Supporting Information

Type 1 Ring-Opening Reactions of Cyclopropanated 7-Azabenzonorbornadienes with Organocuprates

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Contents

Part I: General Information

All experiments were conducted under inert atmosphere of dry argon. Glassware was oven-dried overnight. Column chromatography was performed on 230-400 mesh silica gel using flash column chromatography techniques.[1] Infrared samples were prepared as thin films on NaCl discs or acquired as solids on a Nicolet 380 FTIR spectrophotometer or Bruker ALPHA platinum single reflection diamond ATR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 or 400 MHz spectrometer equipped with a Cryoplatform® Prodigy cryoprobe. Chemical shift (δ) values for ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) with the solvent resonance as the internal standard (deuterochloroform; ^{1}H: δ 7.24 ppm; ^{13}C: δ 77.0 ppm). HRMS was performed at the Mass Spectrometry & Proteomics Services Unit of Queen's University, Kingston, Ontario. The samples were ionized by electron impact (EI) or positive electrospray ionization (ESI) and ion detection was performed by time of flight (TOF).

Reagents: Commercial reagents were purchased from Sigma-Aldrich and used without further purification. Organolithium reagents were titrated against (±)-menthol using 9H-fluorene as an indicator.[2] Dried and degassed solvents were obtained from an LC-SPS solvent purification system supplied with dry packed columns containing 3 Å molecular sieves. Cyclopropanated 7-azabenzonorbornadienes[3] and higher order cyanocuprate reagents[4] were prepared according to literature procedures.

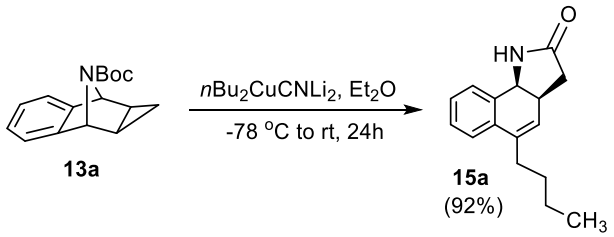
[1] Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[2] (a) Love, B.E.; Jones, E.G. *J. Org. Chem.* **1999**, *64*, 3755. (b) Li, J.J.; Limberakis, C.; Pflum, D.A. Modern Organic Synthesis in the Laboratory; Oxford University Press, Inc.: NY, 2007; Chapter 1.
[3] Carlson, E.; Tam, W. *Synthesis*, in press.
[4] (a) Lipshutz, B.H.; Wilhelm, R.S.; Kozlowski, J.A.; Parker, D. *J. Org. Chem.* **1984**, *49*, 3922. (b) Lipshutz, B.H.; Wilhelm, R.S.; Kozlowski, J.A. *J. Org. Chem.* **1984**, *49*, 3938.

Part II: General Procedure for Type 1 Ring-Opening Reactions

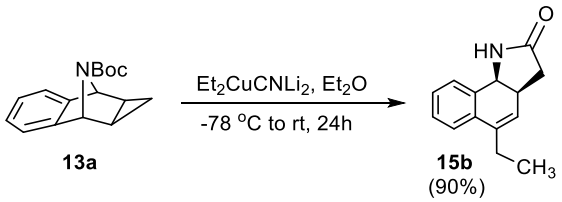
General procedure for Cu-catalyzed ring-opening reactions with higher order cyanocuprates:

CuCN (0.41 mmol, 3 equiv.) was weighed into an oven-dried Schlenk flask with stir bar, which was evacuated and back-filled with nitrogen or argon three times. Et_2O (4 mL) was added, and the suspension was cooled to -78 ˚C. To this, an organolithium reagent (0.83 mmol, 6 equiv.) was added dropwise with constant stirring to prepare the corresponding cyanocuprate. Cyclopropanated 7-azabenzonorbornadiene **13** (0.14 mmol, 1 equiv.), weighed into an oven-dried vial and purged with inert gas, was transferred to the organocuprate solution by cannula with rinses of Et_2O (3 × 0.5 mL). The cooling bath was removed and, once at room temperature, the flask was sealed. Upon completion of the reaction, the mixture was cooled in an ice bath and quenched by dropwise addition of 9:1 saturated aqueous NH_4Cl: conc.NH_4OH solution (pH 9-10). The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and dried over anhydrous $MgSO_4$. The organic extract was concentrated under rotary evaporation and purified by column chromatography (ethyl acetate/methanol mixture).

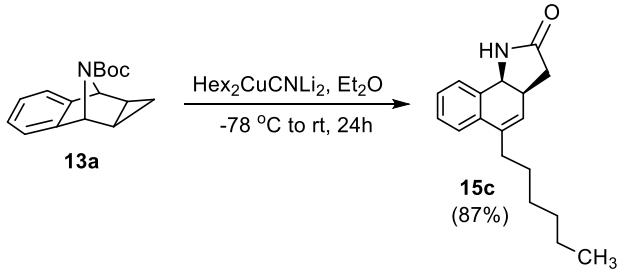
Part III: Characterization Data of Products



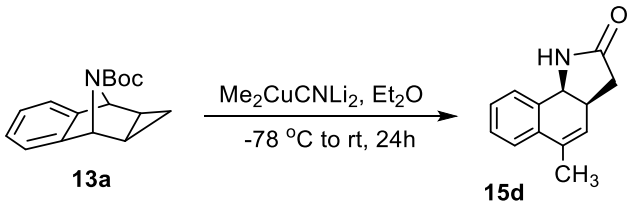
(3a*R,9b*S**)-5-Butyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15a (Table 1, entry 1):** (30.8 mg, 92% yield). White solid; mp: 141-143 ˚C; R_f (EtOAc): 0.14; IR (ν, cm^{-1}): 3194, 2943, 2923, 1683, 1425, 1373; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.30 (m, 2H), 7.23-7.19 (m, 2H), 6.08 (br s 1H), 5.44 (d, *J*=2.8 Hz, 1H), 4.77 (d, *J*=7.2 Hz, 1H), 3.33 (br dd *J*=8.2 Hz, 7.3 Hz, 1H), 2.76 (m, 1H), 2.47-2.34 (m, 2H), 2.30 (dd, *J*=16.5 Hz, 3.0 Hz, 1H), 1.53 (m, 2H), 1.39-1.33 (m, 2H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 135.0, 132.7, 131.4, 129.0, 128.9, 127.7, 125.4, 123.8, 55.2, 37.9, 35.0, 32.3, 30.5, 22.6, 14.0; HRMS: Calculated for $C_{16}H_{19}NO$ $[M]^+$: 241.1467. Found: 241.1471.



(3a*R,9b*S**)-5-Ethyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15b (Table 1, entry 3):** (20.5 mg, 90% yield). White solid; mp: 163-164 ˚C; R_f (EtOAc): 0.14; IR (ν, cm^{-1}): 3182, 3077, 2996, 2905, 1686, 1455, 1371; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.29 (m, 2H), 7.24-7.17 (m, 2H), 6.11 (br s 1H), 5.43 (d, *J*=1.2 Hz, 1H), 4.77 (d, *J*=7.3 Hz, 1H), 3.32 (dd *J*=7.9 Hz, 7.7 Hz, 1H), 2.75 (m, 1H), 2.47-2.41 (m, 2H), 2.31 (dd, *J*=16.5 Hz, 2.9 Hz, 1H), 1.14 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 136.3, 132.7, 131.3, 129.0, 128.8, 127.7, 124.4, 123.6, 55.2, 37.9, 34.9, 25.2, 12.8; HRMS: Calculated for $C_{14}H_{15}NO$ $[M]^+$: 213.1154. Found: 213.1151.

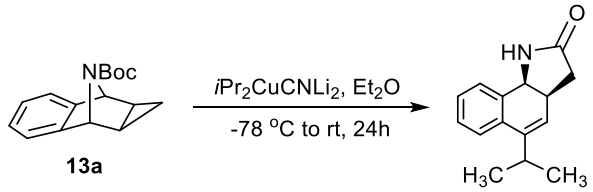


(3a*R,9b*S**)-5-Hexyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15c (Table 1, entry 4):** (34.8 mg, 87% yield). Beige solid; mp: 147-149 ˚C; R_f (EtOAc): 0.15; IR (ν, cm^{-1}): 3433, 3201, 2928, 2859, 1690, 1454, 1377; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.32 (m, 2H), 7.26-7.22 (m, 2H), 6.46 (br s 1H), 5.47 (d, *J*=2.8 Hz, 1H), 4.80 (d, *J*=7.3 Hz, 1H), 3.34 (br dd *J*=7.7 Hz, 7.7 Hz, 1H), 2.78 (m, 1H), 2.51-2.38 (m, 2H), 2.34 (dd, *J*=16.4 Hz, 3.1 Hz, 1H), 1.58-1.51 (m, 2H), 1.42-1.30 (m, 6H), 0.91 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 135.1, 132.7, 131.5, 128.89, 128.86, 127.7, 125.4, 123.8, 55.2, 37.9, 34.9, 32.6, 31.7, 29.3, 28.3, 22.7, 14.1; HRMS: Calculated for $C_{18}H_{23}NO$ $[M]^+$: 269.1780. Found: 269.1785.



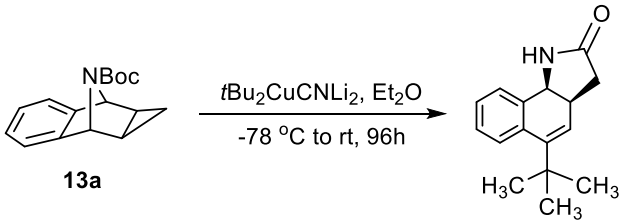
13a **15d** (75%)

(3a*R,9b*S**)-5-Methyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15d (Table 1, entry 7):** (17.0 mg, 75% yield). White solid; dec 152 ˚C; R_f (EtOAc): 0.13; IR (ν, cm^{-1}): 3161, 3065, 1695, 1493, 1440, 1373; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.06 (m, 4H), 6.12 (br s 1H), 5.40 (d, *J*=1.2 Hz, 1H), 4.74 (d, *J*=7.3 Hz, 1H), 3.27 (dd *J*=7.9 Hz, 7.7 Hz, 1H), 2.71 (m, 1H), 2.29 (dd, *J*=16.5 Hz, 2.9 Hz, 1H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.8, 133.3, 130.9, 130.8, 129.0, 128.5, 127.8, 126.3, 123.9, 55.2, 37.7, 34.9, 19.3; HRMS: Calculated for $C_{13}H_{13}NO$ $[M]^+$: 199.0997. Found: 199.0995.



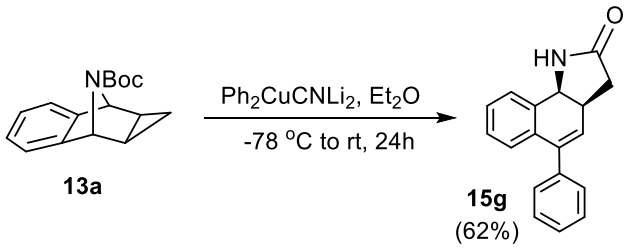
13a **15e** (73%)

(3a*R,9b*S**)-5-*iso*Propyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15e (Table 1, entry 8):** (19.8 mg, 73% yield). White solid; mp: 146-148 ˚C; R_f (EtOAc): 0.17; IR (ν, cm^{-1}): 3173, 3070, 2958, 1689, 1493, 1452, 1369; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J*=7.7 Hz, 1H), 7.35-7.31 (m, 1H), 7.22-7.16 (m, 2H), 5.70 (br s 1H), 5.43 (d, *J*=2.9 Hz, 1H), 4.74 (d, *J*=7.2 Hz, 1H), 3.33 (dd *J*=8.2 Hz, 7.3 Hz, 1H), 2.96-2.89 (m, 1H), 2.81-2.75 (m, 1H), 2.32 (dd, *J*=16.5 Hz, 3.0 Hz, 1H), 1.16 (d, *J*=6.7 Hz, 3H), 1.11 (d, *J*=6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 140.9, 132.5, 131.5, 129.0, 128.9, 127.5, 123.6, 122.2, 55.1, 38.0, 34.8, 28.0, 22.3, 22.0; HRMS: Calculated for $C_{15}H_{17}NO$ $[M]^+$: 227.1310. Found: 227.1315.

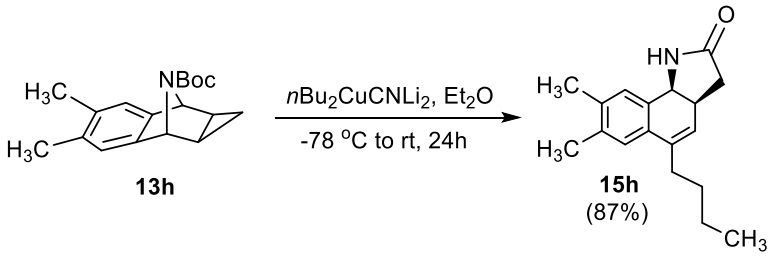


13a **15f** (69%)

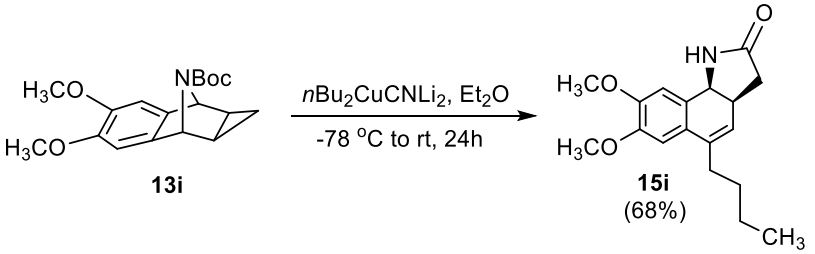
(3a*R,9b*S**)-5-*tert*Butyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15f (Table 1, entry 11):** (20.6 mg, 69% yield). White solid; mp: 156-158 ˚C; R_f (EtOAc): 0.15; IR (ν, cm^{-1}): 3214, 3073, 2958, 2905, 1691, 1488, 1367; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J*= 8.0 Hz, 1H), 7.32-7.27 (m, 1H), 7.18 (d, *J*= 4.2 Hz, 2H), 5.92 (br s 1H), 5.55 (d, *J*=2.8 Hz, 1H), 4.68 (d, *J*=7.0 Hz, 1H), 3.25 (dd *J*=7.6 Hz, 7.6 Hz, 1H), 2.76 (m, 1H), 2.31 (dd, *J*=16.4 Hz, 2.4 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 143.0, 132.4, 132.3, 129.7, 128.2, 127.2, 127.0, 124.8, 55.5, 38.3, 35.1, 35.0, 30.9; HRMS: Calculated for $C_{16}H_{19}NO$ $[M]^+$: 241.1467. Found: 241.1461.



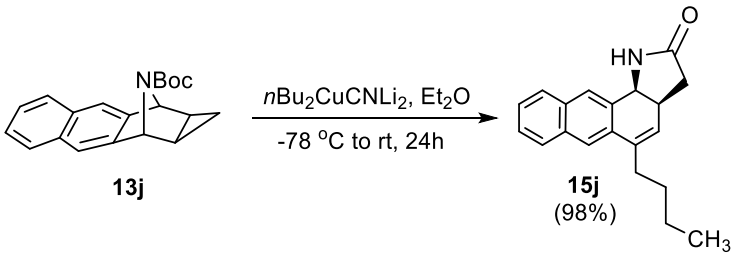
(3a*R,9b*S**)-5-Phenyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15g (Table 1, entry 12):** (19.2 mg, 62% yield). Beige solid; mp: dec 175 ˚C; R_f (EtOAc): 0.14; IR (ν, cm^{-1}) 3289, 2915, 1683, 1670, 1292, 1262; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38-7.19 (m, 8H), 7.03 (d, *J*=1.4 Hz, 1H), 6.39 (br s 1H), 5.60 (d, *J*=3.0 Hz, 1H), 4.87 (d, *J*=7.3 Hz, 1H), 3.50-3.43 (m, 1H), 2.87-2.78 (m, 1H), 2.39 (dd, *J*=16.5 Hz, 3.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.7, 139.6, 138.6, 132.7, 131.3, 128.9, 128.4, 128.2, 127.5, 126.5, 55.2, 37.6, 35.3; HRMS: Calculated for $C_{18}H_{15}NO$ $[M]^+$: 261.1154. Found: 261.1161.



(3a*R,9b*S**)-5-Butyl-7,8-dimethyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15h (Table 2, entry 2):** (18.1 mg, 87% yield); beige solid; mp: 164-165 ˚C; R_f (EtOAc): 0.24; IR (ν, cm^{-1}): 3165, 3078, 2963, 2923, 2860, 1693, 1505, 1470, 1372, 790; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (s, 1H), 6.94 (s, 1H), 5.56 (br s, 1H), 5.36 (d, *J*=2.4 Hz, 1H), 4.70 (d, *J*=7.1 Hz, 1H), 3.29 (br dd *J*=7.6 Hz, 7.5 Hz, 1H), 2.76 (m, 1H), 2.45-2.39 (m, 2H), 2.38 (dd, *J*=16.4 Hz, 2.6 Hz, 1H), 2.27 (s, 3H), 2.25 (s, 3H), 1.53 (m, 2H), 1.49-1.35 (m, 2H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 137.1, 136.0, 135.0, 130.4, 130.3, 128.7, 125.2, 124.6, 55.0, 38.0, 35.1, 32.2, 30.5, 22.6, 19.9, 19.4, 14.0; HRMS: Calculated for $C_{18}H_{23}NO$ $[M]^+$: 269.1780. Found: 269.1785.

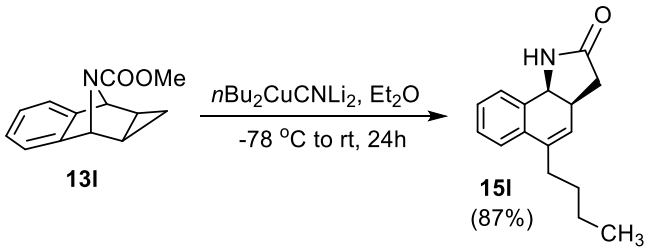


(3a*R,9b*S**)-5-Butyl-7,8-dimethoxy-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15i (Table 2, entry 3):** (13.3 mg, 68% yield); white solid; dec 188 ˚C; R_f (EtOAc): 0.09; IR (ν, cm^{-1}): 3174, 3075, 2950, 2927, 2865, 2834, 1678, 1518, 1231, 1181, 879; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.72 (s, 1H), 5.88 (br s, 1H), 5.34 (d, *J*=3.8 Hz, 1H), 4.71 (d, *J*=7.3 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.32 (br dd *J*=7.6 Hz, 7.5 Hz, 1H), 2.76 (m, 1H), 2.44-2.36 (m, 2H), 2.31 (dd, *J*=12.6 Hz, 3.0 Hz, 1H), 1.55-1.50 (m, 2H), 1.48-1.32 (m, 2H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 148.9, 148.1, 134.6, 126.0, 124.0, 123.7, 112.1, 107.7, 56.1, 55.2, 37.9, 35.2, 32.4, 30.5, 22.6, 14.0; HRMS: Calculated for $C_{18}H_{23}NO_3$ $[M]^+$: 301.1678. Found: 301.1671.



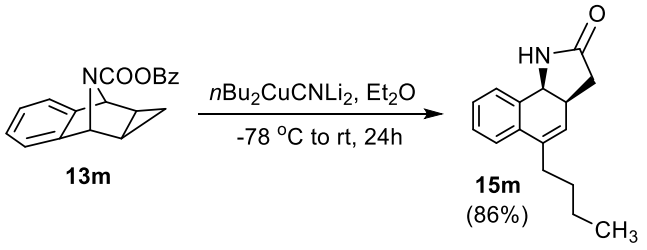
13j **15j** (98%)

(3a*R,11b*S**)-5-Butyl-1,3,3a,11b-tetrahydro-2*H*-naphtho[2,3-*g*]indol-2-one, 15j (Table 2, entry 4):** (20.1 mg, 98% yield); white solid; dec 167 ˚C; R_f (EtOAc): 0.19; IR (ν, cm^{-1}): 3200, 2956, 2922, 1674, 1501, 1426, 1365, 1303, 1254, 1207, 1125, 965, 758, 735; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.78 (m, 1H), 7.76 (s, 2H), 7.63 (s, 1H), 7.49-7.43 (m, 2H), 6.00 (br s, 1H), 5.52 (d, *J*=1.8 Hz, 1H), 4.90 (d, *J*=6.6 Hz, 1H), 3.35 (br dd, *J*=7.6 Hz, 7.6 Hz, 1H), 2.80 (m, 1H), 2.64-2.47 (m, 2H), 2.33 (dd, *J*=16.4 Hz, 2.5 Hz, 1H), 1.64-1.56 (m, 2H), 1.47-1.41 (m, 2H), 0.97 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 135.4, 133.8, 132.5, 130.3, 130.1, 128.2, 127.4, 126.6, 126.3, 126.2, 122.7, 55.6, 38.2, 35.2, 32.4, 30.5, 22.7, 14.1; HRMS: Calculated for $C_{20}H_{21}NO$ $[M]^+$: 291.1623. Found: 291.1620.



13l **15l** (87%)

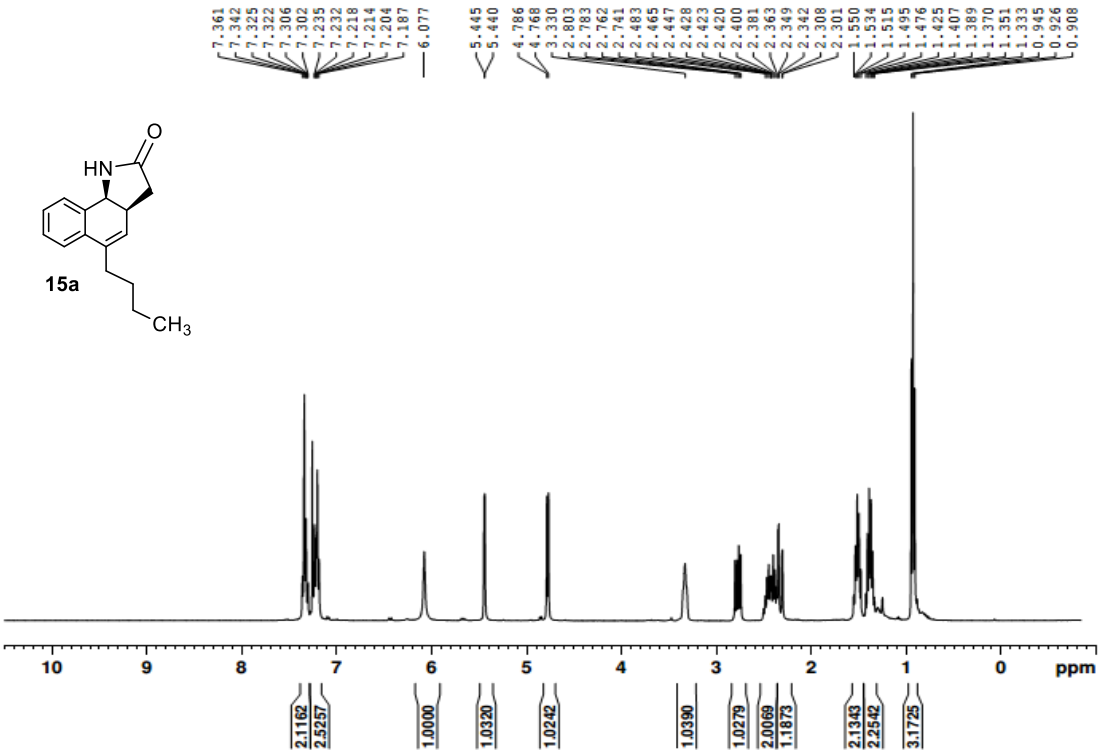
(3a*R,9b*S**)-5-Butyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15l (Table 2, entry 6):** (26.3 mg, 87 % yield). The characterization data for this compound was identical to that of compound **15a**.



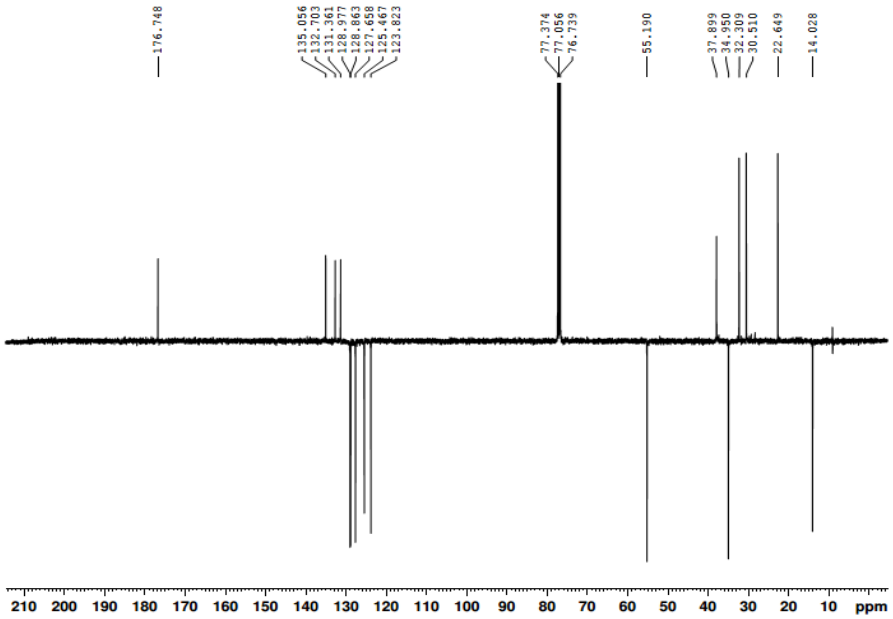
13m **15m** (86%)

(3a*R,9b*S**)-5-Butyl-1,3,3a,9b-tetrahydro-*2H*-benzo[*g*]indol-2one, 15m (Table 2, entry 7):** (27.2 mg, 86 % yield). The characterization data for this compound was identical to that of compound **15a**.

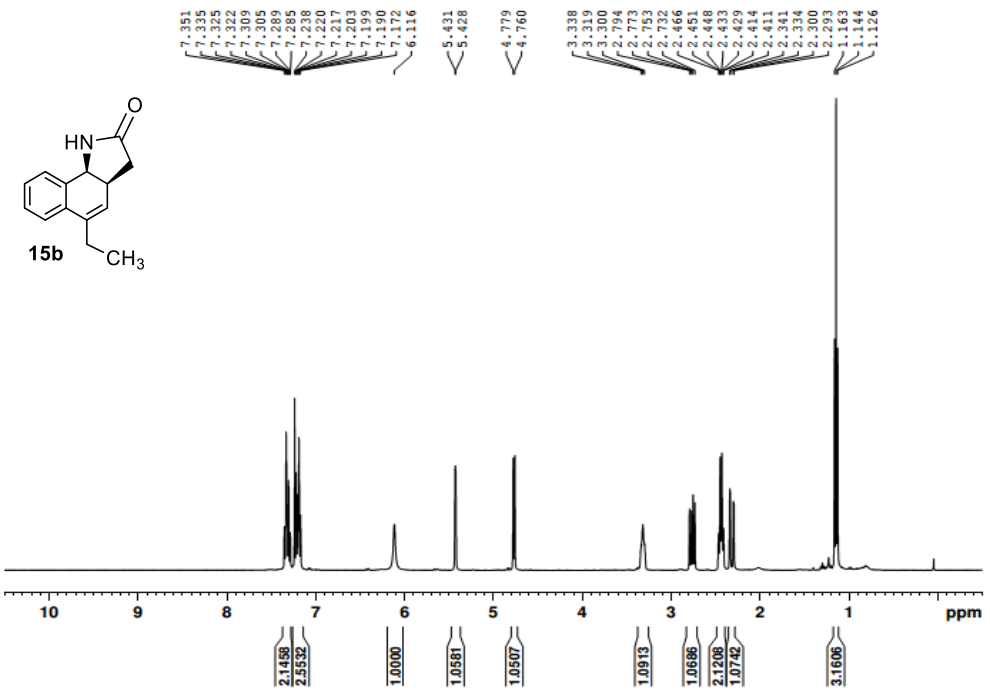
Part IV: ^{1}H and ^{13}C NMR Spectra of Products



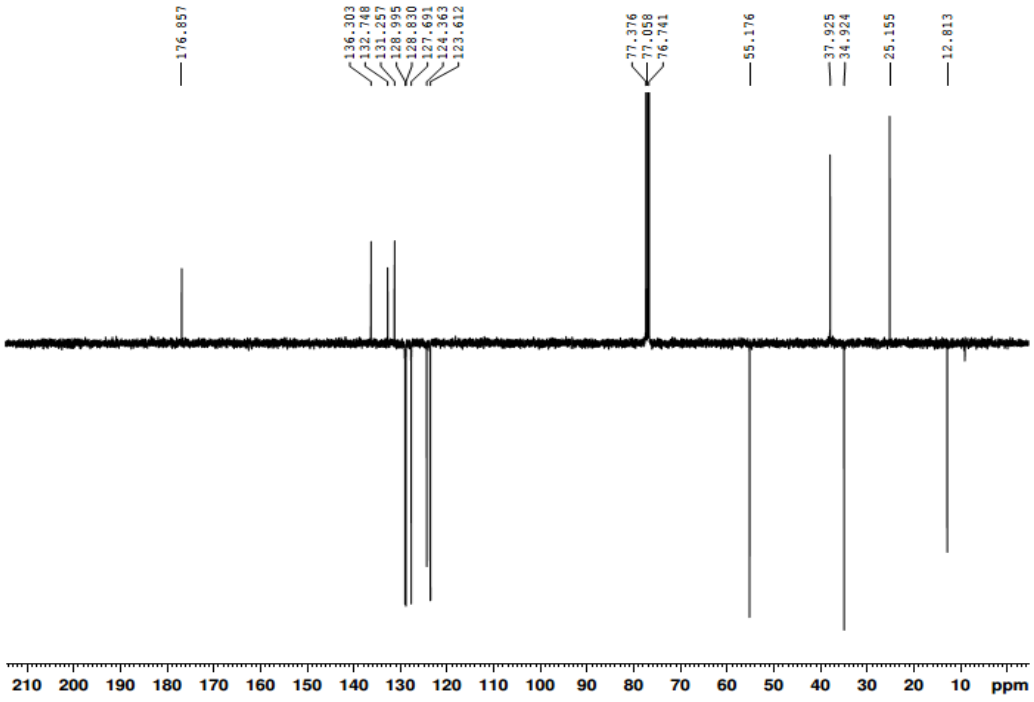
400 MHz ^{1}H NMR spectrum of **15a** in $CDCl_3$



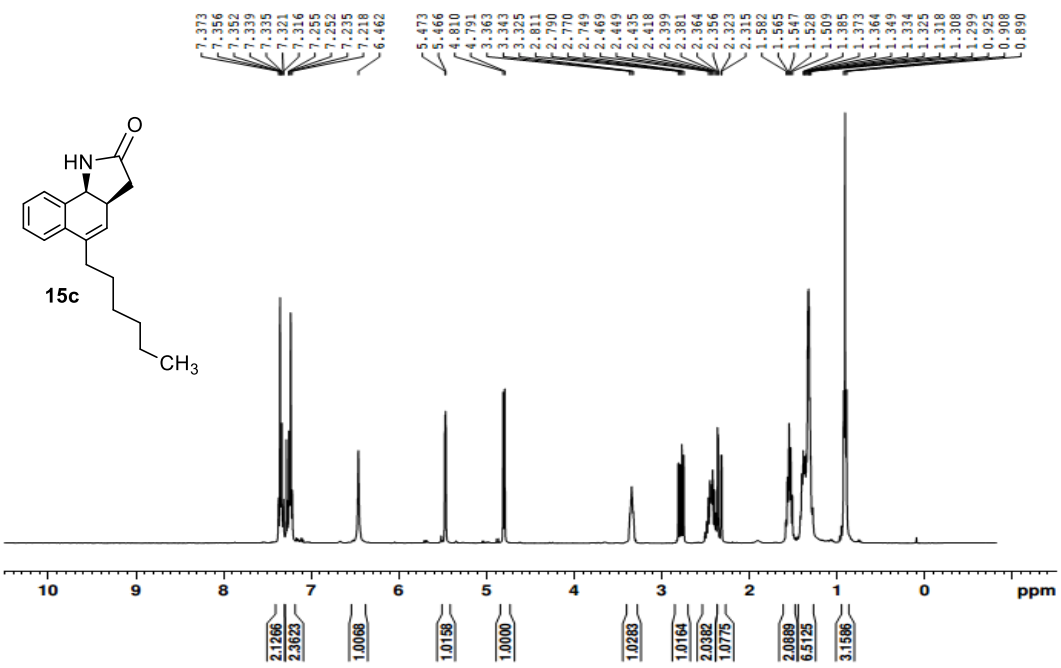
100 MHz ^{13}C NMR spectrum of **15a** in $CDCl_3$



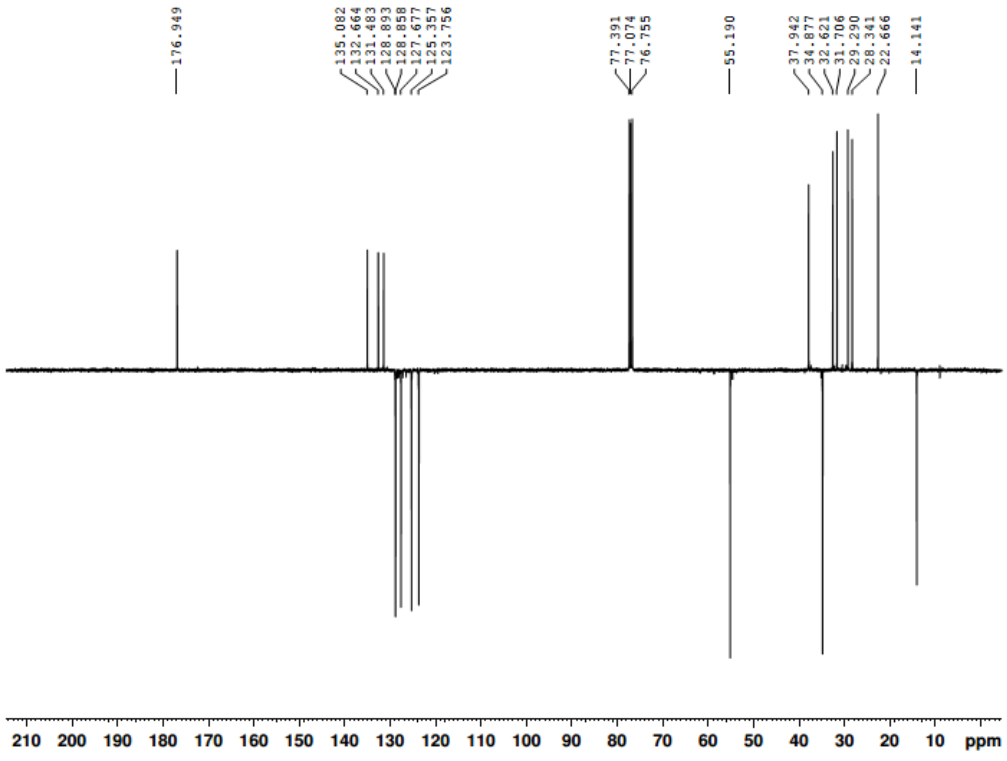
400 MHz ^{1}H NMR spectrum of **15b** in $CDCl_3$



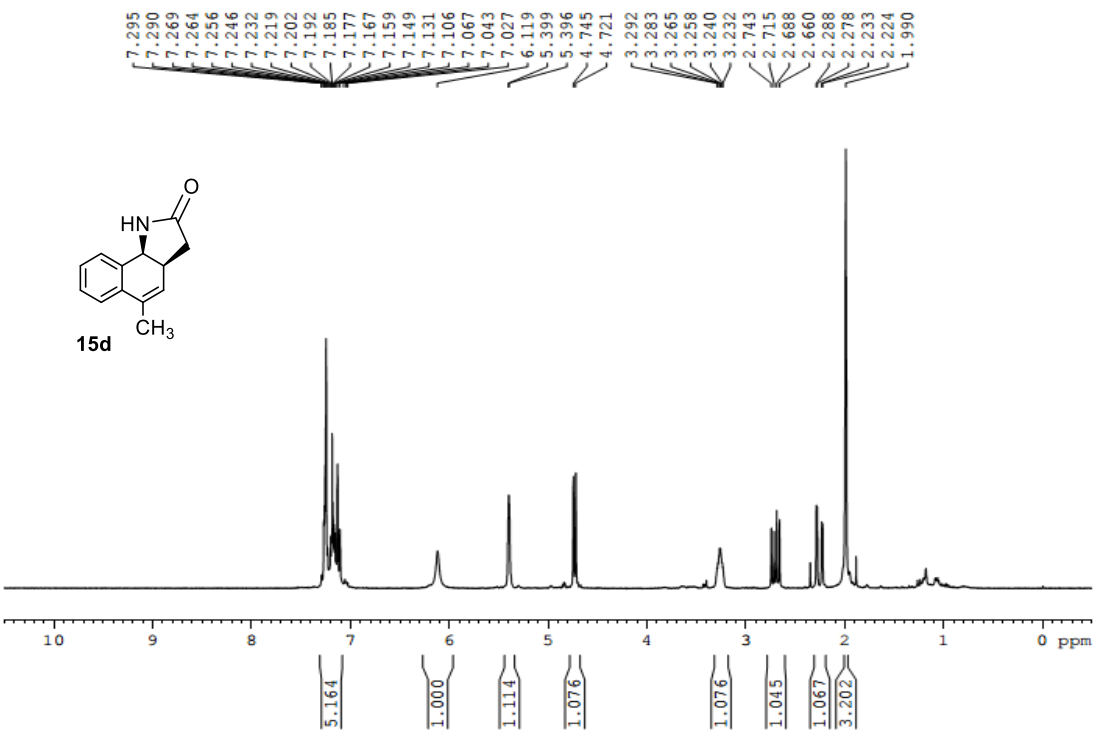
100 MHz ^{13}C NMR spectrum of **15b** in $CDCl_3$



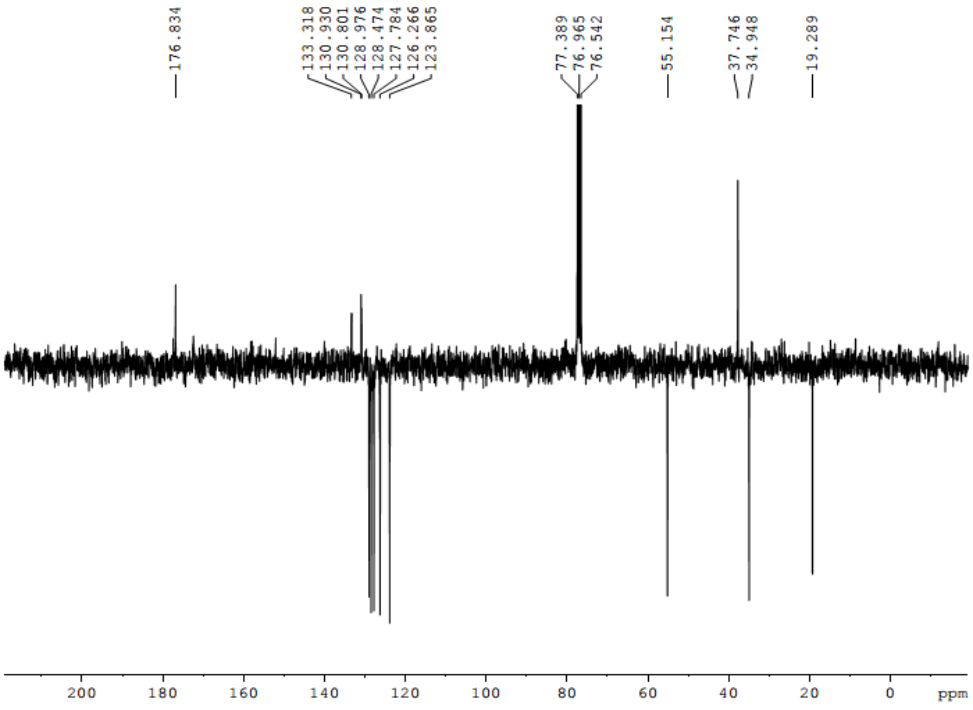
400 MHz ^{1}H NMR spectrum of **15c** in $CDCl_3$



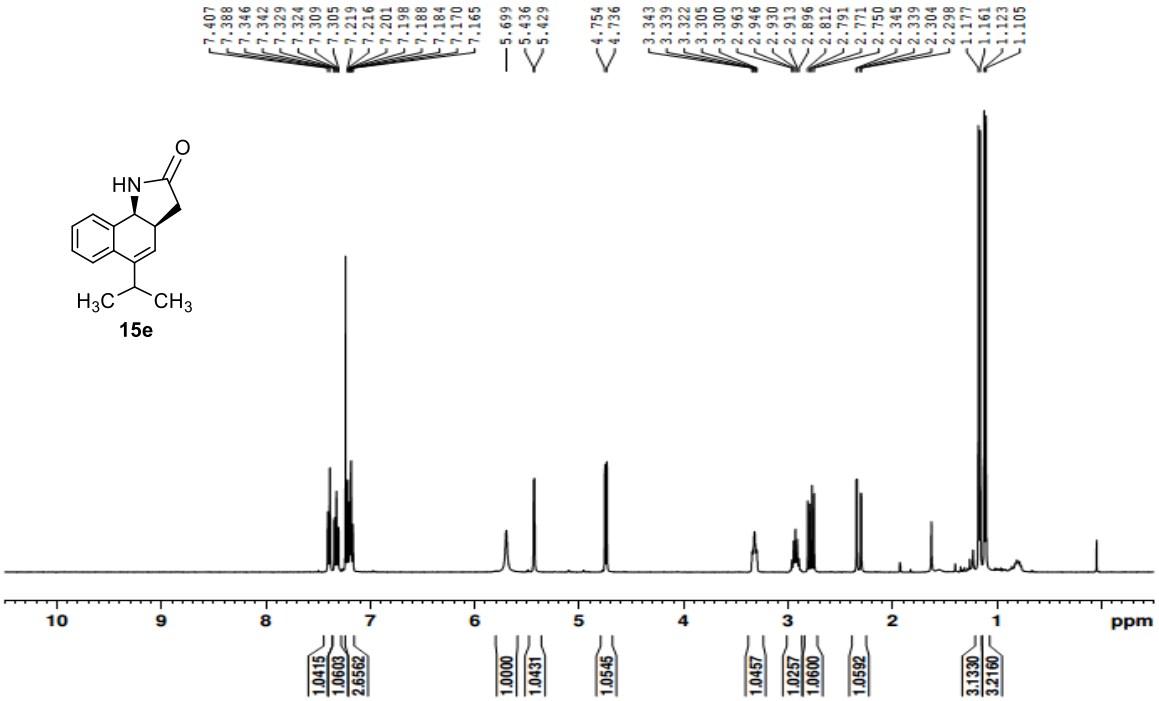
100 MHz ^{13}C NMR spectrum of **15c** in $CDCl_3$



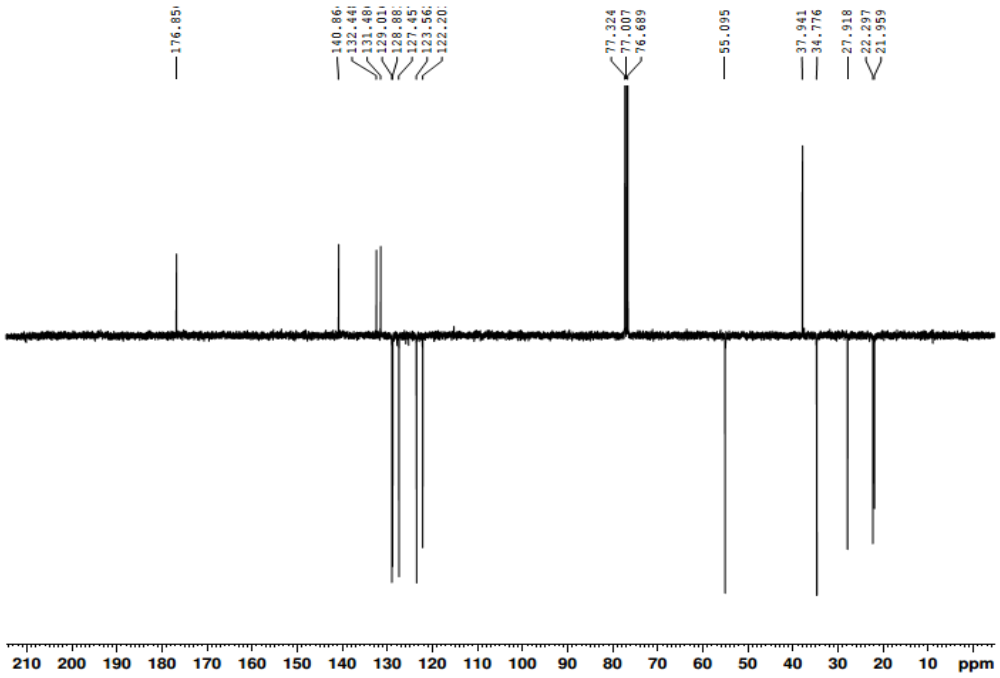
300 MHz ^{1}H NMR spectrum of **15d** in $CDCl_3$



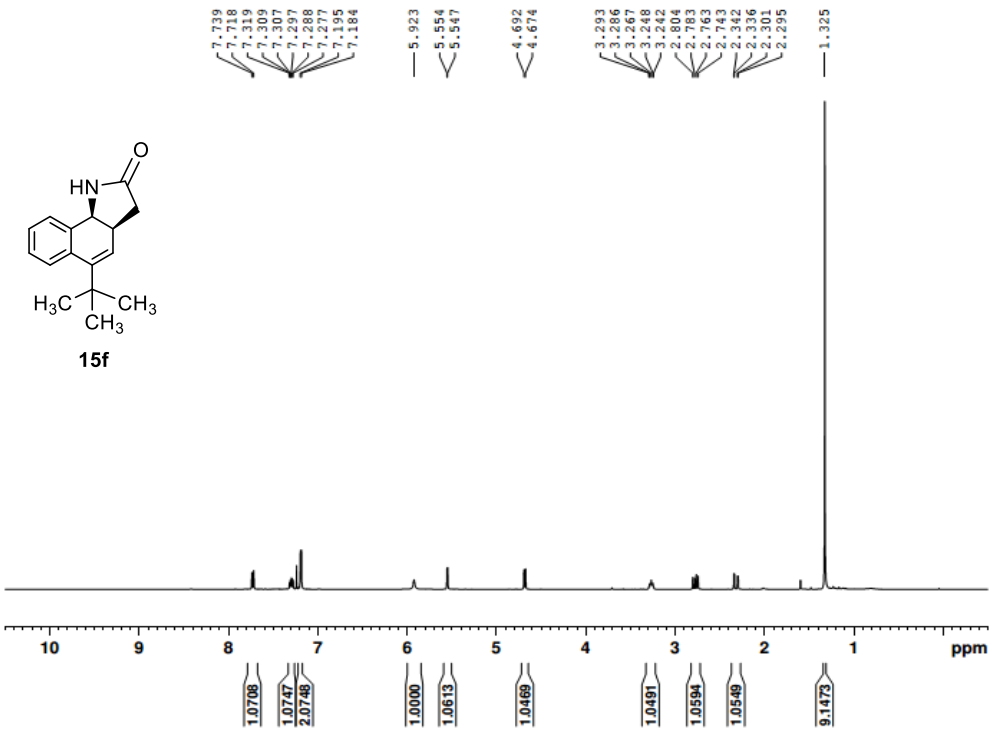
75 MHz ^{13}C NMR spectrum of **15d** in $CDCl_3$



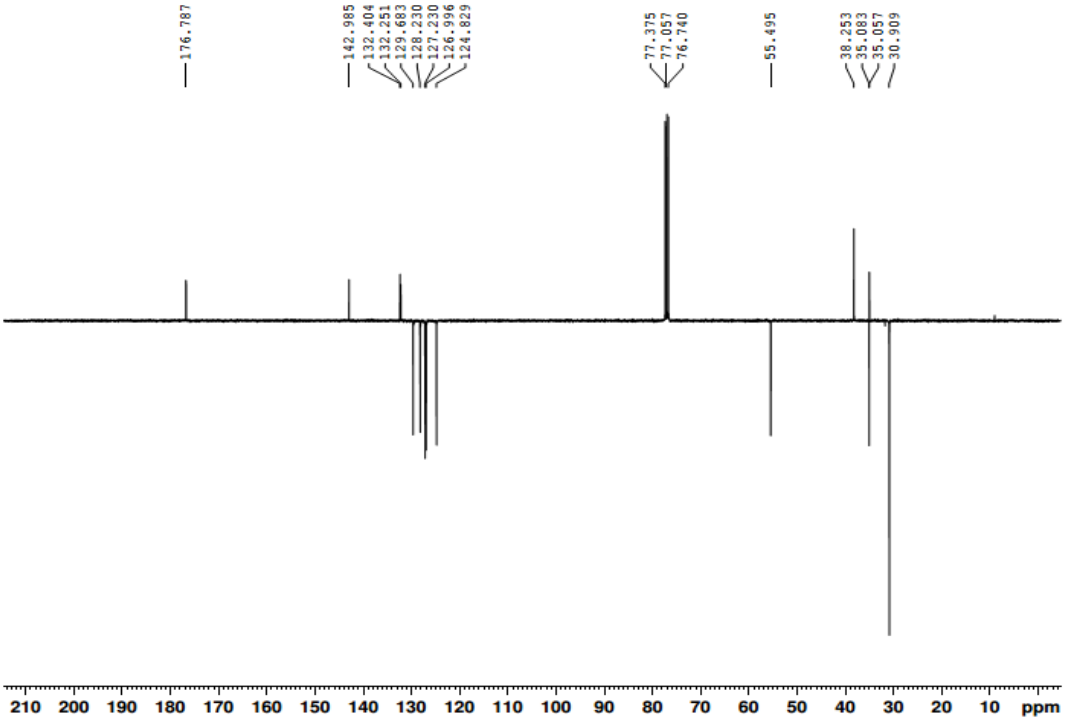
400 MHz ^{1}H NMR spectrum of **15e** in $CDCl_3$



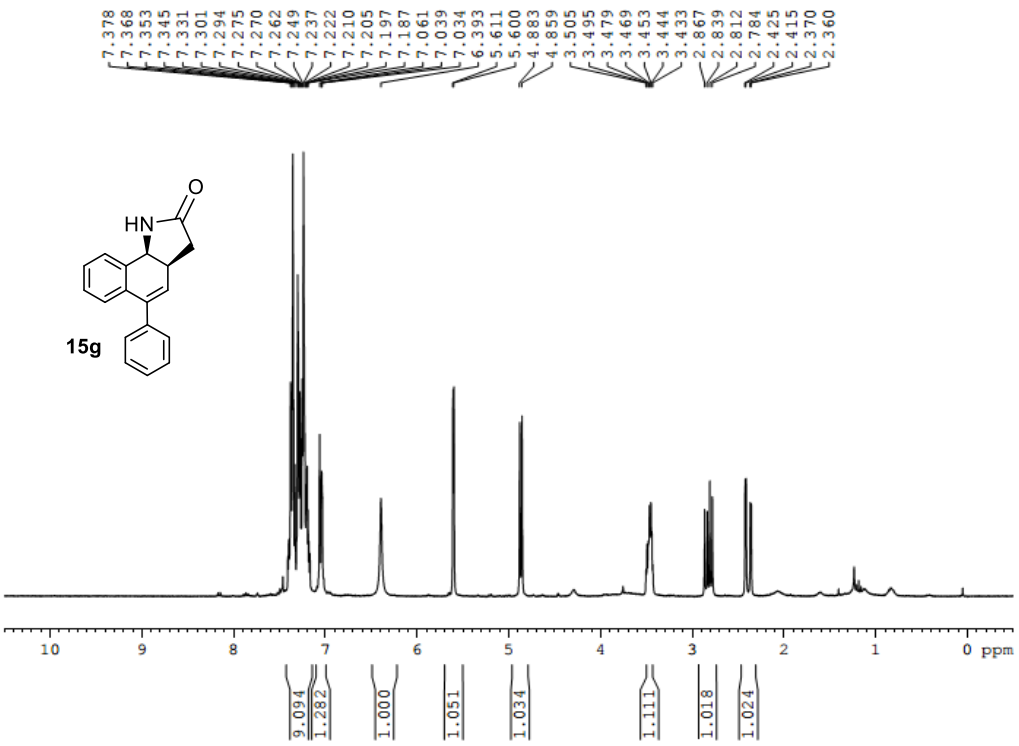
100 MHz ^{13}C NMR spectrum of **15e** in $CDCl_3$



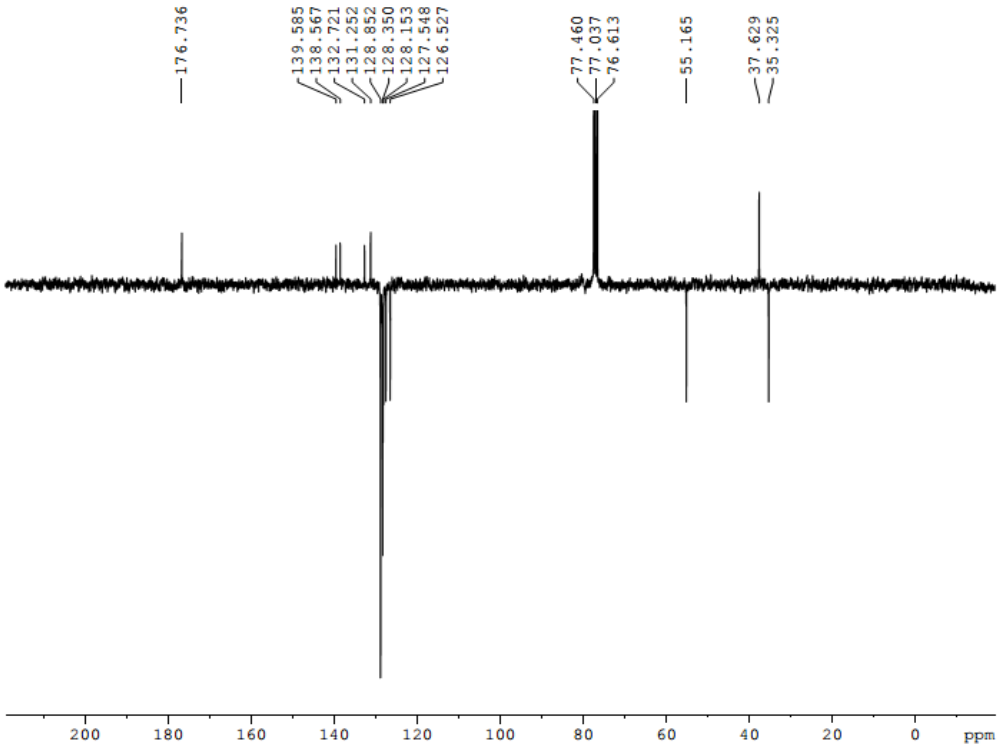
400 MHz ^{1}H NMR spectrum of **15f** in $CDCl_3$



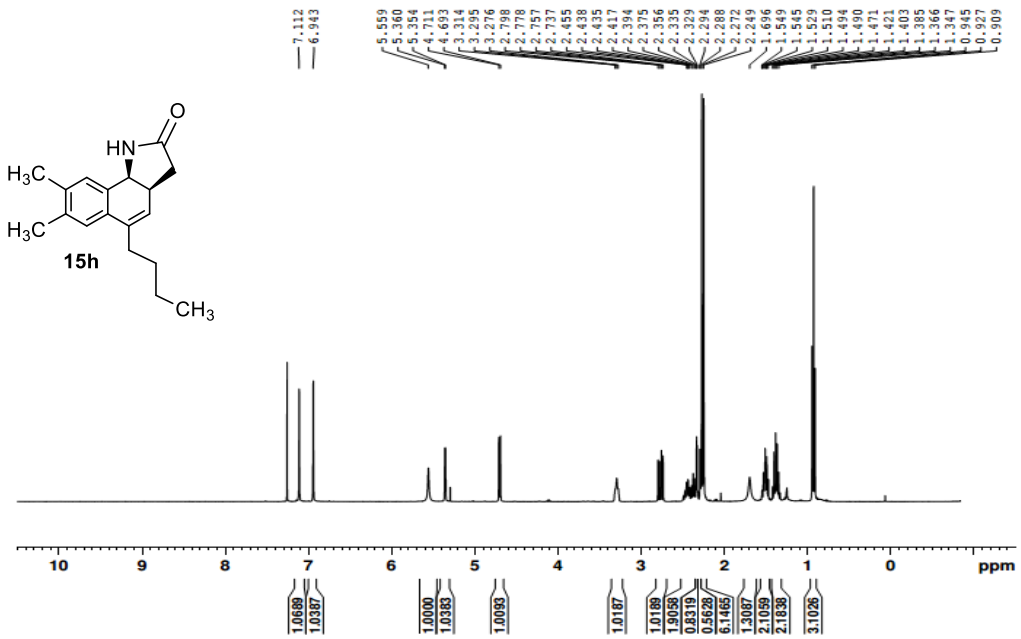
100 MHz ^{13}C NMR spectrum of **15f** in $CDCl_3$



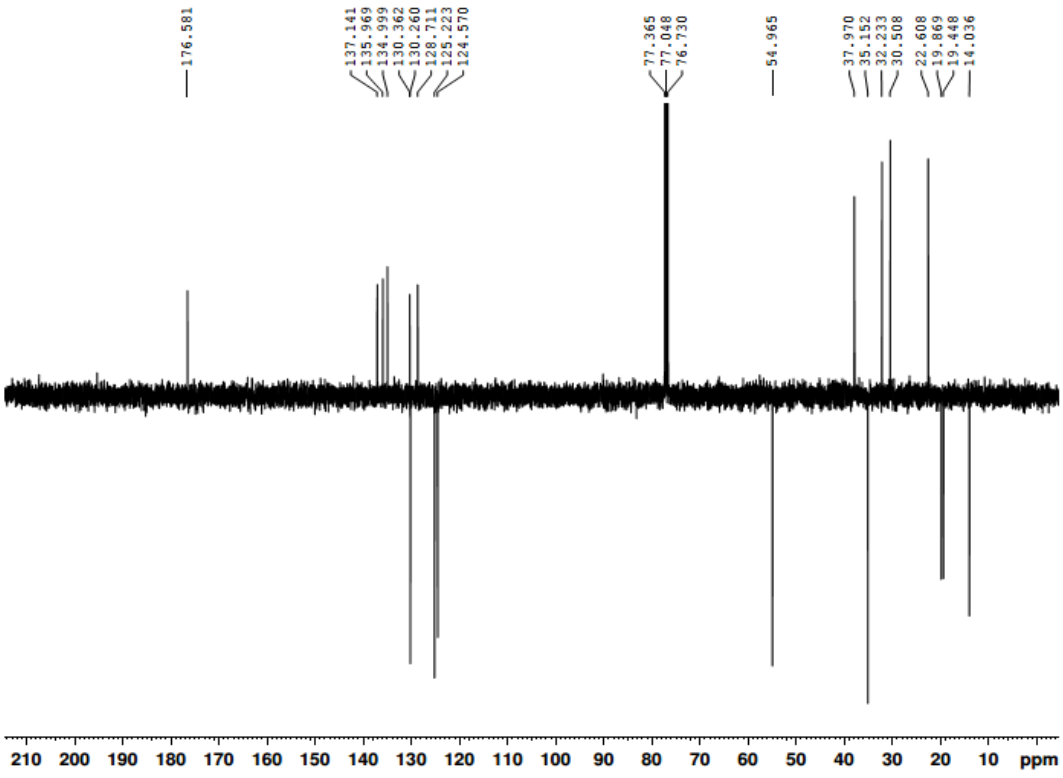
300 MHz ^{1}H NMR spectrum of **15g** in $CDCl_3$



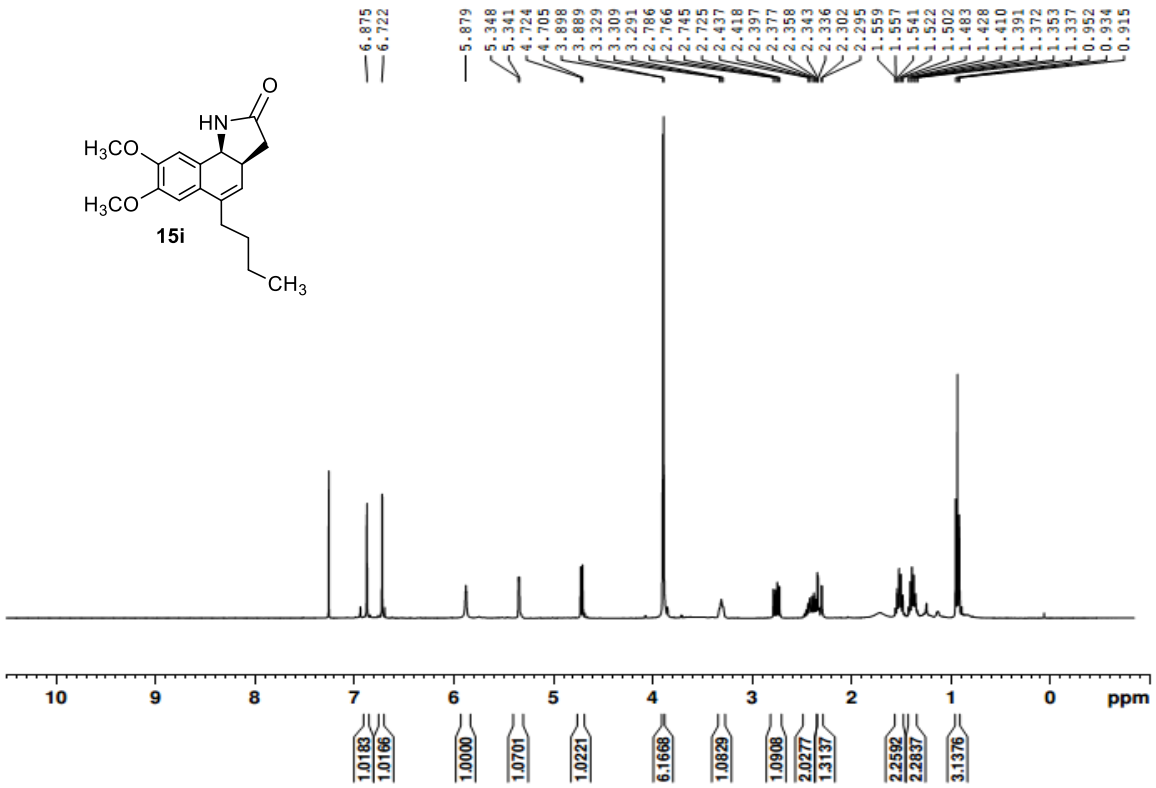
75 MHz ^{13}C NMR spectrum of **15g** in $CDCl_3$



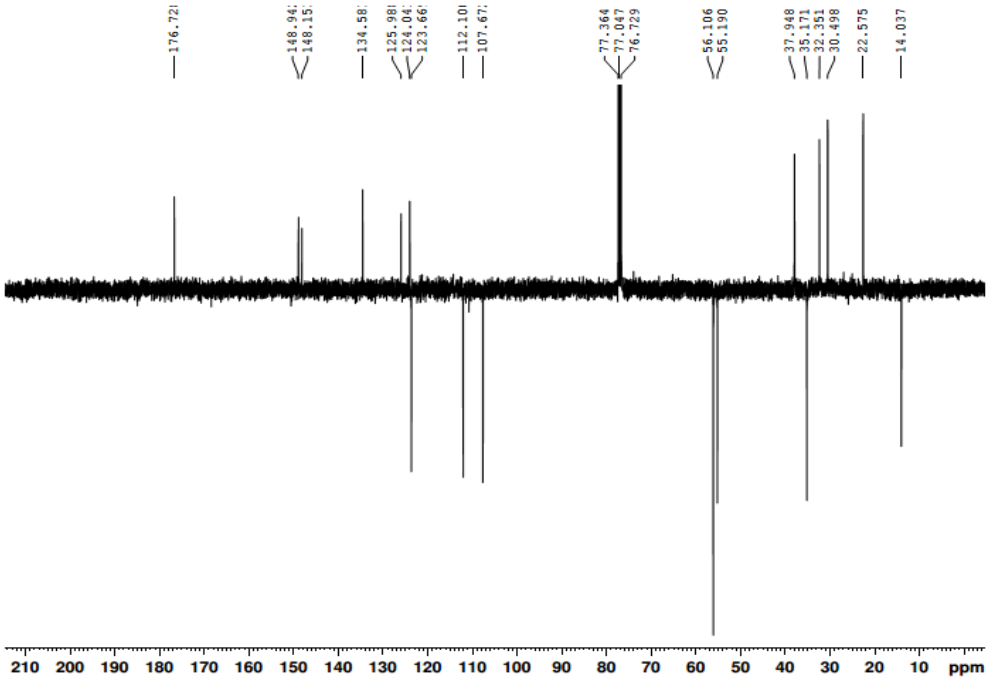
400 MHz ^{1}H NMR spectrum of **15h** in $CDCl_3$



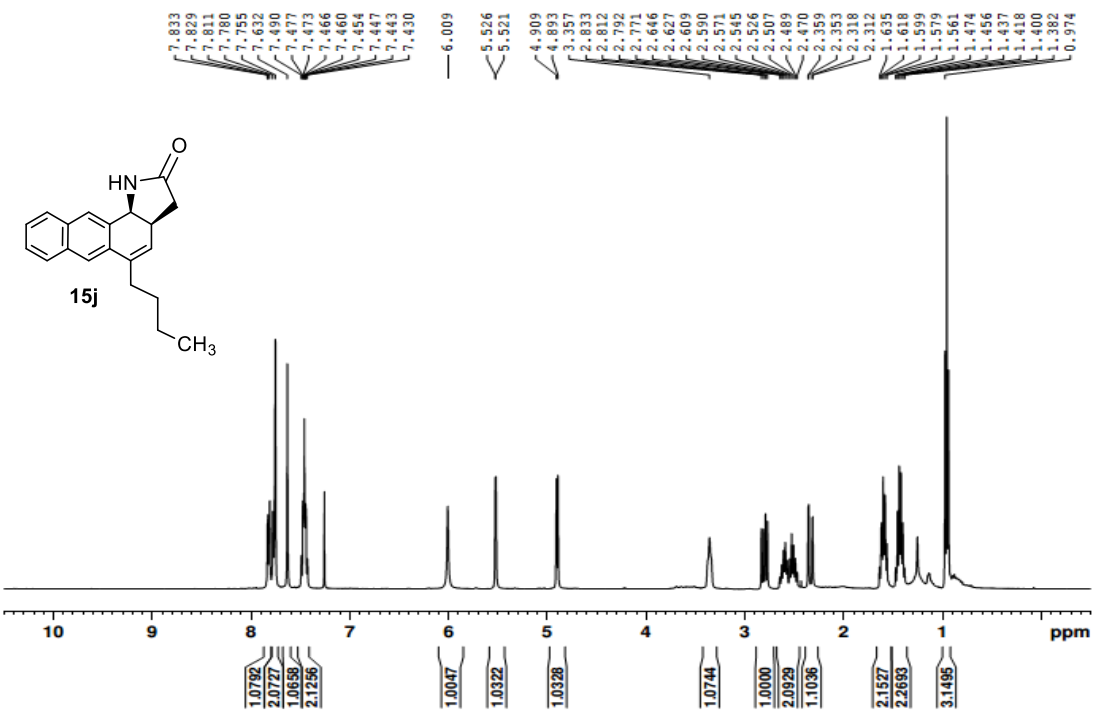
100 MHz ^{13}C NMR spectrum of **15h** in $CDCl_3$



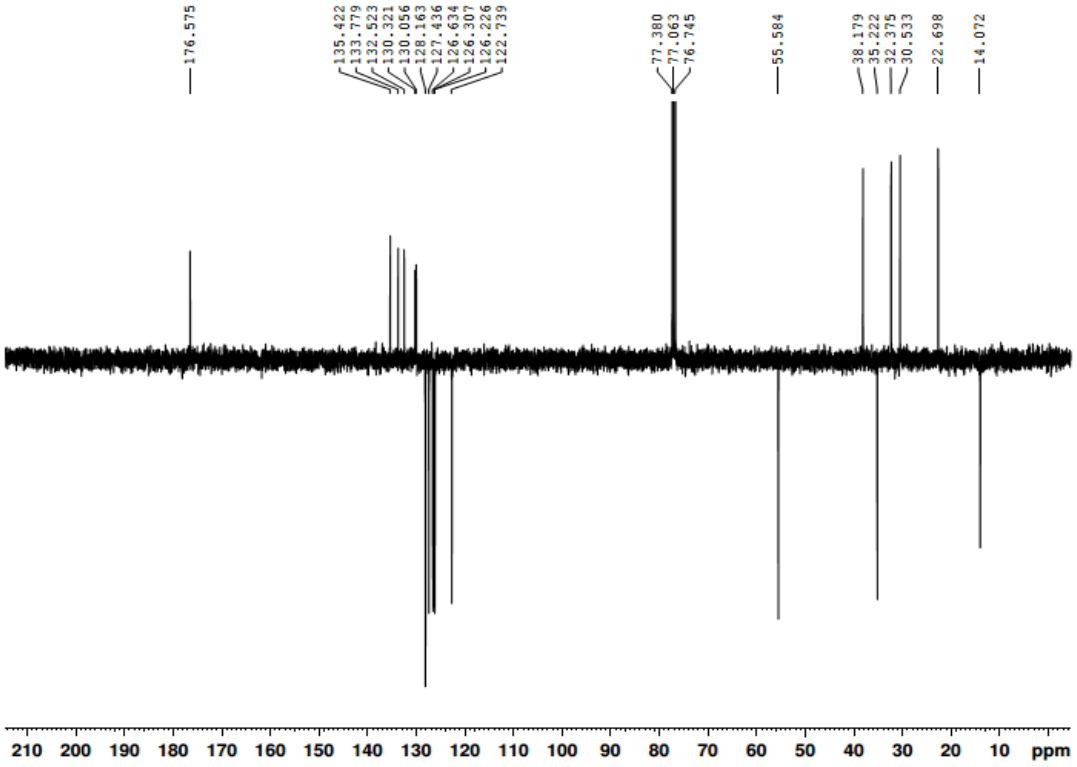
400 MHz ^{1}H NMR spectrum of **15i** in $CDCl_3$



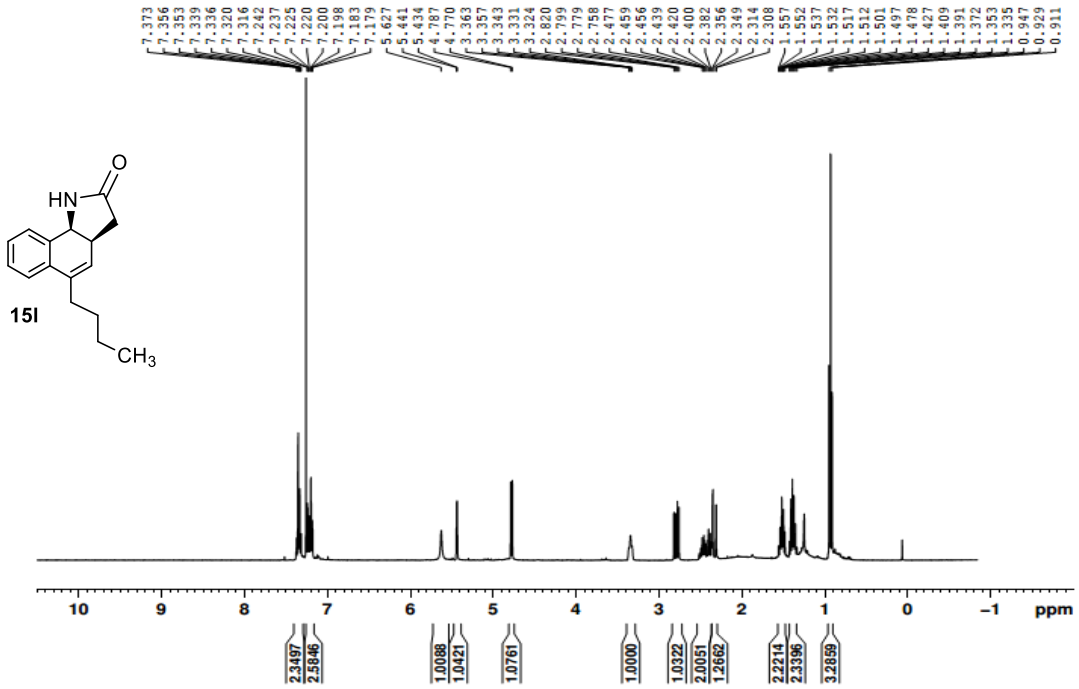
100 MHz ^{13}C NMR spectrum of **15i** in $CDCl_3$



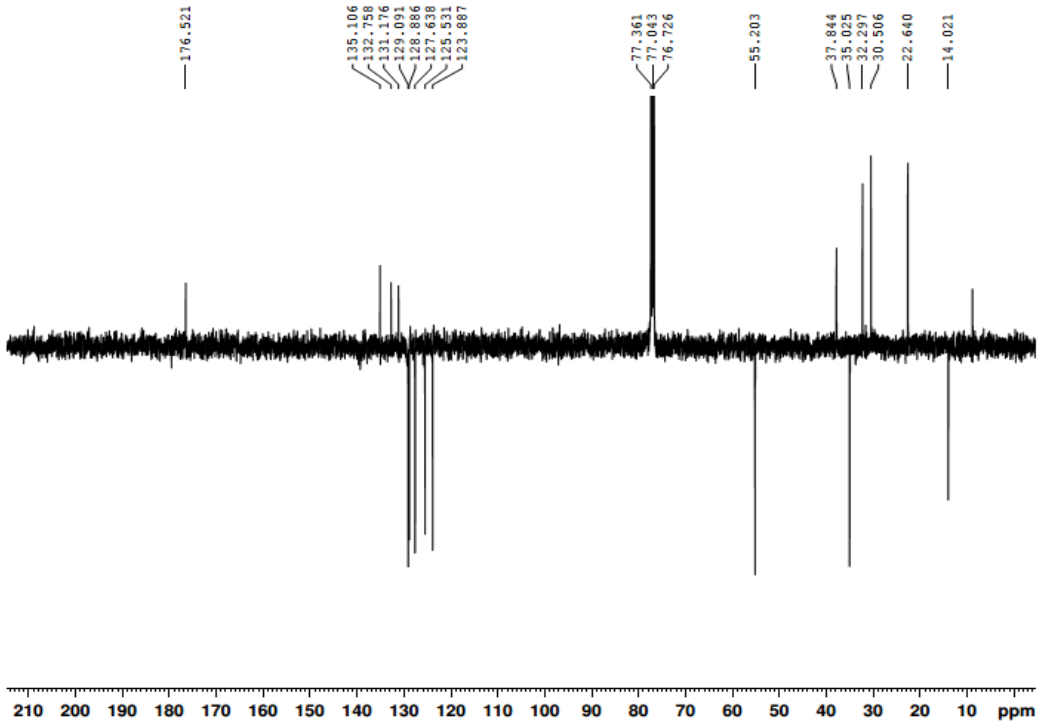
400 MHz ^{1}H NMR spectrum of **15j** in $CDCl_3$



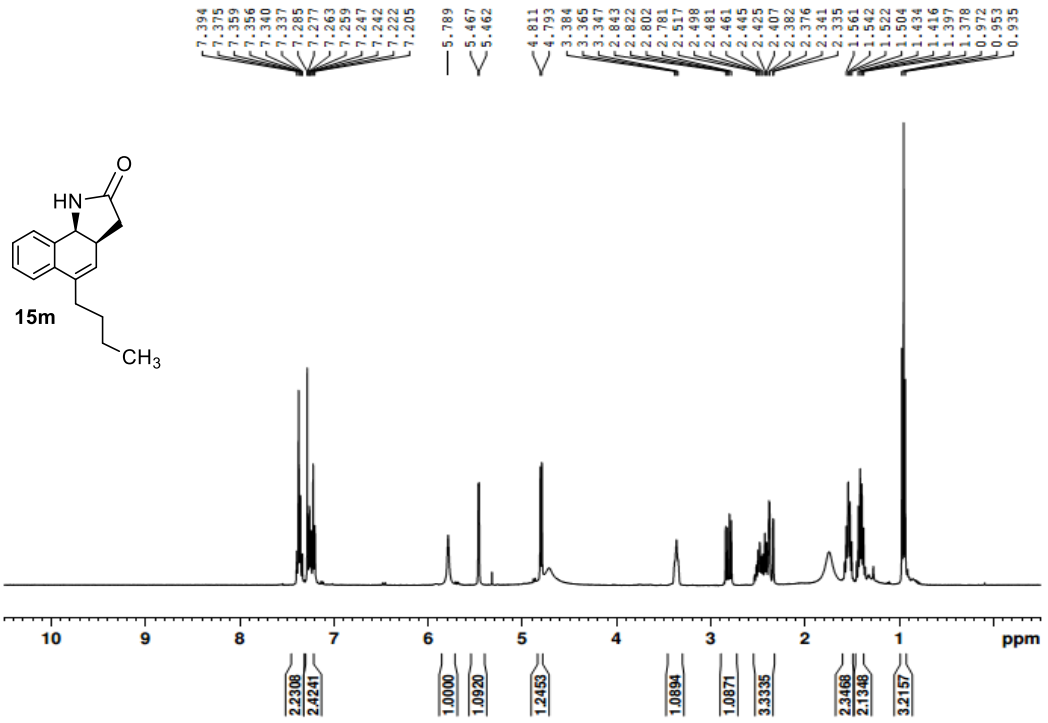
100 MHz ^{13}C NMR spectrum of **15j** in $CDCl_3$



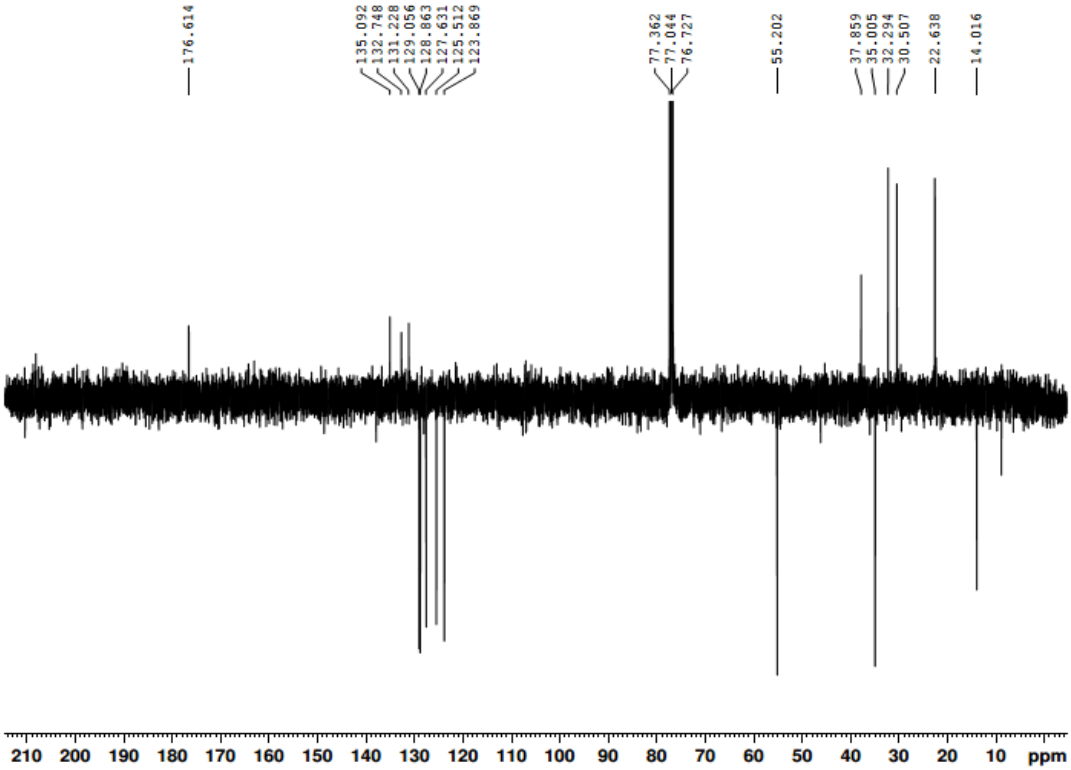
400 MHz ^{1}H NMR spectrum of **15l** in $CDCl_3$



100 MHz ^{13}C NMR spectrum of **15l** in $CDCl_3$



400 MHz ^{1}H NMR spectrum of **15m** in $CDCl_3$



100 MHz ^{13}C NMR spectrum of **15m** in $CDCl_3$