Supporting Information

Anomeric Reactivity-Based One-Pot Synthesis of Heparin-like Oligosaccharides

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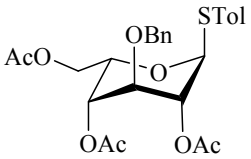
Experimental Section

General Procedures. All chemicals were purchased as reagent grade and used without further purification. Dichloromethane (CH_2Cl_2), toluene, and acetonitrile (CH_3CN) were distilled over calcium hydride whereas tetrahydrofuran (THF) and ether (Et_2O) were distilled over sodium/benzophenone ketyl. Anhydrous DMF and Pyridine were purchased from a commercial source. Trifluoromethanesulfonic anhydride was stirred for 3 hours on P_2O_5 and subsequently distilled. Molecular sieves (MS) used for glycosylation were AW-300, which was ground into powdered form before use. Reactions were performed under an inert atmosphere under strictly anhydrous conditions. Traces of water from reagents used in reactions that require anhydrous conditions were removed by coevaporation with toluene. Reactions were monitored with analytical thin-layer chromatography (TLC) on silica gel 60 F254 plates and visualized under UV (254 nm) and/or by spraying with 20% H_2SO_4 in ethanol or with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ 25 g/L. ^{1}H NMR spectra were recorded on a 400 Hz NMR spectrometer at 20ºC. Chemical shift (in ppm) was determined relative to either tetramethylsilane in deuterated chloroform (δ 0 ppm). Coupling constant(s) in hertz (Hz) were measured from one-dimensional spectra. ^{13}C Attached Proton Test (C-Apt) spectra were obtained with NMR-400 or NMR 500 spectrometer and were calibrated with $CDCl_3$ (δ 77.00 ppm). Mass spectra

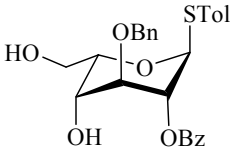
were obtained by the analytical services of this department.

_p_-Methylphenyl 2,4,6-tri-_O_-acetyl-1-thio-α-L-idopyranoside (2):



1,2,4,6-Tetra-*O*-acetyl-3-*O*-benzyl-α/β-D-idopyranoside[13] (12.0 g, 27.4 mmol) was dissolved in CH_2Cl_2 (100 mL) and cooled to 0°C. *p*-Toluenethiol (4.0 g, 32.8 mmol) and $BF_3 \cdot OEt_2$ (10.4 mL, 82.2 mmol) were added and the mixture was stirred for three hours at room temperature. The reaction mixture was diluted with CH_2Cl_2 and washed with 1 M NaOH. Organic phase was washed with H_2O, brine and dried over $MgSO_4$. Solvent was evaporated and the residue was purified by column chromatography on silica gel (Hexane–EtOAc, 3:1), to give compound **2** in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44-7.07 (m, 9H, Ar-H), 5.40 (s, 1H, H-1), 5.15-5.14 (m, 1H, H-6a), 5.01-4.90 (m, 1H, H-5), 4.87-4.86 (m, 1H, H-6b), 4.82 (d, J = 11.7 Hz, 1H, CH_2Ph), 4.68 (d, J = 11 Hz, 1H, CH_2Ph), 4.27-4.15 (m, 2H, H-2, H-4), 3.76-3.74 (m, 1H, H-3), 2.30 (s, 3H, CH_3Ph), 2.07-2.03 (3s, 9H, $COCH_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 170.7, 170.2, 169.7, 137.8, 137.3, 132.2, 129.8-127.9 (CH_{arom}), 86.4, 72.8, 71.7, 68.9, 67.3, 64.7, 63.0, 21.3, 21.1, 21.08, 20.9; m/z (HRMS) calcd for $C_{26}H_{30}O_8S\ Na^+$: 525.1553, found: 525.1550.

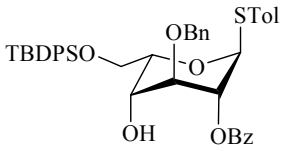
_p_-Methylphenyl 2-_O_-benzoyl-3-_O_-benzyl-1-thio-α-L-idopyranoside (3):



Compound **2** (4.70 g, 9.40 mmol) was dissolved in a mixture of methanol (40 mL) and a catalytic amount of NaOMe was added. The mixture was stirred overnight, after which the mixture was neutralized with amberlite-H^+ resin. The resin was filtered off and the solvents were evaporated. The crude triol was coevaporated with toluene and dissolved in a mixture of CH_3CN/DMF (10/1 v/v, 40 mL). Benzaldehyde dimethyl acetal (2.9 mL, 19.4 mmol) and a catalytic amount of pTsOH were added and the mixture was heated at 50°C for 4 h. After the mixture was cooled to room temperature, saturated aqueous $NaHCO_3$ was added and the mixture was diluted with Et_2O. The layers were separated and the aqueous layer was extracted with Et_2O, after which the combined organic layers were washed with water, dried ($MgSO_4$), filtered and concentrated. The residue was coevaporated with toluene and dissolved in pyridine (25 mL), after which BzCl (3.5 mL, 28.2 mmol) was added at 0°C. The reaction mixture was stirred overnight and then concentrated to a smaller volume, diluted with EtOAc and washed with aqueous 1M HCl and water. After the organic layer was dried ($MgSO_4$) and filtered it was concentrated in *vacuo*. The residue was coevaporated with toluene to remove the last traces of pyridine and then taken up in CH_2Cl_2 (30 mL). 60% Aqueous TFA (3 mL) was added and the reaction mixture was stirred for 2 h. Saturated aqueous $NaHCO_3$ was added and the layers were separated. The aqueous layer was extracted twice with EtOAc, after which the combined organic layers were washed with water and dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography on silica gel (Hexane–EtOAc, 3:1), to give compound **3** in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01-7.11 (m, 14H, Ar-H), 5.54 (bs, 1H, H-1), 5.50 (bs, 1H, H-2), 4.91-4.88 (d, J = 12.0 Hz, 1H, CH_2Ph), 4.80-4.78 (m, 1H, H-5), 4.66-4.63 (d, J = 11.7 Hz, 1H, CH_2Ph),

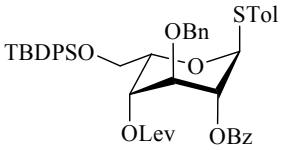
3.97 (dd, J = 12 Hz, 1H, H-6a), 3.89-3.84 (m, 4H, H-6b, H-3, H4), 2.29 (s, 3H, CH_3Ph); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 165.3, 138.2, 137.5, 133.9, 132.8, 132.1-128.0 (CH_{arom}), 87.3, 74.4, 72.6, 70.1, 68.5, 68.4, 63.3, 21.4; m/z (HRMS) calcd for $C_{27}H_{28}O_6S\ Na^+$: 503.1504, found: 503.1507.

_p_-Methylphenyl 2-_O_-benzoyl-3-_O_-benzyl-6-_O_-tert-butyldiphenylsilyl-1-thio-α-L-idopyranoside (4):



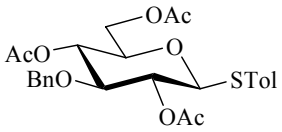
A solution of **3** (3.0 g, 6.2 mmol) in anhydrous pyridine (30 mL), TBDPSCl (1.30 mL, 9.3 mmol) was added. After overnight at room temperature under nitrogen, the reaction mixture was quenched with CH_3OH and evaporated under vacuum. The residue was purified by chromatography on silica gel (Hexane-EtOAc, 5:1) to afford **4** in 91% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01-7.01 (m, 24H, Ar-H), 5.54 (s, 1H, H-1), 5.50 (m, 1H, H-2), 4.92 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.83 (t, J = 5.2 Hz 1H, H-5), 4.67 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.01-3.86 (m, 4H), 2.98 (d, J = 8.8 Hz, 1H), 2.29 (s, 3H, CH_3Ph), 1.07 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 165.3, 137.8, 136.0, 135.9, 133.8, 133.5, 133.2-128.0 (CH_{arom}), 87.5, 74.6, 72.6, 70.4, 68.7, 64.5, 27.1, 21.4, 19.5; m/z (HRMS) calcd for $C_{43}H_{46}O_6SSi\ Na^+$: 741.2676, found: 741.2670.

_p_-Methylphenyl 2-_O_-benzoyl-3-_O_-benzyl-6-_O_-tert-butyldiphenylsilyl-4-_O_-levulinyl-1-thio-α-L-idopyranoside (5):



A solution of **4** (1.0 g, 1.2 mmol) in anhydrous pyridine (8 mL), Lev_2O (0.3 g, 1.5 mmol) was added. After overnight at room temperature under nitrogen, the reaction mixture was evaporated under vacuum. The residue was purified by chromatography on silica gel (Hexane-EtOAc, 4:1) to afford **5** in 89% yield as a white solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02-7.01 (m, 24H, Ar-H), 5.52 (s, 1H, H-1), 5.42 (m, 1H, H-4), 5.13 (bs, 1H, H-2), 4.95-4.86 (m, 2H, H-3, CH_2Ph), 4.78 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.98-3.95 (m, 1H, H-5), 3.83 (d, J = 6.6 Hz, 2H, H-6a, H-6b), 2.54-2.33 (m, 4H, C:OCH_2CH_2C:O), 2.29 (s, 3H, CH_3C:O), 2.11 (s, 3H, CH_3Ph), 1.07 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 205.6, 172.2, 165.5, 137.8, 135.9, 133.7, 133.5, 133.4, 132.7, 132.4-127.8 (CH_{arom}), 86.7, 73.0, 72.7, 70.1, 67.5, 62.8, 38.1, 29.9, 28.1, 27.1, 21.4, 19.5; m/z (HRMS) calcd for $C_{48}H_{52}O_8SSi\ Na^+$: 839.3044, found: 839.3043.

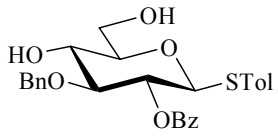
_p_-Methylphenyl 2,4,6-tri-_O_-acetyl-3-_O_-benzyl-1-thio-β-D-glucopyranose (7):



1,2,4,6-_O_-tetra-_O_-acetyl-3-_O_-benzyl-β-D-glucopyranoside[14] (10.0 g) was treated as described for preparation of **2** and **7** was obtained in 87% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44-7.15 (m, 14H, Ar-H), 5.08 (t, J = 9.5 Hz, 1H, H-4), 5.06 (t, J = 9.8 Hz, 1H, H-2), 4.60-4.54 (m, 3H, H-1, CH_2Ph), 4.21-4.16 (m, 2H, H-6a, H-6b), 3.65 (t, J = 9.3 Hz, 1H, H-3), 3.60 (m, 1H, H-5), 2.34 (s, 3H, CH_3Ph),

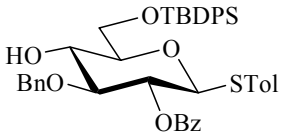
2.07-1.96 (3s, 9H, $COCH_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 170.7, 169.5, 169.4, 138.4, 137.7, 133.3-127.8 (CH_{arom}), 86.4 (C-1), 81.5, 76.0, 74.2, 71.3, 69.6, 62.5, 21.2, 21.0, 20.8, 20.7; m/z (HRMS) calcd for $C_{26}H_{30}O_8S\ Na^+$: 525.1553, found: 525.1554.

***p*-Methylphenyl 2-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-glucopyranose (8):**



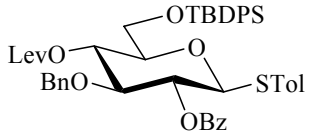
Compound **7** (6.8 g) was treated as described for preparation of **3** and **8** was obtained in 81% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.08-7.07 (m, 14H, Ar-H), 5.22 (t, *J* = 9.3 Hz, 1H, H-2), 4.76 (d, *J* = 10.0 Hz, 1H, H-1), 4.71 (d, *J* = 11.5 Hz, 1H, CH_2Ph), 4.59 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 3.91 (dd, *J* = 3.2 Hz, 1H, H-6), 3.79, (dd, *J* = 4.8, 12.0 Hz, 1H, H-6), 3.71-3.69 (m, 2H, H-3, H-4), 3.47-3.42 (m, 1H, H-5), 2.30 (s, 3H, CH_3Ph); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 165.3, 137.6, 132.7, 129.8, 133.4-128.2 (CH_{arom}), 86.4 (C-1), 83.9, 79.4, 74.7, 72.3, 70.3, 74.2, 71.3; m/z (HRMS) calcd for $C_{27}H_{28}O_6S\ Na^+$: 503.1504, found: 503.1502.

***p*-Methylphenyl 2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-1-thio-β-D-glucopyranose (9):**



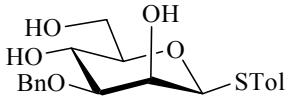
Compound **8** (5.3 g) was treated as described for preparation of **4** and **9** was obtained in 95% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17-7.07 (m, 24H, Ar-H), 5.34 (t, *J* = 9.6 Hz, 1H, H-2), 4.84 (d, *J* = 10.0 Hz, 1H, H-1), 4.77 (dd, *J* = 11.4 Hz, 2H, CH_2Ph), 4.10-4.02 (m, 2H, H-6a, H6b), 3.93 (t, *J* = 9.2 Hz, 1H, H-3), 3.79 (t, *J* = 9.0 Hz, 1H, H-4), 3.61-3.57 (m, 1H, H-5), 2.37 (s, 3H, CH_3Ph), 1.18 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 165.4, 138.2, 138.1, 135.9, 135.8, 133.3, 133.1, 130.2-128.0 (CH_{arom}), 86.8 (C-1), 84.2, 79.7, 75.0, 72.4, 71.4, 64.3, 27.1, 21.4, 19.5; m/z (HRMS) calcd for $C_{43}H_{46}O_6SSi\ Na^+$: 741.2676, found: 741.2658.

***p*-Methylphenyl 2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-levulinyl-1-thio-β-D-glucopyranose (10):**



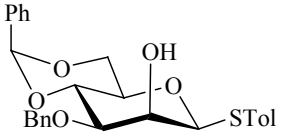
Compound **9** (4.2 g) was treated as described for preparation of **5** and **10** was obtained in 91% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05-6.96 (m, 24H, Ar-H), 5.29 (dd, *J* = 9.9 Hz, 1H, H-2), 5.17 (t, *J* = 9.8 Hz, 1H, H-4), 4.78 (d, *J* = 10.0 Hz, 1H, H-1), 4.55 (s, 2H, CH_2Ph), 3.88 (t, *J* = 9.2 Hz, 1H, H-3), 3.77-3.70 (m, 2H, H-6), 3.61-3.57 (m, 1H, H-5), 2.56-2.28 (m, 4H, $C{:}OCH_2CH_2C{:}O$), 2.27 (s, 3H, $CH_3C{:}O$), 2.10 (s, 3H, CH_3Ph), 1.06 (s, 9H, $(CH_3)_3C$);); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 206.1, 171.3, 165.2, 138.2, 137.9, 136.0, 135.9, 133.5, 133.4, 133.3, 133.2, 130.1-127.8 (CH_{arom}), 100.7, 86.9 (C-1), 81.8, 79.6, 74.2, 72.4, 70.2, 63.2, 37.9, 30.0, 28.0, 27.0, 21.3, 19.5; m/z (HRMS) calcd for $C_{48}H_{52}O_8SSi\ Na^+$: 839.3044, found: 839.3043.

***p*-Methylphenyl 3-*O*-benzyl-1-thio-β-D-mannopyranoside (12):**



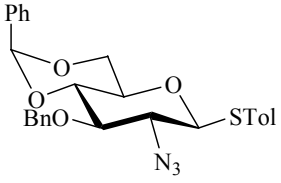
To a solution of *p*-methylphenyl 1-thio-β-D-mannopyranoside[5f] (2.3 g, 8.0 mmol) in anhydrous toluene (100 mL), was added di-n-butyltin oxide (2.2 g, 8.8 mmol) and refluxed with azeotropic removal of water for 6 h using Dean–Stark tube. The reaction was cooled to 60°C, tetra-*n*-butylammonium bromide (2.9 g, 8.9 mmol) and benzyl bromide (1.5 mL, 12.5 mmol) was added the reaction was stirred for overnight at the same temperature. The mixture was concentrated and the residue was purified by column chromatography on silica gel (MeOH–EtOAc, 49:1), to give compound **12** in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.08 (m, 4H, Ar-H), 4.74 (d, *J* = 11.2 Hz, 1H, CH_2Ph), 4.60 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.26 (bs, 1H, H-2), 4.06-4.03 (m, 1H, H-4), 3.86 (bs, 1H, H-6), 3.42 (dd, *J* = 9.4, 9.2 Hz, 1H, H-3), 3.37 (bs, 1H, H-1), 3.26-3.24 (m, 1H, H-5), 3.18 (d, *J* = 3.1 Hz, 1H, H-6), 2.33 (s, 3H, CH_3Ph); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 137.9, 131.8-128.3 (CH_{arom}), 87.6 (C-1), 82.1, 79.9, 71.8, 69.7, 66.0, 62.3, 21.3; m/z (HRMS) calcd for $C_{20}H_{24}O_5S\ K^+$: 415.0976, found: 415.0967.

***p*-Methylphenyl 4,6-*O*-benzylidene-3-*O*-benzyl-1-thio-β-D-mannopyranoside (13):**



To a solution of compound **12** (1.9 g, 4.7 mmol) and benzaldehyde dimethyl acetal (2.1 mL, 14.0 mmol) in dry CH_3CN, was add camphor sulfonic acid (100 mg, 0.43 mmol). The reaction was continued for 4 h and then quenched with triethyl amine. Concentration of the mixture followed by column chromatography on silica gel (Toluene–EtOAc, 5:1), to give compound **13** in 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50-7.18 (m, 14H, Ar-H), 5.60 (s, 1H, CHPh), 4.80 (d, *J* = 9.5 Hz, 1H, H-1), 4.80 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.73 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.32-4.28 (m, 2H, H-2, H-6), 4.18 (t, *J* = 10.3 Hz; 1H, H-4), 3.71 (dd, *J* = 9.0, 9.5 Hz, 1H, H-6), 4.38-4.32 (m, 1H, H-5), 2.33 (s, 3H, CH_3Ph); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 138.1, 137.8, 137.6, 132.2, 130.9-126.3 (CH_{arom}), 101.7, 88.3, 78.4, 77.9, 73.0, 71.5, 71.3, 68.7, 21.4; m/z (HRMS) calcd for $C_{20}H_{24}O_5S\ Na^+$: 487.1555, found: 487.1558.

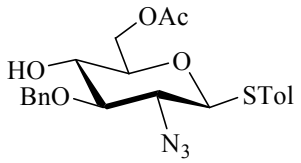
***p*-Methylphenyl 2-azido-4,6-*O*-benzylidene-2-*O*-deoxy-3-*O*-benzyl-1-thio-β-D-glucopyranoside (14):**



To a mixture of mannoside **13** (640mg, 1.29 mmol) in pyridine-CH_2Cl_2 (1:1, 12 mL) at -15ºC under argon, was added liquid trifluoromethanesulfonic anhydride (1 mL). The reaction was allowed to warm to room temperature. The reaction was diluted with EtOAc and quenched with a few drops of H_2O. The mixture was then washed with 2 N HCl, $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was then stirred in anhydrous DMF at 0ºC under argon. Solid NaN_3 (422 mg, 6.48 mmol) was added. The reaction was allowed to warm to room temperature

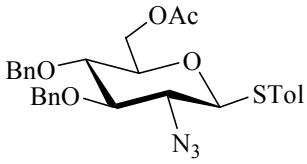
and proceed overnight. The reaction was diluted with EtOAc, washed with H_2O. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was purified by column chromatography (3% EtOAc in toluene) to give **14** in 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.14 (m, 14H, Ar-H), 5.56 (s, 1H, CHPh), 4.90 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.76 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.41 (d, *J* = 10.3 Hz, 1H, H-1), 4.38-4.36 (m, 1H), 3.79-3.74 (m, 1H), 3.67-3.57 (m, 2H), 3.46-3.40 (m, 1H, H-5), 3.34-3.30 (m, 1H), 2.35 (s, 3H, CH_3Ph); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 138.1, 137.5, 129.3-126.25, 101.7, 99.6, 83.0, 76.6, 75.3, 69.1, 63.4, 62.8, 55.6; m/z (HRMS) calcd for $C_{20}H_{24}O_5S\ Na^+$: 512.1620, found: 512.1619.

***p*-Methylphenyl 2-azido-4-*O*-hydroxyl-6-*O*-acetyl-2-*O*-deoxy-3-*O*-benzyl-1-thio-β-D-glucopyranoside (15):**



To a mixture of mannoside **14** (640mg, 1.29 mmol) was added 80% AcOH (10 mL) and the reaction mixture was stirred at 90ºC for 5 h. Solvent was concentrated and the residue was coevaporated with toluene to remove the last traces of water and then taken up in pyridine (4 mL). Reaction mixture was cooled to 0^{o}C and AcCl (0.09 mL, 1.25 mmol) was added. After 4 h, mixture was poured into EtOAc and extracted with 1N HCl, brine, and sat. $NaHCO_3$. The organic phase dried over Na_2SO_4 and filtered. Concentration of the mixture followed by column chromatography on silica gel (Hexane–EtOAc, 3:1), to give compound **15** in 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.18 (m, 9H, Ar-H), 4.90 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.78 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.45 (dd, *J* = 12.2 Hz, 1H, H-2), 4.36 (d, *J* = 10.0 Hz, 1H, H-1), 4.28 (dd, *J* = 12.2 Hz, 1H, H-4), 3.44-3.22 (m, 4H, H-6a, H-6b, H-5, H-3), 2.34 (s, 3H, CH_3Ph), 2.10 (s, 3H, $COCH_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 171.8, 139.0, 137.9, 134.5, 129.9-127.2 (CH_{arom}), 86.3 (C-1), 84.5, 75.8, 70.0, 64.7, 63.3, 21.4, 21.0; m/z (HRMS) calcd for $C_{20}H_{24}O_5S\ Na^+$: 466.1407, found: 466.1411.

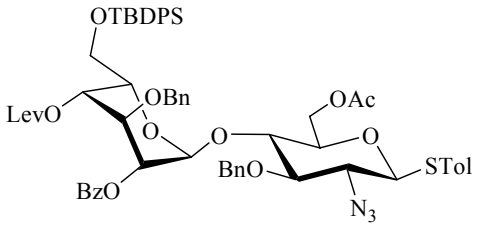
***p*-Methylphenyl 2-azido-6-*O*-acetyl-2-*O*-deoxy-3, 4-*O*-dibenzyl-1-thio-β-D-glucopyranoside (16):**



Compound **14** (0.5 g, 0.98 mmol) and flame activated AW-300 MS were suspended in dry CH_2Cl_2 (5 mL) for 1 h at room temperature under argon and then cooled to -78^{o}C. PhBCl (0.4 mL, 3.3 mmol) and Et_3SiH (0.47 mL, 2.9 mmol) were added and the reaction was allowed to warm to room temperature. After 1 h, reaction mixture was quenched with Et_3N and MeOH. The reaction was diluted with CH_2Cl_2, washed with $NaHCO_3$, the organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. The resulting residue was purified by column chromatography to give corresponding compound in 92% yield. The resulting compound in pyridine (4 mL) was cooled to 0^{o}C and AcCl (0.07 mL, 0.95 mmol) was added. After 4 h, mixture was poured into EtOAc and extracted with 1N HCl, brine, and sat. $NaHCO_3$. The organic phase dried over Na_2SO_4 and filtered. Concentration of the mixture followed by column chromatography on silica gel (Hexane–EtOAc, 3:1), to give compound **16** in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.18 (m, 14H, Ar-H), 4.90 (d, *J* = 10.5 Hz, 1H, CH_2Ph), 4.82 (d, *J* = 10.5 Hz, 2H, CH_2Ph), 4.55 (d, *J* = 10.9 Hz, 1H, CH_2Ph), 4.40 (dd, *J* = 12.0, 11.9 Hz, 1H, H-4), 4.31 (d, *J* = 10.1 Hz, 1H, H-1), 4.15 (dd, *J* = 11.9, 12.0 Hz, 1H, H-2), 3.55-3.40 (m, 3H, H-6a, H-6b, H-5),

3.30 (t, J = 10.0 Hz, 1H, H-3), 2.34 (s, 3H, CH_3Ph), 2.10 (s, 3H, $COCH_3$); m/z (HRMS) calcd for $C_{29}H_{31}N_3O_5S\ Na^+$: 556.1882, found: 556.1879.

***p*-Methylphenyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-1-thio-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-levulinyl-α-L-idopyranosyl)-β-D-glucopyranoside (17):**

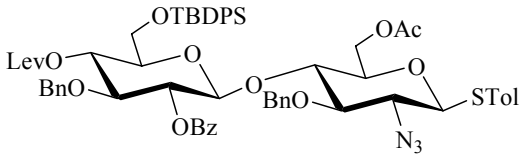


Method a: Idopyranosyl donor **5** (0.3 g, 0.37 mmol), azidoglucosyl acceptor **15** (0.2 g, 0.45 mmol) and flame activated AW-300 MS (0.75 g) were suspended in dry CH_2Cl_2 (3 mL) for 1 h at room temperature under argon and then cooled to -45°C. *N*-iodosuccinimide (NIS) (0.1 g, 0.45 mmol) and 1 M trifluoromethanesulfonic acid (TfOH) in Et_2O (36 µL, 0.11 mmol) were added and the reaction was allowed to warm to room temperature. After 3 h reaction mixture was quenched with sat. $NaHCO_3$ and solid $Na_2S_2O_3$. The mixture was filtered and washed with sat. $NaHCO_3$, H_2O and brine, dried over Na_2SO_4 and concentrated for column chromatography purification (Toluene/EtOAc, 8:1) to yield **17** in 92% yield.

Method b: Idopyranosyl donor **5** (0.3 g, 0.37 mmol), azidoglucosyl acceptor **15** (0.2 g, 0.45 mmol), BSP (0.77 g, 0.37 mmol) and flame activated AW-300 MS (0.75 g) were suspended in dry CH_2Cl_2 (3 mL) at room temperature for 1 h under Ar. The reaction mixture was cooled to -45°C, followed by the addition of Tf_2O (0.07 mL, 0.41 mmol), and the temperature was increased gradually from -45°C to room temperature within 3 h. The reaction was quenched with triethylamine (0.1 mL) at -45°C and diluted with CH_2Cl_2. The reaction mixture was filtered and washed sequentially with sat. $Na_2S_2O_3$, sat. $NaHCO_3$, H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated. The crude mixture was purified by flash column chromatography (Toluene-EtOAc, 8:1) to give **17** in 72% yield.

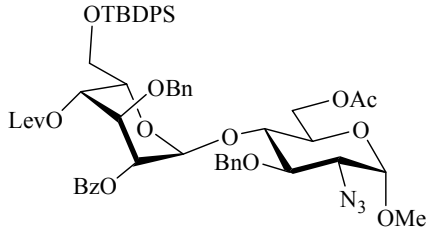
Method c: Idopyranosyl donor **5** (0.3 g, 0.37 mmol), azidoglucosyl acceptor **15** (0.2 g, 0.45 mmol), N-(thiophenyl)-ε-caprolactam (91 mg, 0.41 mmol), and flame activated AW-300 MS were suspended in dry CH_2Cl_2 (3 mL) at room temperature for 1 h under Ar. The reaction mixture was cooled to -45°C, followed by the addition of Tf_2O (0.07 mL, 0.41 mmol), and the temperature was increased gradually from -45°C to room temperature within 3 h. The reaction was quenched with triethylamine (0.1 mL) at -45°C and diluted with CH_2Cl_2. The reaction mixture was filtered and washed sequentially with sat. $Na_2S_2O_3$, sat. $NaHCO_3$, H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated. The crude mixture was purified by flash column chromatography (Toluene-EtOAc, 8:1) to give **17** in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-7.12 (m, 29H, Ar-H), 5.20 (d, J = 2.2 Hz, 1H; H-1′), 5.14-5.10 (m, 2H, H-2′, H-4′), 4.85 (d, J = 10.3 Hz, 1H, CH_2Ph), 4.72 (s, 2H, CH_2Ph), 4.60 (d, J = 10.5 Hz, 1H, CH_2Ph), 4.90-4.42 (m, 2H, H-5′, H-6a), 4.28 (d, J = 10.3 Hz, 1H, H-1), 4.22 (dd, J = 12.2 Hz, 1H, H-6b), 3.98 (t, J = 3.7 Hz, 1H, H-3), 3.76-3.64 (m, 3H, H-6′a, H-6′b, H-4), 3.46-3.40 (m, 1H, H-5), 3.36 (t, J = 9.3 Hz, 1H, H-3), 3.18 (dd, 1H, H-2), 2.60-2.35 (m, 4H, C:OCH_2CH_2C:O), 2.29 (s, 3H, CH_3C:O), 2.11 (s, 3H, CH_3Ph), 2.01 (s, 3H, $COCH_3$), 1.07 (s, 9H, $(CH_3)_3C$); m/z (HRMS) calcd for $C_{63}H_{69}N_3O_{13}SSi\ Na^+$: 1158.4212, found: 1158.4213.

***p*-Methylphenyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-1-thio-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-levulinyl-β-D-glucopyranosyl)-β-D-glucopyranoside (18):**



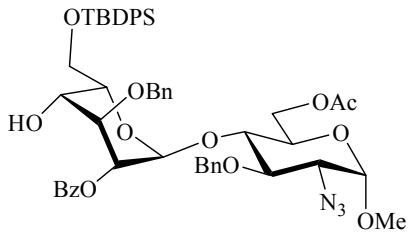
Compound **18** was synthesized as described for preparation of **17**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02-7.05 (m, 29H, Ar-H), 5.30 (dd, *J* = 8.0 Hz, 1H, H-2′), 5.12 (t, *J* = 9.2 Hz, 1H, H-4′), 4.92 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.75 (d, *J* = 11.5 Hz, 1H, CH_2Ph), 4.61 (d, *J* = 7.9 Hz, 1H, H-1′), 4.54-4.51 (m, 2H, CH_2Ph), 4.33-4.29 (m, 1H, H-6a), 4.20 (d, *J* = 10.2 Hz, 1H, H-1), 4.11-4.08 (m, 1H, H-6b), 3.82-3.74 (m, 2H, H-3′, H-4), 3.66-3.61 (m, 2H, H-6′a, H-6′b), 3.45-3.38 (m, 2H, H-5′, H-3), 3.32-3.28 (m, 1H, H-5), 3.16 (t, *J* = 9.6 Hz, 1H, H-2), 2.60-2.32 (m, 4H, C:OCH_2CH_2C:O), 2.29 (s, 3H, CH_3C:O), 2.11 (s, 3H, CH_3Ph), 1.95 (s, 3H, $COCH_3$), 1.07 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 205.7, 172.2, 170.8, 165.4, 138.9, 138.2, 137.8, 136.0, 135.7, 133.6, 133.2, 130.2-127.1 (CH_{arom}), 100.8, 100.7 (C-1, C-1′), 82.1, 80.4, 80.2, 79.5, 76.2, 76.0, 75.9, 75.8, 75.2, 74.2, 73.9, 37.9, 30.1, 29.9, 27.9, 27.1, 26.8,19.4; m/z (HRMS) calcd for $C_{63}H_{69}N_3O_{13}SSi\ Na^+$: 1158.4212, found: 1158.4213.

Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-levulinyl -α-L-idopyranosyl)-β-D-glucopyranoside (19):



Compound **19** was synthesized as described for preparation of **17** (method a). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-7.12 (m, 25H, Ar-H), 5.24 (bs, 1H, H-1′), 5.16-5.10 (m, 2H, H-2′, H-4′), 4.90 (d, 1H, CH_2Ph), 4.81-4.72 (m, 3H, CH_2Ph, H-6a), 4.60 (d, 1H, CH_2Ph), 4.56-4.52 (m, 1H, H-5′), 4.35 (bs, 2H, H-1, H6b), 4.02-3.95 (m, 1H, H-3′), 3.85-3.78 (m, 3H, H-4, H-5, H-3), 3.76-3.64 (m, 2H, H-6′a, H-6′b), 3.42 (s, 3H, OCH_3), 3.38-3.32 (m, 1H, H-2), 2.60-2.44 (m, 4H, C:OCH_2CH_2C:O), 2.08 (s, 3H, CH_3C:O), 1.98 (s, 3H, $COCH_3$), 1.05 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 205.9, 172.0, 170.7, 165.3, 137.8, 137.4, 135.6, 133.4, 133.1, 133.0, 129.8-127.6 (CH_{arom}), 98.5, 98.3 (C-1, C-1′), 79.5, 75.4, 75.3, 73.8, 73.0, 68.9, 68.8, 67.2, 67.1, 63.7, 62.5, 62.2, 55.3, 37.7, 29.7, 27.8, 26.8, 20.8, 19.1; m/z (HRMS) calcd for $C_{57}H_{65}N_3O_{14}Si\ Na^+$: 1066.4128, found: 1066.4143.

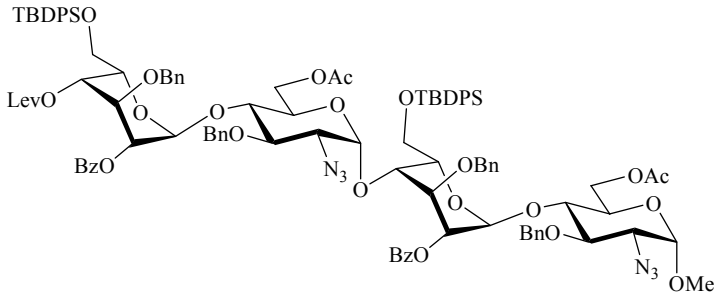
Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-hydroxyl-α-L-idopyranosyl)-β-D-glucopyranoside (20):



Disaccharide precursor **19** (0.3 g, 0.29 mmol) was dissolved in dry pyridine (3 mL) and 1M hydrazine hydrate ($NH_2NH_2{\cdot}xH_2O$) in Pyr/AcOH mixture (vol/vol = 3:2) (0.9 mL) was added. The reaction mixture was stirred at room temperature for 4 h and solvent was removed and purified by column

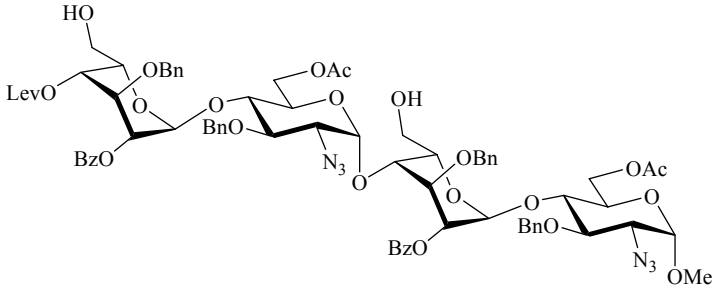
chromatography purification on silica gel (Hexane–EtOAc, 1:1) to provide **20** in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-7.12 (m, 25H, Ar-H), 5.16 (bs, 2H, H-1′, H-2′), 4.82-4.76 (m, 2H, H-1, CH_2Ph), 4.74 (d, J = 10.5 Hz, 1H, CH_2Ph), 4.66 (dd, J = 11.7, 10.5 Hz, 2H, CH_2Ph), 4.46-4.32 (m, 2H, H-6a, H-6b), 4.28-4.25 (m, 1H, H-5′), 4.92-4.78 (m, 4H, H-3, H-5, H-3′, H-4), 3.70 (dd, J = 11.2, 11.0 Hz, 1H, H-6′a), 3.47-3.40 (m, 5H, H-6′b, H-4′, OCH_3), 3.38-3.32 (m, 1H, H-2), 2.02 (s, 3H, $COCH_3$), 1.05 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 172.2, 165.5, 138.0, 137.6, 135.9, 135.8, 133.6, 133.3, 130.0-127.7 (CH_{arom}), 98.7, 98.5 (C-1, C-1′), 79.6, 75.6, 75.5, 73.98, 73.2, 69.1, 67.4, 67.3, 63.9, 62.7, 62.4, 55.5, 20.8, 19.1; m/z (HRMS) calcd for $C_{52}H_{59}N_3O_{12}Si$ Na^+: 968.3766, found: 968.3763.

Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-{2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-[6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-tert-butyldiphenylsilyl-4-*O*-levulinyl-α-L-idopyranosyl)-α-D-glucopyranoside]-α-L-idopyranosyl }-α-D-glucopyranoside (21):



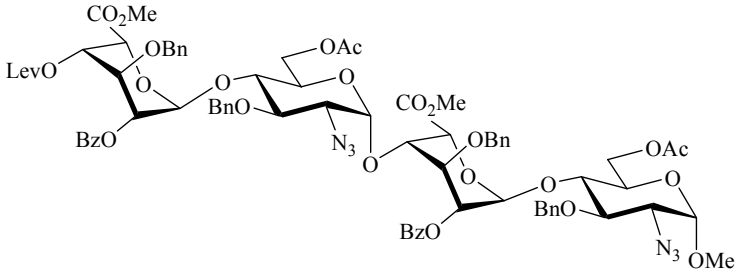
Idopyranosyl donor **5** (0.1 g, 0.12 mmol), azidoglucosyl acceptor **15** (0.064 g, 0.14 mmol) and MS AW-300 (0.3 g) were suspended in dry CH_2Cl_2 (2 mL) for 1 h at room temperature under Ar and then cooled to -45^{o}C. NIS (0.032 g, 0.14 mmol) and 1 M TfOH in Et_2O (36 µL, 0.036 mmol) were added and the reaction was allowed to warm to room temperature. After consumption of donor **5** (TLC, Toluene/EtOAc, 5:1), the disaccharide acceptor **20** (0.17 g, 0.18 mmol) in dry CH_2Cl_2 (2 mL) and MS AW-300 (0.3 g) were added mixture was let to stirred for 30 min at room temperature. Then cooled to -45^{o}C. NIS (0.054 g, 0.24 mmol) and 1 M TfOH (72 µL, 0.072 mmol) were added and the reaction was allowed to warm to room temperature. The reaction mixture was quenched with sat. $NaHCO_3$ and solid $Na_2S_2O_3$. The mixture was filtered and washed with sat. $NaHCO_3$, H_2O and brine, dried (Na_2SO_4) and concentrated for column chromatography purification (Toluene/EtOAc, 5:1) to give **21** in 35% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02-7.05 (m, 50H, Ar-H), 5.28 (d, J = 3.4 Hz, 1H, H-1‴), 5.18-5.07 (m, 4H, H-4′, H-2‴, H-4‴, H-4), 4.91 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.83 (d, J = 3.2 Hz, 1H, H-1″), 4.75 (d, J = 3.3 Hz, 1H, H-1), 4.73-4.63 (m, 6H, CH_2Ph), 4.54-4.49 (m, 1H, H-5‴), 4.25 (d, 2H, H-1′, H6b), 4.17-4.05 (m, 5H, H-3′, H-6″, H6a, CH_2Ph), 3.97-3.92 (m, 2H, H-3‴, H-5′), 3.87-3.68 (m, 7H, H-3, H-2′, H-4″, H-6′, H-5, H-6‴a), 3.65-3.61 (m, 1H, H-6‴b), 3.58-3.55 (m, 1H, H-5″), 3.48 (t, 1H, H-3″), 3.39 (s, 3H, OCH_3), 3.32 (dd, 1H, H-2), 3.17 (dd, 1H, H-2″), 2.55-2.28 (m, 4H, C:OCH_2CH_2C:O), 2.05 (s, 3H, CH_3C:O), 1.98-1.84 (2s, 6H, $COCH_3$), 1.12-1.04 (2s, 18H, $(CH_3)_3C$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 206.7, 172.7, 170.9, 165.3, 138.0, 137.5, 130.1, 129.9, 129.2, 128.9-127.8, 98.8, 98.6, 98.4, 98.2, (C-1, C-1′, C-1″, C-1‴), 79.5, 79.4, 75.7, 75.4, 75.1, 72.9, 72.8, 69.1, 69.0, 68.7, 68.5, 67.1, 66.9, 66.7, 64.3, 64.1, 63.4, 62.5, 55.7, 55.5; m/z (HRMS) calcd for $C_{108}H_{120}N_6O_{25}Si_2$ Na^+: 1979.7733, found: 1979.7870.

Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-{ 2-*O*-benzoyl-3-*O*-benzyl-6-*O*-hydroxyl-4-*O*-[6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-hydroxyl-4-*O*-levulinyl-α-L-idopyranosyl)-α-D-glucopyranoside]-α-L-idopyranosyl }-α-D-glucopyranoside (22):



A solution of **21** (100 mg, 0.3 mmol) in THF (3 mL), HF·Pyridine (0.3 mL) was added at 4°C. After 24 h at room temperature under nitrogen, the reaction mixture was evaporated under vacuum. The residue was dissolved in CH_2Cl_2 and washed with sat. $NaHCO_3$, H_2O and brine, dried (Na_2SO_4) and concentrated for column chromatography purification by chromatography on silica gel (Hexane-EtOAc, 1:1) to afford **22** in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12-7.09 (m, 30H, Ar-H), 5.18 (bt, 1H), 5.12 (m, 2H), 4.98 (s, 1H), 4.90-4.68 (m, 10H), 4.40-4.16 (m, 8H), 4.15 (m, 2H), 3.97-3.76 (m, 6H), 3.65-3.56 (m, 3H), 3.48 (dd, 1H), 3.45 (s, 3H, OCH_3), 3.34-3.3 (m, 3H), 3.01 (bs, 1H), 2.68-2.57 (m, 4H, C:OCH_2CH_2C:O), 2.12 (s, 3H, CH_3C:O), 2.05-1.98 (2s, 6H, $COCH_3$); ^{13}C NMR (400 MHz, $CDCl_3$, 20°C, TMS): δ = 98.8, 98.7, 98.2, 97.9 (C-1, C-1′, C-1″, C-1‴); m/z (HRMS) calcd for $C_{76}H_{84}N_6O_{25}$ Na^+: 1503.5384, found: 1503.5382.

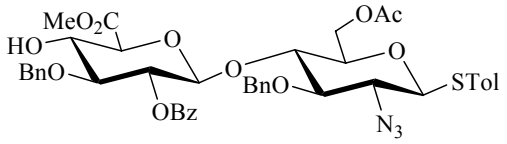
Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-{ methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-[6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-levulinyl-α-L-idopyranosyluronate)-α-D-glucopyranoside]-α-L-idopyranosyluronate }-α-D-glucopyranoside (23):



To a solution of primary alcohols (30 mg, 20 μmol) in CH_2Cl_2 (0.8 mL) was consecutively added H_2O (0.8 mL), 1 M KBr (aq) (40 μL, 40 μmol), TEMPO (6 mg, 40 μmol), 0.5 M $NaHCO_3$ (aq) (0.8 mL), and Bu_4NBr (129 mg, 0.4 mmol) at room temperature. The reaction flask was immersed in an ice-bath, and NaOCl (0.260 mL) was added to the mixture which was simultaneously calibrated with 0.5 N NaOH (aq) through micro-syringe to maintain at pH=10. The resulting solution was gradually warmed up to room temperature, and 0.5 N NaOH (aq) was added to keep at the same pH value. After stirring for 3 h, the mixture was extracted with CH_2Cl_2 (3 mL x 3), and the combined organic layers were acidified with 1 N HCl (aq), dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was coevaporated with toluene to remove the last traces of water and then dissolved in DMF (0.5 mL). MeI (10 μL, 0.16 mmol) and $KHCO_3$ (8 mg, 0.08 mmol) were added to the reaction mixture at 0°C. After 4h at room temperature, the solution was washed with H_2O and dried over $MgSO_4$ and concentrated. Residue was purified by flash column chromatography (EtOAc/Hex = 1/1) to give **23** in 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11-7.20 (m, 30H, Ar-H), 5.45 (d, *J* = 3.9 Hz, 1H, H-1‴), 5.32 (d, *J* = 3.6 Hz, 1H, H-1′), 5.20-5.13 (m, 3H, H-2‴, H-2′, H-4′), 4.90-4.84 (m, 3H, H-1″, H-5′, CH_2Ph), 4.78-4.71 (m, 6H, H-1, 5CH_2Ph), 4.65 (d, 1H, H-6a″), 4.59 (d, *J* = 10.5 Hz, 1H, CH_2Ph), 4.32-3.22 (m, 4H, H-6a, H-6b, H-5″, CH_2Ph), 4.11-4.07 (m, 1H, H-3‴), 3.97-3.74 (m, 8H, H-3, H-3′, H-4, H-4″, H-4‴, H-5, H-5‴, H-6b″), 3.62-3.51 (m, 1H, H-3″), 3.53 (s, 3H, OCH_3), 3.44 (s, 3H, OCH_3), 3.34 (s, 3H, OCH_3), 3.42-3.40 (m, 1H, H-2), 3.30 (dd, *J* = 10.6, 10.2 Hz, 1H, H-2″), 2.68-2.43 (m, 4H, C:OCH_2CH_2C:O), 2.13 (s,

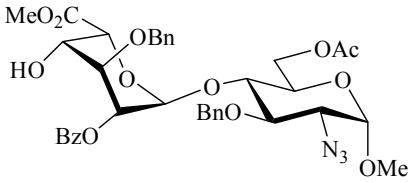
3H, CH_3C:O), 2.07 (s, 3H, CH_3 Ac), 2.06 (s, 3H, CH_3 Ac); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 206.6, 172.2, 170.8, 170.6, 165.6, 165.4, 138.3, 137.8, 138.7, 137.4, 135.9, 133.7, 133.5, 133.2, 133.1, 130.2, 130.0, 129.7, 128.7-127.7, 98.8, 98.6, 98.3, 98.2 (C-1, C-1′, C-1″, C-1‴), 79.4, 79.3, 76.6, 75.7, 75.5, 75.2, 74.8, 74.4, 73.9, 73.3, 71.5, 70.7, 70.1, 69.2, 69.1, 67.3, 63.9, 63.7, 62.8, 62.4, 55.5; m/z (HRMS) calcd for $C_{78}H_{84}N_6O_{27}$ Na^+: 1559.5276, found: 1503.5344.

***p*-Methylphenyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-1-thio-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*-levulinyl-4-*O*-hydroxyl-β-D- glucopyranosyluronate)-β-D-glucopyranoside (24):**



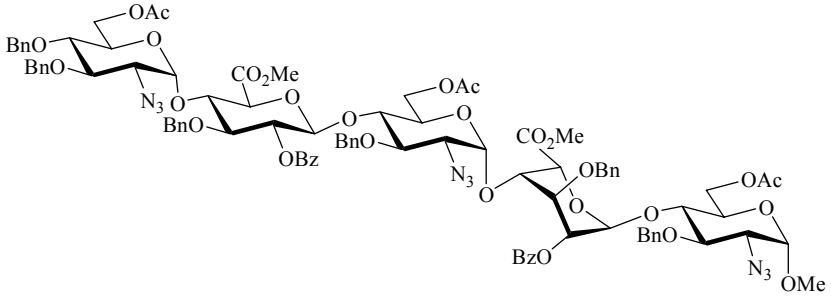
Disaccharide precursor **18** (0.3 g, 0.26 mmol) was dissolved in dry THF (3 mL) and HF·Pyr (0.6 mL) was added at 0°C. The reaction mixture was stirred at room temperature for 12 h and solvent was removed. The residue was dissolved in CH_2Cl_2 and washed with H_2O, dried (Na_2SO_4) and concentrated for column chromatography purification by chromatography on silica gel. To a solution of primary alcohol (60 mg, 67 μmol) in CH_2Cl_2 (3.4 mL) was consecutively added H_2O (3.4 mL), 1 M KBr (aq) (60 μL, 67 μmol), TEMPO (11 mg, 67 μmol), 0.5 M $NaHCO_3$ (aq) (3.4 mL), and Bu_4NBr (216 mg, 0.7 mmol) at room temperature. The reaction flask was immersed in an ice-bath, and NaOCl (0.4 mL) was added to the mixture which was simultaneously calibrated with 0.5 N NaOH (aq) through micro-syringe to maintain at pH=10. The resulting solution was gradually warmed up to room temperature, and 0.5 N NaOH (aq) was added to keep at the same pH value. After stirring for 3 h, the mixture was extracted with CH_2Cl_2 (3 mL x 3), and the combined organic layers were acidified with 1 N HCl (aq), dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was coevaporated with toluene to remove the last traces of water and then dissolved in DMF (1.0 mL). MeI (15 μL, 0.27 mmol) and $KHCO_3$ (12 mg, 0.13 mmol) were added to the reaction mixture at 0°C. After overnight at room temperature, the solution was washed with H_2O and dried over $MgSO_4$ and concentrated. Residue was purified by flash column chromatography. Resulting disaccharide precursor (30 mg, 32 μmol) was dissolved in dry pyridine (1 mL) and 1M hydrazine hydrate ($NH_2NH_2{\cdot}xH_2O$) in Pyr/AcOH mixture (vol/vol = 3:2) (0.1 mL) was added. The reaction mixture was stirred at room temperature for 4 h and solvent was removed, the residue was diluted with H_2O and mixture was extracted by EtOAc (3 mL x 3). The combined organic layers were sequentially washed with saturated $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. Residue was purified by flash column chromatography (Hex/EtOAc = 3/1) to give **24** in 45% yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01-7.05 (m, 19H, Ar-H), 5.30 (dd, *J* = 9.4, 9.3 Hz, 1H, H-2′), 5.08 (d, *J* = 11.2 Hz, 1H; CH_2Ph), 4.78-4.68 (m, 3H, CH_2Ph), 4.65 (d, *J* = 8.0 Hz, 1H, H-1′), 4.25 (dd, *J* = 12.1, 11.9 Hz, 1H, H-H6a), 4.65 (d, *J* = 10.2 Hz, 1H, H-1), 4.12-4.01 (m, 2H, H6b, H-4′), 3.78 (d, *J* = 9.8 Hz, 1H, H-5′), 3.69-3.65 (m, 2H, H-3′, H-4), 3.43 (t, *J* = 9.1 Hz, 1H, H-3), 3.27-3.21 (m, 2H, H-2, H-5), 2.31 (s, 3H, CH_3Ph), 1.92 (s, 3H, $COCH_3$); m/z (HRMS) calcd for $C_{43}H_{45}N_3O_{12}S$ Na^+: 850.2622, found: 850.2628.

Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(2-*O*-benzoyl-3-*O*-benzyl-6-*O*- levulinyl-4-*O*-hydroxyl-α-L- idopyranosyluronate)-β-D-glucopyranoside (25):



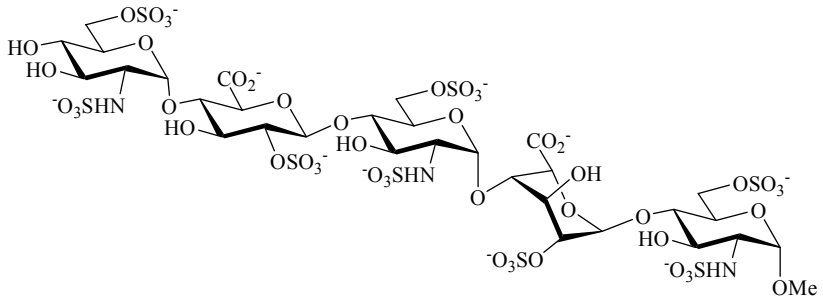
Compound **25** was synthesized as described for preparation of **24**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.23 (m, 15H, Ar-H), 5.27 (bs, 1H, H-1′), 5.17-5.16 (m, 1H, H-2′), 4.94 (d, *J* = 10.5 Hz, 1H, H-5′), 4.83-4.79 (m, 3H, H-1, CH_2Ph), 4.70 (t, *J* = 10.4 Hz, 2H, CH_2Ph), 4.44 (dd, *J* = 12.5, 12.3 Hz, 1H, H6a), 4.32 (dd, *J* = 12.3, 12.5 Hz, 1H, H6b), 4.06-4.02 (m, 1H, H-5), 3.96-3.82 (m, 4H, H-3′, H-4′, H-3, H-4), 3.50 (s, 3H, OCH_3), 3.45-3.40 (m, 4H, H-2, OCH_3), 2.07 (s, 3H, $COCH_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 170.8, 169.8, 165.2, 138.0, 137.5, 134.0, 130.1-127.5 (CH_{arom}), 98.8, 98.3 (C-1, C-1′), 78.9, 75.5, 75.3, 74.9, 72.8, 69.2, 69.1, 68.3, 68.1, 63.9, 62.4, 55.3, 52.3, 32.1, 29.9, 29.5, 22.9, 21.1; m/z (HRMS) calcd for $C_{37}H_{41}N_3O_{13}Na^+$: 758.2537, found: 758.2541.

Methyl 6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-{methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-[6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-(methyl 2-*O*-benzoyl-3-*O*-benzyl-4-*O*-{6-*O*-acetyl-2-azido-3-*O*-benzyl-2-*O*-deoxy-4-*O*-benzyl-α-D-glucopyranoside}-β-D-glucopyranosyluronate)-α-D-glucopyranoside]-α-L-idopyranosyluronate }-α-D-glucopyranoside (26):



Compound **26** was synthesized as described for preparation of **21**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07-7.18 (m, 40H, Ar-H), 5.45 (d, *J* = 4.7 Hz, 1H, H-1′′′′), 5.43 (d, *J* = 3.4 Hz, 1H, H-1′), 5.41 (dd, *J* = 9.0 Hz, 1H, H-2′′′), 5.15 (t, *J* = 5.7 Hz, 1H, H-2′), 4.97 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.88-4.80 (m, 6H, H-1′′, 5 CH_2Ph), 4.76-4.65 (m, 6H, H-1′′′, H-1, 4 CH_2Ph), 4.55 (d, *J* = 10.7 Hz, 1H; CH_2Ph), 4.41 (d, *J* = 5.1 Hz, 1H, H-5′), 4.88-4.81 (m, 5H, H-1′′, CH_2Ph), 4.75 (d, *J* = 11.0 Hz, CH_2Ph), 4.71-4.65 (m, 4H), 4.64 (d, *J* = 7.8 Hz, 1H, H-1′′′), 4.54 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.51 (m, 1H), 4.25-4.19 (m, 8H), 4.12 (m, 1H), 4.03 (m, 1H), 3.95-3.83 (m, 6H), 3.74-3.51 (m, 5H), 3.48-3.35 (3s, 9H, OCH_3), 3.30 (m, 3H), 3.26 (t, 1H), 3.21 (m, 1H), 2.05 (s, 3H, CH_3 Ac), 2.04 (s, 3H, CH_3 Ac), 2.02 (s, 3H, CH_3 Ac); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 170.9, 170.8, 170.6, 169.7, 167.9, 165.5, 164.9, 138.2, 138.1, 138.0, 137.7, 137.6, 137.5, 137.3, 134.1, 133.8, 130.1, 129.9, 129.3-127.7, 125.5, 101.4 (C-1′′′), 98.8, 98.7, 98.2, 97.9 (C-1, C-1′, C-1′′, C-1′′′′), 82.7, 80.4, 80.1, 79.0, 78.6, 78.0, 77.8, 76.3, 75.9, 75.8, 75.5, 75.3, 75.2, 75.0, 74.8, 74.5, 74.2, 73.8, 71.2, 70.8, 70.0, 69.6, 69.0, 63.6, 63.5, 63.1, 62.3, 62.2, 61.7, 55.6, 52.9, 52.0, 32.1, 29.9, 29.8, 29.6, 22.9, 21.7, 21.0; m/z (HRMS) calcd for $C_{95}H_{101}N_9O_{30}Na^+$: 1870.6546, found: 1870.6581.

Methyl (2-deoxy-2-sodium sulfonatamido-6-*O*-sodium sulfonato-4-*O*-{2,6-di-*O*-sodium sulfonato-4-*O*-[2-deoxy-2- sodium sulfonatamido-6-*O*-sodium sulfonato-4-*O*-(2,6-di-*O*-sodium sulfonato-4-*O*-{2-deoxy-2-sodium sulfonatamido-6-*O*-sodium sulfonato-α-D-glucopyranoside}-β-D-glucopyranosyluronate)-α-D-glucopyranoside]-α-L-idopyranosyluronate }-α-D-glucopyranoside (27):



(1) **Saponification.** An aq solution of H_2O_2 (30%, 325 μL) was added to a cooled (-5°C) solution of 26 (15 mg, 8.1 μmol) in THF (0.8 mL) and aq LiOOH (0.7M, 193 μL) was introduced dropwise. After 16 h at room temperature, MeOH (0.8 mL) and NaOH (4M, 212 μL) were added. Twenty-four hours later the mixture was acidified (6M aq HCl) and diluted with H_2O. The compound was extracted with CH_2Cl_2, washed with 10% aq Na_2SO_3, H_2O, dried, and concentrated to give white powder. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.44-7.17 (m, 30H, Ar-H), 5.53 (d, *J* = 3.3 Hz, 1H, H-1‴), 5.24 (bs, 1H, H-1′), 5.10 (d, *J* = 9.3 Hz, 2H, CH_2Ph), 5.03 (d, *J* = 3.8 Hz, 1H, H-1), 4.90 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.79-4.62 (m, 10H, 8 CH_2Ph, H-1″, H-2‴), 4.51 (d, *J* = 10.9 Hz, 1H, H-1‴), 4.44 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.15-4.08 (m, 2H, H-5′, H-5‴), 3.94-3.72 (m, 15H, H-3, H-4, H-6a, H-2′, H-3′, H-4′, H-3″, H-4″, H-6a″, H-6b″, H-3‴, H-4‴, H-5‴, H-6a‴, H-6b‴), 3.67-3.46 (m, 6H, H2, H-5, H6a, H-5″, H-3‴, H-4‴), 3.34-3.27 (3s, 9H, OCH_3), 3.18 (dd, *J* = 10.1 Hz, 10.3 Hz, 2H, H-2″, H-2‴); (HRMS) calcd for $C_{73}H_{83}N_9O_{25}Na^+$: 1508.5392, found: 1508.5385.

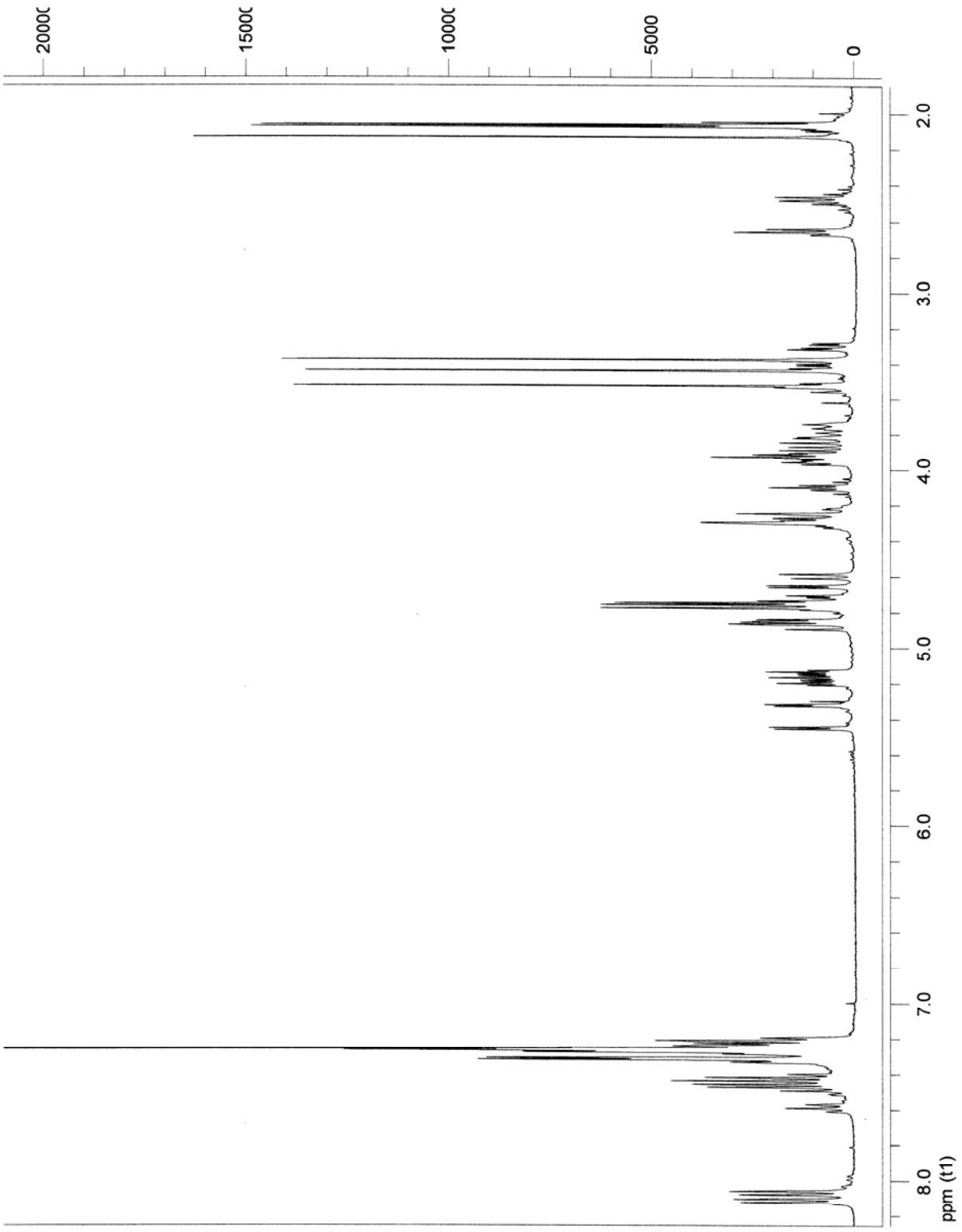
(2) ***O*-Sulfonation**. A solution of this crude triol and sulfur trioxide-triethylamine complex (0.20 g, 1.2 mmol) in DMF (0.6 mL) was stirred at 50°C under nitrogen overnight. The reaction flask was cooled down to room temperature, a solution of $NaHCO_3$ (0.114 g) in H_2O (1.4 mL) was added to the mixture, and the mixture was kept stirring for another 16 h. The solvent was coevaporated with ethanol under reduced pressure, and a mixed solvent of CH_2Cl_2/MeOH (1/1, 10 mL) was added to the residue. The mixture was filtered through paper, and the filtrate was concentrated in vacuo to give a syrup which was dissolved in a mixed solvent CH_2Cl_2/MeOH (4/1, 10 mL). Repeating of the filtration and concentration steps led to the crude sulfonated derivative, which was used for next reaction without further purification. LRMS (ESI negative mode) calcd for $[M-H]^-$ 1884.33, found 1884; calcd for $[M-2H+Na]^-$ 1906.31 found 1906; calcd for $[M-5H+4Na]^-$ 1972.25 found 1972.

(3) **Hydrogenolysis**. A solution of this crude compound in a mixed solvent tert-BuOH/H_2O (13/20, 2 mL) was hydrogenated in the presence of 10% Pd/C (30 mg) under 50 psi pressure at room temperature. After 2 d, the mixture was filtered through celite, and the filtrate was concentrated in vacuo. The same procedure was repeated again until no signals of aryl groups could be detected by 1H NMR spectrum.

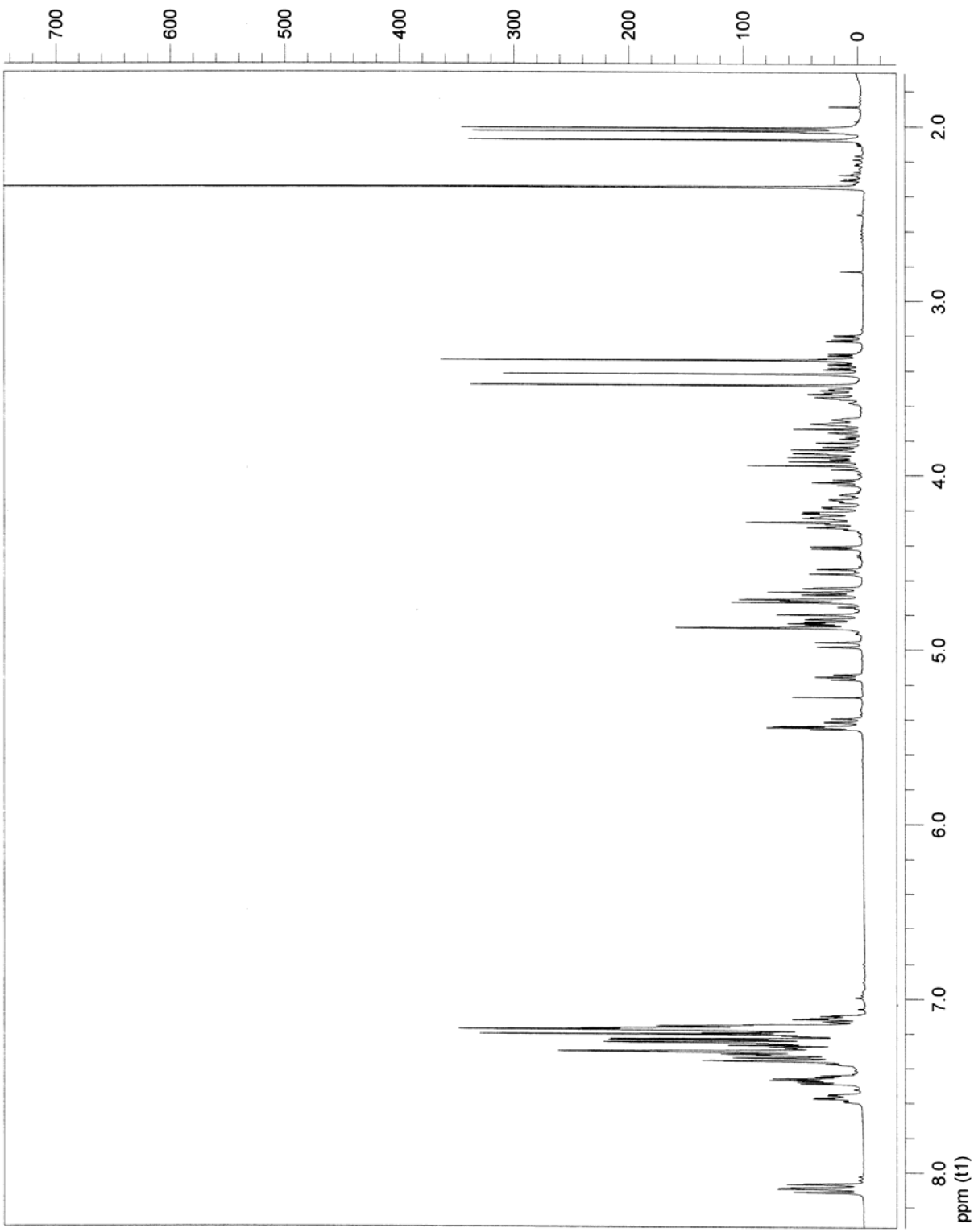
(4) ***N*-Sulfonation**. The above amino-alcohol was dissolved in water (1.5 mL), and the solution was adjusted to pH=9.5 through addition of 2 N NaOH (aq). Sulfur trioxide-pyridine complex (15 mg, 1.0 mmol) was added in five equal portions at half-hour intervals at room temperature, and the pH value was maintained at 9.5 via calibration of 2 N NaOH(aq). After stirring for 3 h, the reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography on Sephadex G-25 using 0.2 N NaCl (aq) as an eluent. The crude product portion was lyophilized followed by desalting through a Sephadex G-25 column eluted with water to give compound **27** (4 mg, 33% over four steps) as a white solid. ^{1}H NMR (400 MHz, D_2O): δ = 5.62 (dd, *J* = 4.8 Hz, 4.7 Hz, 2H, H-1⁗, H-1′), 5.43-5.40 (m, 1H), 5.22-5.20 (m, 1H), 4.62-4.52 (m, 2H), 4.45 (d, *J* = 8.8 Hz, 1H, H-1‴), 4.37-4.28 (m, 4H), 4.22-4.08 (m, 7H), 3.98-3.83 (m, 7H), 3.79-3.67 (m, 5H), 3.64-3.54 (m, 3H), 3.37 (s, 3H, OCH_3), 3.29-3.34 (m, 2H), 3.22 (dd, *J* = 8.7 Hz, 10.3 Hz, 1H); LRMS (ESI negative mode) calcd for $[M-H]^-$ 1505.94

found 1506.14, calcd for $[M-3H+2Na]^-$ 1549.91 found 1549.20, calcd for $[M-5H+4Na]^-$ 1593.87 found 1593.19.

^{1}H NMR Spectrum of Tetrasaccharide **23**



^{1}H NMR Spectrum of Pentasaccharide **26**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200
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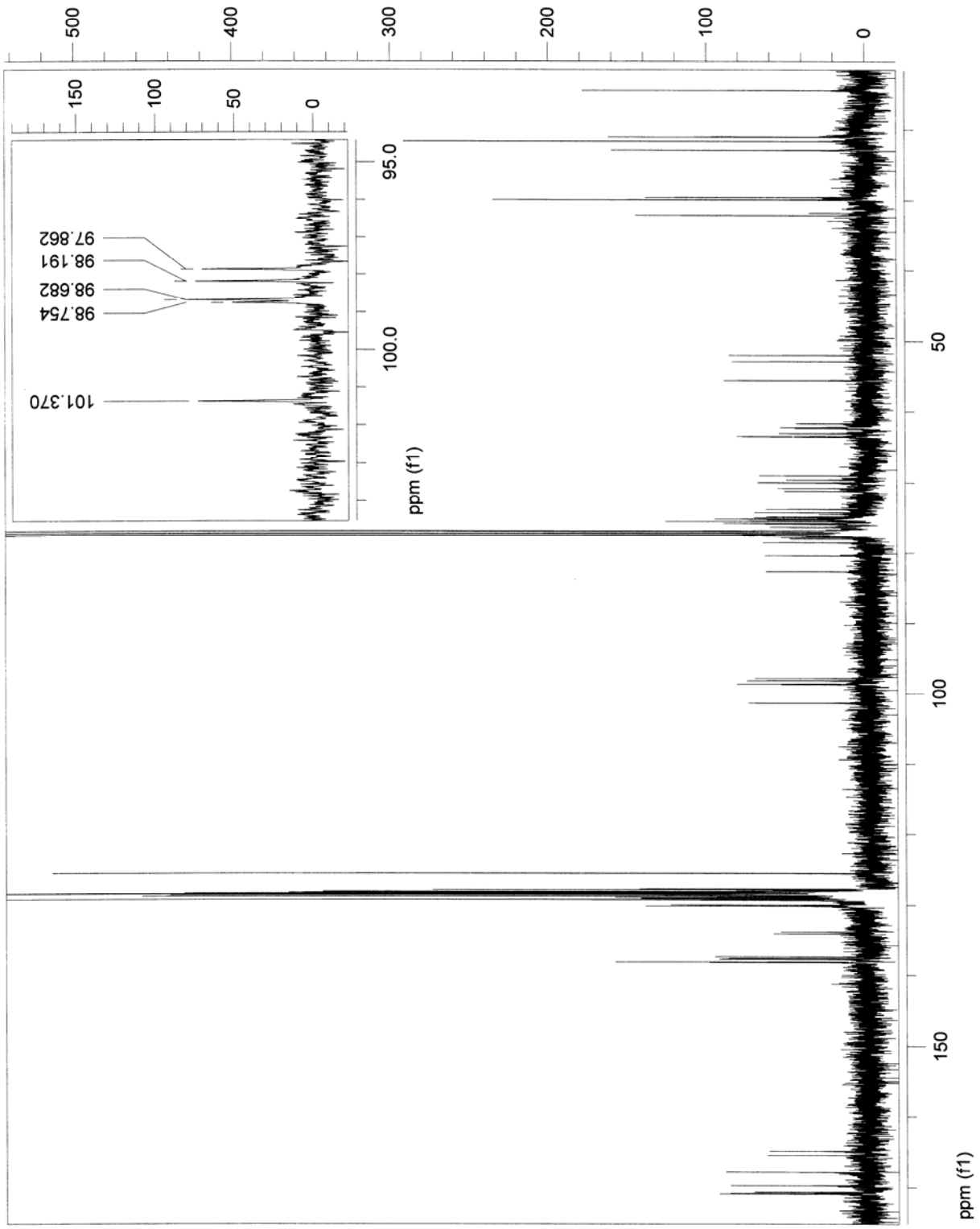
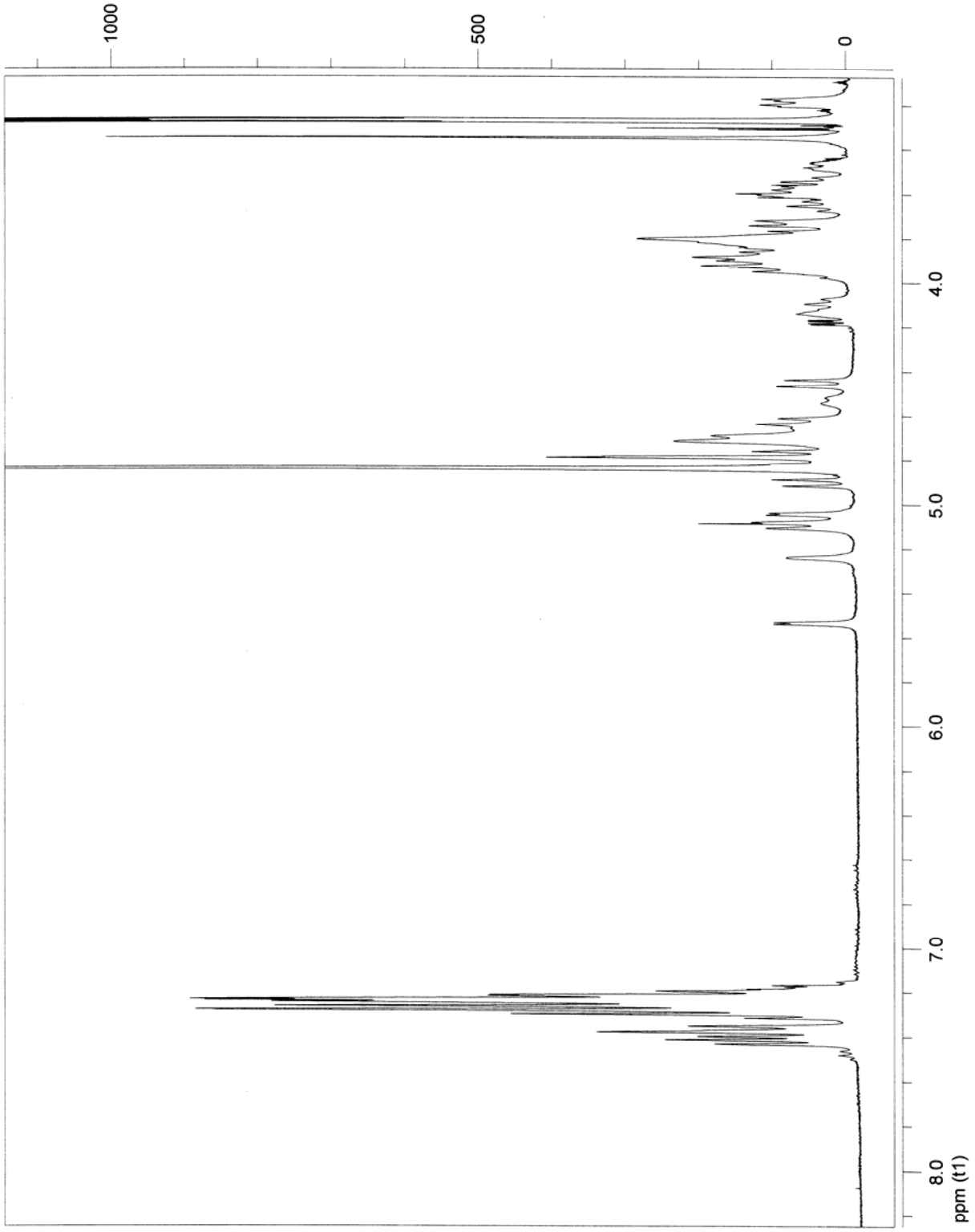
4.0
5.0
6.0
7.0
8.0
ppm (t1)

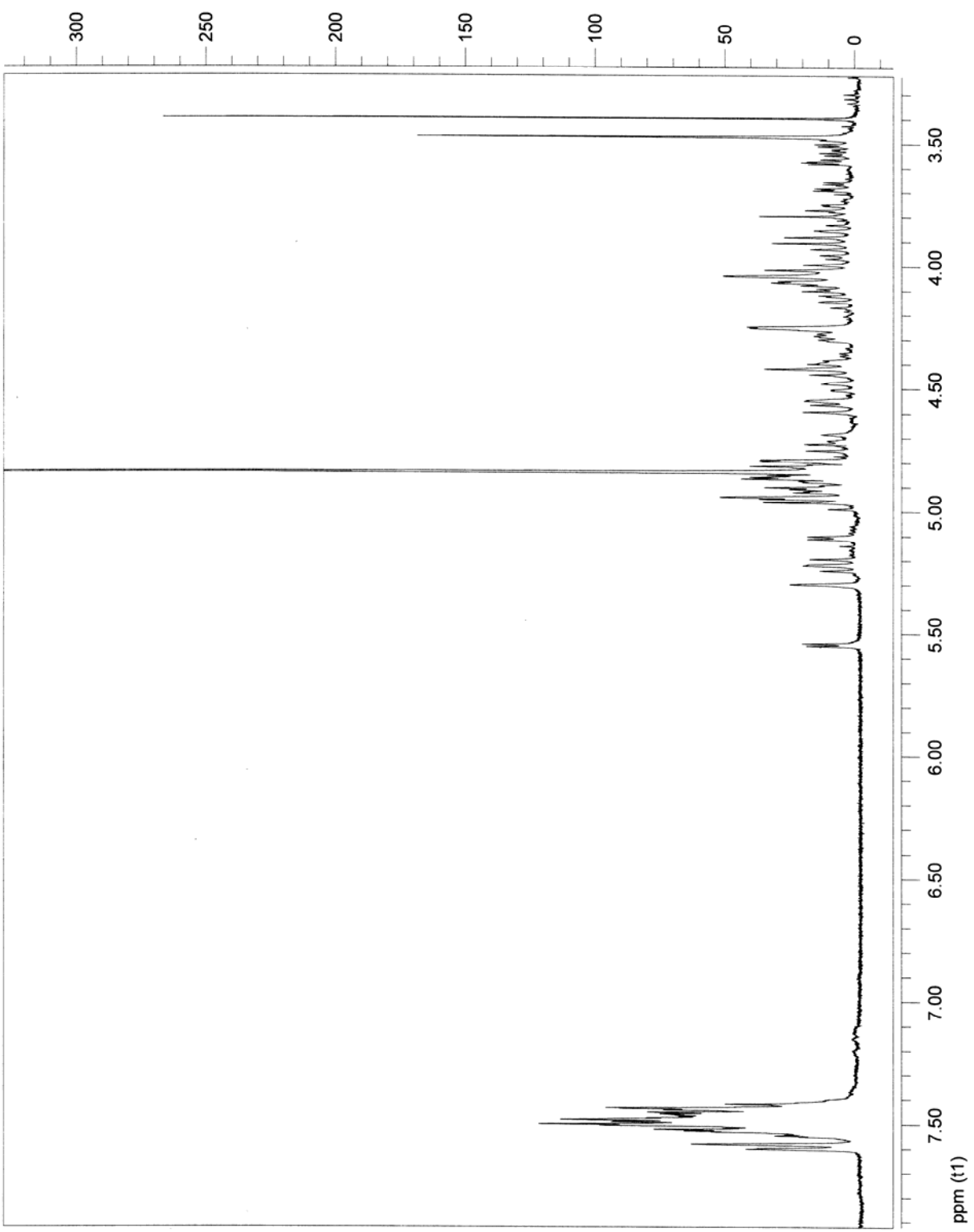
^{13}C NMR Spectrum of Pentasaccharide **26**



^{1}H NMR Spectrum of Saponification (**27-1**)



^{1}H NMR Spectrum O-Sulfation (**27-2**)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100
50
0
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
ppm (t1)

^{1}H NMR Spectrum of **27**