Supporting Information for:

Chemoselective Activation of Ethyl vs Phenyl Thioglycosides: One-pot Synthesis of Oligosaccharides

Cian Mc Carthy and Xiangming Zhu*

Centre for Synthesis and Chemical Biology, UCD School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland

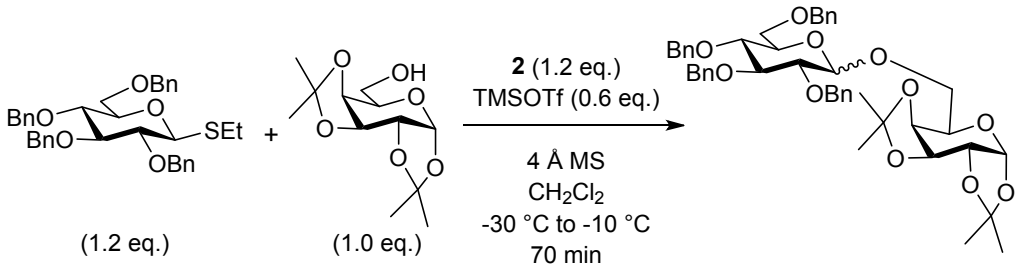
Tel: +353 17162386; Fax: +353 17162501; Email: xiangming.zhu@ucd.ie

Table of Contents

General Methods

All reagents described were reagent grade and used as supplied. Reactions were performed in oven-dried glassware under a nitrogen atmosphere. Solvents were chromatography/HPLC grade, with the exception of anhydrous CH_2Cl_2 (distilled over CaH_2). Reactions were monitored by thin-layer chromatography (TLC) using aluminium-backed silica gel 60 F_{254}, and compounds were visualised by UV or by treatment with 8% H_2SO_4 in MeOH followed by heating. Purification of compounds was carried out by flash chromatography with the appropriate solvent and 40-60 μm silica gel. NMR spectra were recorded using Varian 400, 500 and 600 MHz instruments and reported in parts per million (δ). $CDCl_3$ was used as the solvent with chemical shifts reported relative to the standard reference TMS. Coupling constants (*J*) were reported in units of Hertz (Hz). Signals were assigned with the aid of COSY, DEPT and HSQC spectra. High-resolution mass spectrometry was performed using a VG analytical 70-E mass spectrometer. Optical rotation measurements were recorded using a Schmidt-Haensch Unipol L2000 polarimeter at 589 nm and are quoted in units of deg dm^{-1} cm^3 g^{-1} (concentration *c* is given in g/100 mL).

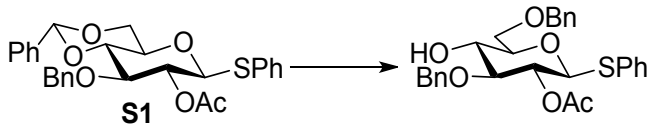
Effects of Different Solvents on Reactions Promoted by 2/TMSOTf



Entry	Solvent	Yield (%)[a]	α/β[b]
1	CH_2Cl_2	77	1:1.8
2	CH_2Cl_2/CH_3CN (5:1)	36	1:17
3	CH_2Cl_2/CH_3CN (10:1)	59	1:4
4	CH_2Cl_2/Et_2O (10:1)	0	-

[a]Isolated yield.[b] Determined by integration of the proton signals in the ^1H NMR spectrum after chromatographic purification.

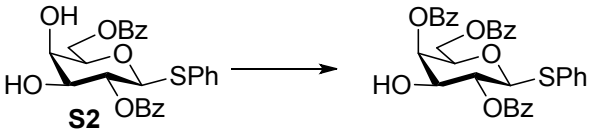
Phenyl 2-*O*-acetyl-3,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (13).



Trifluoroacetic acid (0.37 mL, 4.85 mmol) was slowly added to a solution of **S1**[1] (0.478 g, 0.97 mmol) and triethylsilane (0.77 mL, 4.85 mmol) in CH_2Cl_2 (6 mL) at 0 °C. The mixture was stirred at this temperature for 2 hours until TLC (cyclohexane–EtOAc, 5:2) indicated significant conversion. The mixture was diluted with CH_2Cl_2 and washed with H_2O, $NaHCO_3$ (x2) and brine and dried over $MgSO_4$.

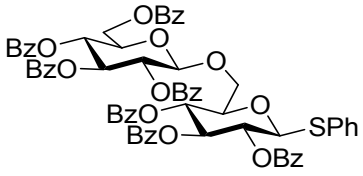
The suspension was concentrated *in vacuo* and the resulting residue was purified by flash chromatography (cyclohexane–EtOAc, 5:1) to afford **13** (0.312 g, 0.63 mmol, 65%) as a colourless oil.[2] $[\alpha]_D$ +85.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.46 (2H, m, CH_{Ar}), 7.37-7.22 (13H, m, CH_{Ar}), 5.01 (1H, dd, J_1 = 10.0 Hz, J_2 = 9.2 Hz, H-2), 4.73 (2H, bs, $PhCH_2$ x2), 4.65 (1H, d, *J* = 10.1 Hz, H-1), 4.57 (2H, AB quartet, $PhCH_2$ x2), 3.78 (2H, dd, J_1 = 4.8 Hz, J_2 = 1.4 Hz, H-6a, H-6b), 3.70 (1H, td, J_1 = 9.3 Hz, J_2 = 2.5 Hz, H-4), 3.55-3.49 (2H, m, H-3, H-5), 2.68 (1H, d, *J* = 2.5 Hz, OH) and 2.04 (3H, s, $COCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.5, 138.1, 137.7, 133.1, 132.1, 128.8, 128.5, 128.4, 127.9, 127.8, 127.8, 127.7, 127.7, 86.3, 83.8, 78.2, 74.6, 73.7, 71.8, 71.4, 70.3 and 21.0; HRMS (ES): calcd for $C_{28}H_{30}O_6SNa$ [M+Na$^+$] 517.1655, found 517.1657.

Phenyl 2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (14).



S2[3] (0.127 g, 0.264 mmol) was dissolved in CH_2Cl_2 (8 mL) in the presence of 4 Å molecular sieves under N_2. Benzoyl cyanide (38 mg, 0.29 mmol) was added to the mixture. The temperature was then lowered to -78 °C and 4-dimethylaminopyridine (3.22 mg, 26 µmol) was added to the mixture. The reaction was stirred at this temperature for 4 hours. The reaction was then quenched by the addition of saturated NH_4Cl and MeOH (250 µL), followed by dilution with CH_2Cl_2 and filtration. The filtrate was washed with saturated NH_4Cl, $Na_2S_2O_3$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (cyclohexane–EtOAc, 4:1) to afford **14** (0.137 g, 0.234 mmol, 89%) as a white solid.[4] $[\alpha]_D$ +3.2 (*c* 1.1 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12-7.93 (6H, m, CH_{Ar}), 7.66-7.19 (14H, m, CH_{Ar}), 5.78 (1H, d, *J* = 3.2 Hz, H-4), 5.29 (1H, t, *J* = 9.7 Hz, H-2), 4.94 (1H, d, *J* = 9.9 Hz, H-1), 4.57 (1H, dd, J_1 = 11.5 Hz, J_2 = 7.2 Hz, H-6a), 4.46 (1H, dd, J_1 = 11.6 Hz, J_2 = 5.3 Hz, H-6b), 4.23-4.20 (1H, m, H-5), 4.16 (1H, ddd, J_1 = 9.6 Hz, J_2 = 6.2 Hz, J_3 = 3.4 Hz, H-3) and 2.75 (1H, d, *J* = 6.2 Hz, OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.8, 166.1, 166.0, 133.8, 133.6, 133.3, 131.3, 130.1, 130.1, 129.8, 129.5, 129.3, 128.9, 128.9, 128.6, 128.5, 128.4, 128.4, 85.4, 75.3, 73.1, 71.6, 70.7 and 62.9; HRMS (ES): calcd for $C_{33}H_{28}O_8SNa$ [M+Na$^+$] 607.1397, found 607.1402.

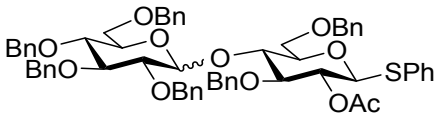
Phenyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (17).



A mixture of donor **3** (71 mg, 0.111 mmol) and acceptor **12** (50 mg, 0.085 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (32 mg, 0.113 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (20 µL, 0.111 mmol) was added successively in one portion. The reaction mixture was allowed to gradually warm to room temperature and was stirred for 40 minutes, and then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 10:1) to afford

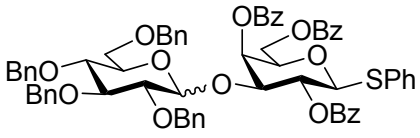
disaccharide **17** (78 mg, 0.067 mmol, 78%) as a white solid.; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07-8.02 (2H, m, CH_{Ar}), 7.97-7.88 (6H, m, CH_{Ar}), 7.87-7.79 (4H, m, CH_{Ar}), 7.79-7.70 (2H, m, CH_{Ar}), 7.58-7.22 (26H, m, CH_{Ar}), 5.84 (1H, t, *J* = 9.6 Hz, H-3'), 5.81 (1H, t, *J* = 9.2 Hz, H-3), 5.60 (1H, t, *J* = 9.4 Hz, H-4'), 5.49 (1H, dd, J_1 = 9.7 Hz, J_2 = 7.9 Hz, H-2'), 5.35 (1H, t, *J* = 9.7 Hz, H-2), 5.26 (1H, t, *J* = 9.8 Hz, H-4), 4.96 (1H, d, *J* = 7.8 Hz, H-1'), 4.91 (1H, d, *J* = 10.0 Hz, H-1), 4.60 (1H, dd, J_1 = 12.1 Hz, J_2 = 2.9 Hz, H-6a'), 4.40 (1H, dd, J_1 = 12.1 Hz, J_2 = 5.2 Hz, H-6b'), 4.08-4.00 (2H, m, H-5, H-5') and 4.01-3.92 (2H, m, H-6a, H-6b); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.1, 165.8, 165.6, 165.3, 165.2, 165.1, 165.0, 133.5, 133.4, 133.3, 133.2, 133.2, 133.0, 131.8, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.7, 129.6, 129.3, 129.2, 129.2, 129.1, 128.9, 128.8, 128.8, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 101.0, 85.9, 78.5, 74.1, 72.9, 72.3, 71.9, 70.5, 69.6, 69.5, 68.2 and 62.9; HRMS (ES): calcd for $C_{67}H_{54}O_{17}SNa$ [M+Na$^+$] 1185.2974, found 1185.2983. The NMR data were in agreement with those reported in literature.[5]

Phenyl-2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (18).



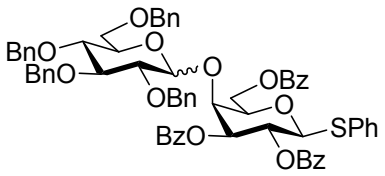
A mixture of donor **4** (100 mg, 0.171 mmol) and acceptor **13** (71 mg, 0.143 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (49 mg, 0.172 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (18.6 µL, 0.103 mmol) was added successively in one portion. The reaction mixture was stirred at this temperature for 40 minutes, after which TLC (cyclohexane–EtOAc, 5:2) showed significant conversion. The reaction was then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 15:1) to afford disaccharide **18** (84 mg, 0.083 mmol, 58%, α/β 1.5:1) as a white solid.; α-anomer which is the major product: $[\alpha]_D$ +19.5 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.48 (2H, m, CH_{Ar}), 7.36-7.08 (33H, m, CH_{Ar}), 5.46 (1H, d, *J* = 3.6 Hz, H-1), 5.10 (1H, dd, J_1 = 9.7 Hz, J_2 = 9.1 Hz, H-2'), 4.88 (1H, d, *J* = 10.9 Hz, $PhCH_2$), 4.84-4.76 (3H, m, $PhCH_2$ x3), 4.64 (1H, d, *J* = 9.9 Hz, H-1'), 4.61-4.50 (6H, m, $PhCH_2$ x6), 4.45 (1H, d, *J* = 10.7 Hz, $PhCH_2$), 4.33 (1H, d, *J* = 12.2 Hz, $PhCH_2$), 4.08 (1H, t, *J* = 9.1 Hz, H-4'), 3.93-3.75 (5H, m, H-3, H-5, H-3', H-6a', H-6b'), 3.68-3.56 (2H, m, H-4, H-5'), 3.55 (1H, dd, J_1 = 10.6 Hz, J_2 = 3.3 Hz, H-6a), 3.49 (1H, dd, J_1 = 9.8 Hz, J_2 = 3.6 Hz, H-2), 3.42 (1H, dd, J_1 = 10.7 Hz, J_2 = 1.7 Hz, H-6b) and 1.93 (3H, s, $COCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.5, 138.7, 138.3, 138.3, 138.2, 137.9, 137.9, 132.3, 128.8, 128.3, 128.3, 128.3, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 127.1, 97.2, 85.9, 84.5, 81.9, 79.4, 79.2, 77.7, 75.5, 75.0, 73.6, 73.5, 73.4, 73.4, 73.3, 71.5, 71.2, 69.1, 68.3 and 20.9; HRMS (ES): calcd for $C_{62}H_{64}O_{11}SNa$ [M+Na$^+$] 1039.4062, found 1039.4063.

Phenyl 2,4,6-tri-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (19).



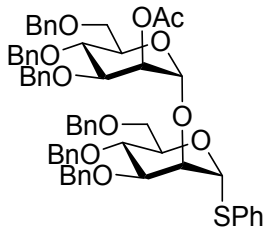
A mixture of donor **4** (63 mg, 0.107 mmol) and acceptor **14** (52 mg, 0.090 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (33 mg, 0.117 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (11.7 µL, 0.065 mmol) was added successively in one portion. The reaction mixture was immediately stirred at room temperature for 40 minutes, and then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 15:1 -> 12:1) to afford disaccharide **19** (81 mg, 0.074 mmol, 82%, α/β 5:1) as a colourless oil.; α-anomer which is the major product: $[\alpha]_D$ +51.3 (*c* 0.27, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08-8.00 (4H, m, CH_{Ar}), 7.95-7.90 (2H, m, CH_{Ar}), 7.63-7.03 (32H, m, CH_{Ar}), 6.84-6.80 (2H, m, CH_{Ar}), 5.92 (1H, d, *J* = 2.6 Hz, H-4'), 5.68 (1H, t, *J* = 9.9 Hz, H-2'), 5.15 (1H, d, *J* = 3.4 Hz, H-1), 4.86 (1H, d, *J* = 9.9 Hz, H-1'), 4.57-4.44 (5H, m, H-6a', H-6b', $PhCH_2$ x3), 4.42 (1H, d, *J* = 12.0 Hz, $PhCH_2$), 4.38 (1H, d, *J* = 11.0 Hz, $PhCH_2$), 4.36 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.31 (1H, d, *J* = 12.0 Hz, $PhCH_2$), 4.24-4.16 (2H, m, H-3', $PhCH_2$), 4.14-4.06 (1H, m, H-5'), 3.63 (1H, dt, J_1 = 10.0 Hz, J_2 = 2.9 Hz, H-5), 3.55 (1H, t, *J* = 9.4 Hz, H-3), 3.37 (1H, dd, J_1 = 9.7 Hz, J_2 = 3.4 Hz, H-2) and 3.34-3.28 (3H, m, H-4, H-6a, H-6b); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.1, 165.9, 165.0, 138.6, 138.5, 138.2, 137.9, 133.3, 133.2, 133.1, 132.1, 130.1, 129.8, 129.8, 129.6, 129.5, 129.1, 128.7, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 128.00, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1, 94.2, 86.3, 81.4, 78.6, 77.1, 75.4, 75.3, 74.6, 74.3, 73.3, 72.3, 70.8, 69.0, 68.2, 66.6 and 63.0; HRMS (ES): calcd for $C_{67}H_{62}O_{13}SNa$ [M+Na$^+$] 1129.3809, found 1129.3799.

Phenyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (20).



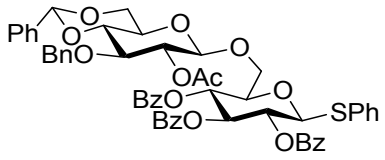
A mixture of donor **4** (49 mg, 0.084 mmol) and acceptor **15** (41 mg, 0.070 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (26 mg, 0.092 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (9.5 µL, 0.053 mmol) was added successively in one portion. The reaction mixture was immediately stirred at room temperature for 40 minutes, and then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 10:1) to afford disaccharide **20** (49 mg, 0.044 mmol, 63%, α/β 3:1) as a colourless oil.; α-anomer which is the major anomer: $[\alpha]_D$ +66.3 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07-8.03 (2H, m, CH_{Ar}), 7.96-7.90 (4H, m, CH_{Ar}), 7.64-7.04 (34H, m, CH_{Ar}), 5.66 (1H, t, *J* = 10.0 Hz, H-2'), 5.30 (1H, dd, J_1 = 9.6 Hz, J_2 = 3.4 Hz, H-3'), 5.00 (1H, d, *J* = 11.0 Hz, $PhCH_2$), 4.93 (2H, d, *J* = 10.1 Hz, $PhCH_2$, H-1'), 4.85 (1H, d, *J* = 3.4 Hz, H-1), 4.81 (1H d, *J* = 10.9 Hz, $PhCH_2$), 4.81-4.74 (3H, m, $PhCH_2$, H-6a', H-6b'), 4.67 (1H, d, *J* = 11.8 Hz, $PhCH_2$), 4.43 (1H, d, *J* = 10.9 Hz, $PhCH_2$), 4.42 (1H, d, *J* = 2.6 Hz, H-4'), 4.38 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.14 (1H, app. t, *J* = 6.3 Hz, H-5'), 4.08 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.01 (1H, t, *J* = 9.5 Hz, H-3), 3.92-3.86 (1H, m, H-5), 3.69 (1H, t, *J* = 9.6 Hz, H-4), 3.52 (1H, dd, J_1 = 9.8 Hz, J_2 = 3.4 Hz, H-2), 3.37 (1H, dd, J_1 = 10.9 Hz, J_2 = 1.7 Hz, H-6a) and 3.03 (1H, dd, J_1 = 10.9 Hz, J_2 = 1.5 Hz, H-6b); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.1, 166.1, 165.1, 138.8, 138.6, 138.0, 137.9, 133.3, 133.2, 133.1, 132.8, 131.9, 130.0, 130.0, 129.8, 129.8, 129.7, 129.7, 129.5, 129.1, 128.8, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.7, 127.5, 127.5, 127.4, 100.4, 86.0, 81.7, 79.8, 77.5, 76.9, 76.2, 75.6, 75.1, 74.8, 74.0, 73.3, 71.4, 67.8, 67.7 and 63.3 ppm; HRMS (ES): calcd for $C_{67}H_{62}O_{13}SNa$ [M+Na$^+$] 1129.3803, found 1129.3803.

Phenyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (21).



A mixture of donor **10** (58 mg, 0.108 mmol) and acceptor **16** (49 mg, 0.090 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (28 mg, 0.099 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (12.3 µL, 0.068 mmol) was added successively in one portion. The reaction mixture was kept at 0 °C and stirred for 40 minutes until TLC (cyclohexane–EtOAc, 3:1), indicated significant conversion and was then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 10:1) to afford disaccharide **21** (54 mg, 0.053 mmol, 59%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45-7.41 (2H, m, CH_{Ar}), 7.39-7.14 (31H, m, CH_{Ar}), 7.11-7.08 (2H, m, CH_{Ar}), 5.63 (1H, d, *J* = 1.6 Hz, H-1'), 5.51 (1H, dd, J_1 = 3.2 Hz, J_2 = 1.9 Hz, H-2), 5.06 (1H, d, *J* = 1.6 Hz, H-1), 4.88 (1H, d, *J* = 10.8 Hz, $PhCH_2$), 4.80 (1H, d, *J* = 10.8 Hz, $PhCH_2$), 4.72 (1H, d, *J* = 11.9 Hz, $PhCH_2$), 4.68 (1H, d, *J* = 11.7 Hz, $PhCH_2$), 4.64 (1H, d, *J* = 11.1 Hz, $PhCH_2$), 4.62-4.57 (2H, m, $PhCH_2$x2), 4.53 (1H, d, *J* = 12.3 Hz, $PhCH_2$), 4.46 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.42 (1H, d, *J* = 10.5 Hz, $PhCH_2$), 4.40 (1H, d, *J* = 10.9 Hz, $PhCH_2$), 4.37 (1H, d, *J* = 12.3 Hz, $PhCH_2$), 4.29-4.25 (1H, m, H-5'), 4.22-4.20 (1H, m, H-2'), 3.97-3.88 (4H, m, H-3, H-5, H-3', H-4'), 3.84-3.79 (2H, m, H-4, H-6a'), 3.71 (1H, dd, J_1 = 11.2 Hz, J_2 = 1.7 Hz, H-6a), 3.68 (1H, dd, J_1 = 10.7 Hz, J_2 = 4.6 Hz, H-6b'), 3.56 (1H, dd, J_1 = 10.7 Hz, J_2 = 1.8 Hz, H-6b) and 2.12 (3H, s, $COCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.2, 138.4, 138.4, 138.3, 138.1, 138.0, 138.0, 134.1, 131.7, 128.9, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 127.3, 99.7, 87.2, 79.9, 78.1, 77.2, 75.2, 75.1, 74.7, 74.3, 73.2, 73.2 72.9, 72.2, 72.0, 71.9, 69.2, 68.8, 68.6 and 21.1; HRMS (ES): calcd for $C_{62}H_{64}O_{11}SNa$ [M+Na$^+$] 1039.4061, found 1039.4062. The NMR data were in agreement with those reported in literature.[6]

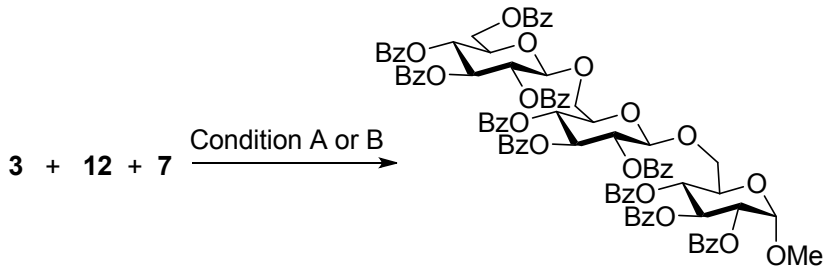
Phenyl 6-*O*-(2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-1-thio-β-D-glucopyranoside (22).



A mixture of donor **11** (53 mg, 0.119 mmol) and acceptor **12** (58 mg, 0.099 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (42 mg, 0.128 mmol) for 15 minutes under N_2. After the mixture was cooled to -25 °C, TMSOTf (12.6 µL, 0.069 mmol) in a solution of CH_2Cl_2 (1 mL) was slowly added dropwise over 1 minute. The reaction mixture was allowed to warm slowly to -15 °C and stirred at that temperature until TLC (cyclohexane–EtOAc, 2:1) indicated significant conversion. The reaction was then quenched with Et_3N. The suspension was diluted with

CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 7:1) to afford disaccharide **22** (70 mg, 0.072 mmol, 73%) as a white solid.; $[\alpha]_D$ +49.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.88 (4H, m, CH_{Ar}), 7.79-7.74 (2H, m, CH_{Ar}), 7.55-7.23 (24H, m, CH_{Ar}), 5.84 (1H, t, *J* = 9.5 Hz, H-3'), 5.53 (1H, s, $PhCHO_2$), 5.43 (1H, t, *J* = 9.7 Hz, H-2'), 5.34 (1H, t, *J* = 9.8 Hz, H-4'), 5.05-5.01 (1H, m, H-2), 4.99 (1H, d, *J* = 10.1 Hz, H-1'), 4.87 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.67 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.57 (1H, d, *J* = 7.9 Hz, H-1), 4.26 (1H, dd, J_1 = 10.5 Hz, J_2 = 5.0 Hz, H-6a), 4.04 (1H, ddd, J_1 = 9.6 Hz, J_2 = 7.2 Hz, J_3 = 1.7 Hz, H-5'), 3.97 (1H, dd, J_1 = 11.4 Hz, J_2 = 1.7 Hz, H-6a'), 3.78 (1H, dd, J_1 = 11.4 Hz, J_2 = 7.3 Hz, H-6b'), 3.72-3.65 (3H, m, H-3, H-4, H-6b), 3.42-3.34 (1H, m, H-5) and 1.99 (3H, s, $COCH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.5, 165.7, 165.3, 165.0, 138.2, 137.1, 133.6, 133.3, 133.2, 132.7, 132.0, 129.9, 129.7, 129.2, 129.2, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 127.8, 127.7, 126.0, 101.6, 101.2, 86.2, 81.5, 78.4, 78.1, 74.2, 74.1, 72.6, 70.4, 69.5, 68.6, 68.5, 66.2 and 20.9; HRMS (ES): calcd for $C_{55}H_{50}O_{14}SNa$ [M+Na$^+$] 989.2813, found 989.2822.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl)-α-D-glucopyranoside (23).



Condition A:

A mixture of donor **3** (90 mg, 0.140 mmol) and acceptor **12** (75 mg, 0.128 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (40 mg, 0.141 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (28.8 µL, 0.166 mmol) was added successively in one portion. The reaction mixture was stirred at this temperature for 40 minutes, after which TLC (cyclohexane–EtOAc, 5:2) showed significant conversion. The reaction temperature then was brought back to 0 °C. Thioperoxide **1** (51 mg, 0.140 mmol) in a solution of dry CH_2Cl_2 (1 mL) was premixed with acceptor **7** (71 mg, 0.140 mmol) and was added dropwise to the reaction mixture. The temperature was allowed to gradually warm to room temperature and it was stirred for 60 minutes, after which TLC (cyclohexane–EtOAc, 2:1) showed significant conversion. The reaction was then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 10:1->5:1) to afford disaccharide **23** (117 mg, 0.075 mmol, 59%) as a white solid.

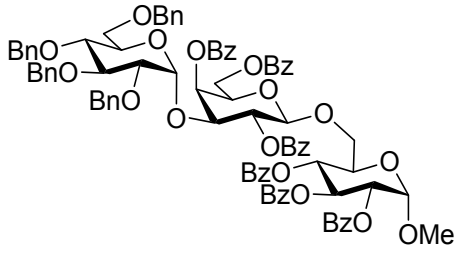
Condition B:

A mixture of donor **3** (56 mg, 0.087 mmol) and acceptor **12** (46 mg, 0.079 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (29 mg, 0.102 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (15.6 µL, 0.087 mmol) was added successively in one portion. The reaction mixture was stirred at this temperature for 40 minutes, after which TLC (cyclohexane–EtOAc, 5:2) showed significant conversion. The reaction temperature then was brought back to -20 °C. Acceptor **7** (44 mg, 0.087 mmol) was added to the reaction mixture followed by the immediate addition of NIS (19 mg, 0.087 mmol). The temperature

was stirred at this temperature for 30 minutes, after which TLC (cyclohexane–EtOAc, 2:1) showed significant conversion. The reaction was then quenched with Et_3N, diluted with CH_2Cl_2 and the mixture was washed with saturated $Na_2S_2O_3$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (cyclohexane–EtOAc, 10:1->5:1) to afford disaccharide **23** (83 mg, 0.053 mmol, 67%) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05-7.08 (50H, m, CH_{Ar}), 6.15-6.07 (2H, m, H-3'', H-3), 5.73 (1H, t, *J* = 9.6 Hz, H-3'), 5.65 (1H, t, *J* = 9.7 Hz, H-4), 5.54 (1H, t, *J* = 9.7 Hz, H-4''), 5.53-5.46 (1H, m, H-2), 5.37-5.31 (1H, m, H-2'), 5.24-5.19 (2H, m, H-2'', H-4'), 5.14 (1H, d, *J* = 7.9 Hz, H-1), 5.11 (1H, d, *J* = 3.5 Hz, H-1''), 4.69 (1H, d, *J* = 7.8 Hz, H-1'), 4.62 (1H, dd, J_1 = 12.1 Hz, J_2 = 2.8 Hz, H-6b), 4.47 (1H, dd, J_1 = 12.1 Hz, J_2 = 5.2 Hz, H-6a), 4.31-4.26 (1H, m, H-5), 4.11-3.97 (3H, m, H-6b', H-5'', H-6b''), 3.93-3.87 (2H, m, H-5', H-6a'), 3.66-3.60 (1H, m, H-6a'') and 3.13 (3H, s, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.1, 165.7, 165.7, 165.7, 165.6, 165.4, 165.3, 165.2, 165.2, 165.0, 133.5, 133.4, 133.3, 133.3, 133.2, 133.2, 133.1, 133.1, 132.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.7, 129.6, 129.6, 129.4, 129.4, 129.3, 129.2, 129.0, 128.9, 128.8, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 101.3, 101.0, 96.6, 74.7, 72.8, 72.7, 72.2, 72.2 72.1, 71.9, 70.3, 70.1, 69.7, 69.6, 68.6, 68.4, 68.2, 63.2 and 55.1; HRMS (ES): calcd for $C_{89}H_{74}O_{26}Na$ [M+Na$^+$] 1581.4366, found 1581.4403. The NMR data were in agreement with those reported in literature.[7]

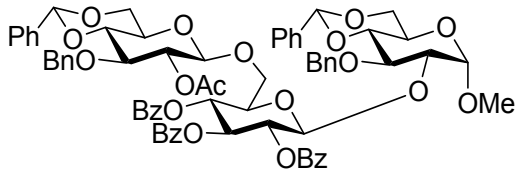
Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,4,6-tri-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α -D-glucopyranosyl)-β-D-galactopyranosyl)-α-D-glucopyranoside (24).



A mixture of donor **4** (57 mg, 0.097 mmol) and acceptor **14** (52 mg, 0.089 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (33 mg, 0.116 mmol) for 15 minutes under N_2. After the mixture was cooled to 0 °C, TMSOTf (12.3 µL, 0.068 mmol) was added successively in one portion. The reaction mixture was immediately stirred at room temperature for 40 minutes, after which TLC (cyclohexane–EtOAc, 2:1) showed significant conversion. The reaction temperature then was brought back to 0 °C and an additional portion of TMSOTf (8.0 µL, 0.044 mmol) was added to the mixture. Thioperoxide **1** (35 mg, 0.097 mmol) in a solution of CH_2Cl_2 (1 mL) was premixed with acceptor **7** (49 mg, 0.097 mmol) and was added dropwise to the reaction mixture. The temperature was allowed to gradually warm to room temperature and it was stirred for 60 minutes, after which TLC (cyclohexane–EtOAc, 2:1) showed significant conversion. The reaction was then quenched with Et_3N. The suspension was diluted with CH_2Cl_2, filtered through a pad of celite, and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography (cyclohexane–EtOAc, 10:1->5:1) to afford trisaccharide **24** (75 mg, 0.050 mmol, 56%) as a white solid.; $[\alpha]_D$ +53.7 (*c* 0.91, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08-7.98 (6H, m, CH_{Ar}), 7.95-7.90 (2H, m, CH_{Ar}), 7.87-7.83 (2H, m, CH_{Ar}), 7.82-7.77 (2H, m, CH_{Ar}), 7.60-7.01 (36H, m, CH_{Ar}), 6.85-6.79 (2H, m, CH_{Ar}), 6.07 (1H, t, *J* = 9.8 Hz, H-3''), 5.90 (1H, d, *J* = 3.1 Hz, H-4'), 5.73 (1H, dd, J_1 = 10.1 Hz, J_2 = 8.1 Hz, H-2'), 5.30 (1H, t, *J* = 9.9 Hz, H-4''), 5.17 (1H, d, *J* = 3.3 Hz, H-1), 5.07 (1H, dd, J_1 = 10.2 Hz, J_2 = 3.6 Hz, H-2''), 4.87 (1H, d, *J* = 3.6 Hz, H-1''), 4.72 (1H, d, *J* = 8.0 Hz, H-1'), 4.55-4.44 (5H, m, $PhCH_2$ x4, H-6a'), 4.42-4.32 (4H, m, $PhCH_2$ x3, H-6b'), 4.26-4.18 (3H, m, $PhCH_2$, H-3', H-5''), 4.12 (1H, d, *J* = 11.2 Hz, H-6a''), 4.03 (1H, app. t, *J* = 6.5 Hz, H-5'), 3.75-3.67 (2H, m, H-5, H-6b''), 3.59 (1H, t, *J* = 9.3 Hz, H-

3), 3.40-3.32 (4H, m, H-6a, H-6b, H-4, H-2) and 3.07 (3H, s, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.0, 165.9, 165.7, 165.6, 165.4, 165.1, 138.6, 138.5, 138.2, 137.9, 133.4, 133.3, 133.2, 133.2, 133.0, 130.1, 129.8, 129.8, 129.8, 129.7, 129.7, 129.6, 129.2, 129.2, 129.0, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.6, 127.6, 127.3, 127.2, 127.2, 127.1, 102.4, 96.3, 94.4, 81.4, 78.7, 77.1, 75.3, 74.2, 73.4, 73.3, 72.3, 72.0, 71.7, 70.8, 70.7, 70.4, 69.7, 69.3, 68.6, 68.2, 66.4, 62.3 and 55.0; HRMS (ES): calcd for $C_{89}H_{82}O_{22}Na$ [M+Na^+] 1525.5190, found 1525.5189.

Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-[6-*O*-(2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl]-α-D-glucopyranoside (26).



A mixture of donor **11** (49 mg, 0.110 mmol) and acceptor **12** (53 mg, 0.091 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature in the presence of 4 Å molecular sieves and **2** (29 mg, 0.118 mmol) for 15 minutes under N_2. After the mixture was cooled to -25 °C, TMSOTf (12.3 µL, 0.068 mmol) in a solution of CH_2Cl_2 (1 mL) was slowly added dropwise over 1 minute. The reaction mixture was allowed to warm slowly to -15 °C and stirred at that temperature until TLC (cyclohexane–EtOAc, 2:1) indicated significant conversion. The reaction temperature then was brought back to -25 °C. Acceptor **25** (41 mg, 0.110 mmol) was added to the reaction mixture followed by the immediate addition of NIS (25 mg, 0.111 mmol). The temperature was allowed to warm slowly to -15 °C, after which TLC (cyclohexane–EtOAc, 2:1) showed significant conversion. The reaction was then quenched with Et_3N, diluted with CH_2Cl_2 and the mixture was washed with saturated $Na_2S_2O_3$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (cyclohexane–EtOAc, 7:1->5:1) to afford disaccharide **26** (46 mg, 0.037 mmol, 41%) as a white solid.; $[\alpha]_D$ -11.0 (*c* 0.56, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.93-7.76 (6H, m, 7H), 7.57-6.98 (29H, m, CH_{Ar}), 5.82 (1H, t, *J* = 9.6 Hz, H-3'), 5.61 (1H, dd, J_1 = 9.6 Hz, J_2 = 7.9 Hz, H-2'), 5.53 (1H, s, $PhCHO_2$), 5.44 (1H, s, $PhCHO_2$), 5.41 (1H, d, *J* = 9.7 Hz, H-4'), 5.14 (1H, d, *J* = 7.8 Hz, H-1'), 5.03-5.00 (1H, m, H-2), 4.95 (1H, d, *J* = 3.6 Hz, H-1''), 4.88 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.65 (1H, d, *J* = 12.1 Hz, $PhCH_2$), 4.57-4.55 (2H, m, H-1, $PhCH_2$), 4.40 (1H, d, *J* = 11.7 Hz, $PhCH_2$), 4.27-4.24 (2H, m, H-6a, H-6a''), 3.98 (1H, ddd, J_1 = 9.6 Hz, J_2 = 6.8 Hz, J_3 = 2.3 Hz, H-5'), 3.95-3.90 (2H, m, H-6a', H-4''), 3.84-3.80 (3H, m, H-3, H-6b', H-2''), 3.71-3.65 (4H, m, H-6b, H-4, H-5'', H-6b''), 3.55 (1H, t, *J* = 9.4 Hz, H-3''), 3.46 (3H, s, OCH_3), 3.38 (1H, dt, J_1 = 9.5 Hz, J_2 = 5.0 Hz, H-5) and 2.05 (3H, s, $COCH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.3, 165.8, 165.3, 165.0, 138.4, 138.2, 137.3, 137.1, 133.5, 133.2, 133.1, 129.8, 129.7, 129.7, 129.7, 129.2, 129.1, 128.9, 128.8, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 127.6, 127.6, 127.5, 127.4, 127.4, 127.3, 126.0, 126.0, 126.0, 102.0, 101.5, 101.3, 101.2, 100.2, 82.1, 81.4, 80.2, 78.8, 77.4, 74.7, 74.2, 74.1, 73.2, 72.5, 72.0, 69.6, 69.1, 68.5, 67.9, 66.2, 62.1, 55.7 and 20.9; HRMS (ES): calcd for $C_{70}H_{68}O_{20}Na$ [M+Na^+] 1251.4196, found 1251.4202.

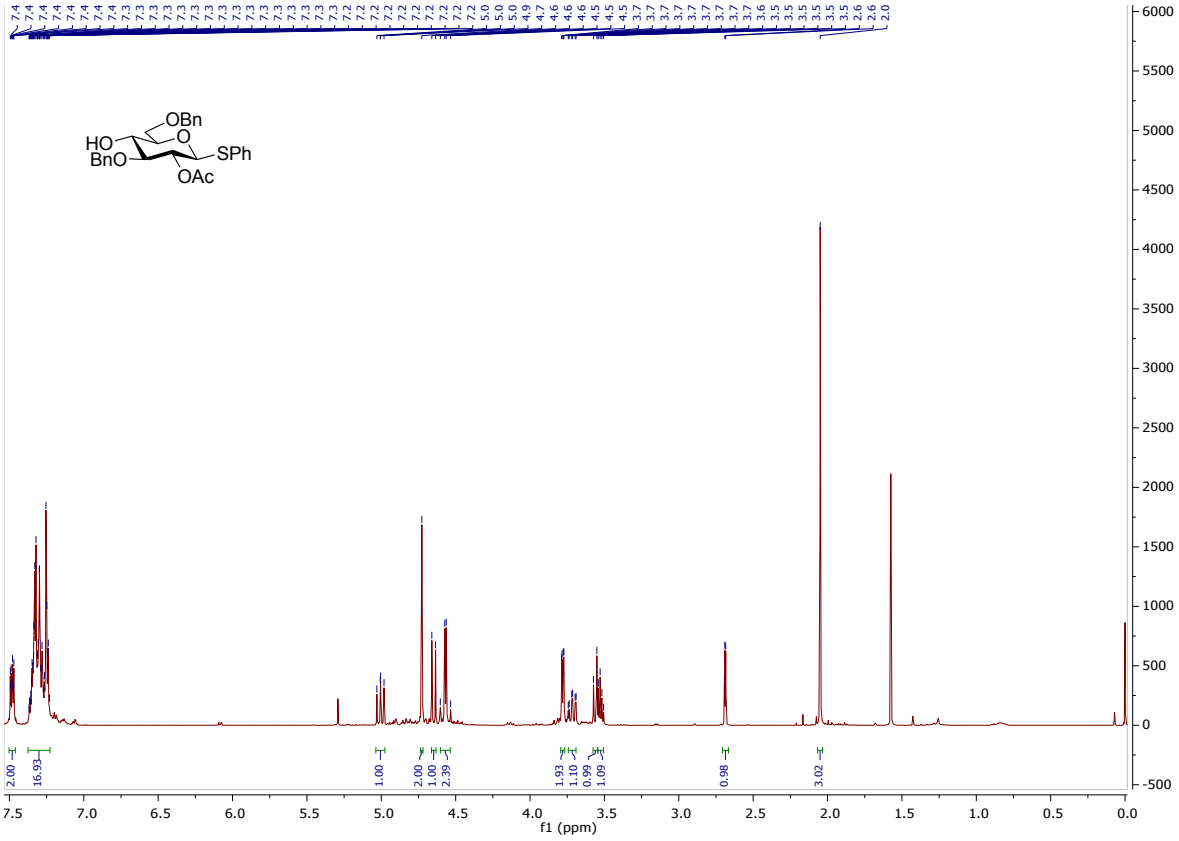
References:

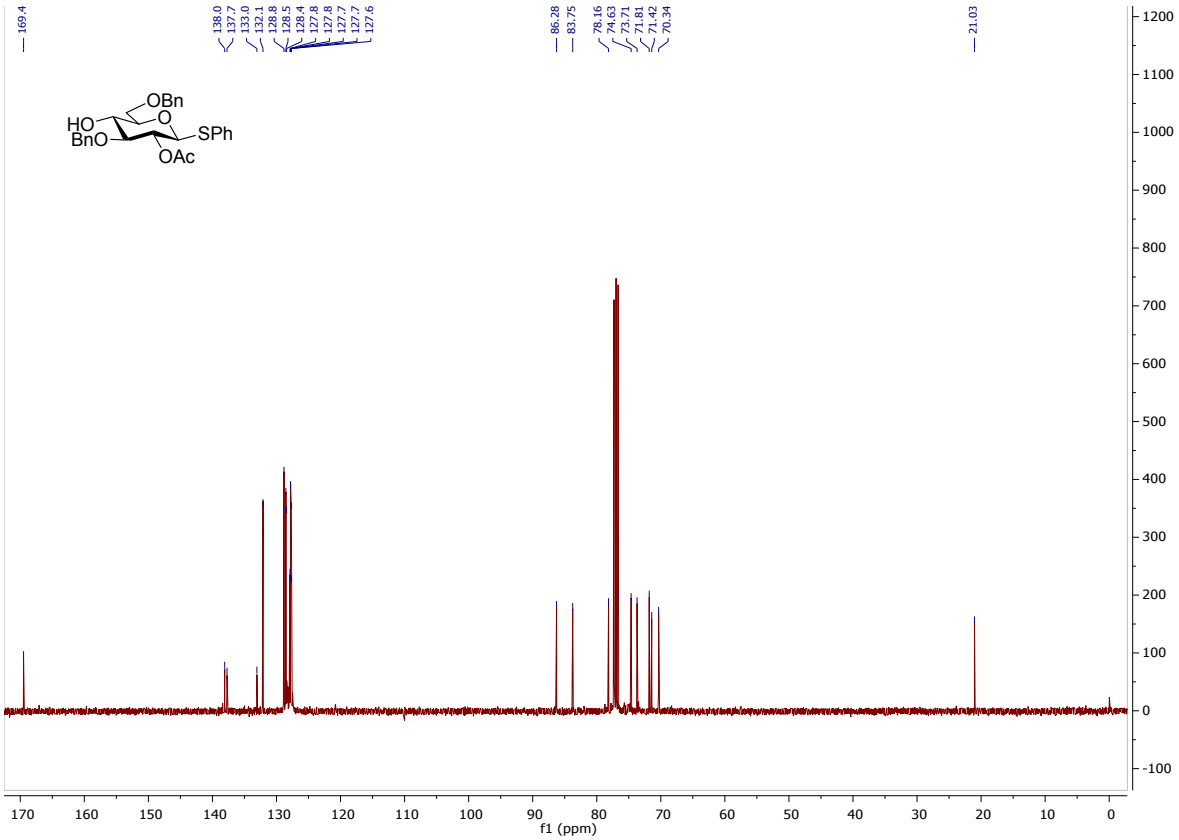
1 E. Bousquet, M. Khitri, L. Lay, F. Nicotra, L. Panza and G. Russo, *Carbohydr. Res.* 1998, **311**, 171-181.

2 R. J. Williams, J. Iglesias-Fernández, J. Stepper, A. Jackson, A. J. Thompson, E. C. Lowe, J. M. White, H. J. Gilbert, C. Rovira, G. J. Davies, and S. J. Williams, *Angew. Chem. Int. Ed.* 2014, **53**, 1087-1091.

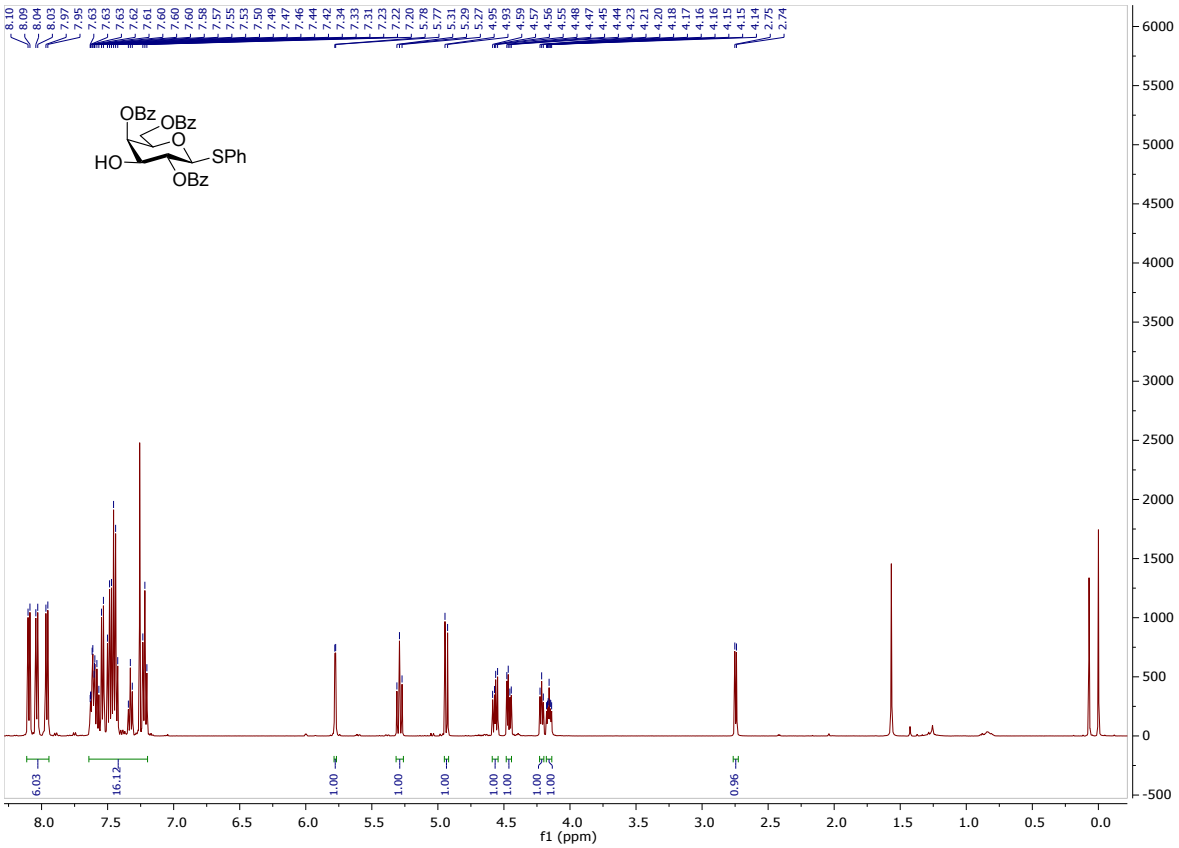
3 T. Ziegler and G. Herold, *Liebigs Ann. Chem.* 1994, 859-866.
4 P. Peng, M. Linseis, R. F. Winter and R. R. Schmidt, *J. Am. Chem. Soc.* 2016, **138**, 6002-6009.
5 M. A. Chaube, V. A. Sarpe, S. Jana, S. S. Kulkarni, *Org. Biomol. Chem.* 2016, **14**, 5595-5598.
6 C. T. Tanifum and C. -W. T. Chang, *J. Org. Chem.* 2009, **74**, 634-644.
7 S. C. Ranade, S. J. Hasty and A. V. Demchenko, *J. Carbohydr. Chem.* 2013, **32**, 360-379.

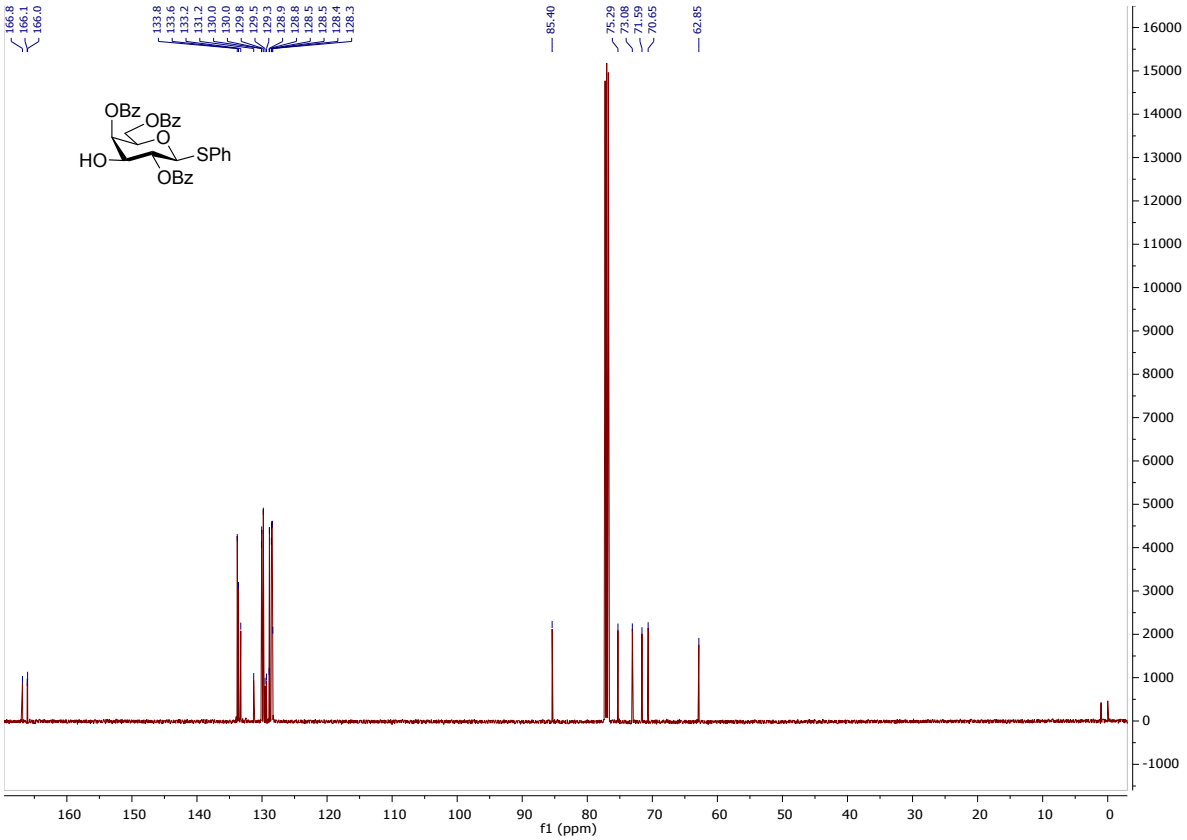
^{1}H and ^{13}C NMR Spectra of Compound **13**



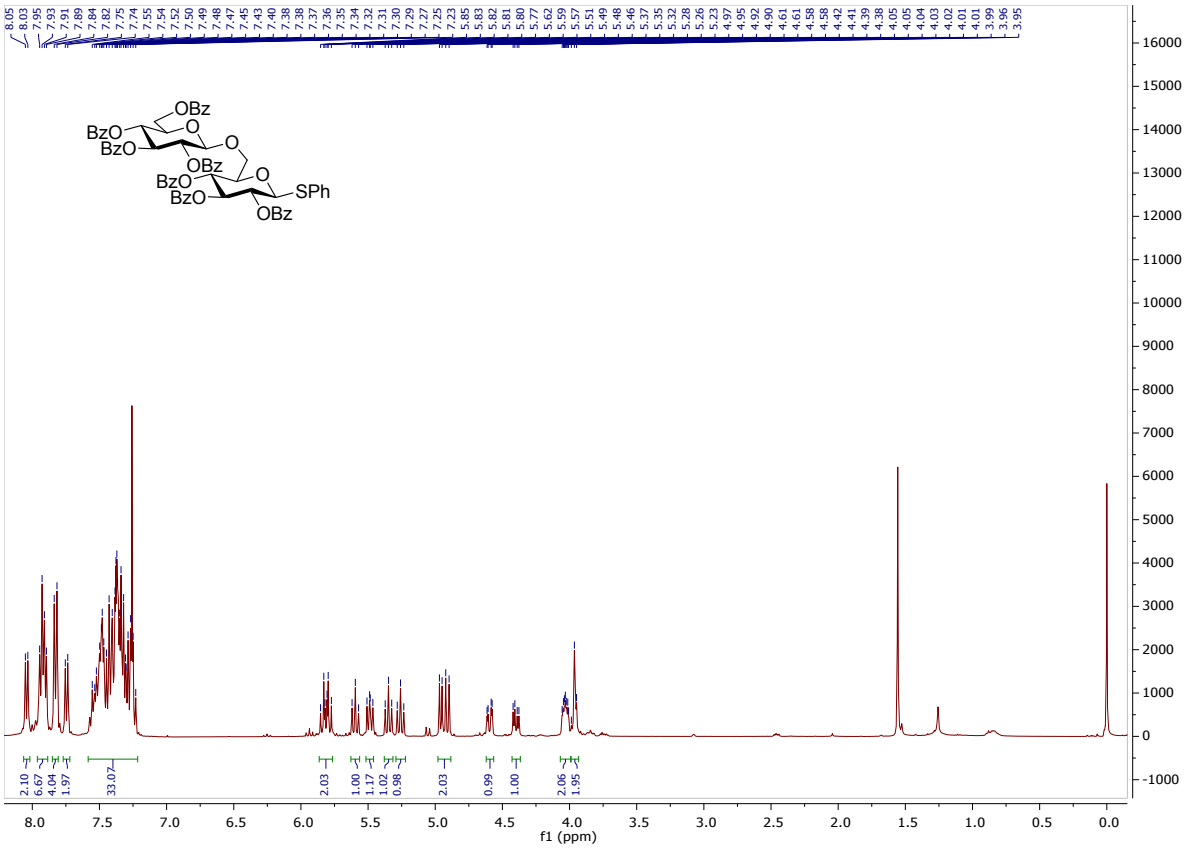


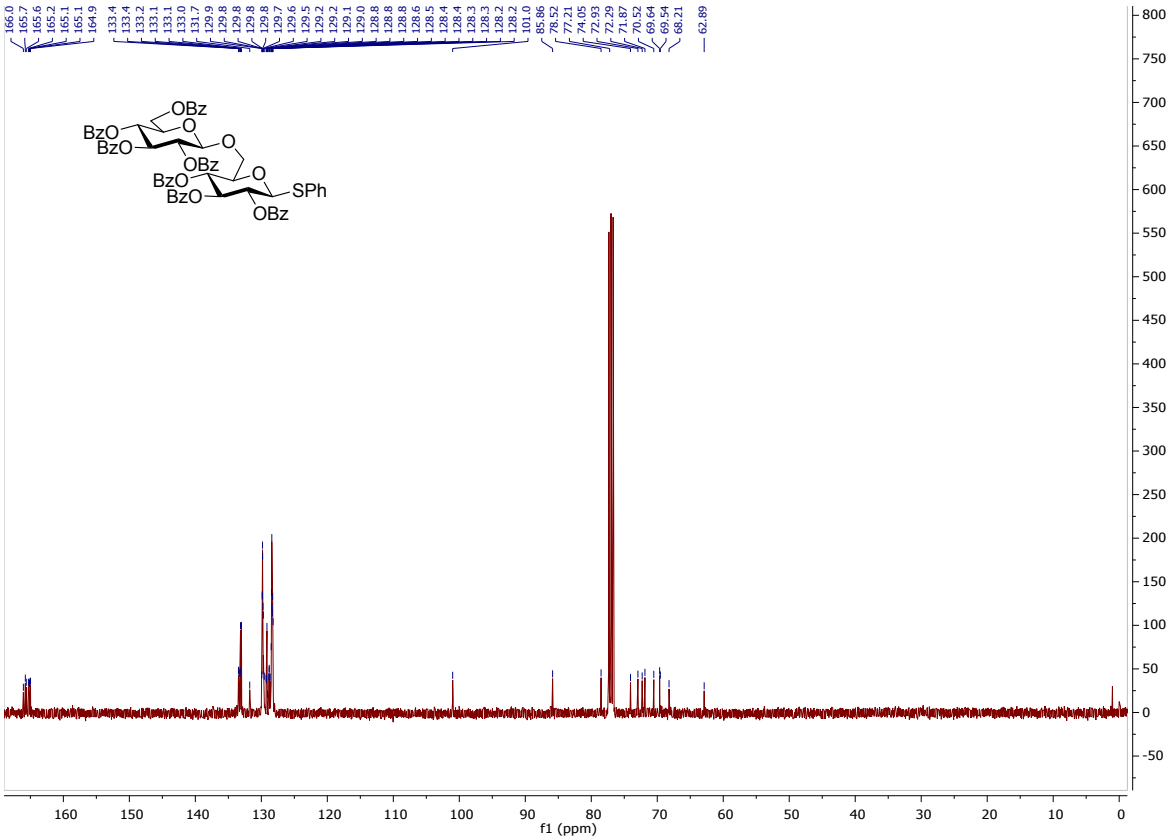
^{1}H and ^{13}C NMR Spectra of Compound **14**



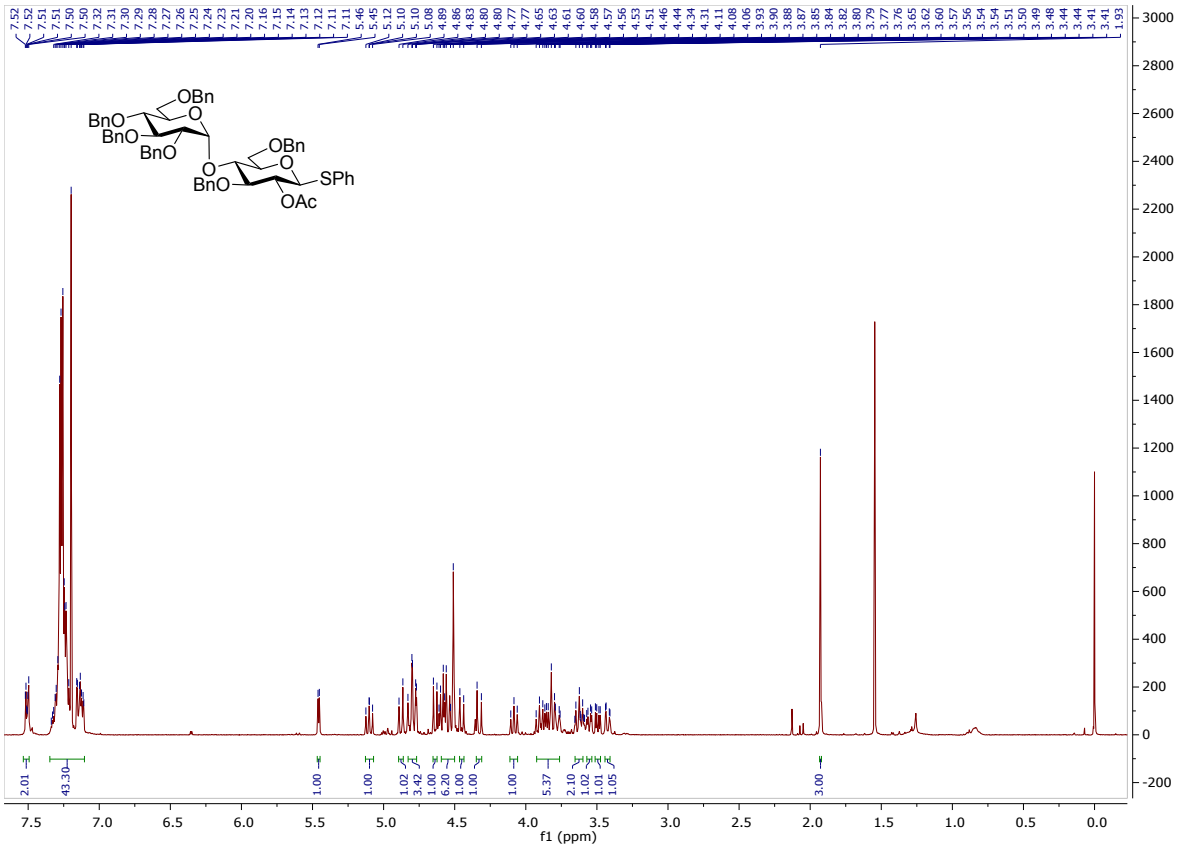


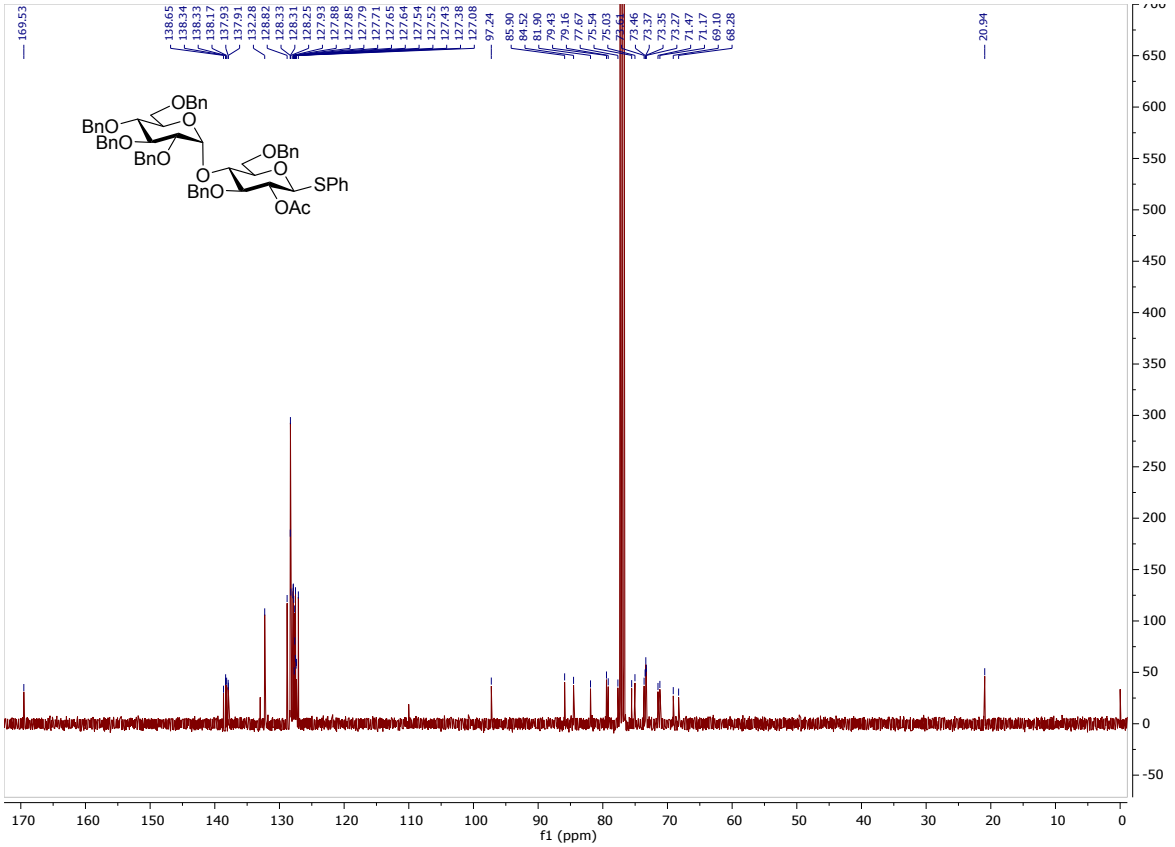
^{1}H and ^{13}C NMR Spectra of Compound **17**



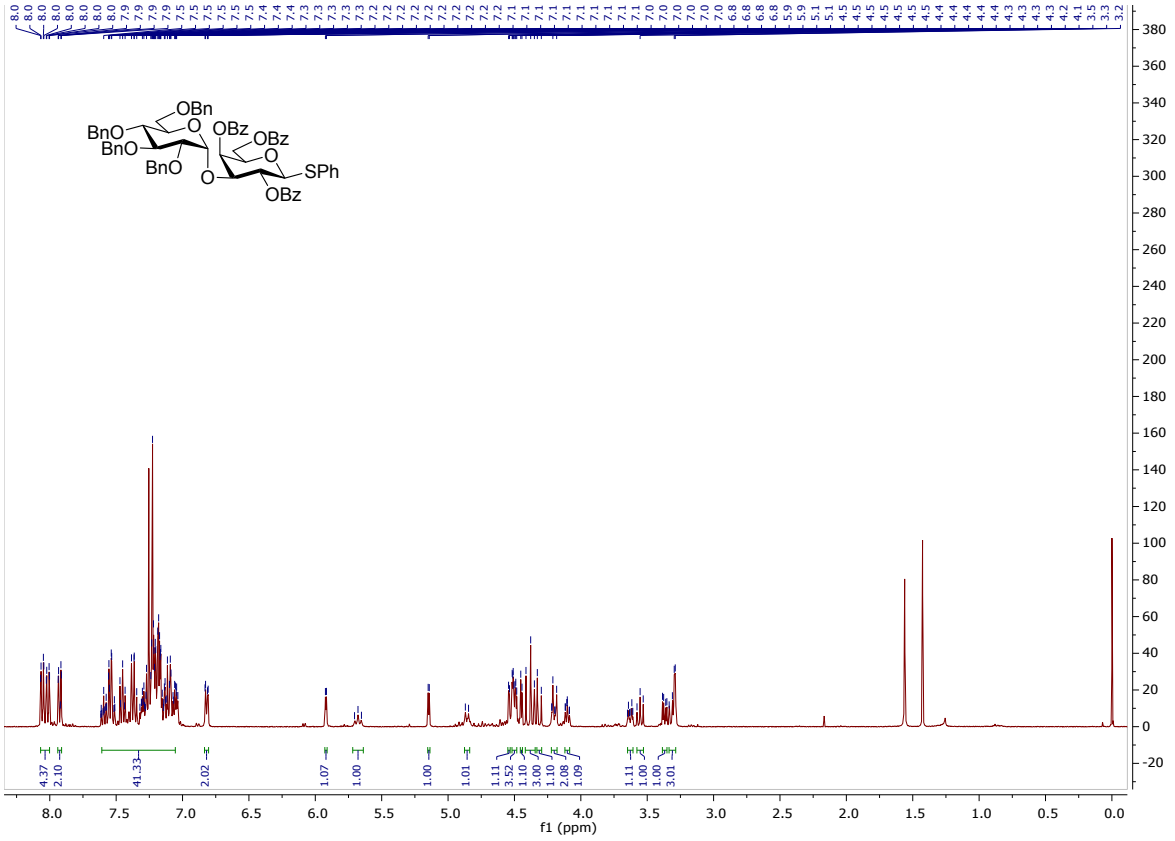


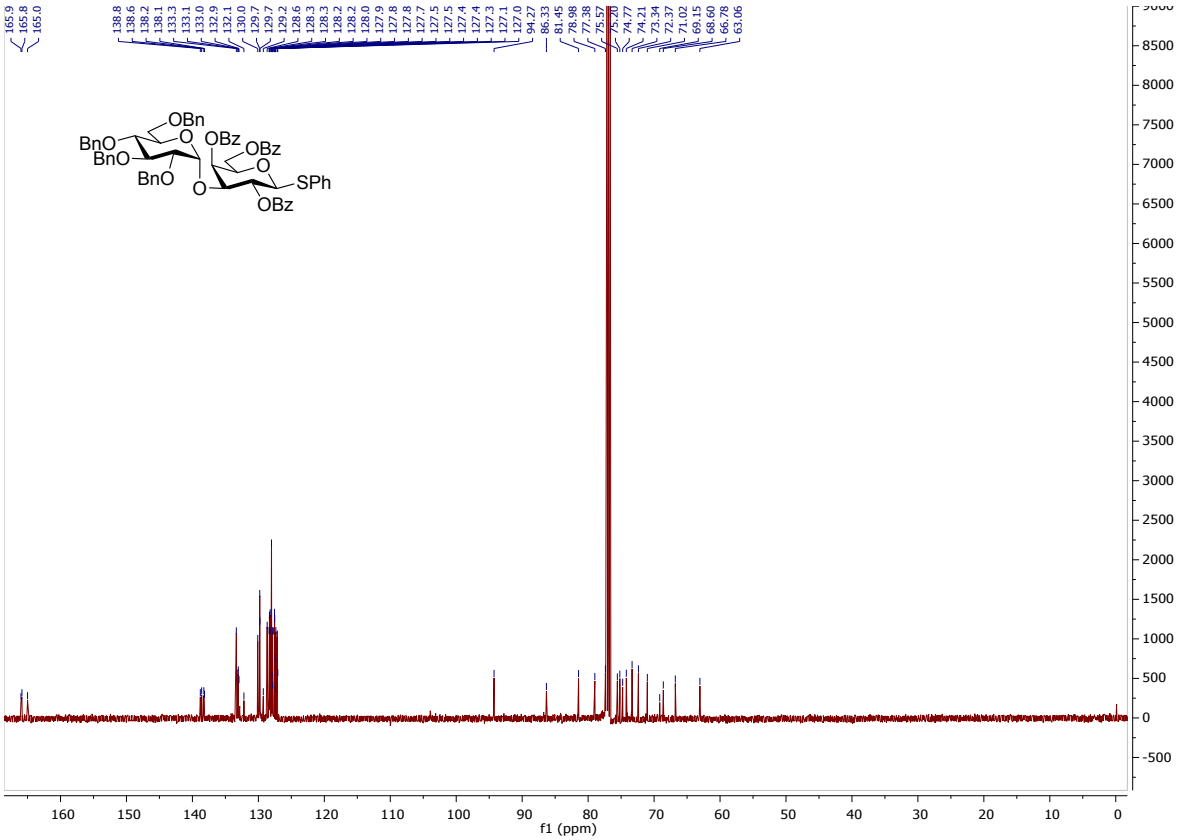
^{1}H and ^{13}C NMR Spectra of Compound **18**



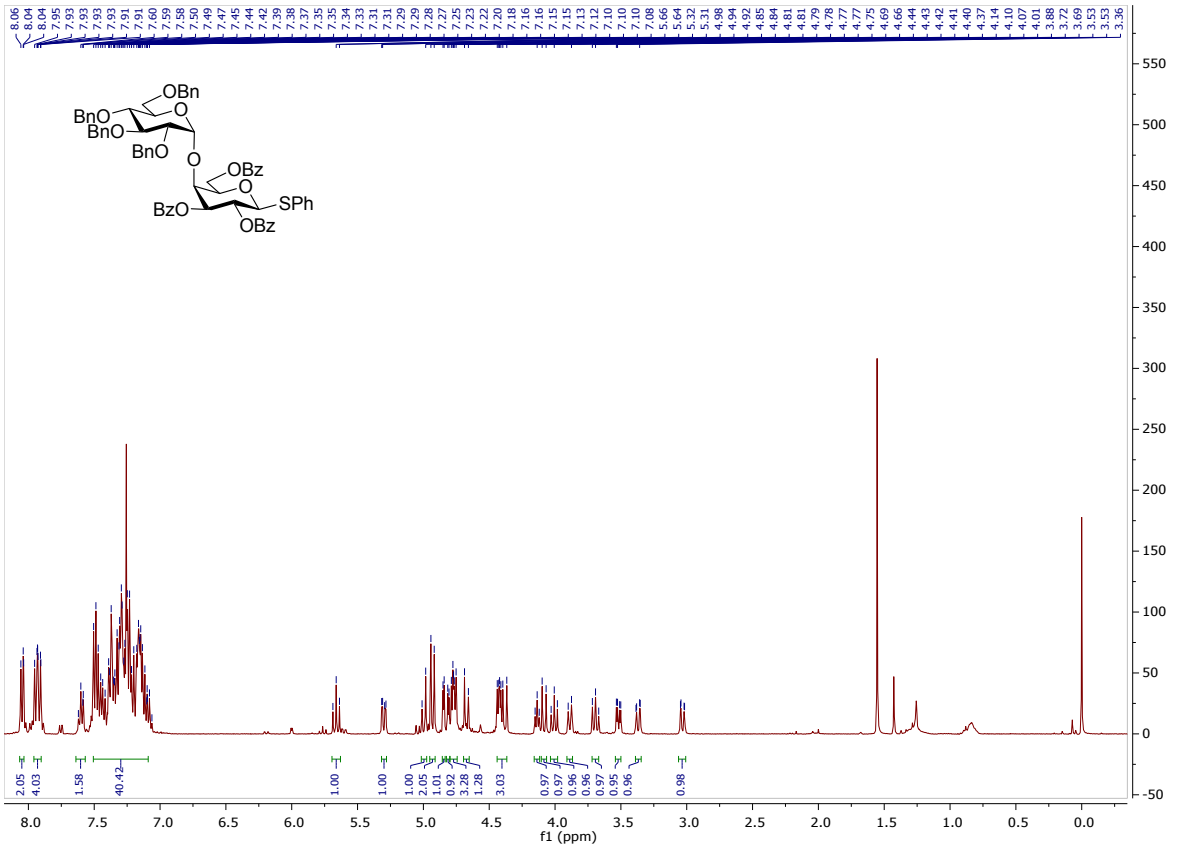


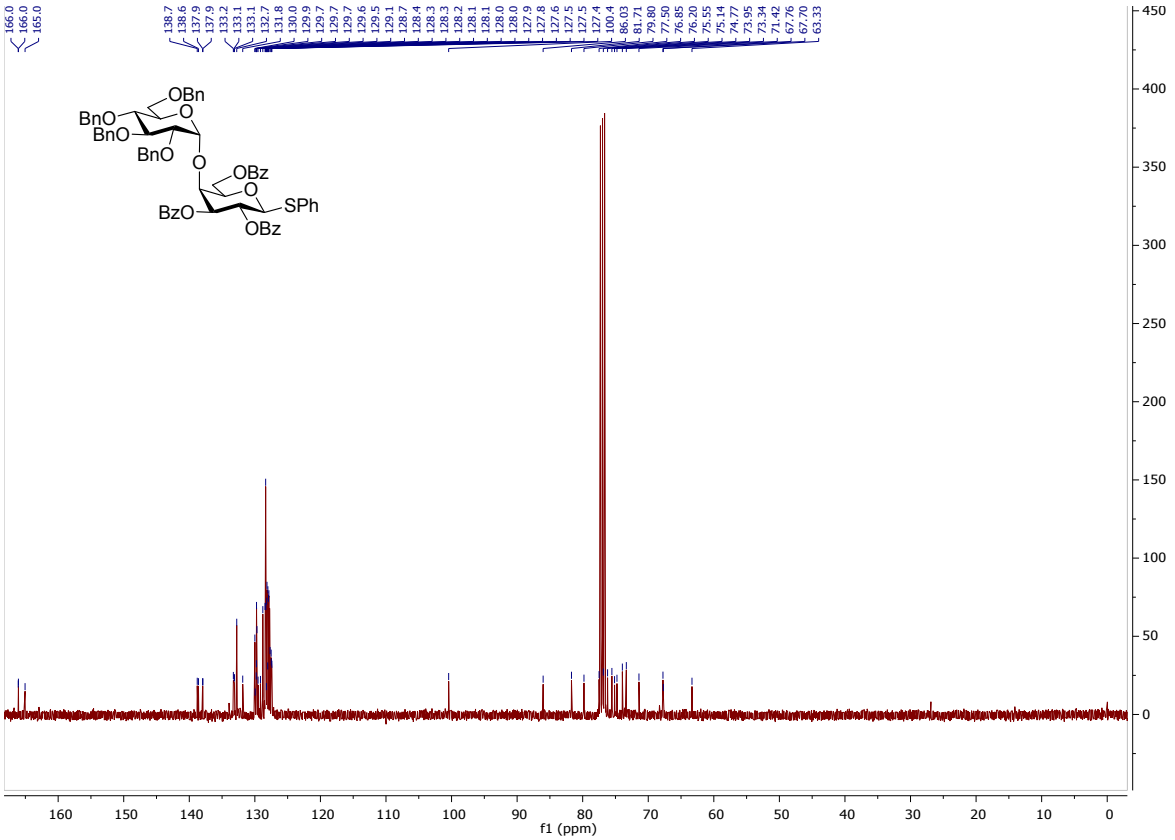
^{1}H and ^{13}C NMR Spectra of Compound **19**



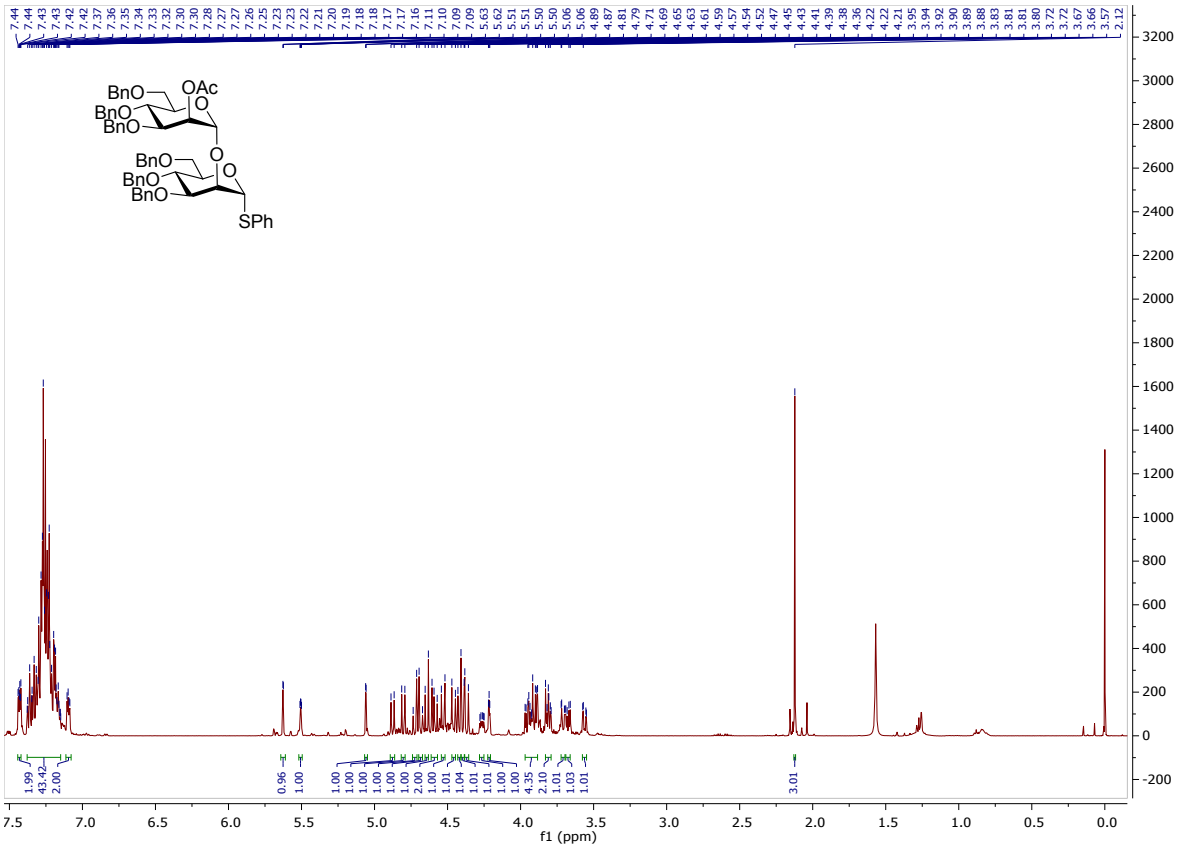


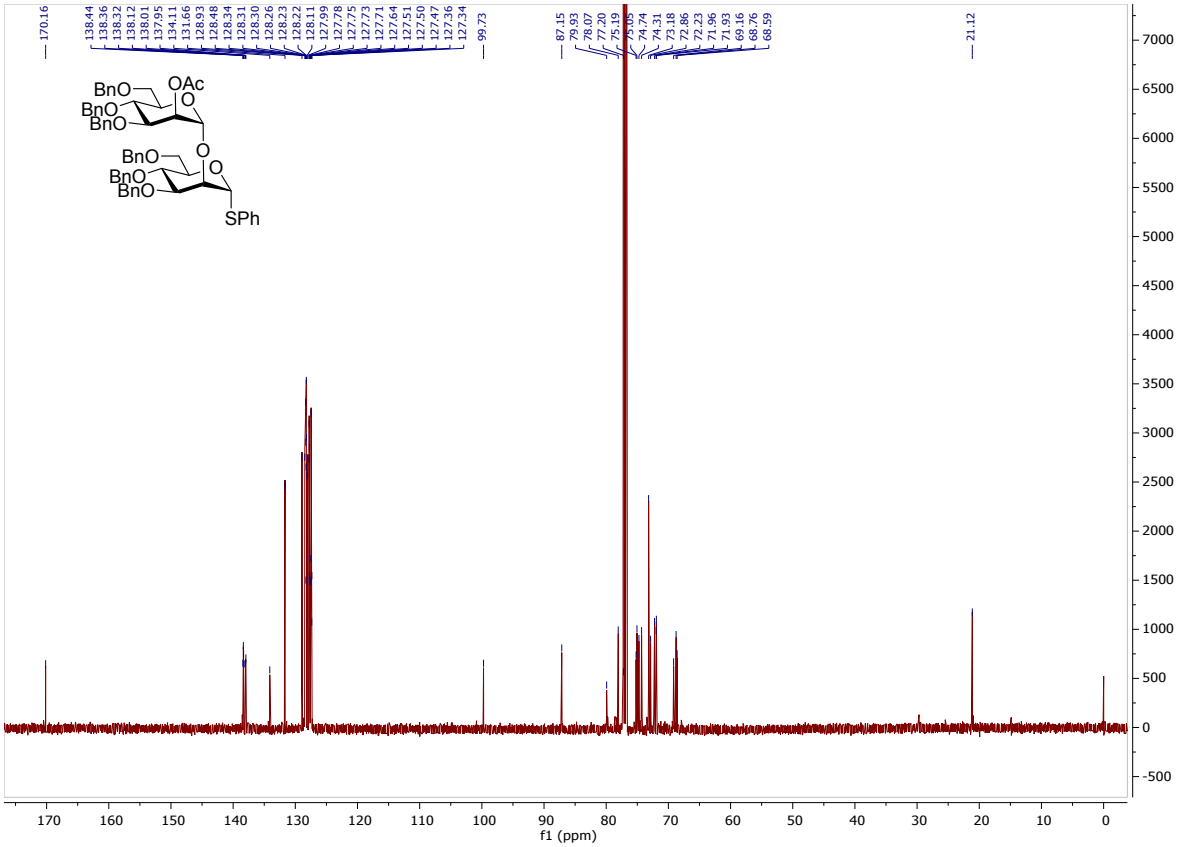
^{1}H and ^{13}C NMR Spectra of Compound **20**



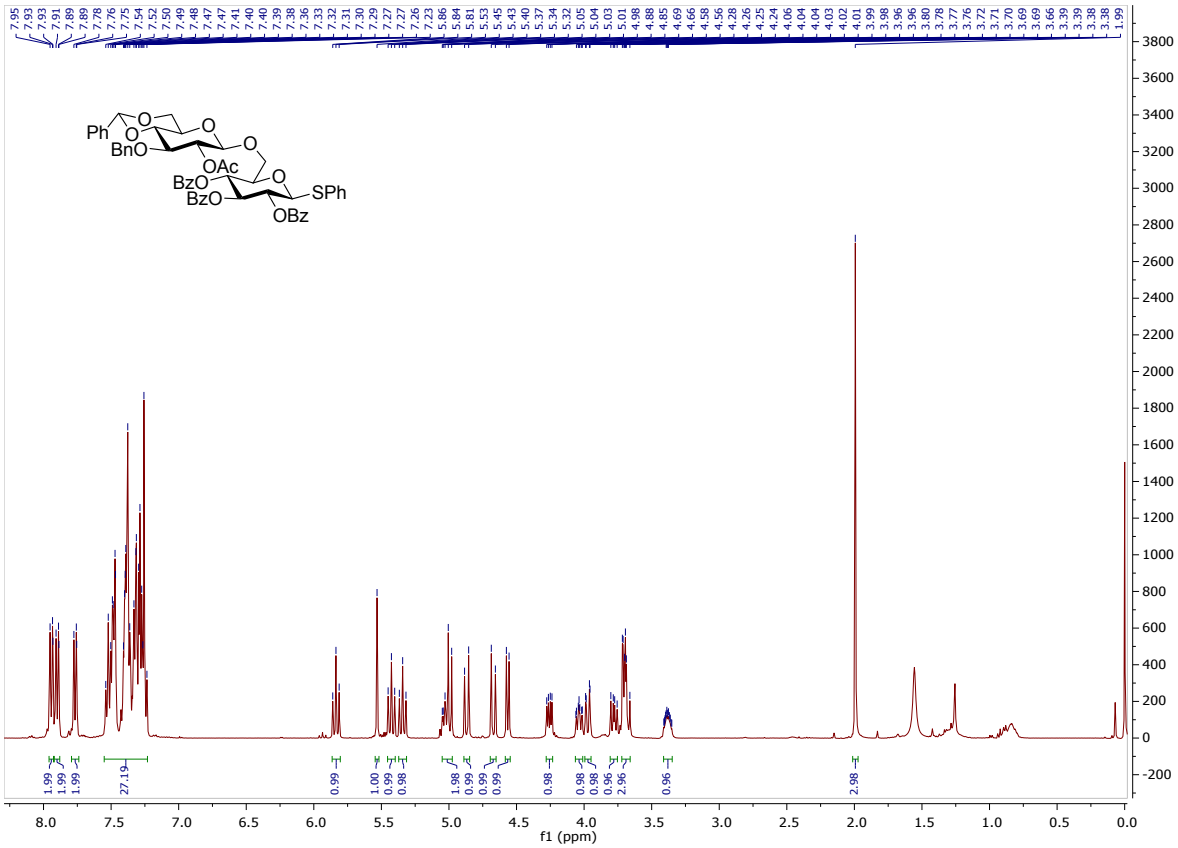


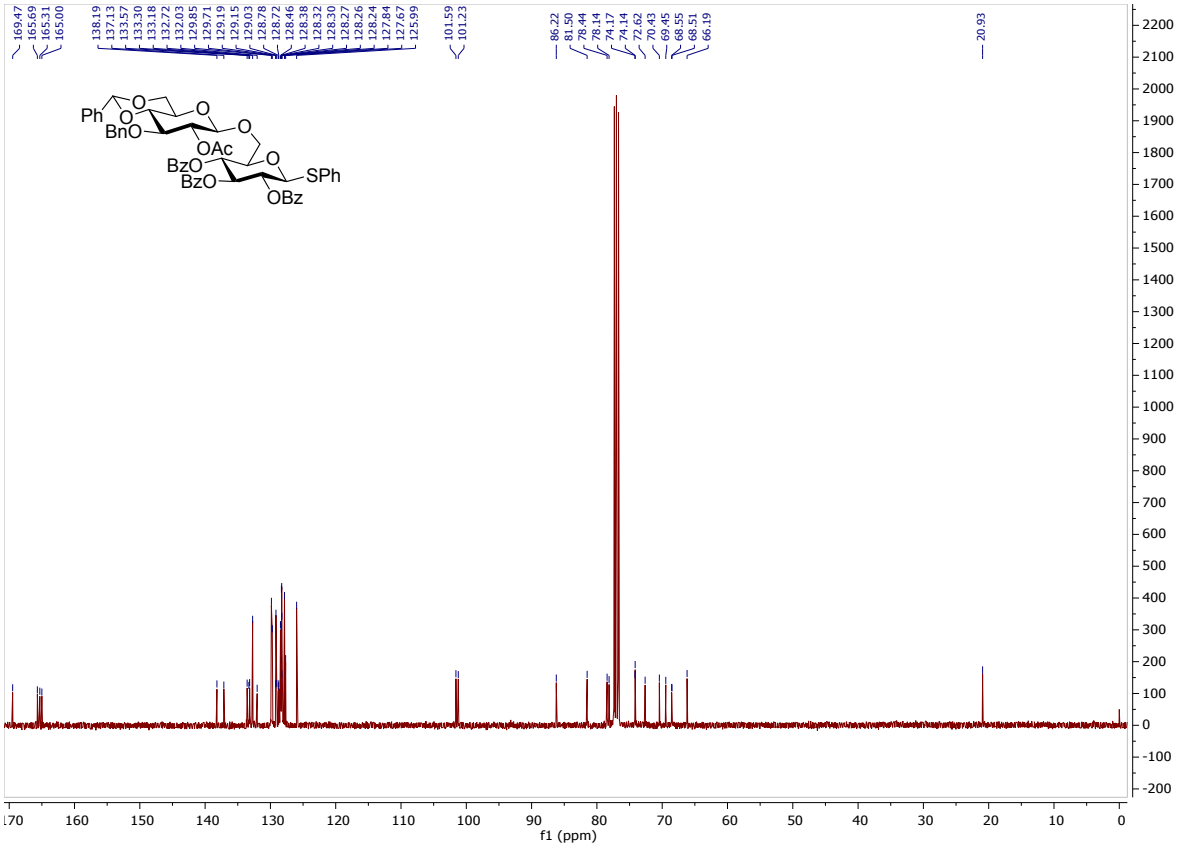
^{1}H and ^{13}C NMR Spectra of Compound **21**



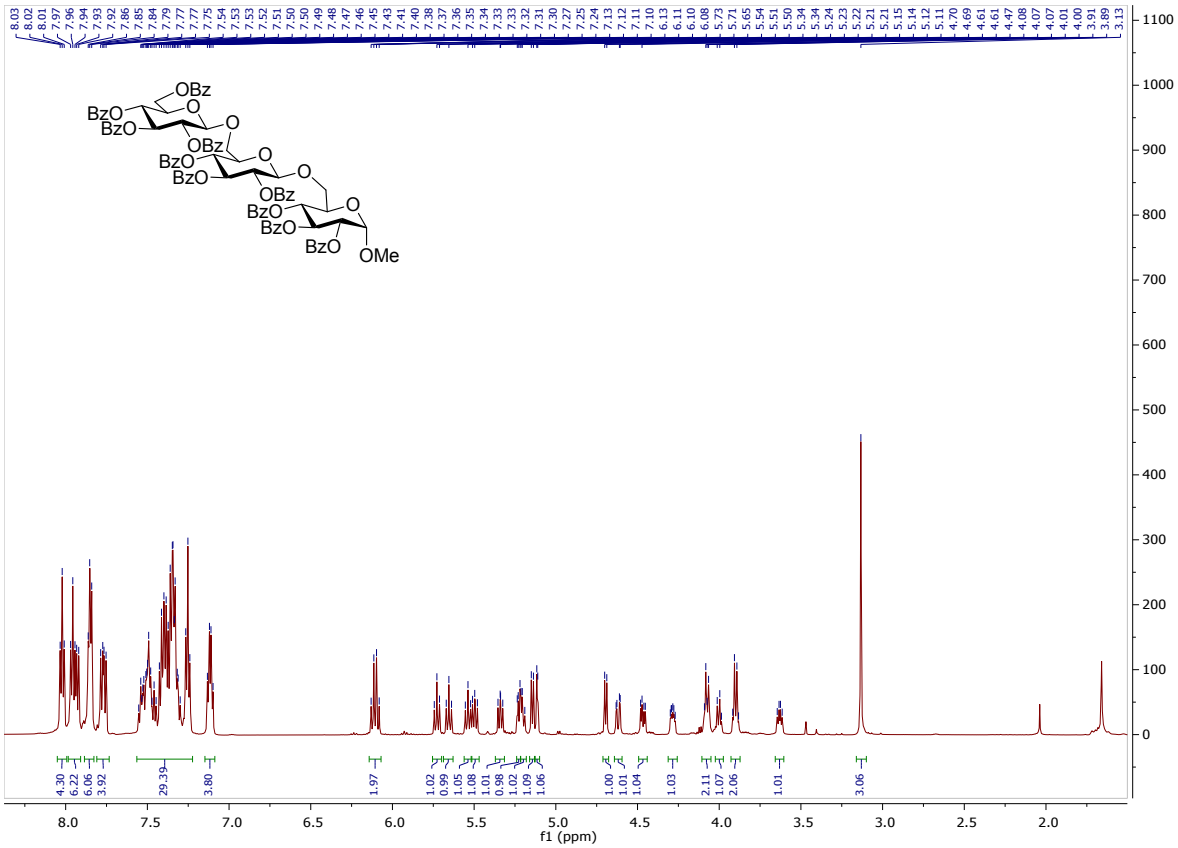


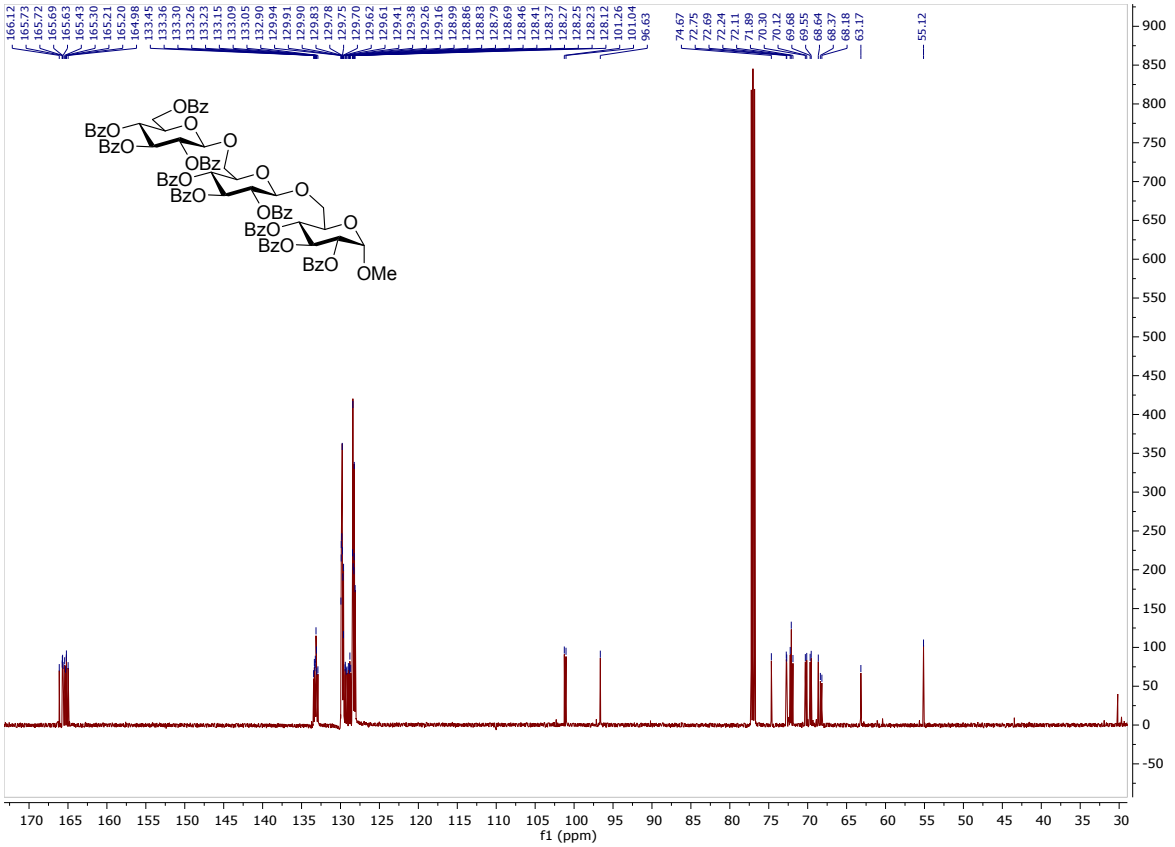
^{1}H and ^{13}C NMR Spectra of Compound **22**



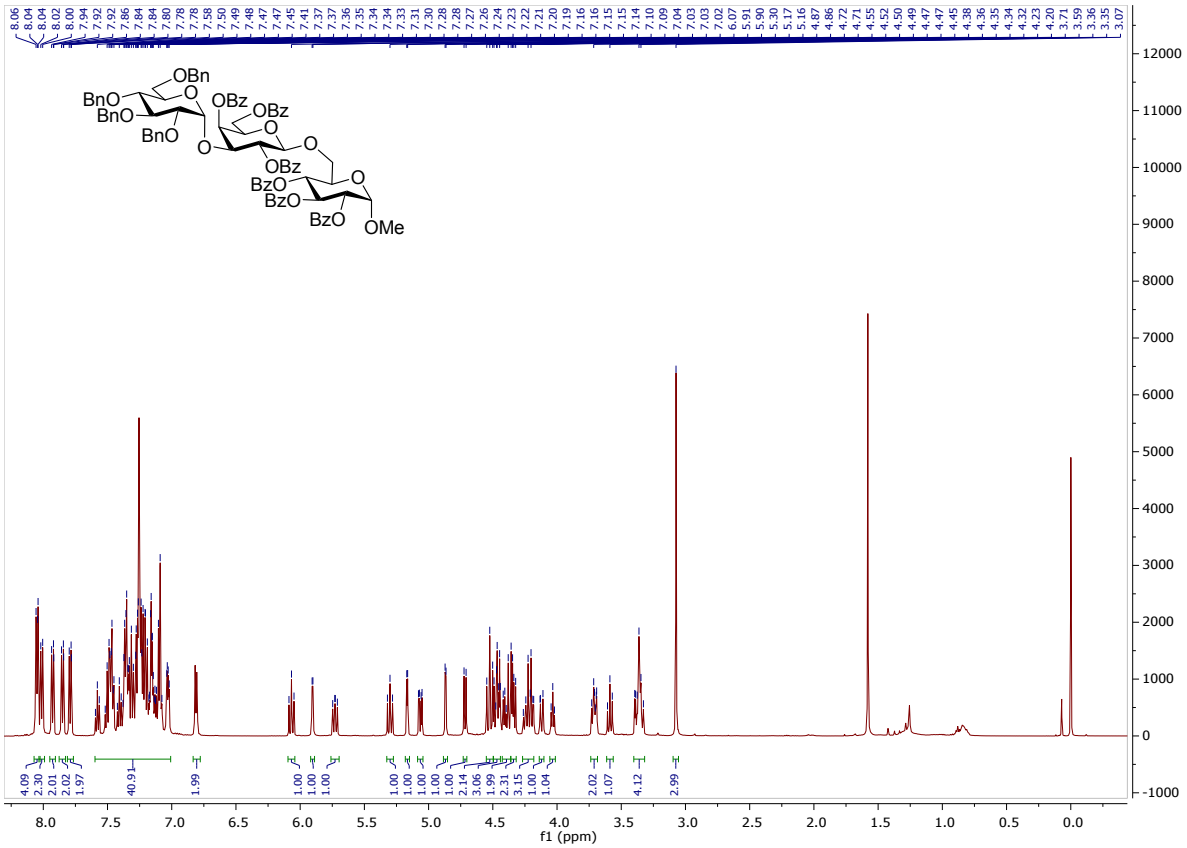


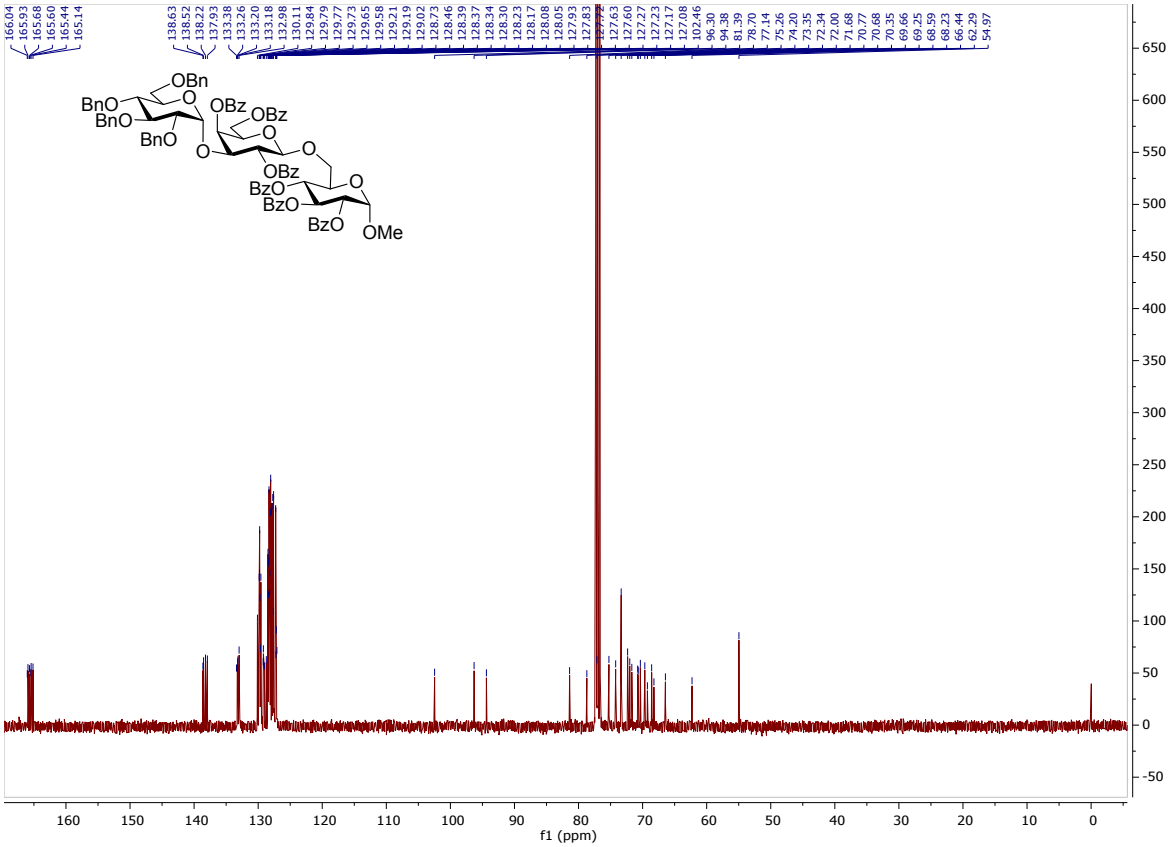
^{1}H and ^{13}C NMR Spectra of Compound **23**



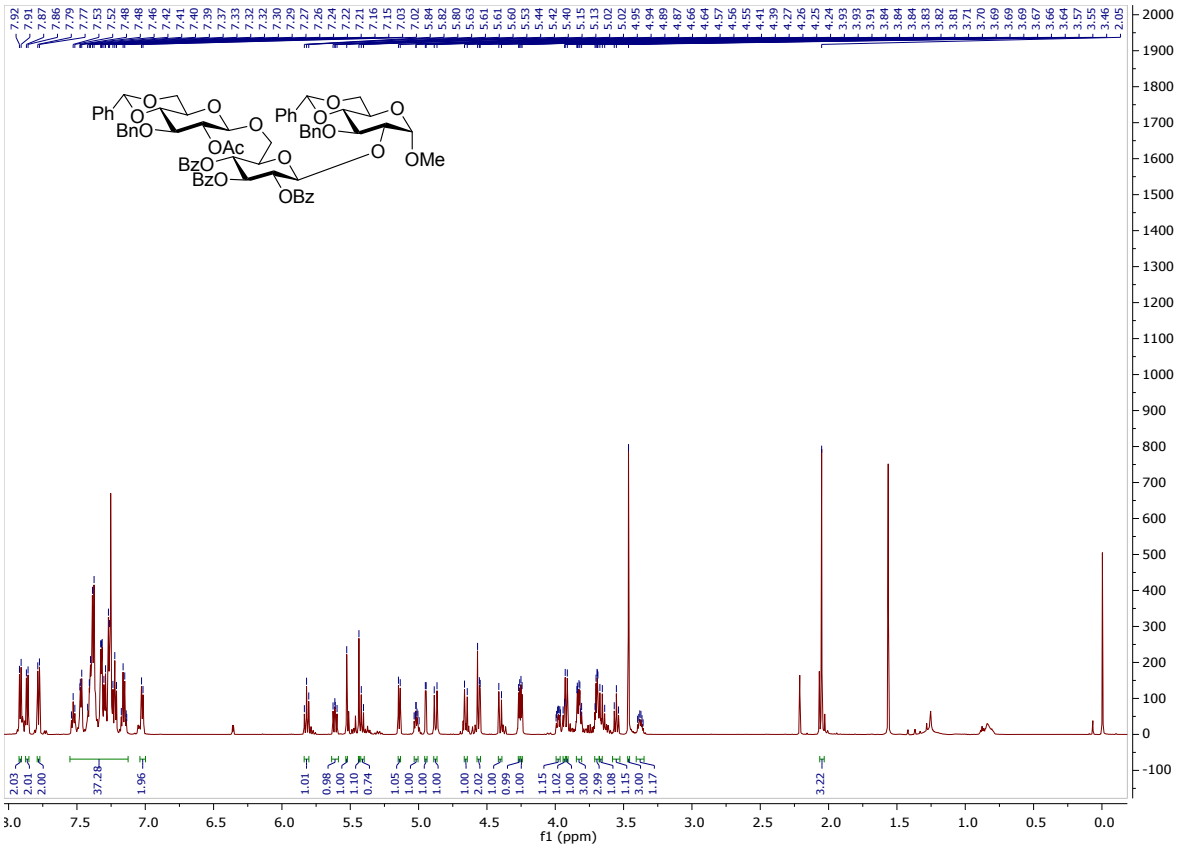


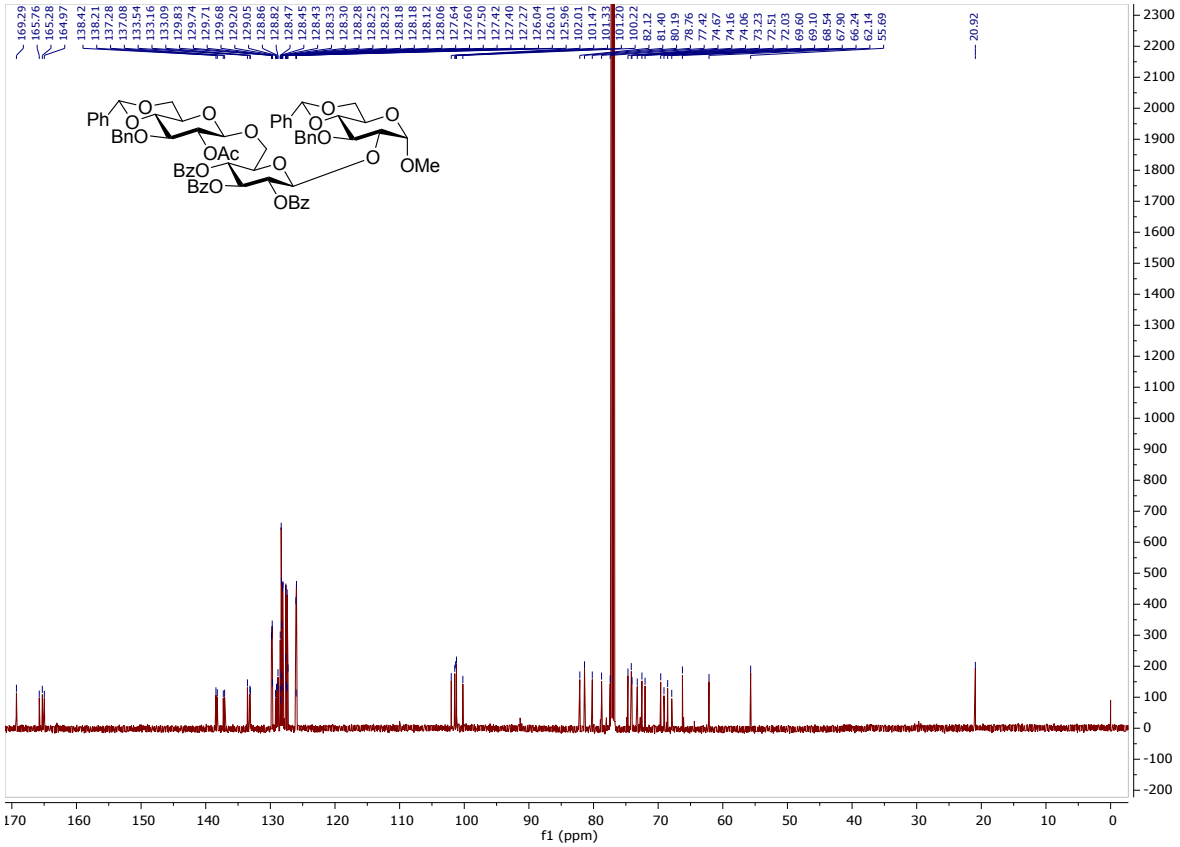
^{1}H and ^{13}C NMR Spectra of Compound **24**





^{1}H and ^{13}C NMR Spectra of Compound **26**




169.29
165.76
165.28
164.97
138.42
138.21
137.28
137.08
133.54
133.16
133.09
129.83
129.74
129.71
129.68
129.20
129.05
128.86
128.82
128.47
128.45
128.43
128.33
128.30
128.28
128.25
128.23
128.18
128.18
128.12
128.06
127.64
127.60
127.50
127.42
127.40
127.27
126.04
126.01
125.96
102.01
101.47
101.33
101.20
100.22
82.12
81.40
80.19
78.76
77.42
74.67
74.16
74.06
73.23
72.51
72.03
69.60
69.10
68.54
67.90
66.24
62.14
55.69
20.92
Ph
O
BnO
O
OAc
BzO
BzO
O
OBz
Ph
O
BnO
O
O
OMe
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)