Simplifying Oligosaccharide Synthesis: Efficient Synthesis of Lactosamine and Siaylated

Lactosamine Oligosaccharide Donors

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Supporting Information Available

N-protected D-glucosamine **5b-c** derivatives were prepared in three steps starting from D-glucosamine hydrochloride **3** as shown in Scheme 2 (ref 15 for **5b**, and ref 14 for **5c**).

Phenyl 2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-1-thio-β-D-glucopyranoside (5b). ¹H NMR (methanol-*d*₄): δ 7.53 (m, 2 H, Ph), 7.33 (m, 3 H, Ph), 4.91 (d, 1 H, *J* = 12.4 Hz, ½ CH₂CCl₃), 4.83 (d, 1 H, *J* = 10.4 Hz, H-1), 4.75 (d, 1 H, *J* = 12.4 Hz, ½ CH₂CCl₃), 3.92 (dd, 1 H, *J* = 12.0 Hz, *J* = 1.5 Hz, H-6), 3.72 (dd, 1 H, *J* = 12.0 Hz, *J* = 5.1 Hz, H-6), 3.51 (m, 2 H, H-3, H-2), 3.39 (t, 1 H, *J* = 9.6 Hz, H-4), 3.34 (m, 1 H, H-5); ¹³C NMR (methanol-*d*₄): δ 156.94 (O=COCH₂CCl₃), 135.91, 132.51, 130.03, 128.40 (6 x C, SPh), 97.30 (CCl₃), 88.86 (C-1), 82.16 (C-5), 77.38 (C-3), 75.73 (CH₂CCl₃), 71.98 (C-4), 62.98 (C-6), 58.38 (C-2).

Phenyl 2-deoxy-2-(2,5-dimethylpyrrol-1-yl)-1-thio-β-D-glucopyranoside (5c). ¹H NMR (D₂O): δ 7.46 (m, 2 H, Ph), 7.38 (m, 3 H, Ph), 5.57 (d, 1 H, *J* = 10.5 Hz, H-1), 4.22 (t, 1 H, *J* = 9.0 Hz, H-3), 4.09 (t, 1 H, *J* = 10.5 Hz, H-2), 3.96 (dd, 1 H, *J* = 12.5 Hz, *J* = 1.5 Hz, H-6), 3.81 (dd, 1 H, *J* = 12.5 Hz, *J* = 5.5 Hz, H-6), 3.68 (m, 1 H, H-5), 3.62 (t, 1 H, *J* = 10.0 Hz, H-4), 2.32 (s, 3 H, CH₃), 2.08 (s, 3 H, CH₃); ¹³C NMR (D₂O): δ 132.25, 131.82, 131.60, 129.56 (6 x C, SPh), 128.38, 127.75 (4 x C, C₄H₂N), 85.68 (C-1), 80.41 (C-5), 74.30 (C-3), 70.62 (C-4), 61.00 (C-6), 60.86 (C-2), 14.36 (CH₃), 12.58 (CH₃).

Ethyl 2,6-di-*O*-benzoyl-3-*O*-levulinoyl-4-*O*-(*R,S*-1-methyl 1'-cyclopropylmethyl)-1-thio-β-D-galactopyranoside (21). 2,6-di-benzoyl-thio-β-D-galactopyranoside **19** (Mehta, S.; Whitfield, D. M. *Tetrahedron* **2000**, *56*, 6415) (14.1 g; 29.4 mmol) was dissolved in pyridine (125 mL) with stirring and the flask placed in a -20 °C cold bath. Then levulinic anhydride (6.3 g, 29.4 mmol) dissolved in pyridine (50 mL) was added dropwise. After 6h at -20 °C the mixture was allowed to slowly warm up

and after a total of 16h the liquids were mostly removed by evaporation. The residue was subjected to chromatography first with 5-10% EtOAc in CH₂Cl₂ and then the fractions containing product were further purified by MPLC eluting with 10% EtOAc in CH₂Cl₂ to yield ethyl 2,6-di-*O*-benzoyl-3-*O*-levulinoyl-1-thio-β-D-galactopyranoside **20** (6.47 g 38% contaminated with some 4-Lev isomer). ¹H NMR δ 8.05 (brd, 2H, *J* = 8 Hz, *o*-Bz), 8.01 (brd, 2H, *J* = 8 Hz, *o*-Bz), 7.56 (m, 2H, *p*-Bz), 7.44 (m, 4H, *m*-Bz), 5.64 (brt, 1H, H-2), 5.10 (dd, 1H, *J* = 9.8 Hz, *J* = 3.1 Hz, H-3), 4.65 (dd, 1H, *J* = 6.2 Hz, *J* = 11.3 Hz, H-6a), 4.64 (d, 1H, *J* = 10.1 Hz, H-1), 4.58 (dd, 1H, *J* = 6.2 Hz, *J* = 11.3 Hz, H-6b), 4.29 (brs, 1H, H-4), 4.00 (brt, 1H, H-5), 2.93 (brd, 1H, *J* = 3.1 Hz, OH-4), 2.73 (m, 4H, CH₂^{Lev}, CH₂^{SEt}), 2.52 (m, 1H, CH₂^{Lev}), 2.42 (m, 1H, CH₂^{Lev}), 2.11 (s, 3H, CH₃^{Lev}), 1.24 (s, 3H, CH₃^{SEt}); ¹³C δ NMR 207.8 (CH₃C=O^{Lev}), 171.9 (OC=O^{Lev}), 166.1 (C=O^{Bz}), 165.4 (C=O^{Bz}), 133.29, 133.25, 129.9, 129.8, 129.6, 128.4 (6 x C, Ph), 83.8 (C-1), 76.1 (C-5), 75.0 (C-3), 67.9 (C-2), 66.9 (C-4), 63.2 (C-6), 38.3 (CH₂^{Lev}), 29.7 (CH₃^{Lev}), 28.3 (CH₂^{Lev}), 24.1 (CH₂^{SEt}), 15.0 (CH₃^{SEt}). Impure alcohol **20** (2.46 g, 4.63 mmol) was dissolved in CH₂Cl₂ (15 mL) with stirring and the flask placed in a -20 °C cold bath. To this solution was added 1-methyl 1'-cyclopropylmethyl trichloroacetimidate (2 mL, 11.6 mmol) followed by silver trifluoromethanesulfonate (1.19 g, 4.6 mmol). After 2h at -20 °C the reaction was quenched with excess NH₄HCO₃, filtered through celite and evaporated. The residue was purified by MPLC eluting with 2% acetone in CHCl₃ to yield **21** (1.12 g, 40 %). ¹H NMR δ 8.02 (m, 8 H, *o*-Bz), 7.57 (m, 4 H, *p*-Bz), 7.44 (m, 8 H, *m*-Bz), 5.71 (brt, 1 H, H-2R), 5.65 (brt, 1 H, H-2S), 5.19 (dd, 1 H, *J* = 9.8 Hz, *J* = 2.9 Hz, H-3R), 5.17 (dd, 1 H, *J* = 9.8 Hz, *J* = 2.9 Hz, H-3S), 4.68 (m, 1 H, H-6), 4.64 (d, 2 H, *J* = 9.7 Hz, H-1RS), 4.59 (m, 3 H, H-6), 4.46 (dd, 1 H, *J* = 6.9 Hz, *J* = 11.6 Hz, H-6), 4.28 (brs, 1 H, H-4S), 4.11 (brs, 1 H, H-4R), 3.97 (m, 2 H, H-5RS), 3.13 (m, 1 H, CHO^{MCPM}-R), 3.03 (m, 1 H, CHO^{MCPM}-S), 2.68 (m, 6 H, CH₂^{Lev}, CH₂^{SEt}), 2.49 (m, 4 H, CH₂^{Lev}, CH₂^{SEt}), 2.31 (m, 2 H, CH₂^{Lev}), 2.03 (s, 3 H, CH₃^{Lev}), 2.02 (s, 3 H, CH₃^{Lev}), 1.36 (d, 3 H, CH₃^{MCPM}-R), 1.26 (m, 9 H, CH₃^{SEt}, CH₃^{MCPM}-S), 0.95 (m, 1 H, CH^{MCPM}-R), 0.85 (m, 1 H, CH^{MCPM}-S), 0.54 (m, 4 H, CH₂^{MCPM}-RS), 0.42 (m, 1 H, CH₂^{MCPM}-S), 0.36 (m, 1 H, CH₂^{MCPM}-S), 0.20 (m, 1 H, CH₂^{MCPM}-R), 0.07 (m, 1 H, CH₂^{MCPM}-R); ¹³C NMR δ 205.7 (CH₃C=O^{Lev}), 172.1

(OC=O^{Lev}), 172.0 (OC=O^{Lev}), 166.2 (C=O^{Bz}), 166.0 (C=O^{Bz}), 165.2 (2 x C=O^{Bz}), 133.2, 129.8, 129.6, 129.5, 128.4 (5 x C, Ph), 83.9 (C-1S), 83.8 (C-1R), 82.1 (CHO^{MCPM}-S), 80.6 (CHO^{MCPM}-R), 76.4 (C-5R), 76.2 (C-5S), 75.4 (C-3S), 75.3 (C-3R), 72.3 (C-4S), 71.1 (C-4R), 68.6 (C-2S), 68.5 (C-2R), 63.8 (C-6S), 62.9 (C-6R), 37.6 (CH₂^{Lev}), 29.6 (CH₃^{Lev}), 28.0 (CH₂^{Lev}), 24.4 (CH₂^{SEt}), 24.3 (CH₂^{SEt}), 21.4 (CH₃^{MCPM}-S), 20.0 (CH₃^{MCPM}-R), 17.1 (CH^{MCPM}-R), 16.6 (CH^{MCPM}-S), 15.0 (CH₃^{SEt}), 5.2 (CH₂^{MCPM}-S), 3.8 (CH₂^{MCPM}-R), 1.9 (CH₂^{MCPM}-R), 0.4 (CH₂^{MCPM}-S).

(MPEG)(DOX)yl 2,6-di-*O*-benzoyl-4-*O*-(*R,S*,1-methyl 1'-cyclopropylmethyl)-β-D-galactopyranoside (10). (MPEG)(DOX)OH (1.5 g, 0.29 mmol), powdered molecular sieves 4Å (1.5 g) and thioglycoside **21** (350 mg, 0.58 mmol) were dried *in vacuo* overnight. The flask was opened to an argon atmosphere and CH₂Cl₂ (25 mL) was added. The reaction mixture was cooled in an ice bath and NIS (202 mg, 0.87 mmol) followed by TfOH (26 μL, 0.29 mmol) were added. After stirring for 1h the reaction was quenched with *N,N*-diisopropylethylamine and worked up as usual to give (MPEG)(DOX)yl 2,6-di-*O*-benzoyl-3-*O*-levulinoyl-4-*O*-(*R,S*,1-methyl 1'-cyclopropylmethyl)-β-D-galactopyranoside **22** (1.62 g). Compound **22** was dissolved in pyridine/acetic acid (4 : 1, 16 mL) and hydrazine hydrate (0.32 mL) was added at 0 °C under an argon atmosphere. The reaction mixture was stirred for 30 minute and worked up as usual to give polymer bound monosaccharide acceptor **10** (1.05 g, 64 %): partial ¹H NMR 7.09 (brd, 8 H, DOX), 5.71 (dd, 1 H, *J* = 10.3 Hz, *J* = 8.1 Hz, H-2R), 5.63 (dd, 1 H, *J* = 10.3 Hz, *J* = 8.1 Hz, H-2S), 5.06 (dd, 1 H, *J* = 10.0 Hz, *J* = 3.0 Hz, H-6R), 5.03 (dd, 1 H, *J* = 10.0 Hz, *J* = 3.0 Hz, H-6S), 4.84 (d, 1 H, *J* = 12.5 Hz, DOXCH-R), 4.58 (m, 6 H, DOXCH-RS, H-6RS, H-1RS), 4.45 (s, 4 H, CH₂OPEGM-RS), 4.21 (brd, 1 H, *J* = 2.5 Hz, H-4R), 4.03 (brd, 1 H, *J* = 2.7 Hz, H-4S), 3.36 (s, 6 H, OCH₃-RS), 3.07 (m, 1 H, CHO^{MCPM}-R), 2.99 (m, 1 H, CHO^{MCPM}-S), 2.44 (m, 4 H, CH₂^{Lev}), 2.31 (m, 4 H, CH₂^{Lev}).

Phenyl *O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-deoxy-3,6-di-*O*-acetyl-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (1b). The disaccharide **6b** (1.0 g, 1.64 mmol) was dissolved in pyridine/acetic anhydride (2 : 1, 10 mL) at 0 °C and stirred at rt for 16h. The

mixture was evaporated, co-evaporated with toluene. The residue was purified by silica gel chromatography (ethyl acetate/hexane, 1 : 1) to afford **1b** (1.4 g, 99 %). ¹H NMR (CDCl₃): δ 7.47 (m, 2 H, Ph), 7.28 (m, 3 H, Ph), 5.45 (d, 1 H, *J* = 9.6 Hz, NH^{GlcN}), 5.34 (d, 1 H, *J* = 2.7 Hz, H-4^{Gal}), 5.15 (t, 1 H, *J* = 9.4 Hz, H-3^{GlcN}), 5.09 (dd, 1 H, *J* = 10.3 Hz, *J* = 8.0 Hz, H-2^{Gal}), 4.95 (dd, 1 H, *J* = 10.3 Hz, *J* = 3.3 Hz, H-3^{Gal}), 4.80 (d, 1 H, *J* = 11.9 Hz, ½ CH₂CCl₃), 4.74 (d, 1 H, *J* = 11.9 Hz, ½ CH₂CCl₃), 4.72 (d, 1 H, *J* = 10.3 Hz, H-1^{GlcN}), 4.50 (d, 1 H, *J* = 11.3 Hz, H-6^{GlcN}), 4.48 (d, 1 H, *J* = 7.8 Hz, H-1^{Gal}), 4.01 (m, 3 H, H-6^{GlcN}, 2 x H-6^{Gal}), 3.87 (t, 1 H, *J* = 6.8 Hz, H-5^{Gal}), 3.78 (t, 1 H, *J* = 9.9 Hz, H-2^{GlcN}), 3.74 (t, 1 H, *J* = 9.0 Hz, H-4^{GlcN}), 3.66 (brs, 1 H, H-5^{GlcN}), 2.11, 2.09, 2.04, 2.03 x 2, 1.96 (s, 18 H, O=CCH₃); ¹³C NMR (CDCl₃): δ 170.40, 170.30, 170.27, 170.08, 170.01, 169.08 (6 x C, O=CCH₃), 154.17 (O=COCH₂CCl₃), 128.99, 128.85, 128.18, 128.01 (6 x C, Ph), 101.03 (C-1^{Gal}), 95.38 (CCl₃), 86.71 (C-1^{GlcN}), 76.67 (C-5^{GlcN}), 76.13 (C-4^{GlcN}), 74.53 (CH₂CCl₃), 73.50 (C-3^{GlcN}), 70.89 (C-3^{Gal}), 70.67 (C-5^{Gal}), 69.05 (C-2^{Gal}), 66.59 (C-4^{Gal}), 62.23 (C-6^{GlcN}), 60.81 (C-6^{Gal}), 55.08 (C-2^{GlcN}), 20.80, 20.77, 20.59, 20.57, 20.54, 20.46 (6 x C, O=CCH₃).

Phenyl *O*-[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosyl-(1'''→2'')-lactone]-(2→3)-*O*-(4,6-di-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-deoxy-3,6-di-*O*-acetyl-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (**8b**).

The trisaccharide **7b** (80 mg, 0.10 mmol) was dissolved in pyridine/acetic anhydride (2 : 1, 3 mL) at 0 °C and heated at 45 °C for 18h. The mixture was evaporated, co-evaporated with toluene. The residue was purified by silica gel chromatography (ethyl acetate/methanol, 97 : 3) to afford **8b** (99 mg, 92 %).

¹H NMR (CDCl₃): δ 7.49 (m, 2 H, Ph), 7.30 (m, 3 H, Ph), 5.53 (d, 1 H, *J* = 10.0 Hz, NH^{GlcN}), 5.43 (d, 1 H, *J* = 10.0 Hz, NH^{Neu}), 5.42 (d, 1 H, *J* = 2.5 Hz, H-4^{Gal}), 5.40 (td, 1 H, *J* = 10.5 Hz, *J* = 5.5 Hz, H-4^{Neu}), 5.28 (dd, 1 H, *J* = 7.0 Hz, *J* = 1.5 Hz, H-7^{Neu}), 5.24 (t, 1 H, *J* = 9.0 Hz, H-3^{GlcN}), 5.08 (m, 1 H, H-8^{Neu}), 4.79 (d, 1 H, *J* = 12.0 Hz, ½ CH₂CCl₃), 4.78 (d, 1 H, *J* = 10.0 Hz, H-1^{GlcN}), 4.72 (d, 1 H, *J* = 12.0 Hz, ½ CH₂CCl₃), 4.68 (dd, 1 H, *J* = 10.5 Hz, *J* = 7.5 Hz, H-2^{Gal}), 4.65 (d, 1 H, *J* = 8.0 Hz, H-1^{Gal}), 4.52 (d, 1

H, $J = 10.5$ Hz, H-6^{GlcN}), 4.40 (dd, 1 H, $J = 11.5$ Hz, $J = 5.5$ Hz, H-6^{GlcN}), 4.26 (dd, 1 H, $J = 12.5$ Hz, $J = 2.5$ Hz, H-9^{Neu}), 4.15 (t, 1 H, $J = 10.5$ Hz, H-5^{Neu}), 4.12 (m, 2 H, 2 x H-6^{Gal}), 4.04 (dd, 1 H, $J = 12.5$ Hz, $J = 6.0$ Hz, H-9^{Neu}), 3.96 (dd, 1 H, $J = 11.0$ Hz, $J = 3.5$ Hz, H-3^{Gal}), 3.93 (t, 1 H, $J = 7.0$ Hz, H-5^{Gal}), 3.88 (t, 1 H, $J = 9.5$ Hz, H-4^{GlcN}), 3.75 (brs, 1 H, H-5^{GlcN}), 3.73 (t, 1 H, $J = 9.5$ Hz, H-2^{GlcN}), 3.65 (dd, 1 H, $J = 10.5$ Hz, $J = 1.5$ Hz, H-6^{Neu}), 2.42 (dd, 1 H, $J = 13.0$ Hz, $J = 5.5$ Hz, H-3_{eq}^{Neu}), 2.20, 2.10, 2.07, 2.06, 2.04 x 3, 2.00, 1.88 (s, 30 H, O=CCH₃), 1.85 (t, 1 H, $J = 13.0$ Hz, H-3_{ax}^{Neu}); ¹³C NMR (CDCl₃): δ 170.92, 170.59, 170.58, 170.38, 170.35 x 2, 169.71, 169.65, 169.56 (9 x C, O=CCH₃), 163.12 (C-1^{Neu}), 154.10 (O=COCH₂CCl₃), 132.82, 132.05, 128.89, 128.10 (6 x C, Ph), 99.56 (C-1^{Gal}), 96.91 (C-2^{Neu}), 95.36 (CCl₃), 86.60 (C-1^{GlcN}), 76.67 (C-5^{GlcN}), 76.24 (C-4^{GlcN}), 74.51 (CH₂CCl₃), 73.55 (C-3^{Gal}), 73.28 (C-2^{Gal}), 72.78 (C-3^{GlcN}), 72.73 (C-6^{Neu}), 71.09 (C-5^{Gal}), 69.53 (C-8^{Neu}), 69.40 (C-4^{Neu}), 67.16 (C-7^{Neu}), 65.88 (C-4^{Gal}), 62.69 (C-6^{GlcN}), 62.02 (C-9^{Neu}), 61.06 (C-6^{Gal}), 55.32 (C-2^{GlcN}), 48.99 (C-5^{Neu}), 37.59 (C-3^{Neu}), 23.09, 20.89, 20.84, 20.72, 20.67, 20.61, 20.56 x 2, 20.39 (9 x C, O=CCH₃).

Phenyl [5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosyl-(1'' $\rightarrow$ 2')-lactone]-(2 $\rightarrow$ 3)-*O*-(4,6-di-*O*-acetyl- β -D-galactopyranosyl)-(1 $\rightarrow$ 4)-2-deoxy-3,6-di-*O*-acetyl-2-phthalimido- β -D-glucopyranoside (8a). The crude **7a** (30 mg) was treated with pyridine/acetic anhydride same as described above to yield **8a** (10 mg). $[\alpha]_D -16.4$ (*c* 0.65, CHCl₃); ¹H NMR (CDCl₃): δ 7.86 (m, 2 H, Phth), 7.76 (m, 2 H, Phth), 7.41 (m, 2 H, Ph), 7.28 (m, 3 H, Ph), 5.80 (t, 1 H, $J = 9.3$ Hz, H-3^{GlcN}), 5.70 (d, 1 H, $J = 10.0$ Hz, NH^{Neu}), 5.43 (d, 1 H, $J = 2.1$ Hz, H-4^{Gal}), 5.41 (td, 1 H, $J = 10.7$ Hz, $J = 5.5$ Hz, H-4^{Neu}), 5.37 (d, 1 H, $J = 10.0$ Hz, H-1^{GlcN}), 5.27 (dd, 1 H, $J = 5.2$ Hz, $J < 1.0$ Hz, H-7^{Neu}), 5.11 (m, 1 H, H-8^{Neu}), 4.73 (dd, 1 H, $J = 10.7$ Hz, $J = 7.6$ Hz, H-2^{Gal}), 4.60 (d, 1 H, $J = 11.5$ Hz, H-6^{GlcN}), 4.58 (d, 1 H, $J = 8.0$ Hz, H-1^{Gal}), 4.47 (dd, 1 H, $J = 12.5$ Hz, $J = 5.0$ Hz, H-6^{GlcN}), 4.26 (t, 1 H, $J = 10.0$ Hz, H-2^{GlcN}), 4.24 (d, 1 H, $J = 11.0$ Hz, H-9^{Neu}), 4.03-4.14 (m, 4 H, H-5^{Neu}, 2 x H-6^{Gal}, H-9^{Neu}), 3.87-3.98 (m, 4 H, H-3^{Gal}, H-4^{GlcN}, H-5^{Gal}, H-5^{GlcN}), 3.66 (d, 1 H, $J = 11.0$ Hz, H-6^{Neu}), 2.43 (dd, 1 H, $J = 13.4$ Hz, $J = 5.5$ Hz, H-3_{eq}^{Neu}), 2.20, 2.13, 2.09, 2.08, 2.05, 2.02, 2.01, 1.89 x 2, 2.00,

1.88 (s, 27 H, O=CCH₃), 1.88 (t, 1 H, $J = 12.8$ Hz, H-3_{ax}^{Neu}); ¹³C NMR (CDCl₃): δ 170.87, 170.69, 170.64, 170.46, 170.32, 169.87, 169.83, 169.74, 169.62 (9 x C, O=CCH₃), 167.86, 167.14 (2 x C, Phth), 163.18 (C-1^{Neu}), 134.52, 134.30 (2 x C, *m*-Phth), 133.41 x 2 (2 x C, Ph), 131.58, 131.12 (2 x C, *p*-Phth), 130.98, 128.85 x 2, 128.41 (4 x C, Ph), 123.64 x 2 (*o*-Phth), 99.55 (C-1^{Gal}), 96.98 (C-2^{Neu}), 82.87 (C-1^{GlcN}), 76.84 (C-4^{GlcN}), 76.55 (C-5^{GlcN}), 73.63 (C-3^{Gal}), 73.37 (C-2^{Gal}), 72.95 (C-6^{Neu}), 71.18 (C-5^{Gal}), 71.01 (C-3^{GlcN}), 69.89 (C-8^{Neu}), 69.39 (C-4^{Neu}), 67.36 (C-7^{Neu}), 65.80 (C-4^{Gal}), 62.54 (C-6^{GlcN}), 62.20 (C-9^{Neu}), 60.95 (C-6^{Gal}), 54.02 (C-2^{GlcN}), 49.00 (C-5^{Neu}), 37.55 (C-3^{Neu}), 23.12, 21.00, 20.88, 20.73, 20.65 x 2, 20.59, 20.43 x 2 (9 x C, O=CCH₃); MS (FAB): Anal. Calcd for C₅₅H₅₉N₂O₂₆S: 1195.3. Found: m/z 1195.2 [M⁺].

Phenyl [5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosyl-(1 $\rightarrow$ 7?)-lactone]-(2 $\rightarrow$ 3)-*O*-(2,4,6-tri-*O*-acetyl- β -D-galactopyranosyl)-(1 $\rightarrow$ 4)-2-deoxy-3,6-di-*O*-acetyl-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)- β -D-glucopyranoside (9). ¹H NMR (CDCl₃): δ 7.48 (m, 2 H, Ph), 7.28 (m, 3 H, Ph), 5.48 (td, 1 H, $J = 11.0$ Hz, $J = 5.4$ Hz, H-4^{Neu}), 5.38 (d, 1 H, $J = 10.3$ Hz, NH^{Neu}), 5.35 (d, 1 H, $J = 9.5$ Hz, NH^{GlcN}), 5.21 (brs, 1 H, H-5^{Gal}), 5.20 (ddd, 1 H, $J = 8.6$ Hz, $J = 6.1$ Hz, $J = 3.4$ Hz, H-8^{Neu}), 5.10 (t, 1 H, $J = 9.5$ Hz, H-3^{GlcN}), 4.96 (d, 1 H, $J = 3.7$ Hz, H-4^{Gal}), 4.84 (dd, 1 H, $J = 9.5$ Hz, $J = 8.0$ Hz, H-2^{Gal}), 4.79 (d, 1 H, $J = 12.0$ Hz, $\frac{1}{2}$ CH₂CCl₃), 4.73 (d, 1 H, $J = 12.0$ Hz, $\frac{1}{2}$ CH₂CCl₃), 4.69 (d, 1 H, $J = 10.5$ Hz, H-1^{GlcN}), 4.62 (dd, 1 H, $J = 12.2$ Hz, $J = 3.4$ Hz, H-9^{Neu}), 4.48 (d, 1 H, $J = 10.2$ Hz, H-6^{GlcN}), 4.39 (d, 1 H, $J = 7.8$ Hz, H-1^{Gal}), 4.27 (m, 2 H, 2 x H-6^{Gal}), 4.09-4.19 (m, 3 H, H-6^{GlcN}, H-5^{Neu}, H-3^{Gal}), 3.39 (dd, 1 H, $J = 12.7$ Hz, $J = 6.1$ Hz, H-9^{Neu}), 3.89 (dd, 1 H, $J = 8.6$ Hz, $J = 3.2$ Hz, H-7^{Neu}), 3.78 (q, 1 H, $J = 10.0$ Hz, H-2^{GlcN}), 3.71 (t, 1 H, $J = 9.0$ Hz, H-4^{GlcN}), 3.64 (br, 1 H, H-5^{GlcN}), 3.62 (dd, 1 H, $J = 9.8$ Hz, H-6^{Neu}), 2.44 (dd, 1 H, $J = 13.7$ Hz, $J = 5.4$ Hz, H-3_{eq}^{Neu}), 2.13, 2.10, 2.08 x 3, 2.04, 2.01, 2.00, 1.87 (s, 27 H, O=CCH₃), 1.78 (dd, 1 H, $J = 13.7$ Hz, $J = 11.7$ Hz, H-3_{ax}^{Neu}); ¹³C NMR (CDCl₃): δ 170.93, 170.67, 170.63, 170.55, 170.47, 170.34, 170.30, 170.00, 169.19 (9 x C, O=CCH₃), 162.75 (C-1^{Neu}), 154.20 (O=COCH₂CCl₃), 132.58, 132.45, 128.89,

128.07 (6 x C, Ph), 99.92 (C-1^{Gal}), 95.35 (C-2^{Neu}), 95.01 (CCl₃), 87.27 (C-1^{GlcN}), 77.26 (C-5^{GlcN}), 76.35 (C-4^{GlcN}), 74.55 (CH₂CCl₃), 72.89 (C-3^{GlcN}), 72.53 (C-6^{Neu}), 72.08 (C-4^{Gal}), 71.73 (C-3^{Gal}), 71.09 (C-7^{Neu}), 70.00 (C-2^{Gal}), 69.19 (C-4^{Neu}), 68.22 (C-8^{Neu}), 66.80 (C-5^{Gal}), 62.43 (C-6^{GlcN}), 62.32 (C-6^{Gal}), 62.26 (C-9^{Neu}), 55.24 (C-2^{GlcN}), 49.29 (C-5^{Neu}), 38.07 (C-3^{Neu}), 23.11, 20.83, 20.78, 20.77, 20.75, 20.70, 20.59 x 2, 20.56 (9 x C, O=CCH₃);

Methyl O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylate)-(2 $\rightarrow$ 3)-O-(2,4,6-tri-O-acetyl- β -D-galactopyranosyl)-(1 $\rightarrow$ 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy- β -D-glucopyranosyl)-(1 $\rightarrow$ 2)-3,4,6-tri-O-benzyl- α -D-mannopyranoside (15). To a solution of **14** (42 mg, 0.026 mmol) in acetic anhydride (2 mL) was added freshly activated zinc powder (100 mg). The mixture was stirred at rt overnight, then diluted with toluene, filtered, and concentrated in vacuo. The residue was purified by preparative TLC (ethyl acetate/acetone/hexane, 1 : 1 : 1) to yield **15** (15 mg, 40 %). ¹H NMR (CDCl₃): δ 7.16-7.36 (m, 15 H, Ph), 5.55 (m, 1 H, H-8^{Neu}), 5.45 (d, 1 H, J = 8.5 Hz, NH^{GlcN}), 5.39 (dd, 1 H, J = 9.0 Hz, J = 2.5 Hz, H-7^{Neu}), 5.32 (t, 1 H, J = 10.0 Hz, H-3^{GlcN}), 5.07 (d, 1 H, J = 10.5 Hz, NH^{Neu}), 4.94 (dd, 1 H, J = 10.0 Hz, J = 8.0 Hz, H-2^{Gal}), 4.89 (td, 1 H, J = 13.3 Hz, J = 4.5 Hz, H-4^{Neu}), 4.88 (d, 1 H, J = 2.5 Hz, H-4^{Gal}), 4.87 (d, 1 H, J = 11.0 Hz, $\frac{1}{2}$ CH₂CCl₃), 4.81 (d, 1 H, J = 8.0 Hz, H-1^{GlcN}), 4.75 (d, 1 H, J = 11.5 Hz, $\frac{1}{2}$ CH₂Ph), 4.68 (d, 1 H, J = 8.0 Hz, H-1^{Gal}), 4.66 (d, 1 H, J = 1.5 Hz, H-1^{Man}), 4.49-4.56 (m, 5 H, H-3^{Gal}, CH₂Ph, H-6^{GlcN}, $\frac{1}{2}$ CH₂Ph), 4.47 (d, 1 H, J = 11.5 Hz, $\frac{1}{2}$ CH₂Ph), 4.44 (dd, 1 H, J = 12.5 Hz, J = 2.5 Hz, H-9^{Neu}), 4.18 (dd, 1 H, J = 12.0 Hz, J = 6.0 Hz, H-6^{GlcN}), 4.12 (t, 1 H, J = 2.5 Hz, H-2^{Man}), 4.05 (t, 1 H, J = 10.0 Hz, H-5^{Neu}), 3.97-4.02 (m, 5 H, 2 x H-6^{Man}, 2 x H-6^{Gal}, H-9^{Neu}), 3.84 (s, 3 H, COOCH₃), 3.80 (t, 1 H, J = 9.0 Hz, H-5^{Man}), 3.80-3.88 (m, 3 H, H-2^{GlcN}, H-4^{Man}, H-5^{GlcN}), 3.64 (dd, 1 H, J = 11.0 Hz, J = 3.0 Hz, H-6^{Neu}), 3.34 (s, 3 H, OCH₃), 2.58 (dd, 1 H, J = 12.7 Hz, J = 4.6 Hz, H-3_{eq}^{Neu}), 2.24, 2.16, 2.09, 2.08, 2.07, 2.07, 2.06, 2.00, 1.99, 1.85, 1.81 (s, 33 H, O=CCH₃), 1.68 (t, 1 H, J = 12.5 Hz, H-3_{ax}^{Neu}); ¹³C NMR (CDCl₃): δ 170.88, 170.68, 170.62, 170.59, 170.42, 170.39, 170.35, 170.34, 170.24, 169.65, 169.60 (11 x C, O=CCH₃), 167.94 (C-1^{Neu}), 138.52, 138.38, 138.27, 128.35, 128.28, 127.97, 127.95,

127.60, 127.57 (18 x C, CH_2Ph), 100.88 (C-1^{Gal}), 98.77 (C-1^{GlcN}), 98.12 (C-1^{Man}), 96.76 (C-2^{Neu}), 78.06 (C-3^{Man}), 76.37 (C-4^{GlcN}), 75.00 (CH_2Ph), 74.42 (C-5^{Man}), 73.30 (C-2^{Man}), 73.18 (CH_2Ph), 72.82 (C-5^{GlcN}), 72.50 (C-3^{GlcN}), 72.05 (C-6^{Neu}), 71.52 (C-5^{Man}), 71.34 (C-3^{Gal}), 70.90 (CH_2Ph), 70.46 (C-5^{Gal}), 69.92 (C-2^{Gal}), 69.29 (C-4^{Neu}), 67.83 (C-8^{Neu}), 67.34 (C-4^{Gal}), 66.93 (C-7^{Neu}), 62.74 (C-6^{GlcN}), 62.21 (C-9^{Neu}), 61.59 (2 x C, C-6^{Man}, C-6^{Gal}), 54.95 (C-2^{GlcN}), 54.80 (OCH_3), 53.14 ($COOCH_3$), 49.14 (C-5^{Neu}), 37.39 (C-3^{Neu}), 23.24, 23.16, 21.51, 20.91, 20.84, 20.75 x 3, 20.72, 20.69, 20.62 (11 x C, $O=CCH_3$); MALDI-MS: Anal. Calcd for $C_{72}H_{92}N_2O_{33}Na$: 1535.55. Found: m/z 1535.34 [$M + Na^+$].

Methyl (5-acetamido-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylate)-(2 $\rightarrow$ 3)-O-(β -D-galactopyranosyl)-(1 $\rightarrow$ 4)-O-(2-acetamido-2-deoxy- β -D-glucopyranosyl)-(1 $\rightarrow$ 2)- α -D-mannopyranoside (18). Tetrasaccharide **15** (12 mg, 0.008 mmol) was dissolved in ethyl acetate (3 mL) and hydrogenated in a Parr apparatus at 50 *psi* of H_2 for 16h in the presence of Pd/C (10 %, 15 mg). The catalyst was removed by filtration through celite. The filtrate was concentrated to give **16**. The crude **16** was dissolved in methanol (2 mL) and 1 M sodium methoxide (0.3 mL) was added. After stirring for 2h the mixture was neutralized with Rexyn 101 (H^+) ion-exchange resin, filtered, and concentrated to yield **17**. Compound **17** was dissolved in water (1 mL) followed by 1 M NaOH (0.2 mL). This solution was stirred overnight and diluted with methanol. The reaction was neutralized with Rexyn 101 (H^+) ion-exchange resin, filtered, and concentrated. The residue was placed on a Sep-Pak C_{18} reversed-phase column and eluted with water to yield the title compound **18** (5 mg, 81 % overall yield from **15**). $[\alpha]_D +15.6$ (c 0.4, H_2O); 1H NMR (D_2O): δ 4.80 (s, 1 H, H-1^{Man}), 4.60 (d, 1 H, J = 8.0 Hz, H-1^{GlcN}), 4.56 (d, 1 H, J = 8.0 Hz, H-1^{Gal}), 4.13 (dd, 1 H, J = 10.0 Hz, J = 2.5 Hz, H-3^{Gal}), 4.07 (d, 1 H, J = 2.5 Hz, H-2^{Man}), 4.00 (dd, 1 H, J = 12.5 Hz, J = 2.5 Hz, H-6^{GlcN}), 3.97 (d, 1 H, J = 3.0 Hz, H-4^{Gal}), 3.86-3.94 (m, 4 H, H-9^{Neu}, H-8^{Neu}, H-6^{Neu}, H-6^{GlcN}), 3.86 (t, 1 H, J = 10.0 Hz, H-5^{Neu}), 3.78 (dd, 1 H, J = 9.5 Hz, J = 4.0 Hz, H-3^{Man}), 3.72-3.78 (m, 5 H, H-2^{GlcN}, 2 x H-6^{Gal}, H-3^{GlcN}, H-4^{GlcN}), 3.70 (td, 1 H, J = 10.0 Hz, J = 4.5 Hz, H-4^{Neu}), 3.69 (brs, 1 H, H-5^{Gal}), 3.67 (d, 1 H, J = 8.5 Hz, H-6^{Man}), 3.65 (d, 1 H, J =

10.0 Hz, $J < 1.0$ Hz, H-6^{Neu}), 3.64 (d, 1 H, $J = 10.5$ Hz, H-9^{Neu}), 3.61 (d, 1 H, $J = 9.0$ Hz, H-7^{Neu}), 3.57 (brs, 1 H, H-5^{Man}), 3.58 (t, 1 H, $J = 8.0$ Hz, H-2^{Gal}), 3.57 (brs, 1 H, H-5^{GlcN}), 3.50 (t, 1 H, $J = 9.5$ Hz, H-4^{Man}), 3.42 (s, 3 H, OCH₃), 2.77 (dd, 1 H, $J = 12.5$ Hz, $J = 4.5$ Hz, H-3_{eq}^{Neu}), 2.06, 2.04 (s, 6 H, O=CCH₃), 1.81 (t, 1 H, $J = 12.5$ Hz, H-3_{ax}^{Neu}); ¹³C NMR (D₂O): δ 175.69, 175.39 (2 x C, O=CCH₃), 175.54 (C-1^{Neu}), 103.27 (C-1^{Gal}), 100.48 (C-2^{Neu}), 100.06 (C-1^{GlcN}), 98.58 (C-1^{Man}), 78.95 (C-4^{GlcN}), 76.83 (C-2^{Man}), 76.13 (C-3^{Gal}), 75.83 (C-4^{Neu}), 75.46 (C-5^{GlcN}), 73.55 (C-6^{Neu}), 73.32 (C-5^{Man}), 72.64 (C-3^{GlcN}), 72.43 (C-8^{Neu}), 70.24 (C-3^{Man}), 70.05 (C-2^{Gal}), 69.02 (C-5^{Gal}), 68.76 (C-7^{Neu}), 68.13 (C-4^{Gal}), 67.96 (C-4^{Man}), 63.24 (C-6^{Man}), 62.25 (C-9^{Neu}), 61.68 (C-6^{Gal}), 60.62 (C-6^{GlcN}), 55.52 (C-2^{GlcN}), 55.47 (OCH₃), 52.34 (C-5^{Neu}), 40.29 (C-3^{Neu}), 22.97, 22.69 (2 x C, O=CCH₃);

JOC-compound 5b

JOC-compound 5c

JOC-compound 6b

JOC-compound 7b

JOC-compound 8a

JOC-compound 8b

JOC-compound 9

JOC-compound 10

JOC-compound 12

JOC-compound 14

JOC-compound 1

JOC-compound 18

JOC-compound 21