

One-Pot Synthesis of Polyrotaxanes via Acyclic Diene Metathesis Polymerization of Supramolecular Monomers

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SUPPORTING INFORMATION

Experimental procedures and characterization data (¹H, ¹³C and 2D NMR spectra, HRMS, GPC) for all compounds.

General Information. NMR spectra were obtained on either a Mercury 300 MHz spectrometer, an INOVA 500 MHz spectrometer equipped with an AutoX broadband probe with z-gradients, or an INOVA 600 MHz spectrometer equipped with an inverse HCN triple resonance probe with x-, y-, and z-gradients. All spectrometers were running Varian VNMRJ software. Chemical shifts for both ¹H and ¹³C spectra are reported in per million (ppm) relative to Si(CH₃)₄ (δ=0) and referenced internally to the protio solvent resonance. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (qt), septuplet (sp), multiplet (m), and broad (br). MestReNova NMR 5.3.2 software was used to analyze all NMR spectra. Molecular mass calculations were performed with ChemBioDraw Ultra 11.0.1 (Cambridge Scientific). Mass spectrometric measurements (FAB, EI, and MALDI) were performed by the California Institute of Technology Mass Spectrometry Facility. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization was performed using UV and iodine stain. Flash column chromatography was performed using silica gel 60 (230-400 mesh) from EM Science. Gel permeation chromatography (GPC) was carried out in 0.2 M LiBr in DMF on two I-series Mixed Bed Low MW ViscoGel columns (Viscotek) connected in series with a DAWN EOS multiangle light scattering (MALS) detector and an Optilab DSP differential refractometer (both from Wyatt

Technology). No calibration standards were used, and dn/dc values were obtained for each injection assuming 100% mass elution from the columns.

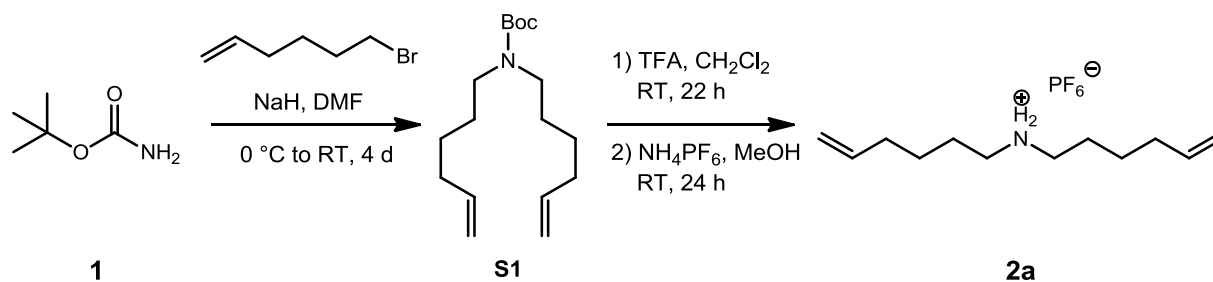
Materials and Methods. Anhydrous *N,N*-dimethylformamide (DMF) was obtained from Acros (99.8% pure, Acrosealed). Dry CH_2Cl_2 was purified by passage through solvent purification columns.¹ All water was deionized. Grubbs-Hoveyda 2nd Generation isopropoxybenzylidene catalyst $(\text{H}_2\text{IMes})(\text{Cl})_2\text{RuCH}(\text{o-OiPrC}_6\text{H}_4)$ (**4**) was obtained as a generous gift from Materia, Inc. All other compounds were purchased from Acros or Aldrich and used as received.

2D-DOSY NMR Spectroscopy. Two-dimensional diffusion-ordered NMR spectroscopy was performed on an INOVA 600 MHz spectrometer equipped with an inverse HCN triple resonance probe with x-, y-, and z-gradients. The spectrometer was running Varian VNMRJ software. Spectra were acquired at 25 °C using the VNMRJ dbppste pulse sequence. Calibration of the instrument was performed using β -cyclodextrin in deuterium oxide (10 mM β -cyclodextrin in 97% H_2O / 3% D_2O), and was recorded at $23.1 \times 10^{-10} \text{ m}^2/\text{sec}$. The difference between this experimental value and the known literature diffusion rate of 3.32×10^{-10} (at 25 °C)² represents the scaling factor for the remainder of the experimentally determined numbers. Values reported in the paper and supporting information are those determined experimentally, and have not been corrected. They should, consequently, be treated as “relative” values, not absolute diffusion rates. Diffusion rates for all samples are in units of $10 \times 10^{-10} \text{ m}^2/\text{sec}$. Concentrations of all samples were $\leq 10 \text{ mg/mL}$.

1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

2) (a) Larive, C. K.; Lin, M.; Piersma, B. J.; Carper, W. R. *J. Phys. Chem.* **1995**, *99*, 12409-12412. (b) Lin, M.; Jayawickrama, D. A.; Rose, R. A.; DelViscio, J. A.; Larive, C. K. *Anal. Chim. Acta* **1995**, *307*, 449-457.

Synthesis of Monomer 2a

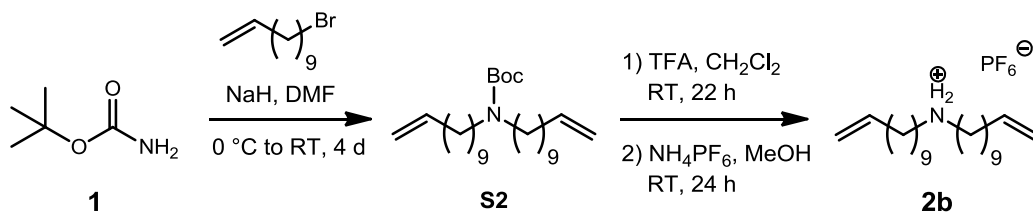


An oven-dried round bottom flask was equipped with a stir bar under nitrogen. To the flask was added NaH (1.04 g, 43.3 mmol, 2.10 eq), 6-bromo-1-hexene (6.87 g, 42.1 mmol, 2.05 eq), and dry DMF (300 mL). The flask was cooled in an ice bath and a solution of *tert*-butyl carbamate **1** (2.41 g, 20.6 mmol, 1.00 eq) in dry DMF (12 mL, 99.8%) was added dropwise to the stirring mixture over 25 min. The ice bath was removed and the reaction mixture was stirred at RT for 4 days. The reaction mixture was then slowly poured onto 200 g of ice and extracted with diethyl ether (3 × 100 mL). The combined ether solutions were washed with H₂O (4 × 200 mL), washed with brine (200 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure to yield carbamate **S1** as a clear liquid (3.01 g, 53% yield). ¹H NMR (500 MHz, CDCl₃) δ 5.83-5.74 (m, 2H), 5.01-4.93 (m, 4H), 3.22-3.10 (m, 4H), 2.06 (qt, *J* = 7.1 Hz, 4H), 1.57-1.46 (m, 4H), 1.44 (s, 9H), 1.42-1.31 (m, 4H). ¹³C NMR (126 MHz, CDCl₃) δ 155.8, 138.6, 114.8, 79.1, 46.9, 33.6, 33.5, 28.6, 28.6, 26.3. HRMS-EI: calcd for C₁₇H₃₁O₂N: 281.2355; found: 281.2360.

To a round bottom flask equipped with a stir bar was added carbamate **S1** (3.01g, 10.7 mmol), CH₂Cl₂ (100 mL), and TFA (12.3g, 107 mmol, 10.0 eq). The mixture was stirred for 22 h, then concentrated under reduced pressure. The crude material was redissolved in CH₂Cl₂ (40 mL) and then concentrated under reduced pressure and dried under high vacuum, yielding light tan needles. The solid product was then dissolved in MeOH (100 mL), and ammonium hexafluorophosphate (17.9 g, 110 mmol, 10.3 eq) was added. The mixture was stirred for 24 h, then poured into 500 mL of H₂O. The resulting suspension stood for 24 h at RT, then at -20 °C for 24 hours. The mixture was then vacuum filtered and the solid was washed with H₂O, yielding light tan crystals (2.586 g, 74% yield) of diene monomer **2a**. ¹H NMR (500 MHz, CD₃CN) δ 5.87-5.78 (m, 2H), 5.07-4.98 (m, 4H), 2.98-2.94 (m, 4H), 2.08 (q, *J* = 7.1 Hz, 4H), 1.62 (qt, *J* =

7.7 Hz, 4H), 1.44 (qt, $J = 7.6$ Hz, 4H). ^{13}C NMR (126 MHz, CD_3CN) δ 139.1, 115.7, 49.0, 33.6, 26.1, 26.0. HRMS-FAB calcd for $\text{C}_{12}\text{H}_{24}\text{N}$: 182.1909; found: 182.1879.

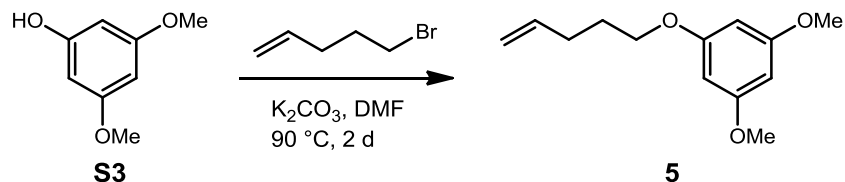
Synthesis of Monomer 2b



In a manner analogous to the synthesis of compound **S1**, dialkyl carbamate **S2** was prepared from **1** (0.75 g, 6.4 mmol, 1.0 eq), NaH (323 mg, 13.5 mmol, 2.10 eq), and 11-bromo-1-undecene (3.06 g, 13.1 mmol, 2.05 eq). Analysis of the crude product mixture indicated an excess of 11-bromo-1-undecene remained. This mixture was resubjected to alkylation conditions using NaH (109 mg, 4.5 mmol) and *tert*-butyl carbamate (256 mg, 2.2 mmol) in dry DMF (100 mL). After workup analogous to that of **S1**, the crude mixture was purified twice by flash chromatography on silica gel (20:1 hexanes/ethyl acetate eluent), yielding the desired product as a clear oil (302 mg, 11% yield). ^1H NMR (500 MHz, CDCl_3) δ 5.88-5.74 (m, 2H), 5.02-4.90 (m, 4H), 3.21-3.06 (br m, 4H), 2.03 (q, $J = 7.0$ Hz, 4H), 1.51-1.19 (m, 27H), 1.44 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 155.8, 139.4, 114.3, 79.0, 47.2, 34.0, 29.7, 29.6, 29.3, 29.1, 28.7, 27.1. HRMS-FAB calcd for $\text{C}_{27}\text{H}_{50}\text{O}_2\text{N}$: 420.3842; found: 420.3824.

In a manner analogous to the synthesis of compound **2a**, monomer **2b** (291 mg, 87% yield) was prepared from **S2** (302 mg, 0.72 mmol), TFA (0.82g, 7.2 mmol, 10 eq), and ammonium hexafluorophosphate (1.17 g, 7.16 mmol, 10.0 eq). ^1H NMR (500 MHz, CD_3CN) δ 5.88-5.80 (m, 2H), 5.02-4.91 (m, 4H), 2.94 (dd, $J = 8.5, 7.0$ Hz, 4H), 2.07-2.02 (m, 4H), 1.64-1.58 (m, 4H), 1.39-1.27 (br m, 26H). ^{13}C NMR (126 MHz, CD_3CN) δ 140.2, 114.8, 49.1, 34.5, 30.0, 29.9, 29.8, 29.7, 29.6, 26.9, 26.5. HRMS-FAB calcd for $\text{C}_{22}\text{H}_{44}\text{N}$: 322.3474; found: 322.3471.

Synthesis of ADMet Chain Transfer Agent 5



A flame dried two-neck round bottom flask and stir bar was fitted with a reflux condenser and placed under Ar. To the flask was added 3,5-dimethoxyphenol **S3** (500 mg, 3.24 mmol, 1.0 eq), anhydrous potassium carbonate (1.35 g, 9.73 mmol, 3 eq), and dry DMF (32 mL). To this stirring mixture was added 5-bromo-1-pentene (532 mg, 0.42 mL, 3.56 mmol, 1.1 eq) in one portion, and the mixture was heated in an oil bath at $90\text{ }^\circ\text{C}$ for 2 d. The reaction mixture was removed from heat, diluted with ethyl acetate (100 mL) and partitioned with water (500 mL). The aqueous layer was extracted with fresh ethyl acetate ($3 \times 50\text{ mL}$), and the combined organic layers were washed with fresh H_2O (100 mL). The organic layer was dried (MgSO_4), filtered, and then concentrated under reduced pressure to afford a brown oil. Purification via flash chromatography on silica gel (10:1 hexanes/acetone eluent) afforded the desired compound as a clear oil (447 mg, 62 % yield). ^1H NMR (500 MHz, CDCl_3): $\delta = 6.08$ (s, 3 H), 5.90-5.80 (m, 1 H), 5.10-4.97 (m, 2 H), 3.93 (t, $J = 6.5$, 2 H), 3.77 (s, 6 H), 2.23 (q, $J = 7.1$, 2 H), 1.87 (qt, $J = 6.5$, 2 H); ^{13}C NMR (126 MHz, CDCl_3): $\delta = 161.6$, 161.1, 137.9, 115.3, 93.6, 93.0, 67.4, 55.5, 30.3, 28.5; HRMS-FAB (m/z): $[\text{M} + \text{H}]$ calcd for $\text{C}_{13}\text{H}_{18}\text{O}_3$: 222.1334; found: 222.1348.

General Procedure for ADMet Polyrotaxane Synthesis using Pseudorotaxane Monomer. A vial with a septum cap was charged with a stir bar, ammonium diene monomer (**2a** or **2b**, 1 eq), and **DB24C8** (1 eq). CH_2Cl_2 was added, and the solution was stirred for 10 min. The solvent was removed under reduced pressure to afford a mixture containing the pseudorotaxane monomer (**3a** or **3b**) as a white solid. The vial was then charged with **5** (0.4 eq) as a solution in dry CH_2Cl_2 (0.5 mL). The solution was frozen in liquid nitrogen, the headspace of the vial was evacuated and filled with argon, the cap was briefly removed, and catalyst **4** (2.5 mol%) was quickly added. The cap was replaced and the headspace was immediately evacuated and backfilled with argon while keeping the mixture frozen in liquid nitrogen. Once the reaction was under positive argon pressure, it was allowed to attain room temperature and then lowered into a oil bath set at $50\text{ }^\circ\text{C}$.

After 30 minutes, the solvent was removed under reduced pressure (10 mTorr), and dry CH₂Cl₂ (0.2 mL) was added. This “cycling” process was repeated at 1 h, 2 h, and 12 h. After 24 h, the reaction mixture was diluted with CH₂Cl₂ (0.5 ml) and added dropwise into 1:1 hexanes/diethyl ether (50 mL) causing precipitation of the desired polymer. The solid was collected via vacuum filtration, rinsed cold hexanes/diethyl ether (1:1 v/v) and dried under vacuum to afford polyrotaxane polymer **6a** or **6b**.

Polyrotaxane 6a. The general polyrotaxane synthetic procedure was employed, using pseudorotaxane **3a** (47.3 mg, 0.06 mmol, 1 eq), cap **5** (5.4 mg, 0.02 mmol, 0.4 eq), and catalyst **4** (1.0 mg, 1.53 μmol, 2.5 mol%). Polyrotaxane **6a** (44 mg, 85% yield) was isolated as an off-white solid. A 10 mg sample of polyrotaxane **6a** was dissolved in deuterated acetonitrile. From this solution, 100 μl was removed and further diluted with an additional 900 μl of solvent (1 mg/mL solution). Both of these samples were studied by one-dimensional ¹H NMR spectroscopy and two-dimensional DOSY spectroscopy (see text). The quantity of free **DB24C8**, and the amount of threaded ammonium moieties were unchanged regardless of concentration. The reported spectral data is for the 10 mg/mL sample. The other spectra are included for reference. ¹H NMR (600 MHz, CD₃CN): δ = 7.06 (m, 0.6 H, free **DB24C8**), 6.93 (m, 7.1 H, complexed **DB24C8**), 6.73 (s, 1.7 H), 6.07 (m, 0.5 H), 5.04 (m, 2 H), 4.24 (m, 0.6 H, free **DB24C8**), 4.14 (br s, 7 H, complexed **DB24C8**), 3.84 (br s, 7 H, complexed **DB24C8**), 3.75 (m, 0.6 H, free **DB24C8**), 3.73 (br s, 1 H), 3.69 (br s, 7 H, complexed **DB24C8**), 3.26 (br s, 3.5 H, **DB24C8**-encircled α-ammonium protons), 2.91 (br s, 0.5 H, uncomplexed α-ammonium protons), 1.80-0.85 (br m, 12 H). 2D-DOSY NMR spectrum (600 MHz, CD₃CN): polyrotaxane **6a** = 1.3x10⁻⁹ m²/s, free **DB24C8** = 2.3x10⁻⁹ m²/s, H₂O = 5.9x10⁻⁹ m²/s, CD₂H₂CN = 4.3x10⁻⁹ m²/s. GPC data: *M*_n = 8.4 kDa, *M*_w = 13.2 kDa, PDI = 1.58

Polyrotaxane 6b. The general polyrotaxane synthetic procedure was employed, using pseudorotaxane **3b** (55.8 mg, 0.061 mmol, 1 eq), cap **5** (5.4 mg, 0.024 mmol, 0.4 eq), and catalyst **4** (1.0 mg, 1.53 μmol, 2.5 mol%). The mixture was precipitated to afford polyrotaxane **6b** (57 mg, 94% yield) as an off-white solid. ¹H NMR (600 MHz, CDCl₃): δ = 6.89 (br s, 7H), 6.71 (br s, 2 H), 6.07 (s, 0.6 H), 5.38 (m, 2 H), 4.31 (m, 0.6 H), 4.17 (br s, 7 H), 3.90 (br s, 7 H),

3.79 (m, 0.6 H), 3.73 (br s, 7 H), 3.23 (br s, 3.5 H), 3.04 (m, 0.5 H), 2.03 (m, 4.7 H), 1.47-0.93 (br m, 38 H). GPC data: $M_n = 7.7$ kDa, $M_w = 11.0$ kDa, PDI = 1.42

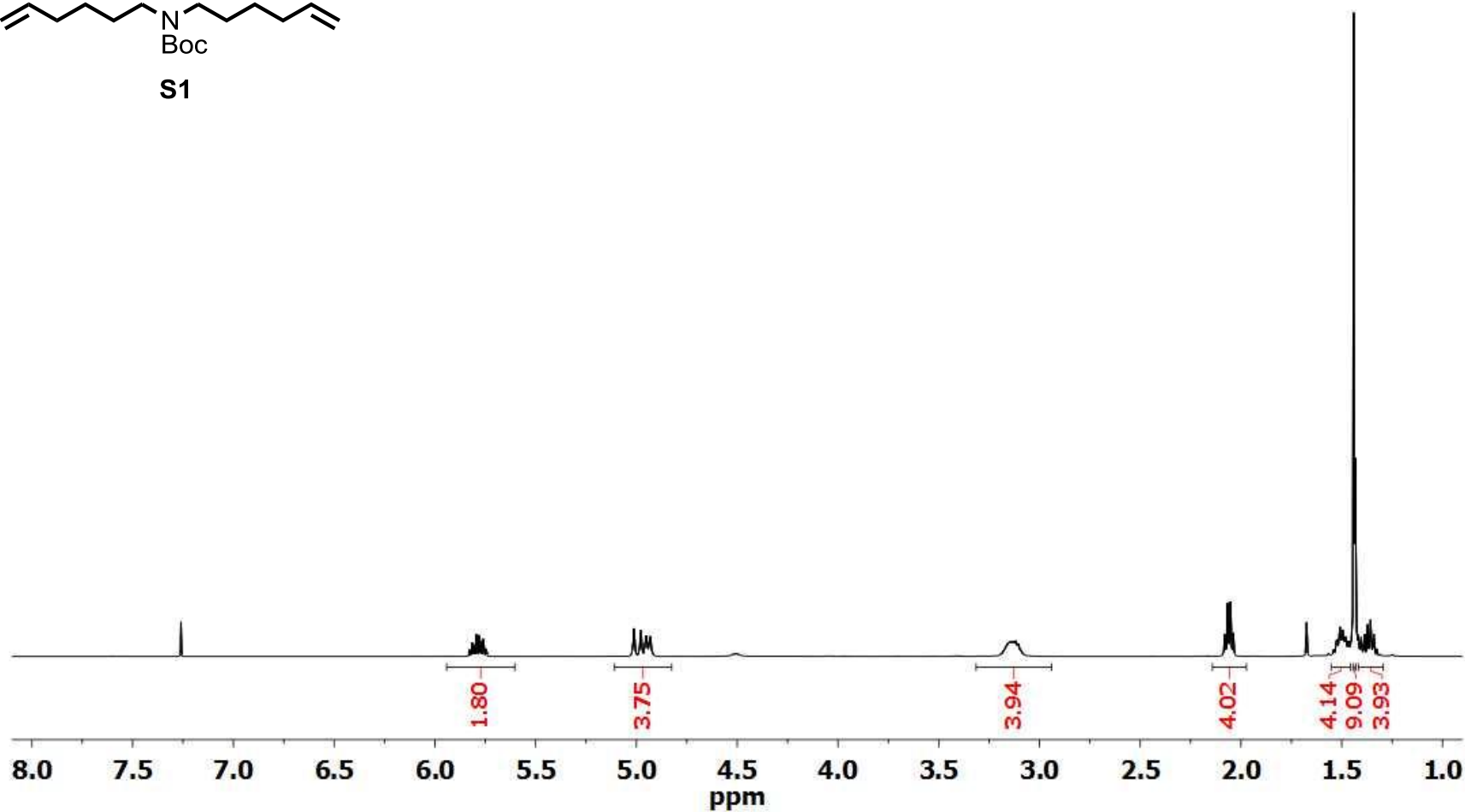
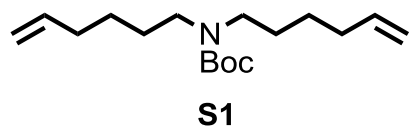
General Procedure for One-Pot ADMet Polyrotaxane Synthesis. A vial with a septum cap was charged with a stir bar, cap **5** (0.4 eq), ammonium diene monomer (**2a** or **2b**, 1 eq), and DB24C8 (1 eq). Dry dichloromethane was added, and the solution was frozen in liquid nitrogen. The headspace of the vial was evacuated and filled with argon, the cap was briefly removed, and catalyst **5** (0.025 eq) was quickly added to the top of the frozen solution. The cap was replaced and the headspace was immediately evacuated and backfilled with argon while keeping the mixture frozen in liquid nitrogen. Once the reaction was under positive argon pressure, it was allowed to attain room temperature and then lowered into an oil bath set at 50 °C. After 30 minutes, the solvent was removed under reduced pressure (10 mTorr), and dry CH₂Cl₂ (0.2 mL) was added. This “cycling” process was repeated at 1 h, 2 h, and 12 h. After 24 h, the reaction mixture was diluted (0.5 mL) and precipitated into 1:1 hexanes:ethyl ether (50 mL) to afford the desired polyrotaxane **6b**.

One-Pot Polyrotaxane 6b (11-carbon chain). The general one-pot polyrotaxane synthetic procedure was employed, using **2b** (47.3 mg, 0.061 mmol, 1 eq), **DB24C8** (27.3 mg, 0.061 mmol, 1 eq), cap **5** (5.4 mg, 0.024 mmol, 0.4 eq), and catalyst **4** (1.0 mg, 1.53 μmol, 2.5 mol%). The mixture was precipitated to afford polyrotaxane **poly3b** (44 mg, 94% yield) as an off-white solid. ¹H NMR (600 MHz, CD₃CN): δ = 6.94 (m, 7.4 H), 6.73 (br s, 2H), 6.07 (s, 0.8 H), 5.38 (m, 2 H), 4.16 (br s, 6 H), 4.13 (m, 1 H), 3.85 (br s, 6 H), 3.79 (m, 1 H), 3.73 (m, 1.8 H), 3.68 (br s, 6 H), 3.24 (br s, 3.3 H), 2.92 (br s, 0.7 H), 1.66-0.84 (m, 30 H). GPC data: $M_n = 16.4$ kDa, $M_w = 19.3$ kDa, PDI = 1.18

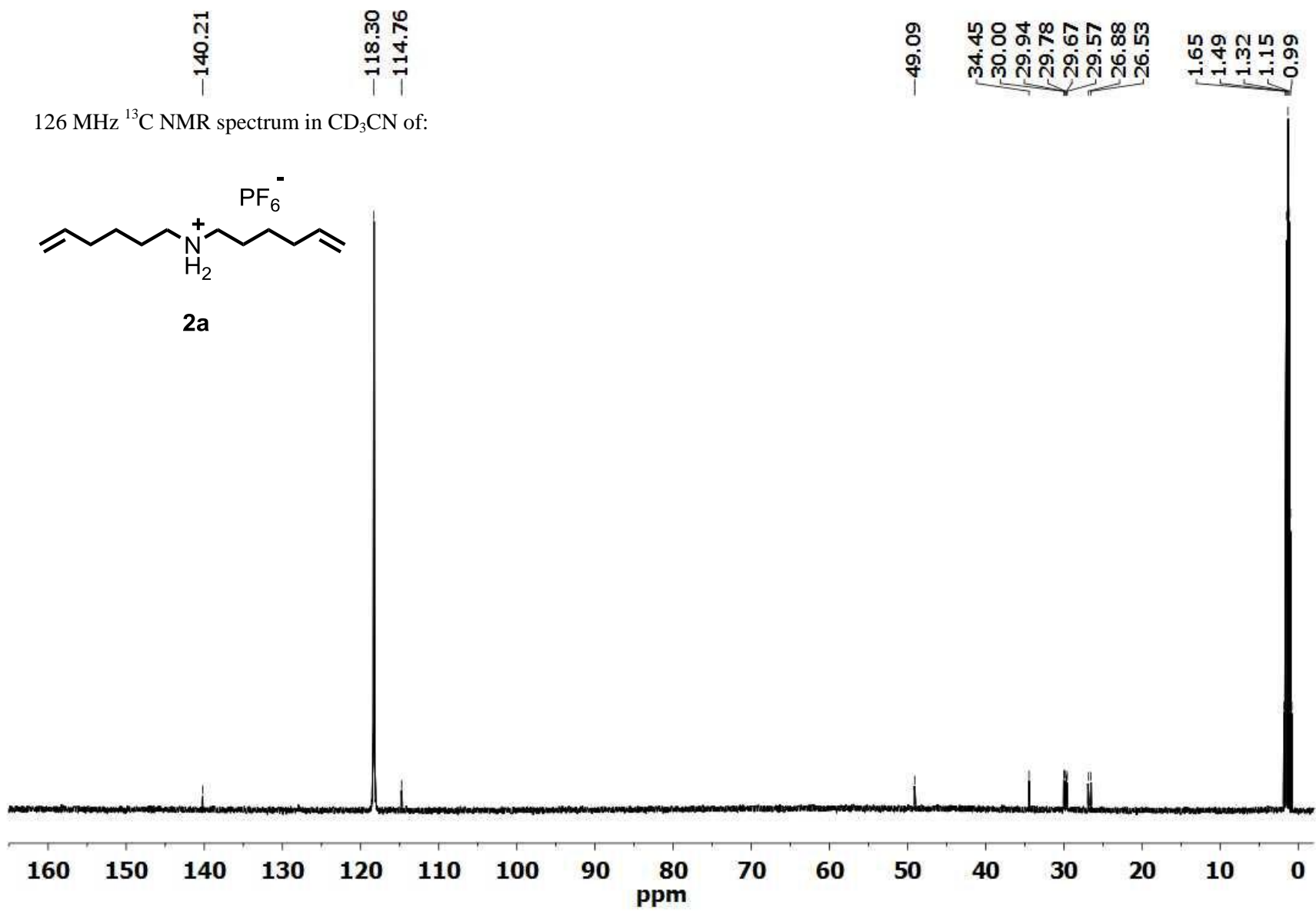
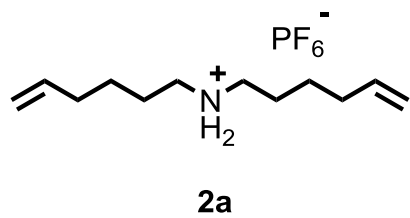
Excess Crown One-Pot Polyrotaxane 6b. The general one-pot polyrotaxane synthetic procedure was employed, using **2b** (28.5 mg, 0.061 mmol, 1 eq), **DB24C8** (136.8 mg, 0.305 mmol, 5 eq), cap **5** (5.4 mg, 0.024 mmol, 0.4 eq), and catalyst **4** (1.0 mg, 1.53 μmol, 2.5 mol%). The mixture was precipitated to afford polyrotaxane **6b** (27.2 mg, 50% yield) as an off-white solid. ¹H NMR (600 MHz, CD₃CN): δ = 6.93 (m, 8 H), 6.73 (br s, 1 H), 6.06 (s, 0.5 H), 5.39 (m, 2 H), 4.15 (br s, 6 H), 4.10 (m, 1.8 H), 3.85 (br s, 6 H), 3.79 (m, 1.8 H), 3.72 (s, 1.3 H), 3.68 (br

s, 7 H), 3.27 (m, 3.3 H), 2.93 (m, 0.7 H), 1.68-0.90 (br m, 30 H). GPC(0.2M LiBr in DMF): $M_n = 10.8$ kDa, $M_w = 14.9$ kDa, PDI = 1.37

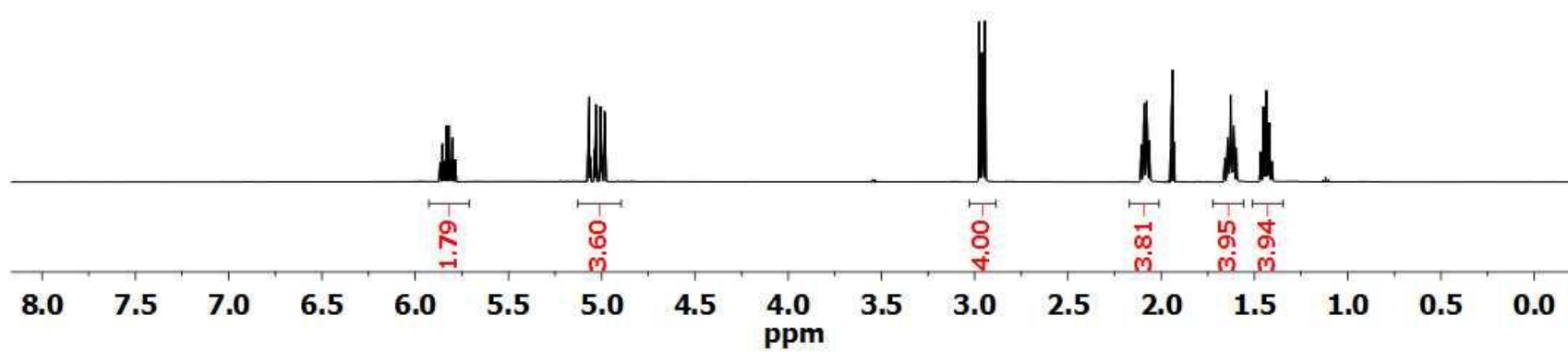
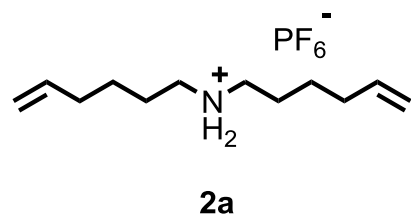
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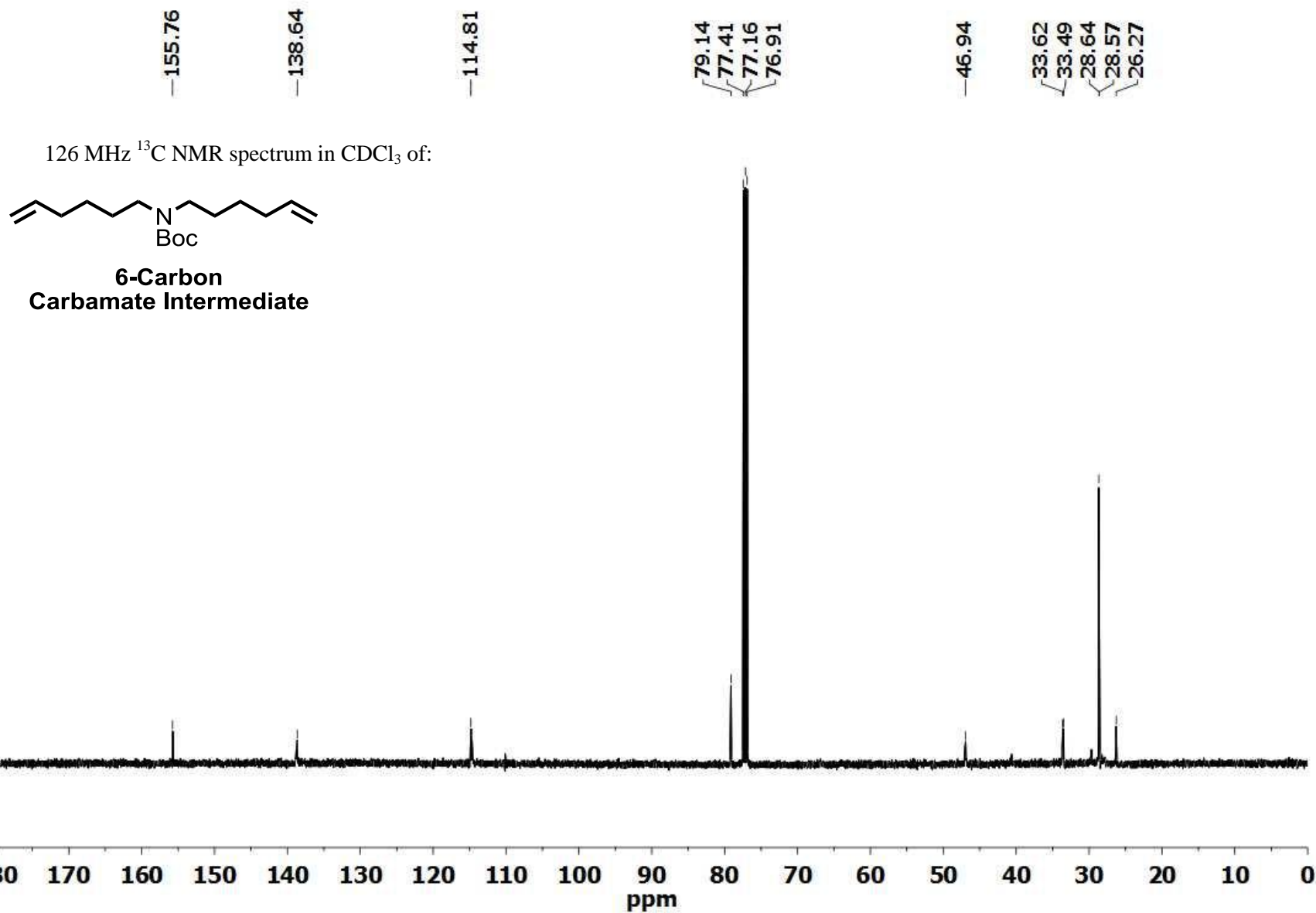


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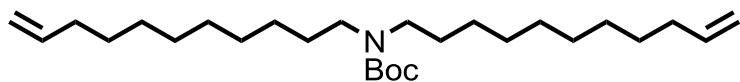


500 MHz ^1H NMR spectrum in CD_3CN of:

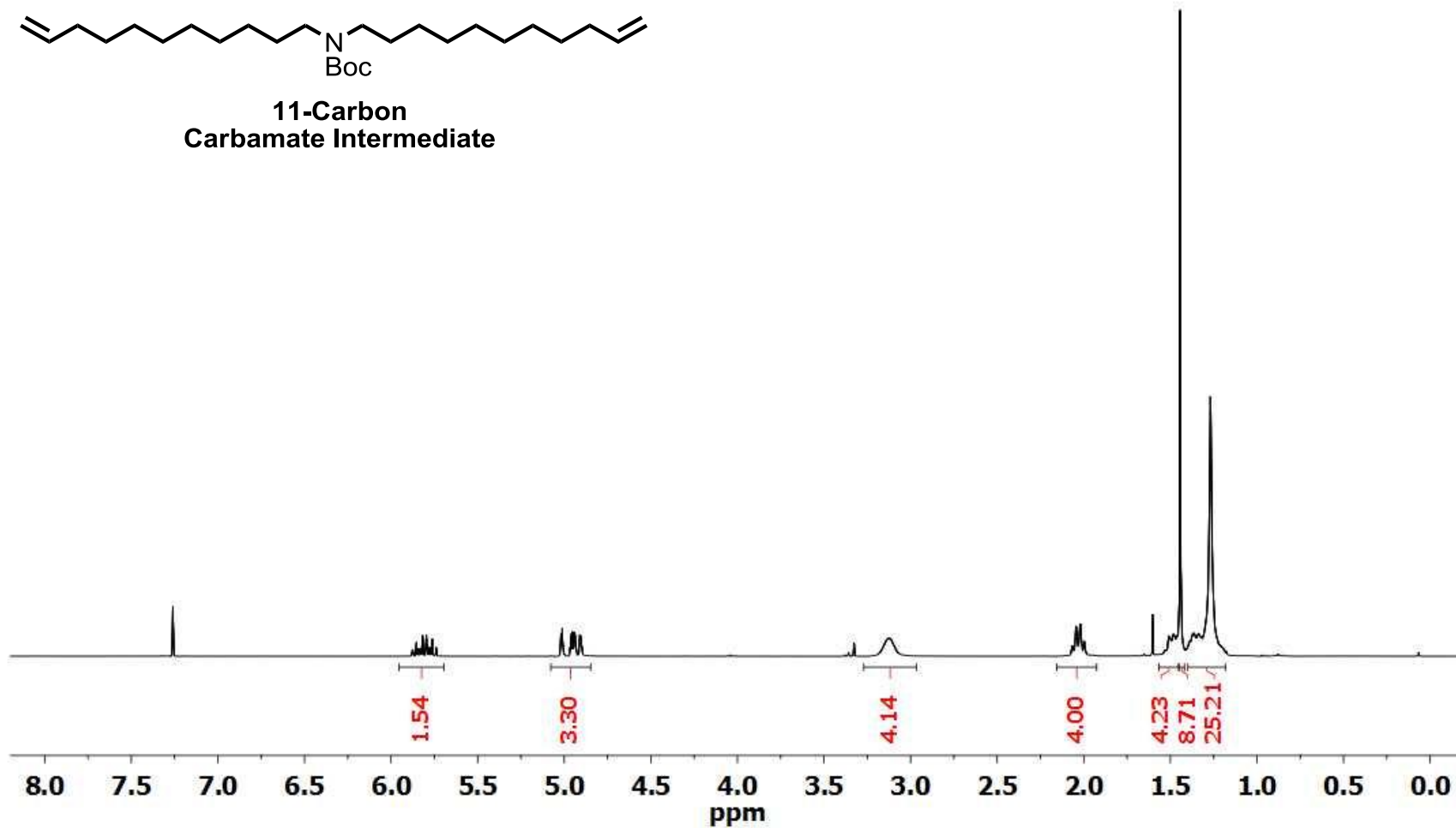


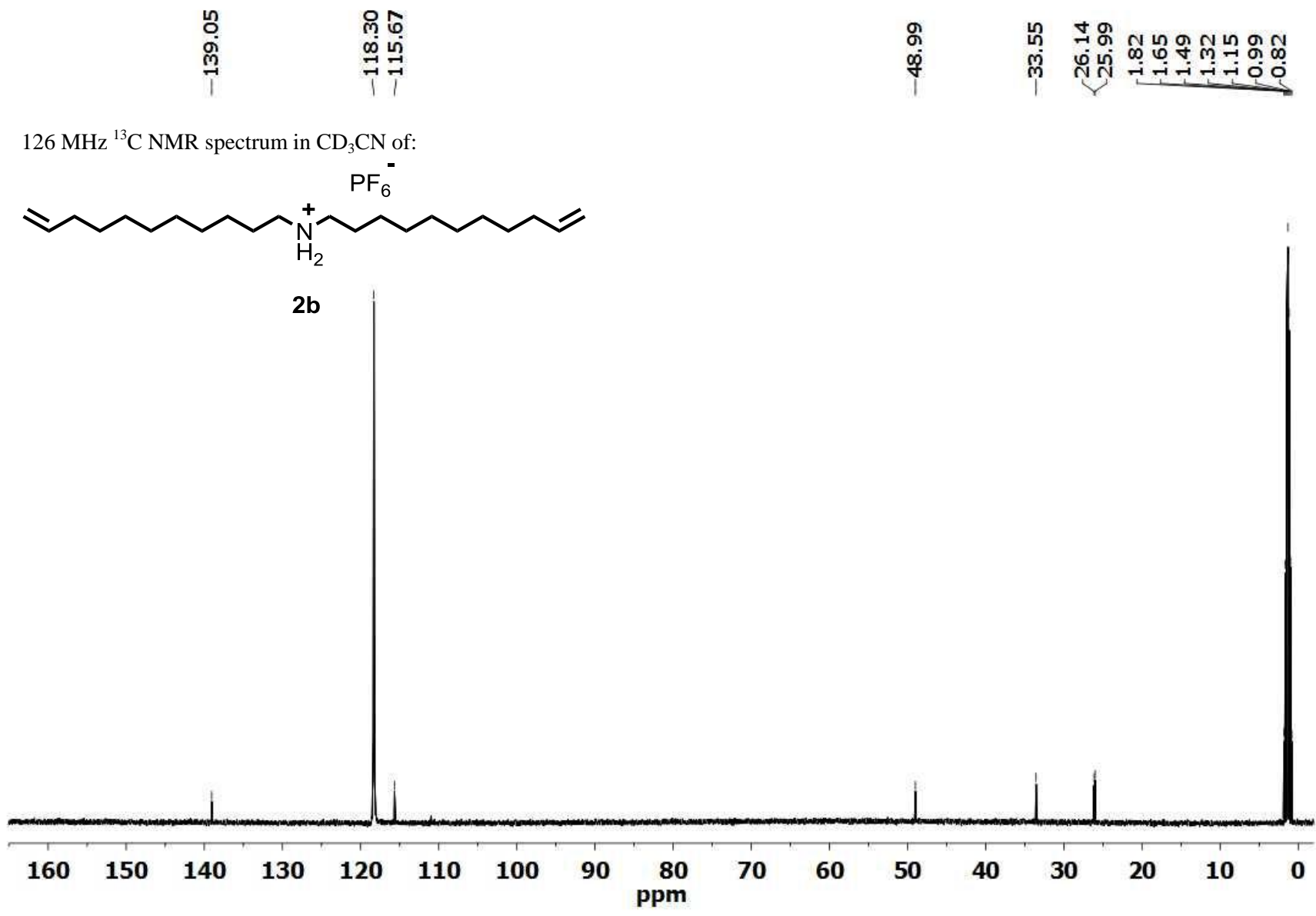


500 MHz ^1H NMR spectrum in CDCl_3 of:

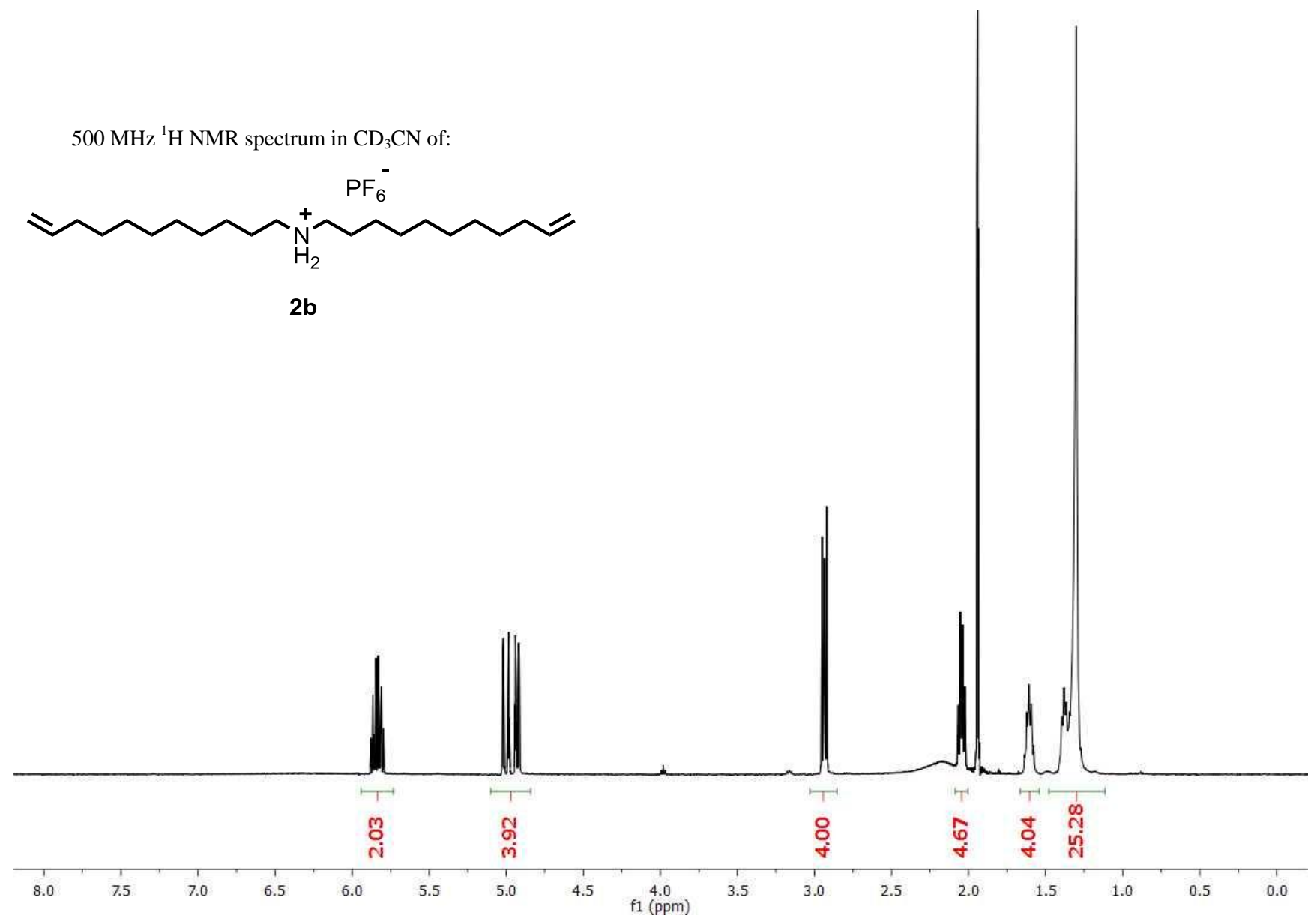
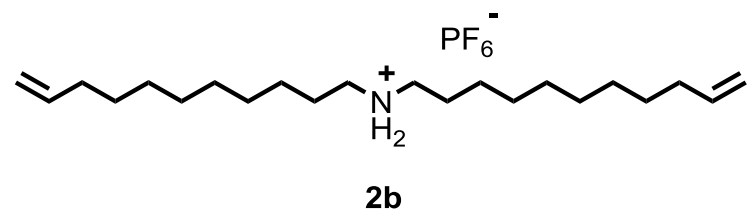


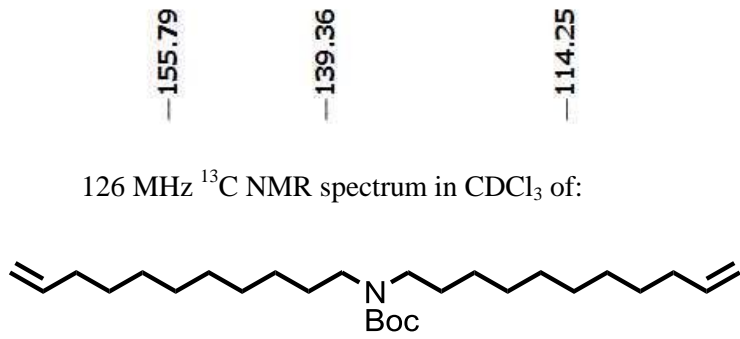
**11-Carbon
Carbamate Intermediate**





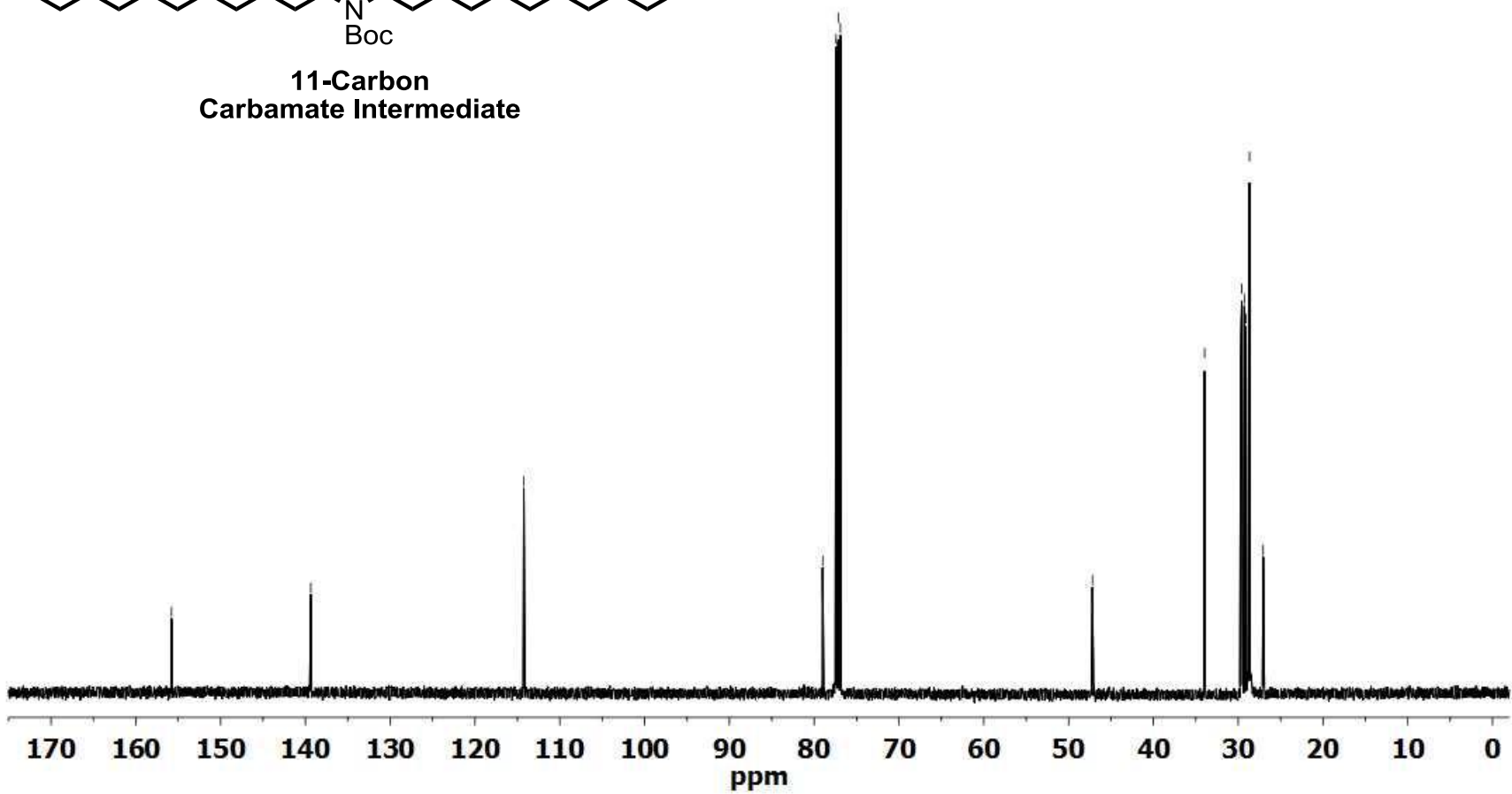
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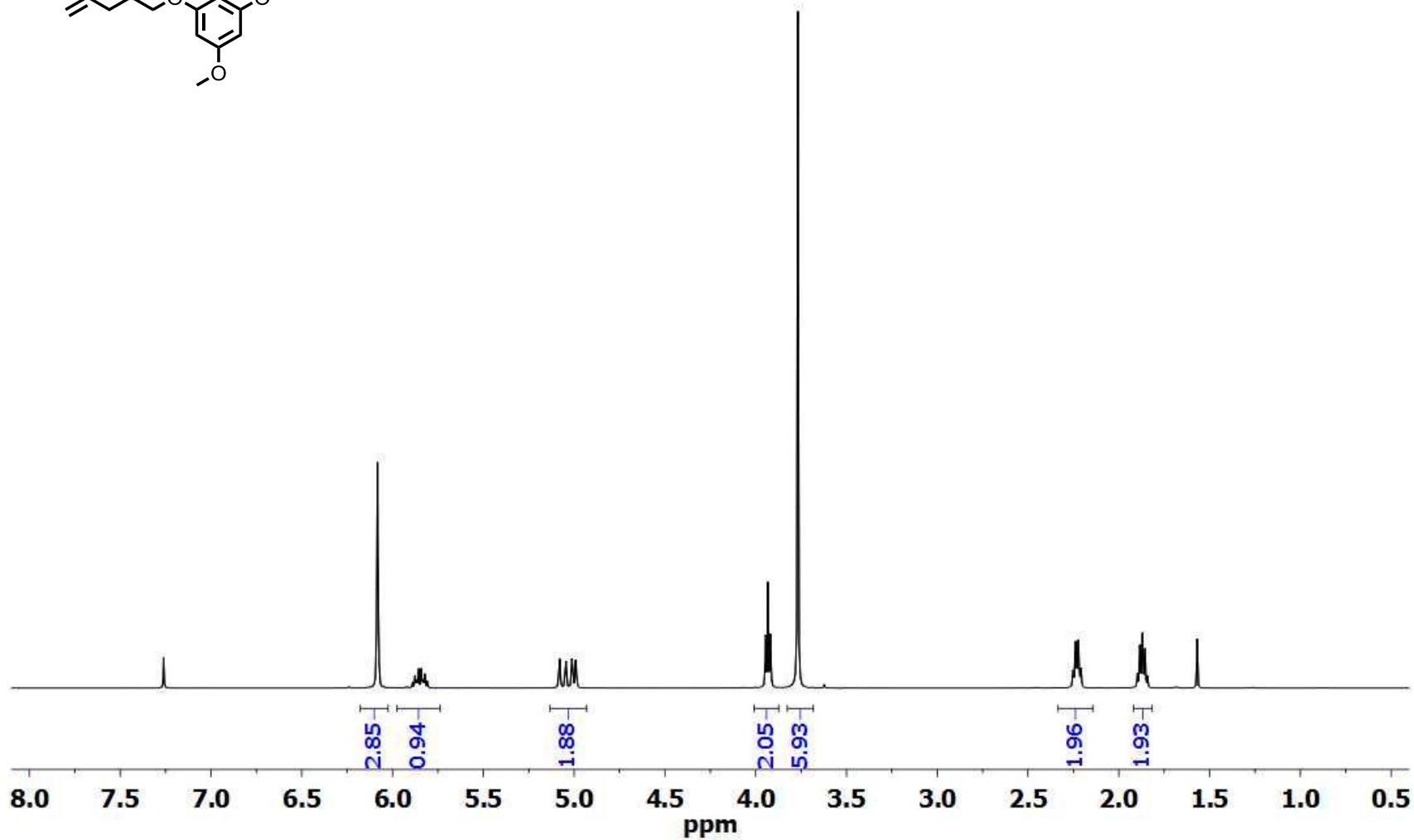
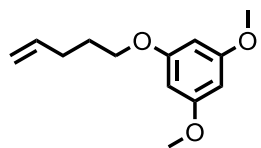


126 MHz ^{13}C NMR spectrum in CDCl_3 of:

**11-Carbon
Carbamate Intermediate**



500 MHz ^1H NMR spectrum in CDCl_3 of:



161.63
161.10

137.92

115.34

93.56
93.03

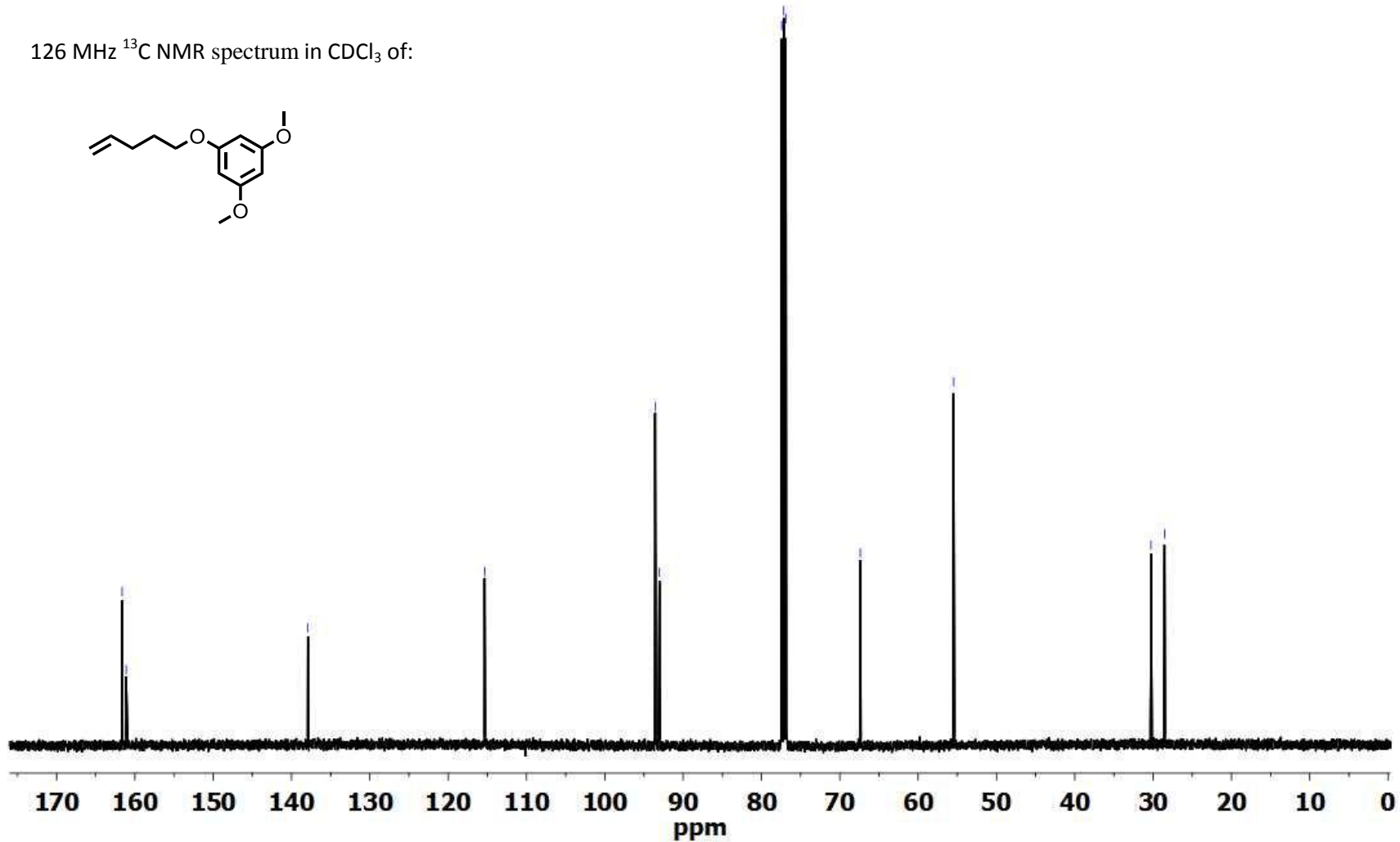
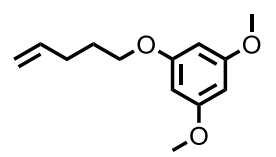
77.41
77.16
76.91

67.37

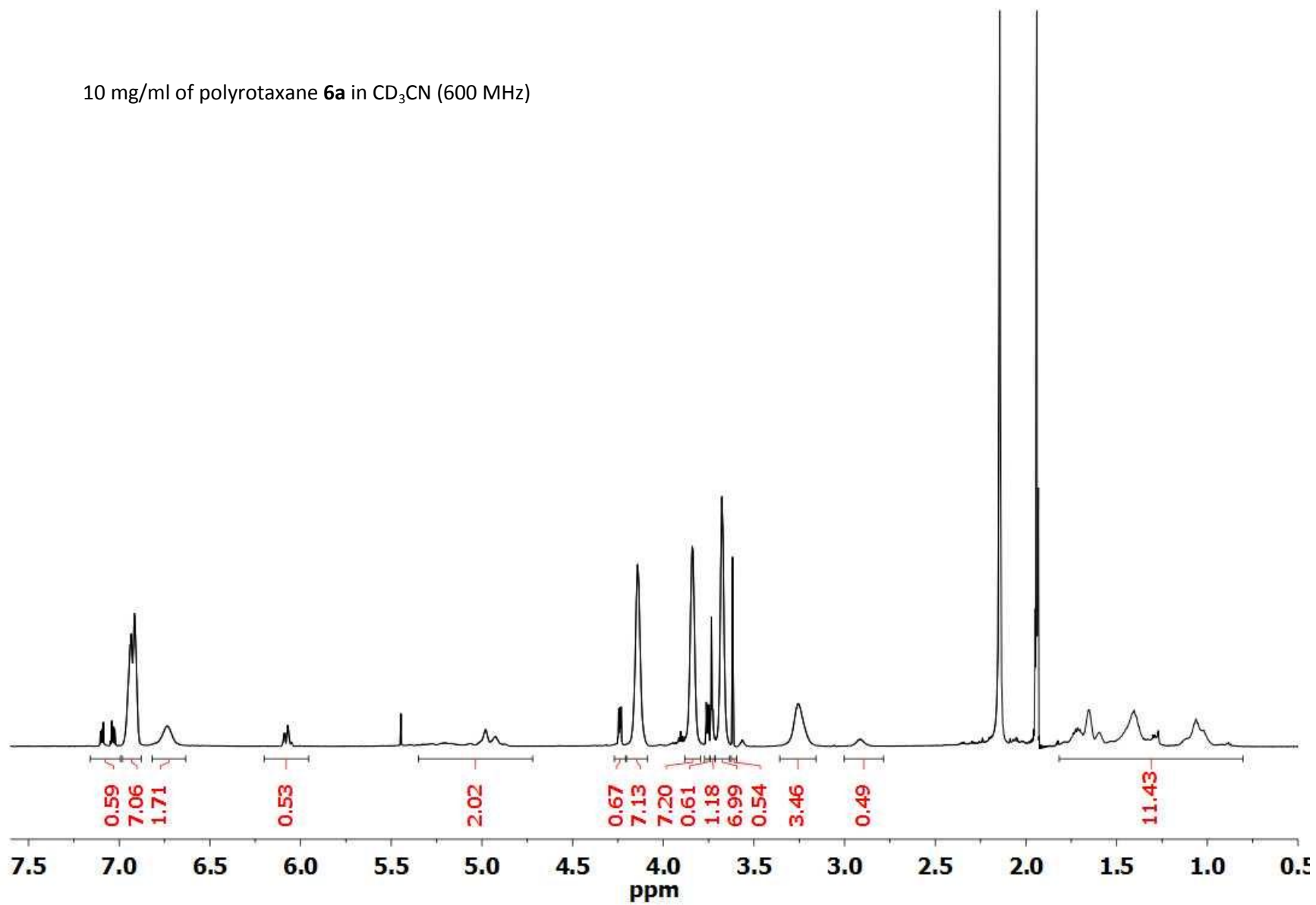
55.47

30.27
28.53

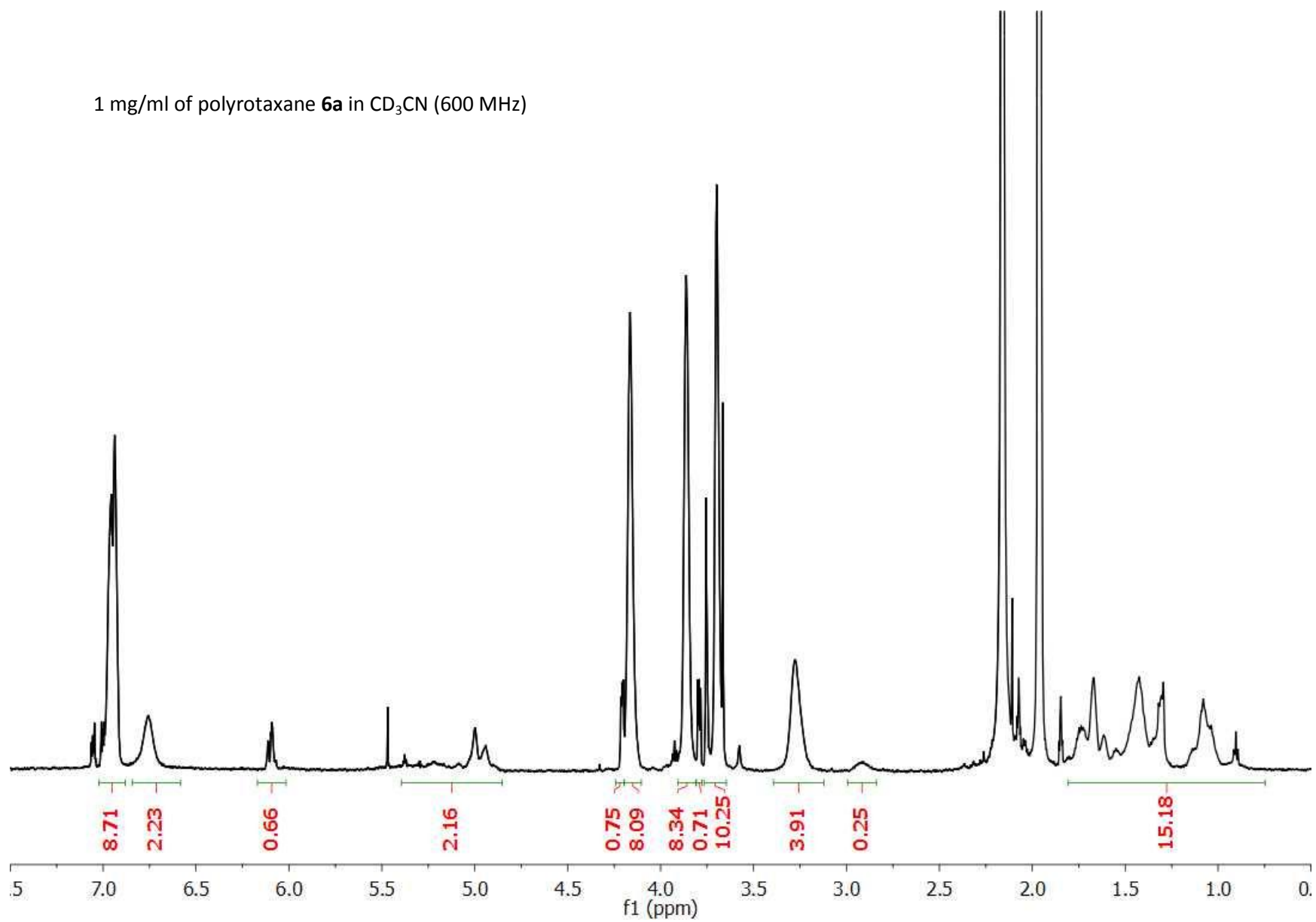
126 MHz ¹³C NMR spectrum in CDCl₃ of:



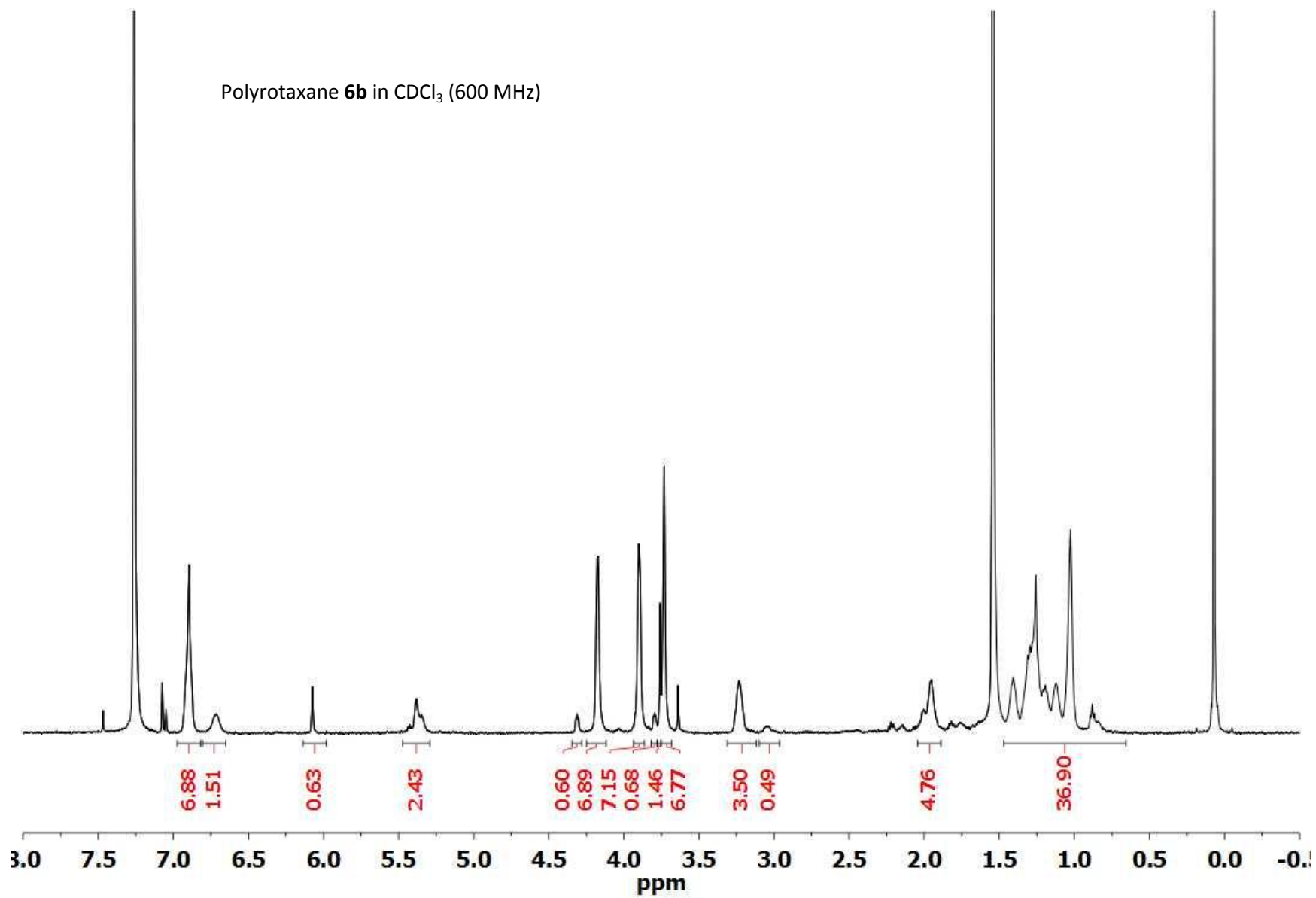
10 mg/ml of polyrotaxane **6a** in CD₃CN (600 MHz)



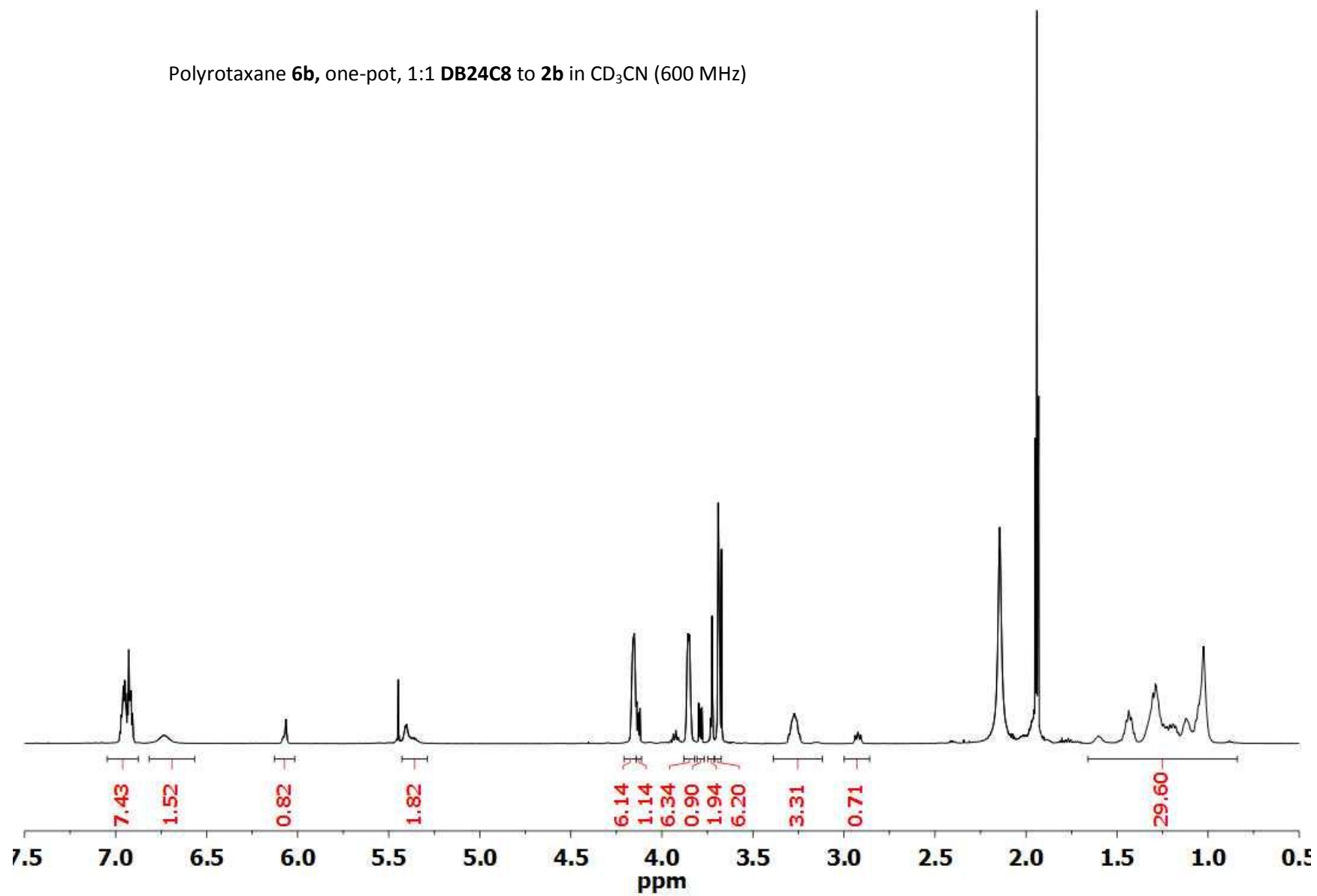
1 mg/ml of polyrotaxane **6a** in CD₃CN (600 MHz)



Polyrotaxane **6b** in CDCl₃ (600 MHz)



Polyrotaxane **6b**, one-pot, 1:1 **DB24C8** to **2b** in CD₃CN (600 MHz)



Polyrotaxane **6b**, one-pot, 5:1 crown to **3b**
in CD₃CN (600 MHz)

