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Stereoselective synthesis of sialyl-lactotetraosylceramide and sialylneolactotetraosylceramide*

Akihiko Kameyama, Hideharu Ishida, Makoto Kiso, and Akira Hasegawa†
Department of Applied Bioorganic Chemistry, Gifu University, Yanagido, Gifu 501-11 (Japan)

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ABSTRACT

The first total syntheses of sialyl-lactotetraosylceramide (**28**, IV^{3}NeuAcLc$_4$Cer) and sialylneolactotetraosylceramide (**32**, IV^{3}NeuAcnLc$_4$Cer) are described. Methyl *O*-(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 (**4**), the key glycosyl donor, was prepared from 2-(trimethylsilyl)ethyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-6-*O*-benzoyl-β-D-galactopyranoside (**1**), *via* benzoylation, replacement of the 2-(trimethylsilyl)ethyl group by acetyl, and introduction of the methylthio group with methylthiotrimethylsilane. Coupling of 2-(trimethylsilyl) ethyl 2,3,6,2′,4′,6′-hexa-*O*-benzyl-β-D-lactoside (**8**), prepared from 2-(trimethylsilyl)ethyl β-D-lactoside (**5**) *via* selective 3′-*O*-(4-methoxybenzylation), benzylation, and selective removal of the 4-methoxybenzyl group, with 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide (**9**) gave a trisaccharide derivative **10**, from which the phthaloyl and *O*-acetyl groups were removed. *N*-Acetylation then gave 2-(trimethylsilyl)ethyl *O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**12**). Dimethyl(methylthio)sulfonium triflate-promoted coupling of **4** with **13**, prepared from **12** by 4,6-*O*-benzylidenation, or with **15**, obtained from **13** by *O*-(4-methoxybenzylation) and reductive opening of the benzylidene acetal, gave the corresponding pentasaccharide derivatives **16** and **20** in good yields. Compounds **16** and **20** were converted into the corresponding α-trichloroacetimidates **19** and **23** which, on coupling with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**24**), gave the β-glycosides **25** and **29**, respectively. Finally, **25** and **29** were transformed, *via* selective reduction of the azide group, condensation with octadecanoic acid, *O*-deacylation, and hydrolysis of the methyl ester group, into **28** and **32**, respectively.

INTRODUCTION

Gangliosides are distinguished from other glycosphingolipids in that they contain sialic acid, usually α-linked to either C-3 of galactose or C-8 of another sialic acid residue.

Various important biological functions of gangliosides have been reported[2-4]. Sialyl-lactotetraosylceramide[5] (**28**, IV^{3}NeuAcLc$_4$Cer) was detected first as a ganglioside antigen in human lung carcinoma by a monoclonal antibody, and is present as a minor component in many different carcinomas. Sialylneolactotetraosylceramide (**32**,

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†Author for correspondence.

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IV^{3}NeuAcnLc$_4$Cer), a positional isomer of IV^{3}NeuAcLc$_4$Cer with regard to the substitution of the GlcNAc residue by the terminal disaccharide, is a major ganglioside of human erythrocytes[6], a receptor of human influenza A virus[7], and induces granulocytic differentiation of human promyelocytic leukemia cell[8].

We have achieved a facile, regio- and stereo-selective α-glycosidation[9,10] of sialic acid and now describe the first total syntheses of sialyl-lactotetraosylceramide and sialylneolactotetraosylceramide.

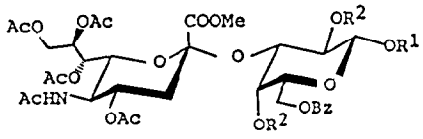
RESULTS AND DISCUSSION

Methyl *O*-(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 (**4**) was selected as the glycosyl donor, and 2-(trimethylsilyl)ethyl *O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**13**) and 2-(trimethylsilyl) ethyl *O*-[2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl]-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**15**) as the acceptors in the syntheses of sialyl-lactotetraosylceramide (**28**) and sialylneolactotetraosylceramide (**32**), respectively.

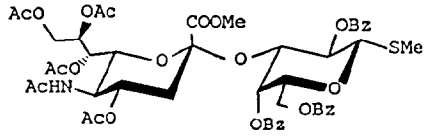
2-(Trimethylsilyl)ethyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-6-*O*-benzoyl-β-D-galactopyranoside[9,10] (**1**) was prepared (46%) by dimethyl(methylthio)sulfonium triflate (DMTST)-promoted glycosylation[9,11] of 2-(trimethylsilyl)ethyl 6-*O*-benzoyl-β-D-galactopyranoside with the methyl α-thioglycoside of *N*-acetylneuraminic acid. Treatment of **1** with benzoyl chloride in pyridine–dichloromethane gave the tribenzoate **2**, which, on treatment[12] with boron trifluoride etherate in toluene–acetic anhydride, gave the β-1-acetate **3** in high yield. The ^{1}H-n.m.r. data for the galactose residue in **3** [δ 6.25 ($J_{1,2}$ 8.3 Hz, H-1), 5.66 ($J_{2,3}$ 10.1 Hz, H-2), and 5.52 ($J_{3,4} = J_{4,5} = 3.3$ Hz, H-4)] are characteristic of the structure assigned. Conversion of the β-1-acetate **3** into the methyl β-thioglycoside **4** (81.7%) was achieved by treatment[13] with methylthiotrimethylsilane and boron trifluoride etherate in dichloromethane. Significant signals in the ^{1}H-n.m.r. spectrum of **4** were at δ 4.84 (d, $J_{1,2}$ 9.9 Hz, H-1), 4.94 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 3.3 Hz, H-3), 5.57 (t, H-2), and 7.39–8.17 (3 Ph). Other ^{1}H-n.m.r. data, given in the Experimental, are consistent with the structure **4**.

Dibutyltin oxide-mediated, selective etherification of 2-(trimethylsilyl)ethyl *O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside[9,15] (**5**), using 4-methoxybenzyl chloride and tetrabutylammonium bromide, gave the 3′-*O*-(4-methoxybenzyl) derivative **6** (74%). Treatment of **6** with benzyl bromide in *N*,*N*-dimethylformamide in the presence of sodium hydride afforded 2-(trimethylsilyl)ethyl *O*-[2,4,6-tri-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**7**, 79%) which, with 2,3-dichloro-5,6-dicyanobenzoquinone[16] in dichloromethane–water for 1 h at room temperature, gave the 3′-hydroxy compound **8** (69.6%).

Glycosylation of **8** with 2,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyra-



1 R^1 = SE, R^2 = H
2 R^1 = SE, R^2 = Bz
3 R^1 = Ac, R^2 = Bz
SE = $Me_3SiCH_2CH_2$



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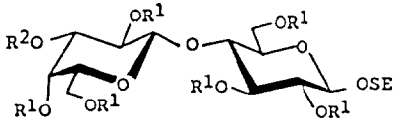
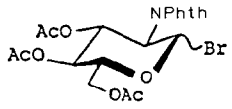


5 R^1 = R^2 = H
6 R^1 = H, R^2 = *p*MeOBn
7 R^1 = Bn, R^2 = *p*MeOBn
8 R^1 = En, R^2 = H



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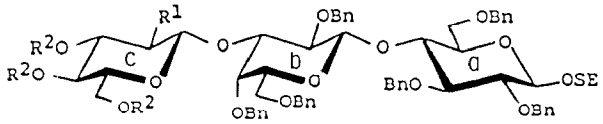
nosyl bromide[17] in dichloromethane in the presence of silver carbonate and silver perchlorate gave the desired β-glycoside **10** (93.7%). Significant signals of the GlcN unit in the ^{1}H-n.m.r. spectrum of **10** were at δ 5.63 (d, $J_{1,2}$ 8.4 Hz, H-1), 5.15 (t, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3), and 5.87 (dd, $J_{4,5}$ 10.6 Hz, H-4), indicating the newly formed glycosidic linkage to be β. *O*-Deacetylation of **10** with sodium methoxide, followed by heating with hydrazine hydrate in aqueous 95% ethanol, and subsequent *N*-acetylation afforded 2-(trimethylsilyl)ethyl *O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**12**, 88.4%), which was used for the preparation of the glycosyl acceptors **13** and **15**.

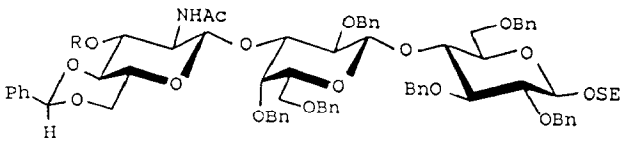
Treatment of **12** with benzaldehyde dimethyl acetal in *N*,*N*-dimethylformamide in the presence of toluene-*p*-sulfonic acid monohydrate gave the 4,6-*O*-benzylidene derivative **13** (83.4%). Treatment of **13** with 4-methoxybenzyl chloride in *N*,*N*-dimethylformamide in the presence of sodium hydride for 3 h at 0° gave the 4-methoxybenzyl derivative **14** (79.6%) which, on reductive ring-opening of the benzylidene group with sodium cyanoborohydride–hydrogen chloride in tetrahydrofuran[18], afforded **15** (52.8%).

Glycosylation of **13** with 1.5 equiv. of **4** in dichloromethane for 12 h at 0° in the presence of 4.0 equiv. of DMTST and powdered molecular sieves 4 Å gave the expected pentasaccharide derivative **16** (87%). The ^{1}H-n.m.r. data for the Neu5Ac–Gal unit in **16** [δ 5.12 (d, $J_{1,2}$ 8.0 Hz, H-1), 5.37 (dd, $J_{2,3}$ 10.0 Hz, H-2), 4.91 (dd, $J_{3,4}$ 2.9 Hz, H-3)] indicated the newly formed glycosidic linkage to be β. In the same way, **4** reacted with **15** to yield the β-glycoside **20** (71.9%).

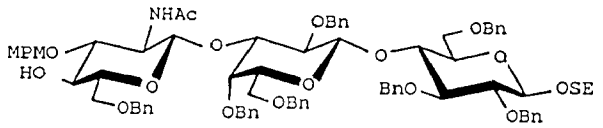
Catalytic hydrogenolysis (Pd–C) in ethanol–formic acid of the benzyl and ben-



10 R^1 = NPhth, R^2 = Ac
11 R^1 = NPhth, R^2 = H
12 R^1 = NHAc, R^2 = H



13 R = H
14 R = *p*MeOBn



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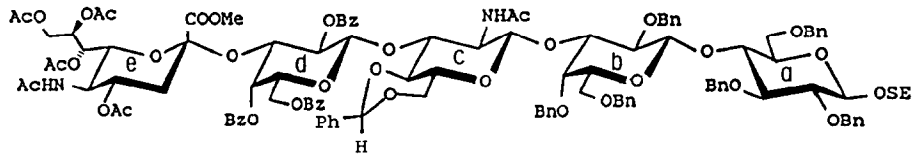
zylidene groups in **16** and subsequent *O*-acetylation gave the pentasaccharide derivative **17** (62.4%). Hydrogenolysis of the benzyl and 4-methoxybenzyl groups in **20** followed by acetylation gave **21** (59.7%). Treatment of compound **17** or **21** with boron trifluoride etherate in dichloromethane for 24 h at 0° gave the corresponding 1-hydroxy compounds **18** and **22** in high yields. Treatment[19,20] of **18** or **22** with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 4 h at 0° gave the corresponding α-trichloroacetimidates **19** (88%) and **23** (87.2%) after column chromatography. Significant signals in the ^{1}H-n.m.r. spectra were at δ 6.48 (d, $J_{1,2}$ 3.8 Hz, H-1) and 8.65 (C=NH) for **19**, and at δ 6.47 (d, $J_{1,2}$ 3.3 Hz, H-1) and 8.64 (C=NH) for **23**, which showed the imidates to be α.

Glycosylation[20,21] of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[22] (**24**) with **19** or **23** in dichloromethane in the presence of boron trifluoride etherate for 8 h at 0° afforded the corresponding β-glycosides **25** (55.3%) and **29** (41.5%). Selective reduction[23,24] of the azide group in **25** or **29** with hydrogen sulfide in aqueous 83% pyridine for 48 h at room temperature gave the corresponding amines (**26** and **30**), which, on condensation with octadecanoic acid, using 1-ethyl-3-(3-dimethylaminopropyl)carbodi-imide hydrochloride (WSC) in dichloromethane, gave the corresponding acylated gangliosides **27** (79.1%) and **31** (83.7%), after chromatography.

O-Deacylation of **27** and **31** with sodium methoxide in methanol, with subsequent saponification of the methyl ester group, yielded the desired sialyl-lactotetraosylcera-



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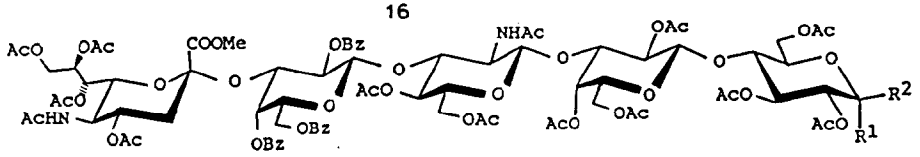
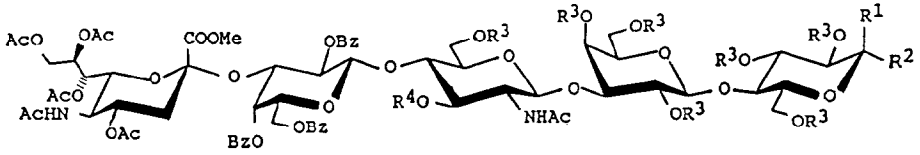


17 R^1 = H, R^2 = OSE
18 R^1, R^2 = H, OH
19 R^1 = OC(=NH)CCl_3, R^2 = H



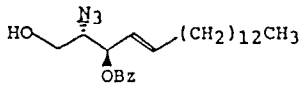
20 R^1 = H, R^2 = OSE, R^3 = Bn, R^4 = *p*MeOBn
21 R^1 = H, R^2 = OSE, R^3 = R^4 = Ac
22 R^1, R^2 = H, OH, R^3 = R^4 = Ac
23 R^1 = OC(=NH)CCl_3, R^2 = H, R^3 = R^4 = Ac

mide (**28**) and sialylneolactotetraosylceramide (**32**), respectively, in almost quantitative yields. The ^{1}H-n.m.r. spectra (400 MHz) of **28** and **32** at 60° in 98:2 $(CD_3)_2SO$–D_2O each contained four signals (d) due to the anomeric protons: **28** at δ 4.17 (J 7.7 Hz, H-1a), 4.19 (J 7.5 Hz, H-1d), 4.29 (J 7.5 Hz, H-1b), and 4.74 (J 8.4 Hz, H-1c); **32** (ref. 25) at δ 4.17 (J 7.7 Hz, H-1a), 4.22 (J 7.9 Hz, H-1d), 4.28 (J 7.0 Hz, H-1b), and 4.67 (J 8.2 Hz, H-1c).

The work described above shows that the use of thioglycosides in the presence of DMTST is effective for the synthesis of complex types of sialoglycoconjugates. The 2-(trimethylsilyl)ethyl group is useful for protecting the anomeric hydroxyl group because of the easy and selective deprotection with boron trifluoride etherate and its stability towards many reagents used in organocarbohydrate syntheses.

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Union PM-201 polarimeter at 25° and i.r. spectra were recorded with a Jasco IRA-100 spectrophotometer. ^{1}H-N.m.r. spectra were recorded at 270 or 400 MHz with a JEOL



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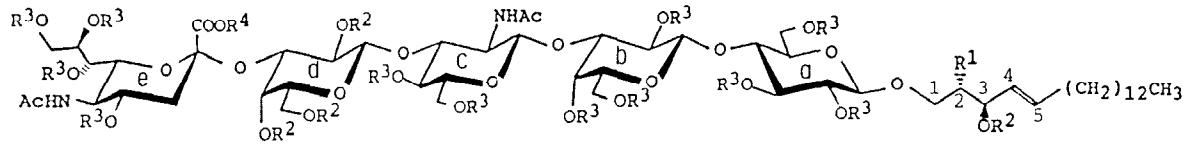
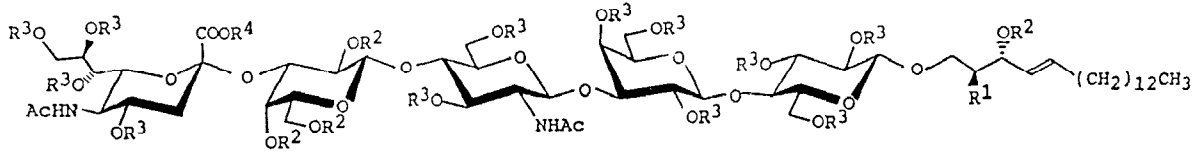


25 $R^1 = N_3$, R^2 = Bz, R^3 = Ac, R^4 = Me
26 $R^1 = NH_2$, R^2 = Bz, R^3 = Ac, R^4 = Me
27 $R^1 = NHCO(CH_2)_{16}Me$, R^2 = Bz, R^3 = Ac, R^4 = Me
28 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = R^3 = R^4$ = H



29 $R^1 = N_3$, R^2 = Bz, R^3 = Ac, R^4 = Me
30 $R^1 = NH_2$, R^2 = Bz, R^3 = Ac, R^4 = Me
31 $R^1 = NHCO(CH_2)_{16}Me$, R^2 = Bz, R^3 = AC, R^4 = Me
32 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = R^3 = R^4$ = H

JNM-GX270 or JNM-GX400 spectrometer, respectively. Preparative chromatography was performed on silica gel (Wako Co., 200 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

2-(Trimethylsilyl)ethyl O-*(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-*galactopyranoside* (**2**). — To a solution of **1** (ref. 9) (1.2 g, 1.4 mmol) in dichloromethane (10 mL) was added, with stirring, a solution of benzoyl chloride (0.68 mL, 5.56 mmol) in dichloromethane (4 mL) at 15°. After completion of the reaction, methanol (1 mL) was added, and the mixture was stirred for 20 min at room temperature, concentrated, and extracted with dichloromethane. The extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (Na_2SO_4), and concentrated. Column chromatography (3:1 ethyl acetate–hexane) of the residue on silica gel (60 g) gave **2** (900 mg, 60.3%), isolated as a syrup, $[\alpha]_D$ +24° (*c* 0.77, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 0.99 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.56 (s, 3 H, AcN), 1.86, 2.00, 2.16, 2.26 (4 s, 12 H, 4 AcO), 1.76 (t, 1 H, $J_{gem} = J_{3'ax,4'} = 12.4$ Hz, H-3′*ax*), 2.75 (dd, 1 H, $J_{3'eq,4'}$ 4.6 Hz, H-3′*eq*), 3.93 (s, 3 H, MeO), 4.92 (m, 1 H, H-4), 4.95 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 5.17 (d, 1 H, $J_{NH,5}$ 7.3 Hz, NH), 5.30 (dd, 1 H, $J_{6',7'}$ 2.6, $J_{7',8'}$ 9.7 Hz, H-7′), 5.46 (d, 1 H, $J_{3,4} = J_{4,5} =$ 3.3 Hz, H-4), 5.53 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2), 5.73 (m, 1 H, H-8′), and 7.36–8.28 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{52}H_{63}NO_{21}Si$ (1066.2): C, 58.58; H, 5.95; N, 1.31. Found: C, 58.55; H, 6.15; N, 1.28.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)-1*-O-*acetyl-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranose* (**3**). — To a solution of **2** (1.84 g, 1.72 mmol) in dry toluene (10 mL) and acetic anhydride (2.6 mL) was added boron trifluoride etherate (0.45 mL), and the mixture was stirred at room temperature. The reaction was monitored by t.l.c. and, after 2 h, **2** was not detectable. Dichloromethane (50 mL) was added, and the solution was washed with M sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (50:1 dichloromethane–methanol) of the residue on silica gel (100 g) afforded **3** (1.61 g, 92.5%), isolated as a syrup, $[\alpha]_D$ +41° (*c* 0.93, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.56 (s, 3 H, AcN), 1.74 (t, 1 H, $J_{gem} = J_{3',4'} = 12.4$ Hz, H-3′*ax*), 1.86, 2.01, 2.10, 2.19, 2.27 (5 s, 15 H, 5 AcO), 2.57 (dd, 1 H, $J_{3',4'}$ 4.5 Hz, H-3′*eq*), 3.72 (dd, 1 H, $J_{5',6'}$ 10.6, $J_{6',7'}$ 2.6 Hz, H-6′), 4.90 (m, 1 H, H-4′), 5.13 (dd, 1 H, $J_{2,3}$ 10.1, $J_{3,4}$ 3.3 Hz, H-3), 5.29 (dd, 1 H, $J_{7',8'}$ 9.2 Hz, H-7′), 5.52 (d, 1 H, $J_{4,5}$ 3.3 Hz, H-4), 5.66 (dd, 1 H, H-2), 5.70 (m, 1 H, H-8′), 6.25 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), and 7.36–8.23 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{49}H_{53}NO_{22}$ (1008.0): C, 58.38; H, 5.29; N, 1.38. Found: C, 58.21; H, 5.34; N, 1.36.

Methyl O-*(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* (**4**). — To a solution of **3** (1.61 g, 1.59 mmol) in dry dichloromethane (10 mL) were added, with stirring, methylthiotrimethylsilane (480 mg, 4.0 mmol) and boron trifluoride etherate (0.4 mL), and the mixture was stirred for 2 h at room temperature. Dichloromethane (50 mL) was added, and the solution was washed with M sodium

hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (80:1 dichloromethane–methanol) of the residue on silica gel (100 g) gave **4** (1.3 g, 81.7%), isolated as a syrup, $[\alpha]_D$ +34° (*c* 0.72, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.48 (s, 3 H, AcN), 1.66 (t, 1 H, $J_{gem} = J_{3',ax,4'}$ = 12.6 Hz, H-3′*ax*), 1.78, 1.92, 2.08, 2.17, 2.27 (5 s, 15 H, 4 AcO and MeS), 2.48 (dd, 1 H, $J_{3'eq,4'}$ 4.6 Hz, H-3*eq*), 3.84 (s, 3 H, MeO), 4.82 (m, 1 H, H-4′), 4.84 (d, 1 H, $J_{1,2}$ 9.9 Hz, H-1), 4.94 (dd, 1 H, $J_{2,3}$ 9.9, $J_{3,4}$ 3.3 Hz, H-3), 5.22 (dd, 1 H, $J_{6',7'}$ 2.6, $J_{7',8'}$ 9.5 Hz, H-7′), 5.44 (d, 1 H, $J_{4,5}$ 3.3 Hz, H-4), 5.57 (t, 1 H, H-2), 5.62 (m, 1 H, H-8′), and 7.39–8.17 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{48}H_{53}NO_{20}S$ (996.0): C, 57.88; H, 5.36; N, 1.40. Found: C, 57.69; H, 5.43; N, 1.35.

2-(Trimethylsilyl)ethyl O-*[3*-O-*(4-methoxybenzyl)*-β-D-*galactopyranosyl]*-*(1→4)*-β-D-*glucopyranoside* (**6**). — A suspension of **5** (refs. 9 and 15) (2.8 g, 6.33 mmol) and dibutyltin oxide (2.38 g) in methanol (28 mL) was stirred and heated for 4 h at 45°, then concentrated. To a solution of the residue in benzene (28 mL) were added 4-methoxybenzyl chloride (2.58 mL), tetrabutylammonium bromide (1.05 g), and molecular sieves 4 Å (2.8 g), and the mixture was stirred and boiled under reflux for 3 h, then concentrated. Column chromatography (30:1 dichloromethane–methanol) of the residue on silica gel (200 g) gave **6** (2.65 g, 74%). Recrystallization from ether gave needles with m.p. 183.5–184.5°, $[\alpha]_D$ −3.2° (*c* 1, 1:1 dichloromethane–methanol). ^{1}H-N.m.r. data ($CDCl_3$): δ 3.36 (m, 1 H, H-5), 3.45 (dd, 1 H, $J_{2',3'}$ 10.1, $J_{3',4'}$ 3.5 Hz, H-3′), 3.76 (m, 1 H, H-5′), 3.80 (s, 3 H, MeO), 4.29, 4.59 (2 d, J_{gem} 11.8 Hz, MeOPhCH_2O), 4.36 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.46 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′), 4.86 (t, 1 H, $J_{2,3}$ 7.8 Hz, H-2), 4.99 (dd, 1 H, $J_{2',3'}$ 10 Hz, H-2′), 5.17 (dd, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 5.44 (dd, 1 H, $J_{4',5'}$ 3.3 Hz, H-4′), and 6.86 and 7.15 (2 d, 4 H, *J* 7.7 Hz, aromatic).

Anal. Calc. for $C_{25}H_{42}O_{12}Si$ (562.7): C, 53.36; H, 7.52. Found: C, 53.29; H, 7.60.

2-(Trimethylsilyl)ethyl O-*[2,4,6-tri*-O-*benzyl-3*-O-*(4-methoxybenzyl)*-β-D-*galactopyranosyl]*-*(1→4)*-*2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**7**). — To a solution of **6** (3.05 g, 5.4 mmol) in *N*,*N*-dimethylformamide (20 mL) was added a suspension of sodium hydride in oil (1.95 g, 60% of sodium hydride by weight). The mixture was stirred for 30 min at 0°, benzyl bromide (5.8 mL, 8.1 mmol) was added dropwise, and stirring was continued for 16 h at room temperature. The reaction was monitored by t.l.c. and, when complete, methanol (1 mL) was added, and the mixture was concentrated and extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (1:6 ethyl acetate–hexane) of the residue on silica gel (300 g) gave **7** (4.75 g, 79.4%), isolated as a syrup, $[\alpha]_D$ −7.5° (*c* 0.4, dichloromethane). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2O$), 3.75 (s, 3 H, MeO), and 6.79–7.33 (m, 34 H, 6 Ph and 4 aromatic).

Anal. Calc. for $C_{67}H_{78}O_{12}Si$ (1103.4): C, 72.93; H, 7.12. Found: C, 72.81; H, 7.15.

2-(Trimethylsilyl)ethyl O-*(2,4,6-tri*-O-*benzyl*-β-D-*galactopyranosyl)*-*(1→4)*-*2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**8**). — To a stirred solution of **7** (4.74 g, 4.3 mmol) in dichloromethane (54 mL) were added 2,3-dichloro-5,6-dicyanobenzoquinone (1.46 g, 6.4 mmol) and water (3 mL), and stirring was continued for 1 h at room temperature. The precipitate was collected and washed with dichloromethane, and the

combined filtrate and washings were washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (1:5 ethyl acetate–hexane) of the residue on silica gel (200 g) gave **8** (2.94 g, 69.6%), isolated as a syrup, $[\alpha]_D$ +0.2° (*c* 0.8, dichloromethane); ν_{max} 3450 cm^{-1} (OH). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$) and 7.10–7.33 (m, 30 H, 6 Ph).

Anal. Calc. for $C_{59}H_{70}O_{11}Si$ (983.3): C, 72.06; H, 7.17. Found: C, 72.05; H, 7.23.

2-(Trimethylsilyl)ethyl O-*(3,4,6-tri*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*benzyl-β-*D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-*D-*glucopyranoside* (**10**). — To a solution of **8** (2.9 g, 2.9 mmol) in dichloromethane (7 mL) were added silver carbonate (1.7 g, 6.2 mmol), silver perchlorate (1.3 g, 6.3 mmol), and powdered molecular sieves 4 Å (3.0 g), and the mixture was stirred for 20 h at room temperature in the dark (mixture *A*). A solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide (**9**; 3.2 g, 6.4 mmol) in dichloromethane (7 mL) was treated with powdered molecular sieves 4 Å (3 g) as above and then added to mixture *A* at room temperature. After vigorous stirring for 16 h, the precipitate was collected and washed with dichloromethane, and the combined filtrate and washings were concentrated. Column chromatography (1:2 ethyl acetate–hexane) of the residue on silica gel (200 g) afforded **10** (3.87 g, 93.7%), isolated as a syrup, $[\alpha]_D$ −3.7° (*c* 1.1, chloroform); ν_{max} 1750 and 1230 (ester), 1720 (imide), 860 and 840 (Me_3Si), and 740, 720, and 700 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.01 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.84, 1.98, 2.05 (3 s, 9 H, 3 AcO), 4.13 (d, 1 H, $J_{1a,2a}$ 7.1 Hz, H-1a), 5.15 (t, 1 H, $J_{2c,3c} = J_{3c,4c}$ = 9.3 Hz, H-3c), 5.63 (d, 1 H, $J_{1c,2c}$ 8.4 Hz, H-1c), 5.87 (dd, 1 H, $J_{4c,5c}$ 10.6 Hz, H-4c), and 6.90–7.34 (m, 34 H, 6 Ph, phthaloyl-H).

Anal. Calc. for $C_{79}H_{89}NO_{20}Si$ (1400.7): C, 67.74; H, 6.40; N, 1.00. Found: C, 67.59; H, 6.60; N, 0.97.

2-(Trimethylsilyl)ethyl O-*(2-acetamido-2-deoxy-β-*D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri-O-benzyl-β-*D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-*D-*glucopyranoside* (**12**). — A solution of **10** (3.87 g, 2.76 mmol) in methanol (15 mL) was stirred with sodium methoxide (100 mg) for 2 h at room temperature. The mixture was treated with Amberlite IR-120 (H^+) resin and concentrated, and a solution of the residue (**11**) in aqueous 95% ethanol (40 mL) was treated with hydrazine hydrate (1 mL) for 2 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 (1 mL) in methanol (50 mL) for 2 h at room temperature, pyridine (1.5 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was washed with 2M hydrochloric acid, water, and M sodium carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (4:1 ethyl acetate–hexane) of the residue on silica gel (200 g) gave **12** (2.9 g, 88.4%), isolated as a syrup, $[\alpha]_D$ −7.3° (*c* 0.41, dichloromethane); ν_{max} 3400 (OH), 1680 and 1560 (amide), 860 and 840 (Me_3Si), and 750 and 700 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.63 (s, 3 H, AcN), and 7.10–7.34 (m, 30 H, 6 Ph).

Anal. Calc. for $C_{67}H_{83}NO_{16}Si$ (1186.5): C, 67.82; H, 7.05; N, 1.18. Found: C, 67.59; H, 7.20; N, 1.21.

2-(Trimethylsilyl)ethyl O-*(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-*D*-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**13**). — To a solution of **12** (2.9 g, 2.44 mmol) in *N,N*-dimethylformamide (15 mL) were added benzaldehyde dimethyl acetal (0.73 mL, 4.88 mmol), toluene-*p*-sulfonic acid monohydrate (30 mg), and Drierite (3.0 g). The mixture was stirred for 16 h at room temperature, then neutralised with Amberlite IR-410 (HO^-) resin, and concentrated. Column chromatography (4:1 ethyl acetate–hexane) of the residue on silica gel (150 g) gave **13** (2.6 g, 83.4%), isolated as a syrup, $[\alpha]_D$ −23° (*c* 1, dichloromethane). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.64 (s, 3 H, AcN), 5.57 (s, 1 H, PhC*H*), and 7.13–7.51 (m, 35 H, 7 Ph).

Anal. Calc. for $C_{74}H_{87}NO_{16}Si$ (1274.6): C, 69.73; H, 6.87; N, 1.09. Found: C, 69.64; H, 6.98; N, 1.05.

2-(Trimethylsilyl)ethyl O-*[2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(4-methoxybenzyl)-β-*D*-glucopyranosyl]-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**14**). — To a solution of **13** (1.27 g, 0.99 mmol) in *N,N*-dimethylformamide (5 mL) was added a suspension of sodium hydride in oil (44 mg, 1.01 mmol; 60% of sodium hydride by weight) at 0°, and the mixture was stirred for 20 min at 0°. 4-Methoxybenzyl chloride (0.17 mL, 1.28 mmol) was added dropwise, and the mixture was stirred for 3 h at room temperature. The solvent was evaporated, the residue was extracted with dichloromethane, and the extract was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (1:3 ethyl acetate–hexane) of the residue on silica gel (200 g) gave **14** (1.12 g, 79.6%), isolated as a syrup, $[\alpha]_D$ −11° (*c* 0.72, dichloromethane). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.44 (s, 3 H, AcN), 3.76 (s, 3 H, MeO), 5.57 (s, 1 H, PhC*H*), and 6.78–7.49 (m, 39 H, 7 Ph, MeO*Ph*).

Anal. Calc. for $C_{82}H_{95}NO_{17}Si$ (1394.7): C, 70.61; H, 6.86; N, 1.00. Found: C, 70.49; H, 6.95; N, 0.98.

2-(Trimethylsilyl)ethyl O-*[2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-β-*D*-glucopyranosyl]-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**15**). — To a solution of **14** (1.02 g, 0.72 mmol) in dry tetrahydrofuran (5 mL) were added powdered molecular sieves 3 Å (2.0 g), the mixture was stirred for 4 h at room temperature, and sodium cyanoborohydride (910 mg) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. T.l.c. indicated that the reaction was complete after 5 min. The mixture was diluted with dichloromethane (50 mL) and water (10 mL), filtered, washed with water and M sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (1:1 ethyl acetate–hexane) of the residue on silica gel (70 g) gave **15** (540 mg, 52.8%), isolated as a syrup, $[\alpha]_D$ −5.1° (*c* 0.98, chloroform); ν_{max} 3400 (OH), 1670 and 1550 (amide), 860 and 840 (Me_3Si), and 740 and 700 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.47 (s, 3 H, AcN), and 3.77 (s, 3 H, MeO), and 6.81–7.31 (m, 39 H, 7 Ph, MeO*Ph*).

Anal. Calc. for $C_{82}H_{97}NO_{17}Si$ (1396.8): C, 70.51; H, 6.99; N, 1.00. Found: C, 70.49; H, 7.15; N, 1.03.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzyl-β*-D-*galactopyranosyl)-(1→3)*-O-*(2-acetamido-4,6*-O-*benzylidene-2-deoxy-β*-D-*glucopyranosyl-(1→3)*-O-*(2,4,6-tri*-O-*benzyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**16**). — To a solution of **4** (472 mg, 0.47 mmol) and **13** (400 mg, 0.31 mmol) in dichloromethane (12 mL) were added powdered molecular sieves 4 Å (1.5 g), and the mixture was stirred for 5 h at room temperature, then cooled to 0°. A mixture of dimethyl(methylthio)sulfonium triflate (DMTST; 490 mg, 1.89 mmol) and molecular sieves 4 Å (500 mg) was added, the mixture was stirred for 12 h at 0°, and the reaction was monitored by t.l.c. The precipitate was collected and washed with dichloromethane, and the combined filtrate and washings were washed with M sodium hydrogen carbonate and water, dried (Na_2SO_4), and concentrated. Column chromatography (4:1 ethyl acetate–hexane) of the residue on silica gel (60 g) gave amorphous **16** (607 mg, 87%), $[\alpha]_D$ +0.37° (*c* 0.79, chloroform); ν_{max} 3400 (NH), 1740 and 1230 (ester), 1680 and 1540 (amide), 860 and 840 (Me_3Si), and 740 and 720 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): δ 0.88, 1.45 (2 s, 6 H, 2 AcN), 0.99 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.59 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.4 Hz, H-3e-*ax*), 1.79, 1.89, 2.02, 2.14 (4 s, 12 H, 4 AcO), 2.42 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.6 Hz, H-3e-*eq*), 3.79 (s, 3 H, MeO), 4.91 (dd, 1 H, $J_{2d,3d}$ 10.0, $J_{3d,4d}$ 2.9 Hz, H-3d), 5.12 (d, 1 H, $J_{1d,2d}$ 8.0 Hz, H-1d), 5.20 (dd, 1 H, $J_{6e,7e}$ 2.6, $J_{7e,8e}$ 9.7 Hz, H-7e), 5.29 (dd, 1 H, $J_{4d,5d}$ 2.9 Hz, H-4d), 5.37 (dd, 1 H, H-2d), 5.56 (s, 1 H, PhC*H*), and 7.08–8.19 (m, 50 H, 10 Ph).

Anal. Calc. for $C_{121}H_{136}N_2O_{36}Si$ (2222.5): C, 65.39; H, 6.16; N, 1.26. Found: C, 65.28; H, 6.25; N, 1.23.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→3)*-O-*(2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranoside* (**17**). — A solution of **16** (380 mg, 0.17 mmol) in ethanol (70 mL) and formic acid (2 mL) was hydrogenolysed in the presence of 10% Pd–C (560 mg) for 48 h at 45°, then filtered, and concentrated. The residue was heated in aqueous 80% acetic acid for 16 h at 45°. The solution was concentrated, and the residue was treated with acetic anhydride (3 mL) and pyridine (5 mL) by heating for 16 h at 45°. Column chromatography (50:1 dichloromethane–methanol) of the product on silica gel (50 g) gave amorphous **17** (206 mg, 62.4%), $[\alpha]_D$ +10° (*c* 1.26, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 0.90 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.62 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.3 Hz, H-3e-*ax*), 1.53, 1.77 (2 s, 6 H, AcN), 1.90–2.15 (11 s, 36 H, 12 AcO), 2.44 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.7 Hz, H-3e-*eq*), 3.81 (s, 3 H, MeO), 4.98 (d, 1 H, $J_{1d,2d}$ 9.7 Hz, H-1d), 5.63 (m, 1 H, H-8e), and 7.40–8.19 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{88}H_{112}N_2O_{44}Si$ (1929.9): C, 54.76; H, 5.84; N, 1.45. Found: C, 54.68; H, 5.93; N, 1.42.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-

2-nonulopyranosylonate)-(2→3)-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→3)*-O-*(2-acetamido-4,6-di*-O-*acetyl-2-deoxy)-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-D-*glucopyranose* (**18**). — To a solution of **17** (210 mg, 0.108 mmol) in dichloromethane (5 mL) was added boron trifluoride etherate (0.14 mL). The mixture was stirred for 24 h at 0°, then diluted with dichloromethane (50 mL), washed with M sodium carbonate and water, dried (Na_2SO_4), and concentrated. Column chromatography (30:1 dichloromethane–methanol) of the residue on silica gel (40 g) gave amorphous **18** (173 mg, 86.7%), $[\alpha]_D$ +30° (*c* 0.82, chloroform); ν_{max} 3400 (NH, OH), 1740 and 1230 (ester), 1680 and 1540 (amide), and 720 cm^{-1} (Ph).

Anal. Calc. for $C_{83}H_{100}N_2O_{44}$ (1829.7): C, 54.48; H, 5.50; N, 1.53. Found: C, 54.35; H, 5.54; N, 1.49.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→3)*-O-*(2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl trichloroacetimidate* (**19**). — To a solution of **18** (172 mg, 0.09 mmol) in dichloromethane (1.5 mL) and trichloroacetonitrile (0.27 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 14 mg) at −5°, and the mixture was stirred for 4 h at 0°, then concentrated. Column chromatography (30:1 dichloromethane–methanol) of the residue on silica gel (20 g) afforded amorphous **19** (163 mg, 88%), $[\alpha]_D$ +39° (*c* 0.69, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.53, 1.77 (2 s, 6 H, 2 AcN), 1.62 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.4 Hz, H-3e-*ax*), 1.90–2.15 (12 s, 36 H, 12 AcO), 2.43 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.6 Hz, H-3e-*eq*), 3.81 (s, 3 H, MeO), 5.51 (t, 1 H, $J_{1d,2d} = J_{2d,3d}$ = 9.5 Hz, H-2d), 5.62 (m, 1 H, H-8e), 6.48 (d, 1 H, $J_{1a,2a}$ 3.8 Hz, H-1a), 7.30–8.19 (m, 15 H, 3 Ph), and 8.65 (s, 1 H, C=NH).

Anal. Calc. for $C_{85}H_{100}Cl_3N_3O_{44}$ (1974.1): C, 51.71; H, 5.10; N, 2.12. Found: C, 51.58; H, 5.32; N, 2.15.

2-(Trimethylsilyl)ethyl O-*(methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→4)*-O-*[2-acetamido-6*-O-*benzyl-2-deoxy-3*-O-*(4-methoxybenzyl)-β*-D-*glucopyranosyl]-(1→3)*-O-*(2,4,6-tri*-O-*benzyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β*-D-*glucopyranoside* (**20**). — Glycosidation of **4** (454 mg, 0.455 mmol) with **15** (430 mg, 0.304 mmol), as described for the synthesis of **16**, gave amorphous **20** (637 mg, 71.9%), $[\alpha]_D$ +7.5° (*c* 1.1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.00 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.44, 1.49 (2 s, 6 H, 2 AcN), 1.78, 1.91, 1.96, 2.14 (4 s, 12 H, 4 AcO), 2.46 (dd, 1 H, J_{gem} 12.4, $J_{3e\text{-}eq,4e}$ 4.5, H-3e-*eq*), 3.64 (s, 3 H, *Me*OPh), 3.82 (s, 3 H, MeO), 5.07 (d, 1 H, $J_{1d,2d}$ 8.1 Hz, H-1d), 5.22 (dd, 1 H, $J_{6e,7e}$ 2.6, $J_{7e,8e}$ 9.7 Hz, H-7e), 5.37 (bt, 1 H, $J_{3d,4d} = J_{4d,5d}$ = 2.8 Hz, H-4d), 5,48 (dd, 1 H, $J_{2d,3d}$ 9.5 Hz, H-2d), 5.67 (m, 1 H, H-8e), and 6.58–8.23 (m, 54 H, 10 Ph, MeO*Ph*).

Anal. Calc. for $C_{129}H_{146}N_2O_{37}Si$ (2344.7): C, 66.08; H, 6.27; N, 1.19. Found: C, 65.86; H, 6.29; N, 1.15.

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

lactopyranosyl)-(1→4)-O-*(2-acetamido-3,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl-β*-D-*glucopyranoside* (**21**). — A solution of **20** (520 mg, 0.22 mmol) in ethanol (70 mL) and formic acid (4 mL) was stirred with 10% Pd–C (980 mg) for 48 h at 45° under hydrogen. The catalyst was collected and washed with methanol, the combined filtrate and washings were concentrated, the residue was heated with acetic anhydride (6 mL) and pyridine (8 mL) for 16 h at 45°, and the mixture was concentrated. Column chromatography (50:1 dichloromethane–methanol) of the reisidue on silica gel (50 g) gave amorphous **21** (260 mg, 59.4%), $[\alpha]_D$ +11° (*c* 0.87, chloroform), ^{1}H-N.m.r. data ($CDCl_3$): δ 1.26 (m, 2 H, $Me_3SiCH_2CH_2O$), 1.52–2.12 (14 s, 42 H, 12 AcO, 2 AcN), 2.46 (dd, 1 H, J_{gem} 12.4, $J_{3e\text{-}eq,4e}$ 4.5 Hz, H-3e-*eq*), 3.80 (s, 3 H, MeO), 5.63 (m, 1 H, H-8e), and 7.43–8.19 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{88}H_{112}N_2O_{44}Si$ (1929.9): C, 54.76; H, 5.84; N, 1.45. Found: C, 54.65; H, 5.99; N, 1.31.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2-acetamido-3,6-di*-O-*(acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*acetyl*-D-*glucopyranose* (**22**). — To a cooled solution of **21** (177 mg, 0.09 mmol) in dichloromethane (4 mL) was added boron trifluoride etherate (0.16 mL), and the mixture was stirred for 8 h at 0° and then worked-up, as described for **18**, to give amorphous **22** (131.7 mg, 78.3%), $[\alpha]_D$ +29° (*c* 1.26, chloroform); ν_{max} 3400 (NH, OH), 1740 and 1230 (ester), 1670 and 1540 (amide), and 720 cm^{-1} (Ph). The ^{1}H-N.m.r. data ($CDCl_3$) showed the loss of the 2-(trimethylsilyl)-ethyl group.

Anal. Calc. for $C_{83}H_{100}N_2O_{44}$ (1829.7): C, 54.48; H, 5.50; N, 1.53. Found: C, 54.45; H, 5.64; N, 1.52.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2-acetamido-3,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl-(1→4)-2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl trichloroacetimidate* (**23**). — A solution of **22** (131 mg, 0.07 mmol) in dichloromethane (1 mL) was treated with trichloroacetonitrile (0.2 mL) and DBU (11 mg), as described for **19**, to give amorphous **23** (123 mg, 87.2%), $[\alpha]_D$ +43° (*c* 0.39, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.53, 1.77 (2 s, 6 H, 2 AcN), 1.59 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.4 Hz, H-3e-*ax*), 1.90–2.12 (12 s, 36 H, 12 AcO), 2.46 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.6 Hz, H-3e-*eq*), 3.80 (s, 3 H, MeO), 5.62 (m, 1 H, H-8e), 6.47 (d, 1 H, $J_{1a,2a}$ 3.3 Hz, H-1a), 7.29–8.18 (m, 15 H, 3 Ph), and 8.64 (s, 1 H, C=NH).

Anal. Calc. for $C_{85}H_{100}Cl_3N_3O_{44}$ (1974.1): C, 51.71; H, 5.10; N, 2.12. Found: C, 51.62; H, 5.25; N, 2.09.

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

syl)-(1→1)-(2S,3R,4E)-2-azido-3-O-benzoyl-4-octadecene-1,3-diol (**25**). — To a solution of **19** (162 mg, 0.08 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[22] (**24**; 68 mg, 0.16 mmol) in dichloromethane (3 mL) were added powdered molecular sieves 4 Å (AW-300, 1.6 g), and the mixture was stirred for 5 h at room temperature, then cooled to 0°. Boron trifluoride etherate (0.05 mL) was added, and the mixture was stirred for 8 h at 0° and then filtered. The insoluble material was washed with dichloromethane, and the combined filtrate and washings were washed with M sodium hydrogen carbonate and water, dried (Na_2SO_4), and concentrated. Column chromatography (50:1 dichloromethane–methanol) of the residue on silica gel (30 g) gave amorphous **25** (101.3 mg, 55.3%), $[\alpha]_D$ +6.5° (*c* 1, chloroform); ν_{max} 3400 (NH), 2100 (N_3), 1750 and 1230 (ester), 1680 and 1540 (amide), and 710 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): (aglycon) δ 0.88 (t, 3 H, CH_3), 1.24 (s, 22 H, 11 CH_2), 5.91 (m, 1 H, $J_{4,5}$ 13.8, $J_{5,6} = J_{5,6'}$ = 7.3 Hz, H-5); (pentasaccharide) δ 1.53; 1.77 (2 s, 6 H, 2 AcN), 1.62 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.4 Hz, H-3e-*ax*), 1.90–2.15 (12 s, 36 H, 12 AcO), 2.44 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.3 Hz, H-3e-*eq*), 3.80 (s, 3 H MeO), and 7.40–8.19 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{108}H_{137}N_5O_{47}$ (2241.3): C, 57.87; H, 6.16; N, 3.12. Found: C, 57.61; H, 6.23; N, 3.05.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-α-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri-O-benzoyl-β-*D-*galactopyranosyl)-(1→3)*-O-*(2-acetamido-4,6-di*-O-*acetyl-2-deoxy-β-*D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-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* (**27**). — Hydrogen sulfide was bubbled through a stirred solution of **25** (100 mg, 44.6 μmol) in aqueous 83% pyridine (12 mL) for 48 h at room temperature. The reaction was monitored by t.l.c. The mixture was concentrated, and the residue (**26**) was stirred with octadecanoic acid (25 mg, 87.8 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC; 25 mg, 130 μmol) in dry dichloromethane (3 mL) for 16 h at room temperature. Dichloromethane (50 mL) was added, and the mixture was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (50:1 dichloromethane–methanol) of the residue on silica gel (20 g) gave amorphous **27** (87.6 mg, 79.1%), $[\alpha]_D$ +14° (*c* 0.87, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): (ceramide) δ 0.87 (t, 6 H, 6.1 Hz, 2 CH_3), 1.25 (~s, 50 H, 25 CH_2), 1.60 (m, 2 H, $COCH_2CH_2$), 5.74 (d, 1 H, $J_{NH,CH}$ 8.9 Hz, NH), and 5.85 (m, 1 H, $J_{4,5}$ 14.1, $J_{5,6} = J_{5,6'}$ = 7.3 Hz, H-5); (pentasaccharide) δ 1.52, 1.77 (2 s, 6 H, 2 AcN), 1.9–2.15 (12 s, 36 H, 12 AcO), 2.45 (dd, 1 H, J_{gem} 13.0, $J_{3e\text{-}eq,4e}$ 4.5 Hz, H-3e-*eq*), 3.80 (s, 3 H, MeO), and 5.61 (m, 1 H, H-8e), and 7.40–8.18 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{126}H_{173}N_3O_{47}$ (2481.8): C, 60.98; H, 7.02; N, 1.69. Found: C, 60.71; H, 7.12; N, 1.65.

Sialyl-lactotetraosylceramide (**28**). — To a solution of **27** (87.6 mg, 35.3 mmol) in methanol (5 mL) was added sodium methoxide (20 mg), the mixture was stirred for 24 h at 40°, and water (0.5 mL) was added. The solution was stirred for 8 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin, and filtered, the resin was washed with 1:1 water–methanol, and the combined filtrate and washings were concen-

trated. Column chromatography (1:1 water–methanol) of the residue on Sephadex LH-20 (40 g) gave amorphous **28** (55.2 mg, quantitative), $[\alpha]_D$ −6.2° (*c* 1.09, water); ν_{max} 3500–3300 (OH, NH), 2940 and 2840 (methyl, methylene), 1720 (COOH), and 1660 and 1540 cm^{-1} (amide). ^{1}H-N.m.r. data [400 MHz, 60°, in 98:2 $(CD_3)_2SO$–D_2O]: (ceramide) δ 0.85 (t, 6 H, 2 CH_3), 1.24 (~s, 50 H, 25 CH_2), 1.46 (bm, 2 H, $COCH_2CH_2$), 1.94 (~q, 2 H, CH=CH-CH_2), 2.04 (t, 2 H, $COCH_2$), 5.37 (~dd, 1 H, $J_{3,4}$ 7.0, $J_{4,5}$ 15.4 Hz, H-4), and 5.55 (m, 1 H, $J_{5,6(6')}$ ~7 Hz, H-5); (pentasaccharide) δ 1.38 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12 Hz, H-3e-*ax*), 1.81, 1.88 (2 s, 6 H, 2 AcN), 2.76 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 5 Hz, H-3e-*eq*), 3.07 (~t, 1 H, *J* 7–8 Hz, H-2a), 3.88 (~d, 1 H, *J* 3 Hz, H-4b), 4.17 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.19 (d, 1 H, $J_{1d,2d}$ 7.5 Hz, H-1d), 4.29 (d, 1 H, $J_{1b,2b}$ 7.5 Hz, H-1b), and 4.74 (d, 1 H, $J_{1c,2c}$ 8.4 Hz, H-1c).

Anal. Calc. for $C_{73}H_{131}N_3O_{31}$ (1546.9): C, 56.68; H, 8.53; N, 2.71. Found: C, 56.48; H, 8.72; N, 2.50.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2-acetamido-3,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl)-(1→1)-(2*S,*3*R,*4*E*)-2-azido-3*-O-*benzoyl-4-octadecene-1,3-diol* (**29**). — Coupling of **23** (110 mg, 0.054 mmol) and **24** (46 mg, 0.1 mmol), as described for **25**, gave amorphous **29** (51.7 mg. 41.5%), $[\alpha]_D$ +5.4° (*c* 1.03, chloroform); ν_{max} 3400 (NH), 2950 and 2840 (methyl, methylene), 2100 (azide), 1740 and 1230 (ester), 1680 and 1540 (amide), and 710 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): (aglycon) δ 0.88 (t, 3 H, CH_3), 1.23 (s, 22 H, 11 CH_2), and 5.91 (m, 1 H, $J_{4,5}$ 14.0, $J_{5,6} = J_{5,6'}$ = 7.1 Hz, H-5); (pentasaccharide) δ 1.53, 1.77 (2 s, 6 H, 2 AcN), 1.63 (t, 1 H, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12.4 Hz, H-3e-*ax*), 1.88–2.12 (12 s, 36 H, 12 AcO), 2.46 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 4.4 Hz, H-3e-*eq*), 3.80 (s, 3 H, MeO), and 7.42–8.21 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{108}H_{137}N_5O_{46}$ (2241.3): C, 57.87; H, 6.16; N, 3.12. Found: C, 57.79; H, 6.25; N, 3.08.

O-*(Methyl 5-acetamido-4,7,8,9-tetra*-O-*acetyl-3,5-dideoxy*-D-glycero-*α*-D-galacto-*2-nonulopyranosylonate)-(2→3)*-O-*(2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2-acetamido-3,6-di*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)*-O-*(2,3,6-tri*-O-*acetyl-β*-D-*glucopyranosyl)-(1→1)-(2*S,*3*R,*4*E*)-3*-O-*benzoyl-2-octadecanamido-4-octadecene-1,3-diol* (**31**) — Selective reduction of the azide group in **29** (51 mg, 22.7 μmol) and subsequent coupling with octadecanoic acid (13 mg, 45.6 μmol), as described for **27**, afforded amorphous **31** (47.3 mg, 83.7%), $[\alpha]_D$ +12.3° (*c* 0.94, chloroform); ν_{max} 3300 (NH), 2940 and 2840 (methyl, methylene), 1740 and 1230 (ester), 1660 and 1530 (amide), and 700 cm^{-1} (Ph). ^{1}H-N.m.r. data ($CDCl_3$): (ceramide) δ 0.87 (t, 6 H, 2 CH_3), 1.25 (~s, 50 H, 25 CH_2), 1.60 (m, 2 H, $COCH_2CH_2$), 5.74 (d, 1 H, $J_{NH,CH}$ 8.8 Hz, NH), and 5.86 (m, 1 H, $J_{4,5}$ 14.2, $J_{5,6} = J_{5,6'}$ = 7.3 Hz, H-5); (pentasaccharide) δ 1.53, 1.77 (2 s, 6 H, 2 AcN), 1.88–2.12 (12 s, 36 H, 12 AcO), 2.46 (dd, 1 H, J_{gem} 12.6, $J_{3e\text{-}eq,4e}$ 4.2 Hz, H-3e-*eq*), 3.80 (s, 3 H, MeO), and 5.62 (m, 1 H, H-8e), and 7.41–8.18 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{126}H_{173}N_3O_{47}$ (2481.8): C, 60.98; H, 7.02; N, 1.69. Found: C, 60.79; H, 7.20; N, 1.63.

Sialylneolactotetraosylceramide (**32**). — Deacylation and saponification of **31** (47.3 mg, 19.0 μmol), as described for **28**, yielded amorphous **32** (26.3 mg, 89.2%), $[\alpha]_D$ −3.8° (*c* 0.79, water); ν_{max} 3500–3350 (OH, NH), 2940 and 2840 (methyl, methylene), 1715 (COOH), and 1660 and 1550 cm^{-1} (amide). ^{1}H-N.m.r. data [400 MHz, 60°, 98:2 $(CD_3)_2SO$–D_2O]: (ceramide) δ 0.85 (t, 6 H, 2 CH_3), 1.24 (~s, 50 H, 25 CH_2) 1.46 (bm, 2 H, $COCH_2CH_2$), 1.94 (~q, 2 H, CH=CH-CH_2), 2.04 (t, 2 H, $COCH_2$), 3.91 (t, 1 H, *J* 7.4 Hz, H-3), 5.37 (~dd, 1 H, $J_{3,4}$ 7.0, $J_{4,5}$ 15.4 Hz, H-4), and 5.55 (m, 1 H, $J_{5,6(6')}$ ~7 Hz, H-5); (pentasaccharide) δ 1.39 (t, $J_{gem} = J_{3e\text{-}ax,4e}$ = 12 Hz, H-3e-*ax*), 1.82, 1.89 (2 s, 6 H, 2 AcN), 2.76 (dd, 1 H, $J_{3e\text{-}eq,4e}$ 5 Hz, H-3e-*eq*), 3.06 (~t, 1 H, *J* 7–8 Hz, H-2a), 3.87 (~s, 1 H, H-4b), 4.17 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.22 (d, 1 H, $J_{1d,2d}$ 7.9 Hz, H-1d), 4.28 (d, 1 H, $J_{1b,2b}$ 7.0 Hz, H-1b), and 4.67 (d, 1 H, $J_{1c,2c}$ 8.2 Hz, H-1c).

Anal. Calc. for $C_{73}H_{131}N_3O_{31}$ (1546.9): C, 56.68; H, 8.53; N, 2.71. Found: C, 56.65; H, 8.61; N, 2.75.

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REFERENCES

1 A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, in press (1989).
2 H. Wiegandt (Ed.), *Glycolipids, New Comprehensive Biochemistry*, Vol. 10, Elsevier, Amsterdam, 1985, pp. 199–260.
3 S. Tsuji, T. Yamakawa, M. Tanaka, and Y. Nagai, *J. Neurochem.*, 50 (1988) 414–423.
4 E. C. Bremor, J. Schlessinger, and S. Hakomori, *J. Biol. Chem.*, 261 (1986) 2434–2440.
5 O. Nilsson, J.-E. Mansson, L. Lindholm, J. Holmgren, and L. Svennerholm, *FEBS Lett.*, 182 (1985) 398–402; J.-E. Mansson, P. Fredman, O. Nilsson, L. Lindholm, J. Holmgren, and L. Svennerholm, *Biochim. Biophys. Acta.*, 834 (1985) 110–117.
6 R. J. Wherret, *Biochim. Biophys. Acta*, 326 (1973) 63–73.
7 Y. Suzuki, Y. Nagao, H. Kato, M. Matsumoto, K. Nerome, K. Nakajima, and E. Nobusawa, *J. Biol. Chem.*, 261 (1986) 17057–17061.
8 H. Nojiri, S. Kitagawa, M. Nakamura, K. Kirito, Y. Enomoto, and M. Saito, *J. Biol. Chem.*, 263 (1988) 7443–7446.
9 T. Murase, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 184 (1988) c1-c4.
10 T. Murase, A. Kameyama, K. P. R. Kartha, H. Ishida, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 265–283.
11 P. Fügedi and P. J. Garegg, *Carbohydr. Res.*, 149 (1986) c9–c12; M. Ravenscroft, R. M. G. Roberts, and J. G. Tillett, *J. Chem. Soc., Perkin Trans. 2*, (1982) 1569–1572.
12 K. Jansson, T. Frejd, J. Kihlberg, and G. Magnusson, *Tetrahedron Lett.*, 27 (1986) 753–756; K. Jansson, S. Ahlfors, T. Frejd, J. Kihlberg, G. Magnusson, J. Dahmen, G. Noori, and K. Stenvall, *J. Org. Chem.*, 53 (1988) 5629–5647.
13 V. Pozsgay and H. J. Jennings, *Tetrahedron Lett.*, 28 (1987) 1375–1376.
14 M. E. Haque, T. Kikuchi, K. Yoshimoto, and Y. Tsuda, *Chem. Pharm. Bull.*, 33 (1985) 2243–2255; J. Alais, A. Maranduba, and A. Veyriéres, *Tetrahedron Lett.*, 24 (1983) 2383–2386.
15 K. P. R. Kartha, A. Kameyama, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 145–158.
16 Y. Oikawa, T. Tanaka, K. Horita, T. Yoshida, and O. Yonemitsu, *Tetrahedron Lett.*, 25 (1984) 5393–5396.

17 R. U. Lemieux, T. Takeda, and B. Y. Chung, *ACS Symp. Ser.*, 39 (1976) 90–115.
18 P. J. Garegg, H. Hultberg, and S. Wallin, *Carbohydr. Res.*, 108 (1982) 97–101.
19 M. Numata, M. Sugimoto, K. Koike, and T. Ogawa, *Carbohydr. Res.*, 163 (1987) 209–225.
20 R. R. Schmidt and G. Grundler, *Synthesis*, (1981) 885.
21 Y. Ito, M. Kiso, and A. Hasegawa, *J. Carbohydr. Chem.*, 8 (1989) 285–294.
22 M. Kiso, A. Nakamura, T. Tomita, and A. Hasegawa, *Carbohydr. Res.*, 158 (1986) 101–111; R. R. Schmidt and P. Zimmermann, *Angew. Chem. Int. Ed. Engl.*, 25 (1986) 725–726.
23 T. Adachi, Y. Yamada, I. Inoue, and M. Saneyoshi, *Synthesis*, (1977) 45–46; H. Paulsen, M. Schultz, J. D. Kamann, B. Waller, and H. Paar, *Liebigs Ann. Chem.*, (1985) 2028–2048.
24 T. Murase, H. Ishida, M. Kiso, and A. Hasegawa, *Carbohydr. Res.*, 188 (1989) 71–80.
25 S. B. Levery, E. Nudelman, R. Kannagi, F. W. Symington, N. H. Andersen, H. Clausen, M. Baldwin, and S. Hakomori, *Carbohydr. Res.*, 178 (1988) 121–144, and references therein.