

Supplementary Information

Systematic synthesis of sulfated oligofucosides and their effect on breast cancer MCF-7 cells

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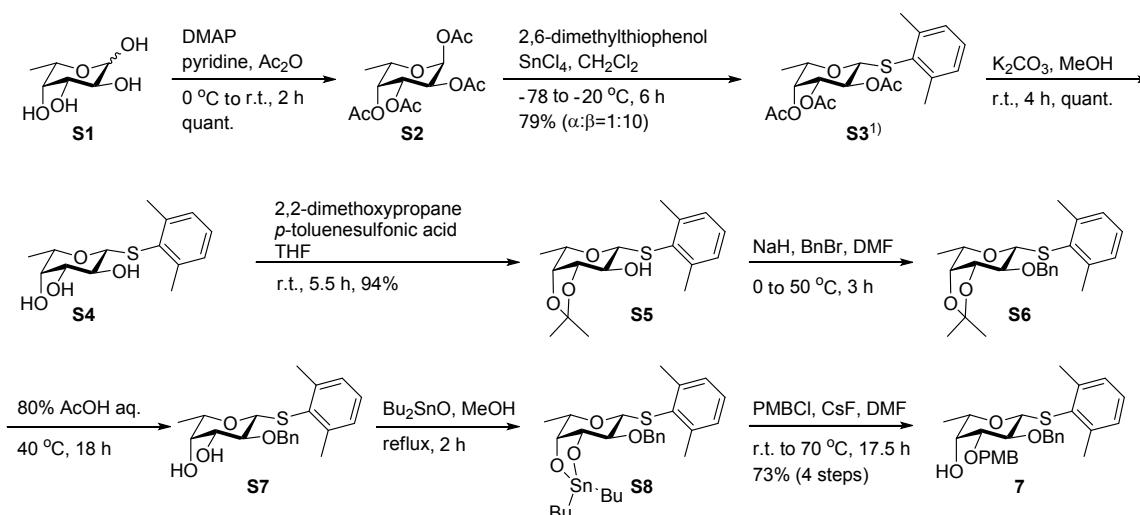
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General methods for synthesis.

NMR spectra were recorded on a JEOL ECA-500 (500 MHz for ^1H , 125 MHz for ^{13}C) spectrometer. ^1H NMR data are reported as follows; chemical shift in parts per million (ppm) downfield or upfield from tetramethylsilane (δ 0.00), CD_3OD (δ 3.31) or CDCl_3 (δ 7.26), integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, d = quartet, and m = multiplet) and coupling constants (Hz). ^{13}C chemical shifts are reported in ppm downfield or upfield from CDCl_3 (δ 77.1), CD_3OD (δ 49.0) or acetone- d_6 (δ 29.8). ESI-TOF Mass spectra were measured on a Waters LCT premier XE. Melting points were determined on a micro hot-stage (Yanako MP-S3) and were uncorrected. Optical rotations were measured on a JASCO P-2200 polarimeter. Silica gel TLC and column chromatography were performed using Merck TLC 60F-254 (0.25 mm) and Silica Gel 60 N (spherical, neutral, 63-210 μm) (Kanto Chemical Co., Inc.), respectively. Gel filtration chromatography separations were performed using Sephadex LH-20 (GE Healthcare). Air- and/or moisture-sensitive reactions were carried out under an argon atmosphere using oven-dried glassware. In general, organic solvents were purified and dried using appropriate procedures, and evaporation and concentration were carried out under reduced pressure below 30 $^\circ\text{C}$, unless otherwise noted.

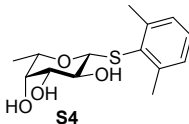
Synthesis of the monosaccharide 7.

Scheme S1. Synthetic scheme of monosaccharide 7



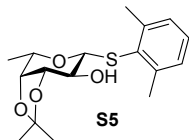
Synthesis of the common key intermediate 12.

2,6-Dimethylphenyl 1-thio- β -L-fucopyranoside (**S4**)



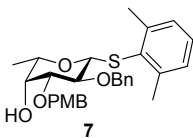
To a solution of **S3**¹⁾ (0.535 g, 1.41 mmol) in MeOH (5.30 mL) was added K₂CO₃ (48.8 mg, 0.354 mmol) at room temperature. After the reaction mixture was stirred for 4 h, the reaction was quenched with Amberlite® IR 120 H⁺ form. The resultant suspension was filtered, and the filtrate was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (4/1 CHCl₃/MeOH) to give **S4** (0.402 g, 1.41 mmol, quant.). White solid; *R*_f 0.55 (4/1 CHCl₃/MeOH); m.p. 188-189 °C; [α]_D²⁷ +10.8° (*c* 1.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.19-7.12 (3H, m, Ar-H), 4.23 (1H, d, *J*_{1,2} = 9.8 Hz, H-1), 3.74 (1H, m, H-4), 3.66 (1H, ddd, *J*_{1,2} = 9.8 Hz, *J*_{2,3} = 9.8 Hz, *J*_{2,OH} = 2.0 Hz, H-2), 3.56 (1H, m, H-3), 3.51 (1H, dq, *J*_{4,5} = 1.7 Hz, *J*_{5,6} = 6.6 Hz, H-5), 2.78 (1H, d, *J* = 5.2 Hz, OH), 2.66 (1H, d, *J* = 2.0 Hz, OH), 2.58 (6H, s, SPhMe₂), 2.22 (1H, d, *J* = 5.5 Hz, OH), 1.28 (3H, d, *J*_{5,6} = 6.6 Hz, H-6); ¹³C-NMR (125 MHz, CD₃OD) δ 145.3, 133.4, 129.8, 129.0, 92.6, 76.5, 75.7, 73.1, 71.9, 22.9×2, 17.0; HRMS (ESI-TOF) *m/z* 307.0968 (307.0980 calcd. for C₁₄H₂₀O₄NaS, [M+Na]⁺).

2,6-Dimethylphenyl 3,4-*O*-acetonide-1-thio- β -L-fucopyranoside (**S5**)



To a solution of **S4** (0.344 g, 1.21 mmol) in THF (6.90 mL) were added *p*-toluenesulfonic acid (46.0 mg, 0.242 mmol) and 2,2-dimethoxypropane (0.297 mL, 2.42 mmol) at room temperature. After the reaction mixture was stirred for 5.5 h, the reaction was quenched with triethylamine (75.7 μ L, 0.543 mmol). And then, water was added to the mixture. The resultant mixture was extracted with EtOAc (10 mL×3), and then the extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (7/3 PhMe/EtOAc) to give **S5** (0.369 g, 1.14 mmol, 94% yield). White solid; *R*_f 0.58 (7/3 PhMe/EtOAc); m.p. 157-158 °C; [α]_D²⁷ +25.2° (*c* 2.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.18-7.11 (3H, m, Ar-H), 4.15 (1H, d, *J*_{1,2} = 10.6 Hz, H-1), 3.99 (2H, m, H-3, 4), 3.68 (1H, dq, *J*_{4,5} = 1.8 Hz, *J*_{5,6} = 6.6 Hz, H-5), 3.61 (1H, m, H-2), 2.58 (7H, m, OH, SPhMe₂), 1.55 (3H, s, Me), 1.36 (3H, s, Me), 1.35 (3H, d, *J*_{5,6} = 6.6 Hz, H-6); ¹³C-NMR (125 MHz, CDCl₃) δ 144.2, 131.5, 129.3, 128.4, 110.0, 90.9, 79.2, 76.3, 72.8, 72.7, 28.4, 26.4, 22.8×2, 17.0; HRMS (ESI-TOF) *m/z* 325.1469 (325.1474 calcd. for C₁₇H₂₅O₄S, [M+H]⁺).

2,6-Dimethylphenyl 2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl-1-thio- β -L-fucopyranoside (**7**)



To a solution of **S5** (0.268 g, 0.829 mmol) in DMF (6.70 mL) was added 55% NaH (0.133 g, dispersion in paraffin liquid, 3.31 mmol) at 0 °C. The mixture was stirred for 5 min at room temperature. And then BnBr (0.394 mL, 3.31 mmol) was added to the reaction mixture at 0 °C. After the reaction mixture was stirred at 50 °C for 3 h, the reaction mixture was poured into water at 0 °C. The resultant mixture was extracted with a mixed solvent of hexane/AcOEt (1/1, v/v, 10 mL×3), and the extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*.

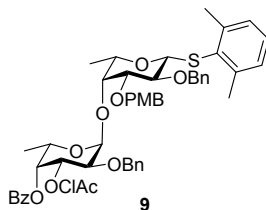
To the above residue was added 80% AcOH aq. (17.0 mL) and then the reaction mixture was stirred at 40 °C for 18 h. After cooling to room temperature, the reaction mixture was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (1/2 *n*-hexane/EtOAc) to give the crude **S7** (0.267 g).

To a solution of the crude **S7** (0.267 g) in MeOH (30.0 mL) was added Bu₂SnO (195 mg, 0.783 mmol) at room temperature, and then the reaction mixture was refluxed. After being stirred for 2 h, the reaction mixture was concentrated in *vacuo*.

To a solution of the above residue in DMF (5.30 mL) were added PMBCl (0.145 mL, 0.802 mmol) and CsF (119 mg, 0.783 mmol) at room temperature, and then the reaction mixture was stirred for 17.5 h at 70 °C. After cooling to room temperature, the reaction mixture was poured into water at room temperature. The resultant mixture was extracted with a mixed solvent of hexane/AcOEt (1/1, v/v, 10 mL×3), and then the extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (1/1 *n*-hexane/EtOAc) to give **7** (0.300 g, 0.606 mmol, 73% yield in 4 steps). White solid; *R*_f 0.69 (1/1 *n*-hexane/EtOAc); m.p. 102-103 °C; [α]_D²⁷ -65.9° (*c* 1.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.45-7.08 (10H, m, Ar-H), 7.85 (2H, m, Ar-H), 5.02 and 4.70 (2H, ABq, *J* = 11.2 Hz, ArCH₂), 4.63 (2H, s, ArCH₂), 4.27 (1H, d, *J*_{1,2} = 10.0 Hz, H-1), 3.80 (3H, s, OMe), 3.73 (1H, m, H-4), 3.65 (1H, dd, *J*_{1,2} = 10.0 Hz, *J*_{2,3} = 8.9 Hz, H-2), 3.48 (1H, dd, *J*_{2,3} = 8.9 Hz, *J*_{3,4} = 3.5 Hz, H-3), 3.32 (1H, q, *J*_{5,6} = 6.6 Hz, H-5), 2.57 (6H, s, SPhMe₂), 2.55 (1H, d, *J* = 2.6 Hz, OH), 1.24 (3H, d, *J*_{5,6} = 6.6 Hz, H-6); ¹³C-NMR (125 MHz, CDCl₃) δ 159.5, 144.5, 138.5, 132.4, 130.0, 129.7, 129.0, 128.4, 128.4, 128.1, 127.8, 114.0×2, 90.4, 82.9, 78.1, 76.2, 73.8, 72.0, 69.5, 55.4, 22.8×2, 16.7; HRMS (ESI-TOF) *m/z* 495.2185 (495.2205 calcd. for C₂₉H₃₅O₅S, [M+H]⁺).

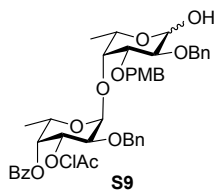
2,6-Dimethylphenyl 4'-O-benzoyl-2'-O-benzyl-3'-O-chloroacetyl- α -L-fucopyranosyl-

(1'→4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl-1-thio-β-*L*-fucopyranoside (9)



To a solution of **8**²⁾ (121 mg, 0.209 mmol) and **7** (51.2 mg, 0.104 mmol) in Et₂O (3.60 mL) was added MS 5A (121 mg, 100 wt% to **8**) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was cooled to −60 °C, and then Yb(OTf)₃ (53.1 mg, 85.6 μmol) was added to the reaction mixture. After the reaction mixture was stirred for 4 h at the same temperature, the reaction was quenched with triethylamine (0.100 mL, 0.717 mmol). The resultant mixture was filtered through Celite. And then, water was added to the filtrate. The resultant mixture was extracted with EtOAc (10 mL×3), and then the extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (2/1 *n*-hexane/EtOAc) to give **9** (94.0 mg, 0.103 mmol, 99% yield). White foam; *R*_f 0.61 (2/1 *n*-hexane/EtOAc); [α]_D²⁷ −119.9° (*c* 3.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 8.04 (2H, m, Ar-H), 7.63-7.08 (18H, m, Ar-H), 6.80 (2H, m, Ar-H), 5.62 (1H, dd, *J*_{2',3'} = 10.6 Hz, *J*_{3',4'} = 3.1 Hz, H-3'), 5.55 (1H, br-d, *J*_{3',4'} = 2.3 Hz, H-4'), 5.10 (1H, d, *J*_{1',2'} = 3.5 Hz, H-1'), 5.04 and 4.94 (2H, ABq, *J* = 10.6 Hz, ArCH₂), 4.81-4.66 (5H, m, ArCH₂×2, H-5), 4.29 (1H, d, *J*_{1,2} = 9.8 Hz, H-1), 4.09 (1H, dd, *J*_{1',2'} = 3.5 Hz, *J*_{2',3'} = 10.6 Hz, H-2'), 3.91 and 3.88 (2H, ABq, *J* = 14.9 Hz, ClAc), 3.77 (5H, m, H-2, 4, OMe), 3.40 (1H, dd, *J*_{2,3} = 9.5 Hz, *J*_{3,4} = 2.9 Hz, H-3), 3.28 (1H, br-q, *J*_{5',6'} = 6.6 Hz, H-5'), 2.56 (6H, s, SPhMe₂), 1.25 (3H, d, *J*_{5',6'} = 6.6 Hz, H-6'), 0.93 (3H, d, *J*_{5,6} = 6.6 Hz, H-6); ¹³C-NMR (125 MHz, CDCl₃) δ 166.8, 166.4, 159.2, 144.7, 138.6, 138.2, 133.5, 132.6, 130.5, 129.9, 129.7, 129.2, 128.8, 128.7, 128.5, 128.5, 128.4, 128.0, 128.0, 127.8, 127.7, 113.8×2, 99.9, 90.3, 82.3, 78.2, 78.0, 75.7, 74.4, 73.6, 72.8, 72.7, 74.5, 72.4, 65.2, 55.4, 40.9, 22.9×2, 17.1, 16.0; HRMS (ESI-TOF) *m/z* 911.3189 (911.3232 calcd. for C₅₁H₅₆O₁₁SCl, [M+H]⁺).

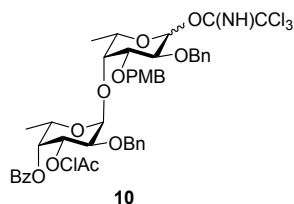
4'-*O*-Benzoyl-2'-*O*-benzyl-3'-*O*-chloroacetyl-α-*L*-fucopyranosyl-(1'→4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl-*L*-fucopyranose (S9)



To a solution of **9** (94.8 mg, 0.104 mmol) in MeCN (2.06 mL) and H₂O (18.6 μL) were added

NIS (46.4 mg, 0.206 mmol) and Sc(OTf)₃ (5.10 mg, 10.3 μmol) at −40 °C. After being stirred for 2 h, the reaction mixture was stirred for 1 h at −20 °C. And then, the reaction mixture was poured into a solution of saturated aq. NaHCO₃ (50 mL) and saturated aq. Na₂S₂O₃ (50 mL) at 0 °C. The resultant mixture was extracted with EtOAc (100 mL×3), and then the extracts were washed with brine (100 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (1/1 *n*-hexane/EtOAc) to give **S9** (66.9 mg, 84.5 μmol, 82% yield, α/β = 1/1). White foam; *R*_f 0.36 (1/1 *n*-hexane/EtOAc); ¹H-NMR (500 MHz, CDCl₃) δ 8.02-7.99 (2H, m, Ar-H), 7.64-7.26 (15H, m, Ar-H), 6.86-6.81 (2H, m, Ar-H), 5.54-5.45 (2H, m), 5.32 (1/2H, dd, *J* = 2.0 Hz, *J* = 3.5 Hz), 5.01 (1/2H, d, *J* = 3.7 Hz), 4.97 (1/2H, ABq, *J* = 11.2 Hz), 4.87 (1/2H, ABq, *J* = 11.2 Hz), 4.96 (1/2H, d, *J* = 3.5 Hz), 4.82 and 4.76 (1H, ABq, *J* = 11.5 Hz, ArCH₂), 4.71-4.57 (11/2H, m), 4.10-4.01 (2H, m), 3.95-3.85 (3H, m), 3.78 (3H, s, OMe), 3.74 (1/2H, d, *J* = 2.9 Hz), 3.63 (1/2H, dd, *J* = 7.5 Hz, *J* = 9.8 Hz), 3.55 (1/2H, q, *J* = 6.3 Hz), 3.42 (1/2H, dd, *J* = 9.8 Hz, *J* = 2.9 Hz), 1.37 (3H, d, *J* = 6.6 Hz), 1.32 (3H, d, *J* = 6.6 Hz), 0.91 (3H, d, *J* = 6.6 Hz), 0.87 (3H, d, *J* = 6.6 Hz); ¹³C-NMR (125 MHz, CDCl₃) δ 166.6, 166.4, 159.3, 138.0, 137.7, 133.5, 130.7, 129.9, 129.7, 129.3, 128.7, 128.6, 128.5, 128.5, 128.2, 128.1, 113.9, 100.0, 99.8, 98.0, 91.7, 80.1, 79.7, 79.1, 78.0, 76.2, 75.9, 74.8, 73.8, 73.4, 72.9, 72.8, 72.7, 72.4, 71.3, 67.1, 65.2, 55.4, 40.8, 31.7, 17.0, 16.6, 15.9, 14.3; HRMS (ESI-TOF) *m/z* 813.2639 (813.2654 calcd. for C₄₃H₄₇O₁₂NaCl, [M+Na]⁺).

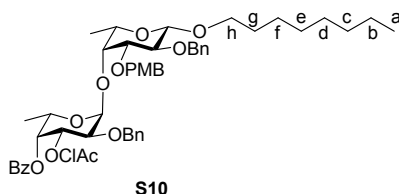
4'-*O*-Benzoyl-2'-*O*-benzyl-3'-*O*-chloroacetyl-α-L-fucopyranosyl-(1'→4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl-L-fucopyranosyl trichloroacetimidate (10**)**



To a solution of **S9** (0.120 g, 0.152 mmol) in CH₂Cl₂ (1.80 mL) were added CCl₃CN (45.7 μL, 0.456 mmol) and DBU (6.80 μL, 45.5 μmol) at room temperature. After being stirred for 15 h, the reaction mixture was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (2/1 *n*-hexane/EtOAc, 1% NEt₃) to give **10** (0.108 g, 0.116 mmol, 76% yield, α/β = 6/1). White foam; *R*_f 0.57, 0.27 (2/1 *n*-hexane/EtOAc, 1% NEt₃); ¹H-NMR (500 MHz, CDCl₃) δ 8.61 (1/7H, s, OC(NH)CCl₃), 8.51 (6/7H, s, OC(NH)CCl₃), 8.01 (2H, m, Ar-H), 7.64-7.22 (15H, m, Ar-H), 6.80 (2H, m, Ar-H), 6.60 (6/7H, d, *J* = 3.2 Hz, Ar-H), 5.72 (1/7H, d, *J* = 7.7 Hz), 5.60-5.48 (2H, m), 4.08 (1/7H, br-q, *J* = 6.6 Hz), 5.00-4.58 (54/7H, m), 4.13 (6/7H, dd, *J* = 3.2, 10.3 Hz), 4.05 (12/7H, m), 3.95-3.85 (18/7H, m), 3.83 (6/7H, br-d, *J* = 2.6 Hz), 3.79 (3H, s), 3.66 (1/7H, br-q, *J* = 6.3 Hz), 3.52 (1/7H, dd, *J* = 2.6, 10.1 Hz), 1.39 (3/7H, d, *J* = 6.6

Hz), 1.32 (18/7H, d, $J = 6.6$ Hz), 0.92 (3/7H, d, $J = 6.3$ Hz), 0.92 (18/7H, d, $J = 6.6$ Hz); ^{13}C -NMR (125 MHz, CDCl_3) α isomer : δ 166.6, 166.3, 161.2, 159.2, 138.3, 137.6, 133.5, 130.5, 129.9, 129.7, 129.6, 128.6, 128.6, 128.5, 128.4, 128.1, 127.9, 127.7, 113.7, 99.8, 95.1, 91.6, 78.8, 75.1, 75.0, 73.9, 73.1, 72.9, 72.8, 72.6, 72.3, 69.9, 65.2, 55.3, 40.8, 16.5, 15.9; LRMS (ESI-TOF) m/z 934.18 (934.19 calcd. for $\text{C}_{45}\text{H}_{48}\text{NO}_{12}\text{Cl}_4$, $[\text{M}+\text{H}]^+$).

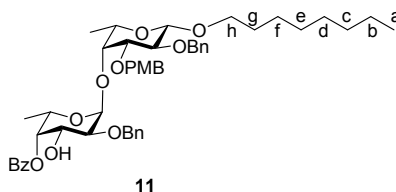
Octyl 4'-O-benzoyl-2'-O-benzyl-3'-O-chloroacetyl- α -L-fucopyranosyl-(1'→4)-2-O-benzyl-3-O-(*p*-methoxy)benzyl- β -L-fucopyranoside (S10)



To a solution of **10** (0.831 g, 0.888 mmol) in CH_2Cl_2 (12.5 mL) were added octanol (0.418 mL, 2.66 mmol) and MS 5A (0.831 g, 100 wt% to **10**) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was cooled to -40 °C, and then $\text{Yb}(\text{OTf})_3$ (0.220 g, 0.355 mmol) was added to the reaction mixture. After the reaction mixture was stirred for 4.5 h at the same temperature, the reaction was quenched with triethylamine (1.00 mL, 7.17 mmol). The resultant mixture was filtered through Celite. And then, water was added to the filtrate. The resultant mixture was extracted with CDCl_3 (20 mL $\times$ 3), and then the extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 , and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (12/1 PhMe/EtOAc) to give **S10** (0.714 mg, 0.790 mmol, 89% yield). Yellow syrup; R_f 0.48 (12/1 PhMe/EtOAc); $[\alpha]_D^{27} -153.0^\circ$ (c 0.12, CHCl_3); ^1H -NMR (500 MHz, CDCl_3) δ 8.02 (2H, m, Ar-H), 7.60-7.25 (15H, m, Ar-H), 6.81 (2H, m, Ar-H), 5.54 (1H, dd, $J_{2',3'} = 10.9$ Hz, $J_{3',4'} = 3.2$ Hz, H-3'), 5.48 (1H, br-d, $J_{3',4'} = 3.2$ Hz, H-4'), 5.03 (1H, d, $J_{1',2'} = 3.8$ Hz, H-1'), 4.97 and 4.80 (2H, ABq, $J = 11.2$ Hz, ArCH_2), 4.73 and 4.61 (2H, ABq, $J = 10.9$ Hz, ArCH_2), 4.67 (2H, s, ArCH_2), 4.59 (1H, br-q, $J_{5,6} = 6.6$ Hz, H-5), 4.29 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 4.04 (1H, dd, $J_{1',2'} = 3.8$ Hz, $J_{2',3'} = 10.9$ Hz, H-2'), 3.95-3.86 (3H, m, ClAc, H-h), 3.79 (3H, s, OMe), 3.68-3.65 (2H, m, H-2, 4), 3.49-3.42 (2H, m, H-5', h), 3.37 (1H, dd, $J_{2,3} = 9.8$ Hz, $J_{3,4} = 2.9$ Hz, H-3), 1.68-1.63 (2H, m, H-g), 1.48-1.20 (13H, m, H-6', b, c, d, e, f), 0.90-0.86 (6H, m, H-6, a); ^{13}C -NMR (125 MHz, CDCl_3) δ 166.6, 166.4, 159.2, 138.8, 138.0, 133.4, 130.8, 129.9, 129.3, 128.6, 128.4, 127.9, 127.7, 113.8, 104.2, 100.1, 79.9, 78.8, 78.6, 74.9, 73.3, 73.1, 72.9, 72.7, 72.4, 70.7, 70.1, 65.2, 55.4, 40.8, 32.0, 29.9, 29.6, 29.4, 26.4, 22.8, 16.8, 16.0, 14.3; HRMS (ESI-TOF) m/z 903.4084 (903.4086 calcd. for $\text{C}_{51}\text{H}_{64}\text{O}_{12}\text{Cl}$, $[\text{M}+\text{H}]^+$).

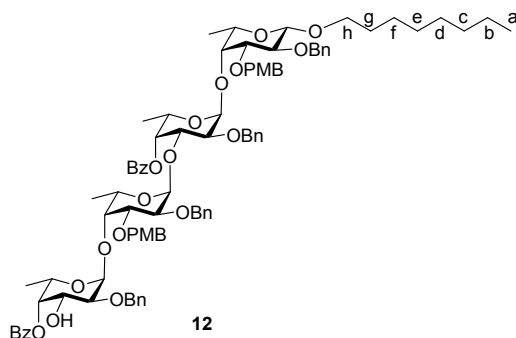
Octyl 4'-O-benzoyl-2'-O-benzyl- α -L-fucopyranosyl-(1'→4)-2-O-benzyl-3-O-

(*p*-methoxy)benzyl- β -L-fucopyranoside (11)



To a solution of **S10** (0.697 g, 0.772 mmol) in DMF (20.9 mL) were added 2,6-lutidine (0.358 mL, 3.09 mmol) and thiourea (0.235 g, 3.09 mmol) at room temperature, and then the reaction mixture was stirred for 16.5 h at 70 °C. After cooling to room temperature, the reaction mixture was poured into water at room temperature. The resultant mixture was extracted with a mixed solvent of hexane/AcOEt (1/1, v/v, 20 mL×3), and then the extracts were washed with brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (6/1 PhMe/EtOAc) to give **11** (0.600 mg, 0.726 mmol, 94% yield) as a single isomer. White foam; *R*_f 0.49 (6/1 PhMe/EtOAc); [α]_D²⁷ -73.3° (*c* 3.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 8.02 (2H, m, Ar-H), 7.60-7.25 (15H, m, Ar-H), 6.81 (2H, m, Ar-H), 5.40 (1H, dd, *J*_{3',4'} = 3.2 Hz, *J*_{4',5'} = 1.2 Hz, H-4'), 5.03 (1H, d, *J*_{1',2'} = 3.4 Hz, H-1'), 4.93 and 4.79 (2H, ABq, *J* = 10.9 Hz, ArCH₂), 4.77 (1H, ABq, *J* = 12.9 Hz, ArCH₂), 4.68 (3H, m, ArCH₂×2), 4.55 (1H, dq, *J*_{4,5} = 0.9 Hz, *J*_{5,6} = 6.6 Hz, H-5), 4.39 (1H, ddd, *J*_{2',3'} = 10.1 Hz, *J*_{3',4'} = 3.2 Hz, *J*_{3',OH} = 3.2 Hz, H-3'), 4.30 (1H, d, *J*_{1,2} = 7.8 Hz, H-1), 3.97-3.92 (1H, m, H-h), 3.88 (1H, dd, *J*_{1',2'} = 3.4 Hz, *J*_{2',3'} = 10.1 Hz, H-2'), 3.78 (3H, s, OMe), 3.70 (1H, d, *J*_{3,4} = 2.9 Hz, H-4), 3.61 (1H, dd, *J*_{1,2} = 7.8 Hz, *J*_{2,3} = 10.0 Hz, H-2), 3.51-3.43 (2H, m, H-5', h), 3.38 (1H, dd, *J*_{2,3} = 10.0 Hz, *J*_{3,4} = 2.9 Hz, H-3), 2.21 (1H, d, *J*_{3',OH} = 3.2 Hz, C_{3'}-OH), 1.72-1.59 (2H, m, H-g), 1.45-1.20 (13H, m, H-6', b, c, d, e, f), 0.92 (3H, d, *J*_{5,6} = 6.6 Hz, H-6), 0.88 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, CDCl₃) δ 166.6, 159.0, 138.7, 138.0, 133.0, 130.6, 130.0, 129.8, 129.1, 128.3, 128.3, 128.2, 127.8, 127.5, 113.6×2, 103.9, 99.5, 79.9, 78.4, 78.1, 76.5, 74.7, 74.6, 72.5, 72.5, 70.5, 69.9, 67.8, 65.6, 55.2, 31.8, 29.8, 29.4, 29.2, 26.2, 22.6, 16.8, 16.1, 14.1; HRMS (ESI-TOF) *m/z* 827.4396 (827.4370 calcd. for C₄₉H₆₃O₁₁, [M+H]⁺).

Octyl 4'''-*O*-benzoyl-2'''-*O*-benzyl- α -L-fucopyranosyl-(1'''→4'')-2''-*O*-benzyl-3''-*O*-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1''→3')-4'-*O*-benzoyl-2'-*O*-benzyl- α -L-fucopyranosyl-(1'→4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl- β -L-fucopyranoside (12)



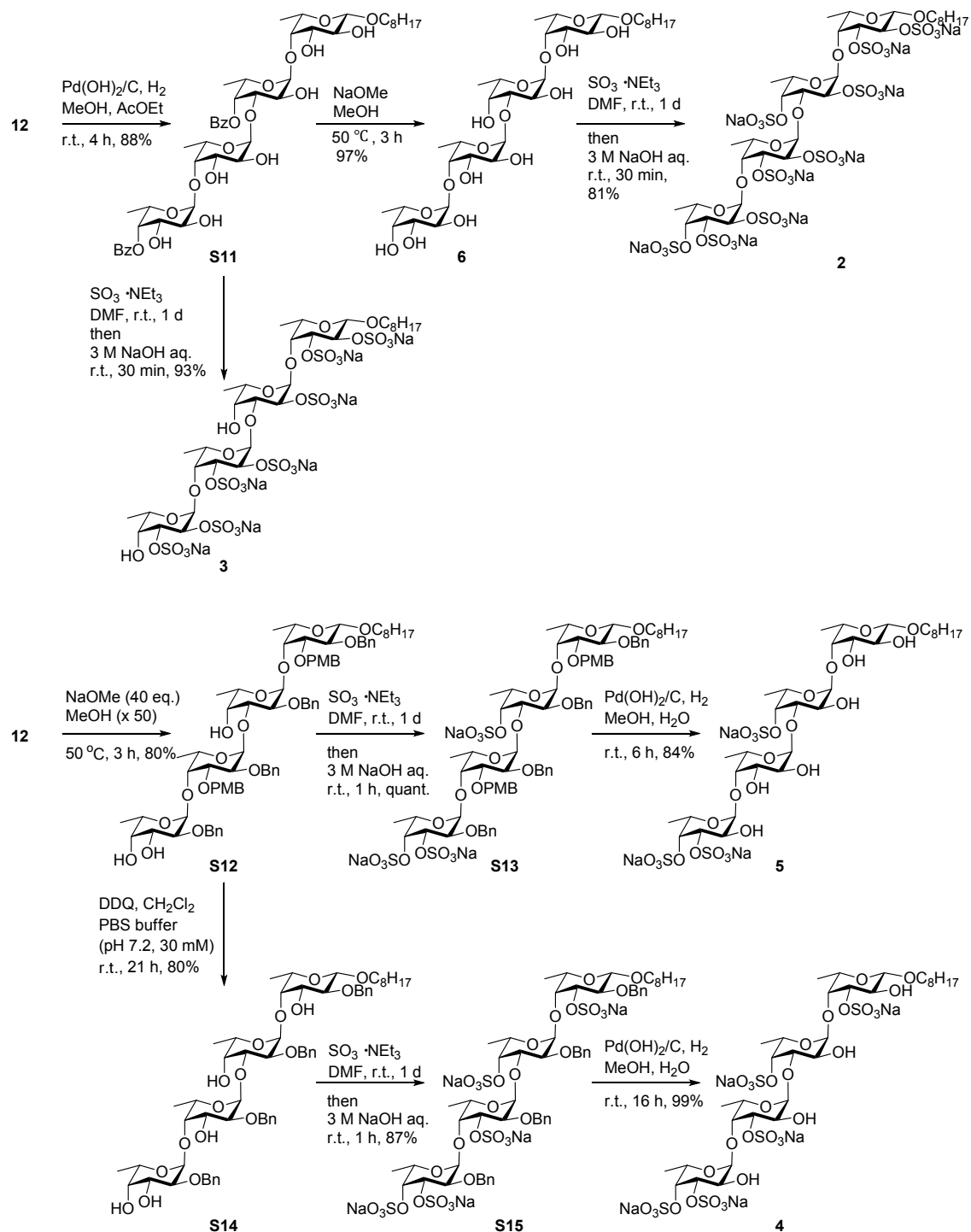
To a solution of **10** (1.15 g, 1.23 mmol) and **11** (0.500 g, 0.605 mmol) in Et₂O (17.0 mL) was added MS 5A (1.15 g, 100 wt% to **10**) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was cooled to $-80\text{ }^{\circ}\text{C}$, and then TMSOTf (11.7 μL , 64.6 μmol) was added to the reaction mixture. After the reaction mixture was stirred for 3.5 h at the same temperature, the reaction was quenched with triethylamine (1.00 mL, 7.17 mmol). The resultant mixture was filtered through Celite. And then, water was added to the filtrate. The resultant mixture was extracted with AcOEt (20 mL $\times$ 3), and then the extracts were washed with brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was passed through silica gel column chromatography (6/1 PhMe/EtOAc) to give the crude product.

To a solution of the above crude product in DMF (29.0 mL) were added 2,6-lutidine (0.280 mL, 2.42 mmol) and thiourea (0.184 g, 2.42 mmol) at room temperature, and then the reaction mixture was stirred for 16 h at $70\text{ }^{\circ}\text{C}$. After cooling to room temperature, the reaction mixture was poured into water at room temperature. The resultant mixture was extracted with a mixed solvent of hexane/AcOEt (1/1, v/v, 30 mL $\times$ 3), and then the extracts were washed with brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (10/1 PhMe/acetone) to give **12** (0.746 g, 0.490 mmol, 81% yield in 2 steps). White foam; R_f 0.42 (10/1 PhMe/acetone); $[\alpha]_D^{27} -152.0^{\circ}$ (c 0.56, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.98 (4H, m, Ar-H), 7.56-7.15 (30H, m, Ar-H), 6.80 (2H, m, Ar-H), 6.65 (2H, m, Ar-H), 5.57 (1H, br-d, $J_{3',4'} = 1.7\text{ Hz}$, H-4'), 5.39 (1H, d, $J_{1'',2''} = 3.5\text{ Hz}$, H-1''), 5.32 (1H, br-d, $J_{3'',4''} = 2.3\text{ Hz}$, H-4''), 4.99 (1H, dd, $J_{1'',2''} = 3.2\text{ Hz}$, H-1''), 4.95 (1H, d, $J_{1',2'} = 3.5\text{ Hz}$, H-1'), 4.91 (2H, ABq, $J = 10.9\text{ Hz}$, ArCH₂), 4.79-4.73 (2H, m, ArCH₂), 4.65 (2H, s, ArCH₂), 4.61 (1H, ABq, $J = 11.8\text{ Hz}$, ArCH₂), 4.56-4.41 (9H, m, H-5 or H-5' or H-5'' or H-5''' $\times$ 2, H-3', ArCH₂ $\times$ 3), 4.30 (1H, d, $J_{1,2} = 7.8\text{ Hz}$, H-1), 4.19 (1H, ddd, $J_{2'',3''} = 10.1\text{ Hz}$, $J_{3'',4''} = 3.2\text{ Hz}$, $J_{3'',\text{OH}} = 3.2\text{ Hz}$, H-3''), 4.55 (1H, br-q, $J = 6.6\text{ Hz}$, H-5 or 5' or 5'' or 5'''), 3.98-3.91 (2H, m, H-2', h), 3.86 (1H, dd, $J_{1'',2''} = 3.5\text{ Hz}$, $J_{2'',3''} = 10.1\text{ Hz}$, H-2''), 3.81 (1H, dd, $J_{1',2'} = 3.2\text{ Hz}$, $J_{2',3'} = 10.3\text{ Hz}$, H-2'), 3.77-3.73 (4H, m, H-3'', OMe), 3.67 (1H, br-d, $J_{3,4} = 3.0\text{ Hz}$, H-4), 3.63-3.57 (5H, m, H-2, 4'', OMe), 3.50 (1H, m, H-h), 3.43 (1H, br-q, $J = 6.3\text{ Hz}$, H-5 or 5' or 5'' or 5'''), 3.36 (1H, dd, $J_{2',3'} = 10.0\text{ Hz}$, $J_{3',4'} = 2.6\text{ Hz}$, H-3'), 2.09 (1H, d,

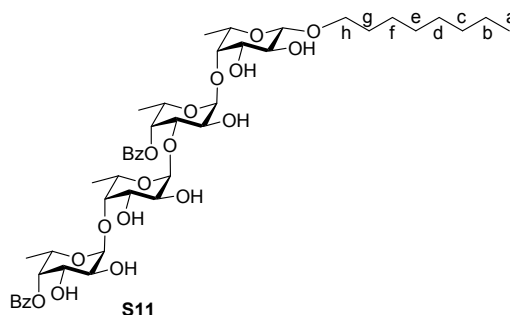
$J_{3''',OH} = 3.2$ Hz, $C_{3'''}-OH$), 1.70-1.59 (2H, m, H-g), 1.45-1.20 (16H, m, H-6 or 6' or 6'' or 6''' $\times$ 2, H-b, c, d, e, f), 0.90-0.82 (9H, m, H-6 or 6' or 6'' or 6''' $\times$ 2, H-a); ^{13}C -NMR (125 MHz, $CDCl_3$) δ 166.7, 166.4, 159.2, 159.0, 138.8, 138.7, 138.5, 137.8, 133.1 $\times$ 2, 133.1 $\times$ 2, 130.9, 130.8, 130.1, 130.1, 130.0, 129.2, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.1, 128.1, 128.0, 127.7, 127.7, 127.3, 113.8, 113.7, 104.0, 99.9, 99.1, 92.0, 80.1, 79.1, 78.8, 77.6, 76.5, 75.7, 75.0, 74.5, 74.4, 74.1, 73.4, 73.1, 72.6, 72.1, 71.5, 70.7, 70.5, 70.0, 69.9, 67.9, 66.7, 65.9, 65.6, 55.4, 55.1, 32.0, 30.0, 29.6, 29.5, 26.3, 22.8, 17.0, 16.3 $\times$ 2, 16.1, 14.3; HRMS (ESI-TOF) m/z 1523.7236 (1523.7305 calcd. for $C_{90}H_{107}O_{21}$, $[M+H]^+$).

Synthesis of the oligofucosides 2-6.

Scheme S2. Synthetic scheme of the oligofucosides 2-6

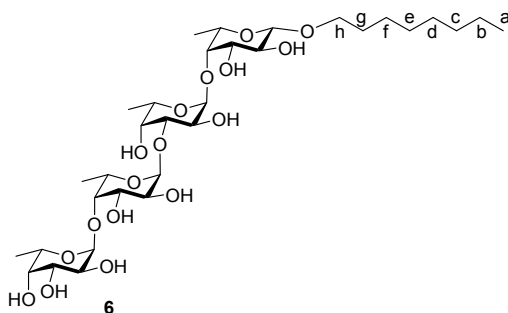


Octyl 4'''-O-benzyl- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-4'-O-benzyl- α -L-fucopyranosyl-(1' $\rightarrow$ 4)- β -L-fucopyranoside (S11)



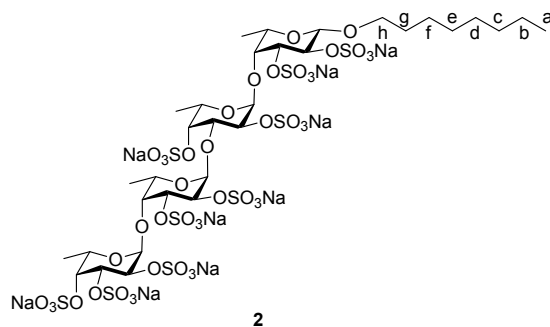
To a solution of **12** (20.4 mg, 13.4 μ mol) in MeOH/AcOEt (4.00 mL, 1/1) was added Pd(OH)₂/C (20.4 mg, 100 wt% to **12**) under H₂ atmosphere at room temperature. After being stirred for 4 h, the reaction mixture was filtered through Celite, and then filtrate was concentrated in *vacuo*. The residue was subjected to reverse phase silica gel column chromatography (8/1 CHCl₃/MeOH) to give **S11** (11.0 mg, 11.9 μ mol, 88% yield). White solid; *R_f* 0.45 (8/1 CHCl₃/MeOH); m.p. 126-127 °C; [α]_D²⁷ -154.2° (*c* 0.62, MeOH); ¹H-NMR (500 MHz, CD₃OD) δ 8.02 (4H, m, Ar-H), 7.57 (2H, m, Ar-H), 7.45 (4H, m, Ar-H), 5.55 (1H, br-d, *J* = 2.9 Hz, H-4' or 4'''), 5.37 (1H, br-d, *J* = 3.5 Hz, H-4' or 4'''), 5.12 (1H, d, *J*_{1'',2''} = 3.9 Hz, H-1''), 4.99 (1H, d, *J* = 3.7 Hz, H-1' or 1'''), 4.93 (1H, d, *J* = 4.2 Hz, H-1' or 1'''), 4.88-4.73 (2H, m, H-5 or 5' or 5'' or 5''' $\times$ 2), 4.26-4.19 (2H, m, H-1, H-5 or 5' or 5'' or 5'''), 4.15 (1H, dd, *J* = 3.2, 10.3 Hz, H-3' or 3'''), 4.06 (1H, dd, *J* = 3.5, 10.6 Hz, H-3' or 3'''), 3.95 (1H, dd, *J* = 3.7, 10.6 Hz, H-2' or 2'''), 3.90-3.83 (2H, m, H-4'', H-h), 3.80-3.67 (5H, m, H-2'', H-2' or 2''', H-3'', 4, H-5 or 5' or 5'' or 5'''), 3.59-3.52 (2H, m, H-3, h), 3.45 (1H, dd, *J*_{1,2} = 7.5 Hz, *J*_{2,3} = 10.0 Hz, H-2), 1.65-1.59 (2H, m, H-g), 1.40-1.20 (16H, m, H-6 or 6' or 6'' or 6''' $\times$ 2, H-b, c, d, e, f), 1.08 (3H, d, *J* = 6.6 Hz, H-6 or 6' or 6'' or 6'''), 1.01 (3H, d, *J* = 6.6 Hz, H-6 or 6' or 6'' or 6'''), 0.87 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, CDCl₃) δ 167.9, 167.0, 133.9, 133.4, 130.1, 130.0, 129.9, 129.5, 128.8, 128.6, 103.5, 101.3, 101.0, 100.8, 80.2, 79.7, 79.5, 74.4, 73.8, 73.5, 72.0, 71.2, 70.8, 70.5, 70.3, 69.6, 69.5, 68.8, 68.0, 66.4, 66.1, 32.0, 29.6, 29.6, 29.4, 26.0, 22.8, 17.0, 16.7, 16.3, 16.2, 14.2; HRMS (ESI-TOF) *m/z* 945.4093 (945.4096 calcd. for C₄₆H₆₆O₁₉Na, [M+Na]⁺).

Octyl α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')- α -L-fucopyranosyl-(1' $\rightarrow$ 4)- β -L-fucopyranoside (6)



To a solution of **S11** (20.2 mg, 21.9 μmol) in MeOH (1.01 mL) was added 28% NaOMe in MeOH (12.8 μL , 87.6 μmol), and then the resultant mixture was stirred at 50 $^{\circ}\text{C}$ for 3 h. After cooling to room temperature, the reaction was quenched with Amberlite[®] IR 120 H⁺ form. The resultant suspension was filtered, the filtrate was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (3/1 CHCl₃/MeOH) to give **6** (15.2 mg, 21.3 μmol , 97% yield). White solid; *R_f* 0.16 (3/1 CHCl₃/MeOH); m.p. 132-133 $^{\circ}\text{C}$; $[\alpha]_D^{27} -179.6^{\circ}$ (*c* 1.0, MeOH); ¹H-NMR (500 MHz, CD₃OD) δ 5.01 (1H, d, *J* = 4.1 Hz, H-1' or 1'' or 1'''), 4.95-4.85 (2H, m, H-1' or 1'' or 1''' $\times$ 2), 4.62-4.49 (2H, m, H-5 or 5' or 5'' or 5''' $\times$ 2), 4.40 (1H, br-q, *J* = 6.6 Hz, H-5 or 5' or 5'' or 5'''), 4.25 (1H, d, *J*_{1,2} = 7.8 Hz, H-1), 3.94 (1H, dd, *J* = 2.9, 10.3 Hz, H-3' or 3'' or 3'''), 3.90-3.68 (11H, m, H-2', 2'', 2''', H-3' or 3'' or 3''' $\times$ 2, H-4, 4', 4'', 4''', H-5 or 5' or 5'' or 5''' $\times$ 2, h), 3.57 (2H, m, H-3, h), 3.43 (1H, dd, *J*_{1,2} = 7.8 Hz, *J*_{2,3} = 10.1 Hz, H-2), 1.70-1.61 (2H, m, H-g), 1.44-1.24 (16H, m, H-6 or 6' or 6'' or 6''' $\times$ 2, H-b, c, d, e, f), 1.20 (6H, m, H-6 or 6' or 6'' or 6''' $\times$ 2), 0.90 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, CD₃OD) δ 105.1, 102.7, 102.6, 98.1, 82.5, 80.5, 78.0, 74.4, 73.8, 72.4, 72.3, 71.5, 71.4, 71.0, 70.6, 70.4, 70.3, 69.2, 68.8, 68.2, 67.4, 33.0, 30.9, 30.6, 30.4, 27.1, 23.7, 16.8, 16.7, 16.5 $\times$ 2, 14.4; HRMS (ESI-TOF) *m/z* 737.3550 (737.3572 calcd. for C₃₂H₅₈O₁₇Na, [M+Na]⁺).

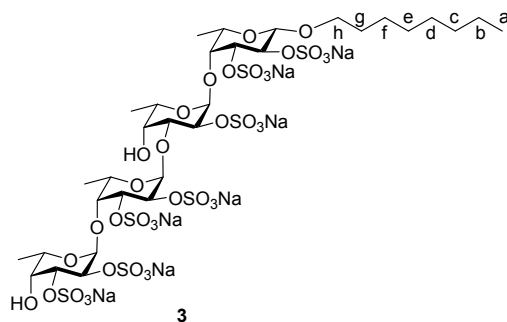
Octyl 2''',3''',4'''-tri-*O*-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2'',3''-di-*O*-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2',4'-di-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2,3-di-*O*-sulfo- β -L-fucopyranoside (2**)**



To a solution of **6** (6.20 mg, 8.67 μmol) in DMF (0.310 mL) was added SO₃•NEt₃ (212 mg, 1.17 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq.

(0.850 mL, 2.55 mmol) was added to the reaction mixture and the mixture was stirred for 30 min. And then, the resultant mixture was subjected to reverse phase silica gel column chromatography (100/0 to 0/50 H₂O/MeOH) and gel filtration chromatography to give **2** (11.5 mg, 7.04 μ mol, 81% yield). White solid; *R_f* 0.25 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; [α]_D²⁷ -41.9° (*c* 0.26, H₂O); ¹H-NMR (500 MHz, D₂O) δ 5.31 (1H, d, *J* = 3.5 Hz, H-1' or 1'' or 1'''), 5.27 (1H, d, *J* = 3.5 Hz, H-1' or 1'' or 1'''), 5.19 (1H, d, *J* = 3.7 Hz, H-1' or 1'' or 1'''), 4.88-4.85 (2H, m, H-4' or 4'' or 4''' $\times$ 2), 4.80-4.61 (2H, m, H-3' or 3'' or 3''' $\times$ 2), 4.56 (1H, dd, *J* = 3.5 Hz, *J* = 10.9 Hz, H-2' or 2'' or 2'''), 4.50-4.35 (6H, m, H-2' or 2'' or 2''' $\times$ 2, H-2, 3, H-5 or 5' or 5'' or 5''' $\times$ 2), 4.34-4.22 (3H, m, H-1, H-3' or 3'' or 3''', H-5 or 5' or 5'' or 5''' $\times$ 2), 4.19-4.13 (2H, m, H-4, H-4' or 4'' or 4'''), 3.78-3.66 (2H, m, H-5 or 5' or 5'' or 5''' $\times$ 2, h), 3.53 (1H, m, H-h), 1.52-1.43 (2H, m, H-g), 1.32-1.10 (22H, m, H-6, 6', 6'', 6''', b, c, d, e, f), 0.72 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, D₂O, acetone-*d*₆) δ 101.4, 99.0, 98.9, 96.9, 80.3, 80.2, 80.1, 79.2, 78.3, 76.2, 74.4, 73.8, 73.0, 72.8, 72.6, 71.2, 70.7, 68.3, 67.9, 67.3, 31.5, 29.1, 28.9, 28.8, 25.3, 22.4, 16.4 $\times$ 2, 16.2, 16.0, 13.8; HRMS (ESI-TOF) *m/z* 1654.8116 (1654.8060 calcd. for C₃₂H₄₉O₄₄Na₁₀S₉, [M+Na]⁺).

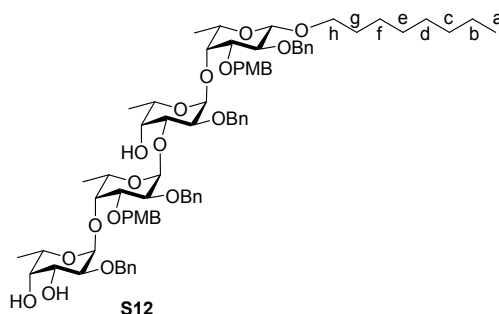
Octyl 2''',3'''-di-*O*-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2'',3''-di-*O*-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2'-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2,3-di-*O*-sulfo- β -L-fucopyranoside (3**)**



To a solution of **S14** (18.0 mg, 19.5 μ mol) in DMF (0.900 mL) was added SO₃•NEt₃ (371 mg, 2.05 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq. (0.680 mL, 2.05 mmol) was added to the reaction mixture and the mixture was stirred for 30 min. And then, the resultant mixture was subjected to reverse phase silica gel column chromatography (100/0 to 0/50 H₂O/MeOH) and gel filtration chromatography to give **3** (25.9 mg, 18.1 μ mol, 93% yield). White solid; *R_f* 0.34 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; [α]_D²⁷ -32.5° (*c* 0.30, H₂O); ¹H-NMR (500 MHz, D₂O) δ 5.28 (1H, d, *J* = 3.7 Hz, H-1'' or 1'''), 5.18 (2H, m, H-1', H-1'' or 1'''), 4.62 (2H, m, H-3'', 3'''), 4.54 (1H, dd, *J* = 4.0, 10.9 Hz, H-2'' or 2'''), 4.50-4.40 (4H, m, H-2', H-2'' or 2''', H-3, H-5 or 5' or 5'' or 5'''), 4.35 (1H, br-q, *J* = 6.3 Hz, H-5 or 5' or 5'' or 5'''), 4.28-4.21 (3H, m, H-1, 2, H-5 or 5' or 5'' or 5'''), 4.15-

4.06 (4H, m, H-3', 4, 4'', 4'''), 3.99 (1H, br-d, $J_{3,4'} = 2.6$ Hz, H-4'), 3.74 (2H, m, H-5 or 5' or 5'' or 5''', H-h), 3.52 (1H, m, H-h), 1.54-1.43 (2H, m, H-g), 1.30-1.10 (22H, m, H-6, 6', 6'', 6''', b, c, d, e, f), 0.72 (3H, t, $J = 6.9$ Hz, H-a); ^{13}C -NMR (125 MHz, D_2O , acetone- d_6) δ 101.4, 99.1, 98.9, 95.3, 80.0, 78.8, 78.1, 76.2, 75.3, 74.2, 74.0, 73.0, 72.8, 71.2, 71.2, 70.8, 69.9, 68.1, 67.4 $\times$ 3, 31.5, 29.4, 29.1, 28.8, 25.3, 22.4, 16.3, 15.9, 15.7, 15.6, 13.8; HRMS (ESI-TOF) m/z 1428.9403 (1428.9465 calcd. for $\text{C}_{32}\text{H}_{52}\text{O}_{38}\text{Na}_7\text{S}_7$, $[\text{M}+\text{H}]^+$).

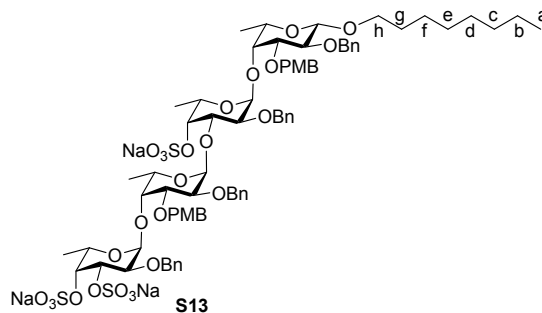
Octyl 2'''-O-benzyl- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2''-O-benzyl-3''-O-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2'-O-benzyl- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-O-benzyl-3-O-(*p*-methoxy)benzyl- β -L-fucopyranoside (S12)



To a solution of **12** (70.9 mg, 47.0 μmol) in MeOH (3.50 mL) was added 28% NaOMe in MeOH (27.5 μL , 188 μmol), and then the resultant mixture was stirred at 50 $^\circ\text{C}$ for 3 h. After cooling to room temperature, the reaction was quenched with Amberlite[®] IR 120 H^+ form. The resultant suspension was filtered, the filtrate was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (4/1 PhMe/acetone) to give **S12** (49.1 mg, 37.4 μmol , 80% yield). White foam; R_f 0.32 (4/1 PhMe/acetone); $[\alpha]^{27}_{\text{D}} -130.2^\circ$ (c 0.43, CHCl_3); ^1H -NMR (500 MHz, CDCl_3) δ 7.39-7.21 (24H, m, Ar-H), 6.85-6.80 (4H, m, Ar-H), 4.96-4.83 (5H, m, H-1, 1', 1'', Ar CH_2), 4.77-4.45 (10H, m, Ar $\text{CH}_2\times$ 5), 4.40 (1H, br-q, $J = 6.1$ Hz, H-5 or 5' or 5'' or 5'''), 4.31 (1H, br-q, $J = 6.3$ Hz, H-5 or 5' or 5'' or 5'''), 4.27 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 4.13 (1H, dd, $J = 3.2$ Hz, $J = 10.1$ Hz, H-3' or 3''), 3.99 (1H, m, H-3'''), 3.95-3.75 (12H, m, H-2', 2'', 4, OMe $\times$ 2, H-h, H-3' or 3'', H-5 or 5' or 5'' or 5'''), 3.70 (1H, dd, $J_{1'',2''} = 3.5$ Hz, $J_{2'',3''} = 10.1$ Hz, H-2'''), 3.68 (1H, m, H-4' or 4''), 3.66 (1H, d, $J_{3,4} = 2.9$ Hz, H-4), 3.62 (1H, br-s, H-4'''), 3.59 (1H, dd, $J_{1,2} = 7.8$ Hz, $J_{2,3} = 10.0$ Hz, H-2), 3.48 (1H, m, H-h), 3.40 (1H, br-q, $J = 6.6$ Hz, H-5 or 5' or 5'' or 5'''), 3.34 (1H, dd, $J_{2,3} = 10.0$ Hz, $J_{3,4} = 2.9$ Hz, H-3), 1.70-1.60 (2H, m, H-g), 1.45-1.20 (13H, m, H-6 or 6' or 6'' or 6''', H-b, c, d, e, f), 1.13-1.07 (9H, m, H-6 or 6' or 6'' or 6''' $\times$ 3), 0.90 (3H, t, $J = 6.9$ Hz, H-a); ^{13}C -NMR (125 MHz, CDCl_3) δ 159.2, 159.1, 139.0, 138.7, 137.9, 137.7, 133.5, 130.9, 130.6, 130.2, 129.3, 129.2, 128.8, 128.6, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 127.8, 127.6, 127.4, 113.9 $\times$ 2, 113.7 $\times$ 2, 104.1, 100.0, 98.8, 94.4, 80.2, 78.7 $\times$ 2, 77.8, 75.3, 75.0, 74.8, 74.6, 74.2, 73.2, 72.7, 72.4, 71.9, 70.8, 70.2, 69.0,

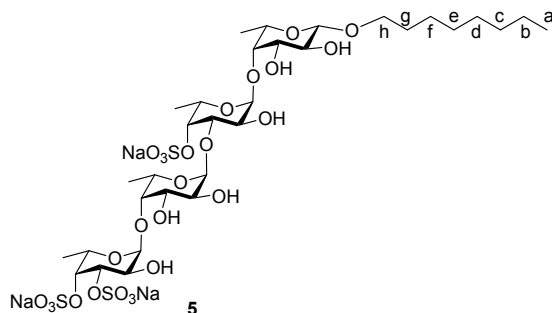
68.6, 67.5, 66.2, 65.6, 55.4, 55.3, 32.0, 29.9, 29.6, 29.4, 26.3, 22.8, 16.9, 16.5, 16.3, 16.2, 14.2; HRMS (ESI-TOF) m/z 1315.6774 (1315.6781 calcd. for $C_{76}H_{99}O_{19}$, $[M+H]^+$).

Octyl 2'''-*O*-benzyl-3''',4'''-di-*O*-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2''-*O*-benzyl-3''-*O*-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2'-*O*-benzyl-3',4'-di-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl- β -L-fucopyranoside (S13)



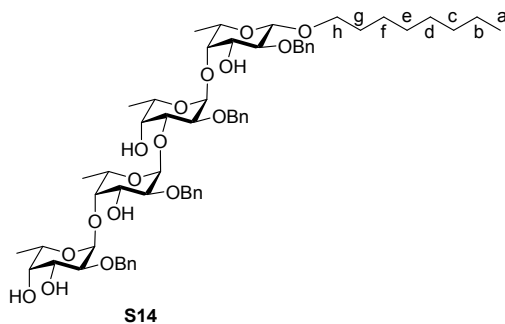
To a solution of **S12** (48.0 mg, 36.5 μ mol) in DMF (2.40 mL) was added $SO_3 \cdot NEt_3$ (280 mg, 1.54 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq. (1.40 mL, 4.20 mmol) was added to the reaction mixture and the mixture was stirred for 1 h. And then, the resultant mixture was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 $H_2O/MeOH$) to give **S13** (59.0 mg, 36.4 μ mol, quant.). White solid; R_f 0.10 (3/1 $CHCl_3/MeOH$); m.p. 148-149 $^{\circ}C$; $[\alpha]^{27}_D -83.4^{\circ}$ (c 0.78, MeOH); 1H -NMR (500 MHz, CD_3OD) δ 7.42-7.06 (24H, m, Ar-H), 6.72 (2H, m, Ar-H), 6.62 (2H, m, Ar-H), 5.41 (1H, d, $J_{1'',2''} = 3.2$ Hz, H-1''), 4.91-4.85 (2H, m, $ArCH_2$), 4.82 (1H, d, $J_{1''',2'''} = 3.4$ Hz, H-1'''), 4.80-4.68 (3H, m, H-1', 3'', 4'''), 4.64 (1H, br-d, $J_{3',4'} = 1.7$ Hz, H-4'), 4.60-4.45 (8H, m, $ArCH_2 \times 4$), 4.37 and 4.33 (2H, ABq, $J = 11.2$ Hz, $ArCH_2$), 4.25-4.17 (4H, m, H-1, 3', H-5 or 5' or 5'' or 5''' $\times 2$), 4.05 (1H, br-q, $J = 6.6$ Hz, H-5 or 5' or 5'' or 5'''), 3.85 (1H, dd, $J_{1'',2''} = 2.9$ Hz, $J_{2'',3''} = 10.2$ Hz, H-2''), 3.82-3.74 (4H, m, H-2', 2''', 3'', h), 3.66 (4H, m, H-4, OMe), 3.55 (4H, m, H-4'', OMe), 3.46 (1H, dd, $J_{1,2} = 7.8$ Hz, $J_{2,3} = 10.0$ Hz, H-2), 3.42-3.36 (2H, m, H-5 or 5' or 5'' or 5''', H-h), 3.30 (1H, dd, $J_{2,3} = 10.0$ Hz, $J_{3,4} = 4.1$ Hz, H-3), 1.55-1.46 (2H, m, H-g), 1.35-1.10 (16H, m, H-6 or 6' or 6'' or 6''' $\times 2$, H-b, c, d, e, f), 0.97 (3H, d, $J = 6.3$ Hz, H-6 or 6' or 6'' or 6'''), 0.85-0.74 (6H, m, H-6 or 6' or 6'' or 6''', H-a); ^{13}C -NMR (125 MHz, CD_3OD) δ 160.6, 160.3, 140.5, 140.4, 140.3, 140.1, 132.7, 132.1, 130.3, 130.1, 129.9, 129.5 $\times 2$, 129.3 $\times 2$, 129.2 $\times 2$, 129.1, 128.9, 128.6, 128.3 $\times 2$, 128.2, 114.6 $\times 2$, 114.5 $\times 2$, 105.0, 101.3, 100.6, 95.0, 81.7, 80.4, 80.2, 80.1, 78.4, 78.1, 77.5, 76.6, 76.5, 76.2, 76.0, 74.8, 74.5, 73.6, 73.3, 73.3, 72.2, 72.1, 70.6, 68.6, 68.2, 67.4, 55.7, 55.5, 33.0, 31.1, 30.8, 30.6, 30.5, 27.4, 23.8, 17.7, 17.5, 17.4, 17.3, 14.5; HRMS (ESI-TOF) m/z 1621.5000 (1621.4943 calcd. for $C_{76}H_{96}O_{28}Na_3S_3$, $[M+H]^+$).

Octyl 3''',4'''-di-*O*-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-4'-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)- β -L-fucopyranoside (5**)**



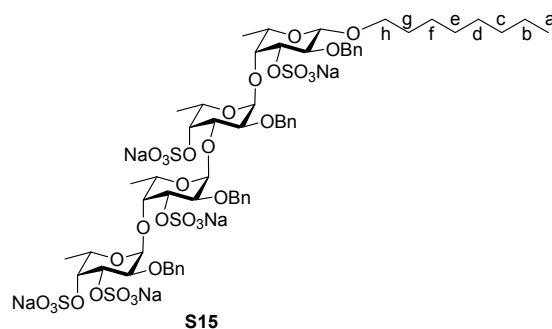
To a solution of **S13** (50.5 mg, 31.1 μ mol) in MeOH/H₂O (10.0 mL, 1/1) was added Pd(OH)₂/C (50.5 mg, 100 wt% to **S13**) under H₂ atmosphere at room temperature. After being stirred for 6 h, the reaction mixture was filtered through Celite, and then filtrate was concentrated in *vacuo*. The residue was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 H₂O/MeOH) to give **5** (26.7 mg, 26.2 μ mol, 84% yield). White solid; *R_f* 0.32 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; [α]_D²⁷ -113.4° (*c* 0.10, H₂O); ¹H-NMR (500 MHz, D₂O) δ 5.02 (1H, d, *J*_{1'',2''} = 4.0 Hz, H-1''), 4/93 (1H, d, *J*_{1''',2'''} = 4.0 Hz, H-1'''), 4.88 (1H, d, *J*_{1',2'} = 4.3 Hz, H-1'), 4.79 (1H, d, *J*_{3''',4'''} = 2.9 Hz, H-4'''), 4.67 (1H, m, H-4'), 4.60 (1H, br-q, *J*_{5''',6'''} = 6.3 Hz, H-5'''), 4.58-4.51 (2H, m, H-3''', 5'), 4.30 (1H, d, *J*_{1,2} = 8.0 Hz, H-1), 4.25 (1H, br-q, *J*_{5'',6''} = 6.6 Hz, H-5''), 3.93 (1H, dd, *J*_{2',3'} = 10.6 Hz, *J*_{3',4'} = 2.9 Hz, H-3'), 3.90-3.85 (2H, m, H-2''', 3''), 3.81-3.67 (6H, m, H-2', 2'', 4, 4'', 5, h), 3.62 (1H, dd, *J*_{2,3} = 10.3 Hz, *J*_{3,4} = 3.4 Hz, H-3), 3.55 (1H, m, H-h), 3.40 (1H, dd, *J*_{1,2} = 8.0 Hz, *J*_{2,3} = 10.3 Hz, H-2), 1.52-1.47 (2H, m, H-g), 1.30-1.10 (22H, m, H-6, 6', 6'', 6''', b, c, d, e, f), 0.75 (3H, t, *J* = 7.2 Hz, H-a); ¹³C-NMR (125 MHz, D₂O, acetone-*d*₆) δ 102.3, 100.7, 100.3, 99.7, 80.3, 80.3, 79.4, 79.2, 77.2, 75.3, 72.5, 71.0, 70.7, 70.6, 69.5, 68.6, 67.8, 67.8, 67.0, 66.7, 66.4, 31.3, 29.0, 28.6, 28.6, 25.3, 22.2, 15.9, 15.8, 15.5 $\times$ 2, 13.6, 15.3; HRMS (ESI-TOF) *m/z* 1021.1868 (1021.1915 calcd. for C₃₂H₅₆O₂₆Na₃S₃, [M+H]⁺).

Octyl 2'''-*O*-benzyl- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2''-*O*-benzyl- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2'-*O*-benzyl- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-*O*-benzyl- β -L-fucopyranoside (S14**)**



To a solution of **S12** (26.1 mg, 19.8 μmol) in $\text{CH}_2\text{Cl}_2/\text{PBS}$ buffer (pH 7.2, v/v, 30 mM) (3.00 mL, 1/1) was added DDQ (13.4 mg, 59.0 μmol) at room temperature. The mixture was stirred for 21 h at the same temperature. The reaction mixture was quenched with saturated aq. NaHCO_3 (10 mL). The resultant mixture was extracted with CHCl_3 (10 mL $\times$ 3), and then the extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4 , and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (3/1 PhMe/acetone) to give **S14** (17.1 mg, 15.8 μmol , 80% yield). White solid; R_f 0.29 (3/1 PhMe/acetone); m.p. 77-78 $^\circ\text{C}$; $[\alpha]_D^{27} -81.4^\circ$ (c 0.35, CHCl_3); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 7.43-7.23 (20H, m, Ar-H), 4.93 (1H, d, $J = 3.8$ Hz, H-1' or 1'' or 1'''), 4.91-4.87 (3H, m, H-1' or 1'' or 1''', ArCH_2), 4.81 (1H, m, H-1' or 1'' or 1'''), 4.81 and 4.65 (2H, ABq, $J = 11.7$ Hz, ArCH_2), 4.65 and 4.49 (2H, ABq, $J = 12.0$ Hz, ArCH_2), 4.58 (2H, s, ArCH_2), 4.31 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 4.13-3.90 (7H, m, H-3', 3'', 3''', 4, H-5 or 5' or 5'' or 5''' $\times$ 3), 3.85-3.83 (2H, m, H-2' or 2'' or 2''', H-4' or 4'' or 4'''), 3.75 (1H, dd, $J = 3.5$ Hz, $J = 10.0$ Hz, H-2' or 2'' or 2'''), 3.71-3.46 (9H, m, H-2' or 2'' or 2''', H-3, H-4' or 4'' or 4''' $\times$ 2, H-5 or 5' or 5'' or 5''' $\times$ 2, OH $\times$ 2, H-h), 3.36 (1H, s, OH), 3.22 (1H, dd, $J_{1,2} = 7.8$ Hz, $J_{2,3} = 9.5$ Hz, H-2), 2.49 (1H, s, OH), 2.38 (1H, s, OH), 1.73-1.63 (2H, m, H-g), 1.45-1.18 (19H, m, H-6 or 6' or 6'' or 6''' $\times$ 3, H-b, c, d, e, f), 1.08 (3H, d, $J = 6.6$ Hz, H-6 or 6' or 6'' or 6'''), 0.88 (3H, t, $J = 6.9$ Hz, H-a); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 138.8, 138.4, 137.8, 137.6, 128.8, 128.4, 128.4, 128.2, 128.1, 127.7, 127.4, 104.1, 100.3, 99.9, 94.4, 85.1, 84.1, 80.0, 76.8, 76.6, 75.3, 74.8, 74.4, 74.4, 74.1, 73.4, 73.0, 71.4, 70.7 $\times$ 2, 70.5, 68.8, 68.3, 67.2, 67.0, 66.7, 32.0, 29.9, 29.6, 29.4, 26.3, 22.8, 16.8, 16.4, 16.3, 16.2, 14.3; HRMS (ESI-TOF) m/z 1075.5585 (1075.5630 calcd. for $\text{C}_{60}\text{H}_{83}\text{O}_{17}$, $[\text{M}+\text{H}]^+$).

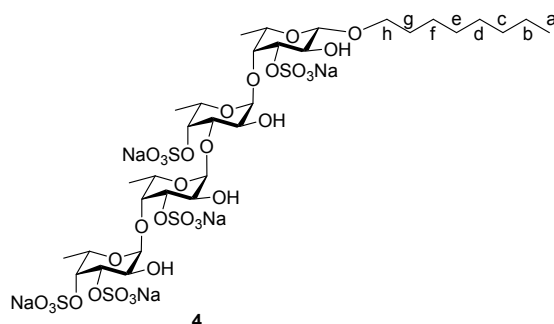
Octyl 2'''-O-benzyl-3''',4'''-di-O-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2''-O-benzyl-3''-O-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-2'-O-benzyl-3',4'-di-O-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-O-benzyl-3-O-sulfo- β -L-fucopyranoside (S15**)**



To a solution of **S14** (17.7 mg, 16.4 μmol) in DMF (0.885 mL) was added $\text{SO}_3\cdot\text{NEt}_3$ (224 mg, 1.23 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq. (0.500 mL, 1.50 mmol) was added to the reaction mixture and the mixture was stirred for 30 min. And then, the resultant mixture was subjected to reverse phase silica gel column

chromatography (100/0 to 0/100 H₂O/MeOH) and gel filtration chromatography to give **S15** (22.7 mg, 14.3 μ mol, 87% yield). White solid; R_f 0.55 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; $[\alpha]_D^{27} -118.0^\circ$ (c 0.31, H₂O); ¹H-NMR (500 MHz, D₂O) δ 7.50-6.90 (20H, m, Ar-H), 5.36 (1H, d, $J_{1'',2''} = 3.4$ Hz, H-1''), 4.80-4.76 (3H, m, H-1', 1''', ArCH₂), 4.73-4.55 (6H, m, H-3'', 4''', ArCH₂), 4.51-4.31 (6H, m, H-1, 3''', 4', ArCH₂), 4.03 (1H, dd, $J_{2,3} = 9.6$ Hz, $J_{3,4} = 2.3$ Hz, H-3), 3.92 (1H, br-q, $J = 6.3$ Hz, H-5 or 5' or 5'' or 5'''), 3.81 (1H, dd, $J_{1'',2''} = 3.4$ Hz, $J_{2'',3''} = 10.9$ Hz, H-2''), 3.79-3.70 (4H, m, H-2', 2''', 4, 4''), 3.66 (1H, dd, $J_{2',3'} = 10.9$ Hz, $J_{3',4'} = 2.9$ Hz, H-3'), 3.61-3.50 (2H, m, H-5 or 5' or 5'' or 5''', H-h), 3.42 (1H, m, H-h), 3.33-3.20 (3H, m, H-2, H-5 or 5' or 5'' or 5''') $\times 2$), 1.47-1.41 (2H, m, H-g), 1.29-0.93 (22H, m, H-6, 6', 6'', 6''', b, c, d, e, f), 0.68 (3H, t, $J = 6.9$ Hz, H-a); ¹³C-NMR (125 MHz, D₂O, acetone-*d*₆) δ 137.9, 137.5, 137.3, 136.3, 130.8, 130.6, 129.5, 128.9, 128.7, 128.6, 128.4, 128.3, 128.2, 103.0, 99.5, 98.8, 91.8, 80.3, 80.0, 78.2, 77.9, 76.9, 75.2, 74.9, 74.8, 73.8, 72.9, 72.4, 70.8, 70.2, 69.9, 69.1, 67.7, 66.6, 66.4, 31.5, 28.9, 25.9, 22.4, 16.4, 16.0 $\times 2$, 15.9, 13.7; HRMS (ESI-TOF) m/z 1585.2606 (1585.2568 calcd. for C₆₀H₇₈O₃₂Na₅S₅, [M+H]⁺).

Octyl 3''',4'''-di-*O*-sulfo- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-3''-*O*-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-4'-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-3-*O*-sulfo- β -L-fucopyranoside (4)

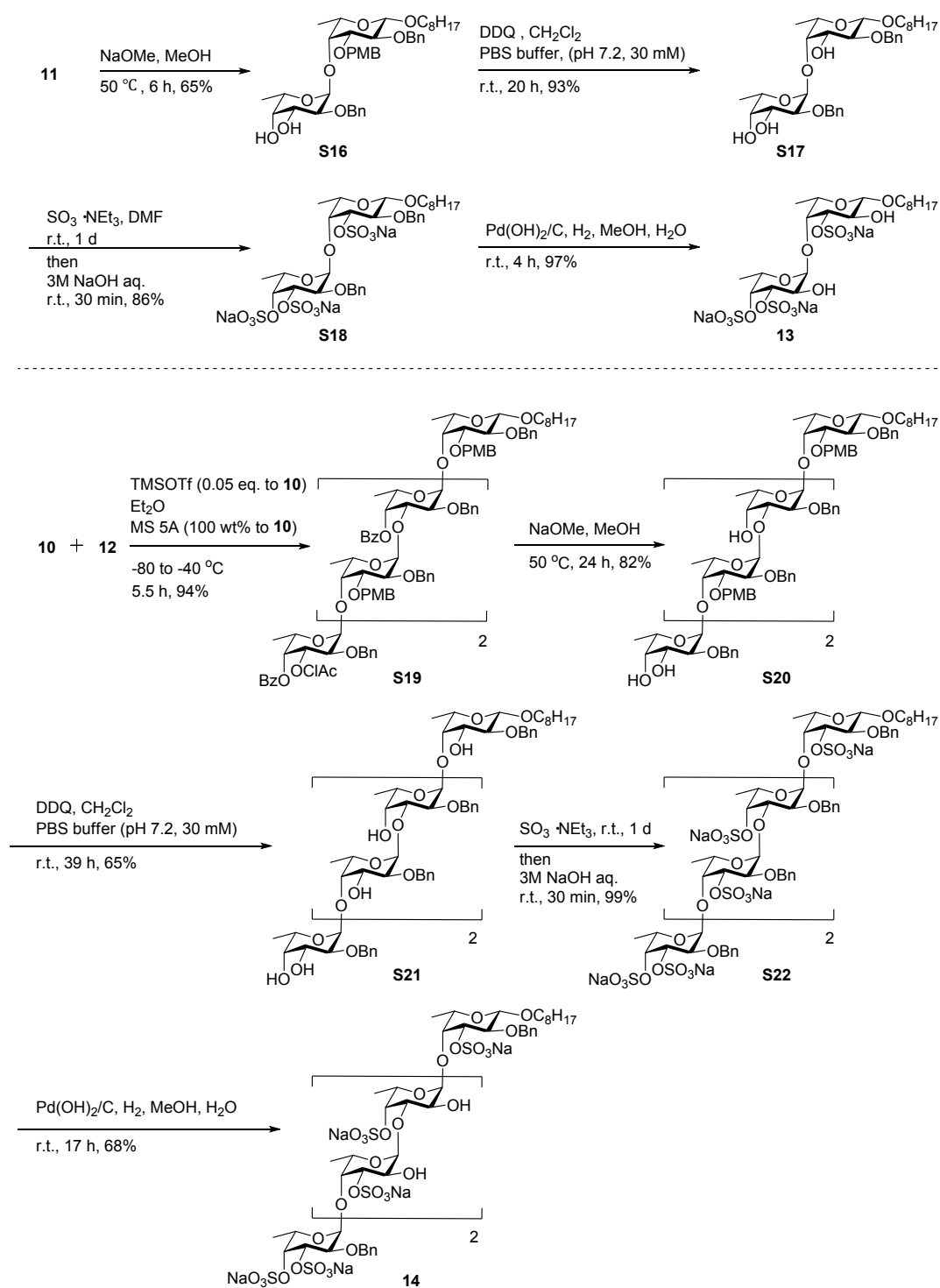


To a solution of **S15** (19.6 mg, 12.4 μ mol) in MeOH/H₂O (7.84 mL, 1/1) was added Pd(OH)₂/C (39.2 mg, 200 wt% to **S15**) under H₂ atmosphere at room temperature. After being stirred for 16 h, the reaction mixture was filtered through Celite, and then filtrate was concentrated in *vacuo*. The residue was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 H₂O/MeOH) to give **4** (15.0 mg, 12.2 μ mol, 99% yield). White solid; R_f 0.54 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; $[\alpha]_D^{27} -135.6^\circ$ (c 0.31, H₂O); ¹H-NMR (500 MHz, D₂O) δ 5.05 (1H, d, $J_{1'',2''} = 4.0$ Hz, H-1''), 4.96 (1H, d, $J_{1''',2'''} = 3.8$ Hz, H-1'''), 4.91 (1H, d, $J_{1',2'} = 4.3$ Hz, H-1'), 4.77 (1H, br-d, $J_{3''',4'''} = 2.9$ Hz, H-4'''), 4.68 (1H, m, H-4'), 4.54-4.46 (3H, m, H-3'', 3''', H-5 or 5' or 5'' or 5'''), 4.44-4.37 (2H, m, H-1, H-5 or 5' or 5'' or 5'''), 4.27 (1H, br-q, $J = 6.9$ Hz, H-5 or 5' or 5'' or 5'''), 4.20 (1H, dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 2.9$ Hz, H-3), 4.08 (1H, br-d, $J_{3'',4''} = 3.2$ Hz, H-4''), 4.02 (1H, br-d, $J_{3,4} = 2.9$ Hz, H-4),

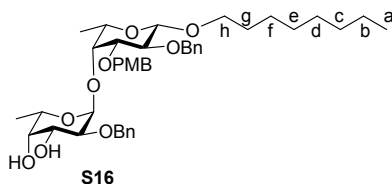
3.95 (1H, dd, $J_{2,3'} = 10.0$ Hz, $J_{3,4'} = 2.3$ Hz, H-3'), 3.90-3.80 (3H, m, H-2', 2'', 2'''), 3.79-3.73 (2H, m, H-5 or 5' or 5'' or 5''', H-h), 3.58-3.49 (2H, m, H-2, h), 1.47-1.45 (2H, m, H-g), 1.25-1.10 (22H, m, H-6, 6', 6'', 6''', b, c, d, e, f), 0.72 (3H, t, $J = 6.9$ Hz, H-a); ^{13}C -NMR (125 MHz, D_2O , acetone- d_6) δ 102.5, 100.5, 100.1, 99.0, 80.1, 79.6, 79.3, 78.0, 76.9, 76.7, 76.3, 75.2, 71.2, 70.8, 69.1, 68.0, 67.5, 67.0, 66.9 $\times$ 2, 66.8, 31.4, 29.1, 28.8, 25.4, 22.4, 16.3, 15.8, 15.6, 13.8; HRMS (ESI-TOF) m/z 589.0416 (589.0408 calcd. for $\text{C}_{32}\text{H}_{53}\text{O}_{32}\text{Na}_3\text{S}_5$, $[\text{M}-2\text{Na}]^{2-}$).

Synthesis of the oligofucosides 13 and 14.

Scheme S3. Synthetic scheme of the oligosaccharides **13** and **14**

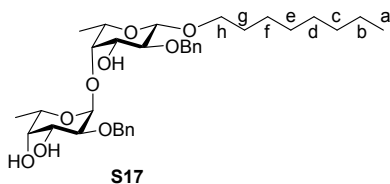


Octyl 2'-*O*-benzyl- α -L-fucopyranosyl-(1'→4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl- β -L-fucopyranoside (S16)



To a solution of **11** (26.0 mg, 31.4 μ mol) in MeOH (2.60 mL) was added 28% NaOMe in MeOH (303 μ L, 2.07 mmol), and then the resultant mixture was stirred at 50 °C for 6 h. After cooling to room temperature, the reaction was quenched with Amberlite® IR 120 H⁺ form. The resultant suspension was filtered, the filtrate was concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (1/1 PhMe/AcOEt) to give **S16** (14.8 mg, 20.5 μ mol, 65% yield). Colorless syrup; R_f 0.50 (1/1 PhMe/EtOAc); $[\alpha]^{23}_D$ -92.4° (*c* 0.41, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.40-7.23 (12H, m, Ar-H), 6.81 (2H, m, Ar-H), 5.03 (1H, d, $J_{1',2'}$ = 3.5 Hz, H-1'), 4.93 (1H, ABq, J = 10.9 Hz, ArCH₂), 4.77-4.73 (2H, m, ArCH₂), 4.69 and 4.64 (2H, ABq, J = 12.3 Hz, ArCH₂), 4.56 (1H, ABq, J = 11.5 Hz, ArCH₂), 4.36 (1H, br-q, $J_{5,6}$ = 6.3 Hz, H-5), 4.29 (1H, d, $J_{1,2}$ = 7.8 Hz, H-1), 4.12 (1H, dd, $J_{1',2'}$ = 3.5 Hz, $J_{2',3'}$ = 10.0 Hz, H-2'), 3.93 (1H, m, H-h), 3.79 (3H, s, OMe), 3.77-3.72 (2H, m, H-3', 4), 3.66 (1H, d, $J_{3',4'}$ = 2.9 Hz, H-4'), 3.58 (1H, dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 3.50-3.41 (2H, m, H-5', h), 3.37 (1H, dd, $J_{2,3}$ = 9.8 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 1.64 (2H, m, H-g), 1.43-1.20 (13H, m, H-6', b, c, d, e, f), 1.08 (3H, d, $J_{5,6}$ = 6.6 Hz, H-6), 0.87 (3H, t, J = 6.6 Hz, H-a); ¹³C-NMR (125 MHz, CDCl₃) δ 159.2, 138.9, 138.1, 130.8, 129.3, 128.7, 128.4, 128.3, 128.3, 128.1, 127.6, 113.8, 104.1, 99.1, 80.3, 78.6, 78.2, 74.9, 72.7, 72.5, 72.1, 70.6, 70.2, 69.0, 66.1, 55.4, 32.0, 29.9, 29.6, 29.4, 26.3, 22.8, 16.9, 16.2, 14.2; HRMS (ESI-TOF) m/z 745.3926 (745.3928 calcd. for C₄₂H₅₈O₁₀Na, [M+Na]⁺).

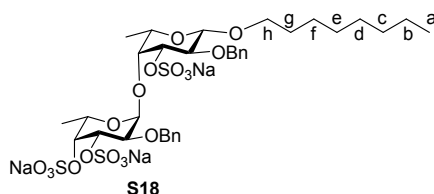
Octyl 2'-*O*-benzyl- α -L-fucopyranosyl-(1'→4)-2-*O*-benzyl- β -L-fucopyranoside (S17)



To a solution of **S16** (14.8 mg, 20.5 μ mol) in CH₂Cl₂/PBS buffer (pH 7.2, v/v, 30 mM) (3.00 mL, 1/1) was added DDQ (21.2 mg, 93.4 μ mol) at room temperature. The mixture was stirred for 20 h at the same temperature. The reaction mixture was quenched with saturated aq. NaHCO₃ (6 mL). The resultant mixture was extracted with CHCl₃ (6 mL×3), and then the extracts were washed with brine (15 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (1/1 PhMe/AcOEt) to give **S17** (11.4 mg, 18.9 μ mol, 93% yield). Colorless syrup; R_f 0.32 (1/1 PhMe/EtOAc); $[\alpha]^{23}_D$

–86.6° (*c* 1.0, CHCl₃); ¹H-NMR (500 MHz, CDCl₃) δ 7.42-7.22 (10H, m, Ar-H), 4.98 (1H, d, *J*_{1',2'} = 3.7 Hz, H-1'), 4.90 and 4.79 (2H, ABq, *J* = 11.5 Hz, ArCH₂), 4.68 and 4.53 (2H, ABq, *J* = 11.8 Hz, ArCH₂), 4.31 (1H, ABq, *J*_{1,2} = 7.5 Hz, H-1), 4.14-4.08 (2H, m, H-4, 5), 3.95 (1H, m, H-h), 3.79-3.73 (3H, m, H-2', 4', OH), 3.49 (1H, m, H-h), 3.25 (1H, dd, *J*_{1,2} = 7.5 Hz, *J*_{2,3} = 9.5 Hz, H-2), 2.47 (1H, s, OH), 2.35 (1H, s, OH), 1.64 (2H, m, H-g), 1.43-1.20 (13H, m, H-6', b, c, d, e, f), 1.17 (3H, d, *J*_{5,6} = 6.6 Hz, H-6), 0.87 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, CDCl₃) δ 138.7, 137.8, 128.8, 128.5, 128.3, 128.3, 128.0, 127.8, 104.1, 99.5, 83.7, 79.5, 74.6, 73.9, 72.9, 71.5, 70.6, 70.5, 68.9, 67.1, 32.0, 29.9, 29.6, 29.4, 26.3, 22.8, 16.7, 16.2, 14.2; HRMS (ESI-TOF) *m/z* 603.3539 (603.3533 calcd. for C₃₄H₅₁O₉, [M+H]⁺).

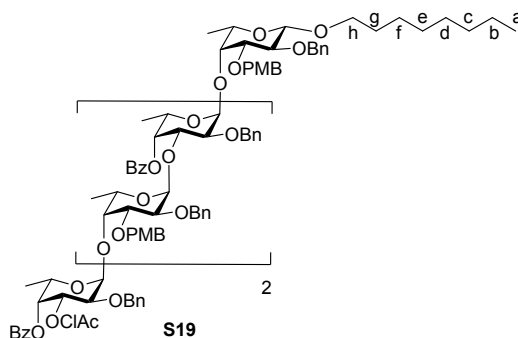
Octyl 2'-*O*-benzyl-3',4'-di-*O*-sulfo-α-L-fucopyranosyl-(1'→4)-2-*O*-benzyl-3-*O*-sulfo-β-L-fucopyranoside (S18)



To a solution of **S17** (11.4 mg, 18.9 μmol) in DMF (0.342 mL) was added SO₃•NEt₃ (103 mg, 0.568 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq. (0.377 mL, 1.13 mmol) was added to the reaction mixture and the mixture was stirred for 30 min. And then, the resultant mixture was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 H₂O/MeOH) and gel filtration chromatography to give **S18** (15.0 mg, 16.5 μmol, 86% yield). White solid; *R_f* 0.55 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; [α]_D²⁶ –75.8° (*c* 1.0, MeOH); ¹H-NMR (500 MHz, CD₃OD) δ 7.57-7.20 (10H, m, Ar-H), 5.21 (1H, d, *J*_{1',2'} = 3.4 Hz, H-1'), 5.02-4.80 (4H, m, H-3', 4', ArCH₂), 4.77-4.71 (2H, m, ArCH₂), 4.45 (1H, br-q, *J*_{5',6'} = 6.3 Hz, H-5'), 4.40-4.36 (2H, m, H-1, 3), 4.21 (1H, d, *J*_{3,4} = 2.6 Hz, H-4), 3.90 (1H, dd, *J*_{1',2'} = 3.4 Hz, *J*_{2',3'} = 10.3 Hz, H-2'), 3.85 (1H, m, H-h), 3.65-3.56 (2H, m, H-2, 5), 3.48 (1H, m, H-h), 1.63-1.54 (2H, m, H-g), 1.37 (3H, d, *J*_{5,6} = 6.3 Hz, H-6), 1.33-1.21 (13H, m, H-6', b, c, d, e, f), 0.89 (3H, t, *J* = 6.9 Hz, H-a); ¹³C-NMR (125 MHz, D₂O, acetone-*d*₆) δ 140.2, 129.4, 129.3, 129.0, 128.3, 104.6, 100.9, 80.8, 80.4, 79.1, 78.2, 76.5, 76.0, 75.7, 74.1, 72.0, 70.9, 67.8, 33.0, 30.9, 30.6, 30.4, 27.3, 23.7, 17.6, 17.3, 14.4; HRMS (ESI-TOF) *m/z* 931.1483 (931.1515 calcd. for C₃₄H₄₇O₁₈Na₄S₃, [M+Na]⁺).

13

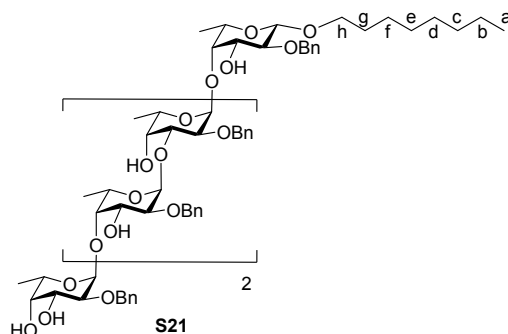
Octyl 4''''-*O*-benzoyl-2''''-*O*-benzyl-3''''-*O*-chloroacetyl- α -L-fucopyranosyl-(1'''' $\rightarrow$ 4''')-2''''-*O*-benzyl-3''''-*O*-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1'''' $\rightarrow$ 3''')-4'''-*O*-benzoyl-2'''-*O*-benzyl- α -L-fucopyranosyl-(1''' $\rightarrow$ 4''')-2''-*O*-benzyl-3''-*O*-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-4'-*O*-benzoyl-2'-*O*-benzyl- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-*O*-benzyl-3-*O*-(*p*-methoxy)benzyl- β -L-fucopyranoside (S19)



S24

added MS 5A (61.6 mg, 100 wt% to **10**) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was cooled to $-80\text{ }^{\circ}\text{C}$, and then TMSOTf (0.700 μL , 3.62 μmol) was added to the reaction mixture. After the reaction mixture was stirred for 5.5 h at the same temperature, the reaction was quenched with triethylamine (0.100 mL, 0.717 mmol). The resultant mixture was filtered through Celite. And then, water was added to the filtrate. The resultant mixture was extracted with AcOEt (5 mL $\times$ 3), and then the extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4 , and concentrated in *vacuo*. The residue was passed through silica gel column chromatography (6/1 PhMe/EtOAc) to give **S19** (78.4 mg, 34.1 μmol , 94% yield). Colorless syrup; R_f 0.42 (10/1 PhMe/acetone); $[\alpha]_D^{24} -145.7^{\circ}$ (c 1.0, CHCl_3); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.01 (2H, m, Ar-H), 7.92 (4H, m, Ar-H), 7.65-7.05 (45H, m, Ar-H), 6.81 (2H, m, Ar-H), 6.60 (4H, m, Ar-H), 5.61 (1H, br-d, $J = 1.8\text{ Hz}$, H-4' or 4'' or 4''' or 4'''' or 4'''''), 5.51 (1H, br-d, $J = 2.3\text{ Hz}$, H-4' or 4'' or 4''' or 4'''' or 4'''''), 5.45-5.43 (4H, m, H-1' or 1'' or 1''' or 1'''' or 1''''') $\times$ 4, 4.97-4.92 (3H, m, H-3' or 3'' or 3''' or 3'''' or 3''''') $\times$ 3, 4.78-4.66 (7H, m), 4.56-4.28 (16H, m), 4.10-3.82 (10H, m), 3.81 (7H, m), 3.65-3.59 (3H, m), 3.55-3.47 (7H, m, OMe $\times$ 2, H-h), 3.44 (1H, br-q, $J = 6.6\text{ Hz}$, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.38 (1H, dd, $J_{2,3} = 10.0\text{ Hz}$, $J_{3,4} = 2.9\text{ Hz}$, H-3), 1.70-1.59 (2H, m, H-g), 1.45-1.20 (19H, m, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''') $\times$ 3, H-b, c, d, e, f), 0.90-0.78 (12H, m, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''') $\times$ 3, H-a); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 166.5, 166.4, 166.4, 166.2, 163.3, 159.2, 158.9, 158.9, 138.9, 138.6, 138.6, 138.5, 138.4, 137.8, 133.4, 133.1, 133.0, 130.8, 130.8, 130.1, 129.9, 129.2, 129.2, 128.8, 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 127.3, 127.2, 113.8 $\times$ 2, 113.6 $\times$ 2, 104.0, 100.1, 100.0 $\times$ 2, 92.0, 91.8, 80.1, 79.3, 79.0, 78.4, 77.8, 76.6, 75.5, 75.4, 75.3, 75.0, 74.9, 73.8, 73.6, 73.3, 73.0, 72.9, 72.6, 72.5, 72.2, 71.9, 71.7, 71.1, 70.7, 70.5, 70.4, 70.0, 69.9, 69.8, 68.1, 66.9, 66.6, 65.9, 65.7, 65.0, 55.4, 55.1, 55.0, 40.8, 32.0, 30.0, 29.6, 29.5, 26.3, 22.8, 17.0, 16.5, 16.4, 16.3, 16.2, 15.9, 14.3; HRMS (ESI-TOF) m/z 2296.0049 (2295.9955 calcd. for $\text{C}_{133}\text{H}_{152}\text{O}_{32}\text{Cl}$, $[\text{M}+\text{H}]^+$).

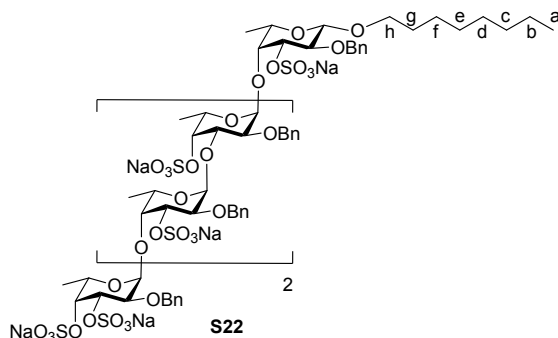
Octyl 2''''''-O-benzyl- α -L-fucopyranosyl-(1'''''' $\rightarrow$ 4''''')-2''''-O-benzyl-3''''-O-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1'''' $\rightarrow$ 3''')-2'''-O-benzyl- α -L-fucopyranosyl-(1''' $\rightarrow$ 4'')-2''-O-benzyl-3''-O-(*p*-methoxy)benzyl- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-2-O-benzyl-3-O-(*p*-methoxy)benzyl- β -L-fucopyranoside (S20)



To a solution of **S20** (21.6 mg, 12.8 μmol) in $\text{CH}_2\text{Cl}_2/\text{PBS}$ buffer (pH 7.2, 30 mM) (4.20 mL, v/v, 1/1) was added DDQ (21.7 mg, 95.7 μmol) at room temperature. The mixture was stirred for 39 h at the same temperature. The reaction mixture was quenched with saturated aq. NaHCO_3 (10 mL). The resultant mixture was extracted with CHCl_3 (15 mL $\times$ 3), and then the extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4 , and concentrated in *vacuo*. The residue was subjected to silica gel column chromatography (3/1 PhMe/AcOEt) to give **S21** (13.0 mg, 8.40 μmol , 65% yield). White solid; R_f 0.21 (1/2 PhMe/AcOEt); m.p. 85-86 $^\circ\text{C}$; $[\alpha]_D^{27} -157.6^\circ$ (c 0.11, CHCl_3); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 7.45-7.20 (30H, m, Ar-H), 4.94-4.88 (5H, m), 4.85-4.78 (4H, m), 4.66-4.61 (3H, m), 4.56 (4H, m), 4.50 (1H, ABq, $J = 11.8$ Hz, ArCH_2), 4.31 (1H, d, $J_{1,2} = 7.5$ Hz, H-1), 4.16-4.01 (8H, m, H-3' or 3'' or 3''' or 3'''' or 3''''' $\times$ 3, H-5 or 5' or 5'' or 5''' or 5'''' or 5''''' $\times$ 5), 3.97-3.92 (4H, m, H-3' or 3'' or 3''' or 3'''' or 3''''' $\times$ 2, H-4, h), 3.85-3.80 (4H, m), 3.76 (1H, dd, $J = 3.4, 10.0$ Hz, H-2' or 2'' or 2''' or 2'''' or 2''''' $\times$ 3), 3.71-3.69 (3H, m, H-4' or 4'' or 4''' or 4'''' or 4''''' $\times$ 3), 3.66-3.46 (10H, m), 3.22 (1H, dd, $J_{1,2} = 7.5$ Hz, $J_{2,3} = 9.5$ Hz, H-2), 2.46 (1H, s, OH), 2.37 (1H, s, OH), 2.04 (1H, s, OH), 1.72-1.61 (2H, m, H-g), 1.40-1.20 (19H, m, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''' $\times$ 3, H-b, c, d, e, f), 1.19 (3H, d, $J = 6.6$ Hz, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''' $\times$ 3), 1.09 (3H, d, $J = 6.6$ Hz, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''' $\times$ 3), 1.06 (3H, d, $J = 6.6$ Hz, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''' $\times$ 3), 0.87 (3H, t, $J = 7.2$ Hz, H-a); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 138.8, 138.4, 138.3, 137.9, 137.9, 137.6, 128.8, 128.8, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 127.8, 127.7, 127.5, 127.5, 104.2, 100.8, 100.4, 99.9, 94.6, 94.4, 85.5, 85.0, 84.1, 80.0, 75.3, 75.1, 74.8, 74.6, 74.5, 74.4, 74.2, 74.1, 73.6, 73.4, 73.0, 71.4, 70.7, 70.7, 70.6, 70.4, 68.8, 68.2, 68.2, 67.2, 67.1, 67.0, 66.9, 66.7, 32.0, 29.9, 29.6, 29.4, 26.3, 22.8; HRMS (ESI-TOF) m/z 1569.7594 (1569.7547 calcd. for $\text{C}_{86}\text{H}_{114}\text{O}_{25}\text{Na}$, $[\text{M}+\text{Na}]^+$).

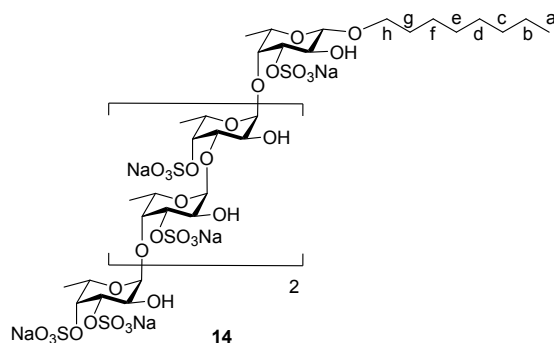
Octyl 2'''''-O-benzyl-3'''''',4'''''-di-O-sulfo- α -L-fucopyranosyl-(1''''' $\rightarrow$ 4''''')-2'''''-O-benzyl-3'''''-O-sulfo- α -L-fucopyranosyl-(1''''' $\rightarrow$ 3''''')-2'''''-O-benzyl-4''''-O-sulfo- α -L-fucopyranosyl-

(1'''→4'')-2''-O-benzyl-3''-O-sulfo- α -L-fucopyranosyl-(1''→3')-2'-O-benzyl-4'-O-sulfo- α -L-fucopyranosyl-(1'→4)-2-O-benzyl-3-O-sulfo- β -L-fucopyranoside (S22)



To a solution of **S21** (13.7 mg, 8.85 μ mol) in DMF (0.665 mL) was added $\text{SO}_3 \cdot \text{NET}_3$ (164 mg, 0.905 mmol) at room temperature. After the reaction mixture was stirred for 1 d, 3 M NaOH aq. (0.450 mL, 1.35 mmol) was added to the reaction mixture and the mixture was stirred for 30 min. And then, the resultant mixture was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 $\text{H}_2\text{O}/\text{MeOH}$) and gel filtration chromatography to give **S22** (20.0 mg, 8.84 μ mol, 99% yield). White solid; R_f 0.54 (10/10/3 $\text{CHCl}_3/\text{MeOH}/\text{H}_2\text{O}$); m.p. >300 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{28} -135.4^\circ$ (c 0.26, H_2O); ^1H -NMR (500 MHz, D_2O) δ 7.49-7.02 (30H, m, Ar-H), 5.34 (1H, d, $J = 3.2$ Hz, H-1' or 1'' or 1''' or 1'''' or 1'''''), 5.22 (1H, d, $J = 3.2$ Hz, H-1' or 1'' or 1''' or 1'''' or 1'''''), 4.90-4.84 (2H, m, H-1' or 1'' or 1''' or 1'''' or 1'''''), 4.80-4.50 (17H, m, H-1' or 1'' or 1''' or 1'''' or 1''''', H-3' or 3'' or 3''' or 3'''' or 3''''') $\times 3$, H-4' or 4'' or 4''' or 4'''' or 4''''', ArCH₂ $\times 6$, 4.48-4.35 (6H, m), 4.11-4.03 (2H, m, H-3, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.80 (1H, br-q, $J = 6.3$ Hz, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.87-3.74 (5H, m), 3.73-3.56 (6H, m), 3.55-3.47 (2H, m, H-4, H-4' or 4'' or 4''' or 4'''' or 4'''''), H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.43 (1H, m, H-h), 3.36 (1H, dd, $J_{1,2} = 7.8$ Hz, $J_{2,3} = 10.6$ Hz, H-2), 3.30 (1H, br-q, $J = 6.3$ Hz, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.21 (1H, br-q, $J = 6.3$ Hz, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 1.42-1.35 (2H, m, H-g), 1.22-1.00 (25H, m, H-6 or 6' or 6'' or 6''' or 6'''' or 6''''') $\times 5$, H-b, c, d, e, f), 0.79 (3H, d, $J = 6.6$ Hz, H-6 or 6' or 6'' or 6''' or 6'''' or 6'''''), 0.68 (3H, t, $J = 7.2$ Hz, H-a); ^{13}C -NMR (125 MHz, D_2O , acetone- d_6) δ 137.9, 137.7, 137.6, 137.3, 137.1, 136.6, 130.7, 130.6, 130.3, 129.4, 129.3, 128.9, 128.7, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 127.9, 102.8, 99.3, 99.1, 98.5, 92.0, 91.6, 80.6, 80.2, 79.9, 78.2, 77.4 $\times 2$, 75.4, 75.2, 75.1, 74.9 $\times 2$, 74.6, 74.2, 73.9, 73.0, 72.3, 72.0, 70.7, 70.3, 70.2, 69.8, 69.1, 68.8, 67.5, 67.0, 66.7, 66.5, 66.3, 31.4, 29.3, 28.7, 25.7, 22.3, 16.4 $\times 2$, 16.3, 16.0, 15.9, 15.4, 13.7; LRMS (ESI-TOF) m/z 2261.37 (2261.34 calcd. for $\text{C}_{86}\text{H}_{108}\text{O}_{46}\text{Na}_7\text{S}_7$, $[\text{M}+\text{H}]^+$).

Octyl 3''''',4'''''-di-*O*-sulfo- α -L-fucopyranosyl-(1'''' $\rightarrow$ 4''''')-3''''-*O*-sulfo- α -L-fucopyranosyl-(1'''' $\rightarrow$ 3'')-4''-*O*-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 4'')-3''-*O*-sulfo- α -L-fucopyranosyl-(1'' $\rightarrow$ 3')-4'-*O*-sulfo- α -L-fucopyranosyl-(1' $\rightarrow$ 4)-3-*O*-sulfo- β -L-fucopyranoside (14**)**



To a solution of **S22** (20.0 mg, 8.84 μ mol) in MeOH/H₂O (8.00 mL, 1/1) was added Pd(OH)₂/C (40.0 mg, 200 wt% to **S22**) under H₂ atmosphere at room temperature. After being stirred for 17 h, the reaction mixture was filtered through Celite, and then filtrate was concentrated in *vacuo*. The residue was subjected to reverse phase silica gel column chromatography (100/0 to 0/100 H₂O/MeOH) to give **14** (10.3 mg, 5.98 μ mol, 68% yield). White solid; *R_f* 0.59 (10/10/3 CHCl₃/MeOH/H₂O); m.p. >300 °C; [α]_D²⁴ -133.2° (*c* 0.33, H₂O); ¹H-NMR (500 MHz, D₂O) δ 5.13 (2H, m, H-1' or 1'' or 1''' or 1'''' or 1''''' $\times$ 2), 5.03 (1H, d, *J* = 4.0 Hz, H-1' or 1'' or 1''' or 1'''' or 1'''''), 5.00 (1H, d, *J* = 4.0 Hz, H-1' or 1'' or 1''' or 1'''' or 1'''''), 4.98 (1H, d, *J* = 4.0 Hz, H-1' or 1'' or 1''' or 1'''' or 1'''''), 4.84 (1H, d, *J* = 2.9 Hz, H-4' or 4'' or 4''' or 4'''' or 4'''''), 4.80-3.60 (5H, m), 4.55 (3H, m, H-3' or 3'' or 3''' or 3'''' or 3''''' $\times$ 2, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 4.50-4.43 (2H, m, H-1, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 4.36 (1H, br-q, *J* = 6.5 Hz, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 4.28 (1H, dd, *J*_{2,3} = 10.3 Hz, *J*_{3,4} = 2.9 Hz, H-3), 4.16 (2H, m, H-4' or 4'' or 4''' or 4'''' or 4''''' $\times$ 2), 4.08 (1H, d, *J*_{3,4} = 2.9 Hz, H-4), 4.06-4.01 (2H, m, H-3' or 3'' or 3''' or 3'''' or 3'''''), H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), 3.98-3.86 (5H, m, H-2', 2'', 2''', 2'''', 2'''''), 3.84-3.78 (2H, m, H-5 or 5' or 5'' or 5''' or 5'''' or 5'''''), H-h), 3.65-3.56 (2H, m, H-2, h), 1.58-1.52 (2H, m, H-g), 1.32-1.20 (28H, m, H-6, 6', 6'', 6''', 6'''', 6''''', b, c, d, e, f), 0.79 (3H, t, *J* = 7.2 Hz, H-a); ¹³C-NMR (125 MHz, D₂O, acetone-*d*₆) δ 102.4, 100.7, 100.5, 100.1, 99.3 $\times$ 2, 80.2, 79.8, 79.4, 78.1, 78.0, 77.1, 76.8, 76.7, 76.6, 76.5, 75.2, 71.2, 70.8, 69.0, 68.7, 68.2, 68.1, 67.6, 67.0 $\times$ 2, 66.9 $\times$ 2, 66.8, 62.7, 31.3, 30.2, 29.1, 28.6 $\times$ 2, 25.4, 22.2, 16.3, 16.2 $\times$ 2, 15.6, 15.5, 15.4, 13.7; HRMS (ESI-TOF) *m/z* 837.0242 (837.0250 calcd. for C₄₄H₇₁O₄₆Na₅S₇, [M-2Na]²⁻).

Materials and methods for biological assay.

Fucoidans isolated from *F. vesiculosus* (ca 600 kDa) and *C. filum* (ca 350 kDa) were purchased from Elicityl (Crolles, France). Antibodies to caspase-8 (1C12) and -9 were purchased from Cell Signaling Technology, Inc. (Beverly, MA). An antibody to α -tubulin (DM1A) and horseradishperoxidase (HRP)-conjugated donkey anti-rabbit IgG (sc-2313) were purchased from Santa Cruz Biotechnology, Inc. (Santa Cruz, CA). HRP-conjugated anti-mouse IgG (NA931A) was purchased from GE healthcare. The caspase inhibitor, Z-VAD-fmk was purchased from Promega Corporation, Madison, WI, USA. Hoechst 33342 was purchased from Dojindo Laboratories. Fetal bovine serum (FBS) was purchased from MP Biomedicals. The human breast cancer MCF-7 was provided by the RIKEN BRC through the National Bio-Resource Project of the MEXT, Japan.

Cell culture.

Human breast cancer MCF-7 and human normal diploid fibroblast WI-38 were grown at 37 °C in 5% CO₂ in air in DMEM medium supplemented with phenol red, L-glutamine (2 mM), penicillin (100 Units/mL), kanamycin (100 µg/mL) and 10% FBS.

MTT assay.

MCF-7 cells or WI-38 cells were seeded at 1.0×10^3 cells/well or 2.5×10^3 cells/well in 96-well in 10% FBS DMEM, respectively. After 24 h, samples were incubated with the indicated concentration of compounds. Cells were then kept for 96 h at 37 °C and in 5% CO₂ in air, and then MTT reagent was added to each well and cells were incubated for up to 3 additional hours at 37 °C. The absorbance at a single wavelength of 540 nm was read on a plate reader SAFIRE (TECAN).

Morphology of nucleus.

MCF-7 cells were cultured on ϕ 18 mm micro cover glass (Matsunami Glass Industrial, Ltd.) in 12-well plate (3.0×10^4 cells/well) in the presence of each compound (1000 µg/mL) or vehicle with or without caspase inhibitor, Z-VAD-fmk (10 µM), for 48 h. And then, the cells were washed three times with PBS and fixed with 4% paraformaldehyde phosphate buffer solution for 15 min at room temperature. After removing paraformaldehyde, cells were washed three times with PBS and blocked with 2% BSA phosphate buffer solution for 30 min at room temperature. After removing BSA, cells were stained with Hoechst 33342 for 10 min. The nucleus morphological changes were observed by inverted fluorescence microscope (EVOS FL

Cell Imaging System; Life Technologies).

Immunoblotting.

MCF-7 cells (4.0×10^5 cells) were plated on 100 mm dishes containing 10% FBS DMEM. After 24 h, samples were incubated with each compound (330 $\mu\text{g/mL}$). The cells were then kept for 1-4 d at 37 °C and in 5% CO₂ in air. After the incubation time, medium was collected and then, adherent cells were scraped with rubber policeman and centrifuged for 5 min at 3000 rpm at 4 °C. The pellet was then resuspended in 100 μL lysis buffer (25 mM Tris-HCl (pH 7.6), 150 mM NaCl, 0.1% SDS, 1% triton X-100, 1 mM EDTA (pH 8.0), 1% sodium deoxycholate) containing protease inhibitor cocktail (NAKARAI TESQUE Inc.) and homogenized with ULTRA SONIC HOMOGENIZER UH-50 (SMT Co., Ltd.). The lysate was centrifuged for 10 min at 14000 rpm at 4 °C. Equal amounts of protein were separated by SDS-PAGE in 10% polyacrylamide gels. Proteins were transferred onto nitrocellulose membranes Hybond™-ECL (GE Healthcare). Membranes were blocked with Tris-buffered saline-0.1% Tween 20 (TBST) containing 5% BSA or 5% nonfat dry milk for 30 min at room temperature and membranes were incubated with appropriately diluted primary antibodies at 4 °C overnight. After washing five times with TBST, the blots were incubated with horseradish peroxidase-conjugated specific secondary antibody for 2 h at 4 °C and then again washed five times. Then the complexes were visualized in Medical Film Processor FPM100 (Fujifilm Co.) using the enhanced chemiluminescence reagents Immobilon™ Western (Millipore Co.). The following primary antibodies were used for detection of the specific bands: caspase-8, caspase-9, and α -tubulin. The following secondary antibodies were used for detection of the specific bands: HRP-conjugated anti-mouse IgG and HRP-conjugated anti-rabbit IgG.

References.

- 1) J. Gildersleeve, R. A. Pascal and D. Kahne, *J. Am. Chem. Soc.*, 1998, **120**, 5961.
- 2) V. B. Krylov, Z. M. Kaskova, D. Z. Vinnitskiy, N. E. Ustyuzhanina, A. A. Grachev, A. O. Chizhov and N. E. Nifantiev, *Carbohydr. Res.*, 2011, **346**, 540.

^1H and ^{13}C NMR spectra

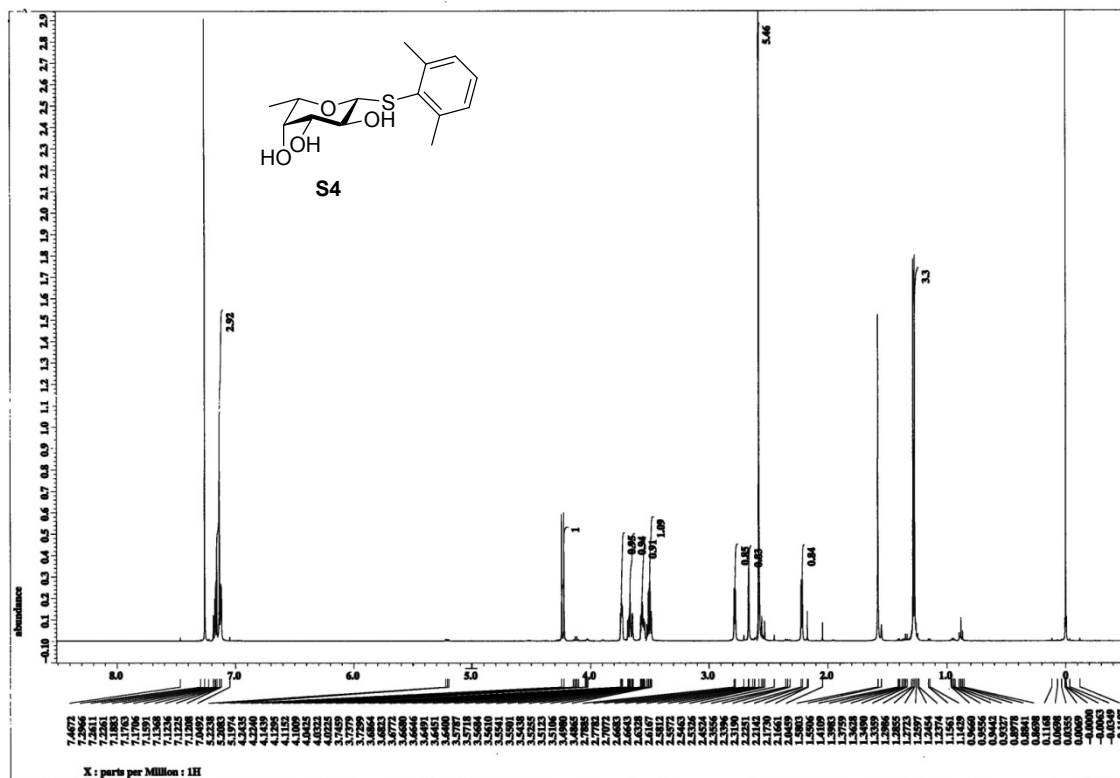


Figure S1 ^1H -NMR spectrum of S4

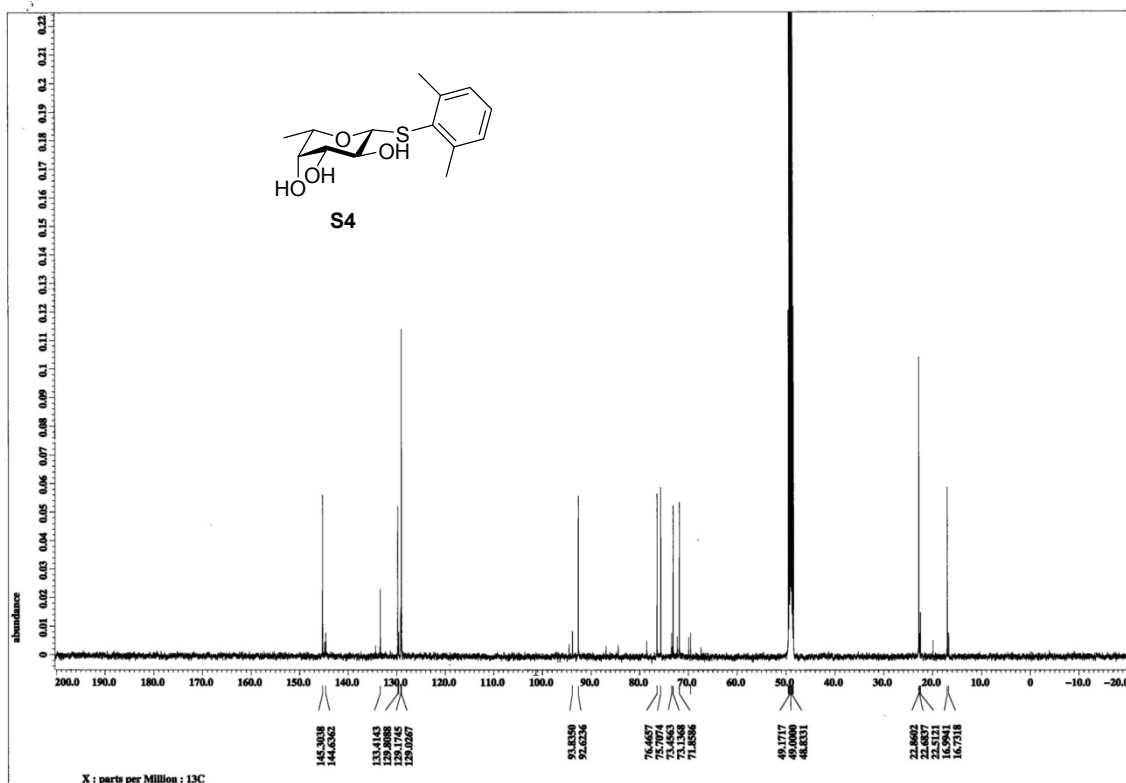


Figure S2 ^{13}C -NMR spectrum of S4

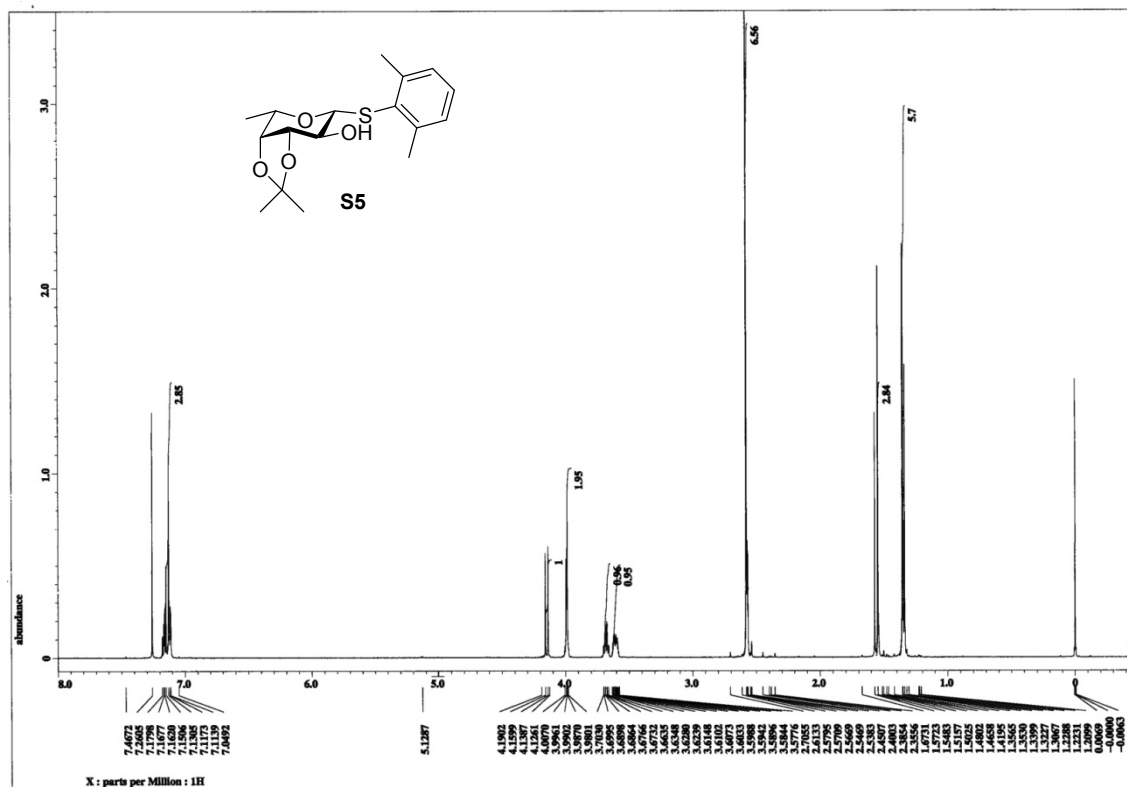


Figure S3 ¹H-NMR spectrum of S5

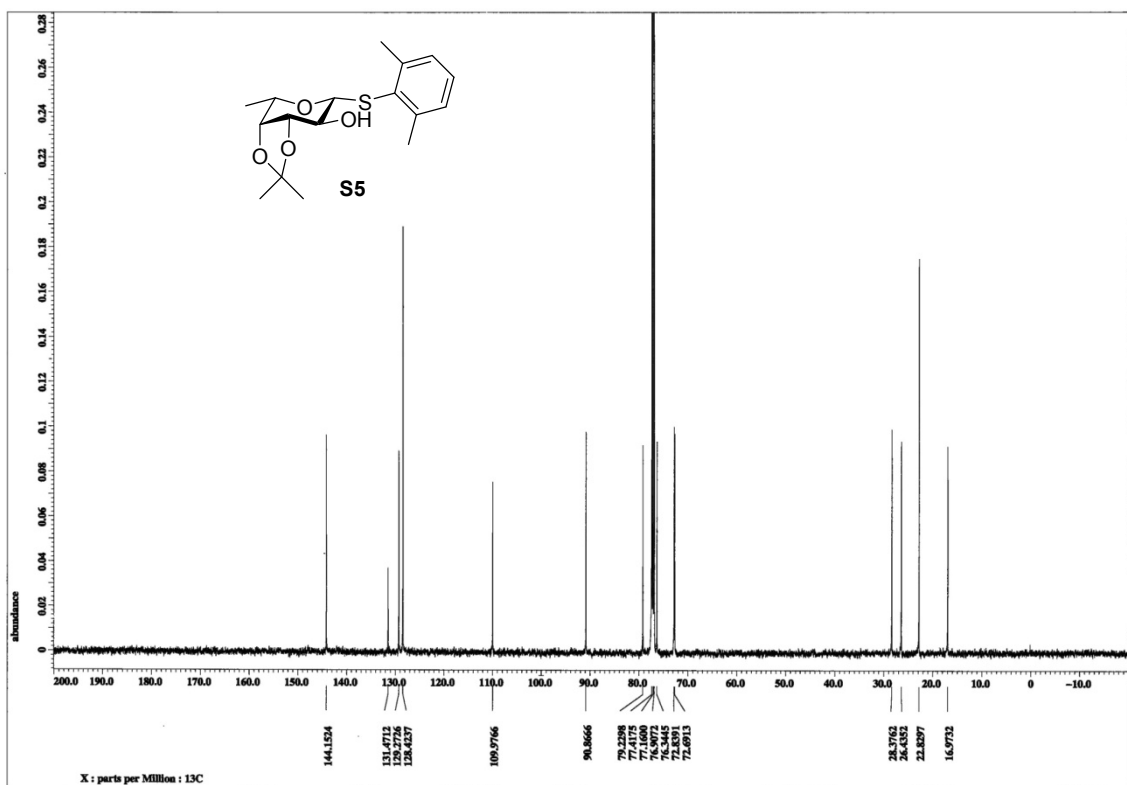


Figure S4 ¹³C-NMR spectrum of S5

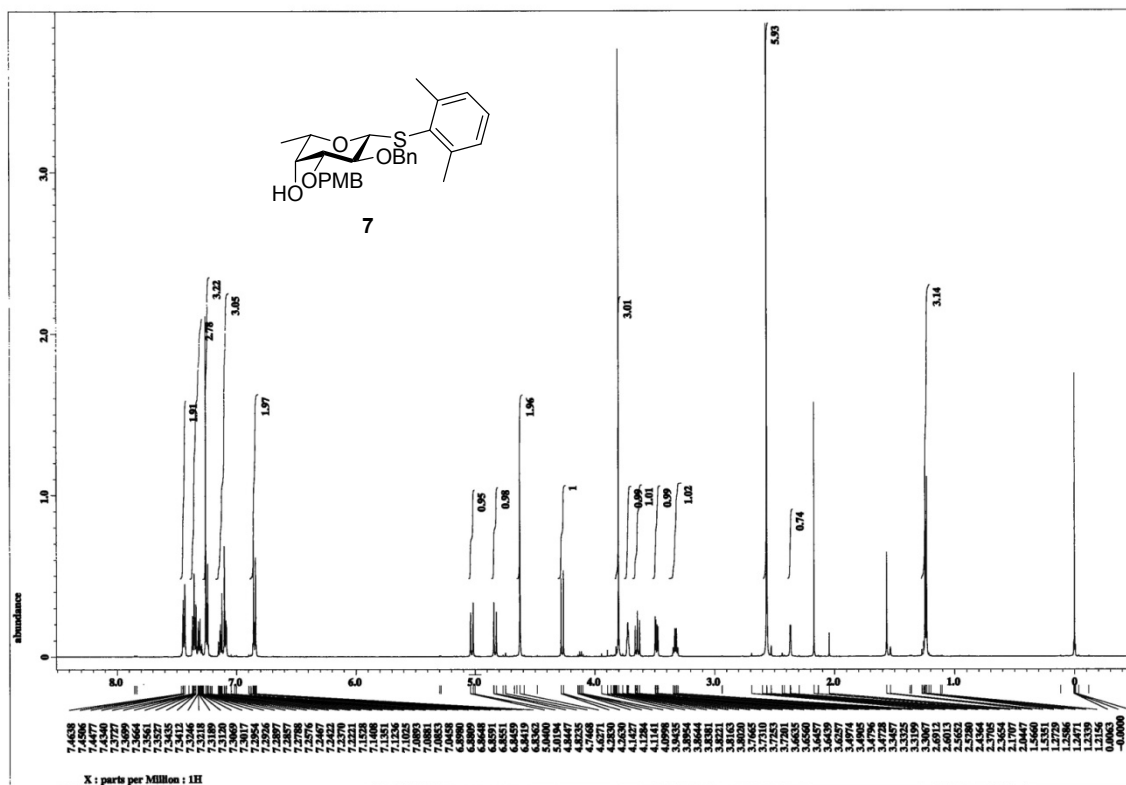


Figure S5 ¹H-NMR spectrum of 7

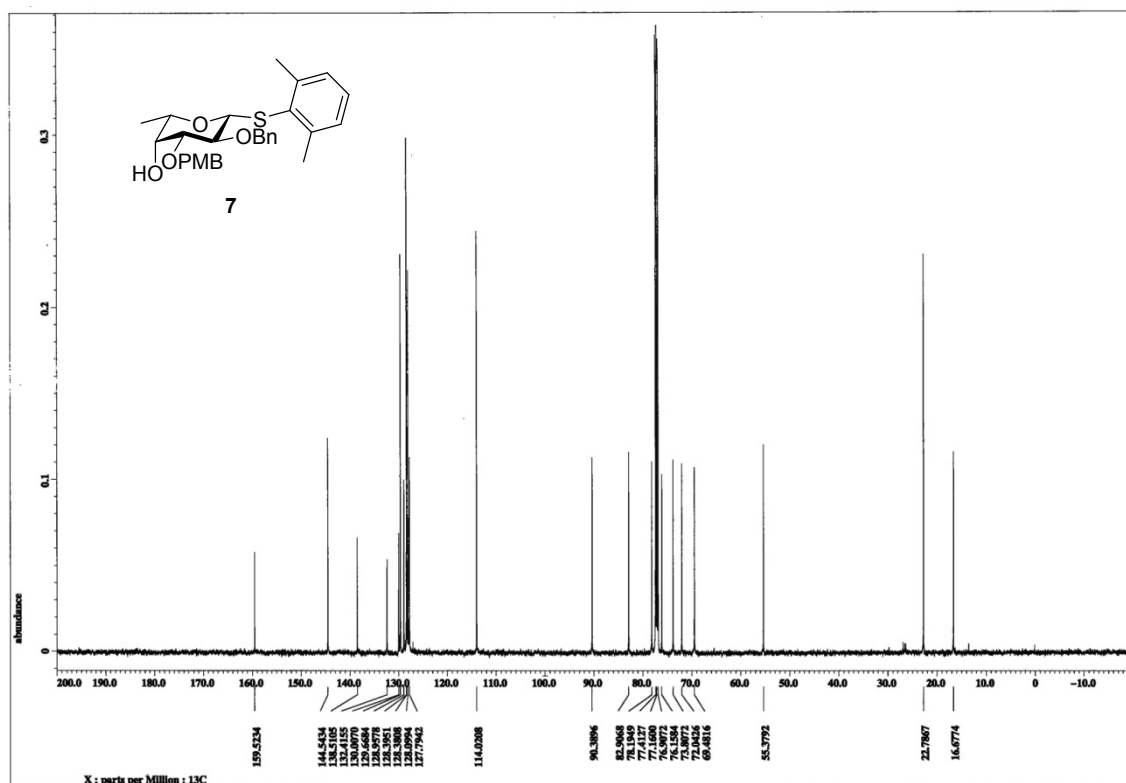


Figure S6 ¹³C-NMR spectrum of 7

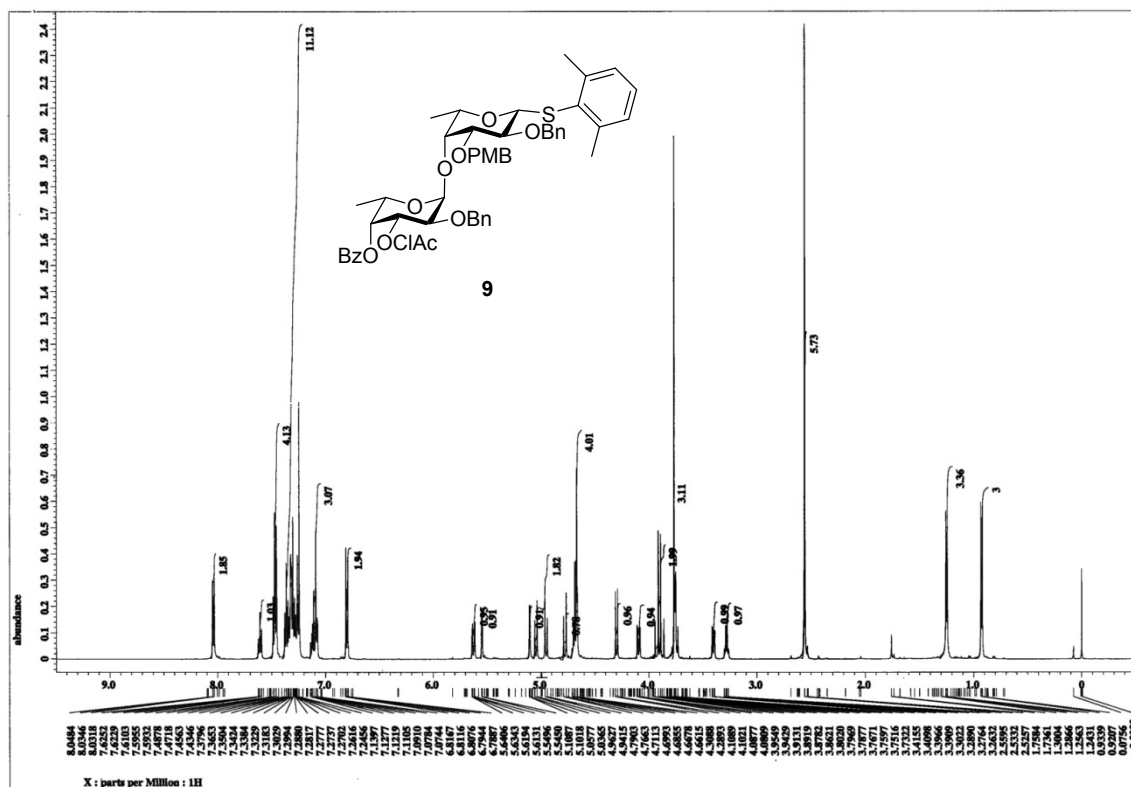


Figure S7 ¹H-NMR spectrum of 9

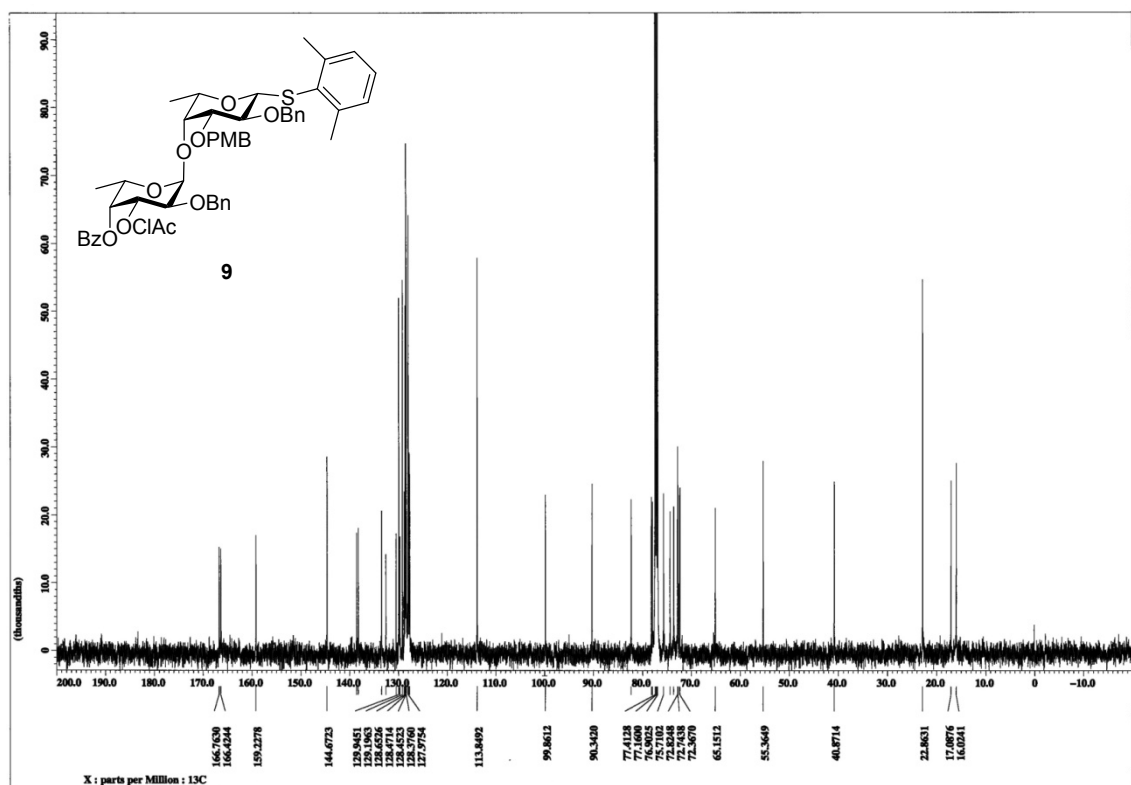


Figure S8 ¹³C-NMR spectrum of 9

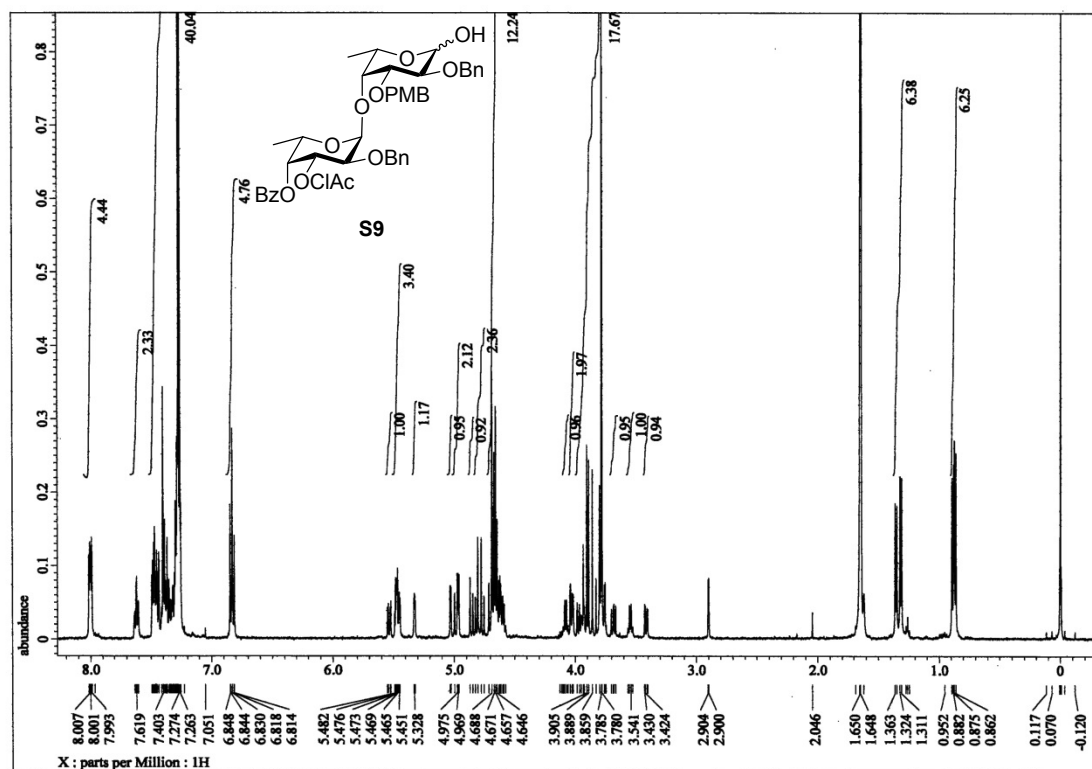


Figure S9 ¹H-NMR spectrum of S9

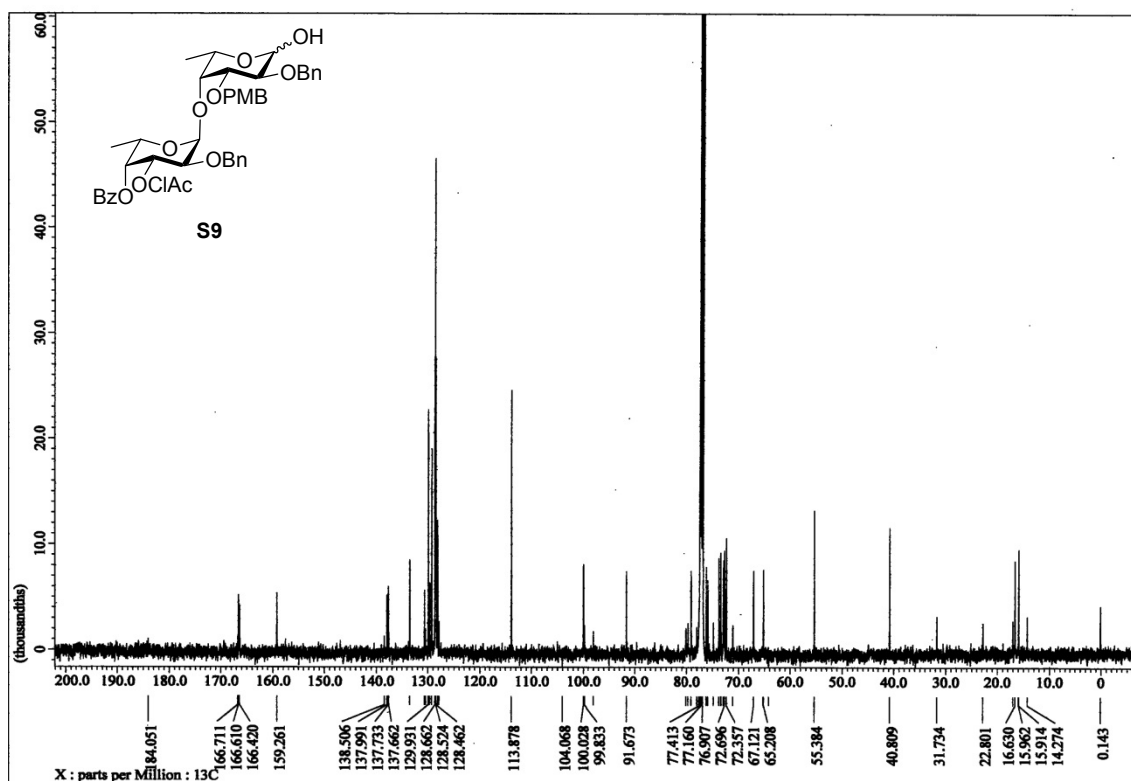


Figure S10 ¹³C-NMR spectrum of S9

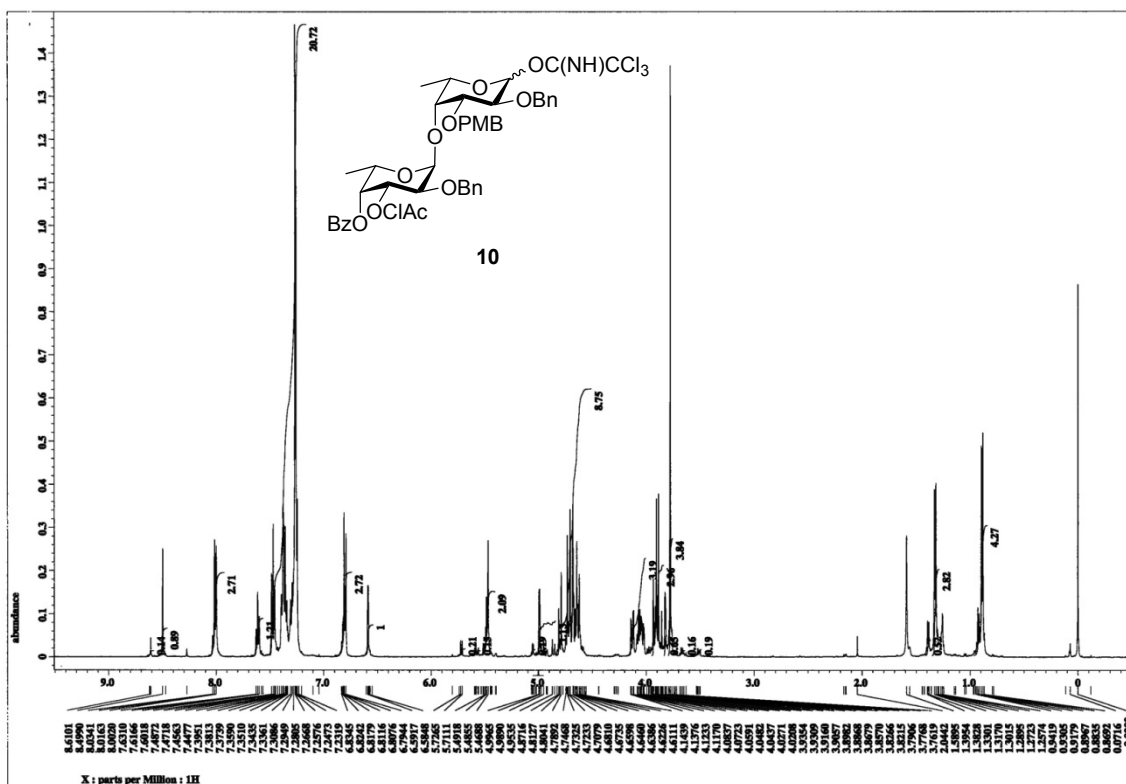


Figure S11 ¹H-NMR spectrum of 10

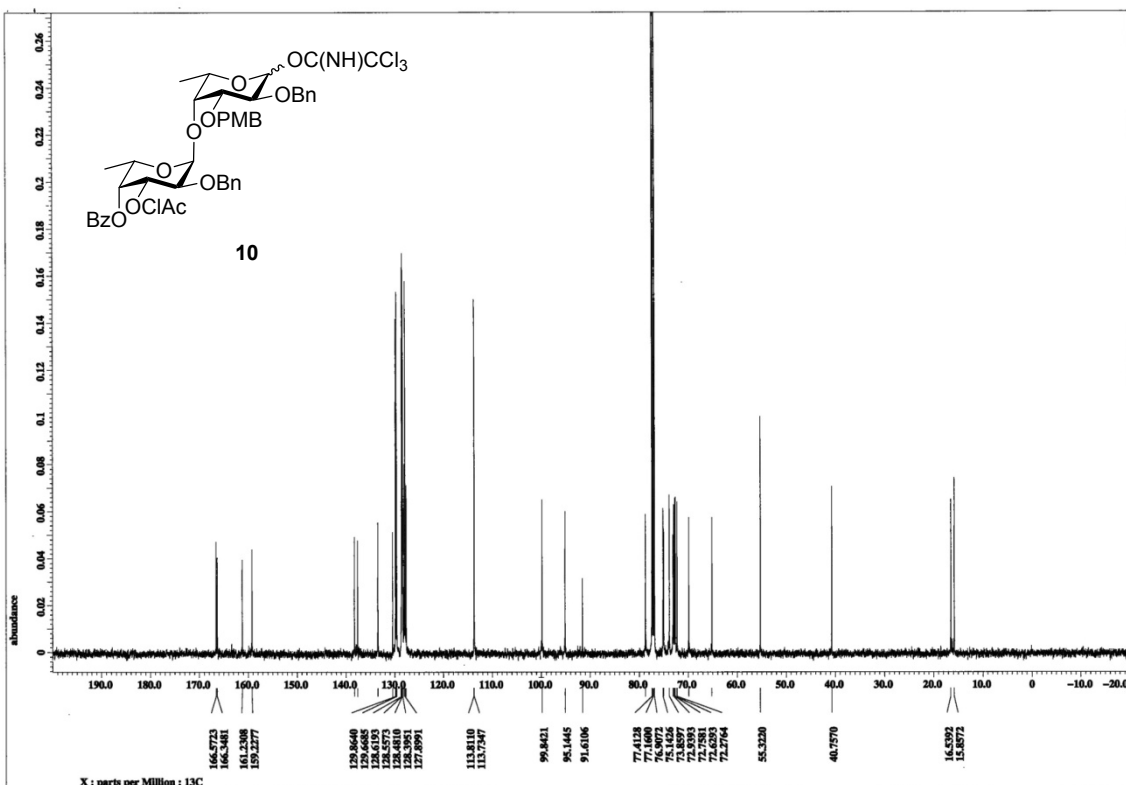


Figure S12 ¹³C-NMR spectrum of 10

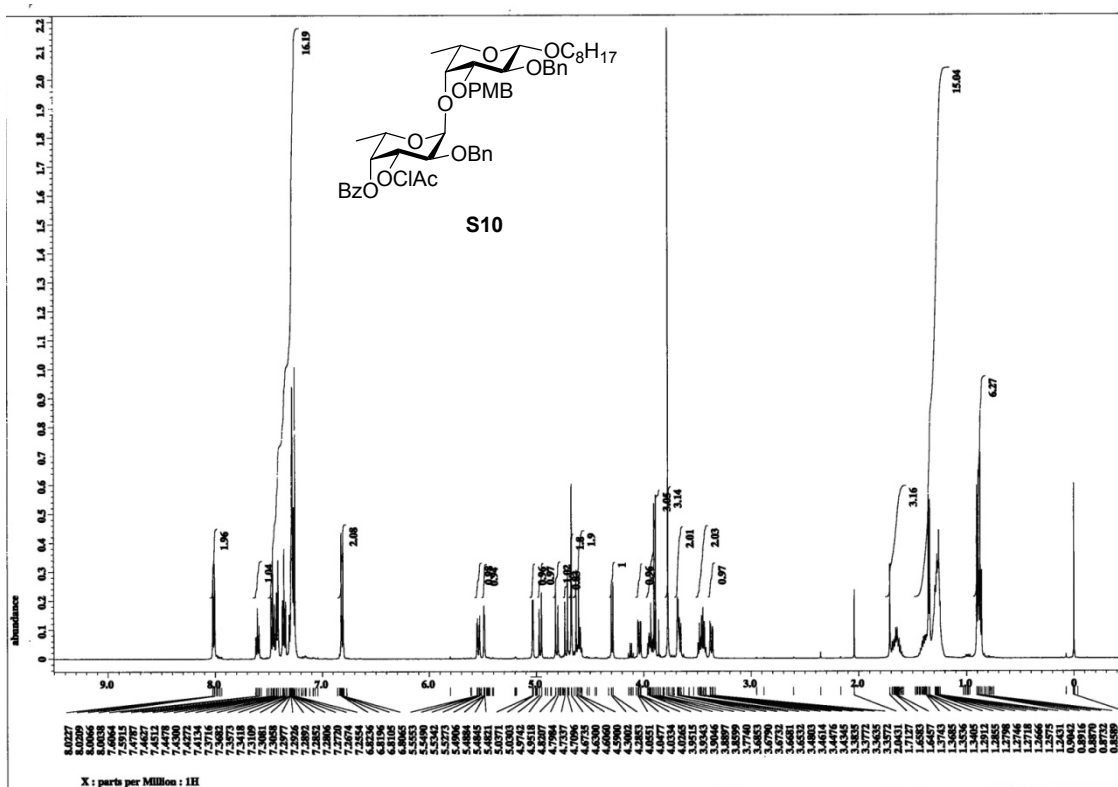


Figure S13 ¹H-NMR spectrum of S10

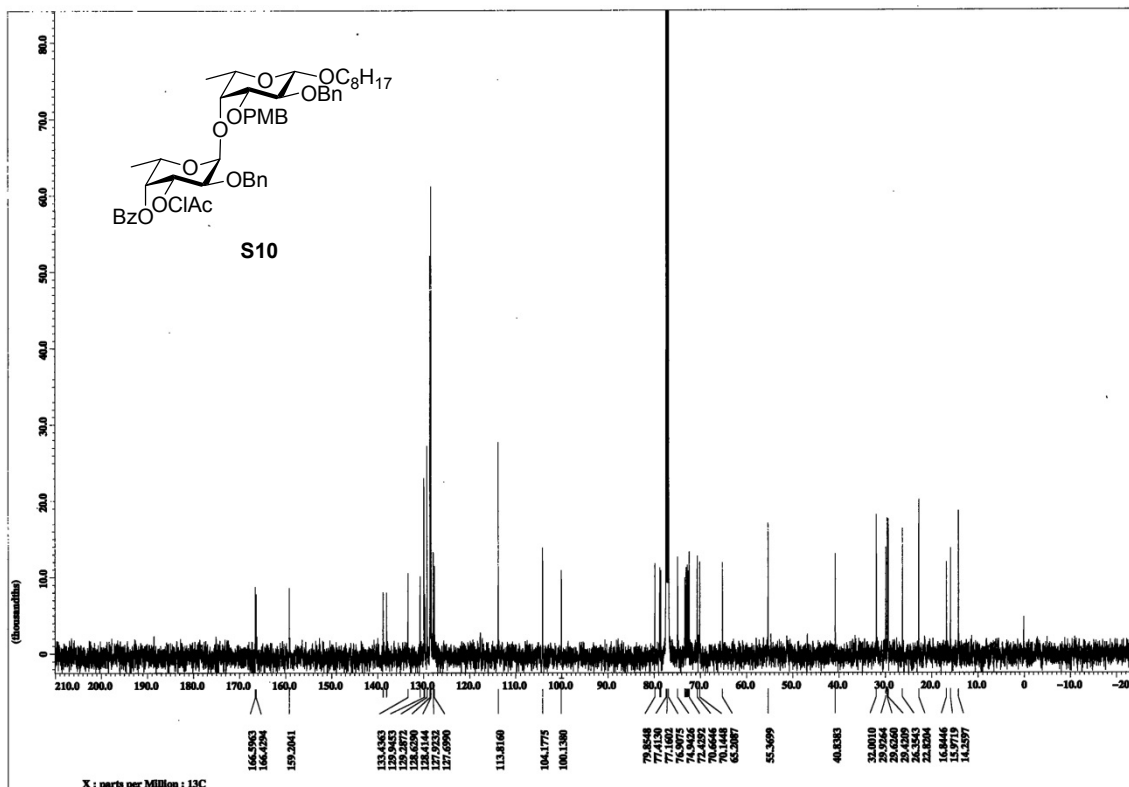


Figure S14 ¹³C-NMR spectrum of S10

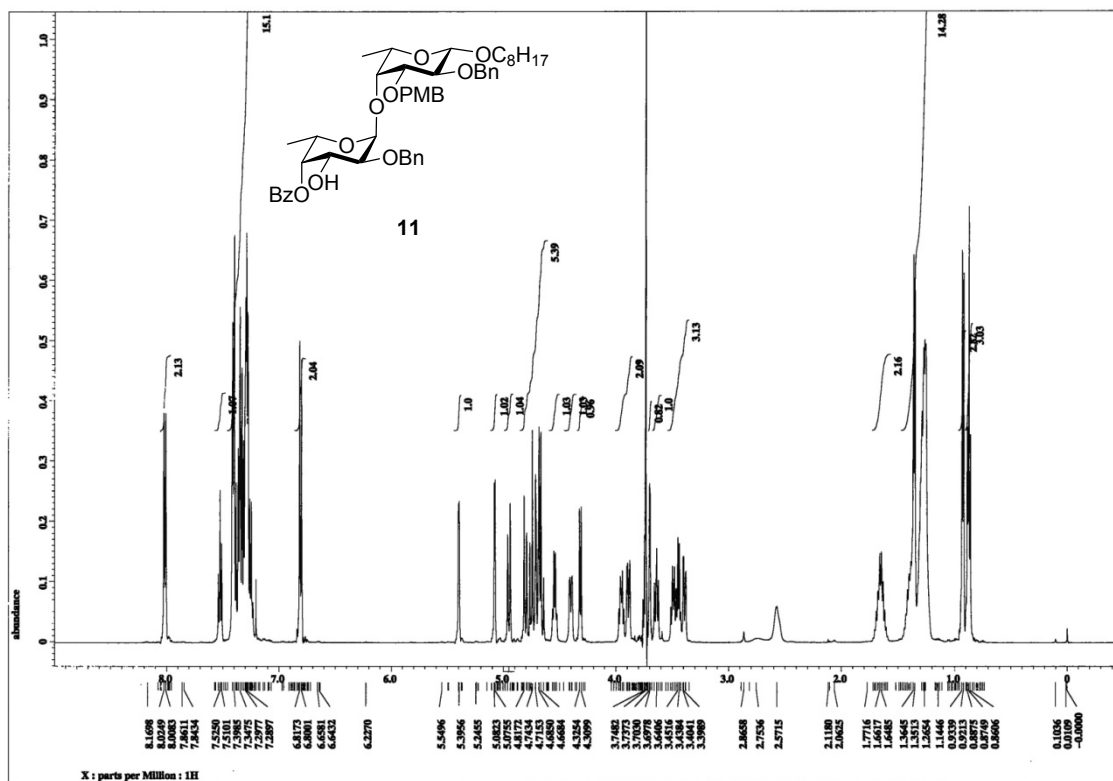


Figure S15 ^1H -NMR spectrum of **11**

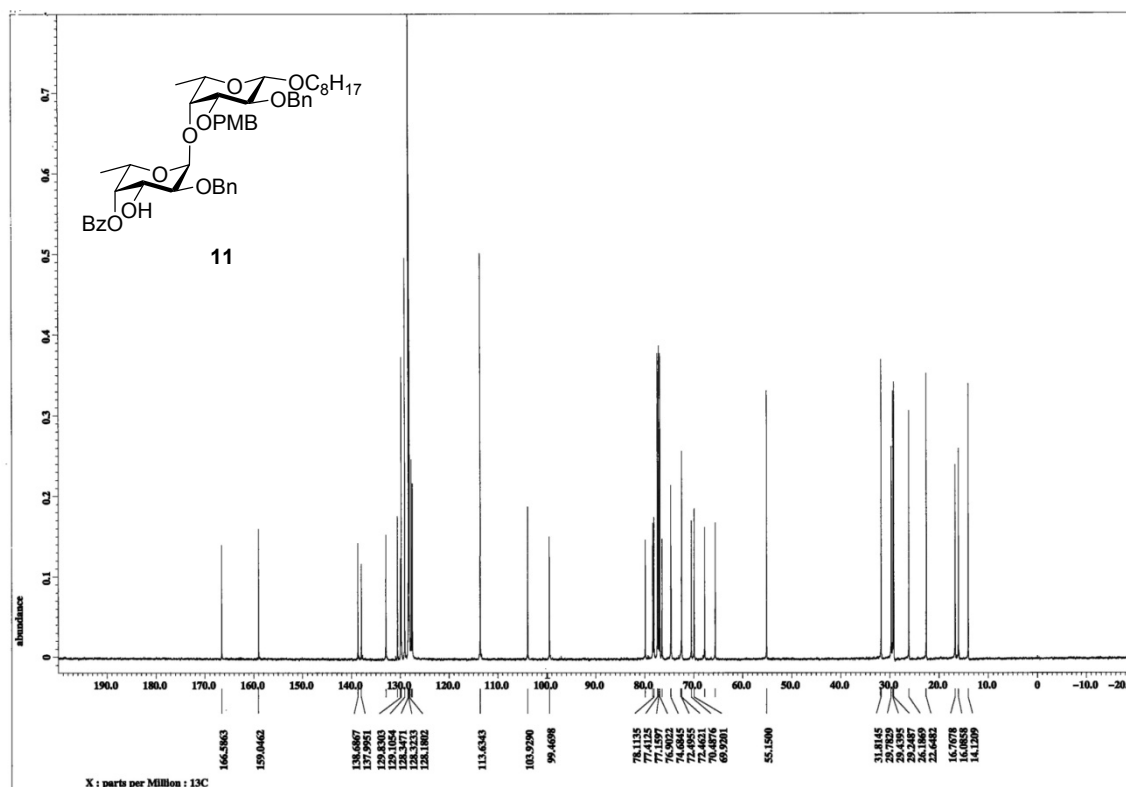


Figure S16 ^{13}C -NMR spectrum of **11**

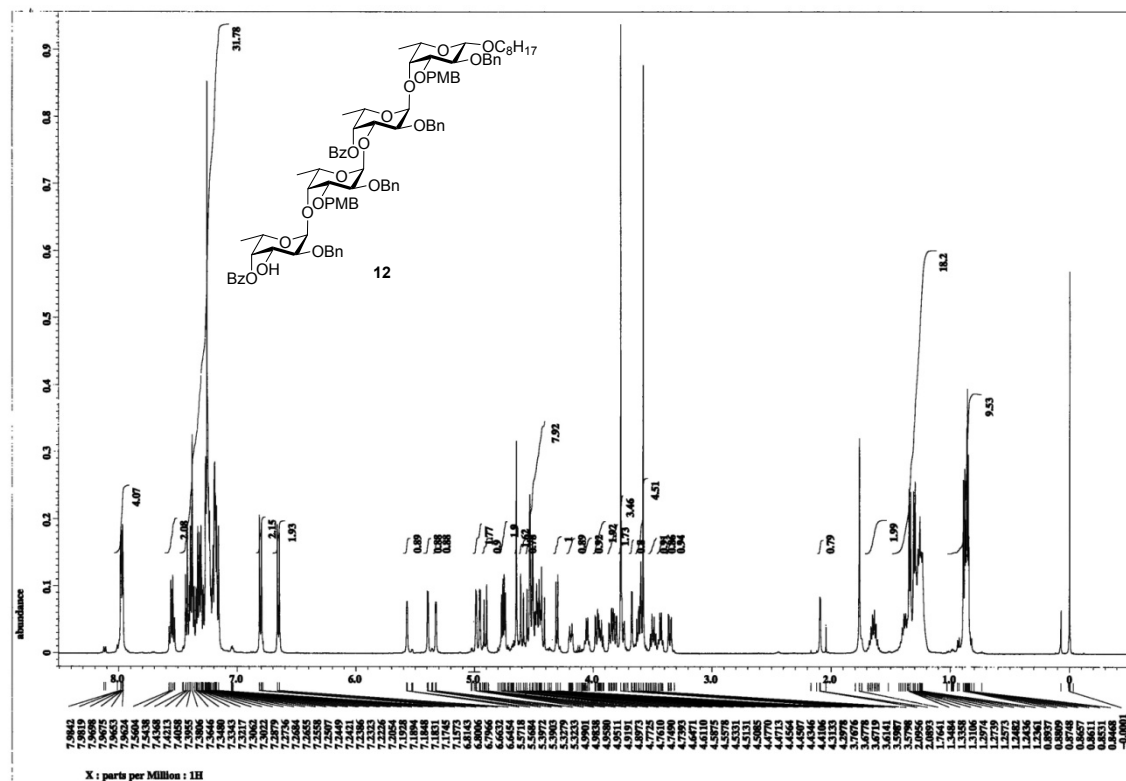


Figure S17 ^1H -NMR spectrum of **12**

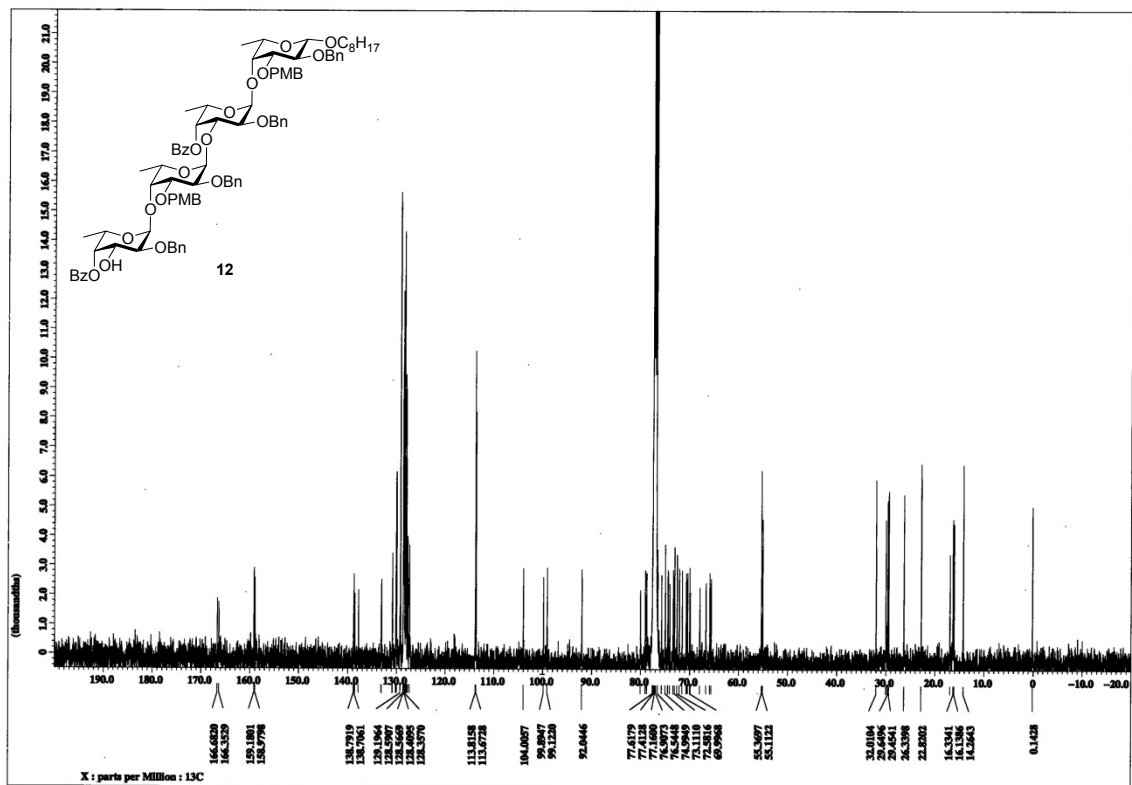


Figure S18 ^{13}C -NMR spectrum of **12**

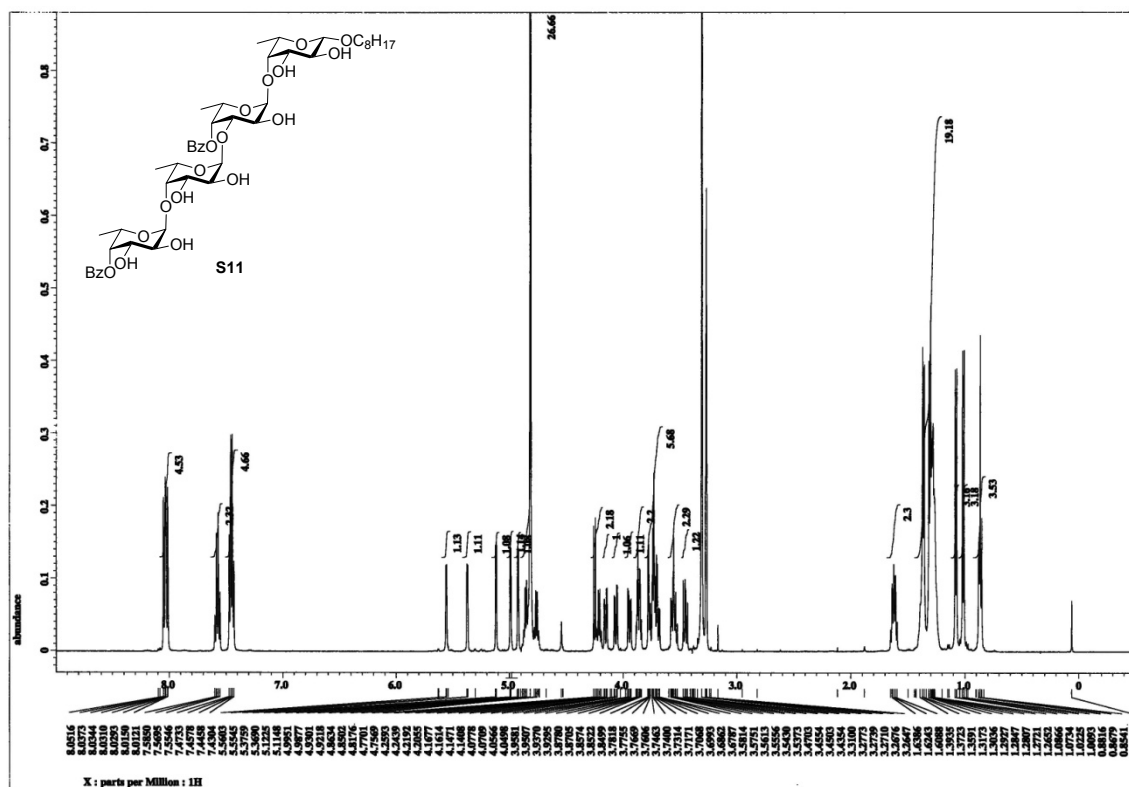


Figure S19 ^1H -NMR spectrum of S11

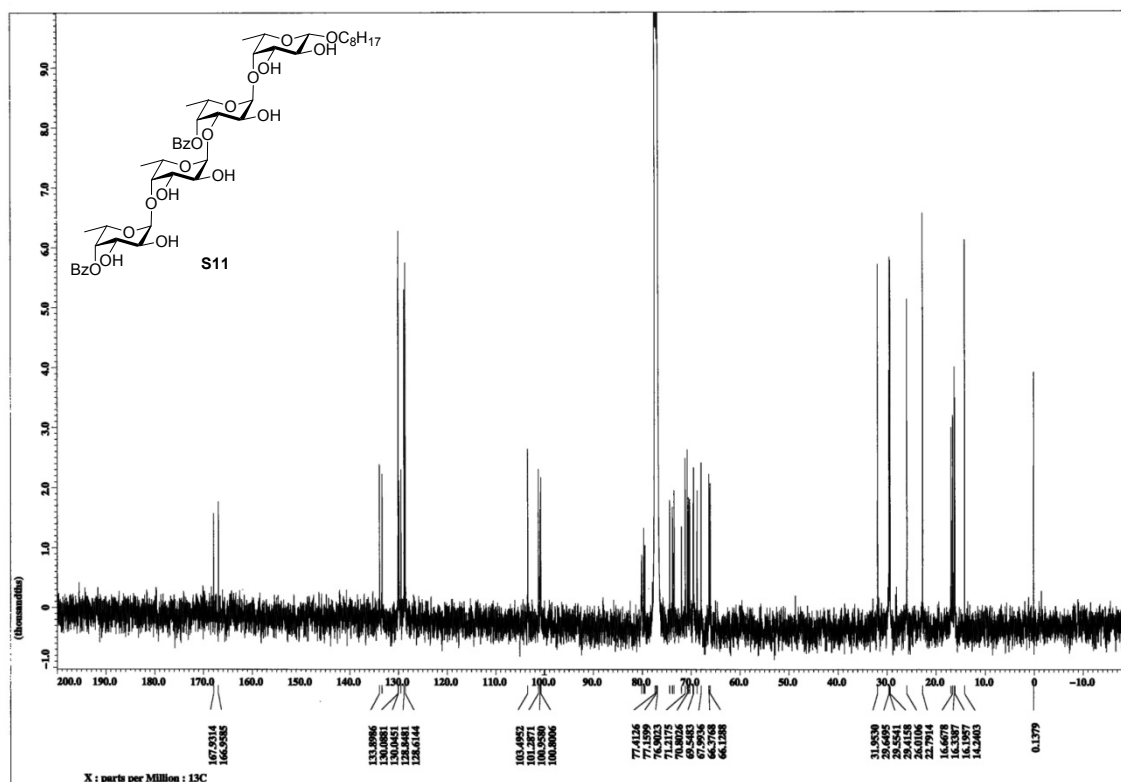


Figure S20 ^{13}C -NMR spectrum of S11

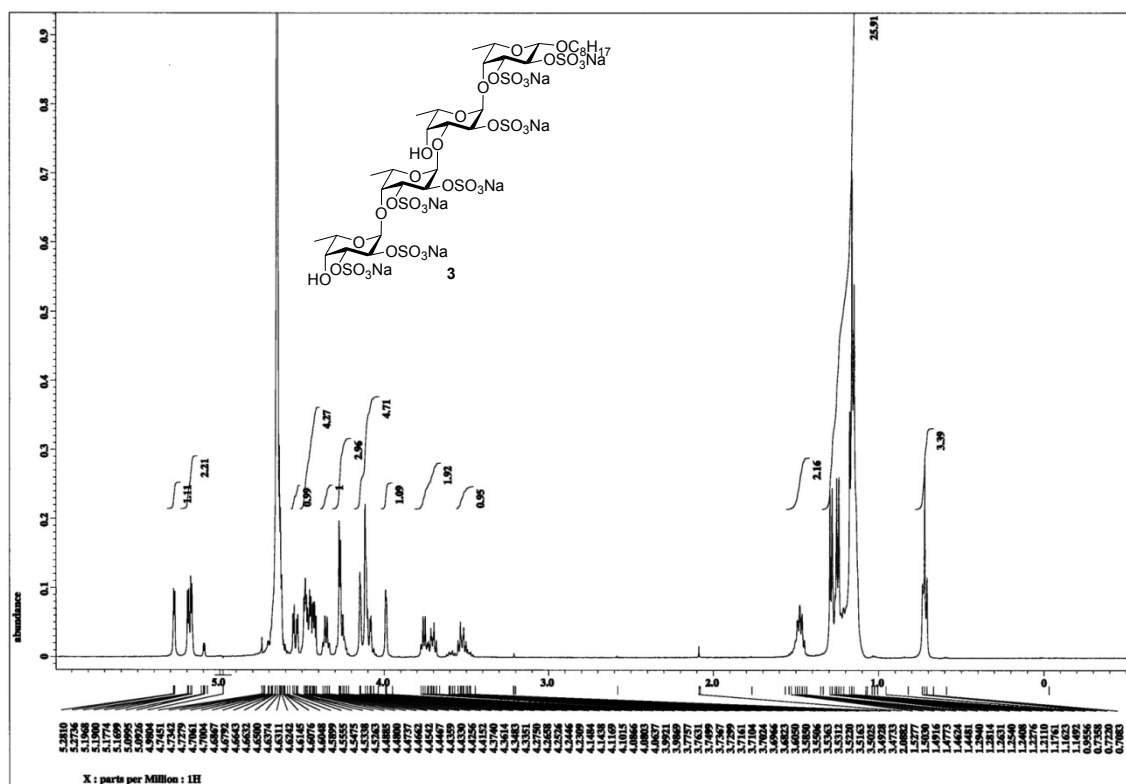


Figure S21 ¹H-NMR spectrum of 3

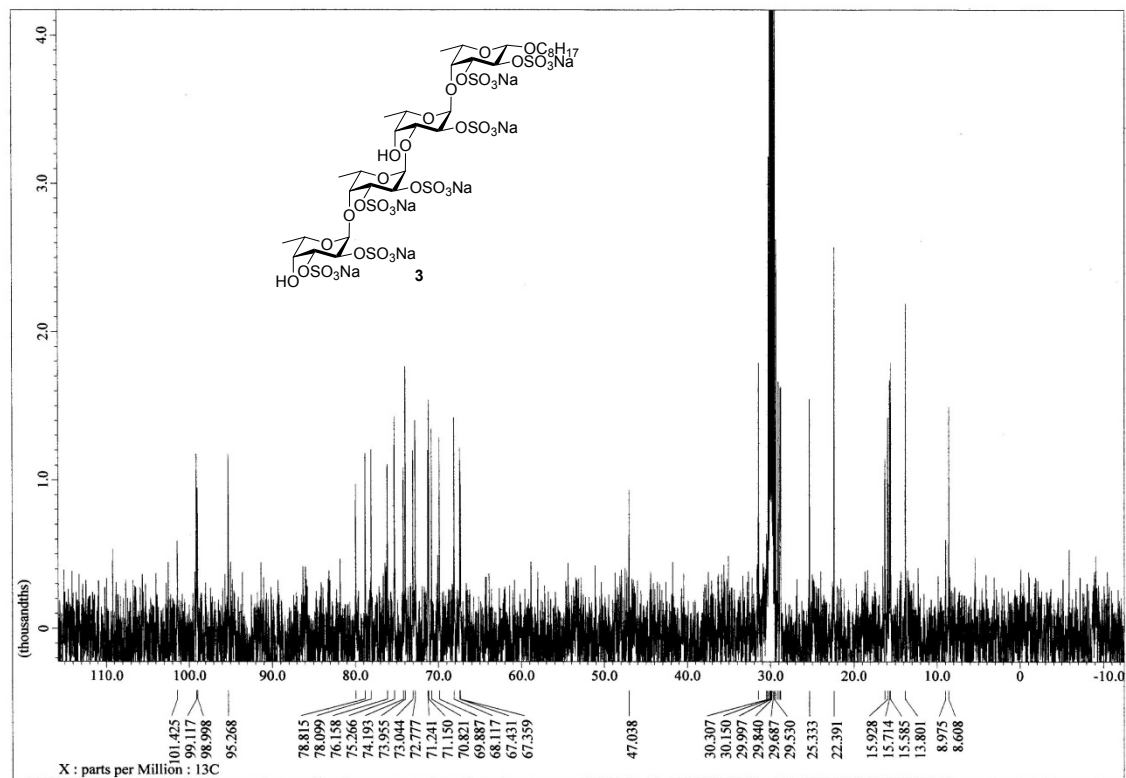


Figure S22 ¹³C-NMR spectrum of 3

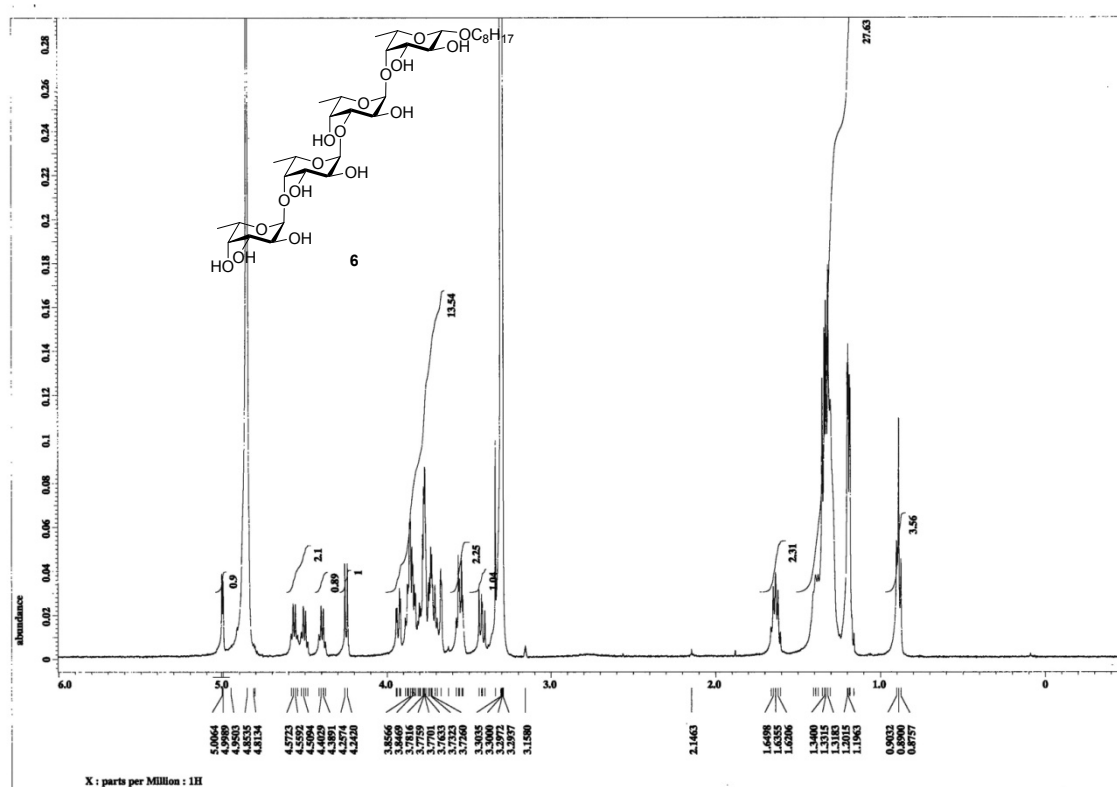


Figure S23 ¹H-NMR spectrum of 6

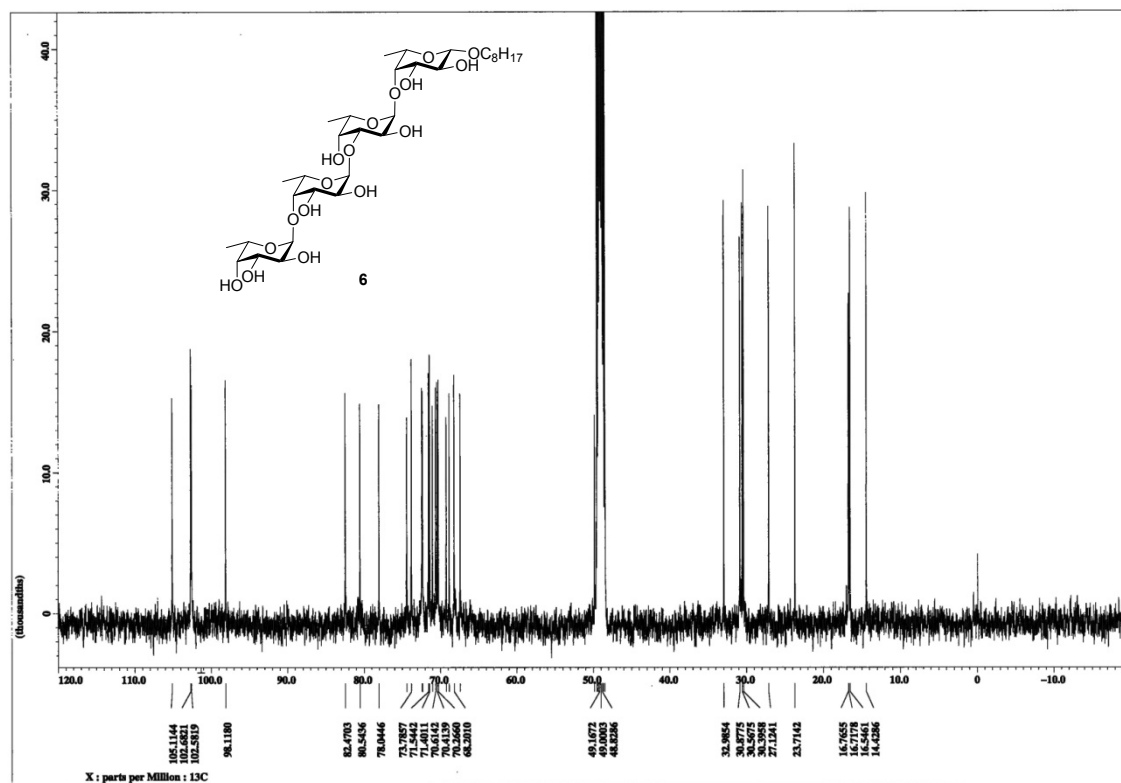


Figure S24 ¹³C-NMR spectrum of 6

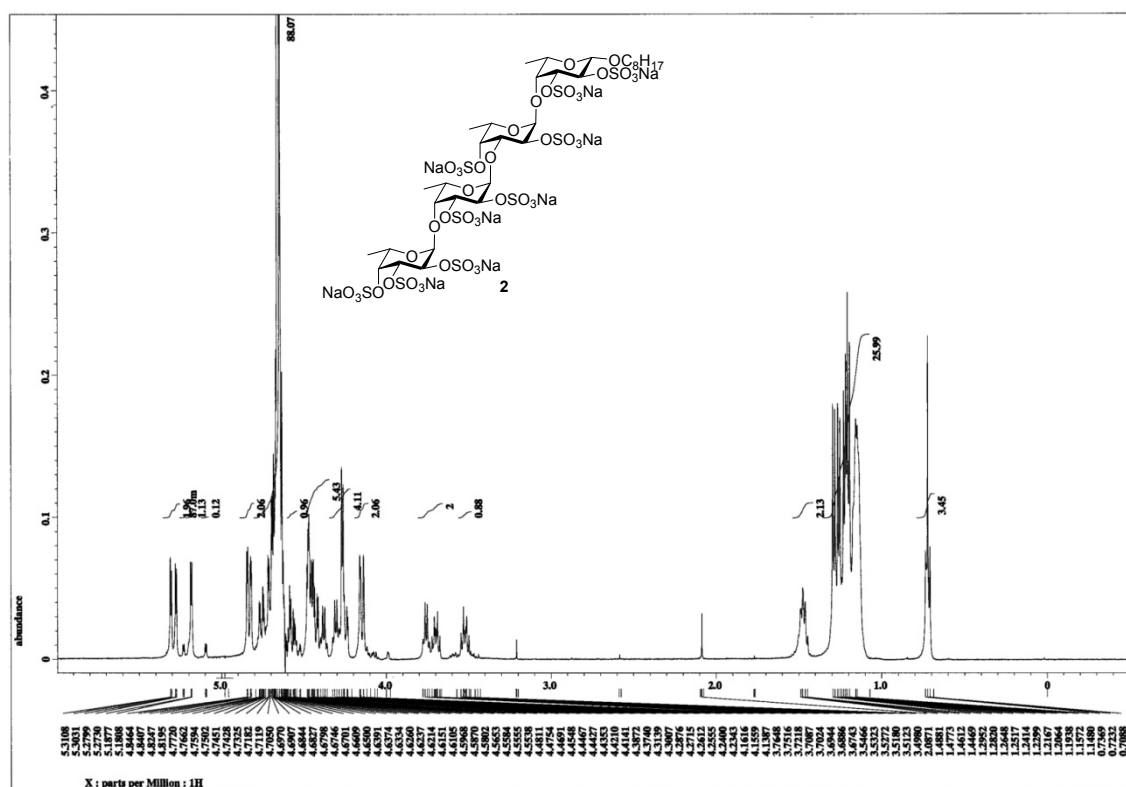


Figure S25 ¹H-NMR spectrum of 2

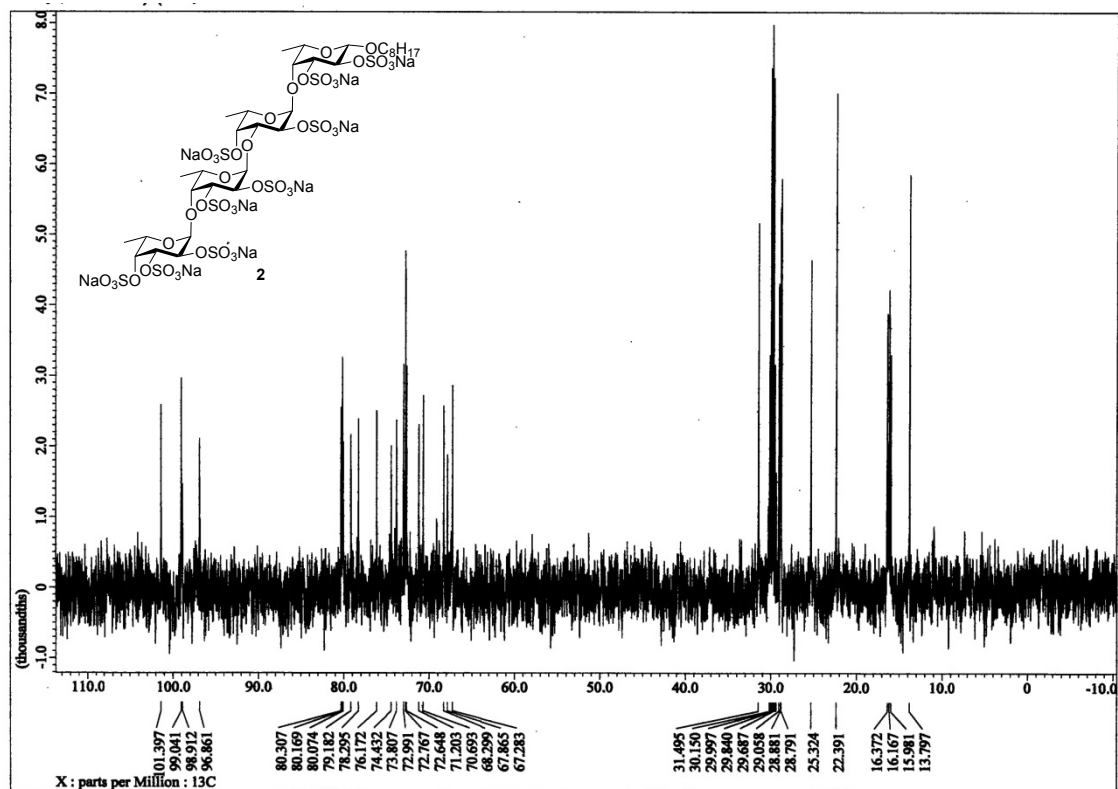


Figure S26 ¹³C-NMR spectrum of 2

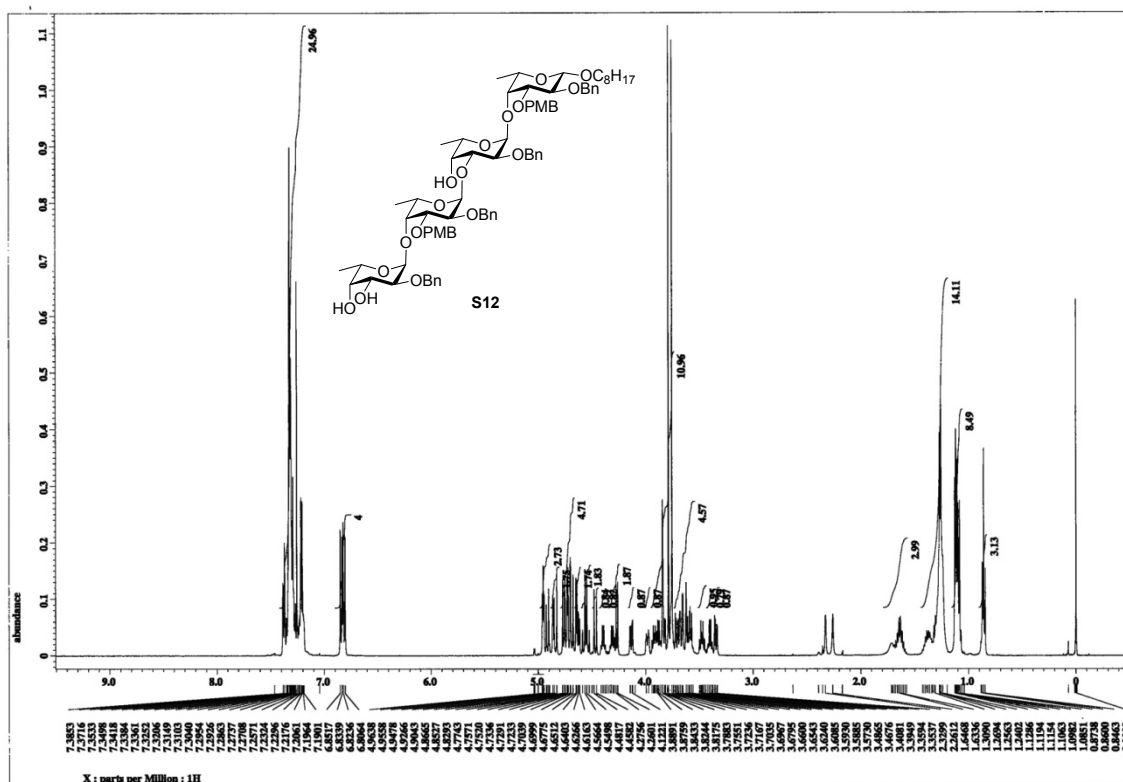


Figure S27 ¹H-NMR spectrum of **S12**

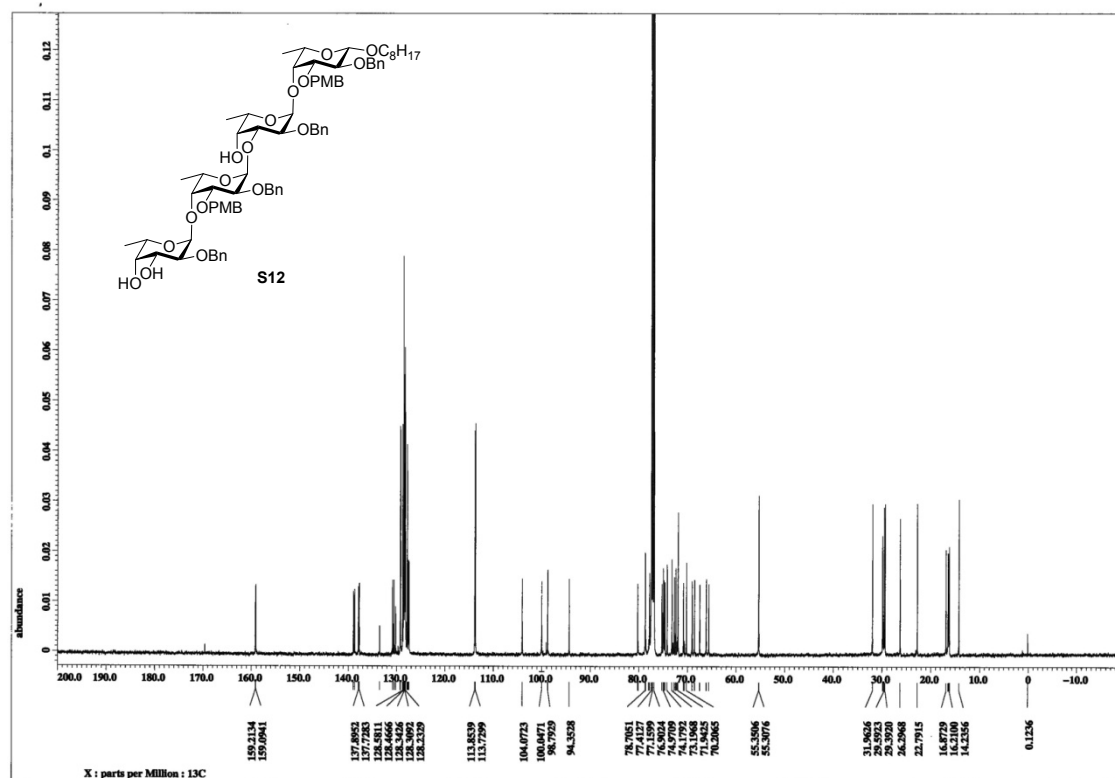


Figure S28 ^{13}C -NMR spectrum of **S12**

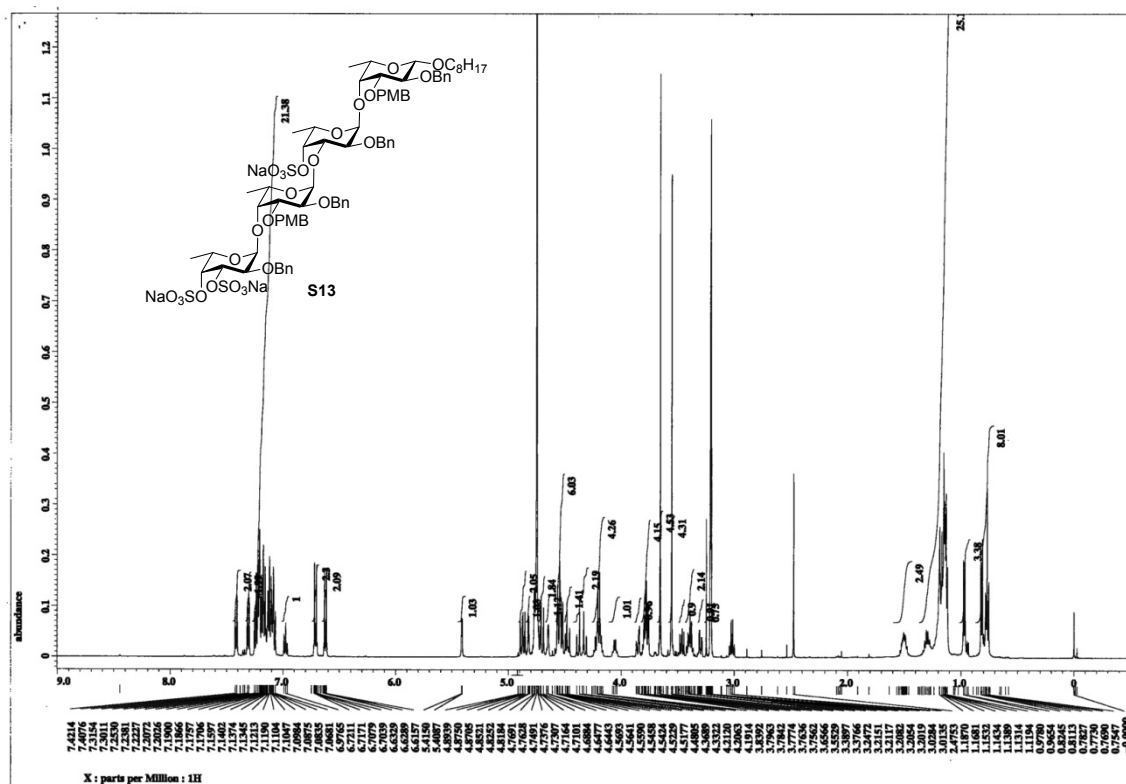


Figure S29 ^1H -NMR spectrum of **S13**

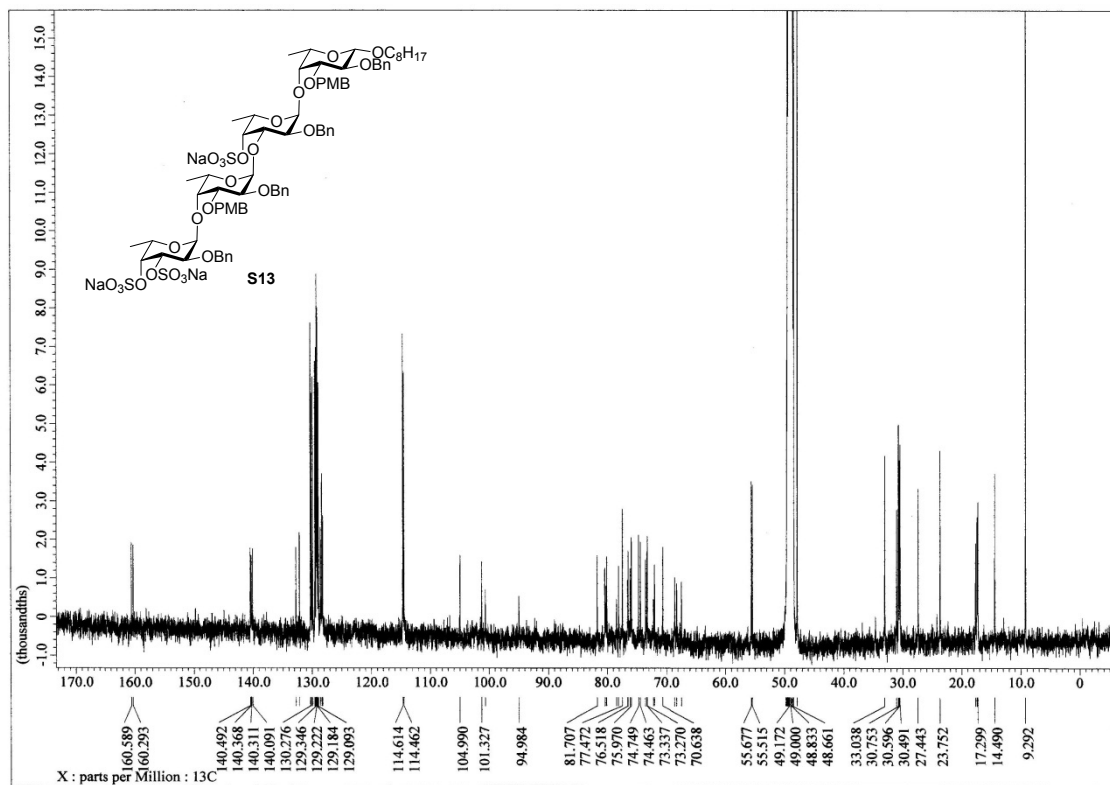


Figure S30 ^{13}C -NMR spectrum of **S13**

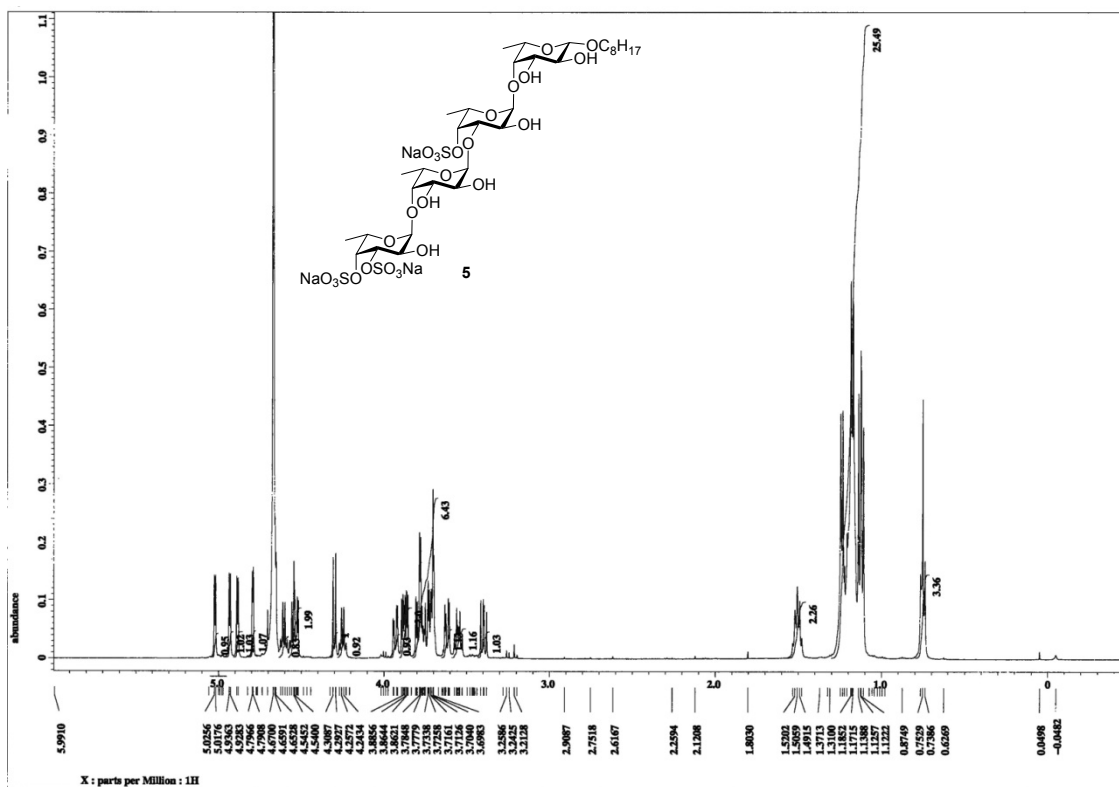


Figure S31 ^1H -NMR spectrum of 5

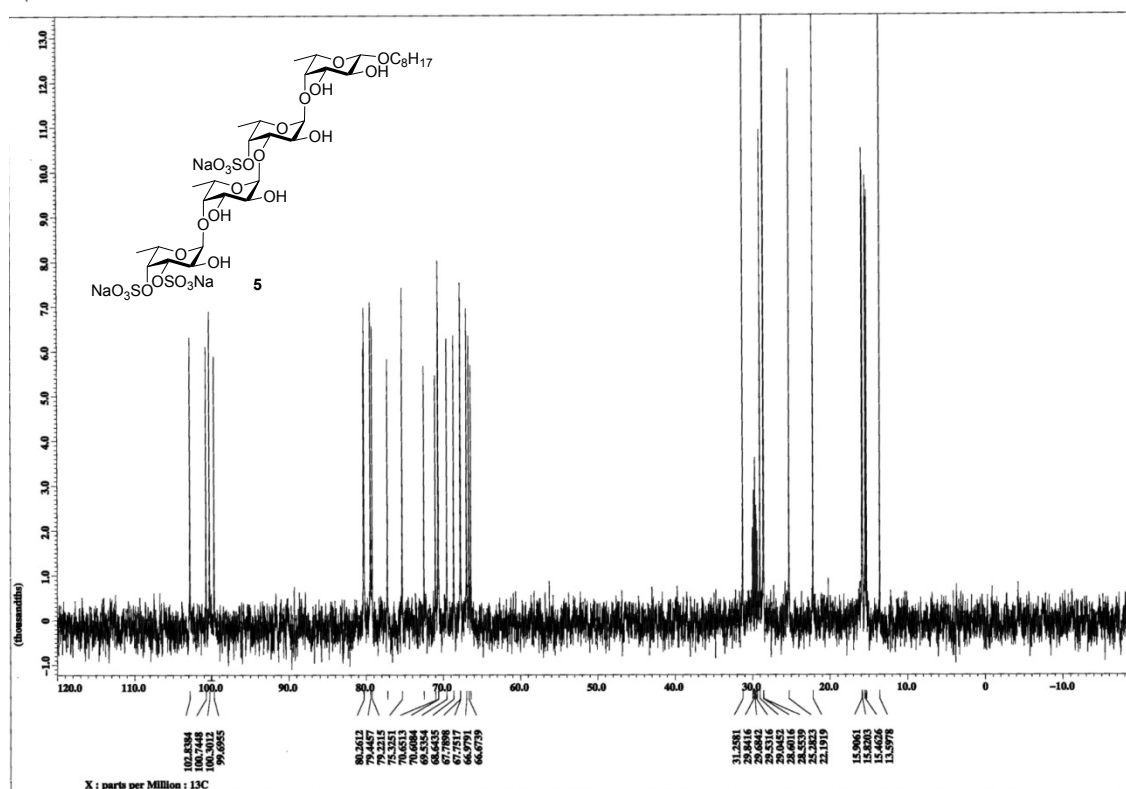


Figure S32 ^{13}C -NMR spectrum of 5

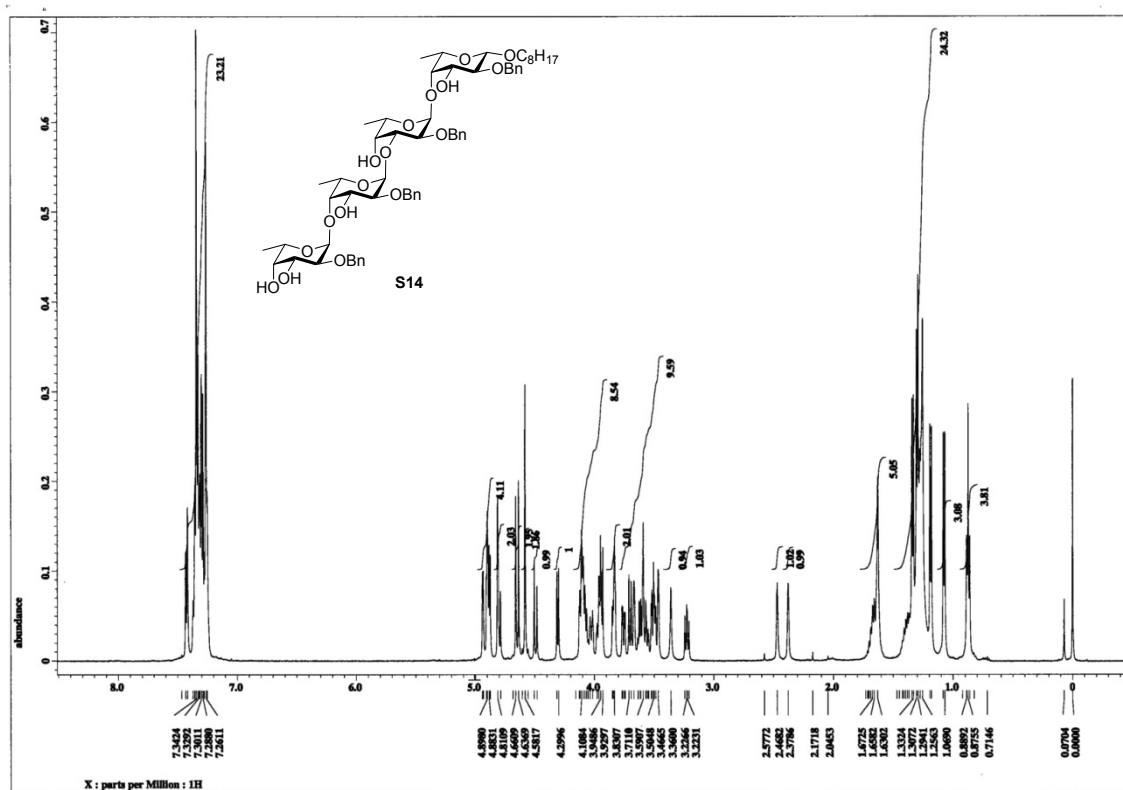


Figure S33 ^1H -NMR spectrum of **S14**

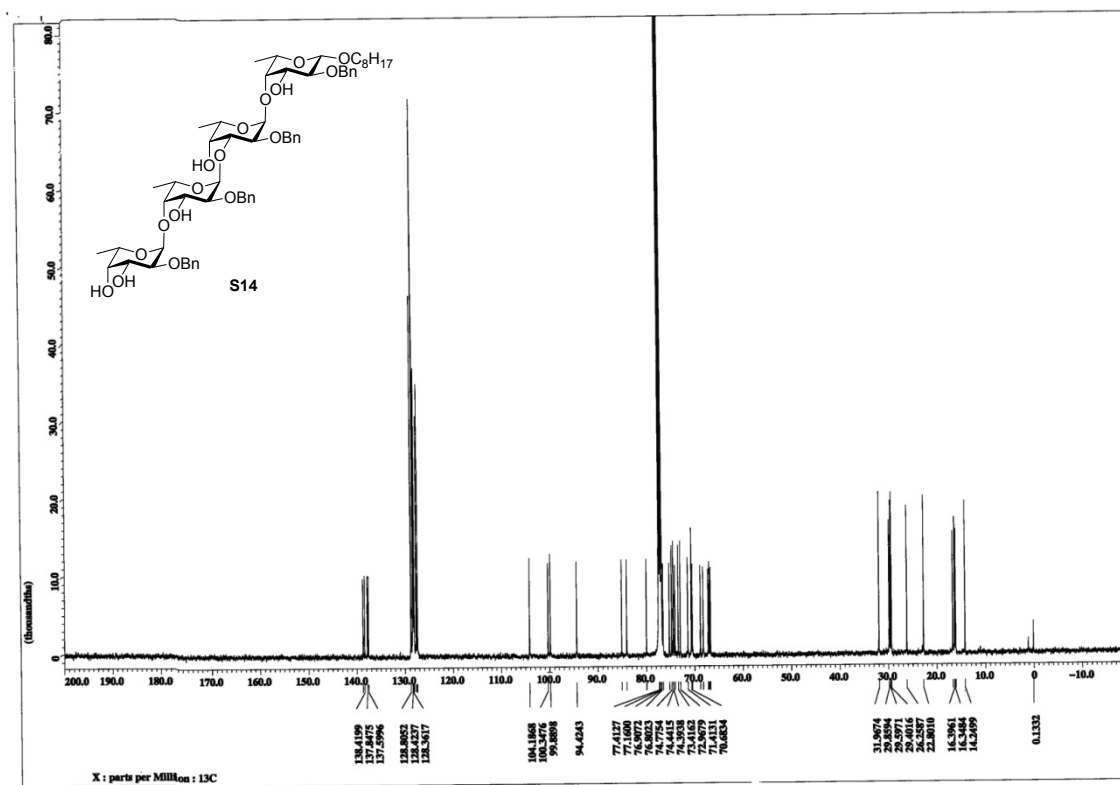


Figure S34 ^{13}C -NMR spectrum of **S14**

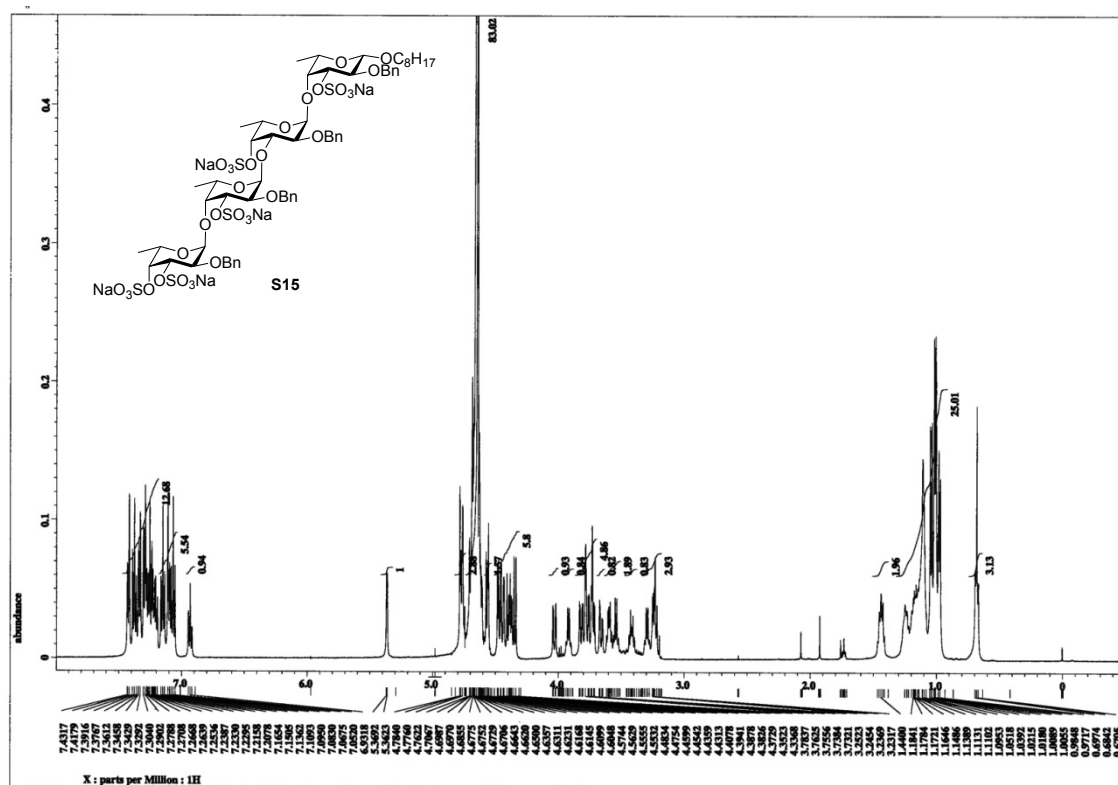


Figure S35 ^1H -NMR spectrum of **S15**

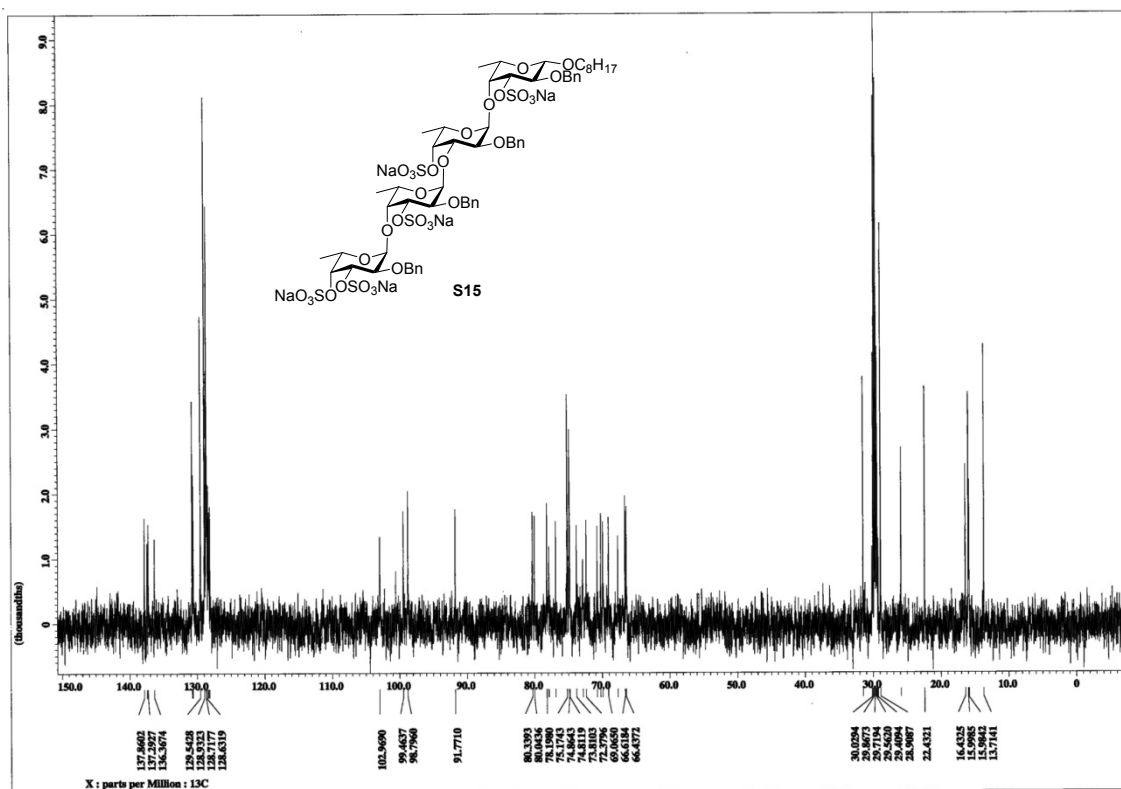


Figure S36 ^{13}C -NMR spectrum of **S15**

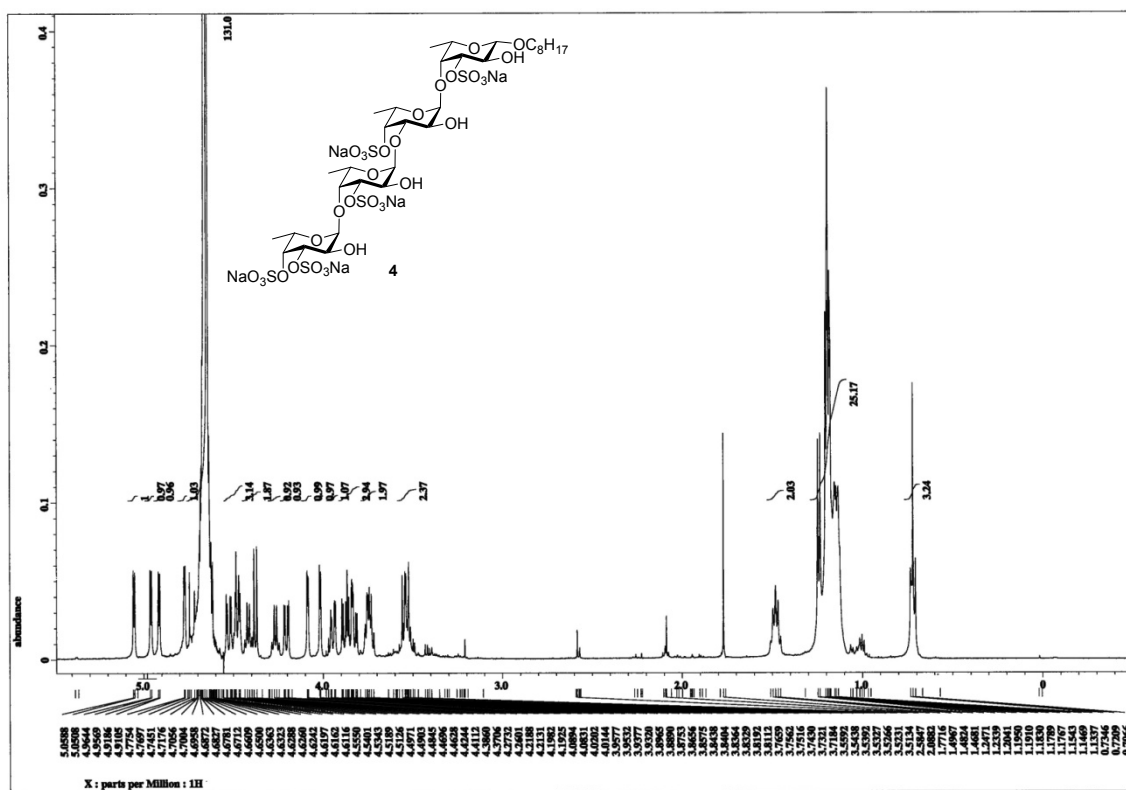


Figure S37 ¹H-NMR spectrum of 4

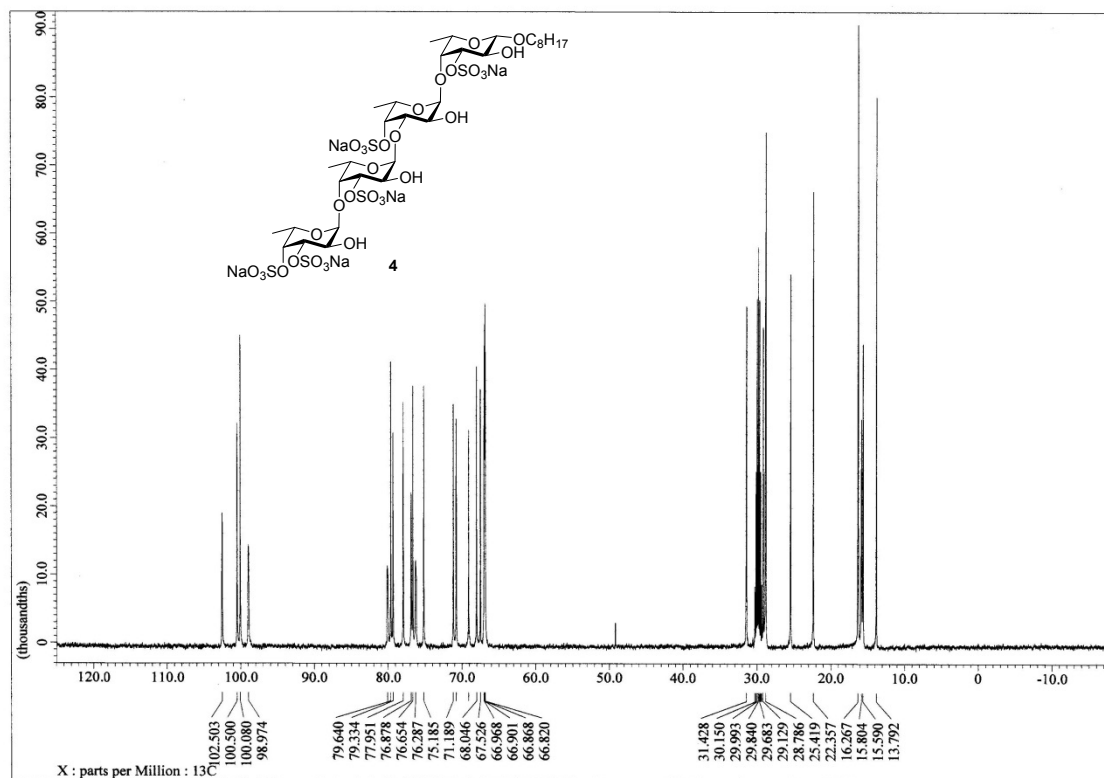


Figure S38 ¹³C-NMR spectrum of 4

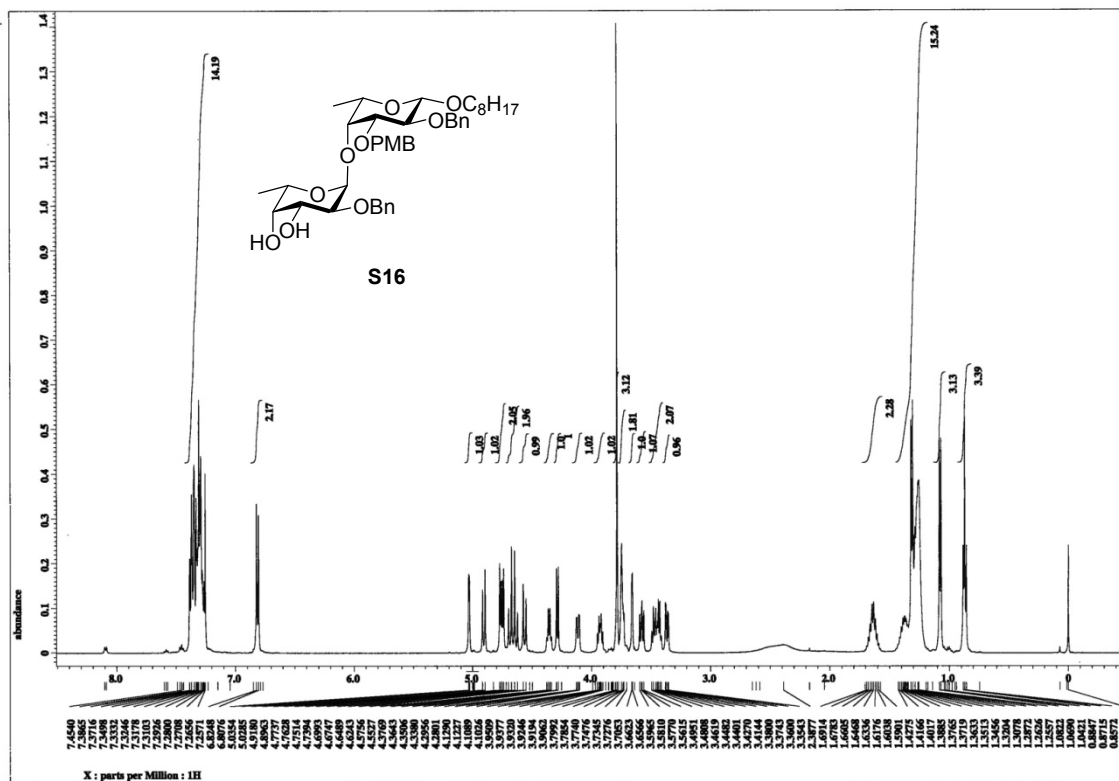


Figure S39 ^1H -NMR spectrum of **S16**

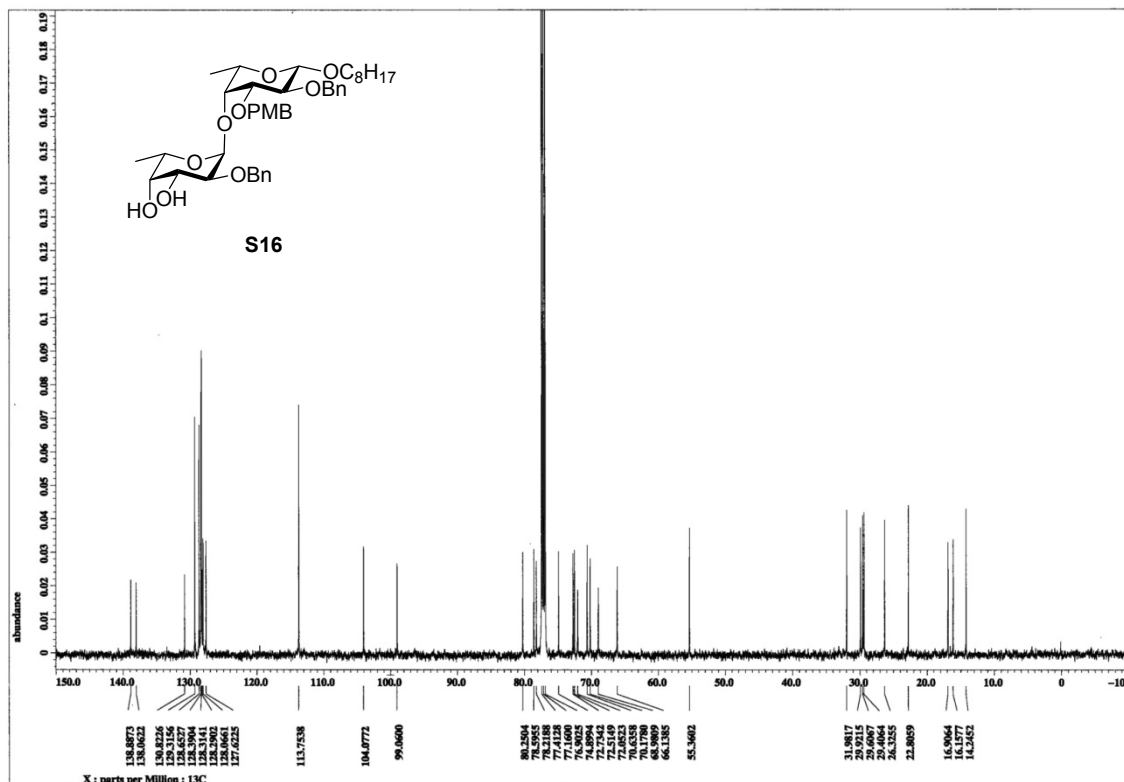


Figure S40 ^{13}C -NMR spectrum of **S16**

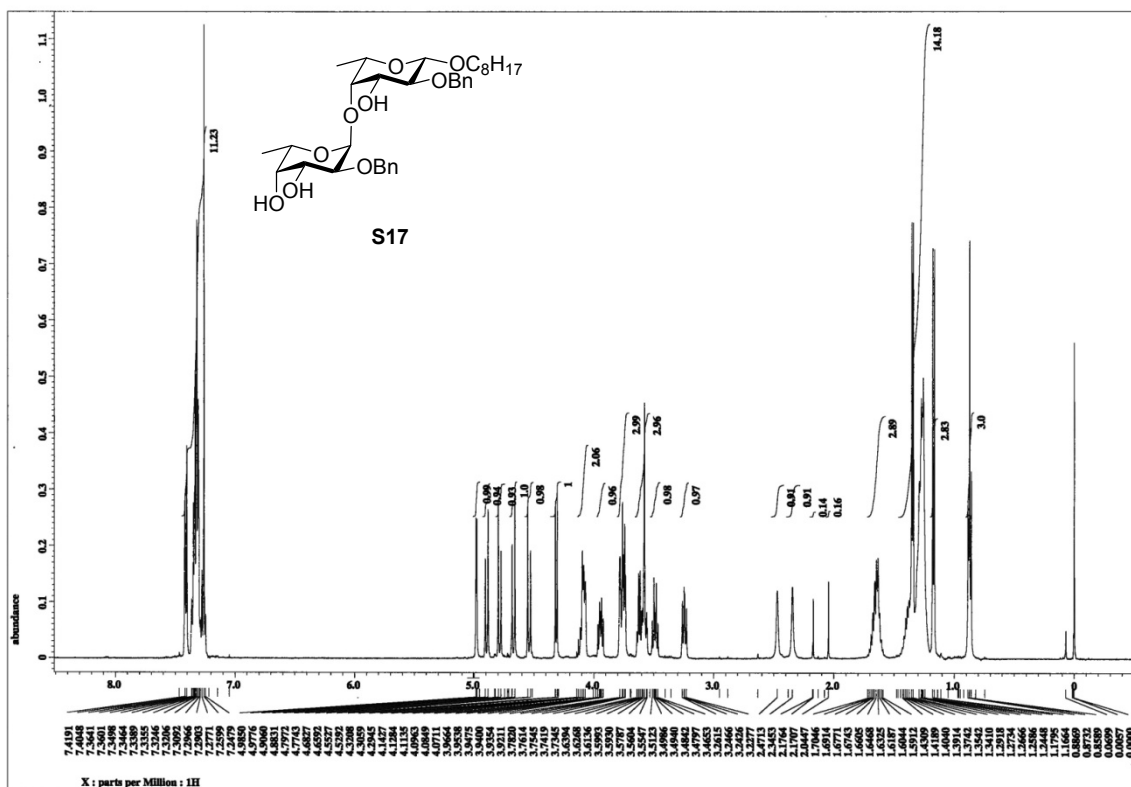


Figure S41 ¹H-NMR spectrum of S17

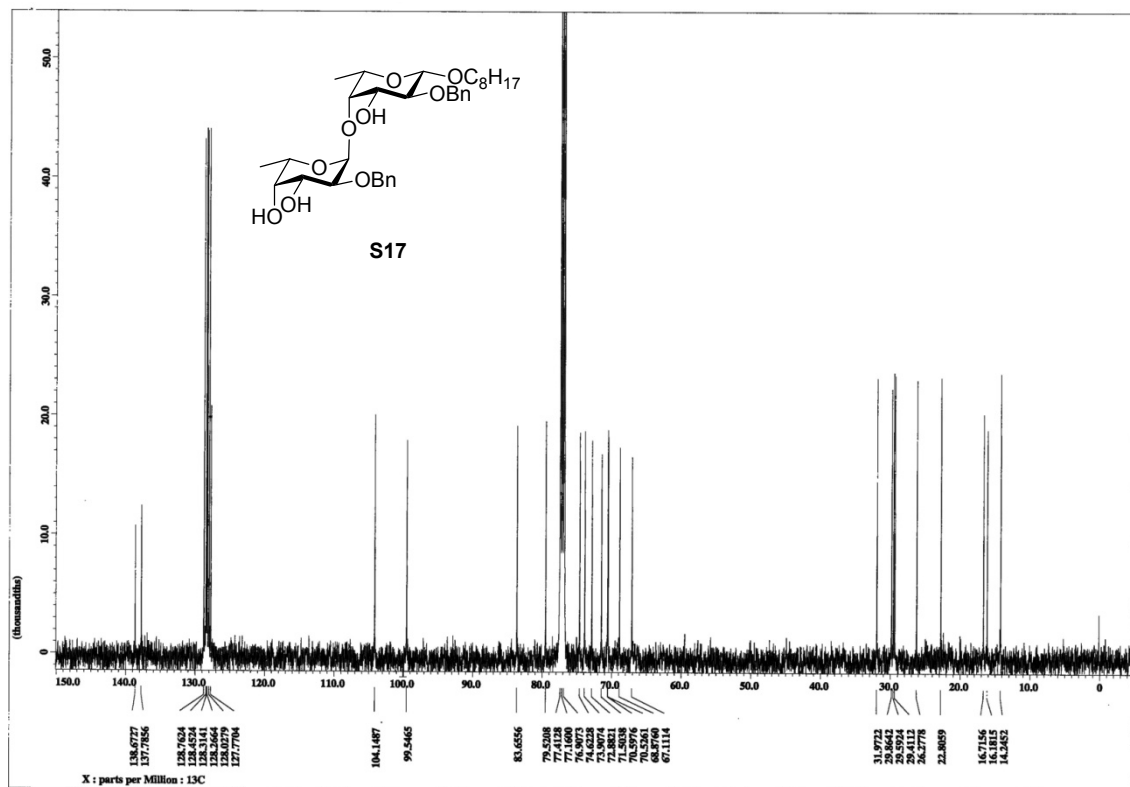


Figure S42 ¹³C-NMR spectrum of S17

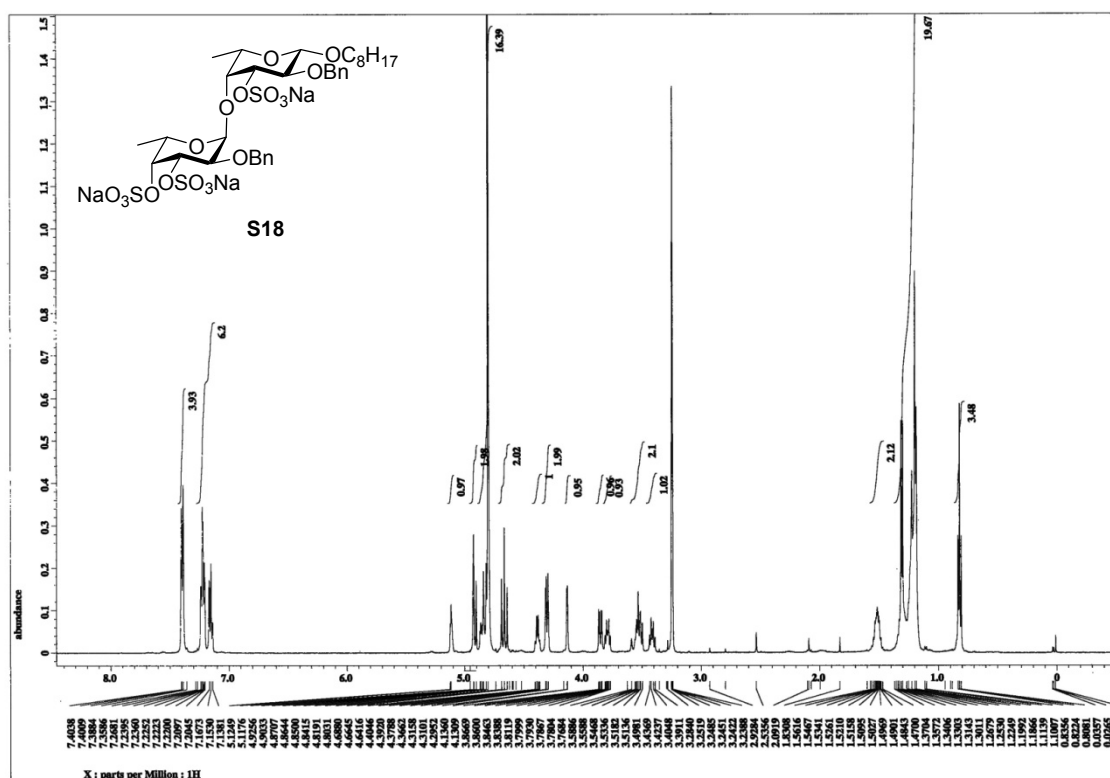


Figure S43 ^1H -NMR spectrum of **S18**

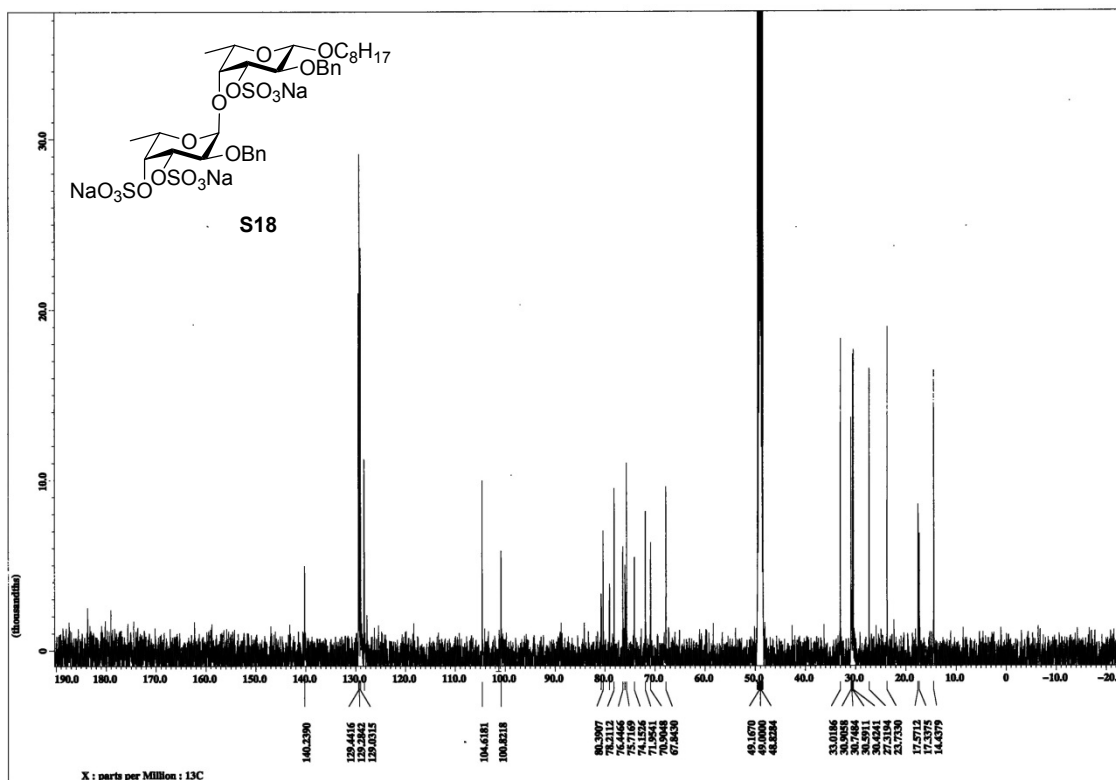


Figure S44 ^{13}C -NMR spectrum of **S18**

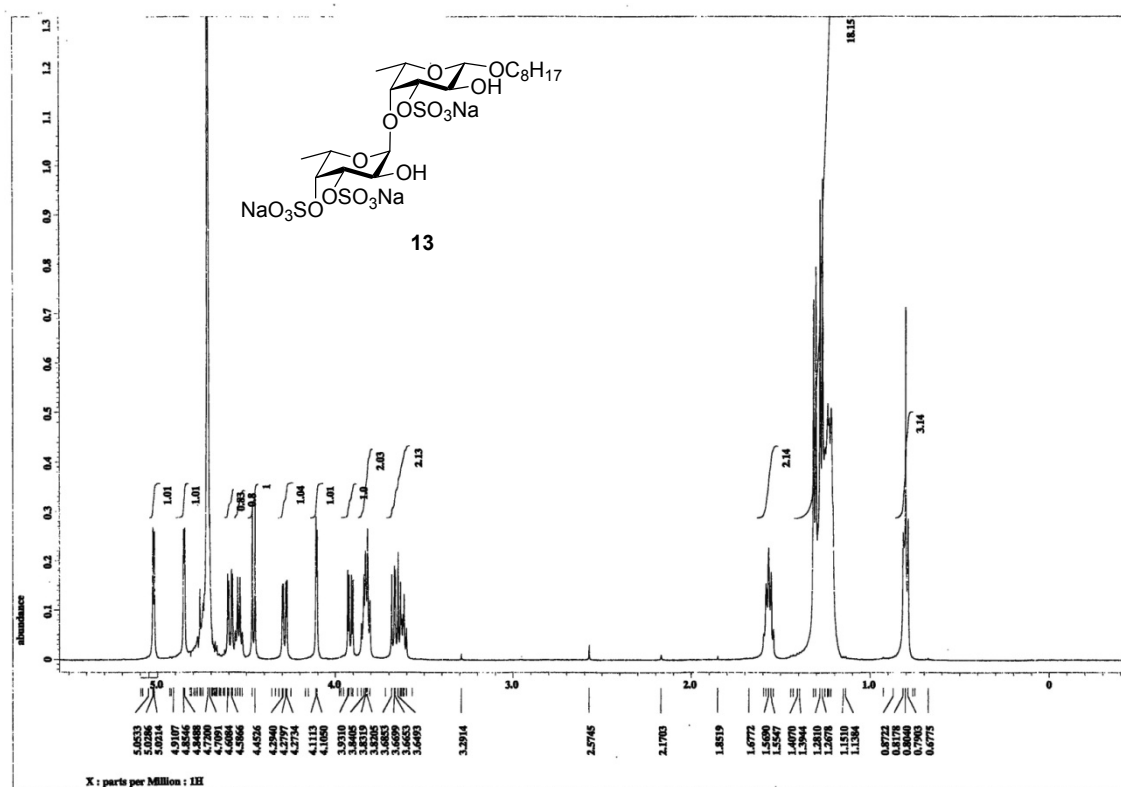


Figure S45 ¹H-NMR spectrum of 13

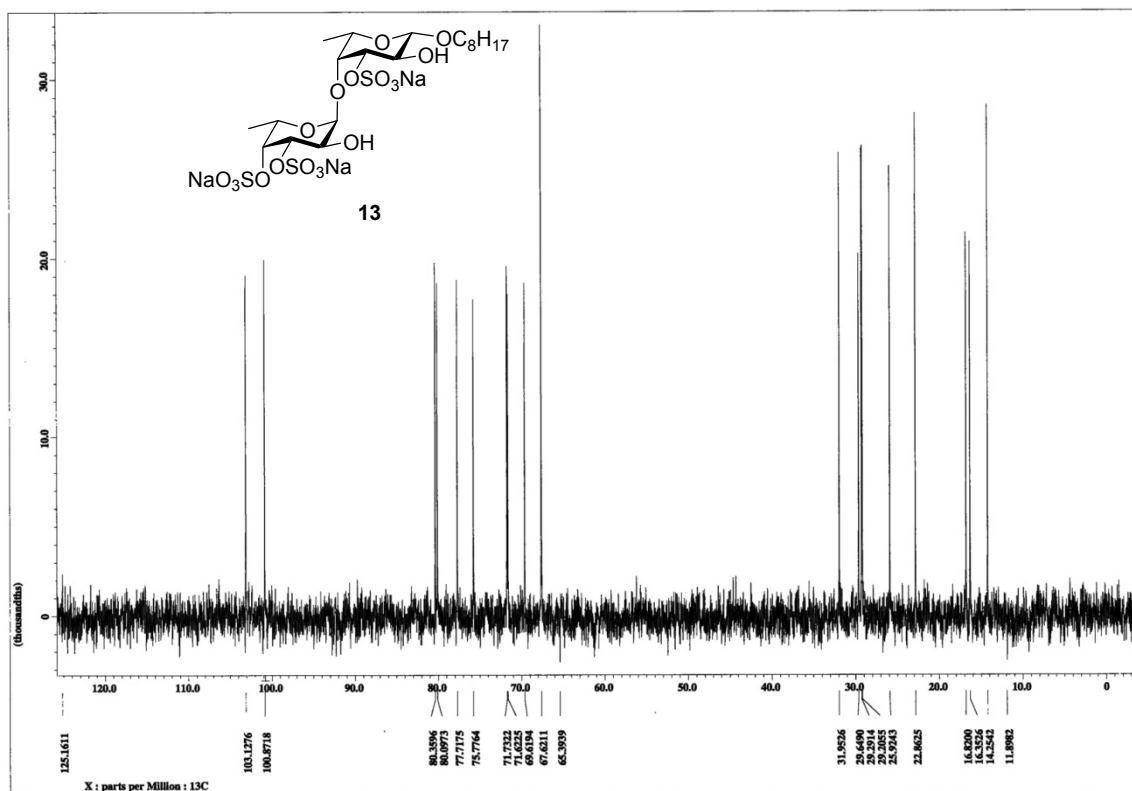


Figure S46 ¹³C-NMR spectrum of 13

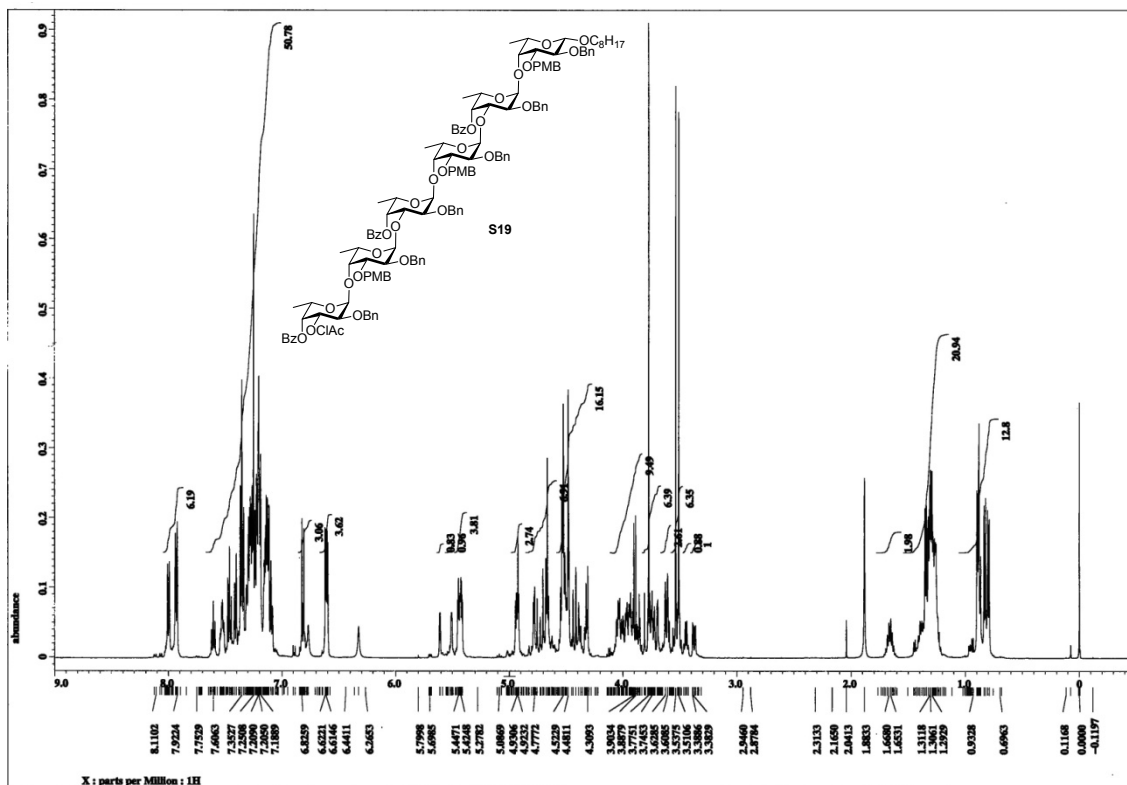


Figure S47 ^1H -NMR spectrum of S19

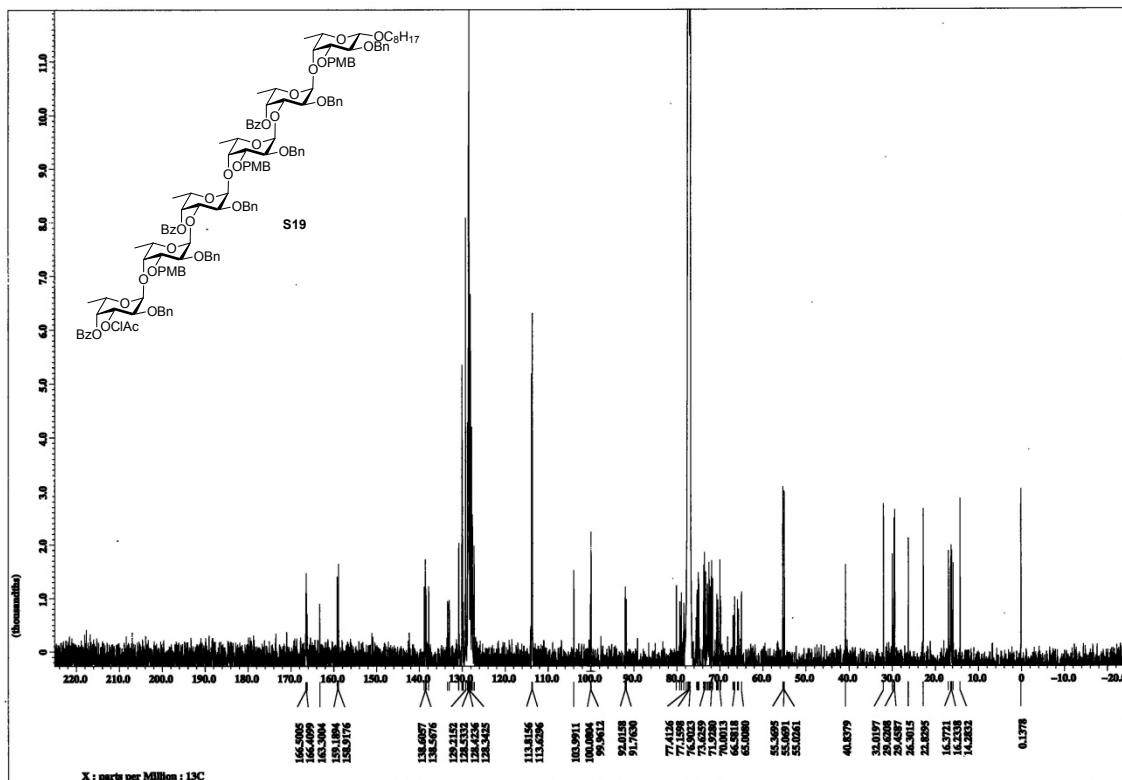


Figure S48 ^{13}C -NMR spectrum of S19

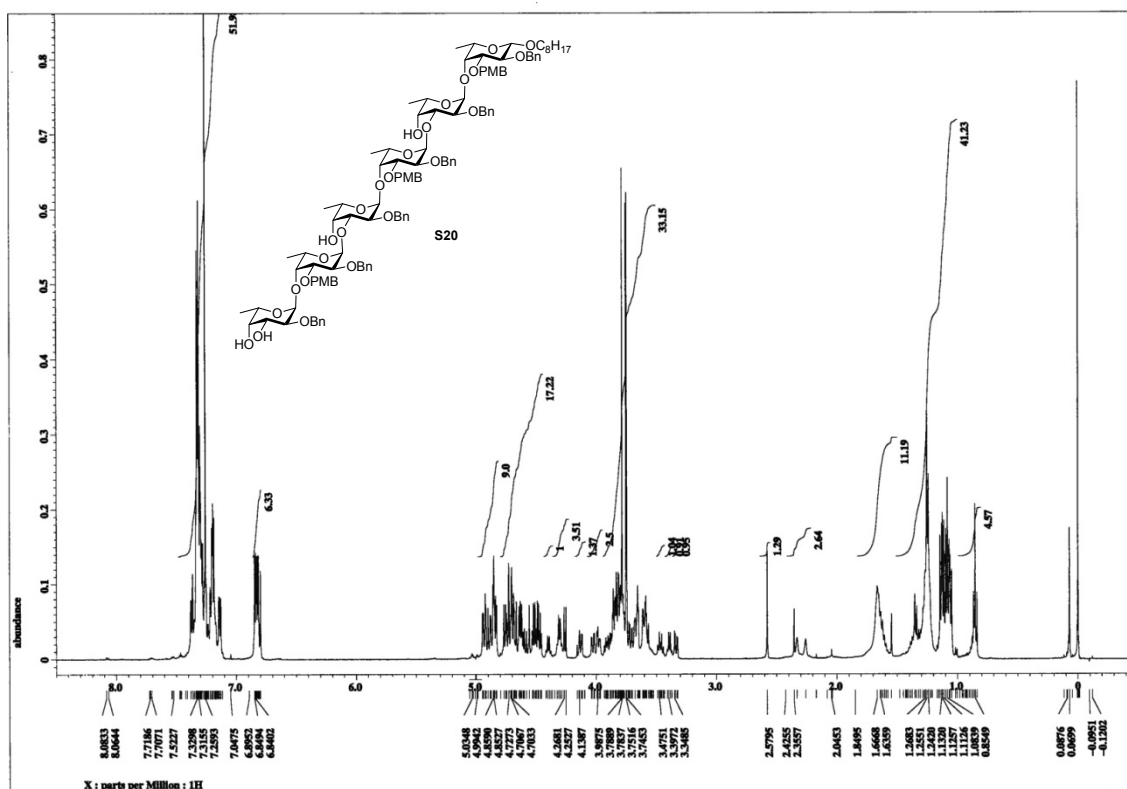


Figure S49 ¹H-NMR spectrum of S20

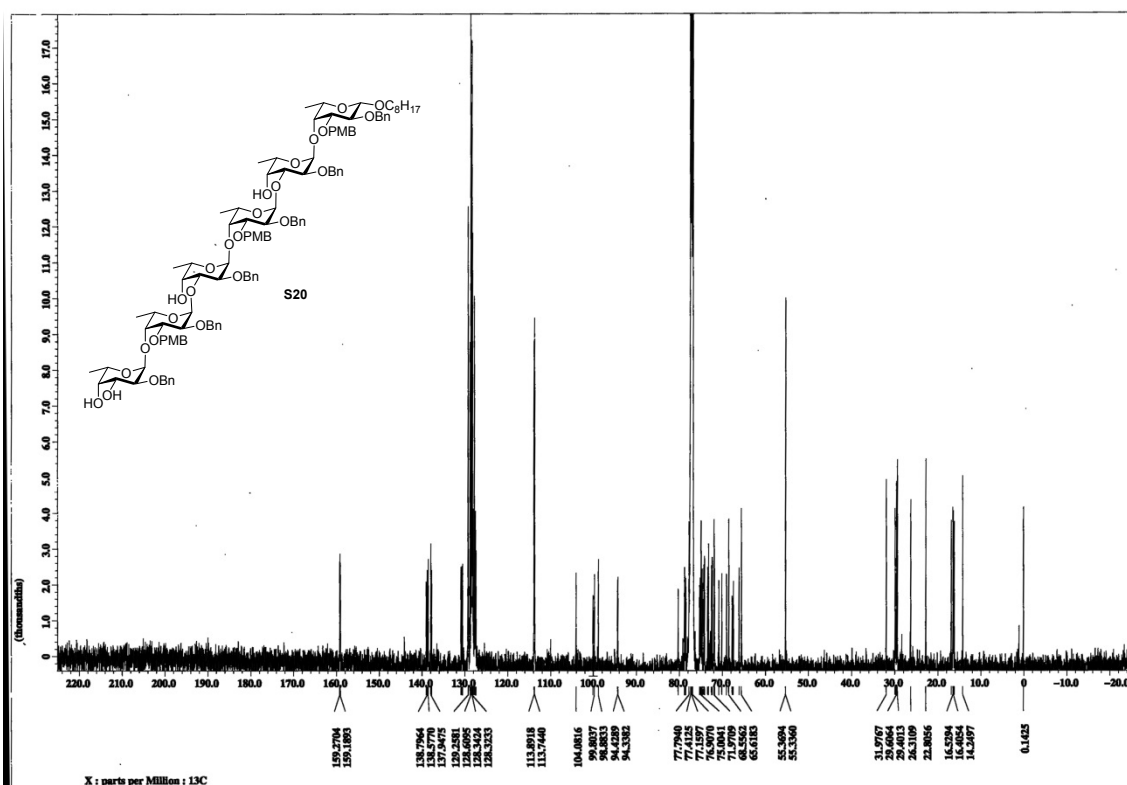


Figure S50 ¹³C-NMR spectrum of S20

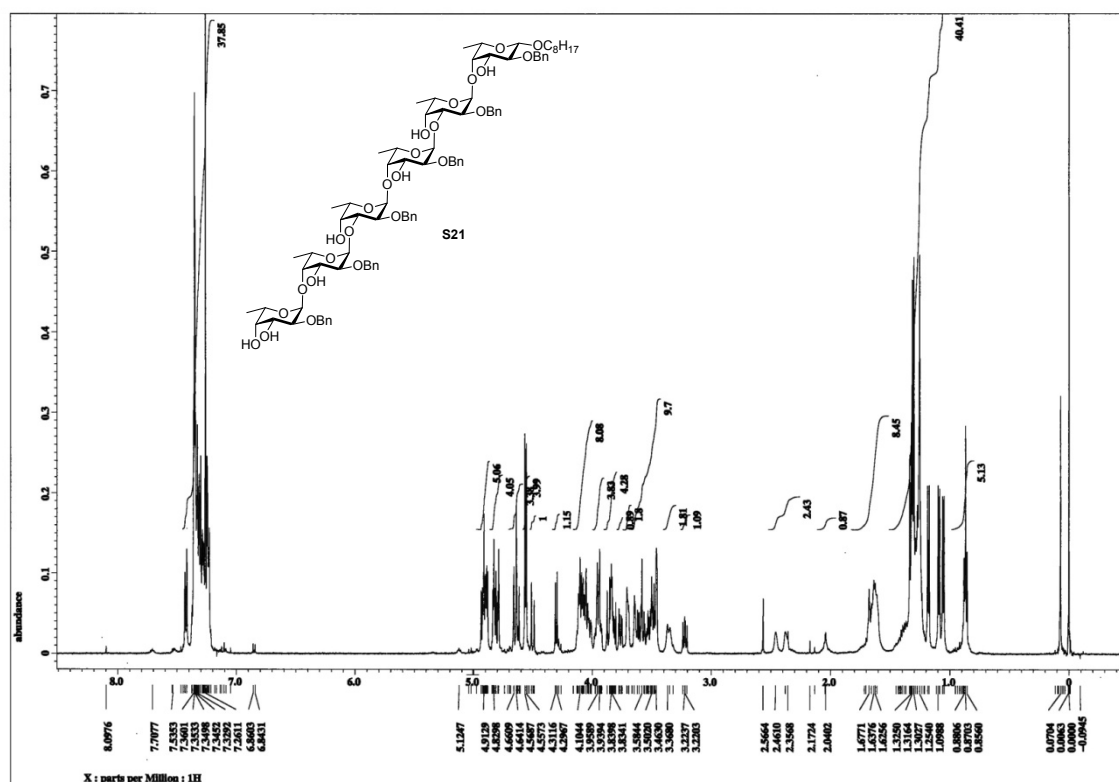


Figure S51 ^1H -NMR spectrum of **S21**

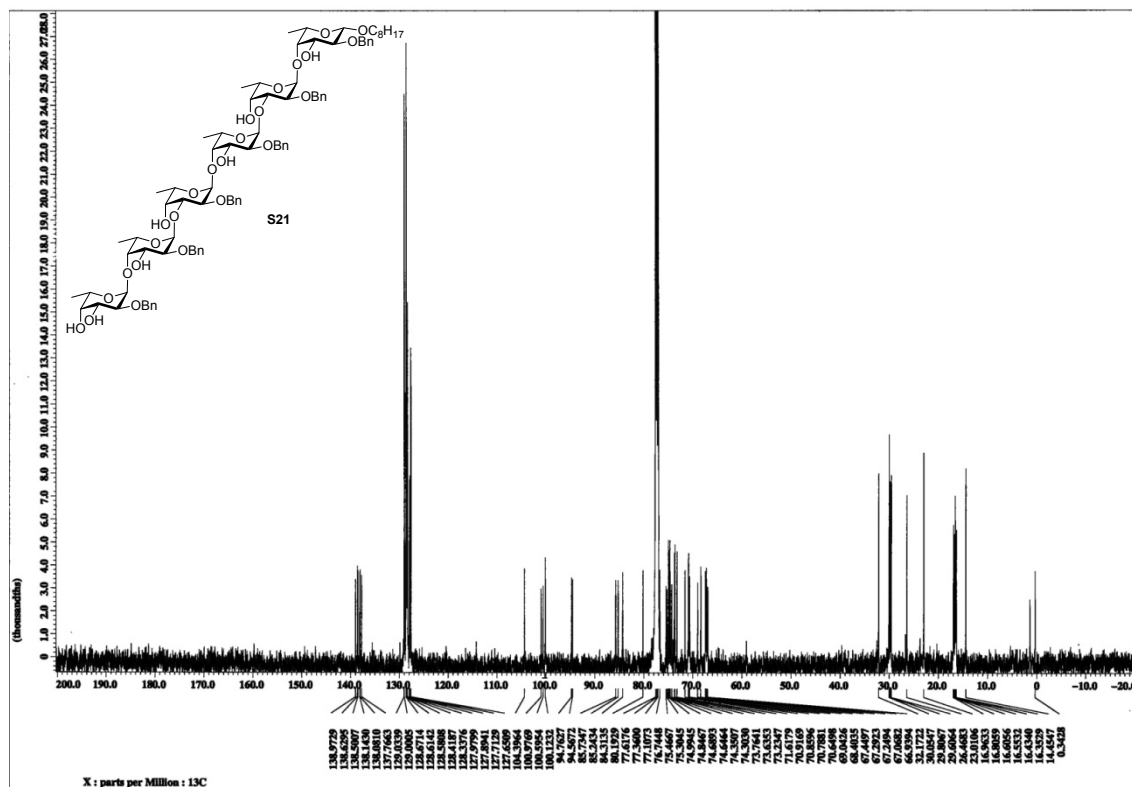


Figure S52 ^{13}C -NMR spectrum of **S21**

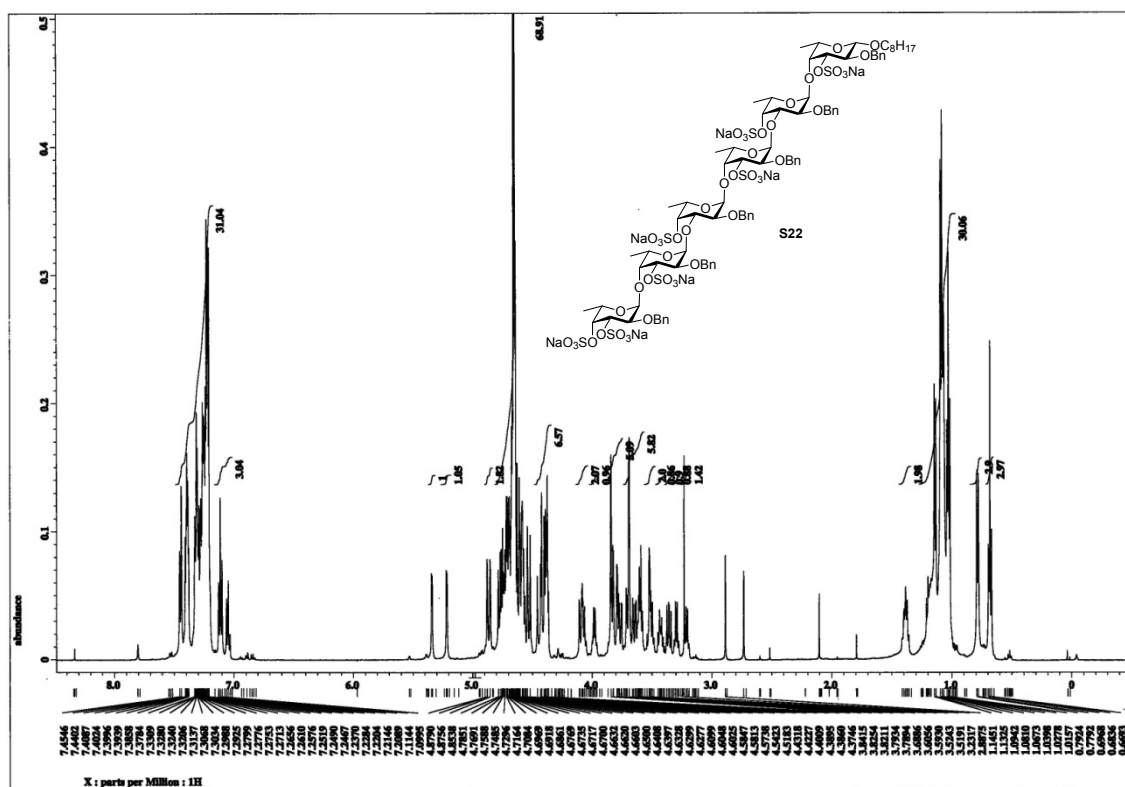


Figure S53 ¹H-NMR spectrum of **S22**

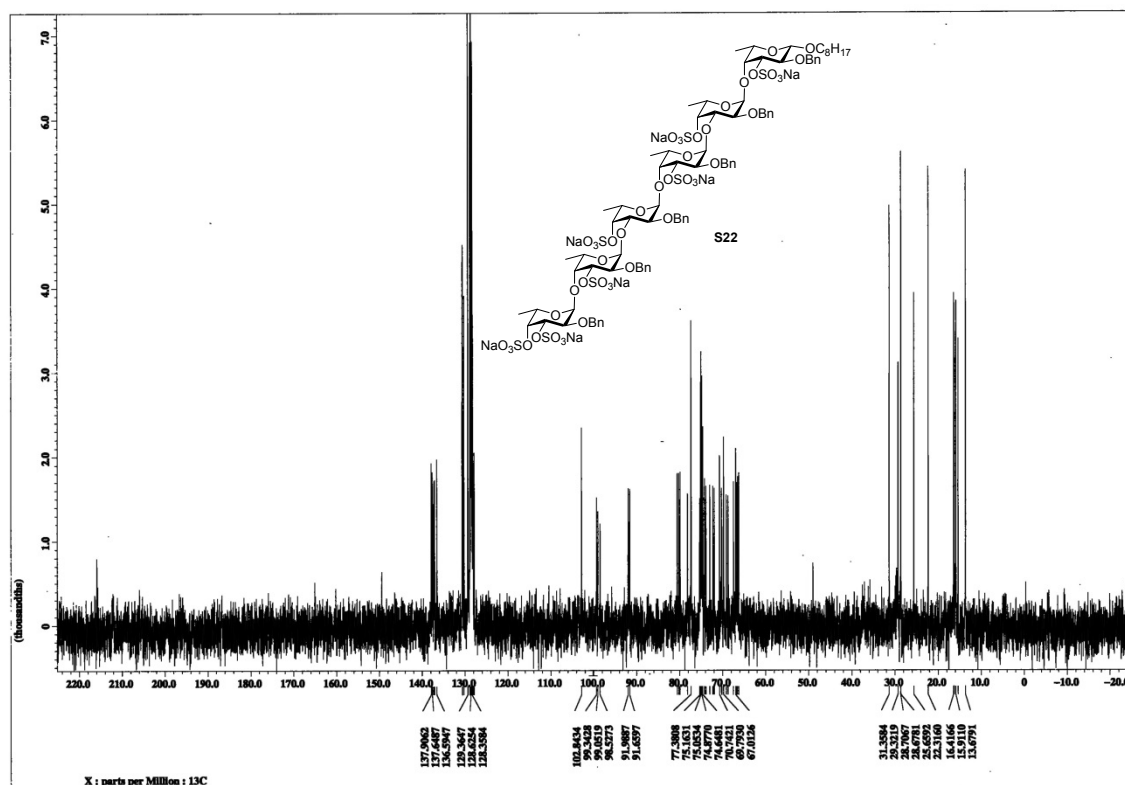


Figure S54 ^{13}C -NMR spectrum of **S22**

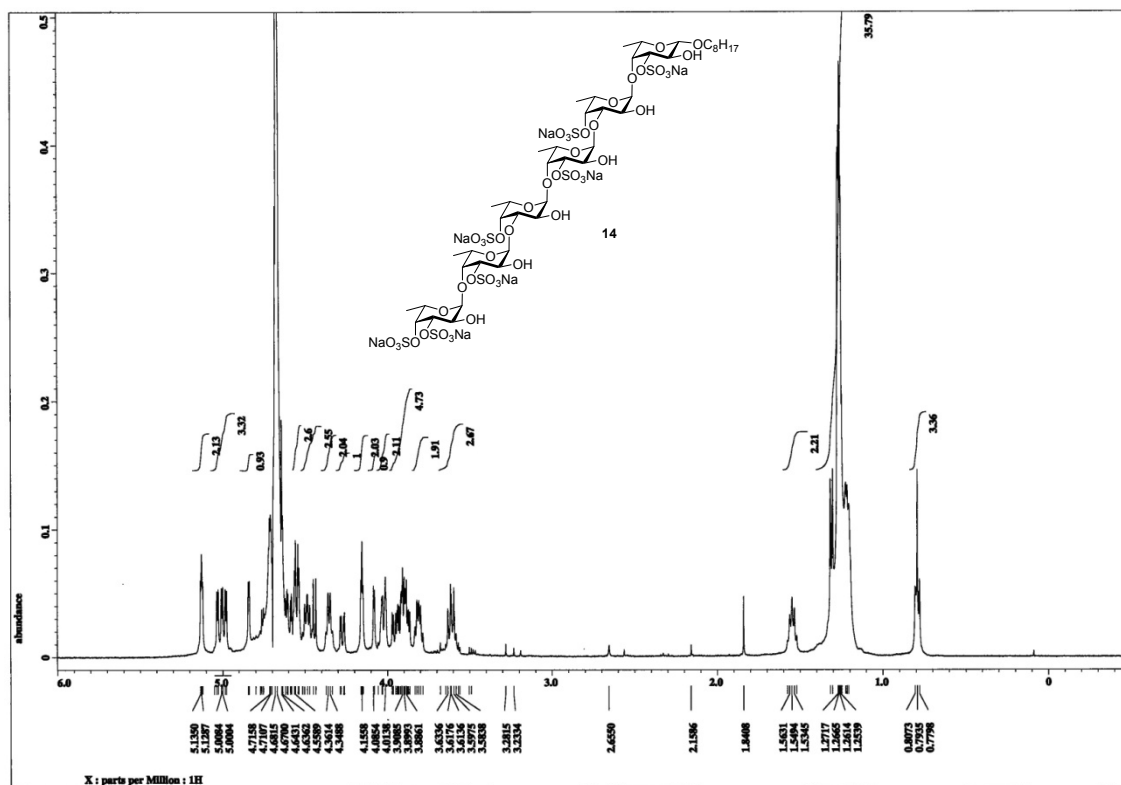


Figure S55 ^1H -NMR spectrum of 14

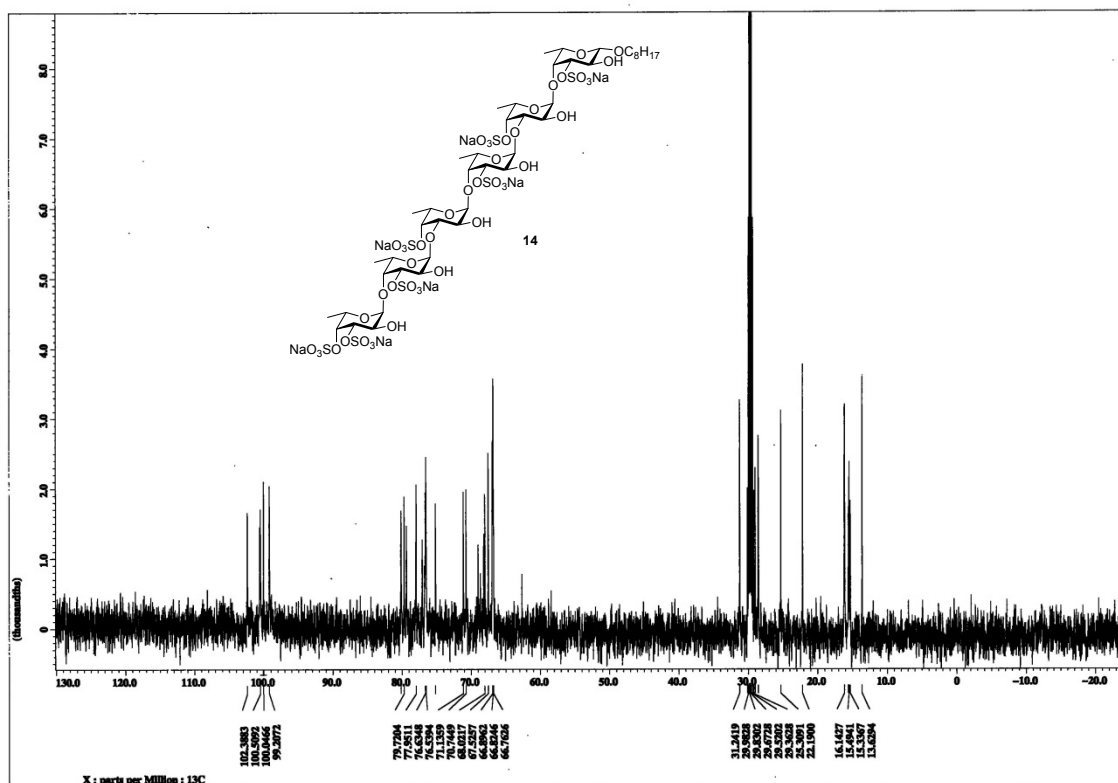


Figure S56 ^{13}C -NMR spectrum of 14