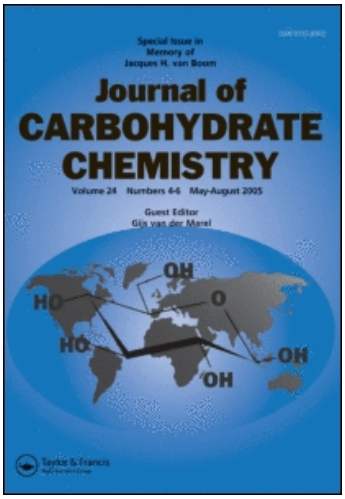

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SYNTHESIS OF SIALYL LEWIS X GANGLIOSIDE ANALOGS CONTAINING A VARIABLE LENGTH SPACER BETWEEN THE SUGAR AND LIPOPHILIC MOIETIES[1]

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ABSTRACT

Five sialyl Lewis X ganglioside analogs containing 4-(2-tetradecylhexadecanoylamino)benzyl group in place of ceramide and a variety of lengths of ethylene glycol chains as the spacer, have been synthesized. Glycosidation of *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetylα-L-fucopyranosyl)-(1→3)]-2,4-di-*O*-benzoyl-α-D-glucopyranosyl trichloroacetimidate (**13**) with oligo ethyleneglycol monobenzyl ether derivatives **9**, **10**, **11** and **12**, prepared from the corresponding oligo ethyleneglycols by 4-nitrobenzylation, reduction and *N*-acylation with 2-tetradecylhexadecanoic acid, using boron trifluoride etherate gave the corresponding glycolipid derivatives **14**, **15**, **16** and **17**. A similar glycosidation of **13** with 4-nitrobenzyl alcohol gave the 4-nitrobenzyl glycoside **18**, which was converted *via* reduction of nitro group and *N*-acylation into the corresponding glycolipid derivative **19**. Compounds **14-17** and **19** were transformed into the title compounds by *O*-deacylation and hydrolysis of methyl ester group in good yields.

INTRODUCTION

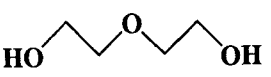
The selectins are a family of cell adhesion molecules that play an important role in the initial interactions of leukocyte homing, platelet binding, and neutrophil extravasation. Recently, it has been demonstrated[2,3] that the selectins, such as E-, P-, and L-selectin, recognize the sialyl Lewis X determinant, α-Neu5Ac-(2→3)-β-D-Gal-(1→4)-[α-L-Fuc-(1→3)]-β-D-GlcNAc, which is found as the terminal carbohydrate structure of both cell membrane glycolipid and glycoprotein. More recent reports[4-7] of *in vivo* experiments suggest that the inhibitions of interaction between selectins and their ligand substantially reduce inflammatory response. A simple saccharide derivative that inhibits the selectin binding to sialyl Lewis X could be clinically useful as anti-inflammatory or anti-cancer metastasis drug. Several groups have reported the syntheses of sialyl Lewis X ganglioside analogs[8,9] as the selectin blocker, but the study concerned with the distance between sugar and lipophilic moiety has not been thus far reported.

We described here the synthesis of novel sialyl Lewis X ganglioside analogs, which contain the 4-(2-tetradecylhexadecanoylamino)benzyl group linked to a variable length ethylene glycol ether chain as the spacer, to examine their potency as selectin blockers.

RESULTS AND DISCUSSION

For the synthesis of the designed sialyl Lewis X ganglioside analogs, we employed *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-2,4-di-*O*-benzoyl-α-D-glucopyranosyl trichloroacetimidate[10] (**13**) as the glycosyl donor, and 4-nitrobenzyl alcohol or the ethylene glycol 4-(2-tetradecylhexadecanoylamino)benzyl ether derivatives (**9**-**12**) as the glycosyl acceptors.

Treatment of the diethylene glycol (**1**) with 4-nitrobenzyl bromide in benzene in the presence of silver(I) oxide for 8 h at room temperature, afforded the mono 4-nitrobenzyl ether **5** in 64% yield. Selective reduction[11] (10% Pd-C) of the nitro group of **5** in ethanol



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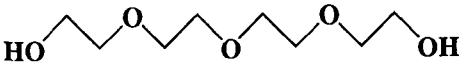

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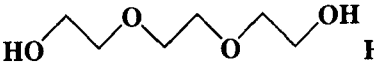

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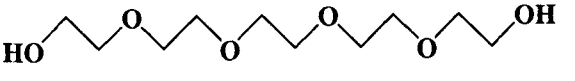

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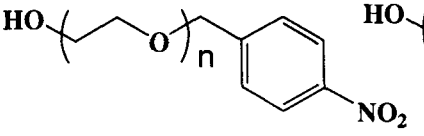

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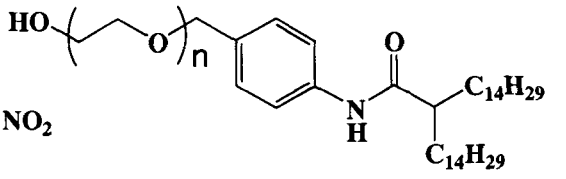
6	n = 3
7	n = 4
8	n = 5



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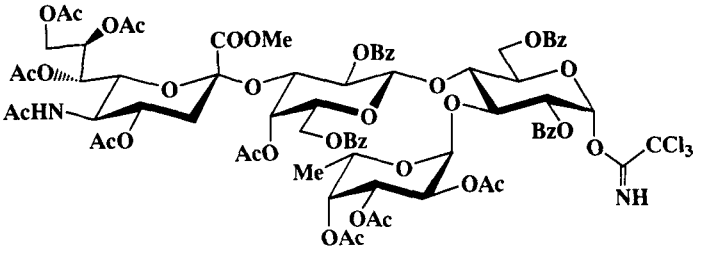
11	n = 4
12	n = 5



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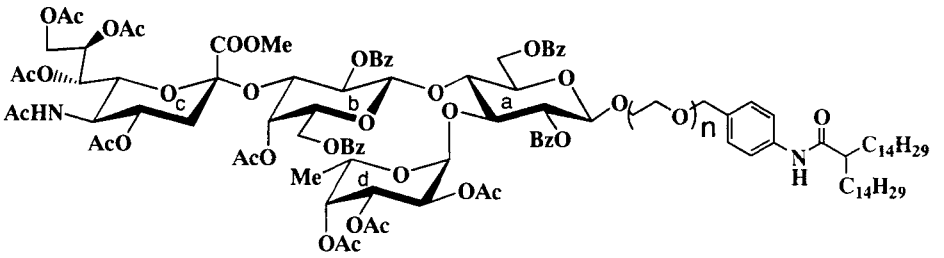

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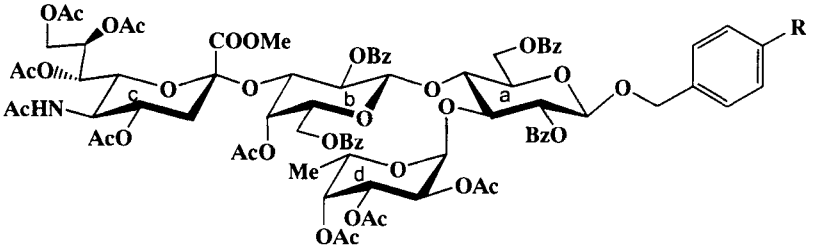
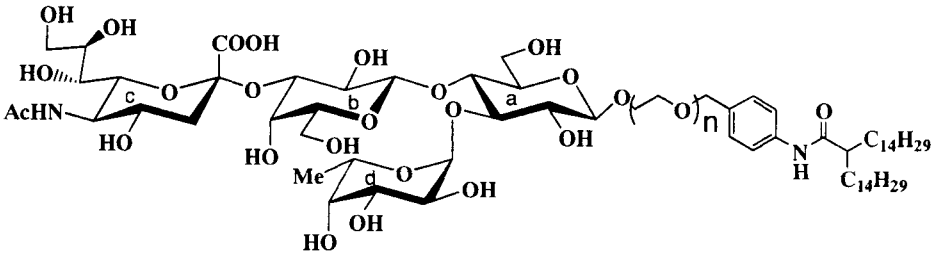


18 $R = NO_2$
19 $R = NH(CO)CH(C_{14}H_{29})_2$



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21 n = 2
22 n = 3
23 n = 4
24 n = 5

for 1 h and subsequent *N*-acylation with 2-tetradecylhexadecanoic acid by the using of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC), gave the 4-(2-tetradecylhexadecanoylamino)benzyl ether derivative **9** in 76% yield. In essentially the same way, 4-(2-tetradecylhexadecanoylamino)benzyl derivatives **10**, **11** and **12** were prepared from the corresponding oligo ethylene glycols in good yields, respectively.

The glycosylation of **9-12** with **13** in dichloromethane in the presence of boron trifluoride etherate[12] for 5 h, afforded the expected β-glycosides **14-17** in high yields respectively. The ^{1}H NMR data for the Glc unit of **14-17**[δ 4.47-4.52 ($J_{1,2}$ = 7.8~8.1 Hz, H-1)] indicated the glycosidic linkages to be β. The glycosylation of 4-nitrobenzyl alcohol with **13** in dichloromethane in the presence of boron trifluoride etherate for 5 h, gave the β-4-nitrobenzyl glycoside **18**. Catalytic hydrogenation of **18** and subsequent *N*-acylation with 2-tetradecylhexadecanoic acid, as described for **9**, gave the fully protected glycolipid derivative **19** in 49% yield.

Finally, *O*-deacylation of **14-17**, **19** with sodium methoxide in methanol, followed by subsequent saponification of the methyl ester group, yielded the corresponding, desired sialyl Lewis X ganglioside analogs (**20-24**) in good yields, respectively.

These compounds were tested[13] for their ability to inhibit the adhesion of HL-60 cells to HUVECs (Normal Human Umbilical Vein Endothelial Cells). Compound **22**, **23** and **24** showed more significant competitive inhibition activity than **20**, **21** and sialyl Lewis X ganglioside.[14] These results suggest that more than two residues of the ethylene glycol chain in the spacer is necessary for expressing potent activity as selectin blockers.

EXPERIMENTAL

General Procedures. Specific rotations were determined with a Jasco DIP-370 digital polarimeter at 25 ℃, and IR spectra were recorded with a Jasco IR-700 infrared spectrometer. ^{1}H NMR spectra were recorded at 300 MHz with General Electric QE-plus spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 300 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

1-(4-Nitrobenzyl)-3-oxapentane-1,5-diol (5). To a solution of diethylene glycol (**1**; 500 mg, 4.7 mmol) in benzene (5 mL) cooled to 10 °C were added silver(I) oxide (3.3 g) and 4-nitrobenzyl bromide (1.0 g, 4.6 mmol), and the mixture stirred for 8 h. After completion of the reaction, the mixture was filtered through Celite, and combined filtrate and washings concentrated. Column chromatography (25:1 CH_2Cl_2-MeOH) of the residue on silica gel (100 g) gave **5** (730 mg, 64%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 3.18 (br s, 1H, OH), 3.63-3.73 (m, 8H, $2OC_2H_4O$), 4.69 (s, 2H, CH_2Ph), and 7.55-8.19 (m, 4H, aromatic protons).

Anal. Calcd for $C_{11}H_{15}NO_5$ (241.2): C, 54.77; H, 6.27; N, 5.81. Found: C, 54.68; H, 6.03; N, 5.70.

1-(4-Nitrobenzyl)-3,6-dioxaoctane-1,8-diol (6). 4-Nitrobenzylation of triethylene glycol (**2**; 500 mg, 3.3 mmol), as described for **5**, afforded compound **6** (485 mg, 51%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 3.12 (br s, 1H, OH), 3.60-3.75 (m, 12H, $3OC_2H_4O$), 4.68 (s, 2H, CH_2Ph), and 7.52-8.20 (m, 4H, aromatic protons).

Anal. Calcd for $C_{13}H_{19}NO_6$ (285.3): C, 54.73; H, 6.71; N, 4.91. Found: C, 54.66; H, 6.58; N, 4.84.

1-(4-Nitrobenzyl)-3,6,9-trioxaundecane-1,11-diol (7). 4-Nitrobenzylation of tetraethylene glycol (**3**; 500 mg, 2.6 mmol), as described for **5**, afforded compound **7** (480 mg, 57%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 2.99 (br s, 1H, OH), 3.60-3.72 (m, 16H, $4OC_2H_4O$), 4.68 (s, 2H, CH_2Ph), and 7.52-8.21 (m, 4H, aromatic protons).

Anal. Calcd for $C_{15}H_{23}NO_7$ (329.4): C, 54.70; H, 7.04; N, 4.25. Found: C, 54.58; H, 6.94; N, 4.04.

1-(4-Nitrobenzyl)-3,6,9,12-tetraoxatetradecane-1,14-diol (8). 4-Nitrobenzylation of pentaethylene glycol (**4**; 500 mg, 2.1 mmol), as described for **5**, afforded compound **8** (536 mg, 68%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 3.06 (br s, 1H, OH), 3.59-3.72 (m, 20H, $5OC_2H_4O$), 4.69 (s, 2H, CH_2Ph), and 7.52-8.20 (m, 4H, aromatic protons).

Anal. Calcd for $C_{17}H_{27}NO_8$ (373.4): C, 54.68; H, 7.29; N, 3.75. Found: C, 54.40; H, 7.03; N, 3.48.

1-[4-(2-Tetradecylhexadecanoylamino)benzyl]-3-oxapentane-1,5-diol (9). A solution of **5** (108 mg, 0.45 mmol) in ethanol (5 mL) was hydrogenated in the presence of 10% Pd-C (50 mg) for 1 h. The catalyst was filtered off and the filtrate was concentrated to dryness. The residue was taken up in dichloromethane (5 mL), and treated with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC; 200 mg, 1.04 mmol) and 2-tetradecylhexadecanoic acid (470 mg, 1.04 mmol) at room temperature for 2 h. The mixture was concentrated to a residue, which was chromatographed (30:1 CH_2Cl_2-MeOH) on a column of silica gel (30 g) to afford **9** (220 mg, 76%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.40-1.72 (m, 4H, $COCH(CH_2)_2$), 2.20 (m, 1H, COCH), 2.95 (br s, 1H, OH), 3.57-3.72 (m, 8H, $2OC_2H_4O$), 4.50 (s, 2H, CH_2Ph), and 7.23-7.87 (m, 5H, NH and aromatic protons).

Anal. Calcd for $C_{41}H_{75}NO_4$ (646.1): C, 76.22; H, 11.70; N, 2.17. Found: C, 76.19; H, 11.63; N, 2.15.

1-[4-(2-Tetradecylhexadecanoylamino)benzyl]-3,6-dioxaoctane-1,8-diol (10). Coupling of **6** (105 mg, 0.34 mmol) and 2-tetradecylhexadecanoic acid (400 mg, 0.88 mmol), as described for **9**, gave **10** (170 mg, 67%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.41-1.71 (m, 4H, $COCH(CH_2)_2$), 2.18 (m, 1H, COCH), 2.75 (br s, 1H, OH), 3.59-3.73 (m, 12H, $3OC_2H_4O$), 4.51 (s, 2H, CH_2Ph), and 7.26-7.61 (m, 5H, NH and aromatic protons).

Anal. Calcd for $C_{43}H_{79}NO_5$ (690.1): C, 74.84; H, 11.54; N, 2.03. Found: C, 74.78; H,11.36; N, 1.98.

1-[4-(2-Tetradecylhexadecanoylamino)benzyl]-3,6,9-trioxaundecane-1,11-diol (11). Coupling of **7** (98 mg, 0.30 mmol) and 2-tetradecylhexadecanoic acid (350 mg, 0.77 mmol), as described for **9**, gave **11** (132 mg, 61%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.44-1.71 (m, 4H, $COCH(CH_2)_2$), 2.16 (m, 1H, COCH), 2.83 (br s, 1H, OH), 3.58-3.72 (m, 16H, $4OC_2H_4O$), 4.51 (s, 2H, CH_2Ph), and 7.27-7.54 (m, 5H, NH and aromatic protons).

Anal. Calcd for $C_{45}H_{83}NO_6$ (734.2): C, 73.62; H, 11.40; N, 1.91. Found: C, 73.50; H, 11.16; N, 1.75.

1-[4-(2-Tetradecylhexadecanoylamino)benzyl]-3,6,9,12-tetraoxatetradecane-1,14-diol (12). Coupling of **8** (120 mg, 0.32 mmol) and 2-tetradecylhexadecanoic acid (370 mg, 0.82 mmol), as described for **9**, gave **12** (194 mg, 78%) as

an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.44-1.69 (m, 4H, $COCH(CH_2)_2$), 2.19 (m, 1H, COCH), 3.02 (br s, 1H, OH), 3.58-3.71 (m, 20H, $5OC_2H_4O$), 4.50 (s, 2H, CH_2Ph), and 7.28-7.80 (m, 5H, NH and aromatic protons).

Anal. Calcd for $C_{47}H_{87}NO_7$ (778.2): C, 72.54; H, 11.27; N, 1.80. Found: C, 72.41; H, 11.16; N, 1.78.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2,6-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3-oxapentane-1,5-diol (14).** To a solution of **9** (85 mg, 0.13 mmol) and **13** (110 mg, 0.065 mmol) in dry CH_2Cl_2 (3 mL) were added MS-4A (AW-300, 2 g) and the mixture was stirred for 1 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (50 μL) was added and the mixture was stirred for 5 h at 0 °C and then filtered. Dichloromethane (50 mL) was added to the filtrate, and the solution was successively washed with M Na_2CO_3 and H_2O, dried (Na_2SO_4), then concentrated. Column chromatography (30:1 CH_2Cl_2-MeOH) of the residue on silica gel (20 g) gave **14** (105 mg, 75%) as an amorphous mass: $[\alpha]_D$ -1.8° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.25 (s, 48H, $24CH_2$), 1.34 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6d), 1.44-2.20 (9s, 27H, 8AcO and AcN), 2.52 (dd, 1H, J_{gem} = 12.4 Hz, $J_{3eq,4}$ = 4.4 Hz, H-3c-*eq*), 3.18-3.47 (m, 8H, $2OC_2H_4O$), 3.76 (s, 3H, MeO), 4.52 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1a), 5.12 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1b), 5.26 (dd, 1H, $J_{6,7}$ = 2.7 Hz, $J_{7,8}$ = 7.0 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.4 Hz, H-1d), 5.64 (m, 1H, H-8c), and 7.16-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{115}H_{156}N_2O_{38}$ (2174.5): C, 63.52; H, 7.23; N, 1.29. Found: C, 63.33; H, 7.15; N, 1.00.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2,6-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6-dioxaoctane-1,8-diol (15).** Coupling of **10** (73 mg, 0.11 mmol) and **13** (90 mg, 0.053 mmol), as described for **14**,

gave **15** (73 mg, 62%) as an amorphous mass: $[\alpha]_D$ -0.1° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.34 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.43-2.20 (9s, 27H, 8AcO and AcN), 2.52 (dd, 1H, J_{gem} = 12.4 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c-*eq*), 3.22-3.48 (m, 12H, $3OC_2H_4O$), 3.76 (s, 3H, MeO), 4.49 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1a), 5.12 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1b), 5.25 (dd, 1H, $J_{6,7}$ = 2.8 Hz, $J_{7,8}$ = 9.7 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.7 Hz, H-1d), 5.63 (m, 1H, H-8c), and 7.23-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{117}H_{160}N_2O_{39}$ (2218.5): C, 63.34; H, 7.27; N, 1.26. Found: C, 63.15; H, 7.06; N, 1.11.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2,6-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6,9-trioxaundecane-1,11-diol (16).** Coupling of **11** (96 mg, 0.13 mmol) and **13** (110 mg, 0.065 mmol), as described for **14**, gave **16** (108 mg, 74%) as an amorphous mass: $[\alpha]_D$ -2.2° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.34 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6d), 1.43-2.20 (9s, 27H, 8AcO and AcN), 2.52 (dd, 1H, J_{gem} = 12.4 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c-*eq*), 3.21-3.58 (m, 16H, $4OC_2H_4O$), 3.76 (s, 3H, MeO), 4.49 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1a), 5.12 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1b), 5.25 (dd, 1H, $J_{6,7}$ = 2.9 Hz, $J_{7,8}$ = 9.5 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1d), 5.63 (m, 1H, H-8c), and 7.25-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{119}H_{164}N_2O_{40}$ (2262.6): C, 63.17; H, 7.31; N, 1.24. Found: C, 63.12; H, 7.14; N, 1.03.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2,6-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6,9,12-tetraoxatetradecane-1,14-diol (17).** Coupling of **12** (101 mg, 0.13 mmol) and **13** (110 mg, 0.065 mmol), as described for **14**, gave **17** (114 mg, 76%) as an amorphous mass: $[\alpha]_D$ +9.0° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.34 (d, 3H, $J_{5,6}$

= 6.6 Hz, H-6d), 1.43-2.20 (9s, 27H, 8AcO and AcN), 2.52 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c-*eq*), 3.21-3.66 (m, 20H, $5OC_2H_4O$), 3.76 (s, 3H, MeO), 4.49 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), 5.12 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1b), 5.25 (dd, 1H, $J_{6,7}$ = 2.8 Hz, $J_{7,8}$ = 9.5 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1d), 5.62 (m, 1H, H-8c), and 7.26-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{121}H_{168}N_2O_{41}$ (2306.6): C, 63.01; H, 7.34; N, 1.21. Found: C, 62.79; H, 7.19; N, 1.18.

4-Nitrobenzyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-2,6-di-*O*-benzoyl-β-D-glucopyranoside (18). Coupling of **13** (300 mg, 0.18 mmol) and 4-nitrobenzyl alcohol (54 mg, 0.35 mmol), as described for **14**, gave **18** (227 mg, 76 %) as an amorphous mass: $[\alpha]_D$ -4.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.34 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.43-2.22 (9s, 27H, 8AcO and AcN), 2.53 (dd, 1H, J_{gem} = 12.2 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c-*eq*), 3.79 (s, 3H, MeO), 4.47 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1a), 5.25 (dd, 1H, $J_{6,7}$ = 2.8 Hz, $J_{7,8}$ = 9.5 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1d), 5.62 (m, 1H, H-8c), and 7.18-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{81}H_{88}N_2O_{37}$ (1681.6): C, 57.86; H, 5.28; N, 1.67. Found: C, 57.72; H, 5.23; N, 1.48.

4-(2-Tetradecylhexadecanoylamino)benzyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-2,6-di-*O*-benzoyl-β-D-glucopyranoside (19). Coupling of **18** (227 mg, 0.13 mmol) and 2-tetradecylhexadecanoic acid (68 mg, 0.15 mmol), as described for **9**, gave **19** (139 mg, 49%) as an amorphous mass: $[\alpha]_D$ -2.4° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2CH_3$), 1.24 (s, 48H, $24CH_2$), 1.34 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.43-2.20 (9s, 27H, 8AcO and AcN), 2.52 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3c-*eq*), 3.76 (s, 3H, MeO), 4.49 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), 5.12 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1b), 5.25 (dd, 1H, $J_{6,7}$ = 2.8 Hz, $J_{7,8}$ = 9.5 Hz, H-7c), 5.45 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1d), 5.62 (m, 1H, H-8c), and 7.26-8.22 (m, 24H, aromatic protons).

Anal. Calcd for $C_{111}H_{148}N_2O_{36}$ (2086.4): C, 63.90; H, 7.15; N, 1.34. Found: C, 63.76; H, 7.14; N, 1.11.

4-(2-Tetradecylhexadecanoylamino)benzyl *O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-[(α-L-fucopyranosyl)-(1→3)]-β-D-glucopyranoside (20). To a solution of **19** (139 mg, 0.067 mmol) in MeOH (5 mL) was added NaOMe (10 mg) and the mixture was stirred for 24 h at 40 °C. H_2O (0.5 mL) was added and the mixture was stirred for an additional 8 h at room temperature, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 $CHCl_3$-MeOH. The filtrate and the washings were combined and concentrated. Column chromatography (5:4:0.7 $CHCl_3$-MeOH-H_2O) of the residue on Sephadex LH-20 (30 g) gave **20** (79 mg, 90%) as an amorphous mass: $[\alpha]_D$ -43.0° (*c* 1.1, 5:4:0.5 $CHCl_3$-MeOH-H_2O); ^{1}H NMR (98:2 CD_3SO-D_2O) δ 0.80 (t, 6H, $2CH_3$), 0.89 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6d), 1.17 (s, 48H, $24CH_2$), 1.87 (s, 3H, AcN), 2.73 (broad, 1H, H-3c-*eq*), 4.24 (m, 2H, H-1a, H-1b), 4.36 (s, 2H, C*H*$_2$Ph), 5.15 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1d), and 7.14-7.53 (2d, 4H, aromatic protons).

Anal. Calcd for $C_{66}H_{114}N_2O_{24}$ (1319.6): C, 60.07; H, 8.71; N, 2.12. Found: C, 59.83; H, 8.57; N, 1.85.

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-[(α-L-fucopyranosyl)-(1→3)]-*O*-(β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3-oxapentane-1,5-diol (21).** Deacylation and saponification of **14** (103 mg, 0.047 mmol), as described for **20**, yielded **21** (61 mg, 91%) as an amorphous mass: $[\alpha]_D$ -31.0° (*c* 1.0, 5:4:0.5 $CHCl_3$-MeOH-H_2O); ^{1}H NMR (98:2 CD_3SO-D_2O) δ 0.80 (t, 6H, $2CH_3$), 0.98 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6d), 1.18 (s, 48H, $24CH_2$), 1.87 (s, 3H, AcN), 2.73 (broad, 1H, H-3c-*eq*), 3.14-3.26 (m, 8H, $2OC_2H_4O$), 4.24 (m, 2H, H-1a, H-1b), 4.37 (s, 2H, C*H*$_2$Ph), 5.15 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1d), and 7.16-7.53 (2d, 4H, aromatic protons).

Anal. Calcd for $C_{70}H_{122}N_2O_{26}$ (1407.7): C, 59.73; H, 8.74; N, 1.99. Found: C, 59.54; H, 8.59; N, 1.83.

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-[(α-L-fucopyra-**

nosyl)-(1→3)]-*O*-(β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6-dioxaoctane-1,8-diol (22). Deacylation and saponification of **15** (72 mg, 0.033 mmol), as described for **20**, yielded **22** (46 mg, 97%) as an amorphous mass: $[\alpha]_D$ -23.5° (*c* 1.0, 5:4:0.5 $CHCl_3$-MeOH-H_2O); ^1H NMR (98:2 CD_3SO-D_2O) δ 0.85 (t, 6H, $2CH_3$), 1.01 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6d), 1.22 (s, 48H, $24CH_2$), 1.90 (s, 3H, AcN), 2.77 (dd, 1H, J_{gem} = 11.7 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3c-*eq*), 3.18-3.42 (m, 12H, $3OC_2H_4O$), 4.22 (s, 2H, CH_2Ph), 4.26 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), 4.30 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1b), 5.18 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1d), and 7.20-7.58 (2d, 4H, aromatic protons).

Anal. Calcd for $C_{72}H_{126}N_2O_{27}$ (1451.8): C, 59.57; H, 8.75; N, 1.93. Found: C, 59.42; H, 8.51; N, 1.72.

O-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-[(α-L-fucopyranosyl)-(1→3)]-*O*-(β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6,9-trioxaundecane-1,11-diol (23). Deacylation and saponification of **16** (104 mg, 0.046 mmol), as described for **20**, yielded **23** (65 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -22.2° (*c* 1.0, 5:4:0.5 $CHCl_3$-MeOH-H_2O); ^1H NMR (98:2 CD_3SO-D_2O) δ 0.79 (t, 6H, $2CH_3$), 0.97 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6d), 1.17 (s, 48H, $24CH_2$), 1.87 (s, 3H, AcN), 2.74 (broad, 1H, H-3c-*eq*), 3.14-3.23 (m, 16H, $4OC_2H_4O$), 4.24 (m, 2H, H-1a, H-1b), 4.36 (s, 2H, CH_2Ph), 5.15 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1d), and 7.14-7.53 (2d, 4H, aromatic protons).

Anal. Calcd for $C_{74}H_{130}N_2O_{28}$ (1495.8): C, 59.42; H, 8.76; N, 1.87. Found: C, 59.25; H, 8.51; N, 1.74.

O-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-[(α-L-fucopyranosyl)-(1→3)]-*O*-(β-D-glucopyranosyl)-(1→1)-5-*O*-[4-(2-tetradecylhexadecanoylamino)benzyl]-3,6,9,12-tetraoxatetradecane-1,14-diol (24). Deacylation and saponification of **17** (105 mg, 0.046 mmol), as described for **20**, yielded **24** (70 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -44.7° (*c* 1.1, 5:4:0.5 $CHCl_3$-MeOH-H_2O); ^1H NMR (98:2 CD_3SO-D_2O) δ 0.80 (t, 6H, $2CH_3$), 0.98 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6d), 1.17 (s, 48H, $24CH_2$), 1.87 (s, 3H, AcN), 2.73 (broad, 1H, H-3c-*eq*), 3.14-3.37 (m,

20H, $5OC_2H_4O$), 4.24 (m, 2H, H-1a, H-1b), 4.36 (s, 2H, CH_2Ph), 5.15 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1d), and 7.14-7.53 (2d, 4H, aromatic protons).

Anal. Calcd for $C_{76}H_{134}N_2O_{29}$ (1539.9): C, 59.28; H, 8.77; N, 1.82. Found: C, 59.23; H, 8.64; N, 1.71.

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