A New Linker for Solid-Phase Synthesis of Heparan Sulfate Precursors by Sequential Assembly of Monosaccharide Building Blocks

Pawel Czechura[a], Nerea Guedes[a], Sebastian Kopitzki[a], Naiara Vazquez[b], Manuel Martin-Lomas[a] and Niels-Christian Reichardt[a]*
[a] Biofunctional Nanomaterials Department, CICbiomaGUNE,
Paseo Miramon 182, 20009 San Sebastian, Spain;
e-mail: nreichardt@cicbiomagune.es

Supporting Information

General Methods

All anhydrous reactions were performed in flame-dried or oven-dried glassware under a positive pressure of dry argon. Air or moisture-sensitive reagents and anhydrous solvents were transferred with oven-dried syringes or cannulae. Purification of compounds was performed on a Biotage SP4 automated flash chromatography system, Biotage AB, Uppsala, Sweden or by conventional flash chromatography using Merck silica gel 60 (63-200 mesh). Size exclusion chromatography was performed on Sephadex LG-20 (Sigma-Aldrich). Pooled glycoside containing fractions were lyophilized on an ALPHA-2-4 LSC freeze-dryer from Christ, Osterode, Germany All solution phase reactions were monitored using analytical thin layer chromatography (TLC) with 0.2 mm pre-coated silica gel aluminum plates 60 F254 (E. Merck). Components were visualized by illumination with a short-wavelength (254 nm) ultra-violet light and/or by charring with vanillin, ceric ammonium molybdate, potassium permanganate, or phosphomolybdate staining solution. All solvents used for anhydrous reactions were distilled. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under Argon. Dichloromethane and acetonitrile were distilled from calcium hydride. Methanol was distilled from calcium sulfate. *N*,*N*-dimethylformamide (DMF) was stored over activated molecular sieves 4Å under argon.

^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded at ambient temperature on a Bruker Avance 500 spectrometer. Deuterated chloroform ($CDCl_3$), methanol (CD_3OD), or water (D_2O) were used as NMR solvents, unless otherwise stated. Chemical shifts are reported in ppm downfield from TMS and corrected using the solvent residual peak or TMS as an internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and br, broad. Low resolution mass spectrometry (LRMS) was performed LCT Time of Flight Premier XE mass spectrometer equipped with electrospray source (Waters) with a pump rate of 5 μL/min using electrospray ionization (ESI) or a Voyager DE-Pro matrix-assisted desorption ionization-time of flight (MALDI-TOF), (Applied Biosystem, Foster City, CA) mass spectrometer operated in the reflectron/positive-ion mode with DHB in MeOH as the MALDI matrix. High resolution mass spectrometry (HRMS) data was acquired on LCT Time of Flight Premier XE mass spectrometer. Samples in CH_2Cl_2/MeOH 1:1 were mixed with Agilent ES tuning mix for internal calibration, and infused into the mass spectrometer at 5 μL/min. Microwave irradiation was performed on Biotage Initiator monomode oven, Biotage AB, Uppsala, Sweden.

Procedure A (preparative cleavage from the resin)

Preparative cleavage of the product from the resin was performed according to Roussel, F., Takhi, M., Schmidt R. R., *J. Org. Chem.* **2001**, *66*, 8540.

To a dry Schlenk flask under Argon, dry resin loaded compound and NaOMe in MeOH (pH=8)/CH_2Cl_2 (1:4) solution were added. The resin was shaken for 2 hours, then filtered and the filtrate was neutralized with Amberlite IR-120 ion acid exchange resin. The cleavage procedure was repeated 2 times and the filtrates were combined and concentrated.

Procedure B (analytical cleavage from the resin)

To a 0.2-0.5 mL Biotage microwave reaction flask, 3-5 mg of resin loaded compound was added. Then NaOMe in MeOH (pH=8)/CH_2Cl_2 (1:4) solution was added and the sealed reaction vessel was heated in microwave at 55ºC for 5 minutes. The crude reaction mixture was analyzed by TLC and MALDI-TOF MS.

Procedure C (Bu_2SnO mediated cleavage from the resin)

To a 0.2-0.5 mL Biotage microwave reaction flask, 3-5mg of resin loaded compound was added. Then 1 eq Bu_2SnO (solution in MeOH) was added and the sealed reaction vessel was heated in microwave at 120ºC for 10 minutes. The crude reaction mixture was analyzed by TLC and MALDI-TOF MS.

***N*-Benzyl-5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentan-1-amine (2)**

To a solution of 5-(benzylamino)pentan-1-ol (**1**) (5.00 g, 25.9 mmol) in dry DMF (25 mL) at 0°C, imidazole (3.52 g, 51.7 mmol) and dimethylthexylsilyl chloride (6.09 mL, 31.0 mmol) were added respectively. The reaction mixture was stirred overnight, then diluted with ether and washed with a saturated solution of ammonium chloride and water. The organic layer was then dried over $MgSO_4$ and concentrated. Flash column chromatography (10% EtOAc/Toluene) afforded compound **2** as a clear oil (6.6 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.15 (5H, m), 3.73 (2H, s), 3.52 (2H, t, *J*=6.5 Hz), 2.58 (2H, t, *J*=6.8 Hz), 1.62-1.51 (1H, m), 1.51-1.41 (4H, m), 1.36-1.24 (2H, m), 0.83 (3H, s), 0.82 (3H, s), 0.78 (6H, s), 0.02 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.58, 128.35, 128.08, 126.83, 62.79, 54.08, 49.46, 34.18, 32.69, 29.88, 25.12, 23.62, 20.36, 18.48, -3.39; HRMS (ESI): Calcd for $C_{20}H_{37}NOSi$ $[M+H]^+$ 336.2723, found 336.2708.

4-(Hydroxymethyl)benzyl 2,2,2-trichloroethyl carbonate (4)

To 1,4-benzene-dimethanol (1.93 g, 14.0 mmol) in dry CH_3CN (50 mL) and pyridine (2.25 mL, 28.0 mmol), a solution of 2,2,2-trichloroethoxycarbonyl-chloride (1.88 mL, 14.0 mmol) in CH_3CN (125 mL) was added dropwise over a period of 3 hours. After 4 hours the reaction was diluted with EtOAc and washed with saturated solution of $CuSO_4$ and water. The organic layer was then dried over $MgSO_4$ and concentrated. Flash column chromatography (30% EtOAc/toluene) afforded **4** as a clear oil (2.23 g, 53%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.33 (4H, m), 5.24 (2H, s), 4.77 (2H, s), 4.71 (2H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.96, 141.63, 133.88, 128.79, 127.18, 94.35, 76.88, 70.44, 64.91; HRMS (ESI): Calcd for $C_{11}H_{11}Cl_3O_4$ $[M+Na]^+$ 334.9621, found 334.9604.

4-(((2,2,2-Trichloroethoxy)carbonyloxy)methyl)benzyl *N*-benzyl *N*-(5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentyl) carbamate (6)

To a solution of 4-(hydroxymethyl)benzyl 2,2,2-trichloroethyl carbonate (**4**) (4.57 g, 14.6 mmol) in CH_2Cl_2 (100 mL) at 0°C, pyridine (2.35 mL, 29.2 mmol) and 4-nitrophenyl-chloroformate (3.52 g, 17.5 mmol) were added. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The solution was then concentrated and the resulting crystals were washed several times with hexanes to remove pyridine. Next, the dried solid was dissolved in DMF and *N*-benzyl-5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentan-1-amine (**2**) (5.87 g, 17.5 mmol) and DIPEA (3.31 mL, 19.0 mmol) were added at 0°C. The reaction mixture was stirred overnight, then diluted with diethyl ether and washed with saturated solution of NH_4Cl. The organic extract was dried over $MgSO_4$ and concentrated. Flash column chromatography (gradient of 10 to 50% EtOAc/hexanes) gave the title product in 79% yield as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.10 (9H, m), 5.31-5.12 (4H, m), 4.79 (2H, s), 4.55-4..47 (2H, m), 3.61-3.50 (2H, m), 3.34-3.16 (2H, m), 1.68-1.41 (5H, m), 1.38-1.22 (2H, m), 0.89 (3H, s), 0.88 (3H, s), 0.85 (6H, s), 0.08 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.59, 156.02, 153.90, 137.87, 137.59, 134.09, 128.59, 128.51, 127.99, 127.68, 127.24, 127.06, 94.32, 76.84, 70.33, 66.60, 62.63, 50.48, 50.19, 47.33, 46.25, 34.16, 32.42, 27.90, 27.49, 25.09, 23.13, 20.34, 18.48, -3.41; HRMS (ESI): Calcd for $C_{32}H_{46}Cl_3NO_6Si$ $[M+Na]^+$ 696,2057, found 696,1990.

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentyl) carbamate (7)

To a solution of 4-(((2,2,2-trichloroethoxy)carbonyloxy)methyl)benzyl benzyl(5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentyl)carbamate (**5**) (6.16 g, 9.12 mmol) in 150 mL of AcOH/THF (1:10) at 0ºC was added freshly activated Zn dust (1.79 g, 27.4 mmol). The reaction mixture was stirred for 4 hours, diluted with EtOAc and the residual zinc was filtered off. The filtrate was concentrated *in vacuo* and after flash column chromatography (gradient 10 to 25% EtOAc/hexanes), compound **6** was obtained as an oil (>95%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.10 (9H, m), 5.24-5.07 (2H, m), 4.75-4.63 (2H, m), 4.56-4.41 (2H, m), 3.61-3.44 (2H, m), 3.33-3.10 (2H, m), 1.71 (1H, s), 1.66-1.38 (5H, m), 1.36-1.15 (2H, m), 0.88 (3H, s), 0.86 (3H, s), 0.83 (6H, s), 0.06 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.93, 128.50, 128.06, 127.79, 127.23, 127.05, 66.85, 65.06, 62.60, 50.18, 47.21, 46.24, 34.17, 32.43, 27.91, 27.52, 25.11, 23.12, 20.34, 18.48, -3.41; HRMS (ESI): Calcd for $C_{29}H_{45}NO_4Si$ $[M+Na]^+$ 522.3016, found 522.2964.

4-((Benzyl(5-hydroxypentyl)carbamoyloxy)methyl)benzyl benzoate (8)

To a cooled solution (0ºC) of **7** (0.958 g, 1.91 mmol) in dry CH_2Cl_2 (6 mL), pyridine (0.46 mL, 5.73 mmol) and benzoyl chloride (0.33 mL, 2.87 mmol) were added and the solution stirred overnight. The mixture was diluted with EtOAc and washed with 1M HCl, saturated solution of $NaHCO_3$ and water. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (1:1 CH_2Cl_2/Hexane) to afford the benzoylated intermediate (1.09 g, 95%).

^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ 8.10-8.09 (2H, d, J = 7.6Hz, aromatic), 7.57-7.24 (12H, m, aromatic), 5.38 (2H, s, CH_2), 5.21 (2H, s, CH_2), 4.52 (2H, s, CH_2), 3.57 (2H, s, CH_2), 1.67 - 1.50 (5H, m, CH_2, TDS), 1.32 (2H, m, CH_2), 0.91 (3H, s), 0.90 (3H, s), 0.86

(6H, s, TDS), 0.09 (6H, s, TDS); ^{13}C NMR (126 MHz, $CDCl_3$, 323K) δ 166.28, 156.42, 138.02, 137.09, 135.84, 132.91, 130.28, 129.67, 128.47, 128.31, 128.21, 128.00, 127.64, 127.22, 66.74, 66.31, 62.57, 50.49, 47.27, 46.41, 34.30, 32.44, 27.75, 25.19, 23.18, 20.39, 18.49, -3.39; HRMS (ESI): Calcd for $C_{36}H_{49}NO_5SiNa$ $[M+Na]^+$ 626.3278, found 626.3289.

HF-pyridine (5 mL) was added to a cooled solution (0ºC) of the intermediate (1.3 g, 2.15 mmol) in dry THF (5 mL). The mixture was stirred overnight then diluted with EtOAc and $NaHCO_3$ (solid) was added. The reaction mixture was then filtered and washed with saturated solution of $NaHCO_3$ and water. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (3:7 EtOAc/hexanes) to afford **8** (0.675 g, 68%).
^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ 8.07-8.06 (2H, d, *J* = 7.6Hz, aromatic), 7.52 - 7.20 (12H, m, aromatic), 5.34 (2H, ps), 5.18 (2H, ps), 4.49 (2H, ps), 3.54 (2H, ps), 3.26 (2H, ps), 2.44 (1H, s), 1.52 (4H, ps**)**, 1.30 (2H, ps); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.05 (qC), 156.12 (qC), 137.68 (qC), 136.71, 135.64, 132.71, 129.94 (qC), 129.38, 128.83, 128.24, 128.08, 127.94, 127.79, 127.00, 66.54, 66.04, 62.06, 50.24, 46.92, 32.02, 27.44, 22.75; HRMS (ESI): Calcd for $C_{28}H_{31}NO_5Na$ $[M+Na]^+$ 484.2100, found 484.2061.

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-((2,3-dimethylbutan-2-yl)dimethylsilyloxy)pentyl) carbamate (9-SP)
To a dry Schlenk flask 500mg of carboxypolystyrene resin (2.19 mmol/g capacity) was added under Argon. The resin was swollen with CH_2Cl_2 for 10 minutes then washed 3 times with CH_2Cl_2. To this resin in 23 mL of CH_2Cl_2, **7** (0.028 g, 0.110 mmol) dissolved in 2 mL of CH_2Cl_2, DIC (0.034 g, 0.548 mmol), and DMAP (0.002 g, 0.022 mmol) were added and the reaction mixture shaken overnight. After complete reaction of the linker with the solid support (determined by TLC), the reaction solution was filtered off and the resulting resin was washed with 3 cycles of CH_2Cl_2, MeOH and CH_2Cl_2. Finally, the resin was washed with 3 times THF and dried under vacuum. Capping of the unreacted carboxylate groups was performed according to Roussel, F., Takhi, M., Schmidt R. R., *J. Org. Chem*. **2001**, *66,* 8540.

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-hydroxypentyl) carbamate (10-SP)

Dry resin (0.50 g) was transferred to a Teflon reaction vessel and swollen with THF (5 mL). Equal volume (5 mL) of HF pyridine (Note: this reagent is extremely toxic!) was added and the reaction mixture was shaken for 3 hours. The reaction mixture was filtered off and the resin was washed 3 times with THF, 3 cycles of MeOH then CH_2Cl_2, and 3 times CH_2Cl_2. The resin was then dried under vacuum.

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-hydroxypentyl) carbamate (10)
Loading of the linker on the solid phase support was determined by cleaving the linker from 0.100 g of the resin according to Procedure A. The loading of 0.2 mmol/g was confirmed based on the obtained weight (7mg, 0.2mmol) of **10**.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.08 (9H, m), 5.22-5.07 (2H, m), 4.67 (2H, m), 4.53-4.43 (2H, m), 3.64-3.38 (2H, m), 3.34-3.10 (2H, m), 2.50-1.90 (2H, m), 1.75-1.05 (7H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.76, 156.34, 140.94, 140.76, 137.86, 136.15,

128.56, 128.42, 128.11, 127.83, 127.34, 127.26, 127.20, 127.08, 67.01, 64.96, 62.58, 50.52, 50.17, 46.94, 46.12, 32.21, 27.83, 27.38, 22.83; HRMS (ESI): Calcd for $C_{21}H_{27}NO_4Na$ $[M+Na]^+$ 380.1838, found 380.1814.

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyloxy)pentyl) carbamate (12-SP)To a dry schlenk flask under Argon, resin loaded with the linker (0.10 g, 0.2 mmol/g), donor **11** (0.146 g, 0.22 mmol) and CH_2Cl_2 (1.5 mL) were added respectively. The resin was shaken for 15 minutes, and the reaction mixture was cooled to 0ºC. TMSOTf (5 μL, 0.022 mmol) was added and the reaction mixture was allowed to warm to room temperature. After 1 hour, the reaction solution was filtered off, washed with 3 times with CH_2Cl_2 and the glycosylation cycle was repeated. The resin was then washed with 3 cycles of CH_2Cl_2 then MeOH, 3 times with CH_2Cl_2 and dried under vacuum.

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyloxy)pentyl) carbamate (12)
Compound **12** (10mg, 79% yield) was obtained by preparative cleavage from 80mg of resin **12-SP** according to Procedure A. ^1H and ^{13}C NMR spectra for this compound were recorded at 50°C to resolve spectra of rotamers. ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.00 (24H, m), 5.14-5.02 (2H, m), 4.80-4.65 (2H, m), 4.64-4.50 (5H, m), 4.49-4.34 (4H, m), 3.95-3.84 (1H, m), 3.82-3.70 (2H, m), 3.70-3.57 (3H, m), 3.57-3.42 (1H, m), 3.35-3.02 (3H, m), 2.75-1.65 (2H, br s), 1.60-1.30 (4H, m), 1.30-1.00 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.52, 141.00, 138.48, 138.41, 138.11, 137.98, 136.19, 128.51, 128.45, 128.28, 128.09, 127.90, 127.77, 127.58, 127.49, 127.28, 126.98, 99.27, 80.35, 75.06, 74.59, 73.50, 71.99, 71.30, 69.31, 68.54, 67.42, 66.96, 64.85, 50.54, 46.39, 28.99, 27.66, 23.32; HRMS (ESI): Calcd for $C_{48}H_{55}NO_9Na$ $[M+Na]^+$ 812.3774, found 812.3718.

5-Aminopentyl α-D-mannopyranoside (13)
To a solution of **12** (40 mg, 0.05 mmol) in MeOH (2 mL) with 10% formic acid, palladium black (40mg) was added and the reaction mixture was stirred overnight under H_2 atmosphere. The reaction mixture was then filtered over Celite, concentrated and the resulting residue was purified by Sephadex column chromatography to afford **13** in quantitative yield.
^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (1H, br s), 4.74 (1H, s), 3.82 (1H, dd, J=4.5, 8.9 Hz), 3.80-3.63 (4H, m), 3.60 (1H, dd, J=9.5, 9.5 Hz), 3.55-3.42 (2H, m), 2.99-2.88 (2H, m), 1.76-1.58 (4H, m), 1.56-1.42 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.54, 101.71, 74.84, 72.79, 72.35, 72.31, 68.81, 68.20, 63.11, 40.81, 30.19, 28.50, 24.48; HRMS (ESI): Calcd for $C_{11}H_{23}NO_6$ $[M+Na]^+$ 288.1423, found 288.1424.

4-(Phenylcarboxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-levulinoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (15)
Idopyranosyl donor **14** (0.106 g, 0.132 mmol), linker acceptor **8** (0.050 g, 0.108 mmol), and activated molecular sieves were suspended in dry CH_2Cl_2 (1 mL) for 1h at room temperature under argon and then cooled to -20ºC. N-iodosuccinimide (NIS) (0.030 g, 0.132 mmol) and trifluoromethanesulfonic acid (TfOH) (2.83 μL, 0.03 mmol) were added and the reaction mixture was allowed to warm to room temperature. After 3h the reaction mixture was quenched with saturated solution of $NaHCO_3$ and solid $Na_2S_2O_3$. The mixture was filtered and washed with saturated solution of $NaHCO_3$, H_2O and brine.

The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (gradient of 95/5 to 50/50 Hexane/EtOAc) to afford **15** (0.100 g, 80%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 - 7.14 (34H, m, aromatic) , 5.35 (2H, ps), 5.19- .18 (3H, m, H-2, CH_2), 5.09 (1H, ps, H-4), 4.97 (1H, ps, H-1), 4.81 (1H, d, *J* = 11.8Hz, CH_2Ph), 4.72 (1H, d, *J* = 11.8Hz, CH_2Ph), 4.48 - 4.41 (m,3H, H-5, CH_2), 3.91 (1H, t, H-3), 3.83 - 3.72 (3H, m, H-6, CH_2), 3.39 - 3.37(1H, m), 3.21 - 3.14 (2H, m), 2.56 - 2.53 (2H; m, CH_2(Lev)), 2.44 - 2.41 (2H; m, CH_2(Lev)), 2.04 (3H, s, CH_3(Lev)), 1.68 - 1.49 (5H, m), 1.33 - 1.25 (2H, m), 1.05 (9H, s, $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.73, 171.96, 166.35, 165.23, 156.60, 156.03 (qC), 137.90, 137.01, 136.88, 135.58, 135.54, 133.33, 133.14, 133.01, 130.04, 129.76, 129.69, 129.66, 129.06, 128.50, 128.38, 128.34, 128.26, 128.19, 127.99, 127.70, 127.65, 127.55, 127.42, 127.20, 127.06, 97.90 (C-1), 73.28 (C-3), 72.13 (CH_2Ph), 68.29 (C-2), 67.80, 67.56 (C-4), 66.72, 66.35 (C-5), 62.66 (C-6), 50.51, 50.20, 47.20, 46.20, 37.76, 29.59, 29.07, 27.98, 27.86, 27.52, 26.72, 23.37, 19.10; HRMS (ESI): Calcd for $C_{69}H_{75}NO_{13}SiNa$ $[M+Na]^+$ 1176.4906, found 1176.4854: $[\alpha]_D^{20}$ = -1.07º (c = 0.8).

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-levulinoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (16)

A solution of **15** (0.020 g) in dry MeOH (0.14 mL) and dibutyltin oxide (0.004 g, 0.017 mmol) was heated under MW irradiation at 120ºC for 40 min. LC-MS analysis of the crude mixture showed the following product distribution: product **16**: 70.5% ; compound with additionally cleaved 2-OBz group: 16.4%, compound with additionally cleaved Lev group: 5.3%; starting material: 7.8%

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 - 7.15 (m, 24H, aromatic), 5.15 (3H, H-2, CH_2), 5.07 (1H, ps, H-4), 4.96 - 4.87 (1H,m, H-1), 4.80 - 4.78 (1H, m), 4.72 - 4.64 (3H, m), 4.48 - 4.39 (3H, m), 3.89 (1H, s, H-3), 3.81 - 3.75 (2H, m, H-6), 3.70 - 3.63 (1H, m), 3.37 - 3.28 (1H, m), 3.21 - 3.12 (2H, m), 2.54 – 2.53 (2H, m, CH_2(Lev)), 2.43 - 2.41 (2H, m, CH_2(Lev)), 2.03 (3H, s, CH_3(Lev)), 1.72 - 1.46 (m, 6H), 1.26 - 1.16 (m, 2H), 1.04 (9H, s, $(CH_3)_3C$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.78, 171.98, 165.30, 156.67, 156.09, 140.90, 137.91, 136.17, 135.59, 135.56, 133.38, 133.15, 129.78, 129.72, 128.50, 128.41, 128.21, 128.09, 127.72, 127.67, 127.57, 127.44, 127.30, 127.10, 127.00, 97.89 (C-1), 73.26 (C-3), 72.13, 68.28 (C-2), 67.54 (C-4), 66.92, 66.36 (C-5), 64.96, 62.64, 50.50, 50.16, 47.13, 46.14, 37.77, 29.09, 28.88, 27.87, 27.51, 26.73, 23.19, 19.12; HRMS (ESI): Calcd for $C_{62}H_{71}NO_{12}SiNa$ $[M+Na]^+$ 1072.4644, found 1072.4539.

4-(Phenylcarboxymethyl)benzyl *N*-benzyl *N*-(5-((3-*O*-benzyl-2-*O*-benzoyl-4-*O*-levulinoyl-α-L-idopyranosyloxy)uronate)pentyl) carbamate (17)

To a cooled solution (0ºC) of **15** (0.076g, 0.065 mmol) in dry THF (3 mL), HF-pyridine (0.3 mL) was added and the solution stirred overnight. The mixture was diluted with EtOAc and $NaHCO_3$ (solid) was added, filtered and washed with saturated solution of $NaHCO_3$ and water. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. The crude was used in the next step without purification. To a solution of the crude intermediate in acetonitrile/water (1/1 v/v, 1 mL), TEMPO (2 mg, 0.013 mmol) and BAIB (46 mg, 0.143 mmol) were added and the reaction mixture was stirred for 4h. The reaction mixture was quenched by the addition of 1M Na_2SO_3 (0.7 mL). The layers were separated and the aqueous layer was acidified with 1M HCl, and extracted 3 times with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and

concentrated. The residue was purified by flash column chromatography (gradient of 80/19/1 to 99/0/1 EtOAc/Hexane/HOAc) to obtain compound **20** as an oil (51 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 - 7.13 (m, 24H, aromatic), 5.35 – 5.32 (3H, m, H-4, CH_2 linker), 5.18 - 5.09 (4H, m, H-1, H-2, CH_2 linker), 4.97 - 4.94 (1H, m, H-5), 4.81 - 4.44 (6H, m), 3.91 (1H, s, H-3), 3.74 - 3.71 (1H, m), 3.52 - 3.46 (1H, m), 3.21 - 3.15 (2H, m), 2.67 - 2.62 (2H, m), 2.51 - 2.42 (2H, m), 2.09 (3H, s), 1.63 - 1.49 (4H, m), 1.32 - 1.27 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.70, 171.52, 170.10, 166.44, 165.14, 156.68 (C carbamato), 156.18 (C carbamato), 137.75, 137.39, 136.75, 135.73, 133.56, 133.06, 130.01, 129.79, 129.67, 129.32, 128.52, 128.44, 128.36, 128.27, 128.04, 127.76, 127.48, 127.27, 127.08, 98.46 (C-1), 72.28 (C-3), 72.14 (CH_2Ph), 68.72, 67.85 (C-4), 66.86, 66.76, 66.38 (C-2), 65.71 (C-5), 50.53, 50.22, 47.11, 46.15, 37.76, 29.55, 28.96, 27.88, 27.32, 23.29; LRMS (ESI): Calcd for $C_{53}H_{55}NO_{14}Na$ $[M+Na]^+$ 952.36, found 952.32; $[\alpha]_D^{20}$ = +2.9º (c = 1.15).

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-levulinoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (18-SP)

To a dry schlenk flask under Argon, resin loaded with the linker (0.50 g, 0.2 mmol/g), donor **14** (0.440 g, 0.550 mmol) and CH_2Cl_2 (10 mL) were added respectively. The resin was shaken for 15 minutes, then NIS (0.160 g, 0.715 mmol) was added and the reaction mixture was cooled to -20ºC. Triflic acid (0.002 μL, 0.015 mmol) was added and the reaction mixture was allowed to warm to room temperature. After 3 hours, the reaction solution was filtered off and resin was washed with 3 cycles of CH_2Cl_2 then MeOH and 3 times with CH_2Cl_2.

4-(Acetoxymethyl)benzyl *N*-benzyl *N*-(5-(2,4-di-*O*-acetyl-3-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (19)

Compound **19** was obtained in 83% overall yield by preparative cleavage (Procedure A) and purification from **18-SP**. Next, the intermediate (0.012 g, 0.014 mmol) was taken up in CH_2Cl_2 (1.5 mL) and treated with pyridine (0.1 mL, 1.3 mmol), acetic anhydride (0.1 mL, 1.0 mmol) and catalytic amount of DMAP. After 12 hours, the reaction mixture was diluted with CH_2Cl_2 and successively washed with saturated solution of $CuSO_4$ and H_2O. The organic phase was then dried over anhydrous $MgSO_4$, filtered and concentrated. Preparative TLC (30% EtOAc/hexanes) afforded compound **19** as a white solid (0.013 g, 96% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.10 (24H, m), 5.21-5.11 (2H, m), 5.08 (2H, s), 5.04-4.95 (1H, m), 4.94-4.88 (1H, m), 4.81-4.71 (3H, m), 4.70-4.64 (1H, m), 4.53-4.41 (2H, m), 4.39-4.31 (1H, m), 3.79-3.70 (3H, m), 3.70-3.60 (1H, m), 3.40-3.26 (1H, m), 3.26-3.08 (2H, m), 2.09 (3H, s), 2.04 (3H, s), 1.97 (3H, s), 1.72-1.42 (4H, m), 1.37-1.17 (2H, m), 1.02 (9H, s);^{13}C NMR (125 MHz, $CDCl_3$) δ 170.85, 170.10, 169.55, 156.62, 156.07, 137.87, 136.89, 135.56, 133.16, 133.07, 129.78, 129.72, 128.53, 128.37, 128.24, 127.98, 127.72, 127.67, 127.63, 127.50, 127.31, 127.27, 127.08, 97.82, 72.69, 71.97, 67.97, 67.76, 67.21, 66.74, 66.03, 65.98, 62.31, 50.52, 50.21, 47.22, 46.21, 29.69, 29.05, 26.72, 23.37, 20.99, 20.86, 19.11; HRMS (ESI): Calcd for $C_{50}H_{61}NO_9SiNa$ $[M+Na]^+$ 870.4013, found 870.3979.

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-levulinoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (20)

Compound **20** was obtained according to cleavage Procedure C. MALDI-TOF MS analysis showed complete retention of all protecting groups. MALDI-TOF MS: Calcd for $C_{62}H_{71}NO_{12}SiNa$ $[M+Na]^+$ 1072.46, found 1072.70.

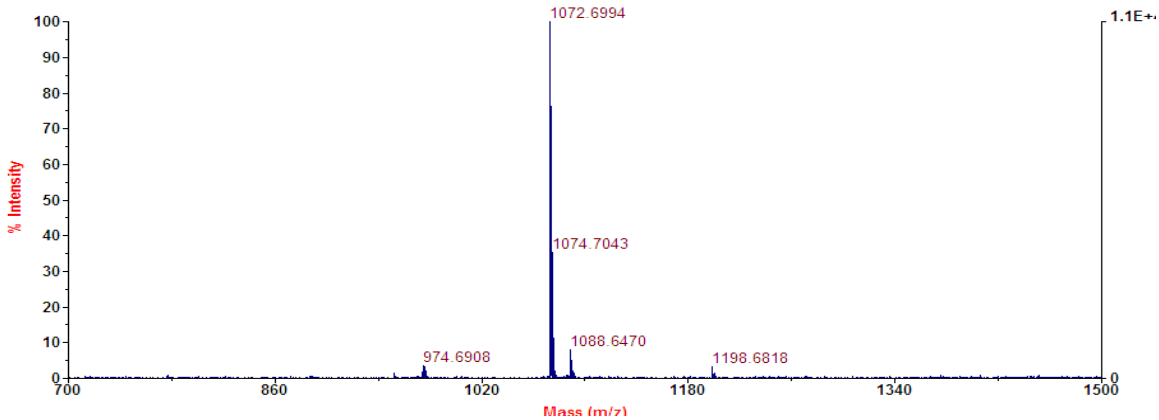


Figure 1 Maldi-Tof MS for glycoconjugate **20**

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (22-SP)

Compound **22-SP** was prepared according to a modified procedure of Roussel, F., Takhi, M., Schmidt R. R., *J. Org. Chem*. **2001**, *66*, 8540.

In a dry Schlenk flask purged with Argon, **18-SP** (0.100 g) was swollen in CH_2Cl_2 (1.5 mL). After 15 minutes of shaking, MeOH (10% by volume) and NH_2NH_2 HOAc (2 equivalents) were added and the agitation was continued for 2 hours. The resin was then filtered washed with CH_2Cl_2 and the cycle was repeated 2 more times. The resin was then filtered, washed with 3 cycles of CH_2Cl_2 then MeOH and 3 times with CH_2Cl_2. Finally, the resin **22-SP** was dried under vacuum.

4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (22)

Compound **22** was obtained according to cleavage Procedure C. MALDI-TOF MS analysis showed complete cleavage of the levulinyl protecting group. MALDI-TOF MS: Calcd for $C_{57}H_{65}NO_{10}SiNa$ $[M+Na]^+$ 974.43, found 975.25.

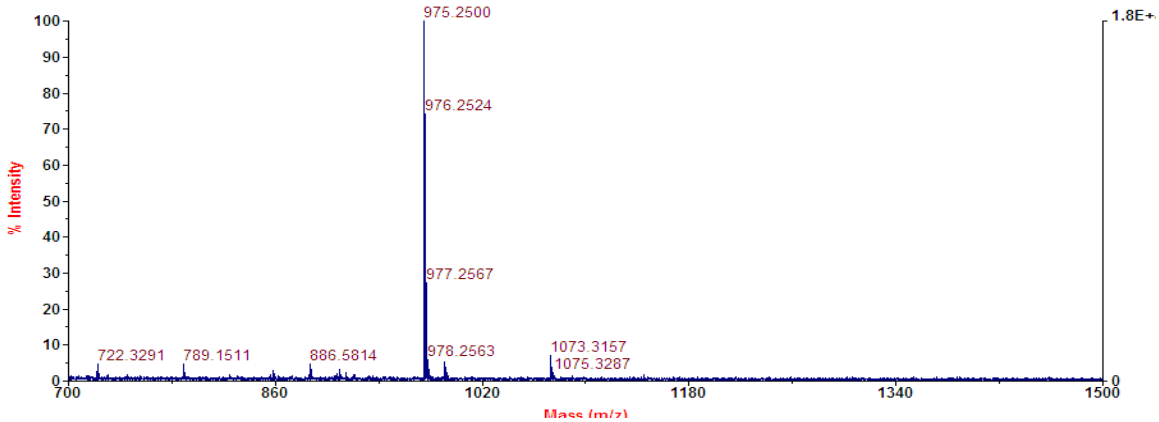


Figure 2 Maldi-Tof MS for glycoconjugate **22**

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-(2-azido-3-*O*-benzyl-6-*O*-benzoyl-2-deoxy-4-*O*-levulinoyl-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (23-SP) and 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-4-*O*-(2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (23)

To a dry Schlenk flask under Argon, **22-SP** (0.5 g, 0.1 mmol), donor **21** (0.320 g, 0.5 mmol) and CH_2Cl_2 (5 mL) were added respectively. The resin was shaken for 15 minutes and then the reaction mixture was cooled to -40ºC. TMSOTf (5 µL, 0.025 mmol) was added and the reaction mixture was allowed to warm to room temperature. After 2 hour, the reaction solution was filtered off, the resin was washed 3 times with dry CH_2Cl_2 and the glycosylation cycle was repeated 4 times. Progress of the glycosylation reaction was monitored by cleavage of a sample aliquot followed by LC-MS analysis. After 5 cycle, LC-MS spectrum indicated 82% conversion of the monosaccharide to the disaccharide derivative. The resin was then washed with 3 cycles of CH_2Cl_2 then MeOH, 3 times with CH_2Cl_2 and dried under vacuum.

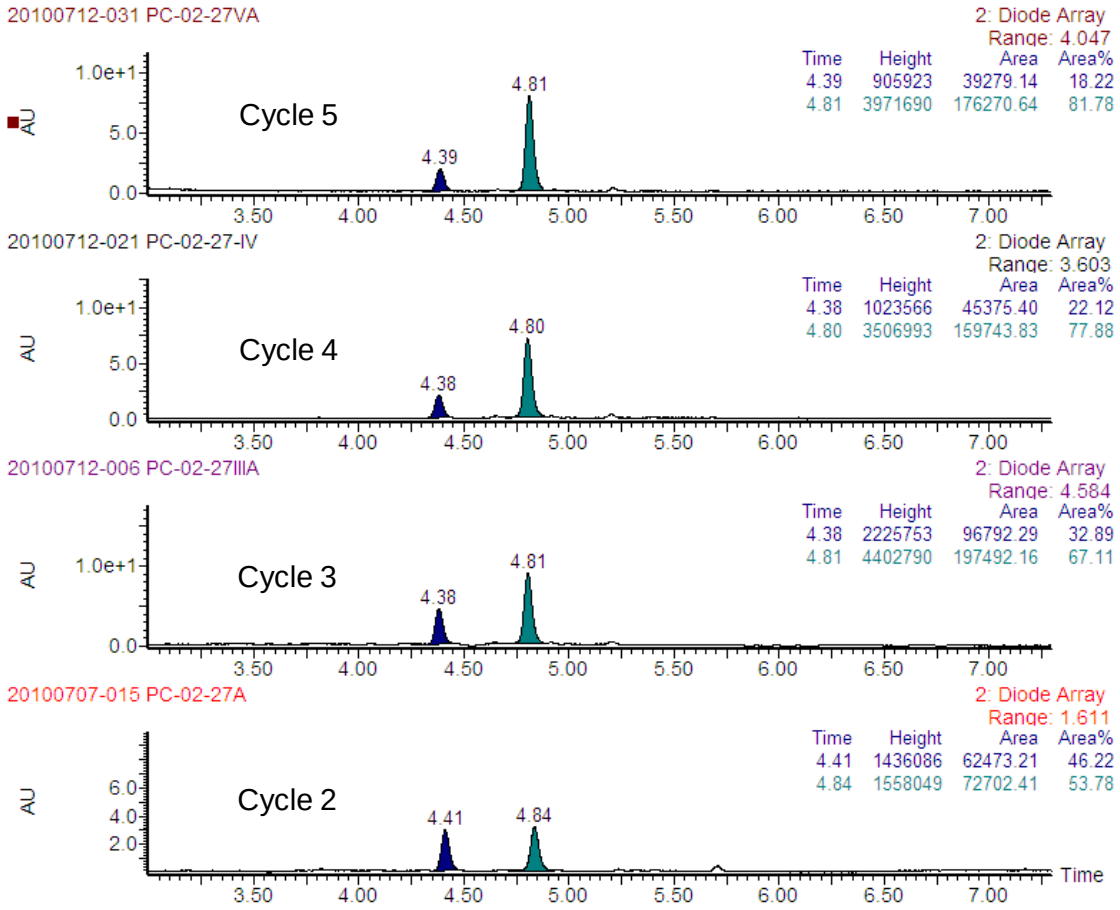


Figure 3 LC-MS data for conversion of monosaccharide **22-SP** (average retention time=4.39 min) to the disaccharide **23-SP** (average retention time=4.81 min) derivative

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-(2-azido-3-*O*-benzyl-6-*O*-benzoyl-2-deoxy-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (24-SP)

Compound **24-SP** was prepared according to a modified procedure of Roussel, F., Takhi, M., Schmidt R. R., *J. Org. Chem*. **2001**, *66*, 8540.

In a dry Schlenk flask purged with Argon, **23-SP** (0.100 g) was swollen in CH_2Cl_2 (1.5 mL). After 15 minutes of shaking, MeOH (10% by volume) and NH_2NH_2 HOAc (2 equivalents) were added and the agitation was continued for 2 hours. The resin was then filtered washed with CH_2Cl_2 and the cycle was repeated 2 more times. The resin was then filtered, washed with 3 cycles of CH_2Cl_2 then MeOH and 3 times with CH_2Cl_2. Finally, the resin **24-SP** was dried under vacuum.

4-(Acetoxymethyl)benzyl *N*-benzyl *N*-(5-(2-*O*-acetyl-3-*O*-benzyl-4-*O*-(4,6-*O*-di-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (24)

Compound **24** was obtained from **23-SP** in 45% overall yield after preparative cleavage according to Procedure A and purification. The intermediate (6mg, 0.005 mmol) was

taken up in CH_2Cl_2 (1.5 mL) and treated with pyridine (0.1 mL, 1.3 mmol), acetic anhydride (0.1 mL, 1.0 mmol), and a catalytic amount of DMAP. After 12 hours, the reaction mixture was diluted with CH_2Cl_2 and successively washed with saturated solution of $CuSO_4$ and H_2O. The organic phase was then dried over anhydrous $MgSO_4$, filtered and concentrated. Preparative TLC (30% EtOAc/hexanes) afforded compound **24** as a white solid (6 mg, 93% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.10 (25H, m), 5.22-5.11 (2H, m), 5.08 (2H, s), 5.01 (1H, dd, J=9.7 Hz), 4.96-4.92 (1H, m), 4.91 (1H, d, J=3.6 Hz), 4.87-4.82 (1H, m), 4.80 (1H, d, J=11.7 Hz), 4.76 (1H, d, J=11.1 Hz), 4.65 (1H, d, J=11.8 Hz), 4.55 (1H, d, J=11.0 Hz), 4.50-4.42 (2H, m), 4.28-4.23 (1H, m), 3.99 (1H, dd, J=4.5, 12.4 Hz), 3.92-3.79 (5H, m), 3.78-3.72 (1H, m), 3.69-3.59 (3H, m), 3.40 (1H, dd, J=3.6, 10.2 Hz), 3.36-3.26 (1H, m), 3.26-3.10 (2H, m), 2.09 (6H, s), 1.94 (3H, s), 1.88 (3H, s), 1.70-1.45 (4H, m), 1.35-1.20 (2H, m), 1.04 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.84, 170.49, 170.05, 169.27, 156.60, 156.06, 137.75, 137.38, 136.89, 135.62, 135.46, 133.14, 132.97, 129.89, 129.83, 128.53, 128.35, 127.99, 127.79, 127.64, 127.35, 127.28, 127.09, 97.84, 95.91, 77.99, 74.94, 72.25, 72.06, 71.44, 69.71, 68.51, 67.87, 67.59, 66.74, 65.97, 63.34, 63.03, 61.70, 50.51, 50.19, 47.19, 46.19, 29.69, 29.08, 26.79, 23.40, 20.99, 20.82, 20.66, 20.59, 19.14.; HRMS (ESI): Calcd for $C_{71}H_{84}N_4O_{17}SiNa$ $[M+Na]^+$ 1315.5498, found 1315.5516.

Resin bound 4-(Hydroxymethyl)benzyl *N*-benzyl *N*-(5-(3-*O*-benzyl-2-*O*-benzoyl-4-*O*-(2-azido-3-*O*-benzyl-4-O-(3-*O*-benzyl-2-*O*-benzoyl-6-*O*-*tert*-butyldiphenylsilyl-4-*O*-levulinoyl–α-L-idopyranosyl)-6-*O*-benzoyl-2-deoxy-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (26-SP)

To a dry Schlenk flask purged with Argon, **24-SP** (0.15 g, 0.03 mmol), donor **25** (0.128 g, 0.15 mmol) and CH_2Cl_2 (2 mL) were added. The resin was shaken for 15 minutes and then the reaction mixture was cooled to -40ºC. TMSOTf (2 μL, 0.007 mmol) was added and the reaction mixture was allowed to warm to room temperature. After 2 hours, the reaction solution was filtered off, the resin was washed 3 times with dry CH_2Cl_2 and the glycosylation was repeated 3 times under the same conditions. Progress of the glycosylation reaction was monitored by analytical cleavage followed by LC-MS analysis. After cycle 4, LC-MS spectrum indicated 53% conversion of the disaccharide to the trisaccharide derivative. The resin was then washed with 3 cycles of CH_2Cl_2 then MeOH, 3 times with CH_2Cl_2 and dried under vacuum.

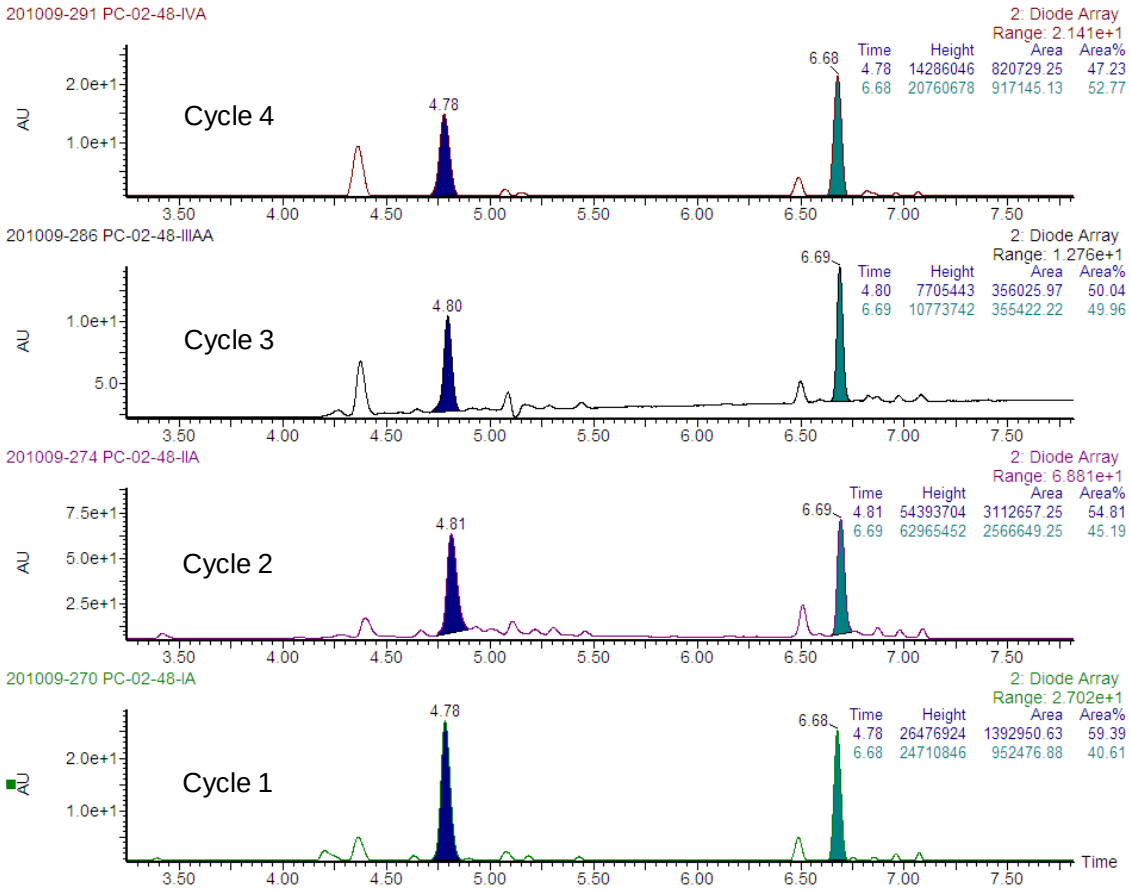


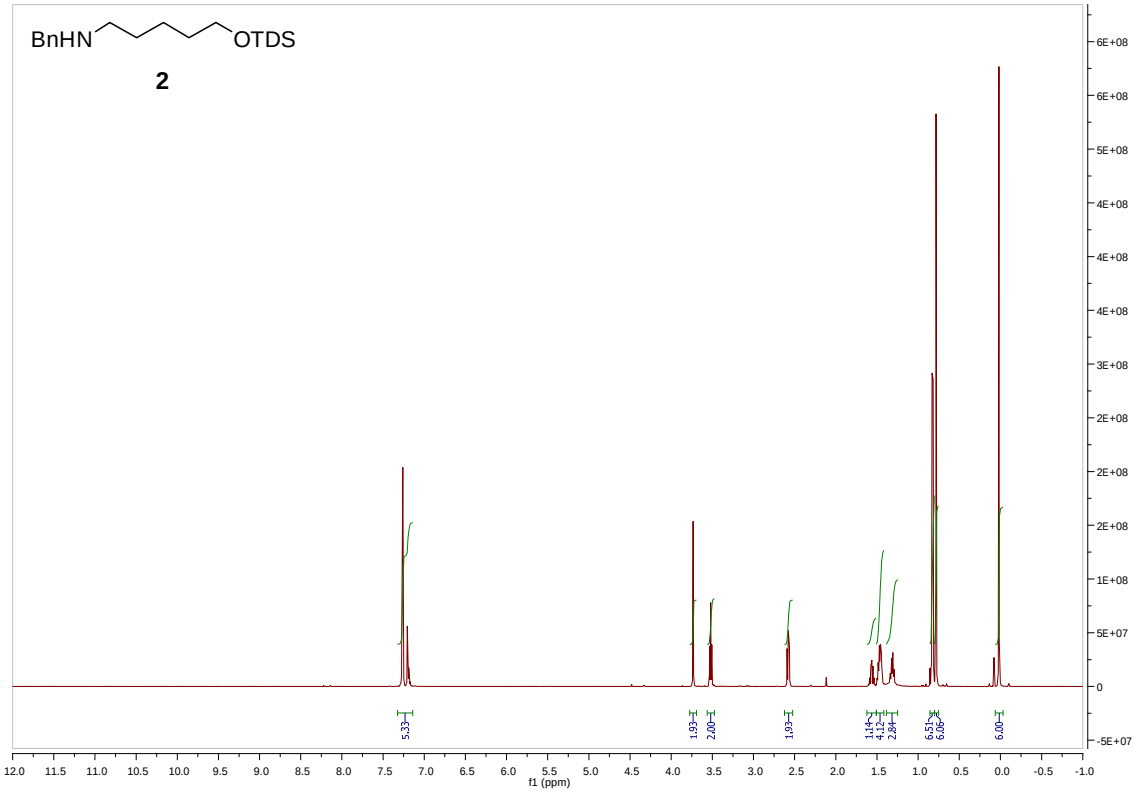
Figure 4 LC-MS data for conversion of disaccharide **23-SP** (average retention time=4.39 min) to trisaccharide **26-SP** (average retention time=6.68 min) derivative

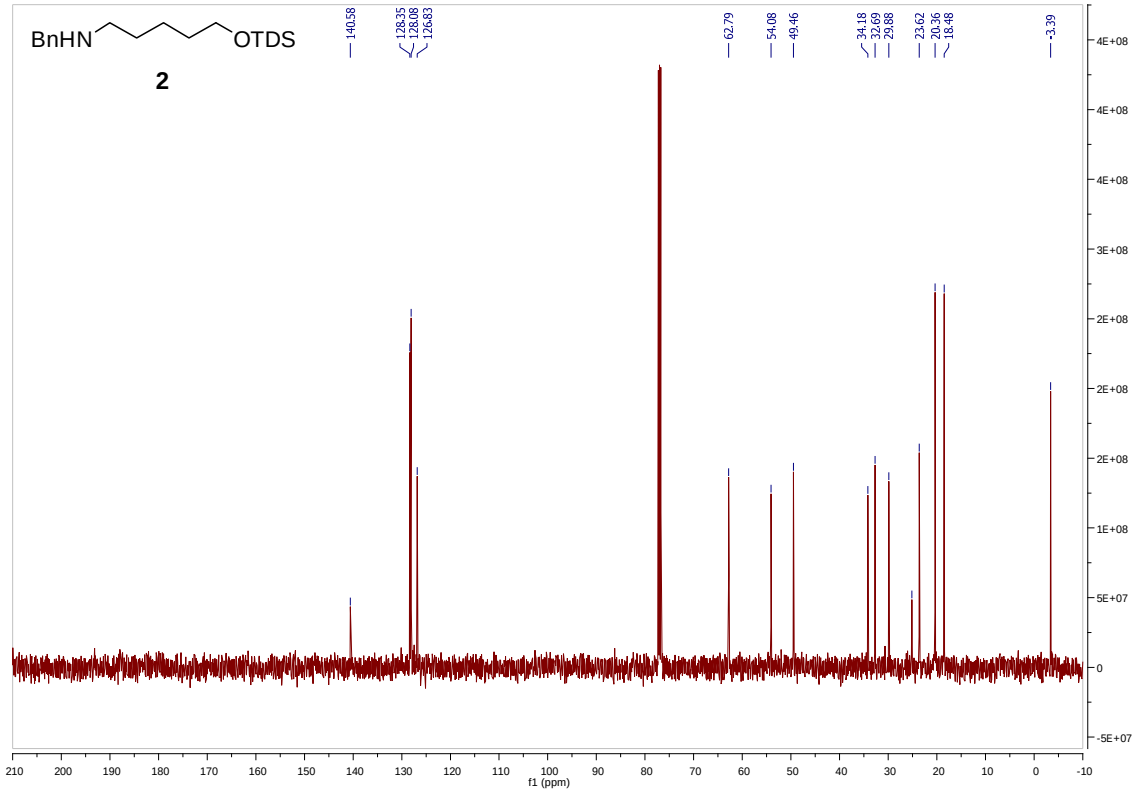
4-(Acetoxymethyl)benzyl *N*-benzyl *N*-(5-(2-*O*-acetyl-3-*O*-benzyl-4-*O*-(6-*O*-acetyl-2-azido-3-*O*-benzyl-4-*O*-(2,4-di-*O*-acetyl-3-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyl)-2-deoxy-α-D-glucopyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-α-L-idopyranosyloxy)pentyl) carbamate (27)

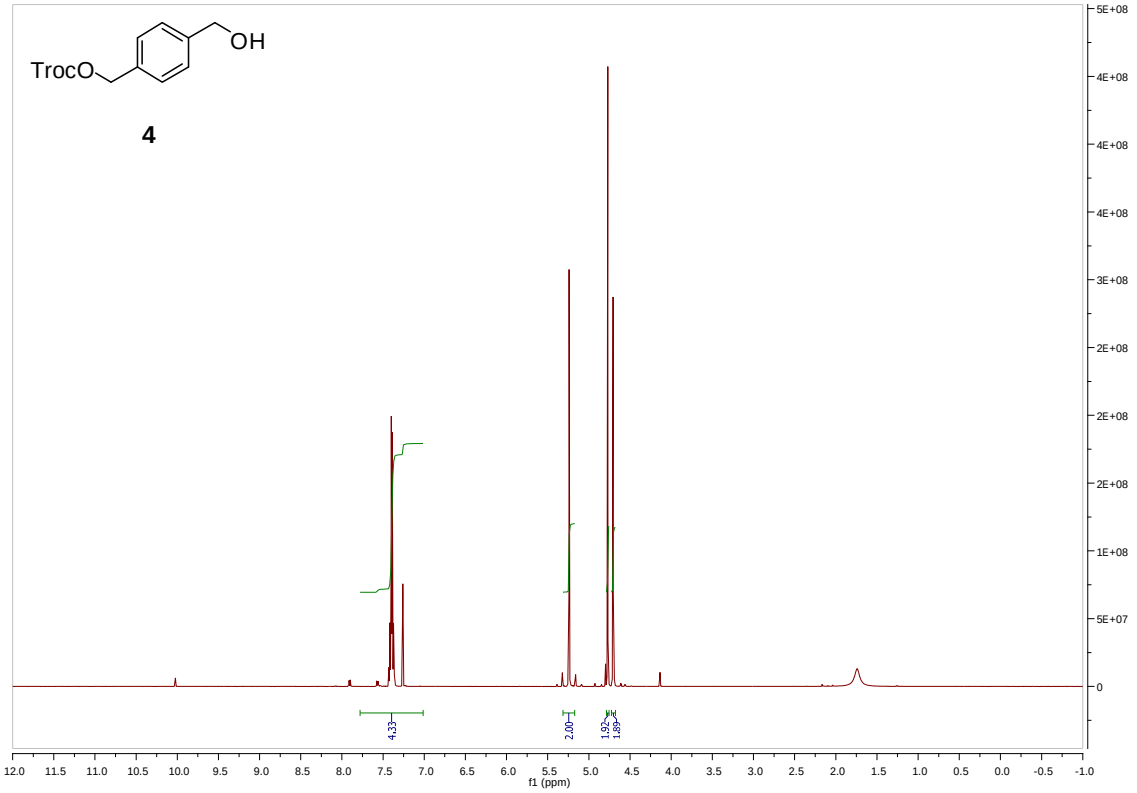
Compound **27** was obtained in 10% overall yield by preparative cleavage (Procedure A) and purification from **26-SP**. Next, the intermediate (4mg, 0.002 mmol) was taken up in CH_2Cl_2 (1.5 mL) and treated with pyridine (0.1 mL, 1.3 mmol), acetic anhydride (0.1 mL, 1.0 mmol), and catalytic amount of DMAP. After 12 hours, the reaction mixture was diluted with CH_2Cl_2 and successively washed with saturated solution of $CuSO_4$ and H_2O. The organic phase was then dried over anhydrous $MgSO_4$, filtered and concentrated. Preparative TLC (30% EtOAc/hexanes) afforded compound **27** as a white solid (4mg, 95% yield).

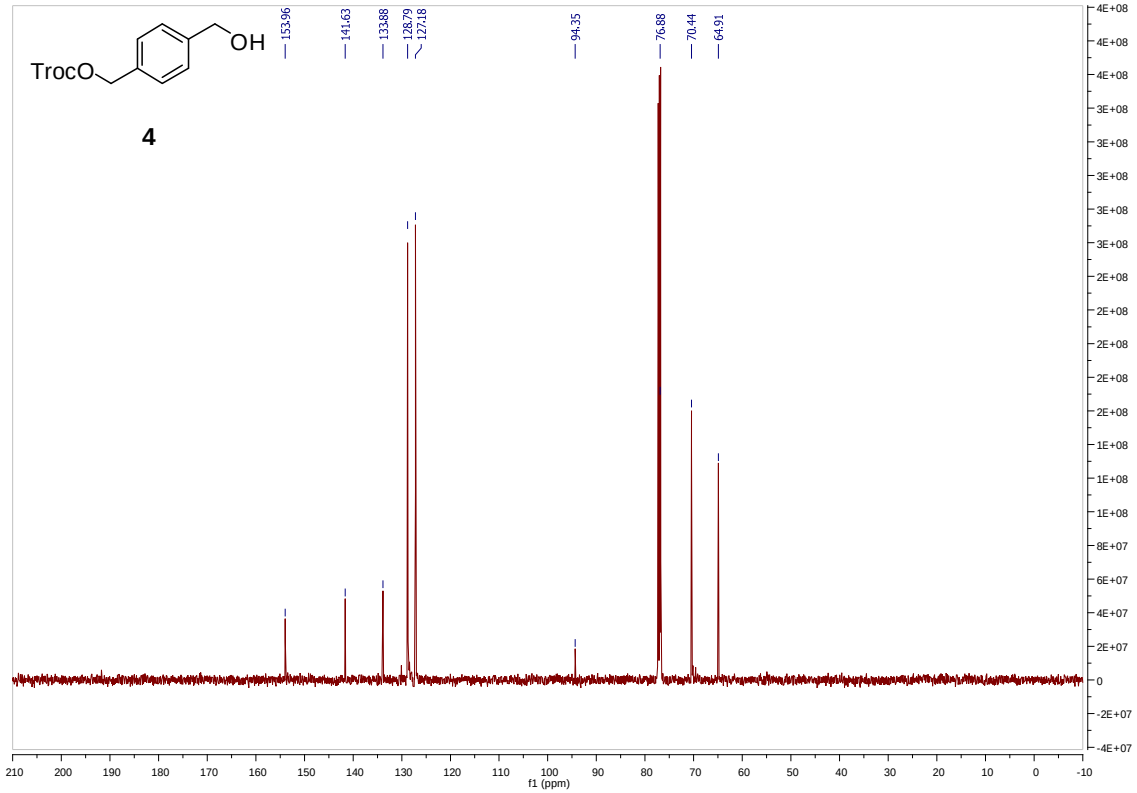
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.09 (44H, m), 5.21-5.11 (2H, m), 5.08 (2H, s), 5.02-4.98 (2H, m), 4.95-4.81 (5H, m), 4.79-4.60 (4H, m), 4.55-4.41 (4H, m), 4.22-4.00 (4H, m), 3.94-3.80 (3H, m), 3.80-3.73 (3H, m), 3.73-3.57 (5H, m), 3.37-3.08 (4H, m), 2.09 (3H, s), 2.03 (3H, s), 1.98 (3H, s), 1.92 (3H, s), 1.90 (3H, s), 1.70-1.40 (4H, m), 1.35-1.20 (2H, m), 1.06 (9H, s), 1.01 (9H, s); ^{13}C NMR shift values taken from HSQC δ 135.56, 135.51, 129.85, 129.69, 128.32, 127.90, 127.85, 127.82, 97.90, 97.77, 96.81, 79.16, 75.40, 75.33, 74.30, 73.23, 72.79, 72.48, 72.34, 69.79, 68.95, 68.51, 68.42, 67.78, 67.55,

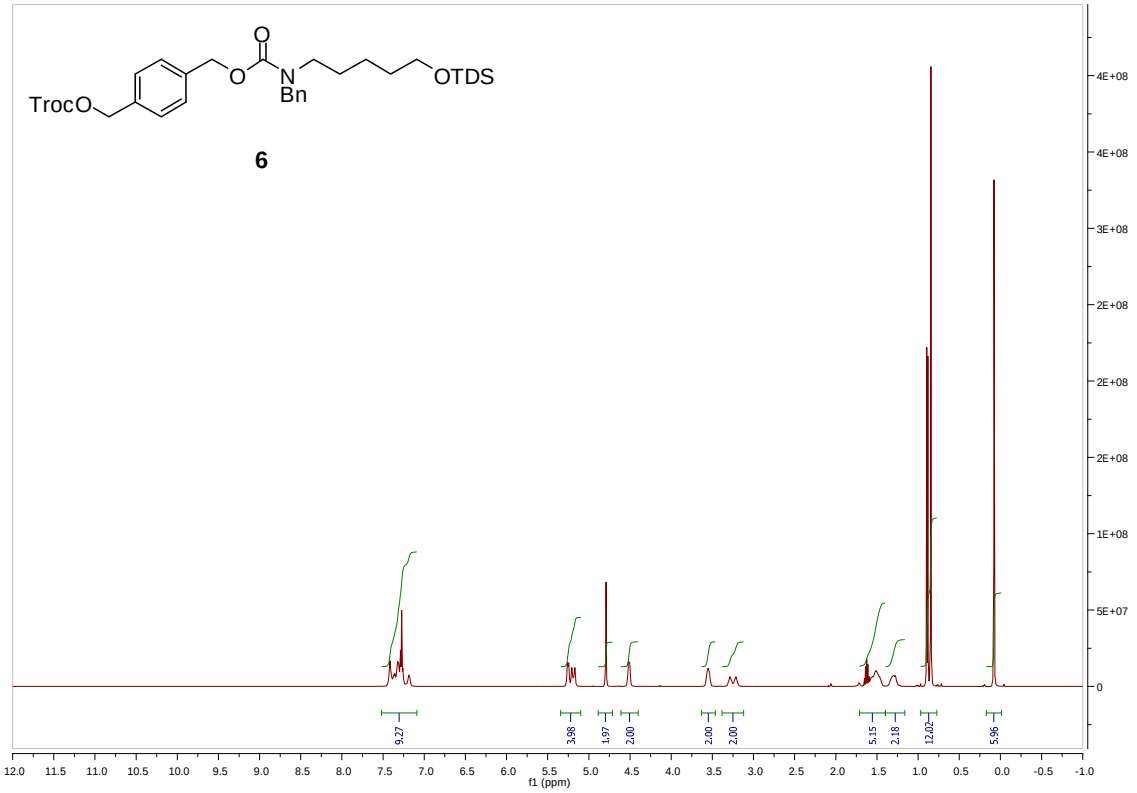
66.69, 66.63, 66.57, 65.88, 63.84, 63.74, 63.36, 62.40, 62.16, 61.82, 61.87, 50.33, 47.16, 46.07, 29.57, 29.19, 26.94, 26.87, 23.00, 21.17, 21.12, 21.01; HRMS (ESI): Calcd for $C_{102}H_{120}N_4O_{23}Si_2Na$ $[M+Na]^+$ 1847.7780, found 1847.7733.

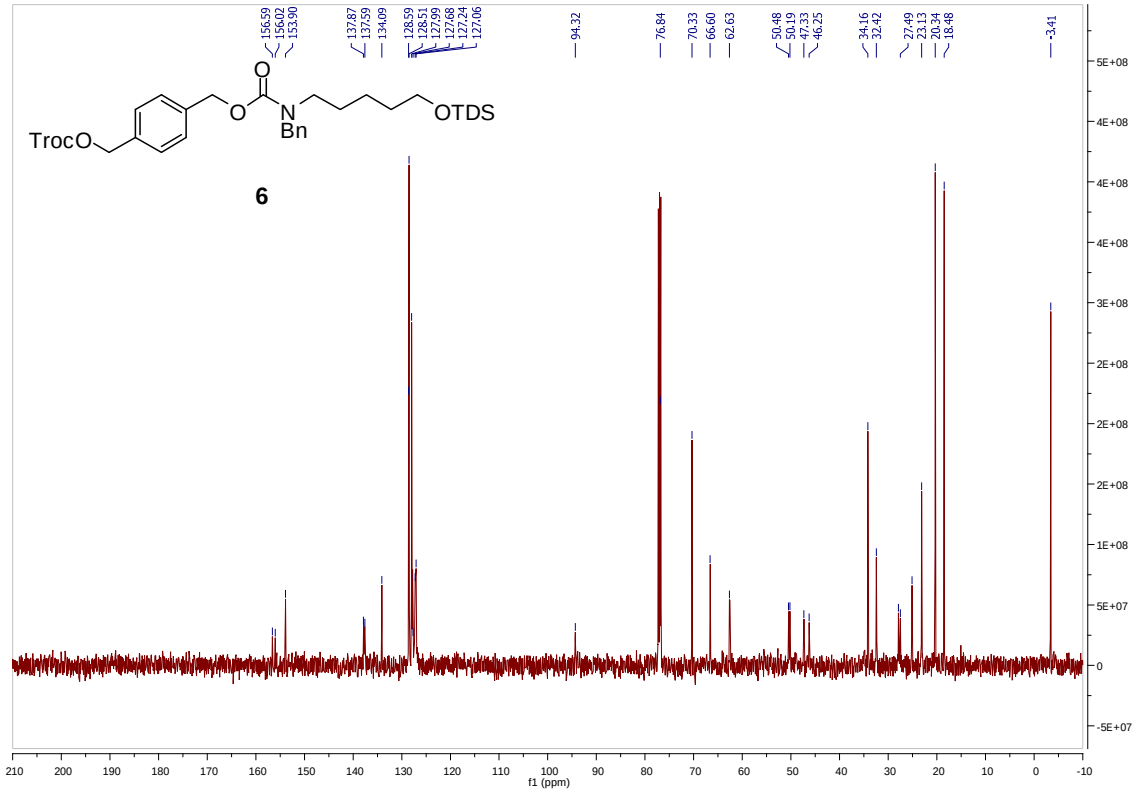

BnHN
OTDS
2
f1 (ppm)

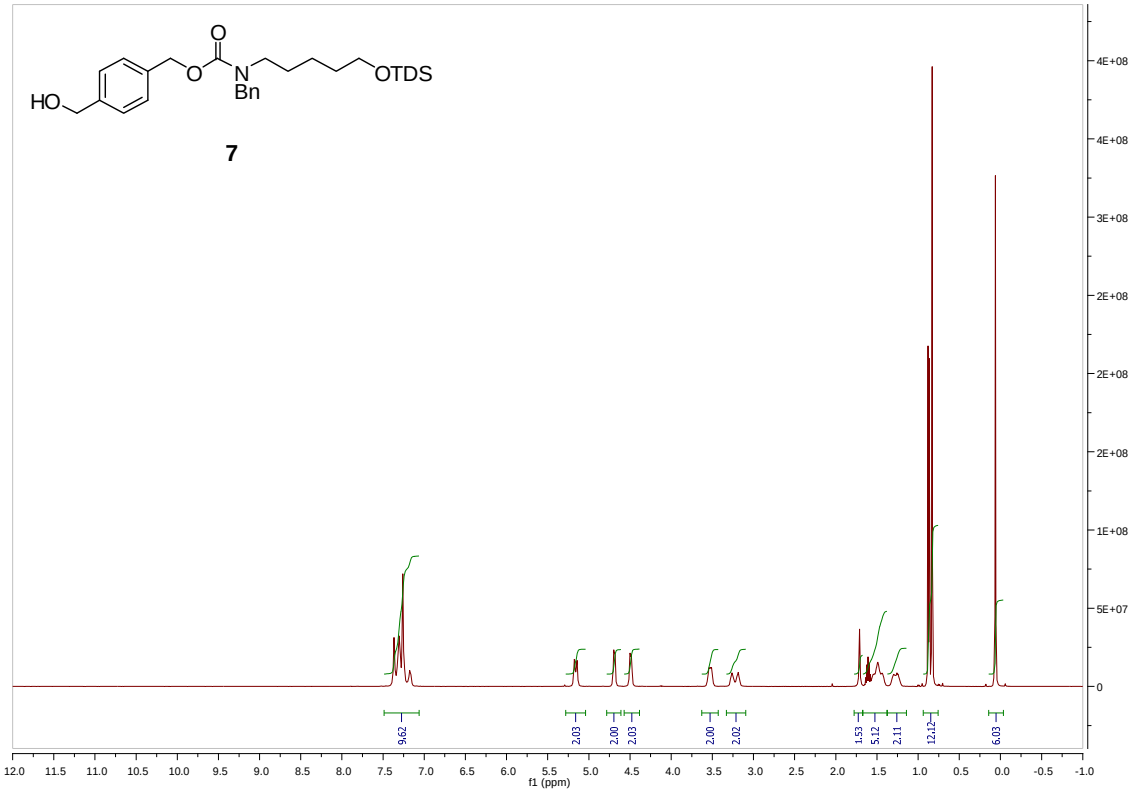

BnHN
OTDS
2
140.58
128.35
128.08
126.83
62.79
54.08
49.46
34.18
32.69
29.88
23.62
20.36
18.48
-3.39
f1 (ppm)

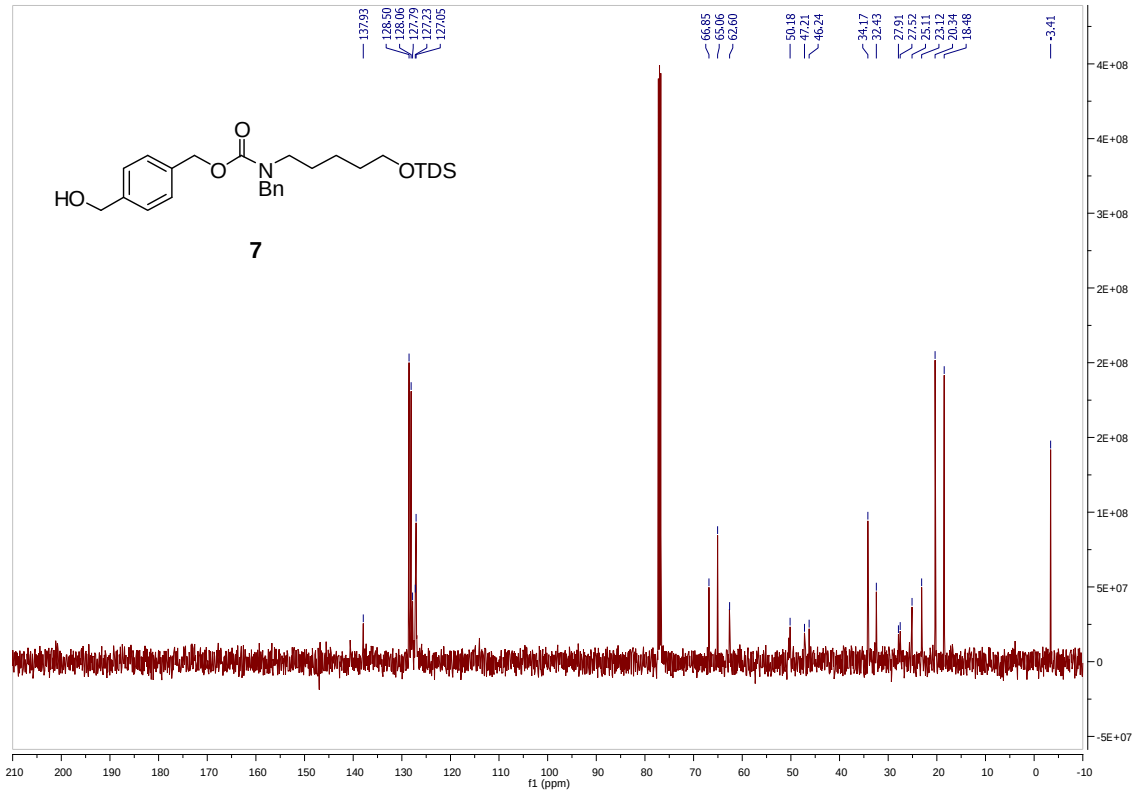

TrocO
OH
4
4.33
2.00
1.92
1.89
f1 (ppm)

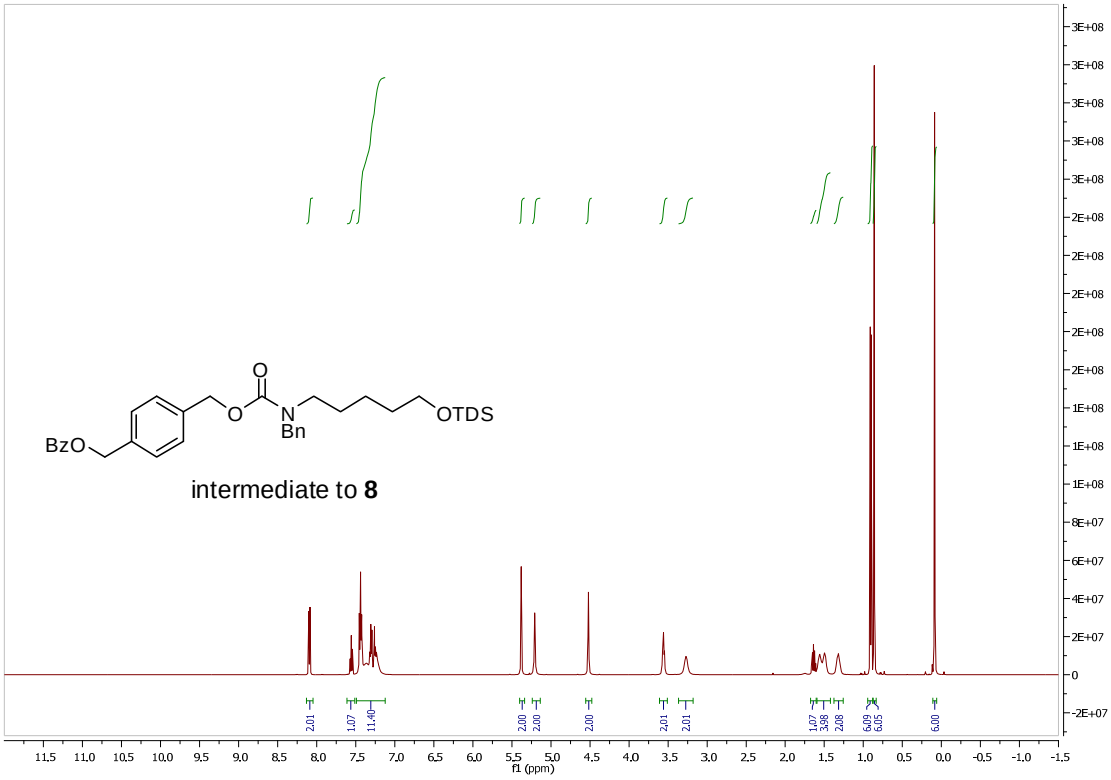

TrocO
OH
4
153.96
141.63
133.88
128.79
127.18
94.35
76.88
70.44
64.91
f1 (ppm)

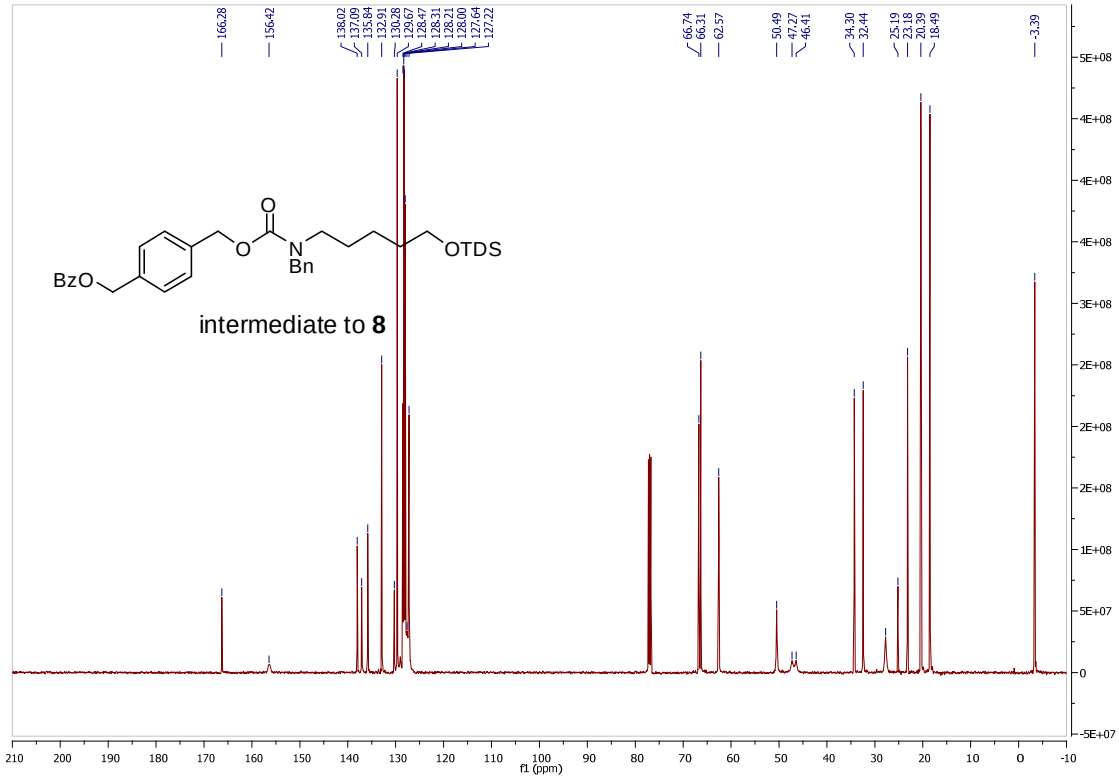

TrocO
O
O
N
Bn
OTDS
6
9.27
3.98
1.97
2.00
2.00
2.00
5.15
2.18
12.02
5.96
f1 (ppm)

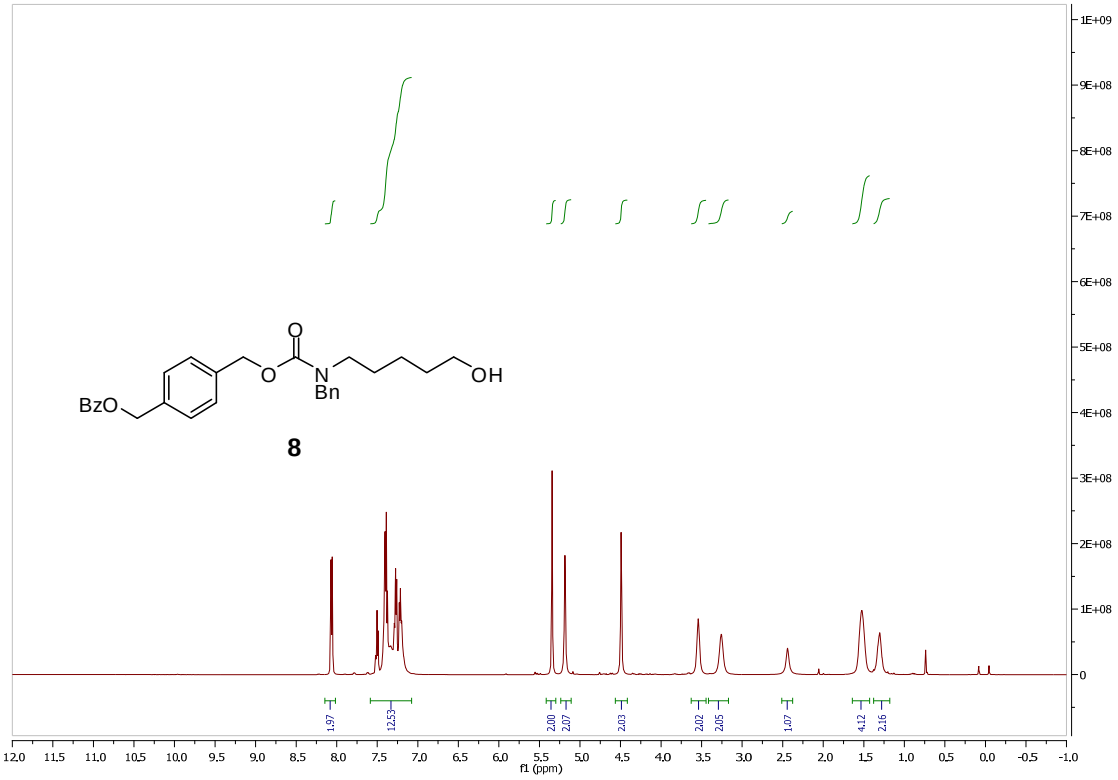

156.59
156.02
153.90
137.87
137.59
134.09
128.59
128.51
127.99
127.68
127.24
127.06
94.32
76.84
70.33
66.60
62.63
50.48
50.19
47.33
46.25
34.16
32.42
27.49
23.13
20.34
18.48
-3.41
TrocO
O
O
N
Bn
OTDS
6
f1 (ppm)

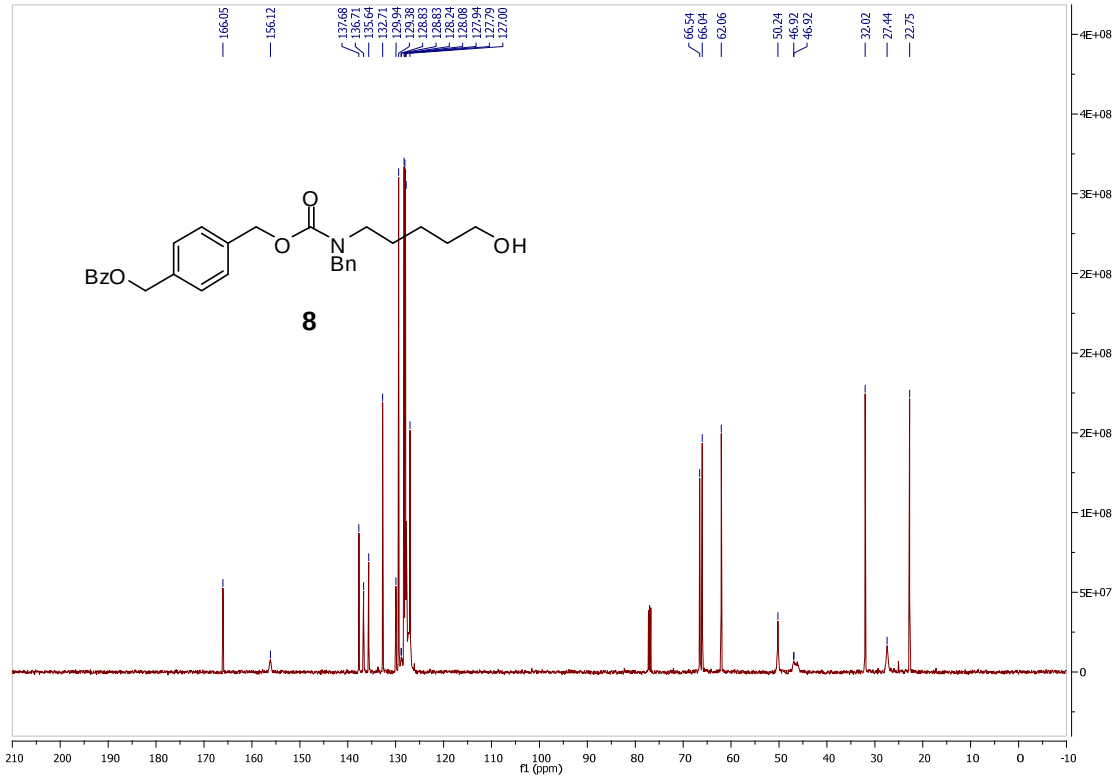


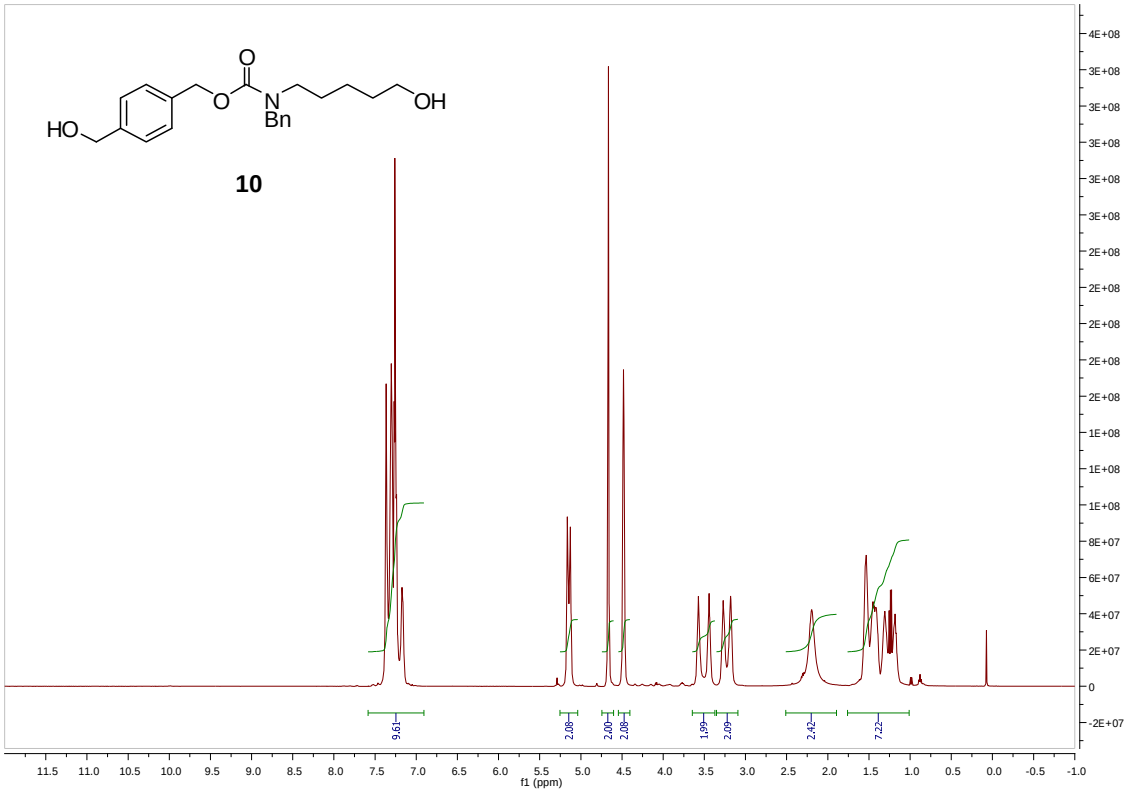


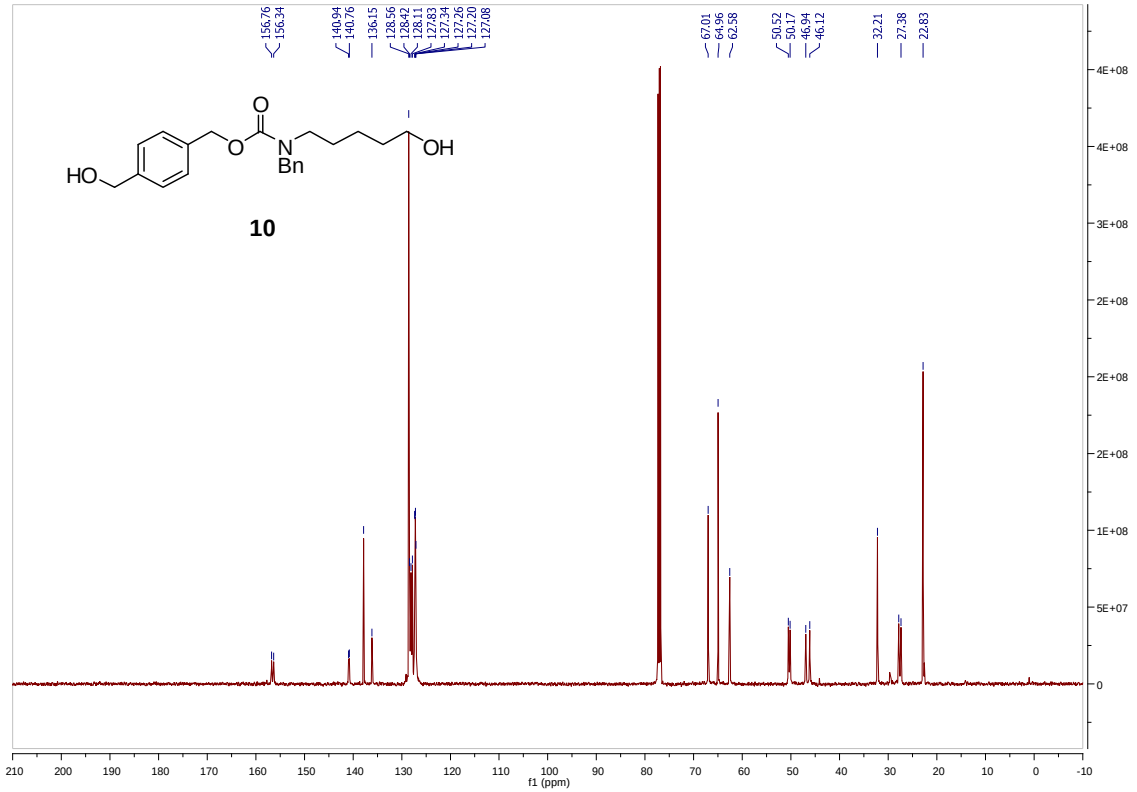

BzO
O
O
N
Bn
OTDS
intermediate to **8**
f1 (ppm)

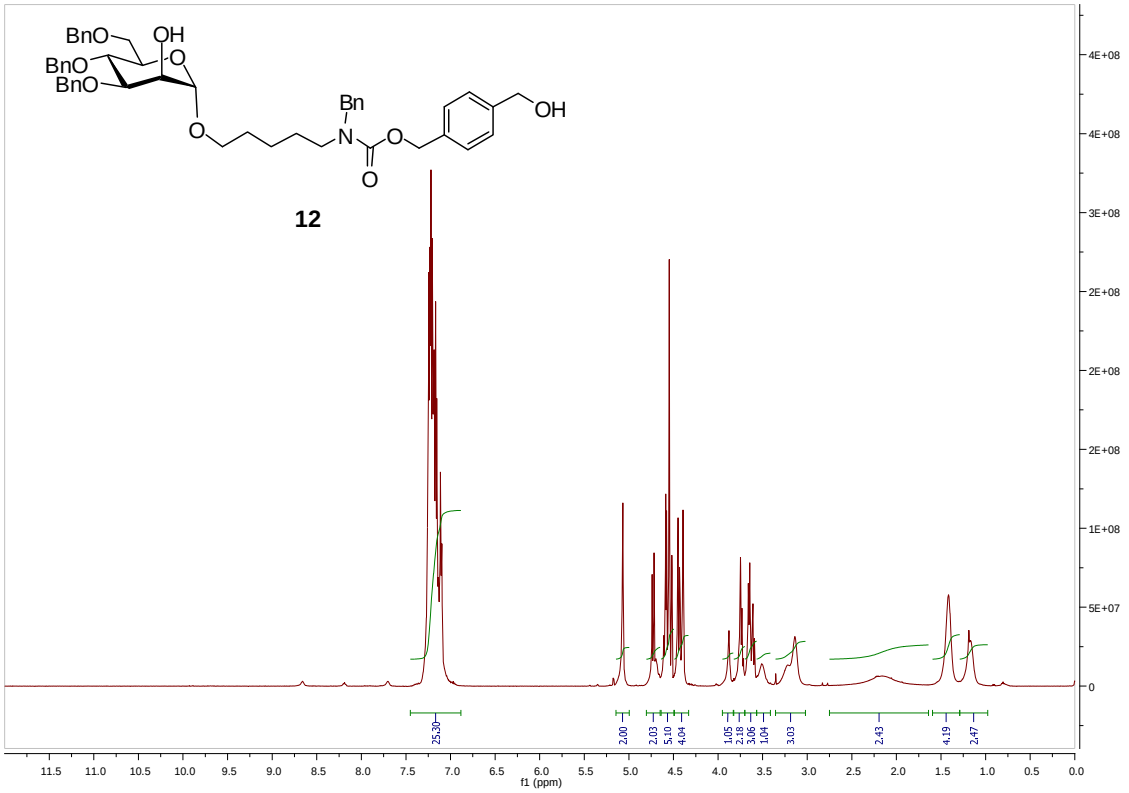

166.28
156.42
138.02
137.09
135.84
132.91
130.28
129.67
128.47
128.31
128.21
128.00
127.64
127.22
66.74
66.31
62.57
50.49
47.27
46.41
34.30
32.44
25.19
23.18
20.39
18.49
-3.39
BzO
O
O
N
Bn
OTDS
intermediate to **8**
f1 (ppm)

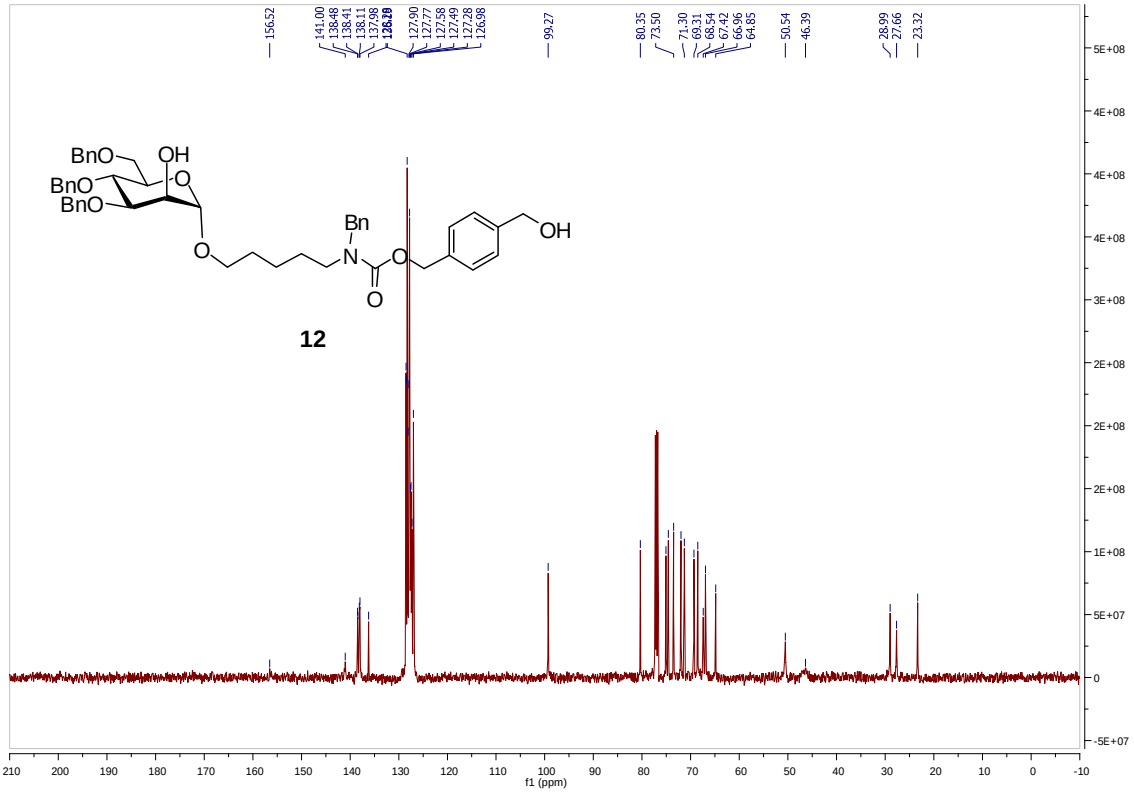

BzO
O
O
N
Bn
OH
8
f1 (ppm)

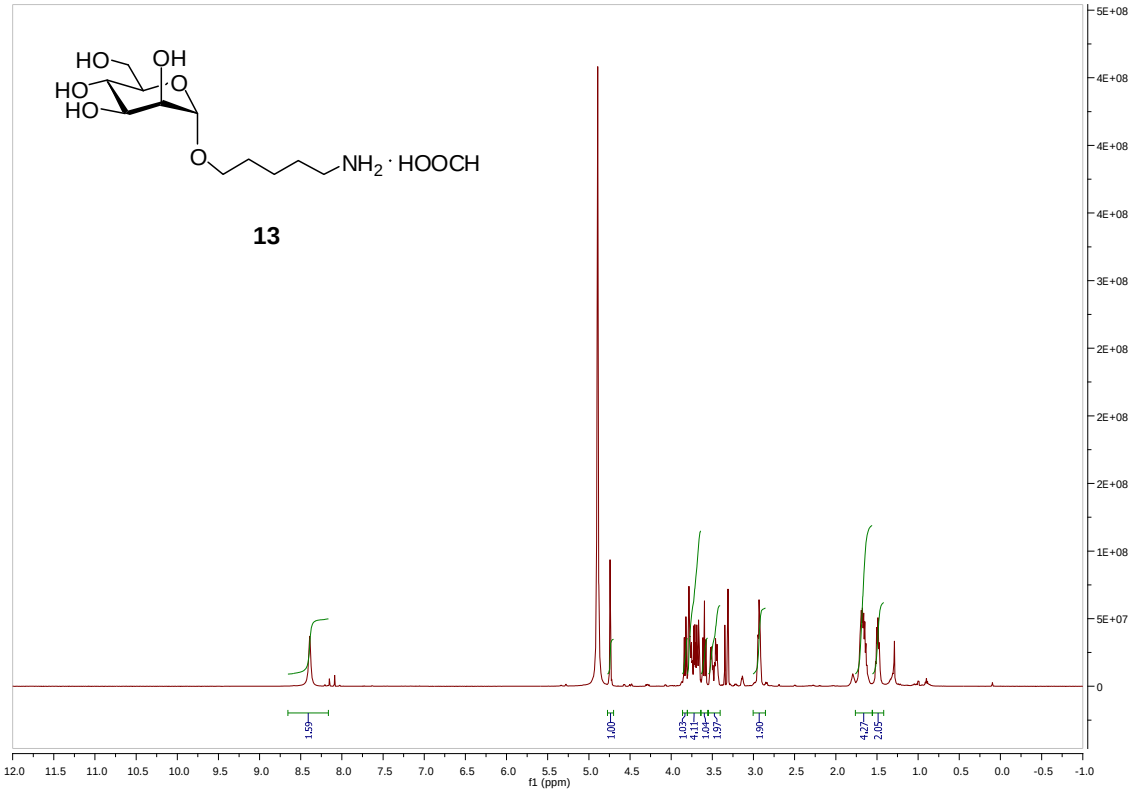

166.05
156.12
137.68
136.71
135.64
132.71
129.94
129.38
128.83
128.24
128.08
127.94
127.79
127.00
66.54
66.04
62.06
50.24
46.92
46.92
32.02
27.44
22.75
BzO
O
O
N
Bn
OH
8
f1 (ppm)

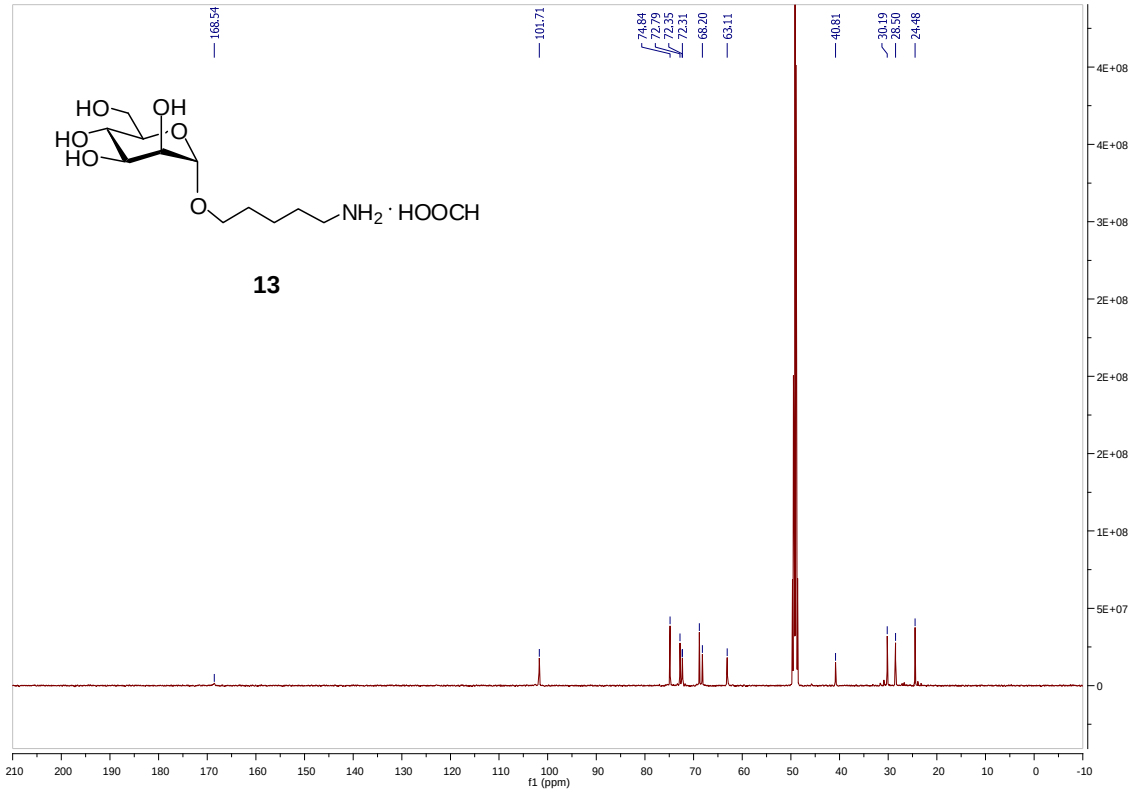

HO
O
O
N
Bn
OH
10
f1 (ppm)

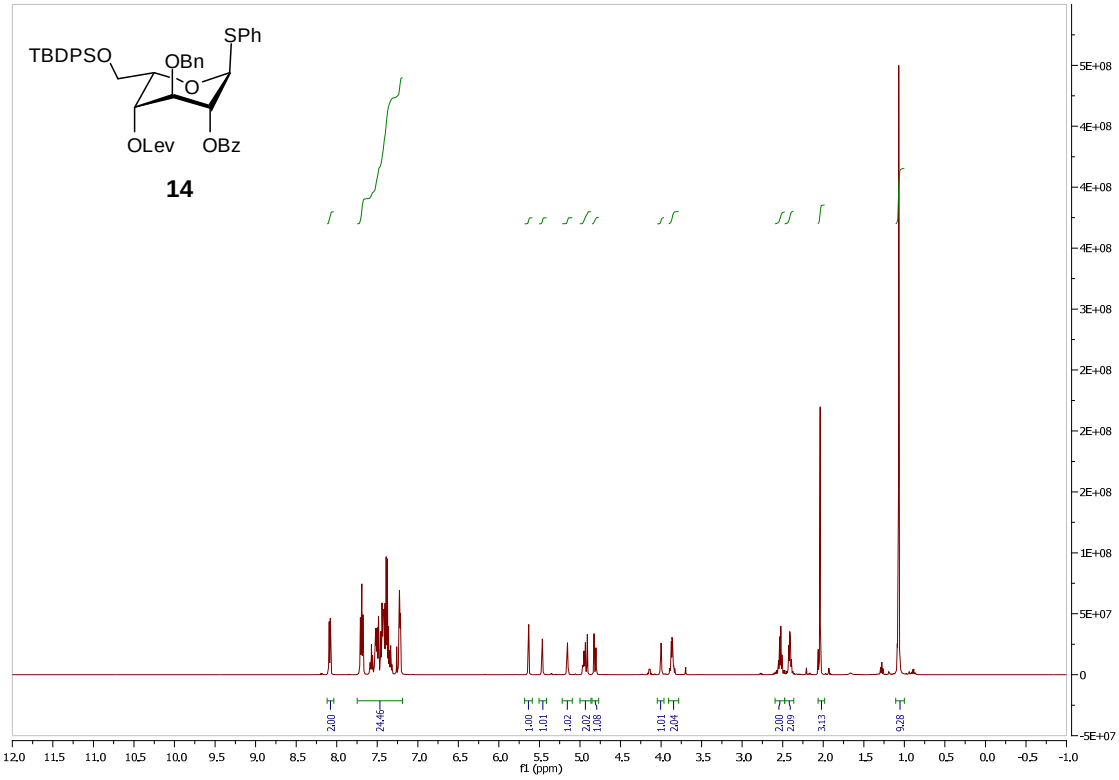

156.76
156.34
140.94
140.76
136.15
128.56
128.42
128.11
127.83
127.34
127.26
127.20
127.08
67.01
64.96
62.58
50.52
50.17
46.94
46.12
32.21
27.38
22.83
HO
O
O
N
Bn
OH
10
f1 (ppm)

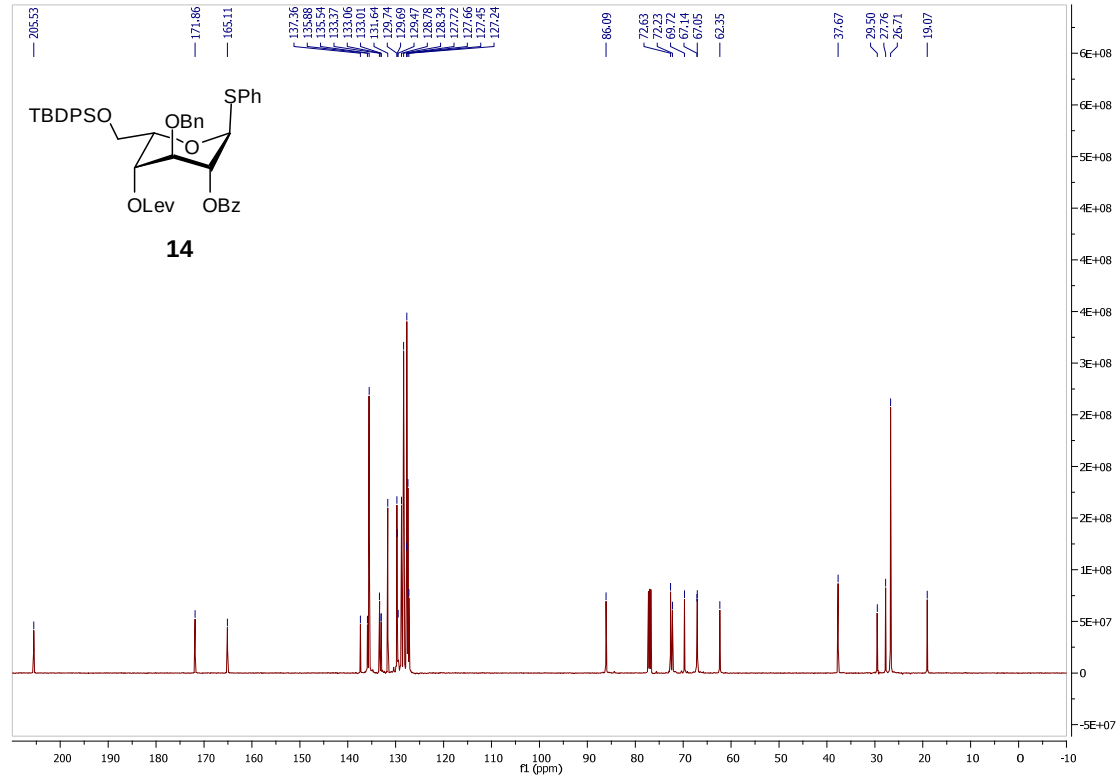

BnO
OH
BnO
O
BnO
Bn
N
O
O
OH
O
12
25.30
2.00
2.03
5.10
4.04
1.05
2.18
3.06
1.04
3.03
2.43
4.19
2.47
f1 (ppm)

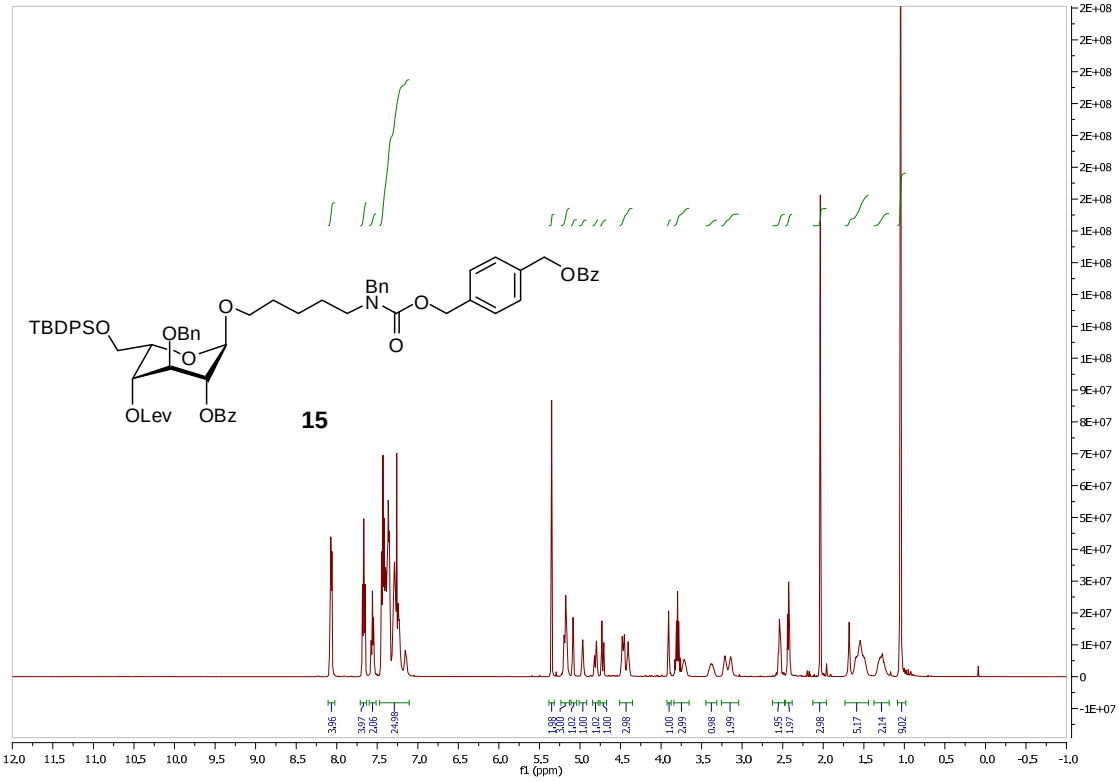

156.52
141.00
138.48
138.41
138.11
137.98
127.90
127.77
127.58
127.49
127.28
126.98
99.27
80.35
73.50
71.30
69.31
68.54
67.42
66.96
64.85
50.54
46.39
28.99
27.66
23.32
BnO
OH
BnO
O
BnO
Bn
N
O
O
OH
O
12
f1 (ppm)

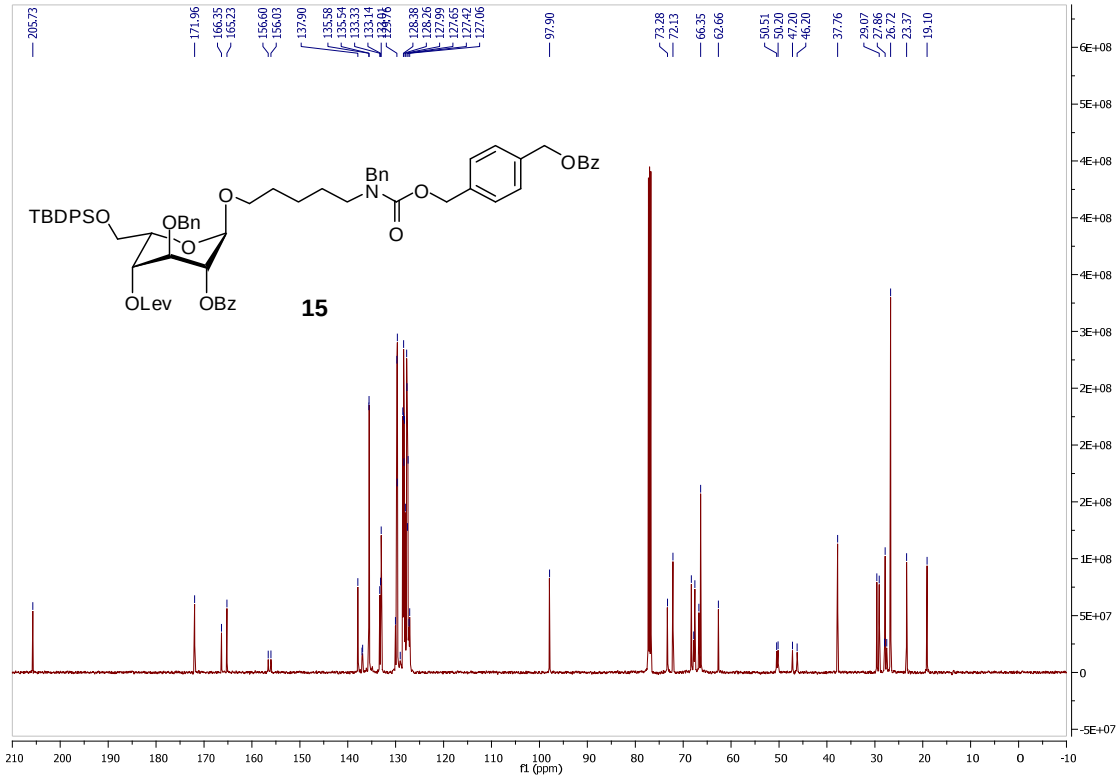

HO
OH
HO
O
HO
O
NH2 · HOOCH
13
1.59
1.00
1.03
4.11
1.04
1.97
1.90
4.27
2.05
f1 (ppm)

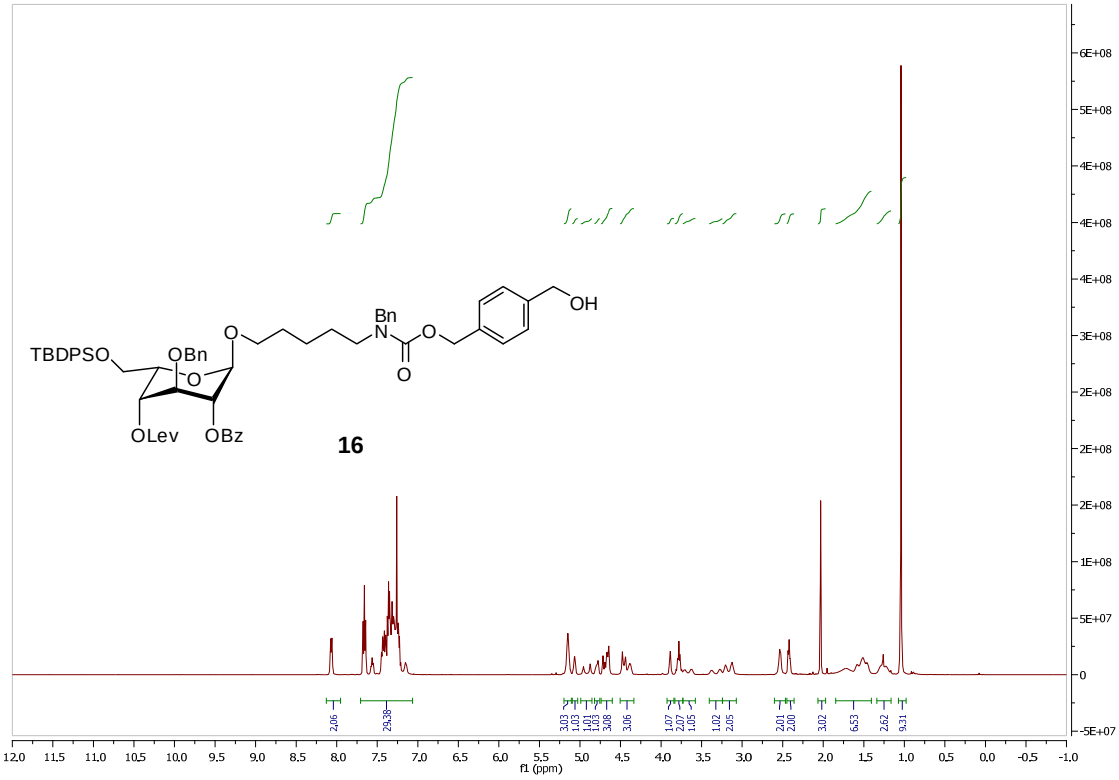

168.54
101.71
74.84
72.79
72.35
72.31
68.20
63.11
40.81
30.19
28.50
24.48
HO
OH
HO
O
HO
O
NH2 · HOOCH
13
f1 (ppm)

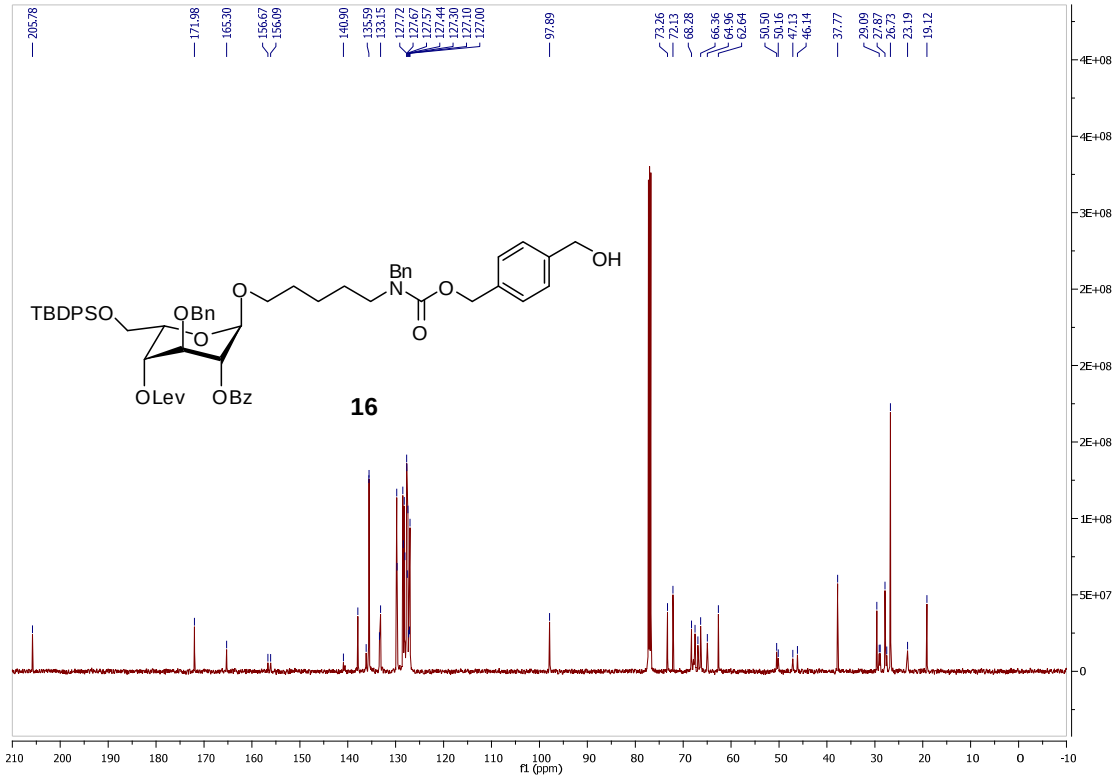

TBDPSO
OBn
O
SPh
OLev
OBz
14
f1 (ppm)

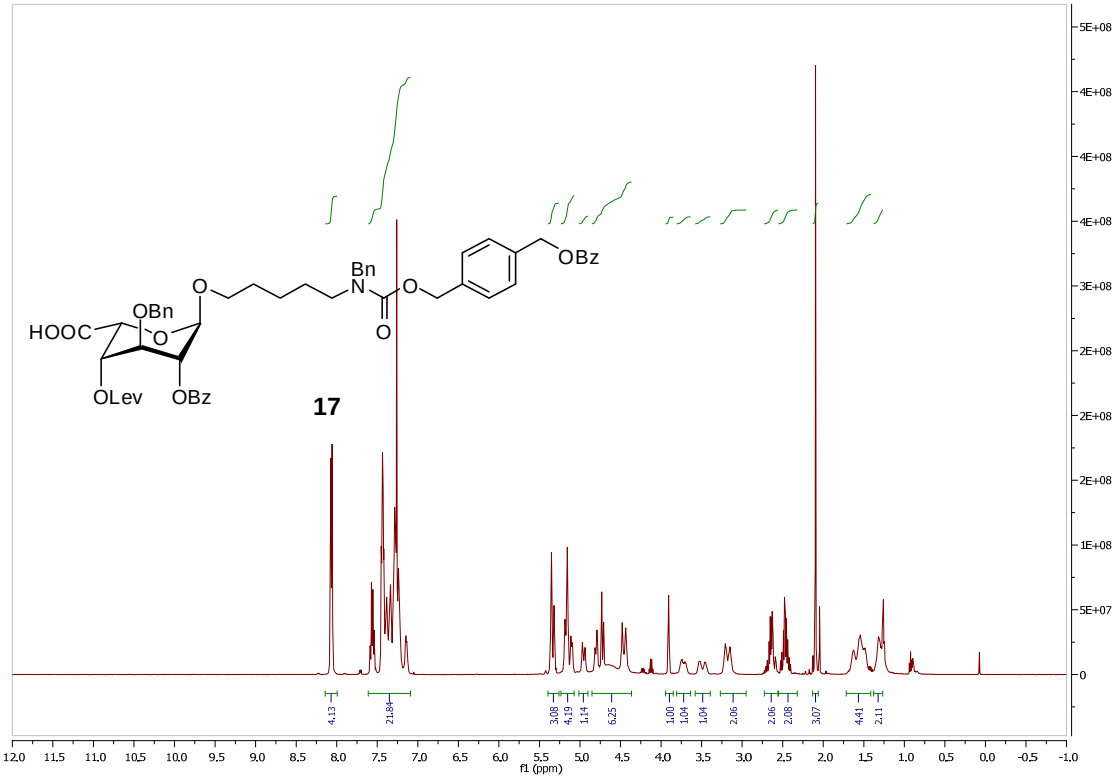

205.53
171.86
165.11
137.36
135.88
135.54
133.37
133.06
133.01
131.64
129.74
129.69
129.47
128.78
128.34
127.72
127.66
127.45
127.24
86.09
72.63
72.23
69.72
67.14
67.05
62.35
37.67
29.50
27.76
26.71
19.07
TBDPSO
OBn
O
SPh
OLev
OBz
14
f1 (ppm)

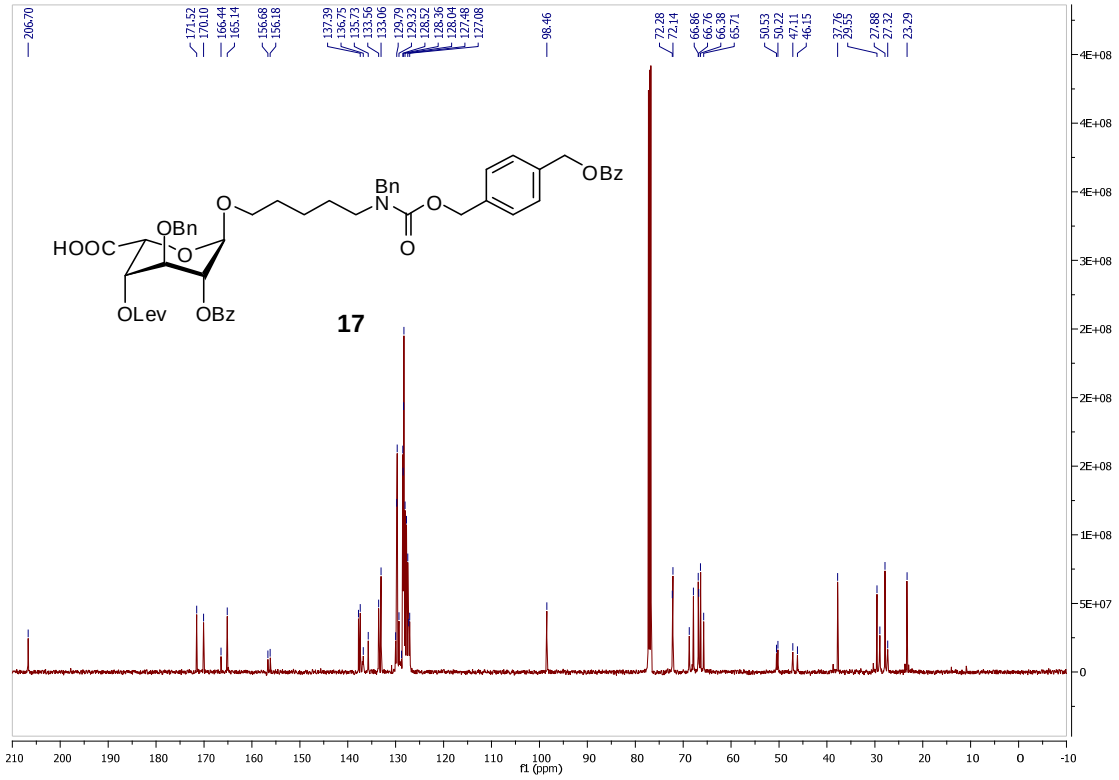

TBDPSO
OBn
O
OLev
OBz
Bn
N
O
O
OBz
15
f1 (ppm)

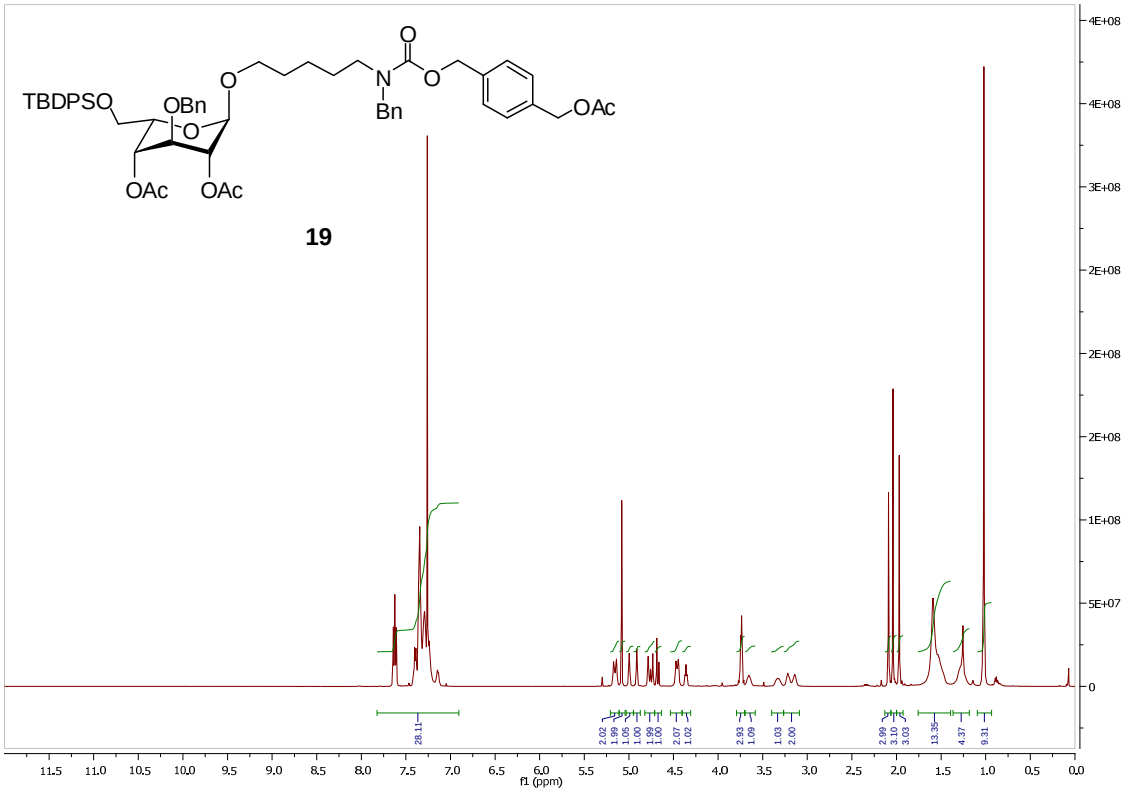

205.73
171.96
166.35
165.23
156.60
156.03
137.90
135.58
135.54
133.33
133.14
128.38
128.26
127.99
127.65
127.42
127.06
97.90
73.28
72.13
66.35
62.66
50.51
50.20
47.20
46.20
37.76
29.07
27.86
26.72
23.37
19.10
TBDPSO
OBn
O
OLev
OBz
Bn
N
O
O
OBz
15
f1 (ppm)

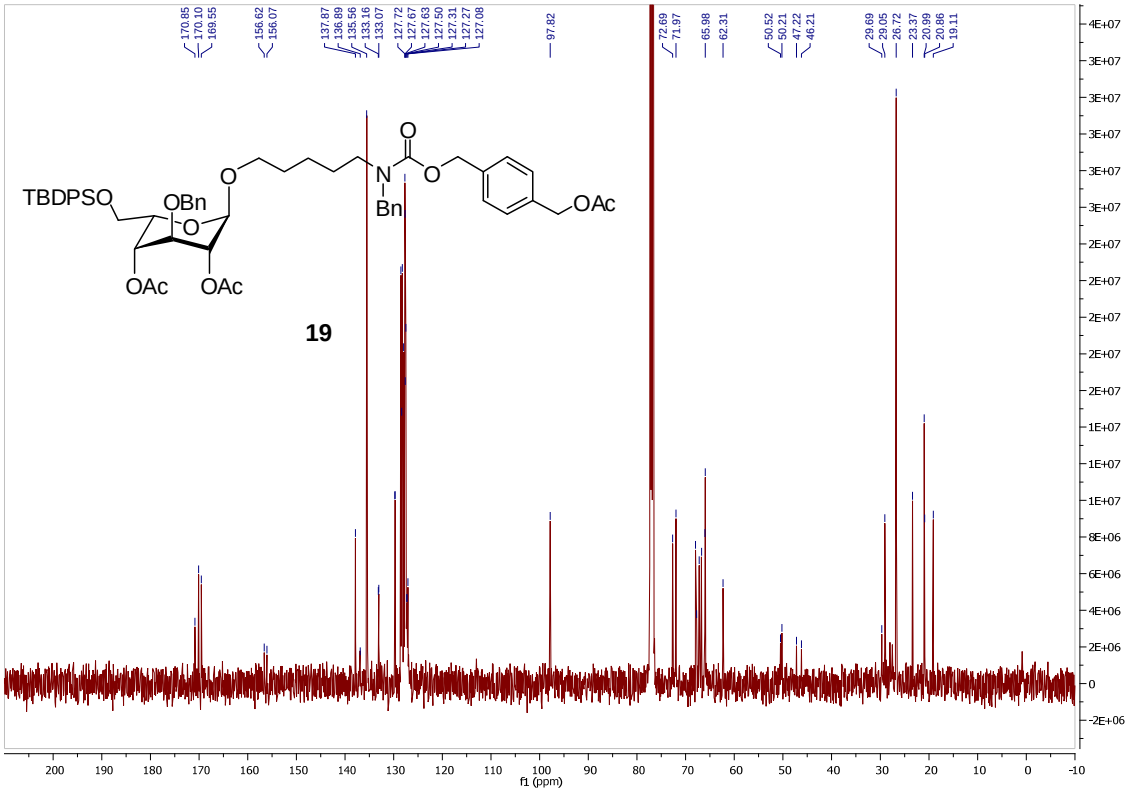

TBDPSO
OBn
O
OLev
OBz
Bn
N
O
O
OH
16
f1 (ppm)

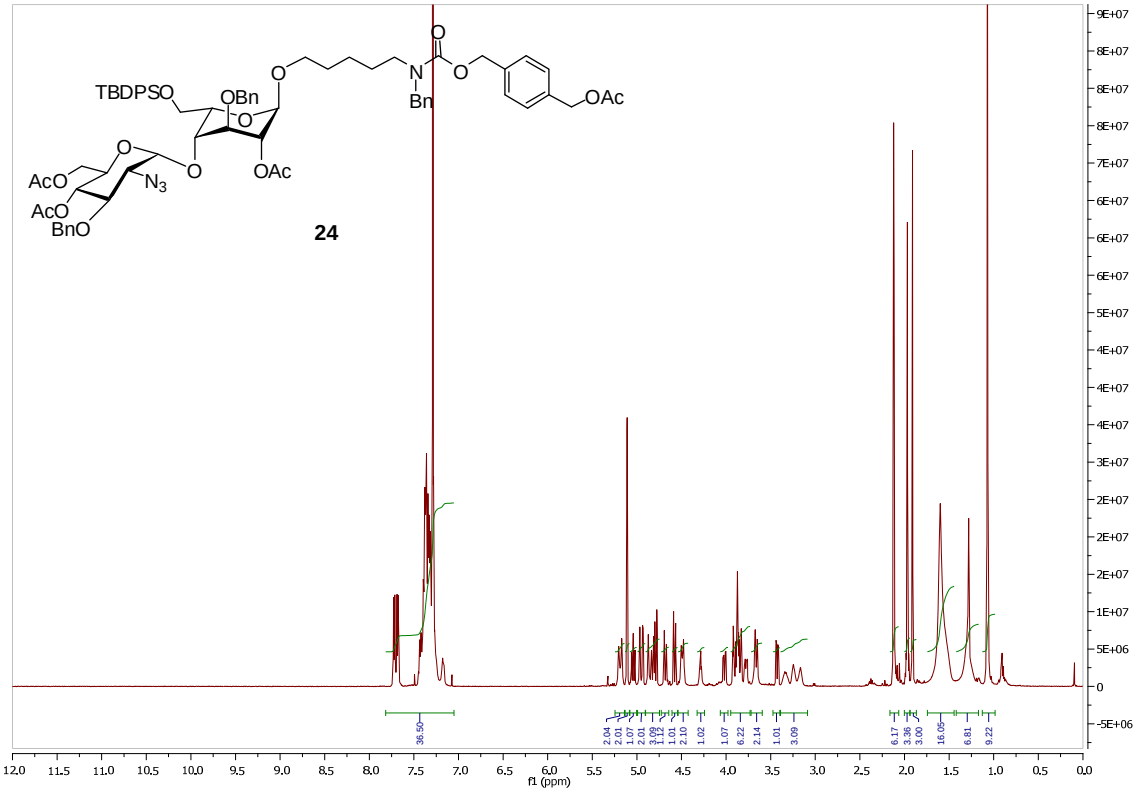

205.78
171.98
165.30
156.67
156.09
140.90
135.59
133.15
127.72
127.67
127.57
127.44
127.30
127.10
127.00
97.89
73.26
72.13
68.28
66.36
64.96
62.64
50.50
50.16
47.13
46.14
37.77
29.09
27.87
26.73
23.19
19.12
TBDPSO
OBn
O
OLev
OBz
Bn
N
O
O
OH
16
f1 (ppm)

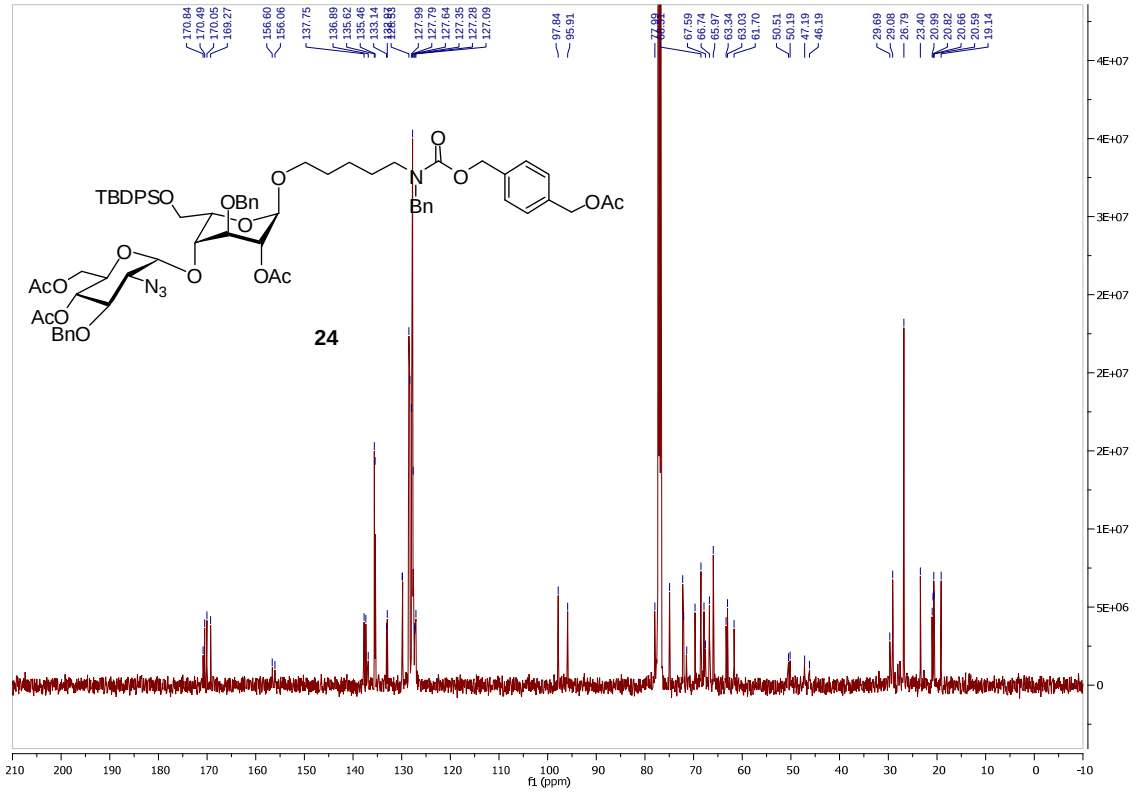

HOOC
OBn
O
OLev
OBz
Bn
N
O
O
OBz
17
f1 (ppm)

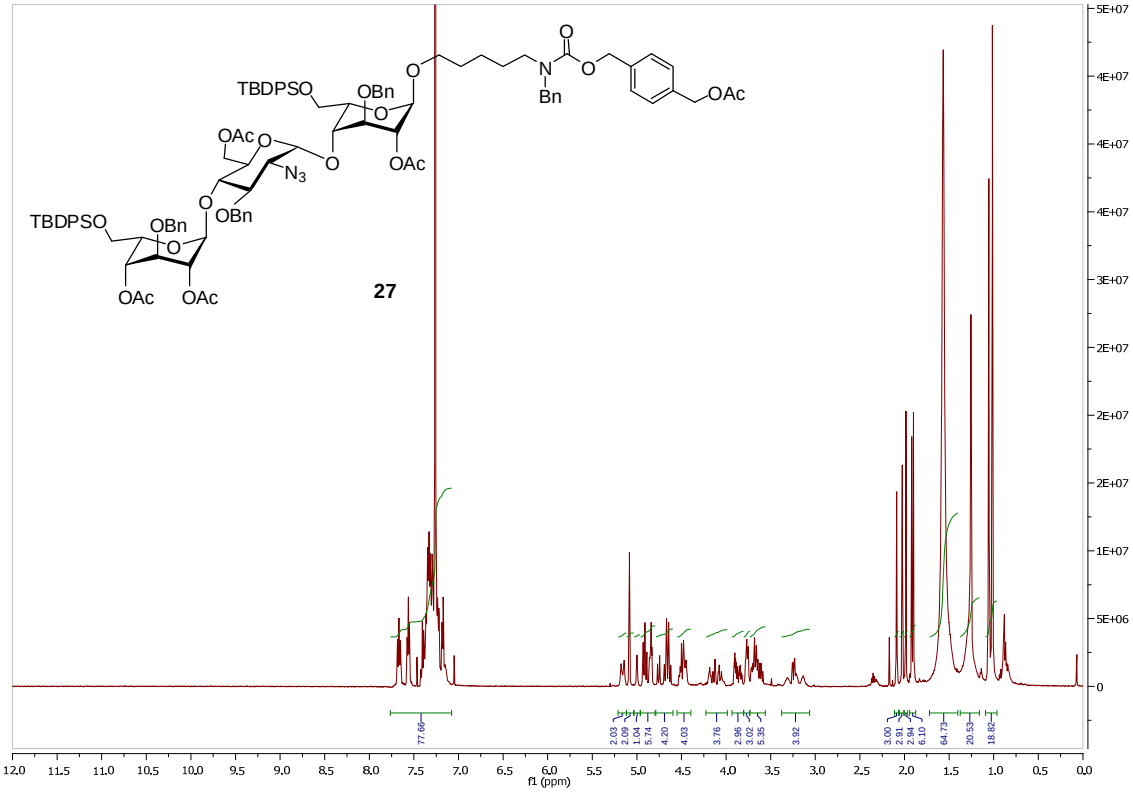

HOOC
OBn
O
OLev
OBz
Bn
N
O
O
OBz
17
f1 (ppm)

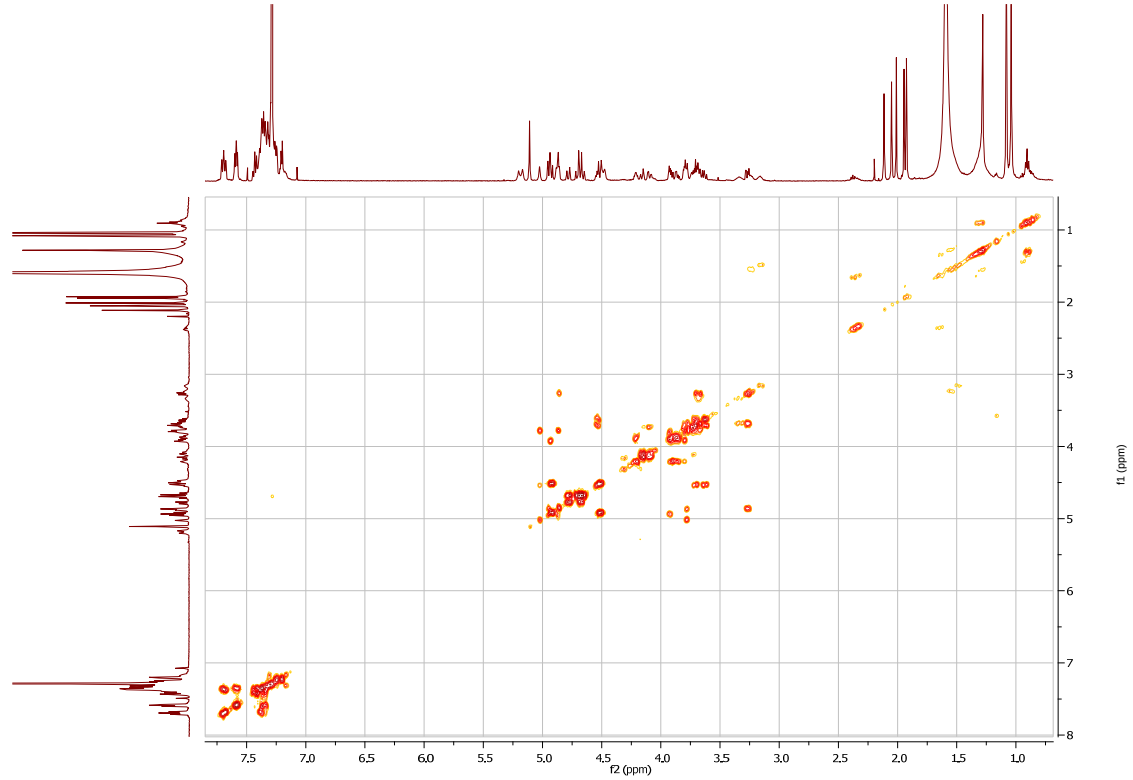

TBDPSO
OBn
O
O
N
Bn
O
O
OAc
OAc
OAc
19
f1 (ppm)


TBDPSO
OBn
O
O
N
Bn
O
O
OAc
OAc
OAc
19
f1 (ppm)

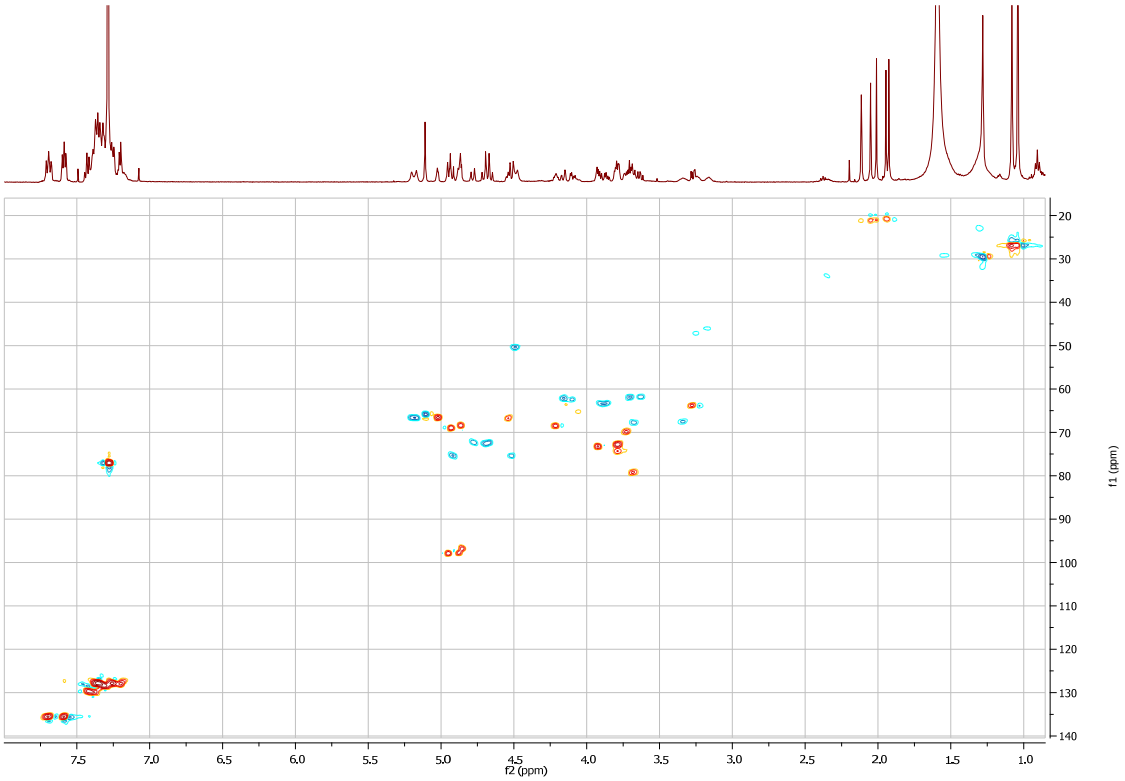

TBDPSO
OBn
O
N
Bn
O
OAc
AcO
AcO
BnO
N3
OAc
24
f1 (ppm)


170.84
170.49
170.05
169.27
156.60
156.06
137.75
136.89
135.62
135.46
133.14
127.99
127.79
127.64
127.35
127.28
127.09
97.84
95.91
77.99
67.59
66.74
65.97
63.34
63.03
61.70
50.51
50.19
47.19
46.19
29.69
29.08
26.79
23.40
20.99
20.82
20.66
20.59
19.14
TBDPSO
OBn
O
N
Bn
O
OAc
AcO
AcO
BnO
N3
OAc
24
f1 (ppm)





COSY spectrum of compound **27**



HSQC spectrum of compound **27**