Supporting Information

Low Temperature Copper-Mediated Two-Component Cross Coupling/Cycloisomerization Approach Towards N-Fused Heterocycles

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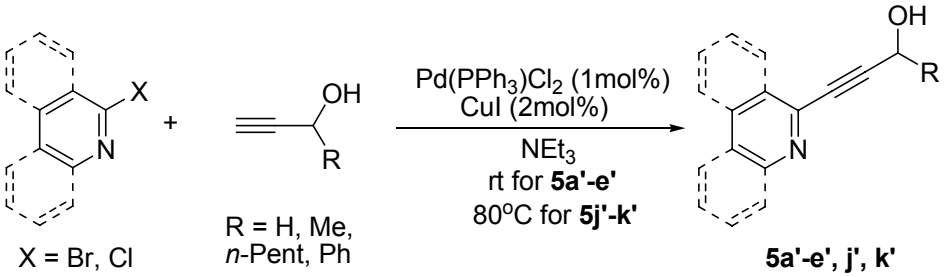
General Information

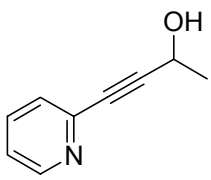
NMR spectra were recorded on a Bruker Avance DRX-500 (500 MHz) or DPX-400 instruments. (+) and (-) represent positive and negative intensities of signals in ^{13}C DEPT-135 experiments. HRMS analysis was performed on Micromass 70 VSE high resolution mass spectrometer. GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). Column chromatography was carried out employing Silicycle Silica-P Flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. Anhydrous solvents were purchased from Aldrich and stored over calcium hydride. Alkynes were commercially available and purchased from Aldrich, Strem Chemicals Inc. or Acros Organics, or synthesized via known literature procedures.

Starting materials

Synthesis of Heterocyclic Propargylic Alcohols (5a'-e', j', k')

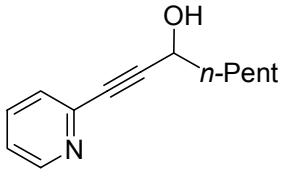


General Procedure: Propargylic alcohols (**5a'-e'**) where prepared from corresponding commercially available bromopyridines, alcohols (**5j'-k'**) from the corresponding commercial chlorinated derivatives. Compounds were synthesized in 5-20 mmol scale using one neck flasks, equipped with inert gas inlet. All reactions were carried out in absolute solvents under argon with syringe Schlenk techniques in oven-dried glassware.
To the flame-dried flask CuI (19 mg, 2 mol%), $Pd(PPh_3)_2Cl_2$ (35 mg, 1 mol%), anhydrous Et_3N (8 mL) 2-bromopyridine (790 mg, 5mmol, 1.0 equiv.) and prop-2-yn-1-ol (348 mg, 6 mmol, 1.2 equiv.) alcohol were successively added. The mixture was stirred at rt for (**5a'-e'**) and heated at 80°C for (**5j'-k'**) until completeness of the reaction (monitored by GC-MS), cooled to rt and quenched with sat. NH_4Cl(aq) 20 mL. The organic layer was separated, the water phase was extracted two times with 20mL portions of EtOAc, the combined organic solution was dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified over a column (Silica gel, dichloromethane-EtOH 40:1) as eluent to afford product (632 mg, 95%).

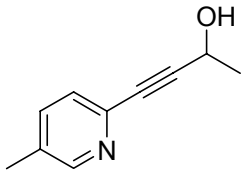


5a': ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.48-8.51 (m, 1 H), 7.58 (dt, *J*=7.60, 1.75 Hz, 1 H), 7.33 - 7.35 (m, 1 H), 7.17 (ddd, *J*=7.60, 5.26, 1.17 Hz, 1 H), 5.07 (d, *J*=5.26 Hz, 1 H), 4.75 - 4.83 (m, 1 H), 1.54 (d,

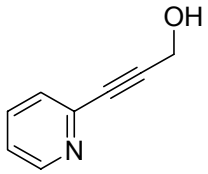
J=7.02 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.34 (+), 142.59, 136.34 (+), 127.03 (+), 122.82 (+), 92.33, 82.25, 57.84 (+), 23.85 (+).



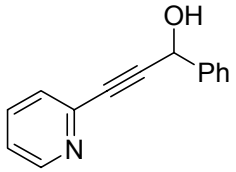
5b': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.52 - 8.59 (m, 1 H), 7.61 - 7.67 (m, 1 H), 7.38 - 7.44 (m, 1 H), 7.19 - 7.26 (m, 1 H), 4.64 (t, *J*=6.69 Hz, 1 H), 2.93 - 3.33 (br s, 1 H), 1.77 - 1.86 (m, 2 H), 1.47 - 1.56 (m, 2 H), 1.26 - 1.38 (m, 4 H), 0.89 (t, *J*=7.06 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 149.62(+), 142.04, 136.30 (+), 127.12 (+), 122.90 (+), 91.20, 83.60, 62.49 (+), 37.49 (-), 31.46 (-), 24.90 (-), 22.52 (-), 13.99 (+).



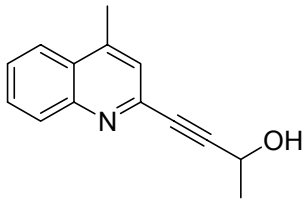
5c': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.37 - 8.39 (m, 1 H), 7.42 - 7.47 (m, 1 H), 7.29 - 7.32 (m, 1 H), 4.79 (q, *J*=6.60 Hz, 1 H), 3.30 – 3.64 (br s, 1 H), 2.32 (s, 3 H), 1.57 (d, *J*=6.69 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 150.18 (+), 139.88, 136.76 (+), 132.89, 126.51 (+), 90.96, 82.87, 58.33 (+), 24.01 (+), 18.40 (+).



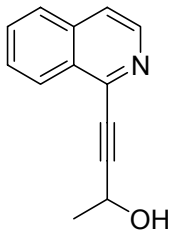
5d': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.52 - 8.56 (m, 1 H), 7.63 - 7.67 (m, 1 H), 7.41 - 7.44 (m, 1 H), 7.22 – 7.27 (m, 1 H), 4.55 (d, *J*=4.86 Hz, 2 H), 4.06 – 4.16 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 149.62 (+), 142.72, 136.43 (+), 127.14 (+), 123.05 (+), 88.56, 84.07, 50.97 (-).



5e': ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.51 - 8.55 (m, 1 H), 7.61 - 7.68 (m, 3 H), 7.30 - 7.47 (m, 1 H), 7.24 (ddd, *J*=7.60, 4.82, 1.17 Hz, 1 H), 5.75 (s, 1 H), 4.00 – 4.40 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.68(+), 142.57, 140.26, 136.36 (+), 128.57 (+), 128.28 (+), 127.27 (+), 126.74 (+), 123.12 (+), 89.71, 85.10, 64.51 (+).



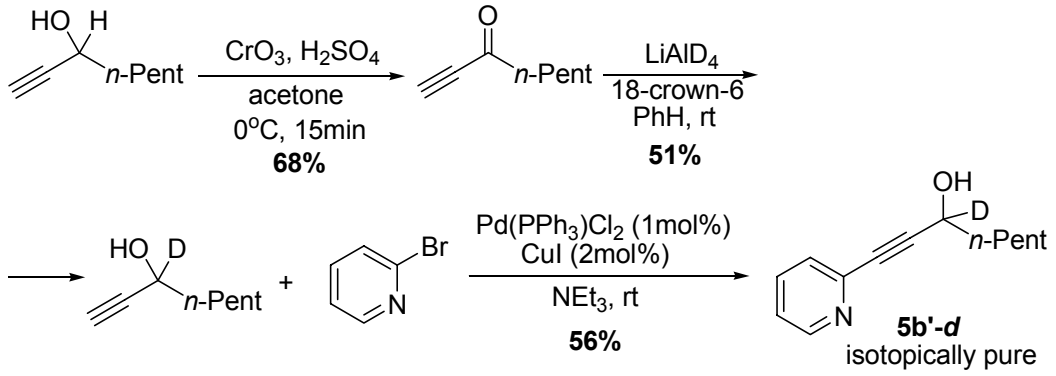
5j': ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.09 (d, *J*=8.48 Hz, 1 H), 7.93 (d, *J*=8.33 Hz, 1 H), 7.67 - 7.73 (m, 1 H), 7.52 - 7.59 (m, 1 H), 7.33 (s, 1 H), 4.88 (q, *J*=6.58 Hz, 1 H), 3.39 - 3.53 (br s, 1 H), 2.65 (s, 3 H), 1.63 (d, *J*=6.58 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 147.59, 144.73, 142.63, 129.74 (+), 129.58 (+), 127.27, 126.90 (+), 124.64 (+), 123.55 (+), 91.85, 83.69, 58.46 (+), 23.94 (+), 18.53 (+).



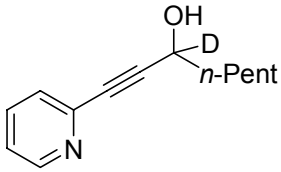
5k': ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (d, *J*=5.70 Hz, 1 H), 8.32 (d, *J*=8.33 Hz, 1 H), 7.69 - 7.75 (m, 1 H), 7.55 - 7.65 (m, 1 H), 7.49 -7.56 (m, 2 H), 5.15 - 5.25 (br s, 1 H), 5.01 (q, *J*=6.58 Hz, 1 H), 1.71 (d, *J*=6.72

Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.68, 142.10 (+), 135.61, 130.61 (+), 129.00, 127.90 (+), 126.97 (+), 126.60 (+), 120.72 (+), 97.23, 80.55, 58.19 (+), 24.08 (+).

Synthesis of Heterocyclic Propargylic Alcohol (5b'-*d*)

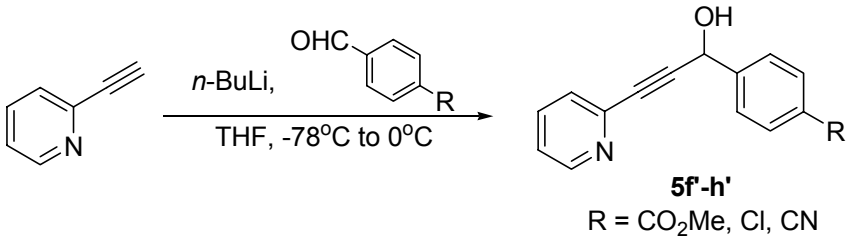


Deuterium labeled propargylic alcohol **5b'-*d*** was prepared starting from 1-octyn-3-ol which was subjected to Jones oxidation giving 1-octyn-3-one in 68% yield followed by reduction with $LiAlD_4$ furnishing deuterated alcohol in 51% yield with complete deuterium incorporation, which was further subjected to Sonogashira reaction conditions with 2-bromopyridine providing compound **5b'-*d*** in 56% isolated yield with complete deuterium incorporation confirmed by NMR.



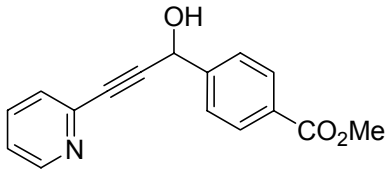
5b'-*d*: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.55 (d, *J*=4.49 Hz, 1 H) 7.63 (td, *J*=7.75, 1.74 Hz, 1 H) 7.41 (d, *J*=7.79 Hz, 1 H) 7.22 (ddd, *J*=7.54, 4.97, 0.87 Hz, 1 H) 3.46 (s, 1 H) 1.79 - 1.87 (m, 2 H) 1.47 - 1.59 (m, 2 H) 1.28 - 1.38 (m, 4 H) 0.89 (t, *J*=6.79 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 149.70 (+), 142.89, 136.21 (+), 127.09 (+), 122.86 (+), 91.08, 83.65, 62.15 (t, *J*=22.20 Hz) 37.40 (-), 31.47 (-), 24.87 (-), 22.52 (-), 13.98 (+); ^{2}H NMR (76.77 MHz, CCl_4) δ ppm 4.74-5.03 (br s, 1 D).

Synthesis of Heterocyclic Propargylic Alcohols (5f'- 5h')

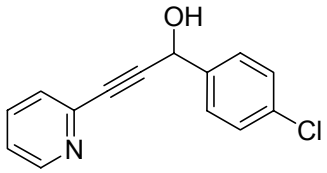


General Procedure: To a solution of 2-ethynyl pyridine (1.03g, 10 mmol) in THF (20 mL) at -78ºC *n*BuLi (2.61M, 4.1 mL, 11 mmol) was added dropwise. The reaction mixture was stirred for 5 minutes before warming to 0ºC and stirred for 20 minutes. The reaction was cooled to -78ºC and 4-chlorobenzaldehyde (1.55g, 11 mmol in 5mL of THF) was added dropwise. The reaction was warmed to 0ºC and stirred for 30 minutes or until TLC analysis indicated the reaction was complete. The reaction mixture was diluted with

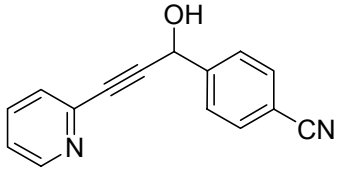
ether (90 mL) and poured into sat. NH_4Cl(aq) (75 mL). The organic phase was washed with sat. NH_4Cl(aq) (75 mL) dried over MgSO4, filtered and concentrated. The residue was purified by column chromatography (Silica gel, EtOAc-Hexanes 1:1) to afford product (1.95g, 80%).



5f': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.48 (d, *J*=4.68 Hz, 1 H), 8.01 (d, *J*=8.33 Hz, 2 H), 7.68 (d, *J*=8.33 Hz, 2 H), 7.61 - 7.66 (m, 1 H), 7.42 (d, *J*=7.75 Hz, 1 H), 7.20 - 7.25 (m, 1 H), 5.80 (s, 1 H), 5.44 - 5.67 (br s, 1 H), 3.90 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.76, 149.47 (+), 145.28, 142.23, 136.57 (+), 129.79 (+), 129.73, 127.41 (+), 126.58 (+), 123.29 (+), 89.64, 84.97, 63.76 (+), 52.10 (+).

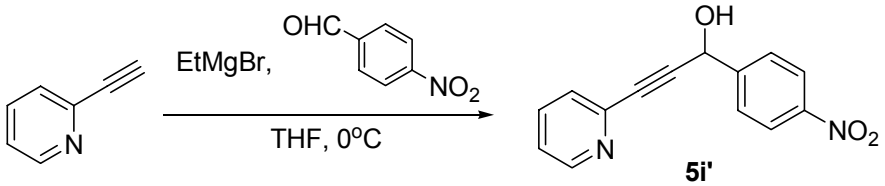


5g': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.46 (d, *J*=4.22 Hz, 1 H), 7.59 – 7.65 (m, 1 H), 7.49 – 7.56 (m, 2 H), 7.37 - 7.42 (m, 1 H), 7.19 – 7.33 (m, 3 H), 5.71 (s, 1 H), 5.43 - 5.63 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 149.50 (+), 142.38, 139.00, 136.48 (+), 133.90, 128.59 (+), 128.10 (+), 127.30 (+), 123.22, (+), 89.79, 84.95, 63.57 (+).

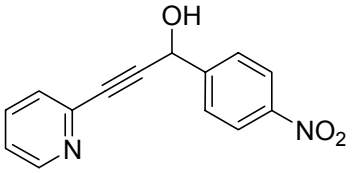


5h': ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.30 - 8.37 (m, 1 H), 7.39 - 7.56 (m, 5 H), 7.23 (d, *J*=7.70 Hz, 1 H), 7.01 - 7.08 (m, 1 H), 5.89 – 6.07 (br s, 1 H), 5.50 (d, *J*=4.95 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 149.31 (+), 145.91, 141.92, 135.71 (+), 131.60 (+), 126.76 (+), 126.68 (+), 122.68 (+), 118.16, 110.81, 88.38, 84.65, 62.60 (+).

Synthesis of Heterocyclic Propargylic Alcohol (5i')



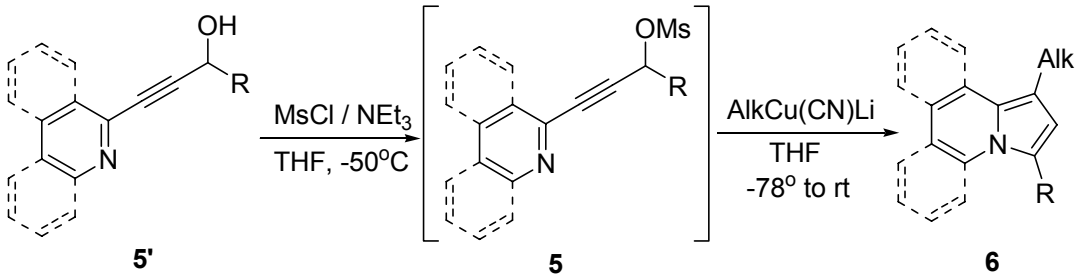
To a stirring solution of the 2-ethynylpyridine (300 mg, 2.9 mmol, 1.2 equiv) in THF (1.0 M) ethylmagnesium bromide (790 µL, 3.0 M in THF, 1.2 equiv) was added at 0°C. The resulting solution was stirred for 30 min. After that solution of 4-nitrobeznaldehyde (366 mg, 2.4 mmol, 1.0 equiv) in THF (0.35 M) was added dropwise at 0°C and stirred for 2 h. The reaction mixture was quenched with sat. NH_4Cl(aq) (40 mL) and extracted three times with EtOAc (20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, the solvent was evaporated under reduced pressure. The residue was purified over a column (Silica gel, dichloromethane-EtOH 40:1) as eluent to afford product (432mg, 70% yield).



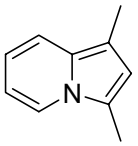
5i': ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 8.54 (d, *J*=2.57 Hz, 1 H), 8.26 (d, *J*=8.16 Hz, 2 H), 7.76 – 7.85 (m, 3 H), 7.52 (d, *J*=7.62 Hz, 1 H), 7.35 – 7.40 (m, 1 H), 6.65 (d, *J*=5.50 Hz, 1 H), 5.83 (d, *J*=5.32 Hz, 1 H);^{13}C NMR (126 MHz, DMSO-d_6) δ ppm 150.11 (+), 148.98, 147.07, 141.84, 136.86 (+), 127.61 (+), 127.23 (+), 123.75 (+), 123.71 (+), 89.33, 84.87, 62.02 (+).

Products

Synthesis of 1-Alkyl-Indolizines (6)

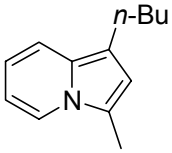


General Procedure: Propargylic alcohol **5a'** (147 mg, 1.0 mmol) was placed into flame-dried round-bottomed flask which was then filled with 6 mL of dry THF and cooled to -50°C under Ar. After that, NEt_3 (121 mg (167 μL), 1.2 mmol) was added neat via a syringe, followed by neat MsCl (137 mg (93 μL), 1.2 mmol). Solution was allowed to stir for 30 min at -50°C, controlling formation of mesylate **5a** by TLC. Meantime, CuCN (116 mg, 1.3 mmol) was placed into another flame-dried round-bottomed flask which was then filled with *ca* 2.5 mL of dry THF and cooled to -50°C under Ar. A 765μL of methyllithium in diethyl ether (1.70 M, 1.3 mmol) was added and the yellowish suspension stirred for 30 min at -50°C, until no CuCN was visible at the bottom of the flask. After complete conversion of alcohol **5a'** to mesylate **5a**, flask with cyanocuprate **7a** was cooled to -78°C and mesylate was transferred to flask with cyanocuprate via canula with cotton at the end avoiding transfer of precipitated triethylammonium chloride. The mixture was stirred for 2h at -78°C, and then it was allowed to warm to room temperature controlling formation of indolizine **6aa** by GC/MS and TLC. After 5h at room temperature reaction was complete and it was quenched with NH_4Cl(aq)-sat. : NH_3(aq)-sat. (10:1) 15 mL and extracted with diethyl ether (3×15mL). Organic extracts were then dried over $MgSO_4$, followed by filtration and evaporation. The column chromatography (Silica gel, EtOAc-Hexanes 1:20) provided 131 mg (90%) of product **6aa**.

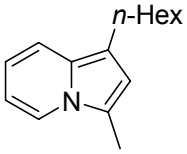


6aa: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 7.21 (d, *J*=8.99 Hz, 1 H), 7.09 (d, *J*=7.06 Hz, 1 H), 6.37 - 6.43 (m, 2 H), 6.17 (t, *J*=6.69 Hz, 1 H), 2.35 (s, 3 H), 2.00 (s, 3 H); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 130.20, 121.88 (+), 118.72 (+), 118.11, 114.84 (+), 113.78 (+), 109.85, 107.66, 11.51; HR EI MS *m/z*

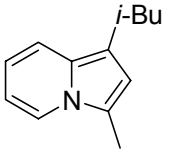
145.0893, Calcd for $C_{10}H_{11}N$ 145.0891.



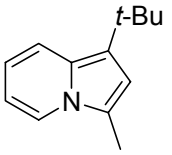
6ab: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.59 (d, *J*=7.06 Hz, 1 H), 7.33 (d, *J*=8.99 Hz, 1 H), 6.51 - 6.57 (m, 1 H), 6.43 - 6.49 (m, 1 H), 2.74 (t, *J*=7.57 Hz, 2 H), 2.44 (s, 3 H), 1.60 - 1.67 (qv, *J*=7.57, 2 H), 1.36 - 1.43 (m, 2 H), 0.95 (t, *J*=7.34 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 128.93, 121.38 (+), 118.41, 117.39 (+), 113.43 (+), 112.87, 112.76 (+), 109.51 (+), 33.79 (-), 25.20 (-), 22.60 (-), 14.03 (+), 11.45 (+); HR EI MS *m/z* 187.1359, Calcd for $C_{13}H_{17}N$ 187.1361.



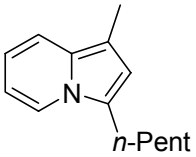
6ac: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 7.31 (d, *J*=8.99 Hz, 1 H), 7.09 (d, *J*=7.15 Hz, 1 H), 6.46 (s, 1 H), 6.42 (dd, *J*=8.89, 6.51 Hz, 1 H), 6.18 (t, *J*=6.33 Hz, 1 H), 2.82 (t, *J*=7.52 Hz, 2 H), 2.02 (s, 3 H), 1.65 - 1.78 (m, 2 H), 1.40 (s, 2 H), 1.22 - 1.33 (m, 4 H), 0.88 (t, *J*=6.97 Hz, 3 H); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 129.89, 121.93 (+), 118.74, 118.13 (+), 113.90 (+), 113.82 (+), 113.61, 109.93 (+), 32.63 (-), 32.44 (-), 29.97 (-), 26.44 (-), 23.48 (-), 14.73 (+), 11.61 (+); HR EI MS *m/z* 215.1672, Calcd for $C_{15}H_{21}N$ 215.1674.



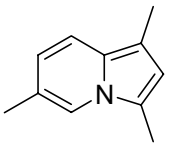
6ad: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 7.30 (d, *J*=9.08 Hz, 1 H), 7.08 (d, *J*=7.06 Hz, 1 H), 6.38 - 6.43 (m, 1 H), 6.18 (t, *J*=6.69 Hz, 1 H), 2.96 (d, *J*=7.15 Hz, 1 H), 2.01 (s, 3 H), 1.65 - 1.76 (m, 2 H), 1.37 (d, *J*=6.97 Hz, 3 H), 0.92 (t, *J*=7.34 Hz, 3 H); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 129.49, 121.94 (+), 118.92, 118.87, 118.14 (+), 113.91 (+), 111.32 (+), 109.97 (+), 33.16 (+), 32.53 (-), 23.26 (+), 13.08 (+), 11.67 (+); HR EI MS *m/z* 187.1359, Calcd for $C_{13}H_{17}N$ 187.1361.



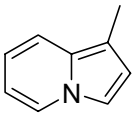
6ae: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.53 - 7.70 (m, 2 H), 6.44 - 6.65 (m, 3 H), 2.47 (s, 3 H), 1.50 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 127.45, 122.32, 121.72 (+), 119.57 (+), 117.45, 113.27 (+), 111.20 (+), 109.32 (+), 31.81 (+), 31.59, 11.51 (+); HR EI MS *m/z* 187.1360, Calcd for $C_{13}H_{17}N$ 187.1361.



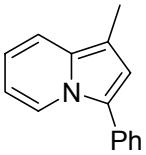
6ba: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 7.27 (d, *J*=7.15 Hz, 1 H), 7.23 (d, *J*=8.89 Hz, 1 H), 6.46 (s, 1 H), 6.41 (dd, *J*=8.71, 6.51 Hz, 1 H), 6.17 - 6.22 (m, 1 H), 2.47 (t, *J*=7.61 Hz, 2 H), 2.37 (s, 3 H), 1.52 - 1.60 (m, 2 H), 1.19 - 1.26 (m, 4 H), 0.85 (t, *J*=6.97 Hz, 3 H); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 123.65, 121.93 (+), 118.34 (+), 113.91 (+), 113.88 (+), 109.84 (+), 107.74, 101.57, 32.35 (-) 27.72 (-) 26.36 (-) 23.22 (-) 14.58 (+) 11.13 (+); HR EI MS *m/z* 201.1519, Calcd for $C_{14}H_{19}N$ 201.1517.



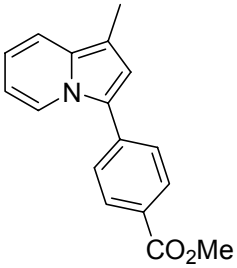
6ca: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.41 (s, 1 H), 7.27 (d, *J*=9.08 Hz, 1 H), 6.46 (d, *J*=8.89 Hz, 1 H), 6.40 (s, 1 H), 2.45 (s, 3 H), 2.39 (s, 3 H), 2.29 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 128.32, 118.81 (+), 118.58, 117.94, 116.80 (+), 116.78 (+), 113.26 (+), 106.69, 18.56 (+), 11.37 (+), 10.44 (+); HR EI MS *m/z* 159.1046, Calcd for $C_{11}H_{13}N$ 159.1048.



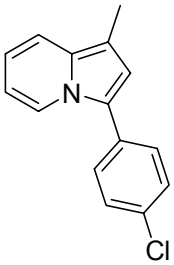
6da: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 7.25 - 7.27 (m, 1 H), 7.22 (d, *J*=9.17 Hz, 1 H), 6.96 (d, *J*=2.57 Hz, 1 H), 6.71 (d, *J*=2.38 Hz, 1 H), 6.43 (dd, *J*=8.53, 6.88 Hz, 1 H), 6.10 (dd, *J*=13.39, 1.10 Hz, 1 H), 2.40 (s, 3 H); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 130.74, 125.52 (+), 118.09 (+), 115.38 (+), 115.27 (+), 111.81 (+), 109.93 (+), 108.46, 11.06 (+); HR EI MS *m/z* 131.08588, Calcd for C_9H_9N 131.17446.



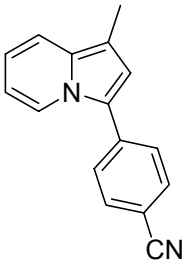
6ea: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.03 (d, *J*=7.09 Hz, 1 H), 7.33 (d, *J*=8.92 Hz, 1 H), 7.07 - 7.19 (m, 4 H), 6.89 - 6.98 (m, 2 H), 6.50 - 6.67 (m, 1 H), 6.34 (t, *J*=6.72 Hz, 1 H), 2.09 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 132.03, 129.95, 129.07 (+), 128.26 (+), 126.16 (+) 121.80 (+), 121.51, 117.47 (+), 115.04 (+), 109.59 (+), 109.54 (+), 109.32, 9.31 (+); HR EI MS *m/z* 207.1044, Calcd for $C_{15}H_{13}N$ 207.1048.



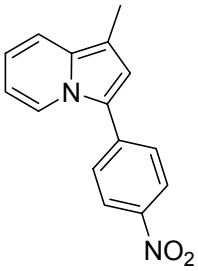
6fa: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.14 - 8.20 (m, 2 H), 8.08 (dd, *J*=7.15, 0.92 Hz, 1 H), 7.52 - 7.60 (m, 2 H), 7.31 - 7.36 (m, 1 H), 6.69 (ddd, *J*=8.94, 6.46, 0.92 Hz, 1 H), 6.38 - 6.47 (m, 2 H), 3.97 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 166.84, 136.52, 133.12, 130.12 (+), 129.07 (+), 128.28, 124.21, 122.04 (+), 118.57 (+), 117.65 (+), 110.21 (+), 101.41 (+), 52.13 (+), 12.54 (+); HR EI MS *m/z* 265.1104, Calcd for $C_{17}H_{15}NO_2$ 265.1103.



6ga: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.20 (d, *J*=8.44 Hz, 1 H), 7.29 - 7.57 (m, 6 H), 6.75 (s, 1 H), 6.68 (s, 1 H), 6.48 (t, *J*=7.43 Hz, 1 H), 2.45 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 132.25, 131.37, 131.04, 129.04 (+), 128.79 (+), 122.79, 121.77 (+), 117.84 (+), 115.59 (+), 115.37 (+), 110.51 (+), 109.12, 10.39 (+); HR EI MS *m/z* 241.0657, Calcd for $C_{15}H_{12}ClN$ 241.0658.

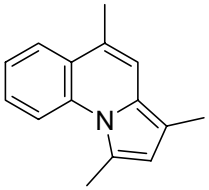


6ha: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.06 (d, *J*=7.15 Hz, 1 H), 7.77 (d, *J*=8.34 Hz, 2 H), 7.58 (d, *J*=8.34 Hz, 2 H), 7.35 (d, *J*=8.89 Hz, 1 H), 6.72 (dd, *J*=8.57, 6.92 Hz, 1 H), 6.46 (dd, *J*=13.62, 1.05 Hz, 1 H), 6.42 (s, 1 H), 2.34 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 136.57, 133.52, 132.62 (+), 129.51 (+), 124.72, 121.77 (+), 120.54, 118.96, 118.71 (+), 118.16 (+), 110.59 (+), 109.93, 101.82 (+), 12.56 (+); HR EI MS *m/z* 232.1000, Calcd for $C_{16}H_{12}N_2$ 232.1001.

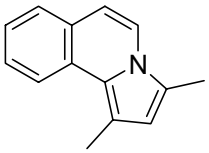


6ia: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.36 (d, *J*=8.71 Hz, 2 H), 8.12 (d, *J*=7.06 Hz, 1 H), 7.64 (d, *J*=8.80 Hz, 2 H), 7.36 (d, *J*=8.99 Hz, 1 H), 6.75 (dd, *J*=8.57, 6.74 Hz, 1 H), 6.49 (t, *J*=6.42 Hz, 1 H), 6.44 (s, 1 H), 2.37 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 145.86, 138.60, 133.92, 129.22 (+), 125.30, 124.30 (+), 121.90 (+), 120.36, 118.78 (+),

118.53 (+), 110.84 (+), 102.23 (+), 12.72 (+); HR EI MS *m/z* 252.0901, Calcd for $C_{15}H_{12}N_2O_2$ 252.0899.

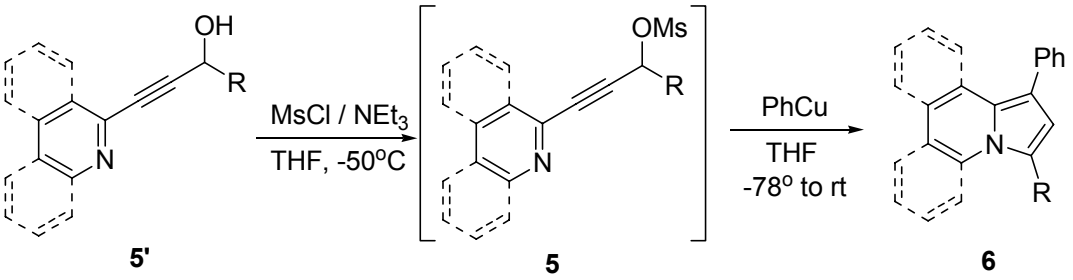


6ja: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.29 (d, *J*=8.44 Hz, 1 H), 7.73 (dd, *J*=7.89, 1.28 Hz, 1 H), 7.42 - 7.47 (m, 1 H), 7.33 (t, *J*=7.20 Hz, 1 H), 7.09 (s, 1 H), 6.34 (s, 1 H), 2.92 (s, 3 H), 2.47 (s, 3 H), 2.33 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 136.07, 128.61, 126.15 (+), 125.90, 124.70 (+), 124.39, 122.56 (+), 121.52, 116.89 (+), 115.74 (+), 115.53 (+), 109.04, 19.20 (+), 18.41 (+), 10.38 (+); HR EI MS *m/z* 209.1206, Calcd for $C_{15}H_{15}N$ 209.1204.



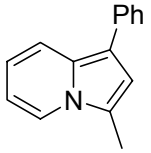
6ka: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.15 (d, *J*=8.25 Hz, 1 H), 7.55 (dd, *J*=7.79, 4.49 Hz, 2 H), 7.47 (dd, *J*=15.22, 1.01 Hz, 1 H), 7.30 (dd, *J*=14.95, 0.73 Hz, 1 H), 6.70 (d, *J*=7.43 Hz, 1 H), 6.34 (s, 1 H), 2.66 (s, 3 H), 2.47 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 128.23, 126.96 (+), 126.57 (+), 123.97 (+), 122.26, 122.09 (+), 121.52 (+), 121.11, 120.47, 113.90 (+), 111.74, 110.10 (+), 14.90 (+), 11.43 (+); HR EI MS *m/z* 195.1050, Calcd for $C_{14}H_{13}N$ 195.1048.

Synthesis of 1-Phenyl-Indolizines (6af, 6jf)

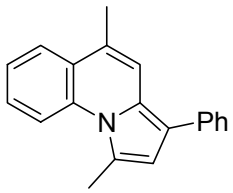


General Procedure: Propargylic alcohol **5a'** (147 mg, 1.0 mmol) was placed into flame-dried round-bottomed flask which was then filled with 6 mL of dry THF and cooled to -50°C under Ar. After that, NEt_3 (121 mg (167 µL), 1.2 mmol) was added neat via a syringe, followed by neat MsCl (137 mg (93 µL), 1.2 mmol). Solution was allowed to stir for 30 min at -50°C, controlling formation of mesylate **5a** by TLC. Meantime, $CuBr{\cdot}SMe_2$ (267 mg, 1.3 mmol) was placed into another flame-dried round-bottomed flask which was then filled with *ca* 4 mL of dry THF and cooled to -50°C under Ar. A 433µL volume of phenyl magnesium bromide in diethyl ether (3.06 M, 1.3 mmol) was added and the yellowish suspension stirred for 30 min at -20°C. After complete conversion of alcohol to mesylate, flask with phenylcopper was cooled to -78°C and mesylate was transferred to flask with phenylcopper via canula with cotton at the end avoiding transfer of precipitated triethylammonium chloride. The mixture was stirred for 2h at -78°C, and then it was allowed to warm to room temperature controlling formation of indolizine by GC/MS and TLC. After 3h at room temperature reaction was complete and it was quenched with NH_4Cl(aq)-sat. : NH_3(aq)-sat. (10:1) 15 mL and extracted with

diethyl ether (3×15mL). Organic extracts were then dried over $MgSO_4$, followed by filtration and evaporation. The column chromatography (Silica gel, EtOAc-Hexanes 1:20) provided 146 mg (71%) of product **6af**.



6af: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J*=9.08 Hz, 1 H), 7.71 (d, *J*=7.06 Hz, 1 H), 7.62 (d, *J*=7.24 Hz, 2 H), 7.44 (t, *J*=7.75 Hz, 2 H), 7.19 - 7.35 (m, 2 H), 6.81 (s, 1 H), 6.68 - 6.78 (m, 2 H), 6.52 - 6.66 (m, 2 H), 2.52 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 136.66, 128.66 (+), 127.37 (+), 125.00 (+), 121.98 (+), 120.10, 118.19 (+), 116.45 (+), 113.50, 112.47 (+), 110.50 (+), 109.55, 11.50 (+); HR EI MS *m/z* 207.1050, Calcd for $C_{15}H_{13}N$ 207.1048.



6jf: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.36 (d, *J*=8.53 Hz, 1 H), 7.77 (dd, *J*=7.93, 1.24 Hz, 1 H), 7.59 (d, *J*=7.06 Hz, 2 H), 7.43 - 7.50 (m, 4 H), 7.38 (t, *J*=7.15 Hz, 1 H), 7.26 - 7.29 (m, 1 H), 6.66 (s, 1 H), 3.00 (s, 3 H), 2.48 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 136.36, 135.96, 130.37, 128.62 (+), 128.12 (+), 126.62 (+), 126.09, 125.79, 125.52 (+), 124.75 (+), 124.42, 123.06 (+), 117.45 (+), 116.13 (+), 115.78, 114.23 (+), 19.29 (+), 18.67 (+); HR EI MS *m/z* 271.1362, Calcd for $C_{20}H_{17}N$ 271.1361.

Attempts on stepwise synthesis of N-fused heterocycles

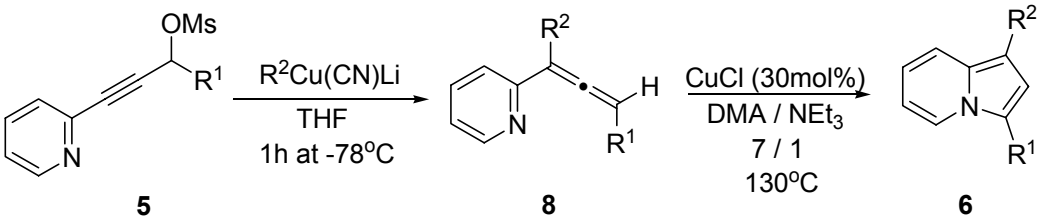


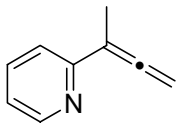
Table 1. Attempts on stepwise synthesis of N-fused heterocycles

Entry	R^1	R^2	Yield[%][a] **8**	Yield[%][a] **6**	Overall Yield[%][b] **6**
1	H	Me	27[c]	0	trace(61)
2	H	*n*-Bu	51	0	0(n/a)
3	Me	Me	43	41	18(90)
4	Me	*s*-Bu	89	42	37(82)
5	Me	*t*-Bu	73	32	23(79)
6	C_6H_4-*p*-CO_2Me	Me	34	27	9(62)

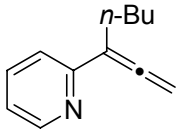
[a] Isolated yield. [b] Overall isolated yield for a stepwise process. Yield for cascade transformation is given in parentheses. [c] Trace amount of **6** were also isolated.

General Procedure: Propargylic alcohol **5a'** (147 mg, 1.0 mmol) was placed into flame-dried round-bottomed flask which was then filled with 6 mL of dry THF and cooled to -50°C under Ar. After that, NEt_3 (121 mg (167 µL), 1.2 mmol) was added neat via a syringe, followed by neat MsCl (137 mg (93 µL), 1.2 mmol). Solution was allowed to stir for 30 min at -50°C, controlling formation of mesylate **5a** by TLC. Meantime, CuCN (116 mg, 1.3 mmol) was placed into another flame-dried round-bottomed flask which was then filled with *ca* 2.5 mL of dry THF and cooled to -50°C under Ar. A 765µL of methyllithium in diethyl ether (1.70 M, 1.3 mmol) was added and the yellowish suspension stirred for 30 min at -50°C, until no CuCN was visible at the bottom of the flask. After complete conversion of alcohol **5a'** to mesylate **5a**, flask with cyanocuprate **7a** was cooled to -78°C and mesylate was transferred to flask with cyanocuprate via canula with cotton at the end avoiding transfer of precipitated triethylammonium chloride. The mixture was stirred for 1h at -78°C, and then it was quenched with NH_4Cl(aq)-sat. : NH_3(aq)-sat. (10:1) 15 mL and extracted with diethyl ether (3×15mL). Organic extracts were then dried over $MgSO_4$, followed by filtration and evaporation. The column chromatography (Silica gel, EtOAc-Hexanes 1:10) provided 62 mg (43%) of product **8** (Entry 3).

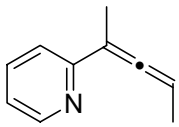
To the 5.0 mL Wheaton microreactor under argon atmosphere CuCl, anhydrous Et_3N and allene **8** in anhydrous DMA were successively added. The mixture was stirred overnight at 130°C with protection from light and then cooled. It was quenched with sat. NH_4Cl(aq) 3 mL and extracted with ethyl acetate (2×7mL) and diethyl ether (7mL). Organic extracts were then dried over $MgSO_4$, followed by filtration and evaporation compound was purified by column chromatography (Silica gel, EtOAc-Hexanes 1:20) providing 25 mg (41%) of product **6aa** with the overall yield (17%) after two steps (Entry 3).



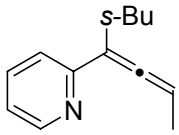
8da: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.56 (1 H, dd, *J*=4.59, 1.28 Hz), 7.57 (1 H, dd, *J*=7.34, 1.83 Hz), 7.50 (1 H, d, *J*=7.89 Hz), 7.06 (1 H, dd, *J*=6.33, 5.78 Hz), 5.06 - 5.13 (2 H, m), 2.11 - 2.17 (3 H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 210.70, 156.03, 149.06 (+), 135.81 (+), 121.41 (+), 120.98 (+) 101.87, 77.69 (+), 15.76 (+).



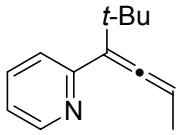
8db: ^{1}H NMR (500 MHz, C_6D_6) δ ppm 8.51 (1 H, d, *J*=4.77 Hz), 7.45 (1 H, d, *J*=8.07 Hz), 7.06 (1 H, t, *J*=7.70 Hz), 6.56 (1 H, dd, *J*=6.97, 4.95 Hz), 4.90 (2 H, t, *J*=3.12 Hz), 2.88 (2 H, dt, *J*=15.31, 3.16 Hz), 1.69 (2 H, ddd, *J*=15.27, 7.57, 7.43 Hz), 1.37 - 1.47 (2 H, m), 0.92 (3 H, t, *J*=7.34 Hz); ^{13}C NMR (126 MHz, C_6D_6) δ ppm 210.63, 155.89, 149.07 (+), 135.20 (+), 121.92 (+), 120.69 (+), 109.56, 78.40 (+), 30.59 (-), 28.42 (-), 22.71 (-), 13.98 (+).



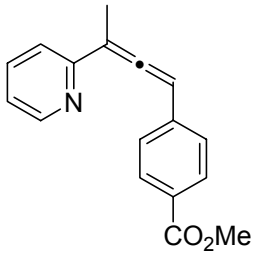
8aa: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.55 (1 H, d, *J*=4.82 Hz), 7.54 (1 H, dd, *J*=7.60, 1.75 Hz), 7.45 - 7.50 (1 H, m), 7.03 (1 H, td, *J*=6.25, 0.80 Hz), 5.48 (1 H, dd, *J*=7.02, 3.07 Hz), 2.13 (3 H, d, *J*=2.78 Hz), 1.77 (3 H, d, *J*=7.16 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 206.76, 156.87, 148.86 (+), 135.58 (+), 121.43 (+), 120.70 (+), 101.78, 88.29 (+), 16.09 (+), 14.03 (+).



8ad: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.52 (1 H, d, *J*=4.53 Hz), 7.49 - 7.56 (1 H, m), 7.42 - 7.47 (1 H, m), 6.98 - 7.03 (1 H, m), 5.50 - 5.59 (1 H, m), 3.01 - 3.11 (1 H, m), 1.68 - 1.95 (4 H, m), 1.33 - 1.47 (1 H, m), 1.05 - 1.12 (3 H, m), 0.86 - 0.94 (3 H, m).

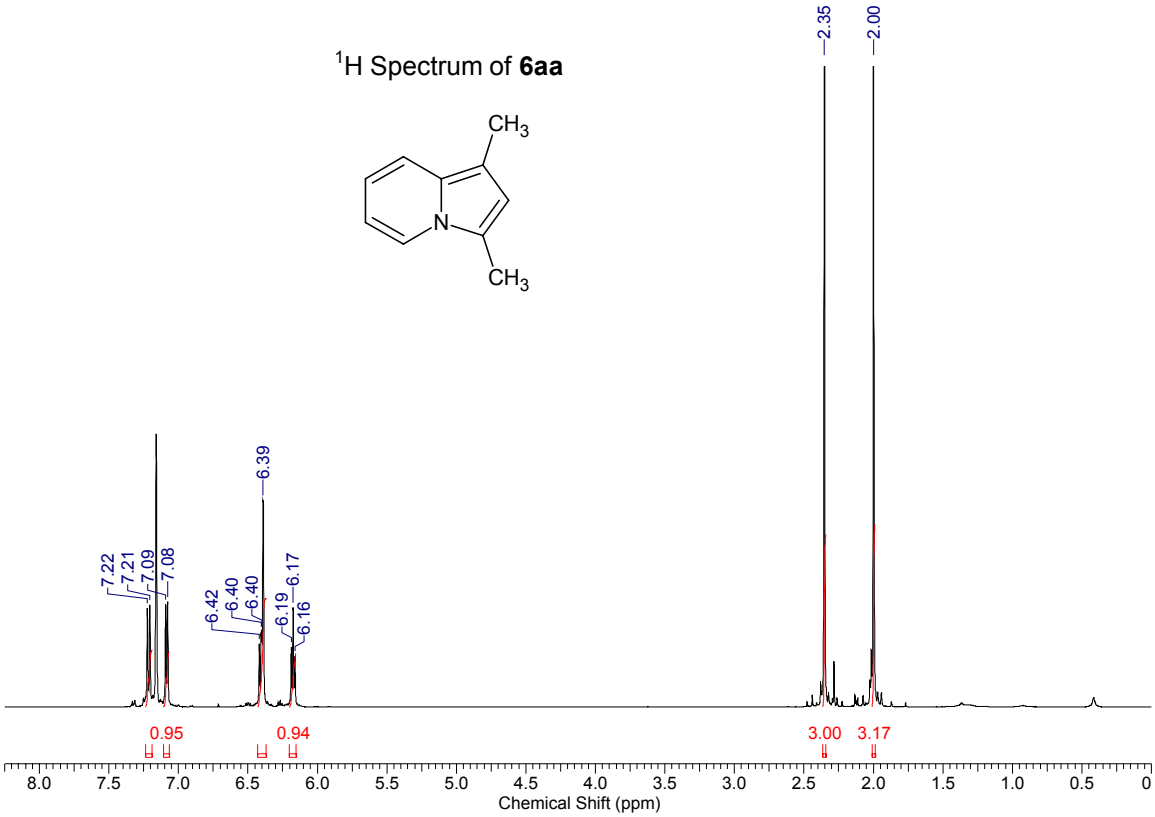


8ae: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 (1 H, d, *J*=3.95 Hz), 7.52 (1 H, td, *J*=7.71, 1.83 Hz), 7.30 (1 H, d, *J*=7.89 Hz), 7.03 (1 H, dd, *J*=6.80, 5.33 Hz), 5.35 (1 H, q, *J*=6.92 Hz), 1.73 (3 H, d, *J*=7.02 Hz), 1.26 (9 H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 205.14, 157.95, 148.13 (+), 135.51 (+), 124.13 (+), 120.61 (+), 115.47, 87.95 (+), 30.06 (+), 29.41, 14.32 (+).

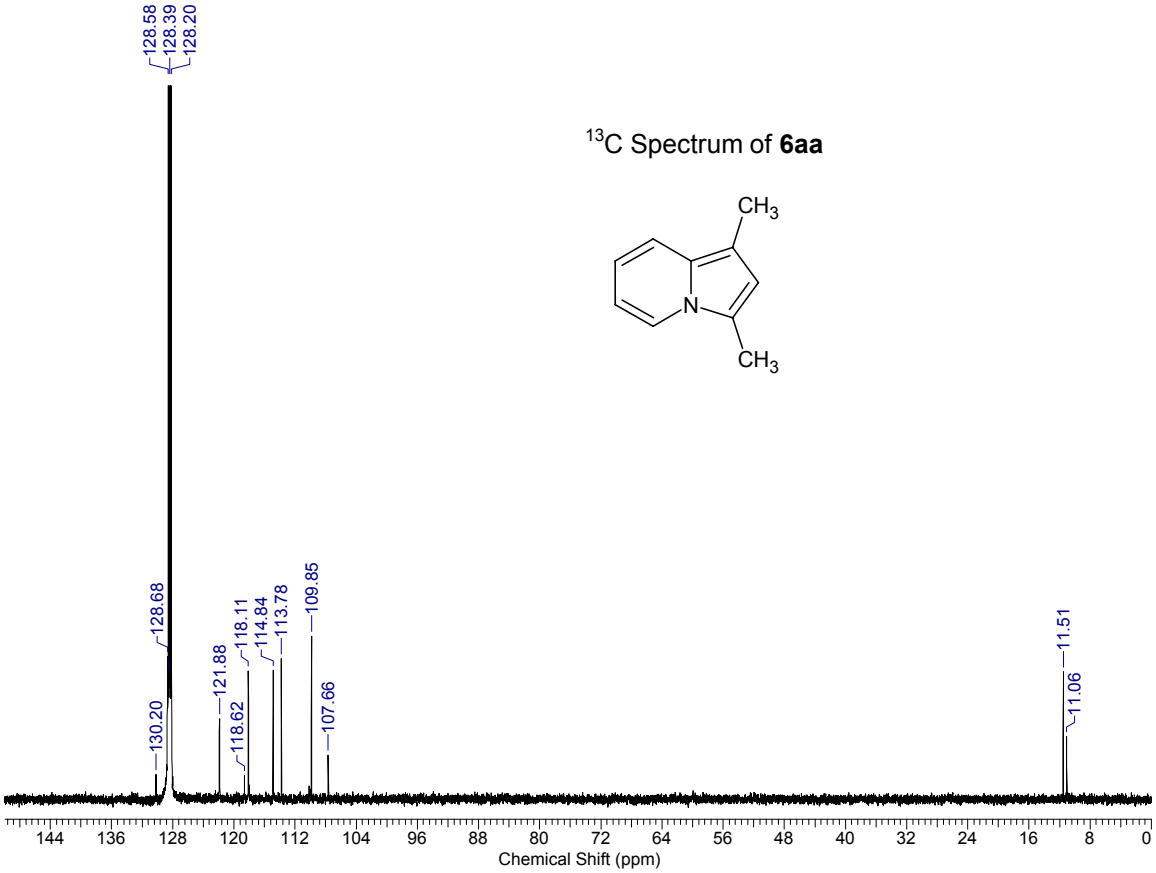


8fa: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.60 (1 H, dd, *J*=6.33, 1.38 Hz), 8.03 (1 H, d, *J*=8.25 Hz), 7.96 (2 H, d, *J*=8.44 Hz), 7.53 - 7.60 (1 H, m), 7.36 (2 H, d, *J*=8.44 Hz), 7.10 (1 H, dd, *J*=6.69, 4.49 Hz), 6.56 (1 H, q, *J*=2.69 Hz), 3.88 (3 H, s), 2.30 (2 H, d, *J*=3.12 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 209.75, 166.71, 149.22 (+), 138.84, 135.95 (+), 129.98 (+), 129.92, 126.75 (+), 125.08, 121.80 (+), 121.60 (+), 106.96, 96.76 (+), 51.96 (+), 18.87 (+).

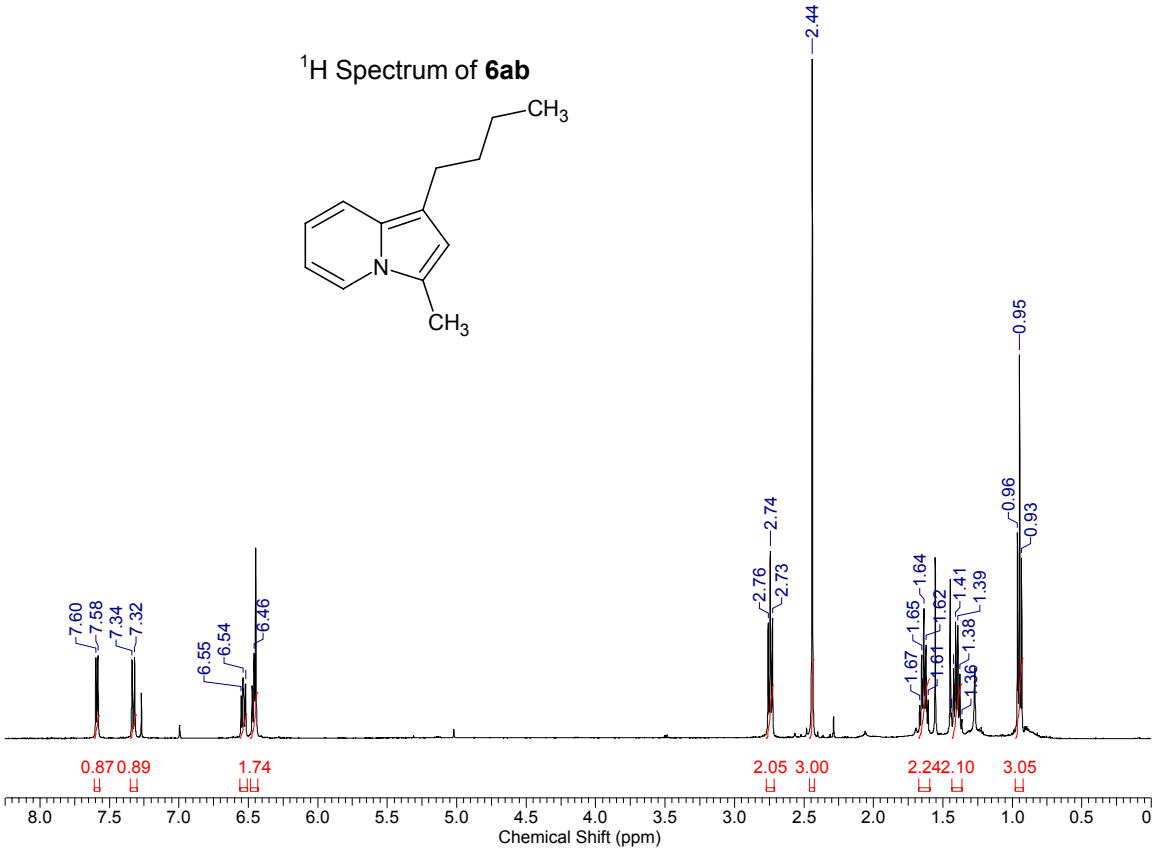
^{1}H Spectrum of **6aa**



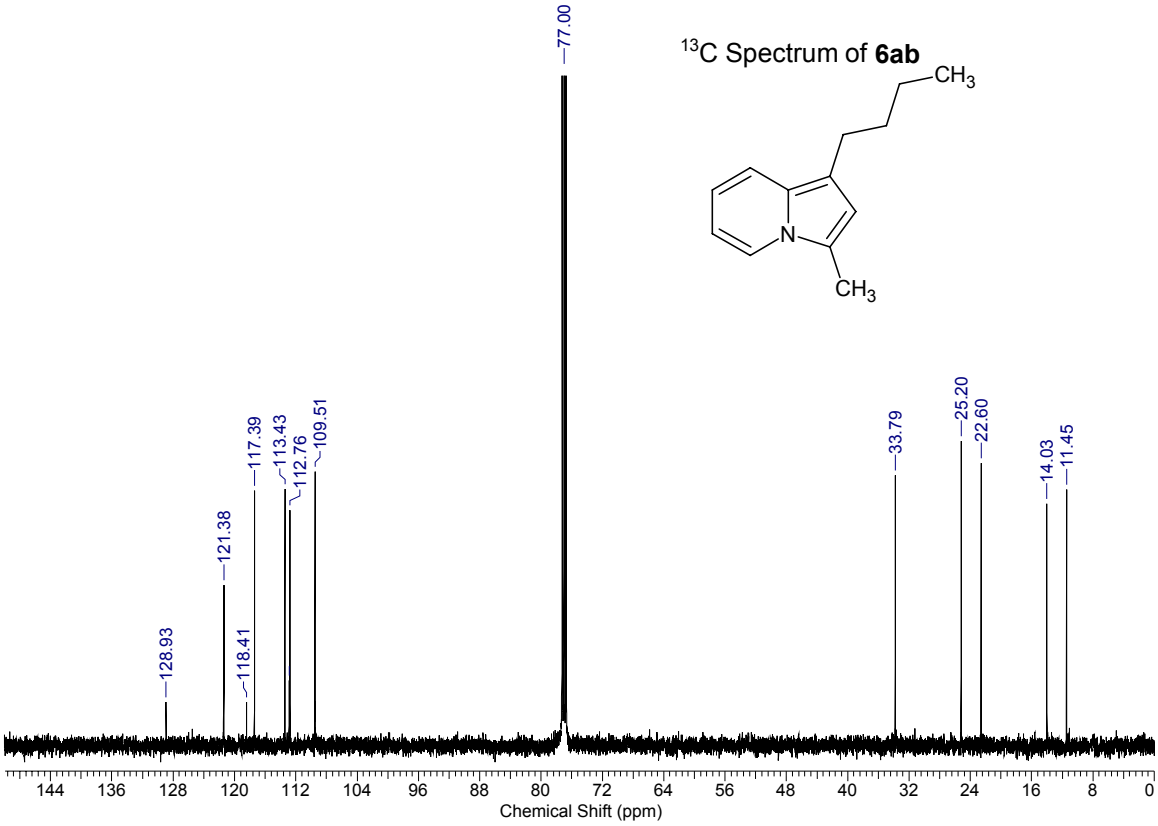
^{13}C Spectrum of **6aa**



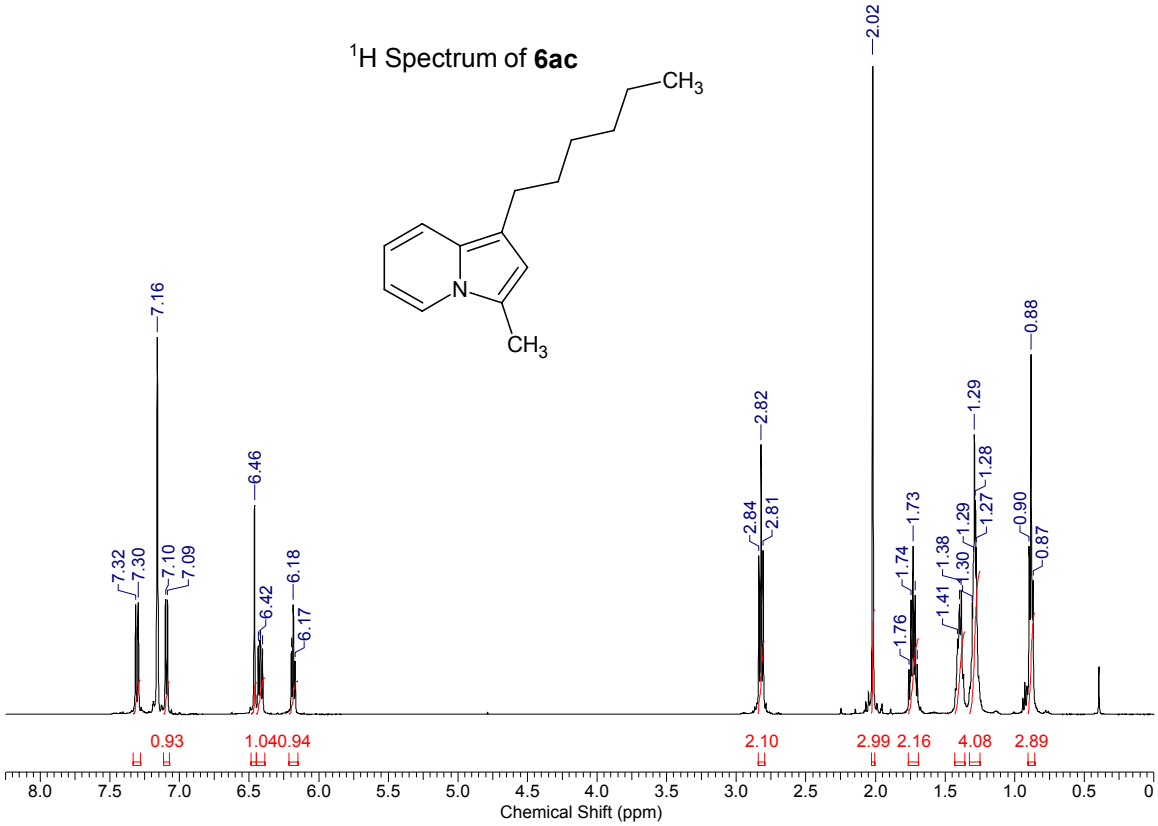
^{1}H Spectrum of **6ab**



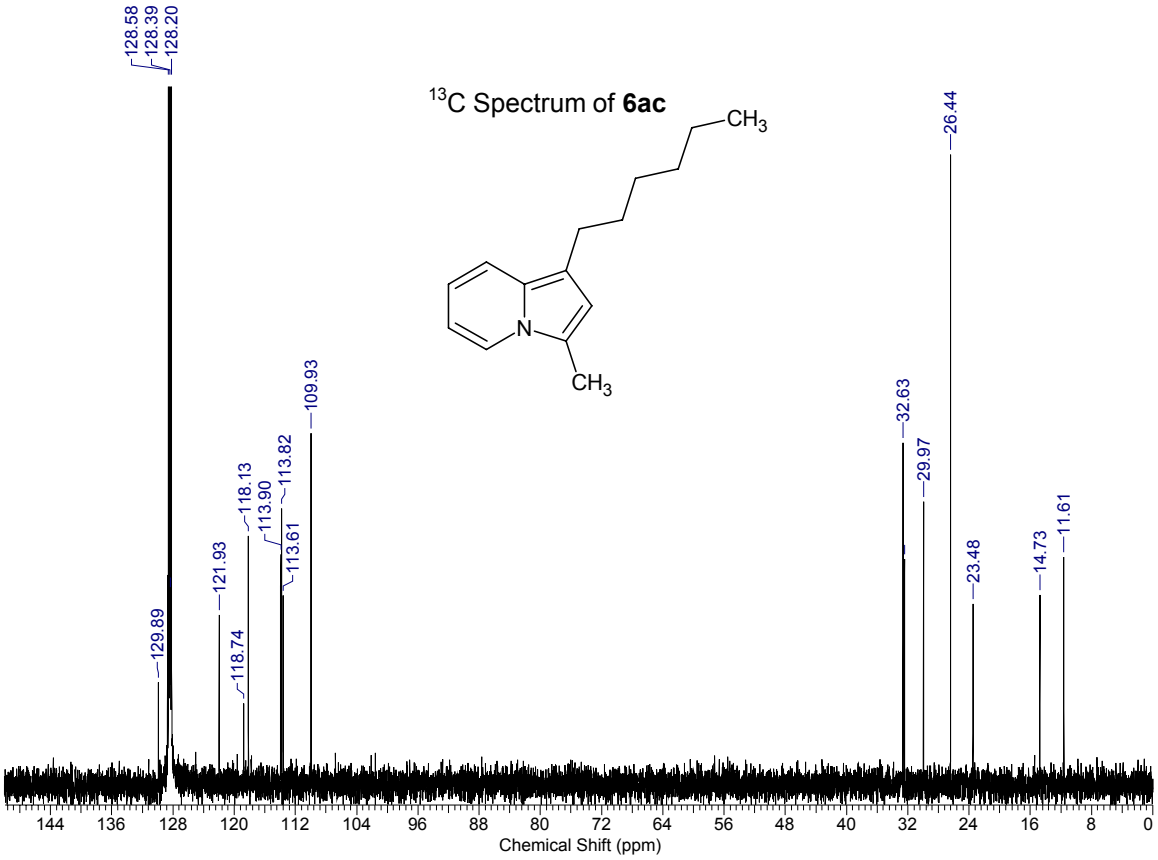
^{13}C Spectrum of **6ab**



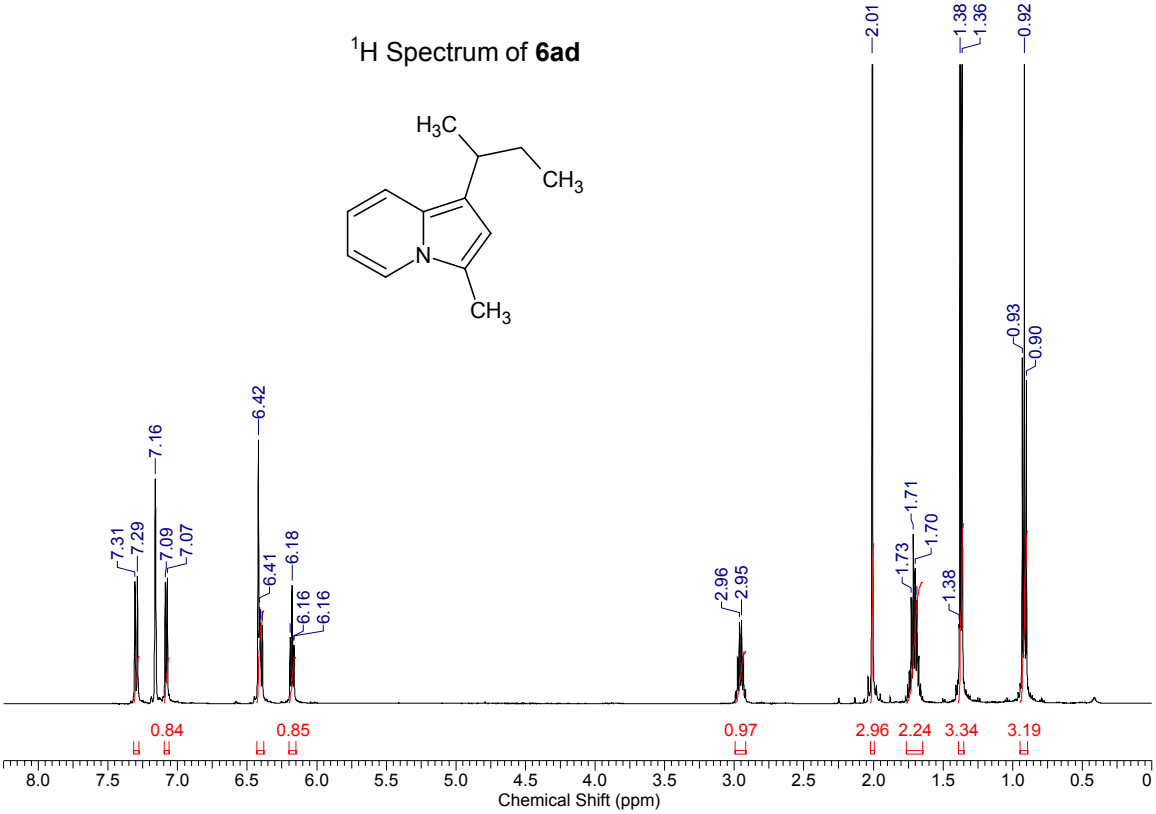
^{1}H Spectrum of **6ac**



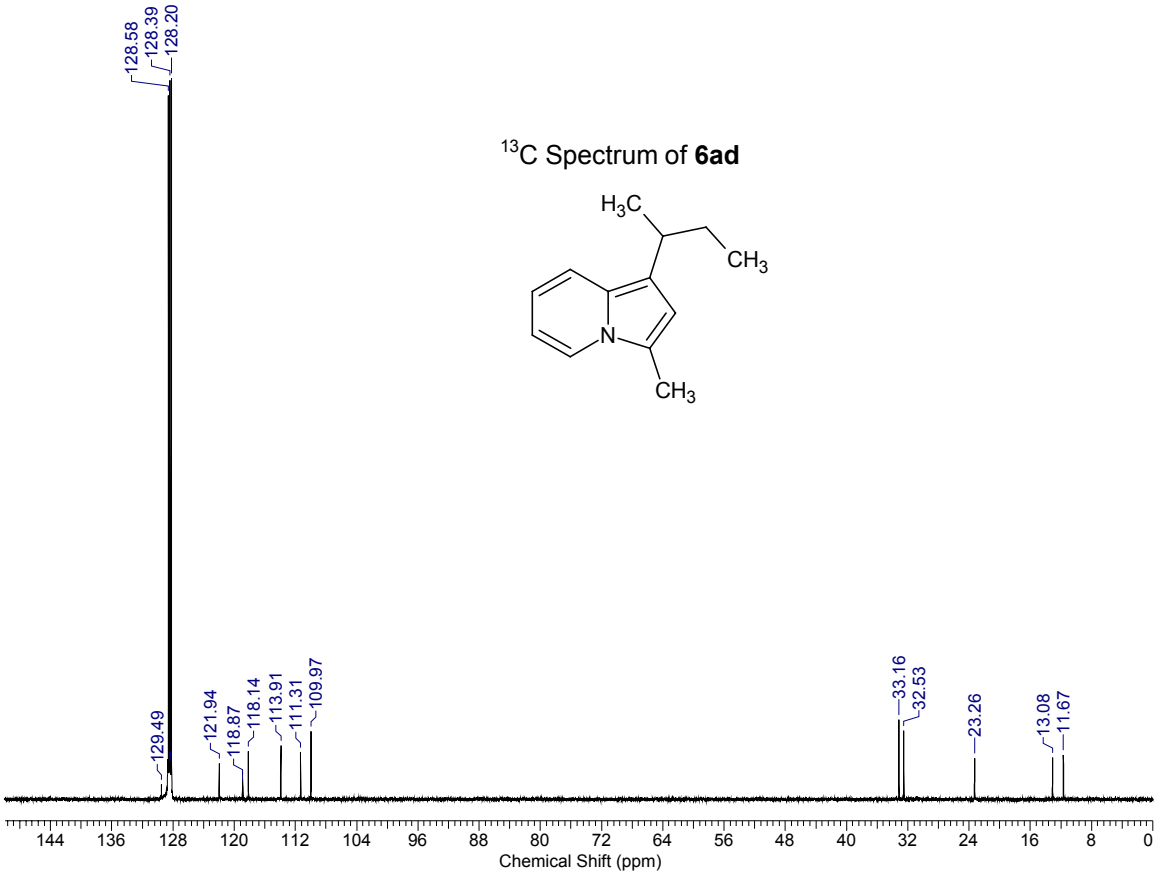
^{13}C Spectrum of **6ac**



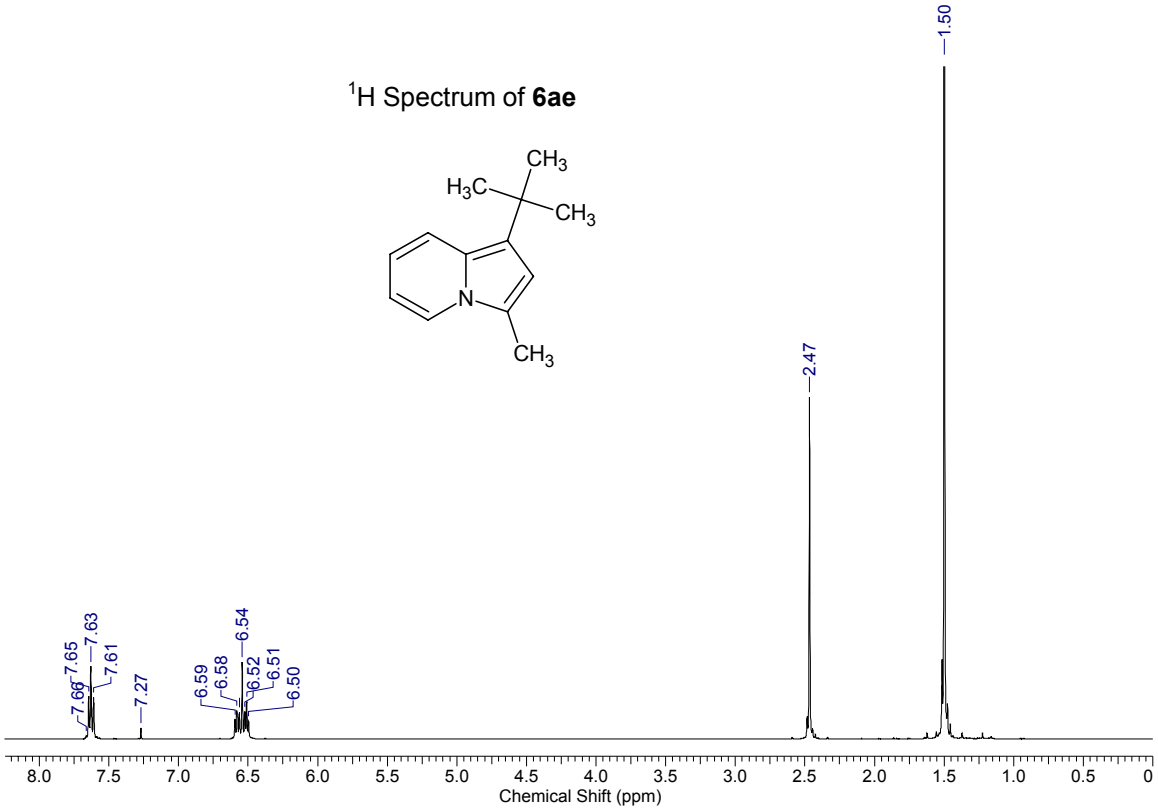
^{1}H Spectrum of **6ad**



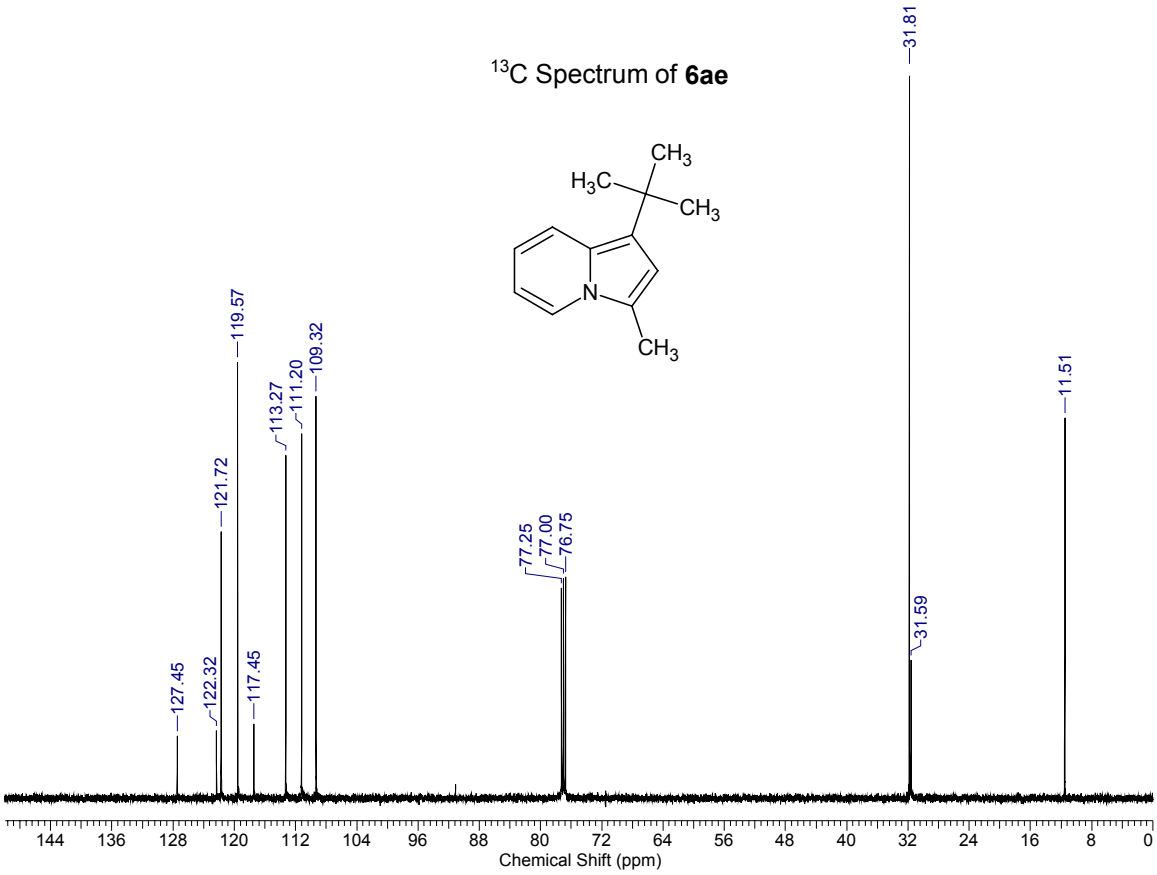
^{13}C Spectrum of **6ad**



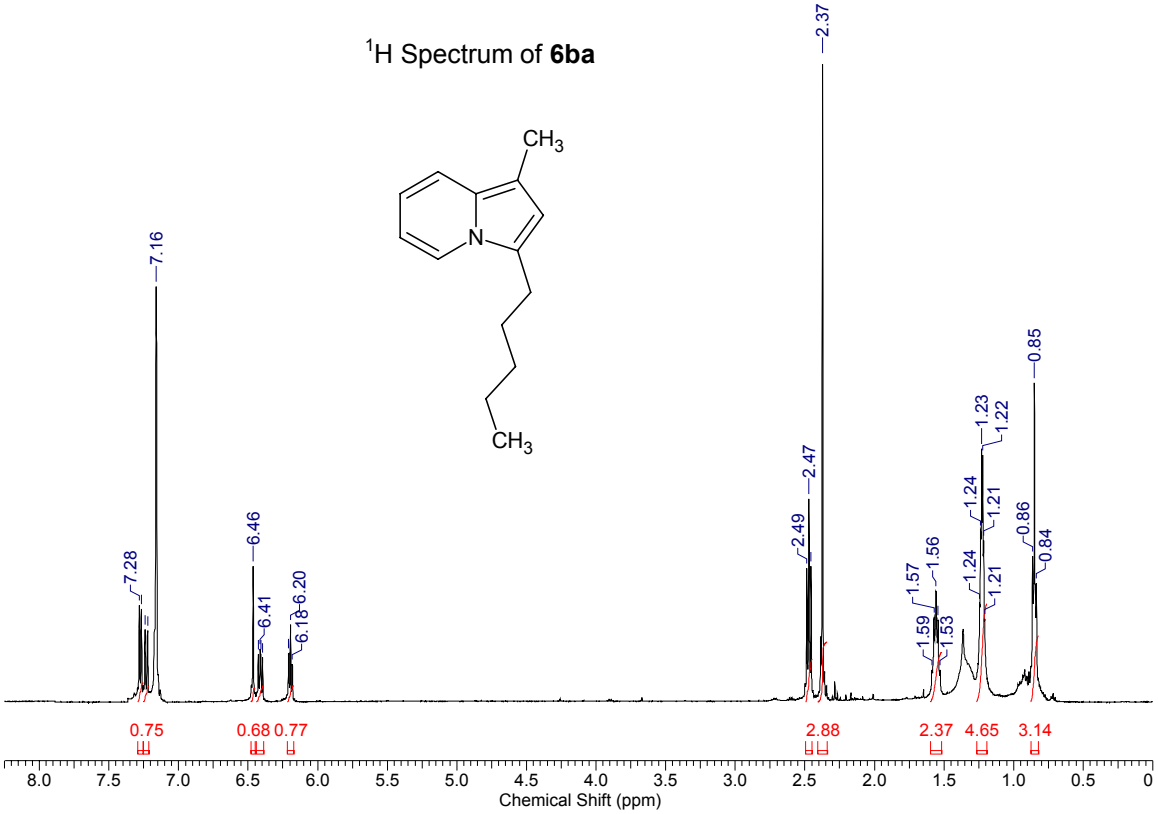
^{1}H Spectrum of **6ae**



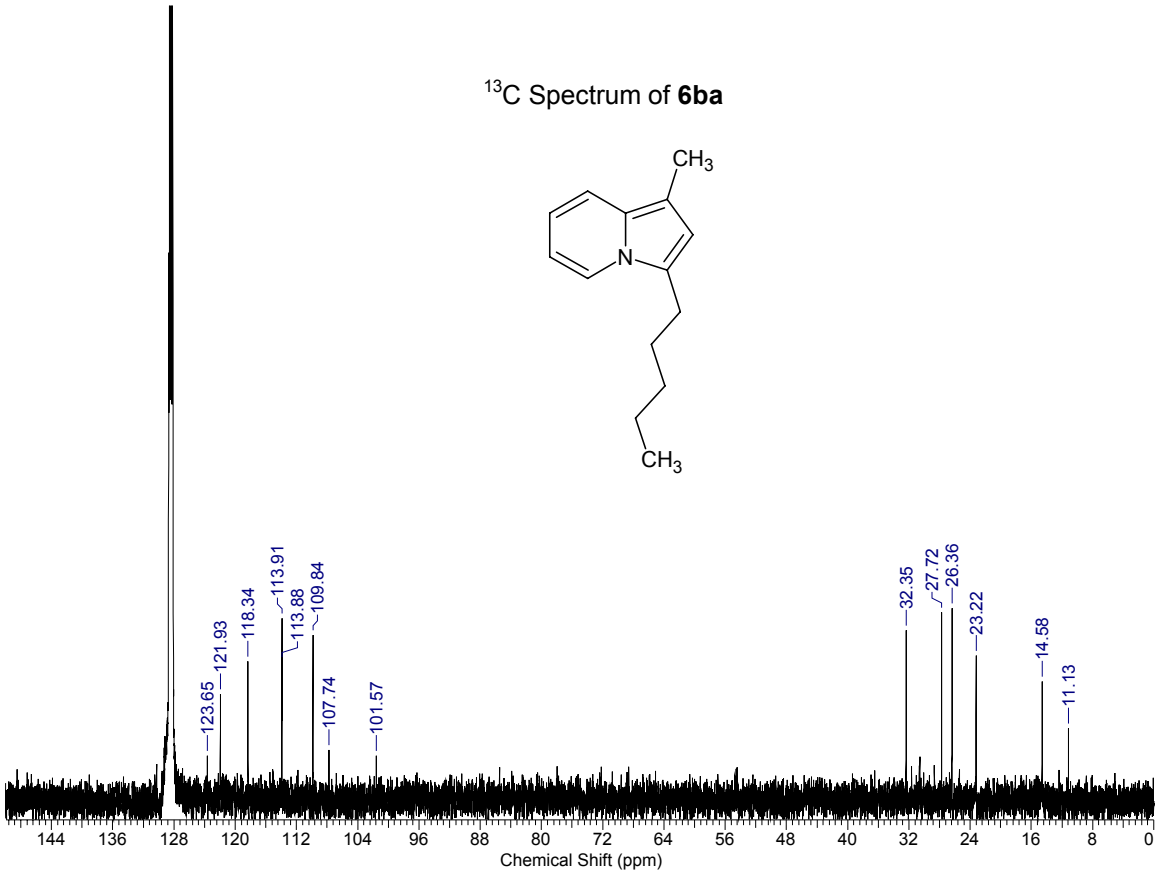
^{13}C Spectrum of **6ae**



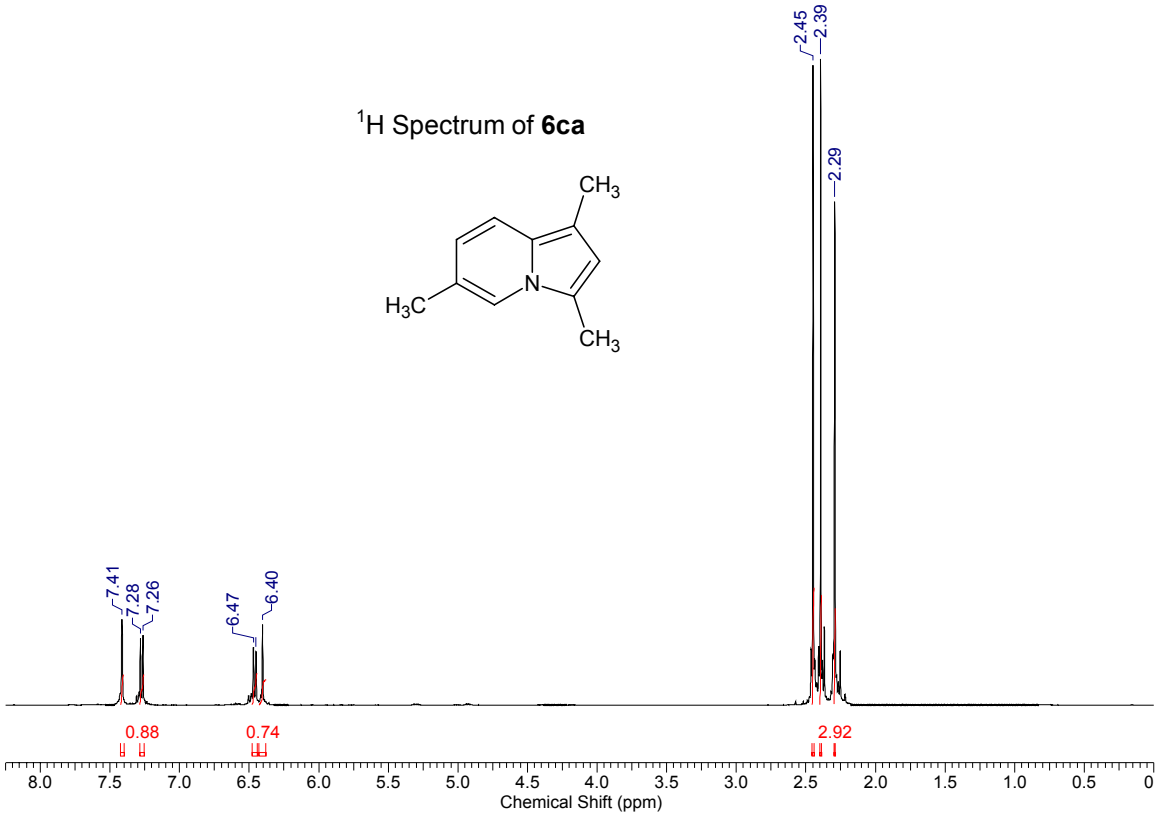
^{1}H Spectrum of **6ba**



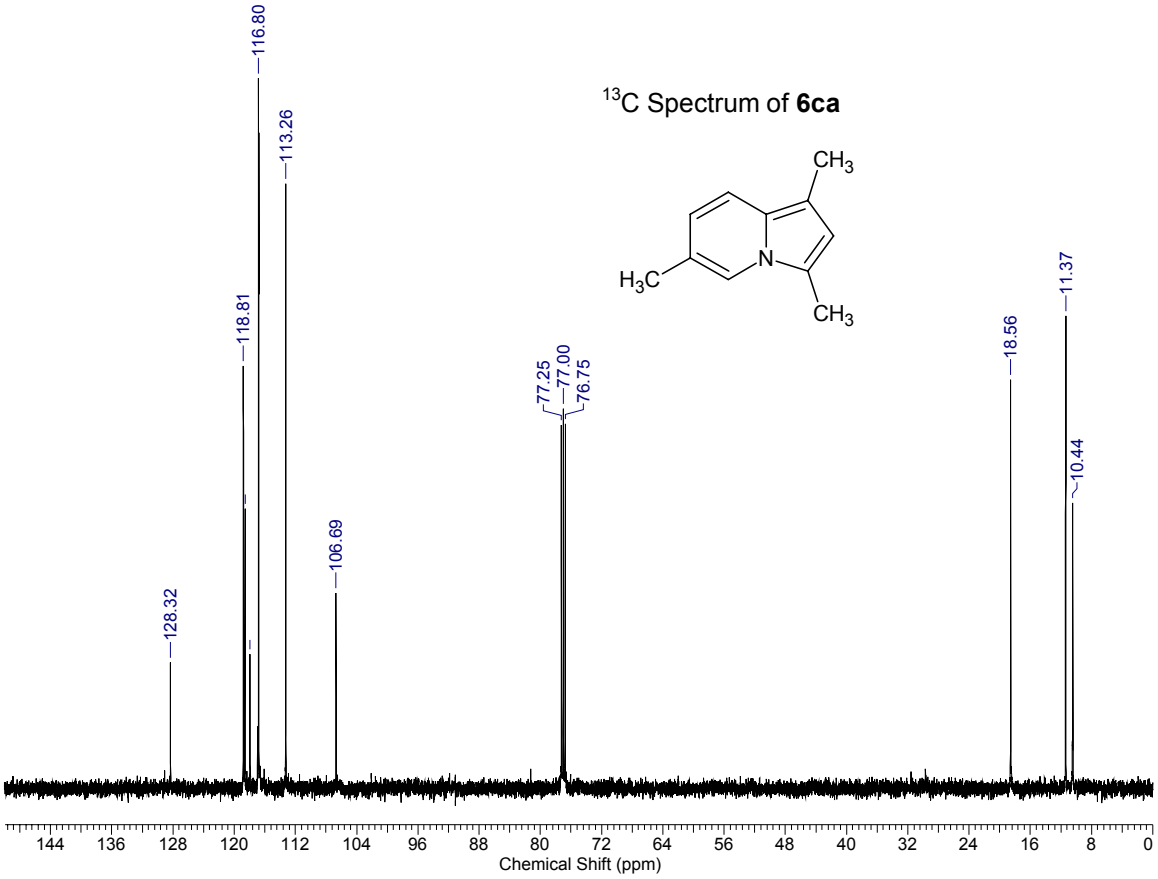
^{13}C Spectrum of **6ba**



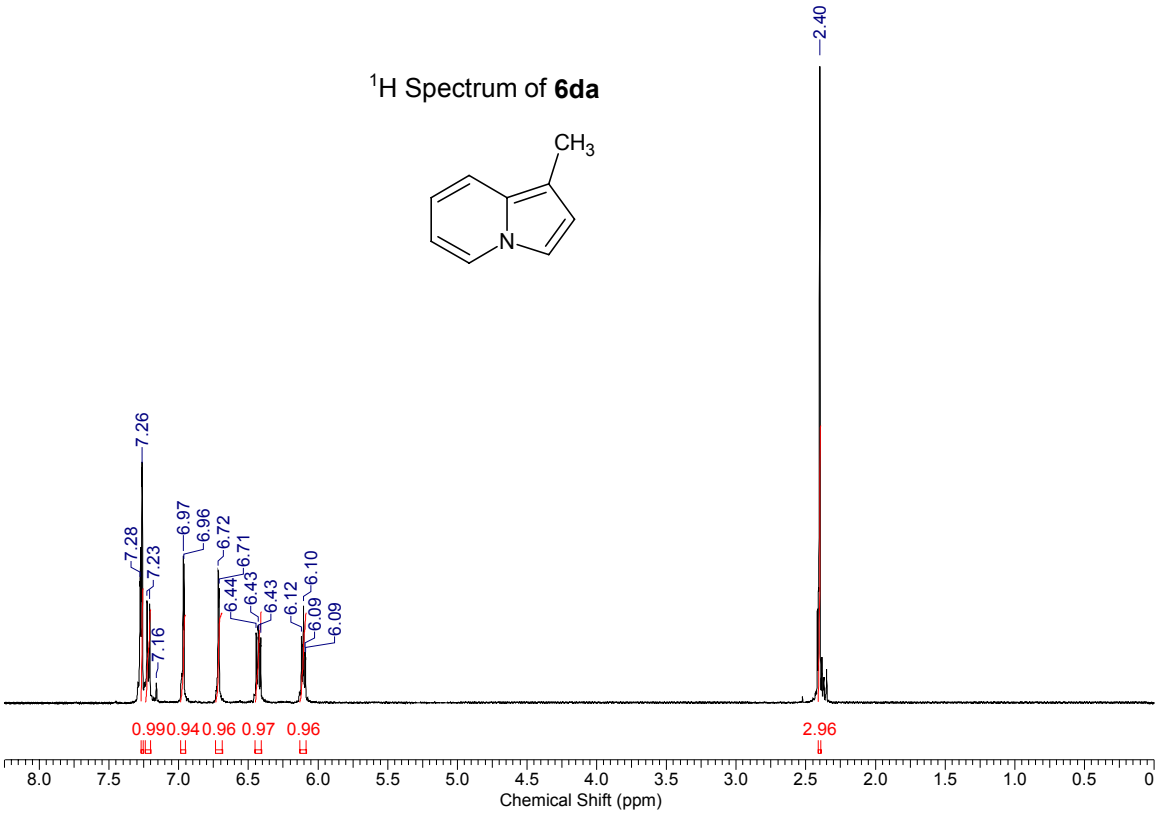
^{1}H Spectrum of **6ca**



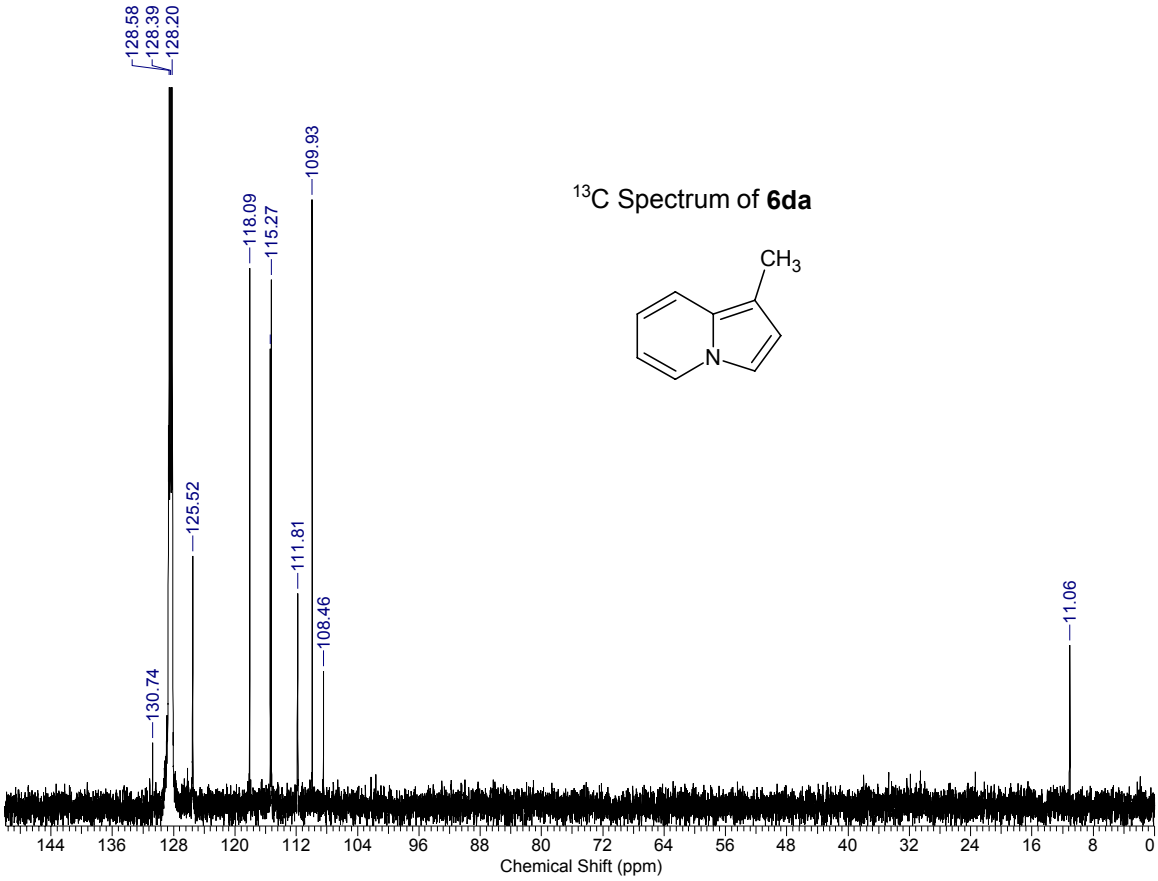
^{13}C Spectrum of **6ca**



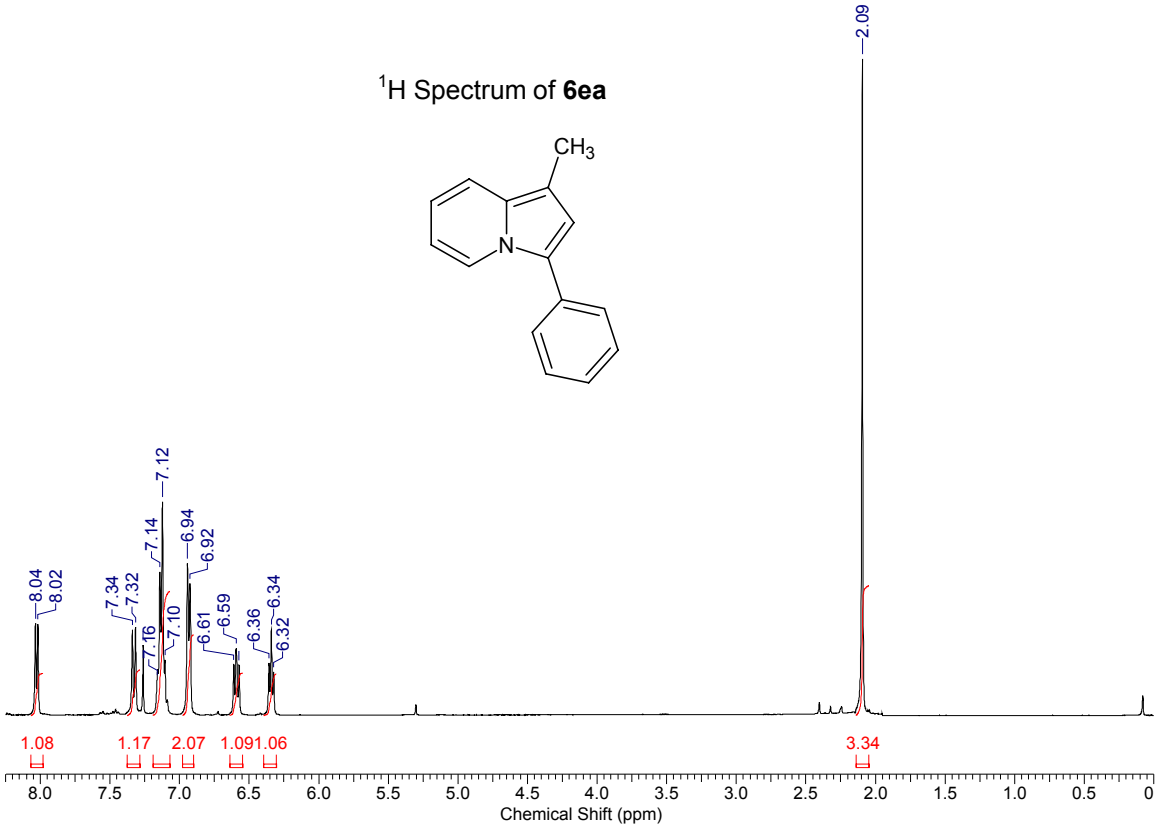
^{1}H Spectrum of **6da**



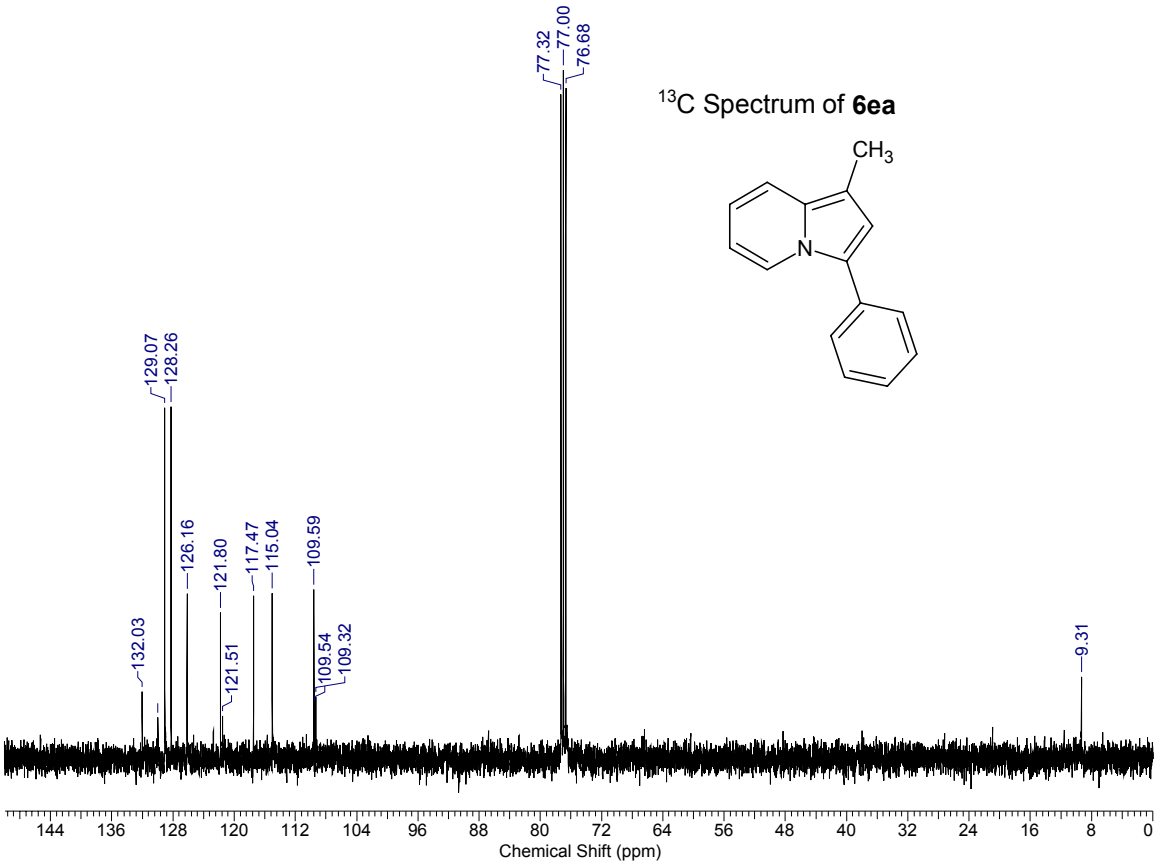
^{13}C Spectrum of **6da**

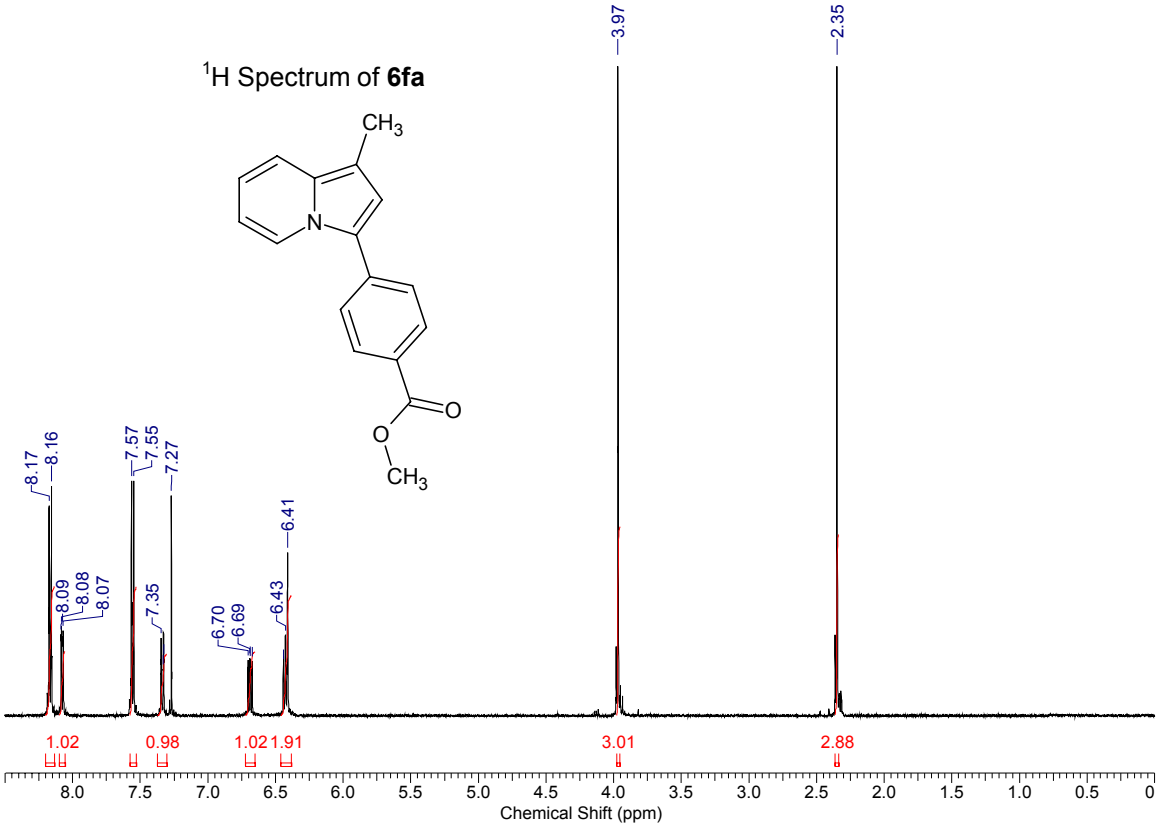


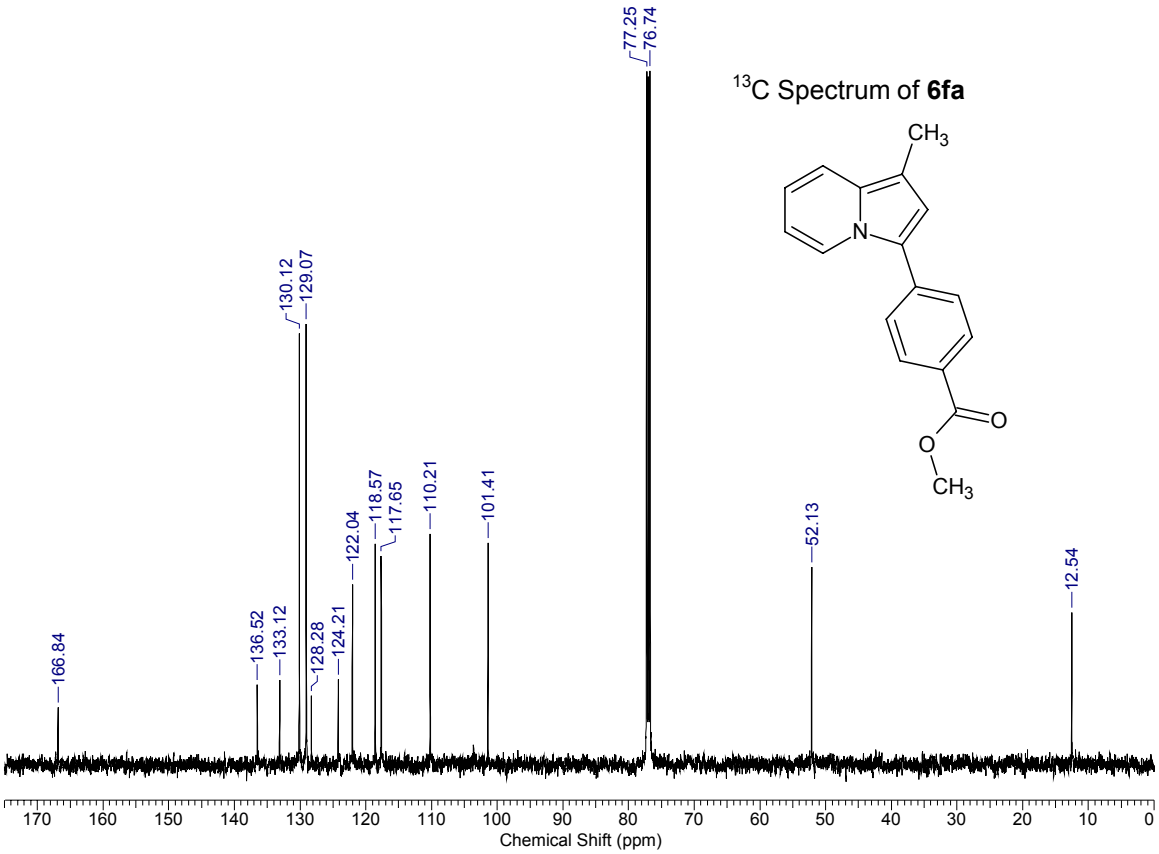
^{1}H Spectrum of **6ea**



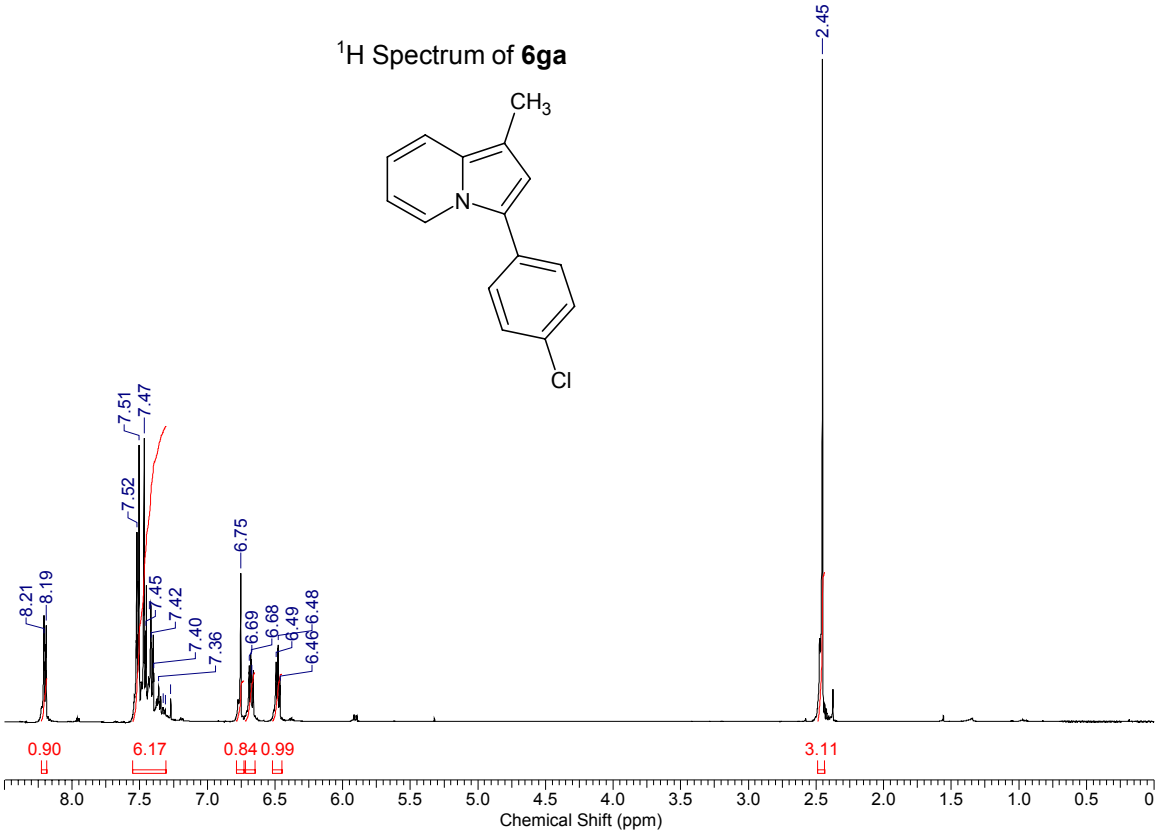
^{13}C Spectrum of **6ea**



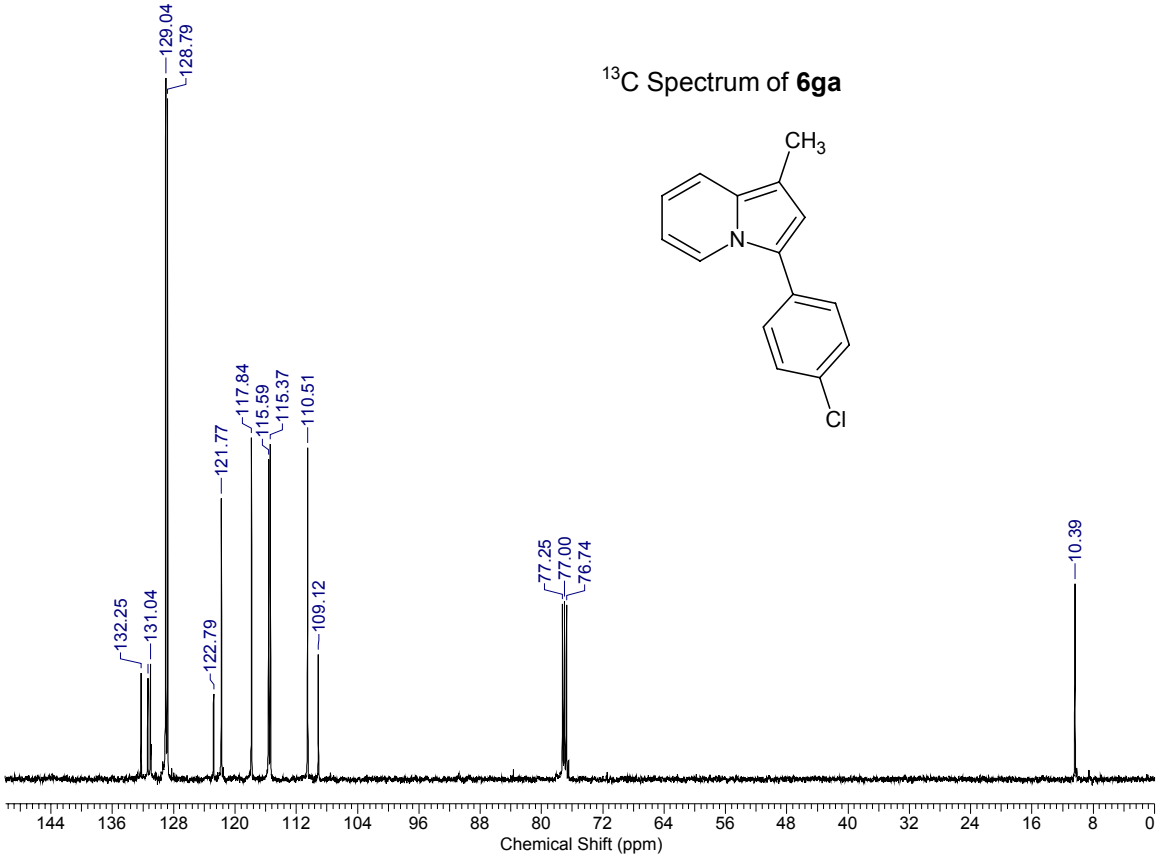

1H Spectrum of 6fa
CH3
N
O
O
CH3
8.17
8.16
8.09
8.08
8.07
7.57
7.55
7.27
7.35
6.70
6.69
6.43
6.41
3.97
2.35
1.02
0.98
1.02
1.91
3.01
2.88
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


13C Spectrum of 6fa
CH3
N
O
O
CH3
77.25
76.74
130.12
129.07
166.84
136.52
133.12
128.28
124.21
122.04
118.57
117.65
110.21
101.41
52.13
12.54
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

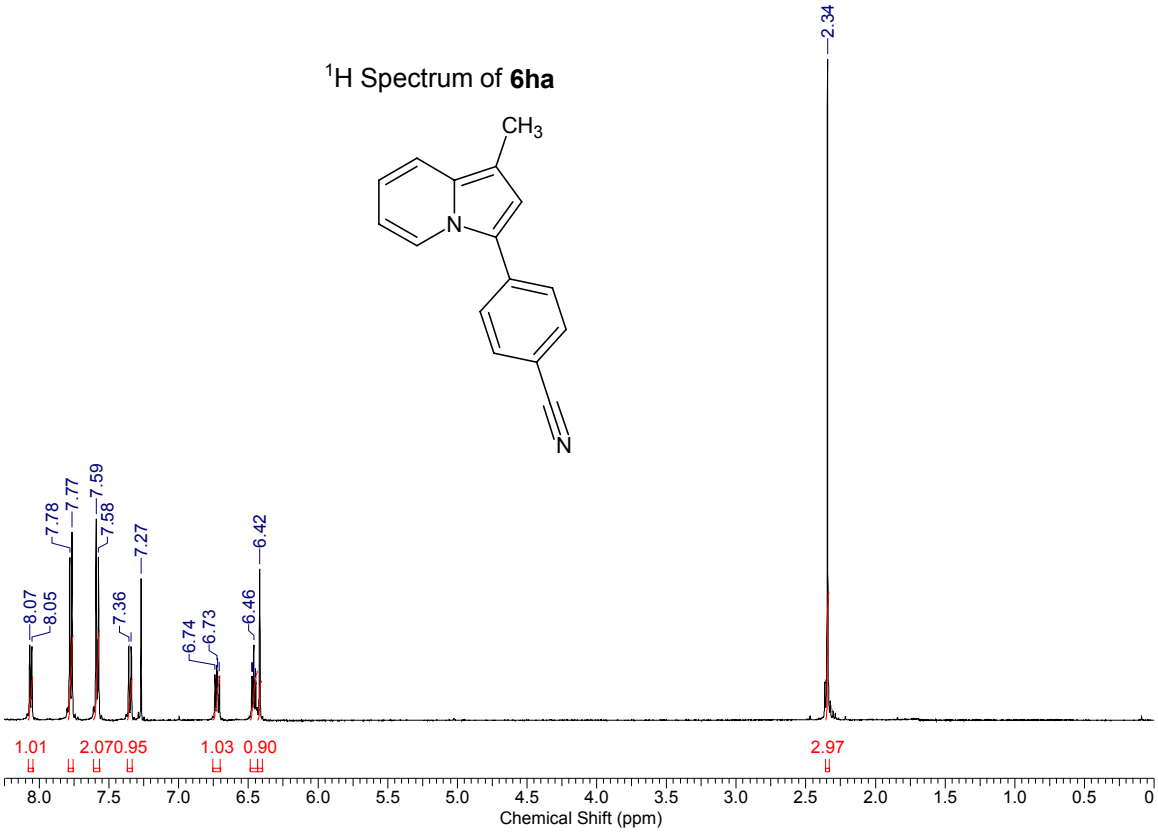
^{1}H Spectrum of **6ga**



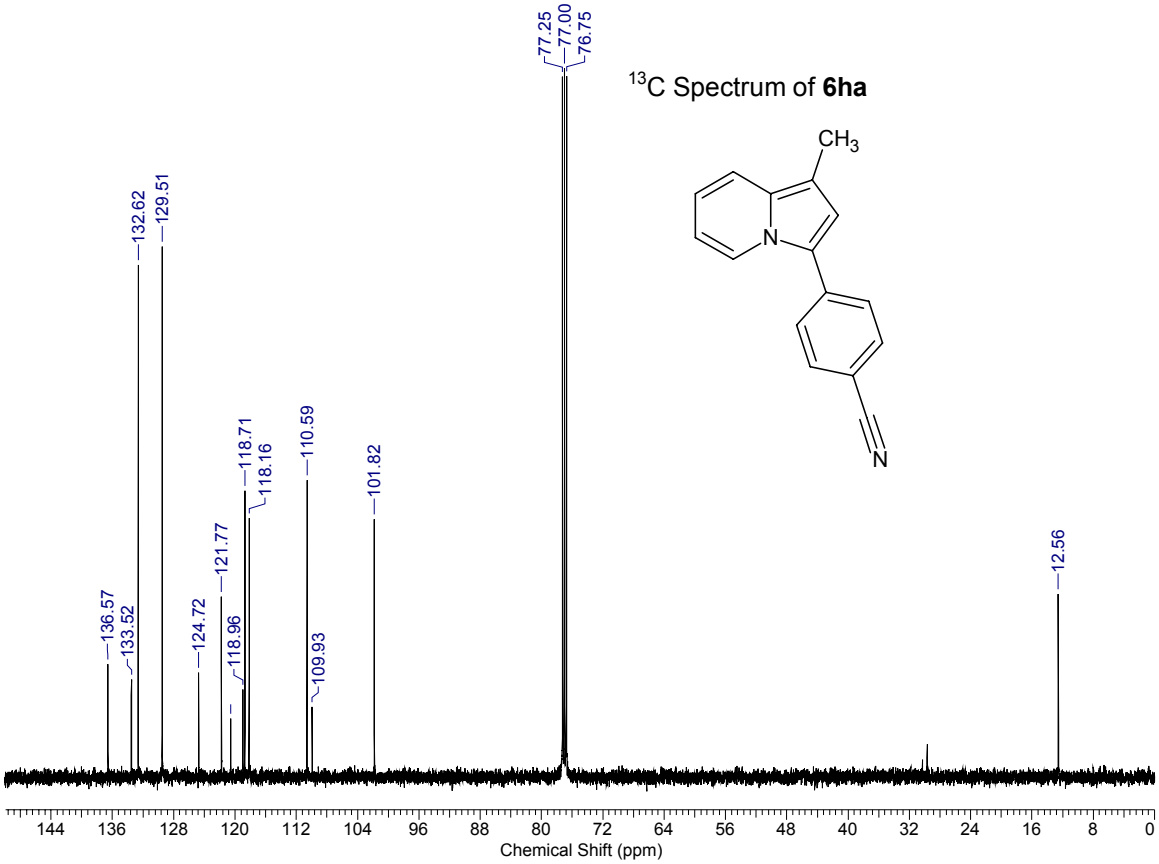
^{13}C Spectrum of **6ga**



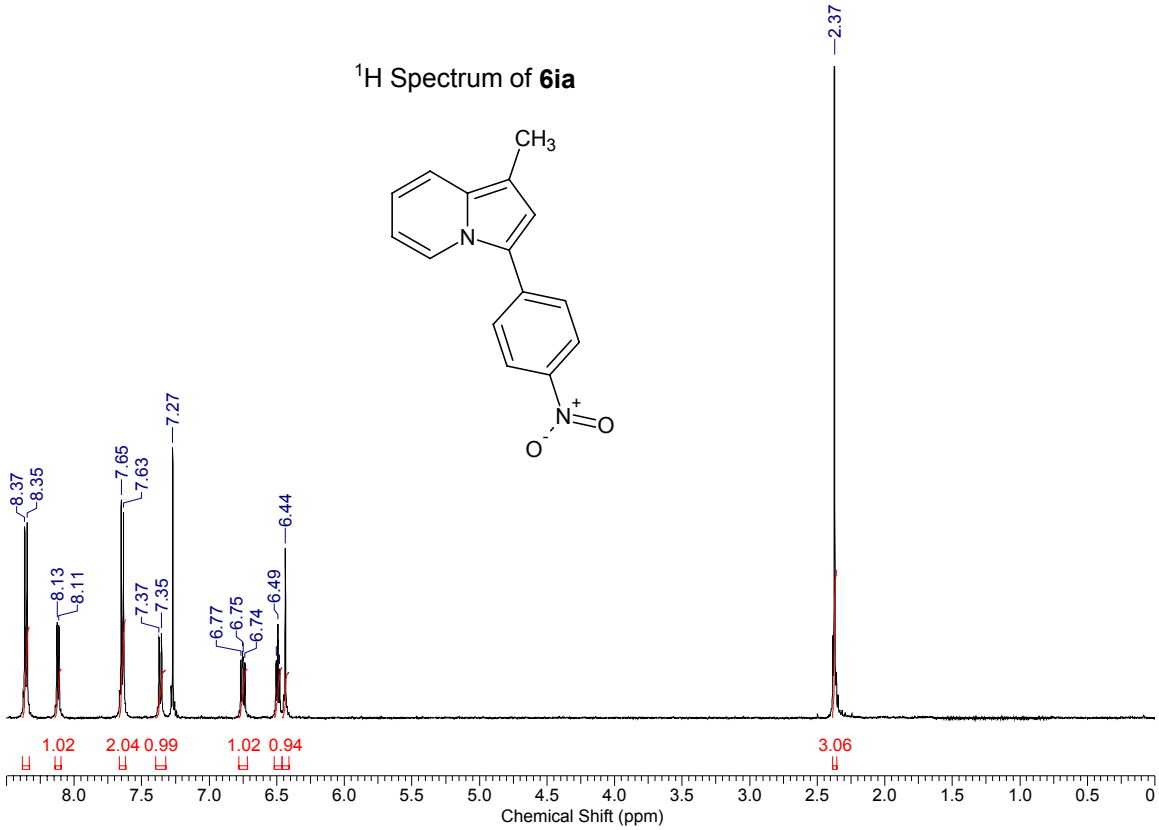
^{1}H Spectrum of **6ha**



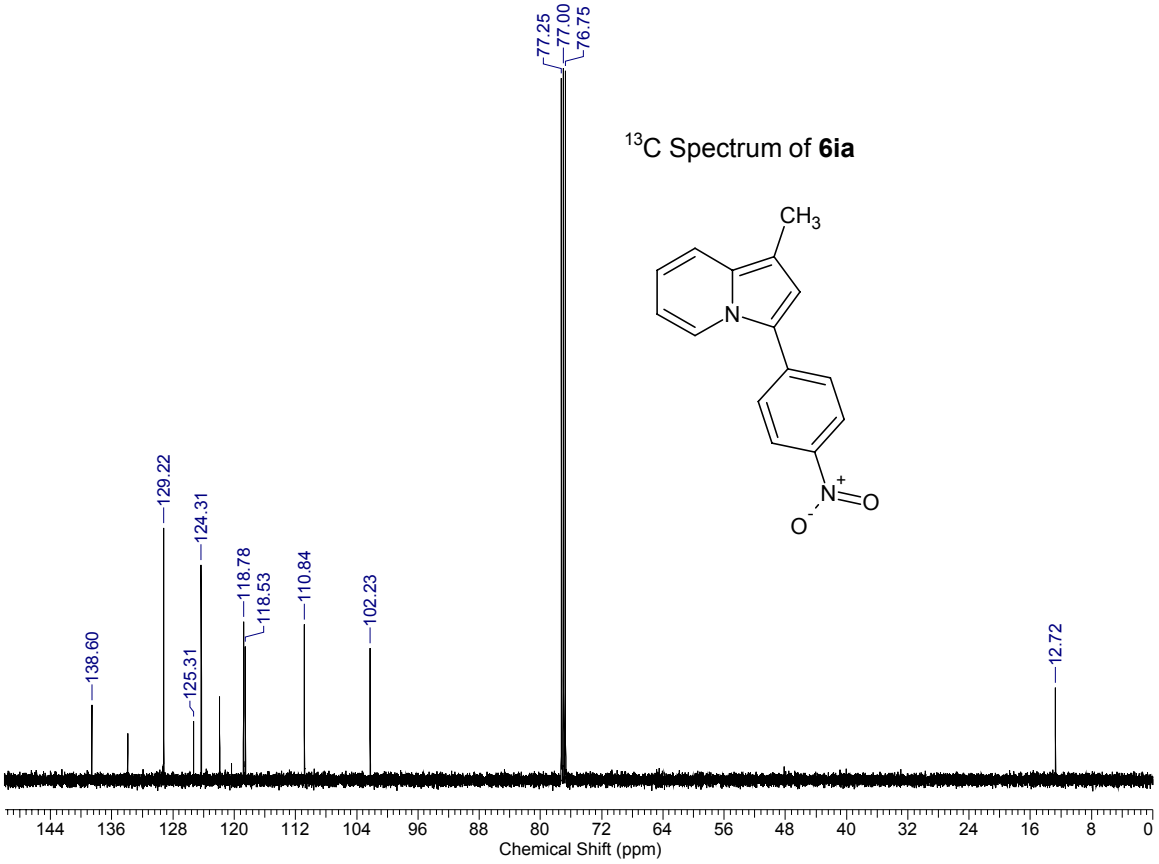
^{13}C Spectrum of **6ha**



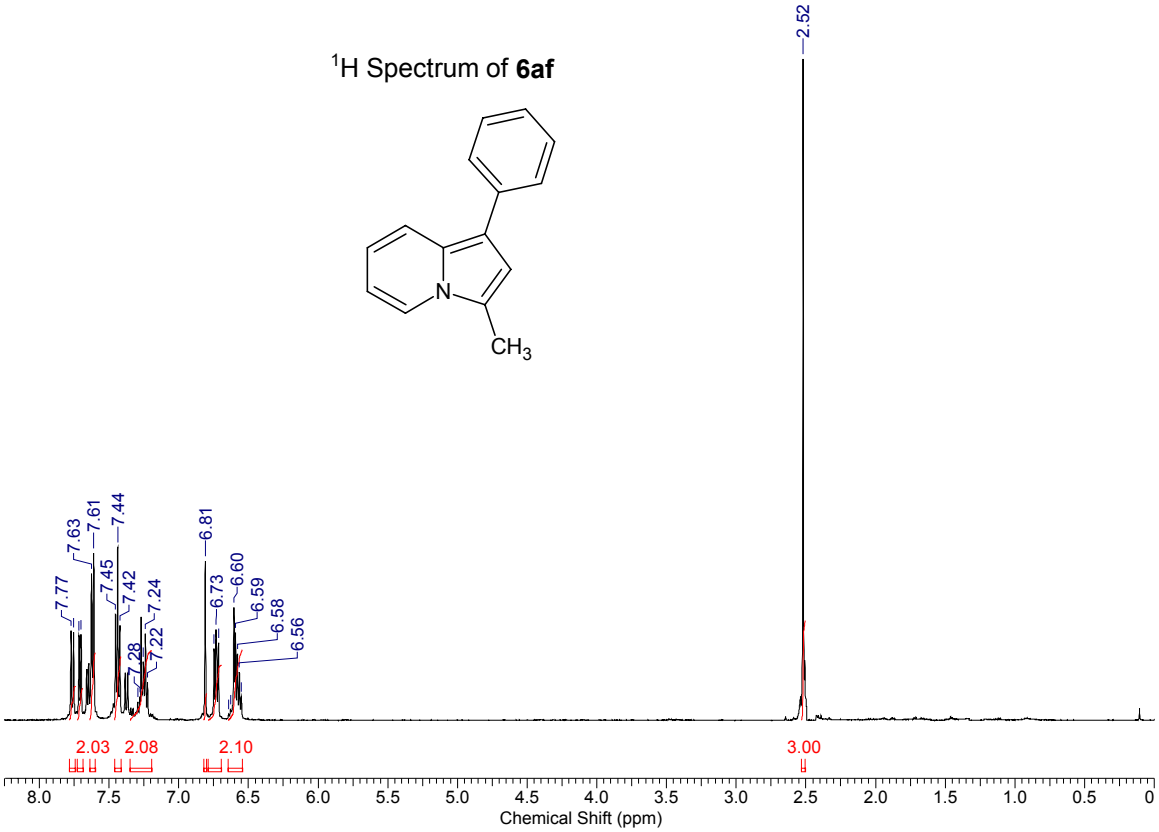
^{1}H Spectrum of **6ia**



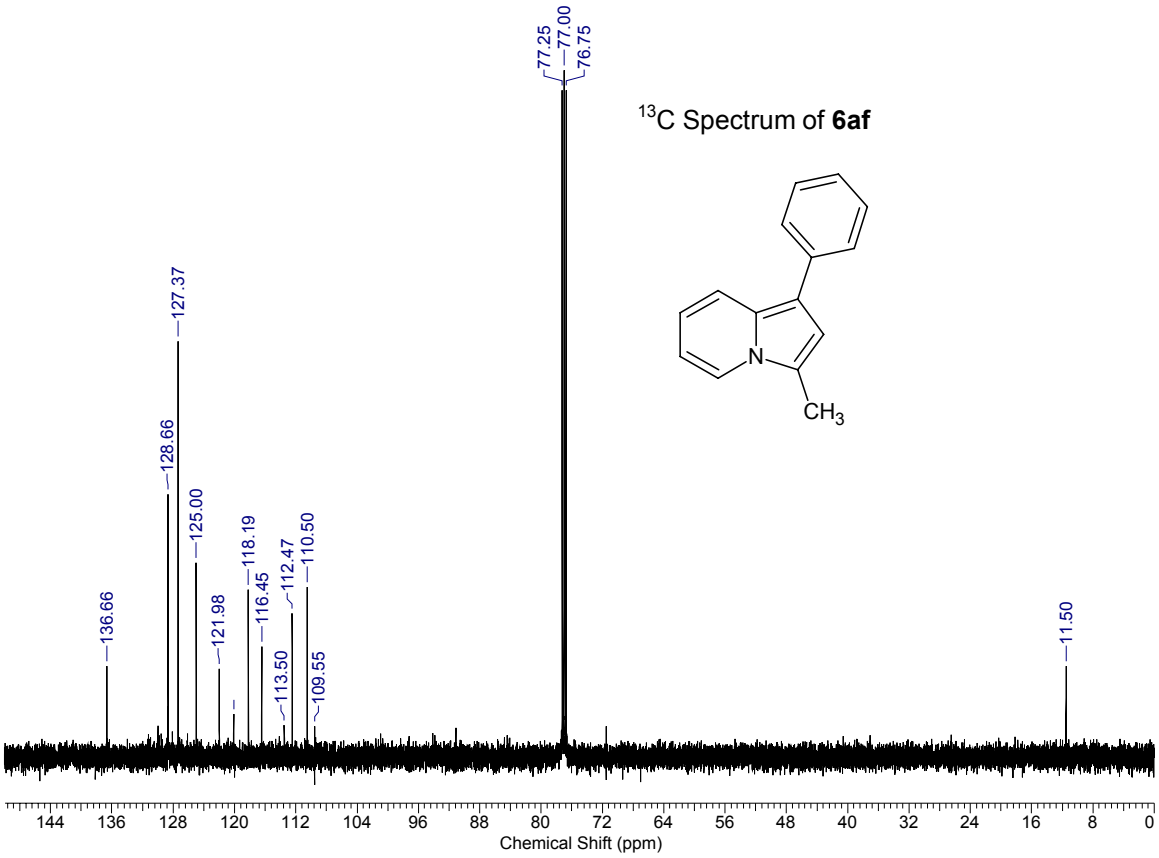
^{13}C Spectrum of **6ia**



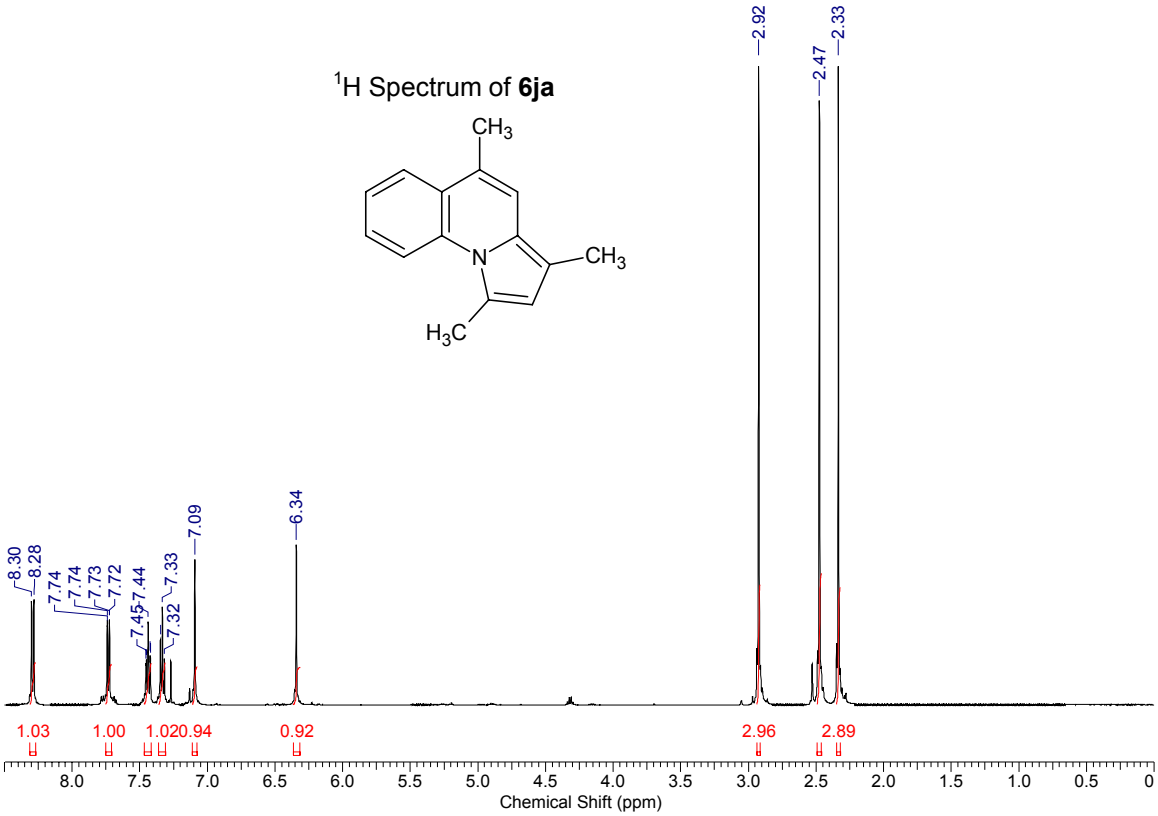
^{1}H Spectrum of **6af**



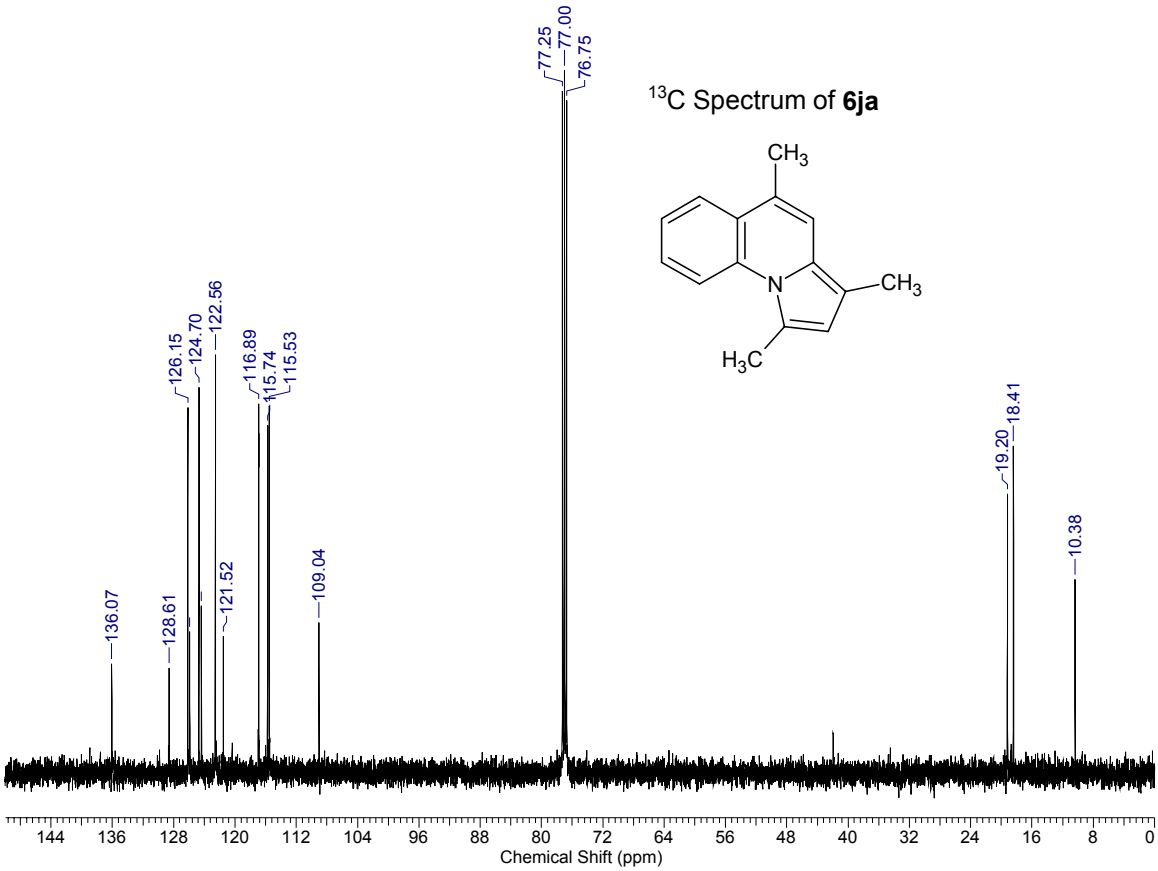
^{13}C Spectrum of **6af**



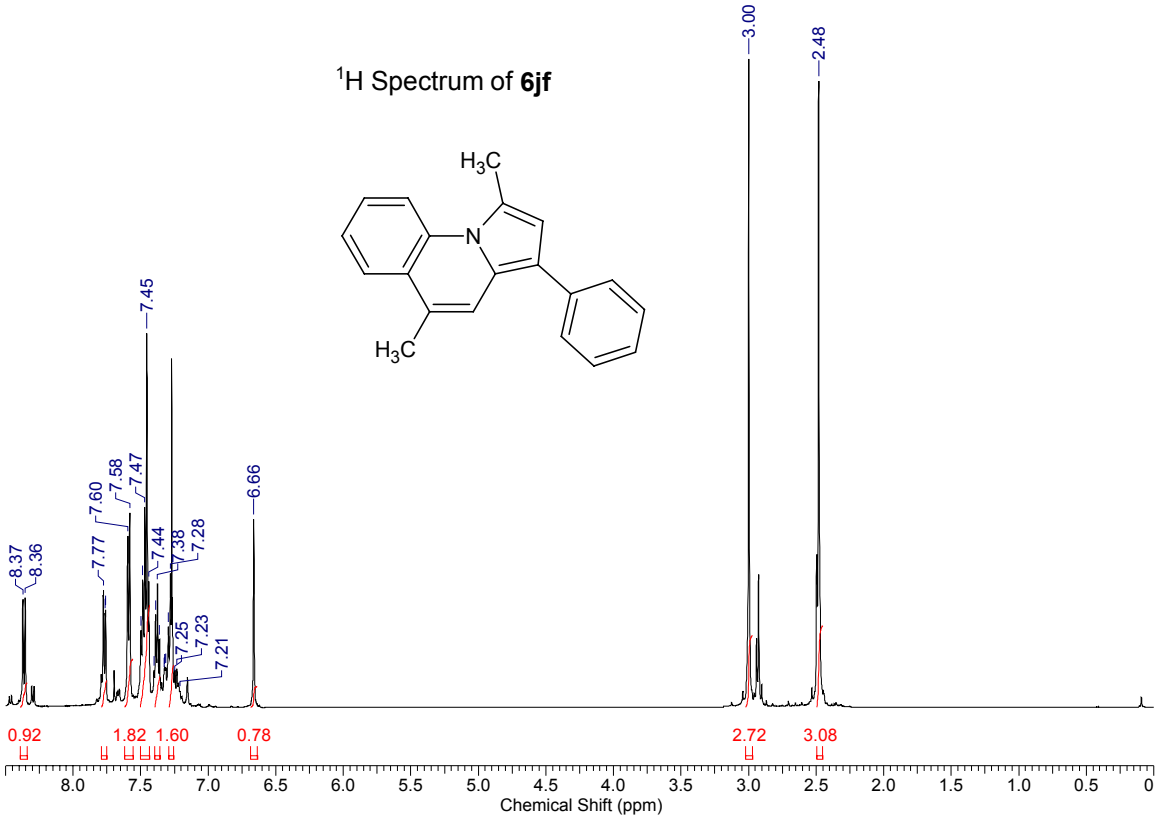
^{1}H Spectrum of **6ja**



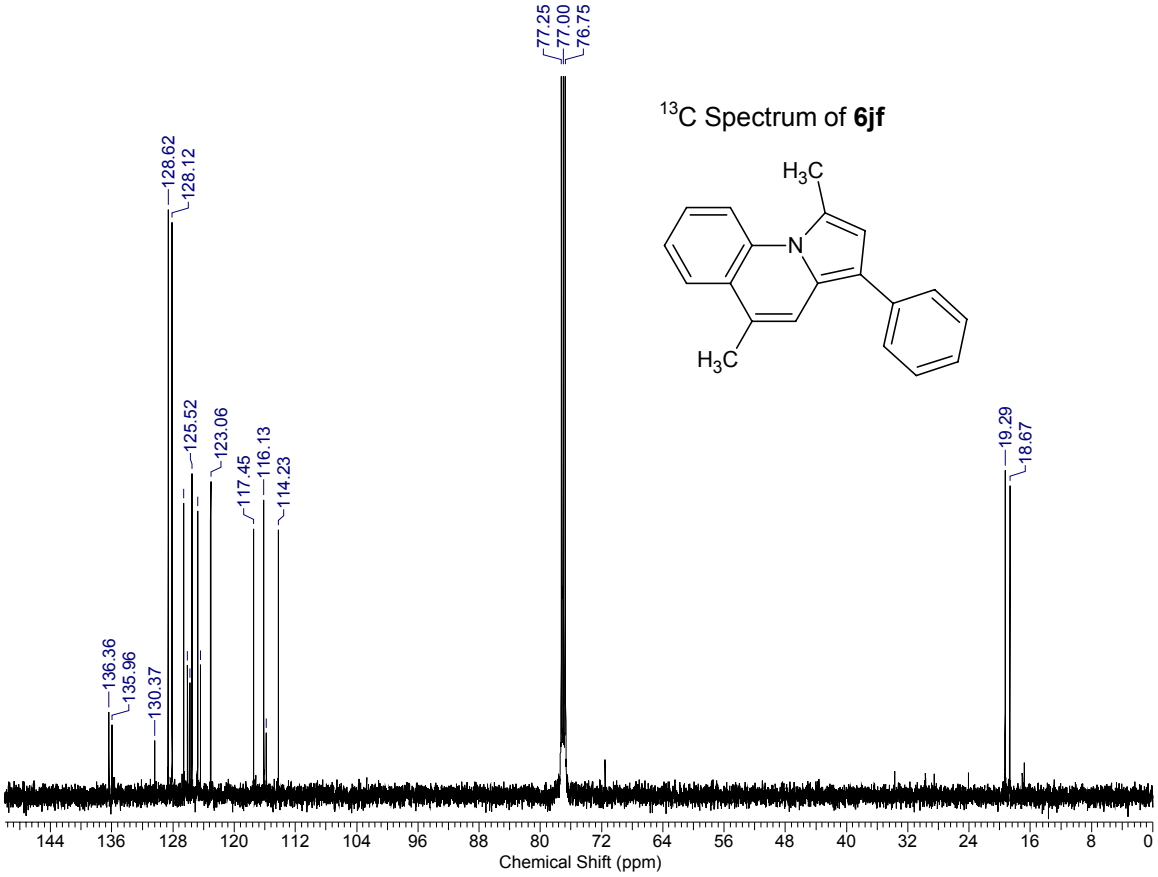
^{13}C Spectrum of **6ja**



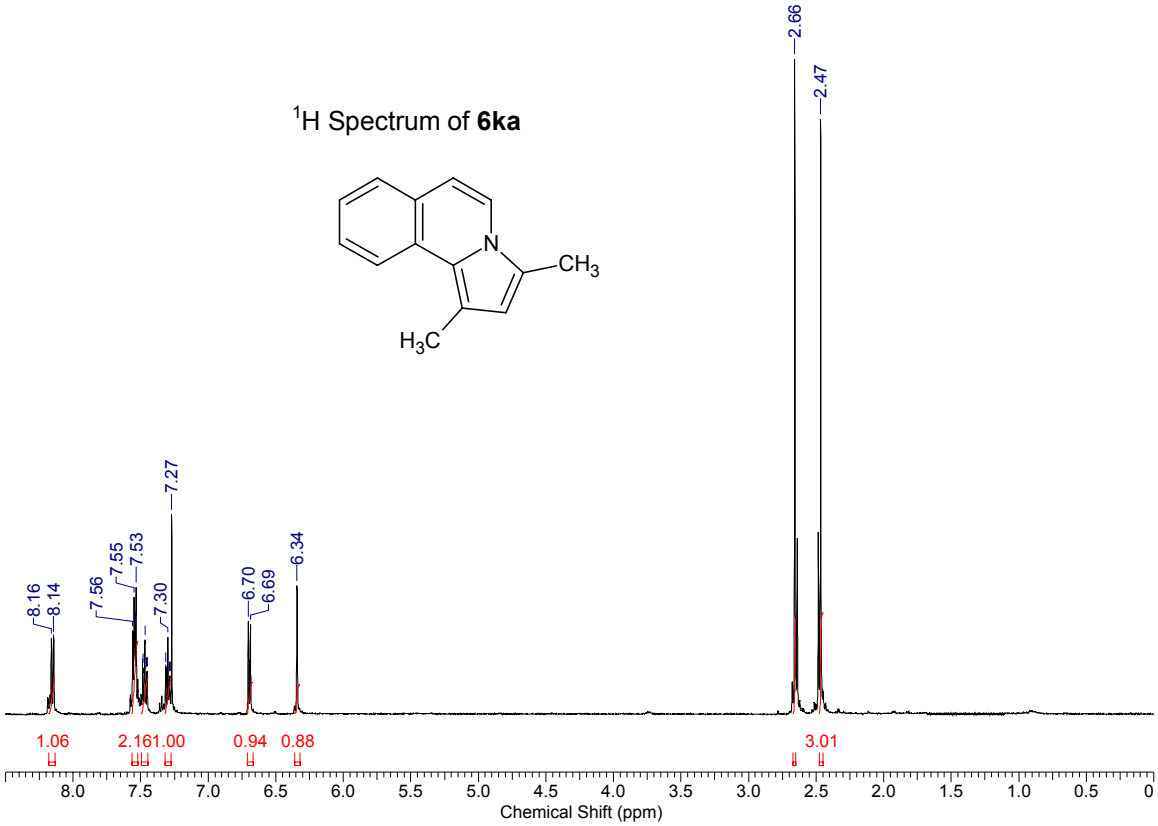
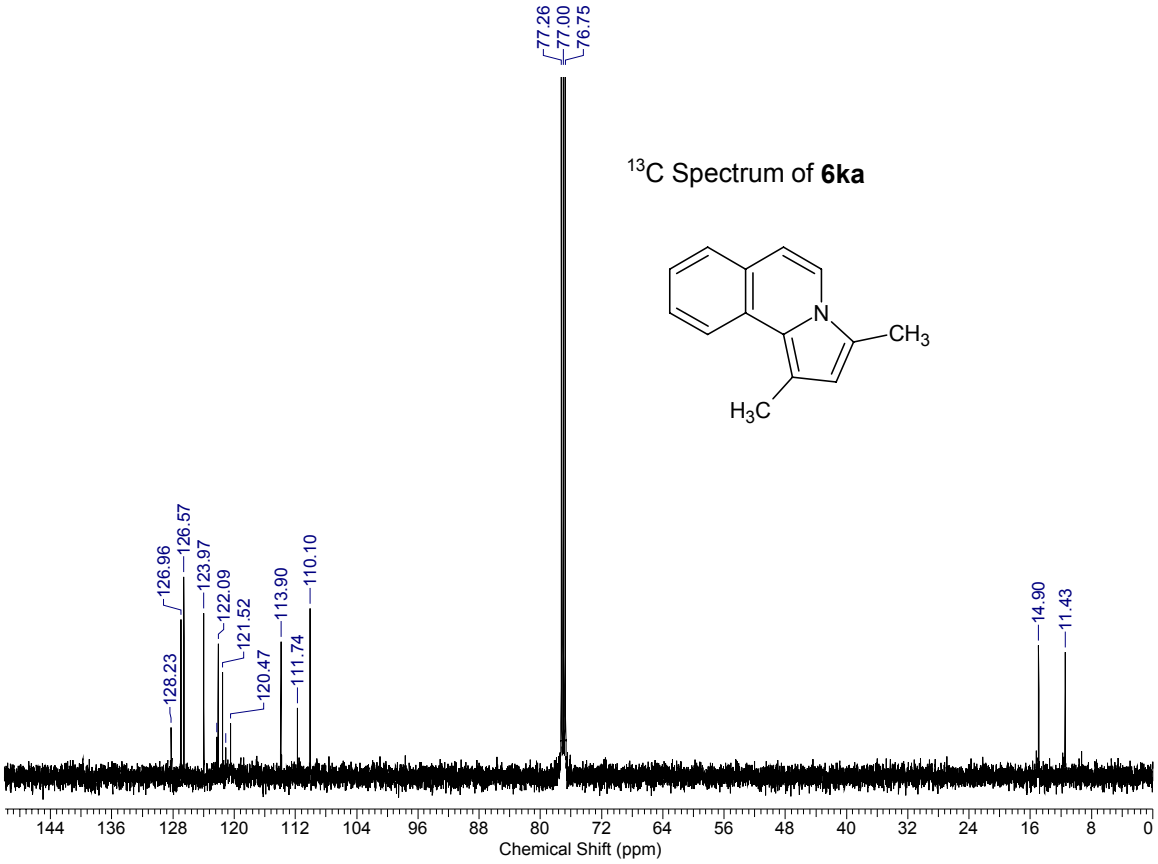
^{1}H Spectrum of **6jf**



^{13}C Spectrum of **6jf**



^{1}H Spectrum of **6ka**



^{13}C Spectrum of **6ka**