Electronic Supplementary Information

IBX mediated reaction of *β*-enamino esters with allylic alcohols: A one pot metal free domino approach to functionalized pyridines

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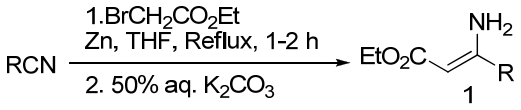
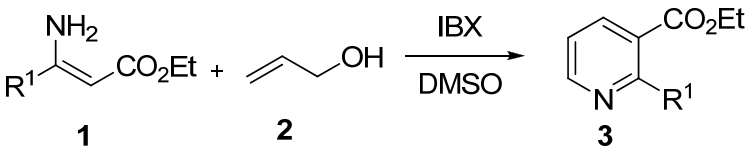
General methods: All reactions were performed in oven-dried glassware and were stirred with Teflon-coated magnetic stirring bars. All solvents were distilled prior to use. Thin layer chromatography was performed using Merck Silica gel 60 F-254 precoated plates (0.25 mm) and visualized by UV irradiation. Silica gel from Merck (particle size 230-400 mesh) was used for flash chromatography. The ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ and the ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ with TMS as internal standard. All coupling constants (J values) were reported in Hertz (Hz).Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR). Data for ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, and number of hydrogens). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), Infrared spectra were recorded on a FT- IR spectrometer and reported in frequency of absorption (cm^{-1}). Only selected IR absorbencies are reported. MS spectra were obtained on a Agilent 6430 series Triple Quard LC-MS / MS spectrometer

General Procedure for Synthesis of *β*-enamino esters 1.[1,2]



To the activated zinc dust (1.31 g, 20 mmol) was added trimithylsilylchloride (3 drops) in dry THF (10 mL) under nitrogen. The mixture was heated to reflux for 10 min and then nitrile (10 mmol) was added all at once. While maintaining the refluxing temperature, ethyl bromoacetate (1.65 mL, 15 mmol in 5 mL THF) was added to the mixture over a period of 1h, and the reaction mixture was further heated to reflux for 1 h. After complete conversion of nitrile, the reaction mixture was cooled to room temperature, quenched with saturated aqueous K_2CO_3 and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography to get *β*-enamino ester.

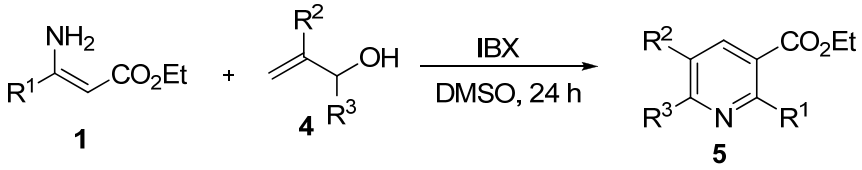
General Procedure for Synthesis of 2–substituted nicotinic esters 3.



1 2 3

A mixture of *β*-enamino ester **1** (0.2 mmol), allyl alcohol **2** (2 equiv.) and IBX (1.2 equiv.) in DMSO (3 mL) was stirred at 70-110 ˚C for 3-12 h (see Table 2). After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature, quenched with sat. $NaHCO_3$ solution (1.5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under low vacuum. The crude compound was purified by using flash chromatography (EtOAc/Hexane).

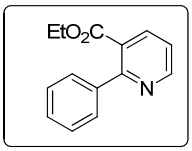
General procedure for the synthesis of unsymmetrical tetra substituted pyridines from substituted allylic alcohols.



1 4 5

A mixture of *β*-enamino ester **1** (0.1 mmol), allyl alcohol **4** (1.1 equiv.) and IBX (1.2 equiv.) in DMSO (3 mL) was stirred at room temperature for 24h (see Table 3). After completion of the reaction (monitored by TLC), the mixture was quenched with sat. $NaHCO_3$ solution (1.5 mL) and extracted with EtOAc (3 x 4 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under low vacuum. The crude compound was purified by using flash chromatography (EtOAc/Hexane).

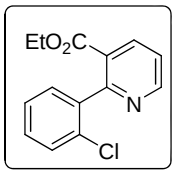
Ethyl 2-phenylnicotinate (3a):



Yellow oil, $\mathbf{R_f}$ = 0.5 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.77 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.10 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.57-7.52 (m, 2H), 7.47-7.40 (m, 3H), 7.34 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 1.04 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz,

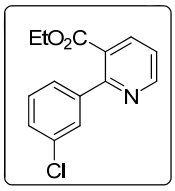
$CDCl_3$) δ ppm 168.1, 158.8, 151.1, 140.2, 137.8, 128.5, 128.5, 128.0, 127.40, 121.5, 61.4, 13.6; **IR** (cm^{-1}): 3053, 2982, 1721, 1565, 1433, 1368, 1053, 754; **MS (ES mass) m/z**: 228.1[M + 1].

Ethyl 2-(2-chlorophenyl)nicotinate (3b):



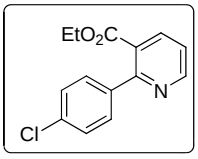
Dark yellow oil, $\mathbf{R_f}$ = 0.4 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.82 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.34 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.47-7.32 (m, 5H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.04 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 165.9, 157.4, 151.7, 139.9, 138.1, 132.2, 130.0, 129.3, 128.8, 127.3, 126.6, 122.5, 61.3, 13.4; **IR** (cm^{-1}): 3053, 2980, 1721, 1562, 1431, 1368, 1138, 1052, 774; **MS (ES mass) m/z**: 262.0 [M + 1].

Ethyl 2-(3-chlorophenyl)nicotinate (3c):



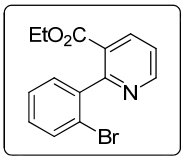
Dark yellow oil, $\mathbf{R_f}$ = 0.35 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.77 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.14 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.54 (s, 1H), 7.42-7.35 (m, 4H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.5, 157.3, 151.2, 141.8, 138.0, 134.0, 129.2, 128.7, 128.6, 127.2, 126.7, 122.0, 61.6, 13.6; **IR** (cm^{-1}): 3053, 2982, 1723, 1585, 1433, 1368, 1050, 774; **MS (ES mass) m/z**: 262.1[M + 1].

Ethyl 2-(4-chlorophenyl)nicotinate (3d):



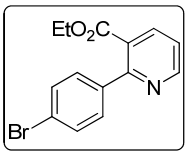
Brownish yellow gum, $\mathbf{R_f}$ = 0.45 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.76 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.12 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.35 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.6, 157.5, 151.1, 138.5, 137.9, 134.7, 129.9, 128.2, 127.1, 121.8, 61.5, 13.6; **IR** (cm^{-1}): 3052, 2981, 1724, 1584, 1434, 1282, 1136, 1051, 781; **MS (ES mass) m/z:** 262.1[M + 1].

Ethyl 2-(2-bromophenyl)nicotinate (3e):



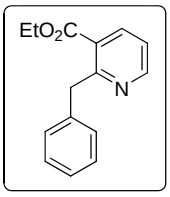
Pale yellow solid, m.p: 55-57 °C; $\mathbf{R_f}$ = 0.33 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.82 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.35 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.45-7.35 (m, 3H), 7.26 (dd, *J* = 6.7, 2.4 Hz, 1H), 4.2-4.07 (m, 2H), 1.03 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 165.9, 159.0, 151.7, 142.0, 138.3, 132.1, 129.9, 129.4, 127.1, 127.1, 122.6, 122.0, 61.3, 13.5; **IR** (cm^{-1}): 3052, 2982, 1722, 1585, 1430, 1388, 1060, 764; **MS (ES mass) m/z:** 306.0[M + 1].

Ethyl 2-(4-bromophenyl)nicotinate (3f):



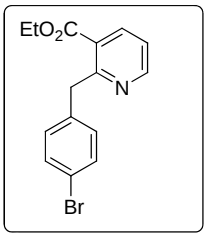
Pale yellow oil; $\mathbf{R_f}$ = 0.3 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.76 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.13 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.36 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.6, 157.7, 151.3, 139.1, 138.0, 131.2, 130.2, 127.1, 123.0, 121.8, 61.6, 13.7; **IR** (cm^{-1}): 3050, 2981, 1723, 1583, 1429, 1393, 1132, 1050, 768; **MS (ES mass) m/z:** 306.0[M + 1].

Ethyl 2-benzylnicotinate (3g):



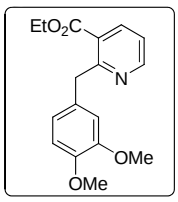
Yellow oil, $\mathbf{R_f}$ = 0.2 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.68 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.16 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.27-7.21 (m, 5H), 7.18-7.11 (m, 1H), 4.59 (s, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.33 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.5, 161.1, 151.8, 139.6, 138.5, 128.9, 128.2, 126.1, 126.0, 121.2, 61.4, 42.3, 14.1; **IR** (cm^{-1}): 3053, 2982, 1721, 1565, 1433, 1368, 1052, 728; **MS (ES mass) m/z:** 242.1[M + 1].

Ethyl 2-(4-bromobenzyl)nicotinate (3h):



Pale yellow oil, $\mathbf{R_f}$ = 0.23 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, *$CDCl_3$*) δ ppm 8.68 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.19 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.25 (dd, *J* = 7.7, 4.6 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 2H), 4.52 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.3, 160.7, 152.0, 138.7, 138.6, 131.2, 130.7, 125.9, 121.4, 120.0, 61.4, 41.7, 14.1; **IR** (cm^{-1}): 3056, 2980, 1722, 1573, 1482, 1368, 1273, 1079, 762; **MS (ES mass) m/z:** 320.0[M + 1].

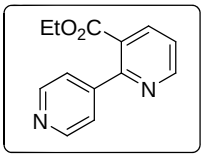
Ethyl 2-(3,4-dimethoxybenzyl)nicotinate (3i):



Yellow oil, $\mathbf{R_f}$ = 0.35 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.68 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.16 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.81 Hz, 1H), 6.87 (s, 1H), 6.82-6.73 (m, 2H), 4.52 (s, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 6H), 1.35 (t, *J* = 7.1 Hz, 3H);

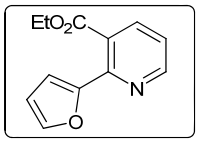
^{13}C NMR (100 MHz, *$CDCl_3$*) δ ppm 166.5, 161.4, 151.8, 148.6, 147.3, 138.5, 132.2, 126.0, 121.1, 120.9, 112.4, 111.0, 61.4, 55.8, 55.7, 41.7, 14.1; **IR** (cm^{-1}): 3050, 2982, 1721, 1565, 1493, 1368, 1050, 1078, 754; **MS (ES mass) m/z:** 302.1[M + 1].

Ethyl 2,4'-bipyridine-3-carboxylate (3j):



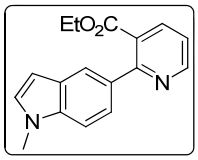
Brown oil, **R_f** = 0.2 (50% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.80 (dd, *J* = 4.6, 1.3 Hz, 1H), 8.68 (d, *J* = 5.5 Hz, 2H), 8.20 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.43 (dd, *J* = 6.6, 2.5 Hz, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.08 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.9, 156.5, 151.5, 149.4, 147.9, 138.3, 127.1, 123.2, 122.8, 61.7, 13.5; **IR** (cm^{-1}): 3044, 2982, 1723, 1574, 1434, 1368, 1057, 777; **MS (ES mass) m/z:** 229.1[M + 1].

Ethyl 2-(furan-2-yl)nicotinate (3k):



Dark brown oil, **R_f** = 0.5 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.68 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.89 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.53 (d, *J* = 0.9 Hz, 1H), 7.24 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.54 (dd, *J* = 3.4, 1.7 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H) **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 168.2, 152.3, 150.7, 146.7, 143.7, 136.8, 126.0, 121.3, 111.9, 111.1, 61.7, 14.1; **IR** (cm^{-1}): 3128, 3047, 2982, 1728, 1584, 1487, 1287, 1052, 776; **MS (ES mass) m/z:** 218.1[M + 1].

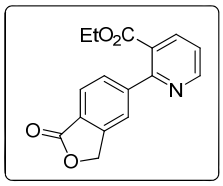
Ethyl 2-(1-methyl-1H-indol-5-yl)nicotinate (3l):



Yellow oil, **R_f** = 0.42 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.77 (dd, *J* =

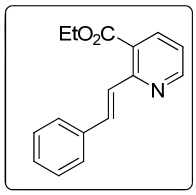
4.8, 1.7 Hz, 1H), 8.04 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.84 (d, *J* = 1.1 Hz, 1H), 7.46 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.32-7.27 (m, 1H), 7.08 (d, *J* = 3.1 Hz, 1H), 6.53 (t, *J* = 4.2 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 159.6, 150.8, 137.5, 136.9, 131.3, 129.4, 128.4, 127.5, 122.5, 121.5, 120.5, 108.8, 101.7, 61.3, 32.9, 13.7; **IR** (cm^{-1}): 3100, 3044, 2970, 1721, 1574, 1430, 1368, 1285, 1093, 775; **MS (ES mass) m/z:** 281.2[M + 1].

Ethyl 2-(1-oxo-1,3-dihydroisobenzofuran-5-yl)nicotinate (3m):



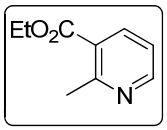
Colorless semisolid, **R_f** = 0.43 (50% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.81 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.24 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.71 (s, 1H), 7.65-7.59 (m, 1H), 7.45 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.38 (s, 2H), 4.21 (q, *J* = 7.14 Hz, 2H), 1.12 (t, *J* = 7.13 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 170.7, 166.9, 157.7, 151.5, 146.5, 146.3, 138.4, 129.9, 127.2, 125.6, 125.2, 122.6, 122.3, 69.6, 61.7, 13.7; **IR** (cm^{-1}): 3059, 2977, 1762, 1727, 1570, 1437, 1358, 1284, 1012, 771; **MS (ES mass) m/z:** 284.1[M + 1].

(E)-ethyl 2-styrylnicotinate (3n):



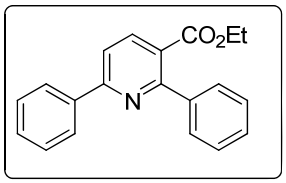
Yellow oil, **R_f** = 0.2 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.75 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.23 (dd, *J* = 7.9, 1.8 Hz, 1H), 8.18 (d, *J* = 15.7 Hz, 1H), 7.96 (d, *J* = 15.7 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.24 (dd, *J* = 7.9, 4.7 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.5, 155.2, 151.9, 138.7, 136.8, 135.9, 128.6, 128.5, 127.5, 125.0, 124.3, 121.3, 61.5, 14.3; **IR** (cm^{-1}): 3031, 2981, 1777, 1572, 1428, 1367, 1263, 1078, 775; **MS (ES mass) m/z:** 254.1[M + 1].

Ethyl 2-methylnicotinate (3o):



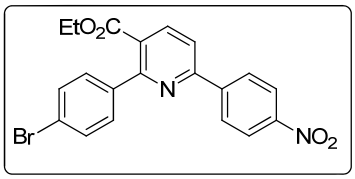
Colorless liquid, $\mathbf{R_f}$ = 0.5 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.61 (dd, *J* = 4.8, 1.62 Hz, 1H), 8.19 (dd, *J* = 7.9, 1.69 Hz, 1H), 7.21 (dd, *J* = 7.9, 4.83 Hz, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 2.84 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.5, 159.7, 151.6, 138.4, 125.7, 120.9, 61.3, 24.7, 14.2 ; **IR** (cm^{-1}): 3020, 2979, 1724, 1572, 1461, 1368, 1293, 1138, 1084; **MS (ES mass) m/z:** 166.2[M + 1].

Ethyl 2,6-diphenylnicotinate (5a):



Yellow oil, $\mathbf{R_f}$ = 0.2 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.20-8.10 (m, 3H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.64 (dd, *J* = 7.4, 2.0 Hz, 2H), 7.52-7.41 (m, 6H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.07 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 168.2, 158.7, 158.3, 140.4, 138.8, 138.2, 129.7, 128.8, 128.7, 128.5, 127.9, 127.2, 125.3, 117.8, 61.3, 13.6; **IR** (cm^{-1}): 3060, 3031, 2980, 1729, 1586, 1435, 1379, 1289,1180, 1052, 1017; **MS (ES mass) m/z:** 304.3[M + 1].

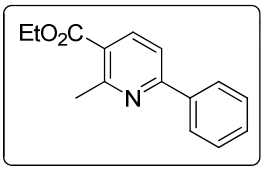
Ethyl 2-(4-bromophenyl)-6-(4-nitrophenyl)nicotinate (5b):



Colorless solid, m.p: 150-152 °C; $\mathbf{R_f}$ = 0.3 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.35 (d, *J* = 9.0 Hz, 2H), 8.31-8.25 (m, 3H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.4, 158.0, 155.9, 148.6, 143.7, 139.5, 138.8, 131.3, 130.4,

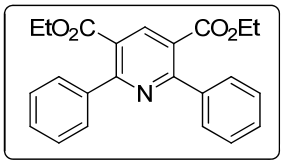
128.1, 126.5, 124.0, 123.4, 118.9, 114.0, 61.8, 13.8; **IR** (cm^{-1}): 3079, 2980, 2853, 1723, 1581, 1445, 1343, 1278, 1107, 1053; **MS (ES mass) m/z:** 427.1[M + 1].

Ethyl 2-methyl-6-phenylnicotinate (5c):



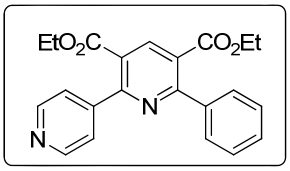
Colorless liquid, $\mathbf{R}_f$ = 0.7 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.27 (d, *J* = 8.2 Hz, 1H), 8.09-8.03 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.52-7.43(m, 3H), 4.40 (q, *J* = 7.2 Hz, 2H), 2.92 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.6, 159.9, 159.0, 139.3, 138.5, 129.6, 128.8, 127.3, 123.6, 117.3, 61.1, 25.3, 14.3; **IR** (cm^{-1}): 3063, 2980, 2872, 1721, 1583, 1452, 1381, 1266, 1152, 1075; **MS (ES mass) m/z:** 242.2[M + 1].

Diethyl 2,6-diphenylpyridine-3,5-dicarboxylate (5d):



Colorless solid, m.p: 61-63 °C; $\mathbf{R}_f$ = 0.7 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) ppm 8.55 (s, 1H), 7.67-7.61 (m, 4H), 7.46-7.41 (m, 6H), 4.20 (q, *J* = 7.1 Hz, 4H), 1.10 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.4, 159.7, 140.3, 139.3, 129.1, 128.9, 128.0, 124.8, 61.6, 13.7; **IR** (cm^{-1}): 3059, 2981, 2872, 1725, 1590, 1447, 1365, 1251, 1105, 1030; **MS (ES mass) m/z:** 376.3[M + 1].

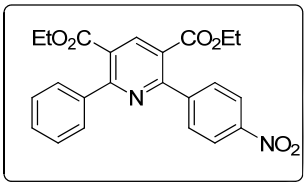
Diethyl 6-phenyl-2,4'-bipyridine-3,5-dicarboxylate (5e):



Color less solid**,** m.p: 63-65 °; $\mathbf{R}_f$ = 0.2 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*)

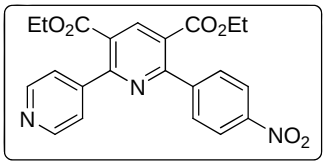
ppm 8.69 (d, *J* = 4.1 Hz, 2H), 8.61 (s, 1H), 7.63-7.58 (m, 2H), 7.50 (d, *J* = 5.7 Hz, 2H), 7.47-7.42 (m, 3H), 4.25-4.18 (m, 4H), 1.15-1.07 (m, 6H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.1, 166.1, 160.2, 157.5, 149.4, 147.2, 140.7, 138.8, 129.5, 128.9, 128.2, 126.2, 124.7, 123.4, 62.0, 61.9, 13.7; **IR** (cm^{-1}): 3060, 3030, 2981, 2855, 1726, 1590, 1447, 1367, 1249, 1105, 1024; **MS (ES mass) m/z:** 377.3 [M + 1].

Diethyl 2-(4-nitrophenyl)-6-phenylpyridine-3,5-dicarboxylate (5f):



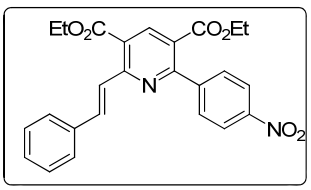
Pale Yellow solid, m.p: 88-90 °C; **R_f** = 0.25 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.65 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.67-7.58 (m, 2H), 7.50-7.43 (m, 3H), 4.3-4.2 (m, 4H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 167.1, 166.0, 160.1, 157.9, 148.0, 145.7, 140.8, 138.7, 130.0, 129.6, 128.9, 128.2, 126.1, 124.5, 123.2, 62.0, 62.0, 13.8, 13.7; **IR** (cm^{-1}): 3031, 2981, 1720, 1570, 1428, 1379, 1249, 1105, 1017; **MS (ES mass) m/z:** 421.3[M + 1].

Diethyl 6-(4-nitrophenyl)-2,4'-bipyridine-3,5-dicarboxylate (5g):



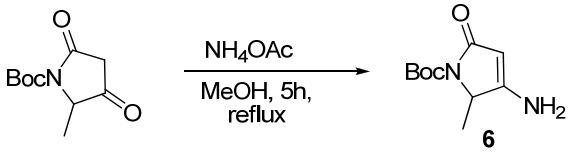
Yellow color solid, m.p: 89-91 °C; **R_f** = 0.3 (50% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.76-8.70 (m, 3H), 8.32 (d, *J* = 8.6 Hz, 2H), 7.77 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 5.6 Hz, 2H), 4.30-4.21 (m, 4H), 1.21-1.13 (m, 6H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 165.8, 165.7, 158.3, 157.9, 149.6, 148.2, 146.6, 145.0, 141.2, 130.0, 126.0, 126.0, 123.3, 123.2, 62.3, 13.8, 13.6; **IR** (cm^{-1}): 3031, 2981, 1725, 1572, 1428, 1367, 1263, 1078; **MS (ES mass) m/z:** 422.3[M + 1].

(E)-diethyl 2-(4-nitrophenyl)-6-styrylpyridine-3,5-dicarboxylate (5h):



Pale yellow solid**,** m.p: 127-129 °C; $\mathbf{R_f}$ = 0.3 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.75 (s, 1H), 8.37-8-32 (m, 2H), 8.23 (d, *J* = 15.6 Hz, 1H), 8.09 (d, *J* = 15.6 Hz, 1H) 7.79 (d, *J* = 8.7 Hz, 2H), 7.65 (d, *J* = 7.0 Hz, 2H), 7.43-7.33 (m, 3H), 4.49 (q, *J* = 7.1 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 166.1, 165.4, 158.6, 156.7, 148.0, 146.1, 141.9, 139.1, 136.2, 129.9, 129.3, 128.8, 127.9, 123.8, 123.2, 122.6, 62.0, 61.8, 14.3, 13.8; **IR** (cm^{-1}): 3050, 2981, 1719, 1573, 1448, 1347, 1236, 1089; **MS (ES mass) m/z:** 447.3[M + 1].

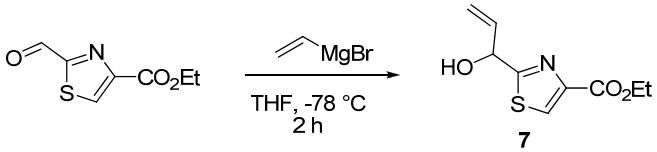
***tert*-Butyl 3-amino-2-methyl-5-oxo-2,5-dihydro-1H-pyrrole-1-carboxylate (6):**



6

To a stirred solution of *tert*-butyl 2-methyl-3,5-dioxopyrrolidine-1-carboxylate[3] (213 mg, 1 mmol) in dry MeOH (15 mL) was added NH_4OAc (385 mg, 5 mmol) under nitrogen. The mixture was heated to reflux and stirred overnight at the same temperature. After completion of the reaction the mixture was cooled to room temperature and evaporated under vacuo. The residue was dissolved in EtOAc (10 mL) and washed with saturated $NaHCO_3$ solution. The aqueous layer was further extracted with EtOAc (3 x 3 mL). The combined organic layers were collected, combined, washed with brine, dried over anhydrous Na_2SO_4, filtered and evaporated under vacuo. The residue was purified by flash chromatography using EtOAc to give the desired compound **6** (0.171 g, 80% yield) as a pale yellow solid; mp 88-90 °C; $\mathbf{R_f}$ = 0.2 (5% MeOH in DCM). **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 5.26 (brs, 2H), 4.79 (s, 1H), 4.39 (q, *J* = 6.5 Hz, 1H), 1.52 (s, 9H), 1.50 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 171.1, 167.2, 149.5, 89.6, 81.8, 56.1, 28.2, 19.0; **IR** (cm^{-1}): 3345, 3271, 2981, 1745, 1672, 1597, 1349, 1255, 1159, 1086; **MS (ES mass) m/z:** 235.2[M + Na].

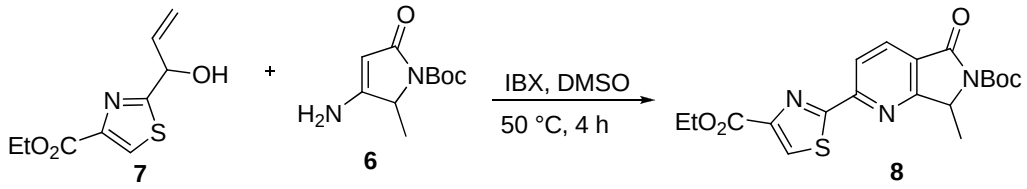
Ethyl 2-(1-hydroxyallyl)thiazole-4-carboxylate (7):



7

To a stirred solution of ethyl 2-formylthiazole-4-carboxylate[4] (0.093 g, 0.05 mmol) in THF (5 mL) at -78 °C was added vinyl magnesium bromide (0.75 mL, 1.5 eq., 1M solution in THF). The mixture was stirred for 2 h and then quenched with saturated ammonium chloride solution. Aqueous layer was further extracted with EtOAc (3 x 5 mL). The organic layers were collected, combined, washed with brine, dried over anhydrous Na_2SO_4 and filtered. After removal of EtOAc under reduced pressure, the residue was purified by flash chromatography using 8% EtOAc in hexane to give the desired compound **7** (0.081 g, 76% yield) as a yellow color oil**;** $\mathbf{R}_f$ = 0.5 (20% EtOAc in hexane); **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.15 (s, 1H), 6.22-6.08 (m, 1H), 5.60 (d, *J* = 5.6 Hz, 1H), 5.54 (d, *J* =17.1 Hz, 1H), 5.33 (d, *J* = 10.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 174.4, 161.3, 146.9, 137.1, 127.8, 117.3, 72.4, 61.5, 14.3. **IR** (cm^{-1}): 3450, 3113, 2981, 1723, 1589, 1482, 1368, 1215, 110, 1053; **MS(ES mass) m/z:** 214.2[M + 1].

Ethyl 2-(6-(tert-butoxycarbonyl)-7-methyl-5-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl)thiazole-4-carboxylate (**8**):

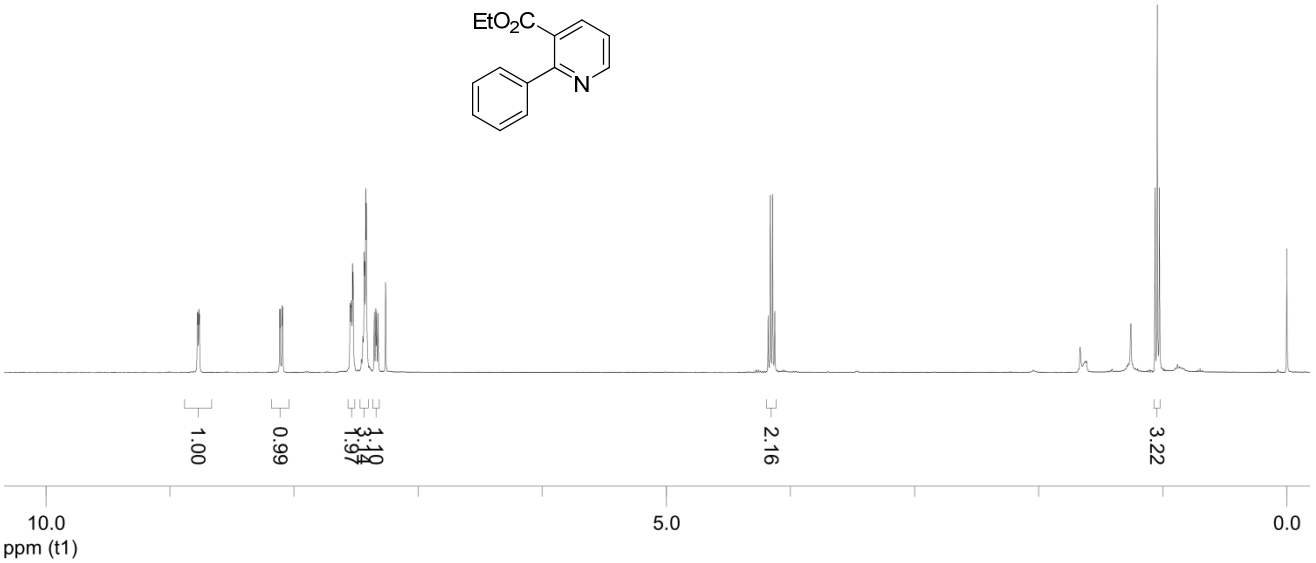


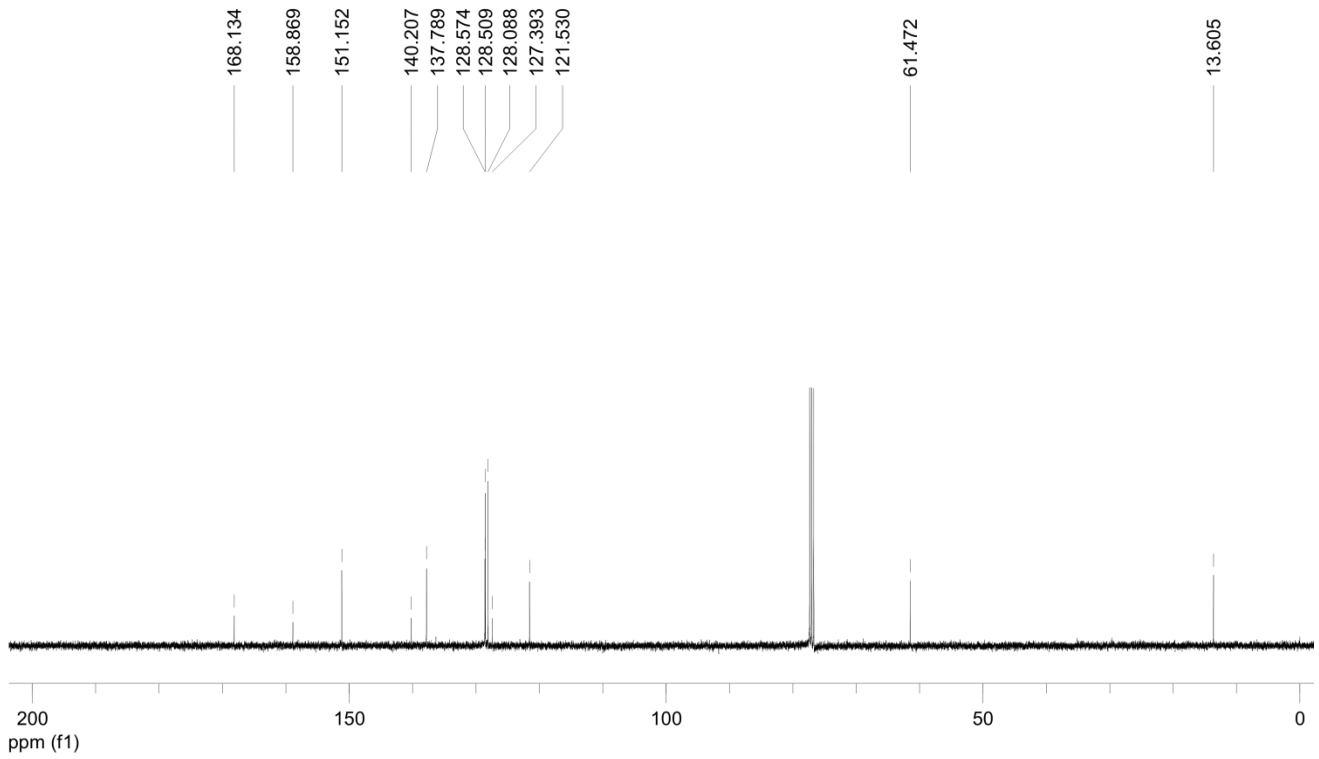
A mixture of enamine **6** (22 mg, 0.1 mmol), allyl alcohol **7** (23 mg, 0.1 mmol) and IBX (1.2 equiv.) in DMSO (2 mL) was stirred at 50 °C for 4h. After completion of the reaction (monitored by TLC), the mixture was quenched with sat. $NaHCO_3$ solution and extracted with EtOAc (3 x 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under low vacuum. The crude compound was purified by flash chromatography using 30% EtOAc in Hexane to give the desired compound **8** (0.029 g, 70% yield) as a colorless solid; mp 161-163 °C; $\mathbf{R}_f$ = 0.3 (30% EtOAc in hexane); **^{1}H NMR** (400 MHz, *$CDCl_3$*) δ ppm 8.47 (d, *J* = 8.0 Hz, 1H), 8.34 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 5.13 (q, *J* = 6.6 Hz, 1H), 4.47 (q, *J* = 7.1 Hz,

2H), 1.75 (d, *J* = 6.6 Hz, 3H), 1.63 (s, 9H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, *$CDCl_3$*) δ ppm 168.2, 165.8, 164.2, 161.1, 154.9, 149.7, 148.8, 134.3, 130.5, 125.0, 120.4, 83.6, 61.6, 57.8, 28.1, 18.8, 14.3; **IR** (cm^{-1}): 2979, 2926, 2851, 1780, 1740, 1721, 1595, 1369, 1208, 1159, 1099, 1015; **MS (ES mass) m/z:** 404.3[M + 1].

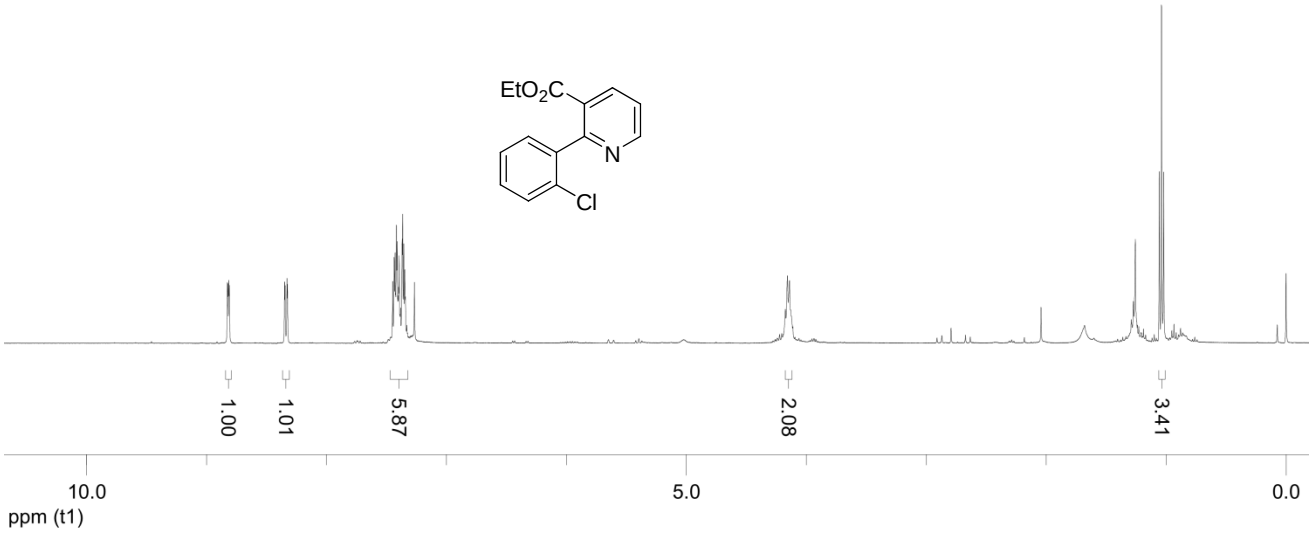
Copies of HMR spectra

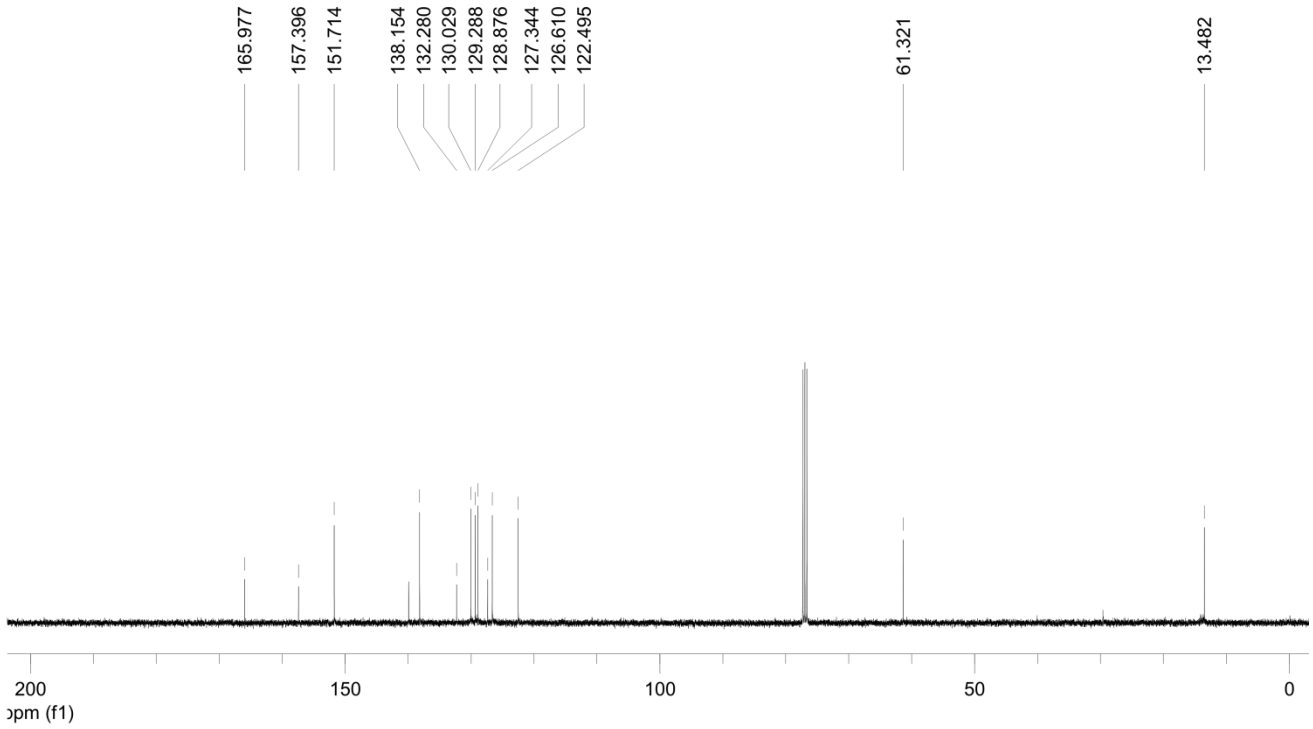
^{1}H & ^{13}C NMR Spectrum of **3a**



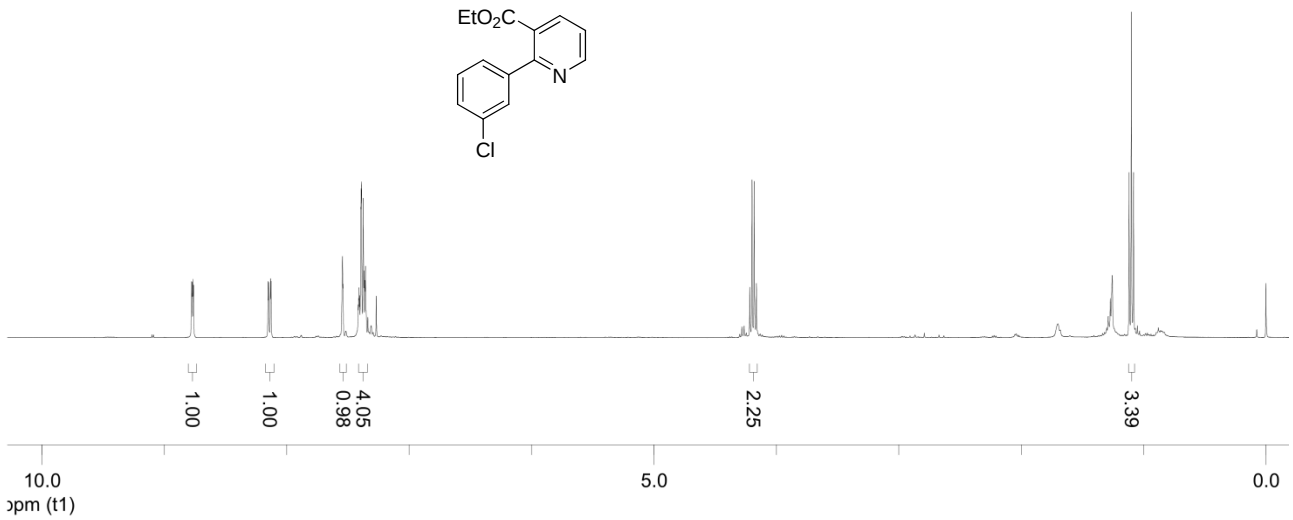


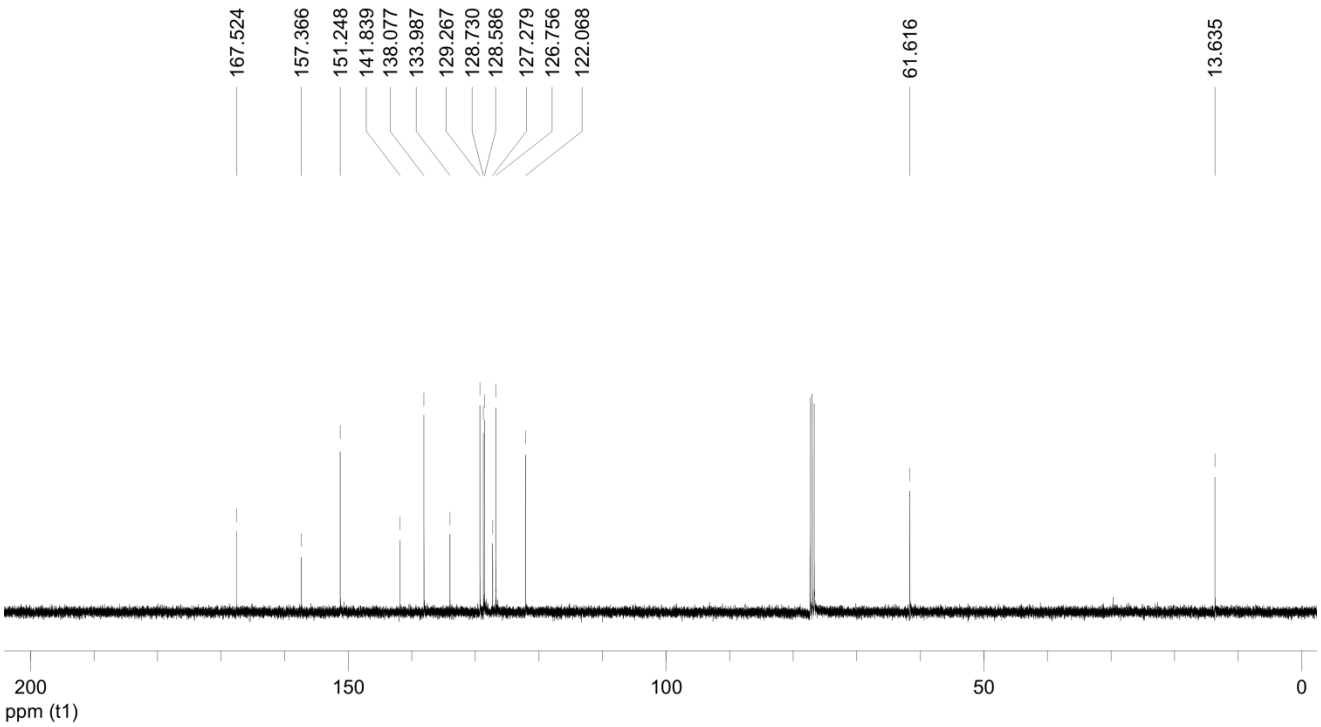
^{1}H & ^{13}C NMR Spectrum of **3b**



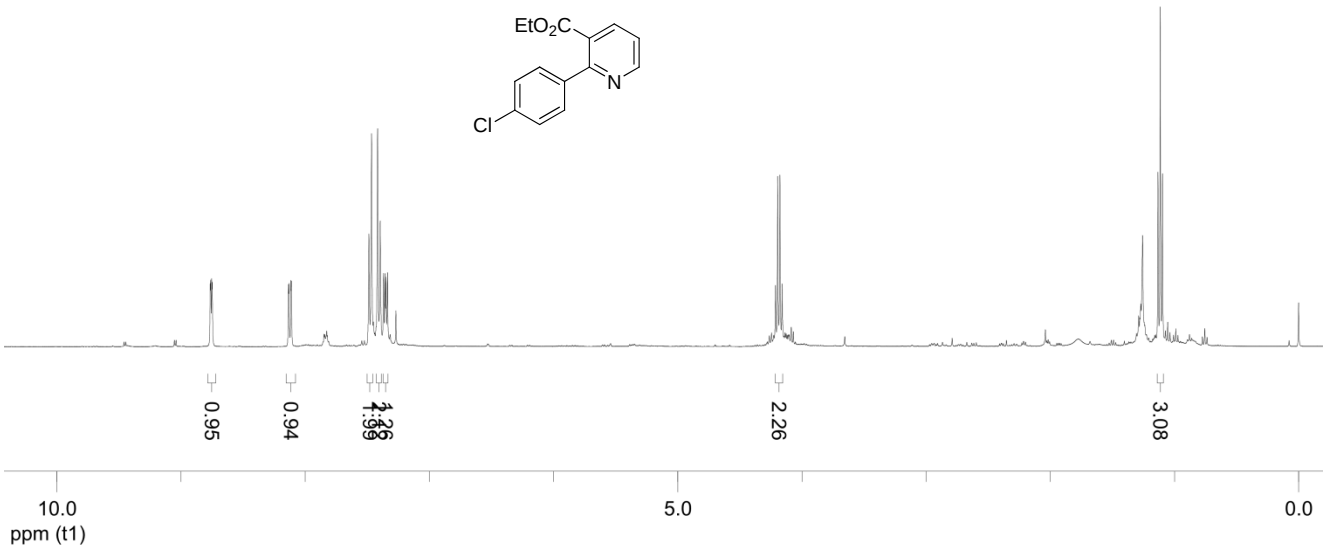


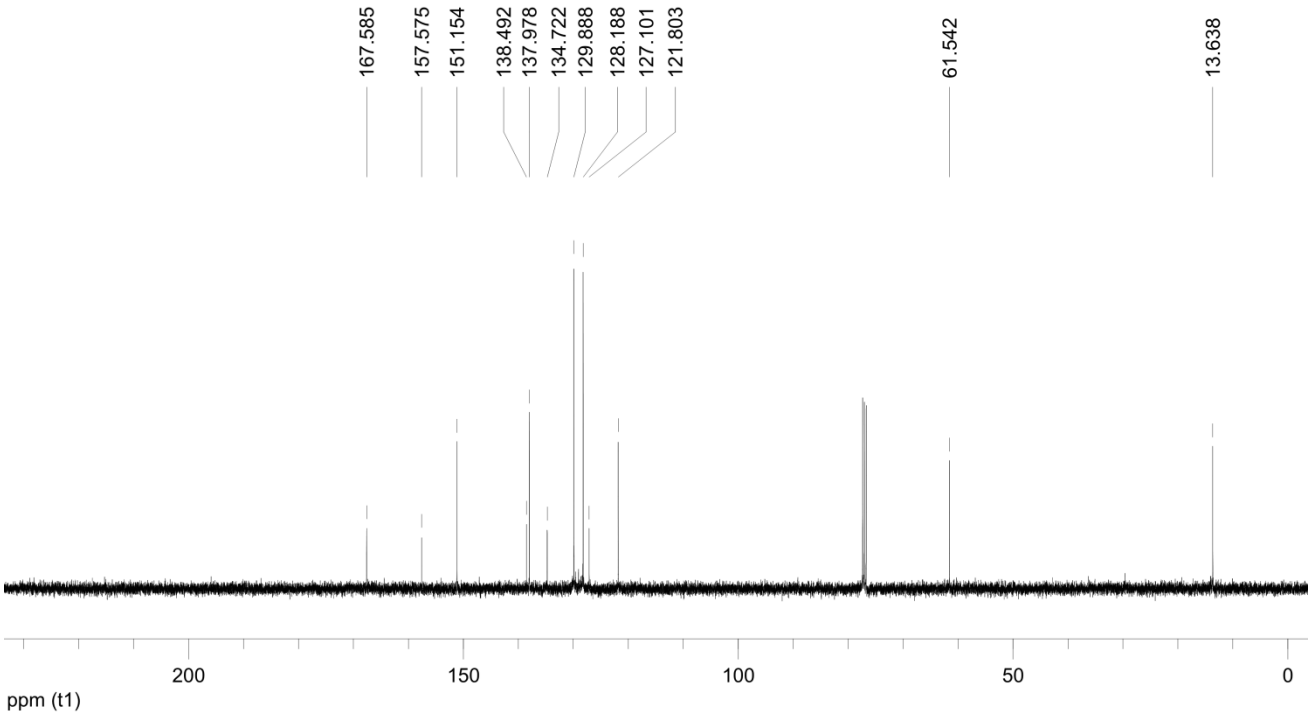
^{1}H & ^{13}C NMR Spectrum of **3c**



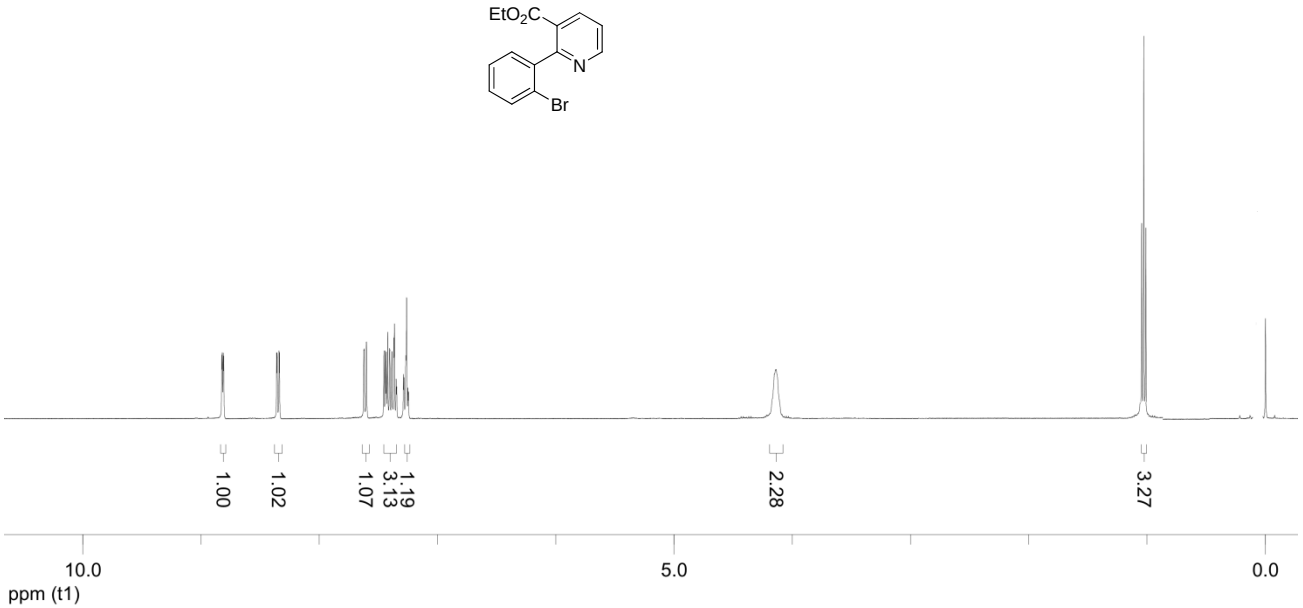


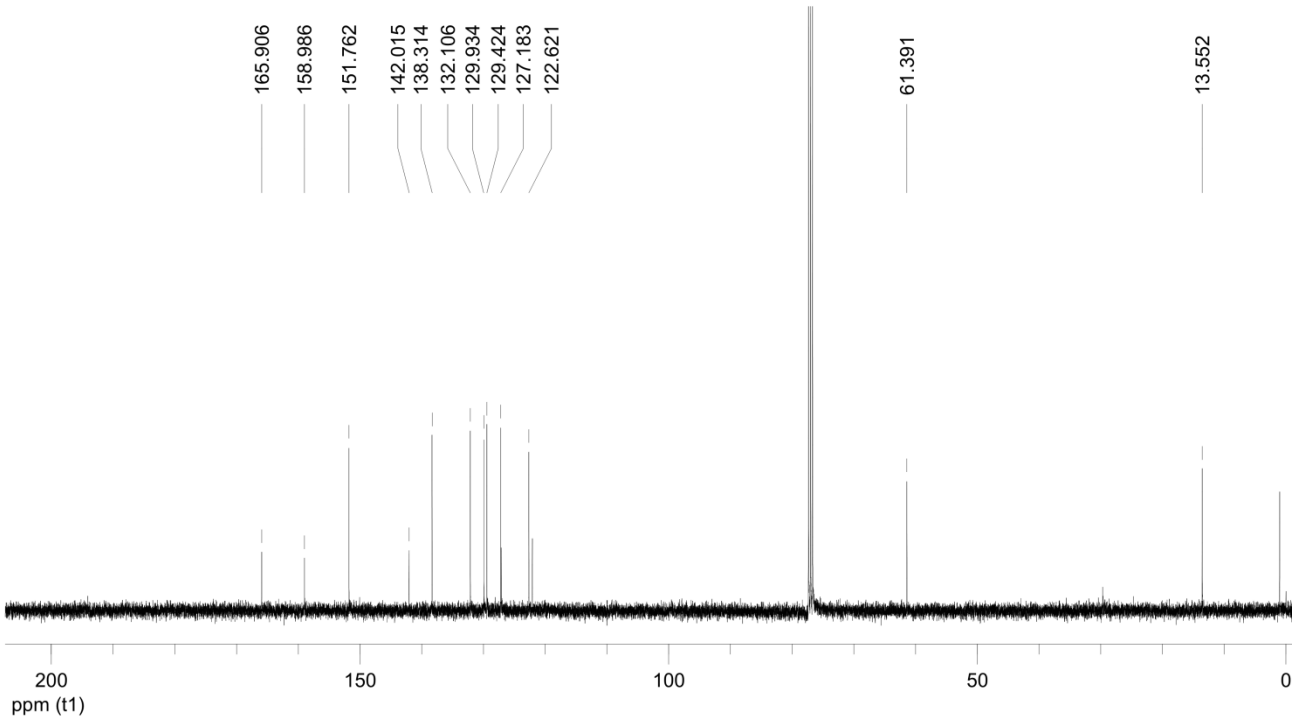
^{1}H & ^{13}C NMR Spectrum of **3d**



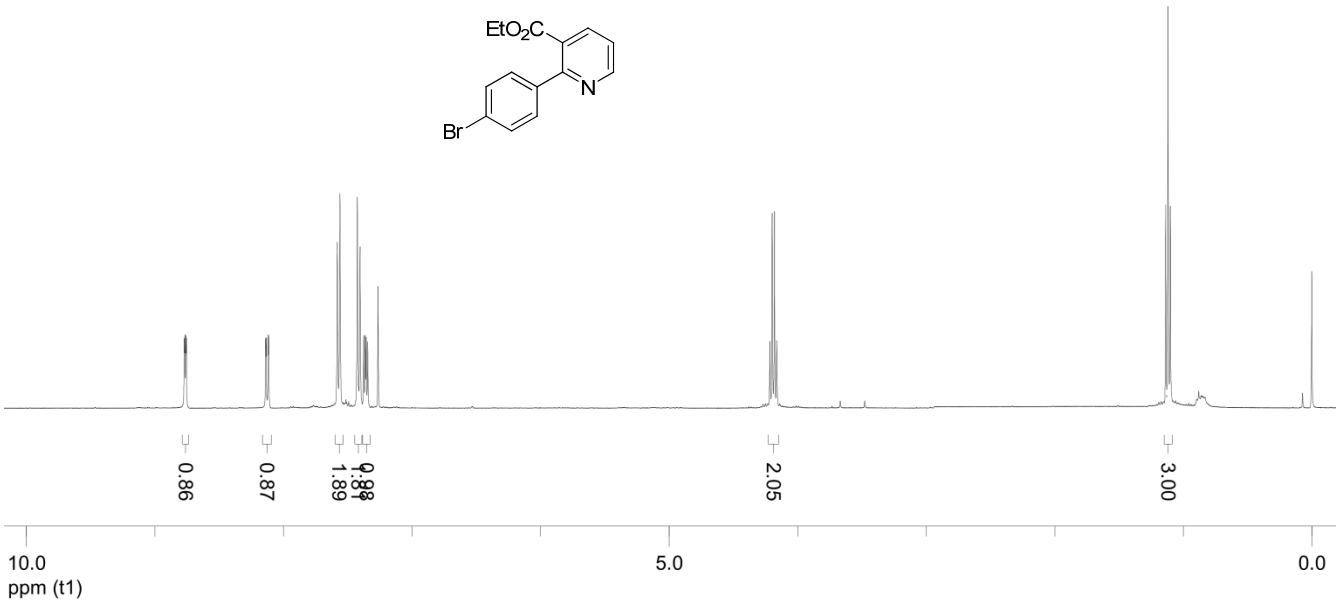


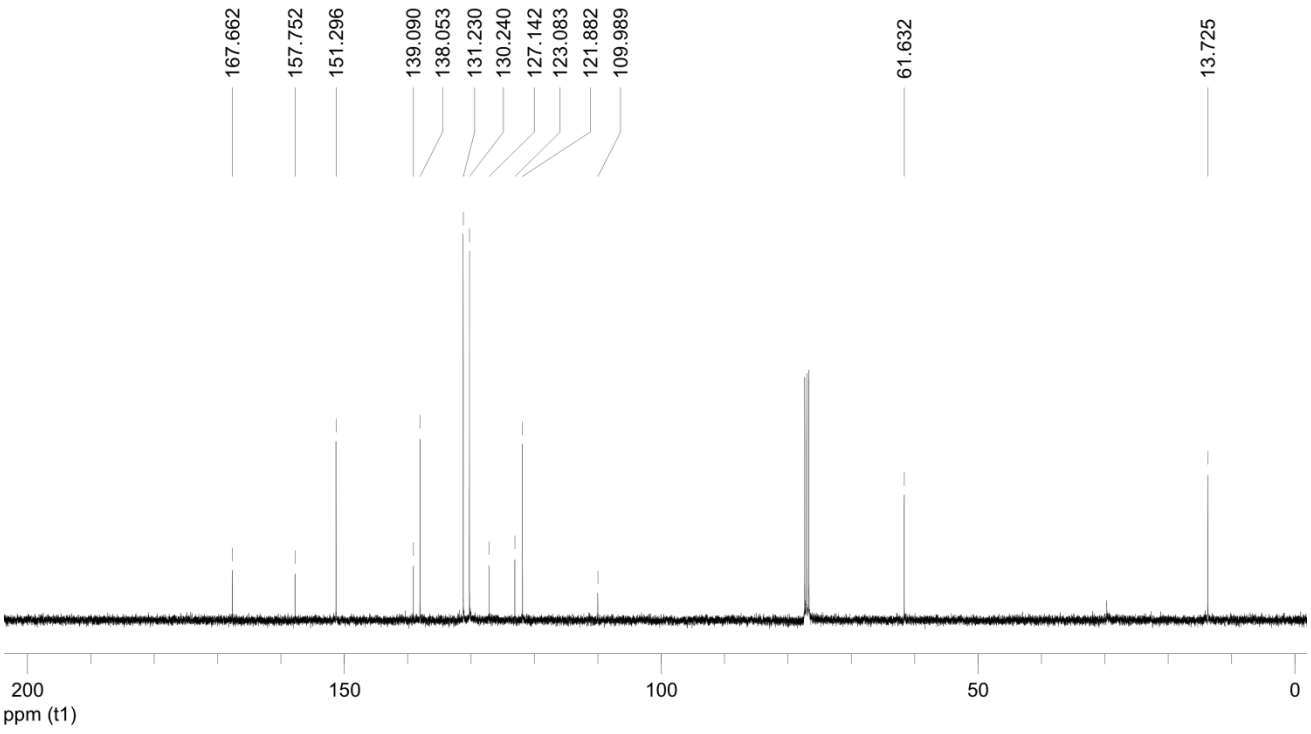
^{1}H & ^{13}C NMR Spectrum of **3e**



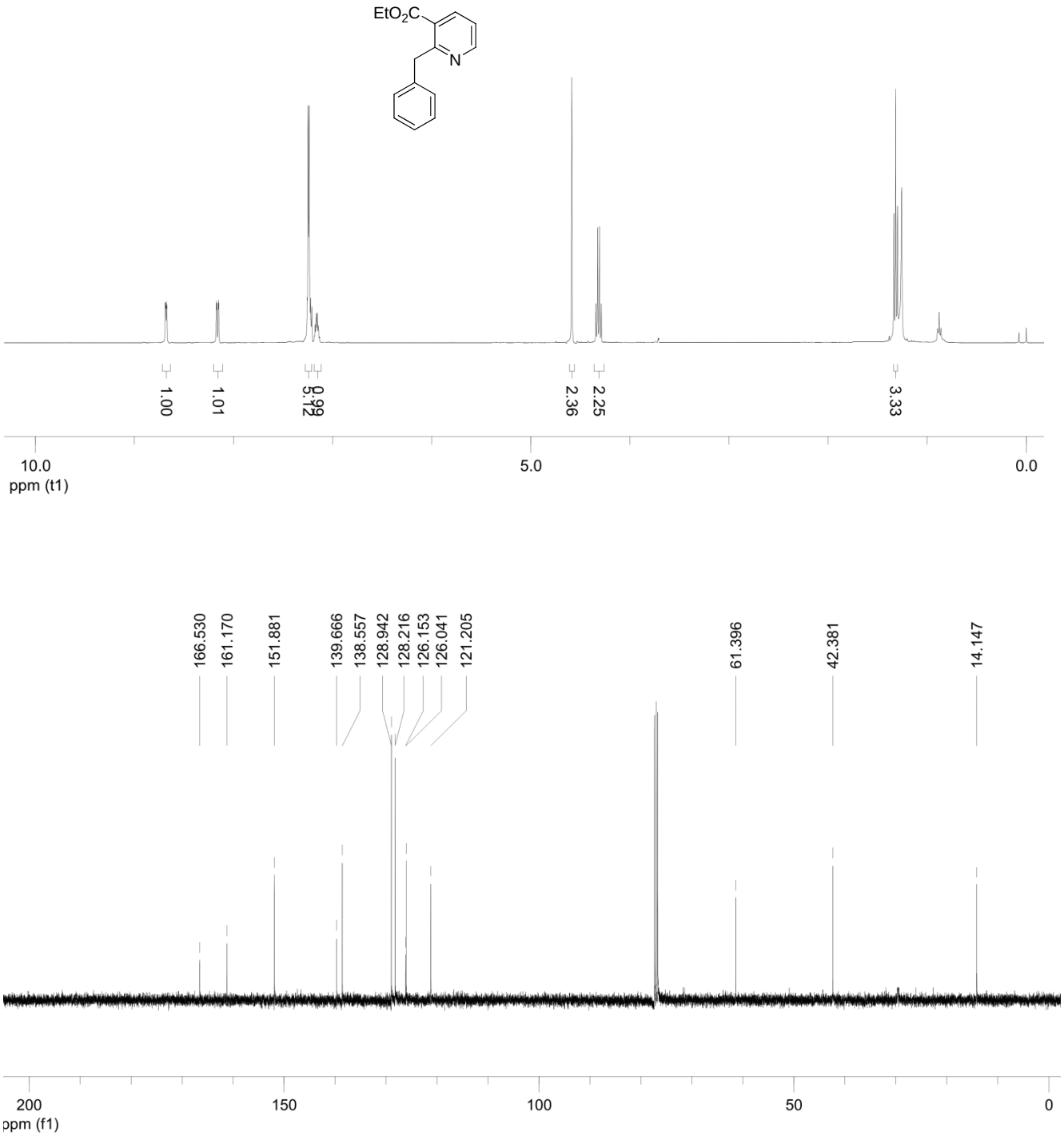


^{1}H & ^{13}C NMR Spectrum of **3f**

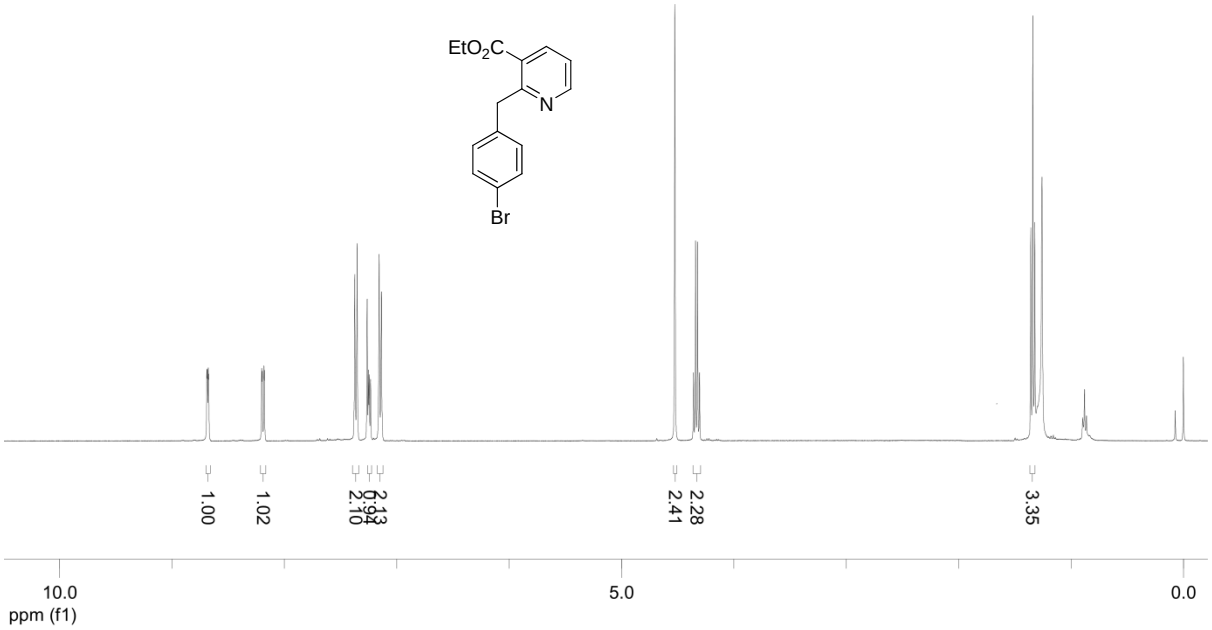


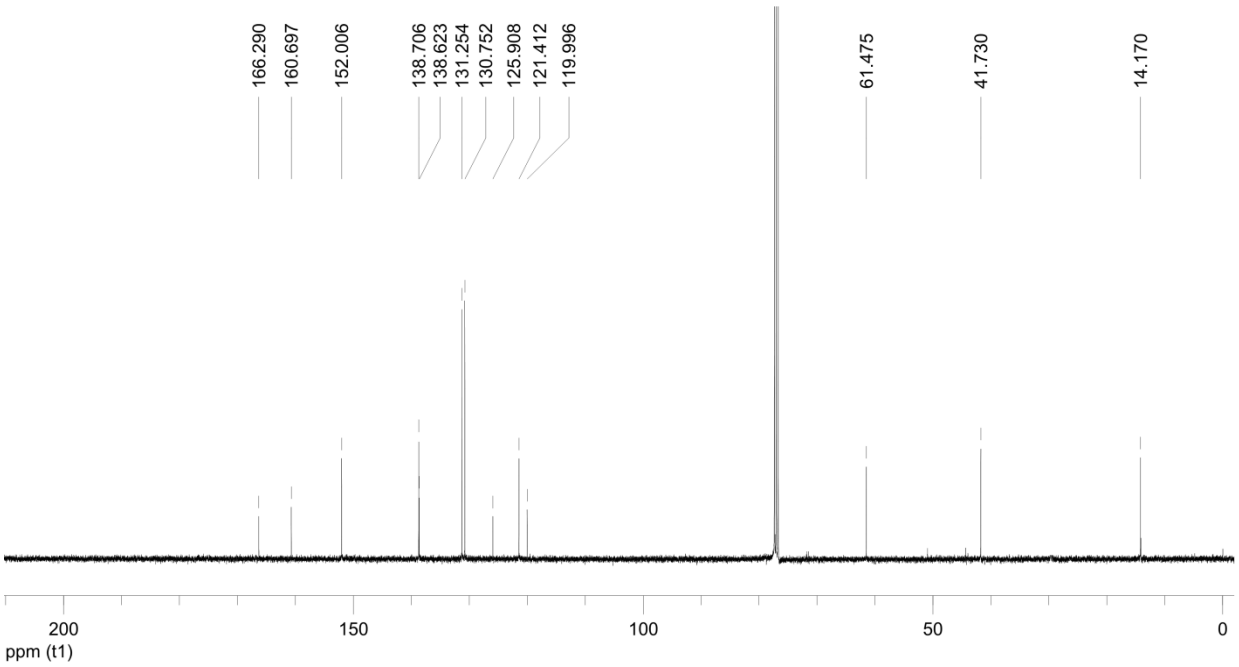


^{1}H & ^{13}C NMR Spectrum of **3g**



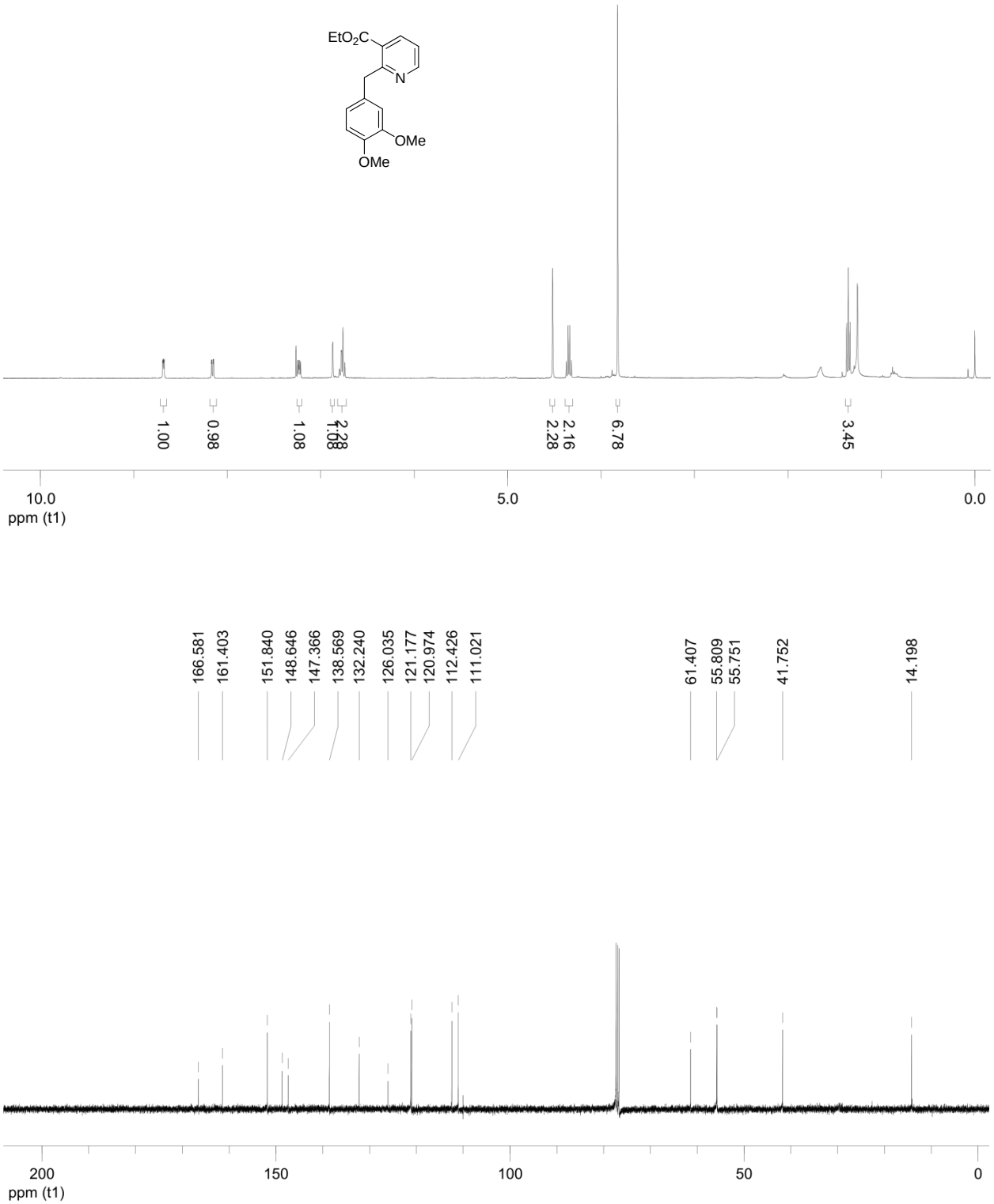
^{1} H & ^{13}C NMR Spectrum of **3h**



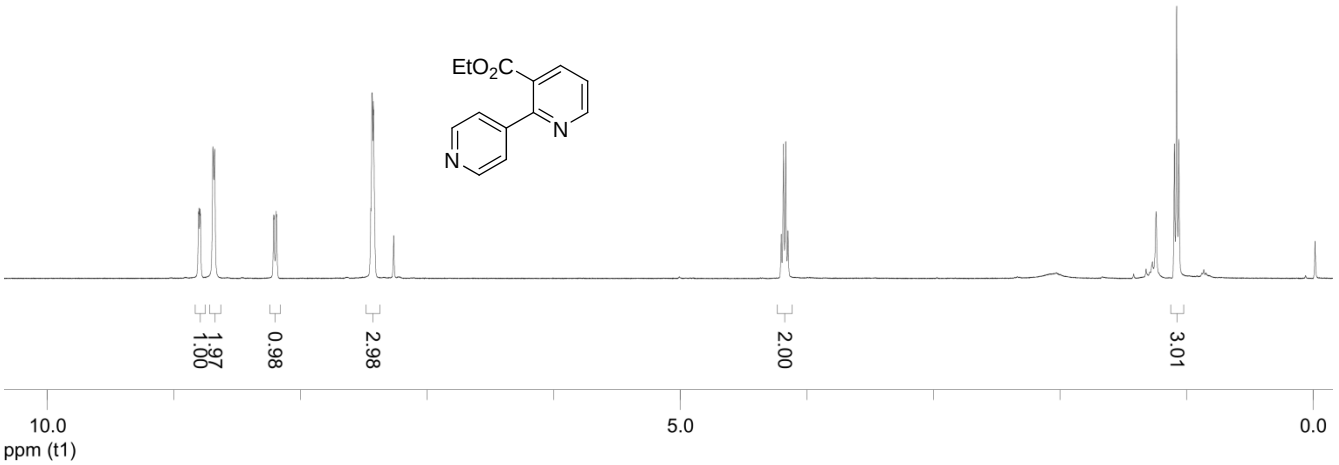


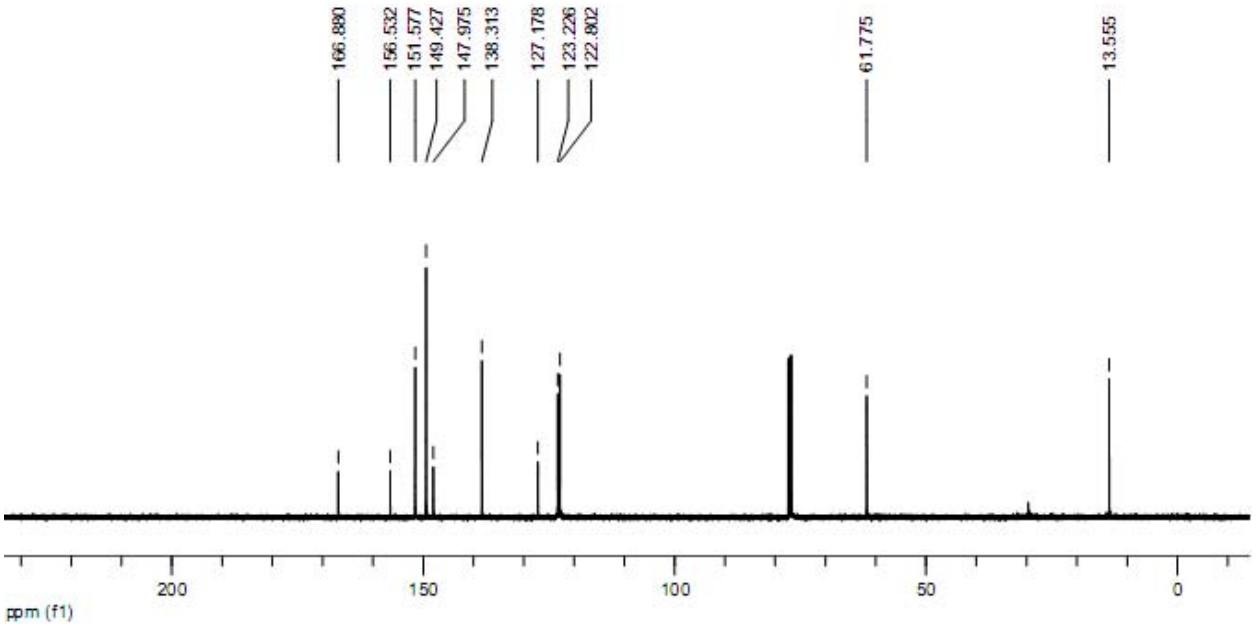
S22

^{1} H & ^{13}C NMR Spectrum of **3i**

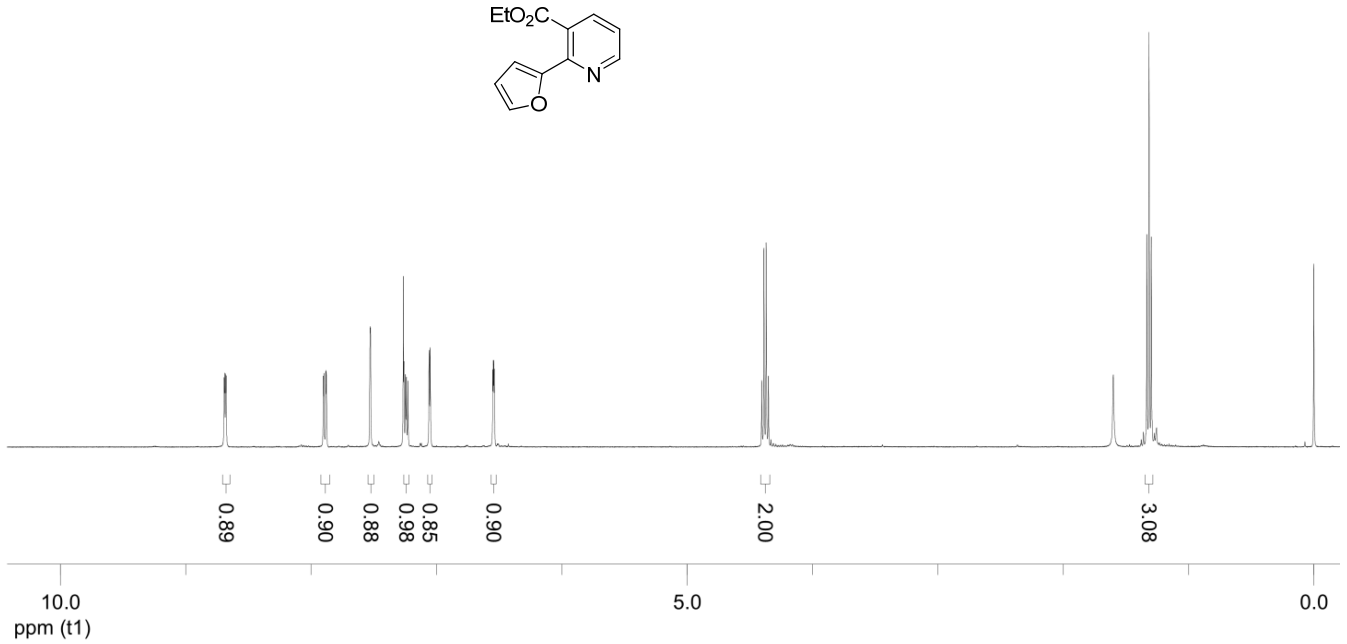


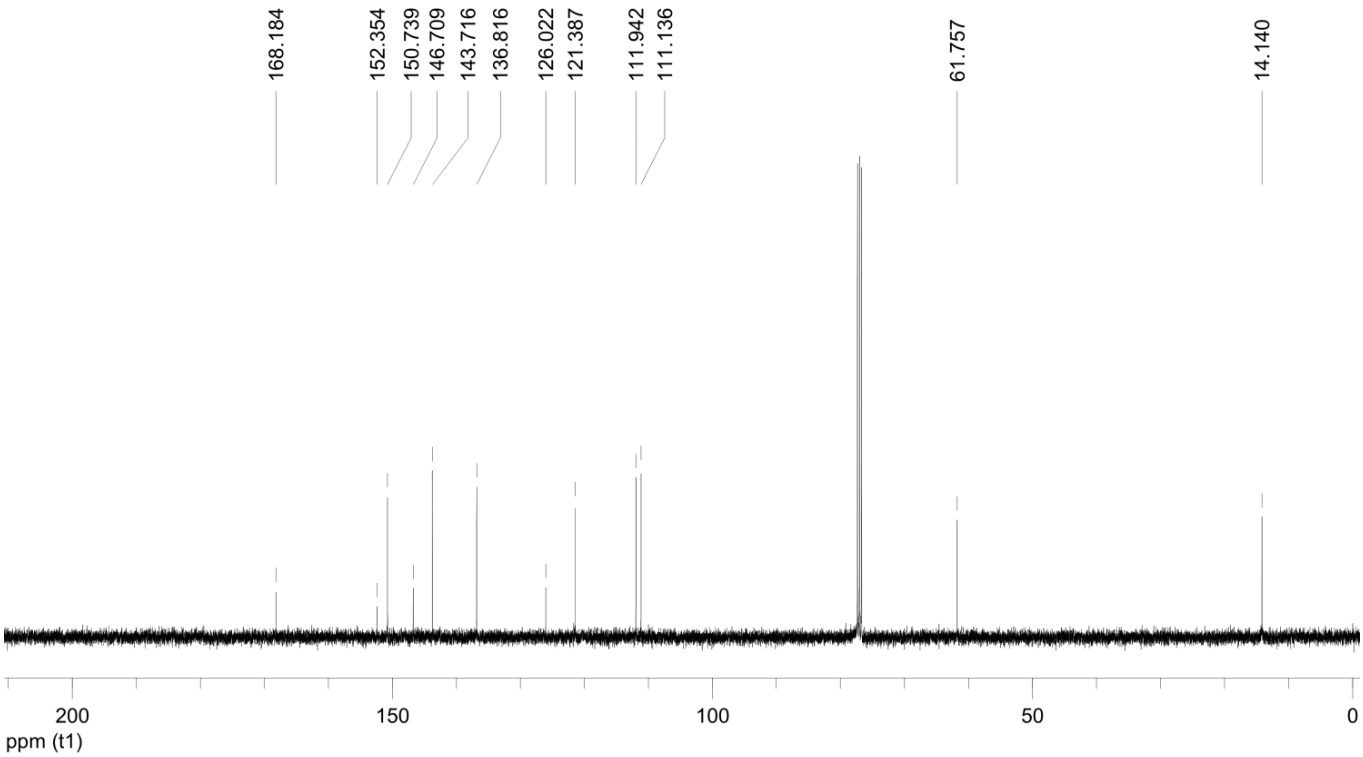
^{1}H & ^{13}C NMR Spectrum of **3j**



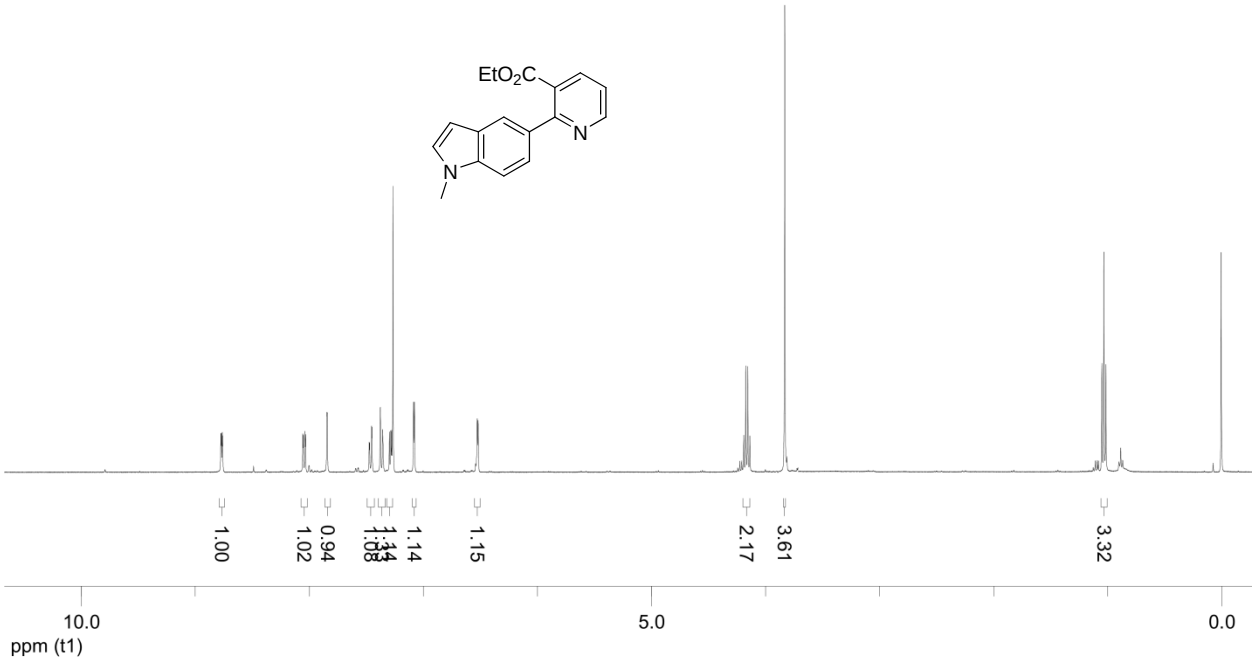


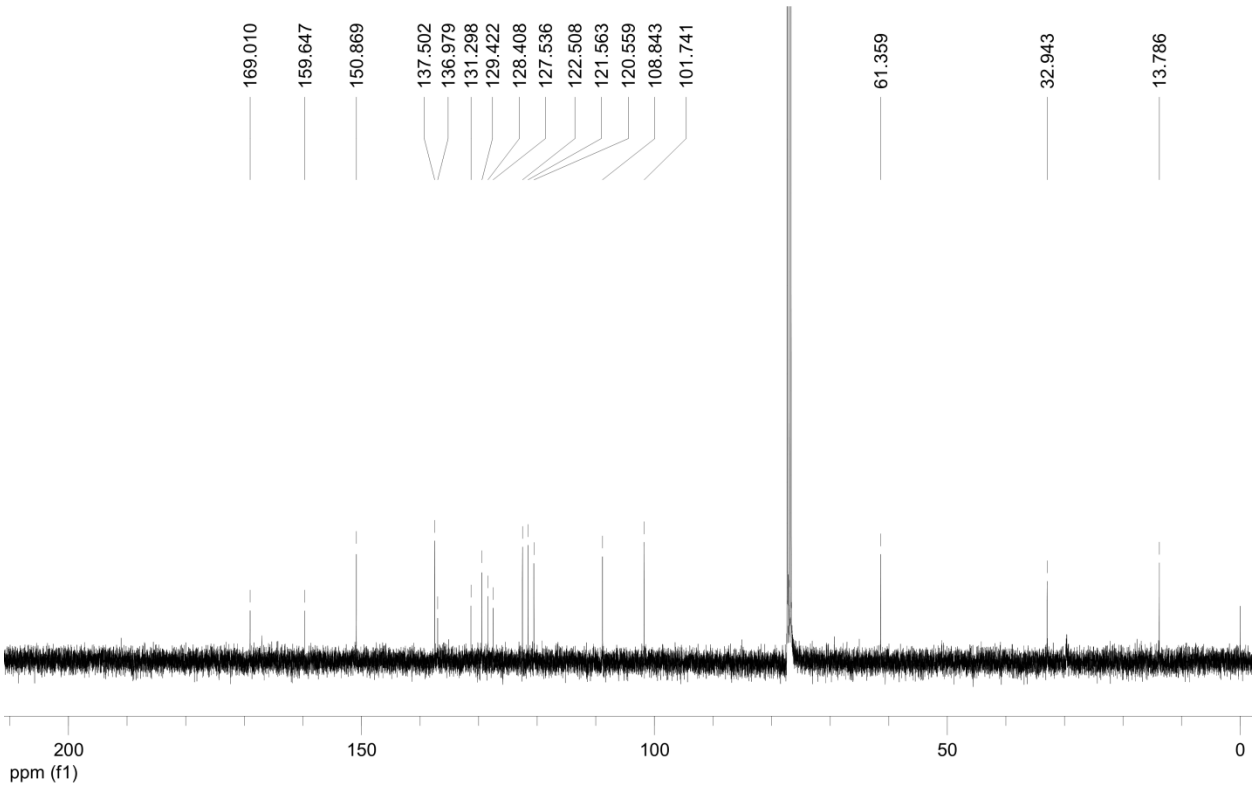
^{1}H & ^{13}C NMR Spectrum of **3k**



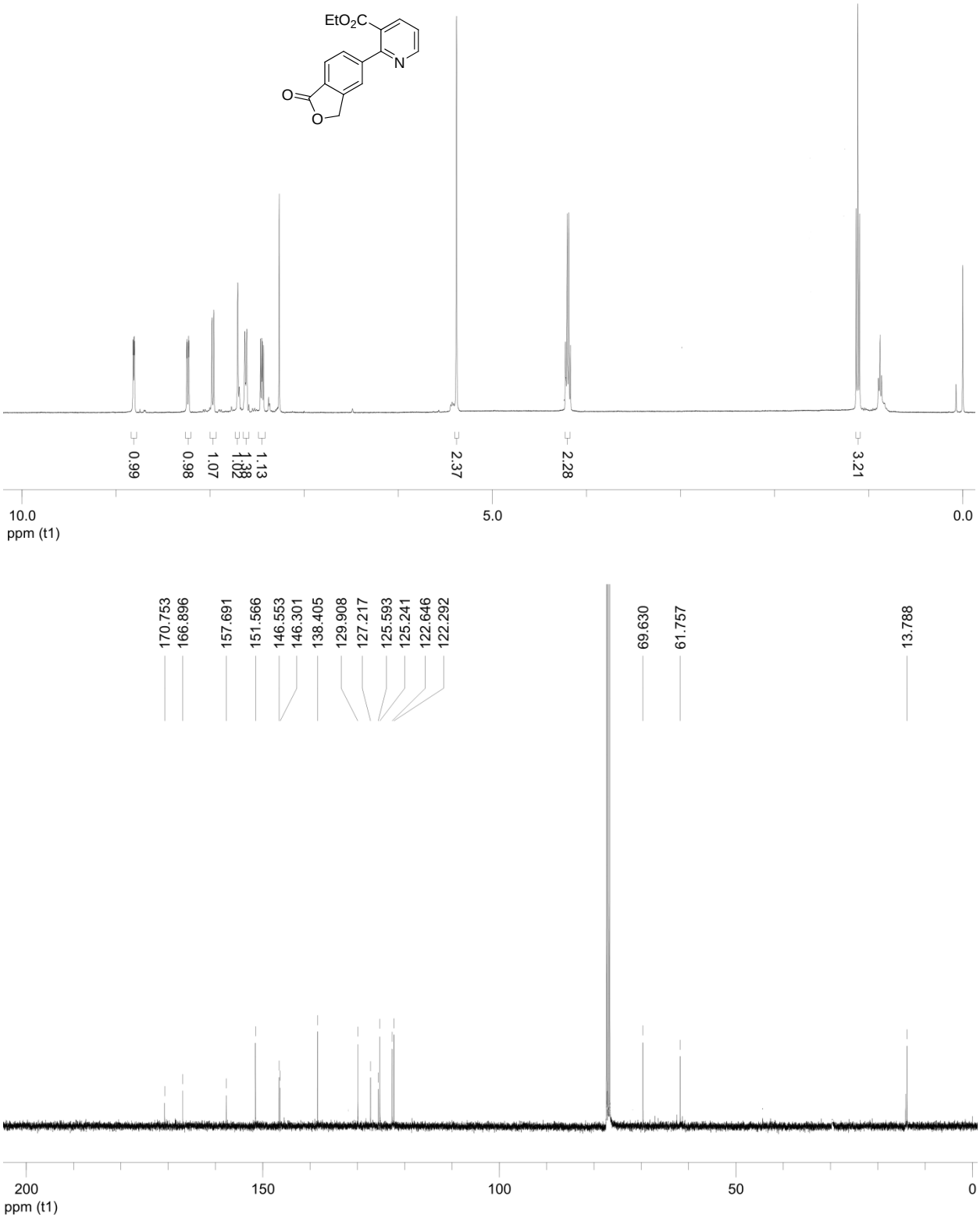


^{1}H & ^{13}C NMR Spectrum of **3l**

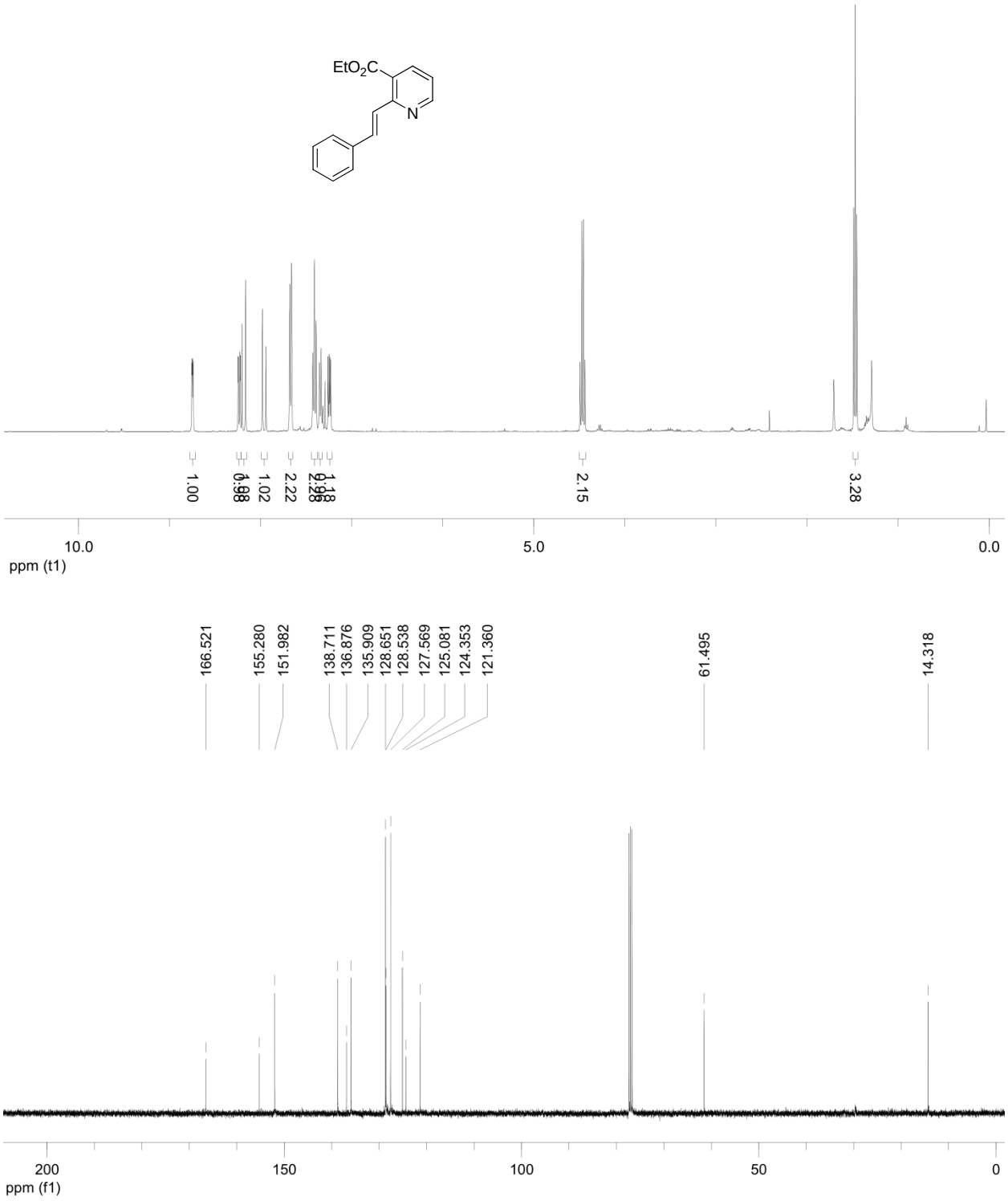




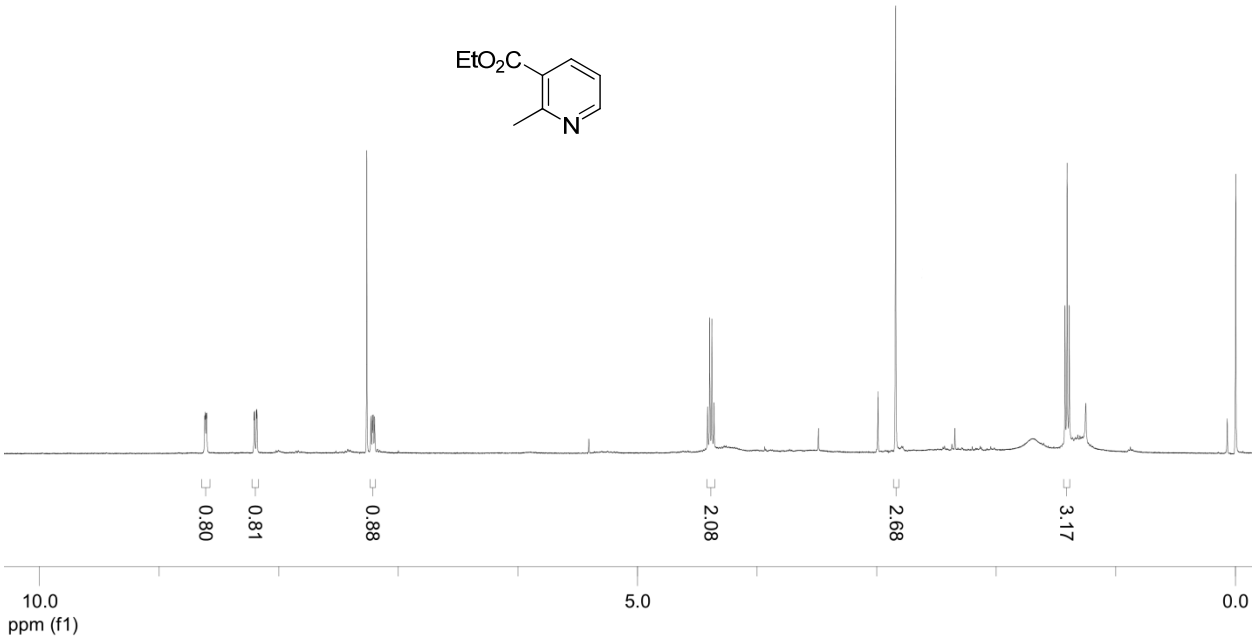
^{1}H & ^{13}C NMR Spectrum of **3m**

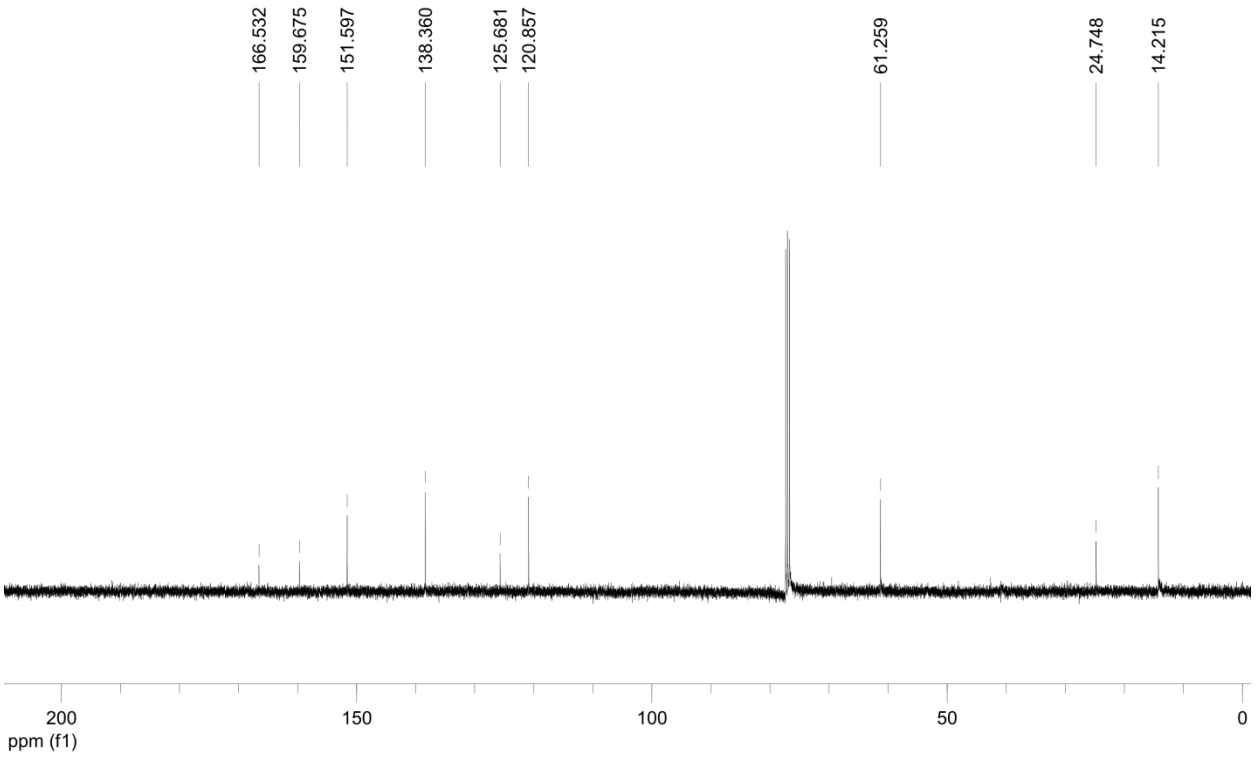


^{1} H & ^{13}C NMR Spectrum of **3n**

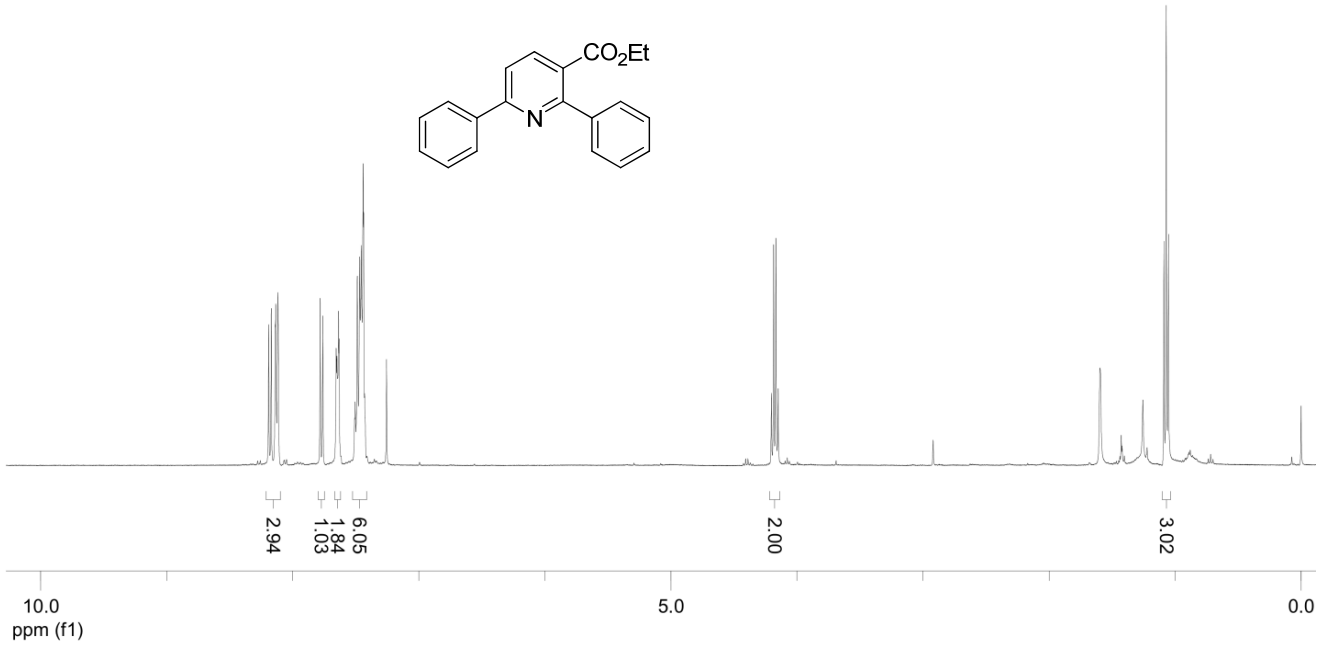


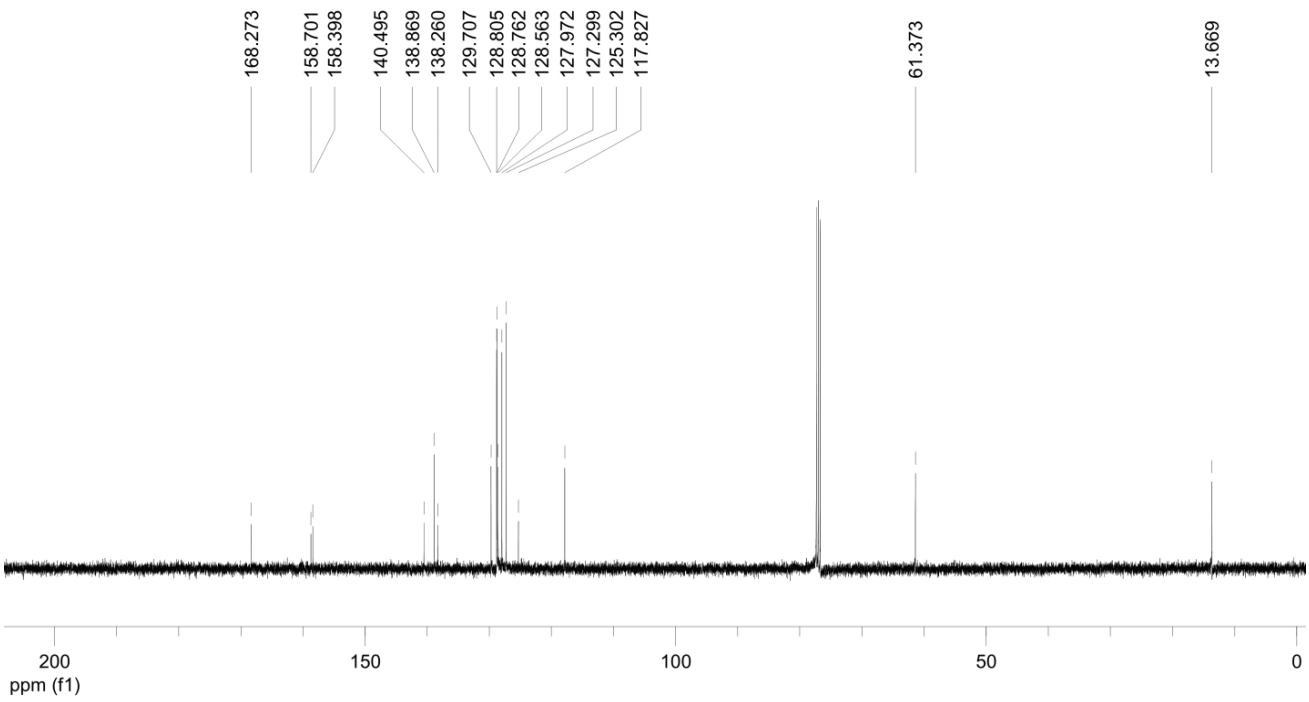
^{1}H & ^{13}C NMR Spectrum of **3o**



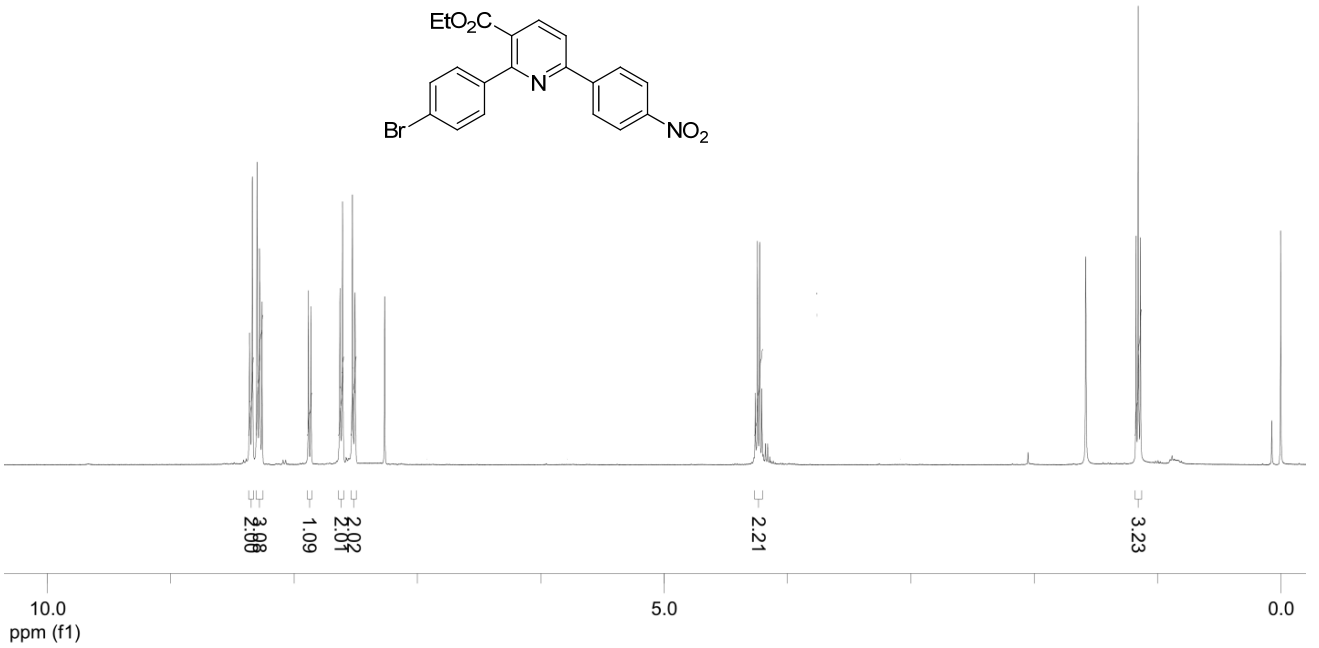


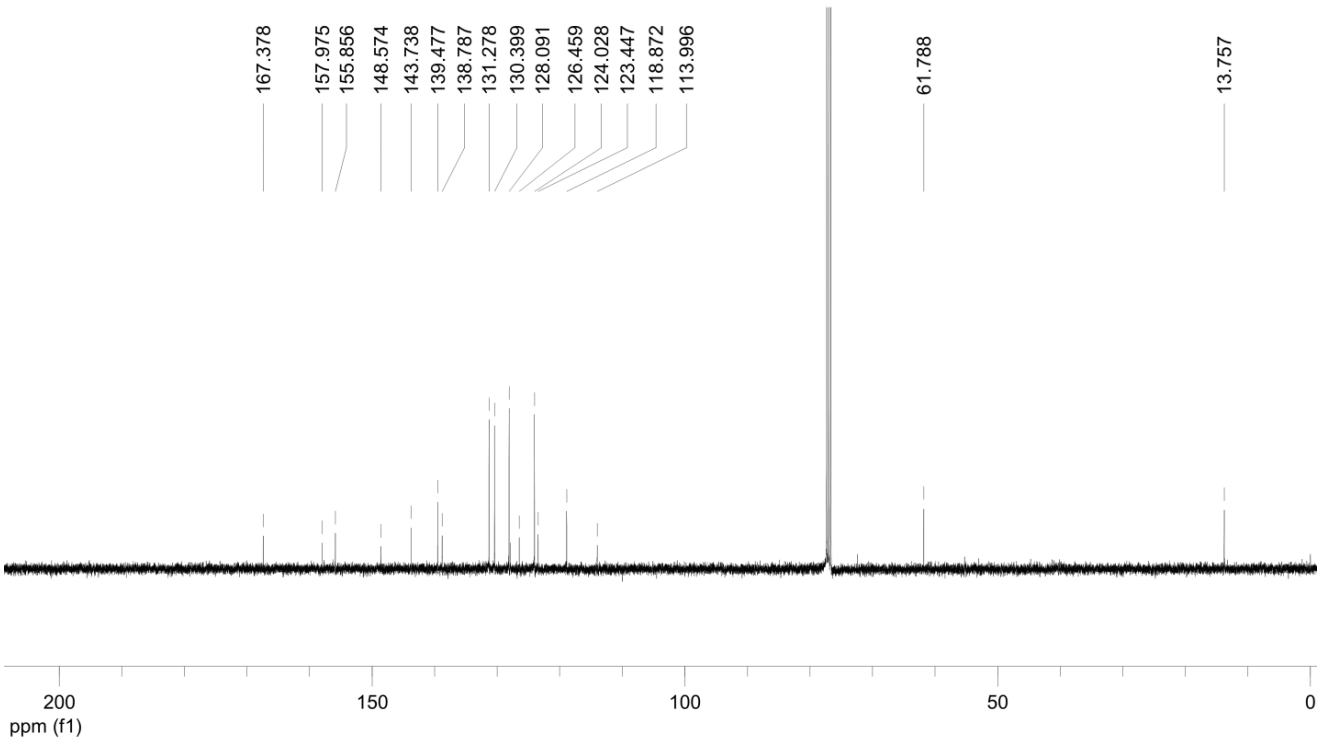
^{1}H & ^{13}C NMR Spectrum of **5a**



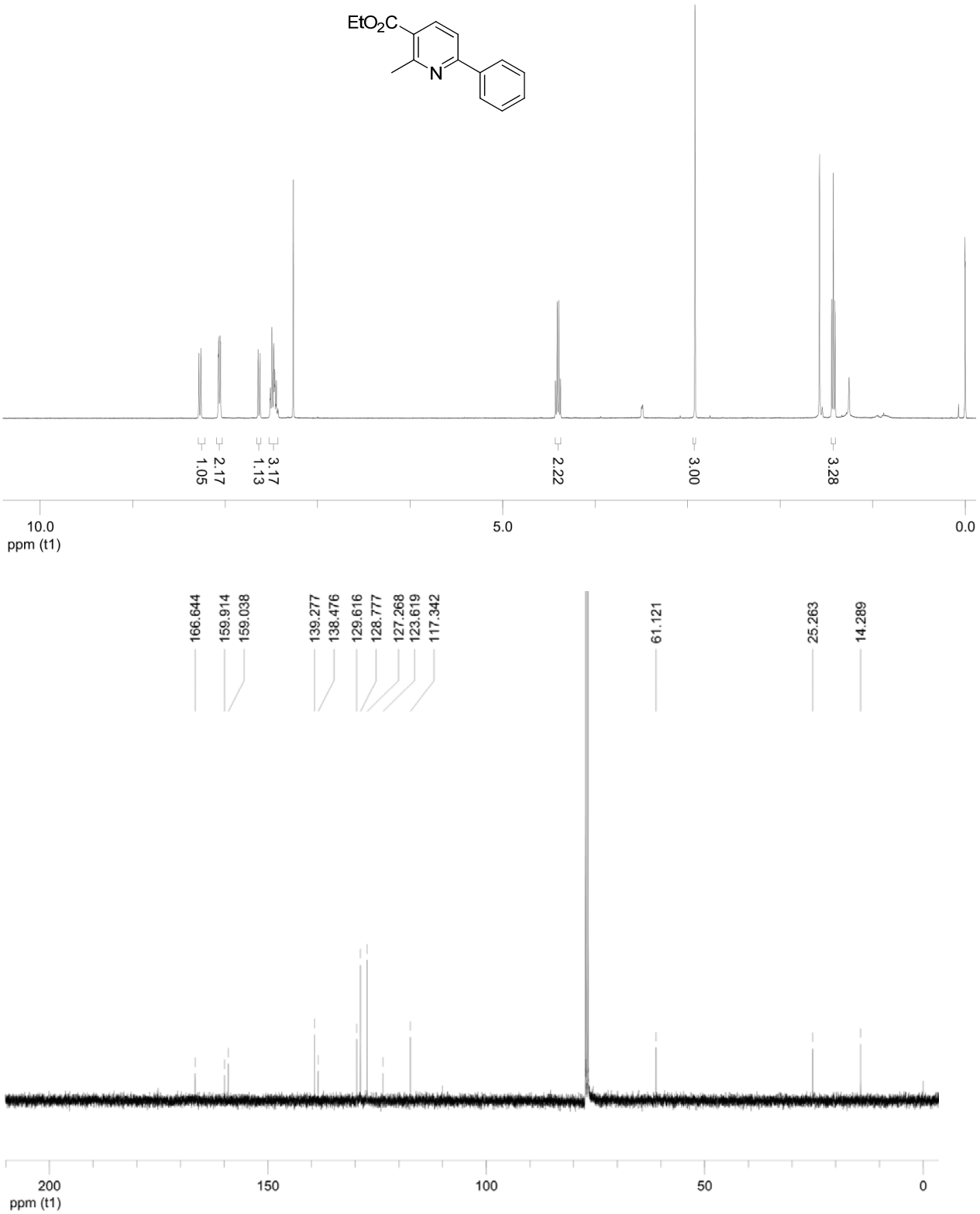


^{1}H & ^{13}C NMR Spectrum of **5b**

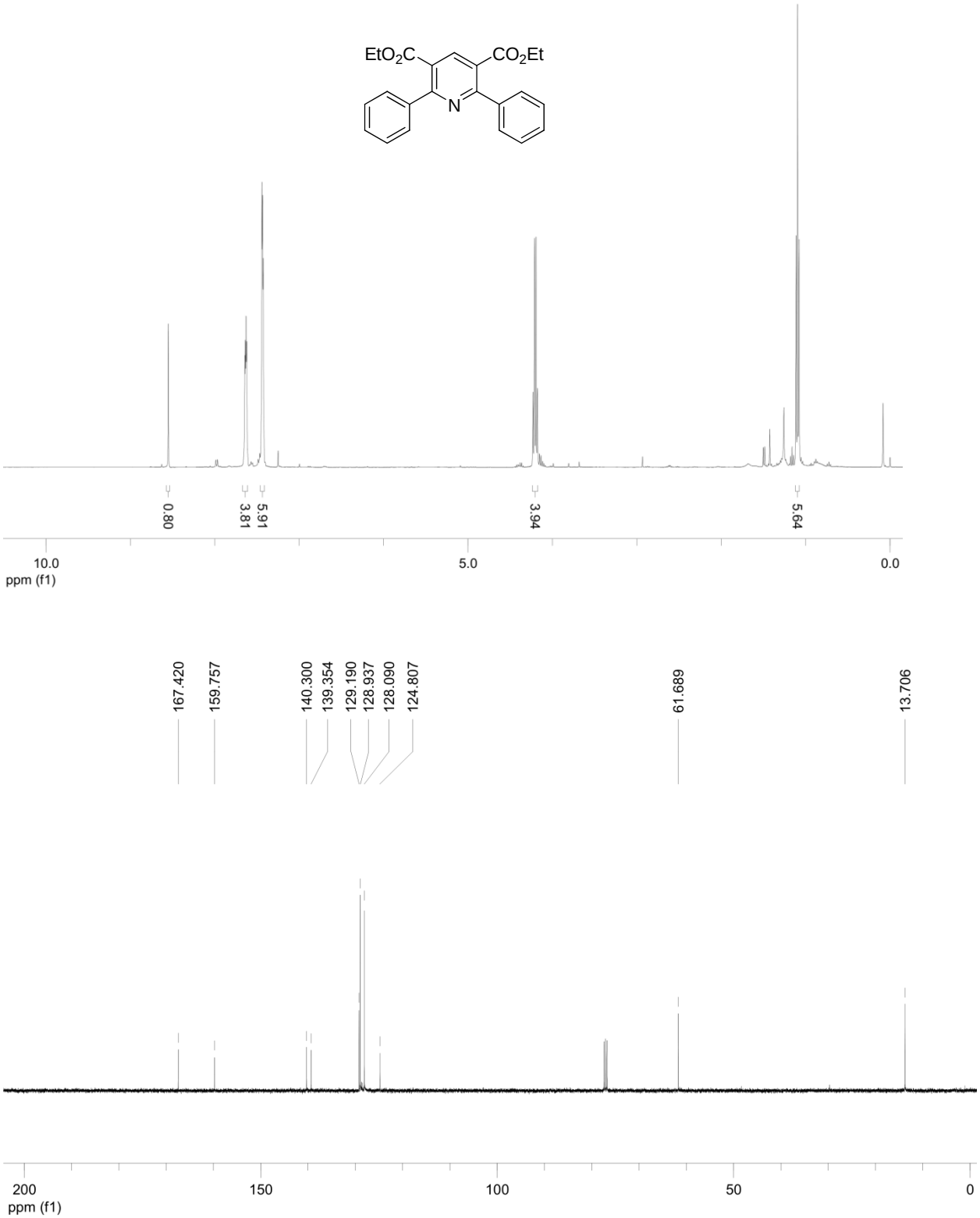




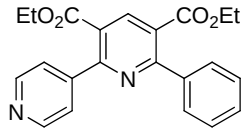
^{1}H & ^{13}C NMR Spectrum of **5c**

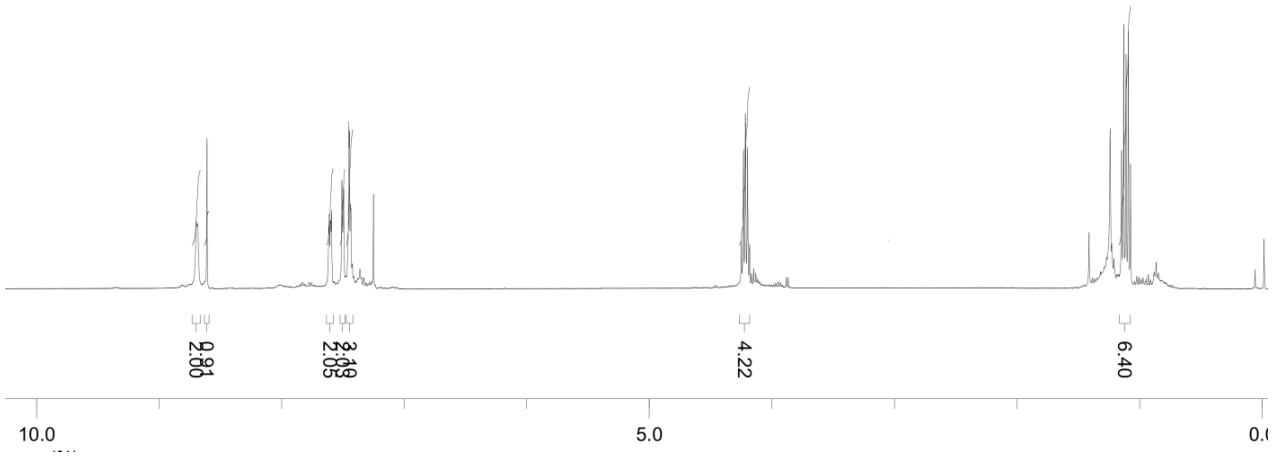


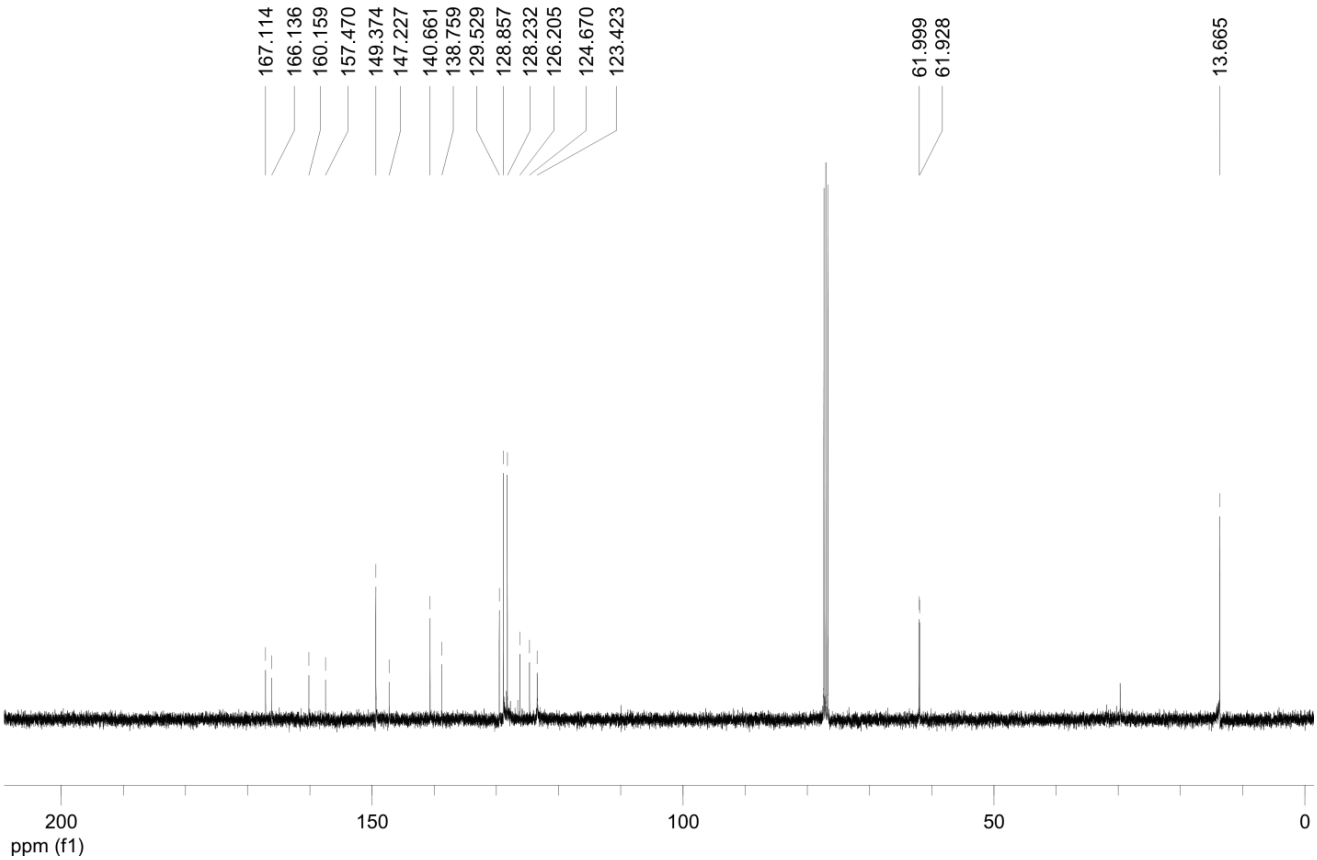
^{1}H & ^{13}C NMR Spectrum of **5d**



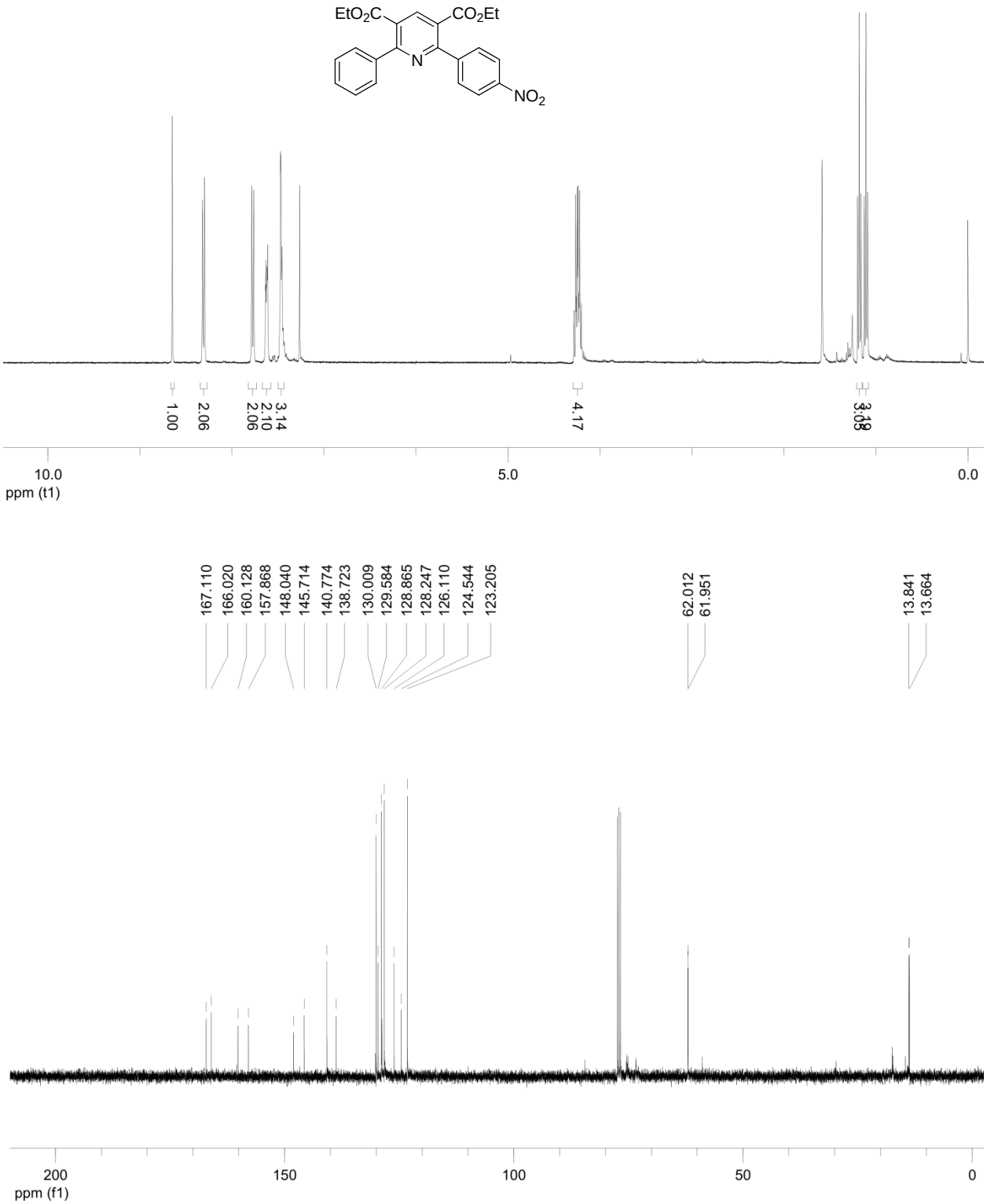
^{1}H & ^{13}C NMR Spectrum of **5e**



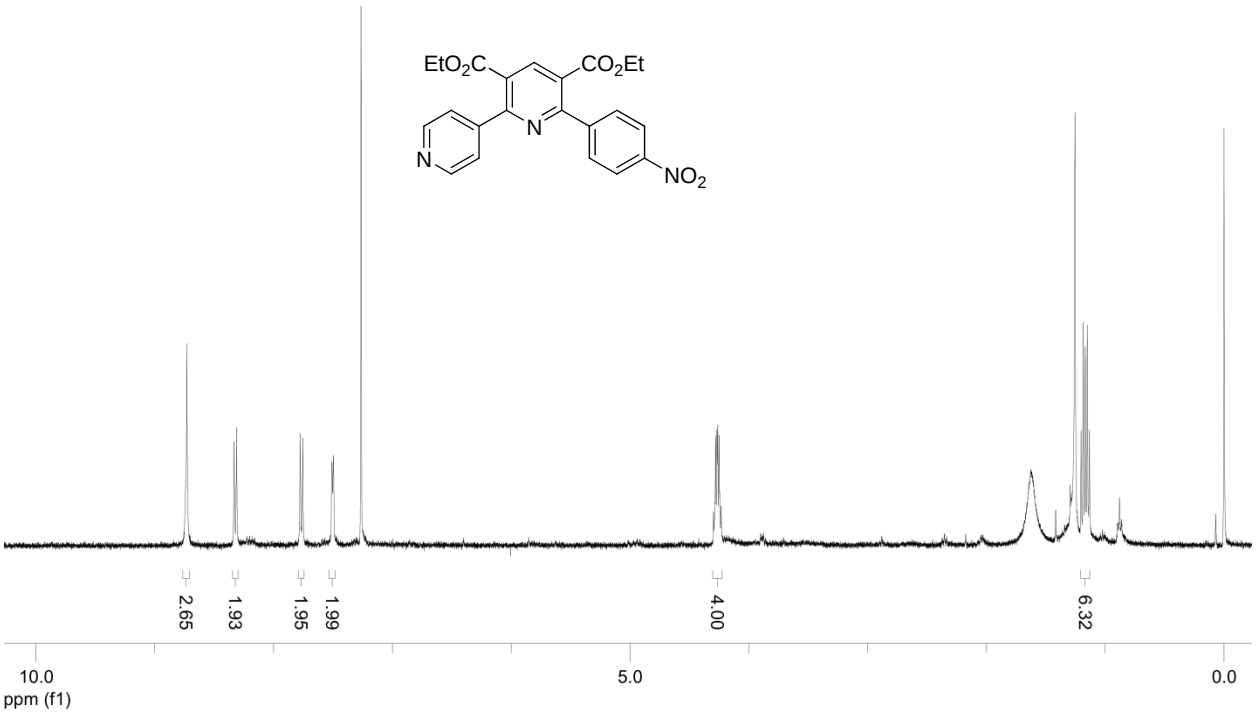


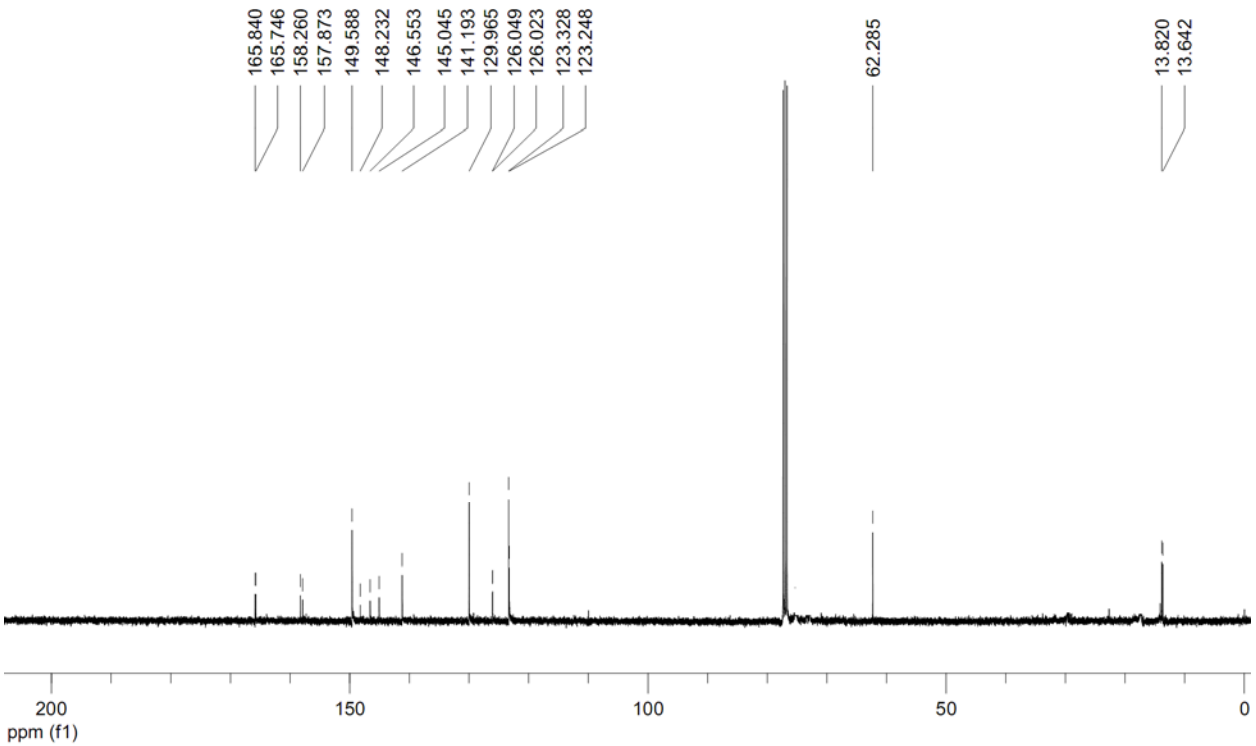


^{1}H & ^{13}C NMR Spectrum of **5f**



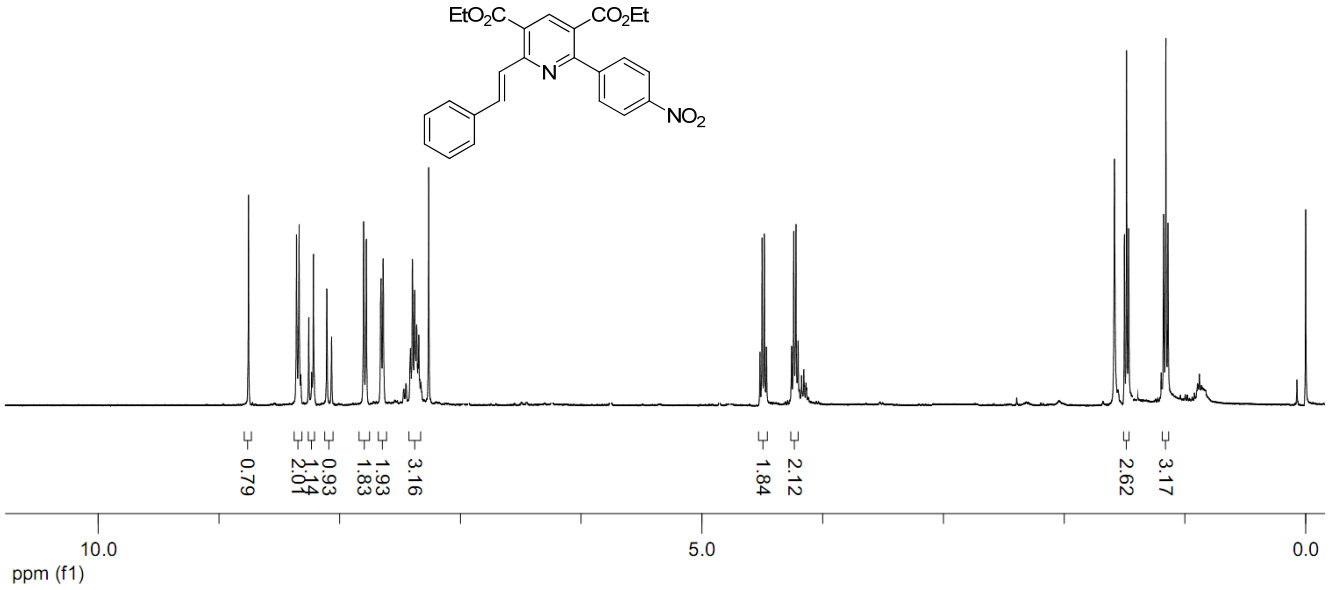
^{1}H & ^{13}C NMR Spectrum of **5g**

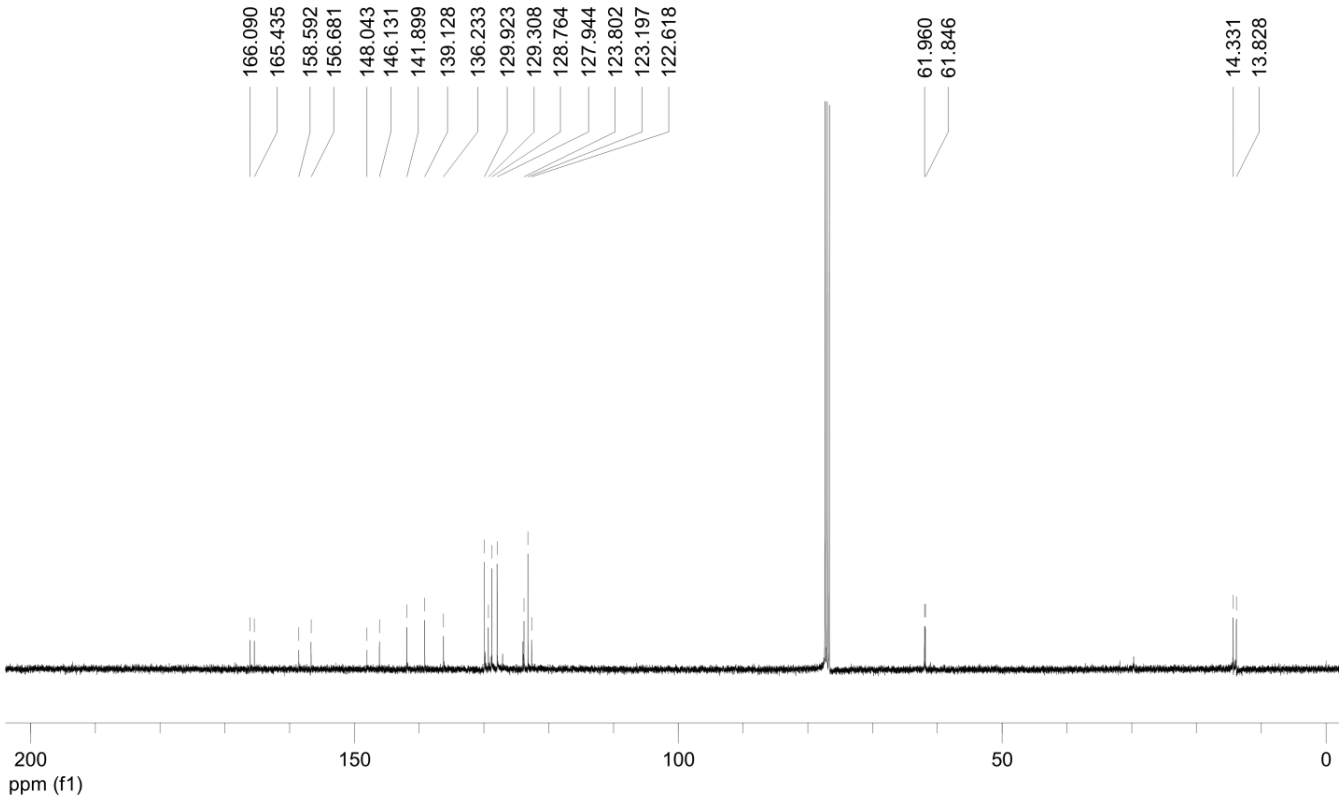




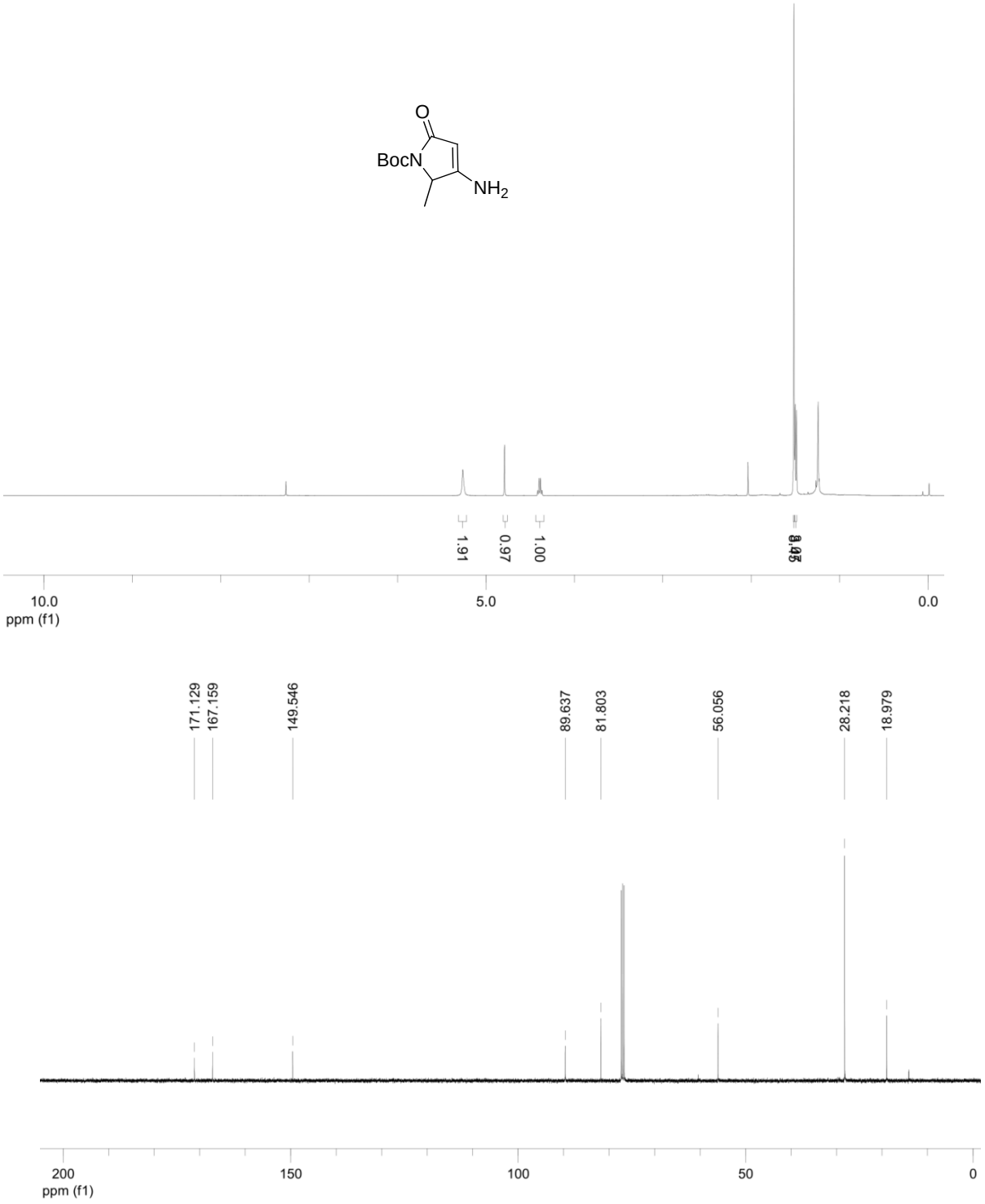
S36

^{1}H & ^{13}C NMR Spectrum of **5h**

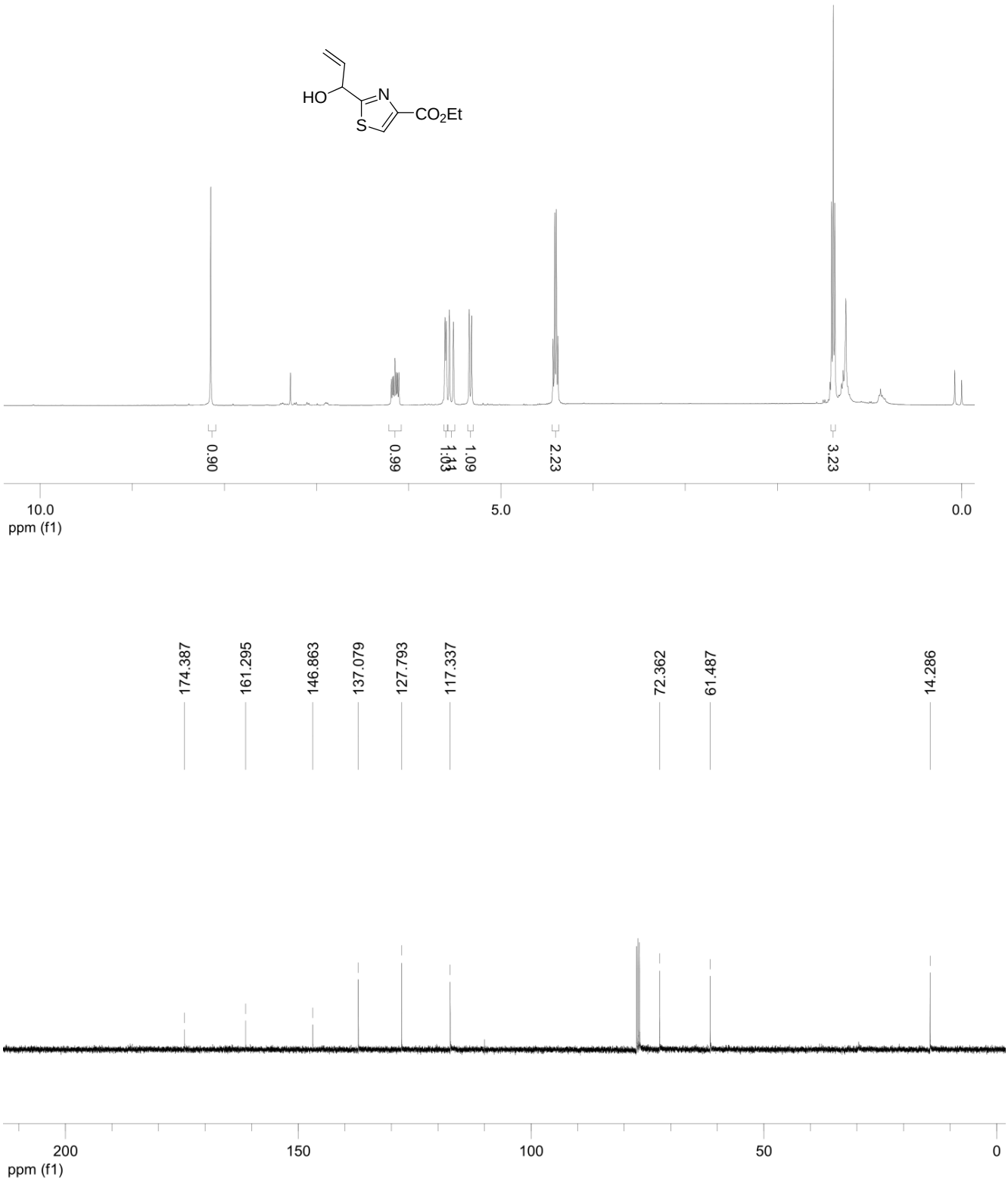




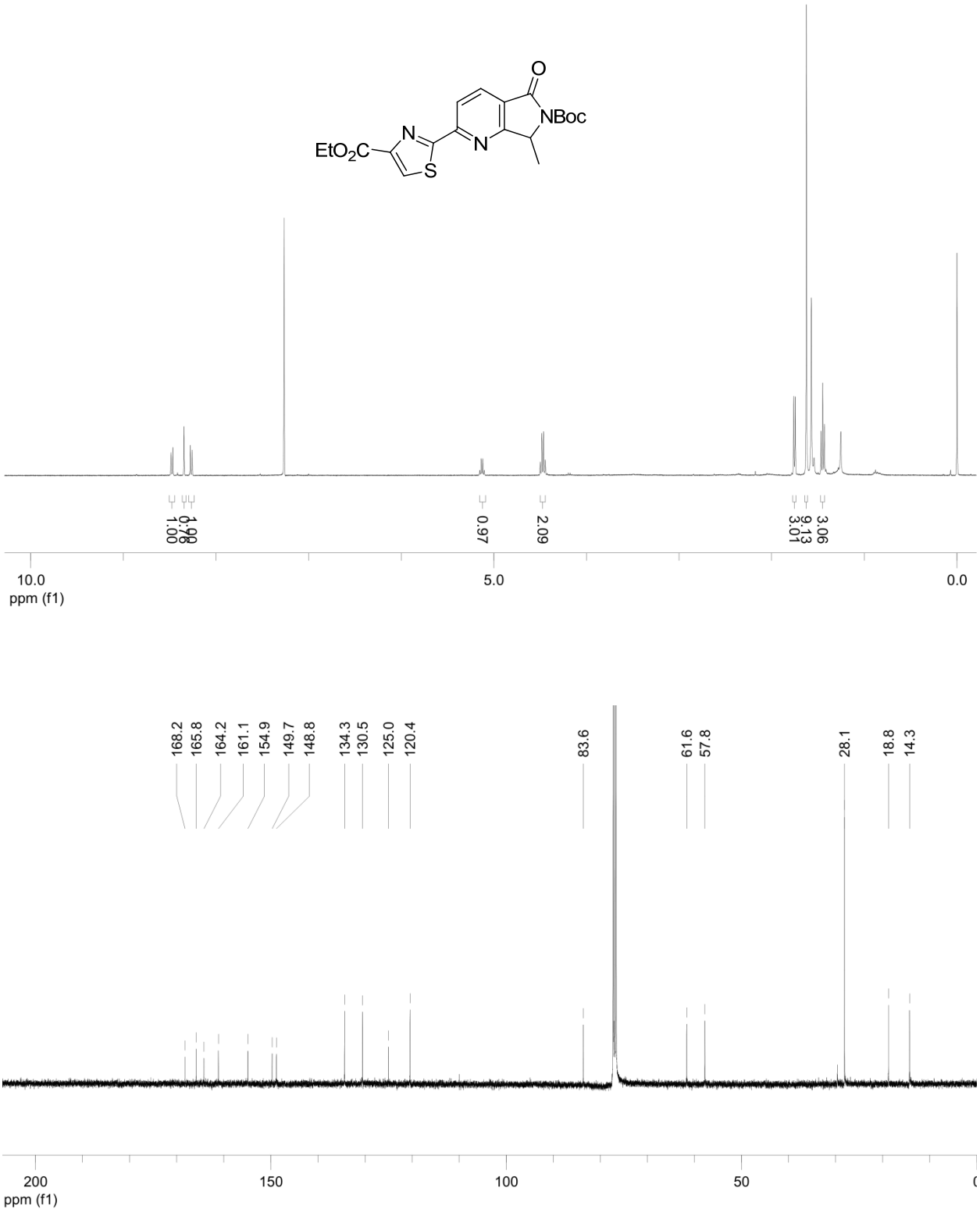
^{1}H & ^{13}C NMR Spectrum of **6**



^{1}H & ^{13}C NMR Spectrum of **7**



^{1}H & ^{13}C NMR Spectrum of **8**



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