{1}H-N.m.r. data [49:1 $(CD_3)_2SO$–D_2O, 65°]: δ 5.557 (td, 1 H, *J* 15.3 and 6.6 Hz, H-5cer), 5.372 (dd, 1 H, *J* 15.3 and 6.8 Hz, H-4cer), 4.193 (d, 1 H, *J* 6.1 Hz, H-1b), 4.176 (d, 1 H, *J* 7.6 Hz, H-1a), and 3.057 (t, 1 H, *J* 8.0 Hz, H-2a), 2.041 (m, 2 H, H-2′cer), 1.934 (m, 2 H, H-6cer), and 0.854 (t, 6 H, *J* 6.5 Hz, CH_2CH_3).

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