Supporting Information

Rhodium-Catalyzed N-H Insertion of Pyridyl Carbenes Derived from Pyridotriazoles: A General and Efficient Approach to 2-Picolylamines and Imidazo[1,2-*a*]pyridines

Yi Shi, Anton V. Gulevich and Vladimir Gevorgyan*

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, 4500 SES, M/C 111, Chicago, Illinois 60607-7061

E-mail: vlad@uic.edu

Table of Contents

General Information

GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). NMR spectra were recorded on Bruker Avance DRX-500 (500 MHz) or DPX-400 (400 MHz) instrument. LRMS and HRMS analyses were performed on Micromass 70 VSE mass spectrometer. Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques unless otherwise noted. Anhydrous DCM, toluene, ethyl ether and THF (BHT-free) was purchased from Aldrich, degassed with argon, and dried by passage through activated alumina on an Innovative Technology PureSolv system. Other dry solvent were prepared using CaH_2. All commercially available compounds were purchased from Acros Organics, Strem Chemicals, Aldrich, Gelest Inc., Alfa Aesar, Oakwood Products, Inc., Ark Pharm, Inc., AK Scientific Inc., Matrix Scientific, or Chem-Impex International and used without further purification.

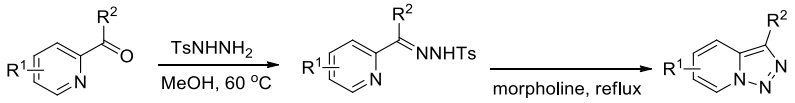
Part I. Preparation of Pyridoriazoles

General Procedure A

Pyridotriazoles (**1a, 1b, 1f-h)** were prepared via the diazotransfer reaction on 2-(pyridin-2-yl) acetate. To a stirred solution of 2-(pyridin-2-yl) acetate (1.0 equiv) and DBU (1.1 equiv) in dry acetonitrile, *p*-ABSA (1.0 equiv) was added at room temperature in small portions over a 5 min period. The resulting yellow solution was stirred overnight. After removal of solvent, the residue was taken up into 150 ml of dichloromethane, washed with water and brine, and dried over sodium sulfate. The product was isolated as white or yellowish solid by Silica Gel column chromatography.

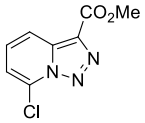
General Procedure B

Pyridotriazoles (**1c-e**) were prepared from the 2-pyridylketone.



A mixture of *p*-toluenesulfonylhydrazide (1.05 equiv) and methanol (1 mL/mmol) was heated at 60 ^{o}C until dissolved. To this solution, 2-pyridylketone in MeOH was added. The reaction was heated at 60 ^{o}C until completion and then cooled in an ice bath, and the hydrazine product was collected by filtration, dried, and directly used in next step without additional purification. The obtained hydrazone was dissolved in morpholine (1.8 mL/g) and heated at 90 °C for 1-4 h. The morpholine was removed in vacuo and the resulting yellow solid was suspended in diethyl ether, and filtered to remove morpholine toluenesulphinate. The filtrate was concentrated in vacuo, and the resulting solid residue was purified by silica gel chromatography to afford the corresponding pyridotriazole.

Methyl 7-chloro-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate 1a:



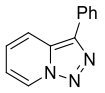
Compound **1a** was prepared according to the literature procedure.[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.24 (s, 1 H), 7.53 (t, *J*=7.89 Hz, 1 H), 7.22 (s, 1 H), 4.03 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 161.34, 136.64, 129.81, 128.40, 117.46, 116.37, 52.09.

Ethyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate 1b:

1b

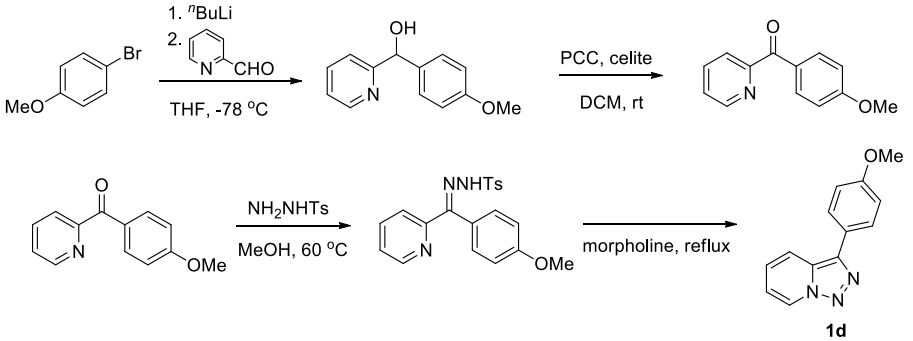
Compound **1b** was prepared from according to the **General Procedure A** (10 mmol scale, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.82 (dt, *J*=7.02, 0.88 Hz, 1 H), 8.25 (d, *J*=8.77 Hz, 1 H), 7.54 (ddd, *J*=8.77, 6.72, 0.88 Hz, 1 H), 7.15 (td, *J*=6.87, 1.17 Hz, 1 H), 4.50 (q, *J*=7.21 Hz, 2 H), 1.46 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 161.36, 135.05, 129.46, 129.08, 125.87, 119.32, 116.31, 61.07, 14.39. HRMS (ESI) calculated for $C_9H_{10}N_3O_2$ $[M+H]^+$: 192.0773, found: 192.0775.

3-Phenyl-[1,2,3]triazolo[1,5-a]pyridine 1c:



Compound **1a** was prepared according to the literature procedure.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.73 (d, *J*=7.02 Hz, 1 H), 7.99 – 7.94 (m, 3 H), 7.50 (t, *J*=7.45 Hz, 2 H), 7.39 – 7.36 (m, 1 H), 7.30 – 7.26 (m, 1 H), 6.98 (t, *J*=6.72 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 137.84, 131.36, 130.34, 128.92, 127.79, 126.54, 125.53, 125.49, 118.29, 115.21.

3-(4-Methoxyphenyl)-[1,2,3]triazolo[1,5-a]pyridine 1d:

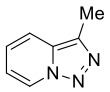


1d

A solution of 1-bromo-4-methoxybenzene (5 mmol) in THF (8 mL) was treated with *n*-BuLi (1.4 equiv., 1.6 M solution in hexane) at -78°C dropwise. After stirring at the same temperature for 1 h, 2-pyridinecarboxaldehyde (1.4 equiv.) was added and the reaction mixture was stirred -78°C for 80 min before warming to room temperature. The solution was then stirred overnight and quenched by addition of water. The product was extracted with ethyl acetate, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by flash silica gel chromatography and used in the next step without additional purification.

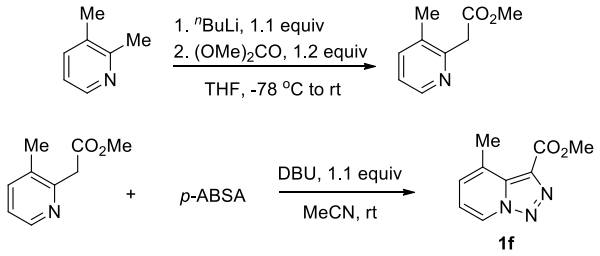
Pyridinium chlorochromate (3.7 mmol) was dissolved in CH_2Cl_2 (~600 mL), and 0.6 g of Celite was added with stirring. The alcohol (~3.5 mmol) was then added and the slurry was stirred at room temperature for 20 min. Upon completion, the solution was concentrated, and crude ketone product was purified by flash chromatography and used in the next step without additional purification. Compound **1d** was prepared form the ketone according to **General Procedure B** (37% yield over 4 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.73 (d, *J*=6.97 Hz, 1 H), 7.95 (d, *J*=9.17 Hz, 1 H), 7.88 (d, *J*=8.80 Hz, 2 H), 7.27 (dd, *J*=8.99, 6.79 Hz, 1 H), 7.05 (d, *J*=8.80 Hz, 2 H), 6.99 (t, *J*=6.60 Hz, 1 H), 3.87 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 159.32, 137.89, 129.99, 127.90, 125.46, 125.14, 123.95, 118.39, 115.21, 114.07, 55.32. HRMS (ESI) calculated for $C_{13}H_{12}N_3O$ $[M+H]^+$: 226.0980, found: 226.0979.

3-Methyl-[1,2,3]triazolo[1,5-*a*]pyridine 1e:



Pyridotriazole **1e** was prepared according to the literature procedure.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.60 (d, *J*=7.31 Hz, 1 H), 7.57 (d, *J*=9.06 Hz, 1 H), 7.13 (dd, *J*=8.77, 6.72 Hz, 1 H), 6.89 (t, *J*=6.87 Hz, 1 H), 2.58 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 134.22, 131.48, 124.94, 123.54, 117.38, 114.83, 10.23.

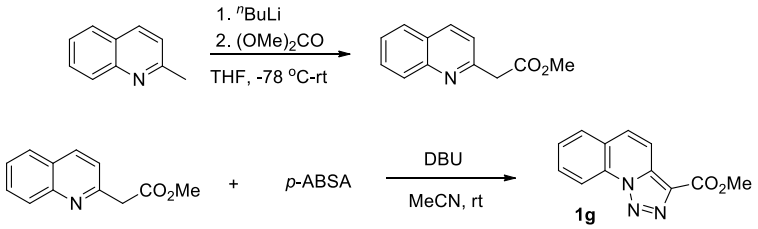
Methyl 4-methyl-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate 1f:



1f

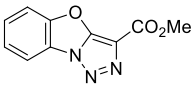
A solution of 2,3-lutidie (5.0 mmol) in THF (20 mL) was cooled to -78 °C. To this solution ^{n}BuLi (1.6 M solution in THF, 3.4 mL) under argon atmosphere. After stirring for 1 h, $CO(OMe)_2$ (6 mmol) was added via syringe. The resulting mixture was allowed to react for 3 h at this temperature and then warm to rt. When complete, the reaction was quenched with saturated ammonium chloride solution. Then the mixture was extracted with ethyl acetate, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by flash silica gel chromatography to afford the pyridyl acetate (64% yield), which was converted into pyridotriazole **1f** according to **General Procedure A** (55% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.68 (d, *J*=6.97 Hz, 1 H), 7.25 (d, *J*=7.70 Hz, 1 H), 7.03 (t, *J*=6.79 Hz, 1 H), 4.02 (s, 3 H), 2.87 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 161.9, 135.03, 130.73, 130.11, 129.23, 123.71, 116.39, 52.20, 21.07. HRMS (ESI) calculated for $C_9H_{10}N_3O_2$ $[M+H]^+$: 192.0773, found: 192.0777.

Methyl [1,2,3]triazolo[1,5-a]quinoline-3-carboxylate 1g:



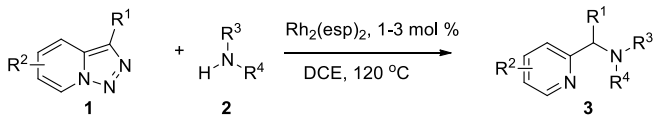
A solution of 2-methylquinoline (5.0 mmol) in THF (20 mL) was cooled to -78 ^{o}C and ^{n}BuLi (1.6 M solution in THF, 3.4 mL) was added to this solution under argon atmosphere. After stirring for 1 h at -78 ^{o}C, $CO(OMe)_2$ (6.0 mmol) was added to the reaction mixture via syringe. The resulting mixture was allowed to react for 3 h at this temperature and then warmed up to room temperature. Saturated ammonium chloride was added and the product was extracted with ethyl acetate, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography to afford quinolinyl acetate in 43% yield. The obtained quinolinyl acetate was converted into pyridotriazole **1g** according to the **General Procedure A** (38% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.84 (d, *J*=8.44 Hz, 1 H), 8.09 (d, *J*=9.17 Hz, 1 H), 7.92 (d, *J*=8.07 Hz, 1 H), 7.85–7.78 (m, 2 H), 7.69 – 7.66 (m, 1 H), 4.07 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 161.98, 133.67, 131.57, 131.08, 130.92, 130.42, 128.72, 127.80, 124.01, 116.55, 115.41, 52.16. HRMS (ESI) calculated for $C_{12}H_{10}N_3O_2$ $[M+H]^+$: 228.0773, found: 228.0772.

Methyl benzo[4,5]oxazolo[3,2-c][1,2,3]triazole-3-carboxylate 1h:



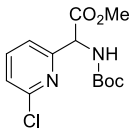
Compound **1h** was prepared according to the literature procedure.[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.66 (d, *J*=7.70 Hz, 1 H), 7.51 (d, *J*=7.70 Hz, 1 H), 7.32–7.25 (m, 2 H), 3.95 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 161.80, 153.93, 150.54, 141.71, 124.65, 124.17, 119.00, 110.25, 52.87. HRMS (ESI) calculated for $C_{10}H_7N_3NaO_3$ $[M+Na]^+$: 240.0385, found: 240.0386.

Part II. Rh(II)-Catalyzed N-H Insertion Reaction



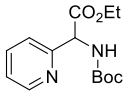
General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1-3 mol %), pyridotriazole (0.2 mmol), amine or amide and DCE (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 120 °C. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the corresponding N-H insertion products.

methyl 2-((tert-butoxycarbonyl)amino)-2-(6-chloropyridin-2-yl)acetate 3aa:



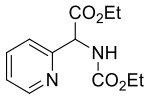
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 74% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.66 (t, *J*=7.70 Hz, 1 H), 7.39 (d, *J*=7.70 Hz, 1 H), 7.28 (d, *J*=7.70 Hz, 1 H), 6.11 (d, *J*=6.97 Hz, 1 H), 5.42 (d, *J*=7.70 Hz, 1 H), 3.74 (s, 3 H), 1.45 (s, 9 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.97, 155.44, 155.17, 151.17, 139.50, 124.04, 121.56, 80.32, 58.23, 52.91, 28.28. HRMS (ESI) calculated for $C_{13}H_{18}ClN_2O_4$ $[M+H]^+$: 301.0955, found: 301.0957.

Ethyl 2-((tert-butoxycarbonyl)amino)-2-(pyridin-2-yl)acetate 3ab:



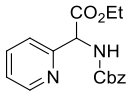
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.54 (d, *J*=4.09 Hz, 1 H), 7.69 (td, *J*=7.67, 1.32 Hz, 1 H), 7.46 (d, *J*=7.89 Hz, 1 H), 7.25 – 7.22 (m, 1 H), 6.27 (d, *J*=7.31 Hz, 1 H), 5.40 (d, *J*=7.60 Hz, 1 H), 4.17 (q, *J*=7.21 Hz, 2 H), 1.43 (s, 9 H), 1.19 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.06, 155.25, 54.47, 149.06, 137.09, 123.22, 123.04, 109.50, 79.93, 61.73, 58.58, 28.24, 13.96. HRMS (ESI) calculated for $C_{14}H_{21}N_2O_4$ $[M+H]^+$: 281.1501, found: 281.1495.

Ethyl 2-((ethoxycarbonyl)amino)-2-(pyridin-2-yl)acetate 3ac:



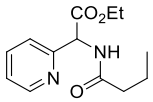
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.55 (d, *J*=4.03 Hz, 1 H), 7.73 – 7.69 (m, 1 H), 7.48 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.25 (m, 1 H), 6.41 (br. s, 1 H), 5.46 (d, *J*=7.34 Hz, 1 H), 4.21 – 4.12 (m, 4 H), 1.26 – 1.19 (m, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.95, 156.04, 154.39, 149.32, 136.95, 123.25, 122.99, 61.82, 61.19, 58.79, 14.49, 13.98. HRMS (ESI) calculated for $C_{12}H_{17}N_2O_4$ $[M+H]^+$: 253.1188, found: 253.1181.

Ethyl 2-(((benzyloxy)carbonyl)amino)-2-(pyridin-2-yl)acetate 3ad:



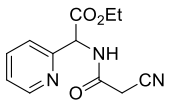
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.56 (d, *J*=4.09 Hz, 1 H), 7.77 – 7.73 (m, 1 H), 7.51 (d, *J*=7.89 Hz, 1 H), 7.36 – 7.29 (m, 6 H), 6.62 (d, *J*=7.02 Hz, 1 H), 5.51 (d, *J*=7.60 Hz, 1 H), 5.14 (s, 1 H), 5.13 (s, 1 H), 4.25 – 4.15 (m, 2 H), 1.21 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 169.55, 155.80, 154.00, 148.76, 137.56, 136.23, 128.45, 128.08, 128.02, 123.49, 123.32, 67.04, 62.02, 58.70, 13.98. HRMS (ESI) calculated for $C_{17}H_{19}N_2O_4$ $[M+H]^+$: 315.1345, found: 315.1335.

Ethyl 2-butyramido-2-(pyridin-2-yl)acetate 3ae:



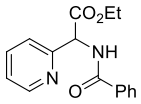
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.53 (d, *J*=4.40 Hz, 1 H), 7.70 (t, *J*=7.70 Hz, 1 H), 7.49 (d, *J*=7.70 Hz, 1 H), 7.29 – 7.23 (m, 2 H), 5.64 (d, *J*=6.97 Hz, 1 H), 4.19 – 4.13 (m, 2 H), 2.29 – 2.26 (m, 2 H), 1.70 – 1.66 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H), 0.93 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 172.71, 169.72, 154.03, 149.12, 137.05, 123.24, 61.76, 57.15, 38.13, 18.89, 13.92, 13.61. HRMS (ESI) calculated for $C_{13}H_{19}N_2O_3$ $[M+H]^+$: 251.1396, found: 251.1391.

Ehyl 2-(2-cyanoacetamido)-2-(pyridin-2-yl)acetate 3af:



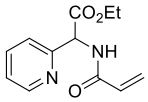
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 (d, *J*=4.68 Hz, 1 H), 8.09 (d, *J*=6.14 Hz, 1 H), 7.74 (td, *J*=7.67, 1.61 Hz, 1 H), 7.51 (d, *J*=7.60 Hz, 1 H), 7.30 – 7.27 (m, 1 H), 5.61 (d, *J*=7.02 Hz, 1 H), 4.21 – 4.14 (m, 2 H), 3.52 (s, 2 H), 1.20 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.74, 161.14, 152.54, 149.11, 137.43, 123.73, 123.26, 114.10, 62.24, 57.58, 25.77, 13.92. HRMS (ESI) calculated for $C_{12}H_{14}N_3O_3$ $[M+H]^+$: 248.1035, found: 248.1033.

Ethyl 2-benzamido-2-(pyridin-2-yl)acetate 3ag:



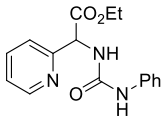
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.59 (d, *J*=4.09 Hz, 1 H), 8.13 – 8.11 (br. s, 1 H), 7.92 – 7.90 (m, 2 H), 7.77 (td, *J*=7.67, 1.61 Hz, 1 H), 7.61 (d, *J*=7.60 Hz, 1 H), 7.53 – 7.43 (m, 3 H), 7.32 – 7.29 (m, 1 H), 5.87 (d, *J*=7.02 Hz, 1 H), 4.26 – 4.19 (m, 2 H), 1.24 (t, *J*=7.02 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 169.55, 166.87, 153.84, 148.80, 137.60, 133.60, 131.77, 128.51, 127.27, 123.58, 123.54, 62.05, 57.48, 14.02. HRMS (ESI) calculated for $C_{16}H_{17}N_2O_3$ $[M+H]^+$: 285.1239, found: 285.1231.

Ethyl 2-acrylamido-2-(pyridin-2-yl)acetate 3ah:



Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.54 (d, *J*=4.77 Hz, 1 H), 7.70 (td, *J*=7.70, 1.47 Hz, 1 H), 7.51 (d, *J*=8.07 Hz, 1 H), 7.44 – 7.43 (br. s, 1 H), 7.26 – 7.24 (m, 1 H), 6.34 – 6.22 (m, 2 H), 5.73 (d, *J*=6.97 Hz, 1 H), 5.67 (dd, *J*=9.90, 1.83 Hz, 1 H), 4.21 – 4.15 (m, 2 H), 1.20 (t, *J*=6.97 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.48, 164.99, 154.01, 149.11, 137.17, 130.30, 127.08, 123.36, 123.33, 61.91, 57.31, 13.95. HRMS (ESI) calculated for $C_{12}H_{15}N_2O_3$ $[M+H]^+$: 235.1083, found: 235.1082.

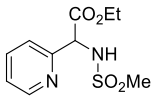
Ethyl 2-(3-phenylureido)-2-(pyridin-2-yl)acetate 3ai:



Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (d, *J*=4.38 Hz, 1 H), 7.79 (s, 1 H), 7.71 (td, *J*=7.75, 1.75 Hz, 1 H), 7.57 (d, *J*=7.89 Hz, 1 H), 7.32 (d, *J*=7.60 Hz, 2 H), 7.24 – 7.17 (m, 4 H), 7.01 – 6.97 (m, 1 H), 5.78 (d, *J*=7.31 Hz, 1 H), 4.19 – 4.10 (m, 2 H), 1.17 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.75, 155.23, 155.11, 148.83, 138.86, 137.55, 128.92,

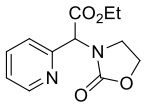
123.73, 123.36, 123.01, 119.92, 62.01, 58.27, 13.92. HRMS (ESI) calculated for $C_{16}H_{18}N_3O_3$ $[M+H]^+$: 300.1348, found: 300.1345.

Ethyl 2-(methylsulfonamido)-2-(pyridin-2-yl)acetate 3aj:



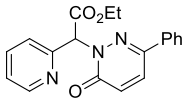
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.57 (d, *J*=4.40 Hz, 1 H), 7.75 (td, *J*=7.70, 1.47 Hz, 1 H), 7.48 (d, *J*=8.07 Hz, 1 H), 7.30 (dd, *J*=6.97, 5.14 Hz, 1 H), 6.25 (d, *J*=7.70 Hz, 1 H), 5.36 (d, *J*=8.07 Hz, 1 H), 4.24 – 4.18 (m, 2 H), 2.95 (s, 3 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.36, 153.67, 149.32, 137.46, 123.74, 123.14, 62.40, 60.26, 42.10, 13.98. HRMS (ESI) calculated for $C_{10}H_{15}N_2O_4S$ $[M+H]^+$: 259.0753, found: 259.0750.

Ethyl 2-(2-oxooxazolidin-3-yl)-2-(pyridin-2-yl)acetate 3ak:



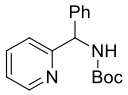
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.58 (d, *J*=4.40 Hz, 1 H), 7.74 (td, *J*=7.70, 1.83 Hz, 1 H), 7.39 (d, *J*=8.07 Hz, 1 H), 7.29 (dd, *J*=6.79, 4.95 Hz, 1 H), 5.80 (s, 1 H), 4.42 – 4.38 (m, 1 H), 4.26 – 4.23 (m, 2 H), 4.12 (td, *J*=8.80, 6.97 Hz, 1 H), 3.33 (td, *J*=8.80, 6.97 Hz, 1 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.86, 158.40, 154.07, 149.40, 137.37, 124.20, 123.46, 62.78, 61.65, 61.95, 42.13, 14.01. HRMS (ESI) calculated for $C_{12}H_{15}N_2O_4$ $[M+H]^+$: 251.1032, found: 251.1026.

Ethyl 2-(6-oxo-3-phenylpyridazin-1(6H)-yl)-2-(pyridin-2-yl)acetate 3al:



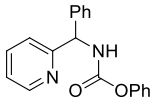
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.68 (d, *J*=4.77 Hz, 1 H), 7.98 (d, *J*=6.97 Hz, 2 H), 7.83 (d, *J*=9.17 Hz, 1 H), 7.78 (td, *J*=7.61, 1.65 Hz, 1 H), 7.66 (d, *J*=7.70 Hz, 1 H), 7.50 – 7.44 (m, 3 H), 7.32 (dd, *J*=6.97, 5.50 Hz, 1 H), 7.26 (d, *J*=9.17 Hz, 1 H), 6.73 (s, 1 H), 4.26 (q, *J*=6.97 Hz, 2 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.35, 162.80, 156.14, 154.23, 149.79, 137.05, 135.99, 129.52, 128.87, 127.67, 126.67, 123.86, 123.24, 117.90, 77.50, 61.81, 13.99. HRMS (ESI) calculated for $C_{19}H_{18}N_3O_3$ $[M+H]^+$: 336.1348, found: 336.1343.

***tert*-Butyl (phenyl(pyridin-2-yl)methyl)carbamate 3am**:



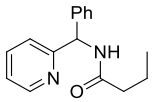
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.56 (d, *J*=4.68 Hz, 1 H), 7.61 (t, *J*=7.60 Hz, 1 H), 7.35 – 7.16 (m, 7 H), 6.53 (br. s, 1 H), 5.87 (d, *J*=6.72 Hz, 1 H), 1.43 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.28, 155.19, 148.83, 142.29, 136.78, 128.56, 127.33, 127.10, 122.41, 122.25, 79.43, 58.86, 28.35. HRMS (ESI) calculated for $C_{17}H_{21}N_2O_2$ $[M+H]^+$: 285.1603, found: 285.1593.

Phenyl (phenyl(pyridin-2-yl)methyl)carbamate 3an:



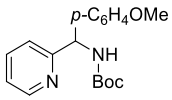
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.62 (d, *J*=4.03 Hz, 1 H), 7.65 (td, *J*=7.61, 1.65 Hz, 1 H), 7.41-7.39 (m, 2 H), 7.34 – 7.31 (m, 4 H), 7.28-7.13 (m, 7 H), 5.97 (d, *J*=6.97 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 158.38, 153.93, 151.08, 148.80, 141.68, 136.93, 129.14, 128.68, 127.67, 127.37, 125.12, 122.53, 122.53, 121.58, 59.15. HRMS (ESI) calculated for $C_{19}H_{17}N_2O_2$ $[M+H]^+$: 305.1290, found: 305.1283.

***N*-(Phenyl(pyridin-2-yl)methyl)butyramide 3ao**:



Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.57 (d, *J*=4.09 Hz, 1 H), 7.64 – 7.58 (m, 2 H), 7.33 – 7.19 (m, 7 H), 6.17 (d, *J*=7.31 Hz, 1 H), 2.27 (t, *J*=9.50 Hz, 2 H), 1.73 – 1.64 (m, 2 H), 0.93 (t, *J*=7.45 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 172.11, 158.85, 148.81, 142.07, 136.87, 128.55, 127.33, 127.24, 122.79, 122.39, 57.13, 38.64, 19.05, 13.73. HRMS (ESI) calculated for $C_{16}H_{19}N_2O$ $[M+H]^+$: 255.1497, found: 255.1493.

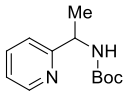
***tert*-Butyl ((4-methoxyphenyl)(pyridin-2-yl)methyl)carbamate 3ap**:



Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.56 (d, *J*=4.40 Hz, 1 H), 7.61 (t, *J*=7.34 Hz, 1 H), 7.26 – 7.15 (m, 4 H), 6.82 (d, *J*=8.44 Hz, 2 H), 6.49 (d, *J*=6.24 Hz, 1 H), 5.81 (d, *J*=6.97 Hz, 1

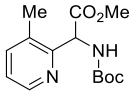
H), 3.76 (s, 3 H), 1.43 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.58, 158.73, 155.16, 14.84, 136.67, 134.59, 128.29, 122.26, 122.13, 113.90, 58.24, 55.14, 28.34, 28.16. HRMS (ESI) calculated for $C_{18}H_{23}N_2O_3$ $[M+H]^+$: 315.1709, found: 315.1702.

***tert*-Butyl (1-(pyridin-2-yl)ethyl)carbamate 3aq**:



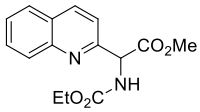
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 – 8.52 (m, 1 H), 7.64 (td, *J*=7.67, 1.90 Hz, 1 H), 7.24 (d, *J*=7.89 Hz, 1 H), 7.17 (ddd, *J*=7.45, 4.97, 1.02 Hz, 1 H), 5.73 (br. s, 1 H), 4.86 – 4.82 (m, 1 H), 1.46 – 1.42 (m, 12 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 161.65, 155.24, 148.90, 136.87, 122.17, 121.19, 79.22, 51.06, 28.39, 22.71. HRMS (ESI) calculated for $C_{12}H_{19}N_2O_2$ $[M+H]^+$: 223.1447, found: 223.1440.

Methyl 2-((tert-butoxycarbonyl)amino)-2-(3-methylpyridin-2-yl)acetate 3ar:



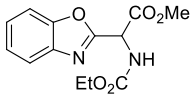
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.39 (d, *J*=4.40 Hz, 1 H), 7.51 (d, *J*=7.34 Hz, 5 H), 7.15 (dd, *J*=7.70, 4.77 Hz, 1 H), 6.18 (d, *J*=8.07 Hz, 1 H), 5.66 (d, *J*=8.44 Hz, 1 H), 3.70 (s, 3 H), 2.50 (s, 3 H), 1.45 (s, 9 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.91, 155.49, 153.32, 146.84, 138.68, 123.20, 79.96, 55.09, 52.56, 28.30, 18.48. HRMS (ESI) calculated for $C_{14}H_{21}N_2O_4$ $[M+H]^+$: 281.1501, found: 281.1500.

Methyl 2-((ethoxycarbonyl)amino)-2-(quinolin-2-yl)acetate 3as:



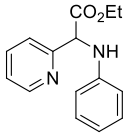
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 63% yield. ^{1}H NMR (500 MHz, acetone-*d*6) δ ppm: 8.39 (d, *J*=8.44 Hz, 1 H), 8.05 (d, *J*=8.44 Hz, 1 H), 7.98 (d, *J*=8.07 Hz, 1 H), 7.79 (t, *J*=7.52 Hz, 1 H), 7.70 (d, *J*=8.44 Hz, 1 H), 7.64 – 7.61 (m, 1 H), 7.08 (br. s, 1 H), 5.66 (d, *J*=7.34 Hz, 1 H), 4.13 – 4.09 (m, 2 H), 3.71 (s, 3 H), 1.23 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ ppm: 170.12, 155.82, 154.69, 147.16, 137.30, 129.95, 129.01, 127.83. 127.77, 126.96, 120.51, 60.58, 59.52, 51.93, 14.04. HRMS (ESI) calculated for $C_{15}H_{17}N_2O_4$ $[M+H]^+$: 289.1188, found: 289.1187.

Methyl 2-(benzo[d]oxazol-2-yl)-2-((ethoxycarbonyl)amino)acetate 3at:



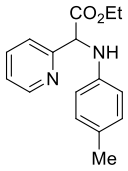
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.73 (d, *J*=6.97 Hz, 1 H), 7.55 (d, *J*=7.34 Hz, 1 H), 7.37 (quin, *J*=7.06 Hz, 2 H), 6.01 (d, *J*=6.24 Hz, 1 H), 5.83 (d, *J*=8.07 Hz, 1 H), 4.19 – 4.15 (m, 2 H), 3.83 (s, 3 H), 1.27 (t, J=7.00 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 167.36, 160.30, 155.61, 150.90, 140.58, 125.75, 124.80, 120.55, 110.97, 61.87, 53.62, 52.73, 14.44. HRMS (ESI) calculated for $C_{13}H_{15}N_2O_5$ $[M+H]^+$: 279.0981, found: 279.0977.

Ethyl 2-(phenylamino)-2-(pyridin-2-yl)acetate 3ba:



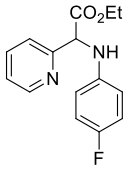
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.63 (d, *J*=4.40 Hz, 1 H), 7.72 – 7.69(m, 1 H), 7.51 (d, *J*=7.70 Hz, 1 H), 7.27 – 7.25 (m, 1 H), 7.17- 7.13 (m, 2 H), 6.74 – 6.71 (m, 1 H), 6.66 (d, *J*=8.44 Hz, 2 H), 5.72 (br. s, 1 H), 5.30 (s, 1 H), 4.24 – 4.17 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.01, 156.27, 149.02, 145.98, 137.39, 129.24, 123.22, 122.14, 118.28, 113.56, 62.13, 61.91, 14.01. HRMS (ESI) calculated for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: 257.1290, found: 257.1286.

Ethyl 2-(pyridin-2-yl)-2-(p-tolylamino)acetate 3bb:



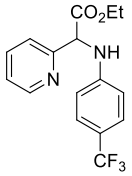
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 63% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.63 – 8.62 (m, 1 H), 7.69 (td, *J*=7.70, 1.83 Hz, 1 H), 7.50 (d, *J*=7.70 Hz, 1 H), 7.25 (ddd, *J*=7.52, 4.95, 1.10 Hz, 1 H), 6.96 (d, *J*=8.07 Hz, 2 H), 6.58 (d, *J*=8.44 Hz, 2 H), 5.26 (s, 1 H), 4.24 – 4.16 (m, 2 H), 2.21 (s, 3 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.21, 156.49, 149.23, 143.68, 137.18, 129.74, 127.45, 123.12, 122.06, 113.67, 62.53, 61.84, 20.36, 14.05. HRMS (ESI) calculated for $C_{16}H_{19}N_2O_2$ $[M+H]^+$: 271.1447, found: 271.1445.

Ethyl 2-((4-fluorophenyl)amino)-2-(pyridin-2-yl)acetate 3bc:



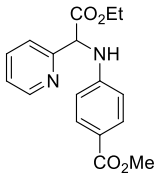
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.63 (d, *J*=4.40 Hz, 1 H), 7.71 (td, *J*=7.70, 1.47 Hz, 1 H), 7.49 (d, *J*=7.70 Hz, 1 H), 7.28 – 7.25 (m, 1 H), 6.88 – 6.83 (m, 2 H), 6.62 – 6.58 (m, 2 H), 5.22 (s, 1 H), 4.22 – 4.16 (m, 2 H), 1.18 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.01, 156.23 (d, *J*=236.9 Hz), 156.01, 149.23, 142.34, 137.30, 123.28, 122.15, 115.73(d, *J*=21.4 Hz), 114.47 (d, *J*=8.82 Hz), 62.70, 61.95, 14.04. HRMS (ESI) calculated for $C_{15}H_{16}FN_2O_2$ $[M+H]^+$: 275.1196, found: 275.1184.

Ethyl 2-(pyridin-2-yl)-2-((4-(trifluoromethyl)phenyl)amino)acetate 3bd:



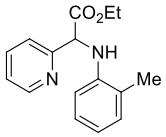
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 86% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.64 (d, *J*=4.03 Hz, 1 H), 7.74 (t, *J*=7.52 Hz, 1 H), 7.51 (d, *J*=8.07 Hz, 1 H), 7.39 (d, *J*=8.44 Hz, 2 H), 7.31 – 7.29 (m, 1 H), 6.67 (d, *J*=8.44 Hz, 2 H), 5.89 (br. s, 1 H), 5.32 (s, 1 H), 4.25 – 4.16 (m, 2 H), 1.20 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.42, 155.19, 149.06, 148.41, 37.69, 126.65 (q, *J*=3.78 Hz), 124.79 (q, *J*=270.9 Hz), 123.57, 122.20, 119.76 (d, *J*=11.3 Hz), 112.71, 62.27, 61.37, 14.03. HRMS (ESI) calculated for $C_{16}H_{16}F_3N_2O_2$ $[M+H]^+$: 325.1164, found: 325.1156.

Methyl 4-((2-ethoxy-2-oxo-1-(pyridin-2-yl)ethyl)amino)benzoate 3be:



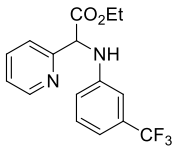
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.62 (d, *J*=4.38 Hz, 1 H), 7.85 – 7.82 (m, 2 H), 7.71 (td, *J*=7.60, 1.75 Hz, 1 H), 7.48 (d, *J*=7.89 Hz, 1 H), 7.29 – 7.25 (m, 1 H), 6.62 (d, *J*=8.48 Hz, 2 H), 6.00 (br. s, 1 H), 5.31 (s, 1 H), 4.19 (qq, *J*=10.75, 7.08 Hz, 2 H), 1.18 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.46, 167.09, 155.07, 149.69, 149.21, 137.40, 131.46, 123.45, 122.10, 119.41, 112.36, 62.16, 61.31, 51.52, 14.01. HRMS (ESI) calculated for $C_{17}H_{19}N_2O_4$ $[M+H]^+$: 315.1345, found: 315.1335.

Ethyl 2-(pyridin-2-yl)-2-(o-tolylamino)acetate 3bf:



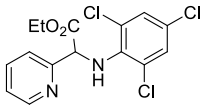
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.65 (d, *J*=4.97 Hz, 1 H), 7.71 (td, *J*=7.67, 1.61 Hz, 1 H), 7.52 (d, *J*=7.89 Hz, 1 H), 7.29 – 7.27 (m, 1 H), 7.09 – 7.01 (m, 2 H), 6.67 (t, *J*=7.31 Hz, 1 H), 6.47 (d, *J*=8.18 Hz, 1 H), 5.34 (s, 1 H), 4.24 – 4.16 (m, 2 H), 2.32 (s, 3 H), 1.20 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.35, 156.49, 149.39, 144.14, 137.02, 130.21, 126.96, 123.08, 122.77, 121.84, 117.80, 110.64, 62.35, 61.85, 17.51, 14.01. HRMS (ESI) calculated for $C_{16}H_{19}N_2O_2$ $[M+H]^+$: 271.1447, found: 271.1444.

Ethyl 2-(pyridin-2-yl)-2-((3-(trifluoromethyl)phenyl)amino)acetate 3bg:



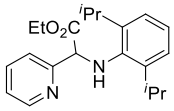
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 71% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.64 (d, *J*=4.04 Hz, 1 H), 7.75 (td, *J*=7.61, 1.65 Hz, 1 H), 7.52 (d, *J*=7.70 Hz, 1 H), 7.32 – 7.22 (m, 2 H), 6.95 (d, *J*=7.70 Hz, 1 H), 6.88 (s, 1 H), 6.80 (dd, *J*=8.25, 1.65 Hz, 1 H), 5.78 (br. s, 1 H), 5.32 (s, 1 H), 4.26 – 4.17 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 170.51, 155.14, 148.93, 146.14, 137.71, 131.55 (d, *J*=31.5 Hz), 129.73, 124.16 (q, *J*=272.2 Hz), 123.55, 122.33, 116.37, 114.68 (q, *J*=3.78 Hz), 109.85 (q, J=3.78Hz). HRMS (ESI) calculated for $C_{16}H_{16}F_3N_2O_2$ $[M+H]^+$: 325.1164, found: 325.1152.

Ehyl 2-(pyridin-2-yl)-2-((2,4,6-trichlorophenyl)amino)acetate 3bh:



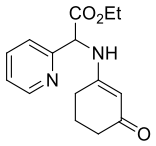
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.60 (d, *J*=4.03 Hz, 1 H), 7.69 (t, *J*=7.52 Hz, 1 H), 7.46 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.23 (m, 1 H), 7.20 (s, 2 H), 6.10 (br. s, 1 H), 5.84 (s, 1 H), 4.18 – 4.12 (m, 2 H), 1.16 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.63, 155.36, 149.23, 139.65, 137.06, 128.53, 125.80, 125.50, 123.27, 122.77, 63.13, 61.87, 13.95. HRMS (ESI) calculated for $C_{15}H_{14}Cl_3N_2O_2$ $[M+H]^+$: 359.0121, found: 359.0113.

Ethyl 2-((2,6-diisopropylphenyl)amino)-2-(pyridin-2-yl)acetate 3bi:



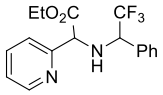
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.64 (d, *J*=4.40 Hz, 1 H), 7.65 (t, *J*=7.34 Hz, 1 H), 7.31 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.23 (m, 1 H), 7.06 – 7.01 (m, 3 H), 4.90 (s, 1 H), 4.17 (qd, *J*=7.09, 2.57 Hz, 2 H), 3.28 – 3.20 (m, 2 H), 1.21 (d, *J*=6.60 Hz, 6 H), 1.16 (t, *J*=7.15 Hz, 3 H), 1.09 (d, *J*=6.60 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.83, 157.27, 149.26, 141.96, 140.89, 136.92, 123.61, 123.56, 122.95, 122.61, 67.90, 61.45, 27.66, 24.08, 14.02. HRMS (ESI) calculated for $C_{21}H_{29}N_2O_2$ $[M+H]^+$: 341.2229, found: 341.2220.

Ethyl 2-((3-oxocyclohex-1-en-1-yl)amino)-2-(pyridin-2-yl)acetate 3bj:



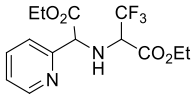
Was prepared according to the general procedure using 1 mol % of $Rh_2(esp)_2$ catalyst in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.56 (d, *J*=4.09 Hz, 1 H), 7.72 (td, *J*=7.67, 1.61 Hz, 1 H), 7.45 (d, *J*=7.89 Hz, 1 H), 7.27 (dd, *J*=4.68, 2.05 Hz, 1 H), 6.37 (d, *J*=5.85 Hz, 1 H), 5.12 (d, *J*=6.72 Hz, 1 H), 5.03 (s, 1 H), 4.21 – 4.13 (m, 2 H), 2.52 – 2.41 (m, 2 H), 2.31 – 2.27 (m, 2 H), 2.01 – 1.93 (m, 2 H), 1.19 (t, *J*=7.02 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.51, 169.17, 162.49, 153.03, 149.33, 137.31, 123.64, 122.67, 98.67, 62.35, 59.81, 36.32, 29.54, 21.77, 13.93. HRMS (ESI) calculated for $C_{15}H_{19}N_2O_3$ $[M+H]^+$: 275.1396, found: 275.1394.

Ethyl 2-(pyridin-2-yl)-2-((2,2,2-trifluoro-1-phenylethyl)amino)acetate 3bk:



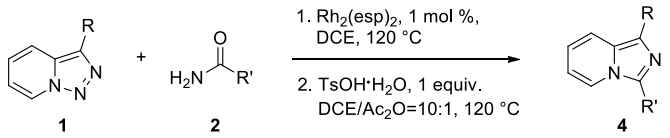
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 87% yield (mixture of diastereomers, *dr* = 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.59 (d, *J*=4.40 Hz, 1 H), 8.55 (d, *J*=4.40 Hz, 1 H), 7.69 (t, *J*=7.70 Hz, 1 H), 7.65 (td, *J*=7.70, 1.10 Hz, 1 H), 7.44-7.21 (m, 14 H), 4.54 (s, 1 H), 4.42-4.38 (m, 2 H), 4.20-4.03 (m, 5 H), 3.34 (br. s, 2 H), 1.17 (t, *J*=7.15 Hz, 3 H), 1.13 (t, *J*=6.97 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 171.23, 171.00, 156.32, 149.57, 149.51, 137.05, 136.95, 133.54, 133.10, 129.35, 129.26, 129.16, 128.80, 128.77, 128.74, 125.30 (d, *J*=278.8 Hz), 125.19 (d, *J*=278.8 Hz), 123.21, 123.13, 123.08, 122.88, 64.12, 63.36, 62.49 (q, *J*=28.75 Hz), 62.17 (q, *J*=28.75 Hz), 61.64, 61.46, 14.10, 13.98. HRMS (ESI) calculated for $C_{17}H_{18}F_3N_2O_2$ $[M+H]^+$: 339.1320, found: 339.1308.

Ethyl 2-((2-ethoxy-2-oxo-1-(pyridin-2-yl)ethyl)amino)-3,3,3-trifluoropropanoate 3bl:



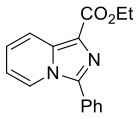
Was prepared according to the general procedure using 3 mol % of $Rh_2(esp)_2$ catalyst in 82% yield (mixture of diastereomers, *dr* = 1 : 0.6). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.56-8.55 (m, 1.6 H), 7.70 (qd, *J*=7.60, 1.46 Hz, 1.6 H), 7.46 (d, *J*=7.60 Hz, 1 H), 7.40 (d, *J*=7.89 Hz, 0.6 H), 7.22-7.25 (m, 1.6 H), 4.76 (s, 0.6 H), 4.66 (s, 1 H), 4.34-4.25 (m, 2 H), 4.23-4.13 (m, 4.4 H), 3.95 (q, *J*=7.31 Hz, 0.6 H), 3.85 (q, *J*=7.50 Hz, 1 H), 3.56 (br. s, 1.6 H), 1.31 (t, *J*=7.16 Hz, 3 H), 1.26-1.15 (m, 6.6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.01, 170.73, 166.54, 156.21, 149.39, 149.18, 137.14, 136.99, 124.79 (d, *J*=5.04 Hz), 123.24, 122.83, 122.72, 122.04 (d, *J*=6.30 Hz), 65.60, 64.85, 62.60, 62.35, 61.72, 61.57, 61.27 (d, *J*=36.54 Hz), 60.12 (*J*=37.80 Hz), 13.96, 13.92, 13.85. HRMS (ESI) calculated for $C_{14}H_{18}F_3N_2O_4$ $[M+H]^+$: 335.1219, found: 335.1217.

Part III. Synthesis of Imidazo[1,2-a]pyridines



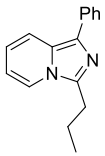
General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1 mol %), pyridotriazole (0.3 mmol), amide **2** and DCE (2 ml) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 120 °C until completion. Then it was cooled down to room temperature and $TsOH \cdot H_2O$ (0.3 mmol) and Ac_2O (0.2 ml) were added under air. The reaction was stirred at 120 ^oC until the N-H insertion product was consumed. Upon completion the mixture was cooled to room temperature, diluted with ethyl acetate and washed with aqueous $NaHCO_3$. Then the organic phase was dried over Na_2SO_4, concentrated under reduced pressure, purified by column chromatography to afford the corresponding imidazo[1,2-*a*]pyridine product (Hexanes: EtOAc).

Ethyl 3-phenylimidazo[1,5-a]pyridine-1-carboxylate 4a:



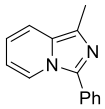
Was prepared according to the general procedure in 70% yield. ^1H NMR (500 MHz, $CDCl_3$) δ ppm 8.31 (d, *J*=7.34 Hz, 1 H), 8.26 (d, *J*=9.17 Hz, 1 H), 7.79 (d, *J*=7.34 Hz, 2 H), 7.55-7.49 (m, 3 H), 7.13 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.78 (t, *J*=6.79 Hz, 1 H), 4.50 (q, *J*=6.97 Hz, 2 H), 1.47 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 163.58, 139.12, 135.42, 129.53, 129.09, 128.96, 128.81, 124.15, 122.49, 121.80, 120.11, 114.37, 60.40, 14.66. HRMS (ESI) calculated for $[M+H]^+$: 267.1134, found: 267.1131.

1-Phenyl-3-propylimidazo[1,5-a]pyridine 4b:



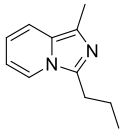
Was prepared according to the general procedure in 77% yield. ^1H NMR (500 MHz, $CDCl_3$) δ ppm 7.87 (d, *J*=7.34 Hz, 2 H), 7.76 (d, *J*=9.17 Hz, 1 H), 7.72 (d, *J*=6.97 Hz, 1 H), 7.44 (t, *J*=7.70 Hz, 2 H), 7.28-7.25 (m, 1 H), 6.70 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.54 (t, *J*=6.60 Hz, 1 H), 3.01 (t, *J*=7.70 Hz, 2 H), 1.90 (sxt, *J*=7.56 Hz, 2H), 1.07 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 138.87, 135.23, 129.96, 128.62, 126.46, 126.34, 126.06, 120.96, 119.02, 118.52, 112.31, 28.63, 20.66, 14.01. HRMS (ESI) calculated for $[M+H]^+$: 237.1392, found: 237.1393.

1-Methyl-3-phenylimidazo[1,5-a]pyridine 4c:



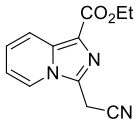
Was prepared according to the general procedure in 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.17 (d, *J*=7.34 Hz, 1 H), 7.78 (d, *J*=7.70 Hz, 2 H), 7.50 (t, *J*=7.70 Hz, 2 H), 7.42-7.38 (m, 2 H), 6.62 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.49 (t, *J*=6.79 Hz, 1 H), 2.58 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 136.27, 129.95, 128.92, 128.49, 127.87, 127.74, 121.08, 118.33, 117.21, 113.06, 12.35. HRMS (ESI) calculated for $[M+H]^+$: 209.1079, found: 209.1078.

1-Methyl-3-propylimidazo[1,5-a]pyridin 4d:



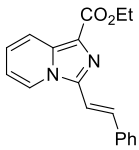
Was prepared according to the general procedure in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.61 (d, *J*=7.02 Hz, 1 H), 7.29 (d, *J*=9.06 Hz, 1 H), 6.53 (dd, *J*=8.92, 6.28 Hz, 1 H), 6.47-6.43 (m, 1 H), 2.92 (t, *J*=7.6 Hz, 2 H), 2.49 (s, 3 H), 1.84 (sxt, *J*=7.48 Hz, 2 H), 1.00 (t, *J*=7.45 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 137.02, 126.28, 125.96, 120.27, 118.17, 115.93, 112.11, 28.31, 20.63, 13.95, 12.18. HRMS (ESI) calculated for $[M+H]^+$: 175.1235, found: 175.1227.

Ethyl 3-(cyanomethyl)imidazo[1,5-a]pyridine-1-carboxylate 4e:



Was prepared according to the general procedure in 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 8.24 (d, *J*=9.35 Hz, 1 H), 8.04 (d, *J*=7.02 Hz, 1 H), 7.22 (dd, *J*=9.06, 6.72 Hz, 1H), 6.97 (t, *J*=6.87 Hz, 1 H), 4.46 (q, *J*=7.21 Hz, 2 H), 2.16 (s, 2 H), 1.45 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 162.79, 135.48, 127.17, 124.56, 121.28, 120.20, 115.36, 113.47, 60.63, 17.08, 14.53. HRMS (ESI) calculated for $[M+H]^+$: 230.0930, found: 230.0932.

(E)-Ethyl 3-styrylimidazo[1,5-a]pyridine-1-carboxylate 4f:

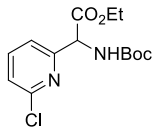


Was prepared according to the general procedure in 78% yield. ^{1}H NMR (500 MHz, acetone-*d*6) δ ppm: 8.78 (d, *J*=6.97 Hz, 1 H), 8.17 (d, *J*=9.17 Hz, 1 H), 7.77-7.68 (m, 4 H), 7.41 (t, *J*=7.70 Hz, 2 H), 7.34-7.31 (m, 1 H), 7.25 (dd, *J*=8.99, 6.42 Hz, 1 H), 7.02-6.99 (m, 1 H), 4.40 (q,

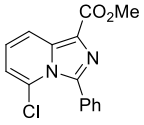
J=7.09 Hz, 2 H), 1.41 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 163.30, 137.37, 136.09, 134.92, 133.95, 128.70, 128.50, 126.78, 124.03, 121.64, 120.05, 114.49, 110.91, 109.47, 60.42, 14.52. HRMS (ESI) calculated for $[M+H]^+$: 293.1290, found: 293.1280.

Part IV. Reactivity Comparison Study

Catalyst Comparison -- General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with pyridotriazole and NH_2Boc (or PhCN) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve. A solution containing Rh(II) catalyst (1 mol %) was then added at room temperature and the reaction mixture was stirred for 5 min (full conversion can be obtained for those using $Rh_2(esp)_2$). Then it was analyzed by NMR.

Ethyl 2-((tert-butoxycarbonyl)amino)-2-(6-chloropyridin-2-yl)acetate 3aa: 

Pyridotriazole **1a** and NH_2Boc (1.5 equiv.) were reacted in $CDCl_3$. 78% NMR yield with $Rh_2(esp)_2$.

Methyl 5-chloro-3-phenylimidazo[1,5-a]pyridine-1-carboxylate 4g: 

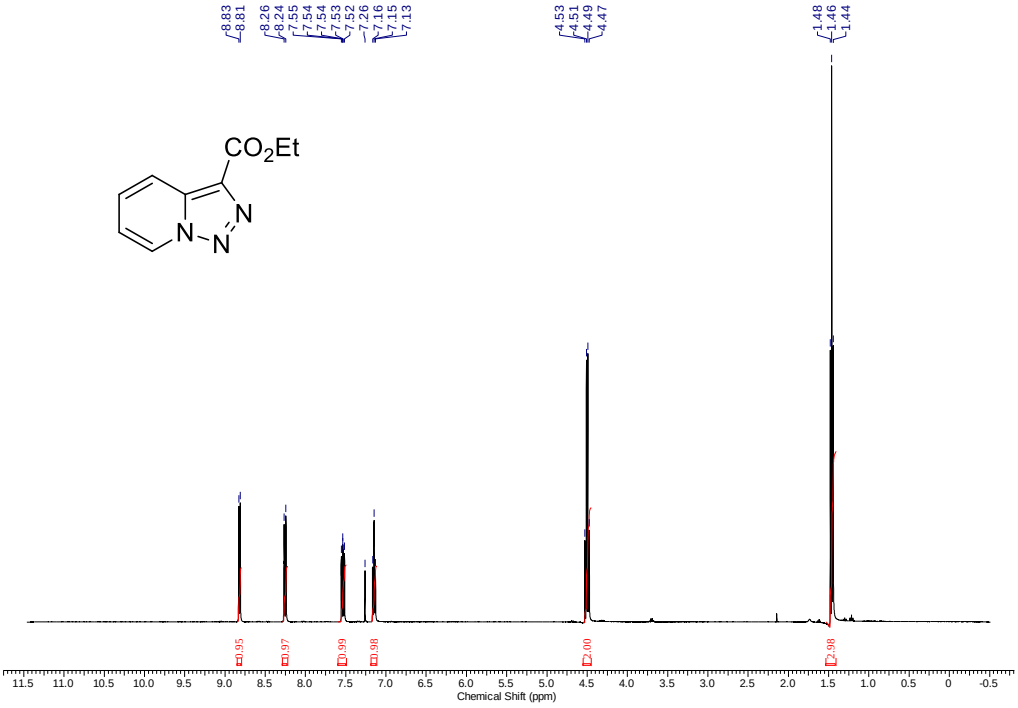
Pyridotriazole **1a** and PhCN (3.0 equiv.) were reacted in Toluene. 74% NMR yield with $Rh_2(esp)_2$

References:

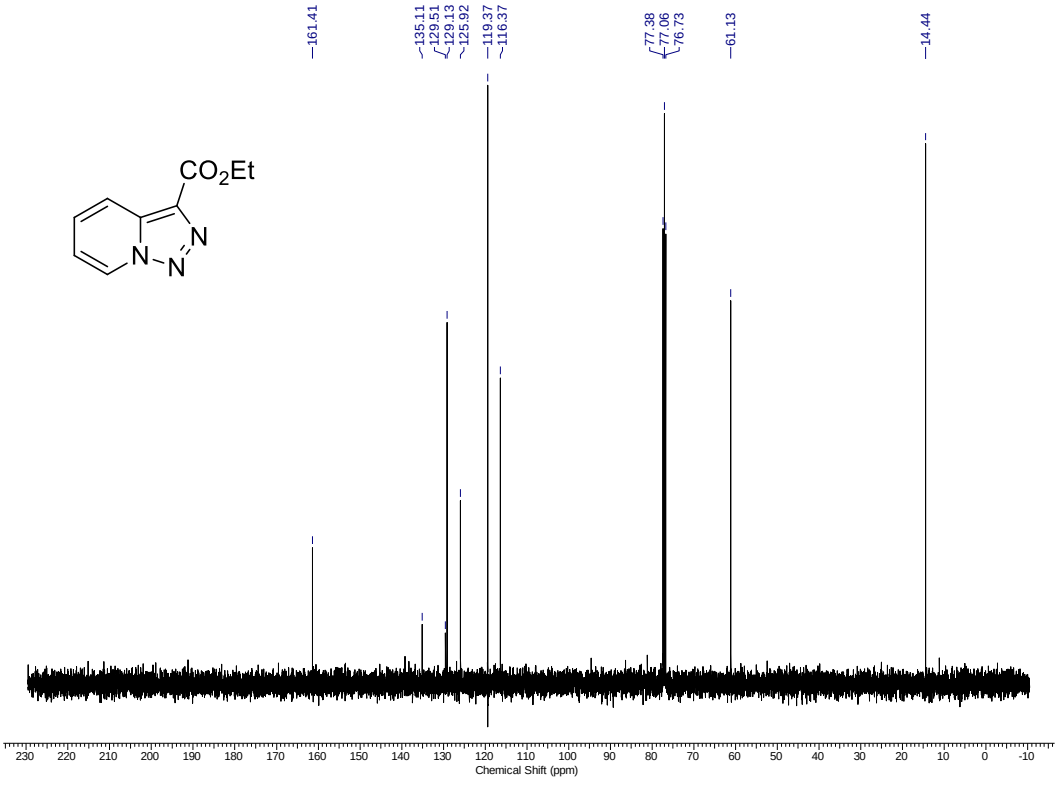
1. S. Chuprakov, F. W. Hwang, V. Gevorgyan, *Angew. Chem., Int. Ed*. **2007**, *46*, 4757.
2. S. Liu, J. Sawicki, T. G. Driver, *Org. Lett*. **2012**, *14*, 3744.
3. H. M. L. Davies, R. T. Townsend, *J. Org. Chem*. **2001**, *66*, 6595.

Copies of ^{1}H and ^{13}C NMR Spectra for Compounds 1,3,4

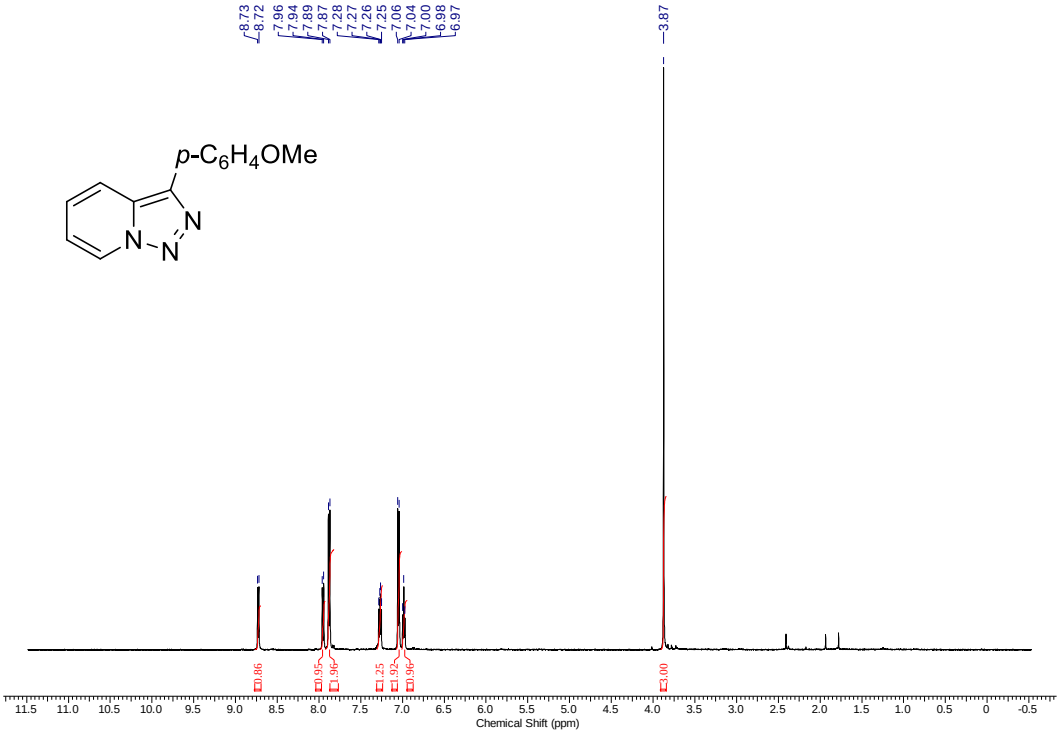
^{1}H NMR Spectrum of **1b**



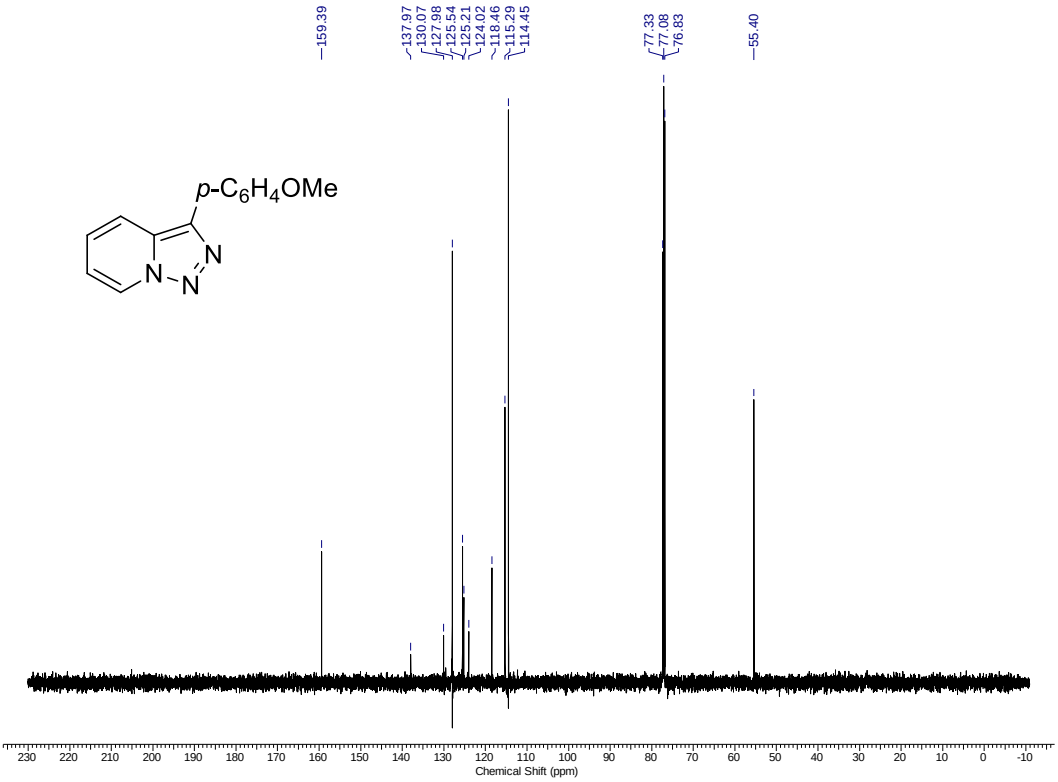
^{13}C NMR Spectrum of **1b**



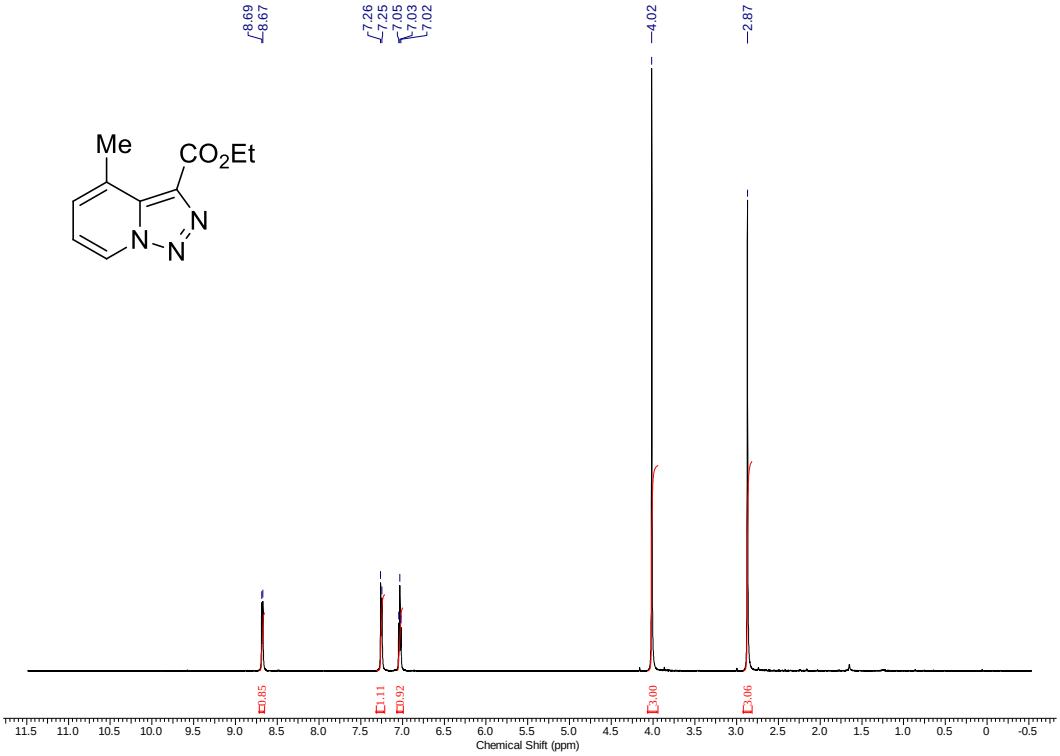
^{1}H NMR Spectrum of **1d**



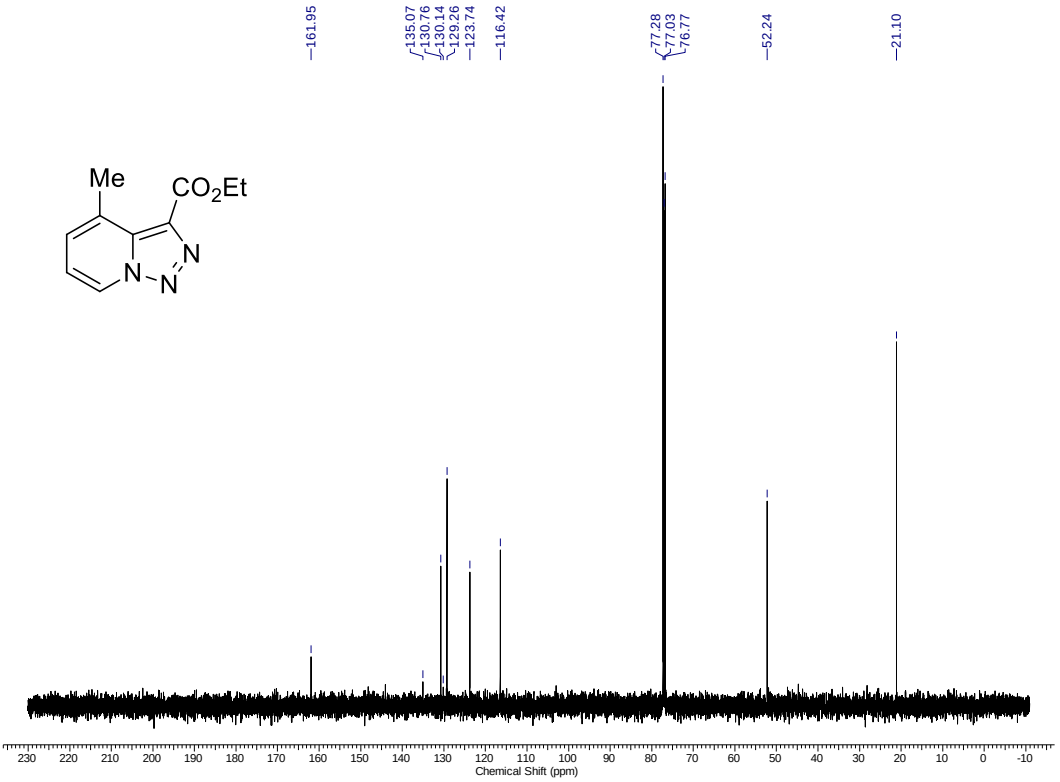
^{13}C NMR Spectrum of **1d**



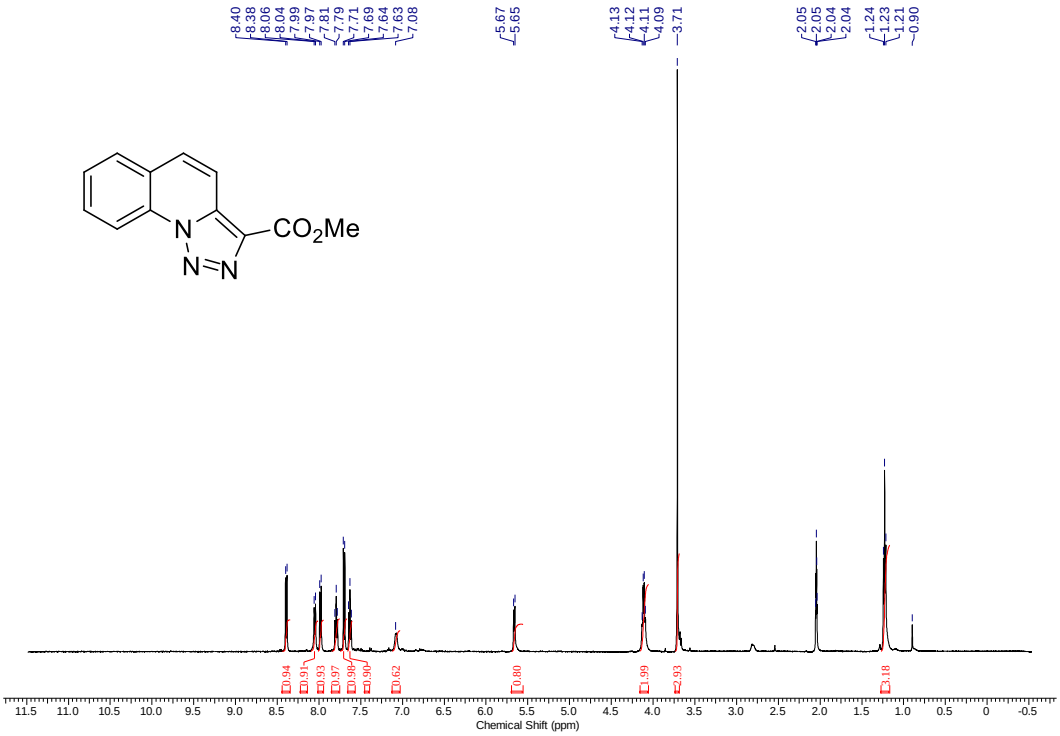
^{1}H NMR Spectrum of **1f**



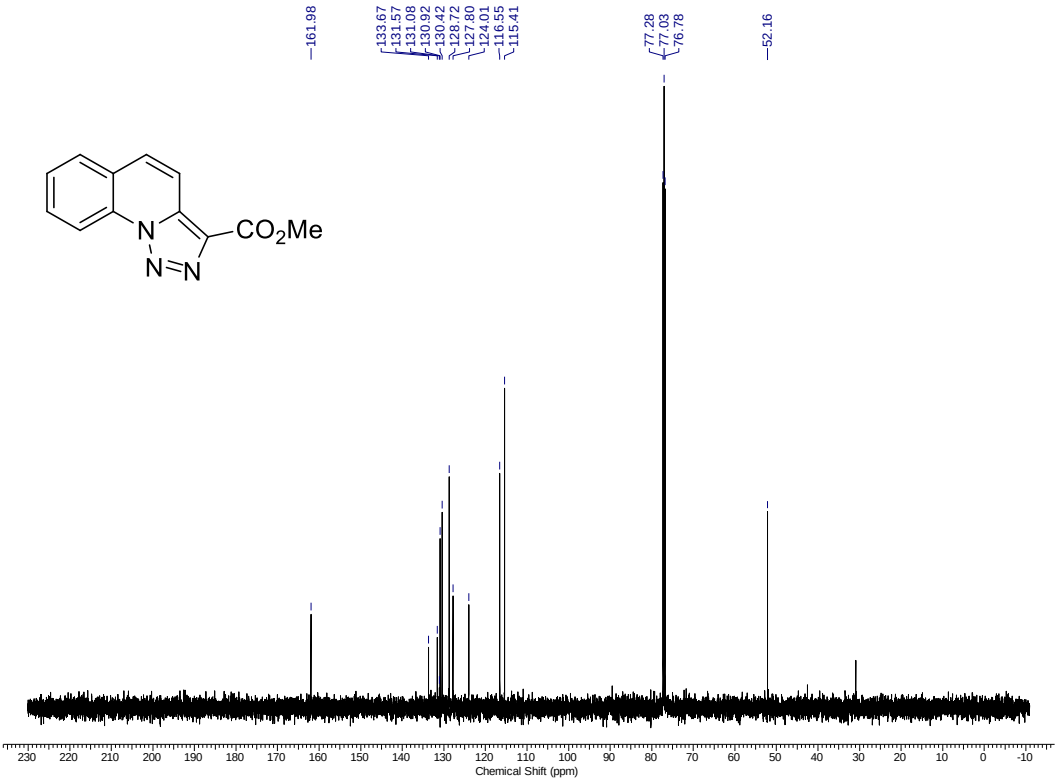
^{13}C NMR Spectrum of **1f**



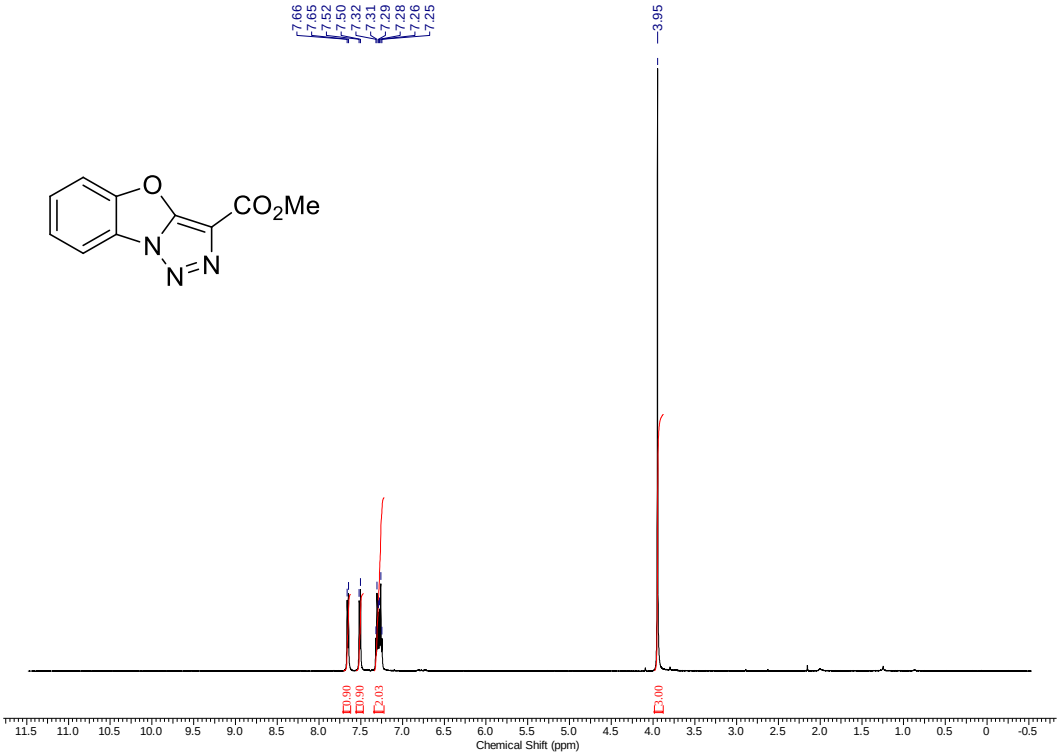
^{1}H NMR Spectrum of **1g**



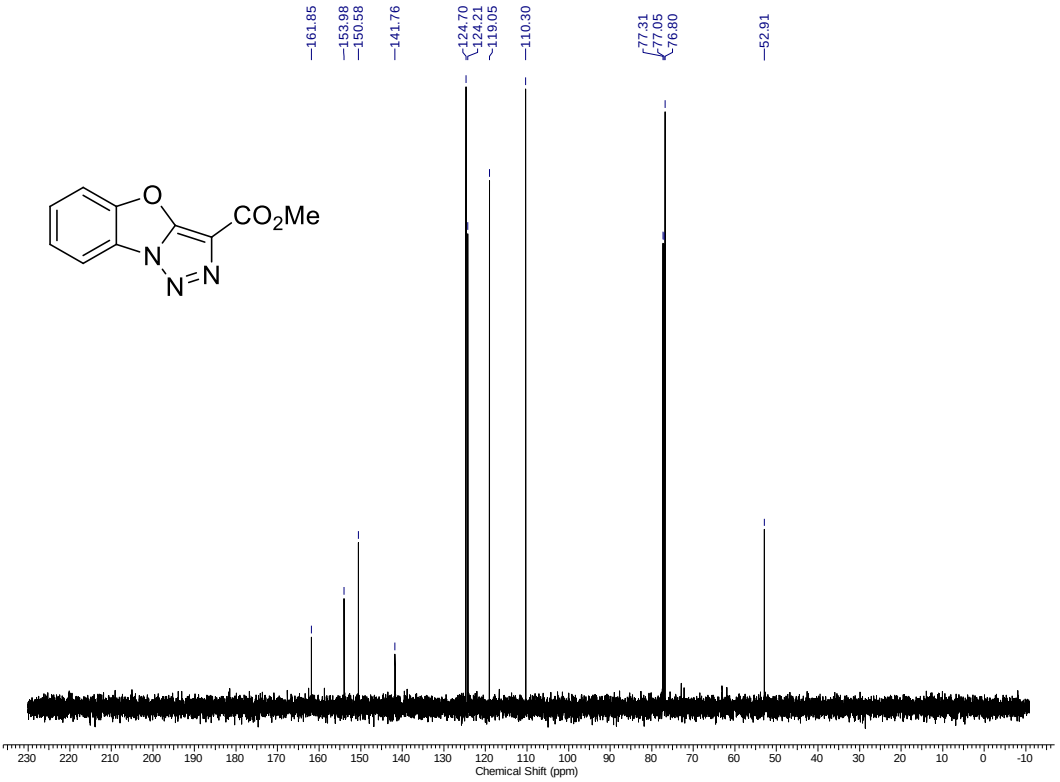
^{13}C NMR Spectrum of **1g**



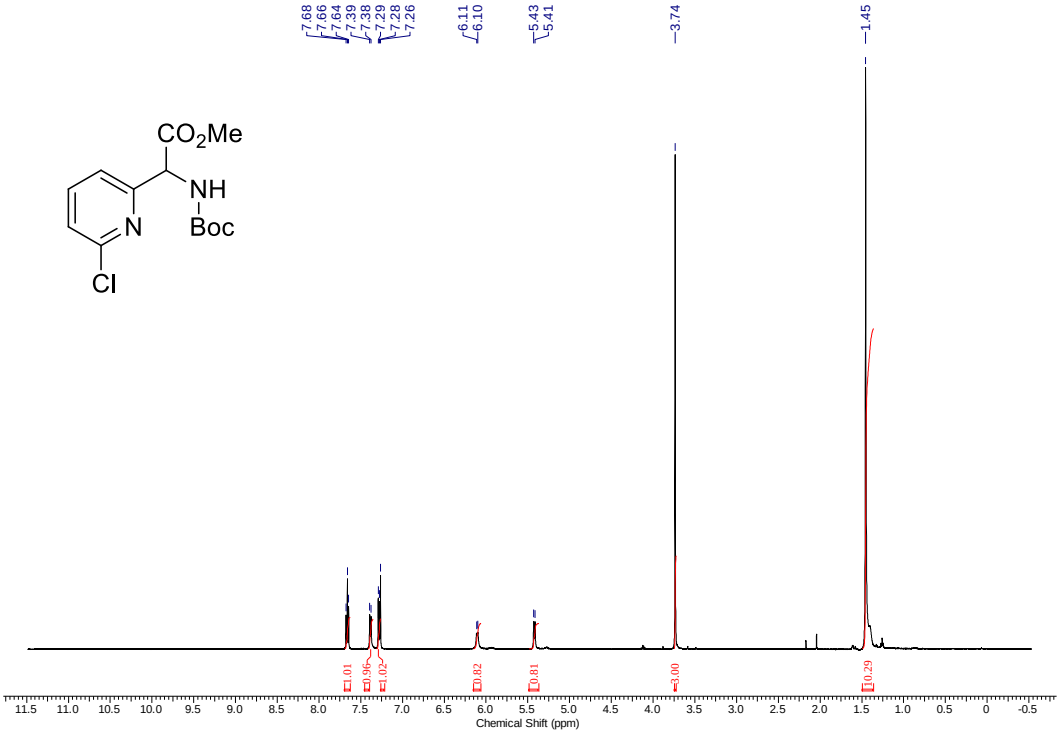
^{1}H NMR Spectrum of **1h**



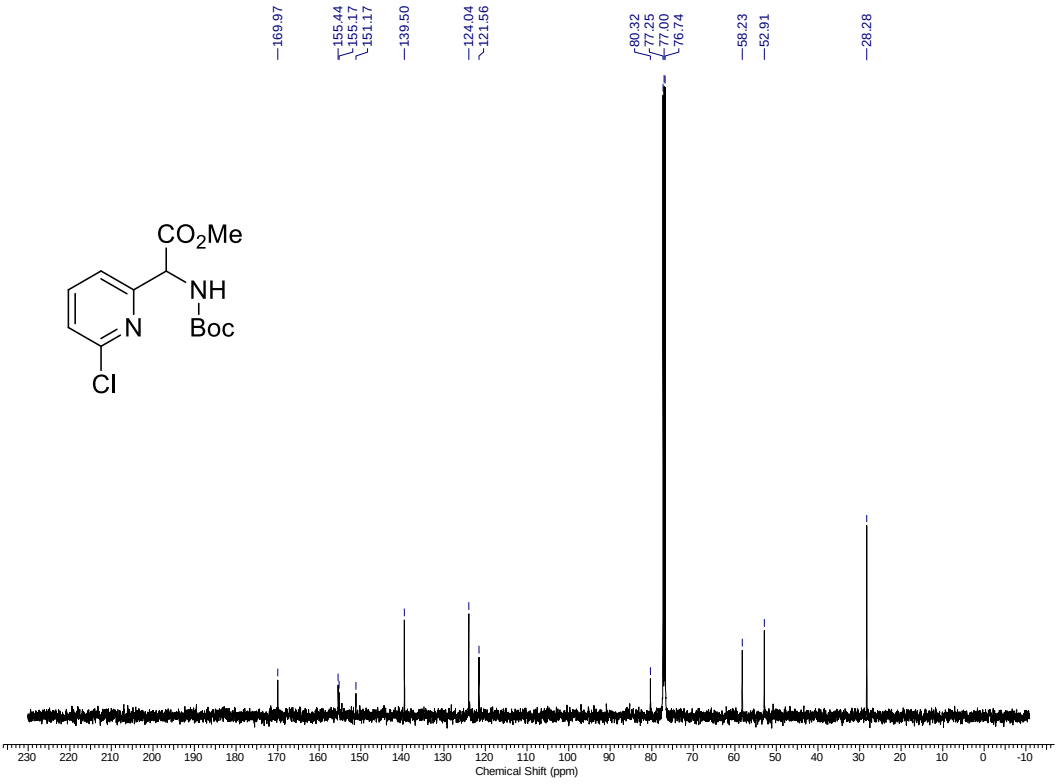
^{13}C NMR Spectrum of **1h**



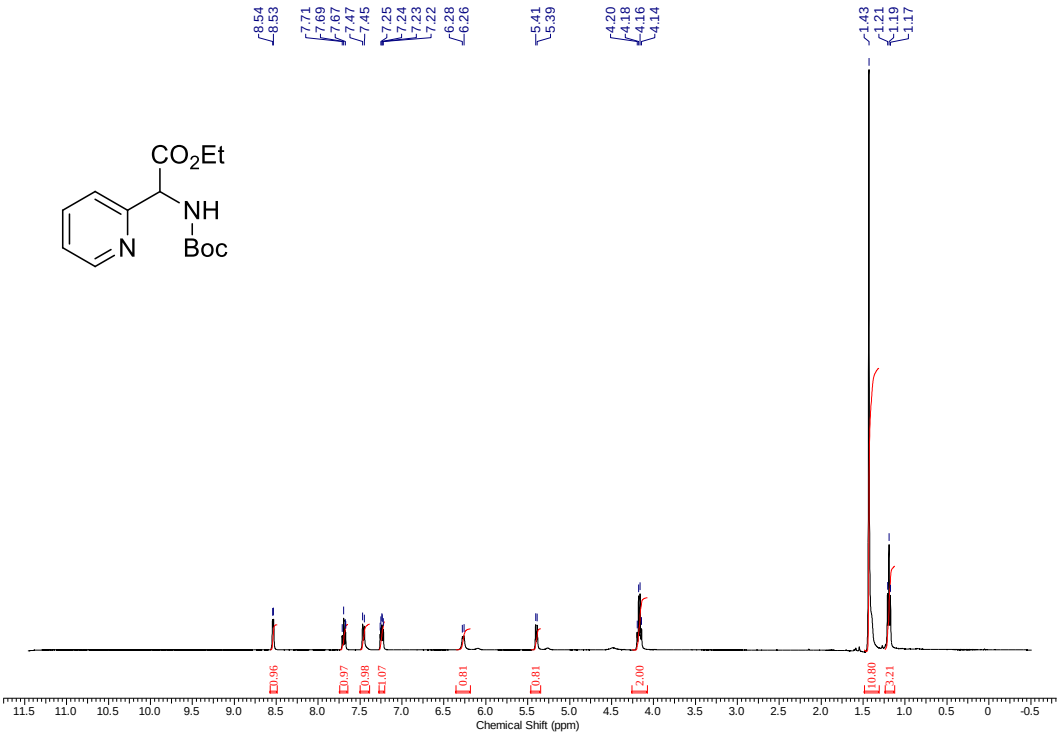
^{1}H NMR Spectrum of **3aa**:



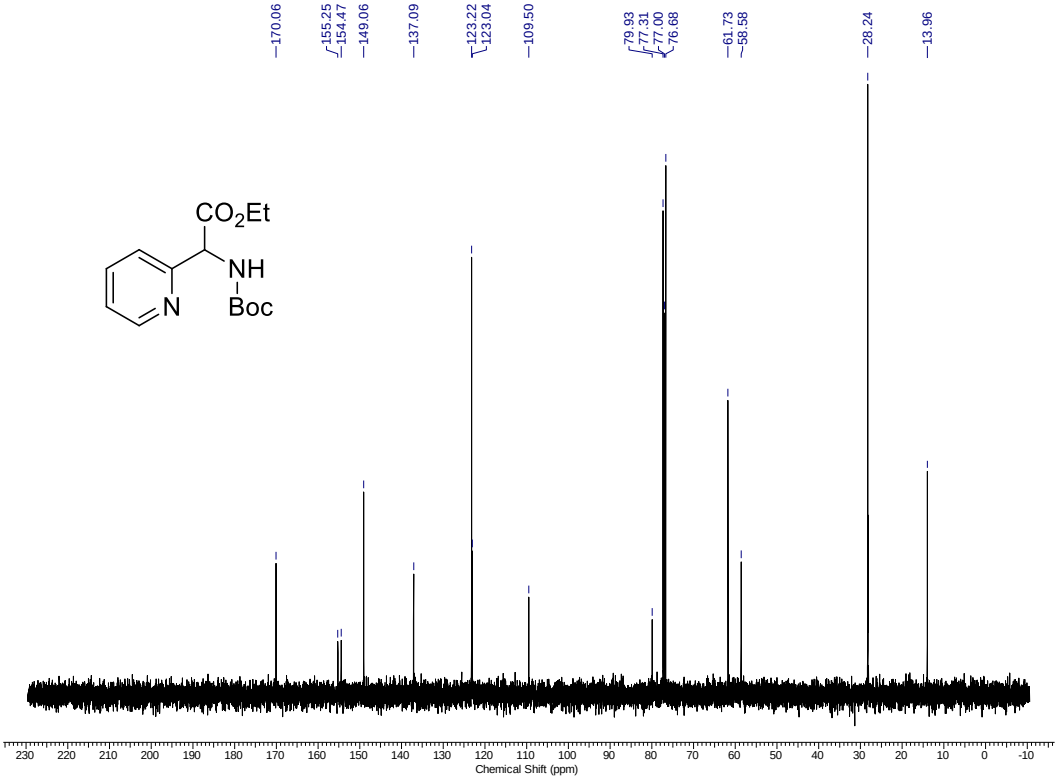
^{13}C NMR Spectrum of **3aa**:



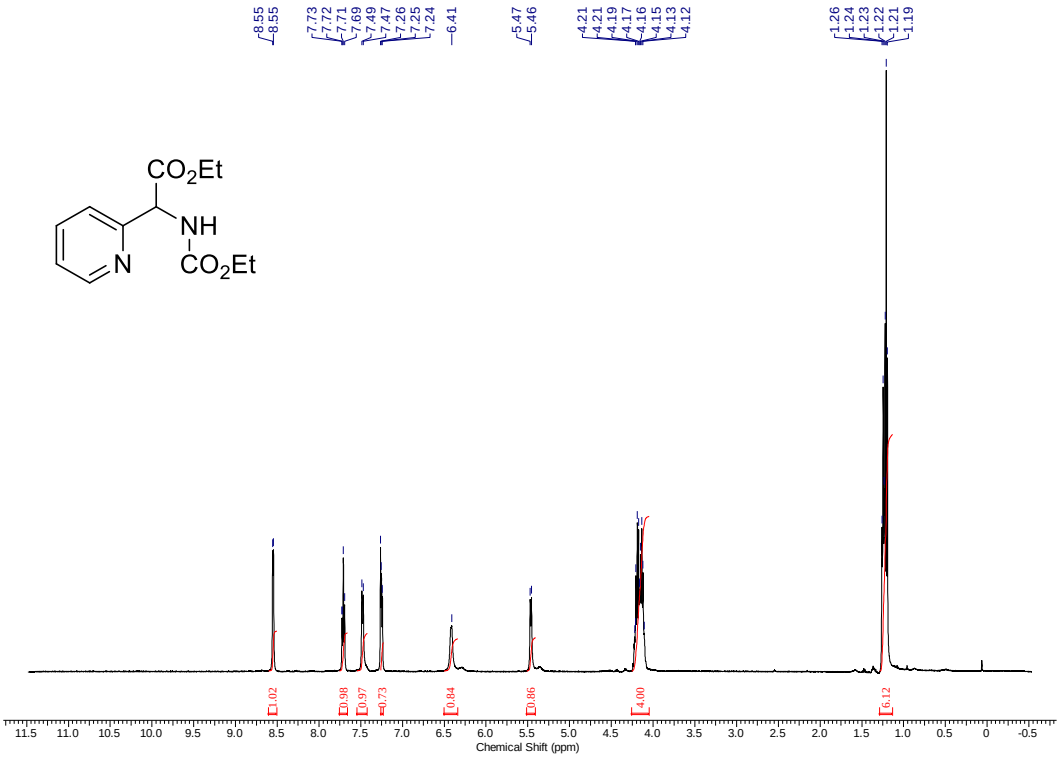
^{1}H NMR Spectrum of **3ab**:



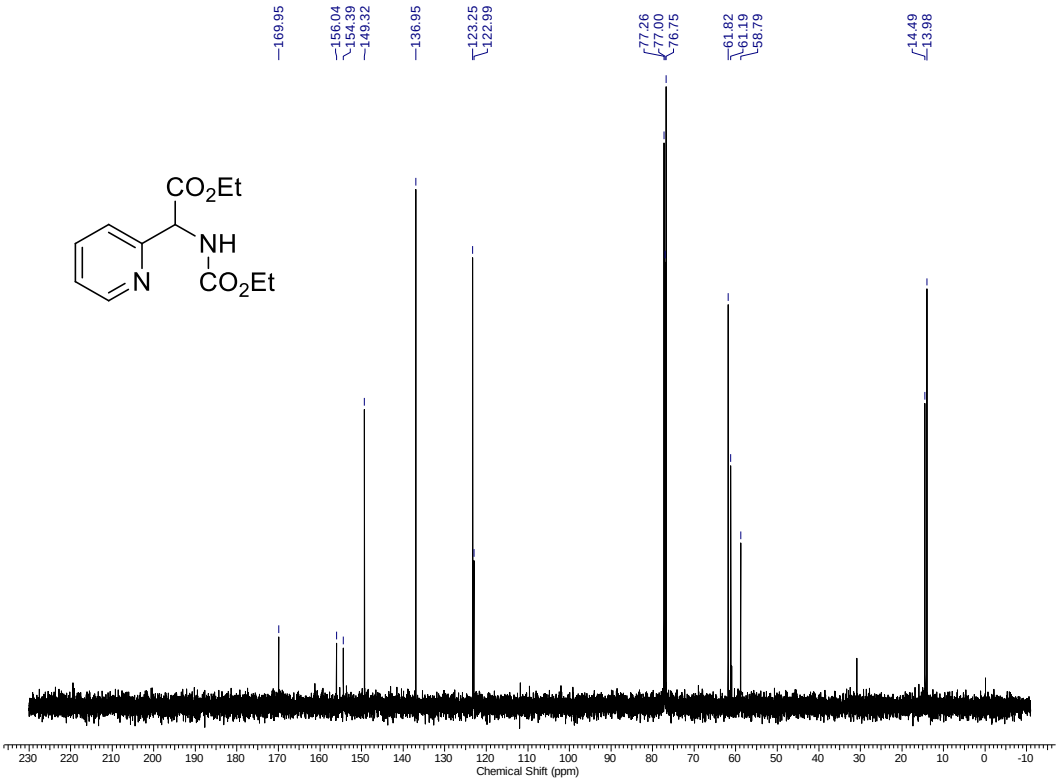
^{13}C NMR Spectrum of **3ab**:



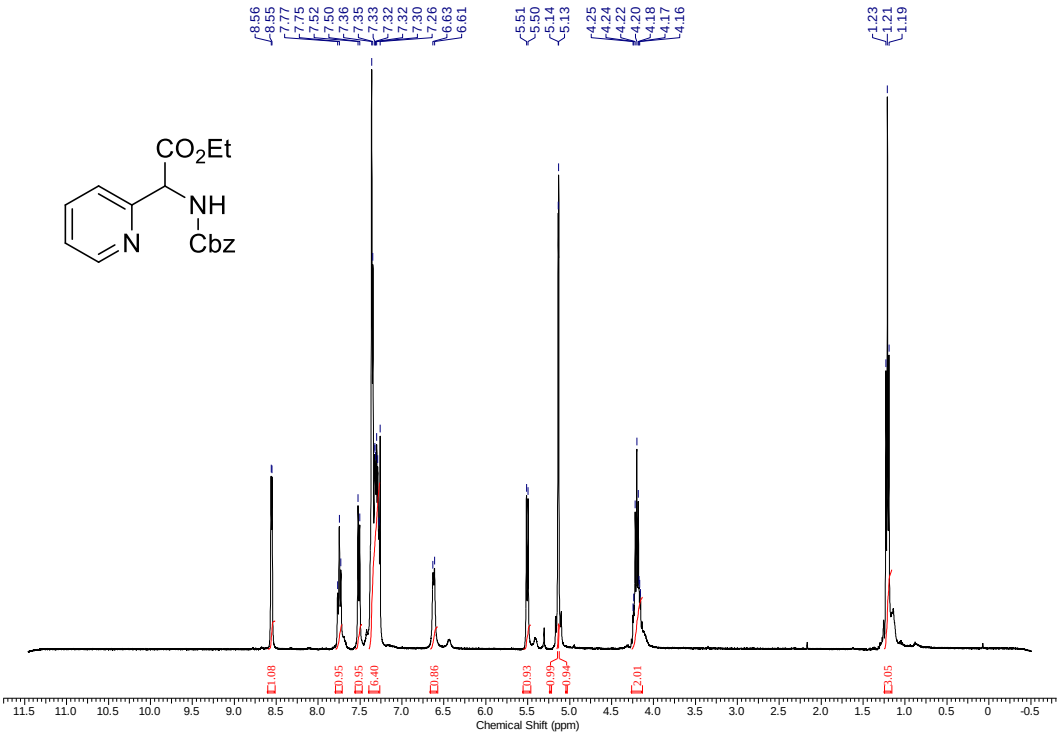
^{1}H NMR Spectrum of **3ac**:



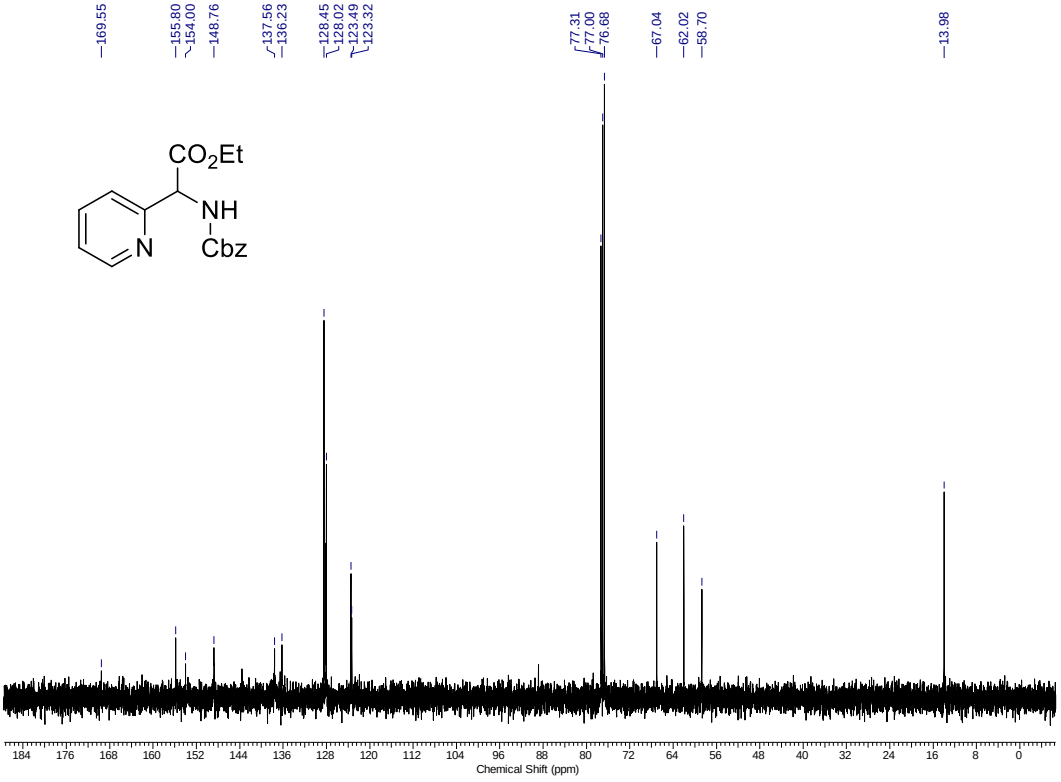
^{13}C NMR Spectrum of **3ac**:



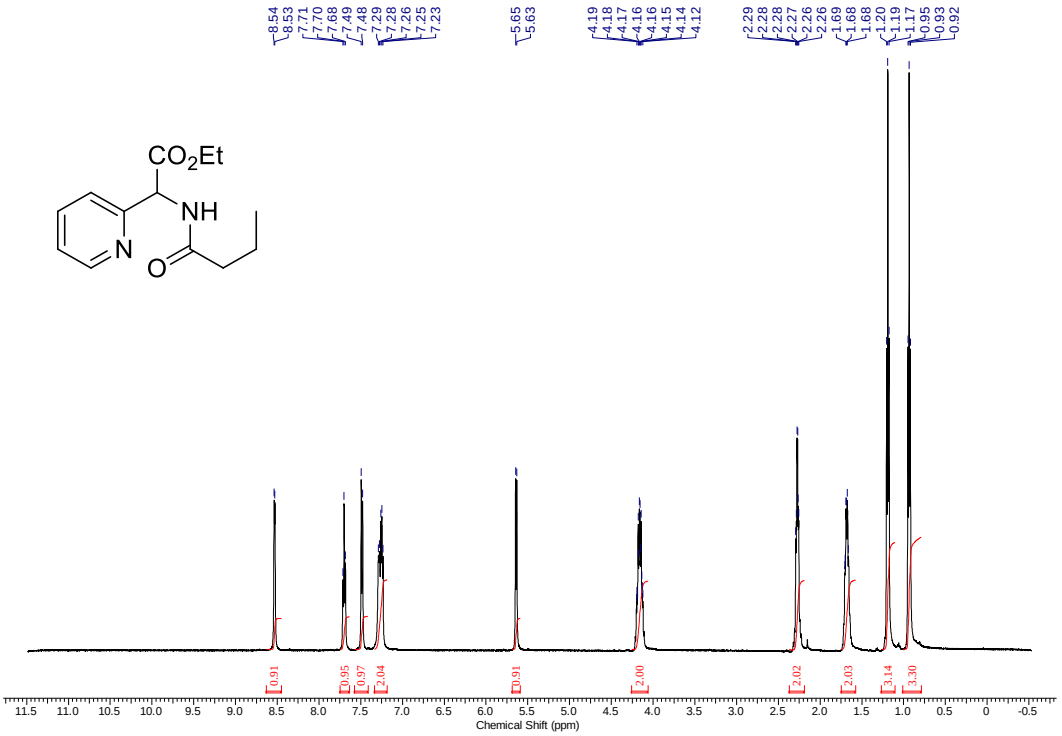
^{1}H NMR Spectrum of **3ad**:



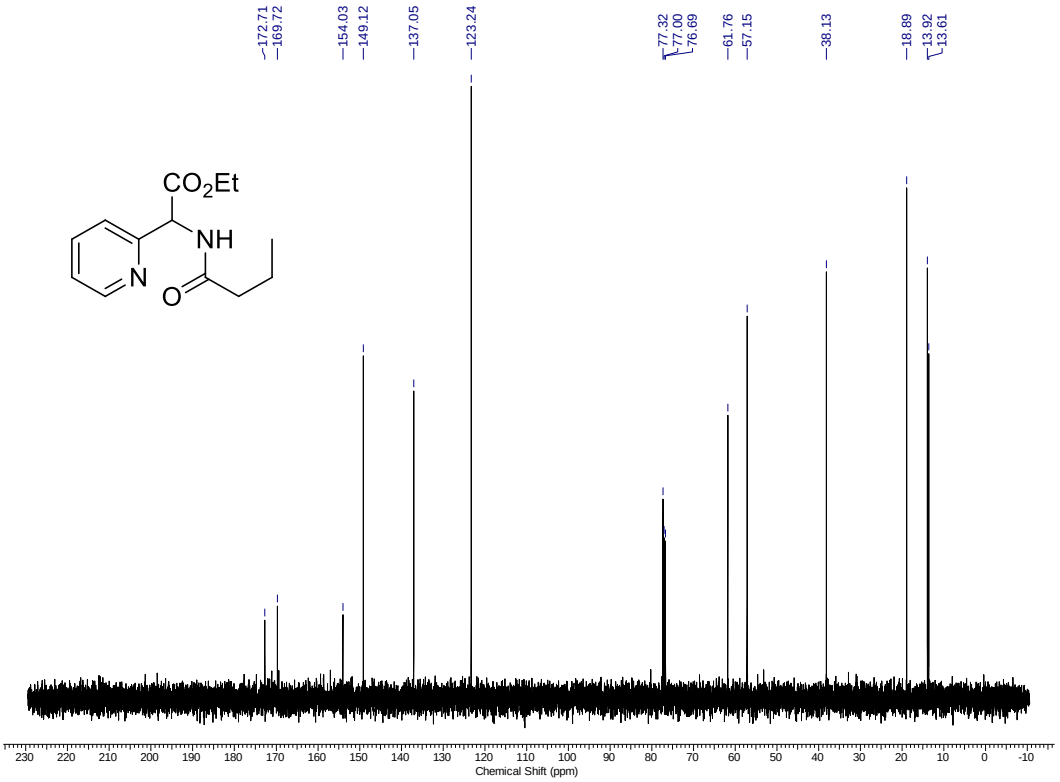
^{13}C NMR Spectrum of **3ad**:



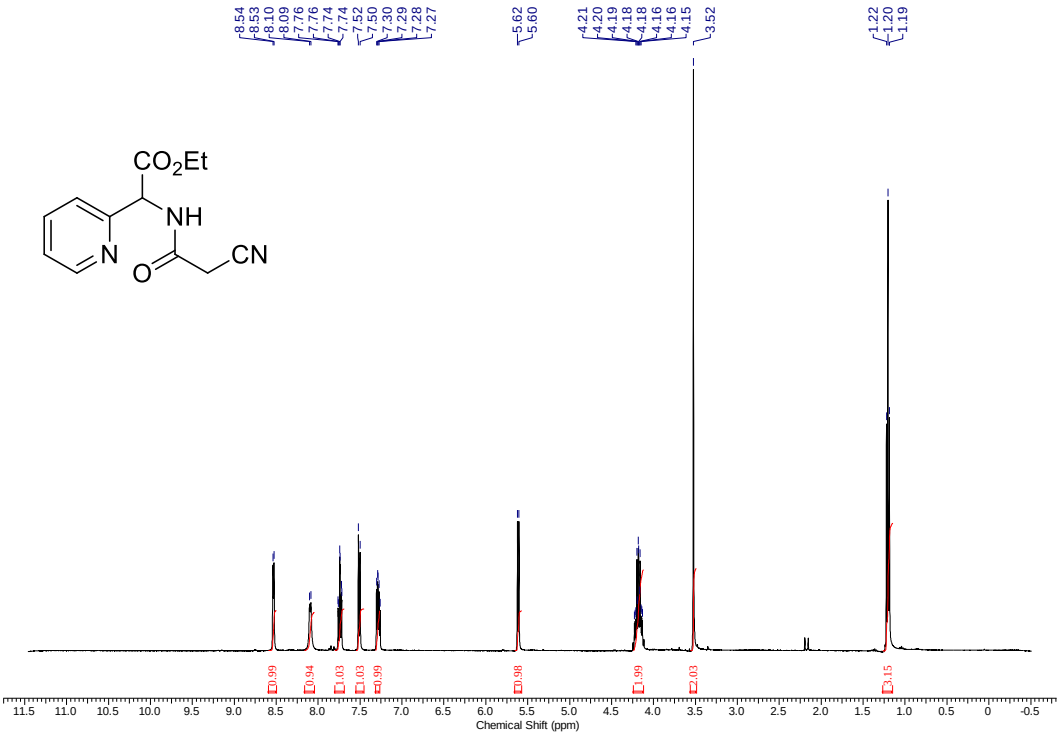
^{1}H NMR Spectrum of **3ae**:



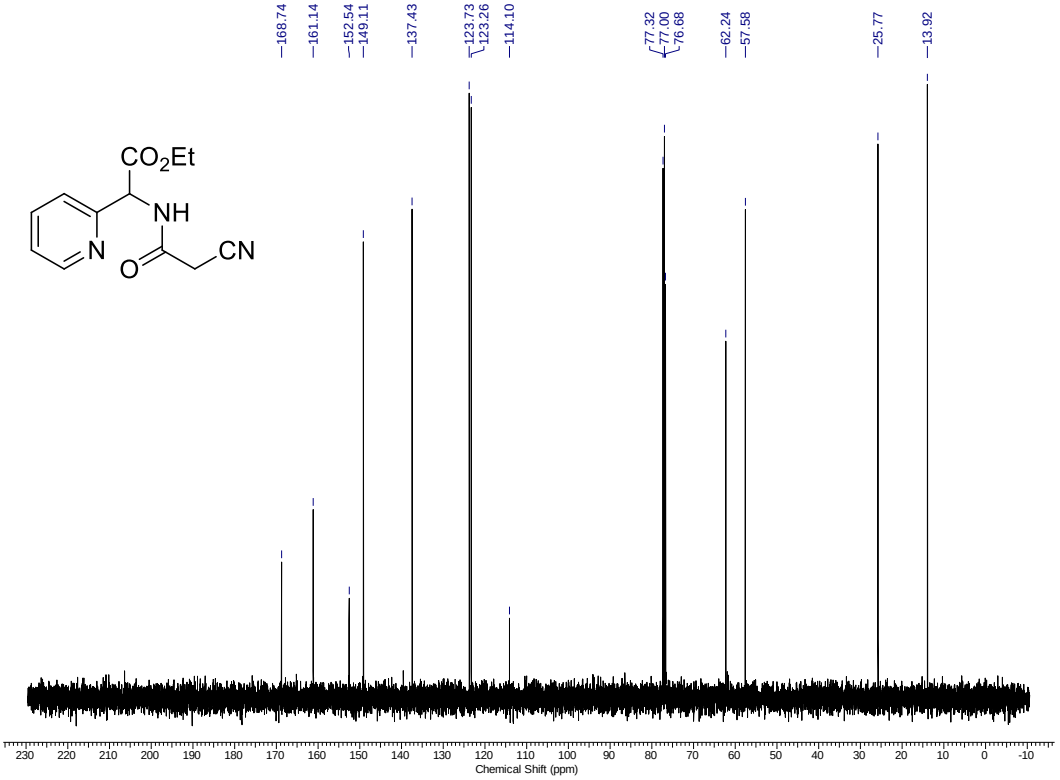
^{13}C NMR Spectrum of **3ae**:



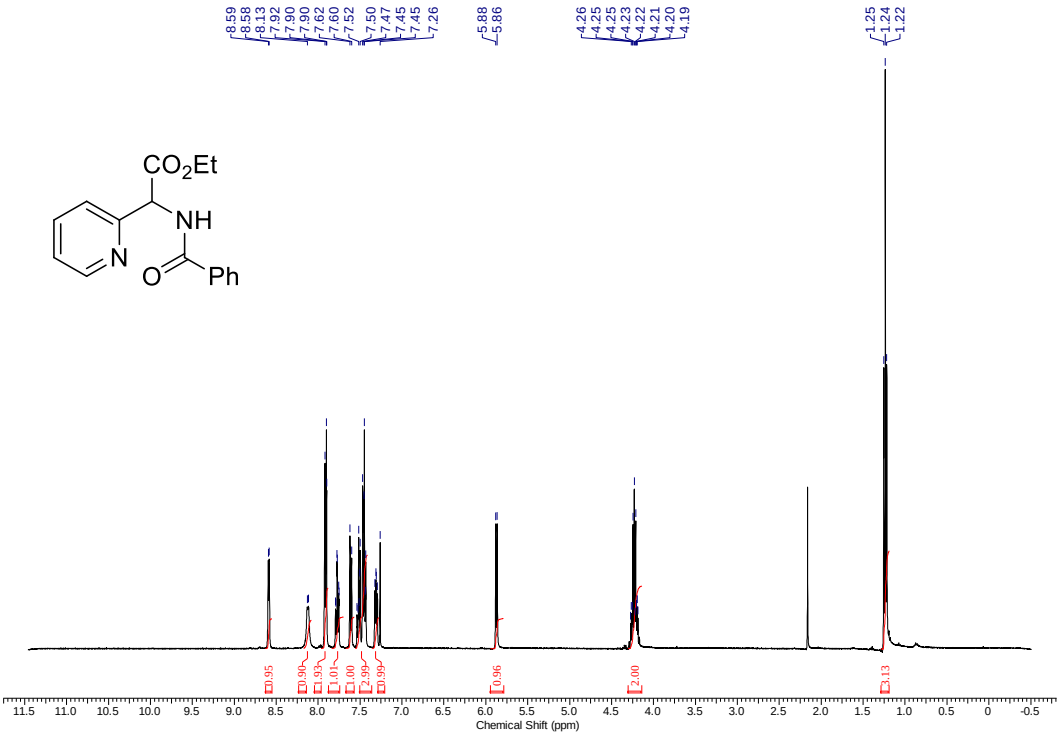
^{1}H NMR Spectrum of **3af**:



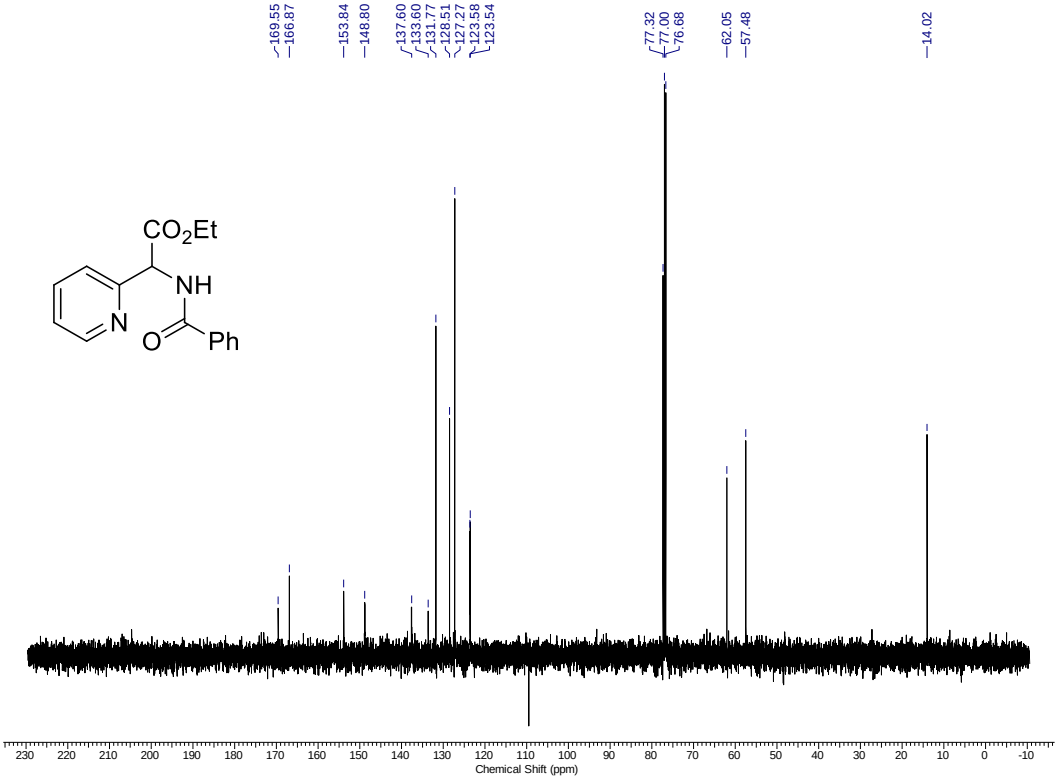
^{13}C NMR Spectrum of **3af**:



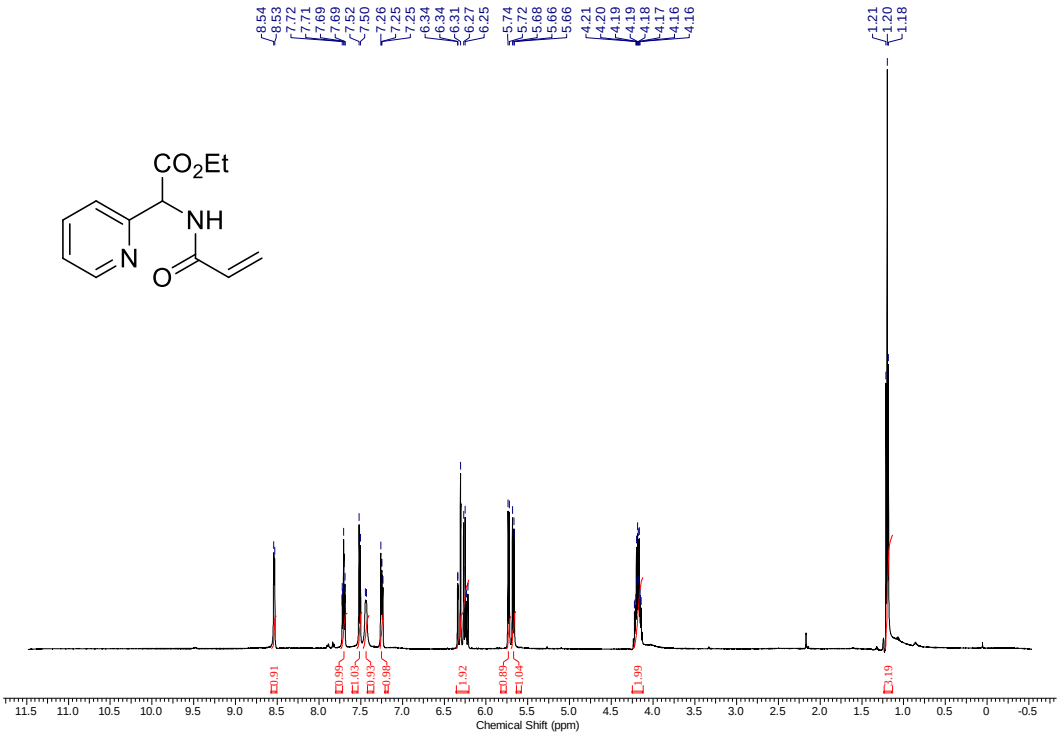
^{1}H NMR Spectrum of **3ag**:



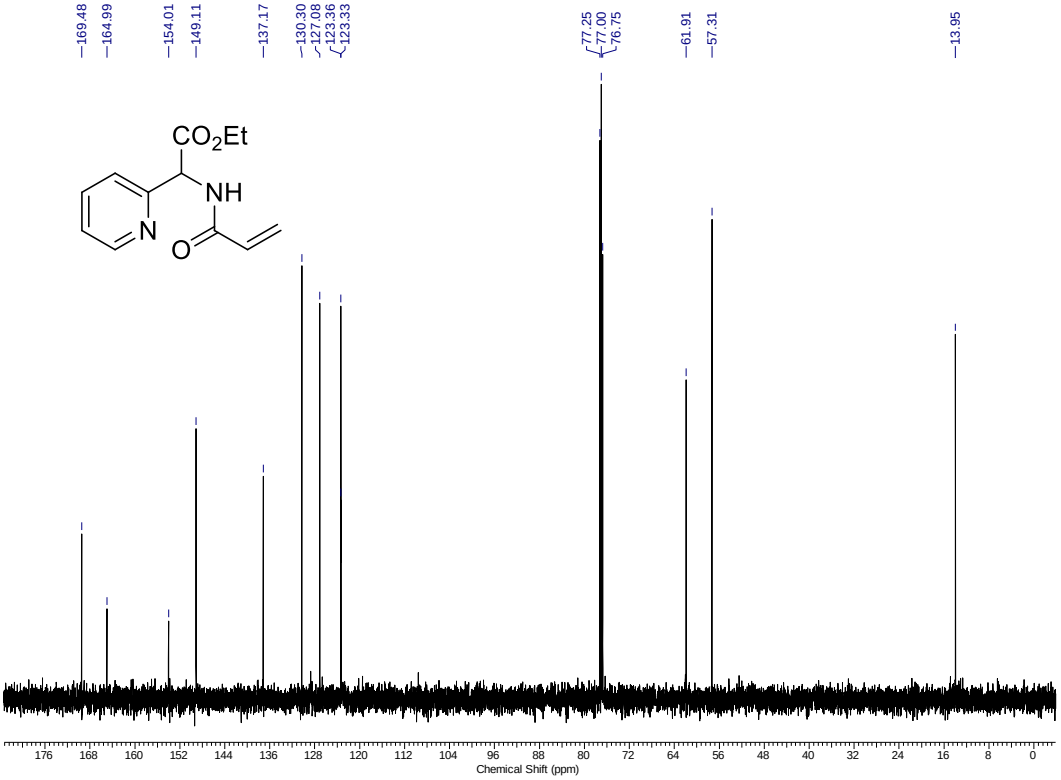
^{13}C NMR Spectrum of **3ag**:



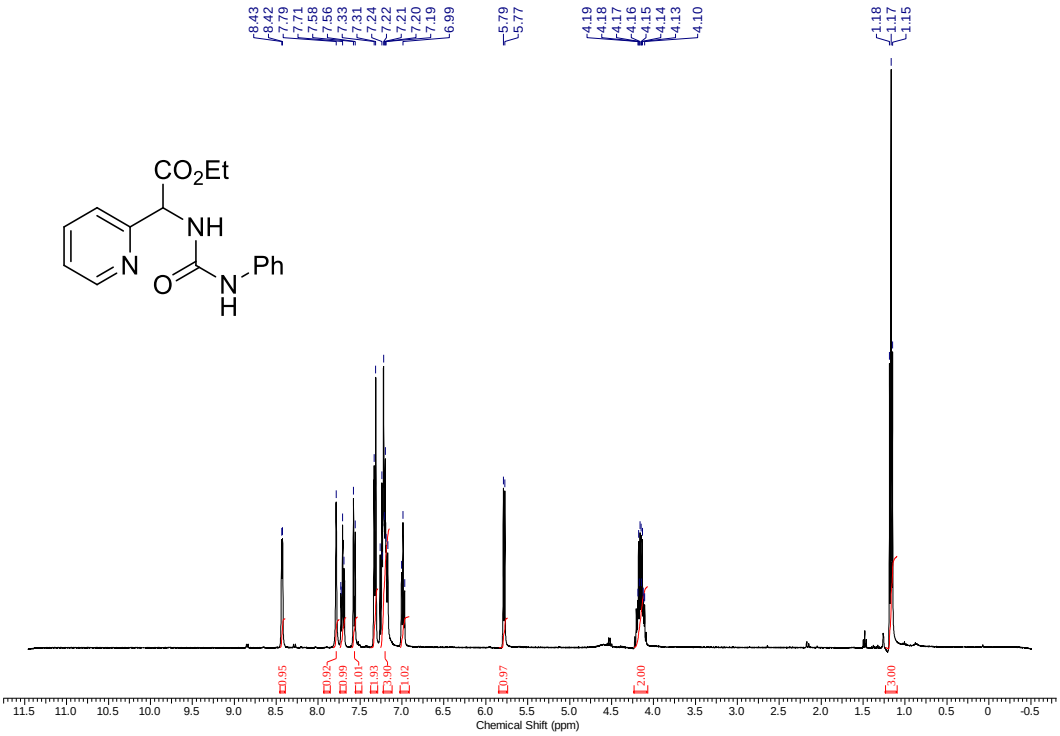
^{1}H NMR Spectrum of **3ah**:



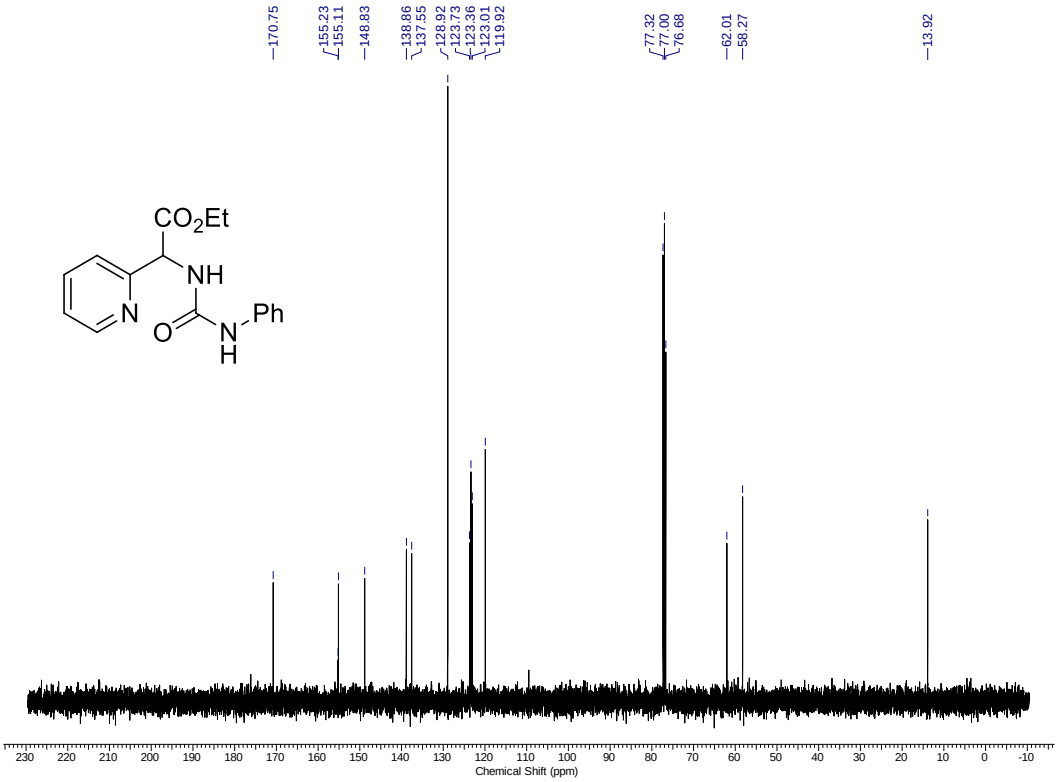
^{13}C NMR Spectrum of **3ah**:



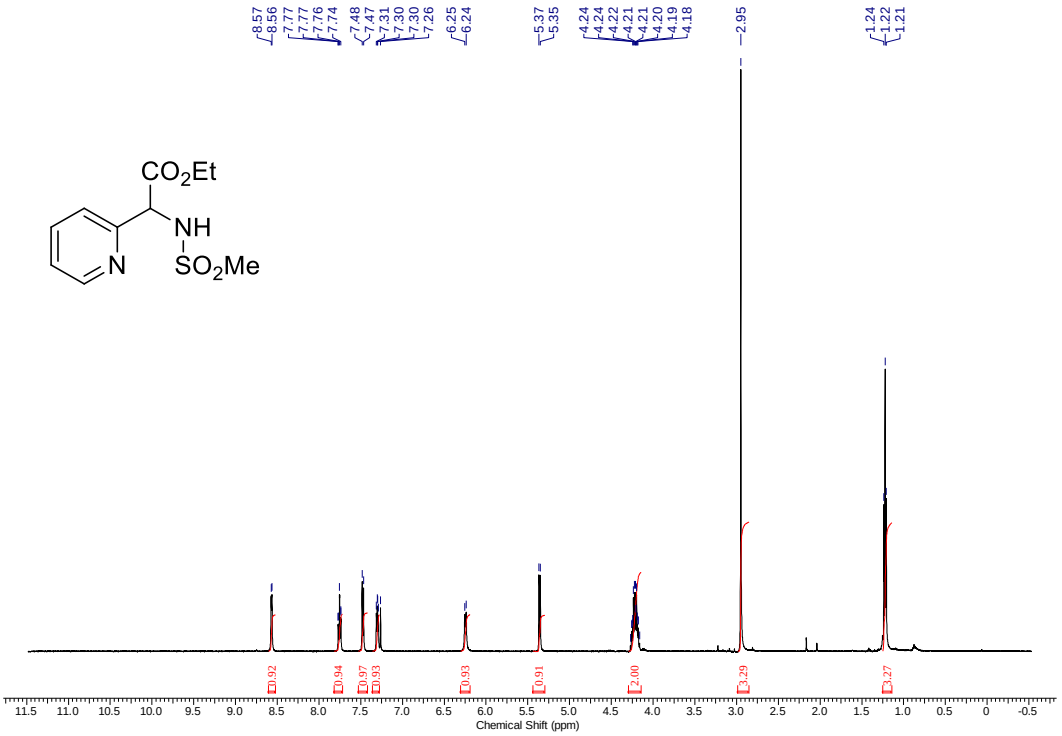
^{1}H NMR Spectrum of **3ai**:



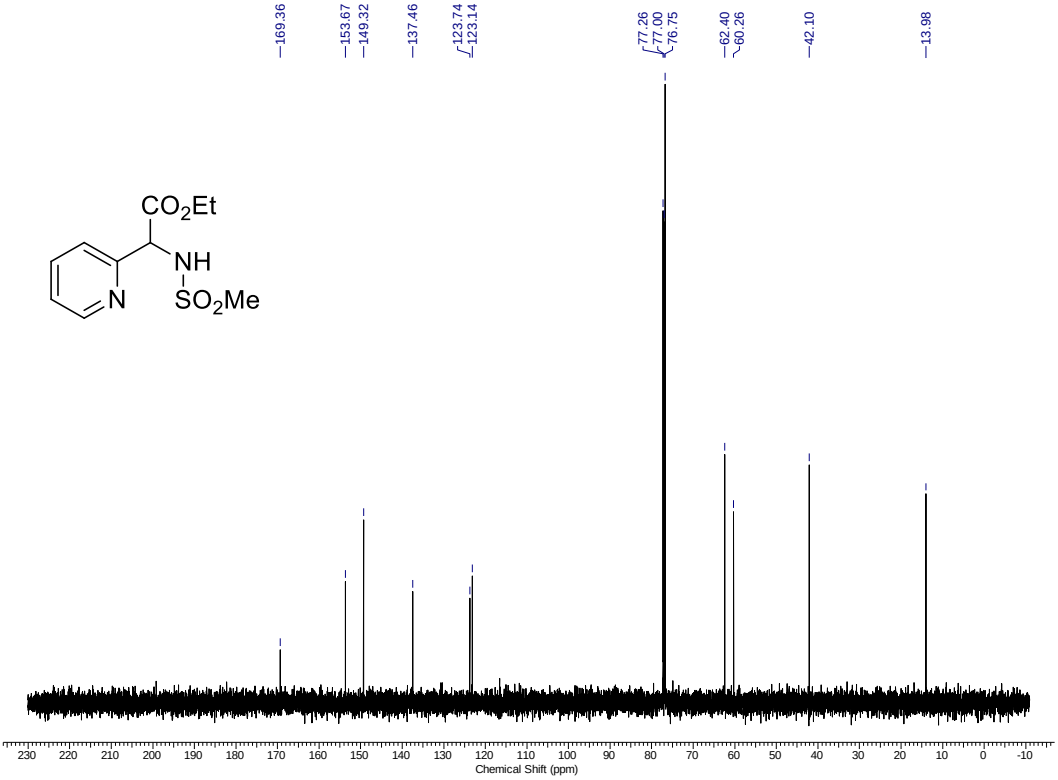
^{13}C NMR Spectrum of **3ai**:



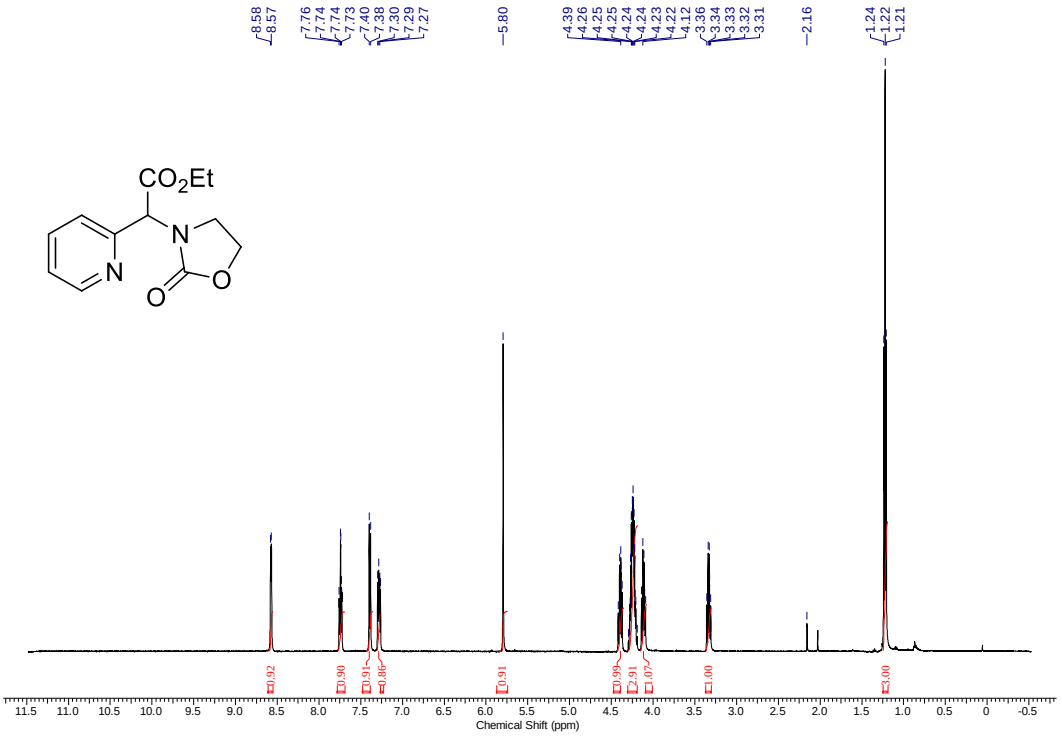
^{1}H NMR Spectrum of **3aj**:



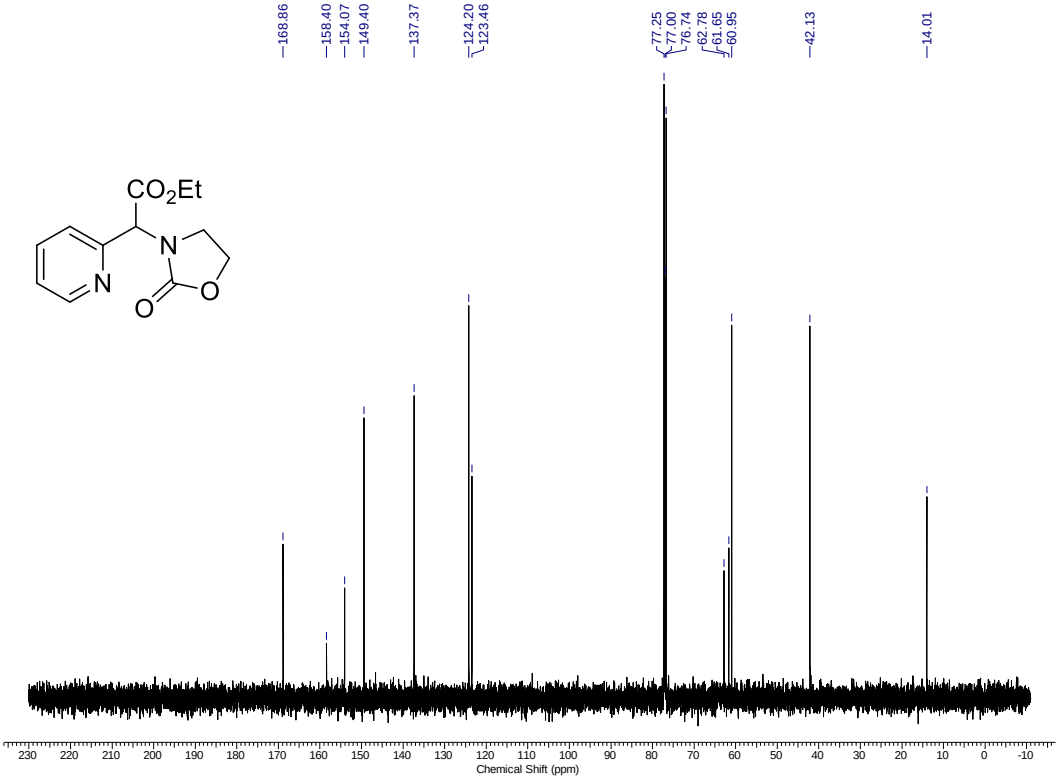
^{13}C NMR Spectrum of **3aj**:



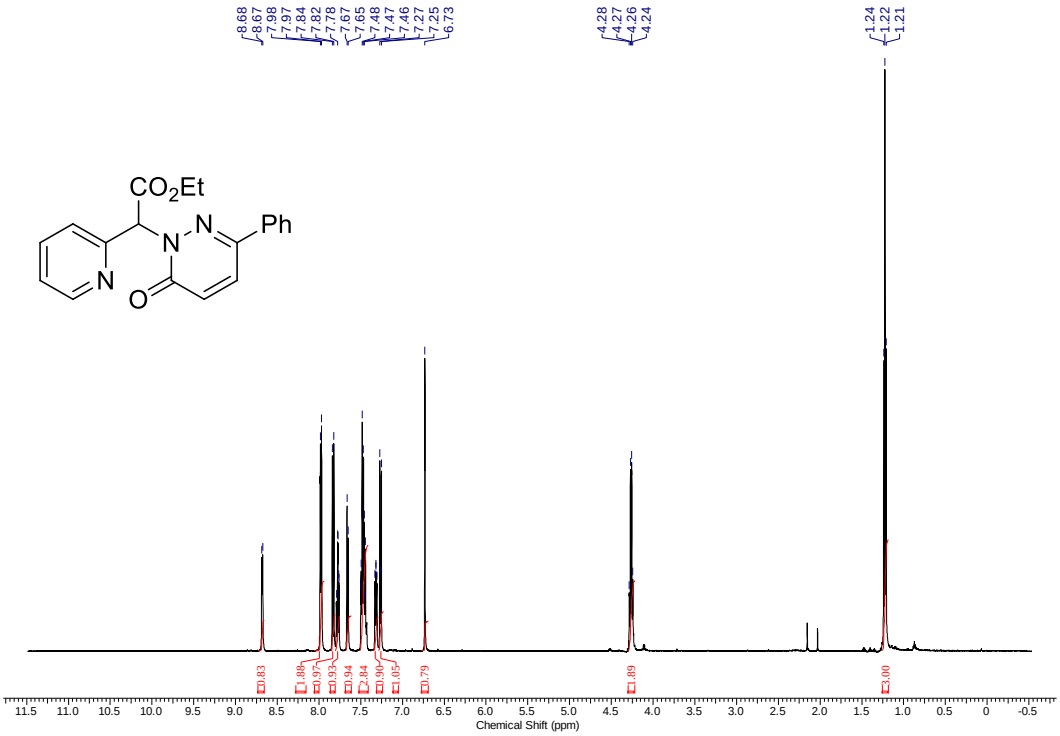
^{1}H NMR Spectrum of **3ak**:



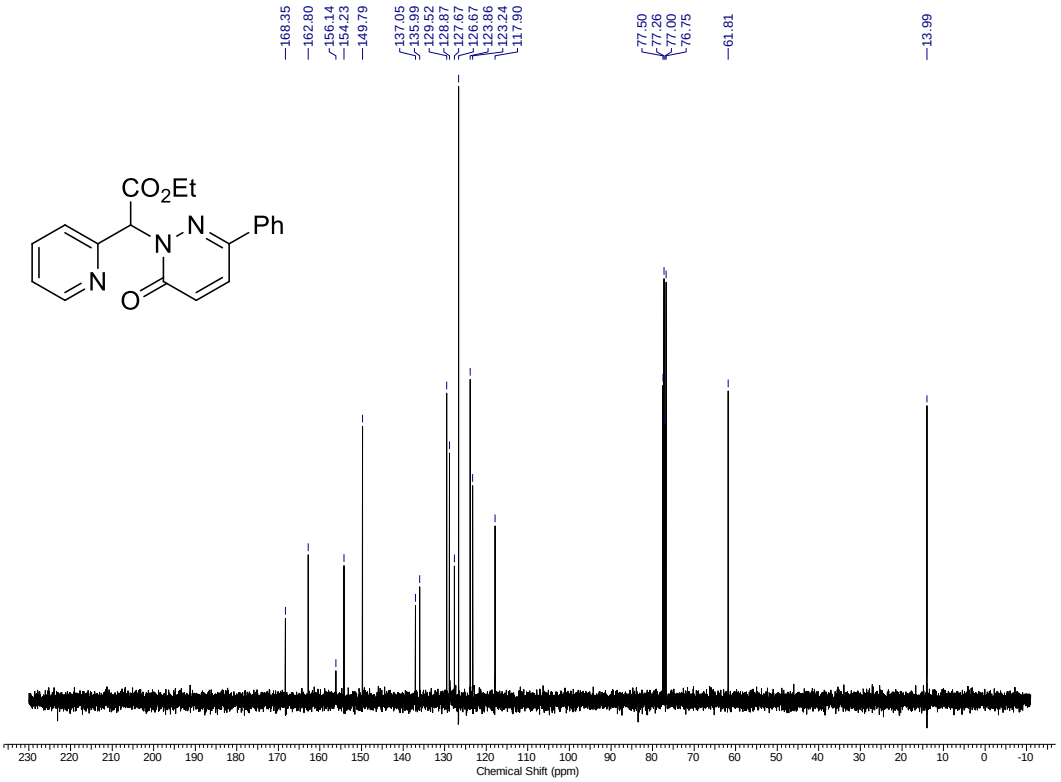
^{13}C NMR Spectrum of **3ak**:



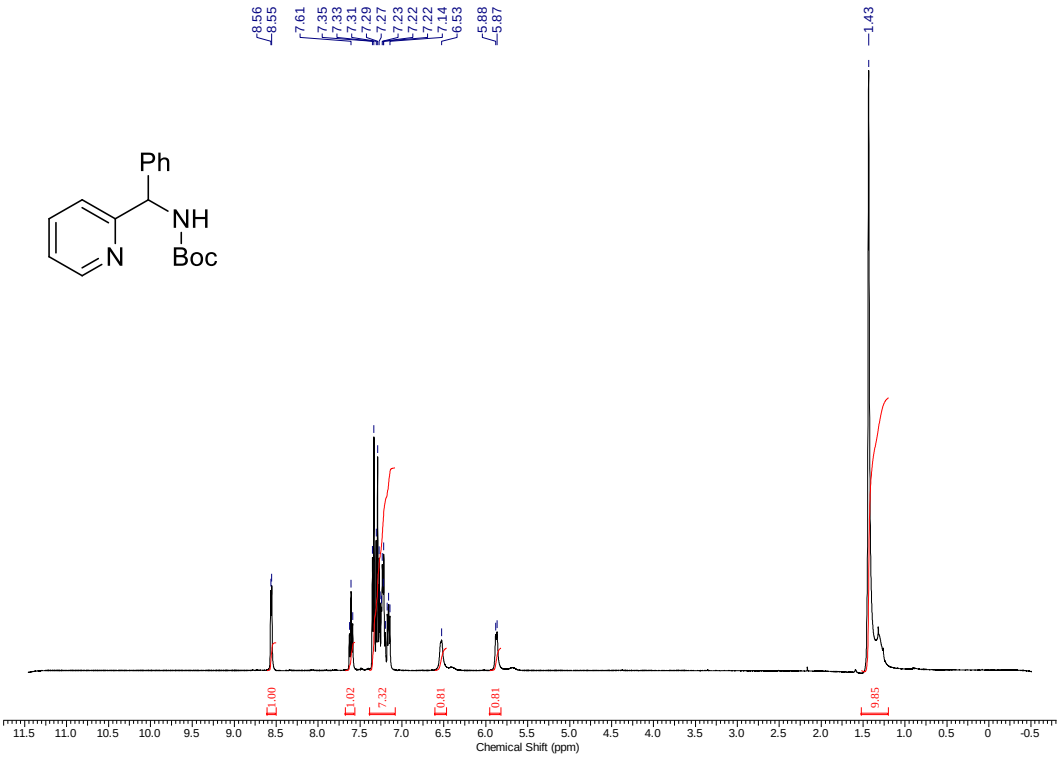
^{1}H NMR Spectrum of **3al**:



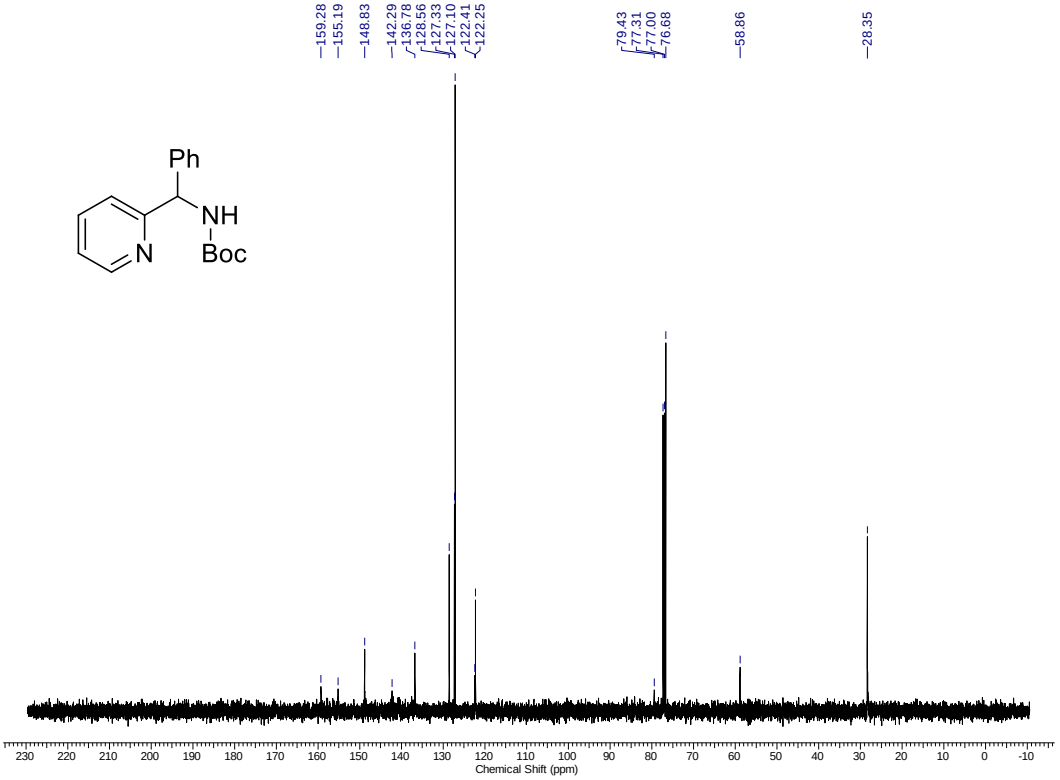
^{13}C NMR Spectrum of **3al**:



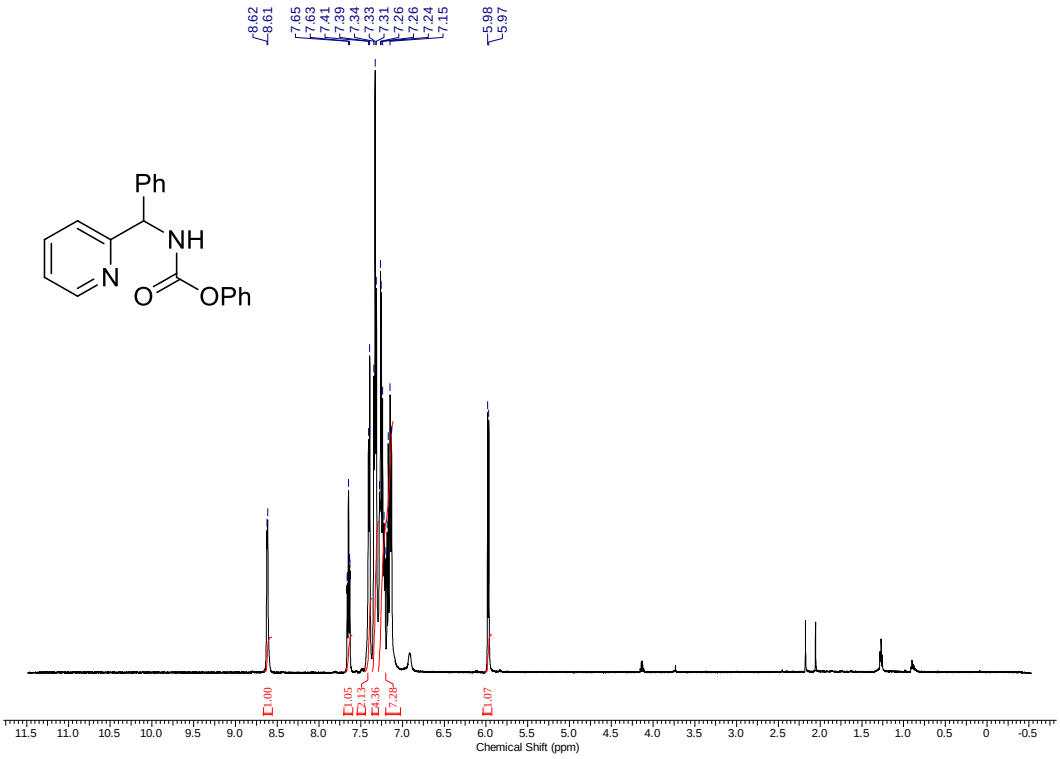
^{1}H NMR Spectrum of **3am**:



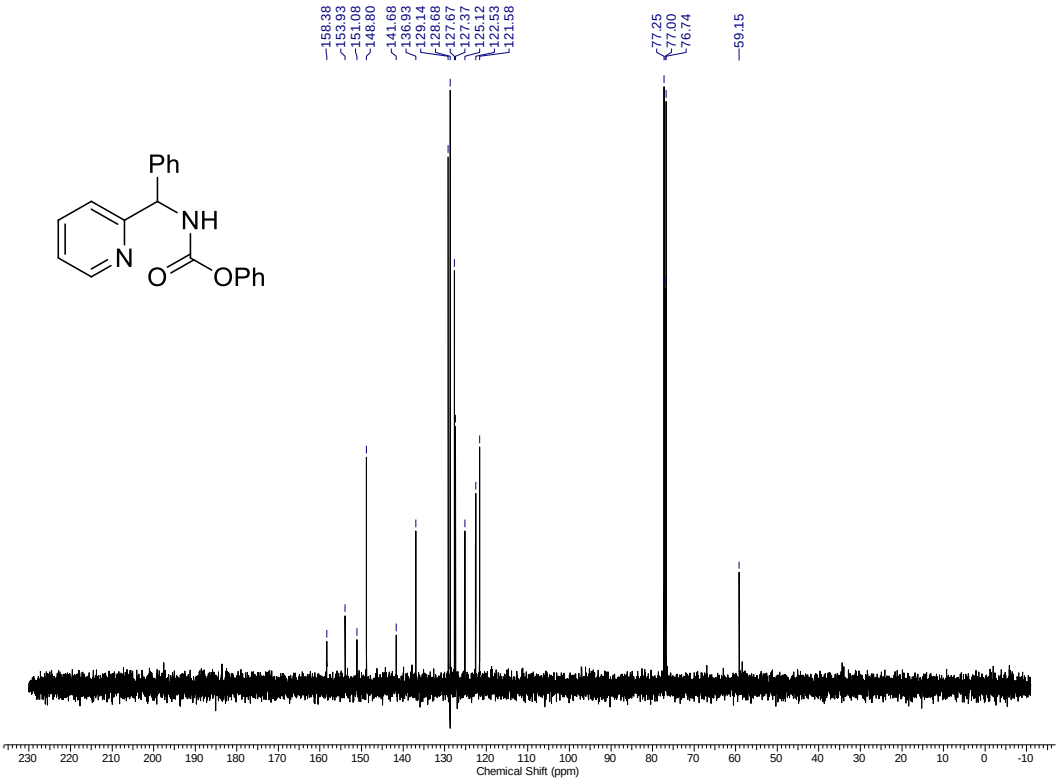
^{13}C NMR Spectrum of **3am**:



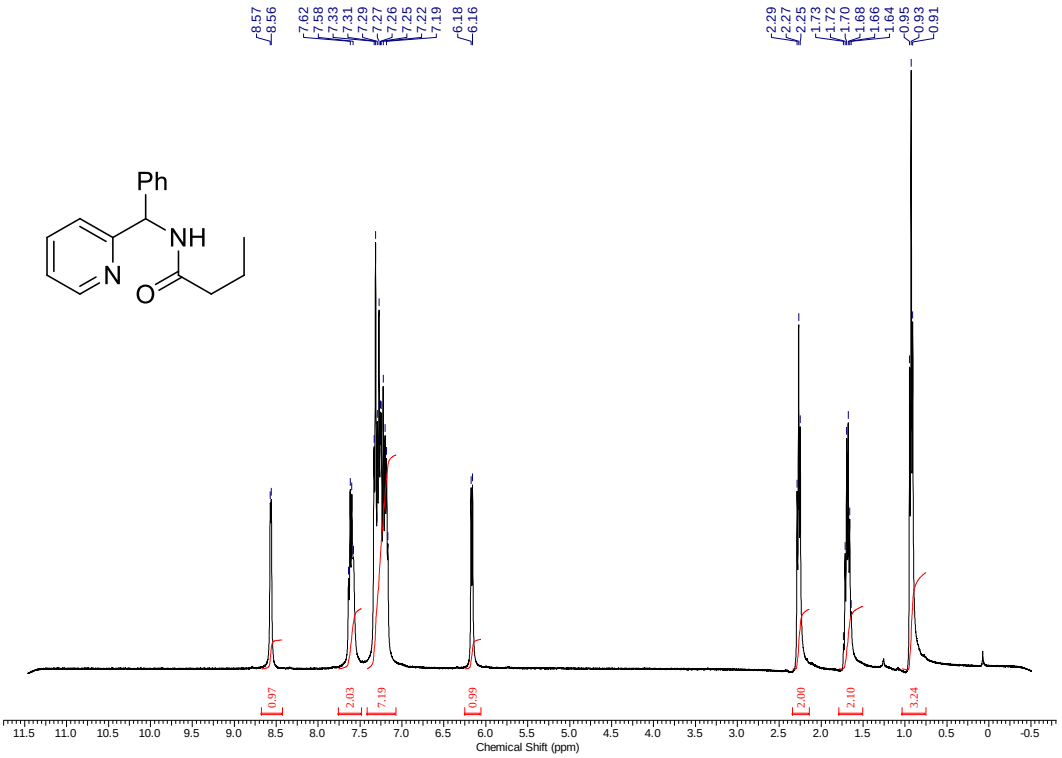
^{1}H NMR Spectrum of **3an**:



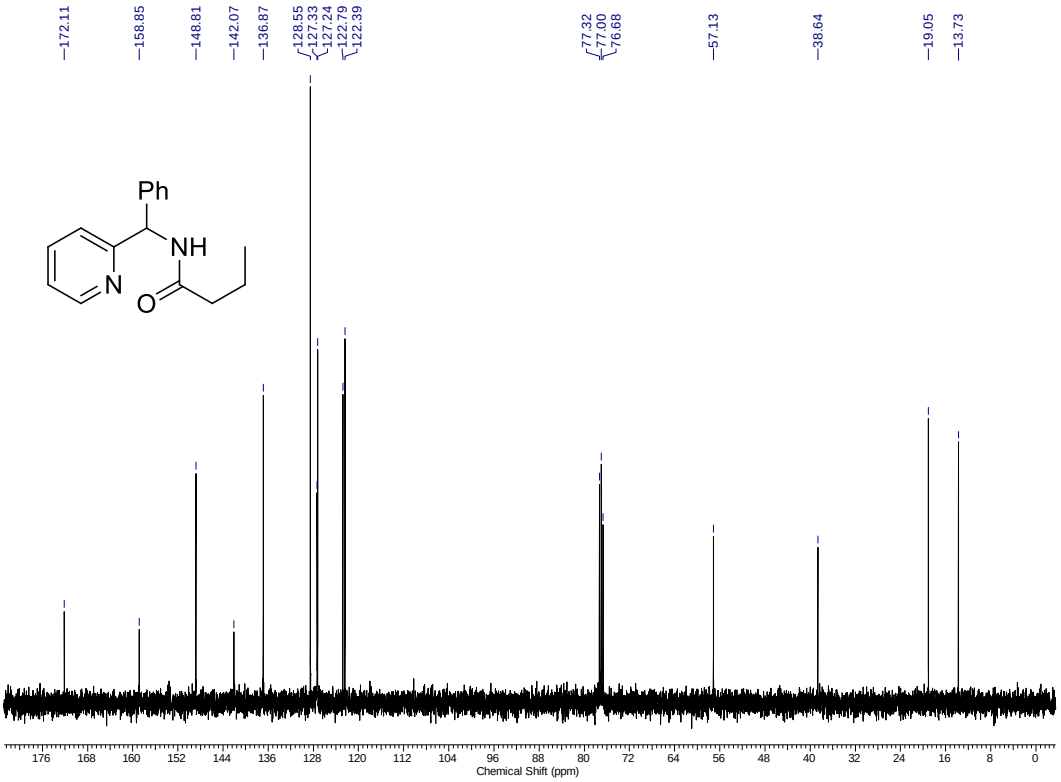
^{13}C NMR Spectrum of **3an**:



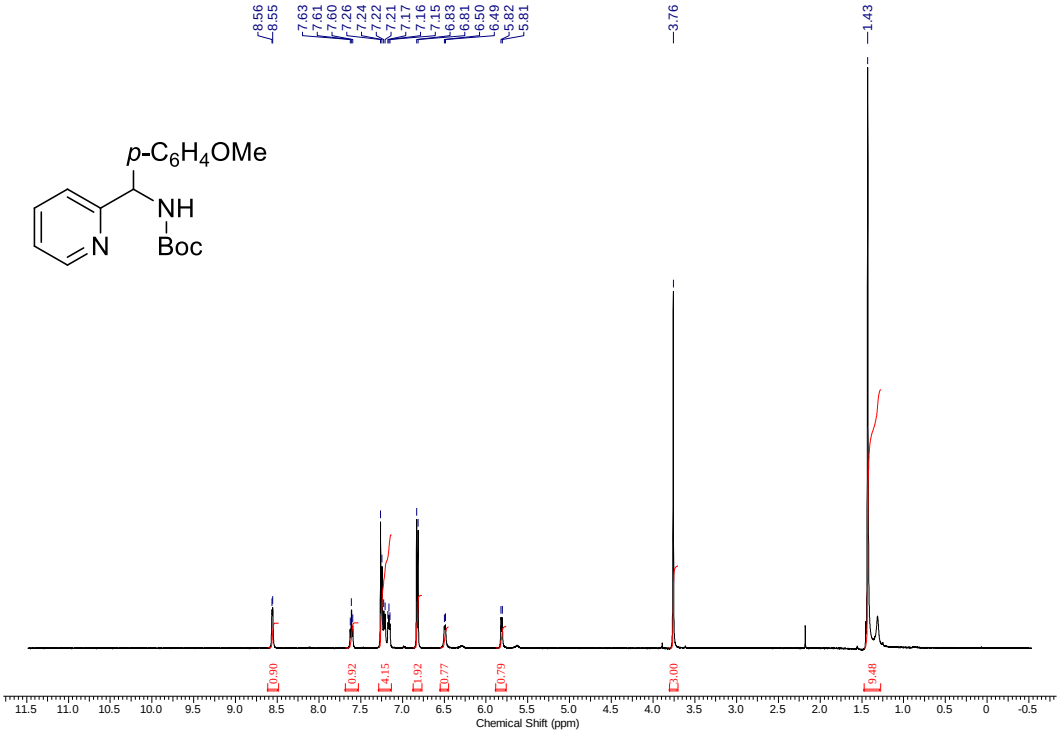
^{1}H NMR Spectrum of **3ao**:



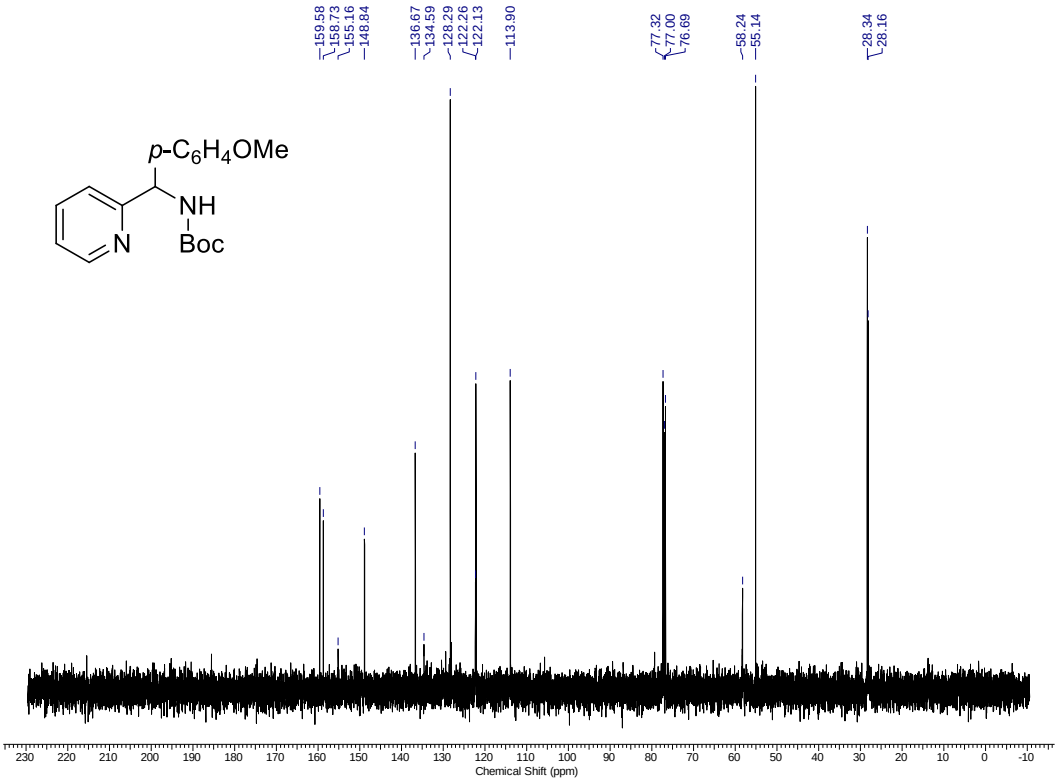
^{13}C NMR Spectrum of **3ao**:



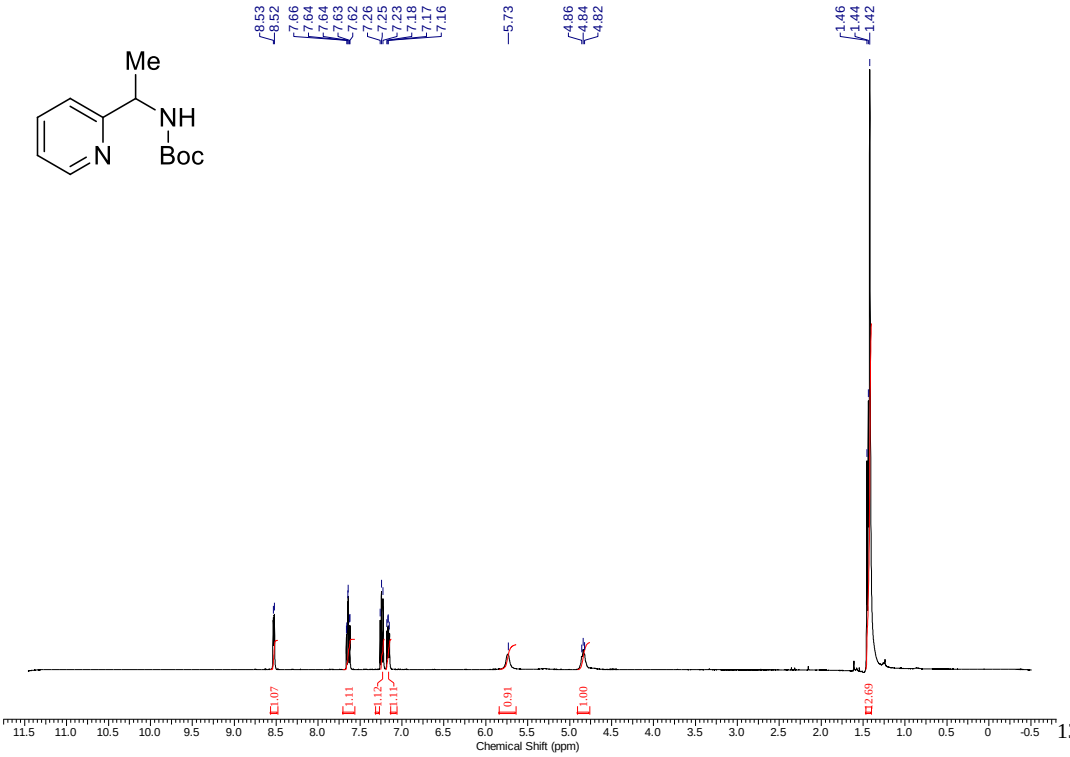
^{1}H NMR Spectrum of **3ap**:



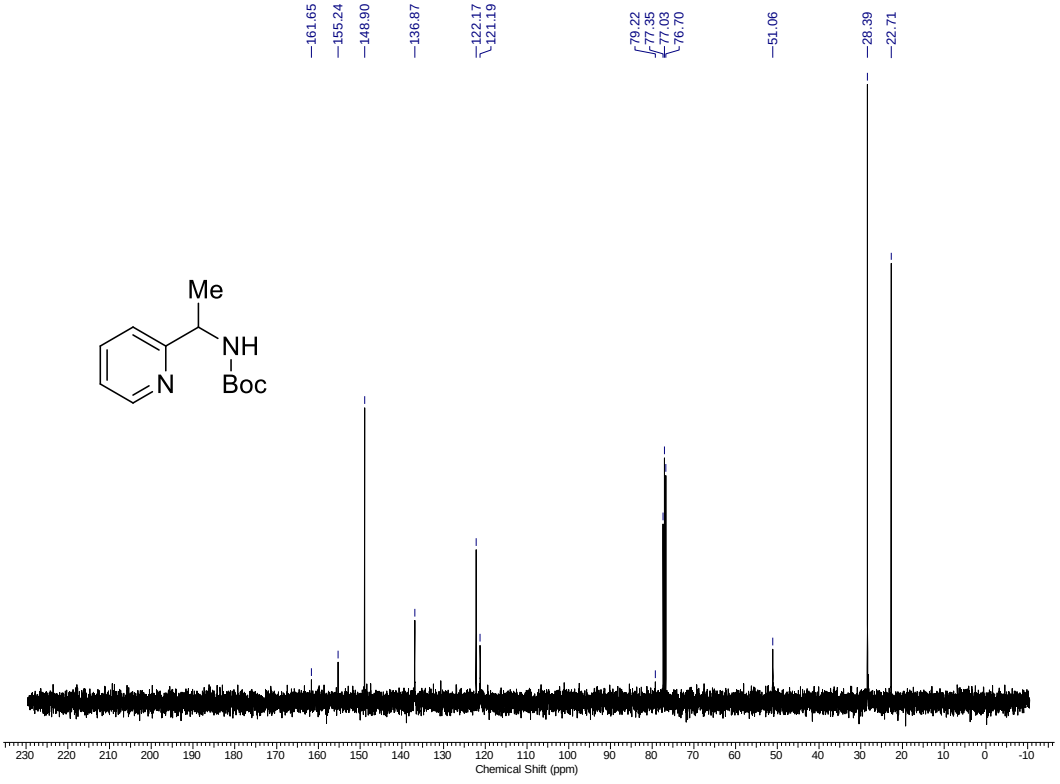
^{13}C NMR Spectrum of **3ap**:



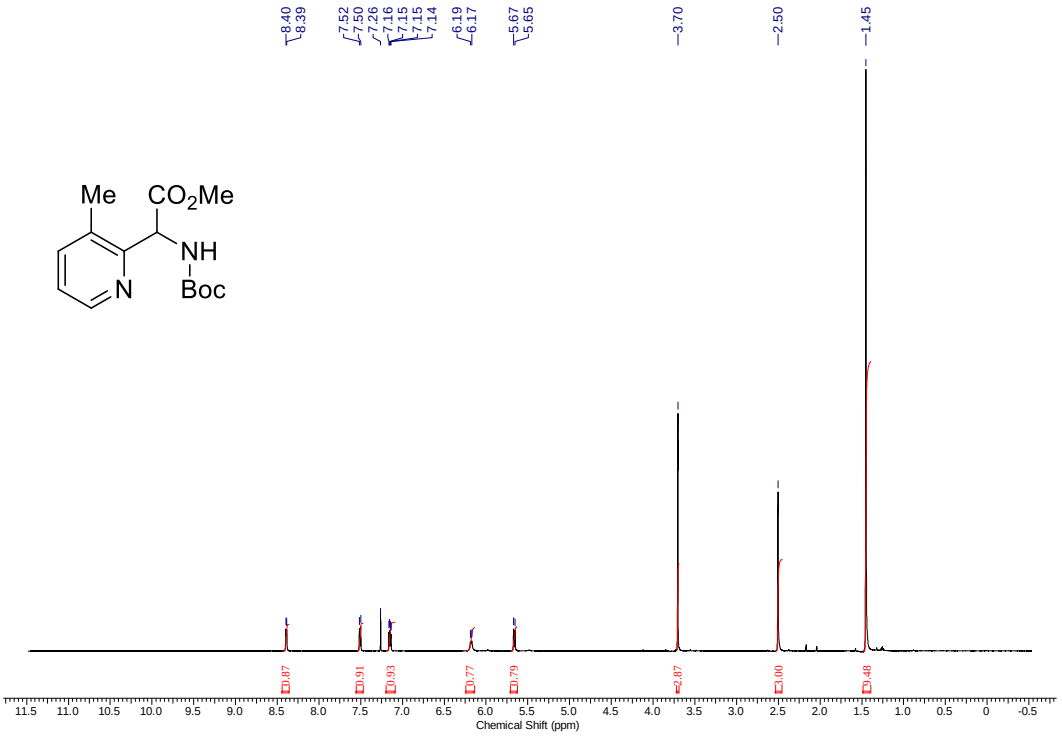
^{1}H NMR Spectrum of **3aq**:



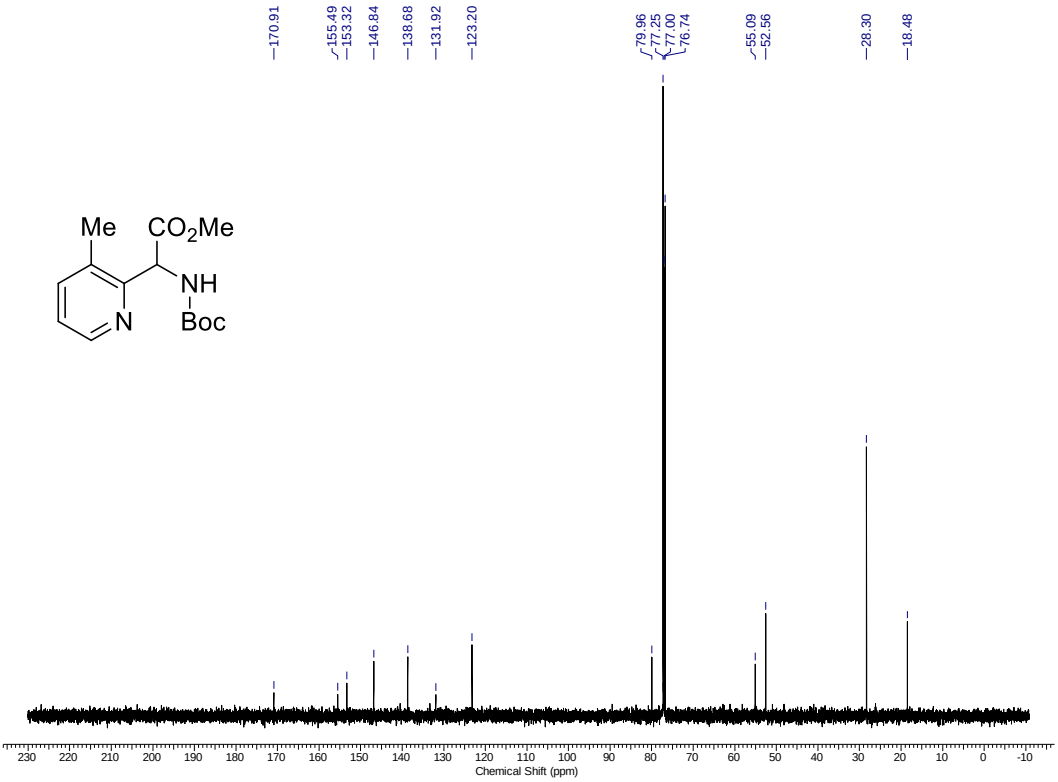
^{13}C NMR Spectrum of **3aq**:



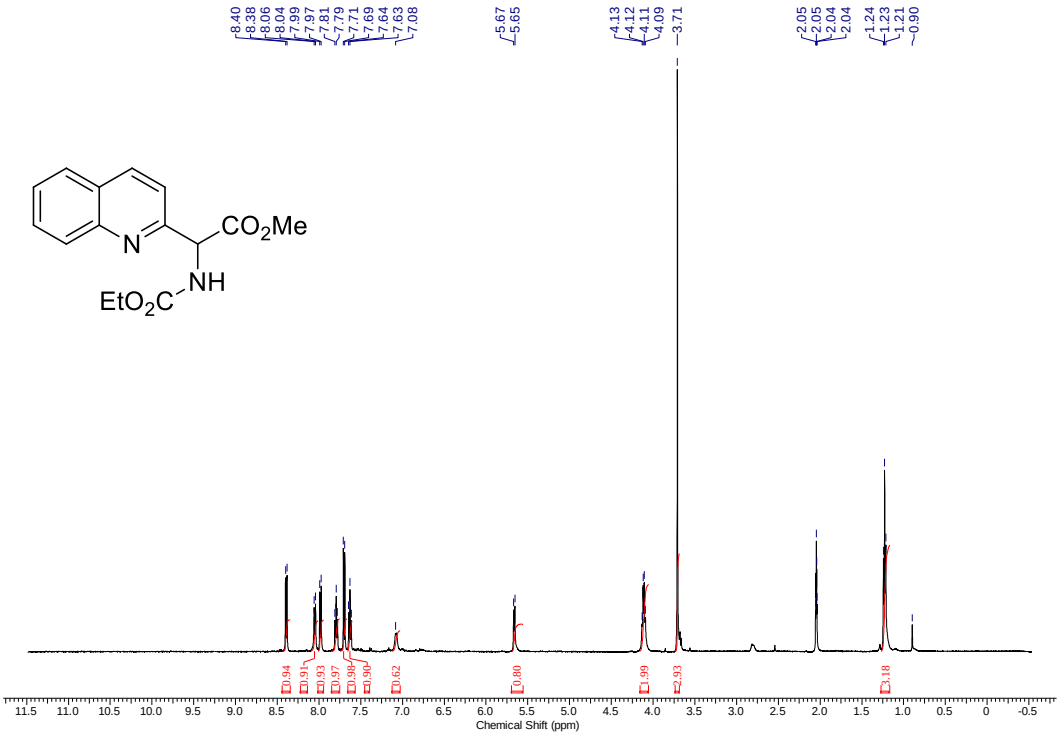
^{1}H NMR Spectrum of **3ar**:



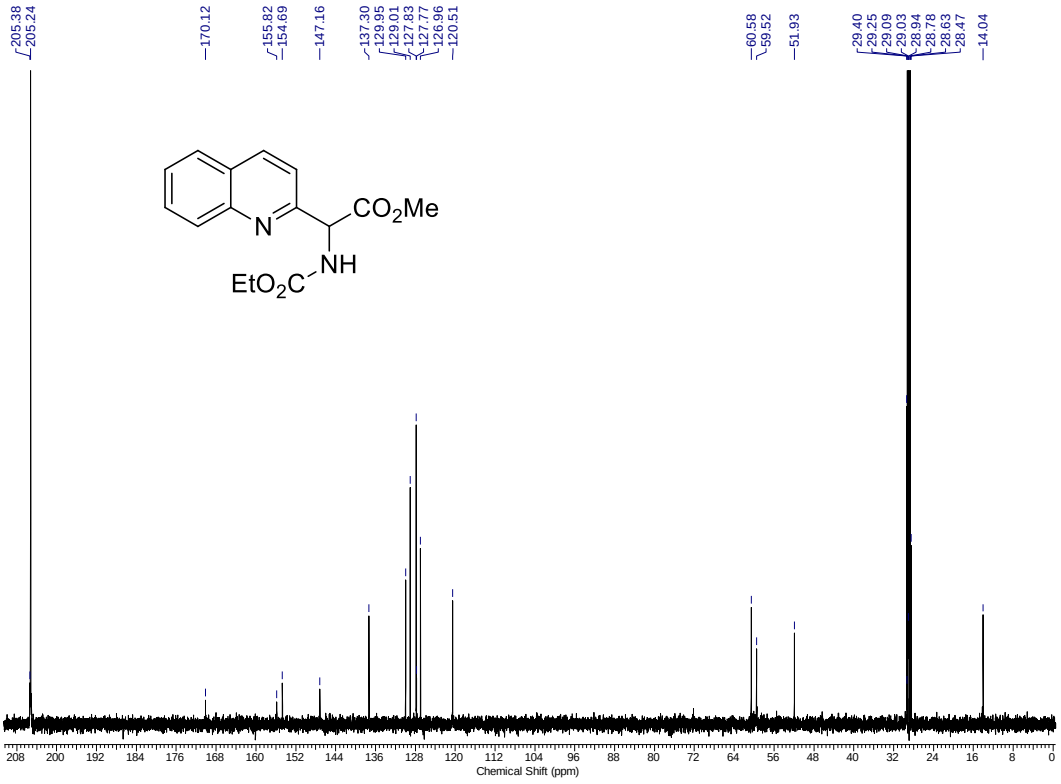
^{13}C NMR Spectrum of **3ar**:



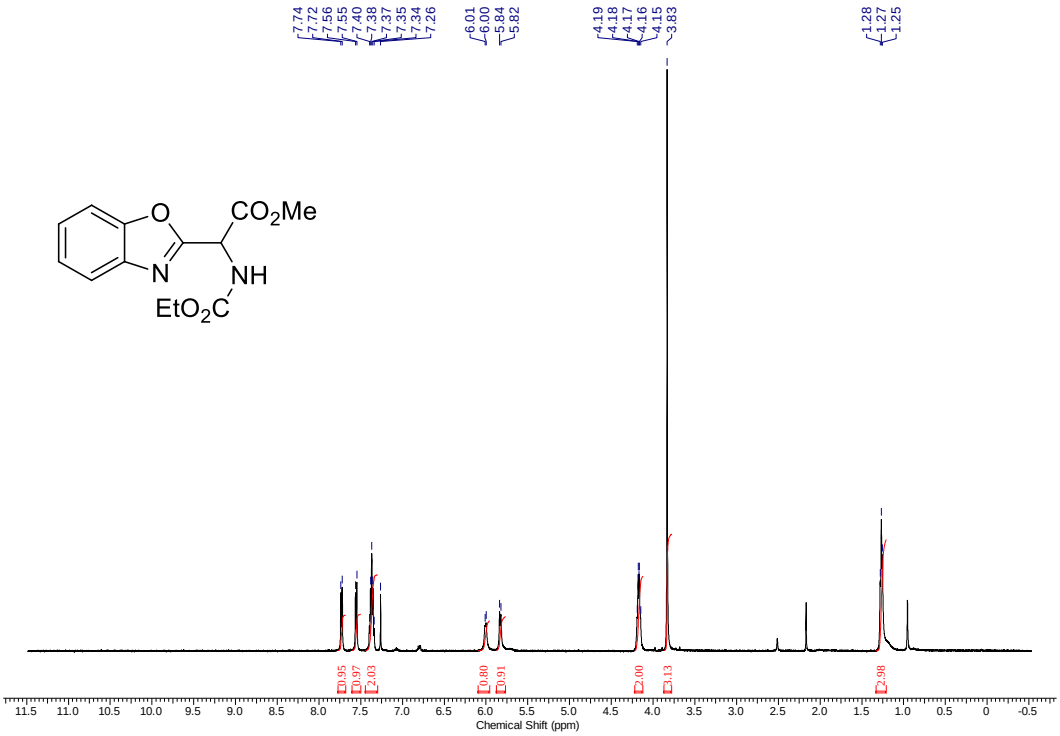
^{1}H NMR Spectrum of **3as**:



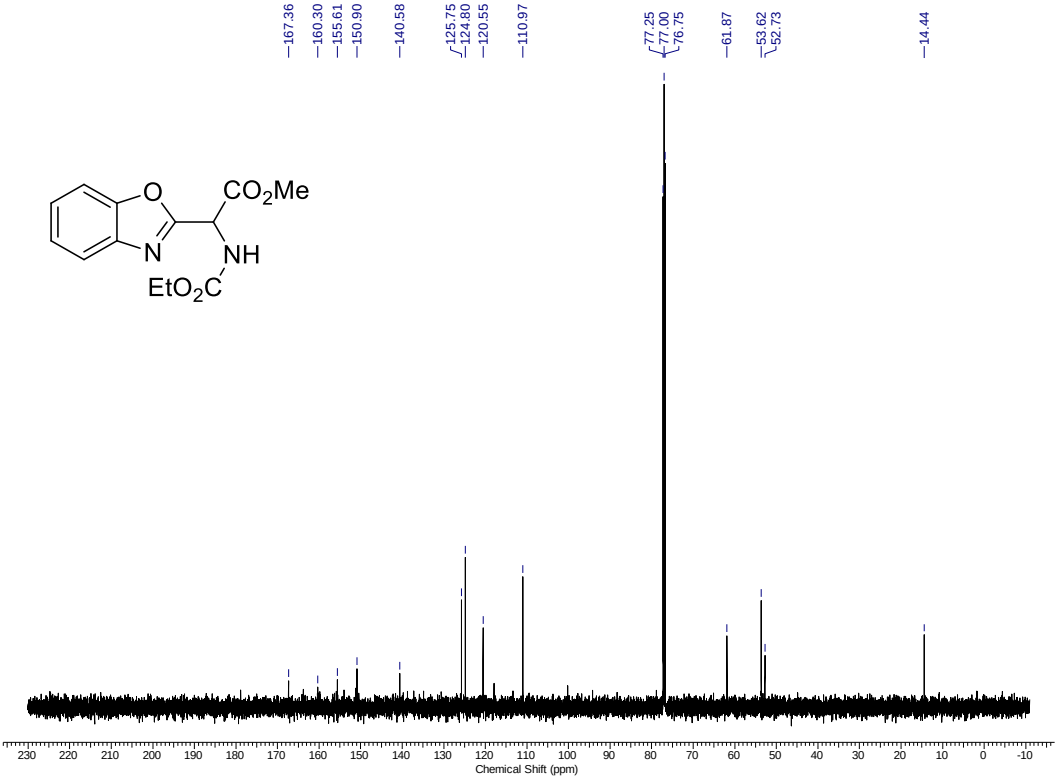
^{13}C NMR Spectrum of **3as**:



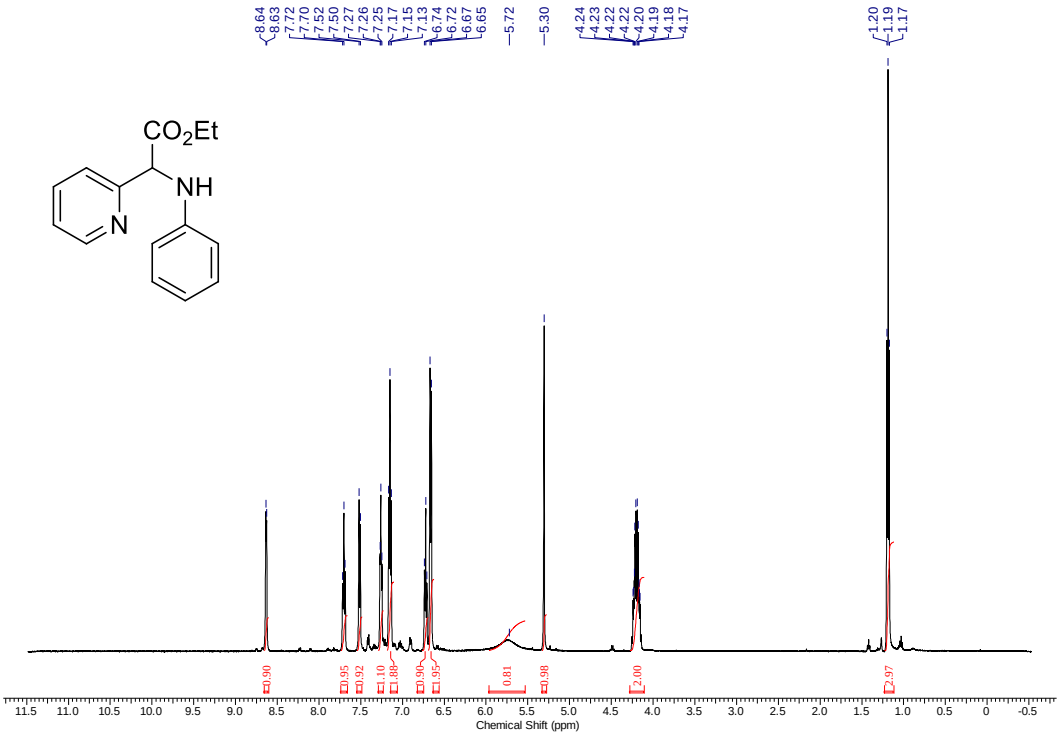
^{1}H NMR Spectrum of **3at**:



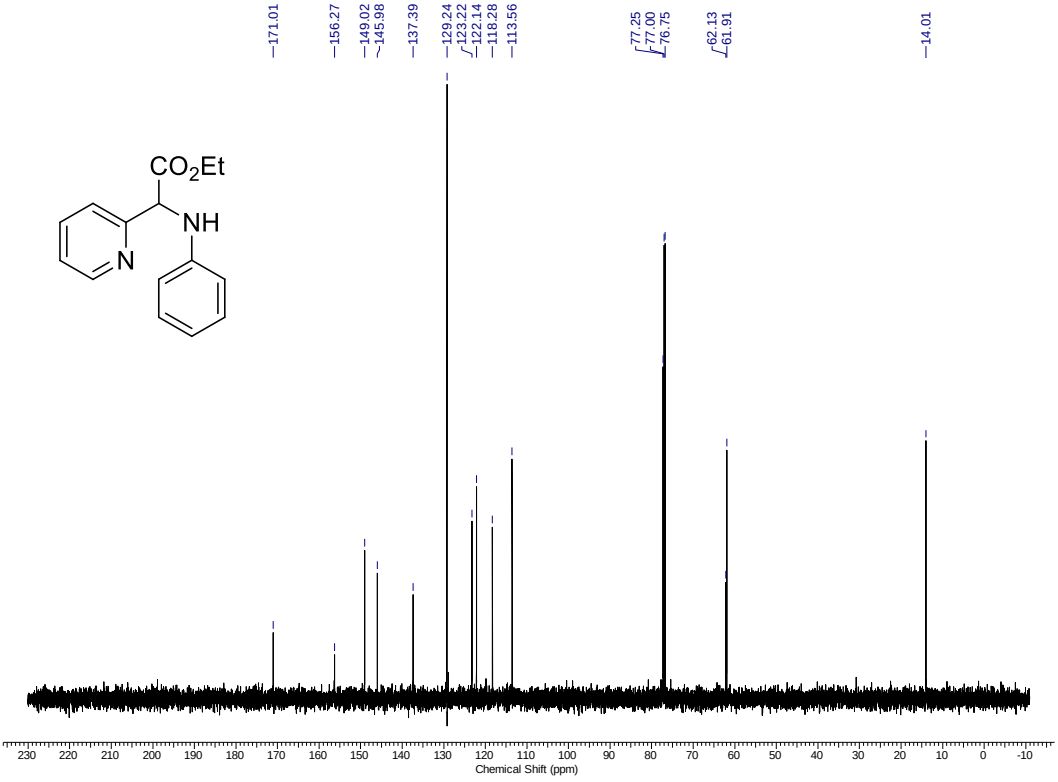
^{13}C NMR Spectrum of **3at**:



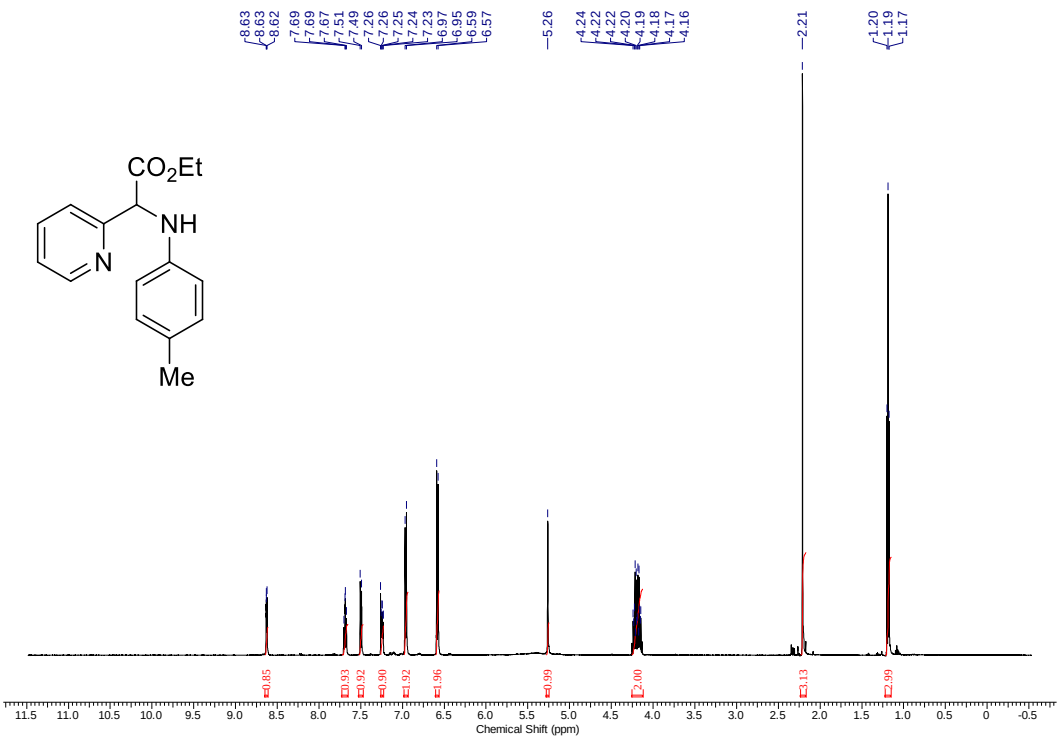
^{1}H NMR Spectrum of **3ba**:



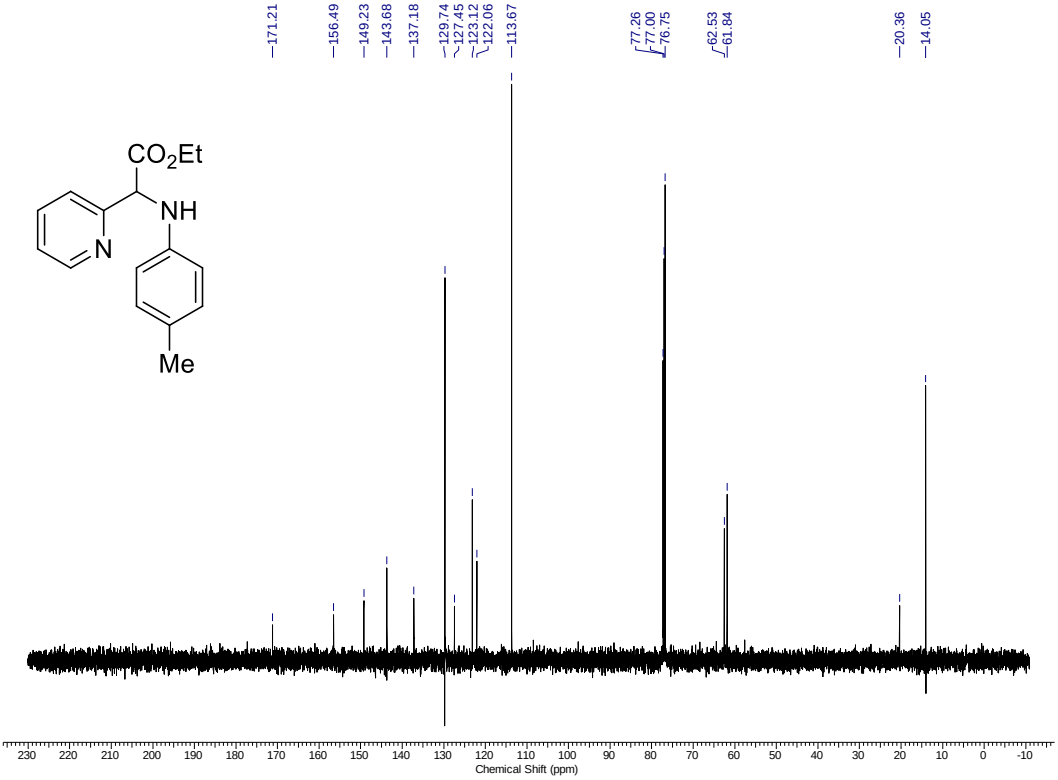
^{13}C NMR Spectrum of **3ba**:



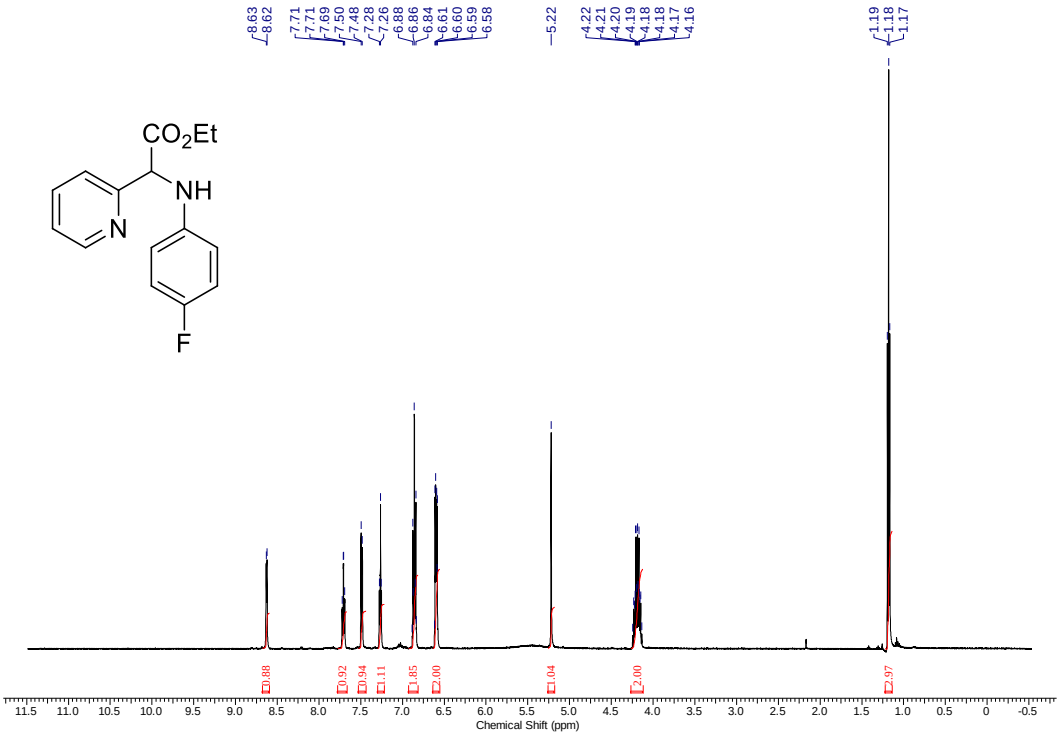
^{1}H NMR Spectrum of **3bb**:



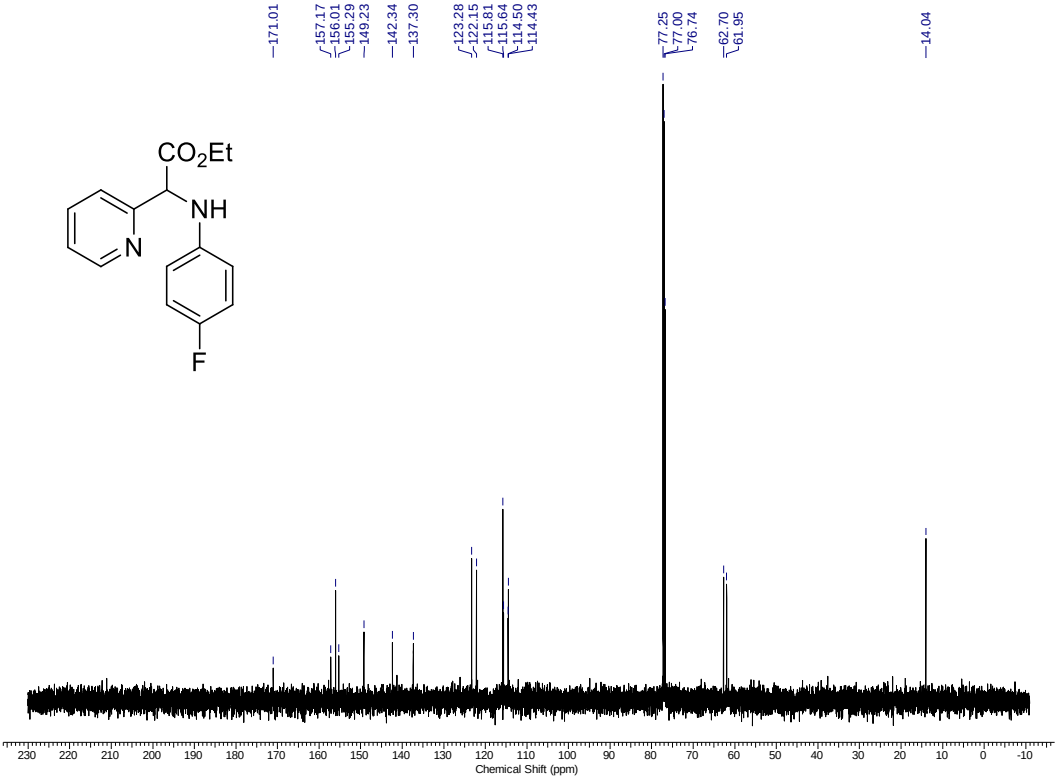
^{13}C NMR Spectrum of **3bb**:



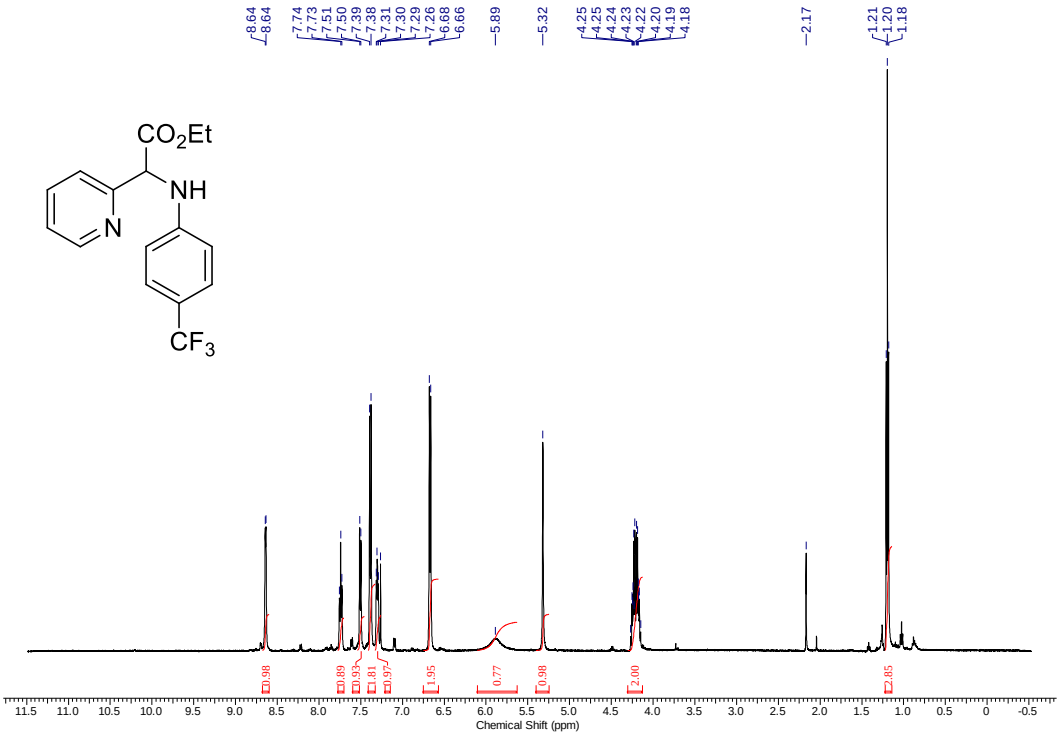
^{1}H NMR Spectrum of **3bc**:



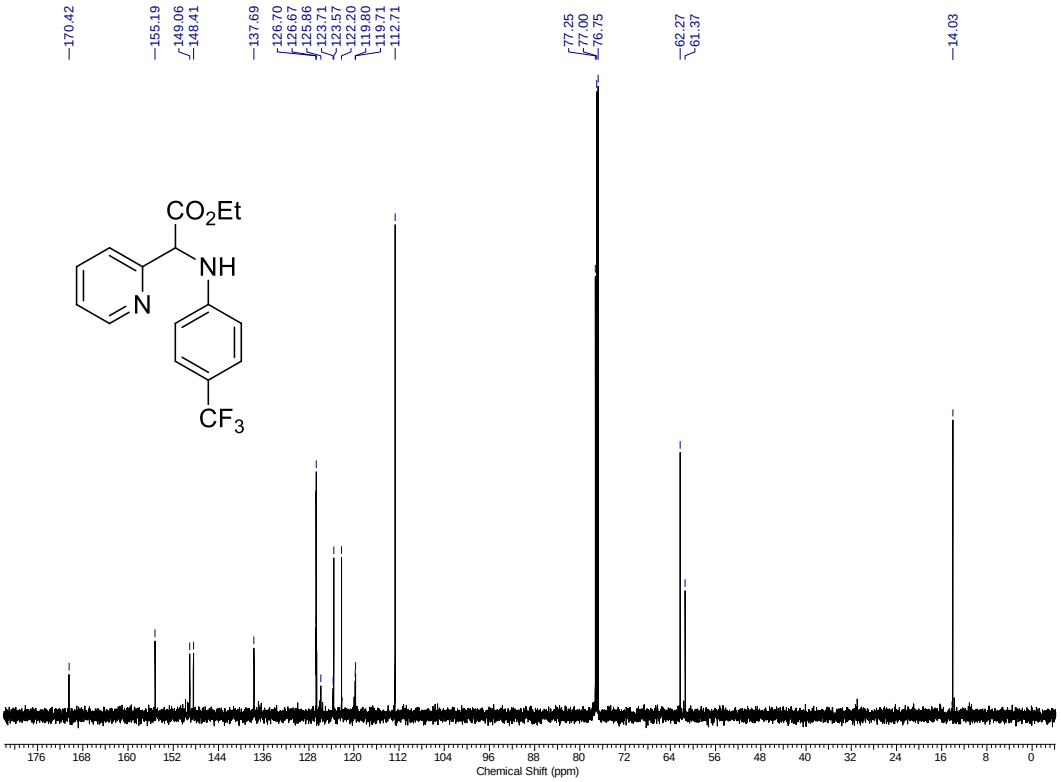
^{13}C NMR Spectrum of **3bc**:



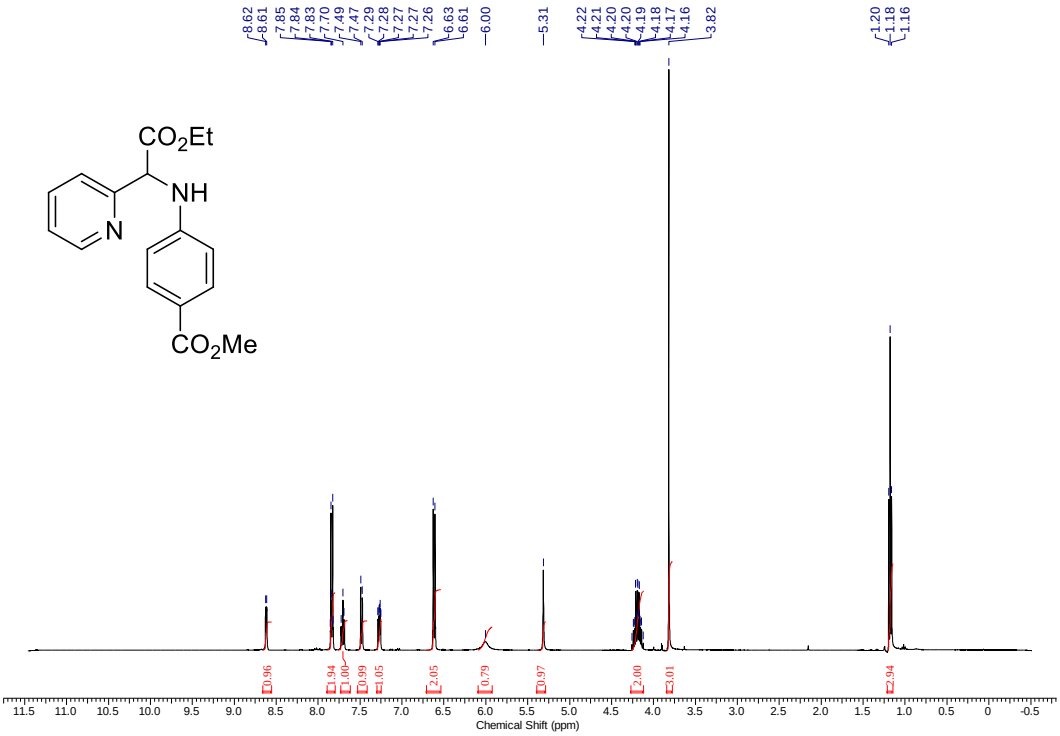
^{1}H NMR Spectrum of **3bd**:



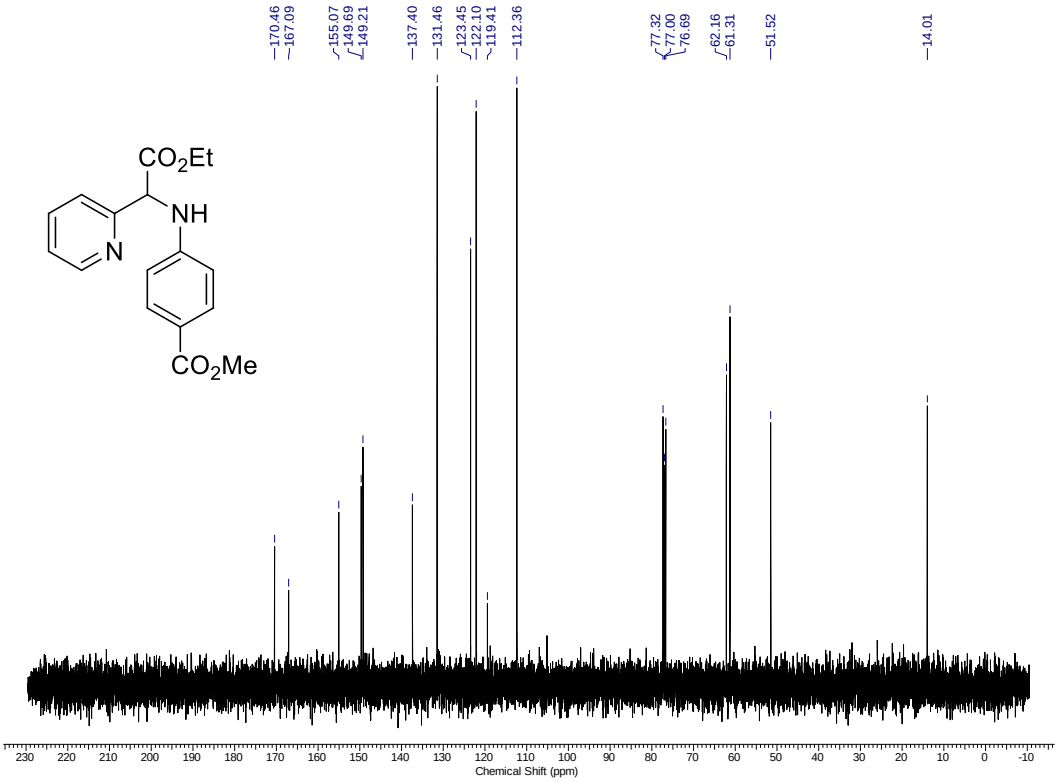
^{13}C NMR Spectrum of **3bd**:



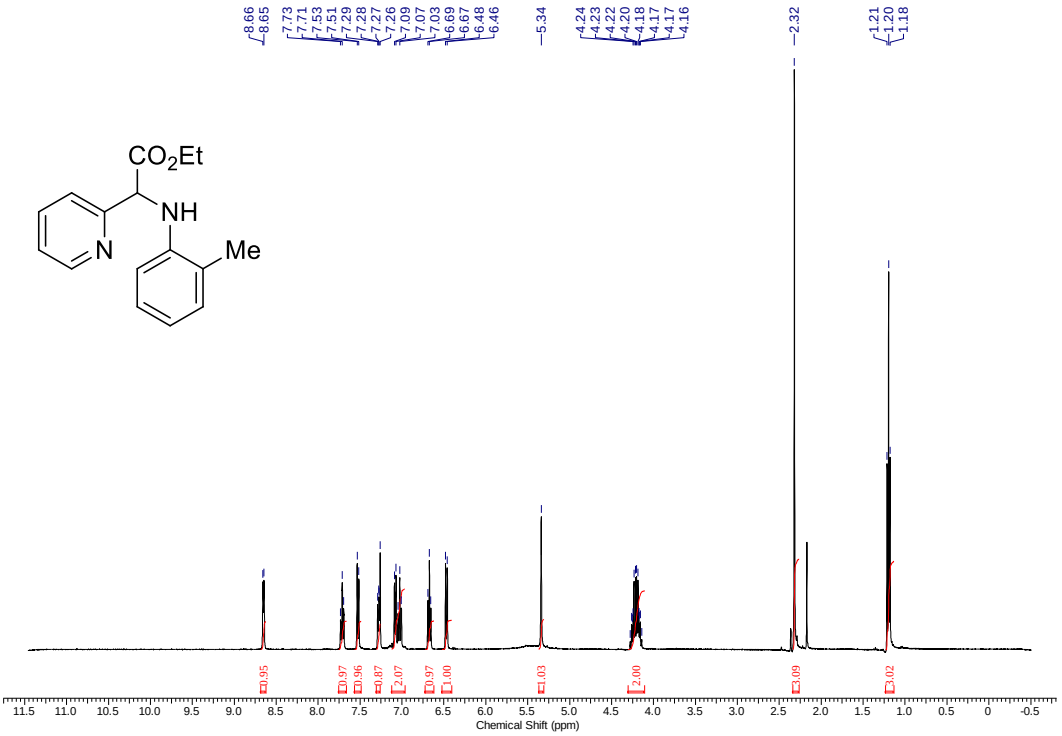
^{1}H NMR Spectrum of **3be**:



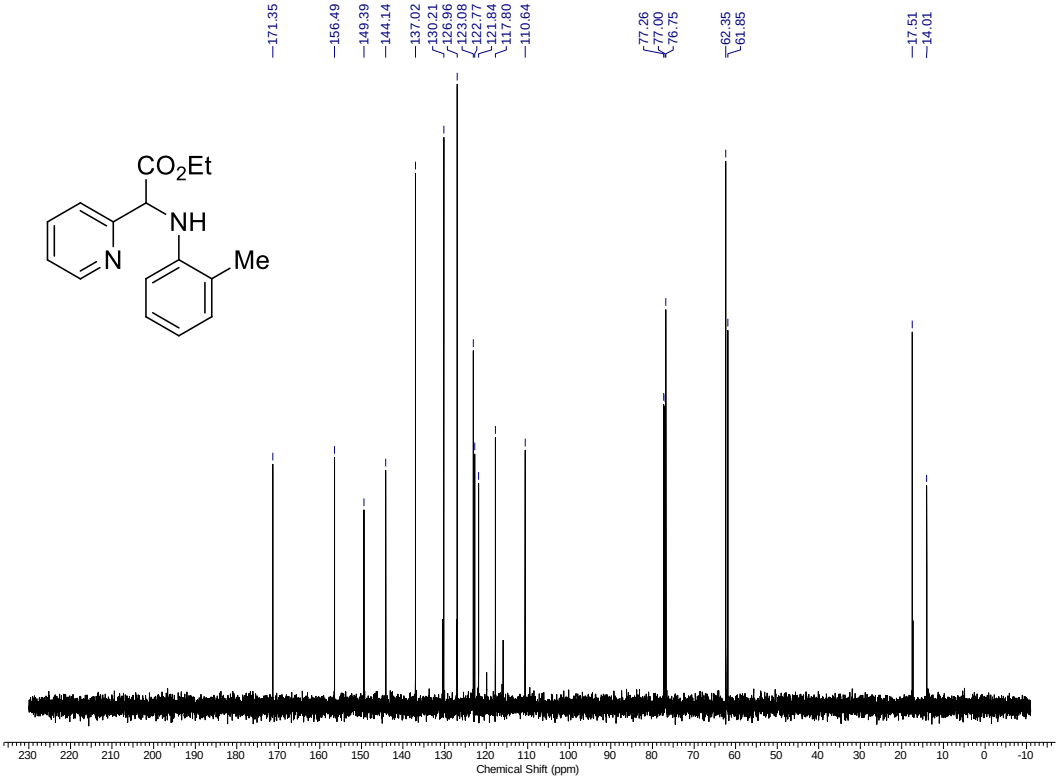
^{13}C NMR Spectrum of **3be**:



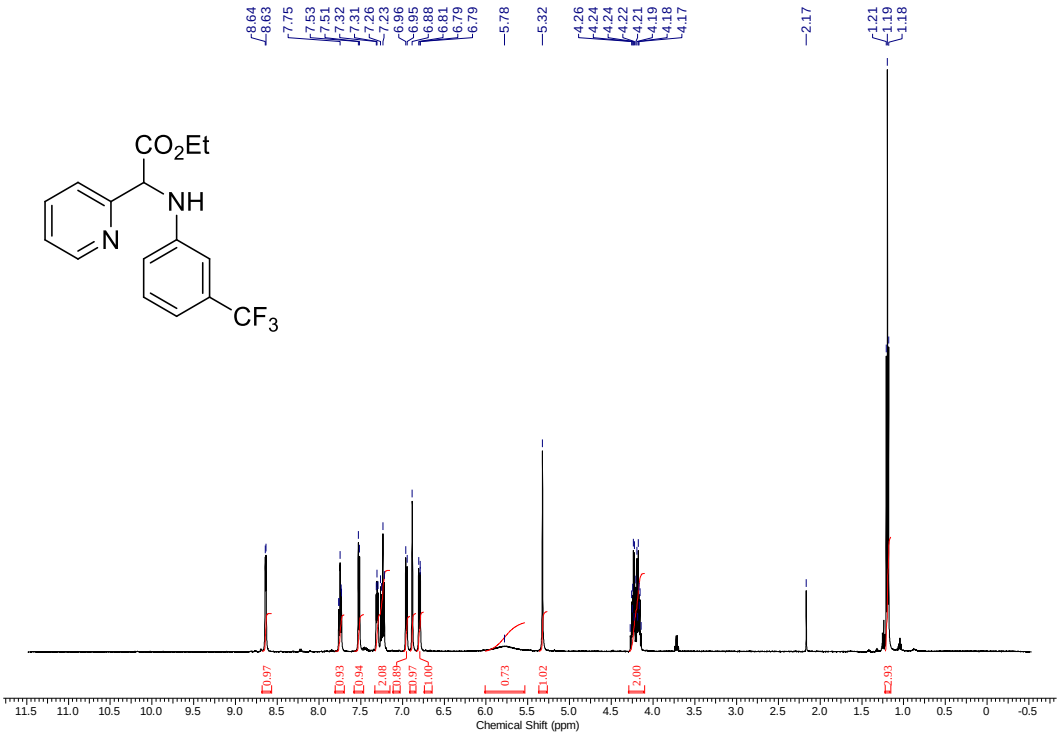
^{1}H NMR Spectrum of **3bf**:



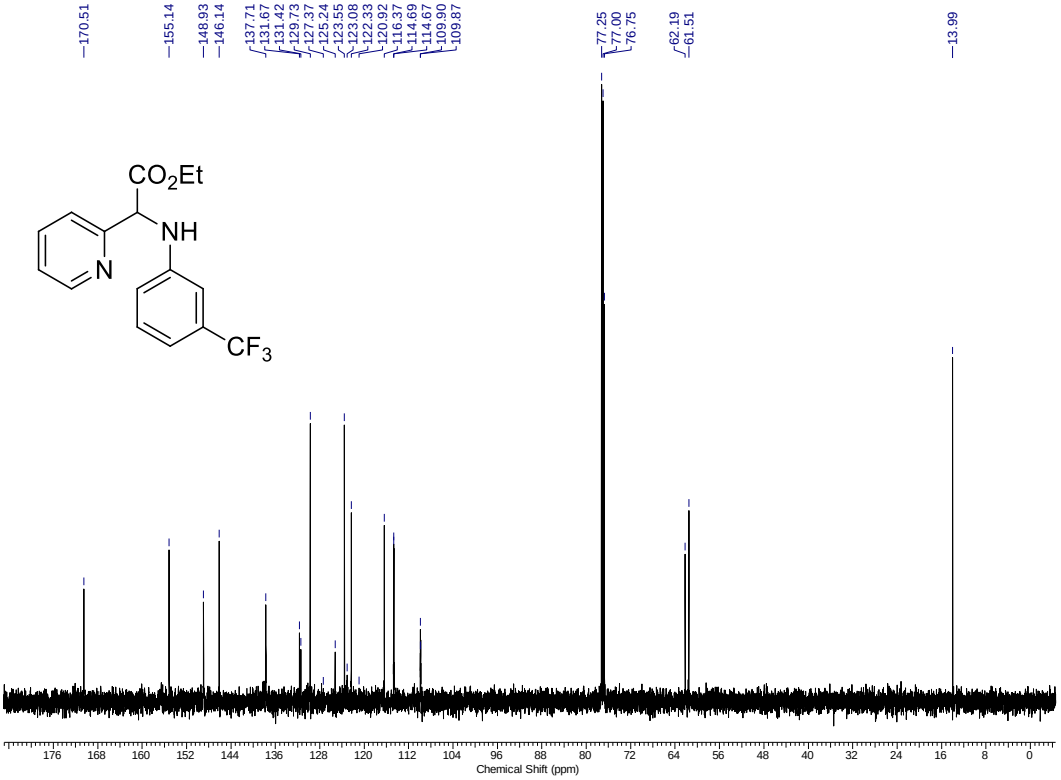
^{13}C NMR Spectrum of **3bf**:



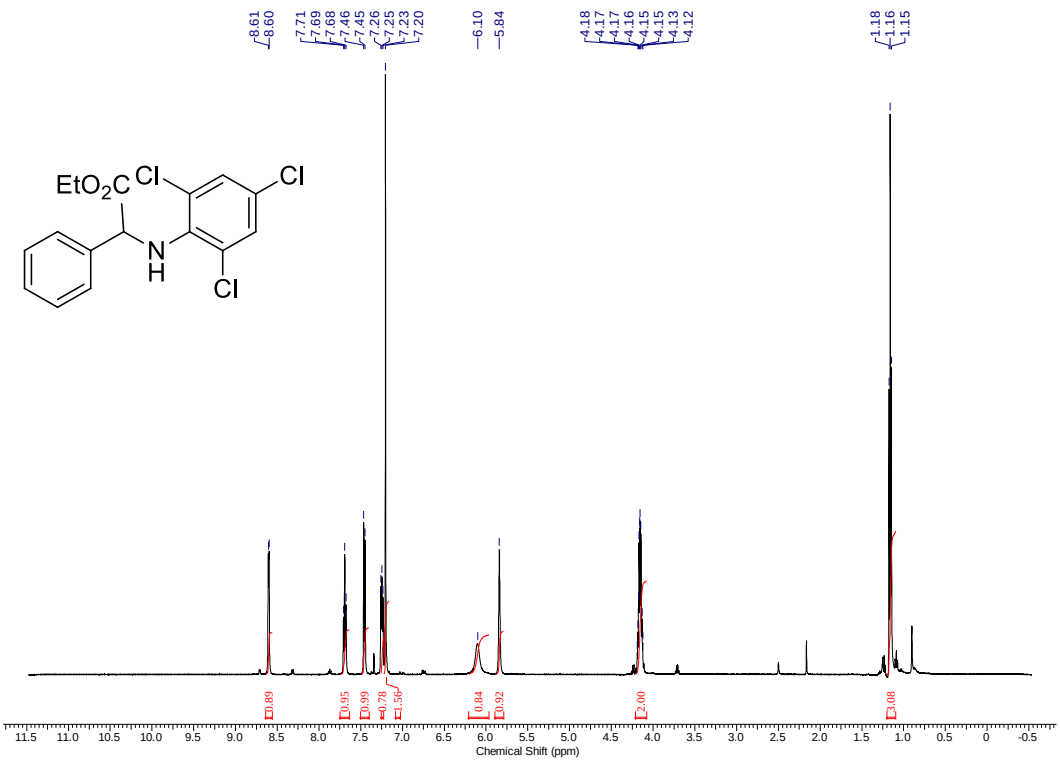
^{1}H NMR Spectrum of **3bg**:



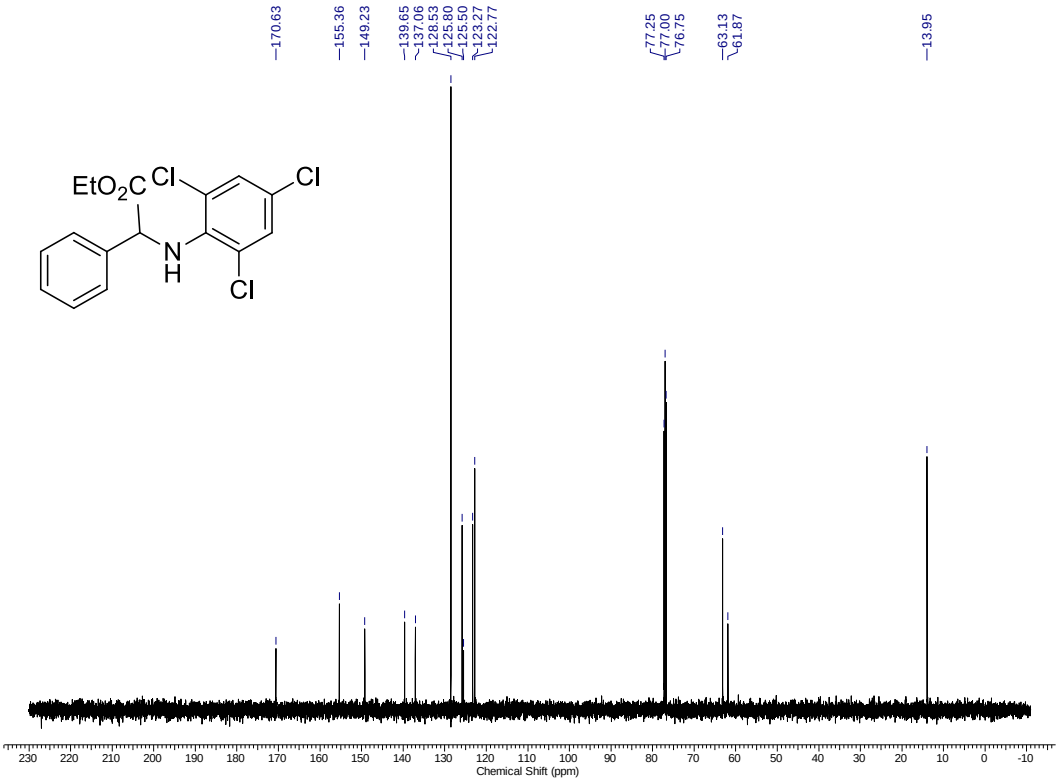
^{13}C NMR Spectrum of **3bg**:



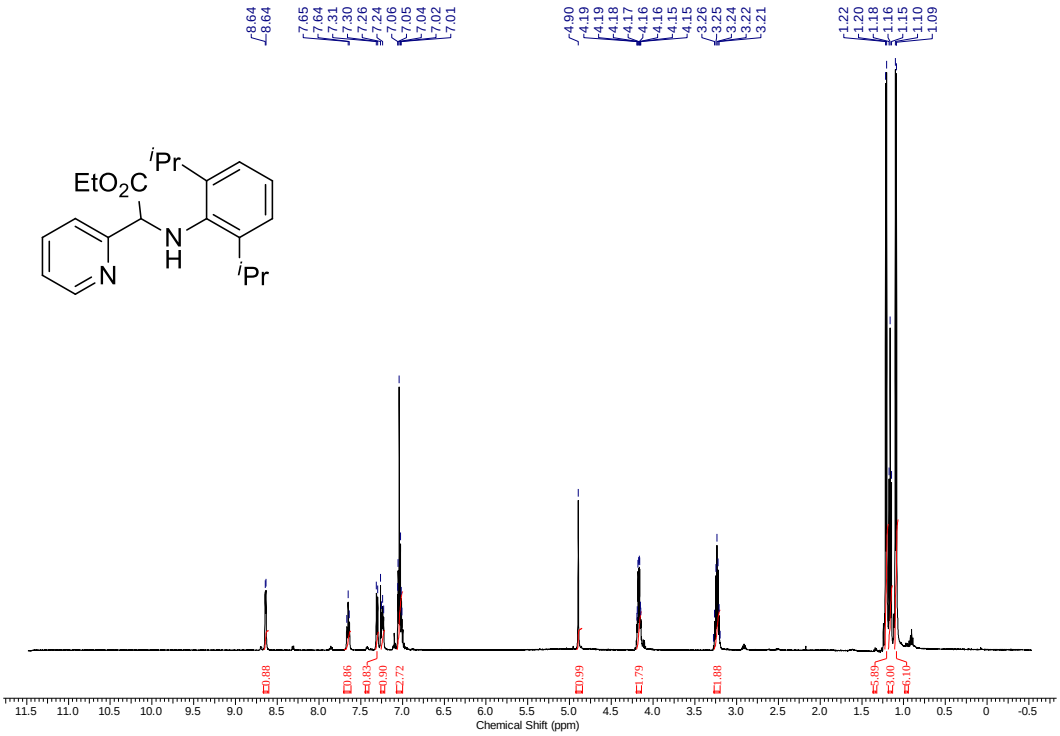
^{1}H NMR Spectrum of **3bh**:



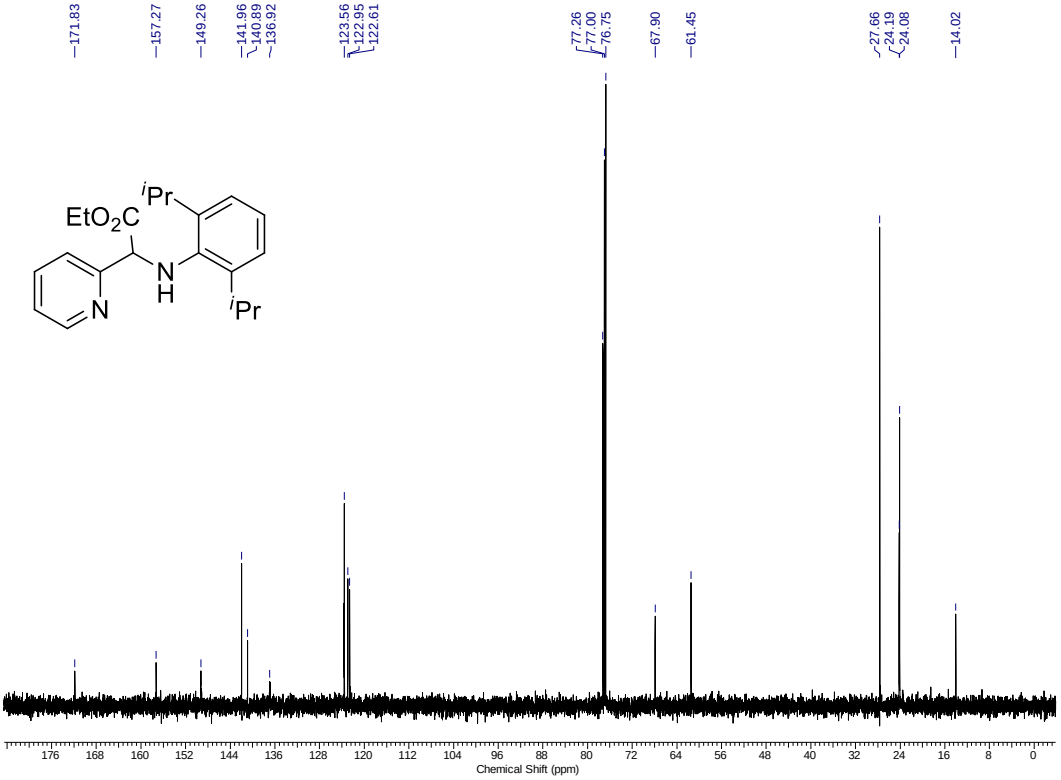
^{13}C NMR Spectrum of **3bh**:



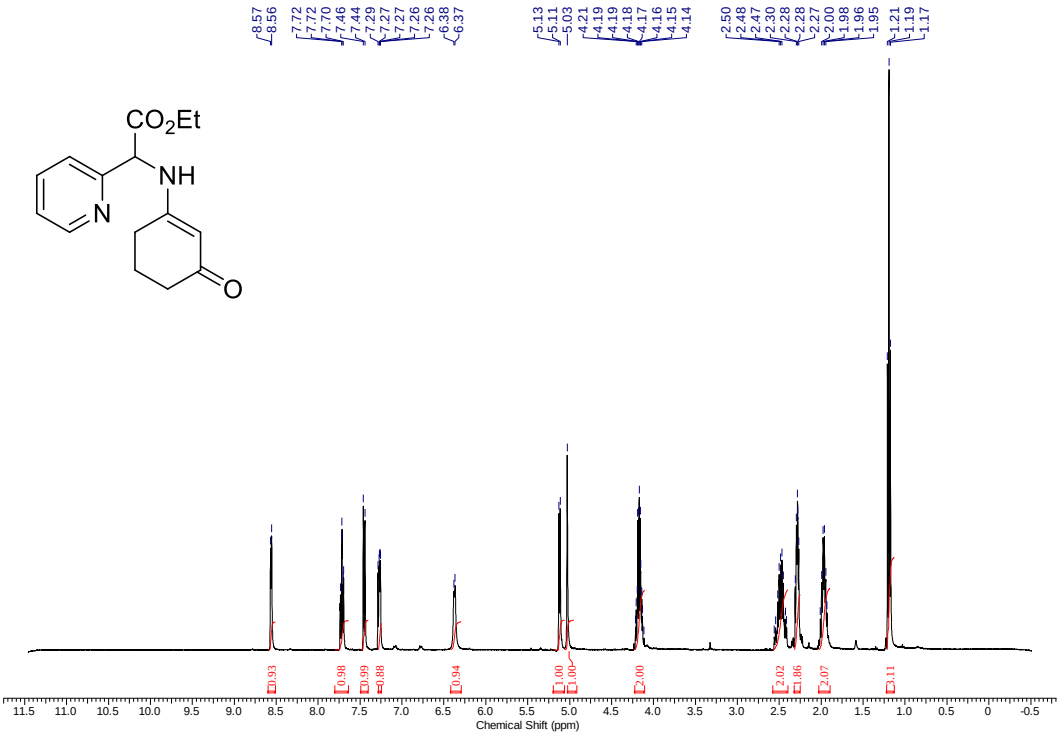
^{1}H NMR Spectrum of **3bi**:



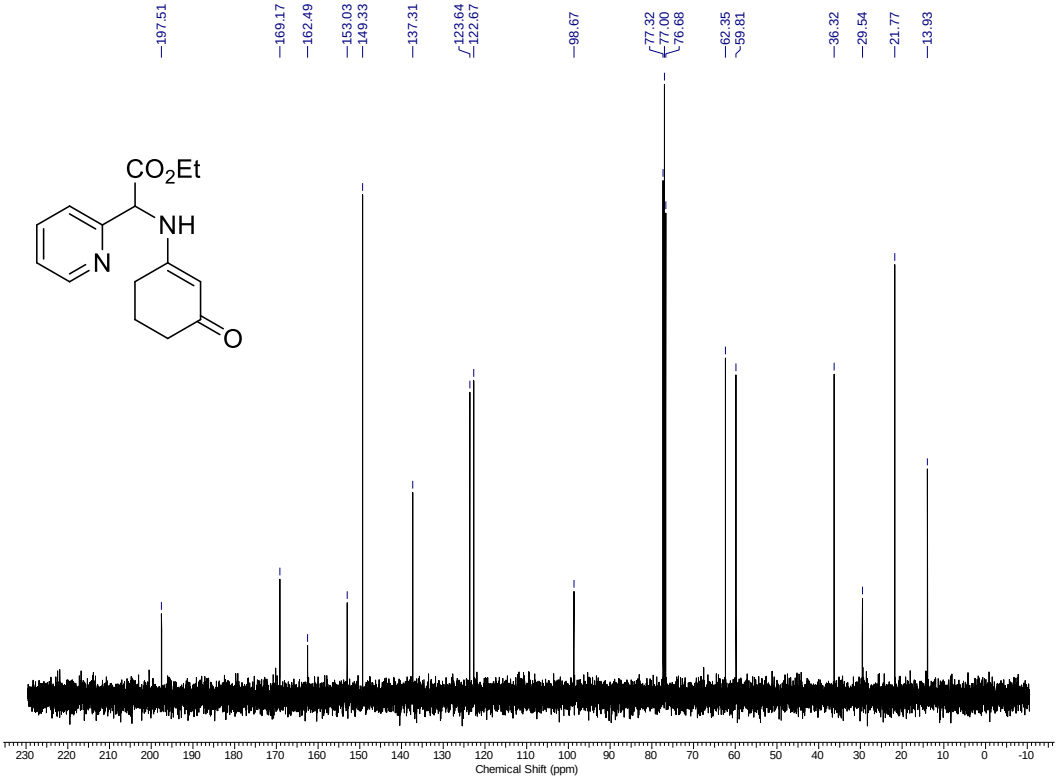
^{13}C NMR Spectrum of **3bi**:



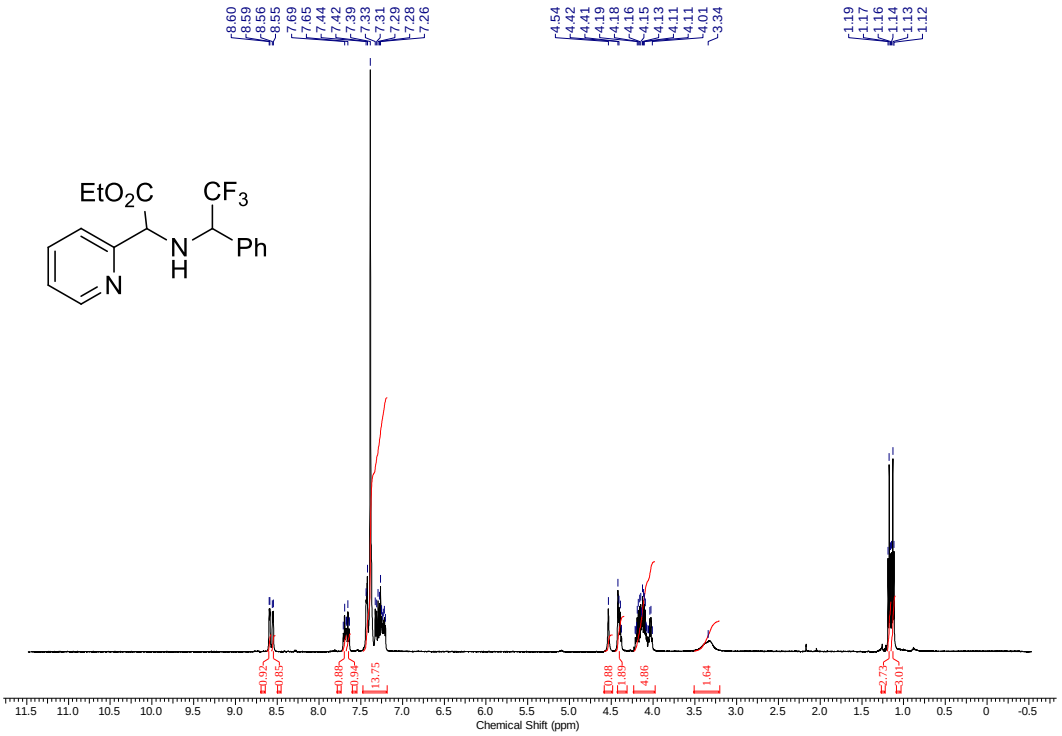
^{1}H NMR Spectrum of **3bj**:



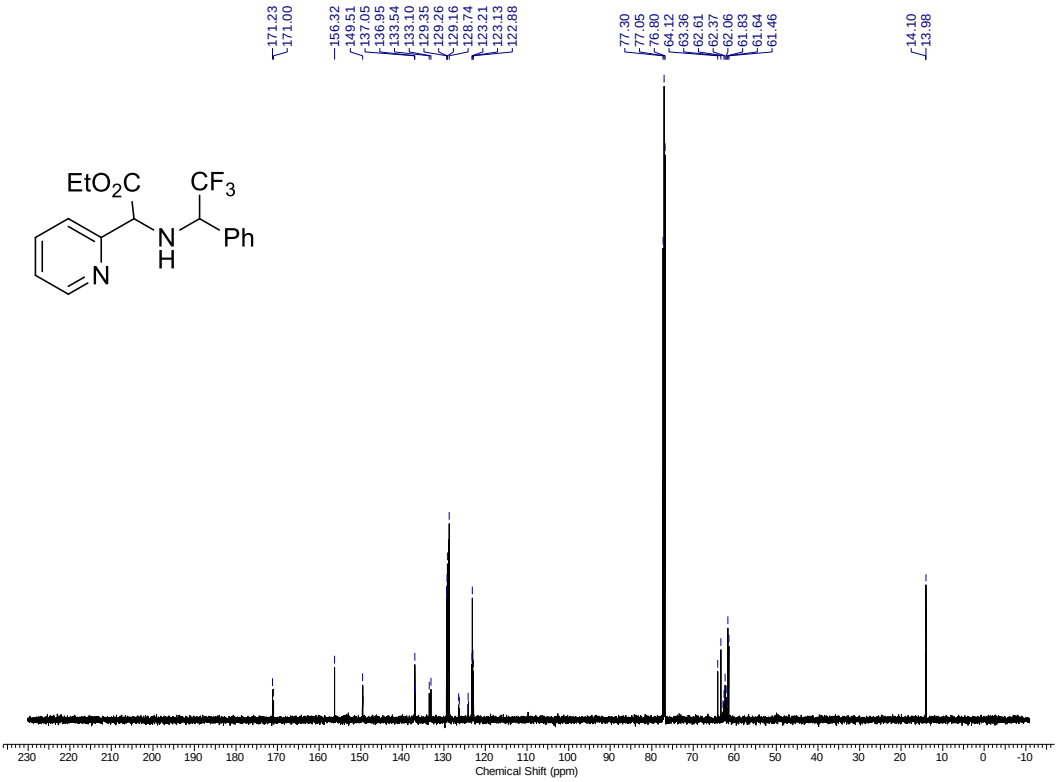
^{13}C NMR Spectrum of **3bj**:



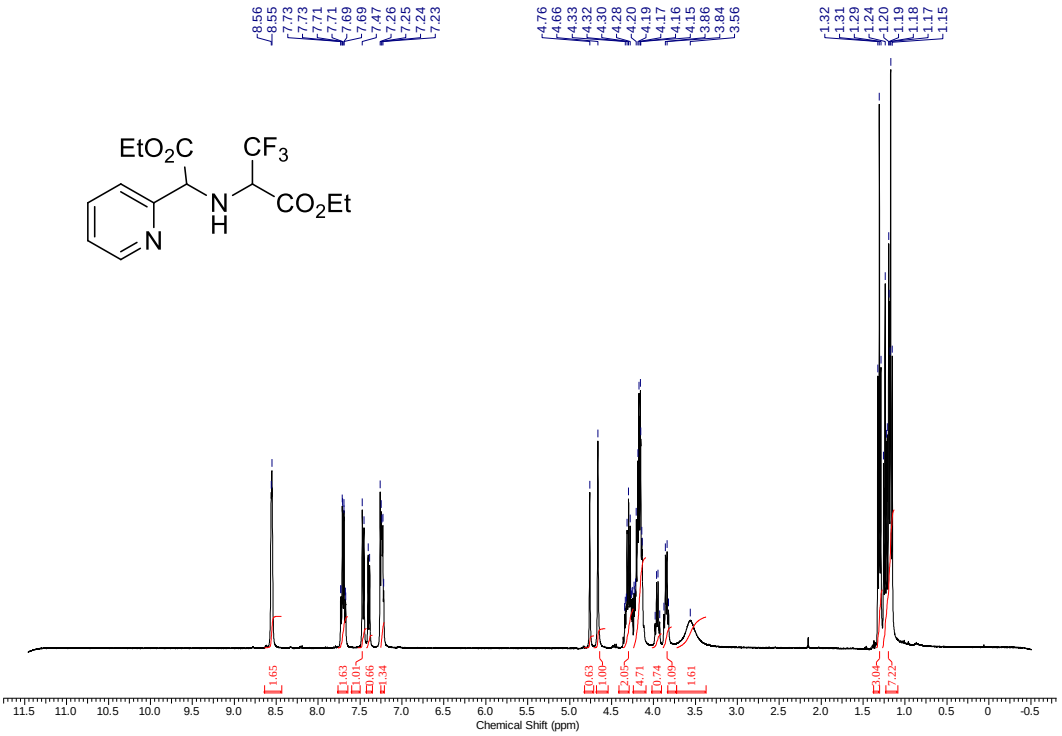
^{1}H NMR Spectrum of **3bk**:



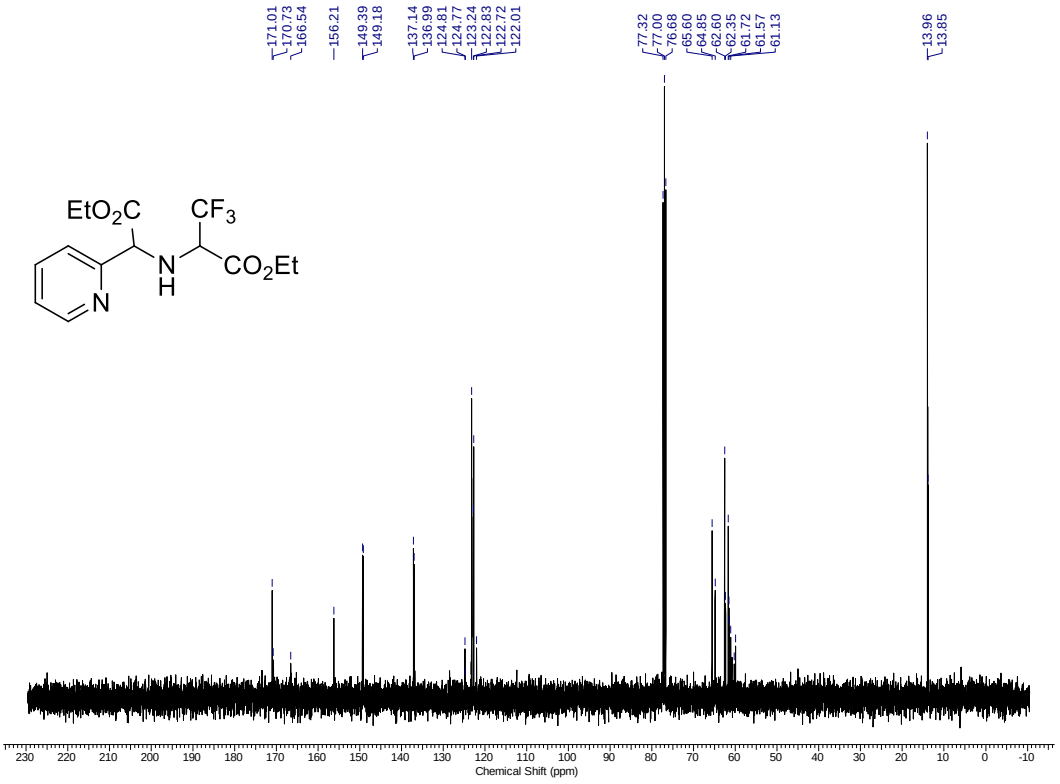
^{13}C NMR Spectrum of **3bk**:



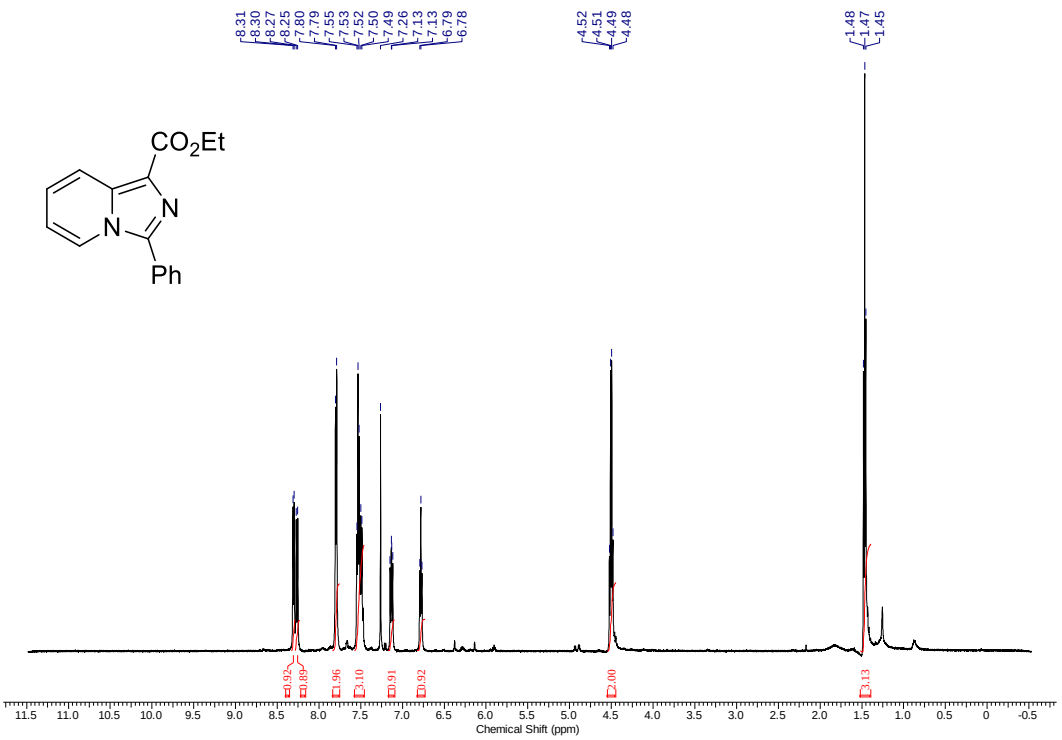
^{1}H NMR Spectrum of **3bl**:



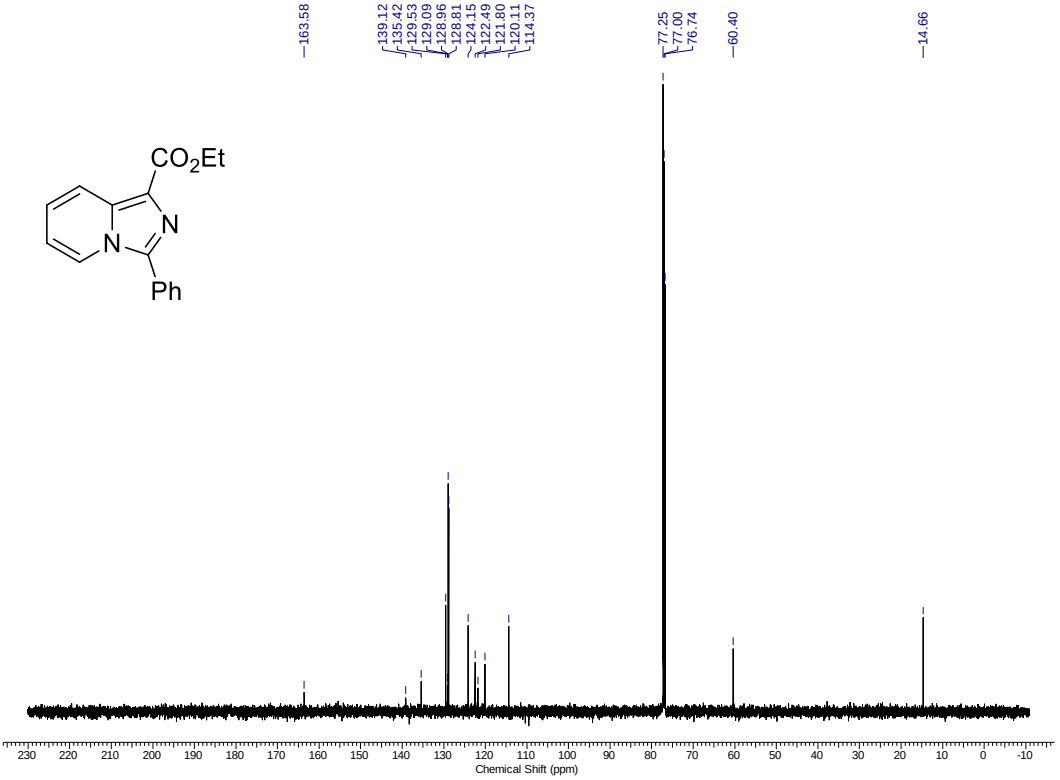
^{13}C NMR Spectrum of **3bl**:



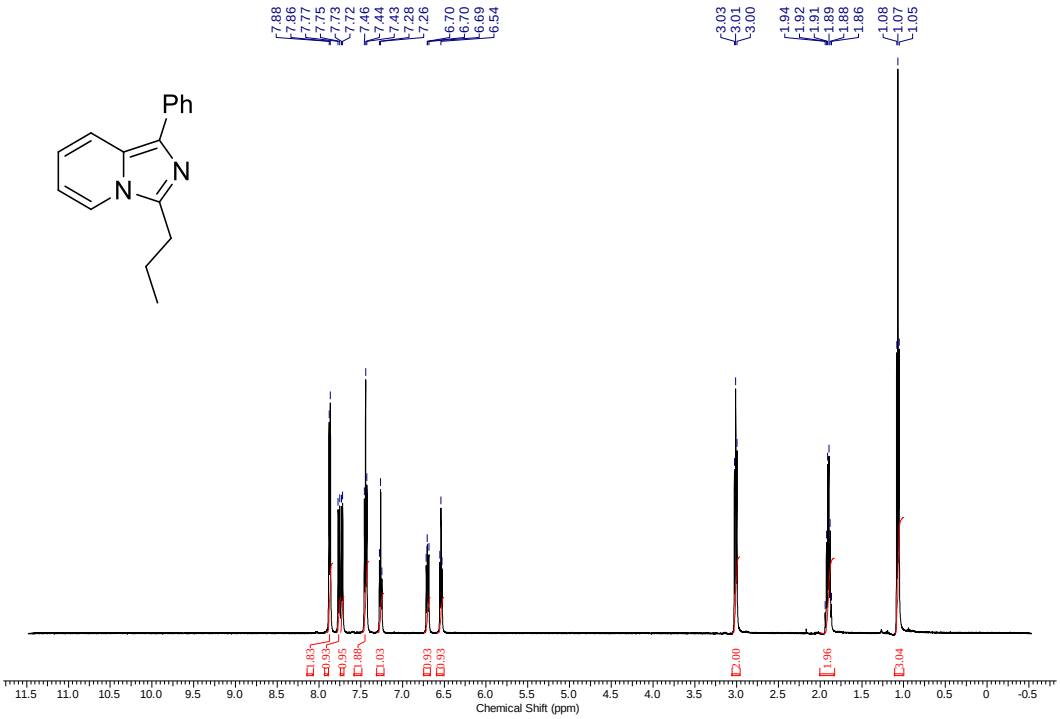
^{1}H NMR Spectrum of **4a**:



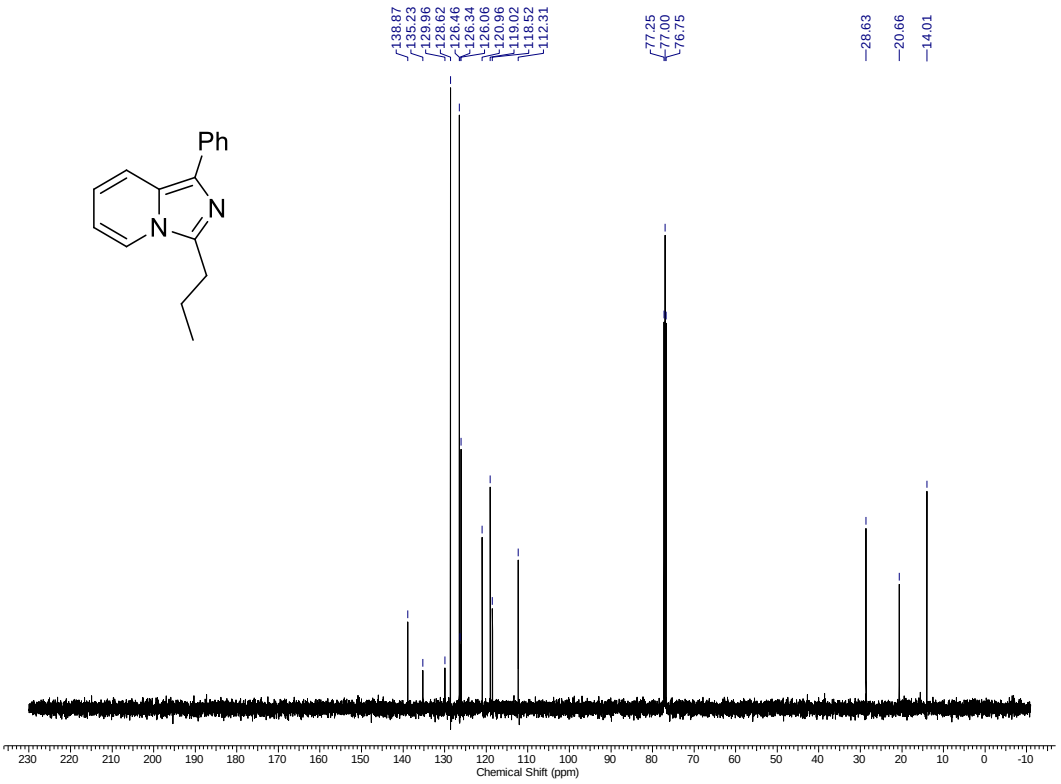
^{13}C NMR Spectrum of **4a**:



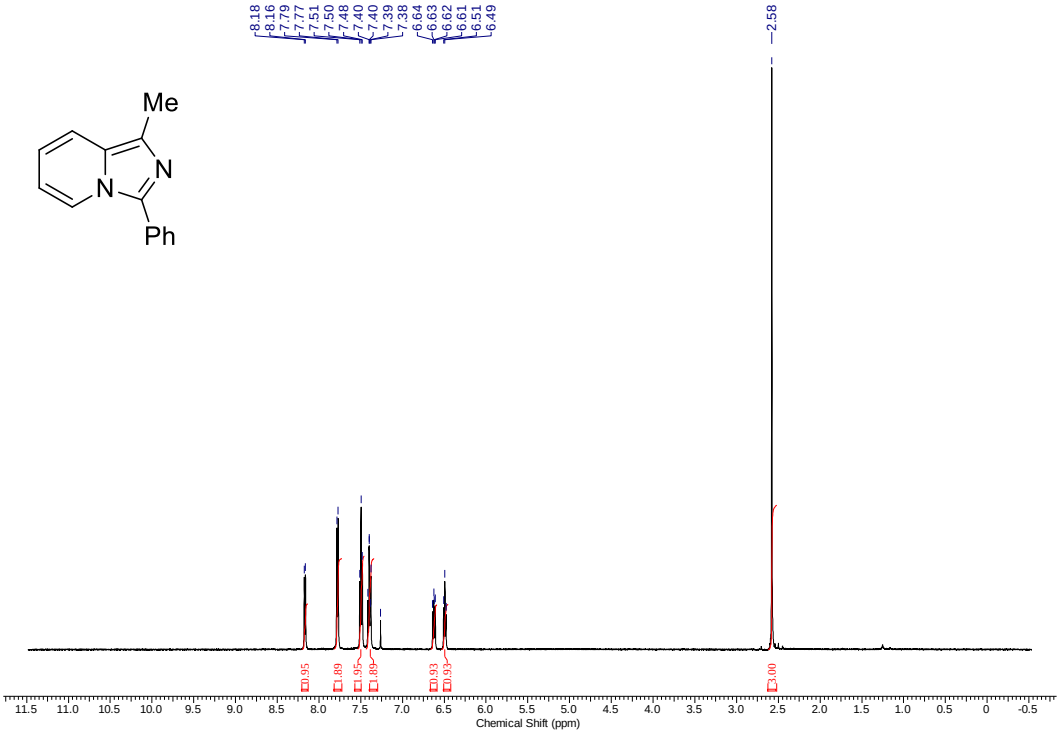
^{1}H NMR Spectrum of **4b**:



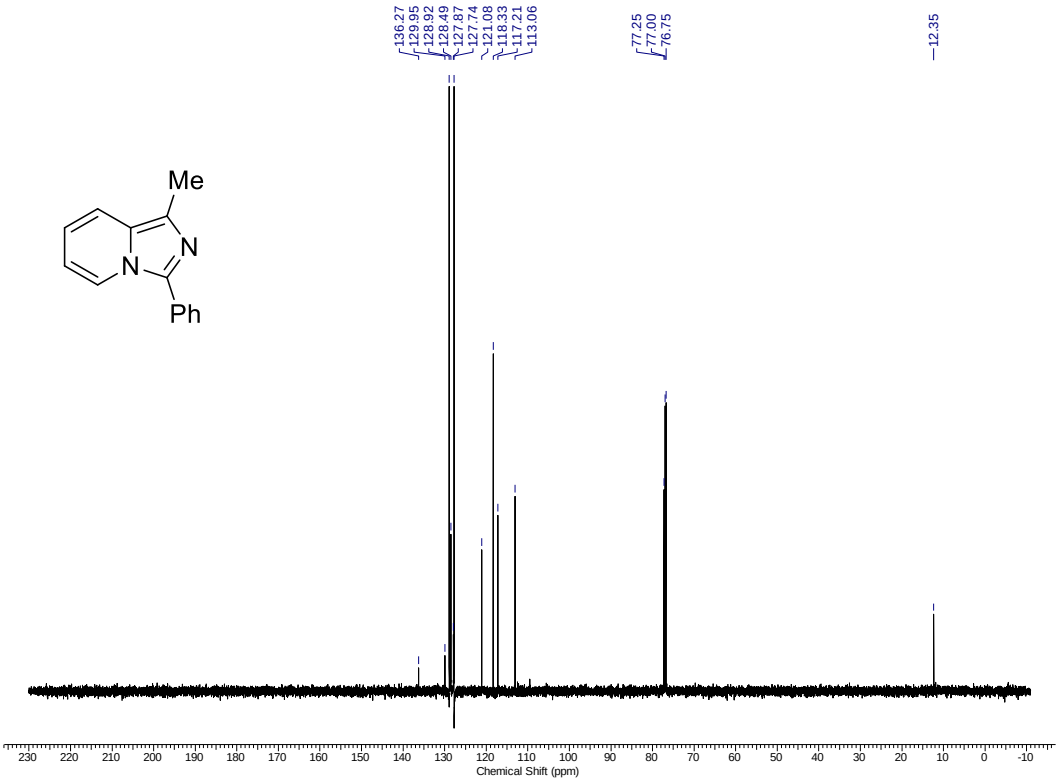
^{13}C NMR Spectrum of **4b**:



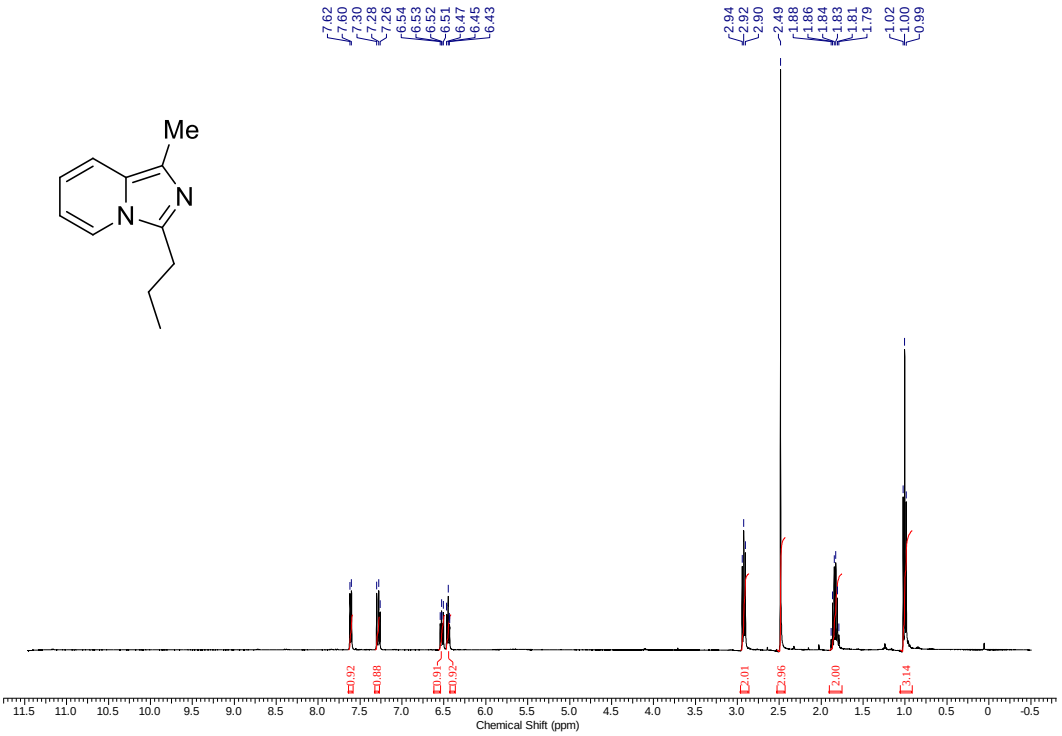
^{1}H NMR Spectrum of **4c**:



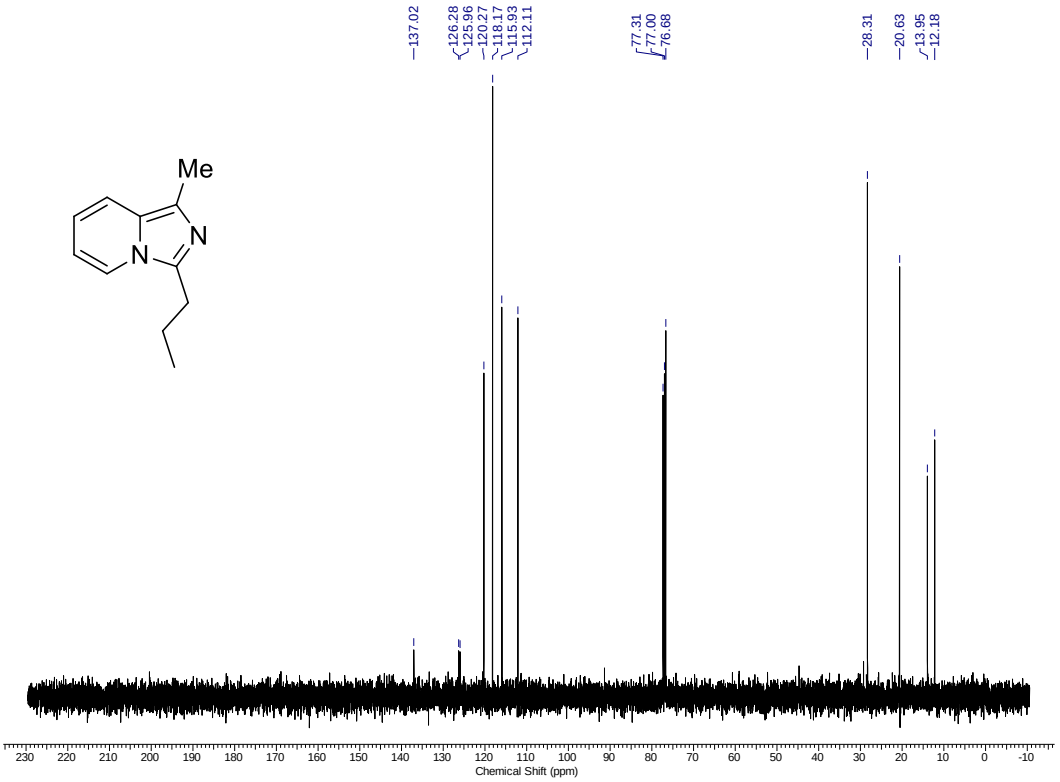
^{13}C NMR Spectrum of **4c**:



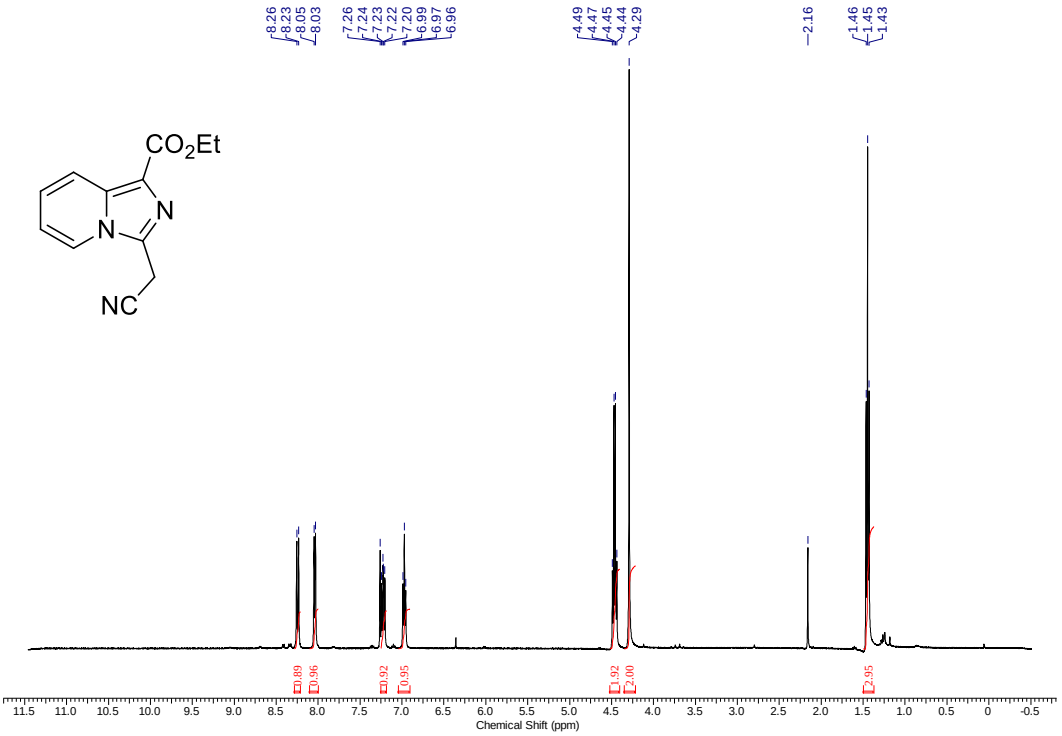
^{1}H NMR Spectrum of **4d**:



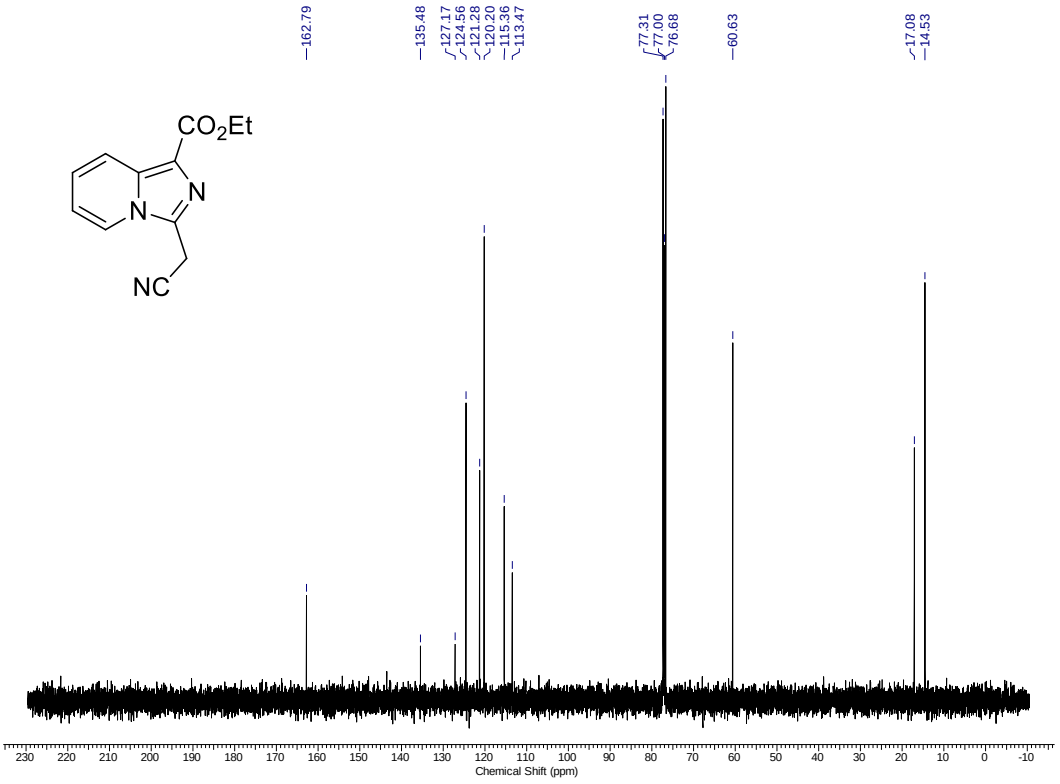
^{13}C NMR Spectrum of **4d**:



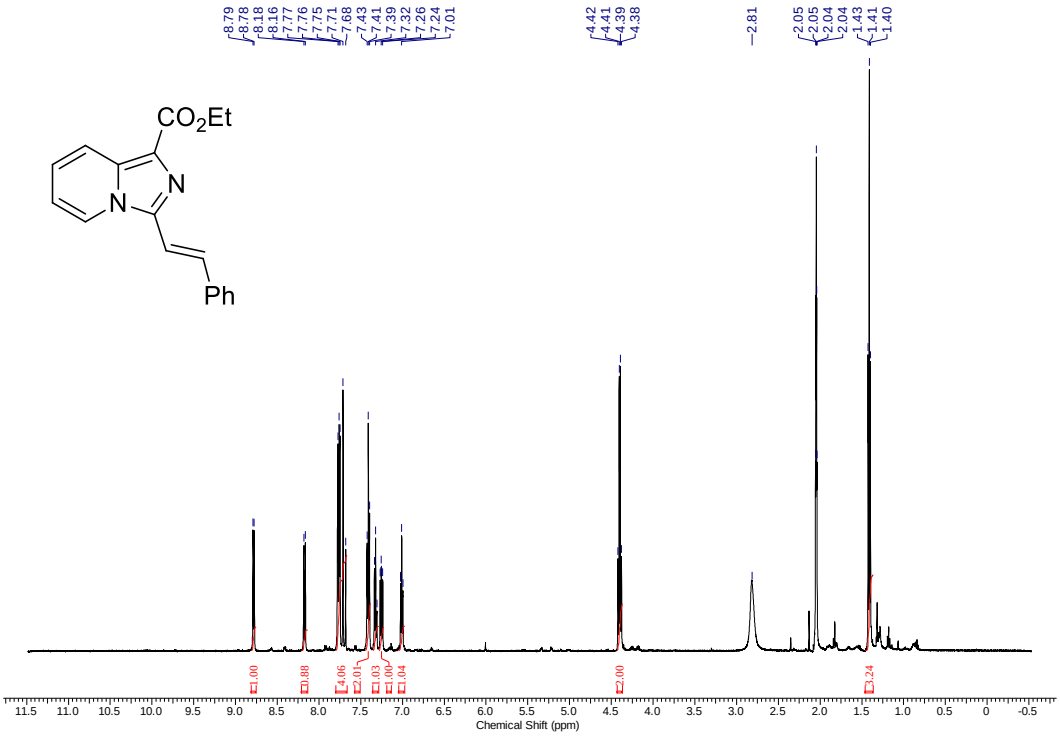
^{1}H NMR Spectrum of **4e**:



^{13}C NMR Spectrum of **4e**:



^{1}H NMR Spectrum of **4f:**



^{13}C NMR Spectrum of **4f**: