Supplementary Information (SI) for Biomaterials Science.

Supplementary Information

Clickable Polyamidosaccharides: Accessing Bottlebrush Inspired Hyaluronic Acid Glycopolymers for CD44 Targeting of Breast Cancer Cells

Kaitlynn A. Sockett[#], Madeline K. Loffredo[#], Christian D. DeMoya, Zoe G. Garman, and Mark W. Grinstaff*

*Corresponding author: mgrin@bu.edu

Boston University, Boston, MA 02215, United States

Table of Contents

Supplemental Figures

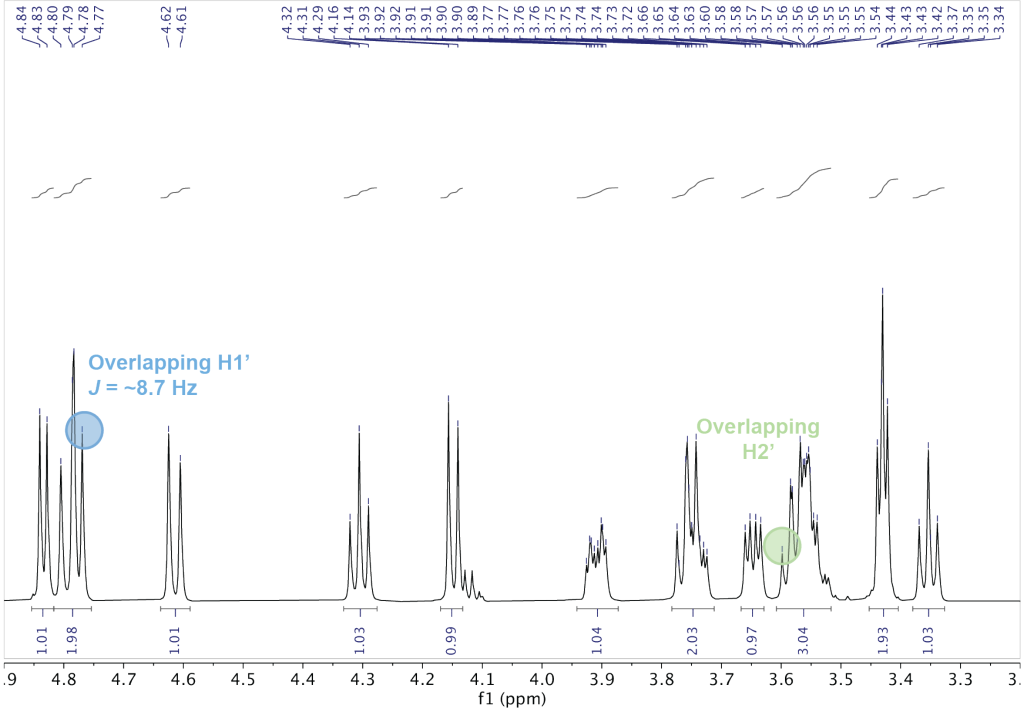


Figure S1. ^{1}H NMR of β-anomer **15** with overlapping peaks and approximate *J*-value of H1' to confirm stereochemistry of isolated disaccharide.

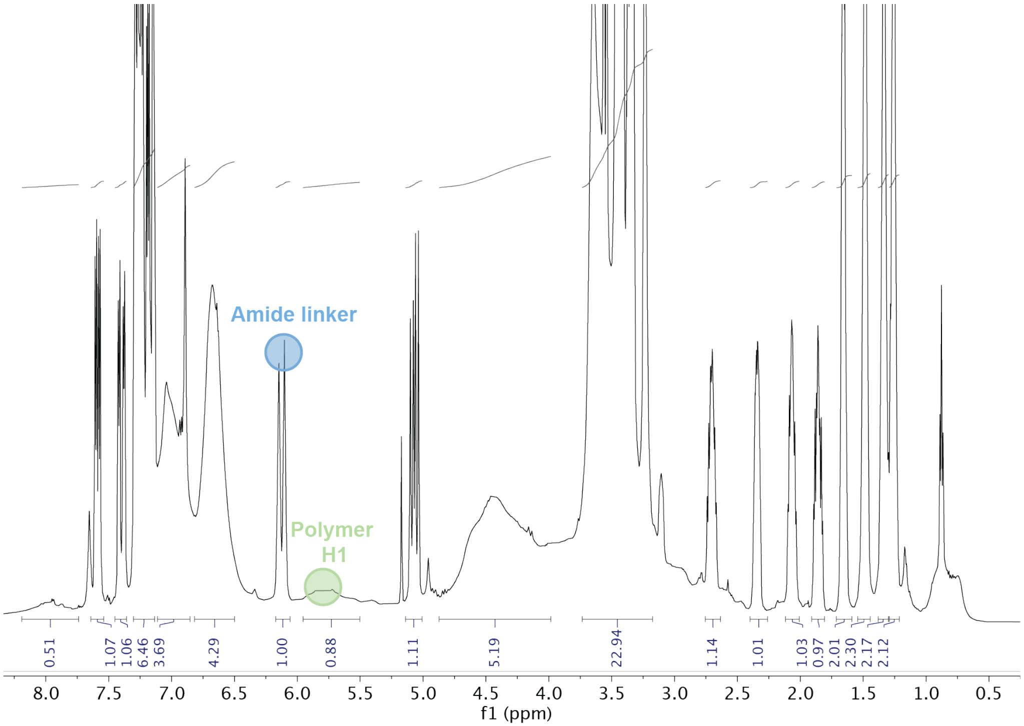


Figure S2. Representative ^{1}H NMR analysis of **P1c** approximating the linker conjugation efficiency by comparing the integrals of the linker amide proton and the polymeric H1.

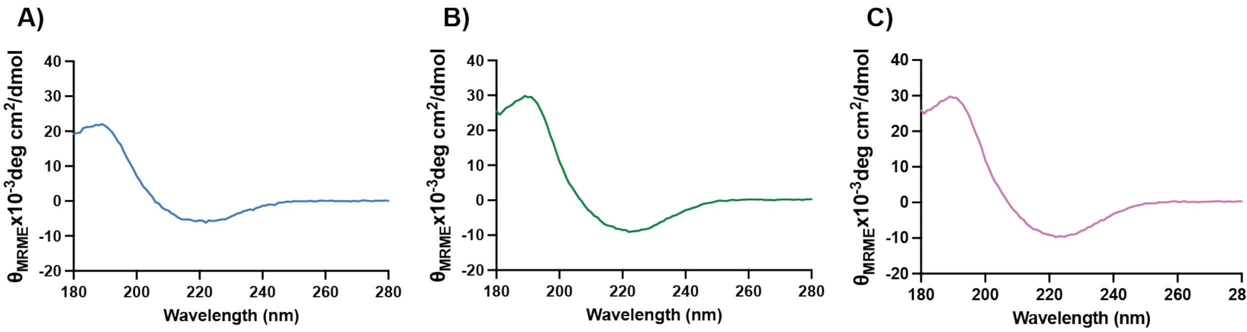


Figure S3. Circular dichroism of polymers, representative N=50 for each polymer class: **A) P2d'**; **B) P5d'**, and; **C) P9d'**.

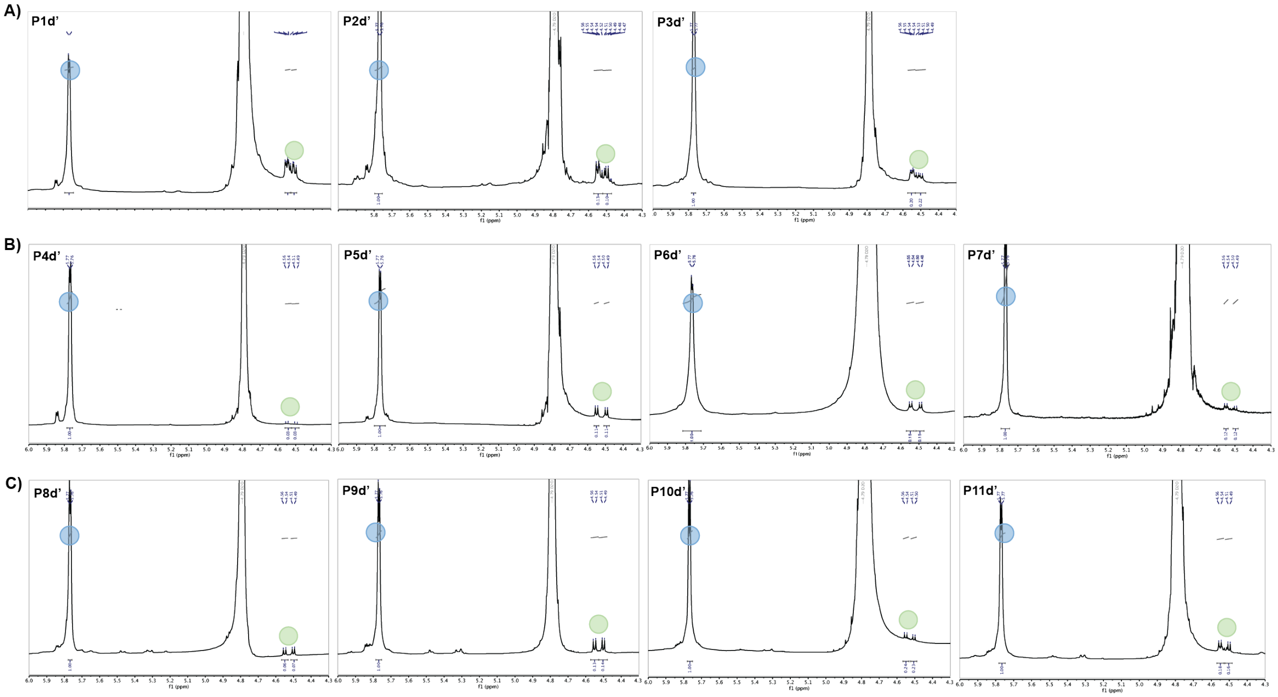


Figure S4. ^{1}H NMR analysis of deprotected polymers and their approximate pendant conjugation. **A)** Polymers **P1d'-P3d' B)** Polymers **P4d'-P7d' C)** Polymers **P8d'-P11d**. Blue circles indicate the polymeric H1 proton while the green circles indicate the pendant disaccharide H1 and H1'.

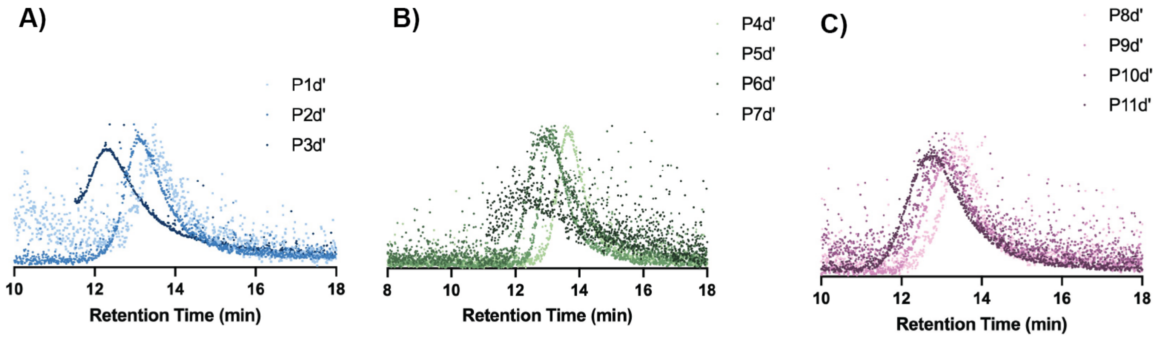


Figure S5. Raw aqueous GPC traces of deprotected polymers **A) P1d'-P3d' B) P4d'-P7d' C) P8d'-P11d'**.

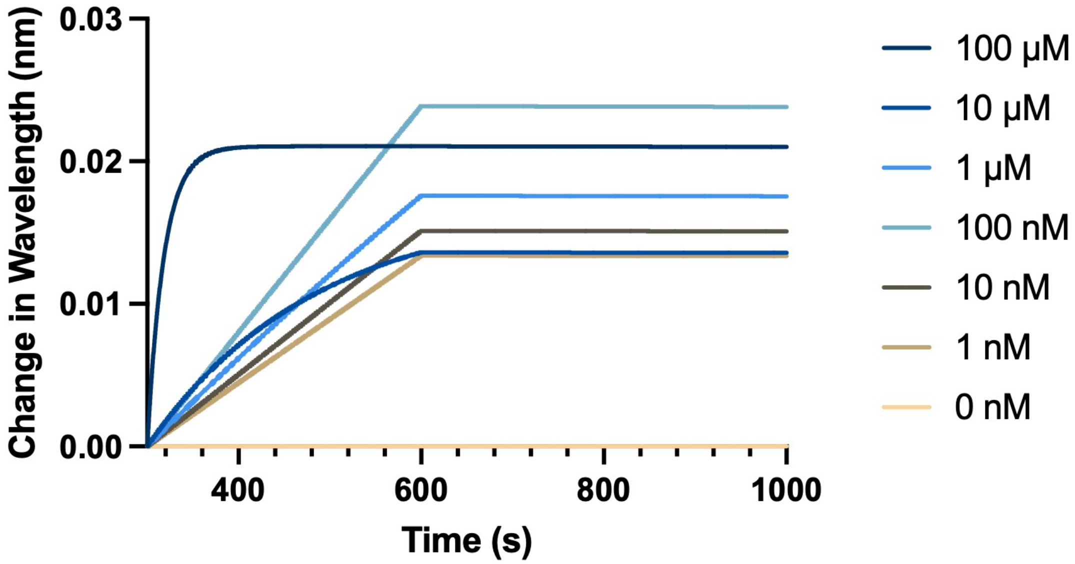


Figure S6. BLI sensogram of association and dissociation curves of **P10d'** and immobilized CD44. Analysis calculated **P10d'** has a K_D = 9. 88 ± 0.96 nM. Association was measured for 240 sec before transferring to a buffer well to measure dissociation for 400 sec. Curves were fit with a Mass Transport model and the K_D was calculated.

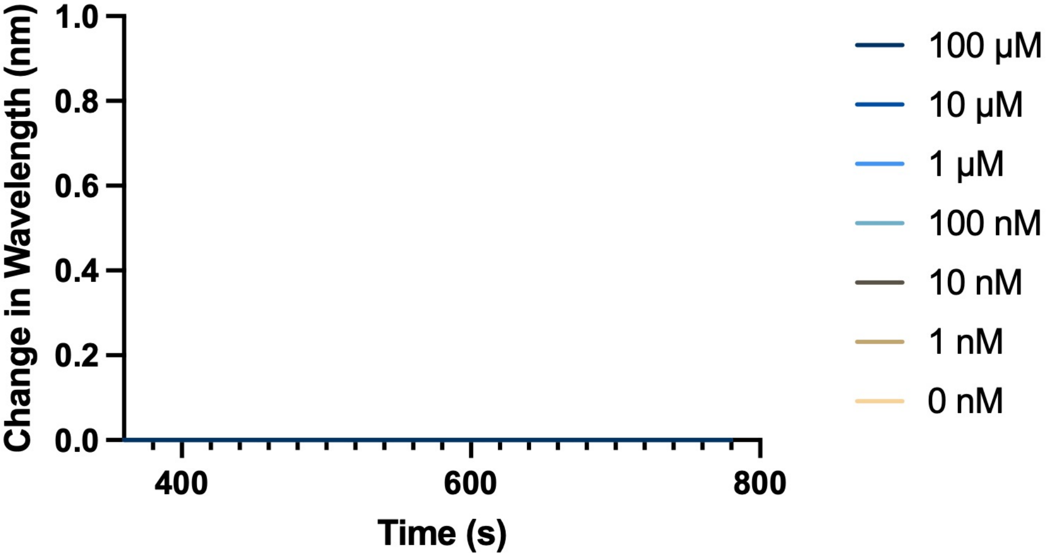


Figure S7. Representative sensogram of no binding observed between glc_{OH}-PAS and immobilized CD44.

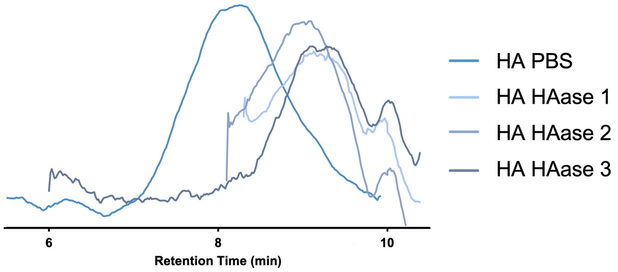


Figure S8. GPC analysis of HA degradation following HAase incubation for 24hrs showing a shift in retention times indicating decreased MW. Samples analyzed include HA, HA incubated with PBS only, and three different HA samples incubated with HAase. GPC chromatograms were fit with a moving average trendline (period of 15).

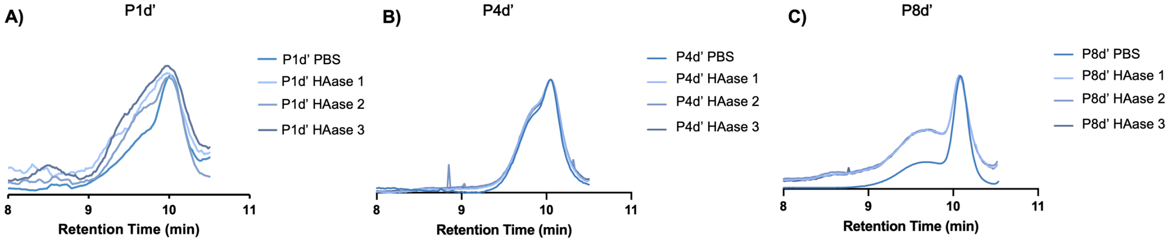


Figure S9. GPC analysis of HA degradation following HAase incubation for 24hrs showing a shift in retention times indicating decreased MW. Samples analyzed include HA, HA incubated with PBS only, and three different HA samples incubated with HAase. **A) P1d'**, GPC chromatograms were fit with a moving average trendline (period of 15); **B) P4d'**; **C) P8d'**.

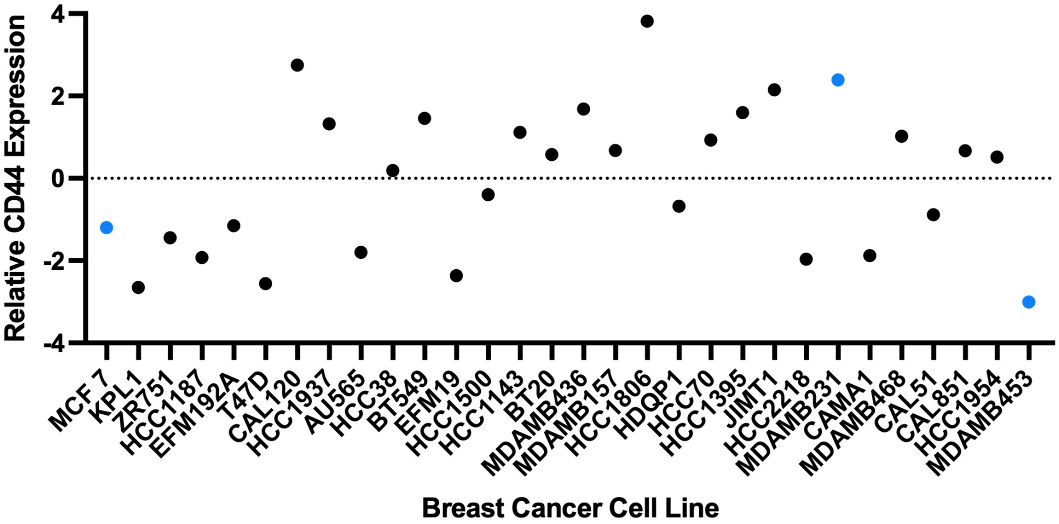


Figure S10. Breast cancer cell line CD44 expression levels. Data was downloaded from DepMap portal where it was normalized to an average of 0. Species with relative expression above 0 exhibit increased CD44 expression while species below 0 exhibit lower than average CD44 expression. Blue points indicate cell lines used for *in vitro* studies.

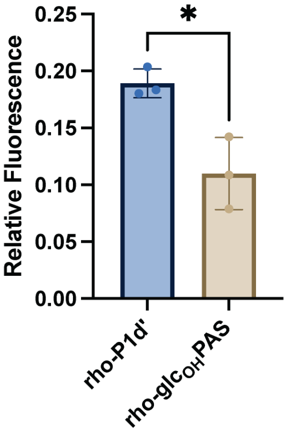


Figure S11. Relative fluorescence quantification of **rho-P1d’** and rho-glc$_{OH}$PAS in MDA-MB-231 cells after a 6hr treatment with 0.250 μg/mL of polymer solutions. Fluorescence was normalized to DAPI fluorescence. Data presented as mean values ± S.D., *= $p < 0.05$ determined by unpaired two-tailed T test with Welch’s correction, n = 3.

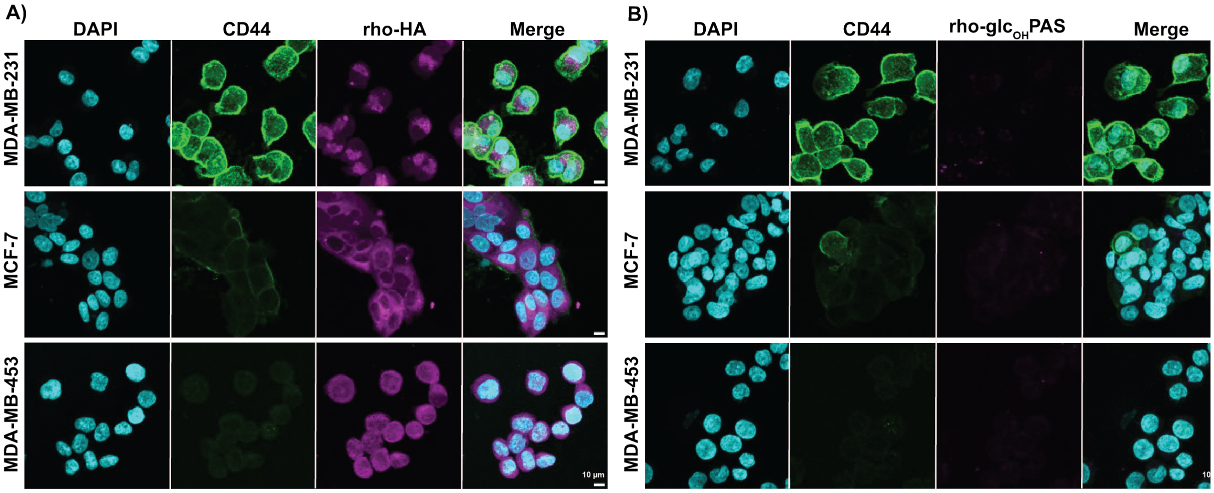


Figure S12. Characterization of rhodamine-labeled positive control, HA and rhodamine-labeled negative control, glc$_{OH}$PAS, cellular uptake in breast cancer cell lines, MDA-MB-231, MCF-7, and MDA-MB-453. **A)** Representative images of rho-HA (pink) cellular uptake following a 6 hr treatment with 250 µg/mL. Cells were stained with DAPI (blue) for nucleus and immunostained for CD44 (green). **B)** Representative images of rho-glc$_{OH}$PAS (pink) cellular uptake after a 6 hr treatment with 250 µg/mL. Cells were stained with DAPI (blue) for nucleus and immunostained for CD44 (green). Scale bars are 10 µm.

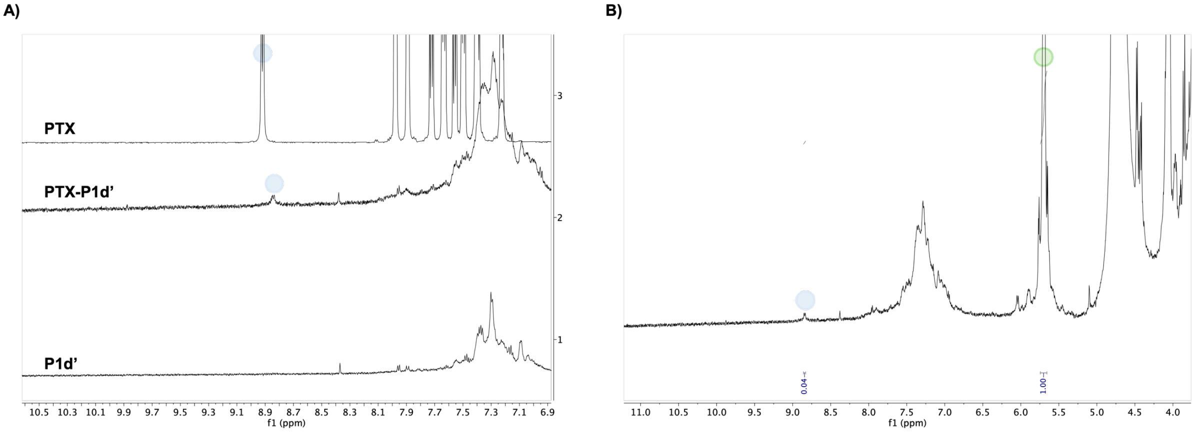


Figure S13. ^{1}H NMR analysis of P1d'-PTX conjugation. **A)** Overlay of PTX alone, **PTX-P1d'**, and **P1d'** alone showing the presence of the PTX aromatic proton following conjugation to indicate a successful coupling to obtain **PTX-P1d'**. **B)** Proton integration of PTX (blue) relative to **P1d'** H1(green) corroborates **PTX-P1d'** conjugation.

Supplemental Experimental Methods

General Methods

Proton (^{1}H), carbon (^{13}C), and fluorine (^{19}F) NMR spectra were acquired on a 600 MHz Bruker NMR Spectrometer at the Boston University Chemical Instrumentation Center (BU-CIC). All NMR spectra were acquired at ambient temperature with spectral references made to residual solvent peaks ($CDCl_3$ = 7.26 ppm, DMSO = 2.50 ppm, and D_2O = 4.79 ppm for ^{1}H NMR, and

$CDCl_3$ = 77.16 ppm and DMSO = 39.52 ppm for ^{13}C NMR). NMR peak splitting abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, ap t = apparent triplet. Chemical shifts (δ) are listed in ppm and coupling constants (*J*) are reported in Hz.

Equations

$$N_{Pa} = \frac{\text{absolute } M_W}{585.81} \qquad N_{Pb} = \frac{\text{absolute } M_W}{429.47} \qquad N_{Pc} = \frac{\text{absolute } M_W}{904.07}$$

$$N_{Pd} = \frac{X(\text{absolute } M_W)}{1994.42} + \frac{(1\text{-}X)(\text{absolute } M_W)}{904.07} \qquad N_{Pd'} = \frac{X(\text{absolute } M_W)}{1277.55} + \frac{(1\text{-}X)(\text{absolute } M_W)}{663.77}$$

Equation S1. Homopolymers; a, b, c, d, d' refer to the previously defined steps of the polymer synthesis (Scheme 3). X represents % conjugation of HA pendant (Table 5, column 3). Denominator values represent molecular weights of the monomer units.

$$N_{Pa} = \frac{.25(\text{absolute } M_W)}{585.81} + \frac{.75(\text{absolute } M_W)}{459.54} \qquad N_{Pb} = \frac{.25(\text{absolute } M_W)}{429.47} + \frac{.75(\text{absolute } M_W)}{459.54}$$

$$N_{Pc} = \frac{.25(\text{absolute } M_W)}{904.07} + \frac{.75(\text{absolute } M_W)}{459.54}$$

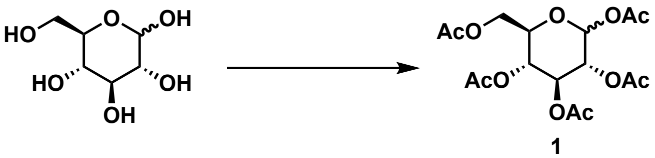
$$N_{Pd} = \frac{X(\text{absolute } M_W)}{1994.42} + \frac{(.25\text{-}X)(\text{absolute } M_W)}{904.07} + \frac{.75(\text{absolute } M_W)}{459.54}$$

$$N_{Pd'} = \frac{X(\text{absolute } M_W)}{1277.55} + \frac{(.25\text{-}X)(\text{absolute } M_W)}{663.77} + \frac{.75(\text{absolute } M_W)}{189.17}$$

Equation S2. Copolymers; a, b, c, d, d' refer to the previously defined steps of the polymer synthesis. X represents % conjugation of HA pendant (Table 5, column 3). Denominator values represent molecular weights of the monomer units.

Small Molecule Synthetic Procedures

1,2,3,4,6-Penta-*O*-acetyl-D-glucopyranose (1)

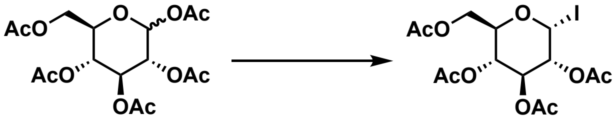


1

Procedure was adapted from previous literature with minor changes.[1] D (+) glucose (20.0 g, 110.99 mmol, 1.0 eq) was dissolved in anhydrous pyridine (123.0 mL) and cooled to 0˚C under N_2 protection. Acetic anhydride (157.4 mL, 1664.91 mmol, 15.0 eq.) was added followed by DMAP (0.542 g, 4.44 mmol, 0.04 eq.). The reaction was stirred at 0˚C until solution turned clear, at which point the reaction was warmed to ambient temperature and stirred overnight. The reaction solution was then added to 220 mL of ice water and allowed to sit for 1 hr. The precipitate was then filtered and washed with water (2x) and diethyl ether (2x) to produce a white solid (31.55 g, >95% yield). Spectral data matches previously reported.[1]

^{1}H NMR (600 MHz, $\mathrm{CDCl_3}$) δ 6.32 (d, *J* = 3.7 Hz, 1H, H-1), 5.50 – 4.51 (ap t, 1H, H-3), 5.17 – 5.11 (ap t, 1H, H-4), 5.09 (dd, *J* = 10.3, 3.7 Hz, 1H, H-2), 4.26 (dd, *J* = 12.2, 3.8 Hz, 1H, H-6), 4.13 – 4.06 (m, 2H, H-5, H-6'), 2.17 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 2.08 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 2.03 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 2.02 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 2.00 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$) ppm; **^{13}C NMR** (151 MHz, $\mathrm{CDCl_3}$) δ 170.6 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 170.2 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 169.6 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 169.4 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 168.7 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 89.1 (C-1), 69.8 (2x *C*H, C-3, C-5), 69.2 (C-2), 67.9 (C-4), 61.5 (C-6), 20.9 ($\mathit{C}\mathrm{H_3COO}$), 20.69 ($\mathit{C}\mathrm{H_3COO}$), 20.66 ($\mathit{C}\mathrm{H_3COO}$), 20.6 ($\mathit{C}\mathrm{H_3COO}$), 20.4 ($\mathit{C}\mathrm{H_3COO}$) ppm; **HRMS:** Calc. for $\mathrm{C_{16}H_{22}O_{11}}$ $[M\mathrm{+Na}]^+$: 413.1060, found 413.1046 m/z.

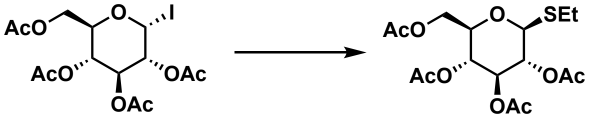
2,3,4,6-tetra-*O*-acetyl-1-iodo-α-D-glucopyranoside



1

Procedure was adapted from previous literature with minor changes.[1] To a refluxing solution of compound **1** (10 g, 25.62 mmol, 1.0 eq.) in anhydrous $\mathrm{CH_2Cl_2}$ (64.3 mL), iodine (8.45 g, 33.30 mmol, 1.3 eq.) was added followed by triethylsilane (5.32 mL, 33.30 mmol, 1.3 eq.). The reaction was stirred for 20 min then cooled to ambient temperature. The reaction was then diluted with $\mathrm{CH_2Cl_2}$ and washed with 1:1 (v/v) sat. $\mathrm{NaHCO_3}$: 10% $\mathrm{Na_2S_2O_3}$, followed by water, brine, dried over $\mathrm{Na_2SO_4}$, filtered, and concentrated under vacuum. Crude material was carried to the next step without further purification.

Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (2)

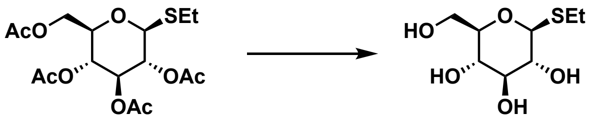


2

Procedure was adapted from previous literature with minor changes.[1] To a solution of crude material in acetonitrile (92.4 mL) under $\mathrm{N_2}$ was added thiourea (2.93 g, 38.43 mmol, 1.5 eq.) and stirred at 60°C for 40 min. The reaction was then cooled to ambient temperature, and iodoethane (10.3 mL, 128.10 mmol, 5.0 eq) was added followed by triethylamine (14.3 mL, 102.48 mmol, 4.0 eq.), followed by stirring overnight at ambient temperature. Resulting precipitate was removed via filtration. Filtrate was concentrated under vacuum and purified by flash column chromatography (3: 10 EtOAc: cyclohexane) to give a white solid (8.632g, 86% over two steps). Spectral data matches previously reported.[1]

^{1}H NMR (600 MHz, $\mathrm{CDCl_3}$) δ 5.19 – 5.15 (ap t, 1H, H-3), 5.07 – 5.02 (ap t, 1H, H-2), 5.02 – 4.96 (ap t, 1H H-4), 4.47 (d, *J* = 10.1 Hz, 1H, H-1), 4.21 (dd, *J* = 12.4, 5.04 Hz, 1H, H-6), 4.10 (dd, *J* = 12.4, 2.3 Hz, 1H, H-6'), 3.68 (ddd, *J* = 10.1, 4.9, 2.3 Hz, 1H, H-5), 2.74 – 2.60 (m, 2H, $\mathrm{SC}\mathit{H}_2\mathrm{CH_3}$), 2.04 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 2.02 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 1.99 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 1.97 (s, 3H, $\mathrm{C}\mathit{H}_3\mathrm{COO}$), 1.23 (t, *J* = 7.5 Hz, 3H, $\mathrm{SCH_2C}\mathit{H}_3$) ppm; **^{13}C NMR** (151 MHz, $\mathrm{CDCl_3}$) δ 170.7 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 170.2 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 169.43 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 169.41 ($\mathrm{CH_3}\mathit{C}\mathrm{OO}$), 83.5 (C-1) 75.8 (C-5), 73.9 (C-3), 69.9 (C-2), 68.3 (C-4), 62.2 (C-6), 23.8 ($\mathrm{S}\mathit{C}\mathrm{H_2CH_3}$), 20.7 ($\mathit{C}\mathrm{H_3COO}$), 20.59 ($\mathit{C}\mathrm{H_3COO}$), 20.56 ($\mathit{C}\mathrm{H_3COO}$), 14.8 ($\mathrm{SCH_2}\mathit{C}\mathrm{H_3}$) ppm; **HRMS:** Calc. for $\mathrm{C_{16}H_{24}O_9S}$ $[M\mathrm{+Na}]^+$: 415.1039, found 415.1028 m/z.

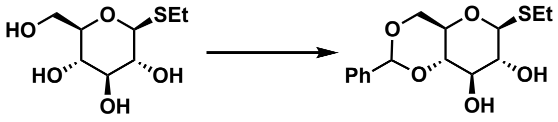
Ethyl 1-thio-β-D-glucopyranoside



2

Procedure was adapted from previous literature with minor changes.[1] Compound **2** (8.63 g, 22.00 mmol, 1.0 eq) was added to a mixture of aqueous 25% NH_3 solution (17.0 mL, 3.10 g, 182.06 mmol, 8.3 eq) in methanol (141.6 mL) and stirred overnight at ambient temperature. Crude material was concentrated and carried to next step without further purification.

Ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (3)

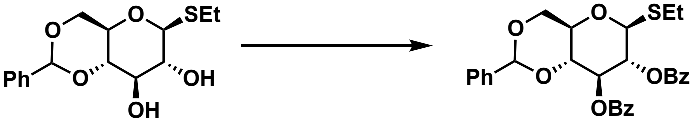


3

Procedure was adapted from previous literature.[2] To an ambient temperature solution of crude material in acetonitrile (121.0 mL) under N_2 was added benzaldehyde dimethyl acetal (5.97 g, 39.77 mmol, 1.5 eq.) followed by (1*S*)-(+)-10-Camphorsulfonic acid (0.62 g, 2.65 mmol, 0.1 eq.). The reaction was warmed to 70˚C and stirred for 2 hr. The reaction was subsequently quenched with triethylamine and concentrated under vacuum. Crude material was triturated with diethyl ether to afford a white solid (4.76 g, 69% over two steps). Spectral data matches previously reported.[2]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.48 (m, 2H, Ph), 7.38 – 7.36 (m, 3H, Ph), 5.54 (s, 1H, PhC*H*), 4.47 (d, *J* = 9.8 Hz, 1H, H-1), 4.36 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6), 3.85 – 3.82 (ap t, 1H, H-3), 3.78 – 3.75 (ap t, 1H, H-6'), 3.59 – 3.56 (ap t, 1H, H-4), 3.52 – 3.50 (m, 2H, H-2, H-5), 2.79 – 2.73 (m, 2H, SCH_2CH_3), 1.34 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 136.8 (Ph), 129.3 (Ph), 128.3 (Ph), 126.2 (Ph), 101.9 (Ph*C*H), 86.6 (C-1), 80.3 (C-4), 74.5 (C-3), 73.1 (C-2), 70.5 (C-5), 68.5 (C-6), 24.7 (SCH_2CH_3), 15.2 (SCH_2CH_3) ppm; **HRMS:** Calc. for $C_{15}H_{20}O_5S$ $[M+Na]^+$: 335.0929, found 335.0927 m/z.

Ethyl 4,6-*O*-benzylidene-2,3-*O*-benzoyl-β-1-thio-β-D-glucopyranoside (4)

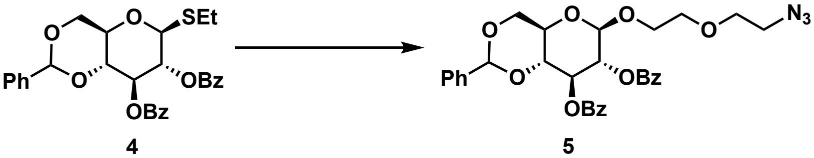


3 4

Procedure was adapted from previous literature with minor changes.[3] To an ambient temperature solution of **3** (4.76 g, 15.23 mmol, 1.0 eq.) in CH_2Cl_2 (41.8 mL) under N_2 was added pyridine (8.0 mL, 99.04 mmol, 6.5 eq.) followed by benzoyl chloride (7.1 mL, 60.95 mmol, 4.0 eq.). The reaction was stirred for 4 hr. The solution was then diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$, water, brine, and dried over Na_2SO_4. Product was filtered and concentrated. The resulting solid was triturated with diethyl ether to produce a white solid (6.25 g, 79%). Spectral data matches previously reported.[3]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.94 (ap t, 4H, Ph), 7.53 – 7.31 (m, 11H, Ph), 5.83 – 5.80 (ap t, 1H, H-3), 5.56 (s, 1H, PhC*H*), 5.54 – 5.50 (ap t, 1H, H-2), 4.83 (d, *J* = 10.0 Hz, 1H, H-1), 4.47 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6), 3.95 – 3.92 (ap t, 1H, H-4), 3.89 – 3.85 (ap t, 1H, H-6'), 3.77 (td, *J* = 9.7, 9.7, 4.9 Hz, 1H, H-5), 2.82 – 2.73 (m, 2H, SCH_2CH_3), 1.28 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.6 (C=O), 165.3 (C=O), 136.8-125.7 (3x C_6H_5), 101.5 (Ph*C*H), 84.5 (C-1), 78.8 (C-4), 73.2 (C-3), 71.1 (C-5), 71.0 (C-2), 69.1 (C-6), 24.4 (SCH_2CH_3), 14.9 (SCH_2CH_3) ppm; **HRMS:** Calc. for $C_{29}H_{28}O_7S$ $[M+Na]^+$: 543.1453, found 543.1464 m/z.

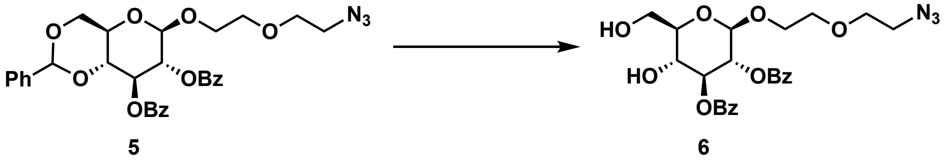
2-(2-azidoethoxy)ethyl 4,6-*O*-benzylidene-2,3-*O*-benzoyl-β-D-glucopyranoside (5)



Procedure was adapted from previous literature with minor changes.[4] 2-(2-azidoethoxy)ethanol (0.59 g, 4.49 mmol, 1.33 eq.) was added to a solution of **4** (1.76 g, 3.39 mmol, 1.0 eq.) in anhydrous CH_2Cl_2 (15.4 mL) over 4Å molecular sieves and under N_2 and stirred at ambient temperature for 30 min. The reaction was then cooled to -20°C followed by the addition of *N*-iodosuccinimide (1.01 g, 4.49 mmol, 1.33 eq.) and trifluoromethanesulfonic acid (0.03 mL, 0.34 mmol, 0.1 eq.). The reaction was warmed to -10°C and stirred for 4.5 hr before quenching with triethylamine and filtering through a pad of celite. Filtrate was washed with sat. $Na_2S_2O_3$, brine, and dried over Na_2SO_4. Product was purified via flash column chromatography (1: 4 EtOAc: cyclohexane) to afford an amber oil (1.72 g, 86%). Spectral data matches previously reported.[4]

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.96 (m, 4H, Ph), 7.54 – 7.47 (m, 2H, Ph), 7.43 – 7.31 (m, 9H, Ph), 5.82 – 5.79 (ap t, 1H, H-3), 5.56 (s, 1H, PhC*H*), 5.51 – 5.48 (ap t, 1H, H-2), 4.92 (d, *J* = 7.9 Hz, 1H, H-1), 4.46 (dd, *J* = 10.6, 4.9 Hz, 1H, H-6), 4.03 – 3.99 (m, 1H, $OCH_2CH_2OCH_2CH_2N_3$), 3.96 – 3.93 (ap t, 1H, H-4), 3.91 – 3.88 (ap t, 1H, H-6'), 3.80 – 3.77 (m, 1H, $OCH_2CH_2OCH_2CH_2N_3$), 3.74 – 3.70 (td, *J* = 9.8, 4.8 Hz, 1H, H-5), 3.63 – 3.56 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$), 3.47 – 3.45 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$), 3.13 – 3.04 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.6 (C=O), 165.2 (C=O), 133.3 (C_6H_5), 133.1 (C_6H_5), 129.8 (C_6H_5), 129.8 (C_6H_5), 129.44 (C_6H_5), 129.38 (C_6H_5), 129.1 (C_6H_5), 128.4 (C_6H_5), 128.3 (C_6H_5), 128.2 (C_6H_5), 126.2 (C_6H_5), 101.9 (C-1), 101.5 (Ph*C*H), 78.9 (C-4), 72.5 (C-2), 72.0 (C-3), 70.4 ($OCH_2CH_2OCH_2CH_2N_3$), 70.1 ($OCH_2CH_2OCH_2CH_2N_3$), 69.7 ($OCH_2CH_2OCH_2CH_2N_3$), 68.7 (C-6), 66.6 (C-5), 50.6 ($OCH_2CH_2OCH_2CH_2N_3$) ppm; **HRMS:** $C_{31}H_{31}N_3O_9$ $[M+Na]^+$: 612.5910, found 612.1951 m/z.

2-(2-azidoethoxy)ethyl 2,3-*O*-benzoyl-β-D-glucopyranoside (6)

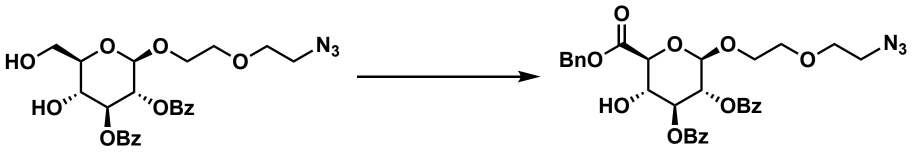


Procedure was adapted from previous literature with minor changes.[5] To a 0°C solution of **5** (2.08 g, 3.5 mmol, 1.0 eq.) dissolved in CH_2Cl_2 (4.4 mL) under N_2 was added 70% TFA solution (aq; 0.74 mL, 0.77 g, 6.73 mmol, 1.9 eq) dropwise. Reaction was warmed to ambient temperature and stirred for 5 hr. The reaction was then diluted with CH_2Cl_2 and quenched with sat. $NaHCO_3$, washed with brine, and dried over Na_2SO_4. Crude was purified via flash column chromatography (7: 10 EtOAc: cyclohexane) to afford an amber oil (1.21 g, 68%). Spectral data matches previously reported.[5]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 4H, Ph), 7.53 – 7.49 (m, 2H, Ph), 7.39 – 7.35 (m, 4H, Ph), 5.46 – 5.40 (m, 2H, H-2, H-3), 4.84 (d, *J* = 7.6 Hz, 1H, H-1), 4.01 – 3.96 (m, 3H, H-4, H-5, H-6), 3.92 (dd, *J* = 12, 4.6 Hz, 1H, H-6'), 3.79 – 3.75 (m, 1H, $OCH_2CH_2OCH_2CH_2N_3$), 3.62 – 3.55 (m, 3H, $OCH_2CH_2OCH_2CH_2N_3$), 3.50 – 3.42 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$), 3.15 – 3.05 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 167.4 (C=O), 165.3 (C=O), 133.6 (Ph), 133.3

(Ph), 123.0 (Ph), 129.8 (Ph), 129.4 (Ph), 128.9 (Ph), 128.5 (Ph), 128.4 (Ph), 101.2 (C-1), 77.0 (C-4, 5 or 6), 75.9 ($OCH_2CH_2OCH_2CH_2N_3$), 70.4 ($OCH_2CH_2OCH_2CH_2N_3$), 70.1 ($OCH_2CH_2OCH_2CH_2N_3$), 69.9 (C-4, 5 or 6), 69.6 ($OCH_2CH_2OCH_2CH_2N_3$), 62.2 (C-6), 50.6 ($OCH_2CH_2OCH_2CH_2N_3$) ppm; **HRMS:** Calc. for $C_{24}H_{28}N_3O_9$ $[M{+}H]^+$: 502.1826, found 502.1822 m/z.

Benzyl (2,3-*O*-benzoyl-β-1-(2-(2-azidoethoxy)ethyl)-β-D-glucopyranosid)uronate (7)

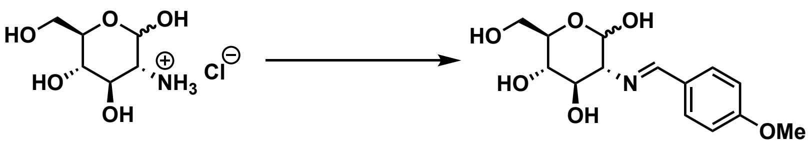


6 7

Procedure was adapted from previous literature.[6] To an ambient temperature solution of **6** (1.21 g, 2.40 mmol, 1.0 eq.) in a 2:1 solution of CH_2Cl_2 (16.0 mL): water (8.0 mL) was added TEMPO (0.079 g, 0.51 mmol, 0.21 eq.) followed by BAIB (1.94 g, 6.01 mmol, 2.5 eq.). The reaction was stirred for 1 hr at ambient temperature. Sat. $Na_2S_2O_3$ was added, and the reaction was stirred for an additional 15 min. before diluting in CH_2Cl_2 and acidifying the aqueous layer with 1M HCl. The aqueous layer was extracted 3 times with CH_2Cl_2 then the organic layers were combined and washed with sat. $NaHCO_3$, water, and brine before drying over Na_2SO_4 and concentrating. Dried crude material was redissolved in dimethyl formamide (13.3 mL) at ambient temperature, and benzyl bromide (0.714 mL, 6.01 mmol, 2.5 eq.) was added followed by K_2CO_3 (1.66g, 12.02 mmol, 5.0 eq.). The reaction was stirred for 30 min before diluting with EtOAc and washing with water (2x). Crude was purified via flash column chromatography (7: 20 EtOAc: cyclohexane) to afford an off-white waxy solid (1.075 g, 74% over two steps). Spectral data matches previously reported.[6]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J = 9.7 Hz, 4H, Ph), 7.58 – 7.45 (m, 2H, Ph), 7.39 – 7.32 (m, 9H, Ph), 5.56 – 5.53 (ap t, 1H, H-3), 5.46 – 5.43 (ap t, 1H, H-2), 5.32 – 5.26 (m, 2H, OCH_2Ph), 4.86 (d, J = 7.7 Hz, 1H, H-1), 4.24 – 4.20 (ap t, 1H, H-4), 4.13 (d, J = 9.8 Hz, 1H, H-5), 4.01 – 3.95 (m, 1H, $OCH_2CH_2OCH_2CH_2N_3$), 3.79 (ddd, J = 11.3, 7.2, 3.3 Hz, 1H, $OCH_2CH_2OCH_2CH_2N_3$), 3.62 – 3.55 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$), 3.44 – 3.43 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$), 3.27 (s, 1H, O*H*), 3.13 – 3.01 (m, 2H, $OCH_2CH_2OCH_2CH_2N_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.5 (C=O), 166.7 (C=O), 165.2 (C=O), 133.5 (Ph), 133.3 (Ph), 130.0 (Ph), 129.8 (Ph), 129.3 (Ph), 129.0 (Ph), 128.7 (Ph), 128.7 (Ph), 128.42 (Ph), 128.36 (Ph), 101.6 (C-1), 75.0 (C-3), 74.8 (C-5), 71.3 (C-2), 70.7 (C-4), 70.4 ($OCH_2CH_2OCH_2CH_2N_3$), 70.1 ($OCH_2CH_2OCH_2CH_2N_3$), 69.8 ($OCH_2CH_2OCH_2CH_2N_3$), 67.7 (OCH_2Ph), 50.6 ($OCH_2CH_2OCH_2CH_2N_3$) ppm; **HRMS:** Calc. for $C_{31}H_{31}N_3O_{10}$ $[M{+}Na]^+$: 628.2009, found 628.1920 m/z.

2-deoxy-2-*p*-methoxybenzylideneamino-D-glucopyranose (8)

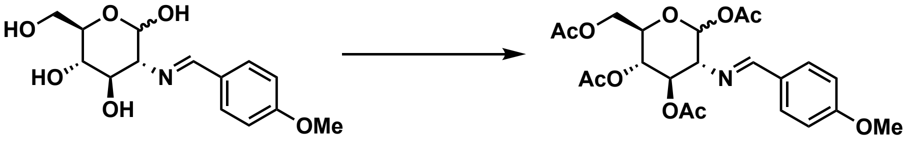


8

Procedure was adapted from literature with minor changes.[1] D-glucosamine hydrochloride (10 g, 46.4 mmol, 1.0 eq.) was dissolved in 1M NaOH (48.0 mL) and stirred for 10 minutes at ambient temperature before addition of *p*-anisaldehyde (5.64 mL, 46.4 mmol, 1.0 eq.). Reaction was stirred for an additional 10 minutes before cooling to 0˚C and stirring for 1 hour at 0˚C. Solution was filtered and precipitate was washed with water (3x), and a 1:1 MeOH: diethyl ether mixture (3x). The resulting solid was concentrated under vacuum to give a white solid (10.49 g, 76% yield). Spectral data matches previously reported.[1]

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.12 (s, 1H, *H*C=N), 7.69 (d, *J* = 8.7 Hz, 2H, C$_{Ar}$*H*), 6.99 (d, *J* = 8.7 Hz, 2H, C$_{Ar}$*H*), 6.53 (d, *J* = 5.2 Hz, 1H, 1-O*H*), 4.93 (d, *J* = 5.3, 1H, 4-O*H*), 4.82 (d, *J* = 5.6 Hz, 1H, 3-O*H*), 4.70 (dd, *J* = 8.1, 4.7 Hz, 1H, H-1), 4.56 – 4.54 (ap. t, 1H, 6-O*H*), 3.79 (s, 3H, OC*H*$_3$), 3.73 (ddd, *J* = 11.7, 5.5, 2.1 Hz, 1H, H-6), 3.49 (ddd, *J* = 11.7, 6.0, 5.9 Hz, 1H, H-6), 3.45 – 3.41 (m, 1H, H-3), 3.24 (ddd, *J* = 9.3, 6.0, 2.1 Hz, 1H, 5-H), 3.15 (ddd, *J* = 9.3, 9.2, 5.1 Hz, 1H, H-4), 2.81 – 2.78 (ap. t, 1H, 2-H) ppm; **^{13}C NMR** (151 MHz, CDCl$_3$) δ 161.3 (H*C*=N), 161.1 (C$_q$, *C*$_{Ar}$OCH$_3$), 129.7 (*C*$_{Ar}$H), 129.1 (C$_q$, *C*$_{Ar}$), 113.9 (*C*$_{Ar}$H), 95.7 (C-1), 78.2 (C-2), 76.9 (C-5), 74.6 (C-3), 70.4 (C-4), 61.3 (C-6), 55.3 (O*C*H$_3$) ppm; **HRMS:** Calc. for C$_{14}$H$_{19}$NO$_6$ [*M*+H]$^+$: 298.1291, found 298.1286 m/z.

Acetyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-p-methoxybenzylideneamino-D-glucopyranose (9)

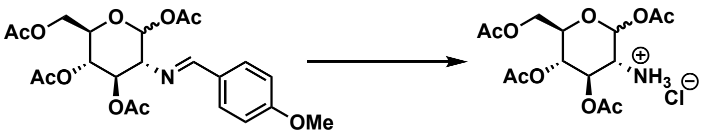


8 9

Procedure was adapted from literature with minor changes.[1] To a 0°C solution of **8** (11.04 g, mmol, 1.0 eq.) dissolved in pyridine (88.0 mL) under nitrogen, was added acetic anhydride (52.7 mL, 557.0 mmol, 15.0 eq.) followed by DMAP (0.181 g, 1.49 mmol, 0.04 eq.). The reaction was stirred at 0°C until the solution became clear (approximately 10 min), at which point it was warmed to ambient temperature and allowed to stir at ambient temperature overnight. The solution was poured into 1L of ice water and sat for 1 hour. The white precipitate was filtered and washed with water (2x) and diethyl ether (2x). The precipitate was collected and dried under vacuum to produce a white solid (9.86 g, 57% yield). Spectral data matches previously reported.[1]

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.15 (s, 1H, *H*C=N), 7.65 (d, *J* = 8.8 Hz, 2H, C$_{Ar}$*H*), 6.91 (d, *J* = 8.8 Hz, 2H, C$_{Ar}$*H*), 5.94 (d, *J* = 8.3 Hz, 1H, H-1), 5.44 –5.40 (ap. t, 1H, H-3), 5.15 – 5.12 (ap. t, 1H, H-4), 4.37 (dd, *J* = 12.4, 4.5 Hz, 1H, H-6), 4.12 (dd, *J* = 12.4, 2.1, 1H, H-6), 3.96 (ddd, *J* = 10.0, 4.5, 2.1 Hz, 1H, H-5), 3.83 (s, 1H, OC*H*$_3$), 3.44 (dd, J = 9.8, 8.3 Hz, 1H, H-2), 2.09 (s, 3H, C*H*$_3$COO), 2.03 (s, 3H, C*H*$_3$COO), 2.01 (s, 3H, C*H*$_3$COO), 1.87 (s, 3H, C*H*$_3$COO) ppm; **^{13}C NMR** (151 MHz, CDCl$_3$) δ 170.8 (CH$_3$*C*OO), 170.0 (CH$_3$*C*OO), 169.7 (CH$_3$*C*OO), 168.9 (CH$_3$*C*OO), 164.4 (H*C*=N), 162.5 (*C*$_{Ar}$OCH$_3$), 130.4 (*C*$_{Ar}$H), 128.4 (*C*$_{Ar}$), 114.2 (*C*$_{Ar}$H), 93.3 (C-1), 73.4 (C-3), 73.1 (C-2), 72.9 (C-5), 68.2 (C-4), 62.0 (C-6), 55.5 (O*C*H$_3$), 20.9 (*C*H$_3$COO), 20.9 (*C*H$_3$COO), 20.8 (*C*H$_3$COO), 20.6 (*C*H$_3$COO) ppm; **HRMS:** Calc. for C$_{22}$H$_{27}$NO$_{10}$ [*M*+H]$^+$: 466.1713, found 466.1747 m/z.

Acetyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-D-glucopyranoside hydrochloride (10)

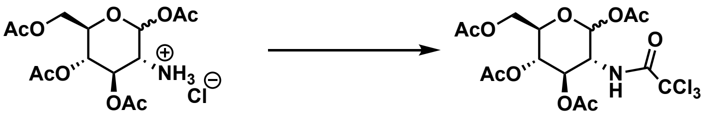


9 10

Procedure was adapted from literature with minor changes.[1] To a refluxing mixture (60°C) of **9** (9.86 g, 21.19 mmol, 1.0 eq) in acetone (51.68 mL) was added, 5M HCl solution (5.16 mL). Upon HCl addition, a white precipitate formed. The suspension was cooled to ambient temperature and the solid was filtered and washed with acetone (2x), followed by diethyl ether (2x). The precipitate was dried under vacuum to give a white solid (2.12 g, 75% yield). Spectral data matches previously reported.[1]

^{1}H NMR (600 MHz, DMSO) δ 8.89 (s, 3H), 5.93 (d, *J* = 8.7 Hz, 1H, H-1), 5.37 (ap. t, 1H, H-3), 4.92 (ap. t, 1H, H-4), 4.18 (dd, *J* = 12.5, 4.3 Hz, 1H, H-6), 4.02 (ddd, *J* = 9.7, 4.3, 2.3 Hz, 1H, H-5), 3.98 (dd, *J* = 12.5, 2.3 Hz, 1H, H-6), 3.53 (ap. t, 1H, H-2), 2.16 (s, 3H, C*H*$_3$COO), 2.02 (s, 3H, C*H*$_3$COO), 1.99 (s, 3H, C*H*$_3$COO), 1.96 (s, 3H, C*H*$_3$COO) ppm; **^{13}C NMR** (151 MHz, DMSO) δ 170.0 (CH$_3$*C*OO), 169.8 (CH$_3$*C*OO), 169.4 (CH$_3$*C*OO), 168.7 (CH$_3$*C*OO), 90.1 (C-1), 71.6 (C-5), 70.4 (C-3), 67.8 (C-4), 61.3 (C-6), 52.2 (C-2), 21.0 (*C*H$_3$COO), 20.9 (*C*H$_3$COO), 20.5 (*C*H$_3$COO), 20.4 (*C*H$_3$COO) ppm; **HRMS:** Calc. for $C_{14}H_{21}NO_9$ [*M*+H]$^+$: 348.1216, found 348.1290 m/z.

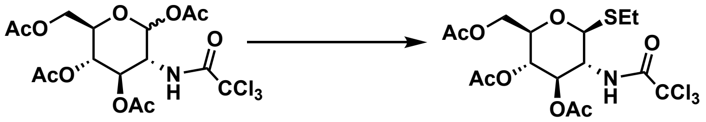
Acetyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-D-glucopyranoside



10

Procedure was adapted from literature with minor changes.[1] To a 0°C solution of **10** (6.68 g, 17.41 mmol, 1.0 eq) was suspended in CH_2Cl_2 (145 mL) under nitrogen was added, triethylamine (4.85 mL, 34.82 mmol, 2.0 eq.) followed by trichloroacetyl chloride (2.52 mL, 22.63 mmol, 1.3 eq.). The reaction as stirred for 1 hr at ambient temperature. The solution was then washed with water (2x), sat. $NaHCO_3$ (2x), and water again (2x). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to produce a white solid. The crude material was taken to the next step without further purification.

Ethyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-2-trichloroacetamido-β-D-glucopyranoside (11)

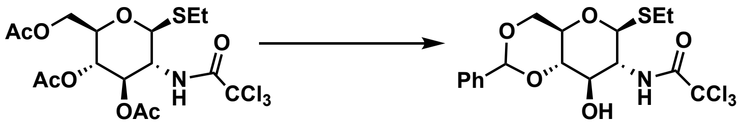


11

Procedure was adapted from literature with minor changes.[2] Starting material (8.58 g, 17.41 mmol, 1.0 eq) was dissolved in CH_2Cl_2 (109.0 mL) and cooled to 0°C under nitrogen. To this was added ethanethiol (1.93, 26.12 mmol, 1.5 eq.) followed by boron trifluoride diethyl etherate (2.15 mL, 17.41 mmol, 1.0 eq.). The reaction was warmed to ambient temperature and stirred for 3 hrs. The solution was diluted in CH_2Cl_2 and washed with sat. $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated. The crude residue was triturated in diethyl ether and the precipitate was filtered to produce a white solid (7.15 g, 83% yield over two steps). Spectral data matches previously reported.[2]

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.79 (d, *J* = 9.2 Hz, 1H, N-*H*), 5.30 (dd, *J* = 10.4, 9.4 Hz, 1H, H-3), 5.13 (ap. t, 1H, H-4), 4.67 (d, *J* = 10.2 Hz, 1H, H-1), 4.30 – 4.23 (m, 1H, H-6), 4.15 (dd, *J* = 12.4, 2.3 Hz, 1H, H-6), 4.09 (ddd, *J* = 10.5, 10.4, 9.3 Hz, 1H, H-2), 3.74 (ddd, *J* = 9.9, 5.0, 2.3 Hz, 1H, H-5), 2.81 – 2.66 (m, 2H, S-C*H*$_2$), 2.09 (s, 3H, C*H*$_3$COO), 2.04 (s, 3H, C*H*$_3$COO), 2.03 (s, 3H, C*H*$_3$COO), 1.28 (t, *J* = 7.4 Hz, 3H, S-CH$_2$C*H*$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.1 (CH$_3$*C*OO), 170.8 (CH$_3$*C*OO), 169.4 (CH$_3$*C*OO), 162.0 (CCl3*C*ONH), 92.3 (*C*Cl$_3$), 84.1 (C-1), 76.3 (C-5), 73.2 (C-3), 68.4 (C-4), 62.4 (C-6), 55.0 (C-2), 24.5 (S-*C*H$_2$), 20.9 (*C*H$_3$COO), 20.7 (2x *C*H$_3$COO), 15.0 (S-CH$_2$*C*H$_3$) ppm; **HRMS:** Calc. for $C_{16}H_{22}Cl_3NO_8S$ [*M*+Na]$^+$: 516.0032, found 516.0272 m/z.

Ethyl 4,6-*O*-benzylidene-2-deoxy-1-thio-2-trichloroacetamido-β-D-glucopyranoside (12)



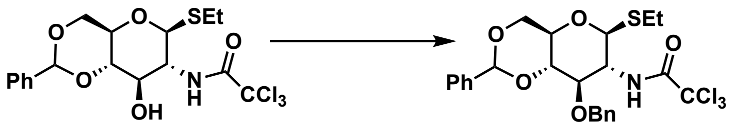
11 **12**

Procedure was adapted from literature with minor changes.[7] To an ambient temperature mixture of **11** (1 g, 2.02 mmol, 1.0 eq.) in MeOH (9.60 mL) under nitrogen was added sodium methoxide (0.011 g, 0.202 mmol, 0.1 eq.). The reaction was stirred overnight at ambient temperature. The reaction was then neutralized with Amberlite™ IRC 120H, hydrogen form cation-exchange resin and filtered. The crude triol was concentrated and used without further purification.

Procedure was adapted from literature with minor changes.[7] To an ambient temperature mixture of triol dissolved in MeCN (9.20 mL) under nitrogen was added benzaldehyde dimethyl acetal (0.45 mL, 3.03 mmol, 1.5 eq.) followed by (±)-camphor-10-sulfonic acid (CSA) (0.05 g, 0.202 mmol, 0.1 eq.). The reaction was warmed to 70°C and stirred for 2 hr before being neutralized with triethylamine and concentrated. The resulting solid was triturated with diethyl ether, filtered, and concentrated in vacuo to produce a tan solid (0.704g, 76% yield over 2 steps). Spectral data matches previously reported.[7]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 – 7.47 (m, 2H, Ph), 7.39 – 7.38 (m, 3H, Ph), 6.88 (d, *J* = 7.9 Hz, 1H, N-*H*), 5.56 (s, 1H, PhC*H*), 4.96 (d, *J* = 10.4 Hz, 1H, H-1), 4.37 (dd, *J* = 10.6, 4.6 Hz 1H, H-6), 4.25 – 4.22 (ap. t, 1H, H-3), 3.78 (dd, *J* = 10.6, 9.4 Hz, 1H, H-6), 3.71 (ddd, *J* = 10.1, 10.1, 7.9 Hz, 1H, H-2), 3.60 – 3.54 (m, 2H, H-4, H-5), 2.84 (br s, 1H O-*H*), 2.80 – 2.70 (m, 2H, S-C*H*$_2$), 1.29 (t, *J* = 7.5 Hz, 3H, S-CH$_2$C*H*$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.5 (CCl3*C*ONH), 137.2 (C_q, Ph), 129.8 (Ph), 128.8 (Ph), 126.6 (Ph), 102.3 (*C*HPh), 92.7 (*C*Cl$_3$), 83.8 (C-1), 81.8 (C-4), 71.8 (C-3), 70.8 (C-5), 68.9 (C-6), 25.0 (S-*C*H$_2$), 15.4 (S-CH$_2$*C*H$_3$) ppm; **HRMS:** Calc. for $C_{17}H_{20}Cl_3NO_5S$ $[M+H]^+$: 456.0206, found 456.0205 m/z.

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-2-trichloroacetamido-β-D-glucopyranoside (13)



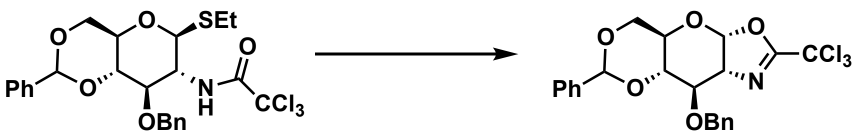
12 **13**

Procedure was adapted from literature with minor changes.[7] To a -20°C solution of **12** (2.0 g, 4.38 mmol, 1.0 eq.) in DMF (24.3 mL) under nitrogen was added NaH (0.315 g, 13.14 mmol, 3.0 eq.). The reaction was stirred for 5 mins before benzyl bromide (0.572 mL, 4.82 mmol, 1.1 eq.) was added dropwise. The reaction was stirred for 1 hr while the cold bath (MeOH/ H_2O/ dry ice) was kept between -14°C and -5°C. The reaction was quenched with the dropwise addition of MeOH and diluted with water. The organic phase was extracted with ethyl acetate. The organic phase was then washed with water (2x), brine (1x), dried over Na_2SO_4, filtered, and concentrated under vacuum to produce a white solid that did not require purification (2.27 g, 95% yield). Spectral data matches previously reported.[7]

^{1}H NMR (600 MHz, CDCl3) δ 7.50 – 7.49 (m, 2H, Ph), 7.42 – 7.38 (m, 3H, Ph), 7.30 – 7.27 (m, 5H, Ph), 6.84 (d, *J* = 8.1 Hz, 1H, N-*H*), 5.60 (s, 1H, PhC*H*), 5.02 (d, *J* = 10.5 Hz, 1H, H-1), 4.91 (d, *J* = 11.3 Hz, 1H, PhC*H2*), 4.71 (d, *J* = 11.3 Hz, 1H, PhC*H2*), 4.38 (dd, *J* = 10.4, 4.9 Hz, 1H, H-6), 4.16 (ap. t, 1H, H-3), 3.82 – 3.75 (m, 2H, H-4, H-6), 3.69 (ddd, *J* = 10.2, 10.1, 8.1 Hz, 1H, H-2), 3.58 (ddd, *J* = 9.8, 9.7, 4.9, 1H, H-5), 2.78 – 2.68 (m, 2H, S-C*H2*), 1.27 (t, *J* = 7.4 Hz, 3H, S-CH2C*H3*) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.8 (CCl3*C*ONH), 137.8 (C_q, Ph), 137.3 (C_q, Ph), 129.2 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.1

(Ph), 126.1 (Ph), 101.4 (Ph*C*H), 92.5 (*C*Cl$_3$), 83.5 (C-1), 82.7 (C-4), 77.4 (C-3), 75.0 (*C*H$_2$Ph), 70.6 (C-5), 68.7 (C-6), 57.6 (C-2), 24.8 (S-*C*H$_2$), 15.2 (S-CH$_2$*C*H$_3$) ppm; **HRMS:** Calc. for $C_{24}H_{26}Cl_3NO_5S$ [*M*+H]$^+$: 546.0676, found 546.0672 m/z.

(4,6-*O*-benzylidene-3-*O*-benzyl-1,2-dideoxy-α-D-glucopyranoso)-4,5-dihydro-2-trichloromethyl-[2,1-d]2-oxazole (14)

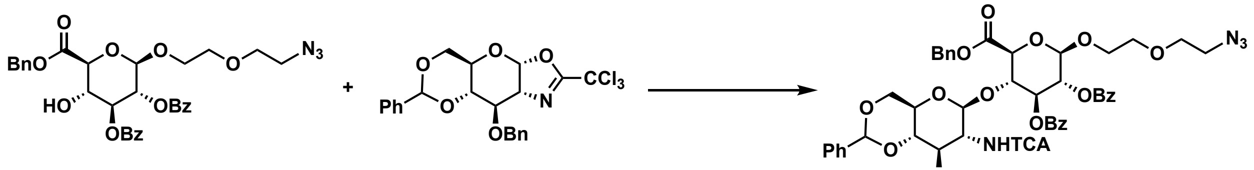


13 14

Procedure was adapted from literature with minor changes.[3] To a flame-dried flask of **13** (0.982 g, 1.80 mmol, 1.0 eq.) dissolved in anhydrous CH_2Cl_2 (8.18 mL) over freshly activated 3Å molecular sieves under N_2 protection cooled to -30˚C (MeOH/ dry ice bath) was added N-iodosuccinimide (0.485 g, 2.15 mmol, 1.2 eq.), followed by trimethylsilyl trifluoromethanesulfonate (0.032 mL, 0.180 mmol, 0.1 eq.). The reaction was stirred at -30˚C for 30 minutes before quenching with NEt_3 (0.5 mL) and filtering through a pad of celite. Filtrate was washed with sat. $NaHCO_3$, sat. $Na_2S_2O_3$, brine, and dried over Na_2SO_4. Crude was purified via flash chromatography (2: 25 EtOAc: cyclohexane) to afford an off-white solid (0.76 g, 87%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 2H, Ph), 7.43 – 7.36 (m, 2H, Ph), 7.37 – 7.31 (m, 2H, Ph), 7.30 (d, *J* = 6.9 Hz, 1H, Ph), 6.30 (d, *J* = 7.7 Hz, 1H, H-1), 5.62 (s, 1H, PhC*H*), 4.87 (d, *J* = 11.7 Hz, 1H, PhC*H$_2$*), 4.83 (d, *J* = 11.7 Hz, 1H, PhC*H$_2$*), 4.45 (dd, *J* = 7.7, 4.0 Hz, 1H, H-2), 4.43 (dd, *J* = 10.4, 5.1 Hz, 1H, H-6), 3.90 (dd, *J* = 8.1, 4.0 Hz, 1H, H-3), 3.84 (dd, *J* = 9.7, 8.1 Hz, 1H, H-4), 3.77 – 3.73 (ap. t, 1H, H-6), 3.67 (ddd, *J* = 9.8, 9.7, 5.1 Hz, 1H, H-5) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.3 (CCl3*C*ON), 137.7 (C$_q$, Ph), 137.0 (C$_q$, Ph), 129.3 (Ph), 128.5 (Ph), 128.4 (Ph), 128.2 (Ph), 128.0 (Ph), 126.2 (Ph), 106.2 (C-1), 101.5 (*C*HPh), 79.5 (C-3), 79.4 (C-4), 73.0 (*C*H$_2$Ph) 69.3 (C-2), 68.6 (C-6), 63.6 (C-5) ppm; **HRMS:** Calc. for $C_{22}H_{20}Cl_3NO_5$ [*M*+H]$^+$: 484.0485, found 484.0478 m/z.

Benzyl *O*-(3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-(1→4)-2,3-*O*-benzoyl-β-1-(2-(2-azidoethoxy)ethyl)-β-D-glucopyranosid)uronate (15)

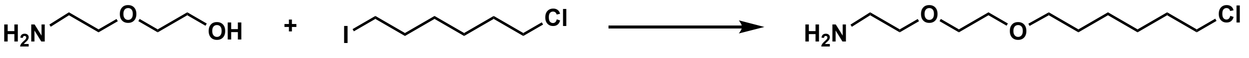


7 14 15

Procedure was adapted from literature with minor changes.[3] To a flame-dried flask of oxazoline **14** (0.224 g, 0.462 mmol, 1.0 eq.) and azido-acceptor **7** (0.308 g, 0.508 mmol, 1.1 eq.) in anhydrous CH_2Cl_2 (4.20 mL) over freshly activated 4Å molecular sieves under N_2 protection cooled to -30˚C (MeOH/ dry ice bath) was added trimethylsilyl trifluoromethanesulfonate (0.017 mL, 0.0924 mmol, 0.2 eq.) dropwise. Reaction was stirred for 2 hrs while bath was kept between -15˚C to -30˚C. Reaction was quenched with NEt_3 (0.5 mL) and diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$, sat. $Na_2S_2O_3$, brine, and dried over Na_2SO_4. Crude was purified via flash chromatography (8: 25 EtOAc: cyclohexane) to afford an off-white solid (0.162 g, 59%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 4H, Ph), 7.57 – 7.47 (m, 2H, Ph), 7.45 – 7.32 (m, 14H, Ph), 7.29 – 7.22 (m, 6H, Ph), 6.66 (d, *J* = 8.3 Hz, 1H, N*H*), 5.63 (ap t, 1H, H-3), 5.41 – 5.36 (overlap, 2H, H-2, PhC*H*$_2$), 5.19 (s, 1H, PhC*H*), 5.15 (d, *J* = 12.1 Hz, 1H, PhC*H*$_2$), 4.83 (d, *J* = 7.3 Hz, 1H, H-1), 4.81 – 4.76 (overlap, 2H, H-1', PhC*H*$_2$), 4.61 (d, *J* = 11.6 Hz, 1H, PhC*H*$_2$), 4.30 (ap. t, 1H, H-4), 4.15 (d, *J* = 9.4, 1H, H-5), 3.94 – 3.88 (m, 1H), 3.79 – 3.71 (m, 2H), 3.65 (dd, *J* = 10.7, 4.9 Hz, 1H, H-6'), 3.61 – 3.52 (m, 3H), 3.43 (t, *J* = 5.1 Hz, 2H), 3.35 (ap t, 1H, H-4'), 3.12 – 3.04 (m, 3H), 2.52 (ap t, 1H, H-6') ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.0 (C=O), 166.1 (C=O), 161.5 (C=O), 137.9 (C_q, Ph), 137.1 (C_q, Ph), 134.9 (C_q, Ph), 133.3, 133.2, 130.0 (Ph), 129.83, 129.79, 129.3, 128.7 (C_q, Ph), 129.1, 128.9, 128.8, 128.7, 128.41, 128.40, 128.37, 128.3 (Ph), 128.1, 127.8, 126.0, 101.5 (C-1), 101.0 (*C*HPh), 99.7 (C-1'), 92.7 (*C*Cl_3), 82.0 (C-4'), 76.5 (C-3'), 76.2 (C-4), 74.3 (C-5), 74.2 (Ph*C*H$_2$), 72.5 (C-3), 71.6 (C-2), 70.3, 70.1, 69.7, 67.9 (Ph*C*H$_2$), 67.7 (C-6'), 65.8, 57.7 (C-2'), 50.5 ppm; **HRMS:** Calc. for $C_{53}H_{51}Cl_3N_4O_{15}$ $[M+Na]^+$: 1111.2314, found 1111.2421 m/z.

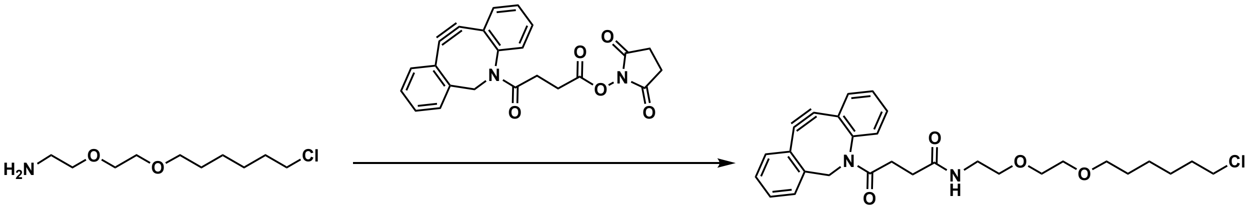
2-(2-((6-chlorohexyl)oxy)ethoxy)ethan-1-amine (16)



16

Procedure was adapted from literature with minor changes.[8] To a flame-dried flask of sodium hydride (0.573 g, 23.88 mmol, 1.2 eq.) in DMF (16.2 mL) under N_2 protection at 0˚C was added 2-(2-aminoethoxy)ethanol (2 mL, 19.9 mmol, 1.0 eq.) and stirred for 45 mins at 0˚C. A solution of 1-chloro-6-iodohexane (3.32 mL, 21.89 mmol, 1.1 eq.) in DMF (16.2 mL) was added dropwise to the reaction and stirred on ice for 4 hrs. The reaction was quenched with MeOH and filtered through celite. The filtrate was diluted with CH_2Cl_2 and washed with water (3x). The organic layer was extracted with CH_2Cl_2. Combined organic layers were washed with sat. $NaHCO_3$, brine and dried over Na_2SO_4. Crude was concentrated and carried to the next reaction without further purification.

2-(2-((6-chlorohexyl)oxy)ethoxy)ethan-1-amido-dibenzocyclooctyne (17)



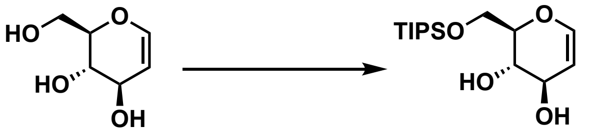
16

17

Procedure was adapted from literature with minor changes.[9] To a flame-dried flask of DBCO-NHS (0.250 g, 0.621 mmol, 1.0 eq.) and **16** (0.222 g, 0.994 mmol, 1.6 eq.) in DMF (7.76 mL) under N_2 protection was added diisopropylethylamine (0.335 mL, 1.93 mmol, 3.1 eq.). The reaction was stirred for 20 min. Reaction was diluted with EtOAc and washed with water (2x), brine, dried over Na_2SO_4, and concentrated under vacuum. Crude was purified via flash column chromatography (19: 20 EtOAc: cyclohexane) to afford an off-white solid (0.233 g, 74%). Spectral data matches previously reported.[9]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.41 – 7.28 (m, 4H), 7.30 – 7.21 (m, 2H), 6.04 (s, 1H), 5.14 (d, *J* = 13.8 Hz, 1H), 3.65 (d, *J* = 13.8 Hz, 1H), 3.59 – 3.48 (m, 6H), 3.48 – 3.40 (m, 4H), 3.33 (q, *J* = 5.4 Hz, 2H), 2.81 (ddd, *J* = 16.8, 8.5, 6.3 Hz, 1H), 2.45 (ddd, *J* = 15.0, 8.5, 6.3 Hz, 1H), 2.15 (dt, *J* = 15.3, 6.2 Hz, 1H), 1.94 (dd, *J* = 16.9, 6.2 Hz, 1H), 1.75 (p, *J* = 6.9 Hz, 2H), 1.57 (p, *J* = 6.9 Hz, 2H), 1.42 (p, *J* = 7.0 Hz, 2H), 1.38 – 1.29 (m, 2H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.4, 172.2, 151.5, 148.2, 132.3, 129.5, 128.8, 128.3, 128.2, 127.8, 127.2, 125.6, 123.3, 122.6, 114.8, 108.0, 71.4, 70.4, 70.1, 69.8, 55.6, 45.2, 39.3, 32.6, 31.3, 30.3, 29.5, 26.8, 25.5 ppm; **HRMS:** Calc. for $C_{29}H_{35}ClN_2O_4$ [*M*+H]$^+$: 511.2364, found 511.2383 m/z.

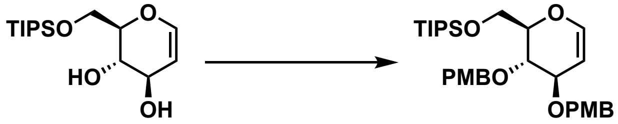
6-*O*-triisopropylsilyl-D-glucal



Procedure was adapted from literature with minor changes.[10] To an ambient temperature mixture of D-glucal (5.0 g, 34.2 mmol, 1.0 eq.) in anhydrous DMF (50.5 mL) under N_2 protection was added imidazole (4.66 g, 68.40 mmol, 2.0 eq.) and stirred for 5 min. The reaction was then cooled to 0˚C and triisopropylsilyl chloride (8.05 mL, 37.6 mmol, 1.1 eq.) was added dropwise. Reaction was warmed to ambient temperature and stirred overnight. The solution was then diluted in 5 reaction volumes of water and extracted with diethyl ether (5x). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under vacuum. Crude was purified via flash column chromatography (1: 4 EtOAc: cyclohexane) to produce a colorless oil (9.0 g, 87%). Spectral data matches previously reported.[10]

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.28 (dd, *J* = 6.1, 1.8 Hz, 1H, H-1), 4.70 (d, *J* = 6.1 Hz, 1H, H-2), 4.36 – 4.20 (m, 1H, H-3), 4.09 – 4.02 (m, 1H, H-6), 4.00 – 3.96 (m, 1H, H-6), 3.81 – 3.79 (m, 2H, H-4, H-5), 3.72 (d, *J* = 2.0 Hz, 1H, O-*H*), 3.08 (d, *J* = 5.4 Hz, 1H, O-*H*), 1.15 – 1.02 (m, 21H, (m, 21H, Si(*i*-Pr)$_3$)) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.1 (C-1), 102.6 (C-2), 76.5, 72.8, 69.5 (C-3), 64.6 (C-6), 18.00 (Si(CH(*C*H$_3$)$_2$), 17.98 (Si(CH(*C*H3)$_2$), 11.9 (Si(*C*H(CH$_3$)$_2$) ppm; **HRMS:** Calc. for $C_{15}H_{30}O_4Si$ [*M*+Na]$^+$: 325.1811, found 325.1738 m/z.

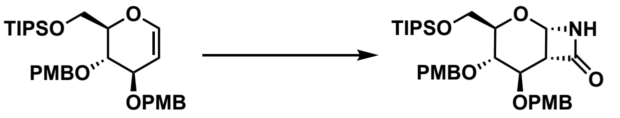
3,4-di-*O*-*para*-methoxybenzyl-6-*O*-triisopropylsilyl-D-glucal



Procedure was adapted from previous literature with minor changes.[11] To a 0˚C anhydrous solution of 6-*O*-triisopropylsilyl glucal (7.89 g, 26.1 mmol, 1.0 eq) in anhydrous DMF (65.25 mL) under N_2 protection, was added NaH (1.5 g, 62.6 mmol, 2.4 eq) in 0.5 g aliquots with 5 minutes of stirring between additions. The reaction was warmed to ambient temperature and stirred for 15 min. The reaction mixture was again cooled to 0˚C and *p*-methoxybenzyl chloride (7.8 mL, 57.4 mmol, 2.2 eq) was added dropwise. The solution was stirred overnight at ambient temperature. The solution was cooled to 0˚C and quenched with dropwise addition of MeOH. The quenched reaction was diluted with water (5x the DMF volume) and the organic phase was extracted with diethyl ether. The aqueous phase was washed with diethyl ether (5x). Combined organic layers were washed with brine and dried over Na_2SO_4. Crude material was filtered, concentrated, and purified by flash column chromatography (1: 24 EtOAc: cyclohexane) to produce a colorless oil (3.36 g, 53%). Spectral data matches previously reported.[11]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (m, 4H, $C_{Ar}H$), 6.81 – 6.77 (m, 4H, $C_{Ar}H$), 6.29 (dd, *J* = 6.2, 1.4 Hz, 1H, H-1), 4.72 (dd, *J* = 6.1, 2.7 Hz, 1H, H-2), 4.70 (d, *J* = 10.9 Hz, 1H, ArC*H*$_2$), 4.60 (d, *J* = 10.9 Hz, 1H, ArC*H*$_2$), 4.49 (d, *J* = 11.4 Hz, 1H, ArC*H*$_2$), 4.43 (d, *J* = 11.4 Hz, 1H, ArC*H*$_2$), 4.09 – 4.05 (m, 1H, H-3), 3.94 – 3.88 (m, 2H, H-6), 3.84 – 3.78 (m, 2H, H-4, H-5), 3.72 (s, 6H, ArOC*H*$_3$), 1.04 – 0.93 (m, 21H, Si(*i*-Pr)$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.4 (C_{Ar}OCH$_3$), 159.3 (C_{Ar}OCH$_3$), 144.8 (C-1), 130.8 (C_{Ar}), 130.7 (C_{Ar}), 129.7 (C_{Ar}H), 129.5 (C_{Ar}H), 113.93 (C_{Ar}H), 113.91 (C_{Ar}H), 99.9 (C-2), 78.3 (C-5), 75.6 (C-3), 73.8 (C-4), 73.6 (C$_{Ar}$*C*H$_2$), 70.5 (C$_{Ar}$*C*H$_2$), 62.1 (C-6), 55.4 (O*C*H$_3$), 18.12 (Si(CH(*C*H$_3$)$_2$), 18.08 (Si(CH(*C*H$_3$)$_2$), 12.1 (Si(*C*H(CH$_3$)$_2$) ppm.

3,4-*O*-*p*-methoxybenzyl-6-*O*-triisopropysilyl-β-lactam (18)

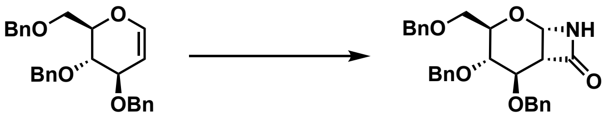


18

The procedure was adapted from previous literature with minor changes.[12] CSI (0.470 mL, 5.42 mmol, 1.4 eq.) which was previously stored over oven-dried Na$_2$CO$_3$ for at least 1 week at 4˚C, was added to an oven dried flask of Na$_2$CO$_3$ (0.697 g, 6.58 mmol, 1.7 eq.) in anhydrous toluene (6.45 mL) at ambient temperature under N$_2$. The solution was then cooled to -78˚C (acetone/ dry ice bath) and a solution of 3,4-*O*-*p*-methoxybenzyl-6-*O*-triisopropylsilyl glucal (**19**) (2.10 g, 3.87 mmol, 1.0 eq.) dissolved in toluene (6.45 mL) was added dropwise via syringe pump. The solution was then warmed to -61˚C (chloroform/ dry ice bath) and stirred for 3 hr. The reaction was then cooled again to -78˚C and diluted with additional toluene (19.35 mL) dropwise via syringe pump. To this, Red-Al (≥60%wt solution in toluene) (2.09 mL, 6.97 mmol, 1.8 eq.) was added dropwise and stirred for 30 min. The reaction was then warmed to -61˚C for 10 min, then -10˚C (sat. NaCl/ ice) for 10 min, after which it was quenched with the dropwise addition of water (1.0 mL) and allowed to stir at 0˚C for an additional 30 min until solution turned white. The solution was then filtered to remove solids and filter cake was washed with diethyl ether. The filtrate was washed with sat. NaHCO$_3$, brine, dried over Na$_2$SO$_4$, and concentrated under vacuum. Crude was purified via flash column chromatography (1: 4 EtOAc: cyclohexane). Fractions were concentrated to give a colorless oil (0.878 g, 39%). Spectral data matches previously reported.[12]

^{1}**H NMR** (600 MHz, CDCl$_3$) δ 7.31 (d, *J* = 8.6 Hz, 1H, C$_{Ar}$*H*), 7.19 (d, *J* = 8.6 Hz, 1H, C$_{Ar}$*H*), 6.88 (d, *J* = 8.7 Hz, 2H, C$_{Ar}$*H*) 6.84 (d, *J* = 8.7 Hz, 2H, C$_{Ar}$*H*), 6.11 (s, 1H, N-*H*), 5.50 (d, *J* = 4.5 Hz, 1H, H-1), 4.70 (d, *J* = 10.7 Hz, 1H, ArC*H*$_2$), 4.64 (d, *J* = 11.4 Hz, 1H, ArC*H*$_2$), 4.55 (d, *J* = 10.7 Hz, 1H, ArC*H*$_2$), 4.51 (d, *J* = 11.4 Hz, 1H, ArC*H*$_2$), 4.08 (dd, *J* = 7.0, 3.0 Hz, 1H, H-3), 3.93 (dd, *J* = 10.9, 4.2 Hz, 1H, H-6), 3.86 (dd, *J* = 10.9, 2.8 Hz, 1H, H-6), 3.84 – 3.82 (m, 1H, H-5), 3.80 (s, 3H, ArOC*H*$_3$), 3.80 (s, 3H, ArOC*H*$_3$), 3.67 (dd, *J* = 8.6, 7.0 Hz, 1H, H-4), 3.39 (dd, *J* = 4.3, 3.0 Hz, 1H, H-2), 1.06 (m, 21H, Si(*i*-Pr)$_3$) ppm; ^{13}**C NMR** (151 MHz, CDCl$_3$) δ 167.4 (*C*=O), 159.5 (C_{Ar}OCH$_3$), 159.3 (C_{Ar}OCH$_3$), 130.7 (C_{Ar}), 129.9 (C_{Ar}H), 129.8 (C_{Ar}), 129.6 (C_{Ar}H), 114.0 (C_{Ar}H), 113.9 (C_{Ar}H), 76.3 (C-1, C-3), 75.2 (C-4), 73.6 (C$_{Ar}$*C*H$_2$), 71.9 (C-5), 71.2 (C$_{Ar}$*C*H$_2$), 63.2 (C-6), 55.4 (O*C*H$_3$), 55.3 (C-2), 18.14 (Si(CH(*C*H$_3$)$_2$), 18.12 (Si(CH(*C*H$_3$)$_2$), 12.1 (Si(*C*H(CH$_3$)$_2$) ppm; **HRMS:** Calc. for C$_{32}$H$_{47}$NO$_7$Si [*M*+H]$^+$: 586.3122, found 586.3206 m/z.

3,4,6-*O*-benzyl-β-lactam (19)

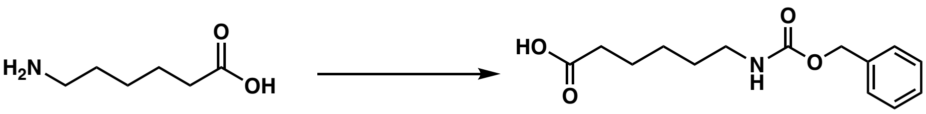


19

The procedure was adapted from previous literature with minor changes.[13] Briefly, chlorosulfonyl isocyanate (CSI) (0.813 mL, 9.36 mmol, 1.3 eq.) which was previously stored over oven-dried Na$_2$CO$_3$ for at least 1 week at 4 ˚C, was added to an oven dried flask of Na$_2$CO$_3$ in anhydrous toluene (12.0 mL) at ambient temperature under N$_2$. The solution was then cooled to -78˚C (acetone/ dry ice bath) and a solution of 3,4,6-*O*-benzyl glucal (3.0 g, 7.20 mmol, 1.0 eq.) dissolved in toluene (12.0 mL) was added dropwise via syringe pump. The solution was then warmed to -61˚C (chloroform/ dry ice bath) and stirred for 3 hours. The reaction was then cooled again to -78˚C and diluted with additional toluene (36.0 mL) dropwise via syringe pump. To this, Red-Al (≥60%wt solution in toluene) (3.27 mL, 2.2 g, 10.9 mmol, 1.5 eq.) was added dropwise and stirred for 30 min. The reaction was then warmed to -61˚C for 10 min, then -10˚C (sat. NaCl/ ice) for 10 min, after which it was quenched with the dropwise addition of water (0.5 mL) and allowed to stir at 0˚C for an additional 30 min until solution turned white. The solution was then filtered to remove solids and filter cake was washed with diethyl ether. The filtrate was washed with sat. $NaHCO_3$, brine, dried over Na_2SO_4, and concentrated under vacuum. Crude was purified via flash column chromatography (1:1 EtOAc: hexanes). Fractions were concentrated to give a white solid (1.18 g, 36%). Spectral data matches previously reported.[13]

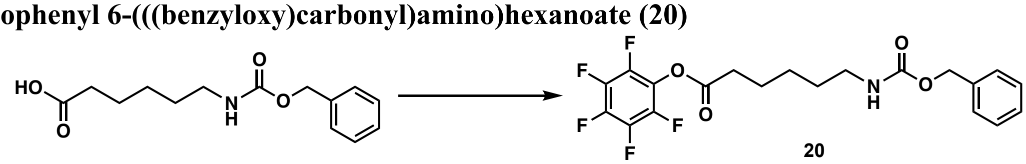
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.18 (m, 13H, PhC*H*), 7.14 – 7.10 (m, 2H), 6.16 (s, 1H, N-*H*), 5.46 (d, *J* = 4.5 Hz, 1H, H-1), 4.69 (d, *J* = 11.3 Hz, 1H, PhCH_2), 4.62 (d, *J* = 11.8 Hz, 1H, PhCH_2), 4.52 – 4.47 (m, 3H), 4.44 (d, *J* = 11.3 Hz, 1H, PhCH_2), 4.04 (dd, *J* = 6.7, 2.8 Hz, 1H, H-3), 3.98 – 3.92 (m, 1H), 3.65 – 3.58 (m, 2H), 3.60 – 3.54 (m, 1H), 3.38 – 3.33 (m, 1H, H-2) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 167.0 (C=O), 138.0, 137.9, 137.5, 128.5, 128.4, 128.4, 128.0, 127.89, 127.87, 127.75, 127.7, 76.4, 76.3, 75.7, 73.6, 73.5, 71.2, 69.8, 69.4, 54.9 ppm; **HRMS:** Calc. for $C_{28}H_{29}NO_5$ $[M+H]^+$: 460.2046, found 460.2106 m/z.

6-(((benzyloxy)carbonyl)amino)hexanoic acid



Procedure was adapted from literature with minor changes.[14] To an ambient temperature solution of 6-aminohexanoic acid (6.42 g, 48.9 mmol, 1.0 eq.) in DI water (25.0 mL) was added $NaHCO_3$ (6.73 g, 80.1 mmol, 1.64 eq.). The reaction was cooled to 0˚C and benzyl chloroformate (7.6 mL, 53.8 mmol, 1.1 eq) was added dropwise. The solution was warmed to ambient temperature and stirred overnight. The reaction was then washed with hexanes and 1M HCl. The organic phase was extracted with chloroform. Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under vacuum. Crude material was purified via flash chromatography (1:2.33 EtOAc: cyclohexane) to give a white solid (2.58 g, 20%). Spectral data matches previously reported.[14]

perfluorophenyl 6-(((benzyloxy)carbonyl)amino)hexanoate (20)



20

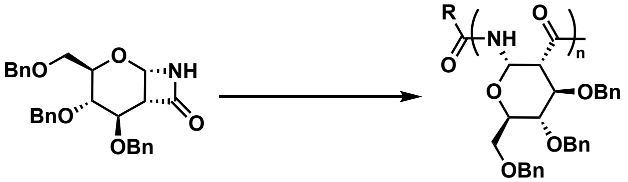
Procedure was adapted from literature with minor changes.[15] To an ambient temperature mixture of 6-(((benzyloxy)carbonyl)amino)hexanoic acid (2.58 g, 9.71 mmol, 1.0 eq.) in anhydrous CH_2Cl_2 (20.0 mL) under N_2 was added DCC (2.20 g, 10.7 mmol, 1.1 eq.) and stirred for 30 min. Once fully dissolved, pentafluorophenol (1.97 g, 10.7 mmol, 1.1 eq.) was added and reaction was stirred overnight at ambient temperature. Crude was concentrated and remaining solids were dissolved in EtOAc to precipitate out DCU byproduct. Solid byproduct was removed via filtration and filtrate was concentrated under vacuum and purified via flash column chromatography (1:9 EtOAc: cyclohexane) to afford a white solid (3.77 g, 90%). Spectral data matches previously reported.[15]

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.32 – 7.22 (m, 5H, C$_{Ar}$*H*), 5.02 (s, 2H, OC*H*$_2$Bn), 4.70 (s, 1H, N*H*), 3.15 (d, *J* = 6.7 Hz, 2H, PfpOCOC*H*$_2$), 2.59 (t, *J* = 7.3 Hz, 2H, PfpOCOCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$), 1.72 (p, *J* = 7.5 Hz, 2H, PfpOCOCH$_2$CH$_2$CH$_2$C*H*$_2$), 1.50 (q, *J* = 7.4 Hz, 2H, PfpOCOCH$_2$C*H*$_2$), 1.38 (p, *J* = 7.6, 7.1 Hz, 2H, PfpOCOCH$_2$CH$_2$C*H*$_2$) ppm; **^{13}C NMR** (151 MHz, CDCl$_3$) δ 169.33 (*C*F), 156.44 (*C*F), 136.57 (*C*F), 128.53 (*C*$_{Ar}$), 128.13 (*C*$_{Ar}$), 66.69 (O*C*H$_2$Bn), 40.75 (C-1), 33.16 (C-5), 29.58 (C-2), 25.92 (C-3), 24.34 (C-4) ppm; **^{19}F NMR** (565 MHz, CDCl$_3$) δ -152.8, -158.1, -162.4 ppm; **HRMS:** Calc. for $C_{20}H_{18}F_5NO_4$ [*M*+H]$^+$: 432.1234, found 432.1229 m/z.

Polymer Synthetic Procedures

Prior to polymerizations, all vials and reaction vessels were flame-dried, evacuated, and backfilled with N$_2$. Distilled THF (without BHT stabilizer) was degassed by purging with N$_2$ for 30 min before addition to reaction vessels.

3,4,6-tri-*O*-benzyl polyamidosaccharide (glc$_{OBn}$PAS)



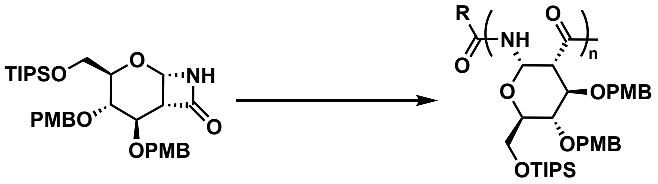
19 glc$_{OBn}$PAS

Procedure was adapted from literature with minor changes.[16] To an ambient temperature solution of lactam **19** (0.200 g, 0.435 mmol, 1.0 eq.) dissolved in anhydrous THF (0.1 M) over freshly activated 3Å molecular sieves and under N$_2$ protection was added Cbz-6-aminohexanoic acid pentafluorophenol ester initiator (1.0 mol% for N$_{theory}$ = 100) from a previously prepared 0.1 M stock solution in THF. The reaction was stirred for 5 min at ambient temperature. The reaction was then cooled to 0˚C and lithium bis(trimethylsilyl)amide (LiHMDS) was added from a 0.5 M THF stock solution (5.0 mol% for N$_{theory}$ = 100). The reaction was then warmed to ambient temperature and allowed to stir overnight. Sat. ammonium chloride (1 mL) was added to quench the reaction, and the solvent was removed under reduced pressure. Crude polymer was redissolved in CH$_2$Cl$_2$ and washed with 1 M HCl, sat. NaHCO$_3$, brine, and dried over Na$_2$SO$_4$. After filtering and concentrating under vacuum, the crude polymer was redissolved in a minimal amount of CH$_2$Cl$_2$ and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford a white solid (0.121 g, 61%). Spectral data matches previously reported.[16]

Supplementary Table 1. Control polymerization M$_w$ characterization via GPC.

Polymer	M$_n$ (kDa)	M$_w$ (kDa)	*Đ*	N	N$_{theory}$
glc$_{OBn}$PAS	48.4	49.2	1.02	107	100

3,4-di-*O*-paramethoxybenzyl-6-*O*-triisopropylsilyl polyamidosaccharide (P1a-P3a)



18 **P1a-P3a**

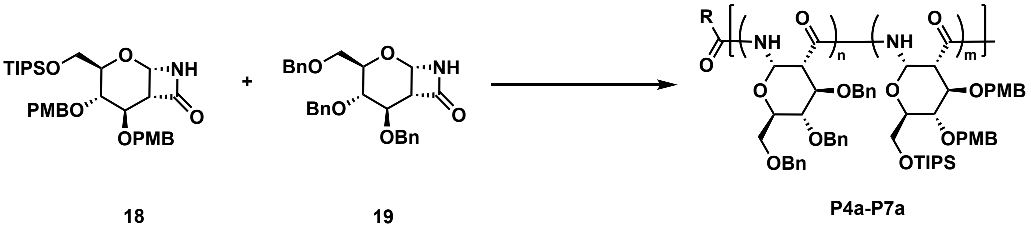
Procedure was adapted from literature with minor changes.[12] To an ambient temperature solution of lactam **18** (0.525-0.521 g depending on sample, 1.0 eq.) dissolved in anhydrous THF (0.1 M) over freshly activated 3Å molecular sieves and under N_2 protection was added Cbz-6-aminohexanoic acid pentafluorophenol ester initiator (4.0 mol% for N_{theory} = 25, 2.0 mol% for N_{theory} = 50, and 1.0 mol% for N_{theory} = 100) from a previously prepared 0.1 M stock solution in THF. The reaction was stirred for 5 min at ambient temperature. The reaction was then cooled to 0˚C and LiHMDS was added from a 0.5 M THF stock solution (10.0 mol% for N_{theory} = 25, 5.0 mol% for N_{theory} = 50, and 5.0 mol% for N_{theory} = 100). The reaction was then warmed to ambient temperature and allowed to stir overnight. Sat. ammonium chloride (1mL) was added to quench the reaction, and the solvent was removed under reduced pressure. Crude polymer was redissolved in CH_2Cl_2 and washed with 1 M HCl, sat. $NaHCO_3$, brine, and dried over Na_2SO_4. After filtering and concentrating under vacuum, the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford a white solid. Spectral data for **P2a**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.75 (br s, 1H, N-*H*), 7.22 – 6.94 (br m, 4H, C_{Ar}*H*), 6.92 – 6.58 (br m, 4H, C_{Ar}*H*), 5.62 – 5.26 (br m, 1H, H-1), 4.84 – 4.23 (br m, 5H), 3.94 – 3.38 (br m, 11H), 1.07 – 0.83 (br m, 21H, Si(*i*-Pr)$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.4 (C=O), 130.4, 130.1, 129.6, 114.3, 114.0, 55.5, 55.3, 18.5, 18.4, 18.4, 18.3, 12.4, 12.3 ppm.

Supplementary Table 2. Polymerization masses and isolated yields.

Polymer	Starting mass (g)	Product mass (g)	Yield (%)
P1a	0.525	0.341	65
P2a	0.513	0.324	63
P3a	0.521	0.367	70

Copolymerization Method A:

3,4-di-*O*-paramethoxybenzyl-6-*O*-triisopropylsilyl-3,4,6-*O*-benzyl-co-polyamidosaccharide (P4a-P7a)



18 **19** **P4a-P7a**

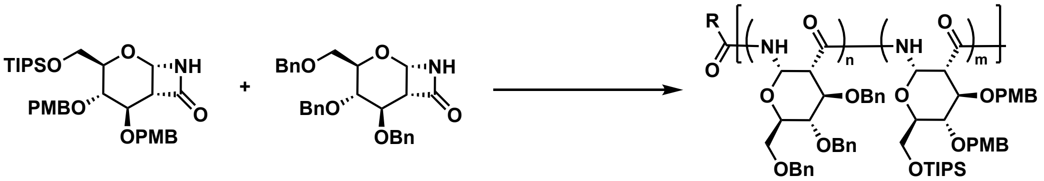
To an ambient temperature solution of 6-*O*-TIPS lactam **18** (0.06-0.49 g depending on sample, 1.0 eq.) and tri-*O*-Bn lactam **19** (0.115-0.141 g depending on sample, 3.0 eq.) in anhydrous THF (0.1 M) over freshly activated 3Å molecular sieves and under N_2 protection was added Cbz-6-aminohexanoic acid pentafluorophenol ester initiator (4.0 mol% for N_{theory} = 25, 2.0 mol% for N_{theory} = 50, 1.0 mol% for N_{theory} = 100, and 0.5 mol% for N_{theory} = 200 with mol% calculated relative to total monomer mmol) from a 0.1 M stock solution of initiator in THF. The reaction was stirred for 5 min at ambient temperature before cooling to 0˚C. LiHMDS was added from a 0.5 M THF stock solution (10.0 mol% for N_{theory} = 25, 5.0 mol% for N_{theory} = 50, 5.0 mol% for N_{theory} = 100, and 5.0 mol% for N_{theory} = 200 with mol% calculated relative to total monomer mmol). The reaction was then warmed to room temperature and allowed to stir overnight. Sat. ammonium chloride (1mL) was added to quench the reaction, and the solvent was removed under reduced pressure. Crude polymer was redissolved in CH_2Cl_2 and washed with 1 M HCl, sat. $NaHCO_3$, brine, and dried over Na_2SO_4. After filtering and concentrating under vacuum, the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford a white solid. Spectral data for **P5a**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.78 (br s, 4H, N*H*), 7.24 – 6.65 (br m, 53H), 5.61 (br s, 4H, H-1, H-1'), 4.68 – 3.26 (br m, 52H), 2.71 (br s, 4H), 0.99 – 0.77 (br m, 21H, Si(*i*-Pr)$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.5 ($C{=}O_{tri\text{-}OBn}$), 159.1 ($C{=}O_{6\text{-}TIPS}$), 138.2, 129.7, 128.3, 128.2, 127.8, 127.6, 113.7, 78.7, 73.7, 73.1, 68.5, 55.2, 51.2, 18.1, 11.8 ppm.

Supplementary Table 3. Method A copolymerization masses and isolated yields.

Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P4a	0.174	0.135	78
P5a	0.171	0.108	63
P6a	0.164	0.094	57
P7a	0.201	0.115	57

Copolymerization Method B:

3,4-di-*O*-paramethoxybenzyl-6-*O*-triisopropylsilyl-co-3,4,6-*O*-benzyl-polyamidosaccharide (P8a-P11a)



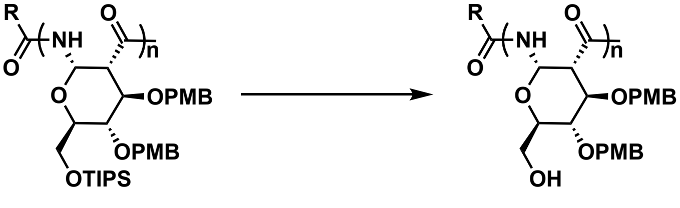
18 **19** **P8a-P11a**

To an ambient temperature solution of 6-*O*-TIPS lactam **18** (0.1 g, 0.171 mmol, 1.0 eq.) in anhydrous THF (1.71 mL, 0.1 M final volume post imitator and LiHMDS addition) over freshly activated 3Å molecular sieves and under N_2 protection was added Cbz-6-aminohexanoic acid pentafluorophenol ester initiator (4.0 mol% for N_{theory} = 25, 2.0 mol% for N_{theory} = 50, 1.0 mol% for N_{theory} = 100, and 0.5 mol% for N_{theory} = 200 with mol% calculated relative to total final monomer mmol) from a 0.1 M stock solution of initiator in THF. The reaction was stirred for 5 min at ambient temperature before cooling to 0°C. LiHMDS was added from a 0.5 M THF stock solution (10.0 mol% for N_{theory} = 25, 5.0 mol% for N_{theory} = 50, 5.0 mol% for N_{theory} = 100, and 5.0 mol% for N_{theory} = 200 with mol% calculated relative to total monomer mmol). The reaction was then warmed to room temperature. Separately, tri-*O*-Bn lactam **19** (0.235 g, 0.512 mmol, 3.0 eq.) was dissolved in anhydrous THF (5.12 mL, 0.1 M) and added to stirring polymerization in 0.5 mL aliquots at time points; 2, 4, 7, 8, 10, 11, 13, 14, 16 and 17 min (time begins at LiHMDS addition). Following tri-O-Bn monomer addition, reaction was stirred overnight at ambient temperature. Sat. ammonium chloride (1mL) was added to quench the reaction, and the solvent was removed under reduced pressure. Crude polymer was redissolved in CH_2Cl_2 and washed with 1 M HCl, sat. $NaHCO_3$, brine, and dried over Na_2SO_4. After filtering and concentrating under vacuum, the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford a white solid. Spectral data for **P9a**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (br s, 4H, N*H*), 7.27 – 6.67 (br m, 53H), 5.63 (br s, 4H, H-1, H-1'), 4.68 – 3.24 (br m, 52H), 2.74 (br s, 4H, H-2, H-2'), 1.14 – 0.62 (br m, 21H, Si(*i*-Pr)$_3$) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.6 ($C{=}O_{tri\text{-}OBn}$), 159.1 ($C{=}O_{6\text{-}TIPS}$) , 138.5, 138.3, 129.6, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 113.8, 113.7, 73.9, 73.1, 68.5, 62.2, 55.3, 55.1, 51.2, 18.1, 12.0 ppm.

Supplementary Table 4. Method B copolymerization masses and isolated yields.

Polymer	**Starting total mass (g)**	**Product mass (g)**	**Yield (%)**
P8a	0.335	0.222	66
P9a	0.335	0.234	70
P10a	0.335	0.244	73
P11a	0.335	0.246	73

Homopolymer 6-triisopropylsilyl deprotection (P1b-P3b)



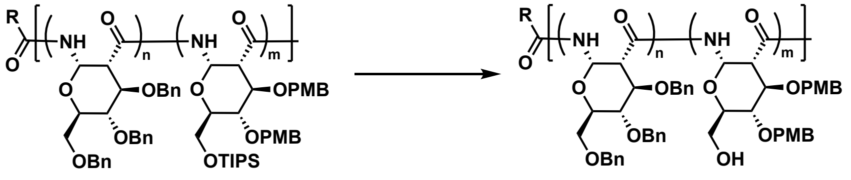
P1a-P3a **P1b-P3b**

Procedure was adapted from literature with minor changes.[12] A flame-dried flask equipped with polymer (0.338-1.15 g depending on sample, 1.0 eq.) over freshly activated 3Å molecular sieves under N_2 protection was cooled to 0˚C. A 1 M THF solution of tetra-n-butylammonium fluoride (4 eq.) was added dropwise. Reaction was warmed to ambient temperature and stirred overnight. The reaction was filtered, concentrated under reduced pressure and redissolved in a 2:1 CH_2Cl_2: MeOH solution (0.125 M). Calcium carbonate (210 mg/ 1 mL to TBAF volume) and Dowex 50WX8 200-400 mesh ion exchange resin (625 mg/ 1 mL to TBAF volume) were added and stirred overnight. The reaction was then filtered through celite to remove solids and successively washed with 2:1 CH_2Cl_2: MeOH. Filtrate was concentrated, redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford polymers as off-white solids. Spectral data for **P2b**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.00 (br s, 1H, N-*H*), 7.24 – 6.90 (br m, 4H, C_{Ar}*H*), 6.88 – 6.59 (br m, 4H, C_{Ar}*H*), 6.06 – 5.51 (br m, 1H, H-1), 4.92 – 4.04 (br m, 5H), 3.82 – 3.31 (br m, 11H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.2 (C=O), 129.7, 113.9, 66.0, 59.1, 55.3, 24.3, 19.9, 15.4, 13.8 ppm.

Supplementary Table 5. Homopolymer triisopropylsilyl deprotection masses and isolated yields.

Polymer	**Starting total mass (g)**	**Product mass (g)**	**Yield (%)**
P1b	0.498	0.158	43
P2b	1.154	0.510	60
P3b	0.338	0.158	64

Copolymer 6-triisopropylsilyl deprotection (P4b-P11b)



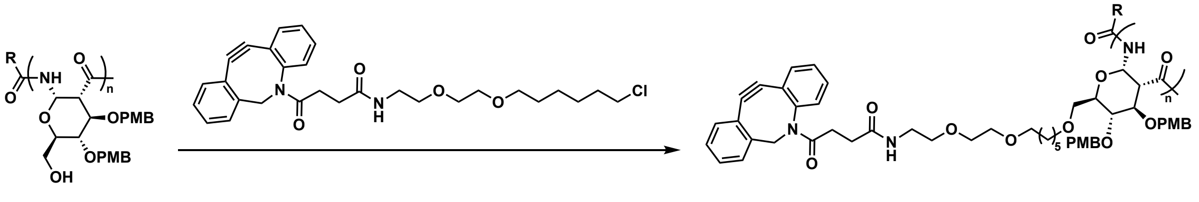
P4a-P11a **P4b-P11b**

Total starting polymer mass was multiplied by 0.25 to estimate amount of 6-*O*-TIPS monomer units present, all calculations were based on this mass. All equivalences and molarities were calculated relative to one 6-*O*-TIPS monomer unit. To a flame-dried flask equipped with polymer (0.027-0.061 g, depending on sample, 1.0 eq.) over freshly activated 3Å molecular sieves under N_2 protection in THF (0.084 M) was cooled to 0˚C. A 1 M THF solution of tetra-*n*-butylammonium fluoride (4 eq.) was added dropwise. Reaction was warmed to ambient temperature and stirred overnight. The reaction was filtered, concentrated under reduced pressure and redissolved in CH_2Cl_2 (0.125 M). Calcium carbonate (210 mg/ 1 mL to TBAF volume) and Dowex 50WX8 200-400 mesh ion exchange resin (625 mg/ 1 mL to TBAF volume) were added and stirred overnight. The reaction was then filtered through celite to remove solids and successively washed with CH_2Cl_2. Filtrate was concentrated, redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford polymers as off-white solids. Spectral data for **P5b**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (br s, 4H, N*H*), 7.25 – 6.64 (br m, 53H), 5.72 (br s, 4H, H-1, H-1'), 4.53 – 3.19 (br m, 52H), 2.72 (br s, 4H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.8 ($C=O_{tri\text{-}OBn}$), 159.1 ($C=O_{6\text{-}OH}$), 139.0, 128.4, 128.3, 128.1, 127.8, 127.6, 113.7, 78.7, 75.1, 73.4, 68.4, 58.9, 55.2, 50.5, 24.1, 19.8, 13.7 ppm.

Supplementary Table 6. Copolymer triisopropylsilyl deprotection masses and isolated yields.

Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P4b	0.124	0.088	76
P5b	0.108	0.068	67
P6b	0.168	0.098	62
P7b	0.115	0.065	61
P8b	0.222	0.172	83
P9b	0.234	0.154	71
P10b	0.244	0.158	69
P11b	0.242	0.176	78

Homopolymer linker substitution (P1c-P3c)



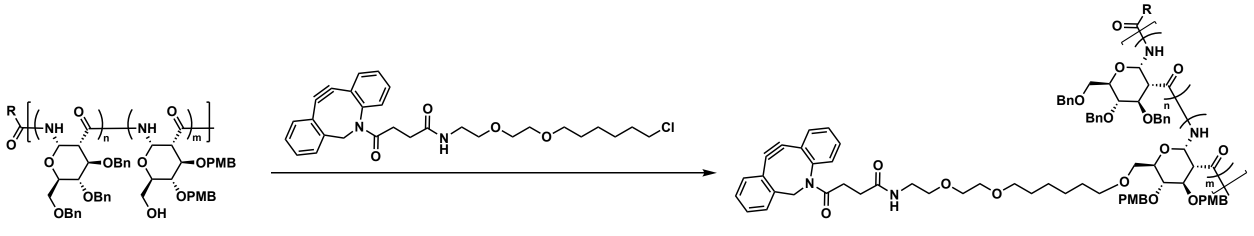
P1b-P3b **P1c-P3c**

To a flame-dried flask of polymer (0.076-0.158 g depending on sample, 1.0 eq. with respect to a single monomer unit) and DBCO linker (1.2 eq.) in anhydrous THF (0.1 M) cooled to 0˚C was added imidazole (2.0 eq.). The reaction was warmed to ambient temperature and stirred overnight. The reaction was diluted in EtOAc and washed with water (3x), brine, and dried over Na_2SO_4. After filtering and concentrating under reduced pressure, the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford polymers as white solids. Spectral data for **P2c**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.91 (br s, 1H, N-*H*), 7.60 (t, *J* = 8.5 Hz, 1H), 7.42 (dd, *J* = 15.0, 6.9 Hz, 1H), 7.35 – 7.13 (m, 6H), 7.12 – 6.80 (m, 4H, C_{Ar}*H*), 6.81 – 6.42 (m, 4H, C_{Ar}*H*), 6.08 – 5.94 (m, 1H), 5.90 – 5.52 (m, 1H, H-1), 5.08 (t, *J* = 14.1 Hz, 1H), 4.78 – 4.02 (m, 5H), 3.93 – 2.95 (m, 23H), 2.73 (dd, *J* = 16.5, 8.1 Hz, 1H), 2.41 – 2.33 (m, 1H), 2.14 – 2.02 (m, 1H), 1.88 (dt, *J* = 16.7, 7.7 Hz, 1H), 1.68 (p, *J* = 7.3 Hz, 2H), 1.50 (p, *J* = 7.9 Hz, 2H), 1.35 (p, *J* = 8.2 Hz, 2H), 1.28 (q, *J* = 8.1 Hz, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.23, 172.15, 172.0, 171.9, 159.1 ($C{=}O_{PAS}$), 151.3, 148.0, 132.20, 132.17, 129.31, 129.28, 128.6, 128.5, 128.2, 128.1, 128.0, 127.63, 127.60, 127.0, 125.39, 125.36, 123.11, 123.09, 122.4, 114.7, 113.8, 113.7, 107.9, 71.1, 70.2, 69.9, 69.63, 69.60, 55.4, 55.12, 55.07, 45.0, 39.1, 32.4, 31.2, 31.1, 30.10, 30.06, 29.4, 26.6, 25.3 ppm.

Supplementary Table 7. Homopolymer linker substitution masses and isolated yields.

Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P1c	0.150	0.183	58
P2c	0.076	0.099	62
P3c	0.158	0.206	62

Copolymer linker substitution (P4c-P11c)



P4b-P11b

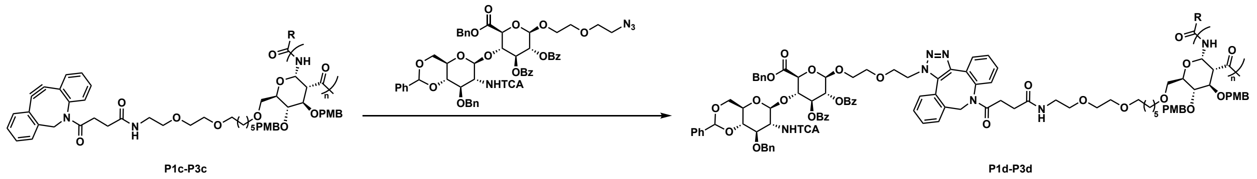
P4c-P11c

Total starting polymer mass was multiplied by 0.25 to estimate amount of 6-OH monomer units present, all calculations were based on this mass. All equivalences and molarities were calculated relative to one 6-OH monomer unit. To a flame-dried flask of polymer (0.0163-0.0413 g depending on sample, 1.0 eq.) and DBCO linker (1.2 eq.) in anhydrous THF (0.026 M) cooled to 0˚C was added imidazole (2.0 eq.). The reaction was warmed to ambient temperature and stirred overnight. The reaction was diluted in EtOAc and washed with water (3x), brine, and dried over Na_2SO_4. After filtering and concentrating under reduced pressure, the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford polymers as white solids. Spectral data for **P5c**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.97 (br s, 4H, N*H*), 7.61 (t, *J* = 7.6 Hz, 1H, C_{Ar}H), 7.44 – 7.43 (m, 1H, C_{Ar}H), 7.32 – 6.64 (m, 59H, C_{Ar}H), 5.93 (br s, 1H), 5.69 (br s, 4H, H-1, H-1’), 5.10 – 5.07 (d, *J* = 13.9 Hz, 1H), 4.39 – 3.90 (m, 27H), 3.60 – 2.72 (m, 42H), 2.41 (dt, *J* = 14.9, 7.4 Hz, 1H), 2.12 – 2.07 (dt, *J* = 14.2, 6.2 Hz, 1H), 1.90 – 1.86 (dt, *J* = 17.0, 6.2 Hz, 1H), 1.69 – 1.68 (m, 2H), 1.52 – 1.50 (m, 2H), 1.38 – 1.35 (m, 2H), 1.29 – 1.27 (m, 2H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.2, 172.0, 170.5 ($C{=}O_{tri\text{-}OBn}$), 159.3 ($C{=}O_{6\text{-}DBCO}$), 151.4, 148.1, 138.2, 132.2, 129.4, 128.65, 128.3, 128.2, 128.1, 127.7, 127.3, 127.1, 125.5, 123.2, 122.5, 114.7, 113.7, 107.9, 77.3, 77.1, 76.8, 74.1, 71.3, 70.3, 70.0, 69.7, 68.6, 55.5, 55.2, 45.1, 39.2, 32.5, 31.3, 30.2, 29.7, 29.5, 26.7, 25.4 ppm.

Supplementary Table 8. Copolymer linker substitution masses and isolated yields.

Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P4c	0.087	0.071	64
P5c	0.068	0.031	36
P6c	0.093	0.072	61
P7c	0.065	0.061	74
P8c	0.165	0.075	36
P9c	0.144	0.155	84
P10c	0.158	0.163	69
P11c	0.140	0.150	78

Homopolymer strain-promoted azide-alkyne cycloaddition (P1d-P3d)

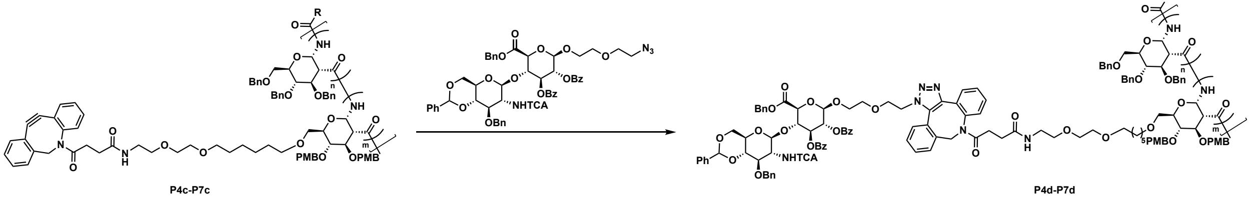


An ambient temperature mixture of polymer (0.161-0.194 g depending on sample, 1.0 eq. with respect to a single monomer unit) and azido-armed disaccharide (1.5 eq.) dissolved in CH_2Cl_2 (0.01 M) was stirred for 24 hrs. Reaction was concentrated and the crude polymer was redissolved in a minimal amount of CH_2Cl_2 and precipitated dropwise into stirring cold MeOH with the exception of P2d which only precipitated in cold n-pentane. The resulting solid was filtered and further dried under high vacuum to afford polymers as white solids. Spectral data for **P1d**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.23 – 7.89 (m, 7H), 7.81 – 6.45 (m, 58H), 6.33 (d, *J* = 18.1 Hz, 1H), 6.21 (dd, *J* = 13.1, 6.2 Hz, 1H), 6.17 – 6.07 (m, 1H), 5.94 (br s, 1H), 5.72 (q, *J* = 8.9 Hz, 1H), 5.65 (q, *J* = 9.4 Hz, 1H), 5.46 (t, *J* = 12.2 Hz, 2H), 5.39 (q, *J* = 8.8, 8.2 Hz, 1H), 5.23 (dd, *J* = 16.5, 9.5 Hz, 1H), 5.03 – 3.33 (m, 68H), 3.16 (q, *J* = 8.4, 5.7 Hz, 2H), 3.04 – 2.68 (m, 2H), 2.61 (td, *J* = 15.9, 15.0, 8.6 Hz, 1H), 2.45 (dq, *J* = 15.3, 6.9 Hz, 1H), 2.32 (q, *J* = 12.5, 10.1 Hz, 1H), 2.22 (dq, *J* = 13.9, 6.8 Hz, 1H), 2.06 (dq, *J* = 15.6, 8.8, 7.3 Hz, 1H), 1.84 (t, *J* = 7.6 Hz, 2H), 1.80 – 1.71 (m, 1H), 1.66 (q, *J* = 7.2 Hz, 2H), 1.51 (d, *J* = 8.3 Hz, 2H), 1.43 (q, *J* = 7.6, 7.0 Hz, 2H), 1.35 (br s, 1H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.0, 171.9, 171.7, 170.8, 170.8, 168.1, 168.0, 168.0, 167.9, 165.3, 165.2, 165.14, 165.12, 165.07, 161.6, 161.5, 159.2 ($C{=}O_{PAS}$), 144.7, 144.6, 143.2, 143.1, 141.3, 140.2, 137.9, 137.1, 135.9, 135.8, 135.4, 135.3, 134.9, 134.8, 133.6, 133.5, 133.35, 133.26, 132.7, 132.1, 132.0, 131.9, 131.6, 131.4, 130.9, 130.6, 130.0, 129.9, 129.84, 129.82, 129.79, 129.73, 129.71, 129.3, 129.10, 129.06, 129.0, 128.93, 128.88, 128.85, 128.82, 128.79, 128.7, 128.5, 128.44, 128.41, 128.3, 128.1, 127.8, 127.5, 127.4, 127.1, 126.0, 125.3, 125.1, 113.8, 101.6, 101.5, 101.3, 101.1, 101.0, 99.84, 99.78, 99.7, 92.84, 92.77, 92.7, 82.0, 76.60, 76.57, 76.3, 76.2, 76.1, 74.27, 74.25, 74.15, 72.7, 72.6, 71.75, 71.67, 71.2, 70.7, 70.5, 70.4, 70.3, 70.3, 70.2, 70.1, 70.05, 70.03, 70.02, 69.9, 69.8, 69.74, 69.65, 69.6, 67.9, 67.7, 65.79, 65.76, 57.7, 55.2, 51.7, 50.5, 48.65, 48.56, 45.11, 45.09, 39.20, 39.16, 32.5, 31.11, 31.06, 31.0, 29.6, 29.5, 29.4, 26.7, 25.4 ppm.

Supplementary Table 9. Homopolymer SPAAC masses and isolated yields. **P2d** could not be isolated from residual azido-disaccharide as it did not precipitate in cold MeOH.

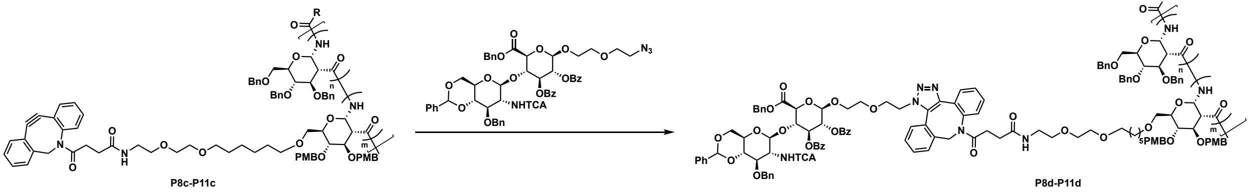
Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P1d	0174	0.129	34
P2d	0.161	0.402	N/A
P3d	0.194	0.076	18

Method A copolymer strain-promoted azide-alkyne cycloaddition (P4d-P7d)



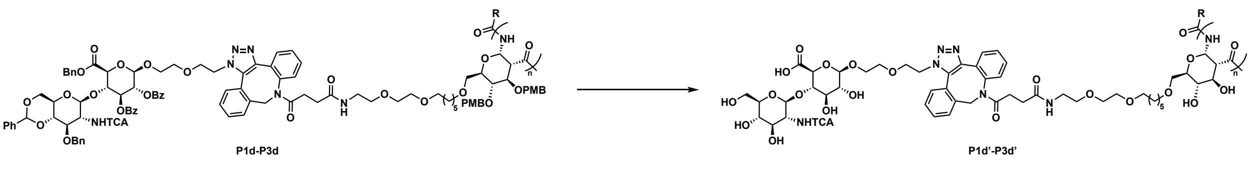
Total starting polymer mass was multiplied by 0.25 to estimate amount of 6-DBCO monomer units present, all calculations were based on this mass. All equivalences and molarities were calculated relative to one 6-DBCO monomer unit. An ambient temperature mixture of polymer (0.010-0.025 g depending on sample, 1.0 eq. with respect to a single monomer unit) and azido-armed disaccharide (2.0 eq.) dissolved in CH_2Cl_2 (0.014 M) was stirred for 24 hrs. Reaction was concentrated and the crude polymer was taken to the next step without further purification.

Method B copolymer strain-promoted azide-alkyne cycloaddition (P8d-P11d)



Total starting polymer mass was multiplied by 0.25 to estimate amount of 6-DBCO monomer units present, all calculations were based on this mass. All equivalences and molarities were calculated relative to one 6-DBCO monomer unit. An ambient temperature mixture of polymer (0.017-0.039 g depending on sample, 1.0 eq. with respect to a single monomer unit) and azido-armed disaccharide (1.5 eq.) dissolved in CH_2Cl_2 (0.0014 M) was stirred for 24 hrs. Reaction was concentrated and the crude polymer was taken to the next step without further purification.

Homopolymer global deprotection (P1d'-P3d')

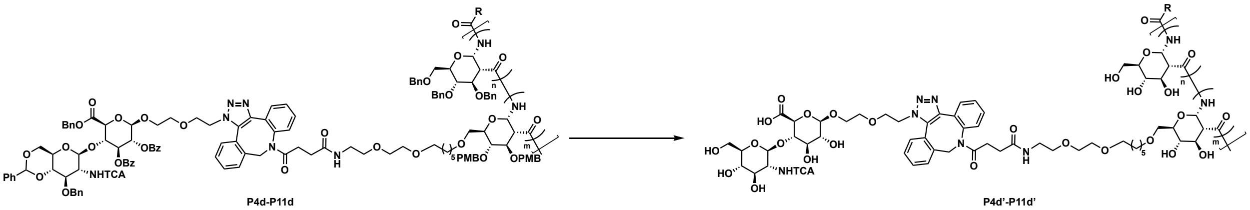


Procedure was adapted from literature with minor changes.[17] To a 0˚C solution of polymer (0.075-0.355 g depending on sample, 1.0 eq. with respect to a single monomer unit) in THF (0.045 M, final concentration post LiHMDS addition) was added LiHMDS (3.0 eq.) dropwise from a previously prepared stock THF solution. The reaction was stirred for 5 min at ambient temperature before adding dropwise into a -61˚C stirring solution of sodium in anhydrous liquid ammonia (10-25 mL depending on sample) under N_2 protection. The deep blue color of the solution was maintained by additional sodium if necessary. The reaction was stirred at -61˚C for 2.5 hrs. The reaction was quenched by the addition of sat. ammonium chloride dropwise until the blue color disappeared. The ammonia was left to evaporate, and the resulting residue was washed with DI water and dialyzed (8.0 kDa MWCO) against DI water for 24 hrs with three water changes. Solutions were lyophilized to give polymers as white fluffy solids. Spectral data for **P2d'**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.77 (d, J = 5.0 Hz, 1H), 4.57 – 4.52 (m, 0.13H), 4.52 – 4.43 (m, 0.10H), 4.24 – 4.09 (m, 1H), 4.09 – 3.18 (m, 9H), 3.15 – 2.13 (m, 2H), 1.73 – 1.42 (m, 1H), 1.28 (s, 1H), 0.86 (0.86, d, 0.26H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.2 (C=O), 74.7, 73.1, 69.9, 68.4, 60.5, 60.3, 55.3, 51.1, 26.4, 22.4, 21.9 ppm.

Supplementary Table 10. Homopolymer deprotection masses and isolated yields.

Polymer	Starting total mass (g)	Product mass (g)	Yield (%)
P1d'	0.119	0.018	24
P2d'	0.355	0.030	13 *(over two steps)*
P3d'	0.075	0.012	25

Copolymer global deprotection (P4d'-P11d')

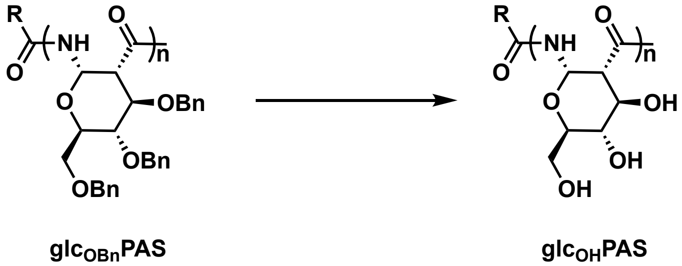


Procedure was adapted from literature with minor changes.[17] Total starting polymer mass was multiplied by 0.25 to estimate amount of 6-disaccharide monomer units present, all calculations were based on this mass. All equivalences and molarities were calculated relative to one 6-disaccharide monomer unit. To a 0˚C solution of polymer (0.010-0.045 g depending on sample, 1.0 eq. with respect to a single monomer unit) in THF (0.01 M, final concentration post LiHMDS addition) was added LiHMDS (22.5 eq.) dropwise from a previously prepared stock THF solution. The reaction was stirred for 5 min at ambient temperature before adding dropwise into a -61˚C stirring solution of sodium in anhydrous liquid ammonia (10-25 mL depending on sample) under N_2 protection. Additional sodium was added to maintain the deep blue color of the solution. The reaction was stirred at -61˚C for 2.5 hrs. The reaction was quenched by the addition of sat. ammonium chloride dropwise until the blue color disappeared. The ammonia was left to evaporate, and the resulting residue was washed with DI water and dialyzed (8.0 kDa MWCO) against DI water for 24 hrs with three water changes. Solutions were lyophilized to give polymers as white fluffy solids. Spectral data for **P5d'**: **^{1}H NMR** (600 MHz, D_2O) δ 7.32 (s, 1H), 5.70 (d, J = 5.1 Hz, 1H, H-1_{PAS}), 4.49 (d, J = 8.4 Hz, 0.11H, H-$1_{disacch}$), 4.43 (d, J = 8.0 Hz, 0.11H, H-$1'_{disacch}$), 4.08 – 4.04 (m, 1H), 3.87 – 3.52 (m, 4H), 3.43 – 3.28 (m, 3H), 2.99 – 2.69 (m, 1H), 2.27 – 2.23 (m, 0.26H), 1.98 (s, 0.30H), 1.61 – 1.51 (m, 0.70H), 1.29 – 0.80 (m, 2.13H) ppm; **^{13}C NMR** (151 MHz, D_2O) δ 170.2 (C=O), 74.7, 73.1, 70.4, 67.7, 59.7, 51.1 ppm.

Supplementary Table 11. Copolymer deprotection masses and isolated yields over two steps.

Polymer	Starting total mass (g)	Product mass (g)	Yield over two steps (%)
P4d’	0.099	0.008	17
P5d’	0.038	0.004	22
P6d’	0.089	0.015	36
P7d’	0.077	0.009	25
P8d’	0.077	0.013	36
P9d’	0.179	0.016	19
P10d’	0.156	0.026	36
P11d’	0.179	0.011	13

Control polymer debenzylation (glc$_{OH}$PAS)



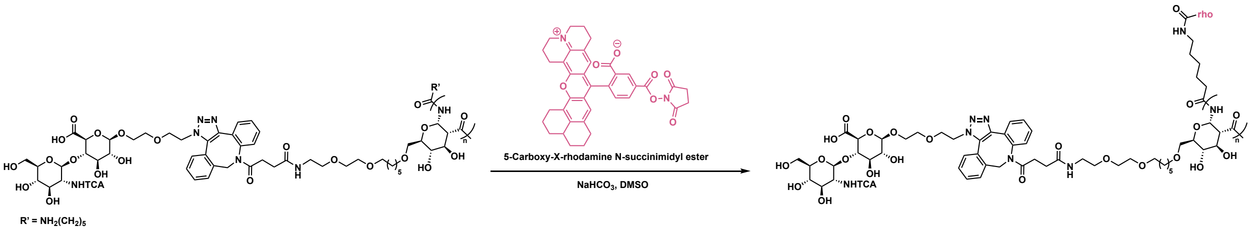
Procedure was adapted from literature with minor changes.[16, 17] To a 0˚C solution of polymer (0.121 g, 1.0 eq. with respect to a single monomer unit) in THF (2.39 mL) was added LiHMDS (0.066 g, 0.395 mmol, 1.5 eq.) dropwise from a previously prepared stock THF solution. The reaction was stirred for 5 min at ambient temperature before adding dropwise into a -61˚C stirring solution of sodium in anhydrous liquid ammonia (25 mL) under N_2 protection. The deep blue color of the solution was maintained by additional sodium if necessary. The reaction was stirred at -61˚C for 2 hrs. The reaction was quenched by the addition of sat. ammonium chloride dropwise until the blue color disappeared. The ammonia was left to evaporate, and the resulting residue was washed with DI water and dialyzed (8.0 kDa MWCO) against DI water for 24 hrs with three water changes. Solutions were lyophilized to afford polymer as a white fluffy solid (0.035 g, 70%). Spectral data matches previously reported.[16]

Supplementary Table 12. Control polymer debenzylation and M_w characterization via GPC.

Polymer	M_n (kDa)	M_w (kDa)	$Đ$	N	N_{theory}
glc$_{OH}$PAS	16.0	21.6	1.35	114	100

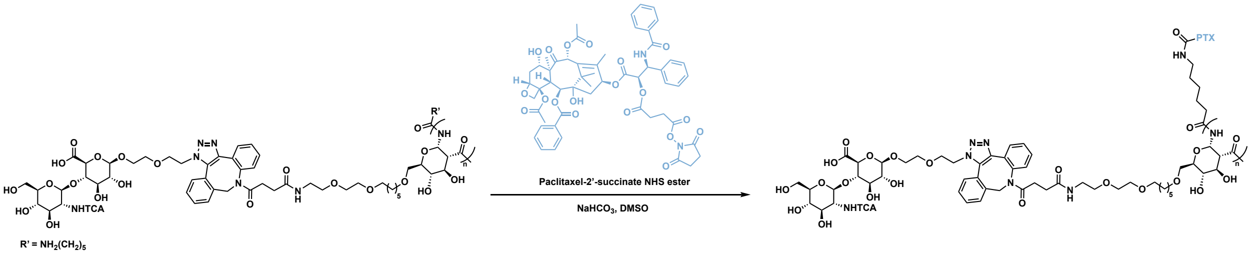
Synthesis of rhodamine labeled HA (rho-HA)

Procedure was adapted from literature with minor changes.[18] To an ambient temperature mixture of HA (8-15 kDa, 10.0 mg, 0.025 mmol, 1.0 eq.) in DI water (0.25 mL) was added a solution of rhodamine isothiocyanate (1.3 mg, 0.0025 mmol, 0.1 eq. relative to HA disaccharide) in DMSO (1.0 mL). The reaction was stirred overnight at ambient temperature. The solution was dialyzed (2.0 kDa MWCO) against DI water for 48 hrs with four water changes. Solution was lyophilized to furnish the rho-HA polymer as a purple fluffy solid (5.59 mg, 56% mass recovery). The reaction and subsequent purifications were carried out under light protection. The rhodamine labelling was confirmed using polyacrylamide gel electrophoresis.



Synthesis of rhodamine labeled P1d' (rho-P1d')

Procedure was adapted from literature with minor changes.[19] **P1d'** or glc$_{OH}$PAS was dissolved at 10 mg/mL in 0.1 M $NaHCO_3$ (8.97 mg, 8.07 mg respectively). Separately, 5-Carboxy-X-rhodamine N-succinimidyl ester was dissolved in DMSO at 2 mg/mL. 100 µL of the rhodamine solution was then added per 400 µL of polymer solution and incubated at ambient temperature for 1 hr before transfer to dialysis (2.0 kDa MWCO) in DI water for 48 hrs with four water changes. Solutions were lyophilized to give purple fluffy solids (**P1d'** = 3.27 mg, 36% mass recovery; glc$_{OH}$PAS = 2.81 mg, 35% mass recovery). All reactions and subsequent dialysis were performed under light protection, and labelling was confirmed via polyacrylamide gel electrophoresis.

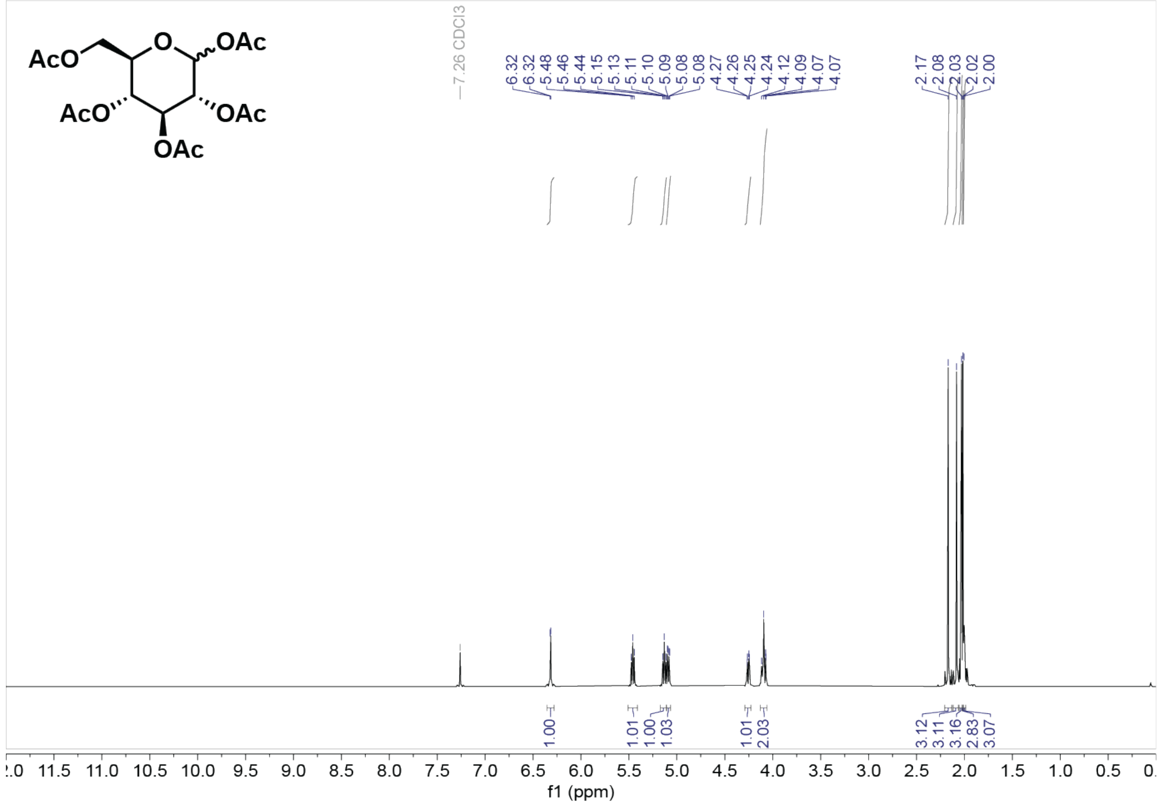


Synthesis of paclitaxel (PTX) and P1d' conjugate (PTX-P1d')

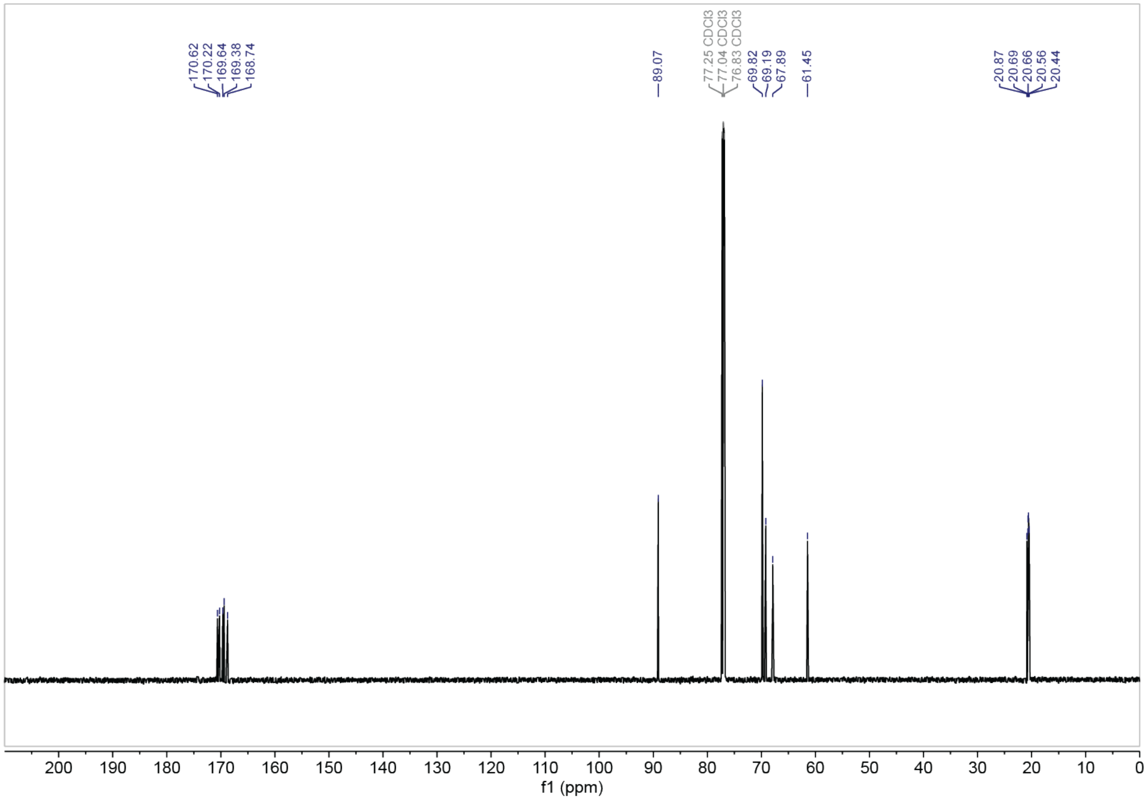
Procedure was adapted from literature with minor changes.[19] Briefly, **P1d'** (10.26 mg) was dissolved at 10 mg/mL in 0.1 M $NaHCO_3$ and paclitaxel-NHS was dissolved at 2 mg/mL in DMSO, separately. 100 µL of the PTX solution was then added per 400 µL of **P1d'** solution and incubated at ambient temperature for 1 hr before dialyzing for 48 hrs against DI water (2.0 kDa MWCO) with four water changes. Lyophilized solutions yielded a fluffy, white solid (5.0 mg, 49% mass recovery). Conjugation was confirmed via ^{1}H NMR.

Small Molecule NMRs

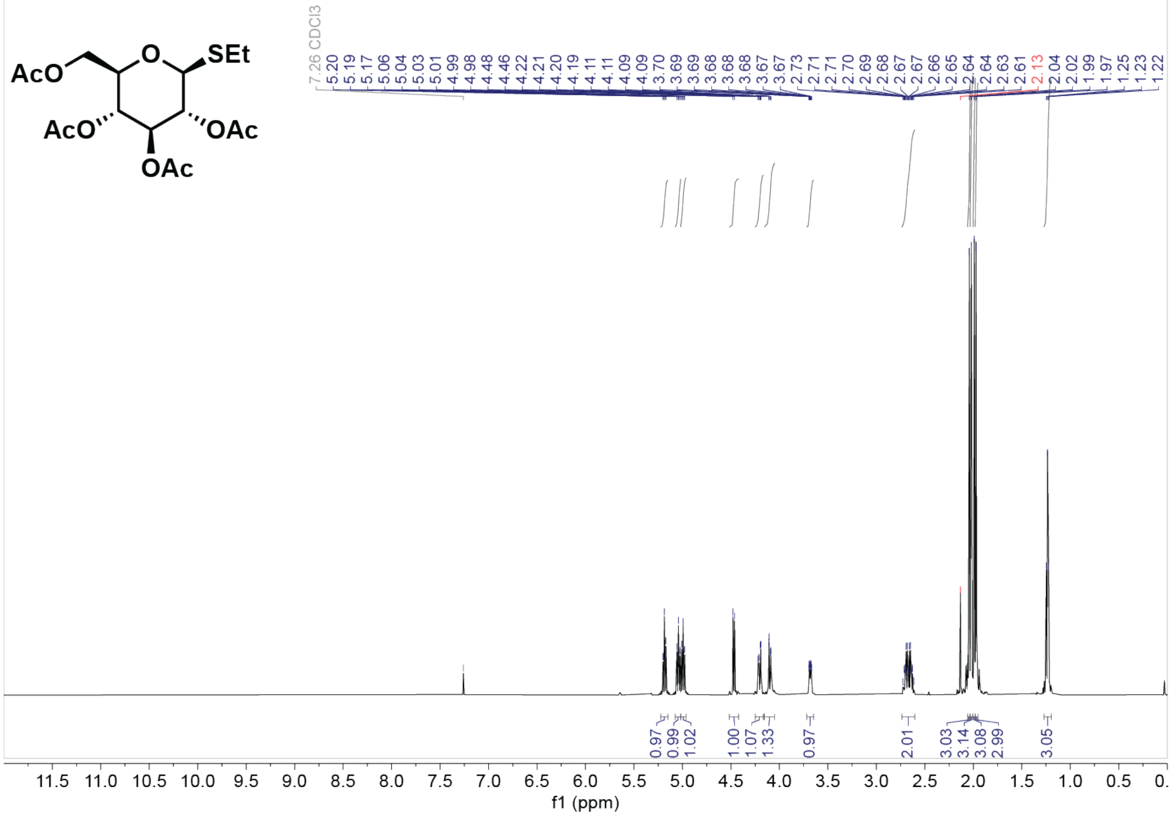
(**1**) – ^{1}H NMR (600 MHz, CDCl$_3$)



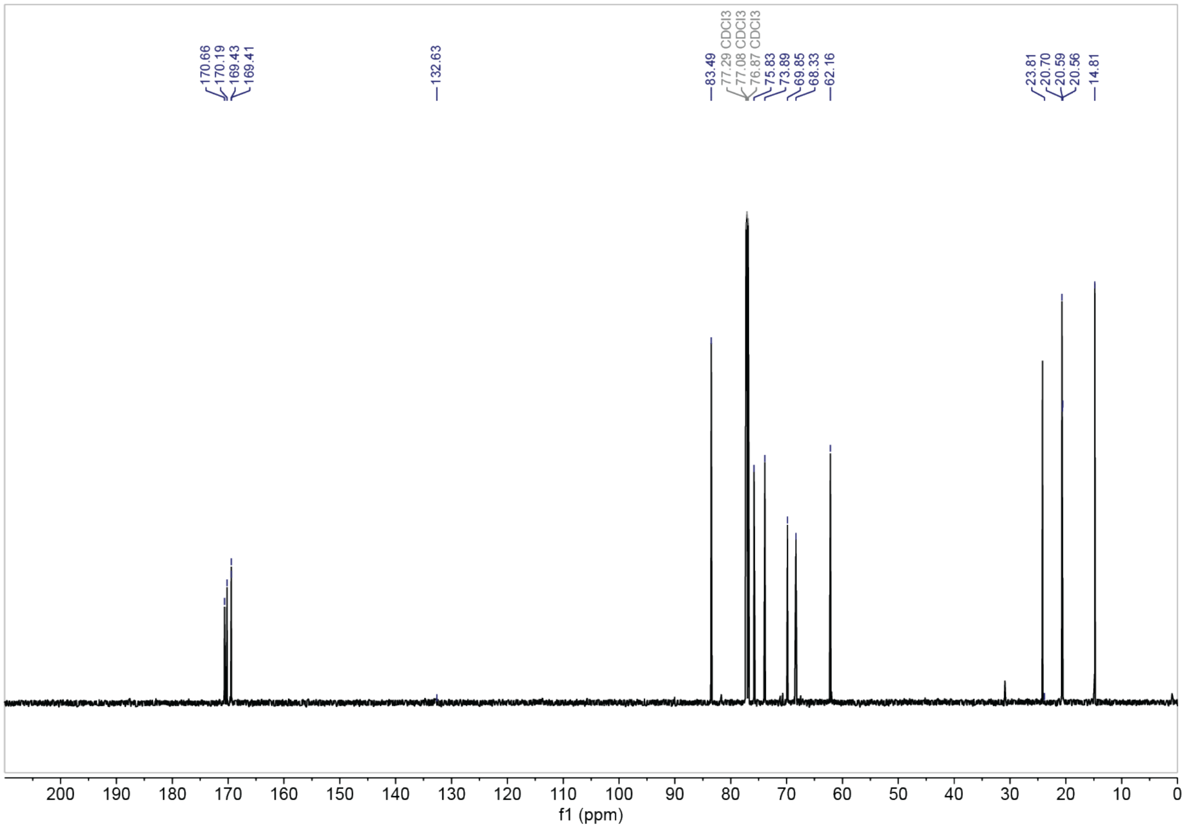
(**1**) – ^{13}C NMR (151 MHz, CDCl$_3$)



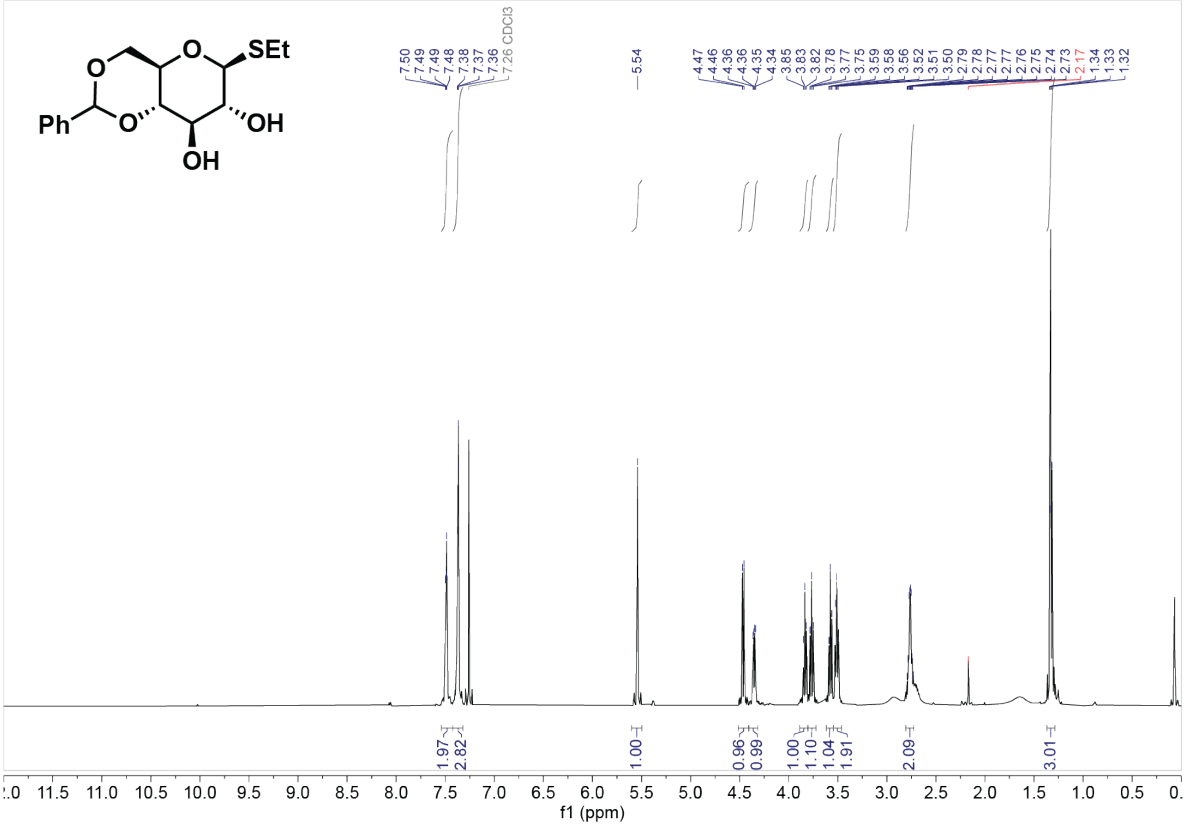
(**2**) – ^{1}H NMR (600 MHz, CDCl$_3$)



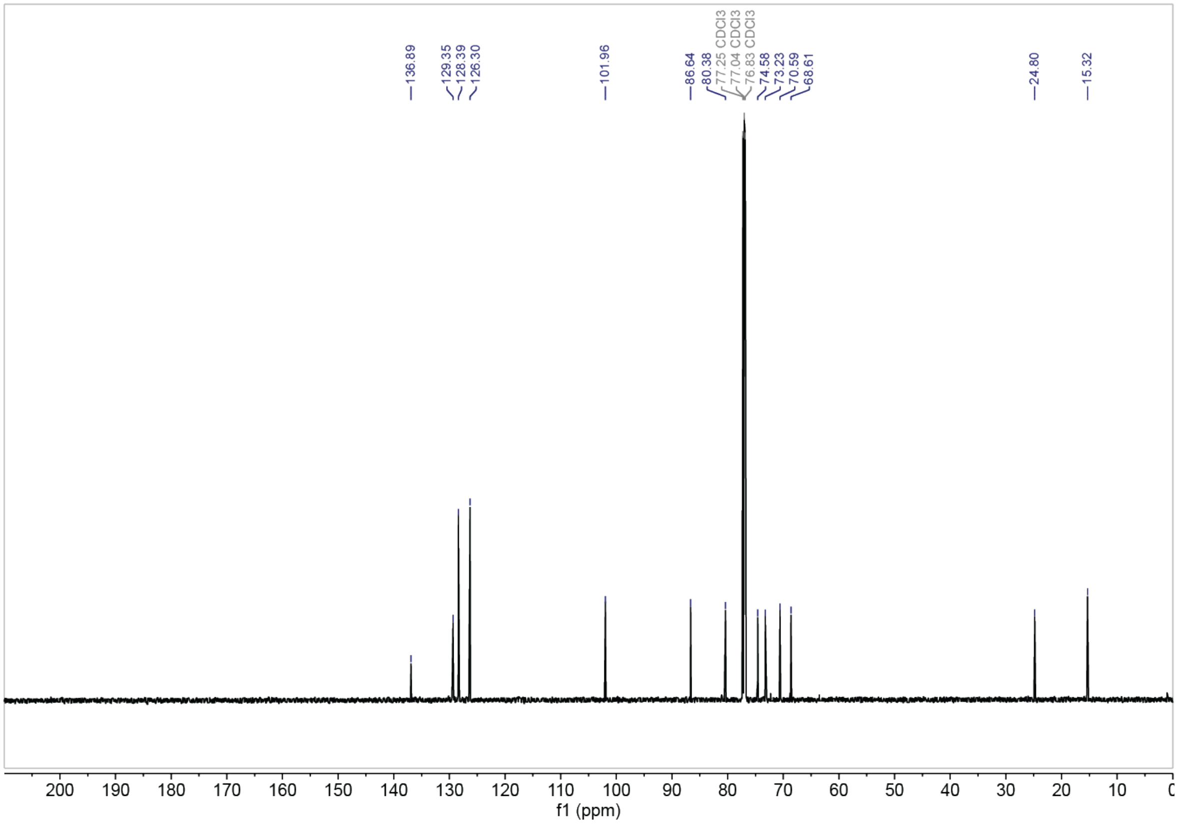
(**2**) – ^{13}C NMR (151 MHz, CDCl$_3$)



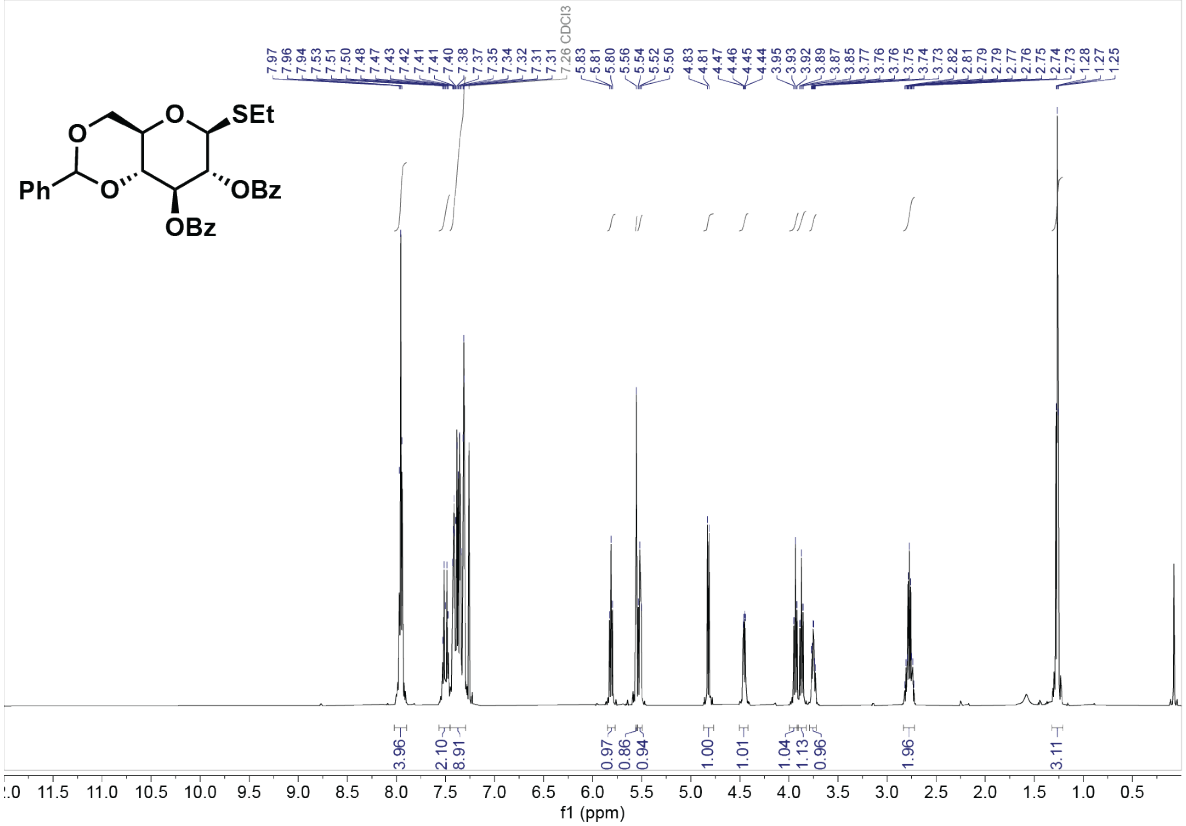
(**3**) – ^{1}H NMR (600 MHz, CDCl$_3$)



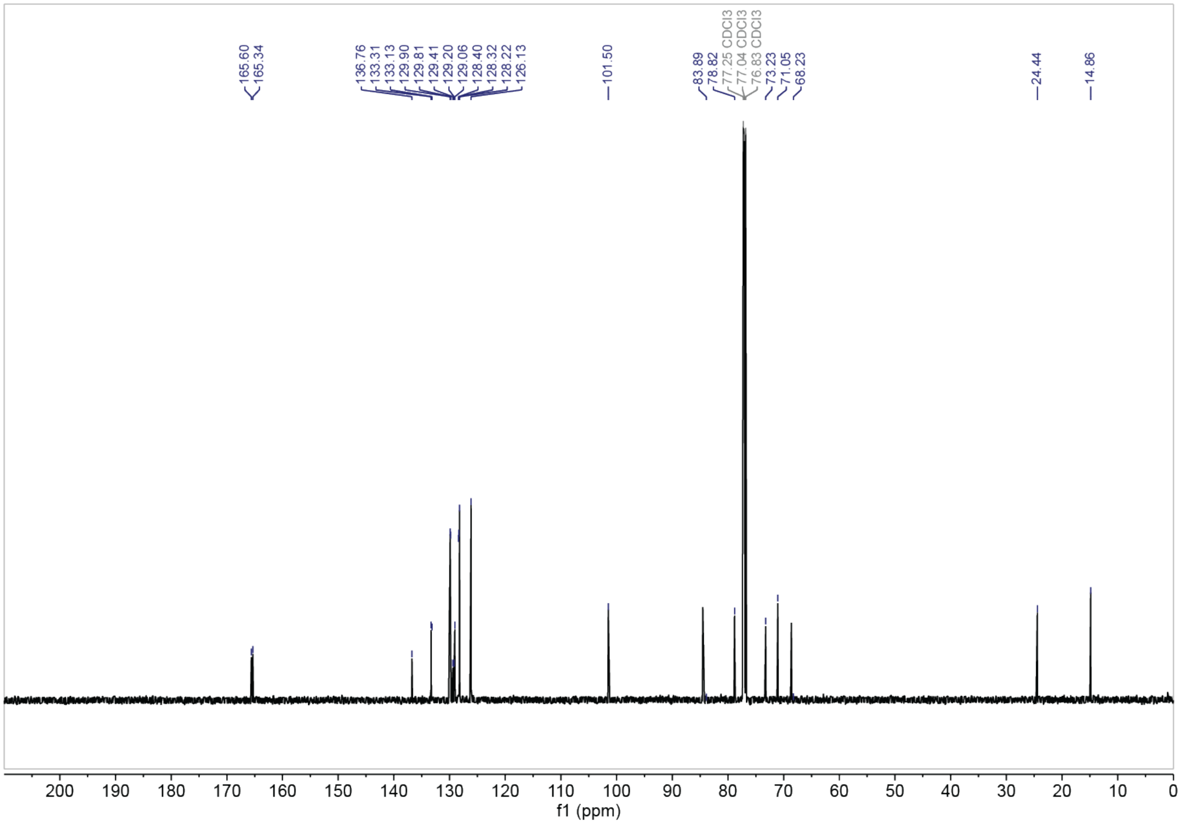
(**3**) – ^{13}C NMR (151 MHz, CDCl$_3$)



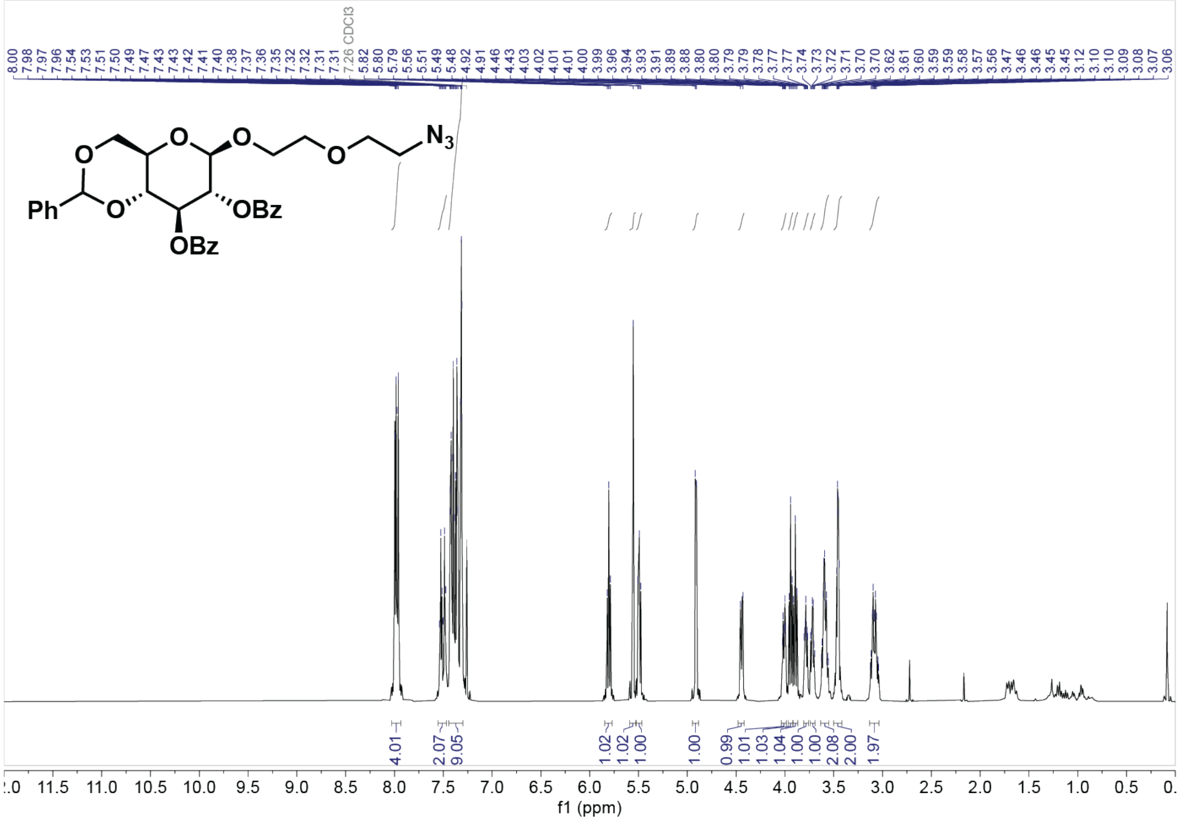
(**4**) – ^{1}H NMR (600 MHz, CDCl$_3$)



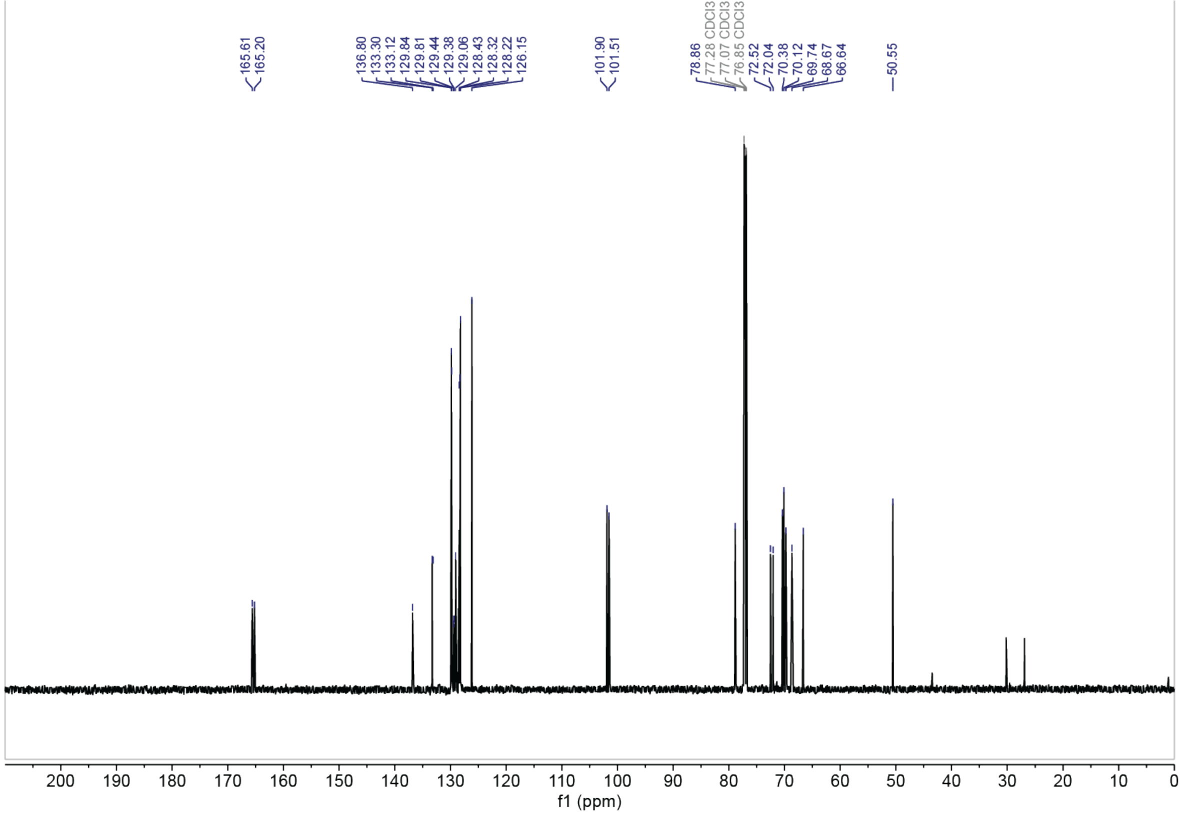
(**4**) – ^{13}C NMR (151 MHz, CDCl$_3$)



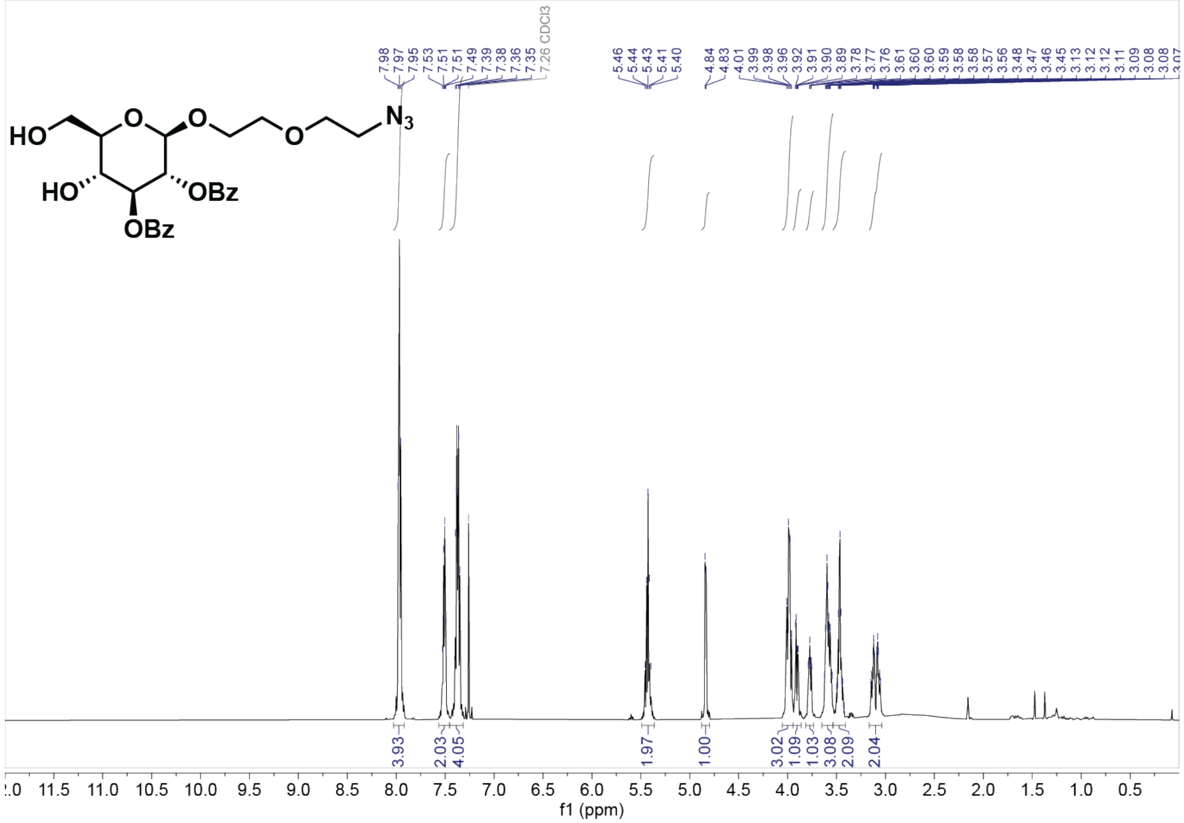
(**5**) – ^{1}H NMR (600 MHz, CDCl$_3$)



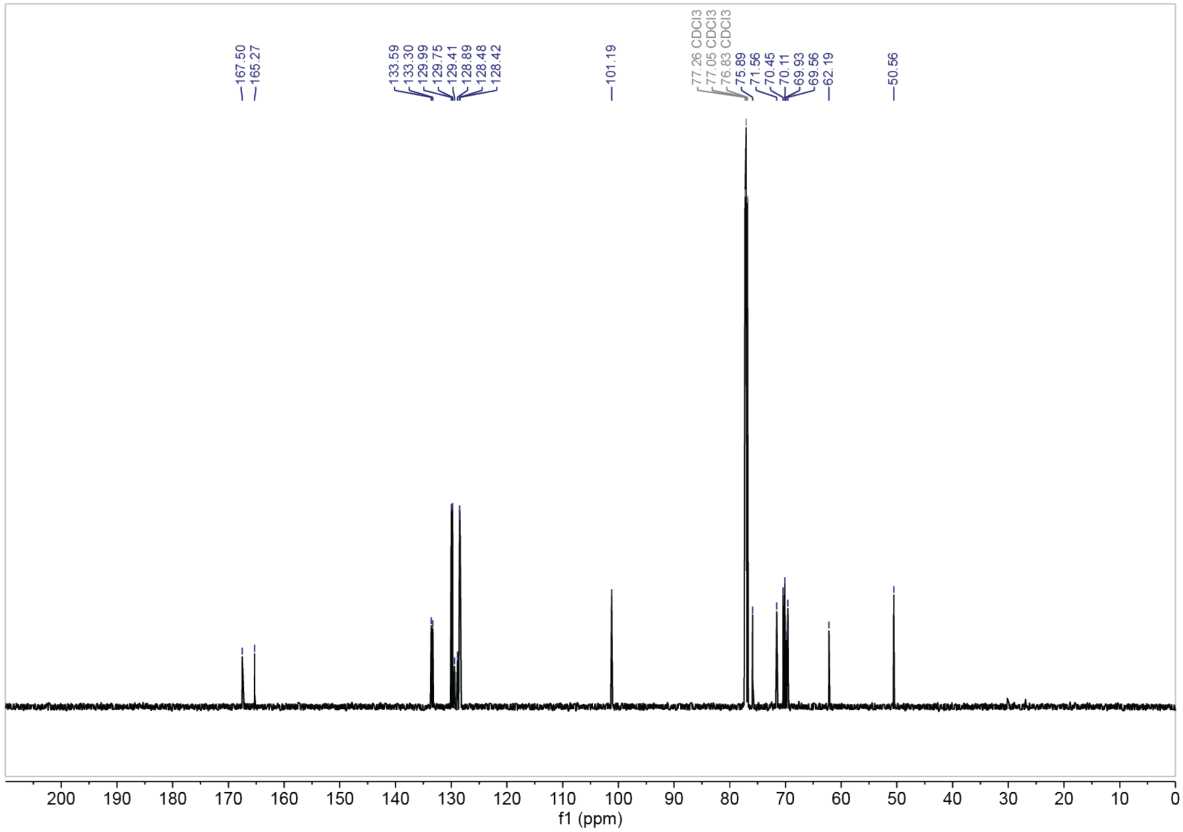
(**5**) – ^{13}C NMR (151 MHz, CDCl$_3$)



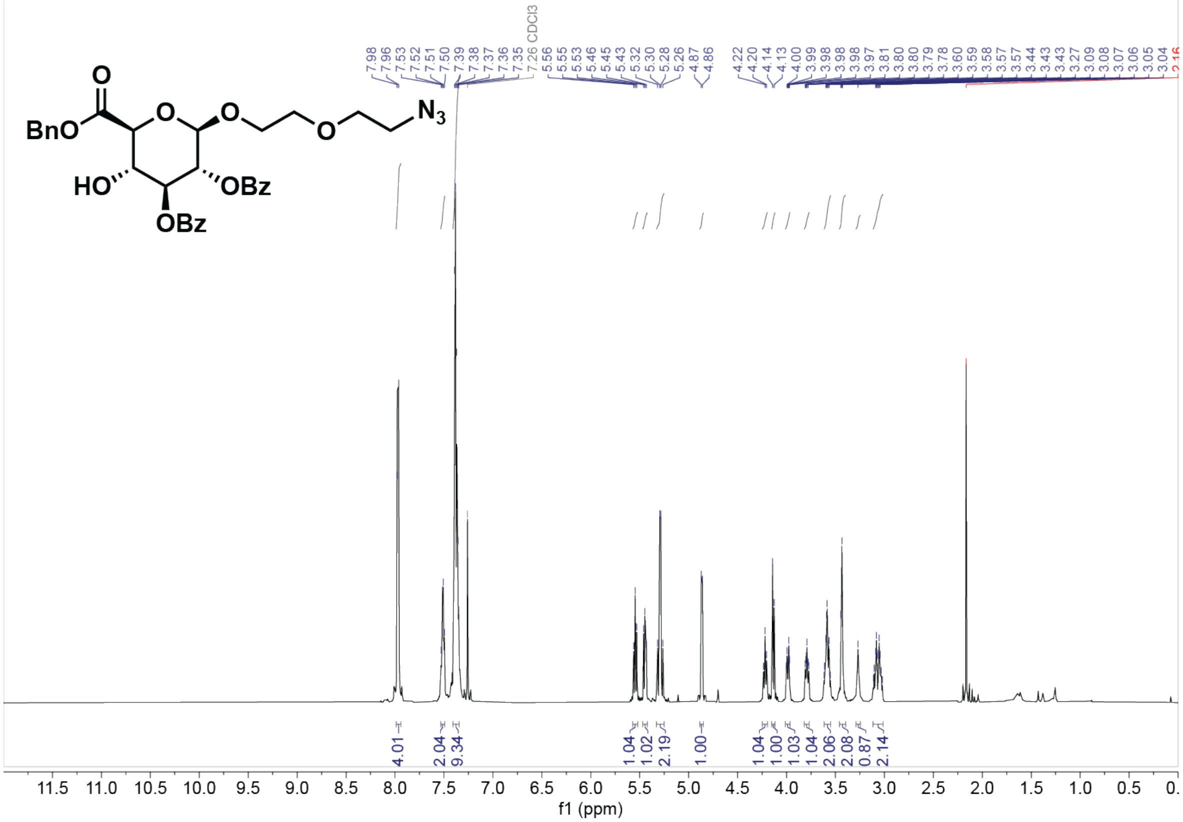
(**6**) – ^{1}H NMR (600 MHz, CDCl$_3$)



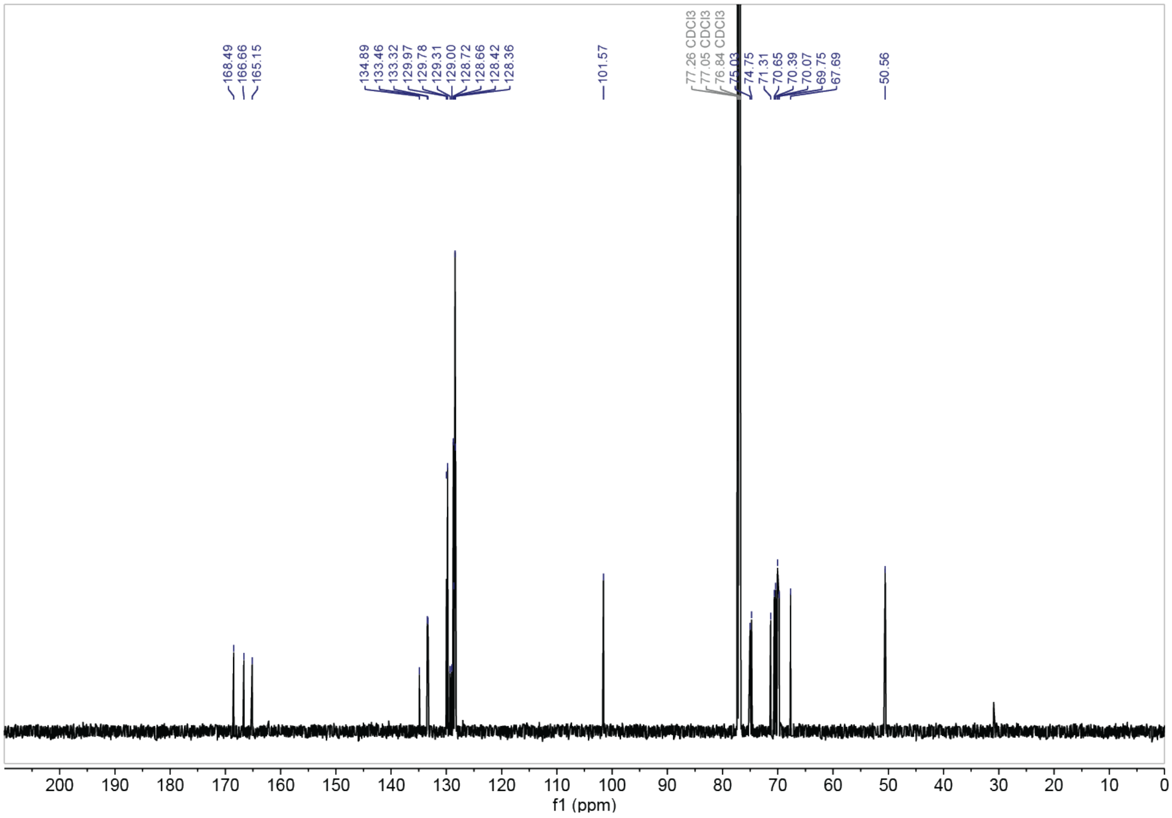
(**6**) – ^{13}C NMR (151 MHz, CDCl$_3$)



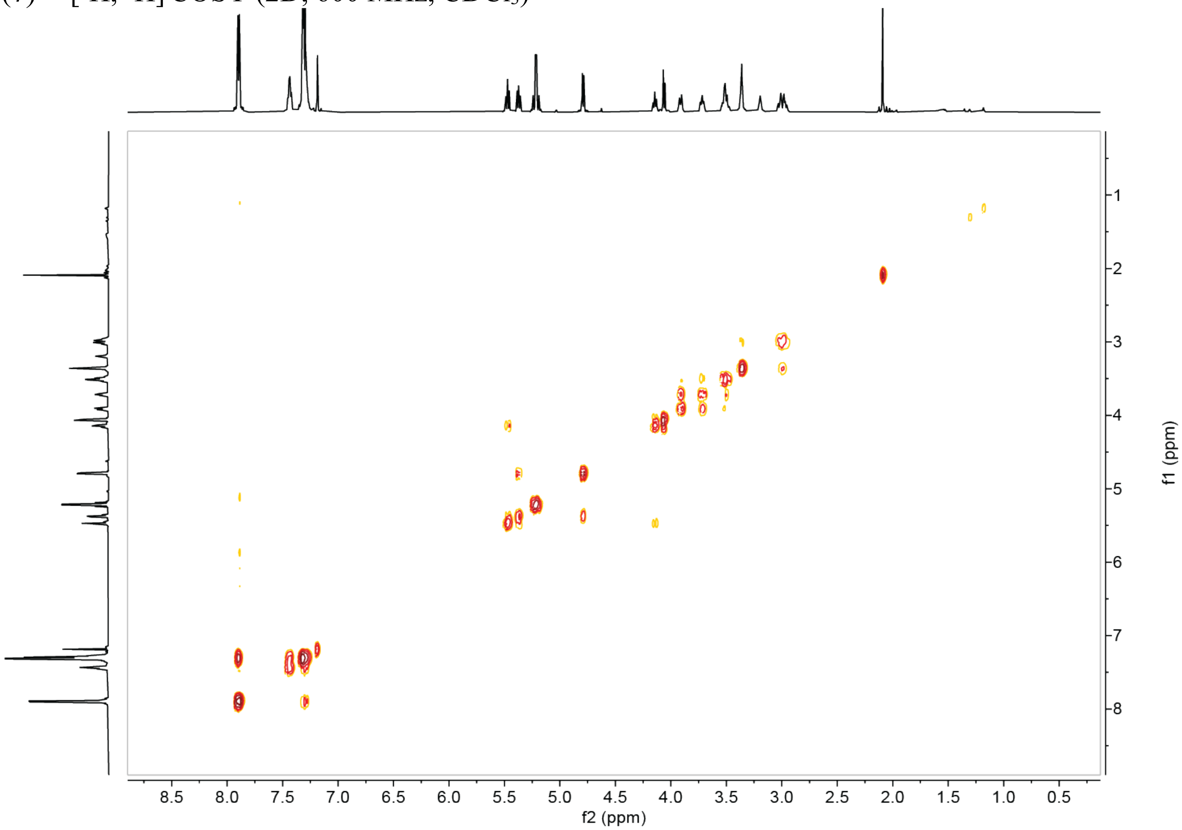
(**7**) – ^{1}H NMR (600 MHz, CDCl$_3$)



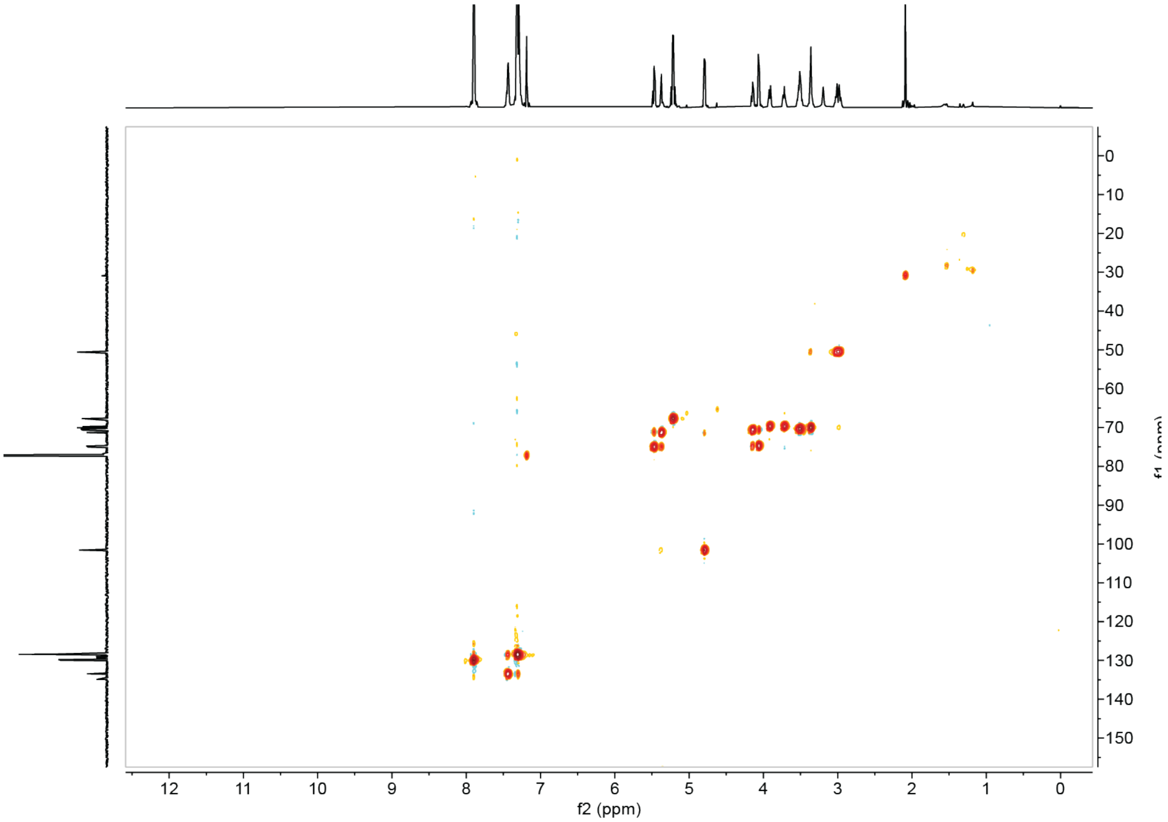
(**7**) – ^{13}C NMR (151 MHz, CDCl$_3$)



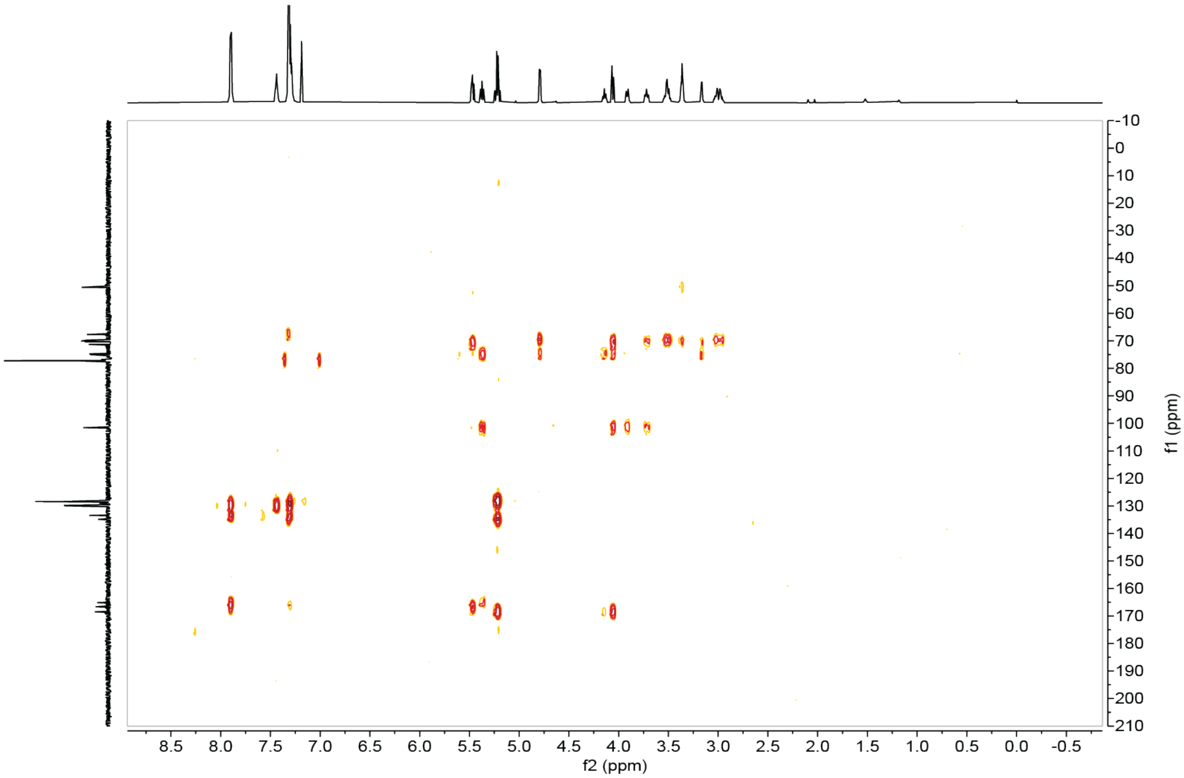
(**7**) – [^{1}H, ^{1}H] COSY (2D, 600 MHz, CDCl$_3$)



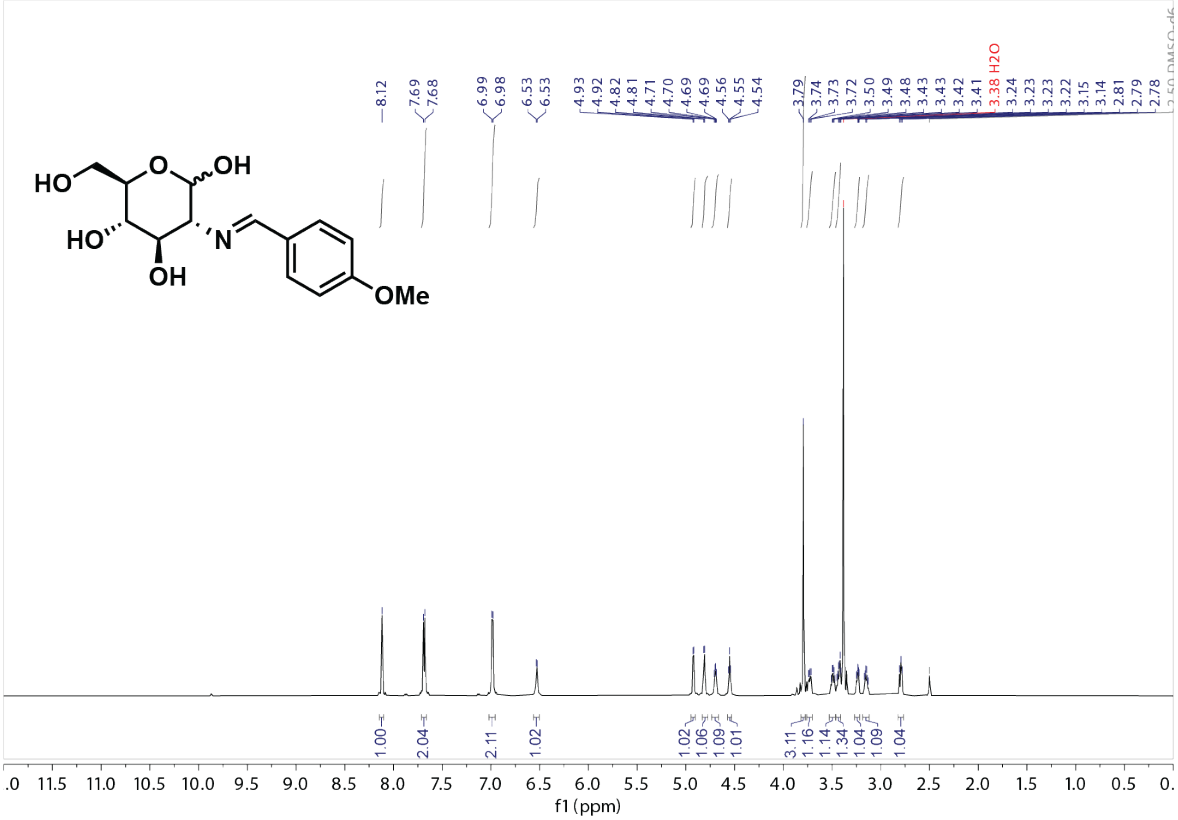
(**7**) – [^{1}H, ^{13}C] HSQC (2D, 600 MHz, CDCl$_3$)



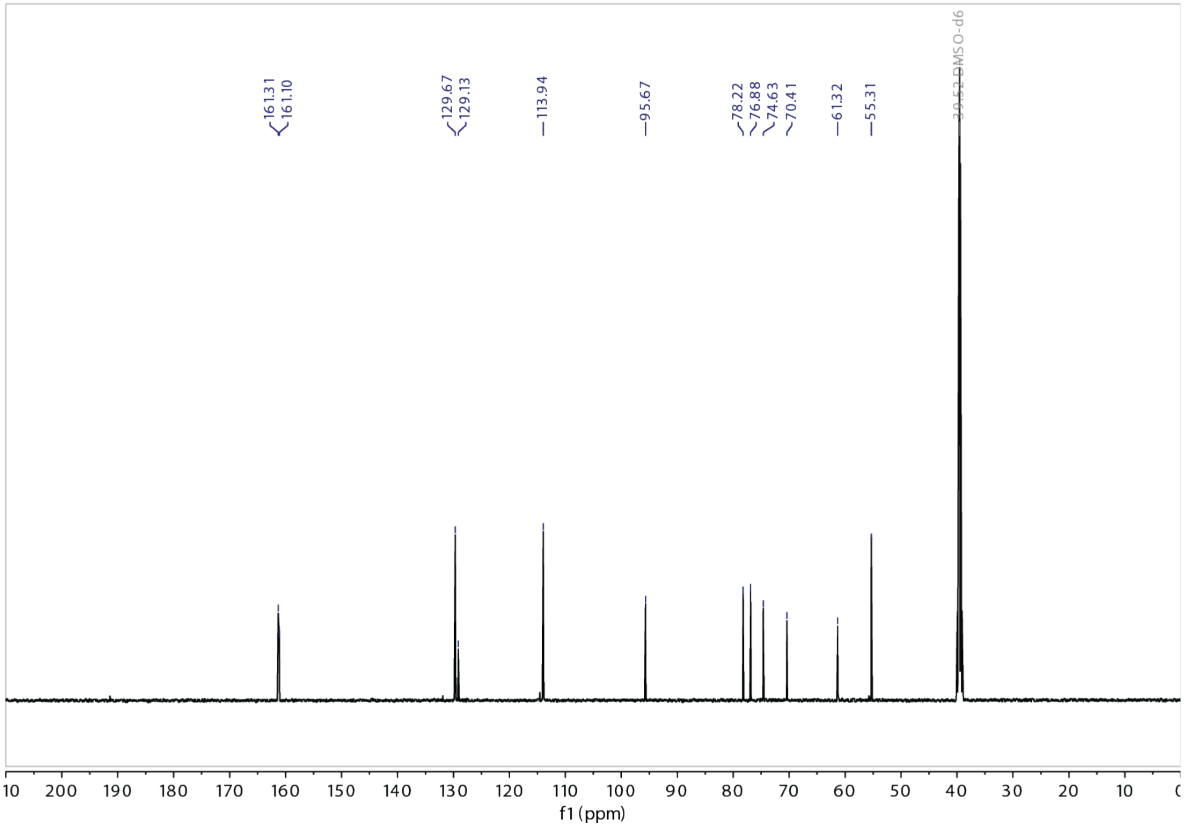
(**7**) – [^{1}H, ^{13}C] HMBC (2D, 600 MHz, CDCl$_3$)



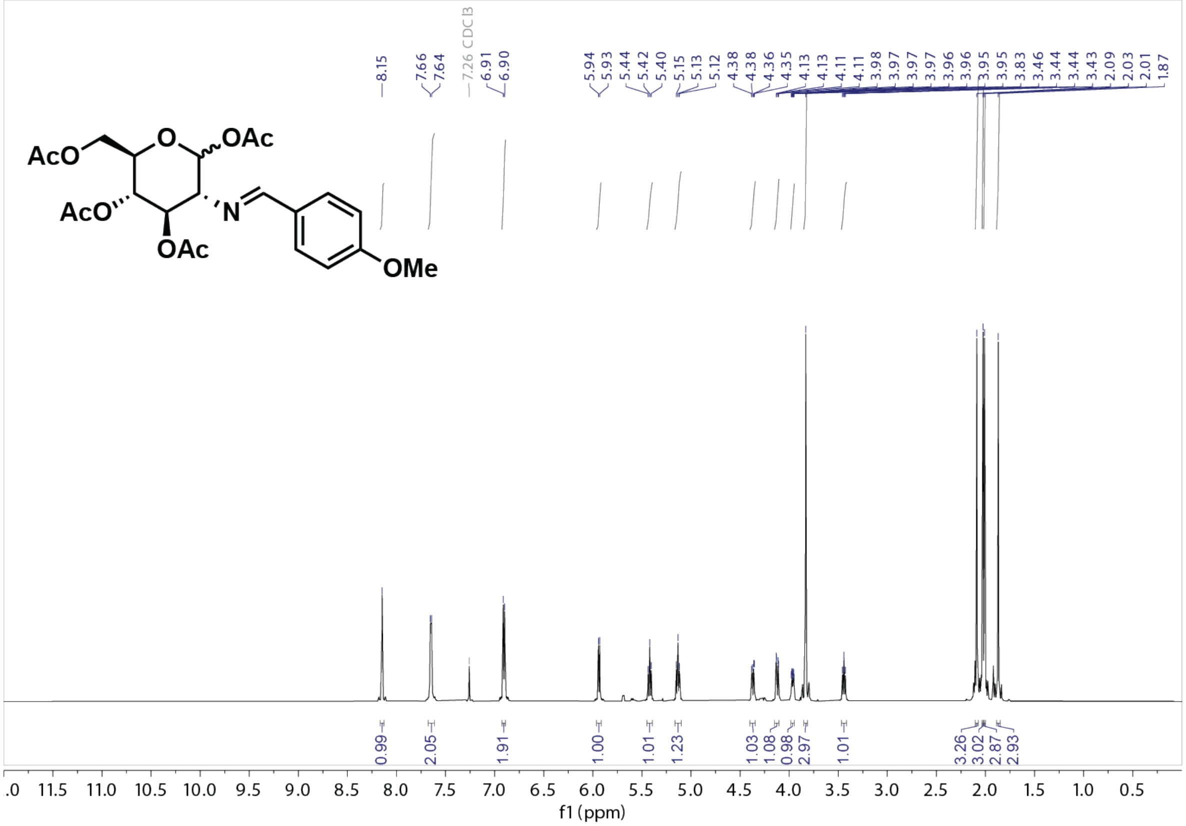
(**8**) – ^{1}H NMR (600 MHz, CDCl$_3$)



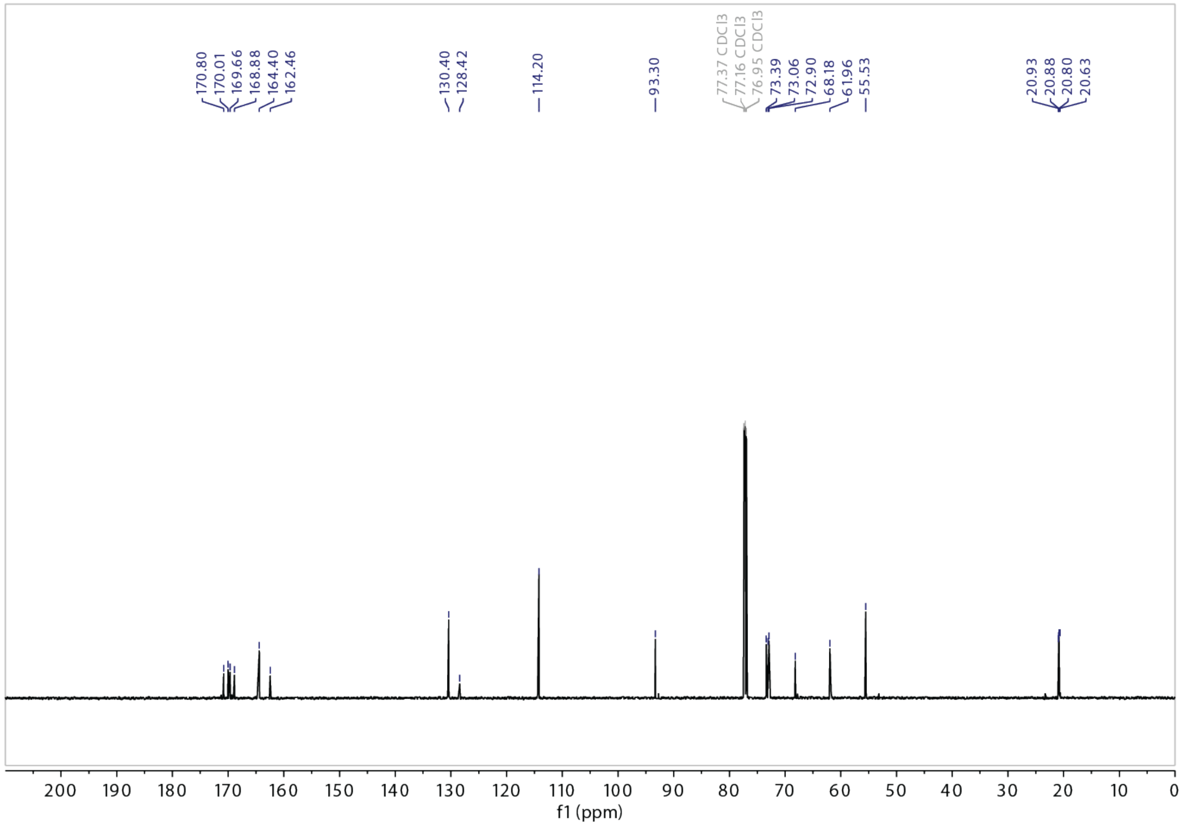
(**8**) – ^{13}C NMR (151 MHz, CDCl$_3$)



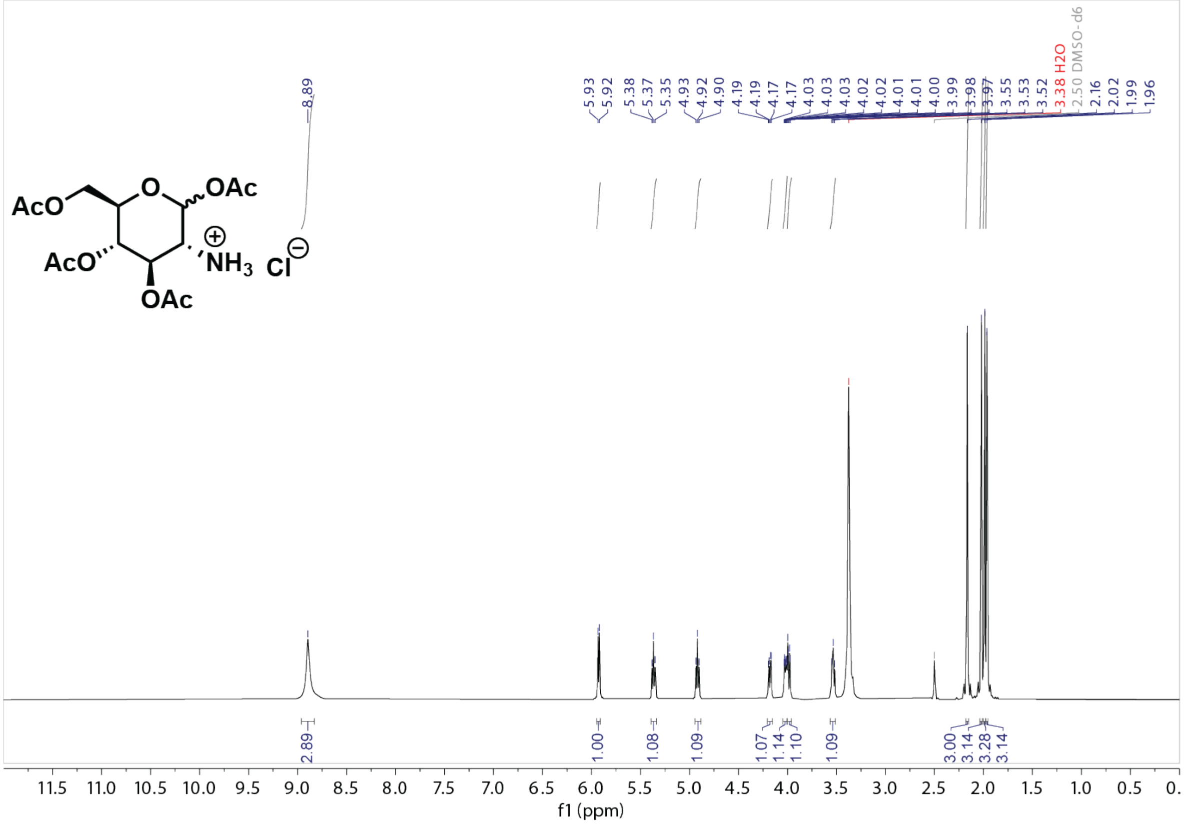
(**9**) – ^{1}H NMR (600 MHz, CDCl$_3$)



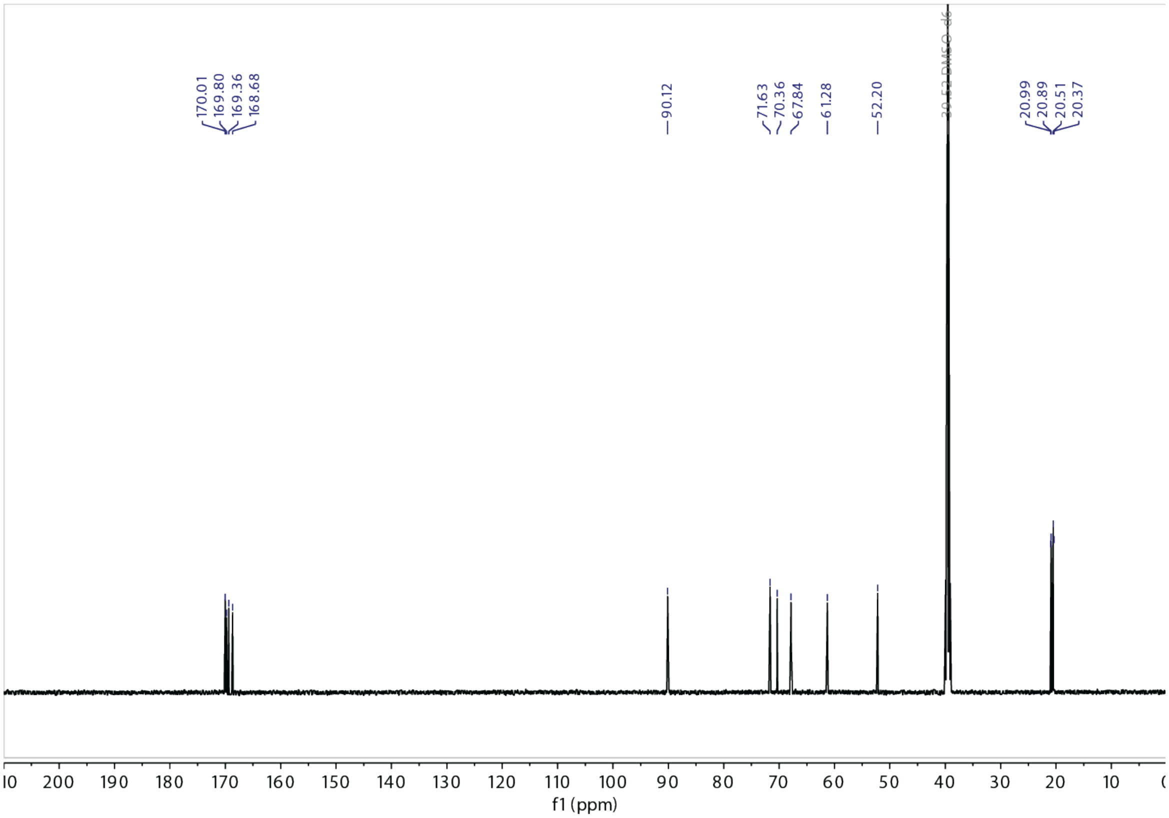
(**9**) – ^{13}C NMR (151 MHz, CDCl$_3$)



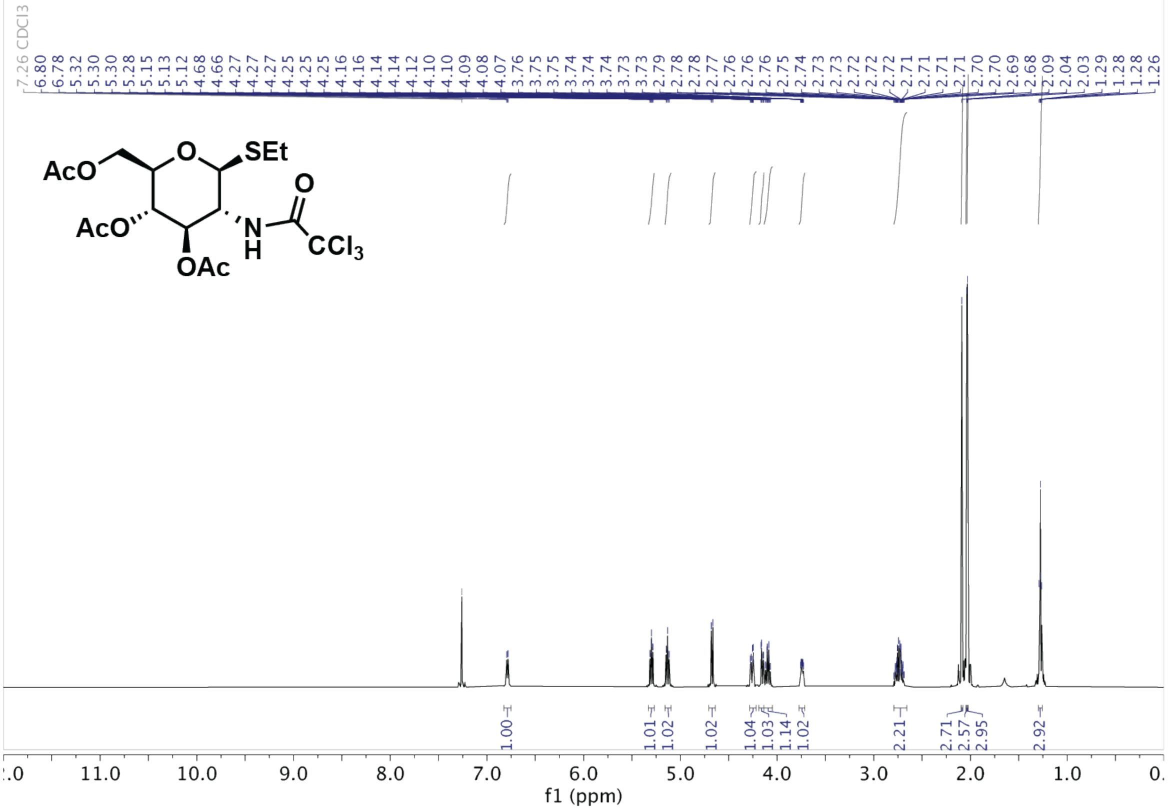
(**10**) – ^{1}H NMR (600 MHz, CDCl$_3$)



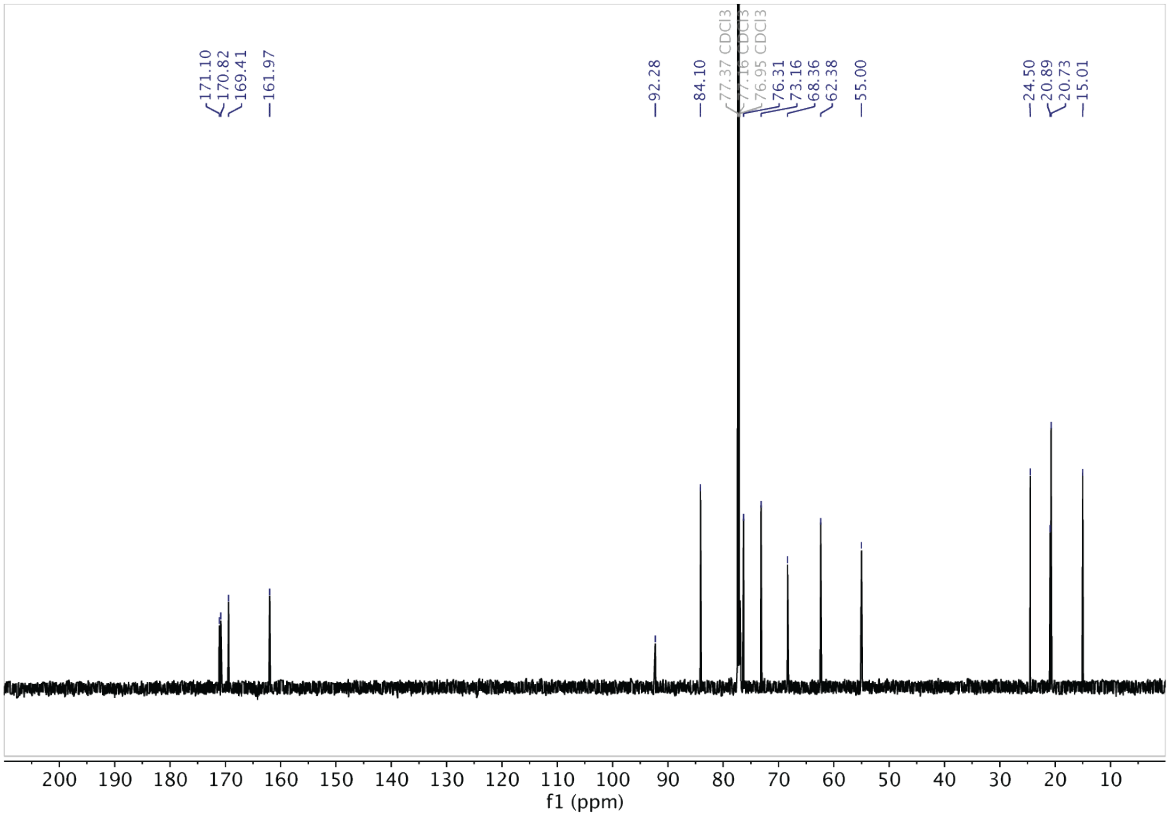
(**10**) – ^{13}C NMR (151 MHz, CDCl$_3$)



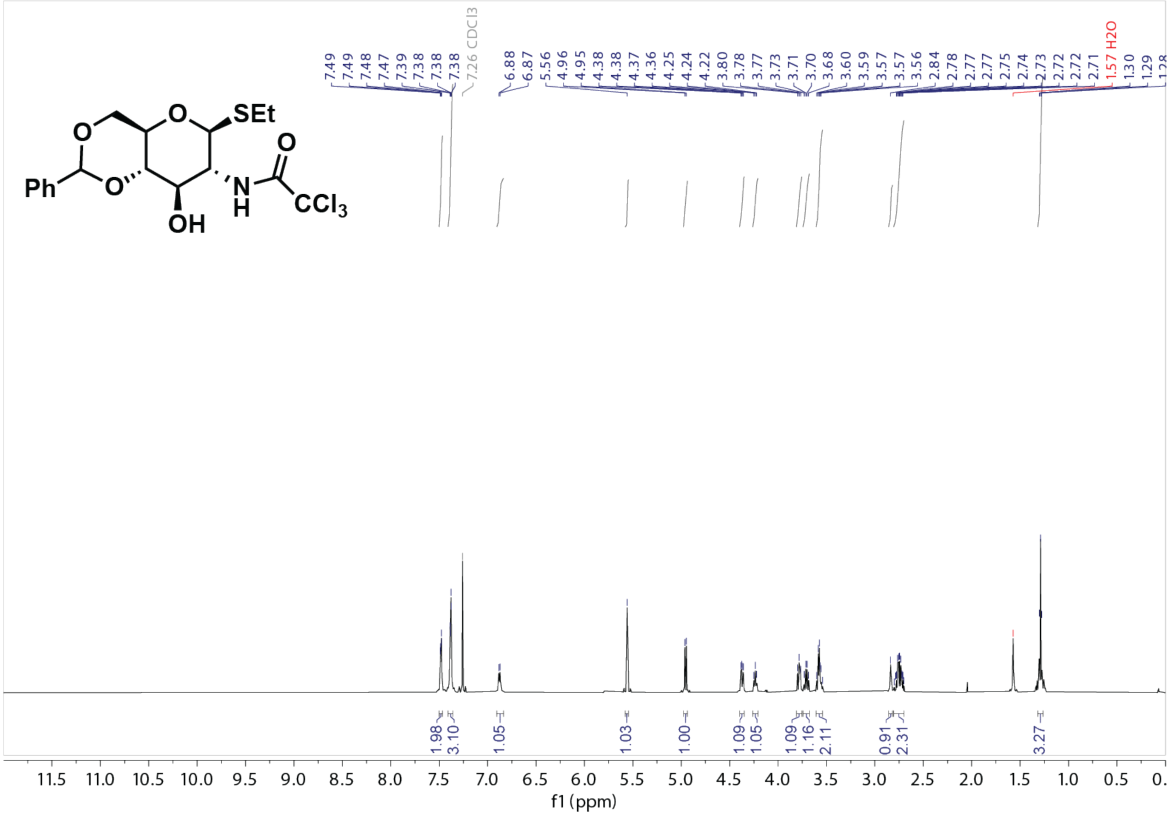
(**11**) – ^{1}H NMR (600 MHz, CDCl$_3$)



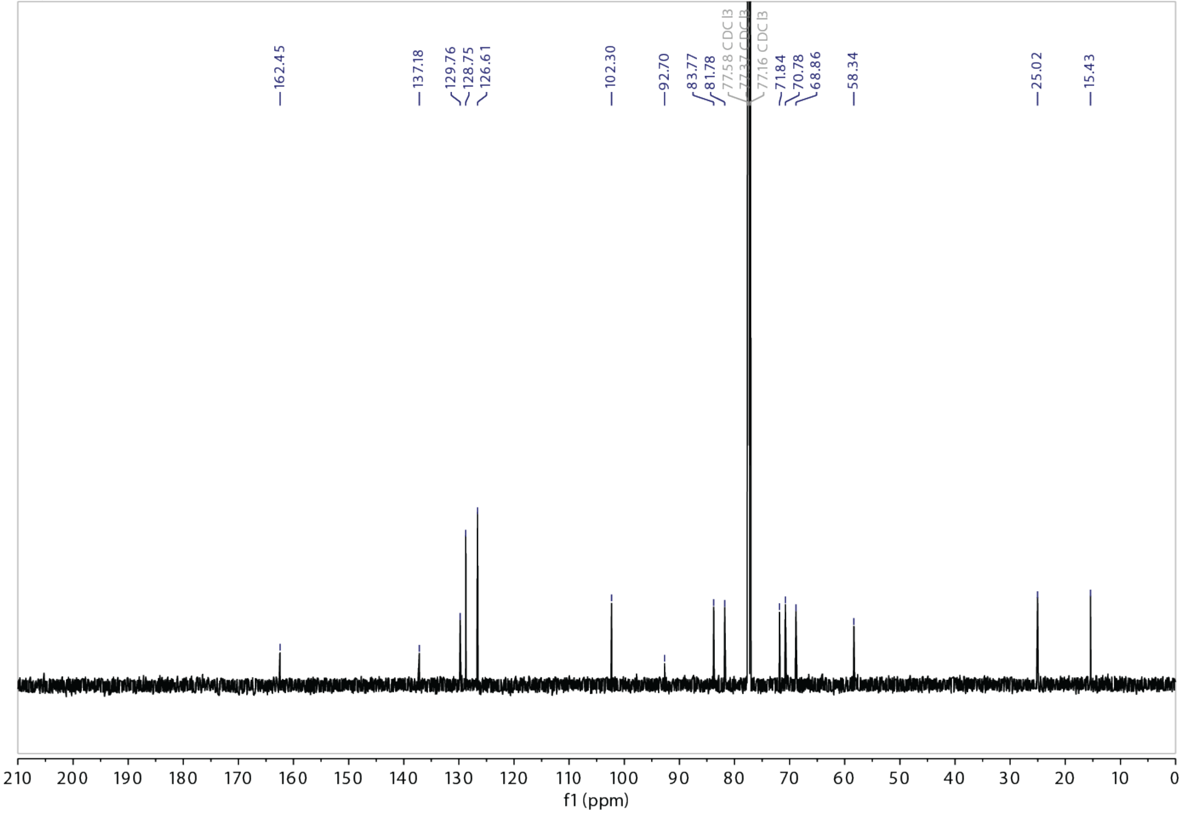
(**11**) – ^{13}C NMR (151 MHz, CDCl$_3$)



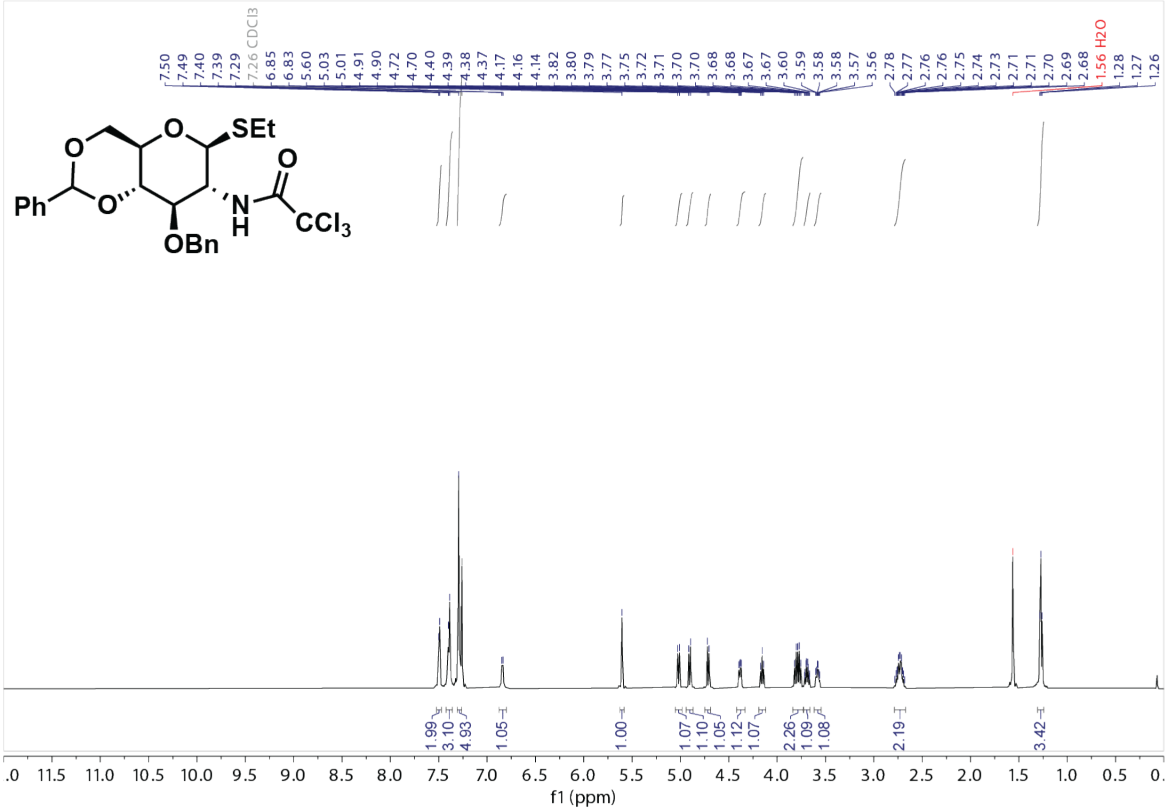
(**12**) – ^{1}H NMR (600 MHz, $CDCl_3$)



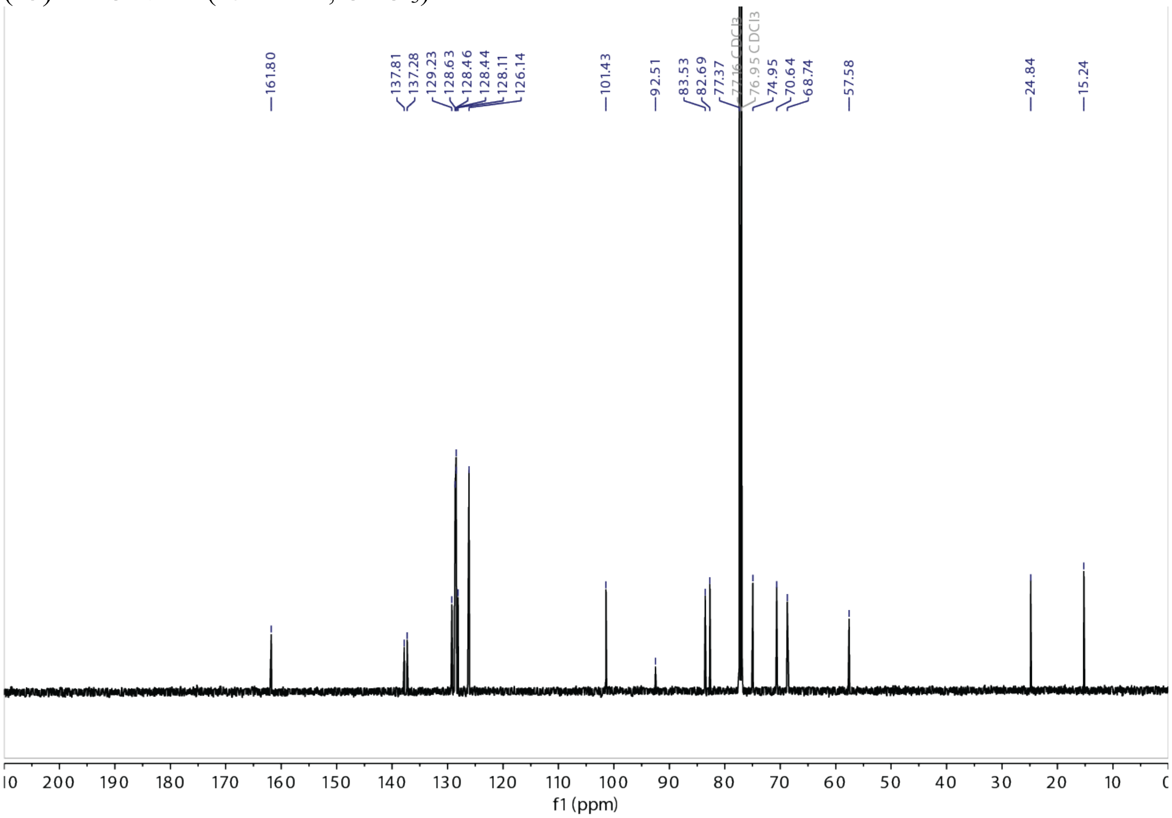
(**12**) – ^{13}C NMR (151 MHz, $CDCl_3$)



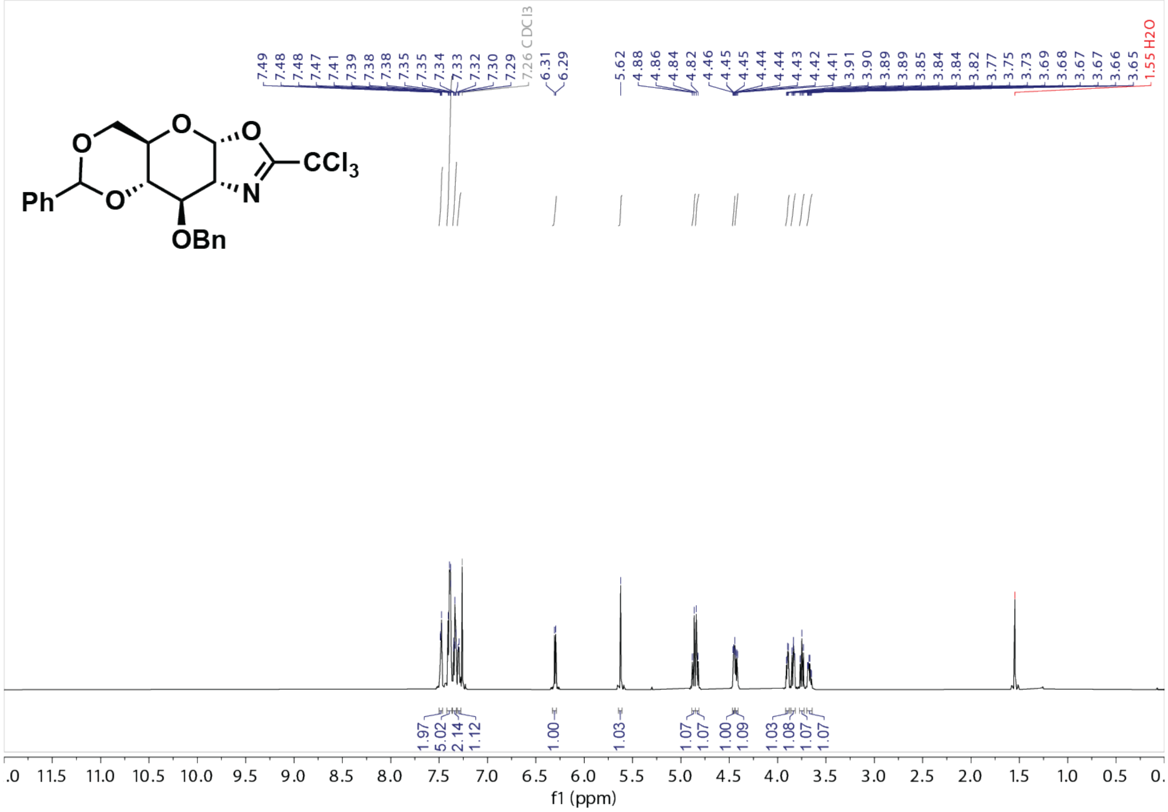
(**13**) – ^{1}H NMR (600 MHz, CDCl$_3$)



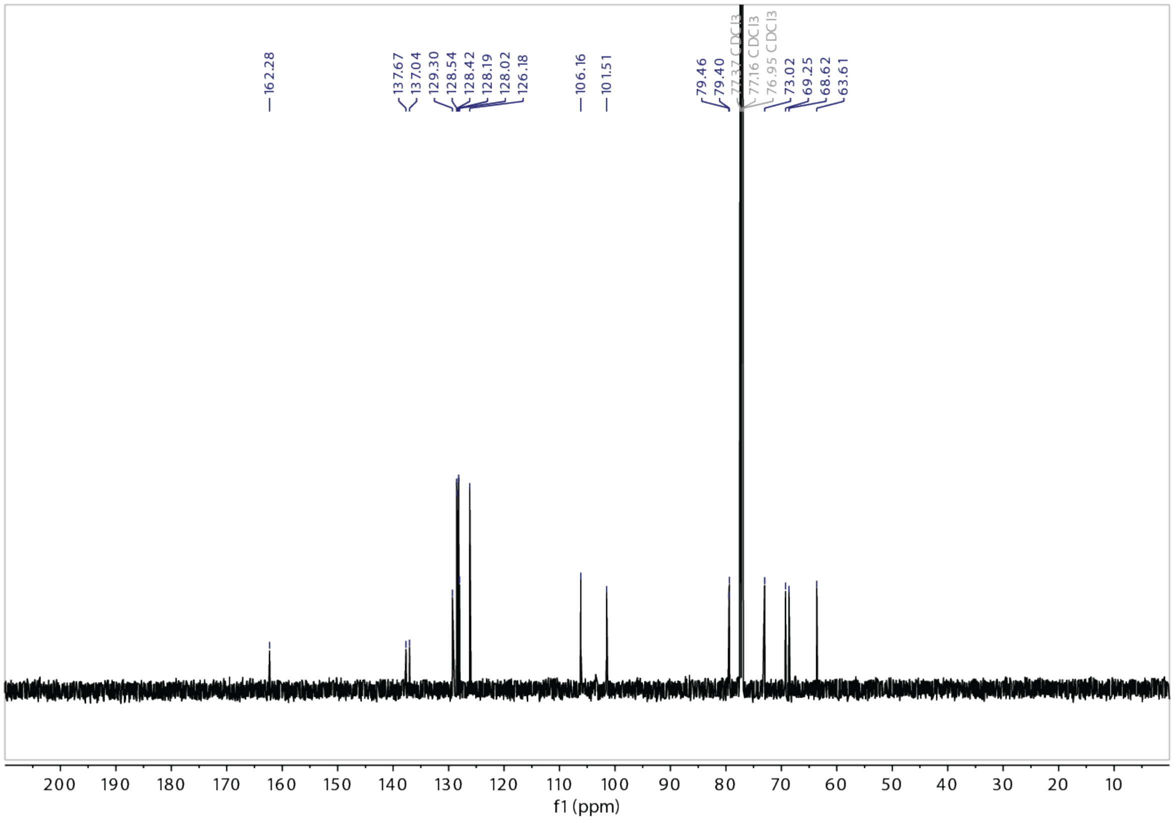
(**13**) – ^{13}C NMR (151 MHz, CDCl$_3$)



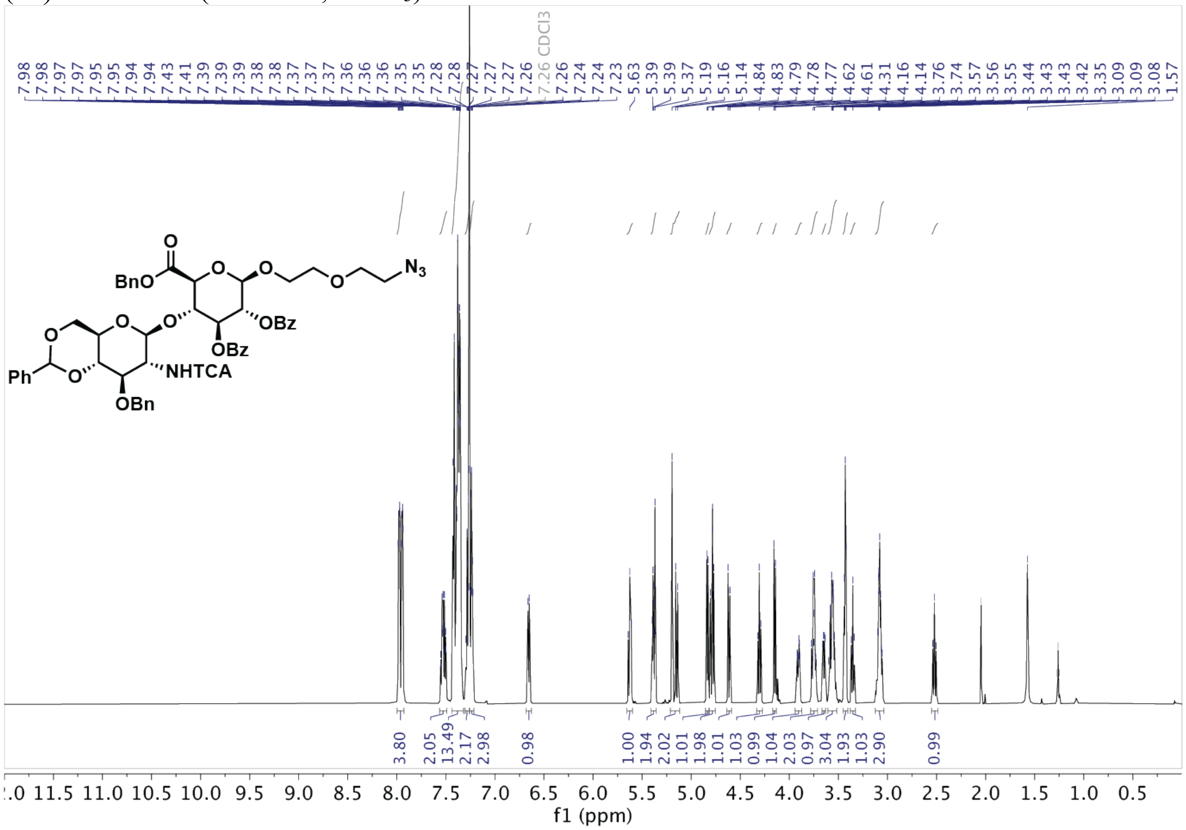
(**14**) – ^{1}H NMR (600 MHz, CDCl$_3$)



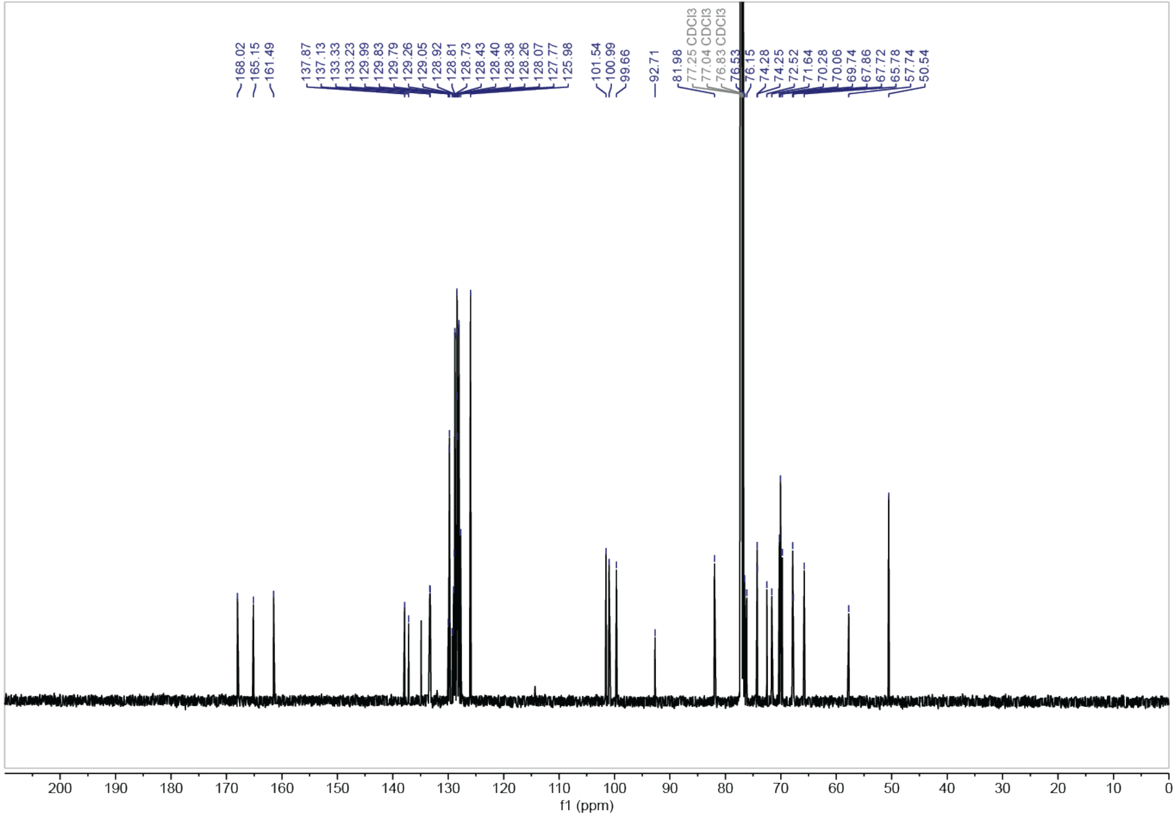
(**14**) – ^{13}C NMR (151 MHz, CDCl$_3$)



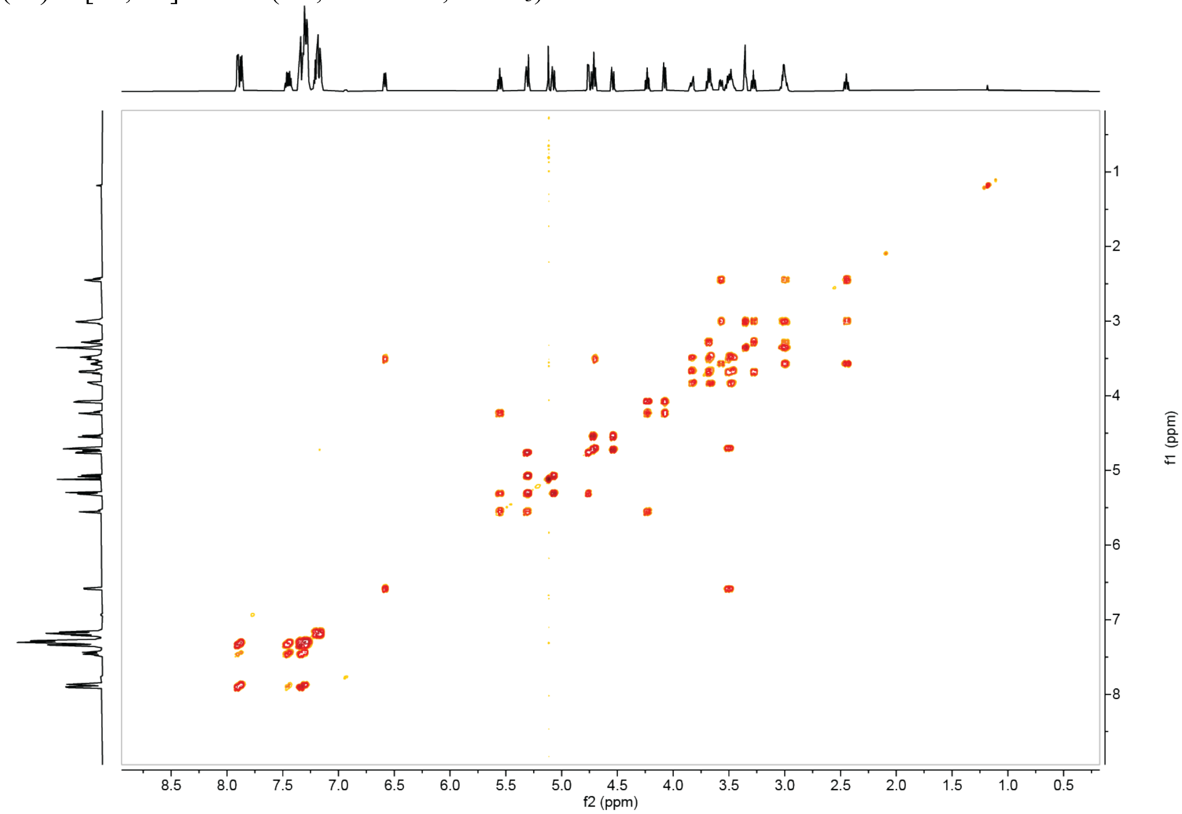
(**15**) – ^{1}H NMR (600 MHz, $CDCl_3$)



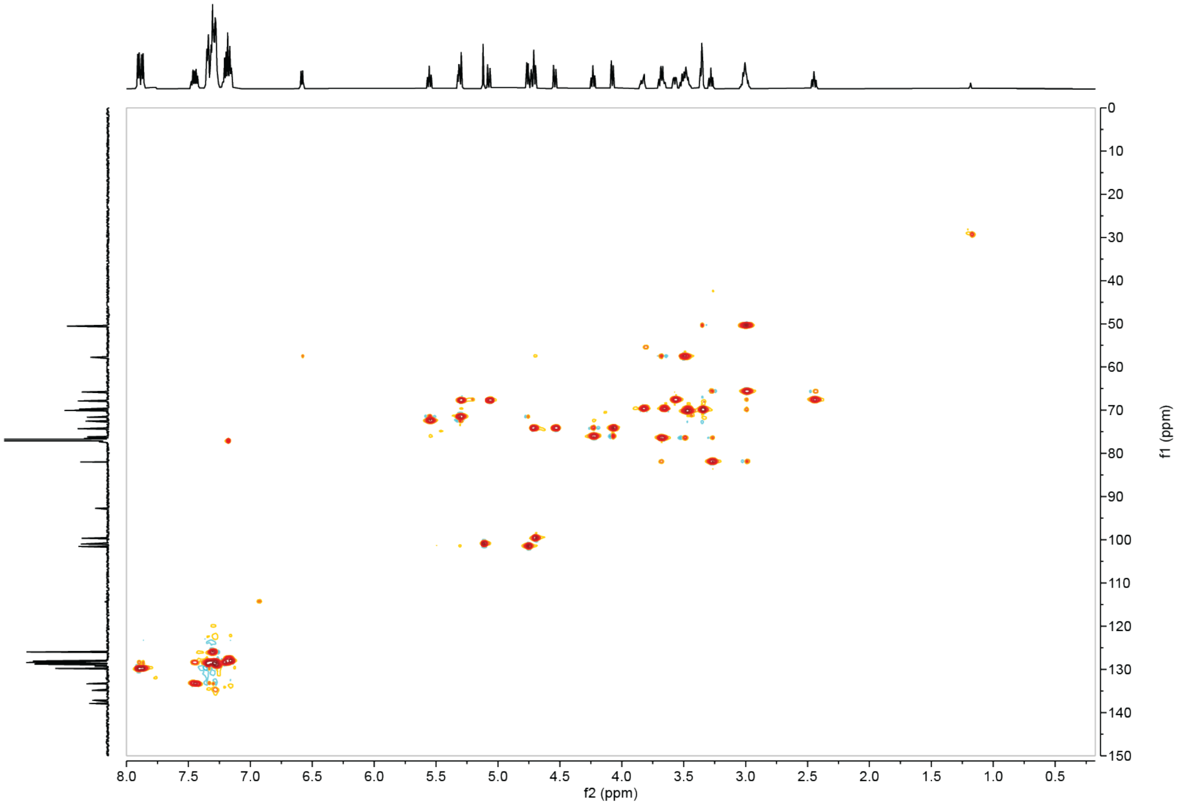
(**15**) – ^{13}C NMR (151 MHz, $CDCl_3$)



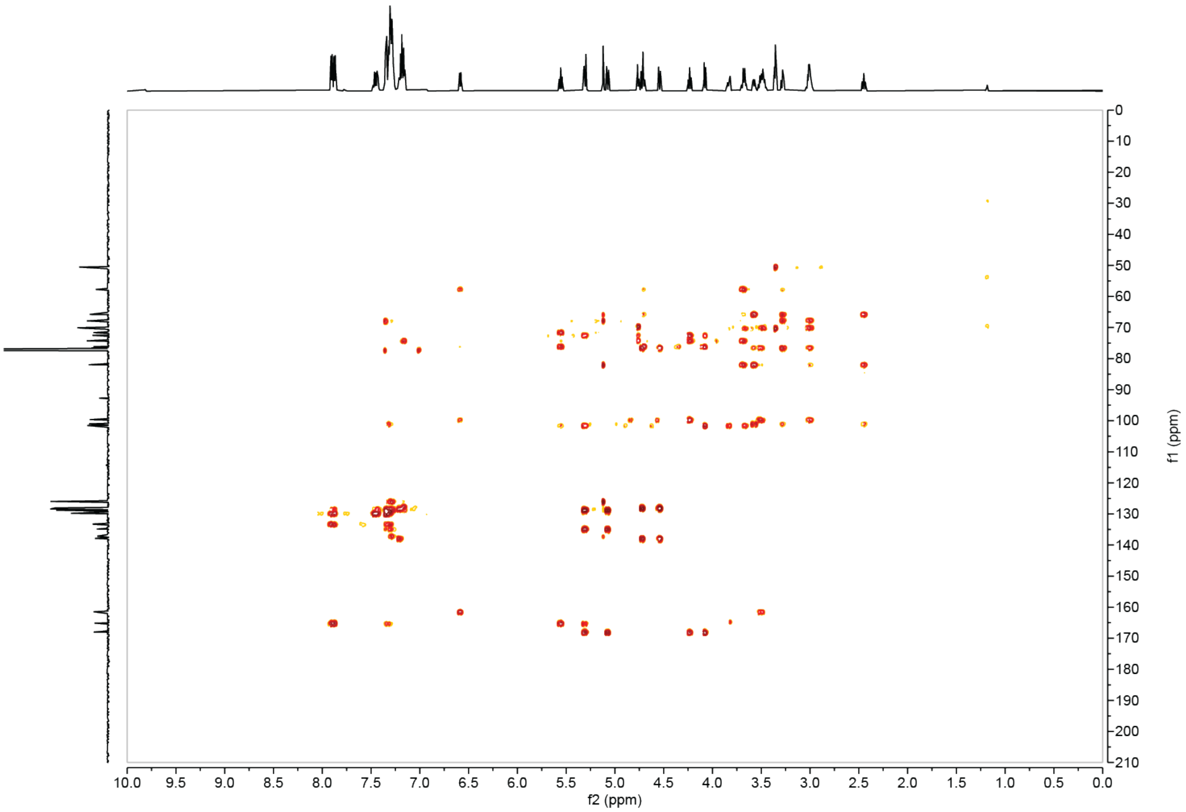
(15) – [^{1}H, ^{1}H] COSY (2D, 600 MHz, CDCl$_3$)



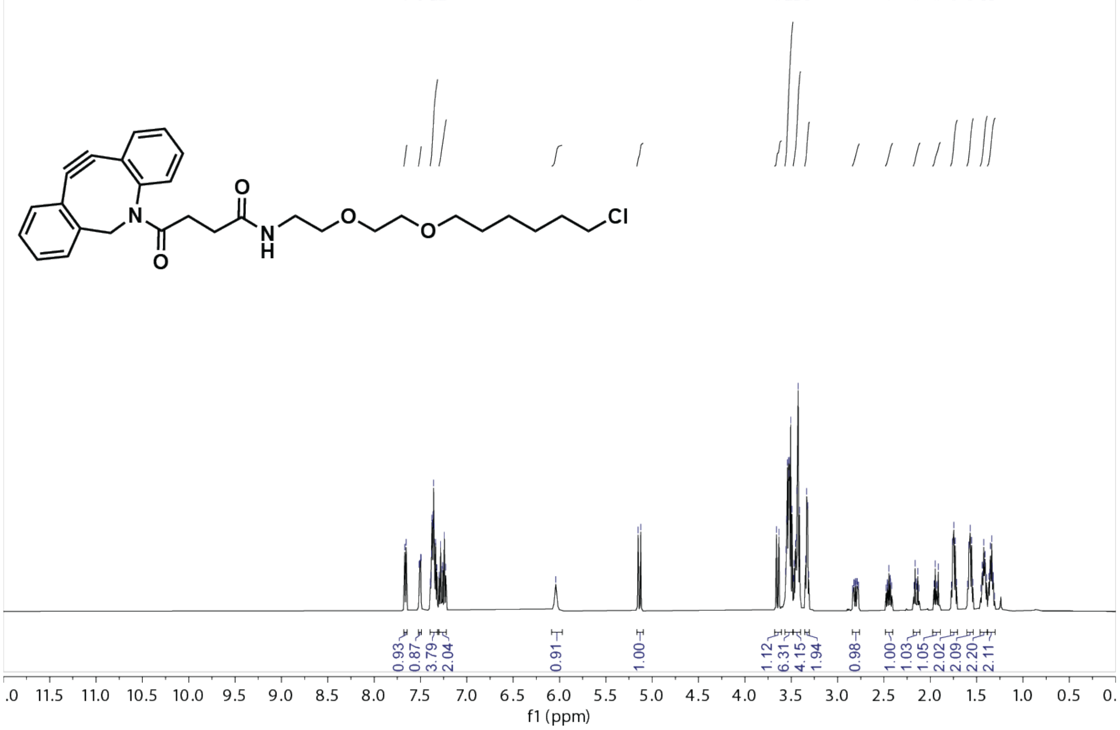
(15) – [^{1}H, ^{13}C] HSQC (2D, 600 MHz, CDCl$_3$)



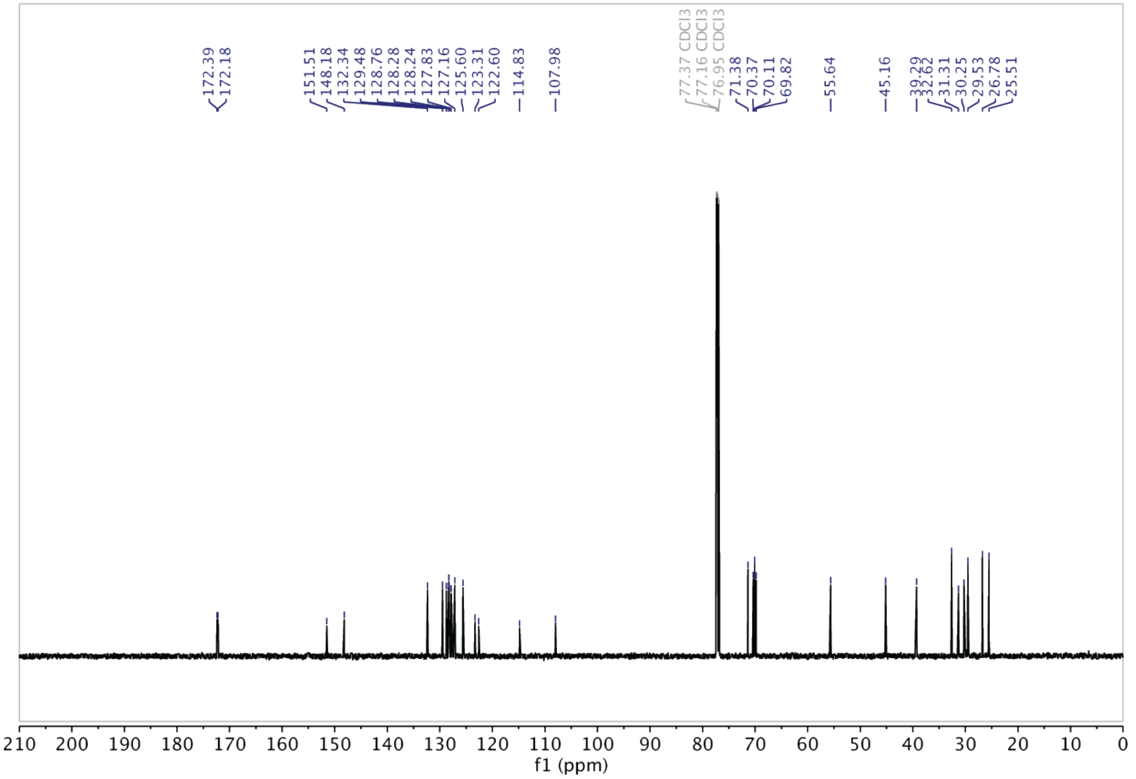
(**15**) – [^{1}H, ^{13}C] HMBC (2D, 600 MHz, CDCl$_3$)



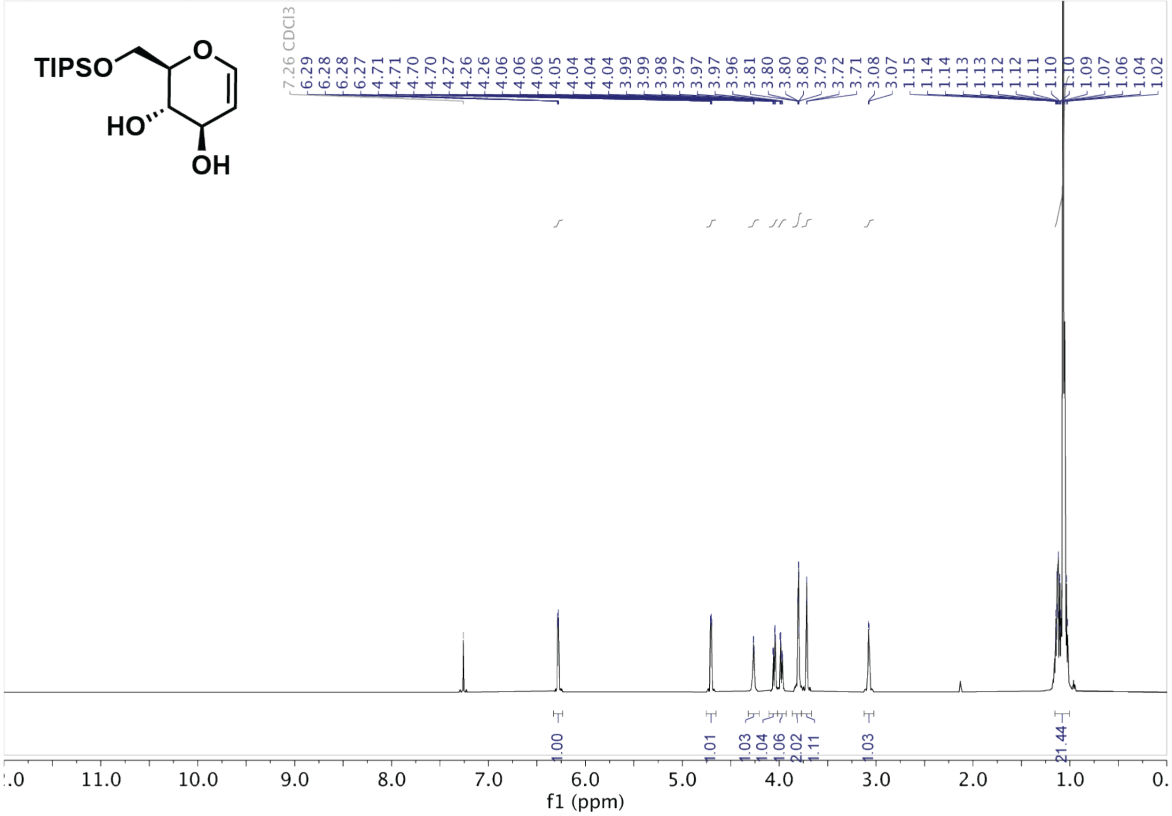
(**17**) – ^{1}H NMR (600 MHz, $CDCl_3$)



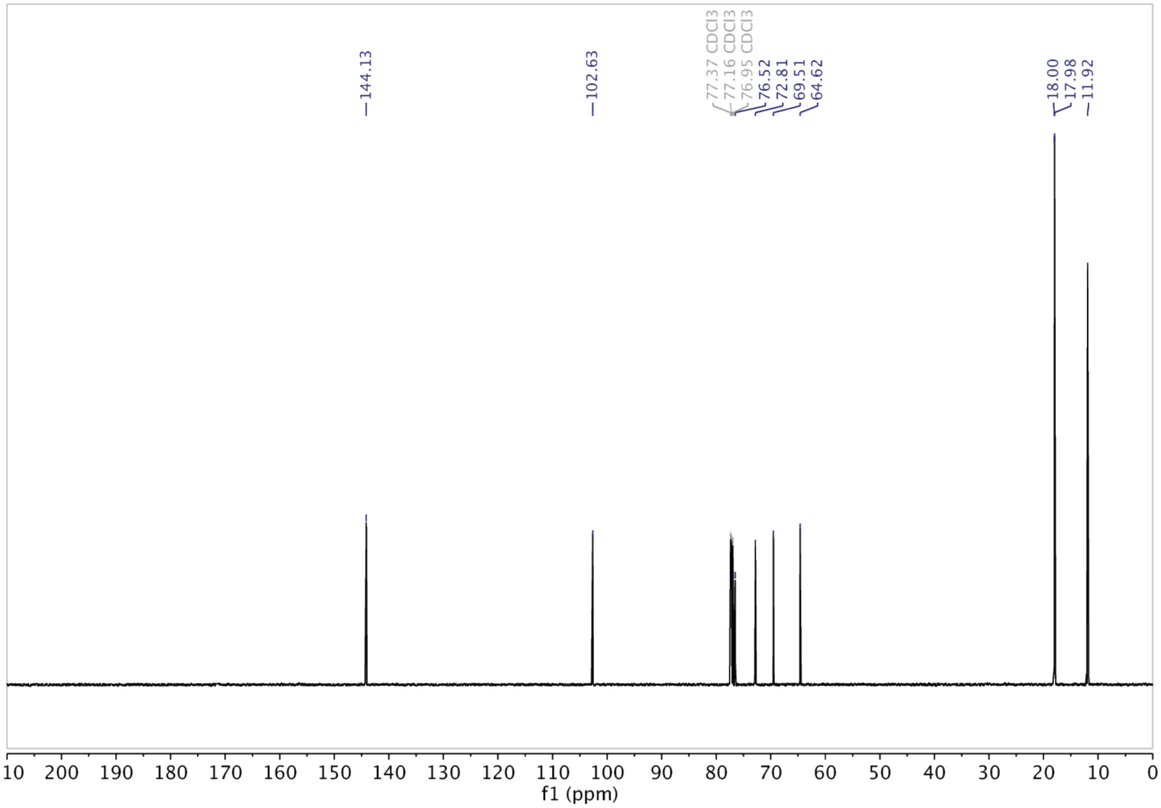
(**17**) – ^{13}C NMR (151 MHz, $CDCl_3$)



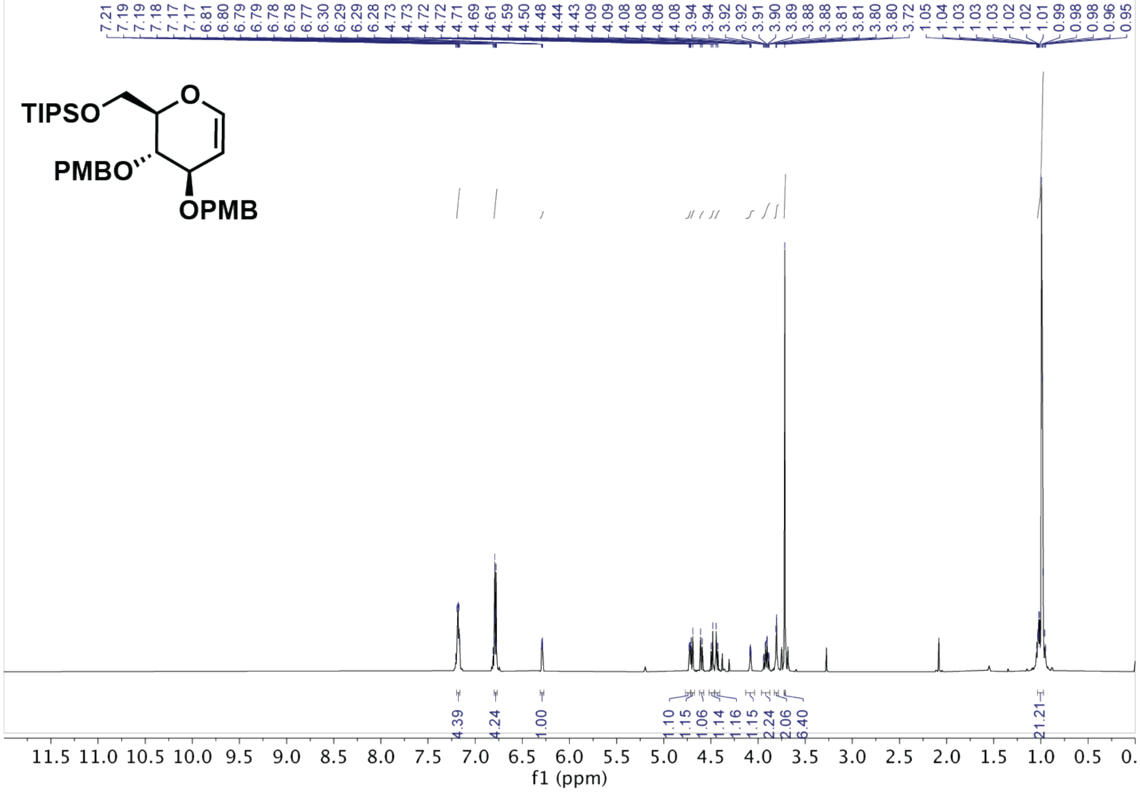
(**18**) – ^{1}H NMR (600 MHz, CDCl$_3$)



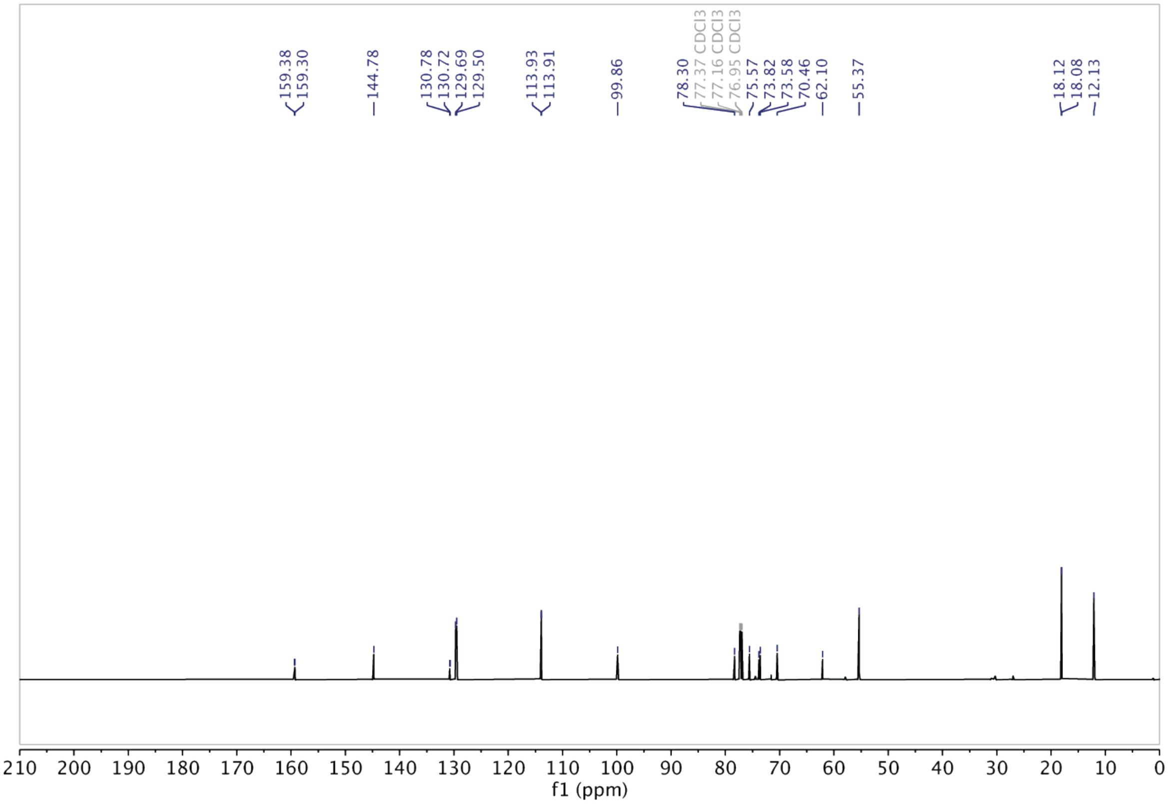
(**18**) – ^{13}C NMR (151 MHz, CDCl$_3$)



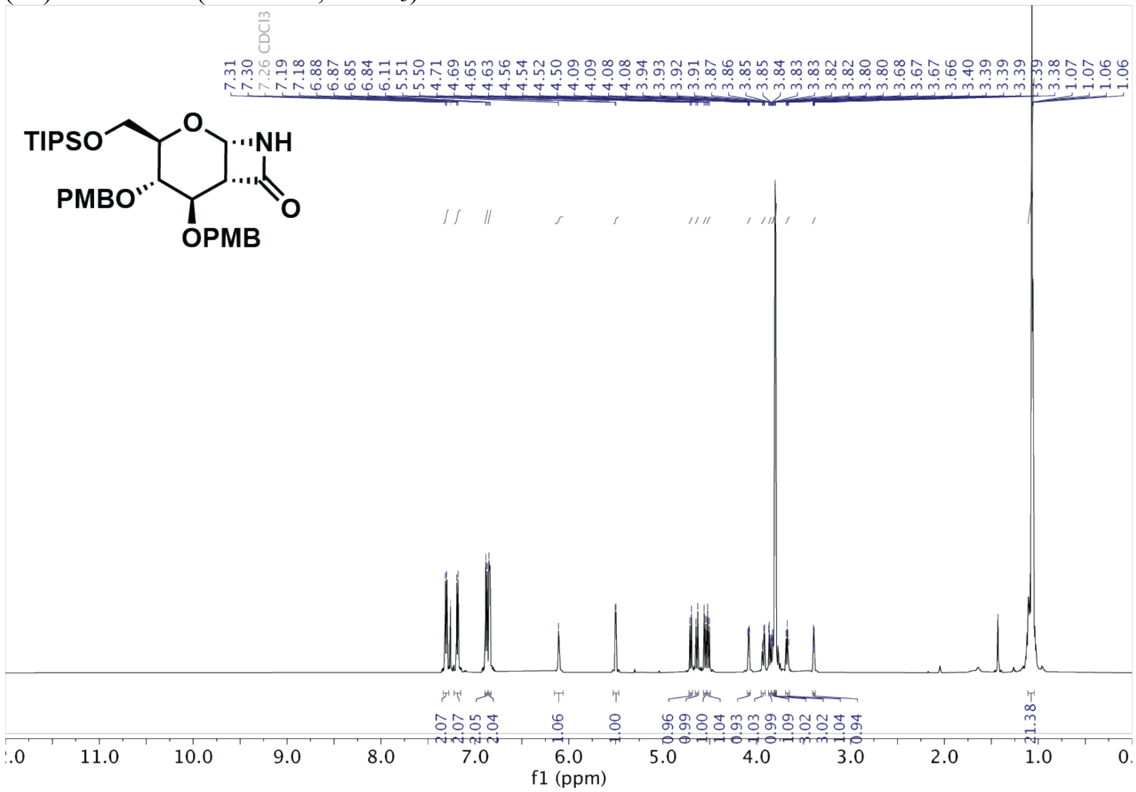
(**19**) – ^{1}H NMR (600 MHz, CDCl$_3$)



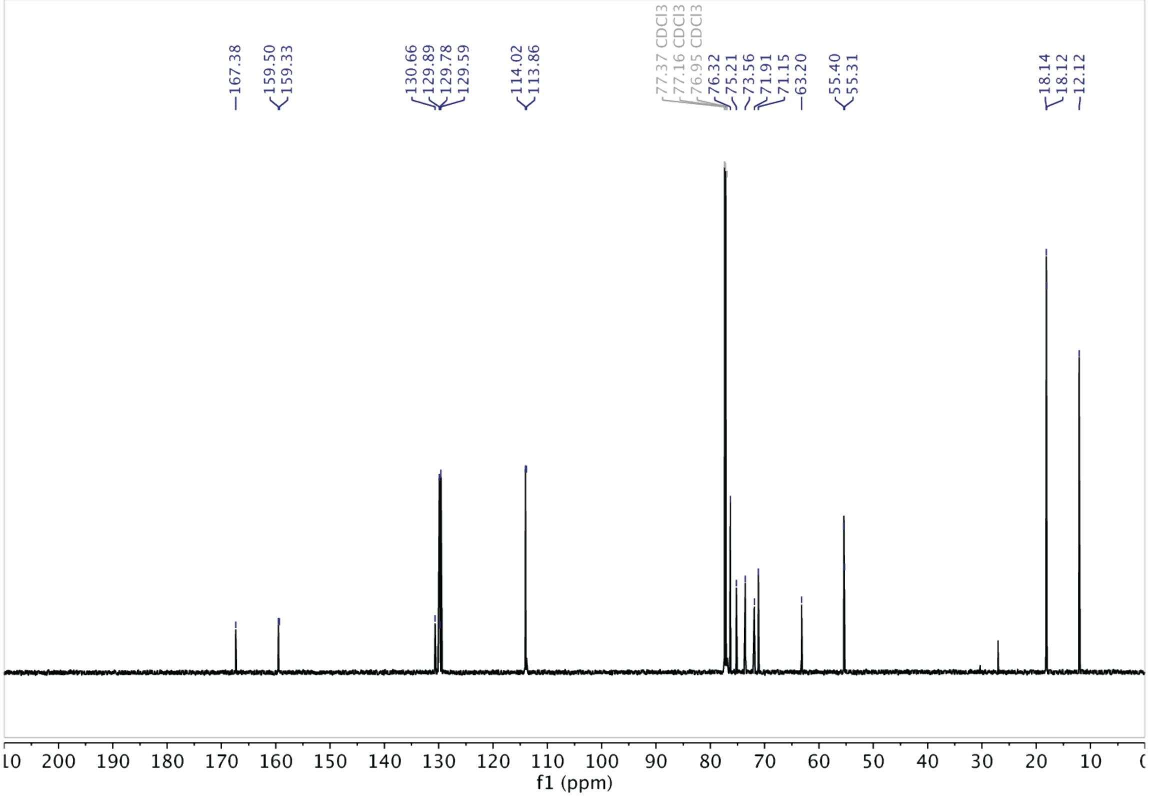
(**19**) – ^{13}C NMR (151 MHz, CDCl$_3$)



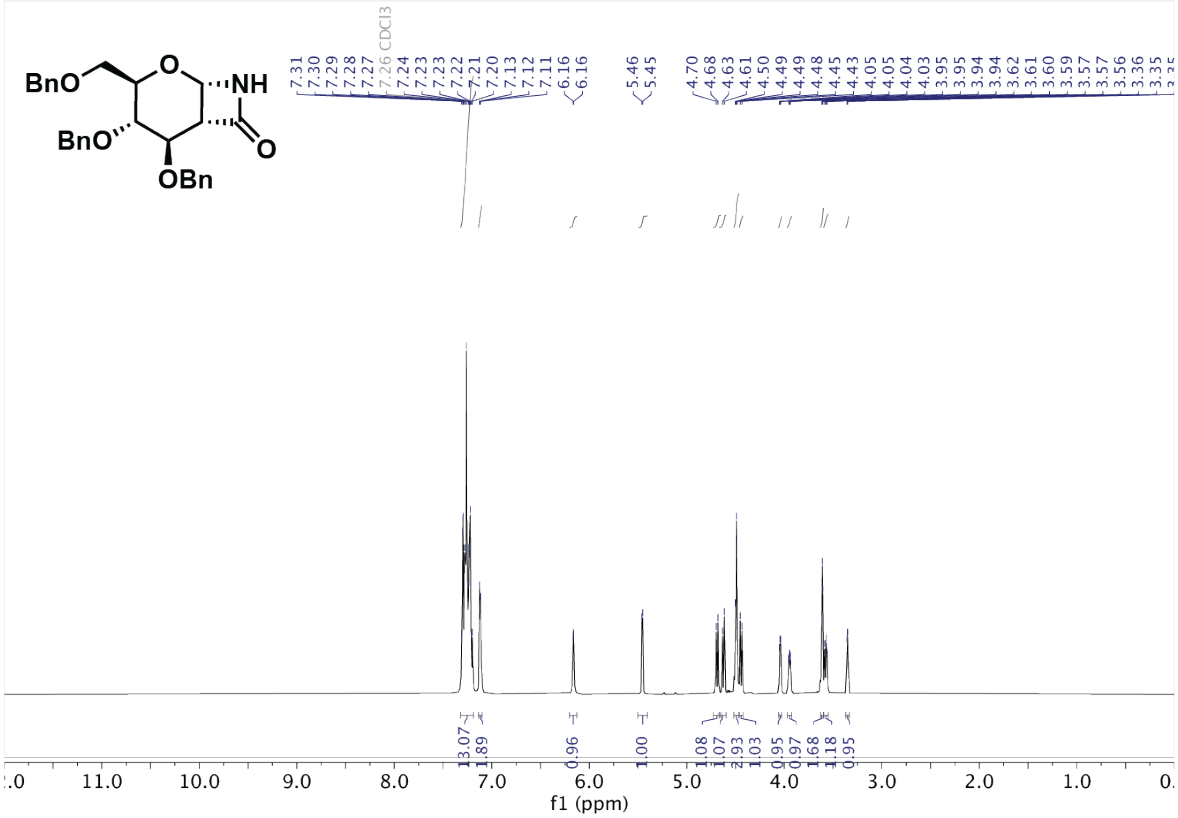
(**20**) – ^{1}H NMR (600 MHz, CDCl$_3$)



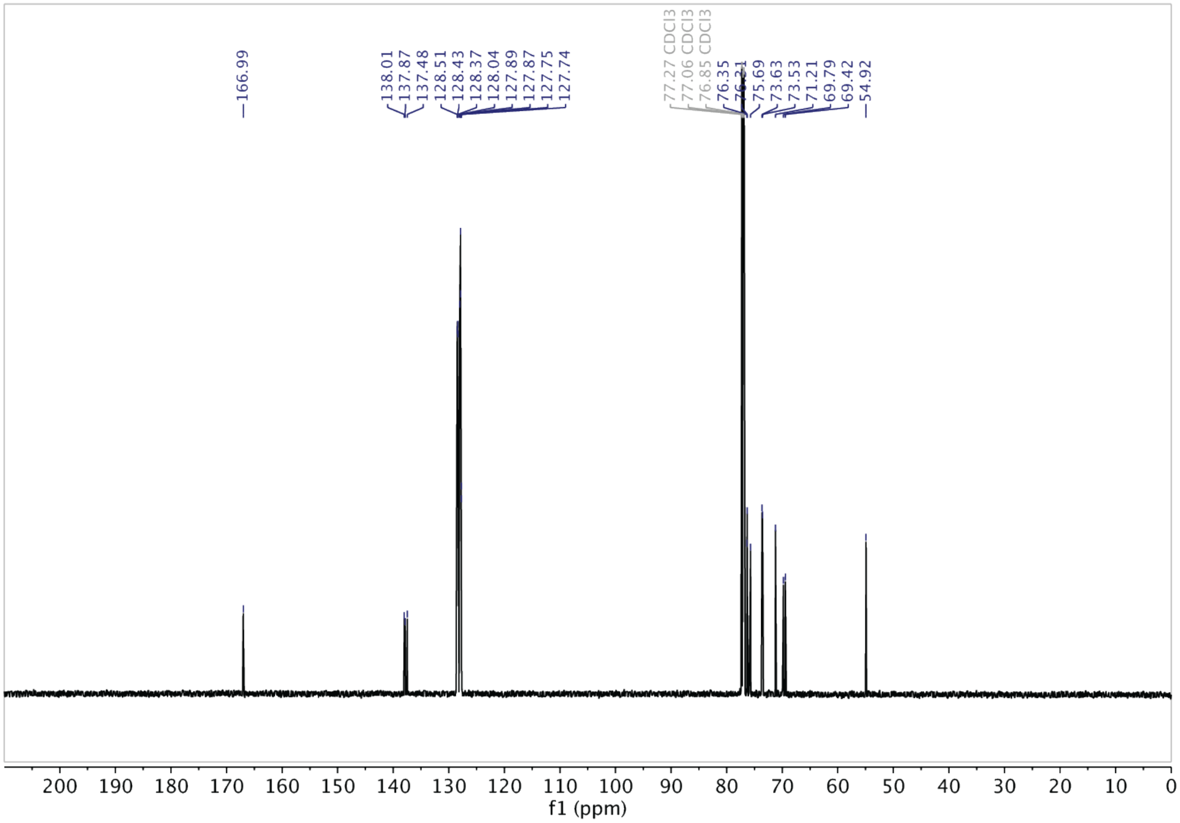
(**20**) – ^{13}C NMR (151 MHz, CDCl$_3$)



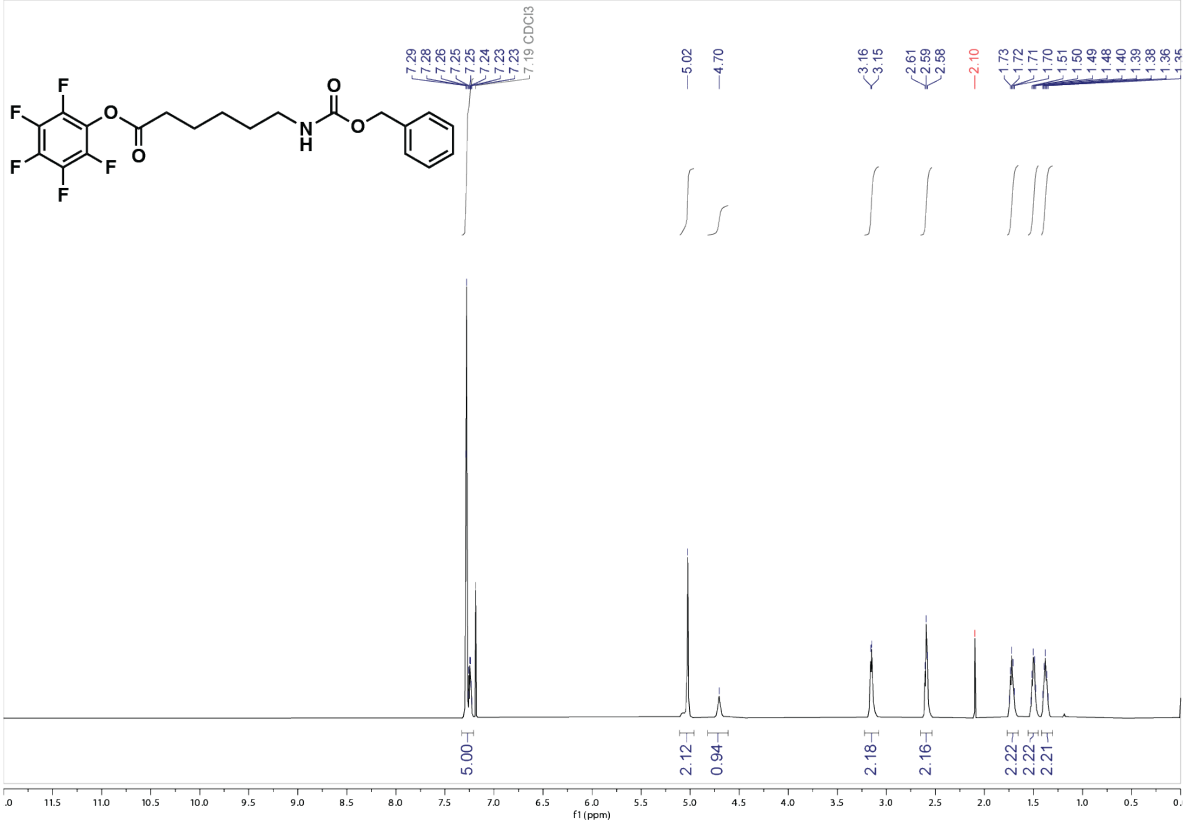
(**21**) – ^{1}H NMR (600 MHz, CDCl$_3$)



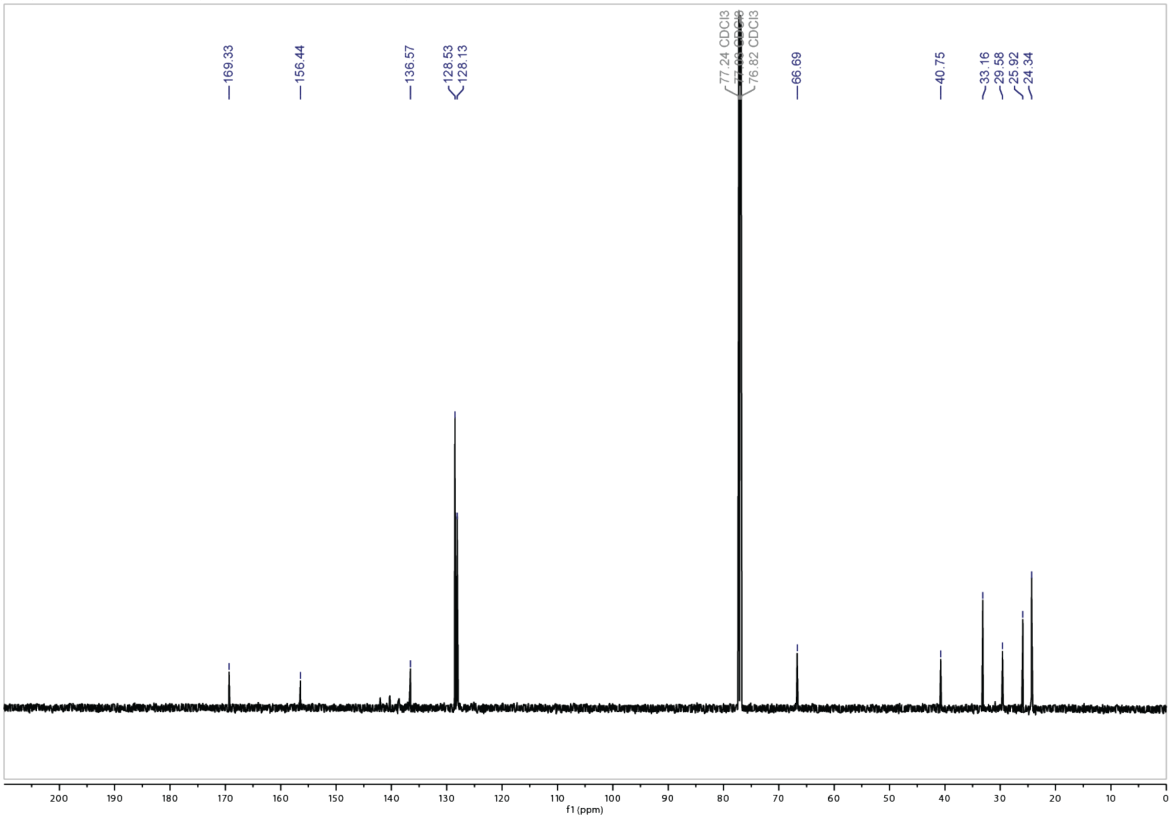
(**21**) – ^{13}C NMR (151 MHz, CDCl$_3$)



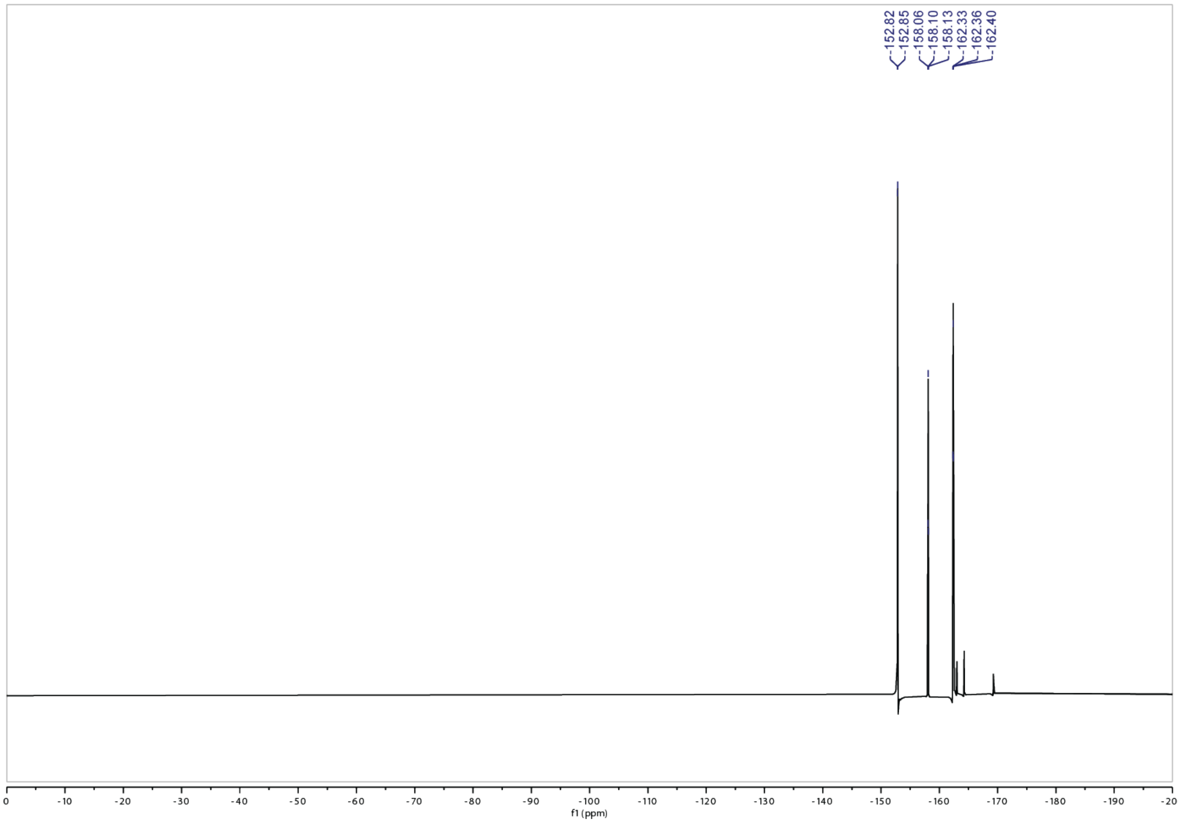
(**22**) – ^{1}H NMR (600 MHz, CDCl$_3$)



(**22**) – ^{13}C NMR (151 MHz, CDCl$_3$)

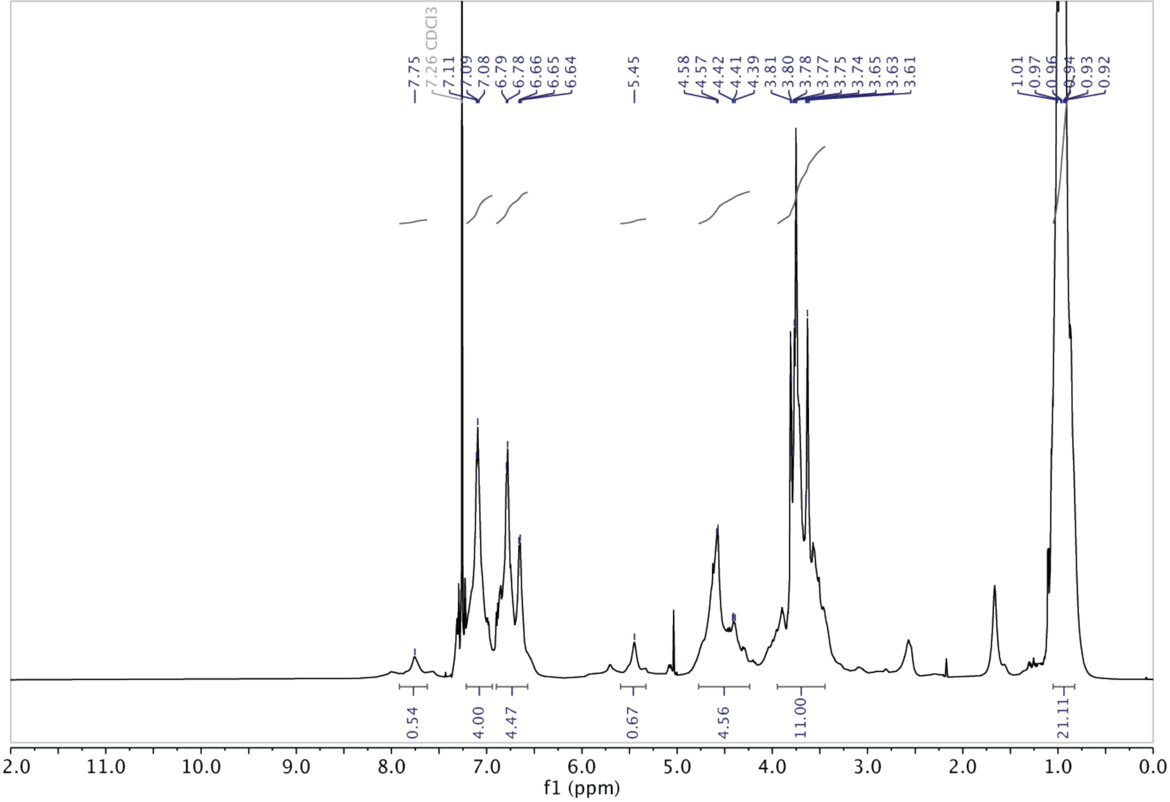


(**22**) – ^{19}F NMR (565 MHz, CDCl$_3$)

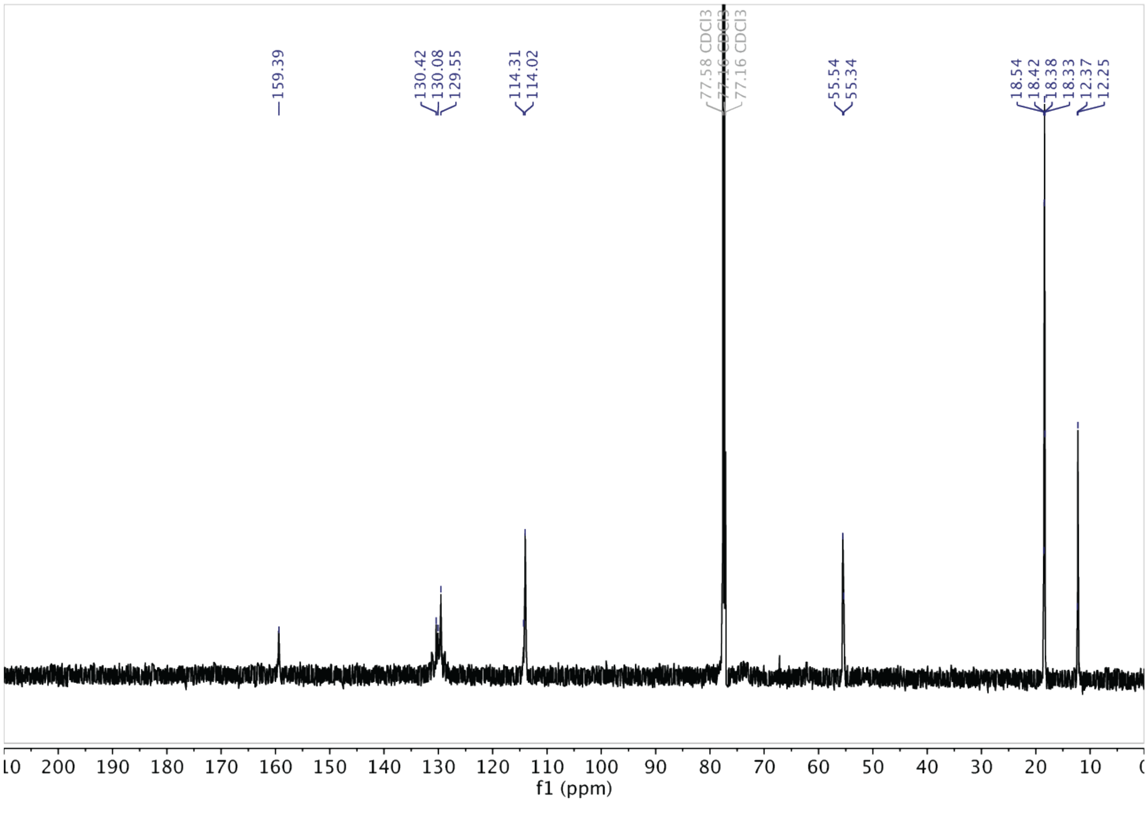


Polymer NMRs

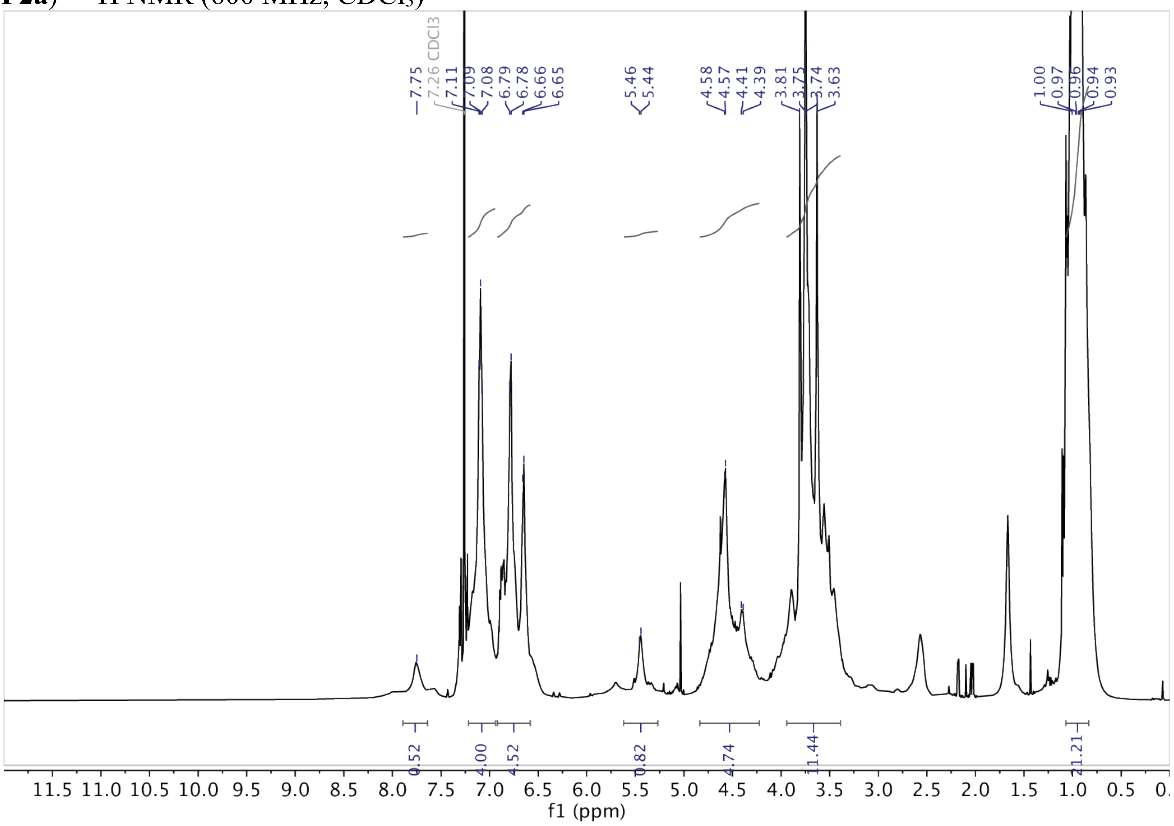
(**P1a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



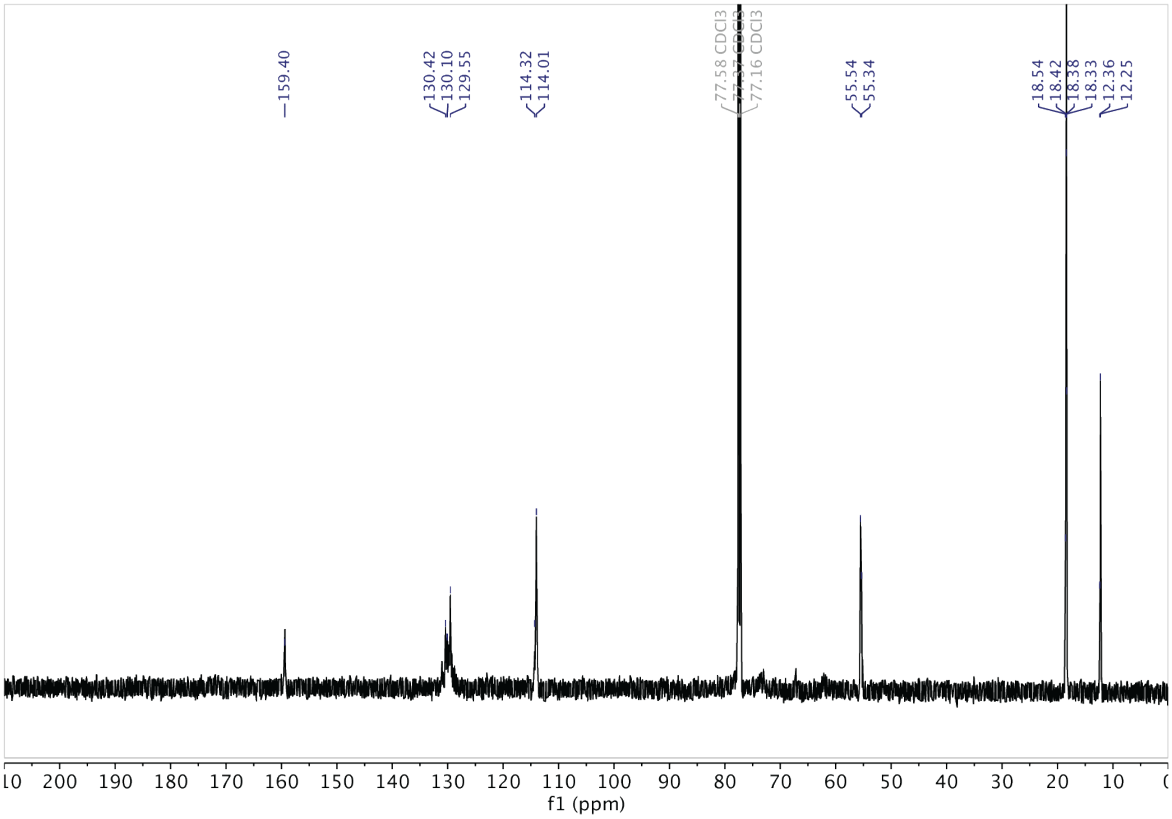
(**P1a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



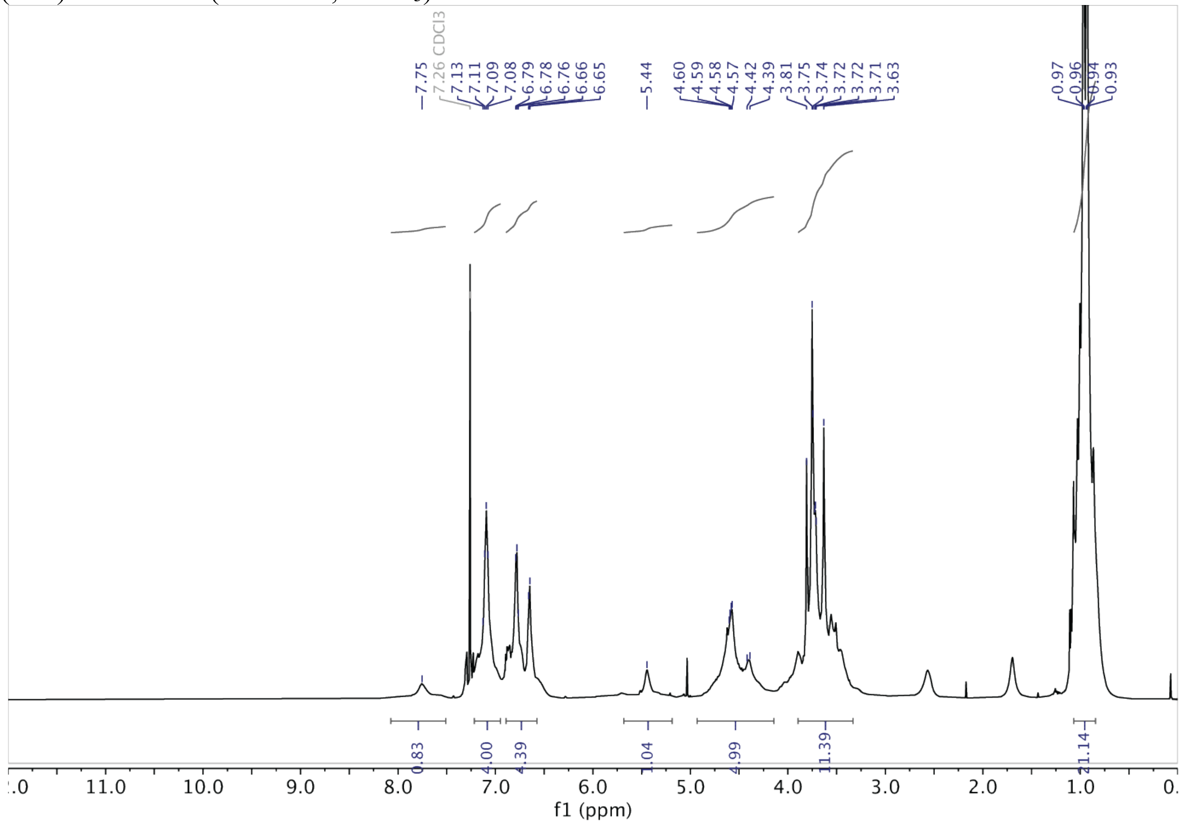
(**P2a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



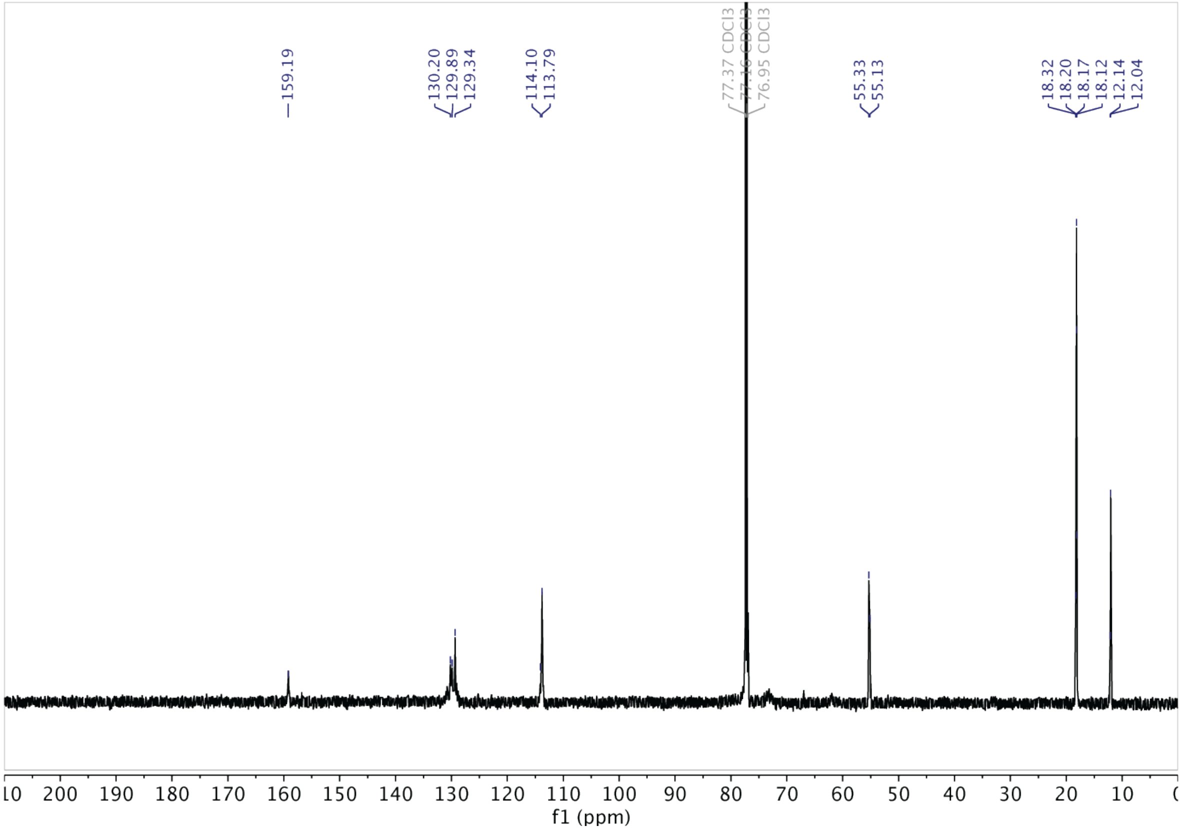
(**P2a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



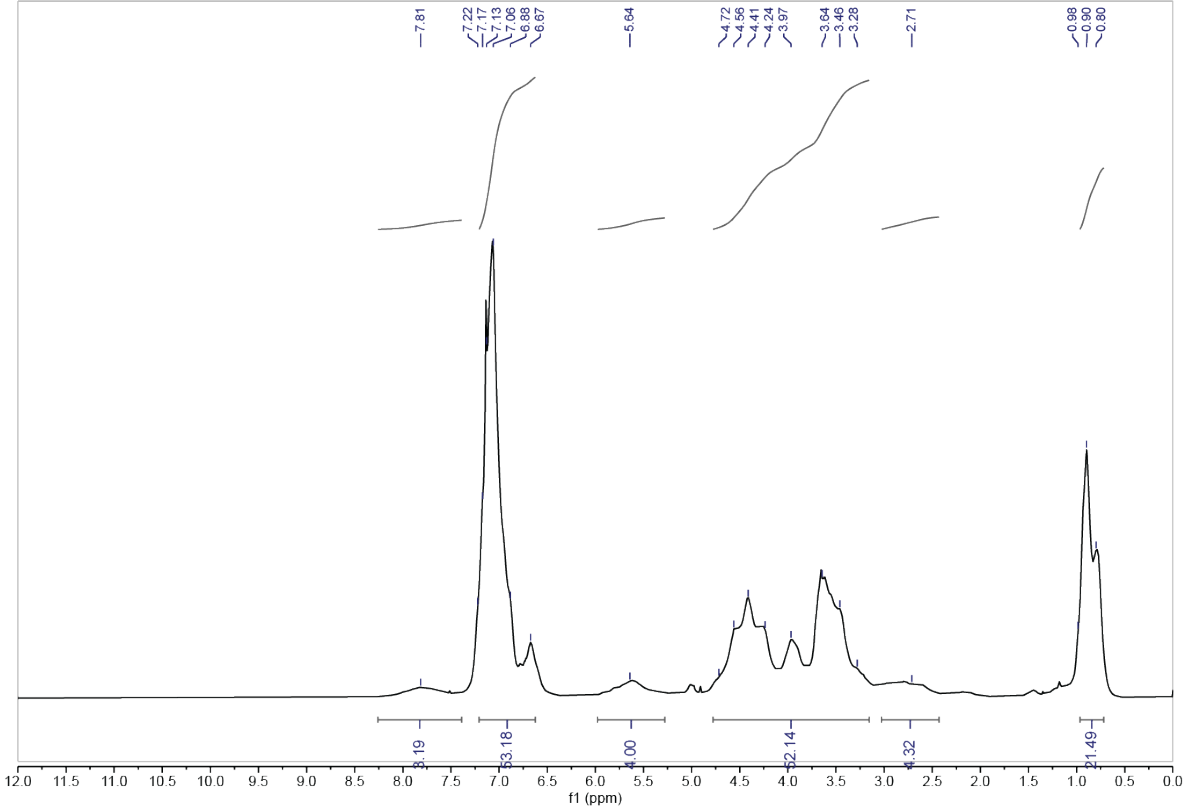
(**P3a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



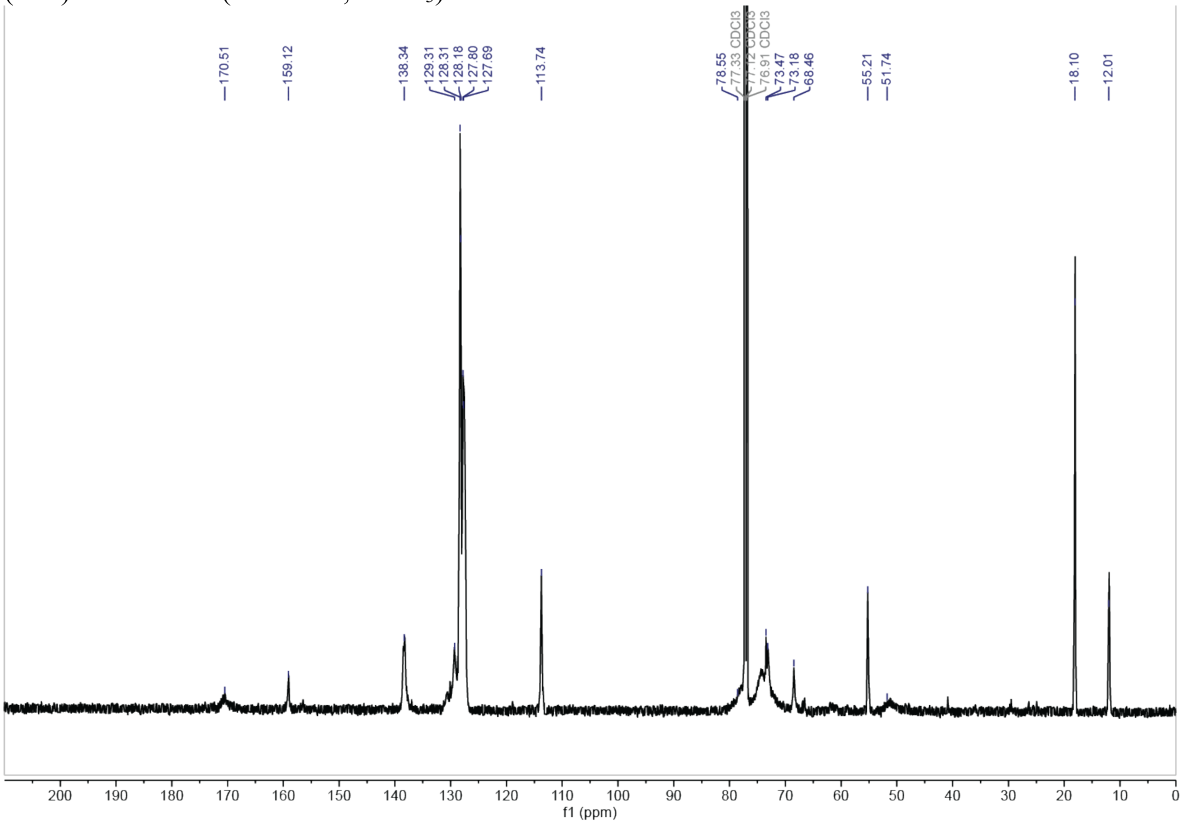
(**P3a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



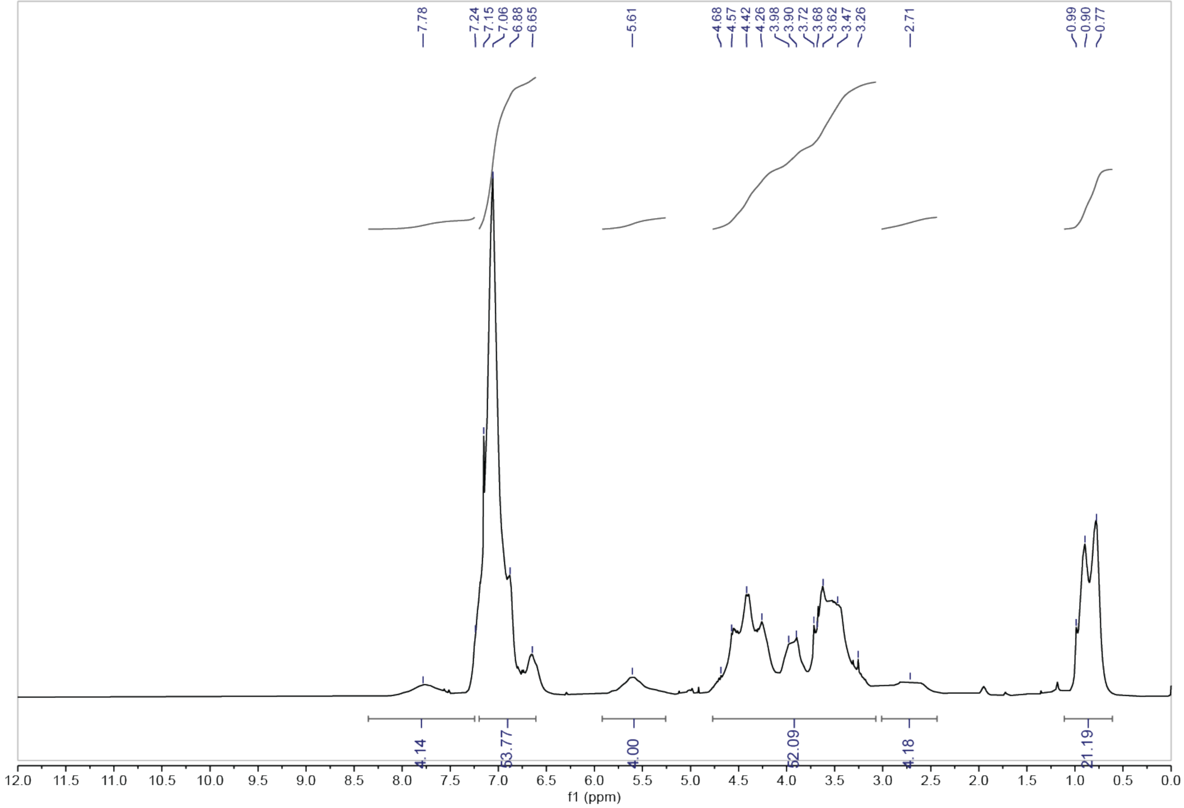
(**P4a**) – ^{1}H NMR (600 MHz, $CDCl_3$)



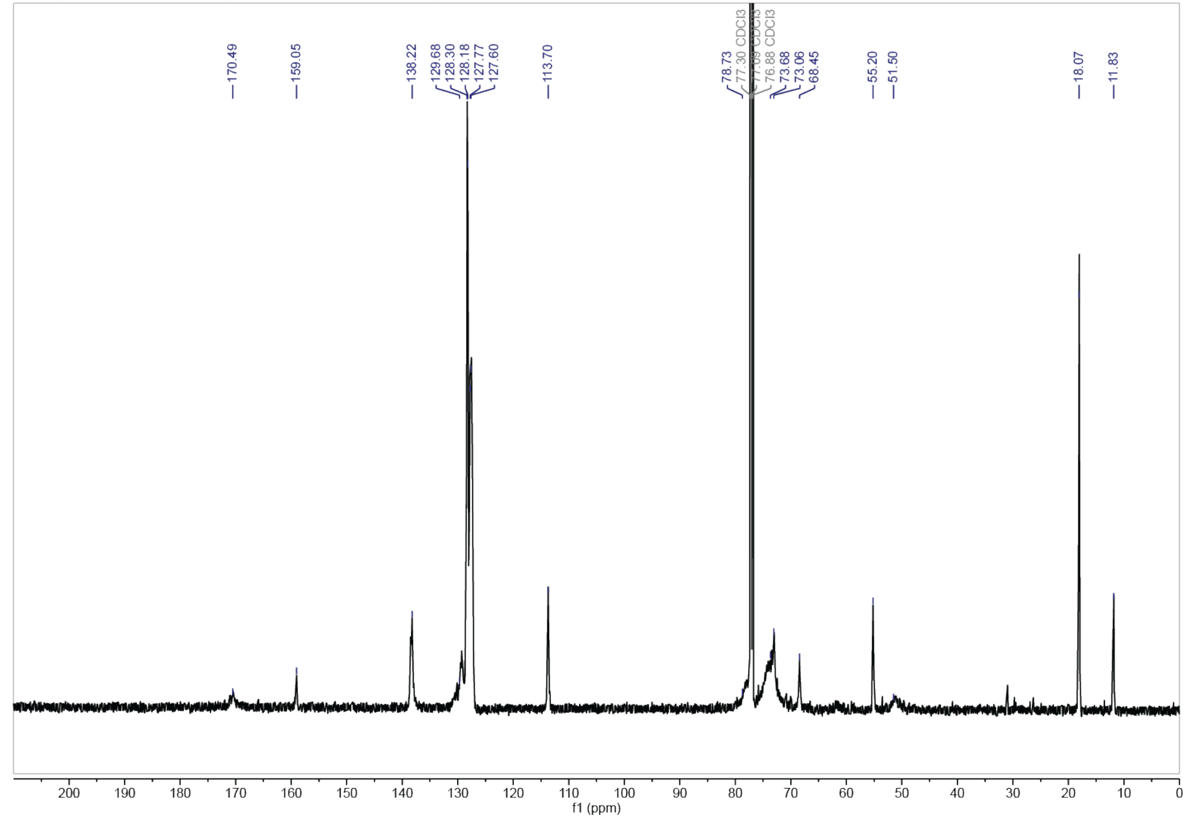
(**P4a**) – ^{13}C NMR (151 MHz, $CDCl_3$)



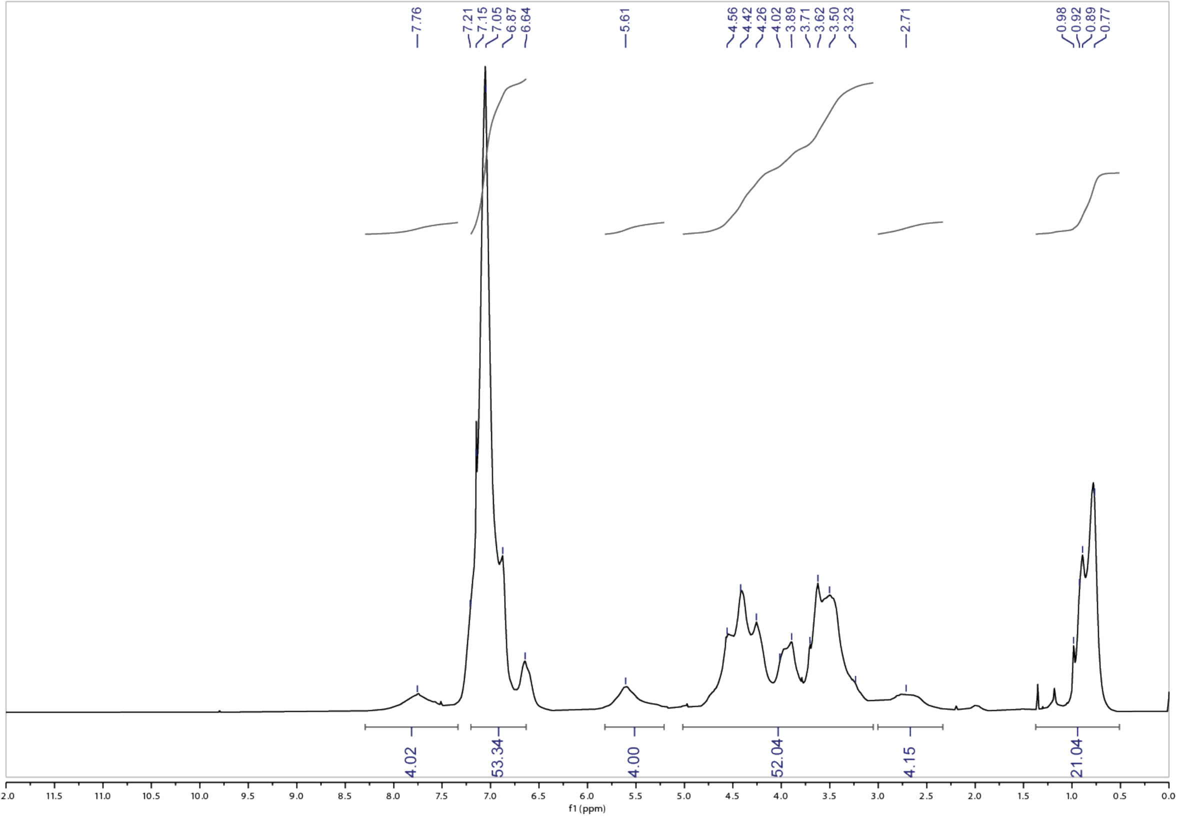
(**P5a**) – ^{1}H NMR (600 MHz, $CDCl_3$)



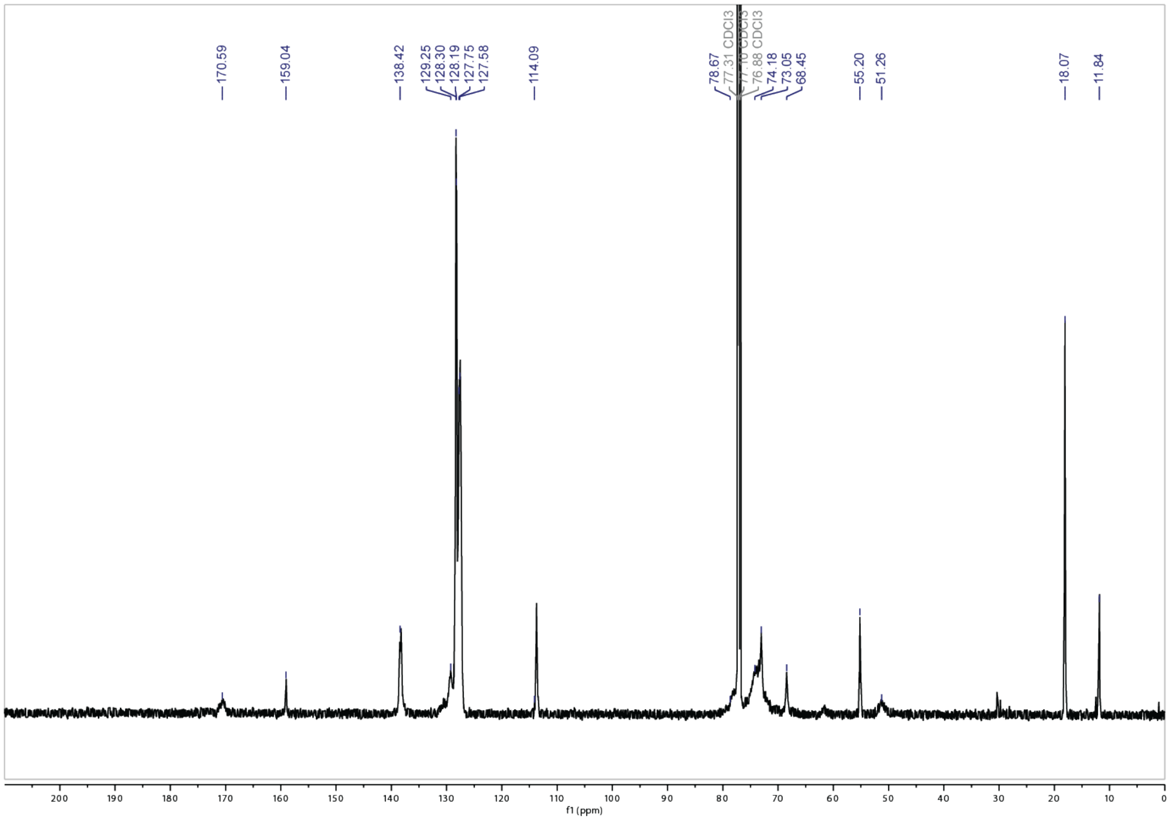
(**P5a**) – ^{13}C NMR (151 MHz, $CDCl_3$)



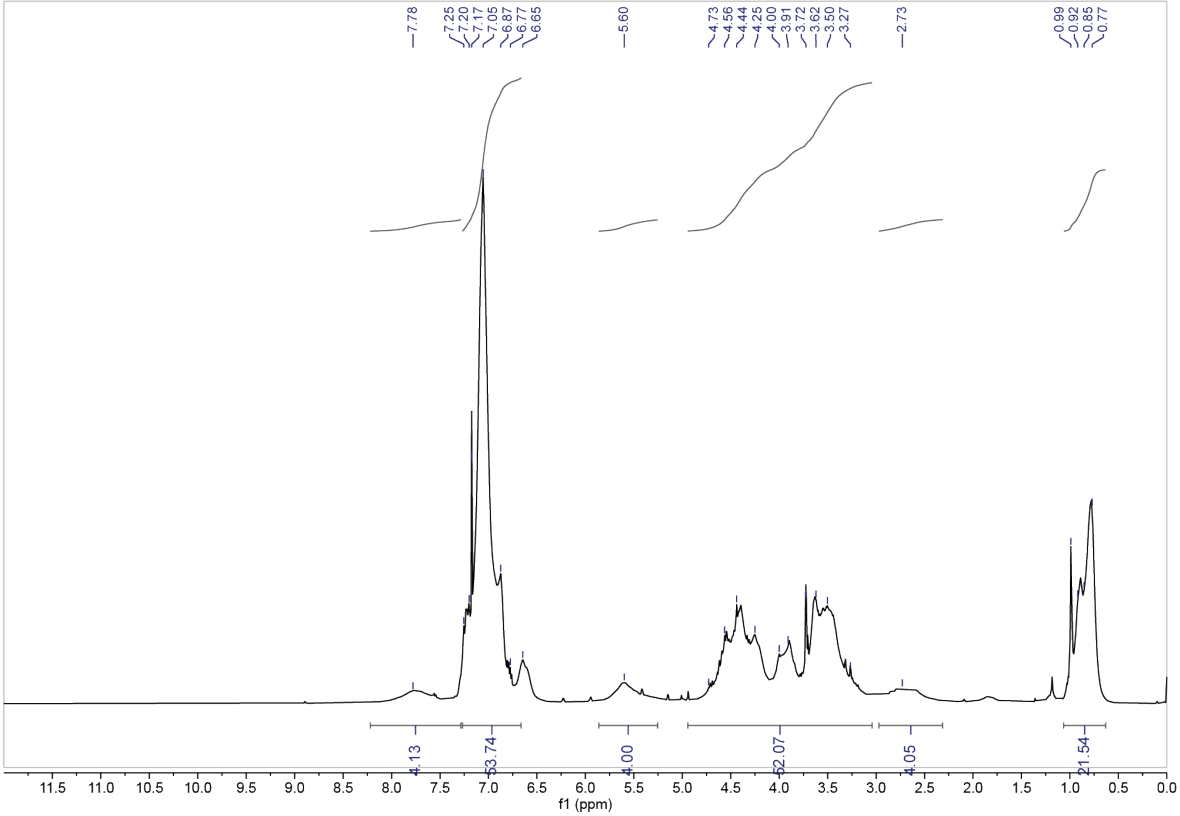
(**P6a**) – ^{1}H NMR (600 MHz, $CDCl_3$)



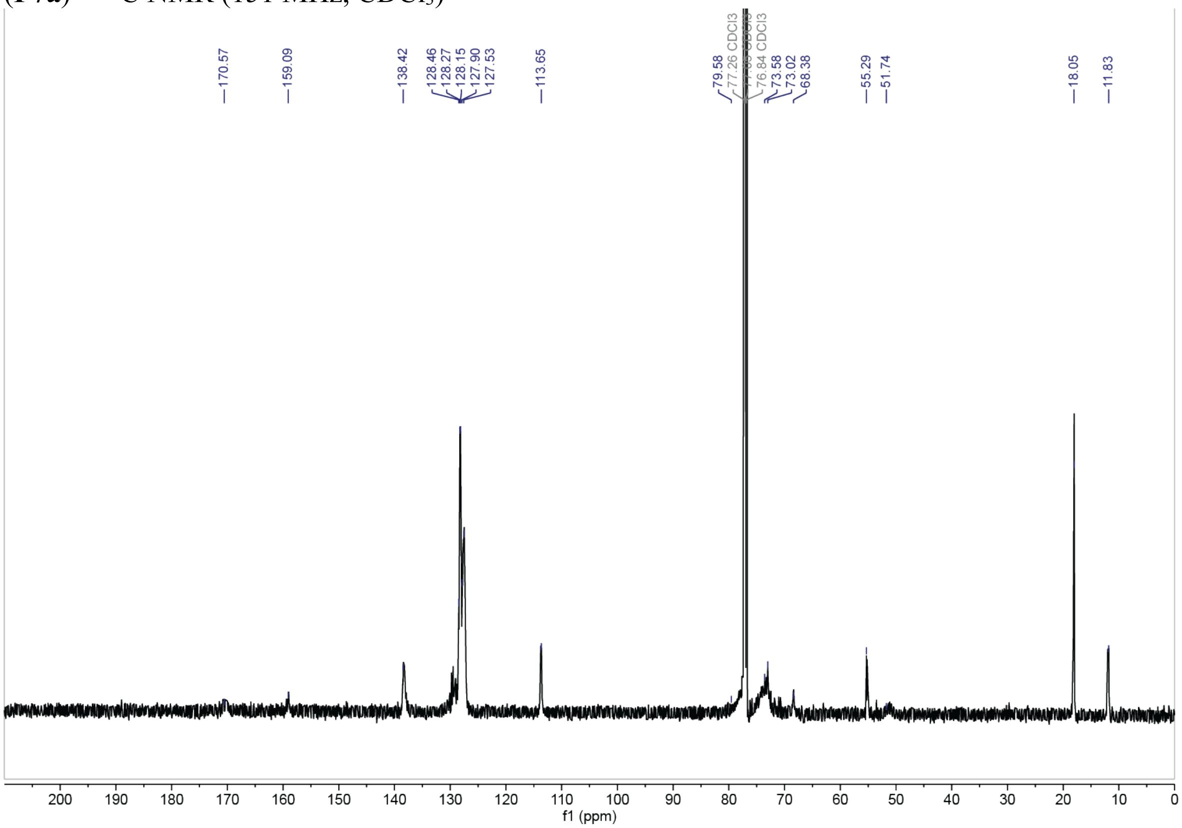
(**P6a**) – ^{13}C NMR (151 MHz, $CDCl_3$)



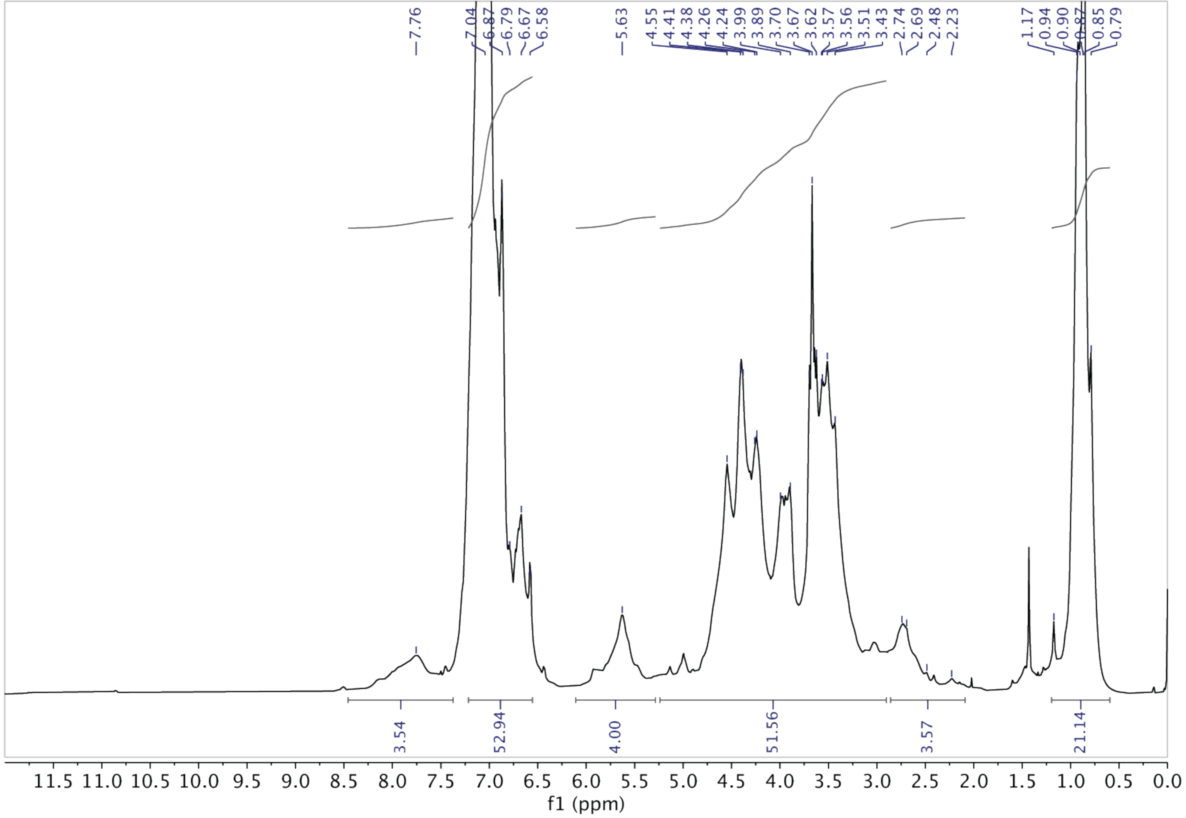
(**P7a**) – ^{1}H NMR (600 MHz, $CDCl_3$)



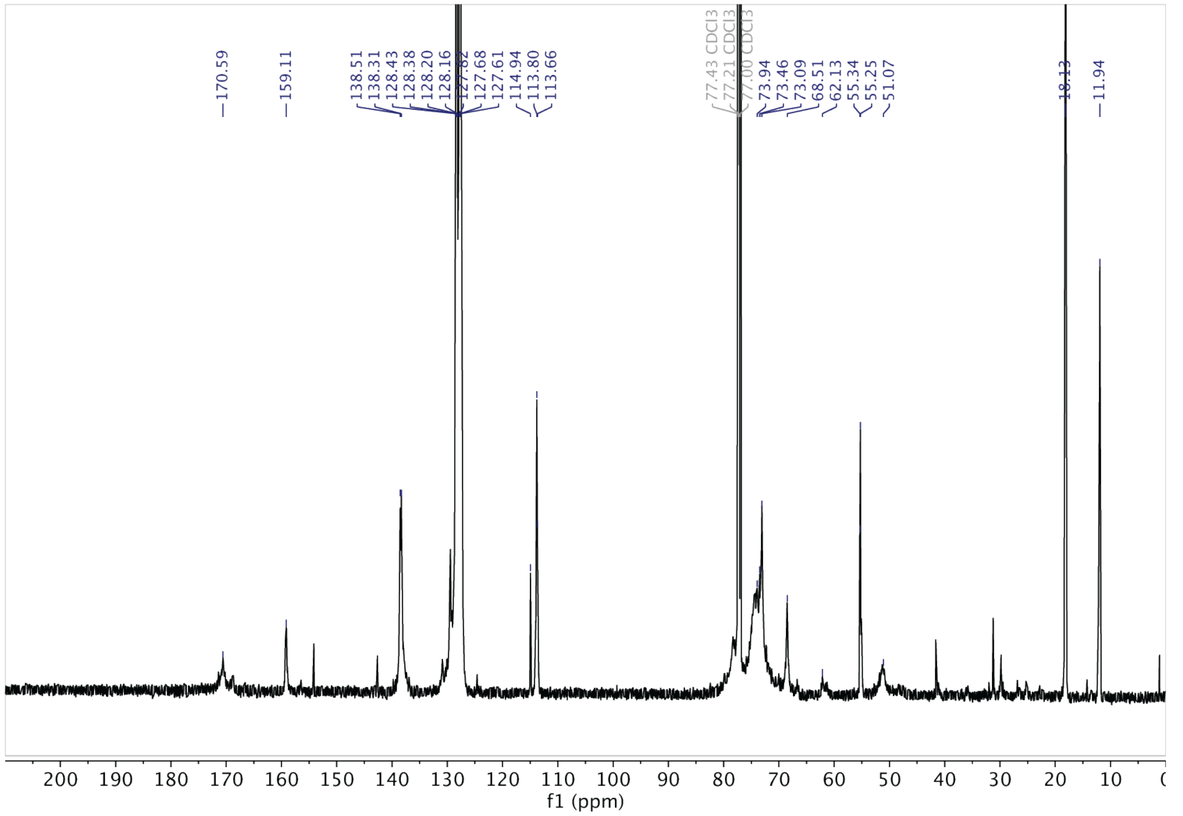
(**P7a**) – ^{13}C NMR (151 MHz, $CDCl_3$)



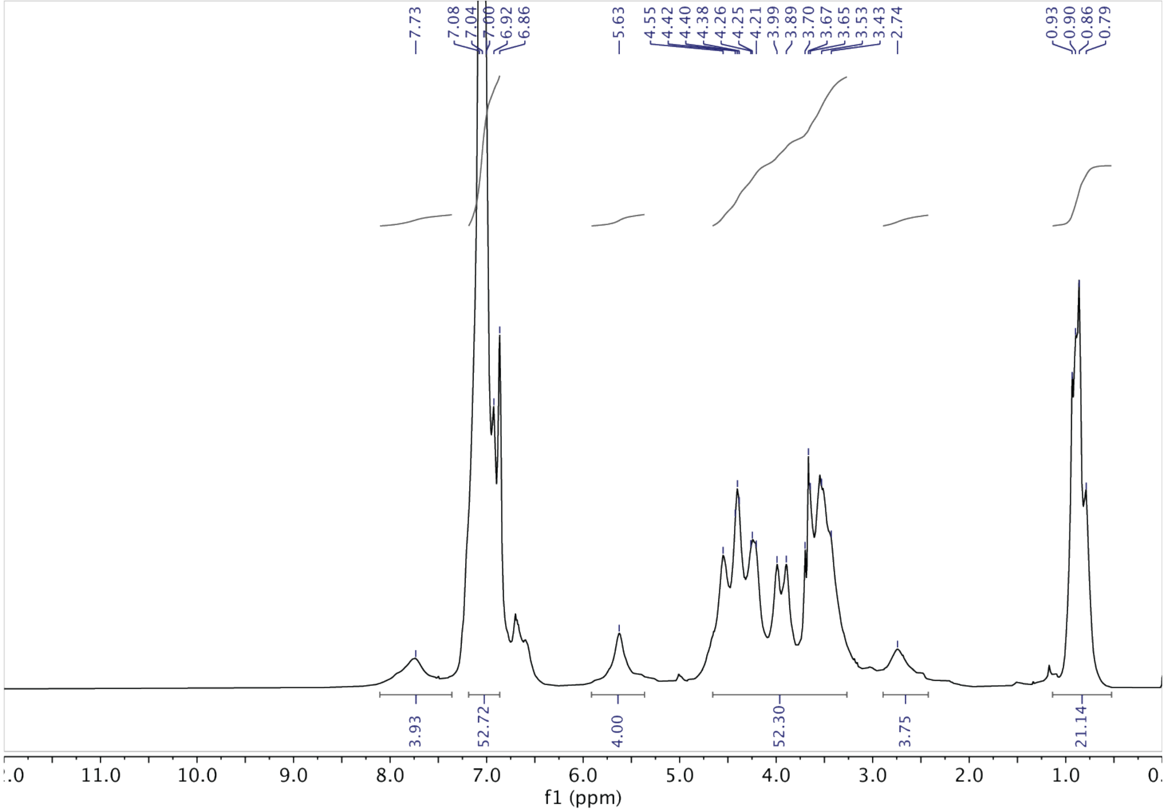
(**P8a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



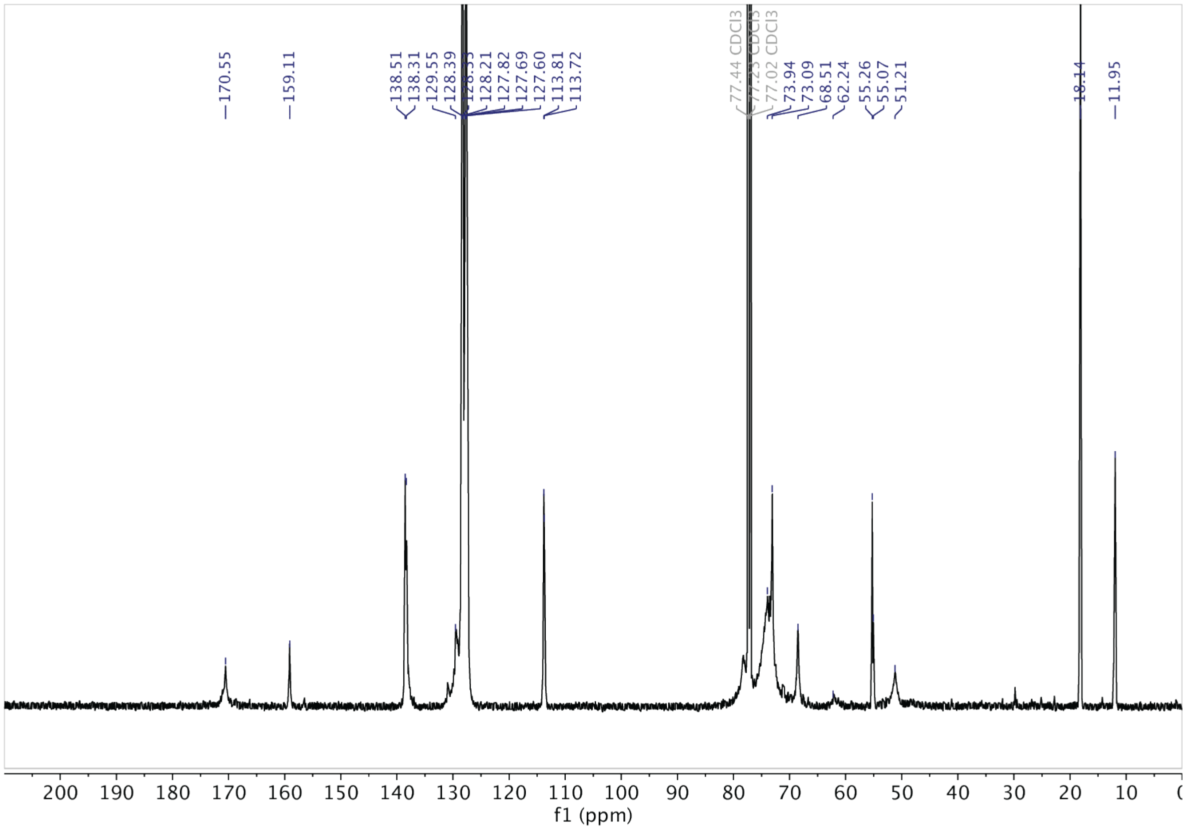
(**P8a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



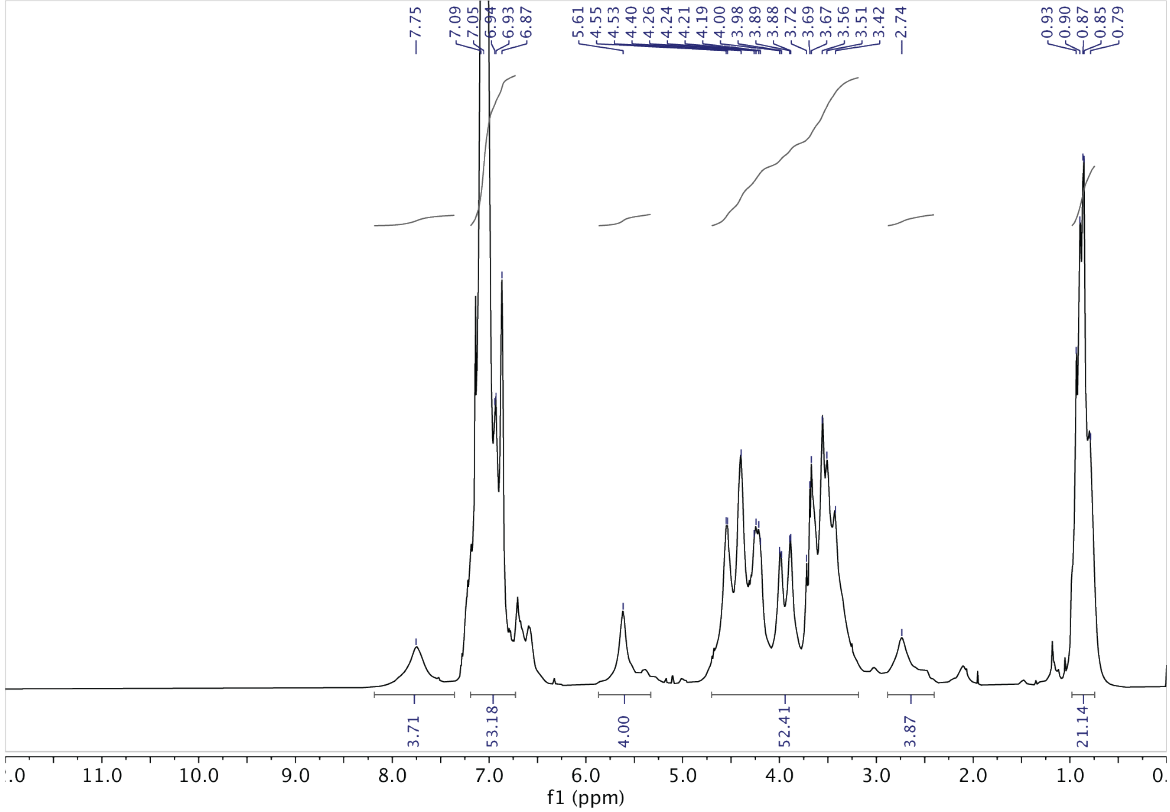
(**P9a**) – ^{1}H NMR (600 MHz, $CDCl_3$)



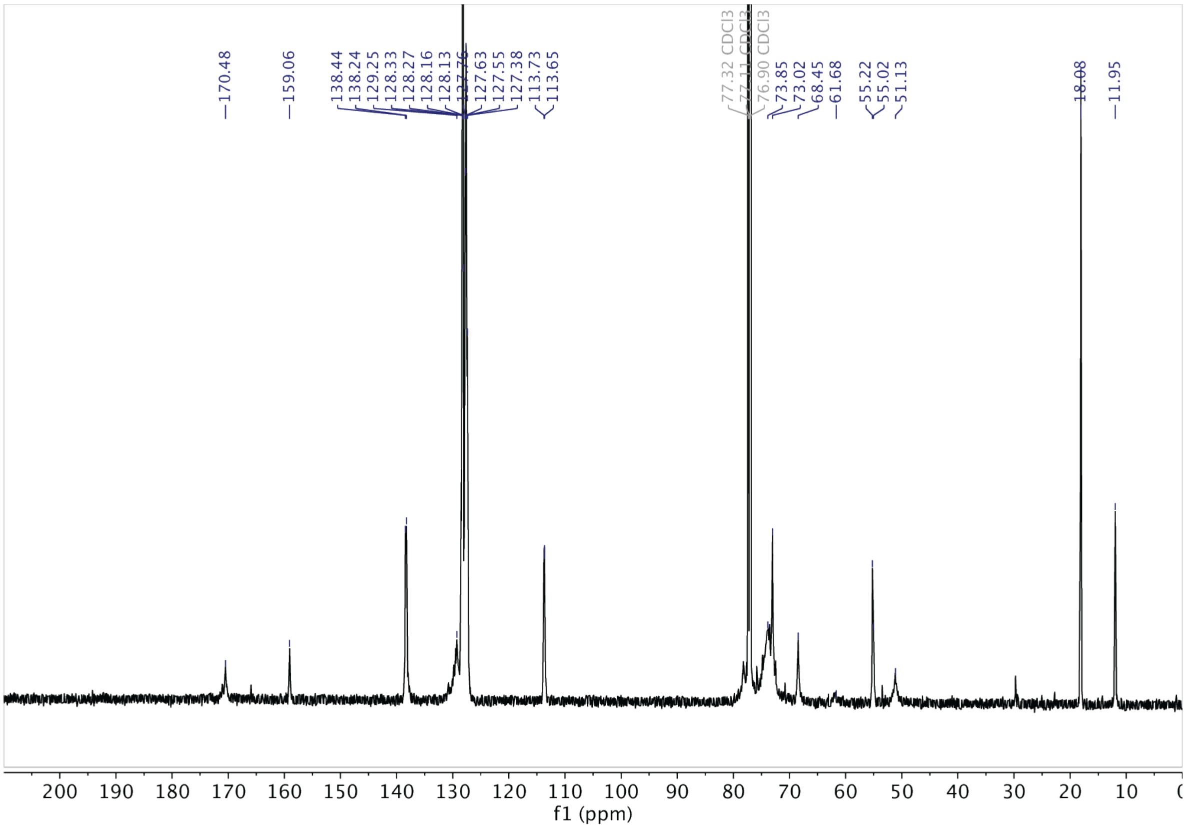
(**P9a**) – ^{13}C NMR (151 MHz, $CDCl_3$)



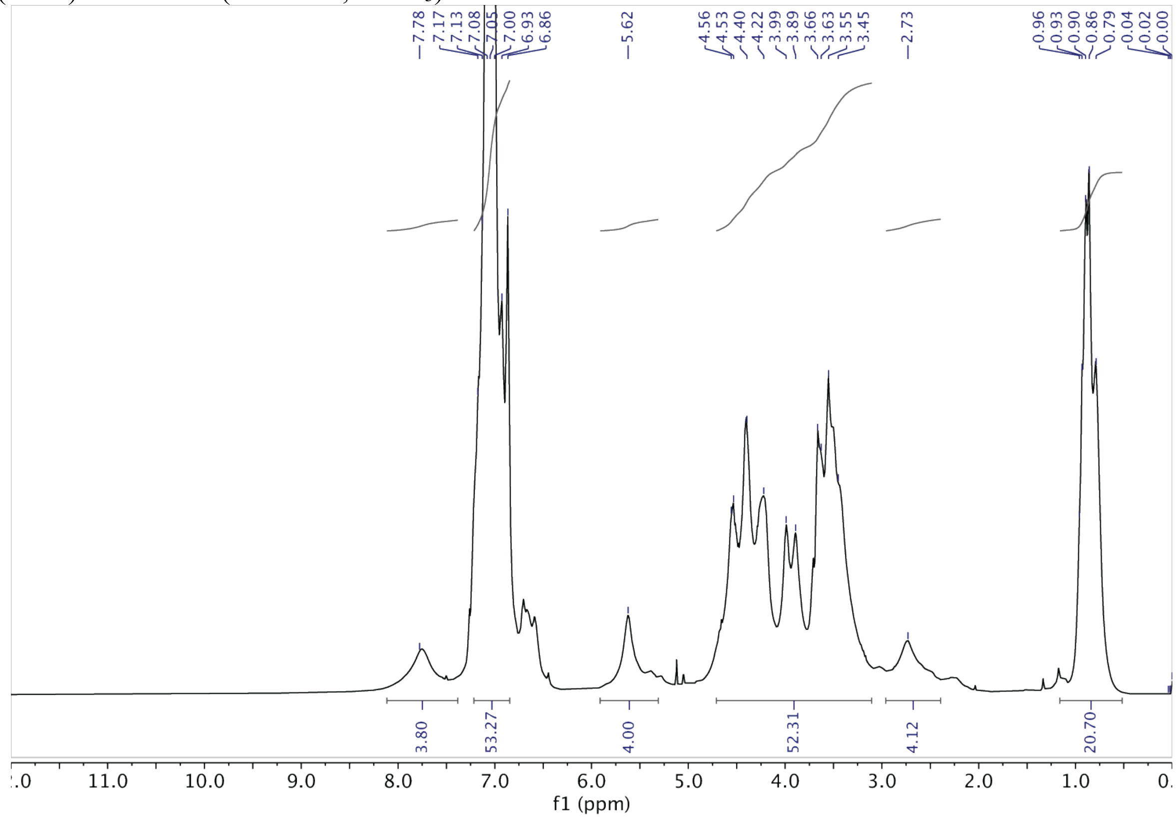
(**P10a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



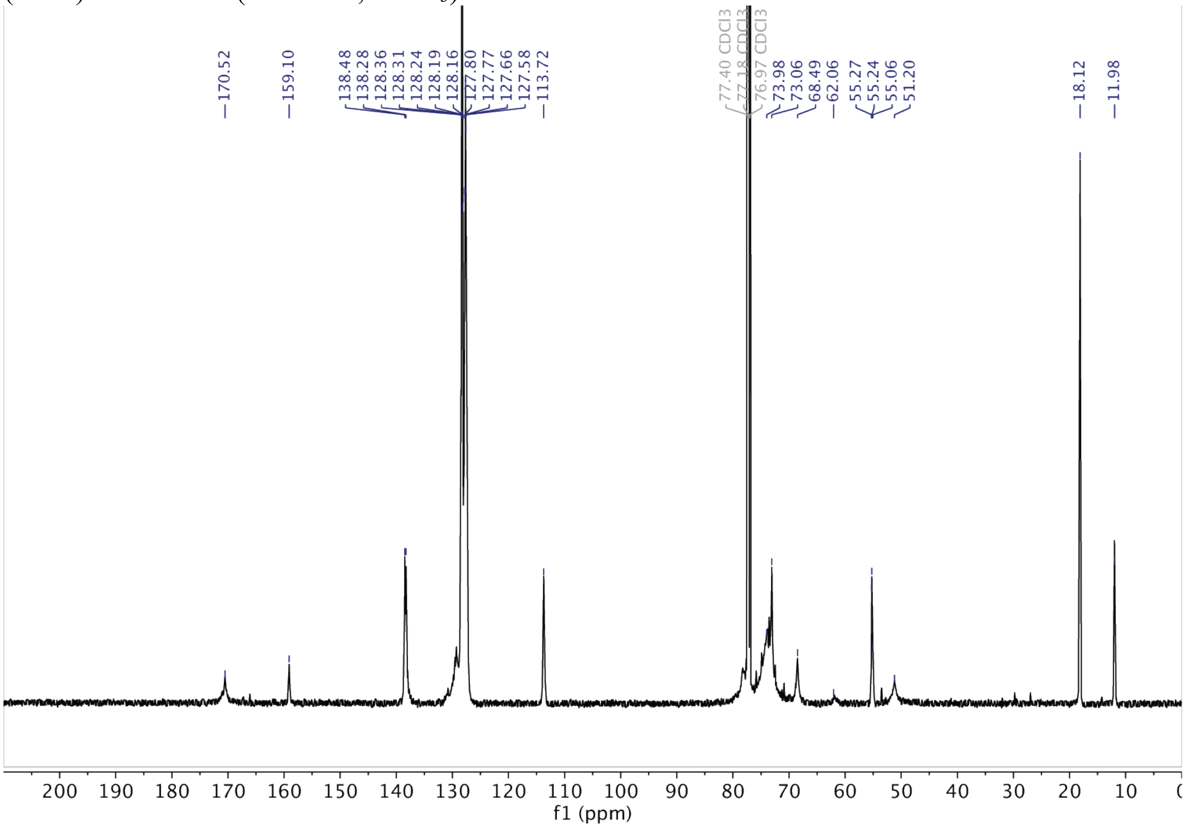
(**P10a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



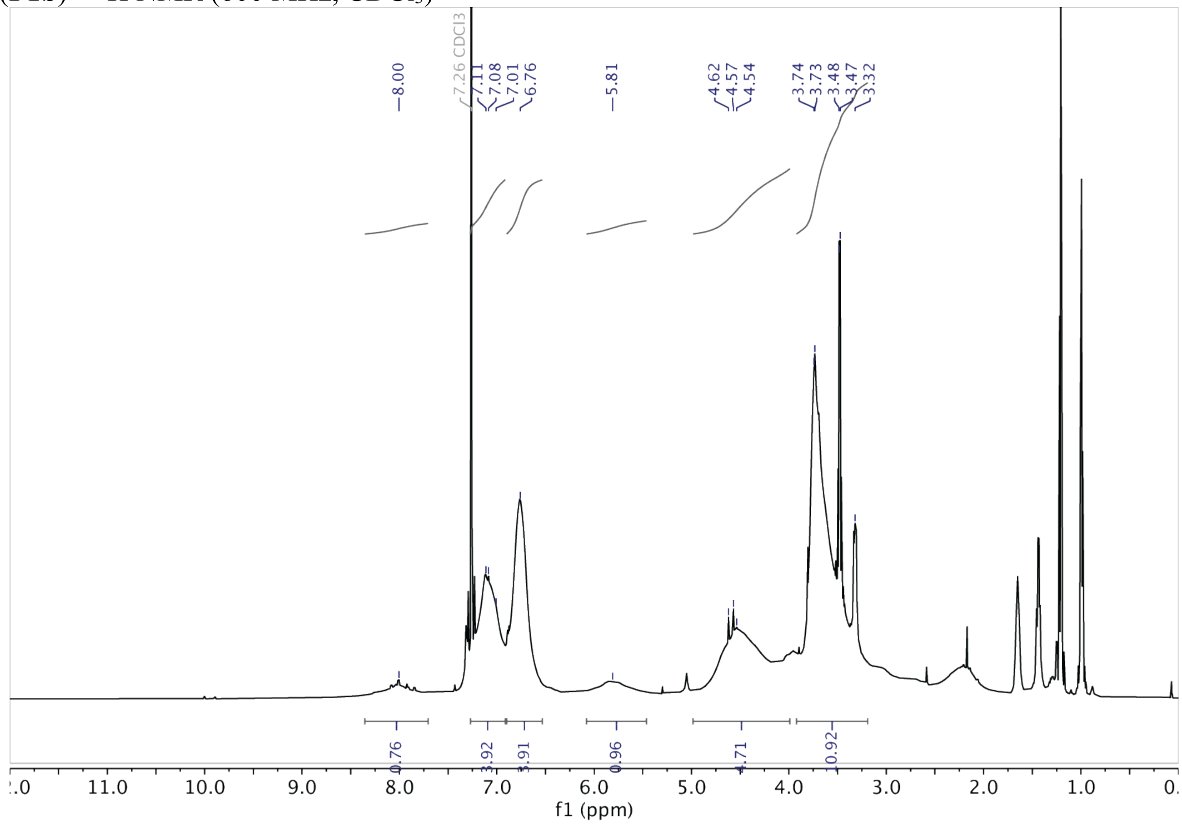
(**P11a**) – ^{1}H NMR (600 MHz, CDCl$_3$)



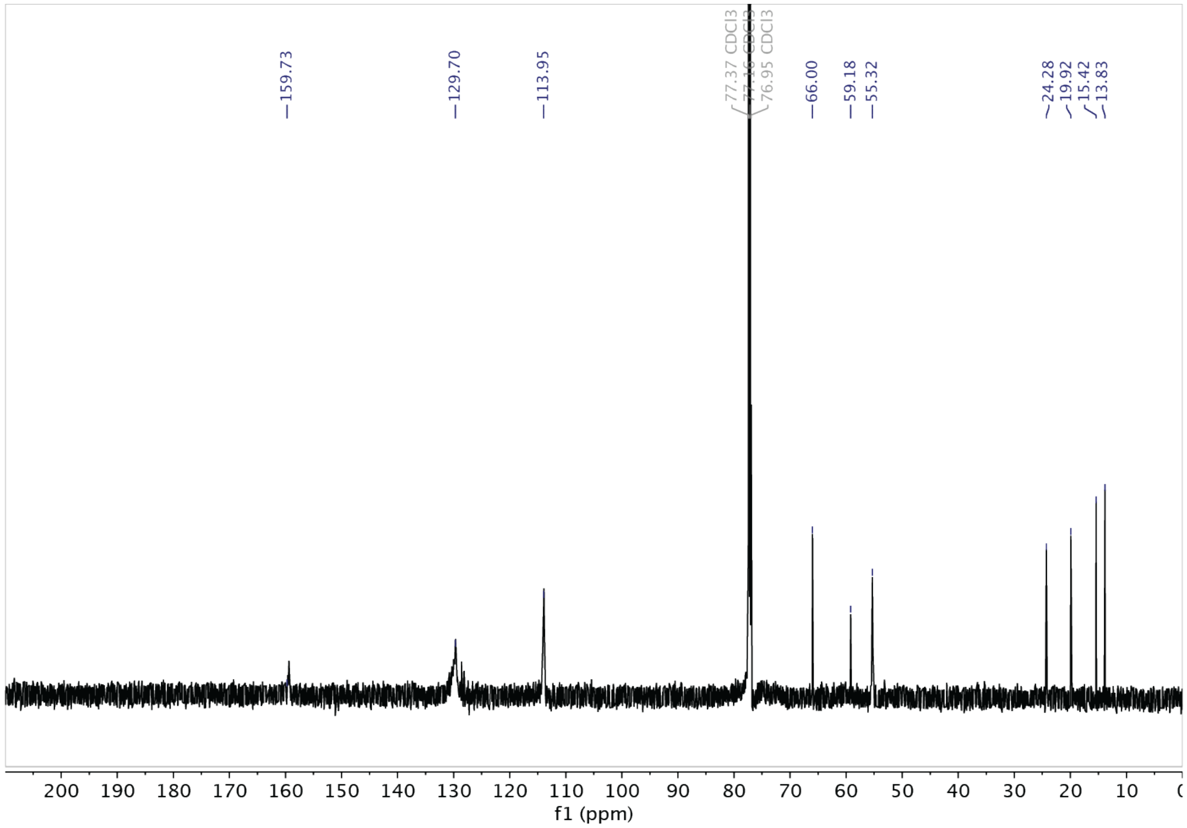
(**P11a**) – ^{13}C NMR (151 MHz, CDCl$_3$)



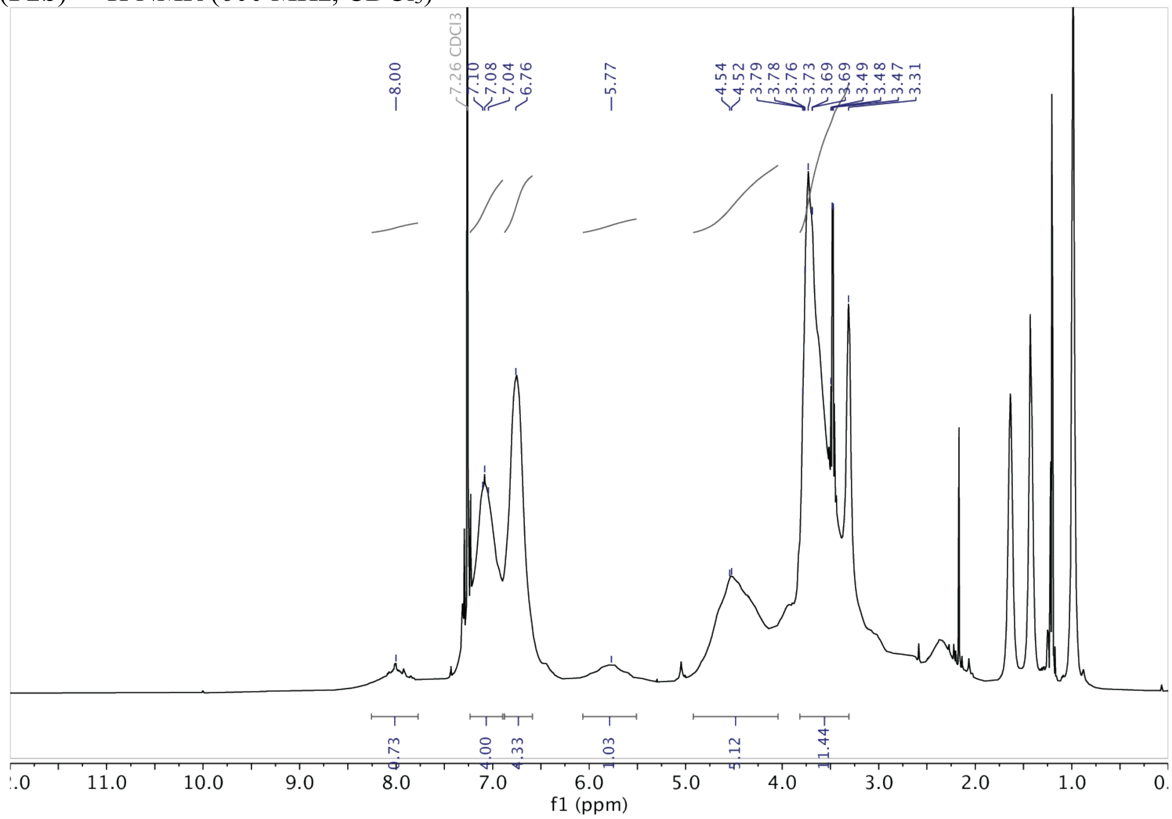
(**P1b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



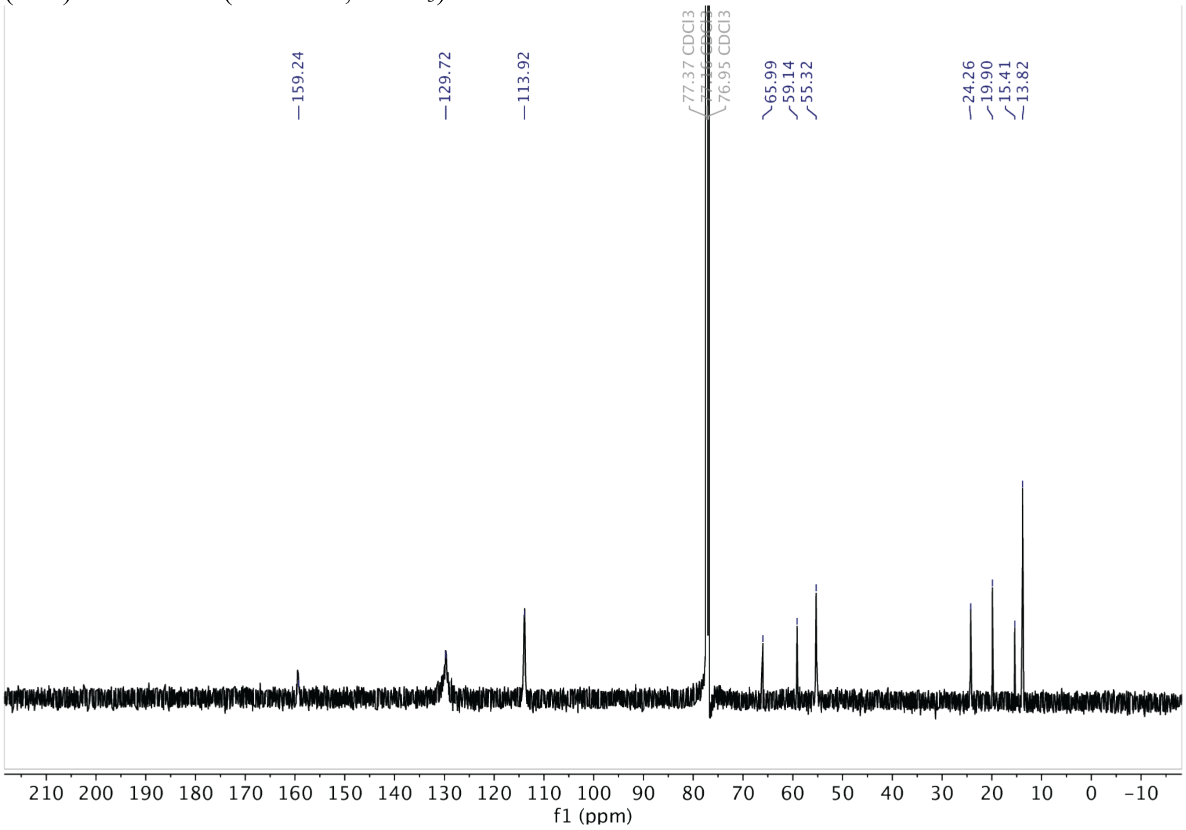
(**P1b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



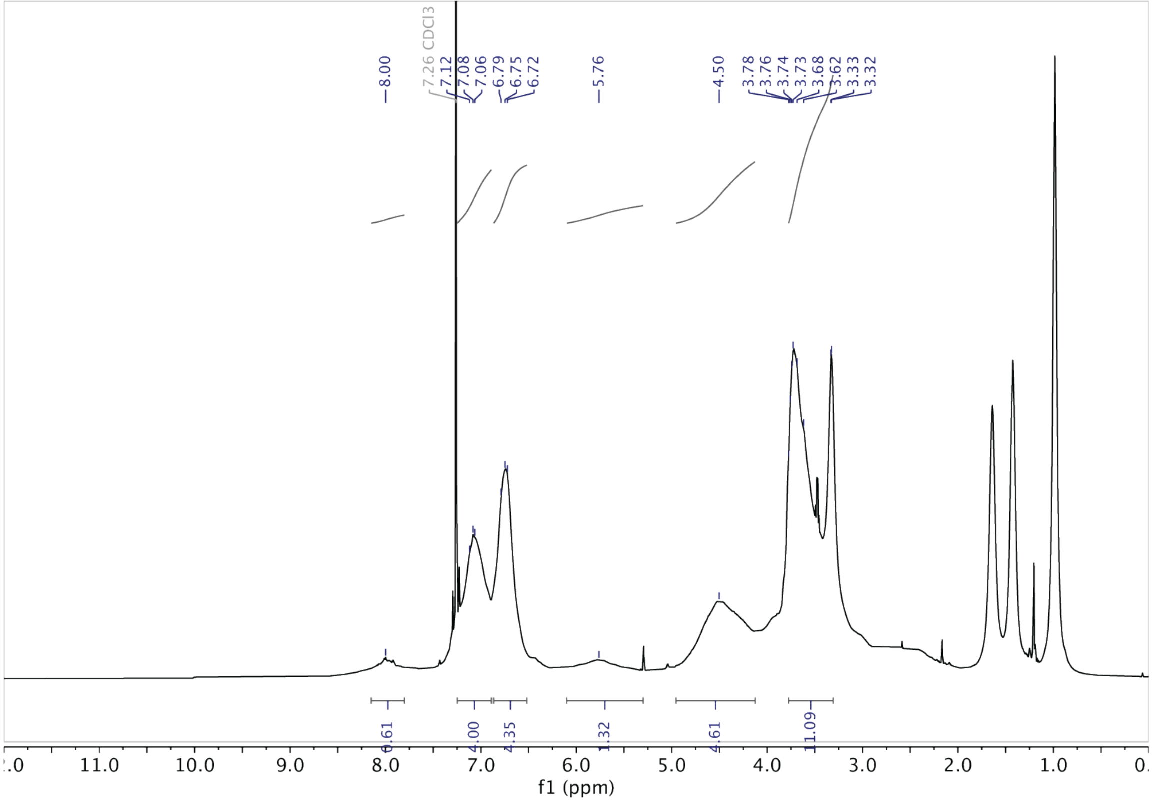
(**P2b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



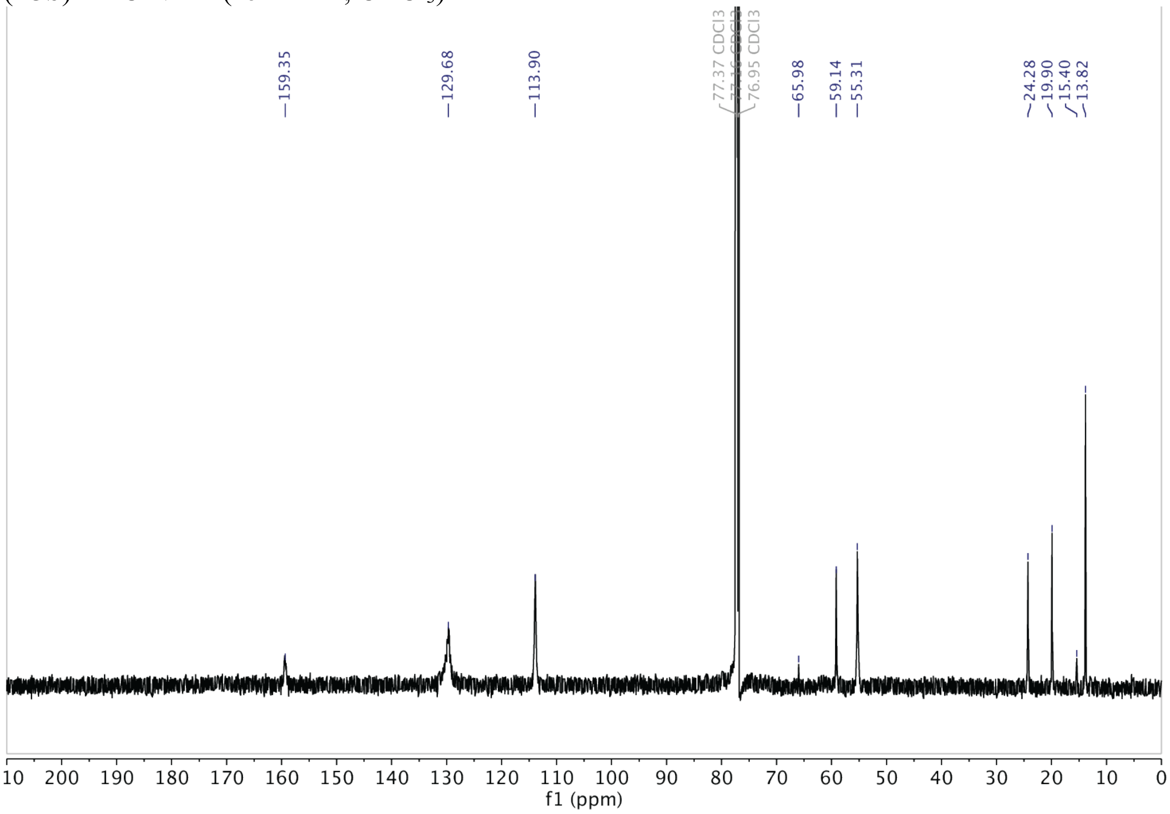
(**P2b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



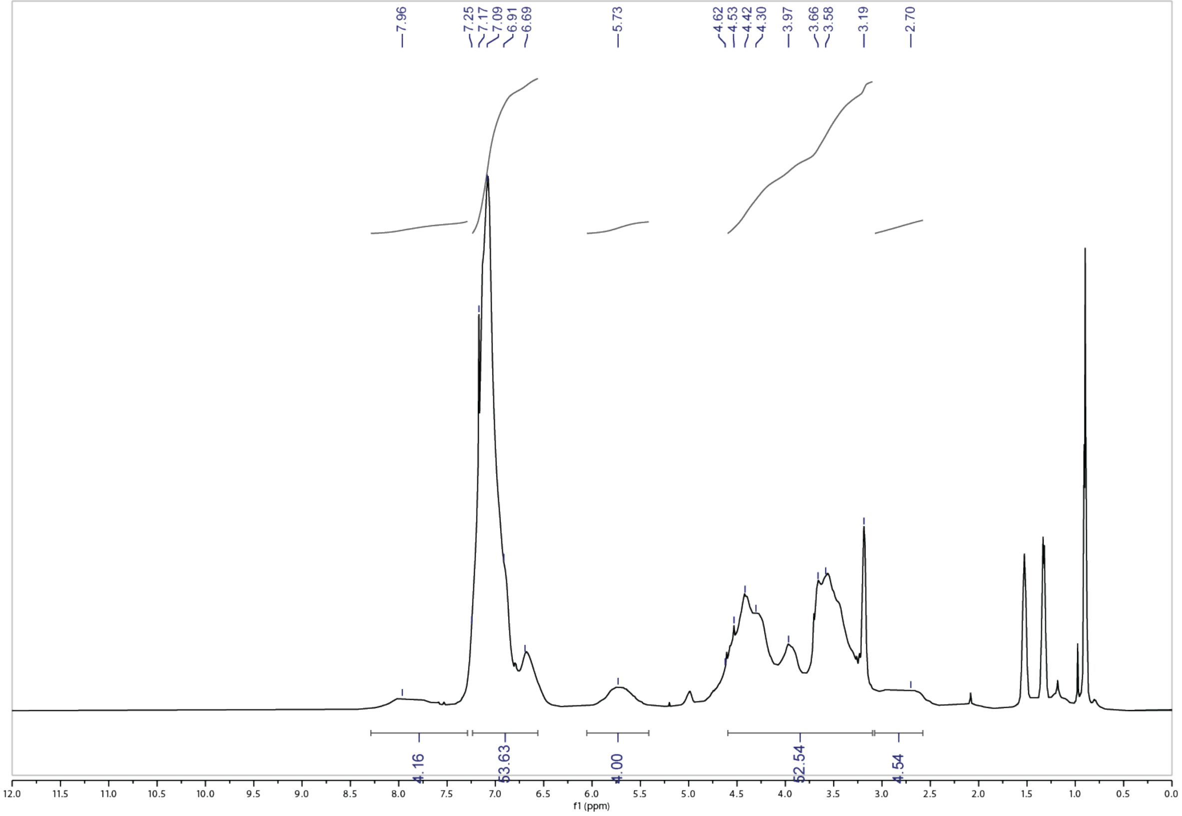
(**P3b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



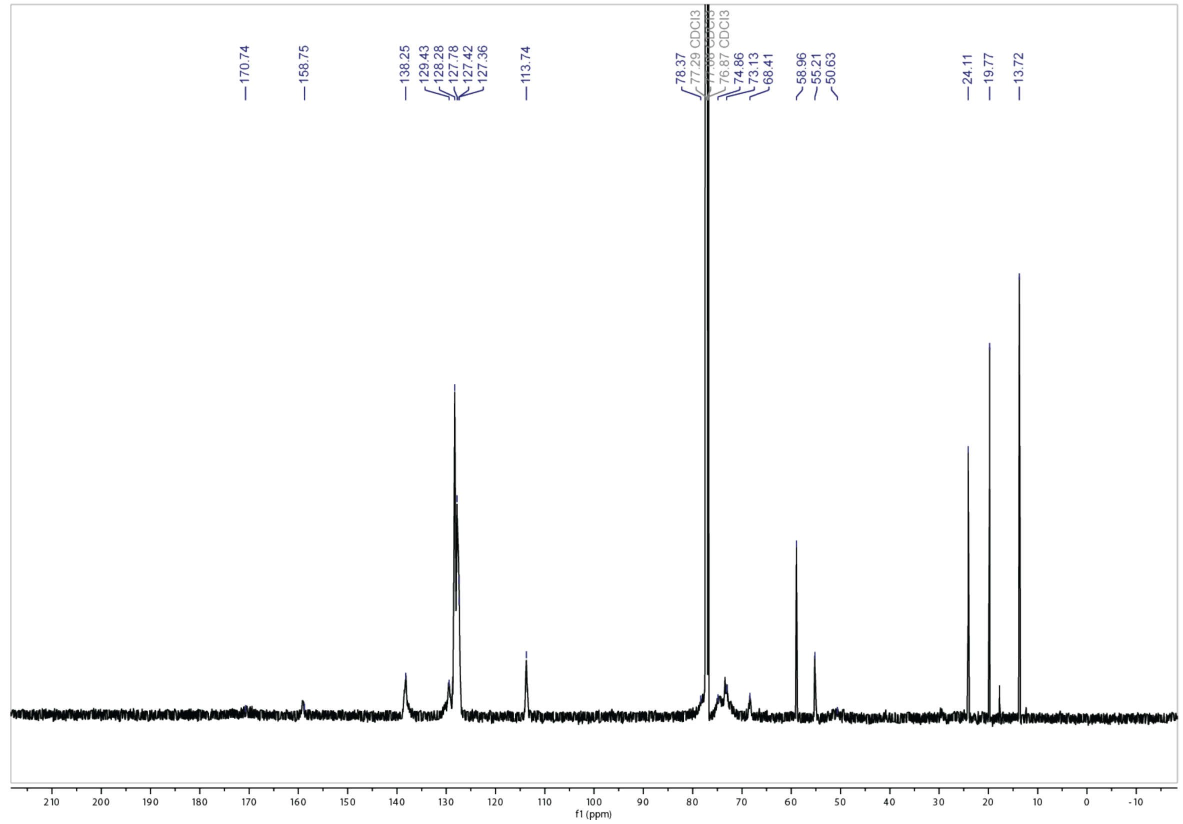
(**P3b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



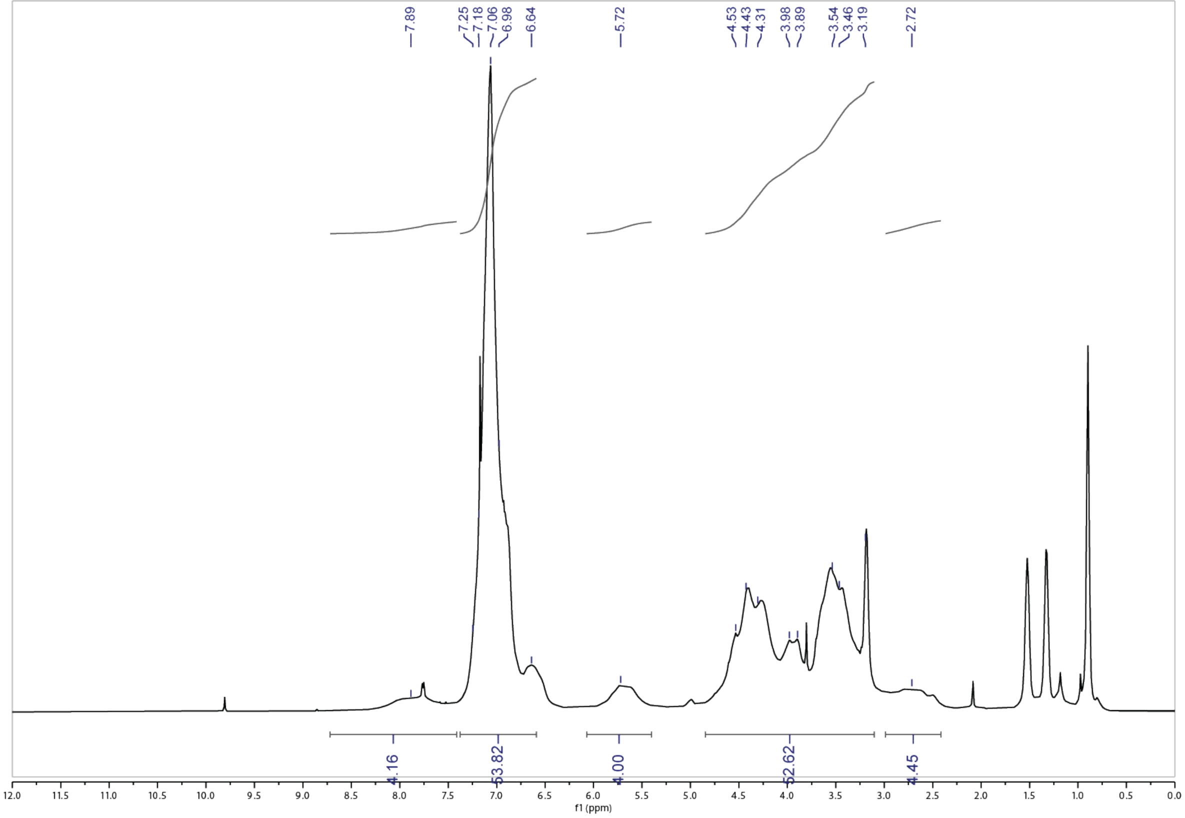
(**P4b**) – ^{1}H NMR (600 MHz, $CDCl_3$)



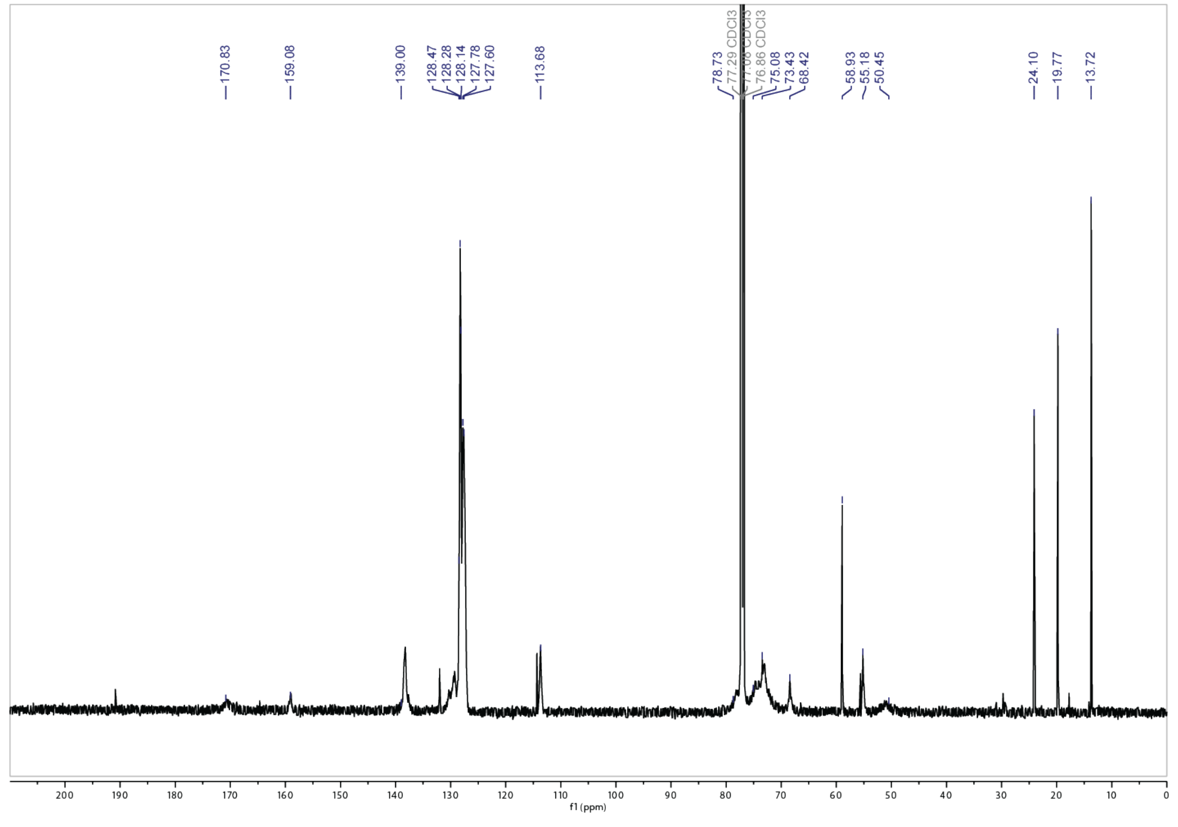
(**P4b**) – ^{13}C NMR (151 MHz, $CDCl_3$)



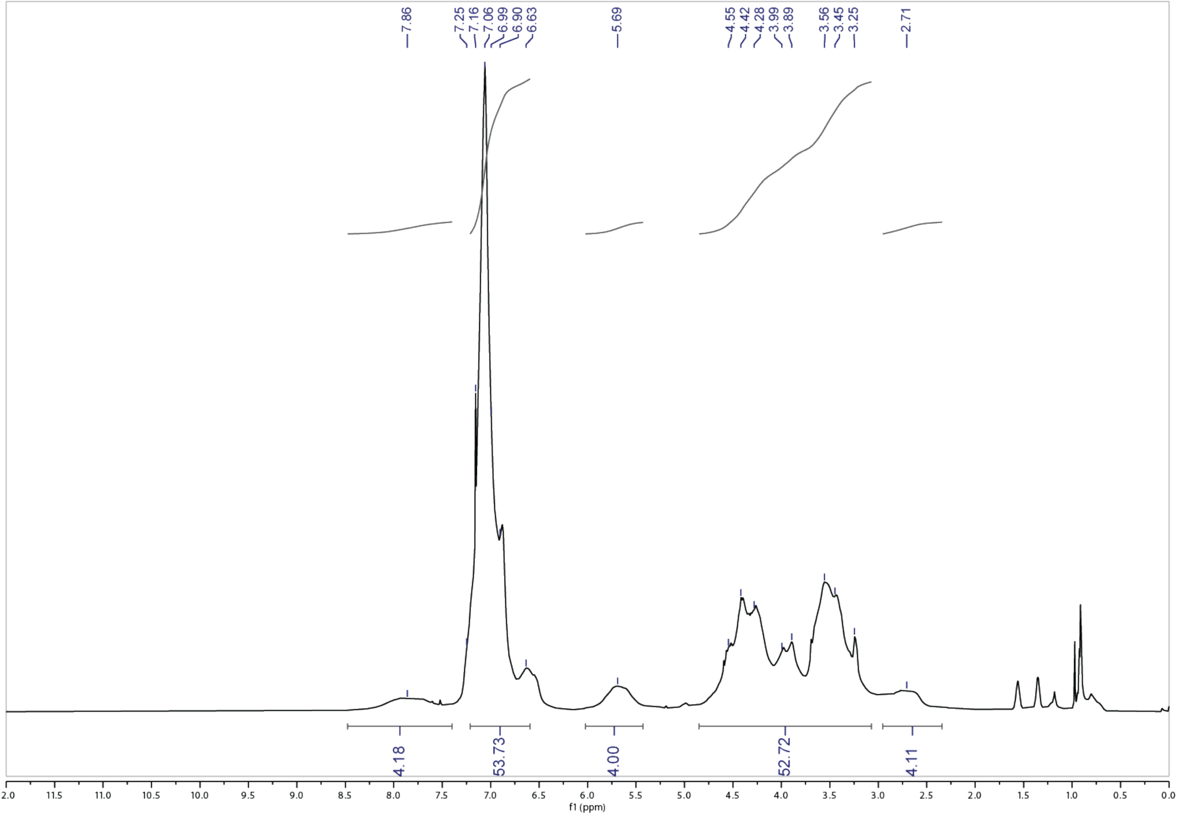
(**P5b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



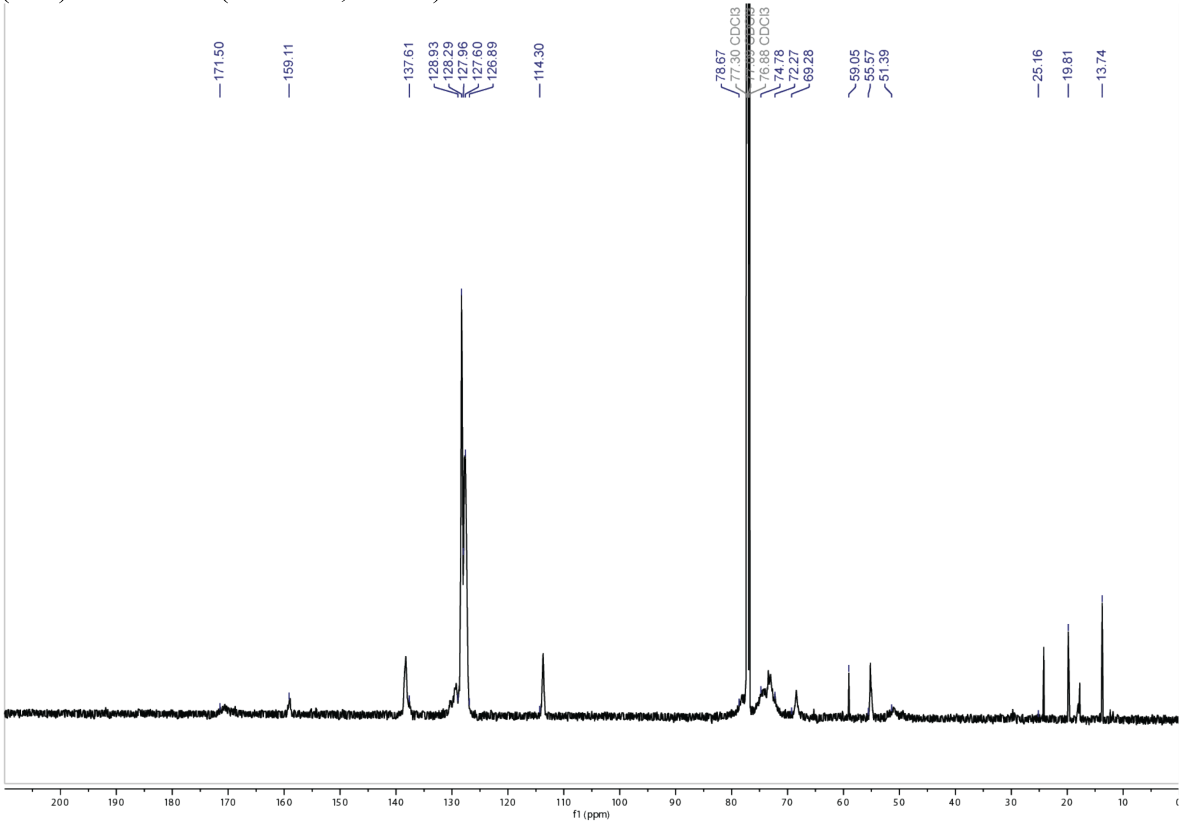
(**P5b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



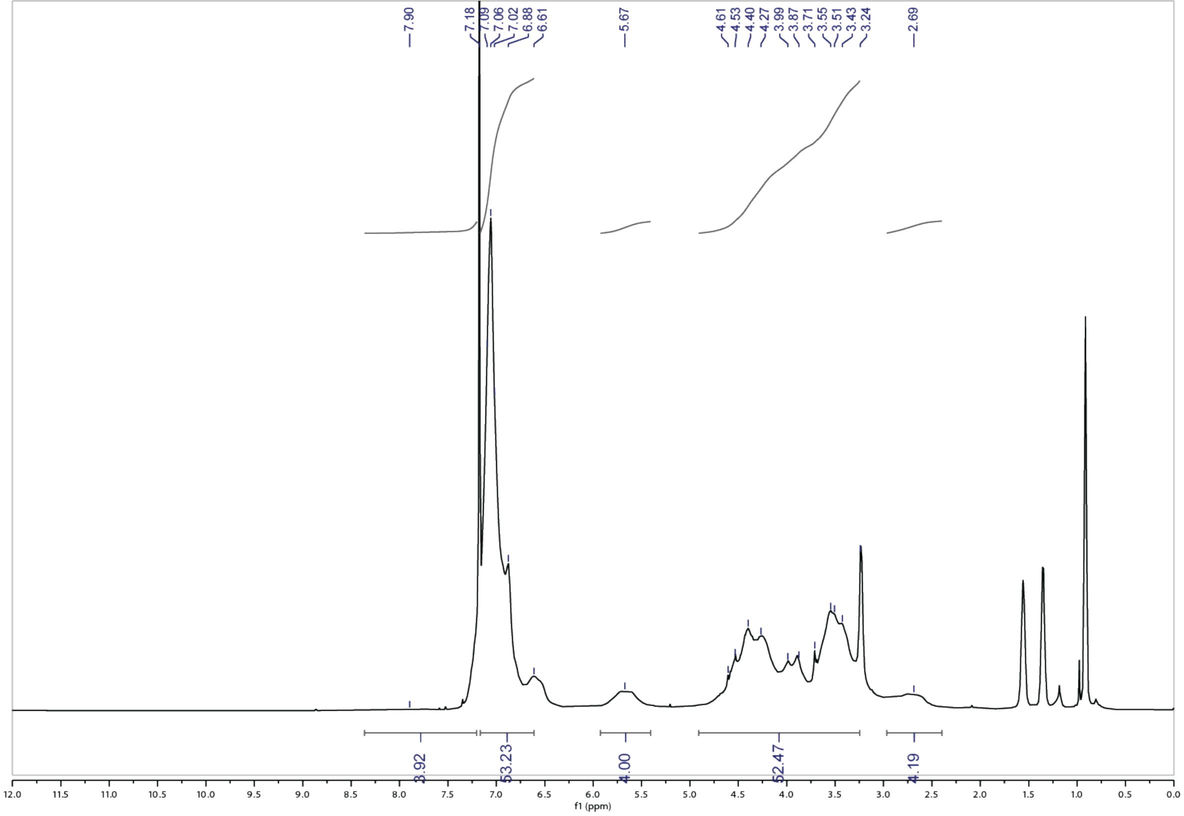
(**P6b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



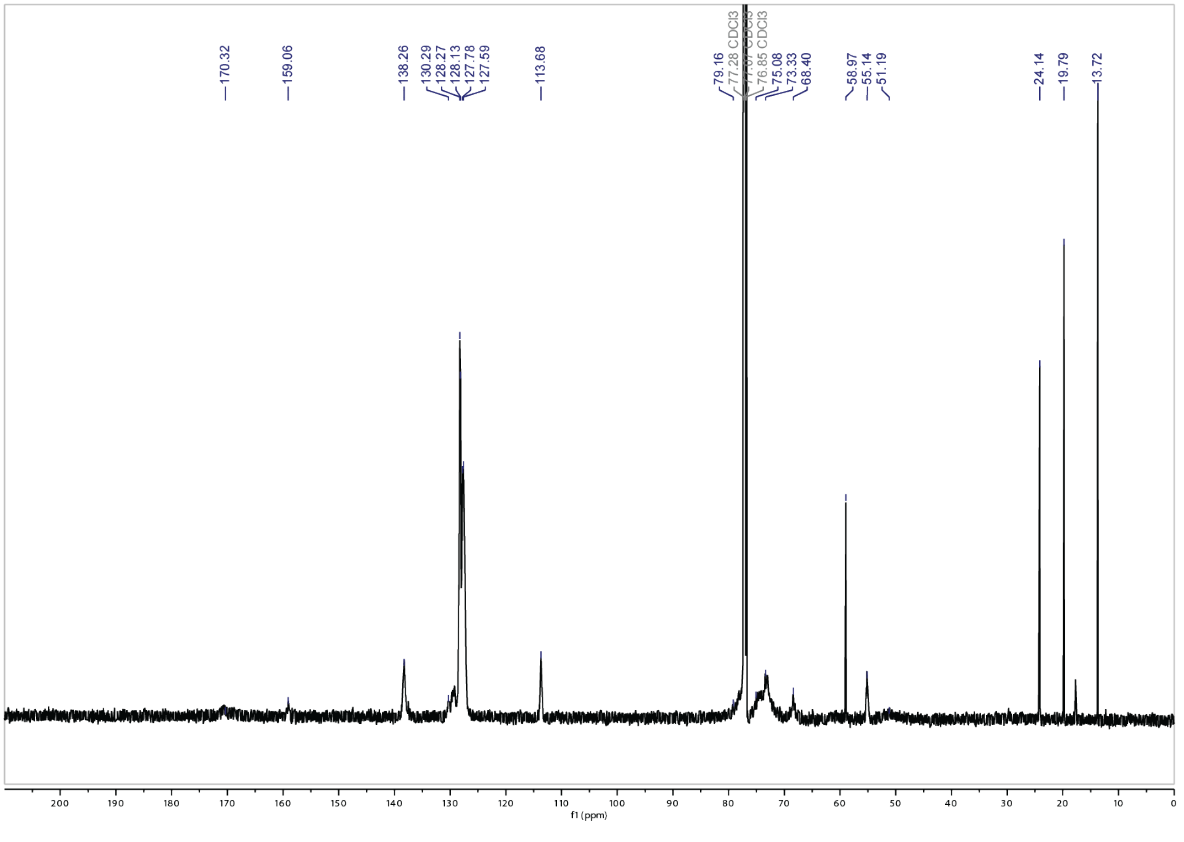
(**P6b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



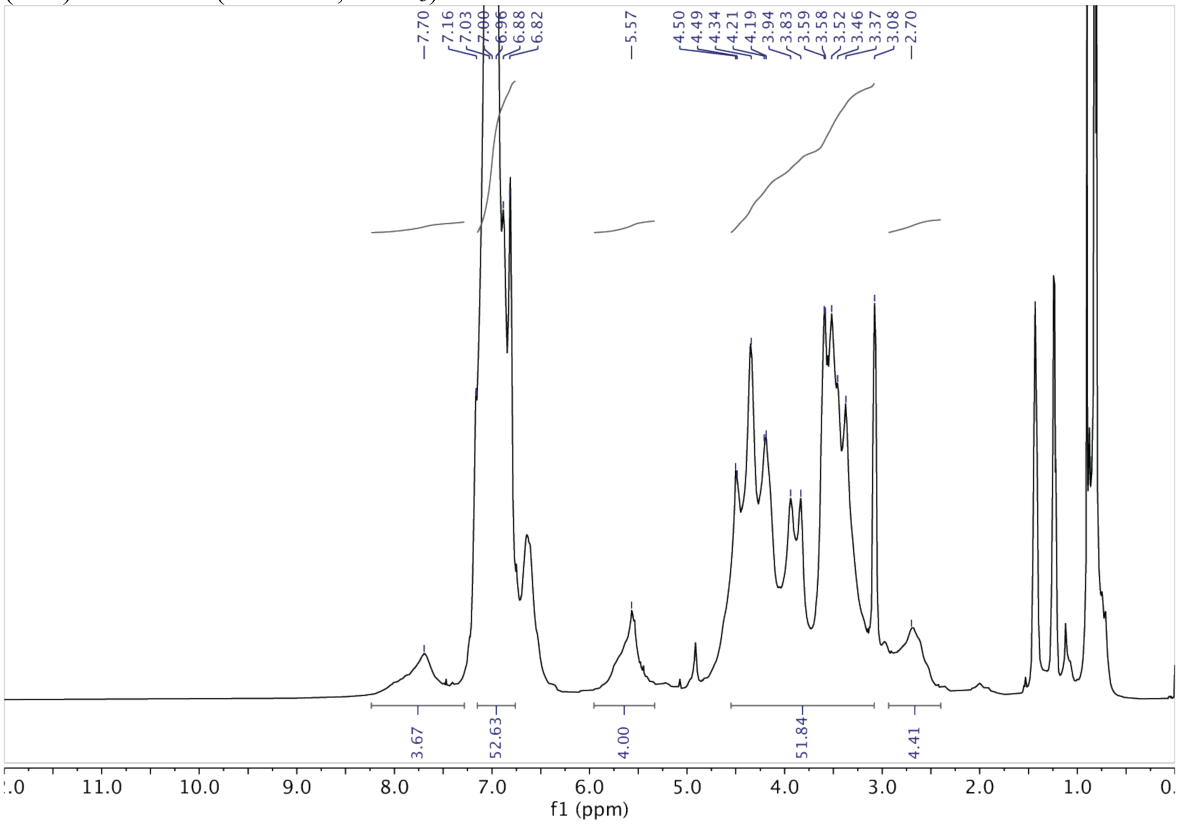
(**P7b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



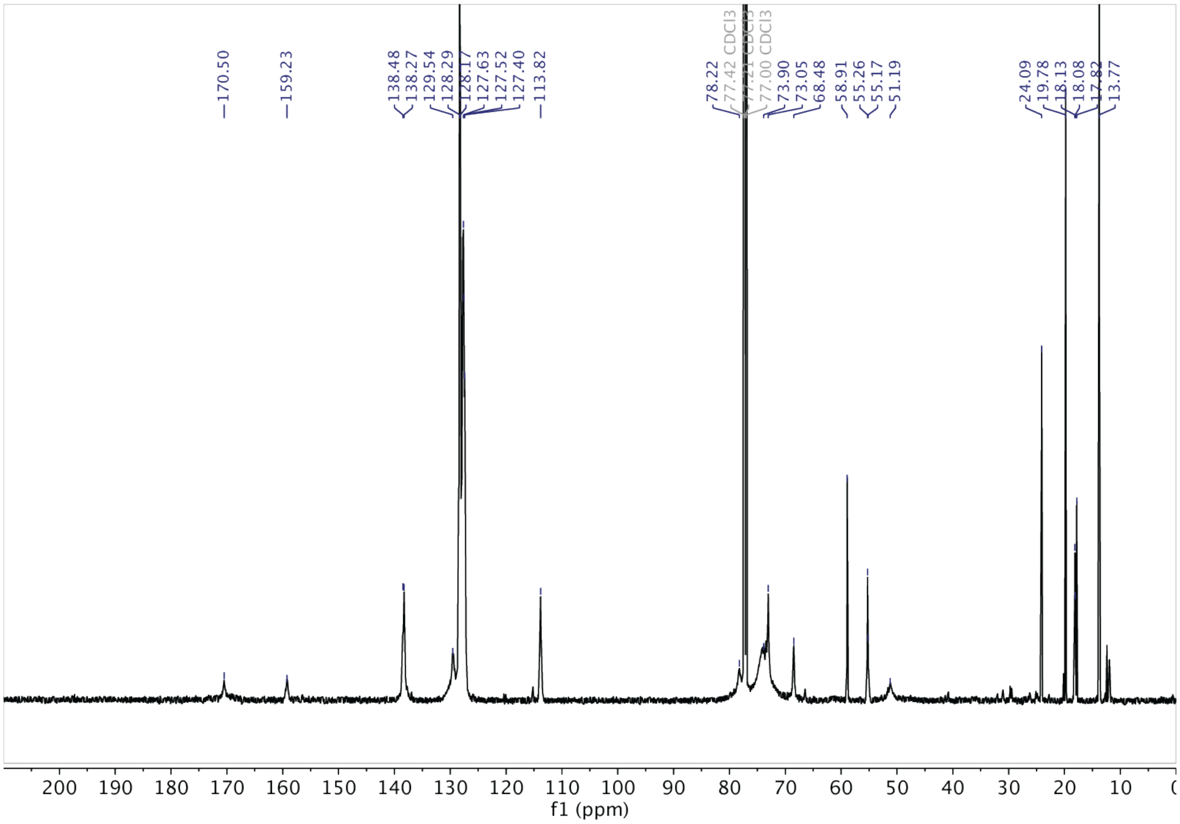
(**P7b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



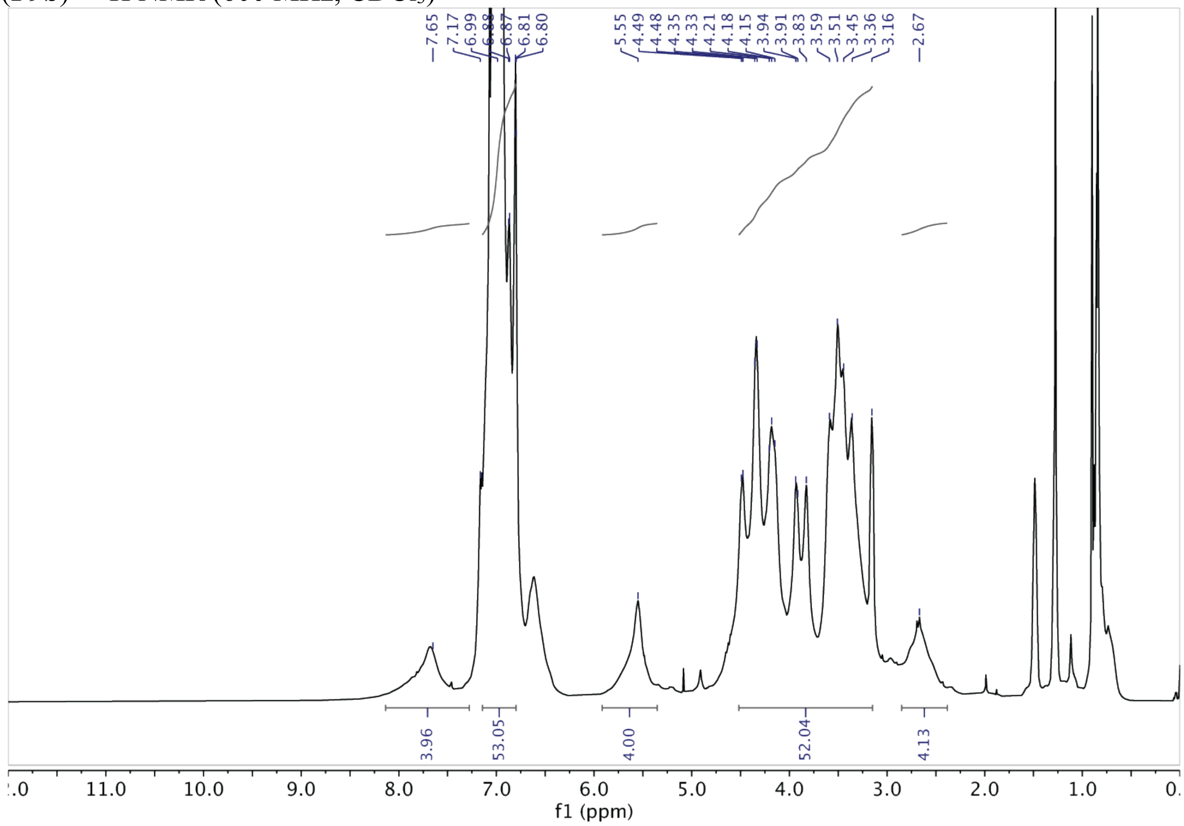
(**P8b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



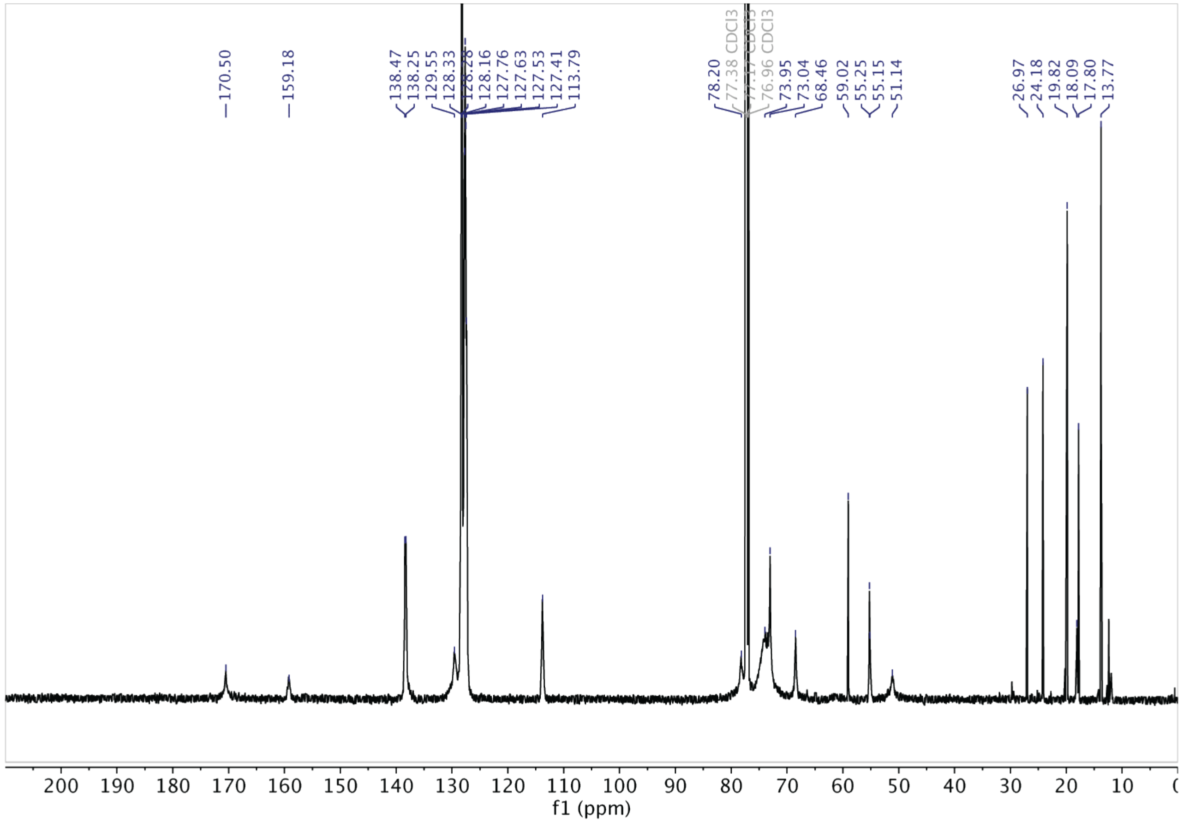
(**P8b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



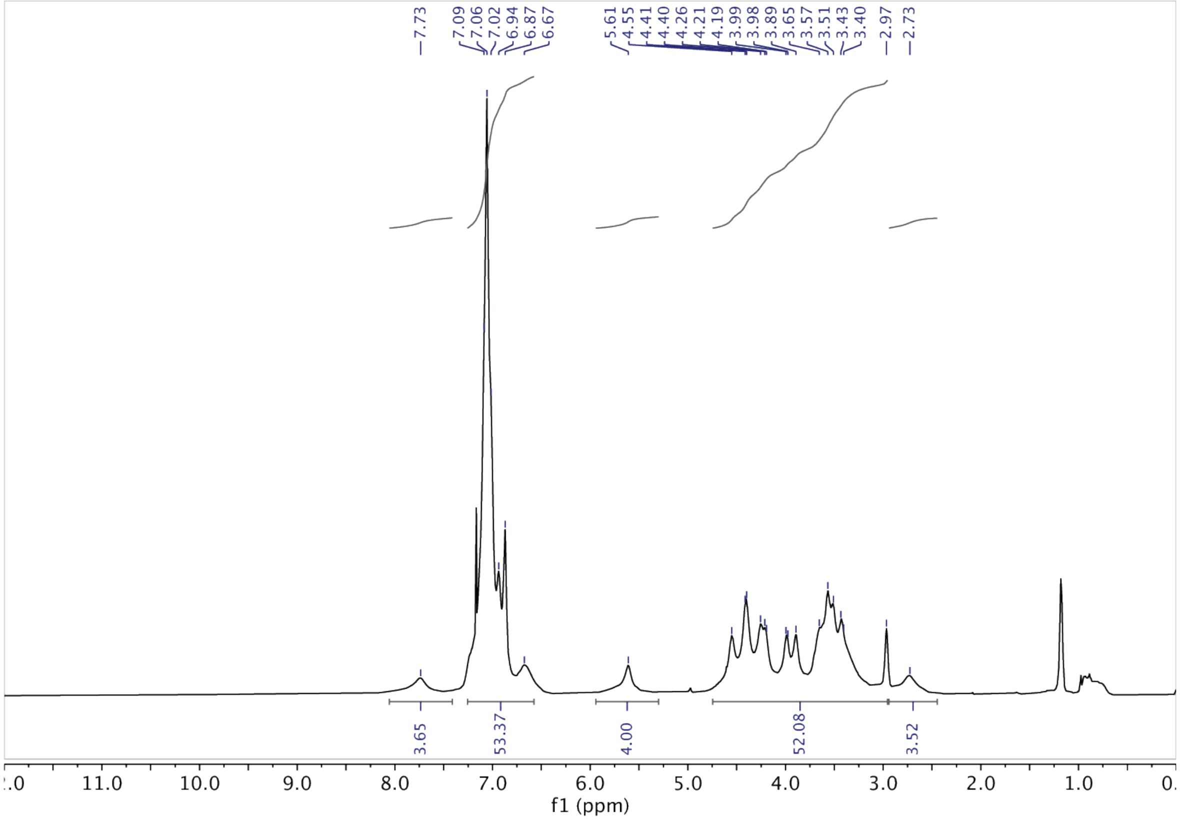
(**P9b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



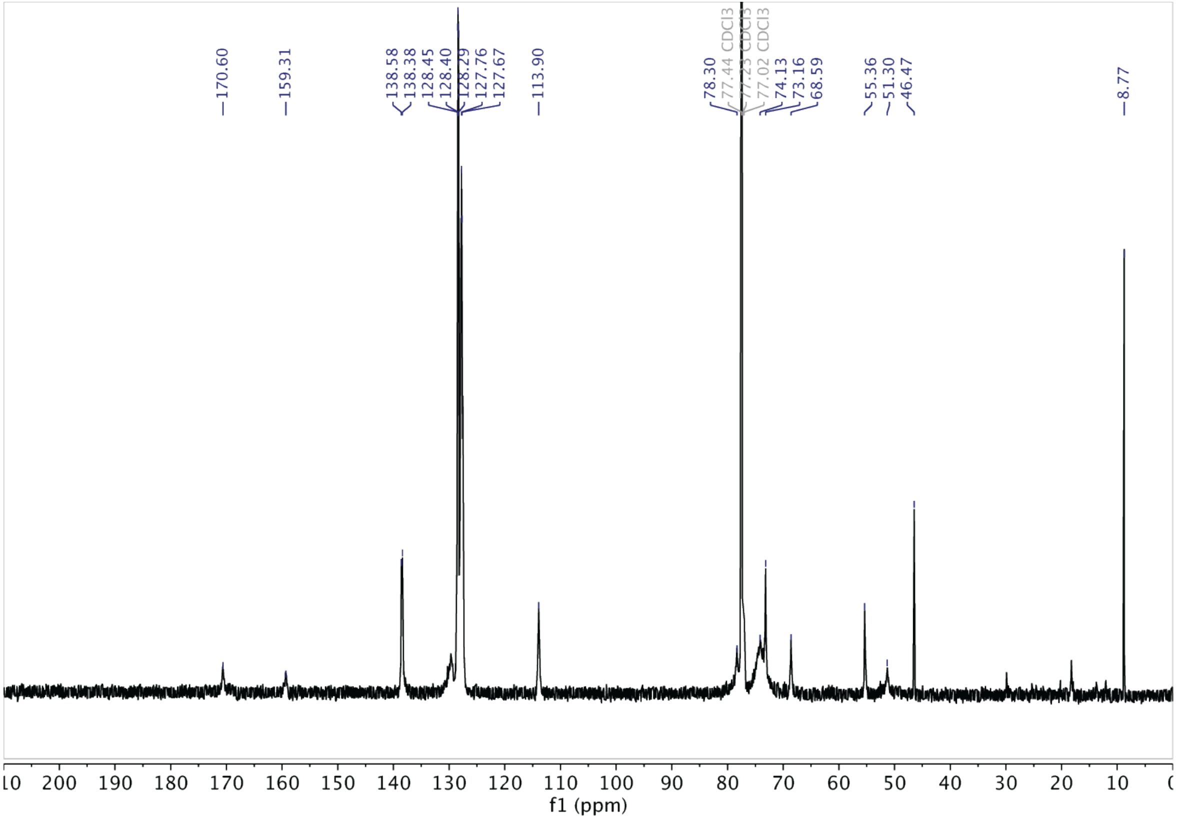
(**P9b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



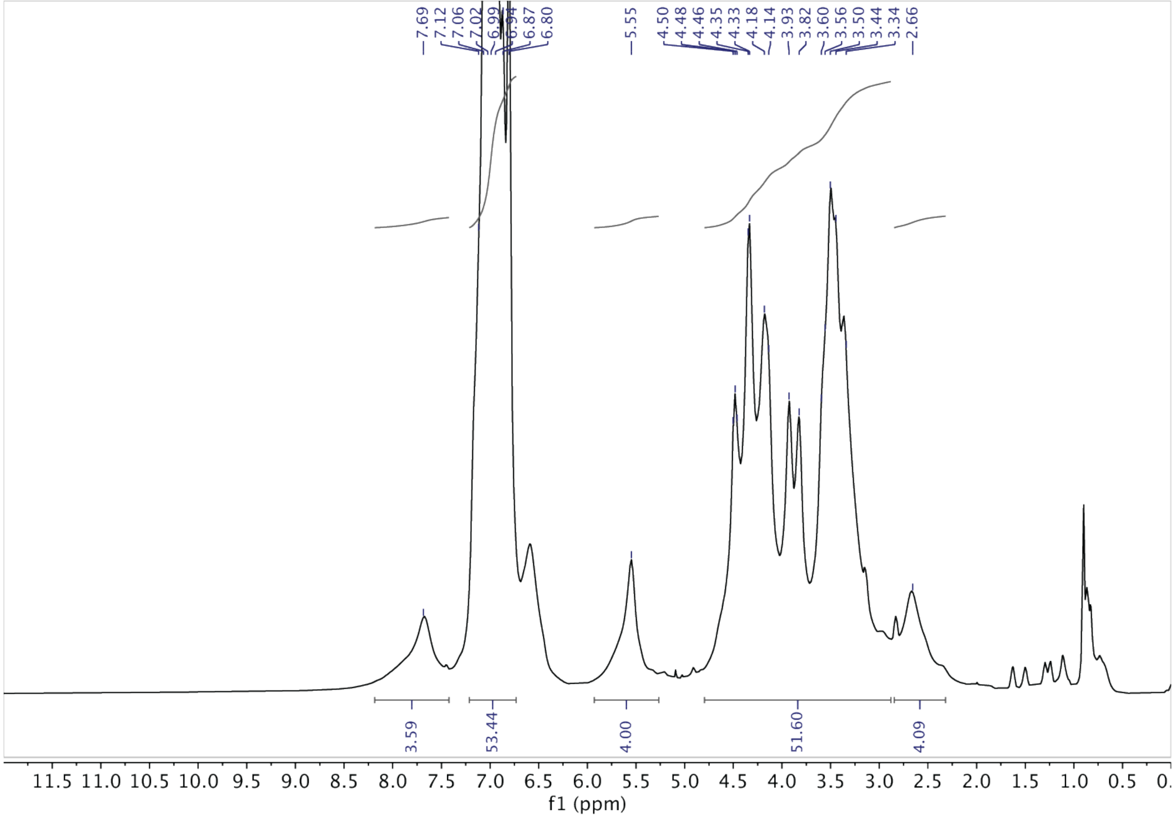
(**P10b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



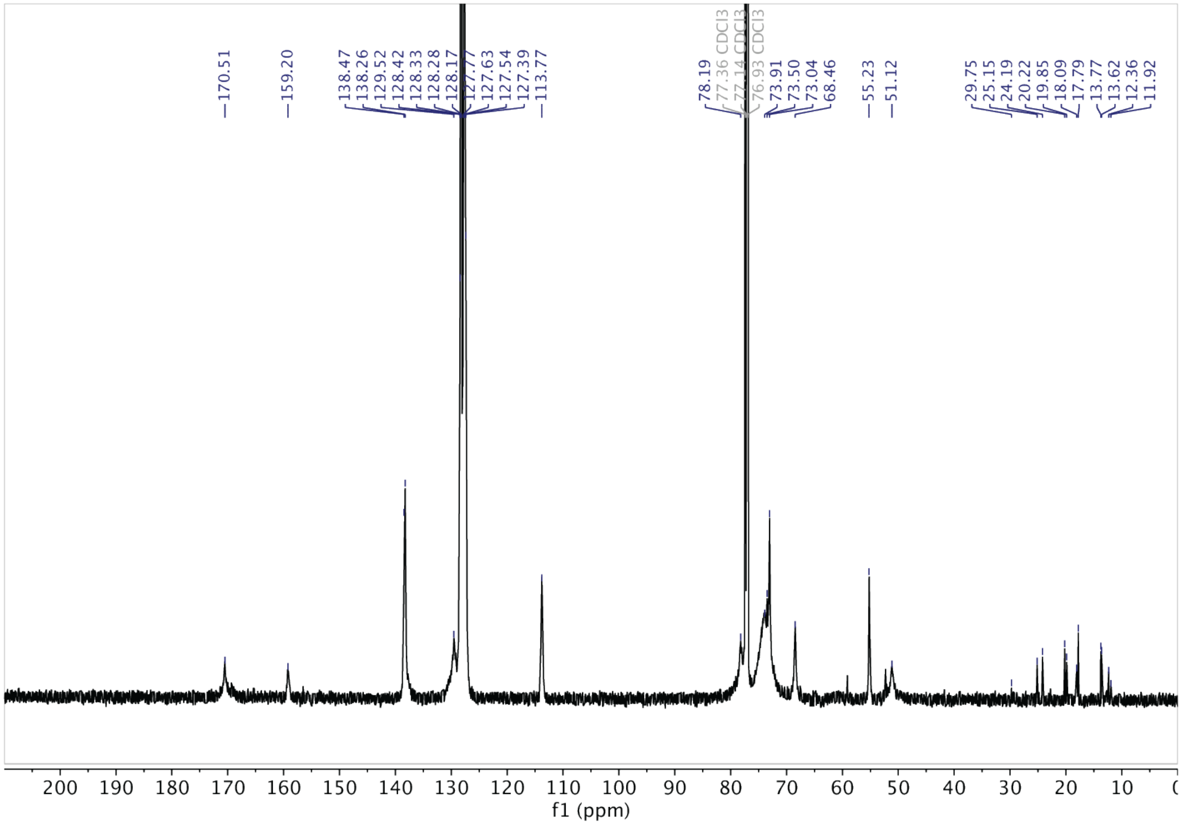
(**P10b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



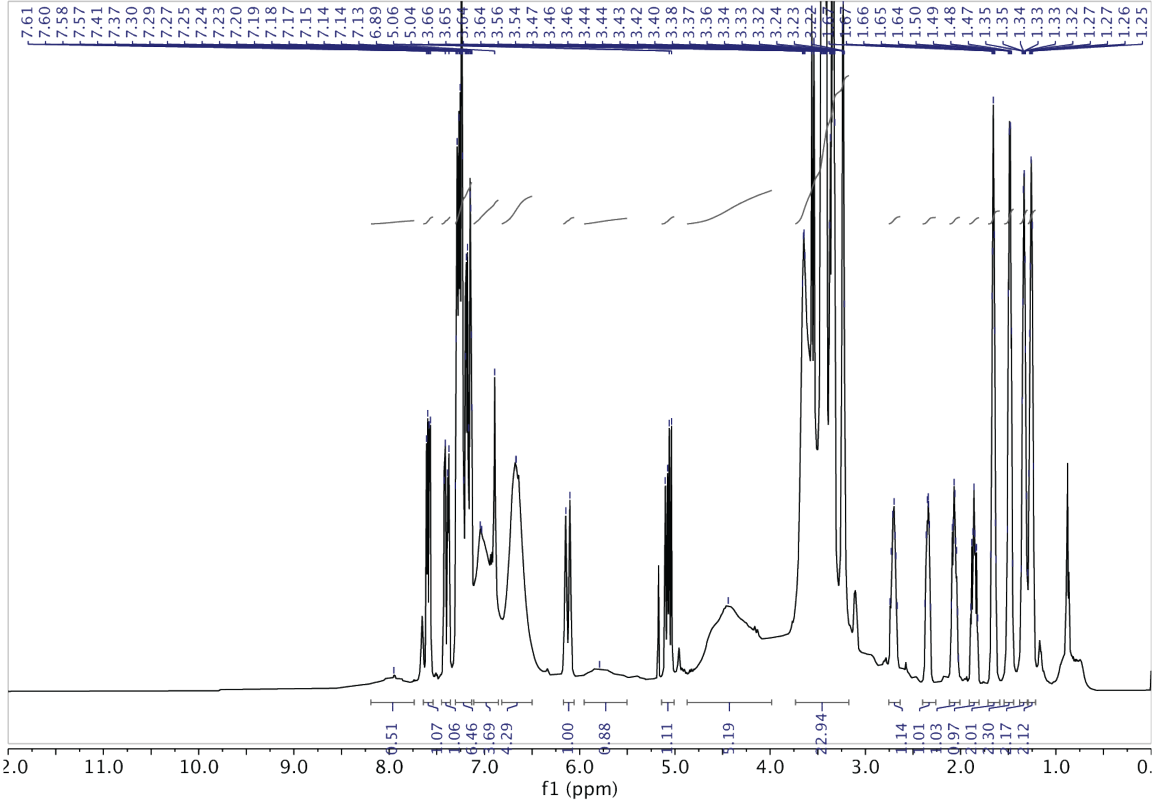
(**P11b**) – ^{1}H NMR (600 MHz, CDCl$_3$)



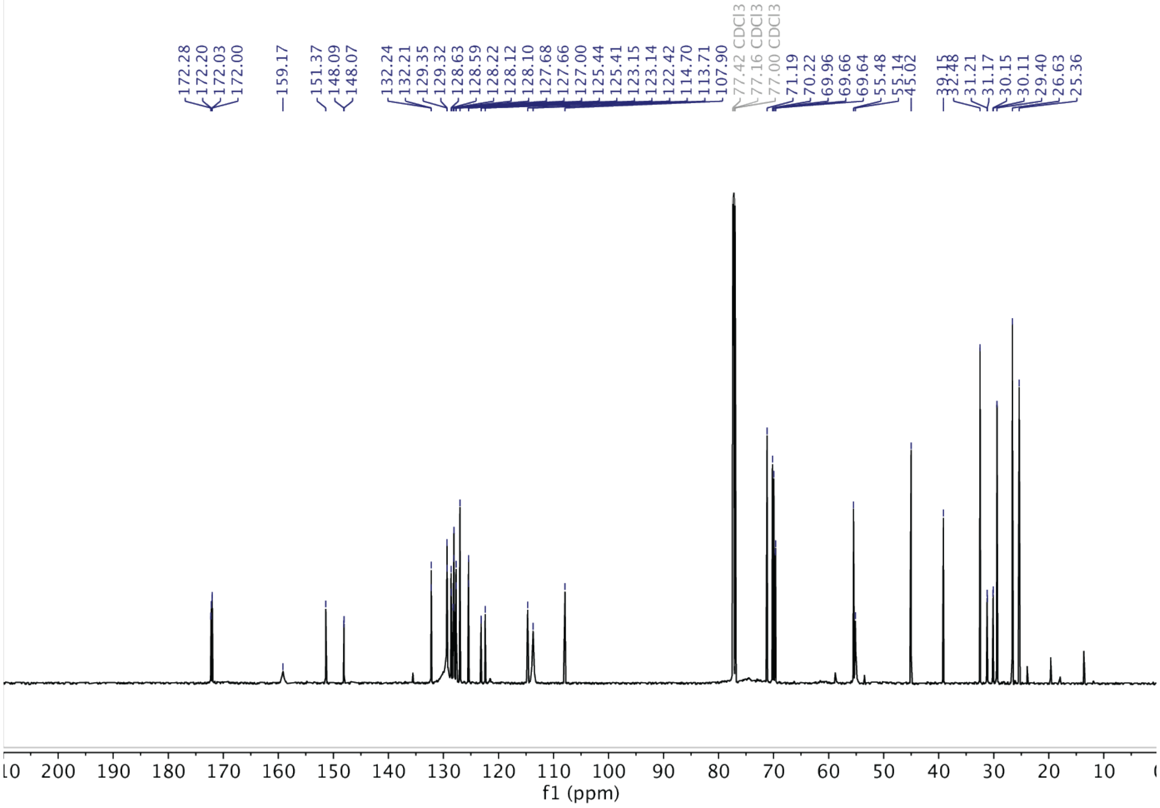
(**P11b**) – ^{13}C NMR (151 MHz, CDCl$_3$)



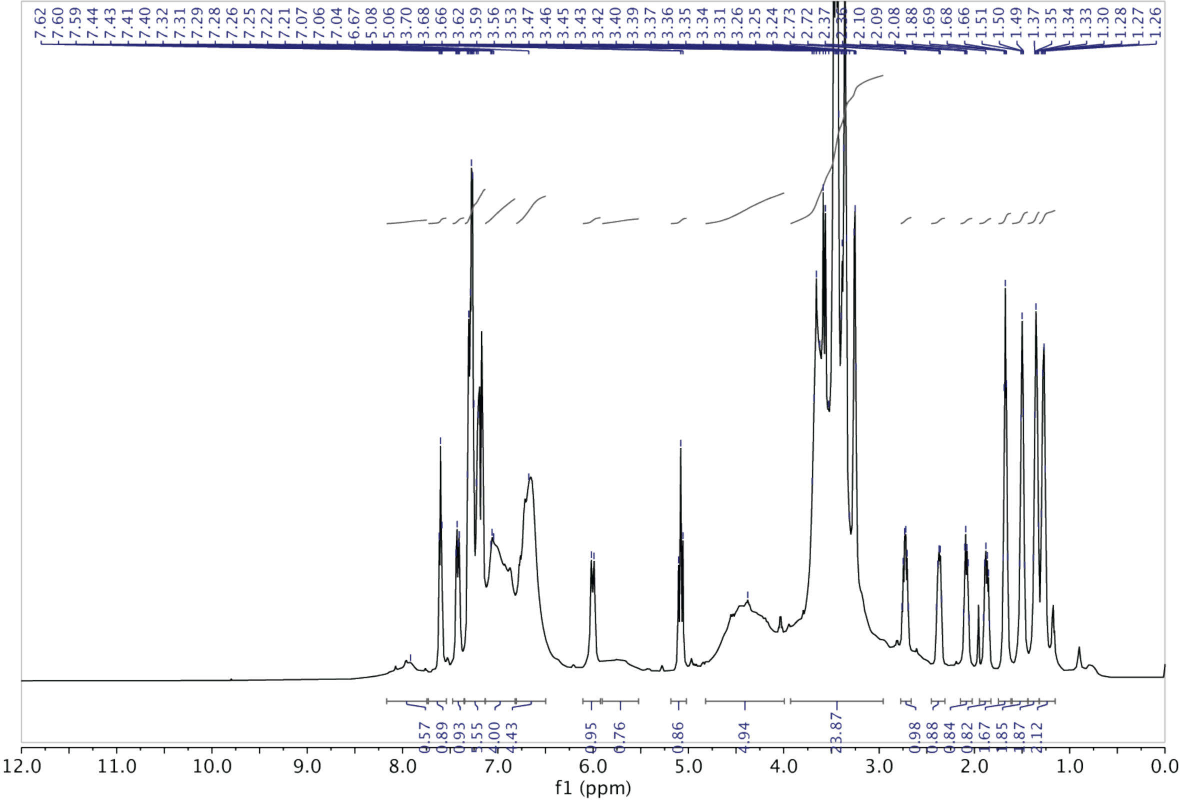
(**P1c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



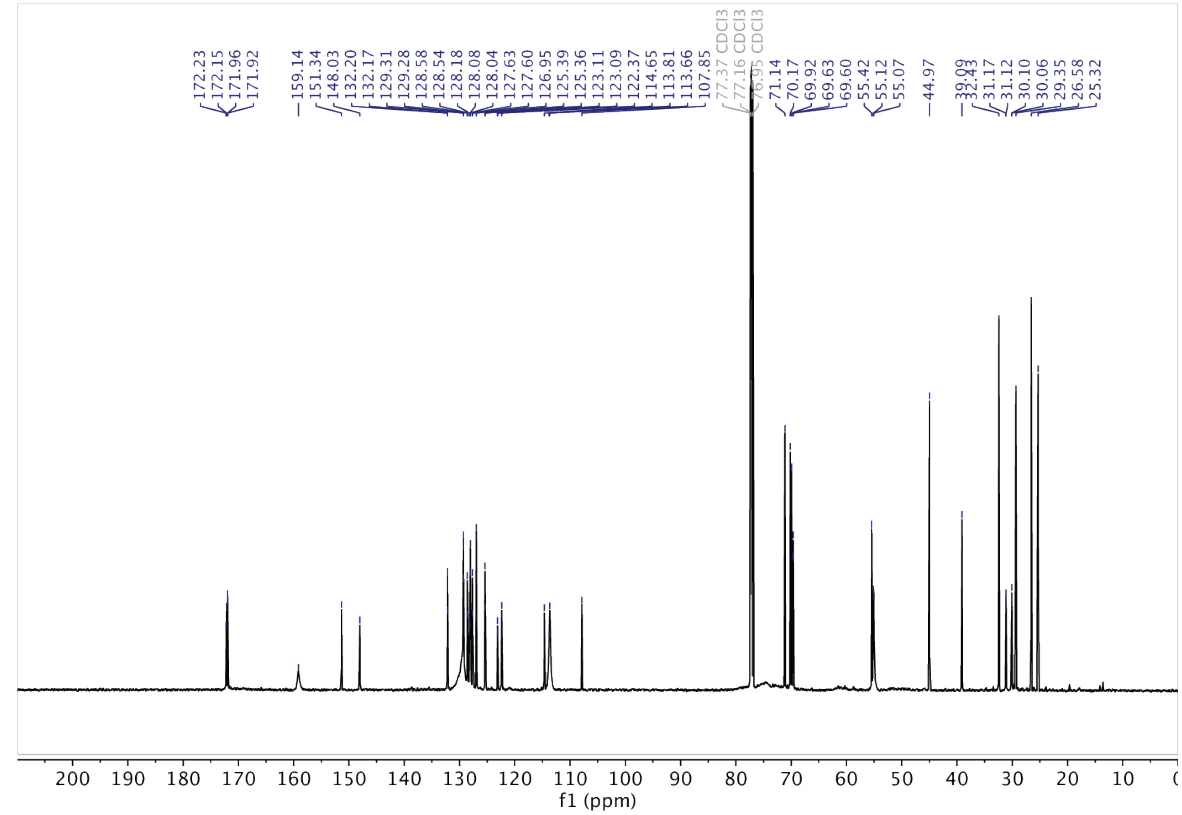
(**P1c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



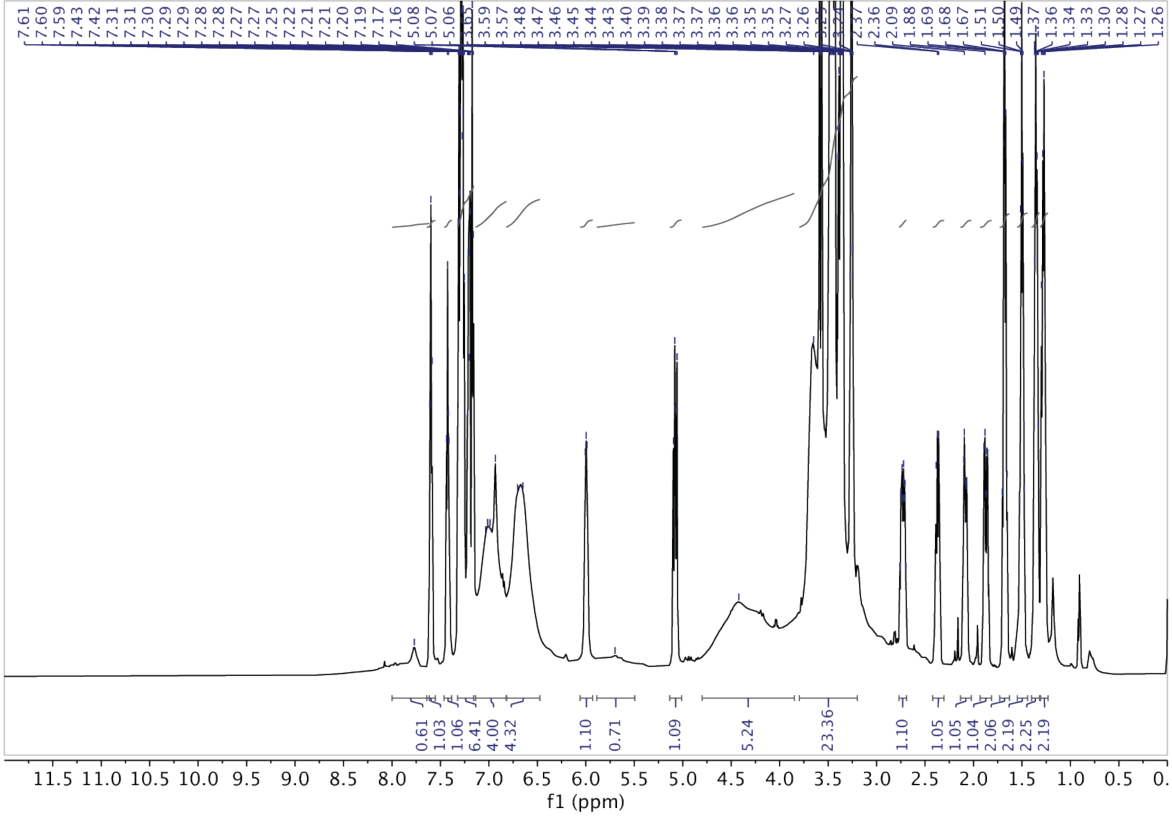
(**P2c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



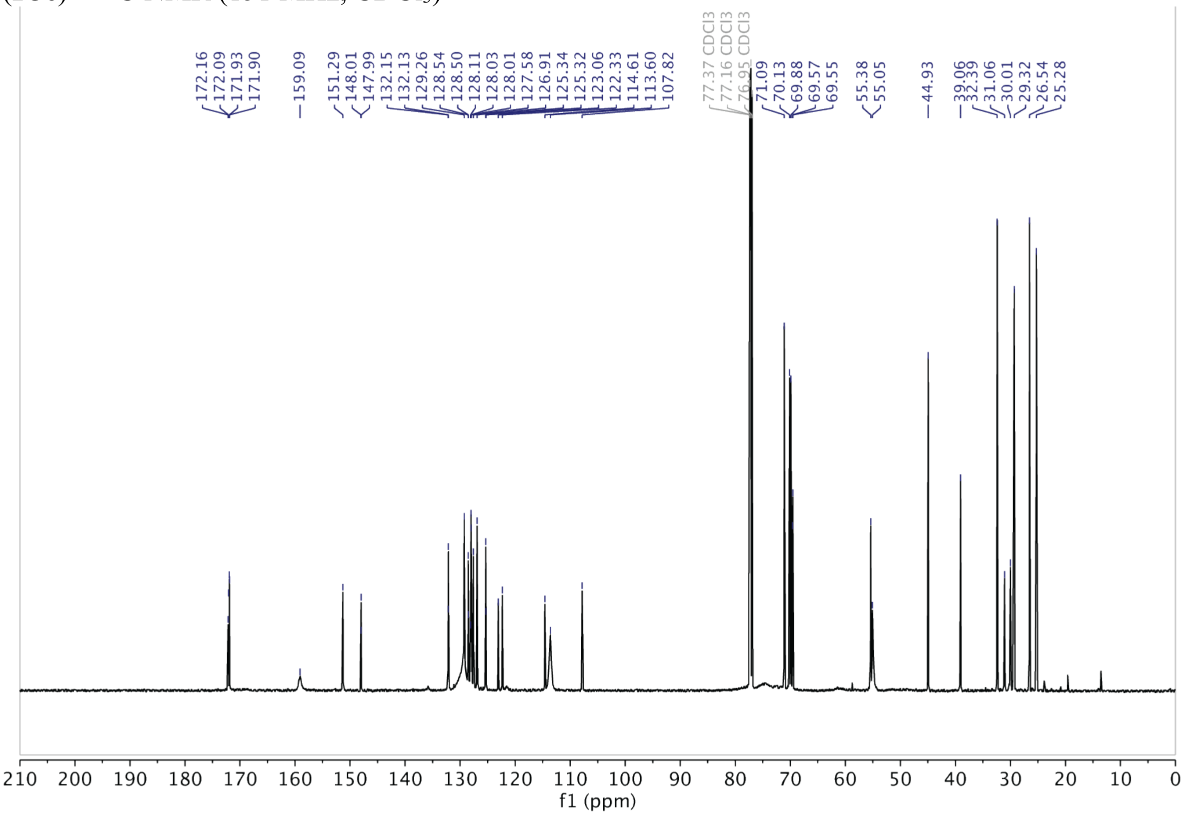
(**P2c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



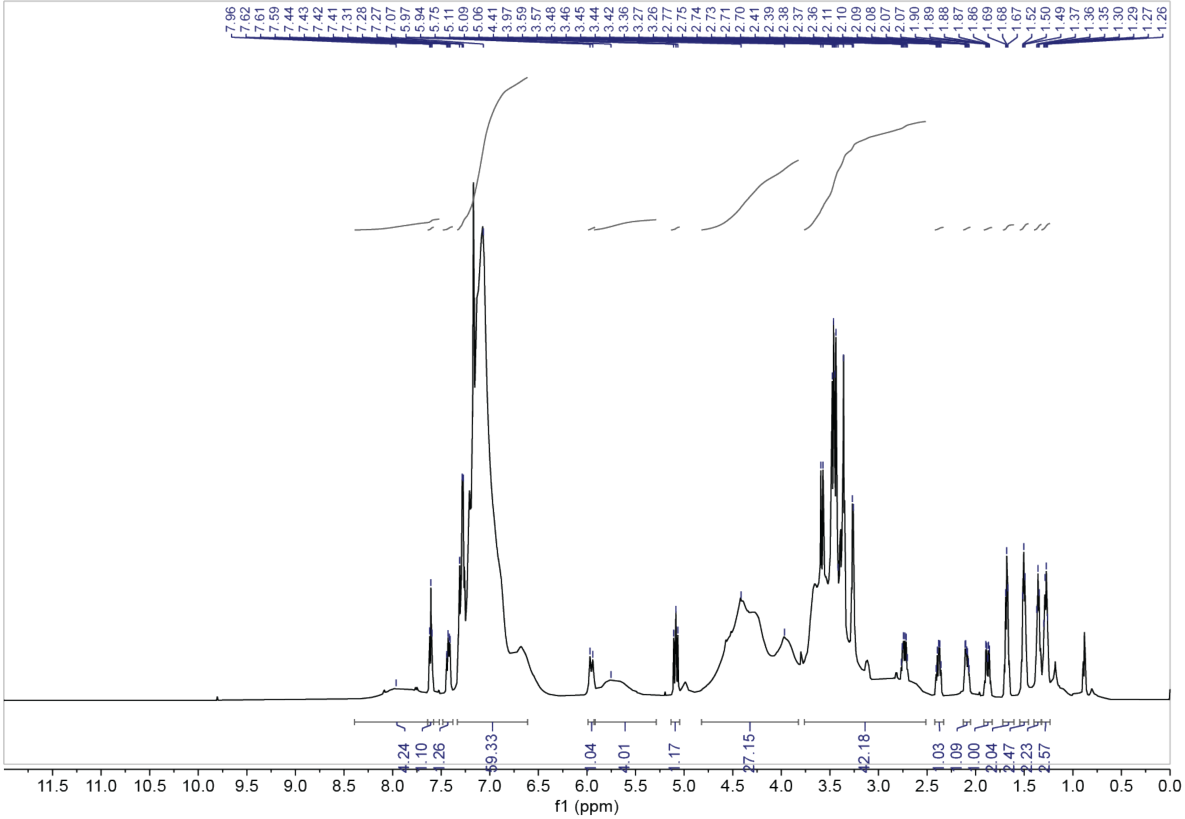
(**P3c**) – ^{1}H NMR (600 MHz, $CDCl_3$)



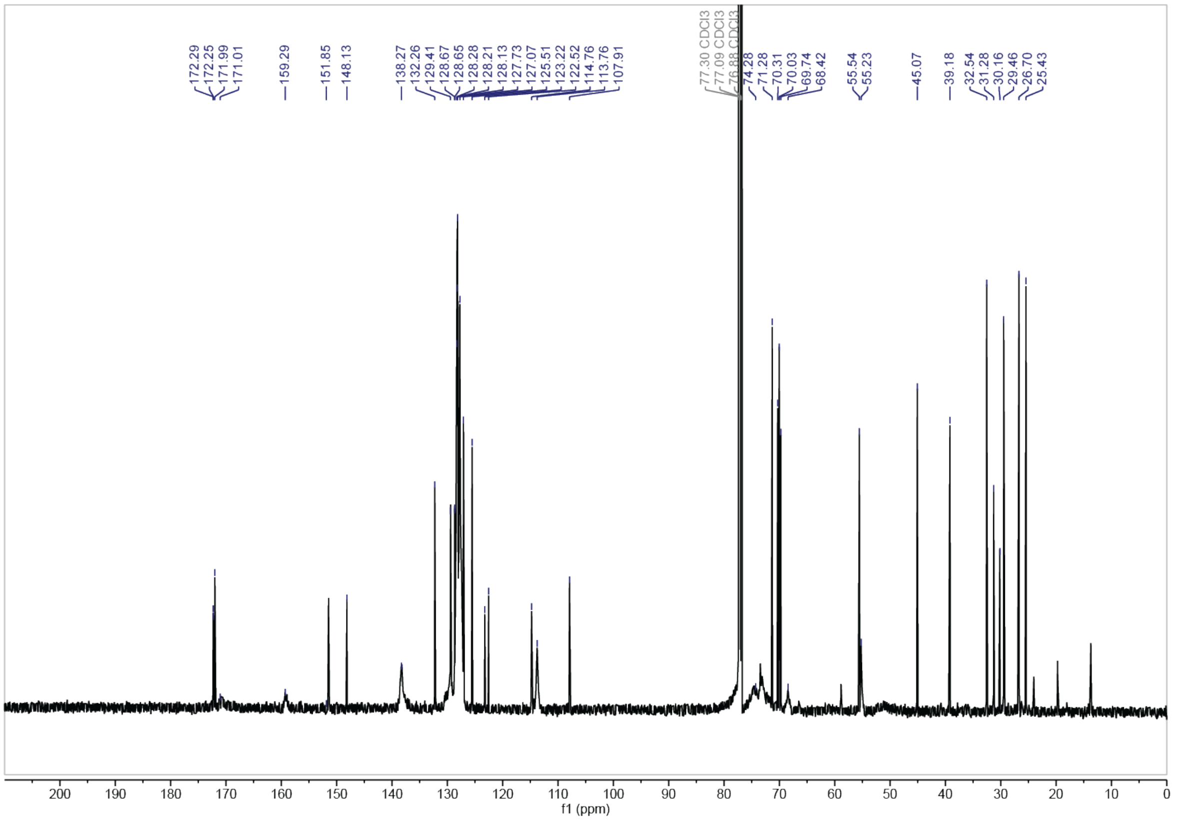
(**P3c**) – ^{13}C NMR (151 MHz, $CDCl_3$)



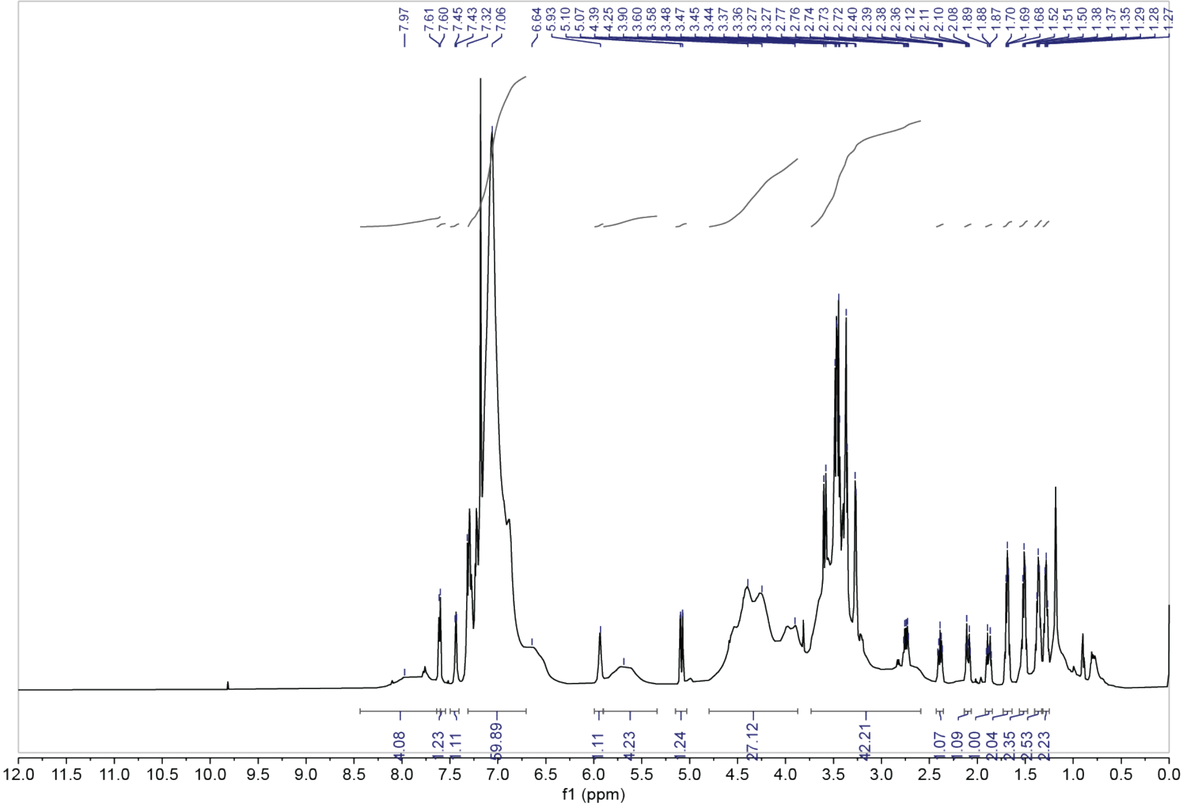
(**P4c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



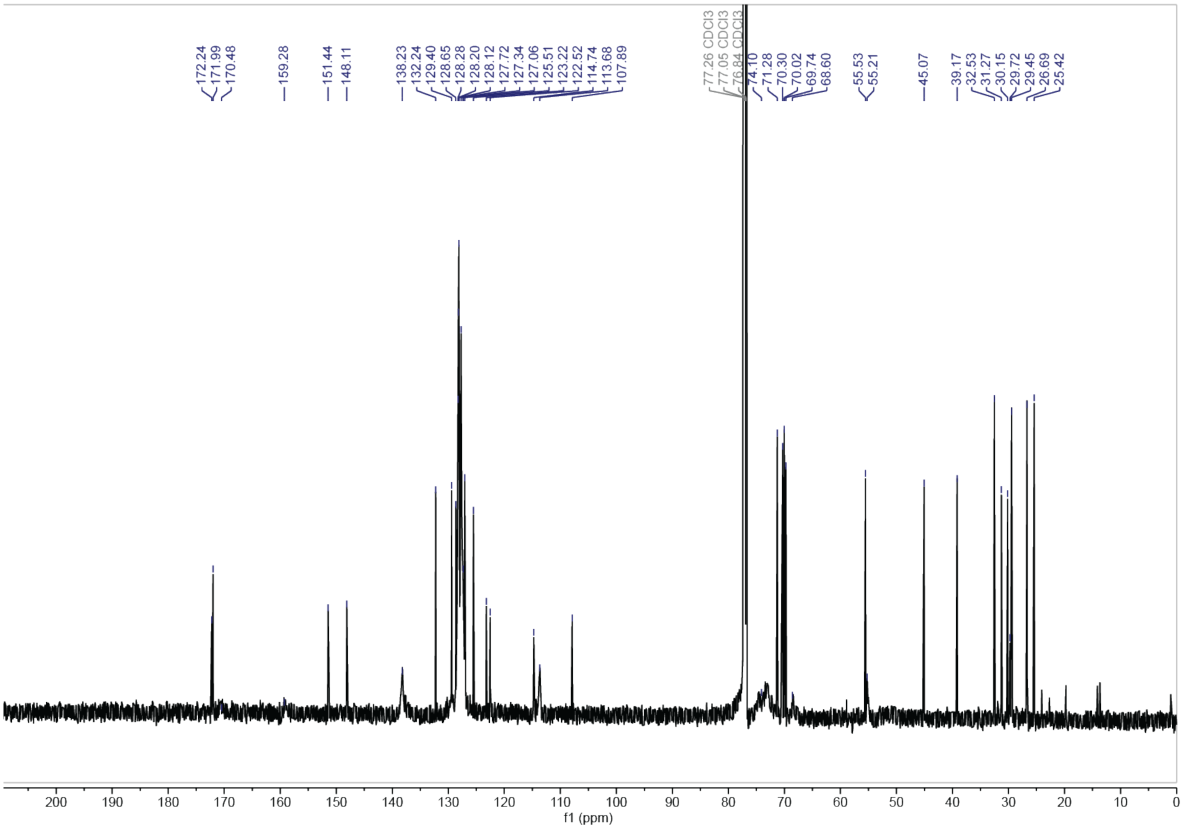
(**P4c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



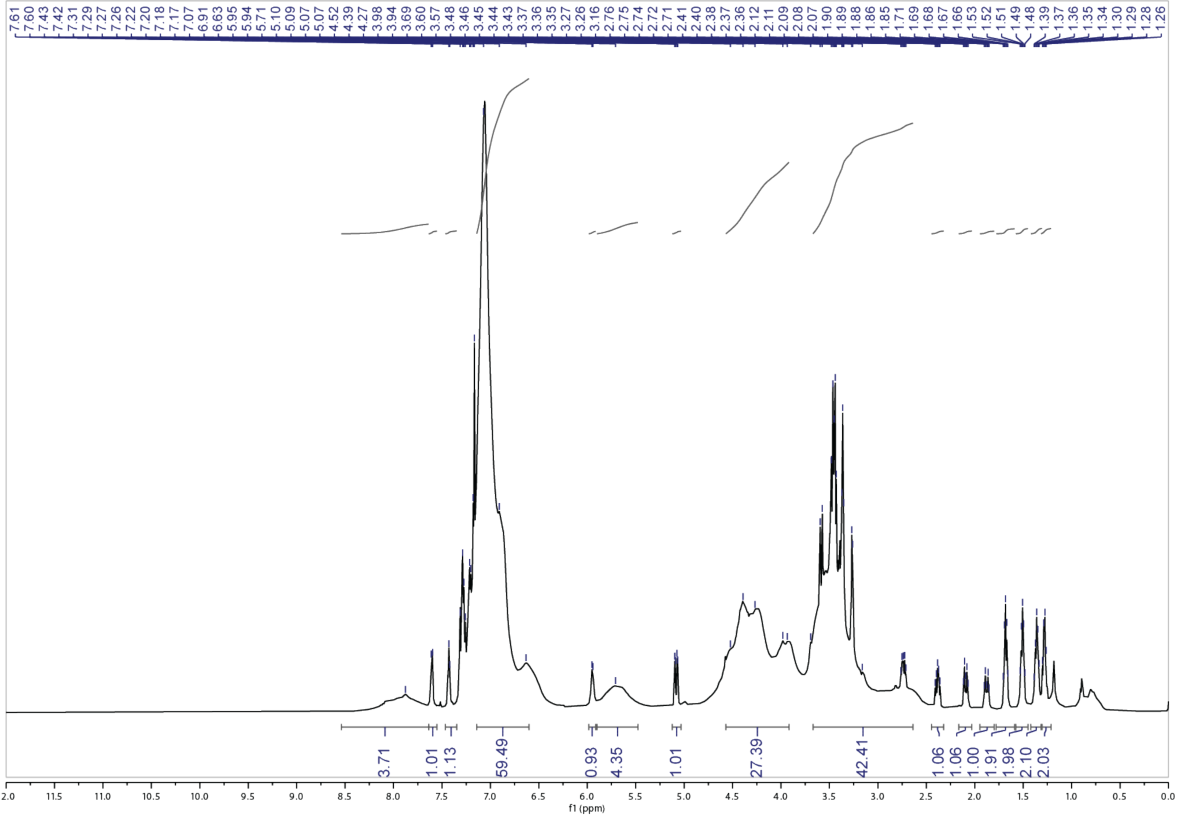
(**P5c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



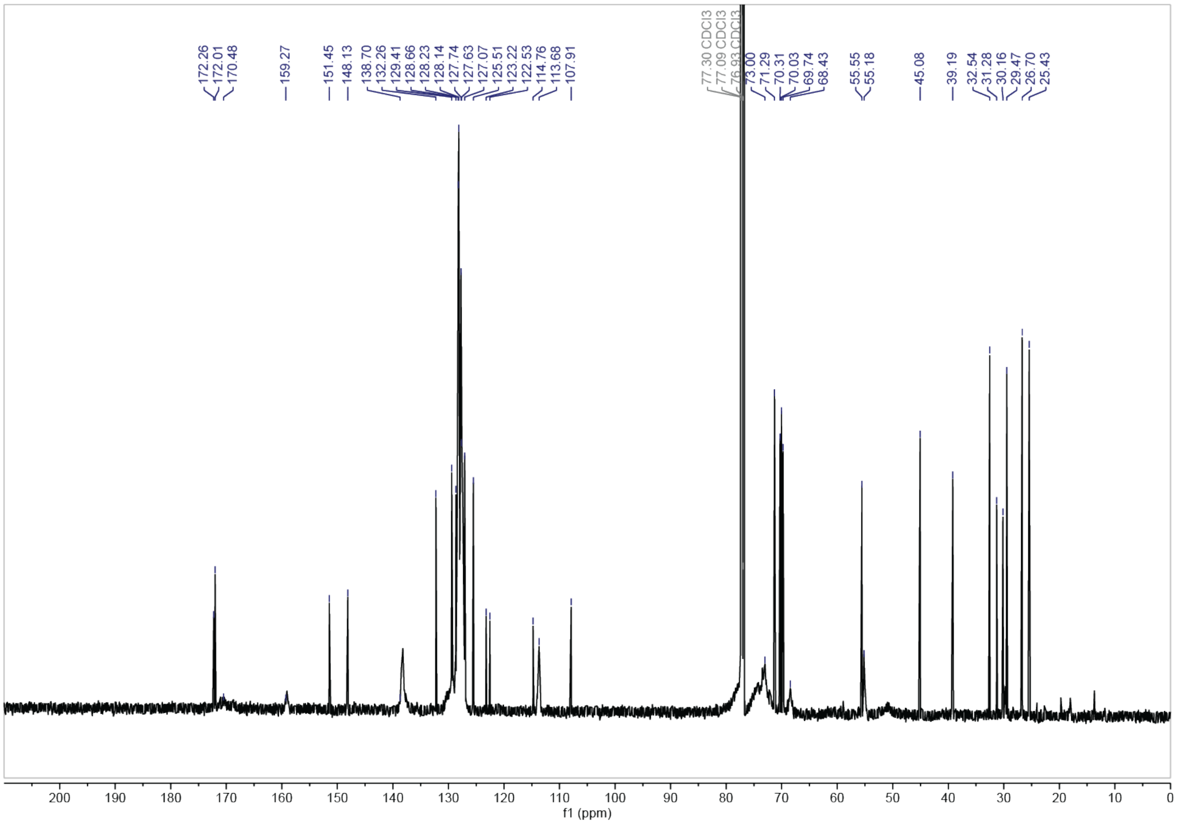
(**P5c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



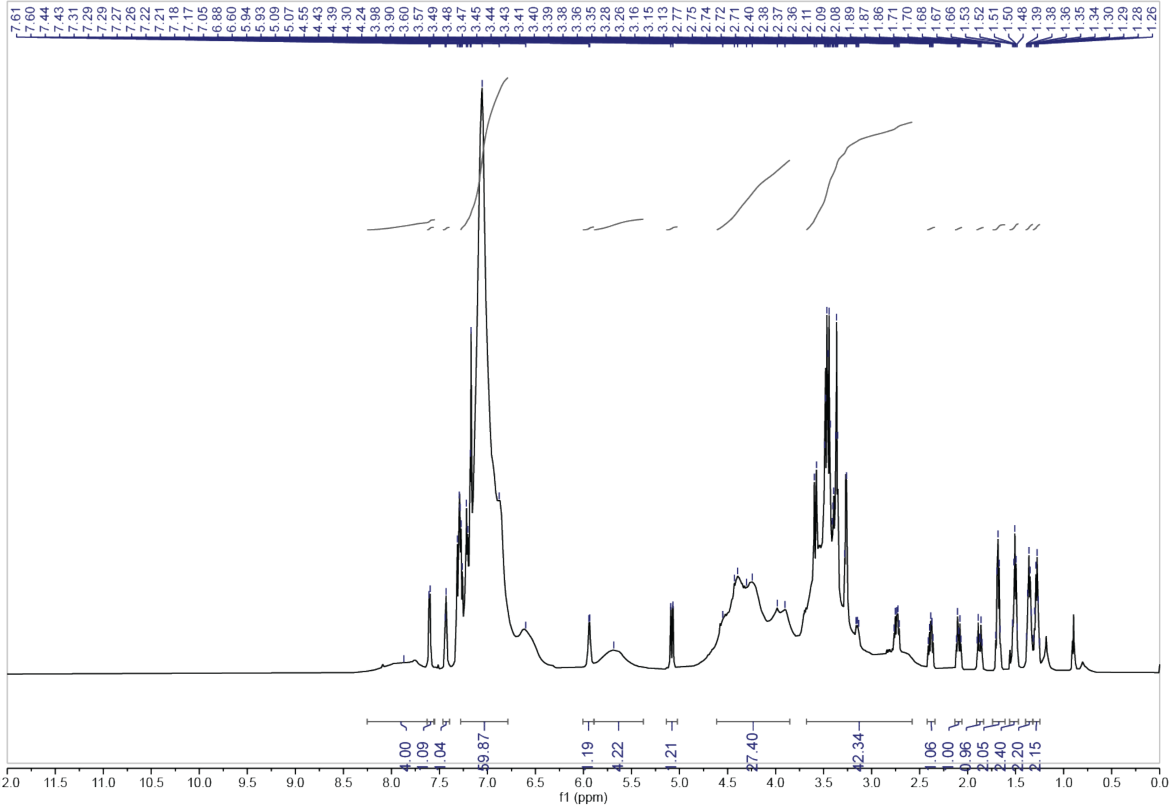
(**P6c**) – ^{1}H NMR (600 MHz, $CDCl_3$)



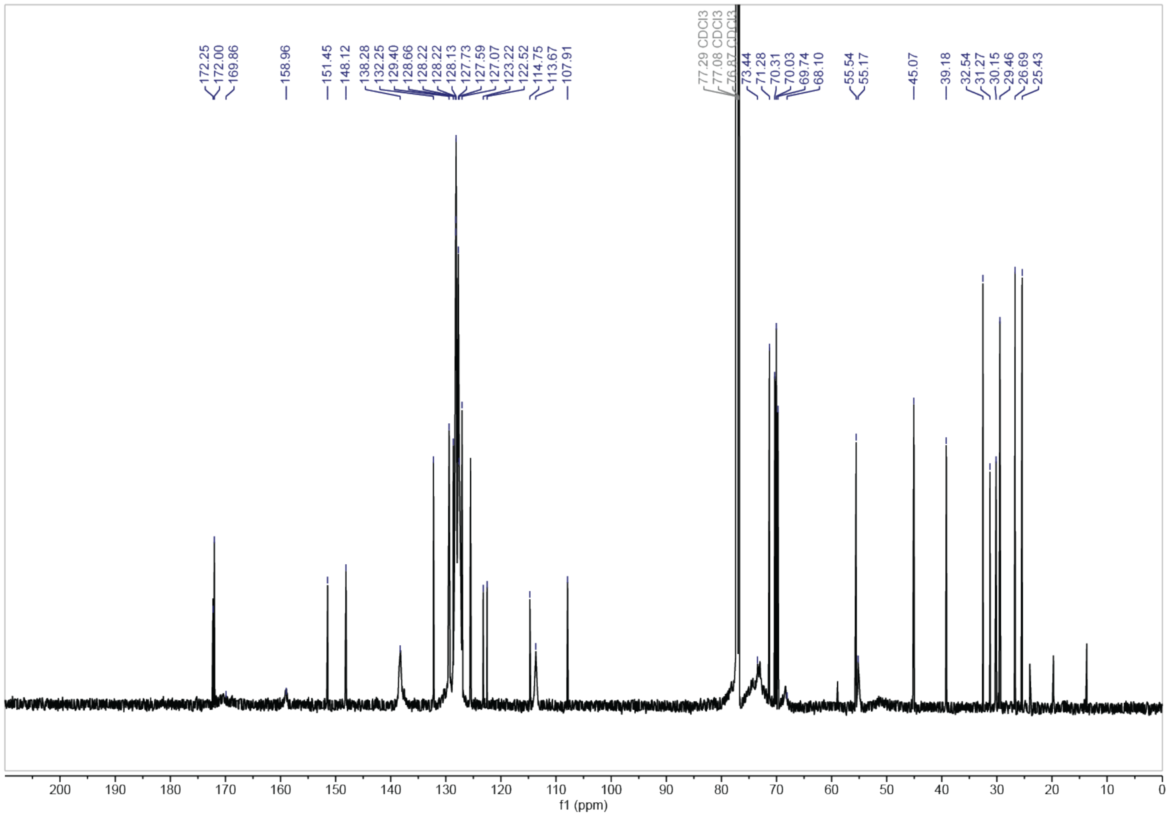
(**P6c**) – ^{13}C NMR (151 MHz, $CDCl_3$)



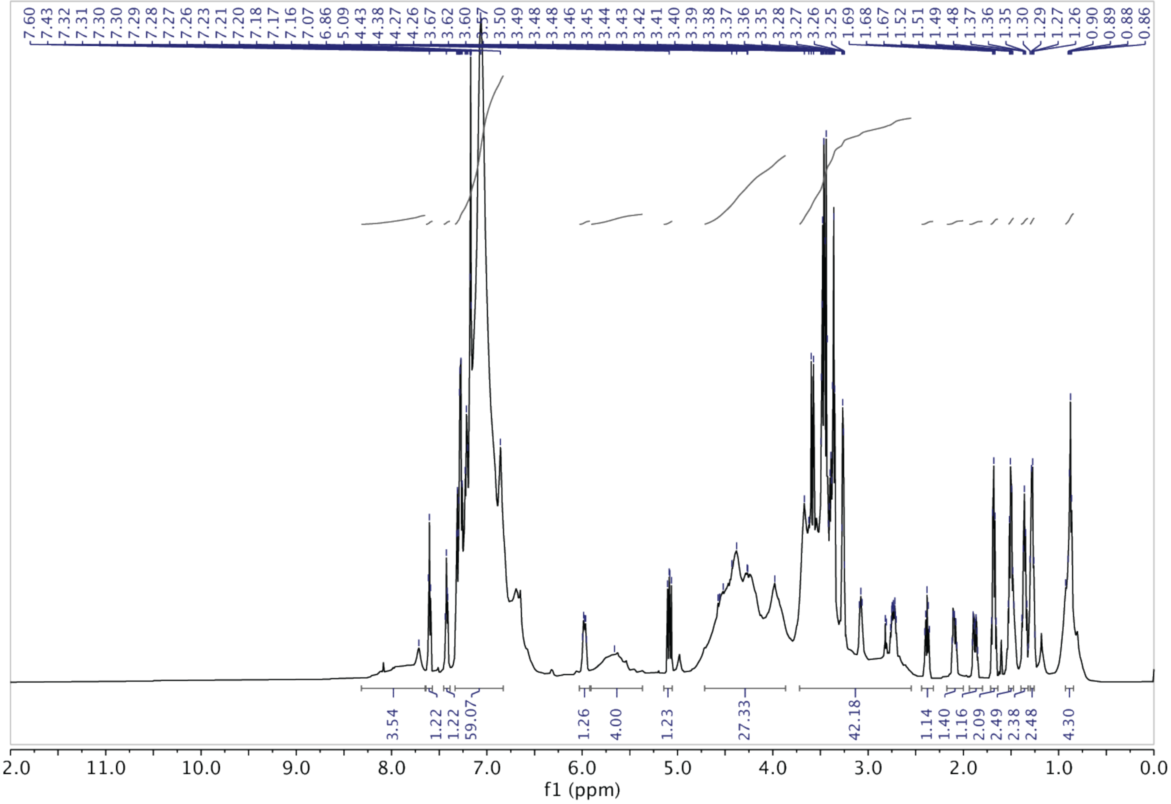
(**P7c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



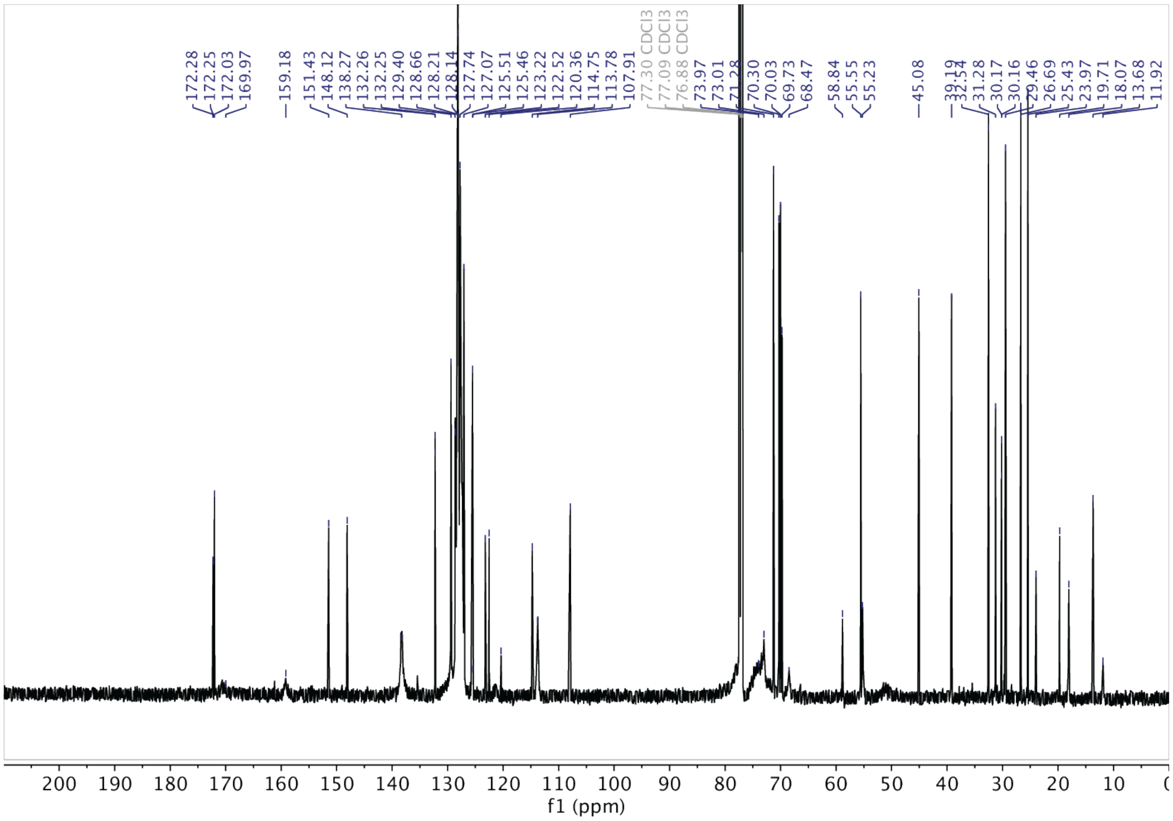
(**P7c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



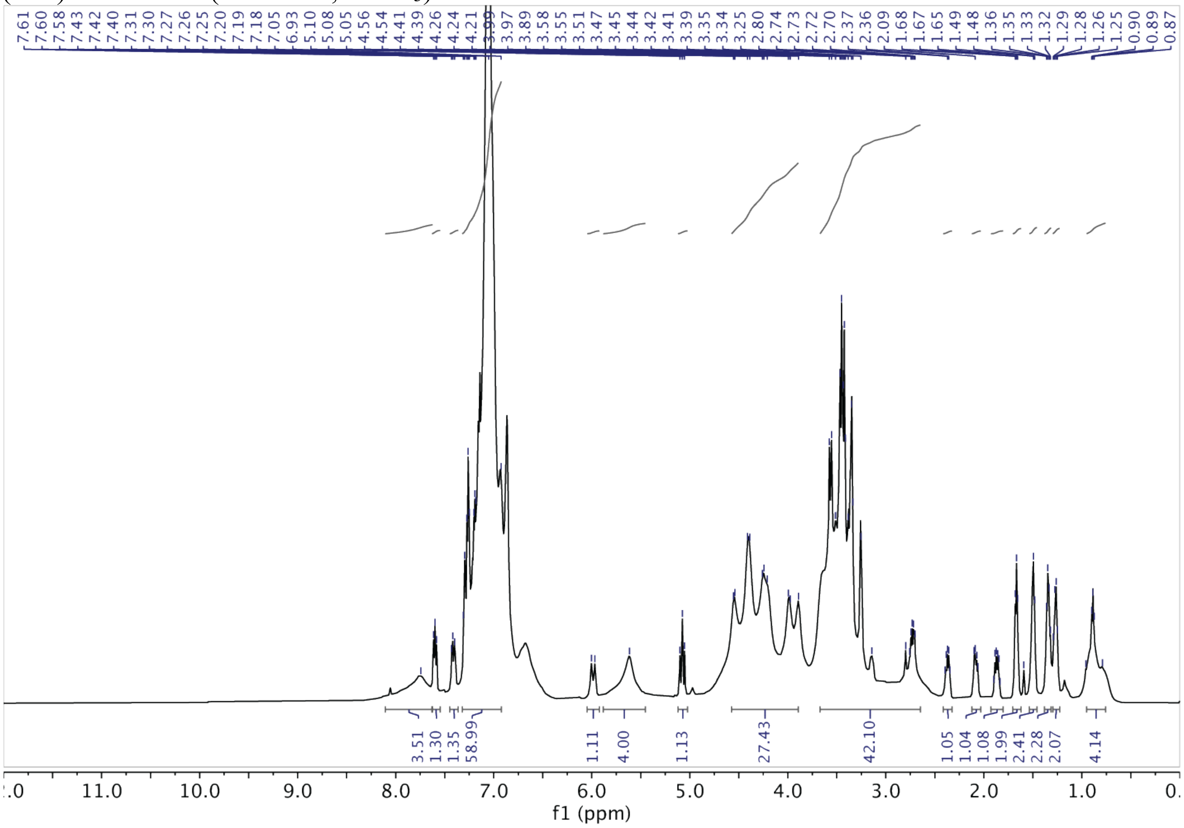
(**P8c**) – ^{1}H NMR (600 MHz, $CDCl_3$)



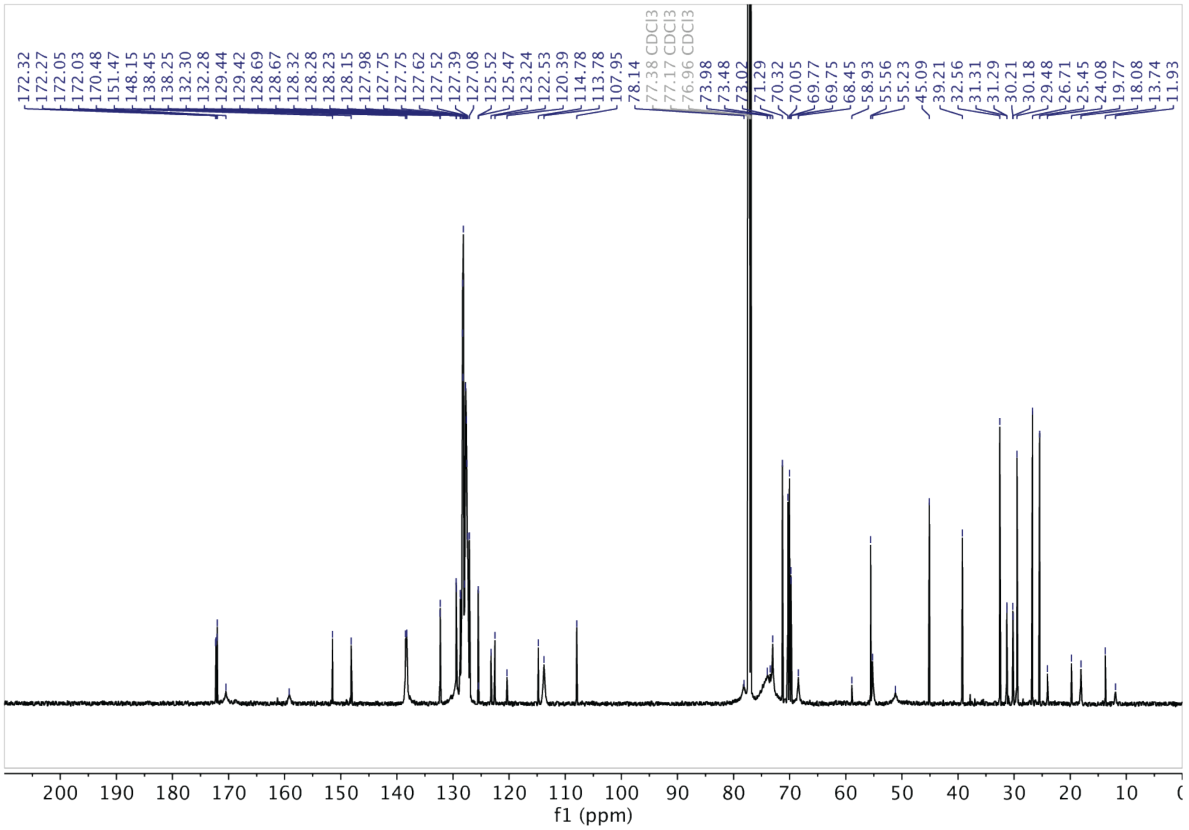
(**P8c**) – ^{13}C NMR (151 MHz, $CDCl_3$)



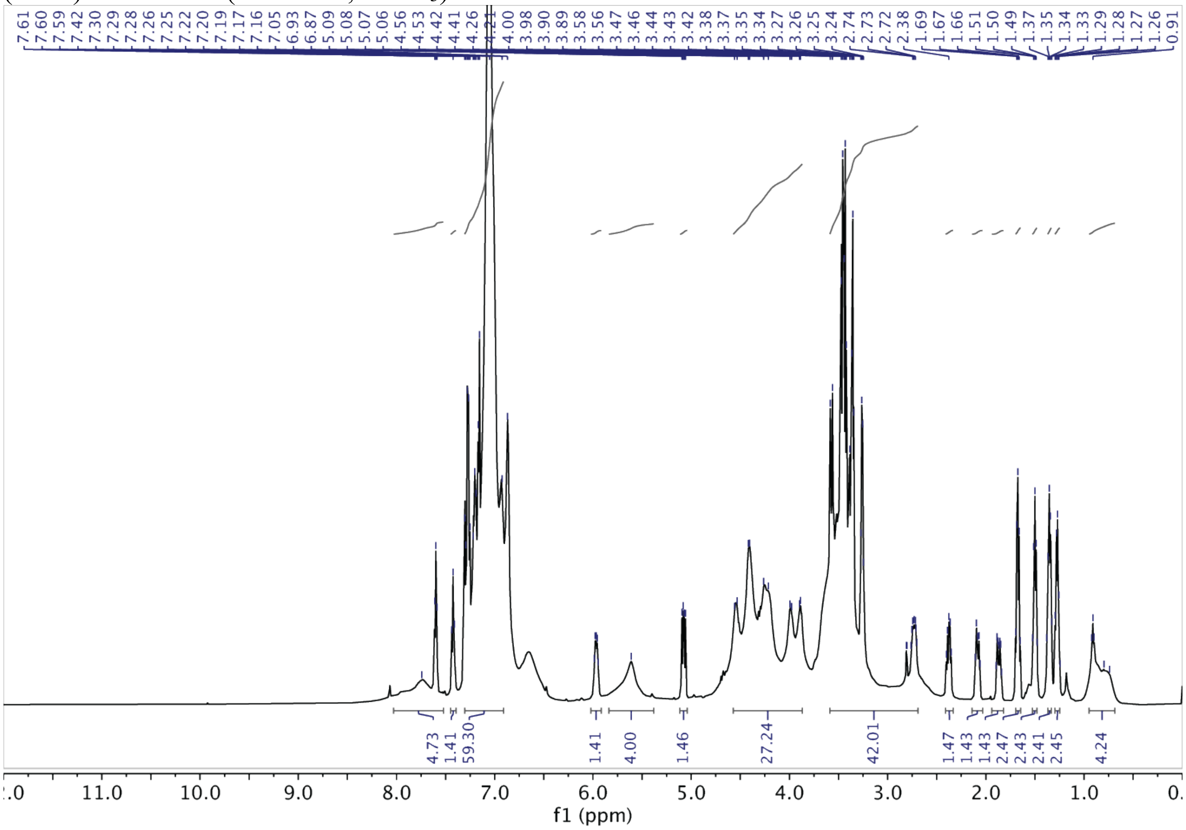
(**P9c**) – ^{1}H NMR (600 MHz, $CDCl_3$)



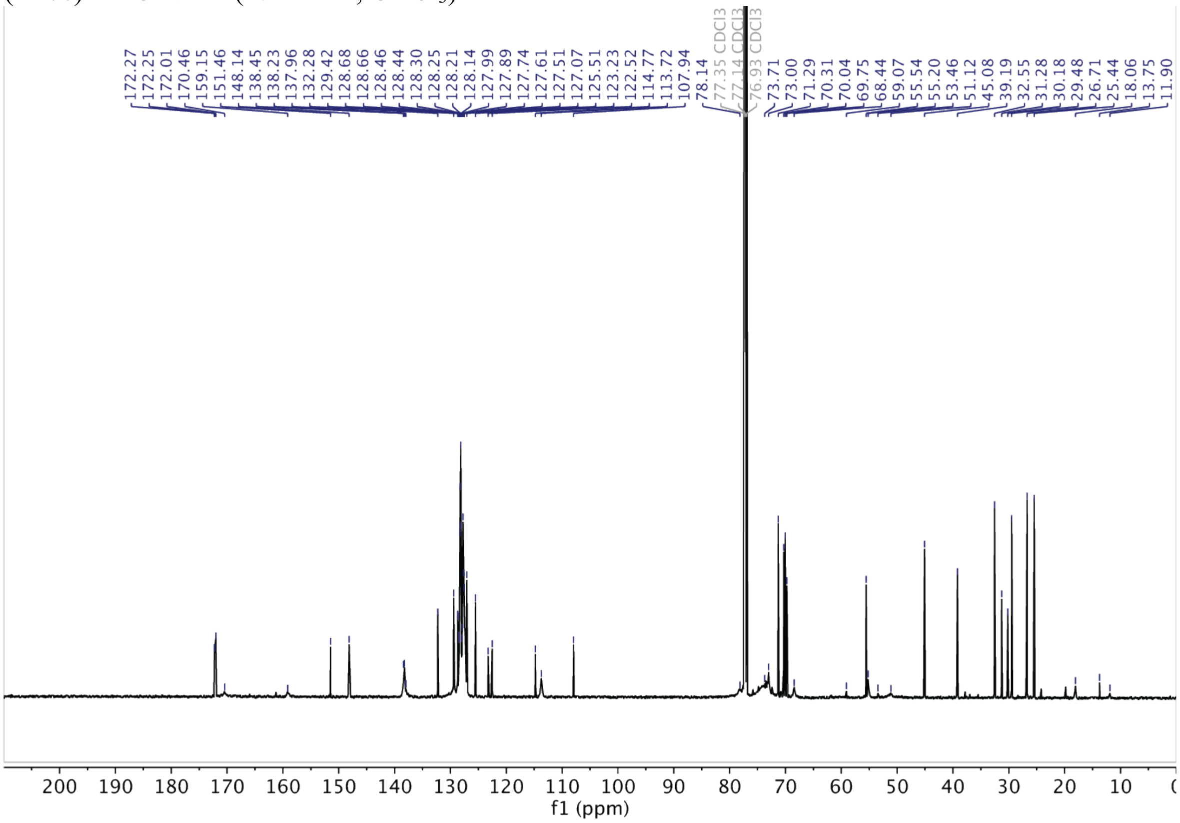
(**P9c**) – ^{13}C NMR (151 MHz, $CDCl_3$)



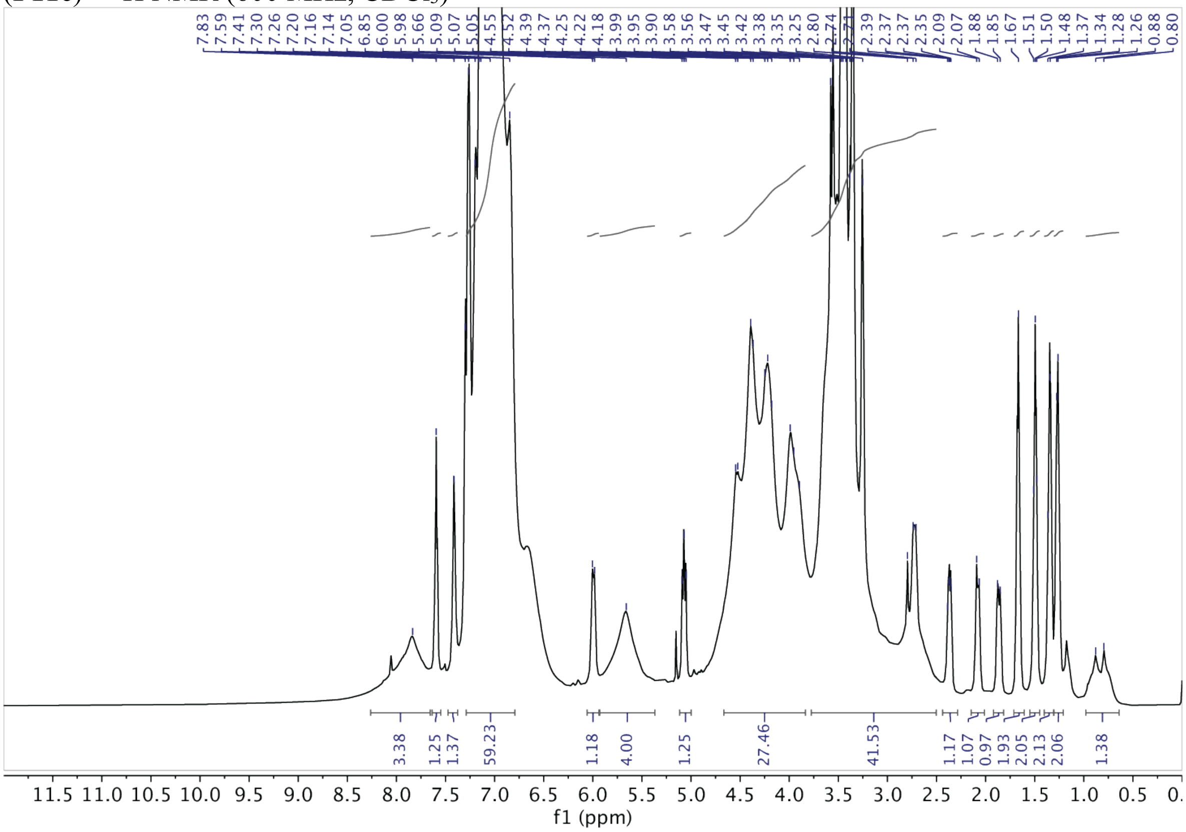
(**P10c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



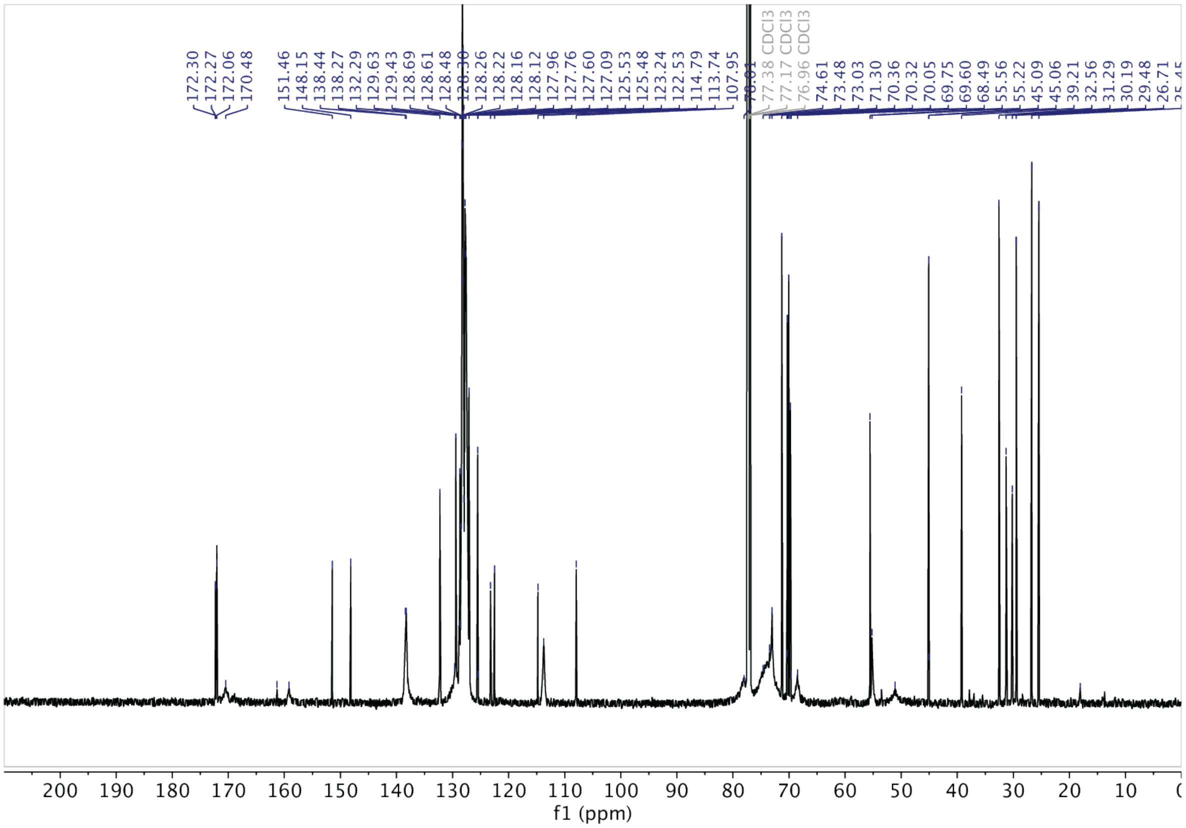
(**P10c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



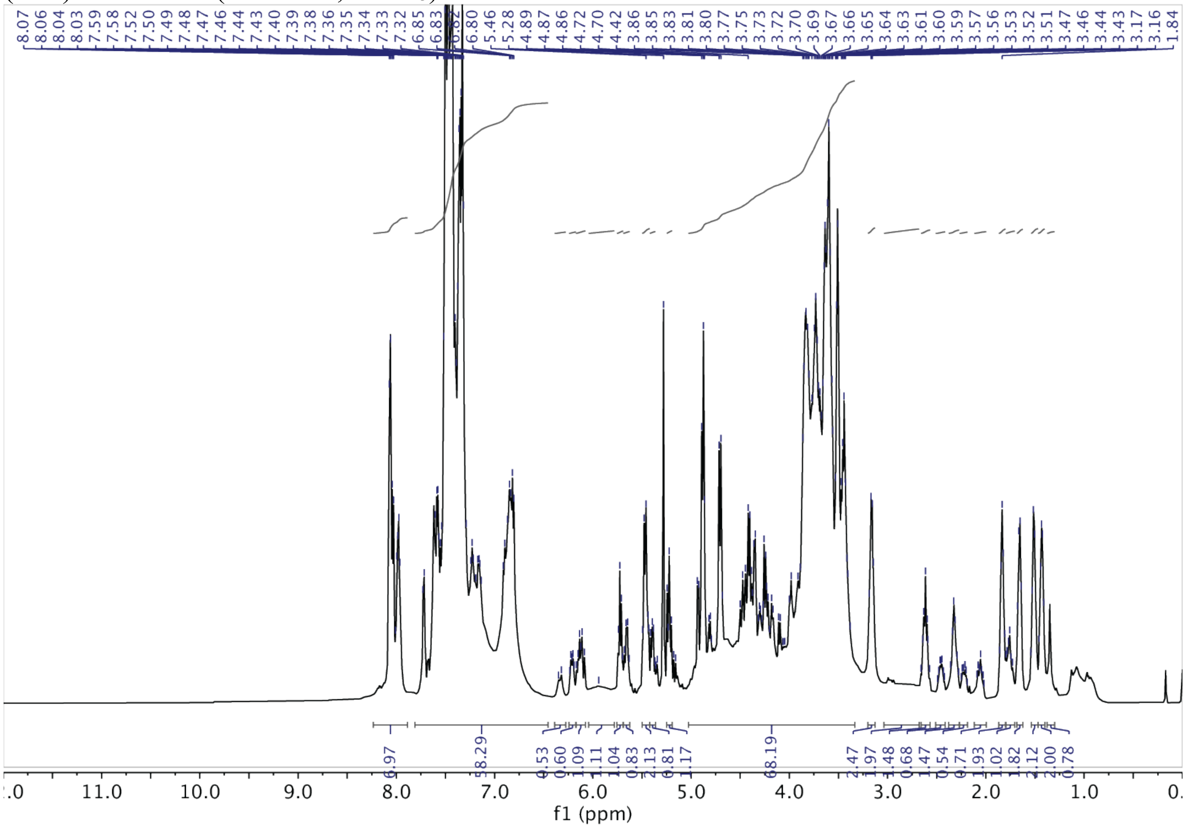
(**P11c**) – ^{1}H NMR (600 MHz, CDCl$_3$)



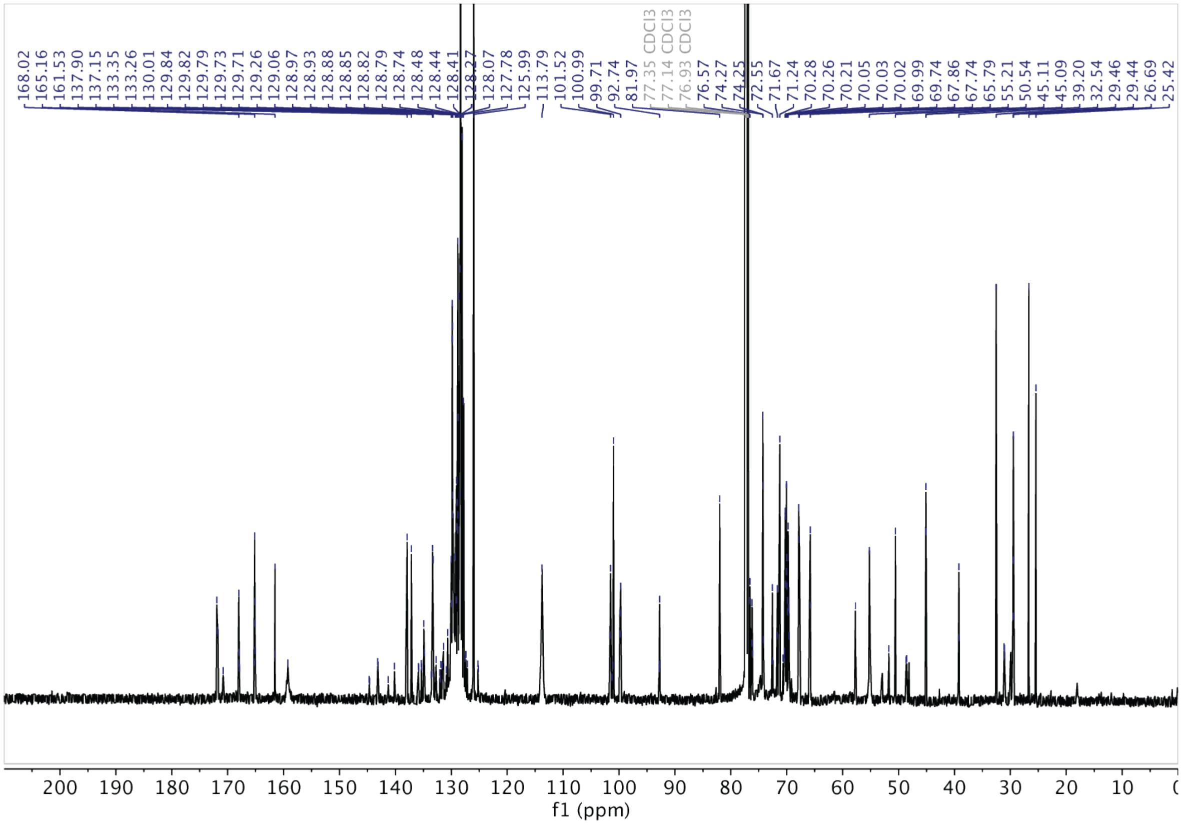
(**P11c**) – ^{13}C NMR (151 MHz, CDCl$_3$)



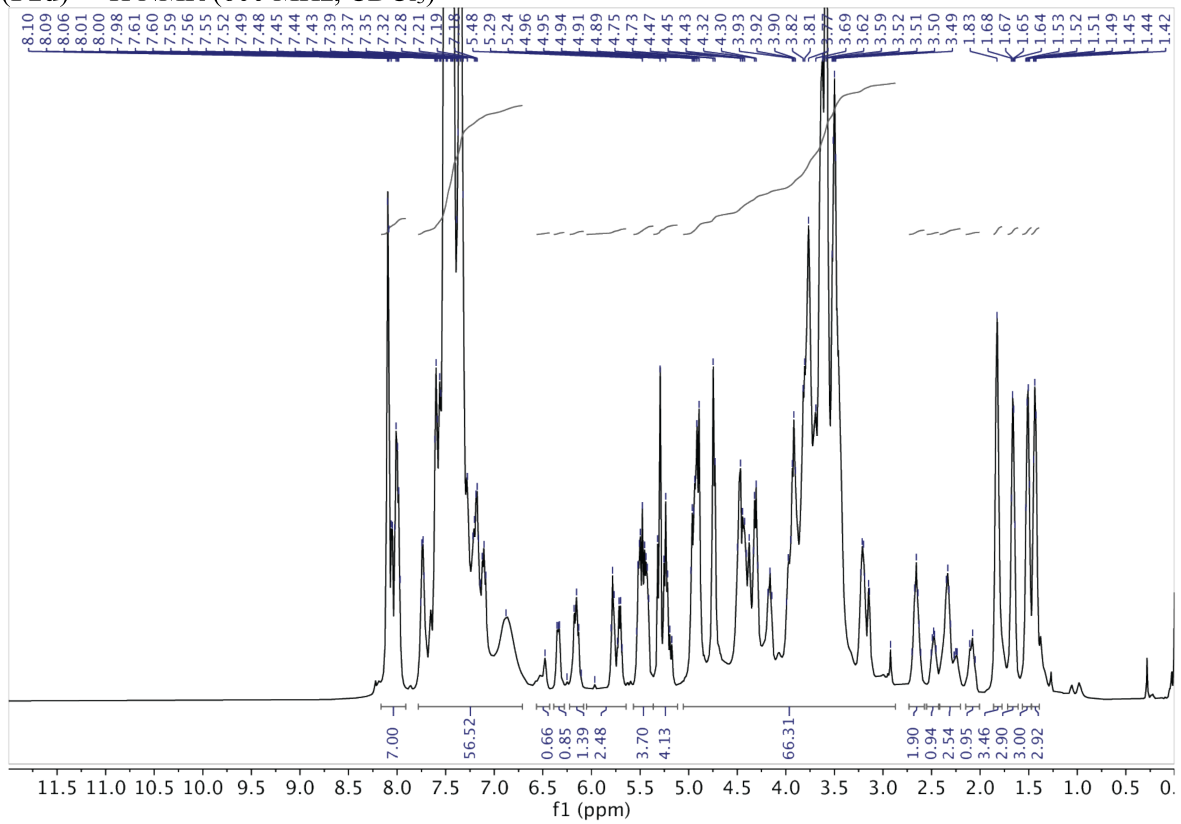
(**P1d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



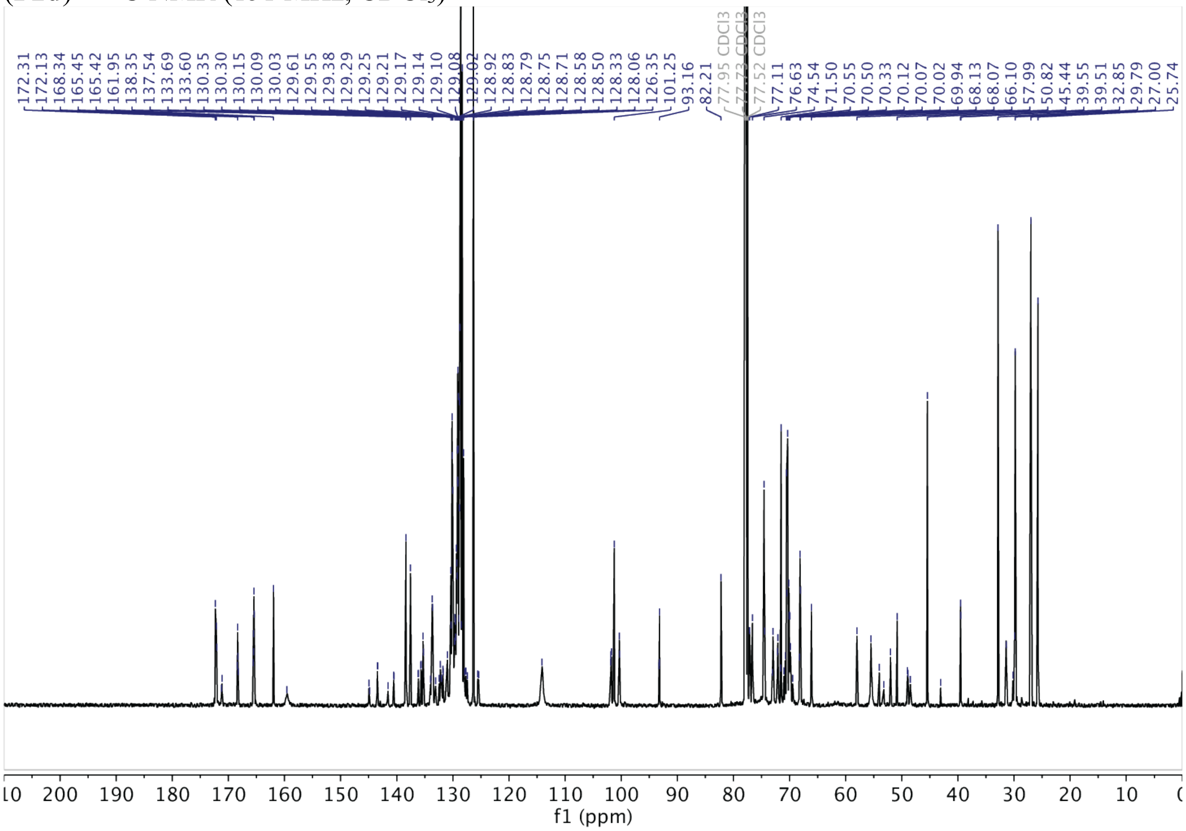
(**P1d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



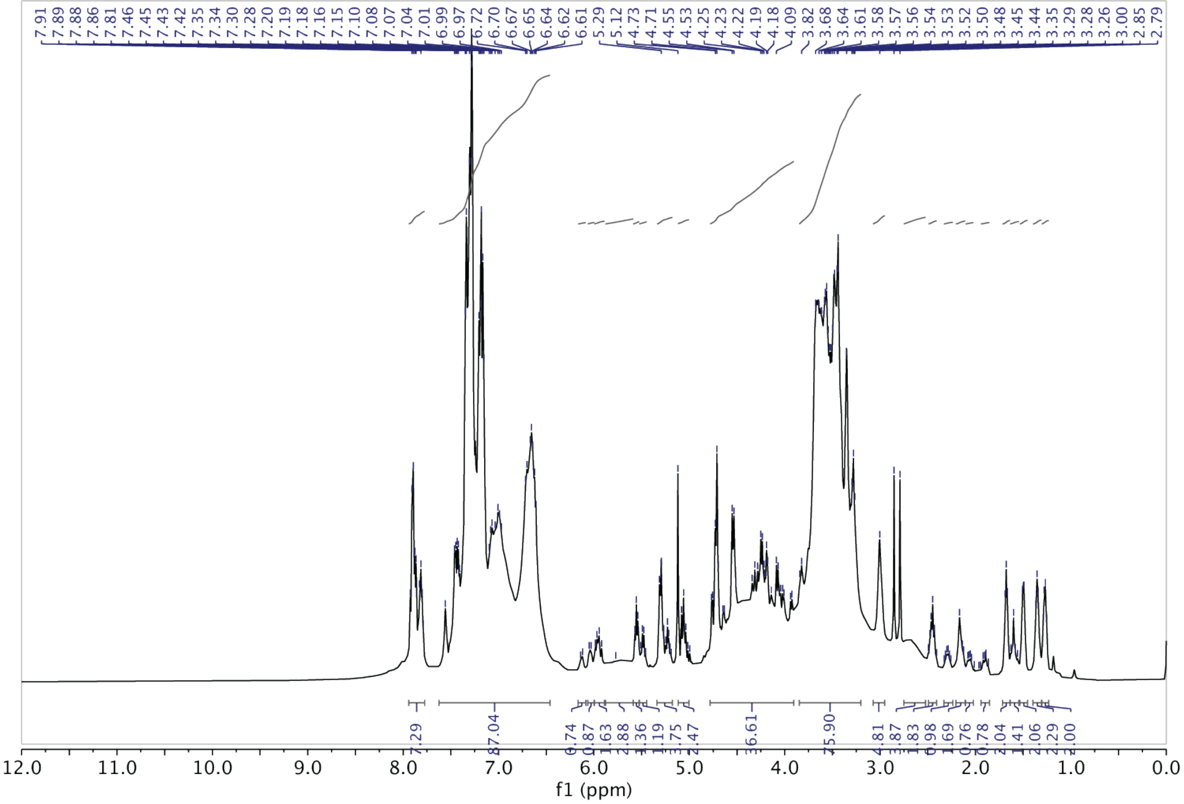
(**P2d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



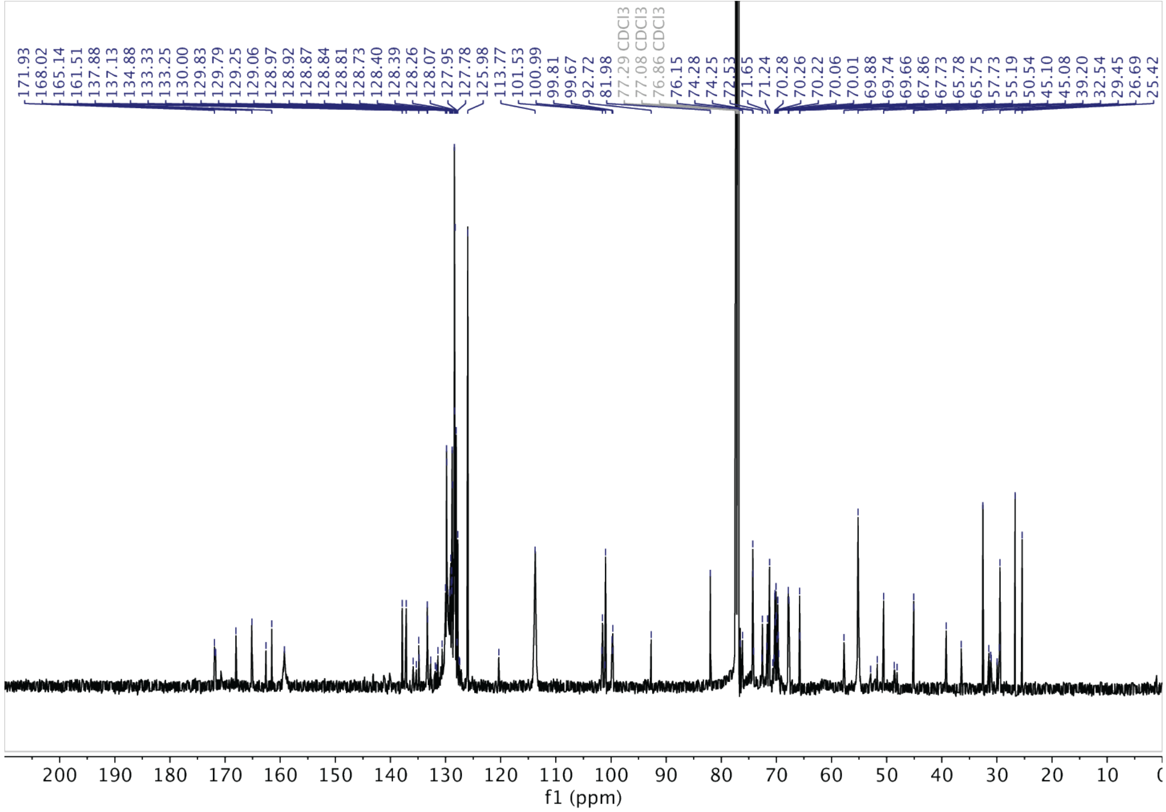
(**P2d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



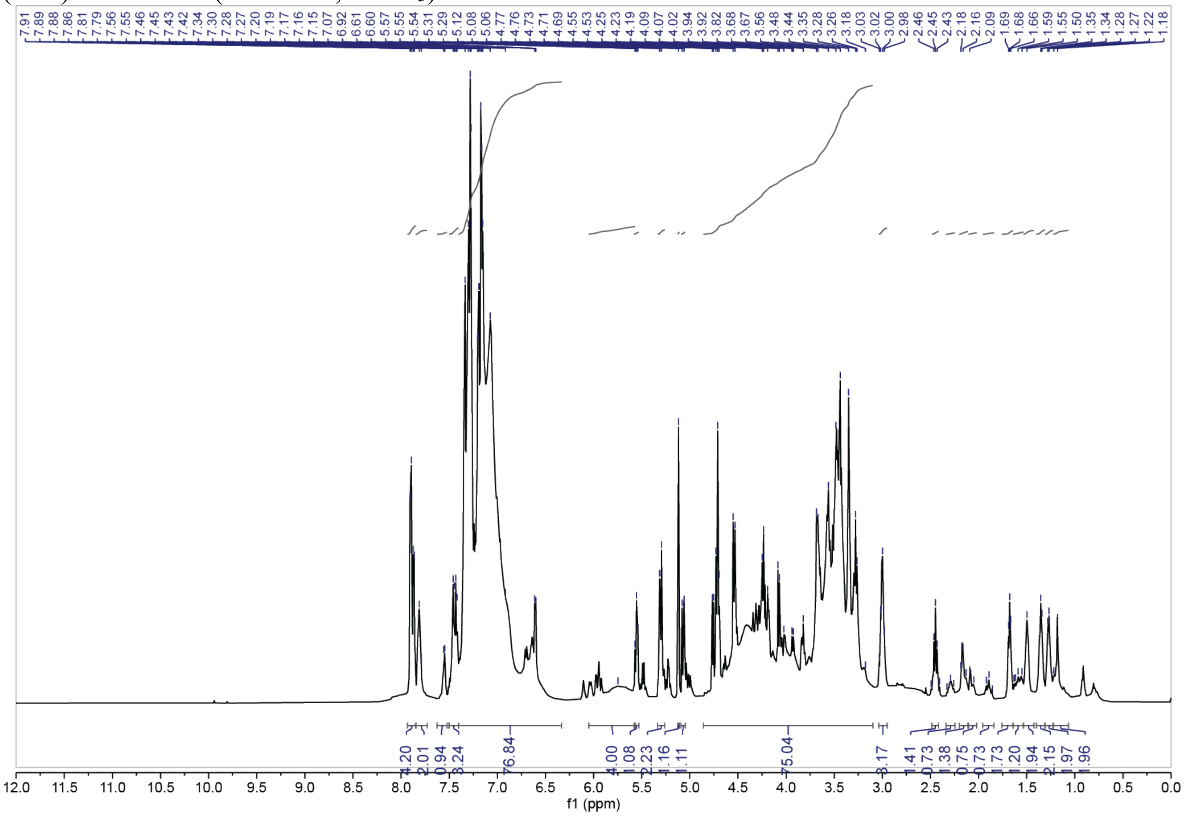
(**P3d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



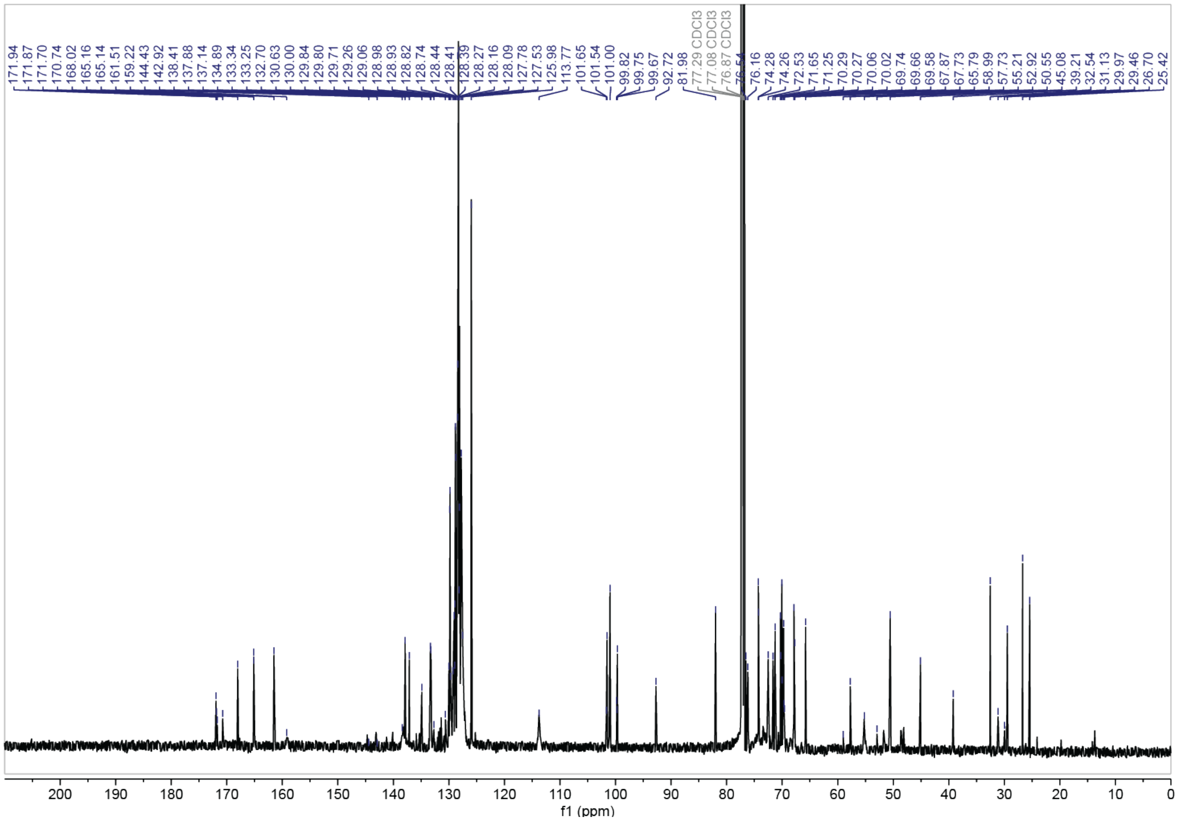
(**P3d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



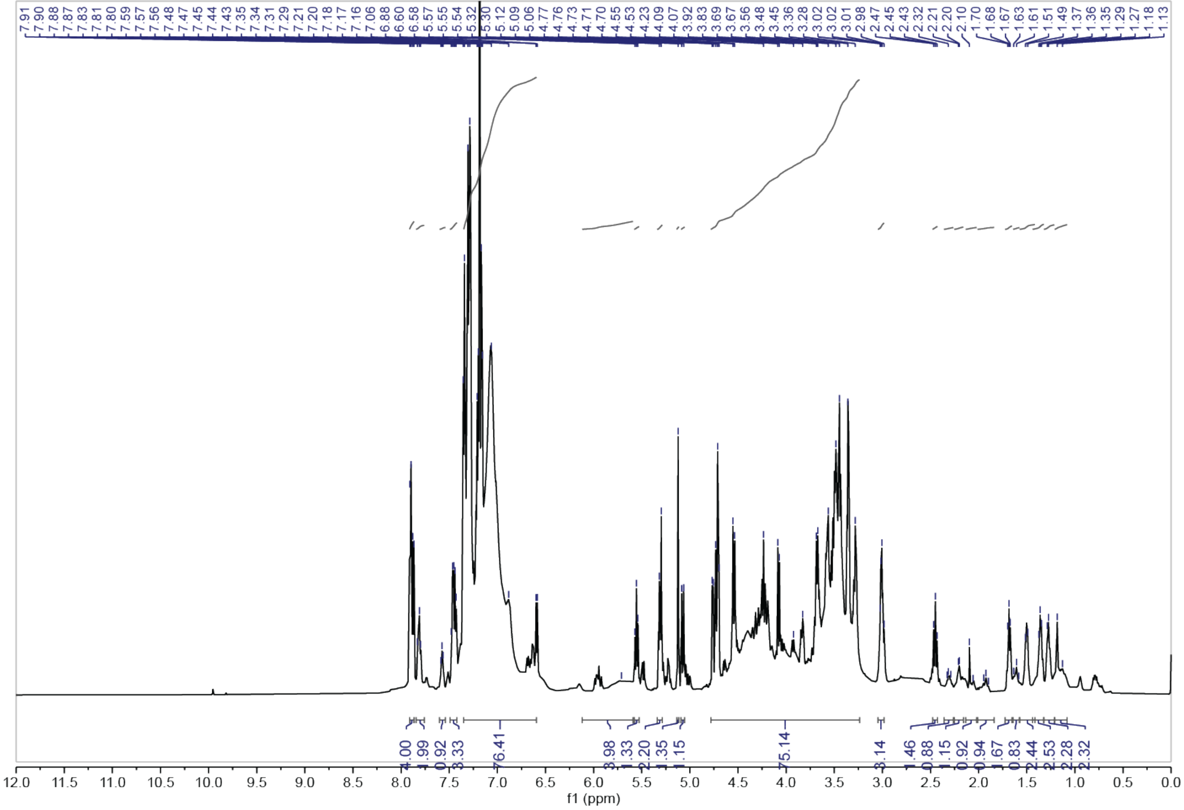
(**P4d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



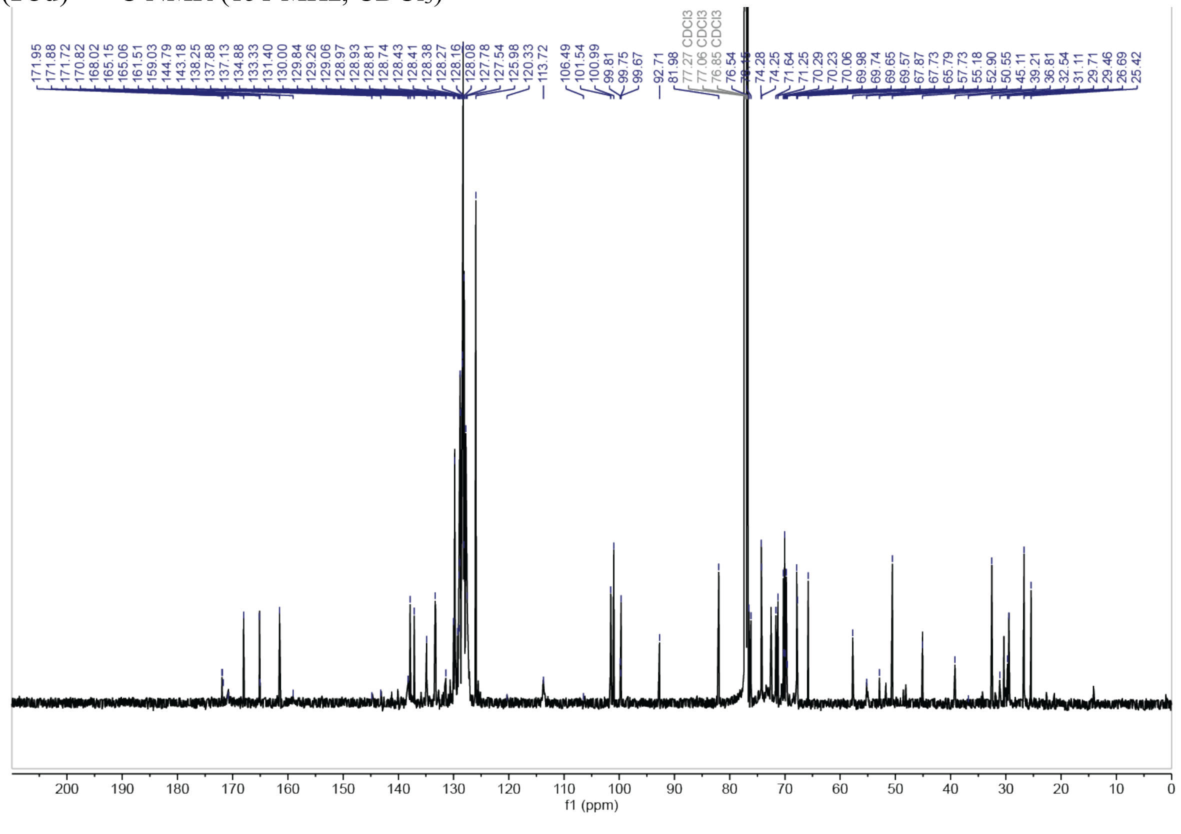
(**P4d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



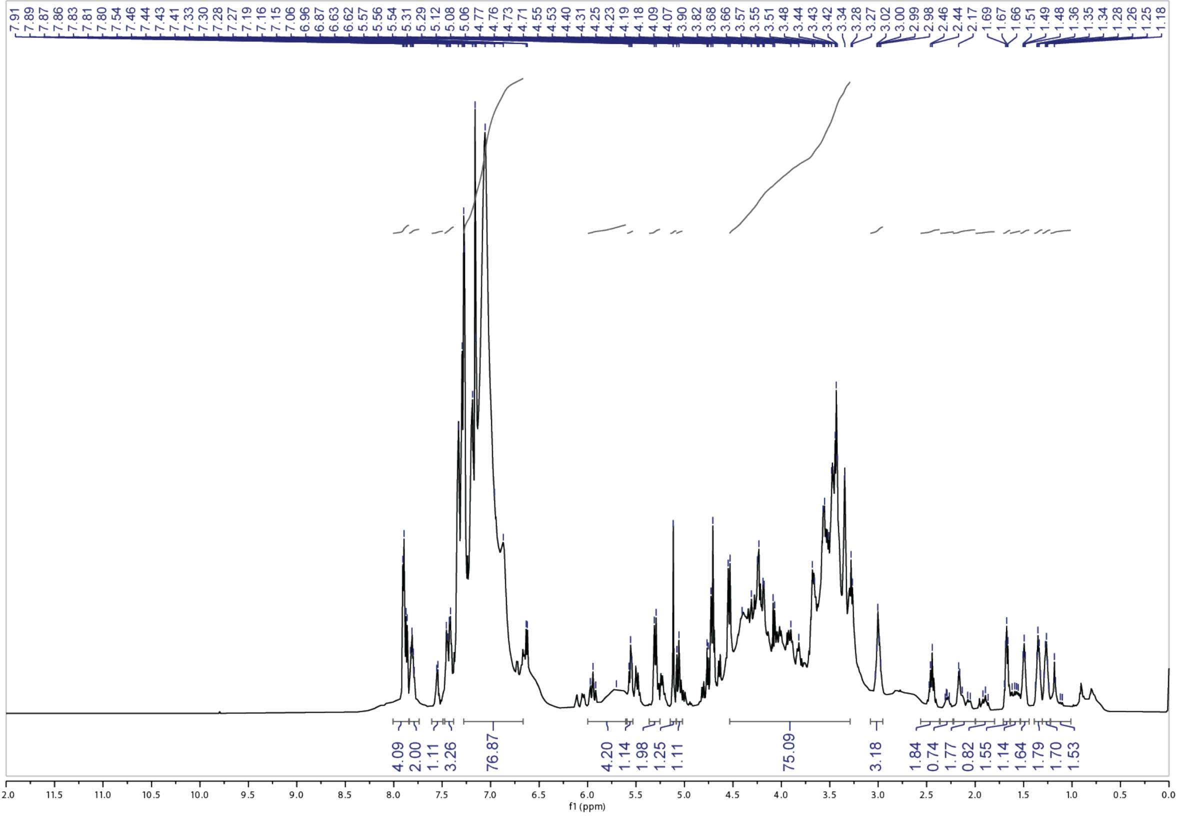
(**P5d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



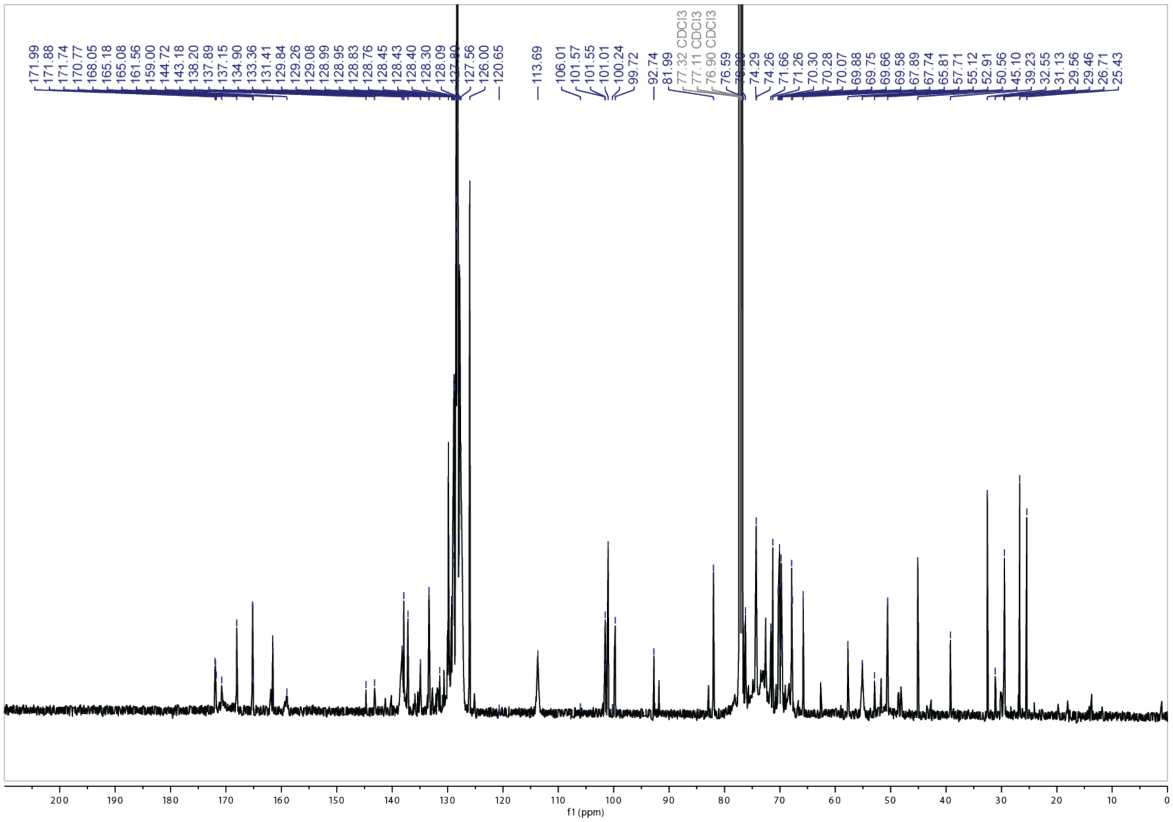
(**P5d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



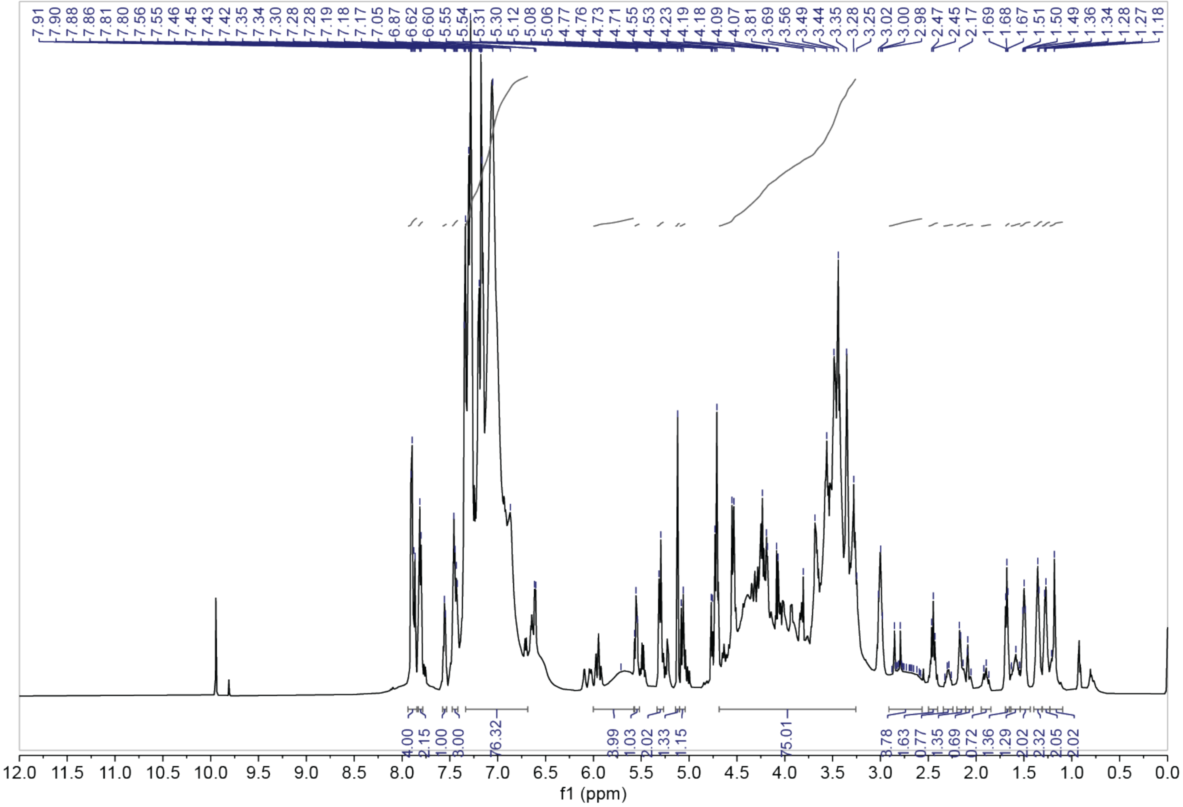
(**P6d**) – ^{1}H NMR (600 MHz, $CDCl_3$)



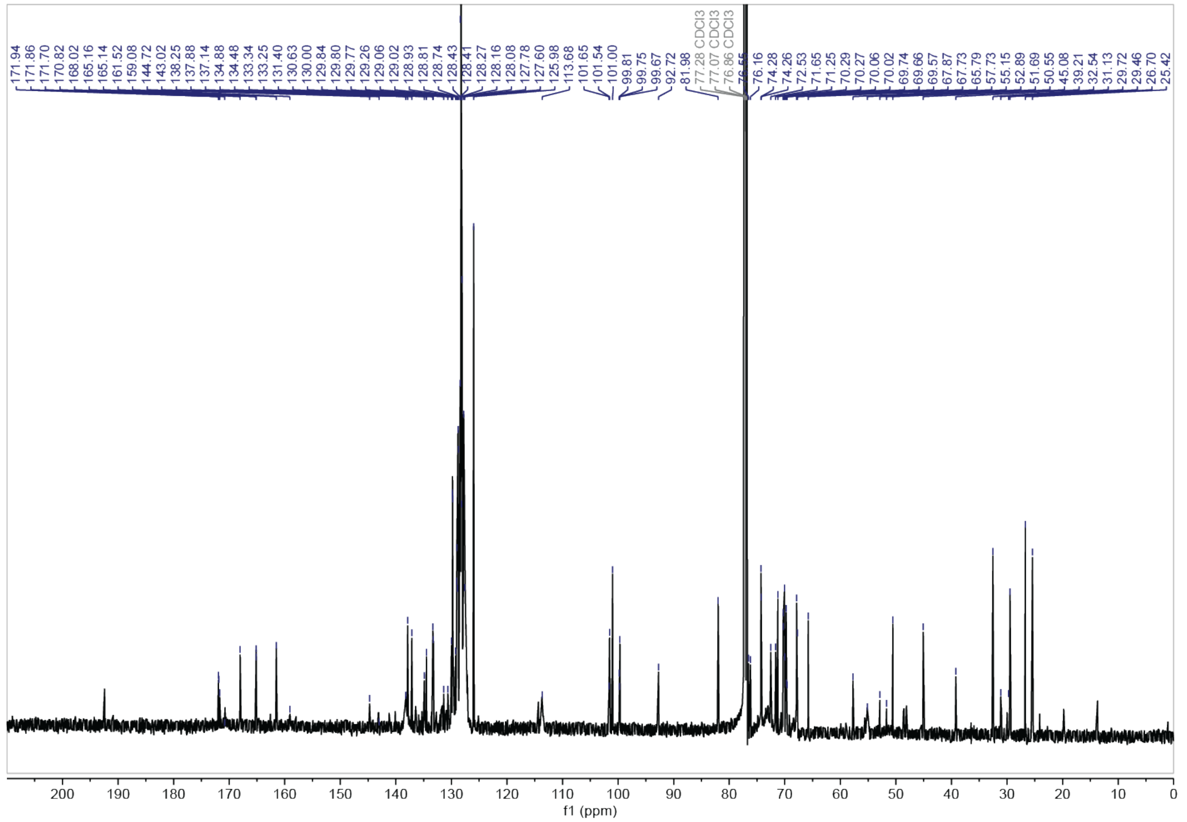
(**P6d**) – ^{13}C NMR (151 MHz, $CDCl_3$)



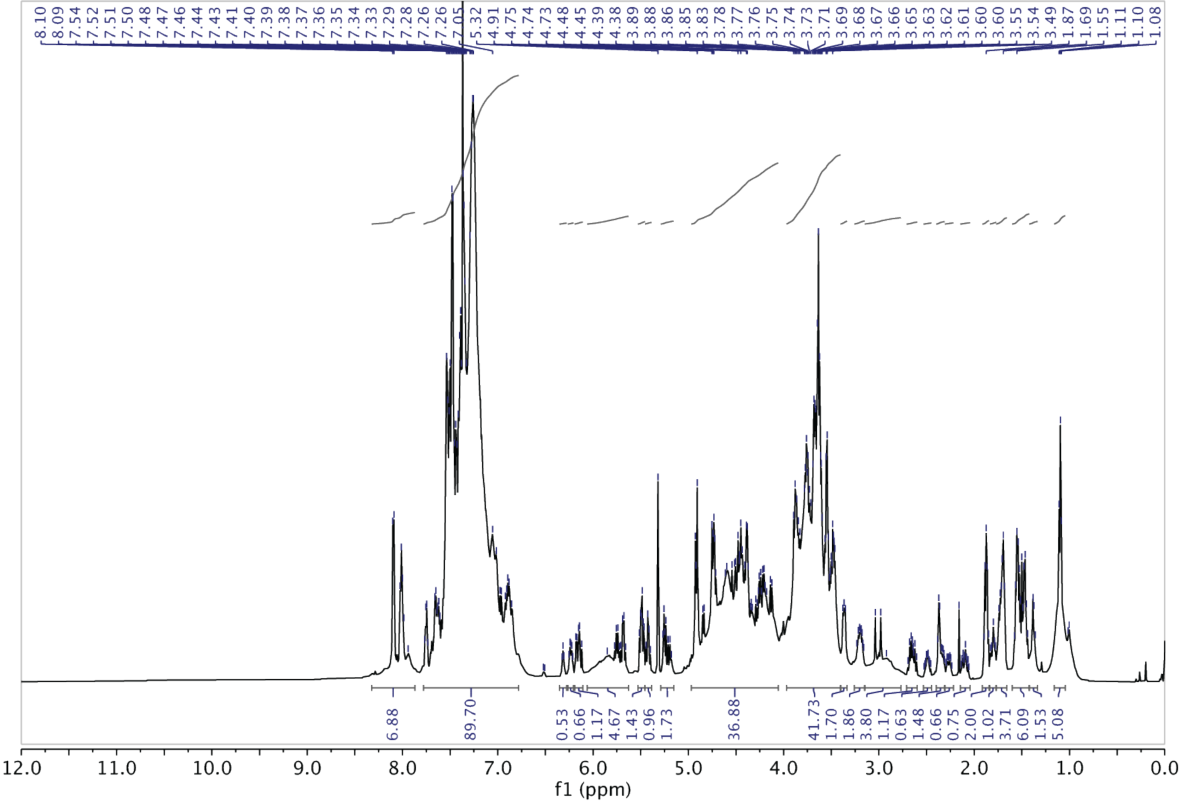
(**P7d**) – ^{1}H NMR (600 MHz, $CDCl_3$)



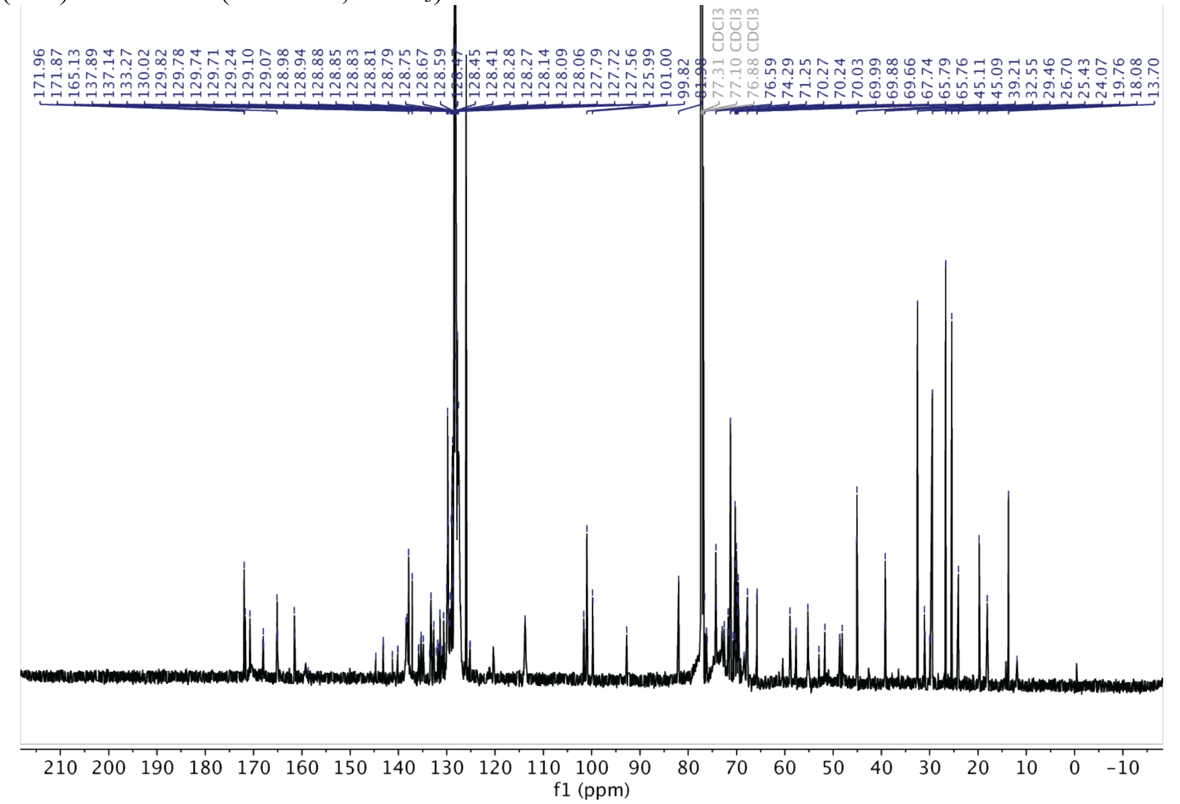
(**P7d**) – ^{13}C NMR (151 MHz, $CDCl_3$)



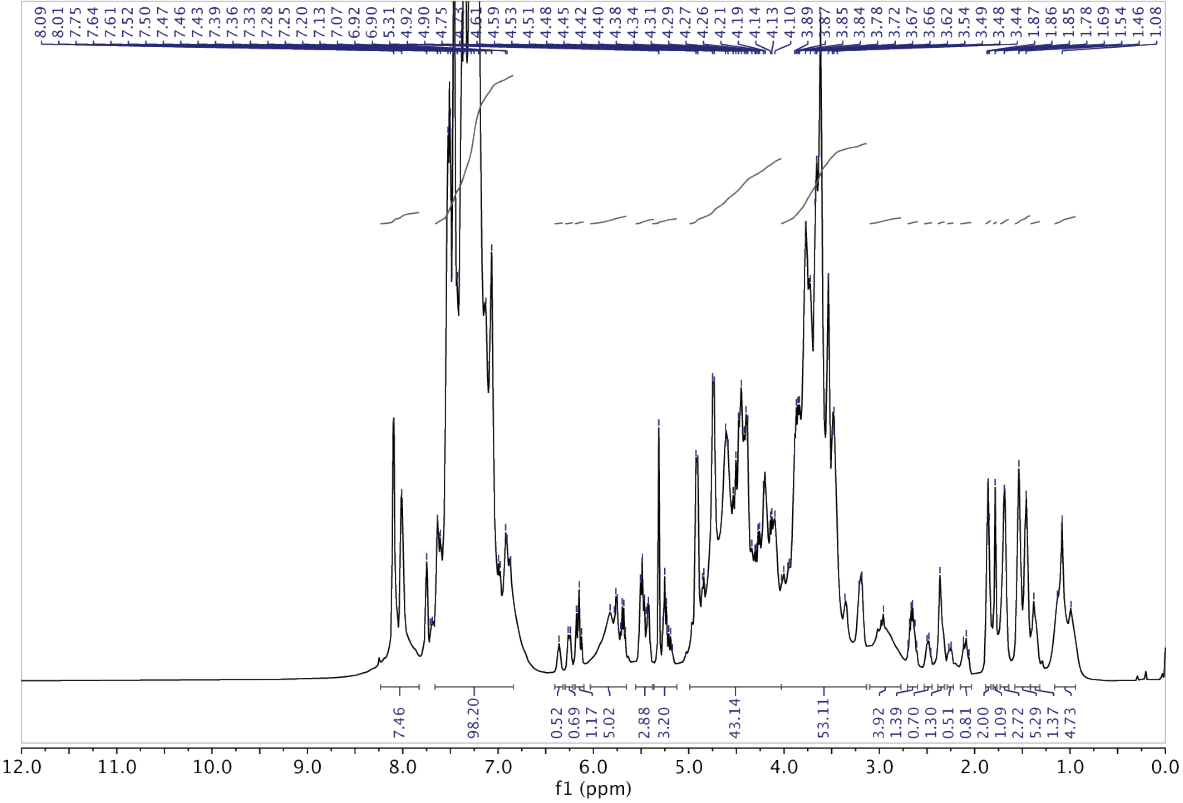
(**P8d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



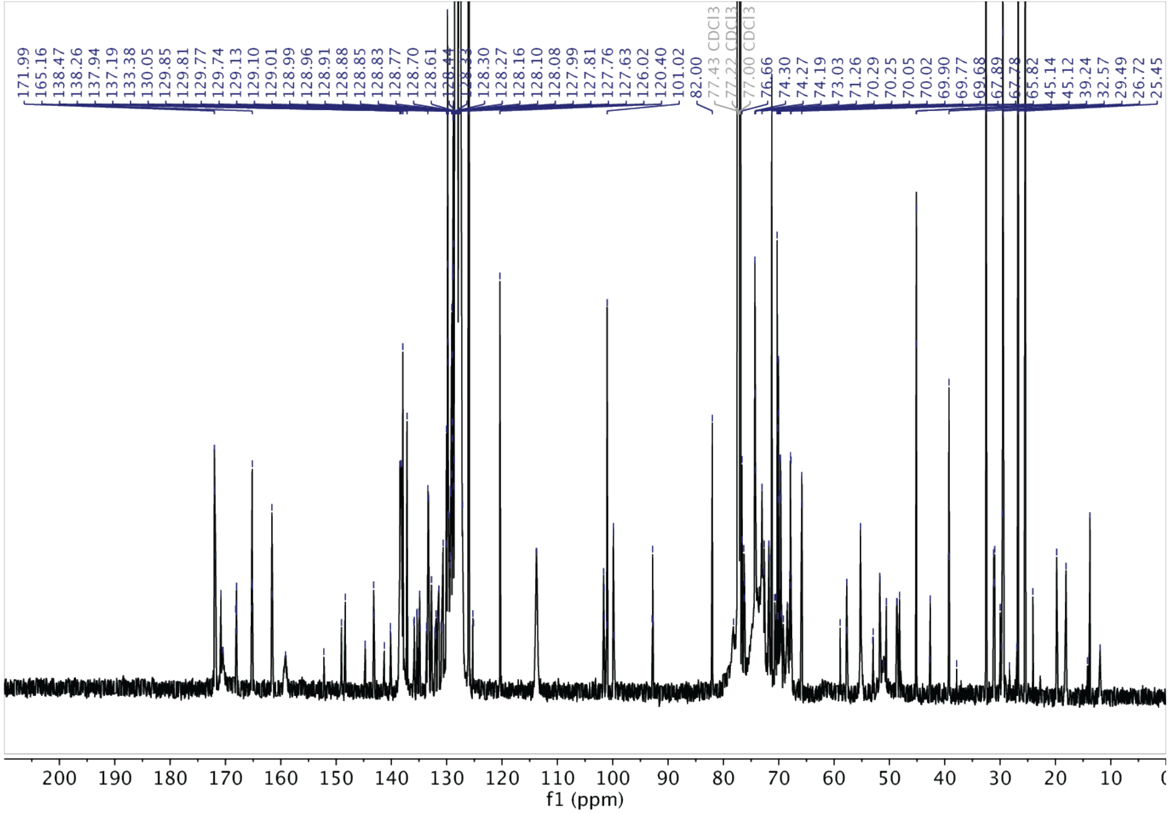
(**P8d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



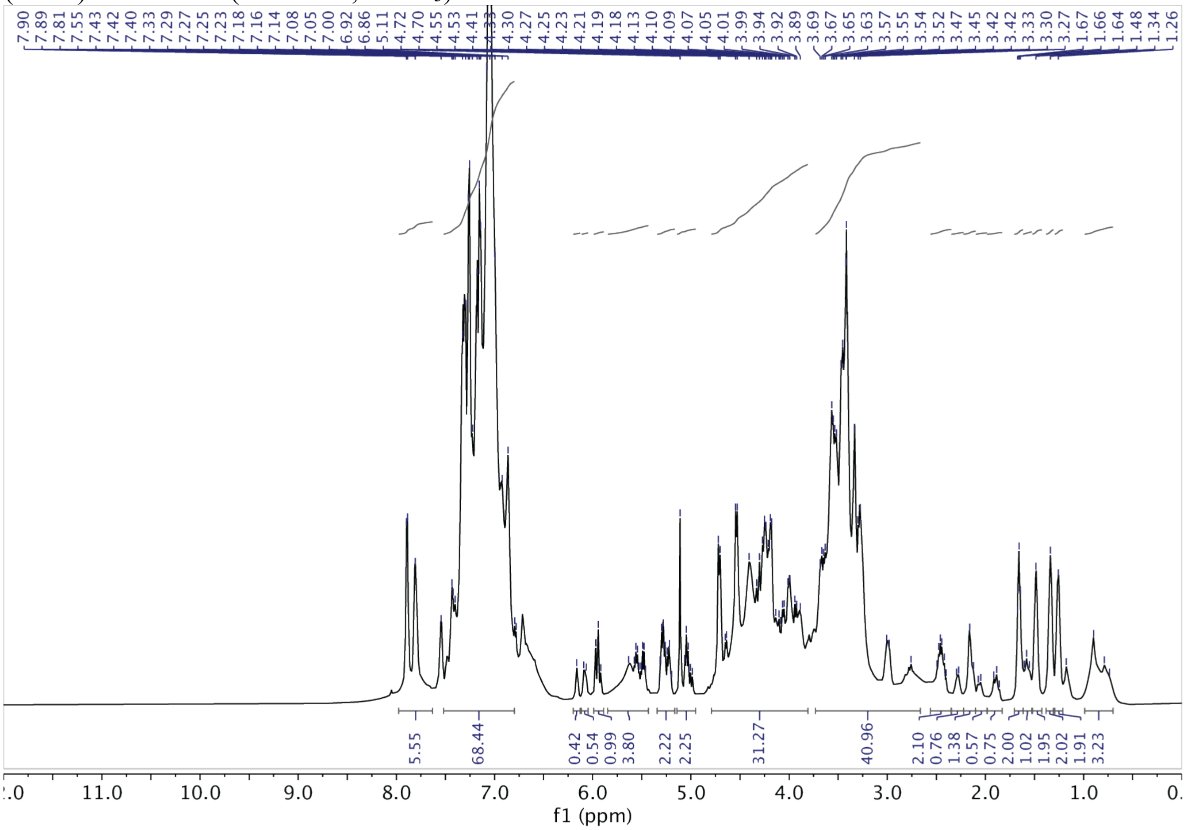
(**P9d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



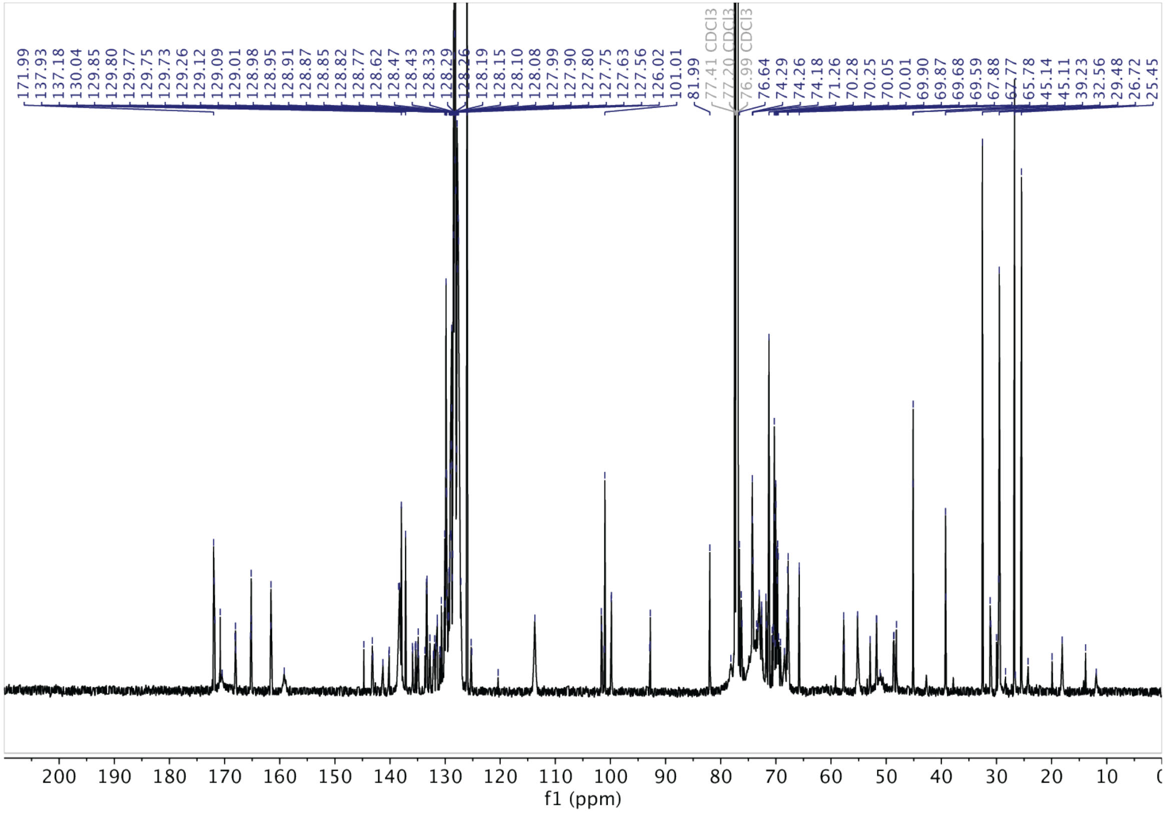
(**P9d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



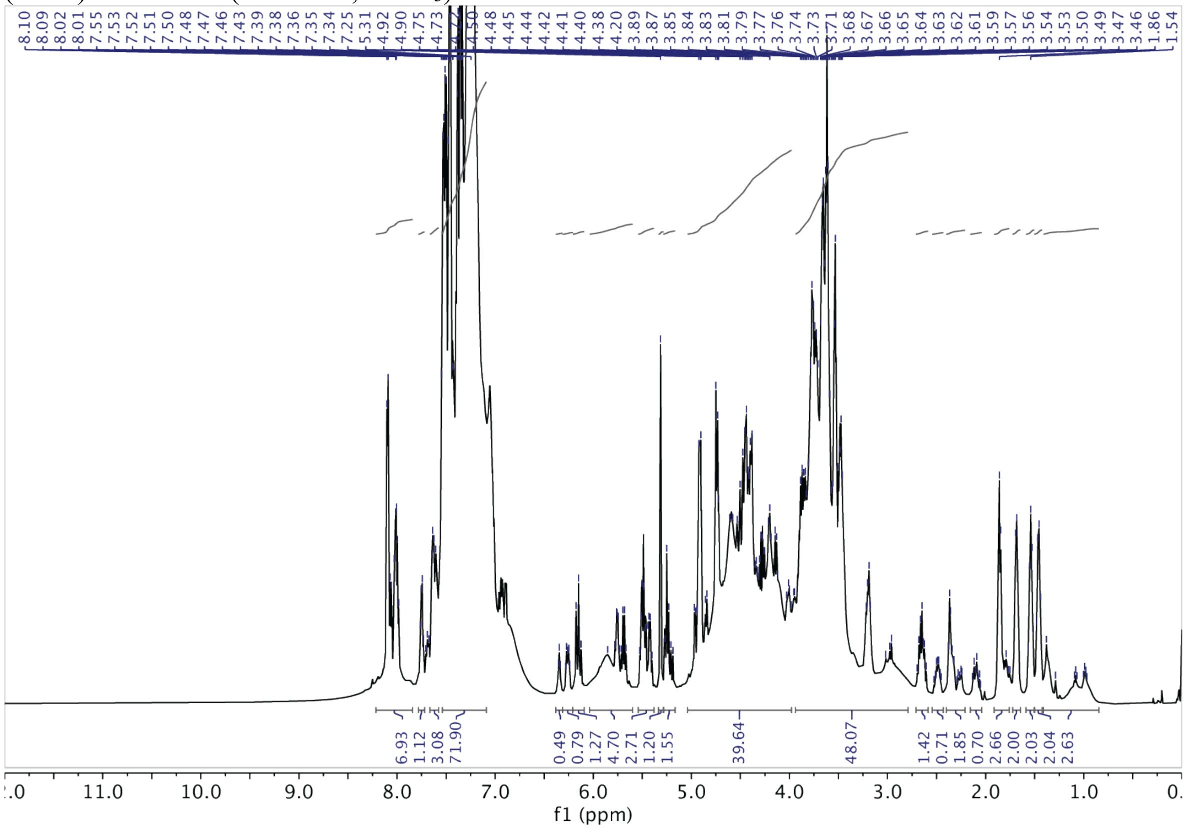
(**P10d**) – ^{1}H NMR (600 MHz, CDCl$_3$)



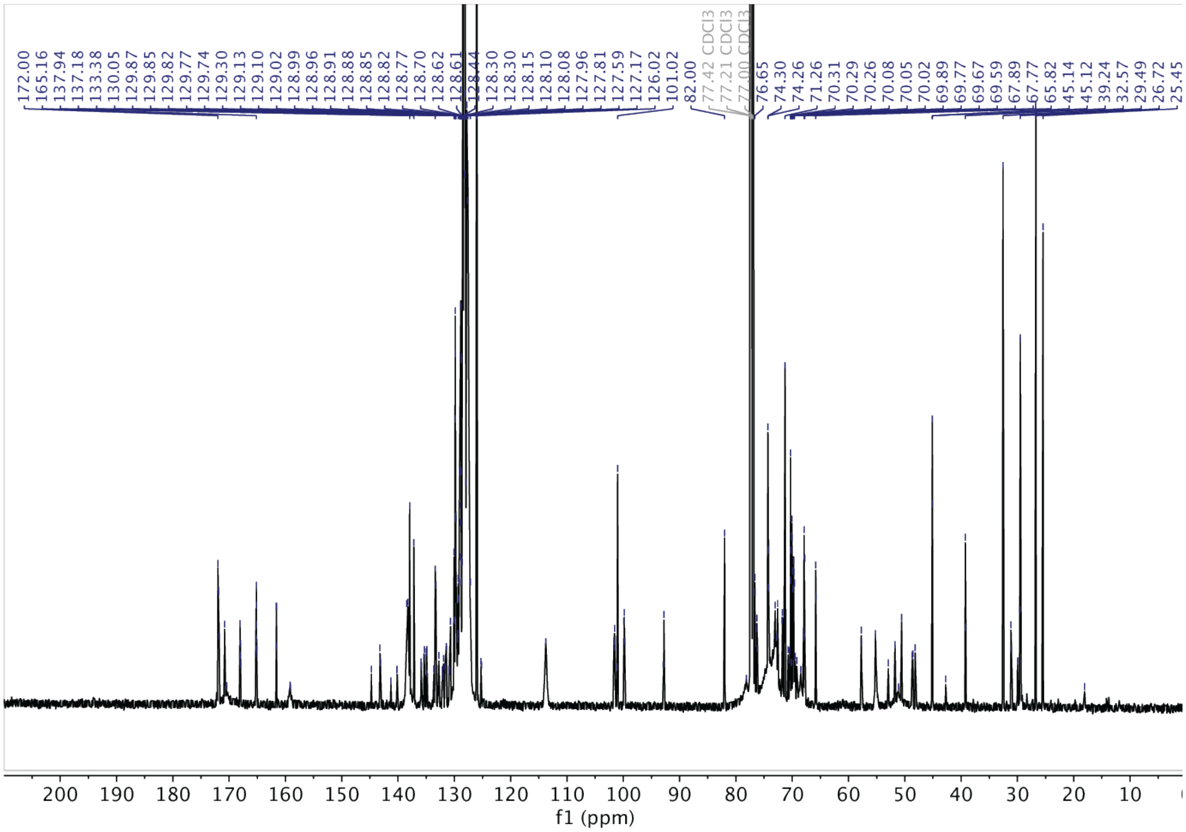
(**P10d**) – ^{13}C NMR (151 MHz, CDCl$_3$)



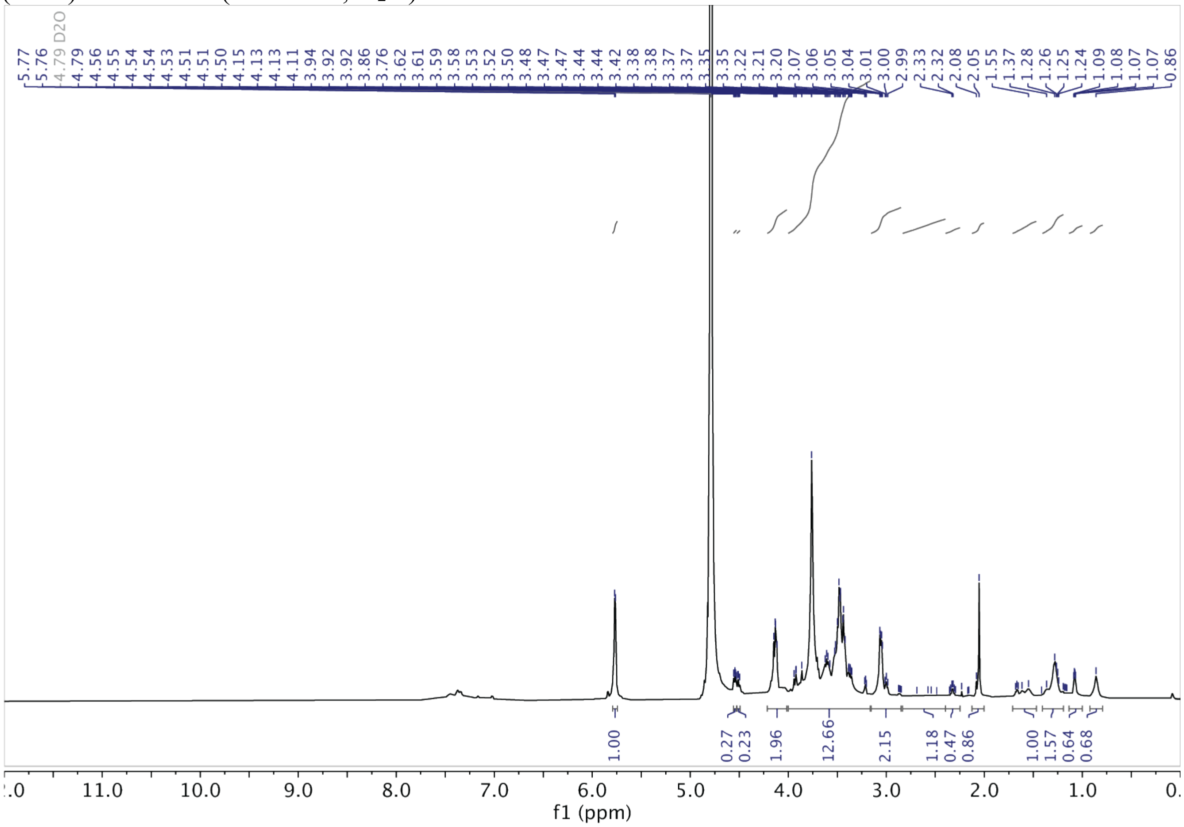
(**P11d**) – ^{1}H NMR (600 MHz, $CDCl_3$)



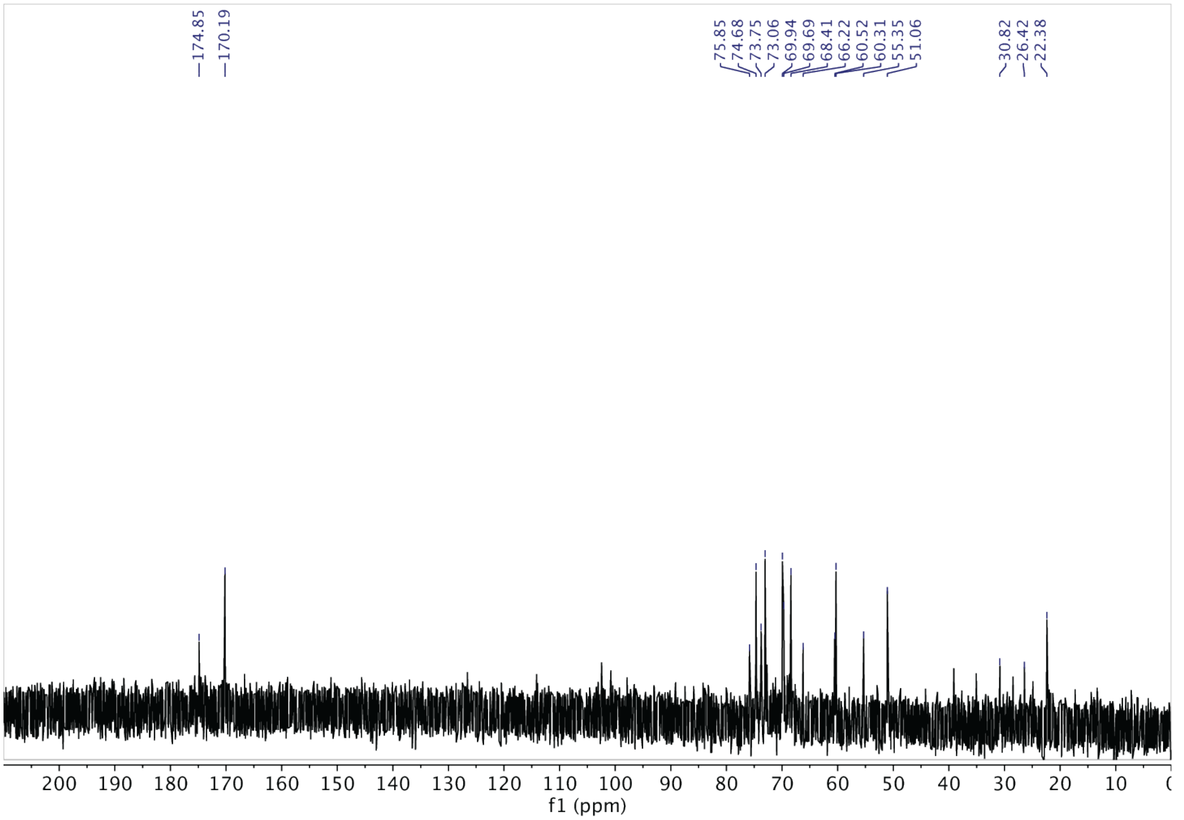
(**P11d**) – ^{13}C NMR (151 MHz, $CDCl_3$)



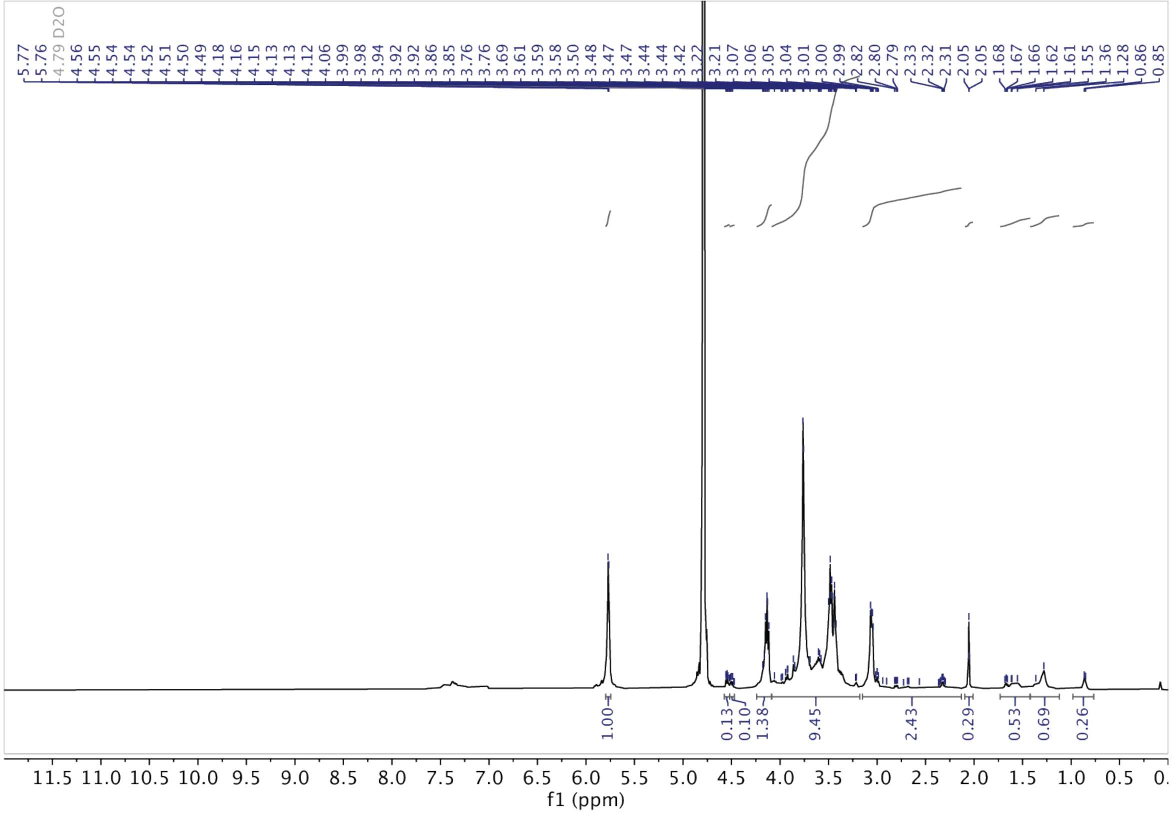
(**P1d'**) – ^{1}H NMR (600 MHz, D_2O)



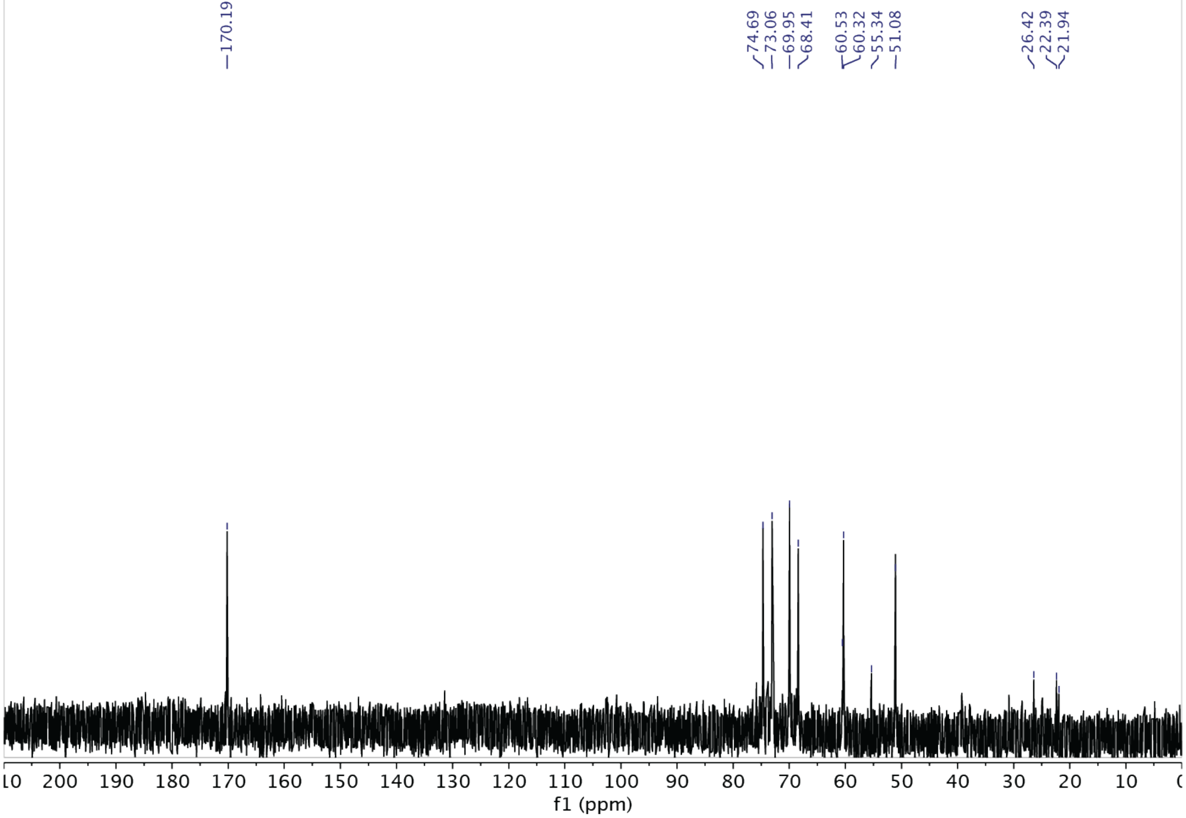
(**P1d'**) – ^{13}C NMR (151 MHz, D_2O)



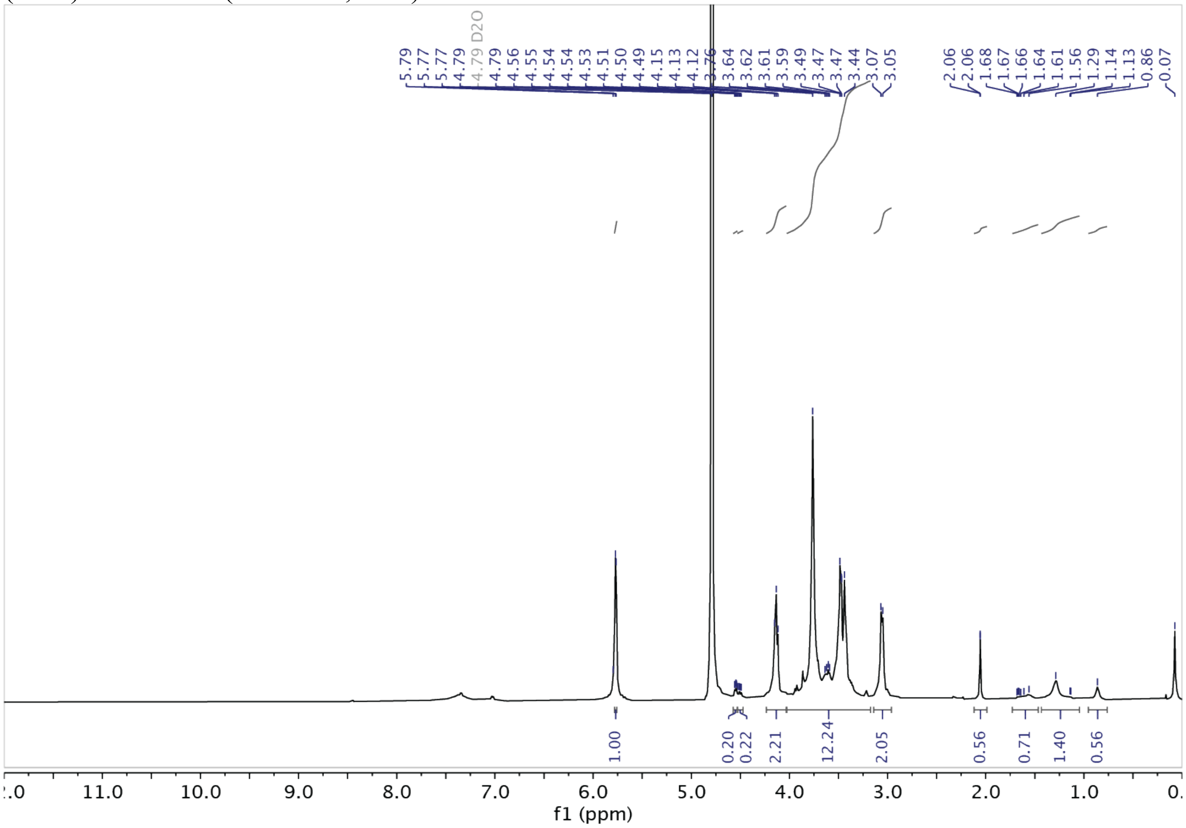
(**P2d'**) – ^{1}H NMR (600 MHz, D_2O)



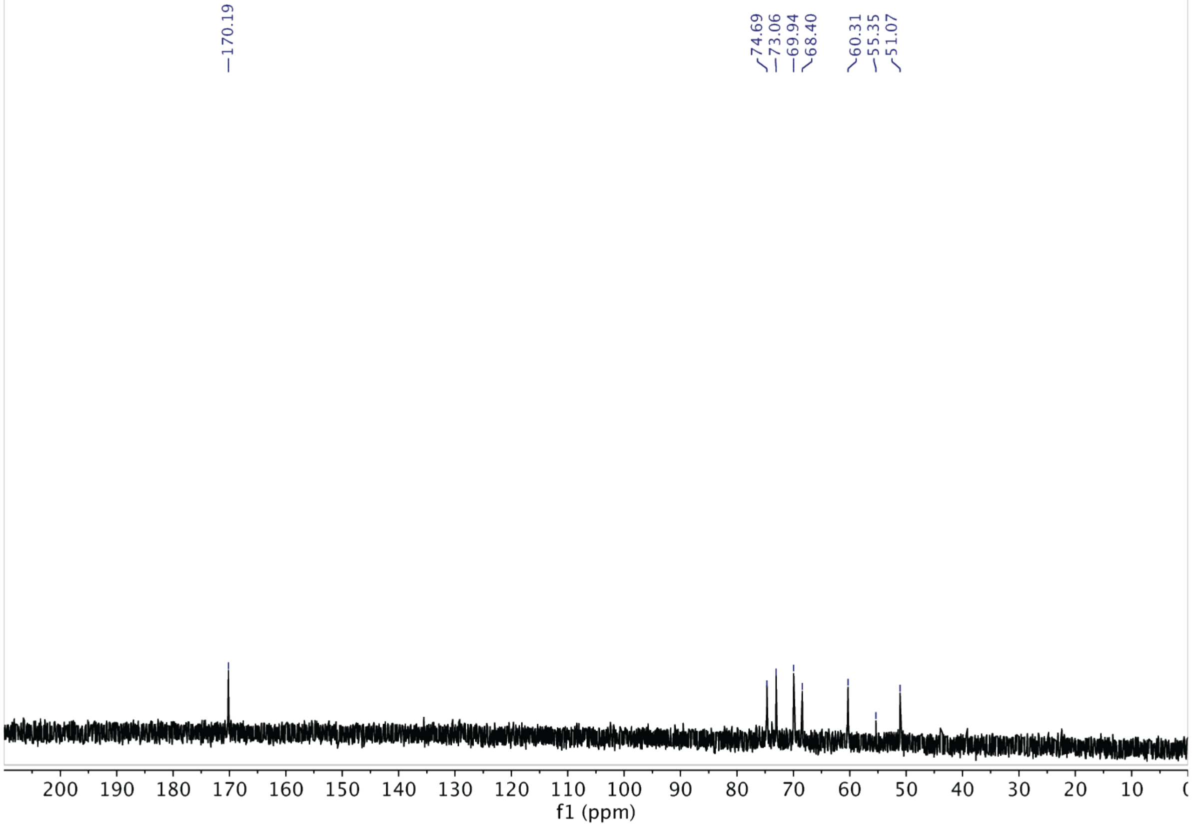
(**P2d'**) – ^{13}C NMR (151 MHz, D_2O)



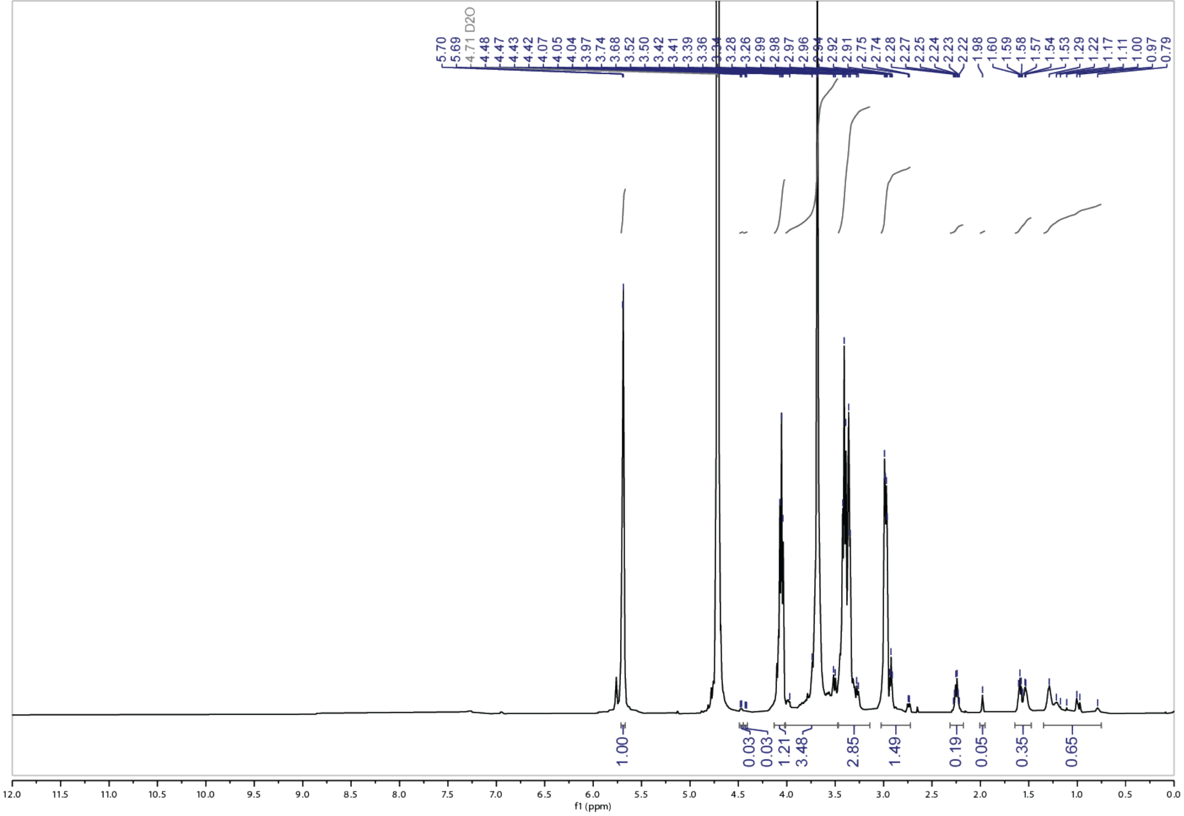
(**P3d'**) – ^{1}H NMR (600 MHz, D_2O)



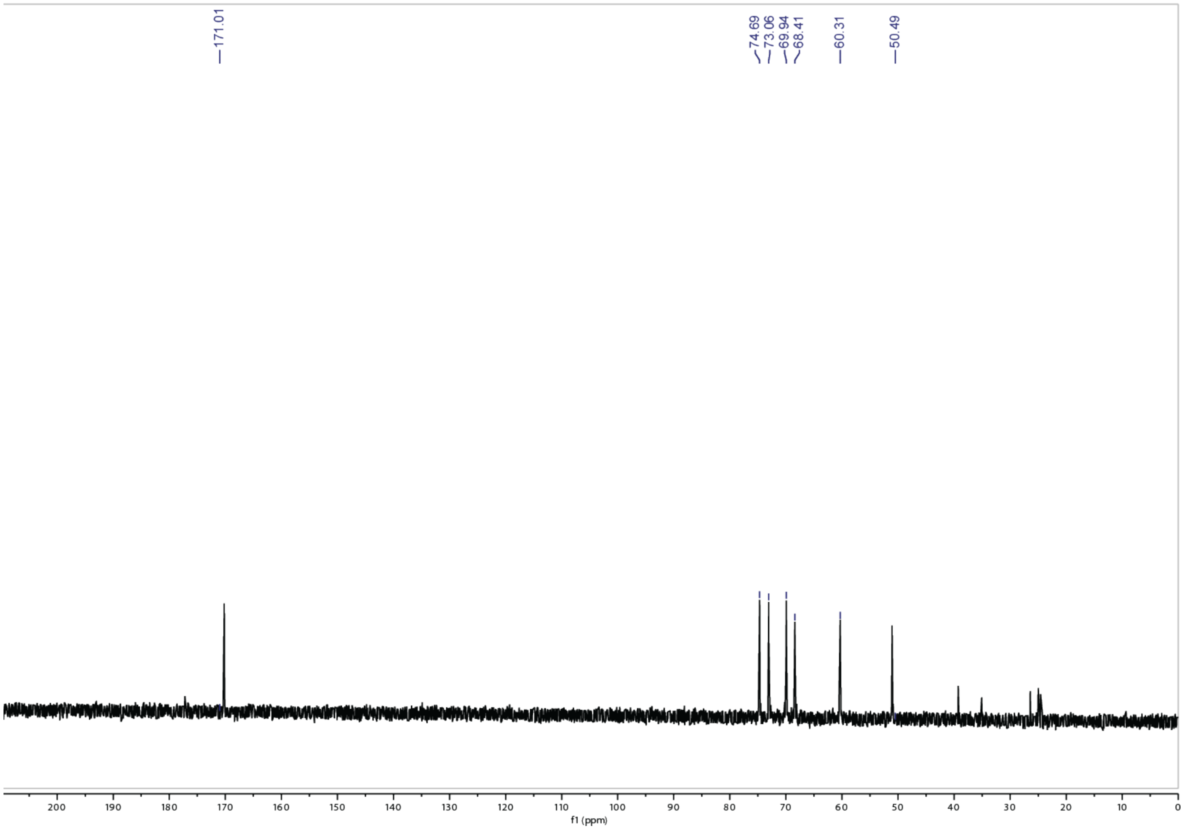
(**P3d'**) – ^{13}C NMR (151 MHz, D_2O)



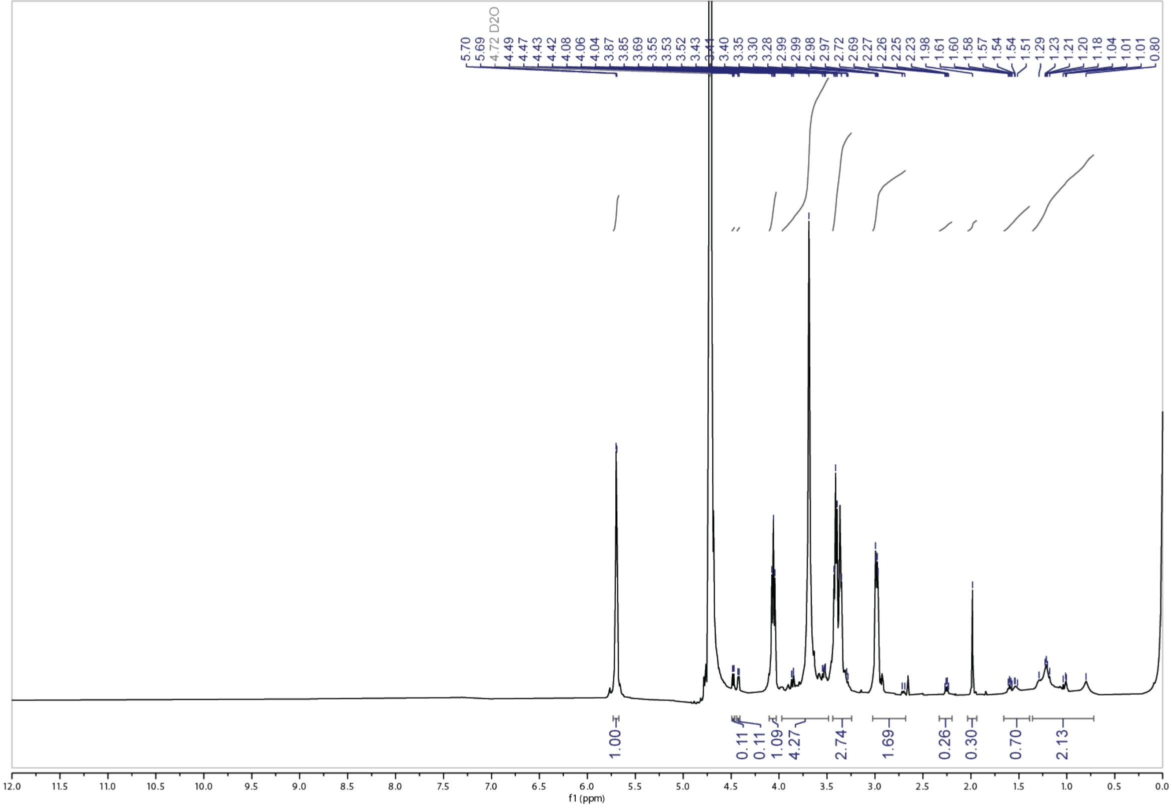
(**P4d'**) – ^1H NMR (600 MHz, D_2O)



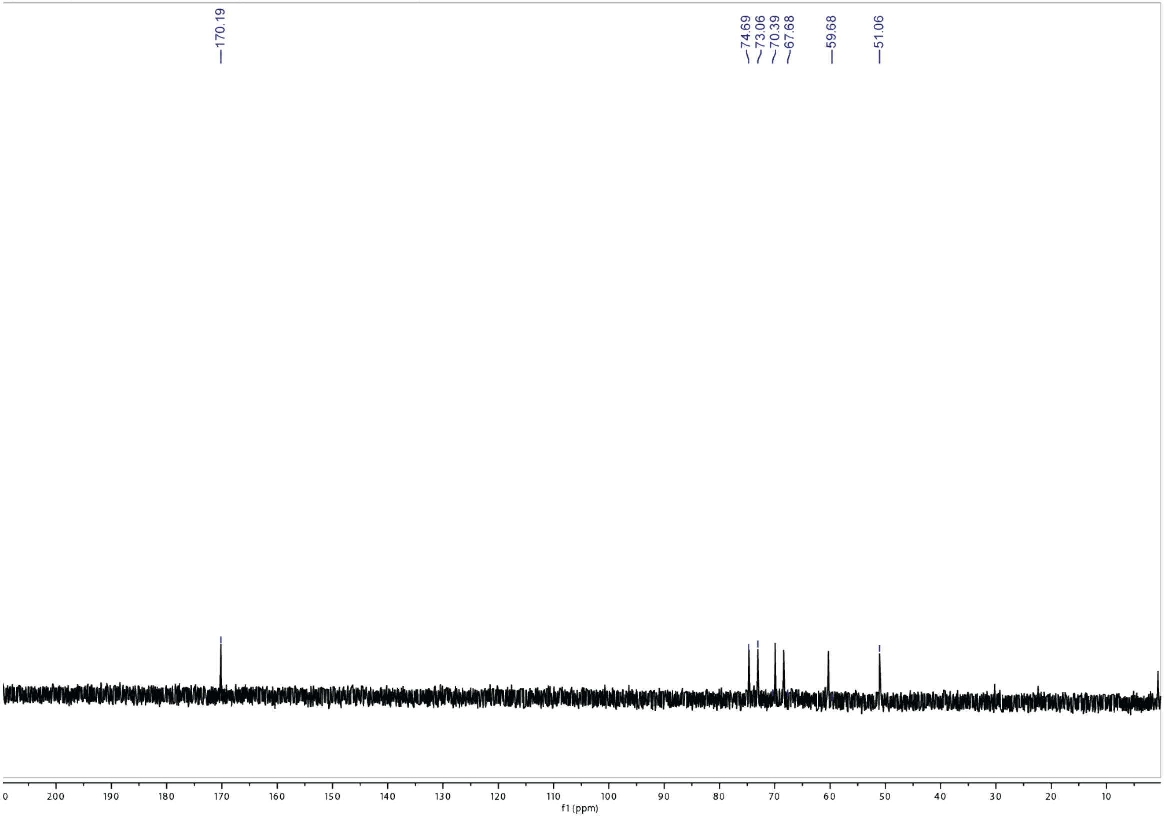
(**P4d'**) – ^{13}C NMR (151 MHz, D_2O)



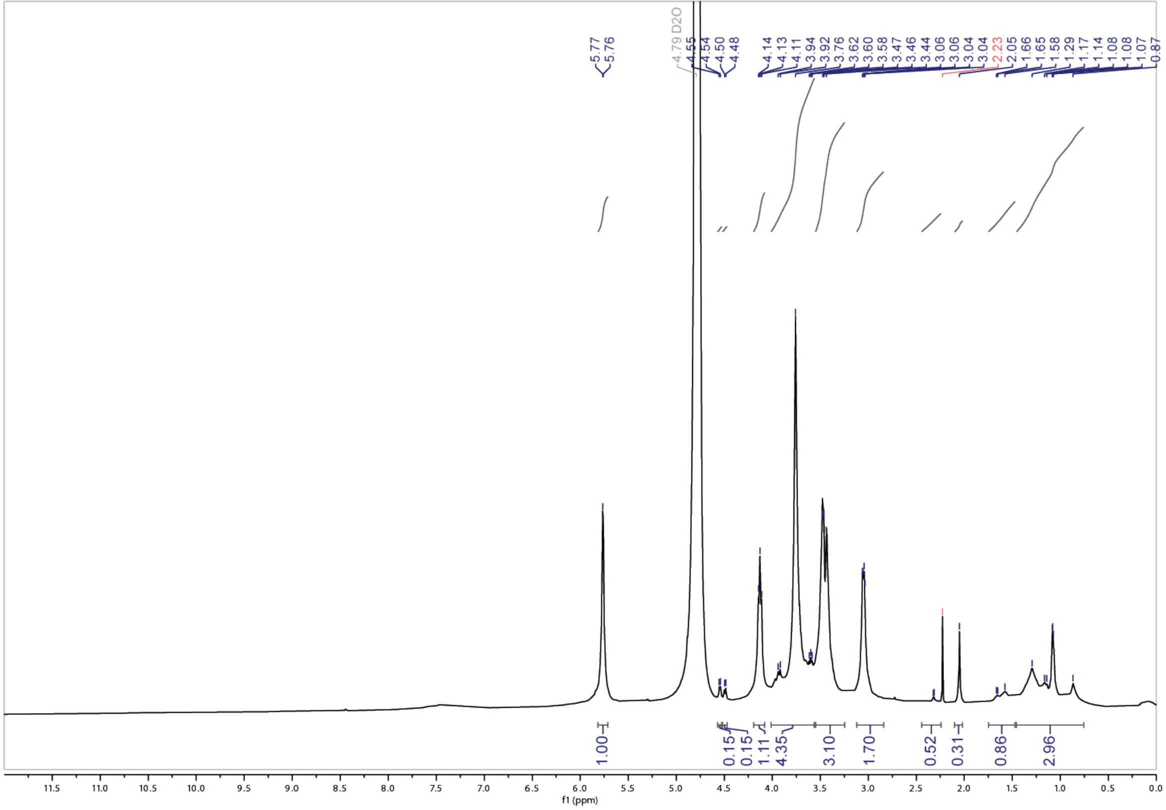
(**P5d'**) – ^{1}H NMR (600 MHz, D_2O)



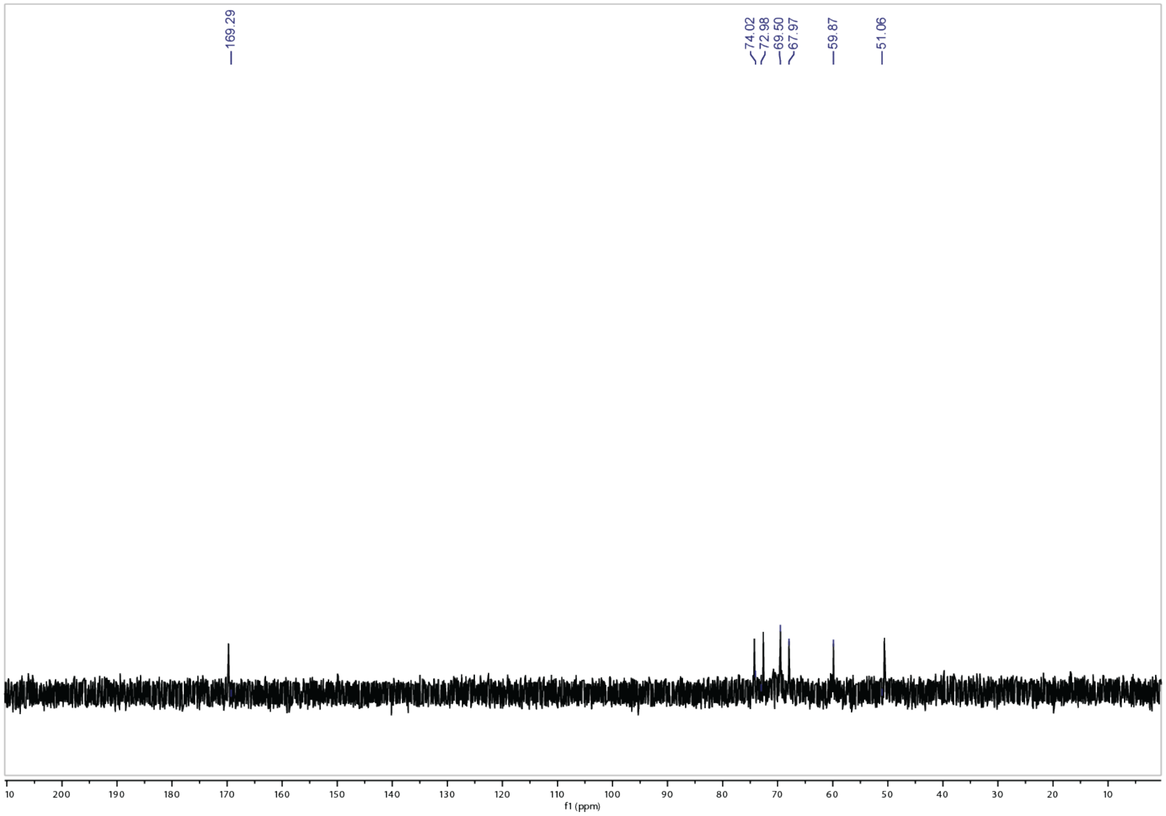
(**P5d'**) – ^{13}C NMR (151 MHz, D_2O)



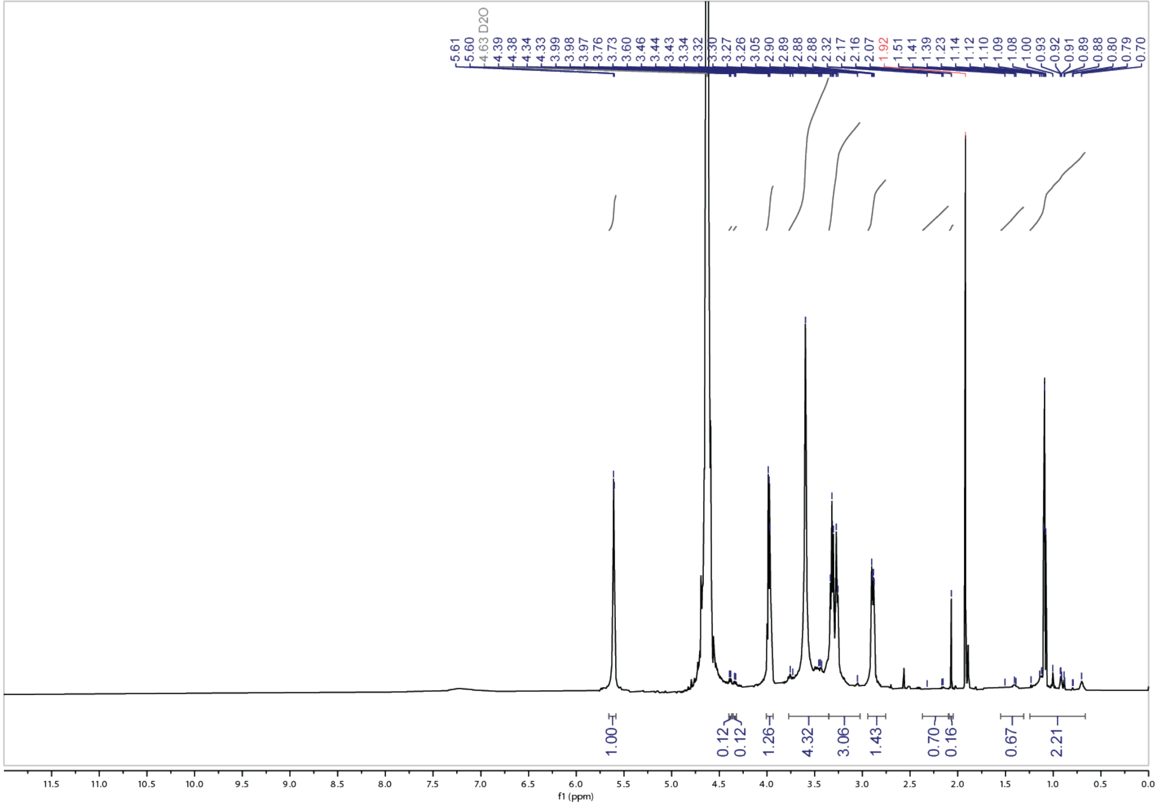
(**P6d'**) – ^{1}H NMR (600 MHz, D_2O)



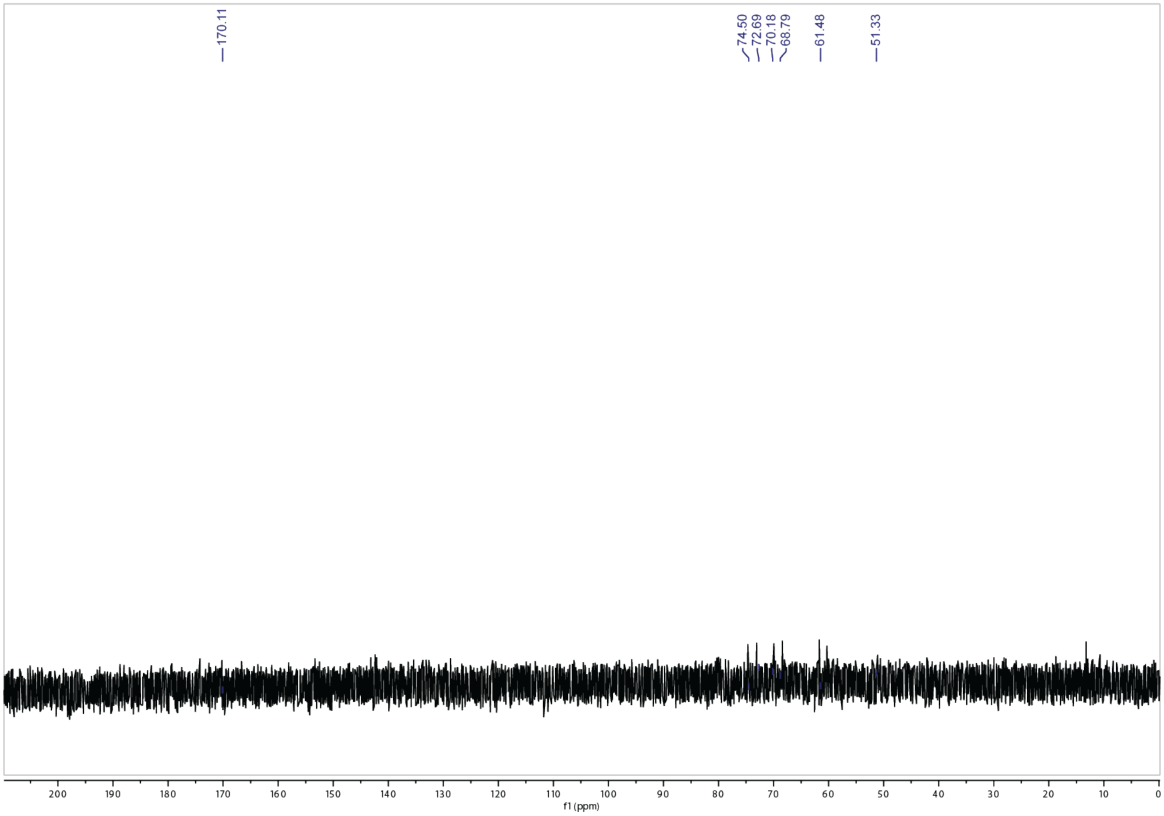
(**P6d'**) – ^{13}C NMR (151 MHz, D_2O)



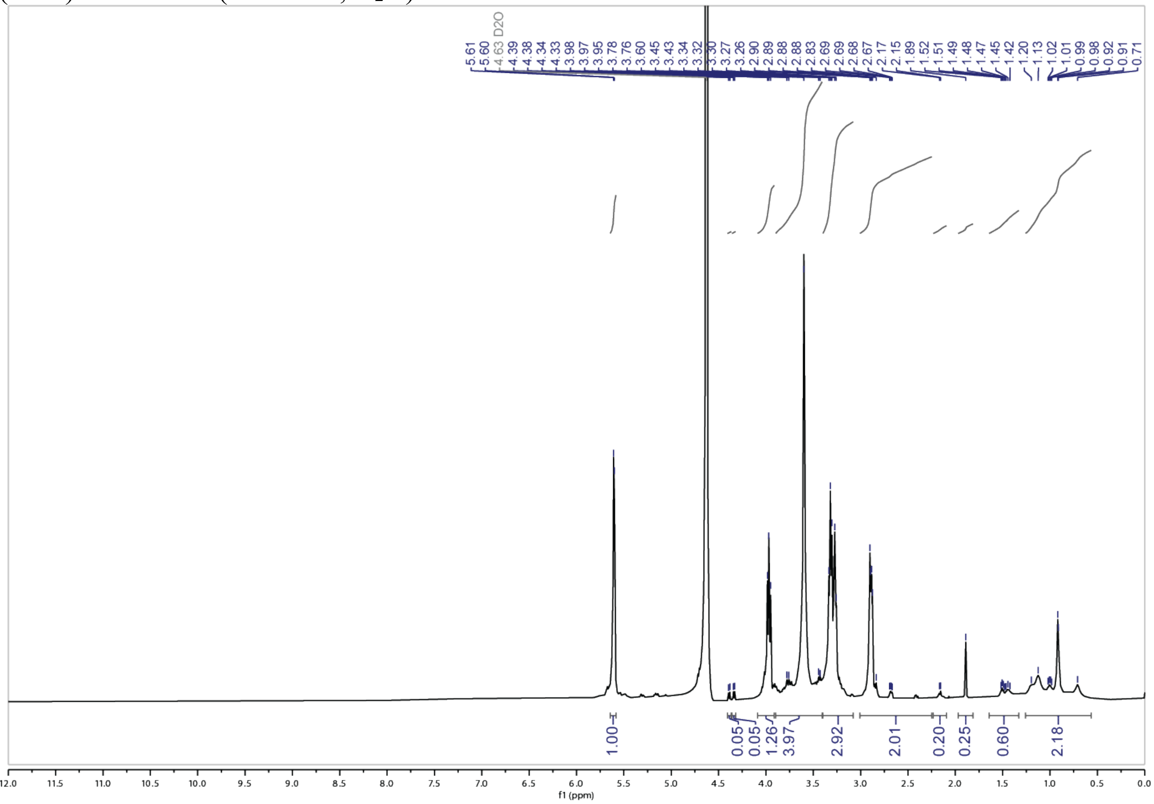
(**P7d'**) – ^{1}H NMR (600 MHz, D$_2$O)



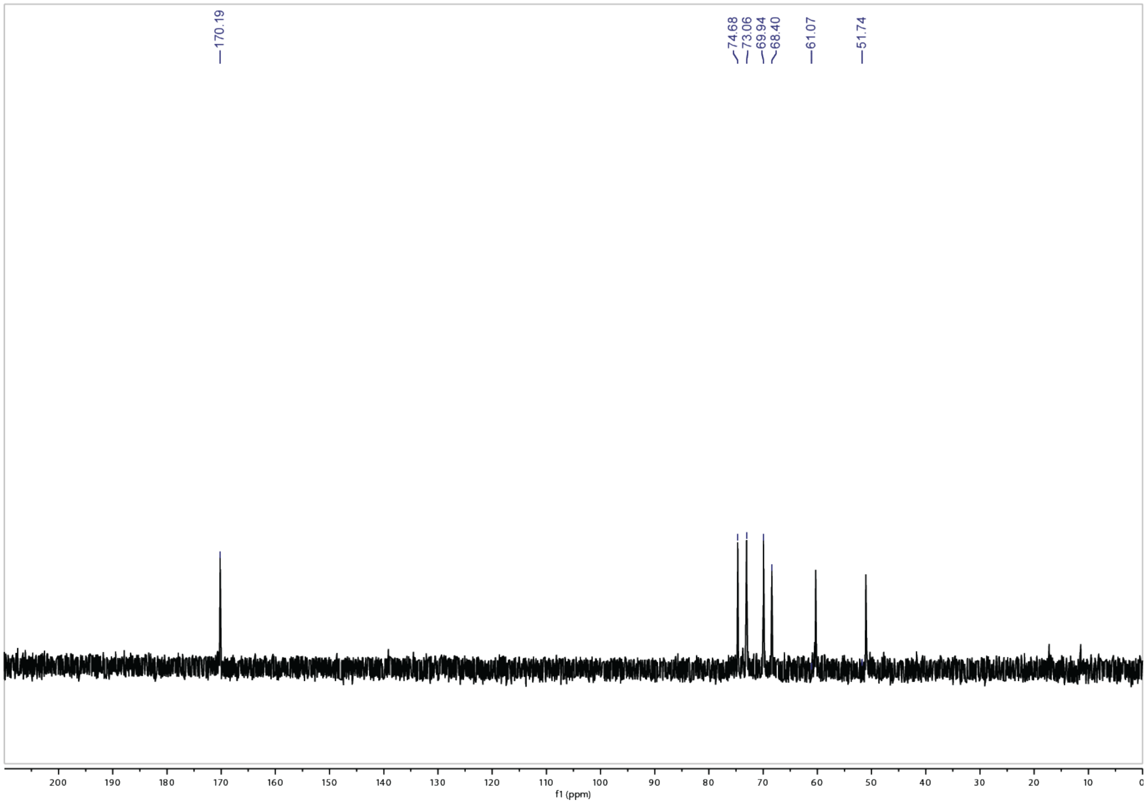
(**P7d'**) – ^{13}C NMR (151 MHz, D$_2$O)



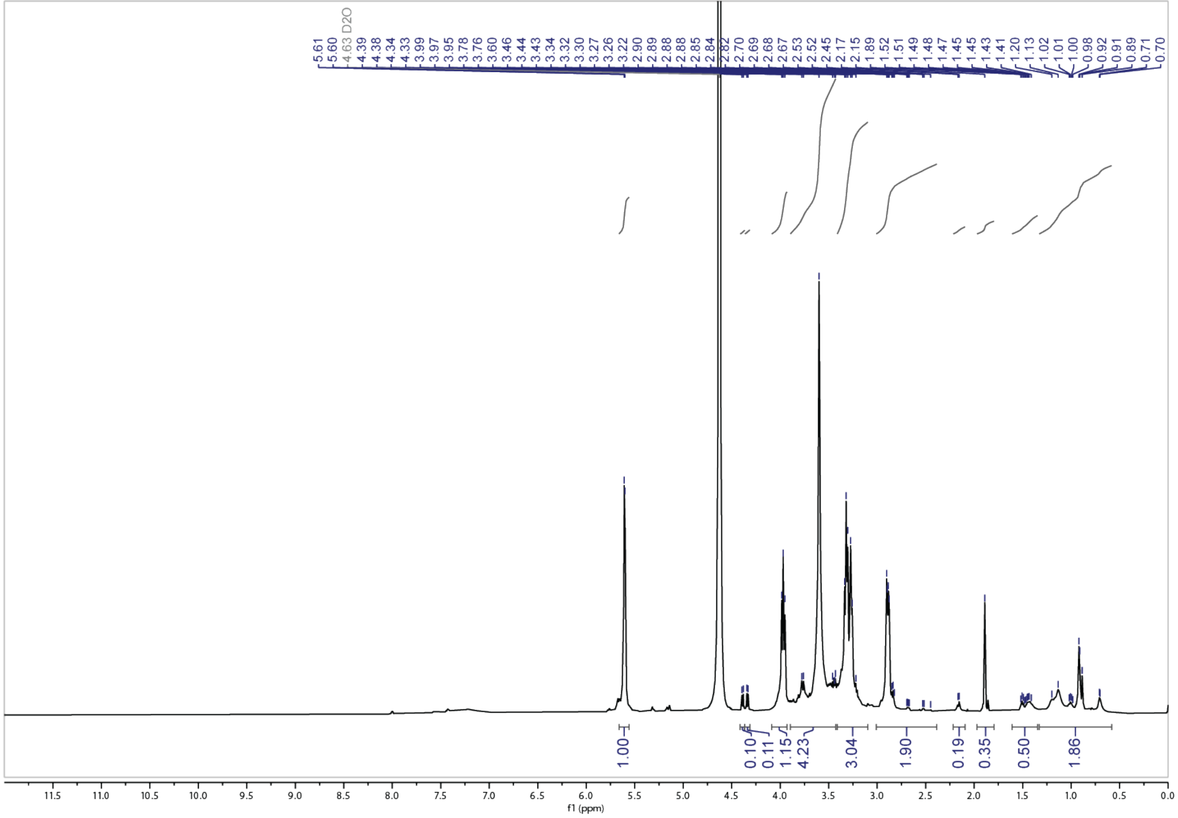
(**P8d'**) – ^{1}H NMR (600 MHz, D_2O)



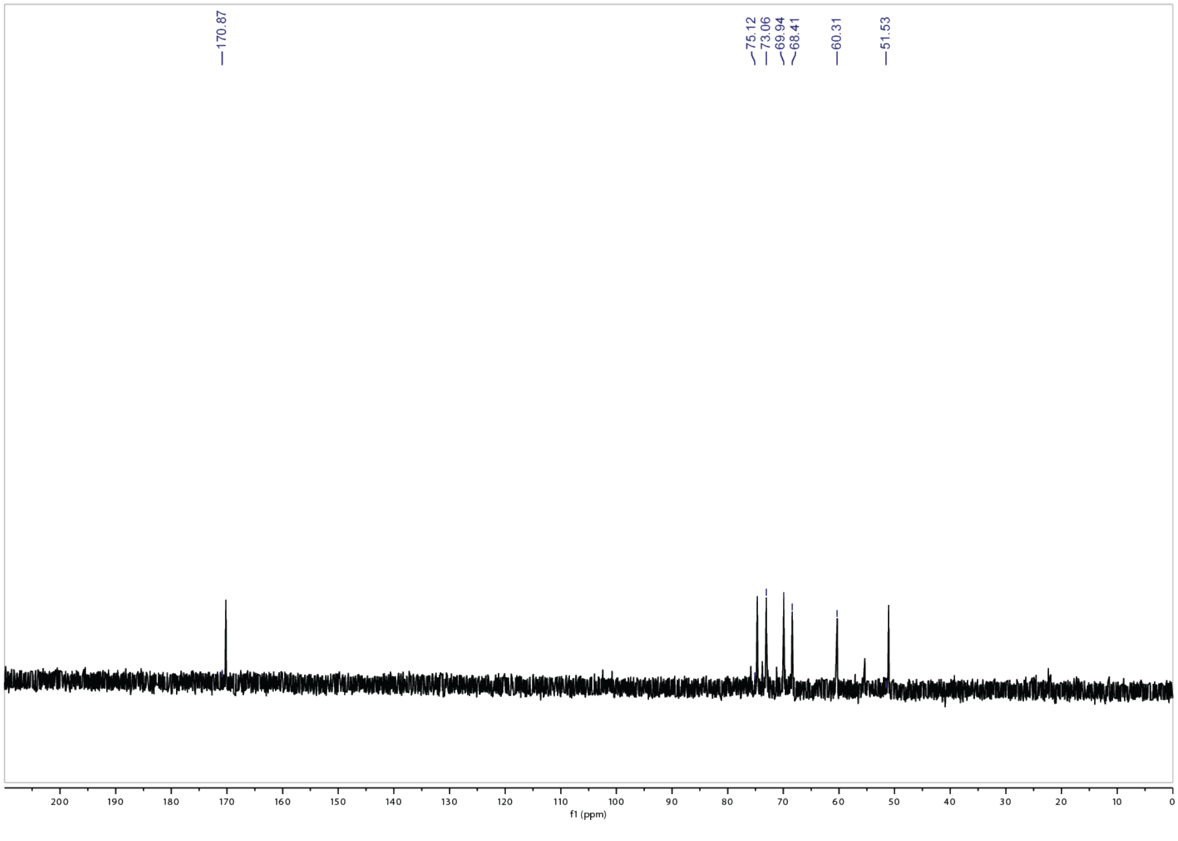
(**P8d'**) – ^{13}C NMR (151 MHz, D_2O)



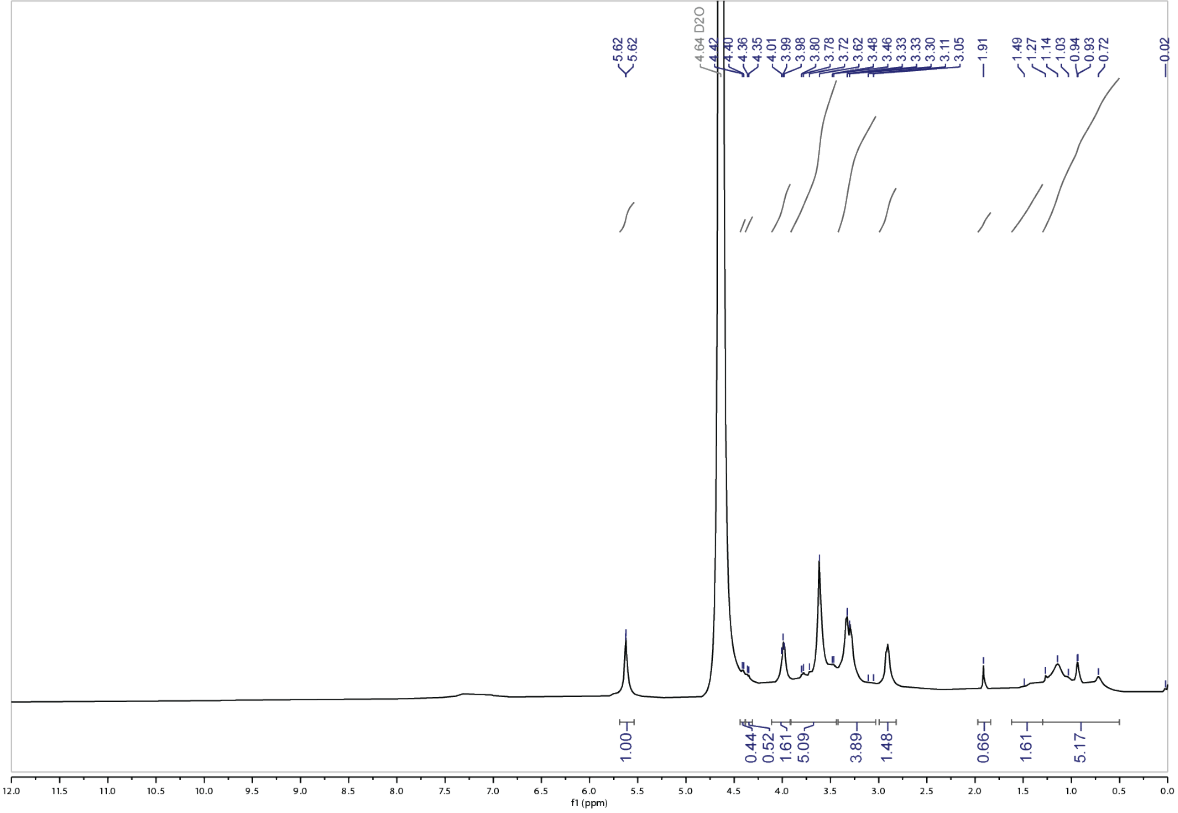
(**P9d'**) – ^{1}H NMR (600 MHz, D_2O)



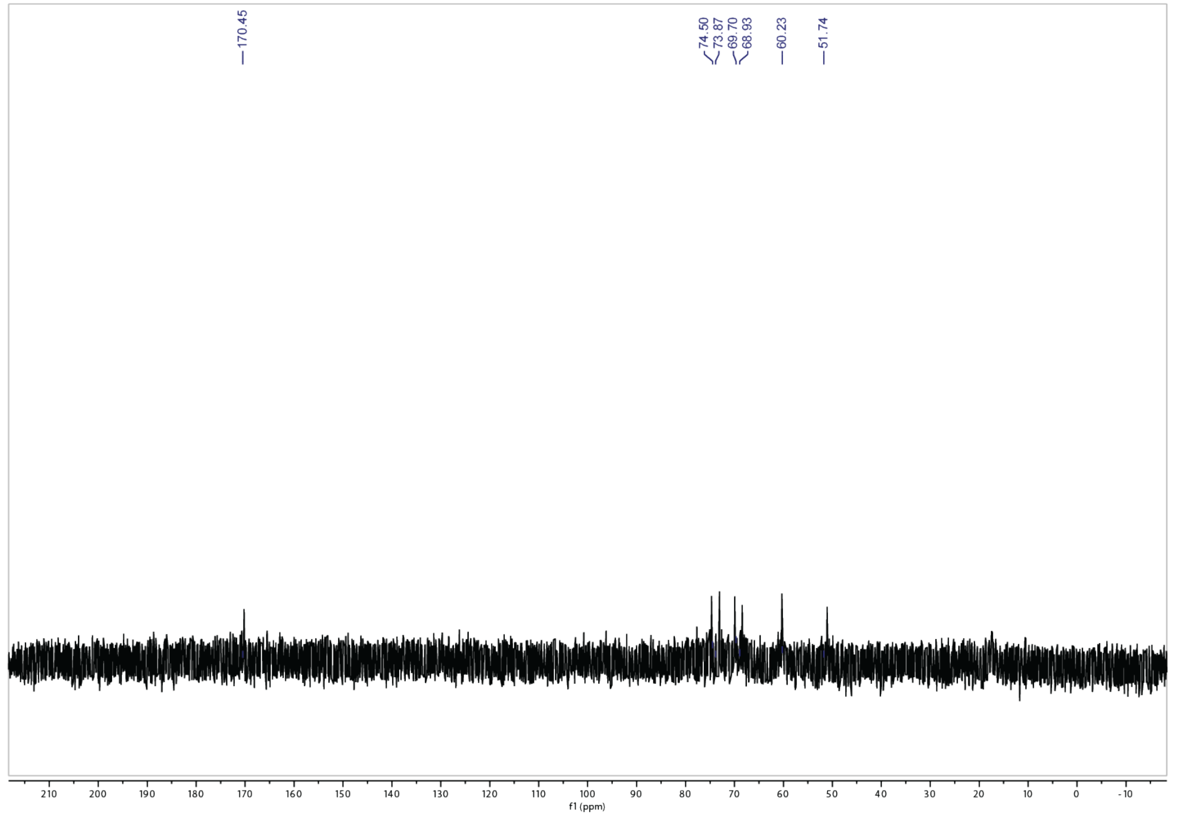
(**P9d'**) – ^{13}C NMR (151 MHz, D_2O)



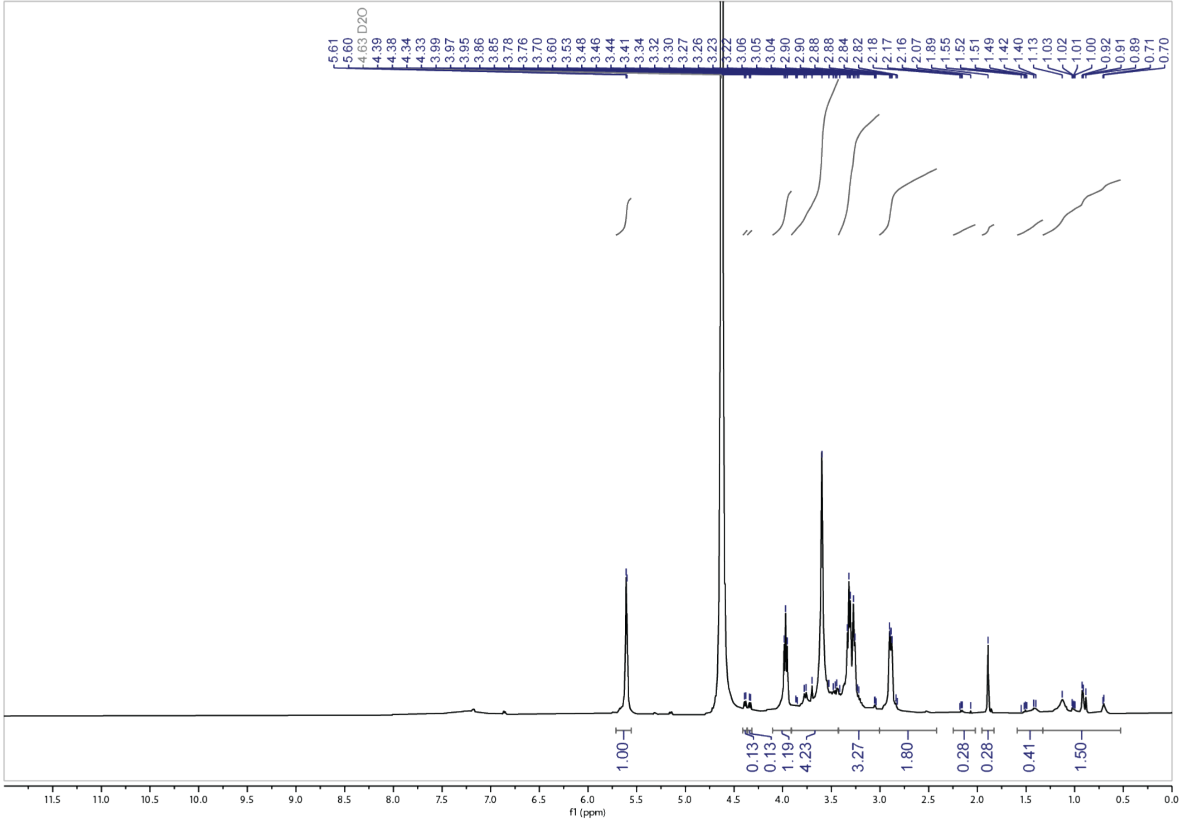
(**P10d'**) – ^{1}H NMR (600 MHz, D_2O)



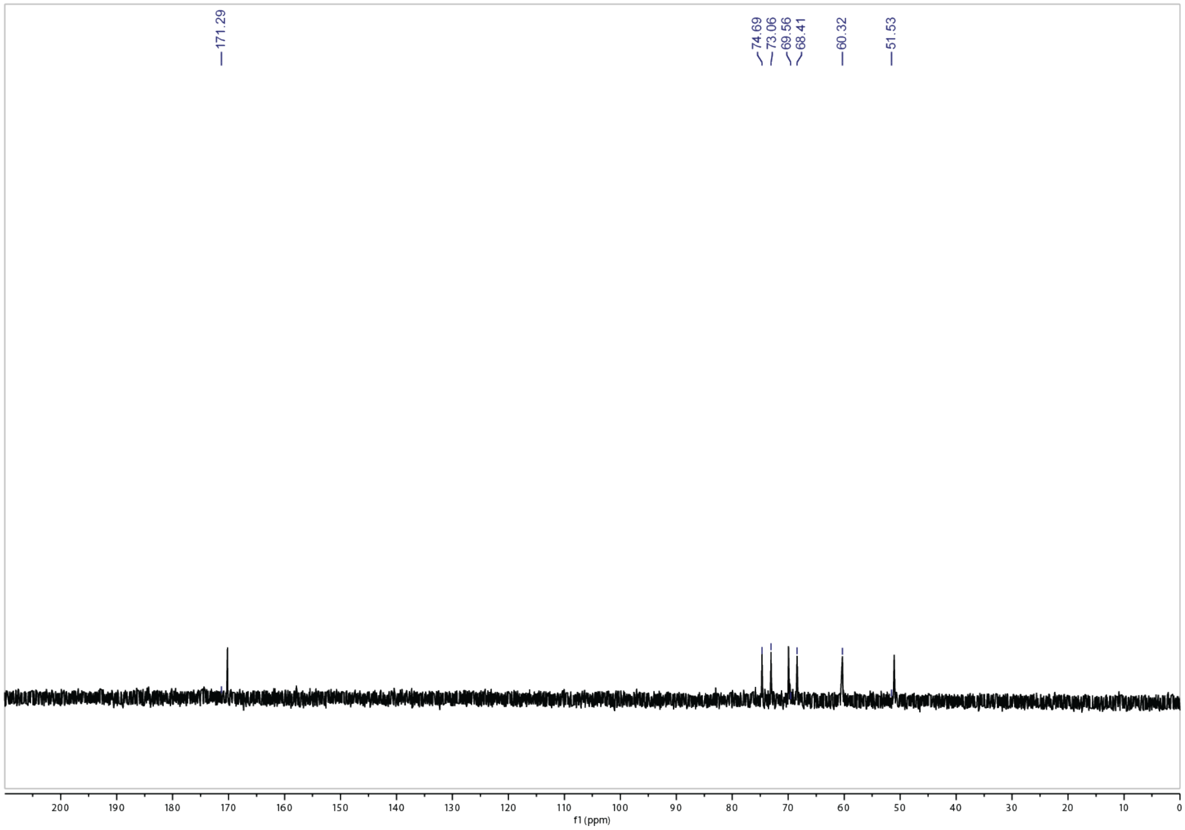
(**P10d'**) – ^{13}C NMR (151 MHz, D_2O)



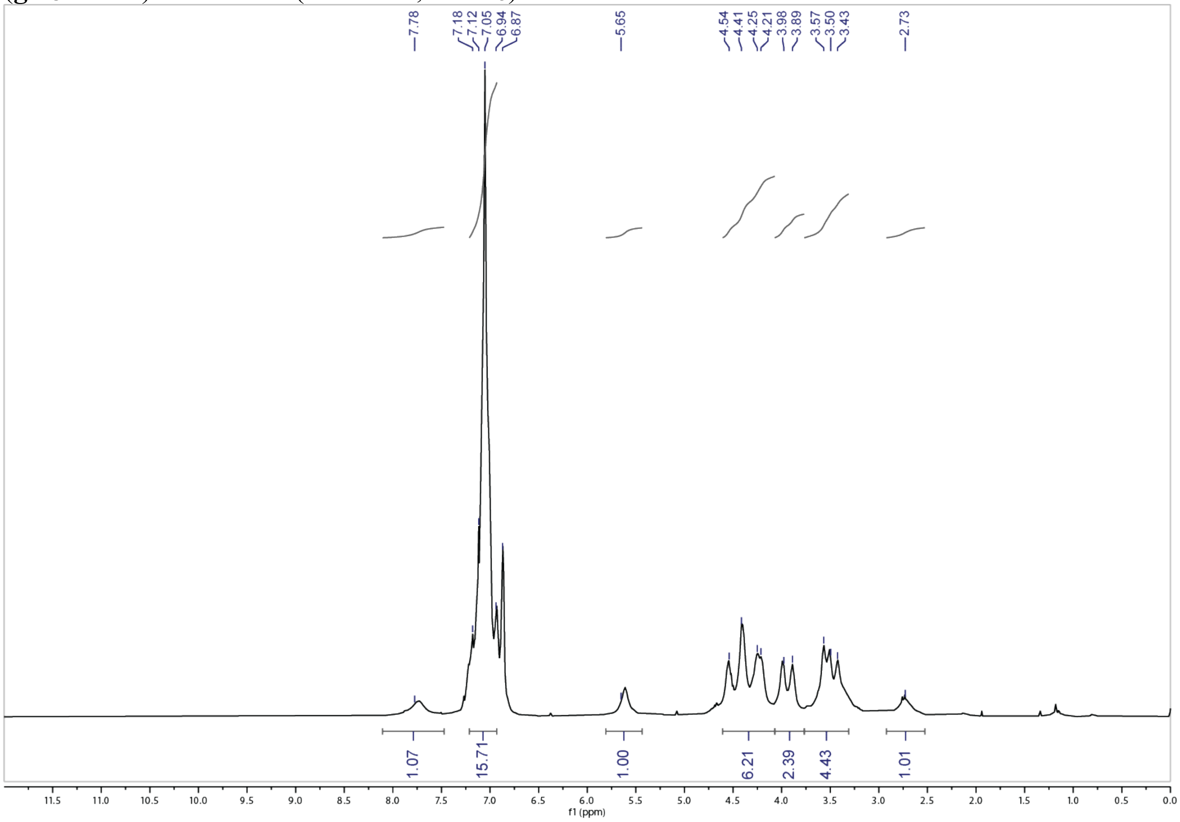
(**P11d'**) – ^{1}H NMR (600 MHz, D_2O)



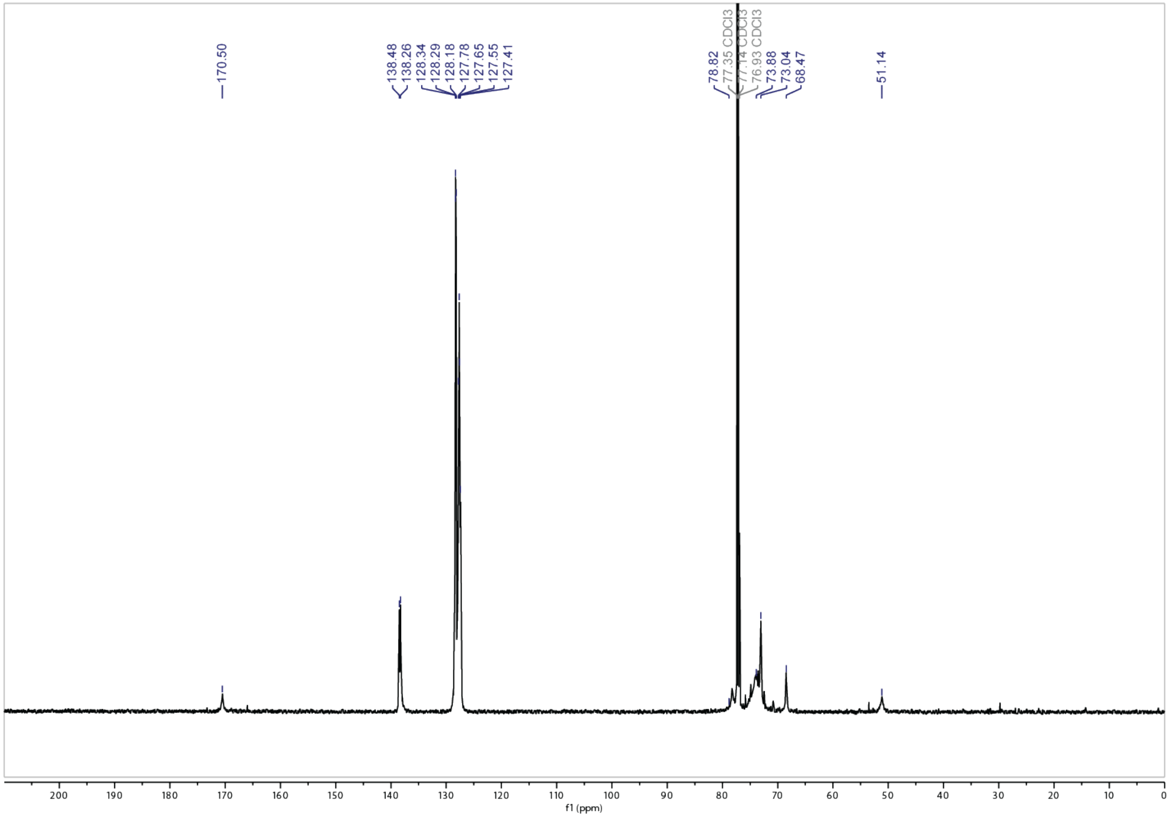
(**P11d'**) – ^{13}C NMR (151 MHz, D_2O)



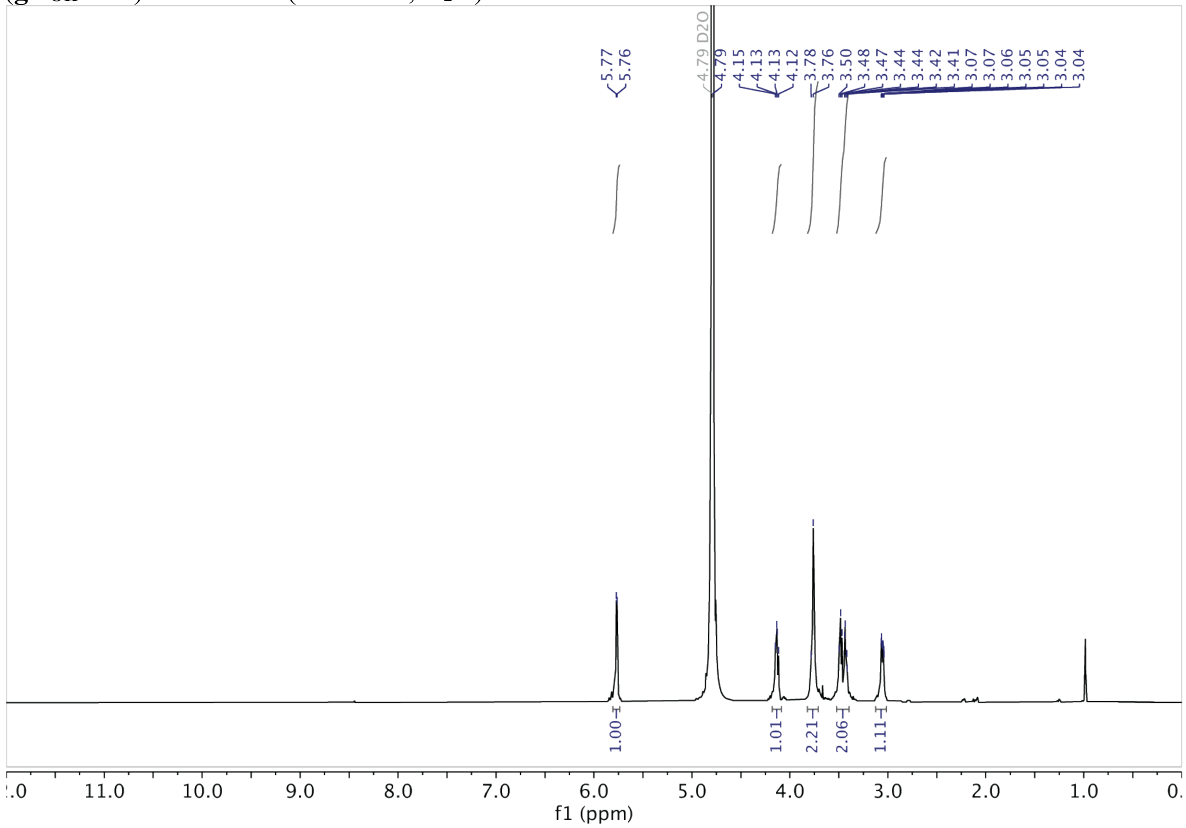
(**glc$_{\mathbf{OBn}}$PAS**) – ^{1}H NMR (600 MHz, CDCl$_3$)



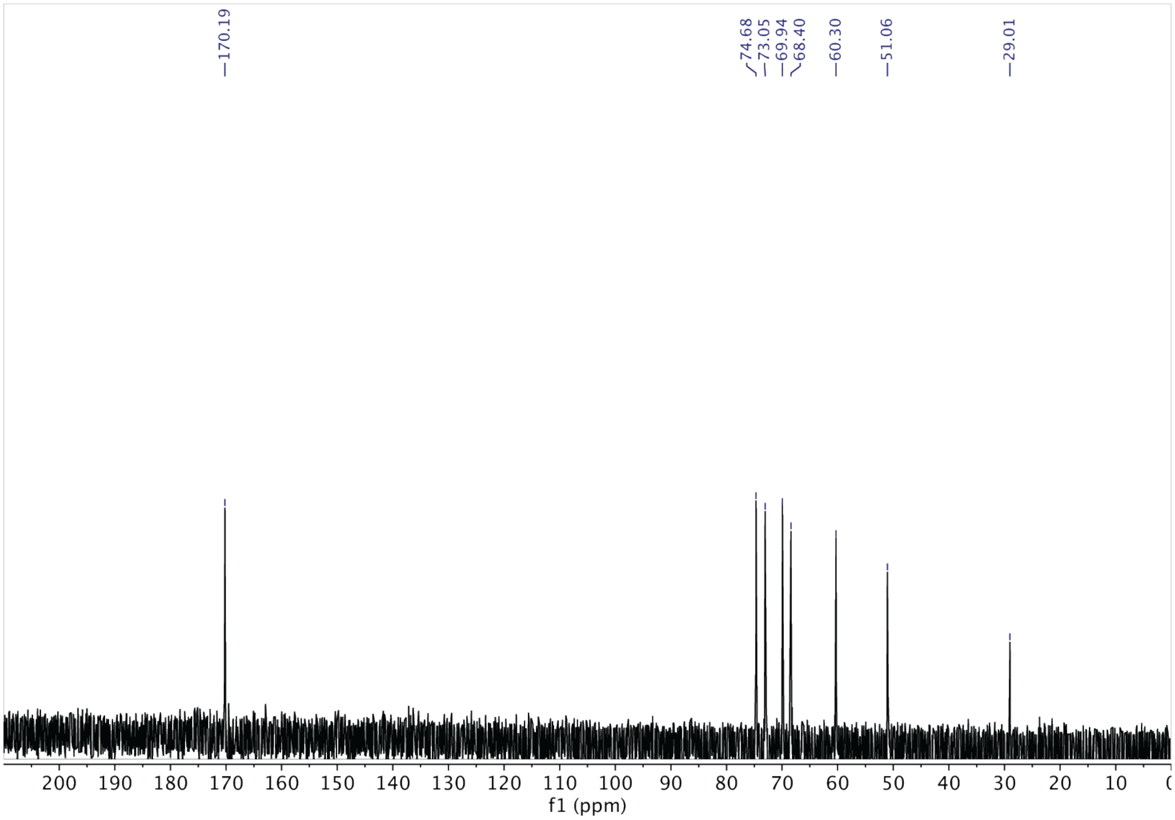
(**glc$_{\mathbf{OBn}}$PAS**) – ^{13}C NMR (151 MHz, CDCl$_3$)



(**glc$_{OH}$PAS**) – ^{1}H NMR (600 MHz, D$_2$O)



(**glc$_{OH}$PAS**) – ^{13}C NMR (151 MHz, D$_2$O)



References

1. M. Mende, M. Nieger and S. Brase, *Chem Eur J*, 2017, **23**, 12283-12296.
2. J. Kandasamy, F. Schuhmacher, H. S. Hahm, J. C. Klein and P. H. Seeberger, *Chem Commun (Camb)*, 2014, **50**, 1875-1877.
3. A. A. Grinkova, E. V. Sukhova, N. E. Ustyuzhanina and N. E. Nifantiev, *Carbohydr Res*, 2022, **522**, 108701.
4. R. Yadav, S. Leviatan Ben-Arye, B. Subramani, V. Padler-Karavani and R. Kikkeri, *Org Biomol Chem*, 2016, **14**, 10812-10815.
5. K. J. Loft, P. Bojarova, K. Slamova, V. Kren and S. J. Williams, *Chem Biochem*, 2009, **10**, 565-576.
6. J. Dinkelaar, L. J. van den Bos, W. F. Hogendorf, G. Lodder, H. S. Overkleeft, J. D. Codee and G. A. van der Marel, *Chem Eur J*, 2008, **14**, 9400-9411.
7. A. A. Sherman, O. N. Yudina, Y. V. Mironov, E. V. Sukhova, A. S. Shashkov, V. M. Menshov and N. E. Nifantiev, *Carbohydr Res*, 2001, **336**, 13-46.
8. G. V. Los, L. P. Encell, M. G. McDougall, D. D. Hartzell, N. Karassina, C. Zimprich, M. G. Wood, R. Learish, R. F. Ohana, M. Urh, D. Simpson, J. Mendez, K. Zimmerman, P. Otto, G. Vidugiris, J. Zhu, A. Darzins, D. H. Klaubert, R. F. Bulleit and K. V. Wood, *ACS Chem Biol*, 2008, **3**, 373-382.
9. H. E. Murrey, J. C. Judkins, C. W. Am Ende, T. E. Ballard, Y. Fang, K. Riccardi, L. Di, E. R. Guilmette, J. W. Schwartz, J. M. Fox and D. S. Johnson, *J Am Chem Soc*, 2015, **137**, 11461-11475.
10. J.-P. Lellouche and S. Koeller, *The Journal of Organic Chemistry*, 2001, **66**, 693-696.
11. A. S. Balijepalli, J. H. McNeely, A. Hamoud and M. W. Grinstaff, *J Org Chem*, 2020, **85**, 12044-12057.
12. M. Varghese, F. Haque, W. Lu and M. W. Grinstaff, *Biomacromolecules*, 2022, **23**, 2075-2088.
13. M. Varghese, H. E. Caputo, X. Ruiqing, A. Balijepalli, A. Hamoud and M. W. Grinstaff, *Org Synth*, 2021, **98**, 491-508.
14. G. Maccari, D. Deodato, D. Fiorucci, F. Orofino, G. I. Truglio, C. Pasero, R. Martini, F. De Luca, J. D. Docquier and M. Botta, *Bioorg Med Chem Lett*, 2017, **27**, 3332-3336.
15. WO2006088490 A2, 2005.
16. E. L. Dane and M. W. Grinstaff, *J Am Chem Soc*, 2012, **134**, 16255-16264.
17. R. Xiao, J. Zeng and M. W. Grinstaff, *ACS Macro Lett*, 2018, **7**, 772-777.
18. A. M. Carvalho, J. Valcarcel, D. Soares da Costa, M. Gomes, J. A. Vazquez, R. L. Reis, R. Novoa-Carballal and I. Pashkuleva, *ACS Appl Mater Interfaces*, 2022, **14**, 41779-41789.
19. E. L. Dane, S. L. Chin and M. W. Grinstaff, *ACS Macro Lett*, 2013, **2**, 887-890.