Comparison of Disaccharide Donors for Heparan Sulfate Synthesis: Uronic Acids vs. their Pyranose Equivalents

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Supplementary Information

Experimental

General

All ^{1}H, ^{13}C, DEPT and 2D NMR spectra were acquired on a Bruker 500 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS). NMR data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), coupling constant (J) in Hertz (Hz), integration. Mass spectra were acquired on a Waters Q-TOF Premier™ Electrospray Mass Spectrometer. TLC analysis was conducted on silica gel F254 (Merck KGaA) with detection by UV absorption (254 nm) or by dipping in cerium molybdate stain (400ml 10% sulfuric acid/water, 20g ammonium molybdate and 0.2g cerium sulfate) where applicable. Column chromatography was carried out using an automated BÜCHI Pure system and pre-packaged BÜCHI FlashPure EcoFlex silica columns (50µm irregular).

X-ray

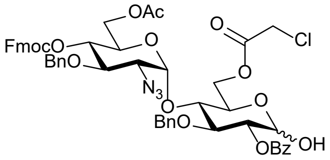
Compound **4** was collected on a Rigaku Spider diffractometer equipped with a MicroMax MM007 rotating-anode generator, high-flux Osmic multilayer mirror optics, and a curved image-plate detector. Compounds **5** and **12** were collected on an Agilent SuperNova diffractometer fitted with an EOS S2 detector.

Crystallographic details

Identification code	**5**	**4**	**12**
CCDC identifier	1987993	1987992	1987991
Empirical formula	$C_{43}H_{45}N_3O_{14}$	$C_{44}H_{46}ClN_3O_{14}$	$C_{59}H_{56}ClN_3O_{14}S$
Formula weight	827.82	876.29	1098.57
Temperature (K)	120.00(10)	164(2)	120.00(10)
Wavelength (Å)	1.54184	1.54178	1.54184
Crystal system	Orthorhombic	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
Unit cell dimensions			
a (Å) b (Å) c (Å)	8.0833(2) 18.7876(7) 26.8116(12)	8.1104(2) 19.5548(6) 27.2321(19)	5.23660(10) 35.3229(3) 14.56840(10)
α (°) β (°) γ (°)	90 90 90	90 90 90	90 95.5220(10) 90
Volume (Å^3)	4071.8(3)	4318.9(4)	2682.24(6)
Z	4	4	2
Density (calculated) (Mg/m^3)	1.350	1.348	1.360
Absorption coefficient (mm^{-1})	0.852	1.389	1.590
F(000)	1744	1840	1152
Crystal size (mm^3)	0.259 × 0.034 × 0.025	1.0 × 0.13 × 0.11	0.484 × 0.098 × 0.055
Theta range for data collection (°)	4.051 to 74.658	6.654 to 58.931	3.944 to 73.534
Index ranges	-9 <= h <= 9 -22 <= k <= 23 -33 <= l < =31	-6 <= h <= 8 -21 <= k <= 21 -30 <= l <= 30	-5 <= h <= 6 -43 <= k <= 43 -18 <= l <= 18
Reflections collected	64624	34329	48369
Independent reflections	8176 [R(int) = 0.0883]	6132 [R(int) = 0.0454]	10328 [R(int) = 0.0367]
Completeness to theta = 67.684°	100%	99.3%	98.9%
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.575	1.0 and 0.717	1.000 and 0.541
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	8176 / 0 / 548	6132 / 10 / 528	10328 / 68 / 914
Goodness-of-fit on F^2	1.054	1.095	1.115
Final R indices [I>2sigma(I)]	R1 = 0.0564 wR2 = 0.1354	R1 = 0.0625 wR2 = 0.1705	R1 = 0.0396 wR2 = 0.1040
R indices (all data)	R1 = 0.0721 wR2 = 0.1464	R1 = 0.0813 wR2 = 0.1892	R1 = 0.0415 wR2 = 0.1051
Absolute structure parameter	-0.06(11)	0.101(9)	-0.005(5)
Largest diff. peak and hole (e.Å^{-3})	0.292 and -0.217	0.429 and -0.339	0.388 and -0.269

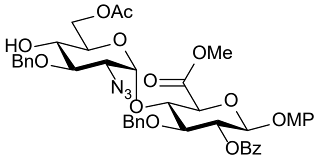
Synthetic Procedures

[6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-6-O-chloroacetyl-β-D-glucopyranoside (2)



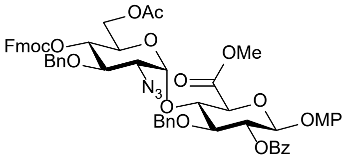
Disaccharide **1** (200 mg, 0.18 mmol) was dissolved in acetonitrile (5 mL), and water (1 mL) was added. Then, ceric ammonium nitrate (3 equiv., 0.3 g, 0.5 mmol) was added and the reaction stirred at room temperature. After 2.5 hours, the mixture was diluted with equal parts toluene and ethyl acetate (20 mL) and washed with water, saturated sodium bicarbonate, brine, dried over $MgSO_4$ and solvents removed in vacuo. The residue was purified by column chromatography to yield **2** as two separate anomers, in the form of a yellow foam (158 mg, 0.16 mmol, 75%); TLC: Rf = 0.45 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 7.8 Hz, 0.05H), 8.09 – 8.03 (m, 2H), 7.90 (dd, J = 7.6, 3.8 Hz, 0.05H), 7.77 – 7.71 (m, 2H), 7.60 (dd, J = 7.5, 1.0 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.45 – 7.34 (m, 4H), 7.31 – 7.13 (m, 12H), 5.64 (d, J = 3.9 Hz, 1H), 5.56 (d, J = 3.9 Hz, 0.05H), 5.50 (t, J = 3.3 Hz, 1H), 5.25 (s, 0.05H), 5.22 – 5.15 (m, 0.05H), 5.12 (dd, J = 9.7, 3.5 Hz, 1H), 4.93 – 4.85 (m, 3H), 4.76 (d, J = 10.9 Hz, 1H), 4.65 (d, J = 10.9 Hz, 1H), 4.62 (dd, J = 12.0, 2.4 Hz, 1H), 4.47 (dd, J = 10.5, 6.8 Hz, 1H), 4.39 (dd, J = 9.7, 8.5 Hz, 1H), 4.37 – 4.22 (m, 4H), 4.18 (t, J = 7.0 Hz, 1H), 4.13 (s, 2H), 4.07 (dd, J = 12.4, 2.8 Hz, 1H), 3.99 (ddd, J = 10.4, 8.1, 5.2 Hz, 2H), 3.91 (dd, J = 9.8, 8.4 Hz, 1H), 3.78 (ddd, J = 9.8, 5.4, 2.5 Hz, 0.05H), 3.60 (d, J = 3.7 Hz, 1H), 3.51 (t, J = 6.6 Hz, 0.05H), 3.37 (dd, J = 10.3, 3.9 Hz, 1H), 2.34 (s, 0.05H), 2.04 (s, 3H), 1.93 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.85, 165.45, 164.01, 152.40, 141.47, 141.24, 139.54, 139.52, 135.98, 135.37, 131.97, 131.75, 128.00, 127.55, 126.82, 126.60, 126.18, 126.13, 125.88, 125.54, 125.46, 123.33, 123.14, 118.33, 118.31, 114.60, 96.27, 93.71, 88.32, 80.66, 77.71, 75.68, 75.56, 75.30, 75.05, 74.48, 73.43, 73.37, 73.06, 72.92, 72.68, 70.72, 68.60, 66.87, 66.25, 63.00, 60.92, 60.15, 44.91, 38.92, 27.90, 18.90; HRMS (ESI+) calculated for $C_{52}H_{50}ClN_3O_{15}$ [M+Na]$^+$ 1014.2828 m/z, found 1014.2823.

Methyl (p-Methoxyphenyl [6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-β-D-glucopyranoside) uronate (5)



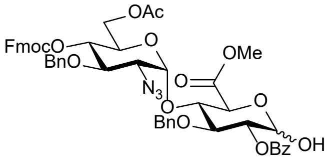
Disaccharide **1** (200 mg, 0.18 mmol) was dissolved in ethanol (10 mL) and acetonitrile (1 mL), and DABCO (6 equiv., 130 mg, 1.1 mmol) was added. The reaction was stirred at 70°C for 1.5 hours. The solvents were removed in vacuo, and the residue dissolved in chloroform and filtered through a silica pad. The pad was washed with equal parts ethyl acetate and petroleum ether, and the solvents removed in vacuo. The residue was then dissolved in acetonitrile (10 mL) and water (2 mL), and iodobenzene diacetate (2.5 equiv., 150 mg, 0.46 mmol) and TEMPO (1 equiv., 30 mg, 0.18 mmol) added. The mixture was stirred at room temperature for 24 hours, and then the solvents were removed in vacuo and the residue was co-evaporated twice with toluene. The residue was then dissolved in MeOH (6 mL) and Et_2O (12 mL) under argon, and trimethylsilyldiazomethane (2.0 mol/L) in hexanes (2 equiv., 0.2 mL, 0.4 mmol) was added. The reaction was allowed to stir for 1 hour before quenching with 4 drops of glacial acetic acid. The solvents were removed in vacuo and the residue co-evaporated twice with toluene. The residue was then purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the title compound as a yellow foam (94 mg, 0.11 mmol, 62%), TLC: Rf = 0.45 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 2H), 7.61 – 7.53 (m, 1H), 7.46 – 7.33 (m, 6H), 7.32 – 7.28 (m, 1H), 7.25 – 7.16 (m, 5H), 6.93 – 6.86 (m, 2H), 6.79 – 6.73 (m, 2H), 5.59 – 5.51 (m, 2H), 5.15 (d, J = 6.7 Hz, 1H), 4.87 (s, 2H), 4.81 (d, J = 10.6 Hz, 1H), 4.75 (d, J = 10.6 Hz, 1H), 4.55 (dd, J = 12.4, 3.4 Hz, 1H), 4.46 (t, J = 8.8 Hz, 1H), 4.23 – 4.04 (m, 4H), 3.76 (dd, J = 10.3, 8.6 Hz, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 3.60 – 3.52 (m, 1H), 3.43 (dd, J = 10.1, 8.7 Hz, 1H), 3.25 (dd, J = 10.2, 3.8 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 168.5, 165.0, 155.7, 150.9, 137.9, 137.3, 133.5, 129.8, 129.4, 128.6, 128.55, 128.35, 128.2, 128.1, 127.85, 127.80, 118.7, 114.5, 100.7, 97.8, 82.0, 79.0, 75.3, 74.5, 74.3, 73.9, 70.9, 70.5, 62.8, 62.6, 55.6, 52.7, 20.8; HRMS (ESI+) calculated for $C_{43}H_{45}N_3O_{14}$ $[M+Na]^+$ 850.2799 m/z, found 850.2795.

Methyl (p-Methoxyphenyl [6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-β-D-glucopyranoside)uronate (6)



Disaccharide **1** (200 mg, 0.18 mmol) was dissolved in ethanol (10 mL) and acetonitrile (1 mL), and thiourea (6 equiv., 85 mg, 1.1 mmol) was added. The reaction was stirred at 70°C for 2 hours, and then left to stir at room temperature for 12 hours. The solvents were removed in vacuo, and the residue dissolved in chloroform and filtered through a silica pad. The pad was washed with equal parts ethyl acetate and petroleum ether, and the solvents removed in vacuo. The residue was then dissolved in acetonitrile (10 mL) and water (2 mL), and iodobenzene diacetate (2.5 equiv., 150 mg, 0.46 mmol) and TEMPO (1 equiv., 30 mg, 0.18 mmol) added. The mixture was stirred at room temperature for 24 hours, and then the solvents were removed in vacuo and the residue was co-evaporated twice with toluene. The residue was then dissolved in MeOH (6 mL) and Et$_2$O (12 mL) under argon, and trimethylsilyldiazomethane (2.0 mol/L) in hexanes (2 equiv., 0.2 mL, 0.4 mmol) was added. The reaction was allowed to stir for 1 hour before quenching with 4 drops of glacial acetic acid. The solvents were removed in vacuo and the residue co-evaporated twice with toluene. The residue was then purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield **6** as a yellow foam (129 mg, 0.12 mmol, 64%), TLC: Rf = 0.7 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.08 – 8.01 (m, 2H), 7.79 – 7.71 (m, 2H), 7.63 – 7.52 (m, 3H), 7.47 – 7.43 (m, 2H), 7.41 – 7.36 (m, 2H), 7.31 – 7.15 (m, 12H), 6.94 – 6.87 (m, 2H), 6.80 – 6.74 (m, 2H), 5.59 – 5.49 (m, 2H), 5.18 (d, J = 6.3 Hz, 1H), 4.89 (dd, J = 10.3, 9.2 Hz, 1H), 4.82 – 4.68 (m, 3H), 4.63 (d, J = 10.9 Hz, 1H), 4.54 – 4.43 (m, 2H), 4.34 – 4.29 (m, 1H), 4.28 – 4.21 (m, 2H), 4.20 – 4.07 (m, 3H), 3.93 (dd, J = 10.3, 9.1 Hz, 1H), 3.83 (ddd, J = 10.1, 3.9, 2.3 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.37 (dd, J = 10.3, 3.7 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 168.4, 165.0, 155.7, 154.2, 150.9, 143.3, 143, 141.35, 141.3, 137.25, 137.2, 133.5, 129.8, 129.4, 128.6, 128.45, 128.4, 128.4, 128.0, 127.95, 127.9, 127.85, 127.8, 127.2, 125.1, 124.9, 120.1, 120.05, 118.5, 114.5, 100.5, 97.6, 81.6, 77.4, 75.0, 74.7, 74.4, 74.35, 74.3, 73.9, 70.3, 68.4, 62.8, 61.5, 60.4, 55.6, 52.7, 46.7, 21.0, 20.7, 14.2; HRMS (ESI+) calculated for C$_{58}$H$_{55}$N$_3$O$_{16}$ [M+Na]$^+$ 1072.3480 m/z, found 1072.3484.

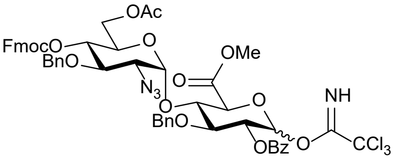
Methyl ([6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-β-D-glucopyranoside)uronate (7)



Compound **6** (850 mg, 0.81 mmol) was dissolved in acetonitrile (10 mL), and water (1 mL) was added. Then, ceric ammonium nitrate (3 equiv., 1.34 g, 2.43 mmol) was added and the reaction stirred at room temperature. After 2.5 hours, the mixture was diluted with equal parts toluene and ethyl acetate (20 mL) and washed with water, saturated sodium bicarbonate, brine, dried over MgSO$_4$ and solvents removed in vacuo. The residue was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the title compound as a mixture of anomers, appearing as a yellow foam (500 mg, 0.53 mmol, 77%), TLC: Rf = 0.45 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.12 – 8.06 (m, 1.7H), 8.06 – 8.04 (m, 0.3H), 7.79 – 7.73 (m, 2H), 7.63 – 7.53 (m, 2H), 7.52 – 7.35 (m, 5H), 7.32 – 7.12 (m, 12H), 5.66 (dd, J = 6.6, 3.0 Hz, 0.85H), 5.44

(d, J = 3.7 Hz, 0.15H), 5.37 (d, J = 3.6 Hz, 0.85H), 5.24 – 5.19 (m, 0.15H), 5.13 (dd, J = 7.4, 3.0 Hz, 0.85H), 4.95 (dd, J = 9.2, 6.5 Hz, 0.15H), 4.87 – 4.78 (m, 3H), 4.76 (d, J = 6.9 Hz, 0.85H), 4.63 – 4.59 (m, 0.15H), 4.56 – 4.48 (m, 1.15H), 4.44 (d, J = 10.9 Hz, 0.85H), 4.39 – 4.29 (m, 3H), 4.26 – 4.15 (m, 3.4H), 4.14 – 4.04 (m, 0.6H), 4.01 (ddd, J = 10.3, 4.7, 2.5 Hz, 0.85H), 3.89 –3.83 (m, 0.3H), 3.77 – 3.74 (m, 0.85H), 3.72 (s, 3H), 3.38 – 3.27 (m, 2H), 2.08 (s, 2.55H), 2.07 (s, 0.45H); ^{13}C NMR (126 MHz, $CDCl_3$) δ170.97, 169.32, 165.69, 154.29, 143.23, 143.09, 141.34, 137.37, 137.25, 133.54, 129.83, 129.34, 128.80, 128.68, 128.41, 128.35, 128.31, 127.97, 127.85, 127.71, 127.63, 127.54, 127.23, 125.00, 124.80, 120.12, 98.58, 95.69, 89.78, 77.36, 77.27, 77.16, 77.02, 76.76, 75.87, 75.00, 74.62, 74.42, 72.10, 71.61, 70.15, 68.41, 62.76, 61.84, 52.57, 46.78, 20.84; HRMS (ESI+) calculated for $C_{51}H_{49}N_3O_{15}$ $[M+Na]^+$ 966.3061 m/z, found 966.3065.

Methyl ([6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-α,β-D-glucopyranoside)uronate trichloroacetimidate (8)



Hemiacetal **7** (300 mg, 0.318 mmol) was dissolved in dry dichloromethane (15 mL per 1 mmol hemiacetal) under argon. The reaction mixture was then treated with excess trichloroacetonitrile (10 equiv.), stirred at room temperature briefly, and then catalytic sodium hydride (0.3 equiv.) was added. The reaction was stirred at room temperature for approximately 1 hour until TLC indicated competition. The reaction mixture was then filtered through a small silica pad, which was rinsed with EtOAc, before being dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the title compound as a mixture of anomers in a foam (204 mg, 0.187 mmol, 59%), TLC: Rf = 0.8 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 0.15H), 8.60 (s, 0.85H), 8.05 – 7.98 (m, 2H), 7.75 (dd, J = 7.6, 3.7 Hz, 2H), 7.63 – 7.52 (m, 3H), 7.46 – 7.35 (m, 4H), 7.32 – 7.13 (m, 12H), 6.58 (d, J = 3.6 Hz, 0.85H), 6.11 (d, J = 6.0 Hz, 0.15H), 5.66 (d, J = 3.9 Hz, 0.85H), 5.59 (t, J = 6.0 Hz, 0.15H), 5.45 (d, J = 3.9 Hz, 0.15H), 5.40 (dd, J = 9.7, 3.7 Hz, 0.85H), 4.94 – 4.84 (m, 3H), 4.78 (d, J = 11.0 Hz, 1H), 4.68 (d, J = 10.9 Hz, 1H), 4.62 (dd, J = 12.0, 2.3 Hz, 1H), 4.47 (dd, J = 10.5, 6.7 Hz, 1H), 4.45 – 4.19 (m, 4H), 4.18– 3.94 (m, 6H), 3.35 (dd, J = 10.3, 3.9 Hz, 1H), 2.06 (s, 0.45H), 2.05 (s, 2.55H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.42, 166.97, 165.26, 160.45, 154.12, 143.22, 142.99, 141.30, 137.44, 137.13, 133.61, 129.74, 129.02, 128.94, 128.54, 128.39, 128.36, 128.21, 127.94, 127.84, 127.75, 127.34, 127.22, 125.09, 124.90, 120.08, 98.40, 93.16, 90.84, 79.89, 75.12, 75.06, 74.62, 72.86, 70.57, 70.40, 68.87, 64.37, 62.51, 61.85, 46.68, 40.58, 20.67; HRMS (ESI+) calculated for $C_{53}H_{49}Cl_3N_4O_{15}$ $[M+Na]^+$ 1109.2158 m/z, found 1109.2167.

General procedure A: Trifluoro-N-phenylacetimidate formation

The appropriate hemiacetal was dissolved in dry dichloromethane (15 mL per 1 mmol hemiacetal) under argon. The reaction mixture was then treated with 2,2,2-trifluoro-N-phenylacetimidoyl chloride (4 equiv.), stirred at room temperature briefly, and then sodium hydride (1 equiv.) was added in small portions. The reaction was stirred at room temperature for approximately 10 minutes until TLC indicated competition. The reaction mixture was then filtered through a small silica pad, which was rinsed with EtOAc, before being dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the desired trifluoro-N-phenylacetimidate as a mixture of anomers.

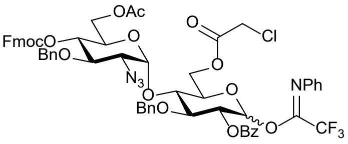
General procedure B: Acetate formation

Sodium acetate (2 equiv.) and acetic anhydride (2 equiv.) was added to toluene (30 mL per 1 mmol hemiacetal) and heated to reflux. The appropriate hemiacetal was dissolved in a small quantity of toluene (1-5 mL) and injected into the reaction vessel. The reaction was then stirred at reflux for around 2-3 hours, until TLC indicated completion. The reaction mixture was then allowed to cool, and then diluted with EtOAc and washed with saturated aqueous sodium bicarbonate, water, brine, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene), with both anomers of the product eluting as one peak.

General procedure C: Thioglycoside formation

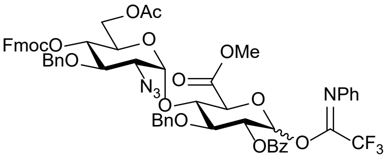
The appropriate disaccharide acetate and a small quantity of molecular sieves was dissolved in dry dichloromethane (15 mL per 1 mmol hemiacetal) under argon. The reaction mixture was then treated with toluenethiol (solution of 1g in 10ml DCM, 1.5 equiv.) followed by boron trifluoride diethyl etherate (0.5 equiv.). The reaction mixture was then stirred at room temperature for around 3 hours, until TLC indicated completion. The reaction mixture was then diluted with EtOAc and washed with saturated aqueous sodium bicarbonate, water, brine, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the desired β thioglycoside.

[6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-6-O-chloroacetyl-α,β-D-glucopyranoside trifluoro-N-phenylacetimidate (9)



Hemiacetal **2** (100 mg, 0.101 mmol) was reacted according to General procedure A to yield the title compound as a yellow foam (100 mg, 0.085 mmol, 85%), TLC: Rf = 0.8 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$)δ 8.10 – 8.04 (m, 1.86H), 8.05 – 8.02 (m, 0.14H), 7.75 (dd, J = 7.7, 3.6 Hz, 2H), 7.63 – 7.52 (m, 3H), 7.47 (t, J = 7.8 Hz, 2H), 7.38 (m, 2H), 7.32 – 7.16 (m, 14H), 7.14 – 7.07 (m, 1H), 6.76 (d, J = 7.8 Hz, 2H), 6.46 (s, 0.07H), 6.09 (s, 0.93H), 5.63 (d, J = 3.9 Hz, 0.07H), 5.56 (t, J = 6.1 Hz, 0.93H), 5.43 (d, J = 3.8 Hz, 1H), 4.89 – 4.82 (m, 2H), 4.78 (d, J = 10.8 Hz, 1H), 4.67 – 4.59 (m, 2H), 4.56 – 4.46 (m, 2H), 4.41 (dd, J = 12.0, 4.8 Hz, 1H), 4.34 (dd, J = 10.6, 7.1 Hz, 1H), 4.26 (dd, J = 12.4, 4.7 Hz, 1H), 4.19 (t, J = 6.9 Hz, 1H), 4.11 – 3.98 (m, 7H), 3.87 (dd, J = 10.3, 9.1 Hz, 1H), 3.40 (dd, J = 10.3, 3.9 Hz, 0.07H), 3.35 (dd, J = 10.3, 3.8 Hz, 0.93H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 167.0, 164.8, 154.2, 143.2, 143.1, 143.0, 141.3, 137.1, 133.7, 129.8, 129.1, 128.8, 128.7, 128.5, 128.4, 127.9, 127.8, 127.6, 127.2, 125.1, 124.9, 124.6, 120.1, 119.3, 98.1, 94.5, 80.9, 77.4, 75.1, 74.7, 73.8, 73.0, 71.3, 70.3, 68.8, 64.6, 62.7, 61.9, 46.7, 40.5, 20.7; HRMS (ESI+) calculated for $C_{60}H_{54}ClF_3N_3O_{15}$ $[M+Na]^+$ 1185.3124 m/z, found 1185.3131.

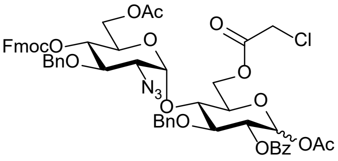
Methyl ([6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-α,β-D-glucopyranoside)uronate trifluoro-N-phenylacetimidate (10)



Hemiacetal **7** (50 mg, 0.053 mmol) was reacted according to General procedure A to yield the title compound (30 mg, 0.27 mmol, 51 %), TLC: Rf = 0.8 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$)δ 8.11 – 8.05 (m, 2H), 7.76 (ddt, J = 7.6, 2.7, 0.9 Hz, 2H), 7.60 (dt, J = 7.5, 0.9 Hz, 1H), 7.61 –

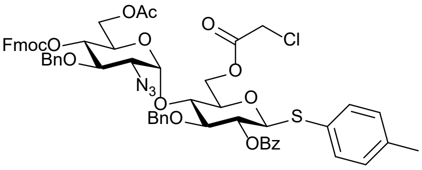
7.49 (m, 2H), 7.48 – 7.41 (m, 2H), 7.39 (tt, J = 7.5, 0.9 Hz, 2H), 7.30 – 7.25 (m, 8H), 7.24 – 7.19 (m, 4H), 7.15 (dd, J = 7.1, 2.6 Hz, 2H), 7.10 (ddt, J = 8.5, 7.2, 1.1 Hz, 1H), 6.82 – 6.76 (m, 2H), 6.25 (s, 1H), 5.49 (dd, J = 5.6, 4.3 Hz, 1H), 5.37 (d, J = 3.7 Hz, 1H), 4.86 – 4.78 (m, 2H), 4.77 (d, J = 10.9 Hz, 1H), 4.58 – 4.49 (m, 3H), 4.46 (d, J = 10.9 Hz, 1H), 4.40 – 4.32 (m, 2H), 4.23 – 4.11 (m, 4H), 4.02 – 3.95 (m, 1H), 3.77 (dd, J = 10.3, 9.1 Hz, 1H), 3.74 (s, 3H), 3.31 (dd, J = 10.3, 3.7 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 168.4, 164.9, 154.2, 143.3, 143.2, 143.1, 141.4, 141.3, 137.2, 137.1, 133.7, 129.9, 129.2, 129.1, 128.8, 128.7, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 127.2, 125.0, 124.8, 124.4, 120.6, 120.1, 119.3, 98.5, 93.9, 77.4, 75.0, 74.8, 74.5, 73.9, 73.5, 70.7, 70.2, 68.7, 62.7, 61.7, 52.7, 46.8, 29.7, 20.65; HRMS (ESI+) calculated for $C_{59}H_{53}F_3N_4O_{15}$ [M+Na]$^+$ 1137.3357 m/z, found 1137.3348.

[6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-6-O-chloroacetyl-β-D-glucopyranosyl acetate (11)



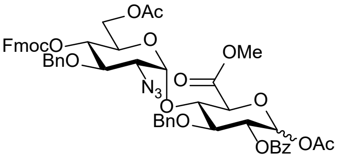
Hemiacetal **2** (675 mg, 0.680 mmol) was reacted according to General procedure B to yield the title compound as a mixture of anomers, appearing as a yellow foam (620 mg, 0.599 mmol, 88%, α/β: 30/70), TLC: Rf = 0.75 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$)δ 8.05 – 8.01 (m, 1.4H), 8.00 – 7.95 (m, 0.6H), 7.78 – 7.73 (m, 2H), 7.62 – 7.52 (m, 3H), 7.45 (td, J = 8.6, 8.0, 1.4 Hz, 2H), 7.41 – 7.36 (m, 2H), 7.32 – 7.11 (m, 12H), 6.40 (d, J = 3.6 Hz, 0.3H), 5.89 (d, J = 7.4 Hz, 0.7H), 5.64 (d, J = 3.9 Hz, 0.3H), 5.51 (d, J = 3.9 Hz, 0.7H), 5.43 (dd, J = 8.1, 7.5 Hz, 0.7H), 5.33 (dd, J = 9.7, 3.7 Hz, 0.3H), 4.93 – 4.83 (m, 1.6H), 4.81 – 4.65 (m, 2.8H), 4.63 – 4.55 (m, 1.6H), 4.52 – 4.45 (m, 1H), 4.41 – 4.23 (m, 3H), 4.18 (t, J = 7.2 Hz, 1H), 4.14 (s, 2H), 4.12 – 4.04 (m, 2H), 4.02 – 3.89 (m, 4H), 3.39 (dd, J = 10.3, 3.9 Hz, 0.3H), 3.36 (dd, J = 10.3, 3.9 Hz, 0.7H), 2.35 (s, 2.1H), 2.17 (s, 0.90H), 2.05 (s, 0.9H), 2.03 (s, 2.1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.4, 169.2, 168.7, 167.0, 165.2, 164.9, 154.1, 143.2, 143.0, 141.35, 141.3, 137.4, 137.2, 137.1, 133.7, 133.6, 129.8, 129.6, 129.1, 129.0, 128.7, 128.6, 128.4, 128.35, 128.2, 128.0, 127.9, 127.8, 127.6, 127.3, 127.2, 125.3, 125.1, 124.9, 120.1, 98.1, 98.0, 91.7, 89.2, 82.1, 79.9, 77.6, 77.4, 75.2, 75.0, 74.8, 74.7, 74.4, 73.1, 72.5, 72.3, 70.4, 70.2, 68.9, 64.6, 64.5, 62.6, 61.9, 61.85, 46.7, 40.65, 40.6, 20.8, 20.7; HRMS (ESI+) calculated for $C_{54}H_{52}ClN_3O_{16}$ [M+NH$_4$]$^+$ 1051.3380 m/z, found 1051.3383.

p-methylphenyl [6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-6-O-chloroacetyl-1-thiol-β-D-glucopyranoside (12)



Acetate **11** (120 mg, 0.115 mmol, α/β: 33/67, containing 0.077 mmol β) was reacted according to General procedure C to yield the title compound (54 mg, 0.049 mmol, 61% based on the amount of β), TLC: Rf = 0.7 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$)δ 8.11 – 8.06 (m, 2H), 7.75 (dd, J = 7.7, 3.9 Hz, 2H), 7.62 – 7.56 (m, 2H), 7.55 (dd, J = 7.5, 1.0 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.41 – 7.33 (m, 5H), 7.28 (tdd, J = 7.5, 3.6, 1.2 Hz, 2H), 7.25 – 7.16 (m, 7H), 7.16 – 7.07 (m, 4H), 5.57 (d, J = 3.9 Hz, 1H), 5.32 – 5.23 (m, 1H), 4.85 (dd, J = 10.2, 9.1 Hz, 1H), 4.79 – 4.63 (m, 6H), 4.47 (dd, J = 10.5, 6.8 Hz, 1H), 4.37 – 4.28 (m, 2H), 4.24 (dd, J = 12.4, 4.7 Hz, 1H), 4.18 (t, J = 6.9 Hz, 1H), 4.09 (s, 1H), 4.08 (s, 1H), 4.07 – 4.00 (m, 2H), 3.97 – 3.90 (m, 2H), 3.87 (dd, J = 9.6, 8.4 Hz, 1H), 3.75 (ddd, J = 9.8, 5.9, 2.5 Hz, 1H), 3.33 (dd, J = 10.3, 4.0 Hz, 1H), 2.34 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 170.48, 166.92, 165.11, 143.23, 143.00, 141.33, 138.62, 137.21, 137.09, 133.74, 133.49, 129.88, 129.62, 128.60, 128.39, 127.97, 127.90, 127.82, 127.64, 127.24, 125.10, 124.92, 120.11, 97.82, 86.06, 84.33, 77.28, 77.02, 76.77, 76.09, 75.13, 74.69, 72.74, 70.41, 68.77, 64.89, 62.54, 61.97, 46.70, 40.64, 21.17, 20.68; HRMS (ESI+) calculated for $C_{59}H_{56}ClN_3O_{14}S$ $[M+NH_4]^+$ 1115.3491 m/z, found 1115.3497.

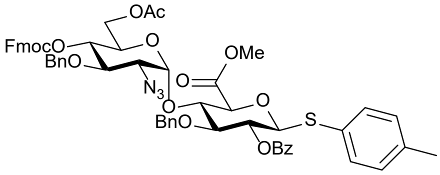
Methyl ([6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-β-D-glucopyranosyl)uronate acetate (13)



Hemiacetal **7** (150 mg, 0.159 mmol) was reacted according to General procedure B to yield the title compound as a mixture of anomers, appearing as a yellow foam (140 mg, 0.142 mmol, 89%, α/β: 45/55), TLC: Rf = 0.75 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$)8.07 – 8.02 (m, 1.2H), 8.02 – 7.99 (m, 0.8H), 7.79 – 7.73 (m, 2H), 7.62 – 7.52 (m, 3H), 7.49 – 7.33 (m, 4H), 7.32 – 7.16 (m, 12H), 6.50 (d, J = 3.5 Hz, 0.4H), 5.97 (d, J = 6.4 Hz, 0.6H), 5.52 (d, J = 3.8 Hz, 0.4H), 5.46 (d, J = 3.7 Hz, 0.6H), 5.42 (dd, J = 7.4, 6.3 Hz, 0.6H), 5.38 – 5.34 (m, 0.4H), 4.90 – 4.82 (m, 2H), 4.80 – 4.72 (m, 1H), 4.71 –

4.60 (m, 1H), 4.59 – 4.46 (m, 2.4H), 4.43 – 4.16 (m, 5H), 4.16 – 4.05 (m, 1.6H), 3.94 – 3.79 (m, 2H), 3.78 (s, 1.2H), 3.76 (s, 1.8H), 3.40 – 3.31 (m, 1H), 2.18 (s, 1.2H), 2.08 (s, 1.8H), 2.07 (s, 1.2H), 2.05 (s, 1.8H).; ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 170.65, 169.1, 168.55, 168.5, 168.3, 165.2, 164.9, 154.2, 143.3, 143.0, 141.35, 141.3, 137.2, 137.15, 137.1, 133.7, 133.6, 129.9, 129.7, 129.1, 128.7, 128.45, 128.4, 128.35, 128.0, 127.9, 127.85, 127.7, 127.5, 127.2, 125.1, 124.9, 120.1, 98.1, 97.9, 91.6, 89.0, 80.4, 78.9, 77.5, 75.1, 75.05, 74.8, 74.5, 74.4, 74.2, 72.5, 71.8, 71.4, 70.3, 68.6, 68.5, 62.7, 62.65, 61.5, 61.45, 52.9, 52.85, 46.7, 20.9, 20.8, 20.75; HRMS (ESI+) calculated for $C_{53}H_{51}N_3O_{16}$ [M+Na]$^+$ 1008.3167 m/z, found 1008.3170.

Methyl (p-methylphenyl [6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-4-O-(9-fluorenylmethyloxycarbonyl)-α- D-glucopyranosyl(1→4)]-2-O-benzoyl-3-O-benzyl-1-thiol-β-D-glucopyranoside)uronate (14)



Acetate **13** (120 mg, 0.122 mmol, α/β: 45/55, containing 0.067 mmol β) was reacted according to General procedure C to yield the title compound (45 mg, 0.043 mmol, 64% based on the amount of β), TLC: Rf = 0.7 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$)δ 8.09 – 8.05 (m, 2H), 7.77 – 7.73 (m, 2H), 7.62 – 7.56 (m, 2H), 7.56 – 7.52 (m, 1H), 7.50 – 7.43 (m, 2H), 7.42 – 7.32 (m, 4H), 7.30 – 7.12 (m, 12H), 7.12 – 7.08 (m, 2H), 5.50 (d, J = 3.7 Hz, 1H), 5.29 (dd, J = 9.7, 8.7 Hz, 1H), 4.86 (dd, J = 10.3, 9.1 Hz, 1H), 4.82 (d, J = 9.7 Hz, 1H), 4.77 – 4.71 (m, 2H), 4.69 – 4.60 (m, 2H), 4.47 (dd, J = 10.5, 6.8 Hz, 1H), 4.33 – 4.28 (m, 1H), 4.26 – 4.20 (m, 2H), 4.18 (t, J = 7.0 Hz, 1H), 4.12 – 4.05 (m, 2H), 4.00 (t, J = 8.6 Hz, 1H), 3.91 (dd, J = 10.3, 9.1 Hz, 1H), 3.81 (s, 3H), 3.73 (ddd, J = 10.2, 3.9, 2.3 Hz, 1H), 3.33 (dd, J = 10.3, 3.8 Hz, 1H), 2.33 (s, 3H), 2.06 (s, 3H)); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.6, 168.1, 164.9, 154.1, 143.3, 143.0, 141.3, 138.6, 137.1, 133.5, 133.4, 129.8, 129.7, 129.6, 129.0, 128.6, 128.3, 128.2, 128.1, 127.9, 127.85, 127.8, 127.75, 127.2, 125.3, 125.1, 124.9, 120.1, 97.5, 87.0, 83.6, 77.9, 75.1, 74.8, 74.3, 72.1, 70.3, 68.4, 62.7, 61.4, 52.8, 46.7, 21.2, 20.7; HRMS (ESI+) calculated for $C_{58}H_{55}N_3O_{16}S$ $[M+Na]^+$ 1072.3302 m/z, found 1072.3311.

General Procedure D: Glycosylation using a trichloroacetimidate donor

Donor **3** or **8** (0.183 mmol, 1.3 equiv.) and acceptor **4** or **5** (0.145 mmol) was dissolved in dry dichloromethane (5 ml) under argon, with 100 mg of 3Å molecular sieves. This mixture was cooled to between -10 and -20°C, and then treated with trimethylsilyl trifluoromethanesulfonate (0.3 equiv.). The reaction was stirred in the cooling bath (reaching 1-2°C) until TLC indicated competition, at which point the reaction was diluted with ethyl acetate, washed with aqueous saturated sodium bicarbonate, water, and brine, dried over $MgSO_4$ and evaporated to dryness. The mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the product.

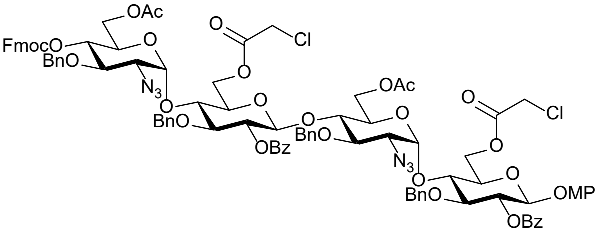
General Procedure E: Glycosylation using a Trifluoro-*N*-phenylacetimidate donor

Donor **9** or **10** (0.172 mmol, 1.3 equiv.) and acceptor **4** or **5** (0.137 mmol) was dissolved in dry dichloromethane under argon, with 100 mg of 3Å molecular sieves. This mixture was cooled to -78°C, and then treated with trimethylsilyl trifluoromethanesulfonate (0.3 equiv.). The reaction was stirred in the cooling bath until TLC indicated competition, at which point the reaction was diluted with ethyl acetate, washed with aqueous saturated sodium bicarbonate, water, and brine, dried over $MgSO_4$ and evaporated to dryness. The mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the product as a yellow foam.

General procedure F: Glycosylation using a Thiogylcoside donor

Donor **12** or **14** (0.178 mmol, 1.3 equiv.) and acceptor **4** or **5** (0.137 mmol) was dissolved in dry dichloromethane under argon, with 100 mg of 3Å molecular sieves. This mixture was cooled to between -10 and -20°C, and then treated with N-iodosuccinimide (1.7 equiv.) and silver trifluoromethanesulfonate (0.4 equiv.). The reaction was stirred at room temperature until TLC indicated competition, at which point the reaction was diluted with ethyl acetate, washed with a 1:1 mixture of aqueous saturated sodium bicarbonate and sodium thiosulfate, water, and brine, dried over $MgSO_4$ and evaporated to dryness. The mixture was purified by column chromatography (gradient of 0-20% EtOAc in toluene) to yield the product as a yellow foam.

Tetrasaccharide 15



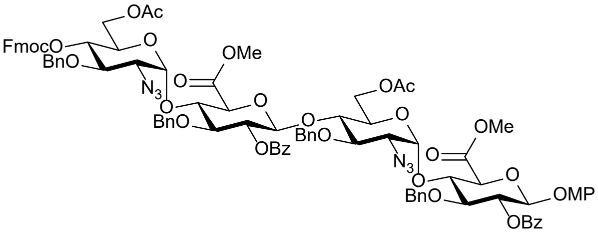
Entry 1: Donor **3** (200 mg, 0.183 mmol, 1.3 equiv.) and acceptor **4** (120 mg, 0.137 mmol) was reacted according to General Procedure D to yield **15** as a foam (230 mg, 0.124 mmol, 90%);

Entry 3: Donor **9** (200 mg, 0.172 mmol, 1.3 equiv.) and acceptor **4** (120 mg, 0.137 mmol) was reacted according to General Procedure E to yield **15** as a foam (220 mg, 0.118 mmol, 87%);

Entry 5: Donor **12** (200 mg, 0.178 mmol, 1.3 equiv.) and acceptor **4** (120 mg, 0.137 mmol) was reacted according to General Procedure F to yield **15** as a foam (120 mg, 0.065 mmol, 53%);

TLC: Rf = 0.65 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.01 (m, 4H), 7.79 – 7.72 (m, 2H), 7.64 – 7.52 (m, 4H), 7.49 – 7.42 (m, 4H), 7.41 – 7.31 (m, 7H), 7.31 – 7.26 (m, 3H), 7.24 – 7.15 (m, 12H), 7.15 – 7.11 (m, 2H), 6.88 – 6.82 (m, 2H), 6.79 – 6.73 (m, 2H), 5.54 – 5.45 (m, 3H), 5.38 (dd, J = 8.8, 7.8 Hz, 1H), 5.11 (d, J = 11.3 Hz, 1H), 5.02 (d, J = 7.2 Hz, 1H), 4.86 (dd, J = 10.2, 9.1 Hz, 1H), 4.81 – 4.61 (m, 8H), 4.48 (dd, J = 10.5, 6.7 Hz, 1H), 4.42 – 4.08 (m, 9H), 4.08 – 3.97 (m, 3H), 3.95 – 3.87 (m, 4H), 3.86 – 3.79 (m, 6H), 3.77 – 3.64 (m, 6H), 3.36 (dd, J = 10.3, 3.9 Hz, 1H), 3.25 (dd, J = 10.2, 3.9 Hz, 1H), 2.03 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 166.9, 166.4, 143.2, 143.0, 141.3, 138.3, 137.2, 133.8, 133.5, 129.8, 129.4, 129.0, 128.8, 128.6, 128.4, 128.35, 128.3, 127.9, 127.7, 127.5, 127.35, 127.25, 125.1, 124.9, 120.1, 118.8, 114.5, 101.0, 100.0, 97.7, 82.7, 77.9, 77.6, 77.5, 75.2, 75.0, 74.7, 74.5, 74.1, 73.5, 72.4, 72.3, 70.4, 69.8, 68.8, 62.6, 55.6, 46.7, 40.4, 20.8, 20.7; HRMS (ESI+) calculated for $C_{96}H_{94}Cl_2N_6O_{28}$ $[M+Na]^+$ 1871.5391 m/z, found 1871.5394.

Tetrasaccharide 16



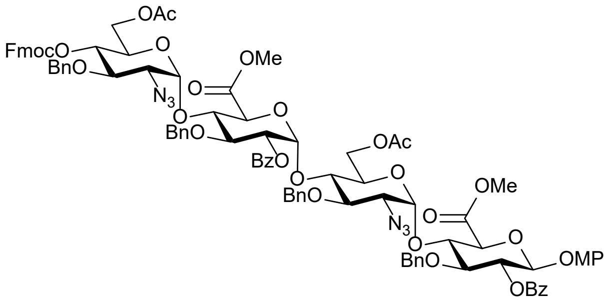
Entry 2: Donor **8** (200 mg, 0.183 mmol, 1.3 equiv.) and acceptor **5** (120 mg, 0.145 mmol) were reacted according to General Procedure E to yield **16** as a foam (120 mg, 0.068 mmol, 47%);

Entry 4: Donor **10** (200 mg, 0.178 mmol, 1.3 equiv.) and acceptor **5** (120 mg, 0.145 mmol) were reacted according to General Procedure F to yield **16** as a foam (5 mg, 0.003 mmol, 5%);

Entry 6: Donor **14** (200 mg, 0.190 mmol, 1.3 equiv.) and acceptor **5** (120 mg, 0.145 mmol) was reacted according to General Procedure G to yield **16** as a foam (140 mg, 0.080 mmol, 56%);

TLC: Rf = 0.65 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.14 – 8.07 (m, 2H), 8.05 – 7.99 (m, 2H), 7.75 (dd, J = 7.7, 3.3 Hz, 2H), 7.61 – 7.51 (m, 4H), 7.50 – 7.32 (m, 10H), 7.30 – 7.14 (m, 16H), 7.11 (dd, J = 7.5, 2.1 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 6.73 (d, J = 8.8 Hz, 2H), 5.53 – 5.46 (m, 3H), 5.42 (t, J = 8.4 Hz, 1H), 5.15 (d, J = 10.9 Hz, 1H), 5.06 (d, J = 6.8 Hz, 1H), 4.88 (t, J = 9.7 Hz, 1H), 4.82 – 4.61 (m, 8H), 4.47 (dd, J = 10.6, 6.6 Hz, 1H), 4.35 – 4.26 (m, 4H), 4.23 (dd, J = 12.6, 3.8 Hz, 1H), 4.20 – 4.12 (m, 2H), 4.11 – 3.99 (m, 3H), 3.98 – 3.86 (m, 3H), 3.83 – 3.67 (m, 6H), 3.55 (s, 3H), 3.46 – 3.40 (m, 1H), 3.37 (dd, J = 10.3, 3.8 Hz, 1H), 3.23 (dd, J = 9.9, 3.8 Hz, 1H), 3.17 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 170.6, 168.1, 167.8, 165.0, 164.7, 155.7, 154.1, 150.9, 143.3, 143.0, 141.35, 141.3, 138.2, 137.2, 137.1, 137.05, 133.8, 133.4, 129.9, 129.8, 129.4, 129.0, 128.9, 128.8, 128.6, 128.4, 128.35, 128.3, 128.2, 128.0, 127.9, 127.9, 127.85, 127.8, 127.75, 127.6, 127.55, 127.2, 125.3, 125.1, 124.9, 120.1, 120.05, 118.7, 114.5, 101.1, 100.7, 97.5, 97.3, 82.5, 82.2, 77.7, 77.5, 75.5, 75.4, 75.2, 74.9, 74.8, 74.5, 74.3, 74.2, 74.1, 73.8, 73.5, 70.3, 69.1, 68.4, 62.8, 61.6, 61.4, 55.6, 52.7, 52.1, 46.7, , 20.9, 20.7; HRMS (ESI+) calculated for C$_{94}$H$_{92}$N$_6$O$_{28}$ [M+Na]$^+$ 1775.5844 m/z, found 1775.5857.

Tetrasaccharide 16a



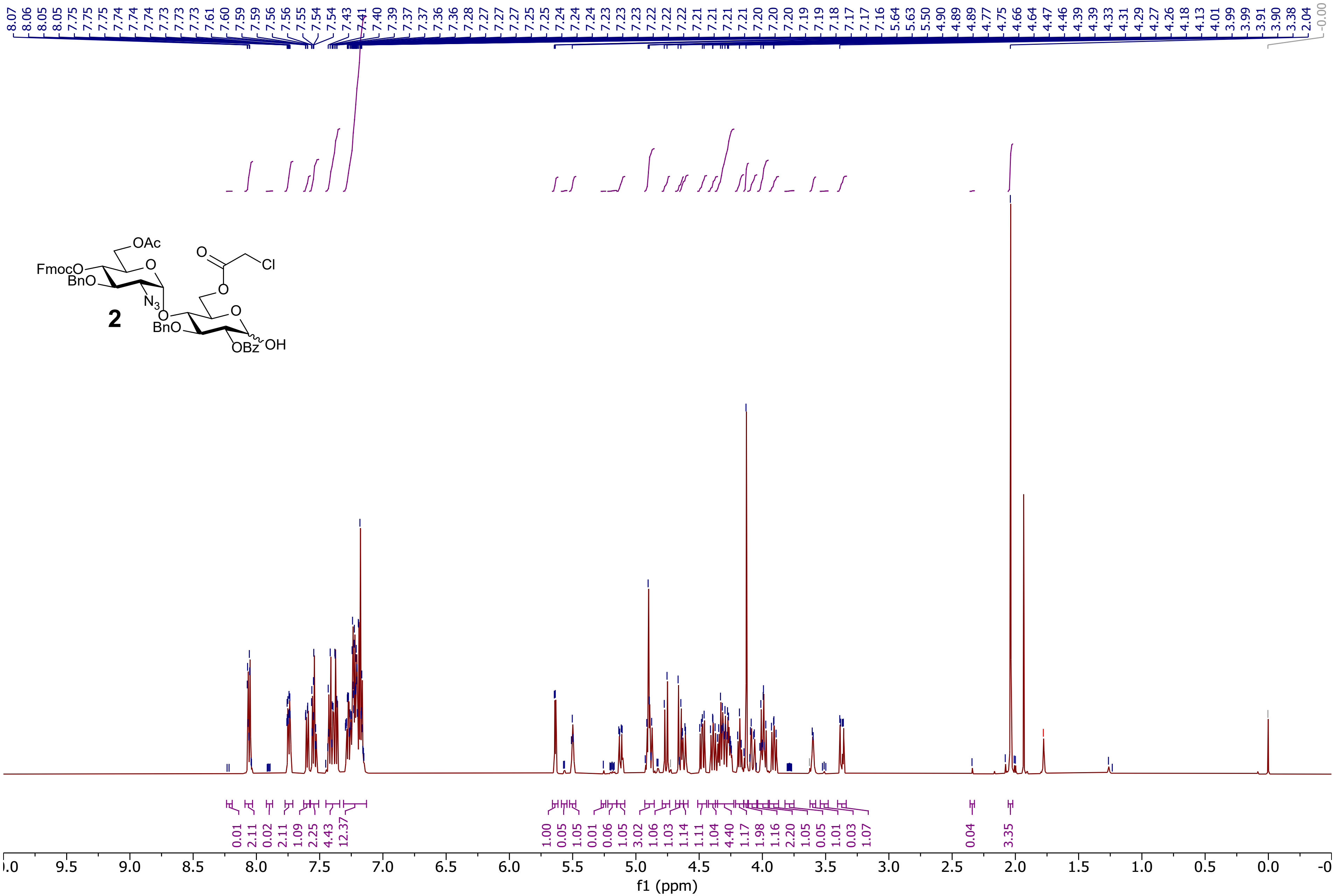
Yield 35%, TLC: Rf = 0.6 (EtOAc/toluene, 1/4 v/v); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.06 – 8.03 (m, 2H), 7.94 – 7.91 (m, 2H), 7.76 – 7.73 (m, 2H), 7.63 – 7.59 (m, 1H), 7.58 – 7.53 (m, 3H), 7.46 – 7.41 (m, 2H), 7.40 – 7.33 (m, 6H), 7.30 – 7.26 (m, 4H), 7.24 – 7.16 (m, 14H), 7.15 – 7.10 (m, 3H), 6.95 – 6.85 (m, 2H), 6.80 – 6.70 (m, 2H), 5.82 (d, J = 5.5 Hz, 1H), 5.59 – 5.51 (m, 3H), 5.31 (s, 1H), 5.15 (d, J = 6.5 Hz, 1H), 4.94 – 4.85 (m, 3H), 4.81 – 4.71 (m, 4H), 4.61 (d, J = 11.1 Hz, 1H), 4.53 – 4.41 (m, 5H), 4.40 – 4.26 (m, 4H), 4.25 – 4.05 (m, 6H), 4.04 – 3.96 (m, 2H), 3.88 – 3.81 (m, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.66

(s, 3H), 3.34 (ddd, J = 13.8, 10.3, 3.7 Hz, 2H), 2.06 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13C NMR (126 MHz, CDCl3) δ 170.55, 170.51, 168.86, 168.38, 165.15, 165.00, 155.67, 154.29, 151.19, 143.29, 143.08, 141.30, 141.26, 137.45, 137.29, 137.23, 136.80, 133.43, 133.34, 129.85, 129.80, 129.44, 129.38, 128.54, 128.45, 128.40, 128.34, 128.33, 128.30, 127.99, 127.93, 127.81, 127.74, 127.22, 125.18, 124.99, 120.05, 120.03, 118.68, 114.49, 100.64, 98.53, 97.53, 81.78, 79.65, 75.21, 74.83, 74.76, 74.59, 74.48, 74.19, 73.68, 72.46, 70.40, 69.30, 68.60, 63.21, 62.67, 62.53, 61.75, 55.61, 52.86, 52.47, 46.68, 20.80, 20.68; HRMS (ESI+) calculated for $C_{94}H_{92}N_6O_{28}$ $[M+Na]^+$ 1775.5844 m/z, found 1775.5861.

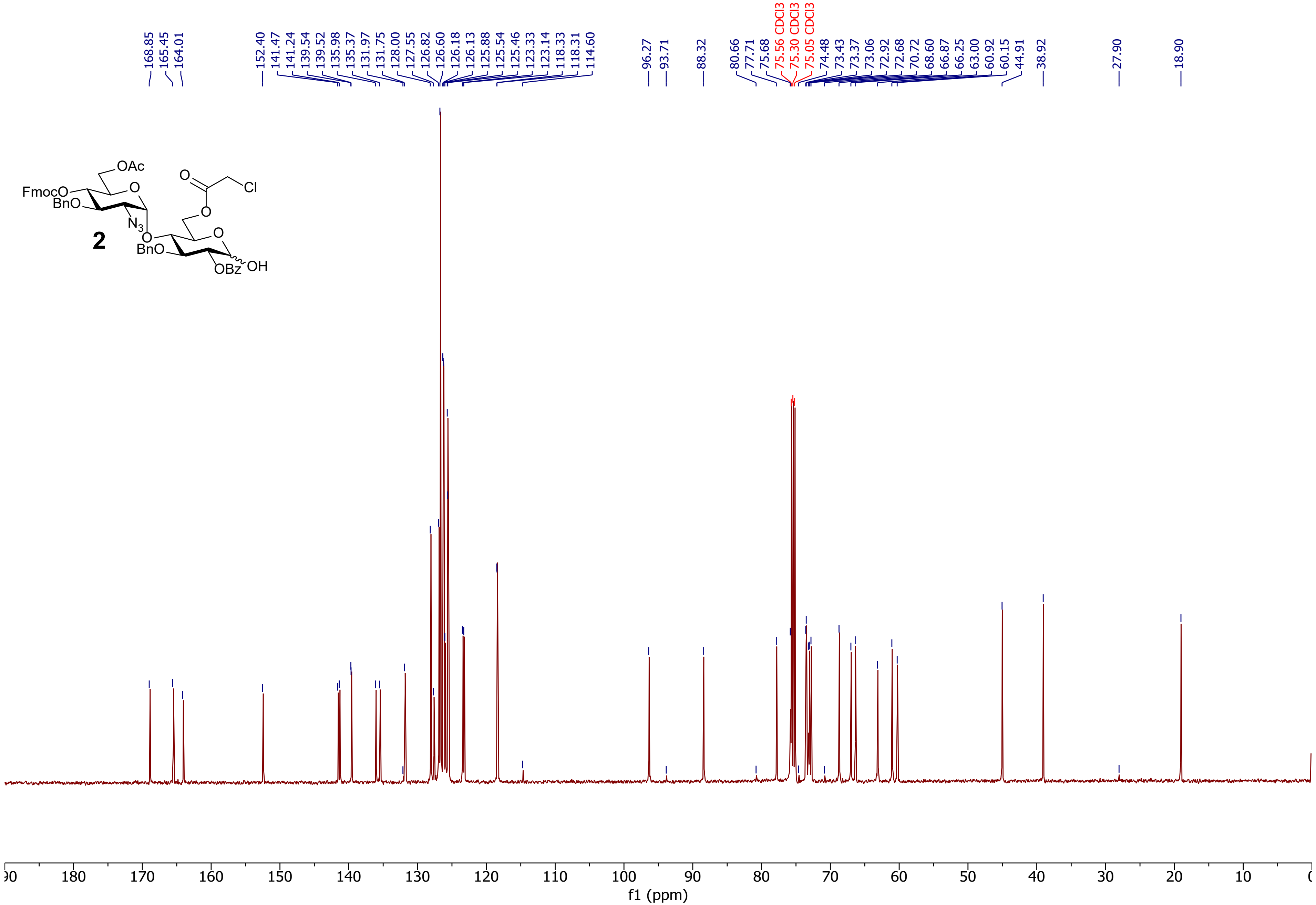
^{1}H and ^{13}C NMR-Spectra

^{1}H NMR (500 MHz, CDCl$_3$)

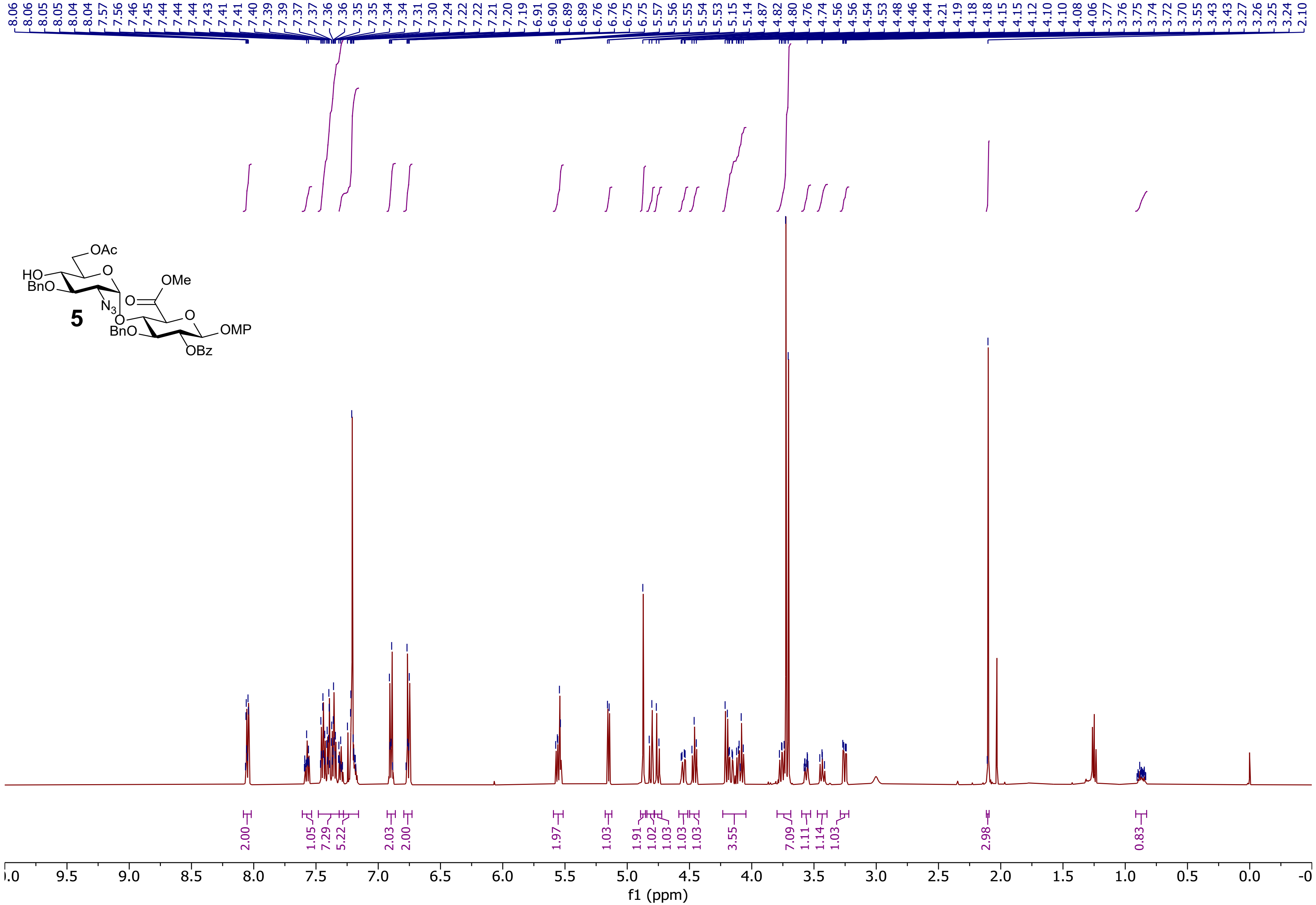
2



^{13}C NMR (126 MHz, CDCl$_3$)

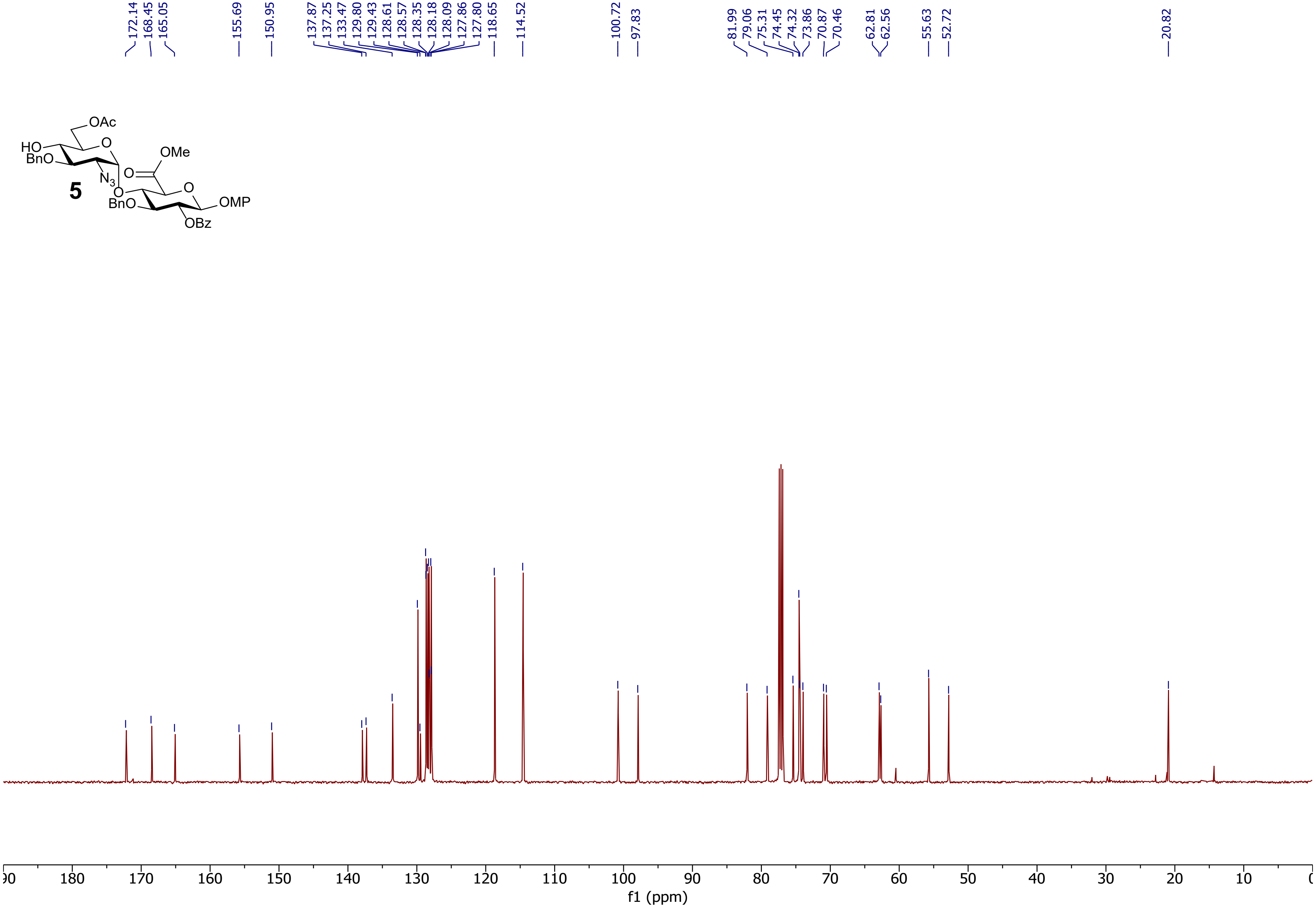


^{1}H NMR (500 MHz, CDCl$_3$)

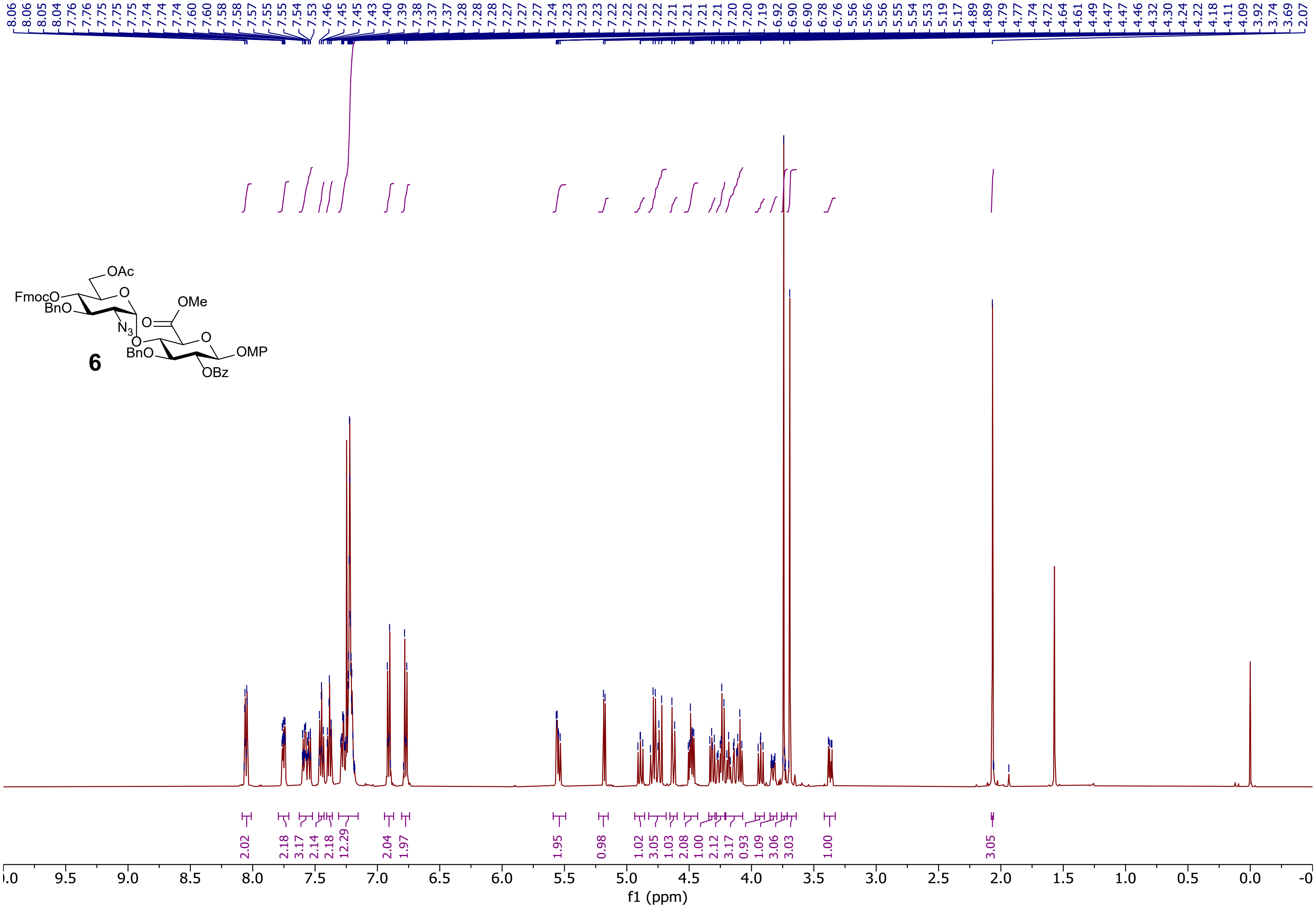


^{13}C NMR (126 MHz, CDCl$_3$)

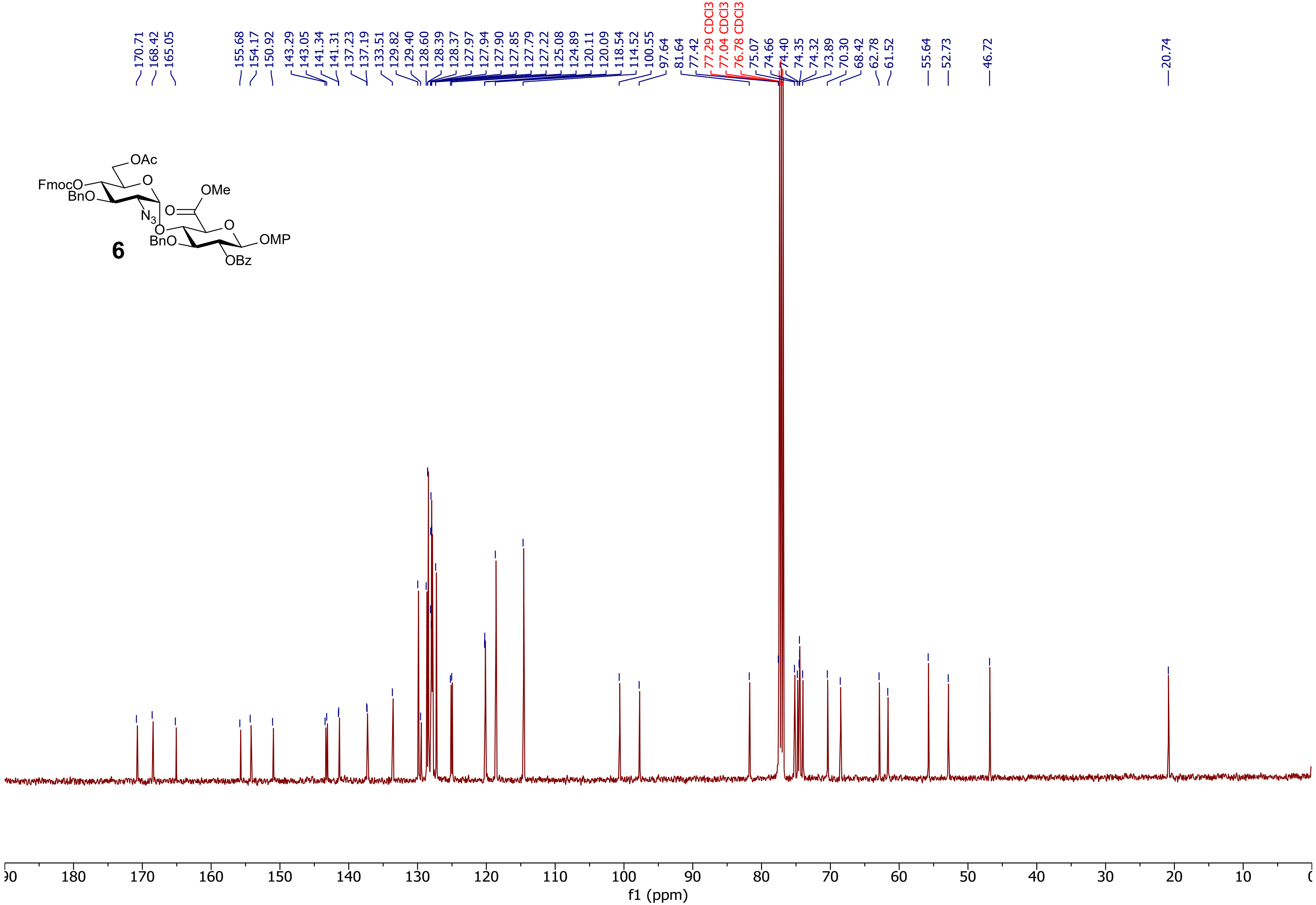
5



¹H NMR (500 MHz, $CDCl_3$)

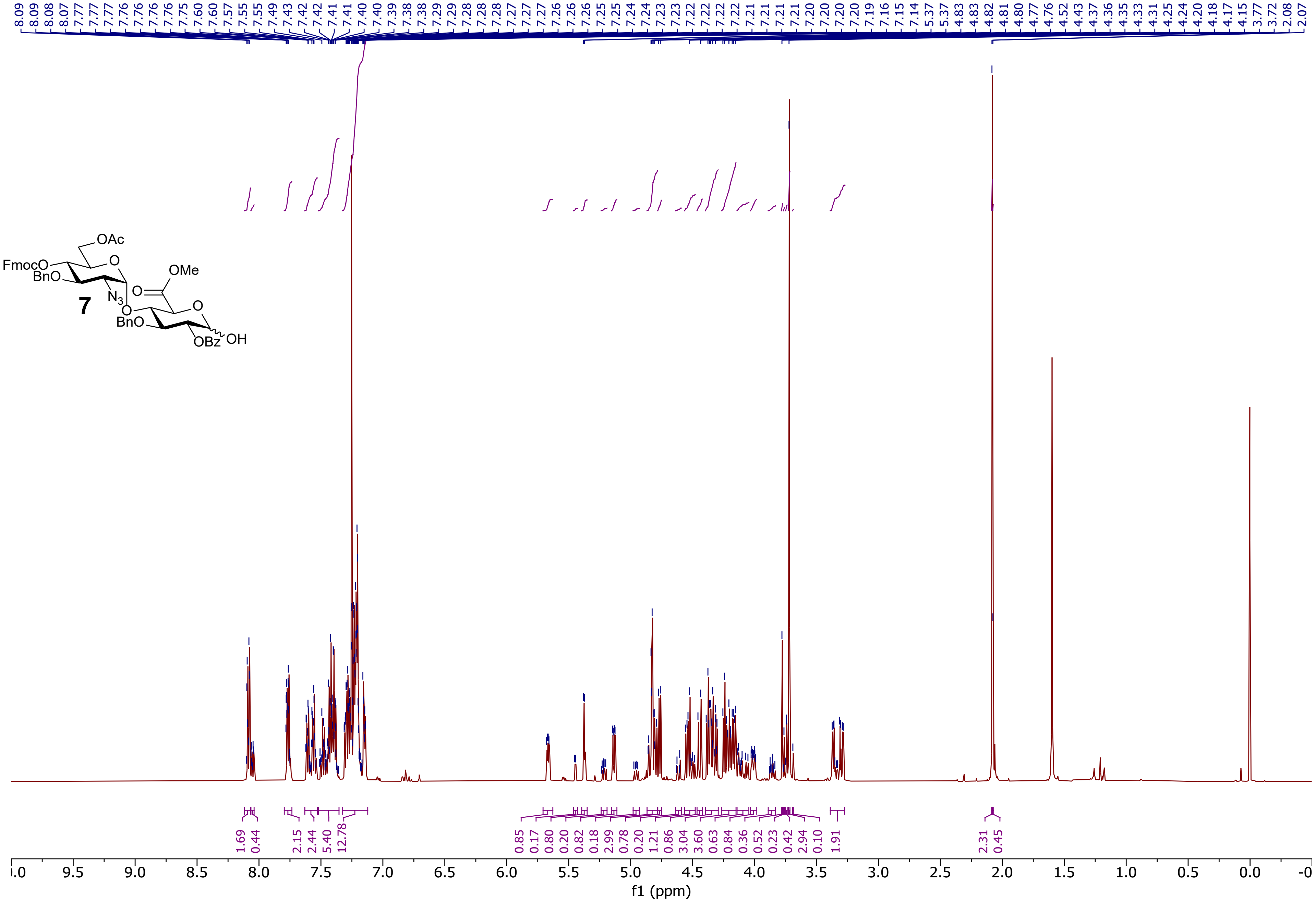


^{13}C NMR (126 MHz, CDCl$_3$)



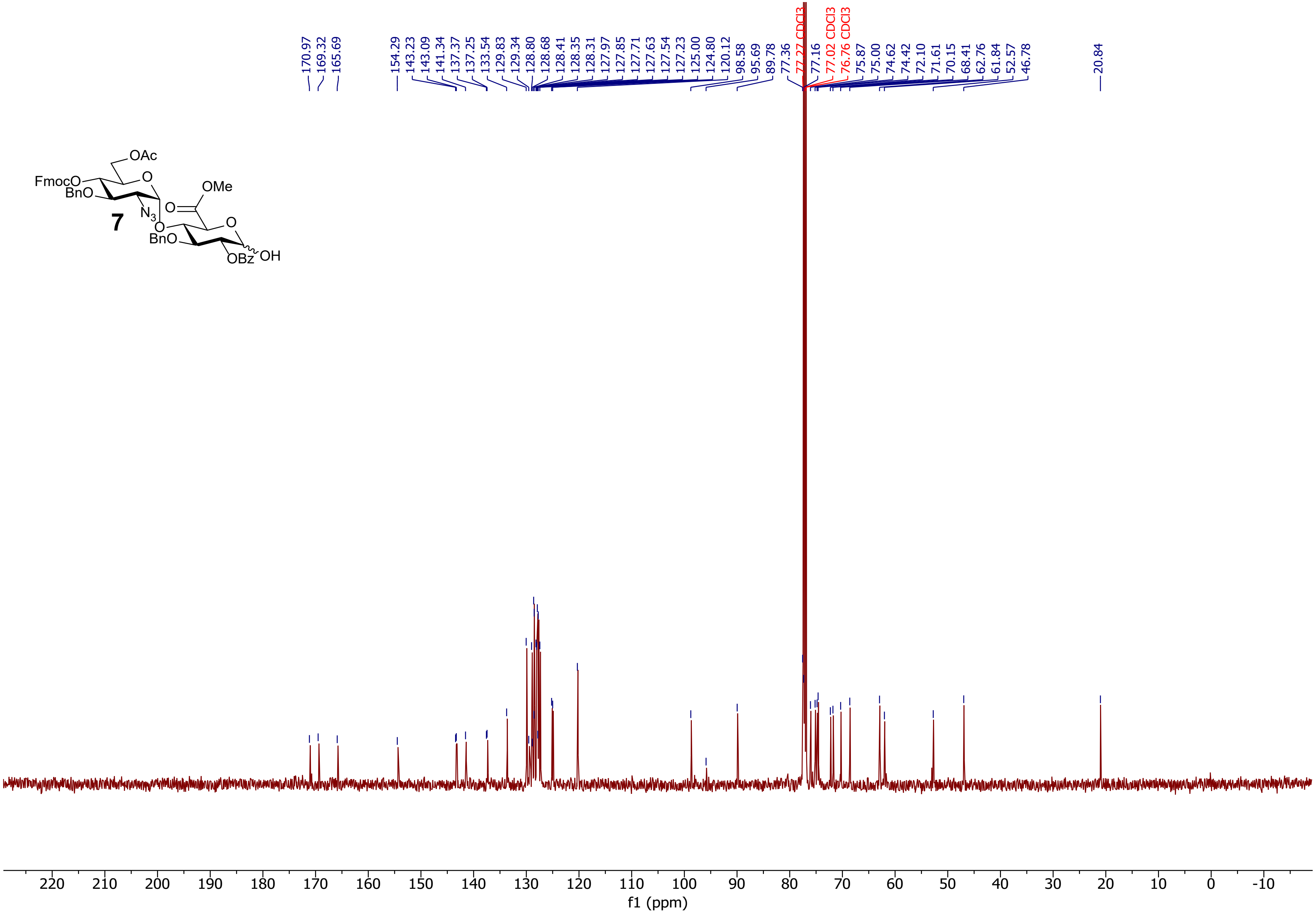
6

¹H NMR (500 MHz, CDCl$_3$)

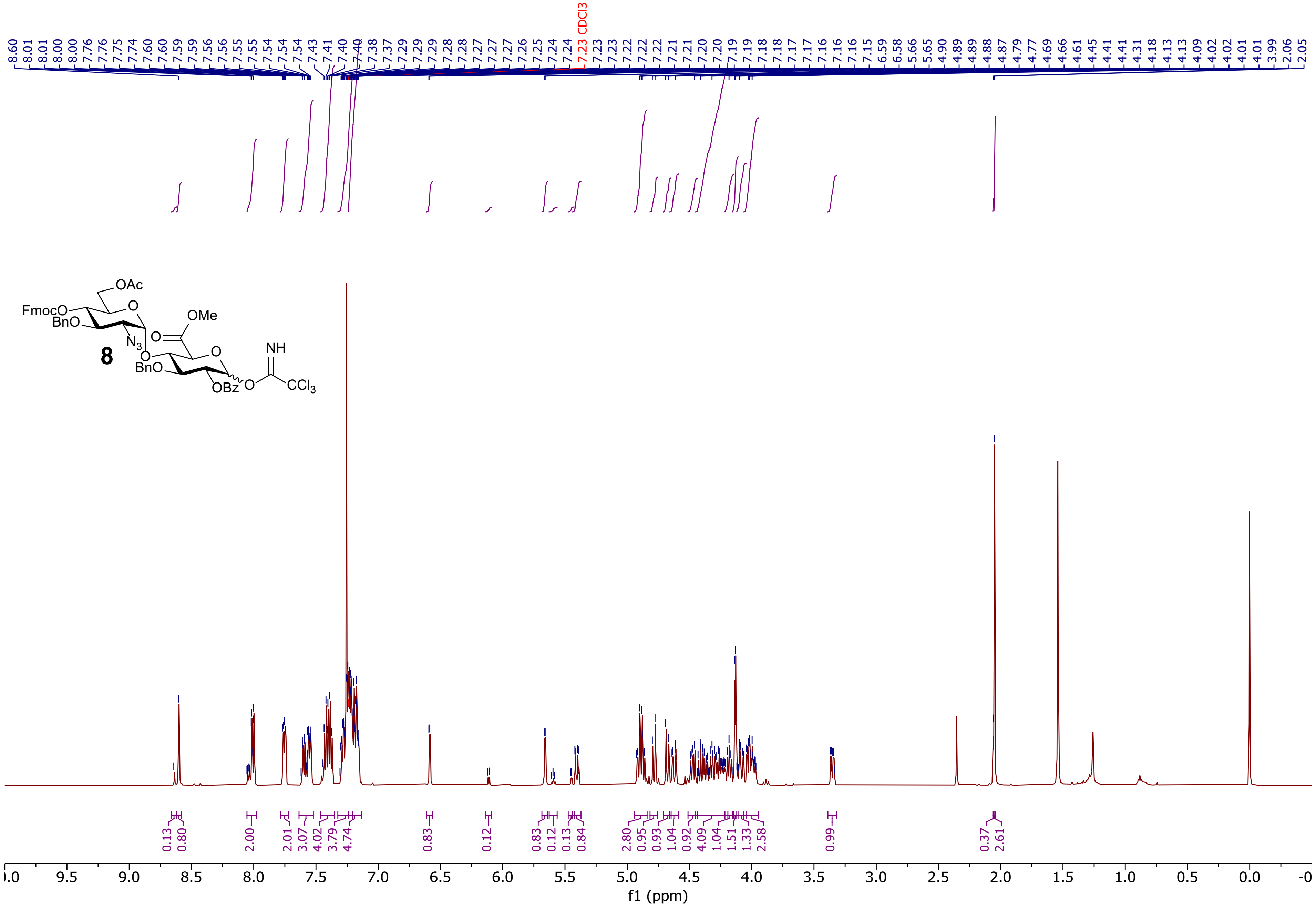


^{13}C NMR (126 MHz, CDCl$_3$)

7

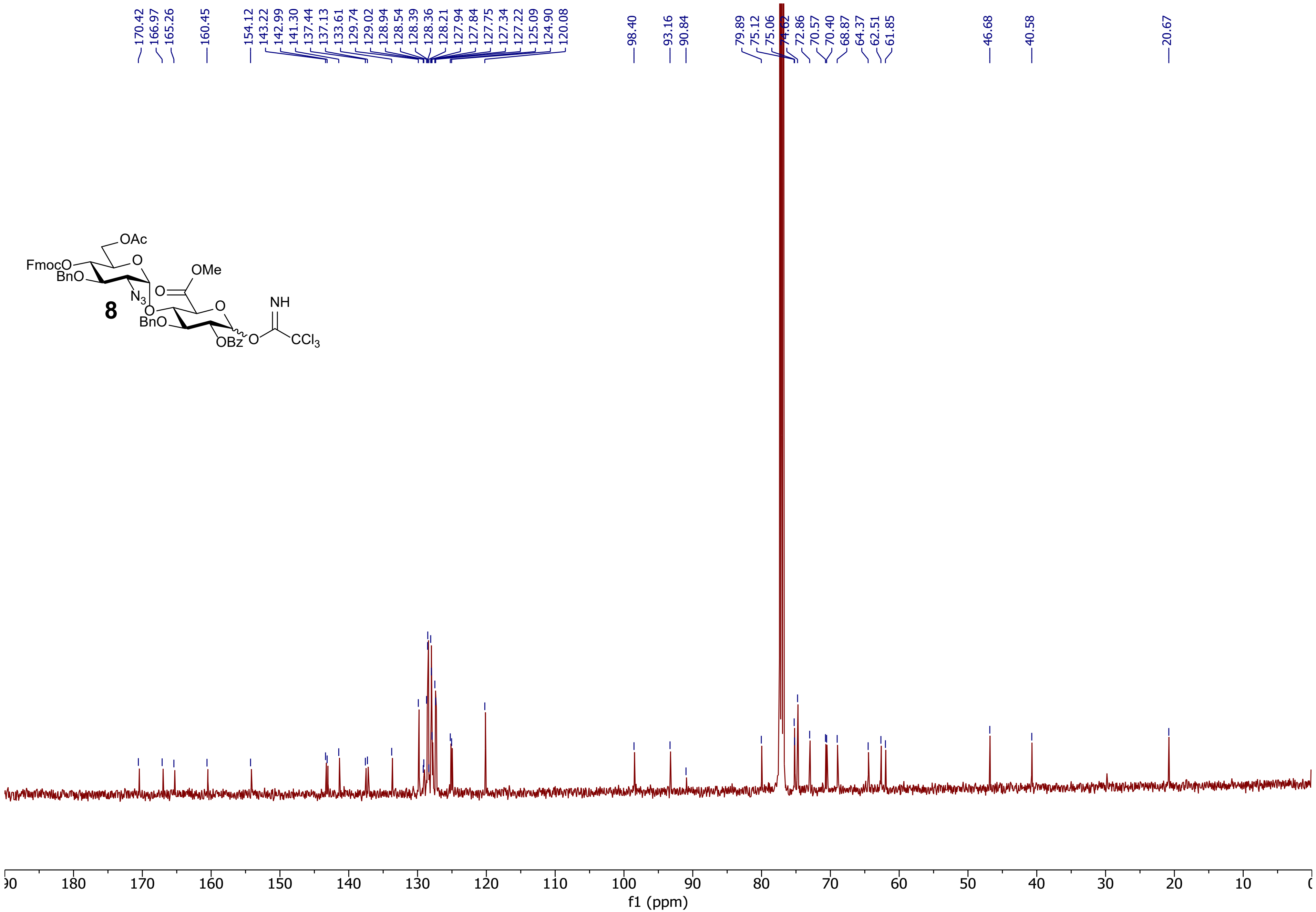


^{1}H NMR (500 MHz, CDCl$_3$)

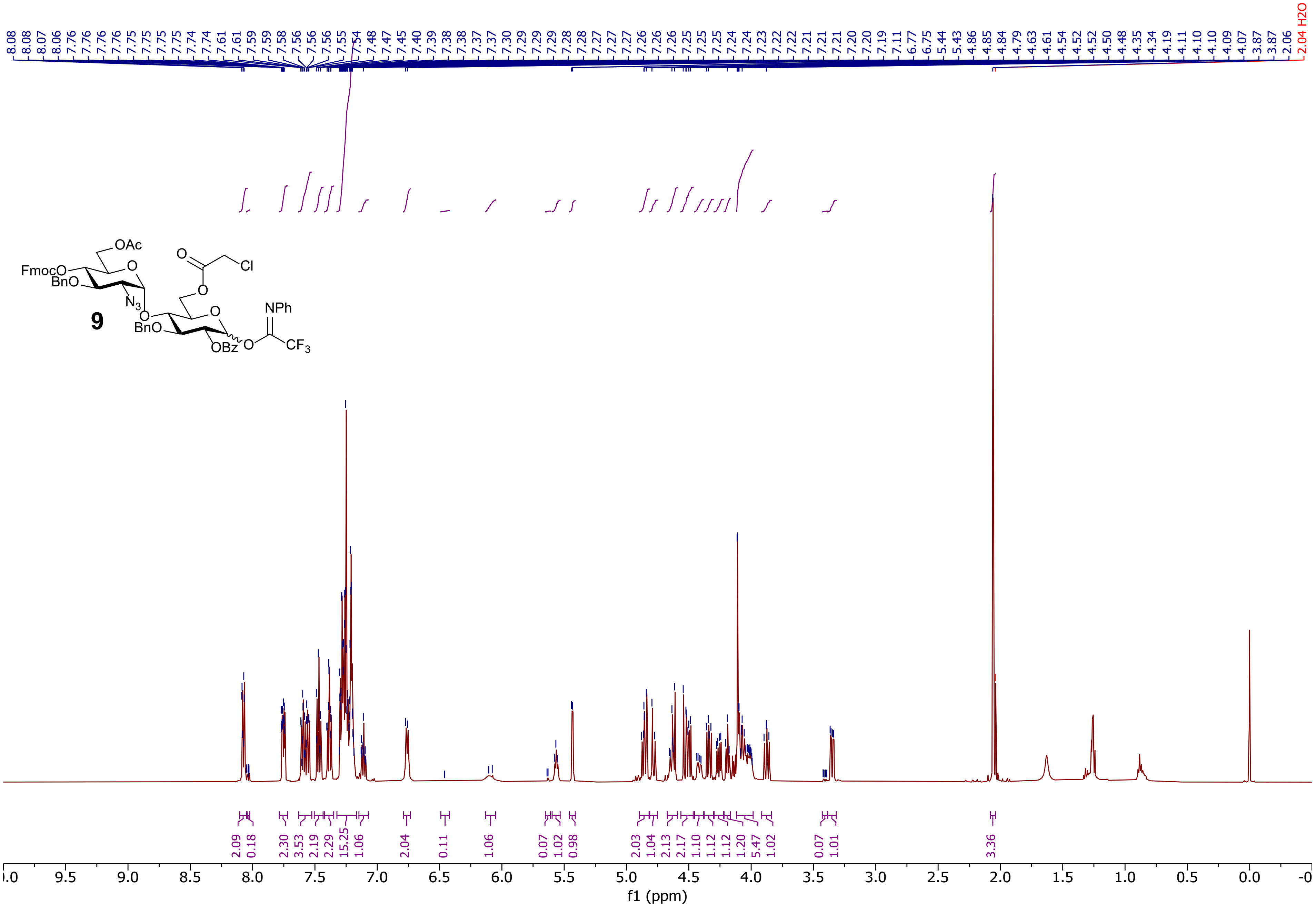


8

^{13}C NMR (126 MHz, $CDCl_3$)

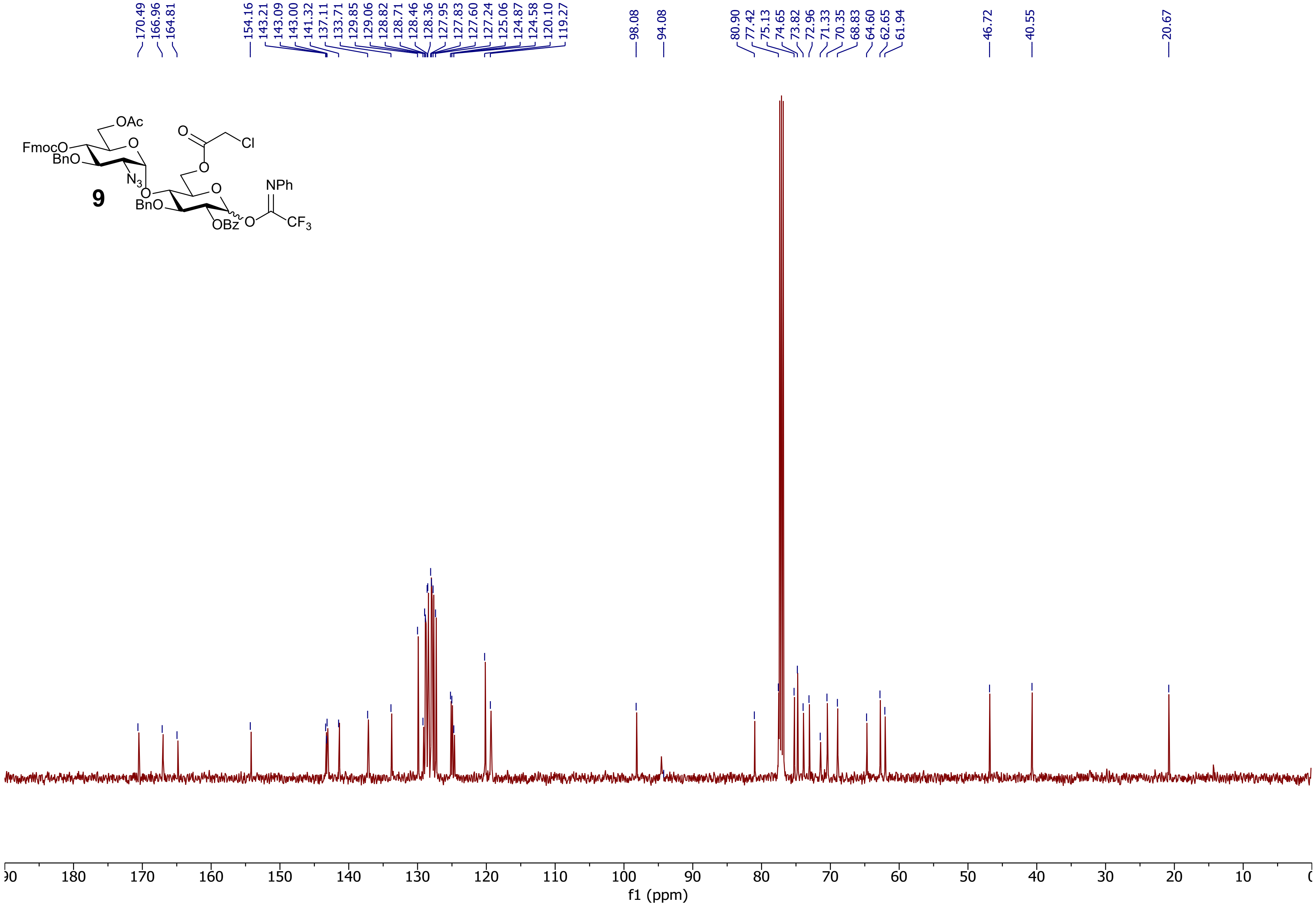


^{1}H NMR (500 MHz, CDCl$_3$)



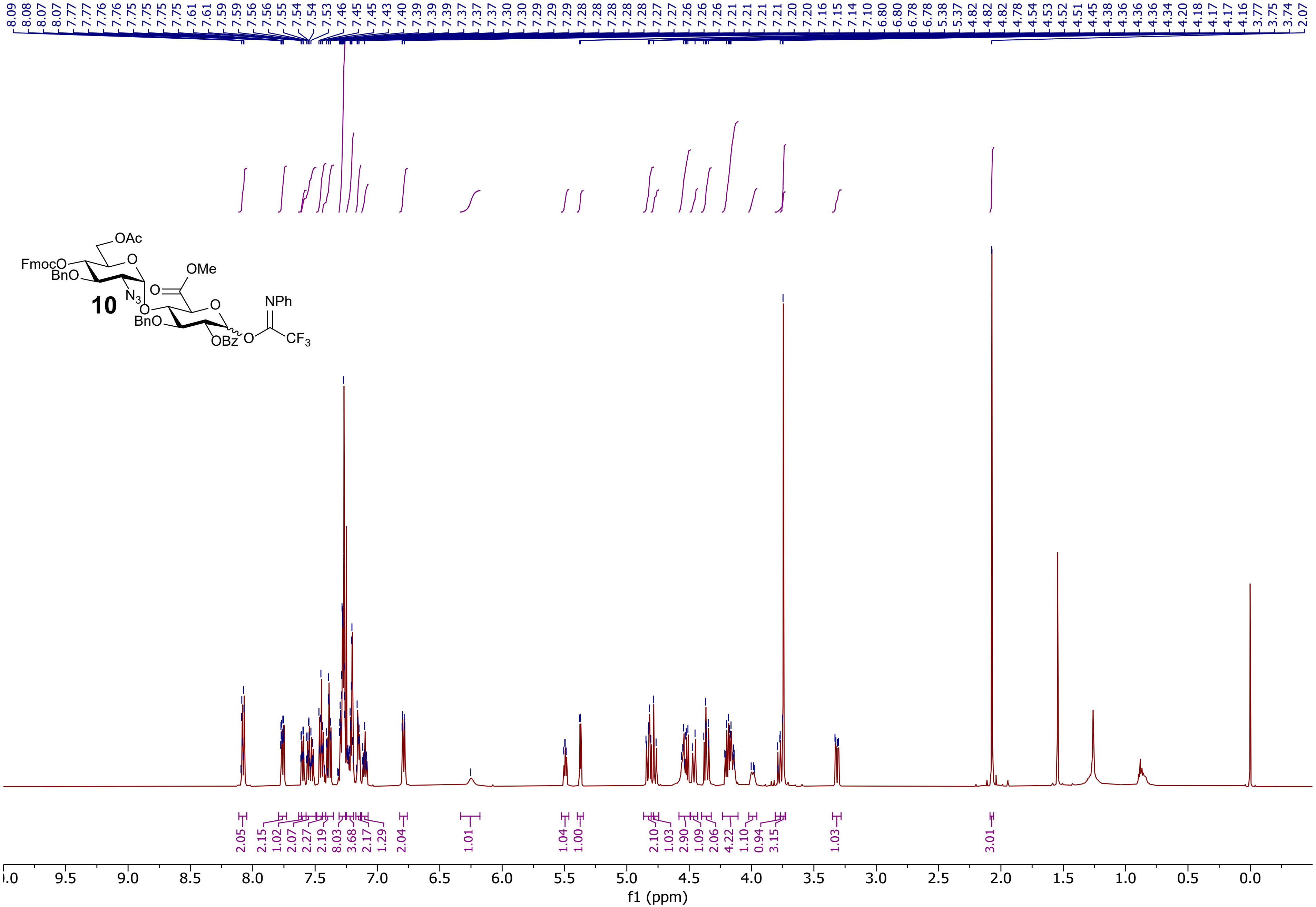
9

^{13}C NMR (126 MHz, CDCl$_3$)

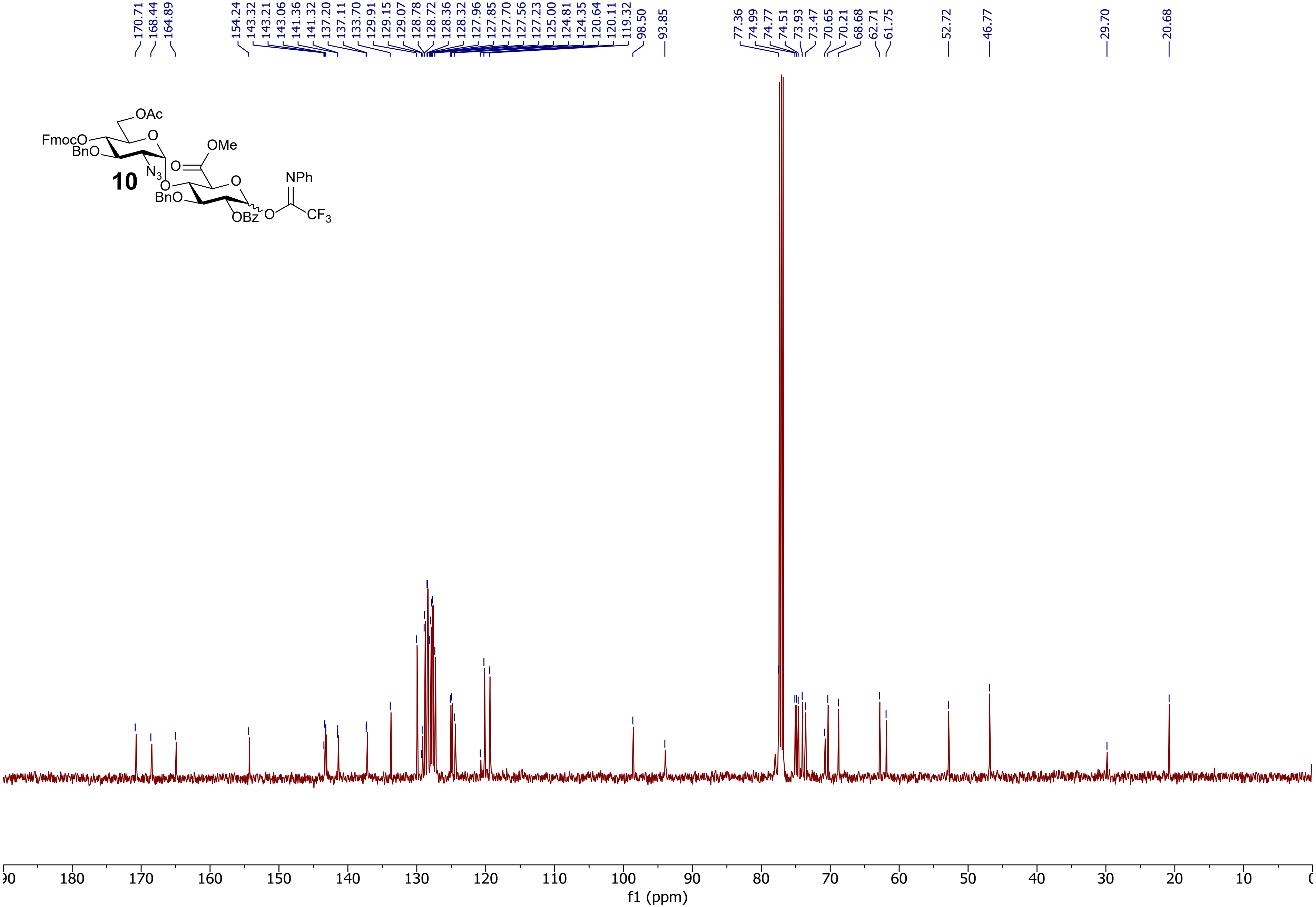


9

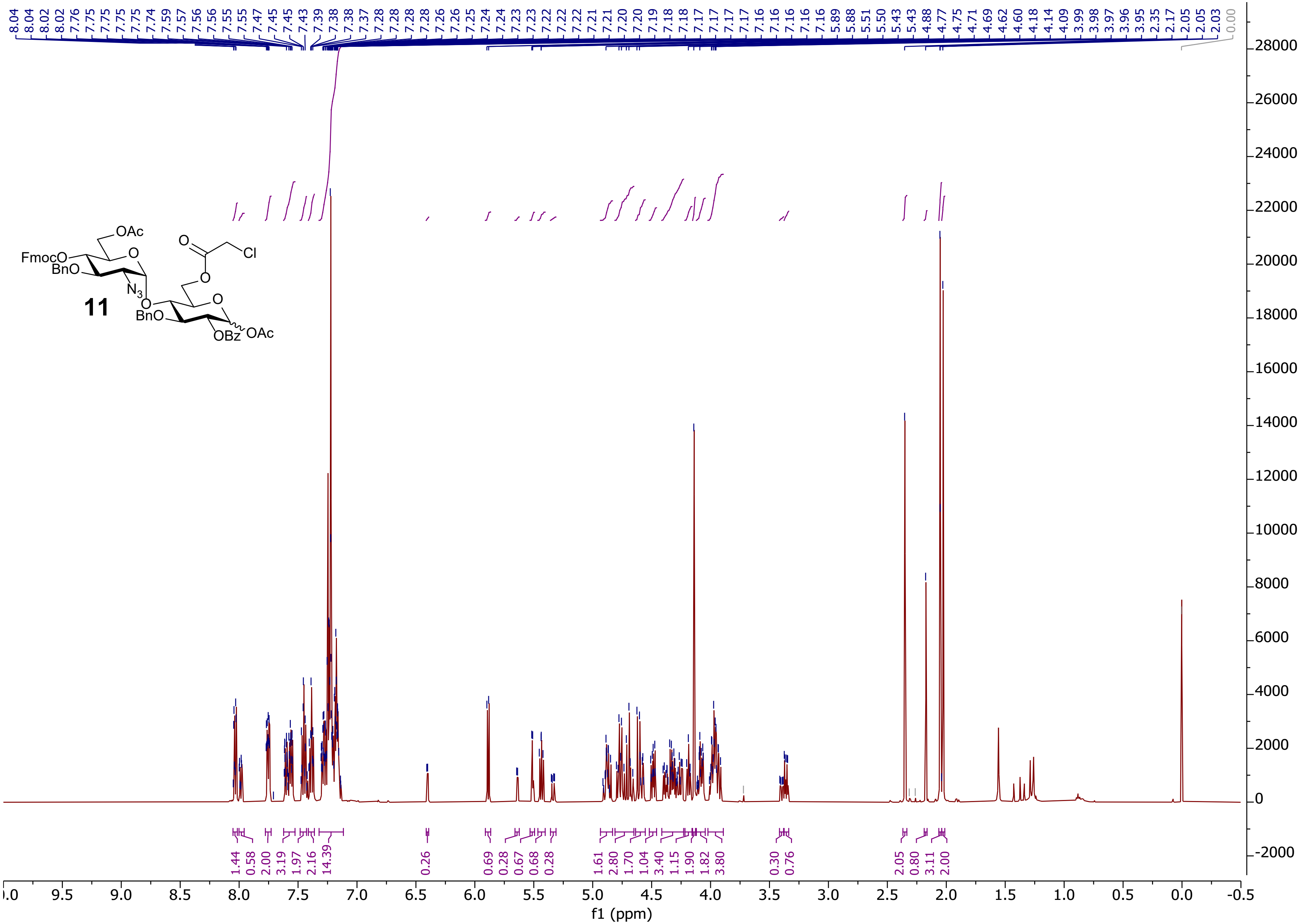
^{1}H NMR (500 MHz, CDCl$_3$)



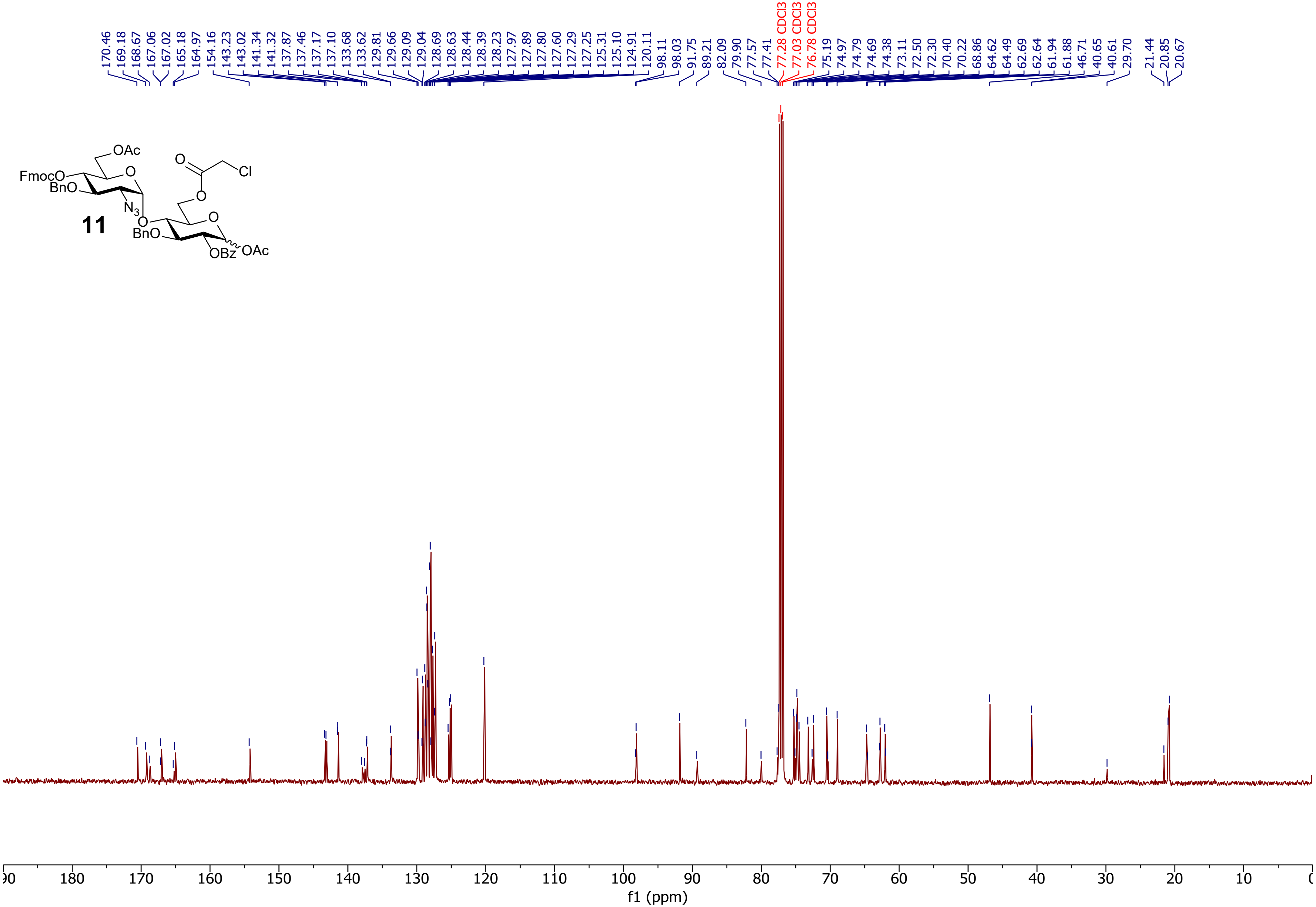
^{13}C NMR (126 MHz, CDCl$_3$)



^{1}H NMR (500 MHz, CDCl$_3$)

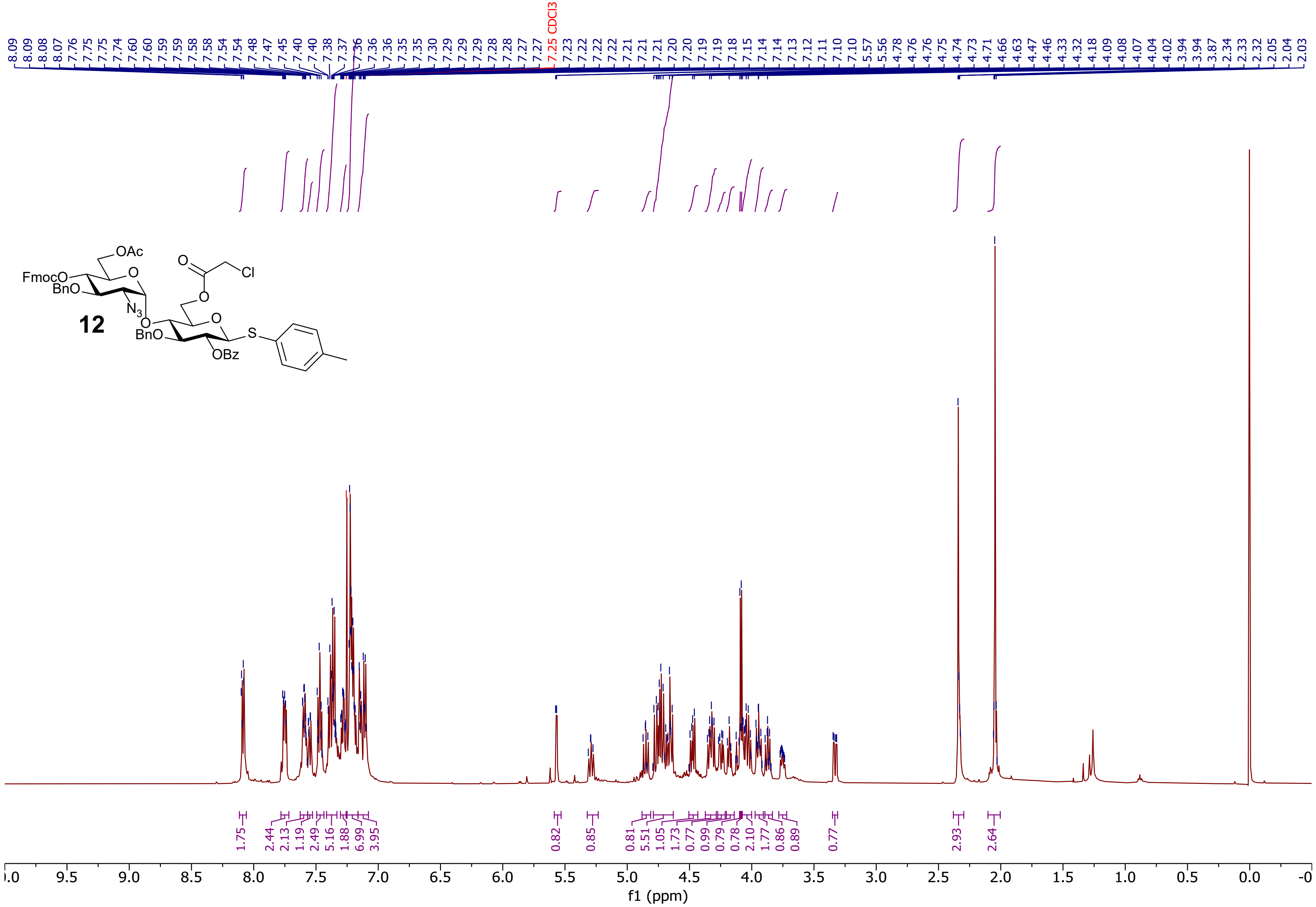


^{13}C NMR (126 MHz, CDCl$_3$)

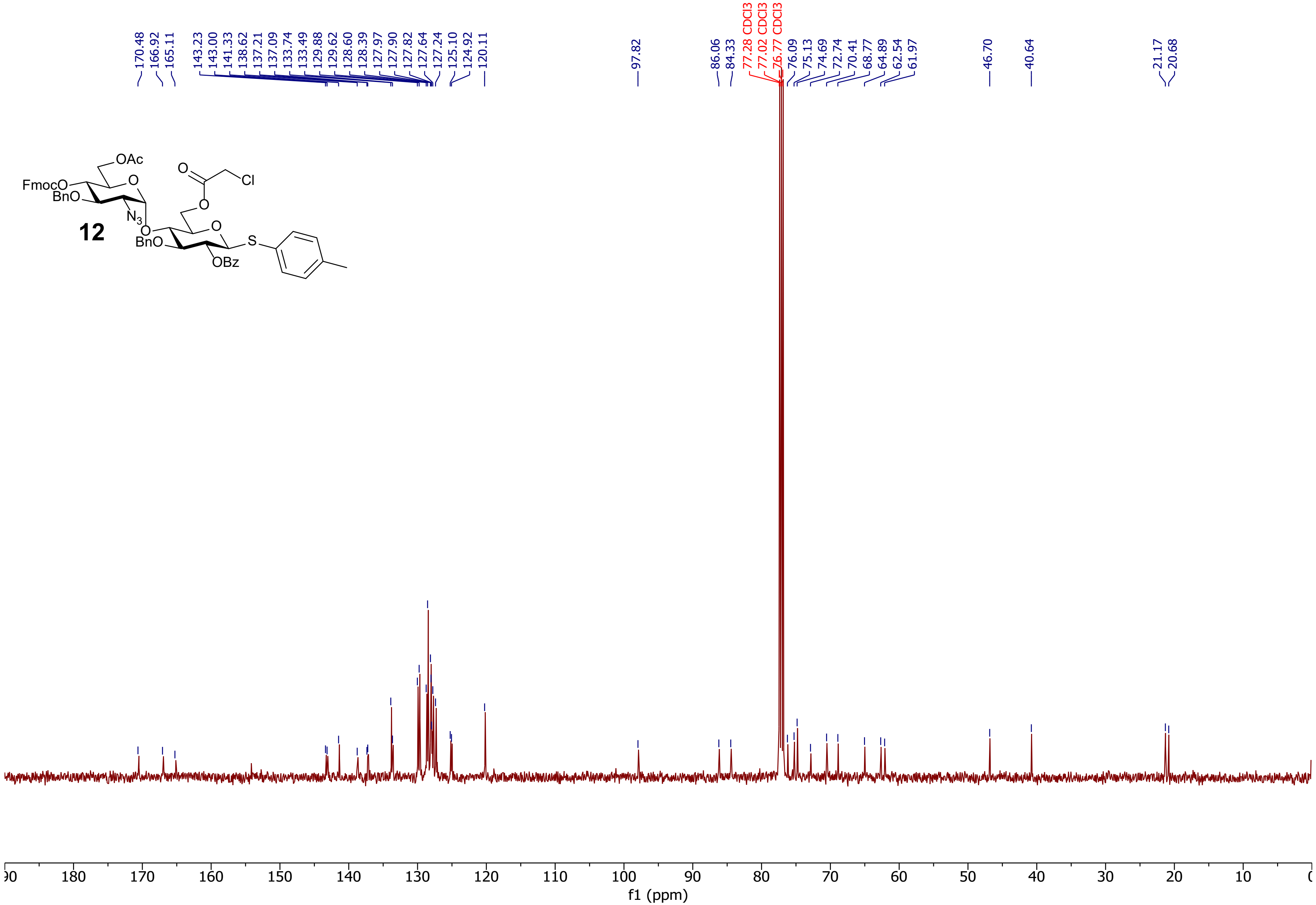


11

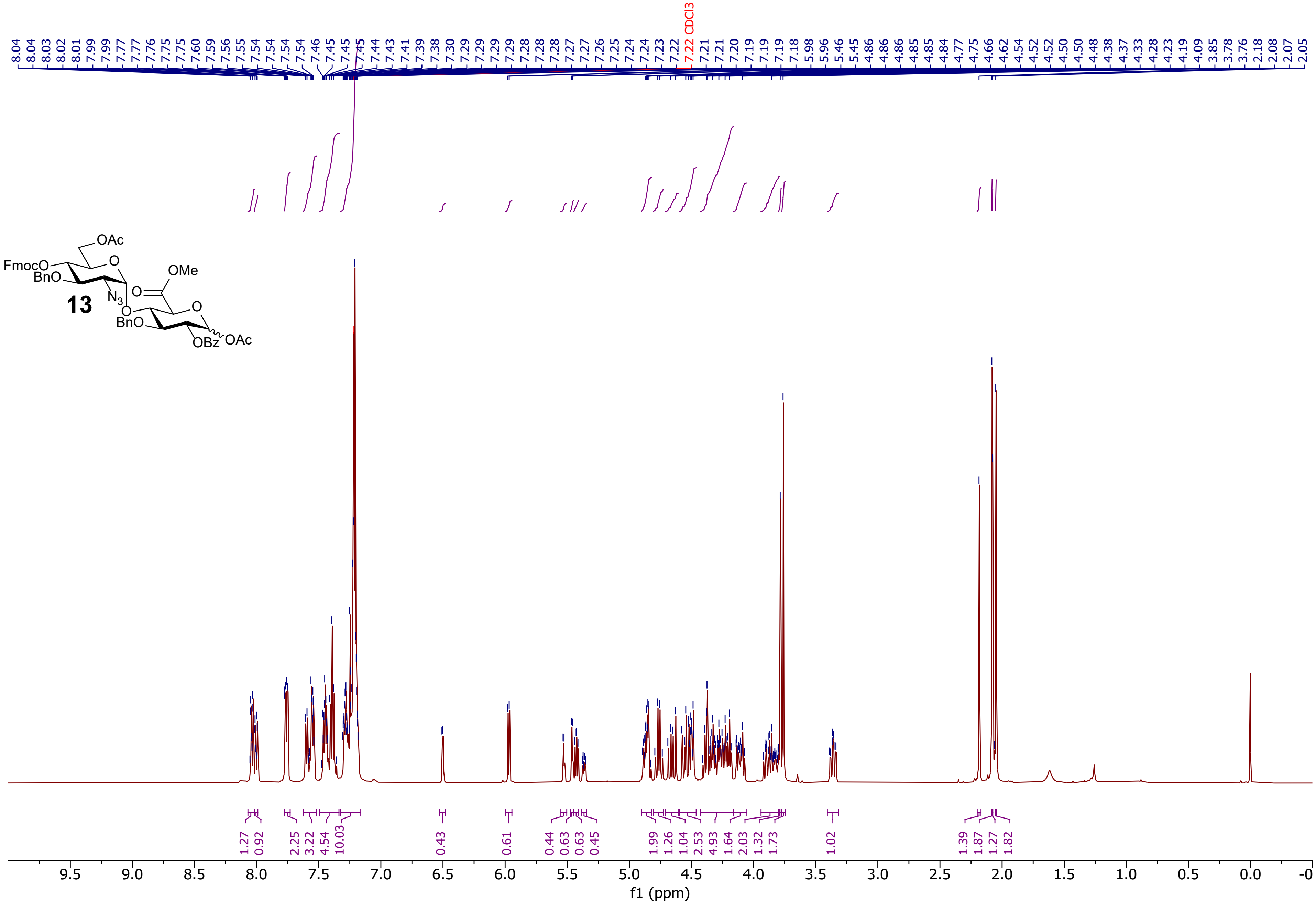
^{1}H NMR (500 MHz, $CDCl_3$)



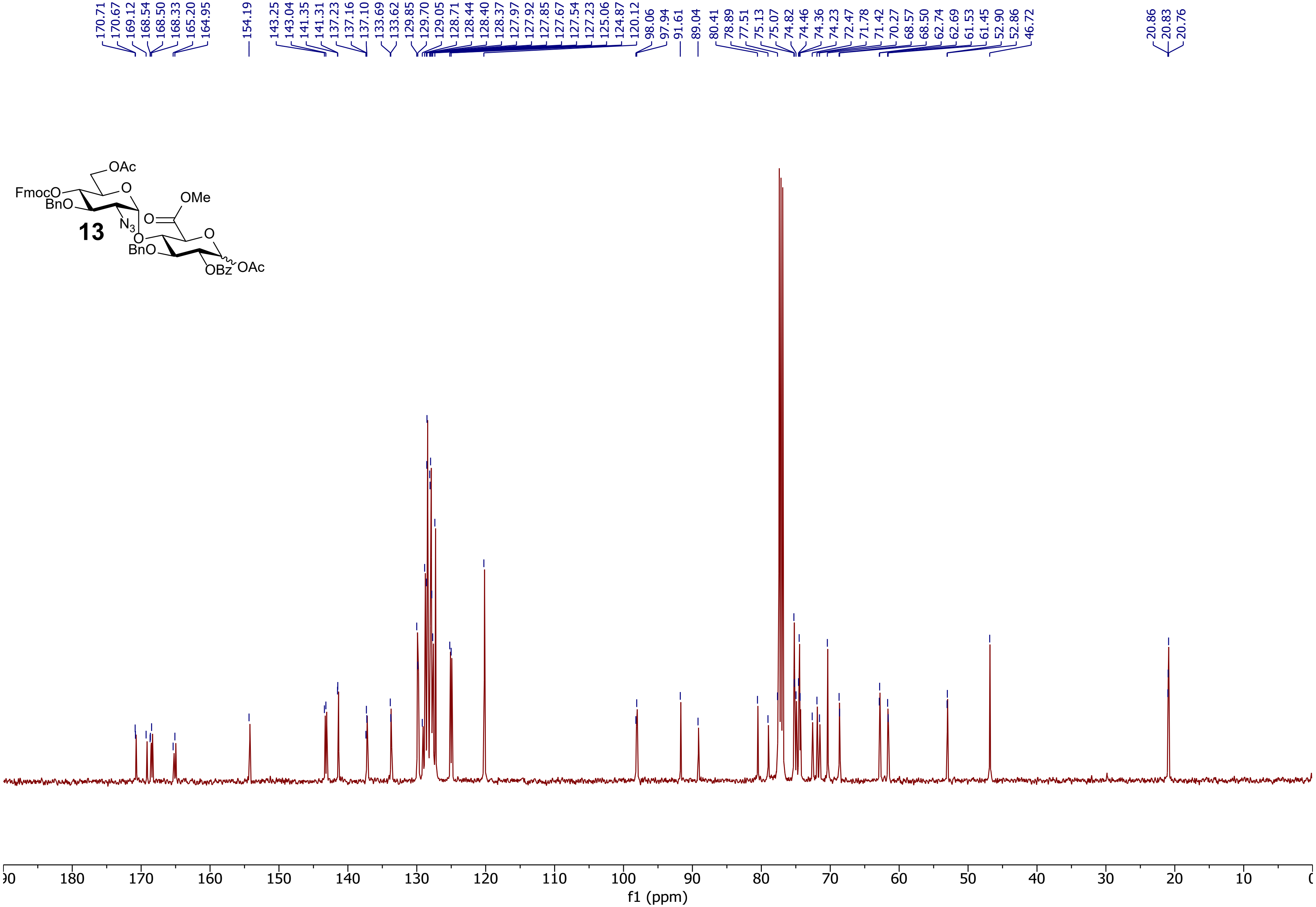
^{13}C NMR (126 MHz, CDCl$_3$)



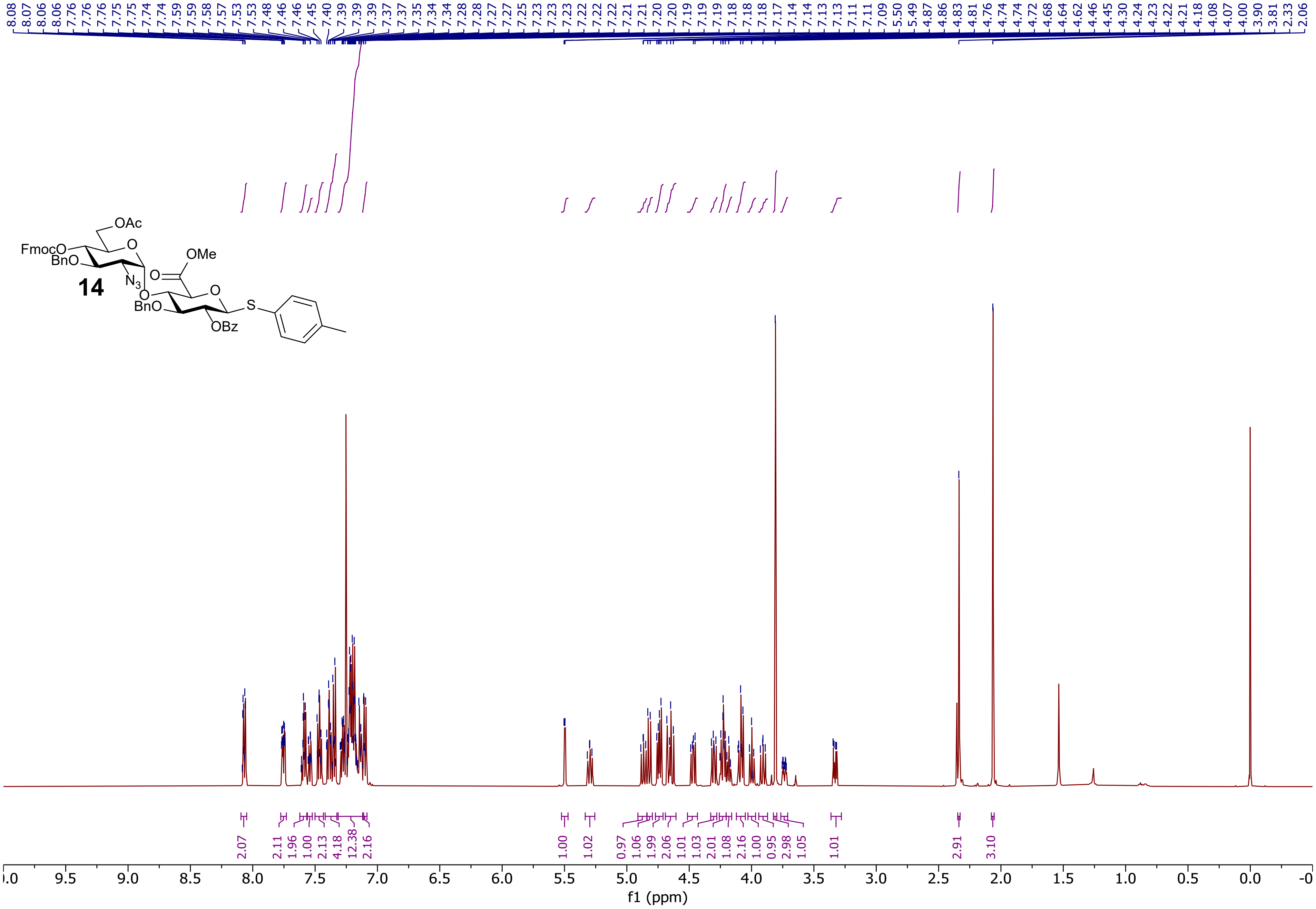
^{1}H NMR (500 MHz, $CDCl_3$)



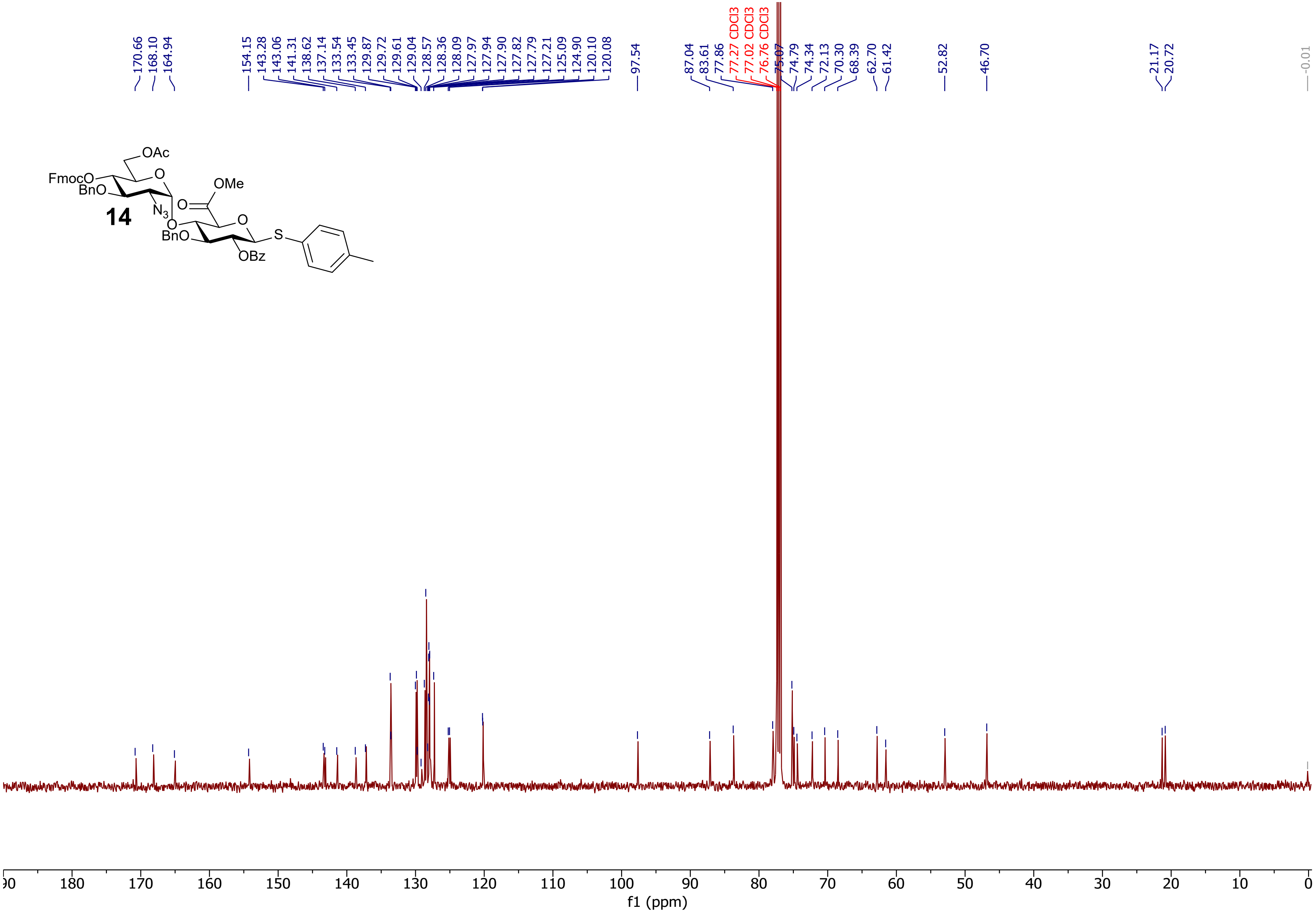
^{13}C NMR (126 MHz, CDCl$_3$)



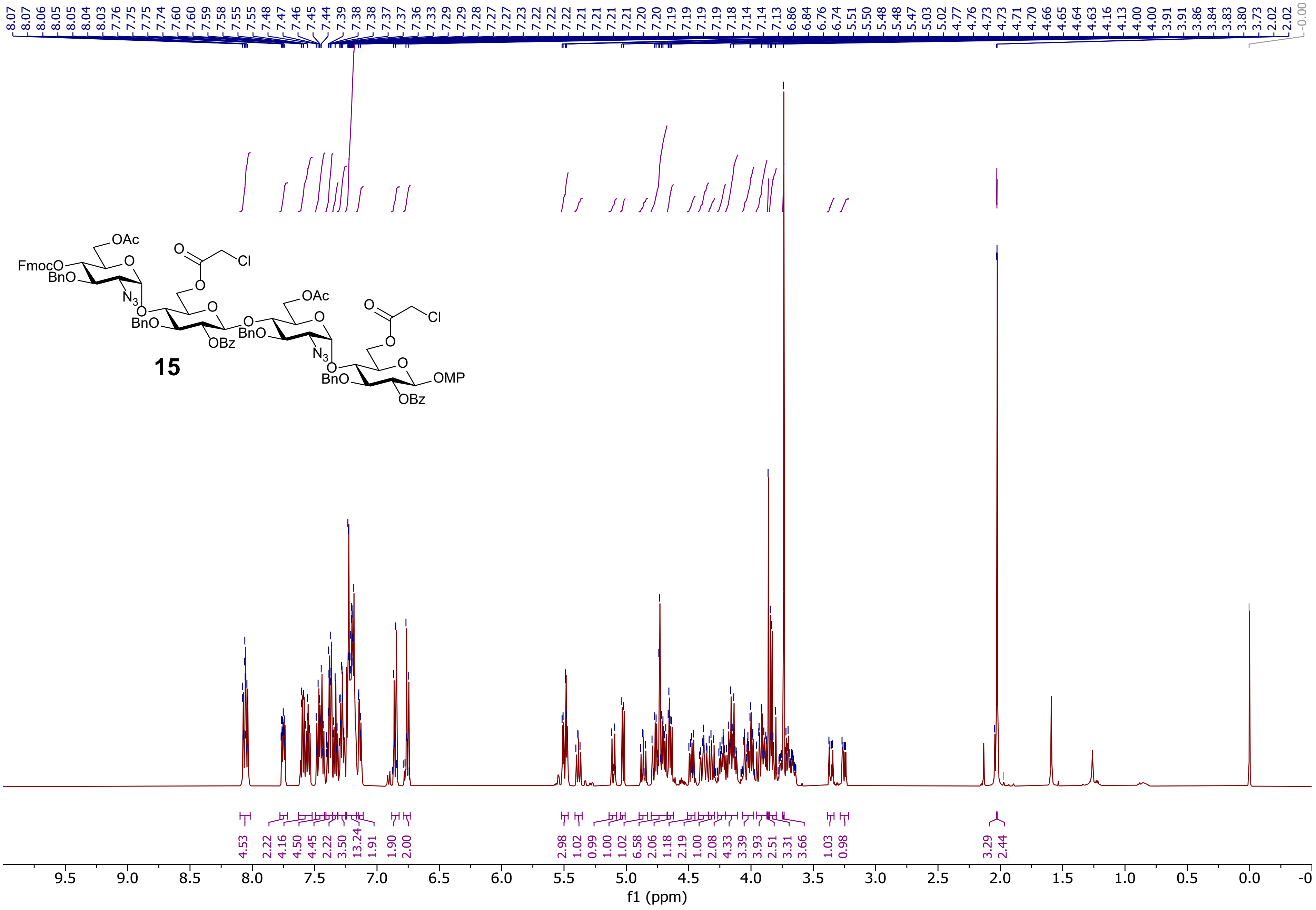
^{1}H NMR (500 MHz, CDCl$_3$)



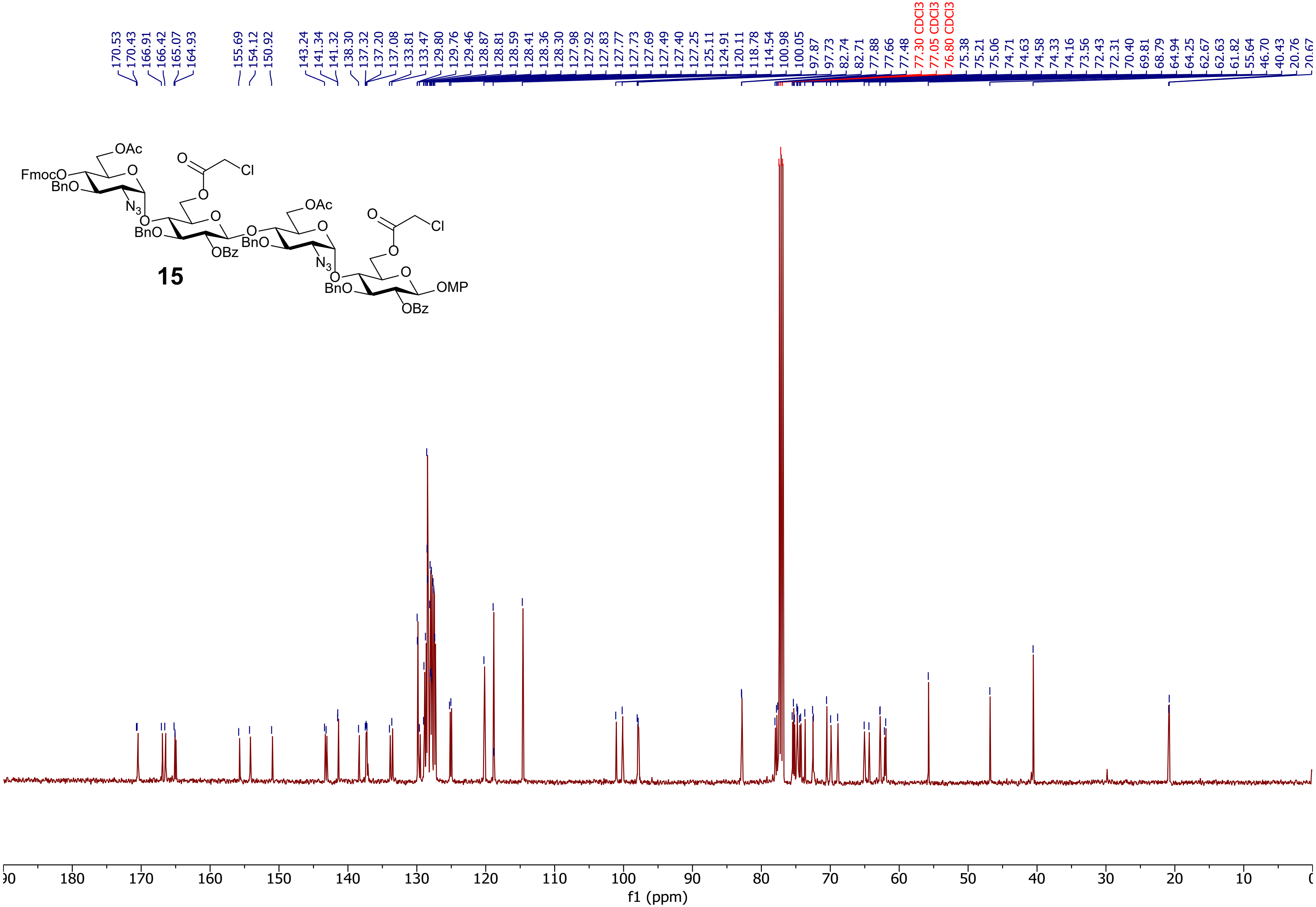
^{13}C NMR (126 MHz, $CDCl_3$)


14

^{1}H NMR (500 MHz, CDCl$_3$)

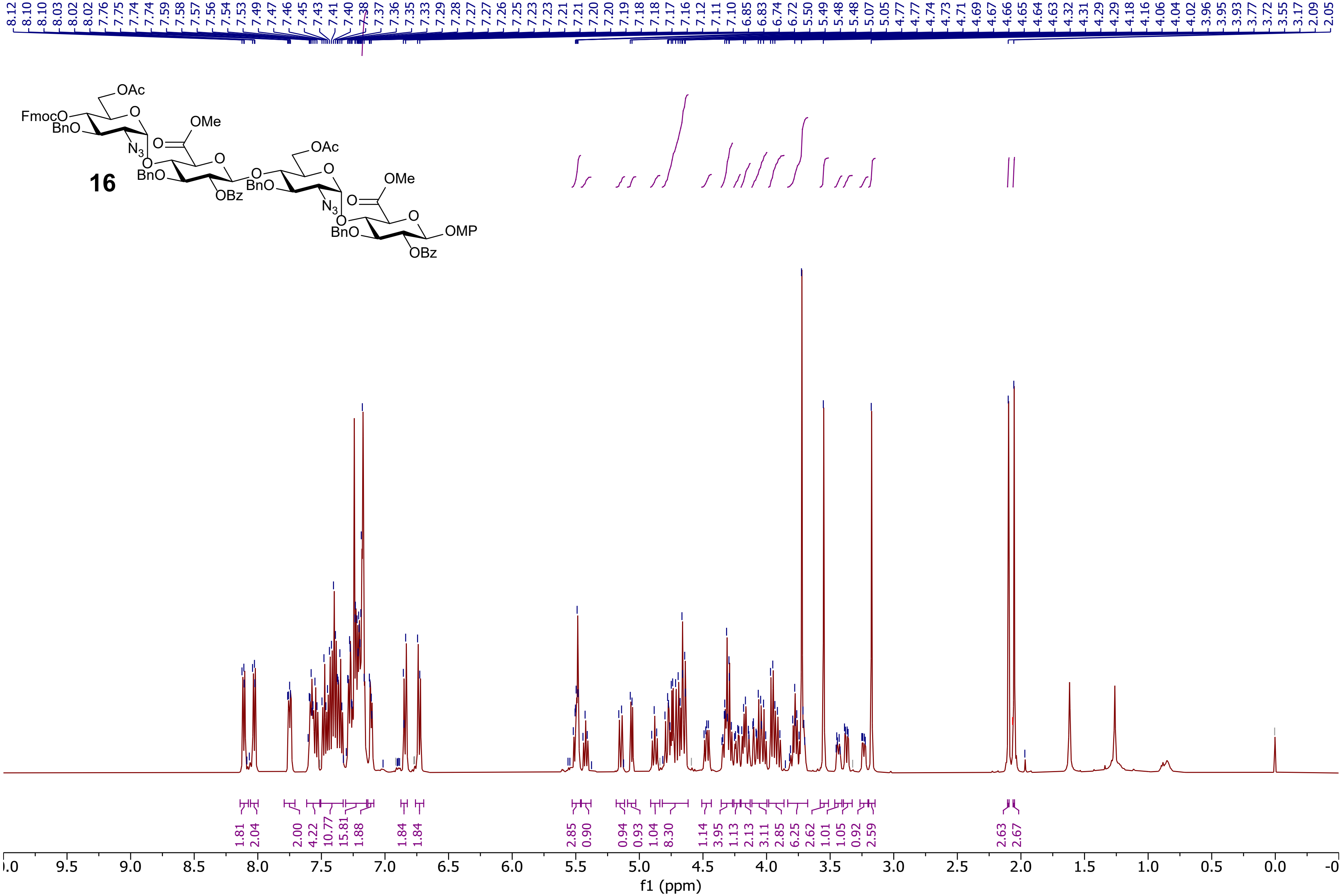


^{13}C NMR (126 MHz, CDCl$_3$)

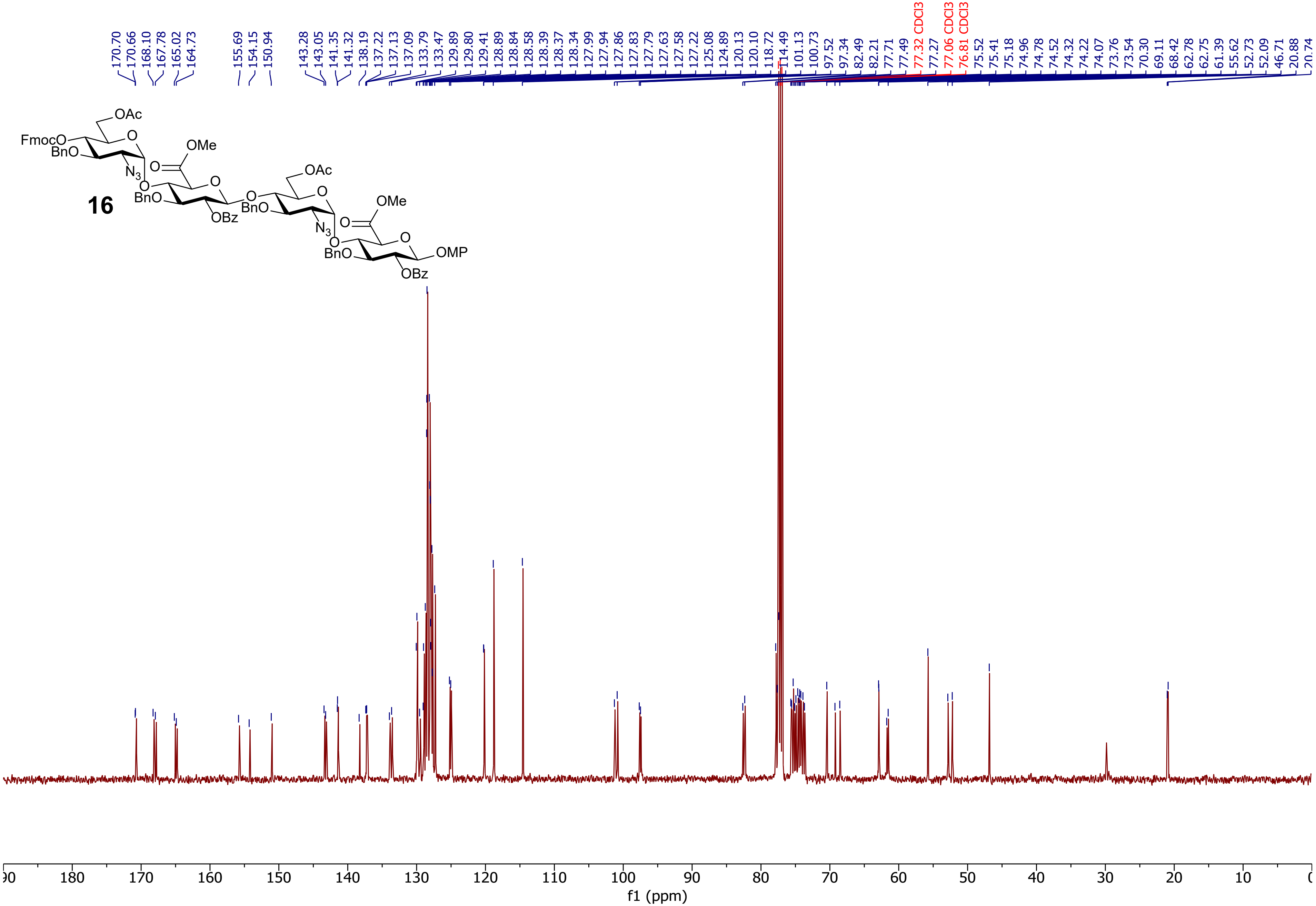


15

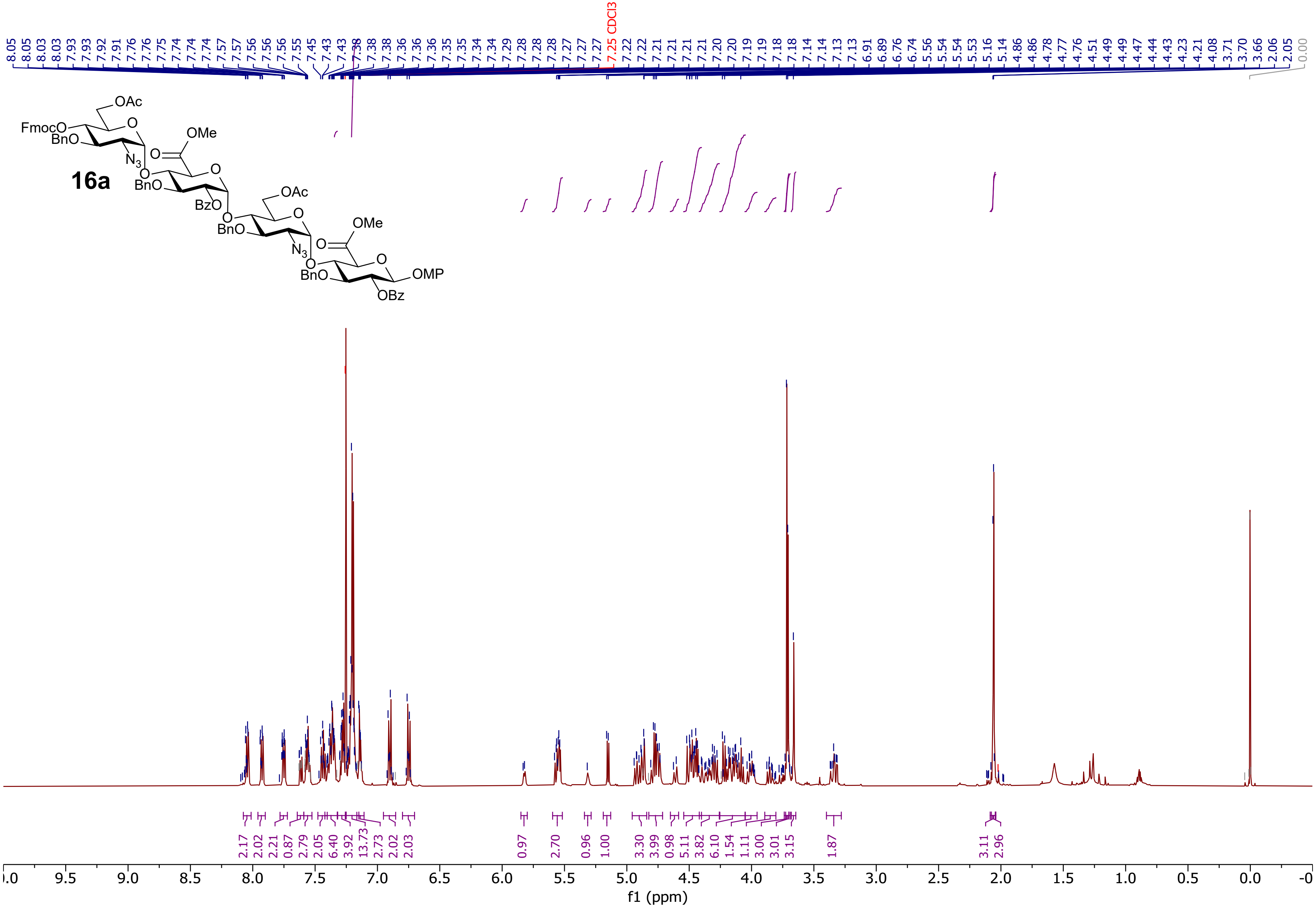
¹H NMR (500 MHz, CDCl₃)



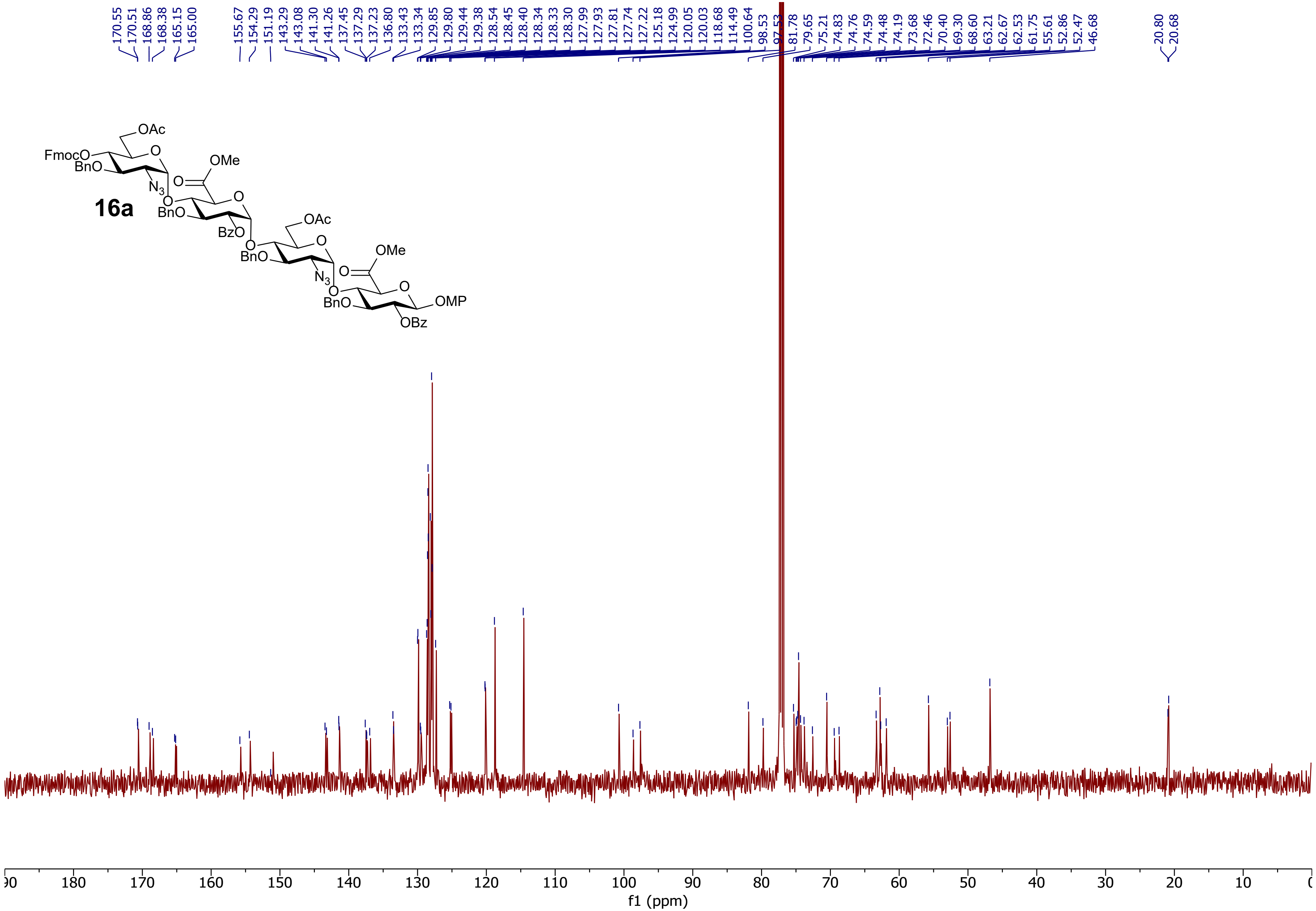
^{13}C NMR (126 MHz, CDCl$_3$)



^1H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, CDCl$_3$)



16a