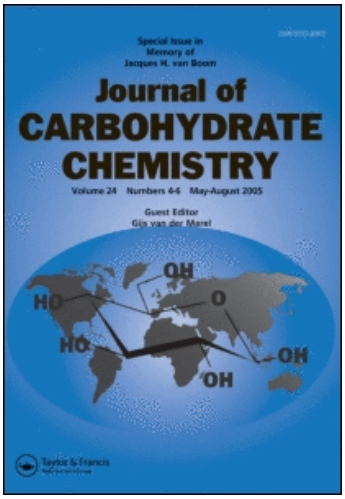

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AN EFFICIENT AND STRAIGHTFORWARD SYNTHESIS OF SIALYL Le^X GLYCOLIPID AS A POTENT SELECTIN BLOCKER[1]

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ABSTRACT

An efficient synthesis of sialyl Lewis X (sLe^x) glycolipid as a potent selectin blocker is described. 2-(Tetradecyl)hexadecanol which functions as an artificial ceramide, was glycosylated with phenyl 4-*O*-acetyl-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-2-phthalimido-1-thio-β-D-glucopyranoside at the first step of the synthetic scheme. The *N*-acetylglucosamine acceptor carrying the hydrophobic aglycon was then coupled with sialyl-α-(2 → 3)galactose donor to afford the trisaccharide which upon successive α-L-fucosylation and deprotections, resulted in sLe^x glycolipid in quite straightforward steps.

Key Words: Sialyl Lewis X; Selectin; Glycolipid

INTRODUCTION

Selectins are a family of carbohydrate-binding proteins that mediate the tethering and rolling of leukocytes in blood vessel endothelium at the sites of inflammation.[2,3] Selectins are also implicated in hematogenous metastasis of some cancer cells.[4,5] Sialyl Lewis X (sLe^x) tetrasaccharide, Neu5Acα2 → 3Galβ1 → 4(Fucα1 → 3) GlcNAc has been generally recognized as a common ligand for all

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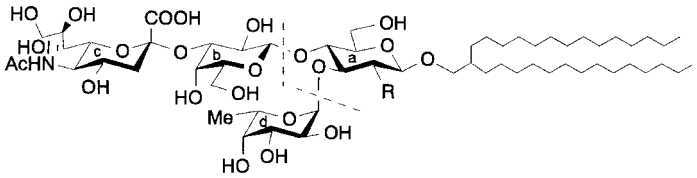


1 R = OH
2 R = NHAc

Scheme 1. Synthetic analogs of sialyl Lewis X ganglioside.

selectins.[6,7] and therefore, many analogs and mimetics of sLe^x have been designed and synthesized[8,9] not only to elucidate the mechanism of selectin recognition but also to present the targets for novel therapeutic agents against allergy, inflammatory diseases, and cancer metastasis.

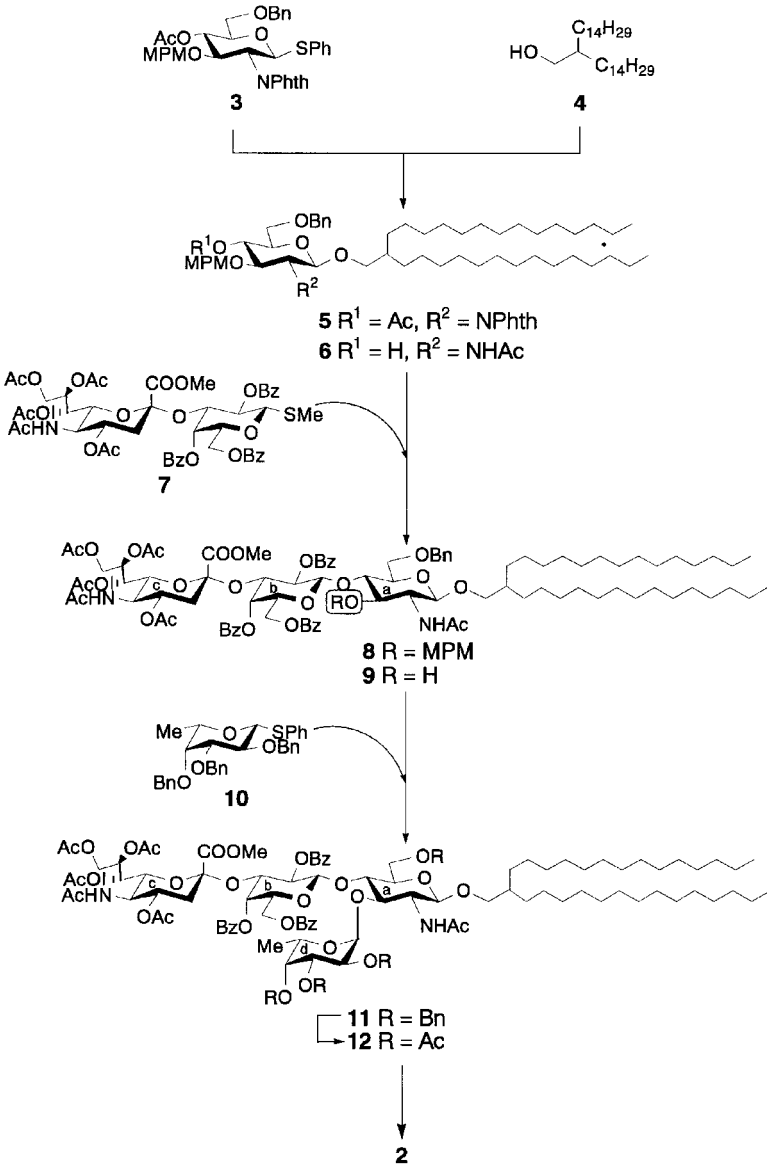
Previously, we have reported that the sLe^x glycolipid (**1**)[10] having 2-(tetradecyl)hexadecanol instead of the ceramide is a potent binding inhibitor of three selectins,[11] in spite of the replacement of *N*-acetyl-D-glucosamine (**2**) with D-glucose (**1**) at the reducing end. As a component of our continuous studies on the structure-activity relationship of selectin ligand/inhibitor, we describe herein the synthesis of the inherent sLe^x glycolipid (**2**) having *N*-acetylglucosamine, based not on the strategy employed for the synthesis of **1** but on a newly developed, straightforward strategy (Scheme 1).

RESULTS AND DISCUSSION

In the retrosynthetic perspective of the glycolipids, the first disconnection of the molecule is generally placed between the oligosaccharide segment and the lipid segment. However, this strategy cannot be applied to the sialooligosaccharide with *N*-acetylglucosamine at the reducing end, due to the presence of the acid labile sialyl glycoside bond and the stability of the oxazoline intermediate. Based on these analyses, we employed a new synthetic strategy where the *N*-acetylglucosamine was first condensed with the lipid segment and subjected to further glycosylations to construct the desired oligosaccharide structures. This strategy eliminated the laborious protection/deprotection processes at the anomeric position and improved the overall efficiency of the synthesis.

Glycosylation of 2-(tetradecyl)hexadecanol (**4**)[12] with phenyl 4-*O*-acetyl-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-2-phthalimido-1-thio-β-D-glucopyranoside (**3**)[13] in dichloromethane for 3 h at room temperature in the presence of *N*-iodosuccinimide (NIS), trifluoromethanesulfonic acid (TfOH) and powdered 4 Å molecular sieves (4 Å MS) resulted in the desired β-glycoside in 84% yield. A significant signal in the ^1H NMR spectrum of **5** to support the stereochemistry of the newly formed glycosidic linkage was a one-proton doublet at δ 5.15 (d, $J_{1,2} = 9.5$ Hz, H-1 of GlcNAc) (Scheme 2).

Removal of phthaloyl and acetyl groups in **5** in the presence of hydrazine monohydrate in ethanol for 10 h at 80°C, and subsequent acetamidation with acetic



Scheme 2. Synthesis of sialyl Lewis X glycolipid.

anhydride in methanol afforded the desired glycosyl acceptor **6** in 96% yield. Glycosylation of **6** with methyl (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 (**7**)[14] was carried out in the presence of dimethyl(methylthio)sulfonium triflate (DMTST)[15,16] and 4 Å MS for 12 h at 0°C, to afford the desired trisaccharide derivative **8** in 70% yield. A significant signal in the ^{1}H NMR spectrum of **8** was a

one-proton doublet at δ 5.09 (d, $J_{1,2}$ = 9.8 Hz, H-1 of Gal), indicating that the α(2 → 3)-sialylgalactose residue was incorporated into the acceptor as a β-glycoside.

For the removal of the 4-methoxybenzyl (MPM) group, the oxidative cleavage by ceric ammonium nitrate (CAN) in acetonitrile–water has generally been employed.[13,17] However, due to the low solubility of **8** in acetonitrile–water, we attempted the cleavage of MPM in the presence of trimethylchlorosilane (TMSCl), tin (II) chloride ($SnCl_2$), and anisole in dichloromethane.[18] Thus, treatment of **8** with the reagent for 3 h at 18°C afforded the desired trisaccharide acceptor **9** in 94% yield. Subsequent α-L-fucosylation of **9** in benzene at 7°C in the presence of phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (**10**),[19] NIS, TfOH and 4 Å MS afforded the protected sLe^x derivative **11** in 95% yield. This structure was supported by a characteristic doublet at δ 5.21 (d, $J_{1,2}$ = 3.4 Hz, H-1 of Fuc). Hydrogenolytic removal of the benzyl group in **11** over palladium hydroxide in ethanol for 24 h at 40°C and subsequent acetylation of the free hydroxyls with acetic anhydride and pyridine for 12 h at room temperature afforded the fully acylated sLe^x derivative **12** in 93% yield. Finally, *O*-deacylation of **12** with sodium methoxide in methanol for 24 h at room temperature, and subsequent saponification of the methyl ester afforded the target sLe^x neoglycolipid **2** in a quantitative yield.

In summary, by using a novel synthetic strategy, we accomplished the efficient and straightforward synthesis of the pharmaceutically active homolog of sLe^x glycolipid in 46% yields over seven steps following the preparations of corresponding building blocks.

EXPERIMENTAL

General Methods. Specific rotations were determined with a Horiba SEPA-300 high sensitive polarimeter at 25°C, and ^1H NMR spectra were recorded at 400 MHz with a Varian Inova 400, or 500 MHz with a Varian Inova 500 spectrometer using deuterated solvents ($CDCl_3$, CD_3OD) with TMS as the internal standard. Preparative TLC was performed on silica gel (E. Merck), and column chromatography on silica gel (Fuji Silysia Co., 300 mesh) was carried out with the solvent system (v/v) specified. Concentrations and evaporations were conducted in vacuo.

2-(Tetradecyl)hexadecyl 4-*O*-acetyl-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-2-phthalimido-β-D-glucopyranoside (5). To a solution of **3** (200 mg, 0.30 mmol) and 2-(tetradecyl)hexadecanol (**4**, 289 mg, 0.76 mmol) in dry CH_2Cl_2 (8 mL) was added powdered 4 Å molecular sieves (4 Å MS, 0.6 g), and the mixture was stirred for 3 h at room temperature. *N*-Iodosuccinimide (NIS, 206 mg, 0.91 mmol) and trifluoromethanesulfonic acid (TfOH, 4.0 μL, 45.2 μmol) were then added to the mixture, and stirred for 3 h at room temperature. The solids were filtered and washed with $CHCl_3$. The combined filtrate and washings were further washed with M $NaHCO_3$ and M $Na_2S_2O_3$, dried (Na_2SO_4) and concentrated. Column chromatography (1:6 EtOAc-hexane) of the residue on silica gel gave **5** (251 mg, 84%) as an amorphous mass: $[\alpha]_D$ + 38.2° (*c* 1.1 $CHCl_3$); IR (film) 2950, 1750, 1720, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.90 (t, 6H, J = 6.9 Hz, $2CH_3$), 1.11–1.43 (m, 53H, $26CH_2$ and CH), 1.99 (s, 3H, AcO), 3.19 (dd, 1H, J_{gem} = 9.1, J_{vic} = 6.6 Hz, OCH_2C), 3.61 (s, 3H, MeO), 3.78 (m, 2H, H-5

and O*CH*$_2$C), 4.22 (dd, 1H, $J_{2,3}$ = 9.5, $J_{3,4}$ = 8.4 Hz, H-3), 4.43 (t, 1H, $J_{1,2}$ = 9.5 Hz, H-2), 5.12 (t, 1H, $J_{4,5}$ = 8.4 Hz, H-4), 5.15 (d, 1H, H-1), 6.44, 6.94 (2d, 4H, J = 8.1, 8.4 Hz, MeO*Ph*), 7.23–7.84 (m, 9H, Ph and phthaloyl-H).

Anal. Calcd for $C_{61}H_{91}NO_9$ (982.40): C, 74.58; H, 9.34; N, 1.43. Found: C, 74.51; H, 9.17; N, 1.34.

2-(Tetradecyl)hexadecyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (6). To a solution of **5** (450 mg, 0.46 mmol) in EtOH (20 mL) was added $NH_2NH_2{\cdot}H_2O$ (1.0 mL, 20.5 mmol), and the mixture was refluxed for 10 h with stirring. The solids were filtered and washed with $CHCl_3$, and the filtrate was concentrated. This residue was dissolved in MeOH (14 mL) and CH_2Cl_2 (4 mL), and treated with Ac_2O (0.42 mL, 4.49 mmol) for 14 h at room temperature, then concentrated. Column chromatography (1:2 EtOAc-hexane) of the residue on silica gel gave **6** (377 mg, 96%) as an amorphous mass: $[\alpha]_D$ − 8.8° (*c* 1.4 $CHCl_3$); IR (film) 3550, 3350, 2950, 1680, 1520, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.91 (t, 6H, J = 6.9 Hz, 2CH_3), 1.20–1.37 (m, 53H, 26CH_2 and CH), 1.92 (s, 3H, AcN), 3.27 (dd, 1H, J_{gem} = 9.5, J_{vic} = 6.6 Hz, O*CH*$_2$C), 3.35 (m, 1H, H-2), 3.53 (m, 1H, H-5), 3.64 (t, 1H, $J_{3,4} = J_{4,5}$ = 8.8 Hz, H-4), 3.76 (m, 3H, H-6, H-6′ and O*CH*$_2$C), 3.80 (s, 3H, MeO), 3.98 (dd, 1H, $J_{2,3}$ = 10.2 Hz, H-3), 4.78 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.69 (d, 1H, $J_{2,NH}$ = 8.1 Hz, NH), 6.86, 7.27 (2d, 4H, J = 8.4 Hz, MeO*Ph*), 7.28–7.37 (m, 5H, Ph).

Anal. Calcd for $C_{53}H_{89}NO_7$ (852.30): C, 74.69; H, 10.53; N, 1.64. Found: C, 74.67; H, 10.49; N, 1.64.

2-(Tetradecyl)hexadecyl (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-galactopyranosyl)-(1 → 4)-2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (8). To a solution of **6** (193 mg, 0.23 mmol) and **7** (352 mg, 0.35 mmol) in dry CH_2Cl_2 (10 mL) was added powdered 4 Å MS (0.8 g), and the mixture was stirred for 5 h at room temperature, then cooled to 0°C. Dimethyl(methylthio)-sulfonium triflate (DMTST, 320 mg, 1.23 mmol) was added to the mixture, and stirred for 10 h at 0°C. The solids were filtered and washed with $CHCl_3$. The combined filtrate and washings were again washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (90:1 $CHCl_3$–MeOH) of the residue on silica gel gave **8** (291 mg, 70%) as an amorphous mass: $[\alpha]_D$ + 9.5° (*c* 1.6 $CHCl_3$); IR (film) 3350, 2950, 1750, 1680, 1520, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 6H, J = 7.3 Hz, 2CH_3), 1.00–1.41 (m, 53H, 26CH_2 and CH), 1.54, 1.78, 1.91, 1.99, 2.16 (5s, 18H, 4AcO, 2AcN), 1.66 (t, 1H, $J_{3ax,4} = J_{gem}$ = 12.3 Hz, H-3*ax*), 2.46 (dd, 1H, $J_{3eq,4}$ = 4.5 Hz, H-3*eq*), 2.94 (dd, 1H, J_{gem} = 8.7, J_{vic} = 7.3 Hz, O*CH*$_2$C), 3.56 (dd, 1H, J_{vic} = 4.8 Hz, O*CH*$_2$C), 3.69 (s, 3H, MeO), 3.82 (s, 3H, COOMe), 3.98 (dd, 1H, $J_{8,9}$ = 6.6, J_{gem} = 12.3 Hz, H-9c), 4.23 (dd, 1H, $J_{8,9'}$ = 6.8 Hz, H-9′c), 4.43 (d, 1H, $J_{1,2}$ = 9.1 Hz, H-1a), 4.83 (m, 1H, H-4c), 4.94 (dd, 1H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 3.2 Hz, H-3b), 5.07 (d, 1H, $J_{5,NH}$ = 7.5 Hz, NH of c), 5.09 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1b), 5.23 (dd, 1H, $J_{6,7}$ = 2.3, $J_{7,8}$ = 9.6 Hz, H-7c), 5.39 (d, 1H, H-4b), 5.48 (t, 1H, H-2b), 5.69 (m, 1H, H-8c), 5.77 (d, 1H, $J_{2,NH}$ = 8.4 Hz, NH-a), 6.71, 7.27 (2d, 4H, J = 8.4 Hz, MeO*Ph*), 7.25–8.23 (m, 20H, 4Ph).

Anal. Calcd for $C_{100}H_{138}N_2O_{27}$ (1800.19): C, 66.72; H, 7.73; N, 1.56. Found: C, 66.64; H, 7.45; N, 1.45.

2-(Tetradecyl)hexadecyl (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-galactopyranosyl)-(1 → 4)-2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (9). To a solution of **8** (512 mg, 0.28 mmol) in CH_2Cl_2 (7 mL) were added trimethylchlorosilane (TMSCl, 107 μL, 0.84 mmol), $SnCl_2$ (5.2 mg, 27.4 μmol) and anisole (46 μL, 0.42 mmol) at 0°C, and the mixture was stirred for 3 h at 18°C. Once the reaction was completed, the mixture was extracted with $CHCl_3$. This extract was successively washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (70:1 $CHCl_3$–MeOH) of the residue on silica gel gave **9** (444 mg, 94%) as an amorphous mass: $[\alpha]_D + 38.7°$ (*c* 1.7 $CHCl_3$); IR (film) 3550, 3350, 2950, 1750, 1680, 1520, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, J = 6.8 Hz, $2CH_3$), 1.11–1.40 (m, 53H, $26CH_2$ and CH), 1.54, 1.76, 1.90, 1.91, 2.03, 2.18 (6s, 18H, 4AcO, 2AcN), 1.62 (t, 1H, $J_{3ax,4} = J_{gem} = 12.3$ Hz, H-3*ax*), 2.43 (dd, 1H, $J_{3eq,4} = 4.6$ Hz, H-3*eq*), 3.20 (dd, 1H, $J_{gem} = 9.3$, $J_{vic} = 6.6$ Hz, O*CH*$_2$C), 3.74 (dd, 1H, $J_{vic} = 5.2$ Hz, O*CH*$_2$C), 3.84 (s, 3H, COOMe), 3.97 (dd, 1H, $J_{8,9} = 6.6$, $J_{gem} = 12.5$ Hz, H-9c), 4.28 (dd, 1H, $J_{8,9'} = 6.9$ Hz, H-9′c), 4.51 (d, 1H, $J_{1,2} = 8.2$ Hz, H-1a), 4.82 (m, 1H, H-4c), 4.95 (dd, 1H, $J_{2,3} = 10.0$, $J_{3,4} = 3.2$ Hz, H-3b), 5.04 (d, 1H, $J_{1,2} = 8.1$ Hz, H-1b), 5.16 (d, 1H, $J_{5,NH} = 10.0$ Hz, NH-c), 5.22 (dd, 1H, $J_{6,7} = 2.7$, $J_{7,8} = 9.4$ Hz, H-7c), 5.39 (d, 1H, H-4b), 5.44 (d, 1H, $J_{2,NH} = 8.4$ Hz, NH-a), 5.48 (dd, 1H, H-2b), 5.67 (m, 1H, H-8c), 7.14–8.24 (m, 20H, 4Ph).

Anal. Calcd for $C_{92}H_{130}N_2O_{26}$ (1680.04): C, 65.77; H, 7.80; N, 1.67. Found: C, 65.72; H, 7.75; N, 1.42.

2-(Tetradecyl)hexadecyl (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-galactopyranosyl)-(1 → 4)-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1 → 3)]-2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (11). To a solution of **9** (195 mg, 0.11 mmol) and **10** (90 mg, 0.17 mmol) in dry benzene (5 mL) was added powdered 4 Å MS (0.3 g), and the mixture was stirred for 3 h at room temperature, then cooled to 0°C. NIS (115 mg, 0.51 mmol) and TfOH (7.5 μL, 84.7 μmol) were added to the mixture and stirred for 2 h at 7°C. The solids were filtered and washed with $CHCl_3$. The combined filtrate and washings were further washed with M $NaHCO_3$ and M $Na_2S_2O_3$, dried (Na_2SO_4) and concentrated. Column chromatography (80:1 $CHCl_3$–MeOH) of the residue on silica gel gave **11** (220 mg, 95%) as an amorphous mass: $[\alpha]_D - 17.9°$ (*c* 1.5 $CHCl_3$); IR (film) 3350, 2950, 1750, 1680, 1520, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, J = 6.8 Hz, $2CH_3$), 1.10 (d, 3H, $J_{5,6} = 6.4$ Hz, H-6d), 1.11–1.37 (m, 53H, $26CH_2$ and CH), 1.57, 1.79, 1.84, 1.92, 2.00, 2.16 (6s, 18H, 4AcO, 2AcN), 1.70 (t, 1H, $J_{3ax,4} = J_{gem} = 12.4$ Hz, H-3*ax*), 2.43 (dd, 1H, $J_{3eq,4} = 4.4$ Hz, H-3*eq*), 2.77 (dd, 1H, $J_{gem} = 9.2$, $J_{vic} = 6.8$ Hz, O*CH*$_2$C), 3.51 (dd, 1H, $J_{vic} = 5.2$ Hz, O*CH*$_2$C), 3.78 (s, 3H, COOMe), 4.83 (m, 1H, H-4c), 4.92 (dd, 1H, $J_{2,3} = 10.0$, $J_{3,4} = 3.6$ Hz, H-3b), 5.03 (d, 1H, $J_{5,NH} = 10.5$ Hz, NH-c), 5.04 (d, 1H, $J_{1,2} = 8.0$ Hz, H-1b), 5.21 (d, 1H, $J_{1,2} = 3.4$ Hz, H-1d), 5.26 (dd, 1H, $J_{6,7} = 2.7$, $J_{7,8} = 9.4$ Hz, H-7c), 5.34 (d, 1H, H-4b), 5.47 (dd, 1H, H-2b), 5.69 (m, 1H, H-8c), 5.93 (d, 1H, $J_{2,NH} = 8.4$ Hz, NH-a), 7.10–8.23 (m, 35H, 7Ph).

Anal. Calcd for $C_{119}H_{158}N_2O_{30}$ (2096.56): C, 68.17; H, 7.60; N, 1.34. Found: C, 67.88; H, 7.40; N, 1.31.

2-(Tetradecyl)hexadecyl (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-galactopyranosyl)-(1 → 4)-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranoside (12). A solution of **11** (70 mg, 33.4 mmol) in EtOH (7 mL) was hydrogenolyzed over $Pd(OH)_2$ (100 mg) for 13 h at 40°C, then filtered and concentrated. The residue was acetylated with Ac_2O (1 mL) and pyridine (2 mL) for 12 h at room temperature. The solution was diluted with $CHCl_3$, and the solution was washed with 2 M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (60:1 $CHCl_3$–MeOH) of the residue on silica gel gave **12** (59 mg, 92%) as an amorphous mass: $[\alpha]_D - 20.4°$ (*c* 1.2 $CHCl_3$); IR (film) 3350, 2950, 1750, 1680, 1520, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.88 (t, 6H, J = 6.8 Hz, $2CH_3$), 1.17 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.18–1.40 (m, 53H, $26CH_2$ and CH), 1.57, 1.78, 1.82, 1.90, 1.96, 2.00, 2.02, 2.07, 2.08, 2.14 (10s, 30H, 8AcO, 2AcN), 1.62 (t, 1H, $J_{3ax,4} = J_{gem}$ = 12.3 Hz, H-3*ax*), 2.42 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, H-3*eq*), 2.94 (dd, 1H, J_{gem} = 9.1, J_{vic} = 6.9 Hz, OCH_2C), 3.57 (dd, 1H, J_{vic} = 5.2 Hz, OCH_2C), 3.82 (s, 3H, COOMe), 3.65 (dd, 1H, $J_{5,6}$ = 10.7, $J_{6,7}$ = 2.7 Hz, H-6c), 4.76 (m, 1H, H-4c), 4.85 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1b), 5.02 (dd, 1H, $J_{2,3}$ = 10.9, $J_{3,4}$ = 3.9 Hz, H-3b), 5.31 (dd, 1H, $J_{7,8}$ = 10.3 Hz, H-7c), 5.44 (dd, 1H, H-2b), 5.47 (d, 1H, H-4b), 5.67 (m, 1H, H-8c), 7.44–8.21 (m, 15H, 3Ph).

Anal. Calcd for $C_{99}H_{142}N_2O_{34}$ (1904.21): C, 62.45; H, 7.52; N, 1.47. Found: C, 62.43; H, 7.29; N, 1.35.

2-(Tetradecyl)hexadecyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2 → 3)-(β-D-galactopyranosyl)-(1 → 4)-[(α-L-fucopyranosyl)-(1 → 3)]-2-acetamido-2-deoxy-β-D-glucopyranoside (2). To a solution of **12** (59 mg, 30.9 mmol) in MeOH (4 mL) was added a catalytic amount of NaOMe, and the mixture was stirred for 18 h at room temperature and then water was added. After completion of the reaction (15 h), the mixture was neutralized with Amberlite IR-120 (H^+) resin and filtered. The resin was washed with MeOH, and combined filtrate and washings were concentrated. Column chromatography (MeOH) of the residue on Sephadex LH-20 (40 g) gave **2** (38 mg, quant.) as an amorphous mass: $[\alpha]_D - 29.7°$ (*c* 0.7 MeOH); ^1H NMR (CD_3OD): δ 0.79 (t, 6H, J = 6.9 Hz, $2CH_3$), 1.05 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.10–1.29 (m, 53H, $26CH_2$ and CH), 1.62 (t, 1H, $J_{3ax,4} = J_{gem}$ = 12.4 Hz, H-3*ax*), 1.84, 1.91 (2s, 6H, 2AcN), 2.78 (dd, 1H, $J_{3eq,4}$ = 3.9 Hz, H-3*eq*), 3.42 (dd, 1H, $J_{1,2}$ = 8.0, $J_{2,3}$ = 9.8 Hz, H-2b), 3.94 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-3b), 4.28 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1a), 4.42 (d, 1H, H-1b), 4.93 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1d). FAB-MS spectrum of **2** (negative ion mode, triethanolamine matrix); *m/z*: 1239.8 $[M\text{-H}]^-$ (Calcd for $C_{61}H_{111}N_2O_{23}$, Exact 1239.7578), 1093.8 [*M*-Fuc], 948.7 [*M*-NeuAc], 786.7 [948.7-Gal], 640.7 [786.7-Fuc].

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