

Supporting Information

**Highly Enantiospecific Platinum-Catalyzed Cycloisomerizations: Synthesis of
Enantioenriched Oxabicycloheptene Derivatives**

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Additional References

Supplemental references related to footnote 5:

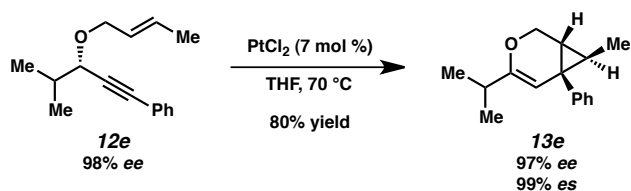
- (a) Brissy, D.; Skander, M.; Retailleau, P.; Marinetti, A. *Organometallics* **2007**, 26, 5782-5785. (b) Brissy, D.; Skander, M.; Retailleau, P.; Frison, G.; Marinetti, A. *Organometallics* **2009**, 28, 140-151. (c) Deschamps, N. M.; Elitzin, V. I.; Liu, B.; Mitchell, M. B.; Sharp, M. J.; Tabet, E. A. *J. Org. Chem.* **2011**, 76, 712-715. (d) Jullien, H.; Brissy, D.; Sylvain, R.; Retailleau, P.; Naubron, J.-V.; Gladiali, S.; Marinetti, A. *Adv. Synth. Catal.* **2011**, 353, 1109-1124. (e) Teller, H.; Fürstner, A. *Chem. Eur. J.* **2011**, 17, 7764-7767. (f) Pradal, A.; Chao, C.-M.; Toullec, P. Y.; Michelet, V. *Beilstein J. Org. Chem.* **2011**, 7, 1021-1029.

Materials and Methods: Reactions were performed under an argon atmosphere unless otherwise noted. Tetrahydrofuran, ether, dichloromethane and toluene were purified by passing through activated alumina columns. All other reagents were used as received unless otherwise noted. Commercially available chemicals were purchased from Alfa Aesar (Ward Hill, MA), Sigma-Aldrich (St. Louis, MO), Oakwood Products, (West Columbia, SC), Strem (Newburyport, MA) and TCI America (Portland, OR). Qualitative TLC analysis was performed on 250 mm thick, 60 Å, glass backed, F254 silica (Silicycle, Quebec City, Canada). Visualization was accomplished with UV light and exposure to *p*-anisaldehyde or KMnO₄ solutions followed by heating. Flash chromatography was performed using Silicycle silica gel (230-400 mesh). ¹H NMR spectra were acquired on either a Varian Mercury 300 (at 300 MHz), or a Varian 400 MR (at 400 MHz) and are reported relative to SiMe₄ (δ 0.00). ¹³C NMR spectra were acquired on a Varian 400 MR (at 100 MHz) and are reported relative to SiMe₄ (δ 0.0). All IR spectra were obtained on NaCl plates (film) with a Bruker Tensor 27. All gas chromatography was performed on a Varian CP-3800 gas chromatograph. All optical rotations were obtained on a Rudolph Research Analytical Autopol III Polarimeter. High resolution mass spectrometry data were acquired by the Colorado State University Central Instrument Facility on an Agilent 6210 TOF LC/MS.

Enyne Cycloisomerizations

General procedure for the platinum catalyzed cycloisomerization of oxygen-tethered 1,6-enynes. To a solution of enyne in THF (0.030 M) under argon was added PtCl_2 (7 mol %). The resulting mixture was sealed and stirred at 70 °C. Upon completion, as determined by TLC, the reaction mixture was allowed to cool to ambient temperature. The mixture was then diluted with hexanes and passed through a small plug of alumina. The solvent was concentrated in vacuo and the crude residue was purified by flash chromatography.

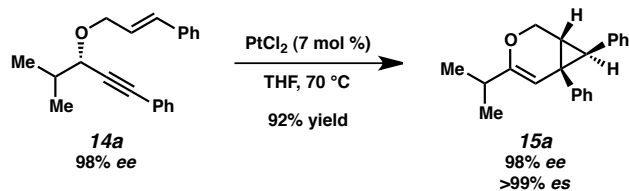
General Notes: Without the addition of triethylamine to the flash chromatography eluent, decreased yields were observed. For ethereal enynes bearing a crotyl substituent (e.g., **12e**), the (*E*)-crotyl bromide that was used as the starting material precursor featured a small amount (~5%) of the corresponding (*Z*)-isomer. This isomer was carried through the enyne synthesis in forming the ether products, as well as the cycloisomerizations to form the bicycles. These isomers were generally inseparable from the major compound, and therefore small amounts are observed in the NMR spectra.



Bicycle 13e. To a solution of enyne **12e** (25.0 mg, 0.109 mmol) in THF (3.63 mL, 0.030 M) under argon was added PtCl_2 (2.0 mg, 0.00763 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 40 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N → 98.5:1:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **13e** (19.9 mg, 80% yield, R_F = 0.63 in 9:1 Hexanes/ Et_2O) as a yellow oil.

Bicycle 13e: ^1H NMR (400 MHz, C_6D_6) δ 7.20-7.18 (m, 4H), 7.10 (dt, J = 8.6, 4.3 Hz, 1H), 5.19 (s, 1H), 4.17 (dd, J = 10.3, 1.4 Hz, 1H), 3.72 (dd, J = 10.4, 2.0 Hz, 1H), 2.27-2.19 (m, 1H), 1.49-1.43 (m, 1H), 1.26-1.20 (m, 1H), 1.07 (d, J = 3.3 Hz, 3H), 1.05 (d, J = 3.3 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.3, 142.5, 129.8, 128.7, 126.5, 104.4, 62.9, 33.0, 30.1, 27.3, 26.1, 20.5, 20.4, 15.0; IR (film) 2972, 2874, 1716, 1493 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{16}\text{H}_{20}\text{O} + \text{H}$] $^+$: 229.1587, found 229.1582; $[\alpha]_D^{31}$ = +18.27 (c = 0.5, CH_2Cl_2).

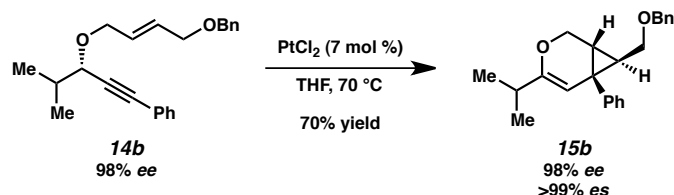
The *ee* was determined to be 97% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1 mL/min, λ = 230 nm, major isomer 5.01 min, minor isomer 5.36 min).



Bicycle 15a. To a solution of enyne **14a** (35.1 mg, 0.121 mmol) in THF (4.03 mL, 0.030 M) under argon was added PtCl_2 (2.3 mg, 0.00847 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 20 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 97.5:2:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **15a** (32.2 mg, 92% yield, R_F = 0.37 in 9:1 hexanes/ Et_2O) as a white solid.

Bicycle 15a: ^1H NMR (400 MHz, C_6D_6) δ 7.07-6.84 (m, 8H), 6.70-6.67 (m, 2H), 5.24 (s, 1H), 4.23 (dd, J = 10.4, 1.3 Hz, 1H), 3.84-3.81 (m, 1H), 2.82 (d, J = 5.8 Hz, 1H), 2.31-2.22 (m, 1H), 2.06 (dt, J = 5.8, 0.9 Hz, 1H), 1.09 (d, J = 6.9 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.0, 141.1, 138.5, 130.4, 128.5, 127.9, 126.6, 125.8, 104.3, 62.6, 36.9, 33.0, 32.4, 29.7, 20.4, 20.2; IR (film) 2975, 1720, 1601, 1496 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{21}\text{H}_{22}\text{O} + \text{H}]^+$: 291.1743, found 291.1742; $[\alpha]_D^{32}$ = +5.32 (c = 1.0, CH_2Cl_2).

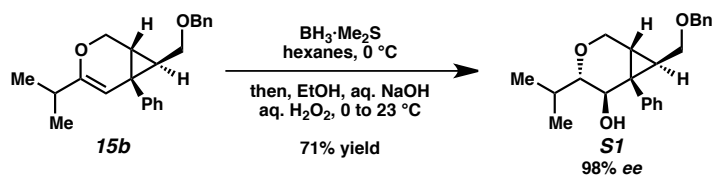
The *ee* was determined to be 98% by HPLC analysis (Chiralpak IC, hexane, 1.0 mL/min, λ = 210 nm, major isomer 8.82 min, minor isomer 8.47 min).



Bicycle 15b. To a solution of enyne **14b** (68.0 mg, 0.203 mmol) in THF (6.78 mL, 0.030 M) under argon was added PtCl_2 (3.8 mg, 0.0142 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 27 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 3 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (97.5:2:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **15b** (47.8 mg, 70% yield, R_F = 0.47 in 9:1 hexanes/ Et_2O) as a colorless oil.

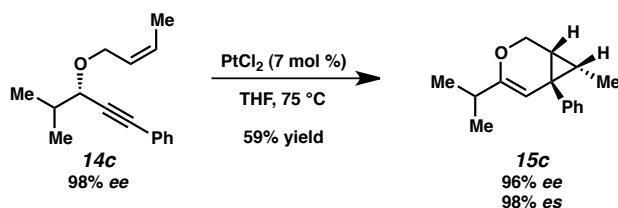
Bicycle 15b: ^1H NMR (400 MHz, C_6D_6) δ 7.25-7.23 (m, 2H), 7.12-6.97 (m, 8H), 5.09 (s, 1H), 4.06 (dd, J = 10.4, 1.4 Hz, 1H), 4.03 (q, J = 9.6 Hz, 2H), 3.64 (dd, J = 10.4, 2.0 Hz, 1H), 3.01-2.90 (m, 2H), 2.12 (dtd, J = 13.7, 6.8, 0.6 Hz, 1H), 1.88 (dt, J = 7.8, 5.8 Hz, 1H), 1.35 (dd, J = 5.1, 2.3 Hz, 1H), 0.95 (d, J = 4.0 Hz, 3H), 0.93 (d, J = 3.9 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.6, 142.1, 139.3, 129.9, 128.7, 128.5, 127.7, 127.5, 126.8, 103.9, 72.9, 70.5, 62.7, 32.9, 31.2, 27.4, 26.9, 20.4, 20.3; IR (film) 2963, 2866, 1664, 1361 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{23}\text{H}_{26}\text{O}_2 + \text{H}]^+$: 335.2011, found 335.2008; $[\alpha]_D^{33}$ = +64.26 (c = 1.0, CH_2Cl_2).

The *ee* was determined to be 98% by hydroboration/oxidation and HPLC analysis:



To a solution of bicyclic **15b** (10.0 mg, 0.030 mmol) in hexanes (300 μL) at 0 °C was added $\text{BH}_3 \cdot \text{Me}_2\text{S}$ (5.6 μL , 2.0 M in hexanes, 0.0105 mmol) dropwise. The resulting solution was stirred at ambient temperature for 3 h, cooled to 0 °C, and EtOH (38 μL) was added, followed by aq. NaOH (12 μL , 3 M), and aq. H_2O_2 (190 μL , 35%). The resulting mixture was allowed to warm to ambient temperature and stirred overnight. The mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with sat. aq. NaHCO_3 (1 x 5 mL), then brine (1 x 5 mL), and then dried over MgSO_4 . The solvent was removed in vacuo and the resulting residue was purified by flash chromatography (9:1 \rightarrow 4:1 hexanes/ Et_2O eluent) affording alcohol **S1** (7.5 mg, 71% yield, R_F = 0.30 in 4:1 hexanes/ Et_2O) as a colorless oil.

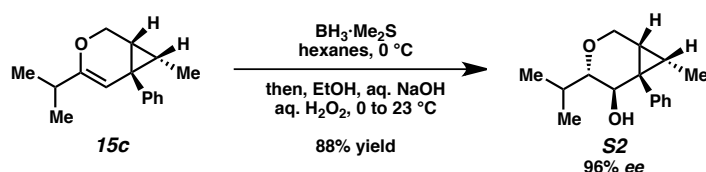
The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel IA, 3% 2-propanol in hexane, 1 mL/min, λ = 210 nm, major isomer 7.96 min, minor isomer 9.08 min).



Bicycle 15c. To a solution of enyne **14c** (44.1 mg, 0.193 mmol) in THF (6.44 mL, 0.030 M) under argon was added PtCl_2 (3.6 mg, 0.0135 mmol). The resulting mixture was sealed, heated to 75 °C and stirred at that temperature for 36 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (90:8:2:1 hexanes/ CH_2Cl_2 / Et_2O / Et_3N \rightarrow 40:8:2:1 hexanes/ CH_2Cl_2 / Et_2O / Et_3N eluent) affording bicyclic **15c** (25.9 mg, 59% yield, R_F = 0.71 in 15:4:1 hexanes/ CH_2Cl_2 / Et_2O) as a yellow oil.

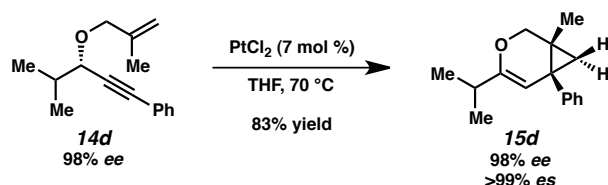
Bicycle 15c: ^1H NMR (400 MHz, C_6D_6) δ 7.29-7.26 (m, 2H), 7.21-7.18 (m, 2H), 7.12-7.07 (m, 1H), 4.93 (s, 1H), 3.99-3.97 (m, 2H), 2.32-2.25 (m, 1H), 1.49-1.41 (m, 1H), 1.19 (dddd, J = 8.7, 3.4, 2.3, 1.0 Hz, 1H), 1.16 (d, J = 6.4 Hz, 3H), 1.10 (d, J = 4.4 Hz, 3H), 1.09 (d, J = 4.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.6, 146.9, 128.7, 128.2, 127.9, 127.6, 126.1, 95.3, 61.9, 22.4, 26.5, 26.2, 24.7, 20.8, 8.7; IR (film) 2963, 2871, 1668, 1492 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{16}\text{H}_{20}\text{O} + \text{H}]^+$: 229.1592, found 229.1587; $[\alpha]_D^{30}$ = +2.13 (c = 0.5, CH_2Cl_2).

The *ee* was determined to be 96% by hydroboration/oxidation and HPLC analysis:



To a solution of bicyclic **15c** (5.3 mg, 0.0232 mmol) in hexane (350 μL) at $0\text{ }^\circ\text{C}$ was added $\text{BH}_3 \cdot \text{Me}_2\text{S}$ (3.8 μL , 2.0 M in hexanes, 0.00690 mmol) dropwise. The resulting solution was stirred at ambient temperature for 3 h, cooled to $0\text{ }^\circ\text{C}$, and EtOH (40 μL) was added, followed by aq. NaOH (12 μL , 3 M), and aq. H_2O_2 (190 μL , 30%). The resulting mixture was allowed to warm to ambient temperature and stirred for 20 h. The mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with sat. aq. NaHCO_3 (1 x 5 mL), then brine (1 x 5 mL), and then dried over MgSO_4 . The solvent was removed in vacuo and the resulting residue was purified by flash chromatography (9:1 hexanes/ Et_2O eluent) affording alcohol **S2** (5.0 mg, 88% yield, $R_F = 0.30$ in 9:1 hexanes/ Et_2O) as a colorless solid.

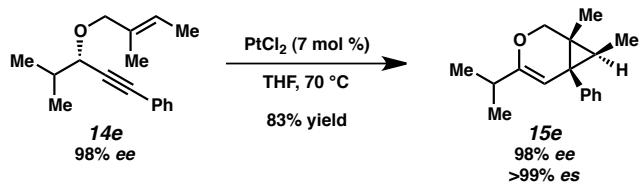
The ee was determined to be 96% by HPLC analysis (Daicel Chiralcel IC, 0.5% 2-propanol in hexane, 1.2 mL/min, $\lambda = 230\text{ nm}$, major isomer 4.76 min, minor isomer 5.14 min).



Bicycle 15d. To a solution of enyne **14d** (29.9 mg, 0.131 mmol) in THF (4.38 mL, 0.030 M) under argon was added PtCl_2 (2.4 mg, 0.00917 mmol). The resulting mixture was sealed, heated to $70\text{ }^\circ\text{C}$ and stirred at that temperature for 26 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ $\text{Et}_3\text{N} \rightarrow 97.5:2:0.5$ hexanes/ Et_2O / Et_3N eluent) affording bicycle **15d** (25.0 mg, 83% yield, $R_F = 0.42$ in 9:1 hexanes/ Et_2O) as a colorless oil.

Bicycle 15d: ^1H NMR (400 MHz, C_6D_6) δ 7.24-7.18 (m, 4H), 7.11-7.07 (m, 1H), 5.10 (s, 1H), 4.00 (d, $J = 10.3\text{ Hz}$, 1H), 3.45 (d, $J = 10.3\text{ Hz}$, 1H), 2.29-2.22 (m, 1H), 1.42 (d, $J = 4.4\text{ Hz}$, 1H), 1.15 (d, $J = 4.3\text{ Hz}$, 1H), 1.07 (d, $J = 6.9\text{ Hz}$, 3H), 1.05 (d, $J = 6.9\text{ Hz}$, 3H), 0.60 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.6, 143.0, 129.5, 128.4, 126.4, 103.7, 68.2, 32.7, 20.3, 28.0, 22.2, 20.6, 20.4, 16.6; IR (film) 2964, 2870, 1666, 1446 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{16}\text{H}_{20}\text{O} + \text{H}]^+$: 229.1592, found 229.1587; $[\alpha]_D^{32} = +55.32$ ($c = 0.1$, CH_2Cl_2).

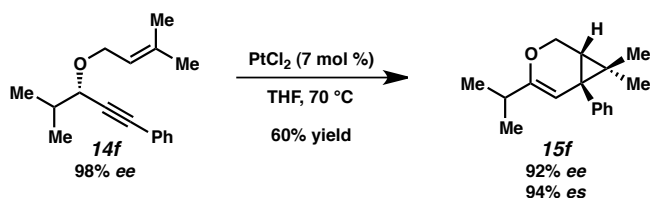
The ee was determined to be 98% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1.0 mL/min, $\lambda = 210\text{ nm}$, major isomer 4.51 min, minor isomer 4.20 min).



Bicycle 15e. To a solution of enyne **14e** (30.1 mg, 0.124 mmol) in THF (4.13 mL, 0.030 M) under argon was added PtCl_2 (2.3 mg, 0.00868 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 24 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 97.5:2:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **15e** (24.9 mg, 83% yield, R_F = 0.86 in 9:1 hexanes/ Et_2O) as a colorless oil.

Bicycle 15e: ^1H NMR (400 MHz, C_6D_6) δ 7.23-7.17 (m, 4H), 7.13-7.08 (m, 1H), 5.01 (s, 1H), 4.00 (d, J = 10.2 Hz, 1H), 3.56 (d, J = 10.1 Hz, 1H), 2.23 (dt, J = 13.4, 6.7 Hz, 1H), 1.69 (q, J = 6.6 Hz, 1H), 1.05 (d, J = 3.4 Hz, 3H), 1.04 (d, J = 3.4 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.1, 141.4, 131.4, 128.7, 126.5, 106.2, 69.0, 32.6, 31.2, 29.8, 26.3, 20.5, 20.4, 12.5, 11.6; IR (film) 2963, 2871, 1663, 1469, 1384 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{17}\text{H}_{22}\text{O} + \text{H}]^+$: 243.1743, found 243.1746; $[\alpha]_D^{32}$ = +351.49 (c = 0.25, CH_2Cl_2).

The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1.0 mL/min, λ = 230 nm, major isomer 4.30 min, minor isomer 3.96 min).

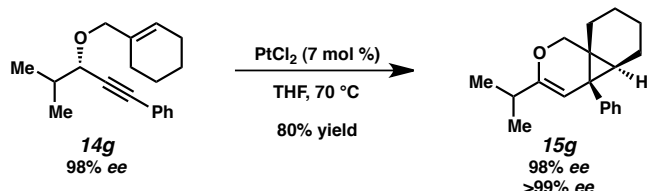


Bicycle 15f. To a solution of enyne **14f** (30.1 mg, 0.124 mmol) in THF (4.13 mL, 0.030 M) under argon was added PtCl_2 (2.3 mg, 0.00868 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 48 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 97.5:2:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **15f** (18.1 mg, 60% yield, R_F = 0.37 in 9:1 hexanes/ Et_2O) as a yellow oil.

Bicycle 15f: ^1H NMR (400 MHz, C_6D_6) δ 7.21-7.17 (m, 4H), 7.11-7.07 (m, 1H), 4.90 (s, 1H), 4.12 (dd, J = 11.3, 1.5 Hz, 1H), 4.05 (dd, J = 11.3, 4.1 Hz, 1H), 2.24 (dq, J = 13.7, 6.8 Hz, 1H), 1.26 (s, 3H), 1.13 (d, J = 4.2 Hz, 1H), 1.07 (d, J = 4.4 Hz, 3H), 1.05 (d, J = 4.4 Hz, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 156.0, 144.5, 129.3, 128.7, 128.1, 127.9, 126.2, 98.8, 62.0, 33.3, 30.5, 29.4, 29.2, 25.3, 20.7, 20.6, 16.6; IR (film) 2966, 2870, 1666, 1492 cm^{-1} ;

HRMS (DART+) m/z calc'd for $(M + H)^+ [C_{17}H_{22}O + H]^+$: 243.1743, found 243.1752; $[\alpha]_D^{30} = +208.09$ ($c = 0.5$, CH_2Cl_2).

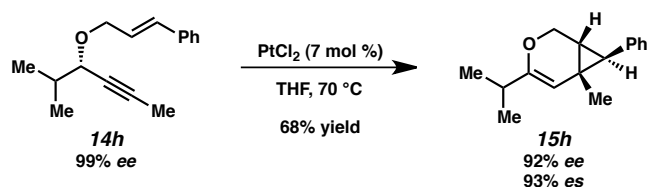
The *ee* was determined to be 92% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1.0 mL/min, $\lambda = 230$ nm, major isomer 4.31 min, minor isomer 4.68 min).



Bicycle 15g. To a solution of enyne **14g** (31.7 mg, 0.188 mmol) in THF (3.93 mL, 0.030 M) under argon was added $PtCl_2$ (2.1 mg, 0.00782 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 26 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a short plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ $Et_3N \rightarrow 97.5:2:0.5$ hexanes/ Et_2O / Et_3N eluent) affording bicycle **15g** (24.0 mg, 80% yield, $R_F = 0.33$ in 9:1 hexanes/ Et_2O) as a colorless oil.

Bicycle 15g: NMR (400 MHz, C_6D_6) δ 7.24-7.18 (m, 4H), 7.11-7.07 (m, 1H), 4.99 (s, 1H), 4.00 (d, $J = 10.2$ Hz, 1H), 3.64 (d, $J = 10.2$ Hz, 1H), 2.22 (dt, $J = 13.6, 6.8$ Hz, 1H), 1.76 (t, $J = 4.9$ Hz, 1H), 1.64 (ddd, $J = 14.2, 7.8, 5.0$ Hz, 1H), 1.27 (ddd, $J = 14.0, 7.6, 6.1$ Hz, 1H), 1.06 (d, $J = 1.9$ Hz, 3H), 1.04 (d, $J = 1.9$ Hz, 3H), 0.97-0.85 (m, 2H), 0.75-0.58 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.7, 142.3, 131.1, 128.8, 128.2, 127.9, 126.4, 106.6, 68.5, 32.63, 32.61, 30.5, 30.0, 29.0, 26.9, 23.1, 21.9, 21.6, 21.3, 20.5, 20.4; IR (film) 2936, 2869, 1664, 1602, 1447 cm^{-1} ; HRMS (DART+) m/z calc'd for $(M + H)^+ [C_{19}H_{24}O + H]^+$: 269.1900, found 269.1900; $[\alpha]_D^{32} = +113.62$ ($c = 1.0$, CH_2Cl_2).

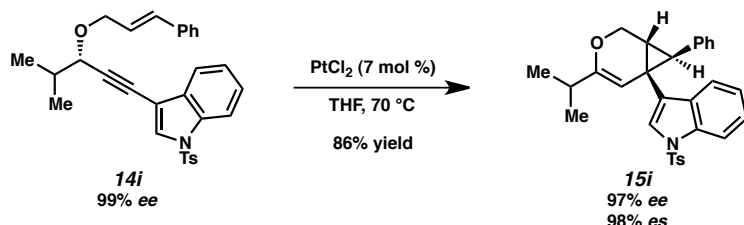
The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OJ-H, 100% hexane, 1.0 mL/min, $\lambda = 210$ nm, major isomer 4.78 min, minor isomer 12.69 min).



Bicycle 15h. To a solution of enyne **14h** (6.5 mg, 0.0285 mmol) in THF (967 μ L, 0.030 M) under argon was added $PtCl_2$ (0.5 mg, 0.00203 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 17 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (97.5:2:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **15h** (4.4 mg, 68% yield, $R_F = 0.42$ in 9:1 hexanes/ Et_2O) as a colorless oil.

Bicycle 15h: ^1H NMR (400 MHz, C_6D_6) δ 7.15-7.01 (comp. m, 5H), 4.99 (s, 1H), 4.09 (dd, J = 10.4, 0.8 Hz, 1H), 3.68 (ddd, J = 10.3, 2.2, 0.4 Hz, 1H), 2.51 (d, J = 5.7 Hz, 1H), 2.31-2.24 (m, 1H), 1.36 (d, J = 5.7 Hz, 1H), 1.11 (t, J = 6.9 Hz, 6H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.5, 138.9, 129.1, 126.1, 103.8, 62.8, 35.1, 33.0, 28.5, 20.6, 20.3, 20.2, 18.4; IR (film) 2974, 1715, 1602, 1498 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{16}\text{H}_{20}\text{O} + \text{H}$] $^+$: 229.1587, found 229.1600; $[\alpha]_{\text{D}}^{33} = -8.40$ (c = 0.076, CH_2Cl_2).

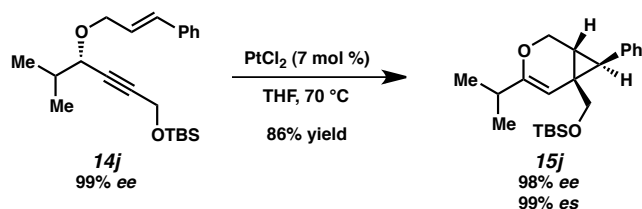
The *ee* was determined to be 92% by HPLC analysis (Daicel Chiralcel IC, 0.1% 2-propanol in hexane, 1 mL/min, λ = 254 nm, major isomer 4.43 min, minor isomer 4.23 min).



Bicycle 15i. To a solution of enyne **14i** (25.0 mg, 0.0517 mmol) in THF (1.73 mL, 0.030 M) under argon was added PtCl_2 (1.0 mg, 0.00364 mmol). The resulting mixture was sealed, heated to 70 $^\circ\text{C}$ and stirred at that temperature for 20 h. Once cooled to ambient temperature, the mixture was diluted with hexanes filtered through a small plug of alumina (0.5 x 2 cm, 1:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (4:1 hexanes/ Et_2O (0.5% Et_3N) eluent) affording bicycle **15i** (21.4 mg, 86% yield, R_{F} = 0.53 in 1:1 hexanes/ Et_2O) as a white semisolid.

Bicycle 15i: ^1H NMR (400 MHz, C_6D_6) δ 8.15-8.12 (m, 1H), 7.59-7.55 (m, 1H), 7.52-7.47 (m, 2H), 7.21-7.18 (s, 1H), 7.08-6.95 (comp. m, 3H), 6.84-6.76 (comp. m, 3H), 6.73-6.69 (m, 2H), 6.55-6.51 (m, 1H), 4.15 (dd, J = 10.6, 1.3 Hz, 1H), 3.80 (dd, J = 10.5, 2.1 Hz, 1H), 2.86 (d, J = 6.0 Hz, 1H), 2.25 (dt, J = 13.5, 6.7 Hz, 1H), 1.91 (d, J = 5.9 Hz, 1H), 1.72 (s, 3H), 1.08 (d, J = 6.9 Hz, 3H), 1.06 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.9, 144.2, 138.0, 136.3, 135.8, 131.6, 129.8, 128.4, 128.2, 128.1, 127.9, 127.0, 126.0, 125.6, 124.9, 123.2, 122.3, 120.8, 114.1, 102.6, 62.5, 36.2, 33.0, 28.8, 23.6, 21.1, 20.4, 20.2; IR (film) 2962, 1494, 1447, 1376 cm^{-1} ; LRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{30}\text{H}_{29}\text{NO}_3\text{S} + \text{H}$] $^+$: 484.2, found 484.2; $[\alpha]_{\text{D}}^{32} = +14.89$ (c = 0.5, CH_2Cl_2).

The *ee* was determined to be 97% by HPLC analysis (Daicel Chiralcel OD-H, 10% 2-propanol in hexane, 1 mL/min, λ = 254 nm, major isomer 5.74 min, minor isomer 7.09 min).

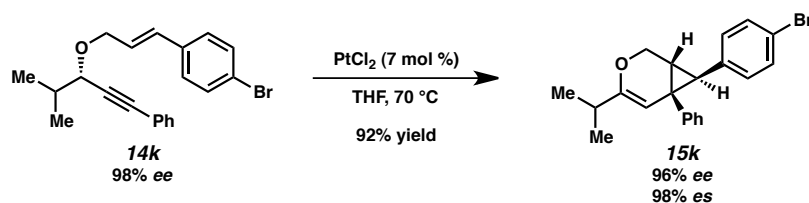


Bicycle 15j. To a solution of enyne **14j** (60.0 mg, 0.167 mmol) in THF (5.57 mL, 0.030 M) under argon was added PtCl_2 (3.2 mg, 0.0117 mmol). The resulting mixture was sealed, heated to

70 °C and stirred at that temperature for 29 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 3 cm, 9:1 hexanes/Et₂O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/Et₃N → 97.5:2:0.5 hexanes/Et₂O/Et₃N eluent) affording bicycle **15j** (51.6 mg, 86% yield, *R*_F = 0.50 in 9:1 hexanes/Et₂O) as a colorless oil.

Bicycle 15j: ¹H NMR (400 MHz, C₆D₆) δ 7.11 (d, *J* = 4.4 Hz, 4H), 7.06-7.02 (m, 1H), 5.51 (s, 1H), 4.12 (dd, *J* = 10.4, 1.2 Hz, 1H), 3.70 (dd, *J* = 10.4, 2.1 Hz, 1H), 3.54 (d, *J* = 10.4 Hz, 1H), 3.23 (d, *J* = 10.5 Hz, 1H), 2.67 (d, *J* = 5.8 Hz, 1H), 2.35-2.28 (m, 1H), 1.52 (dt, *J* = 5.8, 1.0 Hz, 1H), 1.13 (d, *J* = 5.5 Hz, 3H), 1.11 (d, *J* = 5.5 Hz, 3H), -0.09 (s, 3H), -0.16 (s, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 158.0, 138.1, 129.5, 128.3, 126.4, 100.5, 64.5, 62.7, 34.9, 33.1, 26.7, 26.1, 25.5, 20.5, 20.3, 18.5, 5.4; IR (film) 2956, 2858, 1729, 1471, 1255 cm⁻¹; HRMS (DART+) *m/z* calc'd for (M + H)⁺ [C₂₂H₃₄O₂Si + H]⁺: 359.2406, found 359.2403; [α]_D³¹ = -90.21 (*c* = 0.5, CH₂Cl₂).

The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel IC, 100% hexane, 1.5 mL/min, λ = 230 nm, major isomer 4.68 min, minor isomer 4.45 min).



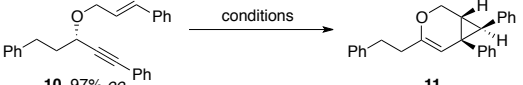
Bicycle 15k. To a solution of enyne **14k** (110 mg, 0.298 mmol) in THF (9.93 mL, 0.030 M) under argon was added PtCl₂ (5.4 mg, 0.0201 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 9 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 4.5 cm, 9:1 hexanes/Et₂O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/Et₃N → 97.5:2:0.5 hexanes/Et₂O/Et₃N eluent) affording bicycle **15k** (101 mg, 92% yield, *R*_F = 0.36 in 9:1 Hexanes/Et₂O) as a white solid.

Bicycle 15k: ¹H NMR (400 MHz, C₆D₆) δ 7.02-6.92 (m, 7H), 6.31-6.28 (m, 2H), 5.18 (s, 1H), 4.16 (dd, *J* = 10.5, 1.3 Hz, 1H), 3.77 (dd, *J* = 10.4, 1.9 Hz, 1H), 2.63 (d, *J* = 5.8 Hz, 1H), 2.30-2.20 (m, 1H), 1.88-1.85 (m, 1H), 1.07 (app. t, *J* = 7.1 Hz, 6H); ¹³C NMR (100 MHz, C₆D₆) δ 157.1, 140.5, 137.6, 131.0, 130.2, 129.6, 128.6, 126.8, 119.7, 104.0, 62.4, 36.1, 33.0, 32.5, 29.8, 20.4, 20.2; IR (film) 3032, 2905, 1620, 1530, 1095 cm⁻¹; HRMS (ESI+) *m/z* calc'd for (M + H)⁺ [C₂₁H₂₀BrO + H]⁺: 369.0849, found 369.0832; [α]_D³² = -15.75 (*c* = 1.0, CH₂Cl₂).

The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OJ-H, 0.5% 2-propanol in hexane, 1 mL/min, λ = 254 nm, major isomer 6.45 min, minor isomer 8.68 min).

Optimization Studies

Catalyst Evaluation



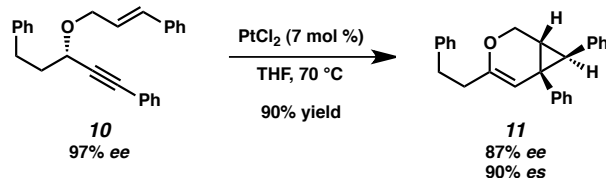
entry	catalyst (mol %)	solvent, temp (°C)	t (h)	yield	ee (%)	es (%) ^a
1	(Ph ₃ P)AuNTf ₂ (5)	CH ₂ Cl ₂ , 23	0.5	52	84	87
2	[Ir(dbcot)Cl] ₂ (2.5) ^{b,c}	PhCH ₃ , 100	3	68	84	87
3	PtCl ₄ (5)	PhCH ₃ , 23	1	27	90	93
4	PtCl ₂ (5)	PhCH ₃ , 60	22	78	86	89
5	PtCl ₂ (5)	THF, 60	18	87	88	91
6	PtCl ₂ (5) ^b	THF, 60	14	86	86	89
7	[(C ₂ H ₄)PtCl ₂] ₂ (2.5)	THF, 23	28	84	86	89
8	Pt(PhCN) ₂ Cl ₂ (7)	THF, 60	48	64	87	90
9	PtCl ₂ (7)	THF, 70	18	90	87	90

^a Enantiospecificity (es) = [(ee_{product}) / (ee_{substrate})] × 100%.

^b Under 1 atm CO.

^c dbcot: dibenzo[a,e]cyclooctatetraene

General Procedure for Experiments in Table 1. To a solution of enyne **10** in the listed solvent under argon was added catalyst. The resulting mixture was sealed, heated to the prescribed temperature and stirred for the listed time. For entry 7, the solution was purged with a balloon of CO prior to heating. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/Et₂O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography. The enantiomeric excess of bicyclic **11** was analyzed by HPLC.

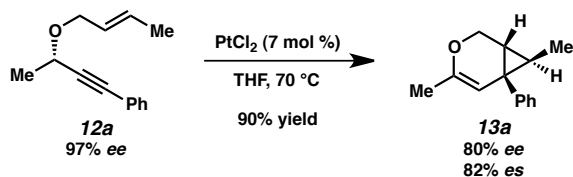


Bicyclic 11, entry 9. To a solution of enyne **10** (20.0 mg, 0.0567 mmol) in THF (1.90 mL, 0.030 M) under argon was added PtCl₂ (0.8 mg, 0.00285 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 18 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/Et₂O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/Et₃N → 98.5:1:0.5 hexanes/Et₂O/Et₃N eluent) affording bicyclic **11** (17.9 mg, 90% yield, R_F = 0.73 in 9:1 hexanes/Et₂O) as a white solid.

Bicyclic 11: ¹H NMR (400 MHz, C₆D₆) δ 7.18 (m, 2H), 7.11-6.85 (comp. m, 11H), 6.72-6.70 (m, 2H), 5.10 (s, 1H), 4.20 (d, *J* = 10.5 Hz, 1H), 3.85 (dd, *J* = 10.5, 2.1 Hz, 1H), 2.87-2.73 (comp. m, 3H), 2.32 (t, *J* = 7.8 Hz, 2H), 2.05 (d, *J* = 5.8 Hz, 1H); ¹³C NMR (100 MHz, C₆D₆) δ 150.9, 142.0, 140.8, 138.4, 130.3, 128.9, 128.6, 128.5, 128.00, 127.97, 126.6, 126.2, 125.8, 107.1, 62.5, 37.2, 36.6, 33.7, 32.4, 29.3; IR (film) 3061, 2923, 2863, 1665, 1497 cm⁻¹; HRMS (ESI+) *m/z* calc'd for (M + H)⁺ [C₂₆H₂₄O + H]⁺: 353.1905, found 353.1891; [α]_D³⁰ = -0.43 (*c* = 1.0, CH₂Cl₂).

The *ee* was determined to be 87% by HPLC analysis (Daicel Chiralcel OD-H, 10% 2-propanol in hexane, 1 mL/min, λ = 210 nm, major isomer 6.04 min, minor isomer 12.23 min).

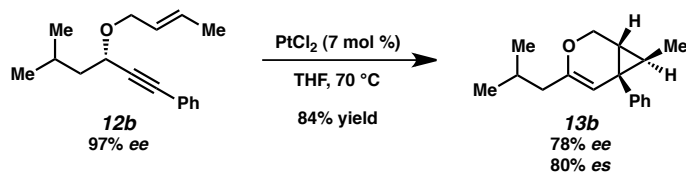
Propargylic Substituent Evaluation



Bicycle 13a. To a solution of enyne **12a** (10.0 mg, 0.0499 mmol) in THF (1.67 mL, 0.030 M) under argon was added PtCl_2 (0.9 mg, 0.00350 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 12 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 98.5:1:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **13a** (9.1 mg, 90% yield, R_F = 0.59 in 9:1 hexanes/ Et_2O) as a yellow oil.

Bicycle 13a: ^1H NMR (400 MHz, C_6D_6) δ 7.25-7.07 (comp. m, 5H), 5.09-5.05 (s, 1H), 4.12 (dd, J = 10.5, 1.1 Hz, 1H), 3.80 (dd, J = 10.5, 2.1 Hz, 1H), 1.67 (s, 3H), 1.43 (quintet, J = 6.0 Hz, 1H), 1.20-1.18 (m, 1H), 1.20-1.13 (comp. m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 147.7, 142.3, 129.7, 128.7, 126.5, 106.7, 62.7, 29.4, 27.5, 26.5, 20.0, 15.0; IR (film) 2929, 1715, 1495, 1447 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{14}\text{H}_{16}\text{O} + \text{H}$] $^+$: 201.1274, found 201.1273; $[\alpha]_D^{31}$ = -31.92 (c = 0.1, CH_2Cl_2).

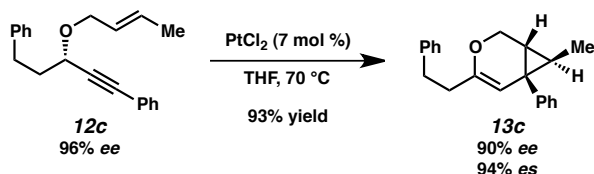
The *ee* was determined to be 80% by HPLC analysis (Daicel Chiralcel OJ-H, 5% 2-propanol in hexane, 1.0 mL/min, λ = 210 nm, major isomer 9.67 min, minor isomer 10.60 min).



Bicycle 13b. To a solution of enyne **12b** (25.0 mg, 0.103 mmol) in THF (3.43 mL, 0.030 M) under argon was added PtCl_2 (1.9 mg, 0.00722 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 24 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 4:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 98.5:1:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **13b** (21.1 mg, 84% yield, R_F = 0.66 in 9:1 hexanes/ Et_2O) as a yellow oil.

Bicycle 13b: ^1H NMR (400 MHz, C_6D_6) δ 7.22-7.18 (comp. m, 4H), 7.13-7.07 (m, 1H), 5.15 (s, 1H), 4.14 (dd, $J = 10.4, 1.3$ Hz, 1H), 3.76 (dd, $J = 10.3, 2.0$ Hz, 1H), 2.03-1.82 (comp. m, 4H), 1.48 (quintet, $J = 6.0$ Hz, 1H), 1.23-1.17 (comp. m, 2H), 0.91 (d, $J = 6.5$ Hz, 3H), 0.88 (d, $J = 6.5$ Hz, 3H), 0.72 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 150.5, 142.3, 129.7, 128.7, 126.5, 107.8, 62.7, 43.9, 29.9, 27.5, 26.42, 26.37, 22.7, 22.6, 15.0; IR (film) 2960, 2872, 1727, 1495 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{17}\text{H}_{22}\text{O} + \text{H}$] $^+$: 243.1744, found 243.1746; $[\alpha]_{\text{D}}^{30} = -13.19$ ($c = 0.5$, CH_2Cl_2).

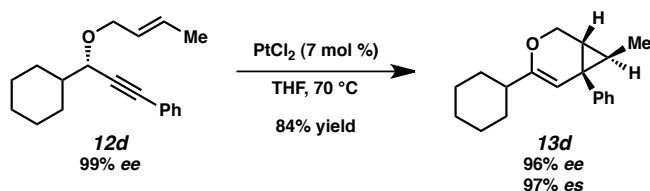
The *ee* was determined to be 78% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1 mL/min, $\lambda = 210$ nm, major isomer 4.91 min, minor isomer 6.01 min).



Bicycle 13c. To a solution of enyne **12c** (10.0 mg, 0.0344 mmol) in THF (1.15 mL, 0.030 M) under argon was added PtCl_2 (0.6 mg, 0.00238 mmol). The resulting mixture was sealed, heated to 70 $^\circ\text{C}$ and stirred at that temperature for 16 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 98.5:1:0.5 hexanes/ Et_2O / Et_3N eluent) affording bicycle **13c** (9.3 mg, 93% yield, $R_F = 0.53$ in 9:1 hexanes/ Et_2O) as a white solid.

Bicycle 13c: ^1H NMR (400 MHz, C_6D_6) δ 7.18-6.98 (comp. m, 10H), 5.06 (s, 1H), 4.11 (dd, $J = 10.4, 1.4$ Hz, 1H), 3.73 (dd, $J = 10.4, 2.2$ Hz, 1H), 2.76-2.71 (m, 2H), 2.28-2.23 (m, 2H), 1.39 (quintet, $J = 6.0$ Hz, 1H), 1.18-1.17 (m, 1H), 0.68 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 150.4, 142.1, 129.7, 128.8, 128.7, 128.6, 126.5, 126.2, 107.1, 62.8, 36.7, 33.9, 29.7, 27.4, 26.4, 15.0; IR (film) 2925, 2855, 1719, 1602 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{21}\text{H}_{22}\text{O} + \text{H}$] $^+$: 291.1744, found 291.1735; $[\alpha]_{\text{D}}^{31} = -8.51$ ($c = 0.1$, CH_2Cl_2).

The *ee* was determined to be 90% by HPLC analysis (Daicel Chiralcel OD-H, 3% 2-propanol in hexane, 1 mL/min, $\lambda = 210$ nm, major isomer 5.62 min, minor isomer 12.79 min).



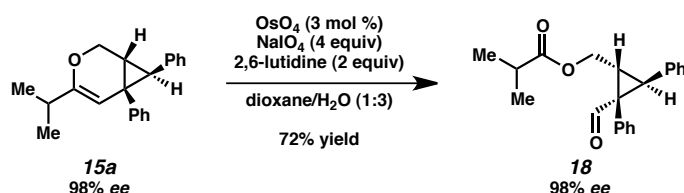
Bicycle 13d. To a solution of enyne **12d** (25.0 mg, 0.0932 mmol) in THF (3.10 mL, 0.030 M) under argon was added PtCl_2 (1.7 mg, 0.00652 mmol). The resulting mixture was sealed, heated to 70 $^\circ\text{C}$ and stirred at that temperature for 24 h. Once cooled to ambient temperature, the mixture was diluted with hexanes and filtered through a small plug of alumina (0.5 x 2 cm, 9:1 hexanes/ Et_2O eluent). The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (99.5:0.5 hexanes/ Et_3N \rightarrow 98.5:1:0.5 hexanes/ Et_2O / Et_3N

eluent) affording bicycle **13d** (21.0 mg, 84% yield, $R_F = 0.85$ in 9:1 hexanes/Et₂O) as a colorless oil.

Bicycle 13d: ¹H NMR (400 MHz, C₆D₆) δ 7.23-7.19 (comp. m, 4H), 7.14-7.09 (m, 1H), 5.17 (s, 1H), 4.18 (dd, $J = 10.3, 1.4$ Hz, 1H), 3.74 (dd, $J = 10.3, 2.0$ Hz, 1H), 1.99-1.83 (comp. m, 4H), 1.70-1.62 (comp. m, 2H), 1.59-1.53 (m, 1H), 1.49 (quintet, $J = 6.0$ Hz, 1H), 1.35-1.02 (comp. m, 7H), 0.74 (d, $J = 6.3$ Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 155.8, 142.6, 129.8, 128.7, 126.5, 104.7, 99.1, 62.8, 42.8, 31.1, 30.9, 30.2, 27.3, 26.69, 26.67, 26.6, 26.1, 15.0; IR (film) 2930, 2856, 1720, 1448 cm⁻¹; HRMS (ESI+) m/z calc'd for (M + H)⁺ [C₁₉H₂₄O + H]⁺: 269.1900, found 269.1901; $[\alpha]_D^{28} = +10.00$ ($c = 1.0$, CH₂Cl₂).

The *ee* was determined to be 96% by HPLC analysis (Daicel Chiralcel OJ-H, 1% 2-propanol in hexane, 1 mL/min, $\lambda = 230$ nm, major isomer 4.15 min, minor isomer 4.56 min).

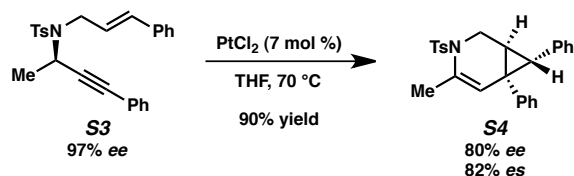
Additional Reactions



Cyclopropane 18. To a solution of bicycle **15a** (36.3 mg, 0.125 mmol) in dioxane (3.75 mL) at 23 °C was added OsO_4 (23.8 μL , 4% in H_2O , 0.00375 mmol) followed by 2,6-lutidine (29.0 μL , 0.250 mmol). To the resulting mixture was added a solution of NaIO_4 (106 mg, 0.500 mmol) in H_2O (1.25 mL). The resulting reaction mixture was stirred vigorously for 48 h, at which time it was diluted with EtOAc (15 mL) and H_2O (10 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (1 x 10 mL), then brine (1 x 10 mL) and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording cyclopropane **18** (28.9 mg, 72% yield, R_F = 0.53 in 4:1 hexanes/EtOAc) as a colorless oil.

Cyclopropane 18: ^1H NMR (400 MHz, CDCl_3) 9.73 (s, 1H), 7.24-7.20 (comp. m, 3H), 7.12-7.07 (comp. m, 3H), 7.06-7.00 (m, 2H), 6.84-6.80 (m, 2H), 4.79 (dd, J = 11.9, 5.6 Hz, 1H), 4.29 (dd, J = 11.9, 9.7 Hz, 1H), 3.34 (d, J = 7.5 Hz, 1H), 2.93-2.87 (m, 1H), 2.60 (septet, J = 7.0 Hz, 1H), 1.21 (d, J = 3.6 Hz, 3H), 1.19 (d, J = 3.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.3, 135.1, 134.6, 131.5, 128.7, 128.1, 128.0, 127.0, 61.3, 49.8, 38.2, 34.6, 34.1, 19.23, 19.16; IR (film) 2969, 1733, 1704, 1191 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{Na})^+ [\text{C}_{21}\text{H}_{22}\text{O}_3 + \text{Na}]^+$: 345.1467, found 345.1466; $[\alpha]_D^{27}$ = -150.43 (c = 1.0 CH_2Cl_2).

The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OD-H, 15% 2-propanol in hexane, 1 mL/min, λ = 210 nm, major isomer 6.30 min, minor isomer 12.41 min).

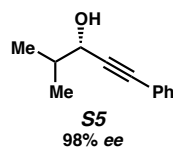


Bicycle S4. To a solution of enyne **S3** (50.0 mg, 0.120 mmol) in THF (4.61 mL, 0.030 M) under argon was added PtCl_2 (2.2 mg, 0.00840 mmol). The resulting mixture was sealed, heated to 70 °C and stirred at that temperature for 15 h. Once cooled to ambient temperature, the solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (4:1 hexanes/EtOAc \rightarrow 1:1 hexanes/EtOAc eluent) affording bicycle **S4** (44.8 mg, 90% yield, R_F = 0.62 in 1:1 hexanes/EtOAc) as a white solid.

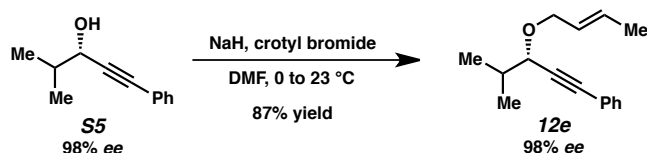
The *ee* was determined to be 80% by HPLC analysis (Daicel Chiralcel IC, 10% 2-propanol in hexane, 1 mL/min, λ = 210 nm, major isomer 17.97 min, minor isomer 14.04 min). *Note:* The absolute configuration of **S4** is preliminarily established.

Substrate Syntheses

General procedure for the synthesis of propargylic alcohols using the Noyori transfer hydrogenation. To a solution of an ynone in 2-propanol (0.1 M) under argon was added Ru[(*S,S*)-TsDPEN(*p*-cymene)] (.04-2 mol %). The resulting purple solution was stirred at ambient temperature until the reaction was complete (2-48 h). The solvent was removed in vacuo and the resulting residue was purified by flash chromatography affording the enantioenriched propargylic alcohol.



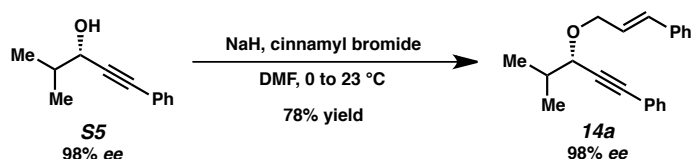
Alcohol S5. Based on the general procedure, alcohol **S5** was produced in >99% yield. All spectra matched those previously reported in the literature.¹ The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OD-H, 5% 2-propanol in hexane, 1 mL/min, λ = 254 nm, *S* isomer 12.18 min, *R* isomer 6.86 min). $[\alpha]_D^{32} = +2.98$ (c = 1.0, CHCl₃) (*S*) (Lit. $[\alpha]_D^{20} = +1.52$ (c = 0.6, CHCl₃) 47.4% *ee* (*S*)).



Enyne 12e. To a solution of alcohol **S5** (90.6 mg, 0.520 mmol) in DMF (1.73 mL) at 0 °C under argon was added NaH (22.9 mg, 60% dispersion in mineral oil, 0.572 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 25 min. Crotyl bromide (53.6 μ L, 0.520 mmol) was added and after 3 h, the reaction was quenched by slow addition of H₂O (3 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 9:1 H/EtOAc eluent) affording enyne **12e** (103 mg, 87% yield, R_F = 0.74 in 4:1 hexanes/EtOAc) as a yellow oil.

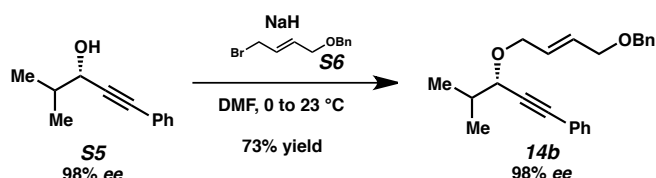
Enyne 12e: ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.42 (m, 2H), 7.33-7.29 (comp. m, 3H), 5.82-5.72 (m, 1H), 5.67-5.57 (m, 1H), 4.28-4.23 (m, 1H), 4.06 (d, J = 5.8 Hz, 1H), 4.00-3.95 (m, 1H), 1.75-1.71 (m, 3H), 1.07 (d, J = 6.7 Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 131.9, 129.8, 128.4, 128.3, 127.6, 123.2, 87.6, 86.4, 74.8, 69.8, 33.4, 19.0, 18.1; IR (film) 2963, 1490, 1444, 1350, cm⁻¹; HRMS (ESI+) m/z calc'd for (M + H)⁺ [C₁₆H₂₀O + H]⁺: 229.1587, found 229.1583; $[\alpha]_D^{31} = -62.55$ (c = 1.0, CH₂Cl₂).

¹ Fang, T.; Du, D-M.; Lu, S-F.; Xu, J. *Org. Lett.* **2005**, 7, 2081–2085.



Enyne 14a. To a solution of alcohol **S5** (100 mg, 0.575 mmol) in DMF (1.91 mL) at 0 °C under argon was added NaH (27.6 mg, 60% dispersion in mineral oil, 0.896 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Cinnamyl bromide (85.2 μ L, 0.575 mmol) was added and after 3 h, the reaction was quenched by slow addition of H₂O (5 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 10:1 hexanes/EtOAc eluent) affording enyne **14a** (130 mg, 78% yield, R_F = 0.55 in 9:1 hexanes/EtOAc) as a colorless oil.

Enyne 14a: ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.44 (m, 2H), 7.42-7.39 (m, 2H), 7.34-7.29 (m, 6H), 6.67 (d, J = 15.9 Hz, 1H), 6.34 (ddd, J = 15.9, 6.7, 5.5 Hz, 1H), 4.50 (ddd, J = 12.7, 5.5, 1.6 Hz, 1H), 4.23 (ddd, J = 12.7, 6.7, 1.3 Hz, 1H), 4.14 (d, J = 5.8 Hz, 1H), 2.06 (dq, J = 12.8, 6.5 Hz, 1H), 1.11 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 137.0, 132.7, 131.9, 128.7, 128.40, 128.36, 127.8, 126.7, 126.2, 123.1, 87.4, 86.7, 75.1, 69.7, 33.5, 18.9, 18.2; IR (film) 3062, 2966, 2874, 1723, 1491 cm⁻¹; HRMS (APCI+) m/z calc'd for (M + H)⁺ [C₂₁H₂₁O + H]⁺: 291.1744, found 291.1752; [α]_D³² = -85.75 (c = 1.0, CH₂Cl₂).

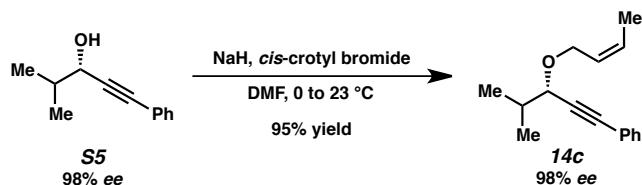


Enyne 14b. To a solution of alcohol **S5** (85.0 mg, 0.488 mmol) in DMF (1.63 mL) at 0 °C under argon was added NaH (23.4 mg, 60% dispersion in mineral oil, 0.585 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Bromide **S6**² (118 mg, 0.488 mmol) was added and after 6 h, the reaction was quenched by slow addition of H₂O (3 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 9:1 hexanes/EtOAc eluent) affording enyne **14b** (119 mg, 73% yield, R_F = 0.47 in 4:1 hexanes/EtOAc) as a colorless oil.

Enyne 14b: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.42 (m, 2H), 7.34 (d, J = 4.4 Hz, 4H), 7.32-7.28 (comp. m, 4H), 5.91-5.88 (comp. m, 2H), 4.53 (s, 2H), 4.37-4.32 (m, 1H), 4.10-4.03 (comp. m, 4H), 2.03 (dq, J = 12.8, 6.5 Hz, 1H), 1.08 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 131.9, 129.7, 129.5, 128.5, 128.39, 128.35, 127.9, 127.4, 87.4, 86.6, 75.2, 72.4, 70.4, 69.0, 33.4, 18.9, 18.1; IR (film) 2962, 2853, 1490, 1454, 1102 cm⁻¹; HRMS

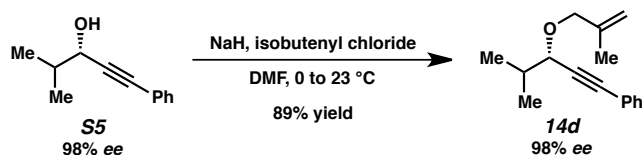
² Kottirsch, G.; Koch, G.; Feifel, R.; Neumann, U. *J. Med. Chem.* **2002**, *45*, 2289–2293.

(APCI) m/z calc'd for $(M + NH_4)^+ [C_{23}H_{26}O_2 + NH_4]^+$: 352.2277, found 352.2276; $[\alpha]_D^{34} = -83.62$ ($c = 1.0$, CH_2Cl_2).



Enyne 14c. To a solution of alcohol **S5** (100 mg, 0.574 mmol) in DMF (1.91 mL) at 0 °C under argon was added NaH (29.8 mg, 60% dispersion in mineral oil, 0.746 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. *Cis*-crotyl bromide³ (77.5 mg, 0.574 mmol) was added and after 3.5 h, the reaction was quenched by slow addition of H_2O (3 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 15:1 hexanes/EtOAc eluent) affording enyne **14c** (125 mg, 95% yield, $R_F = 0.56$ in 4:1 hexanes/EtOAc) as a colorless oil.

Enyne 14c: 1H NMR (400 MHz, $CDCl_3$) δ 7.48–7.43 (m, 1H), 7.33–7.29 (m, 3H), 5.75–5.67 (m, 1H), 5.64–5.57 (m, 1H), 4.34 (dd, $J = 12.0, 5.8$ Hz, 1H), 4.19 (dd, $J = 11.9, 7.2$ Hz, 1H), 4.08 (d, $J = 5.9$ Hz, 1H), 2.02 (dq, $J = 13.2, 6.6$ Hz, 1H), 1.72 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.7$ Hz, 3H), 1.05 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.9, 128.5, 128.4, 128.3, 126.9, 123.2, 87.7, 86.4, 74.86, 74.85, 64.3, 33.4, 18.9, 18.2, 13.4; IR (film) 3023, 2969, 1659, 1490, 1071, 691 cm^{-1} ; HRMS (APCI) m/z calc'd for $(M + H)^+ [C_{16}H_{20}O + H]^+$: 229.1592, found 229.1583; $[\alpha]_D^{30} = -182.55$ ($c = 1.0$, CH_2Cl_2).

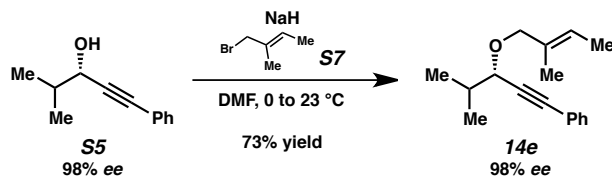


Enyne 14d. To a solution of alcohol **S5** (80.0 mg, 0.459 mmol) in DMF (1.53 mL) at 0 °C under argon was added NaH (22.0 mg, 60% dispersion in mineral oil, 0.551 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Isobutenyl chloride (44.9 μ L, 0.459 mmol) was added and after 2.5 h, the reaction was quenched by slow addition of H_2O (5 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 15:1 hexanes/EtOAc eluent) affording enyne **14d** (93.1 mg, 89% yield, $R_F = 0.83$ in 4:1 hexanes/EtOAc) as a colorless oil.

Enyne 14d: 1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 7.33–7.29 (m, 3H), 5.04 (d, $J = 1.0$ Hz, 1H), 4.92 (d, $J = 0.7$ Hz, 1H), 4.20 (d, $J = 12.5$ Hz, 1H), 4.05 (d, $J = 5.9$ Hz, 1H), 3.98 (d, $J = 12.5$ Hz, 1H), 2.04 (dq, $J = 13.0, 6.6$ Hz, 1H), 1.78 (s, 3H), 1.09 (d, $J = 6.7$ Hz, 3H), 1.06 (d,

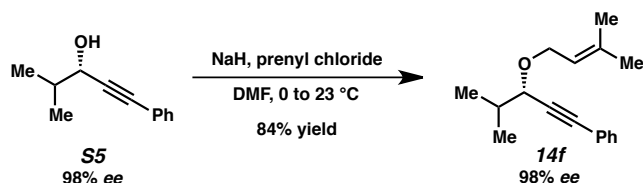
³ Haynes, R. K.; Katsifis, A. G. *Aust. J. Chem.* **1989**, 42, 1455–1471.

$J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.3, 131.9, 128.4, 128.3, 123.2, 112.5, 87.6, 86.4, 74.9, 72.9, 33.5, 19.8, 18.9, 18.3; IR (film) 2963, 2872, 1598, 1490, 1071 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{NH}_4)^+ [\text{C}_{16}\text{H}_{20}\text{O} + \text{NH}_4]^+$: 246.1858, found 246.1859; $[\alpha]_{\text{D}}^{32} = -116.81$ ($c = 1.0$, CH_2Cl_2).



Enyne 14e. To a solution of alcohol **S5** (90.1 mg, 0.517 mmol) in DMF (1.72 mL) at 0 °C under argon was added NaH (24.8 mg, 60% dispersion in mineral oil, 0.628 mmol) in one portion. This mixture was then allowed to warm to ambient temperature and stirred for 20 min. Bromide **S7**⁴ (77.0 mg, 0.517 mmol) was added and after 2 h, the reaction was quenched by slow addition of H_2O (5 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 50:1 hexanes/EtOAc eluent) affording enyne **14e** (91.0 mg, 73% yield, $R_{\text{F}} = 0.59$ in 9:1 hexanes/EtOAc) as a yellow oil.

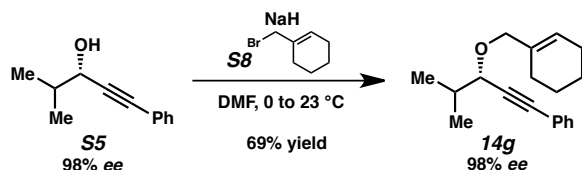
Enyne 14e: ^1H NMR (400 MHz, CDCl_3) δ 7.46-7.43 (m, 2H), 7.32-7.29 (m, 3H), 5.59-5.54 (m, 1H), 4.16 (d, $J = 11.4$ Hz, 1H), 3.99 (d, $J = 6.0$ Hz, 1H), 3.94 (d, $J = 11.4$ Hz, 1H), 2.02 (dq, $J = 13.1$, 6.6 Hz, 1H), 1.68 (s, 1H), 1.64 (dd, $J = 6.7$, 0.9 Hz, 1H), 1.08 (d, $J = 6.7$ Hz, 3H), 1.05 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 132.9, 131.9, 128.4, 128.2, 123.3, 123.0, 87.8, 75.1, 74.4, 33.5, 18.9, 18.3, 13.9, 13.4; IR (film) 2963, 2925, 1723, 1490, 1383 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{NH}_4)^+ [\text{C}_{17}\text{H}_{22}\text{O} + \text{NH}_4]^+$: 260.2014, found 260.2012; $[\alpha]_{\text{D}}^{32} = -47.87$ ($c = 1.0$, CH_2Cl_2).



Enyne 14f. To a solution of alcohol **S5** (90.1 mg, 0.517 mmol) in DMF (1.72 mL) at 0 °C under argon was added NaH (24.8 mg, 60% dispersion in mineral oil, 0.620 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Prenol chloride (58.3 μL , 0.517 mmol) was added and after 2.5 h, the reaction was quenched by slow addition of H_2O (5 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 50:1 hexanes/EtOAc eluent) affording enyne **14f** (105 mg, 84% yield, $R_{\text{F}} = 0.58$ in 9:1 hexanes/EtOAc) as a colorless oil.

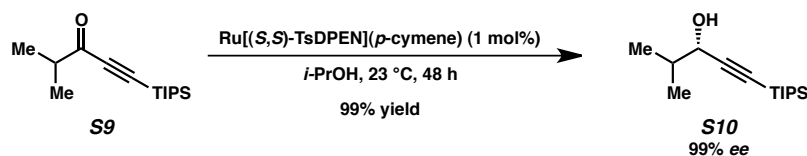
⁴ Lorenz, M.; Kalesse, M. *Org. Lett.* **2008**, *10*, 4371–4374.

Enyne 14f: ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.43 (m, 2H), 7.32-7.29 (m, 3H), 5.41-5.36 (m, 1H), 4.28 (dd, J = 11.5, 6.3 Hz, 1H), 4.07 (dd, J = 11.6, 7.6 Hz, 1H), 4.05 (d, J = 5.9 Hz, 1H), 2.02 (dq, J = 13.0, 6.6 Hz, 1H), 1.77 (s, 3H), 1.73 (s, 3H), 1.07 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.6, 131.9, 128.4, 128.3, 123.3, 121.1, 87.8, 86.3, 74.8, 65.5, 33.4, 26.0, 19.0, 18.3, 18.2; IR (film) 2965, 2930, 1723, 1490, 1444 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{NH}_4)^+ [\text{C}_{17}\text{H}_{22}\text{O} + \text{NH}_4]^+$: 260.2014, found 260.2015; $[\alpha]_{\text{D}}^{31}$ = -249.36 (c = 1.0, CH_2Cl_2).



Enyne 14g. To a solution of alcohol **S5** (80.0 mg, 0.459 mmol) in DMF (1.53 mL) at 0 °C under argon was added NaH (22.0 mg, 60% dispersion in mineral oil, 0.551 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Bromide **S8**⁵ (80.4 mg, 0.459 mmol) was added and after 12 h, the reaction was quenched by slow addition of H_2O (5 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 15:1 hexanes/EtOAc eluent) affording enyne **14g** (85.2 mg, 69% yield, R_{F} = 0.60 in 9:1 hexanes/EtOAc) as a yellow oil.

Enyne 14g: ^1H NMR (400 MHz, C_6D_6) δ 7.45-7.42 (m, 2H), 6.99-6.95 (m, 3H), 5.78-5.76 (m, 1H), 4.30 (d, J = 11.4 Hz, 1H), 4.09 (d, J = 5.7 Hz, 1H), 4.00 (d, J = 11.4 Hz, 1H), 2.14-2.04 (m, 3H), 1.97-1.87 (m, 2H), 1.58-1.43 (m, 4H), 1.19 (d, J = 6.7 Hz, 3H), 1.13 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 135.3, 132.1, 128.6, 128.2, 127.9, 125.0, 123.8, 88.6, 86.7, 74.7, 74.0, 34.0, 26.5, 25.4, 23.0, 22.9, 18.9, 18.5; IR (film) 2928, 2837, 1668, 1490, 1445 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{NH}_4)^+ [\text{C}_{19}\text{H}_{24}\text{O} + \text{NH}_4]^+$: 286.2165, found 286.2163; $[\alpha]_{\text{D}}^{32}$ = -145.32 (c = 1.0, CH_2Cl_2).



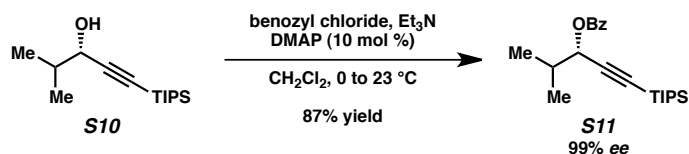
Alcohol S10. To a solution of ketone **S9**⁶ (1.00 g, 3.96 mmol) in 2-propanol (39.6 mL) under argon was added $\text{Ru}[(\text{S},\text{S})\text{-TsDPEN}](p\text{-cymene})$ (23.8 mg, 0.0396 mmol), and the resulting solution was stirred at ambient temperature for 48 h. The solvent was then removed by rotary evaporation and the resulting residue was immediately purified by flash chromatography (9:1 hexanes/EtOAc eluent) to afford alcohol **S10** (993 mg, 99% yield, R_{F} = 0.42 in 4:1 H/EtOAc eluent) as a colorless oil.

⁵ Pagès, L.; Llebaria, A.; Camps, F.; Motins, E.; Miravittles, C.; Moretó, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449–10461.

⁶ Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938–10939.

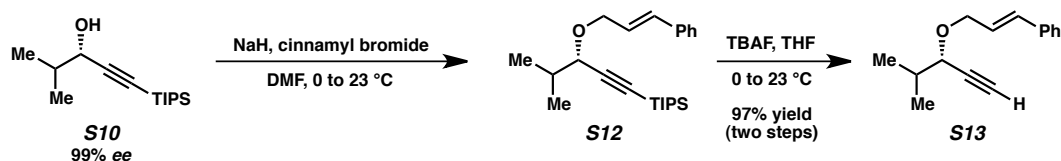
Alcohol S10: ^1H NMR (400 MHz, CDCl_3) δ 4.20 (d, J = 5.5 Hz, 1H), 1.89 (dtd, J = 13.5, 6.7, 5.5 Hz, 1H), 1.68 (br s, 1H), 1.08 (comp. m, J = 2.5 Hz, 17H), 1.03 (d, J = 6.7 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 107.5, 86.4, 85.6, 34.7, 18.8, 18.3, 17.4, 11.3; IR (film) 3356, 2960, 2170, 1464 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{NH}_4)^+$ [$\text{C}_{15}\text{H}_{30}\text{OSi} + \text{NH}_4$] $^+$: 272.2404, found 272.2411; $[\alpha]_{\text{D}}^{30}$ = -10.64 (c = 1.0, CH_2Cl_2).

The *ee* was determined 99% by conversion to the benzoate and HPLC analysis:



To a solution of alcohol **S10** (10.0 mg, .0393 mmol), triethylamine (11.0 μL , .0786 mmol), and DMAP (0.48 mg, .00393 mmol) in CH_2Cl_2 (0.393 mL) at 0 $^\circ\text{C}$ was added benzozyl chloride (5.0 μL , .0432 mmol). The resulting solution was stirred at ambient temperature for 4.5 h. The solvent was then removed in vacuo and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording benzoate **S11** (12.2 mg, 87% yield, R_f = 0.65 in 4:1 hexanes/EtOAc eluent) as a colorless oil.

The *ee* of benzoate **S11** was determined to be 99% by HPLC analysis (Daicel Chiralcel OD-H, 100% hexane, 1.3 mL/min, λ = 280 nm, *S* isomer 4.29 min, *R* isomer 4.08 min).

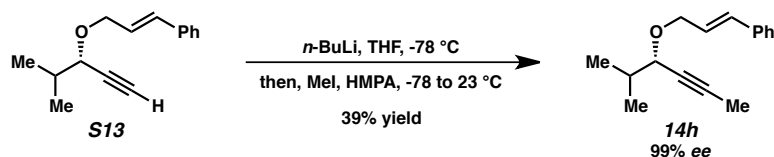


Alkyne S13. To a solution of alcohol **S10** (150 mg, 0.589 mmol) and cinnamyl bromide (116 mg, 0.589 mmol) in DMF (1.96 mL) at 0 $^\circ\text{C}$ under argon was added NaH (30.6 mg, 60% dispersion in mineral oil, 0.766 mmol) in one portion. The mixture was then stirred at 0 $^\circ\text{C}$ for 20 min and ambient temperature for 4 h, at which time the reaction was quenched by slow addition of H_2O (5 mL). The mixture was extracted with hexanes (3 x 30 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (10 mL), and dried over MgSO_4 . The solvent was removed by rotary evaporation to give crude ether **S12**, which was used immediately in the next step.

To crude alkyne **S12** in THF (0.736 mL) at 0 $^\circ\text{C}$ was added TBAF (2.65 mL, 1.0 M in THF, 2.65 mmol) dropwise over 5 min. The resulting solution was allowed to warm to ambient temperature and stirred for 15 min, at which time sat. aq. NaHCO_3 (5 mL) was added. The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed with brine (10 mL) and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 9:1 hexanes/EtOAc eluent) affording alkyne **S13** (122 mg, 97% yield over two steps, R_f = 0.46 in 4:1 hexanes/EtOAc) as a colorless oil.

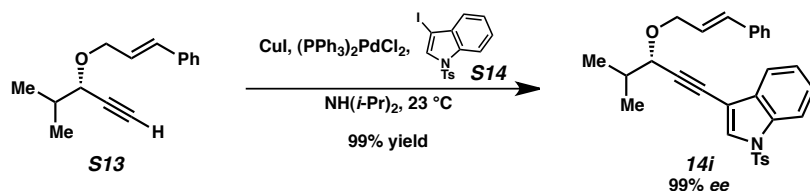
Alkyne S13: ^1H NMR (400 MHz, CDCl_3) δ 7.43-7.38 (m, 2H), 7.35-7.30 (m, 2H), 7.26-7.22 (m, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.33-6.26 (m, 1H), 4.44 (ddd, J = 12.7, 5.4, 1.6 Hz, 1H), 4.15

(ddd, $J = 12.7, 6.8, 1.3$ Hz, 1H), 3.92 (dd, $J = 5.8, 2.1$ Hz, 1H), 2.44 (d, $J = 2.1$ Hz, 1H), 1.98 (dq, $J = 13.0, 6.5$ Hz, 1H), 1.05 (d, $J = 6.7$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 136.9, 132.8, 128.7, 127.8, 126.7, 126.0, 81.9, 74.5, 74.3, 69.6, 33.1, 18.7, 17.9.



Enyne 14h: To terminal alkyne **S13** (30.0 mg, 0.140 mmol) in THF (700 μL) at -78 $^\circ\text{C}$ was added $n\text{-BuLi}$ (91.0 μL , 2.3 M in hexanes, 0.210 mmol). The reaction mixture was stirred at -78 $^\circ\text{C}$ for 1.5 h, then a solution of MeI (34.9 μL , 0.560 mmol) in HMPA (94.7 μL) was added. The mixture was allowed to warm to ambient temperature and stirred for 20 h, at which time it was quenched with H_2O (1 mL). The aqueous layer was extracted with hexanes (3 x 5 mL). The combined organic layers were washed with 10% LiCl (1 x 2 mL), then brine (1 x 3 mL) and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording enyne **14h** (12.5 mg, 39% yield, $R_F = 0.52$ in 4:1 hexanes/EtOAc) as a colorless oil.

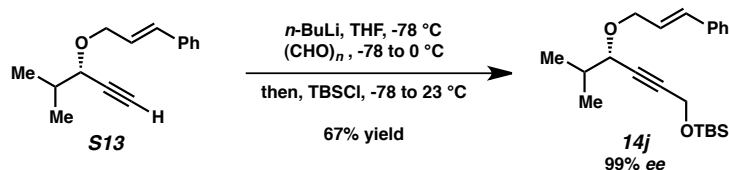
Enyne 14h. ^1H NMR (400 MHz, CDCl_3) δ 7.41-7.38 (m, 2H), 7.33-7.28 (m, 2H), 7.25-7.21 (m, 1H), 6.63 (d, $J = 15.9$ Hz, 1H), 6.30 (ddd, $J = 15.9, 6.6, 5.5$ Hz, 1H), 4.41 (ddd, $J = 12.7, 5.4, 1.6$ Hz, 1H), 4.12 (ddd, $J = 12.7, 6.7, 1.3$ Hz, 1H), 3.87 (dq, $J = 5.8, 2.0$ Hz, 1H), 1.97-1.90 (m, 1H), 1.89 (d, $J = 2.1$ Hz, 3H), 1.02 (d, $J = 6.7$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.0, 132.4, 128.6, 127.7, 126.6, 126.4, 82.4, 74.8, 69.4, 33.3, 18.8, 18.0, 3.8; IR (film) 2961, 2922, 1496, 1072 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{16}\text{H}_{20}\text{O} + \text{H}]^+$: 229.1587, found 229.1590; $[\alpha]_D^{26} = -63.51$ ($c = 2.0$, CH_2Cl_2).



Enyne 14i. To a 2-dram vial under argon containing CuI (3.1 mg, 0.0163 mmol) and $(\text{PPh}_3)_2\text{PdCl}_2$ (5.7 mg, 0.00812 mmol) was added diisopropylamine (0.326 mL) followed by iodindole **S14**⁷ (84.2 mg, 0.212 mmol). This resulting mixture was stirred for 5 min, at which time a solution of ether **S13** (35.0 mg, 0.162 mmol) in THF (0.200 mL) was added via syringe. The reaction mixture was stirred for 3 h then partitioned between ether (4 mL) and 1 M aq. HCl (5 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organics were washed with sat. aq. NaHCO_3 (1 x 5 mL), then brine (1 x 10 mL) and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (9:1 hexanes/ Et_2O eluent) affording enyne **14i** (78.3 mg, 99% yield, $R_F = 0.14$ in 9:1 hexanes/ Et_2O) as a colorless oil.

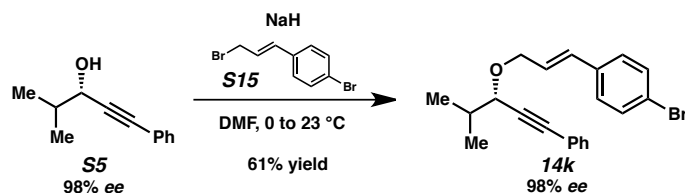
⁷ Witulski, B.; Buschmann, N.; Bergsträßer, U. *Tetrahedron* **2000**, *56*, 8473–8480.

Enyne 14i: ^1H NMR (400 MHz, CDCl_3) δ 7.99-7.96 (m, 1H), 7.80-7.77 (m, 2H), 7.74 (s, 1H), 7.63-7.61 (m, 1H), 7.42-7.28 (comp. m, 5H), 7.25-7.22 (comp. m, 4H), 6.68 (d, $J = 16.0$ Hz, 1H), 6.34 (ddd, $J = 15.9, 6.7, 5.5$ Hz, 1H), 4.51 (dd, $J = 12.7, 5.5$ Hz, 1H), 4.25 (dd, $J = 12.7, 6.7$ Hz, 1H), 4.19 (d, $J = 5.7$ Hz, 1H), 2.35 (s, 3H), 2.13-2.07 (m, 1H), 1.13 (d, $J = 6.7$ Hz, 3H), 1.10 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.5, 136.9, 135.1, 134.3, 132.8, 131.1, 130.2, 129.1, 128.7, 127.8, 127.1, 126.7, 126.1, 125.6, 123.9, 120.6, 113.7, 105.0, 91.8, 75.2, 69.8, 33.4, 21.8, 18.9, 18.2; IR (film) 2962, 2871, 1494, 1376, 1189 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{H})^+ [\text{C}_{30}\text{H}_{29}\text{NO}_3\text{S} + \text{H}]^+$: 484.1941, found 484.1942. $[\alpha]_{\text{D}}^{32} = -114.15$ ($c = 2.0$, CHCl_3).



Enyne 14j: To terminal alkyne **S13** (120 mg, 0.560 mmol) in THF (1.12 mL) at -78 $^\circ\text{C}$ was added $n\text{-BuLi}$ (0.289 mL, 2.13 M in hexanes, 0.616 mmol) dropwise over 2 min. The resulting solution was allowed to warm to 0 $^\circ\text{C}$ and stirred at that temperature for 30 min. The solution was then cooled back down to -78 $^\circ\text{C}$, and finely ground paraformaldehyde (18.7 mg, 0.616 mmol) was added in one portion. The solution was allowed to warm to ambient temperature and stirred for 5 h. The reaction mixture was cooled back to 0 $^\circ\text{C}$ and TBSCl (127 mg, 0.840 mmol) was added. The resulting mixture was stirred at ambient temperature for 1 h and then quenched with sat. aq. NaHCO_3 (10 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed with brine (10 mL) and dried over MgSO_4 . The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (15:1 hexanes/EtOAc eluent) affording enyne **14j** (135 mg, 67% yield, $R_F = 0.83$ in 4:1 hexanes/EtOAc) as a colorless oil.

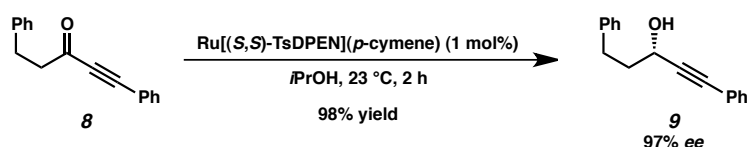
Enyne 14j: ^1H NMR (400 MHz, CDCl_3) δ 7.40-7.37 (m, 2H), 7.35-7.29 (m, 2H), 7.25-7.21 (m, 1H), 6.63 (d, $J = 15.9$ Hz, 1H), 6.28 (ddd, $J = 15.9, 6.7, 5.4$ Hz, 1H), 4.44-4.39 (comp. m, 3H), 4.13 (ddd, $J = 12.6, 6.8, 1.3$ Hz, 1H), 3.94 (dt, $J = 5.8, 1.6$ Hz, 1H), 2.00-1.92 (m, 1H), 1.03 (d, $J = 6.7$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 3H), 0.93-0.92 (m, 9H), 0.14 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.0, 132.7, 128.7, 127.8, 126.6, 126.2, 85.2, 82.8, 74.5, 69.5, 51.9, 33.3, 26.0, 18.8, 18.5, 18.1, 4.9; IR (film) 3028, 2959, 2858, 1728, 1495, 1255 cm^{-1} ; HRMS (DART+) m/z calc'd for $(\text{M} + \text{NH}_4)^+ [\text{C}_{22}\text{H}_{34}\text{O}_2\text{Si} + \text{NH}_4]^+$: 376.2672, found 376.2672; $[\alpha]_{\text{D}}^{33} = -88.30$ ($c = 1.0$, CHCl_3).



Enyne 14k. To a solution of alcohol **S5** (150 mg, 0.861 mmol) in DMF (2.87 mL) at 0 $^\circ\text{C}$ under argon was added NaH (41.2 mg, 60% dispersion in mineral oil, 1.03 mmol) in one portion. The

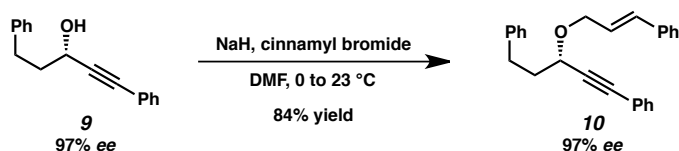
mixture was then allowed to warm to ambient temperature and stirred for 20 min. Bromide **S15**⁸ (186 mg, 0.861 mmol) was added and after 1 h, the reaction was quenched by slow addition of H₂O (5 mL). The mixture was extracted with hexanes (3 x 30 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 7 mL), then brine (7 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes → 9:1 hexanes/EtOAc eluent) affording enyne **14k** (193 mg, 61% yield, R_F = 0.83 in 4:1 hexanes/EtOAc) as a colorless oil.

Enyne 14k: ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.43 (m, 4H), 7.34-7.31 (m, 3H), 7.28-7.25 (m, 2H), 6.62 (d, *J* = 16.0 Hz, 1H), 6.34 (ddd, *J* = 15.9, 6.4, 5.4 Hz, 1H), 4.49 (ddd, *J* = 12.9, 5.4, 1.6 Hz, 1H), 4.21 (ddd, *J* = 12.9, 6.4, 1.4 Hz, 1H), 4.14 (d, *J* = 5.8 Hz, 1H), 2.14-2.02 (m, 1H), 1.12 (d, *J* = 6.7 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 135.9, 131.9, 131.8, 131.2, 128.4, 128.2, 127.2, 123.0, 121.5, 87.3, 86.8, 75.3, 69.5, 33.5, 18.9, 18.1; IR (film) 2964, 2869, 1659, 1491, 1075 cm⁻¹; HRMS (DART+) *m/z* calc'd for (M + NH₄)⁺ [C₂₁H₂₁BrO + NH₄]⁺: 386.1120, found 386.1097; [α]_D³² = -104.68 (*c* = 1.0, CH₂Cl₂).



Alcohol 9. To a solution of ynone **8**⁹ 80.0 mg, 0.341 mmol) in 2-propanol (3.41 mL) under argon was added Ru[(*S,S*)-TsDPEN(*p*-cymene)] (2.1 mg, 0.00341 mmol). The resulting purple solution was stirred at ambient temperature for 2 h. The solvent was removed in vacuo and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording alcohol **9** (79.3 mg, 98% yield, R_F = 0.38 in 4:1 hexanes/EtOAc) as a colorless oil.

Alcohol 9: All spectra matched those previously reported in the literature.¹⁰ The *ee* was determined to be 97% by HPLC analysis (Daicel Chiralcel OD-H, 10% 2-propanol in hexane, 1 mL/min, λ = 254 nm, *S* isomer 25.13 min, *R* isomer 12.59 min). [α]_D²⁶ = +37.45 (*c* = 0.5, CHCl₃) (*S*) (Lit. [α]_D²⁷ = +28.4 (*c* = 1.1, CHCl₃) 49% *ee* (*S*)).



Enyne 10. To a solution of alcohol **9** (400 mg, 1.69 mmol) in DMF (5.64 mL) at 0 °C under argon was added NaH (87.9 mg, 60% dispersion in mineral oil, 2.197 mmol) in one portion. The mixture was allowed to warm to ambient temperature and stirred for 20 min. Cinnamyl bromide (334 mg, 1.69 mmol) was added and after 1 h, the reaction was quenched by slow addition of H₂O (10 mL). The mixture was extracted with hexanes (3 x 50 mL). The combined organic

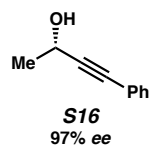
⁸ Hammond, M. L.; Zambias, R. A.; Chang, M. N.; Jensen, N. P.; McDonald, J.; Thompson, K.; Boulton, D. A.; Kopka, I. E.; Hand, K. M.; Opas, E. E.; Luell, S.; Bach, T.; Davies, P.; MacIntyre, D. E.; Bonney, R. J.; Humes, J. L. *J. Med. Chem.* **1990**, 33, 908–918.

⁹ Yamaguchi, M.; Shibato, K.; Fujiwara, S.; Hirao, I. *Synthesis* **1986** 421–422.

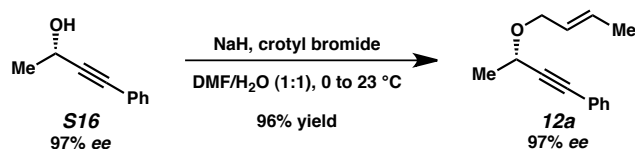
¹⁰ Wu, P.-Y.; Wu, H.-L.; Shen, Y.-Y.; Uang, B.-J. *Tetrahedron: Asymmetry* **2009**, 20, 1837–1841.

layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording enyne **10** (498 mg, 84% yield, R_F = 0.77 in 4:1 hexanes/EtOAc) as a yellow oil.

Enyne 10: ¹H NMR (400 MHz, C₆D₆) δ 7.48-7.45 (m, 2H), 7.25-7.23 (m, 2H), 7.15-6.98 (m, 11H), 6.61 (d, J = 16.0 Hz, 1H), 6.32-6.24 (m, 1H), 4.50 (ddd, J = 12.7, 5.4, 1.6 Hz, 1H), 4.36-4.31 (m, 1H), 4.10 (ddd, J = 12.6, 6.5, 1.4 Hz, 1H), 2.91 (t, J = 7.7 Hz, 2H), 2.34-2.16 (m, 2H).; ¹³C NMR (100 MHz, C₆D₆) δ 141.9, 137.4, 132.6, 132.1, 129.0, 128.82, 128.77, 128.65, 126.9, 126.6, 126.3, 123.5, 89.3, 86.6, 69.7, 68.8, 38.1, 32.0; IR (film) 3060, 2858, 1491, 1453, 1336 cm⁻¹; HRMS (APCI+) m/z calc'd for (M + H)⁺ [C₂₆H₂₄O + H]⁺: 353.1900, found 353.1903; $[\alpha]_D^{26}$ = -43.62 (c = 1.0, CH₂Cl₂).



Alcohol S16. Based on the general procedure, alcohol **S16** was produced in 88% yield. All spectra matched those previously reported in the literature.¹¹ The *ee* was determined to be 97% by HPLC analysis (Daicel Chiralcel OD-H, 20% 2-propanol in hexane, 1 mL/min, λ = 254 nm, *S* isomer 8.89 min, *R* isomer 5.03 min). $[\alpha]_D^{31}$ = -33.40 (c = 1.00, CHCl₃) (*S*) (Lit.¹² $[\alpha]_D^{20}$ = -33.0 (c = 0.94, CHCl₃) >99% *ee* (*S*)).



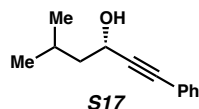
Enyne 12a. To a solution of alcohol **S16** (70.0 mg, 0.479 mmol) in DMF (0.798 mL) and THF (0.798 mL) at 0 °C under argon was added NaH (21.1 mg, 60% dispersion in mineral oil, 0.527 mmol) in one portion. The mixture was allowed to warm to ambient temperature and stirred for 25 min. Crotyl bromide (49.4 μ L, 0.479 mmol) was added and the resulting mixture was stirred for 2.5 h, at which point the reaction was quenched by slow addition of H₂O (4 mL). The volatile solvents were removed by rotary evaporation and the remaining mixture was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (98:2 hexanes/Et₂O eluent) affording enyne **12a** (92.1 mg, 96% yield, R_F = 0.52 in 9:1 hexanes/Et₂O) as a colorless oil.

Enyne 12a: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.41 (m, 2H), 7.33-7.28 (comp. m, 3H), 5.84-5.73 (m, 1H), 5.69-5.57 (m, 1H), 4.42 (q, J = 6.6 Hz, 1H), 4.27-4.22 (m, 1H), 3.99-3.94 (m, 1H), 1.72 (m, J = 1.2 Hz, 3H), 1.53 (d, J = 6.6 Hz, 3H).; ¹³C NMR (100 MHz, CDCl₃) δ 131.9, 130.3, 128.4, 127.4, 123.0, 89.4, 85.0, 69.6, 64.9, 22.4, 18.0; IR (film) 2986, 1490, 1443, 1099 cm⁻¹;

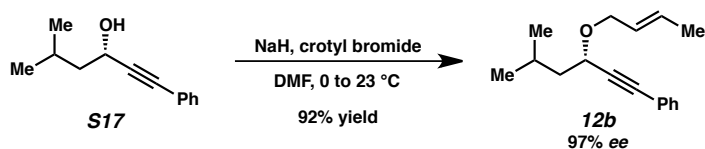
¹¹ Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem.* **2006**, 71, 7035–7044.

¹² Zhang, X.; Lu, Z.; Fu, C.; Ma, S. *Org. Biomol. Chem.* **2009**, 7, 3258–3263.

HRMS (ESI+) m/z calc'd for $(M + H)^+$ $[C_{14}H_{16}O + H]^+$: 201.1274, found 201.1266; $[\alpha]_D^{31} = -75.75$ ($c = 1.0$, CH_2Cl_2).

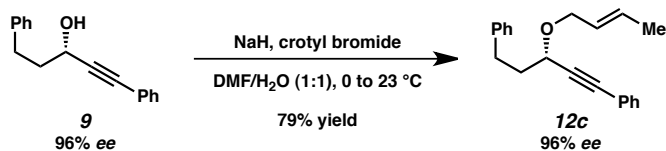


Alcohol S17. Based on the general procedure, alcohol **S17** was produced in 37% yield. All spectra matched those previously reported in the literature.¹³ The *ee* was determined to be 96% by HPLC analysis (Daicel Chiralcel OD-H, 5% 2-propanol in hexane, 1 mL/min, $\lambda = 254$ nm, *S* isomer 14.23 min, *R* isomer 6.98 min). $[\alpha]_D^{31} = -9.79$ ($c = 1.0$, $CHCl_3$) (*S*) (Lit.¹⁴ $[\alpha]_D^{23} = +9.5$ ($c = 3.31$, $CHCl_3$) 94% *ee* (*R*)).



Enyne 12b. To a solution of alcohol **S17** (90.4 mg, 0.480 mmol) in DMF (1.60 mL) at 0 °C under argon was added NaH (21.1 mg, 60% dispersion in mineral oil, 0.528 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 30 min. Crotyl bromide (49.4 μ l, 0.480 mmol) was added and after 2 h, the reaction was quenched by slow addition of H_2O (3 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 15:1 hexanes/EtOAc eluent) affording enyne **12b** (107 mg, 92% yield, $R_F = 0.34$ in 15:1 hexanes/EtOAc) as a yellow oil.

Enyne 12b: 1H NMR (400 MHz, C_6D_6) δ 7.48-7.42 (m, 2H), 7.01-6.94 (comp. m, 3H), 5.71-5.63 (m, 2H), 4.45-4.39 (comp. m, 2H), 4.05-4.01 (m, 1H), 2.09 (app. septet, $J = 6.8$ Hz, 1H), 1.95 (ddd, $J = 13.6, 7.7, 6.6$ Hz, 1H), 1.77 (ddd, $J = 13.5, 7.3, 6.2$ Hz, 1H), 1.53 (d, $J = 4.7$ Hz, 3H), 0.92 (d, $J = 1.8$ Hz, 3H), 0.90 (d, $J = 1.8$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 132.1, 128.9, 128.6, 128.4, 89.9, 86.0, 69.7, 45.4, 25.3, 23.0, 22.6, 17.8; IR (film) 2957, 2869, 1490, 1467 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(M + H)^+$ $[C_{17}H_{22}O + H]^+$: 243.1744, found 243.1730; $[\alpha]_D^{31} = -69.36$ ($c = 1.0$, CH_2Cl_2).



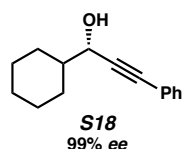
Enyne 12c. (Note: This alcohol **9**, at 96% *ee*, was generated in a separate transfer hydrogenation from the aforementioned one at 97% *ee*.) To a solution of alcohol **9** (35.0 mg, 0.148 mmol) in

¹³ Pathak, K.; Bhatt, A. P.; Abdi, S. H. R.; Kureshy, R. I.; Khan, N. H.; Ahmad, I.; Jasra, R. V. *Chirality* **2007**, 18, 82-88.

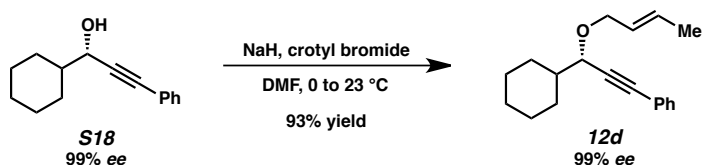
¹⁴ Takita, R.; Yakura, K.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, 127, 13760-13761.

DMF (0.350 mL) and THF (0.350 mL) at 0 °C under argon was added NaH (6.5 mg, 60% dispersion in mineral oil, 0.163 mmol) in one portion. The mixture was allowed to warm to ambient temperature and stirred for 20 min. Crotyl bromide (15.3 μ L, 0.148 mmol) was added and after 4 h, the reaction was quenched by slow addition of H₂O (4 mL). The volatile solvents were then removed by rotary evaporation and the remaining mixture was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (9:1 hexanes/EtOAc eluent) affording enyne **12c** (33.9 mg, 79% yield, *R*_F = 0.73 in 4:1 hexanes/EtOAc) as a yellow oil.

Enyne 12c: ¹H NMR (400 MHz, CDCl₃) δ 7.45 (m, *J* = 1.6 Hz, 2H), 7.34-7.18 (comp. m, 8H), 5.86-5.73 (m, 1H), 5.72-5.56 (m, 1H), 4.31-4.24 (comp. m, 2H), 3.96 (dd, *J* = 11.5, 6.8 Hz, 1H), 2.86 (t, *J* = 7.8 Hz, 2H), 2.23-2.04 (m, 2H), 1.73 (d, *J* = 6.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 141.7, 131.89, 131.87, 130.2, 128.7, 128.5, 128.43, 128.41, 127.4, 126.0, 123.0, 88.4, 86.1, 69.7, 68.3, 37.50, 37.45, 31.73, 31.70, 18.0; IR (film) 2930, 2857, 1491, 1454, 1335 cm⁻¹; HRMS (ESI+) *m/z* calc'd for (M + H)⁺ [C₂₁H₂₂O + H]⁺: 291.1744, found 291.1741; [α]_D³¹ = -17.23 (*c* = 1.0, CH₂Cl₂).



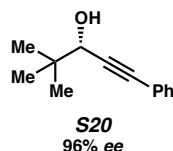
Alcohol S18. Based on the general procedure, alcohol **S18** was produced in 73% yield. All spectra matched those previously reported in the literature.¹⁵ The *ee* was determined to be 98% by HPLC analysis (Daicel Chiralcel OD-H, 15% 2-propanol in hexane, 1 mL/min, λ = 254 nm, *S* isomer 12.18 min, *R* isomer 6.86 min). [α]_D³² = +8.72 (*c* = 1.0, CHCl₃) (*S*) (Lit. [α]_D²⁵ = +11.7 (*c* = 0.63, CHCl₃) 79% *ee* (*S*)).



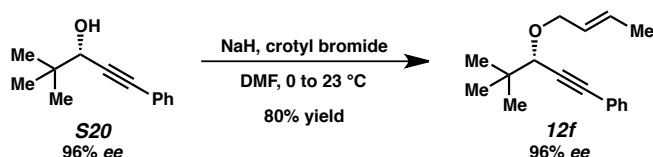
Enyne 12d. To a solution of alcohol **S18** (90.1 mg, 0.420 mmol) in DMF (1.40 mL) at 0 °C under argon was added NaH (18.5 mg, 60% dispersion in mineral oil, 0.462 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Crotyl bromide (43.3 μ L, 0.420 mmol) was added and after 3 h, the reaction was quenched by slow addition of H₂O (3 mL). The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO₄. The solvent was removed by rotary evaporation and the resulting residue was purified by flash chromatography (hexanes \rightarrow 9:1 hexanes/EtOAc eluent) affording enyne **12d** (105 mg, 93% yield, *R*_F = 0.77 in 4:1 hexanes/EtOAc) as a yellow oil.

¹⁵ Zhong, J-C.; Hou, S-C.; Bian, Q-H.; Yin, M-M.; Na, R-S.; Zheng, B.; Li, Z-Y.; Liu, S-Z.; Wang, M. *Chem. Eur. J.* **2009**, *15*, 3069–3071.

Enyne 12d: ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.42 (m, 2H), 7.33-7.29 (comp. m, 3H), 5.82-5.71 (m, 1H), 5.65-5.57 (m, 1H), 4.28-4.22 (m, 1H), 4.06 (d, $J = 6.2$ Hz, 1H), 3.98-3.93 (m, 1H), 1.95-1.88 (m, 2H), 1.78-1.64 (comp. m, 8H), 1.33-1.09 (comp. m, 7H); ^{13}C NMR (100 MHz, CDCl_3) δ 131.9, 129.9, 128.4, 127.6, 123.2, 87.9, 74.1, 69.8, 43.0, 29.4, 28.7, 26.6, 26.2, 26.1, 18.0; IR (film) 2927, 2854, 1490, 1330 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{19}\text{H}_{24}\text{O} + \text{H}$] $^+$: 269.1900, found 269.1903; $[\alpha]_{\text{D}}^{31} = -25.53$ ($c = 0.5$, CH_2Cl_2).



Alcohol S20. Based on the general procedure, alcohol **S20** was produced in 76% yield. All spectra matched those previously reported in the literature.¹⁶ The *ee* was determined to be 96% by HPLC analysis (Diacel Chiralcel OD-H, 3% 2-propanol in hexane, 1 mL/min, $\lambda = 254$ nm, *S* isomer 8.17 min, *R* isomer 6.60 min). $[\alpha]_{\text{D}}^{32} = +1.06$ ($c = 1.0$, CHCl_3) (*S*) (Lit.¹⁷ $[\alpha]_{\text{D}}^{25} = +2.4$ ($c = 4.0$, CHCl_3) 94% *ee* (*S*)).



Enyne 12f. To a solution of alcohol **S20** (90.0 mg, 0.478 mmol) in DMF (1.59 mL) at 0 $^\circ\text{C}$ under argon was added NaH (21.0 mg, 60% dispersion in mineral oil, 0.526 mmol) in one portion. The mixture was then allowed to warm to ambient temperature and stirred for 20 min. Crotyl bromide (49.3 μL , 0.478 mmol) was added and after 4.5 h, H_2O (3 mL) was added dropwise. The mixture was extracted with hexanes (3 x 20 mL). The combined organic layers were washed sequentially with aq. LiCl (10% w/v, 5 mL), then brine (5 mL), and dried over MgSO_4 . The solvent was removed in vacuo and the resulting residue was purified by flash chromatography (100% hexanes \rightarrow 15:1 H/Et $_2$ O eluent) affording enyne **12f** (92.7 mg, 80% yield, $R_{\text{F}} = 0.62$ in 9:1 hexanes/Et $_2$ O) as a yellow oil.

Enyne 12f. ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.42 (m, 2H), 7.32-7.28 (m, 3H), 5.83-5.72 (m, 1H), 5.64-5.55 (m, 1H), 4.31-4.24 (m, 1H), 3.99-3.93 (m, 1H), 3.87 (s, 1H), 1.74-1.70 (m, 3H), 1.07-1.04 (m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 131.9, 129.4, 128.4, 128.2, 127.8, 123.3, 87.9, 86.3, 78.0, 70.3, 35.9, 26.1, 18.0; IR (film) 2969, 2871, 1724, 1489, 1284 cm^{-1} ; HRMS (ESI+) m/z calc'd for $(\text{M} + \text{H})^+$ [$\text{C}_{17}\text{H}_{22}\text{O} + \text{H}$] $^+$: 243.1744, found 243.1736; $[\alpha]_{\text{D}}^{32} = -37.23$ ($c = 1.0$, CH_2Cl_2).

¹⁶ Tanaka, K.; Shoji, T. *Org. Lett.* **2005**, *7*, 3561–3563.

¹⁷ Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806–1807.

Crystallographic dataTable 1. Crystal data and structure refinement for **15k**.

Identification code	ef09_0m	
Empirical formula	C ₂₁ H ₂₁ BrO	
Formula weight	369.29	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	<i>P</i> 2 ₁	
Unit cell dimensions	<i>a</i> = 8.7086(4) Å	α = 90°.
	<i>b</i> = 10.3343(5) Å	β = 113.168(2)°.
	<i>c</i> = 10.3919(5) Å	γ = 90°.
Volume	859.82(7) Å ³	
<i>Z</i>	2	
Density (calculated)	1.426 Mg/m ³	
Absorption coefficient	2.393 mm ⁻¹	
<i>F</i> (000)	380	
Crystal size	0.66 x 0.49 x 0.29 mm ³	
Theta range for data collection	2.13 to 33.29°.	
Index ranges	-13 ≤ <i>h</i> ≤ 12, -15 ≤ <i>k</i> ≤ 14, -16 ≤ <i>l</i> ≤ 15	
Reflections collected	22316	
Independent reflections	5869 [<i>R</i> (int) = 0.0255]	
Completeness to theta = 33.29°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.5447 and 0.3011	
Refinement method	Full-matrix least-squares on <i>F</i> ²	
Data / restraints / parameters	5869 / 1 / 211	
Goodness-of-fit on <i>F</i> ²	1.041	
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> 1 = 0.0281, <i>wR</i> 2 = 0.0692	
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0306, <i>wR</i> 2 = 0.0700	
Absolute structure parameter	0.022(6)	
Largest diff. peak and hole	1.630 and -0.749 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **15k**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	-533(1)	1540(1)	-3037(1)	23(1)
C(1)	597(2)	1364(2)	-1061(2)	14(1)
C(2)	469(2)	202(2)	-452(2)	17(1)
C(3)	1339(2)	48(2)	983(2)	16(1)
C(4)	2330(2)	1043(2)	1812(2)	12(1)
C(5)	2407(2)	2208(2)	1166(2)	14(1)
C(6)	1546(2)	2378(2)	-275(2)	15(1)
C(7)	3336(2)	883(2)	3338(2)	12(1)
C(8)	3157(2)	-277(2)	4146(2)	15(1)
C(9)	4739(3)	-793(2)	5282(2)	24(1)
C(10)	4666(2)	849(2)	6844(2)	17(1)
C(11)	3559(2)	1554(2)	5836(1)	13(1)
C(12)	2550(2)	1011(2)	4433(2)	12(1)
C(13)	717(2)	1321(2)	3890(2)	12(1)
C(14)	-497(2)	385(2)	3694(2)	16(1)
C(15)	-2173(2)	741(2)	3225(2)	21(1)
C(16)	-2639(2)	2029(2)	2947(2)	24(1)
C(17)	-1432(2)	2972(2)	3143(2)	22(1)
C(18)	236(2)	2613(2)	3607(2)	18(1)
C(19)	5627(2)	1234(2)	8346(2)	21(1)
C(20)	5145(3)	357(2)	9319(2)	29(1)
C(21)	5395(3)	2663(2)	8623(2)	24(1)
O(1)	4980(2)	-439(2)	6665(2)	27(1)

Table 3. Bond lengths [Å] and angles [°] for **15k**.

Br(1)-C(1)	1.9045(15)	C(3)-C(4)-C(7)	122.39(15)
C(1)-C(2)	1.382(3)	C(4)-C(5)-C(6)	121.22(15)
C(1)-C(6)	1.385(2)	C(1)-C(6)-C(5)	118.74(16)
C(2)-C(3)	1.392(2)	C(4)-C(7)-C(8)	122.36(14)
C(3)-C(4)	1.400(2)	C(4)-C(7)-C(12)	121.89(13)
C(4)-C(5)	1.393(2)	C(8)-C(7)-C(12)	59.02(10)
C(4)-C(7)	1.489(2)	C(12)-C(8)-C(7)	61.85(11)
C(5)-C(6)	1.397(2)	C(12)-C(8)-C(9)	116.05(14)
C(7)-C(8)	1.506(2)	C(7)-C(8)-C(9)	116.87(15)
C(7)-C(12)	1.547(2)	O(1)-C(9)-C(8)	115.23(15)
C(8)-C(12)	1.505(2)	C(11)-C(10)-O(1)	122.75(17)
C(8)-C(9)	1.515(2)	C(11)-C(10)-C(19)	127.44(17)
C(9)-O(1)	1.416(2)	O(1)-C(10)-C(19)	109.56(14)
C(10)-C(11)	1.328(2)	C(10)-C(11)-C(12)	122.2(2)
C(10)-O(1)	1.385(2)	C(11)-C(12)-C(13)	114.74(13)
C(10)-C(19)	1.506(2)	C(11)-C(12)-C(8)	114.23(14)
C(11)-C(12)	1.485(2)	C(13)-C(12)-C(8)	121.24(14)
C(12)-C(13)	1.504(2)	C(11)-C(12)-C(7)	119.46(13)
C(13)-C(14)	1.387(2)	C(13)-C(12)-C(7)	117.03(13)
C(13)-C(18)	1.396(2)	C(8)-C(12)-C(7)	59.13(11)
C(14)-C(15)	1.394(3)	C(14)-C(13)-C(18)	119.21(15)
C(15)-C(16)	1.389(3)	C(14)-C(13)-C(12)	122.76(15)
C(16)-C(17)	1.388(3)	C(18)-C(13)-C(12)	118.01(14)
C(17)-C(18)	1.389(2)	C(13)-C(14)-C(15)	119.99(17)
C(19)-C(21)	1.533(3)	C(16)-C(15)-C(14)	120.35(18)
C(19)-C(20)	1.534(3)	C(17)-C(16)-C(15)	120.03(18)
		C(16)-C(17)-C(18)	119.44(19)
C(2)-C(1)-C(6)	121.64(14)	C(17)-C(18)-C(13)	120.98(17)
C(2)-C(1)-Br(1)	118.42(13)	C(10)-C(19)-C(21)	112.88(15)
C(6)-C(1)-Br(1)	119.93(13)	C(10)-C(19)-C(20)	110.01(16)
C(1)-C(2)-C(3)	118.83(15)	C(21)-C(19)-C(20)	110.81(16)
C(2)-C(3)-C(4)	121.29(16)	C(10)-O(1)-C(9)	115.23(15)
C(5)-C(4)-C(3)	118.27(14)		
C(5)-C(4)-C(7)	119.31(14)		

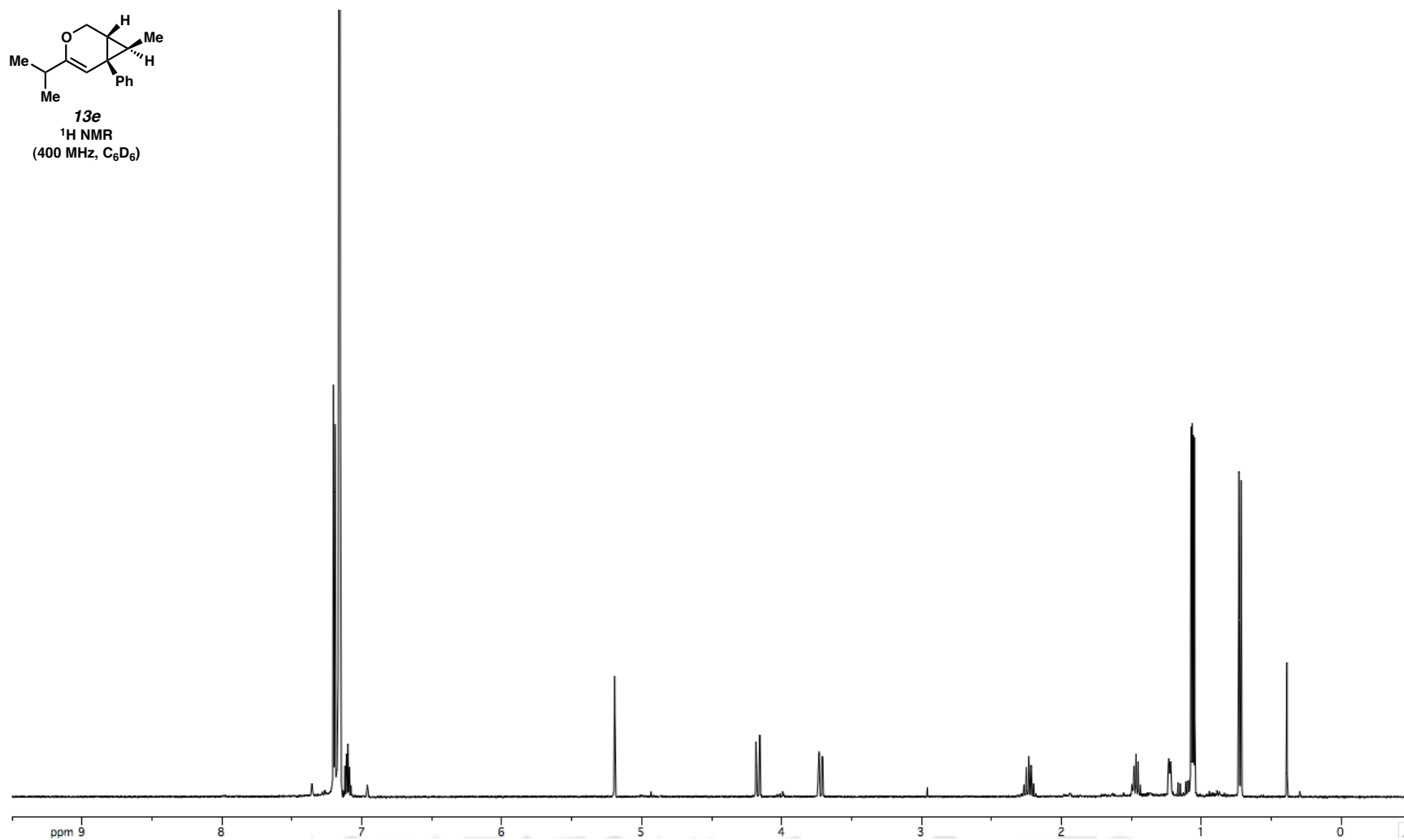
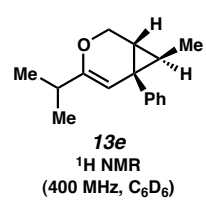
Symmetry transformations used to generate equivalent atoms:

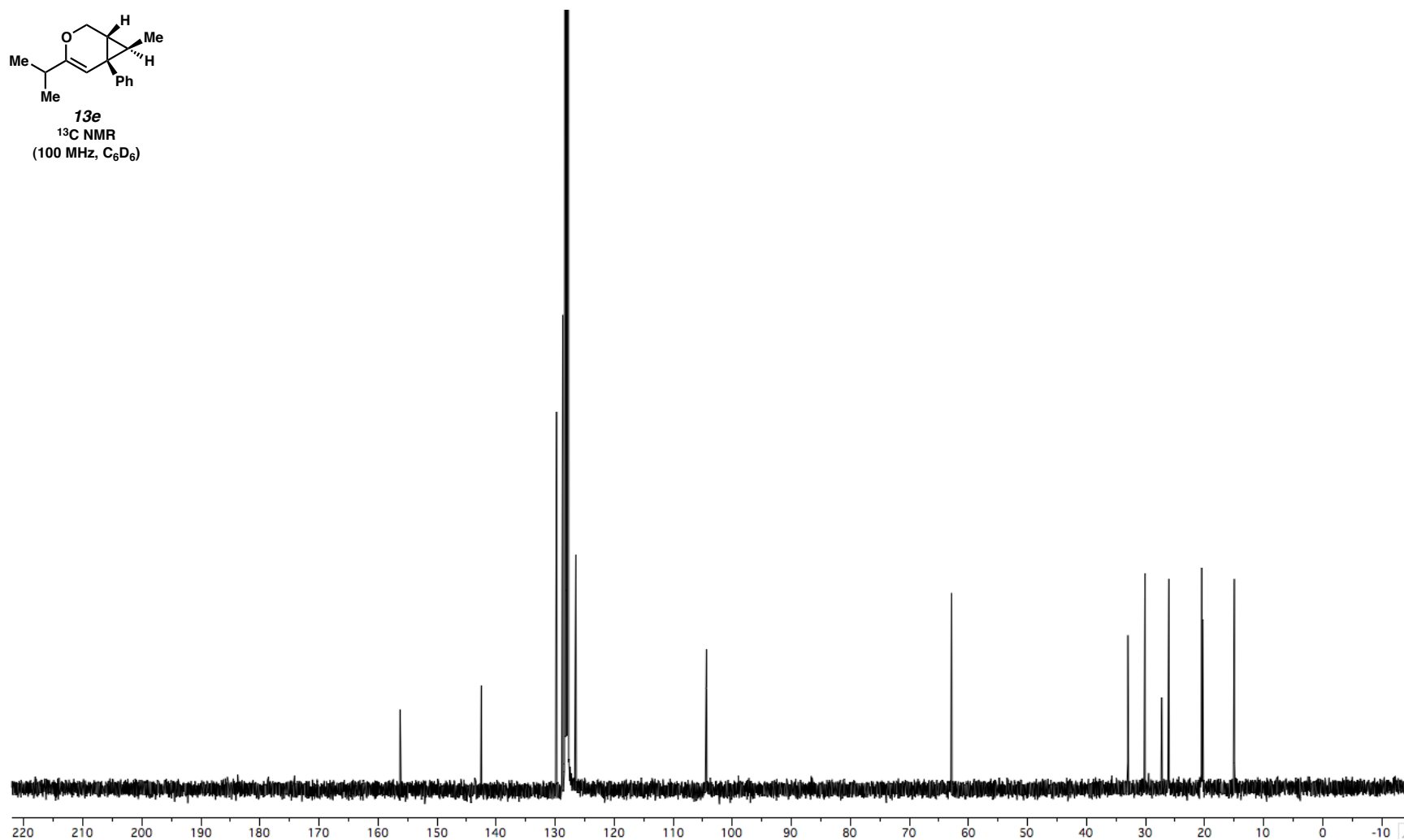
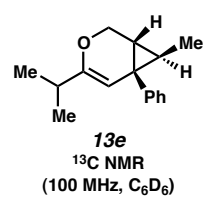
Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **15k**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

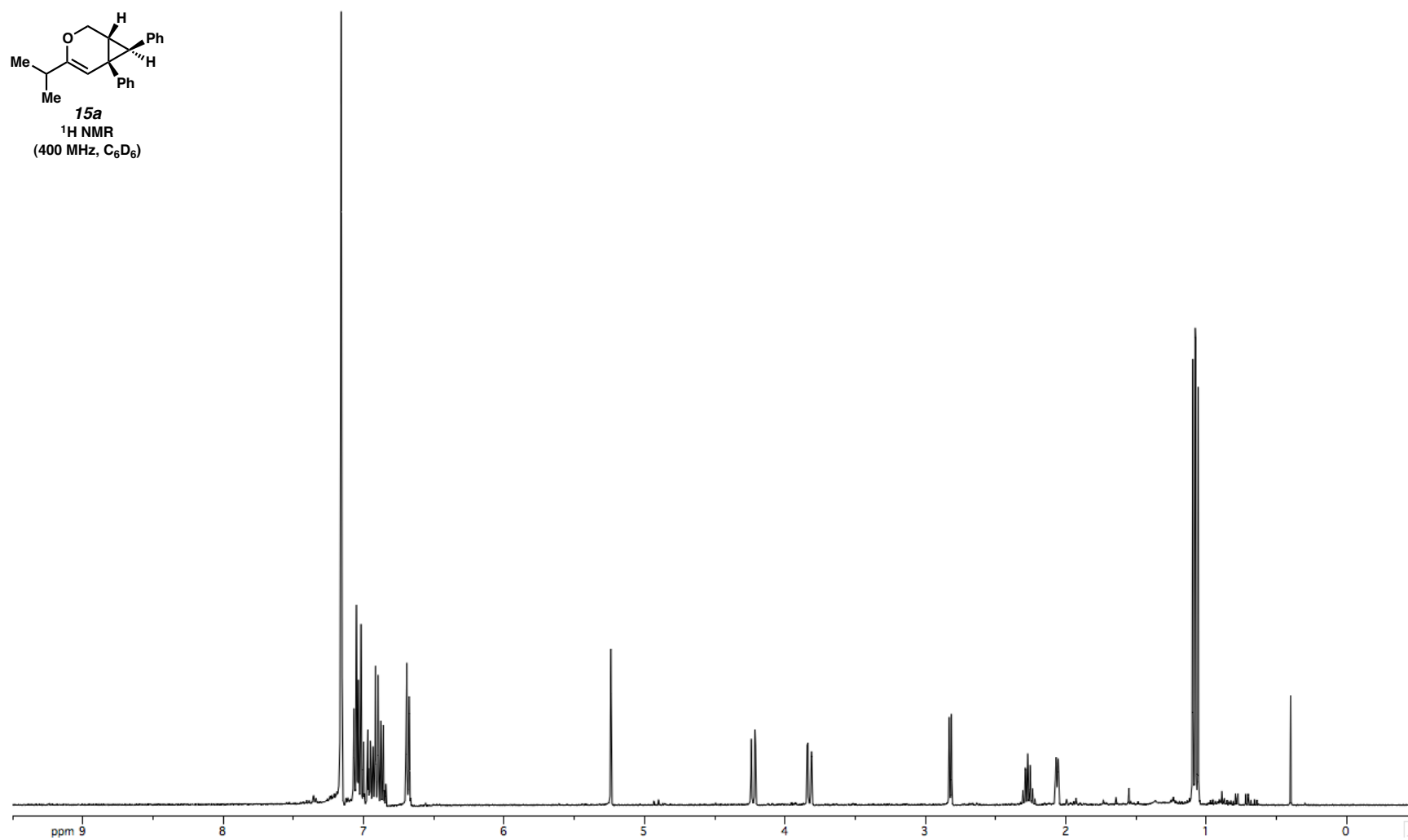
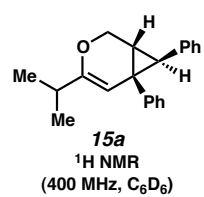
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	36(1)	20(1)	11(1)	2(1)	6(1)	6(1)
C(1)	17(1)	16(1)	11(1)	0(1)	7(1)	3(1)
C(2)	22(1)	15(1)	12(1)	-1(1)	4(1)	-2(1)
C(3)	21(1)	13(1)	12(1)	0(1)	5(1)	-3(1)
C(4)	13(1)	12(1)	12(1)	-1(1)	6(1)	0(1)
C(5)	14(1)	12(1)	16(1)	0(1)	5(1)	-1(1)
C(6)	18(1)	12(1)	16(1)	3(1)	8(1)	3(1)
C(7)	13(1)	12(1)	12(1)	0(1)	5(1)	1(1)
C(8)	21(1)	11(1)	12(1)	0(1)	5(1)	2(1)
C(9)	34(1)	20(1)	15(1)	0(1)	5(1)	13(1)
C(10)	15(1)	18(1)	15(1)	-2(1)	4(1)	3(1)
C(11)	17(1)	11(1)	12(1)	0(1)	5(1)	2(1)
C(12)	16(1)	10(1)	10(1)	1(1)	3(1)	1(1)
C(13)	14(1)	14(1)	10(1)	0(1)	5(1)	0(1)
C(14)	20(1)	14(1)	15(1)	-1(1)	9(1)	-3(1)
C(15)	17(1)	28(1)	17(1)	-1(1)	6(1)	-7(1)
C(16)	13(1)	36(1)	22(1)	4(1)	6(1)	1(1)
C(17)	16(1)	24(1)	27(1)	6(1)	8(1)	5(1)
C(18)	15(1)	16(1)	21(1)	3(1)	7(1)	1(1)
C(19)	18(1)	25(1)	13(1)	-3(1)	-1(1)	5(1)
C(20)	43(1)	24(1)	15(1)	2(1)	6(1)	6(1)
C(21)	30(1)	22(1)	17(1)	-8(1)	6(1)	-4(1)
O(1)	34(1)	24(1)	17(1)	-1(1)	5(1)	11(1)

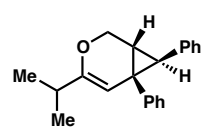
Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **15k**.

	x	y	z	U(eq)
H(2)	-202	-480	-1005	20
H(3)	1259	-749	1410	19
H(5)	3057	2899	1715	17
H(6)	1611	3175	-707	18
H(7)	4502	1225	3658	15
H(8)	2285	-927	3619	18
H(9A)	4726	-1749	5220	29
H(9B)	5707	-481	5096	29
H(11)	3409	2435	6018	16
H(14)	-186	-498	3880	19
H(15)	-3002	98	3094	25
H(16)	-3783	2266	2623	29
H(17)	-1745	3855	2961	27
H(18)	1061	3257	3732	21
H(19)	6840	1093	8564	25
H(20A)	3975	509	9164	43
H(20B)	5860	552	10295	43
H(20C)	5293	-551	9120	43
H(21A)	5686	3205	7978	36
H(21B)	6123	2880	9590	36
H(21C)	4228	2818	8479	36

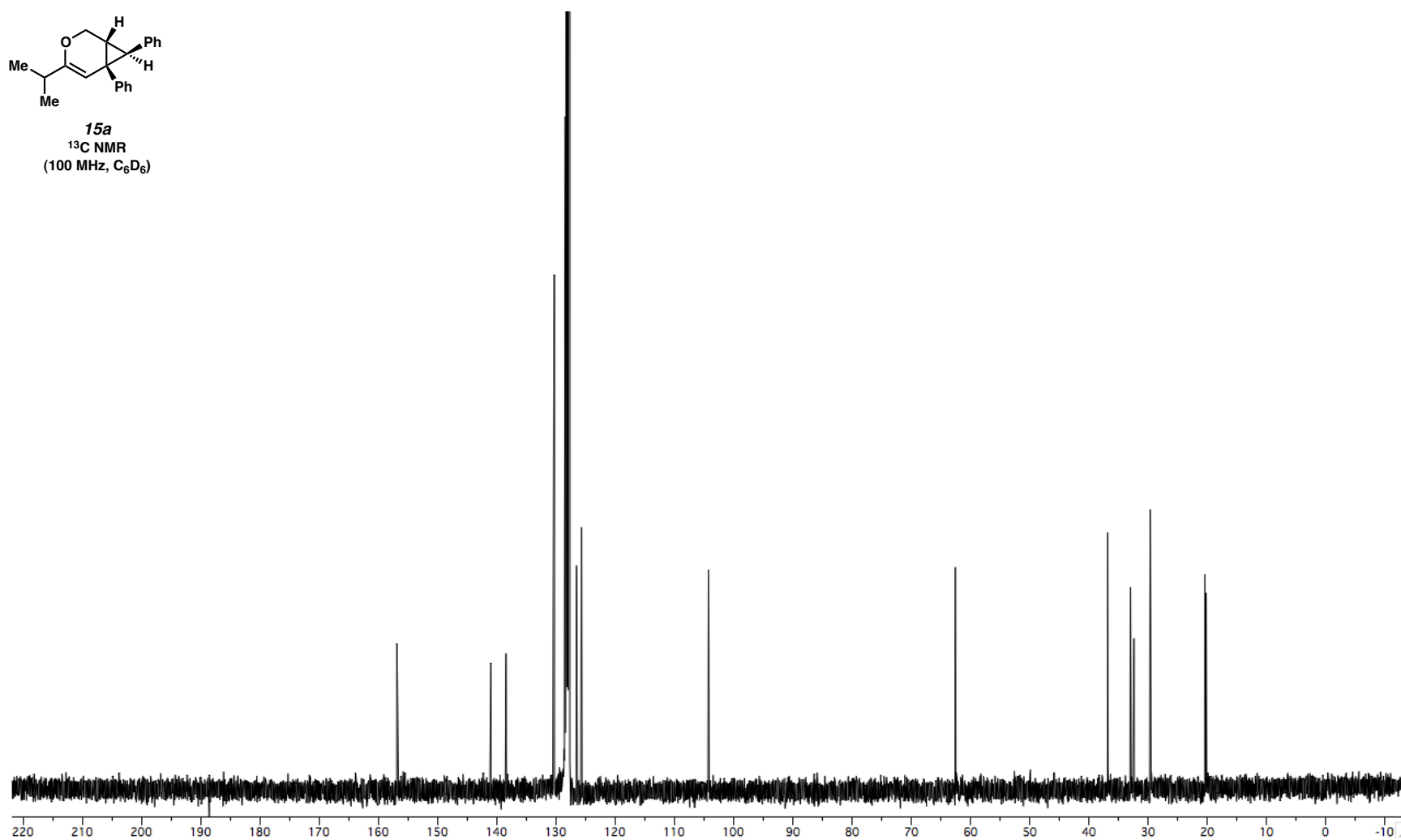


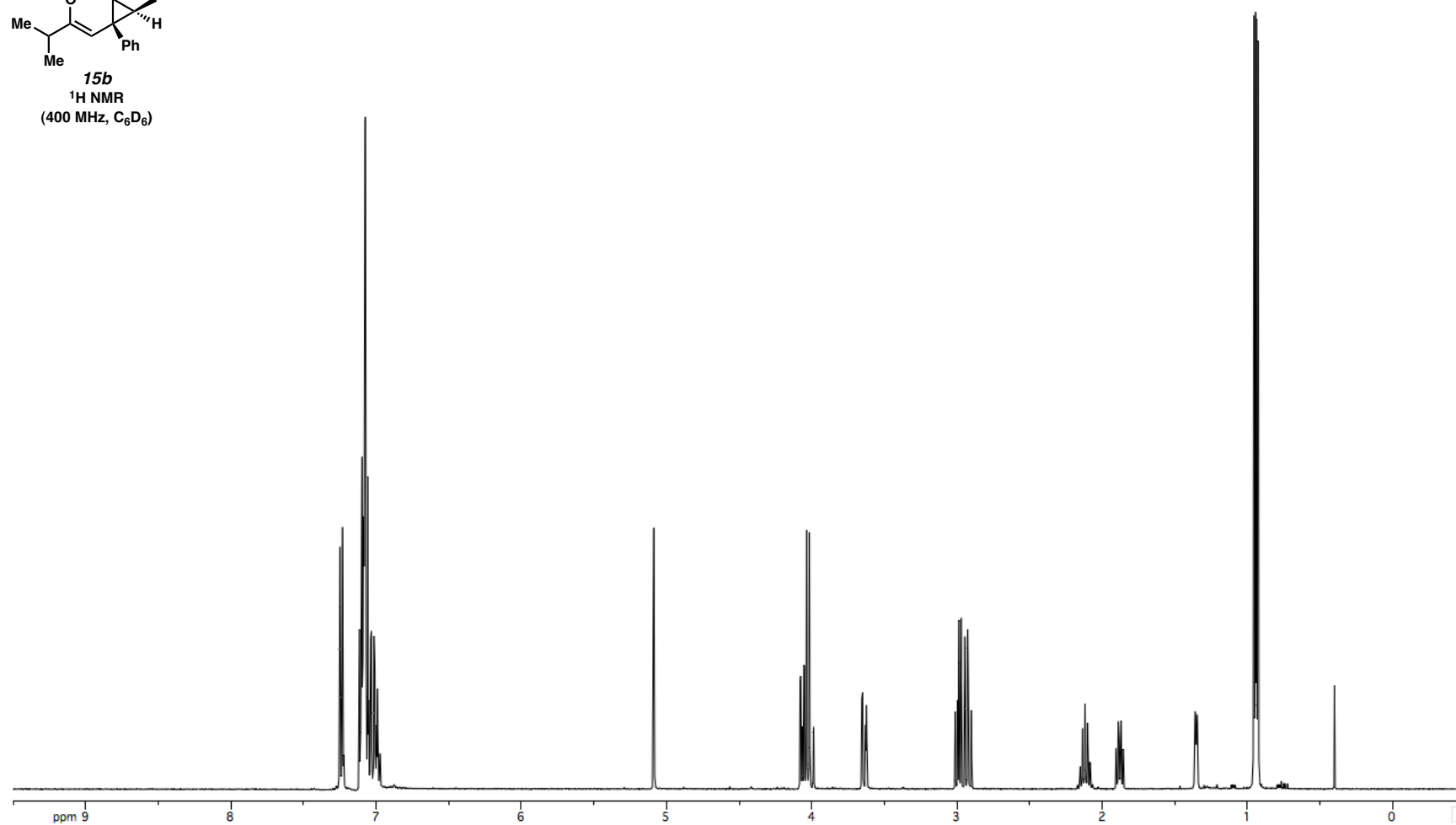
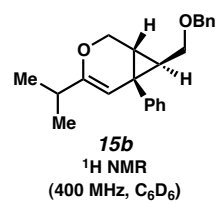


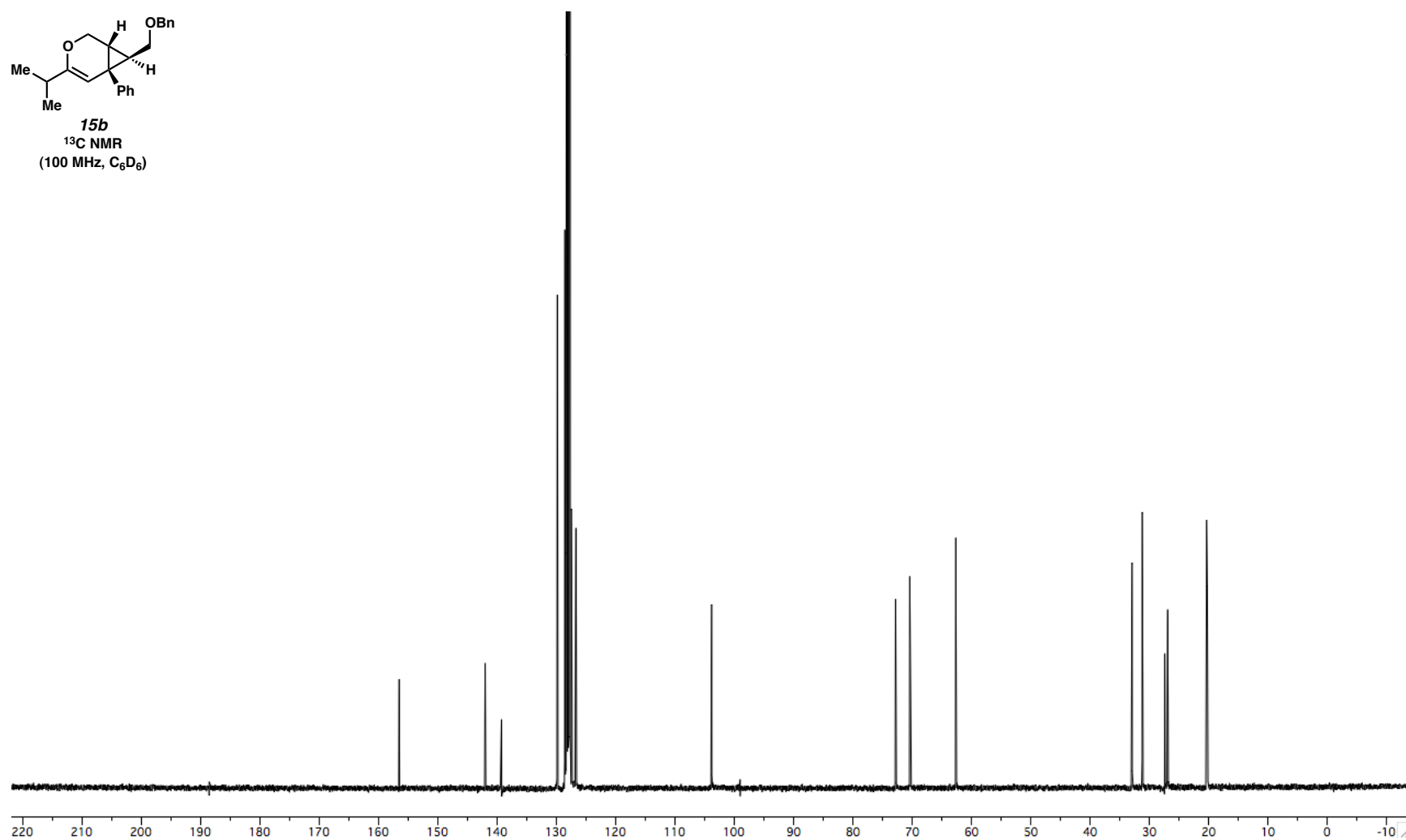
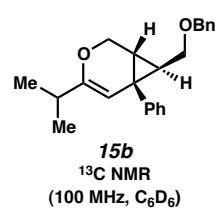


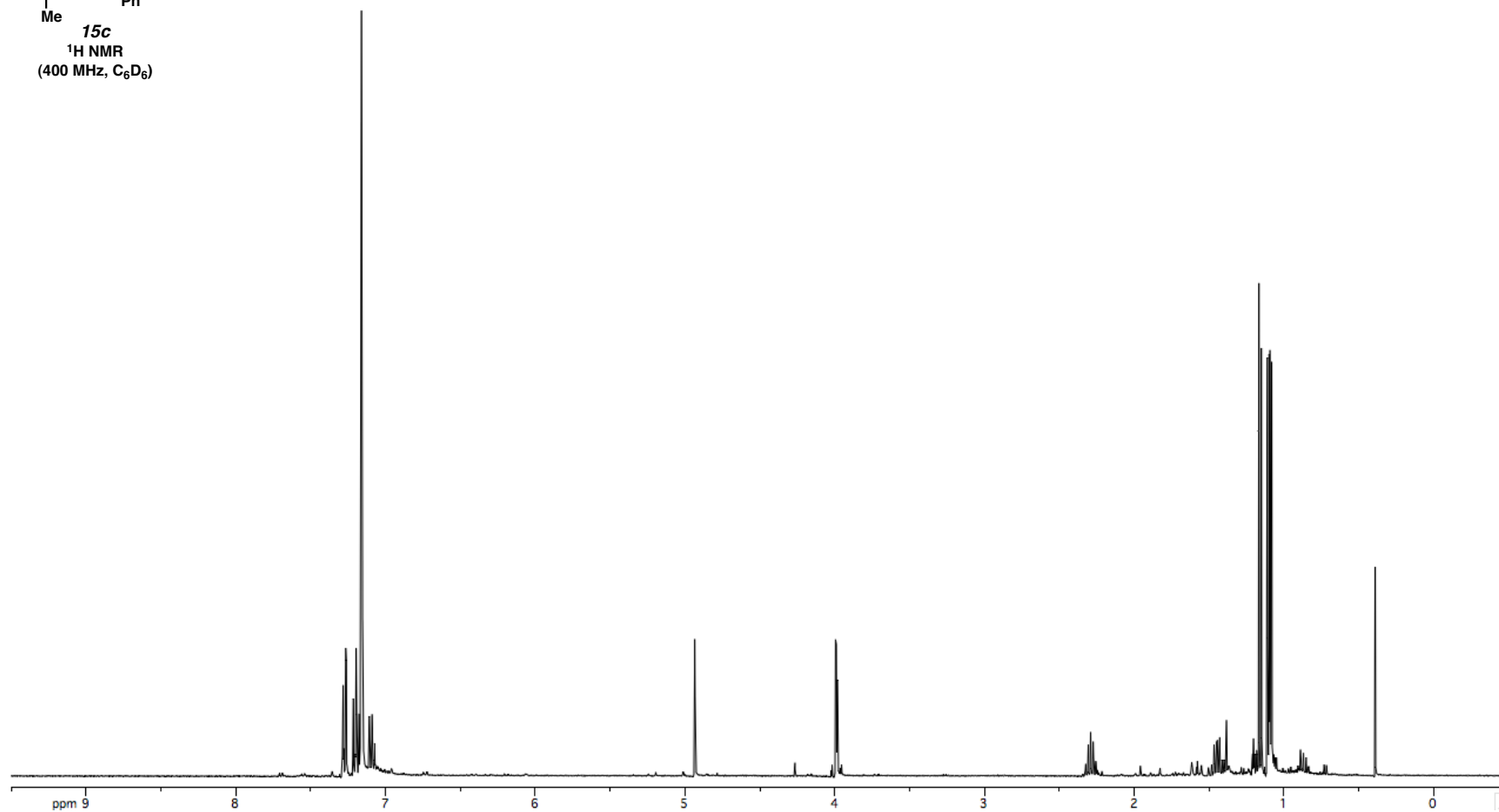
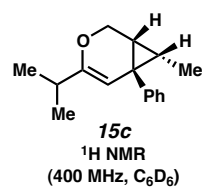


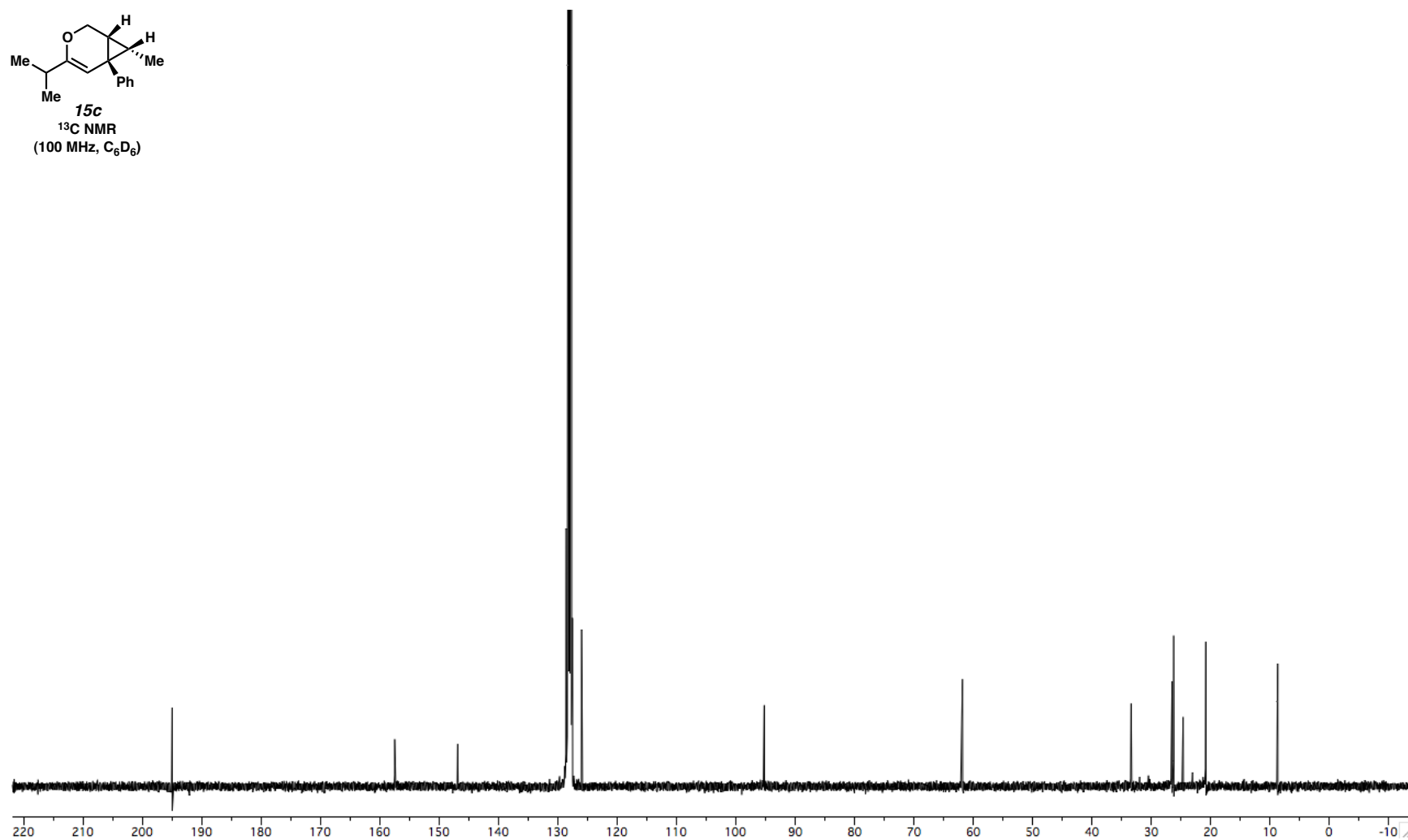
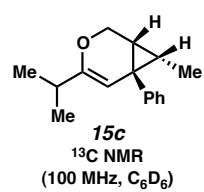
15a
 ^{13}C NMR
(100 MHz, C_6D_6)

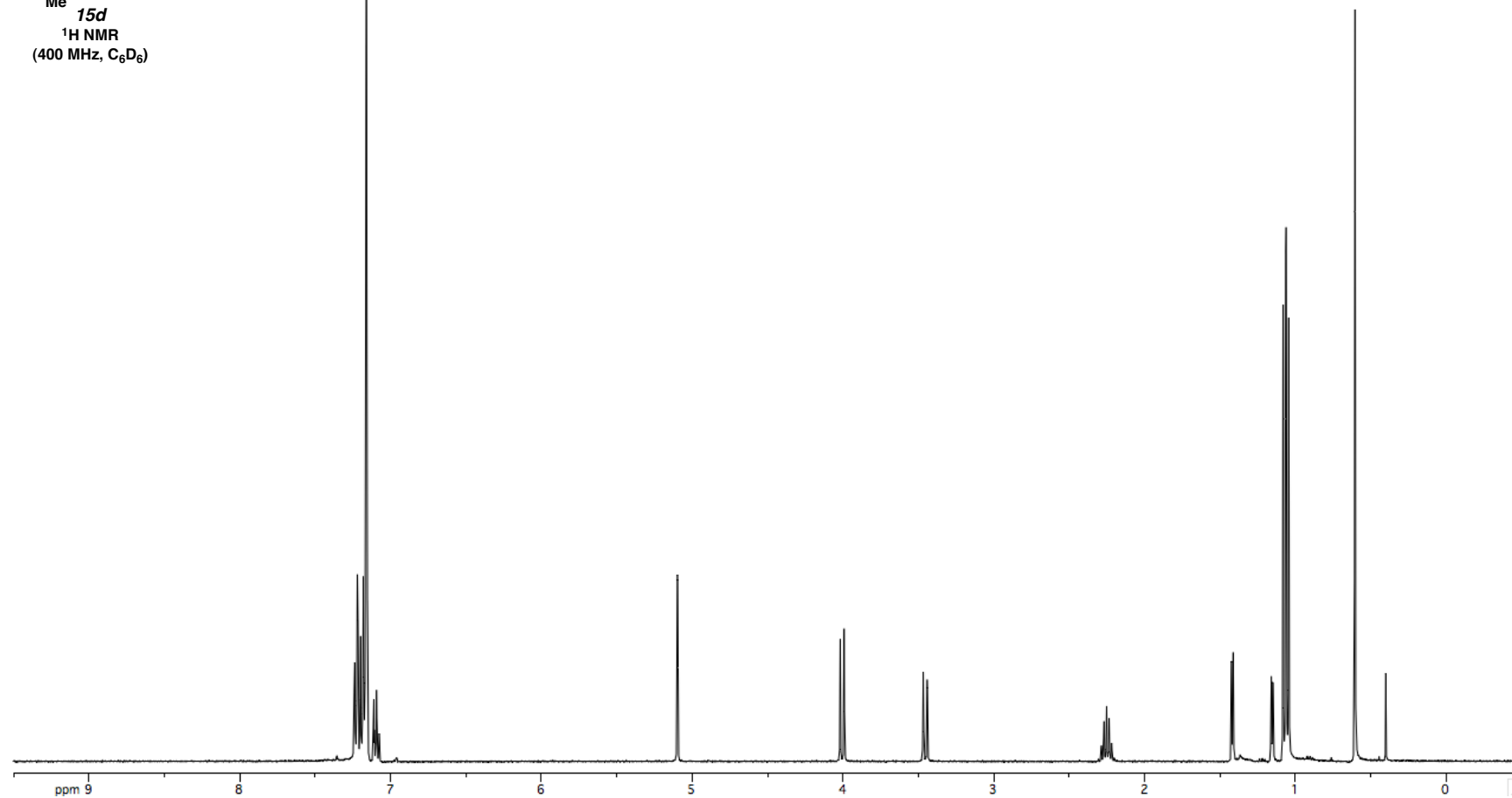
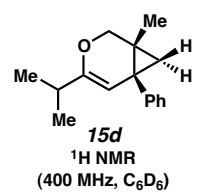


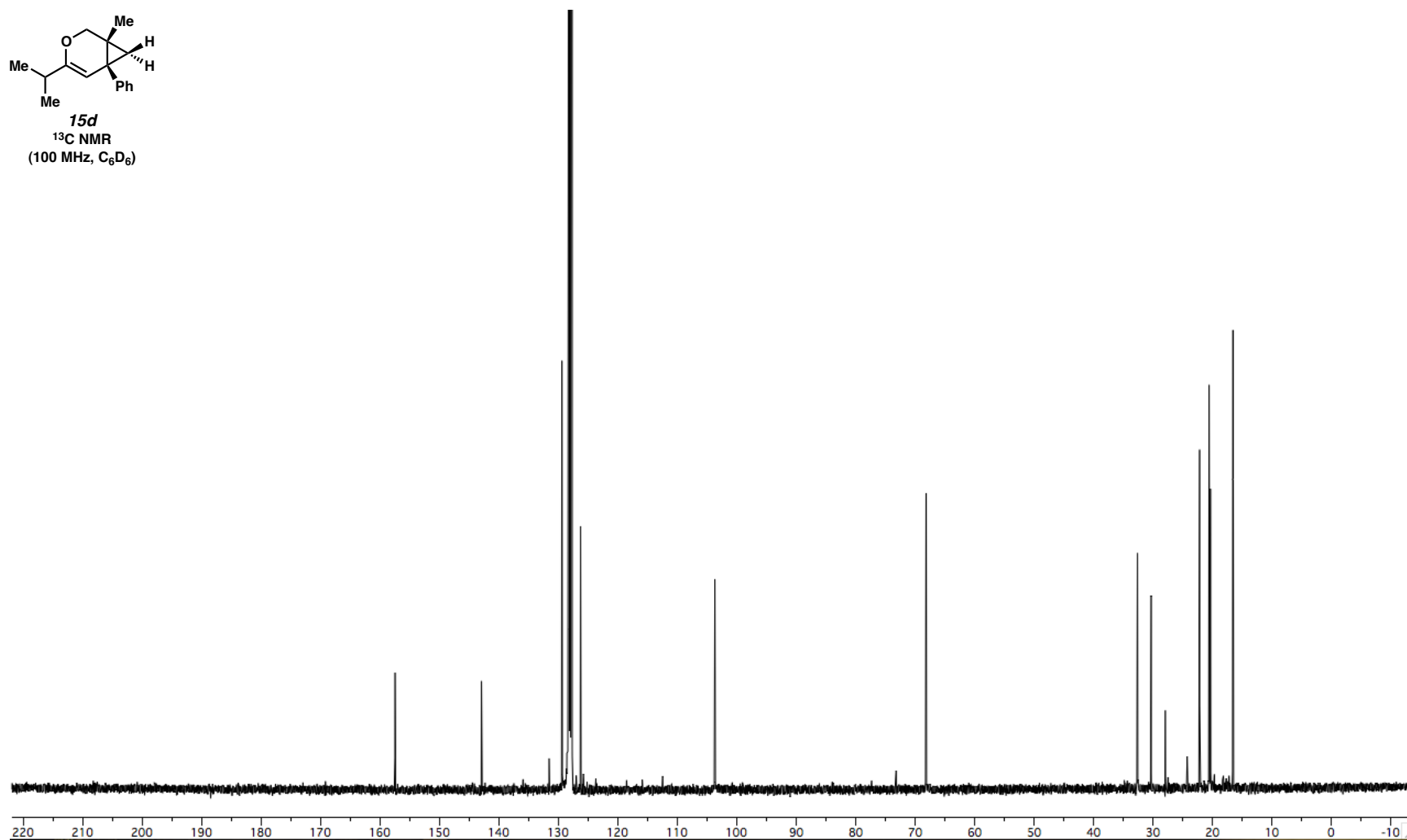
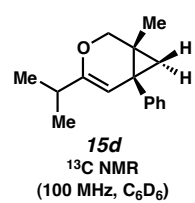


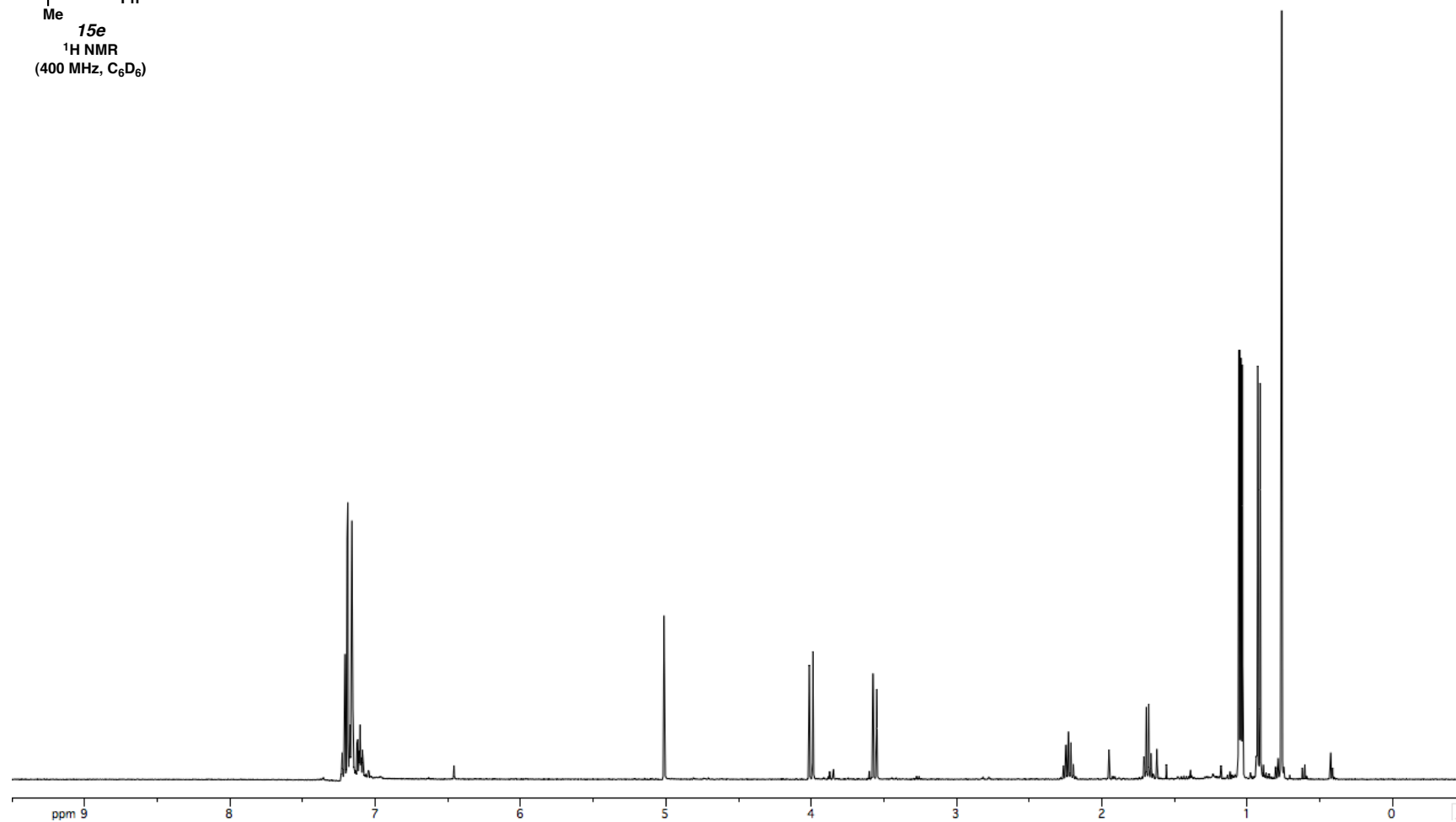
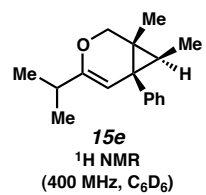


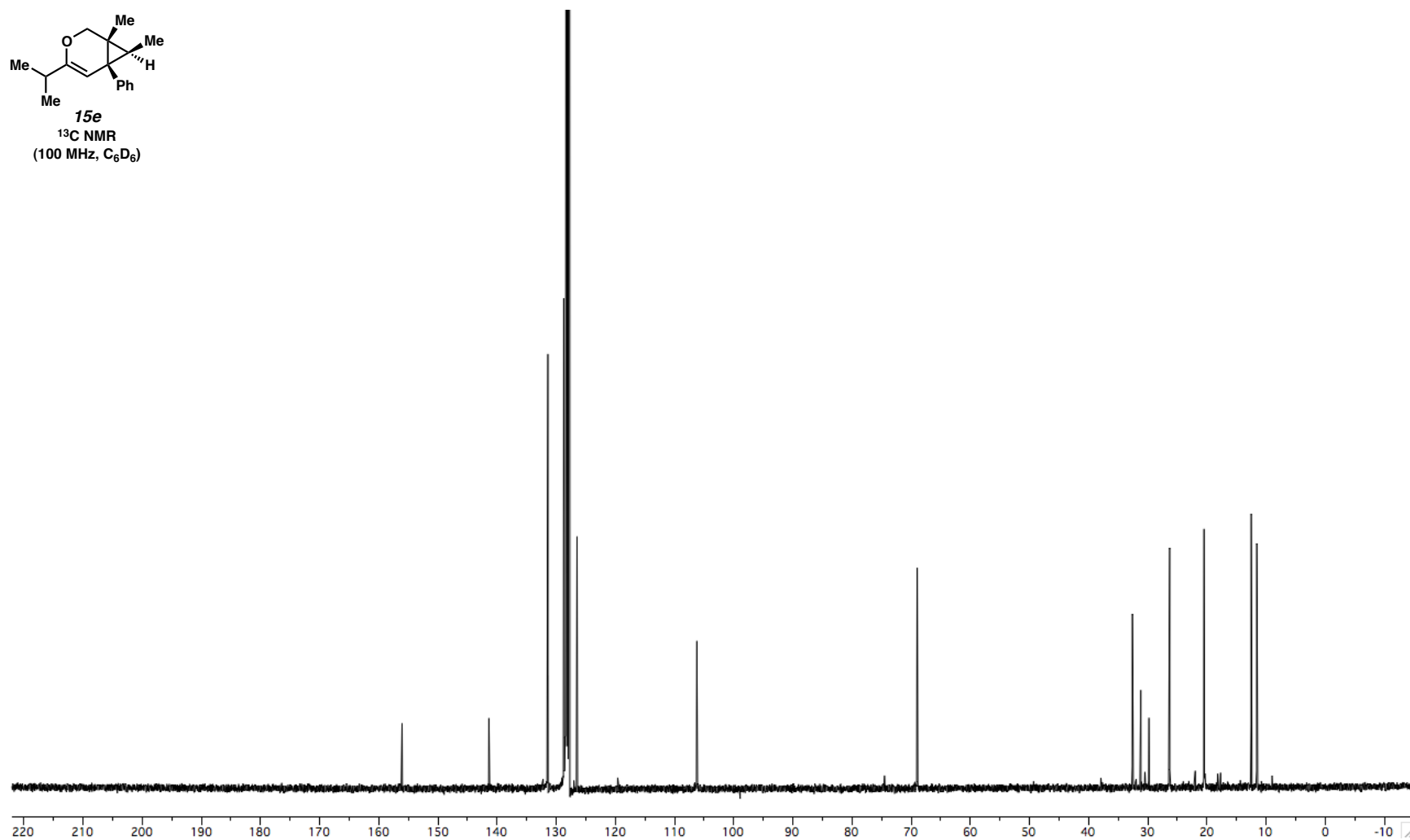
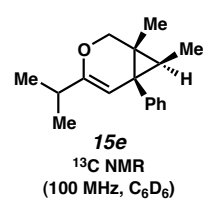


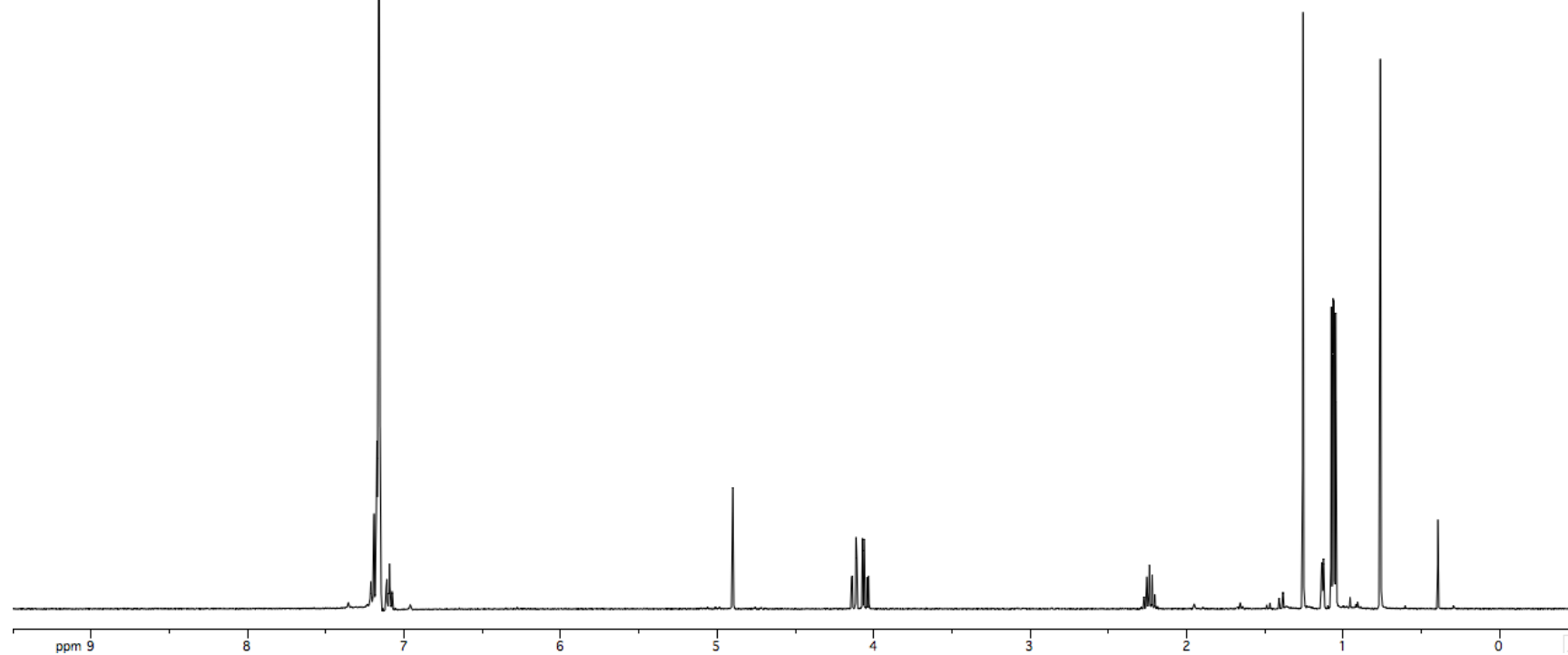
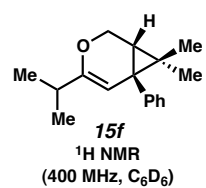


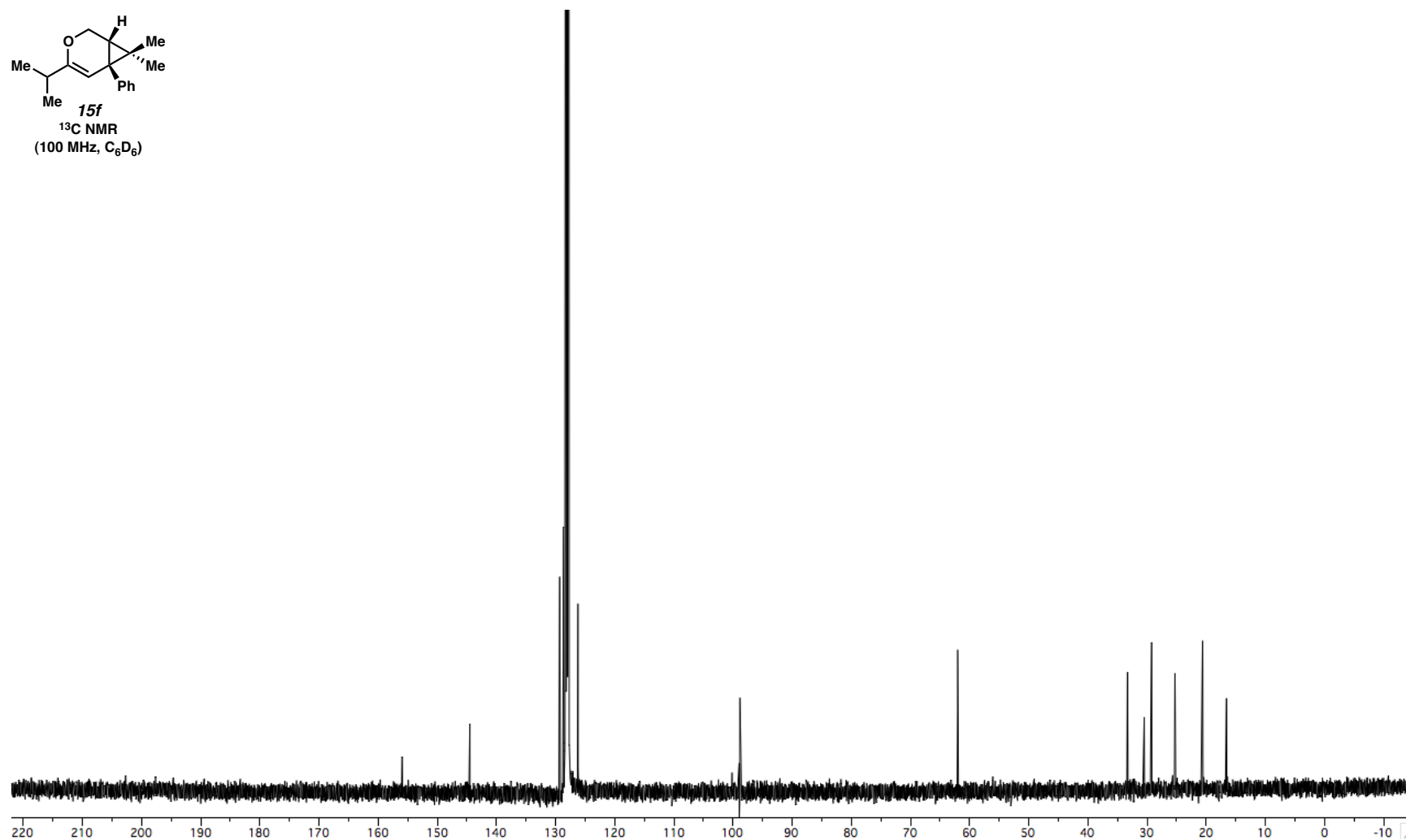
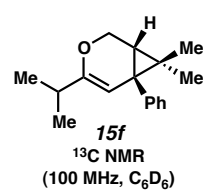


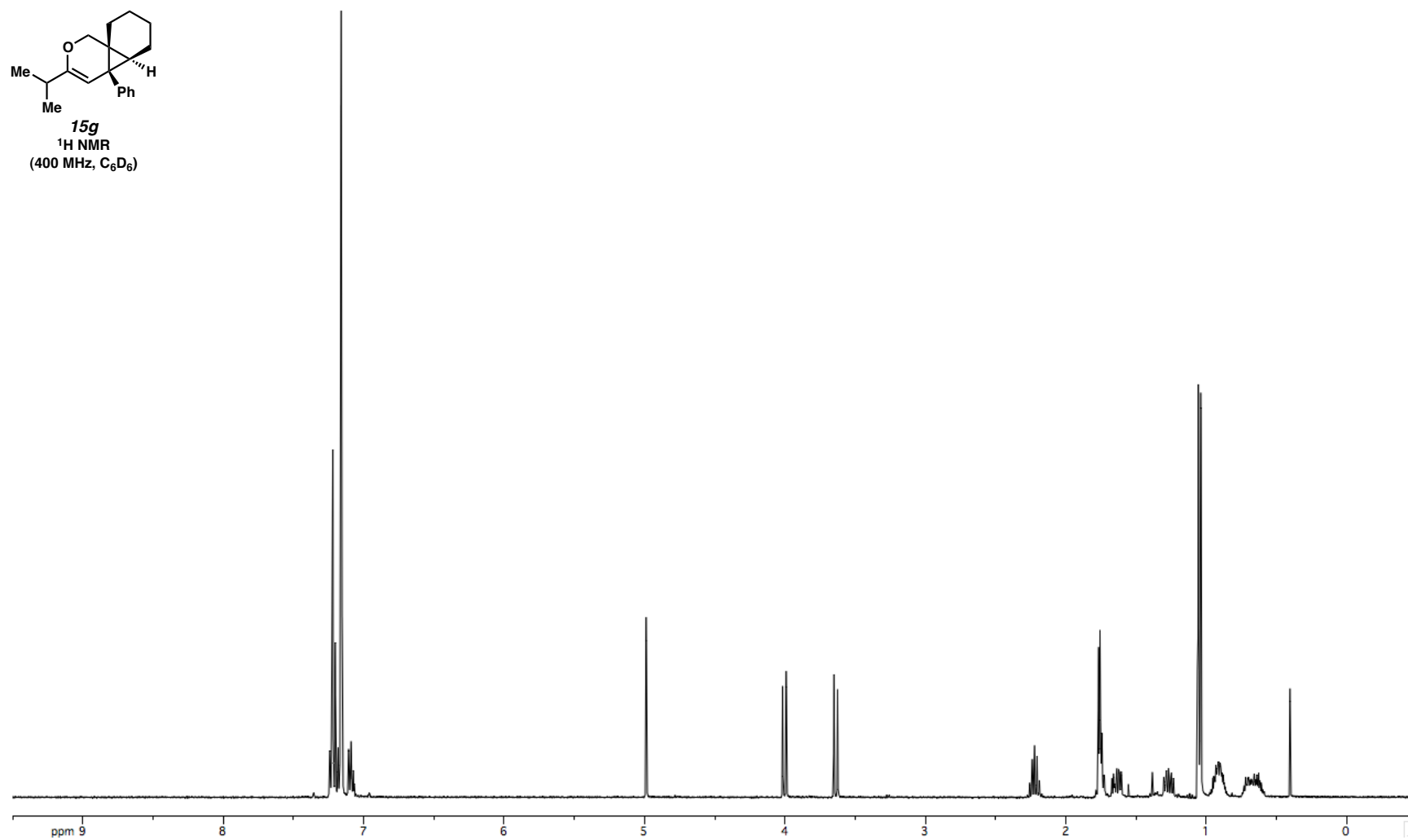
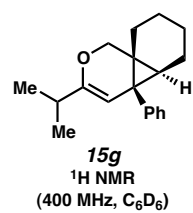


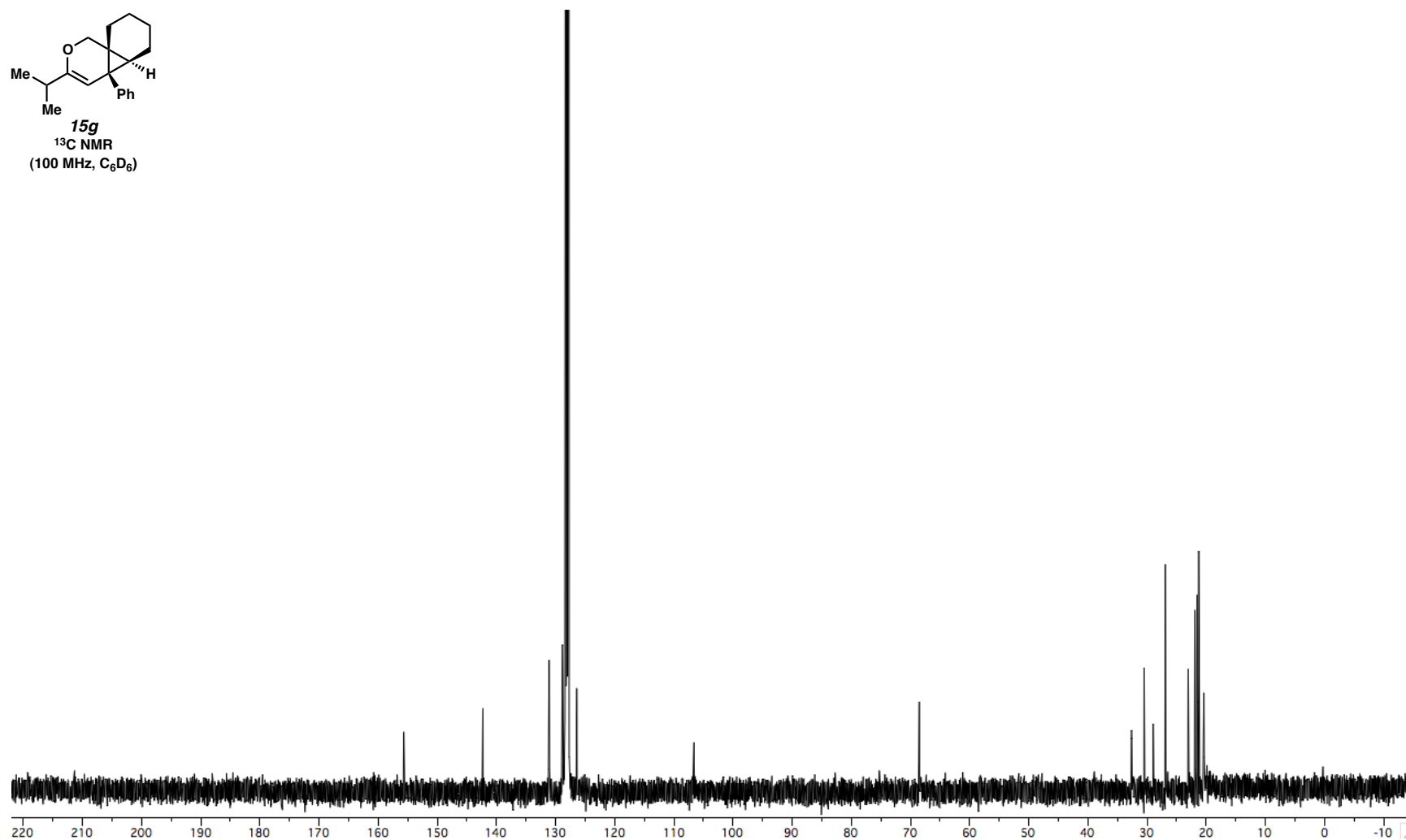
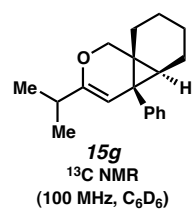


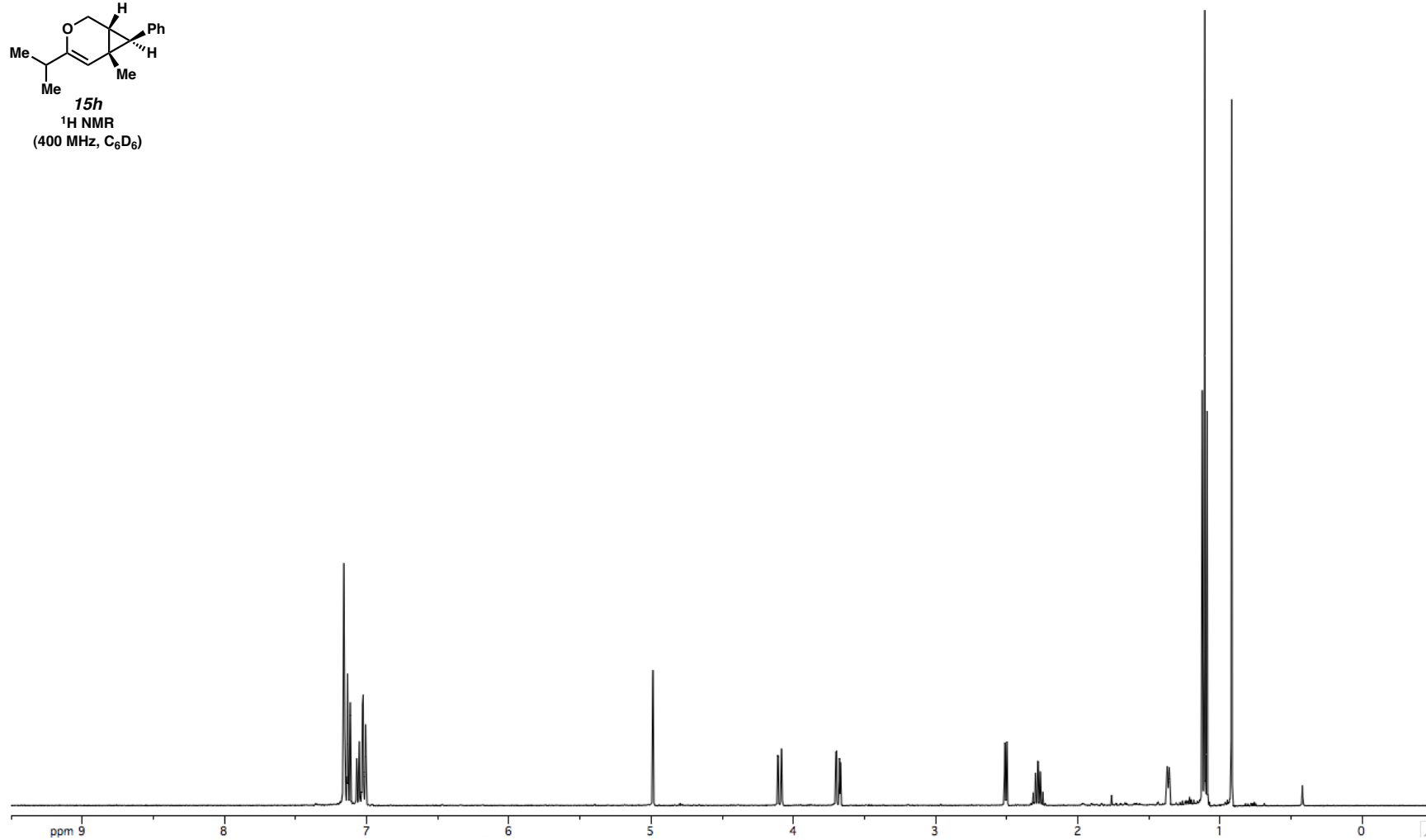
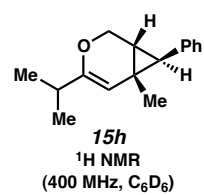


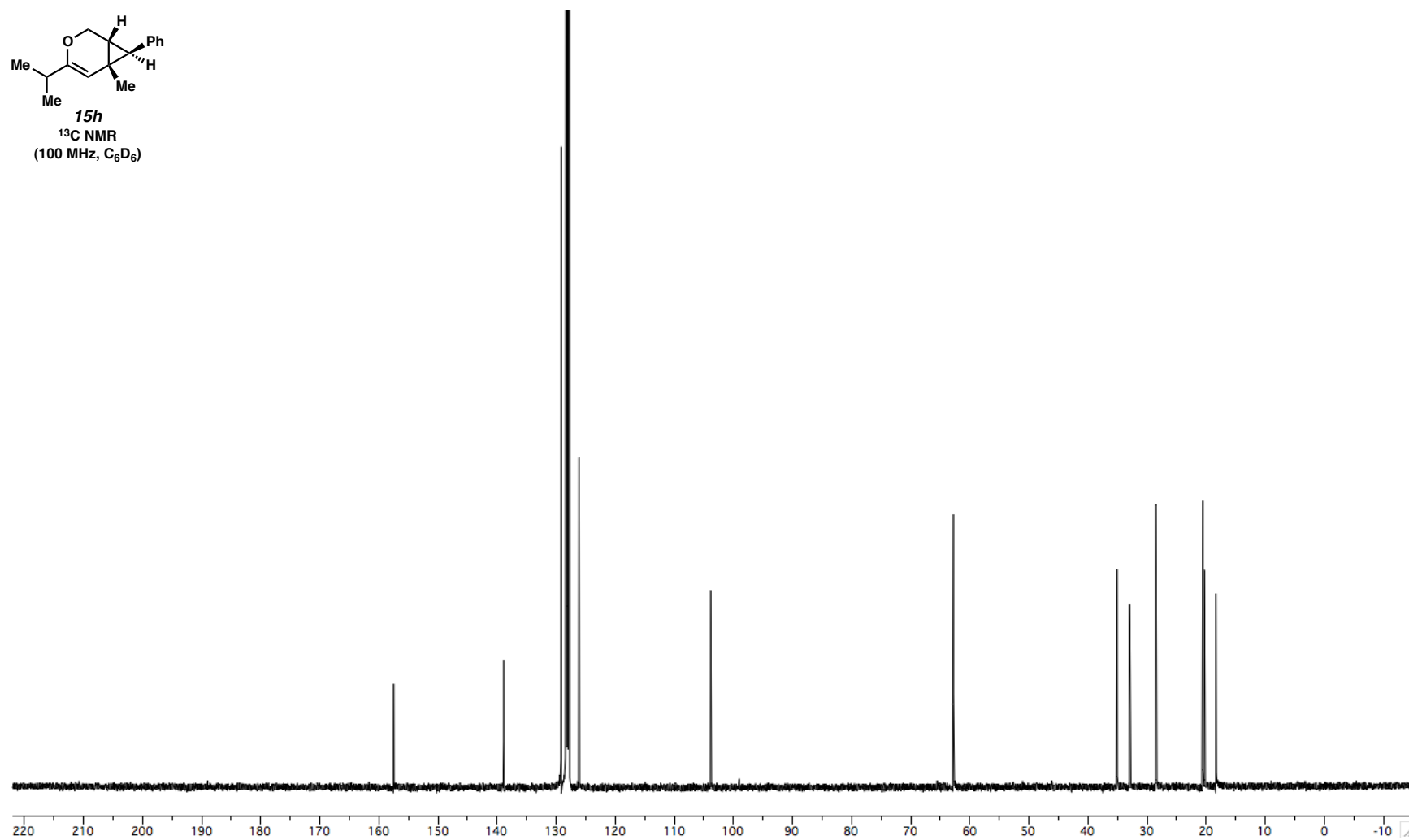
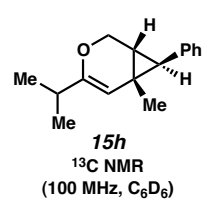


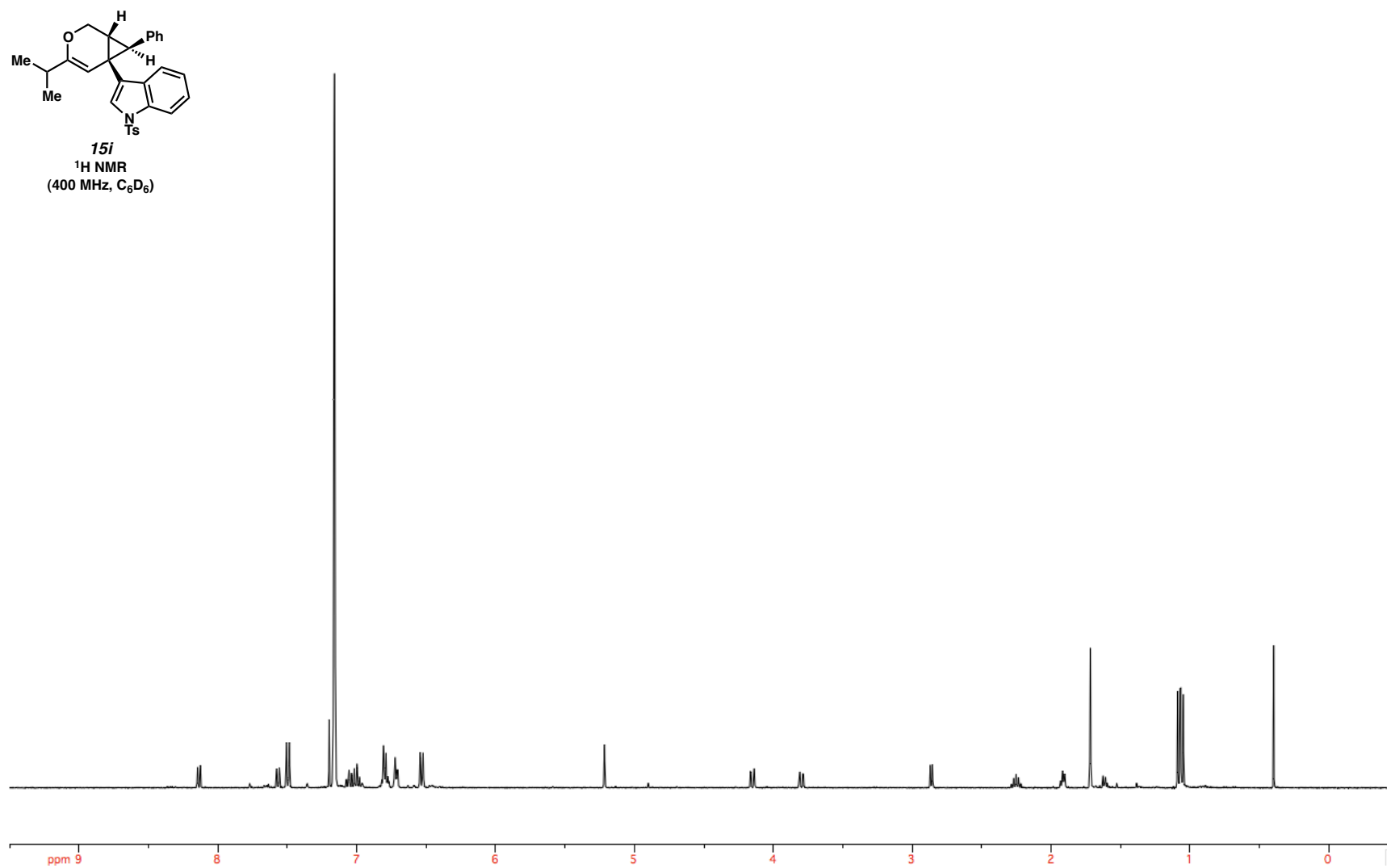


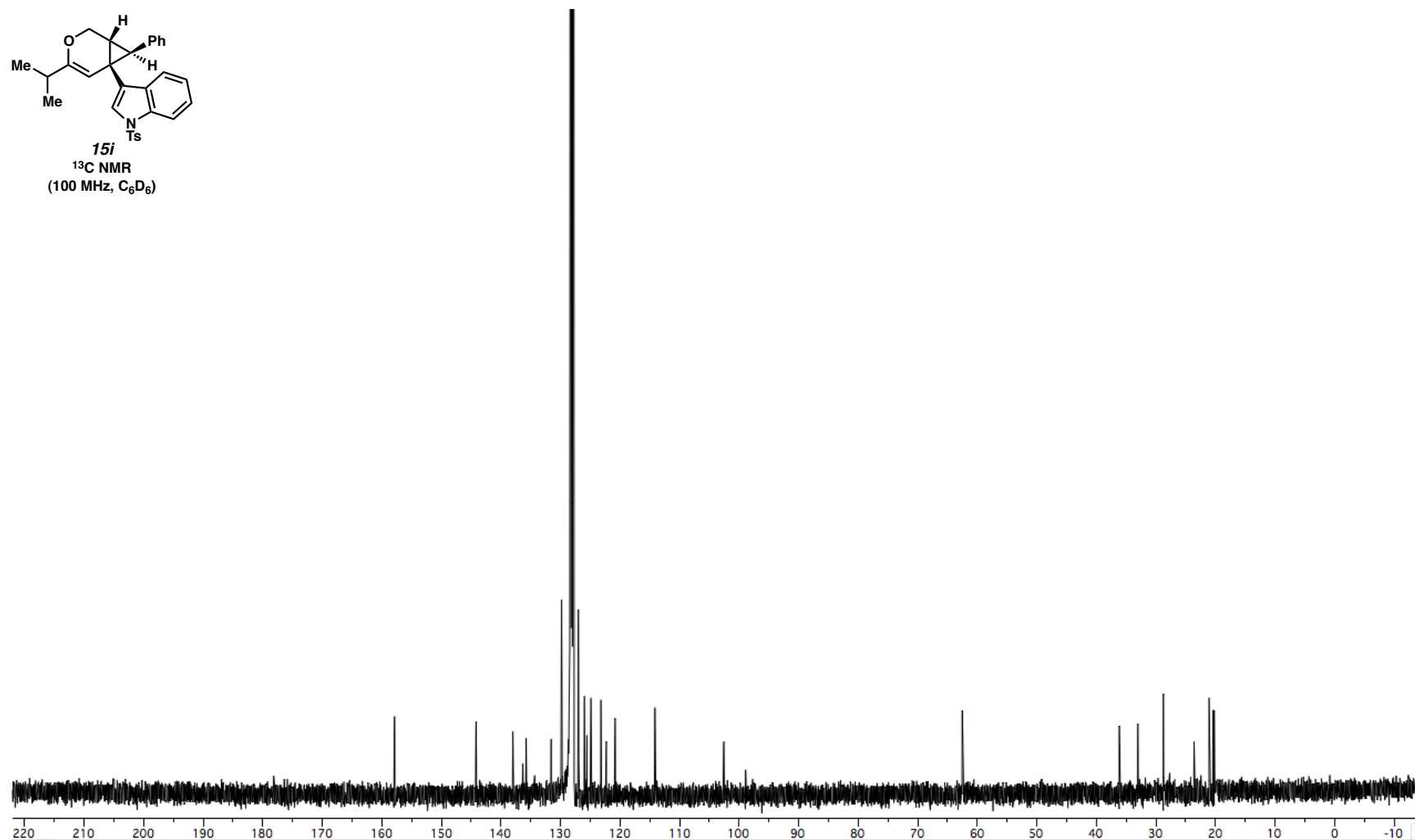


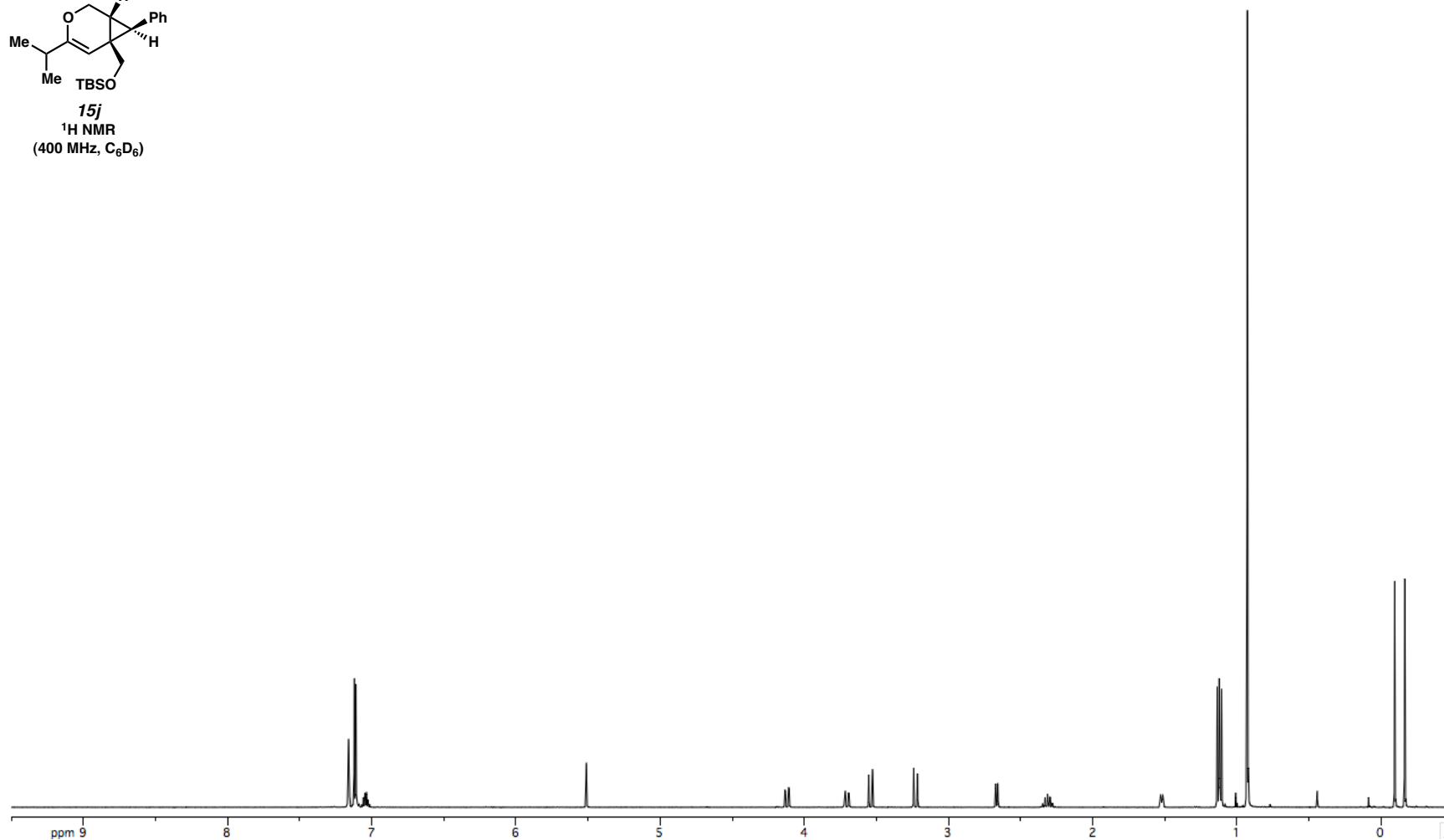
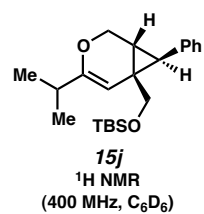


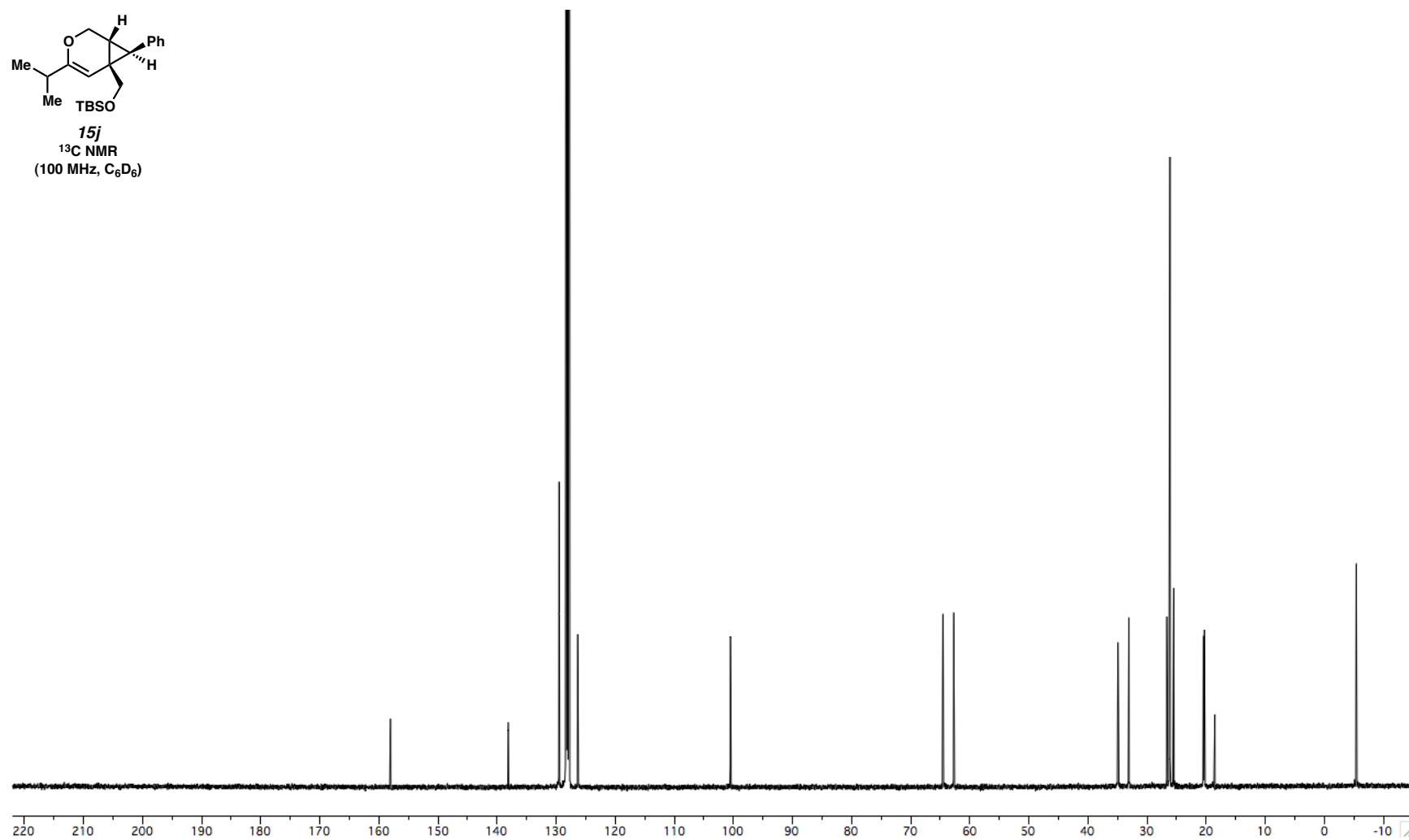
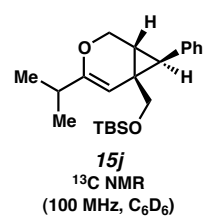


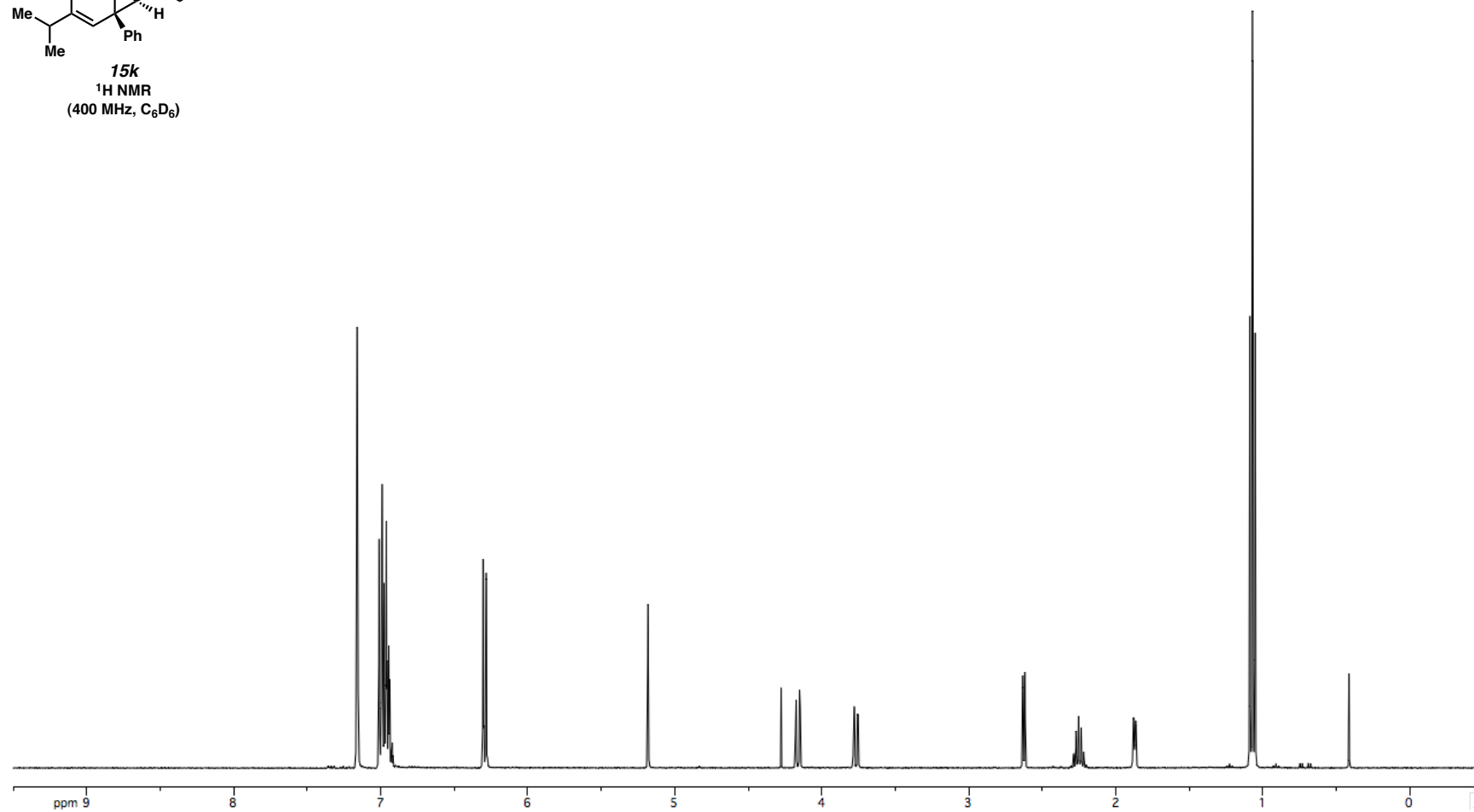
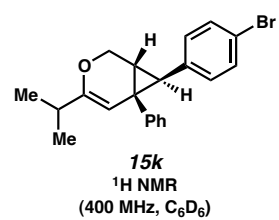


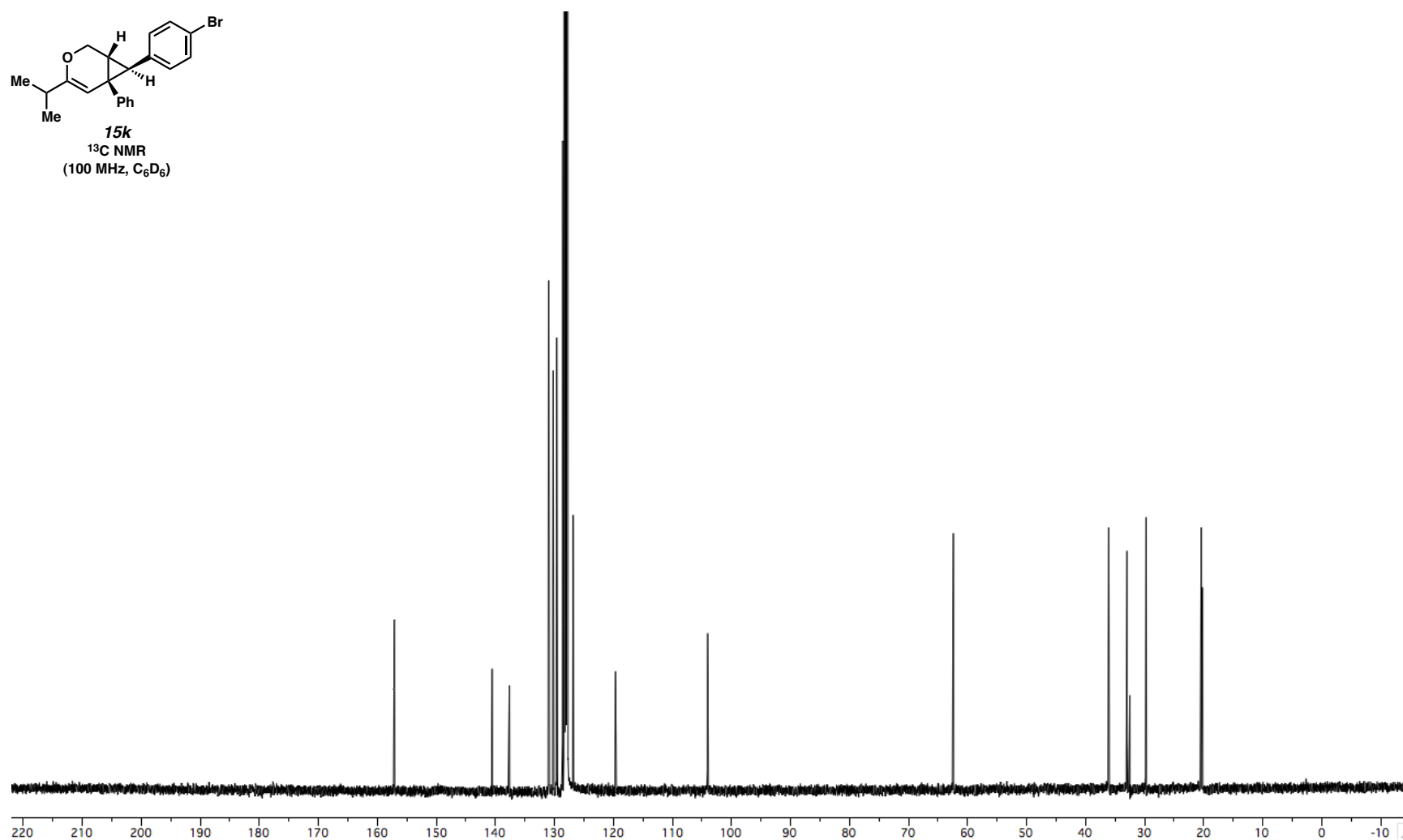
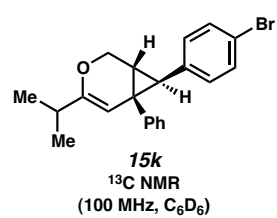


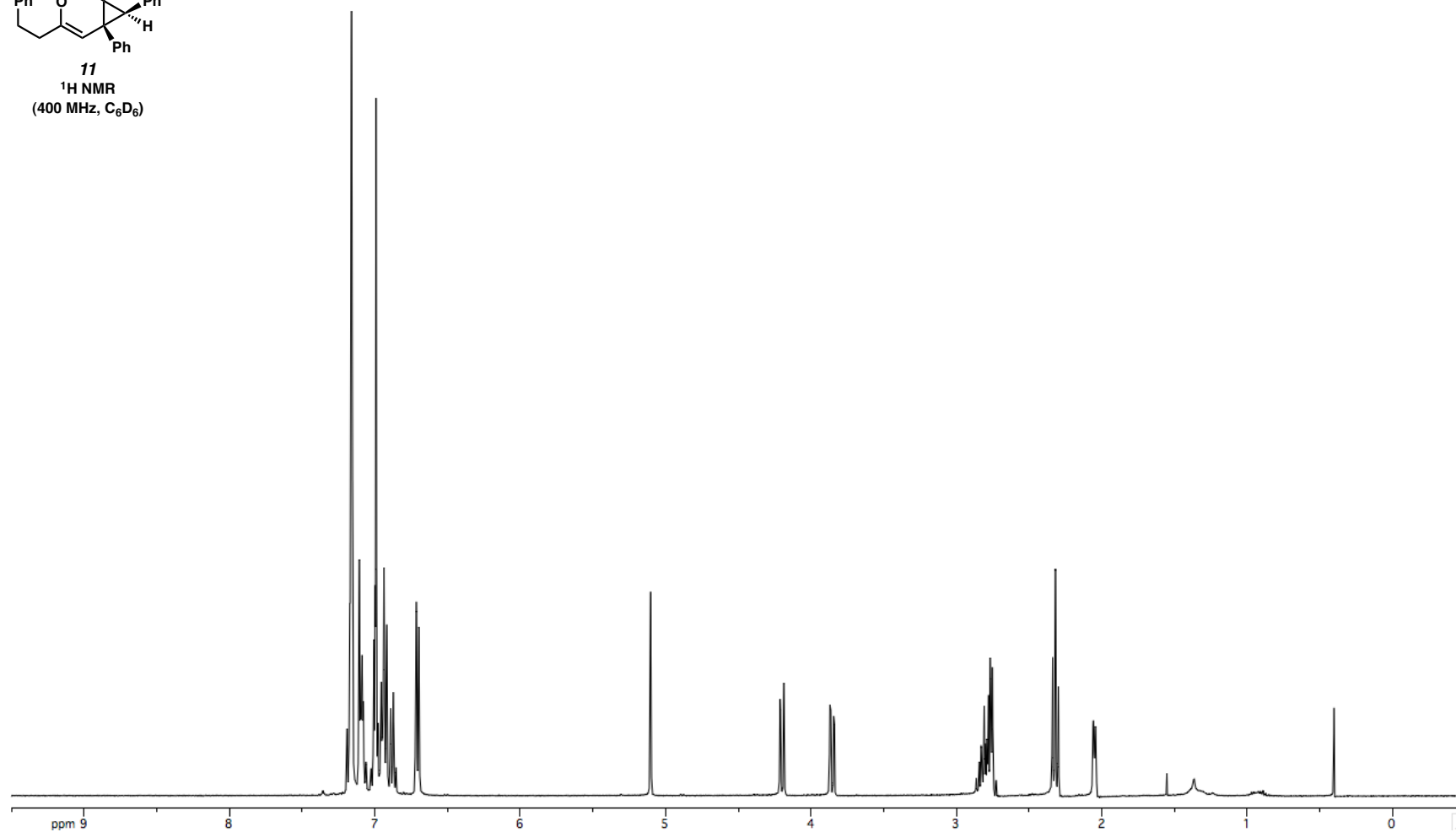
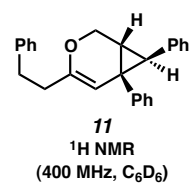


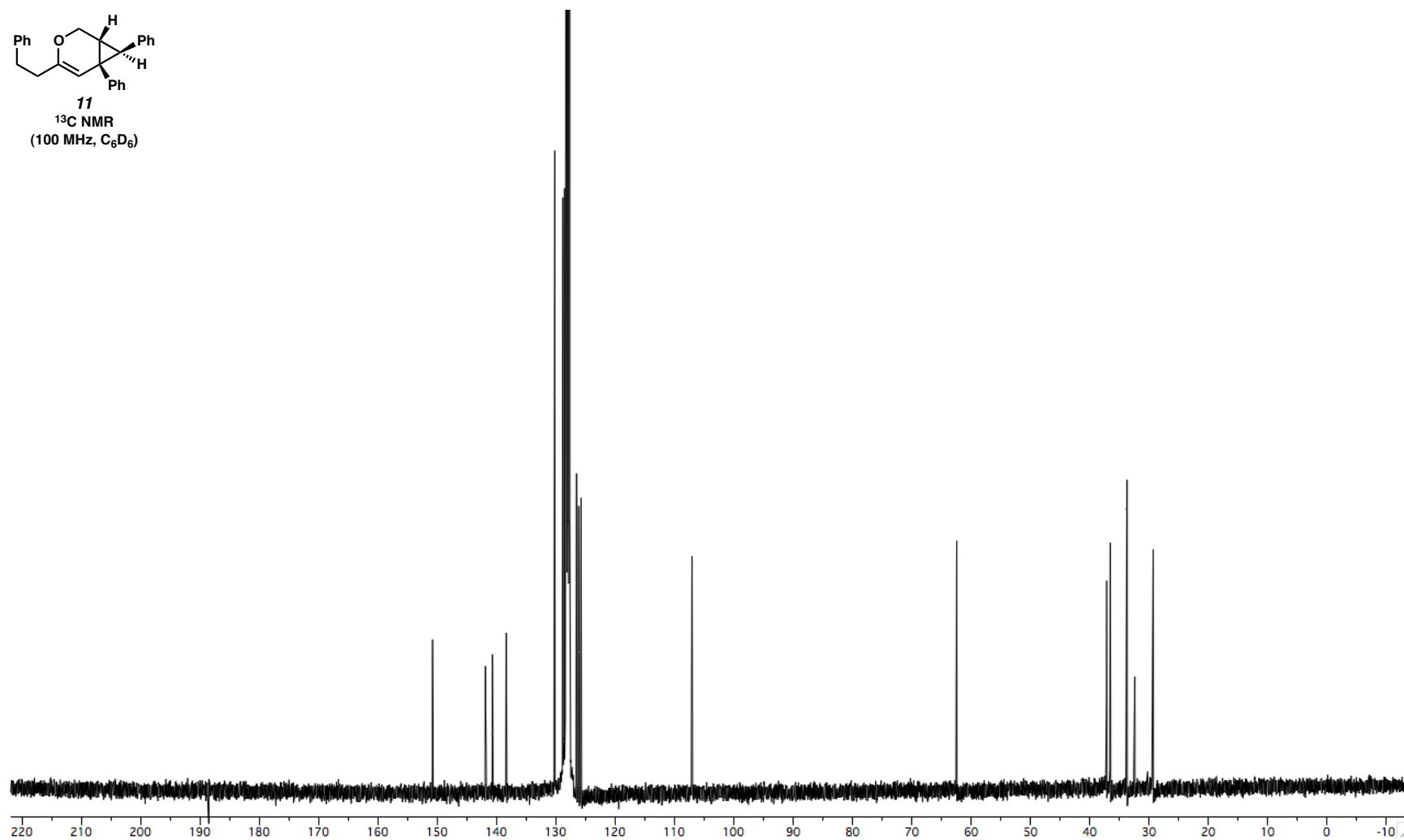
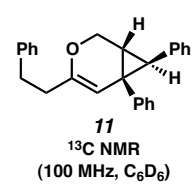


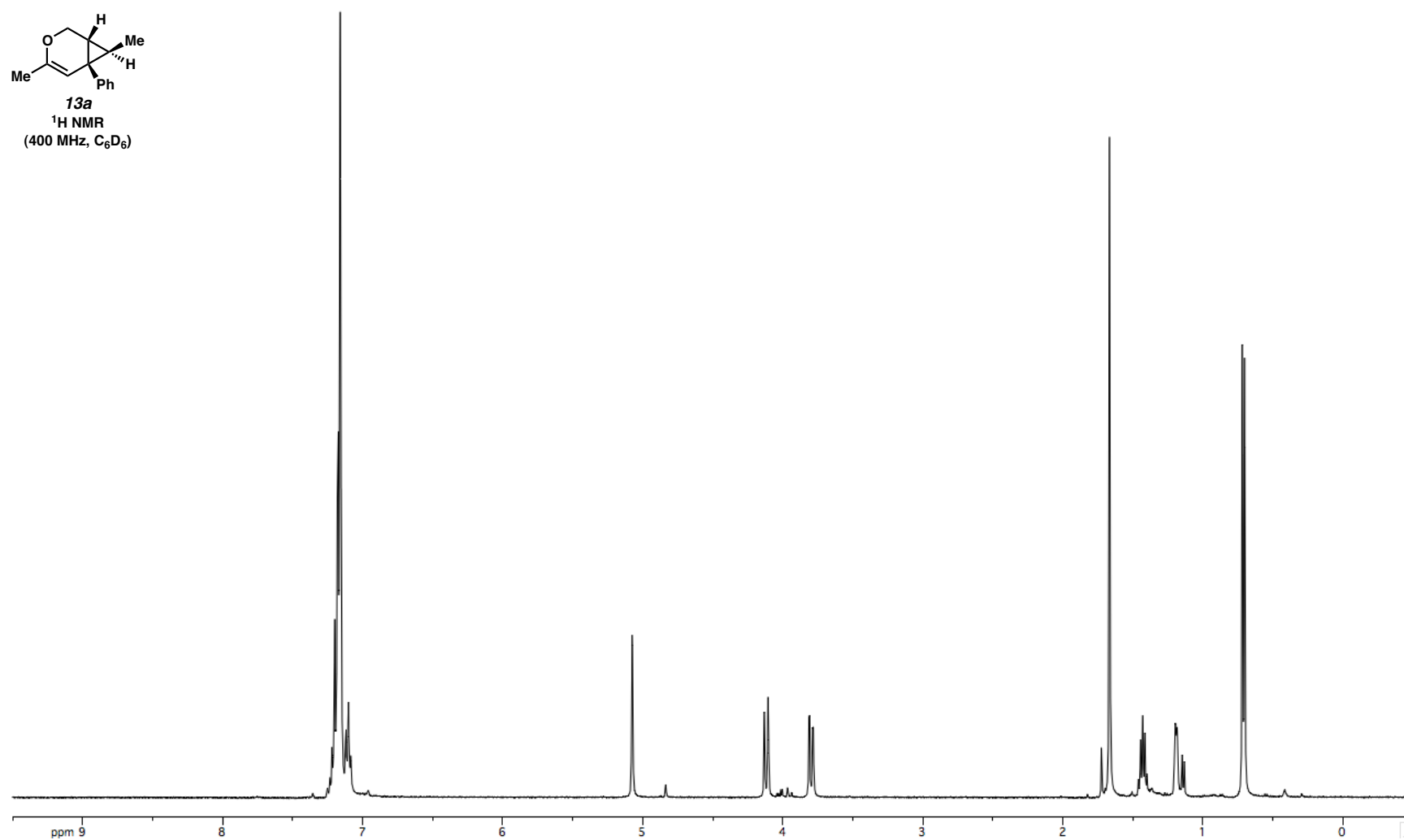
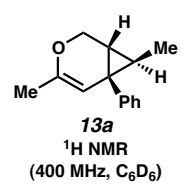


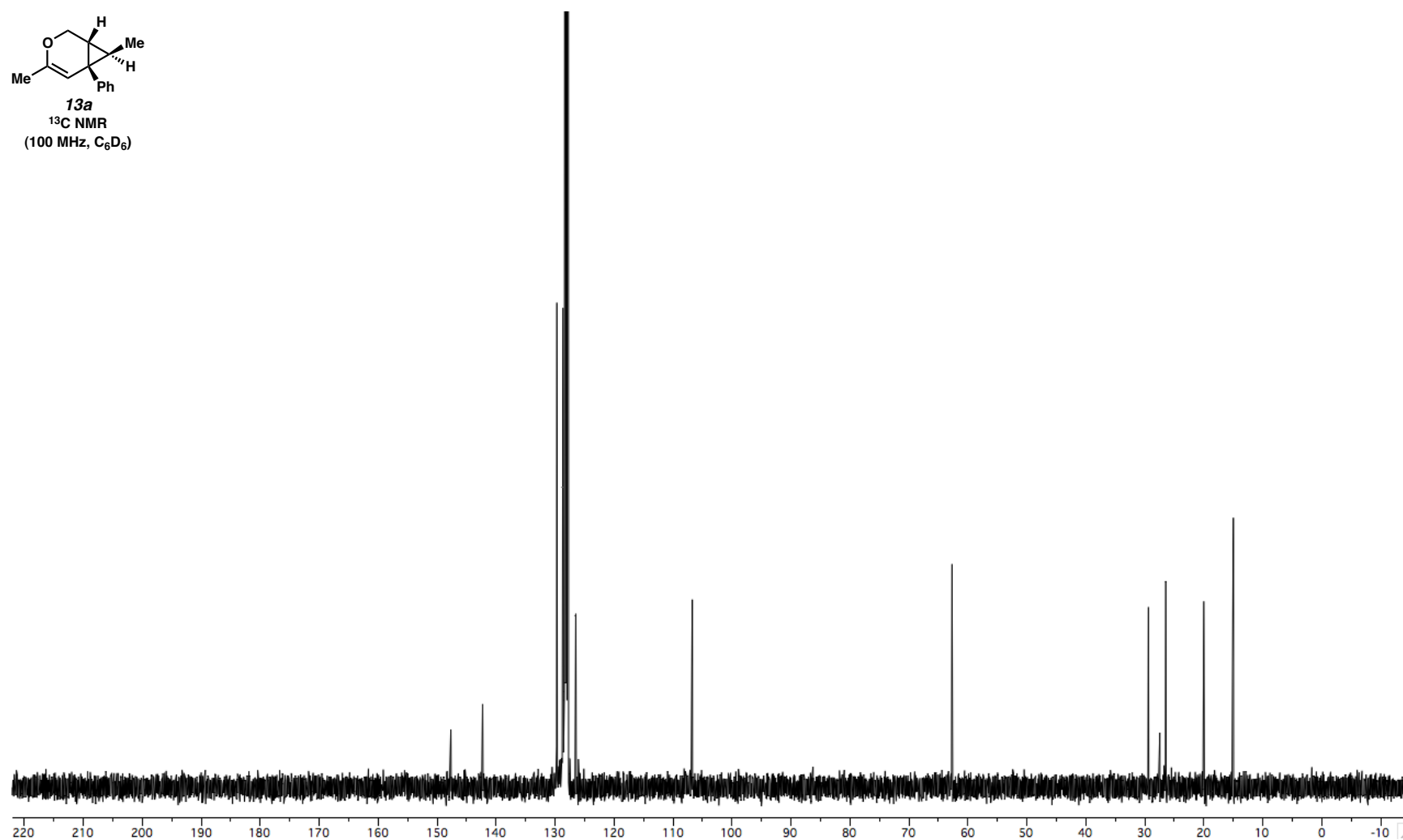
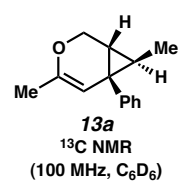


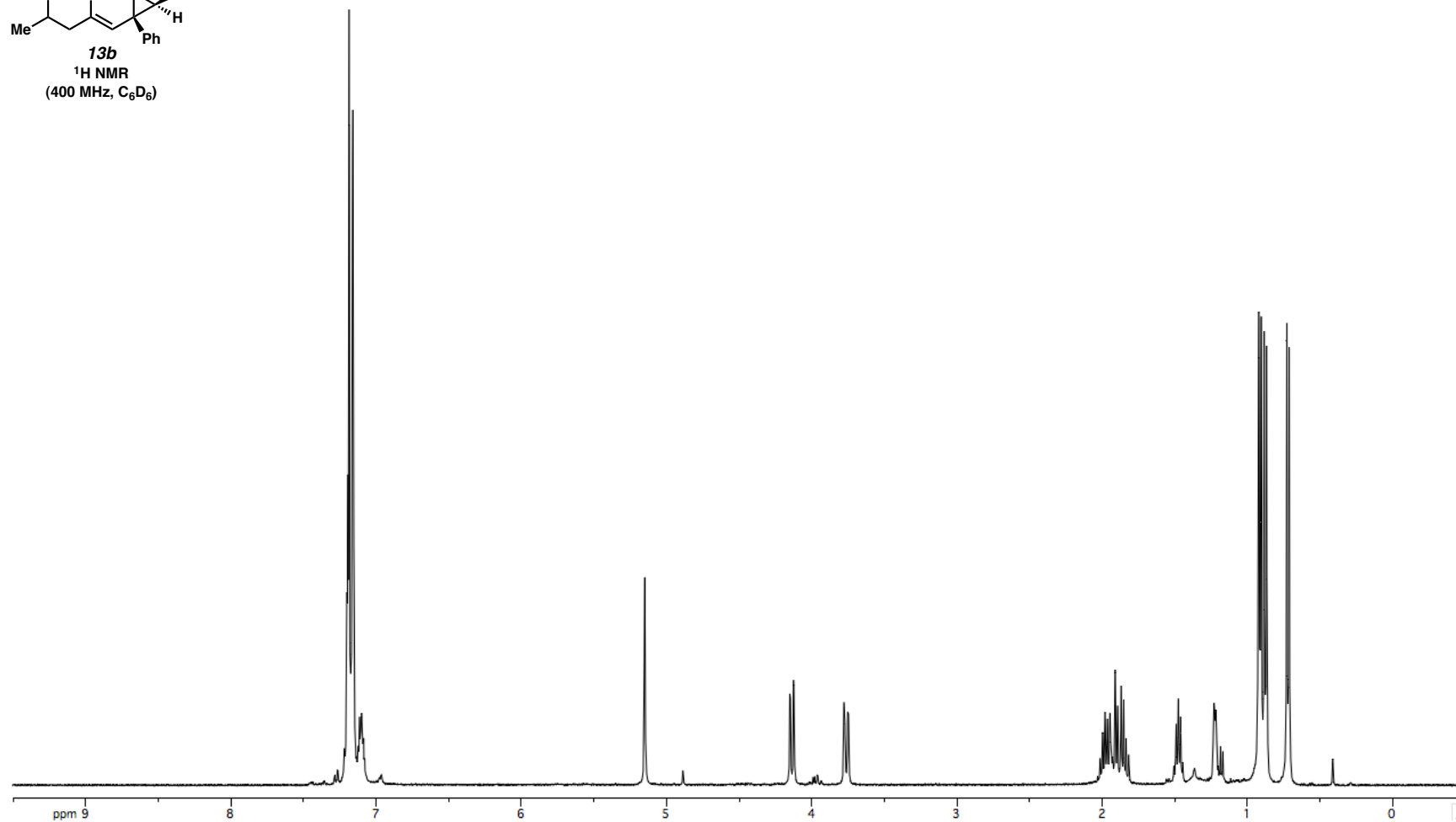
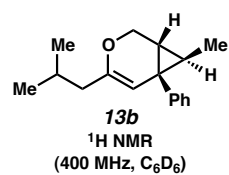


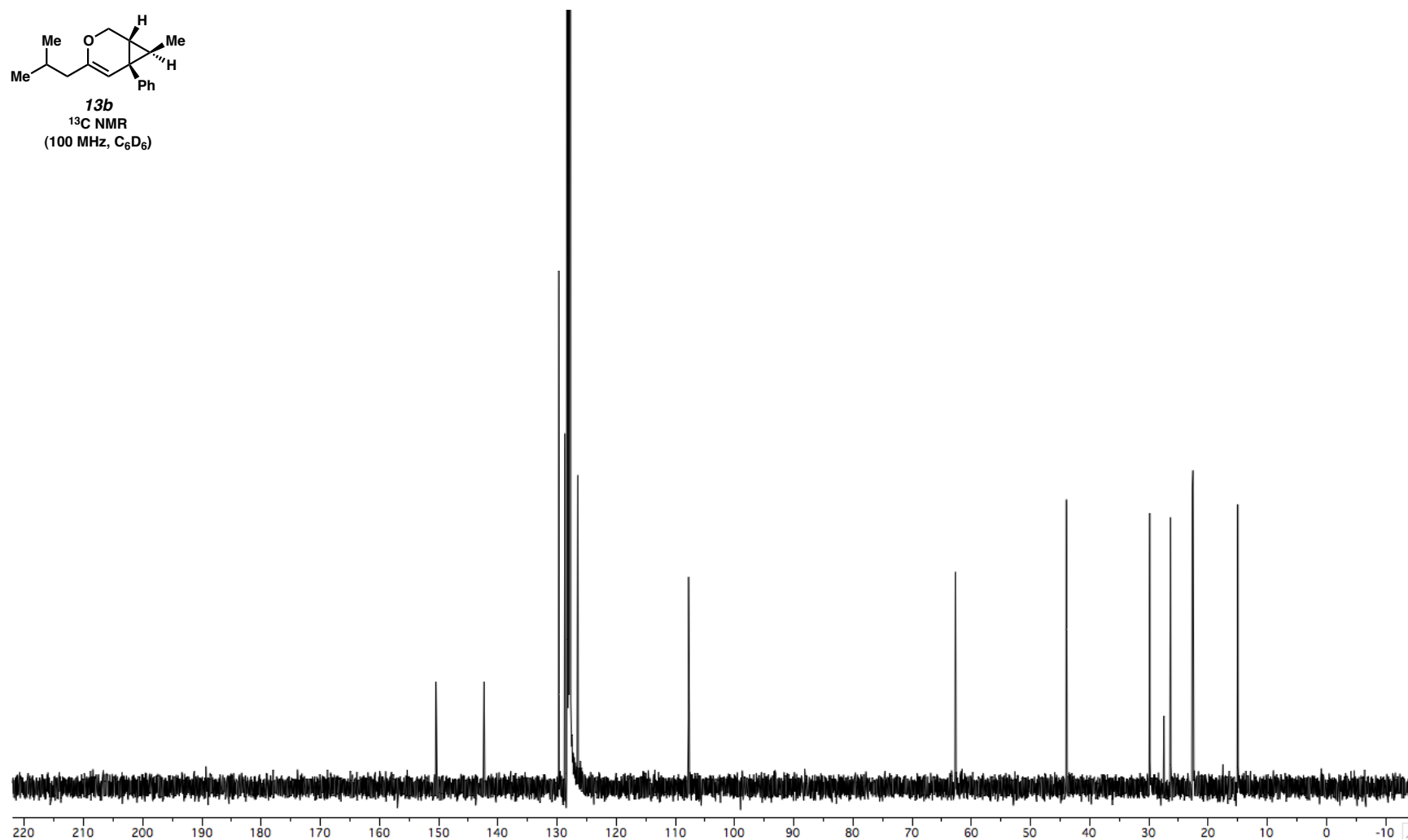
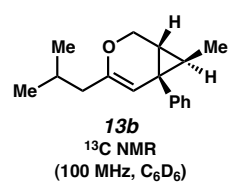


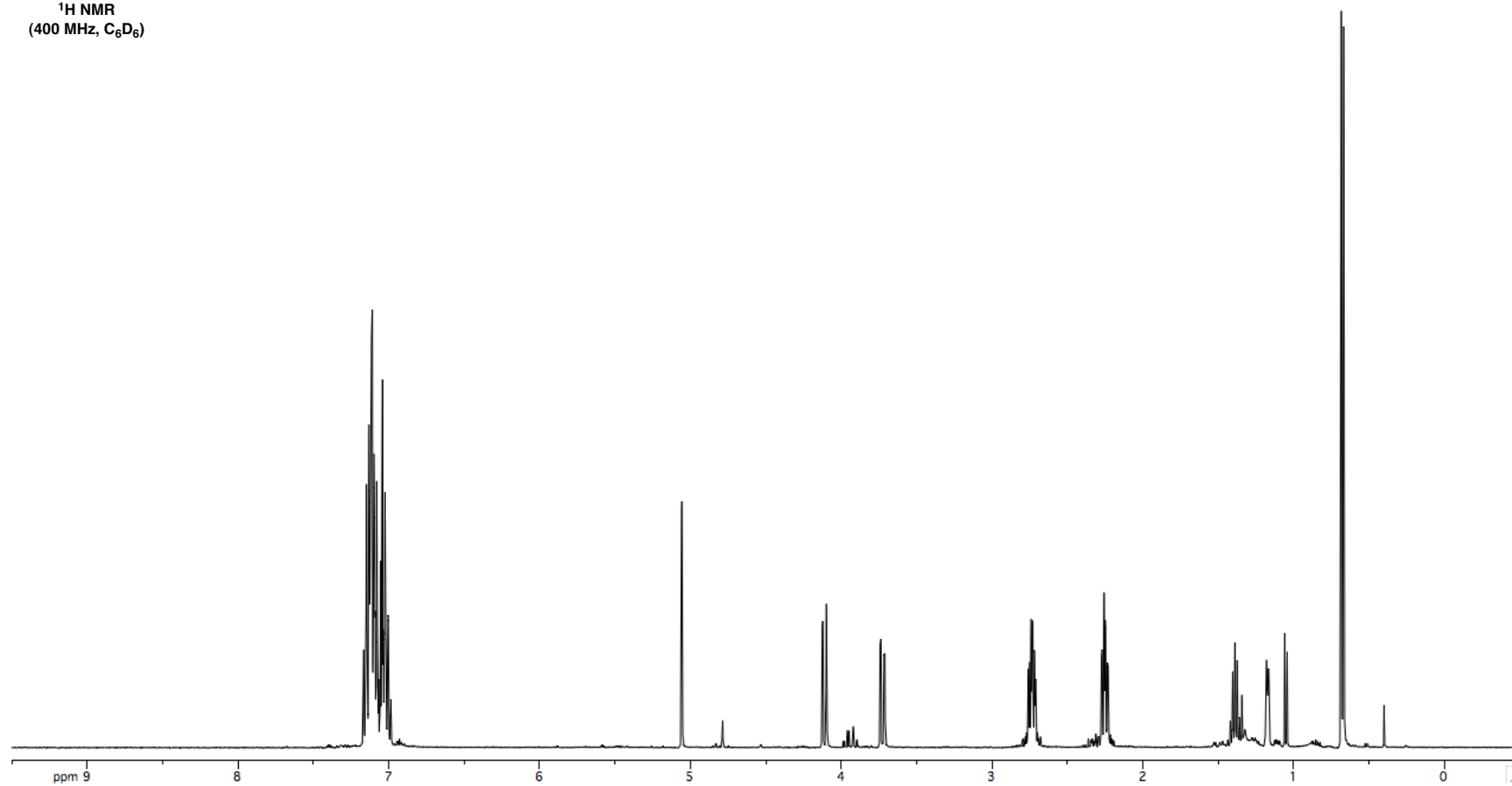
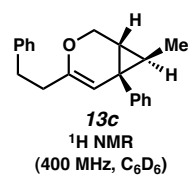


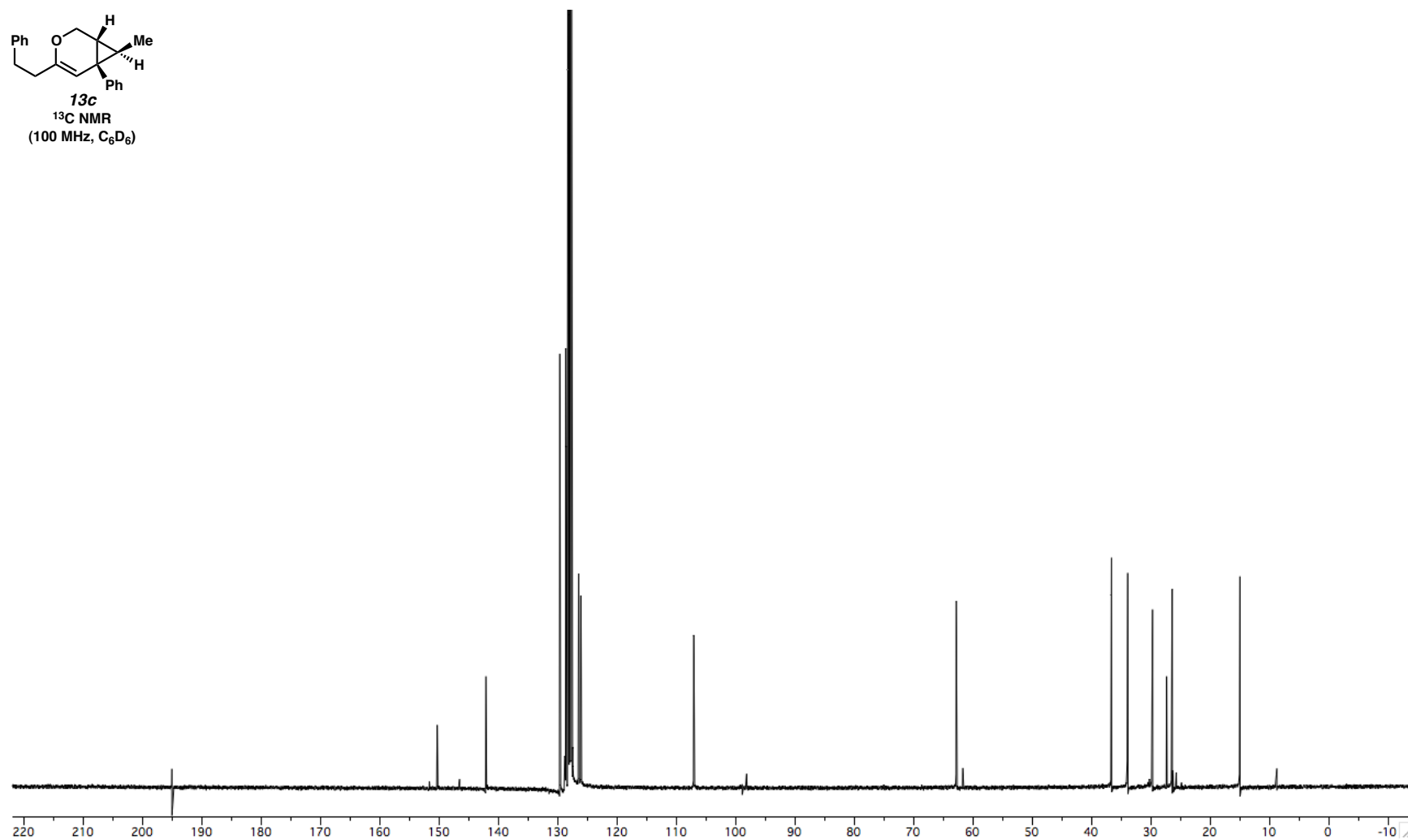
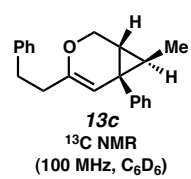


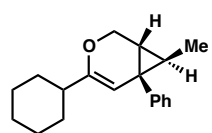




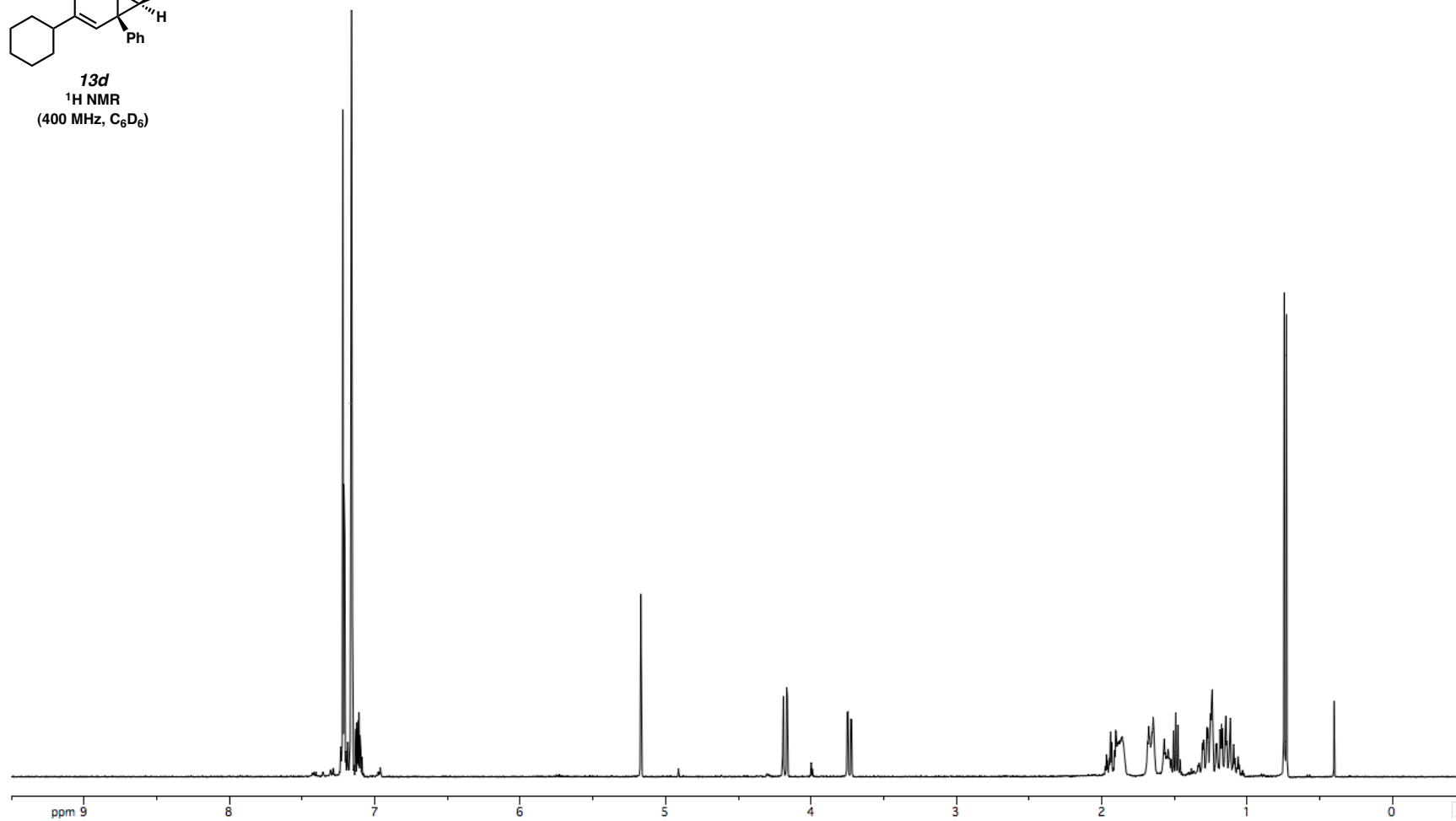


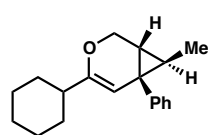




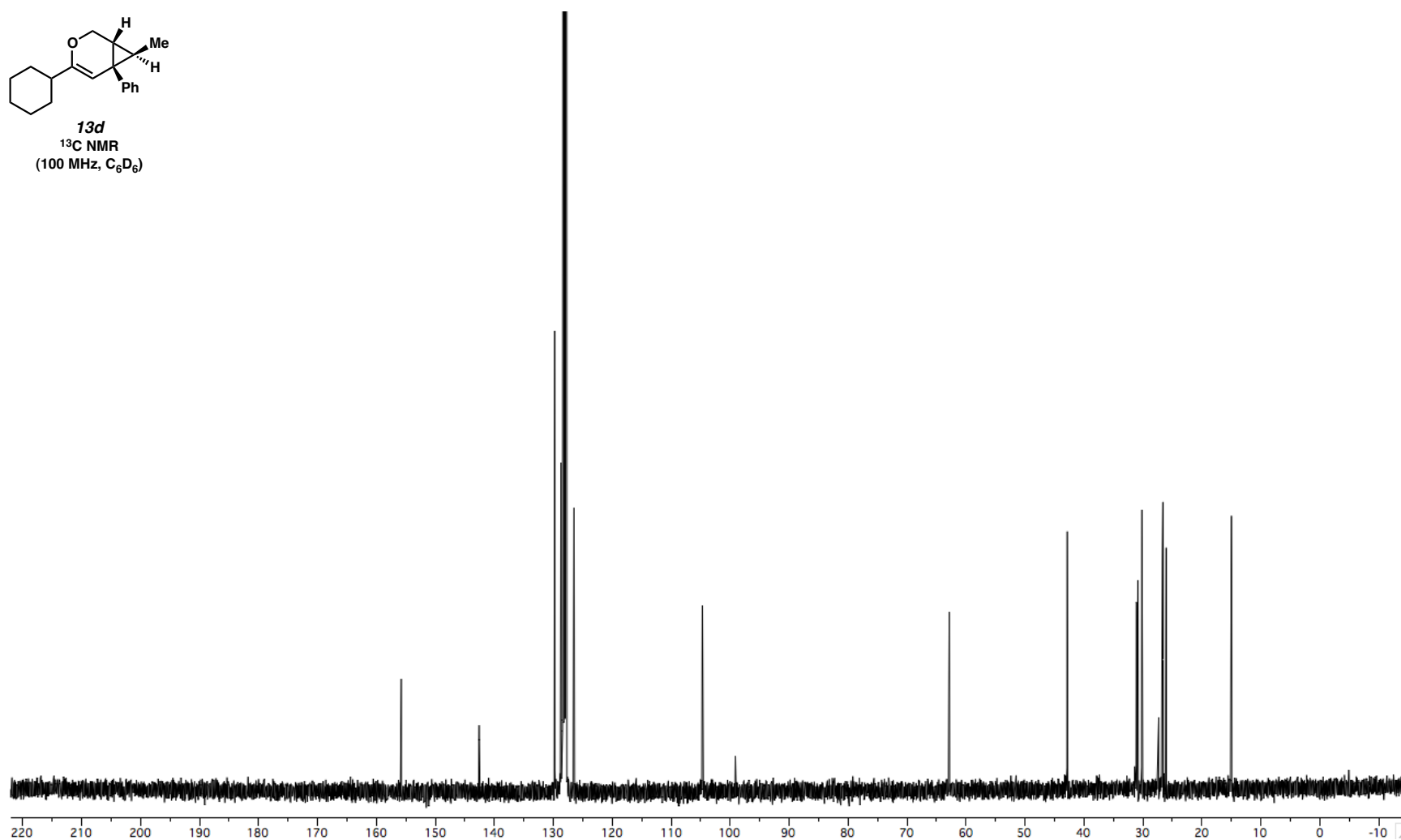


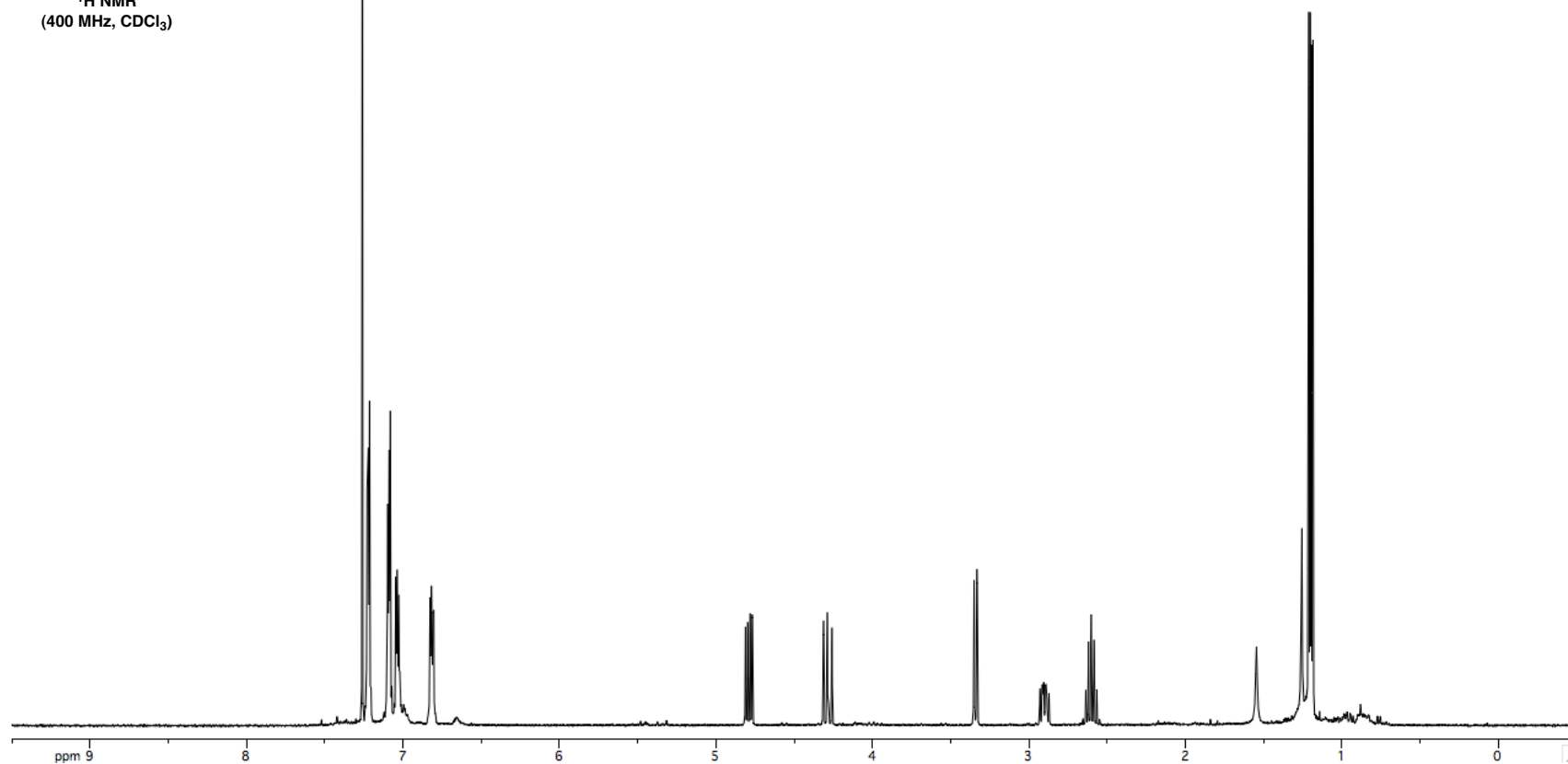
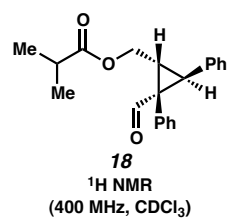
13d
¹H NMR
(400 MHz, C₆D₆)

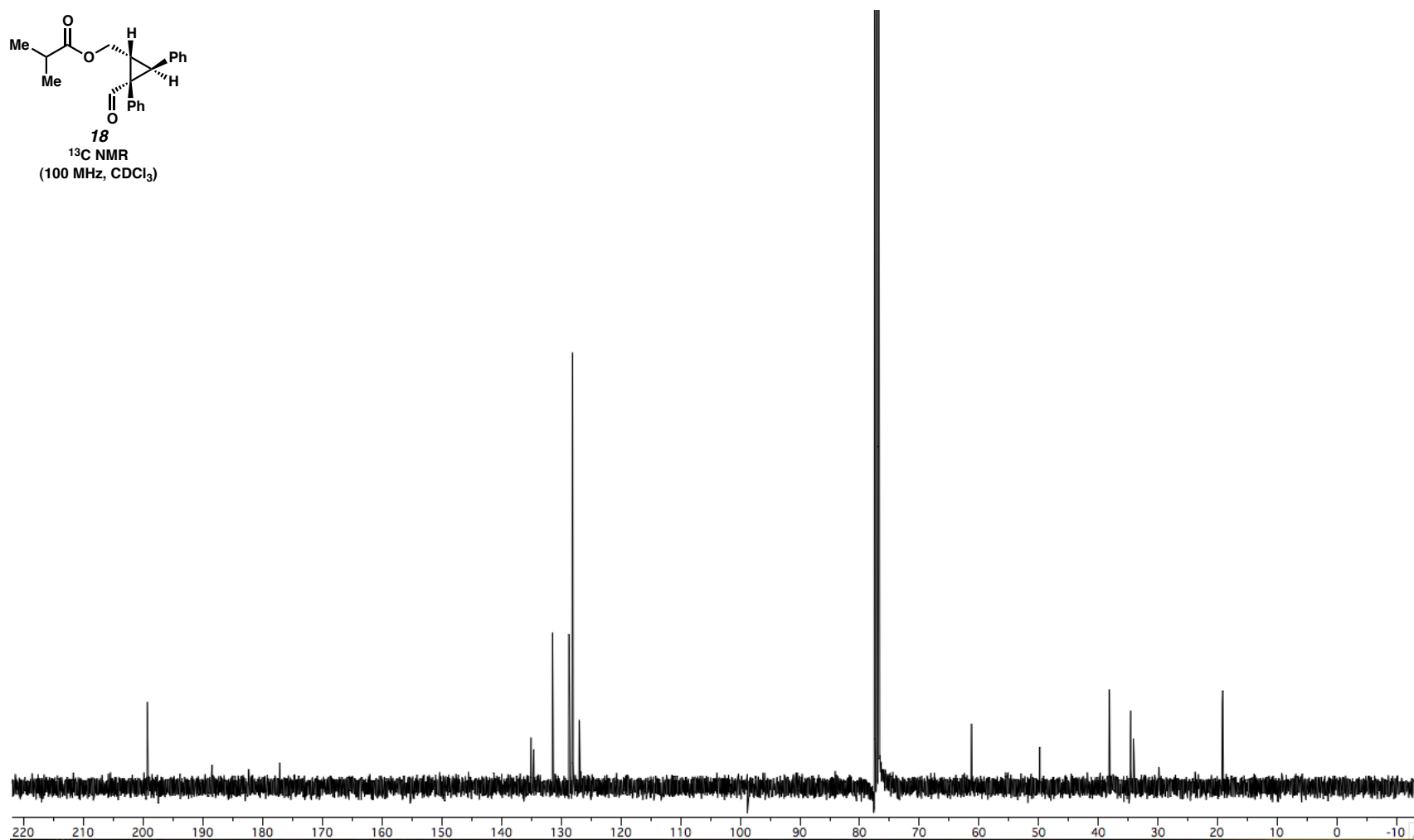
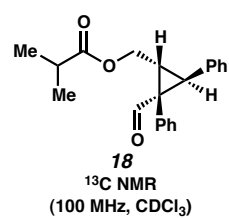


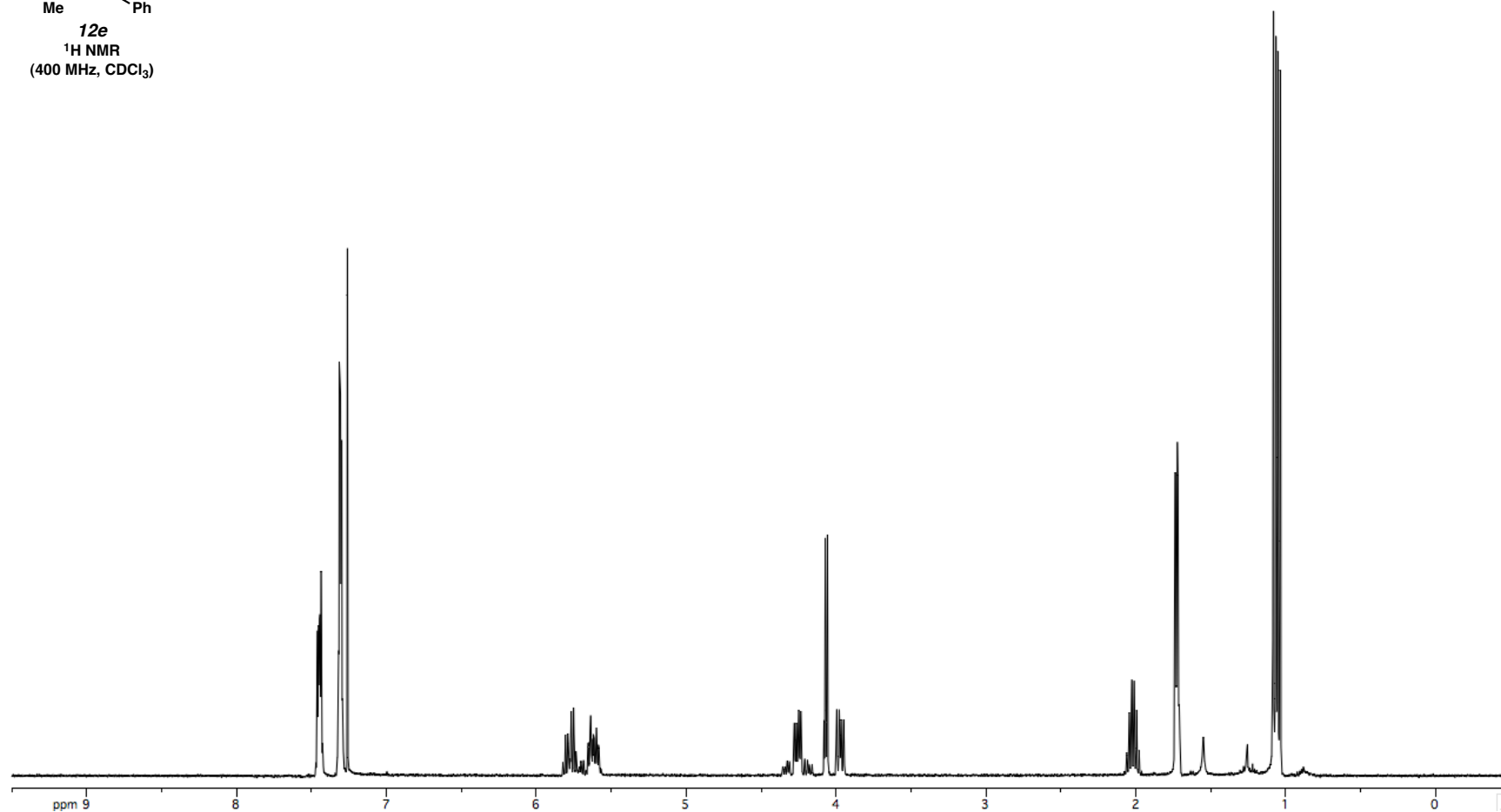
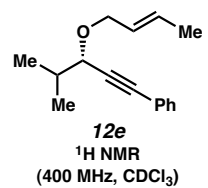


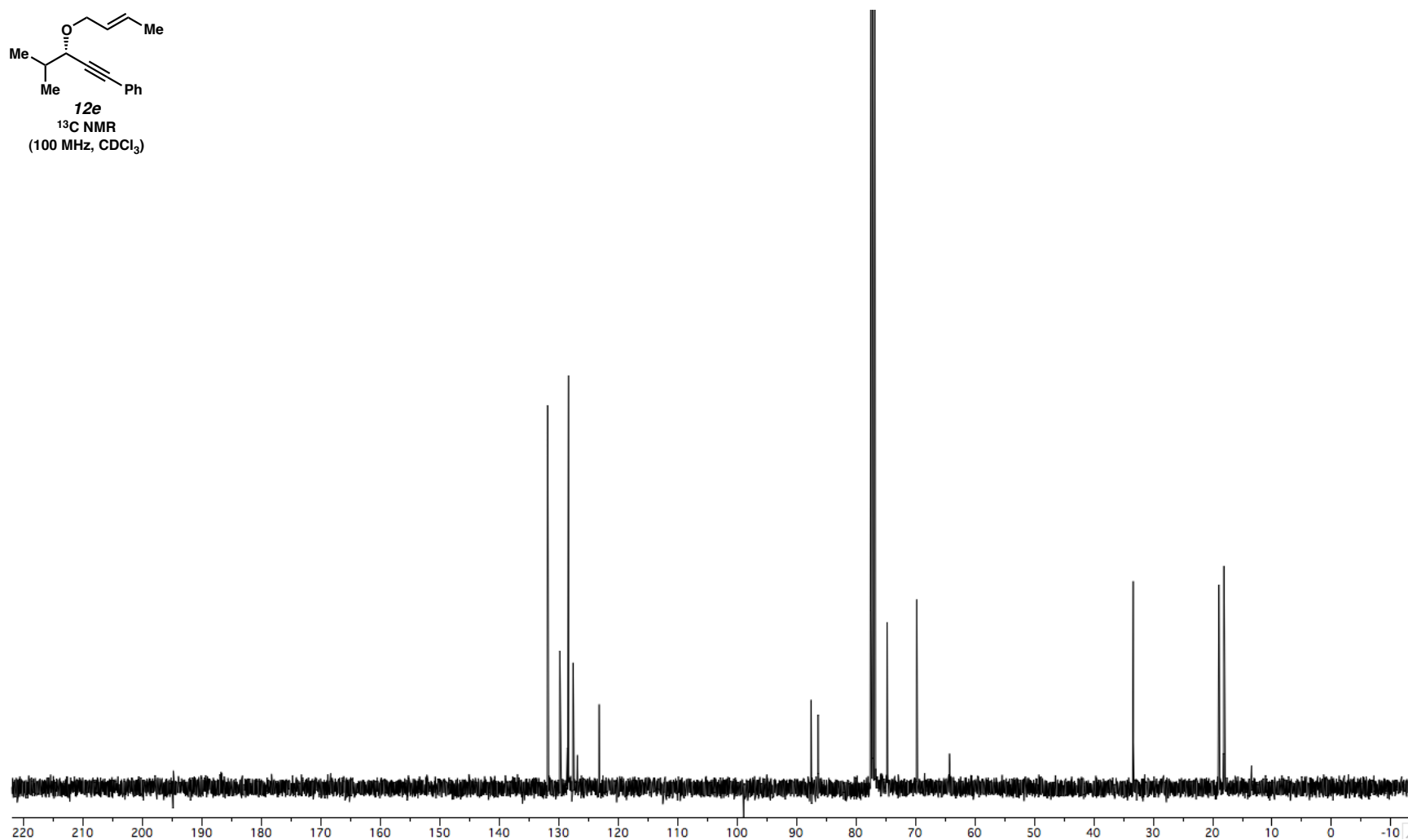
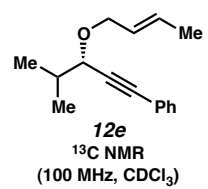
13d
 ^{13}C NMR
(100 MHz, C_6D_6)

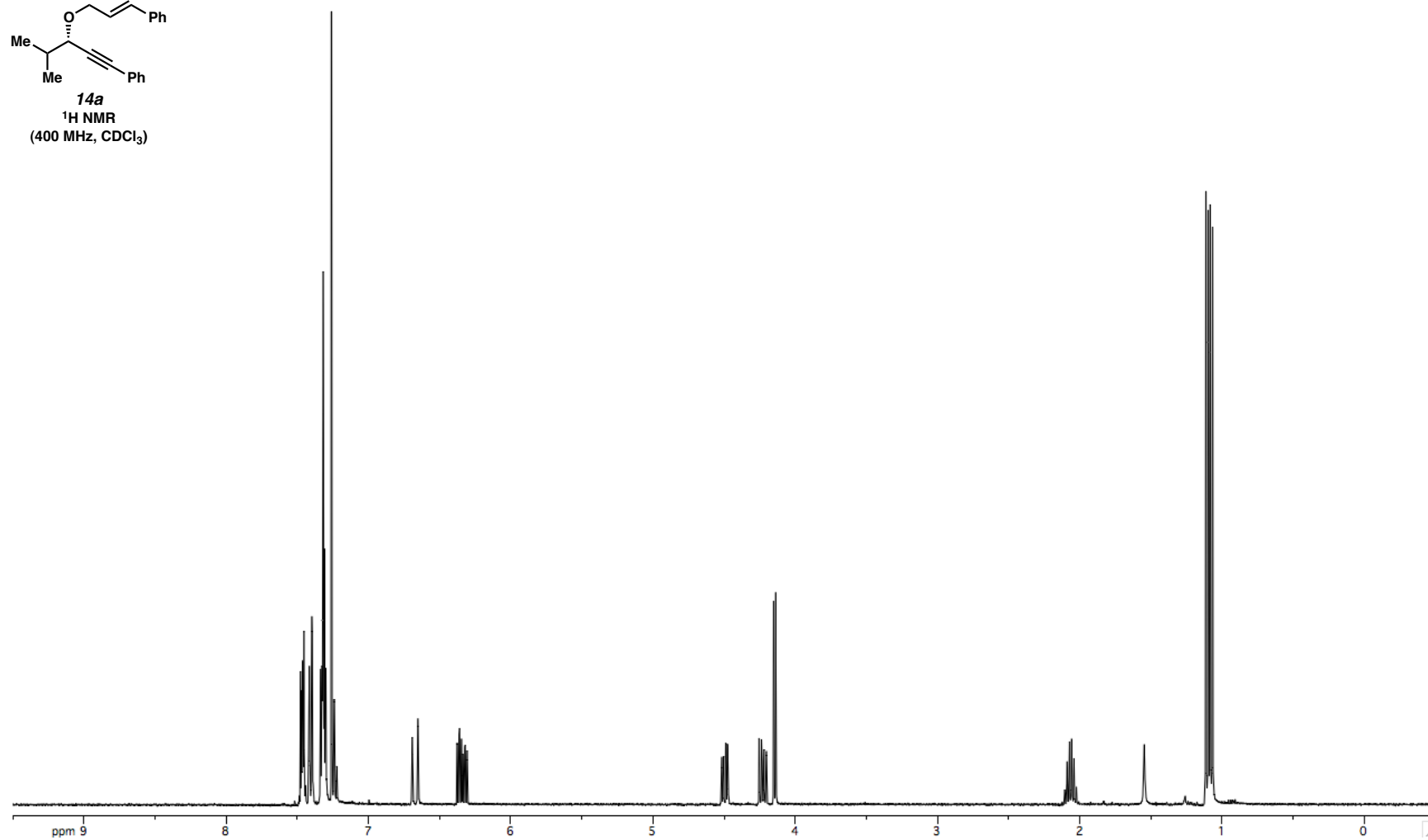
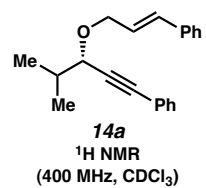


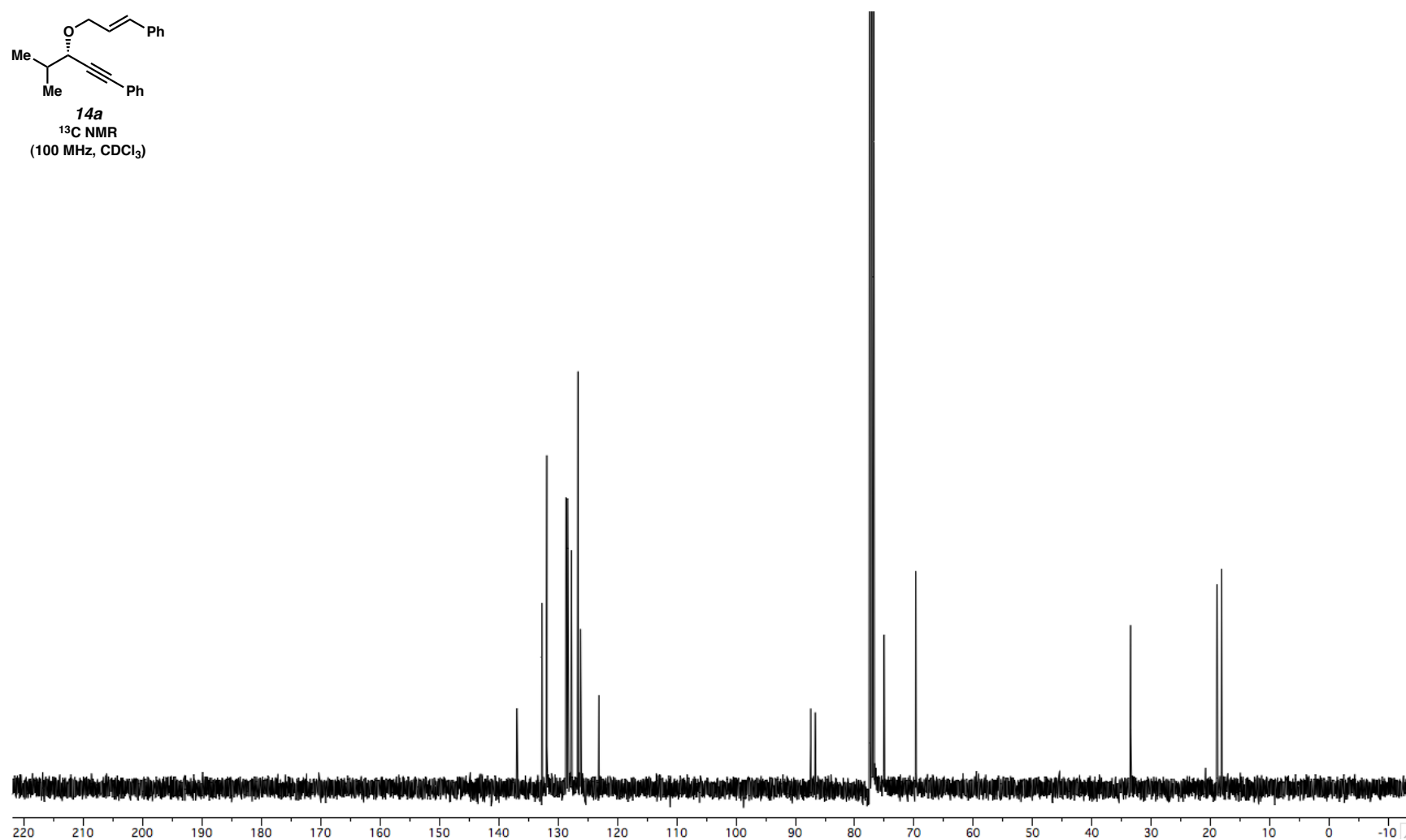
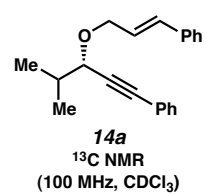


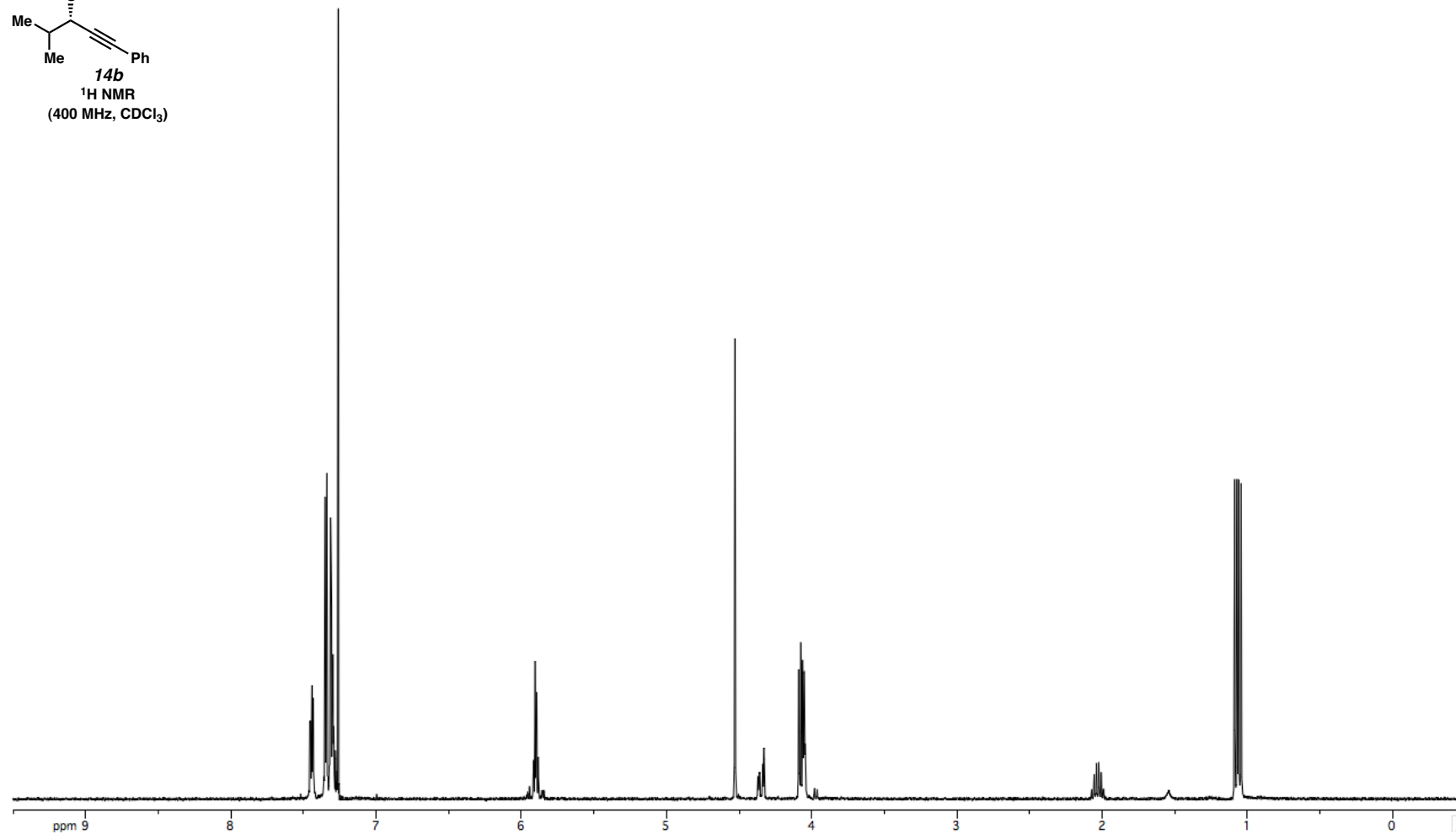
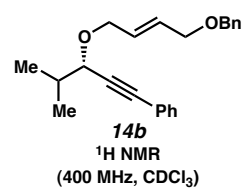


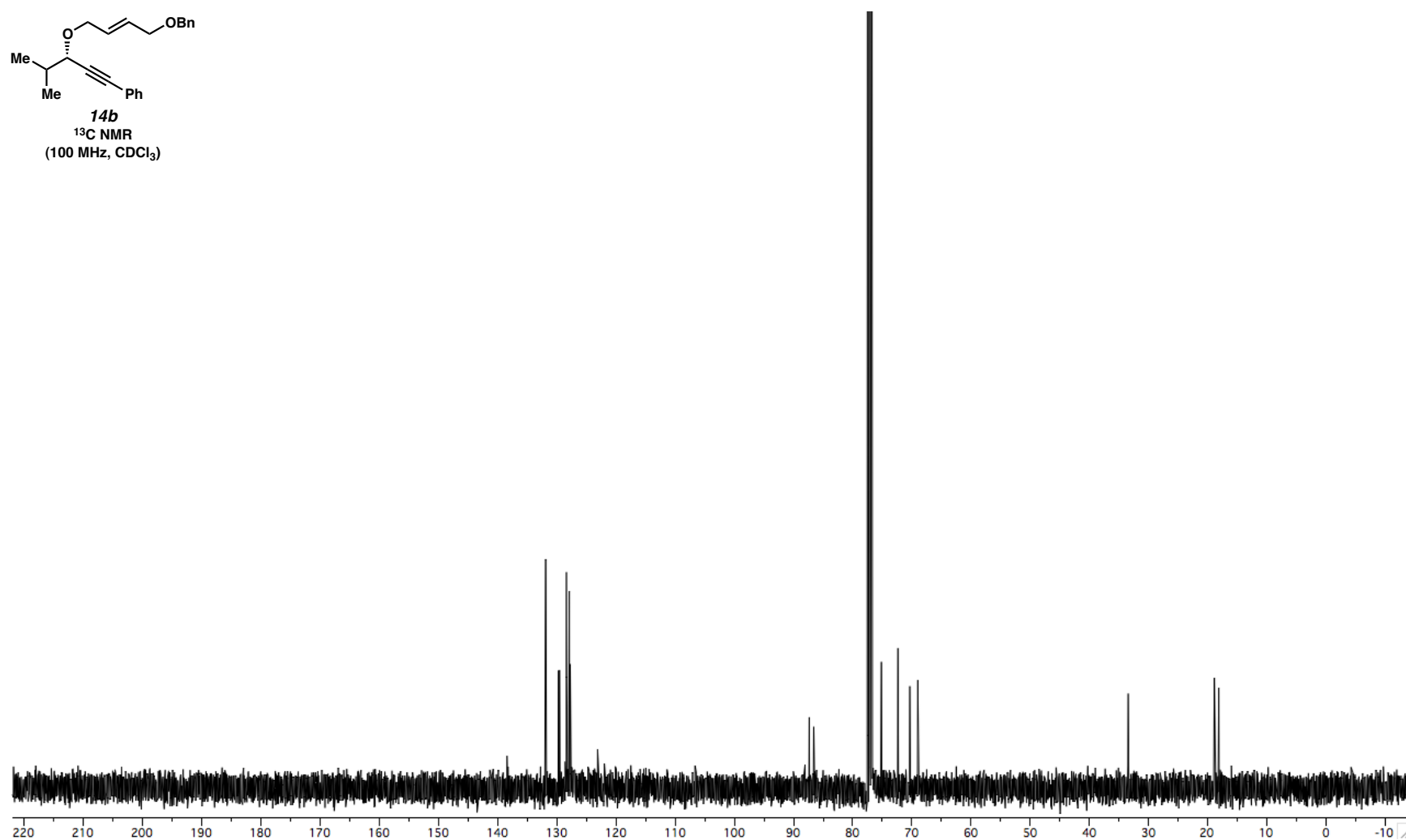
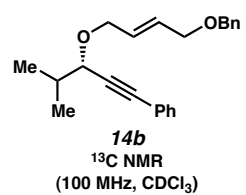


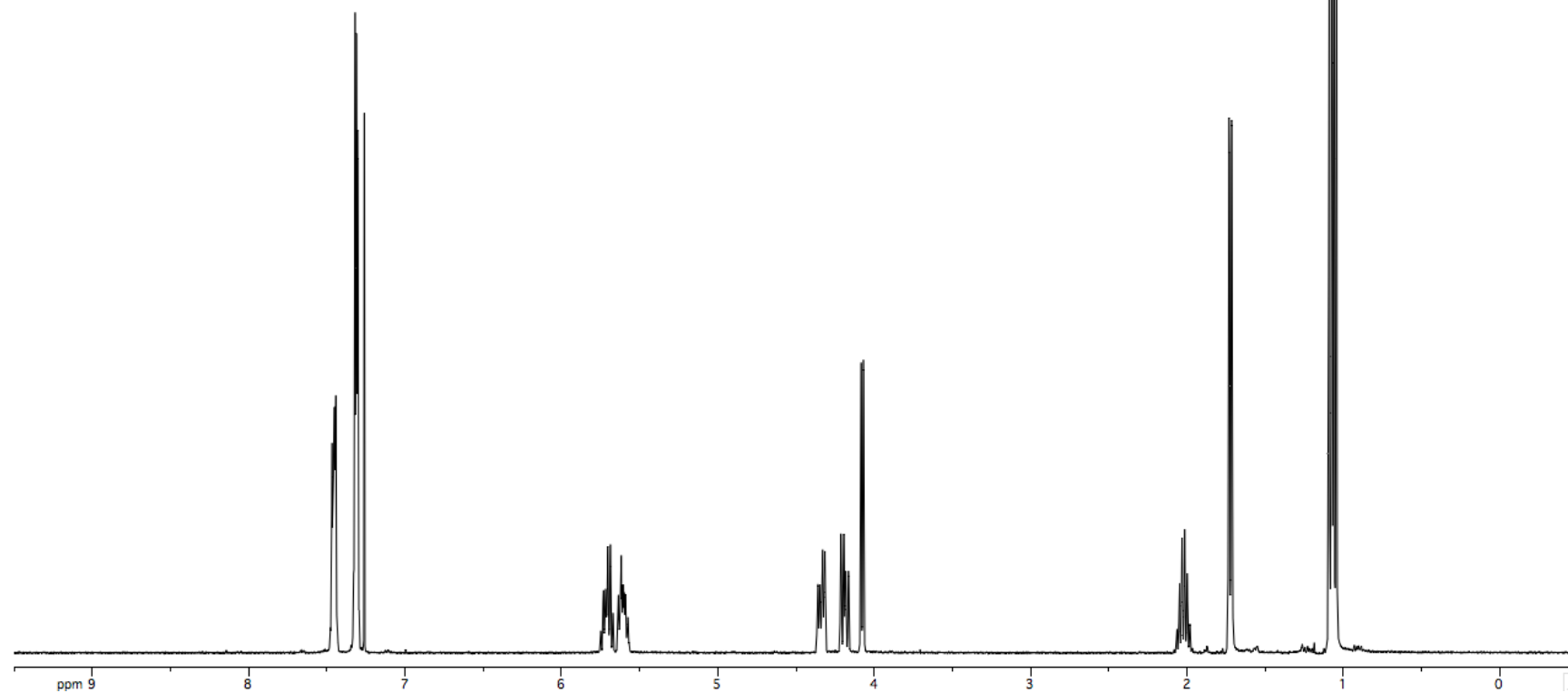
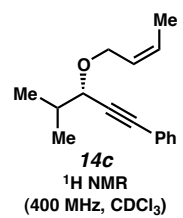


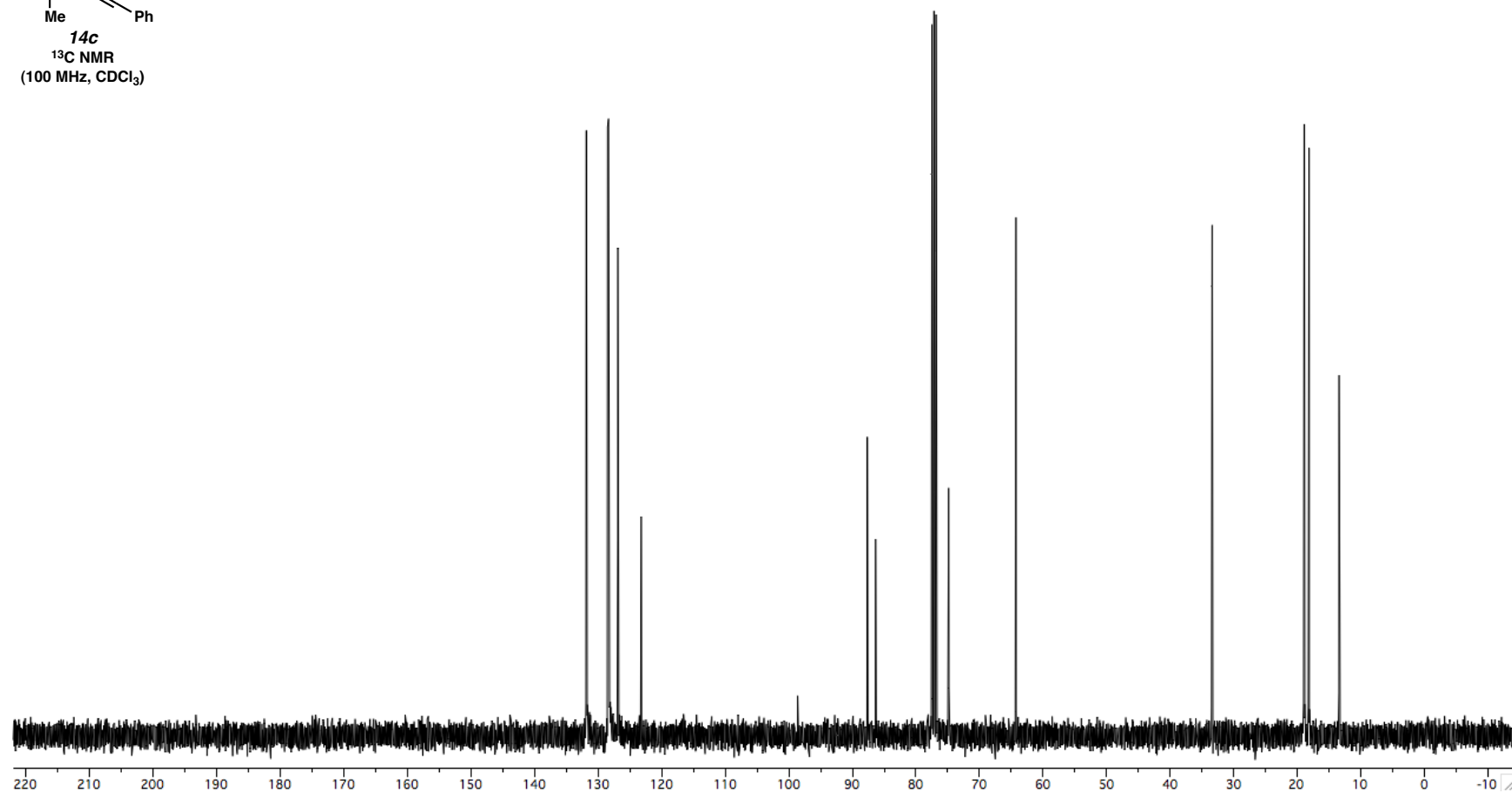
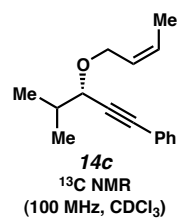


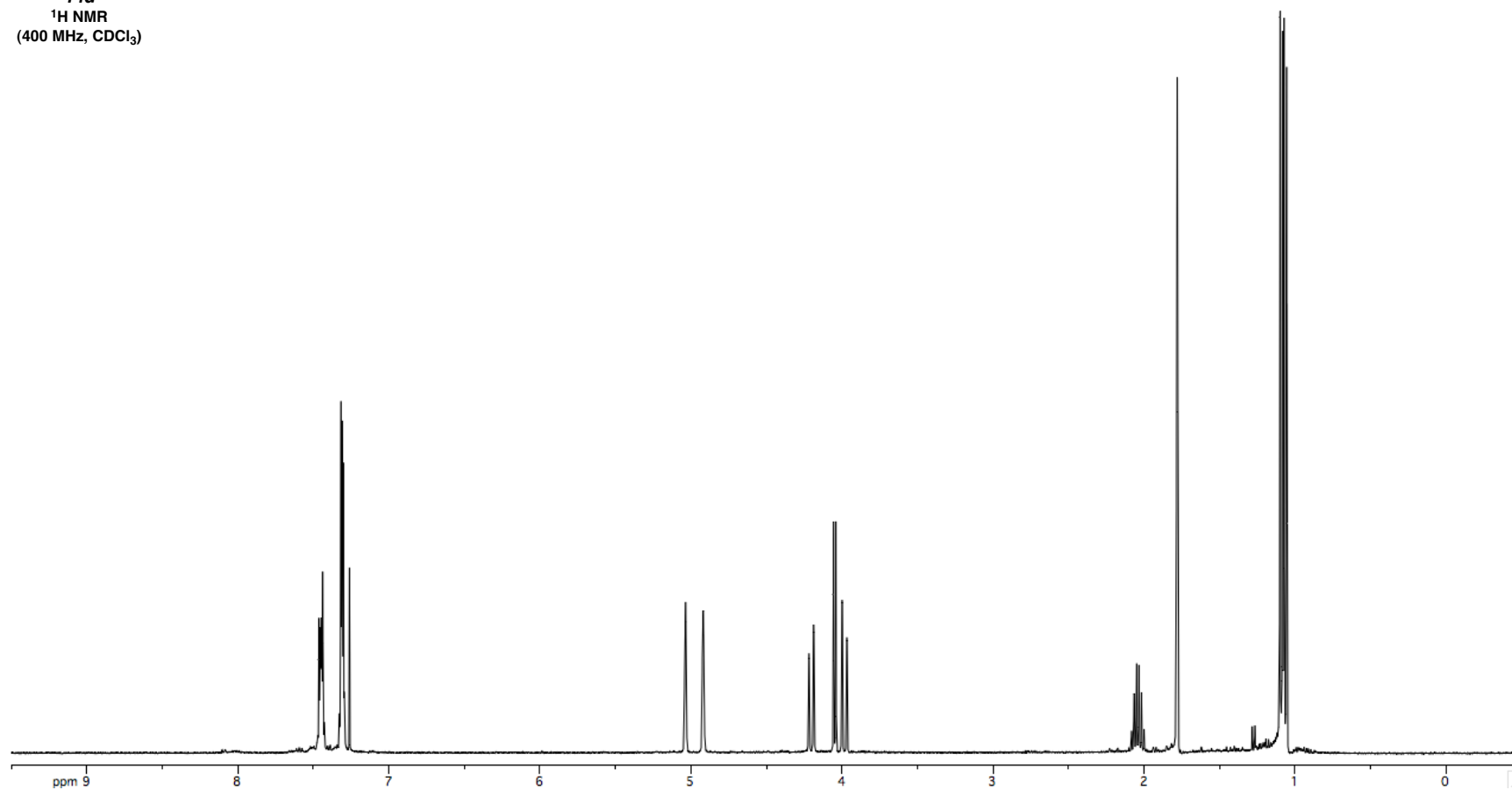
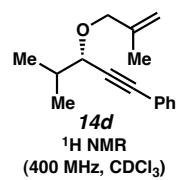


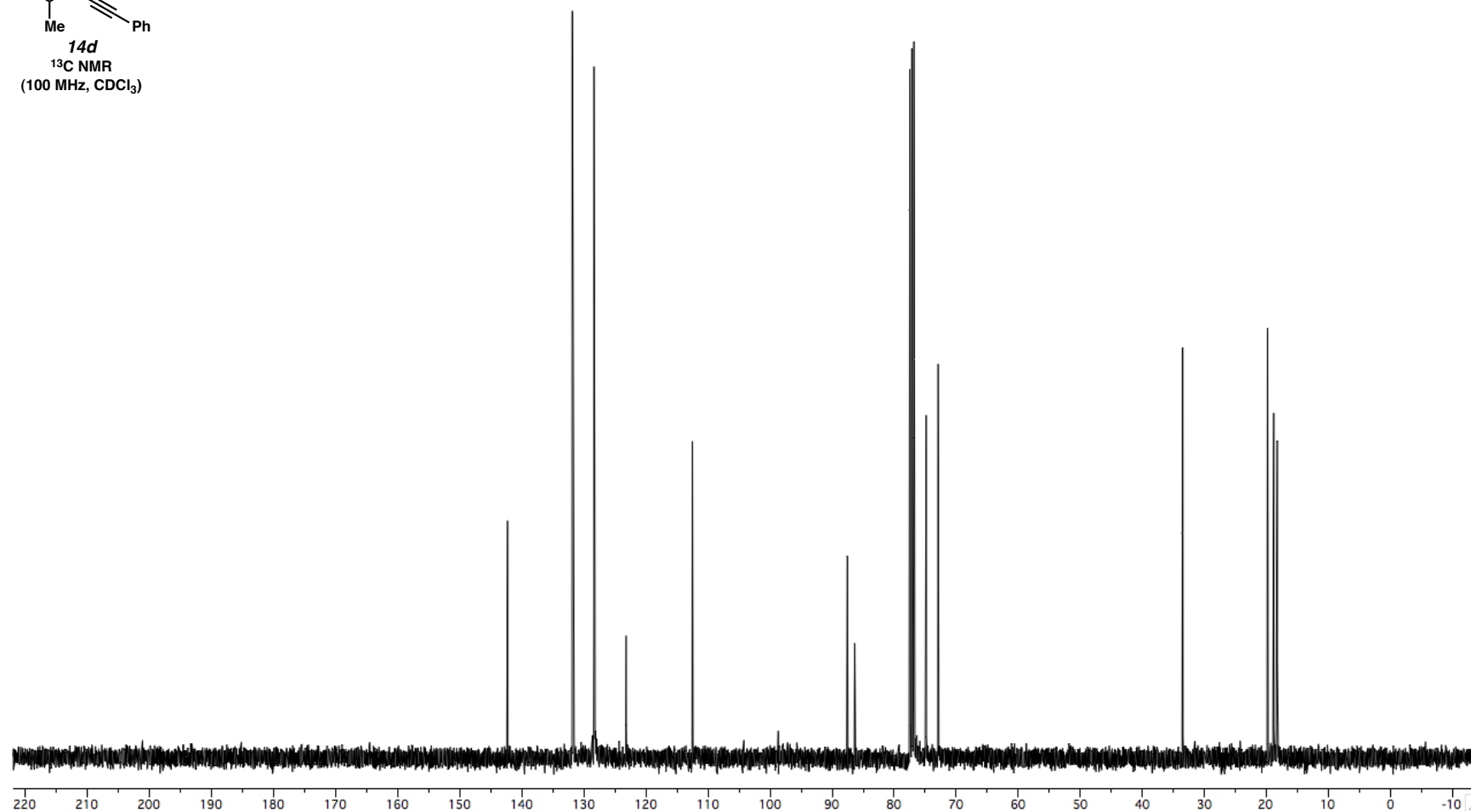
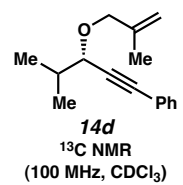


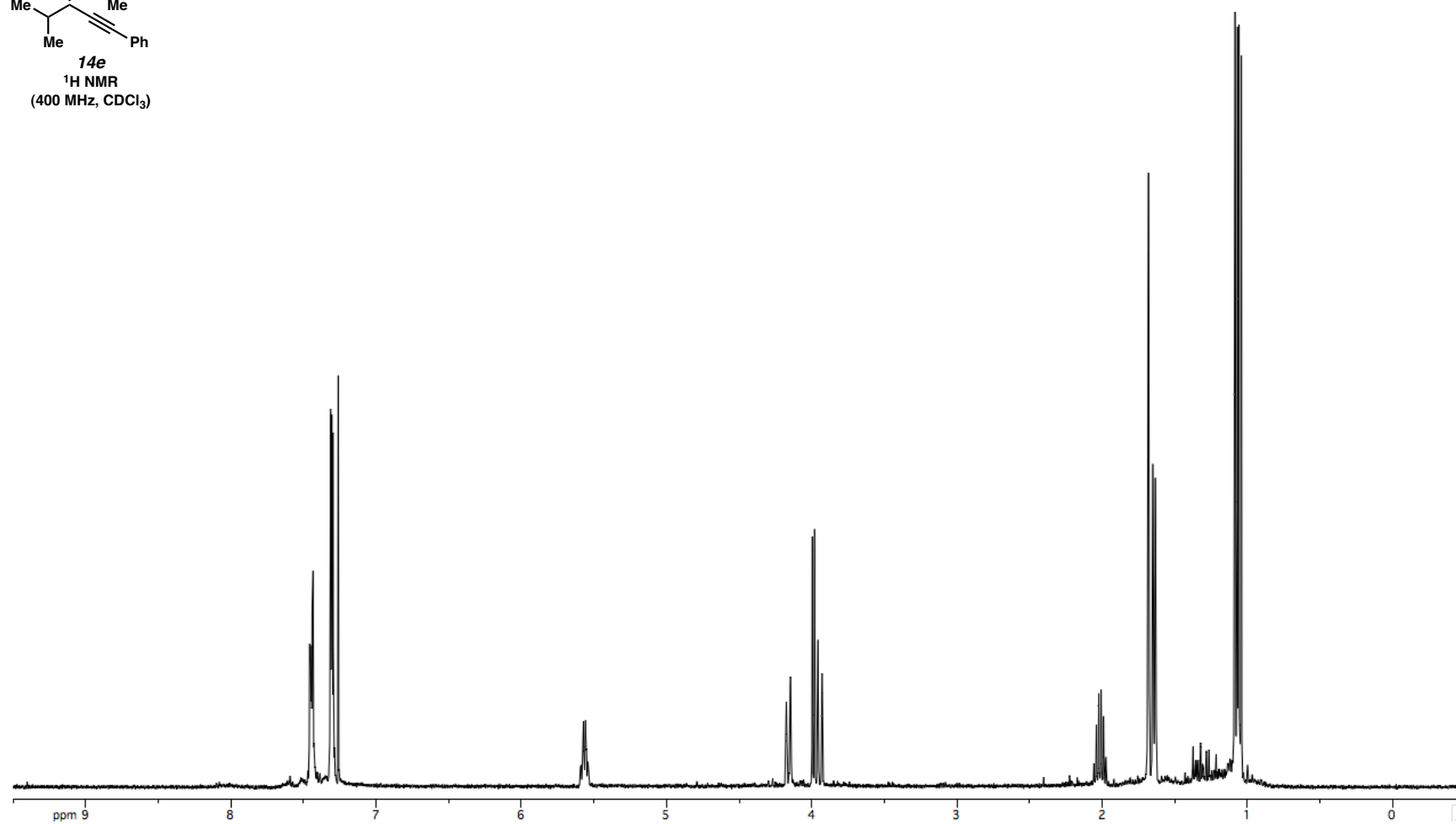
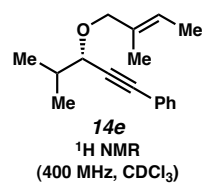


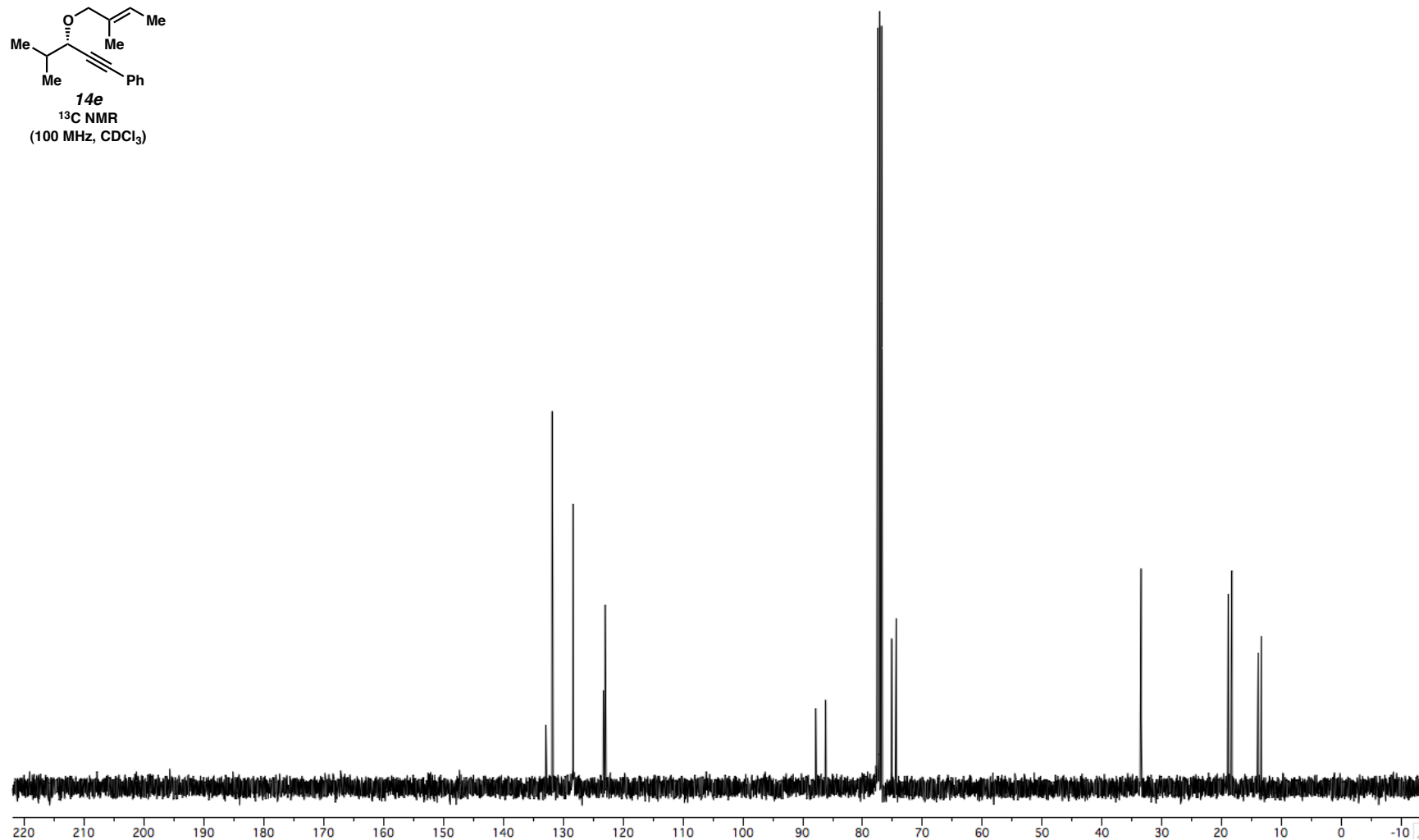
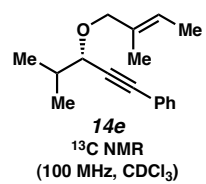


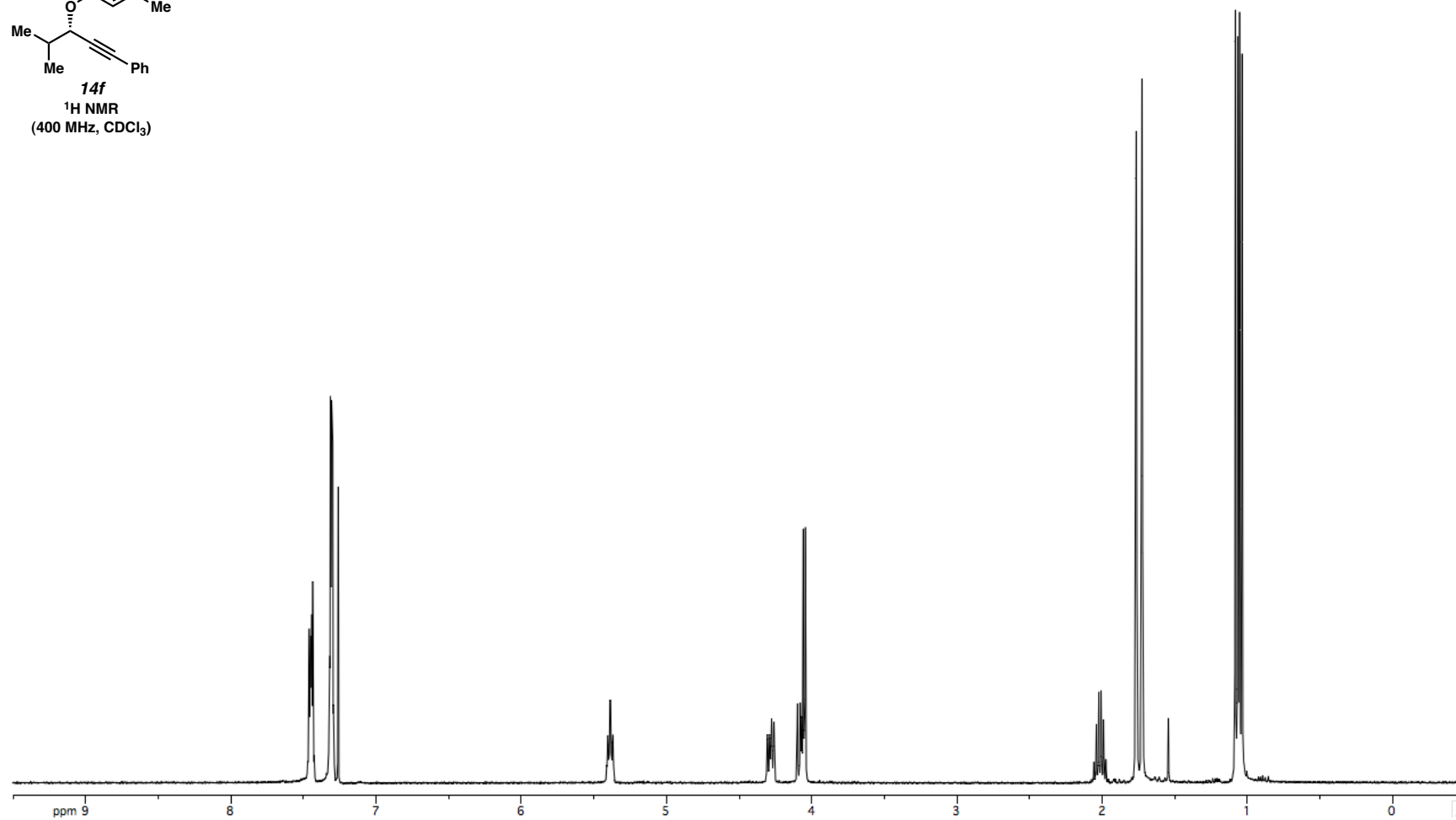
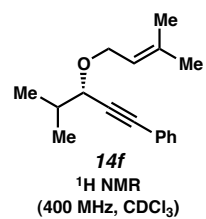


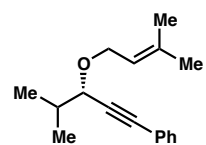




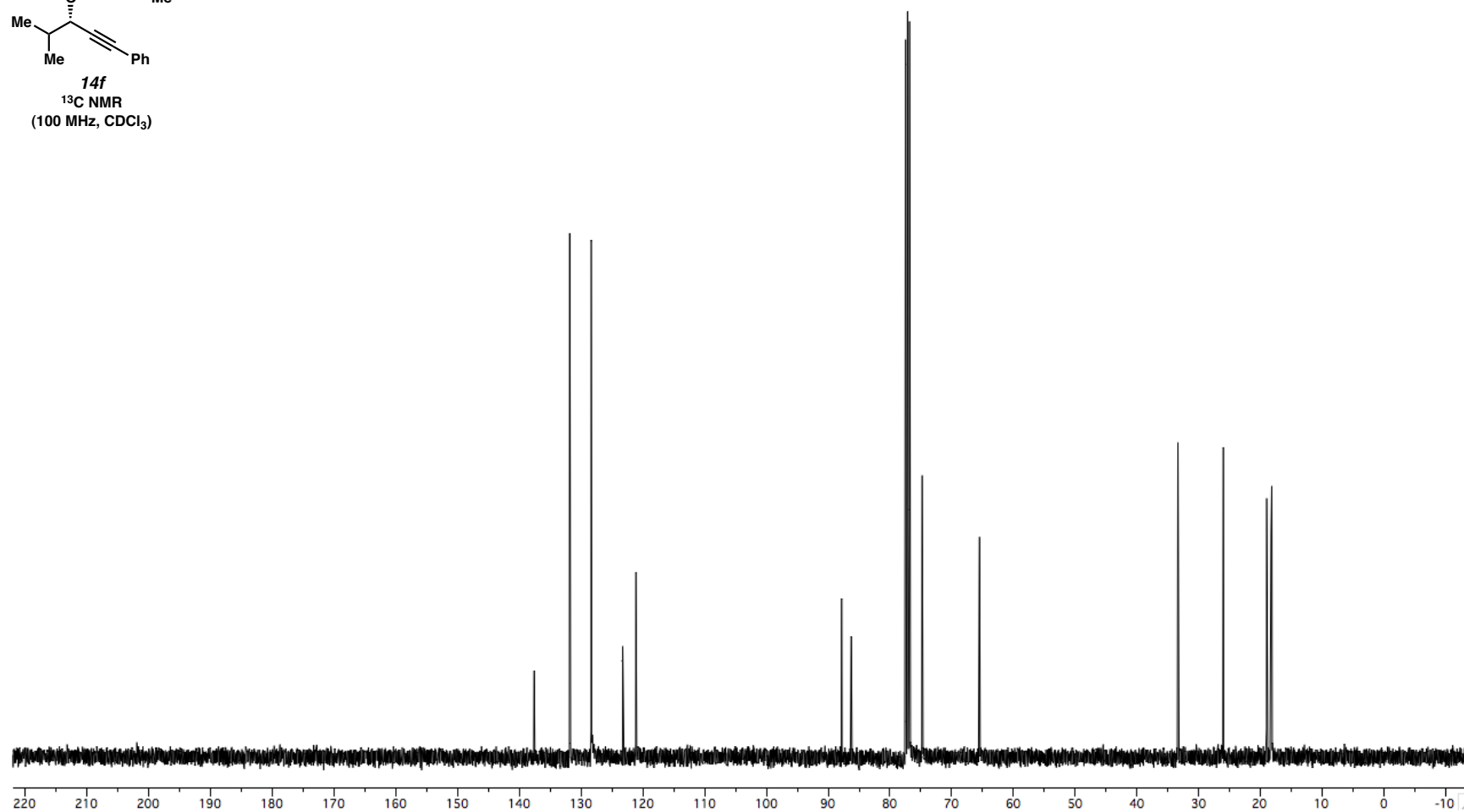


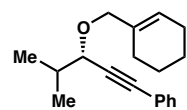




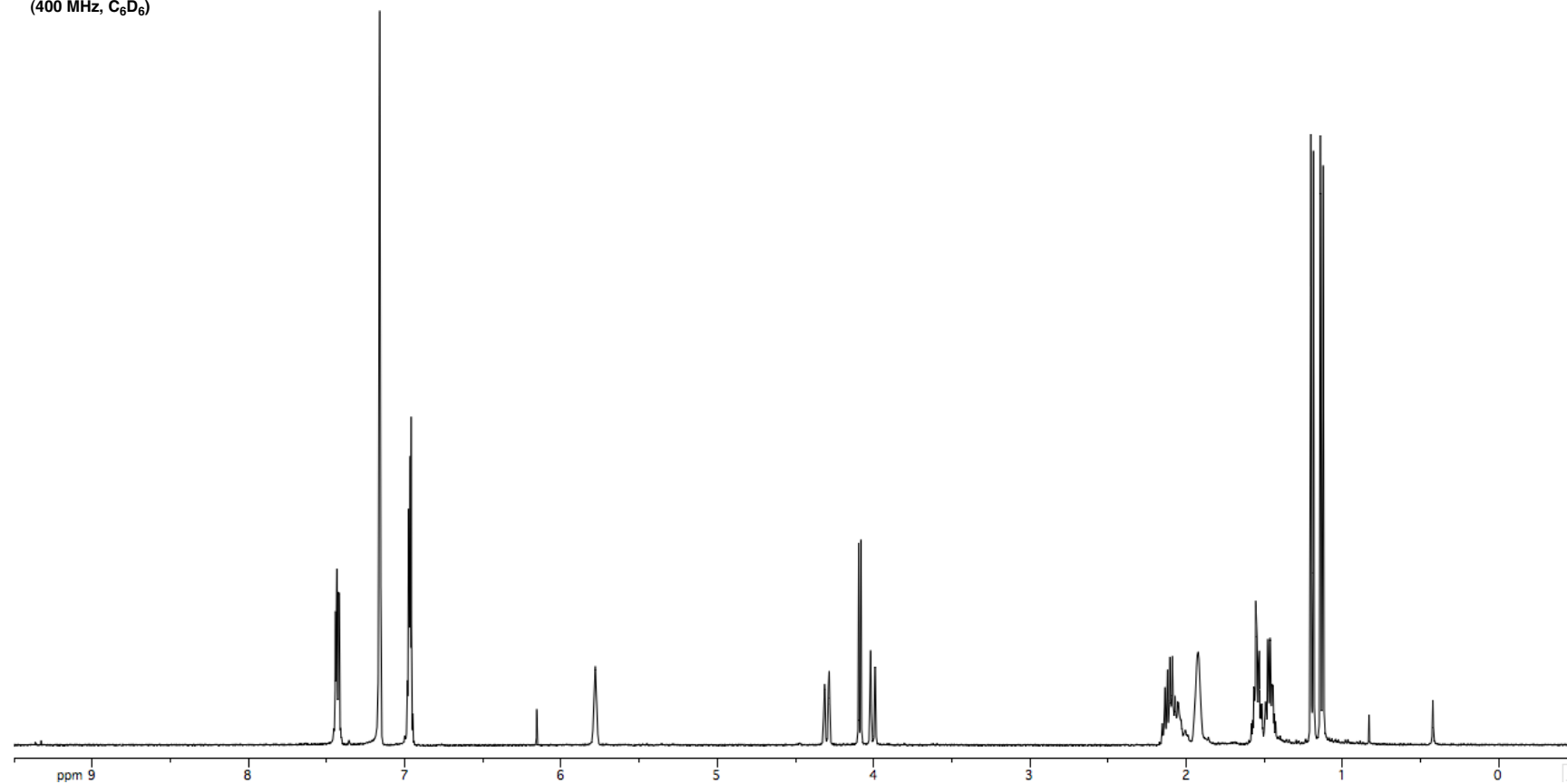


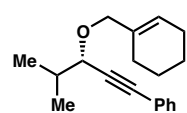
14f
¹³C NMR
(100 MHz, CDCl₃)



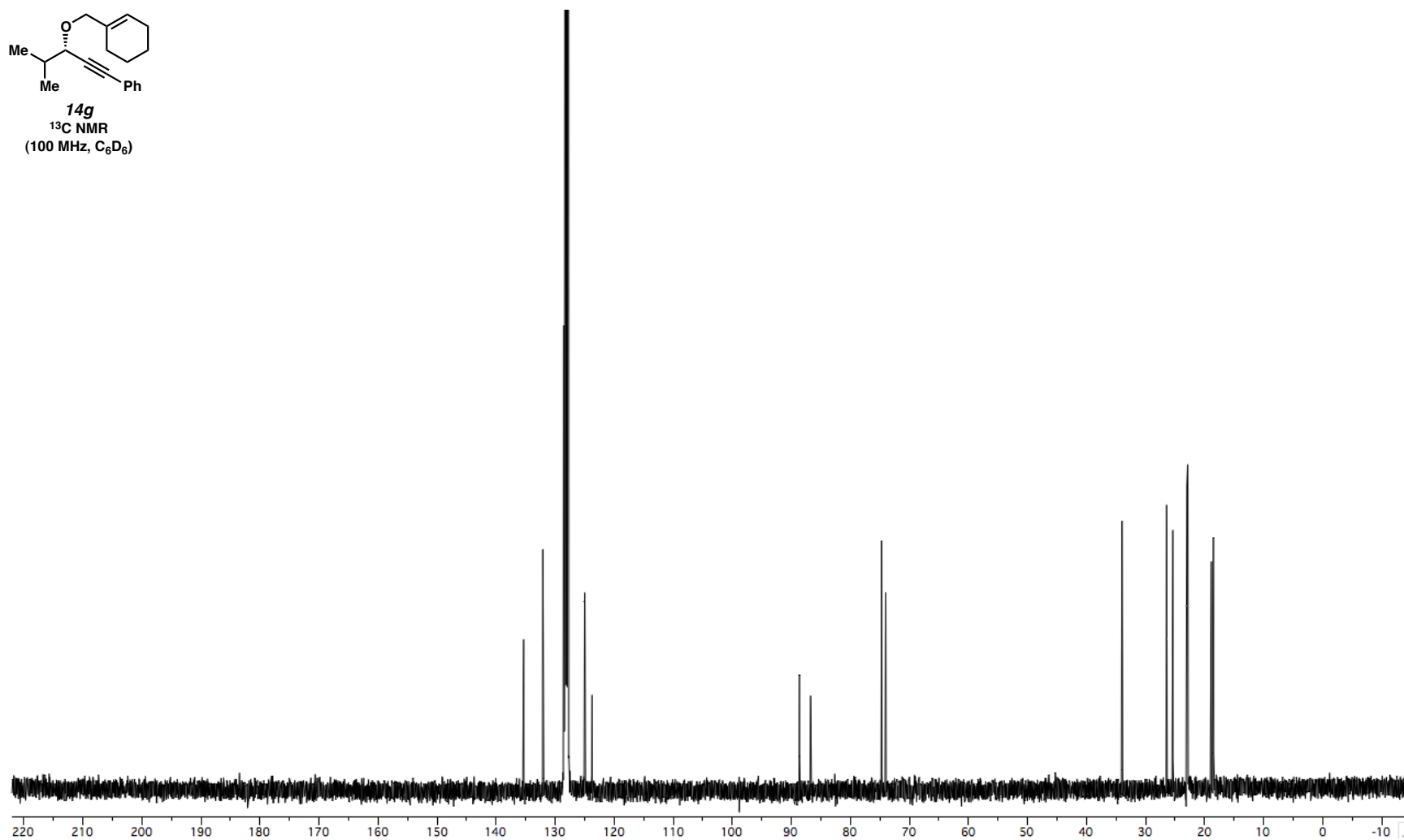


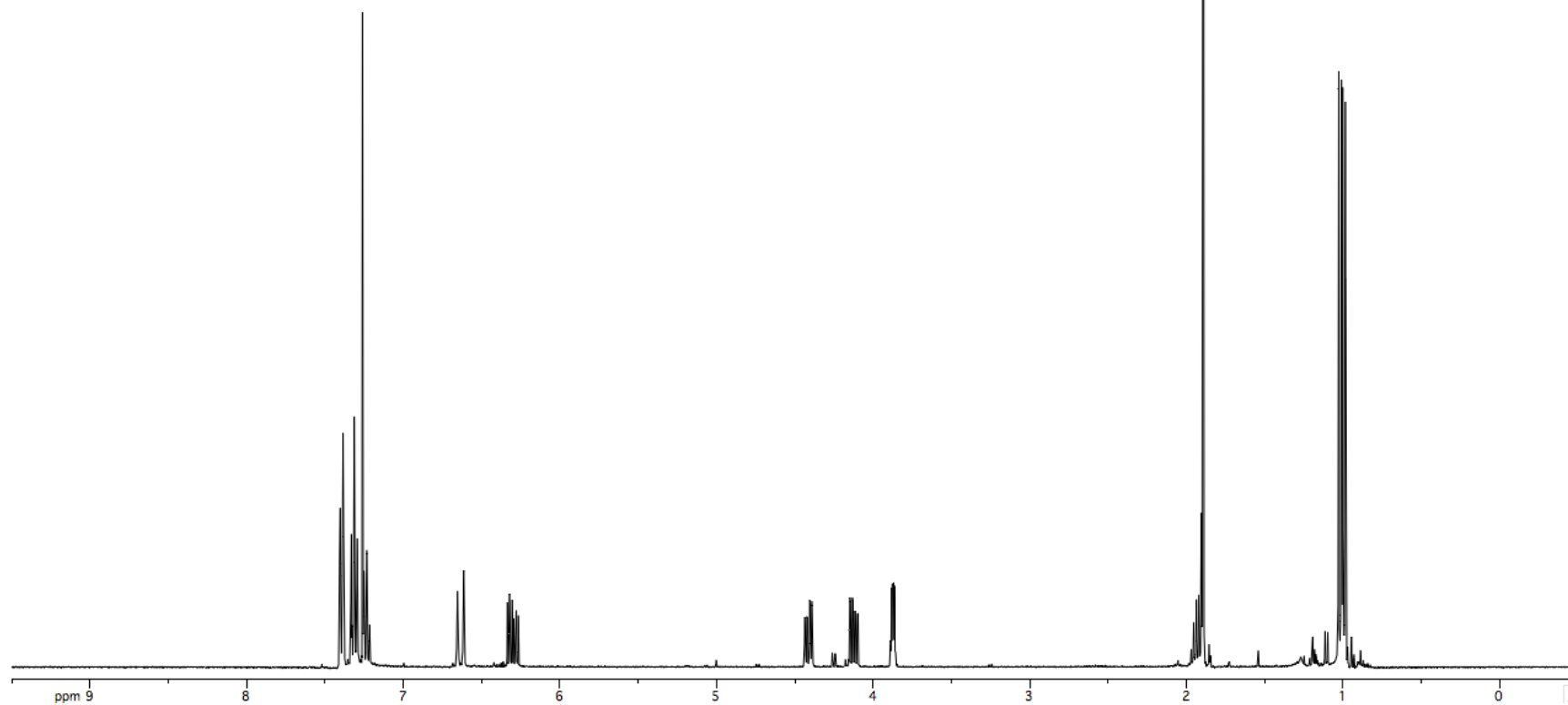
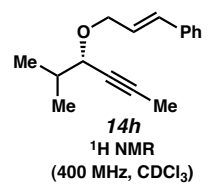
14g
 ^1H NMR
(400 MHz, C_6D_6)

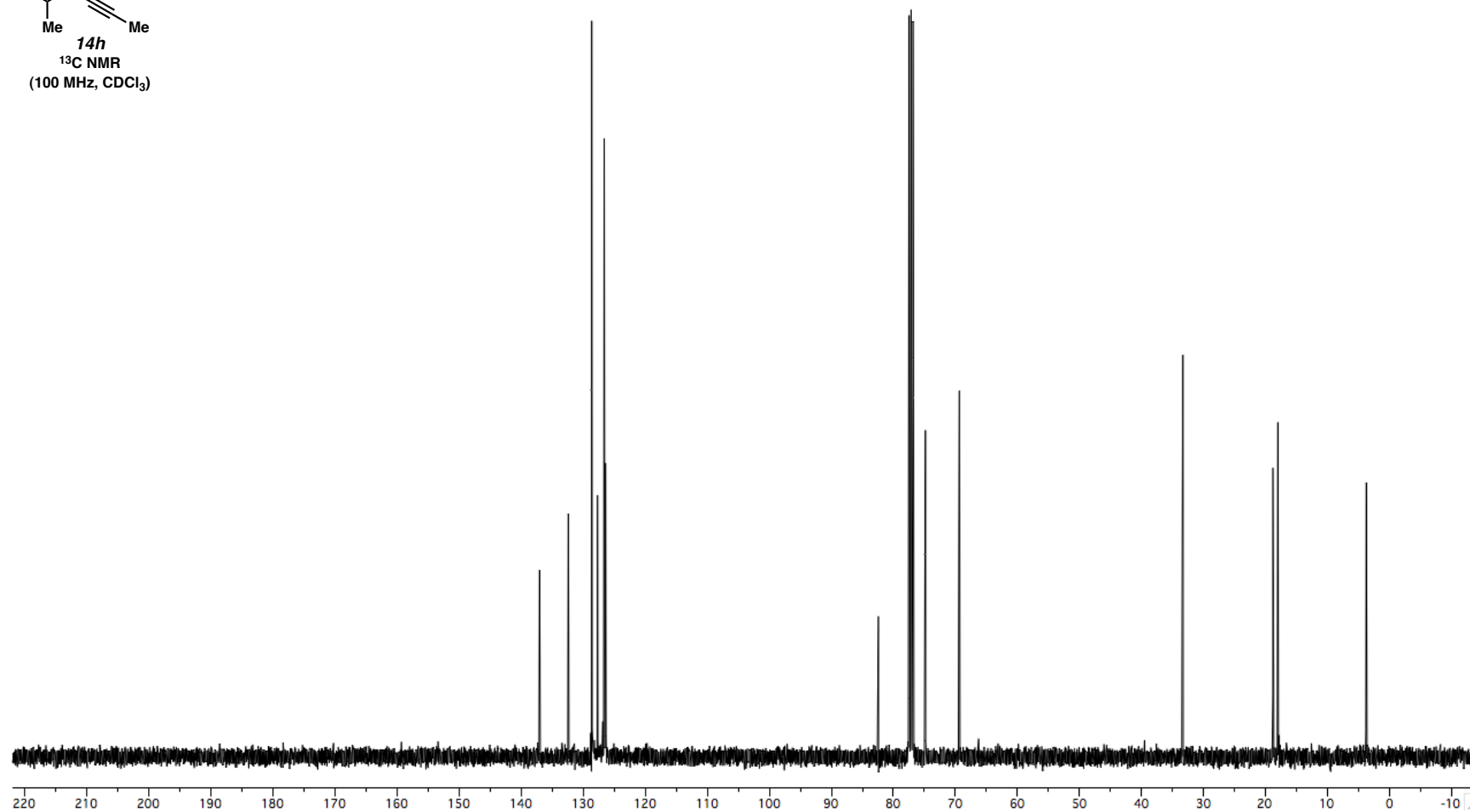
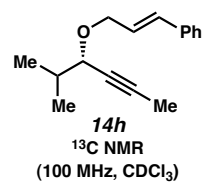


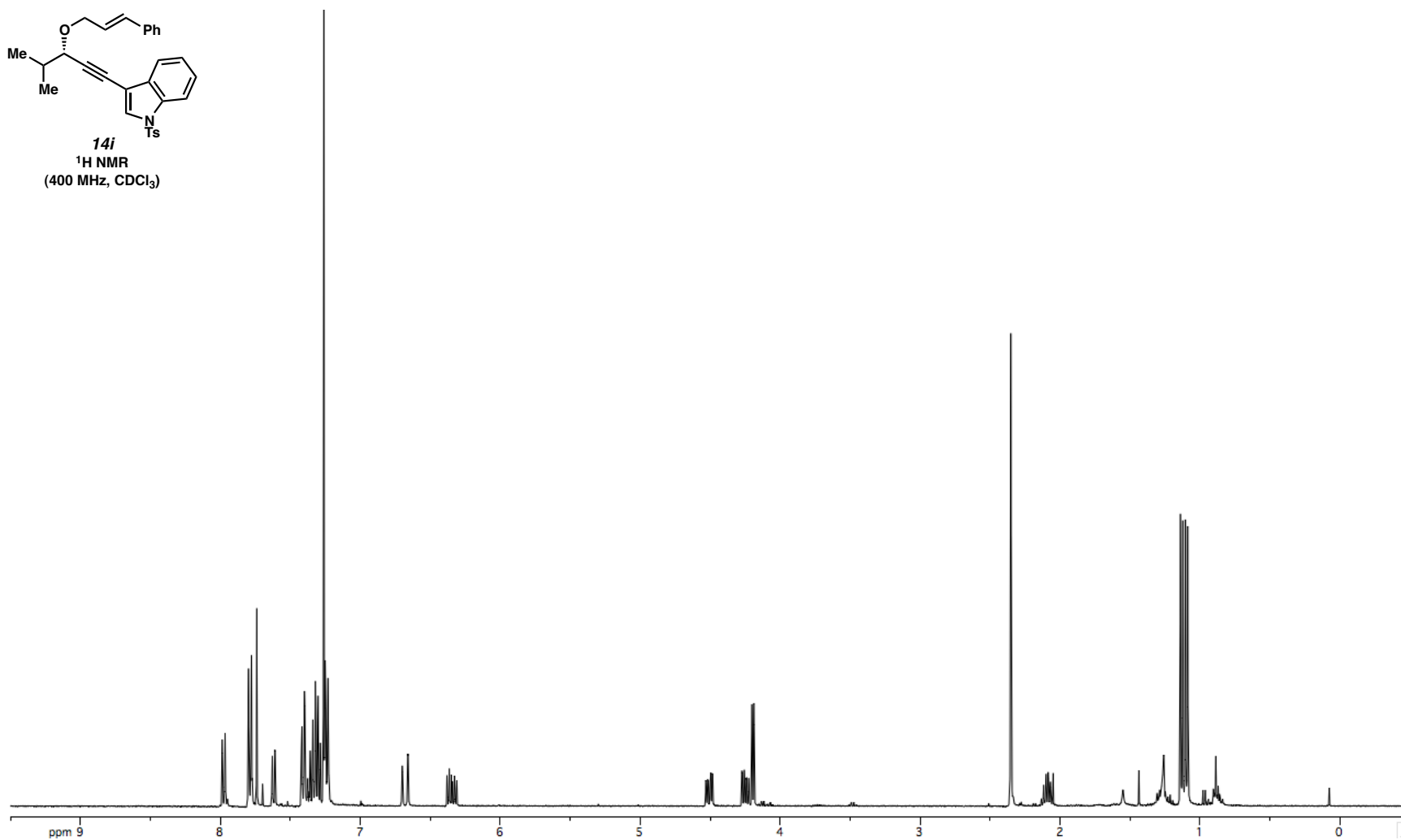
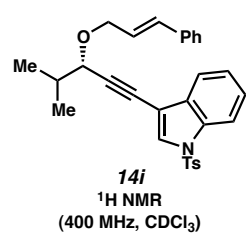


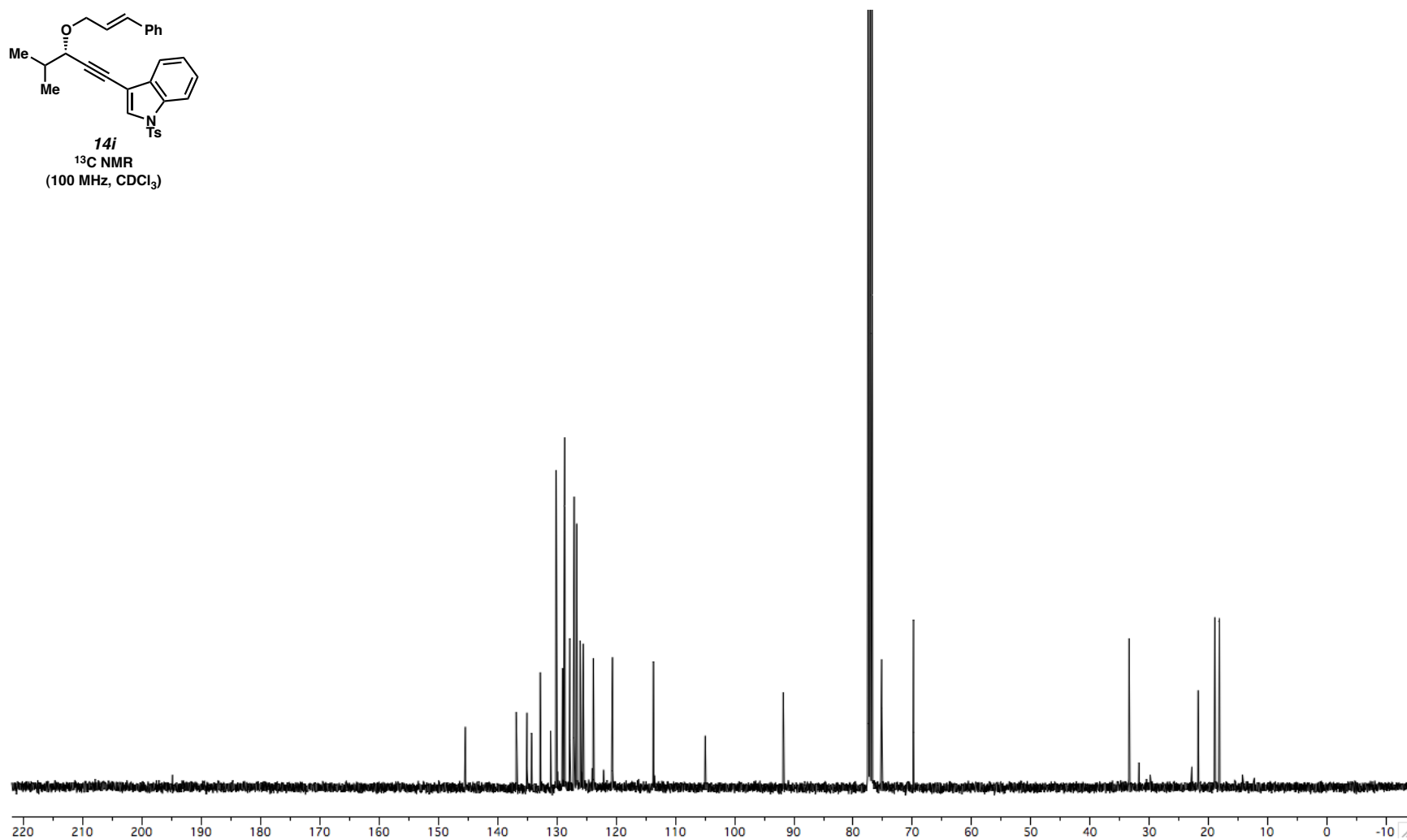
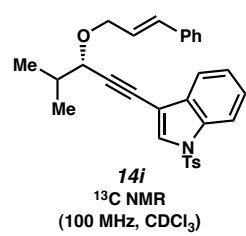
14g
 ^{13}C NMR
(100 MHz, C_6D_6)

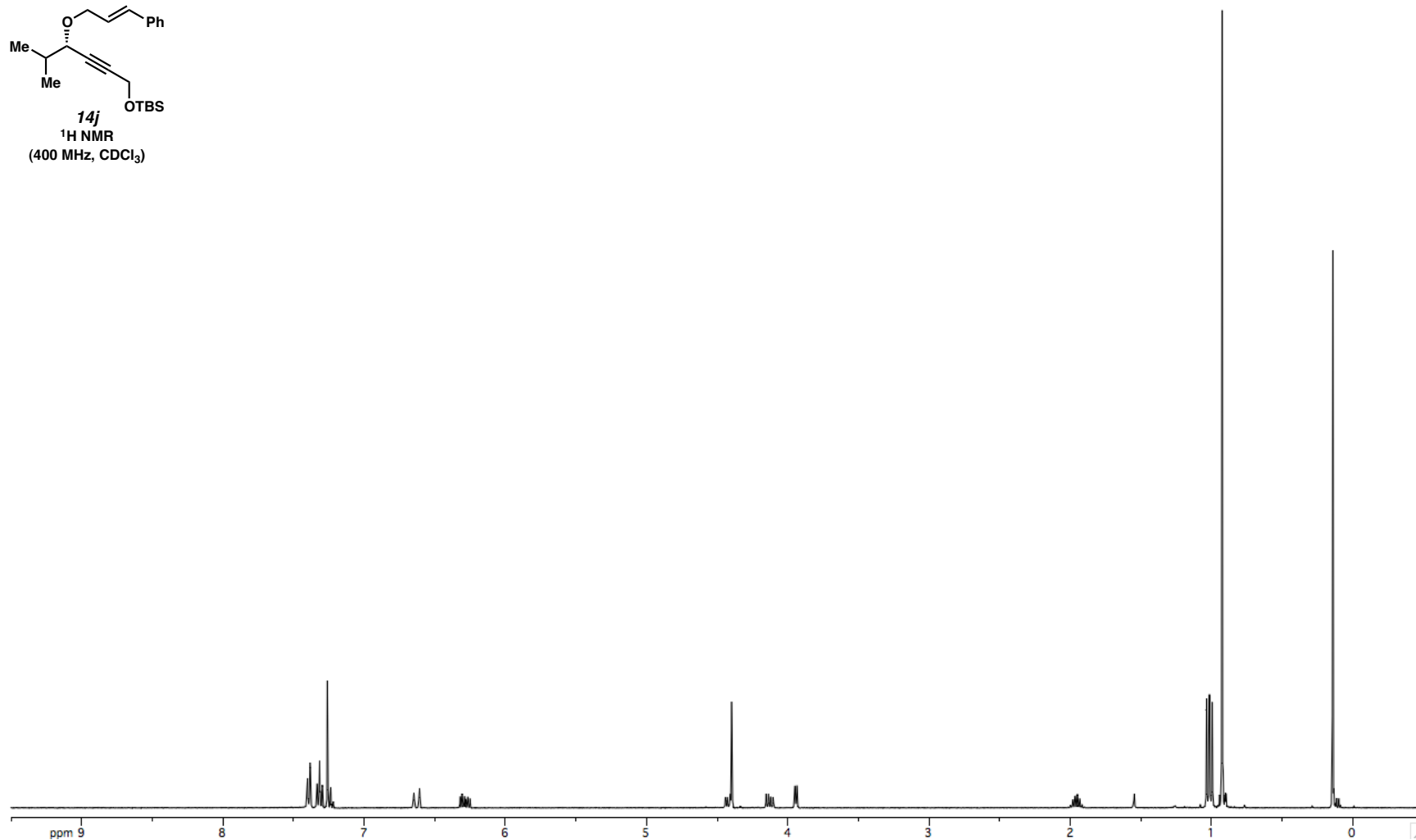
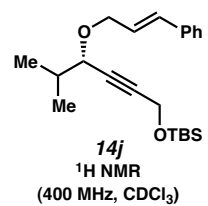


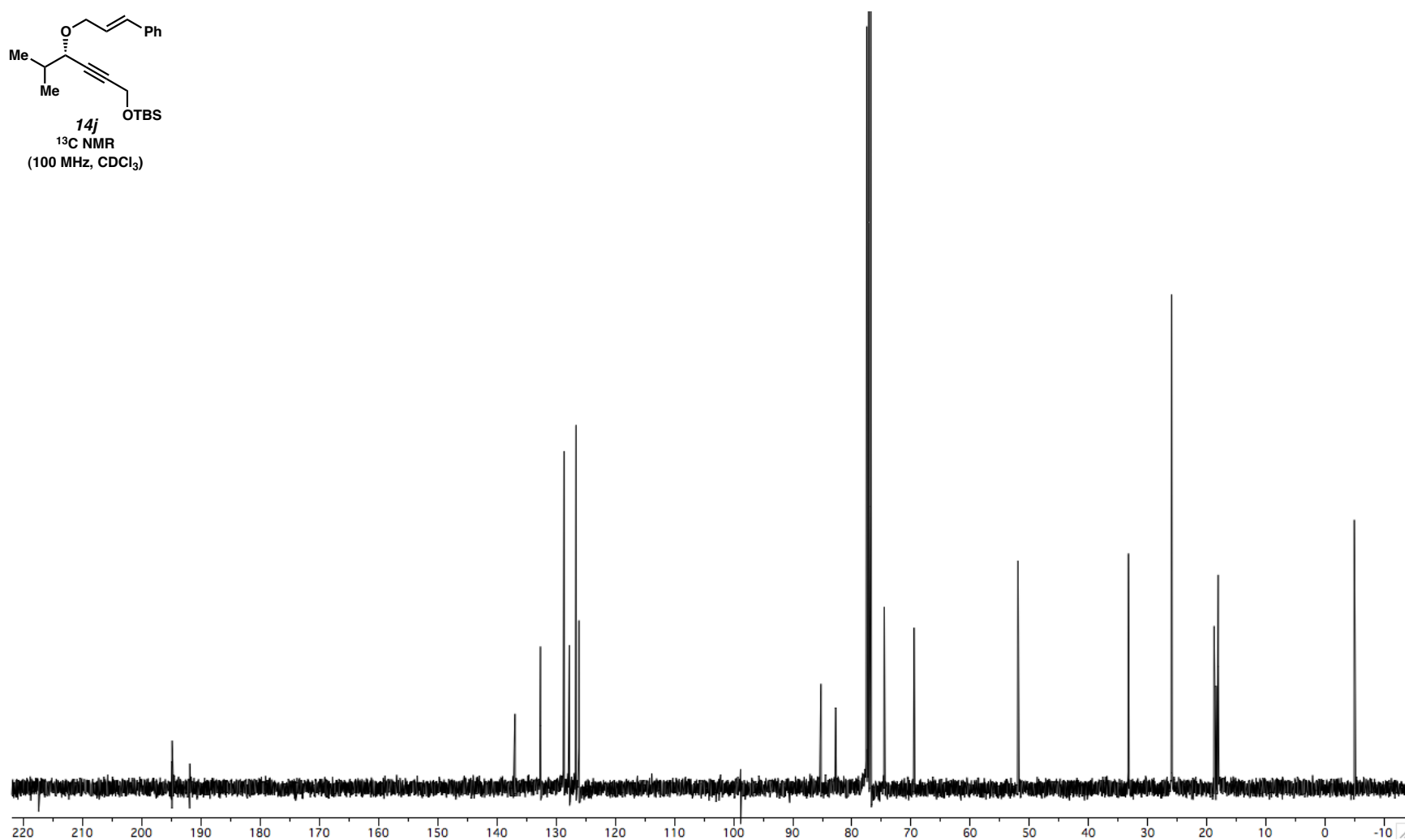
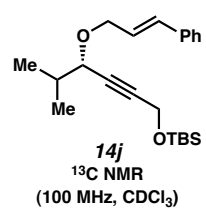


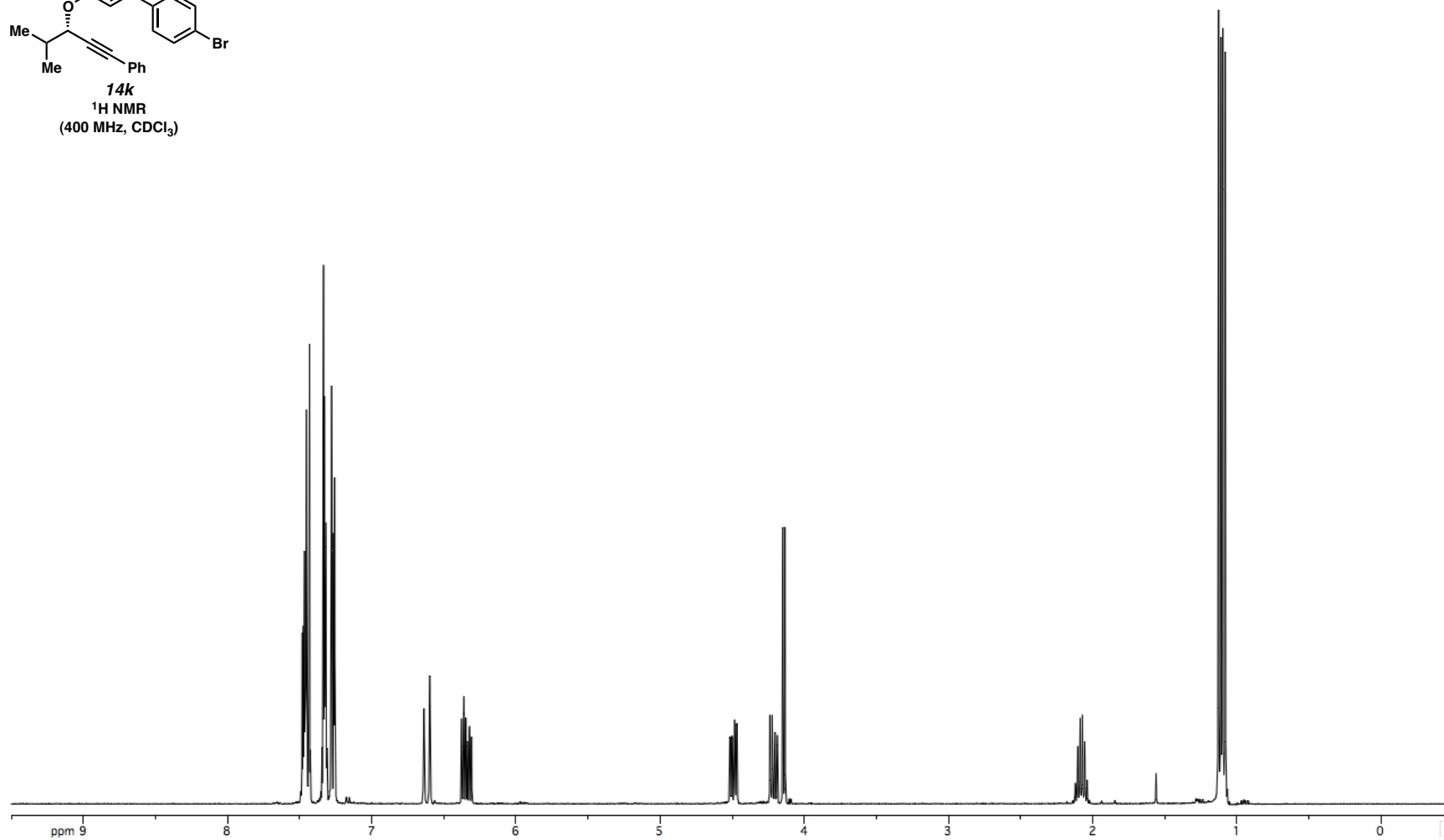
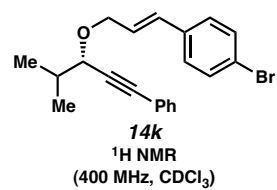


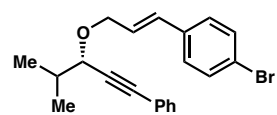




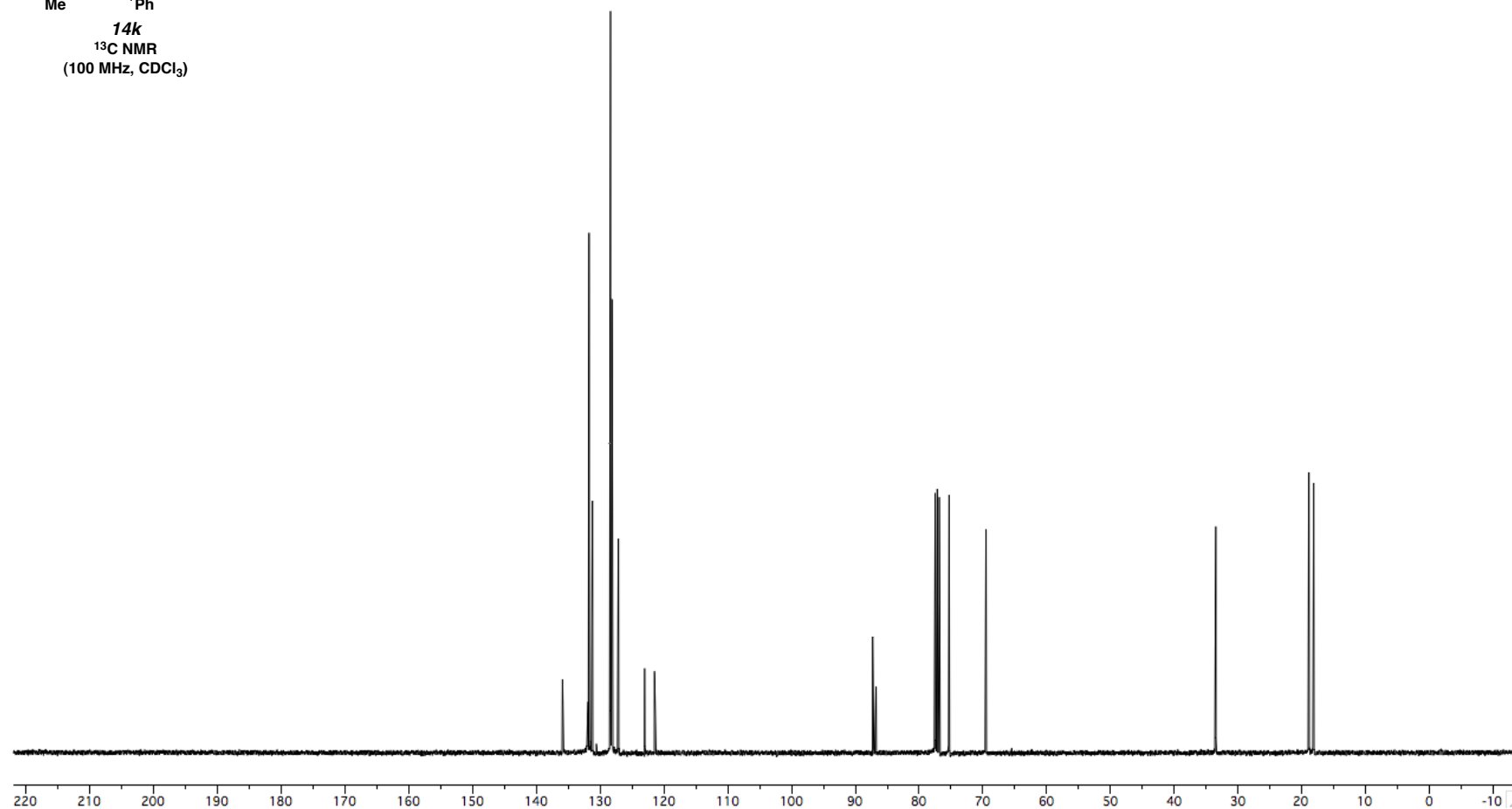


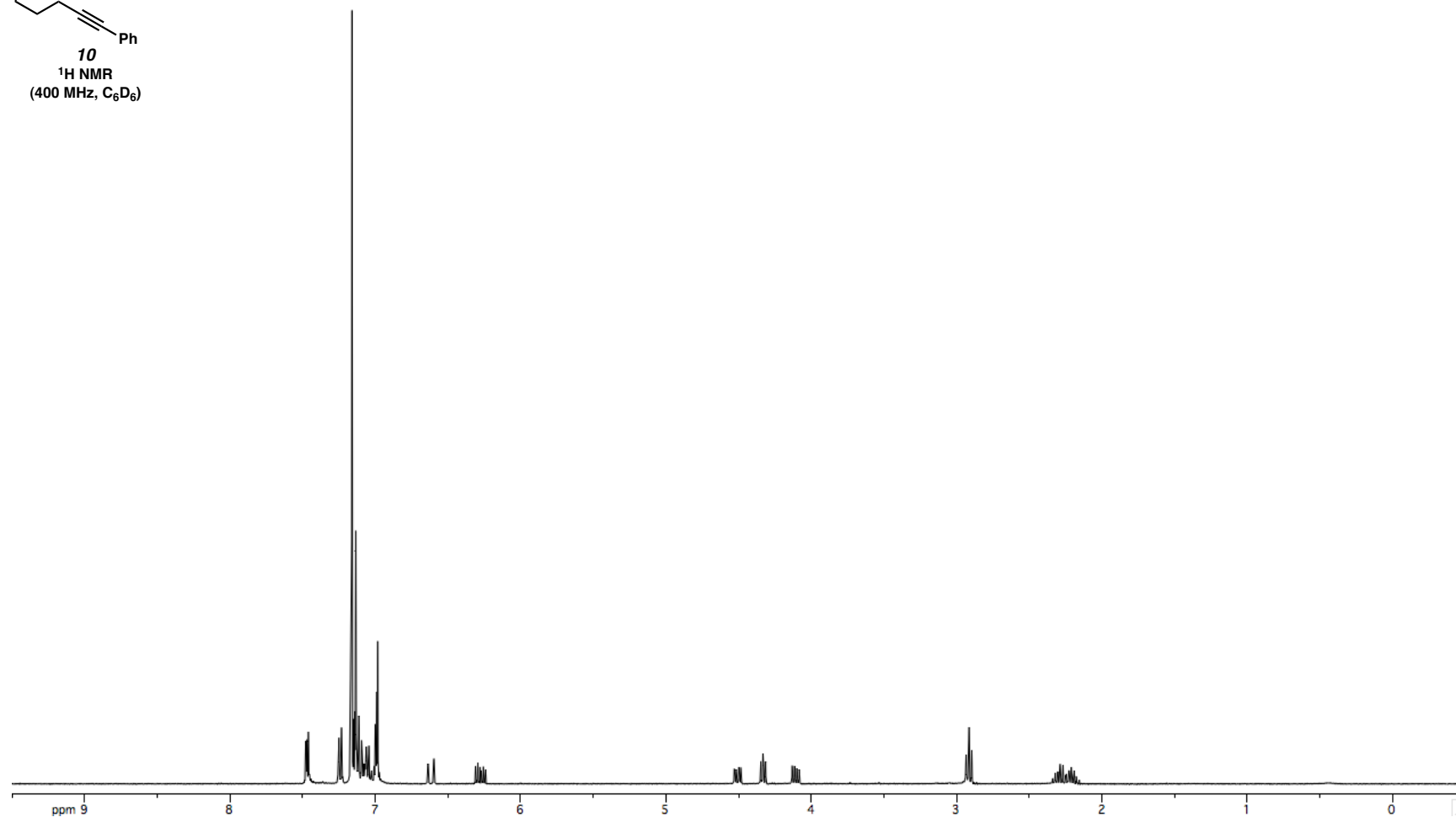
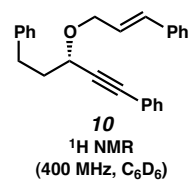


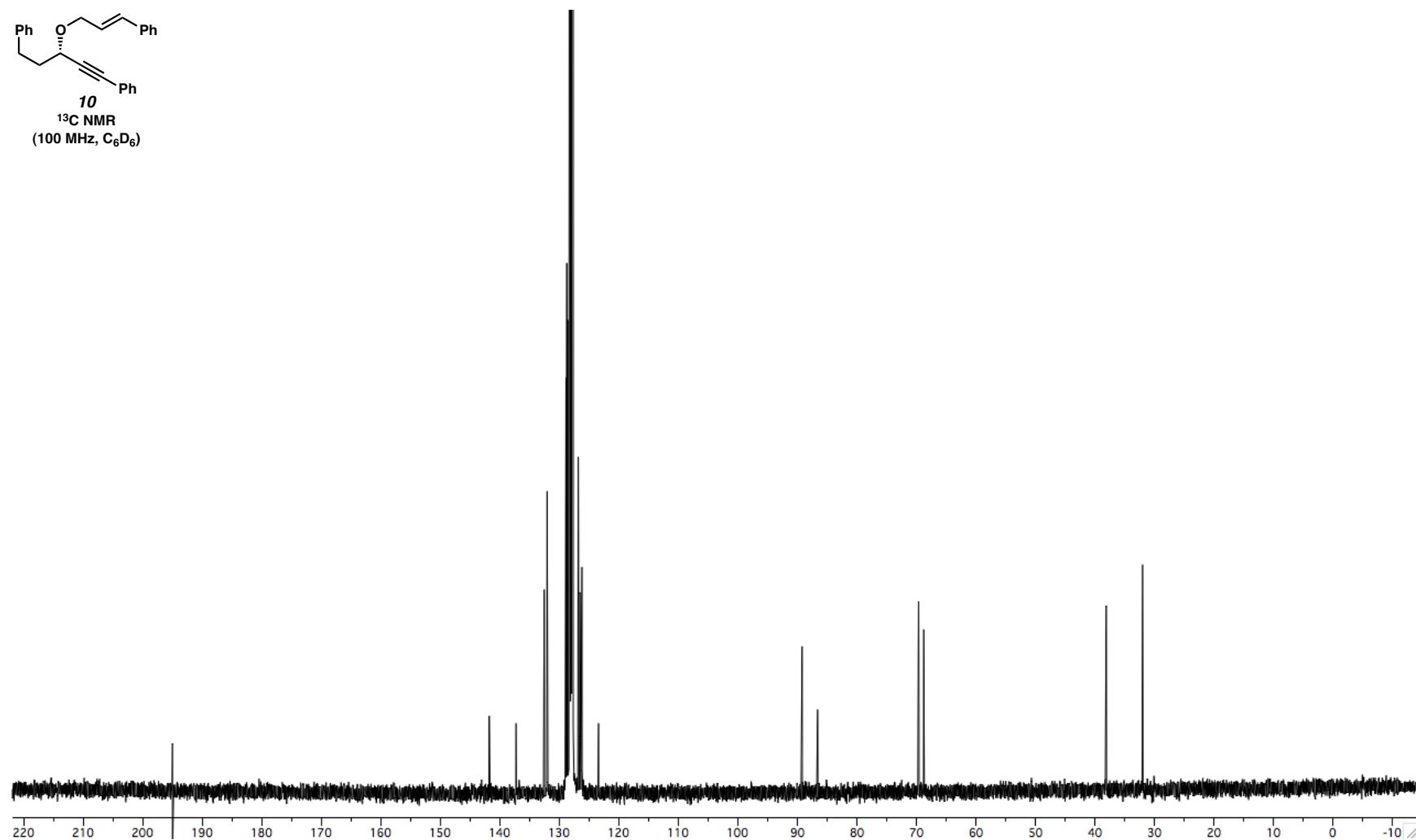


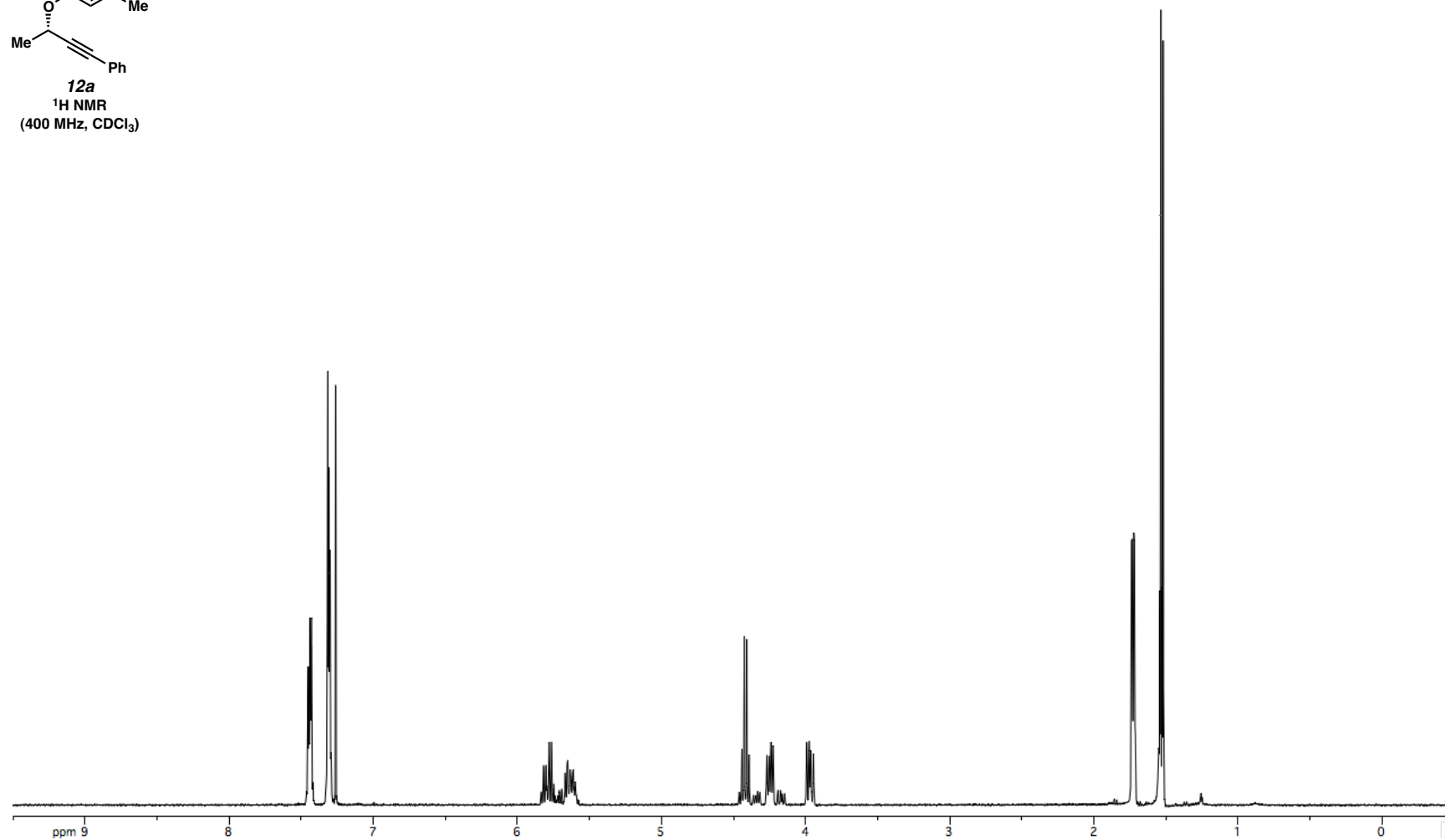
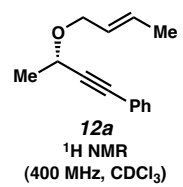


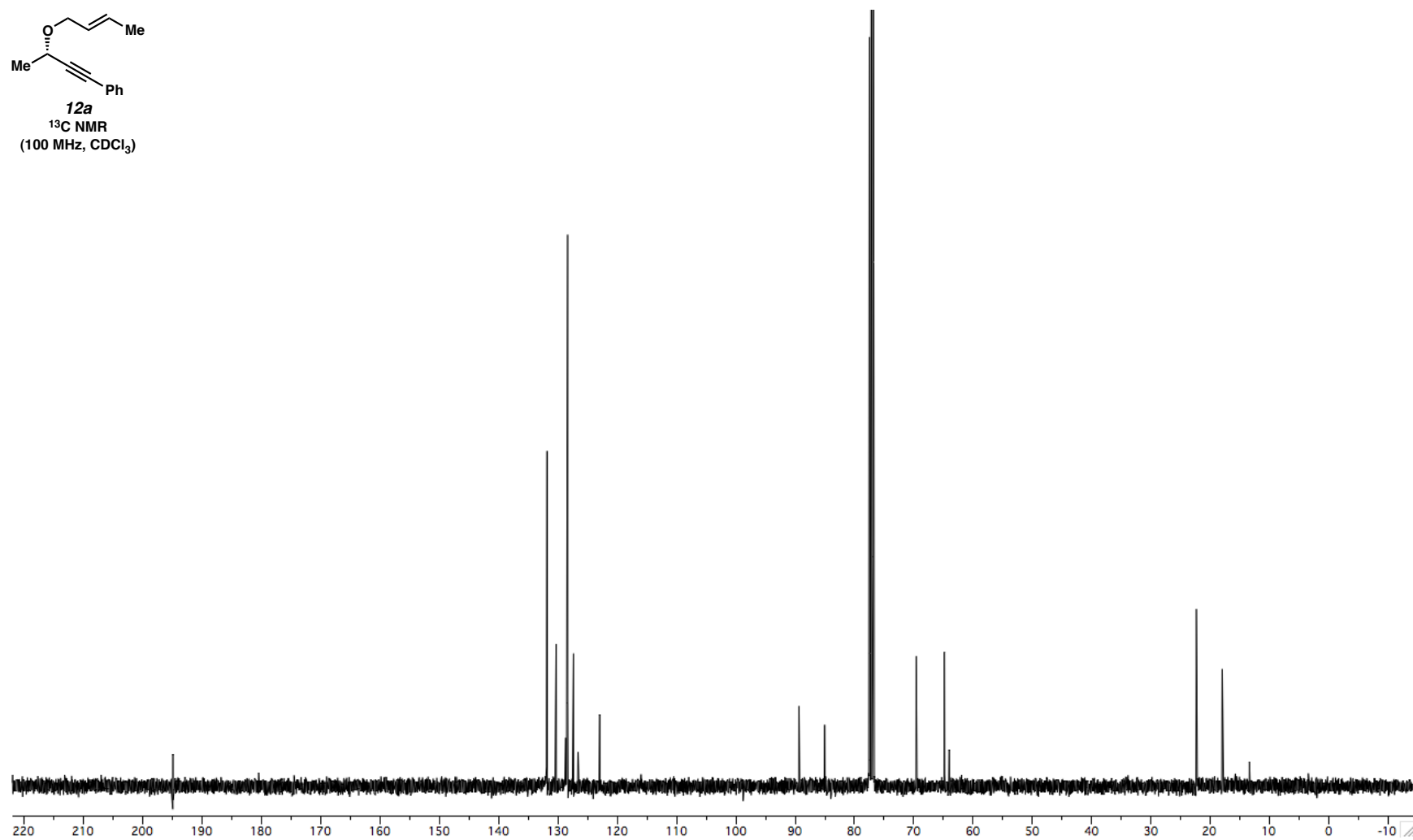
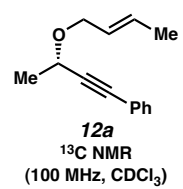
14k
 ^{13}C NMR
(100 MHz, CDCl_3)

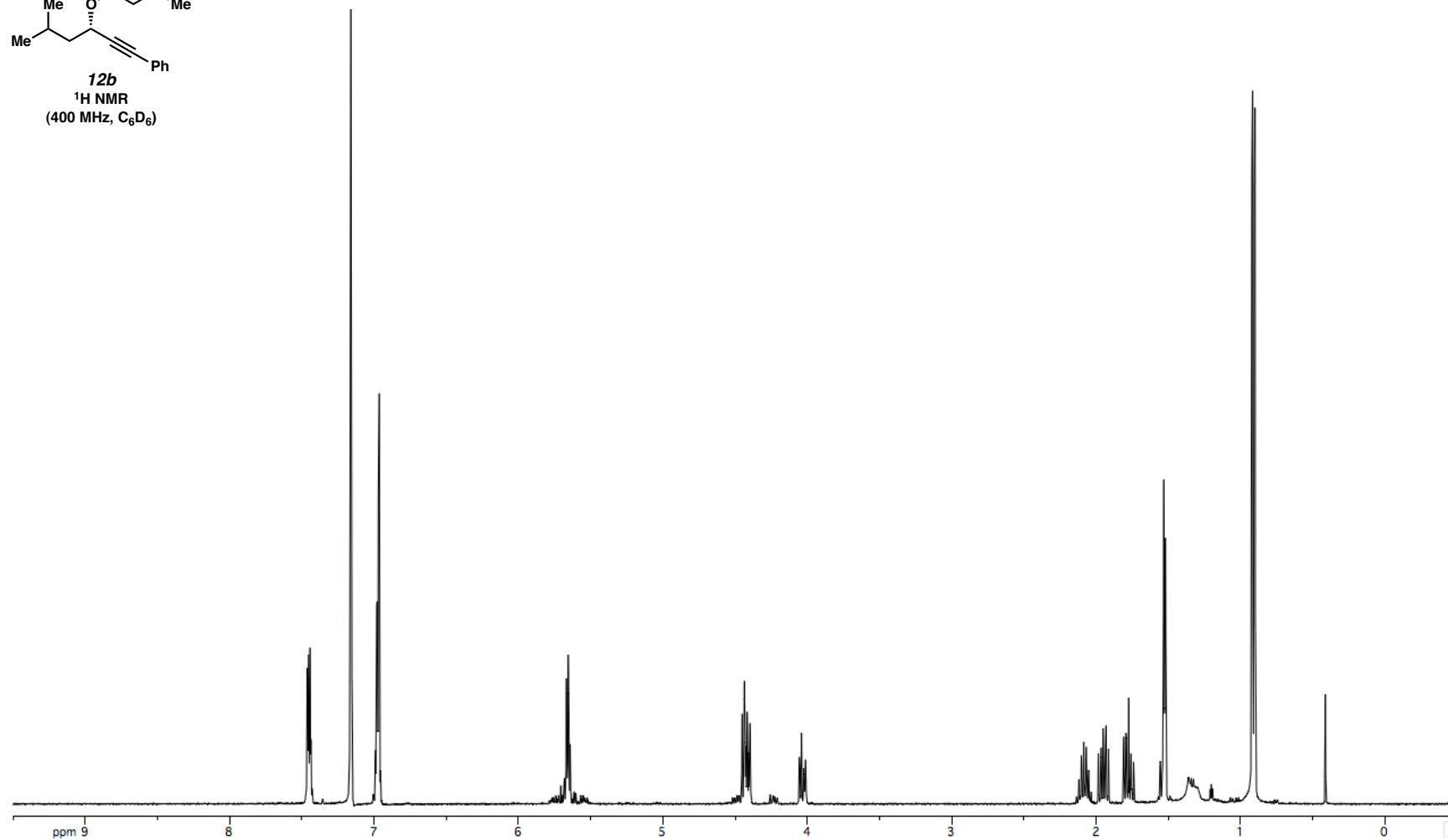
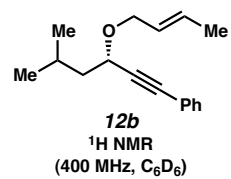


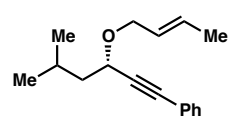




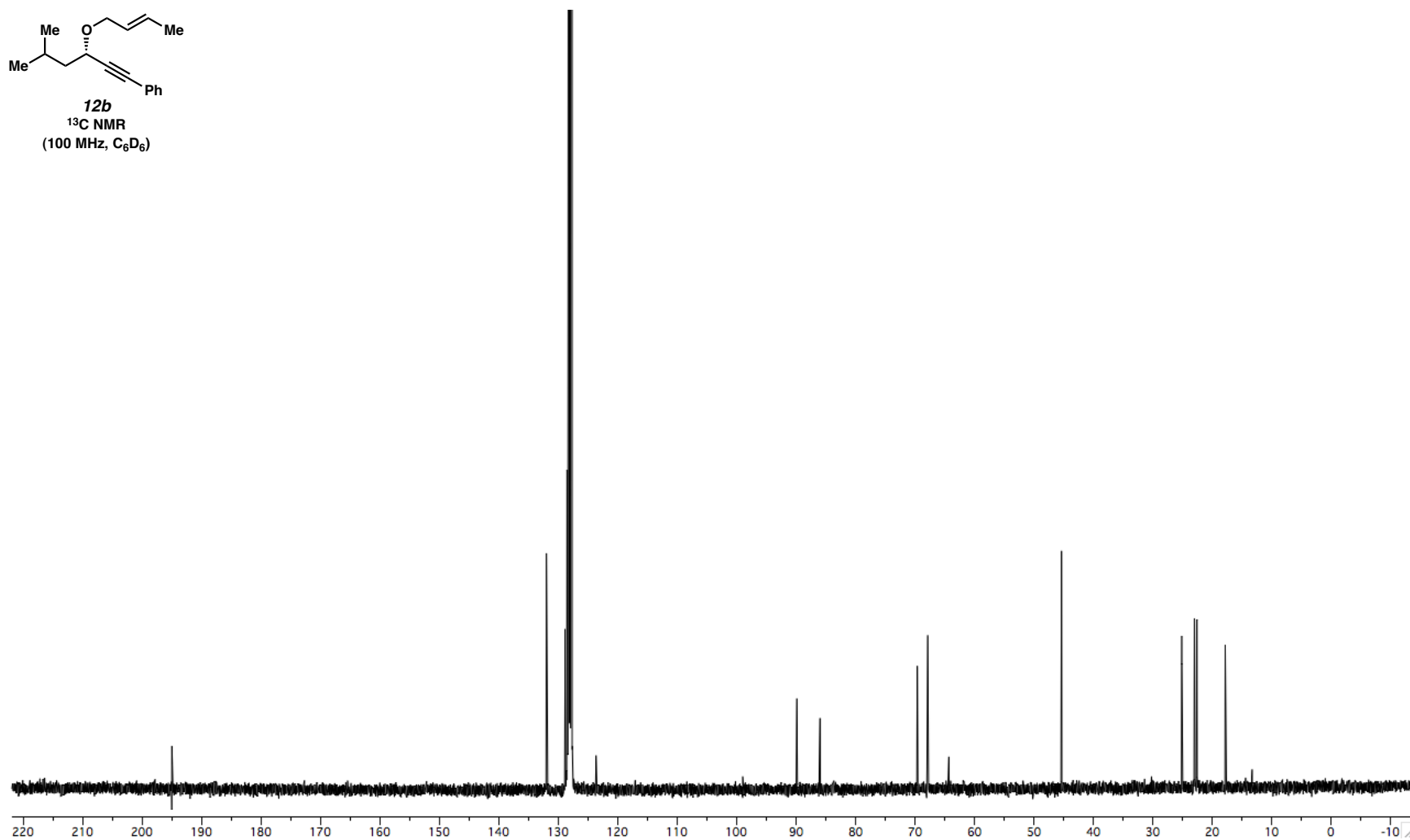


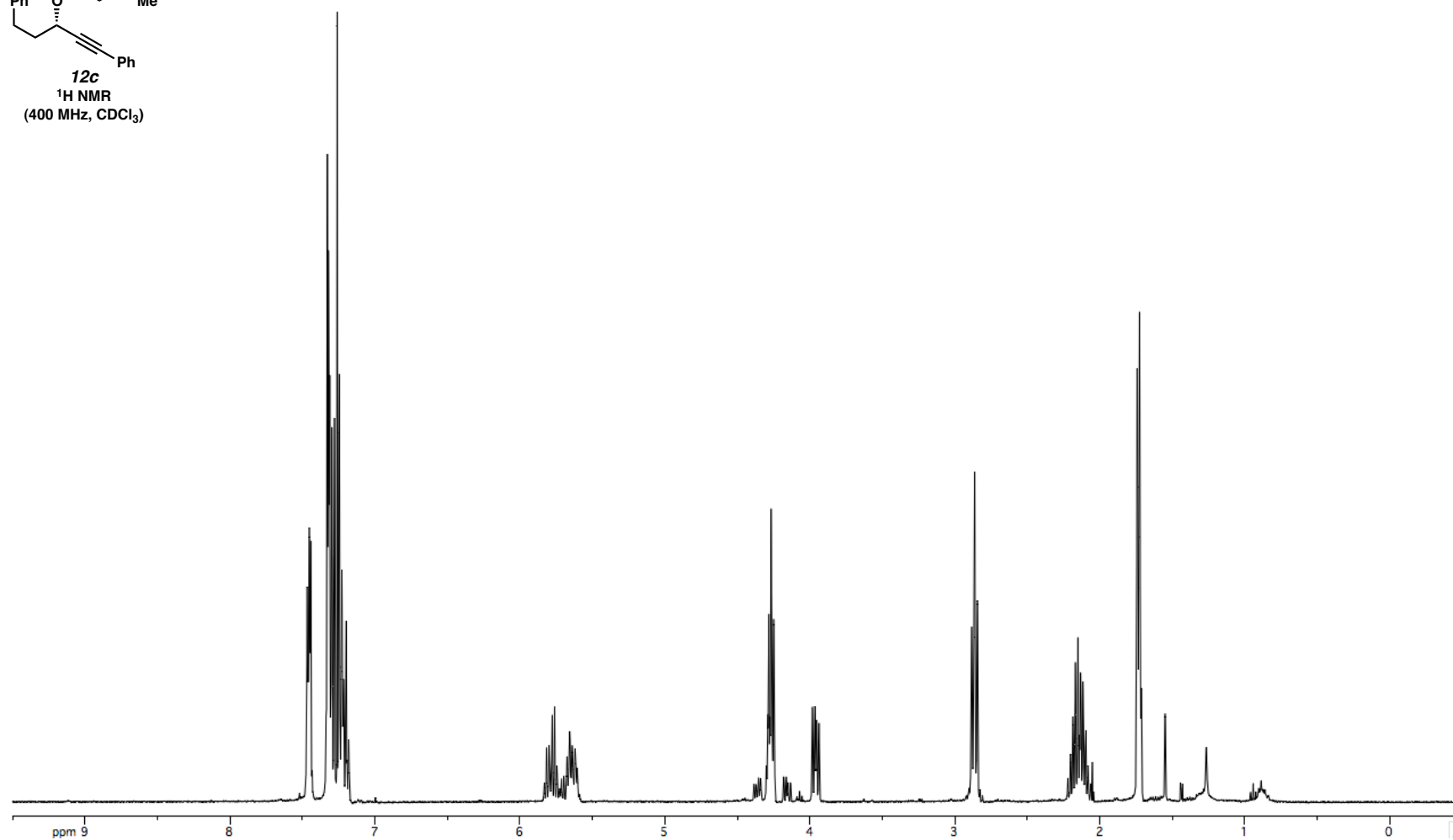
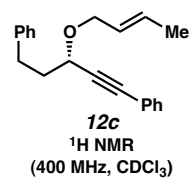


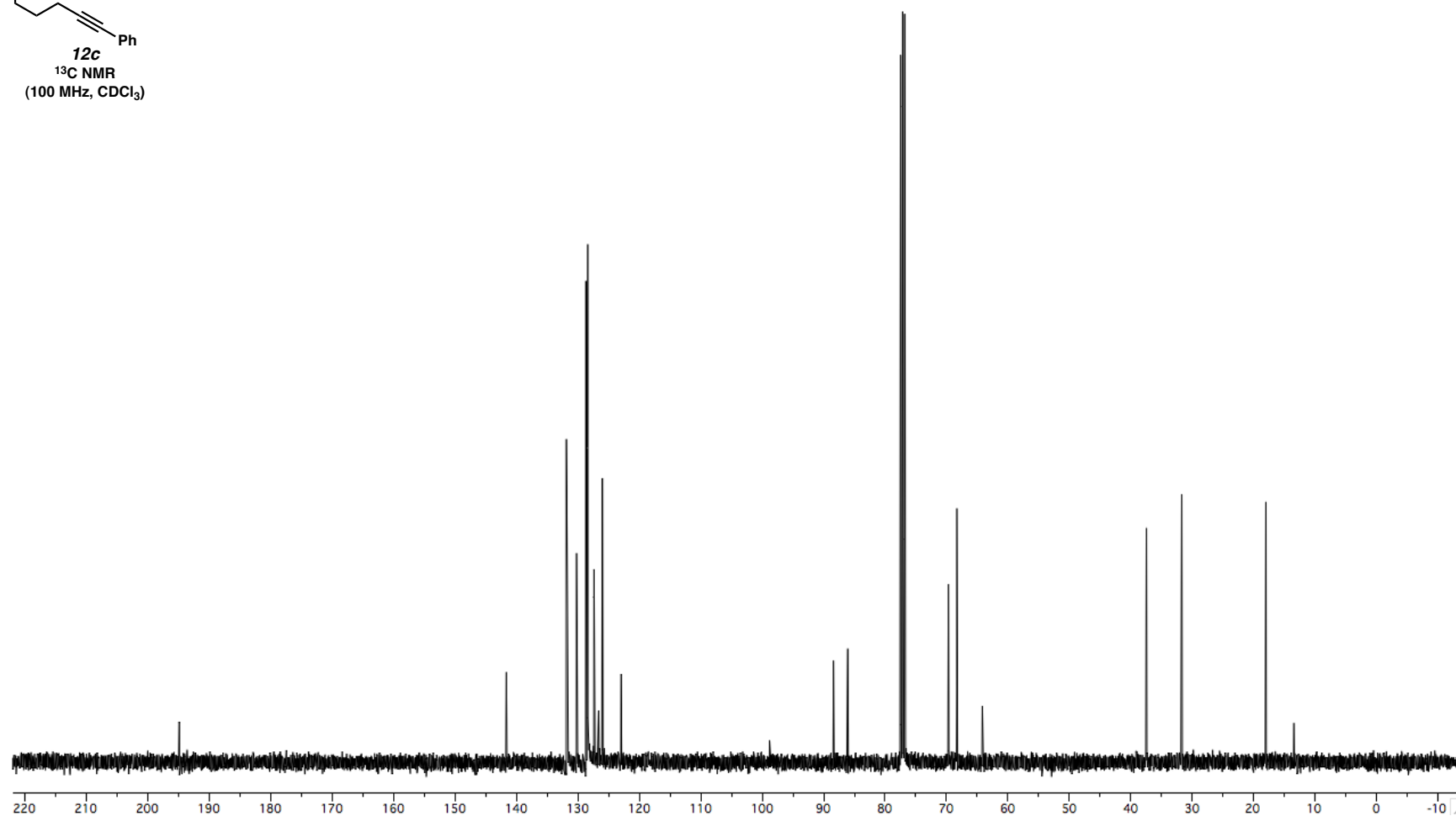
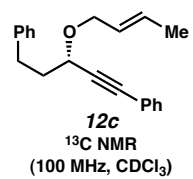


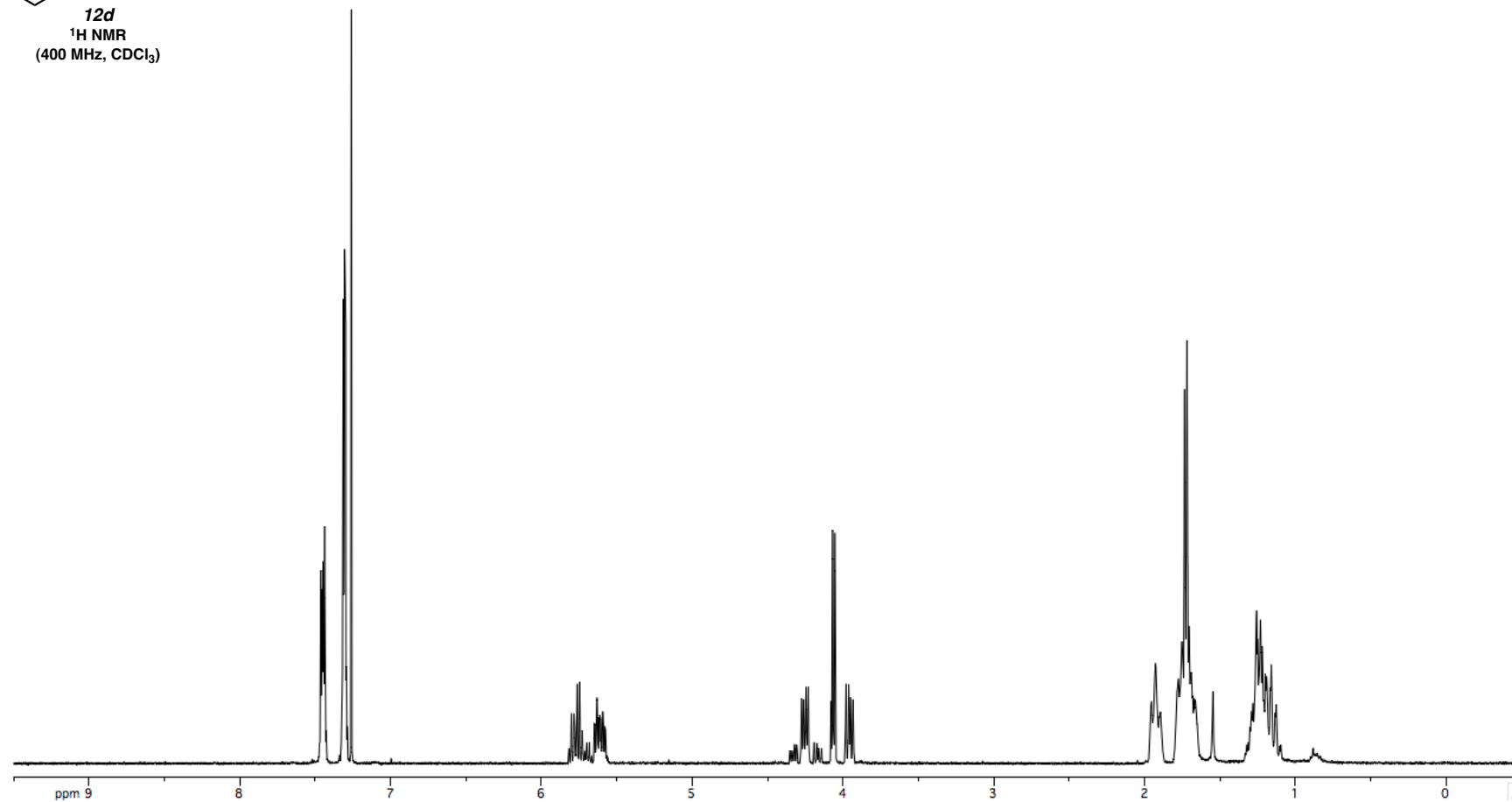
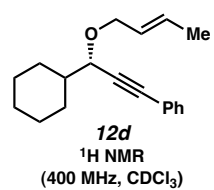


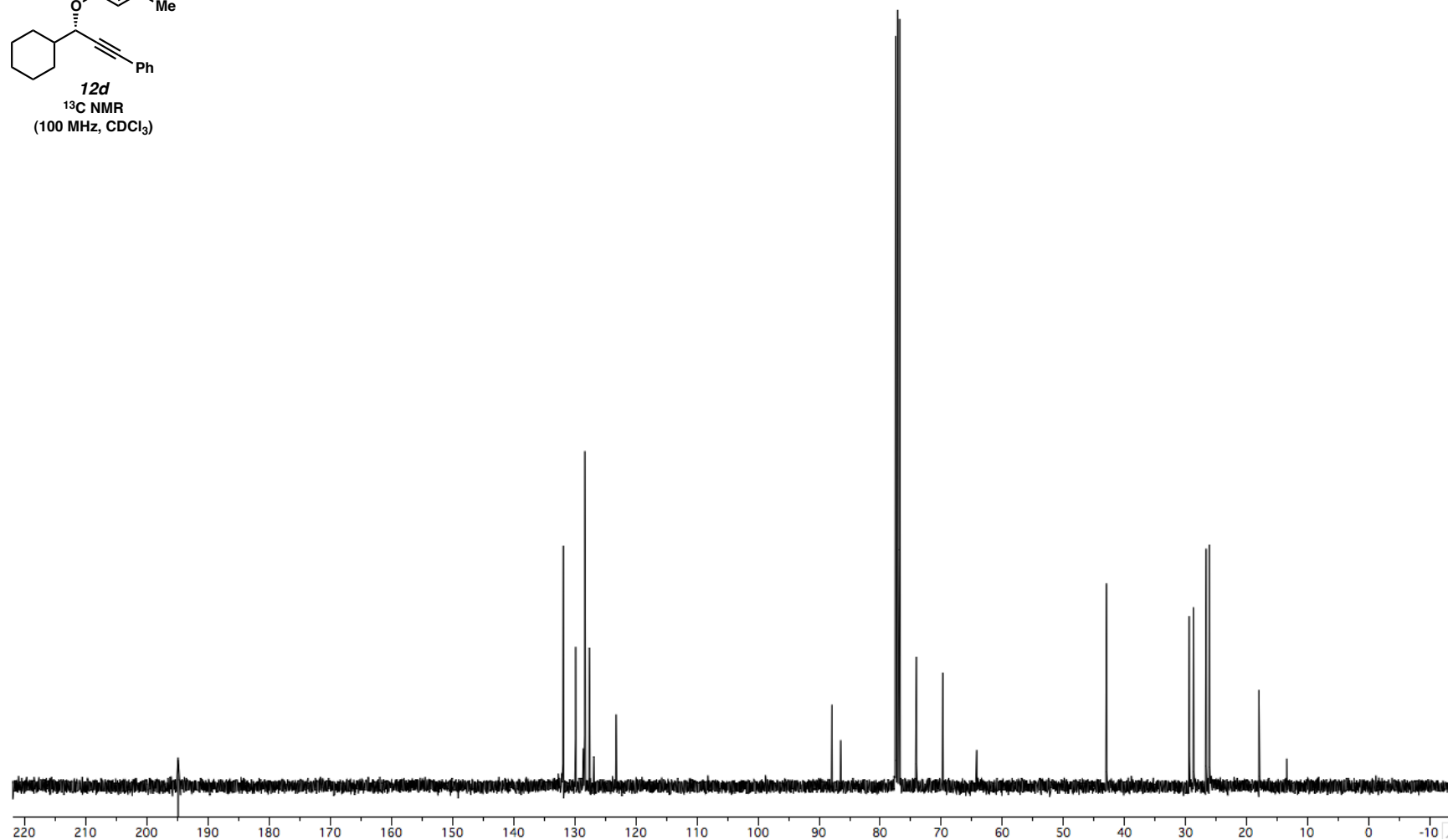
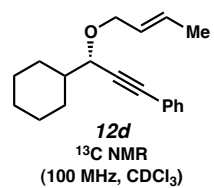
12b
¹³C NMR
(100 MHz, C₆D₆)

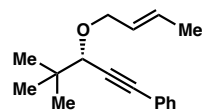




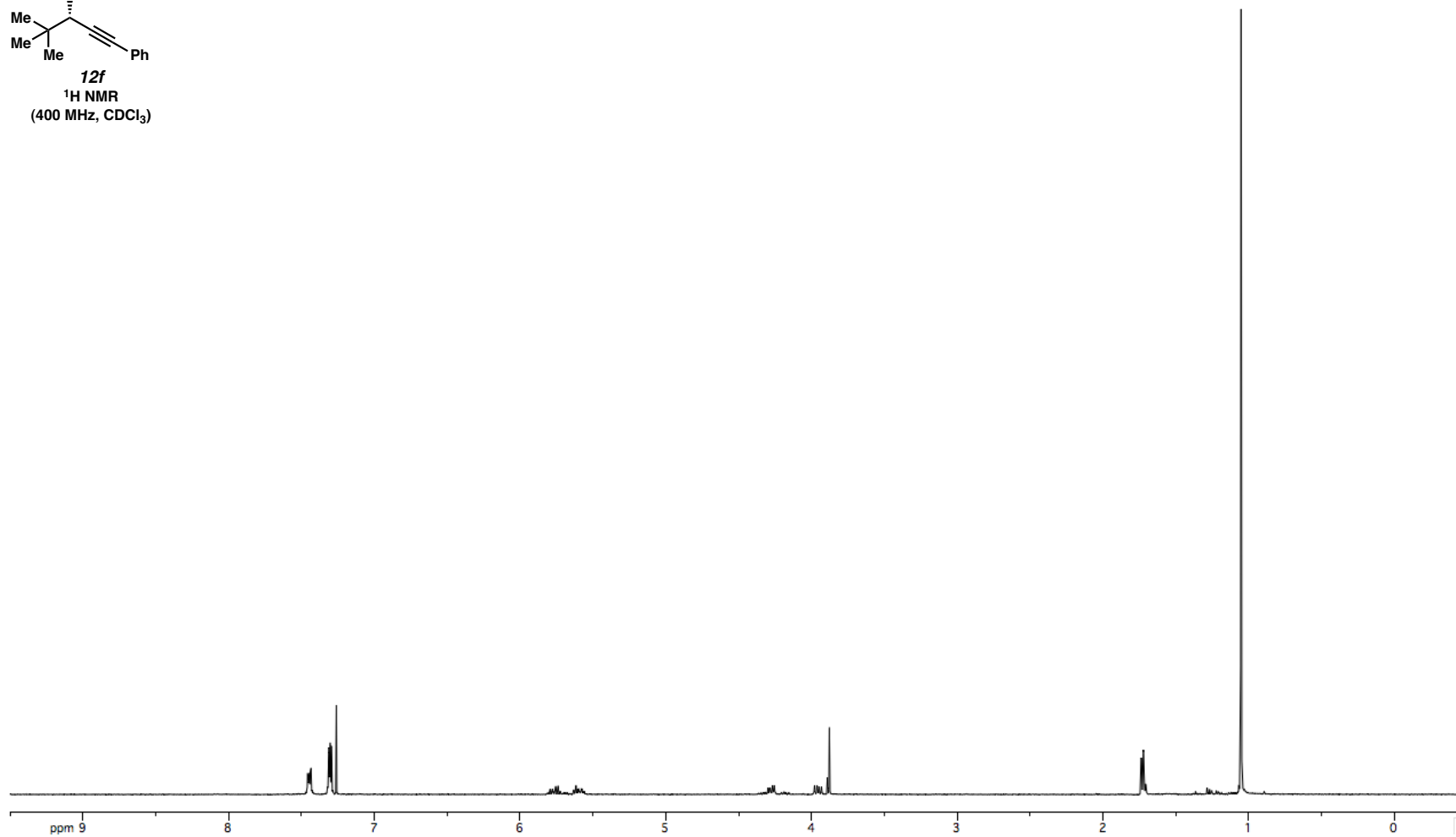


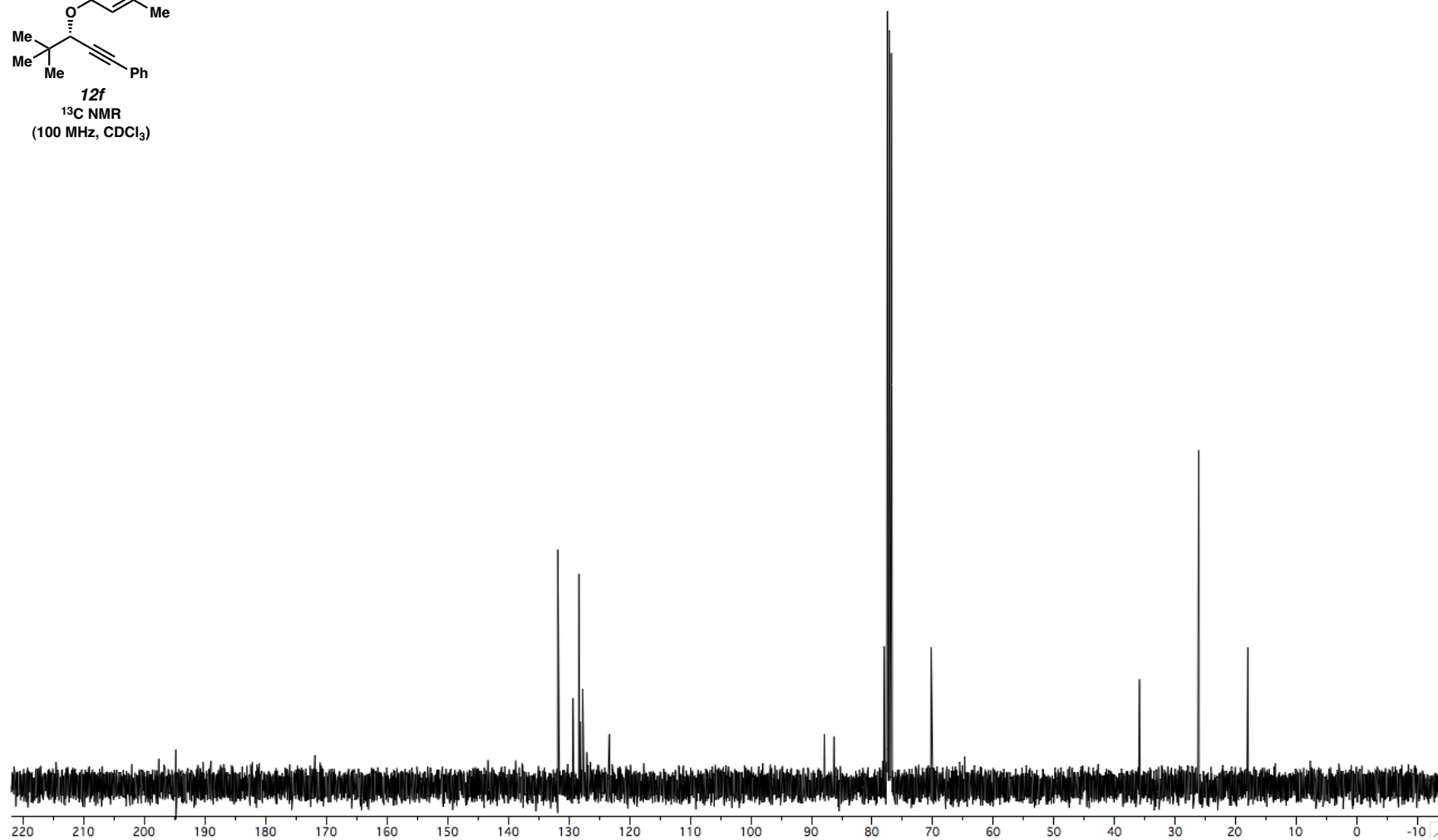
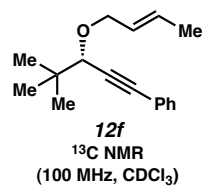






12f
¹H NMR
(400 MHz, CDCl₃)





HPLC Traces

