Supporting Information

Total Synthesis of the Core Tetrasaccharide of Neisseria meningitidis Lipopolysaccharide, a Potential Vaccine Candidate for Meningococcal Diseases

You Yang, Christopher E. Martin, Peter H. Seeberger

Department of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Am Mühlenberg 1, 14476 Potsdam, Germany
and Freie Universität Berlin, Institute of Chemistry and Biochemistry
Arnimallee 22, 14195 Berlin, Germany
Email: peter.seeberger@mpi-kg.mpg.de

Contents

| 1. General information for chemical synthesis          | S2 |
| 2. Experimental details and characterization data of new compounds | S2 |
| 3. References                                       | S18 |
| 4. NMR spectra of new compounds                      | S19 |
1. General information for chemical synthesis. Commercial reagents were used without further purification except where noted. Solvents were dried and redistilled prior to use in the usual way. All reactions were performed in oven-dried glassware under an inert atmosphere unless noted otherwise. Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid) or sulfuric acid-ethanol solution. Column chromatography was performed on Fluka Kieselgel 60 (230-400 mesh). Optical rotations (OR) were measured with a Schmidt & Haensch UniPol L1000 polarimeter at a concentration (c) expressed in g/100 mL. $^1$H and $^{13}$C NMR spectra were measured with a Varian 400-MR or Varian 600 spectrometer with Me$_4$Si as the internal standard. NMR chemical shifts (δ) were recorded in ppm and coupling constants (J) were reported in Hz. High-resolution mass spectra (HRMS) were recorded with an Agilent 6210 ESI-TOF mass spectrometer at the Freie Universität Berlin, Mass Spectrometry Core Facility.

2. Experimental details and characterization data of new compounds

2.1. Synthesis of 2,7-di-O-acetyl-3-O-levulinoyl-4-O-para-bromobenzyl-6-O-benzyl-L-glycero-D-manno-heptopyranosyl levulinoate 10

Compound 8$^1$ (500 mg, 0.49 mmol) was dissolved in THF (2 mL) at room temperature, followed by addition of 70% HF-pyridine (0.4 mL). After stirring for 2 days, the reaction mixture was carefully quenched with sat. aq. NaHCO$_3$ and the resulting solution was diluted with EtOAc. The organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated in vacuo to give the corresponding diol as a colorless syrup. To a solution of the above diol and DMAP (12 mg, 0.1 mmol) in CH$_2$Cl$_2$ (20 mL), was added Ac$_2$O (1 mL). After being stirred at room temperature
for overnight, the mixture was washed with saturated aqueous NaHCO₃ and brine. The organic layer was dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 1/1) to give 10 (300 mg, 82% for 2 steps) as a pale yellow syrup: [α]²⁰ D = +53.3 (c 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.27 (m, 7 H, Ar), 7.03 (m, 2 H, Ar), 6.06 (d, J = 2.4 Hz, 1 H, H-1), 5.31 (dd, J = 3.6, 9.2 Hz, 1 H, H-3), 5.21 (dd, J = 2.4, 3.6 Hz, 1 H, H-2), 4.80 (d-like, J = 12.0 Hz, 1 H, OCH₂Ar), 4.50 (t, J = 11.6 Hz, 2 H, OCH₂Ar), 4.44 (dd, J = 6.0, 11.6 Hz, 1 H, H-7), 4.21 (dd, J = 6.0, 11.6 Hz, 1 H, H-7), 4.14 (d-like, J = 11.6 Hz, 1 H, OCH₂Ar), 4.03 (t, J = 9.6 Hz, 1 H, H-4), 3.98 (m, 1 H, H-5), 3.89 (dd, J = 1.6, 9.6 Hz, 1 H, H-5), 2.77 – 2.57 (m, 6 H, C(O)CH₂), 2.42 (m, 2 H, C(O)CH₂), 2.17 (s, 3 H, C(O)CH₃), 2.14 (s, 3 H, C(O)CH₃), 2.13 (s, 3 H, C(O)CH₃), 2.04 (s, 3 H, C(O)CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 206.1, 205.9, 171.8, 170.6, 170.2, 169.8, 137.9, 137.0, 131.5, 129.0, 128.5, 128.0, 127.9, 121.5, 90.9 (C-1), 73.5, 73.4, 73.3, 73.1, 72.4, 72.2, 72.1, 68.5, 62.8, 37.7, 29.7, 29.6, 27.8, 27.7, 20.9, 20.8; HRMS (ESI) m/z calcd for C₃₅H₄₁BrO₁₃Na [M+Na]+ 773.1608, found 773.1645.

2.2. Synthesis of 2,7-di-O-acetyl-3-O-levulinoyl-4-O-para-bromobenzyl-6-O-benzyl-1-thio-D-glycero-D-manno-heptopyranosyl trichloroacetimidate 4

To a solution of compound 10 (170 mg, 0.227 mmol) in THF and methanol (7:3, 10 mL) at 0 °C, was bubbled through gaseous ammonium at a modest rate. After stirring for 30 min at 0 °C, the solution was evaporated in vacuo to give a residue, which was purified by silica gel column chromatography (CH₂Cl₂/MeOH: 20/1) to afford the corresponding hemiacetal (140 mg, 95%) as a colorless syrup. To a solution of the above hemiacetal (140 mg, 0.215 mmol) in CH₂Cl₂ (5 mL) was added CCl₃CN (107 µL, 1.07 mmol) and DBU (7 µL, 0.046 mmol). After being stirred at room temperature for 2 h, TLC revealed almost complete conversion of the starting material. The solution was concentrated in vacuo to a residue, which was purified by silica gel.
column chromatography (cyclohexane/EtOAc: 2/1) to give 4 (138 mg, 81%) as a colorless syrup: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44 – 7.30 (m, 7 H, Ar), 7.06 (d, $J$ = 8.4 Hz, 2 H, Ar), 6.28 (d, $J$ = 2.0 Hz, 1 H, H-1), 5.44 (dd, $J$ = 2.0, 3.2 Hz, 1 H, H-2), 5.40 (dd, $J$ = 3.2, 9.2 Hz, 1 H, H-3), 4.82 (d-like, $J$ = 12.0 Hz, 1 H, OCH$_2$Ar), 4.56 (d-like, $J$ = 11.6 Hz, 1 H, OCH$_2$Ar), 4.47 (m, 2 H), 4.17 (m, 3 H), 4.02 (m, 2 H), 2.68 (m, 2 H, C(O)CH$_3$), 2.45 (m, 2 H, C(O)CH$_3$), 2.18 (s, 3 H, C(O)CH$_3$), 2.16 (s, 3 H, C(O)CH$_3$); LRMS (ESI) m/z calcd for C$_{32}$H$_{35}$BrCl$_3$NO$_{11}$Na [M+Na]$^+$ 816.0, found 815.9.

2.3. Synthesis of 5-tert-butyl-2-methylphenyl 2,7-di-O-acetyl-3-O-levulinoyl-4-O-para-bromobenzyl-6-O-benzyl-1-thio-1-glycero-D-manno-heptopyranoside 11

To a solution of compound 10 (50 mg, 0.067 mmol) in CH$_2$Cl$_2$ (2.5 mL), was added 5-tert-butyl-2-methylbenzenethiol (61 µL, 0.33 mmol) and BF$_3$OEt$_2$ (18 µL, 0.14 mmol). After being stirred at room temperature for overnight, the mixture was quenched with Et$_3$N and concentrated in vacuo. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 3/1) to give 11 (36 mg, 66%) as a colorless syrup: $[\alpha]^{20}_{D}$ = +98.8 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46 – 7.29 (m, 8 H, Ar), 7.18 (dd, $J$ = 2.0, 8.0 Hz, 1 H, Ar), 7.07 (m, 3 H, Ar), 5.54 (d, $J$ = 2.0 Hz, 1 H, H-1), 5.51 (dd, $J$ = 2.0, 3.2 Hz, 1 H, H-2), 5.37 (dd, $J$ = 3.2, 9.2 Hz, 1 H, H-3), 4.79 (d-like, $J$ = 11.6 Hz, 1 H, OCH$_2$Ar), 4.54 (d-like, $J$ = 12.0 Hz, 1 H, OCH$_2$Ar), 4.50 (d-like, $J$ = 12.0 Hz, 1 H, OCH$_2$Ar), 4.44 (dd, $J$ = 6.0, 11.2 Hz, 1 H, H-7), 4.27 (dd, $J$ = 1.2, 9.6 Hz, 1 H, H-5), 4.18 (d-like, $J$ = 12.0 Hz, 1 H, OCH$_2$Ar), 4.09 (t, $J$ = 9.6 Hz, 1 H, H-4), 4.06 (m, 1 H), 3.99 (m, 1 H), 2.69 (m, 2 H, C(O)CH$_2$), 2.44 (m, 2 H, C(O)CH$_3$), 2.36 (s, 3 H, ArCH$_3$), 2.17 (s, 3 H, C(O)CH$_3$), 2.16 (s, 3 H, C(O)CH$_3$), 1.91 (s, 3 H, C(O)CH$_3$), 1.29 (s, 9 H, C(CH$_3$)$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 206.1, 171.8, 170.4, 170.1, 150.0, 137.8, 137.1, 135.8, 132.1, 131.5, 130.1, 128.9, 128.5, 128.1, 128.0, 127.8, 124.9, 121.5, 85.3 (C-1), 73.5, 73.4, 73.0, 72.9, 72.4, 72.3, 71.6, 62.6, 37.7, 34.5, 31.3, 29.8, 27.8, 26.9, 21.0, 20.7, 20.2; HRMS (ESI) m/z calcd for C$_{41}$H$_{49}$BrSO$_{10}$Na [M+Na]$^+$ 837.2107, found 837.2085.

Compound 9\textsuperscript{1} (930 mg, 1.03 mmol) was dissolved in THF (4 mL) at room temperature, followed by addition of 70% HF-pyridine (0.8 mL). After stirring for 2 days, the reaction mixture was carefully quenched with sat. aq. NaHCO\textsubscript{3} and the resulting solution was diluted with EtOAc. The organic layer was washed with brine, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated in vacuo to give the corresponding diol as a colorless syrup. To a solution of the above diol and DMAP (200 mg, 1.64 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (20 mL), was added Et\textsubscript{3}N (2.0 mL) and benzoyl chloride (1.0 mL). After being stirred at room temperature for overnight, the mixture was concentrated in vacuo to give a residue, which was purified by silica gel column chromatography (cyclohexane/EtOAc: 5/1 to 3/1) to give the corresponding ester (709 mg) as a white solid. To a solution of the above ester (709 mg, 0.93 mmol) and freshly activated 4Å MS in CH\textsubscript{2}Cl\textsubscript{2} (20 mL), was added 5-tert-butyl-2-methylbenzenethiol (0.98 mL, 5.31 mmol) and BF\textsubscript{3}OEt\textsubscript{2} (0.73 mL, 5.77 mmol). After being stirred at room temperature for overnight, the mixture was quenched with Et\textsubscript{3}N and concentrated in vacuo. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 10/1 to 8/1) to provide 12 (531 mg, α/β = 4.0, 60% for 3 steps) as a white foam: [α]\textsuperscript{20}_D = +64.0 (c 0.3, CHCl\textsubscript{3}); β-anomer: +52.3 (c 1.5, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) α-anomer: δ 7.88 – 7.81 (m, 4 H, Ar), 7.51 – 7.15 (m, 14 H, Ar), 7.06 (dd, J = 2.0, 8.0 Hz, 1 H, Ar), 6.96 – 6.81 (m, 3 H, Ar), 5.59 (m, 3 H, H-1/2/3), 4.82 (d-like, J = 11.6 Hz, 1 H, OCH\textsubscript{2}Ar), 4.70 (dd, J = 5.6, 10.8 Hz, 1 H, H-7), 4.51 (d-like, J = 12.0 Hz, 1 H, OCH\textsubscript{2}Ar), 4.42 (m, 2 H), 4.18 (m, 4 H), 2.26 (s, 3 H, ArCH\textsubscript{3}), 2.09 (s, 3 H, C(O)CH\textsubscript{3}), 1.20 (s, 9 H, C(CH\textsubscript{3})\textsubscript{3}); β-anomer: δ 8.07 – 7.92 (m, 4 H, Ar), 7.61 – 7.36 (m, 14 H, Ar), 7.14 (dd, J = 2.0, 8.0 Hz, 1 H, Ar), 7.04 (m, 3 H, Ar), 5.78 (dd, J = 2.0, 3.2 Hz, 1 H, H-2), 5.63 (d, J = 2.0 Hz, 1 H, H-1), 5.51 (dd, J = 3.2, 9.6 Hz, 1 H, H-3), 4.92 (d-like, J = 11.6 Hz, 1 H, OCH\textsubscript{2}Ar), 4.80 (dd, J = 6.0, 10.8 Hz, 1 H, H-7), 4.52 (m, 2 H), 4.47 (dd, J = 1.6, 9.6 Hz, 1 H, H-5), 4.32 (m, 3 H), 4.28 (m, 1 H), 2.38 (s, 3 H, ArCH\textsubscript{3}), 1.91 (s, 3 H, C(O)CH\textsubscript{3}), 1.25 (s, 9 H, C(CH\textsubscript{3})\textsubscript{3}); \textsuperscript{13}C NMR (100 MHz,
CDCl$_3$ α-anomer: δ 169.8, 165.9, 165.2, 149.9, 137.8, 136.7, 135.5, 133.4, 133.0, 132.2, 131.3, 130.1, 129.6, 129.5, 129.4, 129.3, 128.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.3, 124.7, 121.5, 85.2 (C-1), 73.6, 73.5, 73.4, 72.8, 72.6, 72.3, 72.1, 62.3, 34.5, 31.3, 21.0, 20.1; β-anomer: δ 169.8, 166.0, 165.4, 149.9, 138.0, 137.0, 136.1, 133.4, 133.1, 132.1, 131.5, 130.1, 129.9, 129.6, 129.5, 128.7, 128.5, 128.4, 128.3, 127.8, 127.7, 125.0, 121.5, 85.5 (C-1), 74.0, 73.6, 73.3, 72.6, 72.5, 72.4, 72.3, 62.6, 34.5, 31.3, 20.8, 20.3; HRMS (ESI) m/z calcd for C$_{48}$H$_{49}$BrSO$_3$Na [M+Na]$^+$ 905.2158, found 905.2164.

2.5. Synthesis of 5-tert-butyl-2-methylphenyl 3,7-di-O-benzoyl-4-O-para-bromobenzyl-6-O-benzyl-1-thio-L-glycero-D-manno-heptopyranoside 3

To a solution of thioglycoside 12 (220 mg, 0.249 mmol) in MeOH/CHCl$_3$ (5/2, v/v, 12.3 mL), was added acetyl chloride (0.53 mL). After being stirred at room temperature for 1 d, the mixture was diluted with CH$_2$Cl$_2$, washed with saturated aqueous NaHCO$_3$, and brine. The organic layer was dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/EtOAc: 6/1) to afford 3 (160 mg, 76%) as a white solid: [α]$^20_D$ = +79.1 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.02 – 7.83 (m, 4 H, Ar), 7.58 – 7.21 (m, 14 H, Ar), 7.10 (dd, $J$ = 2.0, 8.0 Hz, 1 H, Ar), 7.01 – 6.87 (m, 3 H, Ar), 5.67 (d, $J$ = 2.0 Hz, 1 H, H-1), 5.56 (dd, $J$ = 3.2, 9.2 Hz, 1 H, H-3), 4.85 (d-like, $J$ = 12.0 Hz, 1 H, OCH$_2$Ar), 4.76 (dd, $J$ = 6.0, 11.2 Hz, 1 H, H-7), 4.54 (d-like, $J$ = 11.6 Hz, 1 H, OCH$_2$Ar), 4.46 (m, 3 H), 4.28 (m, 3 H), 4.19 (m, 1 H), 2.30 (s, 3 H, ArCH$_3$), 1.27 (s, 9 H, C(CH$_3$)$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 165.9, 165.5, 149.9, 137.7, 136.8, 134.9, 133.5, 133.0, 132.7, 131.3, 130.0, 129.7, 129.6, 129.5, 129.0, 128.5, 128.2, 128.1, 128.0, 126.4, 124.3, 121.5, 86.9 (C-1), 73.7, 73.5, 73.1, 72.6, 72.2, 71.4, 62.4, 34.5, 31.3, 20.1; HRMS (ESI) m/z calcd for C$_{48}$H$_{49}$BrSO$_3$Na [M+Na]$^+$ 863.2052, found 863.2017.

2.6. Synthesis of methyl (N-benzyl-benzylexocarbonyl-5-aminopentyl 4,5,7,8-
tetra-O-acetyl-3-deoxy-α-D-manno-oct-2-ulopyranosid)onate 15

To a stirred solution of phenylselenyl chloride (2.73 g, 14.3 mmol) in CH$_2$Cl$_2$ (50 mL) was added AgOTf (2.55 g, 9.92 mmol) and TMSOTf (0.16 mL, 0.86 mmol). After stirring at room temperature for 30 min, a solution of glycal 13 (2.85 g, 7.08 mmol) and linker 14 (3.25 g, 9.92 mmol) in CH$_2$Cl$_2$ (70 mL) was added dropwise. After being stirred at room temperature for 2 h, the mixture was diluted with CH$_2$Cl$_2$, washed with saturated aqueous NaHCO$_3$, and brine. The organic layer was dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 3/1) to give a white solid (4.2 g, 67%).

To a solution of the above solid (4.2 g, 4.75 mmol) in toluene (140 mL), was added tri-n-butyltin hydride (3.8 mL, 14.24 mmol) and AIBN (779 mg, 4.75 mmol). After being refluxed for 1.5 h, the mixture was concentrated in vacuo and purified by silica gel column chromatography (cyclohexane/EtOAc: 5/2 to 2/1) to afford 15 (3.26 g, 94%) as a colorless syrup: [$\alpha$]$^2$D = +43.5 (c 0.4, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 – 7.11 (m, 10 H, Ar), 5.29 (br s, 1 H), 5.24 (m, 1 H, H-4), 5.13 (m, 3 H), 4.51 (d-like, J = 12.0 Hz, 1 H), 4.43 (br s, 2 H), 4.05 (dd, J = 3.6, 12.4 Hz, 1 H), 3.98 (m, 1 H), 3.71 (s, 3 H, C(O)OC$_3$H$_7$), 3.37 (m, 1 H, OCH$_2$), 3.16 (m, 3 H, OCH$_2$/NCH$_2$), 2.09 (dd, J = 4.8, 13.2 Hz, 1 H, H-3e), 2.00 (s, 3 H, C(O)CH$_3$), 1.95 (m, 1 H, H-3a), 1.91 (s, 6 H, C(O)CH$_3$), 1.90 (s, 3 H, C(O)CH$_3$), 1.47 (m, 4 H, CCH$_2$C), 1.22 (m, 2 H, CCH$_2$C); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 170.4, 170.3, 169.9, 169.6, 167.8, 137.8, 128.5, 128.4, 127.9, 127.8, 127.3, 127.2, 98.8 (C-2), 68.1, 67.6, 67.1, 66.4, 64.3, 63.8, 62.0, 52.6, 32.1 (C-3), 29.7, 29.2, 23.4, 20.8, 20.7, 20.6; HRMS (ESI) m/z calcd for C$_{37}$H$_{47}$NO$_{14}$Na [M+Na]$^+$ 752.2894, found 752.2921.

2.7. Synthesis of methyl (N-benzyl-benzyloxycarbonyl-5-aminopentyl 4-O-benzyl-7,8-O-isopropylidene-3-deoxy-α-D-manno-oct-2-ulopyranosid)onate 5
To a stirred solution of compound 15 (1 g, 1.37 mmol) in MeOH (25 mL) was added NaOMe (74 mg, 1.37 mmol). The mixture was stirred at room temperature for 4 h, and then neutralized with Amberlite IR120 H+ resin. Filtration, concentration in vacuo, and purification by silica gel column chromatography (CH$_2$Cl$_2$/MeOH: 12/1) gave the corresponding alcohol (710 mg, 92%) as a white solid. To a stirred solution of the above alcohol (500 mg, 0.89 mmol) in DMF (9 mL), was added 2-methoxypropene (153 µL, 1.60 mmol) and p-toluenesulfonic acid monohydrate (40 mg, 0.21 mmol). The mixture was stirred at room temperature for 2 h, and then neutralized with sodium hydrogencarbonate. Filtration, concentration in vacuo, and purification by silica gel column chromatography (CH$_2$Cl$_2$/MeOH: 40/1) afforded 16 (490 mg, 91%) as a colorless syrup: [α]$^2_0$D = +30.3 (c 0.5, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 – 7.10 (m, 10 H, Ar), 5.09 (d-like, J = 12.0 Hz, 2 H), 4.42 (br s, 2 H), 4.32 (m, 1 H), 4.07 (dd, J = 6.0, 8.4 Hz, 1 H), 3.97 (m, 1 H, H-4), 3.88 (m, 2 H), 3.67 (s, 3 H, C(O)OCH$_3$), 3.42 (m, 1 H), 3.31 (m, 1 H, OCH$_2$), 3.15 (m, 3 H, OCH$_2$/NCH$_2$), 2.05 (dd, J = 4.8, 12.8 Hz, 1 H, H-3e), 1.78 (t, J = 12.0 Hz, 1 H, H-3a), 1.44 (m, 4 H, C(CH$_3$)$_2$), 1.32 (s, 3 H, C(CH$_3$)$_2$), 1.29 (s, 3 H, C(CH$_3$)$_2$), 1.18 (m, 2 H, CCH$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.7, 137.8, 128.5, 128.4, 127.9, 127.8, 127.3, 127.2, 109.4 (C(CH$_3$)$_2$), 99.0 (C-2), 73.6, 72.8, 67.2, 67.1, 66.7, 65.7, 63.6, 52.5, 35.0 (C-3), 29.7, 29.2, 26.9, 25.3; HRMS (ESI) m/z calcd for C$_{32}$H$_{43}$NO$_{10}$Na [M+Na]$^+$ 624.2785, found 624.2736.
A mixture of compound 16 (490 mg, 0.81 mmol), dibutyltin oxide (304 mg, 1.22 mmol) and 4Å MS (500 mg) in toluene (15 mL) was heated at 110 °C for 2 h. After cooling to room temperature, benzyl bromide (0.17 mL, 1.47 mmol) and tetrabutylammonium bromide (158 mg, 0.49 mmol) were added, and the mixture was heated at 110 °C for overnight. The cooling mixture was then filtered and the filtrate was evaporated. The residue was dissolved in CH₂Cl₂ and washed with water. The organic layer was dried over Na₂SO₄, filtered and concentrated in vacuo to give a residue, which was purified by silica gel column chromatography (cyclohexane/EtOAc: 4/1) to give a syrup, which was dissolved in MeOH (8 mL) and treated with NaOMe (24 mg, 0.44 mmol). The mixture was stirred at room temperature for 3 h, and then neutralized with Amberlite IR120 H⁺ resin. Filtration, concentration in vacuo, and purification by silica gel column chromatography (cyclohexane/EtOAc: 3/1) provided 5 (418 mg, 74%) as a colorless syrup; [α]²⁰_D = +21.7 (c 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.12 (m, 15 H, Ar), 5.12 (d-like, J = 13.2 Hz, 2 H), 4.53 (dd, J = 11.6, 16.4 Hz, 2 H), 4.41 (m, 3 H), 4.09 (m, 2 H), 3.92 (dd, J = 4.8, 8.8 Hz, 1 H), 3.85 (m, 1 H, H-4), 3.69 (s, 3 H, C(O)OCH₃), 3.42 (m, 1 H), 3.34 (m, 1 H, OCH₂), 3.20 (m, 3 H, OCH₂/NCH₂), 2.16 (dd, J = 4.8, 12.8 Hz, 1 H, H-3α), 1.93 (t, J = 12.8 Hz, 1 H, H-3δ), 1.48 (m, 4 H, CCH₂C), 1.35 (s, 3 H, C(CH₃)₂), 1.32 (s, 3 H, C(CH₃)₂), 1.20 (m, 2 H, CCH₂C); ¹³C NMR (100 MHz, CDCl₃) δ 168.6, 137.9, 137.7, 128.5, 128.4, 127.9, 127.8, 127.7, 127.6, 127.3, 127.1, 109.2 (C(CH₃)₂), 98.9 (C-2), 73.5, 72.9, 72.7, 70.3, 67.1, 67.0, 64.1, 63.5, 52.5, 32.2 (C-3), 29.2, 26.9, 25.3, 23.4; HRMS (ESI) m/z calcd for C₃₉H₄₀NO₁₁Na [M+Na]^+ 714.3254, found 714.3221.

2.8. Synthesis of methyl [N-benzyl-benzylxoycarbonyl-5-aminopentyl (2,7-di-O-acetyl-3-O-levulinoyl-4-O-para-bromobenzyl-6-O-benzyl-L-glycero-α-D-manno-
heptopyranosyl)-(1→5)-4-O-benzyl-7,8-O-isopropylidene-3-deoxy-α-D-manno-oct-2-ulopyranosid]onate 17

To a stirred mixture of the donor 4 (100 mg, 0.126 mmol), acceptor 5 (65 mg, 0.094 mmol), and freshly activated 4Å MS in dry CH₂Cl₂ (5.5 mL) at 0 °C, was added dropwise TMSOTf in CH₂Cl₂ (0.05 M, 138 µL) under nitrogen. After being stirred at 0 °C for 1 h, the mixture was quenched with Et₃N, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography (cyclohexane/EtOAc: 2/1 to 3/2) to afford 17 (110 mg, 88%) as a colorless syrup: [α]²⁰_D = +35.1 (c 1.0, CHCl₃).¹ H NMR (400 MHz, CDCl₃) δ 7.45 – 7.05 (m, 24 H, Ar); 5.40 (dd, J = 3.2, 9.6 Hz, 1 H, H-3), 5.33 (dd, J = 2.0, 3.2 Hz, 1 H, H-2), 5.19 (d, J = 1.6 Hz, 1 H, H-1), 5.16 (m, 2 H), 4.76 (d-like, J = 12.0 Hz, 1 H), 4.64 (d-like, J = 11.6 Hz, 1 H), 4.50 (m, 3 H), 4.42 (m, 2 H), 4.33 (m, 2 H), 4.19 (m, 3 H), 4.09 (br s, 1 H), 4.01 (t, J = 9.6 Hz, 1 H), 3.92 (dd, J = 2.8, 12.4 Hz, 1 H), 3.86 (m, 1 H, H-4'), 3.77 (m, 1 H), 3.76 (s, 3 H, C(O)OCH₃), 3.65 (m, 1 H), 3.25 (m, 5 H), 2.67 (m, 2 H, C(O)CH₂), 2.43 (m, 2 H, C(O)CH₂), 2.30 (dd, J = 3.6, 12.4 Hz, 1 H, H-3'e), 2.15 (s, 3 H, C(O)CH₃), 2.11 (s, 3 H, C(O)CH₃), 2.00 (t, J = 12.0 Hz, 1 H, H-3'a), 1.95 (s, 3 H, C(O)CH₃), 1.49 (m, 4 H, C(CH₂)₂), 1.25 (s, 3 H, C(CH₃)₂), 1.24 (s, 3 H, C(CH₃)₂), 1.23 (m, 2 H, CCH₂C);¹³ C NMR (100 MHz, CDCl₃) δ 206.2, 171.5, 170.4, 170.0, 168.4, 138.5, 137.7, 137.5, 131.3, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 121.3, 109.6 (C(CH₃)₂), 98.8 (C-2), 97.4 (C-1, J_C,H = 173.0 Hz), 77.2, 74.5, 74.4, 73.2, 73.0, 72.6, 72.3, 72.2, 72.1, 71.9, 71.7, 70.2, 70.0, 67.9, 67.1, 66.3, 63.5, 52.4, 37.8, 31.8 (C-3'), 29.8, 29.7, 29.3, 27.9, 26.8, 24.7, 23.4, 22.7, 21.0, 20.9; HRMS (ESI) m/z calcd for C₆₉H₈₂BrNO₂₀Na [M+Na]⁺ 1346.4511, found 1346.4506.

2.9. Synthesis of methyl [N-benzyl-benzylloxycarbonyl-5-aminopentyl (2,7-di-O-
acetyl-4-O-parabromobenzyl-6-O-benzyl-1-L-glycero-α-D-manno-heptopyranosyl)-
(1→5)-4-O-benzyl-7,8-O-isopropylidene-3-deoxy-α-D-manno-oc-t-2-ulopyranosid]

18

To a solution of 17 (105 mg, 0.079 mmol) in DMF (3 mL) at room temperature,
was added hydrazine acetate (30 mg, 0.324 mmol). After being stirred at room
temperature for 40 min, the mixture was diluted with EtOAc, washed with saturated
aqueous NaHCO₃, and brine. The organic layer was dried over Na₂SO₄, filtered, and
concentrated in vacuo. The residue was purified by silica gel column chromatography
(hexane/EtOAc: 1/1) to give 18 (71 mg, 73 %) as a colorless syrup: [α]²⁰_D = +28.6 (c
0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.10 (m, 24 H, Ar), 5.26 (d, J = 1.2
Hz, 1 H, H-1), 5.20 (m, 3 H), 4.76 (d-like, J = 12.0 Hz, 2 H), 4.65 (d-like, J = 11.6 Hz,
1 H), 4.50 – 4.43 (m, 4 H), 4.38 – 4.20 (m, 6 H), 4.11 (m, 2 H), 3.95 (dd, J = 2.4, 12.0
Hz, 1 H), 3.83 (m, 2 H), 3.76 (s, 3 H, C(O)OCH₃), 3.68 (m, 1 H), 3.35 (m, 2 H), 3.25
(m, 3 H), 2.32 (dd, J = 4.0, 12.8 Hz, 1 H, H-3'e), 2.13 (s, 3 H, C(O)CH₃), 1.96 (s, 3 H,
C(O)CH₃), 1.94 (t, J = 12.0 Hz, 1 H, H-3'a), 1.51 (m, 4 H, CCH₂C), 1.27 (s, 3 H,
C(CH₃)₂), 1.26 (s, 3 H, C(CH₃)₂), 1.25 (m, 2 H, CCH₂C); ¹³C NMR (100 MHz, CDCl₃)
δ 171.1, 170.6, 170.5, 168.5, 138.5, 137.9, 137.8, 137.7, 137.1, 131.4, 131.2, 129.0, 128.6,
128.5, 128.4, 128.0, 127.9, 127.8, 127.5, 127.6, 127.3, 127.1, 121.3, 109.6 (C(CH₃)₂), 98.8 (C-2'),
97.0 (C-1), 77.2, 75.7, 74.8, 74.5, 73.4, 72.7, 72.6, 72.2, 72.1, 71.6, 70.6, 70.2, 67.9, 67.1, 66.8, 63.6, 60.4, 52.5, 31.9 (C-3'), 29.2, 26.9, 24.8,
23.4, 21.1, 21.0; HRMS (ESI) m/z calcd for C₆₄H₇₆BrNO₁₈Na [M+Na]^+ 1250.4123,
found 1250.4144.

2.10. Synthesis of 5-tert-butyl-2-methylphenyl (3,4,6-tri-O-acetyl-2-azido-
2-deoxy-α-D-glucopyranosyl)-(1→2)-3,7-di-O-benzoyl-4-O-para-bromobenzyl-6-O-benzyl-1-thio-L-glycero-D-manno-heptopyranoside 19

To a stirred mixture of the donor 2\(^4\) (70 mg, 0.147 mmol), acceptor 3 (28 mg, 0.033 mmol), and freshly activated 4Å MS in dry Et\(_2\)O (3 mL) at 0 °C, was added dropwise TMSOTf in CH\(_2\)Cl\(_2\) (0.05 M, 0.34 mL) under nitrogen. After 0.5 h, the temperature was allowed to warm up naturally to room temperature and the stirring continued for overnight. The mixture was then filtered and concentrated \textit{in vacuo}. The residue was purified silica gel column chromatography (hexane/EtOAc: 7/1 to 6/1) provided 19 (26 mg, 68%) as a white solid: [α]\(^{20D}\) = +78.61 (c 0.8, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.07 – 7.91 (m, 4 H, Ar), 7.58 – 7.21 (m, 14 H, Ar), 7.16 (dd, \(J = 2.0, 8.0\) Hz, 1 H, Ar), 7.08 – 6.85 (m, 3 H, Ar), 5.83 (d, \(J = 2.0\) Hz, 1 H, H-1’), 5.66 (dd, \(J = 9.2, 10.4\) Hz, 1 H, H-3/H-4), 5.58 (m, 1 H, H-3’), 5.07 (dd, \(J = 9.2, 10.4\) Hz, 1 H, H-3/H-4), 5.05 (d, \(J = 3.2\) Hz, 1 H, H-1), 4.85 (d-like, \(J = 12.0\) Hz, 1 H), 4.77 (dd, \(J = 5.6, 10.8\) Hz, 1 H), 4.58 (m, 2 H), 4.55 (m, 1 H), 4.42 (m, 3 H), 4.32 (m, 2 H), 4.17 (t, \(J = 6.8\) Hz, 1 H), 3.98 (m, 2 H), 3.41 (dd, \(J = 3.6, 10.4\) Hz, 1 H, H-2), 2.36 (s, 3 H, ArCH\(_3\)), 2.13 (s, 3 H, C(O)CH\(_3\)), 1.95 (s, 3 H, C(O)CH\(_3\)), 1.85 (s, 3 H, C(O)CH\(_3\)), 1.28 (s, 9 H, C(CH\(_3\)))\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.5, 169.8, 169.7, 166.0, 165.9, 150.0, 137.9, 136.9, 135.7, 133.4, 133.0, 132.6, 131.2, 130.2, 129.7, 129.6, 129.5, 129.3, 129.0, 128.7, 128.5, 128.3, 128.1, 127.9, 124.9, 121.3, 99.1 (C-1), 85.9 (C-1’), 73.3, 73.1, 72.6, 72.2, 71.7, 70.7, 70.5, 68.6, 68.4, 68.2, 62.6, 61.6, 61.2, 34.5, 31.3, 20.7, 20.5, 20.3, 20.2; HRMS (ESI) \textit{m/z} calcd for C\(_{58}\)H\(_{62}\)BrS\(_3\)O\(_{15}\)Na[M+Na]\(^{+}\) 1176.2962, found 1176.2992.

2.11. Synthesis of N-Phenyl Trifluoroacetimidate (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→2)-3,7-di-O-benzoyl-4-O-para-bromobenzyl-6-O-benzyl-1-L-glycero-D-manno-heptopyranoside 20
To a solution of compound 19 (83 mg, 0.072 mmol) in acetone/H₂O (10/1, v/v, 2.2 mL), was added NBS (38 mg, 0.22 mmol). After being stirred at room temperature for 1 h, the mixture was diluted with EtOAc, washed with saturated aqueous NaHCO₃ and brine. The organic layer was dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/EtOAc: 2/1) to afford 5 (87%) as a colorless syrup.

To a solution of the above hemiacetal (69 mg, 0.070 mmol) and K₂CO₃ (27 mg, 0.195 mmol) in acetone (1.5 mL), was added 2,2,2-trifluoro-N-phenylacetimidoyl chloride to a residue, which was purified by silica gel column chromatography (hexane/EtOAc: 3/1) to afford 20 (70 mg, 87%) as a colorless syrup: [α]²⁰D = +47.32 (c 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.06 – 8.01 (m, 4 H, Ar), 7.61 – 7.09 (m, 18 H, Ar), 6.86 – 6.81 (m, 4 H, Ar), 5.62 (dd, J = 9.2, 10.4 Hz, 1 H), 5.59 (dd, J = 2.8, 9.2 Hz, 1 H), 5.05 (dd, J = 9.6, 10.4 Hz, 1 H), 4.85 (d-like, J = 12.0 Hz, 1 H, OCH₂Ar), 4.77 (dd, J = 5.2, 10.8 Hz, 1 H), 4.60 (d-like, J = 12.4 Hz, 1 H, OCH₂Ar), 4.49 – 4.40 (m, 5 H), 4.27 (dd, J = 4.0, 12.4 Hz, 1 H), 4.15 (t, J = 6.4 Hz, 1 H), 4.08 (d-like, J = 9.6 Hz, 1 H), 3.99 (d-like, J = 12.4 Hz, 1 H), 3.40 (dd, J = 4.0, 10.8 Hz, 1 H, H-2), 2.12 (s, 3 H, C(O)CH₃), 2.01 (s, 3 H, C(O)CH₃), 1.95 (s, 3 H, C(O)CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 169.8, 169.7, 166.2, 165.9, 143.2, 137.8, 136.7, 133.6, 133.3, 131.4, 129.8, 129.7, 129.6, 129.3, 129.2, 128.9, 128.8, 128.6, 128.5, 128.2, 128.1, 124.6, 121.6, 119.4, 99.3 (C-1), 77.3, 73.6, 73.5, 72.7, 72.5, 72.2, 70.4, 68.5, 68.2, 62.3, 61.5, 61.1, 20.8, 20.7, 20.6; HRMS (ESI) m/z calcd for C₅₅H₅₂BrF₇N₇O₁₆Na [M+Na]+ 1185.2400, found 1185.2423.

(1→3)-(2,7-di-O-acetyl-4-O-para-bromobenzyl-6-O-benzyl-L-glycero-α-D-manno-heptopyranosyl)-(1→5)-4-O-benzyl-7,8-O-isopropylidene-3-deoxy-α-D-manno-oct-2-ulopyranosiduronate 21

To a stirred mixture of the disaccharide donor 20 (49 mg, 42 µmol), disaccharide acceptor 18 (38 mg, 31 µmol), and freshly activated 4Å MS in dry diethyl ether and dichloromethane (1/1, v/v, 3.6 mL) at 0 °C, was added TMSOTf in CH₂Cl₂ (0.05 M, 90 µL) under nitrogen. The temperature was allowed to warm up naturally to room temperature and the stirring continued for 1 h. The mixture was quenched with Et₃N, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by silica gel column chromatography (hexane/EtOAc/TEA: 5/2/0.07) to afford 21 (49 mg, 72%) as a white solid: [α]²⁰_D = +19.3 (c 1.0, CHCl₃); ¹H NMR (600 MHz, Pyridine-d₅) δ 8.49 – 8.33 (m, 4 H, Ar), 7.85 (m, 2 H, Ar), 7.66 – 7.31 (m, 33 H, Ar), 7.16 (d, J = 7.8 Hz, 2 H, Ar), 6.96 (d, J = 7.8 Hz, 2 H, Ar), 6.11 (dd, J = 2.4, 9.0 Hz, 1 H), 6.04 (m, 1 H), 6.02 (br s, 1 H, H-1”), 5.84 (br s, 1 H, H-1), 5.50 (t, J = 9.6 Hz, 1 H), 5.45 – 5.37 (m, 3 H), 5.20 (m, 2 H), 5.02 (m, 4 H), 4.93 – 4.83 (m, 7 H), 4.77 (d-like, J = 11.4 Hz, 2 H), 4.73 – 4.62 (m, 6 H), 4.56 (m, 3 H), 4.48 (m, 1 H), 4.43 (m, 2 H), 4.28 (d-like, J = 11.4 Hz, 1 H), 4.18 (m, 2 H), 4.07 – 4.01 (m, 3 H), 3.91 (m, 1 H), 3.89 (s, 3 H, C(O)CH₃), 3.76 (m, 1 H), 3.42 (m, 3 H), 3.29 (m, 1 H), 2.62 (d-like, J = 9.6 Hz, 1 H, H-3”e), 2.32 (t, J = 12.0 Hz, 1 H, H-3”a), 2.27 (s, 3 H, C(O)CH₃), 2.16 (s, 3 H, C(O)CH₃), 2.15 (s, 3 H, C(O)CH₃), 2.01 (s, 3 H, C(O)CH₃), 1.99 (s, 3 H, C(O)CH₃), 1.55 (m, 4 H, CCH₂C), 1.41 (s, 3 H, C(CH₃)₂), 1.35 (s, 3 H, C(CH₃)₂), 1.26 (m, 2 H, CCH₂C); ¹³C NMR (150 MHz, Pyridine-d₅) δ 171.1, 171.0, 170.9, 170.7, 170.4, 169.1, 167.2, 166.7, 150.7, 140.2, 139.4, 139.3, 139.0, 138.9, 138.5, 138.3, 136.3, 134.1, 134.0, 132.3, 131.8, 131.2, 130.9, 130.8, 130.5, 130.3, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 128.7, 128.6, 128.2, 128.0, 124.3, 123.6, 122.1, 121.7, 110.4 (C(CH₃)₂), 101.1 (C-1”), 99.8 (C-2”), 98.1 (C-1), 76.7, 

S14

To a solution of compound 21 (37 mg, 0.017 mmol) in dry pyridine (0.3 mL), was added thioacetic acid (0.3 mL, 4.18 mmol). After being stirred at room temperature for 24 h, the solution was coevaporated with toluene to give a residue, which was purified by silica gel column chromatography (hexane/EtOAc/TEA: 3/2/0.05 to 1/1/0.02) to give 22 (34 mg, 91%) as a pale yellow solid: [α]_D^20 = +26.1 (c 0.8, CHCl₃); ^1H NMR (400 MHz, Pyridine-d₅) δ 8.51 – 8.19 (m, 4 H, Ar), 7.79 – 7.18 (m, 37 H, Ar), 6.99 (d, J = 8.4 Hz, 2 H, Ar), 6.12 (m, 2 H, H-1°), 6.04 (br s, 1 H), 5.88 (m, 1 H), 5.83 (br s, 1 H, H-1), 5.56 (t, J = 10.0 Hz, 1 H), 5.39 (m, 4 H), 5.24 (d-like, J = 12.0 Hz, 1 H), 5.05 – 4.89 (m, 9 H), 4.86 – 4.68 (m, 8 H), 4.64 – 4.54 (m, 6 H), 4.39 (m, 2 H), 4.17 (m, 2 H), 4.07 (m, 2 H), 4.00 (m, 2 H), 3.93 (s, 3 H, C(O)OCH₃), 3.75 (d-like, J = 8.8 Hz, 1 H), 3.46 (m, 3 H), 3.29 (m, 1 H), 2.63 (m, 1 H, H-3°e), 2.28 (s, 3 H, C(O)CH₃), 2.25 (m, 1 H, H-3°a), 2.23 (s, 3 H, C(O)CH₃), 2.02 (s, 3 H, C(O)CH₃), 1.98 (s, 3 H, C(O)CH₃), 1.97 (s, 6 H, C(O)CH₃), 1.55 (m, 4 H, CCH₂C),
1.41 (s, 3 H, C(CH$_3$)$_2$), 1.34 (s, 3 H, C(CH$_3$)$_2$), 1.25 (m, 2 H, CCH$_2$C); $^{13}$C NMR (100 MHz, Pyridine-$d_5$) δ 171.6, 171.1, 171.0, 170.4, 170.3, 169.0, 167.3, 166.2, 140.2, 139.5, 139.4, 138.9, 138.6, 138.3, 134.4, 134.0, 132.4, 131.9, 131.2, 130.8, 130.5, 130.4, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 128.7, 128.6, 128.3, 128.1, 128.0, 122.2, 110.4 (C(CH$_3$)$_2$), 100.6 (C-1'), 99.8 (C-2'''), 98.2 (C-1), 76.0, 75.3, 74.8, 73.7, 73.5, 73.1, 72.5, 72.0, 70.9, 69.7, 68.5, 67.7, 67.2, 64.4, 62.9, 60.7, 53.5, 53.0, 51.2, 50.8, 48.0, 47.1, 30.5 (C-3'''), 30.0, 27.4, 25.7, 24.1, 22.8, 21.6, 21.4, 21.3, 21.2, 21.1, 20.9; HRMS (ESI) m/z calcd for C$_{113}$H$_{126}$Br$_2$N$_2$O$_{34}$Na [M+Na]$^+$ 2238.6476, found 2238.6545.

2.14. Synthesis of 2-N-acetyl-2-deoxy-α-D-glucopyranosyl-(1→2)-L-glycero-α-D-manno-heptopyranosyl-(1→3)-L-glycero-α-D-manno-heptopyranosyl-(1→5)-2-(5-amino)pentyl-3-deoxy-α-D-manno-oct-2-ulopyranosidonic acid 1

A solution of compound 22 (35 mg, 0.016 mmol) in acetic acid/water (8/1, v/v, 1.80 mL) was stirred at 70 °C for overnight. TLC indicated complete conversion of starting material. The mixture was covaporated with toluene and dried in vacuo to give the corresponding diol as a pale yellow syrup. The above diol was dissolved in a mixture of dioxane, methanol and 1 M aq NaOH (3/1/1, v/v/v, 1.25 mL). After being stirred at room temperature for overnight, the reaction mixture was diluted with methanol and neutralized with Amberlite IR120 H$^+$ resin. After filtration, the filtrate was concentrated in vacuo to give the corresponding tetrasaccharide as a white solid. A mixture of the above tetrasaccharide and Pd/C (70 mg, 10%) in methanol, water and acetic acid (50/25/1, v/v/v, 3.04 mL) was stirred under an atmosphere of H$_2$ at room temperature for 24 h. Filtration, concentration in vacuo and elution through Sephadex LH-20 column (H$_2$O) provided 1 (12 mg, 82% for 3 steps) as a white solid:
[α]$_D^{20}$ = +64.2 (c 0.3, H$_2$O); $^1$H NMR (600 MHz, D$_2$O) δ 5.42 (br s, 1 H, H-1' of B ring), 5.12 (d, $J$ = 3.6 Hz, 1 H, H-1 of A ring), 5.09 (d, $J$ = 1.2 Hz, 1 H, H-1'' of C ring), 4.16 (m, 2 H, H-4''''), 4.09 (m, 2 H), 4.06 – 4.01 (m, 4 H), 3.98 (m, 3 H), 3.95 (dd, $J$ = 3.0, 12.0 Hz, 1 H), 3.91 (dd, $J$ = 3.6, 10.8 Hz, 1 H), 3.85 – 3.76 (m, 6 H), 3.73 – 3.63 (m, 6 H), 3.49 (t, $J$ = 9.6 Hz, 1 H), 3.44 (m, 1 H, OCH$_3$), 3.30 (m, 1 H, OCH$_2$), 3.01 (t, $J$ = 7.8 Hz, 2 H, NCH$_2$), 2.10 (dd, $J$ = 4.8, 12.6 Hz, 1 H, H-3''e), 2.07 (s, 3 H, C(O)CH$_3$), 1.84 (t, $J$ = 12.6 Hz, 1 H, H-3''a), 1.69 (m, 2 H, CCH$_2$C), 1.62 (m, 2 H, CCH$_2$C), 1.44 (m, 2 H, CCH$_2$C), 1.41 (s, 3 H, C(O)CH$_3$), 1.39 (m, 1 H, OCH$_2$), 1.35 (m, 1 H, OCH$_2$), 1.17 (m, 2 H, CCH$_2$C), 1.11 (m, 2 H, CCH$_2$C), 1.06 (m, 2 H, CCH$_2$C); $^{13}$C NMR (150 MHz, D$_2$O) δ 175.0, 174.4, 101.3 (C-1" of C ring, $J_{C,H} = 169.7$ Hz), 100.3 (C-1' of B ring, $J_{C,H} = 172.1$ Hz), 99.7 (C-2" of D ring), 99.2 (C-1 of A ring, $J_{C,H} = 171.6$ Hz), 78.6, 76.7, 75.0, 72.2, 71.9, 71.6, 71.3, 70.6, 70.4, 70.1, 69.9, 69.2, 68.7, 68.5, 66.3, 65.9, 65.6, 63.3, 63.2, 62.9, 60.4, 53.9, 39.3(NCH$_2$), 34.8 (C-3"'), 28.1, 26.4, 22.4, 21.9; HRMS (ESI) $m/z$ calcd for C$_{35}$H$_{61}$N$_2$O$_{25}$ [M–H]$^-$ 909.3563, found 909.3629.
3. References


Coupled carbon

AcO

BnO

PBB

LevO

BnO

COOMe

Bn-N

Obz

S42

Electronic Supplementary Material (ESI) for Chemical Science
This journal is © The Royal Society of Chemistry 2011
Electronic Supplementary Material (ESI) for Chemical Science
This journal is © The Royal Society of Chemistry 2011
Electronic Supplementary Material (ESI) for Chemical Science
This journal is © The Royal Society of Chemistry 2011

 Karnowski, A.; Grandi, S. A.; Fanuzzo, M.; della Torre, M.; Pugliese, A.; De Santis, L.; Marchetti, E. O.; Frediani, F.; Torrisi, F.; Scorzelli, A.; Storari, S.; Infante, P.; Tommasi, O.; Saraceno, G. A.; Bazzicalupi, C.; Di Renzo, C.; Scandurra, L.; Di Stefano, A. \(\text{1}^{\text{H}}\)NMR and \(\text{13}^{\text{C}}\)NMR spectra of a novel pectin derivative synthesized by the transglucosylation of pectin with D-galactose. \(\text{J}\) Am. \(\text{Chem}\) Soc. 2022, \text{144}, 14303-14314. doi:10.1021/jacs.2c03957

S61
Coupled carbon

![Diagram of coupled carbon structure](image-url)