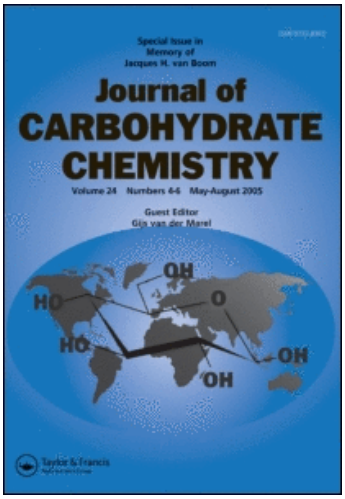

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 23: TOTAL SYNTHESIS OF SIALYL-α(2→6)-LACTOTETRAOSYLCERAMIDE AND SIALYL-α(2→6)-NEOLACTOTETRAOSYLCERAMIDE

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ABSTRACT

The first total syntheses of sialyl-α(2→6)-lactotetraosylceramide (29, $IV^6NeuAcLc_4Cer$) and sialyl-α(2→6)-neolactotetraosylceramide (33, $IV^6NeuAcnLc_4Cer$) 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→6)-2,4-di-O-benzoyl-3-O-benzyl-1-thio-ß-D-galactopyranoside (11), the key glycosyl donor was prepared, via glycosylation of 2-(trimethylsilyl)ethyl 3-O-benzyl-ß-D-galactopyranoside (2) with the methyl α-thioglycoside 3 of N-acetylneuraminic acid, benzoylation, replacement of the 2-(trimethylsilyl)ethyl group by acetyl, and introduction of the methylthio group with (methylthio)trimethylsilane. Each coupling of 2-(trimethylsilyl)ethyl O-(2-acetamido-4,6-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1→3')-per-O-benzyl-ß-lactoside (12) or 2-(trimethylsilyl)ethyl O-(2-acetamido-3-O-acetyl-6-O-benzyl-2-deozy-ß-D-glucopyranosyl)-(1→3')-per-O-benzyl-ß-D-lactoside (14) prepared from 12 by O-acetylation and reductive opening of the benzylidene acetal, with 11 gave the pentasaccharides 16 and 20 in good yields. Compounds 16 and 20 were converted into the corresponding α-trichloroacetimidates 19 and 24 which, on coupling with (2S,3R,4E)-2-azido-3-O-benzoyl-4-octadecene-1,3-diol (25), gave the ß-glycosides 26 and 30, respectively. Finally, 26 and 30 were transformed, via selective reduction of the azide group, condensation with octadecanoic acid, O-deacylation, and hydrolysis of the methyl ester group, into 29 and 33, respectively.

INTRODUCTION

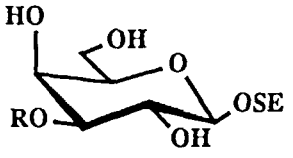
Recently, glycoconjugates, especially gangliosides which contain sialic acid as an essential constituent, have received much attention

owing to their important biological functions[1-5] in biological systems. Consequently, a facile, regio- and α-stereo-selective glycoside synthesis of sialic acid is critically important for the synthesis of a variety of gangliosides and their analogs, in order to investigate the functions of sialoglycoconjugates at the molecular level. Previously, we demonstrated[6,7] a new efficient α-glycosylation of sialic acids by use of dimethyl(methylthio)sulfonium triflate (DMTST)[8,9] as the glycosyl promoter and the suitably protected glycosyl acceptors in acetonitrile under kinetically controlled conditions, and accomplished[10-12] the synthesis of a variety of gangliosides and their analogs. As a part of our continuing efforts, on the synthesis and elucidation of the functions of gangliosides, we describe here the first total synthesis of sialyl-α(2-6)-lactotetraosylceramide 29 and sialyl-α(2-6)-neolactotetraosylceramide 33 which was isolated[13] as a minor component of human erythrocytes, and not only found[14] to be the major ganglioside in human neconium, but also found[15] in carcinomas of all organs and in different histopathological types of carcinomas such as small cell lung carcinomas and squamous lung carcinomas.

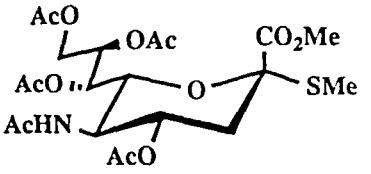
RESULTS AND DISCUSSION

Methyl O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2-6)-2,3,4-tri-O-benzoyl-1-thio-ß-D-galactopyranoside (7) and methyl O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2-6)-2,4-di-O-benzoyl-3-O-benzyl-1-thio-ß-D-galactopyranoside (11) were selected as the key glycosyl donors, and 2-(trimethylsilyl)ethyl O-(2-acetamido-4,6-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1-3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (12) and 2-(trimethylsilyl)ethyl O-(2-acetamido)-3-O-acetyl-6-O-benzyl-2-deoxy-ß-D-glucopyranosyl)-(1-3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (14) as the acceptors in the synthesis of the title gangliosides 29 and 33, respectively.

Treatment of 2-(trimethylsilyl)ethyl O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2-6)-O-benzoyl-ß-D-galactopyranoside[16] (4) prepared by dimethyl(methylthio)sulfonium triflate (DMTST)-promoted glycosylation of 2-(trimethylsilyl)ethyl 3-O-benzoyl-ß-D-galactopyranoside[16] (1) with the methyl α-thioglycoside[16] (3) of N-acetylneuraminic acid, with benzoyl chloride in pyridine-dichloromethane gave the tribenzoate 5, which, on treatment[17,18]

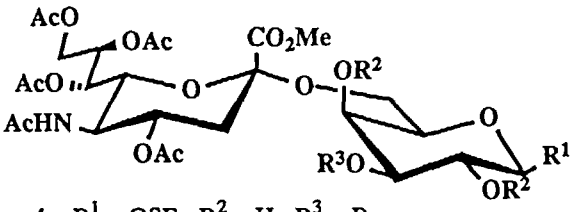


1 R = Bz
2 R = Bn

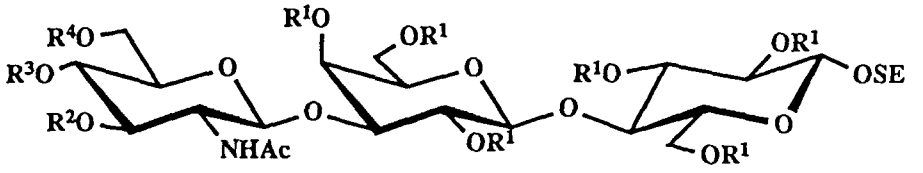


3

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



4 R^1 = OSE, R^2 = H, R^3 = Bz
5 R^1 = OSE, R^2 = R^3 = Bz
6 R^1 = OAc, R^2 = R^3 = Bz
7 R^1 = SMe, R^2 = R^3 = Bz
8 R^1 = OSE, R^2 = H, R^3 = Bn
9 R^1 = OSE, R^2 = Bz, R^3 = Bn
10 R^1 = OAc, R^2 = Bz, R^3 = Bn
11 R^1 = SMe, R^2 = Bz, R^3 = Bn



12 R^1 = Bn, R^2 = H, R^3 , R^4 = benzylidene
13 R^1 = Bn, R^2 = Ac, R^3 , R^4 = benzylidene
14 R^1 = R^4 = Bn, R^2 = Ac, R^3 = H

with boron trifluoride etherate in toluene-acetic anhydride, gave the ß-1-acetate 6 quantitatively. Significant signals in the ^{1}H NMR of 6 were at δ 6.14 (d, $J_{1,2}$ = 8.1 Hz, H-1), 5.83 (dd, $J_{2,3}$ = 10.3 Hz, H-2), 5.71 (dd, $J_{3,4}$ = 3.3 Hz, H-3), and 6.03 (broad d, H-4), indicating the structure assigned. Conversion of the ß-1-acetate 6 into the methyl ß-thioglycoside 7 (70%) was achieved by treatment[18,19] with (methylthio)trimethylsilane and boron trifluoride etherate in dichloromethane. The ^{1}H NMR data for the galactose residue in 7 were at δ 4.84 (d, $J_{1,2}$ = 9.7 Hz, H-1), 5.81 (dd, $J_{2,3}$ = 10.1 Hz, H-2), 5.70 (dd, $J_{3,4}$ = 3.1 Hz, H-3), 6.05 (broad d, H-4), indicating the ß-configuration of the glycoside linkage.

By essentially the same way described for 7, condensation of 2-(trimethylsilyl)ethyl 3-O-benzyl-ß-D-galactopyranoside[16] (2) with 3, O-benzoylation, replacement of the 2-(trimethylsilyl)ethyl group by acetyl, and then introduction of the methylthio group with (methylthio)trimethylsilane, afforded the another glycosyl donor 11 in good yield. The structure of 11 was unambiguously proved by 270 MHz ^{1}H NMR spectroscopy. The observed signals exhibited seven sharp singlets, each integrating for three protons, which demonstrated the presence of one N-acetyl (δ 1.87), four O-acetyl (δ 2.02, 2.03, 2.09, and 2.13), one S-methyl (δ 2.28), and one methyl ester (δ 3.34) groups; H-3e appeared at δ 2.55 (J_{gem} = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e; Neu5Ac unit), H-4 at δ 4.79 (ddd; Neu5Ac unit), H-1 at δ 4.55 (d, $J_{1,2}$ = 9.9 Hz; Gal unit), H-2 at δ 5.55 (t, $J_{2,3}$ = 9.9 Hz; Gal unit), H-4 at δ 5.97 (broad d; Gal unit), and phenyl protons (15H) at δ 7.05-8.02, indicating the structure assigned.

Acetylation of 2-(trimethylsilyl)ethyl O-(2-acetamido-4,6-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside[18] (12), followed by reductive ring-opening of the benzylidene acetal with sodium cyanoborohydride-hydrogen chloride in tetrahydrofuran[20], afforded the glycosyl acceptor 14 (91%) which has free hydroxyl group at C-4 of the glucosamine residue in the trisaccharide for the synthesis of sialyl-α(2→6)-neolactotetraosylceramide.

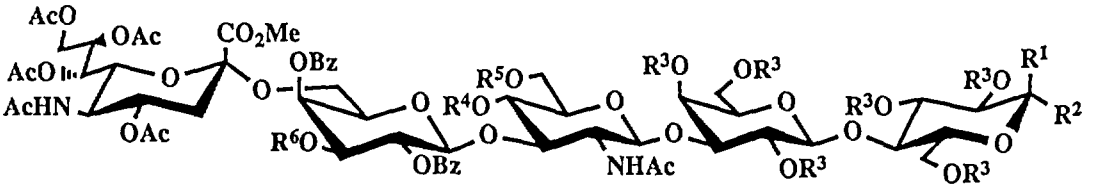
Glycosylation of 12 with 7 or 11 in dichloromethane for 14 h at 0 °C in the presence of 4.0 equiv. of DMTST to the glycosyl donor and powdered molecular sieves 4A gave the expected pentasaccharide derivatives 15 (52%) and 16 (58%), respectively. Removal of the benzylidene acetal in 16 by heating with aqueous 80% acetic acid and subsequent catalytic hydrogenolysis over 10% Pd-C in 4:1 ethanol-acetic acid at 45 °C, followed by O-acetylation, gave 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→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-ß-D-glucopyranoside (17) in 64% yield. The ^{1}H NMR data for Neu5Ac-Gal unit in 17 [δ 4.63 (d, $J_{1,2}$ = 7.7 Hz, H-1; Gal), 5.38 (t, $J_{2,3}$ = 7.7 Hz, H-2; Gal), 5.71 (broad d, H-4; Gal)] indicated that the newly formed glycosidic linkage to be ß. Other ^{1}H NMR data, given in the Experimental, are consistent with the structure 17. Treatment of 17 with trifluoroacetic acid in dichloromethane for 2 h at room temperature gave the 1-hydroxy compound 18 in 77% yield, after chromatography. When treated with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 3 h at 0 °C, 18 gave the α-trichloroacetimidate 19 in 90% yield. Significant signals in the ^{1}H NMR spectrum were at δ 6.47 (d, $J_{1,2}$ = 3.3 Hz, H-1) and 8.65 (s, C=NH), which showed the imidate to be α.

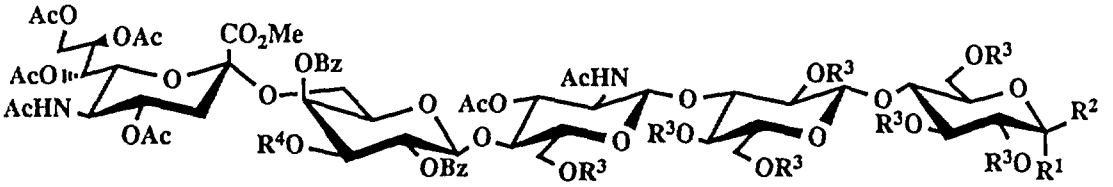
In order to prepare the pentasaccharide for the synthesis of sialyl-α(2→6)-neolactotetraosylceramide, glycosylation of 14 with 7 or 11 was attempted in the same way as described for the preparation of 15. When the glycosyl donor 11 having the benzyl group at C-3 of the galactose residue was used, the expected pentasaccharide 21 was obtained in 55% yield. In contrast, in the case of the donor 7, carrying the benzoyl group at C-3, the yield (25%) of pentasaccharide 20 was very low. It is rationalized that the benzoyl group at C-3 together with those at C-4 and C-6 of the galactose residue in the donor encroaches upon the anomeric carbon from the ß-side of the donor, while that at C-2 from the α-side, and, consequently, an approach of the acceptor nucleophile to the ß-phase of the donor might be strongly prevented.

Catalytic hydrogenolysis using 10% Pd-C in ethanol-acetic acid of the benzyl groups in 21 and subsequent O-acetylation gave 22 in 81% yield. Compound 22 was converted, via selective removal of the 2-(trimethylsilyl) ethyl group and subsequent imidate formation as described for 19, into O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α-D-glucopyranosyl trichloroacetimidate (24) in 77% yield. Significant signals in the ^{1}H NMR spectrum were at δ 6.48 (d, $J_{1,2}$ = 3.3 Hz, H-1) and 8.67 (s, C=NH), which showed the imidate to be α.

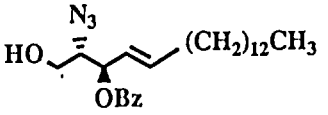
Glycosylation of (2S,3R,4E)-2-azido-3-O-benzoyl-4-octadecene-1,3-diol[21] (25) with 19 or 24 in dichloromethane in the presence of boron trifluoride etherate[21a,22] for 8 h at 0 °C afforded the corresponding ß-glycosides 26



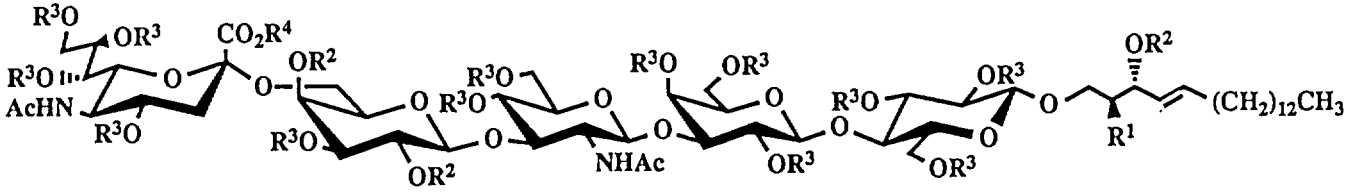
15 $R^1 = H$, $R^2 = OSE$, $R^3 = Bn$, R^4, R^5 = benzylidene, $R^6 = Bz$
16 $R^1 = H$, $R^2 = OSE$, $R^3 = R^6 = Bn$, R^4, R^5 = benzylidene
17 $R^1 = H$, $R^2 = OSE$, $R^3 = R^4 = R^5 = R^6 = Ac$
18 R^1, $R^2 = H$, OH, $R^3 = R^4 = R^5 = R^6 = Ac$
19 $R^1 = OC(=NH)CCl_3$, $R^2 = H$, $R^3 = R^4 = R^5 = R^6 = Ac$



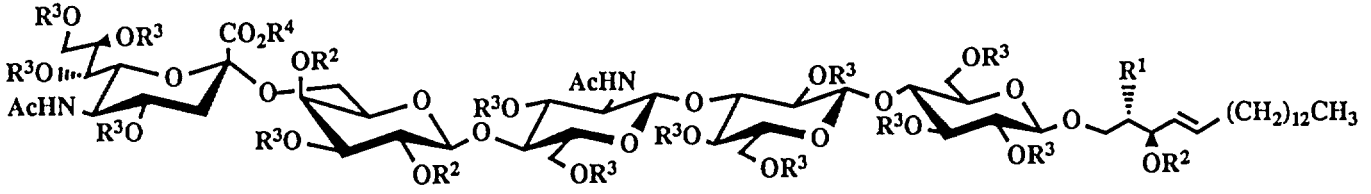
20 $R^1 = H$, $R^2 = OSE$, $R^3 = Bn$, $R^4 = Bz$
21 $R^1 = H$, $R^2 = OSE$, $R^3 = R^4 = Bn$
22 $R^1 = H$, $R^2 = OSE$, $R^3 = R^4 = Ac$
23 R^1, $R^2 = H$, OH, $R^3 = R^4 = Ac$
24 $R^1 = OC(=NH)CCl_3$, $R^2 = H$, $R^3 = R^4 = Ac$



25



26 $R^1 = N_3$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
27 $R^1 = NH_2$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
28 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
29 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = R^3 = R^4 = H$



30 $R^1 = N_3$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
31 $R^1 = NH_2$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
32 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = Bz$, $R^3 = Ac$, $R^4 = Me$
33 $R^1 = NHCO(CH_2)_{16}Me$, $R^2 = R^3 = R^4 = H$

(43%) and 30 (42%), respectively. Selective reduction[21a,23] of the azide group in 26 or 30 with hydrogen sulfide in aqueous 83% pyridine for 48 h at 0 °C gave the corresponding amines (27 and 31), which, on condensation with octadecanoic acid, using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC) in dichloromethane, gave the corresponding acylated gangliosides 28 and 32 in good yields, after chromatography.

Finally, O-deacylation of 28 and 32 with sodium methoxide in methanol, and subsequent saponification of the methyl ester group, yielded the desired sialyl-α(2→6)-lactotetraosylceramide (29) and sialyl-α(2→6)-neolactotetraosylceramide (33), respectively, in good yields. The ^{1}H NMR spectra of 29 and 33 in 98:2 $(CD_3)_2SO$-D_2O each contained four signals (d) due to the anomeric protons: 29 at δ 4.17 (2d, $J_{1,2}$ = 8.1 Hz, H-1a, H-1d), 4.28 ($J_{1,2}$ = 7.1 Hz, H-1b), and 4.79 ($J_{1,2}$ = 8.0 Hz, H-1c); 33 at δ 4.17 ($J_{1,2}$ = 7.7 Hz, H-1a), 4.27 ($J_{1,2}$ = 7.7 Hz, H-1d), 4.29 ($J_{1,2}$ = 7.1 Hz, H-1b), and 4.72 ($J_{1,2}$ = 8.4 Hz, H-1c).

The work described above shows that the use of the thioglycosides in the presence of DMTST is effective for the synthesis of the glycosides and the thioglycoside 11 of sialyl-α(2→6)-galactose is the useful building unit for the synthesis of complex types of sialoglycoconjugates.

EXPERIMENTAL

General Procedures. Specific rotations were determined with a Union PM-201 polarimeter at 25 °C, and IR spectra were recorded with a JASCO A-100 spectrophotometer. ^{1}H NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer. 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→6)-2,3,4-tri-O-benzoyl-β-D-galactopyranoside (5). To a solution of 4[16] (750 mg, 0.87 mmol) in dichloromethane (5 mL) was added, with stirring, a solution of benzoyl chloride (0.3 mL, 2.61 mmol) in pyridine (0.5 mL). After completion of the reaction, methanol (1 mL) was added, and the mixture was stirred for 20 min, 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 (25:1 toluene-methanol) of the residue on silica gel (150 g) gave 5 (770 mg, 82.6%) as an amorphous mass; $[\alpha]_D$ +46.5° (c 0.93, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.93 (s, 3H, AcN), 2.06, 2.10, 2.17, 2.26

(4s, 12H, 4AcO), 2.53 (dd, 1H, J_{gem} = 13.2 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.42 (s, 3H, MeO), 4.43 (dd, 1H, $J_{8,9}$ = 3.1 Hz, J_{gem} = 12.6 Hz, H-9), 4.82 (m, 1H, H-4), 5.35 (dd, 1H, H-7), and 5.45 (m, 1H, H-8); Gal unit δ 0.90 (m, 2H, $Me_3SiCH_2CH_2$), 4.91 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 5.65 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.5 Hz, H-3), 5.77 (dd, 1H, H-2), 6.04 (broad d, 1H, H-4), and 7.24-8.14 (m, 15H, 3Ph).

Anal. Calcd for $C_{52}H_{63}NO_{21}Si$ (1066.2): C, 58.58; H, 5.96; N, 1.31. Found: C, 58.44; H, 6.04; N, 1.38.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-1-O-acetyl-2,3,4-tri-O-benzoyl-β-D-galactopyranose (6). To a solution of 5 (4.9 g, 4.6 mmol) in dry toluene (50 mL) and acetic anhydride (7 mL, 69.5 mmol) was added boron trifluoride etherate (1.2 mL), and the mixture was stirred at room temperature. The reaction was monitored by TLC and, after 1 h, 5 was not detectable. Dichloromethane (100 mL) was added, and the solution was washed with M sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (3:1 ethyl acetate-hexane) of the residue on silica gel (500 g) afforded 6 (4.85 g, quantitative) as an amorphous mass; $[\alpha]_D$ +73.0° (c 1.1, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.87 (s, 3H, AcN), 2.47 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.36 (s, 3H, MeO), 4.80 (m, 1H, H-4), 5.27 (d, 1H, $J_{7,8}$ = 9.0 Hz, H-7), and 5.44 (m, 1H, H-8); Gal unit δ 5.71 (dd, 1H, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 5.83 (dd, 1H, $J_{1,2}$ = 8.1 Hz, H-2), 6.03 (broad d, 1H, H-4), 6.14 (d, 1H, H-1), and 7.02-8.38 (m, 15H, 3Ph); O-acetyl groups δ 2.00, 2.05, 2.08, 2.09, 2.20 (5s, 15H, 5AcO).

Anal. Calcd for $C_{49}H_{53}NO_{22}$ (1008.0): C, 58.39; H, 5.30; N, 1.39. Found: C, 58.38; H, 5.42; N, 1.49.

Metyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-2,3,4-tri-O-benzoyl-1-thio-β-D-galactopyranoside (7). To a solution of 6 (530 mg, 0.53 mmol) in dry dichloromethane (5 mL) were added, with stirring, (methylthio)trimethylsilane (158 mg, 1.29 mmol) and boron trifluoride etherate (0.14 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 (3:1 ethyl acetate-hexane) of the residue on silica gel (60 g) gave 7 (392 mg, 75%) as an amorphous mass; $[\alpha]_D$ +59.5° (c 0.96, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.86 (s, 3H, AcN), 2.00, 2.04, 2.11, 2.21 (4s, 12H, 4AcO), 2.48 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.42 (s, 3H, MeO), 4.77 (m, 1H, H-4), 5.30 (dd, 1H, $J_{6,7}$ = 1.5 Hz, $J_{7,8}$ = 8.4 Hz, H-7), and

5.45 (m, 1H, H-8); Gal unit δ 4.84 (d, 1H, $J_{1,2}$ = 9.7 Hz, H-1), 5.70 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 5.81 (dd, 1H, H-2), 6.05 (broad d, 1H, H-4), and 7.02-8.39 (m, 15H, 3Ph).

Anal. Calcd for $C_{48}H_{53}NO_{20}S$ (996.0): C, 57.88; H, 5.36; N, 1.41. Found: C, 57.60; H, 5.51; N, 1.43.

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→6)-3-O-benzyl-ß-D-galactopyranoside (8). To a solution of 2-(trimethylsilyl)-ethyl 3-O-benzyl-ß-D-galactopyranoside 2[16] (1.0 g, 2.7 mmol) and 3[16] (2.2 g, 4.37 mmol) in dry acetonitrile (2.5 mL) were added molecular sieves 3A (MS-3A; 2.0 g), and the mixture was stirred for 16 h at room temperature, and cooled to -40 °C. Dimethyl(methylthio)sulfonium triflate[24] (DMTST) (5.8 g, 22.4 mmol) was added to the mixture at -40 °C, and vigorously stirred for 24 h at -15 °C; the course of the reaction was monitored by TLC. The precipitates were filtered off, and washed with dichloromethane. The filtrate and washings were combined, and the solution was washed with M sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (200 g) afforded 8 (1.03 g, 45%) as an amorphous mass; $[\alpha]_D$ -16.2° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.83 (s, 3H, AcN), 1.99, 2.00, 2.09, 2.11 (4s, 12H, 4AcO), 2.16 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.79 (s, 3H, MeO), 4.75 (m, 1H, H-4), 5.29 (dd, 1H, $J_{6,7}$ = 2.0 Hz, $J_{7,8}$ = 8.1 Hz, H-7), and 5.33 (m, 1H, H-8); Gal unit δ 0.98 (m, 2H, $Me_3Si\underline{CH_2}\underline{CH_2}$), 4.27 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.67, 4.74 (2d, 2H, $Ph\underline{CH_2}O$), and 7.02-7.46 (m, 5H, Ph).

Anal. Calcd for $C_{38}H_{57}NO_{18}Si$ (843.9): C, 54.08; H, 6.81; N, 1.66. Found: C, 53.87; H, 7.07; N, 1.50.

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→6)-2,4-di-O-benzoyl-3-O-benzyl-ß-D-galactopyranoside (9). To a solution of 8 (395 mg, 0.47 mmol) in dichloromethane (5 mL) was added, with stirring, a solution of benzoyl chloride (0.16 mL, 1.33 mmol) in pyridine (0.5 mL) at 0 °C, and the mixture was stirred for 24 h at room temperature. After completion of the reaction, methanol (1 mL) was added, and the mixture was stirred for 20 min, 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 (2:1 ethyl acetate-hexane) of the residue on silica gel (40 g) gave 9 (301 mg, 61%) as an amorphous mass; $[\alpha]_D$ +39.0° (c 1.26, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.96 (s, 3H, AcN), 2.11, 2.12, 2.18, 2.22

(4s, 12H, 4AcO), 2.64 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.37 (s, 3H, MeO), 4.41 (dd, 1H, $J_{8,9}$ = 2.6 Hz, J_{gem} = 12.5 Hz, H-9), and 5.46 (m, 1H, H-8); Gal unit δ 0.97 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.88 (dd, 1H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.61, 4.84 (2d, 2H, $Ph\underline{CH_2}O$), 4.70 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 5.55 (dd, 1H, H-2), 6.02 (broad d, 1H, H-4), and 7.12-8.26 (m, 15H, 3Ph).

Anal. Calcd for $C_{52}H_{65}NO_{20}Si$ (1052.2): C, 59.36; H,6.23; N, 1.33. Found: C, 59.41; H, 6.43; N, 1.30.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-1-O-acetyl-2,4-di-O-benzoyl-3-O-benzyl-ß-D-galactopyranose (10). To a solution of 9 (301 mg, 0.29 mmol) in dry toluene (3 mL) and acetic anhydride (0.4 mL) was added boron trifluoride etherate (0.08 mL), and the mixture was stirred for 1 h at room temperature. Dichloromethane (10 mL) was added, and the solution was washed with M sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (4:1 ethyl acetate-hexane) of the residue on silica gel (40 g) gave 10 (174 mg, 61%) as an amorphous mass; $[\alpha]_D$ +58.5° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.87 (s, 3H, AcN), 2.55 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.29 (s, 3H, MeO), and 5.38 (m, 1H, H-8); Gal unit δ 4.29 (dd, 1H, $J_{2,3}$ = 12.5 Hz, $J_{3,4}$ = 2.6 Hz, H-3), 4.53, 4.77 (2d, 2H, $Ph\underline{CH_2}O$), 5.58 (dd, 1H, $J_{1,2}$ = 8.4 Hz, H-2), 5.87 (d, 1H, H-1), 5.96 (broad d, 1H, H-4), and 7.03-8.16 (m, 15H, 3Ph); O-acetyl groups δ 2.02, 2.03, 2.04, 2.07, 2.13 (5s, 15H, 5AcO).

Anal. Calcd for $C_{49}H_{55}NO_{21}$ (994.0): C, 59.21; H, 5.58; N, 1.41. Found: C, 59.08; H, 5.71; N, 1.35.

Methyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-2,4-di-O-benzoyl-3-O-benzyl-1-thio-ß-D-galactopyranoside (11). To a solution of 10 (174 mg, 0.17 mmol) in dichloromethane (2 mL) were added, with stirring, (methylthio)trimethylsilane (52.6 mg, 0.43 mmol) and boron trifluoride etherate (0.4 mL), and the mixture was stirred for 2 h at room temperature. Dichloromethane (30 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 (30 g) gave 11 (150 mg, 87%) as an amorphous mass; $[\alpha]_D$ +53.0° (c 0.96, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.87 (s, 3H, AcN), 2.02, 2.03, 2.09, 2.13 (4s, 12H, 4AcO), 2.55 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.34 (s, 3H, MeO), 4.79 (m, 1H, H-4), and 5.38 (m, 1H, H-8); Gal unit δ 2.29 (s, 3H, MeS), 4.54, 4.79 (2d, 2H, $Ph\underline{CH_2}O$), 4.55 (d, 1H, $J_{1,2}$ =

9.9 Hz, H-1), 5.55 (t, 1H, $J_{1,2} = J_{2,3}$ = 9.9 Hz, H-2), 5.97 (broad s, 1H, $J_{3,4}$ = 2.7 Hz, H-4), and 7.05-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{45}H_{55}NO_{19}S$ (982.0): C, 58.71; H, 5.65; N, 1.43. Found: C, 58.71; H, 5.78; N, 1.42.

2-(Trimethylsilyl)ethyl O-(2-Acetamido-3-O-acetyl-4,6-di-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (13). Compound 12[18] (2.71 g, 2.12 mmol) was acetylated with acetic anhydride (15 mL) in pyridine (30 mL) for 16 h at room temperature, to give 13 (2.46 g, 88%) as an amorphous mass; $[\alpha]_D$ -35.0° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.51 (s, 3H, AcN), 1.99 (s, 3H, AcO), 5.51 (s, 1H, PhCH), and 7.09-7.47 (m, 35H, 7Ph).

Anal. Calcd for $C_{76}H_{89}NO_{17}Si$ (1316.6): C, 69.33; H, 6.81; N, 1.06. Found: C, 69.31; H, 6.99; N, 1.18.

2-(Trimethylsilyl)ethyl O-(2-Acetamido-3-O-acetyl-6-O-benzyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (14). To a solution of 13 (167 mg, 0.13 mmol) in dry tetrahydrofuran (2 mL) was added MS-3A (400 mg), and the mixture was stirred for 4 h at room temperature, and sodium cyanoborohydride (120 mg) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added at room temperature until the evolution of gas ceased. TLC indicated that the reaction was completed after 6 min. The mixture was diluted with dichloromethane (50 mL) and water (10 mL), and the mixture was 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 (20 g) gave 14 (152 mg, 91%) as an amorphous mass; $[\alpha]_D$ -20.6° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.46 (s, 3H, AcN), 1.97 (s, 3H, AcO), and 7.10-7.34 (m, 35H, 7Ph).

Anal. Calcd for $C_{76}H_{91}NO_{17}Si$ (1318.6): C, 69.23; H, 6.96; N, 1.06. Found: C, 69.34; H, 6.96; N, 1.02.

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→6)-O-(2,3,4-tri-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (15). To a solution of 7 (250 mg, 0.25 mmol) and 12[18] (212 mg, 0.16 mmol) in dichloromethane (7 mL) was added powdered MS-4A (700 mg), and the mixture was stirred for 5 h at room temperature, then cooled to 0 °C. DMTST (260 mg, 1.0 mmol)

was added, the mixture was stirred for 14 h at 0 °C, and the reaction was monitored by TLC. The precipitates were collected and washed with dichloromethane, and the combined filtrate and washings were washed with water, dried (Na_2SO_4), and concentrated. Column chromatography(4:1ethyl acetate-hexane) of the residue on silica gel (50 g) gave 15 (190 mg, 51.5%) as an amorphous mass; $[\alpha]_D$ +26.0° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3H, AcN), 1.00 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.87, 1.89, 2.01, 2.04, 2.09 (5s, 15H, 4AcO, AcN), 3.02 (s, 3H, MeO), 4.96 (dd, 1H, $J_{2d,3d}$ = 10.4 Hz, $J_{3d,4d}$ = 3.5 Hz, H-3d), 5.32 (dd, 1H, $J_{6e,7e}$ = 2.2 Hz, $J_{7e,8e}$ = 9.4 Hz, H-7e), 5.58 (dd, 1H, $J_{2d,3d}$ = 10.4 Hz, H-2d), 5.78 (broad d, 1H, H-4d), 5.80 (s, 1H, Ph$\underline{CH}$), and 7.08-8.05 (m, 50H, 10Ph).

Anal. Calcd for $C_{121}H_{138}N_2O_{35}Si$ (2208.5): C, 65.81; H, 6.30; N, 1.27. Found: C, 65.78; H, 6.31; N, 1.28.

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→6)-O-(2,4-di-O-benzoyl-3-O-benzyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-O-benzylidene-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (16). Glycosylation of 12 (38.4 mg, 0.03 mmol) with 11 (60 mg, 0.06 mmol), as described for the synthesis of 15, gave 16 (39 mg, 58%) as an amorphous mass; ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.68, 1.87 (2s, 6H, 2AcN), 1.87-2.09 (4s, 12H, 4AcO), 2.58 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3e\text{-}eq,4e}$ = 4.4 Hz, H-3e-eq), 3.06 (s, 3H, MeO), 4.34 (d, 1H, $J_{1b,2b}$ = 7.3 Hz, H-1b), 4.63 (d, 1H, $J_{1d,2d}$ = 7.9 Hz, H-1d), 5.39 (m, 1H, H-8e), 6.93-8.16 (m, 50H, 10Ph).

Anal. Calcd for $C_{121}H_{138}N_2O_{35}Si$ (2208.5): C, 68.81; H, 6.30; N, 1.27. Found: C, 68.65; H, 6.49; N, 1.26.

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→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-ß-D-glucopyranoside (17). A solution of 16 (647 mg, 0.29 mmol) in aqueous 80% acetic acid (60 mL) was heated for 24 h at 60 °C and concentrated. A solution of the residue in ethanol (80 mL) and acetic acid (20 mL) was hydrogenolysed in the presence of 10% Pd-C (1.2 g) for 48 h at 45 °C, then filtered, and concentrated. The residue was treated with acetic anhydride (6 mL) and pyridine (8 mL) by heating for 3 days at 45 °C. Column chromatography (50:1 dichloromethane-methanol) of the product on silica gel (100 g) gave 17 (350 mg, 64%) as an amorphous mass; $[\alpha]_D$ +23.6° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.89 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.85, 1.88 (2s, 6H, 2AcN), 1.99-2.17 (13s,

39H, 13AcO), 2.50 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3e\text{-}eq,4e}$ = 4.0 Hz, H-3e-eq), 3.29 (s, 3H, MeO), 4.10 (dd, 1H, J_{gem} = 12.5 Hz, $J_{8e,9e}$ = 4.0 Hz, H-9e), 4.25 (dd, 1H, H-9'e), 4.32 (d, 1H, $J_{1b,2b}$ = 7.7 Hz, H-1b), 4.45 (d, 1H, $J_{1a,2a}$ = 7.7 Hz, H-1a), 4.63 (d, 1H, $J_{1d,2d}$ = 7.7 Hz, H-1d), 4.80 (m, 1H, H-4e), 4.86 (dd, 1H, $J_{2a,3a}$ = 9.1 Hz, H-2a), 4.90 (t, 1H, $J_{2b,3b}$ = 7.7 Hz, H-2b), 5.12 (d, 1H, $J_{5e,NH}$ = 9.2 Hz, NH), 5.14 (t, 1H, $J_{3a,4a}$ = 9.2 Hz, H-3a), 5.29 (dd, 1H, $J_{6e,7e}$ = 4.3 Hz, $J_{7e,8e}$ = 12.1 Hz, H-7e), 5.38 (t, 1H, $J_{2d,3d}$ = 7.7 Hz, H-2d), 5.71 (broad d, 1H, $J_{3d,4d}$ = 2.9 Hz, H-4d), and 7.45-8.12 (m, 10H, 2Ph).

Anal. Calcd for $C_{83}H_{110}N_2O_{44}Si$ (1867.9): C, 53.37; H, 5.94; N, 1.50. Found: C, 53.19; H, 6.14; N, 1.51.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-D-glucopyranose (18). To a solution of 17 (329 mg, 0.18 mmol) in dichloromethane (2 mL) was added trifluoroacetic acid (1.0 mL), and the mixture was stirred for 2 h at room temperature and then concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (30 g) gave 18 (240 mg, 77%) as an amorphous mass; $[\alpha]_D$ +26.0° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.85, 1.88 (2s, 6H, 2AcN), 2.00-2.17 (13s, 39H, 13AcO), 3.30 (s, 3H, MeO), 4.80 (t, 1H, $J_{1a,2a}$ = $J_{2a,3a}$ = 6.4 Hz, H-2a), 4.31 (d, 1H, $J_{1b,2b}$ = 7.7 Hz, H-1b), 4.63 (d, 1H, $J_{1d,2d}$ = 7.7 Hz, H-1d), 4.80 (m, 1H, H-4e), 5.12 (d, 1H, $J_{5e,NH}$ = 8.1 Hz, NH), 5.35 (m, 1H, H-8e), 5.71 (broad d, 1H, $J_{3d,4d}$ = 3.1 Hz, H-4d), and 7.45-8.12 (m, 10H, 2Ph).

Anal. calcd for $C_{78}H_{98}N_2O_{44}$ (1767.6): C, 53.00; H, 5.59; N, 1.58. Found: C, 52.79; H, 5.71; N, 1.55.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α-D-glucopyranosyl trichloroacetimidate (19). To a solution of 18 (212 mg, 0.12 mmol) in dichloromethane (2 mL) and trichloroacetonitrile (0.35 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 18 mg) at 0 °C, and the mixture was stirred for 3 h at 0 °C, then concentrated. Column chromatography (30:1 dichloromethane-methanol) gave 19 (206 mg, 90%) as an amorphous mass; $[\alpha]_D$ +30.3° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.85, 1.88 (2s, 6H, 2AcN), 2.00-2.17 (13s, 39H, 13AcO), 251 (dd,

1H, J_{gem} = 13.2 Hz, $J_{3e\text{-}eq,4e}$ = 4.6 Hz, H-3e-eq), 3.29 (s, 3H, MeO), 4.12 (dd, 1H, J_{gem} = 12.5 Hz, $J_{8e,9e}$ = 2.4 Hz, H-9e), 4.25 (dd, 1H, H-9'e), 4.35 (d, 1H, $J_{1b,2b}$ = 7.5 Hz, H-1b), 4.62 (d, 1H, $J_{1d,2d}$ =7.5 Hz, H-1d), 4.80 (m, 1H, H-4e), 4.92 (dd, 1J, $J_{1a,2a}$ = 4.0 Hz, $J_{2a,3a}$ = 8.2 Hz, H-2a), 5.12 (d, 1H, $J_{5e,NH}$ = 8.1 Hz, NH), 5.30 (dd, 1H, $J_{6e,7e}$ = 3.5 Hz, $J_{7e,8e}$ = 10.2 Hz, H-7e), 5.38 (dd, 1H, $J_{2d,3d}$ = 10.6 Hz, H-2d), 5.71 (broad d, 1H, $J_{3d,4d}$ = 3.1 Hz, H-4d), 6.47 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1a), 7.46-8.11 (m, 10H, 2Ph), and 8.65 (s, 1H, C=NH).

Anal. Calcd for $C_{80}H_{98}N_3O_{44}Cl_3$ (1912.0): C, 50.25; H, 5.17; N, 2.20. Found: C, 49.95; H, 5.31; N, 2.09.

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→6)-O-(2,3,4-tri-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3-O-acetyl-6-O-benzyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (20). To a solution of 7 (79 mg, 79 μmol) and 14 (70 mg, 53μmol) in dichloromethane (2 mL) was added MS-4A (300 mg), and the mixture was stirred for 8 h at room temperature, then cooled to 0 °C. DMTST (82 mg, 0.32 mmol) and MS-4A (78 mg) were added, the mixture was stirred for 24 h at 0 °C, and the reaction was monitored by TLC. Methanol (1 mL) and triethylamine (0.5 mL) were added, and the precipitates were collected and washed with dichloromethane. The filtrate and washings were combined, and concentrated. A solution in dichloromethane (50 mL) of the residue was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (4:1 ethyl acetate-hexane) of the residue on silica gel (30 g) gave 20 (30 mg, 25%) as an amorphous mass; $[\alpha]_D$ +6.8° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.48, 1.78 (2s, 6H, 2AcN), 1.86-2.11 (5s, 15H, 5AcO), 2.57 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3e\text{-}eq,4e}$ = 4.6 Hz, H-3e-eq), 3.36 (s, 3H, MeO), 5.35 (m, 1H, H-8e), 5.85 (broad d, 1H, $J_{3d,4d}$ = 3.1 Hz, H-4d), and 7.07-8.12 (m, 50H, 10Ph).

Anal. Calcd for $C_{123}H_{140}N_2O_{37}Si$ (2266.5): C, 65.18; H, 6.23; N, 1.24. Found: C, 65.13; H, 6.45; N, 1.20.

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→6)-O-(2,4-di-O-benzoyl-3-O-benzyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3-O-acetyl-6-O-benzyl-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-ß-D-glucopyranoside (21). To a solution of 11 (265 mg, 0.27 mmol) and 14 (237 mg, 0.18 mmol) in dichloromethane (2 mL) was added MS-4A (500 mg), and the mixture was stirred for 5 h at room temperature, and cooled to 0 °C. DMTST (280 mg, 1.08

mmol) was added, and the mixture was stirred at 0 °C; after 5 h, the reaction was completed. A similar work-up, as described for 20, gave 21 (220 mg, 55%) as an amorphous mass; $[\alpha]_D$ +28.0° (c 1.1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.48, 1.78 (2s, 6H, 2AcN), 1.86-2.11 (5s, 15H, 5AcO), 2.57 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3e\text{-}eq,4e}$ = 4.6 Hz, H-3e-eq), 3.36 (s, 3H, MeO), 4.91 (d, 1H, $J_{1d,2d}$ = 7.1 Hz, H-1d), 5.29 (dd, 1H, $J_{6e,7e}$ = 4.2 Hz, $J_{7e,8e}$ = 10.9 Hz, H-7e), 5.35 (m, 1H, H-8e), 5.85 (broad d, $J_{3d,4d}$ = 3.1 Hz, H-4d), and 7.07-8.12 (m, 50H, 10Ph).

Anal. Calcd for $C_{123}H_{142}N_2O_{36}Si$ (2252.6): C, 65.59; H, 6.35; N, 1.24. Found: C, 65.41; H, 6.46; N, 1.25.

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→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-ß-D-glucopyranoside (22). A solution of 21 (520 mg, 0.23 mmol) in ethanol (80 mL) and acetic acid (20 mL) was stirred with 10% Pd-C (1.0 g) for 48 h at 45 °C under hydrogen. The catalyst was collected and washed with ethanol, the combined filtrate and washings were concentrated, and the residue was heated with acetic anhydride (6 mL) and pyridine (8 mL) for 24 h at 45 °C. The mixture was concentrated and extracted with dichloromethane, and the extract was successively washed with 2M hydrochloric acid and M sodium carbonate, dried (Na_2SO_4), and concentrated. Column chromatography (50:1 dichloromethane-methanol) of the residue on silica gel (50 g) gave 22 (348 mg, 81%) as an amorphous mass; $[\alpha]_D$ +1.4° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.91 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.85, 1.89 (2s, 6H, 2AcN), 1.91-2.19 (13s, 39H, 13AcO), 2.51 (dd, J_{gem} = 12.8 Hz, $J_{3e\text{-}eq,4e}$ = 4.6 Hz, H-3e-eq), 3.43 (s, 3H, MeO), 3.69 (t, 1H, $J_{3a,4a}$ = $J_{4a,5a}$ = 9.2 Hz, H-4a), 4.31 (d, 1H, $J_{1b,2b}$ = 8.1 Hz, H-1b), 4.46 (d, 1H, $J_{1a,2a}$ = 8.1 Hz, H-1a), 4.82 (d, 1H, $J_{1d,2d}$ = 7.7 Hz, H-1d), 4.86 (dd, 1H, $J_{2a,3a}$ = 9.5 Hz, H-2a), 4.96 (dd, 1H, $J_{2b,3b}$ = 9.5 Hz, H-2b), 5.15 (dd, 1H, H-3a), 5.40 (m, 1H, H-8e), 5.77 (broad d, 1H, $J_{3d,4d}$ = 3.3 Hz, H-4d), and 7.42-8.11 (m, 10H, 2Ph).

Anal. Calcd for $C_{83}H_{110}N_2O_{44}Si$ (1867.9): C, 53.37; H, 5.94; N, 1.50. Found: C, 53.33; H, 5.98; N, 1.48.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-D-glucopyranose (23). To a solution of 22 (343 mg, 0.18 mmol) in dry dichloromethane (1.8 mL) was added trifluoroacetic acid

(0.8 mL), the mixture was stirred for 2 h at room temperature and concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (30 g) gave 23 (310 mg, 95%) as an amorphous mass; $[\alpha]_D$ +20.0° (c 1.3, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.84, 1.88 (2s, 6H, 2AcN), 1.90-2.18 (13s, 39H, 13AcO), 2.50 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3e\text{-}eq,4e}$ = 4.0 Hz, H-3e-eq), 3.41 (s, 3H, MeO), 5.45 (m, 1H, H-8e), and 7.42-8.11 (m, 10H, 2Ph).

Anal. calcd for $C_{78}H_{98}N_2O_{44}$ (1767.6): C, 53.00; H, 5.59; N, 1.58. Found: C, 53.01; H,5.80; N, 1.46.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4,-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α-D-glucopyranosyl trichloroacetimidate (24). To a solution of 23 (217 mg, 0.122 mmol) in dichloromethane (2 mL) and trichloroacetonitrile (0.4 mL) was added DBU (18 mg) at -5 °C, and the mixture was stirred for 3 h at 0 °C, then concentrated. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel (40 g) gave 24 (190 mg, 81%) as an amorphous mass; $[\alpha]_D$ +27.5° (c 1.3, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.74-2.19 (15s, 45H, 2AcN, 13AcO), 3.41 (s, 3H, MeO), 4.34 (d, 1H, $J_{1b,2b}$ = 10.3 Hz, H-1b), 4.81 (d, 1H, $J_{1d,2d}$ = 9.2 Hz, H-1d), 5.47 (m, 1H, H-8e), 6.48 (d, 1H, $J_{1a,2a}$ = 3.3 Hz, H-1a), 7.35-8.11 (m, 10H, 2Ph), and 8.67 (s, 1H, C=NH).

Anal. Calcd for $C_{80}H_{98}N_3O_{44}Cl_3$ (1912.0): C, 50.25; H, 5.17; N, 2.20. Found: C, 50.08; H, 5.32; N, 2.19.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-O-2,3,6-tri-O-acetyl-ß-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-2-azido-3-O-benzoyl-4-octadecene-1,3-diol (26). To a solution of 25[21] (44 mg, 0.1 mmol) and 19 (102 mg, 0.053 mmol) in dichloromethane (3 mL) was added MS-4A (AW-300; 800 mg), and the mixture was stirred for 1 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (0.04 mL) was added, and the mixture was stirred for 8 h at 0 °C, and then filtered. The insoluble materials were 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 26 (49.3

mg, 43%) as an amorphous mass, $[\alpha]_D$ +4.3° (c 0.9, chloroform); IR (KBr) 3390 (NH), 2950 and 2870 (Me, methylene), 2110 (azide), 1750 and 1230 (ester), 1680 and 1540 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, J_{Me,CH_2} = 6.6 Hz, $\underline{Me}CH_2$), 1.25 (s, 22H, $11CH_2$), 1.85, 1.88 (2s, 6H, 2AcN), 2.00-2.11 (13s, 39H, 13AcO), 3.30 (s, 3H, MeO), 4.31 (d, 1H, $J_{1b,2b}$ = 8.1 Hz, H-1b), 4.49 (d, 1H, $J_{1a,2a}$ = 7.3 Hz, H-1a), 4.63 (d, 1H, $J_{1d,2d}$ = 6.6 Hz, H-1d), 4.80 (m, 1H, H-4e), 4.91 (t, 1H, $J_{2b,3b}$ = 8.2 Hz, H-2b), 5.12 (d, 1H, $J_{5e,NH}$ = 8.4 Hz, NH), 5.91 (m, 1H, H-5; sphingosine), and 7.42-8.11 (m, 15H, 3Ph).

Anal. Calcd for $C_{103}H_{135}N_5O_{46}$ (2179.2): C, 56.77; H, 6.24; N, 3.21. Found: C, 56.51; H, 6.34; N, 3.25.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-4,6-di-O-acetyl-ß-D-glyco-pyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-ß-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (28). Hydrogen sulfide was bubbled through a stirred solution of 26 (49 mg, 22 μmol) in aqueous 83% pyridine (6 mL) for 48 h at 0 °C. The mixture was concentrated, and the residue 27 was stirred with octadecanoic acid (13 mg, 45 μmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC; 13 mg, 70 μmol) in dry dichloromethane (1.5 mL) for 20 h at room temperature. Dichloromethane (20 mL) was added, and the mixture was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave 28 (54 mg, quantitative) as an amorphous mass; $[\alpha]_D$ +8.6° (c 1.3, chloroform); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, J_{Me,CH_2} = 6.4 Hz, $2\underline{Me}CH_2$), 1.26 (s, 52H, $26CH_2$), 1.84, 1.88 (2s, 6H, 2AcN), 1.94-2.16 (13s, 39H, 13AcO), 2.51 (dd, 1H, J_{gem} = 13.2 Hz, $J_{3e\text{-}eq,4e}$ = 4.4 Hz, H-3e-eq), 3.31 (s, 3H, MeO), 4.28 (d, 1H, $J_{1b,2b}$ = 7.9 Hz, H-1b), 4.42 (d, 1H, $J_{1a,2a}$ = 7.7 Hz, H-1a), 4.64 (d, 1H, $J_{1d,2d}$ = 7.5 Hz, H-1d), 4.80 (m, 1H, H-4e), 4.86 (t, 1H, $J_{2a,3a}$ = 7.8 Hz, H-2a), 5.11 (d, 1H, $H_{5e,NH}$ = 9.4 Hz, NH), 5.44 (t, 1H, $J_{2d,3d}$ = 8.0 Hz, H-2d), 5.70 (broad d, 1H, $J_{3d,4d}$ = 2.7 Hz, H-4d), 5.85 (m, 1H, H-5; sphingosine), and 7.41-8.12 (m, 15H, 3Ph).

Anal. Calcd for $C_{121}H_{171}N_3O_{49}$ (2419.7): C, 60.06; H, 7.12; N, 1.74. Found: C, 59.81; H, 7.30; N, 1.74.

O-(5-Acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-(2→6)-O-(ß-D-galactopyranosyl)-(1→3)-O-(2-acetamido-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(ß-D-galactopyranosyl)-(1→4)-O-(ß-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol (29). To a so-

lution of 28 (54 mg, 21.8 μmol) in methanol (3 mL) was added sodium methoxide (10 mg), the mixture was stirred for 24 h at 0 °C, and water (0.3 mL) was added. The solution was stirred for 16 h at room temperature, neutralized with Amberlite IR-120 (H^+) resin and filtered. The resin was washed with 50:40:7 dichloromethane-methanol-water, and the combined filtrate and washings were concentrated. Column chromatography (50:40:7 dichloromethane-methanol-water) of the residue on Sephadex LH-20 (30 g) gave 29 (29 mg, 83%) as an amorphous mass; $[\alpha]_D$ -5.2° (c 0.6, 1:1:0.2 dichloromethane-methanol-water), ^1H NMR [98:2 $(CD_3)_2SO$-D_2O] pentasaccharide unit δ 1.82, 1.88 (2s, 6H, 2AcN), 2.64 (broad dd, 1H, H-3e-eq), 4.17 (2d, 2H, $J_{1a,2a} = J_{1d,2d} = 8.1$ Hz, H-1a, H-1d), 4.28 (d, 1H, $J_{1b,2b} = 7.1$ Hz, H-1b), and 4.79 (d, 1H, $J_{1c,2c} = 8.0$ Hz, H-1c); ceramide unit δ 0.85 (2t, 6H, 2MeCH_2), 1.24 (s, 50H 25CH_2), 1.45 (m, 2H, CO$CH_2$$CH_2$), 2.03 (t, 2H, CO$CH_2$), 5.36 (dd, 1H, $J_{3,4} = 7.1$ Hz, $J_{4,5} = 15.2$ Hz, H-4), and 5.54 (m, 1H, $J_{5,6} = J_{5,6'} = 6.6$ Hz, H-5).

Anal. Calcd for $C_{73}H_{131}N_3O_{31}$ (1546.8): C, 56.68; H, 8.54; N, 2.72. Found: C, 56.41; H, 8.66; N, 2.59.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-ß-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-2-azido-3-O-benzoyl-4-octadecene-1,3-diol (30). Coupling of 24 (78 mg, 41 μmol) and 25 (35 mg, 78 μmol), as described for 26, gave 30 (37 mg, 42%) as an amorphous mass; $[\alpha]_D$ -0.65 (c 1.2, chloroform); IR (KBr) 3390 (NH), 2950 and 2870 (Me, methylene), 2110 (azide), 1750 and 1230 (ester), 1670 and 1540 (amide), and 720 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, MeCH_2), 1.25 (s, 22H, 11CH_2), 1.60 (t, 1H, $J_{gem} = J_{3e-ax} = 12.3$ Hz, H-3e-ax), 1.84-2.18 (15s, 45H, 2AcN, 13AcO), 3.41 (s, 3H, MeO), and 7.74-8.14 (m, 15H, 3Ph).

Anal. Calcd for $C_{103}H_{135}N_5O_{46}$ (2179.2): C, 56.77; H, 6.24; N, 3.21. Found: C, 56.57; H, 6.41; N, 3.20.

O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-O-(3-O-acetyl-2,4-di-O-benzoyl-ß-D-galactopyranosyl)-(1→4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-ß-D-glucopyranosyl)-(1→3)-O-(2,4,6-tri-O-acetyl-ß-D-galactopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-ß-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (32). Selective reduction of the azide group in 30 (71 mg, 33 μmol) and subsequent coupling of the amine 31 with octadecanoic acid (18 mg, 63 μmol), as described for 28, afforded

32 (49.3 mg, 63%) as an amorphous mass; $[\alpha]_D$ +6.2° (c 0.94, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.90 (2t, 6H, J_{Me,CH_2} = 6.2 Hz, 2$\underline{Me}CH_2$), 1.25 (s, 52H, 26CH_2), 1.84-2.17 (15s, 45H, 2AcN, 13AcO), 2.50 (dd, 1H, J_{gem} = 13.2 Hz, $J_{3e\text{-}eq,4e}$ = 4.8 Hz, H-3e-eq), 3.42 (s, 3H, MeO), 4.42 (d, 1H, $J_{1a,2a}$ = 7.7 Hz, H-1a), 4.26 (d, 1H, $J_{1b,2b}$ = 8.1 Hz, H-1b), 4.82 (d, 1H, $J_{1d,2d}$ = 7.7 Hz, H-1d), 5.46 (dd, 1H, $J_{2d,3d}$ = 10.3 Hz, H-2d), 5.85 (m, 1H, H-5; sphingosine), and 7.41-8.11 (m, 15H, 3Ph).

Anal. Calcd for $C_{121}H_{171}N_3O_{49}$ (2419.7): C, 60.06; H, 7.12; N, 1.74. Found: C, 60.13; H, 7.19; N, 1.76.

O-(5-Acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-(2→6)-O-(β-D-galactopyranosyl)-(1→4)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-O-(β-D-galactopyranosyl)-(1→4)-O-(β-D-glucopyranosyl)-(1→1)-(2S,3R,4E)-2-octadecanamido-4-octadecene-1,3-diol (33). O-Deacylation and saponification of 32 (47 mg, 19 μmol), as described for 29, yielded 33 (28 mg, 93%) as an amorphous mass; $[\alpha]_D$ -1.5° (c 0.9, 1:1:0.2 dichloromethane-methanol-water); ^{1}H NMR [98:2 $(CD_3)_2SO$-D_2O] pentasaccharide unit δ 1.86, 1.90 (2s, 6H, 2AcN), 2.66 (broad dd, 1H, H-3e-eq), 4.17 (d, 1H, $J_{1a,2a}$ = 7.7 Hz, H-1a), 4.27 (d, 1H, $J_{1d,2d}$ = 7.7 Hz, H-1d), 4.29 (d, 1H, $J_{1b,2b}$ = 7.1 Hz, H-1b), and 4.72 (d, 1H, $J_{1c,2c}$ = 8.4 Hz, H-1c); ceramide unit δ 0.86 (t, 6H, 2$\underline{Me}CH_2$), 1.24 (s, 50H, 25CH_2), 1.46 (m, 2H, $COCH_2\underline{CH_2}$), 5.37 (dd, 1H, $J_{4,5}$ = 15.5 Hz, $J_{3,4}$ = 6.8 Hz, H-4), and 5.55 (m, 1H, $J_{5,6}$ = $J_{5,6'}$ = 6.6 Hz, H-5).

Anal. Calcd for $C_{73}H_{131}N_3O_{31}$ (1546.8): C, 56.68; H, 8.54; N, 2.72. Found: C, 56.49; H, 8.80; N, 2.61.

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REFERENCES AND FOOTNOTES

1. a) Glycolipids, New Comprehensive Biochemistry, Vol. 10: H. Wiegandt Ed.; Elsevier, Amsterdam, 1985; b) Gangliosides and Moduration of Neuronal Functions, NATO ASI Series, Series H; Cell Biology Vol. 7; H. Rahmann Ed.; Springer-Verlag, Berlin-Heiderberg, 1987; c) Sialic Acids 1988, Proceeding of the Japanese-German Symposium on Sialic Acids; R. Schauer, T. Yamakawa Eds.; Barbel Mende, Kiel, 1988.

2. S. Tsuji, T. Yamakawa, M. Tanaka, and Y. Nagai, J. Neurochem., 50, 414 (1988).

3. H. Nakamura, T. Kawaguchi, A. Koito, T. Hattori, T. Kagimoto, and K. Takatsuki, Jpn. J. Cancer Res., 80, 702 (1989).

4. C. D. Deal and H. C. Krivan, J. Biol. Chem., 265, 12774 (1990).

5. M. Tiemeyer, P. S-Hill, and R. L. Schnaar, J. Biol. Chem., 265, 11990 (1990).

6. T. Murase, H. Ishida, M. Kiso, and A. Hasegawa, Carbohydr. Res., 184, c1 (1988).

7. A. Hasegawa, H. Ohki, T. Nagahama, H. Ishida, and M. Kiso, Carbohydr. Res., in press.

8. P. Fügedi and P. J. Garegg, Carbohydr. Res., 149, c9 (1986).

9. O. Kanie, M. Kiso, and A. Hasegawa, J. Carbohydr. Chem., 7, 501 (1988).

10. A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, Carbohydr. Res., 209, in press.

11. A. Hasegawa, T. Murase, K. Adachi, M. Morita, H. Ishida, and M. Kiso, J. Carbohydr. Chem., 9, 181 (1990), and the references cited therein.

12. A. Hasegawa, M. Morita, Y. Kojima, H. Ishida, and M. Kiso, Carbohydr. Res., in press.

13. K. Watanabe, M. E. Powell, and S. Hakomori, J. Biol. Chem., 254, 8223 (1979).

14. O. Nilsson, J. E. Mansson, E. Tibblin, and L. Svennerholm, FEBS Lett., 133, 197 (1981).

15. O. Nilsson, L. Lindholm, J. Holmgren, and L. Svennerholm, Biochem. Biophys. Acta, 835, 577 (1985).

16. T. Murase, A. Kameyama, K. P. R. Kartha, H. Ishida, M. Kiso, and A. Hasegawa, J. Carbohydr. Chem., 8, 265 (1989).

17. K. Jansson, A. Ahlfors, T. Freid, J. Kihlberg, G. Magnusson, J. Dahmén, G. Noori, and K. Stenvall, J. Org. Chem., 53, 5629 (1988).

18. A. Kameyama, H. Ishida, M. Kiso, and A. Hasegawa, Carbohydr. Res., 200, 269 (1990).

19. V. Pozsgay and H. J. Jennings, Tetrahedron Lett., 28, 1375 (1987).

20. P. J. Garegg, H. Hultberg, and S. Wallin, Carbohydr. Res., 108, 97 (1982).

21. a) Y. Ito, M. Kiso, and A. Hasegawa, J. Carbohydr. Chem., 8, 285 (1989); b) R. R. Schmidt and P. Zimmermann, Angew. Chem. Int. Ed. Engl., 25, 725 (1986).

22. R. R. Schmidt and G. Grundler, Synthesis, 885 (1981).

23. T. Adachi, Y. Yamada, I. Inoue, and M. Saneyoshi, Synthesis, 45 (1977).

24. M. Ravenscroft, R. M. G. Roberts, and J. G. Tillett, J. Chem. Soc. Perkin Trans. II, 1569 (1982).