Synthesis and Growth Inhibitory Properties of Glucosamine-derived Glycerolipids

Guangli Yang, Richard W. Franck,* Robert Bittman, Pranati Samadder, and Gilbert Arthur

Department of Chemistry, Hunter College/CUNY, 695 Park Avenue, New York, New York 10021, Queens College/CUNY, Flushing, New York 11367, and Department of Biochemistry and Medical Genetics, University of Manitoba, Winnipeg, Manitoba, Canada R3E 0W3

rfranck@shiva.hunter.cuny.edu

Experimental Section

General Methods. All air-moisture sensitive reactions were performed under positive Ar or N_2. All solvents and reagents were distilled, dried, and /or recrystallized prior to use according to standard laboratory procedures. Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica 60 F_{254} plates. Column chromatography was accomplished with E. Merck silica gel (230–400 mesh). NMR spectra were obtained on a GE QE 300 MHz spectrometer. All ^{1}H chemical shifts are reported in ppm relative to the internal standard tetramethylsilane (TMS, δ 0.00). ^{13}C chemical shifts are reported in ppm relative to $CDCl_3$ (center of triplet, δ 77.23). Mass spectra were recorded on a Hewlet Packard 5989A GC mass spectrometer (EI). Optical rotations were measured at 23 °C with an Autopol III automatic polarimeter in a cell of 1-dm pathlength. Melting points were determined on a Fisher-Johns melting point apparatus and uncorrected.

(R)-2-Phenyl-(S)-4-hydroxymethyl-1,3-dioxane A sample of 2.6 g (20.6 mmol) of commercially available (Aldrich) (*S*)-(-)-1,2,4-butanetriol **2**, benzaldehyde (3.47 mL, 29 mmol) and trimethyl orthoformate (3.74 mL, 29 mmol) was dissolved in 80 mL of CH_2Cl_2, and 1 mL of CF_3CO_2H was added. After 24 h at rt, the reaction was quenched by the addition of NaOMe (20 mg) and diluted with 100 mL of ether and filtered. After the filtrate was concentrated under reduced pressure, the residue was purified by column chromatography on silica gel, eluting with PE-EtOAc (5:1~1:1) to afford 3.6 g of the product as a colorless oil (90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.33 (m, 5H), 5.51 (s, 1H), 4.29 (dd, *J* = 4.1, 10.7 Hz, 1H), 3.95 (m, 2H), 3.60 (m, 2H), 2.85 (s, 1H, OH), 1.85 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.10, 129.58, 128.90, 126.85, 101.96, 78.35, 67.36, 66.29, 27.69.

(R)-2-Phenyl-(S)-4-hexadecyloxymethyl-1,3-dioxane (3) To a suspension of NaH (3 g, 60% in mineral oil) in 30 mL of dry THF was added a solution of (R)-2-phenyl-(S)-4-hydroxymethyl-1,3-dioxane (1.47 g, 7.6 mmol) in 10 mL of THF at 0 °C. After 30 min, hexadecyl bromide (3 mL, 9.88 mmol) and tetrabutylammonium iodide (0.28 g, 0.76 mmol) were added. The mixture was stirred overnight, and the reaction was quenched by addition of 5 mL of

MeOH. After the solvent was removed under reduced pressure, ether and water were added. The product was extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated. The product was purified by column chromatography on silica gel, eluting with EtOAc-PE (5%) to afford 1.55 g of white solid **3** (50%); mp 51-54 °C. MS: m/z 441 (M^++Na^+), (calcd. for $C_{27}H_{45}O_3$, 418.662). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.31 (m, 5H, Ph), 5.54 (s, PhCH-), 4.32-4.27 (m, -CHO), 4.10-3.94 (m, 2H, -CH_2O-), 3.65-3.59 (m, 4H, -CH_2O), 1.89-1.83 (m, 2H, -CH_2-), 1.62-1.54 (m, 2H), 1.25 (s, 26H), 0.88 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.28, 129.32, 128.77, 126.79, 101.88, 77.09, 74.44, 72.61, 67.61, 32.74, 30.51, 30.30, 30.18, 29.18, 26.93, 23.51, 14.94.

(3S)-4-*O*-Hexadecyl-1,3-butanediol Ether **3** (0.836 g, 2 mmol) was dissolved in 8 mL of 80% acetic acid at 90 °C. The mixture was heated at this temperature for 1 h. The mixture was quenched with $NaHCO_3$. The mixture was then extracted with ether (30 mL× 3). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The product was purified by column chromatography on silica gel, eluting with EtOAc-PE (50%) to afford 0.55 g of a white solid (82%). mp. 48 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.01 (m, 1H), 3.83 (q, 2H), 3.45 (m, 3H), 3.33 (m, 1H), 2.74 (d, *J* = 5.9 Hz, 1H, OH), 2.55 (t, *J* = 5.5 Hz, 1H, OH), 1.71 (m, 2H), 1.57 (m, 2H), 1.25 (s, 28H), 0.88 (t, *J* = 6.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 75.02, 71.86, 70.46, 61.25, 35.32, 32.22, 29.99, 29.77, 29.65, 26.42, 22.99, 14.41.

(3S)-4-*O*-Hexadecyl-1-*O*-*tert*-butyldimethylsilyl-3-butanol (4) To a solution of 4-*O*-hexadecyl-1,3-butanediol (0.5 g, 1.52 mmol) in 10 mL of CH_2Cl_2 was added TBDMSCl (0.259 g, 1.66 mmol) followed by imidazole (0.227 g, 3.33 mmol). The mixture was stirred at rt for 1 h. The mixture was filtered and the filtrate was rinsed with 20mL CH_2Cl_2. The solution was then extracted with H_2O (20mL×2). The organic layer was concentrated and purified by column chromatography on silica gel (eluting with EtOAc-PE 20%) to afford 0.65 g (97%) of compound **4**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.97 (m, 1H), 3.82 (m, 2H), 3.47-3.34 (m, 4H), 3.11 (d, *J* = 2.6Hz, 1H, OH), 1.69 (m, 2H), 1.57 (m, 2H), 1.25 (s, 28H), 0.89 (m, 12H), 0.07 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 75.17, 71.81, 69.69, 61.54, 35.92, 32.23, 29.99, 29.91, 29.78, 29.65, 26.43, 26.20, 22.99, 18.51, 14.41, -5.13.

(3S)-4-*O*-Hexadecyl-3-*O*-methyl-1-butanol (5) To a suspension of 600 mg NaH (60% in mineral oil) in THF (10 mL) was added 1.185 g (2.669 mmol) of **4**. After H_2 evolution ceased, 0.67mL (10.67 mmol) of CH_3I was added, followed by Bu_4NI (10mg, 0.03mmol). After 4 h, the reaction was quenched by addition of 2 mL of MeOH. After concentration under reduced pressure, the residue was treated with 20 mL of water and extracted with CH_2Cl_2 (30 mL×3). The organic layer was dried over Na_2SO_4. After concentration, a 1.22 g sample of a colorless oil was obtained.

To a solution of the above crude product (1.22 g, 2.669 mmol) in 10 mL of THF was added 5.3 mL of Bu_4NF (a 1 M solution in THF). After the mixture was stirred at rt for 2 h, and then concentrated, the residue was treated with water and extracted with ether (30mL×3). The organic layer was dried over Na_2SO_4. After concentration, 0.748 of **5** (93% for two steps) was obtained as a white amorphous solid after purification by chromatography on

silica gel (elution with 30% EtOAc/PE). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (q, 2H), 3.57-3.40 (m, 8H), 2.66 (t, *J* = 5.5Hz, 1H, OH), 1.80 (q, 2H), 1.56 (m, 2H), 1.26 (s, 28H), 0.88 (t, *J* = 5.5 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 79.70, 72.67, 72.00, 60.56, 57.83, 34.70, 32.19, 29.87, 29.73, 29.63, 26.38, 22.96, and 14.39.

(3S)-4-*O*-Hexadecyl-3-*O*-methyl-1-iodobutane (6)[1] To a solution of alcohol **5** (0.748 g, 2.174 mmol) in toluene (20 mL) was added Ph_3P (0.684 g, 2.61 mmol) and imidazole (0.325g, 4.18mmol) followed by iodine (0.717 g, 2.83 mmol). The mixture was heated at reflux (120 °C) for 1 h. The reaction was cooled and filtered through Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel (eluting with 5% EtOAc/PE) to afford 0.73 g (75%) of product **6**; mp 27-28 °C; $[\alpha]^{23}$ -16.67° (*c* 6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.44 (s, 3H, OMe), 4.43-3.38 (m, 5H), 3.28 (m, 2H), 2.00 (q, 2H), 1.59 (m, 2H), 1.25 (s, 28H), 0.88 (t, *J* = 6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 79.92, 72.08, 72.03, 58.27, 36.37, 32.21, 29.99, 29.77, 29.65, 26.43, 22.99, 14.41, 2.99.

1-*S*-Acetyl-2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranose (8) [2] After a mixture of 2-acetamido-2-deoxy-D-glucose **7** (2.0 g, 9.04 mmol) and acetyl chloride (3 mL) was stirred overnight, 30 mL of chloroform was added and the solution was poured into 20 mL of ice water. The mixture was rapidly shaken, the organic layer was run into saturated sodium bicarbonate solution containing cracked ice, and the mixture was stirred at first, shaken until the acid was neutralized. The chloroform layer was separated and dried over anhydrous Na_2SO_4. The solution was concentrated in vacuo to afford a 2.88 g of a yellow solid, which was used in the next step without purification.

A mixture of the above crude product (2.0 g, 5.46 mmol), potassium thioacetate (0.624 g, 5.5 mmol), and dry acetone (20 mL) was shaken for 6 h. The solution was filtered to remove inorganic material, and the combined filtrate and chloroform washings were concentrated. The residue was purified by chromatography on silica gel (eluting with 5% EtOH/$CHCl_3$) to afford 2.04 g (92%) of product **8**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.01(d, *J* = 9.9 Hz, 1H, NH), 5.18-5.06 (m, 3H), 5.35 (q, 1H), 4.23 (dd, *J* = 4.4, 12.5 Hz, 1H), 4.05 (dd, *J* = 2.2, 12.4 Hz, 1H), 3.77 (m, 1H), 2.35 (s, 3H, SAc), 2.05 (s, 3H, OAc), 2.02 (s, 6H, OAc), 1.90 (s, 3H, NAc).

(3S)-(3-*O*-Methyl-4-*O*-hexadecyl-1-butylthio) 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (9)[3] To a degassed solution of 0.60 g (1.476 mmol) of thioacetate **8** in 3mL of DMF was added NH_2NH_2·HOAc (0.14 g, 1.48 mmol). The solution was degassed at rt for 1 h. Iodide **6** (0.67 g, 1.47 mmol) was added, followed by triethylamine (0.24 mL, 1.47mmol). After 5 h, 40 mL of ethyl acetate and 20 mL of water were added. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvent, the residue was purified by chromatography on silica gel (eluting with 50% EtOAc/hexane) to afford 0.874 g (87%) of β-thioglycoside **9** as a white solid; mp: 129-131 °C. $[\alpha]^{23}$ -36.92° (*c* 6.5, $CHCl_3$). MS: *m/z* 712 (M^++Na^+), (calcd. $C_{35}H_{63}O_{10}NS$, 689). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.77 (d, *J* = 9.5 Hz, 1H, NH), 5.12 (m, 2H), 4.58 (d, *J* = 10.6 Hz, 1H, H-1), 4.20 (dd, 1H), 4.11 (m, 2H), 3.69 (m, 1H), 3.45-3.37 (m, 8H), 2.79 (m, 2H), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.92 (s, 3H, NAc), 1.76 (m, 2H), 1.53 (m, 2H), 1.22 (s, 26H), 0.85

(t, J = 6.2Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.99, 170.61, 169.99, 169.26, 84.59, 78.78, 76.09, 74.11, 72.53, 71.92, 68.73, 62.55, 57.91, 53.51, 32.12, 32.07, 29.90, 29.70, 29.56, 26.51, 26.36, 23.45, 22.90, 20.92, 20.82, 14.33.

(3S)-(3-*O*-Methyl-4-*O*-hexadecyl-1-butylthio) 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (10)[4] To a solution of acetate **9** (0.205 g, 0.297 mmol) in 2 mL of EtOH/CH_2Cl_2 (9:1) was added a solution of guanidine by making a solution of guanidine hydrochloride (36 mg, 0.3 mmol) in 2mL EtOH, which was passed through a small column of basic ionic exchange resin (Dowex SBR) The mixture was stirred at rt for 20 min, then filtered and washed with EtOH to afford 0.13 g of a white solid.

To a solution of above solid (0.121 g, 0.214 mmol) in 1 mL of DMF was added $PhCH(OMe)_2$ (98 μL, 0.63mmol), followed by *p*-TsOH (4 mg). After the mixture was stirred at rt overnight, the reaction was quenched with saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvents, the residue was purified by chromatography on silica gel (eluting with 50% EtOAc/hexane) to afford 0.123 g (90%) of β-thioglycoside **10** as a white amorphous solid; $[\alpha]^{23}$ -63.68° (*c* 9.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.37-7.34 (m, 3H), 5.88 (d, J = 7.0 Hz, 1H, NH), 5.54 (s, 1H), 4.70 (d, J =10.2 Hz, 1H, H-1), 4.32 (dd, J = 5.8, 10.2 Hz, 1H, H-2), 3.97 (m, 2H), 3.75 (m, 2H), 3.61-3.35 (m, 10H), 2.82 (m, 2H), 2.04 (s, 3H, NAc), 1.82 (m, 2H), 1.57 (m, 2H), 1.25 (s, 26H), 0.88 (t, J = 6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.74, 137.31, 129.26, 128.35, 126.50, 101.86, 84.61, 81.60, 78.83, 77.44, 77.41, 76.94, 73.07, 72.49, 71.96, 70.68, 68.67, 57.92, 56.46, 32.15, 30.36, 30.22, 29.92, 29.74, 29.59, 26.64, 26.38, 23.65, 22.92, 14.37.

3(S)-(3-*O*-Methyl-4-*O*-hexadecyl-1-butylsulfonyl) 2-acetamido-4,6-O-benzylidene-3-*O*-(*tert*-butyldimethyl-silyl)-2-deoxy-β-D-glucopyranoside (11) To a solution of thioglycoside **10** (0.12 g, 0.185 mmol) in 2 mL of DMF was added TBDMSCl (0.096 g, 0.55 mmol), followed by imidazole (0.056 g, 0.83 mmol). The mixture was stirred at rt for 5 h, then filtered and rinsed with CH_2Cl_2. The solution was concentrated and purified by column chromatography on silica gel (eluting with EtOAc-PE 20%) to afford 0.132 g (93%) of thioglycoside as a colorless oil; $[\alpha]^{23}$ -42.60° (*c* 10, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.45-7.43 (m, 2H), 7.34-7.32 (m, 3H), 5.77 (d, J =8.8 Hz, 1H, NH), 5.47 (s, 1H), 4.88 (m, 1H), 4.31 (m, 1H), 4.10 (m, 1H), 3.75-3.32 (m, 12H), 2.80 (m, 2H), 1.98 (s, 3H, NAc), 1.78 (m, 2H), 1.54 (m, 2H), 1.24 (s, 26H), 1.02-0.84 (m, 12H), 0.01 (s, 3H, CH_3), -0.05 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.98, 137.30, 129.09, 128.19, 126.41, 102.00, 84.44, 82.54, 78.72, 73.13, 72.60, 71.91, 70.63, 68.87, 57.92, 57.85, 32.15, 29.94, 29.74, 29.59, 26.65, 26.39, 26.13, 25.98, 23.98, 22.93, 18.37, -3.77, -4.59.

A solution of MMPA (0.166 g, 0.336 mmol) in H_2O (1 mL) was added to a solution of the above sulfide (0.128 g, 0.168 mmol) in EtOH (1 mL) and THF (1 mL). The mixture was kept at 55 °C for 1 h, then concentrated in vacuo to dryness. The residue was treated with 20 mL of saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc (20mL×3), dried over Na_2SO_4, and evaporated to dryness. The residue was purified by

chromatography on silica gel (eluting with 50% EtOAc/PE) to afford 1.11g (95%) of pure sulfone **11** as a white solid; mp: 50-53 °C. $[\alpha]^{23}$ -13.0° (*c* 5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46-7.43 (m, 2H), 7.34-7.33 (m, 3H), 6.33 (d, *J* = 7.3Hz, 1H, NH), 5.48 (s, 1H), 5.28 (m, 1H), 4.57 (t, 1H), 4.32 (m, 1H), 3.77-3.66 (m, 2H), 3.52-3.41 (m, 8H), 3.35-3.19 (m, 2H), 1.97 (m+s, 5H), 1.55 (m, 2H), 1.25 (s, 26H), 0.89-0.82 (m, 12H), 0.01 (s, 3H), -0.05 (s, 3H). ^{13}C NMR ($CDCl_3$, 75MHz): δ 171.50, 137.00, 129.22, 128.24, 126.41, 102.13, 86.43, 82.02, 78.07, 78.03, 77.37, 72.04, 70.99, 70.71, 68.43, 57.79, 53.92, 46.66, 32.18, 30.32, 30.27, 30.25, 29.94, 29.76, 29.60, 26.38, 25.99, 23.96, 23.59, 22.95, 18.42, 14.38, -3.95, -4.63.

(3S)-3-*O*-Methyl-4-*O*-hexadecyl 2′-acetamido-4′,6′-*O*-benzylidene-3′-*O*-(*tert*-butyldimethyl-silyl)-2′-deoxy-D-glucopyranosylidene butane (12) [5] To a solution of 0.12 g (0.15 mmol) of **11** in 1.5 mL of *t*-BuOH and 2 mL of CF_2BrCF_2Br was added 0.3 g (25% by weight) of KOH/Al_2O_3 (prepared one day earlier). The mixture was heated at 47 °C overnight. The solution was filtered through a pad of Celite which was washed with CH_2Cl_2. The residue was purified by column chromatography on silica gel (eluting with 40% EtOAc-PE) to afford 0.056 g (70%, Z isomer only) of **12** as a colorless oil. MS: *m/z* 754 (M^++Na^+), (calcd. $C_{42}H_{73}O_7NSi$, 731). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48-7.45 (m, 2H), 7.37-7.34 (m, 3H), 5.54 (s, 1H), 5.38 (d, *J* =9.3 Hz, 1H, NH), 4.88 (t, *J* = 6.8 Hz, 1H, vinyl H), 4.62 (t, *J* =8.8 Hz, 1H, H-2), 4.38 (dd, *J* =5.1, 10.5 Hz, 1H, H-6), 3.80 (t, *J* = 10.3 Hz, 1H, H-6), 3.63 (m, 2H), 3.43-3.34 (m, 9H), 2.45 (m, 1H), 2.24 (m, 1H), 2.05 (s, 3H, NAc), 1.57 (m, 2H), 1.25 (s, 24H), 0.87 (t, *J* =6.6 Hz, 3H, CH_3), 0.82 (s, 9H), 0.03 (s, 3H, CH_3), -0.04 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.46, 150.38, 137.15, 129.19, 128.25, 126.41, 105.65, 102.09, 82.26, 79.83, 74.59, 72.63, 71.96, 70.64, 68.95, 57.48, 54.59, 32.19,29.96, 29.79, 29.63, 26.43, 26.33, 25.91, 23.84, 22.96, 18.37, 14.39, -3.66, -4.54.

(3S)-3-*O*-Methyl-4-*O*-hexadecyl 2′-acetamido-3′-*O*-(*tert*-butyldimethyl-silyl)-2′-deoxy-β-D-glucopyranosyl butane (13) To a solution of 30 mg (0.041mmol) of **12** in 5 mL of EtOAc was added 20 mg of 10% Pd/C. After the flask was degassed under H_2 three times, the mixture was stirred overnight under H_2 at rt. After filtration of the catalyst, washing with EtOAc, and evaporation of the solvent in vacuo, 23 mg (85%) of **13** was obtained. MS: *m/z* 668 (M^++Na^+), (calcd. $C_{35}H_{71}O_7NSi$, 645). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (d, *J* = 8.3Hz, 1H, NH), 3.85 (m, 1H, H-6), 3.71 (m, 1H, H-6), 3.59 (m, 2H), 3.49-3.28 (m, 14H), 2.20 (t, 1H, OH), 2.10 (d, 1H, OH), 1.97 (s, 3H, NAc), 1.68 (m, 2H), 1.55 (m, 2H), 1.24 (s, 26H), 0.88 (s, 12H), 0.11 (s, 3H), 0.07 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.82, 79.82, 79.00, 78.50, 77.57, 72.85, 71.95, 63.20, 57.56, 56.77, 32.19, 29.96, 29.91, 29.77, 27.79, 27.72, 26.39, 26.05, 24.06, 22.96, 18.42, 14.39, -3.55, -4.09.

(3S)-3-*O*-Methyl-4-*O*-hexadecyl 2′-acetamido-2′-deoxy-β-D-glucopyranosyl butane (14) [6] To a solution of **13** (30 mg, 0.046 mmol) in 1mL of CH_3CN was added $BF_3{\cdot}Et_2O$ (20 μL) at 0 °C. After 1h, saturated aqueous $NaHCO_3$ solution was added, followed by extraction with EtOAc (20 mL×2). The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (eluting with 5:1 $CHCl_3$/MeOH) to afford 23 mg (94%) of **14** as a white solid; mp: 146-149 °C. $[\alpha]^{23}$ 11.18° (*c* 11, $CHCl_3$:MeOH

1:1). MS: *m/z* 554 (M^++Na^+), (calcd. $C_{29}H_{57}O_7N$, 531). ^{1}H NMR ($CDCl_3$ and a few drops of MeOH-d_4, 300 MHz): δ 7.99 (d, *J* = 8.4 Hz, 1H, NH), 3.80 (dd, *J* = 2.8, 12.1 Hz, 1H, H-6), 3.67 (dd, *J* = 4.7, 12.1 Hz, 1H, H-6), 3.55 (t, *J* = 7.7 Hz, 1H), 3.41-3.30 (m, 10H), 3.19 (m, 2H), 2.65 (broad peak), 1.97 (s, 3H, NAc), 1.63-1.49 (m, 6H), 1.21 (s, 24H), 0.84 (t, *J* = 6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.27, 79.88, 79.31, 78.26, 77.09, 72.79, 71.97, 71.79, 62.59, 57.50, 55.98, 32.12, 30.01, 29.90, 29.69, 29.55, 27.84, 27.67, 26.29, 23.15, 22.88, 14.29.

(3S)-3-*O*-Methyl-4-*O*-hexadecyl 2′-amino-2′-deoxy-β-D-glucopyranosyl butane (1b)[7] *N*-Acetyl-β-*C*-glycoside **14** (20 mg, 0.0377 mmol) was dissolved in 2 mL of 2 N KOH/EtOH. After the mixture was degassed and refluxed under N_2 at 120 °C for 6 h, the reaction was quenched with 5mL of saturated NH_4Cl solution, then extracted with $CHCl_3$ (20 mL×3). The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (eluting with 5:1 $CHCl_3$/MeOH) to afford 13 mg (74%) of **1b** as a white amorphous solid; $[\alpha]^{23}$ -4.67° (*c* 6, $CHCl_3$:MeOH 2:1). ^{1}H NMR ($CDCl_3$ and a few drops of MeOH-d_4, 300 MHz): δ 3.73 (dd, 1H), 3.66-3.17 (m, 14H), 2.52 (broad peak), 1.72-1.1.45 (m, 6H), 1.20 (s, 24H), 0.81 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$ and a few drops of MeOH-d_4, 75 MHz): δ 79.91, 79.66, 77.50, 77.42, 76.44, 72.75, 71.90, 71.10, 62.24, 57.69, 32.03, 29.81, 29.69, 29.47, 27.40, 26.91, 26.18, 22.81, 14.17.

---

[1] Spak, S. J.; Martin, O. R. *Tetrahedron* **2000**, *56*, 217–224.
[2] Horton, D.; Wolfrom, M. L. *J. Org. Chem.* **1962**, *27*, 1794–1799
[3] Park, W. K. C.; Meunier, S. J.; Zanini, D.; Roy, R. *Carbohydr. Lett*. 1**995,** *1*, 179–184.
[4] Kunesch, N.; Meit, C.; Poisson, J. *Tetrahedron Lett.* **1987**, *28*, 3569.
[5] Yang, G.; Franck. R. W; Byun, H.-C.; Bittman, R.; Samadder, P.; Arthur, G. *Org. Lett*.; **1999**, *1*, 2149–2151.
[6] King, S. A.; Pipik, B.; Thompson, A. S.; Decamp, A.; Verhoeven, T. R. *Tetrahedron Lett*. **1995**, *36*, 4563–4566.
[7] Erukulla, R. K.; Zhou, X.; Samadder, P.; Arthur, G.; Bittman, R. *J. Med. Chem*. **1996**, *39*, 1545–1548.