Supporting Information

Decarboxylative Hydroalkylation of Alkynes

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1) General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was prepared according to the literature procedure.[2] All solvents were purified with a J. C. Meyer Solvent Purification System. Non-aqueous reagents were transferred under nitrogen or argon via syringe. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on Sigma Aldrich 320–400 mesh silica gel (63 μM particle size). Thin-layer chromatography (TLC) was performed on Silicycle 0.25 mm silica gel F-254 plates. Visualization of the developed chromatogram was performed by $KMnO_4$ stain. R_f values of 0.2 can be obtained for all isolated compounds within the following range of TLC conditions: in 0-30% EtOAc in hexane. ^{1}H NMR spectra were recorded on a Bruker UltraShield Plus 500 MHz and are internally referenced to residual protio $CDCl_3$ signals (7.26 ppm) or protio DMSO-d_6 signals (2.50 ppm). $CDCl_3$ was stored over K_2CO_3. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br = broad), and coupling constant (Hz). ^{13}C NMR spectra were recorded on a Bruker UltraShield Plus 500 MHz and data are reported in terms of chemical shift relative to $CDCl_3$ (77.0 ppm) or DMSO-d_6 (39.52 ppm). For ^{1}H NMR analysis of crude reaction mixtures, methyl benzoate or mesitylene were used as internal standards, added as pure liquids. IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer and are reported in wavenumbers (cm^{-1}). High Resolution Mass Spectra were obtained from the Princeton University Mass Spectral Facility.

2) Preparation of carboxylic acids

The following carboxylic acid was prepared according to a literature procedure: (4*S*,5*S*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid.[3] All remaining carboxylic acid substrates are commercially available.

3) Preparation of alkynes

The following alkynes were prepared according to literature procedures: *tert*-butyl but-2-yn-1-ylcarbamate[4] and 2-(prop-1-yn-1-yl)-1,3-dioxolane[5]. All remaining alkyne substrates are commercially available.

4) Hydroalkylation Procedures

Decarboxylative hydroalkylation with α-amino and α-oxy acids (procedure A):

To an oven-dried 8 mL vial equipped with a stir bar, carboxylic acid (0.50 mmol, 1.0 equiv) was added. $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (11.2 mg, 10 μmol, 2 mol%), $NiCl_2$·glyme (11.0 mg, 50 μmol, 10 mol%) and dtbbpy (13.4 mg, 50 μmol, 10 mol%) were added as a 0.1 M solution in DMF (5.0 mL). The reaction mixture was degassed by sparging with N_2 while stirring for 10 min. To the degassed solution, alkyne (0.65 mmol, 1.3 equiv), TMG (6.3 μL, 50 μmol, 10 mol%), and separately degassed H_2O (180 μL, 10 mmol, 20 equiv) were added before sealing the vial with Parafilm. The reaction was stirred and irradiated with a 40 W blue LED kessil lamp for 24 hours (vial placed 6 cm from lamp, with fan positioned directly above reaction – reactions reach 30 °C in this setup) and diluted with EtOAc (20 mL). The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography to yield the desired product.

Decarboxylative hydroalkylation with α-carbon carboxylic acids (procedure B):

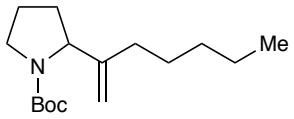
To an oven-dried 8 mL vial equipped with a stir bar, cesium fluoride (38 mg, 0.25 mmol, 0.5 equiv) was added in a nitrogen-filled glovebox. Following removal from the glovebox, carboxylic acid (0.50 mmol, 1.0 equiv) was added to this vial. $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (11.2 mg, 10 μmol, 2 mol%), $NiCl_2$·glyme (11.0 mg, 50 μmol, 10 mol%) and dtbbpy (13.4 mg, 50 μmol, 10 mol%) were added as a 0.1 M solution in DMSO (5.0 mL). The reaction mixture was degassed by sparging with N_2 while stirring for 10 min. To the degassed solution, alkyne (0.65 mmol, 1.3 equiv) was added before sealing the vial with Parafilm. The reaction was stirred and irradiated with 450 nm blue LEDs in the integrated photoreactor at 100% LED intensity, 1000 rpm stirring, and 5000 rpm fan speed[6] for 12 hours (reactions reach 30 °C in this setup) and

diluted with EtOAc (20 mL). These reactions can be performed in front of Kessil lamps, but in 5-15% lower yield. The organic layer was washed with brine (3 x 20 mL), dried over $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography to yield the desired product.

HAT hydroalkylation with α-amino C–H nucleophiles (procedure C):

To an oven-dried 8 mL vial equipped with a stir bar C–H nucleophile (2.5 mmol, 5.0 equiv) was added. $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (11.2 mg, 10 μmol, 2 mol%), $NiCl_2$·glyme (11.0 mg, 50 μmol, 10 mol%) and dtbbpy (13.4 mg, 50 μmol, 10 mol%) were added as a 0.1 M solution in EtOAc (5.0 mL). The reaction mixture was degassed by sparging with N_2 while stirring for 10 min at 0 ºC. To the degassed solution, alkyne (0.50 mmol, 1.0 equiv), 3-acetoxyquinuclidine (73 μL, 0.5 mmol, 100 mol%), and separately degassed H_2O (180 μL, 10 mmol, 20 equiv) were added before sealing the vial with Parafilm. The reaction was stirred and irradiated with 450 nm blue LEDs (reactions reach 30 °C in this setup) in the integrated photoreactor at 100% LED intensity, 1000 rpm stirring, and 5000 rpm fan speed[6] for 6 hours and diluted with EtOAc (20 mL). These reactions can be performed in front of Kessil lamps, but in 5-15% lower yield. The organic layer was washed with saturated ammonium chloride and brine (1 x 20 mL and 2 x 20 mL, respectively), dried over $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography to yield the desired product.

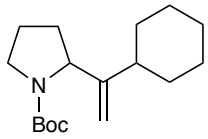
5) Experimental Data for Decarboxylative Hydroalkylation Products



***tert*-butyl 2-(hept-1-en-2-yl)pyrrolidine-1-carboxylate (11)**

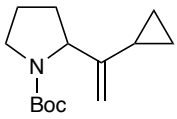
Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 1-heptyne (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (107 mg, 0.40 mmol, 80%) as a colorless oil. IR (film) ν_{max} 2960, 2929, 2873, 1694, 1389, 1364 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.81 – 4.67 (m, 2H), 4.30 – 4.13 (m, 1H), 3.48 – 3.34 (m, 2H), 2.04 – 1.87 (m, 3H),

1.87 – 1.73 (m, 2H), 1.72 – 1.65 (m, 1H), 1.47 – 1.24 (m, 15H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 154.3, 150.3, 149.7, 107.2, 106.9, 79.0, 61.4, 61.3, 46.9, 46.5, 33.1, 32.9, 31.9, 31.8, 31.4, 30.6, 28.5, 28.4, 27.8, 27.4, 23.3, 22.6, 22.5, 14.0; HRMS (ESI-TOF) m/z calcd. For $C_{16}H_{29}NNaO_2$ ($[M+Na]^+$) 290.2096, found 290.2091.



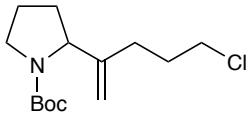
***tert*-butyl 2-(1-cyclohexylvinyl)pyrrolidine-1-carboxylate (12)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and cyclohexylacetylene (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (108 mg, 0.39 mmol, 77%) as a colorless oil. IR (film) ν_{max} 2975, 2925, 2853, 1693, 1389, 1364 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.75 (s, 1H), 4.72 – 4.63 (m, 1H), 4.37 – 4.16 (m, 1H), 3.52 – 3.31 (m, 2H), 2.04 – 1.62 (m, 9H), 1.48 – 1.37 (m, 9H), 1.36 – 1.00 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) 155.9, 154.6, 105.3, 105.1, 79.1, 78.9, 60.8, 60.6, 47.0, 46.6, 41.8, 34.2, 33.9, 32.6, 31.6, 30.9, 28.5, 27.0, 26.9, 26.4, 23.0, 22.1; HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{29}NNaO_2$ ($[M+Na]^+$) 302.2096, found 302.2088.



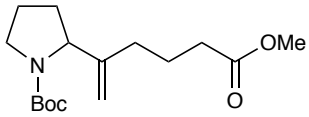
***tert*-butyl 2-(1-cyclopropylvinyl)pyrrolidine-1-carboxylate (13)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and cyclopropylacetylene (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (69 mg, 0.29 mmol, 58%) as a colorless oil. IR (film) ν_{max} 2974, 2931, 2877, 1699, 1388, 1364 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.60 – 4.51 (m, 1H), 4.49 (s, 1H), 4.25 – 4.11 (m, 1H), 3.32 – 3.27 (m, 2H), 2.07 – 1.92 (m, 1H), 1.81 – 1.70 (m, 3H), 1.41 – 1.27 (m, 9H), 1.28 – 1.16 (m, 1H), 0.69 – 0.59 (m, 2H), 0.52 – 0.33 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.4, 153.0, 151.9, 151.0, 104.1, 78.0, 61.1, 46.5, 46.3, 31.3, 30.4, 28.1, 22.9, 22.1, 13.1, 6.9, 6.3, 6.0, 5.7; HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{23}NNaO_2$ ($[M+Na]^+$) 260.1626, found 260.1619.



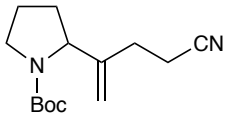
***tert*-butyl 2-(5-chloropent-1-en-2-yl)pyrrolidine-1-carboxylate (14)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 5-chloropent-1-yne (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (116 mg, 0.43 mmol, 85%) as a colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.84 – 4.76 (m, 2H), 4.31 – 4.13 (m, 1H), 3.63 – 3.54 (m, 2H), 3.49 – 3.35 (m, 2H), 2.23 – 2.15 (m, 1H), 2.15 – 2.05 (m, 1H), 2.04 – 1.90 (m, 3H), 1.88 – 1.75 (m, 2H), 1.73 – 1.66 (m, 1H), 1.49 – 1.37 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.5, 148.5, 148.0, 108.4, 79.2, 61.1, 47.0, 46.6, 44.8, 44.5, 31.4, 30.8, 30.6, 30.5, 30.0, 29.8, 28.5, 28.5, 23.3, 22.5. This NMR data is consistent with previously reported synthesis[7].



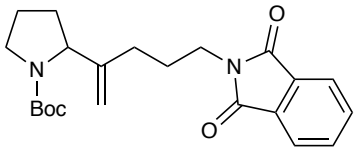
***tert*-butyl 2-(6-methoxy-6-oxohex-1-en-2-yl)pyrrolidine-1-carboxylate (15)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and methyl hex-5-ynoate (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (123 mg, 0.42 mmol, 83%) as a colorless oil. IR (film) ν_{max} 2962, 1737, 1691, 1391, 1365, 1161 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.83 – 4.74 (m, 2H), 4.29 – 4.14 (m, 1H), 3.67 (s, 3H), 3.48 – 3.35 (m, 2H), 2.41 – 2.29 (m, 2H), 2.08 – 1.92 (m, 3H), 1.92 – 1.73 (m, 4H), 1.71 – 1.64 (m, 1H), 1.48 – 1.37 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 154.4, 154.1, 148.9, 148.3, 108.0, 107.8, 79.1, 79.0, 61.1, 61.0, 51.4, 46.8, 46.4, 33.5, 32.2, 31.9, 31.3, 30.5, 29.6, 28.4, 28.3, 23.2, 23.0, 22.8, 22.4; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{16}H_{27}NNaO_4$ ($[M+Na]^+$) 320.1838, found 320.1836.



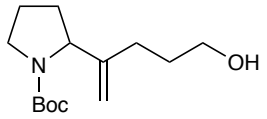
***tert*-butyl 2-(4-cyanobut-1-en-2-yl)pyrrolidine-1-carboxylate (16)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and pent-4-ynenitrile (procedure A). Purification by flash column chromatography (0-25% EtOAc/hexane) provided the title compound (94 mg, 0.38 mmol, 75%) as a colorless oil. IR (film) ν_{max} 2976–2930, 1786, 1365, 1391, 1160 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 4.94 (s, 1H), 4.92 – 4.82 (m, 1H), 4.31 – 4.12 (m, 1H), 3.55 – 3.36 (m, 2H), 2.53 (s, 2H), 2.42 – 2.25 (m, 2H), 2.10 – 1.96 (m, 1H), 1.90 – 1.78 (m, 2H), 1.71 – 1.65 (m, 1H), 1.49 – 1.38 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.5, 146.9, 146.6, 119.7, 119.4, 110.0, 109.5, 79.7, 79.6, 61.1, 47.2, 46.8, 31.8, 31.0, 28.6, 23.6, 22.8, 16.3, 16.0; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{14}H_{22}N_2NaO_2$ ($[M+Na]^+$) 273.1579, found 273.1572.



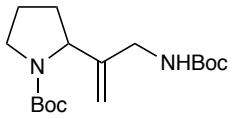
***tert*-butyl 2-(5-(1,3-dioxoisoindolin-2-yl)pent-1-en-2-yl)pyrrolidine-1-carboxylate (17)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 2-(pent-4-yn-1-yl)isoindoline-1,3-dione (procedure A) with one modification: alkyne was added as a solid along with carboxylic acid before dissolution. Purification by flash column chromatography (0-30% EtOAc/hexane) provided the title compound (138 mg, 0.36 mmol, 72%) as a colorless, viscous oil. IR (film) ν_{max} 2974, 2932, 2877, 1708, 1688, 1363 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.89 – 7.81 (m, 4H), 4.82 – 4.72 (m, 1H), 4.65 (s, 1H), 4.16 – 4.05 (m, 1H), 3.60 (t, *J* = 7.1 Hz, 2H), 3.29 (t, *J* = 6.9 Hz, 2H), 2.05 – 1.87 (m, 3H), 1.87 – 1.57 (m, 5H), 1.38 – 1.24 (m, 9H); ^{13}C NMR (126 MHz, DMSO) δ 168.0, 153.4, 149.8, 148.8, 134.4, 131.6, 123.0, 107.2, 79.2, 60.8, 60.7, 46.5, 46.3, 37.4, 31.0, 30.2, 29.6, 28.1, 28.0, 26.3, 26.2, 22.9, 22.1; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{22}H_{28}N_2NaO_4$ ($[M+Na]^+$) 407.1947, found 407.1938.



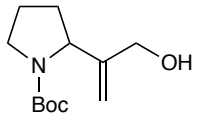
***tert*-butyl 2-(5-hydroxypent-1-en-2-yl)pyrrolidine-1-carboxylate (18)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and pent-4-yn-1-ol (procedure A). Purification by flash column chromatography (0-25% EtOAc/hexane) provided the title compound (97 mg, 0.38 mmol, 76%) as a colorless oil. IR (film) ν_{max} 3423, 2974, 2932, 2876, 1674, 1392 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 4.76 – 4.68 (m, 1H), 4.62 (s, 1H), 4.43 – 4.35 (m, 1H), 4.16 – 4.09 (m, 1H), 3.47 – 3.37 (m, 2H), 3.31 – 3.26 (m, 1H), 2.08 – 1.88 (m, 3H), 1.79 – 1.69 (m, 2H), 1.66 – 1.49 (m, 3H), 1.42 – 1.28 (m, 9H); ^{13}C NMR (126 MHz, DMSO) δ 153.4, 153.1, 150.4, 149.5, 106.8, 106.7, 78.0, 60.7, 60.4, 46.5, 46.3, 30.9, 30.7, 30.0, 28.9, 28.2, 28.1, 22.9, 22.1; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{14}H_{25}NNaO_3$ ($[M+Na]^+$) 278.1732, found 278.1731.



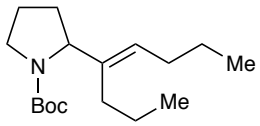
***tert*-butyl 2-(3-((*tert*-butoxycarbonyl)amino)prop-1-en-2-yl)pyrrolidine-1-carboxylate (19)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and *N*-Boc-propargylamine (procedure A) with one modification: alkyne was added as a solid along with carboxylic acid before dissolution. Purification by flash column chromatography (0-30% EtOAc/hexane) provided the title compound (137 mg, 0.42 mmol, 84%) as a white solid. IR (film) ν_{max} 3368, 2973, 2931, 2895, 1684, 1521 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.03 (t, J = 5.8 Hz, 1H), 4.81 (s, 1H), 4.66 (s, 1H), 4.19 – 4.09 (m, 1H), 3.56 – 3.42 (m, 2H), 3.33 – 3.28 (m, 2H), 2.03 – 1.87 (m, 1H), 1.83 – 1.63 (m, 3H), 1.41 – 1.31 (m, 18H); ^{13}C NMR (126 MHz, DMSO) δ 155.5, 155.4, 153.3, 153.1, 148.8, 147.7, 106.9, 78.1, 77.6, 59.2, 59.0, 46.4, 46.2, 42.1, 31.1, 30.3, 28.3, 28.2, 28.0, 27.5, 23.0, 22.2; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{17}H_{30}N_2NaO_4$ ($[M+Na]^+$) 349.2103, found 349.2092.



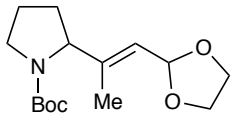
***tert*-butyl 2-(3-hydroxyprop-1-en-2-yl)pyrrolidine-1-carboxylate (20)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and propargyl alcohol (procedure A). Purification by flash column chromatography (0-40% EtOAc/hexane) provided the title compound (75 mg, 0.33 mmol, 66%) as a colorless oil. IR (film) ν_{max} 3413, 2974, 2931, 2877, 1671, 1393, 1364 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.08 (s, 1H), 4.91 (s, 1H), 4.50 – 4.23 (m, 1H), 4.19 – 4.04 (m, 2H), 3.50 – 3.40 (m, 2H), 3.01 (s, 0.5H) 2.04 (s, 1H), 1.93-1.73 (m, 3.5H), 1.44 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.1, 154.6, 150.4, 149.8, 110.3, 109.2, 79.8, 79.5, 64.8, 64.4, 59.1, 58.1, 46.9, 46.6, 32.2, 31.0, 28.6, 23.8, 22.8; HRMS (ESI-TOF) *m*/*z* calcd. For $C_{12}H_{21}NNaO_3$ ($[M+Na]^+$) 250.1419, found 250.1417.



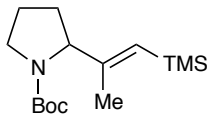
***tert*-butyl (*E*)-2-(oct-4-en-4-yl)pyrrolidine-1-carboxylate (21)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 1-heptyne (procedure A). Purification by flash column chromatography (0-15% EtOAc/hexane) provided the title compound (85 mg, 0.30 mmol, 60%) as a colorless oil. IR (film) ν_{max} 2959, 2930, 2871, 1693, 1390, 1364 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.04 (t, *J* = 7.2 Hz, 3H), 4.33 – 4.13 (m, 1H), 3.48-3.31 (m, 2H), 2.19-2.05 (m, 1H), 2.04-1.87 (m, 3H), 1.86 – 1.70 (m, 3H), 1.69-1.63 (m, 1H), 1.52 – 1.31 (m, 13H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 139.3, 122.9, 78.9, 61.2, 46.6, 31.5, 31.2, 29.6, 28.5, 23.2, 22.2, 22.1, 14.6, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{17}H_{31}NNaO_2$ ($[M+Na]^+$) 304.2252, found 304.2249.



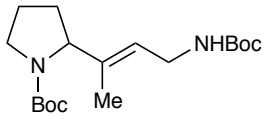
***tert*-butyl (*E*)-2-(1-(1,3-dioxolan-2-yl)prop-1-en-2-yl)pyrrolidine-1-carboxylate (22)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 2-(prop-1-yn-1-yl)-1,3-dioxolane (procedure A) with one modification: prior to loading the crude material, the silica gel column was washed with a solution of 1% triethylamine in hexane (3 column volumes). Purification by flash column chromatography (0-25% EtOAc/hexane) provided the title compound as a mixture of rotamers (101 mg, 0.36 mmol, 71%) as a white solid, which was immediately stored at -20 °C. IR (film) ν_{max} 2971, 2929, 2881, 1680, 1392, 1367 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.51 (d, *J* = 6.9 Hz, 1H), 5.25 (d, *J* = 6.9 Hz, 1H), 4.29 – 4.04 (m, 1H), 4.02 – 3.92 (m, 2H), 3.91 – 3.82 (m, 2H), 3.55 – 3.35 (m, 2H), 2.09 – 1.91 (m, 1H), 1.90 – 1.81 (m, 1H), 1.81 – 1.66 (m, 5H), 1.46 – 1.36 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 154.4, 144.6, 144.2, 120.4, 119.6, 100.7, 100.5, 79.5, 79.3, 65.0, 64.9, 63.4, 62.7, 47.2, 47.0, 31.6, 30.5, 28.6, 28.5, 23.5, 23.3, 14.7, 13.7; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{15}H_{25}NNaO_4$ ($[M+Na]^+$) 306.1681, found 306.1677.



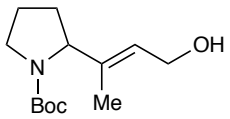
***tert*-butyl (*E*)-2-(1-(trimethylsilyl)prop-1-en-2-yl)pyrrolidine-1-carboxylate (23)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and trimethyl(prop-1-yn-1-yl)silane (TMS acetylene) (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of rotamers (105 mg, 0.37 mmol, 74%) as a colorless oil. IR (film) ν_{max} 2963, 1694, 1389, 1364, 1247, 1164, 1111 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.09 (s, 1H), 4.09 – 3.95 (m, 1H), 3.31 – 3.26 (m, 2H), 2.07 – 1.88 (m, 1H), 1.74 – 1.67 (m, 5H), 1.64 – 1.57 (m, 1H), 1.42 – 1.29 (m, 9H), 0.08 (s, 9H).; ^{13}C NMR (126 MHz, DMSO) δ 155.4, 153.4, 119.2, 118.9, 77.9, 64.7, 64.1, 46.6, 31.3, 30.3, 28.1, 27.9, 23.0, 22.6, 18.3, 18.1, 0.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{15}H_{29}NNaO_2Si$ ($[M+Na]^+$) 306.1865, found 306.1861.



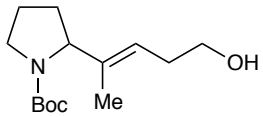
***tert*-butyl (*E*)-2-(4-((*tert*-butoxycarbonyl)amino)but-2-en-2-yl)pyrrolidine-1-carboxylate (24)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and *tert*-butyl but-2-yn-1-ylcarbamate (procedure A) with one modification: alkyne was added as a solid along with carboxylic acid before dissolution. Purification by flash column chromatography (0-30% EtOAc/hexane) provided the title compound as a mixture of rotamers (109 mg, 0.32 mmol, 64%) as a light yellow solid. IR (film) ν_{max} 3349, 2975, 2931, 1689, 1517, 1395, 1365 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.18 (t, *J* = 6.7 Hz, 1H), 4.43 (m, 1H), 4.14 (d, *J* = 60.7 Hz, 1H), 3.75 (s, 2H), 3.54 – 3.32 (m, 2H), 2.05 – 1.90 (m, 1H), 1.87 – 1.72 (m, 2H), 1.48 – 1.37 (m, 18H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8, 155.7, 154.6, 154.3, 139.4, 138.8, 119.7, 119.1, 79.1, 79.0, 63.3, 62.8, 47.0, 46.8, 38.2, 38.1, 31.4, 30.5, 28.4, 28.4, 23.3, 23.0, 13.7, 13.2; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{18}H_{32}N_2NaO_4$ ($[M+Na]^+$) 363.2260, found 363.2254.



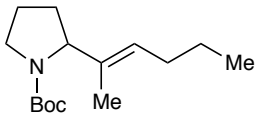
***tert*-butyl (*E*)-2-(4-hydroxybut-2-en-2-yl)pyrrolidine-1-carboxylate (25)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and but-2-yn-1-ol (procedure A). Purification by flash column chromatography (0-30% EtOAc/hexane) provided the title compound as a mixture of rotamers (77 mg, 0.32 mmol, 64%) as a colorless oil. IR (film) ν_{max} 33418, 2975, 2931, 2875, 1675, 1395, 1365 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 5.20 (s, 1H), 4.49 (t, *J* = 5.3 Hz, 1H), 4.11 – 3.99 (m, 1H), 3.96 (s, 2H), 3.30 – 3.21 (m, 1H), 2.01 – 1.85 (m, 1H), 1.79 – 1.67 (m, 2H), 1.62 (s, 1H), 1.49 (s, 3H), 1.43 – 1.28 (m, 9H); ^{13}C NMR (126 MHz, DMSO) δ 153.5, 153.2, 136.0, 135.3, 124.2, 123.6, 78.0, 63.0, 62.3, 57.5, 46.6, 46.6, 30.9, 30.0, 28.2, 28.0, 23.0, 22.6, 13.5, 12.8; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{23}NNaO_3$ ($[M+Na]^+$) 264.1576, found 264.1568.



***tert*-butyl (*E*)-2-(5-hydroxypent-2-en-2-yl)pyrrolidine-1-carboxylate (26)**

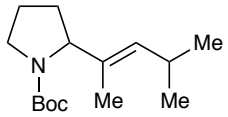
Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and pent-3-yn-1-ol (procedure A). Purification by flash column chromatography (0-25% EtOAc/hexane) provided the title compound (26-A) and minor regioisomer (26-B) (A: 74 mg, 0.29 mmol, 58%, B: 16 mg, 0.6 mmol, 13%) as light yellow oils. 26-A (shown above): IR (film) ν_{max} 3427, 2973, 2930, 2875, 1679, 1365 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.25 – 5.09 (m, 1H), 4.23 – 4.06 (m, 1H), 3.69 – 3.55 (m, 2H), 3.55 – 3.30 (m, 2H), 2.41 (s, 1H), 2.37 – 2.21 (m, 2H), 2.05 – 1.96 (m, 1H), 1.90 – 1.74 (m, 2H), 1.74 – 1.66 (m, 1H), 1.59 (s, 3H), 1.47 – 1.37 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 154.5, 139.6, 138.7, 120.8, 118.7, 79.4, 79.2, 64.1, 63.7, 62.3, 62.0, 47.5, 47.0, 31.7, 31.3, 30.6, 28.6, 23.9, 23.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{14}H_{25}NNaO_3$ ($[M+Na]^+$) 278.1732, found 278.1721. 26-B (minor regioisomer): IR (film) ν_{max} 3393, 2973-2875, 1680, 1403, 1366 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.37 (q, *J* = 6.8 Hz, 1H), 4.24 (s, 1H), 3.90 – 3.61 (m, 3H), 3.49 – 3.29 (m, 2H), 2.59 – 2.45 (m, 1H), 2.13 – 1.94 (m, 2H), 1.87 (s, 1H), 1.81 – 1.75 (m, 1H), 1.68 – 1.59 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 138.6, 119.4, 79.6, 61.4, 61.3, 47.4, 31.9, 31.5, 28.7, 23.3, 13.3; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{14}H_{25}NNaO_3$ ($[M+Na]^+$) 278.1732, found 278.1722.



***tert*-butyl (*E*)-2-(hex-2-en-2-yl)pyrrolidine-1-carboxylate (27)**

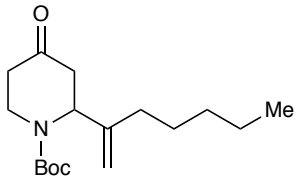
Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 2-hexyne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of regioisomers (2.0:1 r.r. by both GC and ^1H NMR analysis of the crude reaction mixture) (80 mg, 0.32 mmol, 63%) as a light yellow oil. Isolated as a mixture of regioisomers and rotamers. IR (film) ν_{max} 2964, 2930, 2872, 1692, 1389, 1364 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ (both

isomers) 5.23 – 5.08 (m, 1H), (both isomers) 4.32 – 4.02 (m, 1H), (both isomers) 3.54 – 3.31 (m, 2H), (both isomers) 2.17 – 1.71 (m, 5H), (both isomers) 1.71 – 1.62 (m, 1H), (minor) 1.59 (d, J = 6.7 Hz, 3H), (major) 1.53 (s, 3H), (both isomers) 1.49 – 1.31 (m, 11H), (minor) 0.92 (t, J = 7.3 Hz, 3H), (major) 0.88 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 154.9, 154.4, 140.3, 135.5, 123.5, 123.1, 117.1, 79.0, 78.9, 63.7, 63.1, 61.6, 46.9, 46.8, 31.7, 31.6, 30.9, 29.8, 28.6, 28.6, 23.5, 23.3, 23.1, 23.0, 22.4, 22.0, 14.7, 14.0, 13.3, 13.1; HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{27}NNaO_2$ ($[M+Na]^+$) 276.1939, found 276.1937.



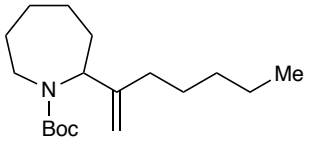
***tert*-butyl (*E*)-2-(4-methylpent-2-en-2-yl)pyrrolidine-1-carboxylate (28)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (L)-Boc-proline and 4-methylpent-2-yne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of regioisomers (6.8:1 r.r. by both GC and ^{1}H NMR analysis of the crude reaction mixture) (55 mg, 0.22 mmol, 43%) as a light yellow oil. IR (film) ν_{max} 2962-2871, 1691, 1389, 1364, 1163 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.09 (minor) (m, 1H) and 4.93 (major) (d, J = 8.2 Hz, 1H), 4.37 – 3.98 (both isomers) (m, 2H total), 3.42 (both isomers) (m, 4H total), 2.65 (minor) (m, 1H), 2.50 (major) (m, 1H), 1.96 (both isomers) (m, 2H total), 1.85-1.69 (both isomers) (m, 2H total), 1.69-1.60 (both isomers) (m, 5H total), 1.54 (major) (s, 3H), 1.42 (both isomers) (s, 18H total), 1.18 – 1.09 (minor) (m, 3H), 1.06 (minor) (d, J = 7.2 Hz, 3H), 0.92 (major) (dd, J = 6.6, 1.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8, 133.0, 130.8, 130.5, 115.9, 78.7, 63.3, 62.6, 59.2, 46.8, 32.8, 31.5, 30.5, 28.6, 28.4, 26.8, 23.1, 22.9, 22.1, 21.6, 13.8, 13.2, 12.9; HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{27}NNaO_2$ ($[M+Na]^+$) 276.1939, found 276.1932.



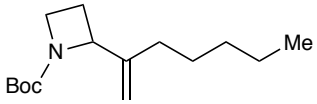
(*E*)-tert-butyl (1-phenyldec-3-en-2-yl)carbamate (29)

Prepared following the general procedure outlined above including the above outlined workup procedure using 1-(*tert*-butoxycarbonyl)-4-oxopiperidine-2-carboxylic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-20% EtOAc/hexane) provided the title compound (118 mg, 0.40 mmol, 80%) as a colorless oil. IR (film) ν_{max} 2959, 2930, 2872, 1719, 1691, 1408, 1156 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.02 (m, 2H), 4.87 (s, 1H), 4.19 (s, 1H), 3.11-3.01 (m, 1H), 2.75-2.67 (m, 1H), 2.66-2.58 (m, 1H), 2.41 (s, 1H), 2.35-2.27 (m, 1H), 2.02-1.88 (m, 2H), 1.49 (s, 9H), 1.48 – 1.22 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.9, 154.6, 147.5, 113.4, 80.5, 54.2, 43.3, 40.6, 38.0, 33.4, 31.6, 28.4, 27.4, 22.5, 14.0; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{18}H_{33}NNaO_2$ ($[M+Na]^+$) 295.2511, found 295.2512.



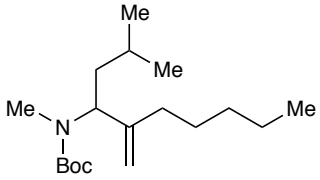
***tert*-butyl 2-(hept-1-en-2-yl)azepane-1-carboxylate (30)**

Prepared following the general procedure outlined above including the above outlined workup procedure using 1-(*tert*-butoxycarbonyl)azepane-2-carboxylic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (118 mg, 0.40 mmol, 80%) as a colorless oil. IR (film) ν_{max} 2927, 2857, 1689, 1407, 1364 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 4.74 – 4.64 (m, 2H), 4.40 (dd, *J* = 11.6, 6.5 Hz, 0.5H), 4.25 (dd, *J* = 11.9, 6.0 Hz, 0.5H), 3.74 (d, *J* = 14.2 Hz, 0.5H), 3.60 (d, *J* = 14.4 Hz, 0.5H), 2.68 (m, 1H), 2.16 – 2.03 (m, 1H), 2.02 – 1.90 (m, 2H), 1.84 – 1.66 (m, 2H), 1.64 – 1.55 (m, 1H), 1.47 – 1.32 (m, 13H), 1.32 – 1.05 (m, 6H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 154.9, 154.7, 150.2, 149.8, 107.7, 107.4, 78.3, 78.2, 59.2, 57.6, 42.3, 42.0, 33.1, 33.0, 32.1, 31.6, 31.1, 31.0, 28.9, 28.9, 28.6, 28.5, 28.1, 28.1, 27.1, 27.1, 25.3, 24.8, 22.0, 22.0, 14.0, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{17}H_{29}NNaO_3$ ($[M+Na]^+$) 318.2045, found 318.2035.



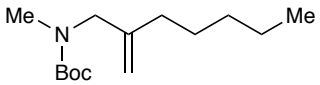
***tert*-butyl 2-(hept-1-en-2-yl)azetidine-1-carboxylate (31)**

Prepared following the general procedure outlined above including the above outlined workup procedure using 1-(*tert*-butoxycarbonyl)azetidine-2-carboxylic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (94 mg, 0.37 mmol, 74%) as a colorless oil. IR (film) ν_{max} 2960, 2929, 2892, 1701, 1363 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 4.93 (s, 1H), 4.80 (s, 1H), 4.59 – 4.52 (m, 1H), 3.77 (q, J = 8.3 Hz, 1H), 3.72 – 3.64 (m, 1H), 2.37 (m, 1H), 1.99 (m, 2H), 1.82 (m, 1H), 1.42 (p, J = 7.5 Hz, 2H), 1.35 (s, 9H), 1.28 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 155.7, 148.6, 108.4, 78.3, 64.6, 46.0, 31.0, 30.6, 28.0, 26.8, 22.4, 22.0, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{15}H_{27}NNaO_2$ ($[M+Na]^+$) 276.1939, found 276.1933.



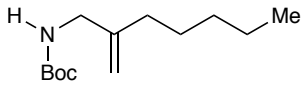
***tert*-butyl methyl(2-methyl-5-methylenedecan-4-yl)carbamate (32)**

Prepared following the general procedure outlined above including the above outlined workup procedure using *N*-(*tert*-butoxycarbonyl)-*N*-methylleucine and 1-heptyne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (110 mg, 0.37 mmol, 74%) as a colorless oil. IR (film) ν_{max} 2957, 2929, 2871, 1691, 1390 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 4.96 (s, 1H), 4.86 (s, 1H), 4.69-4.47 (m, 1H), 2.43 (s, 3H), 1.88 (m, 2H), 1.61-1.42 (m, 2H), 1.40 (s, 9H), 1.33-1.14 (m, 7H), 0.94 – 0.82 (m, 9H); ^{13}C NMR (126 MHz, DMSO) δ 155.5, 155.0, 148.1, 147.8, 111.6, 111.3, 78.6, 78.5, 53.9, 53.3, 37.8, 37.6, 34.3, 34.2, 31.1, 28.1, 28.0, 27.6, 27.2, 27.0, 24.5, 24.3, 23.5, 22.0, 21.9, 21.8, 21.6, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{18}H_{35}NNaO_2$ ($[M+Na]^+$) 320.2565, found 320.2561.



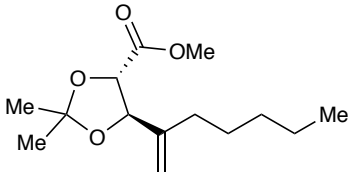
***tert*-butyl methyl(2-methyleneheptyl)carbamate (33)**

Prepared following the general procedure outlined above including the above outlined workup procedure using *N*-(*tert*-butoxycarbonyl)-*N*-methylglycine and 1-heptyne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (94 mg, 0.37 mmol, 78%) as a colorless oil. IR (film) ν_{max} 2960, 2929, 2861, 1696, 1390 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 4.83 (s, 1H), 4.74 (s, 1H), 3.74 (s, 2H), 2.69 (s, 3H), 1.95 – 1.85 (m, 2H), 1.45 – 1.34 (m, 11H), 1.32-1.20 (m, 4H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 154.7, 145.1, 110.4, 78.5, 52.6, 52.0, 33.4, 32.9, 31.0, 28.0, 26.8, 26.7, 22.0, 21.9, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{14}H_{27}NNaO_2$ ($[M+Na]^+$) 264.1939, found 264.1933.



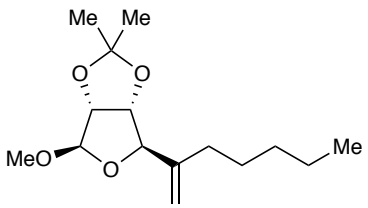
***tert*-butyl (2-methyleneheptyl)carbamate (34)**

Prepared following the general procedure outlined above including the above outlined workup procedure using (*tert*-butoxycarbonyl)glycine and 1-heptyne (procedure A). Purification by flash column chromatography (0-20% EtOAc/hexane) provided the title compound (47 mg, 0.21 mmol, 41%) as a colorless oil. IR (film) ν_{max} 3351, 2958, 2930, 2862, 1700, 1366 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 6.99 and 6.66 (t, J = 5.6 Hz, and s respectively, 1H), 4.77 (s, 1H), 4.72 (s, 1H), 3.47 (d, J = 5.9 Hz, 2H), 1.94 (t, J = 7.6 Hz, 2H), 1.37 (m, 11H), 1.25 (m, 4H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 155.6, 147.0, 108.6, 77.5, 44.2, 33.3, 31.0, 28.3, 26.7, 21.9, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{25}NNaO_2$ ($[M+Na]^+$) 250.1783, found 250.1779.



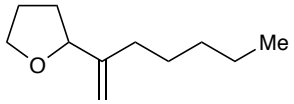
methyl (4*S*,5*R*)-5-(hept-1-en-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (35)

Prepared following the general procedure outlined above including the above outlined workup procedure using (4*S*,5*S*)-5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-20% EtOAc/hexane) provided the title compound (72 mg, 0.28 mmol, 56%) as a light yellow oil in ≥20:1 d.r. by ^{1}H NMR. IR (film) ν_{max} 2990, 2956, 2931, 2861, 1761, 1378, 1205 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.19 (s, 1H), 5.02 – 5.00 (m, 1H), 4.62 (d, *J* = 7.5 Hz, 1H), 4.27 (d, *J* = 7.5 Hz, 1H), 3.78 (s, 3H), 2.07 (m, 2H), 1.54 – 1.44 (m, 8H), 1.32 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 145.2, 113.1, 111.3, 82.3, 78.3, 52.4, 31.7, 30.7, 27.6, 26.8, 25.7, 22.5, 14.0; HRMS (EI-TOF) *m*/*z* calcd. for $C_{14}H_{24}O_4$ ([M•]$^{+}$) 256.1575, found 256.1585.



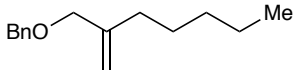
(3a*R*,4*R*,6*R*,6a*R*)-4-(hept-1-en-2-yl)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (36)

Prepared following the general procedure outlined above including the above outlined workup procedure using (3a*S*,4*S*,6*R*,6a*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-20% EtOAc/hexane) provided the title compound (97 mg, 0.36 mmol, 72%) as a light yellow oil in ≥20:1 d.r. by ^{1}H NMR. IR (film) ν_{max} 2989, 2956, 2930, 2860, 1460, 1381, 1372 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.06 (s, 1H), 4.95 (s, 1H), 4.82 (s, 1H), 4.68 (dd, *J* = 6.0, 2.2 Hz, 1H), 4.51 (d, *J* = 6.0 Hz, 1H), 4.47 (s, 1H), 3.30 (s, 3H), 2.10 – 1.93 (m, 2H), 1.47 – 1.22 (m, 12H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 147.4, 112.0, 109.4, 109.2, 88.5, 84.7, 82.3, 55.0, 31.8, 31.1, 26.7, 26.6, 25.0, 22.0, 13.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{15}H_{26}NaO_4$ ([M+Na]$^{+}$) 293.1729, found 293.1728.



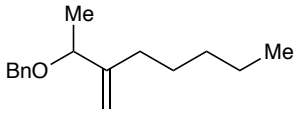
2-(hept-1-en-2-yl)tetrahydrofuran (37)

Prepared following the general procedure outlined above including the above outlined workup procedure using (*tert*-butoxycarbonyl)glycine and 1-heptyne (procedure A). Purification by flash column chromatography (0-5% EtOAc/hexane) provided the title compound (39 mg, 0.23 mmol, 46%, by ^{1}H NMR analysis of crude reaction: 60 mg, 0.36 mmol, 71%) as a colorless oil. Discrepancy in NMR and isolated yields is attributable to product volatility. IR (film) ν_{max} 2957, 2928, 2859, 1461, 1062, 896 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.03 (s, 1H), 4.79 (s, 1H), 4.27 (t, *J* = 7.2 Hz, 1H), 3.95 – 3.90 (m, 1H), 3.84 – 3.76 (m, 1H), 2.08 – 1.85 (m, 5H), 1.64 (m, 1H), 1.46 (m, 2H), 1.37 – 1.25 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3, 108.0, 81.5, 68.2, 32.1, 31.8, 31.1, 27.6, 25.8, 22.6, 14.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{11}H_{20}NaO$ ($[M+Na]^+$) 191.1412, found 191.1405.



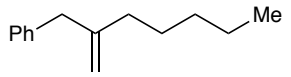
(((2-methyleneheptyl)oxy)methyl)benzene (38)

Prepared following the general procedure outlined above including the above outlined workup procedure using 2-(benzyloxy)acetic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-5% EtOAc/hexane) provided the title compound (71 mg, 0.33 mmol, 65%) as a light yellow oil. IR (film) ν_{max} 2956, 2928, 2857, 1454, 1092 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.38 – 7.26 (m, 5H), 5.00 (s, 1H), 4.88 (s, 1H), 4.44 (s, 2H), 3.91 (s, 2H), 2.01 (t, *J* = 7.6 Hz, 2H), 1.45-1.36 (m, 2H), 1.32 – 1.19 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 146.1, 138.4, 128.2, 127.4, 127.4, 110.8, 72.2, 71.2, 32.6, 31.0, 26.7, 22.0, 13.9; HRMS (EI-TOF) *m*/*z* calcd. for $C_{15}H_{22}O$ ($[M\bullet]^+$) 218.1671, found 218.1670.



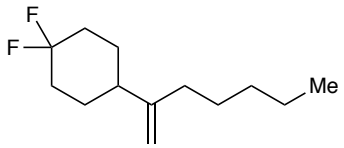
(((3-methyleneoctan-2-yl)oxy)methyl)benzene (39)

Prepared following the general procedure outlined above including the above outlined workup procedure using 2-(benzyloxy)propanoic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-5% EtOAc/hexane) provided the title compound (81 mg, 0.35 mmol, 70%) as a light yellow oil. IR (film) ν_{max} 2957, 2929, 2859, 1454, 1088 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.35 – 7.26 (m, 5H), 5.03 (s, 1H), 4.92 (d, *J* = 1.4 Hz, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 4.30 (d, *J* = 11.9 Hz, 1H), 3.92 (q, *J* = 6.5 Hz, 1H), 2.1-1.96 (m, 2H), 1.53 – 1.45 (m, 2H), 1.37-1.31 (m, 4H), 1.29 (d, *J* = 6.5 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 138.9, 128.3, 127.6, 127.3, 110.5, 78.6, 69.9, 31.9, 30.3, 27.5, 22.6, 20.7, 14.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{16}H_{24}NaO$ ($[M+Na]^+$) 255.1725, found 255.1716.



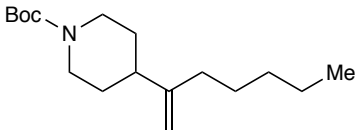
(2-methyleneheptyl)benzene (40)

Prepared following the general procedure outlined above including the above outlined workup procedure using phenylacetic acid and 1-heptyne (procedure A). Purification by flash column chromatography (0-1% EtOAc/hexane) provided the title compound (51 mg, 0.27 mmol, 54%, by ^1H NMR analysis of crude reaction: 60 mg, 0.30 mmol, 64%) as a colorless oil. Discrepancy in NMR and isolated yields is attributable to product volatility. NMR data matches previously reported synthesis[8]: ^1H NMR (500 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 7.4 Hz, 1H), 7.23-7.18 (m, 3H), 4.83 (s, 1H), 4.73 (s, 1H), 3.34 (s, 1H), 1.97 (t, *J* = 7.5 Hz, 2H), 1.49-1.41 (m, 2H), 1.35 – 1.21 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 139.9, 129.0, 128.2, 126.0, 110.9, 43.0, 35.4, 31.5, 27.3, 22.5, 14.1.



1,1-difluoro-4-(hept-1-en-2-yl)cyclohexane (41)

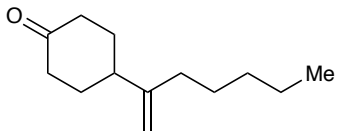
Prepared following the general procedure outlined above including the above outlined workup procedure using 4,4-difluorocyclohexane-1-carboxylic acid and 1-heptyne (procedure B). Purification by flash column chromatography (0-1% EtOAc/hexane) provided the title compound as a mixture of regioisomers (branched:linear 13:1 by ^{1}H NMR analysis of crude reaction mixture) (65 mg, 0.30 mmol, 60%) as a clear oil. IR (film) ν_{max} 2957, 2932, 2861, 1449, 1108 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.51 – 5.27 (m, 1H), (major) 4.76 (s, 1H), (major) 4.76 – 4.74 (m, 1H), all remaining peaks correspond to both isomers: 2.18 – 2.09 (m, 2H), 2.00 (t, *J* = 8.3 Hz, 2H), 1.98 – 1.89 (m, 1H), 1.84 – 1.65 (m, 4H), 1.58 – 1.48 (m, 1H), 1.47 – 1.39 (m, 2H), 1.36 – 1.23 (m, 5H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 123.5 (dd, *J* = 242.1, 239.5 Hz), 107.9, 42.1, 34.9, 33.9 (dd, *J* = 25.5, 22.3 Hz), 31.7, 28.3, 28.2, 27.8, 22.6, 14.1; HRMS (EI-TOF) *m*/*z* calcd. for $C_{13}H_{22}F_2$ ($[M\bullet]^+$) 216.1690, found 216.1695.



***tert*-butyl 4-(hept-1-en-2-yl)piperidine-1-carboxylate (42)**

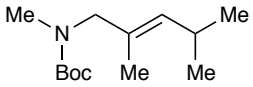
Prepared following the general procedure outlined above including the above outlined workup procedure using 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid and 1-heptyne (procedure B). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of regioisomers (branched:linear 13:1 by ^{1}H NMR analysis of crude reaction mixture) (80 mg, 0.29 mmol, 57%) as a clear oil. IR (film) ν_{max} 2929, 2856, 1693, 1419, 1365, 1165 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.44 – 5.29 (m, 1H), (major) 4.75 – 4.73 (m, 1H), (major) 4.72 (s, 1H), all remaining peaks correspond to both isomers: 4.16 (s, 2H), 2.77-2.61 (m, 1H), 2.05 – 1.92 (m, 3H), 1.69 (d, *J* = 12.8 Hz, 1H), 1.46 (s, 9H), 1.45-1.39 (m, 1H), 1.36-1.24 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8,

153.4, (minor) 134.1, (minor) 129.2, (major) 107.6, 79.3, 42.2, 34.7, 31.7, 31.3, 28.5, 27.8, 22.6, 14.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{17}H_{31}NNaO_2$ ($[M+Na]^+$) 304.2252, found 304.2246.



4-(hept-1-en-2-yl)cyclohexan-1-one (43)

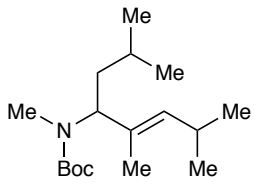
Prepared following the general procedure outlined above including the above outlined workup procedure using 4-oxocyclohexane-1-carboxylic acid and 1-heptyne (procedure B). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of regioisomers (branched:linear 13:1 by ^{1}H NMR analysis of crude reaction mixture) (54 mg, 0.28 mmol, 56%) as a clear oil. IR (film) ν_{max} 2955, 2928, 2861, 1716, 1461 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.53 – 5.36 (m, 1H), (major) 4.78 (s, 2H), all remaining peaks correspond to both isomers: 2.47 – 2.31 (m, 5H), 2.14 – 1.96 (m, 4H), 1.72 – 1.60 (m, 2H), 1.46 (p, *J* = 7.5 Hz, 2H), 1.38-1.23 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (minor) 211.9, (major) 211.7, (major) 152.4, (minor) 132.8, (minor) 130.1, (major) 108.1, (major) 42.2, (major) 41.2, (minor) 40.6, (minor) 38.7, (major) 35.1, (minor) 32.8, (minor) 32.6, (major) 32.0, (major) 31.7, (minor) 31.3, (minor) 29.7, (minor) 29.2, (major) 27.9, (major) 22.6, (minor) 22.5, (both) 14.1; HRMS (EI-TOF) *m*/*z* calcd. for $C_{13}H_{22}O$ ($[M\bullet]^+$) 194.1671, found 194.1675.



***tert*-butyl (*E*)-(2,4-dimethylpent-2-en-1-yl)(methyl)carbamate (46)**

Prepared following the general procedure outlined above including the above outlined workup procedure using *N*-(*tert*-butoxycarbonyl)-*N*-methylglycine and 4-methylpent-2-yne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of rotamers and regioisomers (4.4:1 r.r. by both GC and ^{1}H NMR analysis of the crude reaction mixture) (51 mg, 0.22 mmol, 45%) as a clear oil. IR (film) ν_{max} 2961, 2929, 2870, 1695, 1365, 1140 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.17 – 5.09 (m, 1H), (major) 5.04 (d, *J* = 8.8 Hz, 4H), (both isomers) 3.85 – 3.62 (m, 2H), (minor)2.83 (dt, *J* = 14.2, 7.1 Hz, 1H), (both isomers) 2.80 – 2.64 (m, 3H), (major) 2.53 (ddt, *J* = 13.3, 9.1,

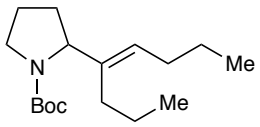
6.7 Hz, 4H), (both isomers) 1.45 (s, 9H), (minor) 1.01 (d, *J* = 7.1 Hz, 3H), (major) 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 139.3, 135.4, 134.8, 128.7, 79.2, 56.3, 55.5, 50.6, 49.9, 33.0, 32.6, 28.4, 27.0, 23.0, 20.5, 13.7, 13.6, 12.7, 12.6; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{25}NNaO_2$ ($[M+Na]^+$) 250.1783, found 250.1772.



***tert*-butyl (*E*)-methyl(2,5,7-trimethyloct-5-en-4-yl)carbamate (47)**

Prepared following the general procedure outlined above including the above outlined workup procedure using *N*-(*tert*-butoxycarbonyl)-*N*-methylleucine and 4-methylpent-2-yne (procedure A). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of rotamers and regioisomers (16:1 r.r. by GC analysis of the crude reaction mixture, 14:1 r.r. by GC analysis of the isolated material) (32 mg, 0.11 mmol, 23%) as a clear oil. IR (film) ν_{max} 2956, 2928, 2869, 1965, 1320, 1144 cm^{-1}; ^{1}H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.37 – 5.28 (m, 1H), (major) 5.06 (d, *J* = 9.0 Hz, 1H), 4.72 – 4.40 (m, 1H), 2.60 – 2.43 (m, 4H), 1.55 (s, 3H), 1.49 – 1.45 (m, 10H), 1.38 – 1.22 (m, 2H), 0.96 – 0.91 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 133.8, 131.7, 79.2, 57.5, 56.4, 38.1, 29.7, 28.5, 27.1, 24.6, 23.8, 23.1, 22.9, 22.0, 15.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{25}NNaO_2$ ($[M+Na]^+$) 306.2409, found 306.2400.

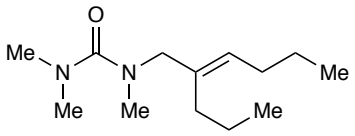
6) Experimental Data for HAT Vinylation Products



***tert*-butyl (*E*)-2-(oct-4-en-4-yl)pyrrolidine-1-carboxylate (21)**

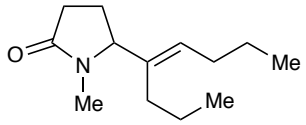
Prepared following the general HAT procedure outlined above including the above outlined workup procedure using *tert*-butyl pyrrolidine-1-carboxylate and 4-octyne (procedure C).

Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (109 mg, 0.39 mmol, 77%) as a colorless oil. See above for characterization data (**21**).



(*E*)-1,1,3-trimethyl-3-(2-propylhex-2-en-1-yl)urea (44)

Prepared following the general HAT procedure outlined above including the above outlined workup procedure using 1,1,3,3-tetramethylurea and 4-octyne (procedure C). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound (81 mg, 0.36 mmol, 72%) as light yellow oil. IR (film) ν_{max} 2957, 2930, 2871, 1645, 1493, 1373 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ 5.30 (t, *J* = 7.2 Hz, 1H), 3.67 (s, 2H), 2.79 (s, 6H), 2.68 (s, 3H), 2.03 (q, *J* = 7.3 Hz, 2H), 1.95 – 1.90 (m, 2H), 1.43-1.33 (m, 4H), 0.89 (q, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 134.9, 127.4, 56.1, 38.6, 35.9, 30.4, 29.6, 23.0, 21.5, 14.1, 13.8; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{27}N_2O$ ($[M+H]^+$) 227.2123, found 227.2119.



(*E*)-1-methyl-5-(oct-4-en-4-yl)pyrrolidin-2-one (45)

Prepared following the general HAT procedure outlined above including the above outlined workup procedure using 1,1,3,3-tetramethylurea and 4-octyne (procedure C). Purification by flash column chromatography (0-10% EtOAc/hexane) provided the title compound as a mixture of regioisomers (5:1 r.r. by ^1H NMR analysis of crude reaction mixture, where r.r. refers to α-amino methyl and methylene functionalization) (61 mg, 0.28 mmol, 58%) as light yellow oil. IR (film) ν_{max} 2958, 2930, 2871, 1689, 1458, 1394 cm^{-1}; ^1H NMR (500 MHz, Chloroform-*d*) δ (minor) 5.26 (t, *J* = 7.3 Hz, 1H), (major) 5.22 (t, *J* = 7.2 Hz, 1H), (major) 3.86 (dd, *J* = 8.4, 4.5 Hz, 1H), (minor) 3.79 (s, 2H), (minor) 3.26 – 3.18 (t, *J* = 7.1 Hz, 2H), (major) 2.68 (s, 3H), all remaining peaks attributable to both isomers: 2.49 – 2.38 (m, 1H), 2.36 – 2.26 (m, 1H), 2.23 – 2.12 (m, 1H), 2.06 – 1.70 (m, 5H), 1.46 – 1.32 (m, 4H), 0.96 – 0.87 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (major) 175.6, (minor) 174.8, (major) 137.3, (minor) 134.1, (minor) 129.2,

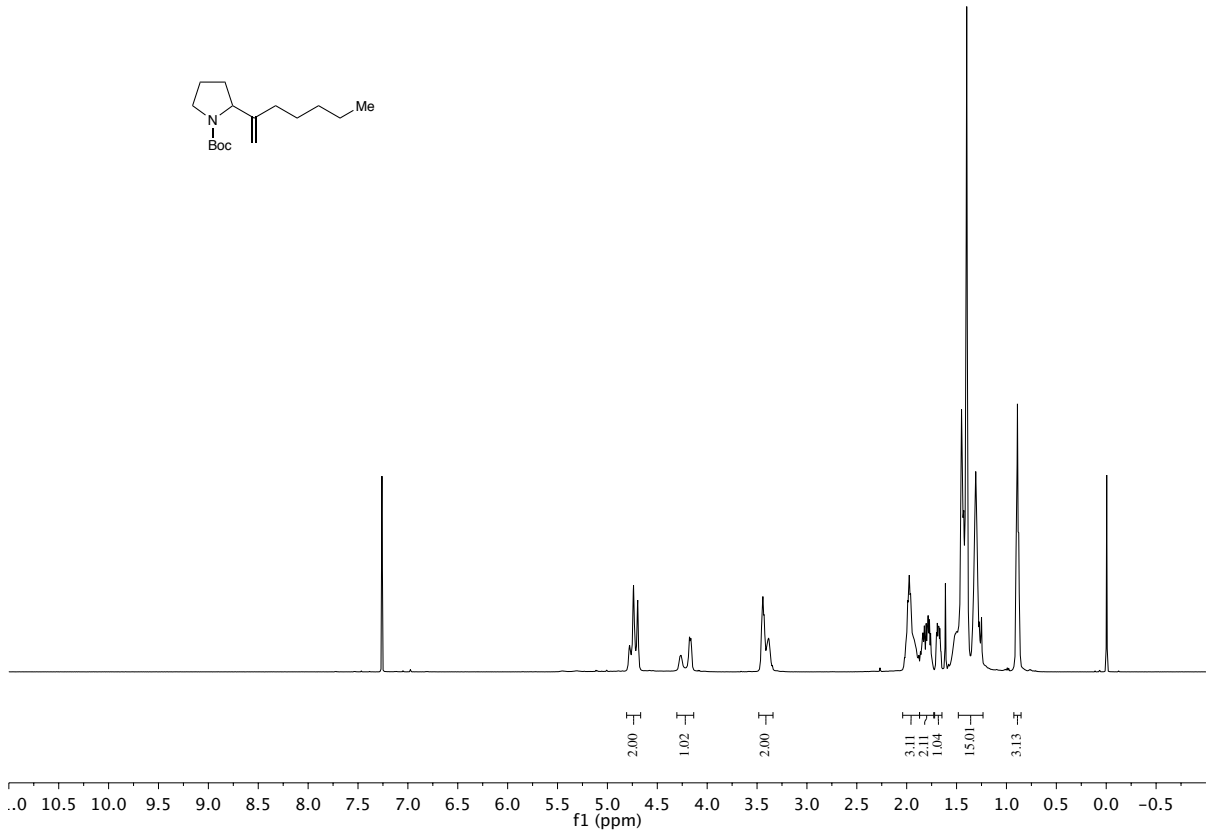
(major) 128.1, (major) 66.3, (minor) 48.4, (minor) 46.5, (minor) 31.2, (minor) 30.2, (major) 29.9, (major) 29.9, (major) 29.7, (minor) 28.0, (major) 24.7, (minor) 22.9, (major) 22.8, (major) 22.7, (minor) 21.3, (minor) 17.8, (major) 14.6, (minor) 14.1, (minor) 13.8, (major) 13.8; HRMS (ESI-TOF) *m*/*z* calcd. for ($[M+H]^+$) 210.1858, found 210.1854.

SI References

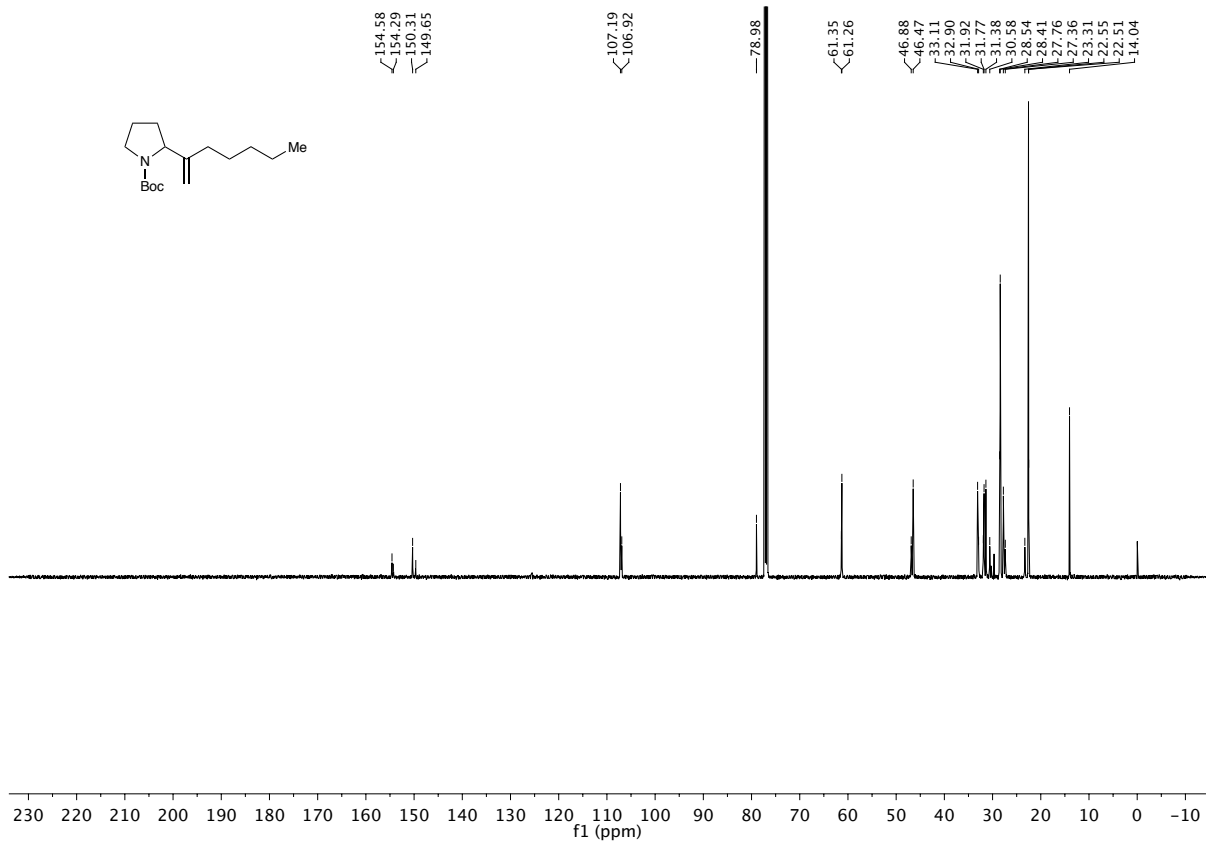
(1) Perrin, D. D.; Armarego, W. L. F., Purification of Laboratory Chemicals *3rd ed.;* Pergamon Press: Oxford, 1988.
(2) Lowry, M. S.; Goldsmith, J. I.; Slinker, J. D.; Rohl, R.; Pascal, R. A.; Malliaras, G. G.; Bernhard, S. *Chem. Mater.* **2005**, *17*, 5712–5719.
(3) Trost, B. M.; Miege, F. *J. Am. Chem. Soc.* **2014**, *136*, 3016–3019.
(4) Anderson, J. C.; Flaherty, A.; Swarbrick, M. E. *J. Org. Chem.* **2000**, *65*, 9152–9156.
(5) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **2003**, *68*, 1319–1333.
(6) Le, C. "Chip"; Wismer, M. K.; Shi, Z.-C.; Zhang, R.; Conway, D. V.; Li, G.; Vachal, P.; Davies, I. W.; MacMillan, D. W. C. *ACS Cent. Sci.* **2017**, *3*, 647–653.
(7) Dieter, R. K.; Chen, N.; Watson, R. T. *Tetrahedron* **2005**, *61*, 3221–3230.
(8) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *Synthesis* **1987**, *1987*, 1034–1036.

7) Spectral Data

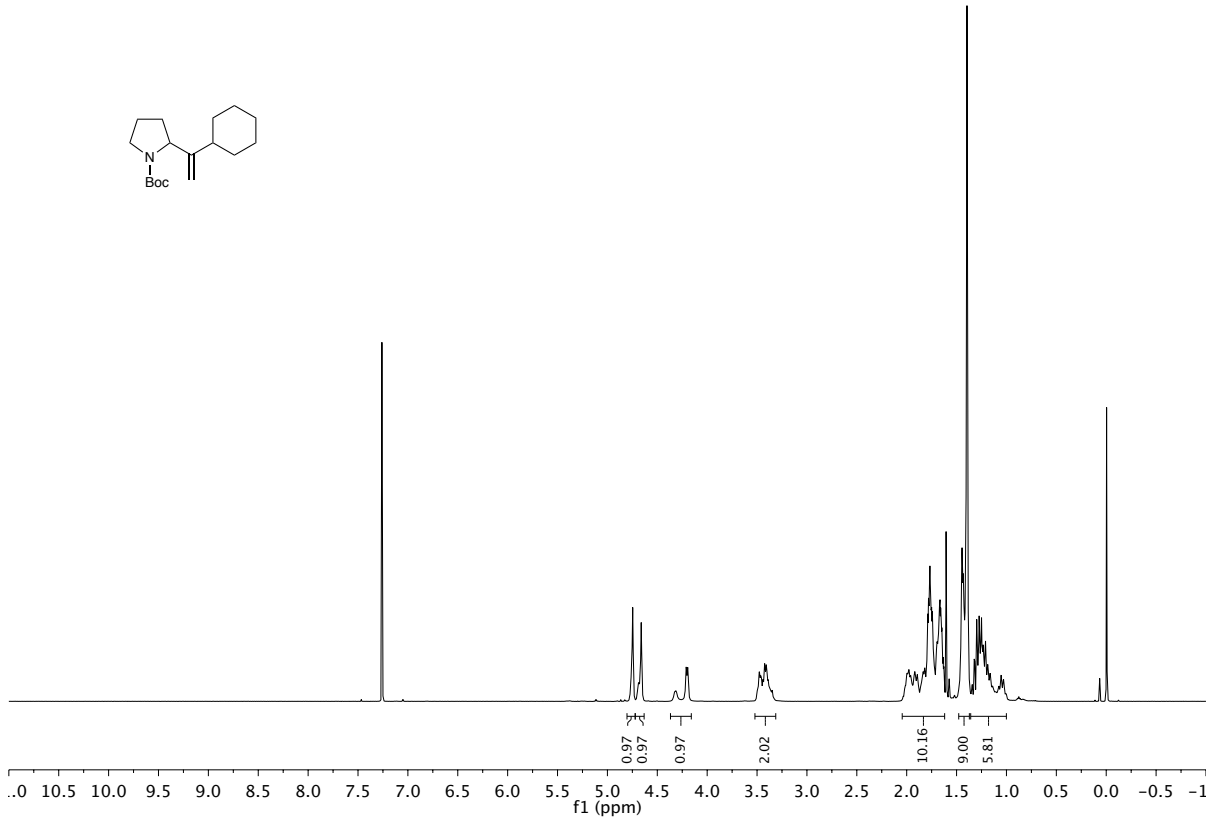
[1]H NMR Spectrum for compound **11**



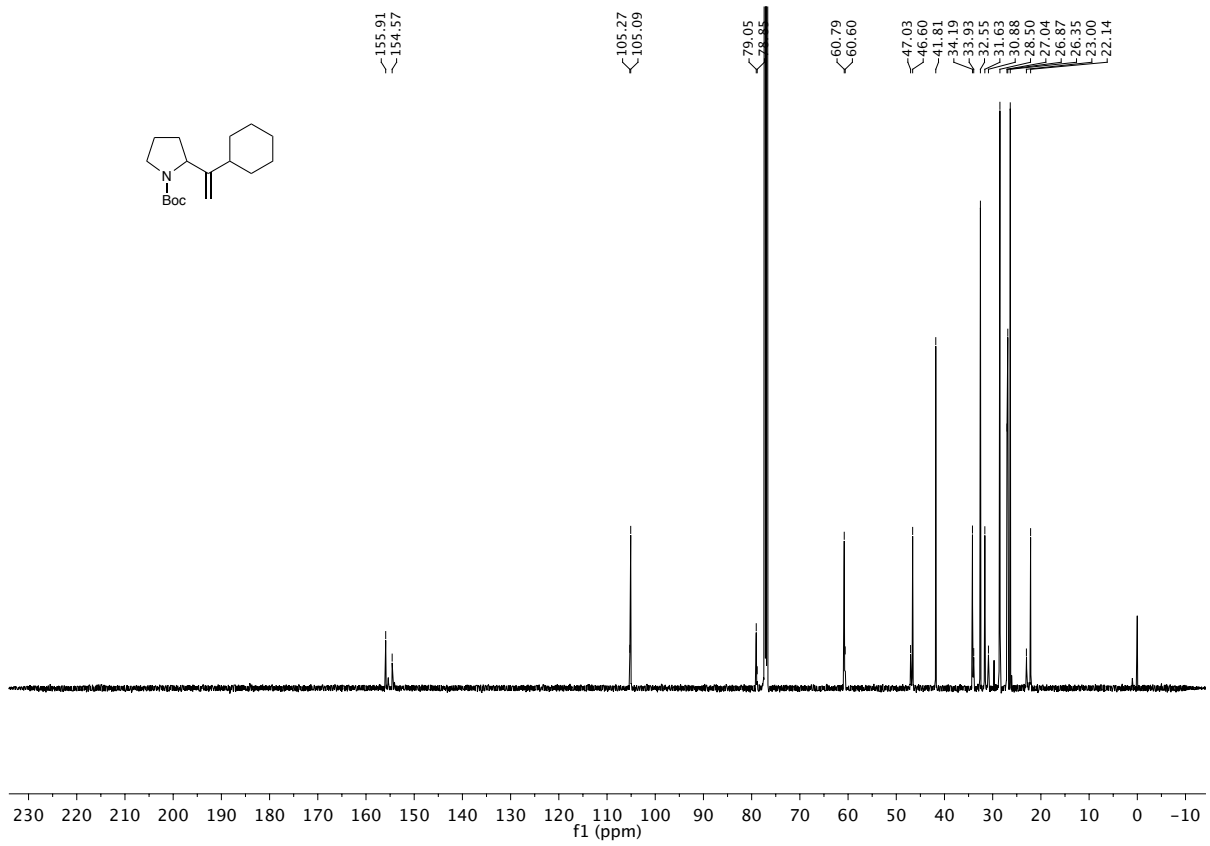
[13]C NMR Spectrum for compound **11**



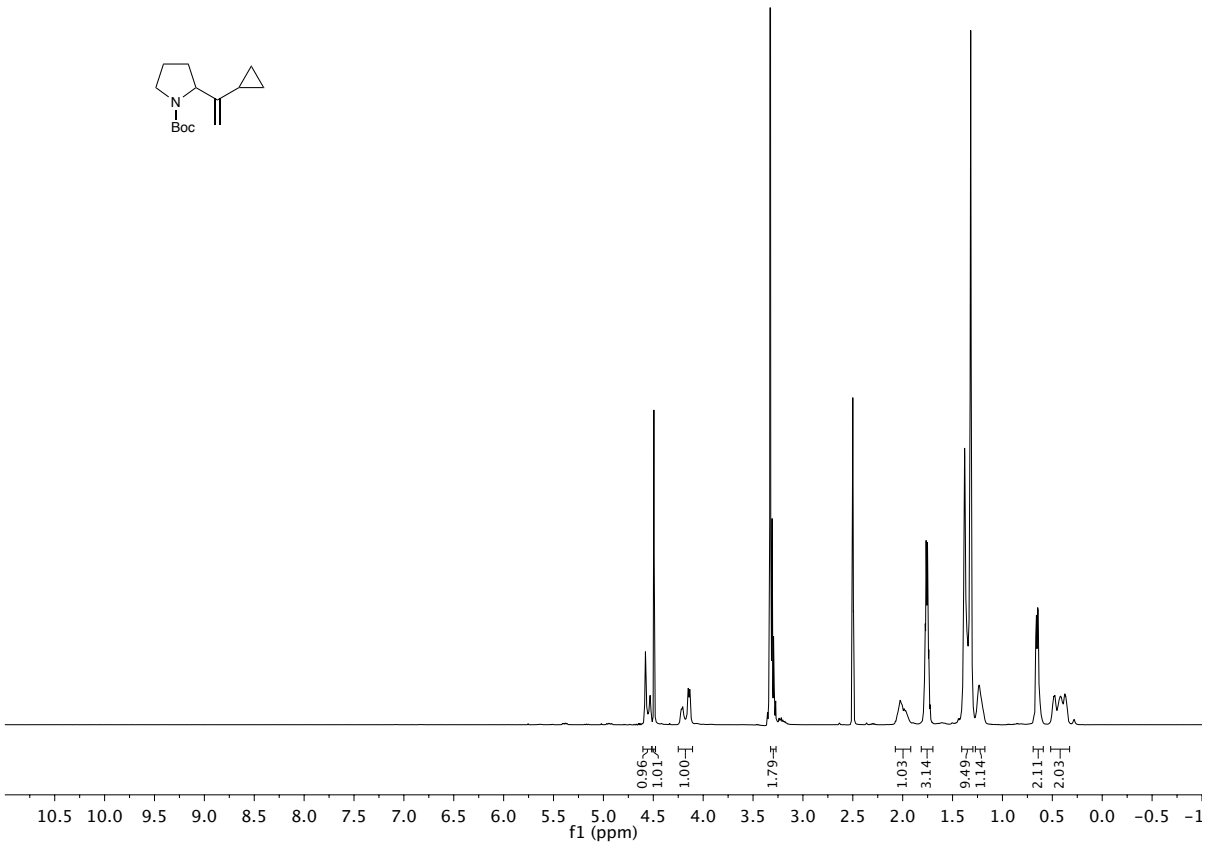
^{1}H NMR Spectrum for compound **12**



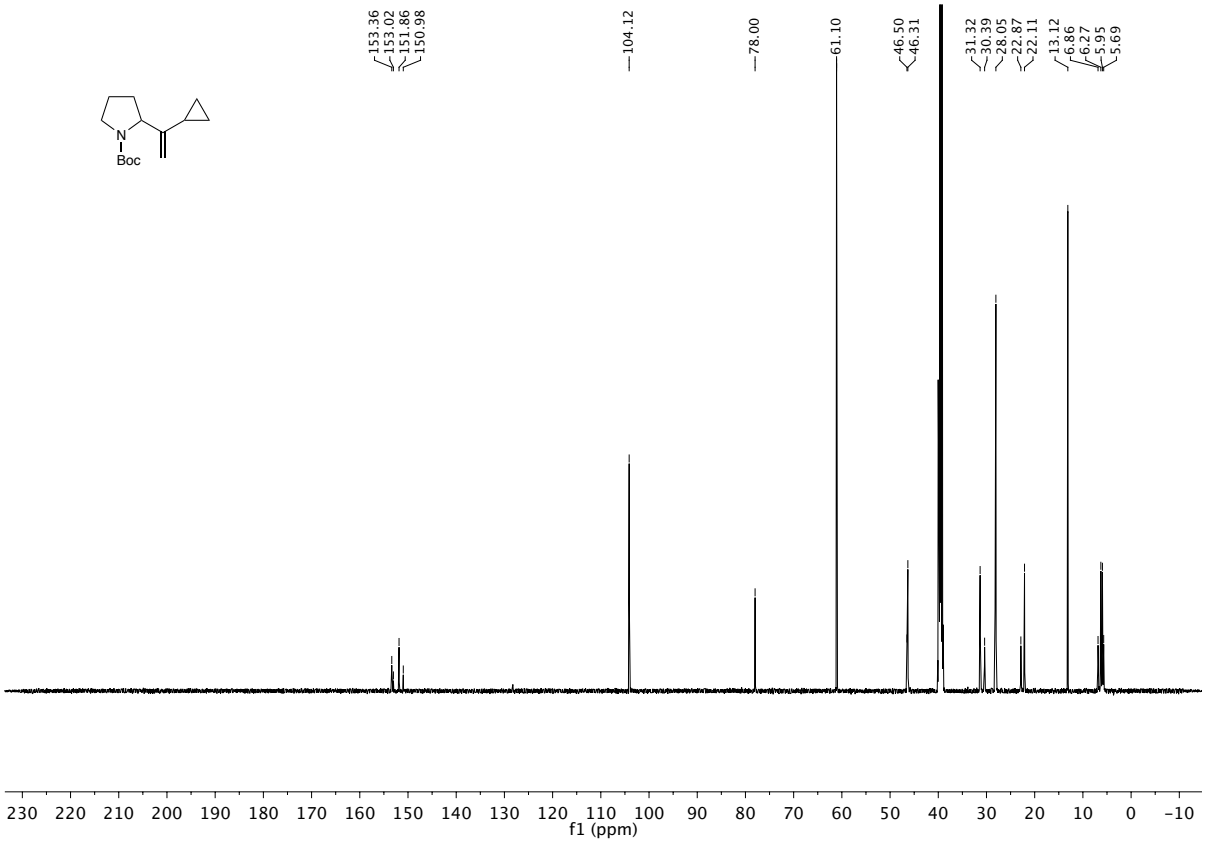
^{13}C NMR Spectrum for compound **12**



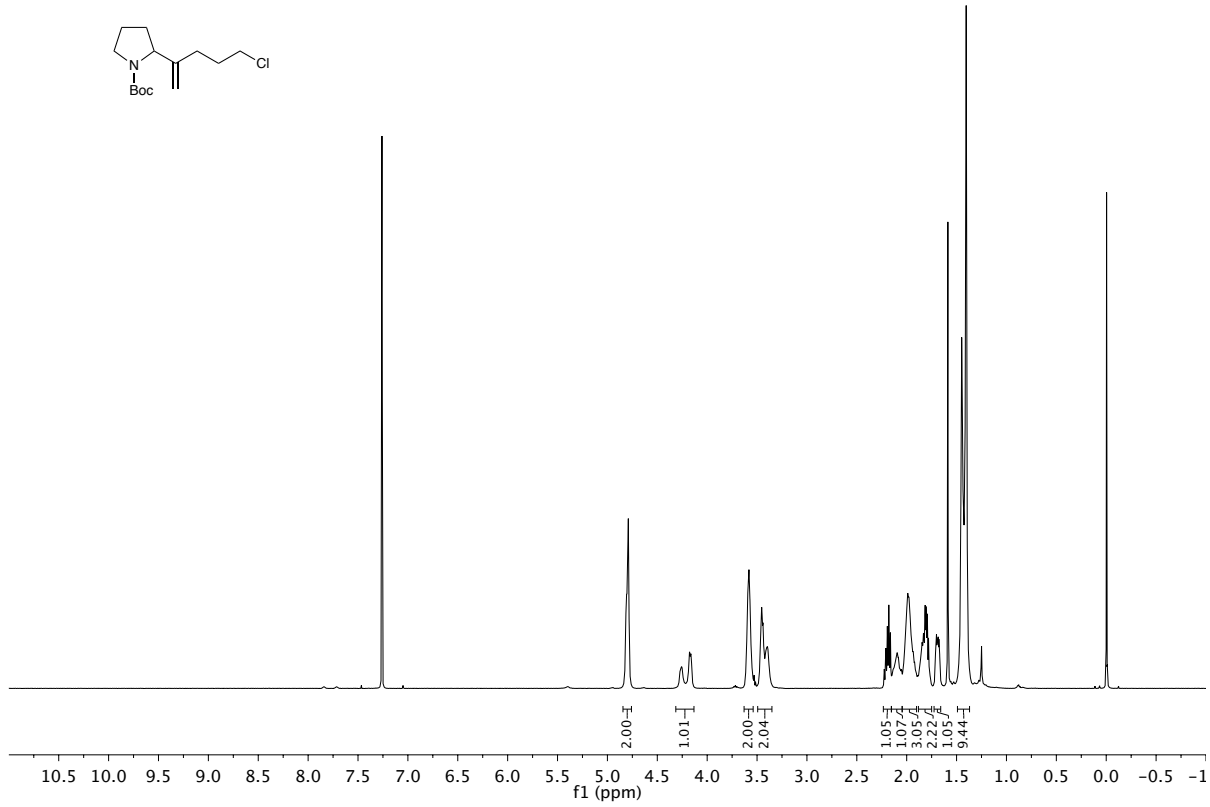
^{1}H NMR Spectrum for compound **13**



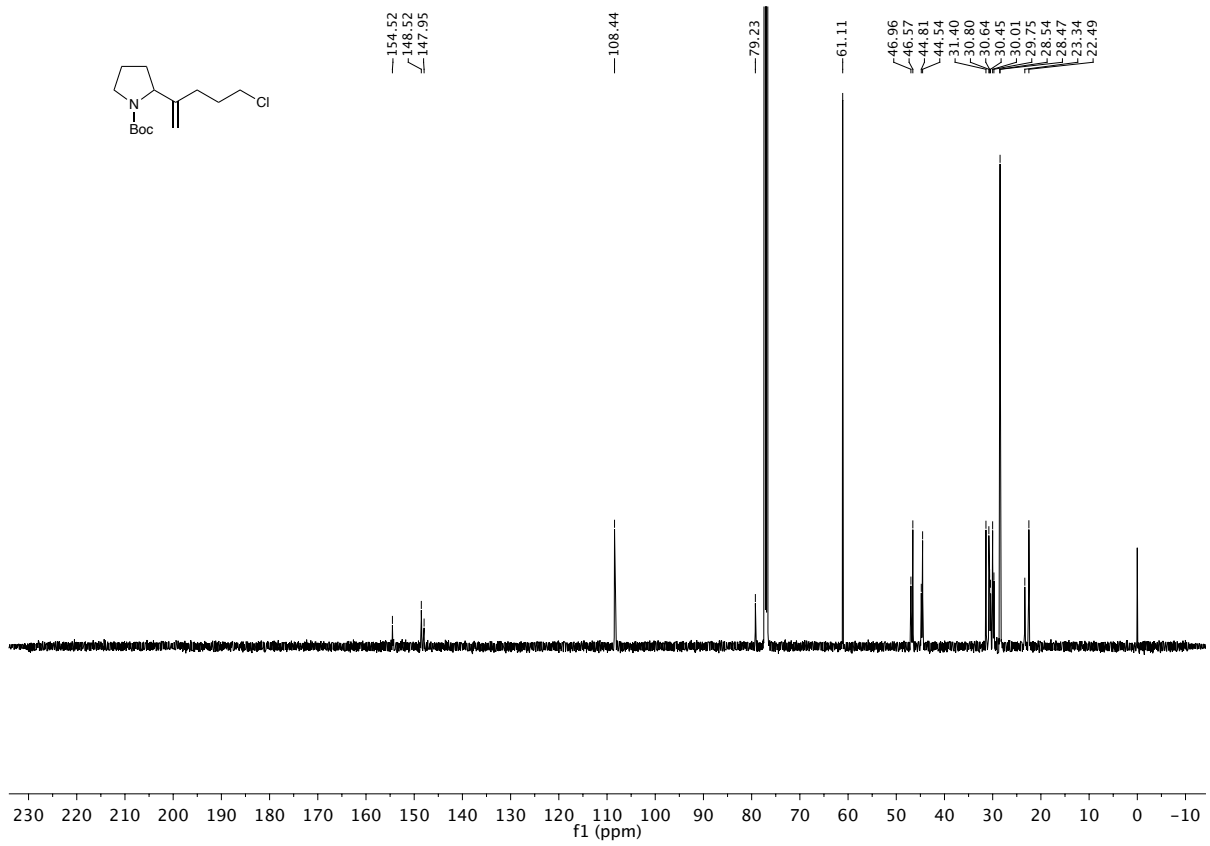
^{13}C NMR Spectrum for compound **13**



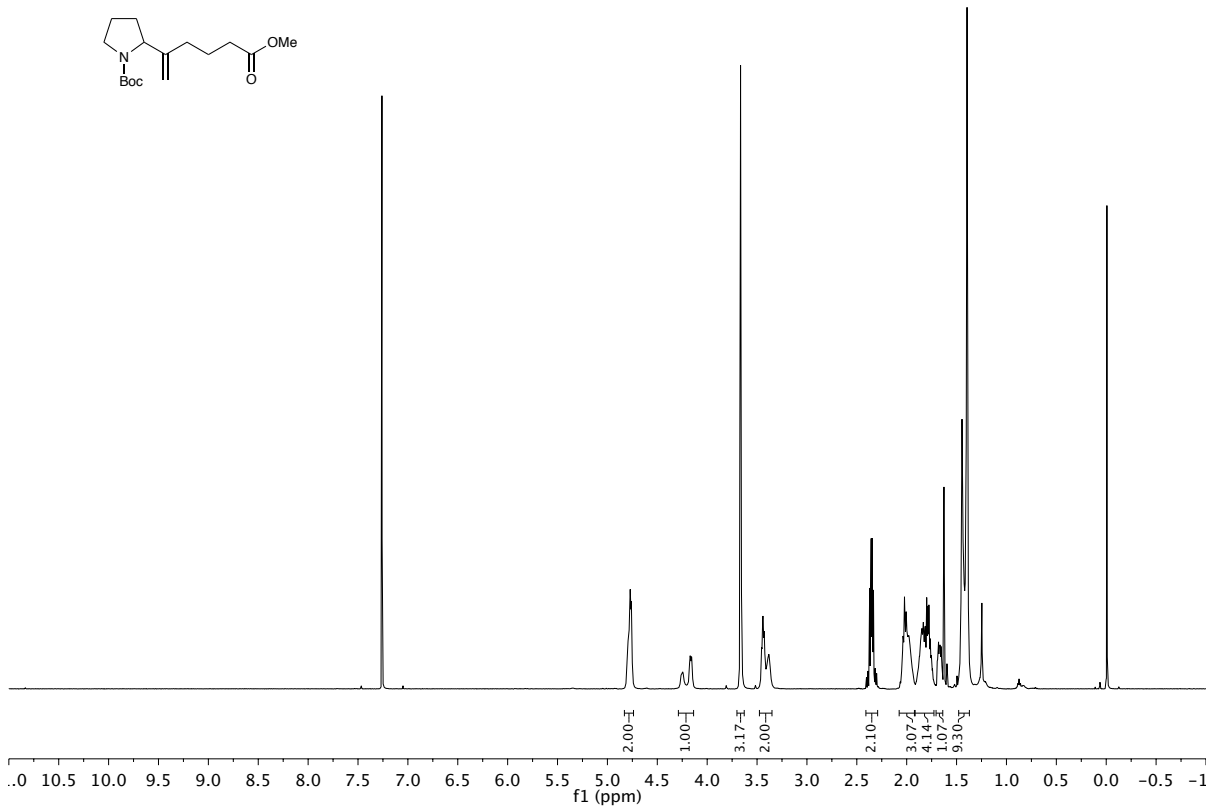
^{1}H NMR Spectrum for compound **14**



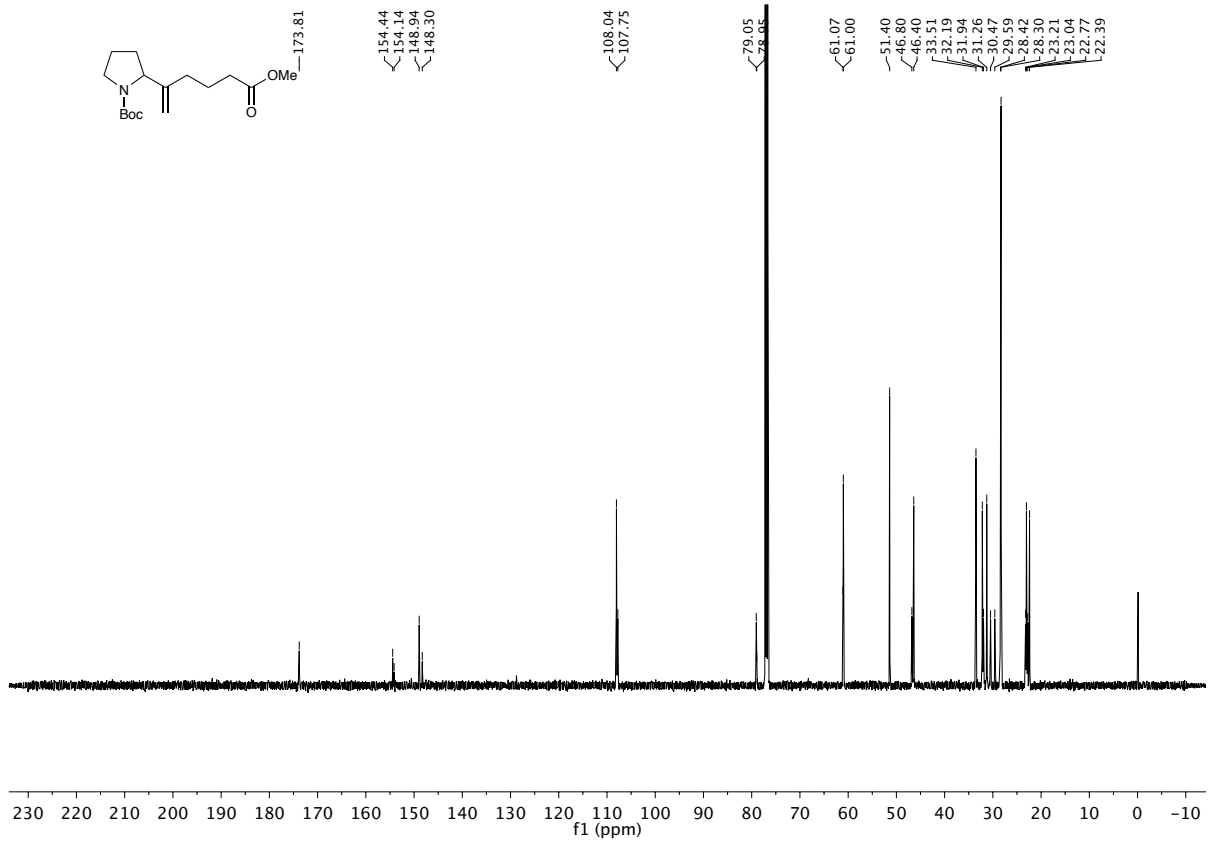
^{13}C NMR Spectrum for compound **14**



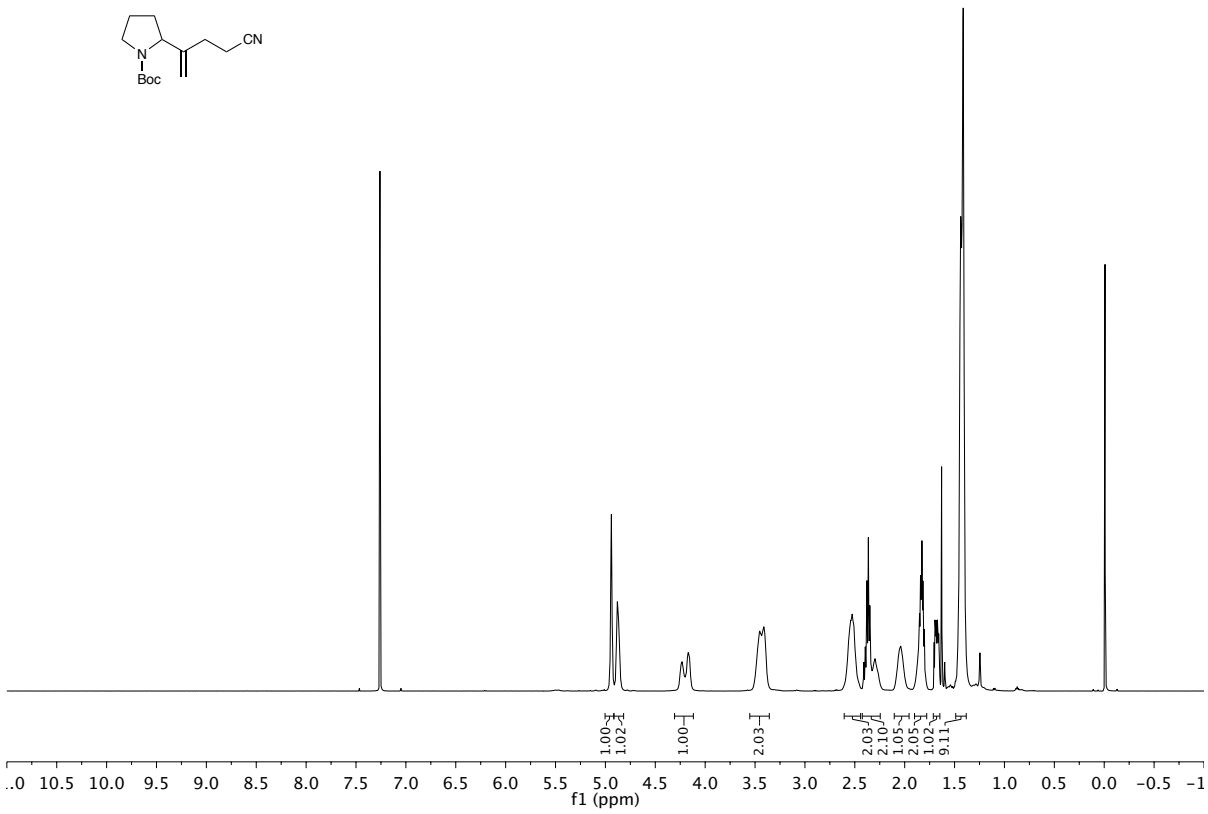
^{1}H NMR Spectrum for compound **15**



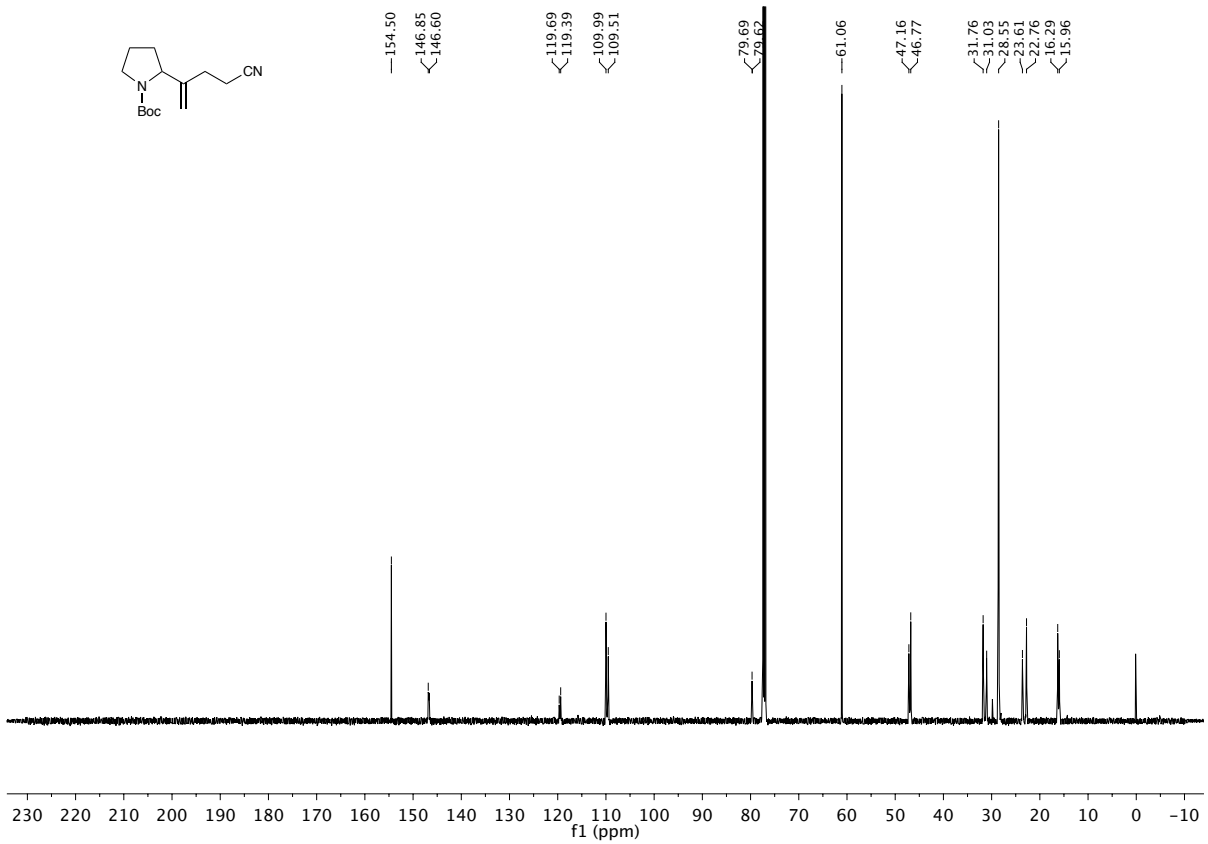
^{13}C NMR Spectrum for compound **15**



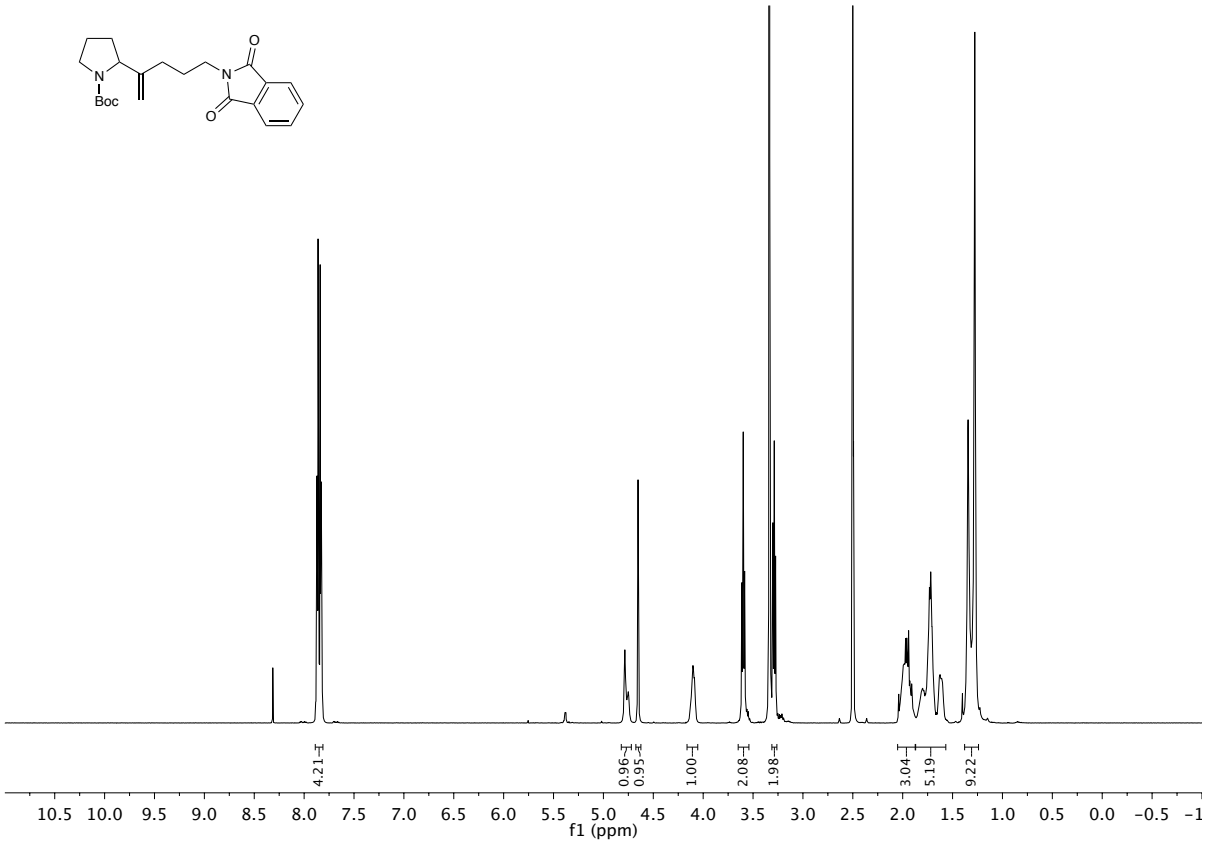
^{1}H NMR Spectrum for compound **16**



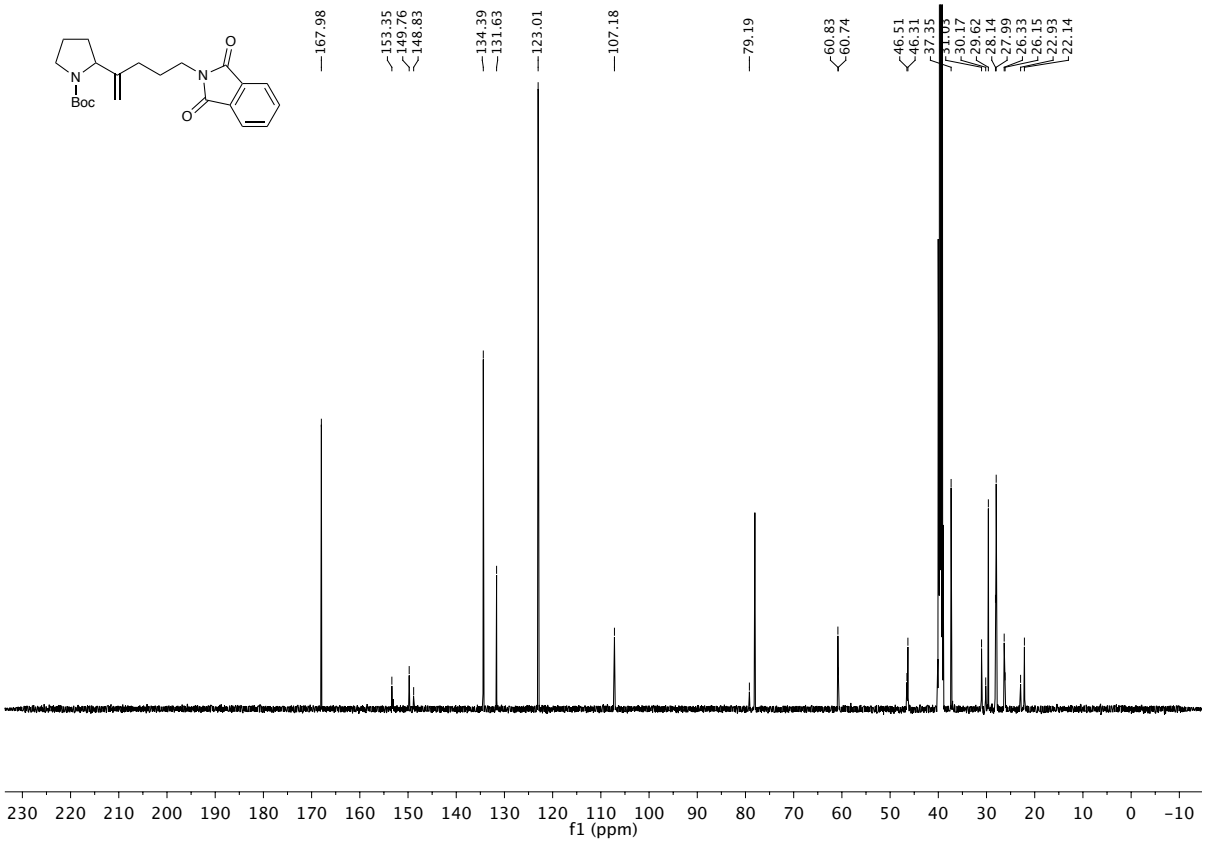
^{13}C NMR Spectrum for compound **16**



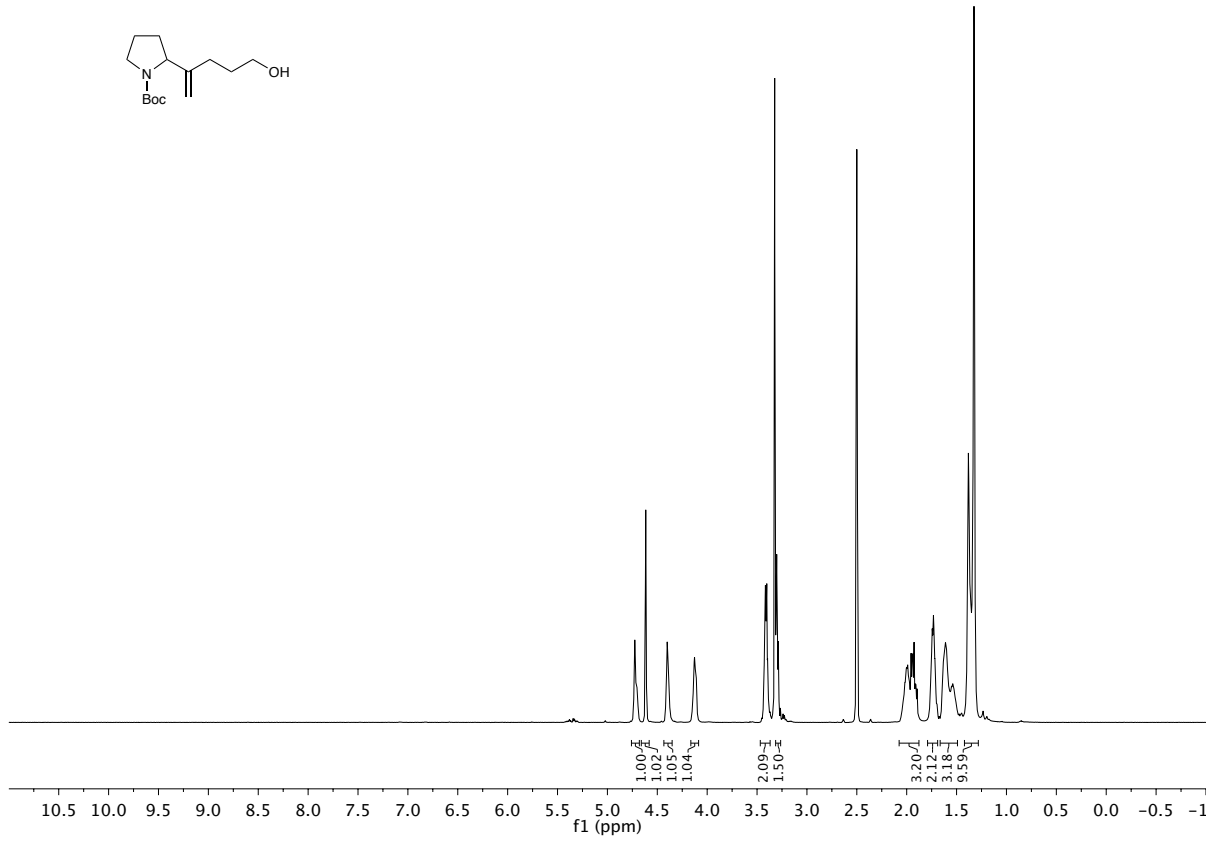
^{1}H NMR Spectrum for compound **17**



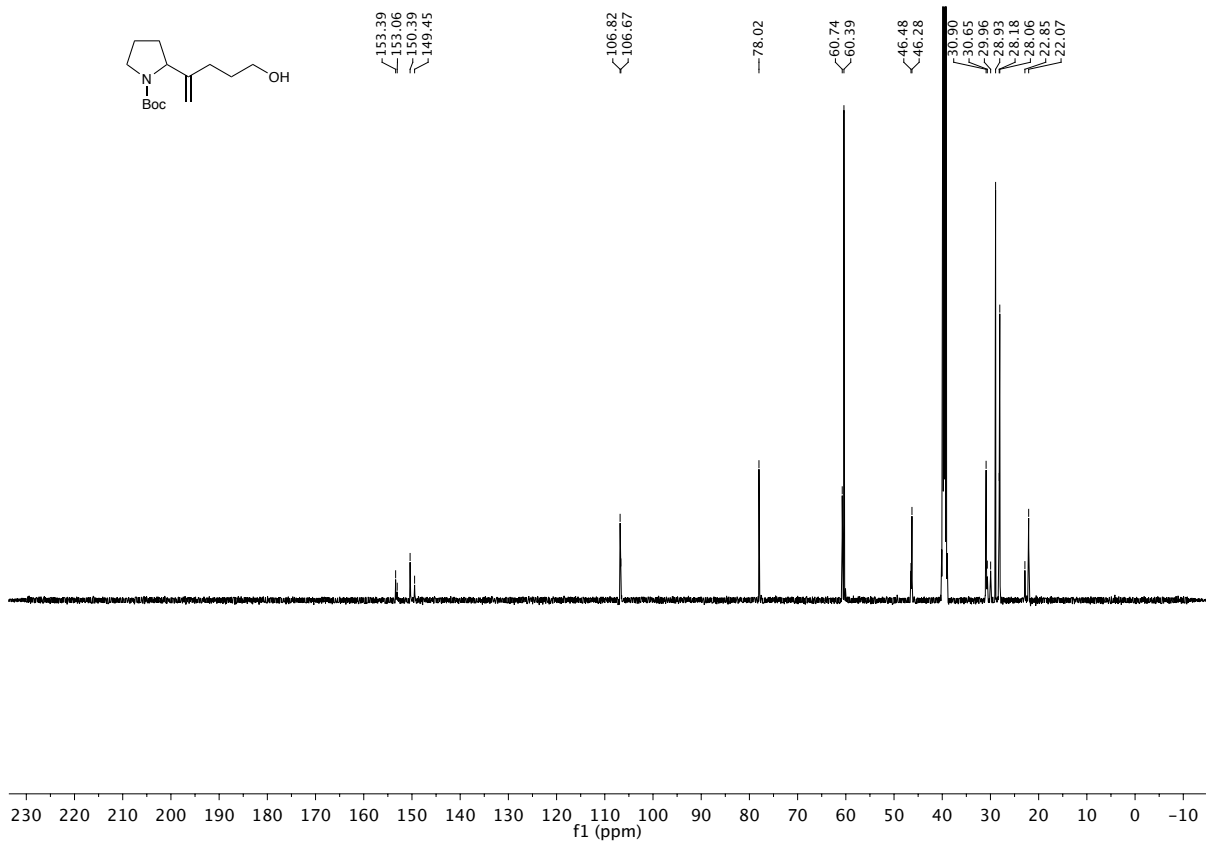
^{13}C NMR Spectrum for compound **17**



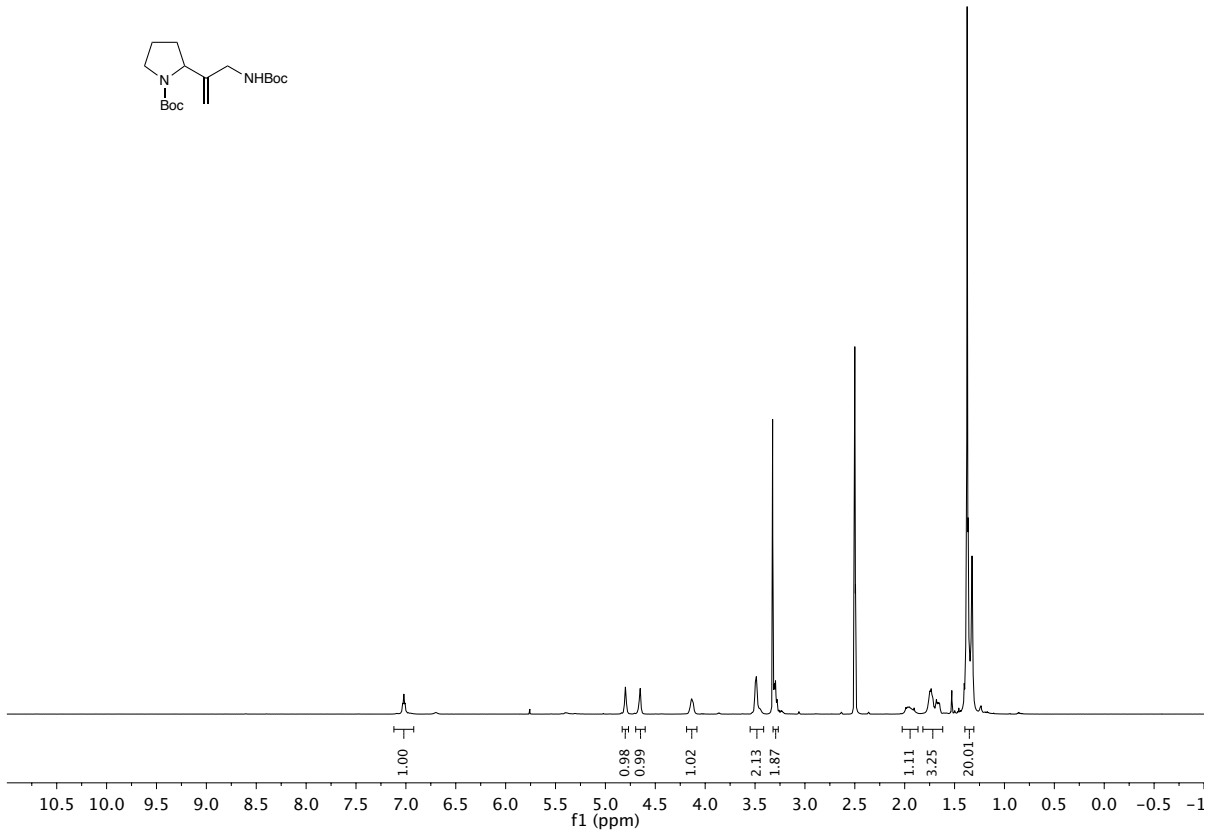
^{1}H NMR Spectrum for compound **18**



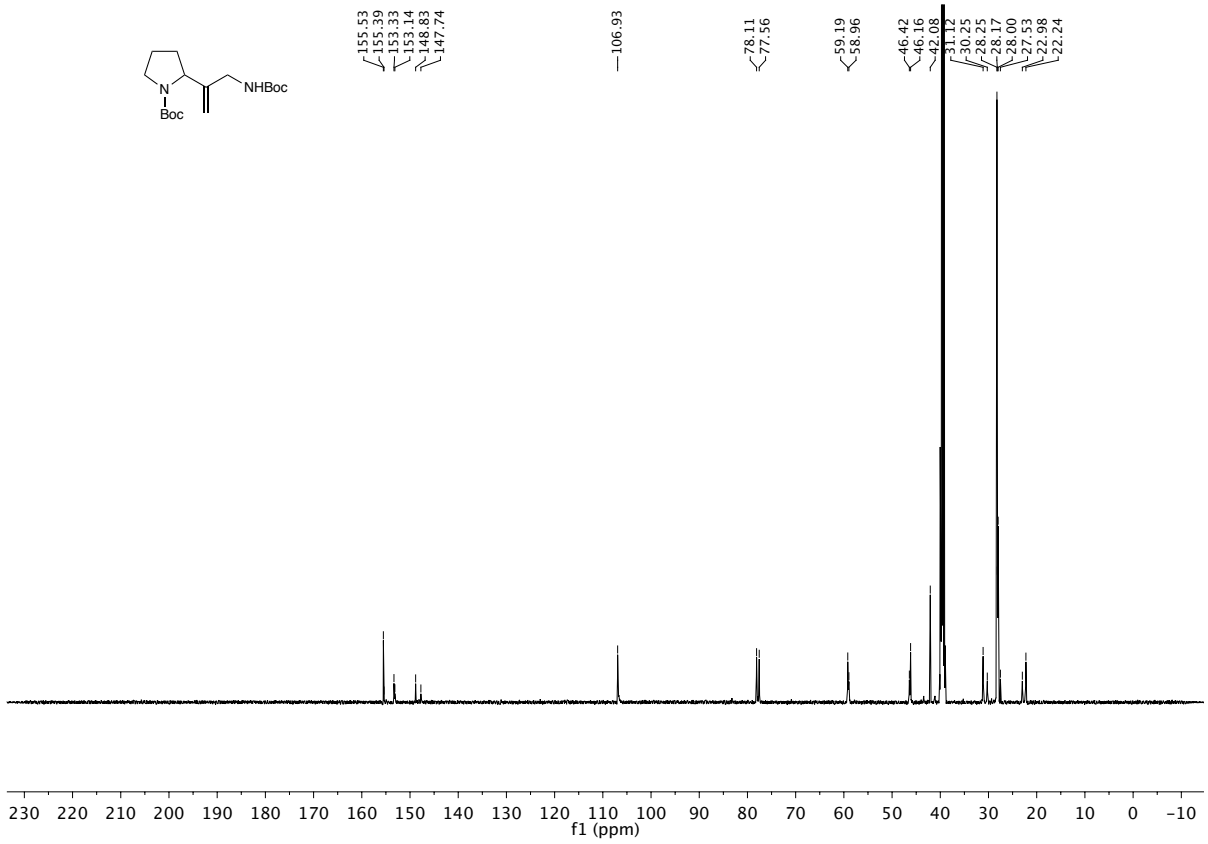
^{13}C NMR Spectrum for compound **18**



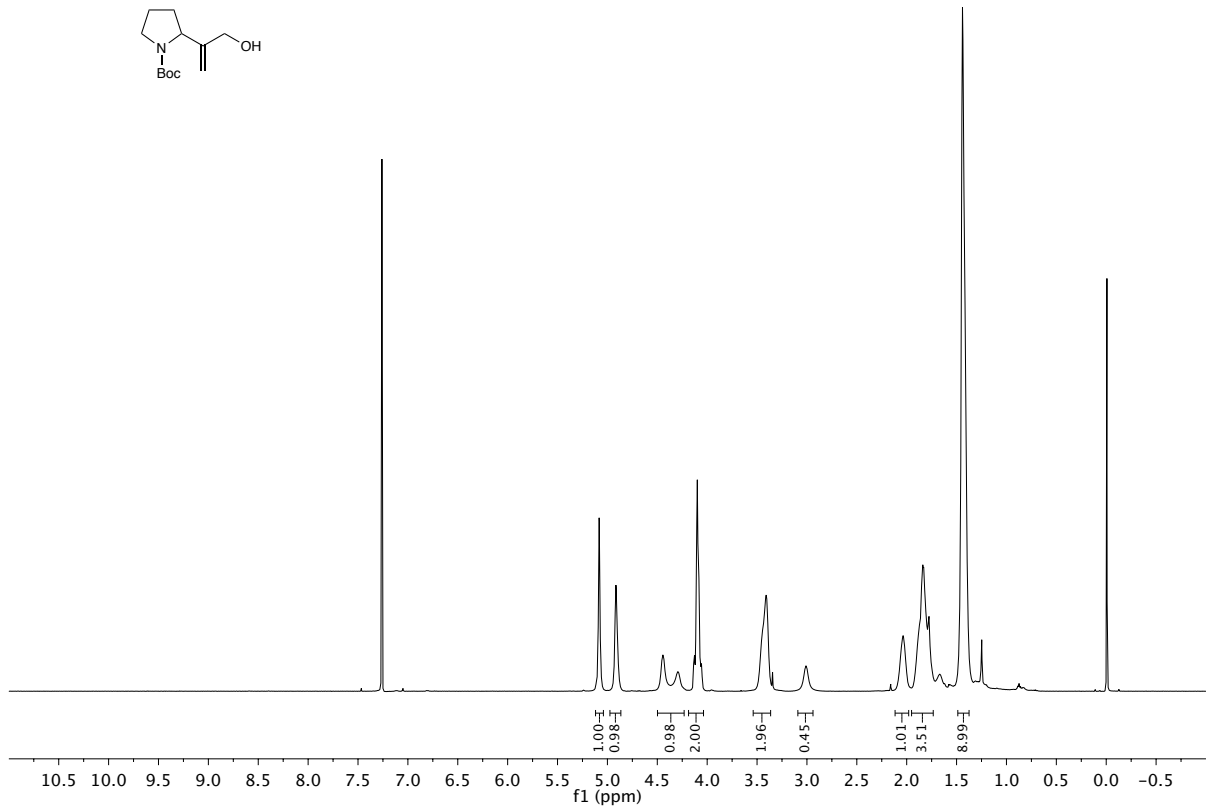
^{1}H NMR Spectrum for compound **19**



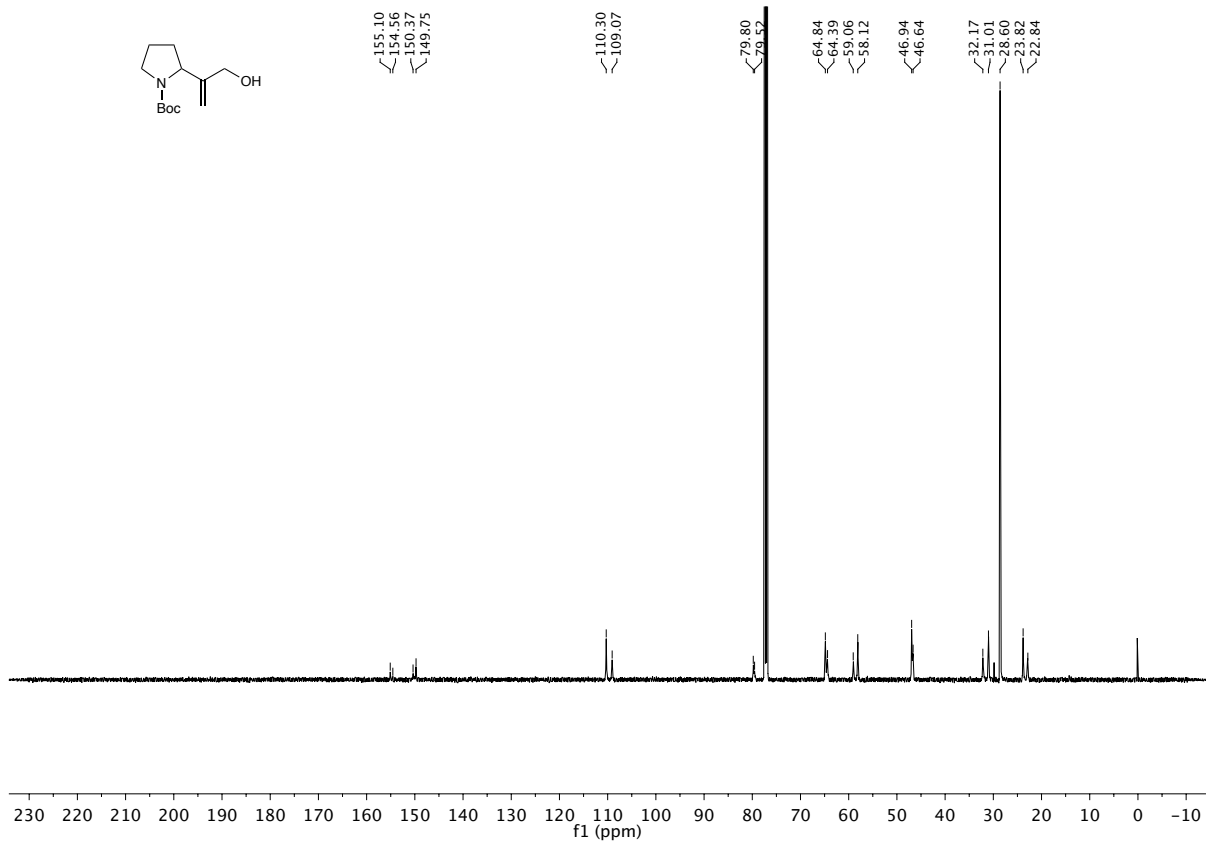
^{13}C NMR Spectrum for compound **19**



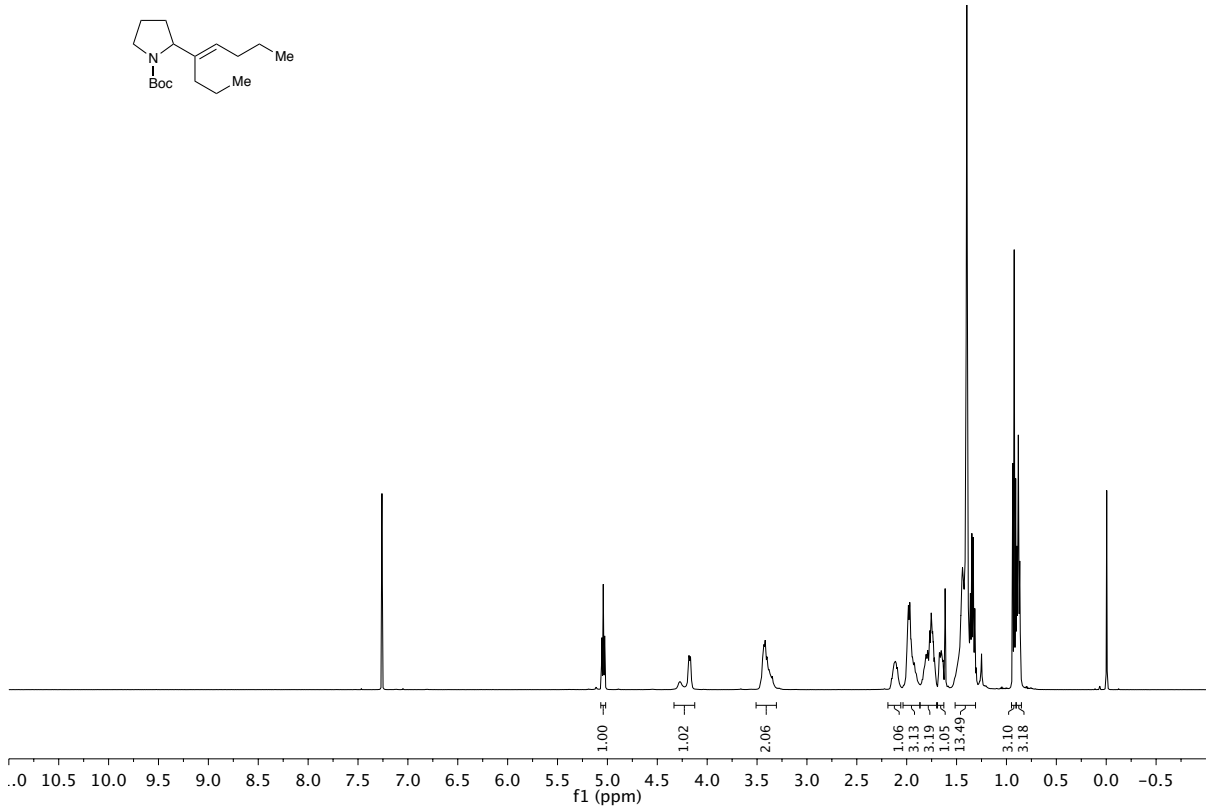
^{1}H NMR Spectrum for compound **20**



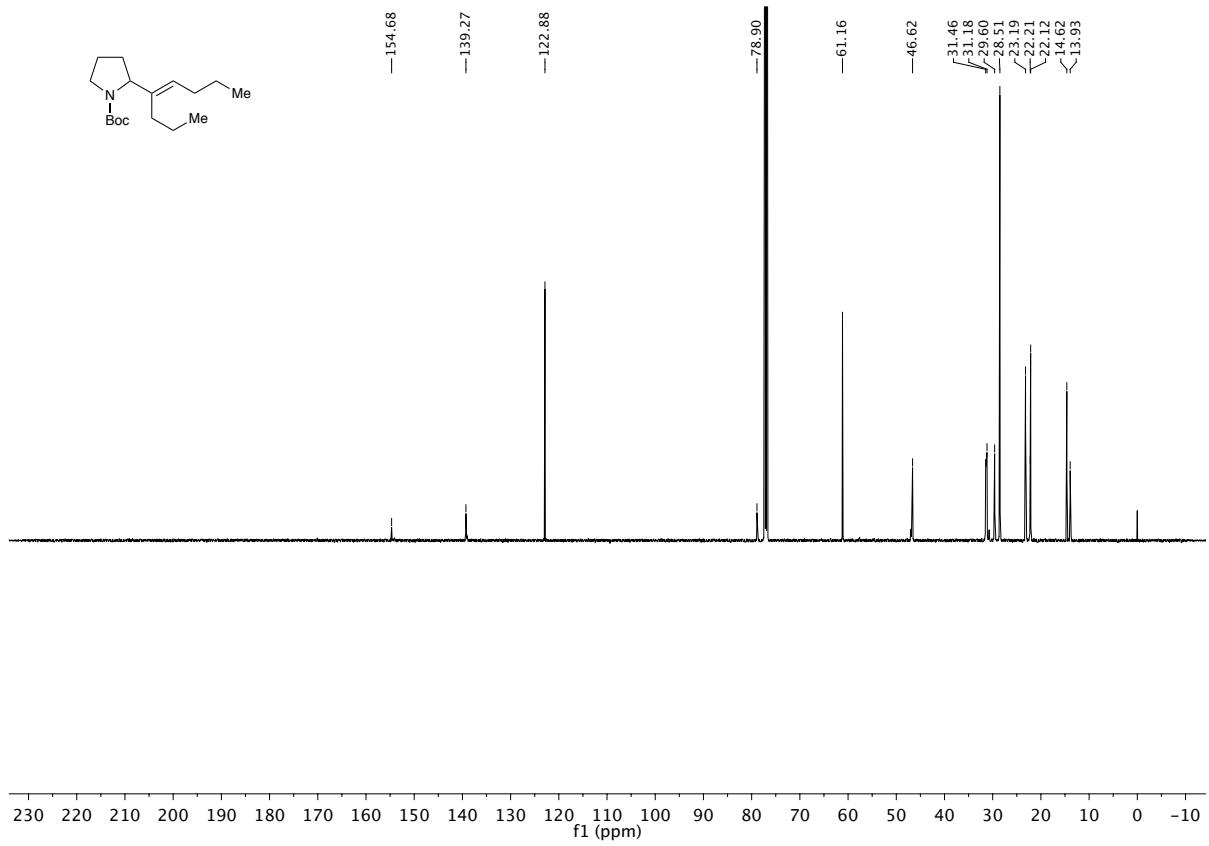
^{13}C NMR Spectrum for compound **20**



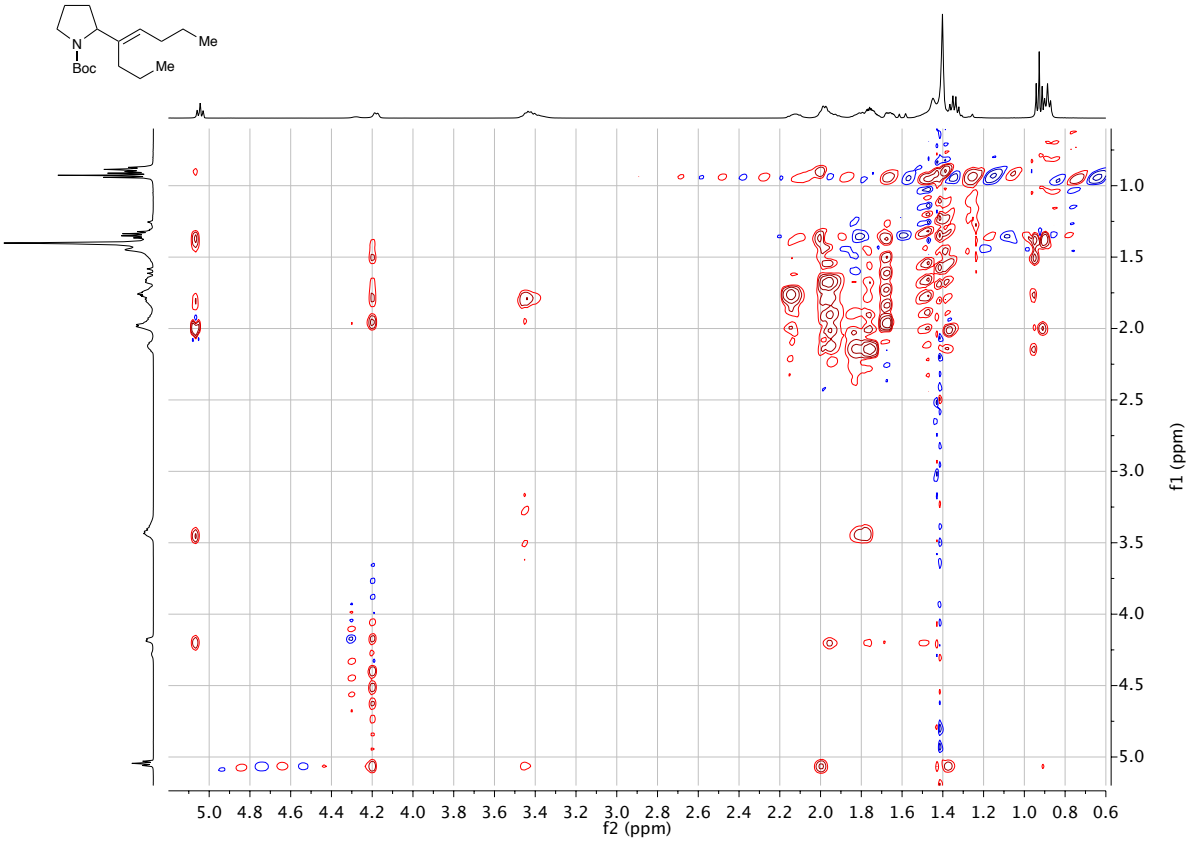
^{1}H NMR Spectrum for compound **21**



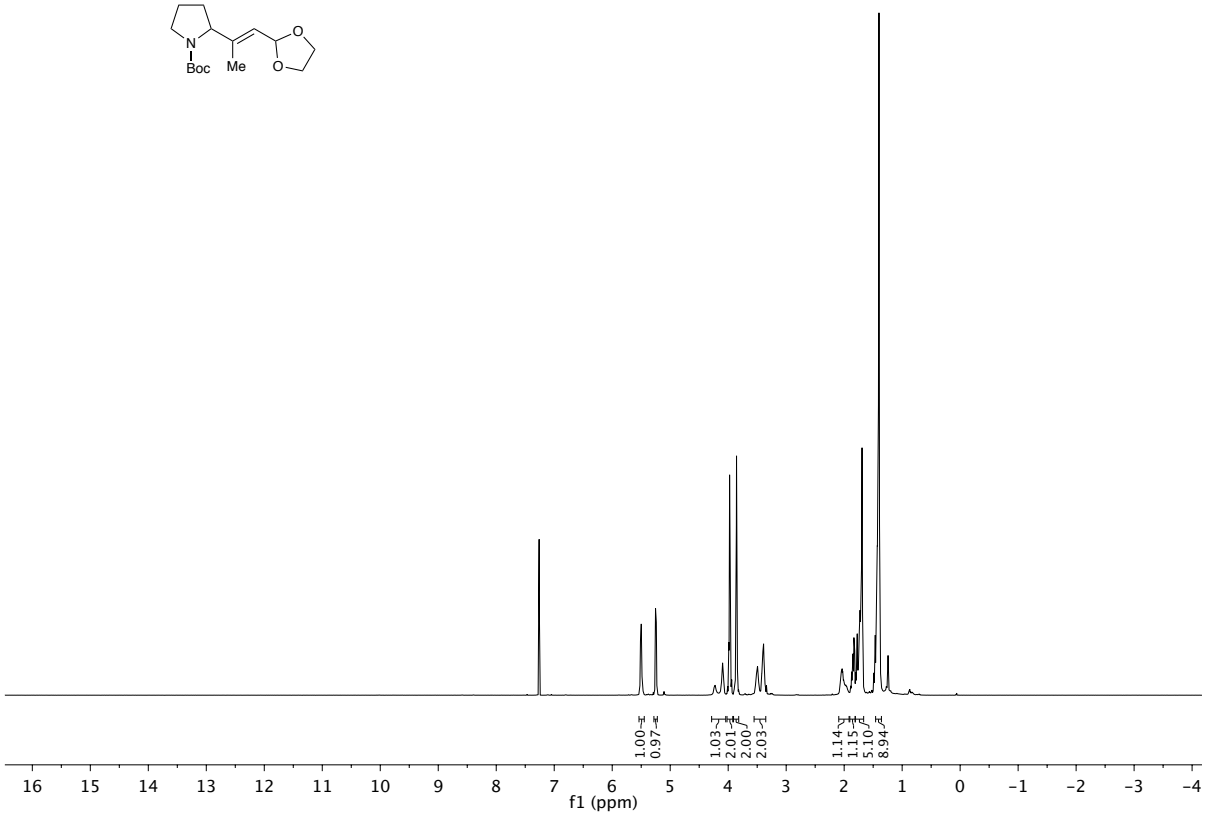
^{13}C NMR Spectrum for compound **21**



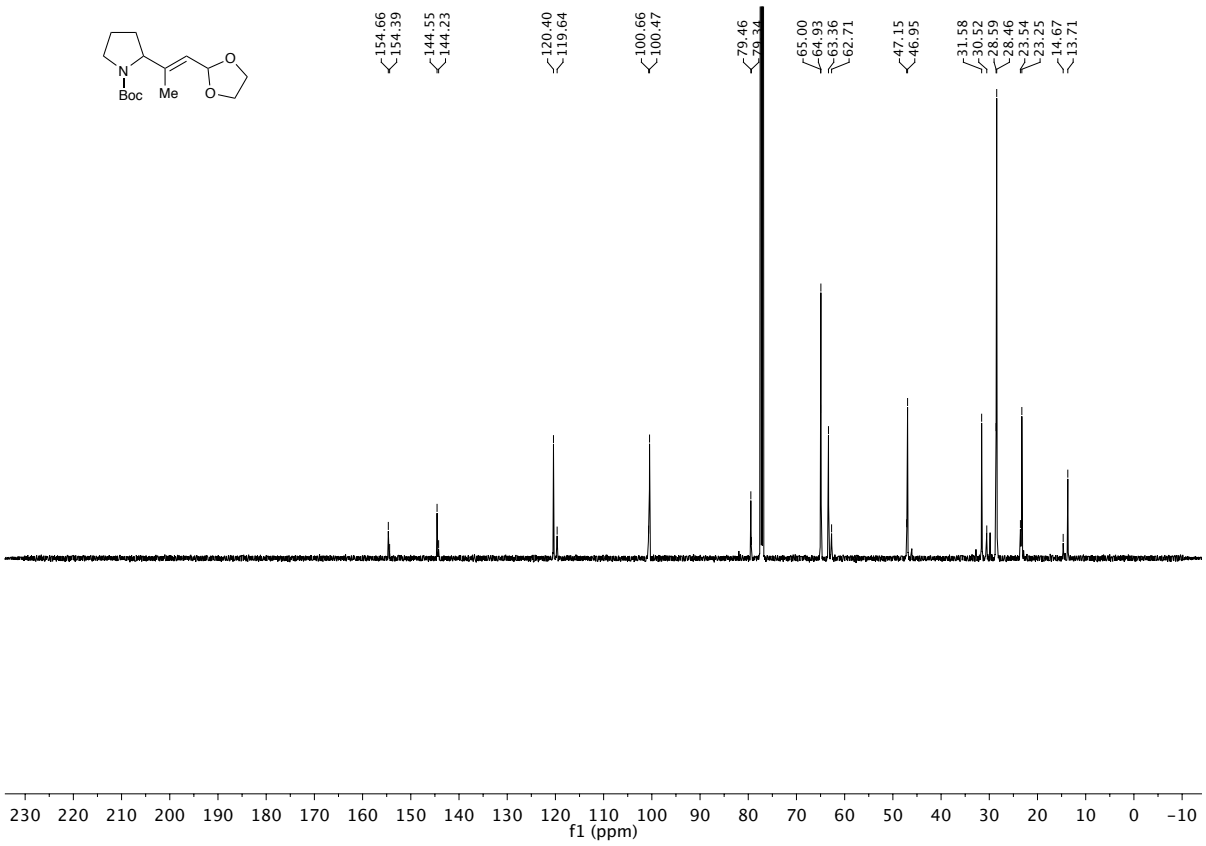
NOESY Spectrum for compound **21**



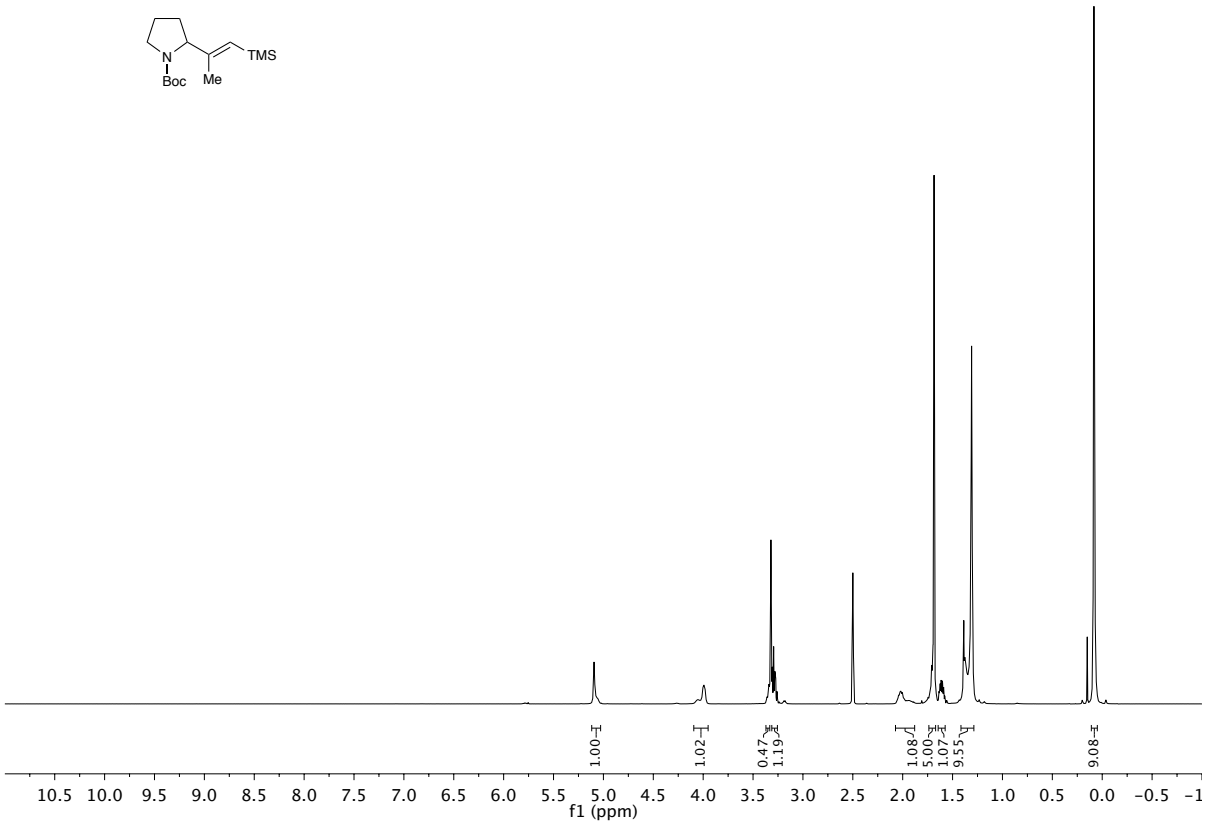
^{1}H NMR Spectrum for compound **22**



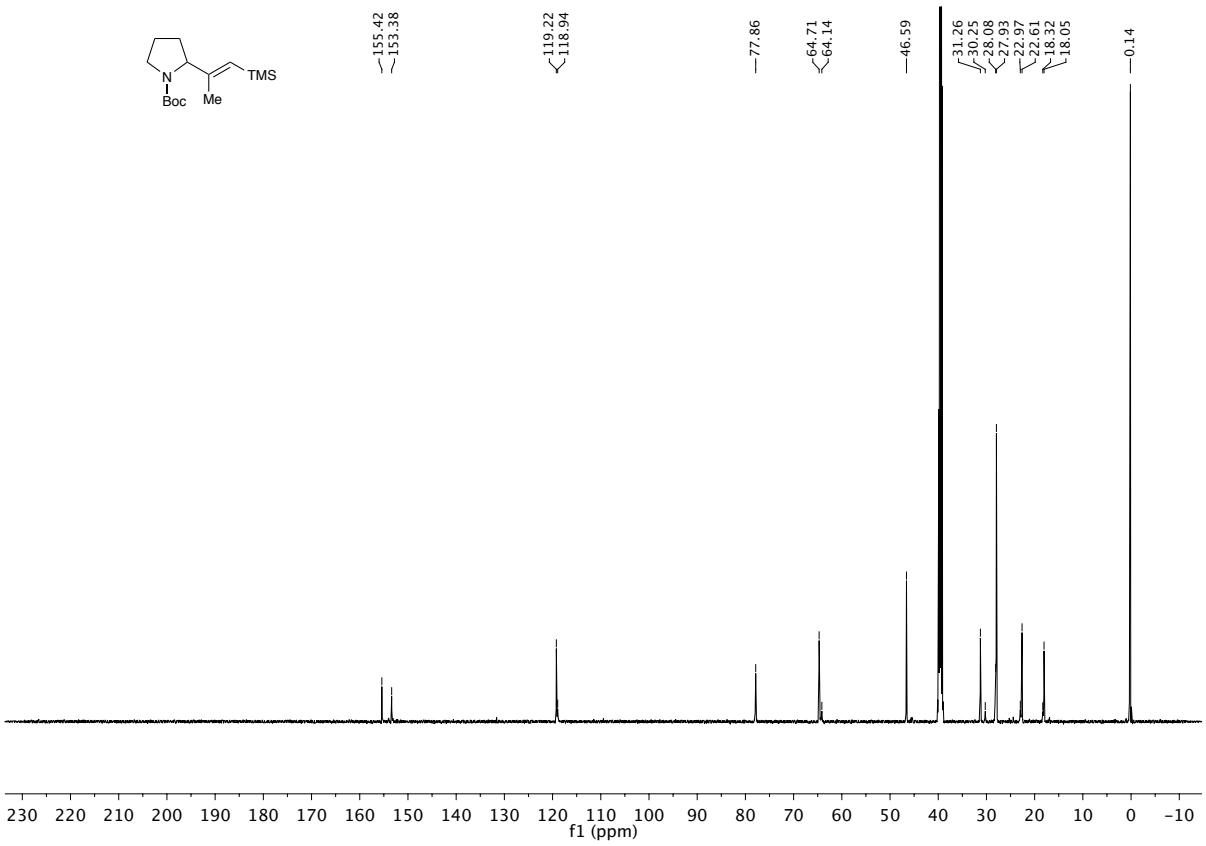
^{13}C NMR Spectrum for compound **22**



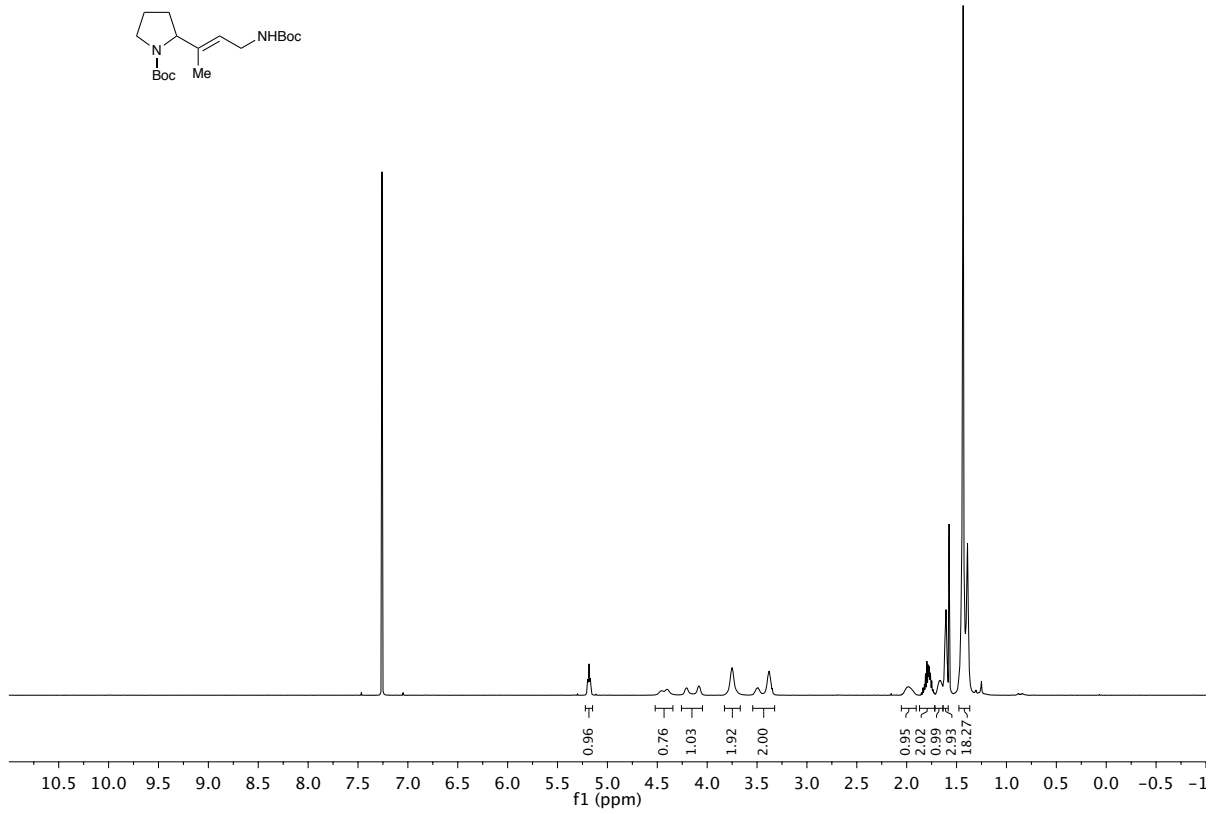
^{1}H NMR Spectrum for compound **23**



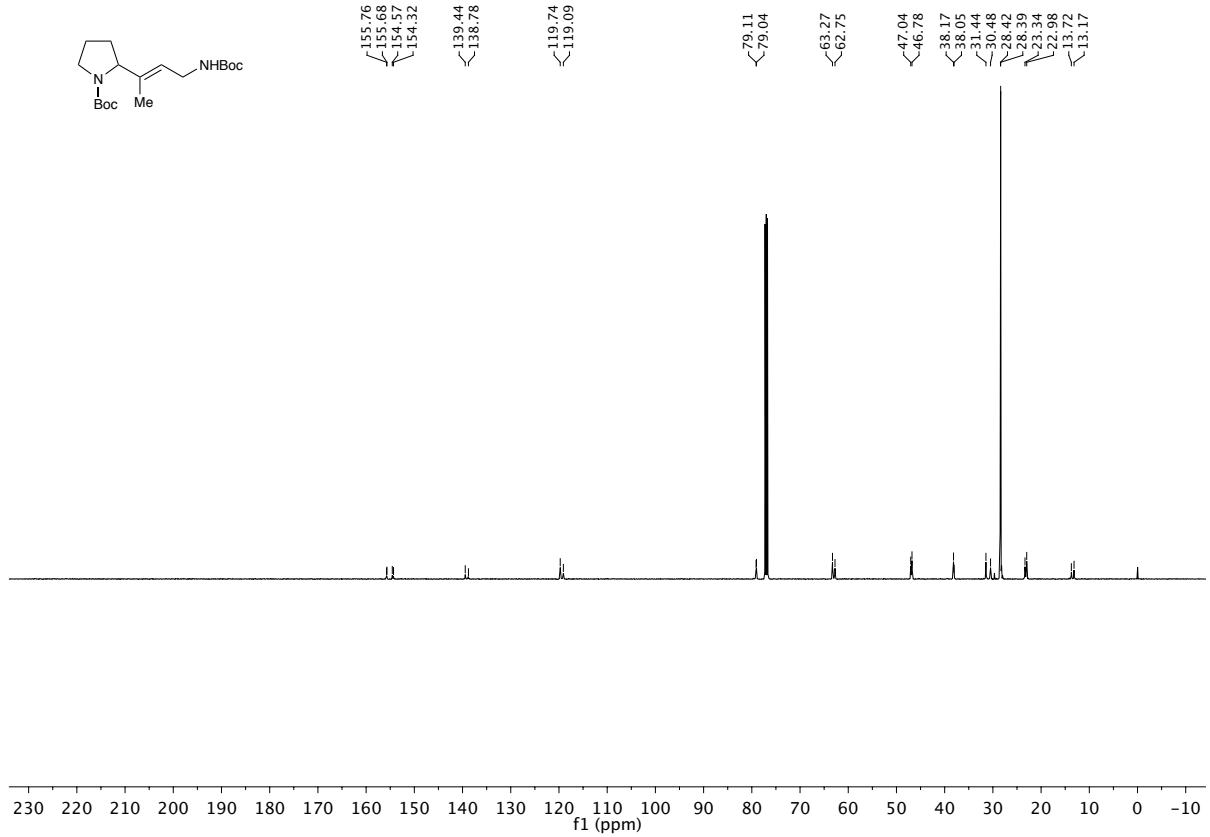
^{13}C NMR Spectrum for compound **23**



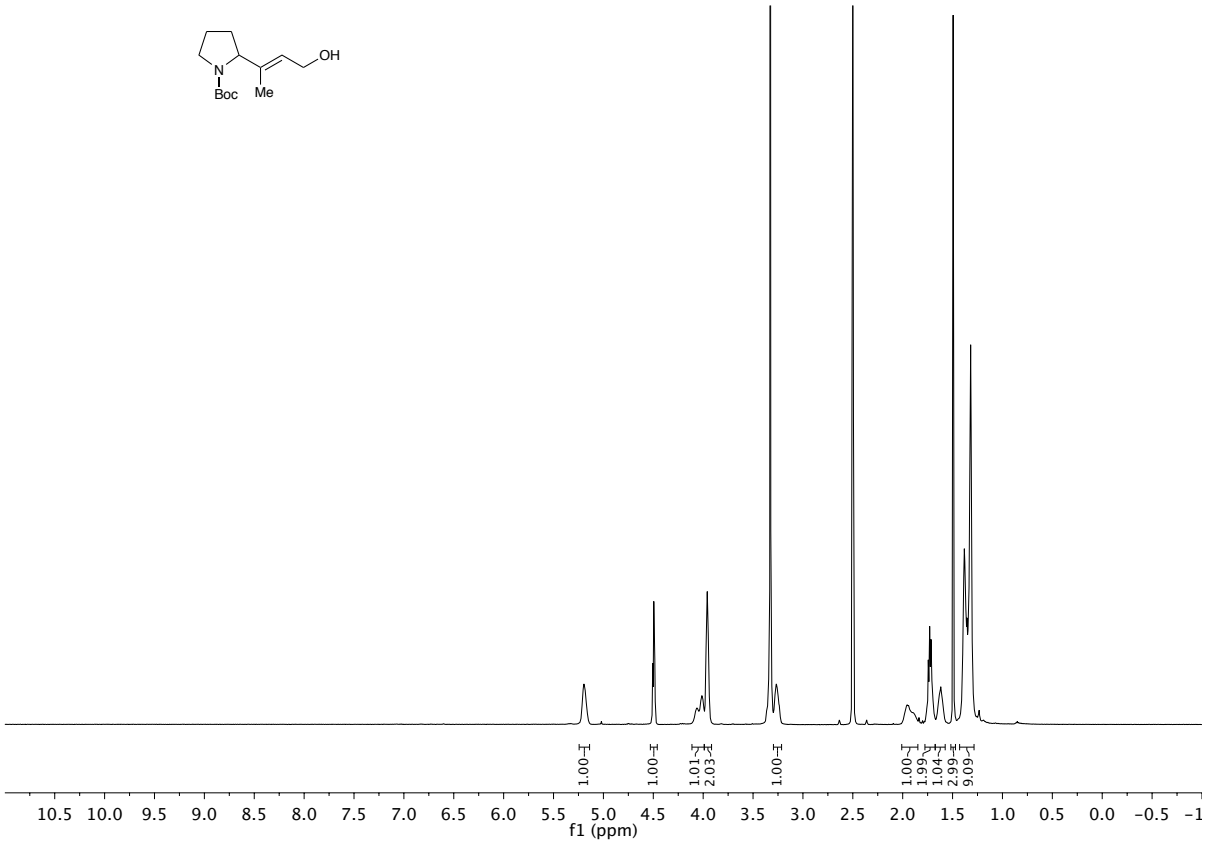
^{1}H NMR Spectrum for compound **24**



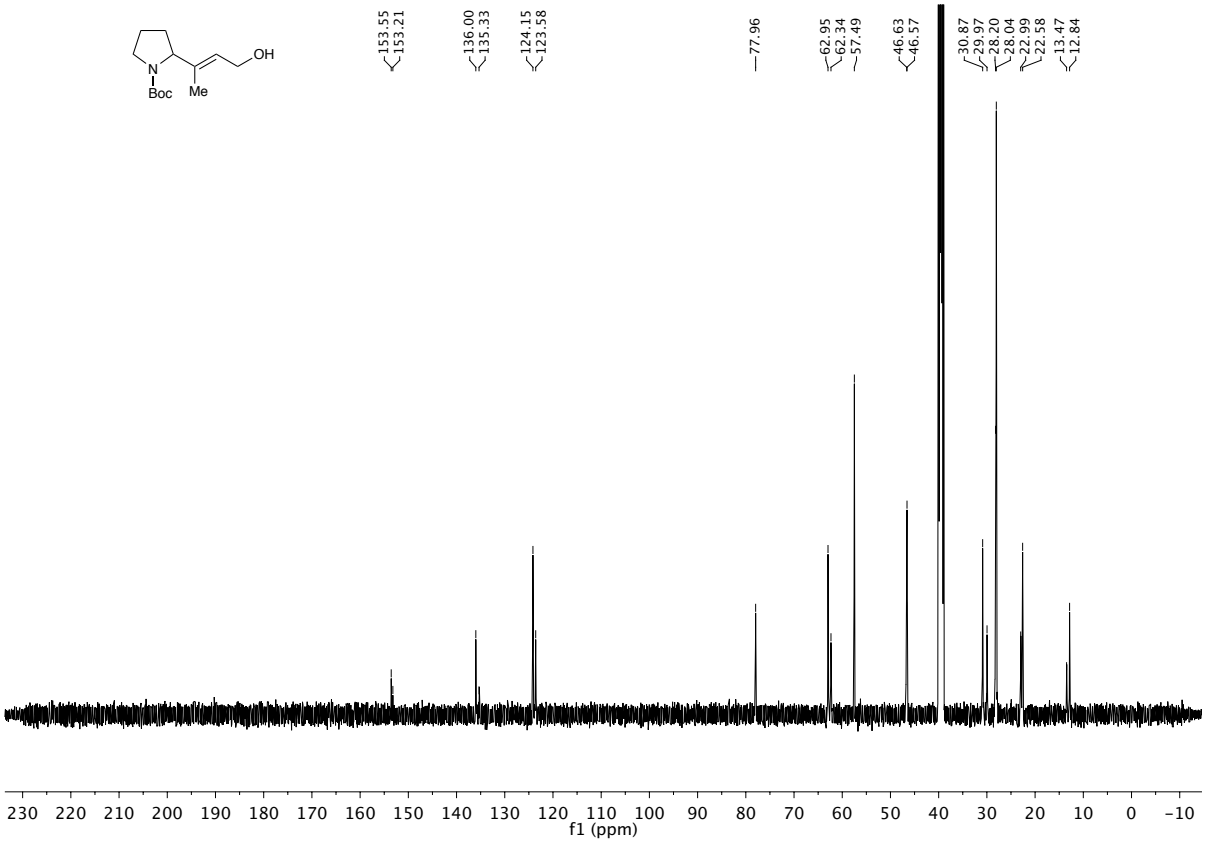
^{13}C NMR Spectrum for compound **24**



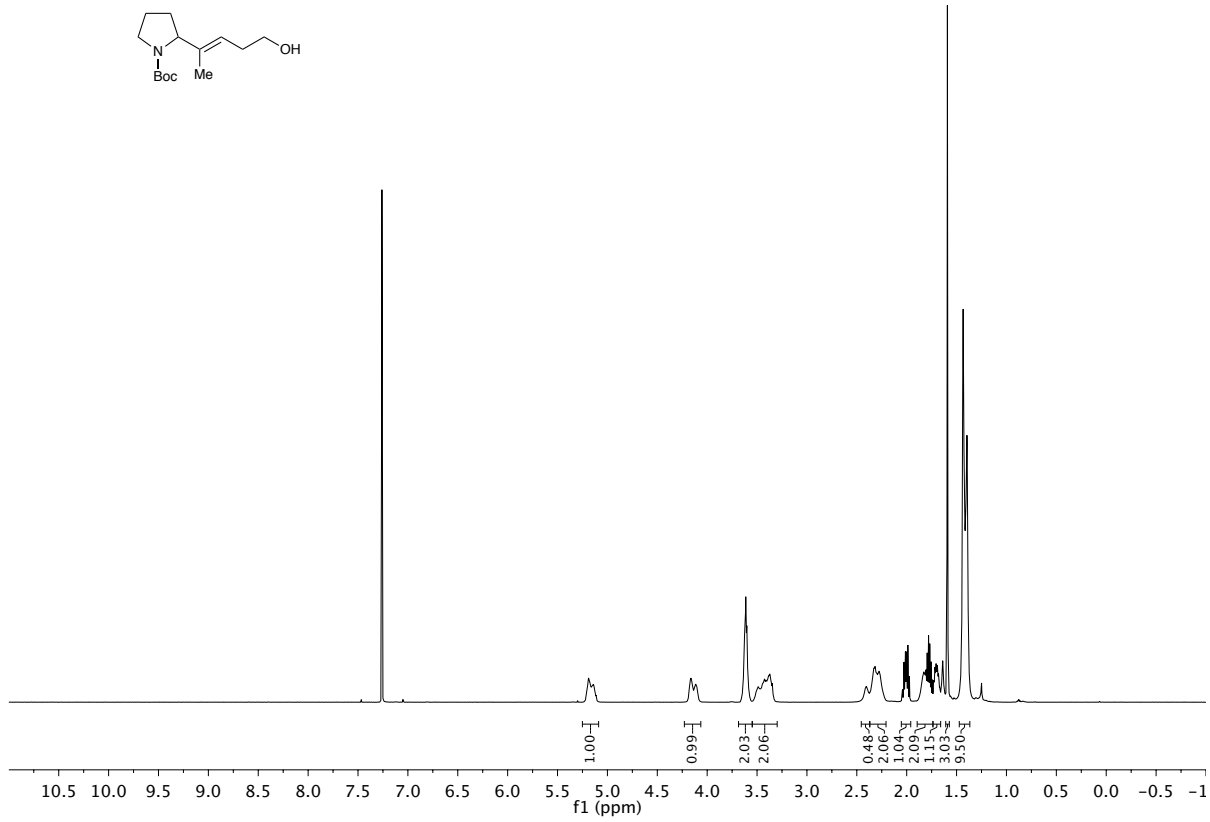
^{1}H NMR Spectrum for compound **25**



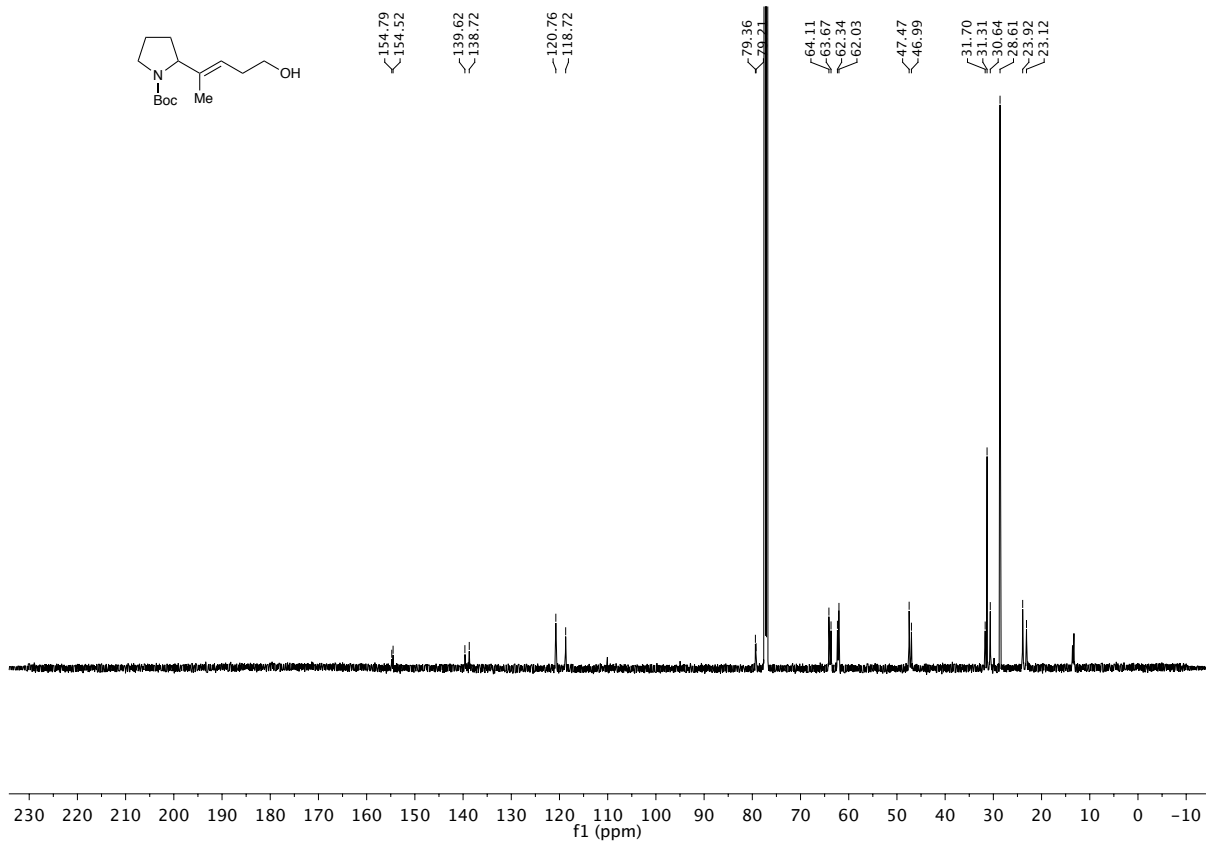
^{13}C NMR Spectrum for compound **25**



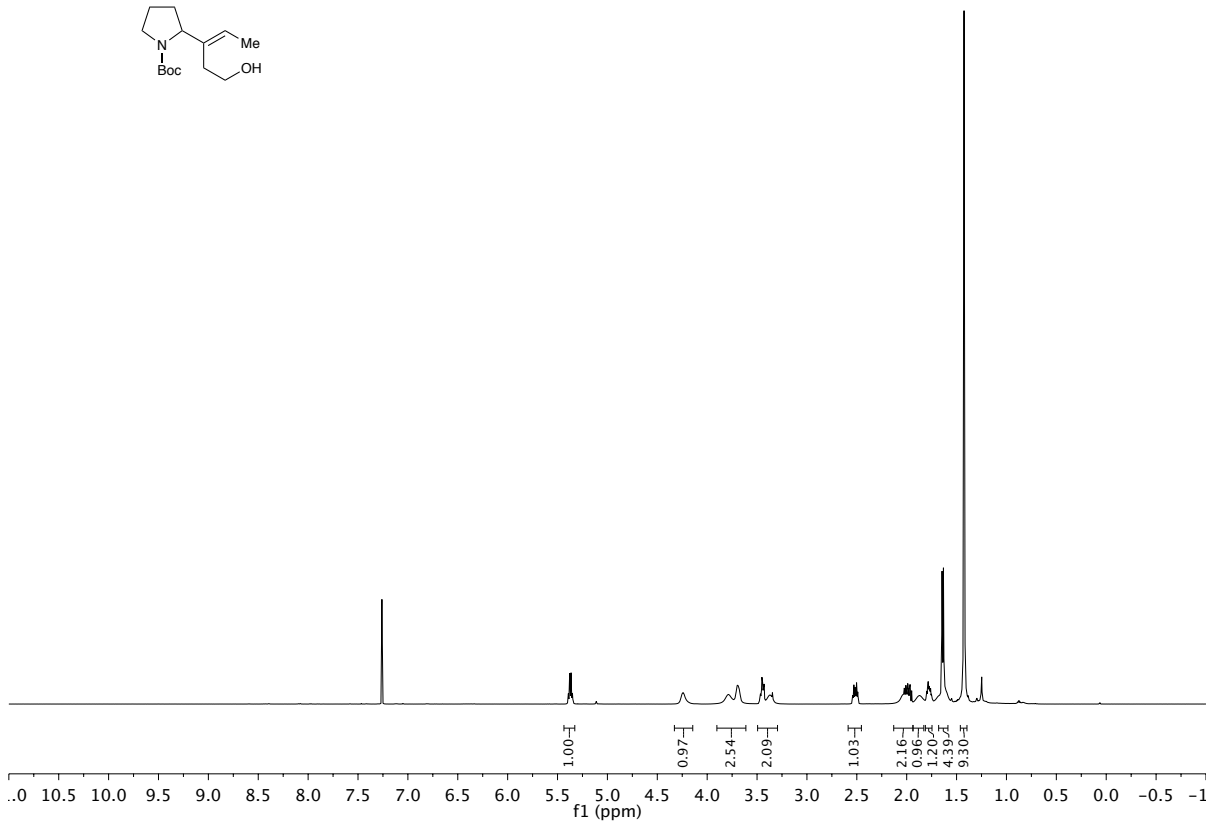
^{1}H NMR Spectrum for compound **26-A**



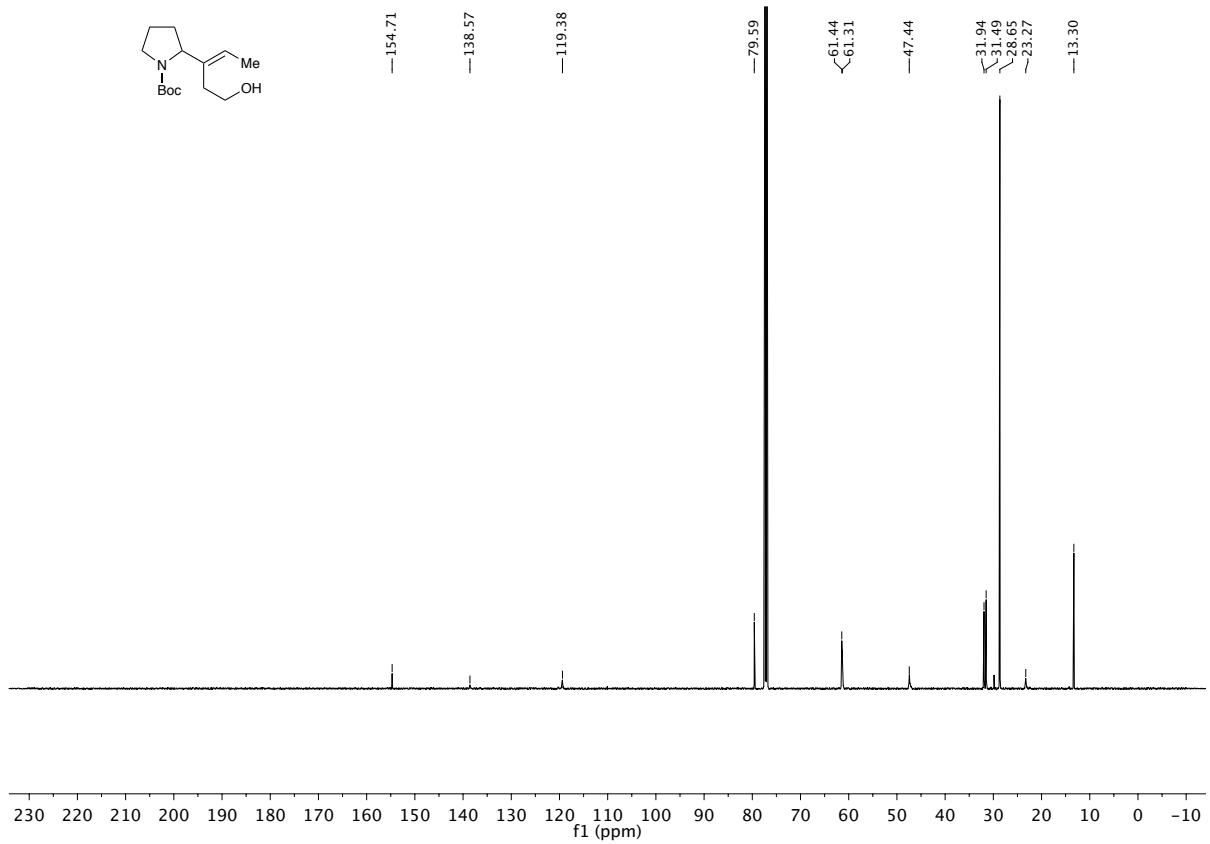
^{13}C NMR Spectrum for compound **26-A**



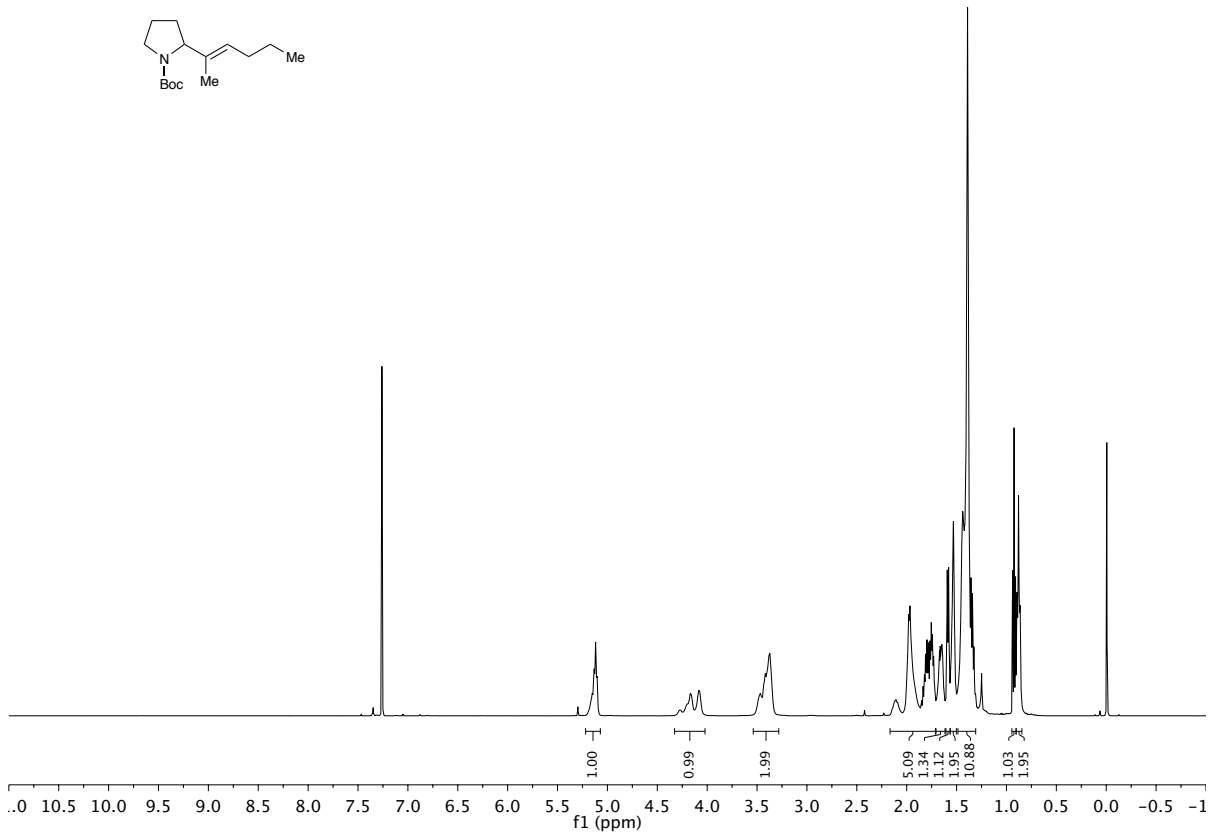
^{1}H NMR Spectrum for compound **26-B**



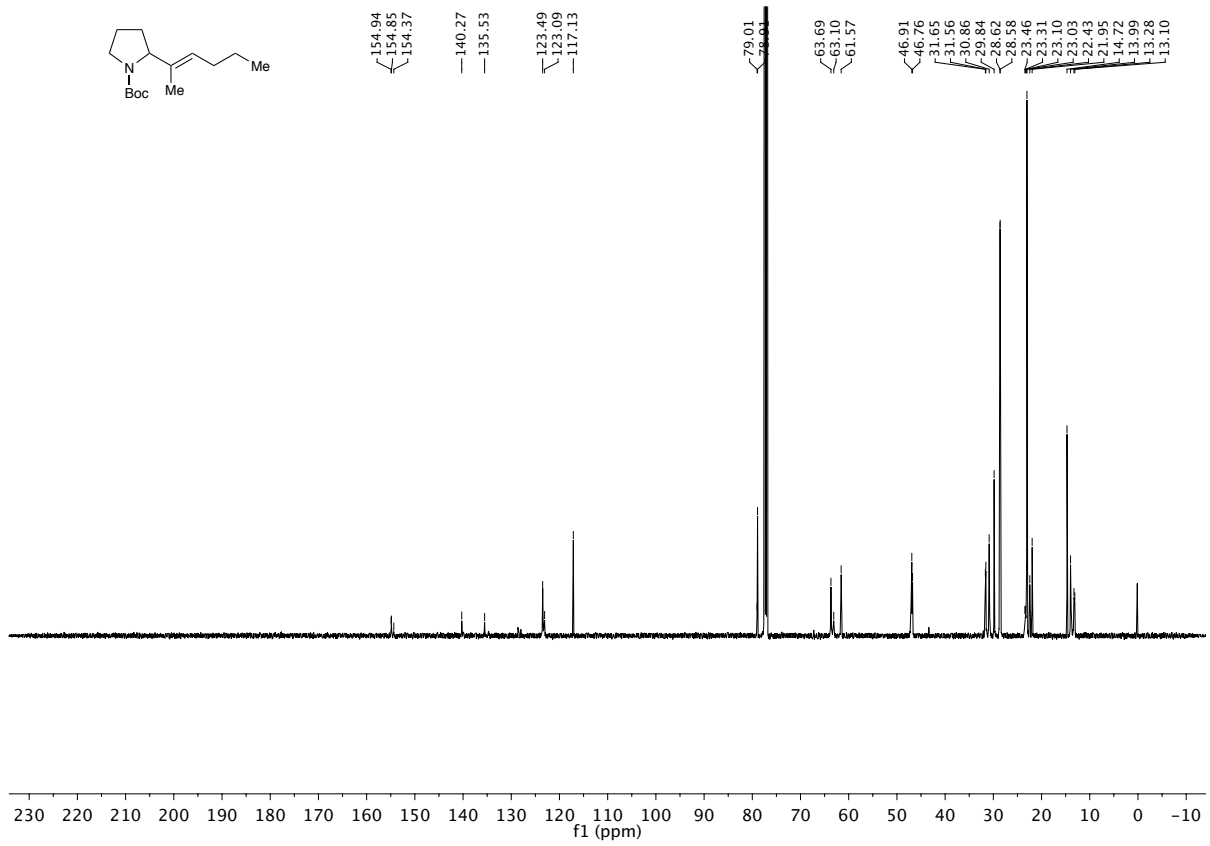
^{13}C NMR Spectrum for compound **26-B**



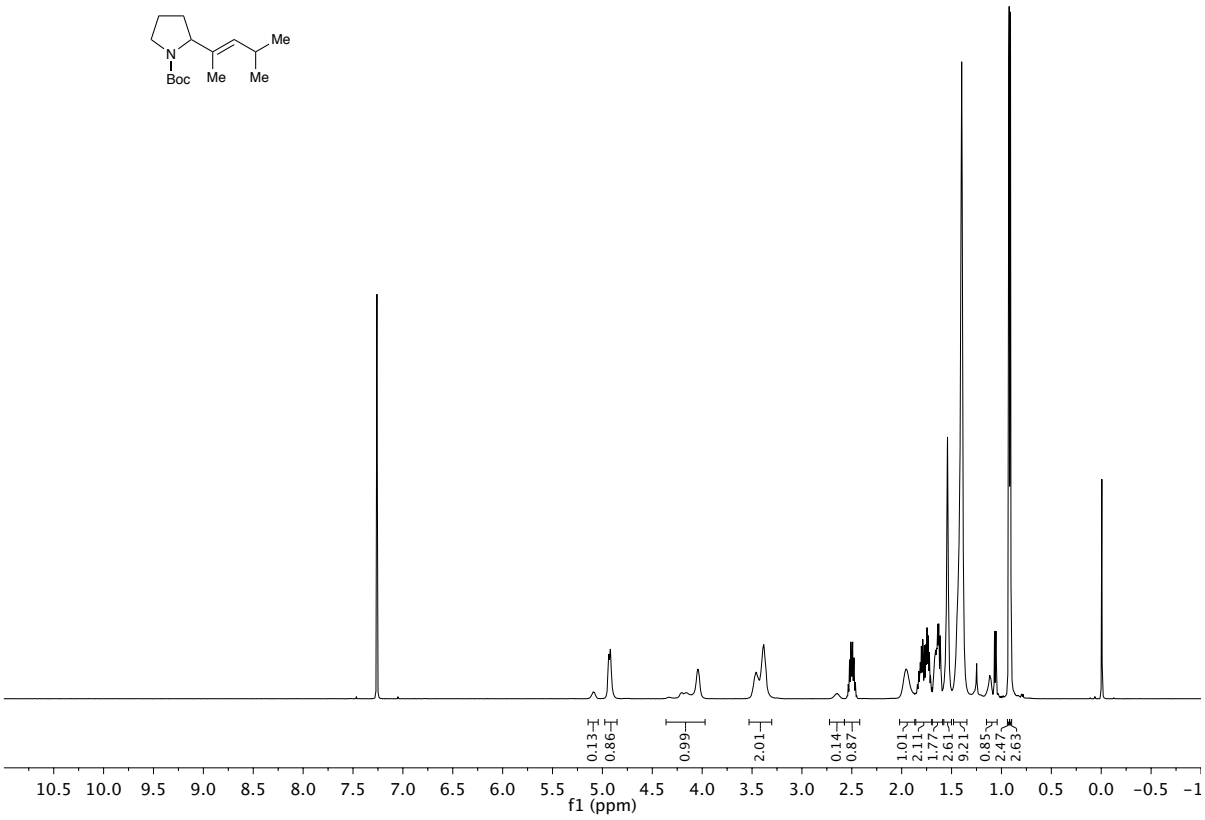
^{1}H NMR Spectrum for compound **27**



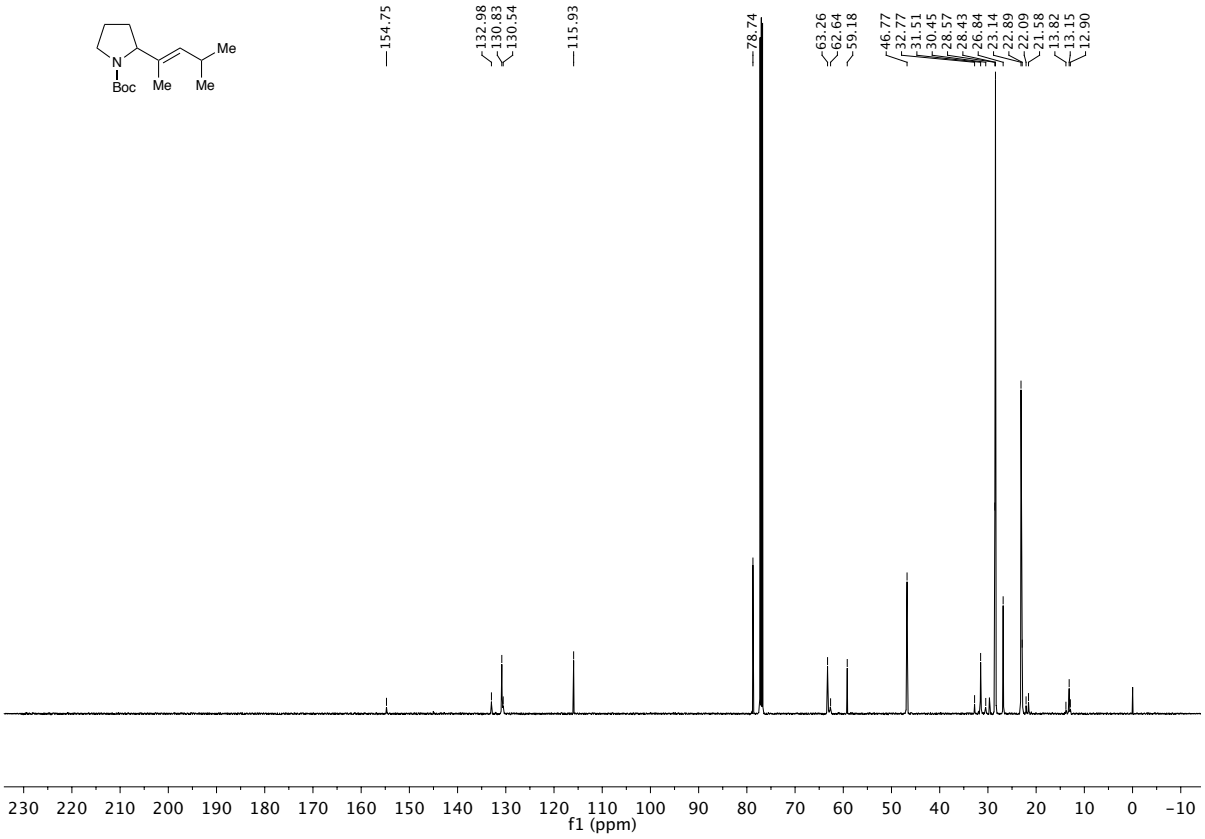
^{13}C NMR Spectrum for compound **27**



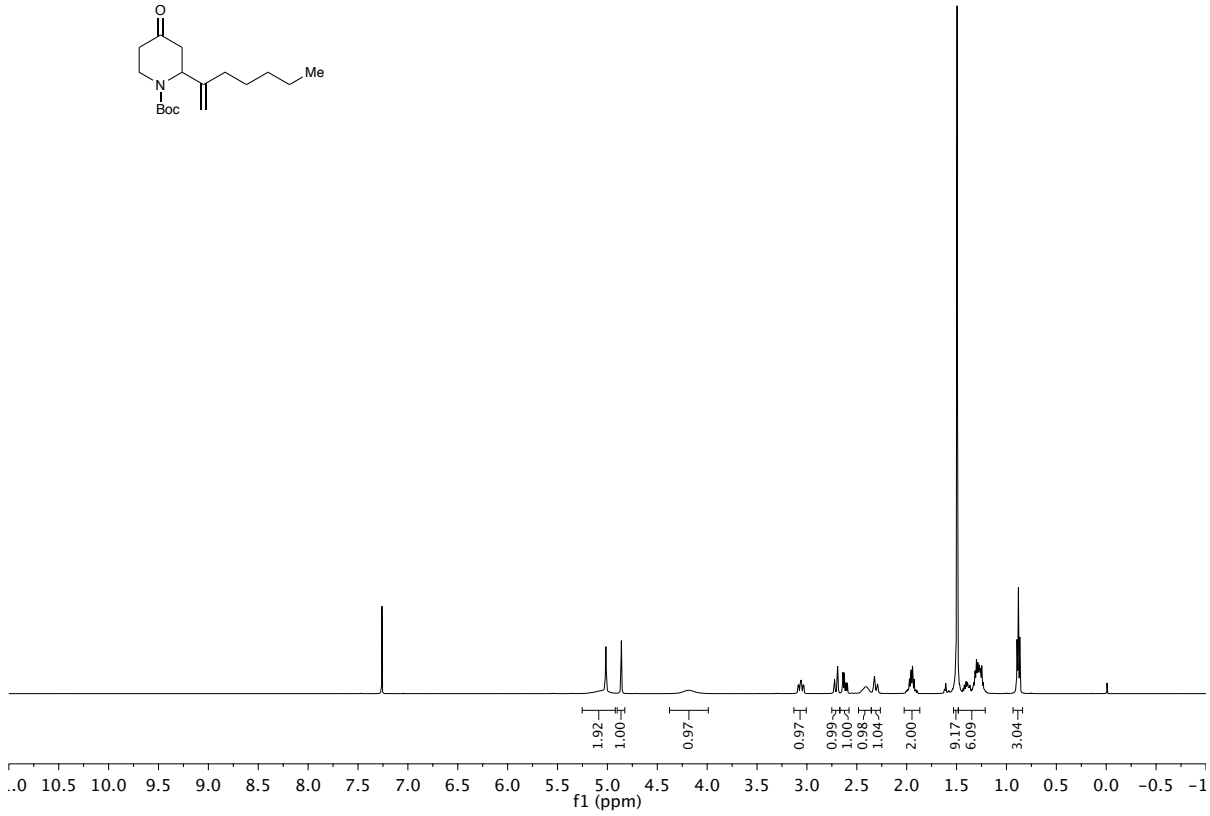
^{1}H NMR Spectrum for compound **28**



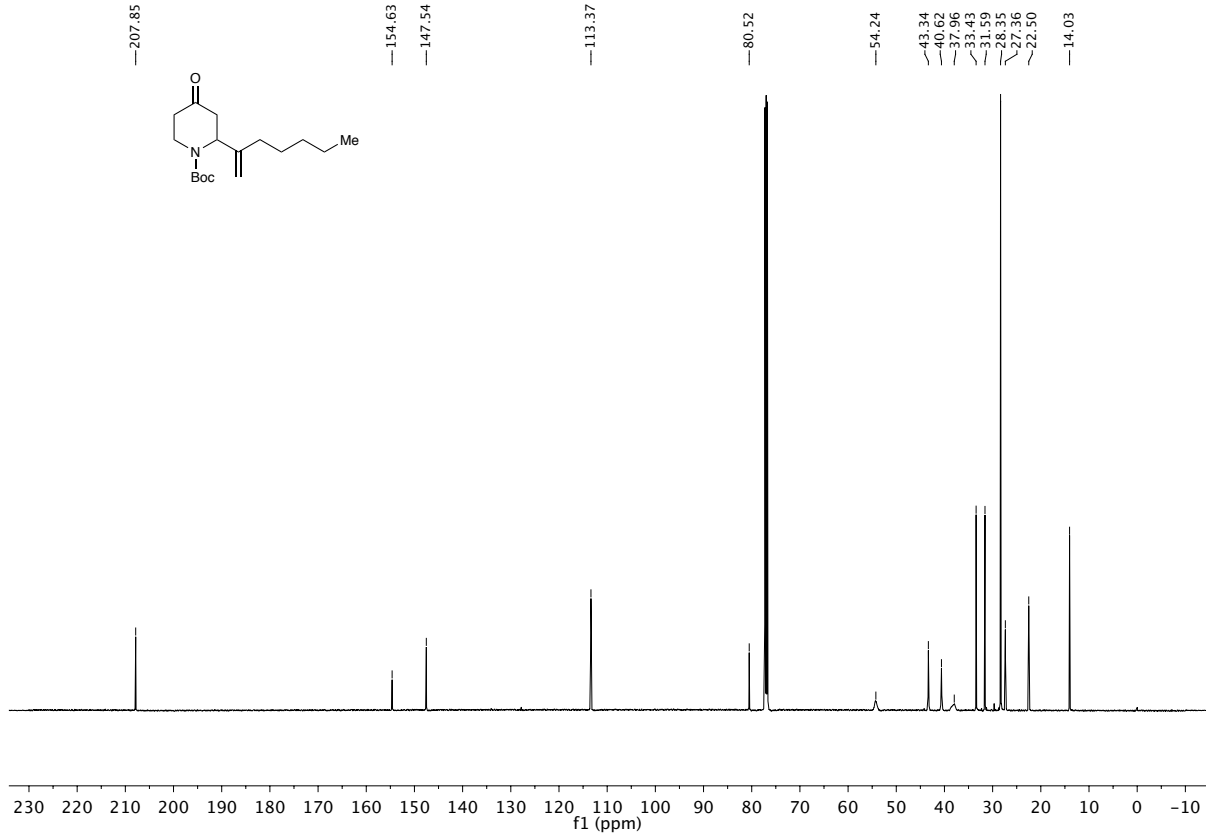
^{13}C NMR Spectrum for compound **28**



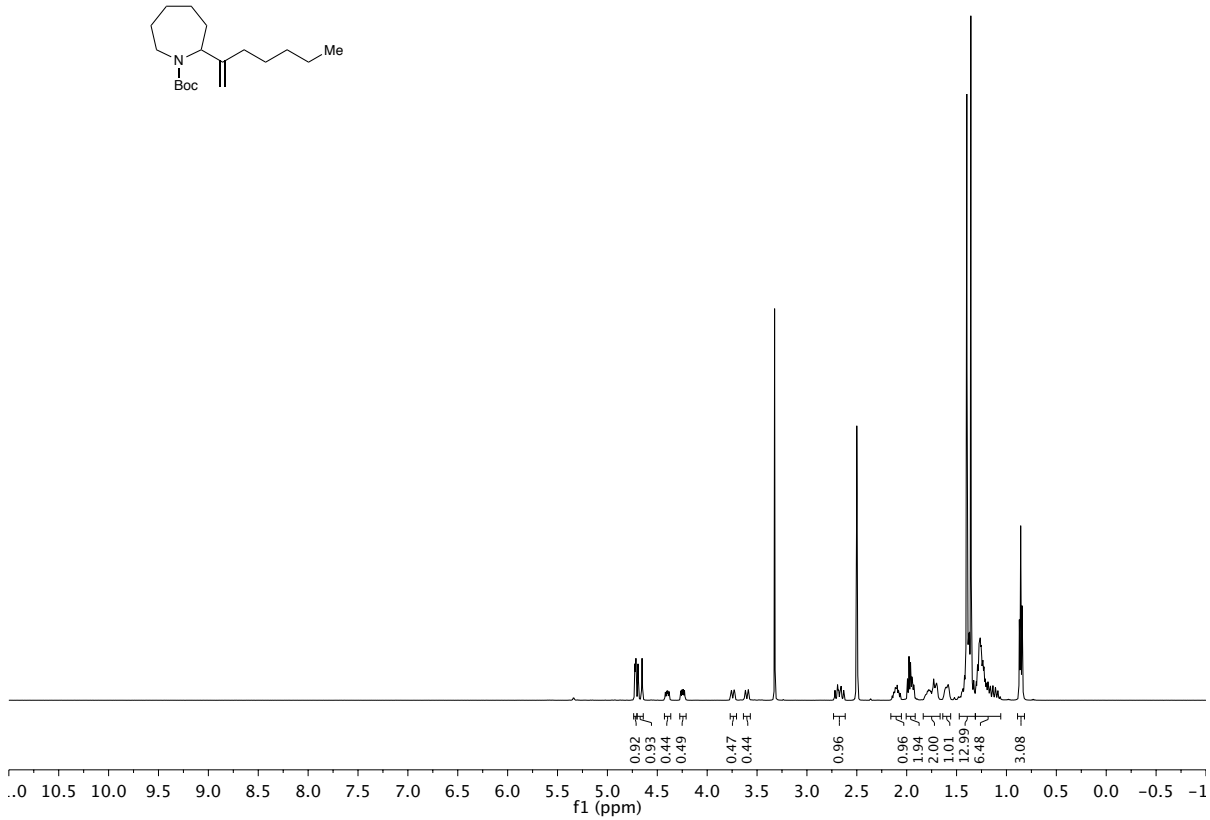
^{1}H NMR Spectrum for compound **29**



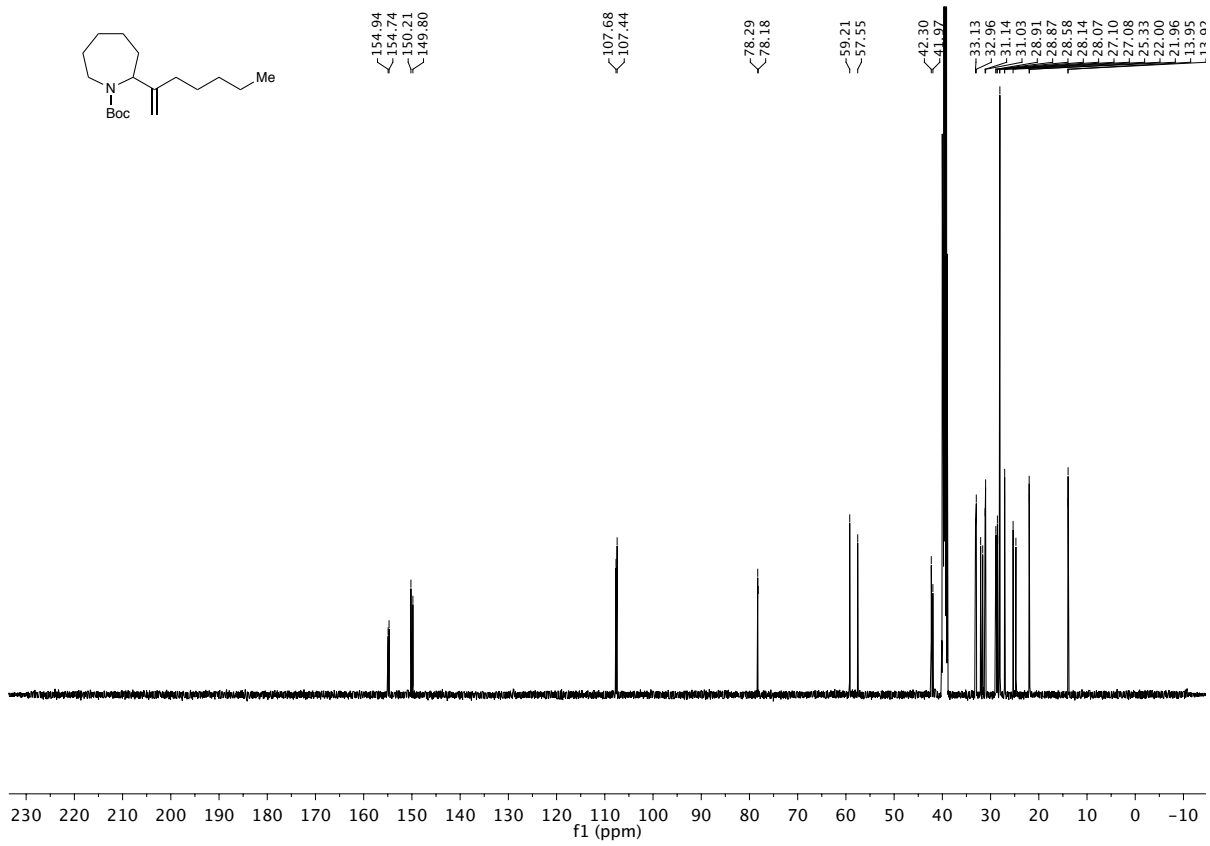
^{13}C NMR Spectrum for compound **29**



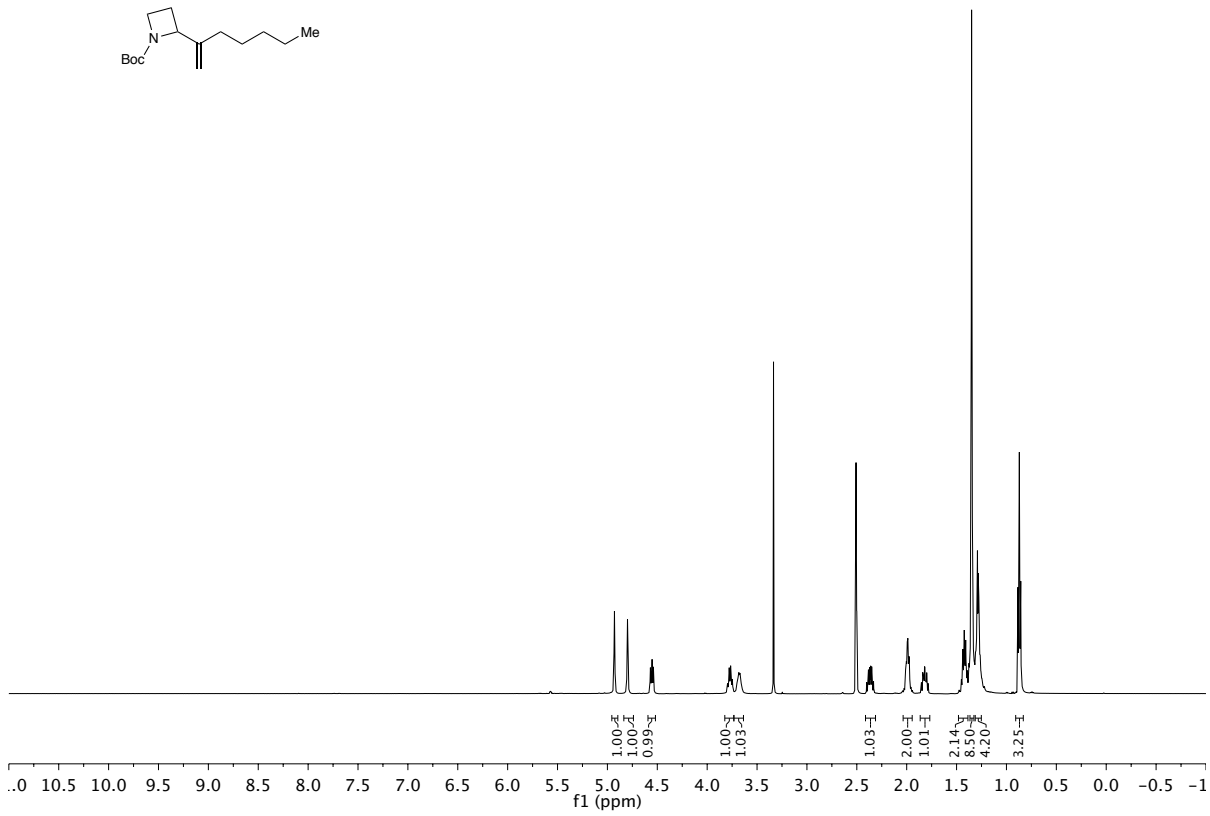
^{1}H NMR Spectrum for compound **30**



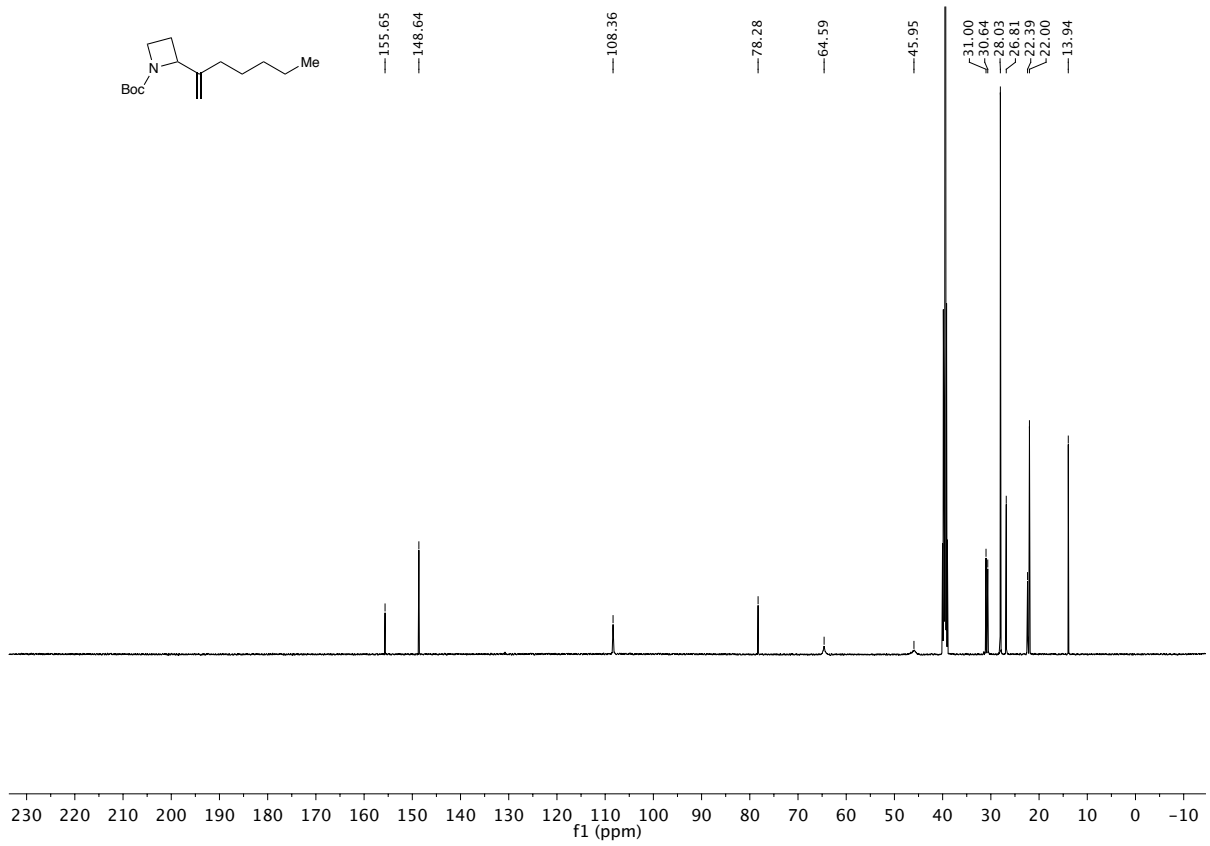
^{13}C NMR Spectrum for compound **30**



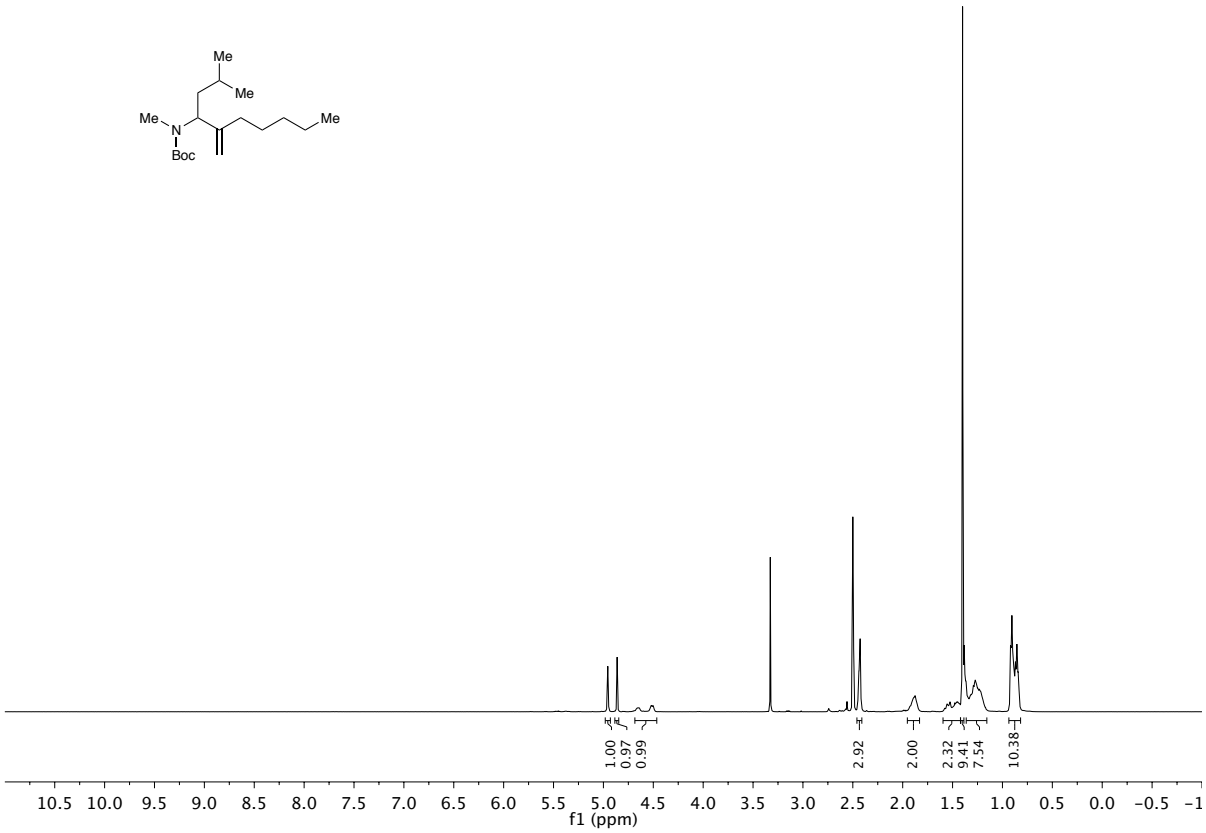
^{1}H NMR Spectrum for compound **31**



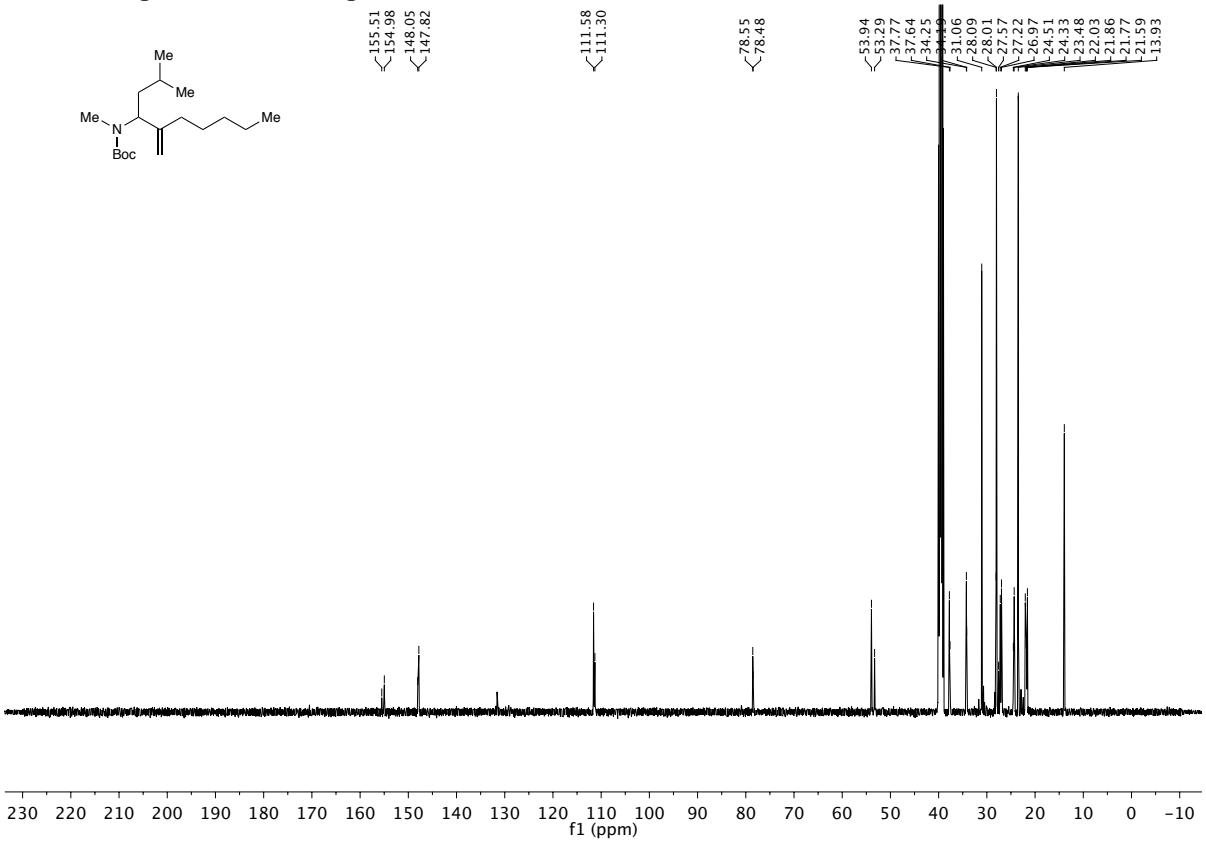
^{13}C NMR Spectrum for compound **31**



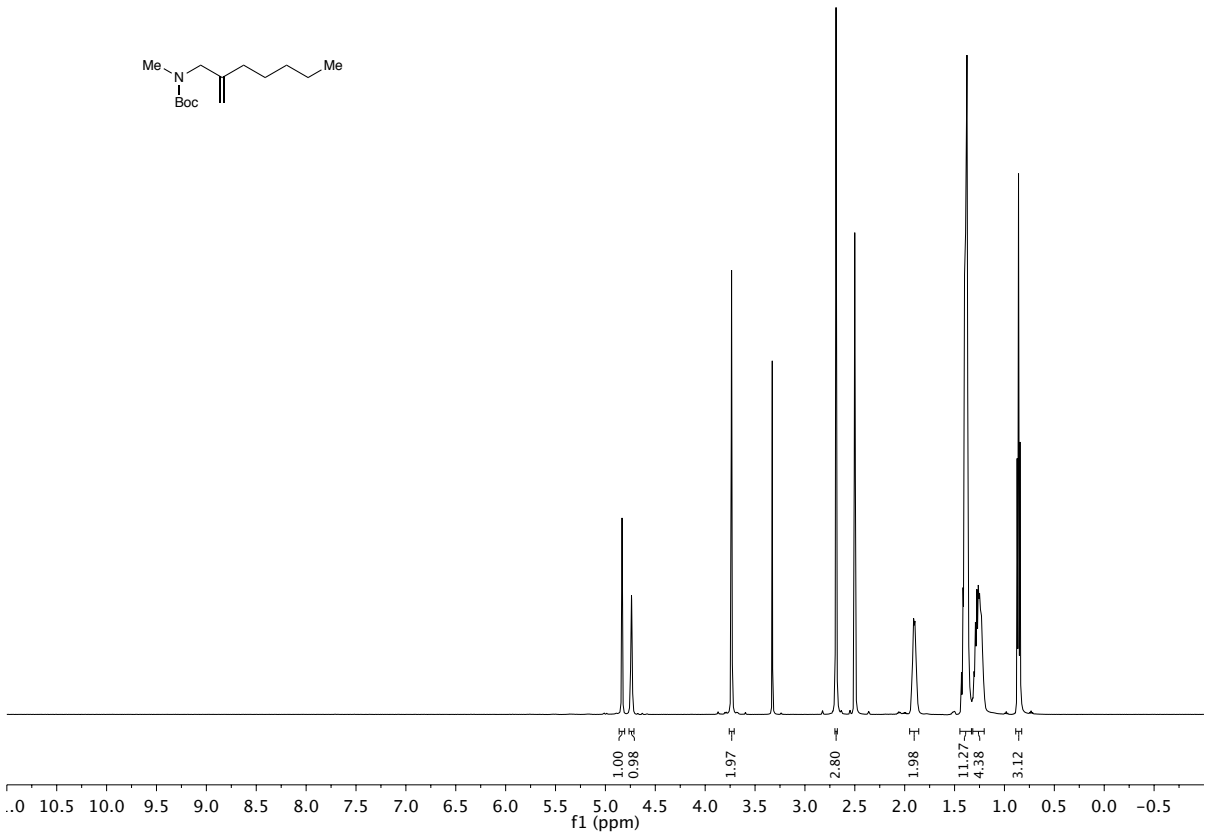
^{1}H NMR Spectrum for compound **32**



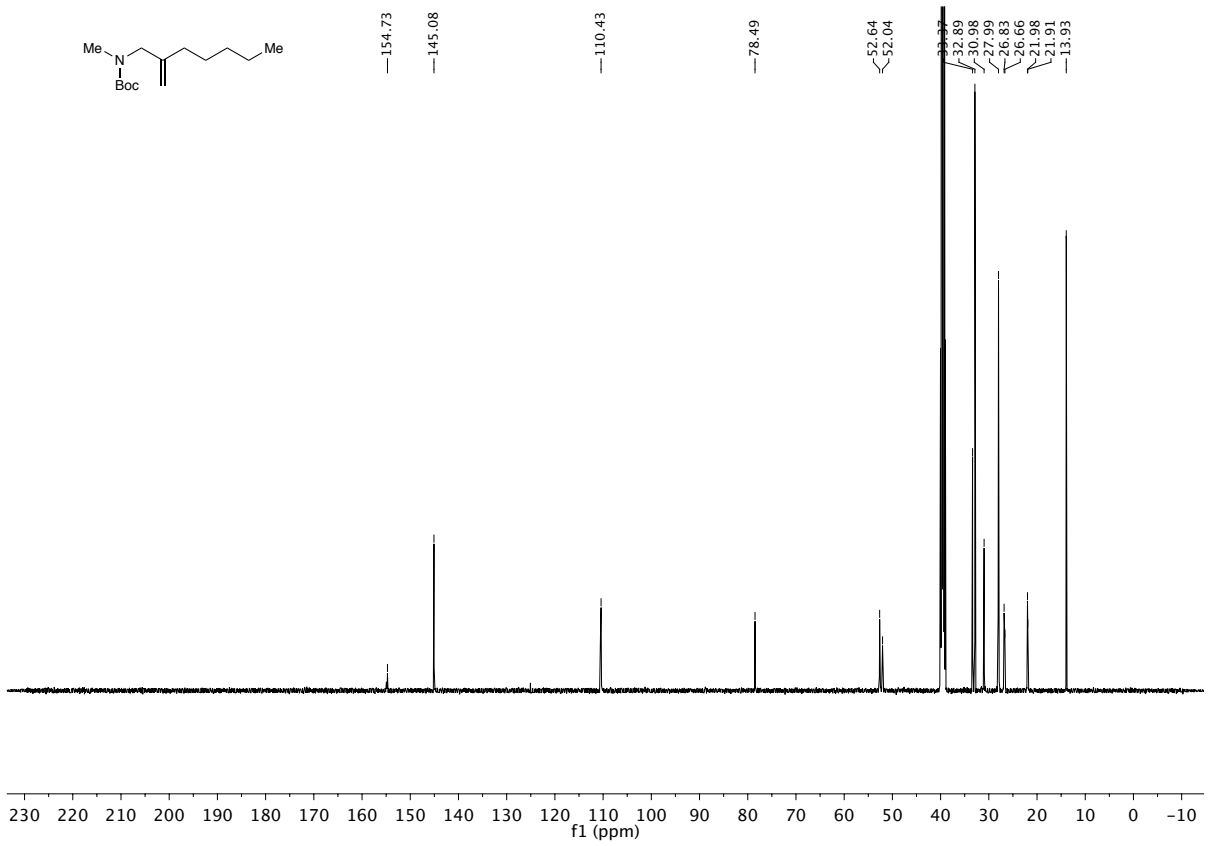
^{13}C NMR Spectrum for compound **32**



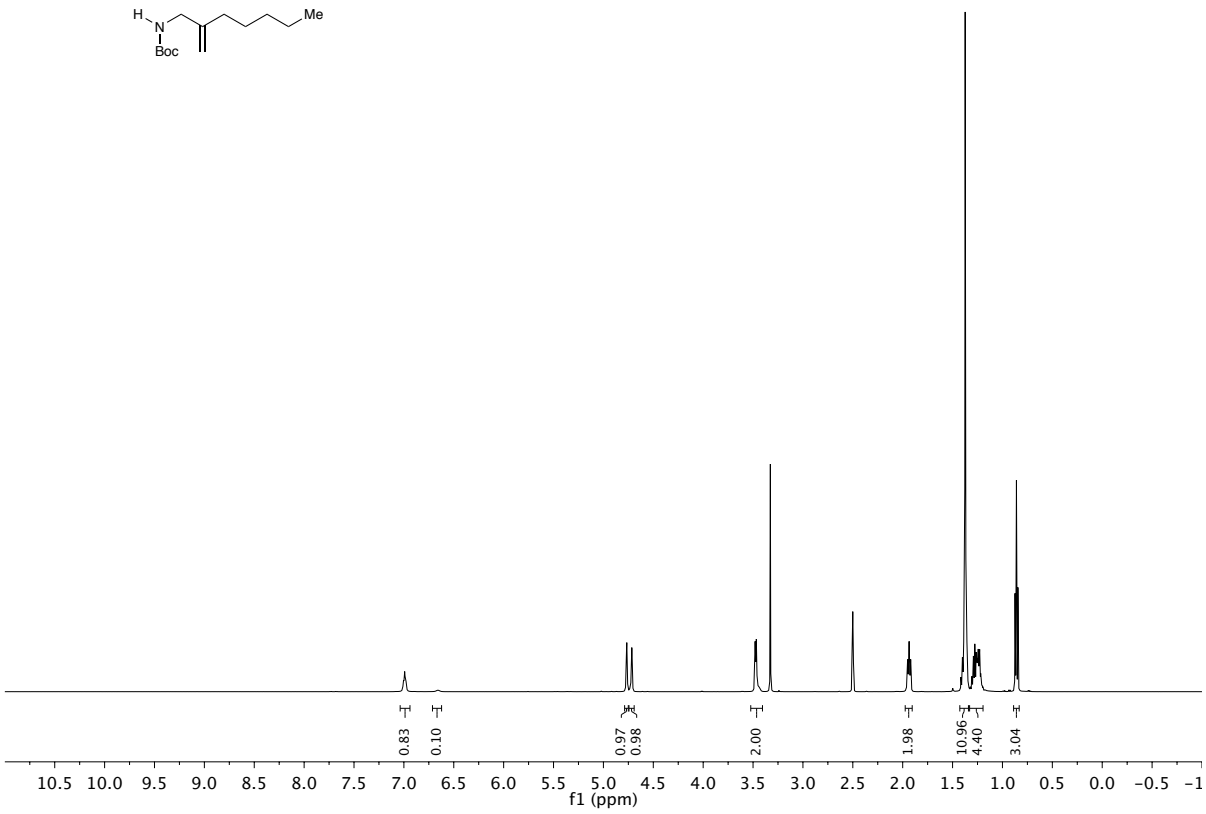
^{1}H NMR Spectrum for compound **33**



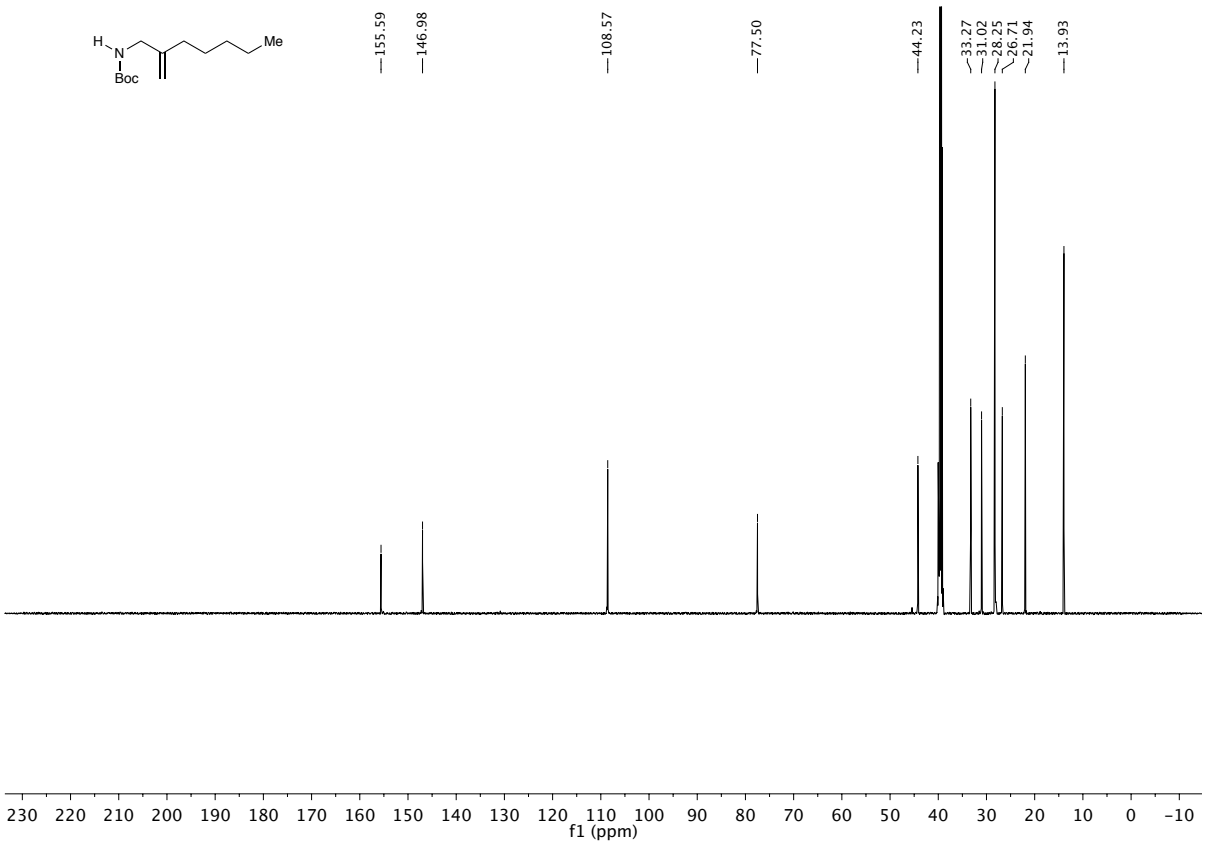
^{13}C NMR Spectrum for compound **33**



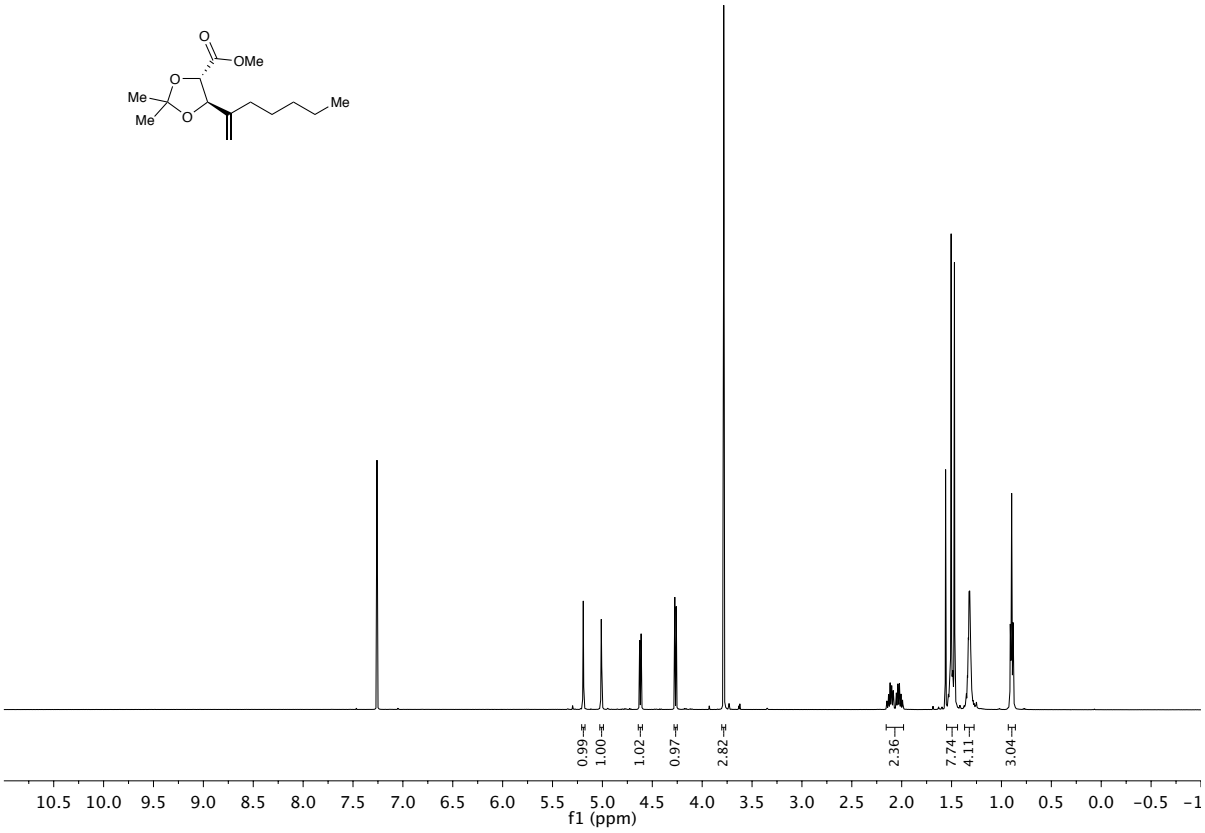
^{1}H NMR Spectrum for compound **34**



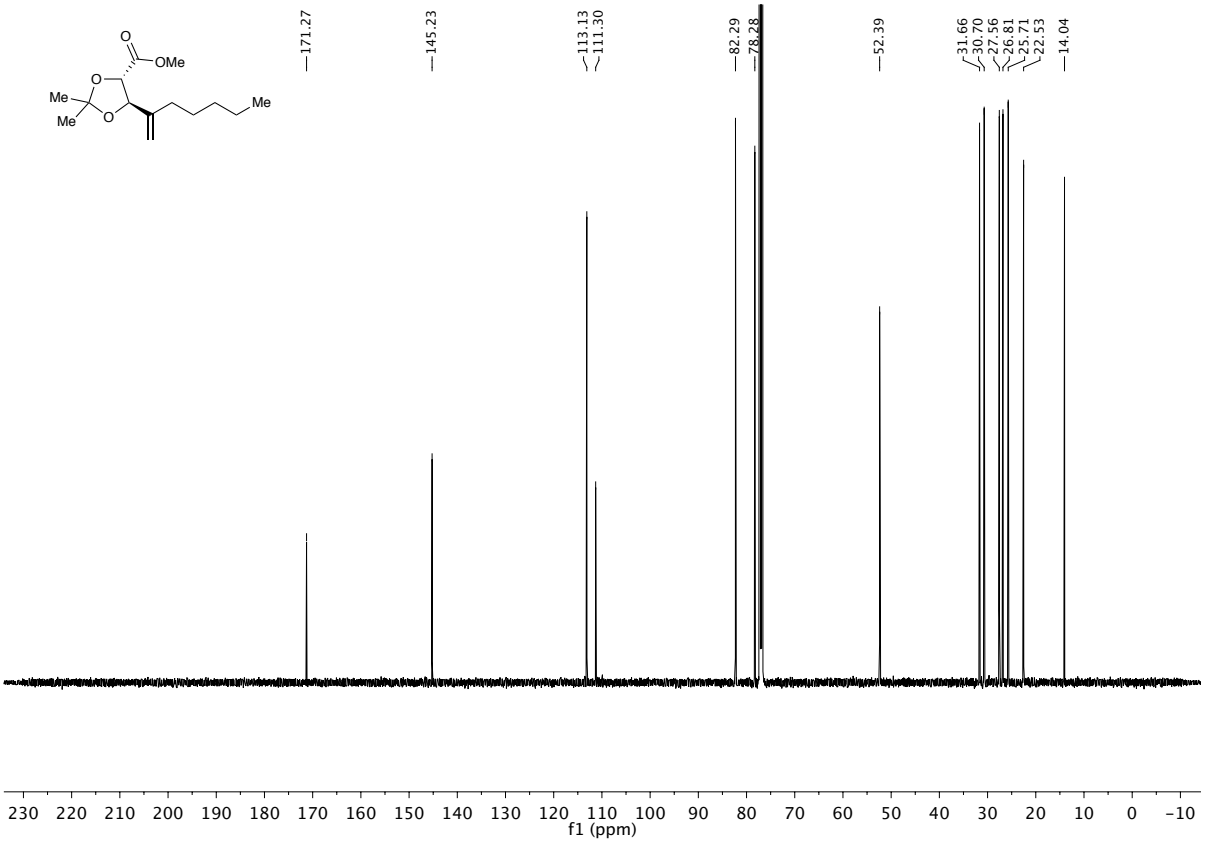
^{13}C NMR Spectrum for compound **34**



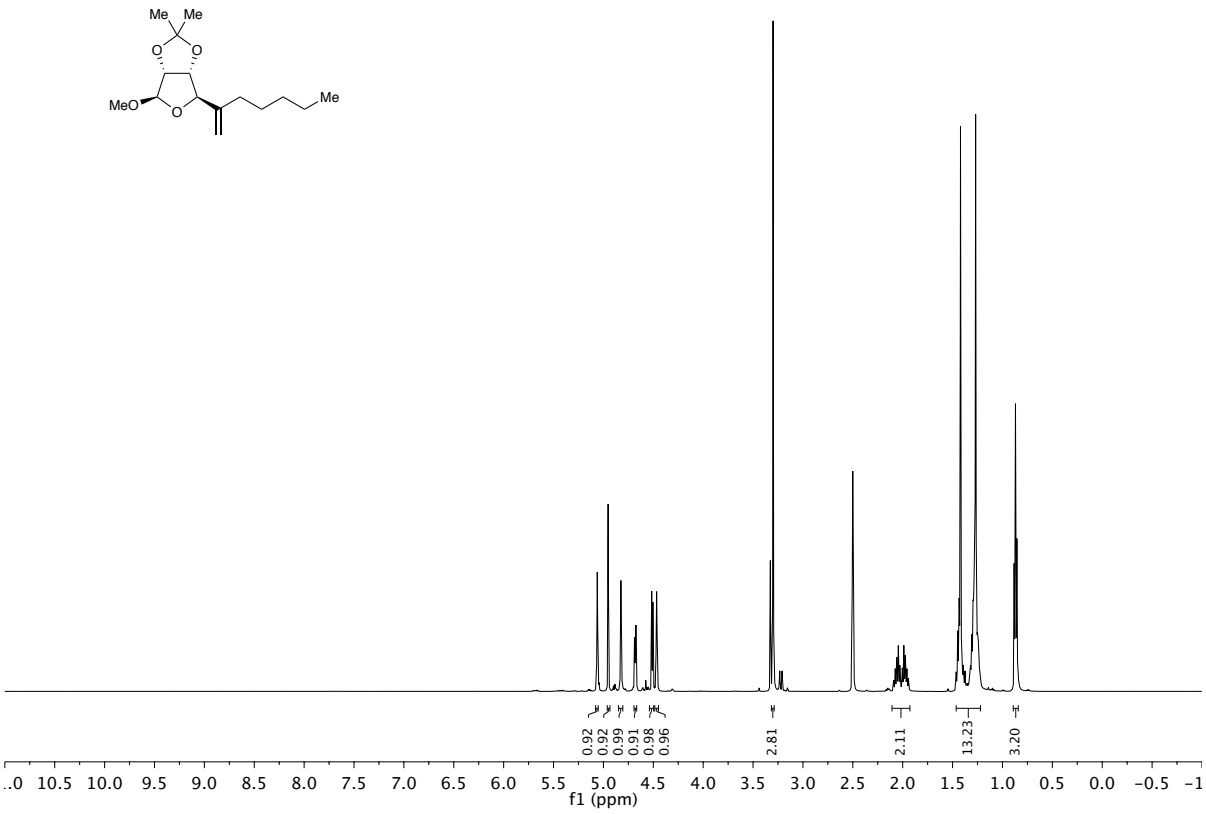
^{1}H NMR Spectrum for compound **35**



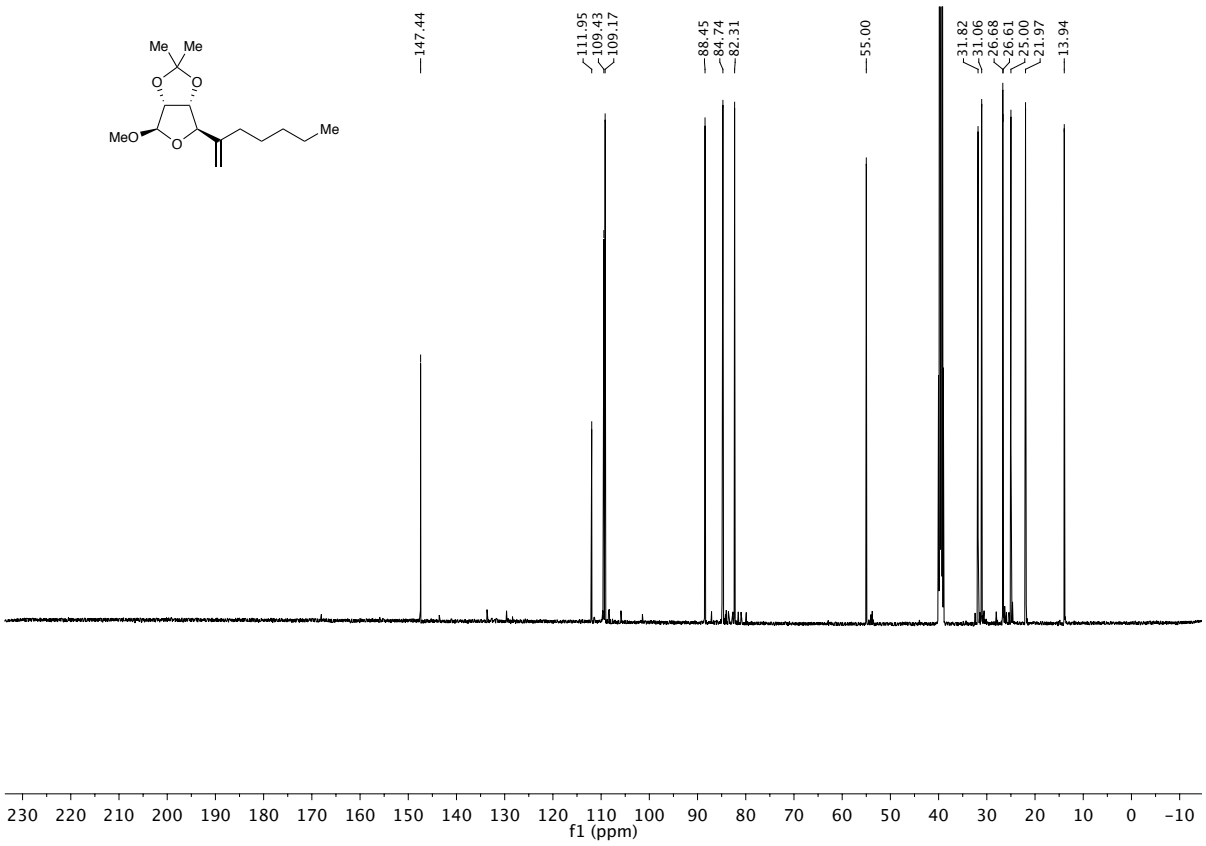
^{13}C NMR Spectrum for compound **35**



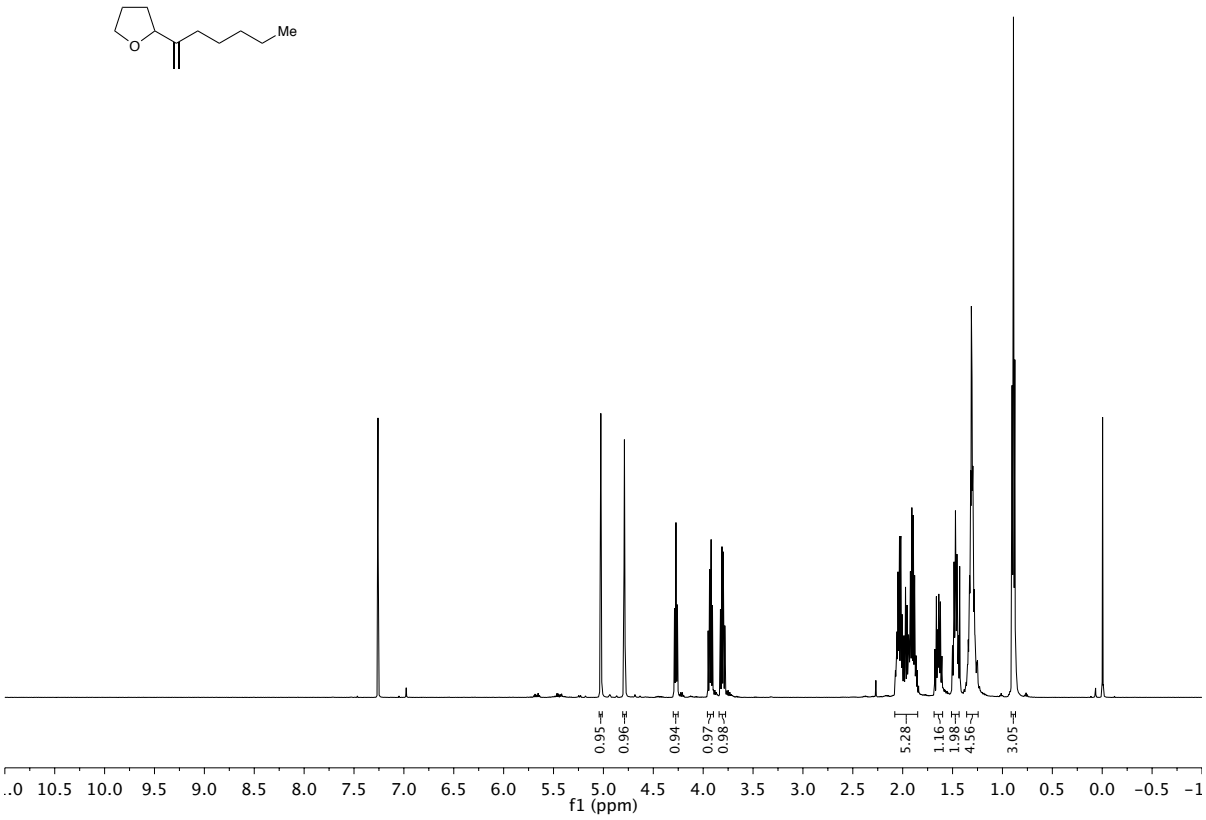
^{1}H NMR Spectrum for compound **36**



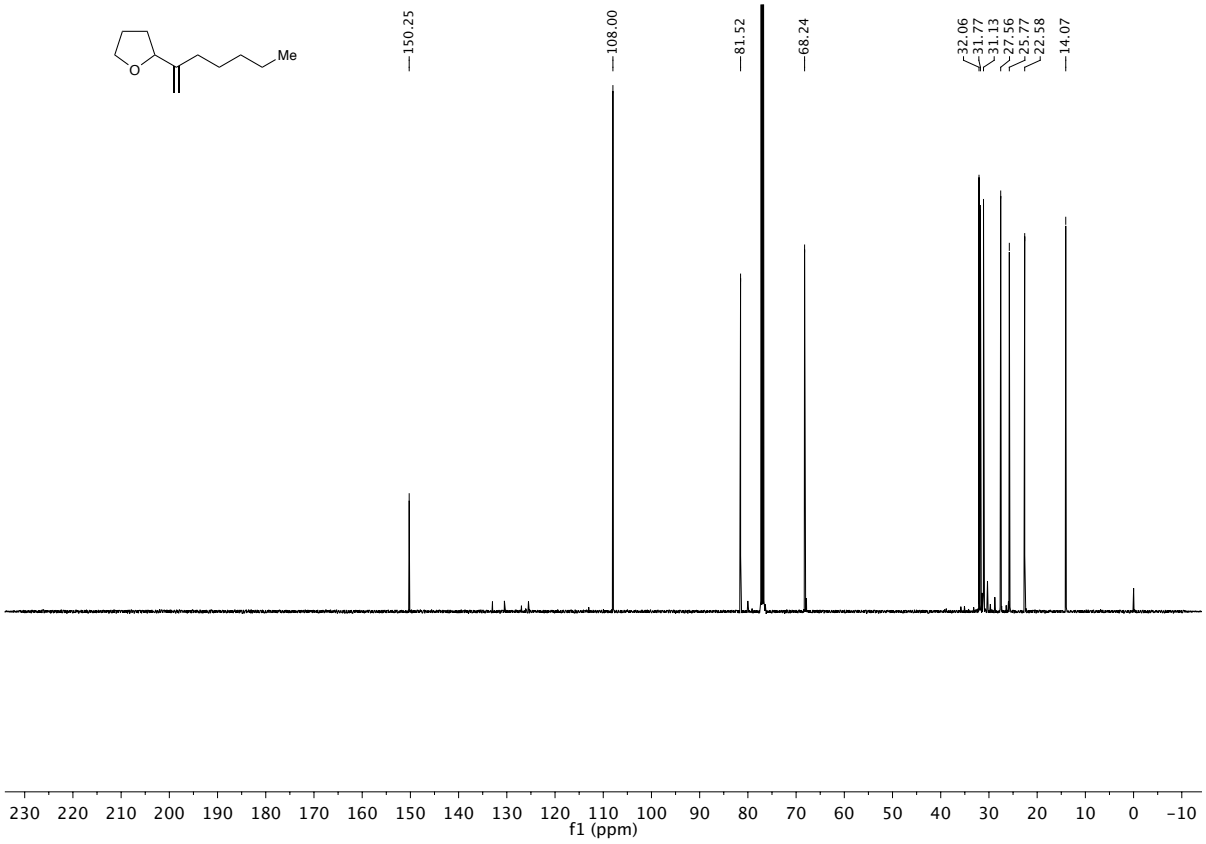
^{13}C NMR Spectrum for compound **36**



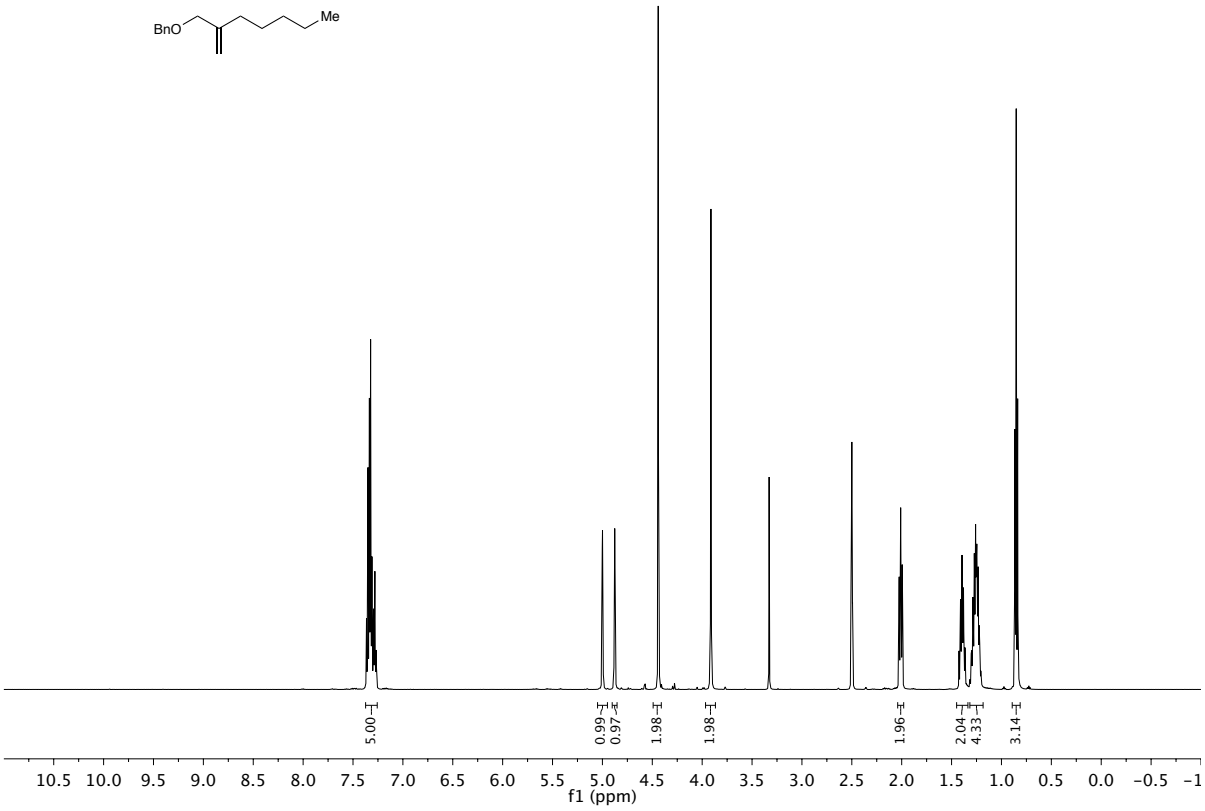
^{1}H NMR Spectrum for compound **37**



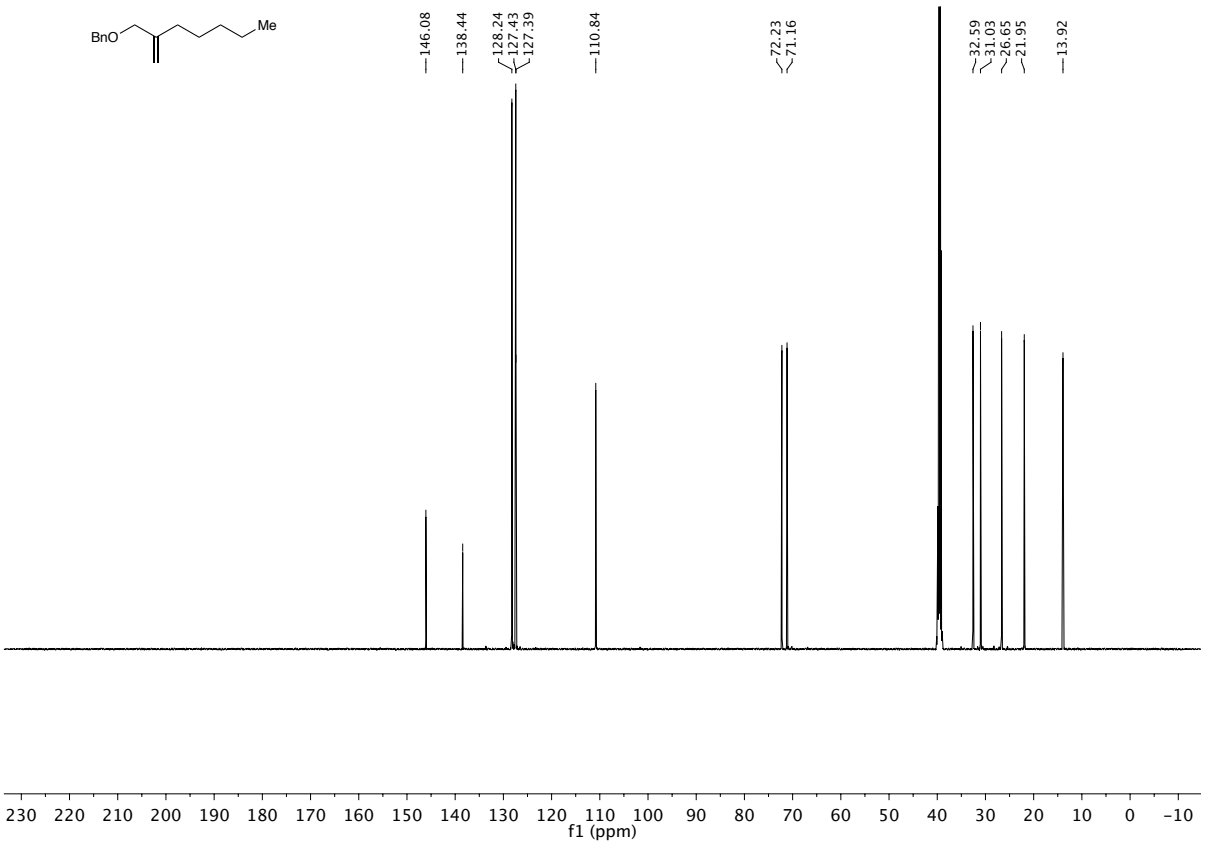
^{13}C NMR Spectrum for compound **37**



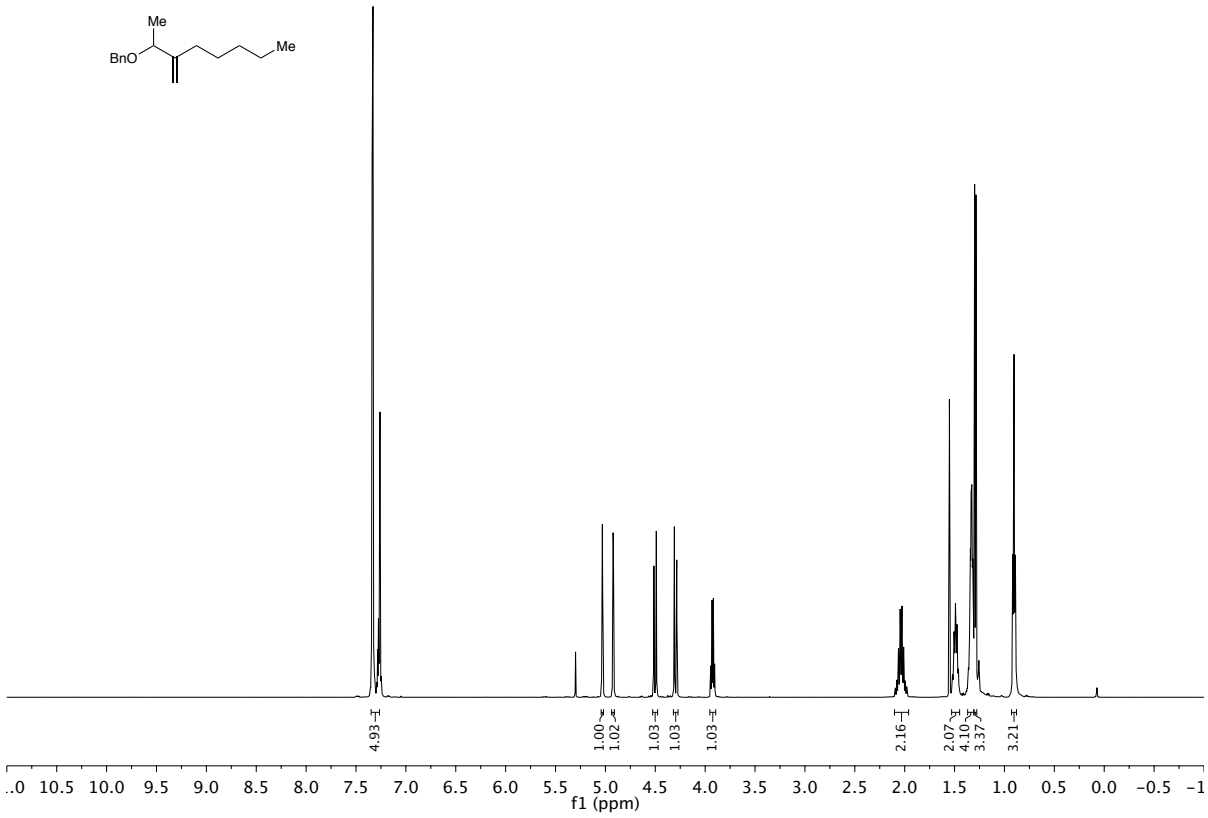
^{1}H NMR Spectrum for compound **38**



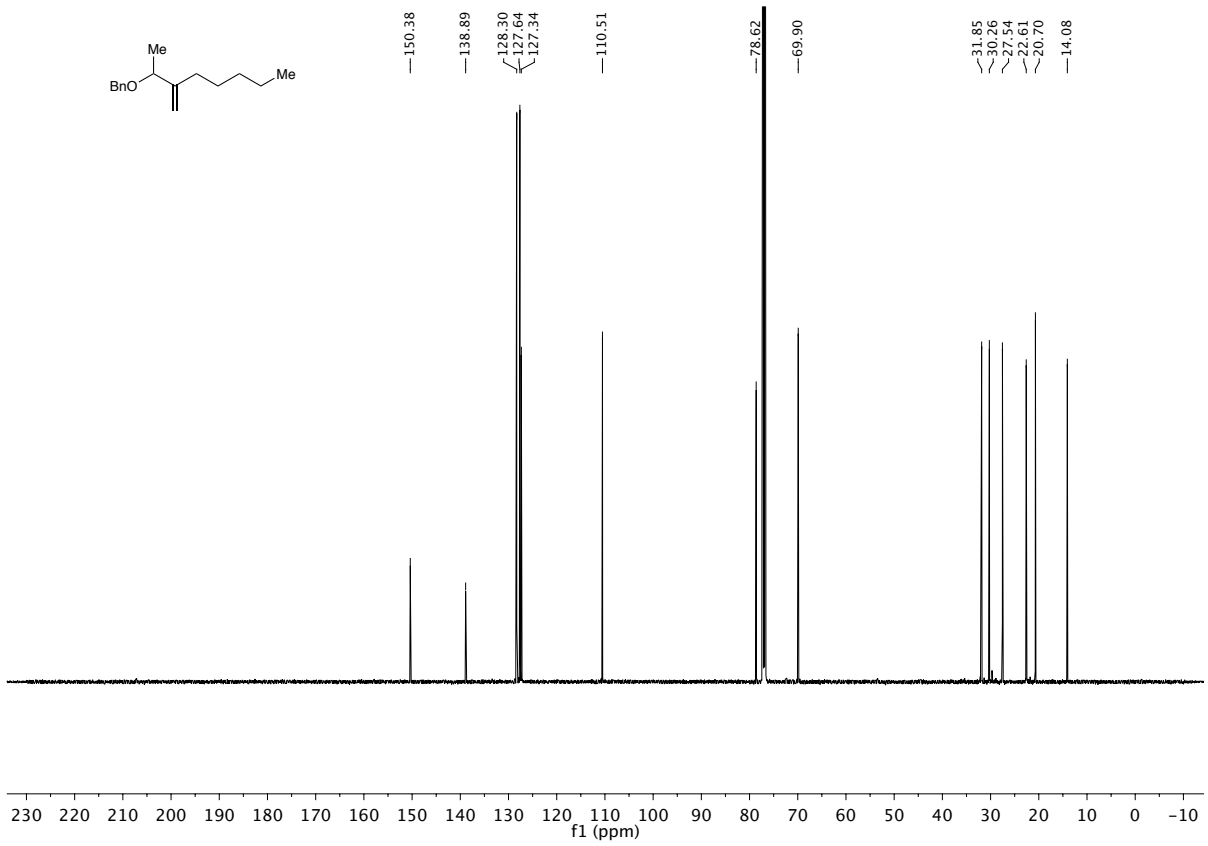
^{13}C NMR Spectrum for compound **38**



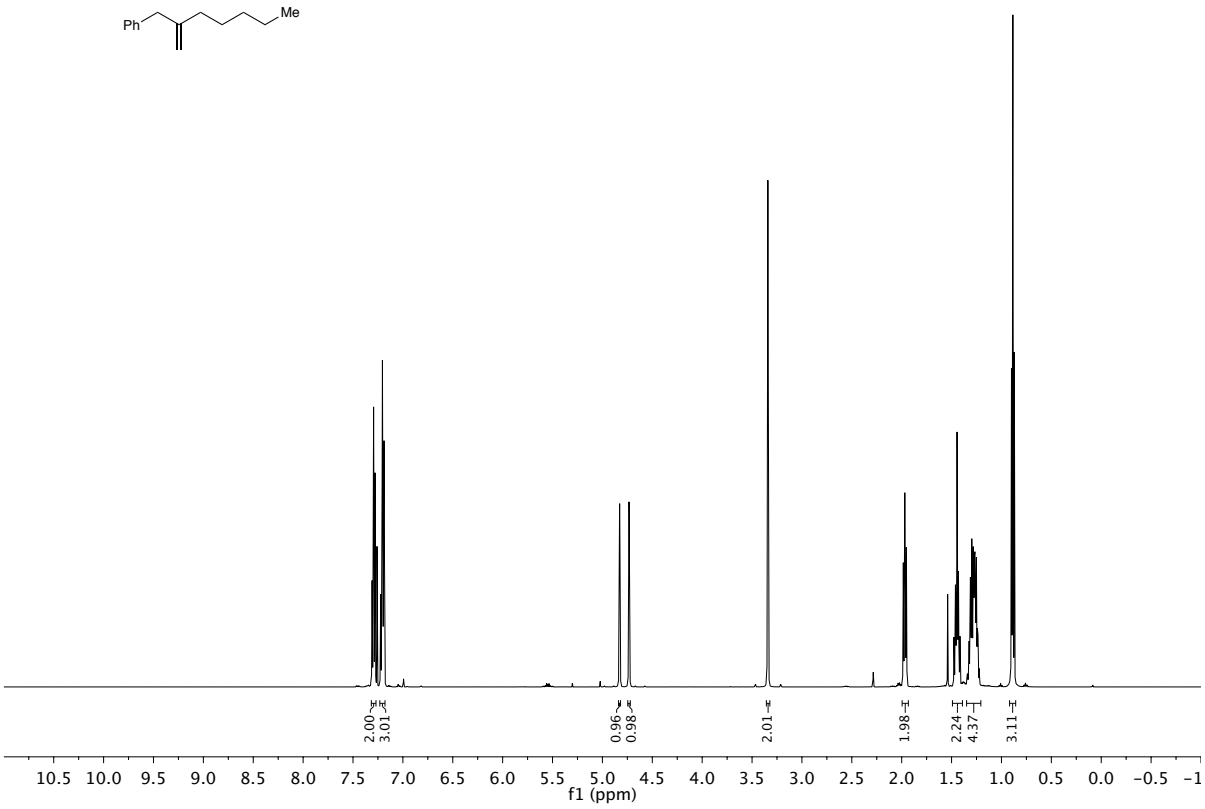
^{1}H NMR Spectrum for compound **39**



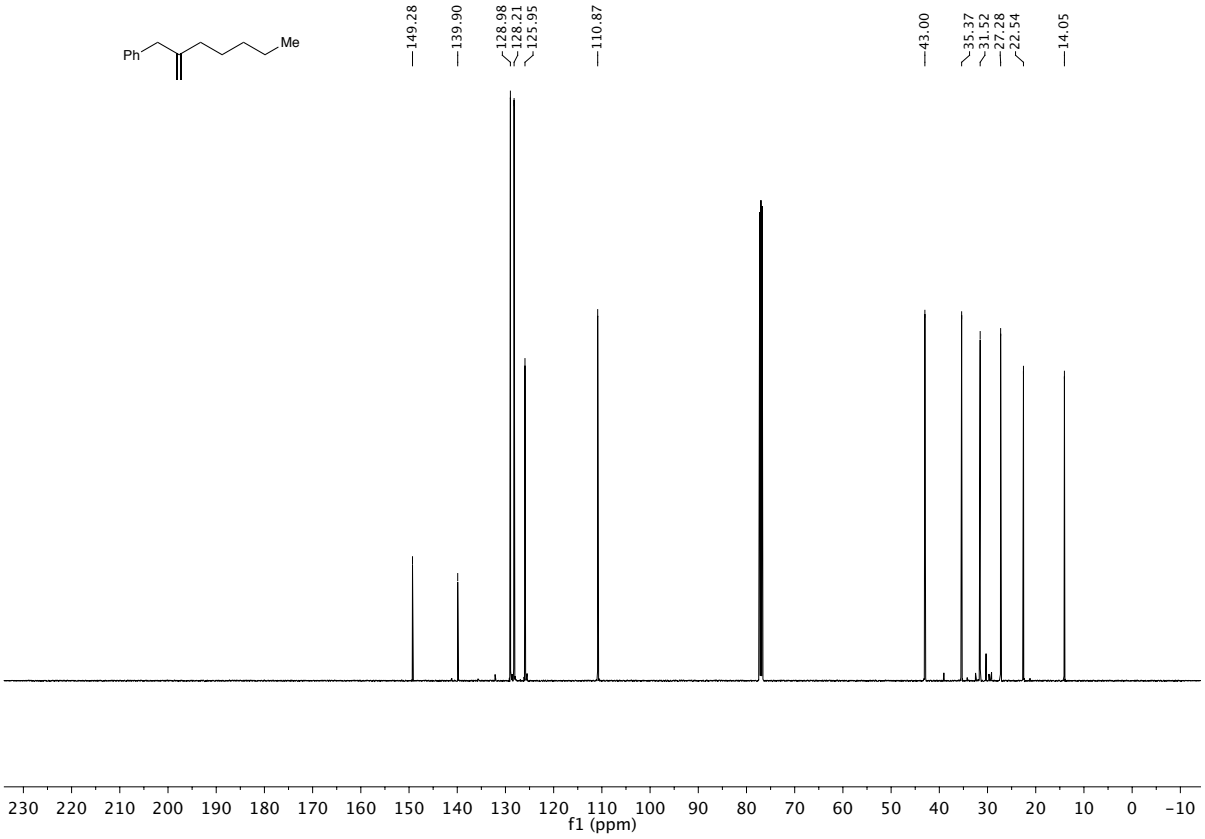
^{13}C NMR Spectrum for compound **39**



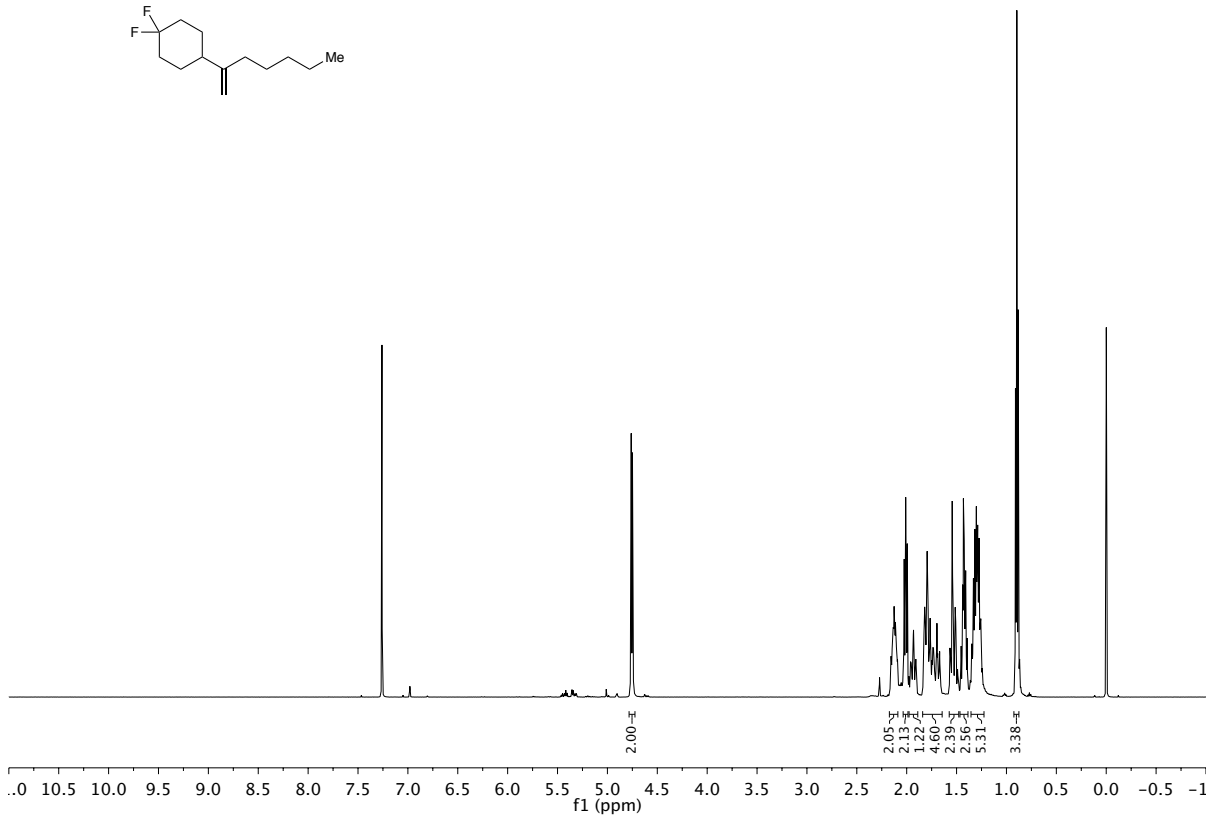
^{1}H NMR Spectrum for compound **40**



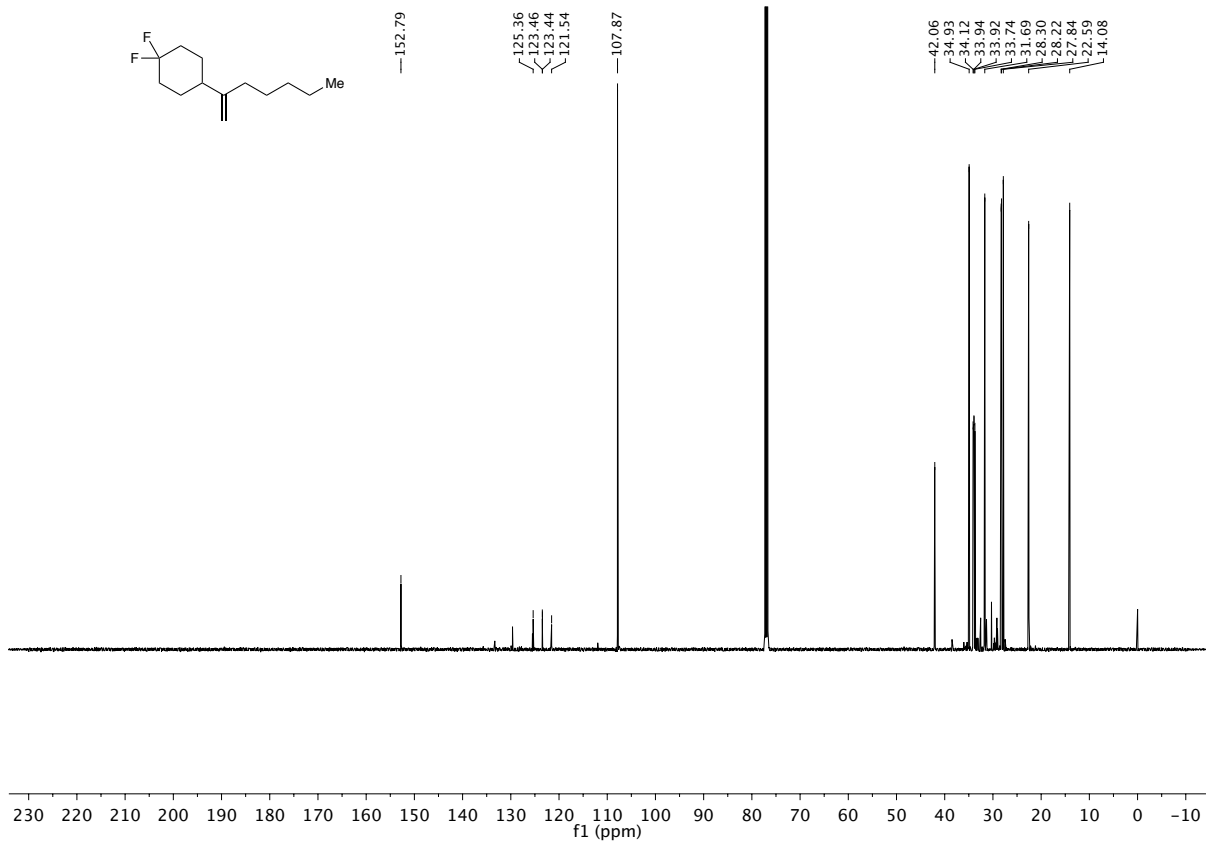
^{13}C NMR Spectrum for compound **40**



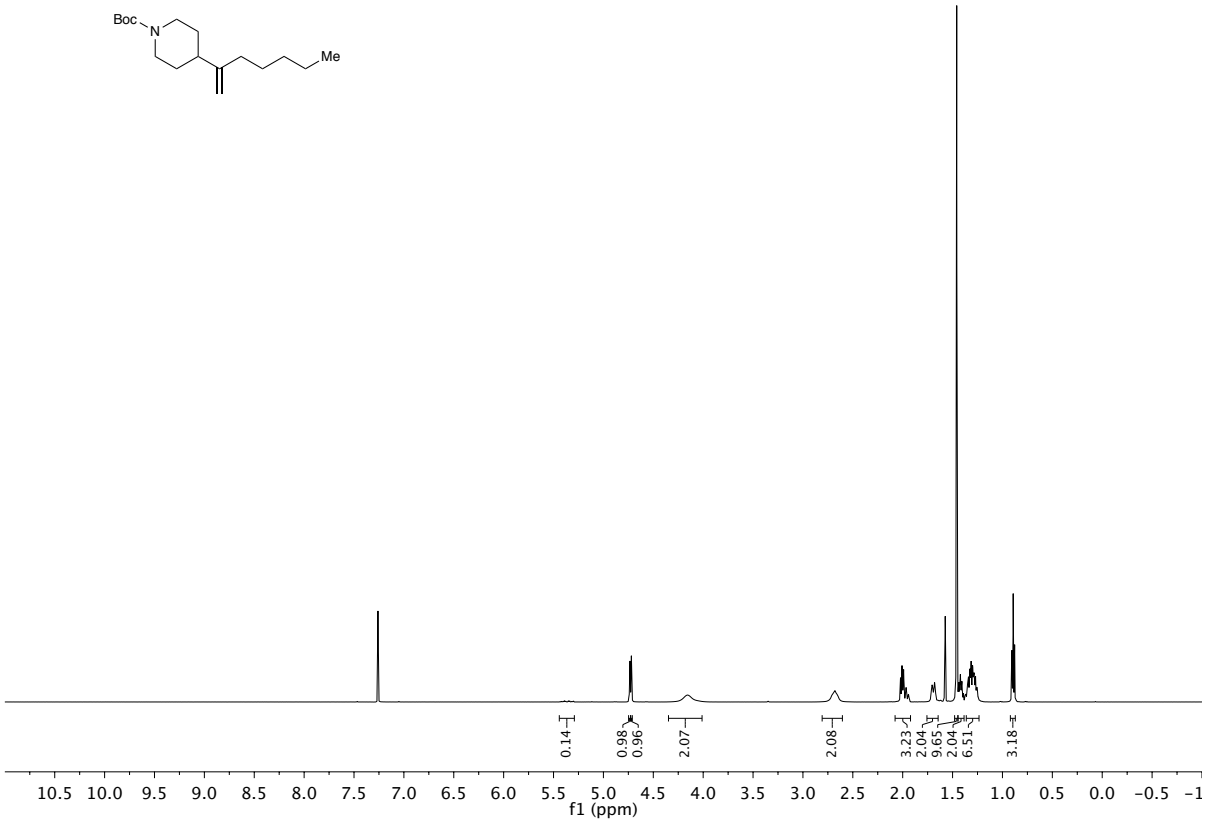
^{1}H NMR Spectrum for compound **41**



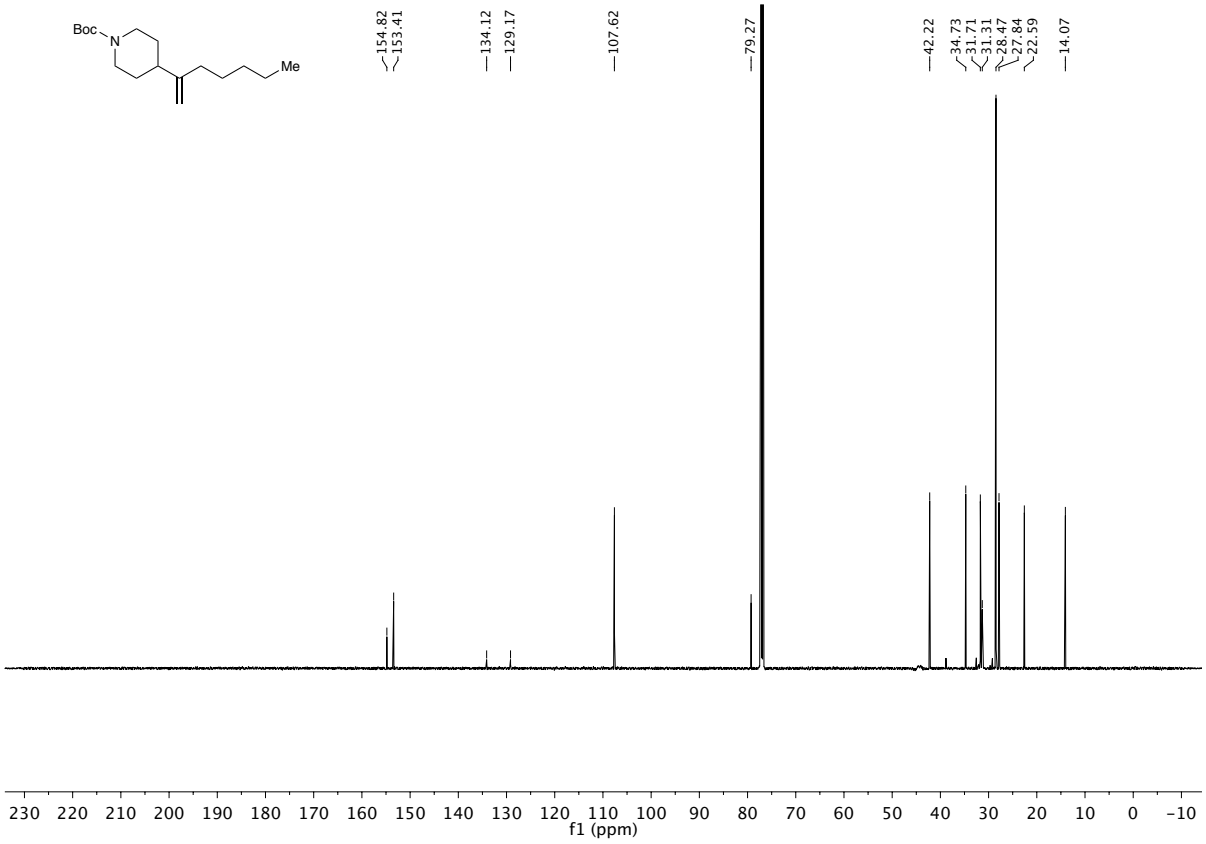
^{13}C NMR Spectrum for compound **41**



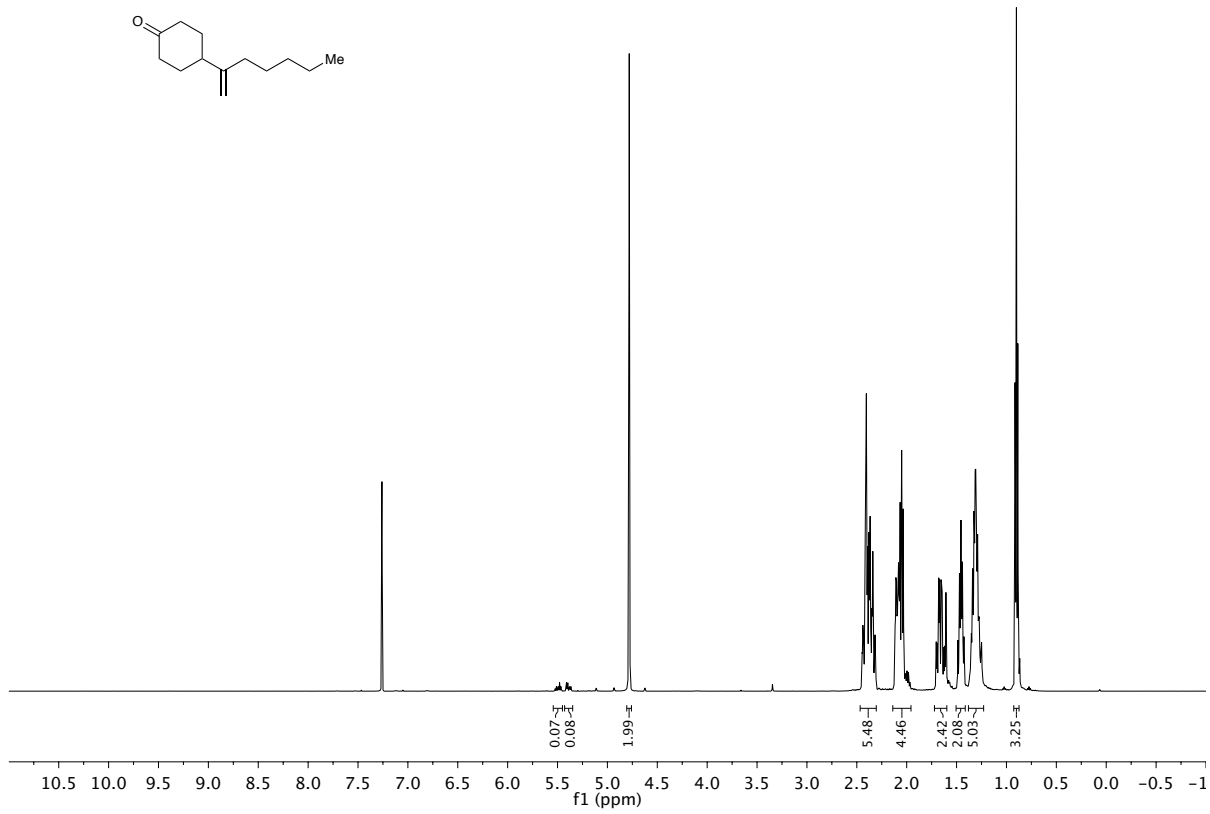
^{1}H NMR Spectrum for compound **42**



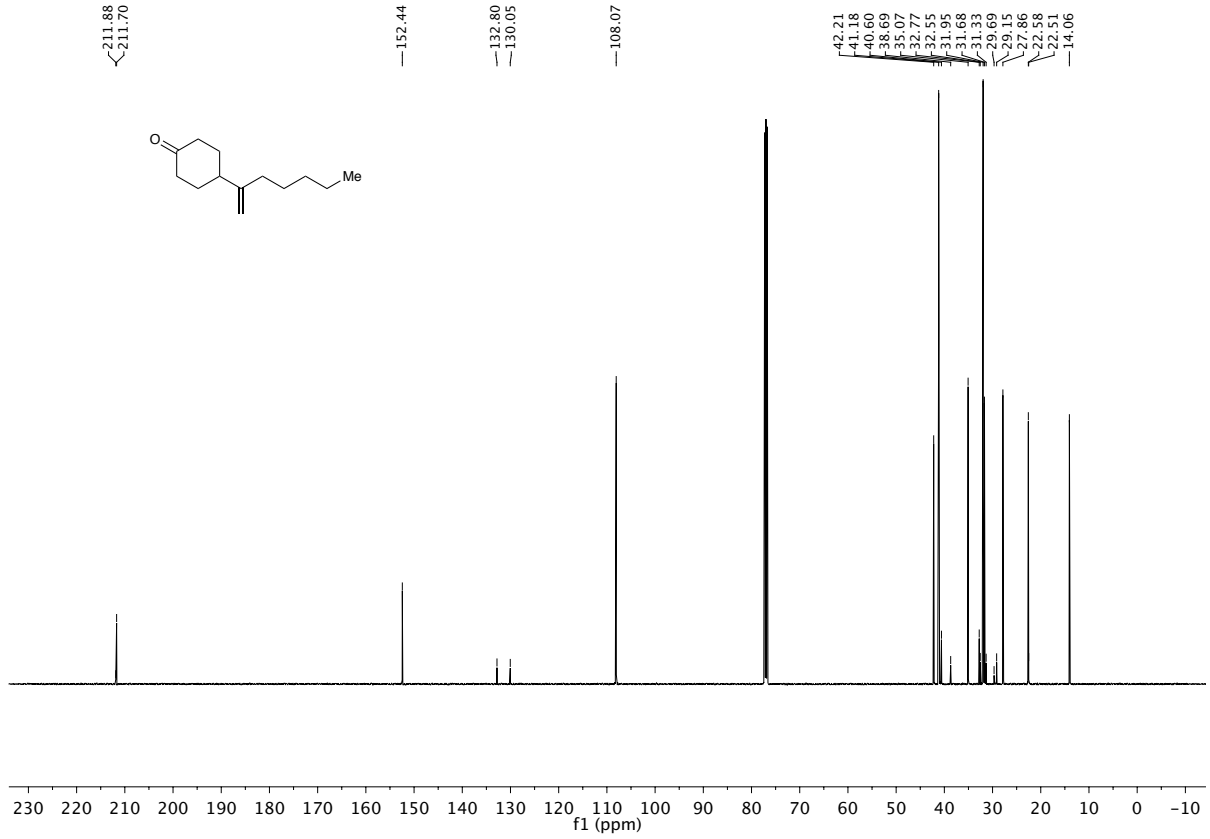
^{13}C NMR Spectrum for compound **42**



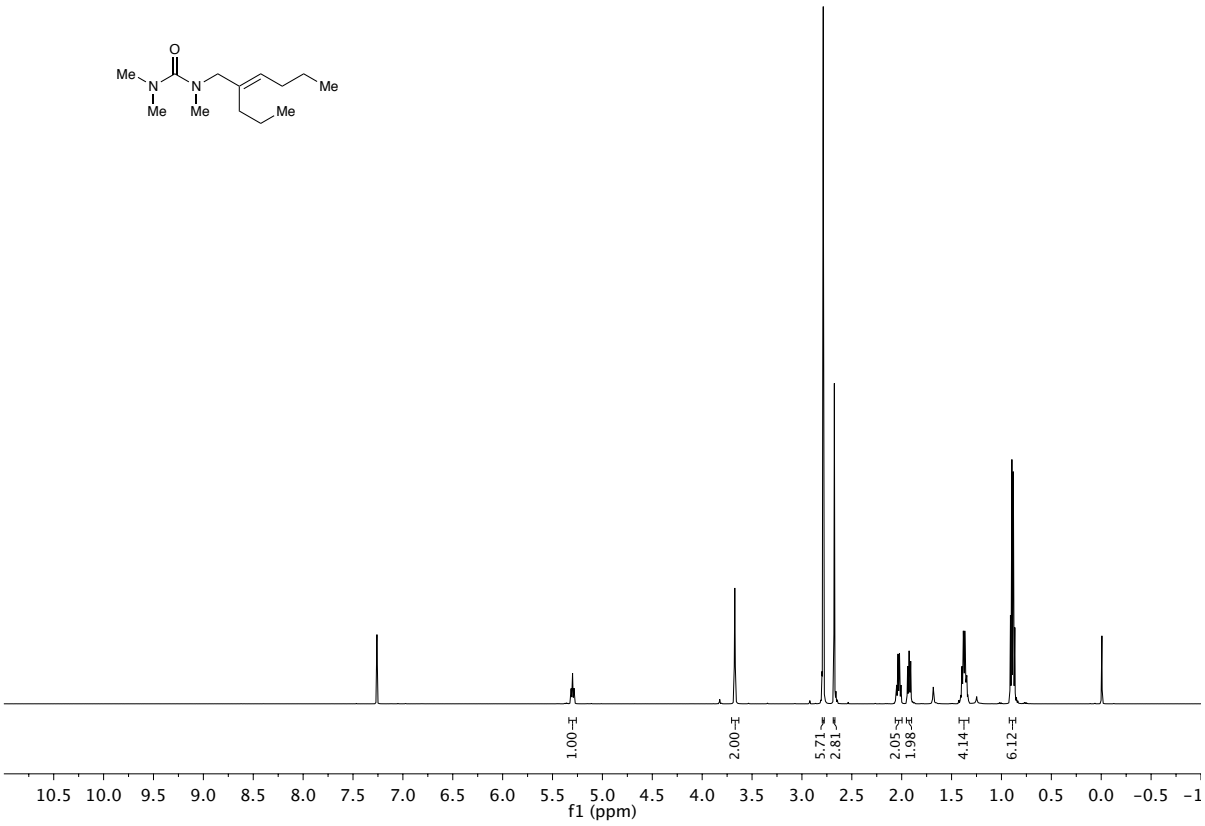
^{1}H NMR Spectrum for compound **43**



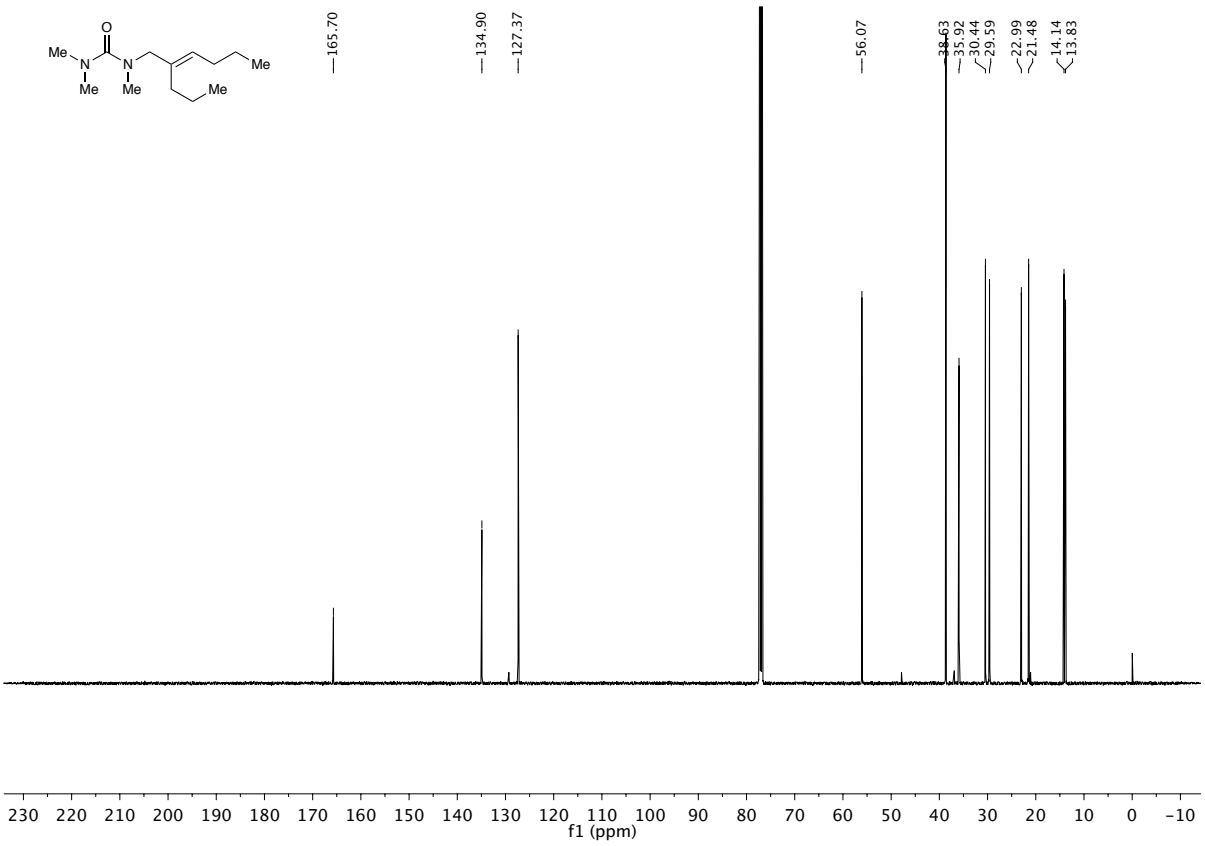
^{13}C NMR Spectrum for compound **43**



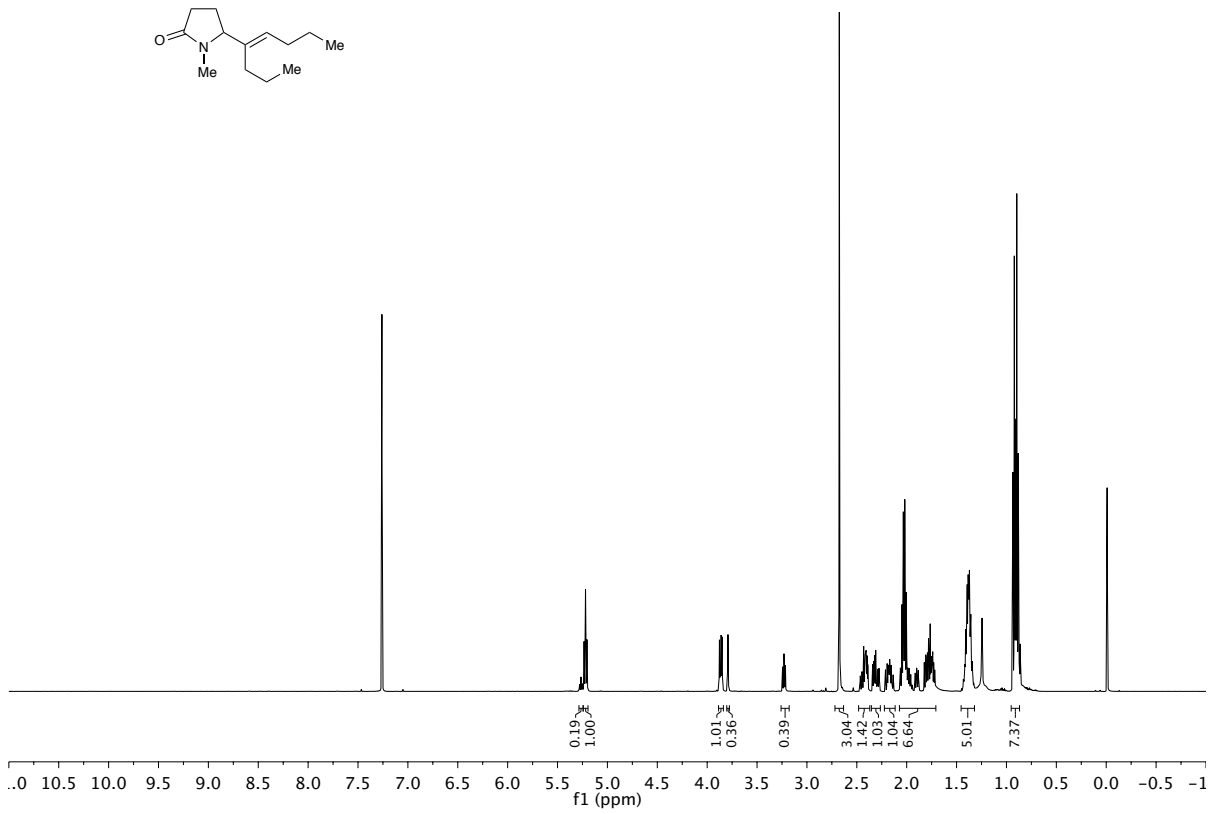
^{1}H NMR Spectrum for compound **44**



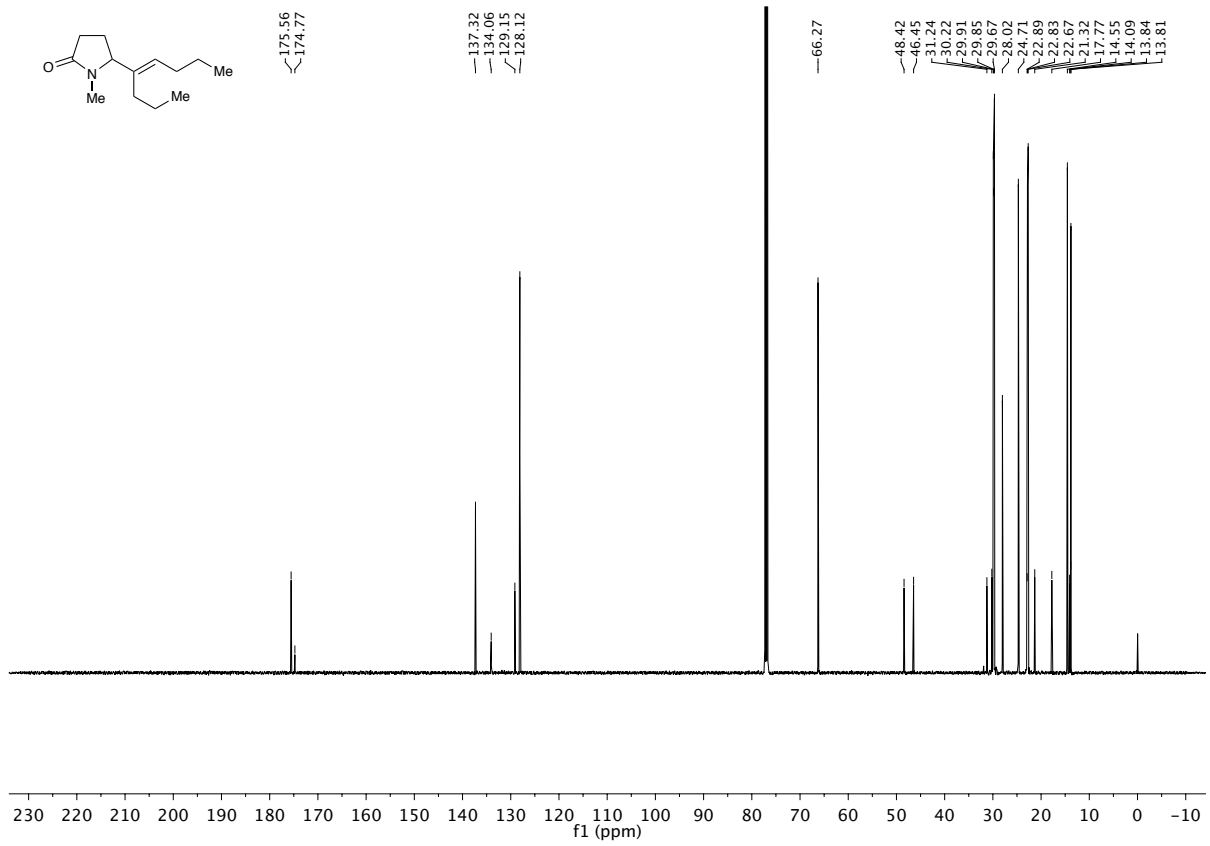
^{13}C NMR Spectrum for compound **44**



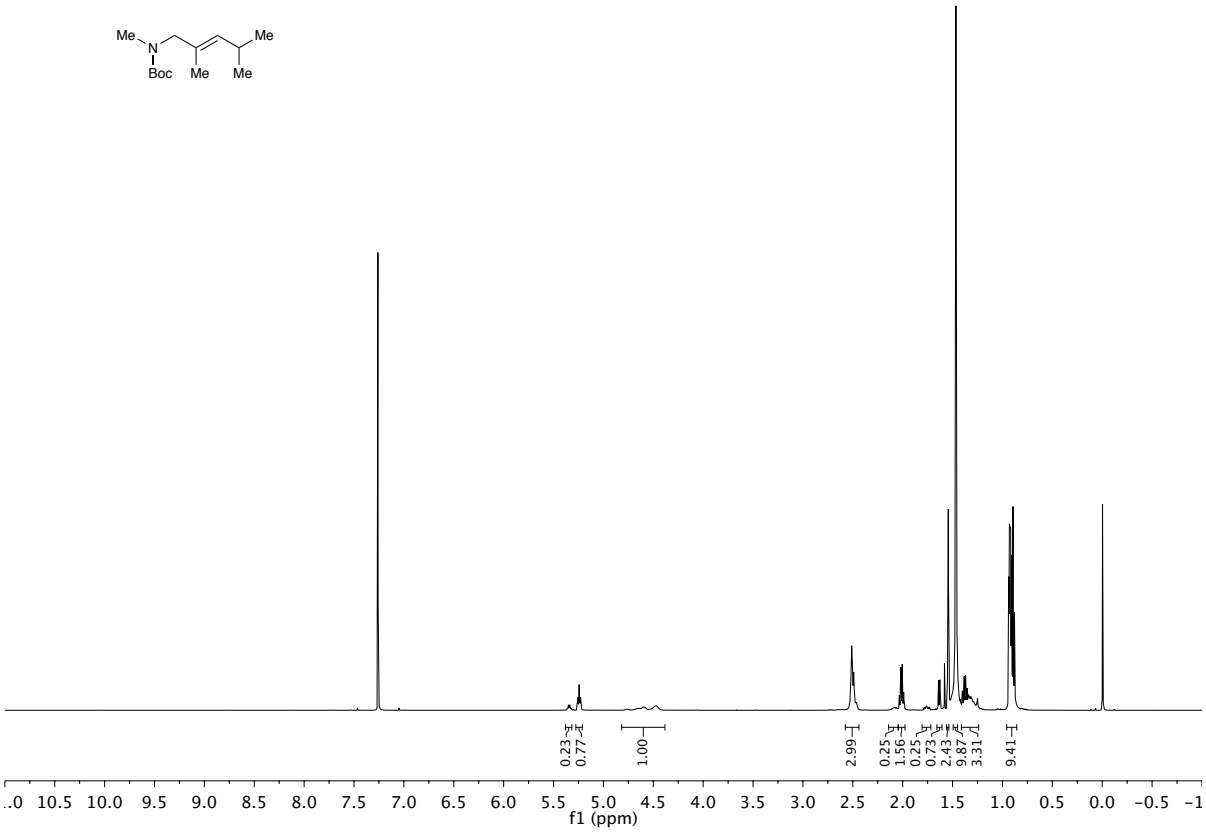
^{1}H NMR Spectrum for compound **45**



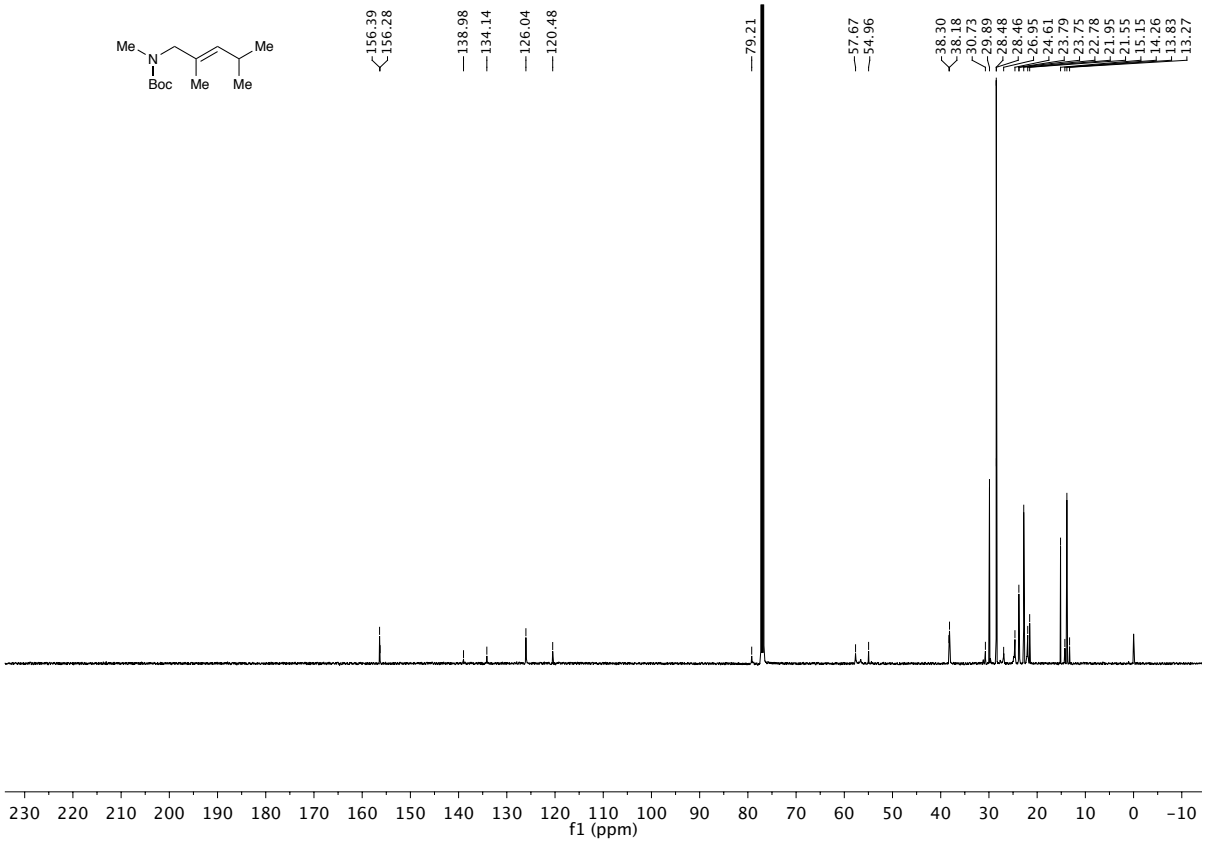
^{13}C NMR Spectrum for compound **45**



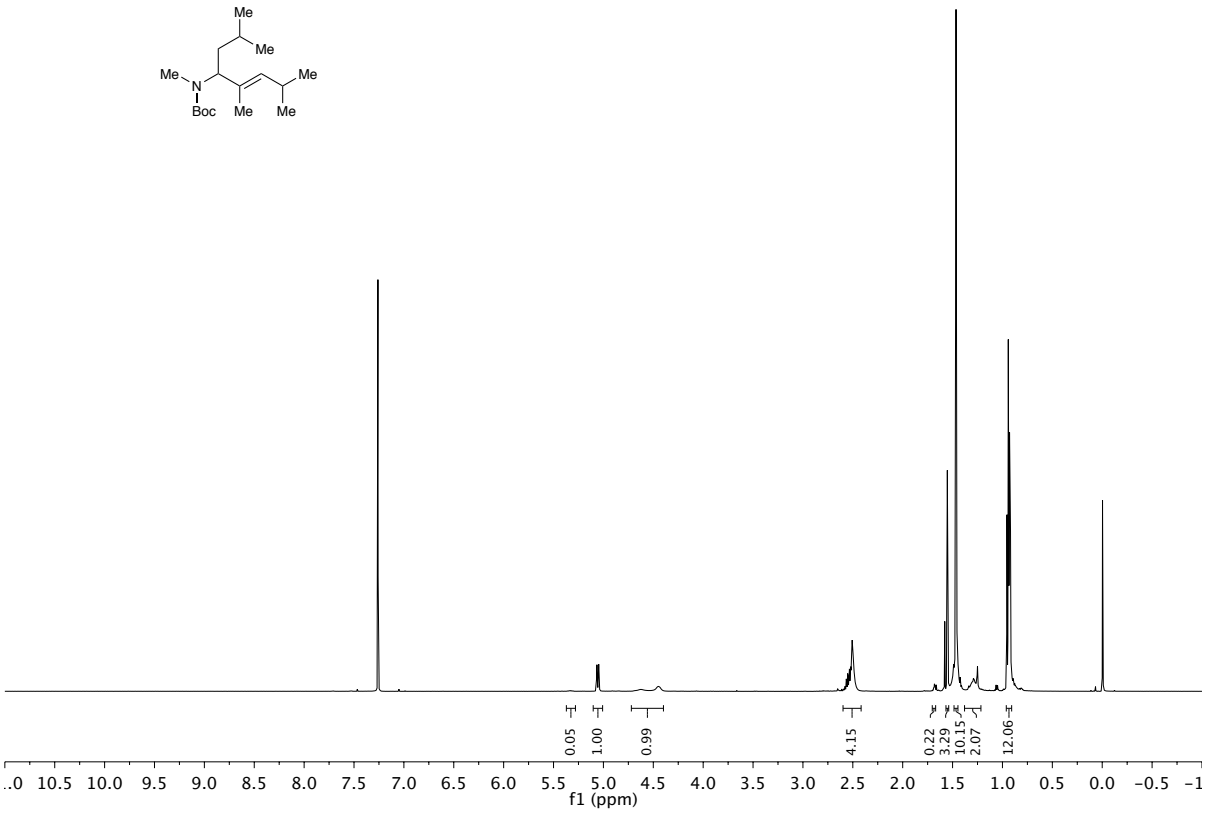
^{1}H NMR Spectrum for compound **46**



^{13}C NMR Spectrum for compound **46**



^{1}H NMR Spectrum for compound **47**



^{13}C NMR Spectrum for compound **47**