Supporting Information for

Palladium-Catalyzed Highly Efficient Synthesis of Functionalized Indolizines via Cross-Coupling/Cycloisomerization Cascade

Liangwei Zhang,[a,b] Xiangdong Li,[b] Yuanhong Liu*,[b] and Dayong Zhang*,[a]

[a]*Center of Drug Discovery, College of Pharmacy, China Pharmaceutical University, 24 Tongjia Xiang Road, Nanjing 210009, China*

[b]*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China*

Contents:

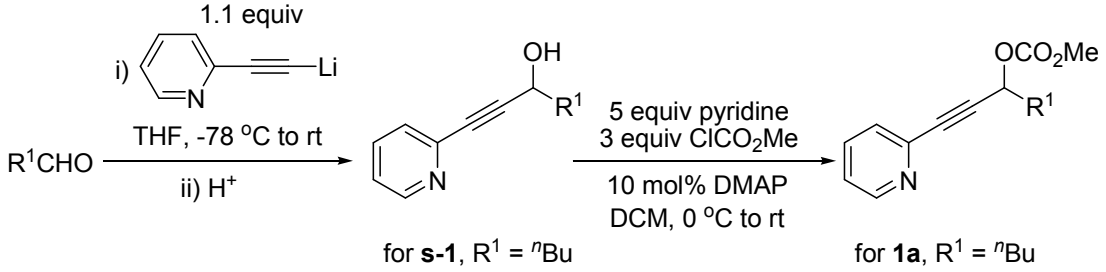
General Methods. All reactions were carried out using standard Schlenk techniques under Argon. MeCN was purified using Innovative Technology Solvent Purifier. THF was distilled from sodium and benzophenone. $Pd(PPh_3)_4$ was purchased from Sigma-Aldrich chemical company. *N*,*N*-dimethylformamide (DMF) was purchased from *J&K* chemical company. 2-Ethynylpyridine was purchased from Rui yi Medical Technology Co. Ltd., and purified by distillation under the reduced pressure before

use. Unless noted, all commercial reagents were used without further purification.

^{1}H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ (containing 0.03% TMS) or C_6D_6 (containing 0.03% TMS) solutions on Varian XL-400 MHz spectrometer or Agilent 400-MR NMR spectrometer. ^{1}H NMR spectra was recorded at 400 MHz, ^{13}C NMR spectra was recorded at 100 or 150 MHz. ^{1}H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) as internal reference in $CDCl_3$ or C_6D_6, and ^{13}C NMR spectra was recorded with $CDCl_3$ (δ = 77.00 ppm) or C_6D_6 (δ = 128.06 ppm). High-resolution mass spectra was obtained by using Waters Micromass GCT, Agilent Technologies 6224 TOF LC/MS mass spectrometer. Single crystal X-ray diffraction data were collected at 293(2) K for **3za** and **3zc** on Bruker SMART diffractometer, 130 K for the HCl salts of **4a** and **4b** on Bruker APEX-II diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å).

Synthesis of propargyl carbonates 1a-1e, 1i-1q.

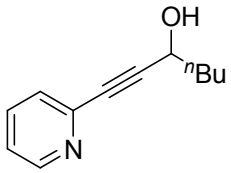
Typical procedure for the synthesis of methyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate (1a)



To a solution of 2-ethynylpyridine (0.61 mL, 6 mmol) in THF (20.0 mL) was added *n*-BuLi (2.2 mL, 5.5 mmol, 2.5 M in hexanes) at -78 °C. After stirring at the same temperature for 30 min, valeraldehyde (0.53 mL, 5 mmol) was added at -78 °C. Then the dry-ice/ acetone bath was removed. The reaction mixture was warmed up to room temperature and stirred for 1 h. Then the resulting mixture was quenched with saturated ammonium chloride solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether

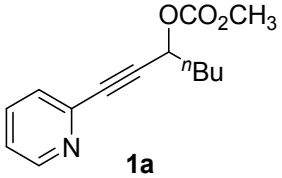
/ acetone = 8:1-4:1) to afford **s-1** in 96% yield (0.91 g) as a brown oil.

To a solution of above alcohol in DCM (10 mL) were added pyridine (1.93 mL, 24 mmol) and DMAP (58.6 mg, 0.48 mmol). Then the mixture was cooled to 0 °C, and methyl chloroformate (1.12 mL, 14.4 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 2 h. Then the mixture was quenched with saturated ammonium chloride solution, extracted with dichloromethane, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 8:1-4:1) to afford propargyl carbonate **1a** in 98% yield (1.16 g) as a yellow oil.



s-1

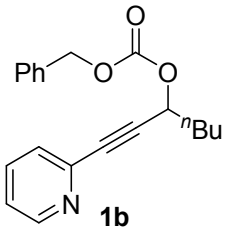
1-(Pyridin-2-yl)hept-1-yn-3-ol (s-1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (dd, *J* =4.4, 0.8 Hz, 1H), 7.66-7.62 (m, 1H), 7.43-7.41 (m, 1H), 7.24-7.21 (m, 1H), 4.66 (t, *J* = 6.8 Hz, 1H), 4.22 (bs, 1H), 1.88-1,82 (m, 2H), 1.56-1.48 (m, 2H), 1.42-1.33 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.55, 142.81, 136.28, 127.11, 122.83, 91.45, 83.34, 62.24, 37.17, 27.33, 22.33, 13.92. IR (film): 2955, 2931, 2860, 2227, 1585, 1562, 1464, 1428, 1379, 1335, 1266, 1151, 1124, 1046, 999, 955, 899, 777, 740 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{16}NO$ $[M+H]^+$: 190.1226, found 190.1227.



1a

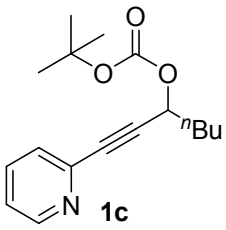
Methyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate (1a). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59-8.57 (m, 1H), 7.66 (td, *J* = 8.0, 1.6 Hz, 1H), 7.46-7.43 (m, 1H), 7.27-7.24 (m, 1H), 5.48 (t, *J* = 6.8 Hz, 1H), 3.82 (s, 3H), 1.97-1.91 (m, 2H), 1.55-1.49 (m,

2H), 1.41-1.36 (m, 2H), 0.93 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.70, 149.70, 142.10, 135.90, 127.10, 122.99, 85.48, 84.90, 67.96, 54.69, 34.08, 26.70, 21.92, 13.58. IR (film): 3008, 2957, 2923, 2864, 2271, 1748, 1582, 1562, 1463, 1441, 1428, 1254, 1115, 1043, 1007, 949, 932, 876, 778, 739 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{18}NO_3$ $[M+H]^+$: 248.1281, found 248.1290.



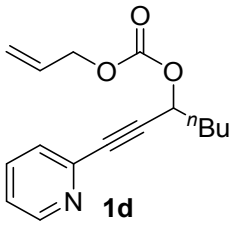
1b

Benzyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate (1b). To a solution of **s-1** (0.95 g, 5 mmol) in DCM (20 mL) were added pyridine (2 mL, 25 mmol) and DMAP (61 mg, 0.5 mmol). Then the mixture was cooled to 0 °C, and $ClCO_2Bn$ (2.11 mL, 15 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 2.5 h. Then the mixture was quenched with saturated ammonium chloride solution, extracted with dichloromethane, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 4:1) to afford propargyl carbonate **1b** in 56% yield (0.91 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (dd, J = 4.8, 0.8 Hz, 1H), 7.64 (td, J = 7.8, 2.0 Hz, 1H), 7.43-7.33 (m, 6H), 7.27-7.22 (m, 1H), 5.49 (t, J = 6.4 Hz, 1H), 5.22-5.15 (m, 2H), 1.97-1.91 (m, 2H), 1.56-1.47 (m, 2H), 1.40-1.34 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.27, 149.90, 142.36, 136.05, 134.92, 128.50, 128.48, 128.30, 127.32, 123.14, 85.70, 85.17, 69.82, 68.33, 34.30, 26.91, 22.13, 13.79. IR (film): 3028, 2956, 2864, 2271, 1745, 1582, 1562, 1463, 1428, 1382, 1236, 1150, 985, 942, 873, 779, 738, 696 cm^{-1}. HRMS (ESI) calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$: 324.1594, found 324.1603.



1c

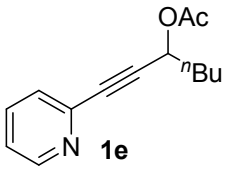
***tert*-Butyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate (1c).** To a solution of **s-1** (0.95 g, 5 mmol) in DCM (20 mL) were added Et_3N (2.1 mL, 15 mmol) and DMAP (61 mg, 0.5 mmol). Then the mixture was cooled to 0 °C, and Boc_2O (2.2 g, 10 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 3 h. Then the mixture was quenched with saturated ammonium chloride solution, extracted with dichloromethane, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 4:1) to afford the title product in 82% yield (1.18 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.65 (td, *J* = 7.6 Hz, 2.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.26-7.22 (m, 1H), 5.44 (t, *J* = 6.8 Hz, 1H), 1.95-1.89 (m, 2H), 1.56-1.48 (m, 11H), 1.41-1.36 (m, 2H), 0.93 (t, *J* = 7.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.50, 149.79, 142.45, 135.97, 127.21, 122.98, 86.16, 84.68, 82.52, 66.97, 34.35, 27.59, 26.93, 22.08, 13.74. IR (film): 3053, 2957, 2933, 2170, 1740, 1582, 1562, 1463, 1428, 1394, 1272, 1158, 1112, 985, 968, 891, 779, 739 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{24}NO_3$ $[M+H]^+$: 290.1751, found 290.1757.



1d

Allyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate (1d). To a solution of **s-1** (0.95 g, 5 mmol) in DCM (20 mL) were added pyridine (2 mL, 25 mmol) and DMAP (61 mg, 0.5 mmol). Then the mixture was cooled to 0 °C, and AllocCl (1.6 mL, 15 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 3 h.

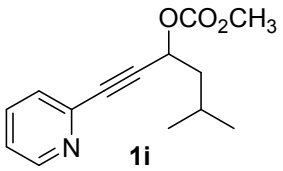
Then the mixture was quenched with saturated ammonium chloride solution, extracted with dichloromethane, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 4:1) to afford the title product in 70% yield (0.95 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.66 (td, *J* = 7.8, 2.4 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 1H), 6.00-5.91 (m, 1H), 5.48 (t, *J* = 6.4 Hz, 1H), 5.41-5.27 (m, 2H), 4.68-4.66 (m, 2H), 1.98 -1.92 (m, 2H), 1.57-1.49 (m, 2H), 1.43-1.36 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.11, 149.89, 142.36, 136.06, 131.29, 127.30, 123.13, 118.98, 85.67, 85.10, 68.65, 68.22, 34.30, 26.91, 22.12, 13.78. IR (film): 3045, 2957, 2931, 2865, 2211, 1745, 1582, 1562, 1463, 1428, 1370, 1237, 1114, 985, 948, 871, 778, 739 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{20}NO_3$ $[M+H]^+$: 274.1438, found 274.1440.



1e

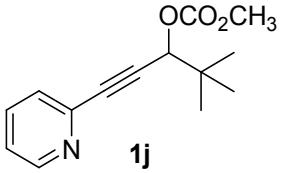
1-(Pyridin-2-yl)hept-1-yn-3-yl acetate (1e). To a solution of **s-1** (0.28 g, 1.5 mmol) in DCM (5 mL) were added Et_3N (0.42 mL, 3 mmol) and DMAP (18 mg, 0.15 mmol). Then the mixture was cooled to 0 °C, and Ac_2O (0.42 ml, 4.5 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 7 h. The mixture was quenched with saturated ammonium chloride solution, extracted with dichloromethane, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 4:1-2:1) to afford the title product in 86% yield (0.3 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58-8.57 (m, 1H), 7.65 (td, *J* = 7.8, 1.6 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.25-7.22 (m, 1H), 5.61 (t, *J* = 6.8 Hz, 1H), 2.11 (s, 3H), 1.92-1.86 (m, 2H), 1.52-1.46 (m, 2H), 1.41-1.35 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.95, 149.93,

142.56, 136.07, 127.28, 123.07, 86.59, 84.27, 64.12, 34.30, 27.09, 22.19, 20.96, 13.84. IR (film): 3053, 2957, 2931, 2863, 2215, 1740, 1582, 1563, 1463, 1428, 1371, 1349, 1268, 1224, 1018, 986, 779, 740 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{18}NO_2$ $[M+H]^+$: 232.1332, found 232.1331.



1i

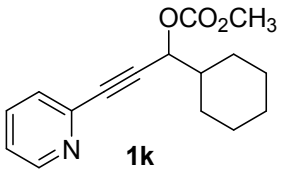
Methyl (5-methyl-1-(pyridin-2-yl)hex-1-yn-3-yl) carbonate (1i). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1) afforded the title product in 78% yield over two steps as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 4.4 Hz, 1H), 7.66 (td, J = 7.2, 1.6 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.25-7.23 (m, 1H), 5.52 (t, J = 7.2 Hz, 1H), 3.83 (s, 3H), 1.91-1.80 (m, 3H), 0.98 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.95, 149.93, 142.38, 136.08, 127.33, 123.17, 85.85, 85.09, 67.00, 54.95, 43.33, 24.56, 22.31, 22.28. IR (film): 3052, 2958 2872, 2251, 1748, 1582, 1562, 1464, 1441, 1428, 1370, 1253, 984, 779, 740 cm^{-1}. HRMS (EI) calcd for $C_{14}H_{17}NO_3$: 247.1208, found 247.1207.



1j

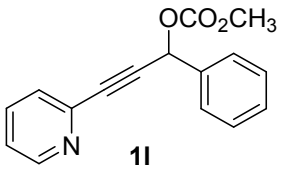
4,4-Dimethyl-1-(pyridin-2-yl)pent-1-yn-3-yl methyl carbonate (1j). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1) afforded the title product in 75% yield over two steps as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 4.4 Hz, 1H), 7.65 (td, J = 7.8, 2.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.26-7.23 (m, 1H), 5.21 (s, 1H), 3.83 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.17, 149.88, 142.41, 136.00, 127.35, 123.07, 85.76, 84.61, 76.18, 54.90, 35.55, 25.45. IR (film): 2961, 2915, 2870, 2259, 1749, 1583, 1562, 1481, 1464, 1429,

1397, 1256, 987, 779, 740 cm^{-1}. HRMS (EI) calcd for $C_{14}H_{17}NO_3$: 247.1208, found 247.1211.



1k

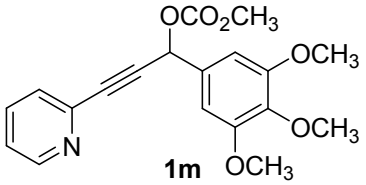
1-Cyclohexyl-3-(pyridin-2-yl)prop-2-yn-1-yl methyl carbonate (1k). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1-4:1) afforded the title product in 68% yield over two steps as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.65 (td, *J* = 7.6 Hz, 2.0 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.26-7.23 (m, 1H), 5.31 (d, *J* = 6.0 Hz, 1H), 3.82 (s, 3H), 1.96-1.67 (m, 6H), 1.29-1.18 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.10, 149.95, 142.48, 136.06, 127.40, 123.12, 85.89, 84.83, 72.54, 54.95, 41.89, 28.37, 28.13, 25.98, 25.61, 25.57. IR (film): 3008, 2854, 2929, 2267, 1747, 1582, 1561, 1463, 1428, 1347, 1249, 1142, 1106, 987, 966, 891, 779, 740 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{19}NO_3$: 273.1365, found 273.1369.



1l

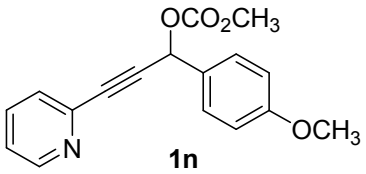
Methyl (1-phenyl-3-(pyridin-2-yl)prop-2-yn-1-yl) carbonate (1l). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate =8:1-4:1) afforded the title product in 94% yield over two steps as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (dd, *J* = 4.4, 0.4 Hz, 1H), 7.67-7.61 (m, 3H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.42 -7.37 (m, 3H), 7.27-7.23 (m, 1H), 6.55 (s, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.75, 150.00, 142.18, 136.10, 135.82, 129.29, 128.72, 127.78, 127.40, 123.36, 86.87, 84.53, 69.74, 55.10. IR (film): 3065, 3004, 2956, 2850, 2211,

1747, 1582, 1562, 1463, 1440, 1428, 1326, 1244, 951, 778, 695 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{14}NO_3$ $[M+H]^+$: 268.0968, found 268.0969.



1m

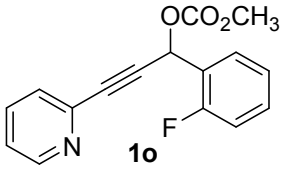
Methyl (3-(pyridin-2-yl)-1-(3,4,5-trimethoxyphenyl)prop-2-yn-1-yl) carbonate (1m). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1-2:1) afforded the title product in 70% yield over two steps as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 5.2 Hz, 1H), 7.67 (td, *J* = 8.0, 1.6Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.28-7.25 (m, 1H), 6.84 (s, 2H), 6.47 (s, 1H), 3.90 (s, 6H), 3.85 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.72, 153.35, 150.04, 142.14, 138.67, 136.15, 131.41, 127.35, 123.42, 104.87, 86.86, 84.50, 69.91, 60.77, 56.15, 55.17. IR (film): 3004, 2941, 2839, 2170, 1749, 1593, 1582, 1428, 1248, 1151, 1123, 975, 948, 907, 780 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{19}NO_6$: 357.1212, found 357.1211.



1n

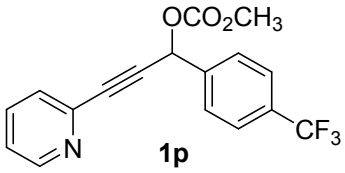
1-(4-Methoxyphenyl)-3-(pyridin-2-yl)prop-2-yn-1-yl methyl carbonate (1n). Column chromatography on silica gel (eluent: petroleum ether: acetone =6:1-4:1) afforded the title product in 78% yield over two steps as a brown oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.66 (td, *J* = 7.6, 2.0 Hz, 1H), 7.57-7.55 (m, 2H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.27-7.24 (m, 1H), 6.93-6.91 (m, 2H), 6.50 (s, 1H), 3.812 (s, 3H), 3.808 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.34, 154.79, 150.01, 142.27, 136.11, 129.49, 128.06, 127.39, 123.33, 114.03, 86.69, 84.79, 69.56, 55.28, 55.03. IR (film): 3053, 3008, 2957, 2838, 2235, 1746, 1582, 1561, 1463, 1440, 1428,

1325, 1239, 1030, 912, 777 cm^{-1}. HRMS (EI) calcd for $C_{17}H_{15}NO_4$: 297.1001, found 297.1005.



1o

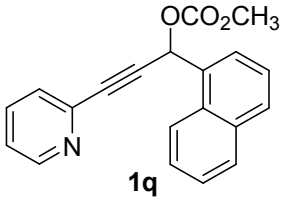
1-(2-Fluorophenyl)-3-(pyridin-2-yl)prop-2-yn-1-yl methyl carbonate (1o). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1-4:1) afforded the title product in 77% yield over two steps as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 4.6 Hz, 1H), 7.78 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.68-7.64 (m, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.41-7.35 (m, 1H), 7.29-7.18 (m, 2H), 7.12-7.07 (m, 1H), 6.83 (s, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.06 (d, J_{F-C} = 249.1 Hz), 154.54, 150.05, 142.07, 136.18, 131.31 (d, J_{F-C} = 8.5 Hz), 129.68 (d, J_{F-C} = 2.8 Hz), 127.54, 124.49 (d, J_{F-C} = 3.8 Hz), 123.51, 123.19 (d, J_{F-C} = 13.2 Hz), 115.71 (d, J_{F-C} = 20.9 Hz), 86.87, 83.56, 63.75 (d, J_{F-C} = 5.1 Hz), 55.24. IR (film): 3061, 3008, 2958, 2846, 2243, 1750, 1582, 1562, 1461, 1441, 1429, 1247, 1175, 1098, 926, 778 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{13}FNO_3$ $[M+H]^+$: 286.0874, found 286.0881.



1p

Methyl (3-(pyridin-2-yl)-1-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl) carbonate (1p). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1-4:1) afforded the title product in 45% yield over two steps as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, J = 5.0, 0.4 Hz, 1H), 7.76-7.74 (m, 2H), 7.70-7.65 (m, 3H), 7.50-7.48 (m, 1H), 7.29-7.26 (m, 1H), 6.59 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.60, 150.11, 141.88, 139.71 (q, J_{F-C} = 0.9 Hz), 136.20, 131.34 (q, J_{F-C} = 32.0 Hz), 128.02, 127.46, 125.78 (q, J_{F-C} = 4.0 Hz), 123.76 (q, J_{F-C} =

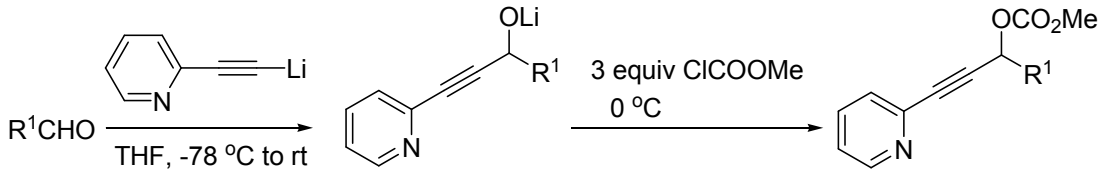
271.0 Hz), 123.61, 87.46, 83.63, 68.86, 55.32. IR (film): 3053, 2960, 2846, 2308, 1750, 1583, 1563, 1464, 1442, 1429, 1246, 1166, 1122, 930, 778 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{13}F_3NO_3$ $[M+H]^+$: 336.0842, found 336.0844.



1q

Methyl (1-(naphthalen-1-yl)-3-(pyridin-2-yl)prop-2-yn-1-yl) carbonate (1q). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 4:1) afforded the title product in 32% yield over two steps as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 4.8 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 7.90-7.88 (m, 3H), 7.64-7.58 (m, 2H), 7.54-7.43 (m, 3H), 7.24-7.21 (m, 1H), 7.17 (s, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.85, 150.01, 142.26, 136.09, 133.97, 131.20, 130.42, 130.30, 128.80, 127.49, 126.99, 126.84, 126.03, 125.14, 123.66, 123.35, 87.36, 84.63, 68.33, 55.21. IR (film): 3052, 2956, 2842, 2267, 1746, 1581, 1562, 1463, 1439, 1428, 1247, 1167, 1092, 948, 776 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{15}NO_3$: 317.1052, found 317.1055.

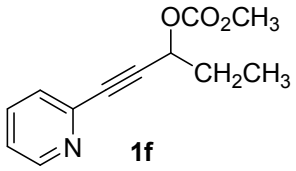
Synthesis of propargyl carbonates 1f, 1g and 1h.[1]



For **1f**, R^1 = Et

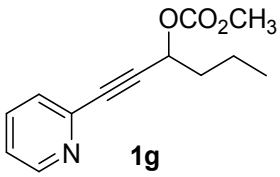
To a solution of 2-ethynylpyridine (0.61 mL, 6.0 mmol) in THF (20.0 mL) was added *n*-BuLi (2.2 mL, 5 mmol, 2.5 M in hexanes) at -78 °C. After stirring at the same temperature for 1 h, propionaldehyde (0.36 mL, 5 mmol) was added at -78 °C. Then the dry-ice/ acetone bath was removed. The reaction mixture was warmed up to room temperature and stirred for 1 h. Then the mixture was cooled to 0 °C. Methyl chloroformate (1.16 mL, 15 mmol) was added to the mixture and stirred for 1 h. The

resulting solution was quenched with saturated ammonium chloride solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 8:1-4:1) to afford **1f** in 80% yield (0.88 g) as a yellow oil.



1f

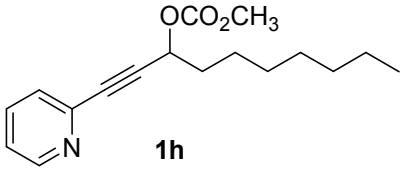
Methyl (1-(pyridin-2-yl)pent-1-yn-3-yl) carbonate (1f). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, *J* = 4.4 Hz, 1H), 7.66 (td, *J* = 7.6, 2.0 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.27-7.23 (m, 1H), 5.44 (t, *J* = 6.8 Hz, 1H), 3.83 (s, 3H), 1.99-1.94 (m, 2H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.88, 149.88, 142.30, 136.06, 127.29, 123.15, 85.40, 85.15, 69.26, 54.90, 27.87, 9.25. IR (film): 3045, 2974, 2883, 2846, 2283, 1747, 1582, 1562, 1463, 1428, 1247, 1151, 945, 778, 740 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{13}NO_3$: 219.0893, found 219.0890.



1g

Methyl (1-(pyridin-2-yl)hex-1-yn-3-yl) carbonate (1g). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1-6:1) afforded the title product in 83% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.65 (td, *J* = 7.8, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 1H), 5.49 (t, *J* = 6.8 Hz, 1H), 3.83 (s, 3H), 1.96-1.89 (m, 2H), 1.61-1.55 (m, 2H), 0.98 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.94, 149.94, 142.38, 136.09, 127.33, 123.16, 85.67, 85.13, 68.04, 54.94, 36.57, 18.21, 13.51. IR (film): 2960, 2935, 2875, 2247,

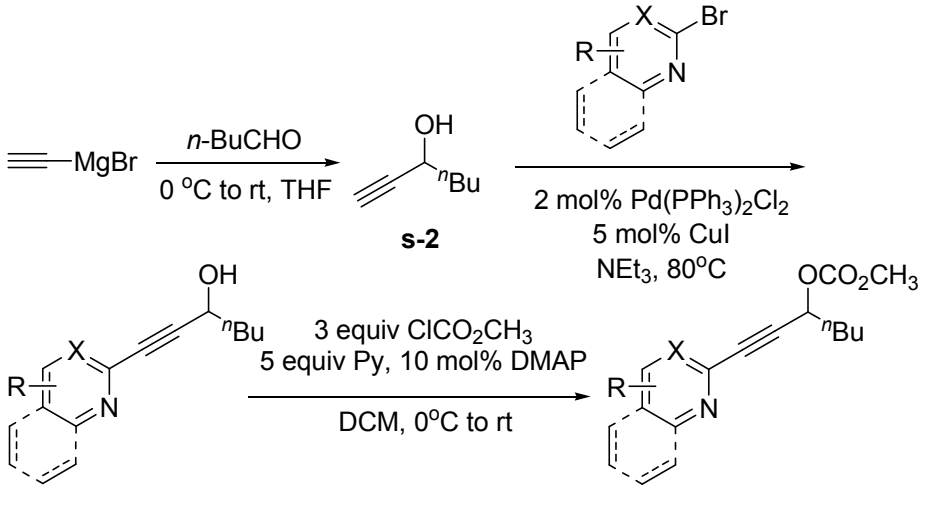
1747, 1582, 1562, 1463, 1441, 1428, 1350, 1251, 991, 779, 740 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{15}NO_3$: 233.1052, found 233.1054.



1h

Methyl (1-(pyridin-2-yl)dec-1-yn-3-yl) carbonate (1h). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1-4:1) afforded the title product in 69% yield as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.59-8.57 (m, 1H), 7.65 (td, *J* = 7.6, 1.6 Hz, 1H), 7.46-7.43 (m, 1H), 7.26-7.23 (m, 1H), 5.47 (t, *J* = 6.4 Hz, 1H), 3.82 (s, 3H), 1.96-1.90 (m, 2H), 1.55-1.52 (m, 2H), 1.36-1.28 (m, 8H), 0.88 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.93, 149.91, 142.37, 136.07, 127.32, 123.15, 85.73, 85.08, 68.25, 54.92, 34.59, 31.64, 28.97, 24.85, 22.52, 13.99. IR (film): 2951, 2927, 2856, 2304, 1750, 1582, 1561, 1464, 1428, 1255, 945, 779, 740 cm^{-1}. HRMS (EI) calcd for $C_{17}H_{23}NO_3$: 289.1678, found 289.1683.

Synthesis of propargyl carbonates 1r, 1s, 1t and 1u.



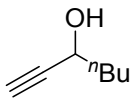
For **1r**, R = CH_3, X = C

To a solution of ethynylmagnesium bromide (48 mL, 24 mmol, 0.5 M in THF) in THF (40.0 mL) was added butyraldehyde (2.13 mL, 20 mmol) at 0 °C. Then the

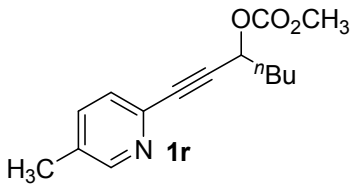
reaction mixture was warmed up to room temperature and stirred for 3 h. The resulting mixture was quenched with saturated ammonium chloride solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 8:1-4:1) to afford hept-1-yn-3-ol (**s-2**) in 63% yield (1.42 g) as a yellow oil.

To a solution of hept-1-yn-3-ol **s-2** (679 mg, 6.05 mmol) in Et_3N (25 mL) were added 2-bromo-5-methylpyridine (946 mg, 5.5 mmol), $Pd(PPh_3)_2Cl_2$ (77 mg, 0.11 mol) and CuI (52 mg, 0.275 mol), and the mixture was stirred at 80 ^oC for 2 h. Then the resulting mixture was quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was used directly for the next step.

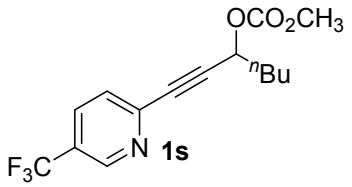
To a solution of above alcohol in DCM (20 mL) were added pyridine (2.2 mL, 27.5 mmol) and DMAP (67.2 mg, 0.55 mmol). Then the mixture was cooled to 0 ^oC, and methyl chloroformate (1.3 mL, 16.5 mmol) was added. The resulting solution was warmed up to room temperature and stirred for 3 h. The mixture was quenched with saturated ammonium chloride solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 10:1-8:1) to afford propargyl carbonate **1r** in 75% yield (1.08 g) over two steps from **s-2** as a brown oil.



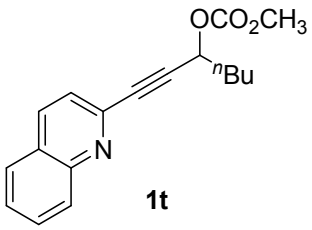
Hept-1-yn-3-ol (s-2). ^1H NMR (400 MHz, $CDCl_3$): δ 4.37 (t, *J* = 6.0 Hz, 1H), 2.47-2.44 (m, 1H), 2.34 (bs, 1H), 1.77-1.69 (m, 2H), 1.46-1.33 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 85.02, 72.73, 62.18, 37.26, 27.10, 22.27, 13.91. The spectroscopic data are in agreement with that previously reported.[2]



Methyl (1-(5-methylpyridin-2-yl)hept-1-yn-3-yl) carbonate (1r). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41-8.40 (m, 1H), 7.47-7.44 (m, 1H), 7.35-7.33 (m, 1H), 5.47 (t, *J* = 6.8 Hz, 1H), 3.82 (s, 3H), 2.34 (s, 3H), 1.96-1.91 (m, 2H), 1.56-1.48 (m, 2H), 1.43-1.35 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.92, 150.40, 139.47, 136.51, 133.12, 126.77, 85.15, 84.98, 68.29, 54.85, 34.35, 26.92, 22.11, 18.37, 13.76. IR (film): 3007, 2957, 2864, 2223, 1748, 1594, 1561, 1477, 1441, 1254, 1114, 1027, 1005, 950, 833, 790 cm^{-1}. HRMS (EI) calcd for $C_{15}H_{19}NO_3$: 261.1365, found 261.1360.

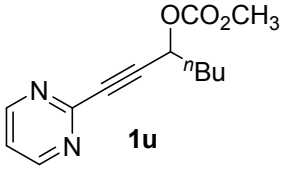


Methyl (1-(5-(trifluoromethyl)pyridin-2-yl)hept-1-yn-3-yl) carbonate (1s). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1-8:1) afforded the title product in 75% yield over two steps from **s-2** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.85-8.84 (m, 1H), 7.90 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 5.48 (t, *J* = 6.4 Hz, 1H), 3.84 (s, 3H), 1.97 -1.94 (m, 2H), 1.55-1.51 (m, 2H), 1.42-1.37 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.91, 146.79 (q, $J_{F\text{-}C}$ = 4.9 Hz), 145.77 (q, $J_{F\text{-}C}$ = 1.7 Hz), 133.34 (q, $J_{F\text{-}C}$ = 3.4 Hz), 126.87, 125.71 (q, $J_{F\text{-}C}$ = 33.9 Hz), 123.15 (q, $J_{F\text{-}C}$ = 271.0 Hz), 88.49, 84.14, 68.02, 55.05, 34.17, 26.94, 22.15, 13.80. IR (film): 2960, 2931, 2866, 2235, 1752, 1600, 1566, 1443, 1326, 1260, 1128, 1081, 1013, 935, 848, 790 cm^{-1}. HRMS (EI) calcd for $C_{15}H_{16}F_3NO_3$: 315.1082, found 315.1079.



1t

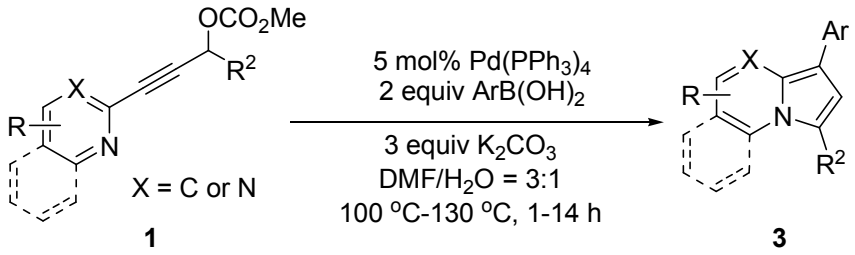
Methyl (1-(quinolin-2-yl)hept-1-yn-3-yl) carbonate (1t). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1-8:1) afforded the title product in 57% yield over two steps from **s-2** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12-8.08 (m, 2H), 7.80-7.78 (m, 1H), 7.74-7.70 (m, 1H), 7.57-7.50 (m, 2H), 5.54 (t, *J* = 6.4 Hz, 1H), 3.84 (s, 3H), 2.00-1.96 (m, 2H), 1.58-1.54 (m, 2H), 1.43-1.37 (m, 2H), 0.94 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.97, 147.98, 142.54, 136.13, 130.05, 129.29, 127.43, 127.26, 127.21, 124.23, 86.40, 85.74, 68.29, 54.97, 34.35, 27.01, 22.17, 13.82. IR (film): 3066, 2956, 2864, 2245, 1748, 1593, 1554, 1500, 1441, 1257, 1234, 1119, 1010, 951, 830, 788 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{19}NO_3$: 297.1365, found 297.1368.



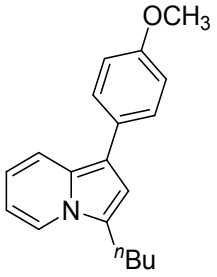
1u

Methyl (1-(pyrimidin-2-yl)hept-1-yn-3-yl) carbonate (1u). Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 4:1-3:1) afforded the title product in 77% yield over two steps from **s-2** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, *J* = 4.8 Hz, 2H), 7.29 (t, *J* = 5.0 Hz, 1H), 5.49 (t, *J* = 6.6 Hz, 1H), 3.83 (s, 3H), 1.99-1.94 (m, 2H), 1.56-1.50 (m, 2H), 1.42-1.36 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.14, 154.78, 152.21, 120.11, 84.45, 84.25, 67.76, 54.90, 34.02, 26.80, 22.04, 13.68. IR (film): 3032, 2958, 2923, 2865, 2244, 1751, 1554, 1442, 1411, 1261, 1116, 1016, 975, 932, 813, 790 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{16}N_2O_3$: 248.1161, found 248.1158.

Typical procedure for the Synthesis of Functionalized Indolizines.



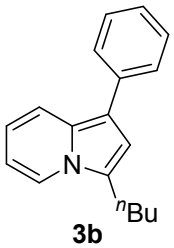
All reactions were carried out on 0.3 mmol scale. To a solution of methyl (1-(pyridin-2-yl)hept-1-yn-3-yl) carbonate **1a** (74 mg, 0.3 mmol) in DMF (2 mL) were added $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), K_2CO_3 (124 mg, 0.9 mmol), DMF (1 mL) and H_2O (1 mL) successively at room temperature. Then the reaction mixture was stirred at 100 °C for 1 h. After the reaction was complete as monitored by TLC, the resulting mixture was quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 30:1-20:1) to afford **3a** in 74% yield (62 mg) as a yellow oil.



3a

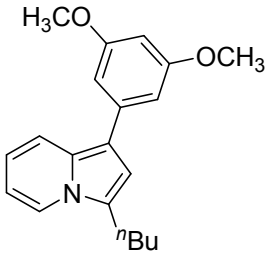
3-Butyl-1-(4-methoxyphenyl)indolizine (3a). ^{1}H NMR (400 MHz, C_6D_6): δ 7.68 (d, *J* = 9.2 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.77 (s, 1H), 6.44 (dd, *J* = 8.6, 6.4 Hz, 1H), 6.12-6.18 (m, 1H), 3.41 (s, 3H), 2.44 (t, *J* = 7.6 Hz, 2H), 1.55-1.49 (m, 2H), 1.29-1.23 (m, 2H), 0.85 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.24, 130.08, 129.07, 128.94, 124.64, 122.05, 118.84, 116.04, 114.71, 114.39, 111.99, 110.29, 54.92, 29.56, 25.74, 22.92, 14.14. IR (film): 3036, 2954, 2928, 2858, 2833, 1611, 1549, 1518, 1463, 1415, 1313, 1282, 1241,1176, 1101, 1033, 824, 737, 722 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{22}NO$ $[M+H]^+$: 280.1696,

found 280.1696.



3b

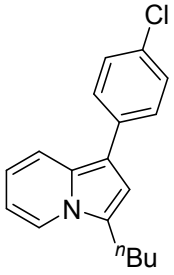
3-Butyl-1-phenylindolizine (3b). Column chromatography on silica gel (eluent: *n*-pentane) afforded the title product in 55% yield (41 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.69-7.67 (m, 3H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.15-7.13 (m, 1H), 6.77 (s, 1H), 6.42 (dd, *J* = 9.0, 6.4 Hz, 1H), 6.19-6.15 (m, 1H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.53-1.46 (m, 2H), 1.29-1.22 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 137.52, 129.25, 129.11, 127.99, 125.38, 124.92, 122.13, 118.79, 116.57, 114.49, 112.07, 110.42, 29.48, 25.69, 22.90, 14.13. IR (film): 3054, 2955, 2928, 2859, 1600, 1549, 1514, 1445, 1416, 1314, 1071, 1029, 940, 826, 731, 697 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{19}N$: 249.1517, found 249.1521.



3c

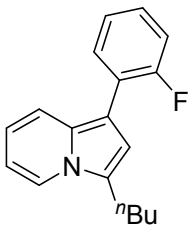
3-Butyl-1-(3,5-dimethoxyphenyl)indolizine (3c). Column chromatography on Al_2O_3 (neutral) (eluent: petroleum ether: ethyl acetate = 30:1-20:1) afforded the title product in 64% yield (60 mg) as a yellow semisolid. ^{1}H NM R (400 MHz, C_6D_6): δ 7.81 (d, *J* = 9.2 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 2H), 6.85 (s, 1H), 6.57 (t, *J* = 2.0 Hz, 1H), 6.44 (dd, *J* = 9.2, 6.4 Hz, 1H), 6.19 (t, *J* = 6.8 Hz, 1H), 3.45 (s, 6H), 2.41 (t, *J* = 7.6 Hz, 2H), 1.53-1.47 (m, 2H), 1.28-1.22 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 161.95, 139.43, 129.49, 124.87, 122.20, 118.90,

116.72, 114.71, 112.18, 110.48, 106.36, 98.02, 54.92, 29.51, 25.72, 22.93, 14.13. IR (film): 2992, 2955, 2930, 2858, 1589, 1513, 1456, 1424, 1408, 1280, 1203, 1152, 1064, 1041, 1100, 927, 823, 737, 721 cm^{-1}. HRMS (ESI) calcd for $C_{20}H_{24}NO_2$ $[M+H]^+$: 310.1802, found 310.1805.



3d

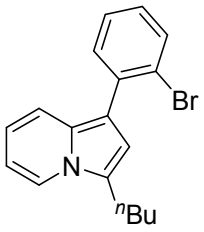
3-Butyl-1-(4-chlorophenyl)indolizine (3d). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane) afforded the title product in 67% yield (57 mg) as a yellow solid. M.p. 57.5-58.6 °C. ^1H NMR (400 MHz, C_6D_6): δ 7.49 (d, *J* = 9.2 Hz, 1H), 7.36-7.25 (m, 4H), 7.19 (d, *J* = 7.2 Hz, 1H), 6.61 (s, 1H), 6.42 (dd, *J* = 8.8, 6.4 Hz, 1H), 6.17 (t, *J* = 6.8 Hz, 1H), 2.37 (t, *J* = 8.0 Hz, 2H), 1.53-1.45 (m, 2H), 1.28-1.22 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 135.92, 130.84, 129.23, 129.19, 128.93, 125.14, 122.22, 118.47, 117.00, 112.98, 111.85, 110.55, 29.46, 25.65, 22.91, 14.13. IR (film): 3045, 2956, 2929, 2870, 1594, 1511, 1490, 1465, 1418, 1314, 1207, 1160, 1090, 1011, 939, 820, 735, 720 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{18}NCl$: 283.1128, found 283.1126.



3e

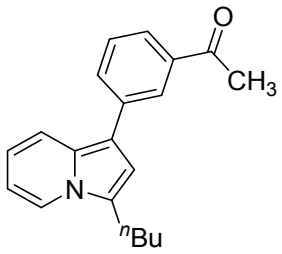
3-Butyl-1-(2-fluorophenyl)indolizine (3e). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate =100:0-100:0.1) afforded the title product in 62% yield (50 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.56-7.52 (m, 2H), 7.21

(d, J = 7.2 Hz, 1H), 7.07-7.02 (m, 1H), 7.00-6.89 (m, 3H), 6.46-6.42 (m, 1H), 6.19-6.16 (m, 1H), 2.38 (t, J = 8.0 Hz, 2H), 1.52-1.44 (m, 2H), 1.28-1.20 (m, 2H), 0.82 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 160.35 (d, $J_{F\text{-}C}$ = 244.6 Hz), 131.07 (d, $J_{F\text{-}C}$ = 3.6 Hz), 130.08, 127.04 (d, $J_{F\text{-}C}$ = 7.7 Hz), 125.09 (d, $J_{F\text{-}C}$ = 14.5 Hz), 124.97, 124.46 (d, $J_{F\text{-}C}$ = 2.3 Hz), 122.11, 119.02 (d, $J_{F\text{-}C}$ = 3.9 Hz), 116.74, 116.36 (d, $J_{F\text{-}C}$ = 23.1 Hz), 113.51 (d, $J_{F\text{-}C}$ = 3.2 Hz), 110.45, 107.61, 29.42, 25.66, 22.89, 14.08. IR (film): 2956, 2928, 2857, 1632, 1612, 1515, 1489, 1456, 1411, 1220, 1120, 1103, 1090, 1033, 946, 813, 754, 740, 724 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{18}NF$: 267.1423, found 267.1427.



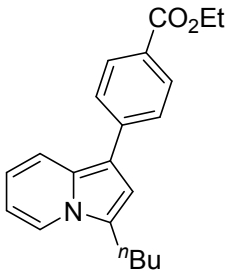
3f

1-(2-Bromophenyl)-3-butylindolizine (3f). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane) afforded the title product in 48% yield (47 mg) as a deep green oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.64 (d, J = 8.4 Hz, 1H), 7.43-7.40 (m, 1H), 7.31 (d, J = 9.2 Hz, 1H), 7.21 (d, J = 6.8 Hz, 1H), 7.04-7.00 (m, 1H), 6.90 (s, 1H), 6.80-6.76 (m, 1H), 6.41 (dd, J = 8.6, 6.8, 1H), 6.18 (t, J = 6.4 Hz, 1H), 2.40 (t, J = 7.6 Hz, 2H), 1.53-1.47 (m, 2H), 1.28-1.23 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 137.90, 133.86, 132.65, 130.06, 127.68, 127.42, 124.64, 124.20, 122.03, 118.86, 116.55, 113.98, 113.05, 110.39, 29.46, 25.65, 22.87, 14.10. IR (film): 3051, 2955, 2927, 2858, 1631, 1589, 1513, 1475, 1435, 1407, 1251, 1114, 1053, 1024, 1006, 941, 831, 763, 752, 736, 722 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{18}NBr$: 327.0623, found 327.0621.



3g

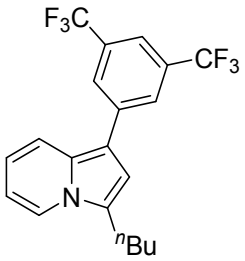
1-(3-(3-Butylindolizin-1-yl)phenyl)ethanone (3g). Column chromatography on Al_2O_3 (basic) (eluent: *n*-hexane: ethyl acetate = 20:1-15:1) afforded the title product in 70% yield (61 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 8.42 (s, 1H), 7.72-7.66 (m, 3H), 7.25-7.22 (m, 2H), 6.76 (s, 1H), 6.45 (dd, *J* = 8.8, 6.8 Hz, 1H), 6.20 (t, *J* = 6.8 Hz, 1H), 2.40 (t, *J* = 7.6 Hz, 2H), 2.22 (s, 3H), 1.52-1.46 (m, 2H), 1.29-1.23 (m, 2H), 0.85 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 197.09, 138.33, 137.85, 131.80, 129.46, 129.13, 127.32, 125.35, 125.20, 122.34, 118.35, 117.32, 113.26, 111.94, 110.65, 29.45, 26.36, 25.66, 22.92, 14.12. IR (film): 3061, 2955, 2928, 2858, 1681, 1598, 1547, 1511, 1452, 1354, 1259, 1081, 951, 910, 791, 735, 720, 693 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{21}NO$: 291.1623, found 291.1626.



3h

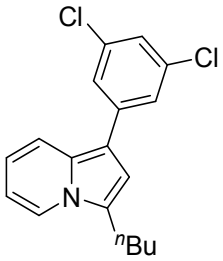
Ethyl 4-(3-butylindolizin-1-yl)benzoate (3h). Column chromatography on Al_2O_3 (basic) (eluent: *n*-hexane: ethyl acetate = 25:1-20:1) afforded the title product in 62% yield (60 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 8.34 (d, *J* = 8.0 Hz, 2H), 7.64-7.59 (m, 3H), 7.21 (d, *J* = 6.8 Hz, 1H), 6.7 (s, 1H), 6.48-6.44 (m, 1H), 6.19 (t, *J* = 6.4 Hz, 1H), 4,23 (q, *J* = 6.8 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 1.50-1.45 (m, 2H), 1.23-1.22 (m, 2H), 1.11 (t, *J* = 6.8 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 166.57, 142.00, 130.67, 129.90, 127.31, 127.06, 125.63, 122.43,

118.63, 117.78, 113.17, 112.09, 110.81, 60.65, 29.41, 25.64, 22.90, 14.47, 14.12. IR (film): 2956, 2928, 2870, 1705, 1603, 1523, 1513, 1464, 1422, 1386, 1212, 1095, 940, 858, 774, 735, 720, 703 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{24}NO_2$ $[M+H]^+$: 322.1802, found 322.1803.



3i

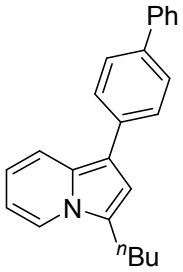
1-(3,5-Bis(trifluoromethyl)phenyl)-3-butylindolizine (3i). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane) afforded the title product in 55% yield (64 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.95 (s, 2H), 7.67 (s, 1H), 7.44 (dd, J = 9.2, 5.2 Hz, 1H), 7.15-7.14 (m, 1H), 6.48 (s, 1H), 6.40-6.36 (m, 1H), 6.15-6.12 (m, 1H), 2.33 (t, J = 7.6 Hz, 2H), 1.49-1.41 (m, 2H), 1.30-1.21 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 139.70, 132.20 (q, $J_{F\text{-}C}$ = 32.0 Hz), 129.90, 126.93 (q, $J_{F\text{-}C}$ = 3.7 Hz), 126.02, 124.39 (q, $J_{F\text{-}C}$ = 271.5 Hz), 122.52, 118.68, 118.08 (q, $J_{F\text{-}C}$ = 3.7 Hz), 117.52, 111.77, 111.08, 110.92, 29.38, 25.56, 22.90, 14.05. IR (film): 2964, 2933, 2862, 1615, 1513, 1386, 1354, 1276, 1176, 1126, 1097, 886, 846, 815, 736, 723, 704 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{17}NF_6$: 385.1265, found 385.1268.



3j

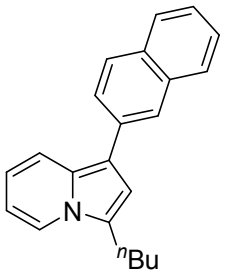
3-Butyl-1-(3,5-dichlorophenyl)indolizine (3j). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane) afforded the title product in 64% yield (61 mg) as a yellow

oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.49 (d, *J* = 1.6 Hz, 2H), 7.41 (d, *J* = 9.2 Hz, 1H), 7.12-7.09 (m, 2H), 6.45 (s, 1H), 6.37-6.33 (m, 1H), 6.12 (t, *J* = 6.4 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.47-1.39 (m, 2H), 1.28-1.18 (m, 2H), 0.85 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 140.56, 135.56, 129.65, 125.57, 125.55, 124.78, 122.35, 118.03, 118.01, 111.75, 111.20, 110.82, 29.33, 25.56, 22.91, 14.13. IR (film): 3065, 2955, 2928, 2859, 1630, 1583, 1556, 1509, 1464, 1389, 1126, 1094, 1011, 871, 840, 797, 734, 720, 682 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{17}NCl_2$: 317.0738, found 317.0737.



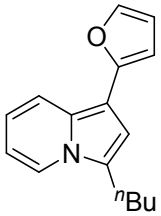
3k

1-(Biphenyl-4-yl)-3-butylindolizine (3k). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 200:1-200:0) afforded the title product in 61% yield (60 mg) as a yellow solid. M.p. 70.8-71.6 °C. ^{1}H NMR (400 MHz, C_6D_6): δ 7.75-7.72 (m, 3H), 7.64-7.60 (m, 4H), 7.30-7.17 (m, 4H), 6.83 (s, 1H), 6.48-6.44 (m, 1H), 6.19 (t, *J* = 6.8 Hz, 1H), 2.41 (t, *J* = 7.6 Hz, 2H), 1.56-1.48 (m, 2H), 1.29-1.23 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 141.77, 138.21, 136.57, 129.40, 129.14, 128.21, 127.87, 127.27, 127.18, 125.12, 122.23, 118.87, 116.78, 114.00, 112.04, 110.51, 29.49, 25.72, 22.92, 14.15. IR (film): 3057, 2954, 2928, 2869, 1627, 1546, 1524, 1505, 1488, 1378, 1314, 1104, 1075, 844, 826, 765, 737, 725, 696 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{24}N$ $[M+H]^+$: 326.1903, found 326.1909.



3l

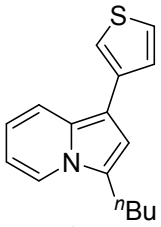
3-Butyl-1-(naphthalen-2-yl)indolizine (3l). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane) afforded the title product in 63% yield (57 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 8.14 (s, 1H), 7.87-7.72 (m, 5H), 7.34-7.24 (m, 3H), 6.88 (s, 1H), 6.47 (dd, *J* = 8.8, 6.8 Hz, 1H), 6.21 (t, *J* = 7.2 Hz, 1H), 2.43 (t, *J* = 7.6 Hz, 2H), 1.58 -1.50 (m, 2H), 1.31-1.25 (m, 2H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 135.04, 134.92, 132.33, 129.62, 128.67, 128.12, 127.42, 126.37, 125.50, 125.16, 122.23, 118.89, 116.87, 114.44, 112.36, 110.58, 29.51, 25.73, 22.92, 14.14. IR (film): 3052, 2954, 2925, 2856, 1626, 1599, 1548, 1514, 1465, 1317, 1234, 1100, 1016, 931, 888, 815, 731 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{21}N$: 299.1674, found 299.1677.



3m

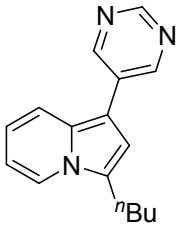
3-Butyl-1-(furan-2-yl)indolizine (3m). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 200:1) afforded the title product in 35% yield (25 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.96 (d, *J* = 9.2 Hz, 1H), 7.27 (d , *J* = 1.2 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.89 (s, 1H), 6.48 (dd, *J* = 9.0, 6.4 Hz, 1H), 6.40- 6.34 (m, 2H), 6.14 (t, *J* = 6.8 Hz, 1H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.46-1.42 (m, 2H), 1.23-1.17 (m, 2H), 0.81 (t, *J* = 7.6 Hz, 3H).^{13}C NMR (100 MHz, C_6D_6): δ 152.85, 139.97, 128.91, 125.17, 122.14, 119.79, 116.98, 111.59, 110.57, 110.00, 105.26, 102.31, 29.31, 25.54, 22.83, 14.09. IR (film): 3114, 2955, 2928, 2859, 1634, 1604,

1518, 1335, 1153, 1123, 1010, 955, 878, 823, 780, 720 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{17}NO$: 239.1310, found 239.1307.



3n

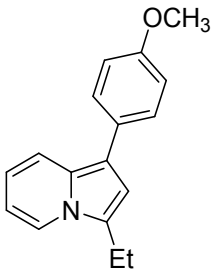
3-Butyl-1-(thiophen-3-yl)indolizine (3n). Column chromatography on silica gel (eluent: *n*-pentane) afforded the title product in 53% yield (41 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.57 (d, *J* = 9.2 Hz, 1H), 7.33 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.12-7.06 (m, 2H), 6.72 (s, 1H), 6.43 (dd, *J* = 8.4, 6.4 Hz, 1H), 6.17 (t, *J* = 6.4 Hz, 1H), 2.38 (t, *J* = 7.6 Hz, 2H), 1.51-1.47 (m, 2H), 1.27-1.21 (m, 2H), 0.83 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 137.75, 129.23, 127.89, 125.51, 124.55, 122.04, 118.95, 117.77, 116.27, 112.00, 110.30, 109.77, 29.50, 25.64, 22.88, 14.11. IR (film): 3101, 2954, 2927, 2858, 1629, 1563, 1533, 1512, 1454, 1360, 1311, 1217, 1109, 879, 852, 715, 679 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{17}NS$: 255.1082, found 255.1081.



3o

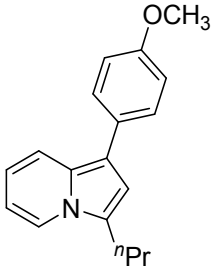
3-Butyl-1-(pyrimidin-5-yl)indolizine (3o). Column chromatography on silica gel (eluent: *n*-pentane: ethyl acetate = 4:1) afforded the title product in 50% yield (38 mg) as a yellow solid. M.p. 75.2-76.3 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 9.03 (s, 1H), 8.94 (s, 2H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 9.2 Hz, 1H), 6.84-6.80 (m, 2H), 6.63 (t, *J* = 7.2 Hz, 1H), 2.83 (t, *J* = 7.2 Hz, 2H), 1.80-1.76 (m, 2H), 1.52-1.46 (m, 2H), 1.00 (t, *J* = 7.6 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 154.77, 154.18, 130.70,

129.50, 126.35, 122.45, 118.48, 117.23, 111.05, 110.63, 105.45, 29.09, 25.43, 22.56, 13.84. IR (film): 3103, 2955, 2926, 2861, 1631, 1572, 1555, 1508, 1422, 1377, 1307, 1231, 1193, 1169, 939, 889 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{18}N_3$ $[M+H^+]$: 252.1495, found 252.1498.



3p

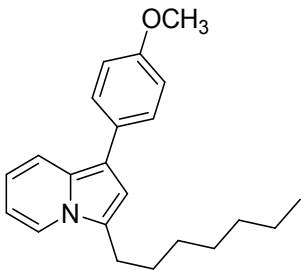
3-Ethyl-1-(4-methoxyphenyl)indolizine (3p). Column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 50:1-30:1) afforded the title product in 66% yield (50 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.68 (d, J = 9.2 Hz, 1H), 7.60-7.58 (m, 2H), 7.17 (d, J = 7.2 Hz, 1H), 6.97-6.95 (m, 2H), 6.76 (s, 1H), 6.46-6.42 (m, 1H), 6.20-6.16 (m, 1H), 3.41 (s, 3H), 2.35 (q, J = 7.6 Hz, 2H), 1.12 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.22, 130.10, 129.06, 128.96, 125.97, 121.94, 118.81, 116.11, 114.71, 114.36, 111.16, 110.27, 54.91, 19.16, 11.71. IR (film): 3040, 2967, 2934, 2834, 1611, 1550, 1519, 1462, 1415, 1299, 1283, 1239, 1178, 1101, 1034, 827, 739, 723 cm^{-1}. HRMS (EI) calcd for $C_{17}H_{17}NO$: 251.1310, found 251.1309.



3q

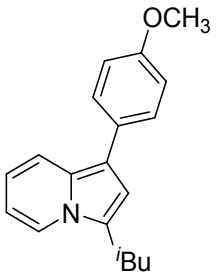
1-(4-Methoxyphenyl)-3-propylindolizine (3q). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 80:1-50:1) afforded the title product in 65%

yield (52 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.69 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 6.8 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 2H), 6.76 (s, 1H), 6.44 (t, *J* = 8.0 Hz, 1H), 6.19 (t, *J* = 6.4 Hz, 1H), 3.41 (s, 3H), 2.39 (t, *J* = 7.2 Hz, 2H), 1.57-1.52 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.23, 130.07, 129.08, 128.96, 124.48, 122.06, 118.82, 116.05, 114.71, 114.38, 112.07, 110.28, 54.91, 28.01, 20.72, 14.21. IR (film): 2957, 2930, 2871, 2834, 1652, 1549, 1518, 1463, 1416, 1312, 1282, 1241, 1176, 1101, 1032, 940, 826, 738, 722 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{19}NO$: 265.1467, found 265.1468.



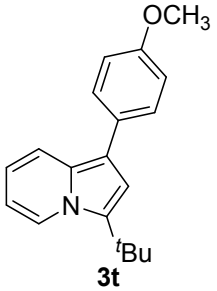
3r

3-Heptyl-1-(4-methoxyphenyl)indolizine (3r). Column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 50:1-30:1) afforded the title product in 56% yield (54 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.69 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.80 (s, 1H), 6.45 (dd, *J* = 9.0, 6.8 Hz, 1H), 6.21 (t, *J* = 6.8 Hz, 1H), 3.41 (s, 3H), 2.47 (t, *J* = 7.6 Hz, 2H), 1.60-1.57 (m, 2H), 1.31-1.23 (m, 8H), 0.91 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.24, 130.07, 129.07, 128.95, 124.72, 122.04, 118.87, 116.05, 114.71, 114.42, 111.99, 110.31, 54.91, 32.23, 29.91, 29.60, 27.52, 26.09, 23.13, 14.40. IR (film): 2926, 2854, 1611, 1551, 1519, 1464, 1415, 1313, 1283, 1243, 1178, 1121, 1036, 940, 832, 737, 722 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{27}NO$: 321.2093, found 321.2096.



3s

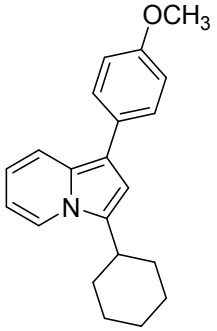
3-Isobutyl-1-(4-methoxyphenyl)indolizine (3s). Column chromatography on Al_2O_3 (basic) (eluent: petroleum ether: ethyl acetate = 50:1-30:1) afforded the title product in 56% yield (47 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.76 (s, 1H), 6.43 (dd, *J* = 8.6, 7.2 Hz, 1H), 6.19 (t, *J* = 6.8 Hz, 1H), 3.41 (s, 3H), 2.40 (d, *J* = 6.8 Hz, 2H), 1.85-1.82 (m, 1H), 0.84 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.27, 130.01, 129.14, 129.05, 123.77, 122.19, 118.88, 116.03, 114.72, 114.50, 113.18, 110.32, 54.92, 35.27, 27.08, 22.82. IR (film): 2954, 2919, 2867, 2834, 1611, 1549, 1517, 1463, 1415, 1333, 1282, 1243, 1177, 1121, 1033, 940, 828, 738, 723 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{21}NO$: 279.1623, found 279.1618.



3t

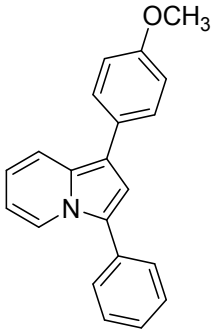
3-(*tert*-Butyl)-1-(4-methoxyphenyl)indolizine (3t). Column chromatography on Al_2O_3 (basic) (eluent: petroleum ether: ethyl acetate = 100:1-50:1) afforded the title product in 66% yield (55 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.79 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.83 (s, 1H), 6.42 (dd, *J* = 8.8, 6.0 Hz, 1H), 6.18 (t, *J* = 6.4 Hz, 1H), 3.41 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.30, 132.73, 130.38, 129.99, 129.32, 124.76, 119.26, 115.70, 114.69, 114.33, 111.31, 110.00, 54.90, 31.78, 28.39. IR (film):

2964, 2930, 2869, 2833, 1611, 1549, 1508, 1462, 1417, 1335, 1284, 1242, 1223, 1174, 1142, 1036, 1014, 939, 823, 740, 722 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{21}NO$: 279.1623, found 279.1627.



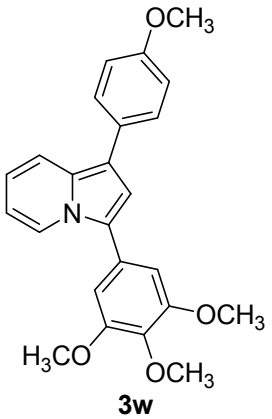
3u

3-Cyclohexyl-1-(4-methoxyphenyl)indolizine (3u). Column chromatography on Al_2O_3 (basic) (eluent: petroleum ether: ethyl acetate = 100:1-50:1) afforded the title product in 65% yield (60 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.68 (d, *J* = 9.2 Hz, 1H), 7.61-7.58 (m, 2H), 7.38 (d, *J* = 7.2 Hz, 1H), 6.98-6.95 (m, 2H), 6.80 (s, 1H), 6.44 (dd, *J* = 8.8, 6.4 Hz, 1H), 6.19 (t, *J* = 6.4 Hz, 1H), 3.41 (s, 3H), 2.52-2.47 (m, 1H), 1.95-1.92 (m, 2H), 1.70-1.63 (m, 3H), 1.38-1.14 (m, 5H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.24, 130.15, 130.06, 129.14, 128.96, 122.14, 119.04, 116.09, 114.70, 114.54, 110.25, 109.96, 54.92, 35.29, 31.94, 26.81, 26.69. IR (film): 3045, 2996, 2924, 2851, 1611, 1549, 1513, 1463, 1415, 1339, 1284, 1243, 1178, 1133, 1103, 1035, 1006, 941, 823, 738, 723 cm^{-1}. HRMS (EI) calcd for $C_{21}H_{23}NO$: 305.1780, found 305.1777.



3v

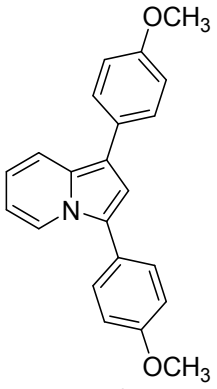
1-(4-Methoxyphenyl)-3-phenylindolizine (3v). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 30:1-20:1) afforded the title product in 42% yield (38 mg) as a yellow solid. M.p. 106.8-108.5 °C. ^{1}H NMR (400 MHz, C_6D_6): δ 7.95 (d, *J* = 7.2 Hz, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.11-7.10 (m, 1H), 7.03 (s, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.43-6.39 (m, 1H), 6.06 (t, *J* = 6.8 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.52, 132.84, 130.44, 129.43, 129.26, 129.22, 128.52, 127.32, 125.78, 122.62, 118.98, 117.63, 116.07, 114.76, 114.40, 111.06, 54.92. IR (film): 3052, 2992, 2930, 2833, 1600, 1551, 1522, 1463, 1418, 1301, 1285, 1243, 1179, 1140, 1110, 1033, 1012, 962, 827, 795, 727 cm^{-1}. HRMS (EI) calcd for $C_{21}H_{17}NO$: 299.1310, found 299.1313.



3w

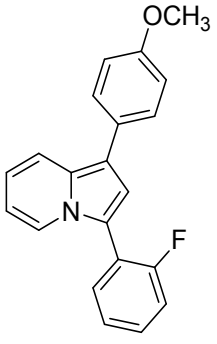
1-(4-Methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)indolizine (3w). Column chromatography on Al_2O_3 (basic) (eluent: petroleum ether: ethyl acetate = 15:1-10:1) afforded the title product in 34% yield (40 mg) as a yellow solid. M.p. 134.6-135.8 °C. ^{1}H NMR (400 MHz, C_6D_6): δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.13 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.66 (s, 2H), 6.47 (dd, *J* = 8.4, 6.4 Hz, 1H), 6.17 (t, *J* = 6.0 Hz, 1H), 3.91 (s, 3H), 3.43 (s, 3H), 3.39 (s, 6H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.57, 154.63, 138.99, 130.11, 129.46, 129.25, 127.99, 126.20, 122.91, 119.05, 117.54, 115.83, 114.84, 114.11, 111.10, 106.56, 60.62, 55.87, 54.94. IR (film): 2996, 2924, 2853, 1580, 1550, 1524, 1504, 1463, 1431, 1411, 1343, 1283, 1236, 1125, 1035, 1005, 943, 826, 743, 727 cm^{-1}. HRMS (EI) calcd for

$C_{24}H_{23}NO_4$: 389.1627, found 389.1625.



3x

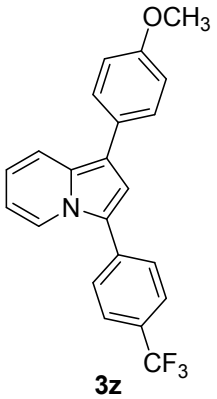
1,3-Bis(4-methoxyphenyl)indolizine (3x). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 20:1-15:1) afforded the title product in 35% yield (35 mg) as a yellow solid. M.p. 110.2-111.5 ^oC. ^1H NMR (400 MHz, C_6D_6): δ 7.95 (d, J = 7.2 Hz, 1H), 7.69 (d, J = 9.2 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 7.03 (s, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.43 (dd, J = 9.0, 6.4 Hz, 1H), 6.10 (t, J = 6.4 Hz, 1H), 3.42 (s, 3H), 3.34 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 159.49, 158.47, 130.11, 129.97, 129.63, 129.25, 125.73, 125.20, 122.62, 118.98, 117.29, 115.78, 114.77, 113.95, 110.91, 54.93, 54.89. IR (film): 3036, 2992, 2931, 2834, 1610, 1574, 1552, 1529, 1505, 1463, 1440, 1340, 1307, 1283, 1243, 1212, 1177, 1139, 1109, 1033, 963, 826, 742, 727 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{19}NO_2$: 329.1416, found 329.1418.



3y

3-(2-Fluorophenyl)-1-(4-methoxyphenyl)indolizine (3y). Column chromatography

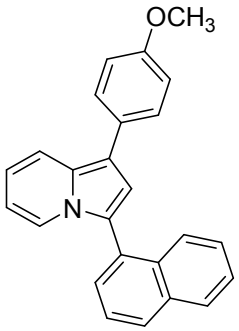
on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 30:1-20:1) afforded the title product in 47% yield (45 mg) as a yellow semisolid. ^{1}H NMR (400 MHz, C_6D_6): δ 7.65-7.60 (m, 2H), 7.56-7.52 (m, 2H), 7.23 (t, J = 7.6 Hz, 1H), 7.07 (s, 1H), 6.95-6.85 (m, 5H), 6.43 (dd, J = 9.4, 6.8 Hz, 1H), 6.13-6.10 (m, 1H), 3.40 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 161.49 (d, $J_{F\text{-}C}$ = 247.5 Hz), 158.53, 131.93 (d, $J_{F\text{-}C}$ = 3.8 Hz), 130.81, 129.45 (d, $J_{F\text{-}C}$ = 7.5 Hz), 129.31, 129.27, 124.75 (d, $J_{F\text{-}C}$ = 3.6 Hz), 123.71 (d, $J_{F\text{-}C}$ = 4.2 Hz), 120.60 (d, $J_{F\text{-}C}$ = 14.8 Hz), 119.60, 118.69, 117.93, 116.32 (d, $J_{F\text{-}C}$ = 21.9 Hz), 116.10, 115.60, 114.73, 111.04, 54.90. IR (film): 3040, 3000, 2928, 2834, 1612, 1576, 1552, 1524, 1502, 1469, 1453, 1343, 1308, 1284, 1245, 1222, 1179, 1103, 1034, 967, 829, 768, 726 cm^{-1}. HRMS (EI) calcd for $C_{21}H_{16}NOF$: 317.1216, found 317.1211.



3z

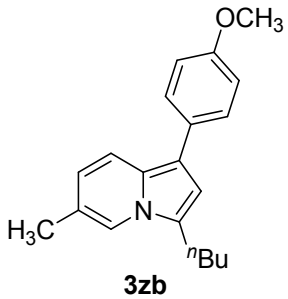
1-(4-Methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)indolizine (3z). Column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 40:1-20:1) afforded the title product in 26% yield (29 mg) as a yellow solid. M.p. 154.5-155.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 7.2 Hz, 1H), 7.73-7.69 (m, 5H), 7.53 (d, J = 8.4 Hz, 2H), 7.02-6.99 (m, 3H), 6.76 (dd, J = 9.0, 6.4 Hz, 1H), 6.53 (t, J = 7.2 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.93, 135.77, 130.77, 128.73, 128.70 (q, $J_{F\text{-}C}$ = 32.1 Hz), 128.35, 127.73, 125.97 (q, $J_{F\text{-}C}$ = 3.9 Hz), 124.18 (q, $J_{F\text{-}C}$ = 270.6 Hz), 123.87, 118.71, 118.33, 115.70, 114.52, 114.30, 111.59, 55.33. IR (film): 2929, 2822, 1614, 1552, 1532, 1505, 1465, 1411, 1324, 1302, 1283, 1246, 1120, 1066, 1015, 964, 851, 743, 726 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{16}NOF_3$: 367.1184, found

367.1182.



3za

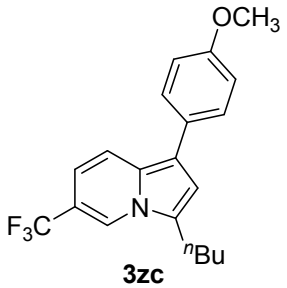
1-(4-Methoxyphenyl)-3-(naphthalen-1-yl)indolizine (3za). Column chromatography on Al_2O_3 (basic) (eluent: petroleum ether: ethyl acetate = 30:1-20:1) afforded the title product in 46% yield (48 mg) as a yellow solid. M.p. 135.7-136.5 ^oC. ^1H NMR (400 MHz, C_6D_6): δ 7.75 (d, J = 9.2 Hz, 1H), 7.70-7.62 (m, 5H), 7.41 (d, J = 6.8 Hz, 1H), 7.30-7.22 (m, 3H), 7.12-7.09 (m, 2H), 6.97 (d, J = 9.2 Hz, 2H), 6.43 (dd, J = 9.2, 6.4 Hz, 1H), 5.95 (t, J = 7.2 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.47, 134.48, 132.89, 130.30, 129.92, 129.56, 129.32, 129.20, 129.02, 128.86, 127.01, 126.42, 125.97, 123.72, 123.57, 118.78, 117.63, 115.72, 115.59, 114.82, 110.80, 54.93. IR (film): 3045, 3000, 2923, 2853, 1610, 1547, 1515, 1505, 1463, 1421, 1339, 1305, 1284, 1266, 1242, 1177, 1034, 951, 828, 762, 741, 726 cm^{-1}. HRMS (EI) calcd for $C_{25}H_{19}NO$: 349.1467, found 349.1468.



3zb

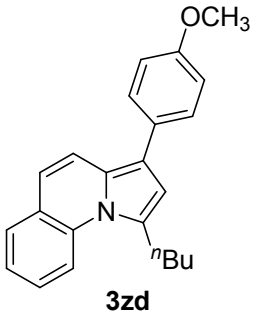
3-Butyl-1-(4-methoxyphenyl)-6-methylindolizine (3zb). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 50:1-30:1) afforded the title product in 62% yield (55 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6): δ 7.68-7.62

(m, 3H), 7.22 (s, 1H), 6.97 (d, J = 8.4 Hz, 2H), 6.77 (s, 1H), 6.34 (d, J = 9.2 Hz, 1H), 3.42 (s, 3H), 2.50 (t, J = 7.6 Hz, 2H), 1.98 (s, 3H), 1.62-1.58 (m, 2H), 1.34-1.28 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.19, 130.34, 129.01, 124.32, 119.63, 119.39, 119.29, 118.46, 114.74, 114.30, 111.58, 54.92, 29.62, 25.86, 22.98, 18.50, 14.16. IR (film): 2955, 2928, 2859, 2831, 1651, 1613, 1557, 1511, 1463, 1440, 1379, 1300, 1243, 1177, 1034, 952, 832, 782 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{23}NO$: 293.1780, found 293.1778.



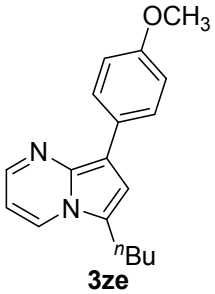
3zc

3-Butyl-1-(4-methoxyphenyl)-6-(trifluoromethyl)indolizine (3zc). Column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 40:1-20:1) afforded the title product in 43% yield (45 mg) as a yellow solid. M.p. 86.5-88.1 ^{o}C. ^{1}H NMR (400 MHz, C_6D_6): δ 7.73 (s, 1H), 7.49-7.45 (m, 3H), 6.96-6.94 (m, 2H), 6.70 (s, 1H), 6.56 (d, J = 9.2 Hz, 1H), 3.42 (s, 3H), 2.19 (t, J = 7.6 Hz, 2H), 1.45-1.42 (m, 2H), 1.22-1.16 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.78, 129.20, 128.81, 128.20, 126.79, 125.32 (q, $J_{F\text{-}C}$ = 268.9 Hz), 121.24 (q, $J_{F\text{-}C}$ = 6.1 Hz), 119.57, 116.28, 114.81, 114.36 (q, $J_{F\text{-}C}$ = 32.7 Hz), 113.83, 111.30 (q, $J_{F\text{-}C}$ = 2.0 Hz), 54.94, 29.24, 25.14, 22.79, 14.08. IR (film): 2955, 2931, 2862, 2830, 1642, 1609, 1573, 1515, 1456, 1423, 1384, 1342, 1323, 1285, 1208, 1179, 1115, 1075, 1033, 949, 855, 791 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{20}NOF_3$: 347.1497, found 347.1499.



3zd

1-Butyl-3-(4-methoxyphenyl)pyrrolo[1,2-*a*]quinoline (3zd). Column chromatography on Al_2O_3 (basic) (eluent: *n*-pentane: ethyl acetate = 50:1-40:1) afforded the title product in 75% yield (74 mg) as a yellow solid. M.p. 100.5-101.6 ^oC. ^1H NMR (400 MHz, C_6D_6): δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.8, 3H), 7.37 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.18-7.14 (m, 1H), 7.08-7.04 (m, 1H), 6.96 (t, *J* = 8.8 Hz, 2H), 6.70-6.67 (m, 2H), 3.42 (s, 3H), 2.99 (t, *J* = 8.0 Hz, 2H), 1.67-1.63 (m, 2H), 1.34-1.28 (m, 2H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.73, 136.30, 131.53, 129.82, 129.46, 128.67, 128.56, 126.73, 126.53, 123.22, 118.86, 118.48, 117.91, 116.81, 114.69, 113.54, 54.94, 31.58, 31.11, 22.93, 14.22. IR (film):3051, 2955, 2930, 2869, 2828, 1609, 1560, 1518, 1481, 1446, 1365, 1309, 1283, 1245, 1218, 1177, 1141, 1038, 835, 788, 755, 739 cm^{-1}. HRMS (EI) calcd for $C_{23}H_{23}NO$: 329.1780, found 329.1777.

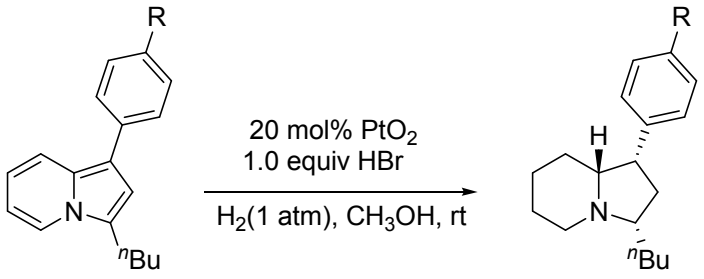


3ze

6-Butyl-8-(4-methoxyphenyl)pyrrolo[1,2-*a*]pyrimidine (3ze). Column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 10:1-8:1) afforded the title product in 33% yield (28 mg) as a red oil. ^1H NMR (400 MHz, C_6D_6): δ 8.45 (d, *J* = 8.4 Hz, 2H), 7.88 (dd, *J* = 3.6, 1.6 Hz, 1H), 7.08-7.05 (m, 3H), 6.99 (s, 1H), 5.78 (dd, *J* = 7.2, 3.6 Hz, 1H), 3.40 (s, 3H), 2.24 (t, *J* = 7.6 Hz, 2H),

1.44-1.41 (m, 2H), 1.25-1.20 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.26, 140.87, 136.46, 128.84, 128.38, 127.93, 121.39, 114.43, 112.47, 111.81, 105.94, 54.84, 29.41, 25.08, 22.85, 14.12. IR (film): 3085, 3028, 2955, 2928, 2858, 2830, 1610, 1560, 1517, 1501, 1464, 1438, 1398, 1278, 1245, 1179, 1125, 1100, 1035, 942, 828, 763, 743 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{20}N_2O$: 280.1576, found 280.1573.

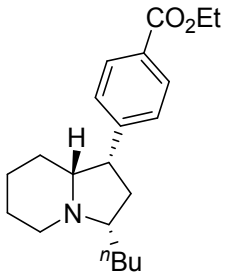
Synthesis of 4a, 4b



3

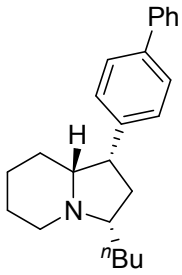
For **4a**, R = CO_2Et
For **4b**, R = Ph

To a solution of ethyl 4-(3-butylindolizin-1-yl)benzoate **3h** (160.7 mg, 0.5 mmol) in CH_3OH (10 mL) were added PtO_2 (22.7 mg, 0.1 mmol) and HBr (0.25 mL, 0.5 mmol, 2 M solution in water). The mixture was stirred under H_2 (1 atm) at room temperature for 6 h. Then the resulting mixture was quenched with saturated sodium bicarbonate solution, extracted with ethyl acetate, and dried over Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1-20:1) to afford **4a** in 72% yield (118 mg) as a yellow oil.



4a

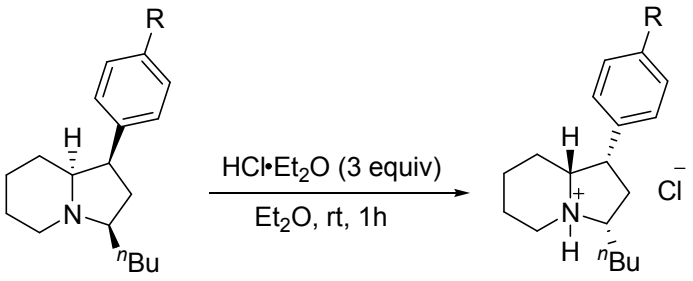
4a. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.24-3.14 (m, 2H), 2.49-2.41 (m, 1H), 2.17-2.08 (m, 2H), 1.85-1.81 (m, 1H), 1.73-1.67 (m, 1H), 1.61-1.55 (m, 2H), 1.52-1.43 (m, 1H), 1.39-1.20 (m, 9H), 1.17-1.08 (m, 2H), 0.92 (t, *J* = 6.4 Hz, 3H), 0.70-0.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.67, 150.98, 128.92, 128.88, 127.92, 69.29, 65.78, 60.55, 52.15, 45.84, 38.99, 32.66, 28.53, 28.03, 25.08, 24.40, 23.05, 14.27, 14.04. IR (film): 2931, 2856, 2790, 2755, 2709, 1716, 1608, 1573, 1502, 1441, 1419, 1390, 1366, 1339, 1309, 1271, 1218, 1178, 1147, 1105, 1061, 1022, 866, 776, 752, 719, 691 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{32}NO_2$ $[M+H]^+$: 330.2428, found 330.2427.



4b

4b. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1-15:1) afforded **4b** as a yellow oil in 74% yield (135 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.42-7.39 (m, 2H), 7.35-7.28 (m, 3H), 3.26 (d, *J* = 10.4 Hz, 1H), 3.19-3.14 (m, 1H), 2.51-2.43 (m, 1H), 2.17-2.08 (m, 2H), 1.87-1.83 (m, 1H), 1.75-1.69 (m, 1H), 1.64-1.50 (m, 3H), 1.41-1.11 (m, 8H), 0.92 (t, *J* = 6.4 Hz, 3H), 0.81-0.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.66, 141.14, 138.47, 129.36, 128.62, 126.93, 126.84, 126.36, 69.62, 65.99, 52.41, 45.47, 39.20, 32.83, 28.72, 28.29, 25.22, 24.55, 23.14, 14.13. IR (film): 3027, 2927, 2854, 2788, 2754, 2707, 1730, 1601, 1514, 1486, 1450, 1369, 1338, 1265, 1220, 1147, 1116, 1062, 1041, 1008, 908, 852, 830, 765, 739, 697 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{32}N$ $[M+H]^+$: 334.2529, found 334.2530.

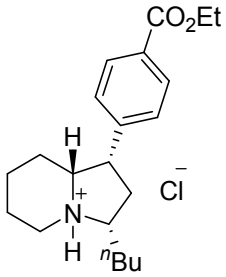
Synthesis of HCl salts of **4a** and **4b**



4

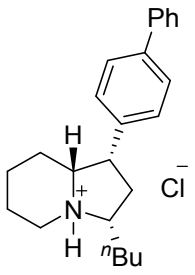
For HCl salt of **4a**, R = CO_2Et, 87%
For HCl salt of **4b**, R = Ph, 86%

To a solution of **4a** (395 mg, 1.2 mmol) in Et_2O (20 mL) was added $HCl \cdot Et_2O$ (9.5 mL, 3.6 mmol, 0.38 M). The mixture was stirred at room temperature for 1 h. Then the resulting mixture was evaporated under the reduced pressure and the residue was washed by Et_2O to afford the HCl salt of **4a** in 87% yield (382 mg) as a white solid. M.p. 101.5-102.7 °C.



HCl salt of **4a**

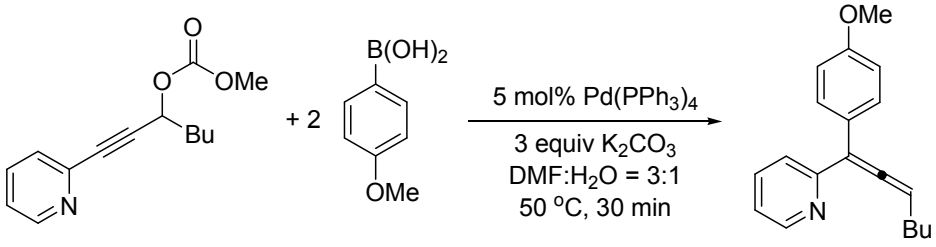
HCl salt of **4a**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.16 (bs, 1H), 8.02 (d, *J* = 7.6 Hz, 2H), 7.87 (d, *J* = 7.6 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.94-3.79 (m, 3H), 3.49 (bs, 1H), 3.08-3.00 (m, 1H), 2.88-2.81 (m, 1H), 2.45-2.21 (m, 3H), 2.09-2.05 (m, 1H), 1.88-1.85 (m, 2H), 1.69-1.57 (m, 2H), 1.41-1.25 (m, 8H), 0.92 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.02, 143.50, 129.67, 129.36, 129.26, 70.17, 67.16, 60.58, 50.85, 42.98, 37.06, 28.46, 27.55, 25.26, 23.05, 22.24, 21.61, 13.99, 13.63. IR (film): 2955, 2953, 2864, 1715, 1611, 1448, 1423, 1366, 1278, 1187, 1106, 1022, 866, 778, 735, 717 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{32}NO_2$ $[(M\text{-}HCl)+H]^+$: 330.2428, found 330. 2431.



HCl salt of **4b**

HCl salt of **4b**. The residue was washed by Et_2O to afford HCl salt of **4b** as a white solid in 86% yield (127 mg). M.p. 98-99.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.84 (bs, 1H), 7.80 (d, *J* = 7.6 Hz, 2H), 7.61-7.56 (m, 4H), 7.44-7.40 (m, 2H), 7.35-7.31 (m, 1H), 3.90-3.88 (m, 1H), 3.72-3.65 (m, 1H), 3.29-3.21 (m, 1H), 3.02-3.00 (m, 1H), 2.78-2.73 (m, 1H), 2.62-2.30 (m, 4H), 2.09-1.79 (m, 4H), 1.42-1.24 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.44, 140.02, 137.25, 130.20, 128.65, 127.16, 127.07, 126.82, 71.00, 67.70, 51.30, 43.05, 37.43, 28.76, 27.58, 25.45, 23.41, 22.38, 21.75, 13.85. IR (film): 3028, 2955, 2932, 2863, 1599, 1563, 1523, 1487, 1447, 1418, 1379, 1266, 1209, 1177, 1120, 1076, 1044, 1007, 938, 905, 849, 769, 737, 698 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{32}N$ [(M-HCl)+H]$^+$: 334.2529, found 334.2541.

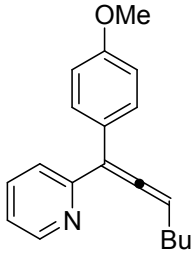
Synthesis of 2a



1a **2a**

To a solution of **1a** (74 mg, 0.3 mmol) in DMF (2 mL) were sequentially added $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), K_2CO_3 (124 mg, 0.9 mmol), DMF (1 mL) and H_2O (1 mL). After stirring at 50 °C for 30 min, the reaction mixture was quenched with H_2O, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated and C_6D_6 and CH_2Br_2 (21 μL, 0.3 mmol) was added. Allene **2a** was obtained in 63%

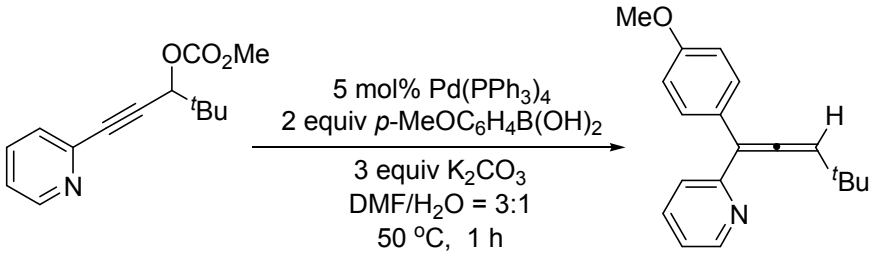
NMR yield. Then the sample was recovered and purified by column chromatography (petroleum ether/ethyl acetate = 20:1) on silica gel to afford **2a** as a colorless oil in 56% yield (46.6 mg), which decomposed slightly under air.



2a

2-(1-(4-Methoxyphenyl)hepta-1,2-dien-1-yl)pyridine (2a). ^{1}H NMR (400 MHz, C_6D_6): δ 8.54-8.53 (m, 1H), 7.61-7.59 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.12 (td, *J* = 8.4, 2.0 Hz, 1H), 6.87-6.85 (m, 2H), 6.64-6.61 (m, 1H), 5.62 (t, 6.8 Hz, 1H), 3.31 (s, 3H), 2.04 (q, *J* = 7.2 Hz, 2H), 1.42-1.37 (m, 2H), 1.27-1.21 (m, 2H), 0.79 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100.5 MHz, C_6D_6): δ 207.92, 159.45, 157.45, 149.60, 135.89, 130.53, 129.06, 123.41, 121.40, 114.04, 110.94, 95.18, 54.82, 31.59, 28.94, 22.60, 14.03. HRMS (ESI) for $C_{19}H_{22}NO$ $[M+H]^+$: calcd 280.1696, found 280.1697.

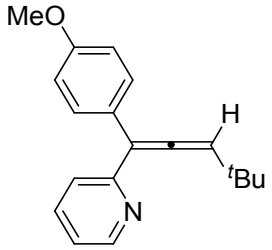
Synthesis of allene 2t.



1j **2t**

To a solution of **1j** (74 mg, 0.3 mmol) in DMF (3 mL) were added $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), K_2CO_3 (124 mg, 0.9 mmol) and H_2O (1 mL) successively at room temperature. Then the reaction mixture was stirred at 50 °C for 1 h. The resulting mixture was quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column

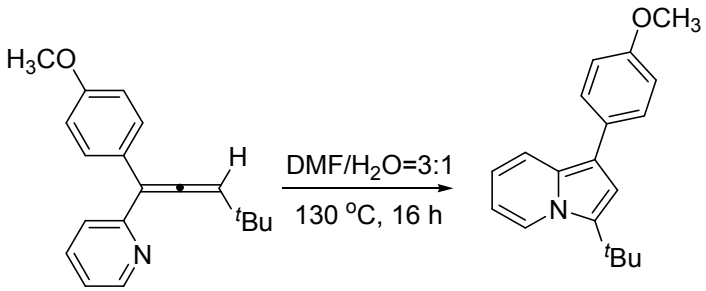
chromatography on silica gel (eluent: petroleum ether: ethyl acetate =30:1-15:1) to afford **2t** in 84% yield (70 mg) as a yellow oil.



2t

2-(1-(4-Methoxyphenyl)-4,4-dimethylpenta-1,2-dien-1-yl)pyridine (2t). ^{1}H NMR (400 MHz, C_6D_6): δ 8.53 (d, *J* = 4.8 Hz, 1H), 7.61 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.11 (td, *J* = 7.6, 1.6 Hz, 1H), 6.85 (dd, *J* = 7.0, 1.6 Hz, 2H), 6.63-6.60(m, 1H), 5.64 (s, 1H), 3.31 (s, 3H), 1.10 (s, 9H). ^{13}C NMR (100 MHz, C_6D_6): δ 205.18, 159.44, 157.45, 149.63, 135.90, 130.34, 129.13, 123.17, 121.40, 114.06, 112.40, 106.73, 54.81, 33.44, 30.34. IR (film): 3061, 3000, 2957, 2901, 2864, 1942, 1606, 1564, 1465, 1429, 1362, 1246, 1174, 1035, 919, 832, 784, 743 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{22}NO$ $[M+H]^+$: 280.1696, found 280.1704.

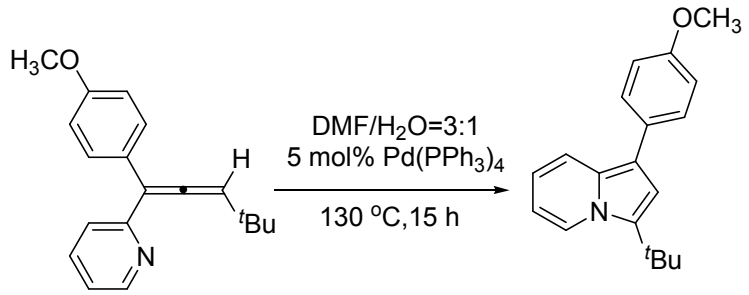
Control Experiments



2t **3t**

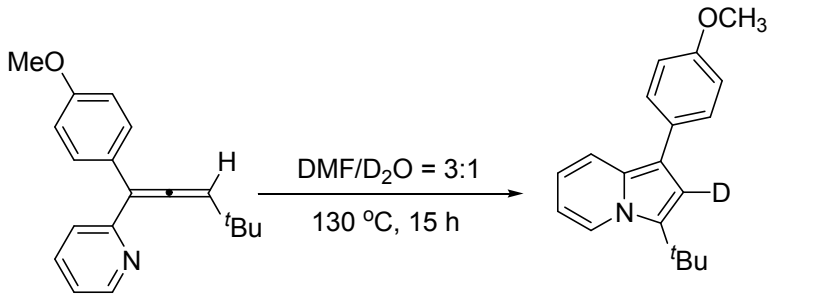
To a solution of **2t** (56 mg, 0.2 mmol) in DMF (3 mL) was added H_2O (1 mL) at room temperature. Then the reaction mixture was stirred at 130 °C for 16 h. The resulting mixture was quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and

the residue was purified by column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 40:1 - 30:1) to afford **3t** in 73% yield (41 mg) as a yellow oil.



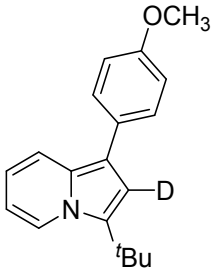
2t **3t**

To a solution of **2t** (70 mg, 0.25 mmol) in DMF (3 mL) was added $Pd(PPh_3)_4$ (14 mg, 0.0125 mmol) and H_2O (1 mL) at room temperature. Then the reaction mixture was stirred at 130 °C for 15 h. The resulting mixture was quenched with water, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 30:1) to afford **3t** in 63% yield (44 mg) as a yellow oil.



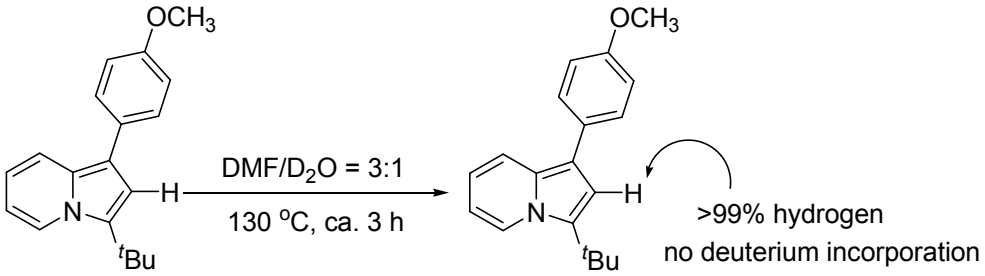
2t **3t-*d*** (D = 99%)

To a solution of **2t** (70 mg, 0.25 mmol) in anhydrous DMF (3 mL) was added D_2O (1 mL) at room temperature. Then the reaction mixture was stirred at 130 °C for 15 h. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on Al_2O_3 (neutral) (eluent: *n*-pentane: ethyl acetate = 30:1) to afford **3t-*d*** in 66% yield (46 mg) with 99% deuterium incorporation as a yellow oil.



3t-*d*

3t-*d*. ^{1}H NMR (400 MHz, C_6D_6): δ 7.79 (d, *J* = 7.2 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.42 (dd, *J* = 9.0, 6.0 Hz, 1H), 6.18 (t, *J* = 6.4 Hz, 1H), 3.40 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, C_6D_6): δ 158.31, 132.65, 130.38, 129.98, 129.33, 124.76, 119.28, 115.69, 114.69, 114.26, 111.08 (t, *J* = 24.2 Hz), 109.99, 54.90, 31.77, 28.38. IR (film): 2962, 2929, 2869, 2834, 1611, 1544, 1510, 1462, 1441, 1335, 1291, 1244, 1217, 1179, 1152, 1037, 1014, 960, 832, 747, 724 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{21}DNO$ $[M+H]^+$: 281.1759, found 281.1757.



3t **3t**

To a solution of **3t** (56 mg, 0.20 mmol) in anhydrous DMF (3 mL) was added D_2O (1 mL) at room temperature. Then the reaction mixture was stirred at 130 °C for ca. 3 h. The solvent was evaporated under the reduced pressure and the residue was purified by chromatography on Al_2O_3 (neutral) (eluent: petroleum ether: ethyl acetate = 30:1-20:1) to afford **3t** in 93% yield (52 mg) as a yellow oil. The results indicated that deuterium was not incorporated in **3t** during the above reaction process.

References:

1 R. Hardin,; R. Sarpong, *Org. Lett.,* 2007, **9**, 4057.

2 M. Beshai, B. Dhudshia, R. Mills, A. N. Thadani, *Tetrahedron Lett.,* 2008, **49**, 6794.

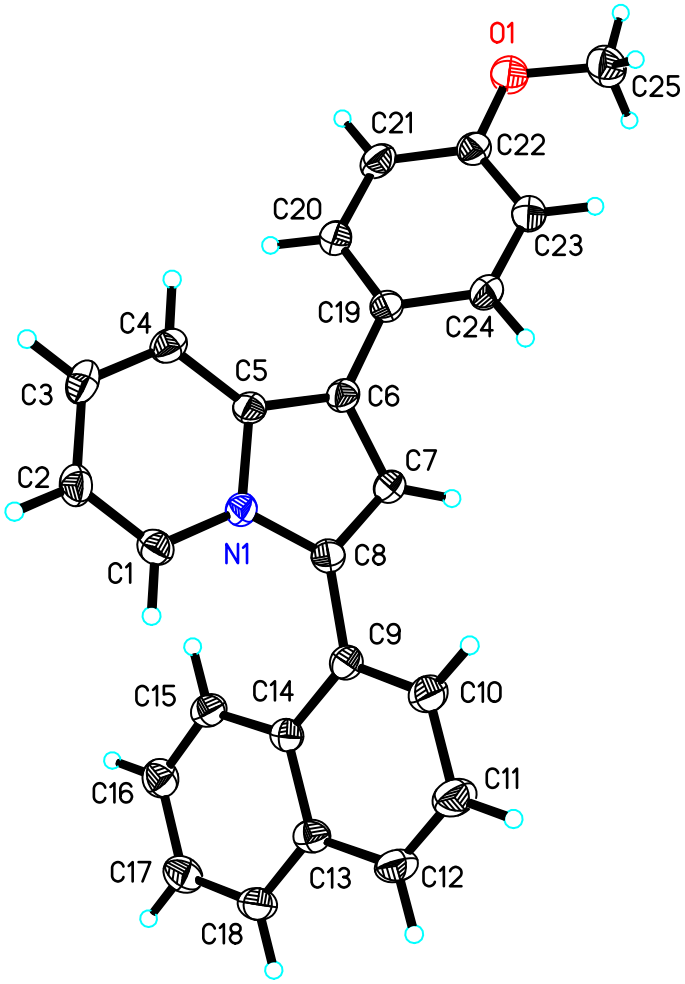


Figure S1. X-ray crystal structure of **3za**

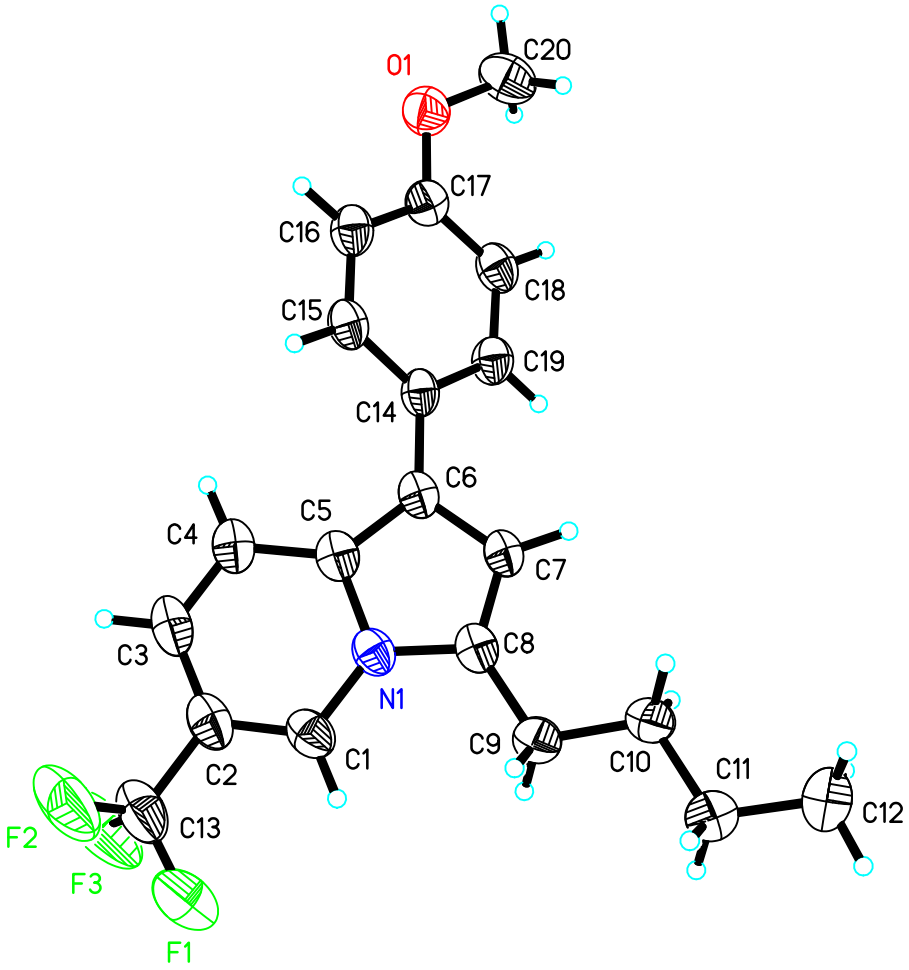


Figure S2. X-ray crystal structure of **3zc**

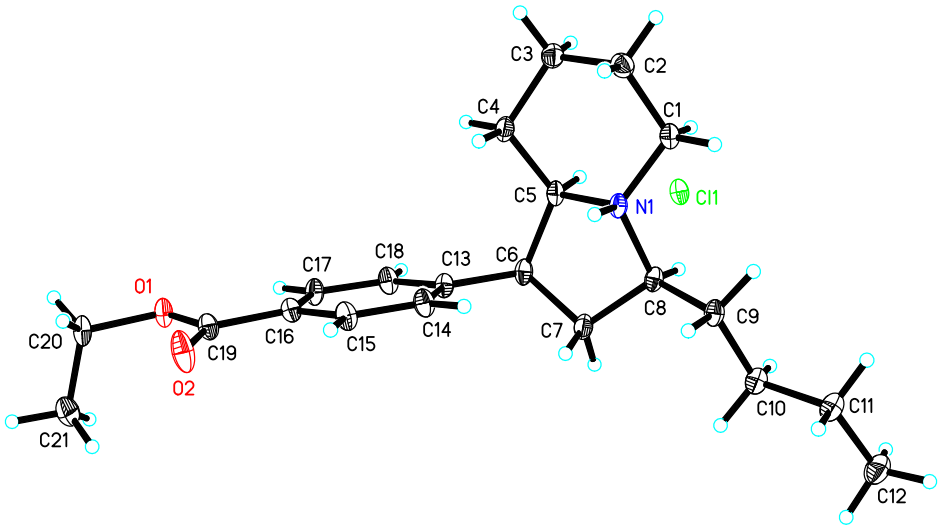


Figure S3. X-ray crystal structure of HCl salt of **4a**

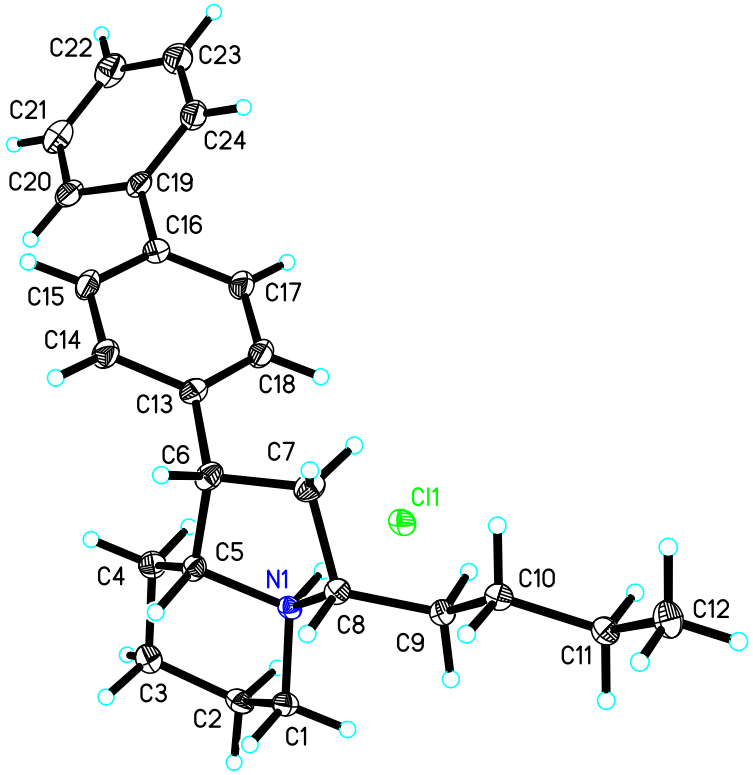
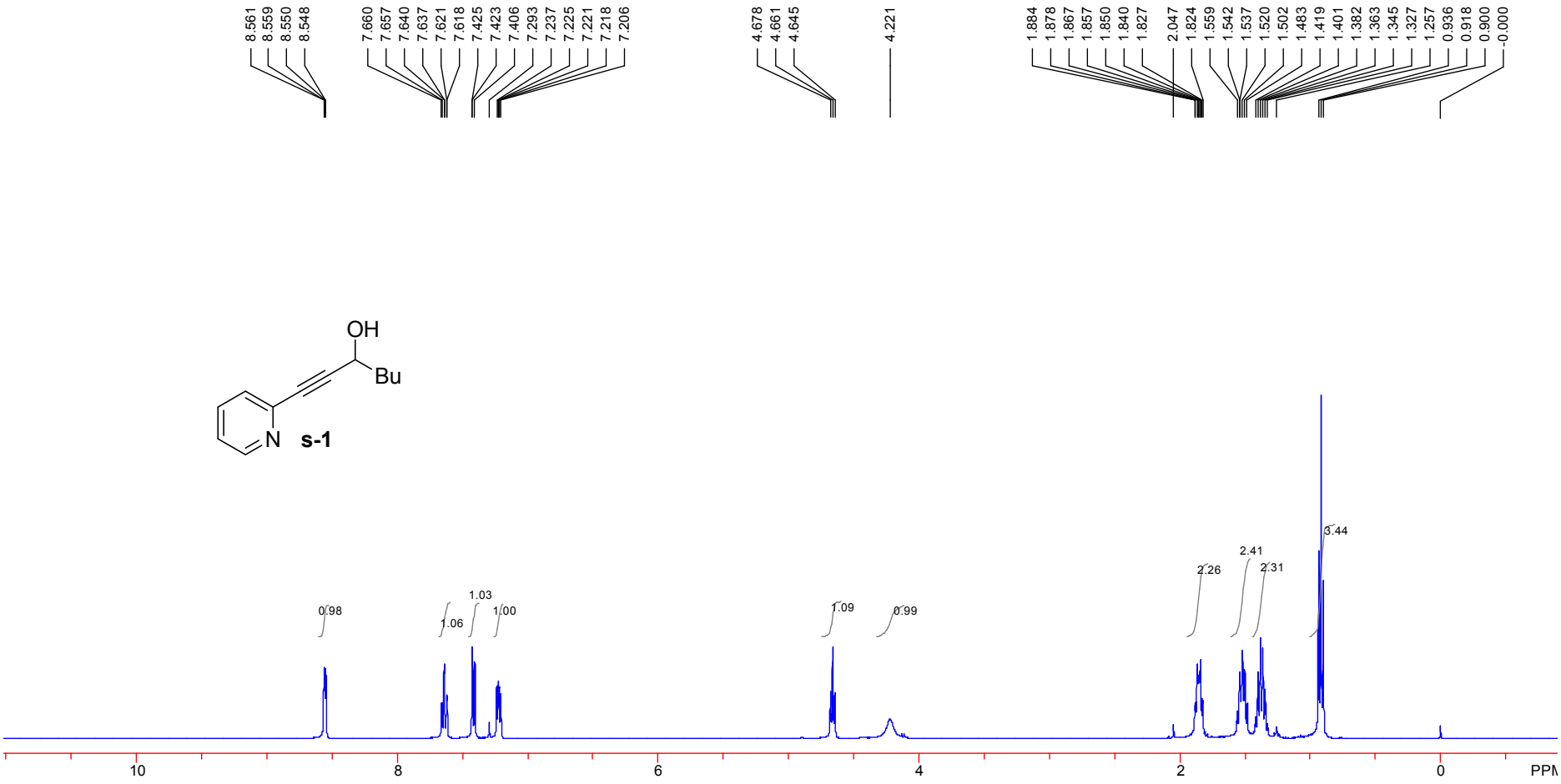
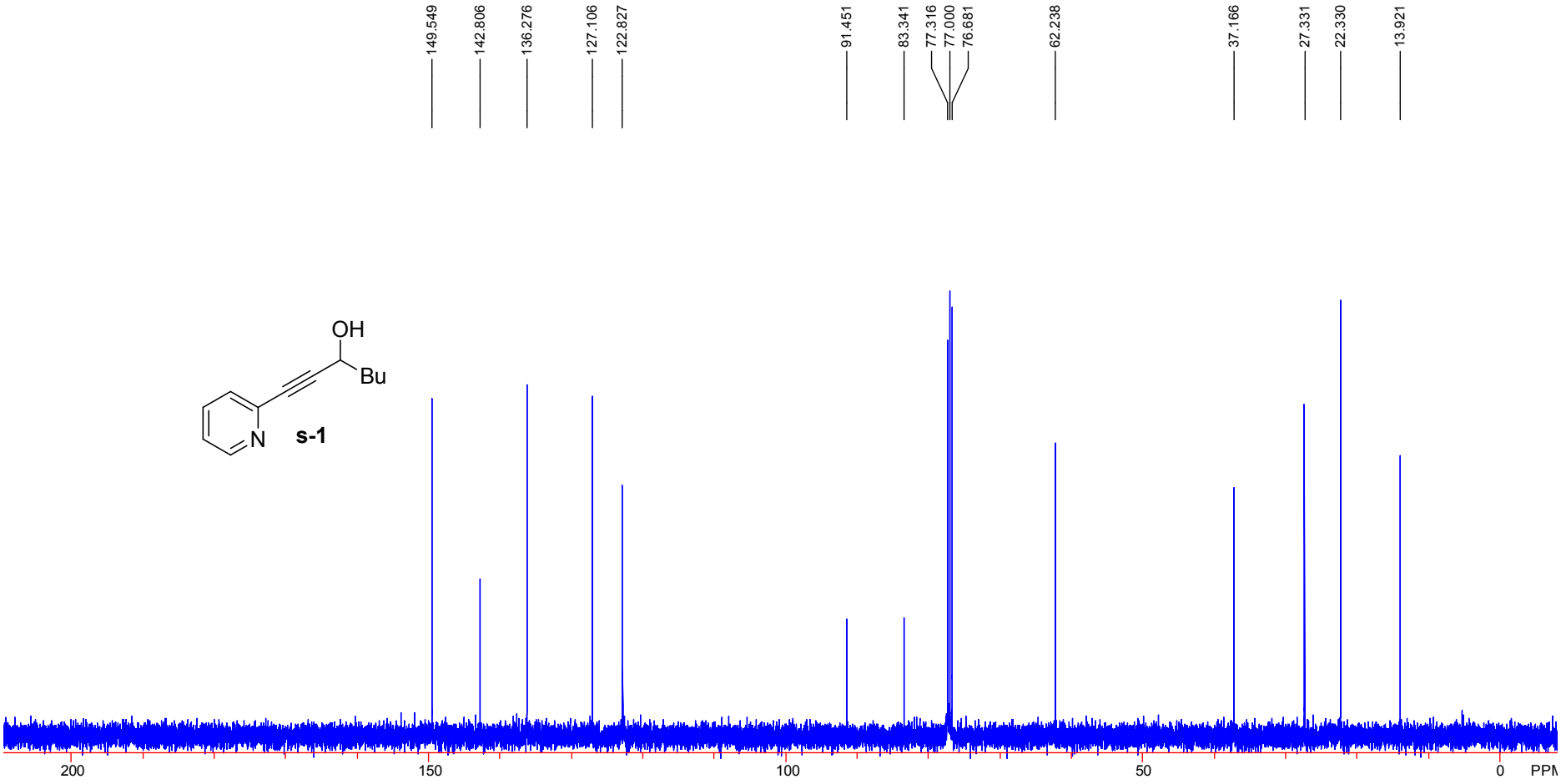


Figure S4. X-ray crystal structure of HCl salt of **4b**

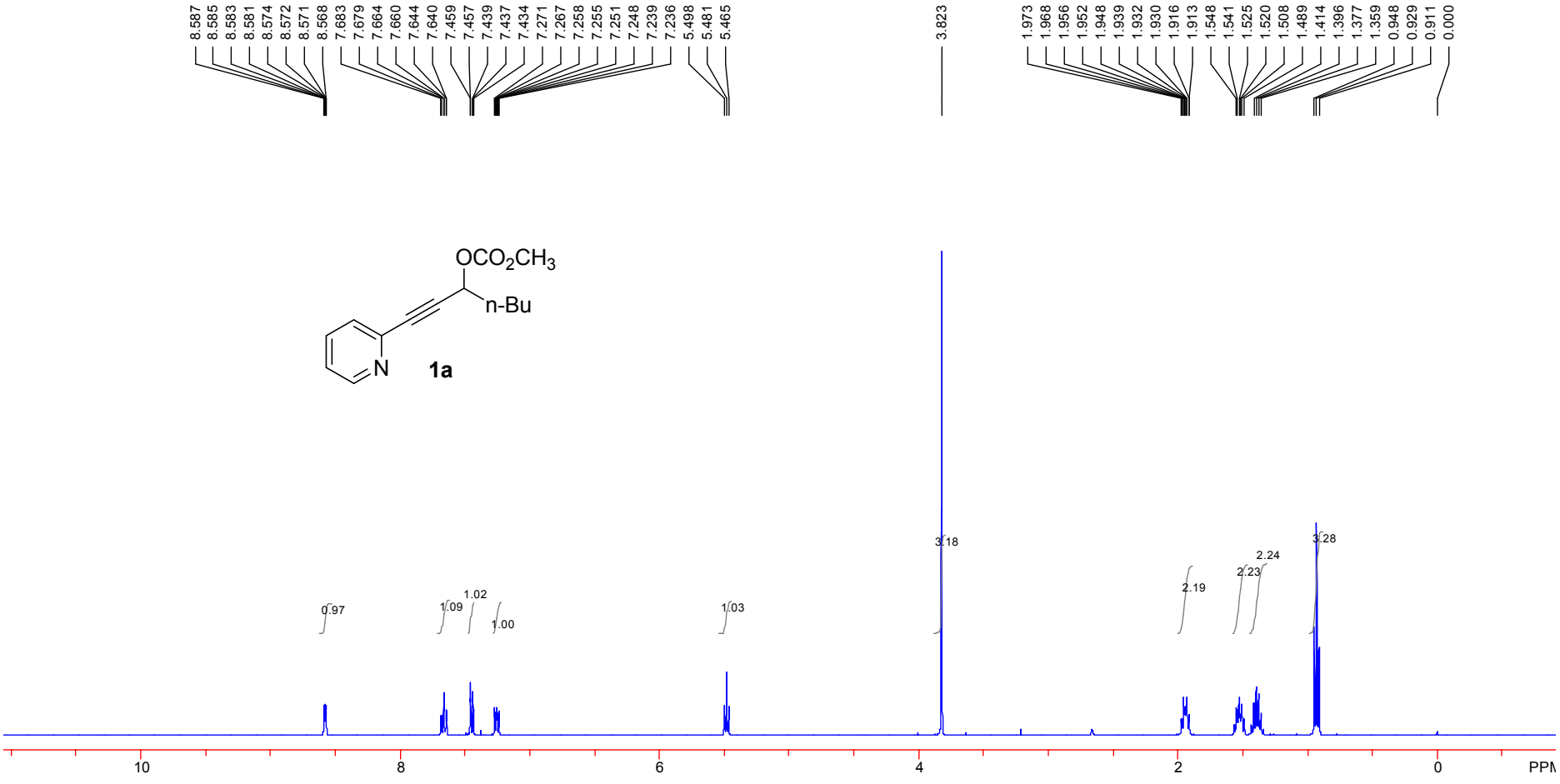
^{1}H NMR (400 MHz, $CDCl_3$)



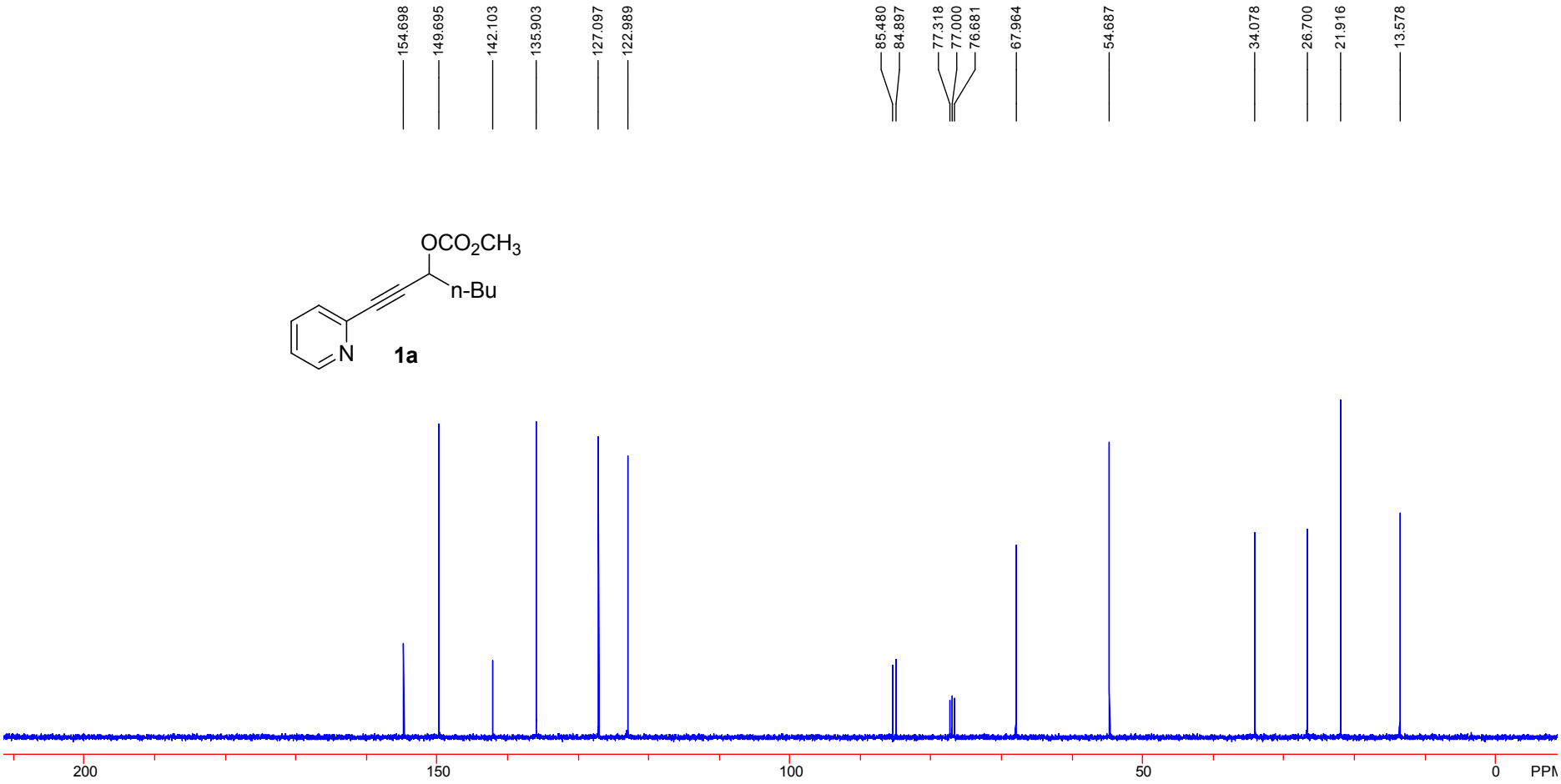
^{13}C NMR (100 MHz, $CDCl_3$)



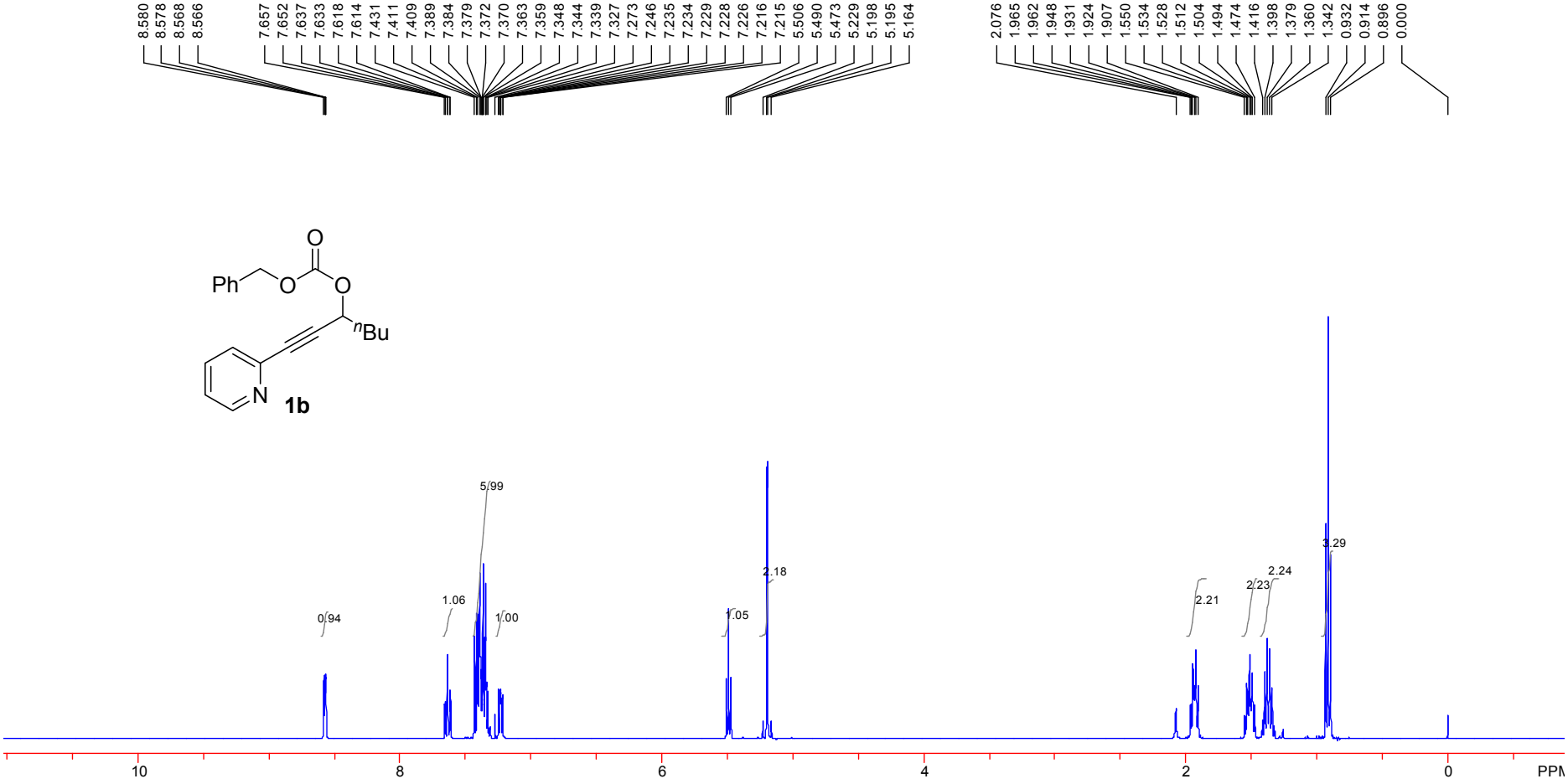
^{1}H NMR (400 MHz, $CDCl_3$)



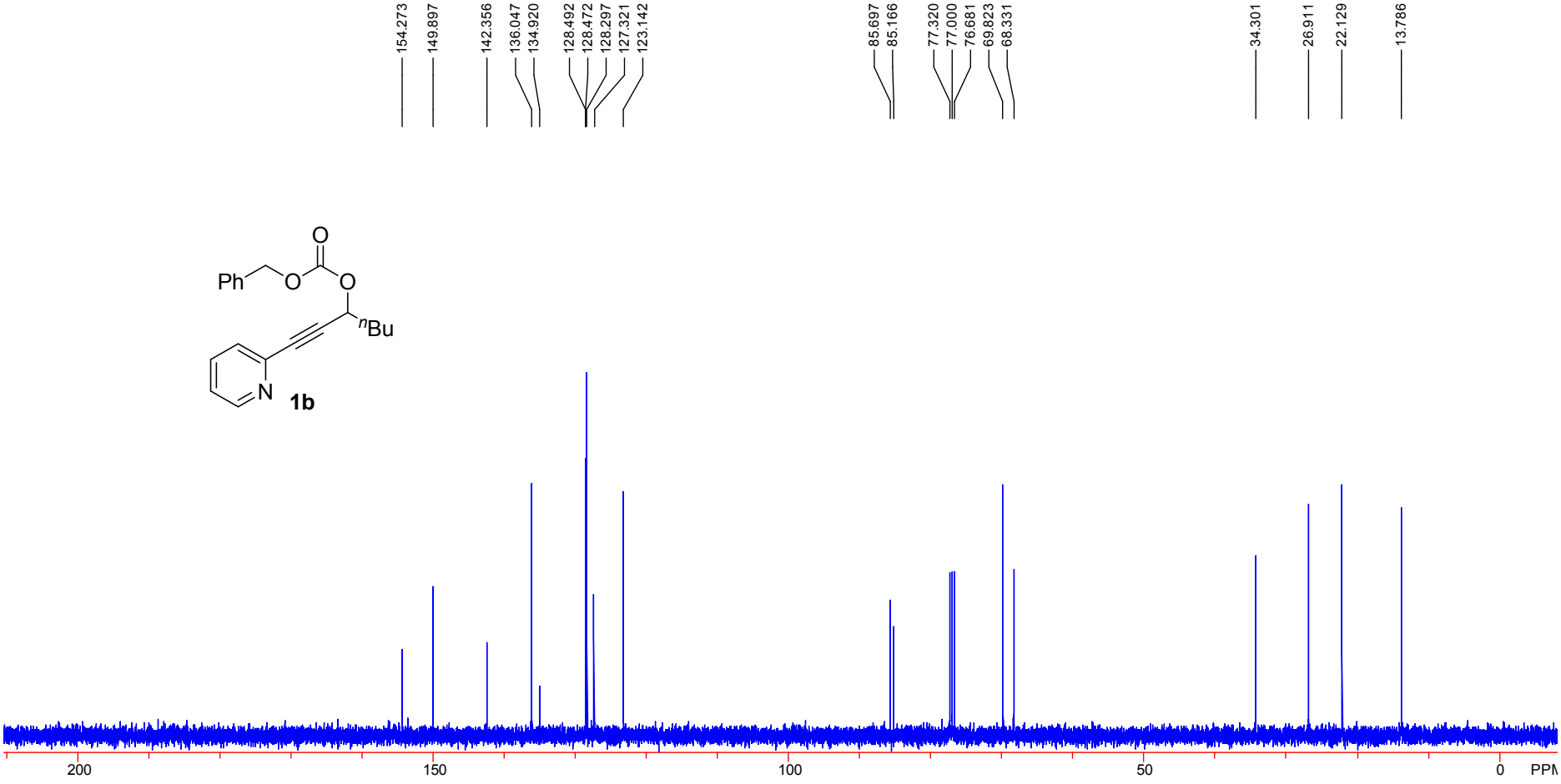
^{13}C NMR (100 MHz, $CDCl_3$)



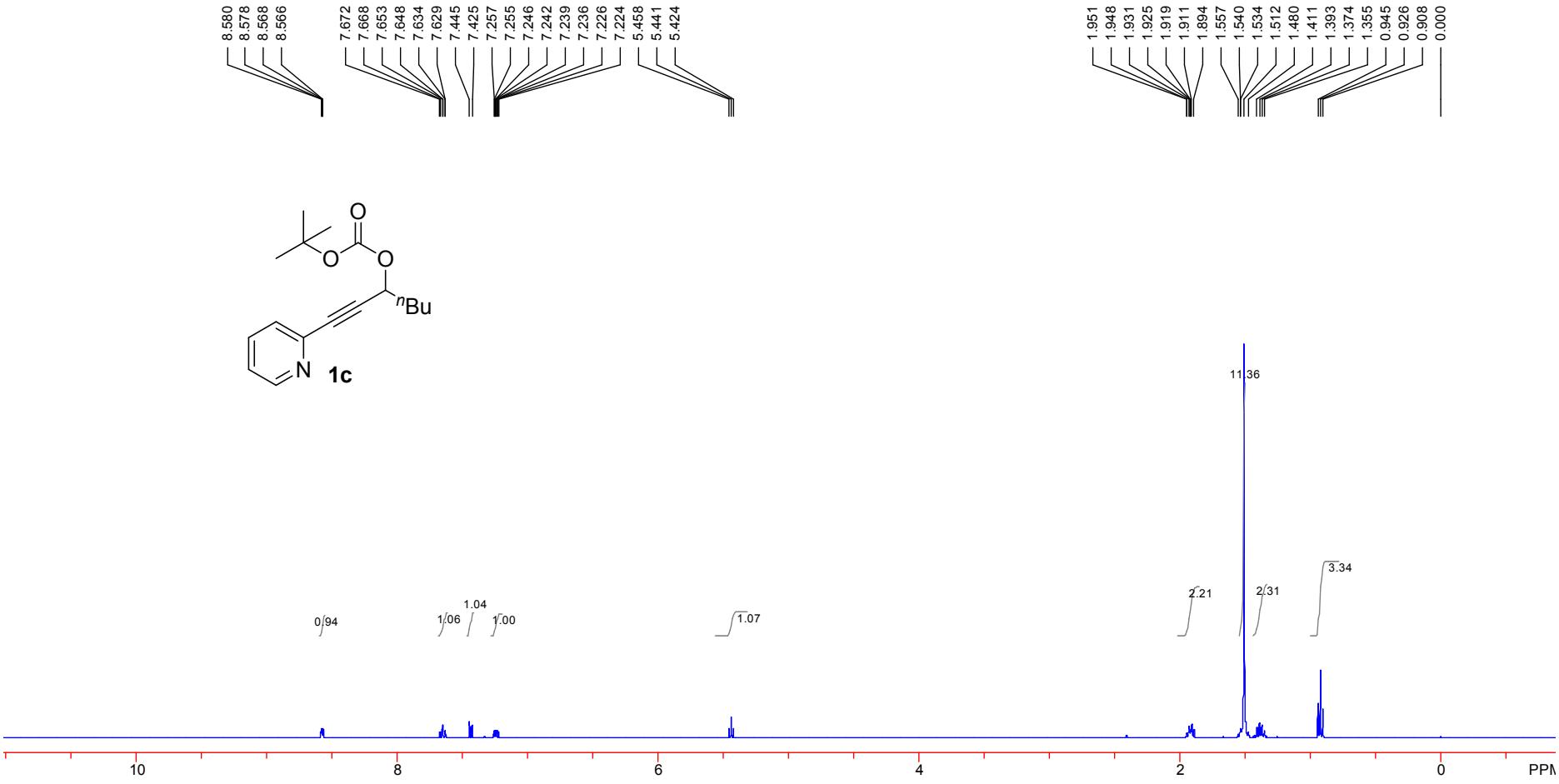
^{1}H NMR (400 MHz, $CDCl_3$)



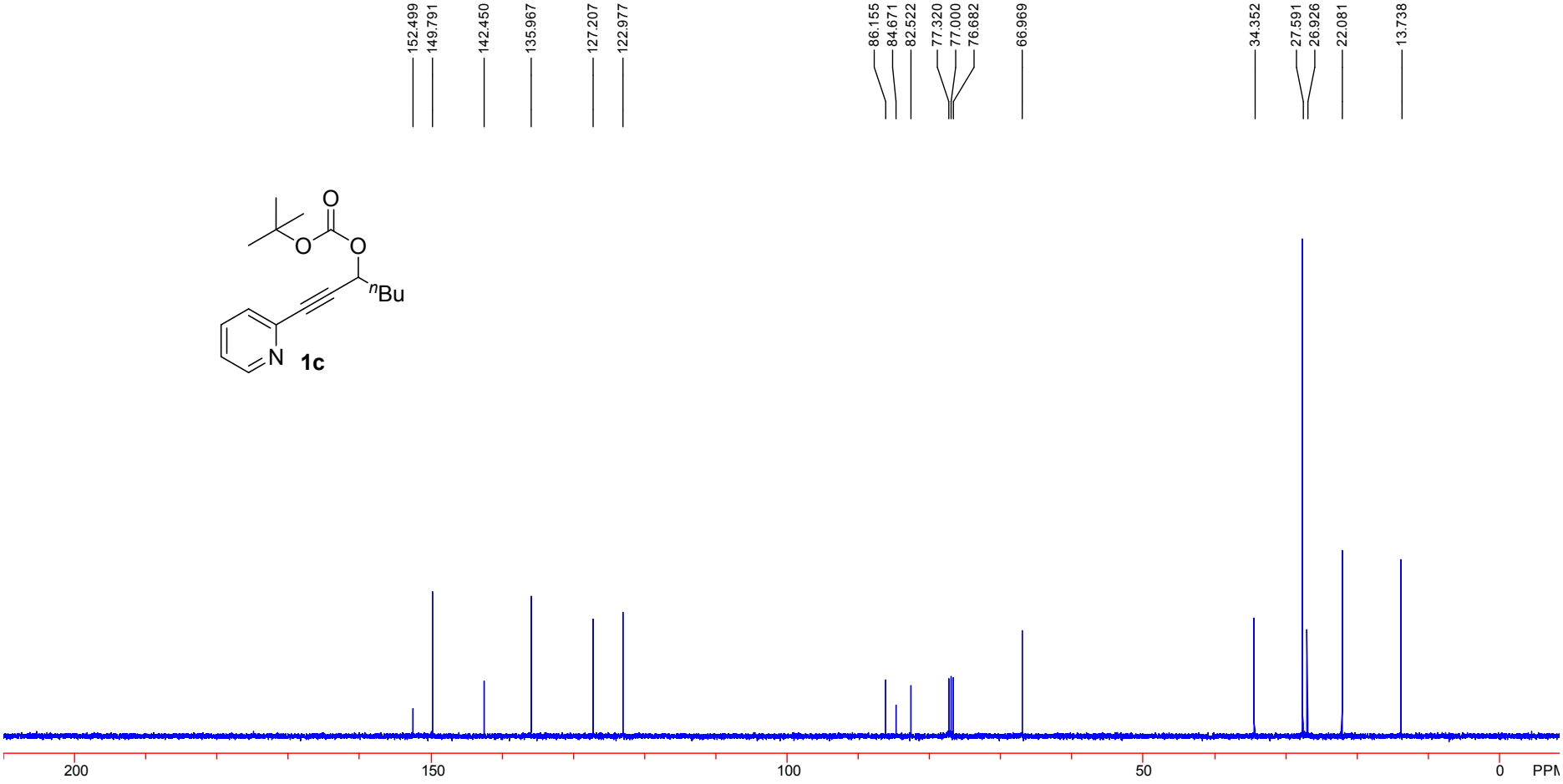
^{13}C NMR (100 MHz, $CDCl_3$)



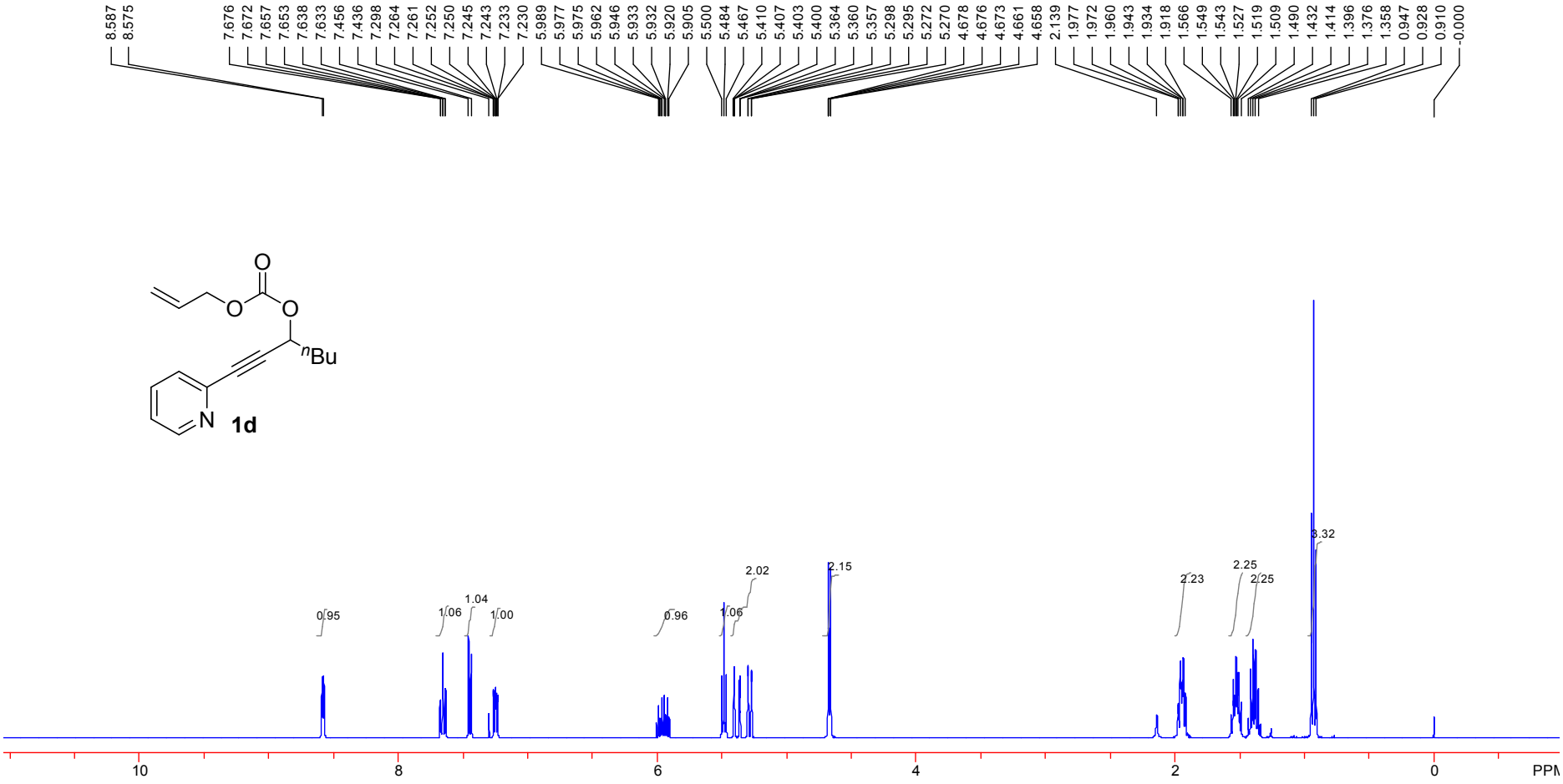
^{1}H NMR (400 MHz, $CDCl_3$)



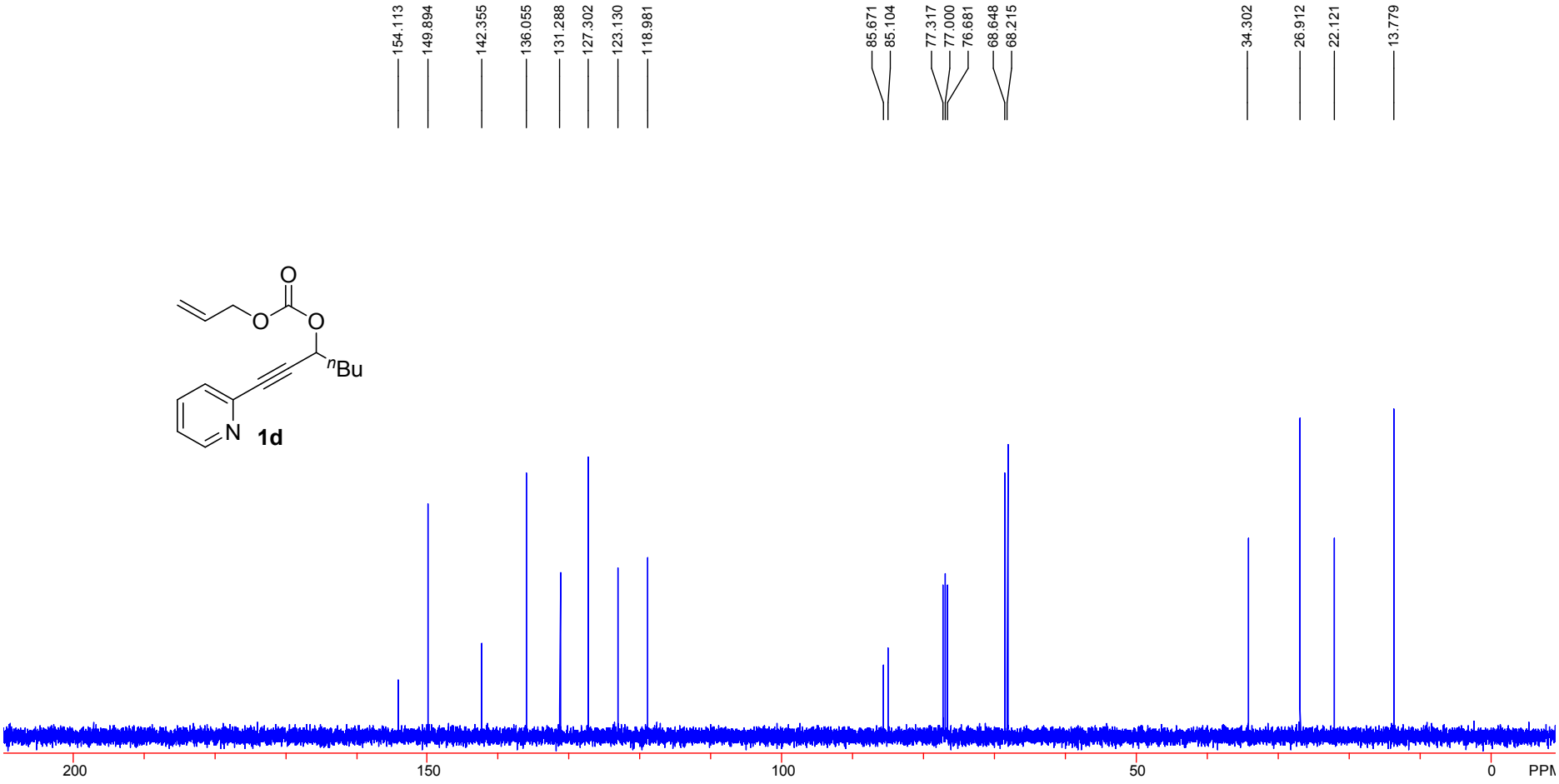
^{13}C NMR (100 MHz, $CDCl_3$)



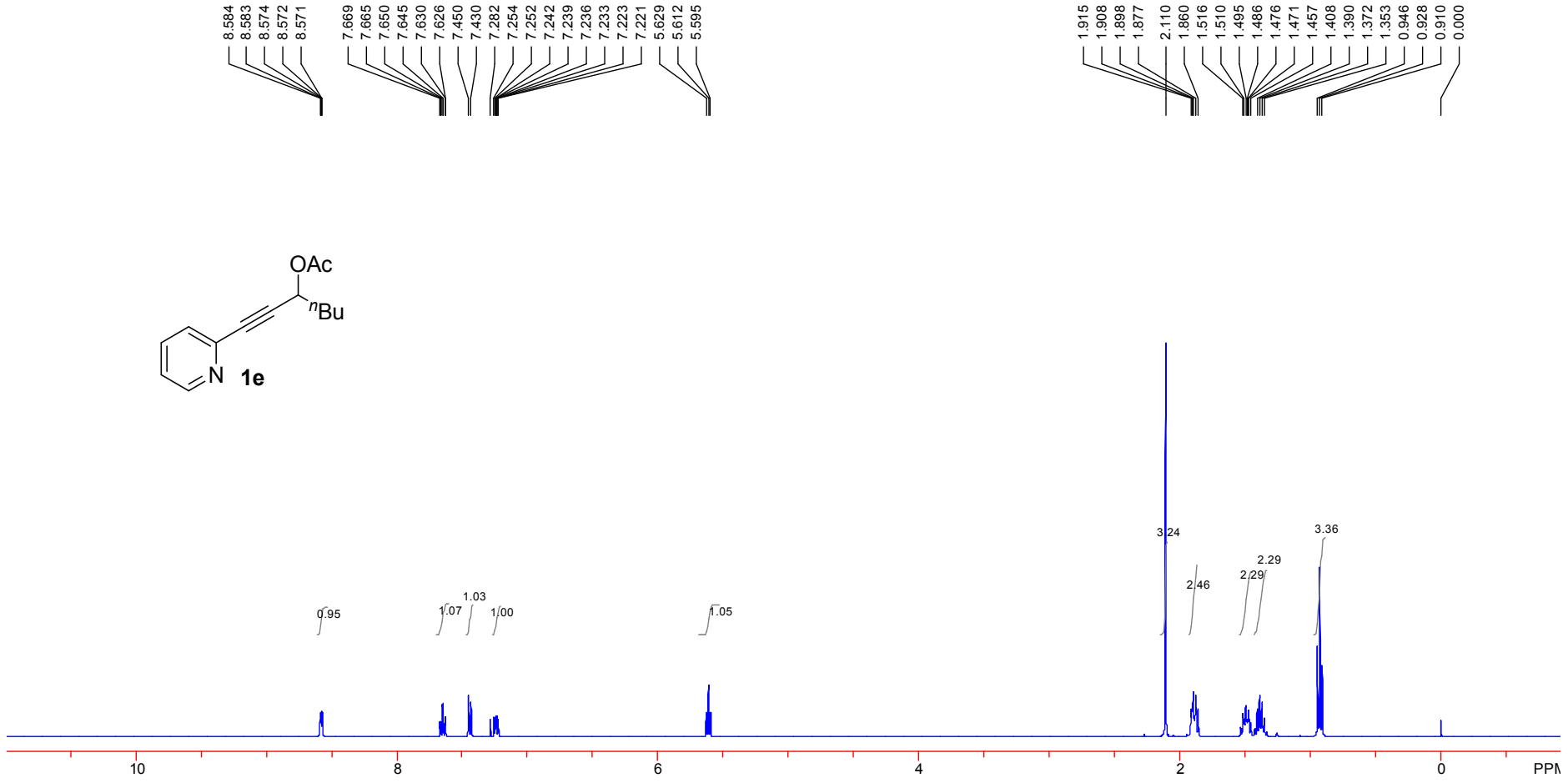
^{1}H NMR (400 MHz, $CDCl_3$)



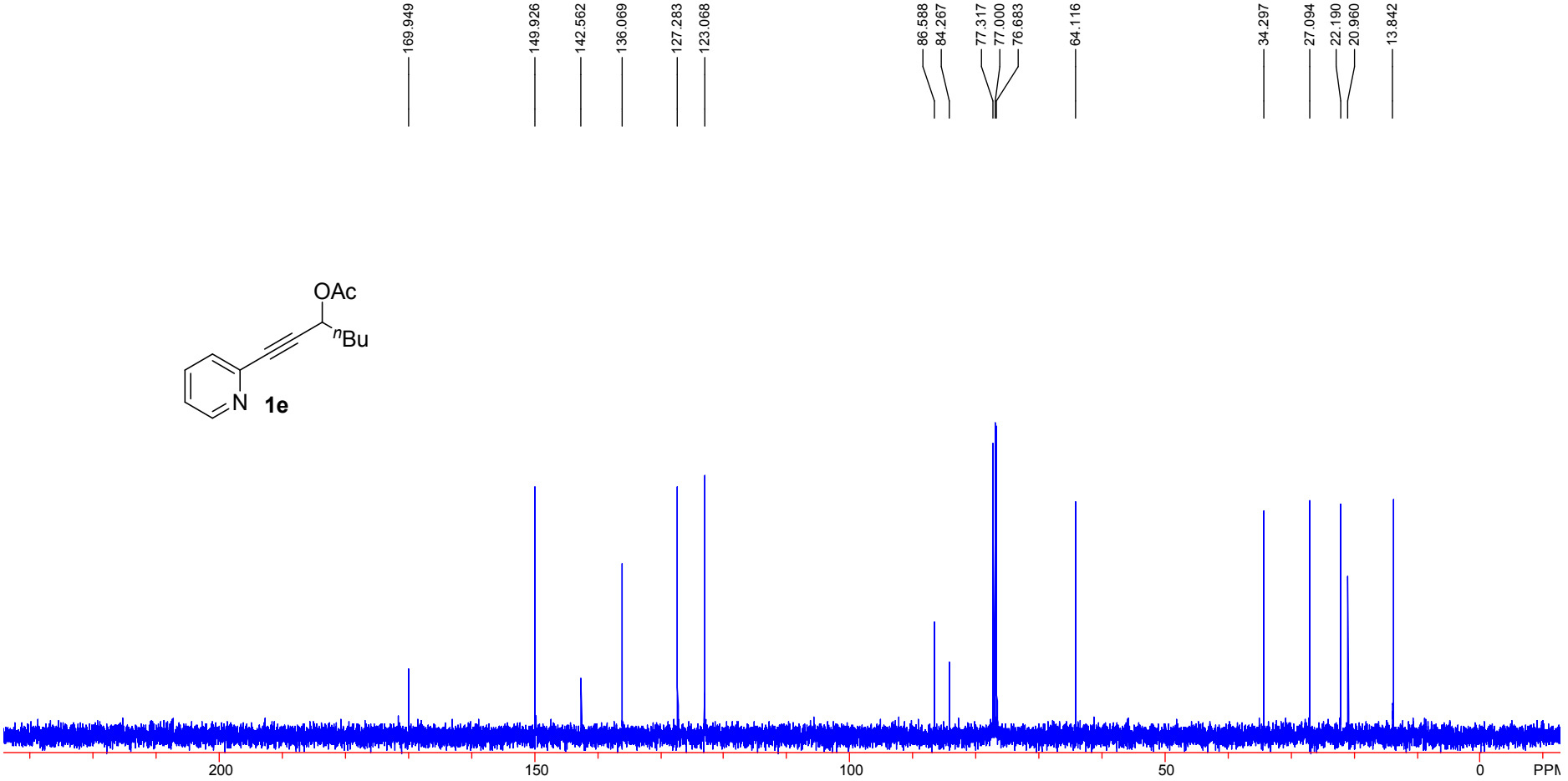
^{13}C NMR (100 MHz, $CDCl_3$)



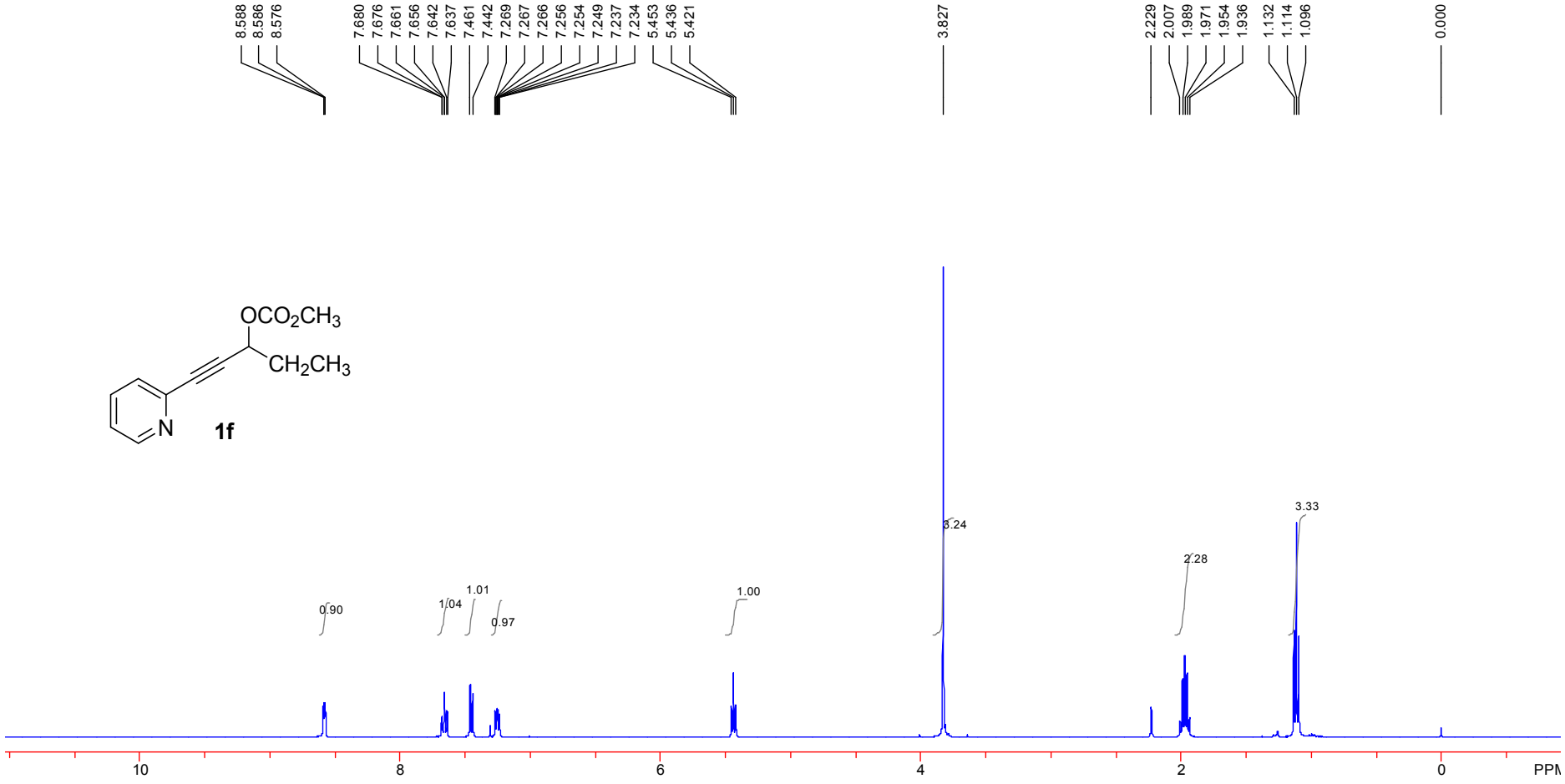
^{1}H NMR (400 MHz, $CDCl_3$)



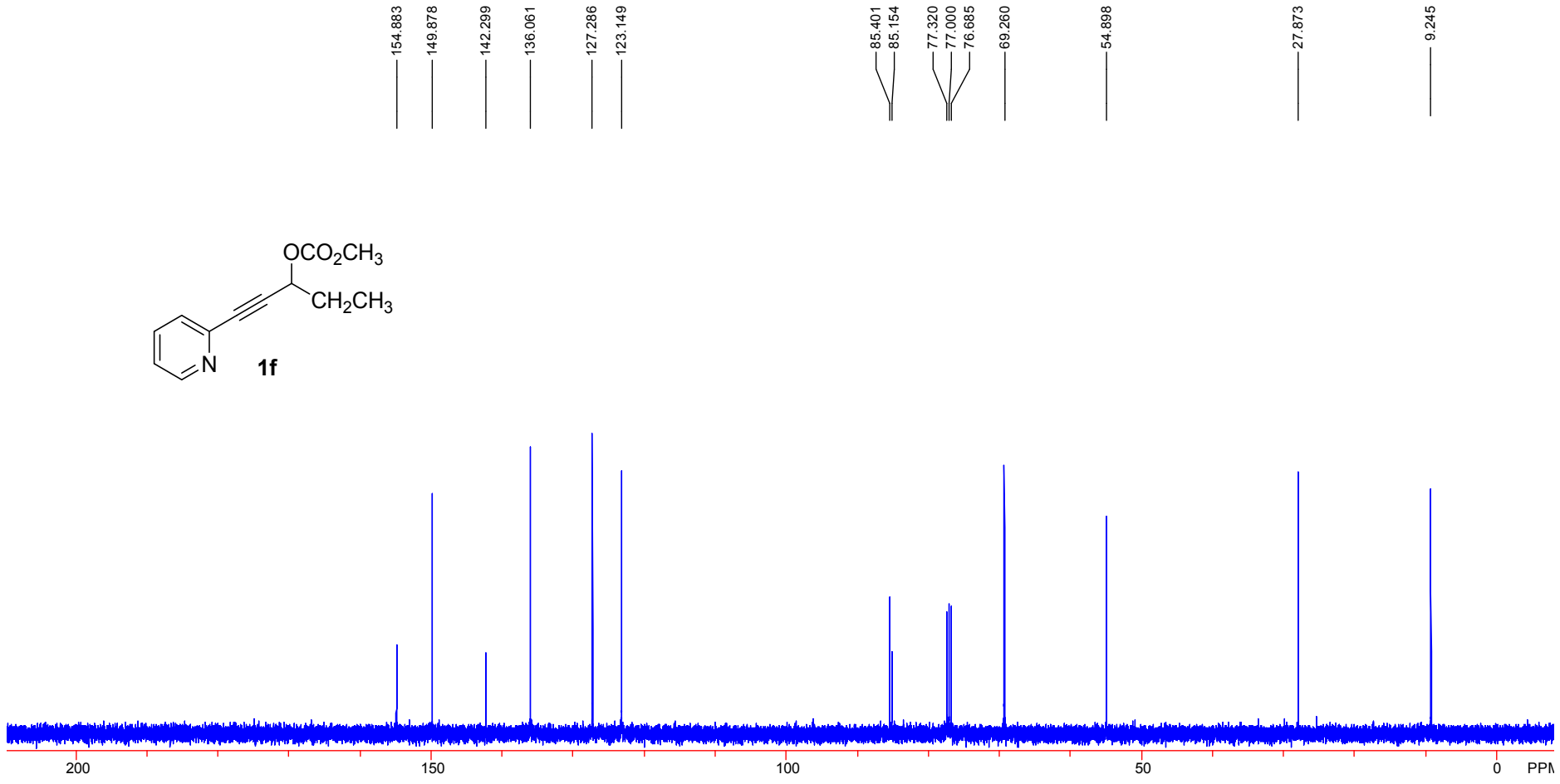
^{13}C NMR (100 MHz, $CDCl_3$)



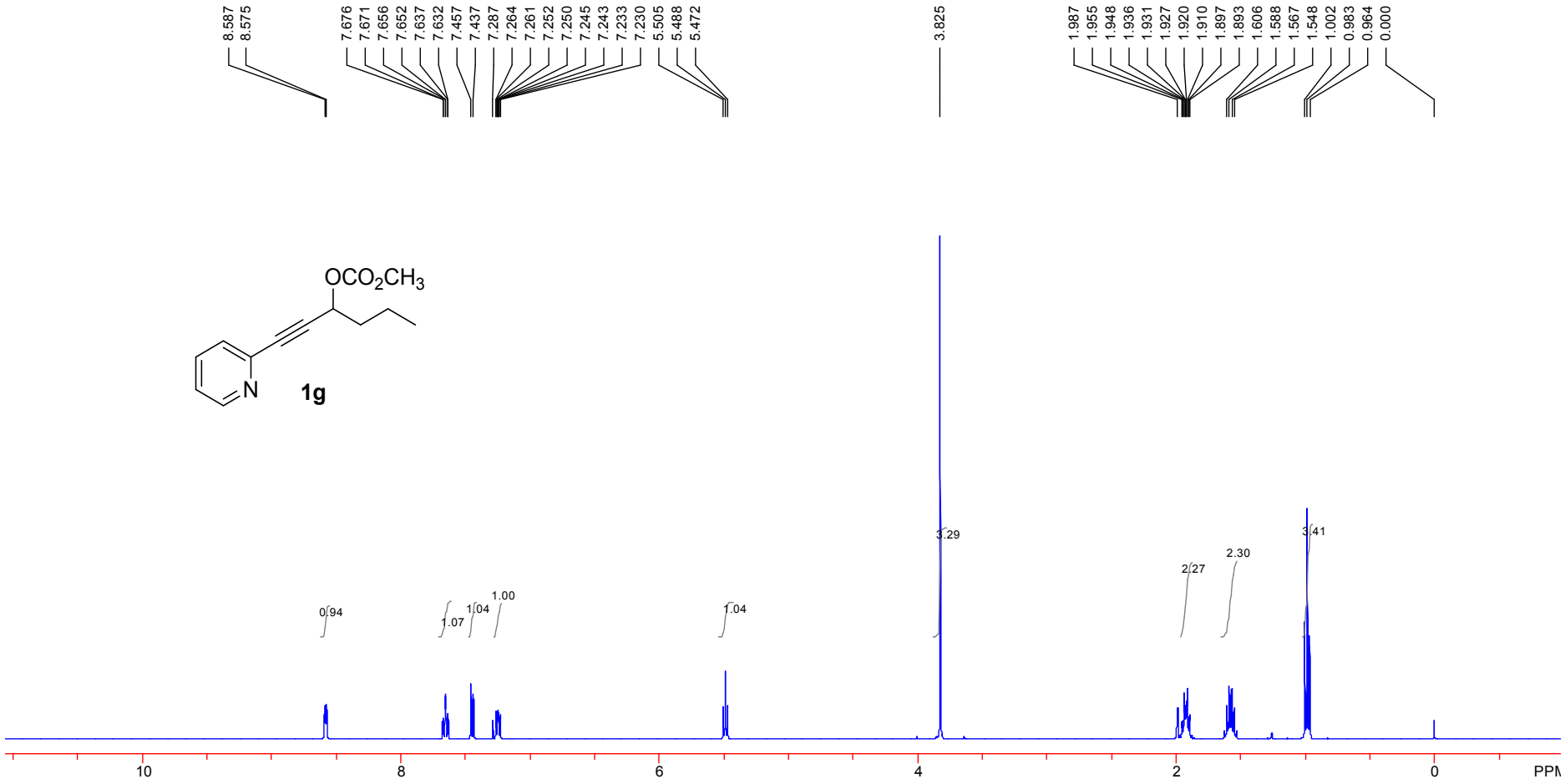
^{1}H NMR (400 MHz, $CDCl_3$)



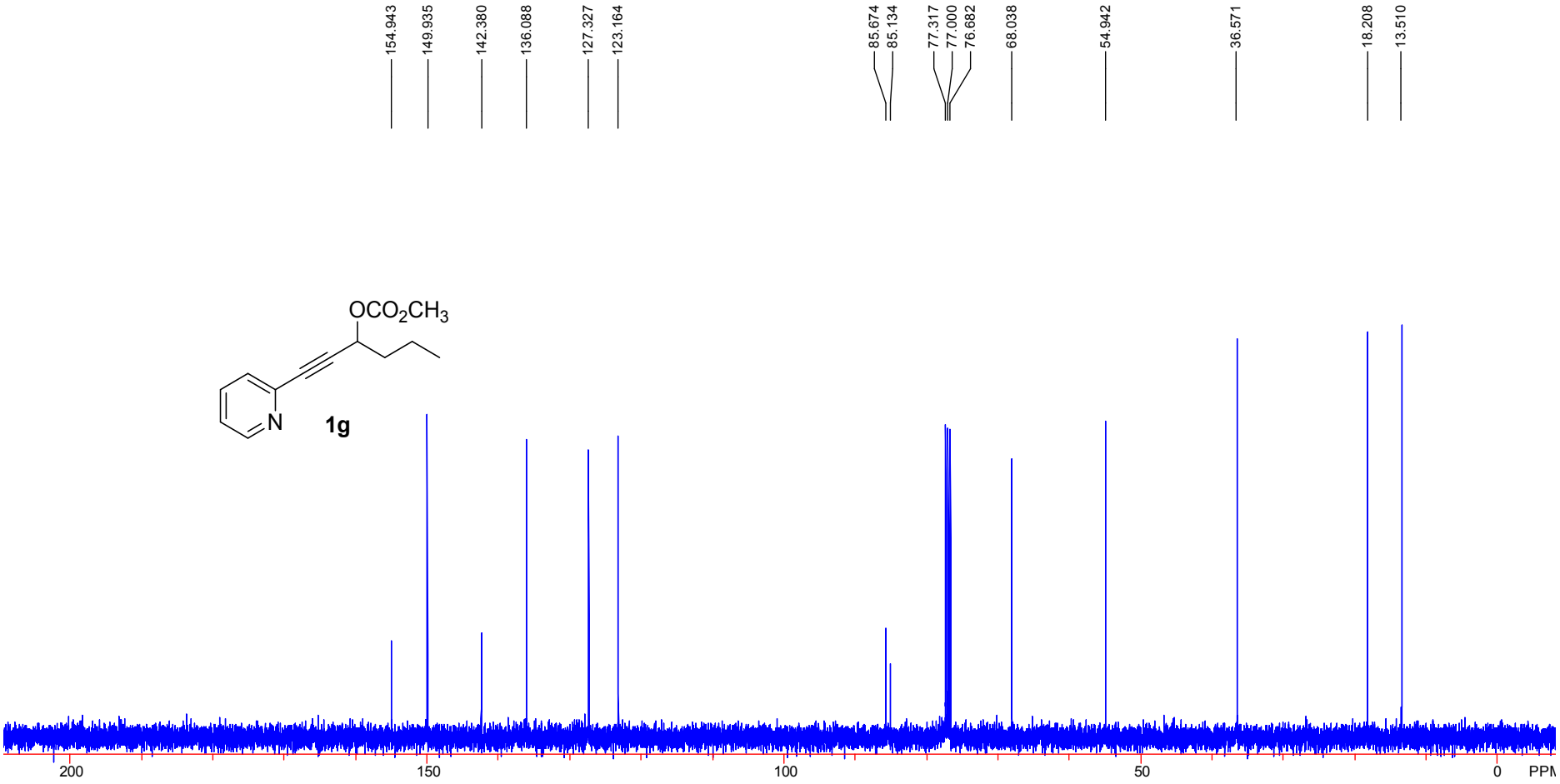
^{13}C NMR (100 MHz, $CDCl_3$)



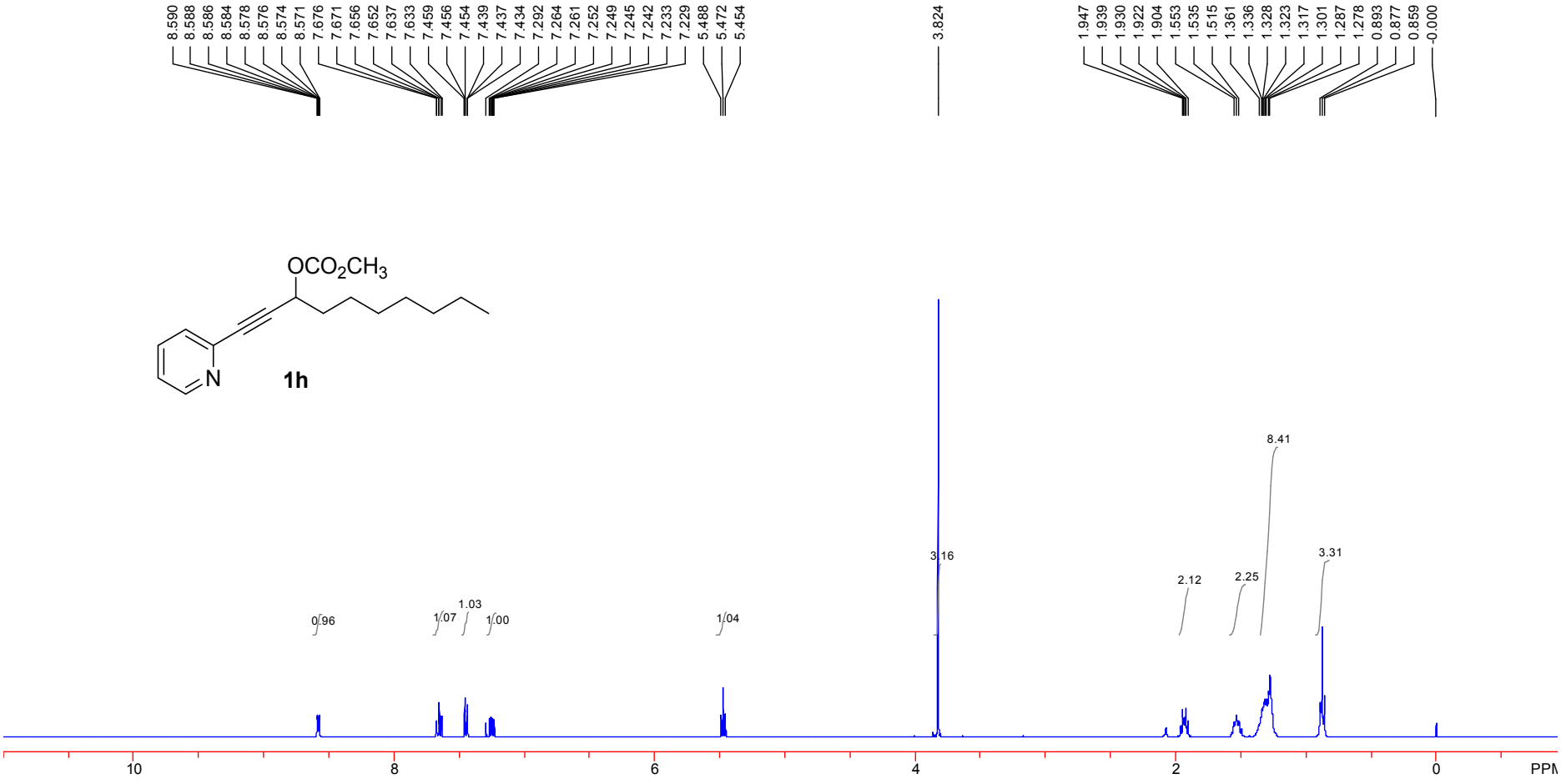
^{1}H NMR (400 MHz, $CDCl_3$)



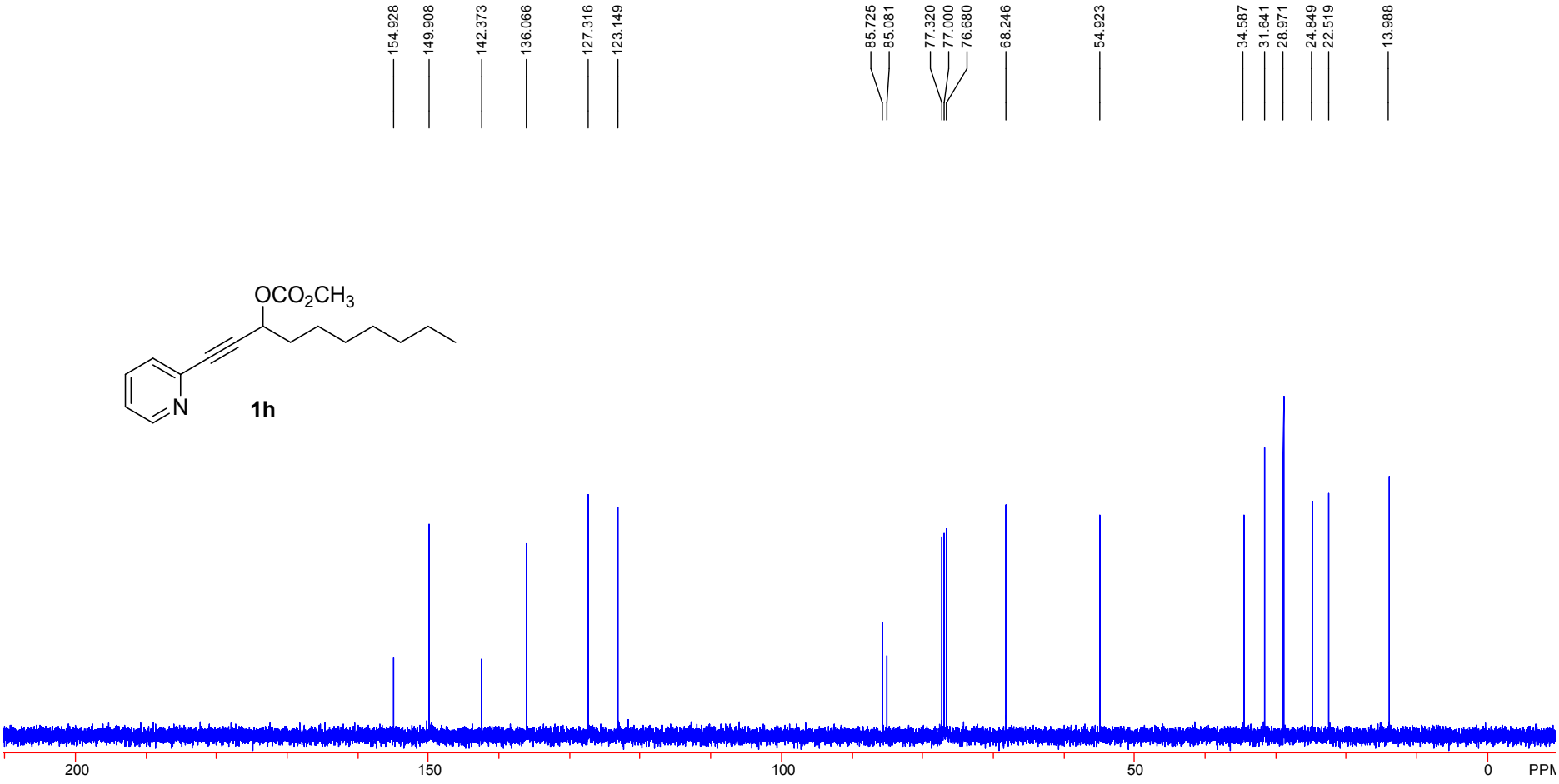
^{13}C NMR (100 MHz, $CDCl_3$)



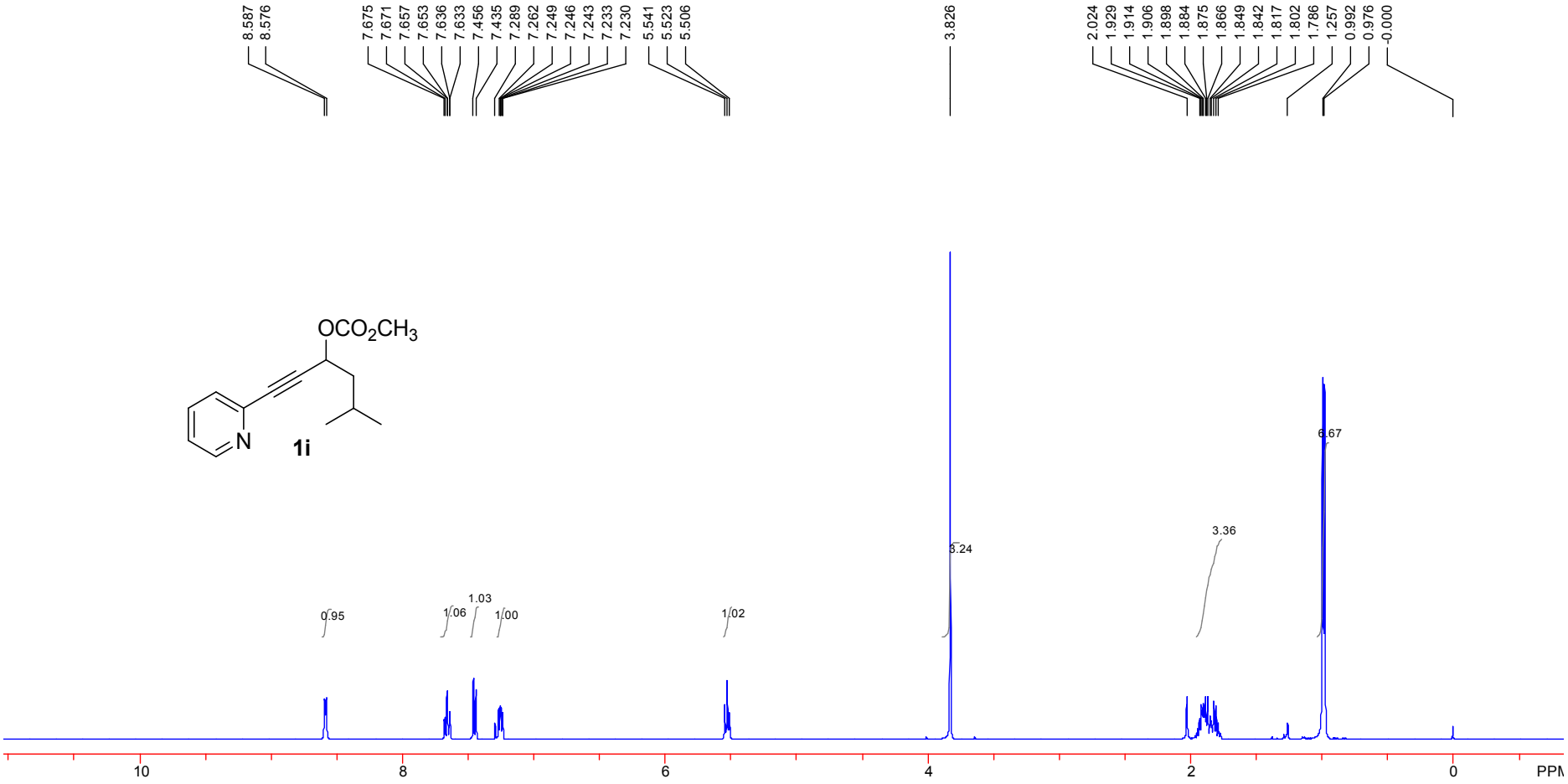
^{1}H NMR (400 MHz, $CDCl_3$)



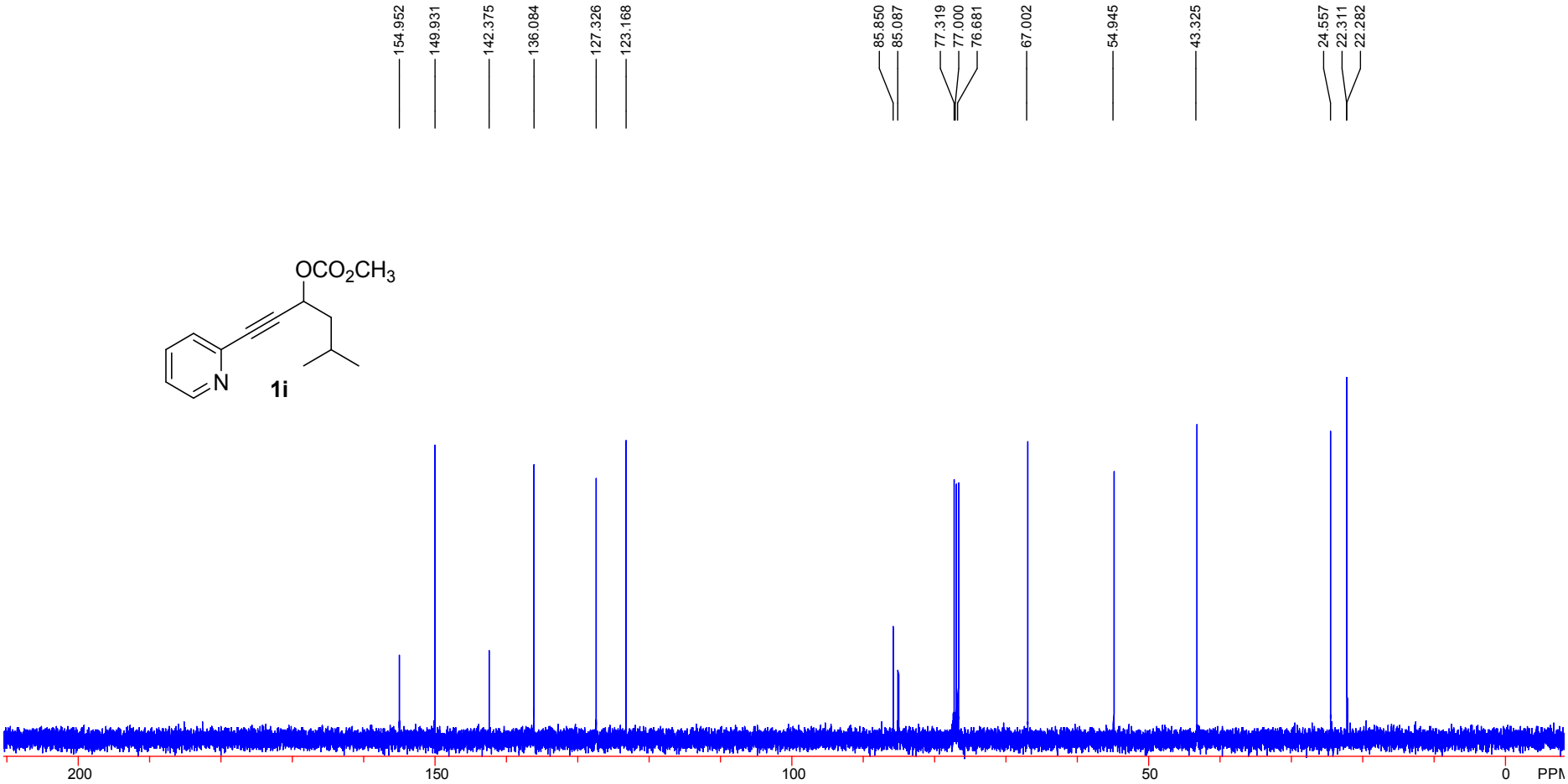
^{13}C NMR (100 MHz, $CDCl_3$)



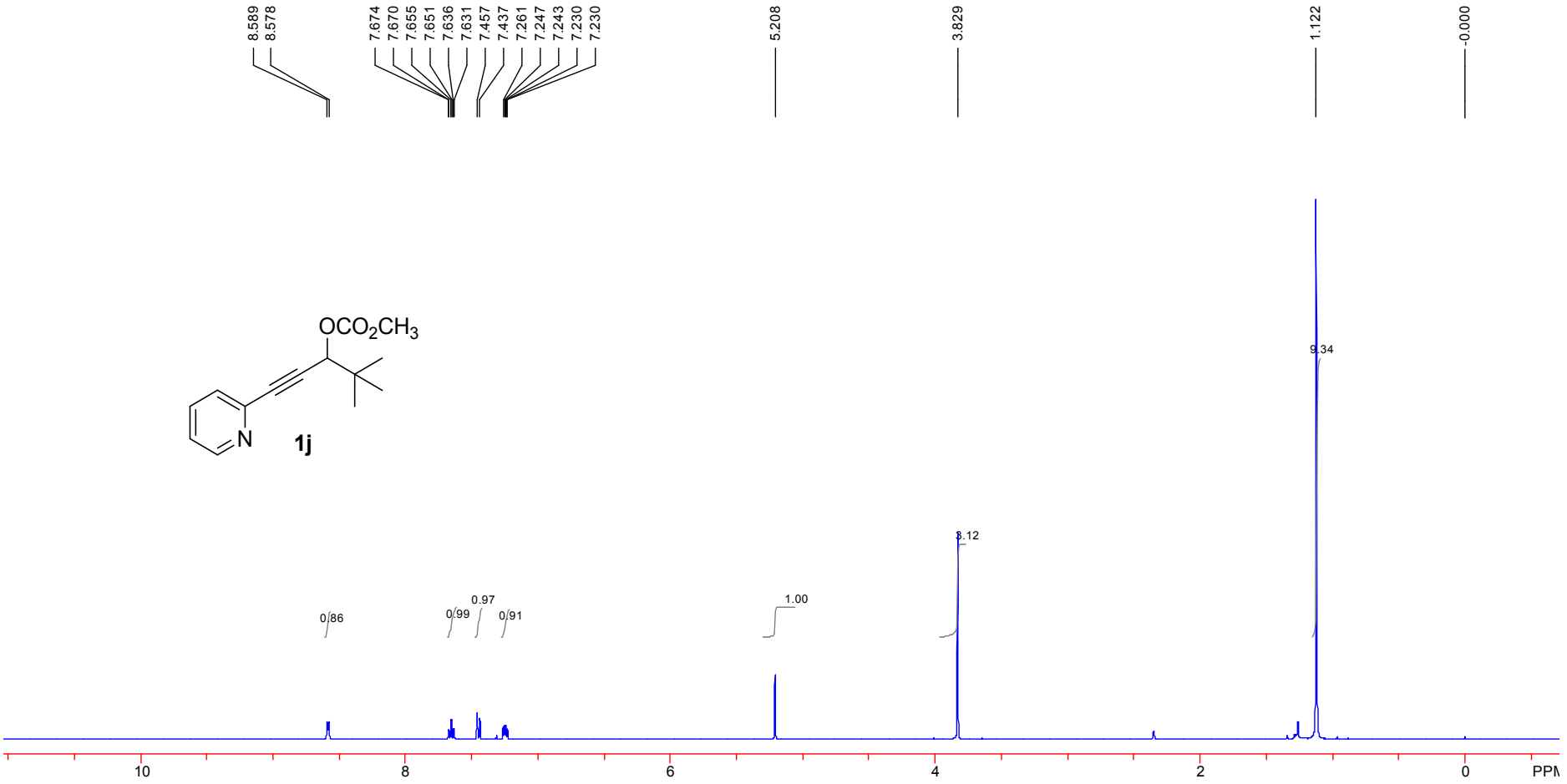
^{1}H NMR (400 MHz, $CDCl_3$)



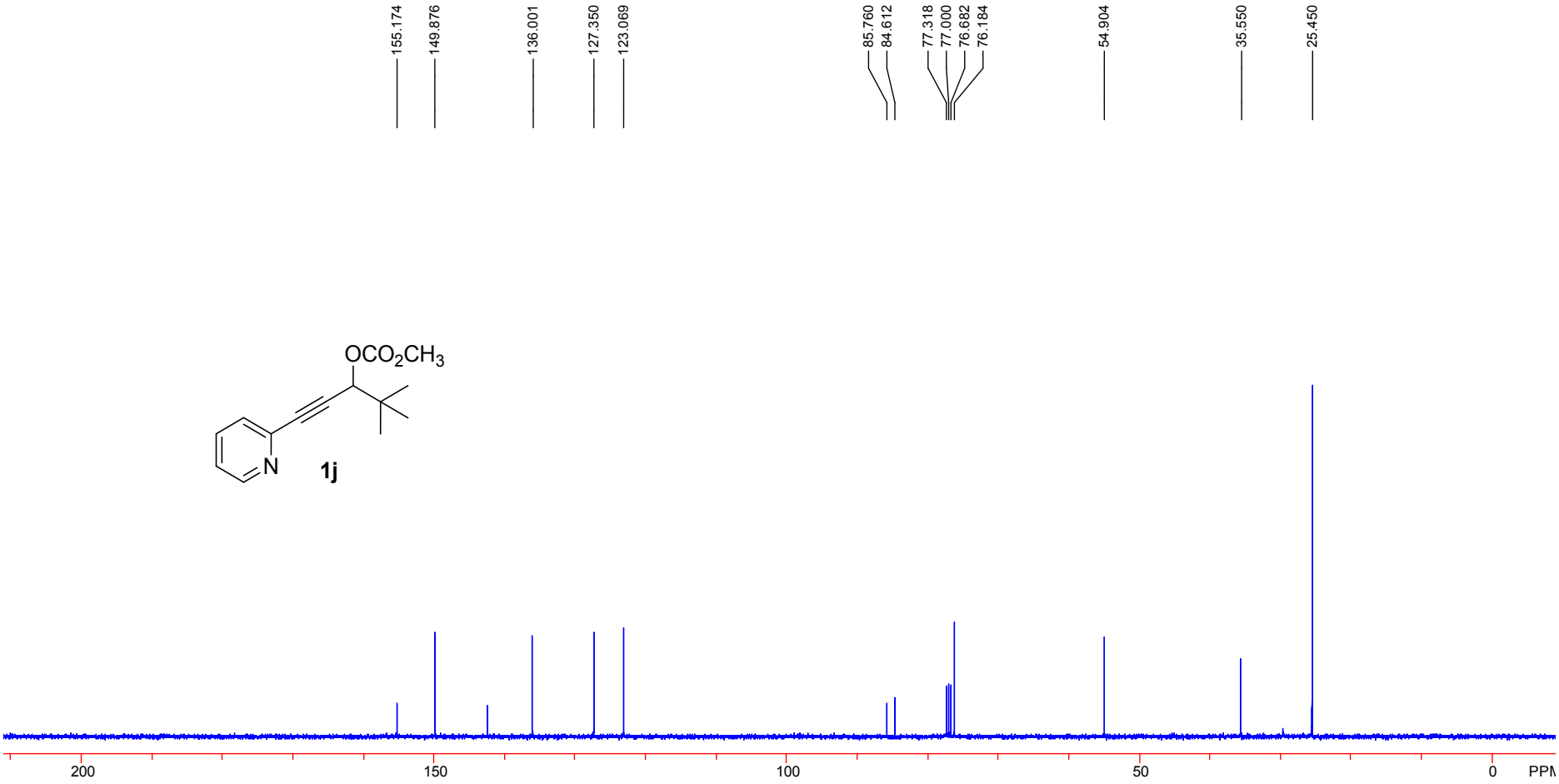
^{13}C NMR (100 MHz, $CDCl_3$)



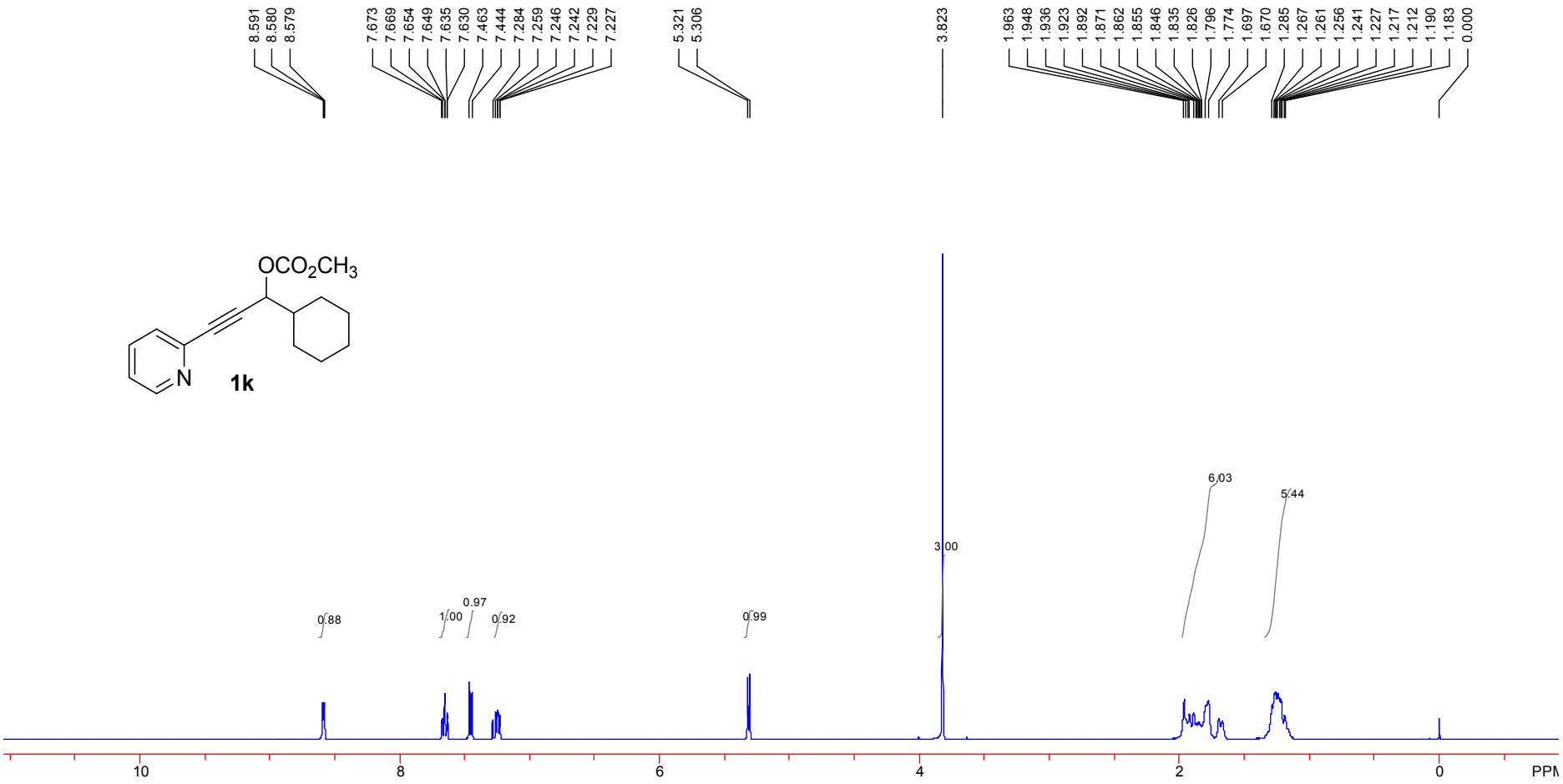
^{1}H NMR (400 MHz, $CDCl_3$)



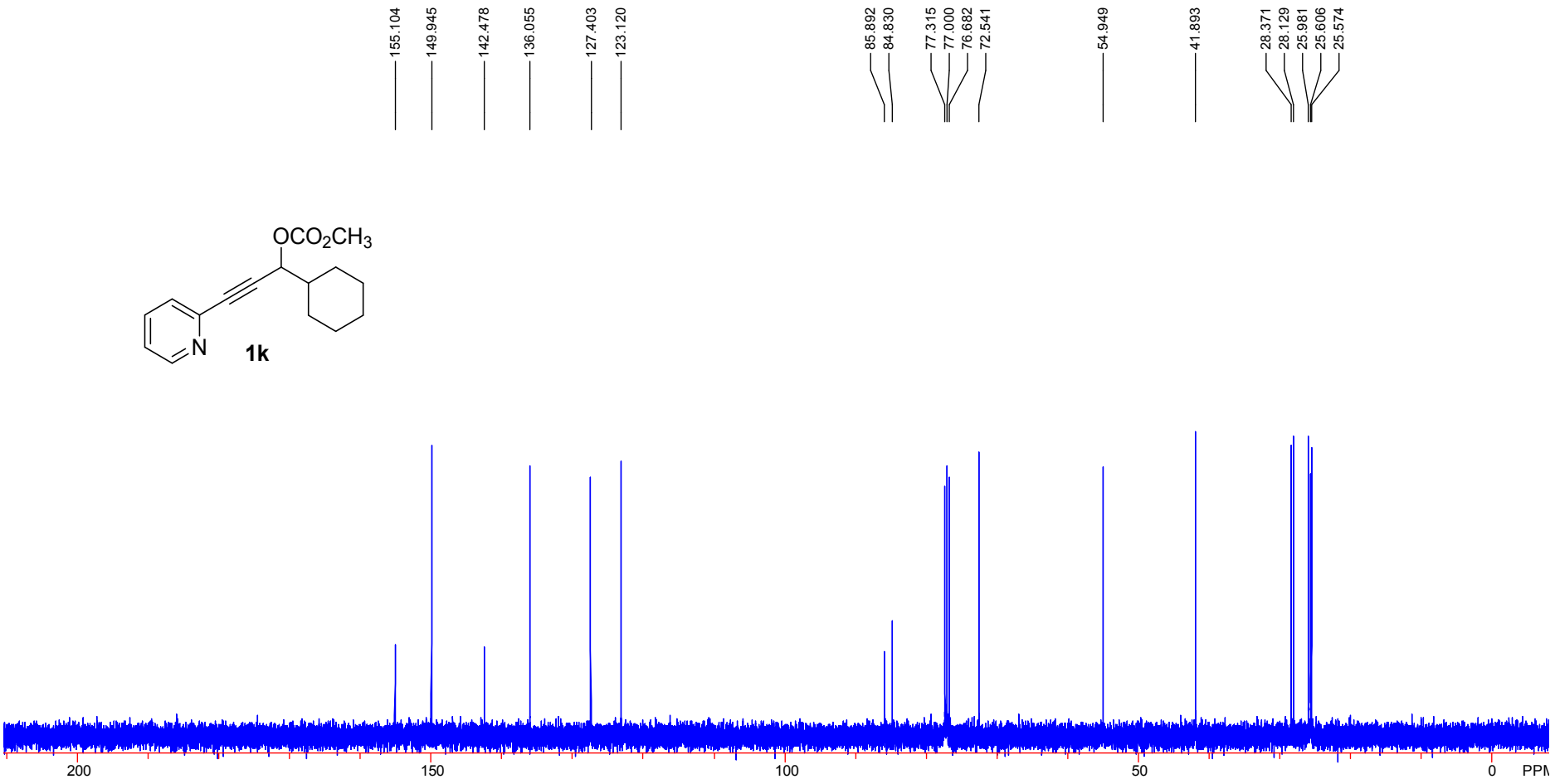
^{13}C NMR (100 MHz, $CDCl_3$)



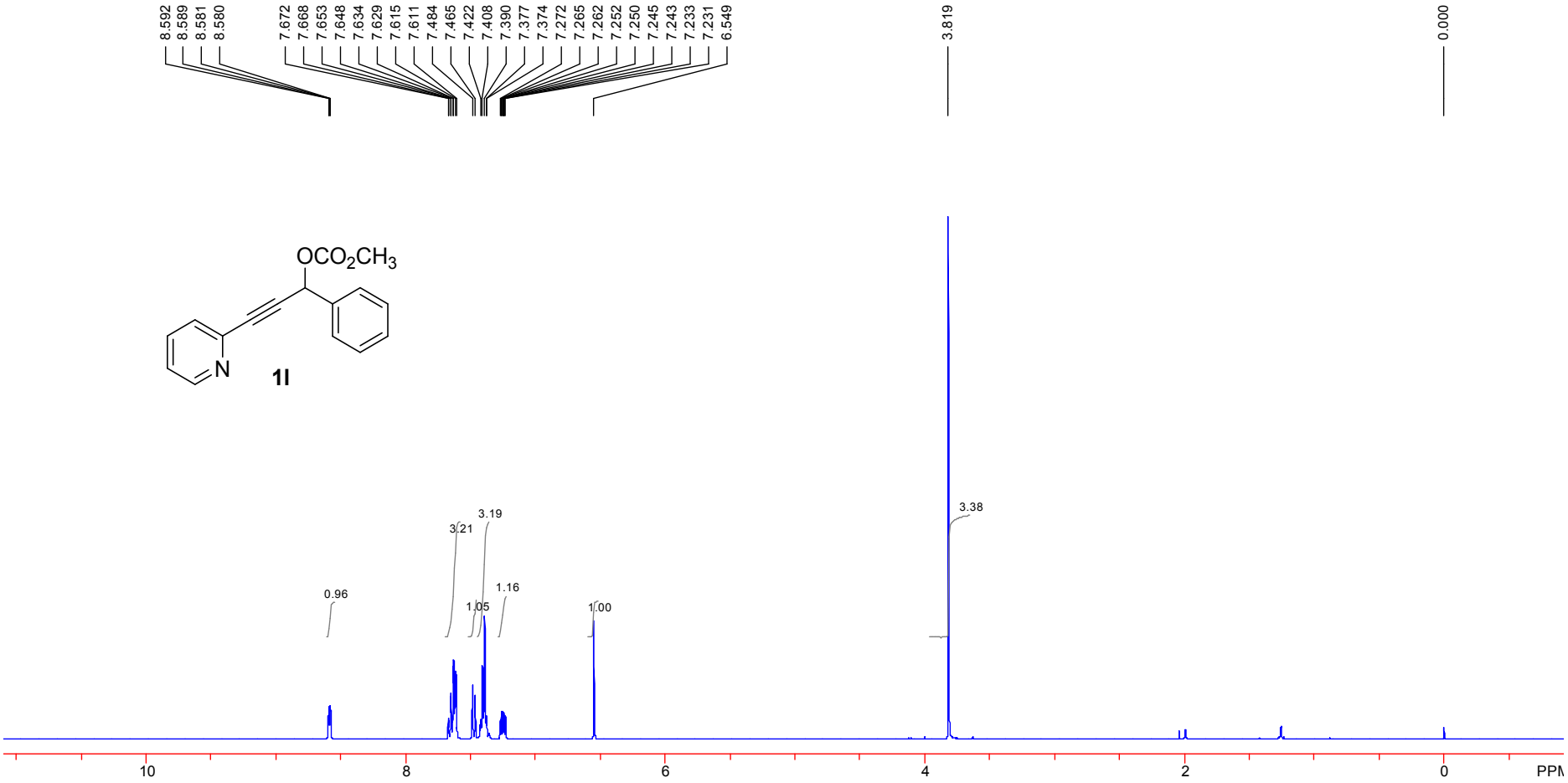
^{1}H NMR (400 MHz, $CDCl_3$)



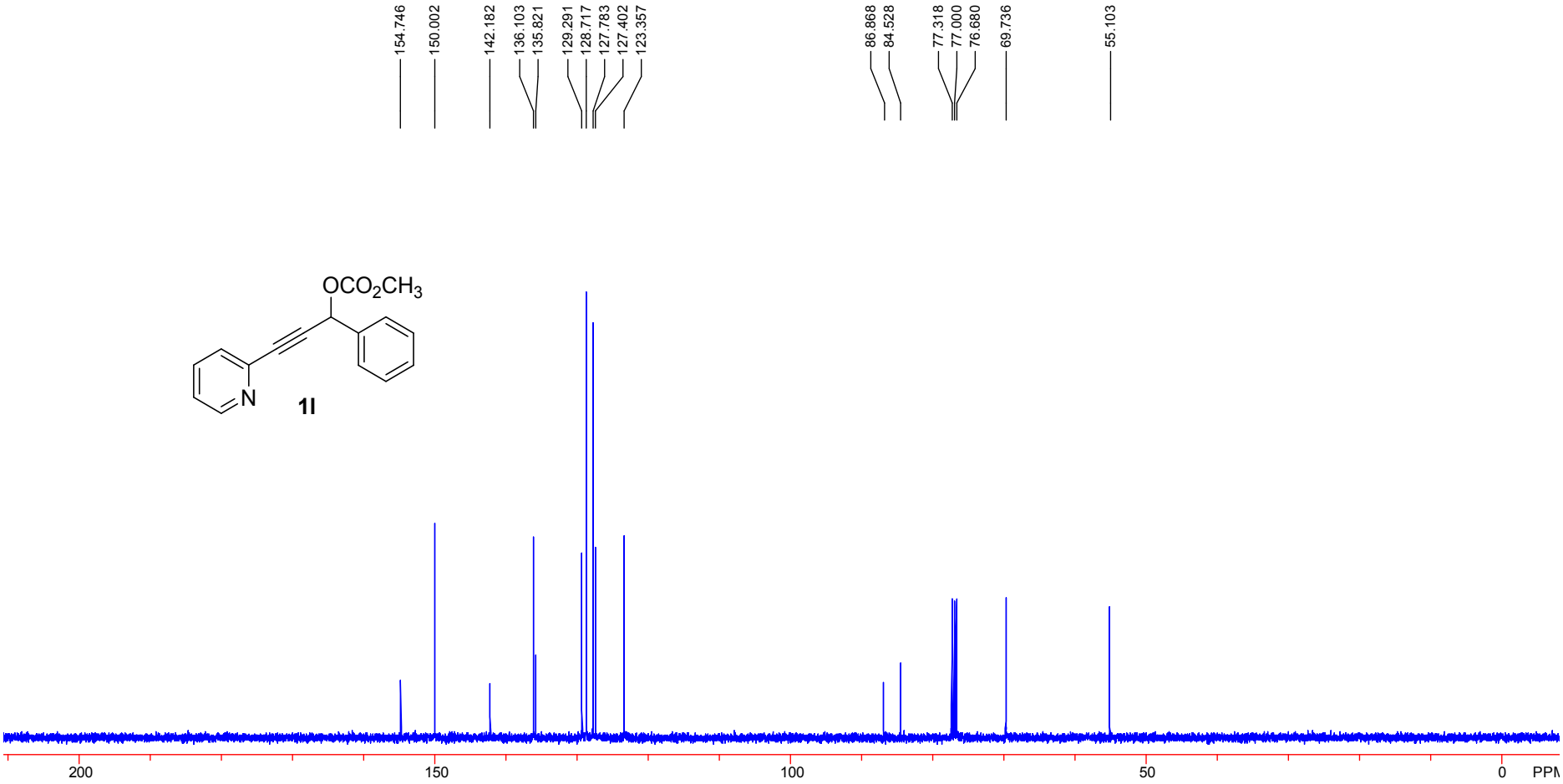
^{13}C NMR (100 MHz, $CDCl_3$)



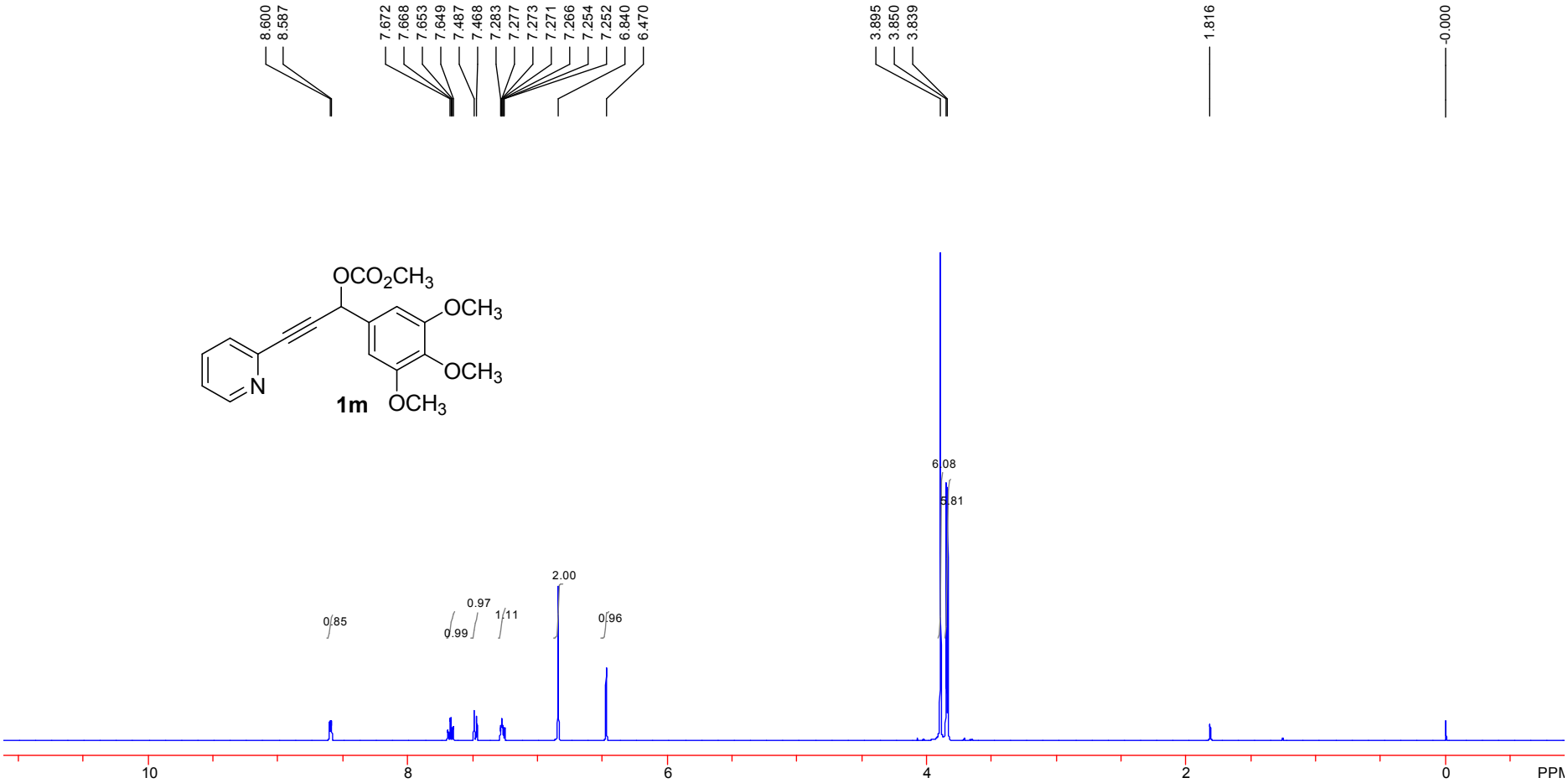
^{1}H NMR (400 MHz, $CDCl_3$)



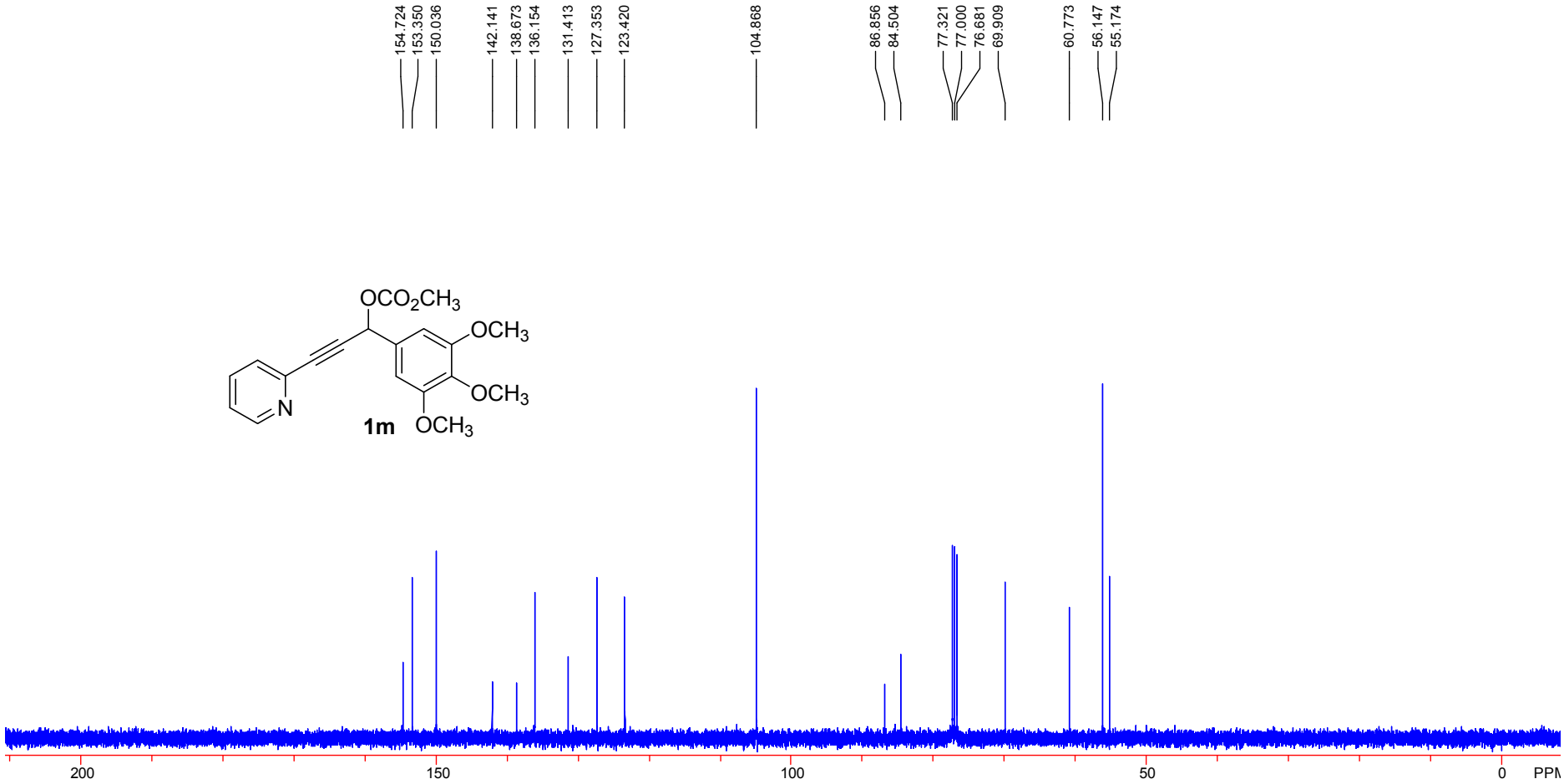
^{13}C NMR (100 MHz, $CDCl_3$)



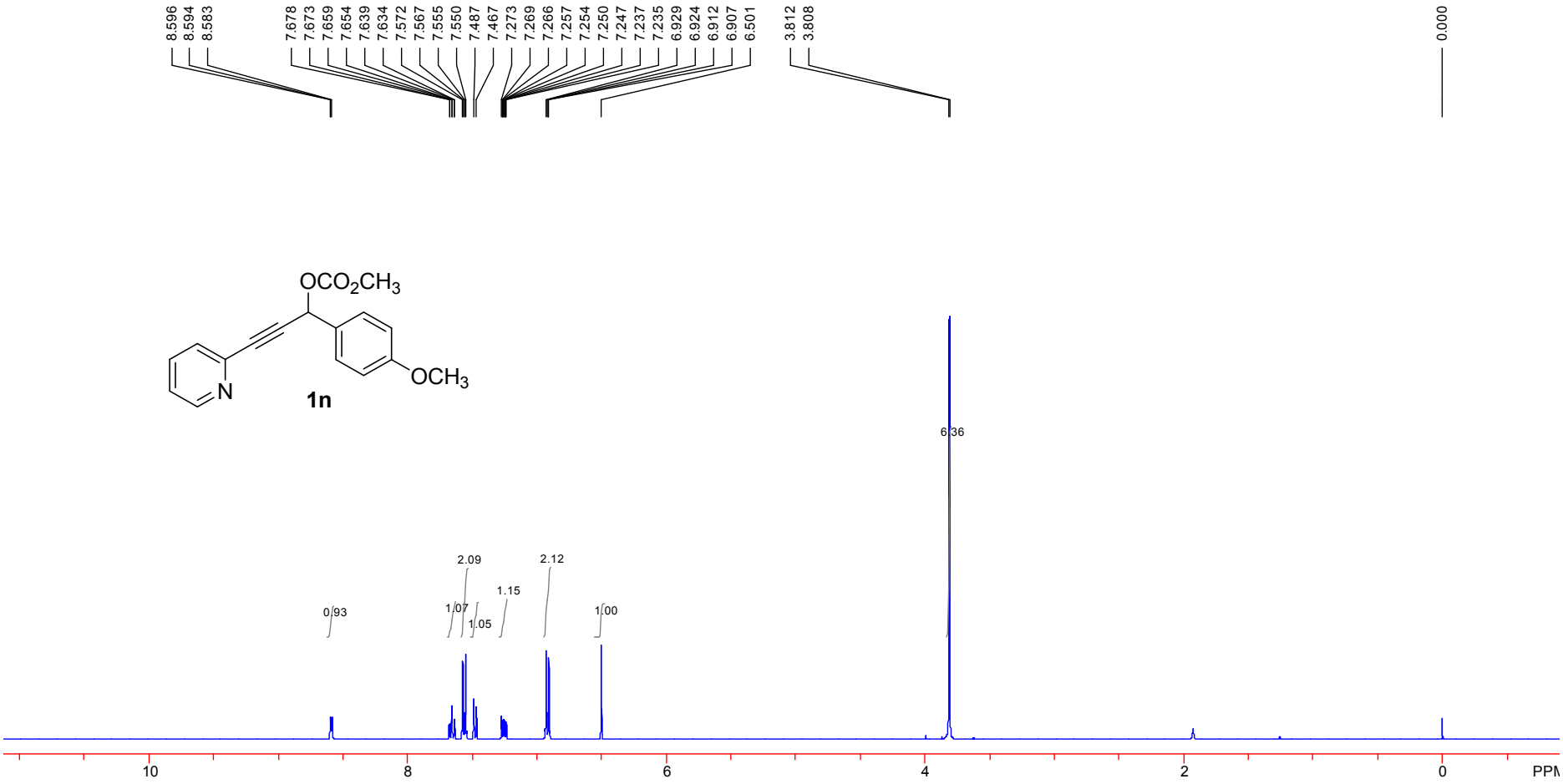
^{1}H NMR (400 MHz, $CDCl_3$)



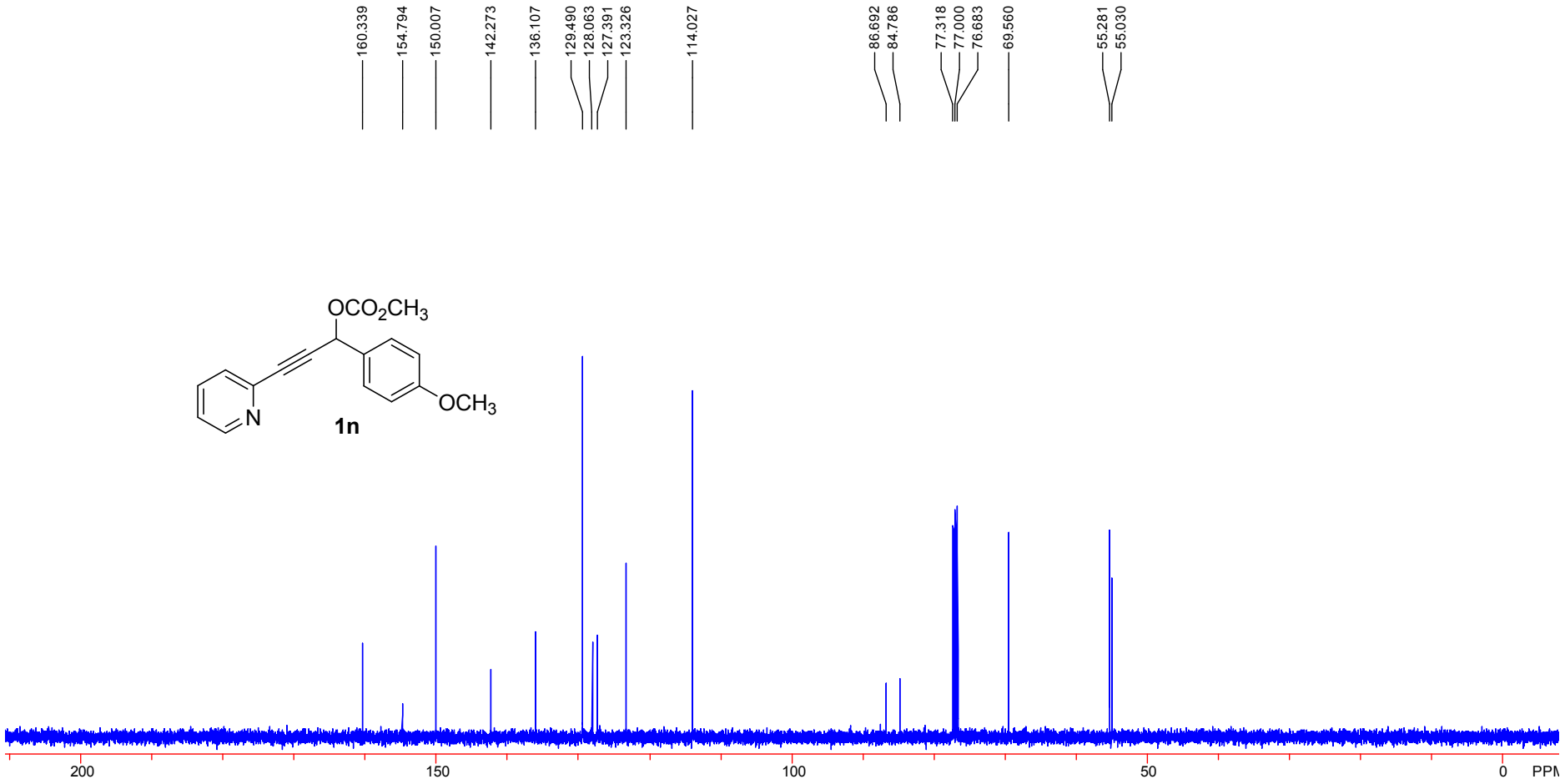
^{13}C NMR (100 MHz, $CDCl_3$)



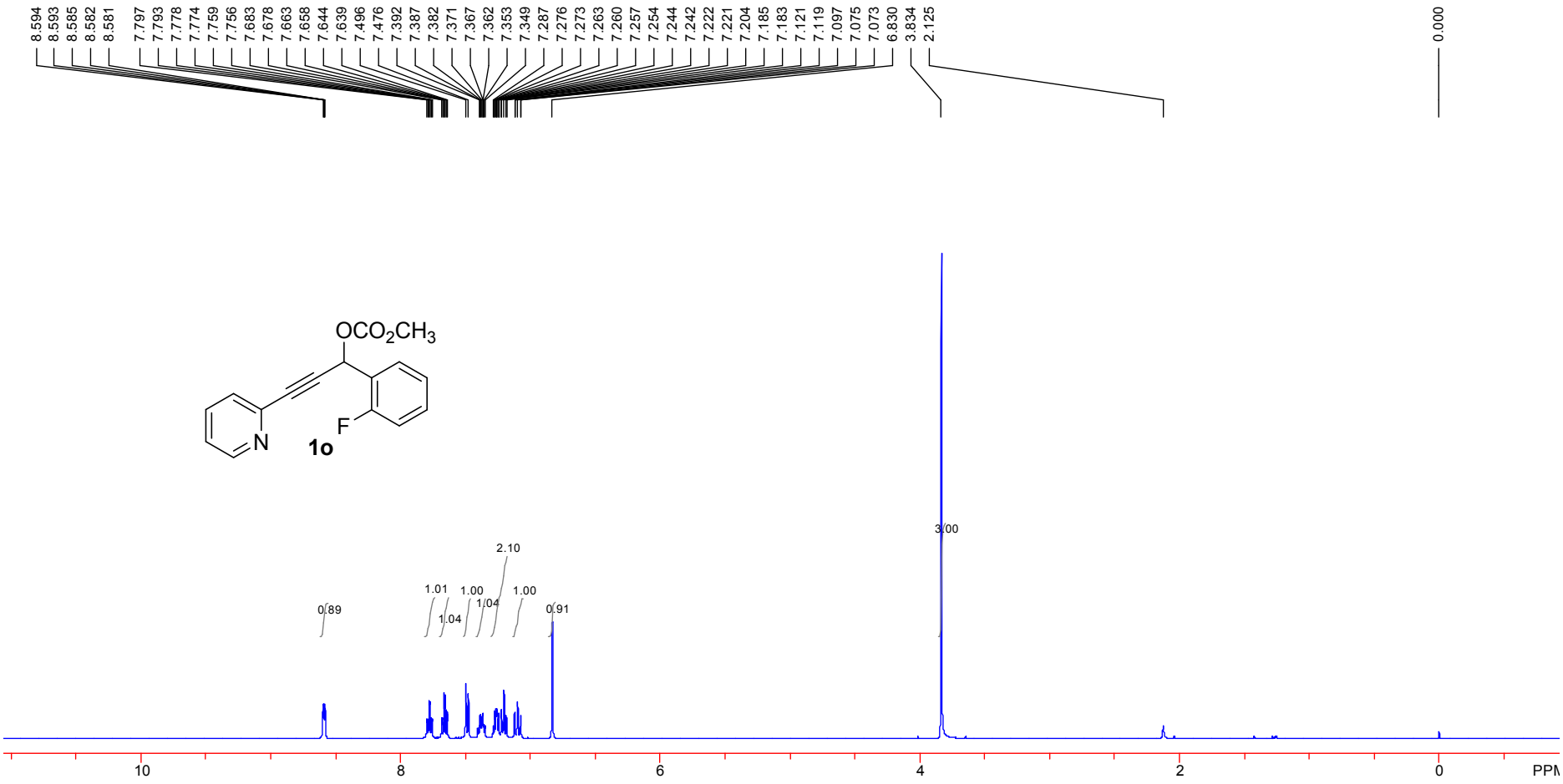
^{1}H NMR (400 MHz, $CDCl_3$)



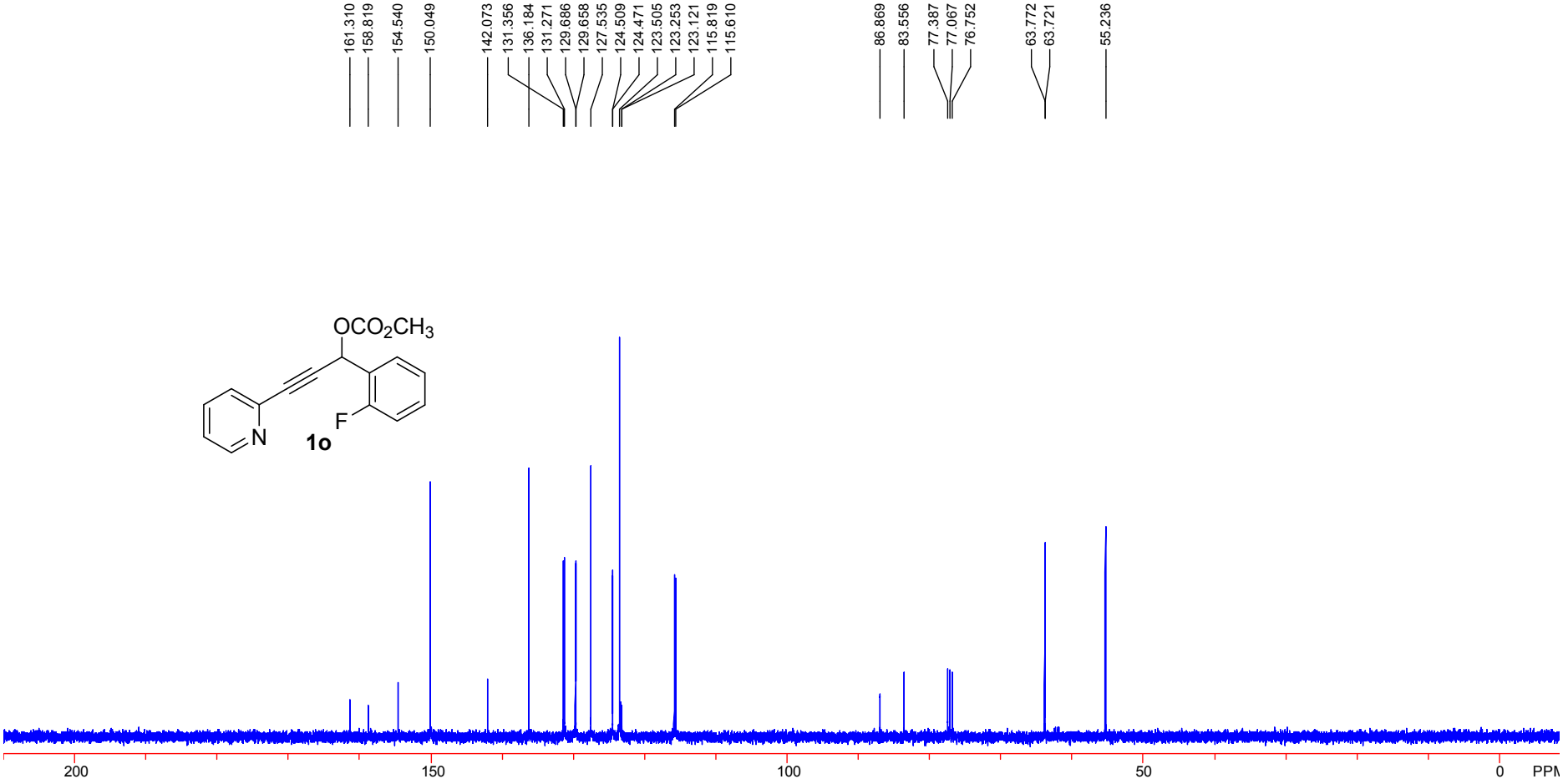
^{13}C NMR (100 MHz, $CDCl_3$)



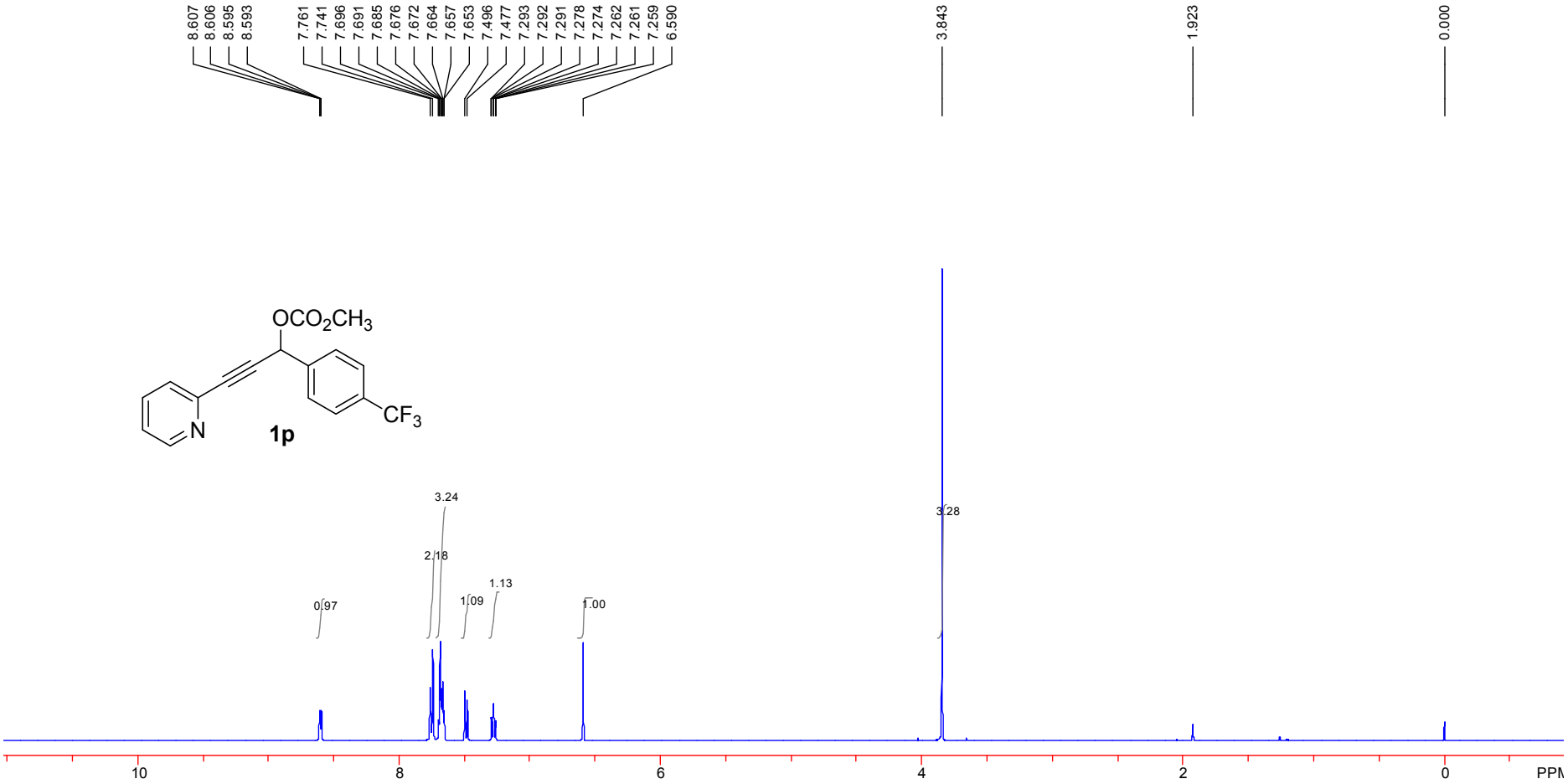
^{1}H NMR (400 MHz, $CDCl_3$)



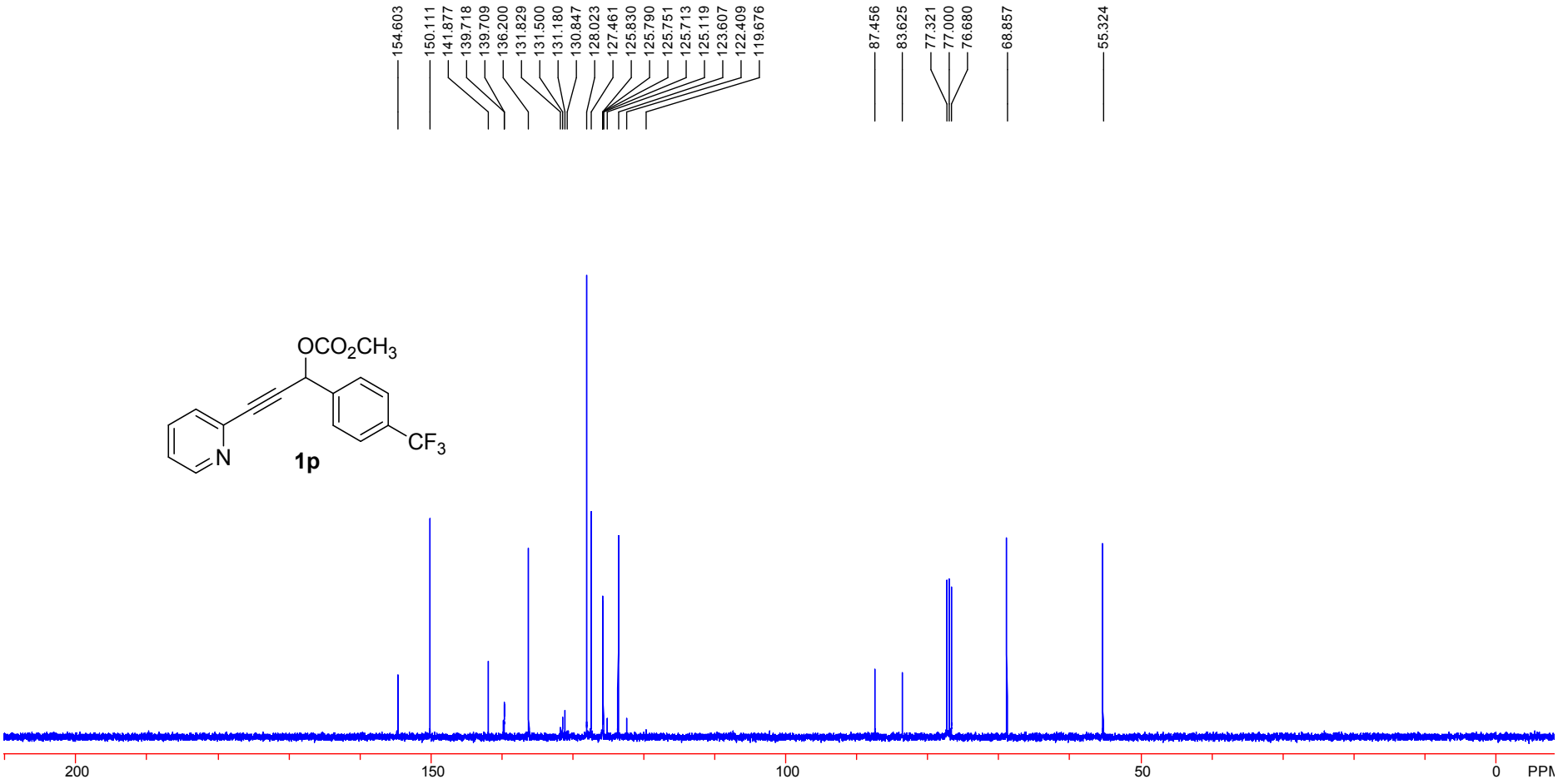
^{13}C NMR (100 MHz, $CDCl_3$)



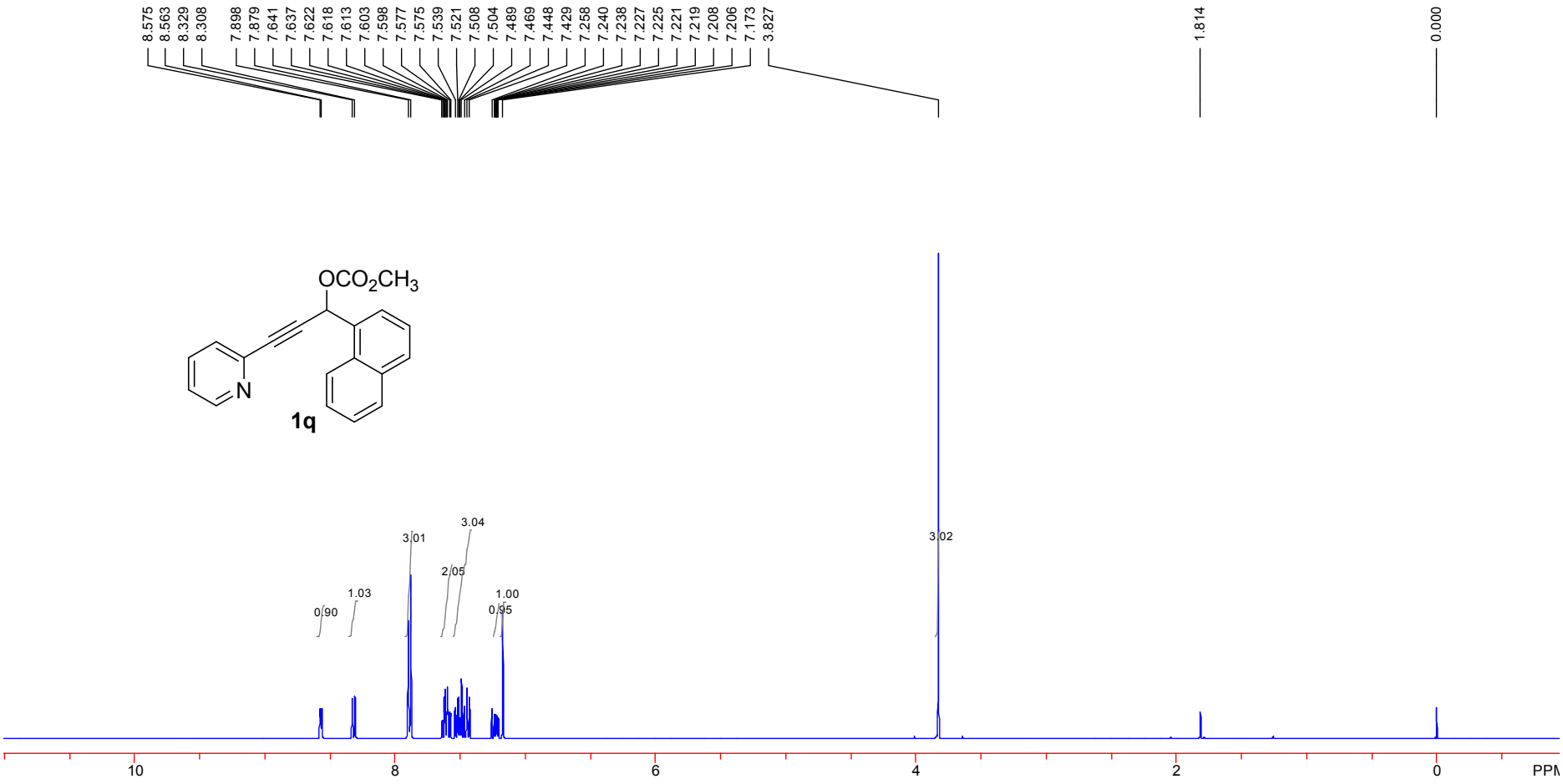
^{1}H NMR (400 MHz, $CDCl_3$)



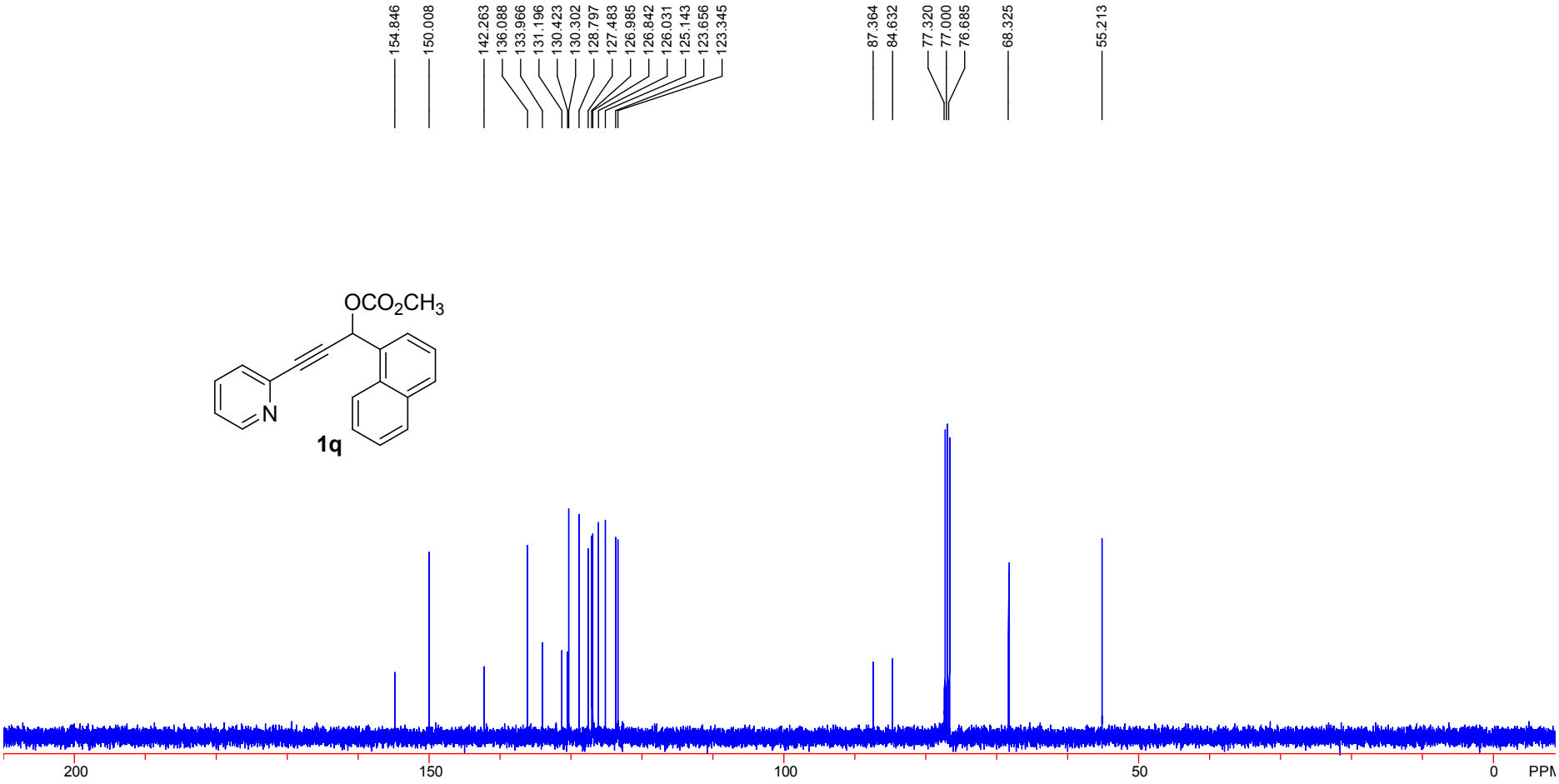
^{13}C NMR (100 MHz, $CDCl_3$)



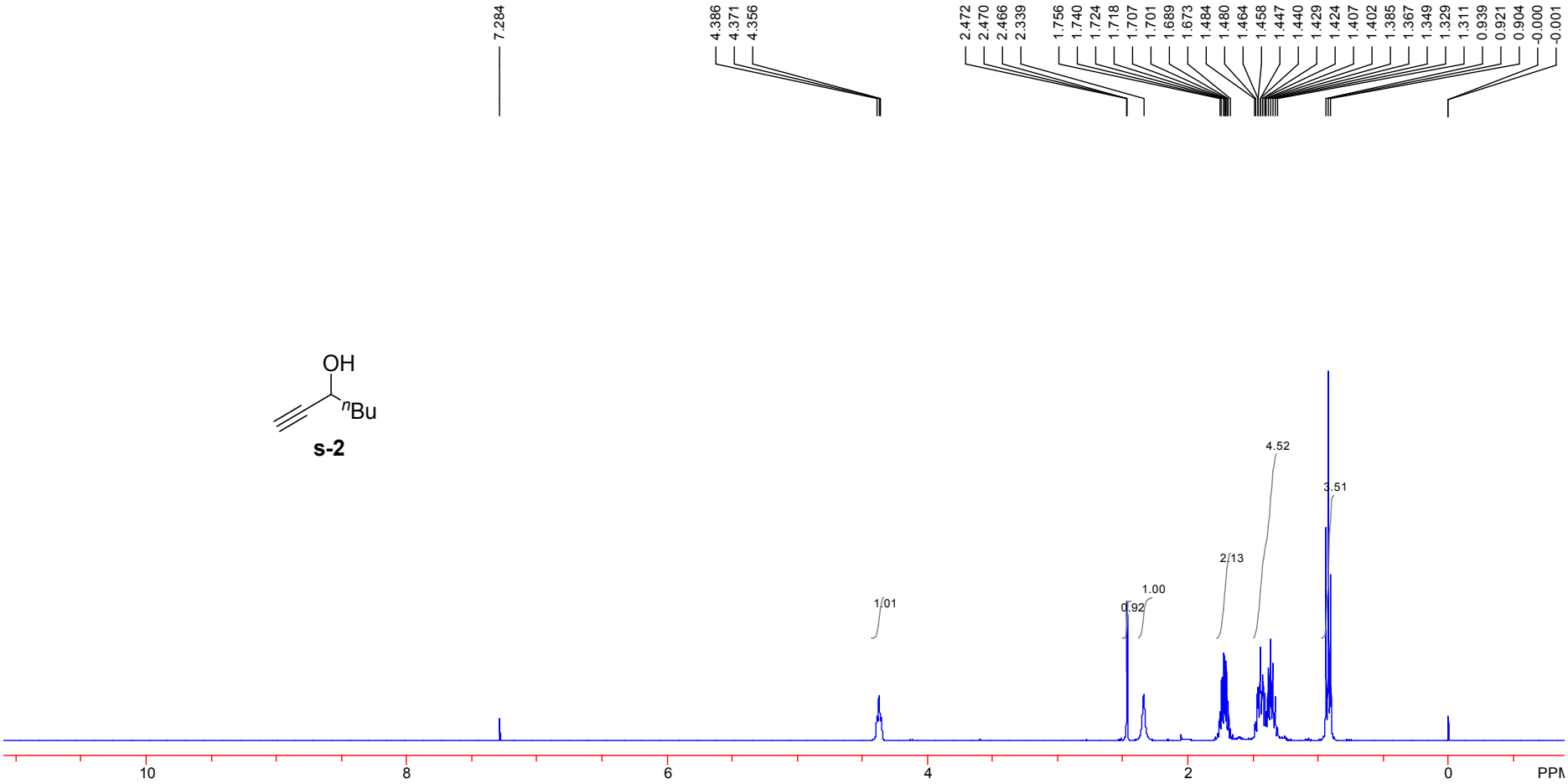
^{1}H NMR (400 MHz, $CDCl_3$)



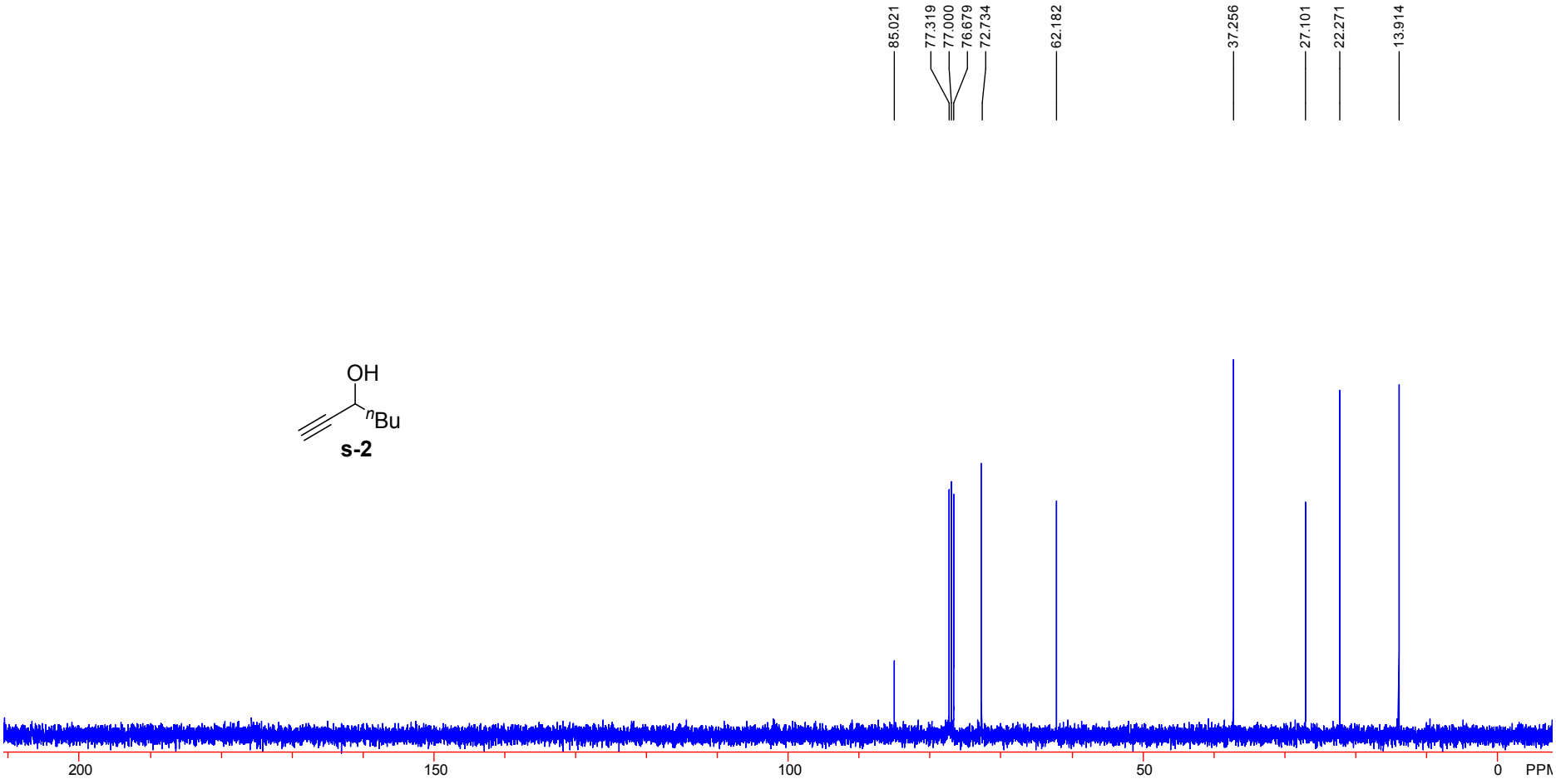
^{13}C NMR (100 MHz, $CDCl_3$)



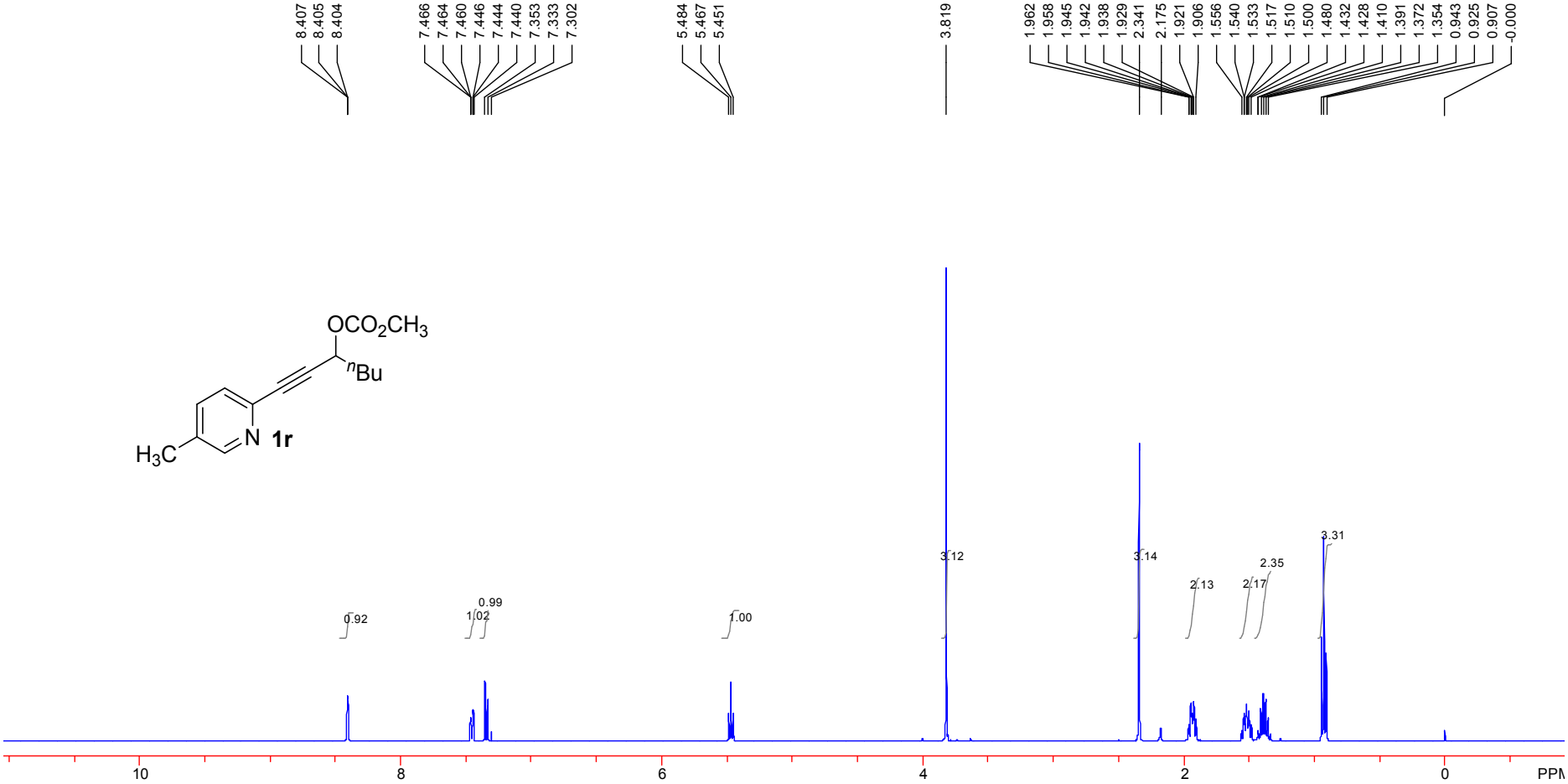
^{1}H NMR (400 MHz, $CDCl_3$)



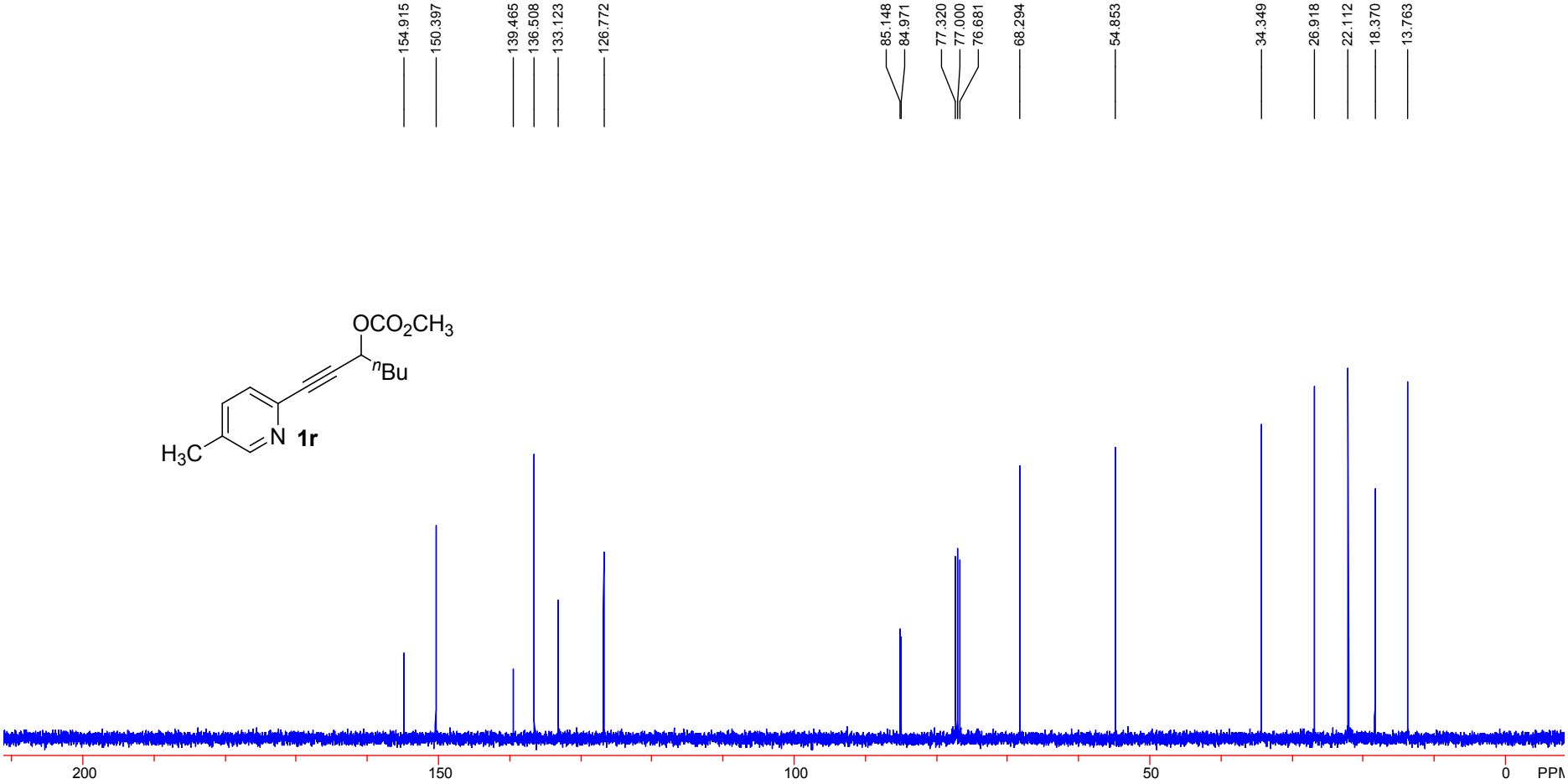
^{13}C NMR (100 MHz, $CDCl_3$)



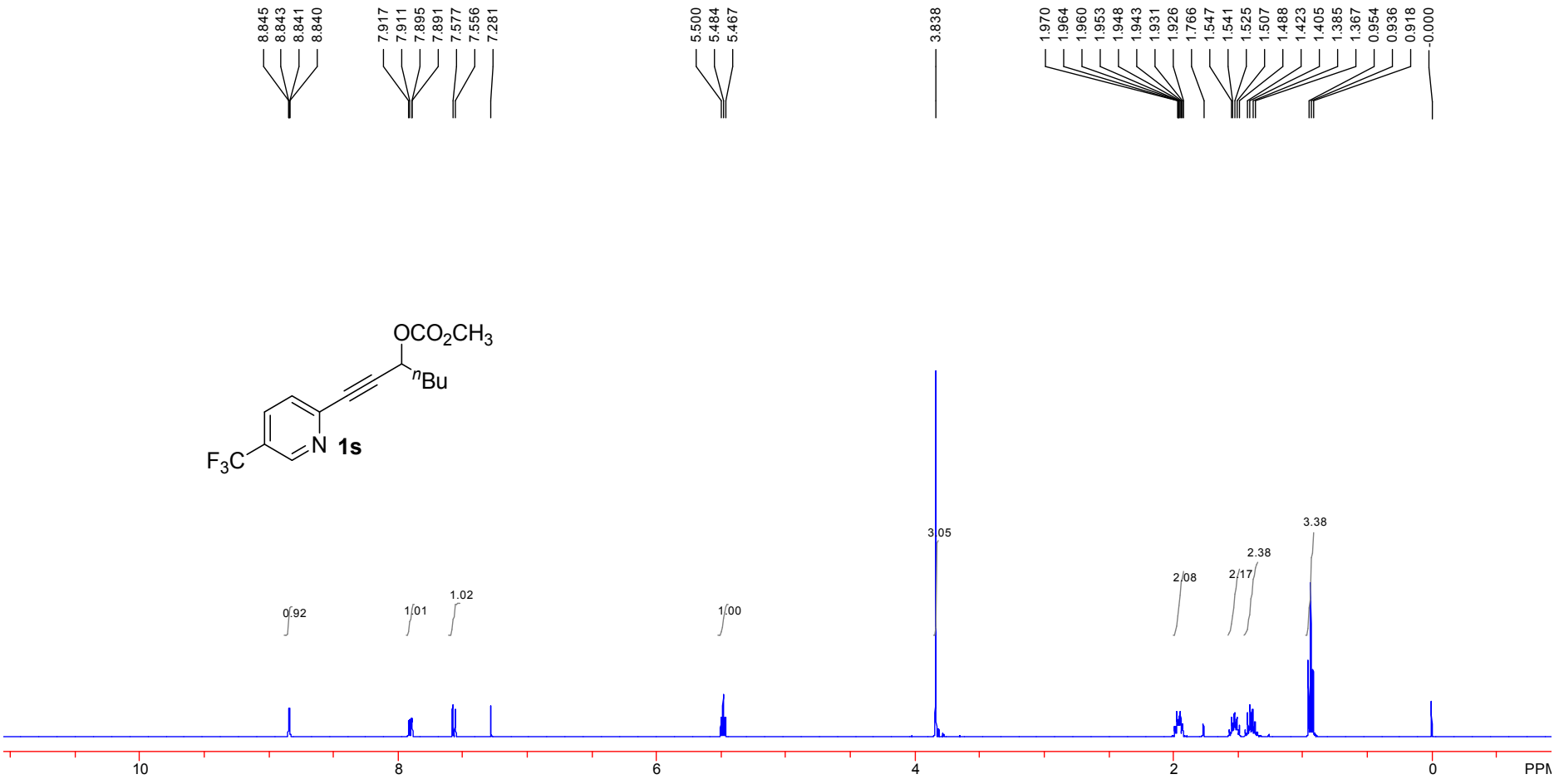
^{1}H NMR (400 MHz, $CDCl_3$)



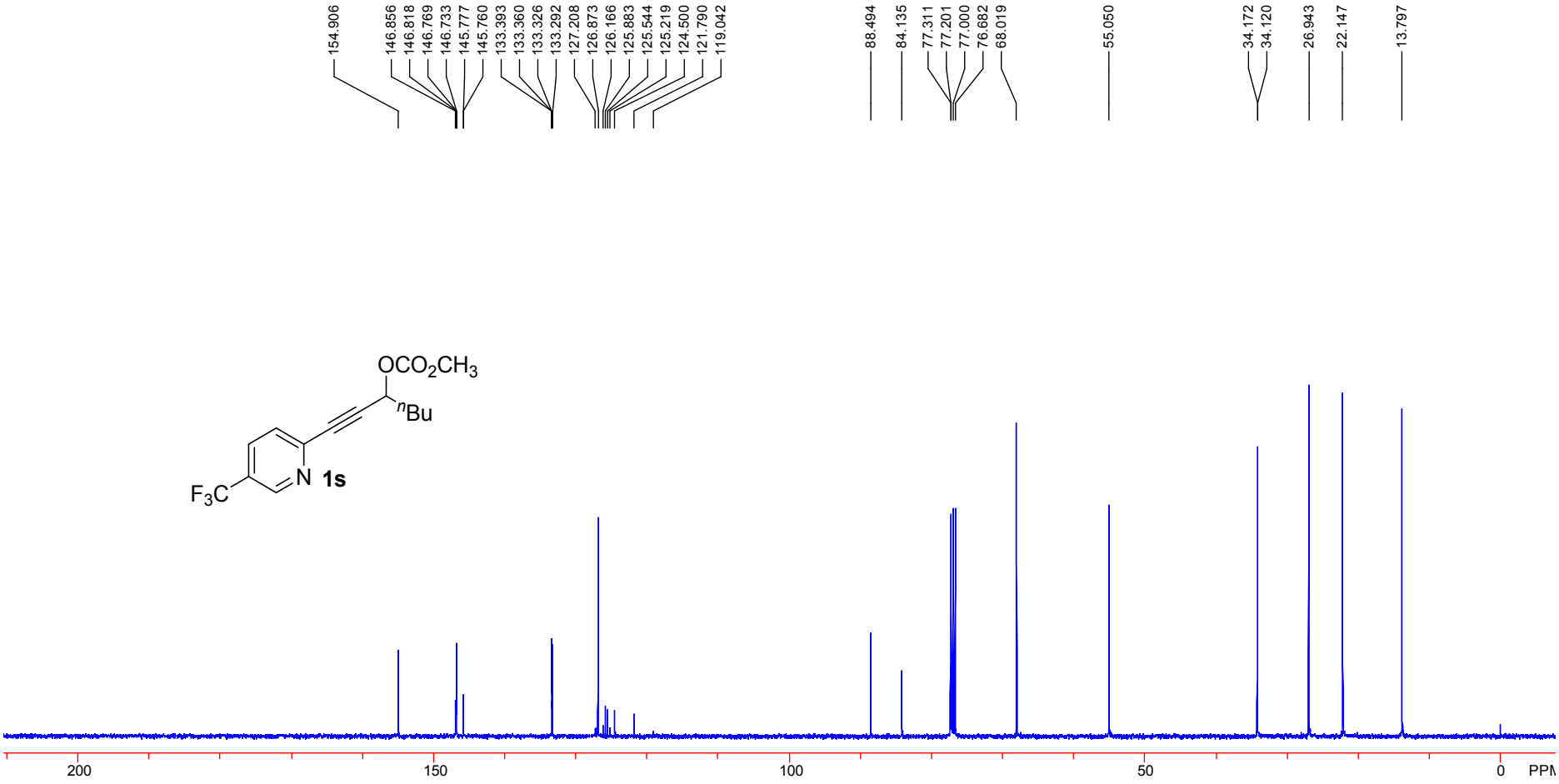
^{13}C NMR (100 MHz, $CDCl_3$)



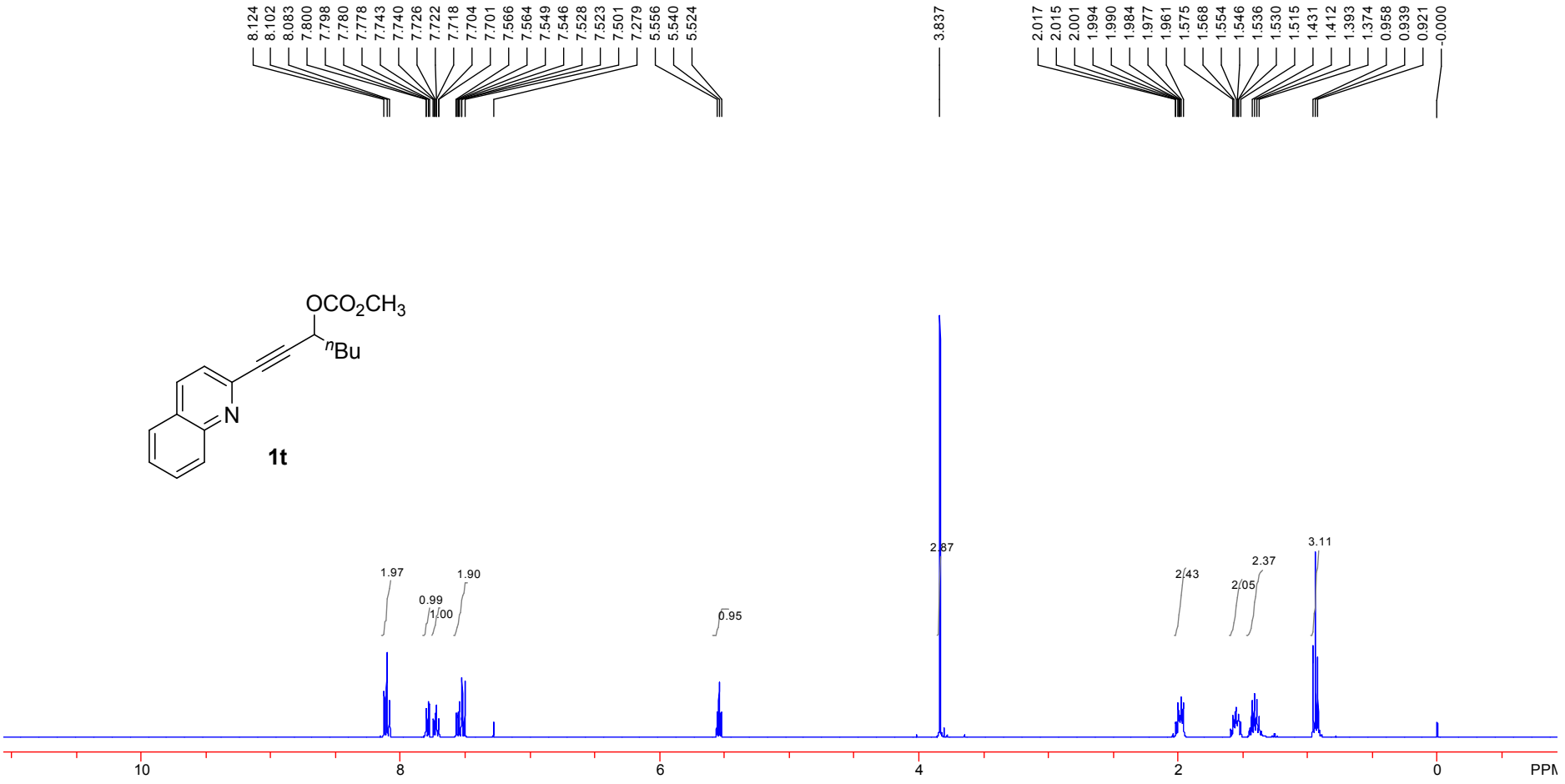
^{1}H NMR (400 MHz, $CDCl_3$)



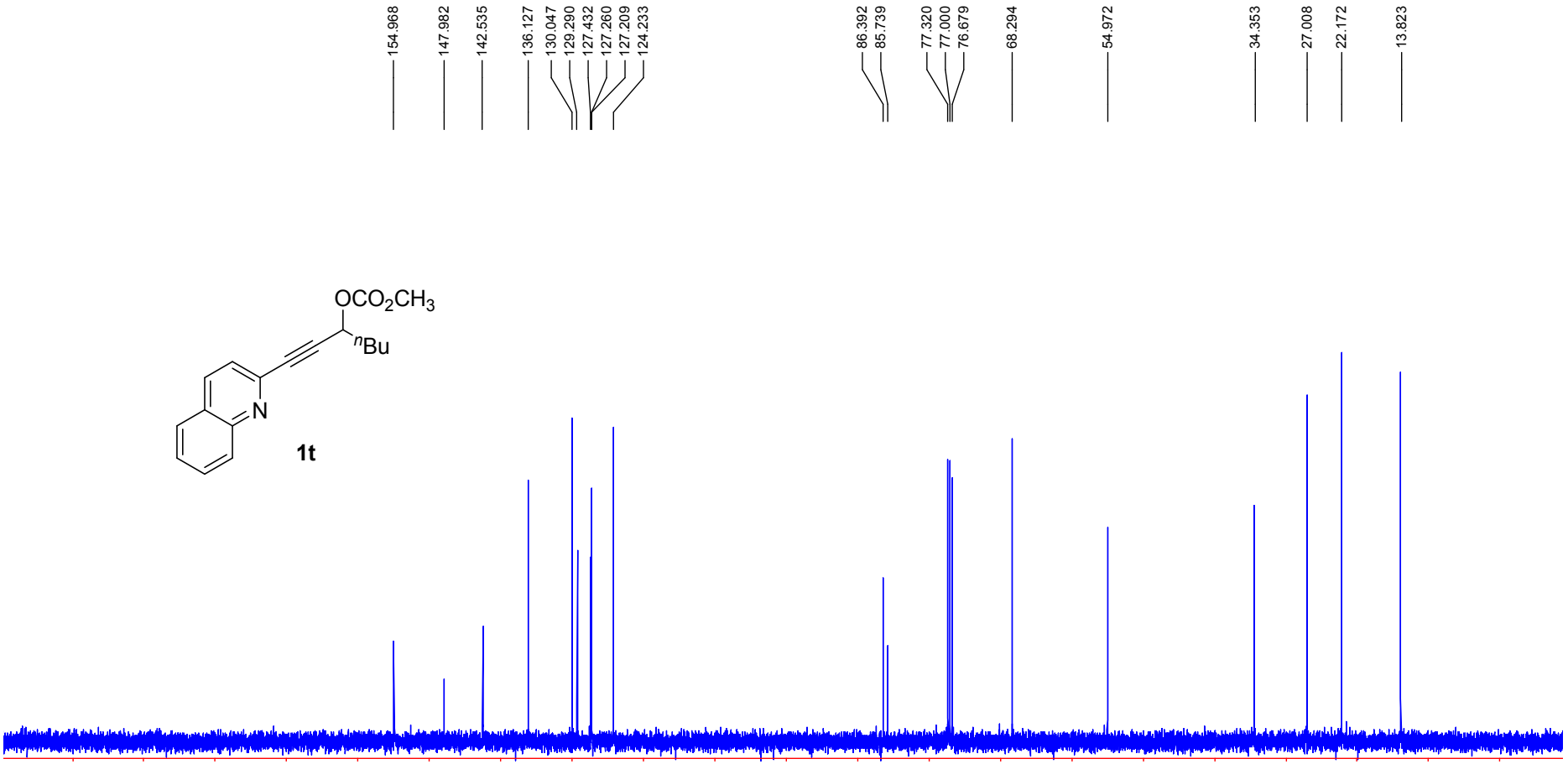
^{13}C NMR (100 MHz, $CDCl_3$)



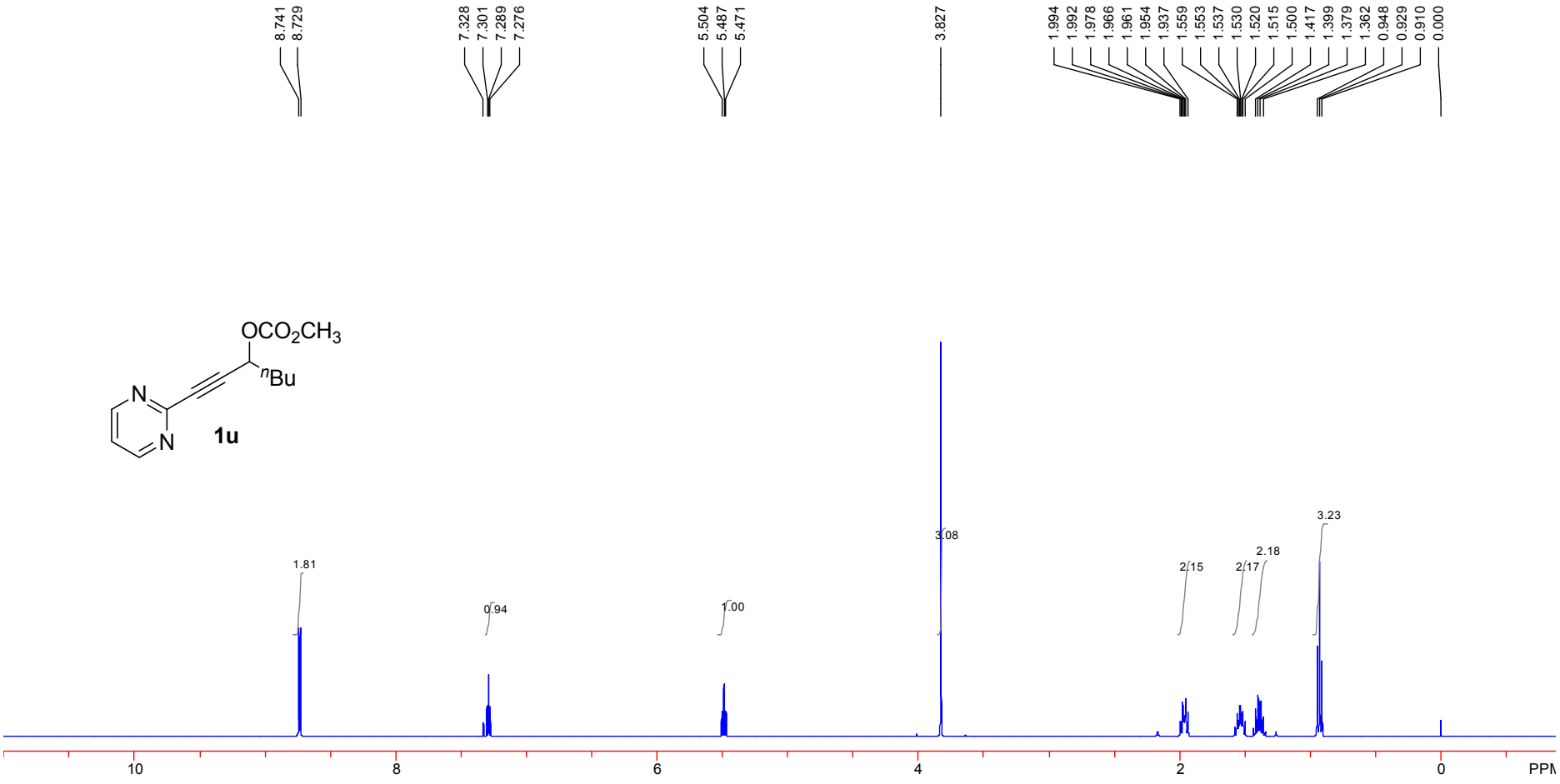
^{1}H NMR (400 MHz, $CDCl_3$)



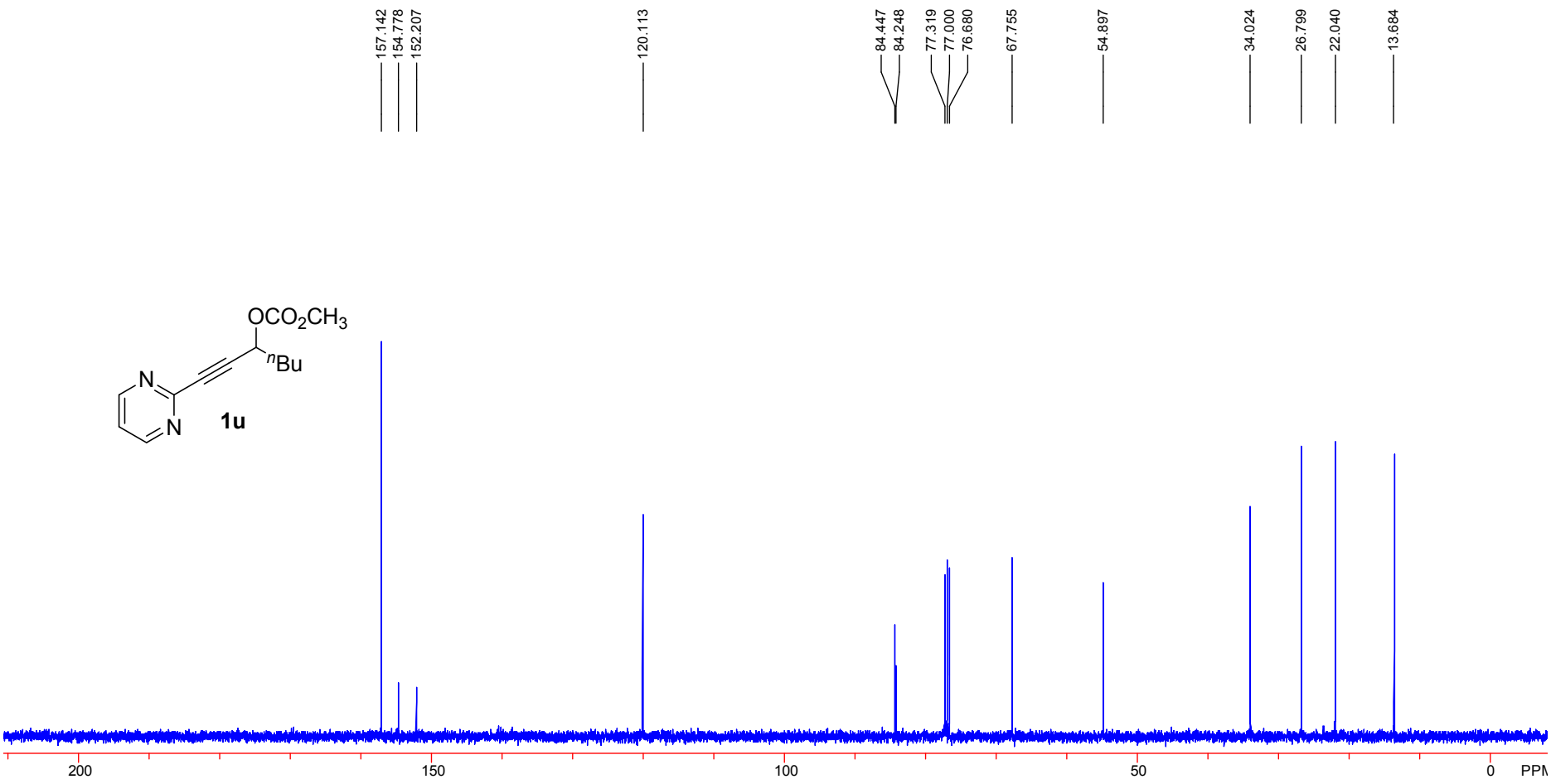
^{13}C NMR (100 MHz, $CDCl_3$)



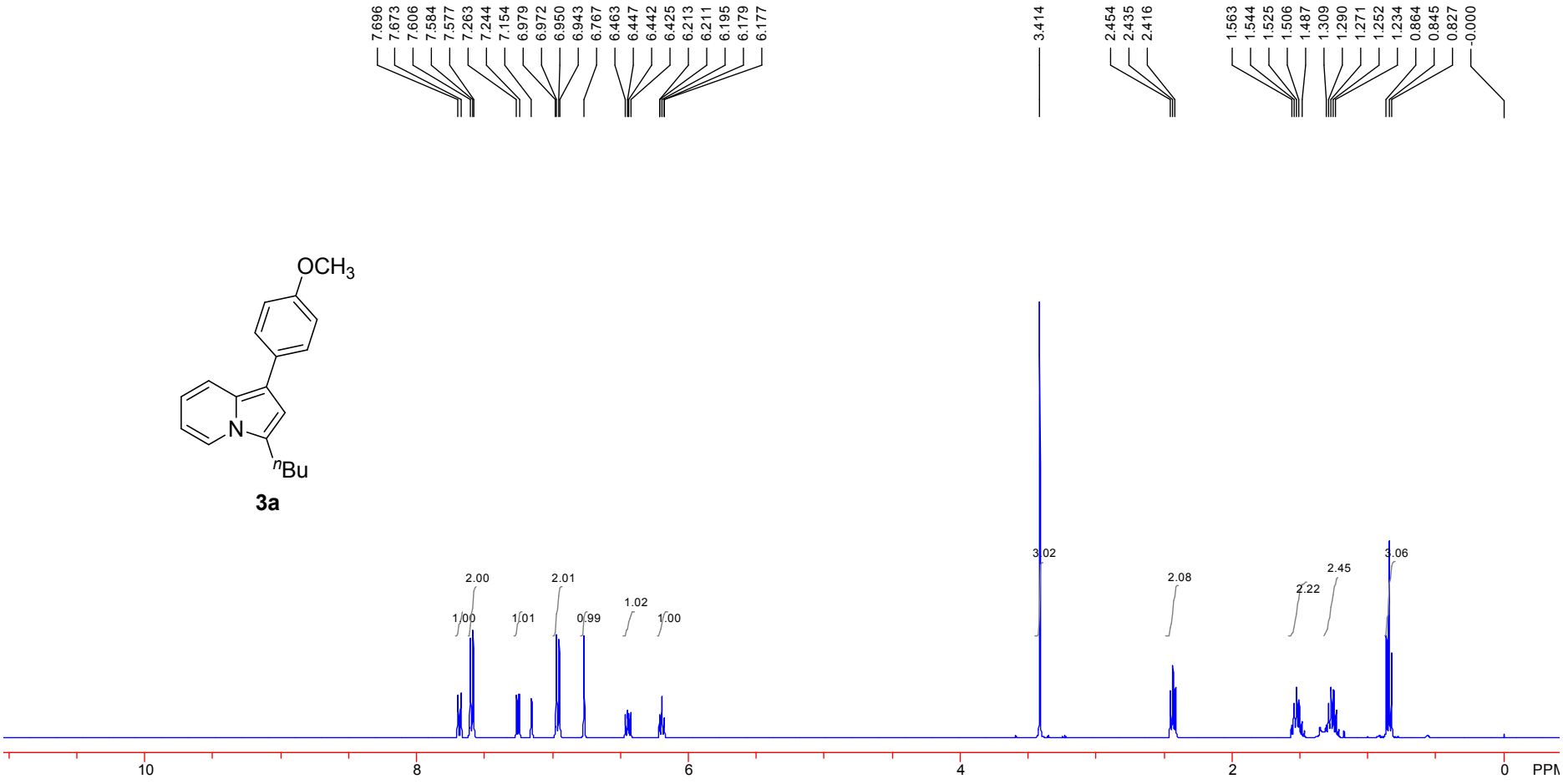
^{1}H NMR (400 MHz, $CDCl_3$)



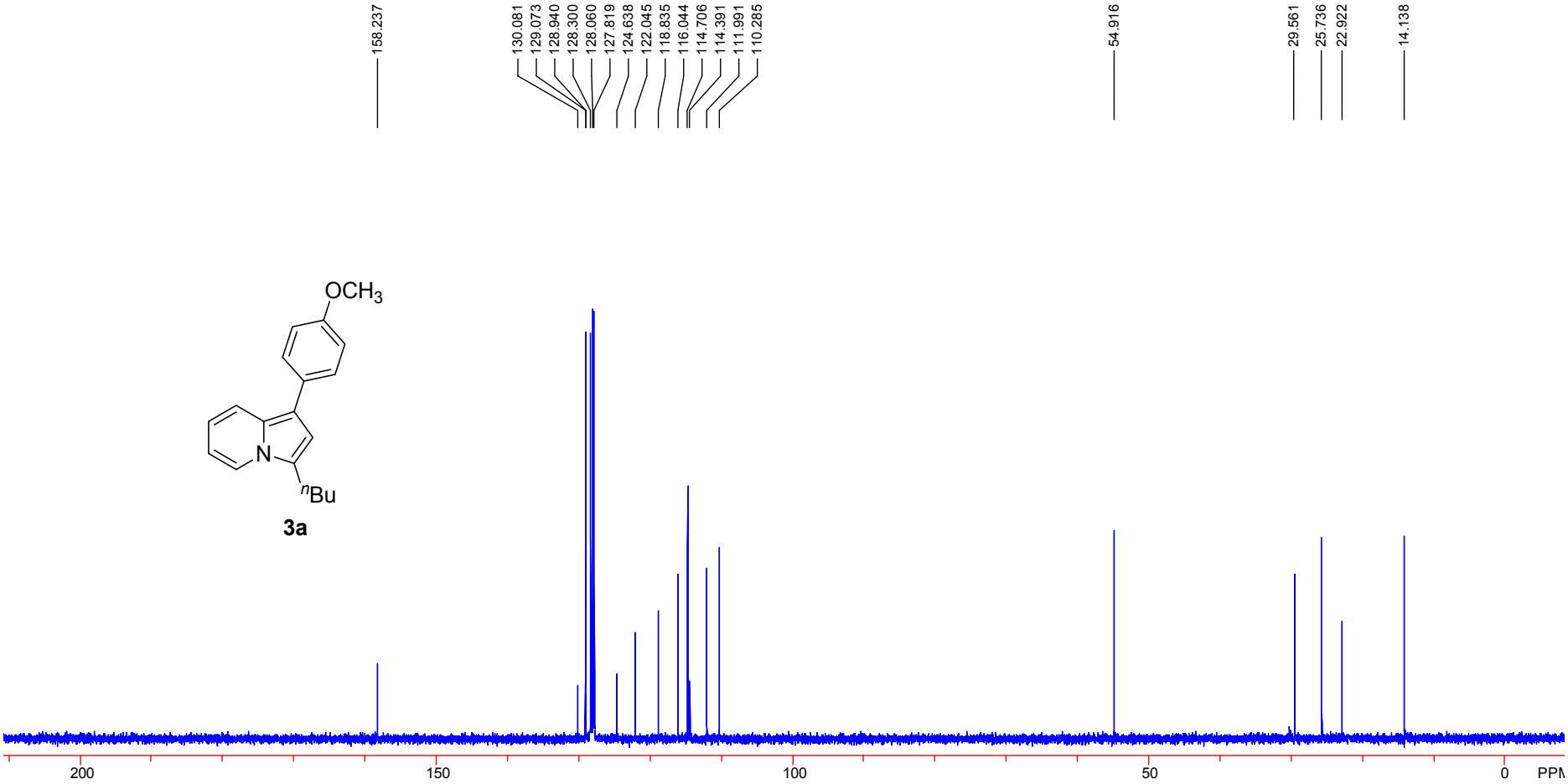
^{13}C NMR (100 MHz, $CDCl_3$)



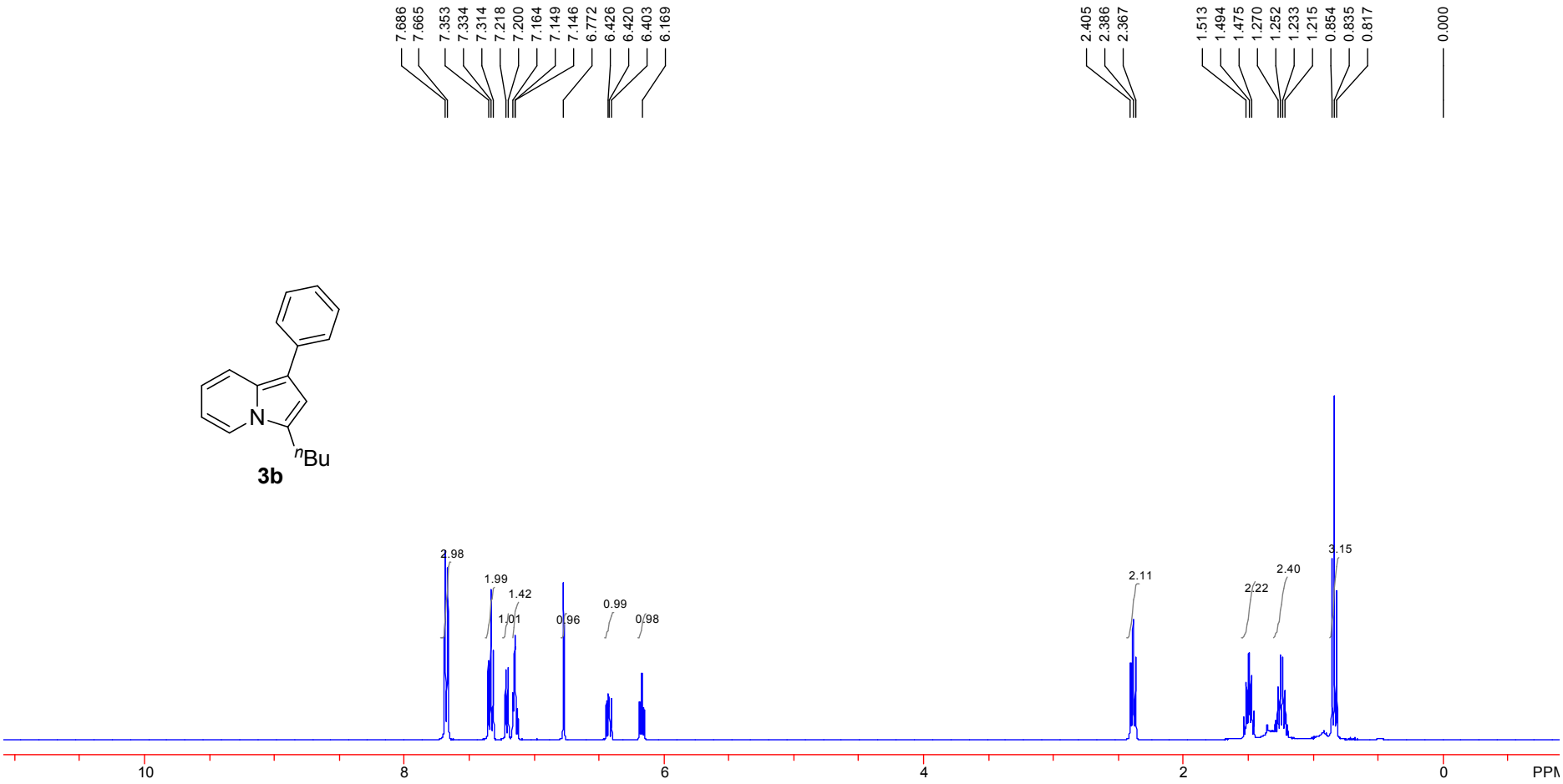
^{1}H NMR (400 MHz, C_6D_6)



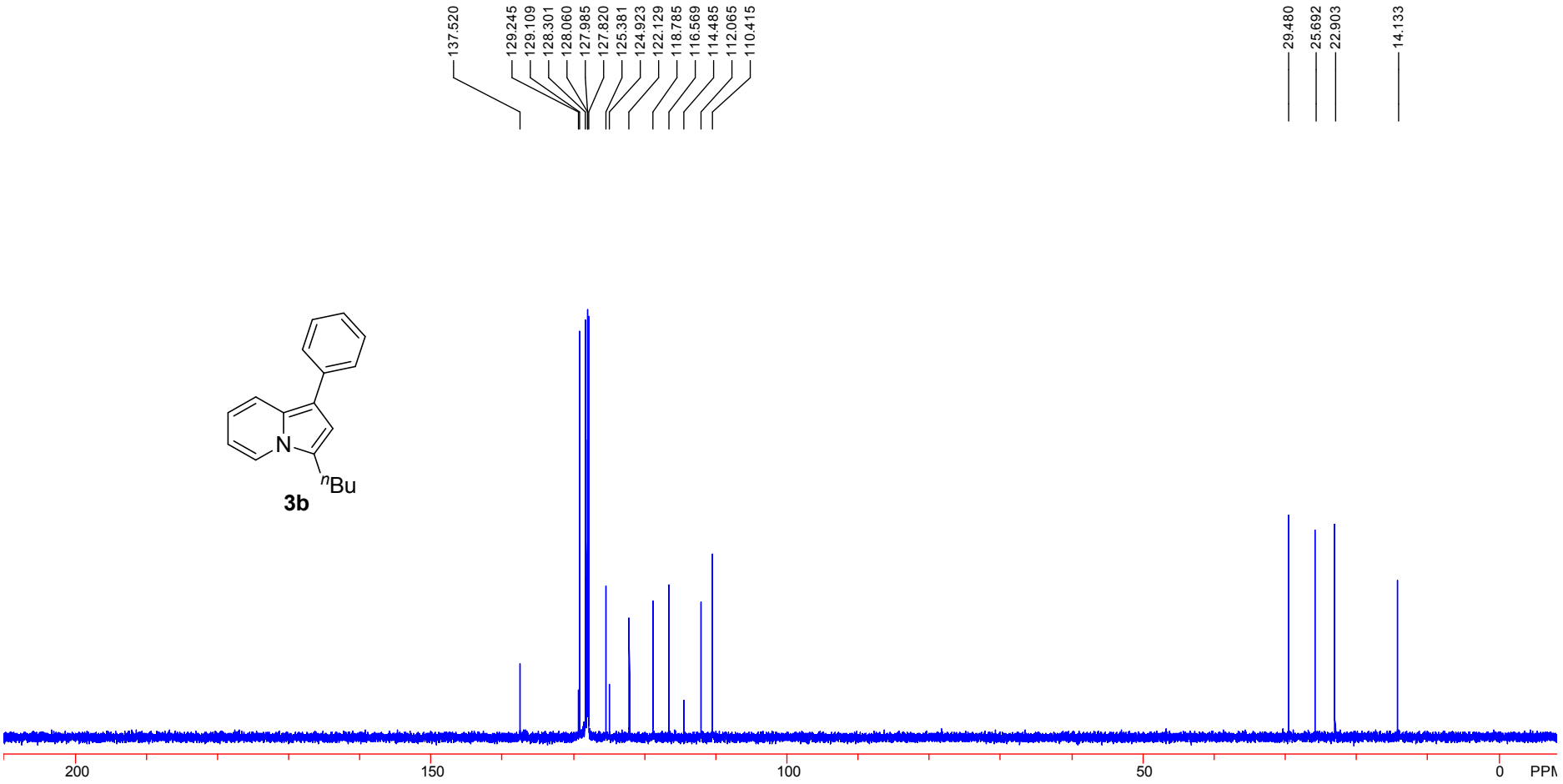
^{13}C NMR (100 MHz, C_6D_6)



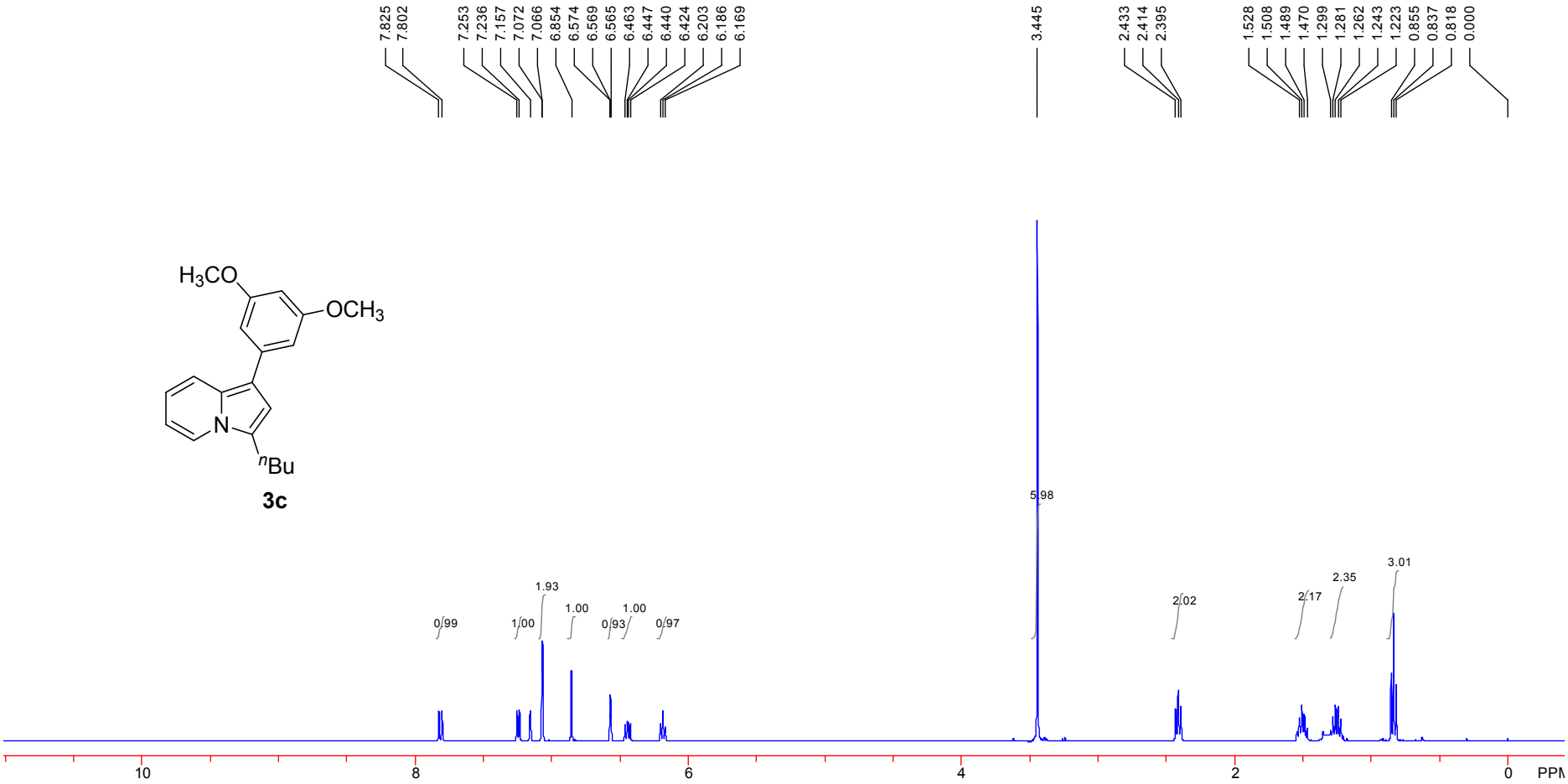
^{1}H NMR (400 MHz, C_6D_6)



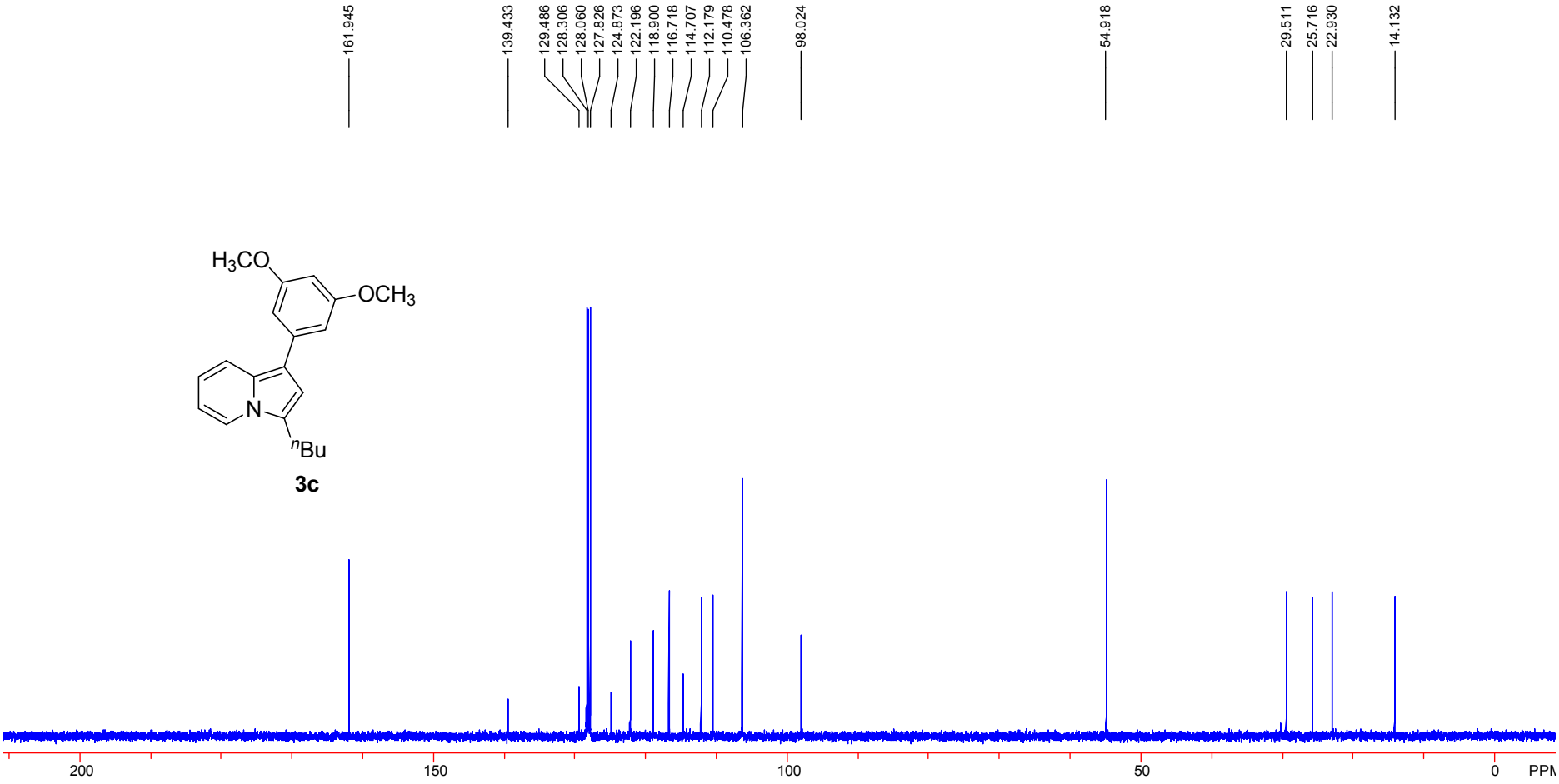
^{13}C NMR (100 MHz, C_6D_6)



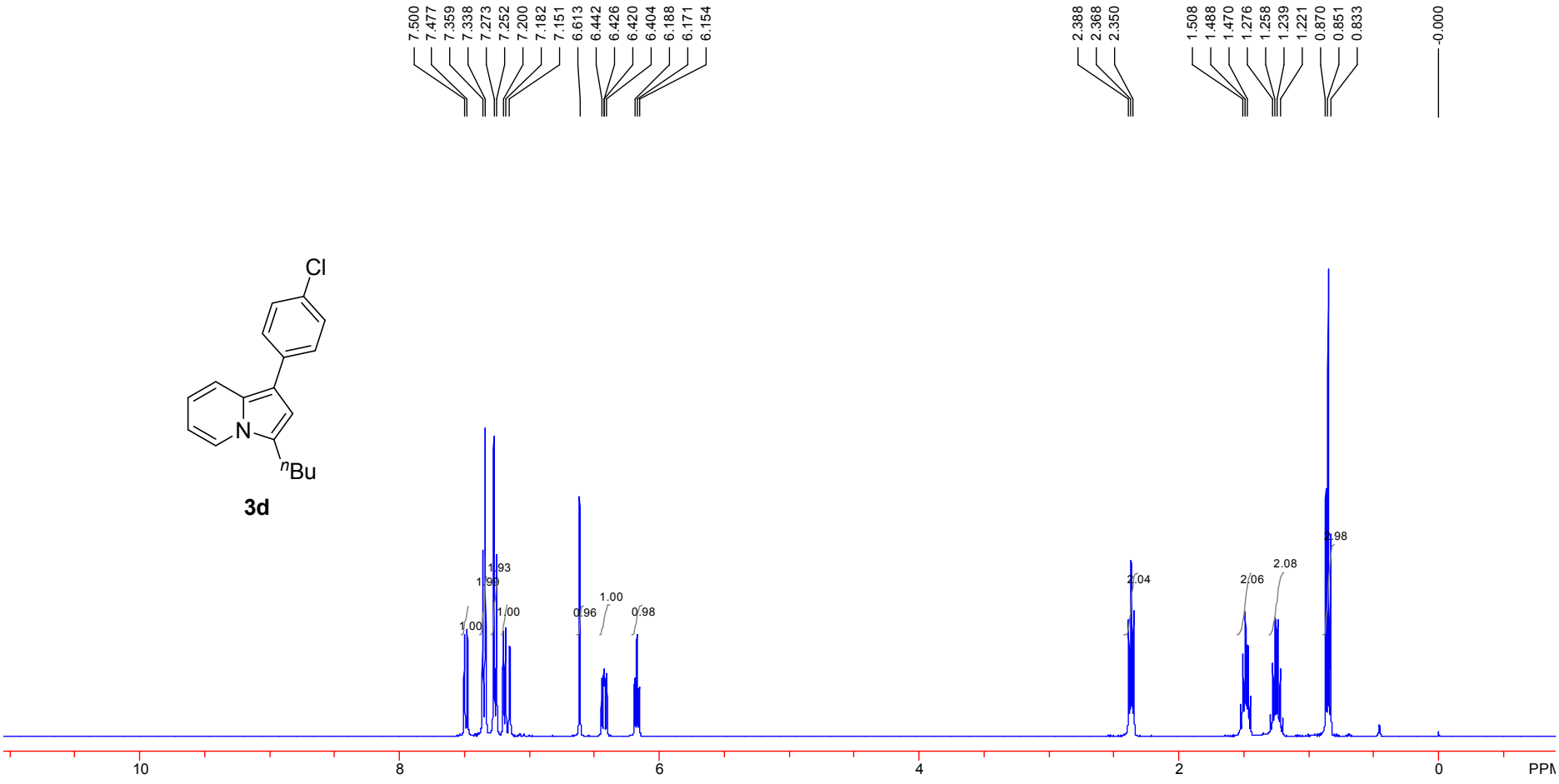
^{1}H NMR (400 MHz, C_6D_6)



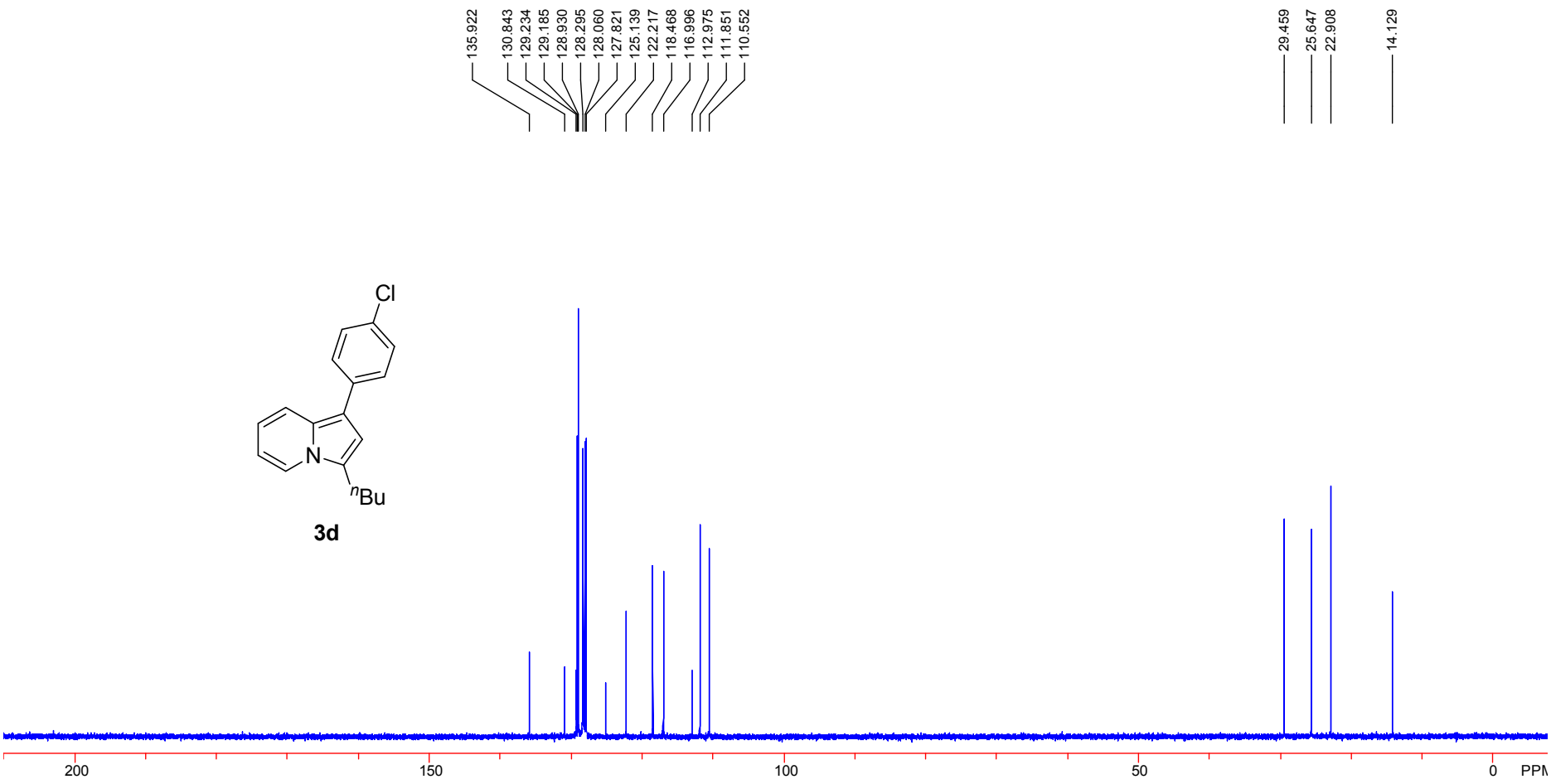
^{13}C NMR (100 MHz, C_6D_6)



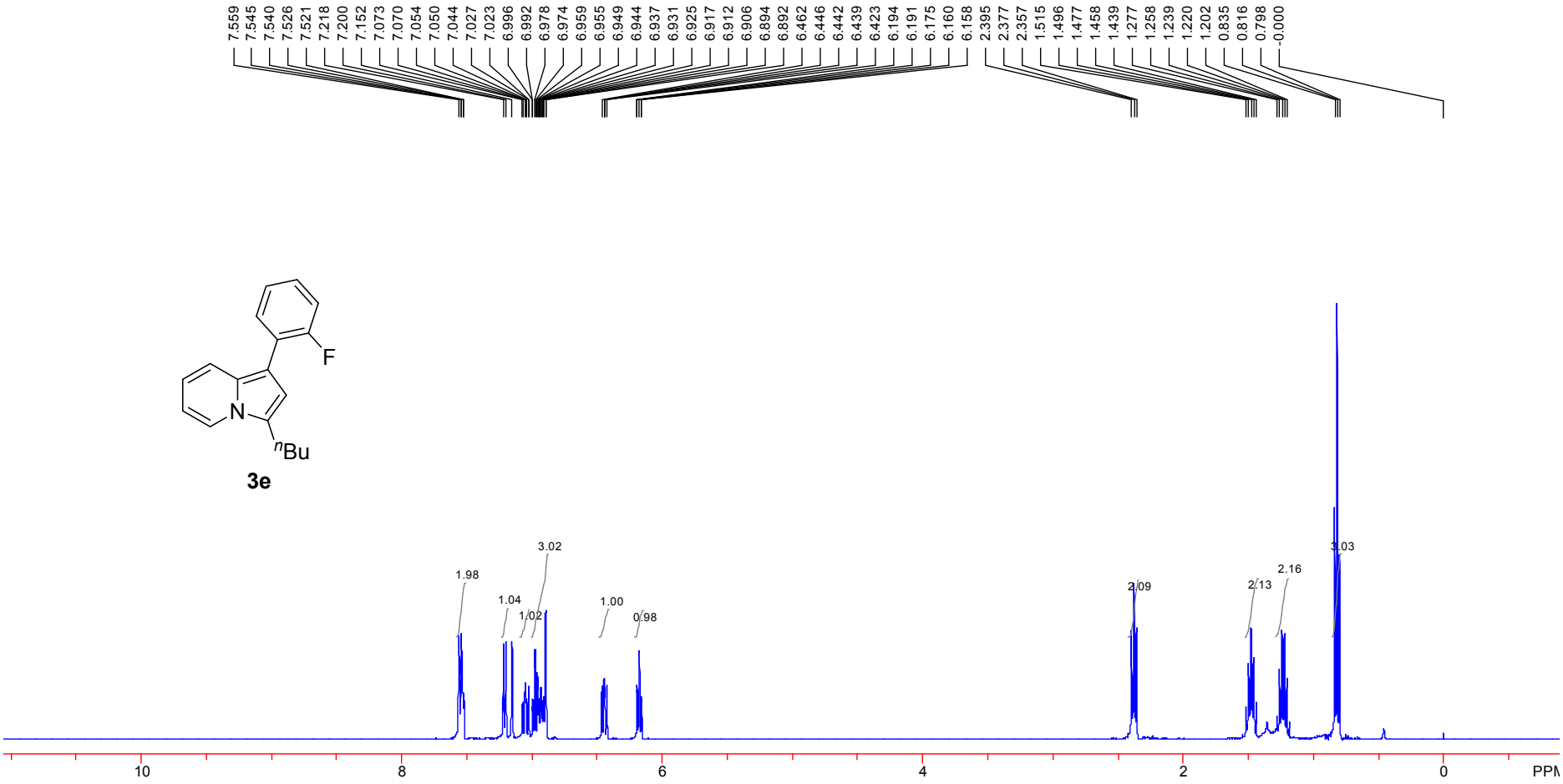
^{1}H NMR (400 MHz, C_6D_6)



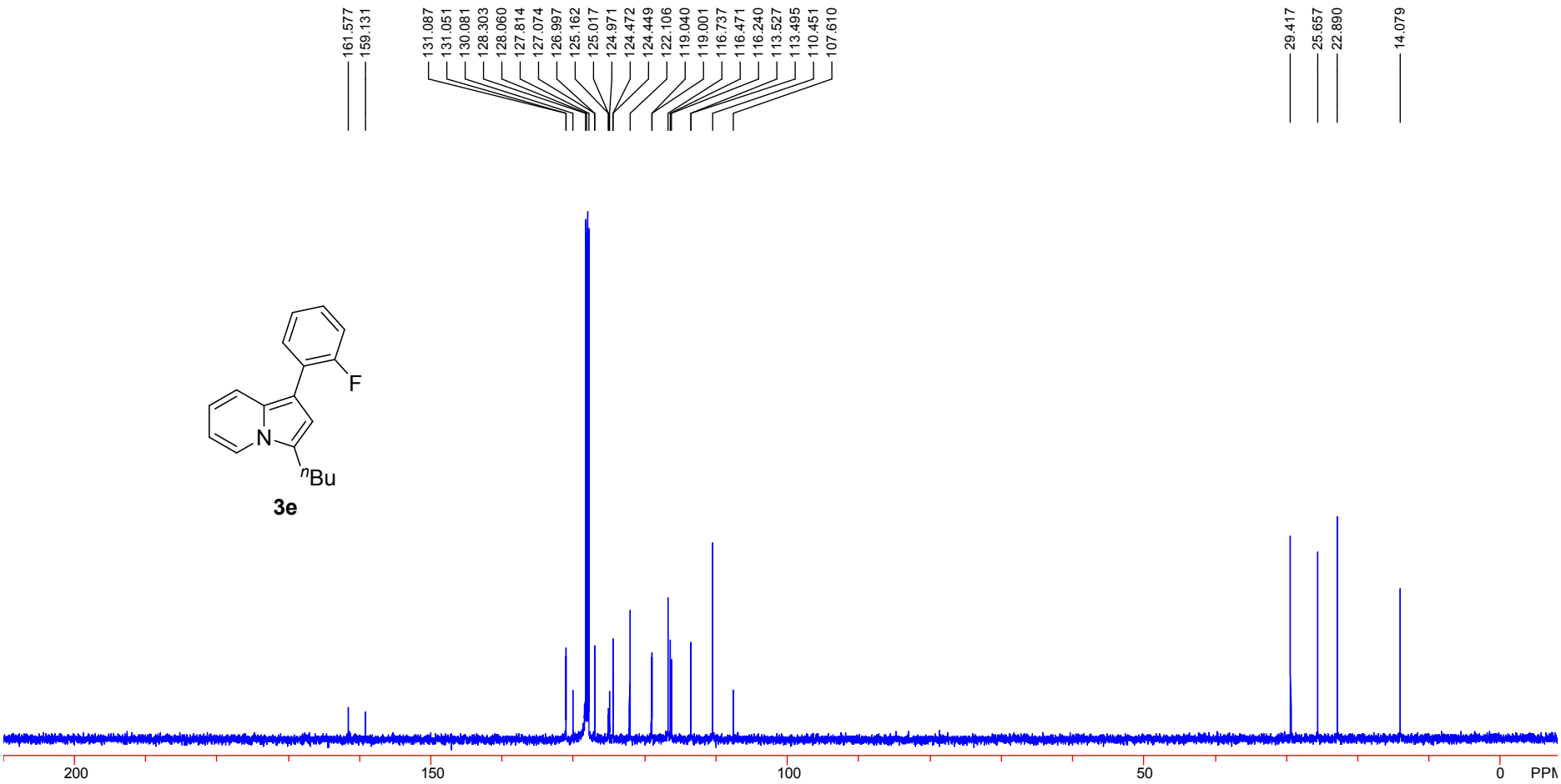
^{13}C NMR (100 MHz, C_6D_6)



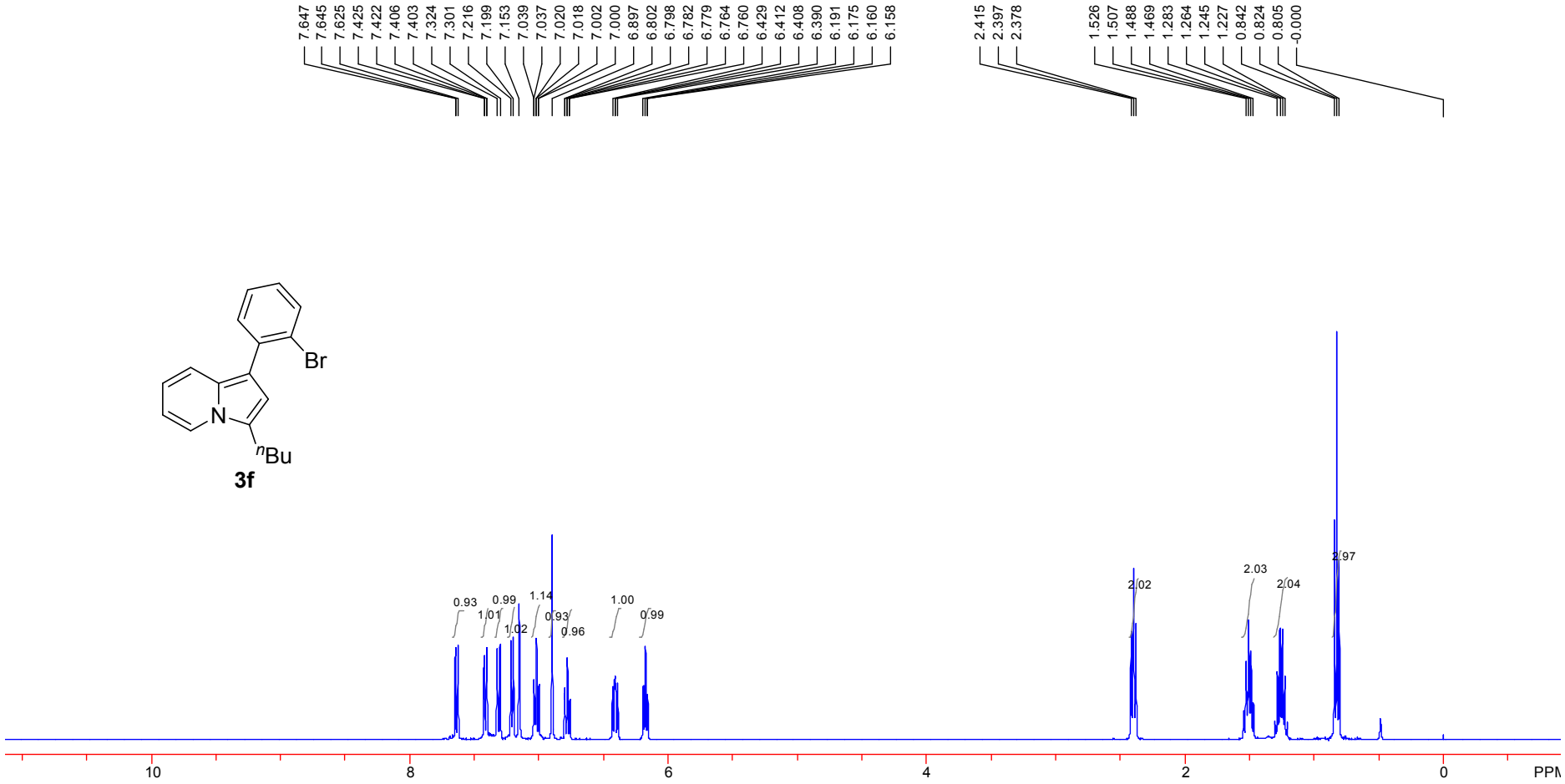
^{1}H NMR (400 MHz, C_6D_6)



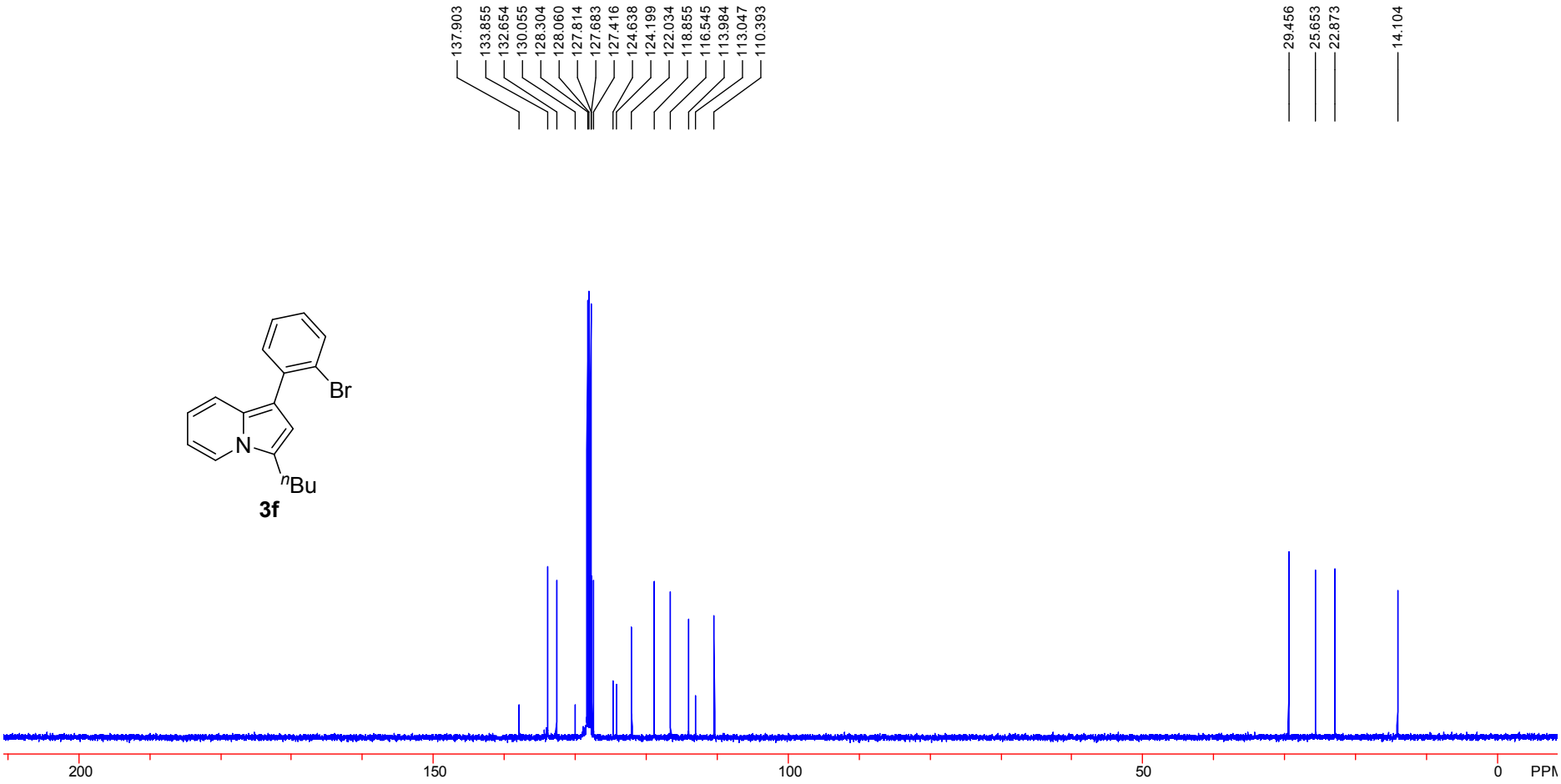
^{13}C NMR (100 MHz, C_6D_6)



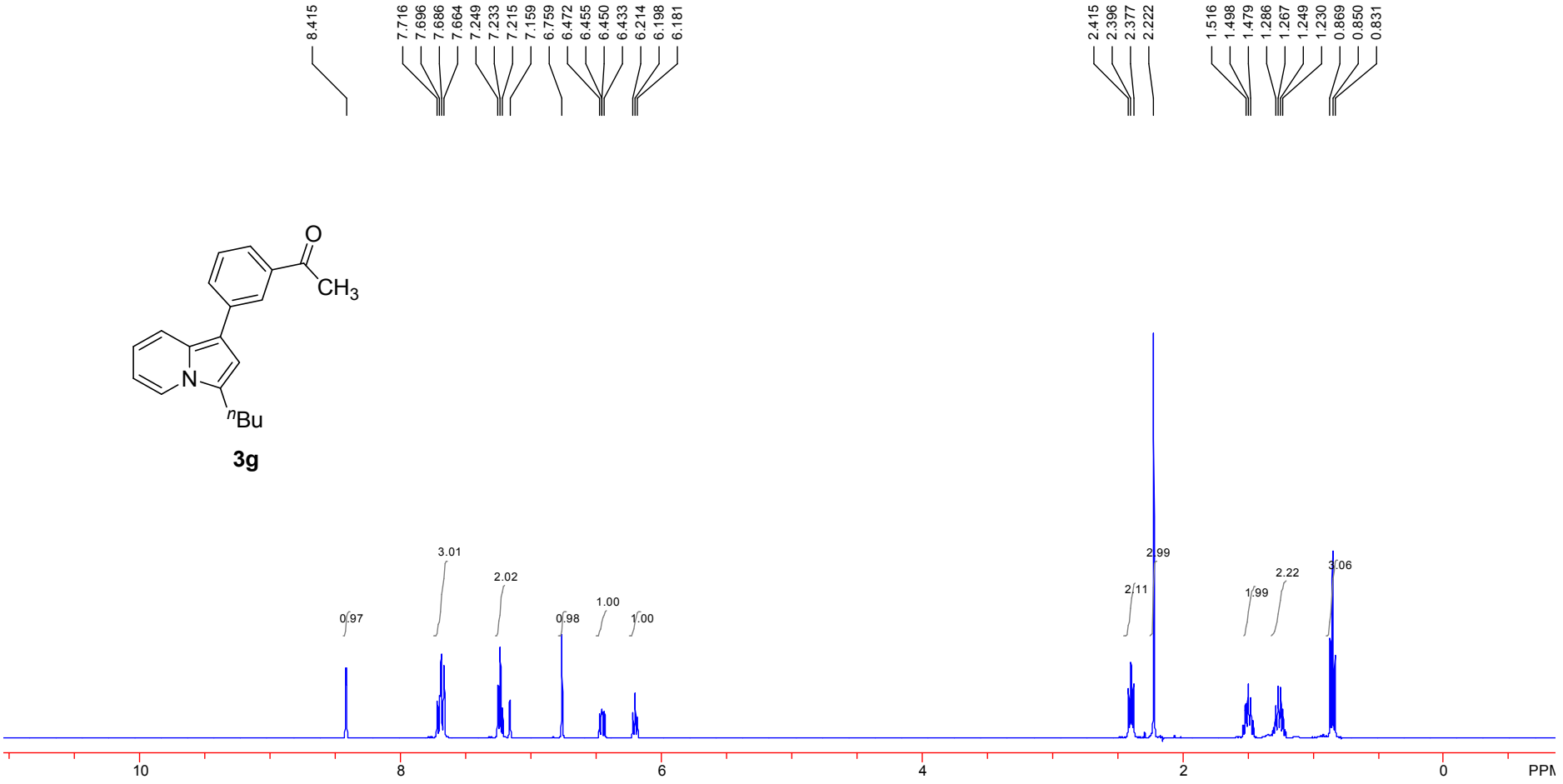
^{1}H NMR (400 MHz, C_6D_6)



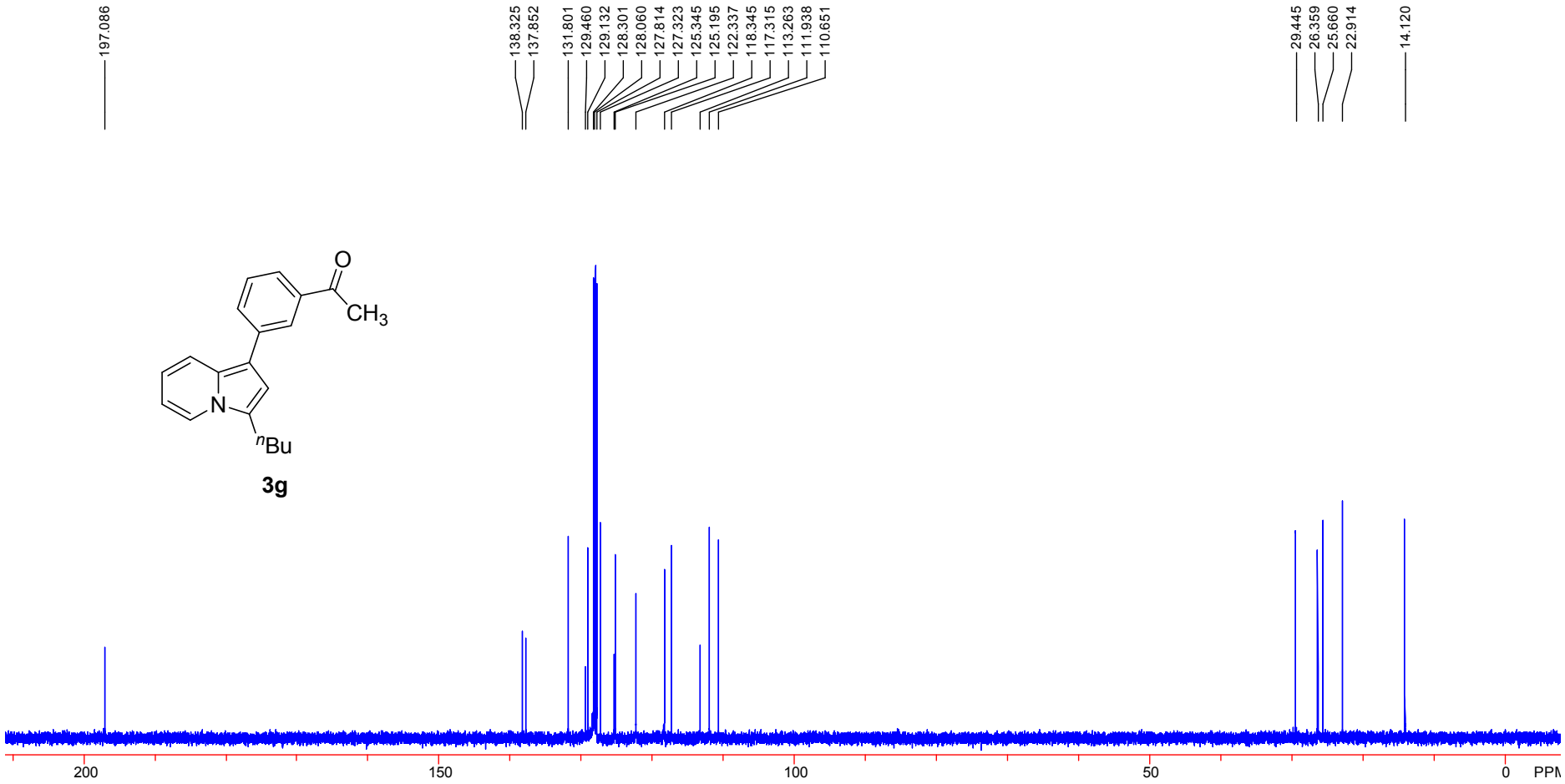
^{13}C NMR (100 MHz, C_6D_6)



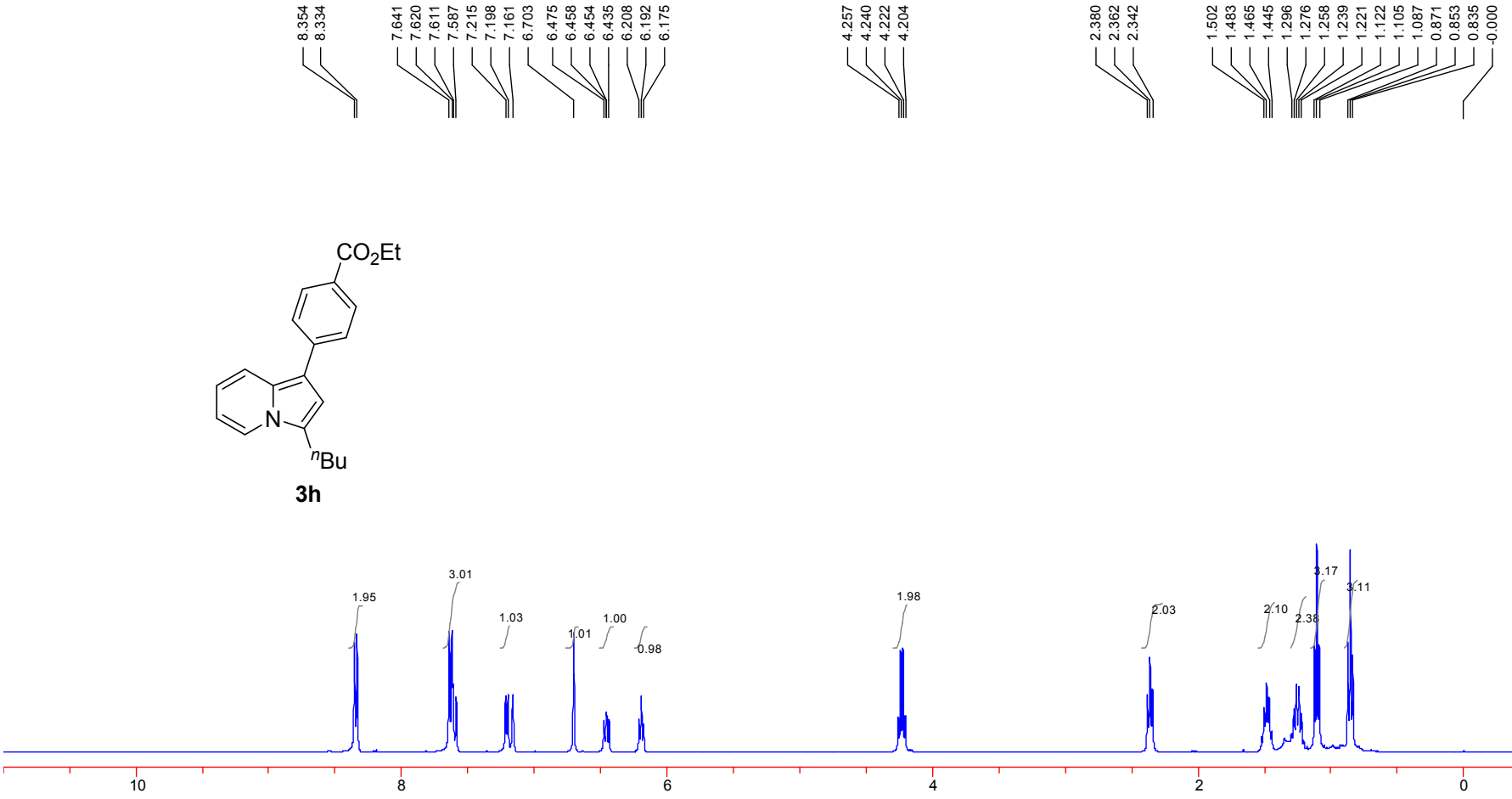
^{1}H NMR (400 MHz, C_6D_6)



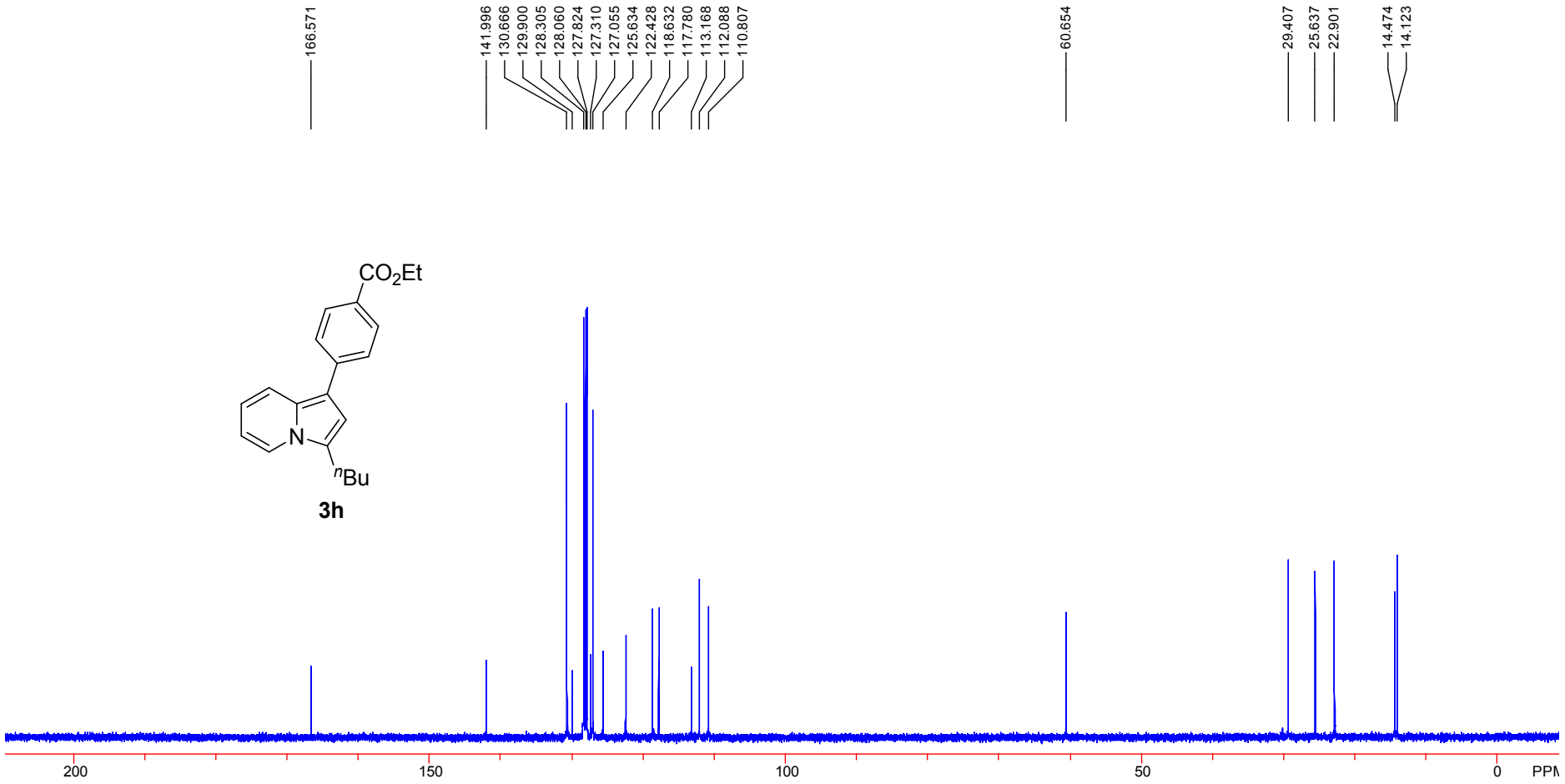
^{13}C NMR (100 MHz, C_6D_6)



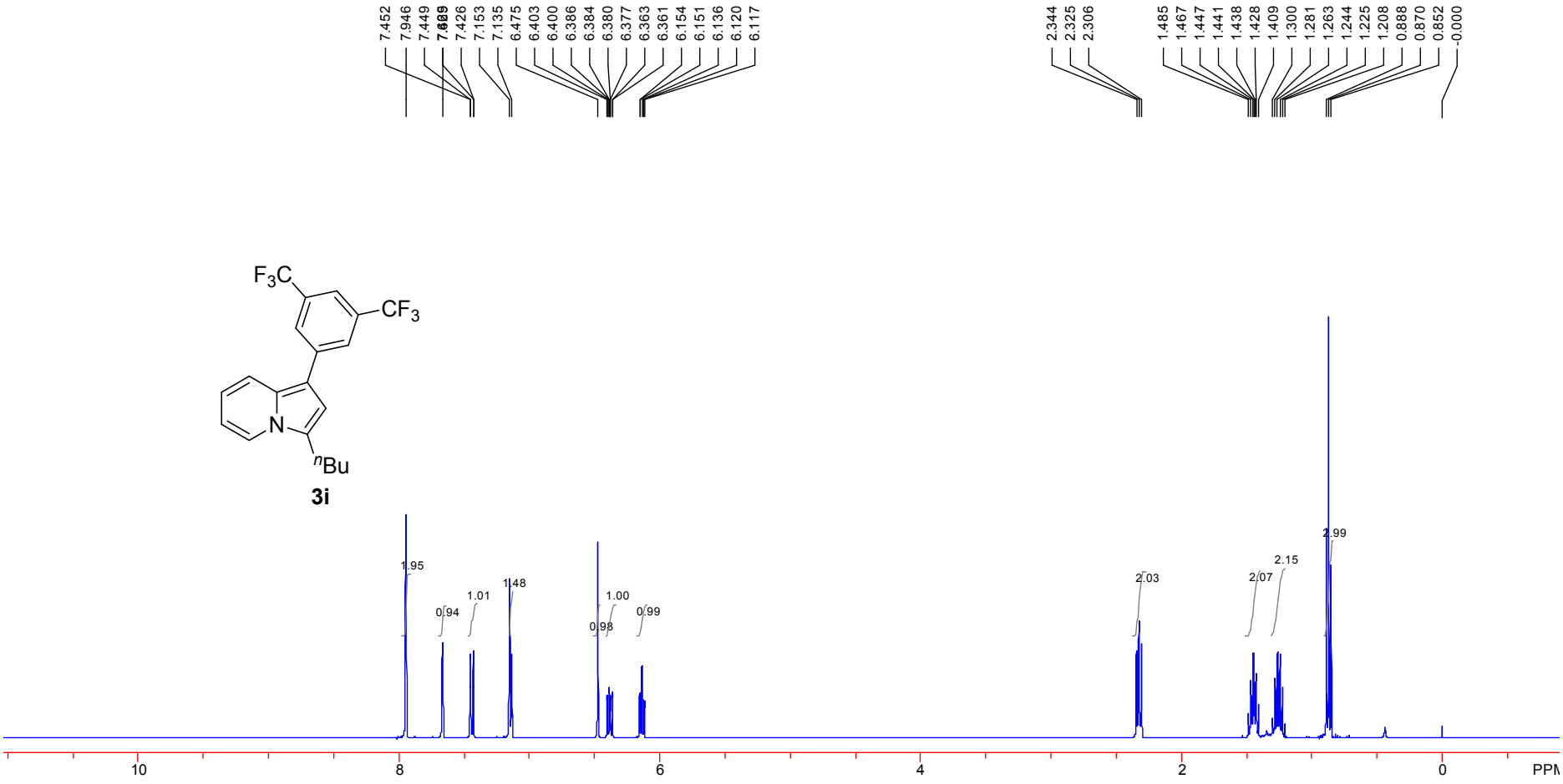
^{1}H NMR (400 MHz, C_6D_6)



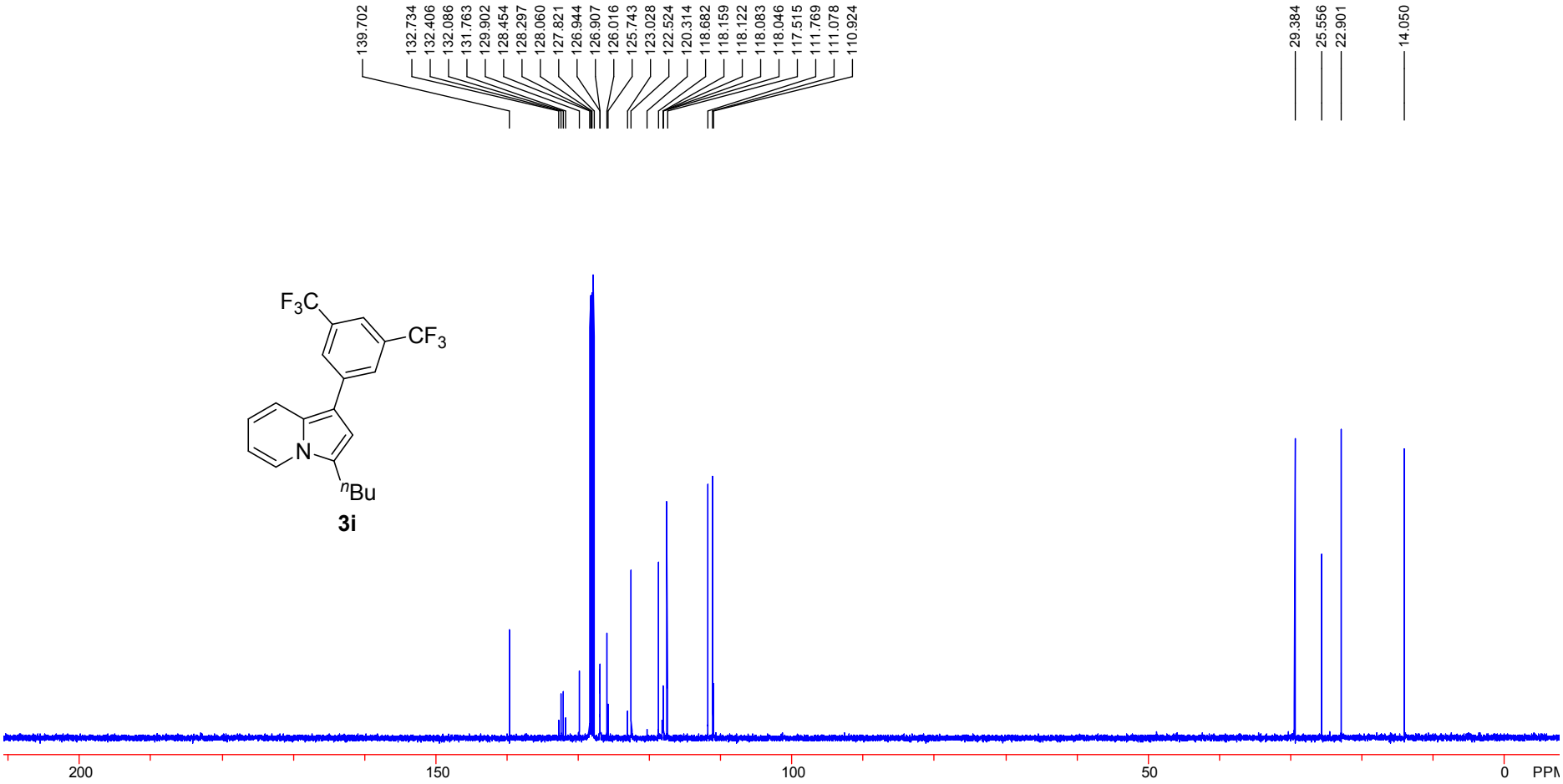
^{13}C NMR (100 MHz, C_6D_6)



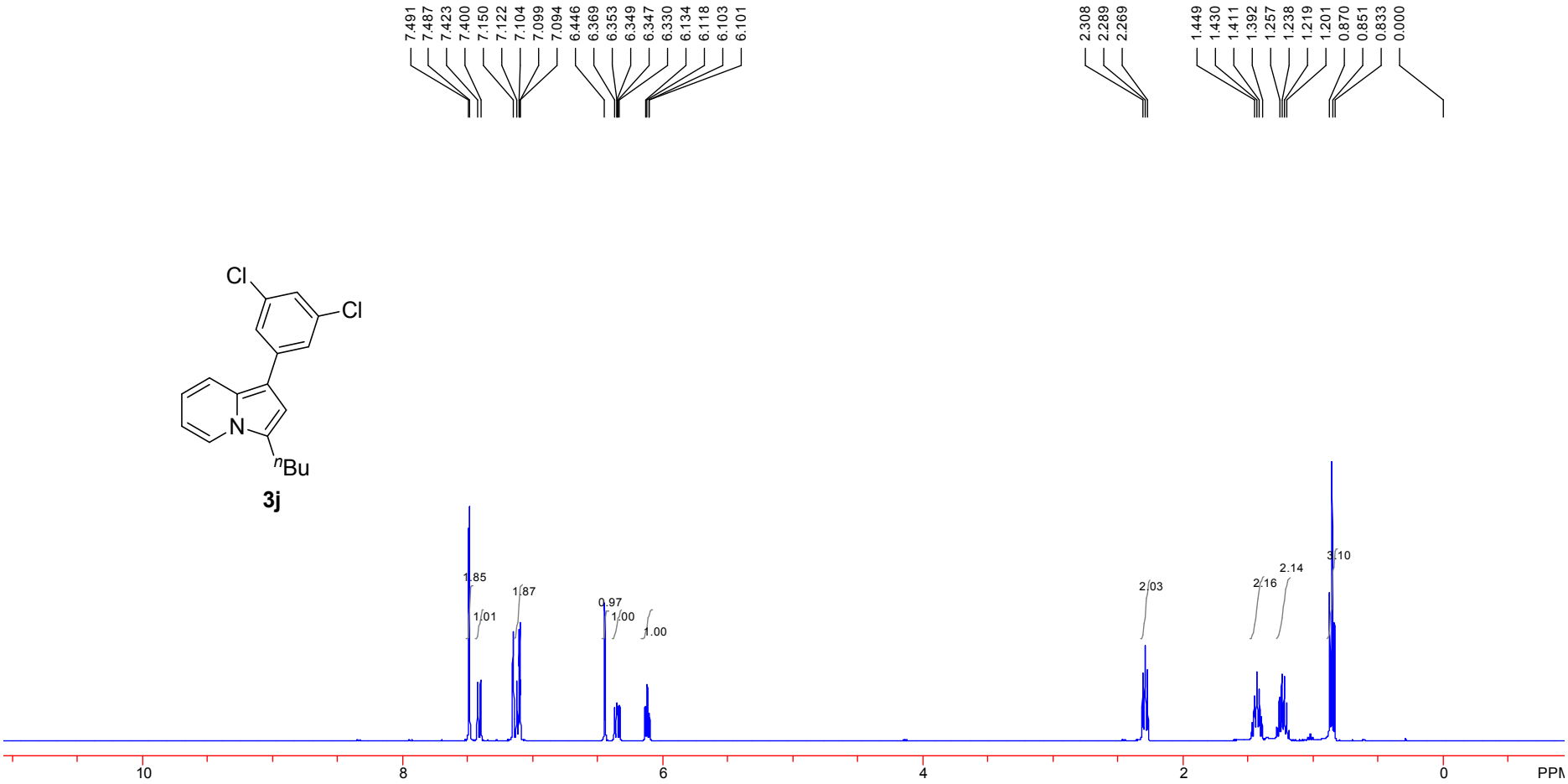
^{1}H NMR (400 MHz, C_6D_6)



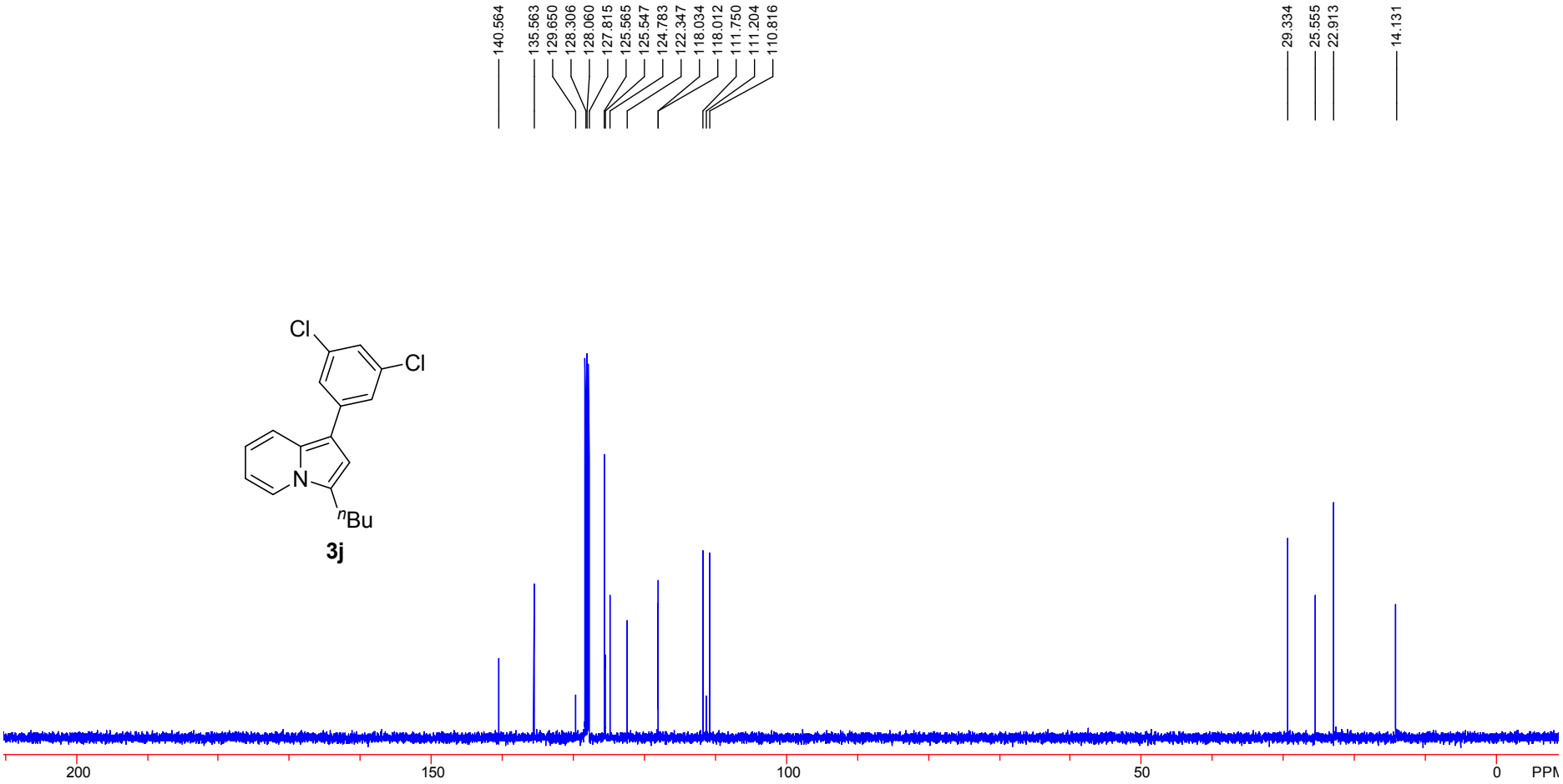
^{13}C NMR (100 MHz, C_6D_6)



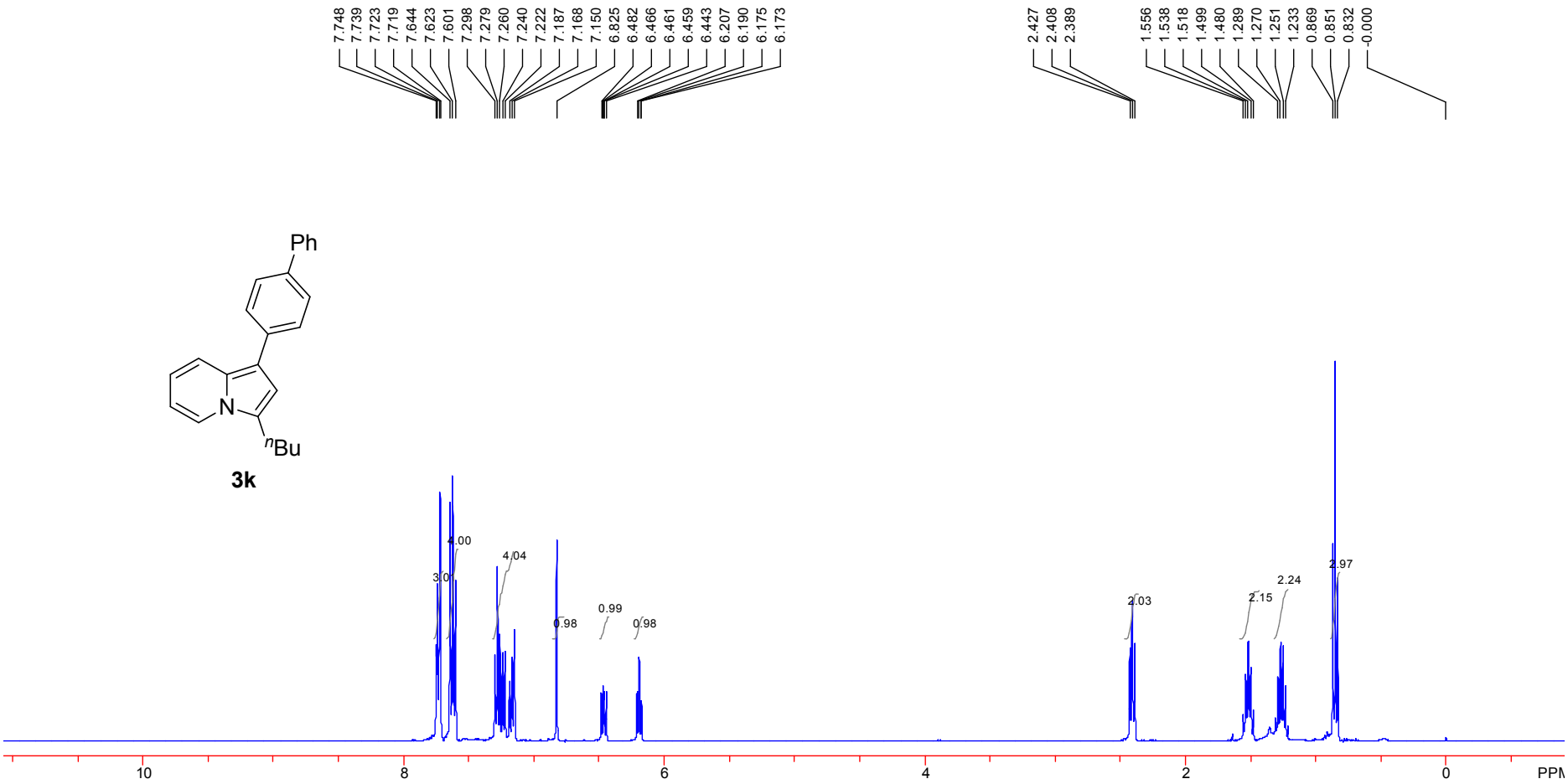
^{1}H NMR (400 MHz, C_6D_6)



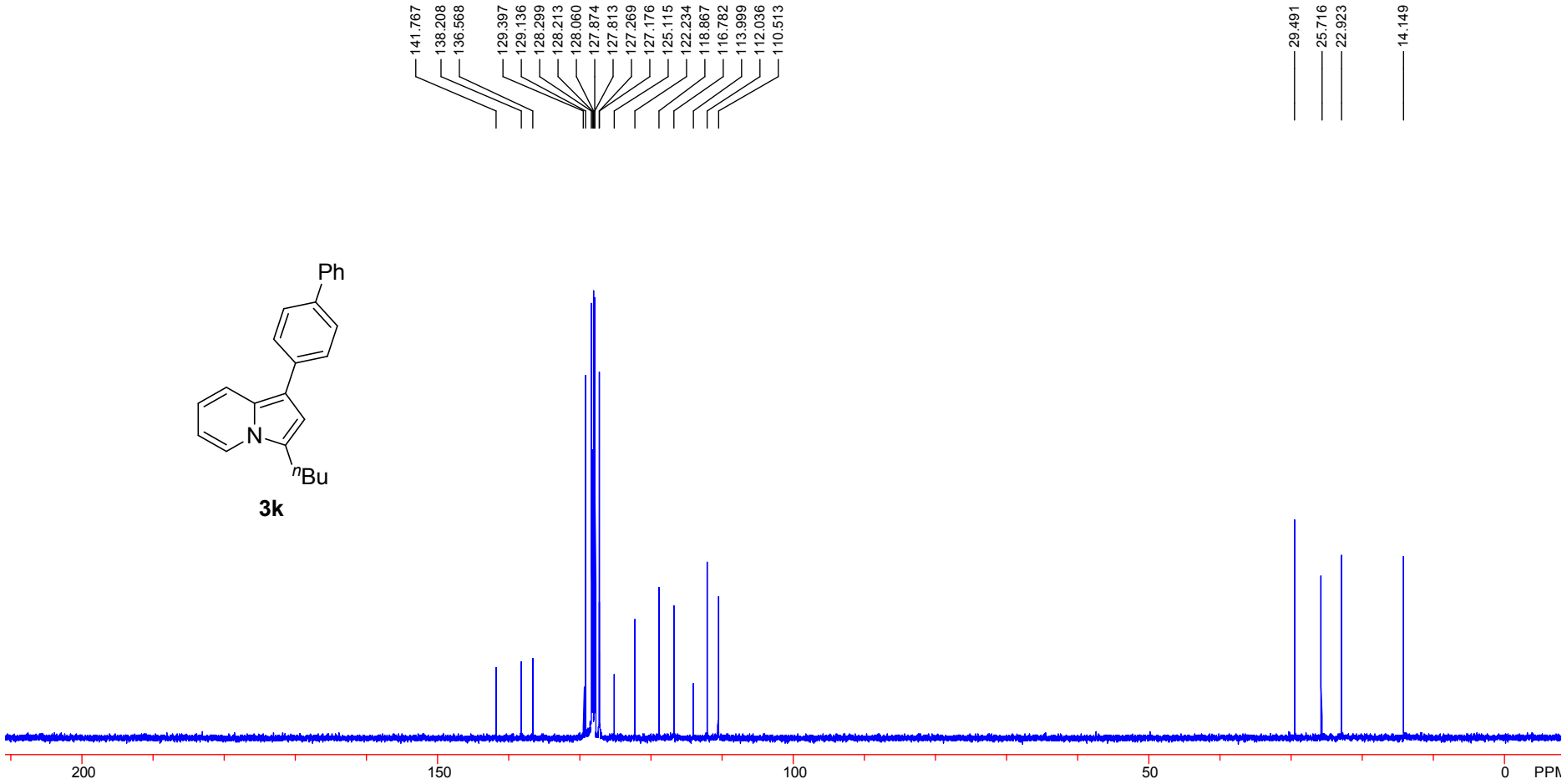
^{13}C NMR (100 MHz, C_6D_6)



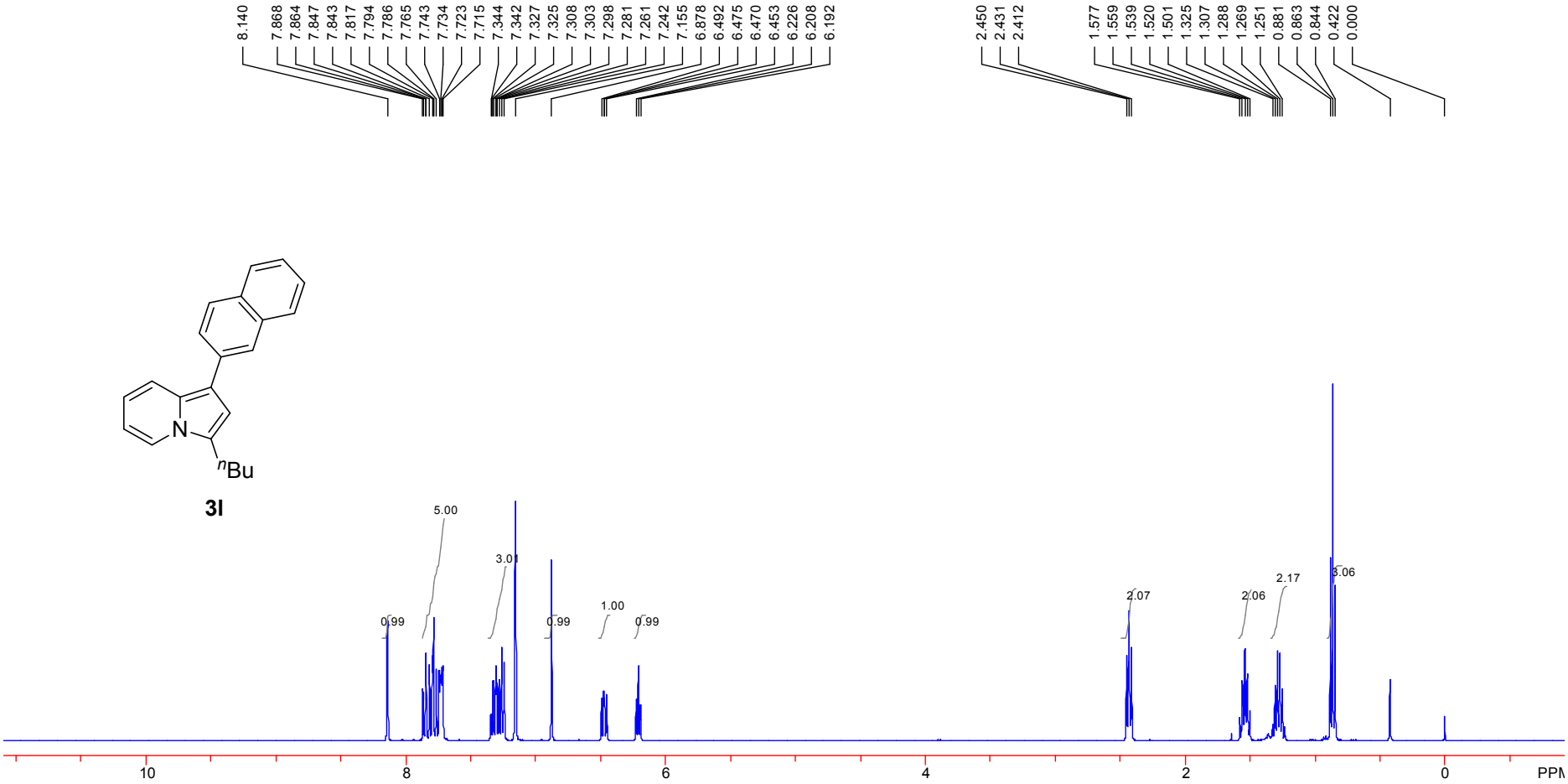
^{1}H NMR (400 MHz, C_6D_6)



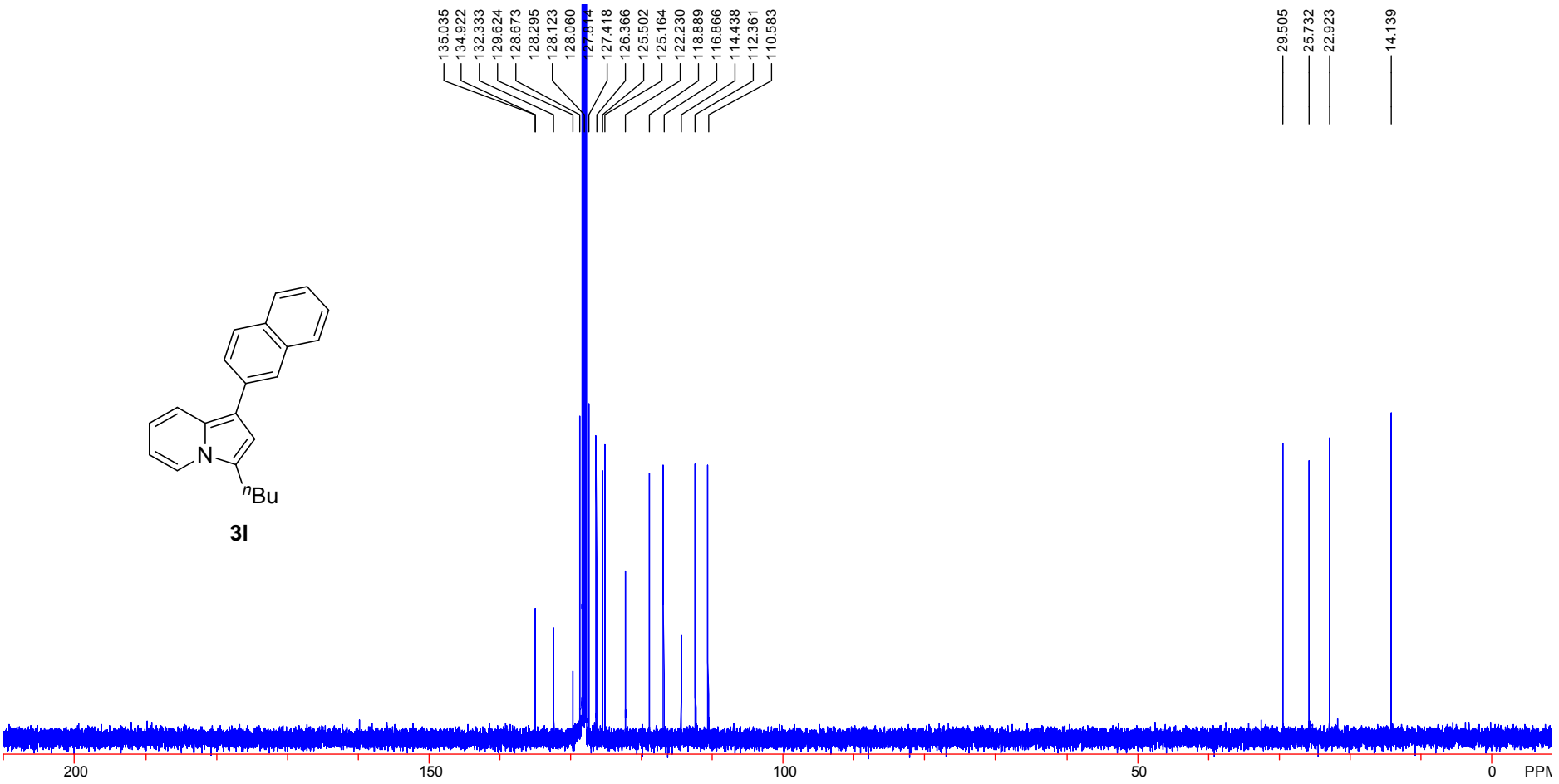
^{13}C NMR (100 MHz, C_6D_6)



^{1}H NMR (400 MHz, C_6D_6)

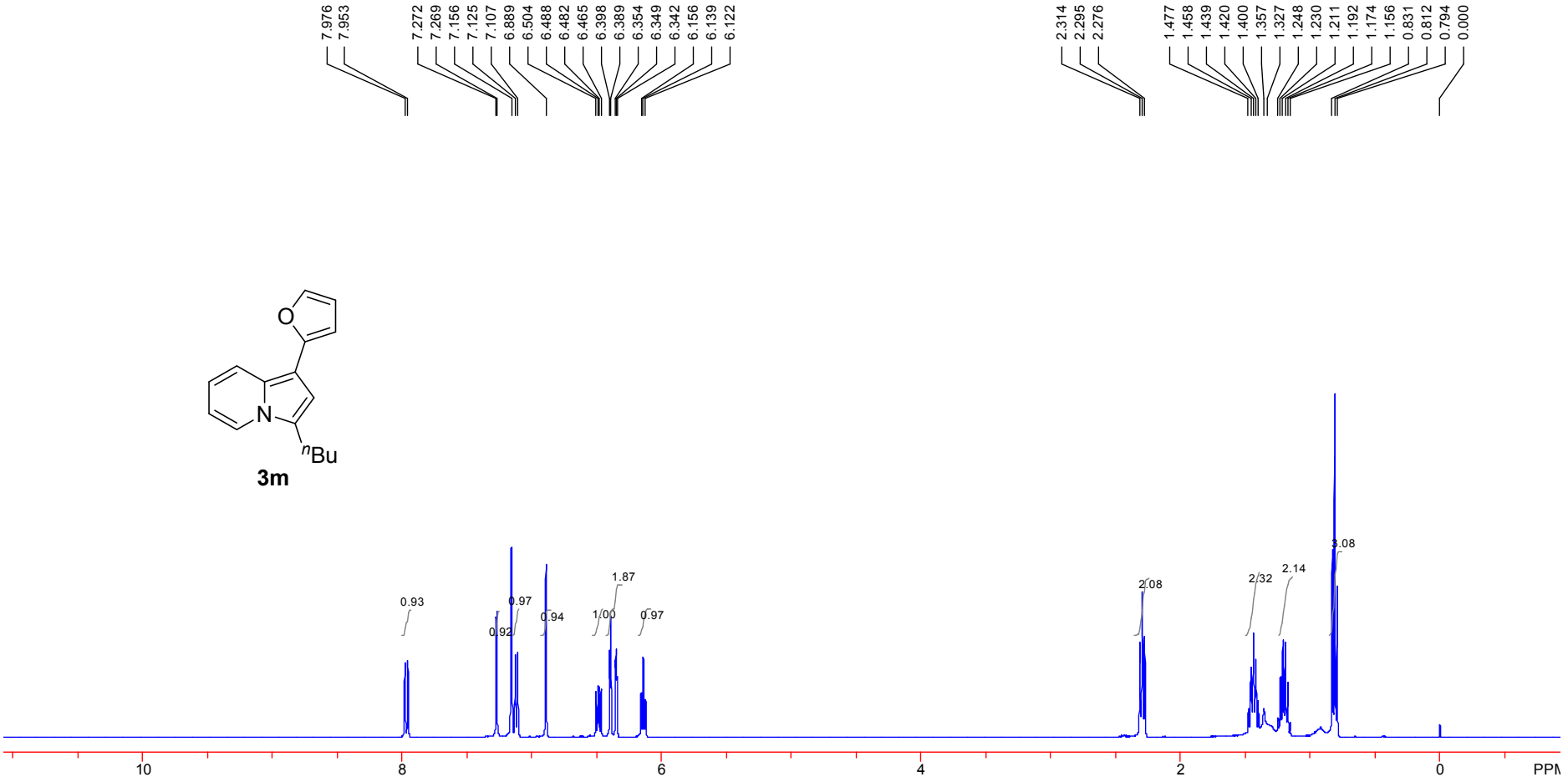


^{13}C NMR (100 MHz, C_6D_6)

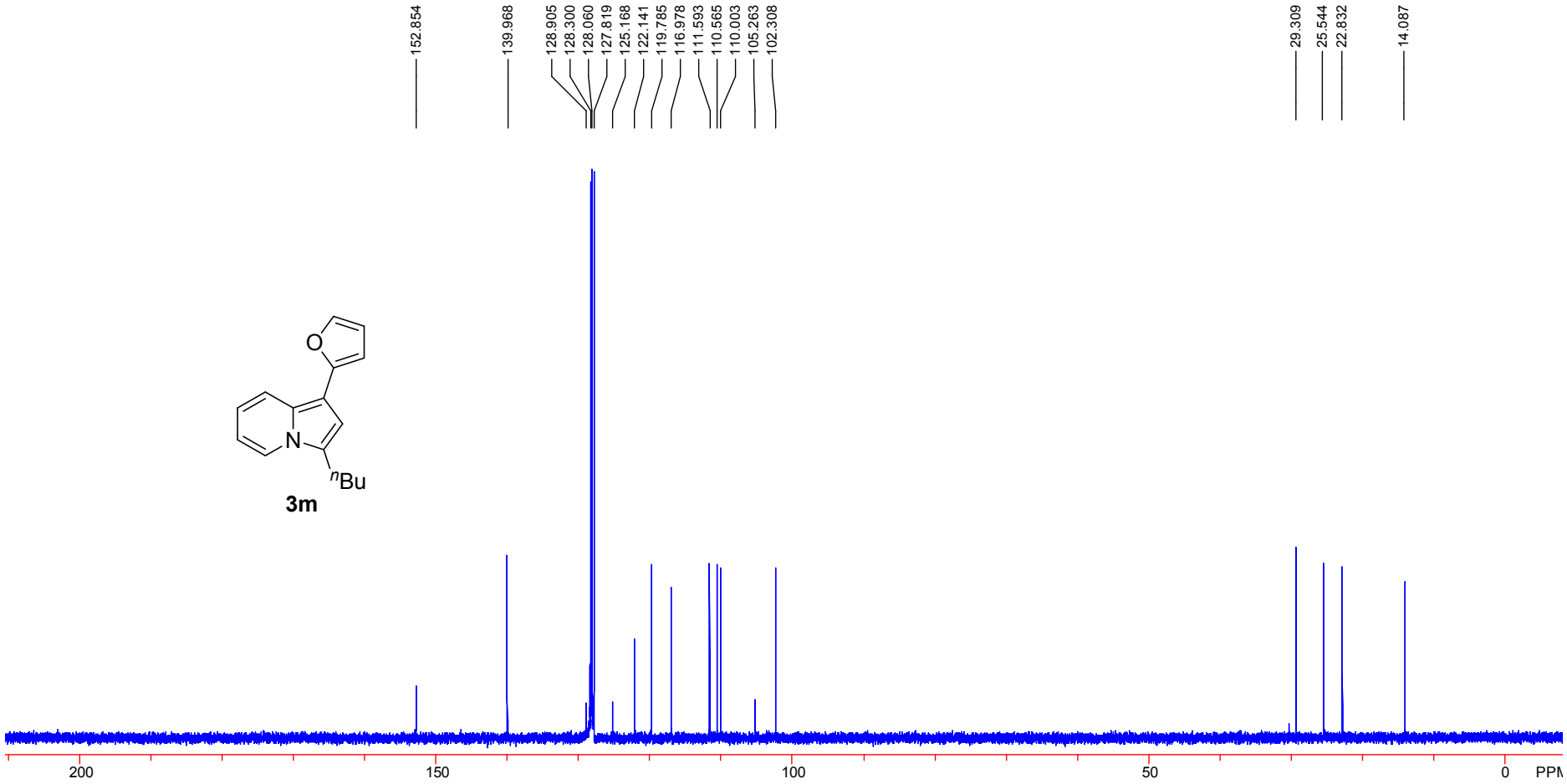


3l

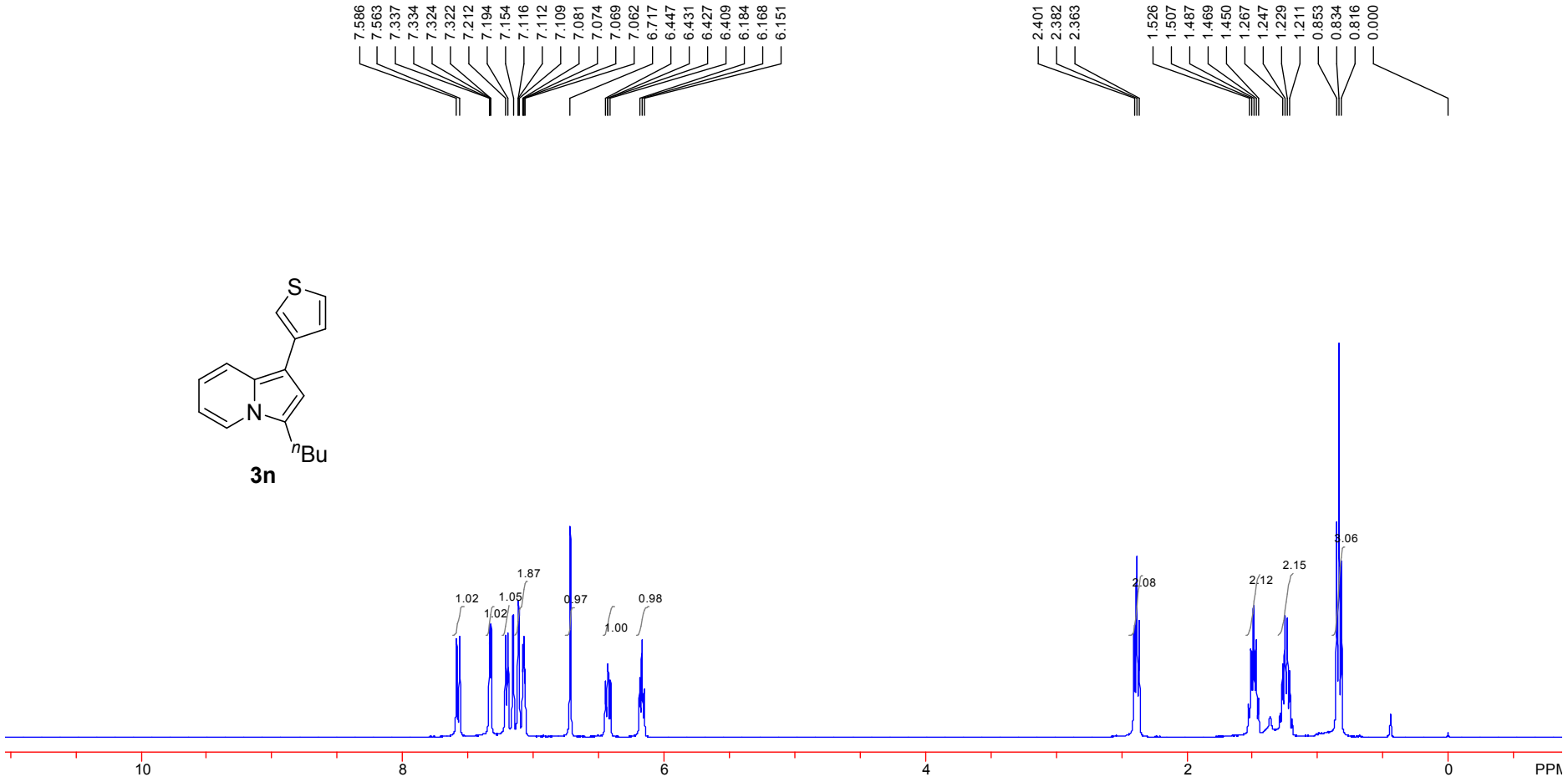
^{1}H NMR (400 MHz, C_6D_6)



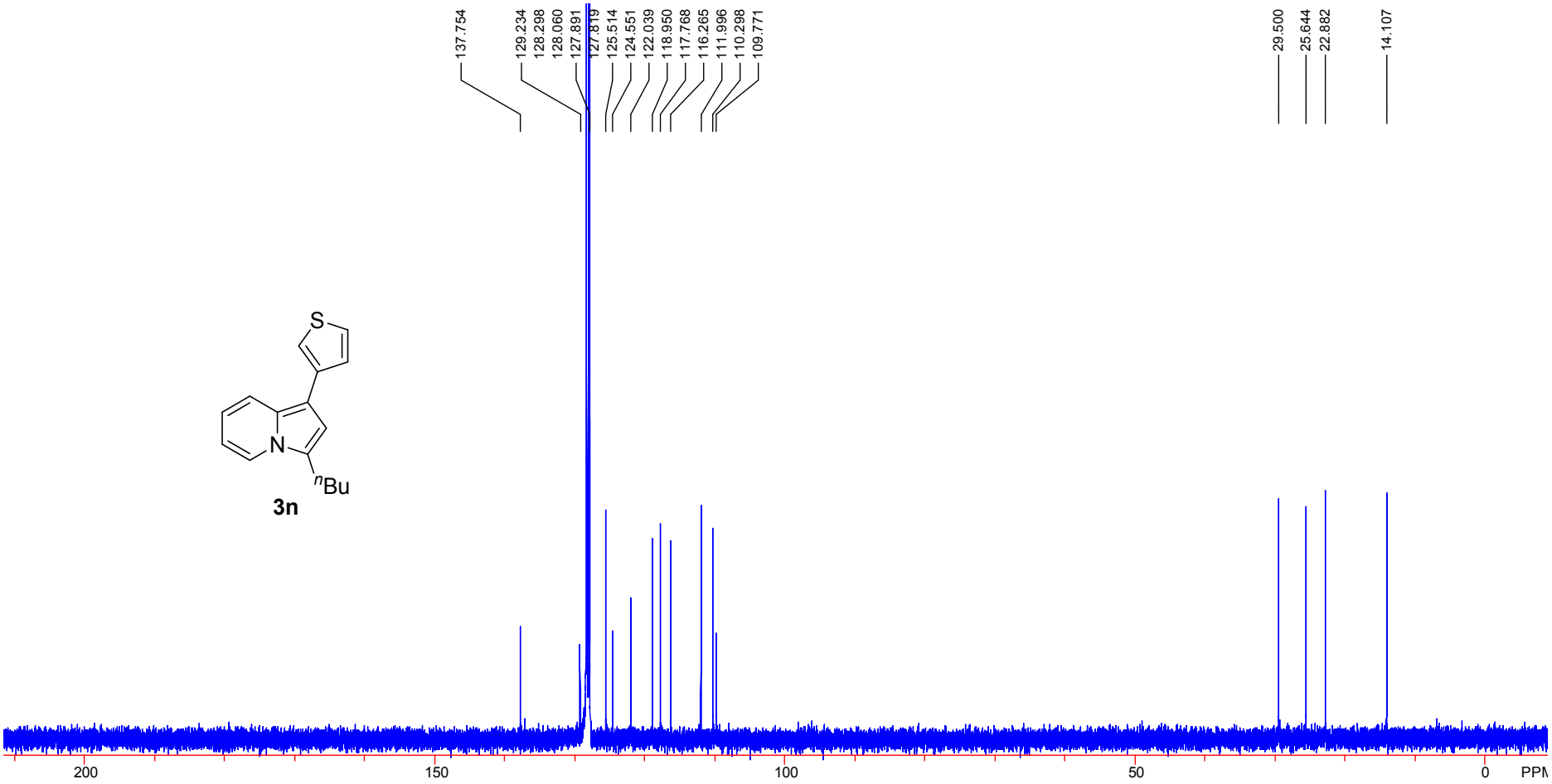
^{13}C NMR (100 MHz, C_6D_6)



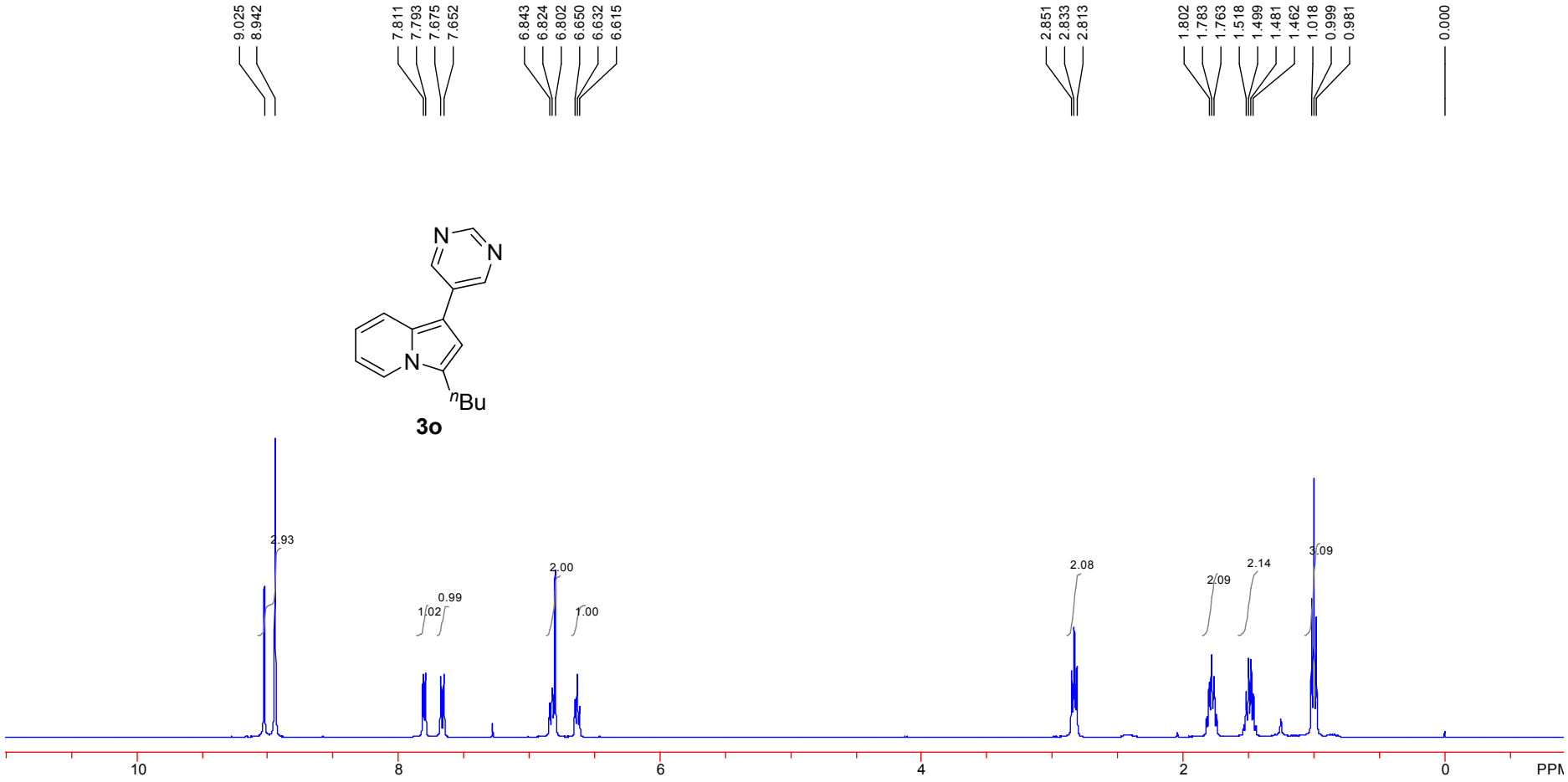
^{1}H NMR (400 MHz, C_6D_6)



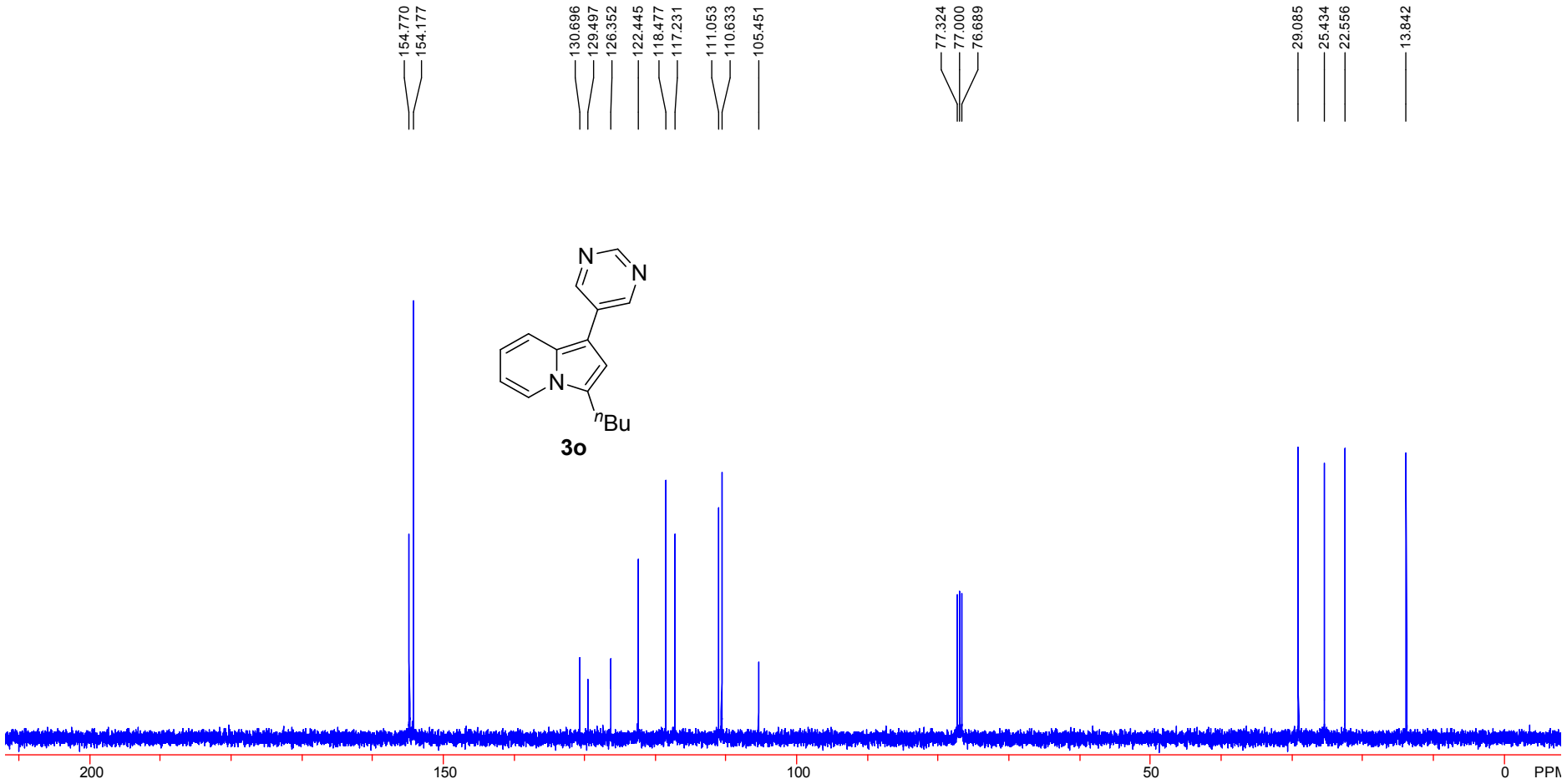
^{13}C NMR (100 MHz, C_6D_6)



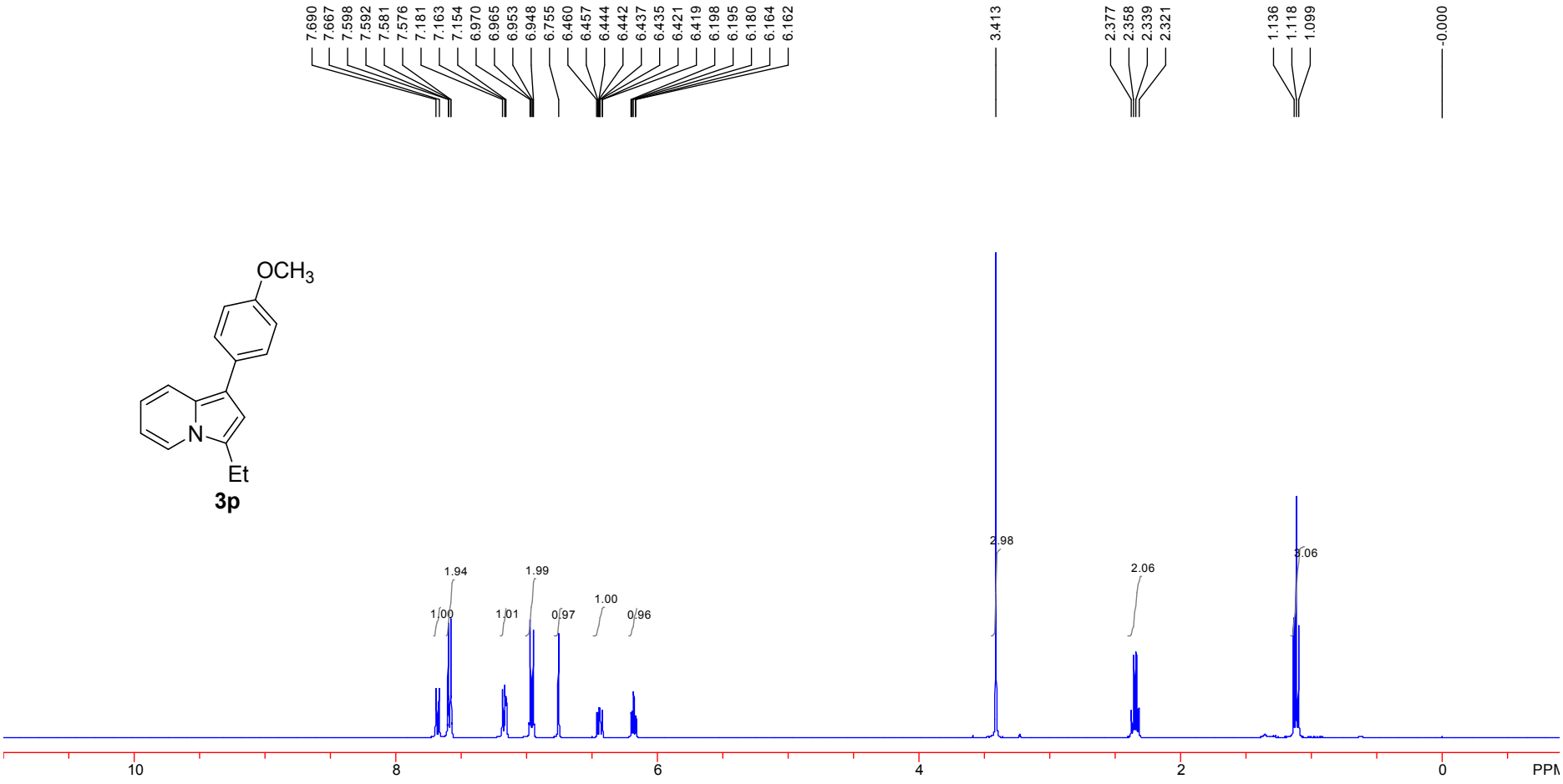
^{1}H NMR (400 MHz, $CDCl_3$)



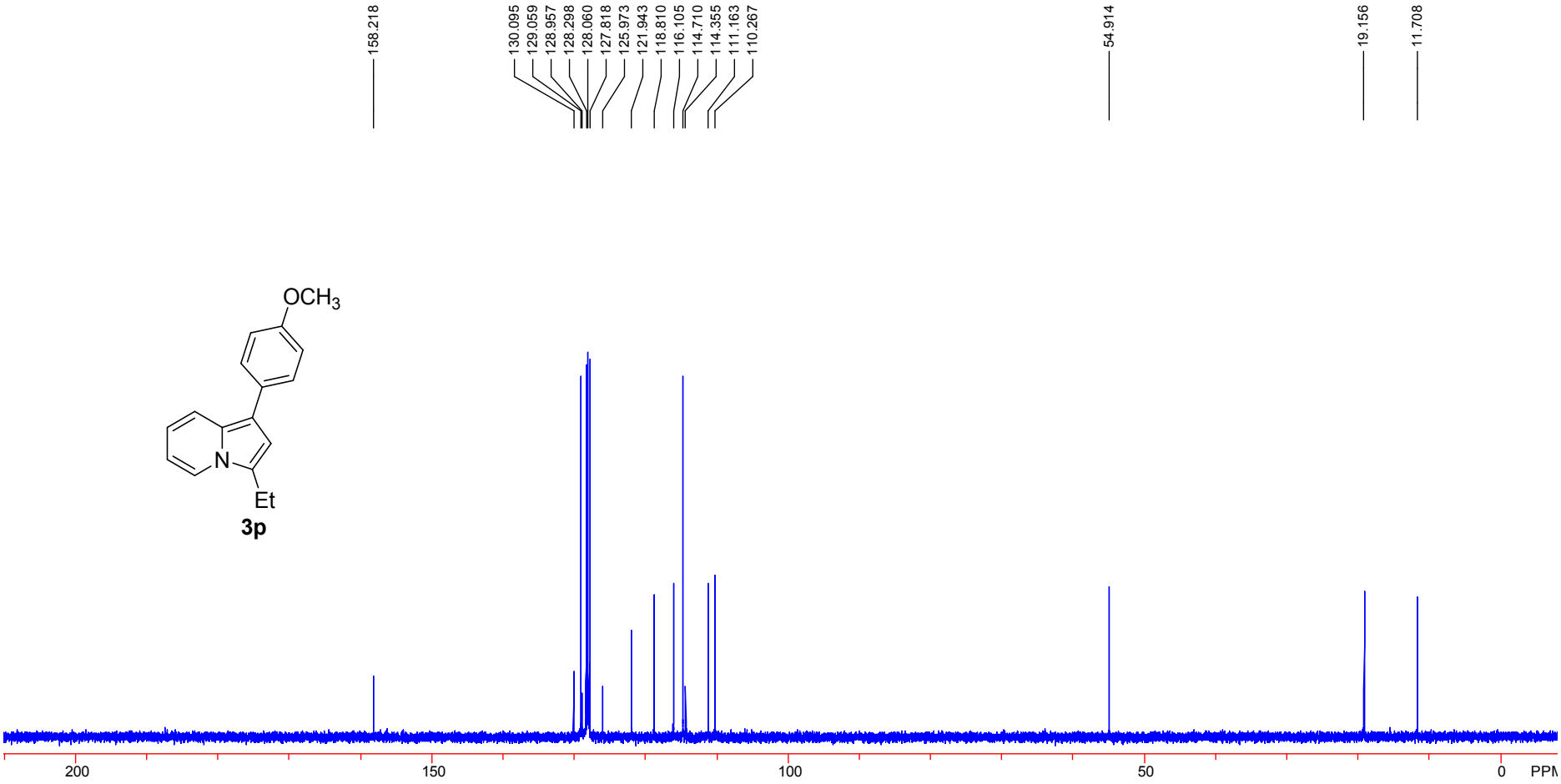
^{13}C NMR (100 MHz, $CDCl_3$)



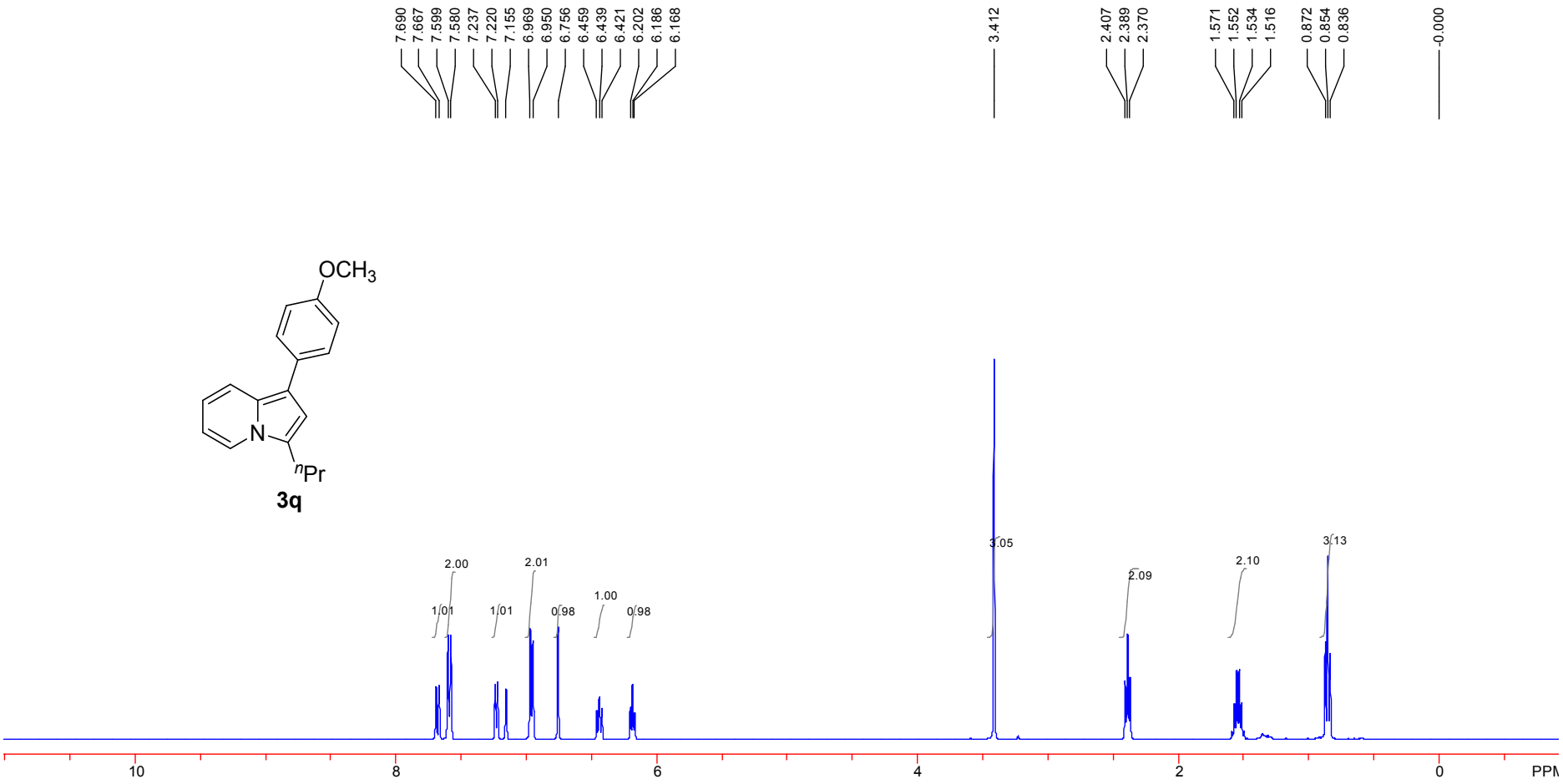
^{1}H NMR (400 MHz, C_6D_6)



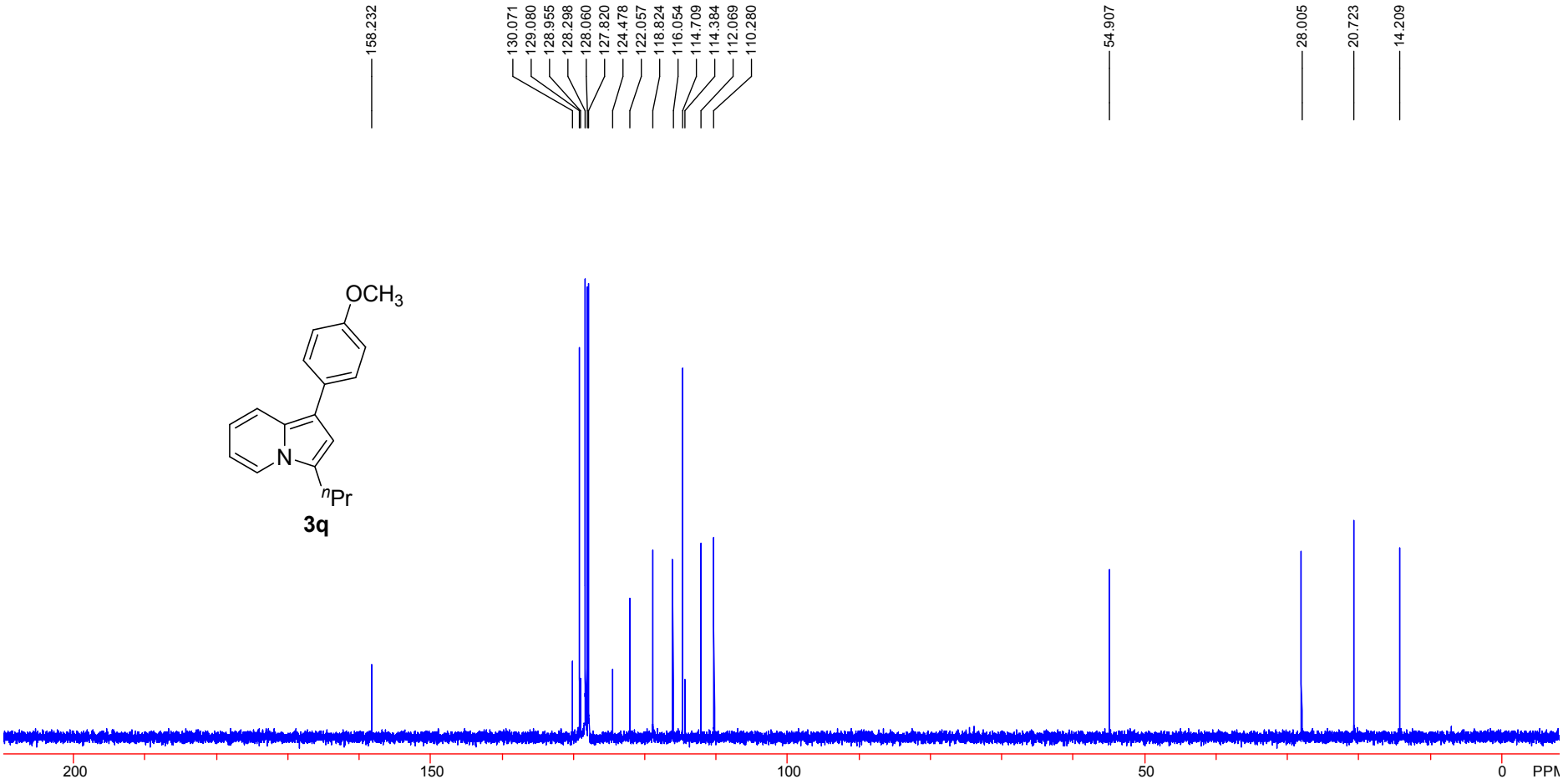
^{13}C NMR (100 MHz, C_6D_6)



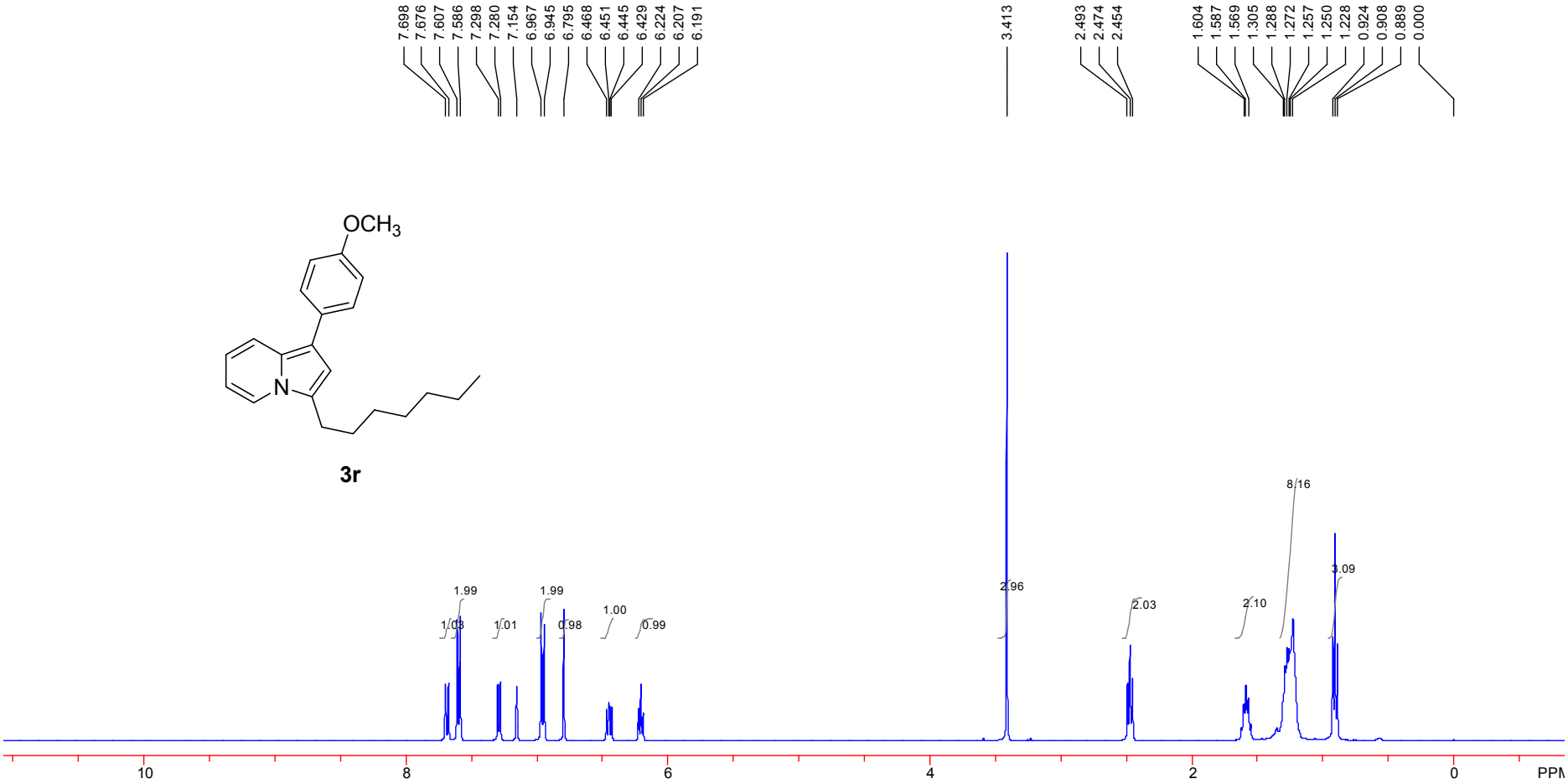
^{1}H NMR (400 MHz, C_6D_6)



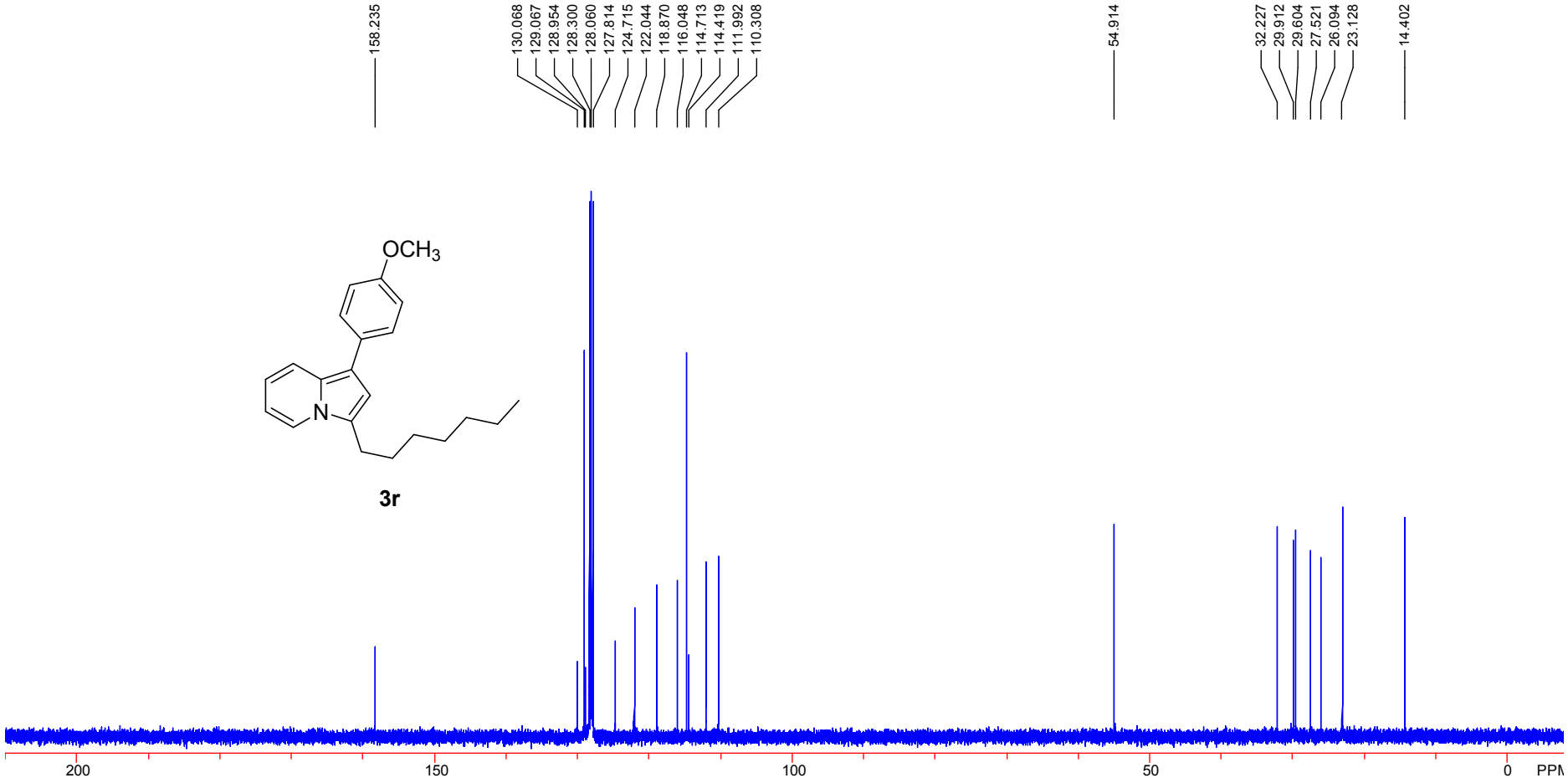
^{13}C NMR (100 MHz, C_6D_6)



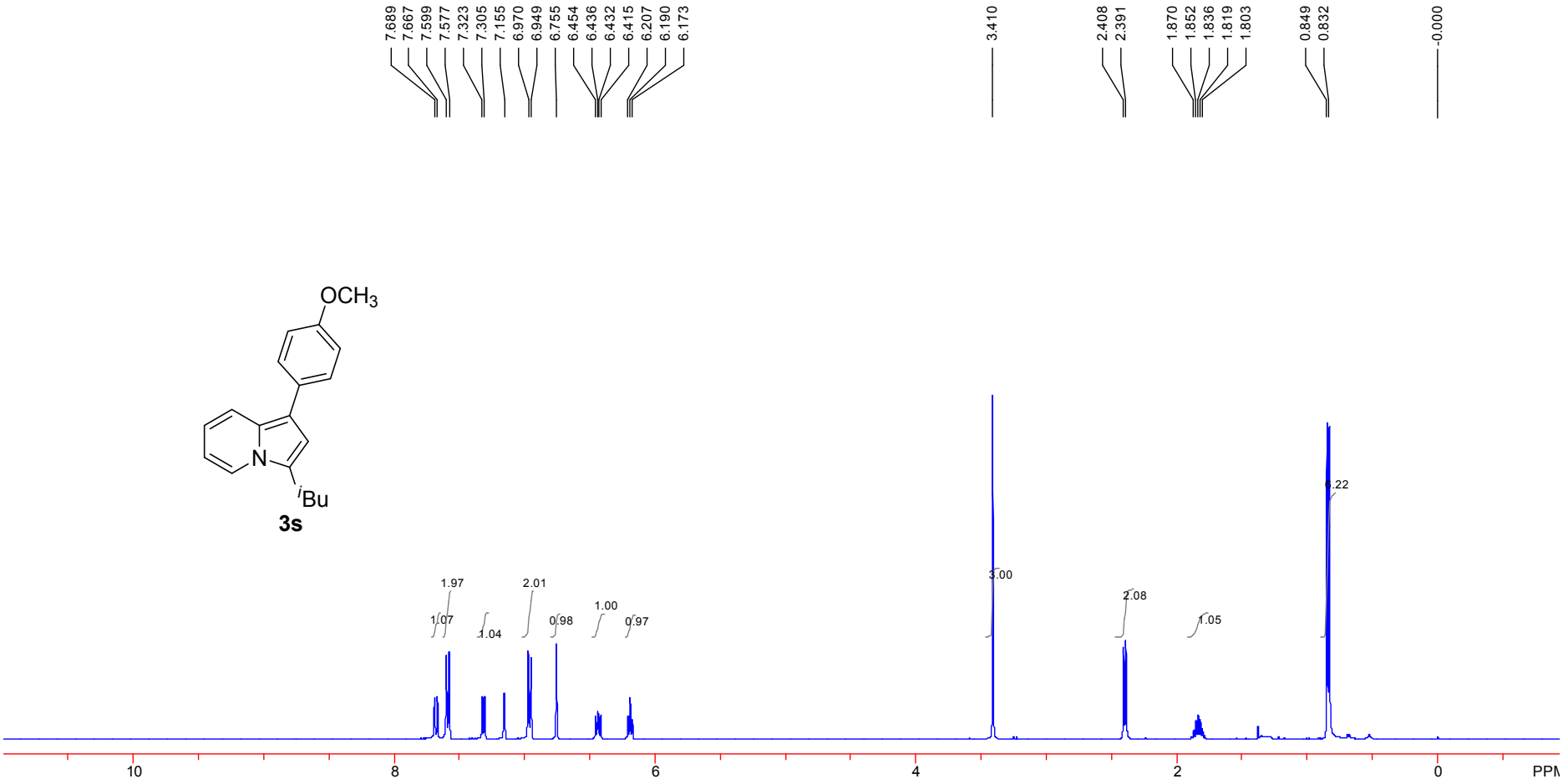
^{1}H NMR (400 MHz, C_6D_6)



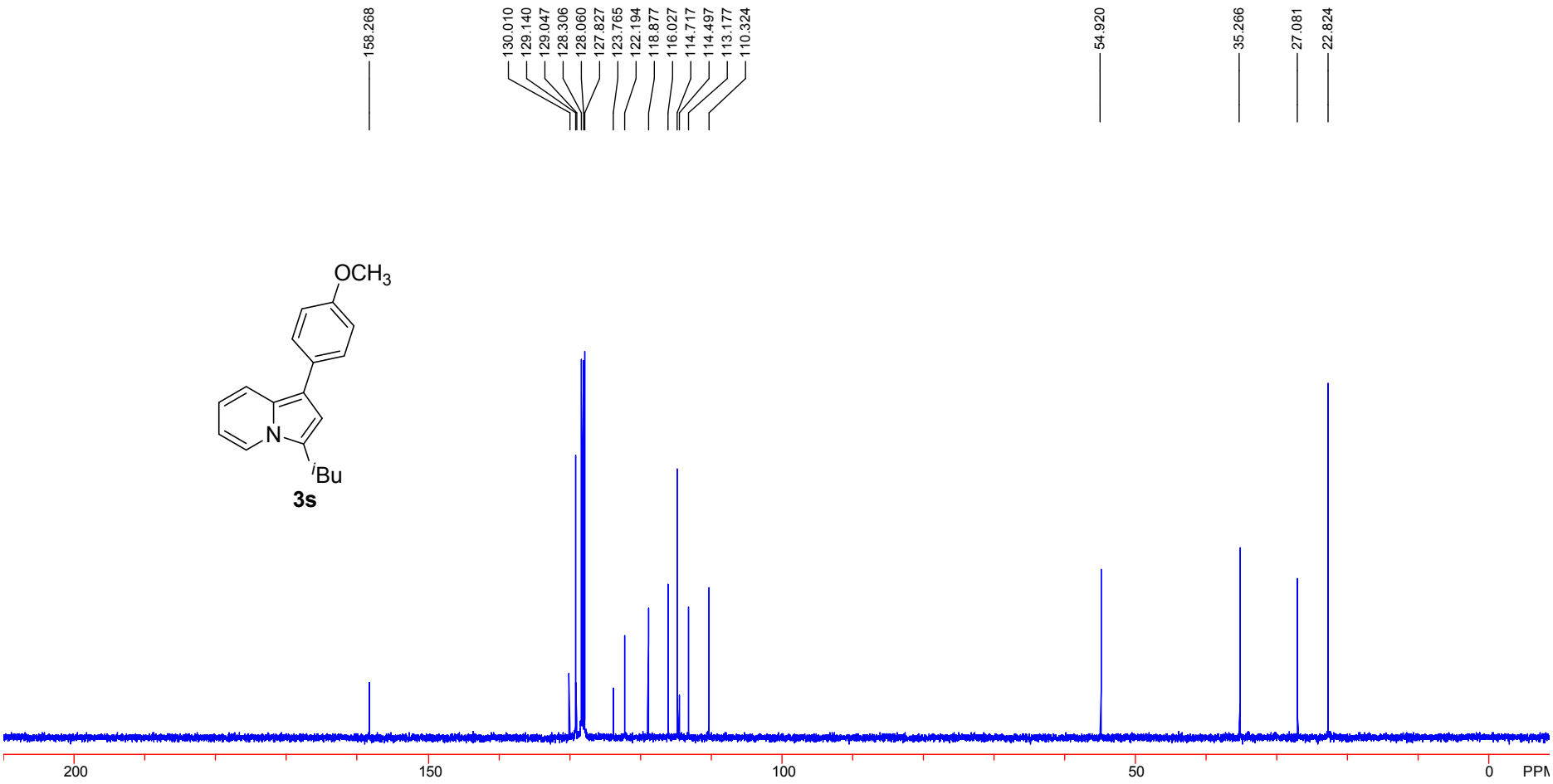
^{13}C NMR (100 MHz, C_6D_6)



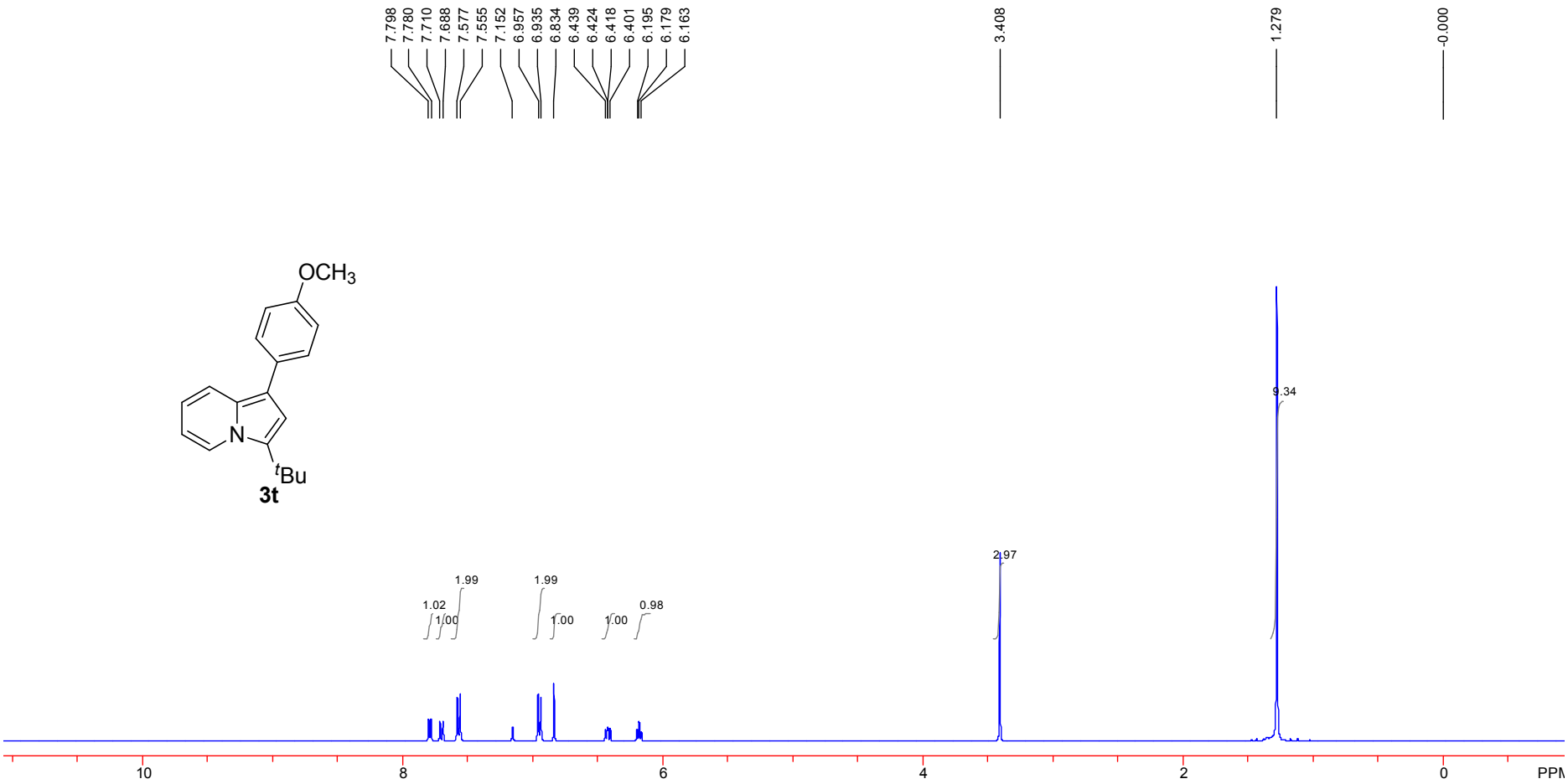
^{1}H NMR (400 MHz, C_6D_6)



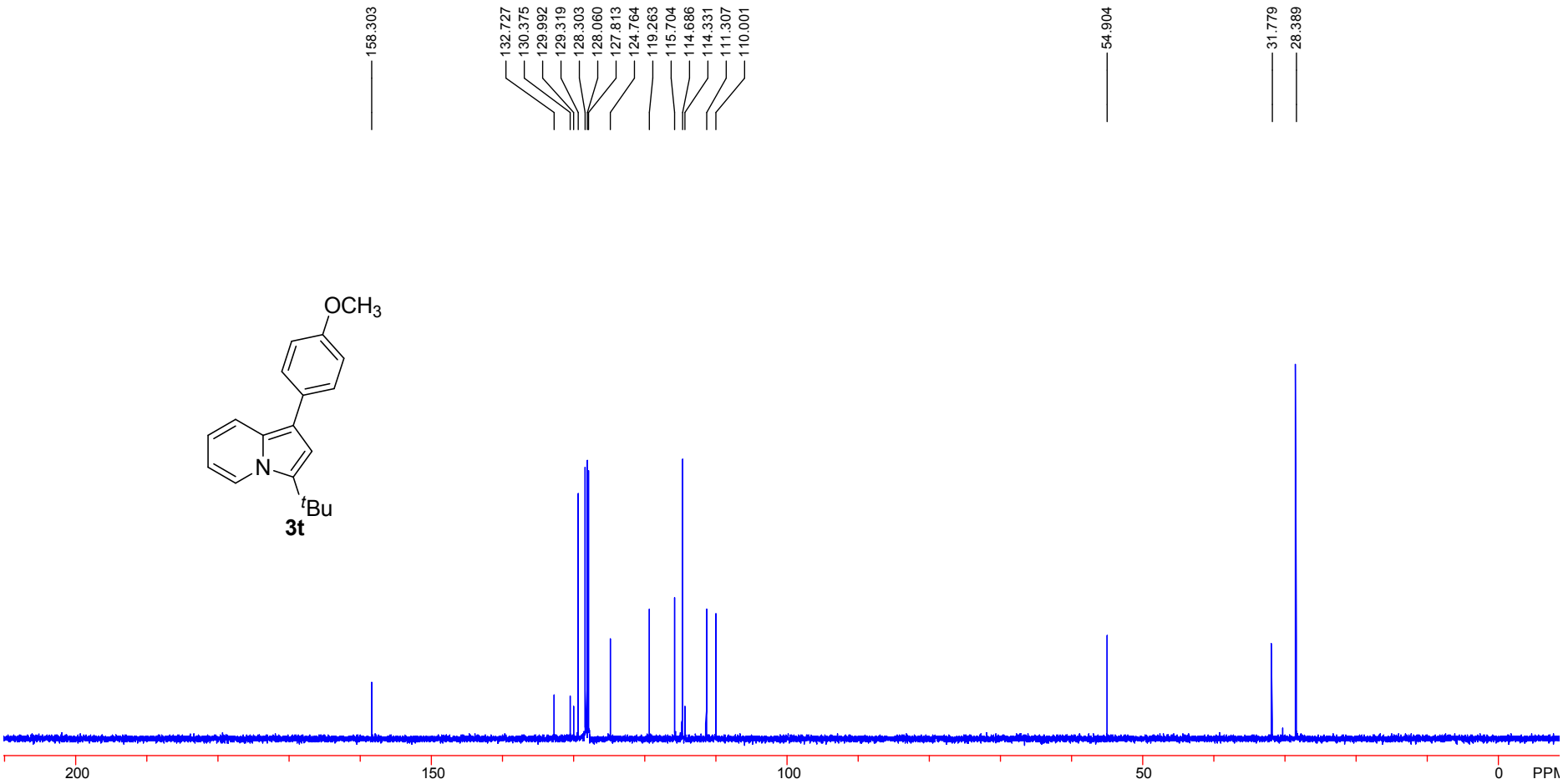
^{13}C NMR (100 MHz, C_6D_6)



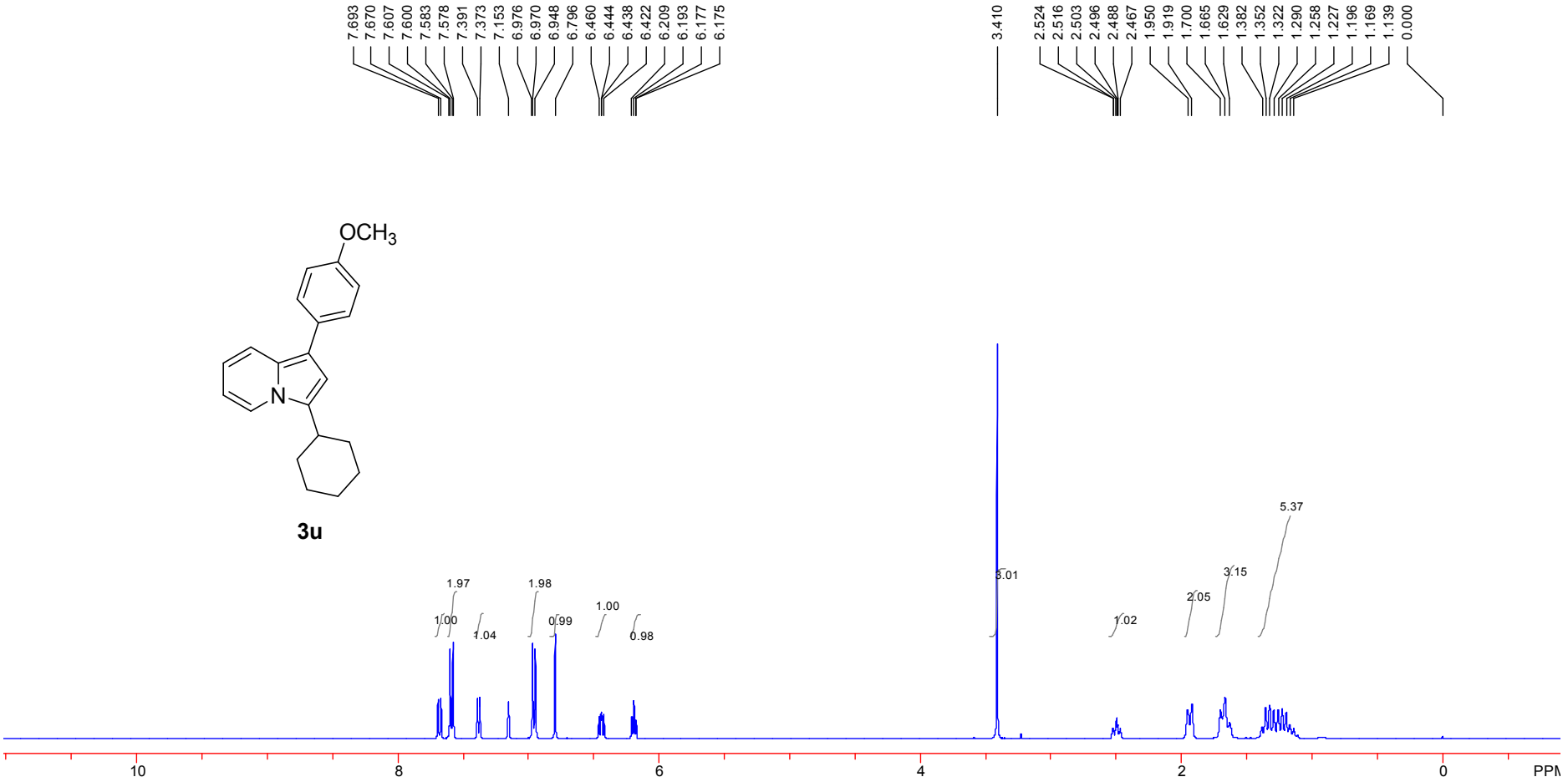
^{1}H NMR (400 MHz, C_6D_6)



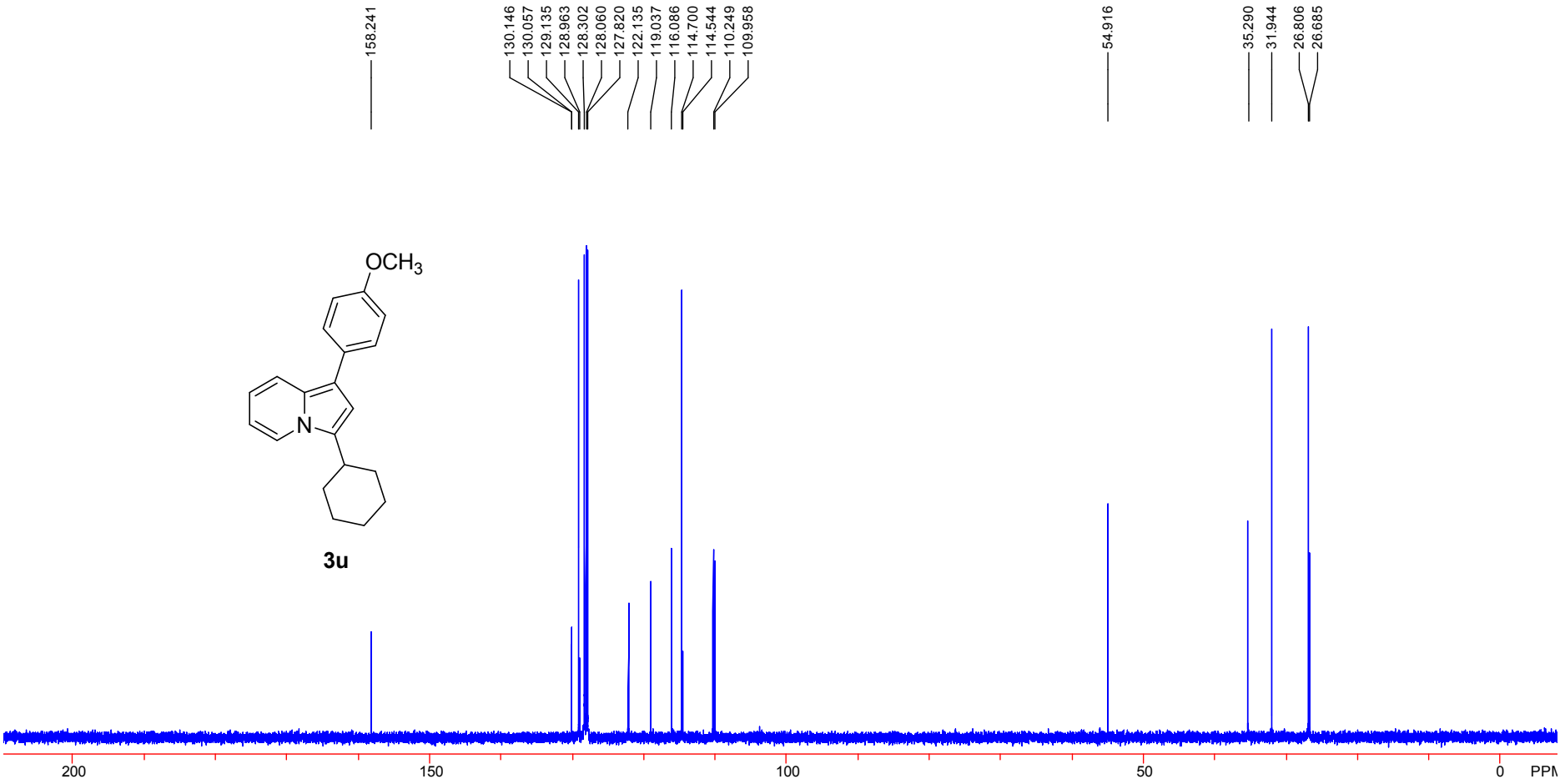
^{13}C NMR (100 MHz, C_6D_6)



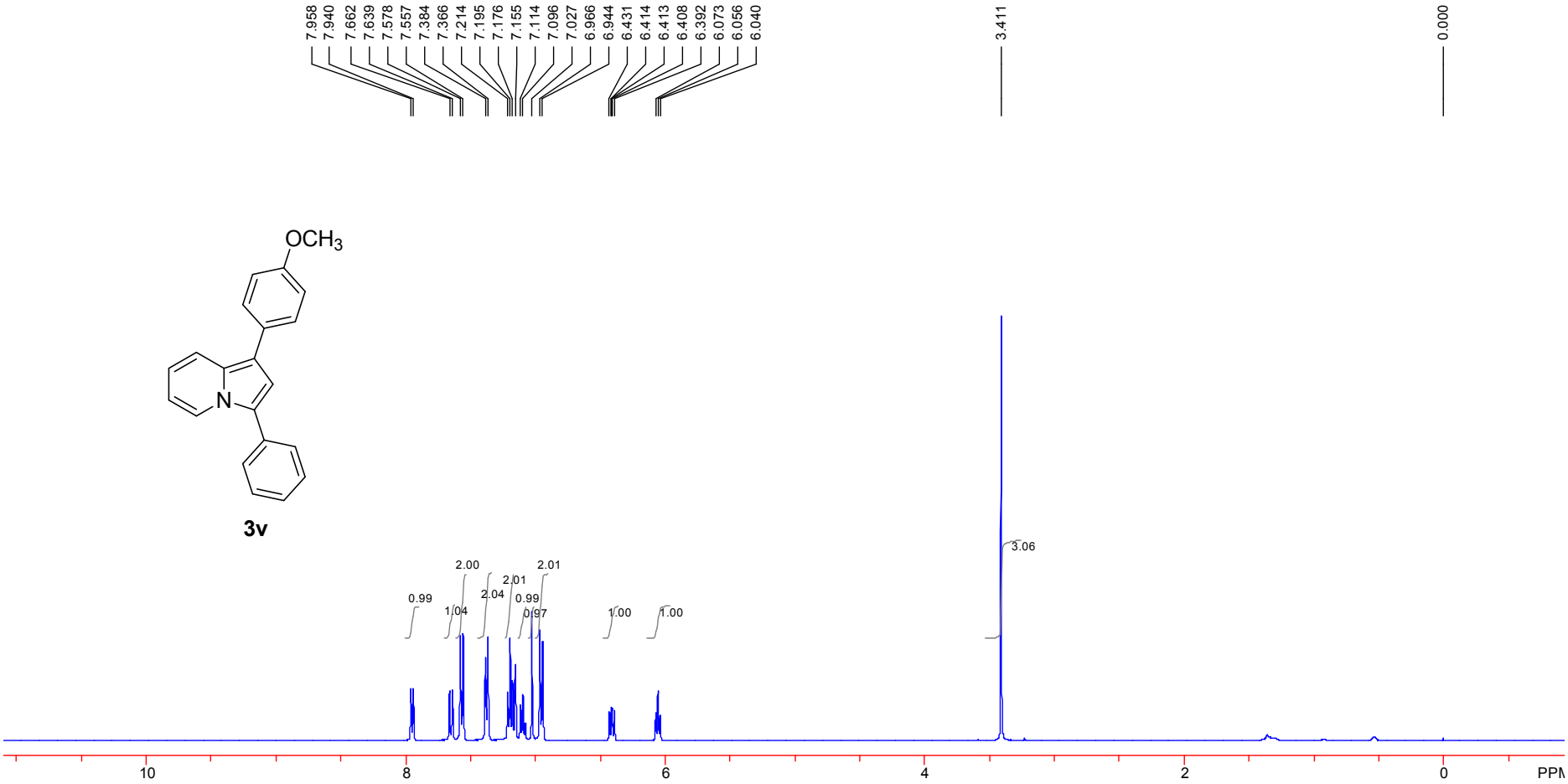
^{1}H NMR (400 MHz, C_6D_6)



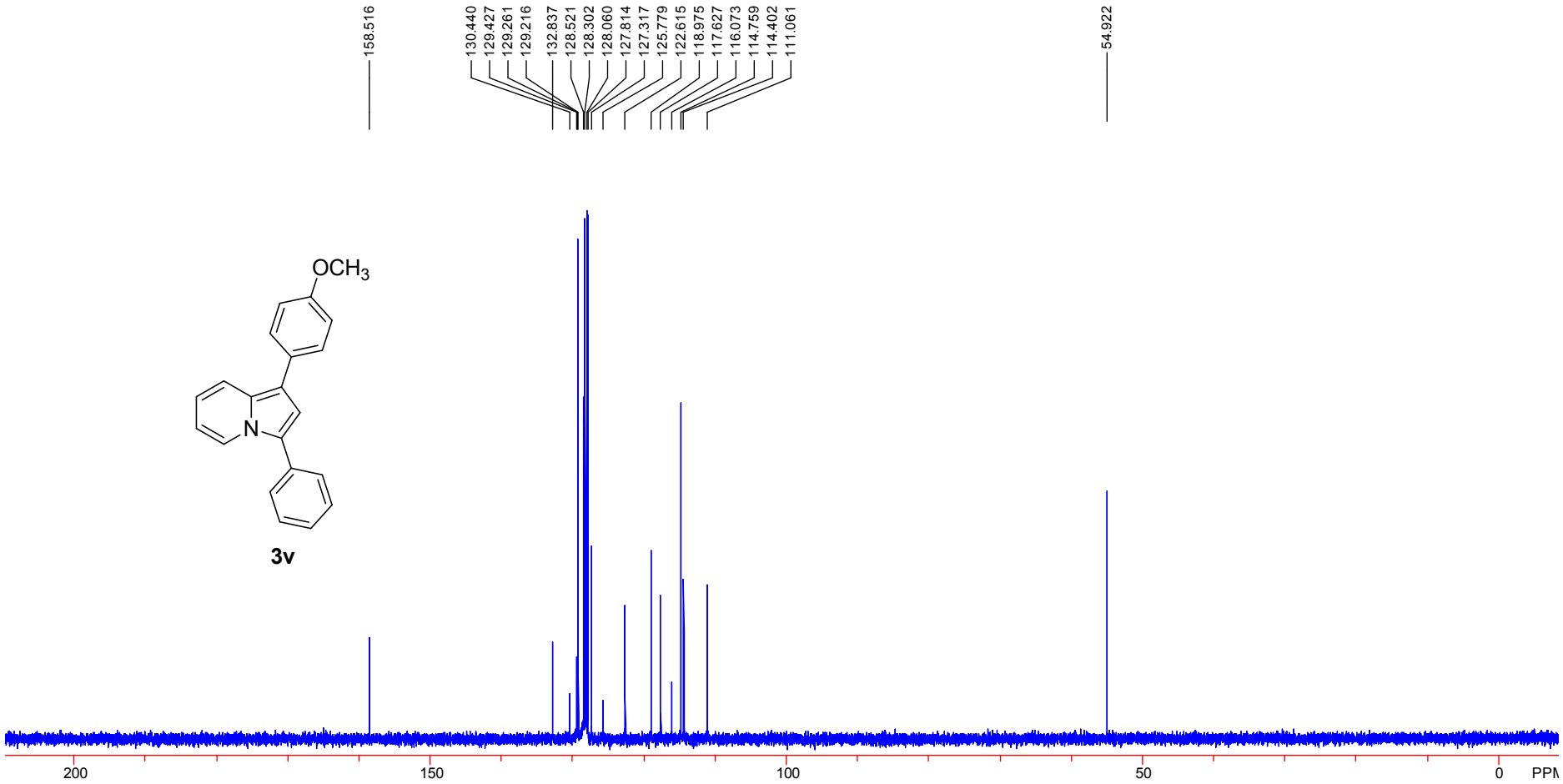
^{13}C NMR (100 MHz, C_6D_6)



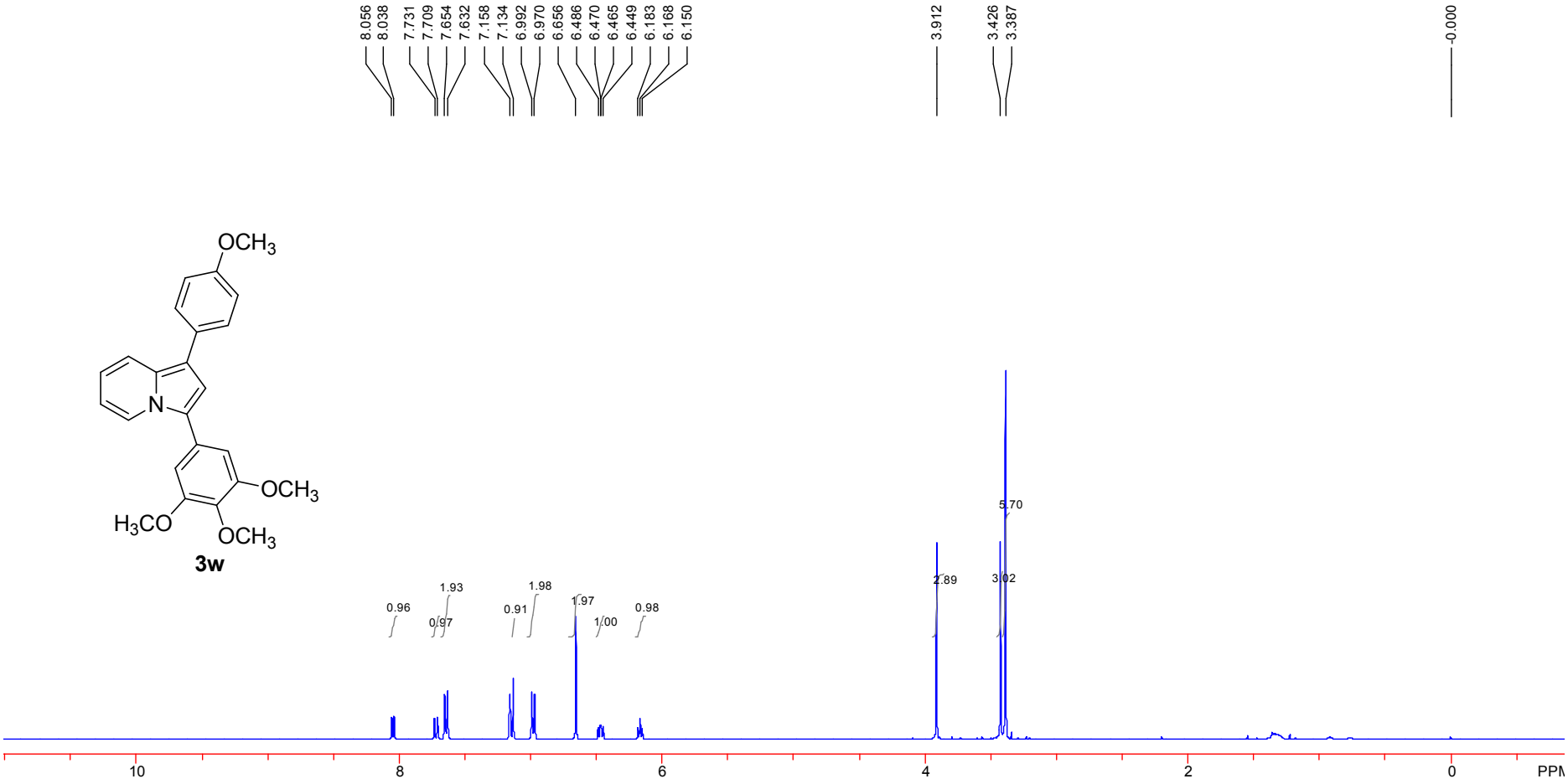
^{1}H NMR (400 MHz, C_6D_6)



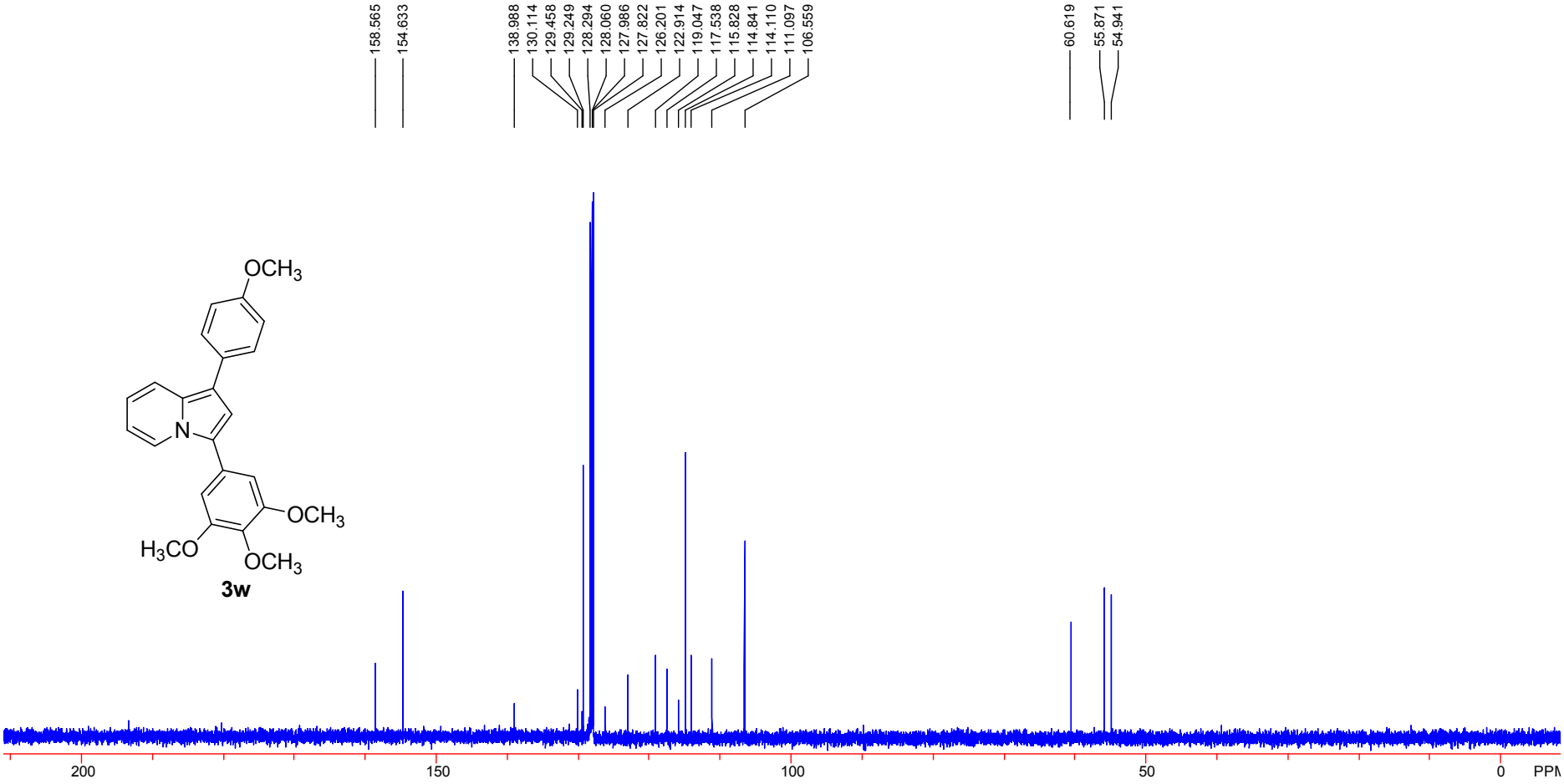
^{13}C NMR (100 MHz, C_6D_6)



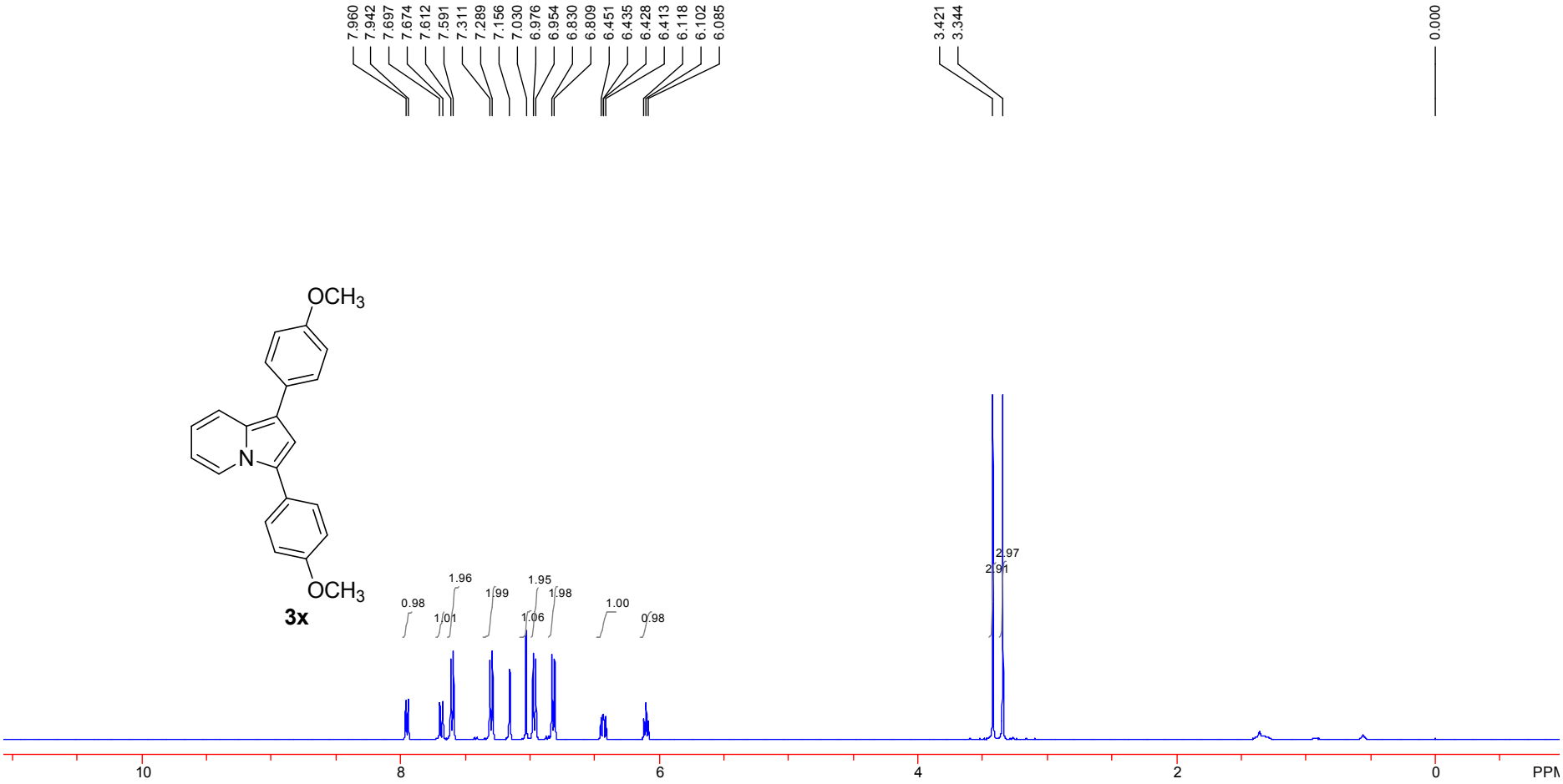
^{1}H NMR (400 MHz, C_6D_6)



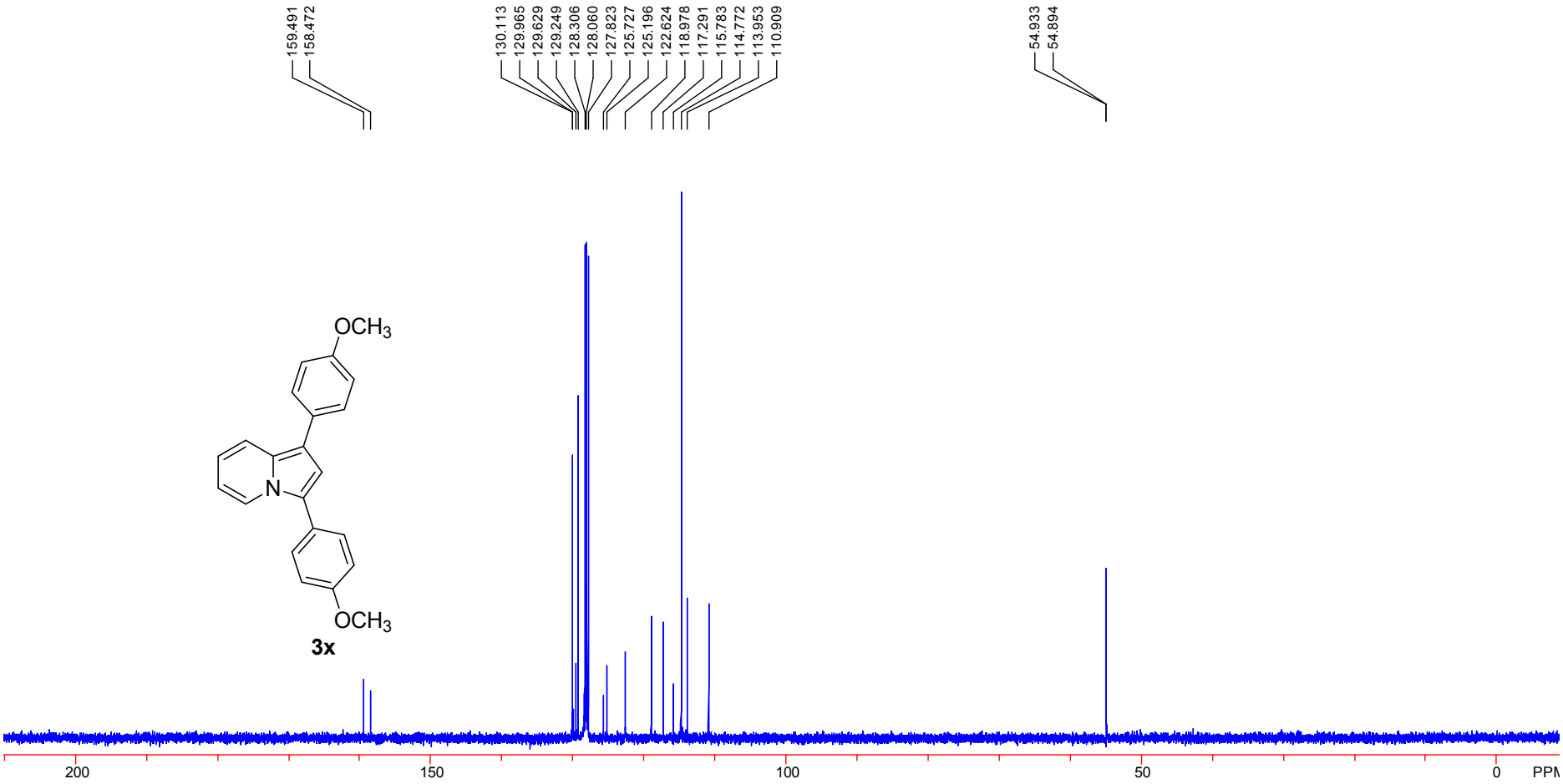
^{13}C NMR (100 MHz, C_6D_6)



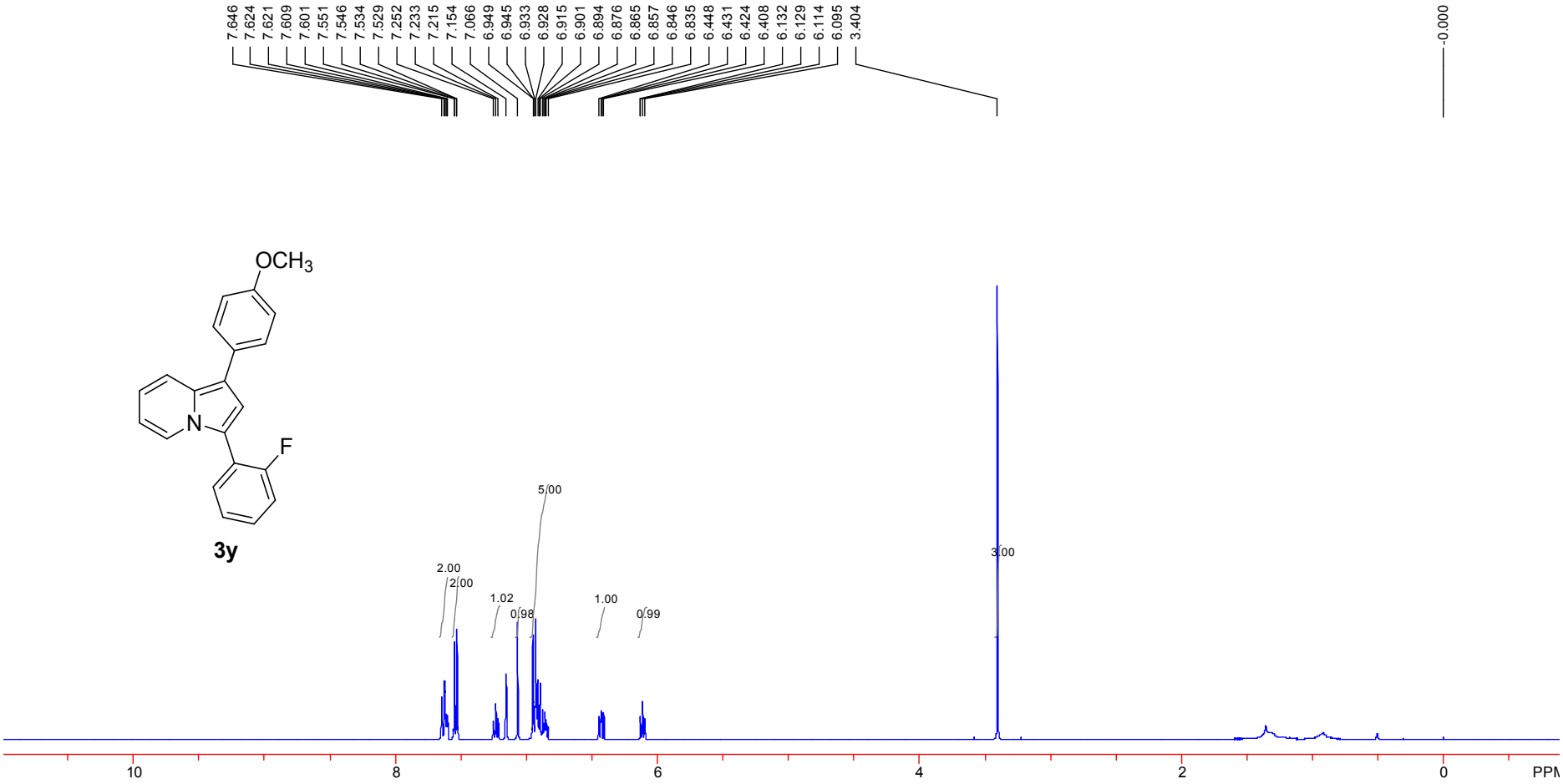
^{1}H NMR (400 MHz, C_6D_6)



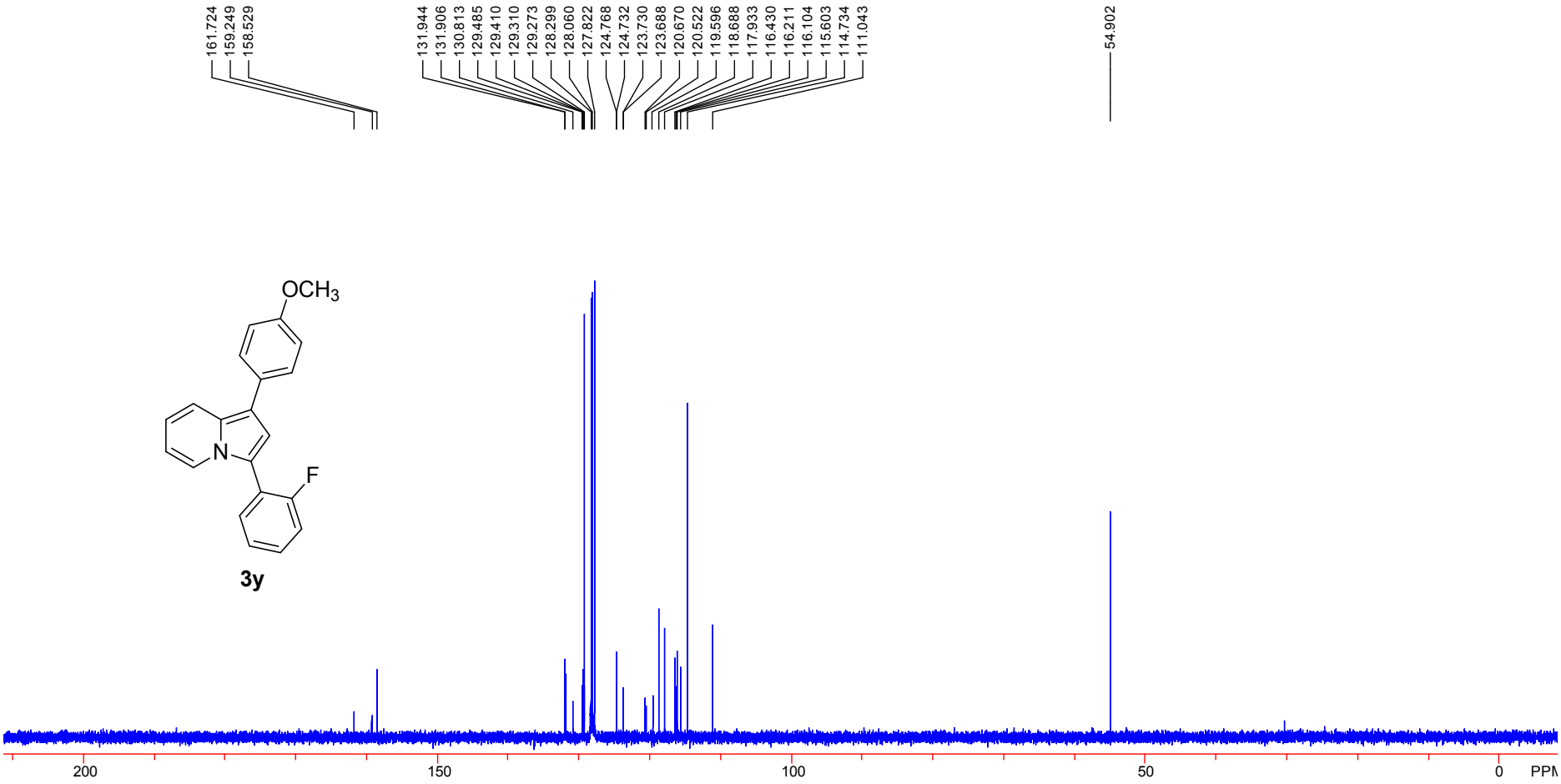
^{13}C NMR (100 MHz, C_6D_6)



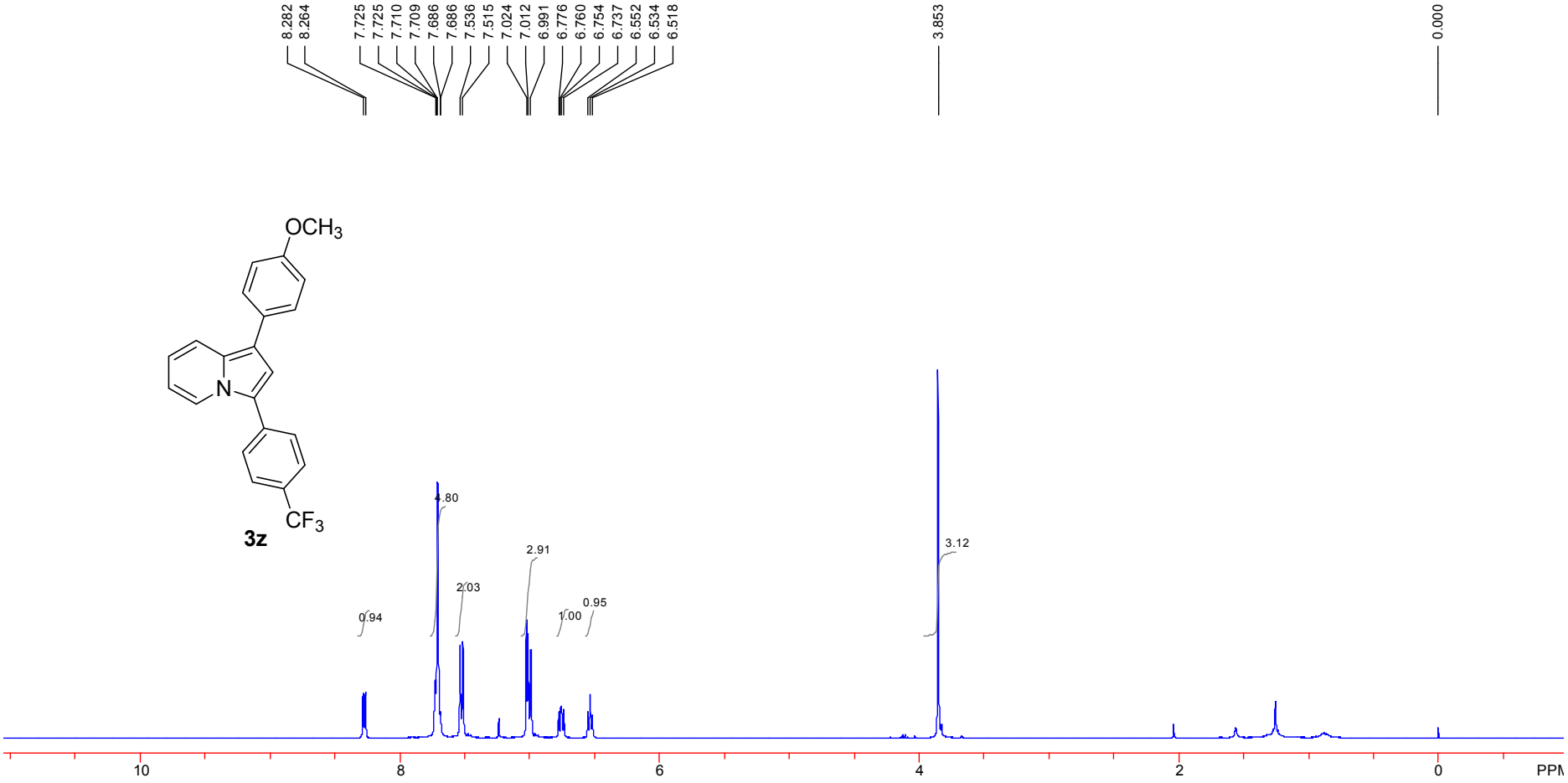
^{1}H NMR (400 MHz, C_6D_6)



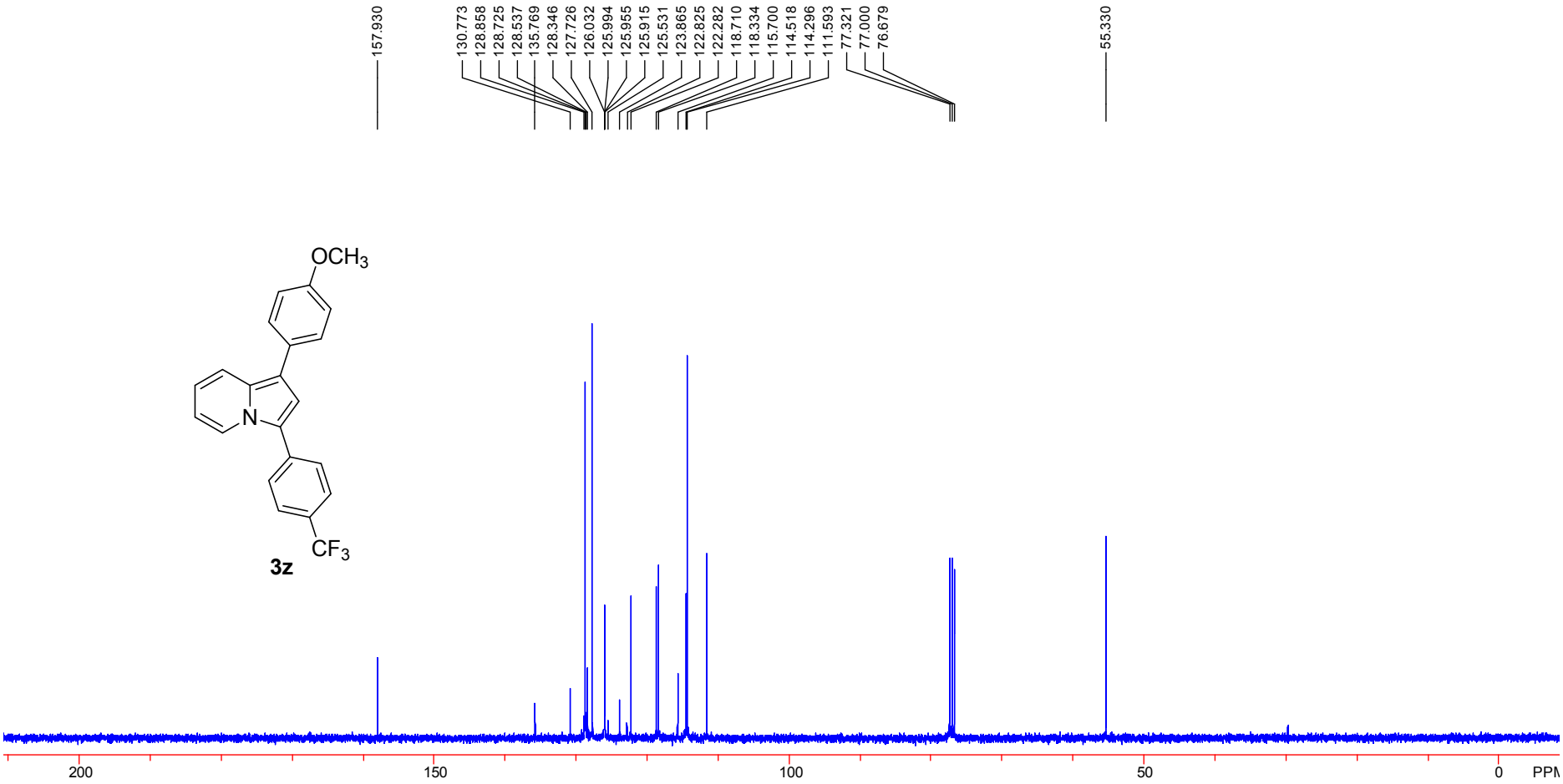
^{13}C NMR (100 MHz, C_6D_6)



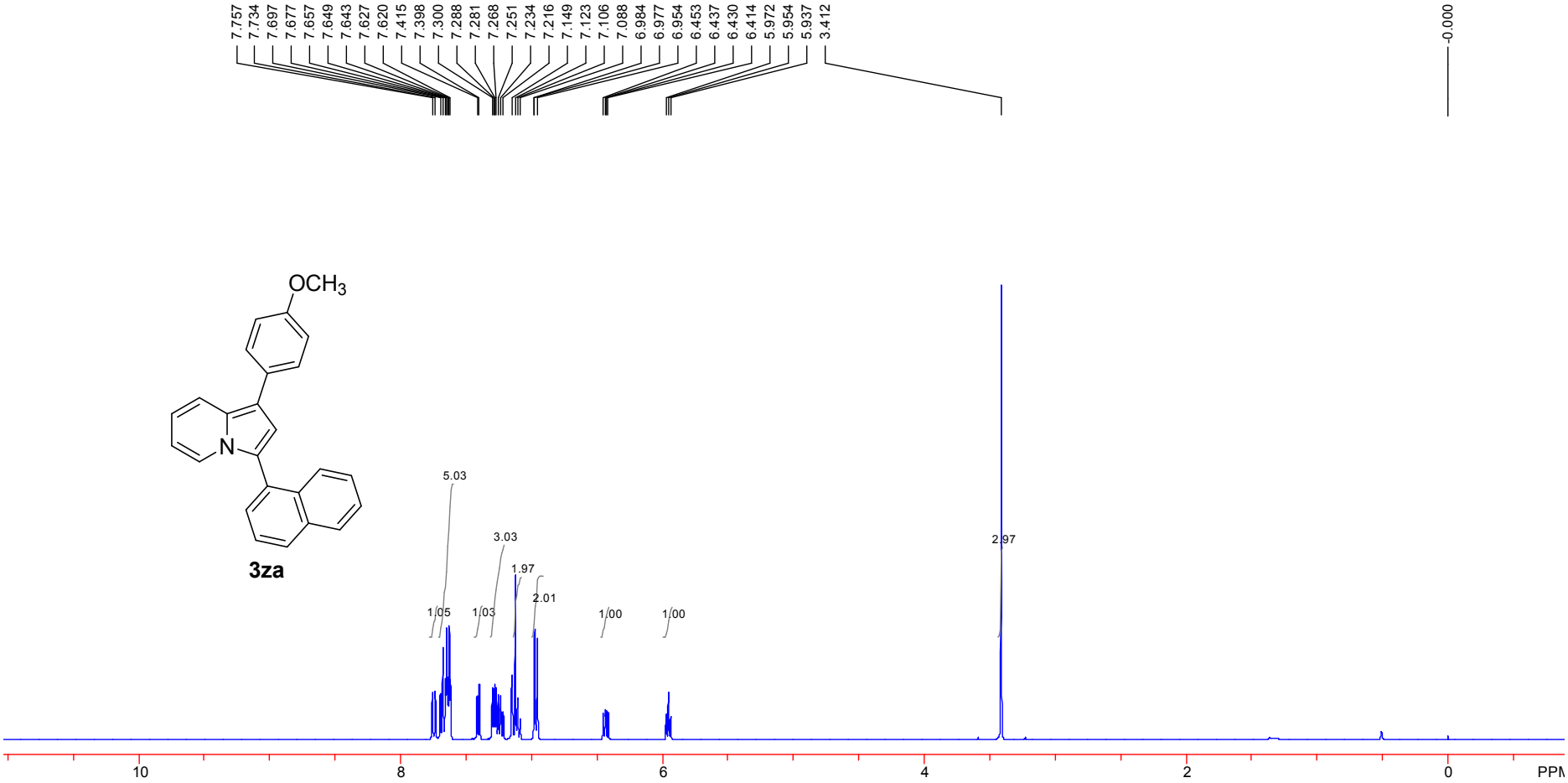
^{1}H NMR (400 MHz, C_6D_6)



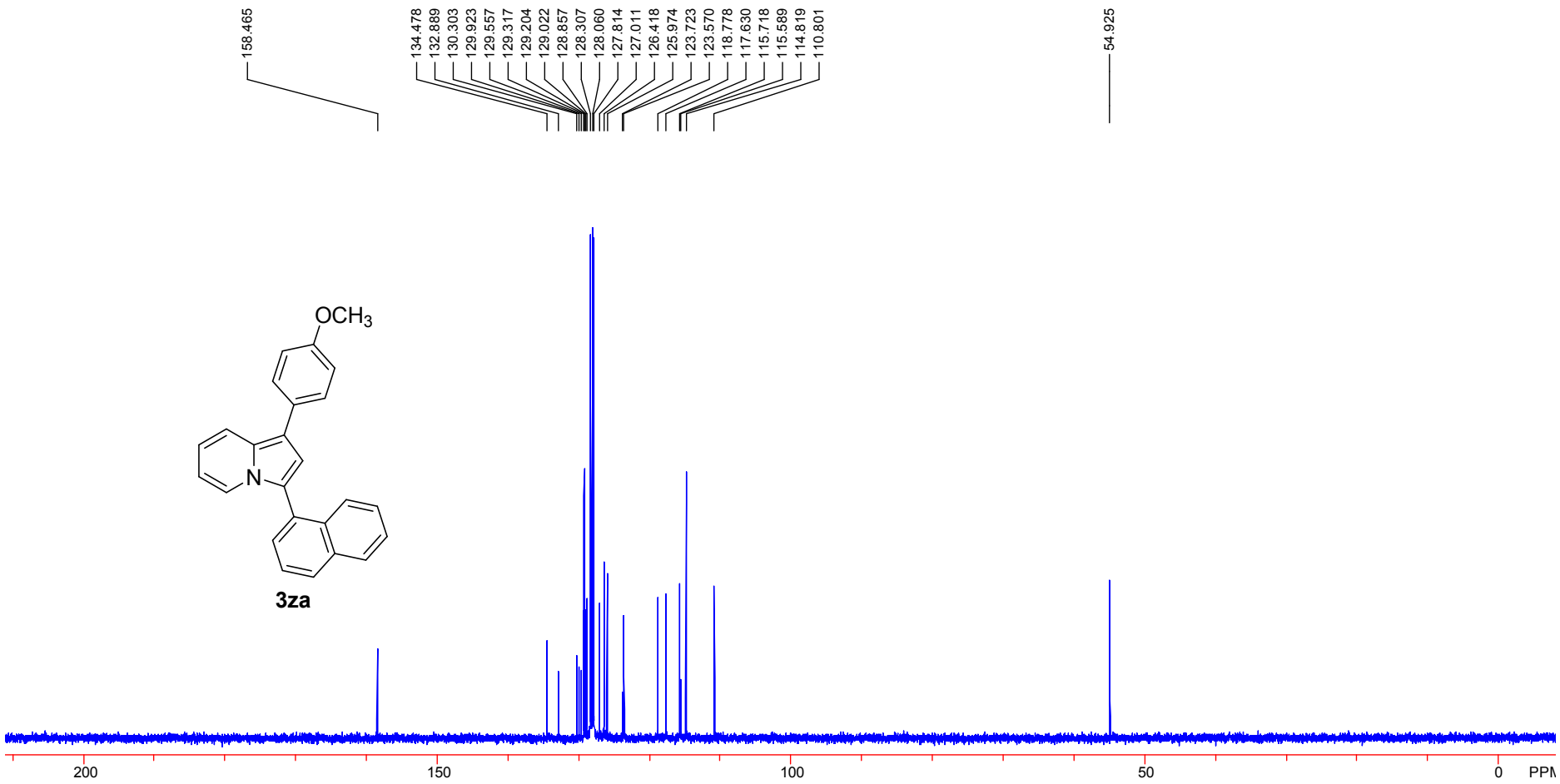
^{13}C NMR (100 MHz, C_6D_6)



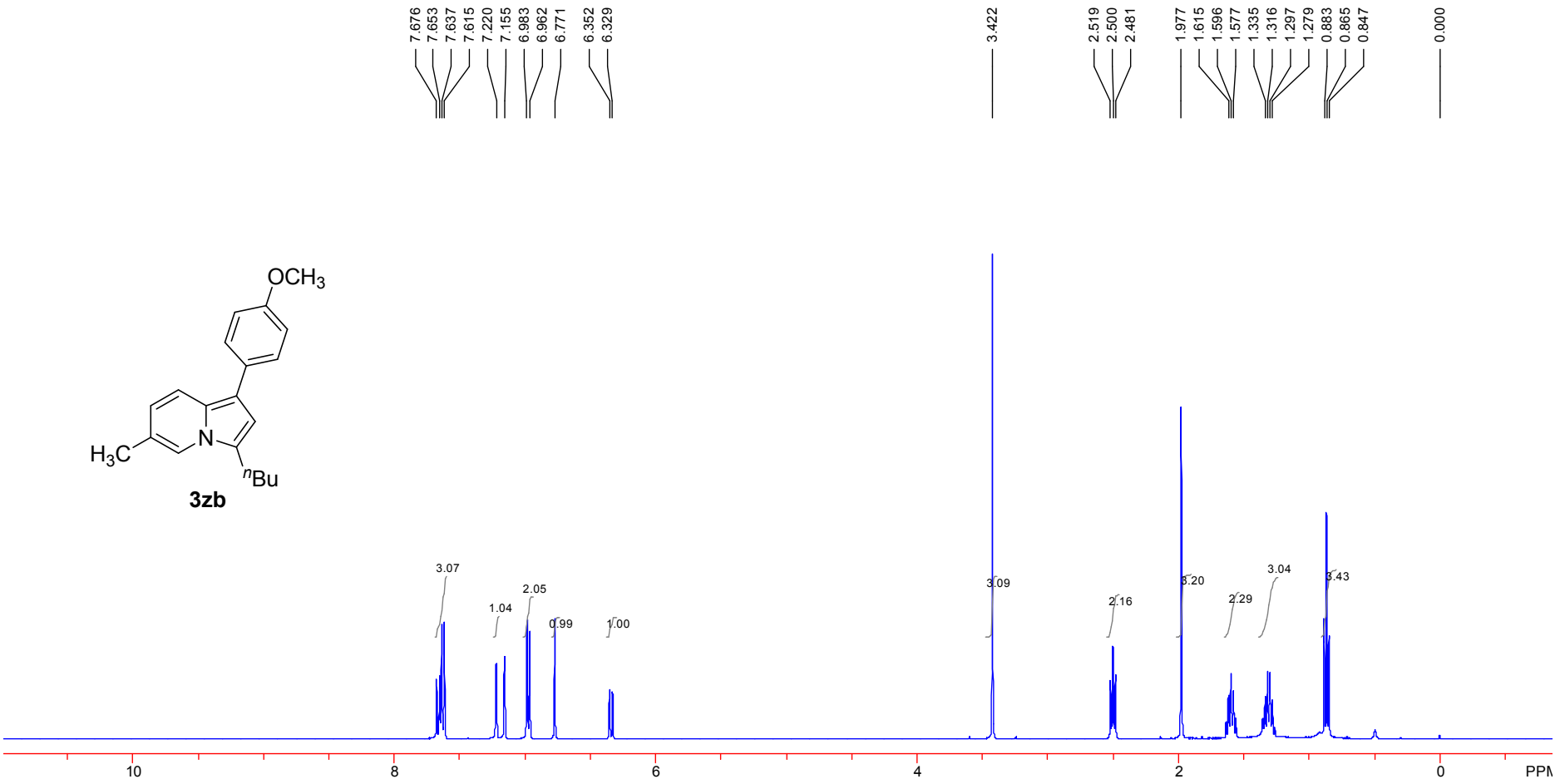
^{1}H NMR (400 MHz, C_6D_6)



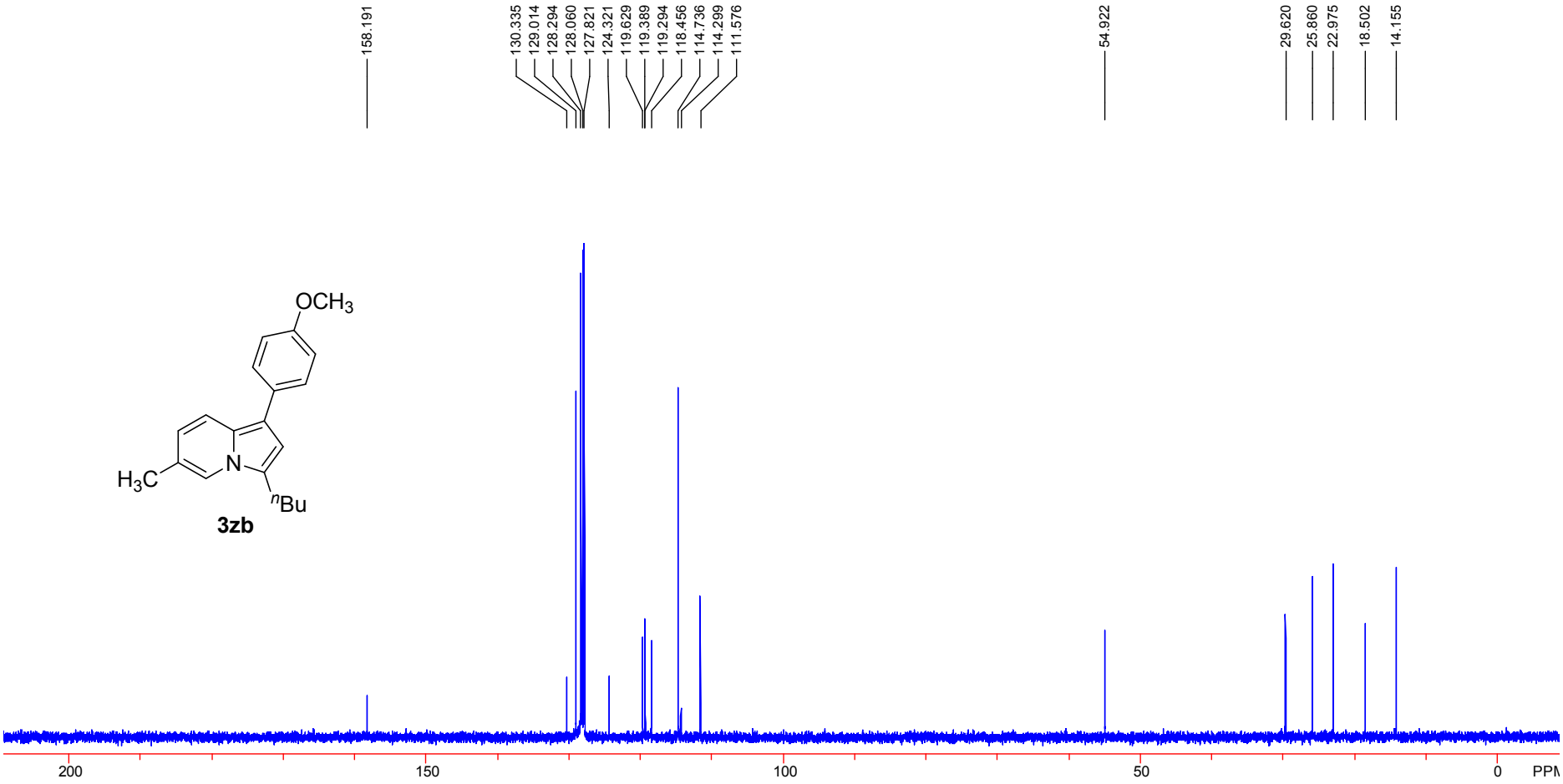
^{13}C NMR (100 MHz, C_6D_6)



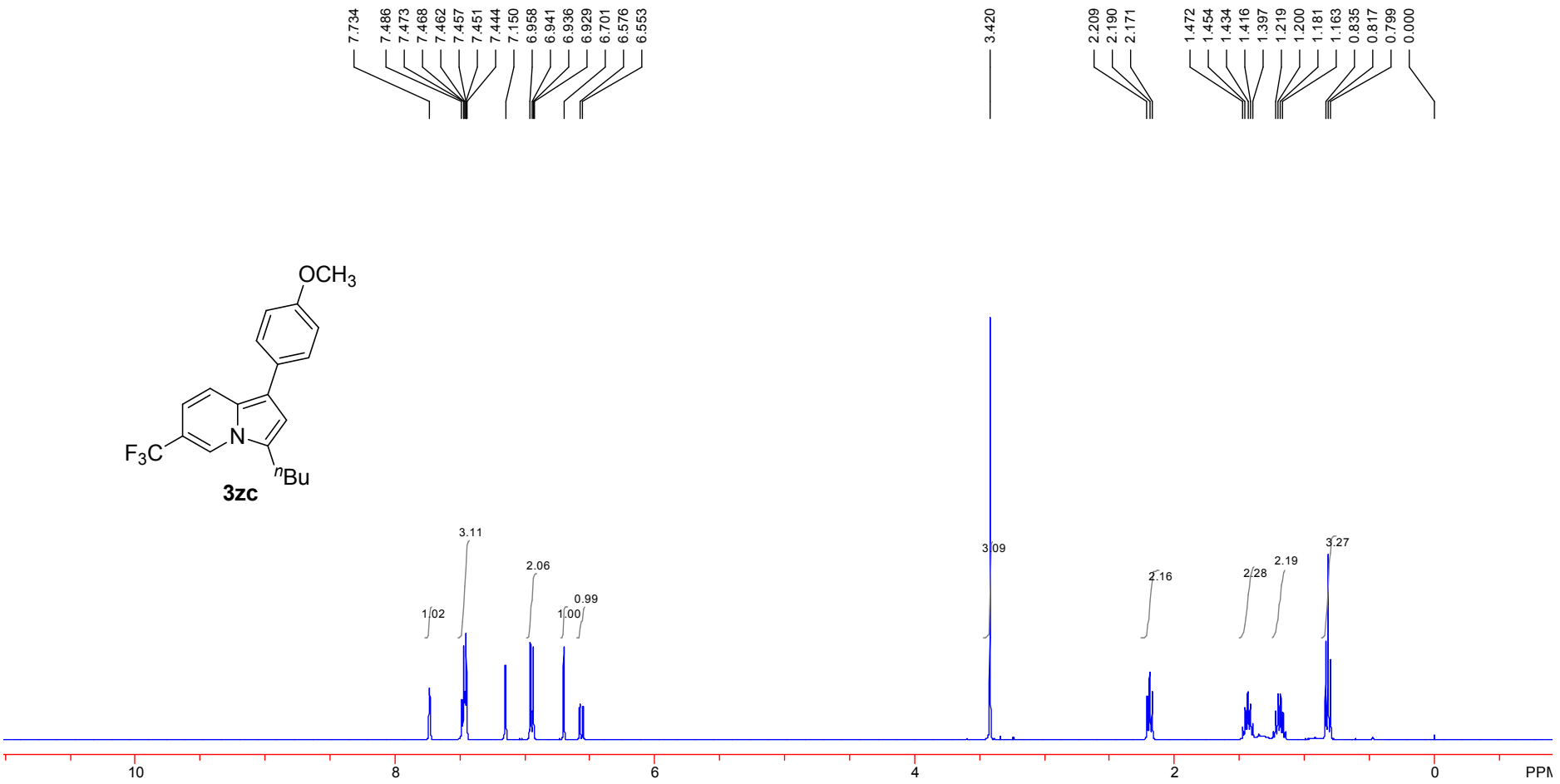
^{1}H NMR (400 MHz, C_6D_6)



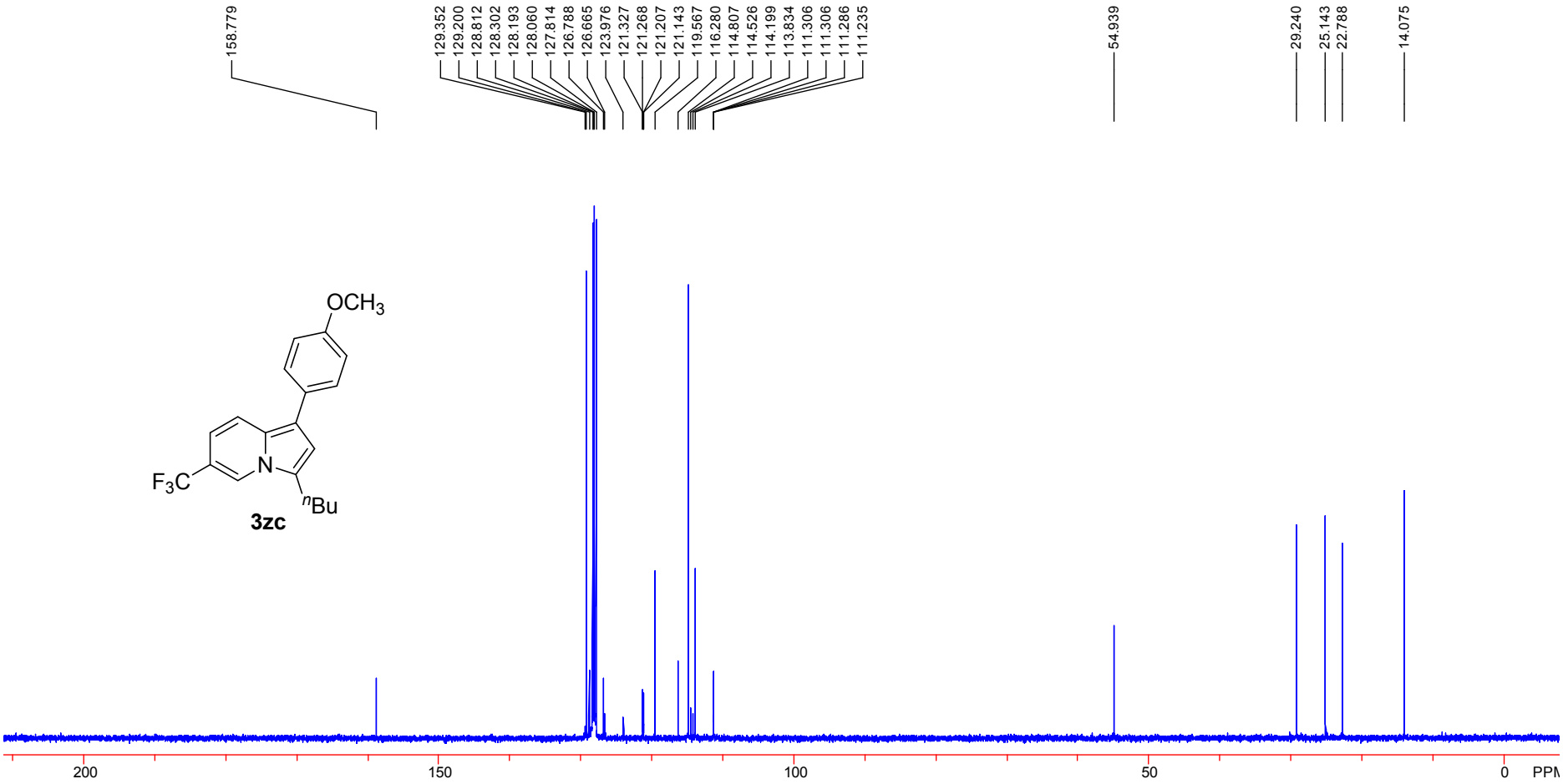
^{13}C NMR (100 MHz, C_6D_6)



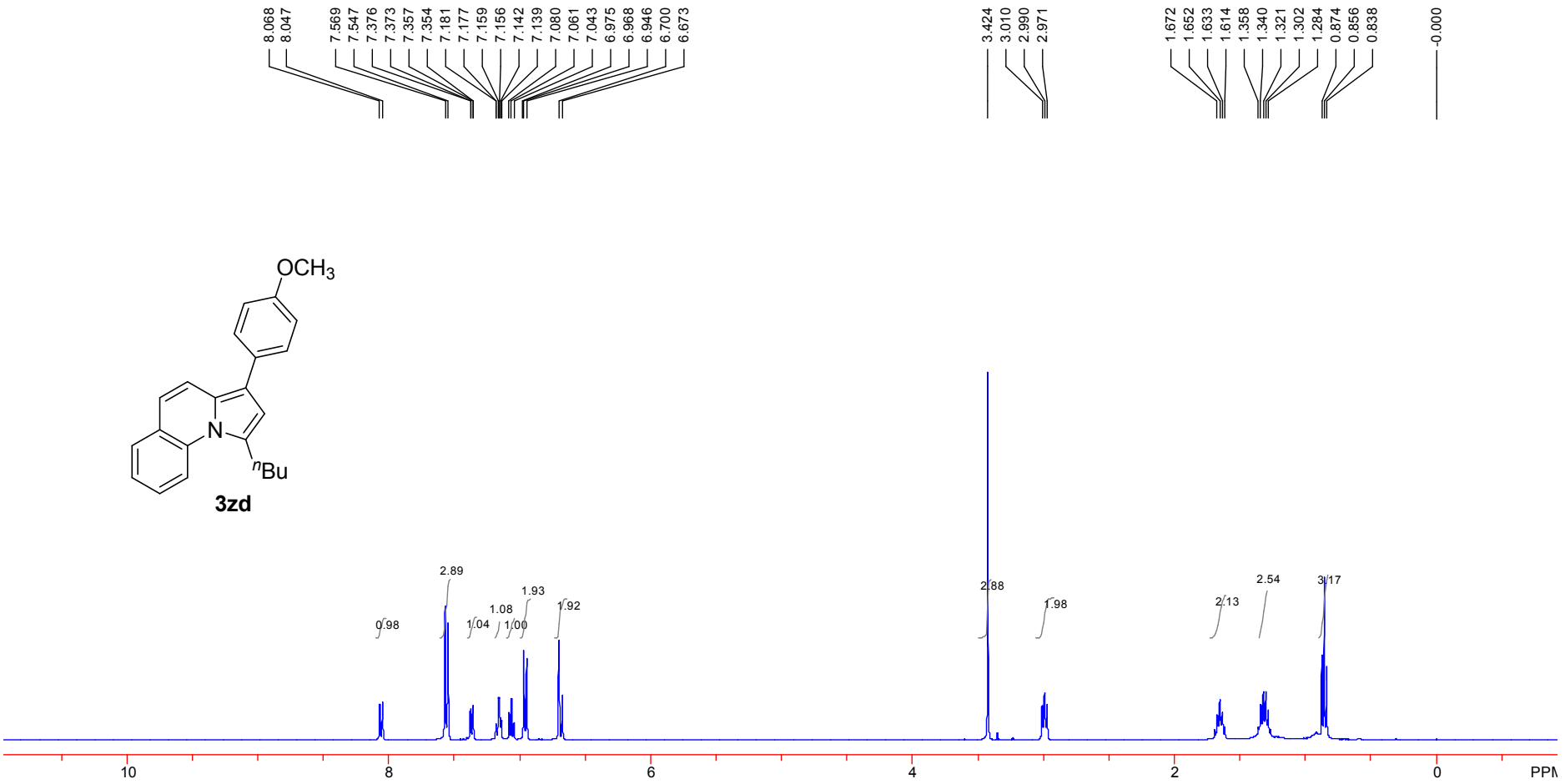
^{1}H NMR (400 MHz, C_6D_6)



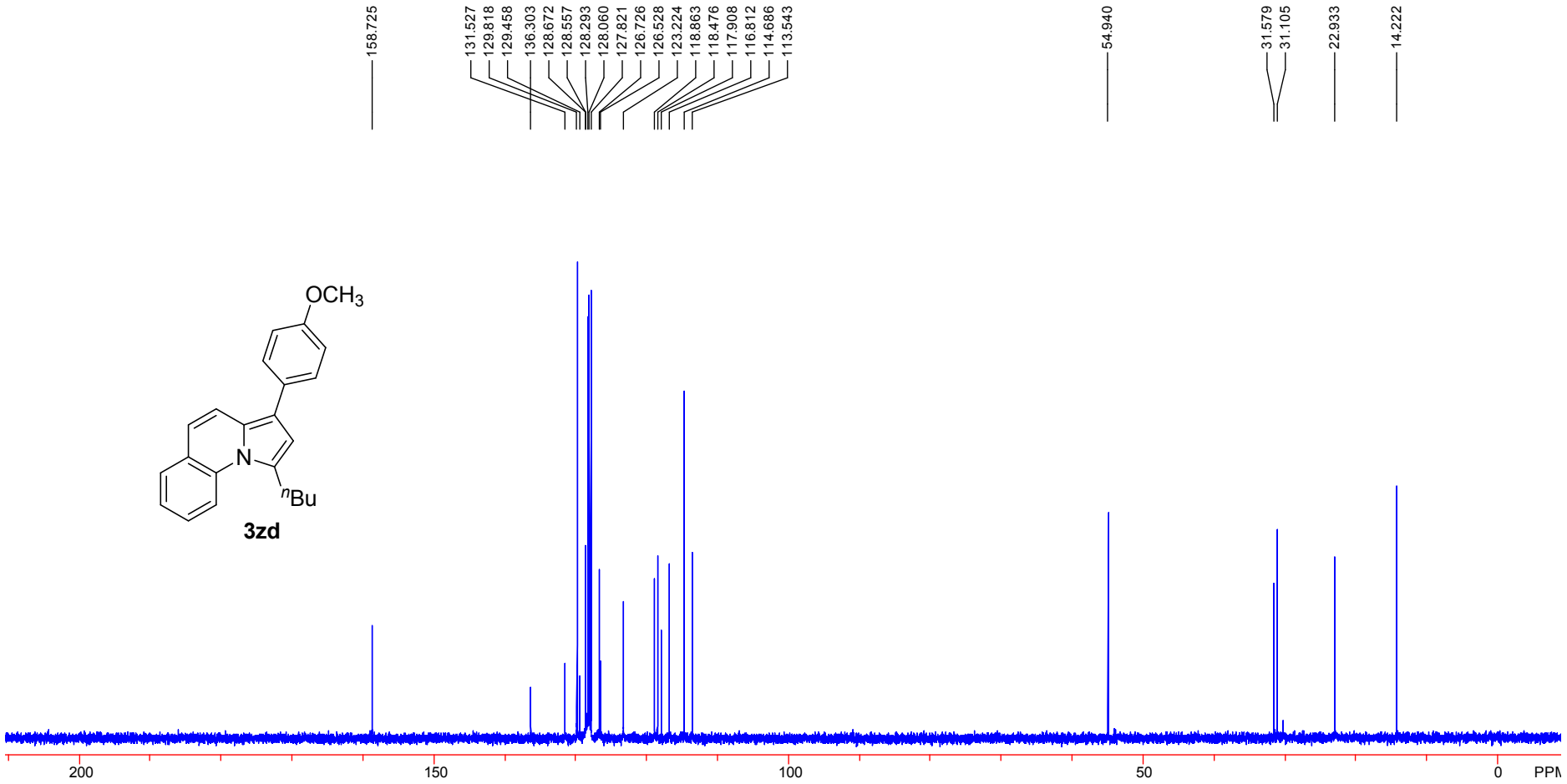
^{13}C NMR (100 MHz, C_6D_6)



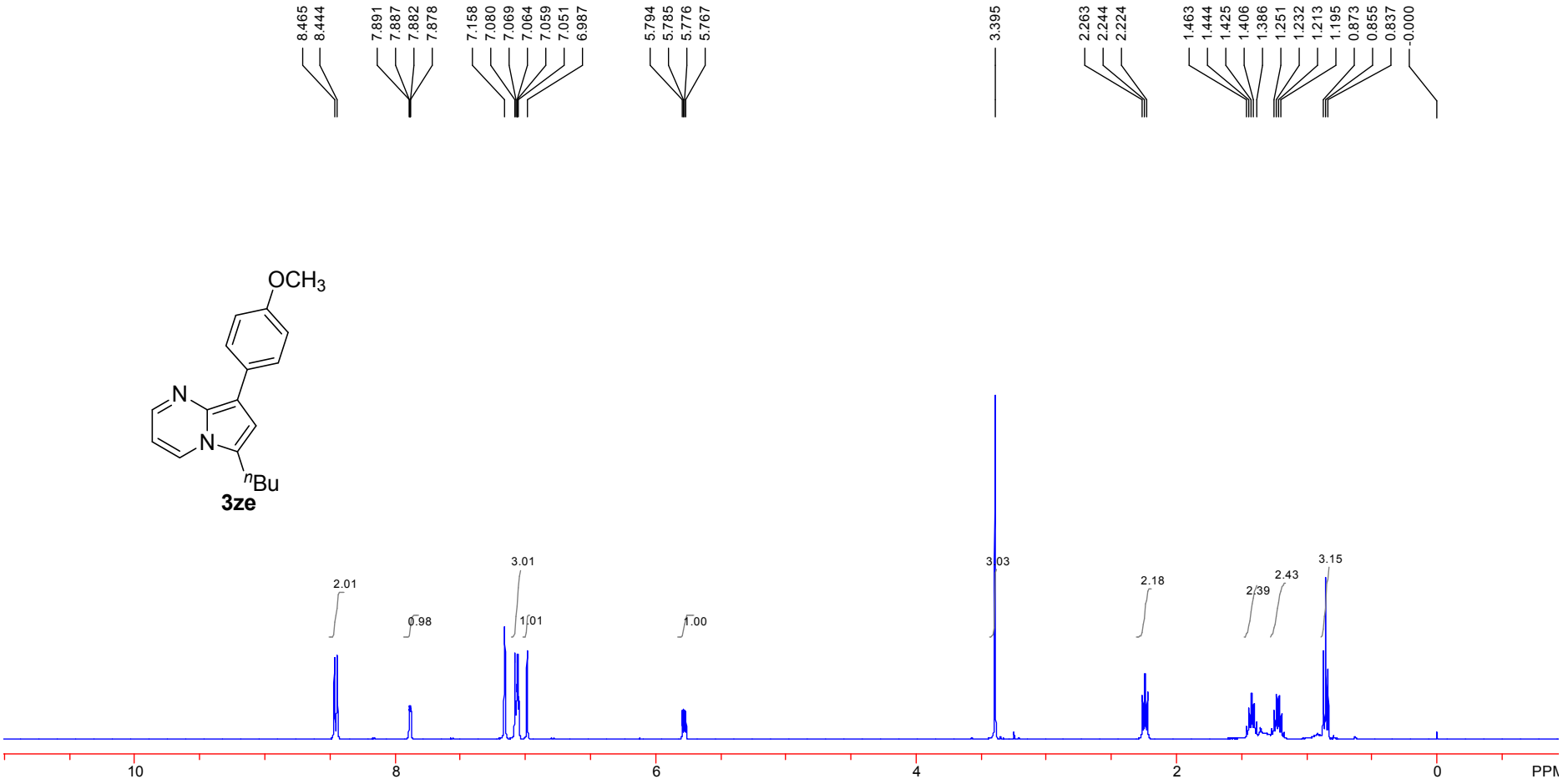
^{1}H NMR (400 MHz, C_6D_6)



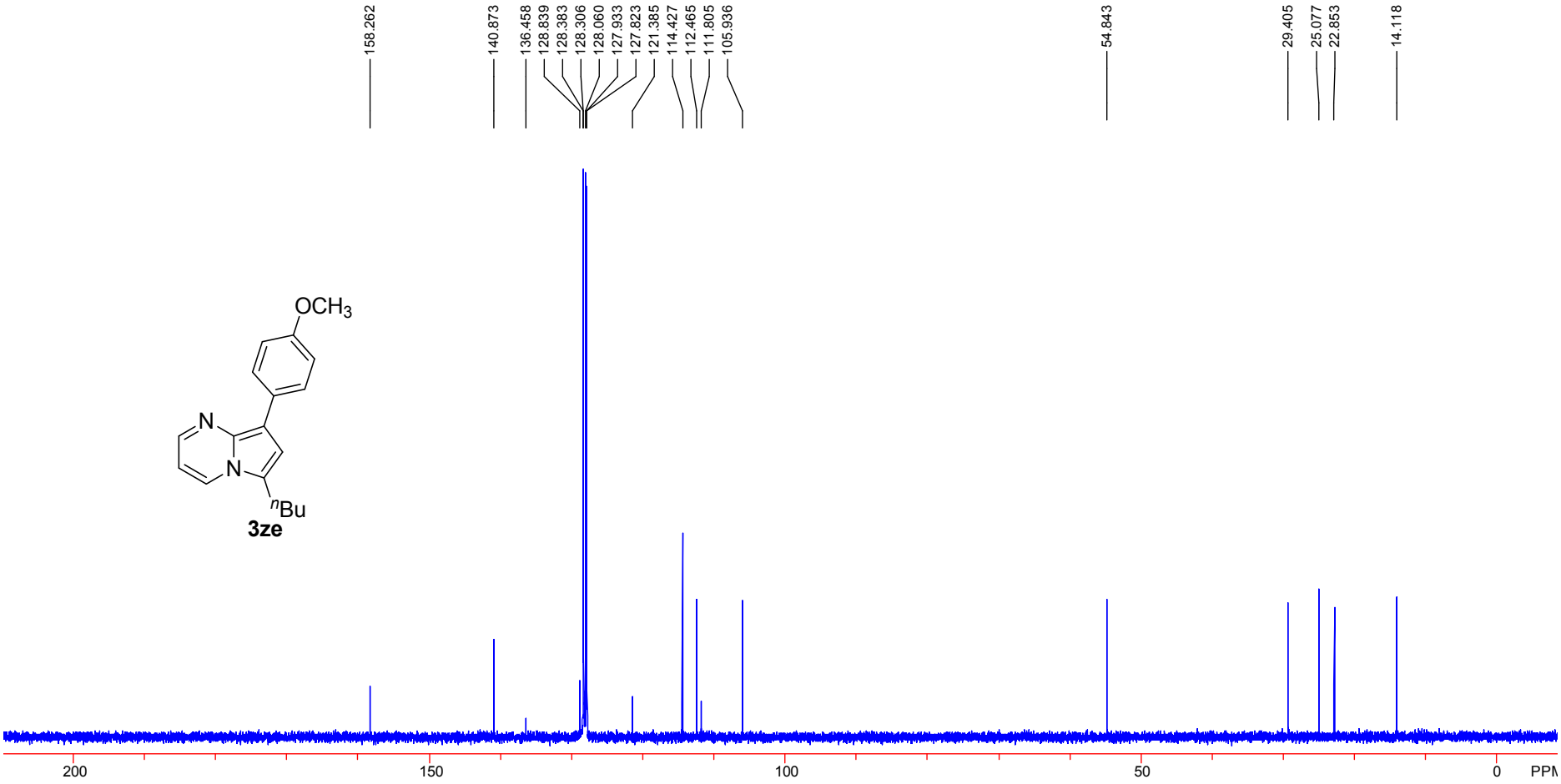
^{13}C NMR (100 MHz, C_6D_6)



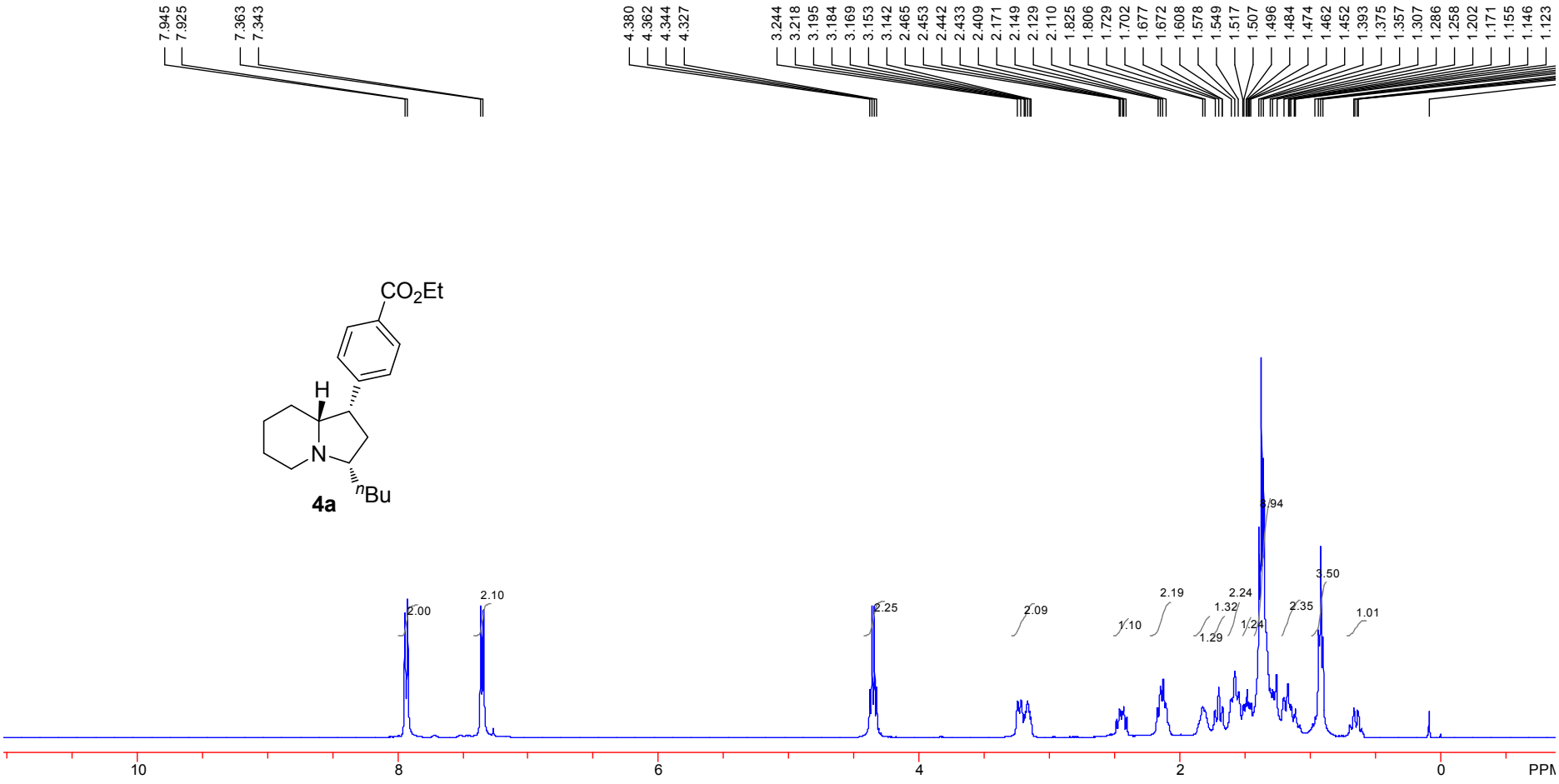
^{1}H NMR (400 MHz, C_6D_6)



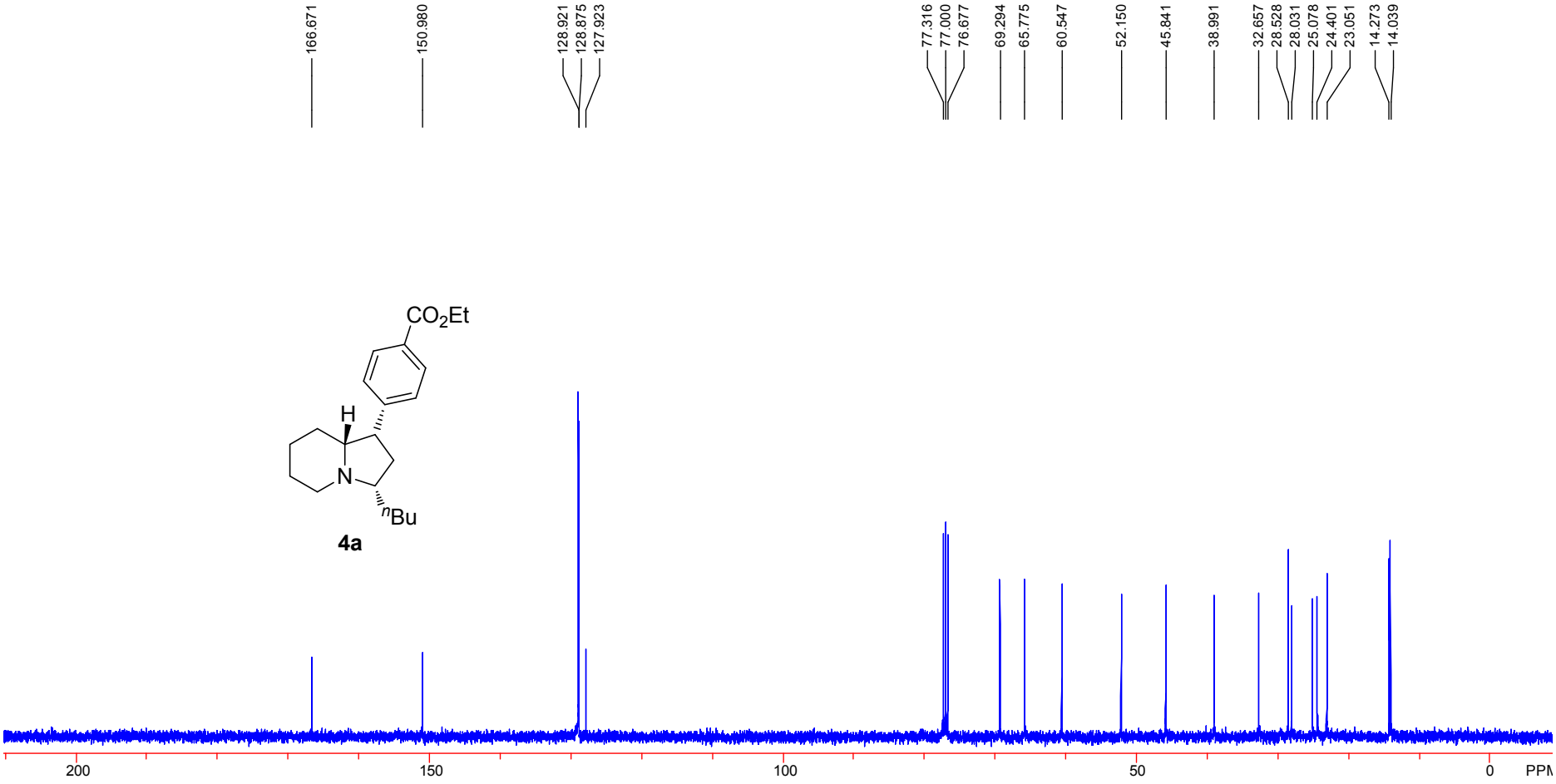
^{13}C NMR (100 MHz, C_6D_6)



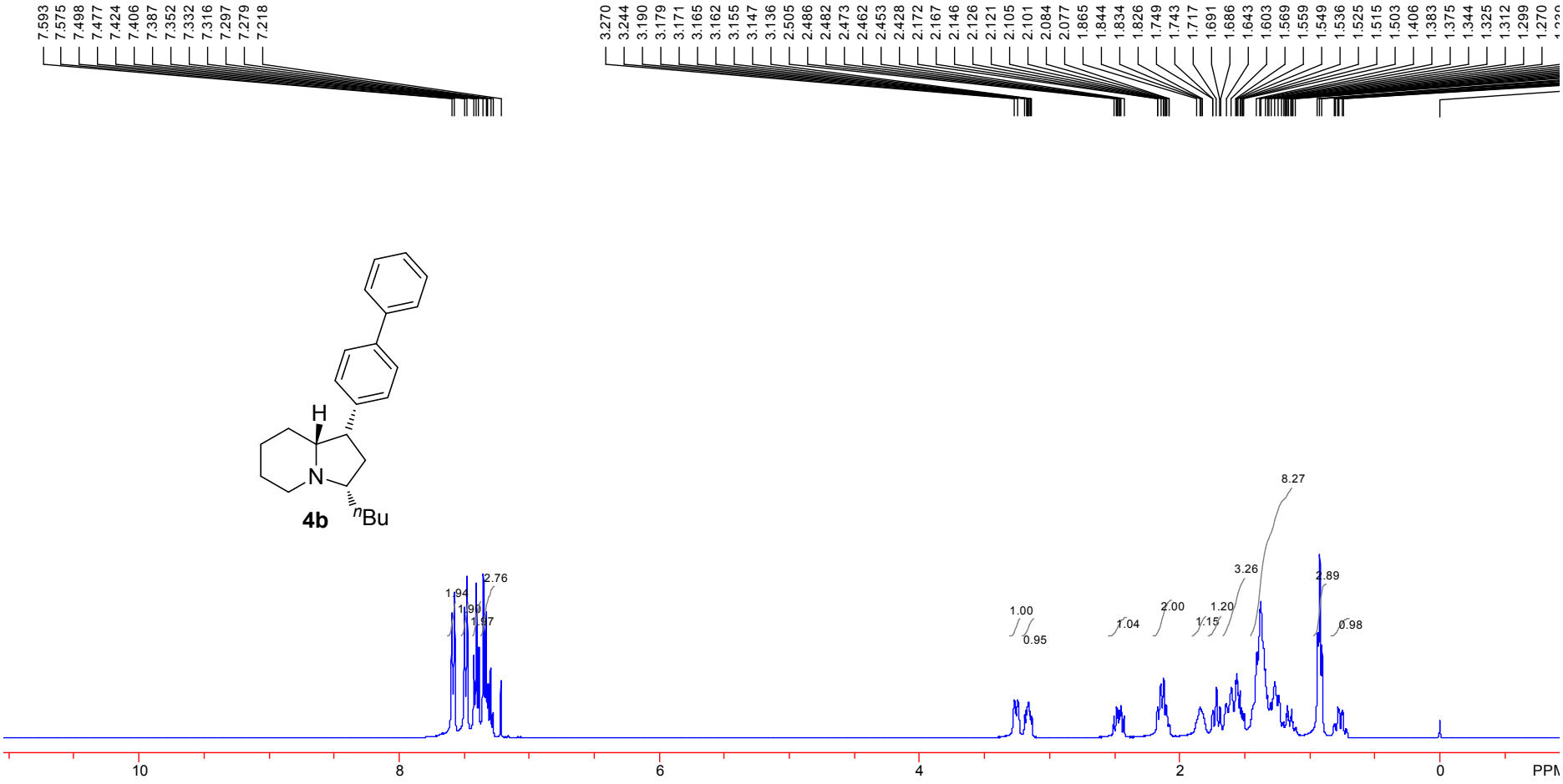
^{1}H NMR (400 MHz, $CDCl_3$)



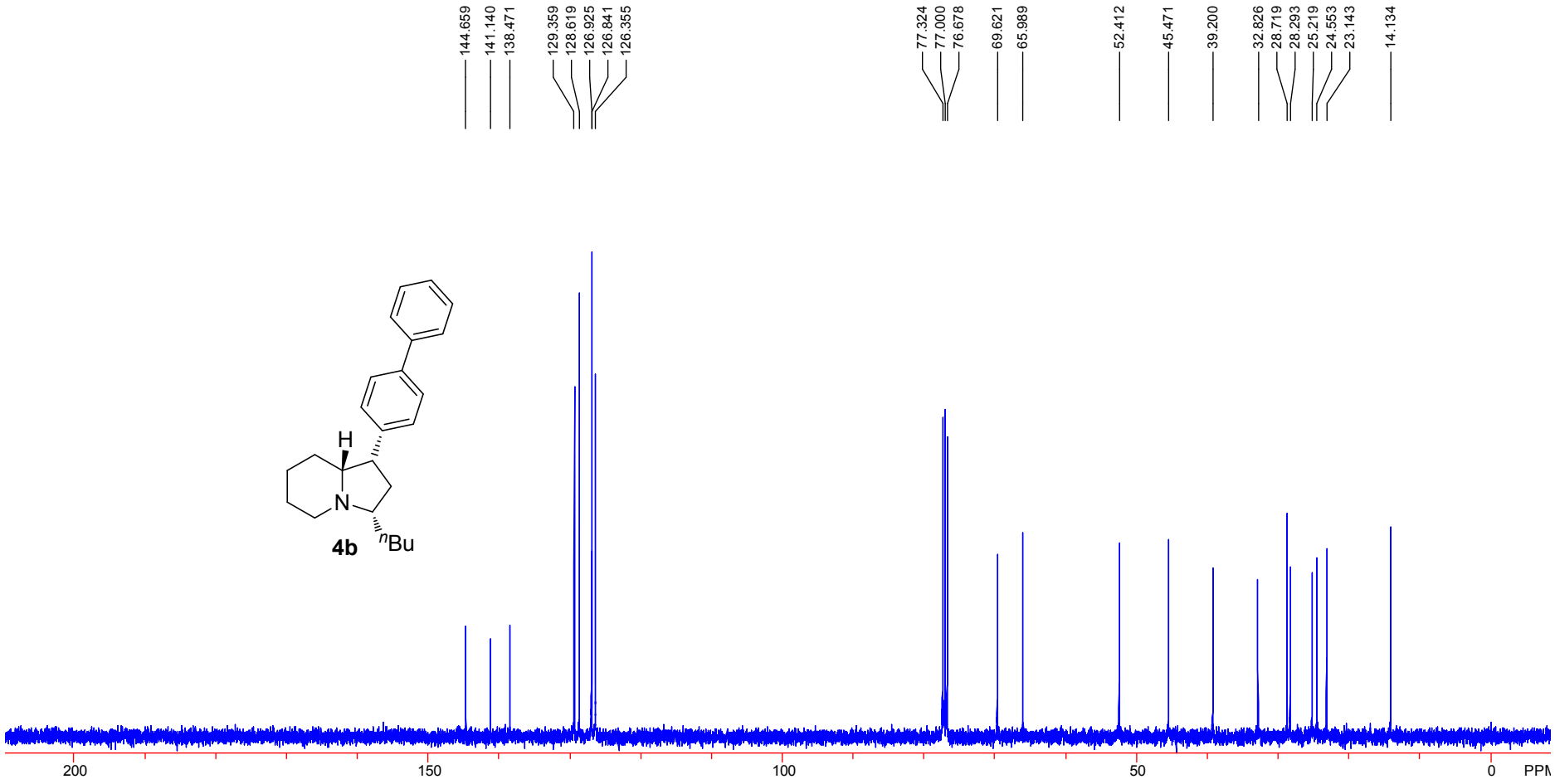
^{13}C NMR (100 MHz, $CDCl_3$)



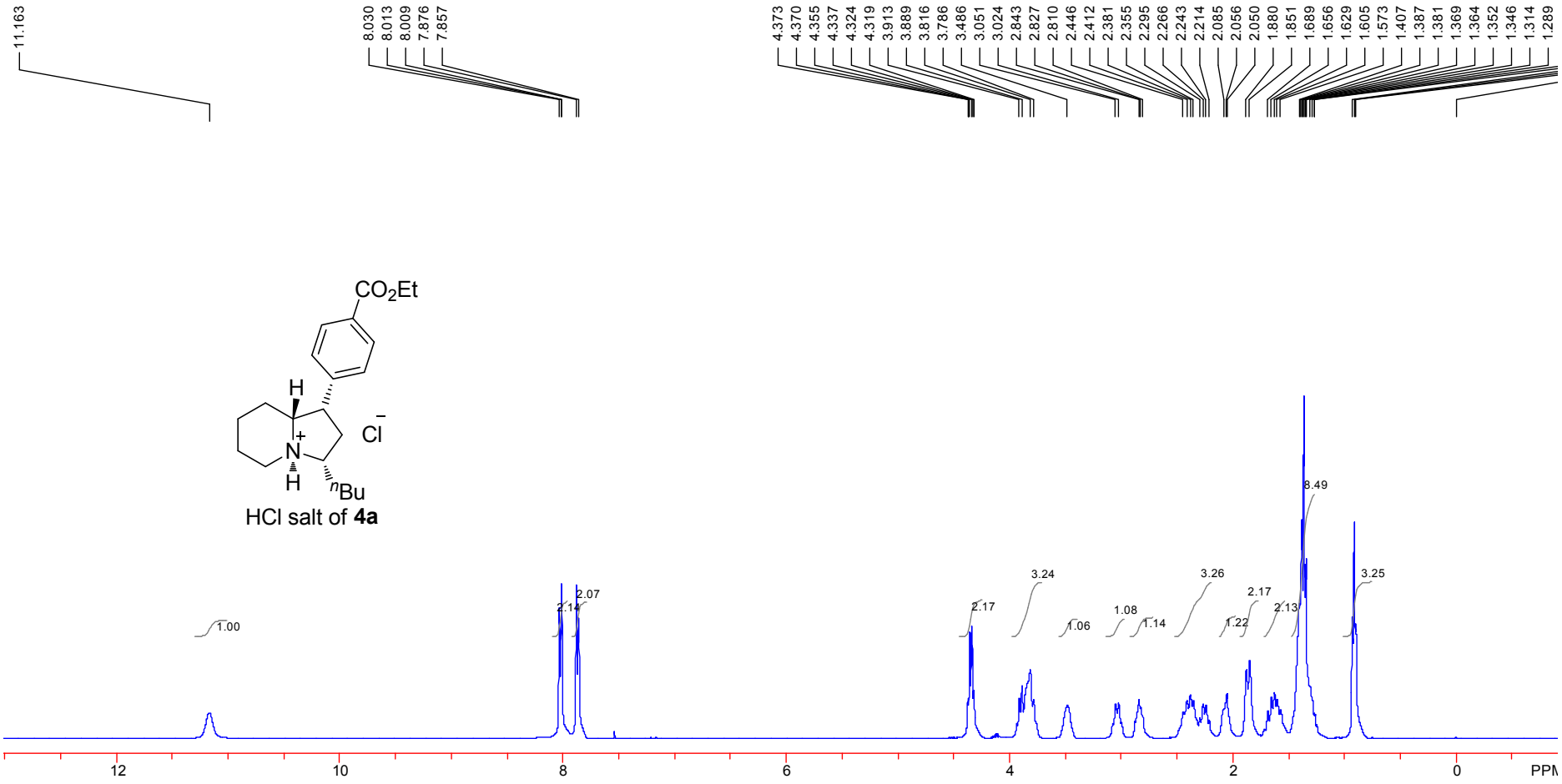
^{1}H NMR (400 MHz, $CDCl_3$)



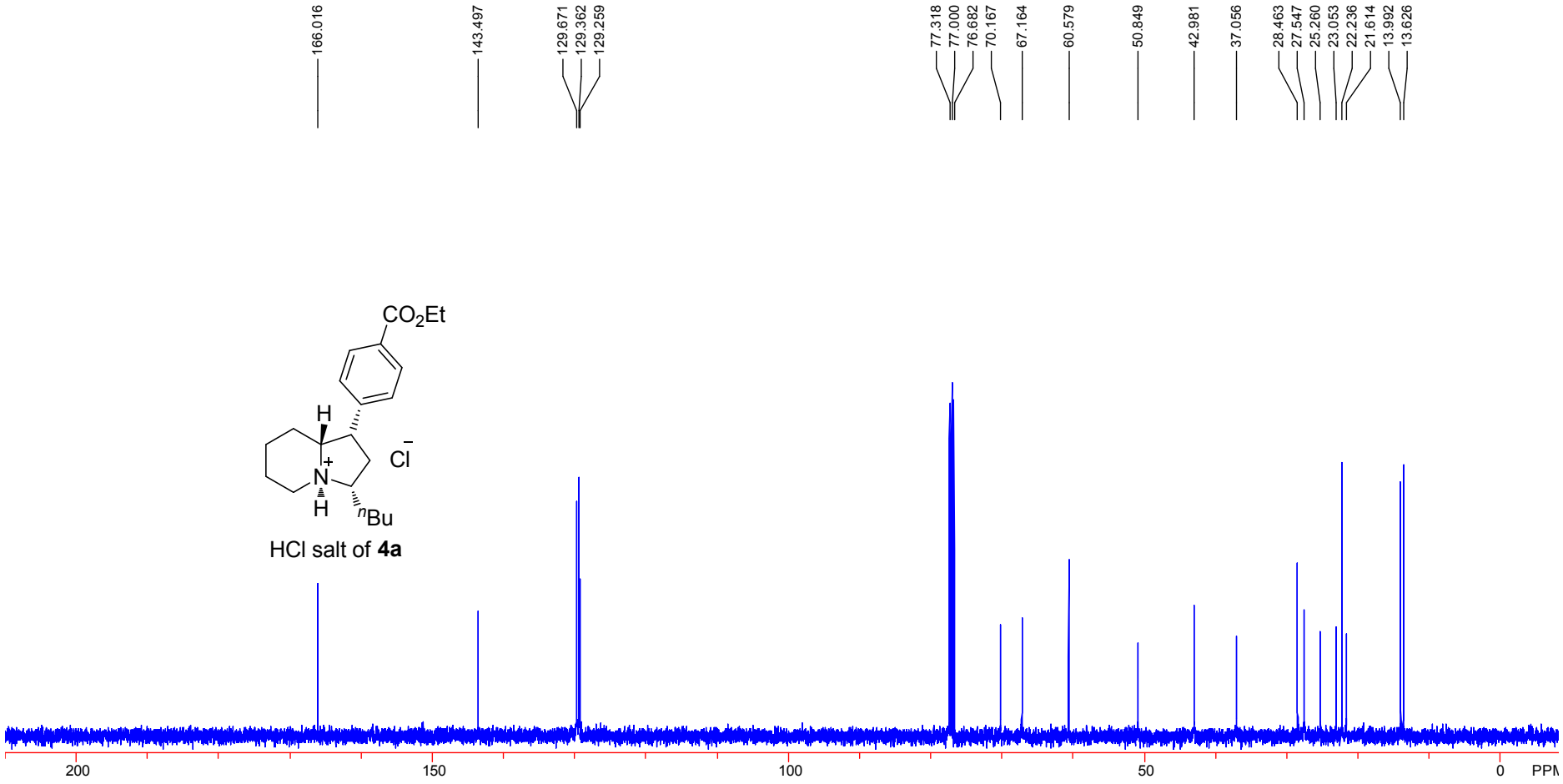
^{13}C NMR (100 MHz, $CDCl_3$)



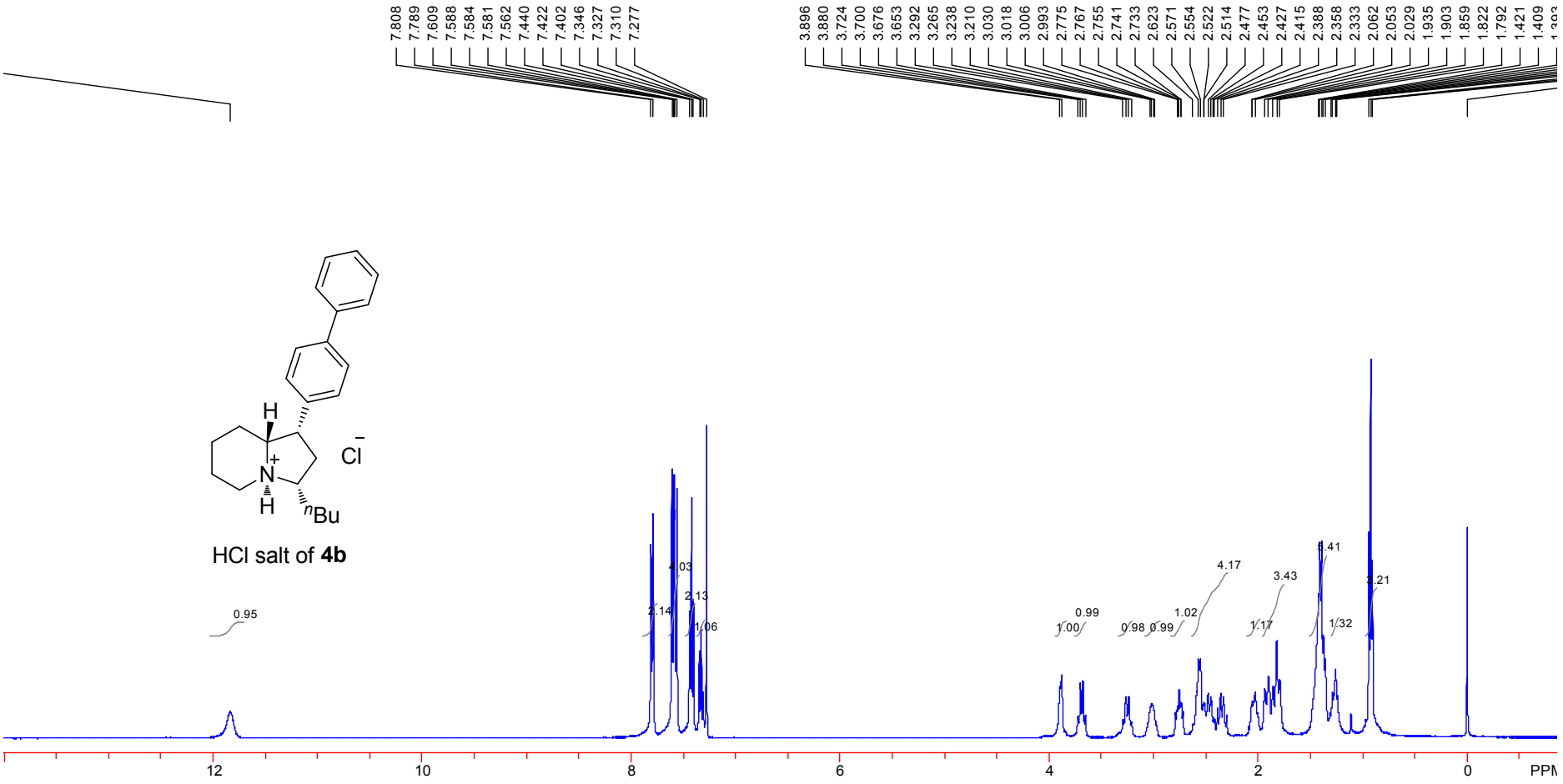
^{1}H NMR (400 MHz, $CDCl_3$)



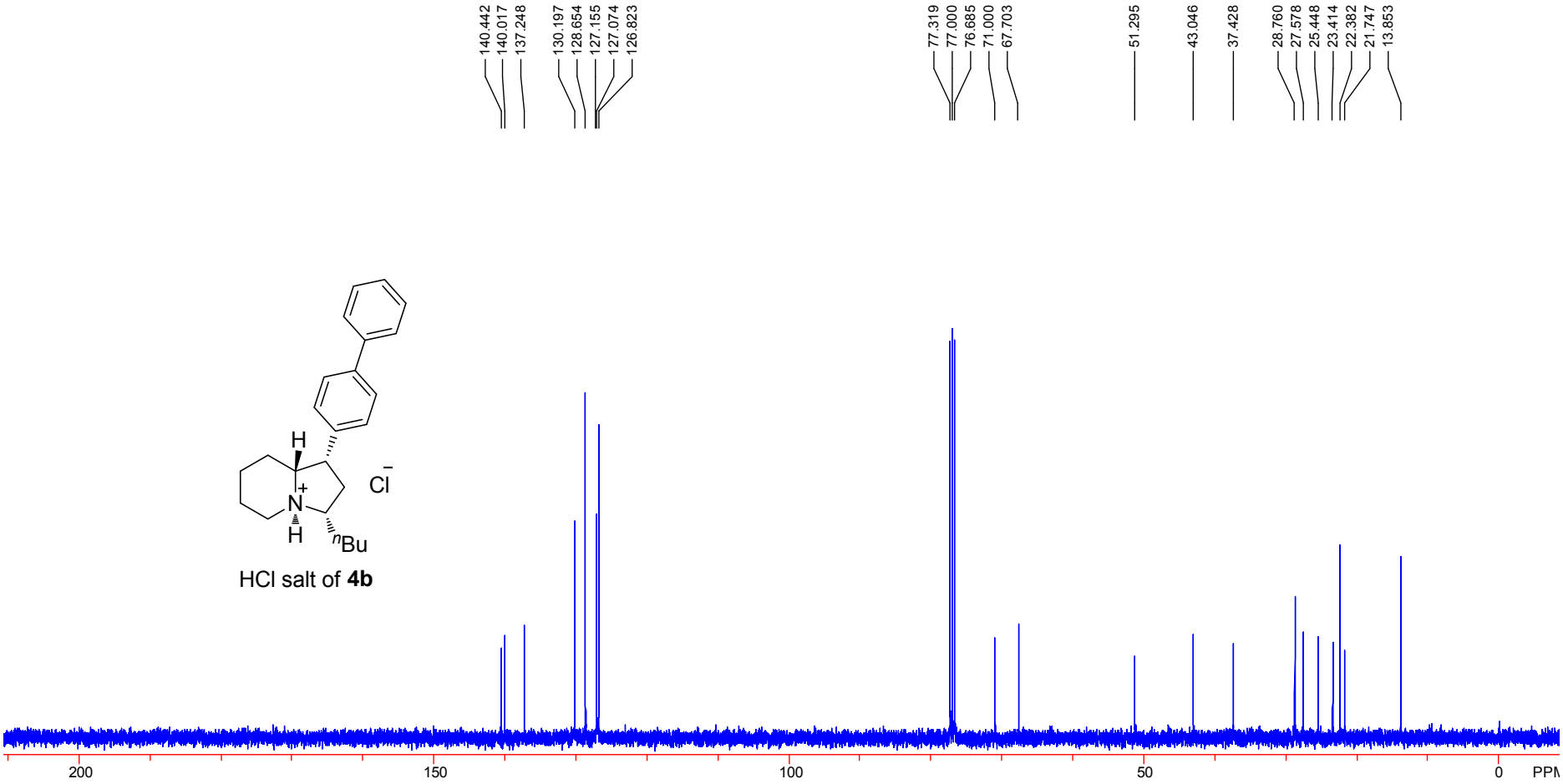
^{13}C NMR (100 MHz, $CDCl_3$)



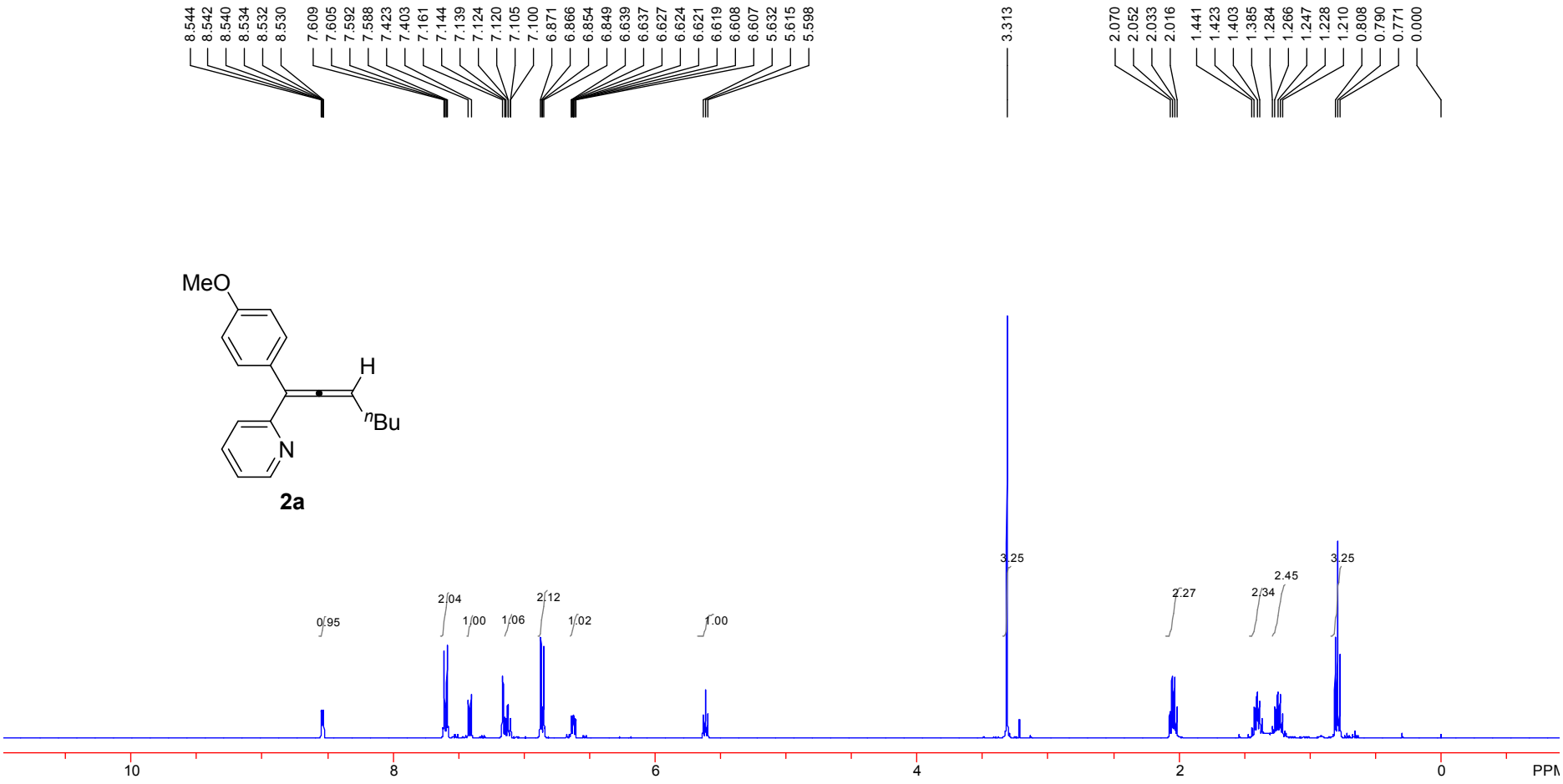
^{1}H NMR (400 MHz, $CDCl_3$)



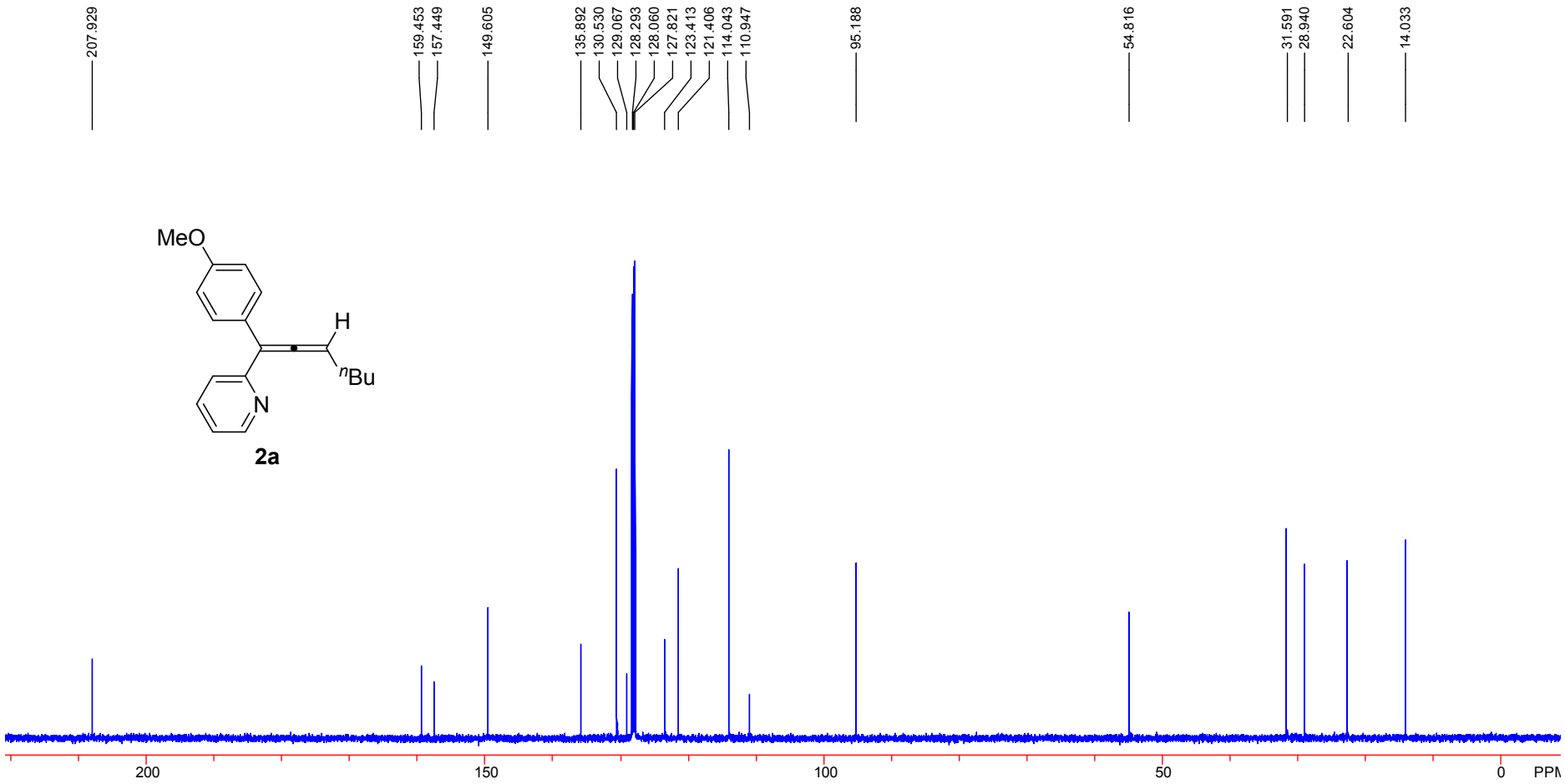
^{13}C NMR (100 MHz, $CDCl_3$)



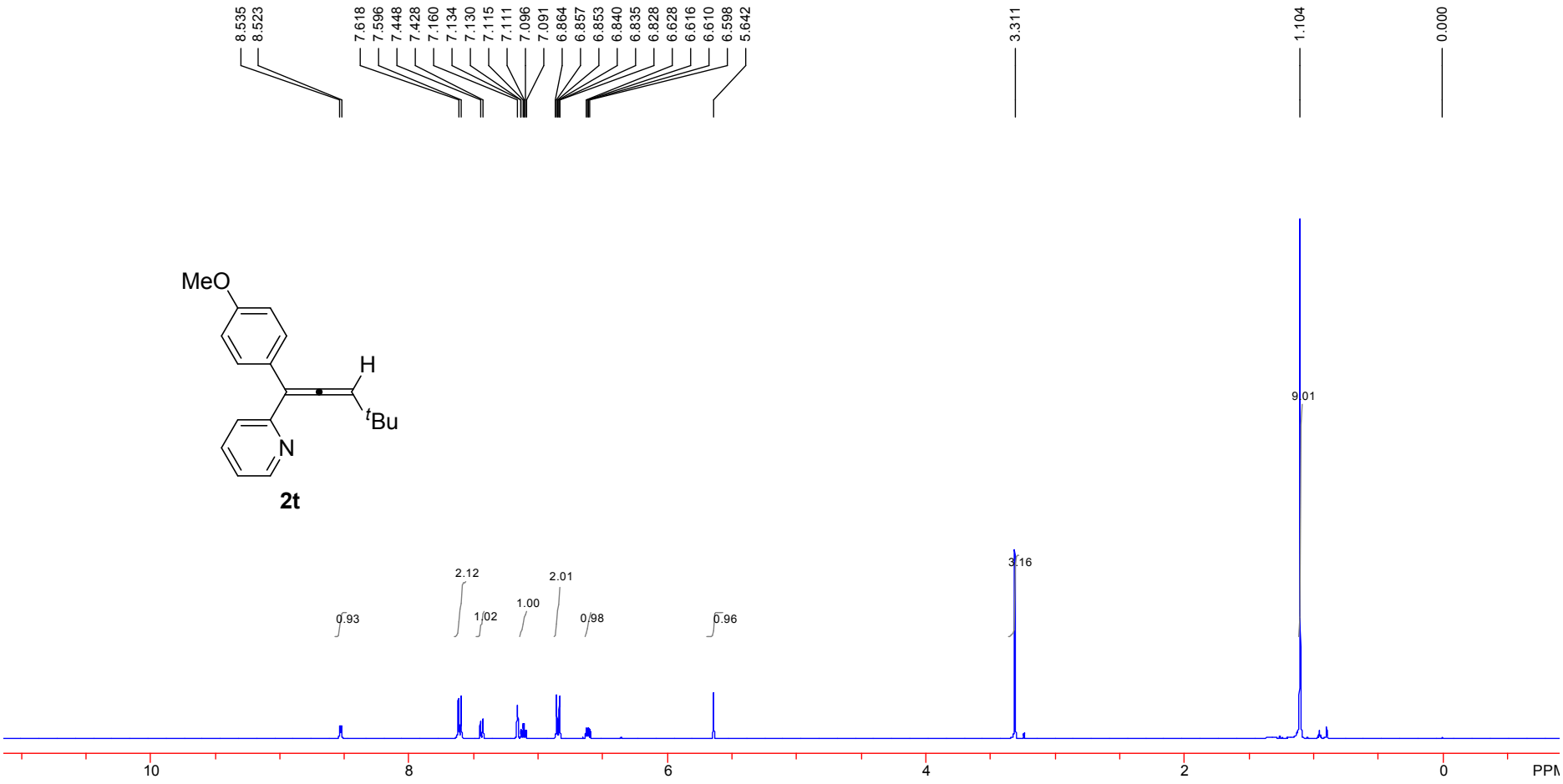
^{1}H NMR (400 MHz, C_6D_6)



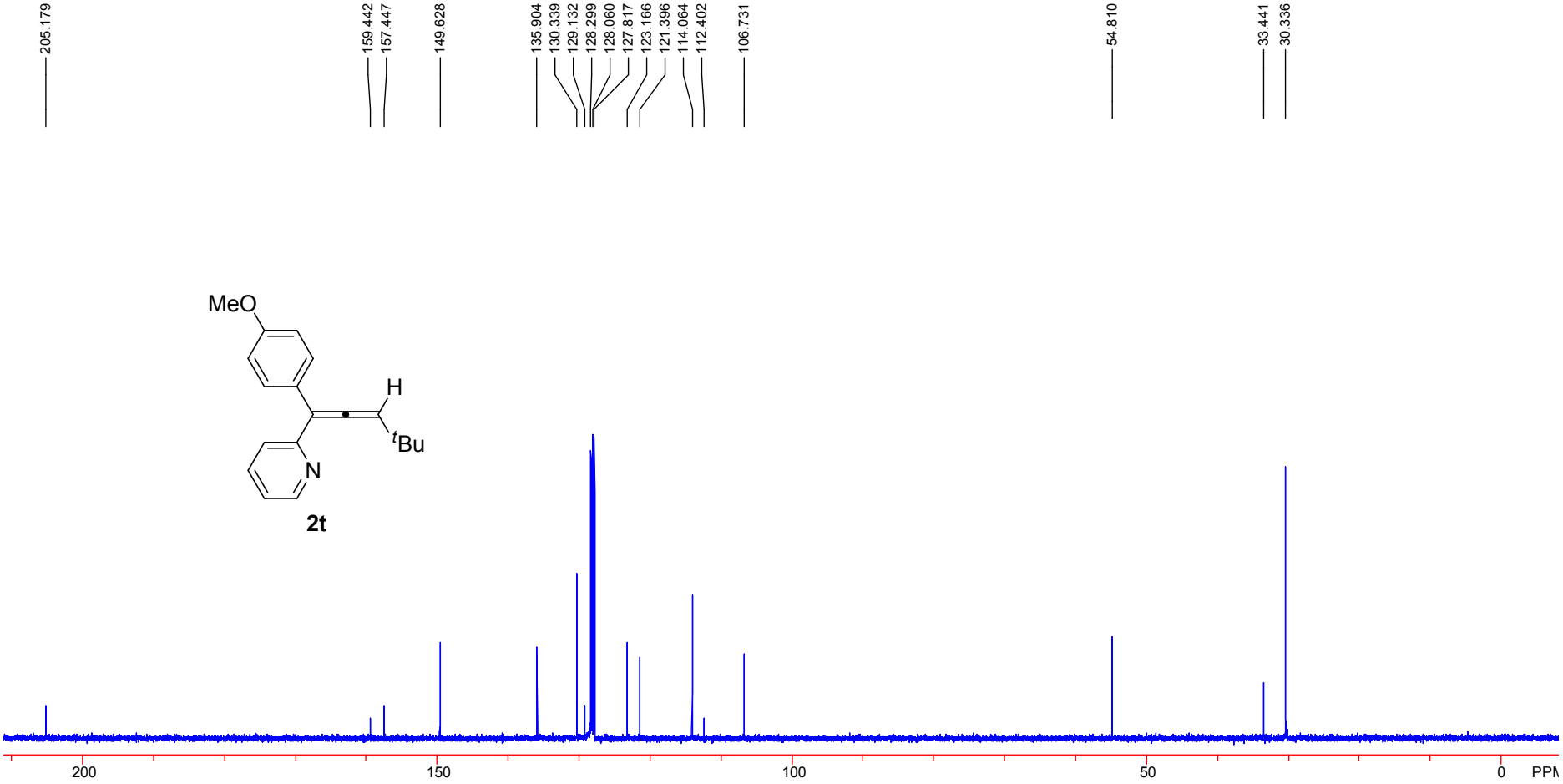
^{13}C NMR (100 MHz, C_6D_6)



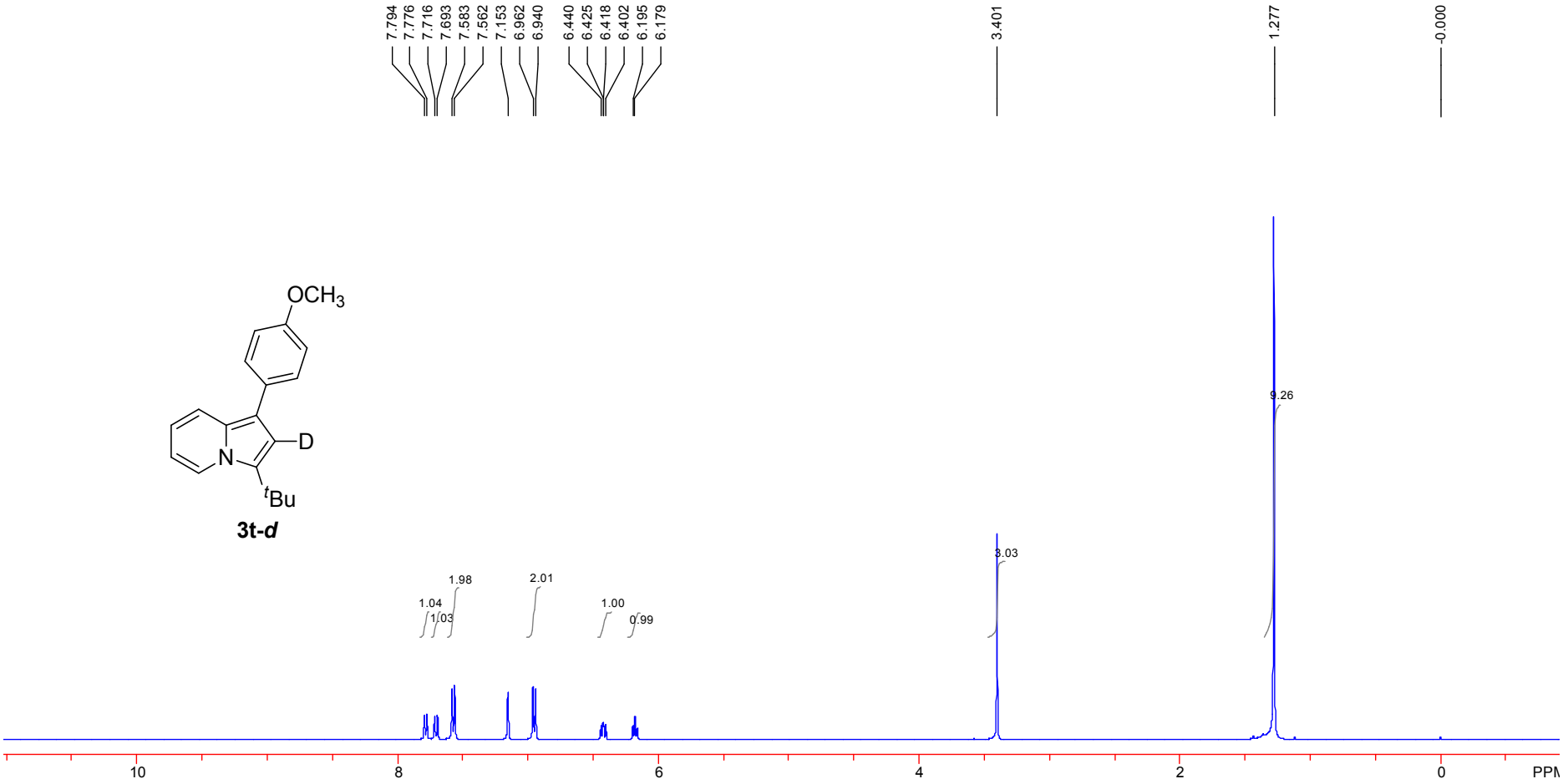
^{1}H NMR (400 MHz, C_6D_6)



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



^{1}H NMR (400 MHz, C_6D_6)



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