

Supporting Information

Magnetically Recoverable Cu⁰/Fe₃O₄ Catalyzed Highly Regioselective Synthesis of 2,3,4-Trisubstituted Pyrroles From Unactivated Terminal Alkynes and Isocyanides

Dipak Kumar Tiwari,^a Mandalaparthi Phanindrudu,^a Vinod Kumar Aravilli,^a B. Sridhar,^b Pravin R. Likhari,^a and Dharmendra Kumar Tiwari*^a

^aInorganic and Physical Chemistry Division, CSIR- Indian Institute of Chemical Technology, Hyderabad -500007, India

^bX-Ray Crystallography Centre, CSIR-Indian Institute of Chemical Technology, Hyderabad-500007, India

Fax (+91)-40-2716-0921; phone (+91)-40-2719-3510 & (+91)-40-2719-1667

email dktiwari@iict.res.in and dkt80.org@gmail.com

Table of Contents:

1	General Techniques	1-2
2	Synthesis of Cu(0)/Fe ₃ O ₄	2-3
3	Catalyst Characterisation XPS- Analysis XRD- Analysis SEM- Analysis	3-6
4	Recovery and reusability of catalyst	6
5	General Procedure for the synthesis of alkyne	7
6	General Experimental procedure	7-8
7	Spectral Data of compounds 3aa-3vb	8-24
8	Soft copy of ¹ H and ¹³ C NMR	25-65
9	Details of Single crystal X-ray of compound (3pa)	65-66
10	References	66

1. General Techniques:

All reagents were purchased from Sigma Aldrich and Alfa Aesar and were used without further purification. All experiments were carried out under nitrogen atmosphere. All the solvents used for the reaction were distilled before use. The product purification by column chromatography was accomplished using silica gel 100-200 mesh. Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection. Infrared spectra were recorded using a FT-IR spectrophotometer and values reported in cm⁻¹. ¹H and ¹³C NMR spectra were recorded with 300, 400 and 500 MHz NMR instruments with tetramethylsilane (TMS) as an internal standard. High-resolution mass spectra (ESI-HRMS) were recorded on ESI-QTOP mass spectrometer. Chemical shifts (δ =)

are reported in ppm using TMS as an internal standard, and spin-spin coupling constants (J) are given in Hz. Multiplicities in the ^1H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, bs = broad singlet; coupling constants are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra were recorded on a Waters 2695 and Thermo Scientific Exactive spectrometer respectively and mass/charge (m/z) ratios are reported as values in atomic mass units. All the melting points are uncorrected. X-ray powder diffraction (XRD) data were collected on a Siemens/D-5000 diffractometer using Cu $K\alpha$ radiation. XPS spectra were recorded on a Kratos AXIS 165 with a dual anode (Mg and Al) apparatus using the Mg $K\alpha$ anode. The pressure in the spectrometer was about 10^{-9} Torr. The particle size and external morphology of the samples were observed on a JEOL JEM-2100 high resolution transmission electron microscope (HRTEM). Auger electron spectroscopic (AES) analysis is conducted, at a base pressure of 10^{-10} Torr, within the K.E. range of 110-700 eV (beam voltage of 3 kV, eV/step 1 eV, time/step 50 ms). X-ray absorption spectra were recorded using a Rigaku spectrometer with a rotating anode X-ray generator (Ru-200B, Rigaku, Japan).

2. Synthesis of copper nanoparticles on Fe_3O_4 :

The stable copper nanoparticles on Fe_3O_4 , $\text{Cu}(0)/\text{Fe}_3\text{O}_4$ were synthesized from copper-Iron hydrotalcite successively by coprecipitation and Hydrothermal methods followed reduction by with Hydrogen gas. The detailed procedure is provided in our experimental procedure.

Copper- Iron Hydrotalcite Cu- Fe HT (Cu-Fe HT):

In a 250 mL four necked round bottomed flask with an overhead stirrer a mixture of copper nitrate trihydrate (0.0375 mole, 9.03 gm) and $\text{FeNO}_3 \cdot 9\text{H}_2\text{O}$ (0.15 moles, 6.06 gm) metal nitrates. NaOH (1.5 moles, 6.0 gm) and Na_2CO_3 (0.5 moles, 5.5 gm) were added from their respective additional burettes into the flask under stirring condition and precipitated at pH 8 with continuous stirring condition. After complete addition of metal nitrates, the greenish brown coloured precipitate was obtained which was aged at 333 K for 2h followed by filtration, washing with copious amount of distilled water to make the solid catalyst free from base and then dried in an oven at 383 K for 12h. The dried catalyst is then crushed into fine powder to obtain copper iron hydrotalcite Cu Fe HT.

Synthesis of calcined copper iron hydrotalcite (CuO/ Fe₃O₄)

5.0 gm of Cu Fe HT catalyst was taken in a tubular furnace and calcined in a static of air at 200 °C for a period of 5h. Calcined copper iron hydrotalcite CuO/Fe₃O₄ is obtained as a grey powder.

Synthesis of copper nanoparticles Cu(0)/ Fe₃O₄:

2.0 gm of calcined CuO/Fe₃O₄ was placed in the sample holder of the closed furnace. The furnace was facilitated with gas inlet and outlet. The inlet was connected to hydrogen gas with the flow rate 1 mL/ min. The furnace was slowly heated to 250 °C and CuO/Fe₃O₄ was kept at this temperature for 2 h. CuO/Fe₃O₄ which was in grey colour was reduced to Cu(0)/Fe₃O₄ (black powder). The furnace was cooled to room temperature under the N₂ flow (for 6-7h).

Iron ratio (Cu:Fe) in the synthesized catalysts was determined by Inductively Coupled Plasma-Atomic Optical Emission Spectroscopy (ICP-OES) and it is found to be 3:1 and showed 8 wt % of copper in Cu(0)/Fe₃O₄.

Cu/ α -Al₂O₃, Cu/La₂O₃, Cu/Y₂O₃, Cu/CeO₂, Cu/ZrO₂, Cu/TiO₂, Cu/Nb₂O₅, Cu/SnO₂ with same 8wt% of copper (ICP-OES) was reduced in same procedure as Cu(0)/Fe₃O₄. Copper nanoparticles on Fe₃O₄ Cu(0)/Fe₃O₄ was characterized and confirmed by various XRD, XPS, OES, and BET analytical methods.

3. Characterizations of Cu(0)/Fe₃O₄:

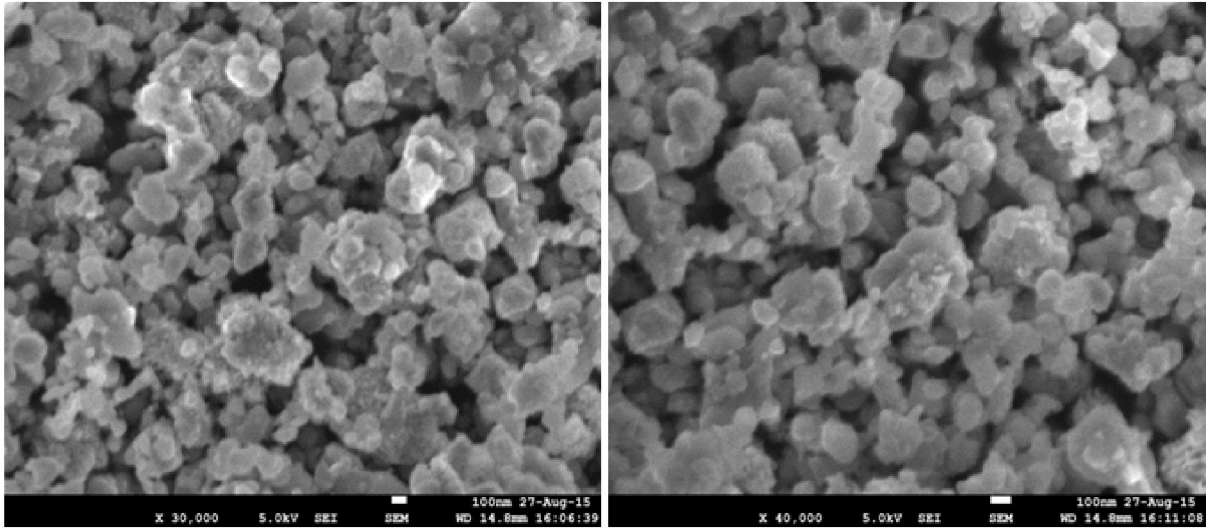


Figure S1: FE-SEM images of Cu(0)/Fe₃O₄

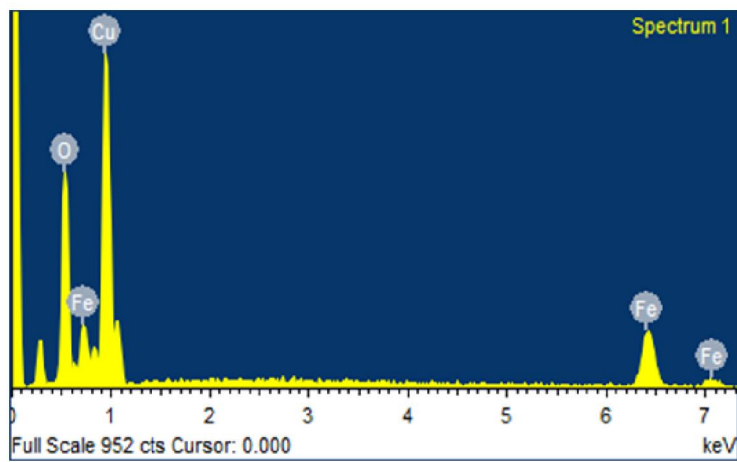
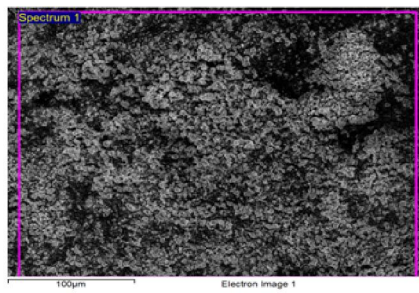


Figure S2: Energy dispersive X-ray spectrum of Cu(0)/Fe₃O₄

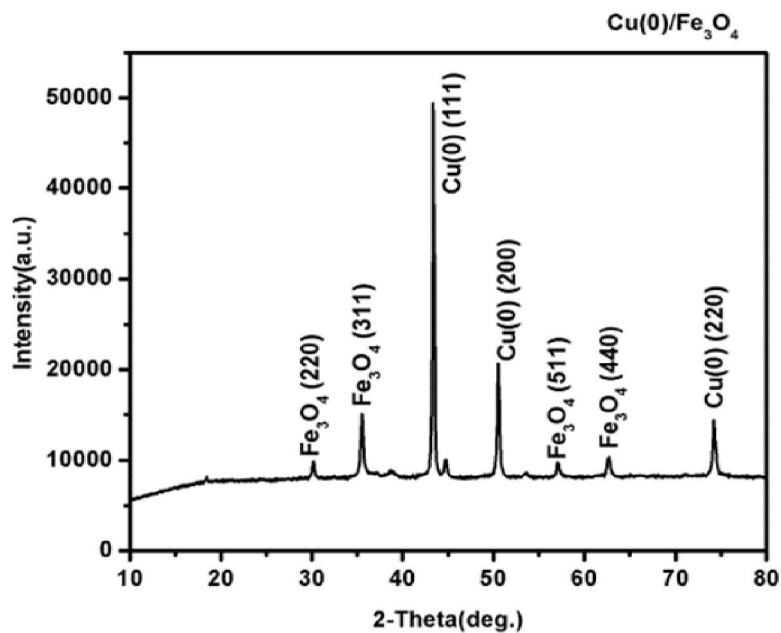


Figure S3: Wide angle powder X-ray diffraction pattern of Cu(0)/Fe₃O₄

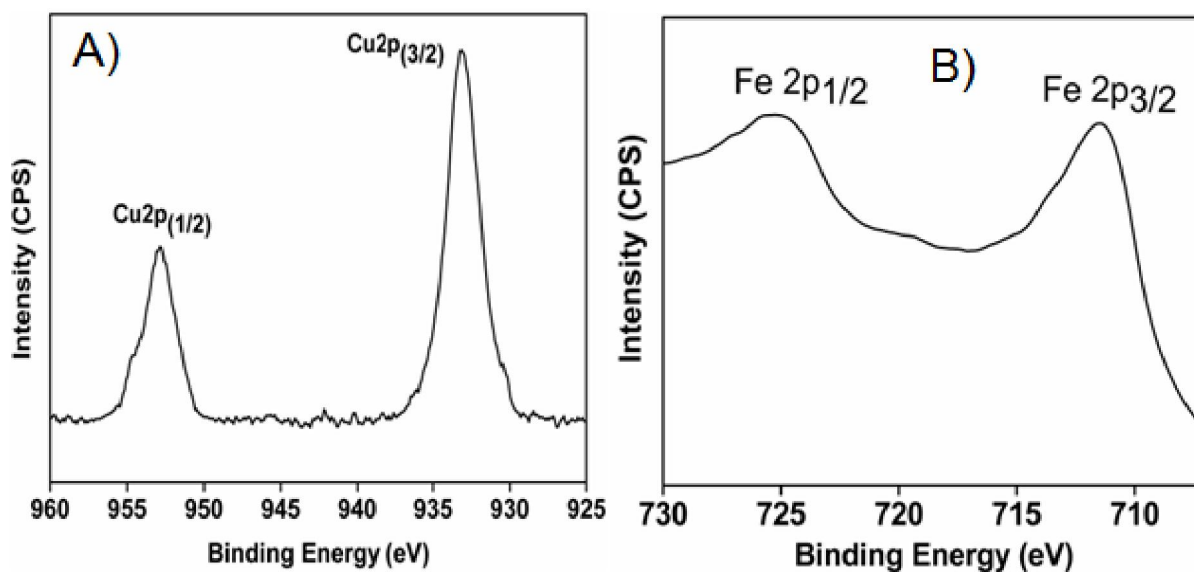


Figure S4: XPS spectra of Cu 2p region (A) and Fe 2p region (B) of Cu(0)/Fe₃O₄

4. Reusability of Cu(0)/Fe₃O₄:

Magnetic separation is a more attractive and simple technique than the filtration or centrifugation techniques as it prevents the loss of the catalyst and increases the reusability of the catalyst. Due to the superparamagnetic nature of Fe₃O₄ nanoparticles at room temperature separation of the Cu(0)/Fe₃O₄ nanocatalyst from the reaction mixture becomes very easy. In

the magnetic separation technique the catalyst became adsorbed onto the magnetic stirring bar when the stirring was stopped. Then the catalyst was washed with diethyl ether, oven dried at 100 °C and then directly used for the next cycle reaction without further purification. A recyclability test was performed under optimised conditions using fresh phenyl acetylene, isocyanides and anhydrous K_2CO_3 . Recyclable potential plot of $Cu(0)/Fe_3O_4$ nanocatalyst suggested that the nanocatalyst can be effectively reused for five consecutive catalytic cycles (ESI, Fig. XX) without significant loss in catalytic activity. A slight drop in the conversion (%) from the 5th to 6th cycles is observed which is due to the clogging of some catalytic active sites with organic reagents during the course of reaction. In every case our recovery of catalyst from the reaction mixture is almost 100%. We have also provided the distribution of product yield which remains consistent in each catalytic cycle.

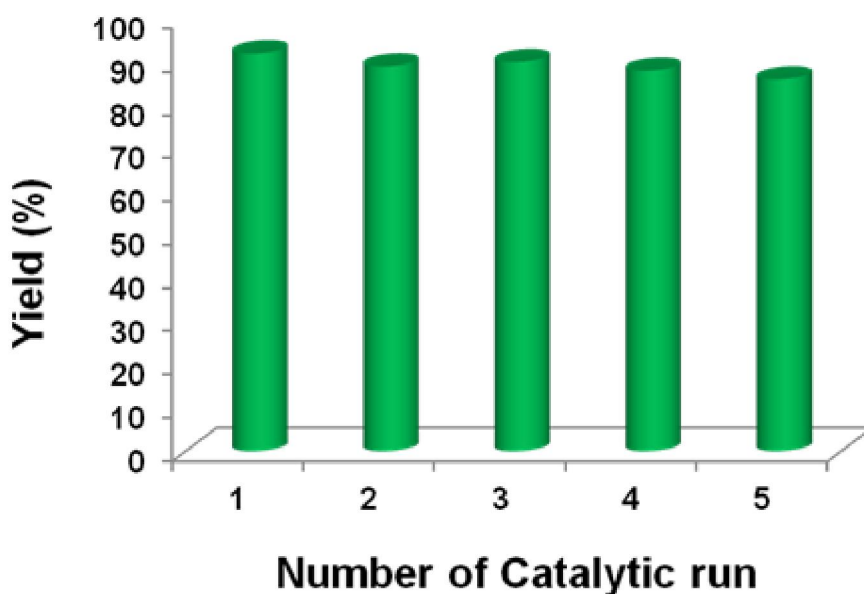
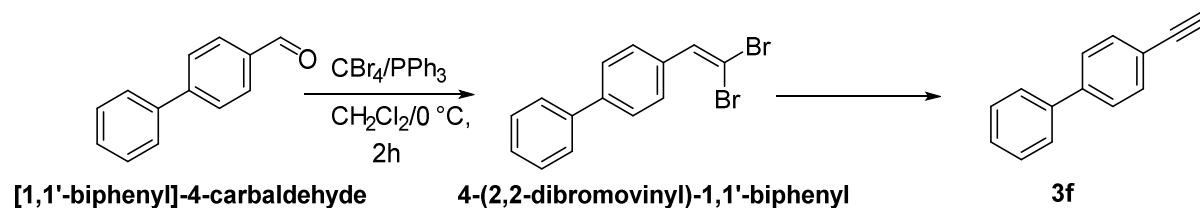


Figure S5: Recycling efficiency of $Cu(0)/Fe_3O_4$ nanocatalyst for five reaction cycles.

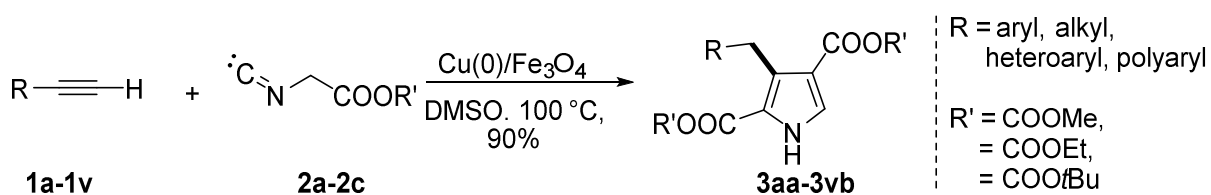
5. General Procedure of synthesis of 4-ethynyl-1,1'-biphenyl: (**3f**)³:



To a stirred solution of [1,1'-biphenyl]-4-carbaldehyde (2.55 g, 14.0 mmol) and carbon tetrabromide (9.27 g, 28.0 mmol) in anhydrous dichloromethane (40 mL) was added triphenylphosphine (14.6 g, 56.0 mmol,) in portions over a period of 30 mins at 0 °C temperature under inert atmosphere. The reaction mixture was turned brown that was allowed to stir at 0 °C temperature for 2 h. After completion of reaction (monitored by TLC), reaction mixture was quenched with water (30 mL). The reaction mixture was extracted with dichloromethane (2 x 60 mL); organic layers were washed with brine (20 mL). The organic layers were dried over anhydrous Na_2SO_4 ; solvent was evaporated under reduced pressure to afford a crude residue. The crude was purified on silica-gel (100 - 200 mesh) to give the dibromo compounds as white solid (3.4 g, 72 % yield). mp. 106-108 °C.; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.69 – 7.57 (m, 6H), 7.52 (s, 1H), 7.45 (t, $J = 7.3$ Hz, 2H), 7.36 (t, $J = 7.2$ Hz, 1H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) $\delta = 141.32, 140.35, 136.50, 134.22, 128.87, 127.67, 127.05, 89.50$.

To a stirred solution of dibromoalkene (3.38 g, 10.0 mmol) in anhydrous CH_3CN (25 mL) was added DBU (5.9 mL, 40.0 mmol, 4 equiv) drop wise over a period of 10 mins at ambient temperature (25-30 °C). The reaction mixture was allowed to stir at ambient temperature for 16 h. After completion of reaction (monitored by TLC), reaction mixture was cooled at 15 °C and quenched by drop wise addition of 5N aqueous HCl (50 mL) over a period of 15 mins then continued stirring for 5 mins. The reaction mixture was extracted with EtOAc/hexane (1:1, 2 x 40 mL); organic layers were washed with water (50 mL). The organic layers were dried over anhydrous K_2CO_3 , solvent was evaporated under reduced pressure, and resulting residues were dried in high vacuum to afford the analytically pure **3f** as white solid (1.4 g, 78 % yield). $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 7.61 - 7.54$ (m, 6H), 7.45 (dd, $J = 10.7, 4.5$ Hz, 2H), 7.42 – 7.33 (m, 1 H), 3.13 (s, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) $\delta = 141.60, 140.27, 132.57, 128.89, 127.75, 127.08, 127.03, 120.99, 83.57, 77.76$.

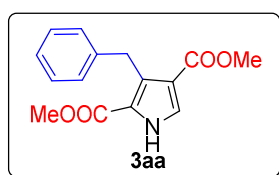
6. General experimental Procedure for the synthesis of 2,3,4-trisubstituted pyrroles (3aa-3vb):



To a solution of alkynes (1.0 mmol), isocyanides (2.0 mmol) and anhydrous K_2CO_3 (3.0 mmol) in dry DMSO (4.0 mL) was added $\text{Cu(0)/Fe}_3\text{O}_4$ nano catalyst (30 mg, 8%, 3.3 mol%) at room temperature under argon atmosphere. The reaction temperature was increased up to 100 °C and stirred for 1 h. The reaction mixture was then allowed to attain room temperature and diluted with ethyl acetate (50 mL). The catalyst was recovered magnetically and the organic layer was washed successively with water (20 mL) and brine (20 mL). The organic layer was further dried over anhydrous sodium sulphate and evaporation of solvent under reduced pressure produced crude product which was purified by column chromatography using 100-200 mesh silica gel.

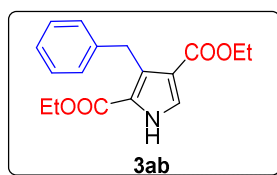
7. Spectral Data of compounds (3aa -3vb)

Dimethyl 3-benzyl-1H-pyrrole-2,4-dicarboxylate (3aa)



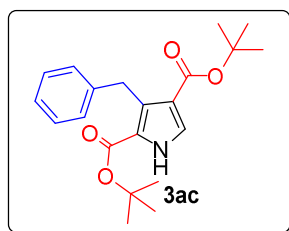
Yield: 85%; White solid, **M.p.** 120 – 122 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.38 (s, 1H), 7.51 (d, J = 3.5 Hz, 1H), 7.28 – 7.25 (m, 2H), 7.22 (dd, J = 10.3, 4.9 Hz, 2H), 7.14 – 7.11 (m, 1H), 4.52 (s, 2H), 3.86 (s, 3H), 3.77 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 164.58, 161.58, 141.17, 132.09, 128.55, 128.06, 127.46, 125.64, 121.02, 116.50, 51.62, 51.04, 30.34; **IR** (neat): 3300, 1714, 1697, 1559, 1277 1147 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{15}\text{H}_{16}\text{NO}_4$ [$\text{M}+\text{H}$] is 274.10738 and found 274.10752.

Diethyl 3-benzyl-1H-pyrrole-2,4-dicarboxylate (3ab):



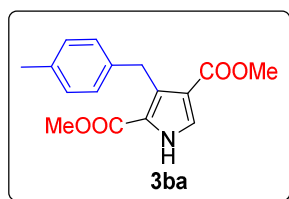
Yield: 89%; Yellow solid, **M.p.** 95 – 97 °C; **¹H NMR** (400 MHz, CDCl₃) δ = 9.51 (s, 1H), 7.53 (d, *J* = 3.5 Hz, 1H), 7.24 – 7.19 (m, 4H), 7.12 (t, *J* = 7.0 Hz, 1H), 4.53 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.33 – 1.29 (t, *J* = 7.6 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); **¹³C NMR** (125 MHz, CDCl₃) δ = 164.32, 161.35, 141.24, 131.63, 128.51, 127.99, 127.40, 125.54, 121.27, 116.89, 60.73, 59.85, 30.38, 14.37; **IR** (neat): 3228, 2952, 1724, 1673, 1441, 1278 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₁₇H₂₀NO₄ [M+H] is 302.13868 and found 302.13814.

Di-tert-butyl 3-benzyl-1H-pyrrole-2,4-dicarboxylate (3ac):



Yield: 86%; White solid; **M.p.** 96 – 98 °C; **¹H NMR** (400 MHz, CDCl₃) δ = 9.44 (s, 1H), 7.46 (d, *J* = 3.4 Hz, 1H), 7.25 – 7.17 (m, 4H), 7.14 – 7.08 (m, 1H), 4.51 (s, 2H), 1.48 (s, 9H), 1.44 (s, 9H); **¹³C NMR** (125 MHz, CDCl₃) δ = 163.98, 161.06, 141.40, 129.61, 128.93, 128.16, 127.84, 126.79, 125.29, 122.48, 118.68, 81.85, 80.24, 30.25, 28.33, 28.28; **IR** (neat): 3284, 2926, 1702, 1670, 1295, 1150 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₂₁H₂₈NO₄ [M+H] is 358.20128 and found 358.20158.

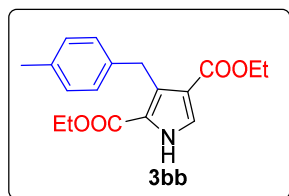
Dimethyl 3-(4-methylbenzyl)-1H-pyrrole-2,4-dicarboxylate (3ba):



Yield: 81%; Colourless thick oil; **¹H** (500 MHz, CDCl₃) δ = 9.23 (s, 1H), 7.51 (d, *J* = 3.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 7.9 Hz, 2H), 4.47 (s, 2H), 3.86 (s, 3H), 3.77 (s,

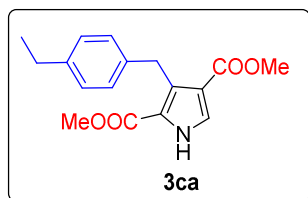
3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.56, 161.55, 138.10, 135.04, 132.40, 128.78, 128.42, 127.36, 120.92, 116.47, 51.62, 51.04, 29.72, 21.02; IR (neat): 3218, 2923, 1699, 1277, 768 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{16}\text{H}_{18}\text{NO}_4$ [M+H] is 288.12303 and found 288.12341.

Diethyl 3-(4-methylbenzyl)-1H-pyrrole-2,4-dicarboxylate (3bb):



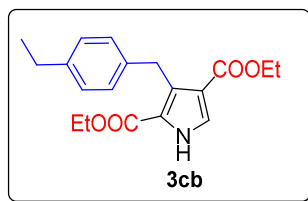
Yield: 82%; Colourless oil; ^1H NMR (500 MHz, CDCl_3) δ = 9.31 (s, 1H), 7.51 (d, J = 3.5 Hz, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.02 (d, J = 7.9 Hz, 2H), 4.48 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 2.27 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.28, 161.28, 138.17, 134.93, 132.01, 128.70, 128.42, 127.25, 121.14, 116.85, 60.70, 59.82, 29.89, 21.01, 14.39; IR (neat): 3295, 2927, 1693, 1271, 1083 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_4$ [M+H] is 316.15433 and found 316.15483.

Dimethyl 3-(4-ethylbenzyl)-1H-pyrrole-2,4-dicarboxylate (3ca):



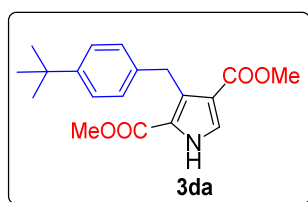
Yield: 82%; Yellow thick oil, ^1H NMR (500 MHz, CDCl_3) δ = 9.30 (s, 1H), 7.50 (d, J = 3.5 Hz, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.1 Hz, 2H), 4.48 (s, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 2.58 (q, J = 7.6 Hz, 2H), 1.19 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 164.60, 161.60, 141.42, 138.35, 132.41, 128.47, 127.57, 127.40, 120.93, 118.23, 116.47, 51.62, 51.04, 29.91, 28.42, 15.56; IR (neat): 3296, 2958, 1700, 1438, 1274, 1020 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_4$ [M+H] is 306.13868 and found 306.138647.

Diethyl 3-(4-ethylbenzyl)-1H-pyrrole-2,4-dicarboxylate (3cb):



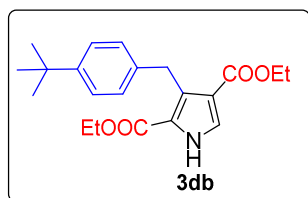
Yield: 81%; Sticky solid; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 9.29 (s, 1H), 7.51 (d, J = 3.5 Hz, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 4.49 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 2.58 (q, J = 7.6 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.19 (t, J = 7.6 Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.29, 161.26, 141.00, 138.44, 128.47, 127.49, 127.21, 121.16, 116.91, 60.69, 59.82, 29.91, 28.42, 15.59, 14.41, 14.38; **IR** (KBr): 3271, 2965, 1701, 1451, 1271, 998 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]$ is 330.16998 and found 330.17014.

Dimethyl 3-(4-(tert-butyl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3da):



Yield: 79%; Colourless liquid; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.26 (s, 1H), 7.51 (d, J = 3.4 Hz, 1H), 7.25 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 4.48 (s, 2H), 3.87 (s, 3H), 3.78 (s, 3H), 1.27 (s, 9H); $^{13}\text{C NMR}$ (125MHz, CDCl_3) δ = 164.43, 161.56, 148.27, 132.40, 128.20, 127.32, 124.99, 120.93, 116.53, 51.61, 51.04, 34.31, 31.42, 29.79; **IR** (neat): 3299, 2957, 1701, 1272, 1022 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]$ is 330.16998 and found 330.170574.

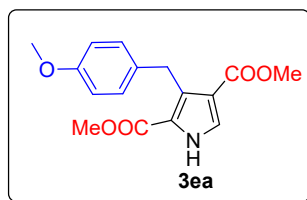
Diethyl 3-(4-(tert-butyl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3db):



Yield: 76%; Colourless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.29 (s, 1H), 7.51 (d, J = 3.4 Hz, 1H), 7.24 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H), 4.49 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 1.27 (s, 9H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.31, 161.29,

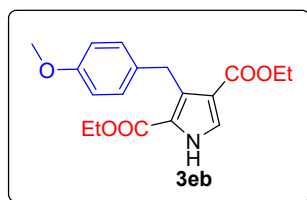
148.18, 138.20, 132.02, 128.18, 127.21, 124.90, 121.16, 116.92, 60.69, 59.82, 34.30, 31.43, 29.80, 14.38; **IR** (neat): 3291, 2945, 1685, 1445, 1265, 1029 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{21}\text{H}_{28}\text{NO}_4$ [M+H] is 358.20128 and found 358.20170.

Dimethyl 3-(4-methoxybenzyl)-1H-pyrrole-2,4-dicarboxylate (3ea):



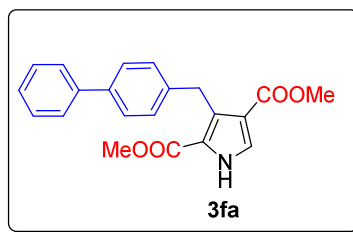
Yield: 71%; White solid; **M.p.** 136 – 138 $^{\circ}\text{C}$; **^1H NMR** (400 MHz, CDCl_3) δ = 9.55 (s, 1H), 7.49 (d, J = 3.5 Hz, 1H), 7.20 (d, J = 8.5 Hz, 2H), 6.78 – 6.76 (m, 2H), 4.45 (s, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H); **^{13}C NMR** (125 MHz, CDCl_3) δ = 164.67, 161.67, 157.61, 133.43, 132.76, 129.50, 127.64, 120.79, 116.22, 113.51, 55.21, 51.61, 51.05, 29.41; **IR** (KBr): 3358, 3299, 2956, 1680, 1509, 1436, 1278, 1020 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{16}\text{H}_{18}\text{NO}_5$ [M+H] is 304.11795 and found 304.11815.

Diethyl 3-(4-methoxybenzyl)-1H-pyrrole-2,4-dicarboxylate (3eb):



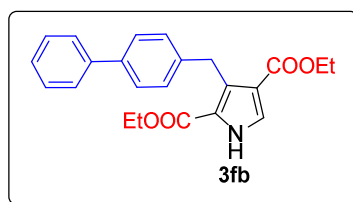
Yield: 73%; Sticky solid; **^1H NMR** (400 MHz, CDCl_3) δ = 9.44 (s, 1H), 7.51 (d, J = 3.5 Hz, 1H), 7.20 (d, J = 8.7 Hz, 2H), 6.78 – 6.75 (m, 2H), 4.46 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3) δ = 164.31, 161.31, 157.57, 133.48, 132.30, 129.47, 127.35, 121.05, 116.73, 113.43, 60.72, 59.84, 55.22, 29.42, 14.41; **IR** (neat): 3257, 2930, 1718, 1423, 1280 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_5$ [M+H] is 332.14925 and found 332.14963.

Dimethyl 3-([1,1'-biphenyl]-4-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3fa):



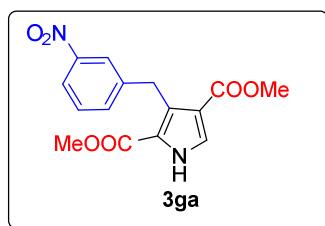
Yield: 86%; Colourless liquid, $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.30 (s, 1H), 7.57 – 7.51 (m, 3H), 7.47 – 7.45 (m, 2H), 7.40 (dd, J = 10.5, 4.9 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.32 – 7.27 (m, 1H), 4.56 (s, 2H), 3.88 (s, 3H), 3.79 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.54, 161.46, 141.25, 140.32, 138.57, 132.02, 128.95, 128.65, 127.38, 127.00, 126.86, 121.04, 116.54, 51.67, 51.09, 29.99; **IR** (neat): 3266, 2961, 1705, 1438, 1266 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_4$ [$\text{M}+\text{H}$] is 350.13868 and found 350.13692.

Diethyl 3-([1,1'-biphenyl]-4-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3fb):



Yield: 84%; Colourless liquid, $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.44 (s, 1H), 7.56 – 7.53 (m, 3H), 7.47 – 7.44 (m, 2H), 7.40 (dd, J = 10.5, 4.9 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.29 (ddd, J = 8.5, 2.3, 1.2 Hz, 1H), 4.57 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 164.28, 161.22, 141.28, 140.42, 138.47, 131.60, 128.94, 128.66, 127.30, 127.00, 126.88, 126.78, 121.28, 116.92, 60.77, 59.90, 30.03, 14.43; **IR** (neat): 3290, 2975, 1703, 1426, 1271 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{23}\text{H}_{24}\text{NO}_4$ [$\text{M}+\text{H}$] is 378.16998 and found 378.16994.

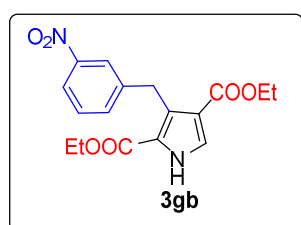
Dimethyl 3-(3-nitrobenzyl)-1H-pyrrole-2,4-dicarboxylate (3ga):



Yield: 93%; White solid, **M.p.** 124 – 126 $^{\circ}\text{C}$; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ = 9.58 (s, 1H), 8.11 (bs, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 7.4 Hz, 1H), 7.56 (d, J = 3.4 Hz, 1H),

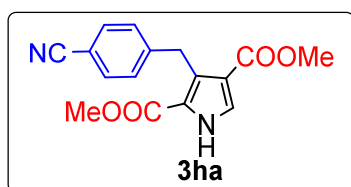
7.48 – 7.37 (m, 1H), 4.62 (s, 2H), 3.90 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ = 164.42, 161.20, 148.16, 144.19, 143.19, 135.04, 130.42, 128.84, 127.66, 123.41, 121.16, 120.93, 116.25, 51.82, 51.21, 30.02; IR (KBr): 3275, 2966, 1715, 1675, 1531, 1275 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_6$ [M+H] is 319.09246 and found 319.09195.

Diethyl 3-(3-nitrobenzyl)-1H-pyrrole-2,4-dicarboxylate (3gb):



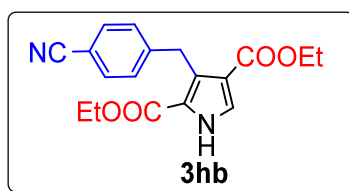
Yield: 91%; White solid, **M.p.** 95 - 97 °C; ^1H NMR (400 MHz, CDCl_3) δ = 9.50 (s, 1H), 8.11 (bs, 1H), 8.00 (dd, J = 8.2, 1.3 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.56 (d, J = 3.5 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 4.62 (s, 2H), 4.35 (q, J = 7.1 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ = 164.11, 160.95, 148.15, 143.30, 135.02, 129.96, 128.79, 127.54, 123.38, 121.38, 120.87, 116.63, 60.96, 60.03, 30.06, 14.34; IR (KBr): 3228, 2926, 1717, 1677, 1531, 1350, 1275 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_6$ [M+H] is 347.12376 and found 347.12313.

Dimethyl 3-(4-cyanobenzyl)-1H-pyrrole-2,4-dicarboxylate (3ha):



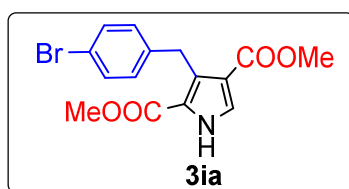
Yield: 91%; White solid, **M.p.** 109 – 111 °C; ^1H NMR (500 MHz, CDCl_3) δ = 9.29 (s, 1H), 7.53 (d, J = 3.5 Hz, 1H), 7.51 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 4.57 (s, 2H), 3.86 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.30, 161.00, 146.80, 131.95, 130.51, 129.33, 127.35, 121.15, 119.31, 116.43, 109.48, 51.75, 51.17, 30.51; IR (KBr): 3305, 2954, 2224, 1719, 1680, 1453, 1283 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_4$ [M+H] is 299.10263 and found 299.10295.

Diethyl 3-(4-cyanobenzyl)-1H-pyrrole-2,4-dicarboxylate (3hb):



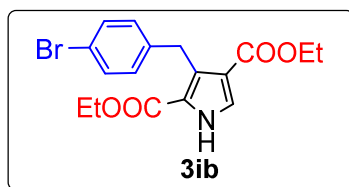
Yield: 92%; Crystalline solid; **M.p.** 101 – 103 °C; **¹H NMR** (500 MHz, CDCl₃) δ = 9.66 (s, 1H), 7.55 (d, *J* = 3.5 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 4.59 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.29 (dt, *J* = 14.2, 7.1 Hz, 6H); **¹³C NMR** (125 MHz, CDCl₃) δ = 164.13, 161.02, 147.05, 132.66, 131.87, 129.98, 129.26, 125.44, 121.40, 119.32, 112.47, 109.24, 60.85, 59.97, 30.63, 14.35; **IR** (KBr): 3301, 2967, 2258, 1715, 1684, 1283 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₁₈H₁₉N₂O₄ [M+H] is 327.13393 and found 327.13441.

Dimethyl 3-(4-bromobenzyl)-1H-pyrrole-2,4-dicarboxylate (3ia):



Yield: 87%; Semi solid, **¹H NMR** (500 MHz, CDCl₃) δ = 9.28 (s, 1H), 7.51 (d, *J* = 3.5 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 4.46 (s, 2H), 3.86 (s, 3H), 3.77 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ = 164.40, 161.27, 140.14, 139.74, 131.08, 130.33, 127.35, 120.97, 119.45, 116.39, 51.68, 51.10, 29.73; **IR** (neat): 3415, 2927, 1701, 1438, 1279 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₁₅H₁₅BrNO₄ [M+H] is 352.01790 and found 352.01835.

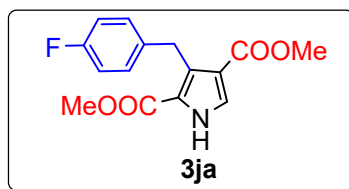
Diethyl 3-(4-bromobenzyl)-1H-pyrrole-2,4-dicarboxylate (3ib):



Yield: 88%; Brown oil, **¹H NMR** (500 MHz, CDCl₃) δ = 9.30 (s, 1H), 7.45 (d, *J* = 3.4 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 4.40 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ = 163.13, 160.07, 139.20, 130.07, 129.99, 129.27, 126.32, 120.20, 118.32,

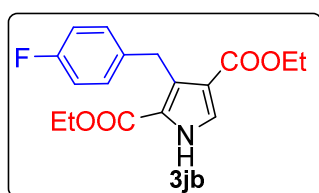
115.74, 59.79, 58.89, 28.78, 13.35; **IR** (neat): 3411, 2937, 1698, 1430, 1271, 1020 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{17}\text{H}_{19}\text{BrNO}_4$ $[\text{M}+\text{H}]$ is 380.04920 and found 380.04969.

Dimethyl 3-(4-fluorobenzyl)-1H-pyrrole-2,4-dicarboxylate (3ja):



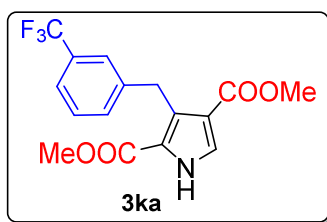
Yield: 90%; White solid, **M.p.** 84 – 86 °C; **^1H NMR** (400 MHz, CDCl_3) δ = 9.45 (s, 1H), 7.51 (d, J = 3.5 Hz, 1H), 7.22 (dd, J = 8.1, 2.5 Hz, 2H), 6.92 – 6.87 (m, 2H), 4.47 (s, 2H), 3.86 (s, 3H), 3.78 (s, 3H); **^{13}C NMR** (125 MHz, CDCl_3) δ = 164.51, 162.13, 161.40, 160.20, 136.81, 132.17, 129.94, 129.87, 127.47, 120.88, 116.31, 114.82, 114.65, 51.65, 51.08, 29.48; **IR** (KBr): 3310, 2925, 1697, 1508, 1275, 1150 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{15}\text{H}_{15}\text{FNO}_4$ $[\text{M}+\text{H}]$ is 292.09796 and found 292.09856.

Diethyl 3-(4-fluorobenzyl)-1H-pyrrole-2,4-dicarboxylate (3jb):



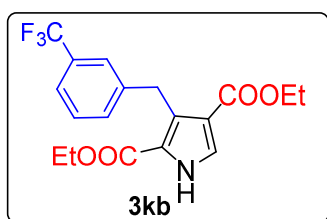
Yield: 88%; White solid, **M.p.** 83 – 84 °C; **^1H NMR** (400 MHz, CDCl_3) δ = 9.46 (s, 1H), 7.22 (dd, J = 8.6, 5.6 Hz, 2H), 6.91 – 6.87 (m, 1H), 4.49 (s, 3H), 4.33 (q, J = 7.1 Hz, 3H), 4.25 (q, J = 7.1 Hz, 3H), 1.30 (dt, J = 14.2, 7.1 Hz, 6H); **^{13}C NMR** (125 MHz, CDCl_3) δ = 164.21, 162.09, 161.14, 160.16, 136.85, 131.68, 129.87, 129.81, 127.34, 121.15, 116.73, 114.74, 114.57, 60.76, 59.88, 29.53, 14.37; **IR** (KBr): 3300, 2932, 1699, 1520, 1292, 1158 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{17}\text{H}_{19}\text{FNO}_4$ $[\text{M}+\text{H}]$ is 320.12926 and found 320.12988.

Dimethyl 3-(3-(trifluoromethyl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3ka):



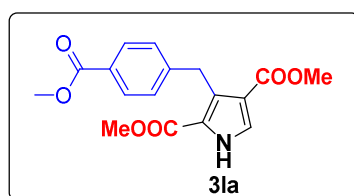
Yield: 87%; White solid, **M.p.** 134 – 136 °C; **¹H NMR** (400 MHz, CDCl₃) δ = 9.57 (s, 1H), 7.72 – 7.53 (m, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 4.72 (s, 2H), 3.75 (s, 3H), 3.68 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ = 164.43, 161.60, 139.82, 131.59, 128.97, 128.32, 127.69, 125.56, 125.44, 122.10, 117.55, 51.71, 51.09, 27.21; **IR** (KBr): 3290, 2925, 1718, 1687, 1315, 1119 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₁₆H₁₅F₃NO₄ [M+H] is 342.09477 and found 342.09539.

Diethyl 3-(3-(trifluoromethyl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3kb):



Yield: 89%; White solid **M.p.** 118 – 120 °C; **¹H NMR** (400 MHz, CDCl₃) δ = 9.53 (s, 1H), 7.66 (d, *J* = 3.5 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.76 (s, 2H), 4.20 (t, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ = 164.18, 161.39, 139.99, 131.54, 128.36, 128.23, 127.73, 126.22, 125.53, 125.48, 125.34, 122.34, 117.93, 60.81, 59.91, 27.33, 14.02, 13.97; **IR** (KBr): 3298, 2915, 1716, 1321, 1110 cm⁻¹; **HRMS** (ESI, Orbitrap) calcd for C₁₆H₁₉F₃NO₄ [M+H] is 370.12607 and found 370.12607.

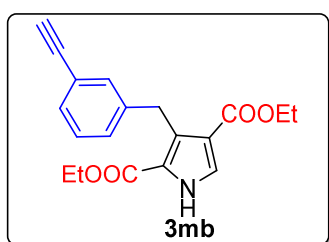
Dimethyl 3-(4-(methoxycarbonyl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3la)



Yield: 86%; White solid, **M.p.** 155 – 157 °C; **¹H NMR** (400 MHz, CDCl₃) δ = 9.30 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 3.4 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.57 (s, 2H), 3.87

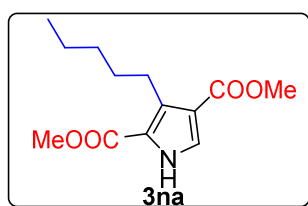
(s, 3H), 3.85 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 167.29, 164.43, 161.30, 146.71, 131.01, 129.46, 128.49, 127.59, 127.44, 121.16, 116.51, 51.94, 51.67, 51.09, 30.48; IR (KBr): 3303, 2951, 1710, 1608, 1437, 1138, 1007 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_6$ $[\text{M}+\text{H}]$ is 332.11286 and found 332.11292.

Diethyl 3-(3-ethynylbenzyl)-1H-pyrrole-2,4-dicarboxylate (3mb):



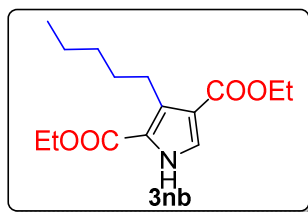
Yield: 86%; Colourless oil; ^1H NMR (500 MHz, CDCl_3) δ = 9.62 (s, 1H), 7.54 (d, J = 3.5 Hz, 1H), 7.35 (s, 1H), 7.26 (dd, J = 9.8, 5.5 Hz, 2H), 7.17 (t, J = 7.7 Hz, 1H), 4.51 (s, 2H), 4.32 (q, J = 7.1 Hz, 2H), 4.24 (q, J = 7.1 Hz, 2H), 3.00 (s, 1H), 1.30 (t, J = 7.3 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.31, 161.37, 144.10, 141.45, 132.12, 130.80, 129.44, 129.26, 127.97, 127.64, 121.57, 121.38, 116.78, 84.17, 60.82, 59.92, 30.15, 14.34; IR (neat): 3283, 2987, 1698, 1667, 1419, 1285 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_4$ $[\text{M}+\text{H}]$ is 326.13868 and found 326.13776.

Dimethyl 3-pentyl-1H-pyrrole-2,4-dicarboxylate (3na):



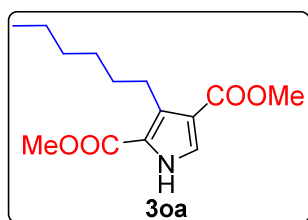
Yield: 72%; Colourless oil; ^1H NMR (500 MHz, CDCl_3) δ = 9.27 (s, 1H), 7.47 (d, J = 3.5 Hz, 1H), 3.88 (s, 3H), 3.81 (s, 3H), 3.08 (t, J = 7.3 Hz, 2H), 1.59 – 1.51 (m, 2H), 1.39 – 1.30 (m, 4H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.80, 161.92, 135.39, 127.43, 120.27, 115.99, 51.49, 50.98, 31.93, 30.84, 24.99, 22.48, 14.08; IR (neat): 3300; 2938, 1694, 1557, 1438, 1280, 1105 cm^{-1} ; HRMS (ESI, Orbitrap) calcd for $\text{C}_{13}\text{H}_{20}\text{NO}_4$ $[\text{M}+\text{H}]$ is 254.13868 and found 254.13875.

Diethyl 3-pentyl-1H-pyrrole-2,4-dicarboxylate (3nb):



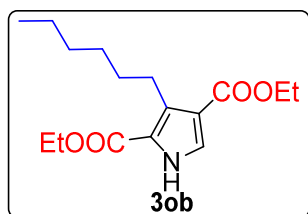
Yield: 70%; Colourless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.65 (s, 1H), 7.43 (d, J = 3.9 Hz, 1H), 4.29 q, J = 7.1 Hz, 2H), 4.23 q, J = 7.1 Hz, 2H), 3.04 – 2.98 (m, 2H); 1.56 – 1.48 (m, 2H), 1.32 – 1.218 (m, 9H), 0.82 (t, J = 7.1 Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.56, 161.74, 134.99, 127.39, 120.50, 116.35, 60.55, 59.73, 32.12, 30.98, 25.23, 22.59, 14.39, 14.37, 14.13; **IR** (neat): 3308; 2945, 1699, 1441, 1267, 1098 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{15}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]$ is 282.16998 and found 282.16107.

Dihyl 3-hexyl-1H-pyrrole-2,4-dicarboxylate (3oa):



Yield: 71%; Colourless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.30 (s, 1H), 7.48 (d, J = 3.5 Hz, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.10 – 3.06 (m, 2H), 1.60 – 1.51 (m, 2H), 1.40 - 1.35 (m, 2H), 1.33 – 1.25 (m, 4H), 0.88 (t, J = 6.9 Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.80, 161.92, 135.38, 127.44, 120.26, 115.98, 51.47, 50.96, 31.67, 31.13, 29.43, 25.07, 22.67, 14.12; **IR** (neat): 3295, 2931, 1701, 1576, 1420, 1296, 1101 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{14}\text{H}_{22}\text{NO}_4$ $[\text{M}+\text{H}]$ is 258.15433 and found 258.15493.

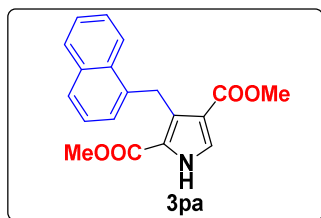
Diethyl 3-hexyl-1H-pyrrole-2,4-dicarboxylate (3ob):



Yield: 69%; Colourless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 9.26 (s, 1H), 7.48 (d, J = 3.5 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 3.08 (t, J = 6.8 Hz, 2H), 1.59 – 1.49 (m, 2H), 1.41 – 1.33 (m, 8H), 1.33 – 1.27 (m, 3H), 0.88 (t, J = 7.0 Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.61, 161.86, 135.00, 127.59, 120.48, 116.20, 60.51, 59.70, 31.78, 31.28, 29.60, 25.31, 22.70, 14.37, 14.08; **IR** (neat): 3299, 2923, 1703, 1556, 1438, 1301,

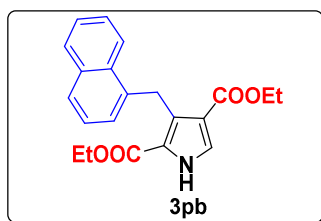
1099 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{16}\text{H}_{26}\text{NO}_4$ $[\text{M}+\text{H}]$ is 296.18563 and found 296.18591.

Dimethyl 3-(naphthalen-1-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3pa):



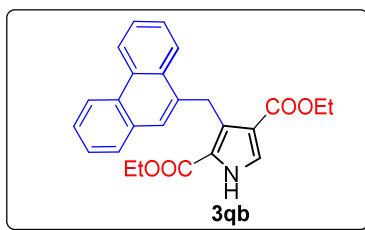
Yield: 90%; crystalline solid, **M.p.** 165 – 166 °C; **^1H NMR** (400 MHz, CDCl_3) δ = 9.73 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 8.9 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.52 – 7.46 (m, 1H), 7.26 – 7.22 (m, 1H), 6.78 (dd, J = 7.1, 0.7 Hz, 1H), 4.96 (s, 2H), 3.66 (s, 3H), 3.60 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3) δ = 164.49, 161.69, 137.11, 133.59, 132.11, 130.69, 128.61, 127.59, 126.14, 125.73, 125.43, 125.34, 123.85, 123.50, 121.99, 117.38, 51.68, 51.05, 27.26; **IR** (KBr): 3282, 2923, 1724, 1673, 1441, 1279, 1018 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{19}\text{H}_{18}\text{NO}_4$ $[\text{M}+\text{H}]$ is 324.12303 and found 324.12251.

Diethyl 3-(naphthalen-1-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3pb):



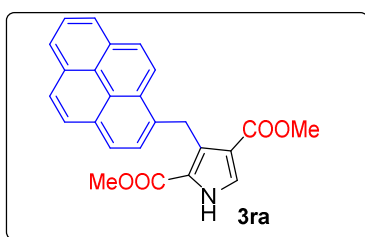
Yield: 89%; White Solid, **M.p.** 115 – 118 °C; **^1H NMR** (400 MHz, CDCl_3) δ = 9.83 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.64 (dd, J = 8.8, 2.3 Hz, 2H), 7.55 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.25 (dd, J = 9.3, 6.0 Hz, 1H), 6.78 (dd, J = 7.2, 1.0 Hz, 1H), 4.98 (s, 2H), 4.13 (q, J = 7.1 Hz, 2H), 4.07 (q, J = 7.1 Hz, 2H), 0.99 – 0.95 (m, 6H); **^{13}C NMR** (100 MHz, CDCl_3) δ = 164.33, 161.47, 137.28, 133.53, 132.14, 130.30, 128.57, 127.62, 126.00, 125.66, 125.43, 125.28, 123.79, 123.42, 122.21, 117.81, 60.63, 59.79, 27.54, 14.01; **IR** (KBr): 3290, 2929, 1721, 1675, 1436, 1288, 1001 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_4$ $[\text{M}+\text{H}]$ is 352.15433 and found 352.15374.

Diethyl 3-(phenanthren-9-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3qb):



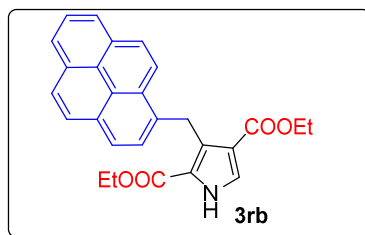
Yield: 91%; Brown solid, **M.p.** 120 – 122 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.55 (s, 1H), 8.77 – 8.71 (m, 1H), 8.63 (d, J = 8.2 Hz, 1H), 8.35 – 8.28 (m, 1H), 7.71 - 7.67 (m, 3H), 7.61 (d, J = 7.8 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.48 (dd, J = 10.9, 3.9 Hz, 1H), 6.96 (s, 1H), 4.84 (s, 2H), 4.13 (q, J = 7.1 Hz, 2H), 4.06 (q, J = 7.1 Hz, 2H), 0.99 (t, J = 7.6 Hz, 3H), 0.96 (t, J = 7.7 Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ = 164.29, 161.43, 135.56, 131.97, 131.77, 130.34, 129.93, 129.44, 128.22, 127.63, 126.55, 126.27, 126.05, 125.64, 124.05, 123.84, 123.01, 122.33, 117.85, 60.65, 59.80, 28.02, 14.00; **IR** (KBr): 3258, 2924, 1707, 1658, 1383, 1284 1161 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{25}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]$ is 402.16998 and found 402.16934.

Dimethyl 3-(pyren-1-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3ra):



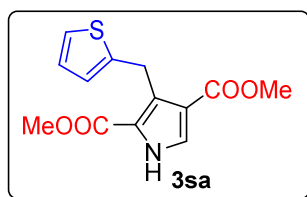
Yield: 85%; White solid, **M.p.** 182 – 184 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.50 (s, 1H), 8.55 (d, J = 9.3 Hz, 1H), 8.18 (dd, J = 8.4, 5.5 Hz, 2H), 8.15 (d, J = 7.6 Hz, 1H), 8.02 – 7.95 (m, 4H), 7.66 (s, 1H), 7.43 (d, J = 7.9 Hz, 1H), 5.25 (s, 2H), 3.67 (s, 3H), 3.58 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.52, 161.61, 135.14, 131.52, 131.01, 129.44, 128.61, 127.59, 127.12, 126.41, 125.69, 125.08, 124.78, 124.72, 124.65, 123.40, 122.06, 117.49, 51.70, 51.09, 27.54; **IR** (KBr): 3320, 2924, 1718, 1675, 1435, 1281, 1016 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{25}\text{H}_{20}\text{NO}_4$ $[\text{M}+\text{H}]$ is 398.13868 and found 398.13896.

Diethyl 3-(pyren-1-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3rb):



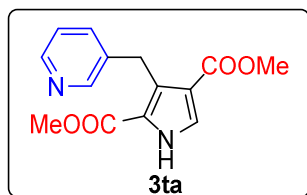
Yield: 84%; White solid, **M.p.** 207 – 209 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.52 (s, 1H), 8.52 (d, J = 9.2 Hz, 1H), 8.23 – 8.12 (m, 3H), 8.04 – 7.93 (m, 4H), 7.68 (d, J = 3.5 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 5.26 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.05 (q, J = 7.1 Hz, 2H), 0.96 (td, J = 7.1, 1.6 Hz, 7H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.30, 161.38, 135.30, 131.53, 131.02, 130.49, 129.38, 128.58, 127.62, 127.08, 126.33, 125.66, 125.01, 124.92, 124.75, 124.69, 124.66, 123.33, 122.28, 117.89, 77.32, 77.07, 76.81, 60.67, 59.83, 27.90, 14.07; **IR** (KBr) 3310, 2931, 1714, 1663, 1287, 1007 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{27}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]$ is 426.16998 and found 426.17039.

Dimethyl 3-(thiophen-2-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3sa):



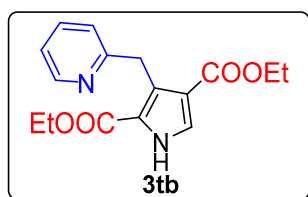
Yield: 88%; Brown liquid; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.29 (s, 1H), 7.49 (d, J = 3.5 Hz, 1H), 7.16 (dd, J = 4.9, 3.0 Hz, 1H), 7.06 – 7.02 (m, 2H), 4.49 (s, 2H), 3.89 (s, 3H), 3.80 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.52, 161.40, 141.28, 132.25, 128.65, 127.25, 124.56, 120.94, 116.18, 51.63, 51.07, 25.35; **IR** (neat): 3345, 3014, 1701, 1691, 1410, 1274, 950 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_4\text{S}$ $[\text{M}+\text{H}]$ is 280.06381 and found 280.06353.

Dimethyl 3-(pyridin-3-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3ta)



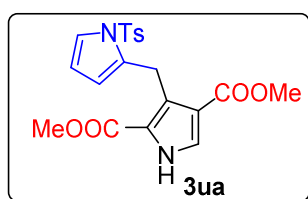
Yield: 88%; White solid, **M.p.** 105 – 107 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 10.11 (bs, 1H), 8.50 (bs, 1H), 7.51 (bs, 2H), 7.05 (d, J = 13.7 Hz, 2H), 4.75 (s, 2H), 3.73 (s, 3H), 3.69 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 164.52, 161.46, 160.97, 148.71, 136.23, 129.40, 127.57, 122.24, 121.86, 120.74, 116.82, 77.30, 77.05, 76.79, 51.52, 50.99, 33.46. **IR** (KBr) 3075, 2967, 1718, 1414, 1301, 1176 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_4$ [M+H] is 275.10263 and found 275.10301.

Diethyl 3-(pyridin-2-ylmethyl)-1H-pyrrole-2,4-dicarboxylate (3tb):



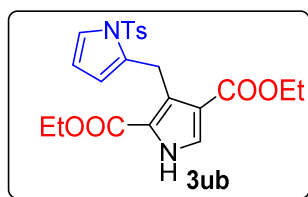
Yield: 89%; White solid, **M.p.** 134 – 136 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.78 (s, 1H), 8.50 (d, J = 4.3 Hz, 1H), 7.56 (s, 1H), 7.51 (dd, J = 10.8, 4.6 Hz, 1H), 7.07 – 7.03 (m, 1H), 6.96 (d, J = 7.8 Hz, 1H), 4.76 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ = 164.21, 161.09, 161.13, 148.69, 136.12, 128.94, 127.37, 121.97, 120.61, 117.06, 60.60, 59.78, 33.55, 14.21, 14.14; **IR** (KBr): 3052, 2985, 2701, 1713, 1566, 1415, 1299 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_4$ [M+H] is 303.13393 and found 303.13415.

Dimethyl 3-((1-tosyl-1H-pyrrol-2-yl)methyl)-1H-pyrrole-2,4-dicarboxylate (3ua):



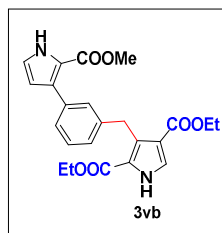
Yield: 81%; Colourless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.44 (s, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 3.2 Hz, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.23 (s, 1H), 6.05 (t, J = 3.3 Hz, 1H), 5.37 – 5.32 (m, 1H), 4.55 (s, 2H), 3.67 (s, 3H), 3.60 (s, 3H), 2.43 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.18, 161.42, 156.36, 144.55, 136.73, 134.92, 129.92, 128.15, 127.26, 127.14, 121.82, 117.05, 111.57, 111.23, 51.63, 50.96, 23.90, 21.64; **IR** (KBr): 3301, 2936, 1705, 1354, 1289, 1171 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_6\text{S}$ [M+H] is 417.11148 and found 417.11152.

Diethyl 3-((1-tosyl-1H-pyrrol-2-yl)methyl)-1H-pyrrole-2,4-dicarboxylate (3ub):



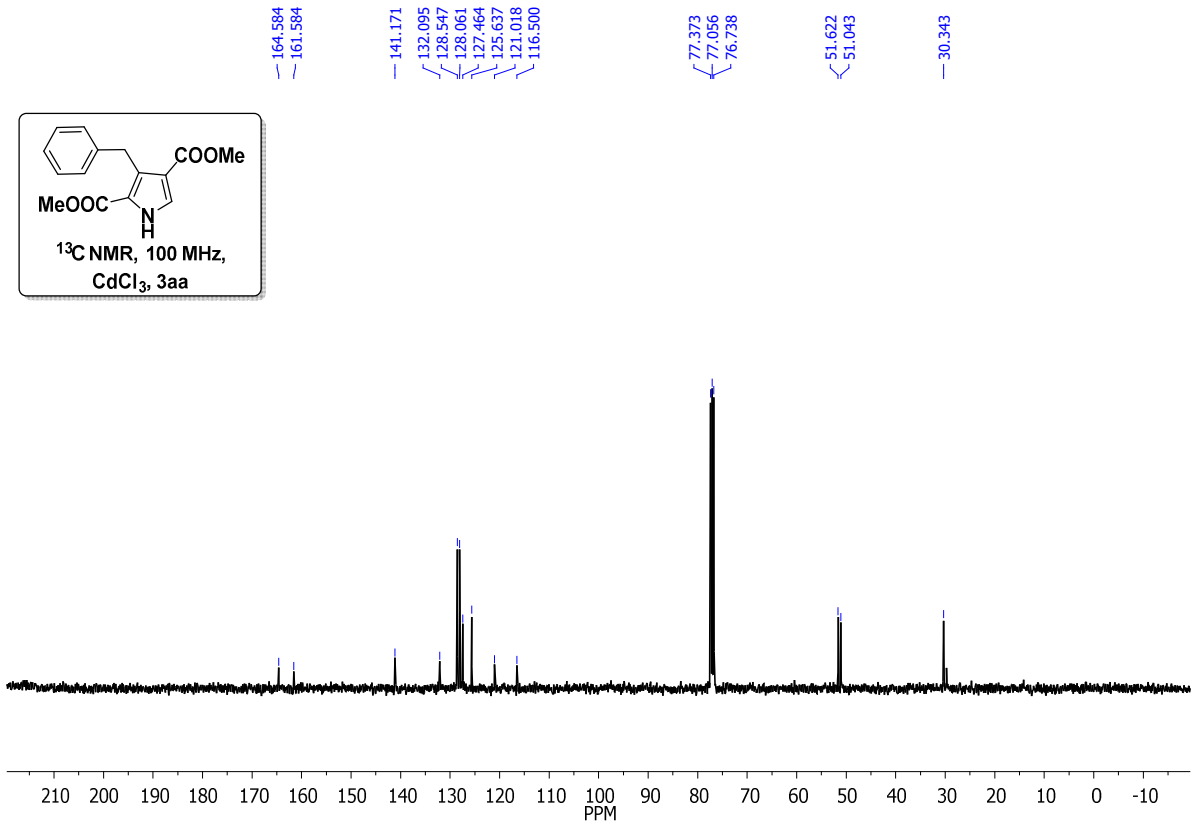
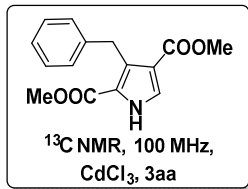
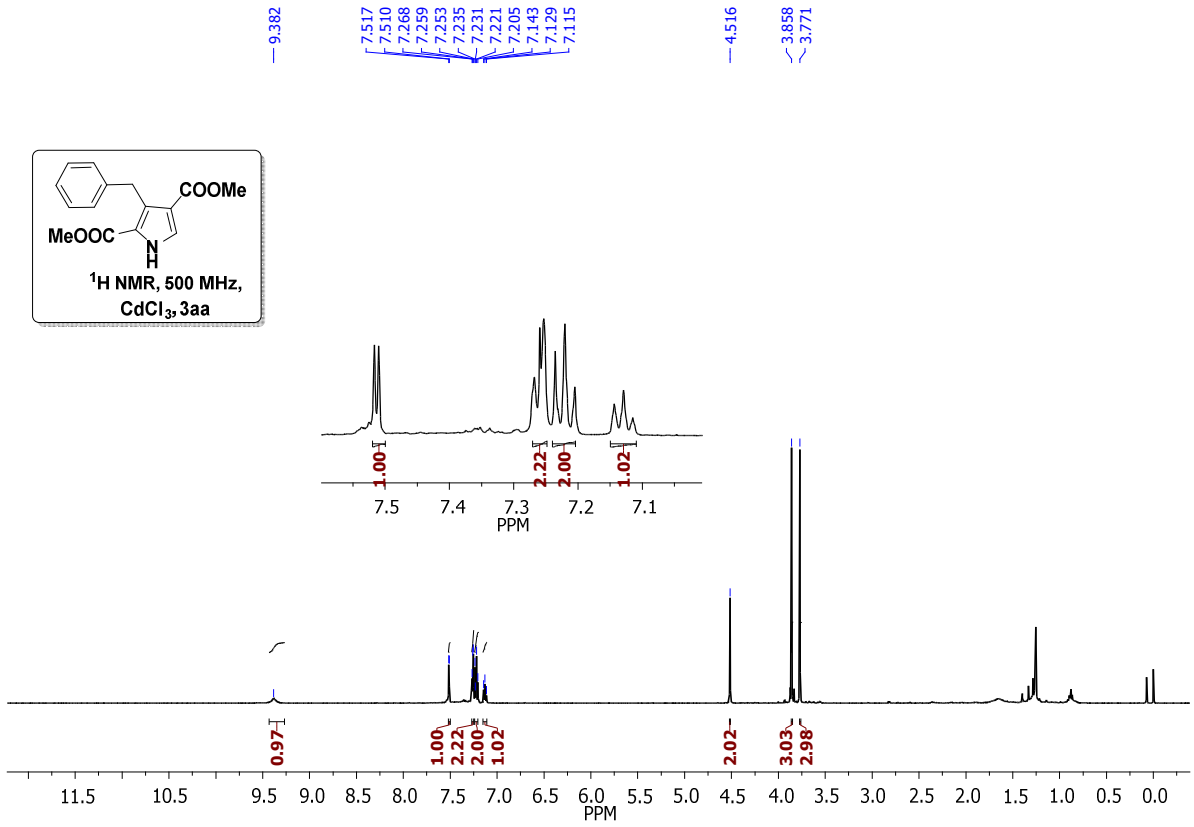
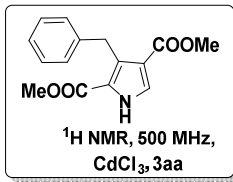
Yield: 82%; Colourless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 9.50 (s, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 3.4 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.26 – 7.24 (m, 1H), 6.05 (t, J = 3.3 Hz, 1H), 5.36 (dd, J = 3.2, 1.6 Hz, 1H), 4.57 (s, 2H), 4.16 (q, J = 7.1 Hz, 2H), 4.09 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.11 (q, J = 7.1 Hz, 6H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 163.96, 161.11, 144.57, 136.69, 135.07, 129.92, 127.82, 127.14, 121.69, 117.49, 111.68, 111.21, 60.66, 59.77, 23.94, 21.61, 14.14; **IR** (KBr): 3298, 2928, 1700, 1367, 1277, 1175 1032 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_6\text{S}$ [M+H] is 445.14278 and found 445.14301.

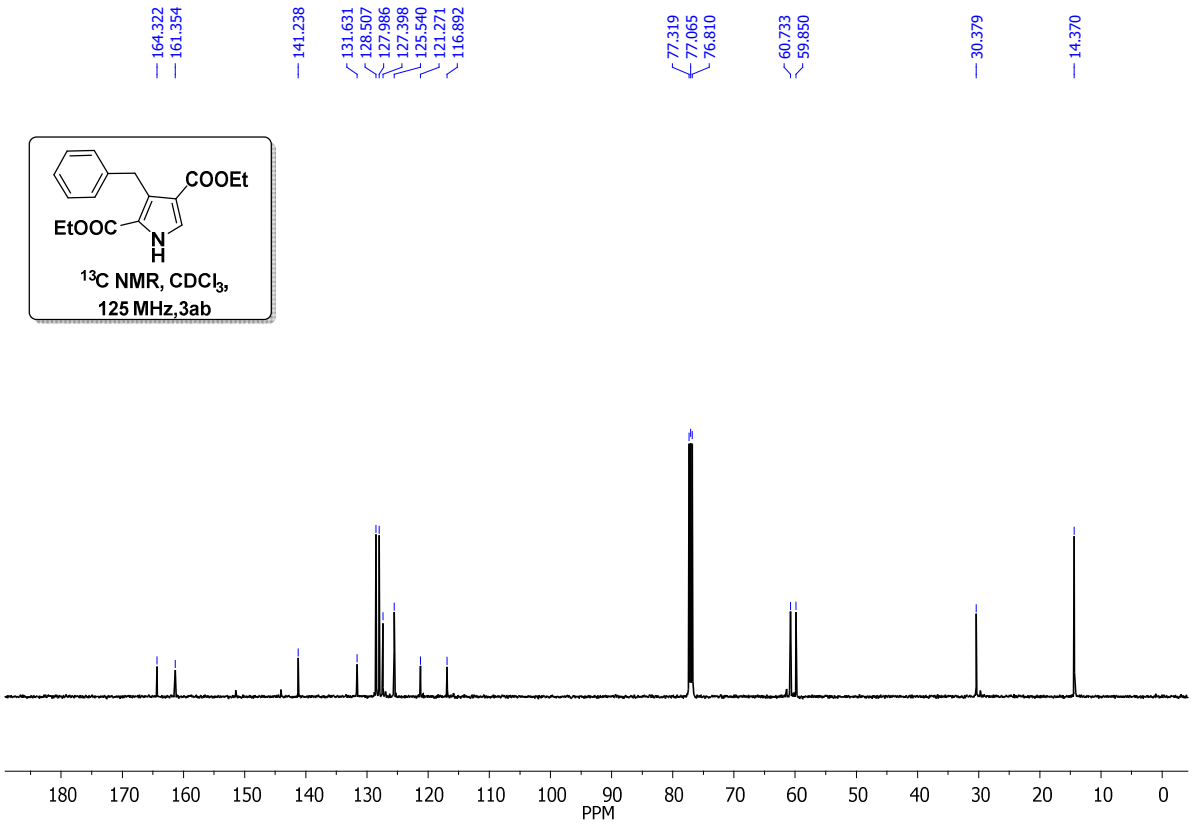
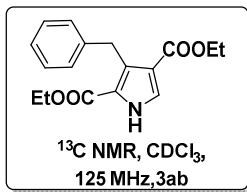
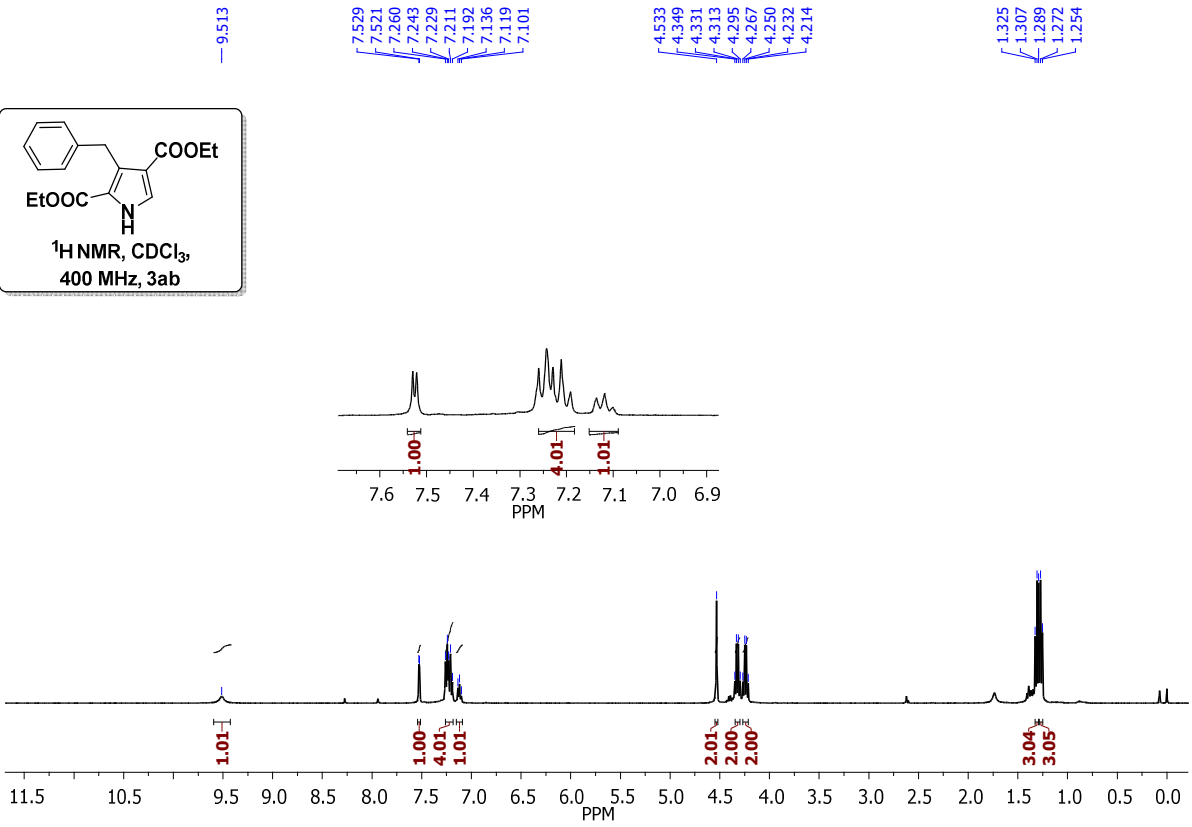
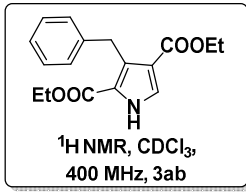
diethyl 3-(3-(2-(methoxycarbonyl)-1H-pyrrol-3-yl)benzyl)-1H-pyrrole-2,4-dicarboxylate (3vb):

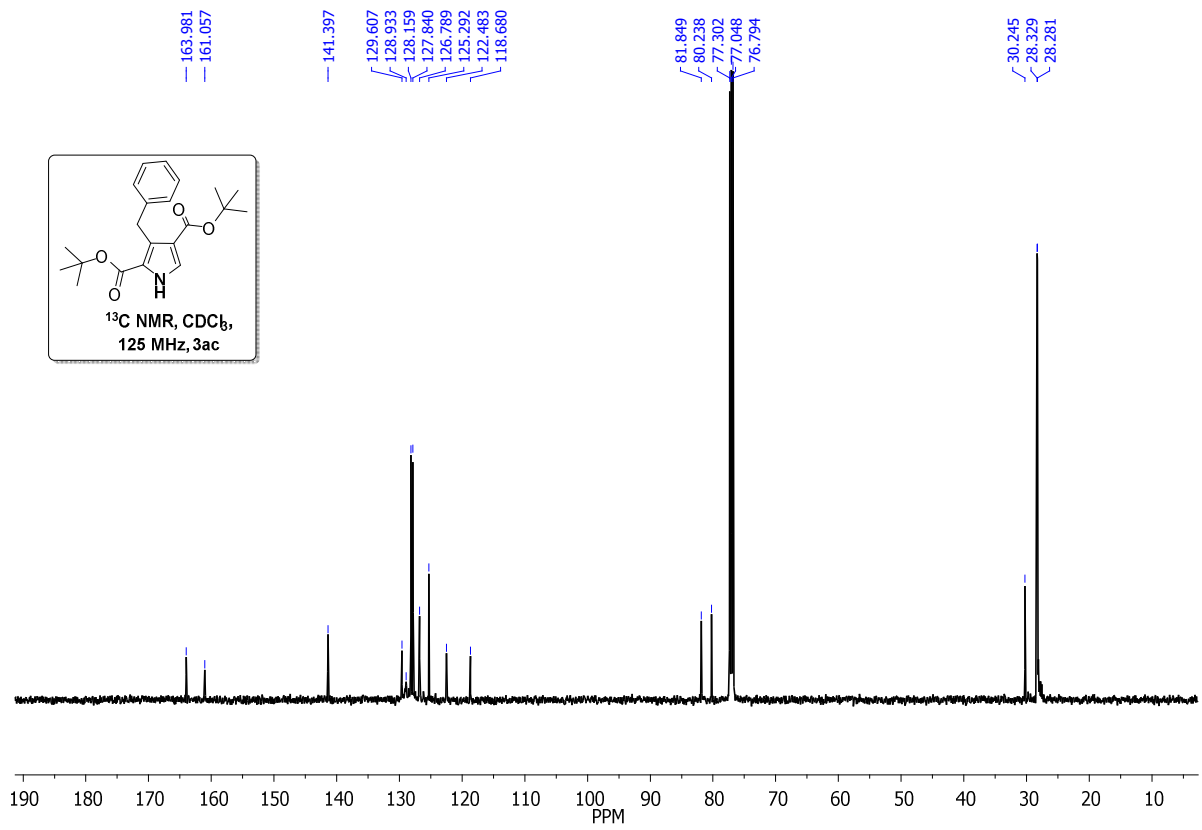
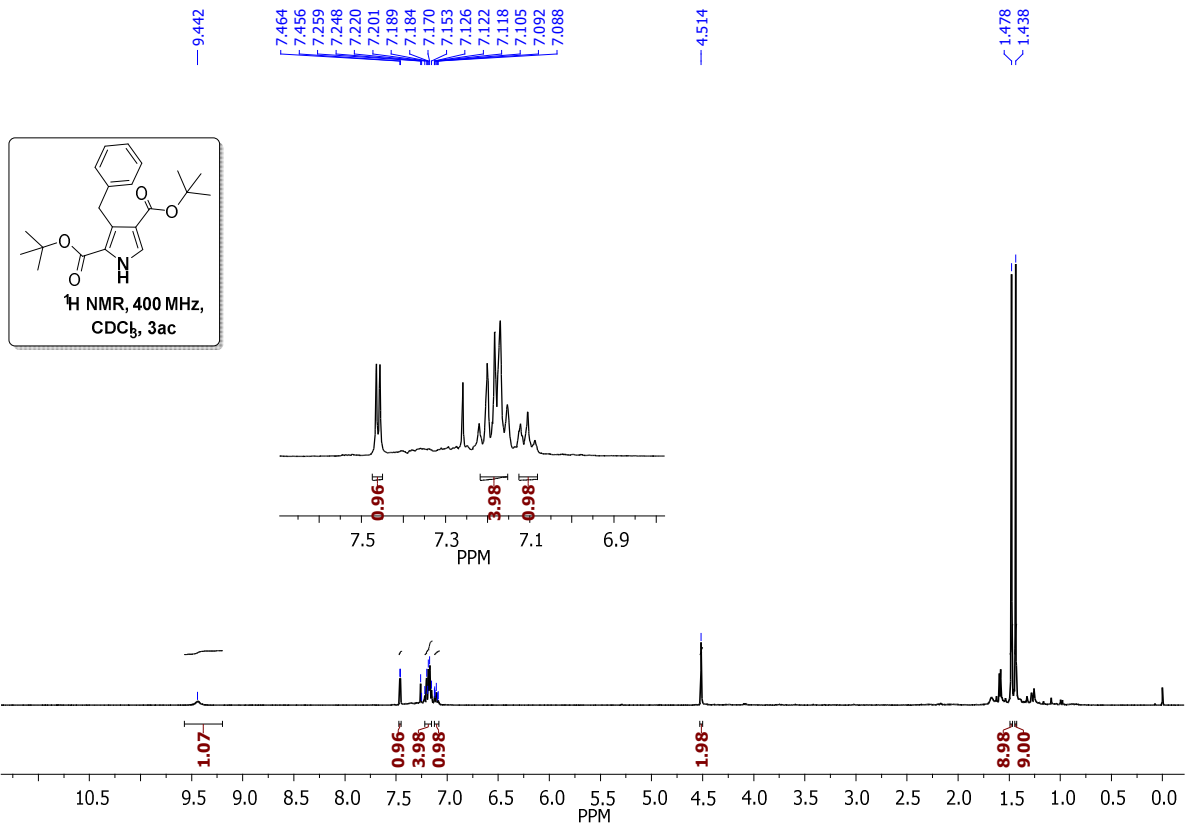


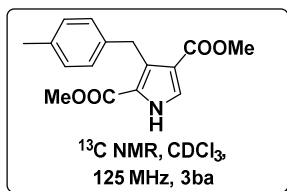
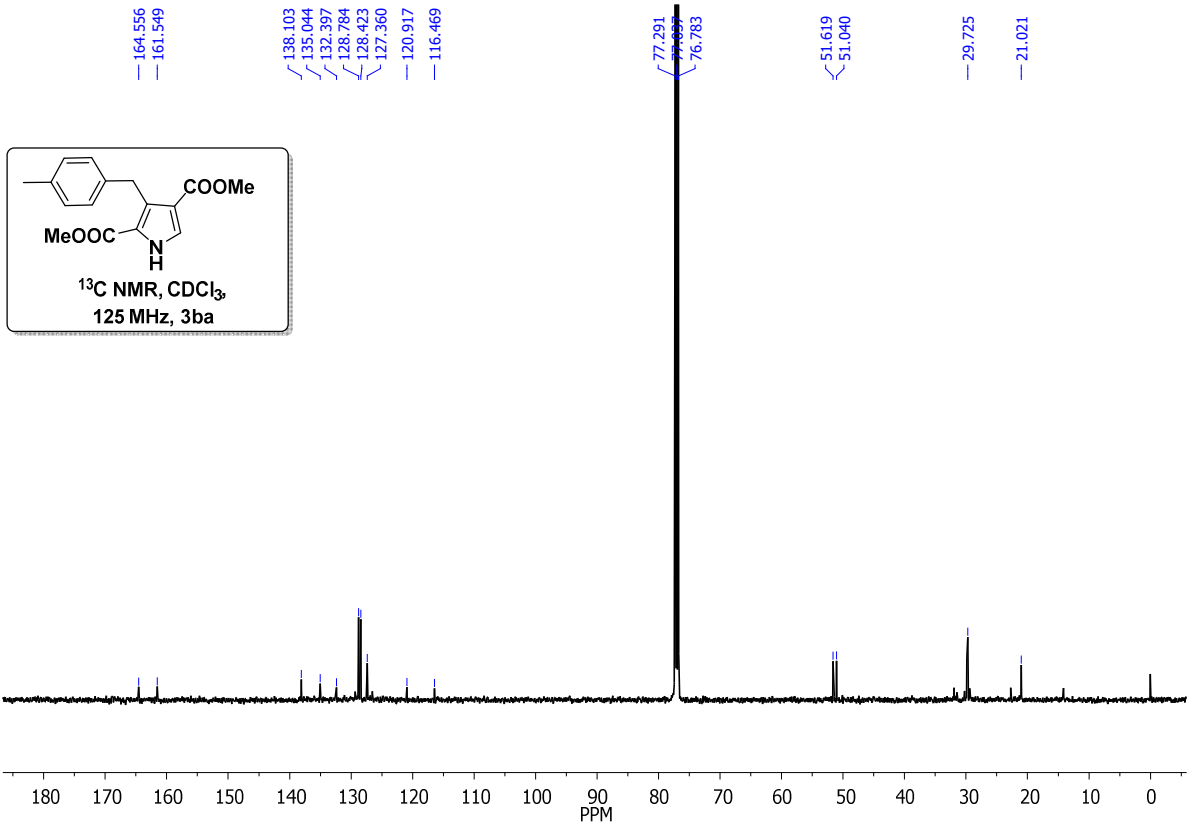
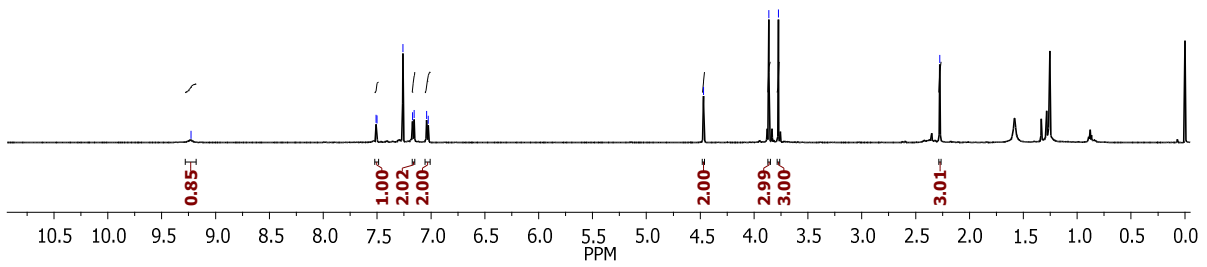
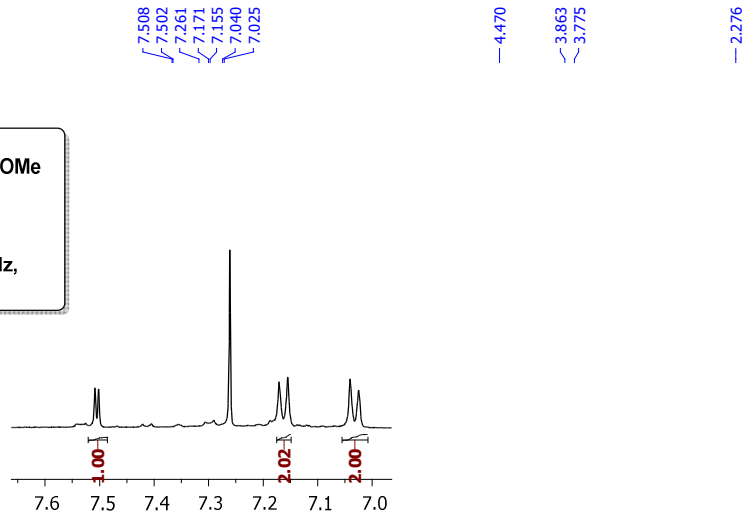
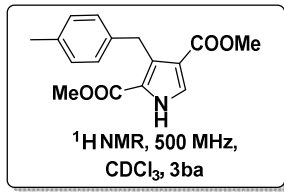
Yield: 82%; colourless liquid, $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 9.50 (s, 1H), 9.28 (s, 1H), 7.52 (d, J = 3.4 Hz, 1H), 7.41 (s, 1H), 7.37 – 7.31 (m, 1H), 7.25 – 7.19 (m, 2H), 6.91 (t, J = 2.8 Hz, 1H), 6.28 (t, J = 2.7 Hz, 1H), 4.57 (s, 2H), 4.32 (q, J = 7.1 Hz, 2H), 4.24 (q, J = 7.1 Hz, 2H), 3.69 (s, 3H), 1.30 (t, J = 6.9 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ = 164.33, 161.85, 161.39, 140.64, 134.73, 132.46, 131.70, 129.67, 127.35, 126.84, 121.86, 121.30, 117.81, 116.98, 112.67, 60.73, 59.83, 51.21, 30.33, 14.36; **IR** (KBr): 3319, 2928, 1692, 1441, 1276, 1143, 1029 cm^{-1} ; **HRMS** (ESI, Orbitrap) calcd for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_6$ [M+H] is 425.17071 and found 425.17099.

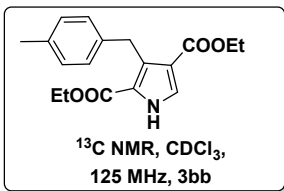
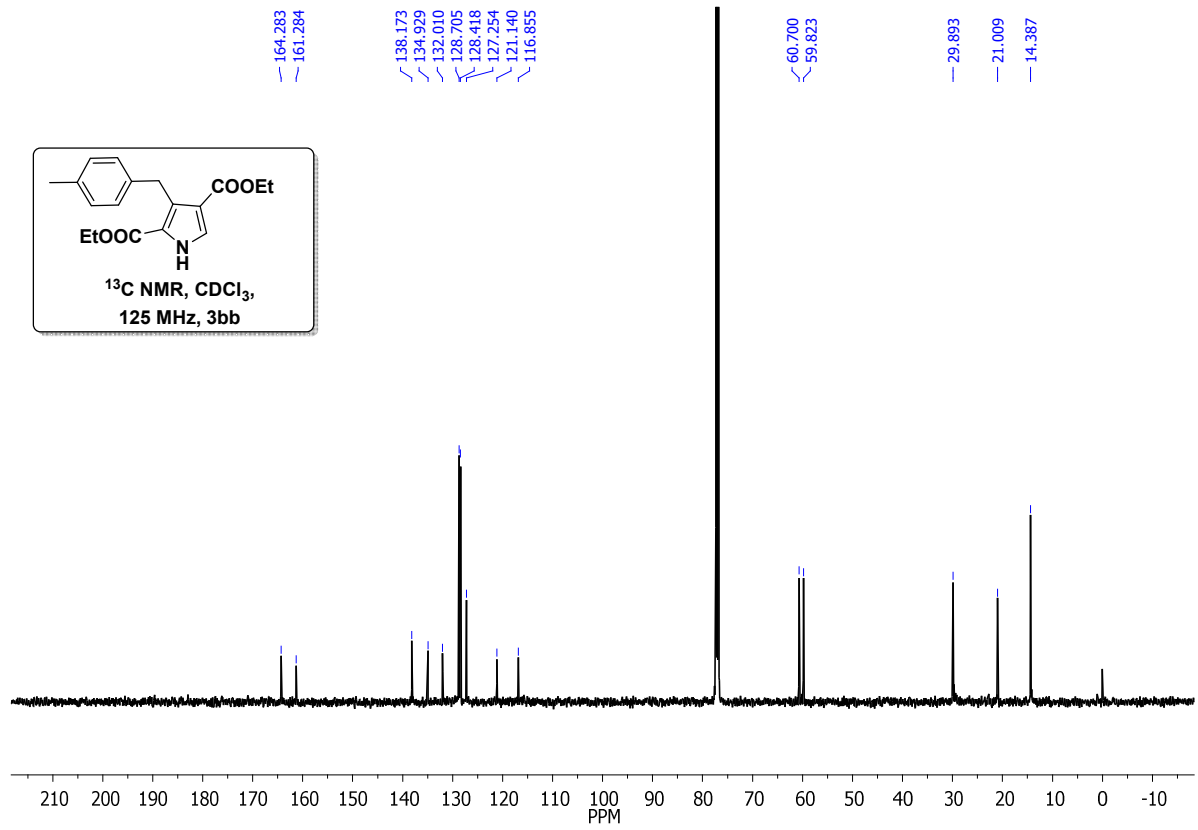
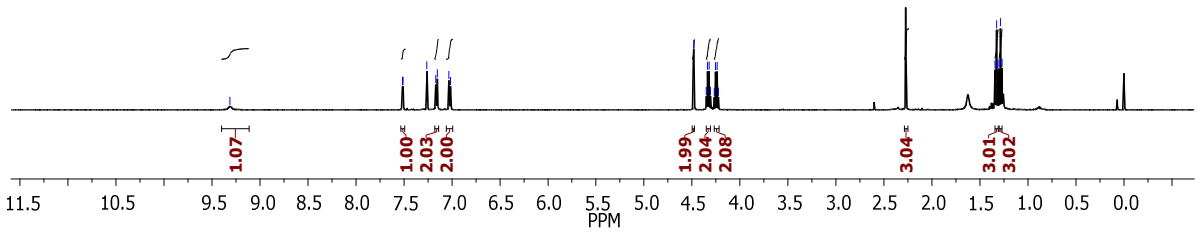
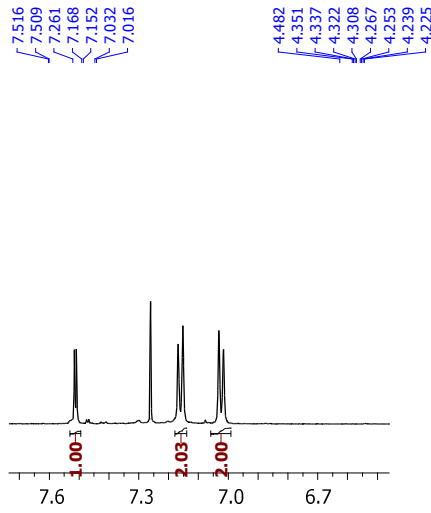
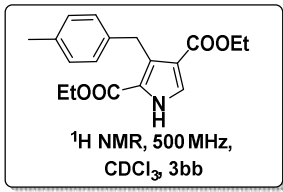
8. Soft copy of ^1H and ^{13}C NMR of compounds (3aa-3vb):

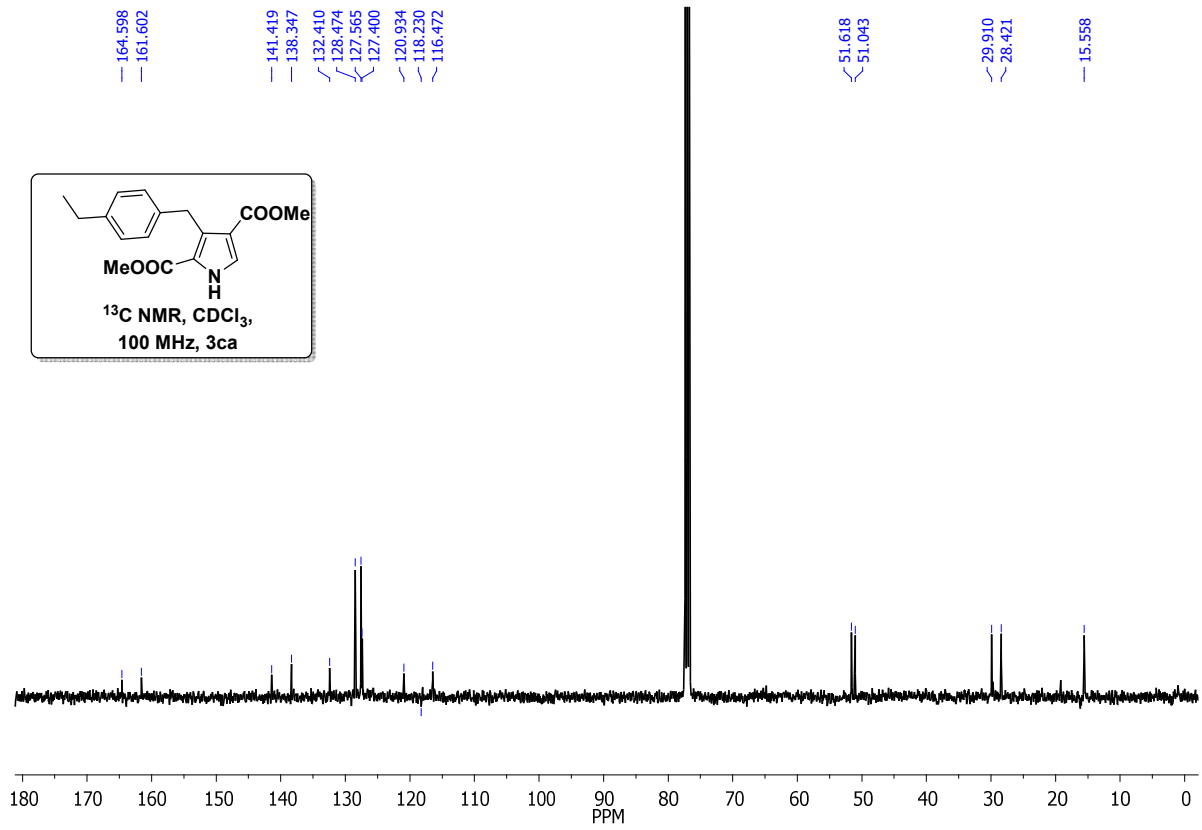
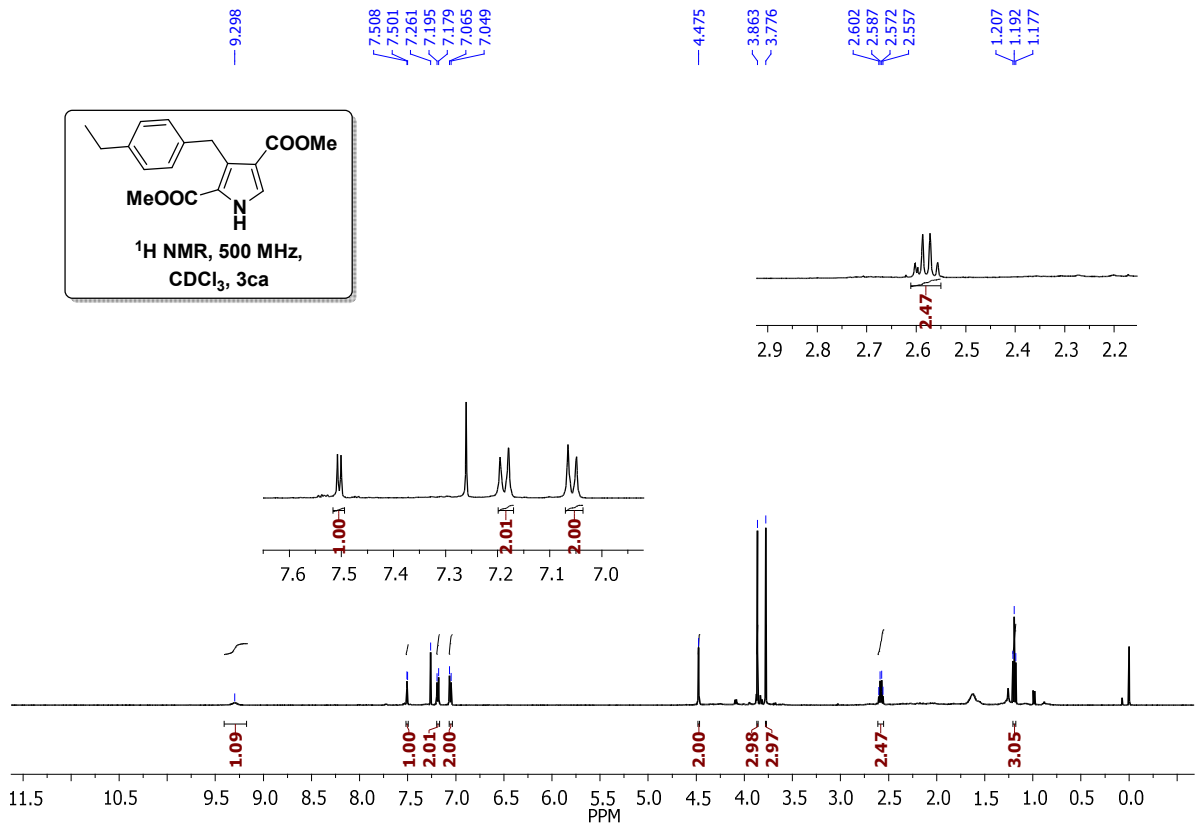


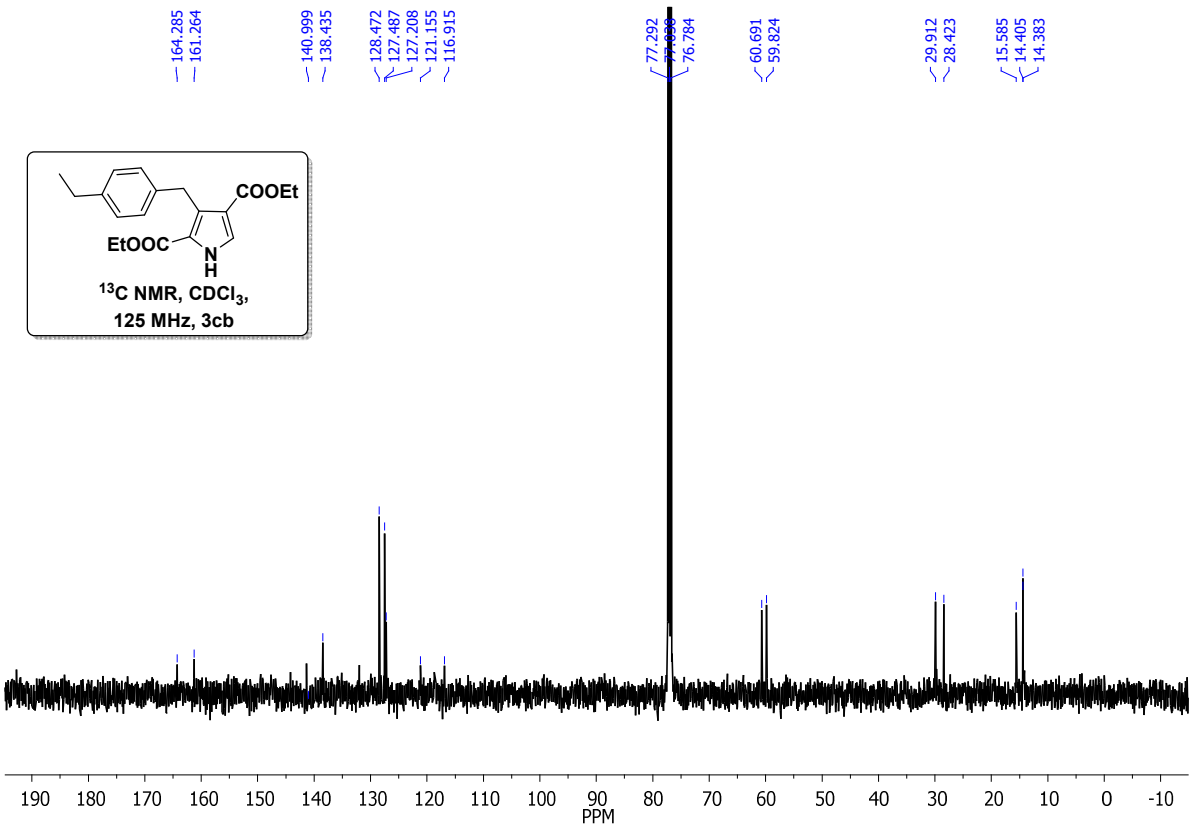
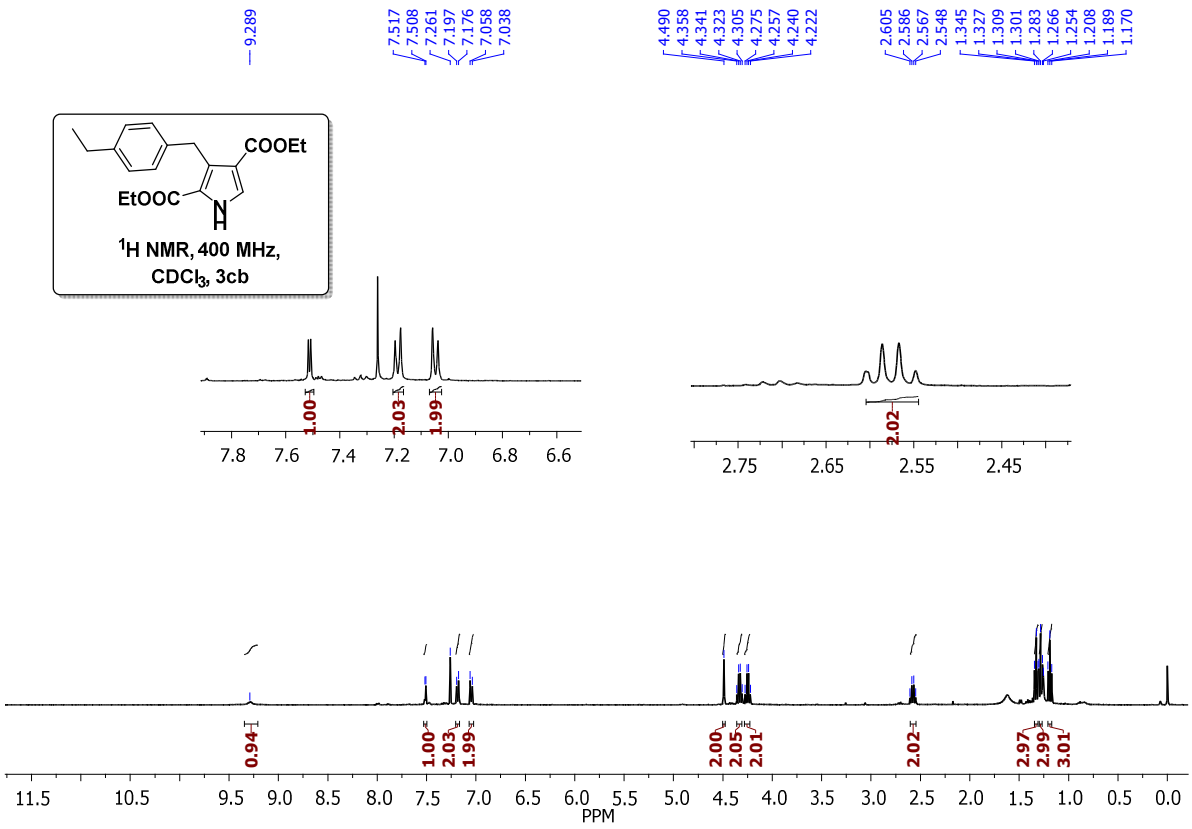


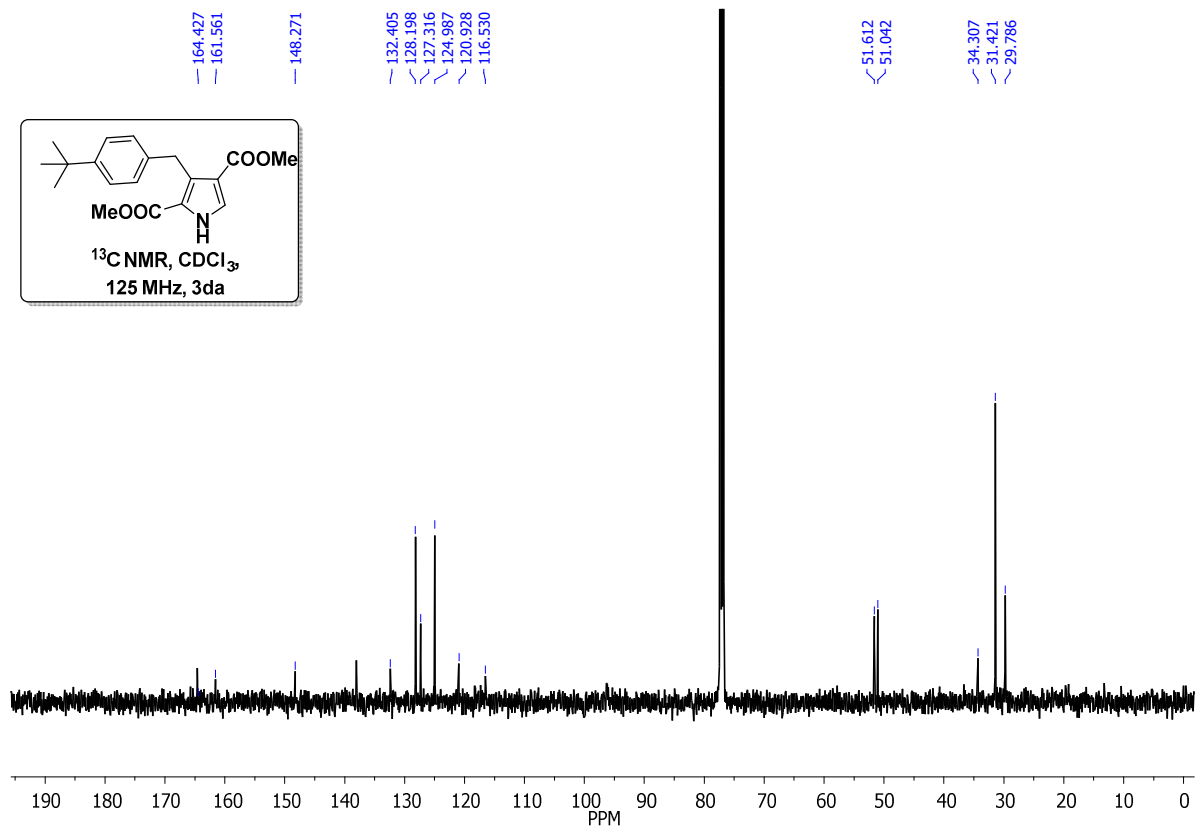
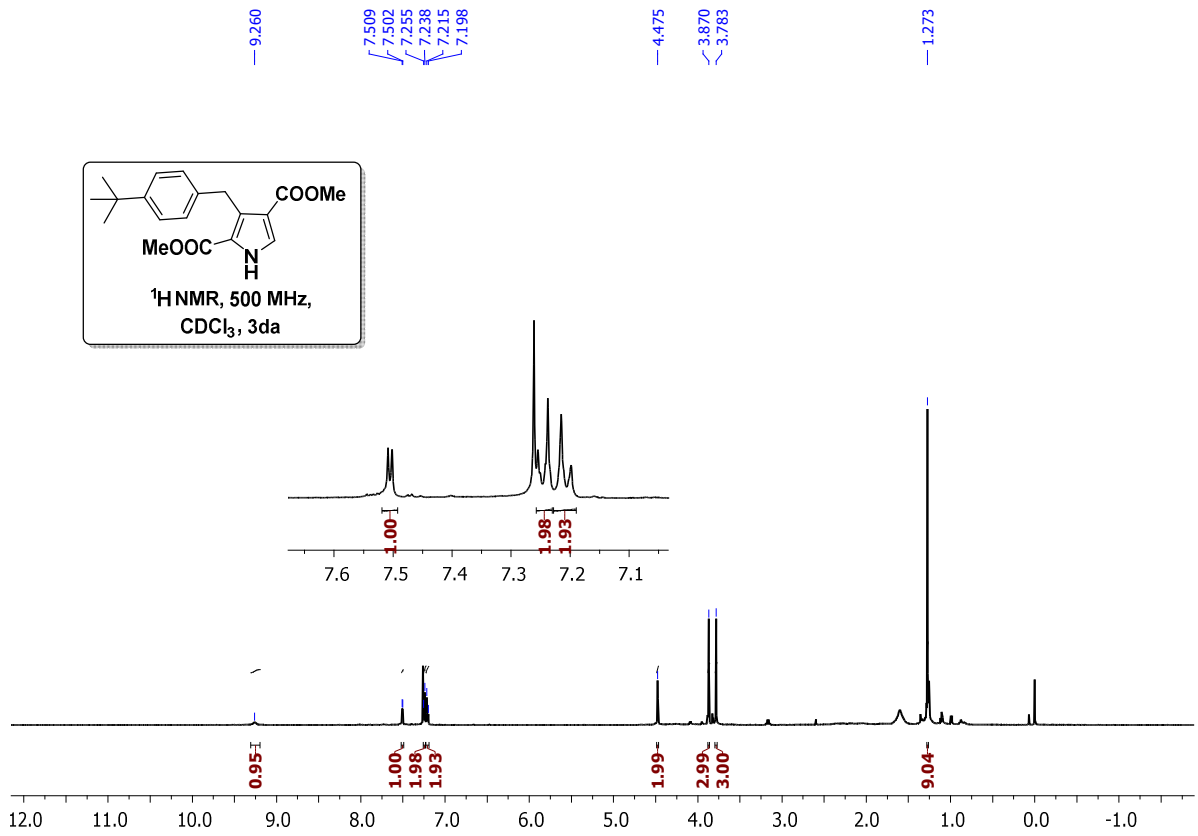


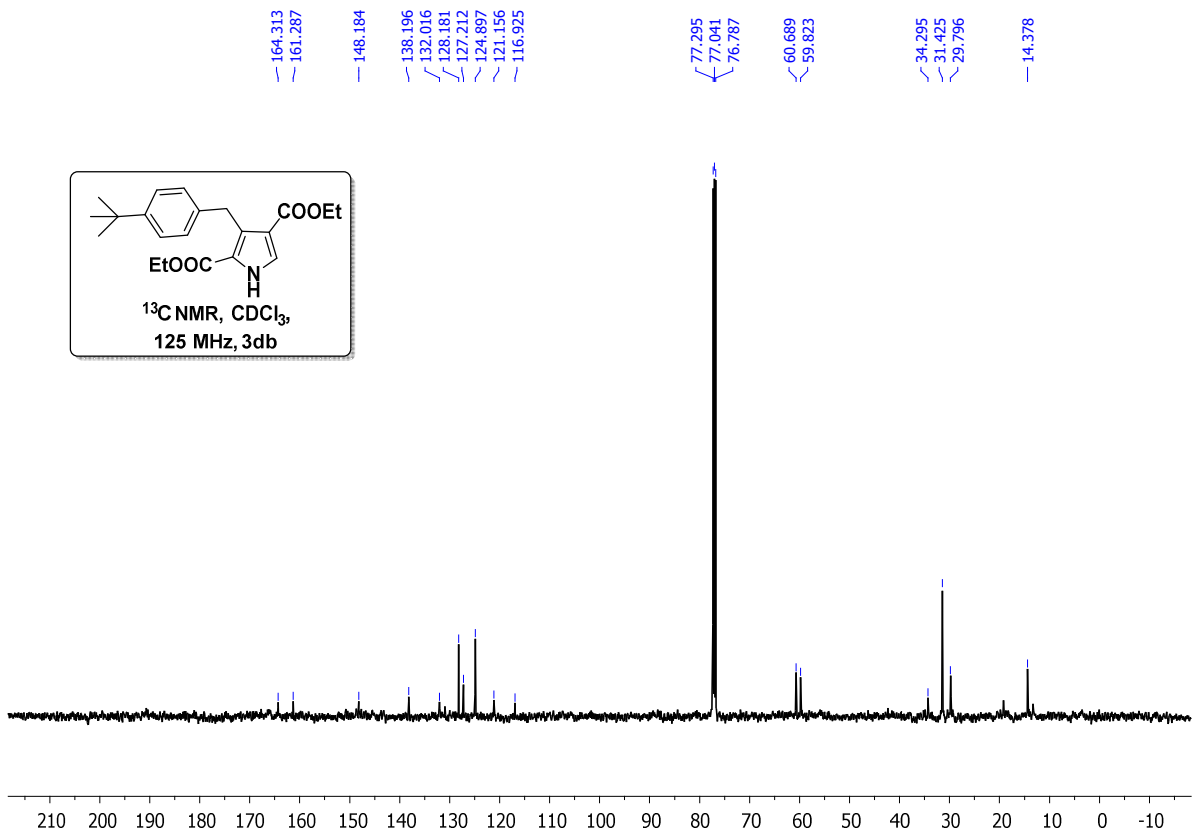
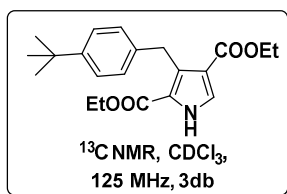
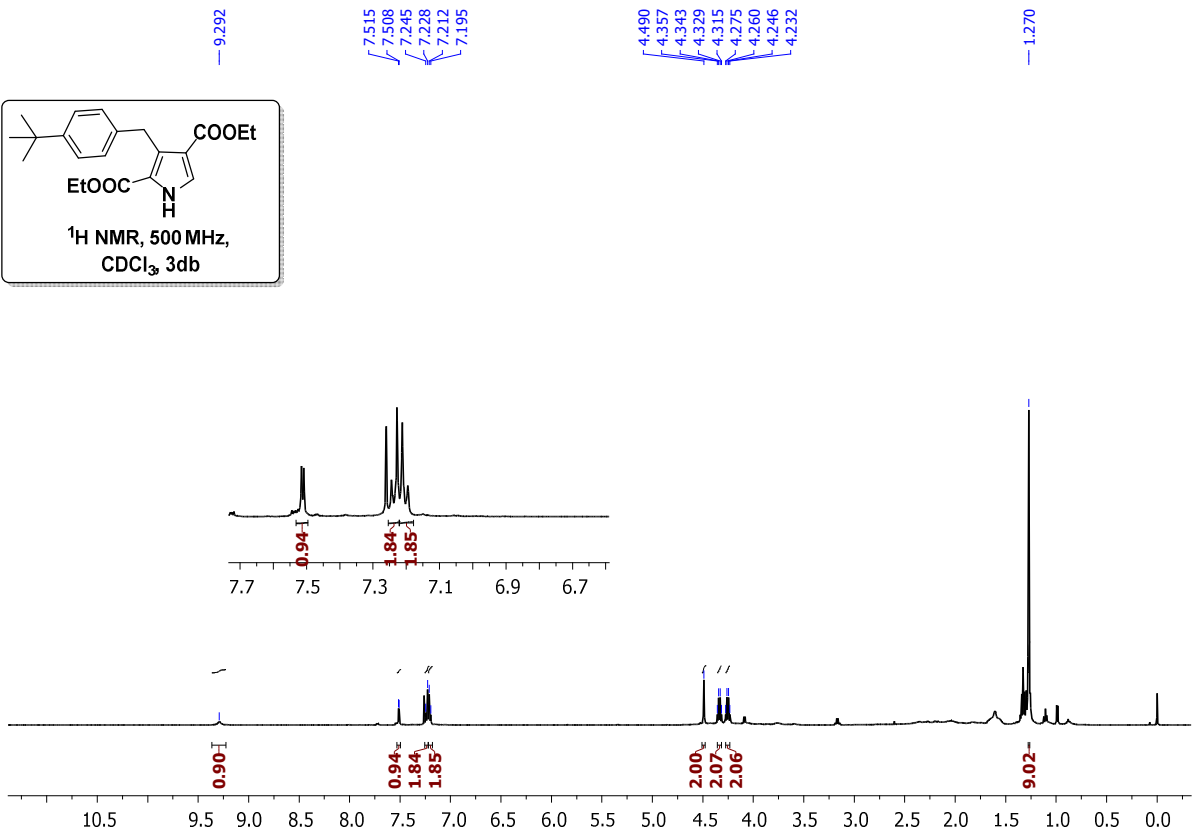
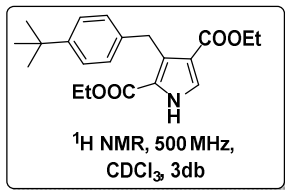


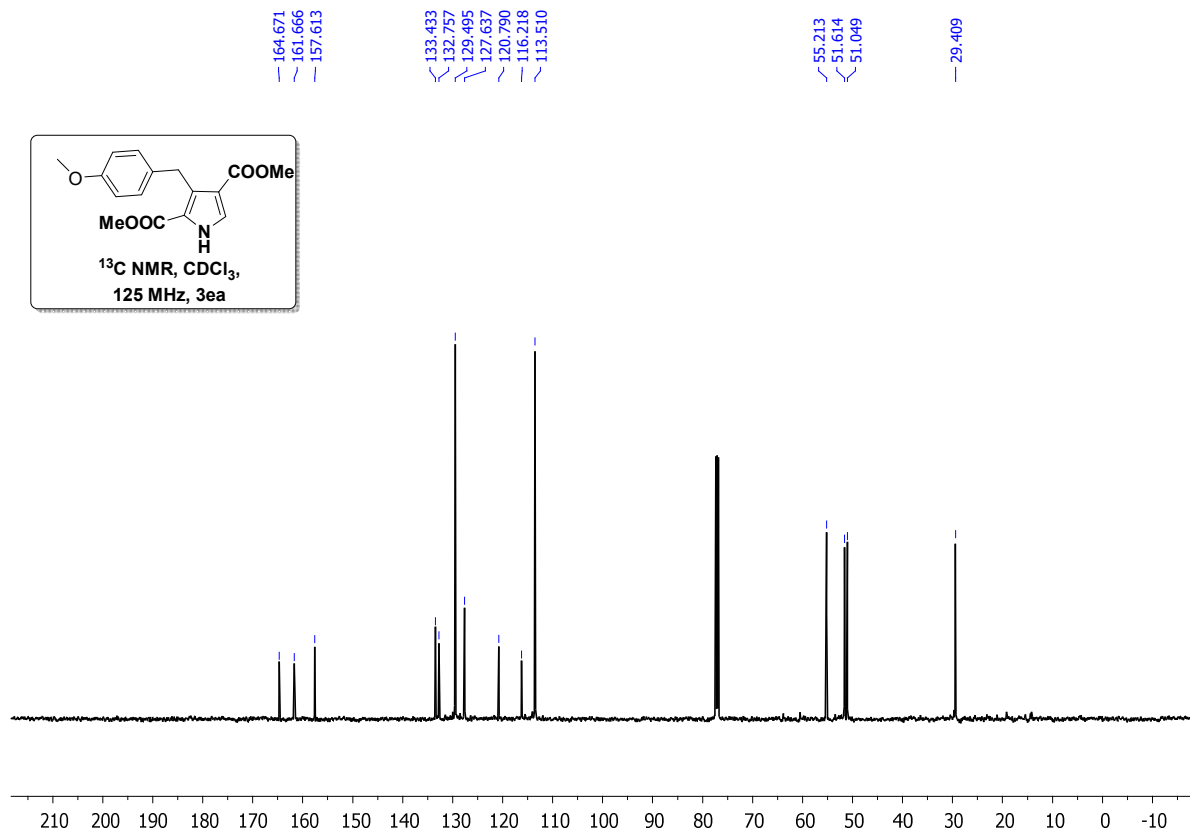
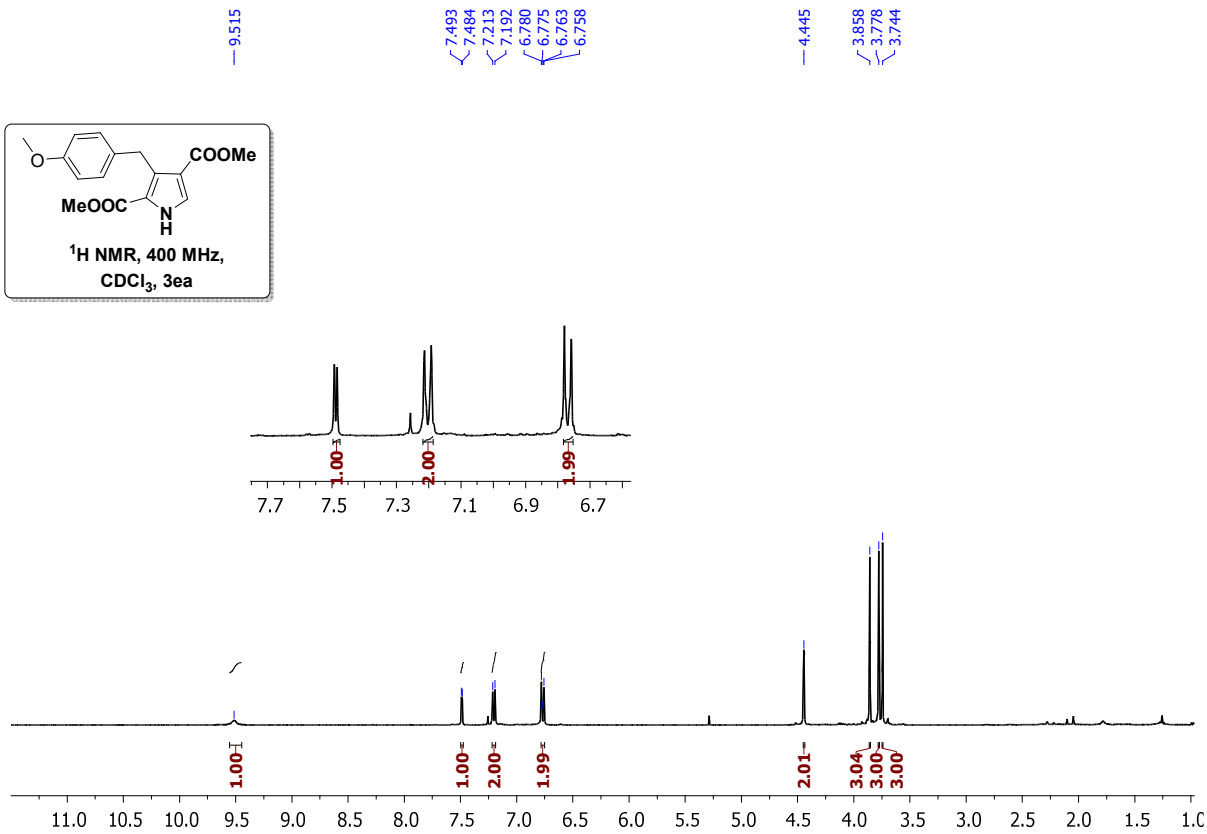


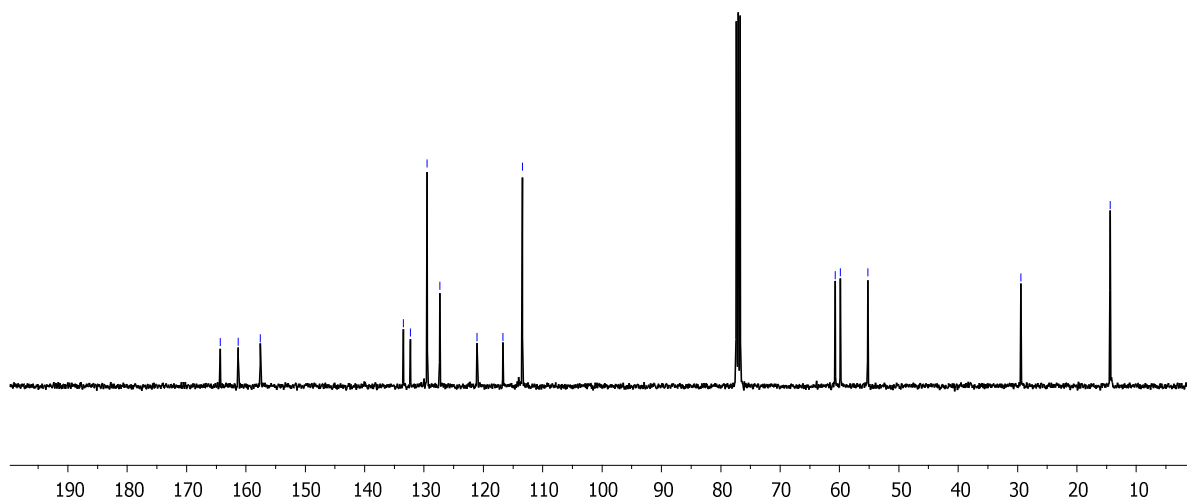
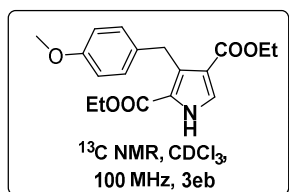
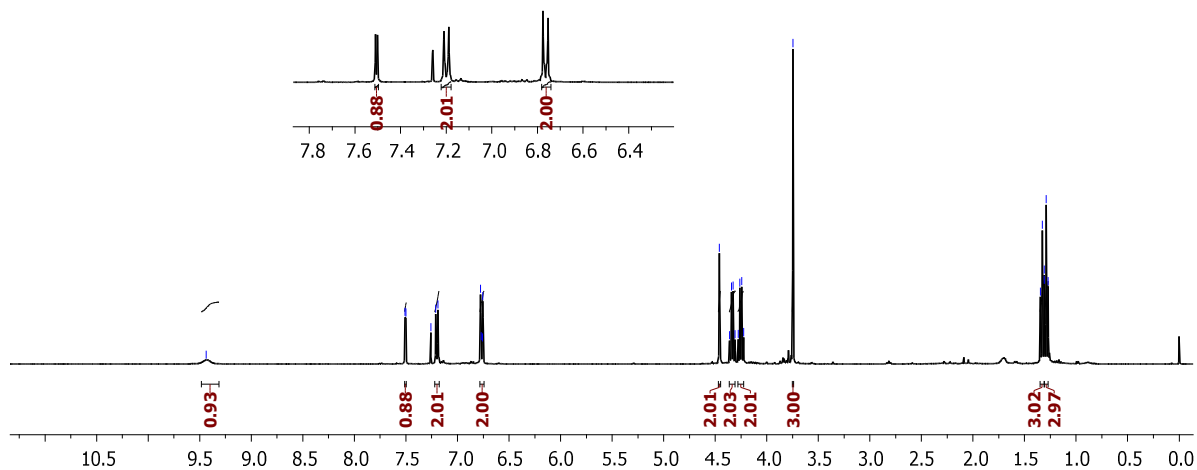
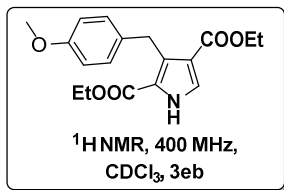


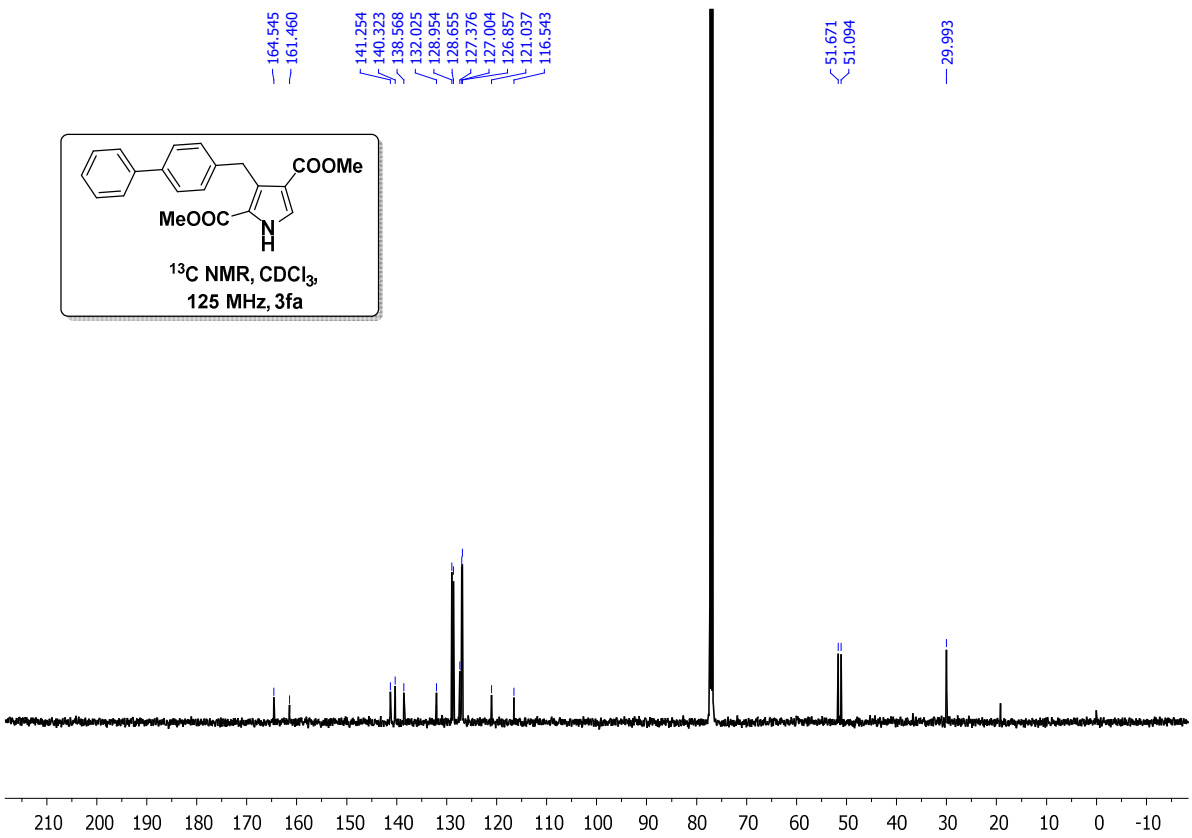
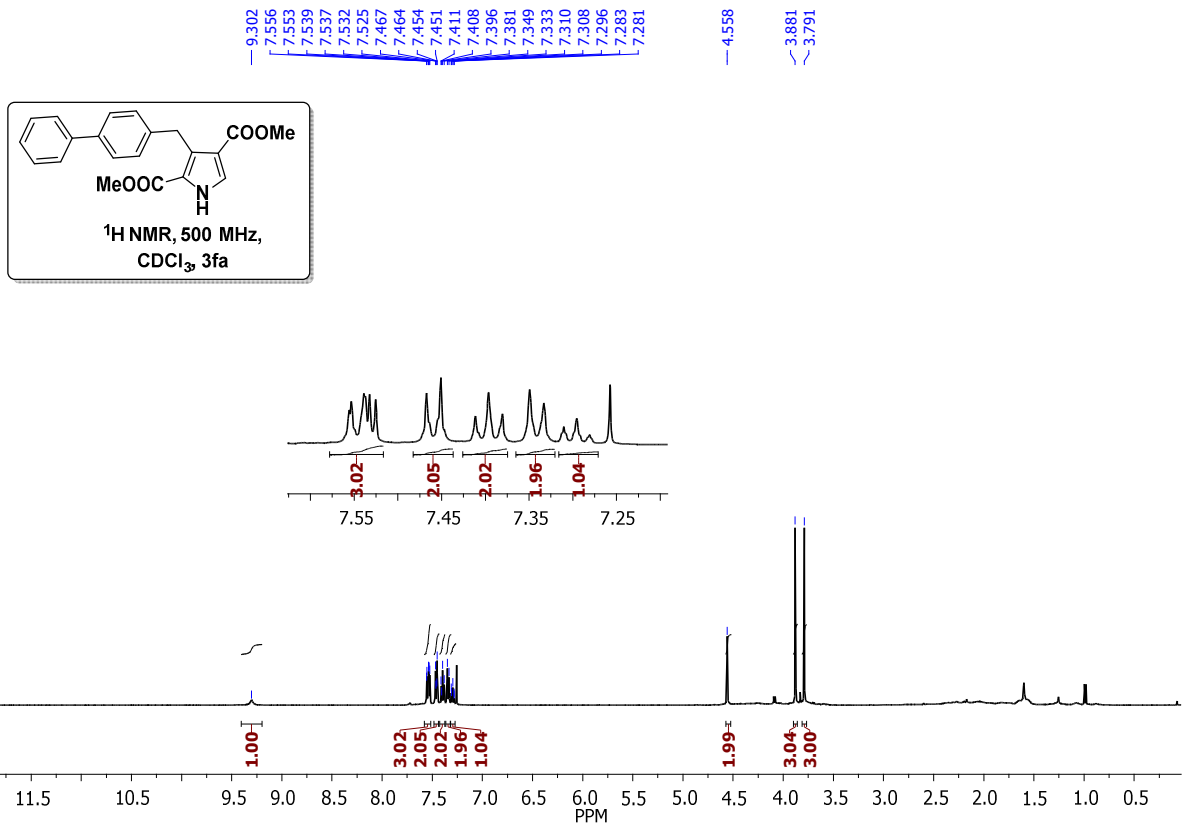


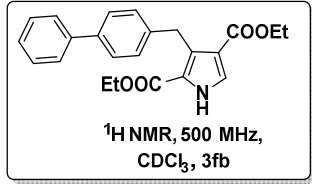






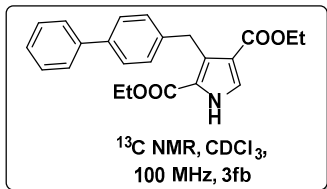
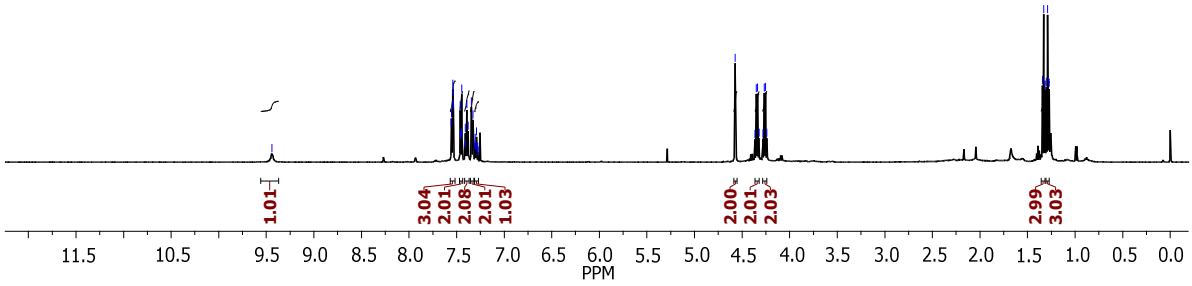
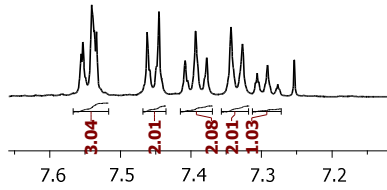






9.441, 7.516, 7.553, 7.541, 7.540, 7.537, 7.534, 7.462, 7.458, 7.449, 7.445, 7.408, 7.405, 7.393, 7.377, 7.343, 7.327, 7.308, 7.306, 7.295, 7.304, 4.291, 4.365, 4.351, 4.336, 4.322, 4.281, 4.267, 4.253, 4.238

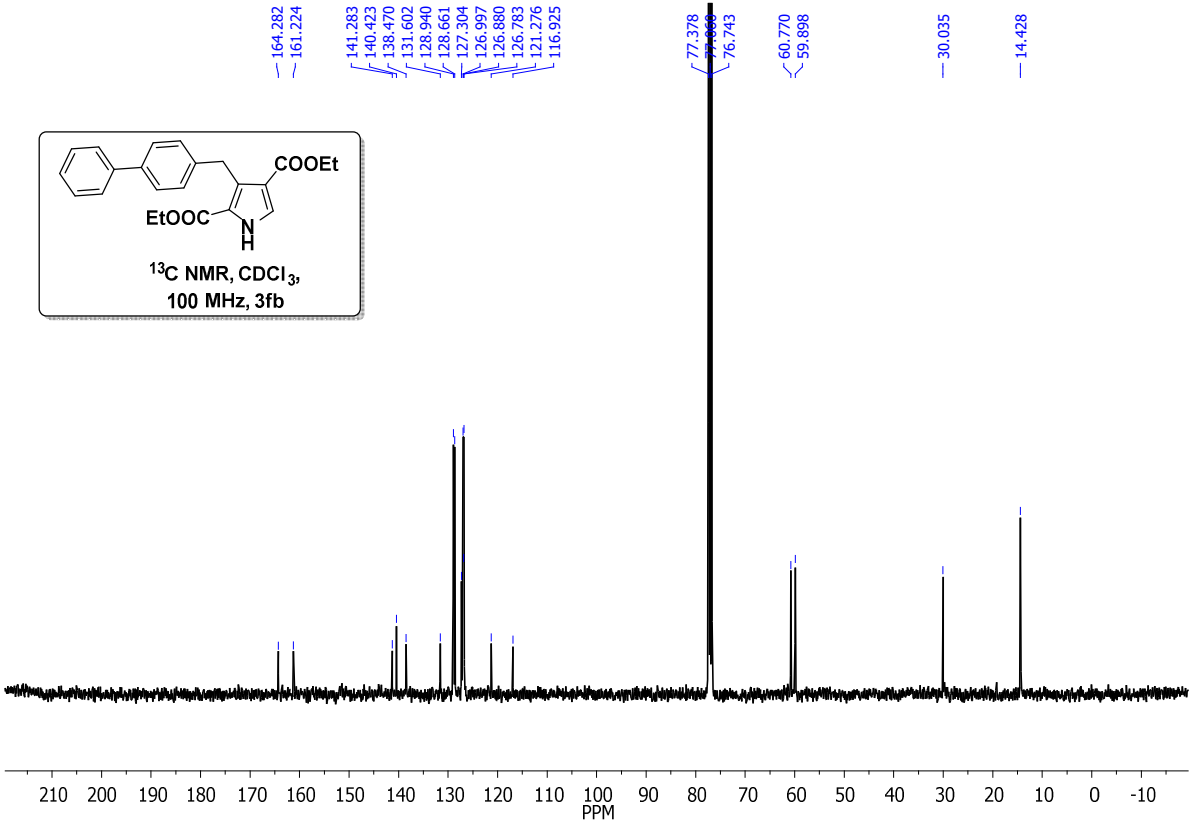
1.344, 1.330, 1.316, 1.302, 1.288, 1.274

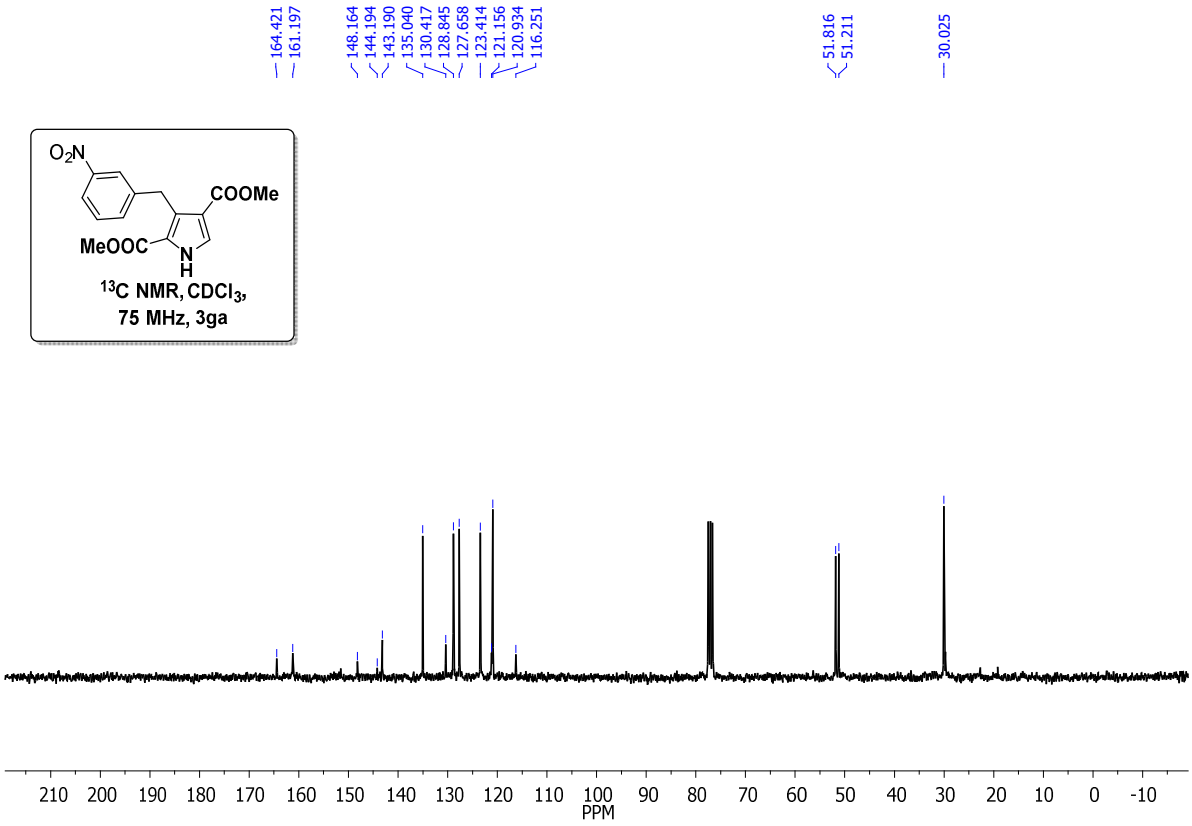
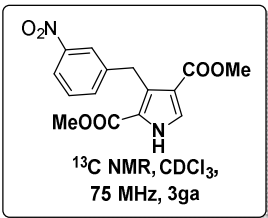
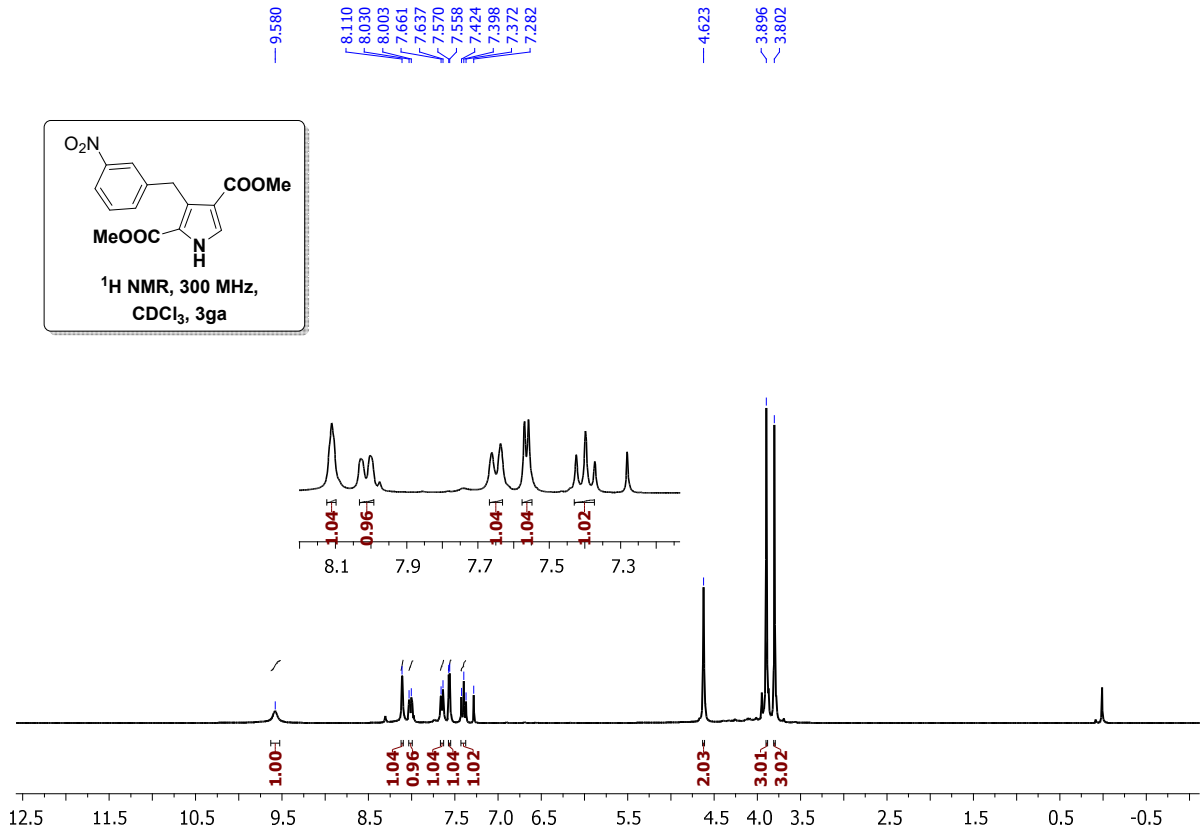
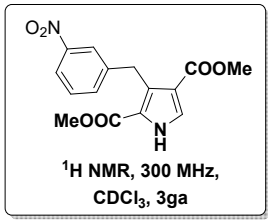


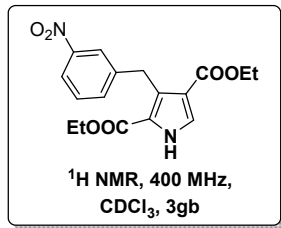
164.282, 161.224, 141.283, 140.423, 138.470, 131.602, 128.940, 128.661, 127.304, 126.997, 126.880, 126.783, 121.276, 116.925

77.378, 77.066, 76.743, 60.770, 59.898

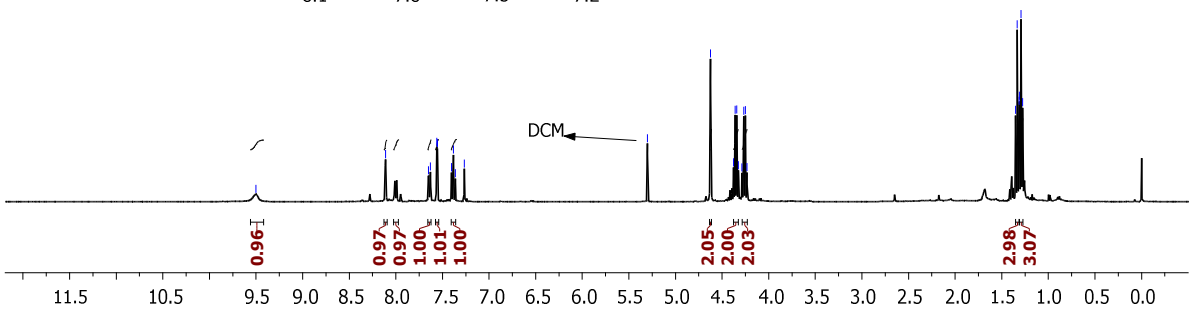
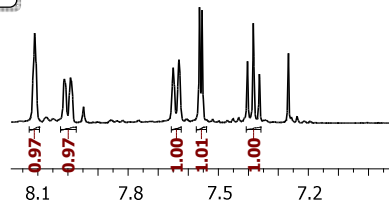
30.035, 14.428



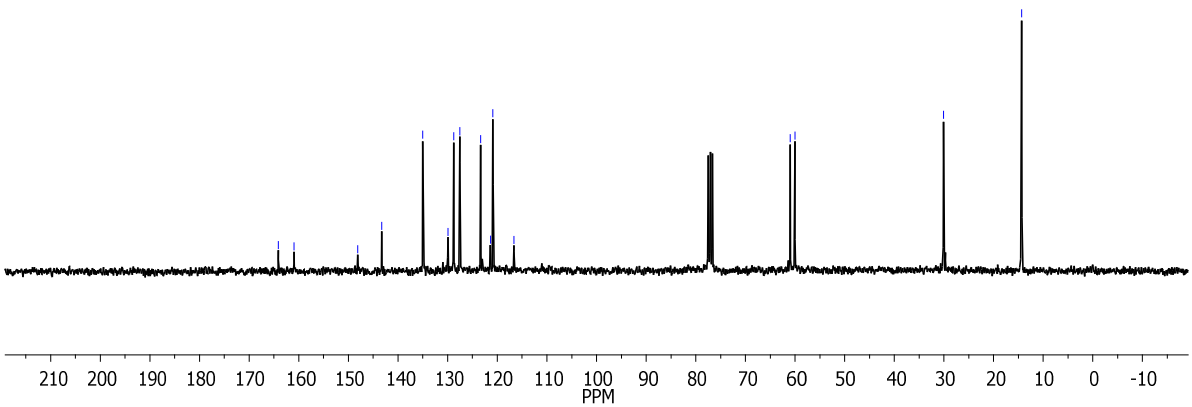
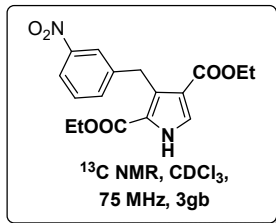


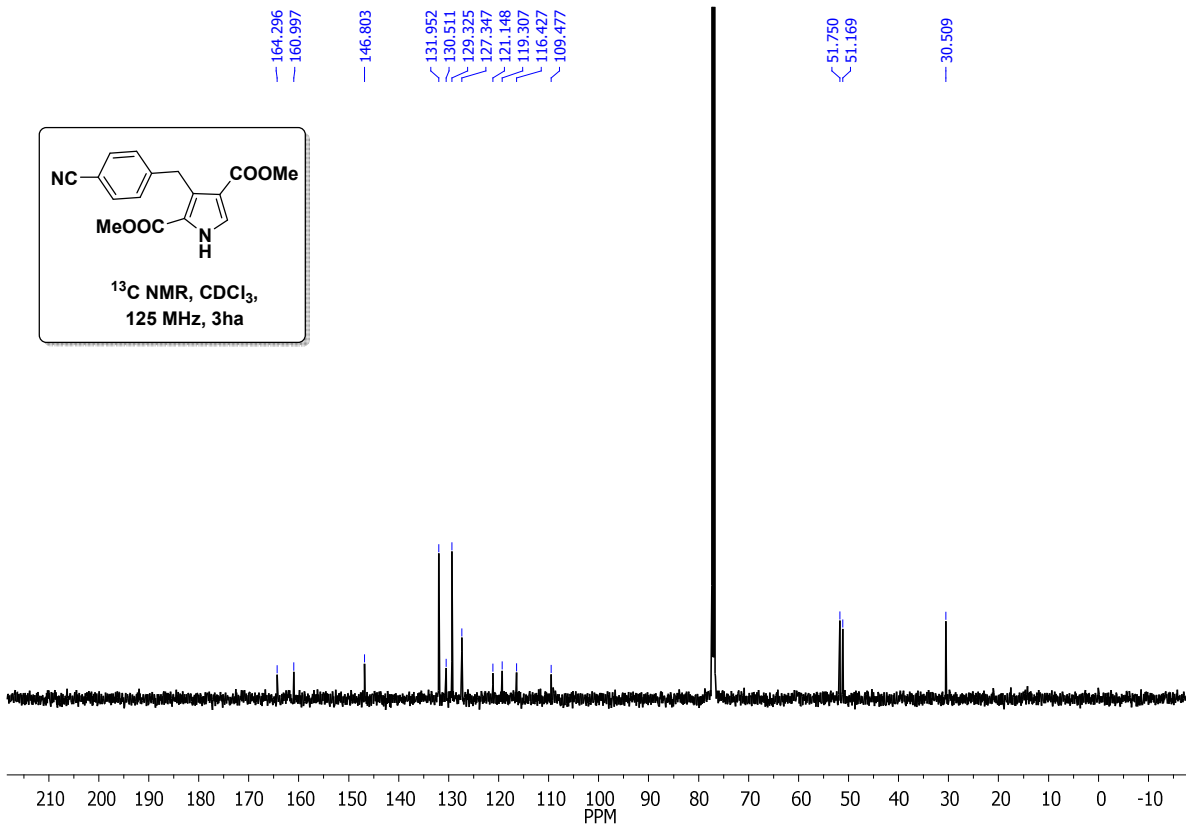
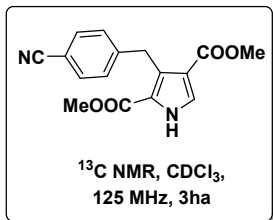
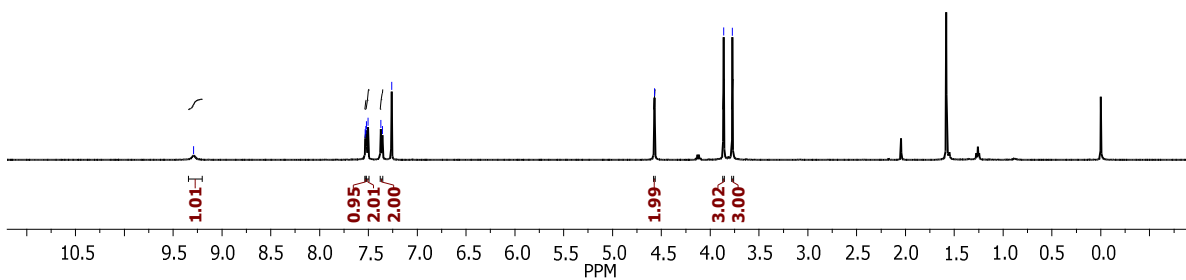
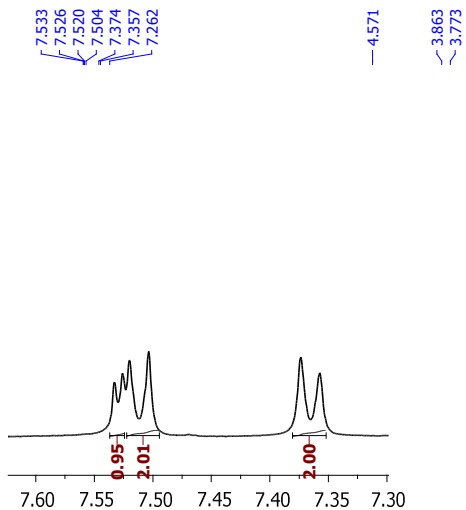
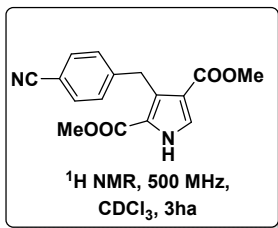


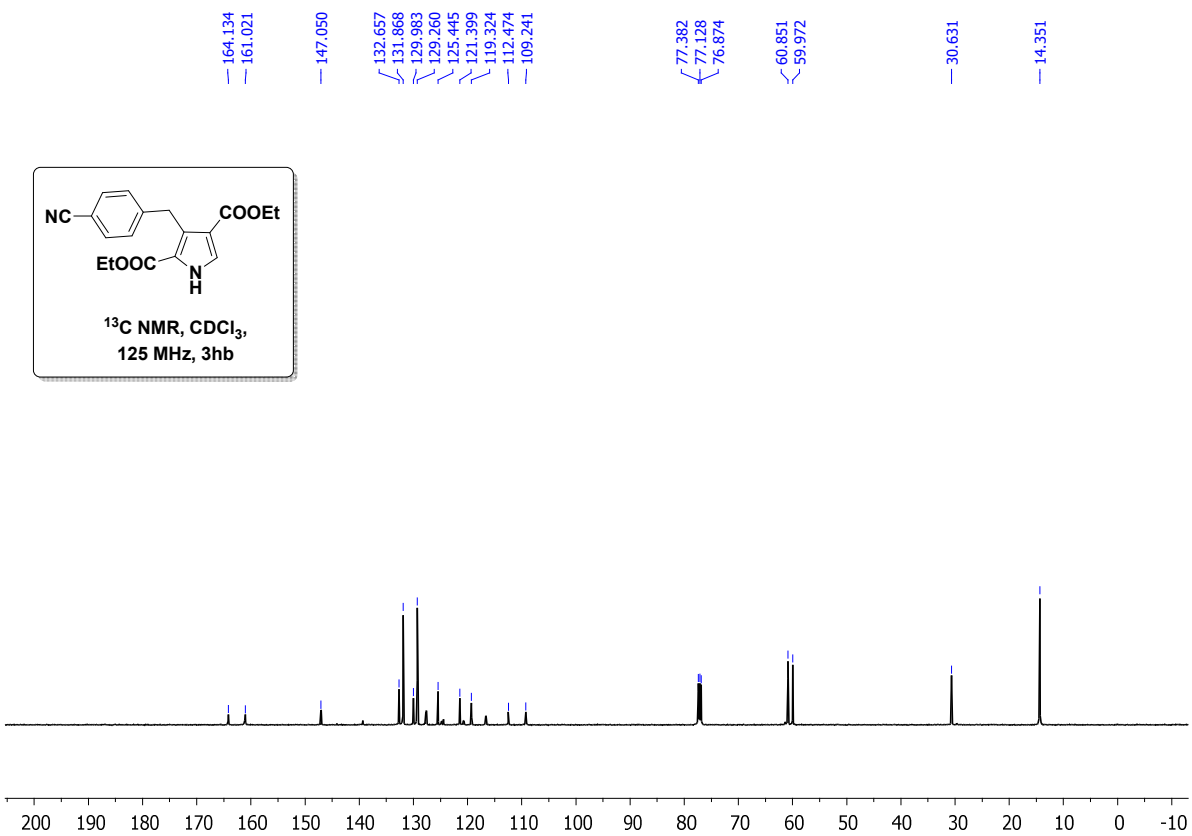
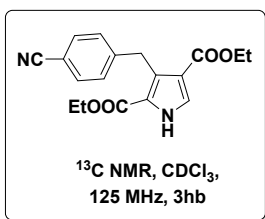
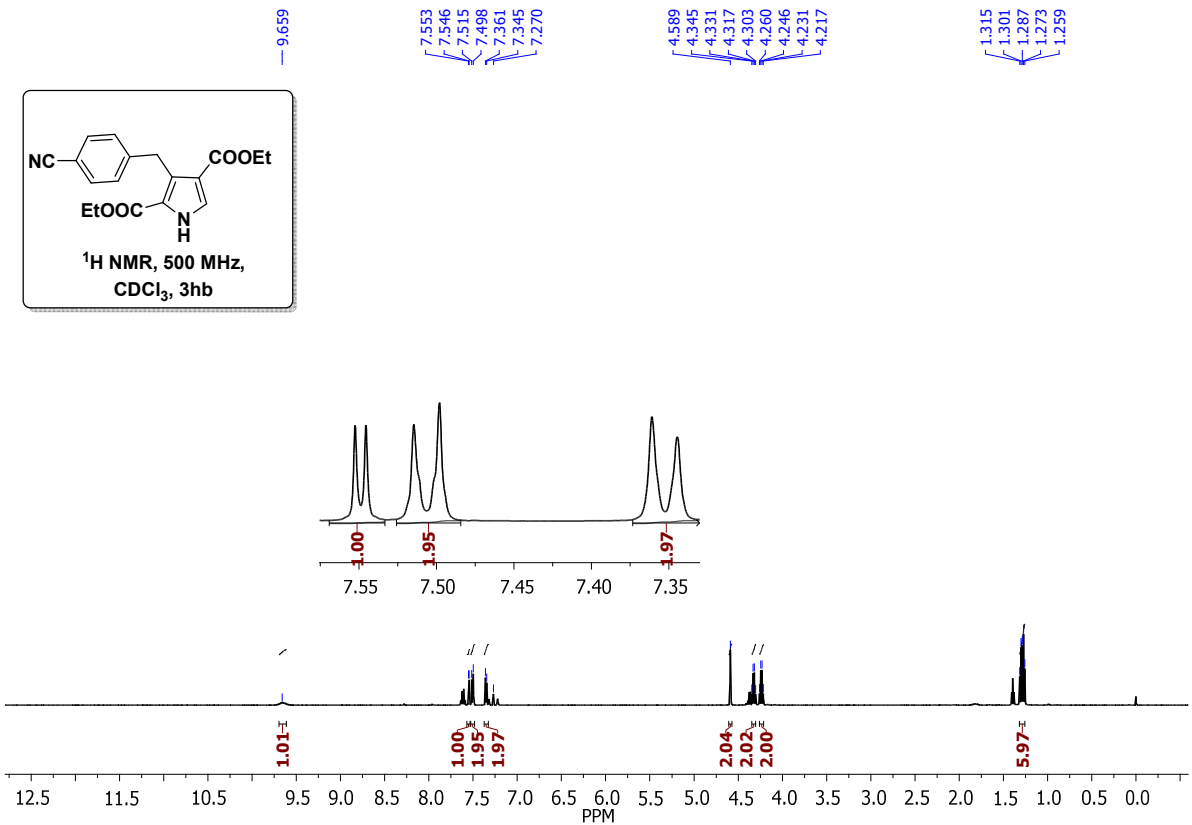
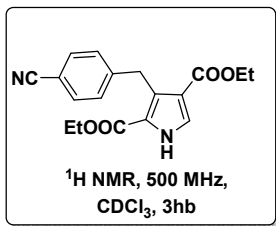
9.503
 8.111, 7.650, 7.631, 7.562, 7.554, 7.403, 7.383, 7.363, 7.267
 5.300, 4.625, 4.379, 4.361, 4.343, 4.325, 4.286, 4.269, 4.251, 4.233
 1.351, 1.334, 1.316, 1.311, 1.293, 1.276

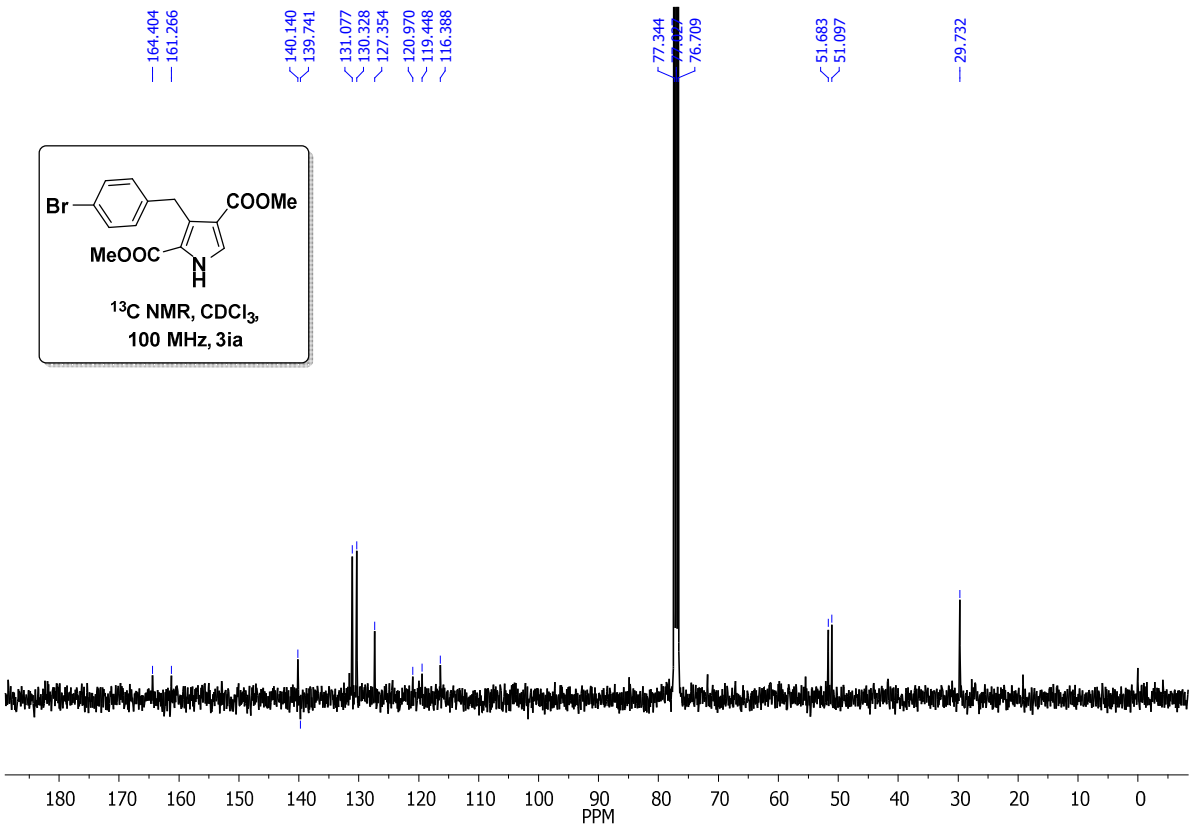
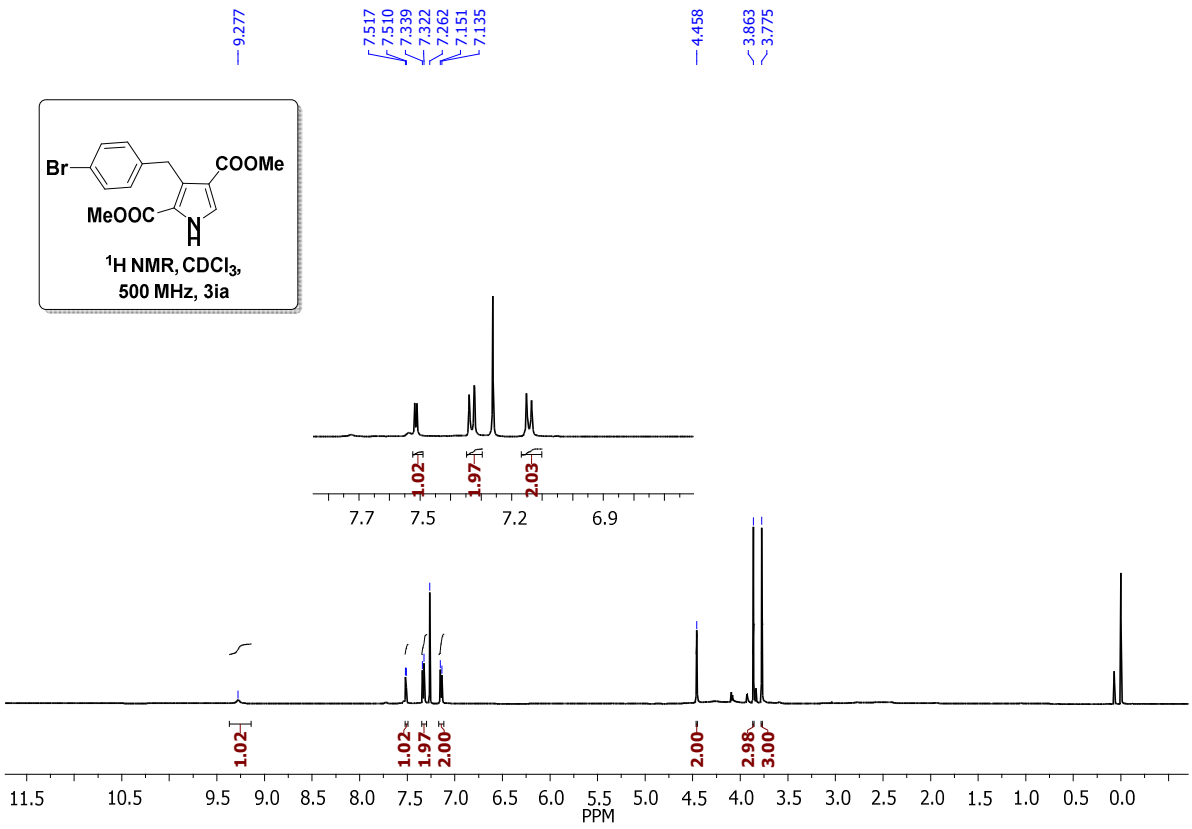


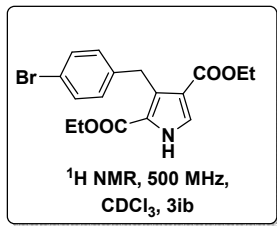
164.114, 160.949
 148.146, 143.300, 135.017, 129.960, 128.791, 127.544, 123.375, 121.382, 120.870, 116.628
 60.963, 60.033
 30.058, 14.339



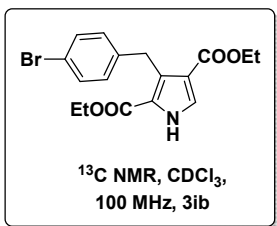
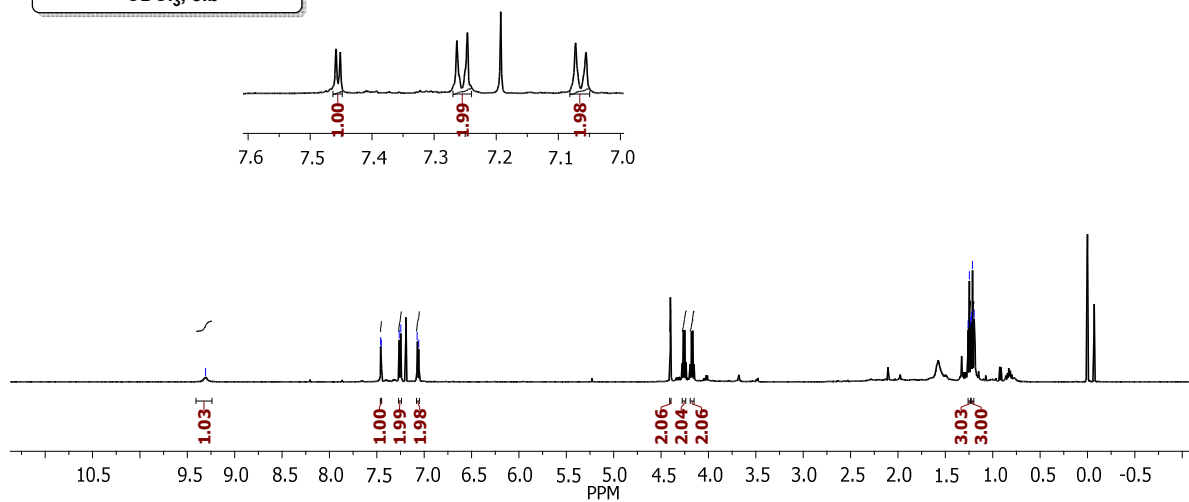




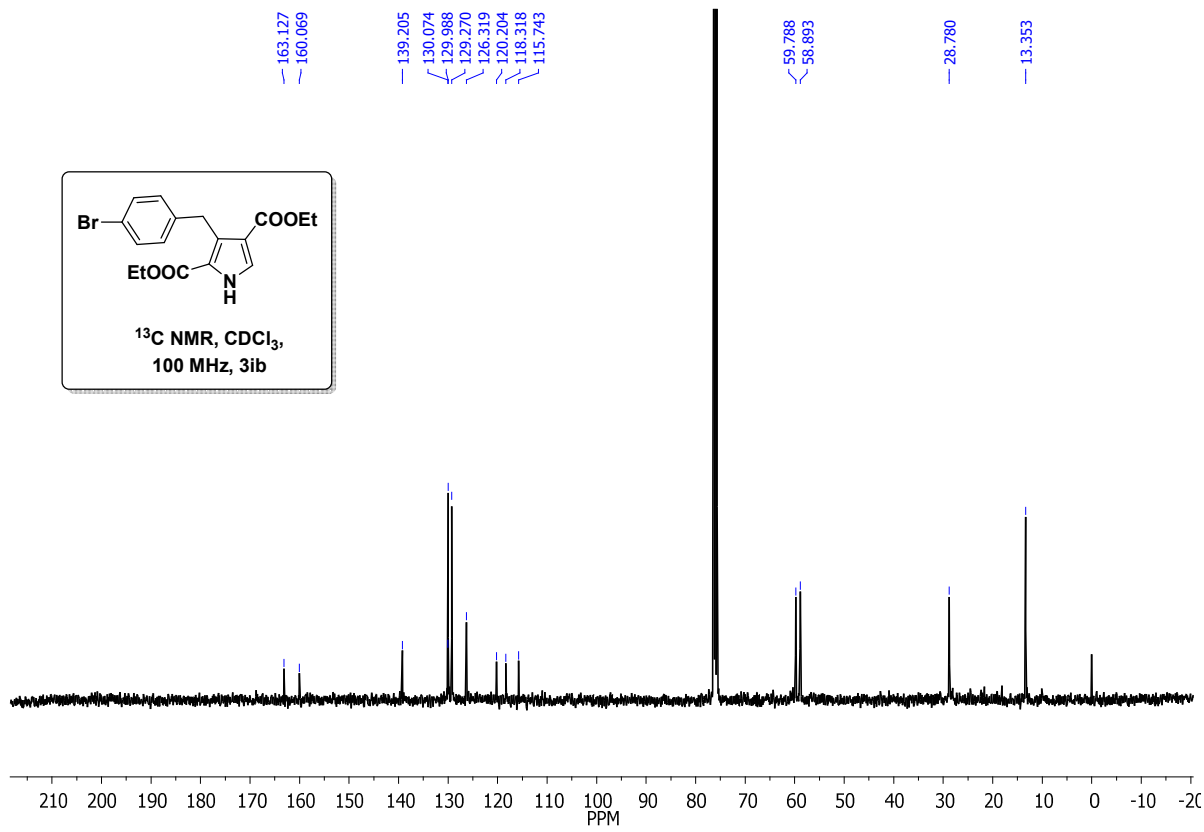


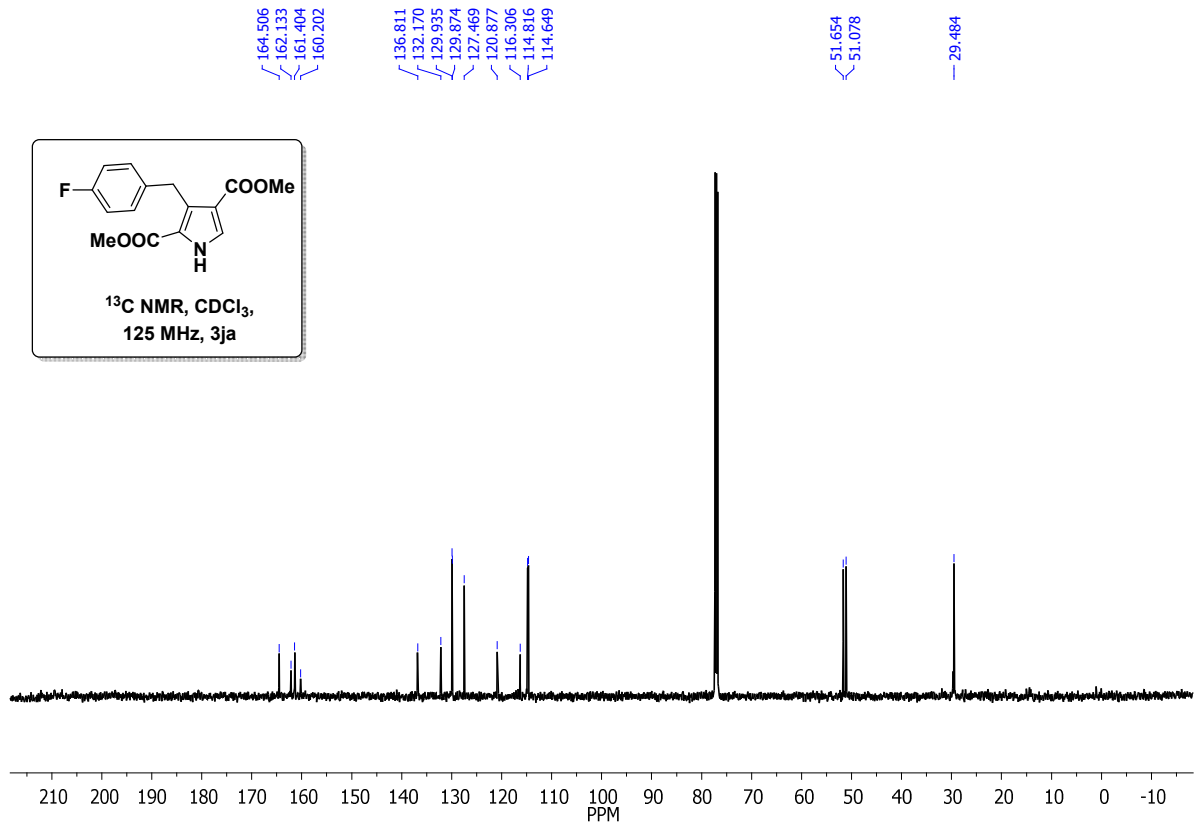
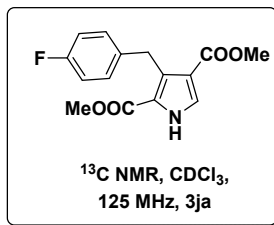
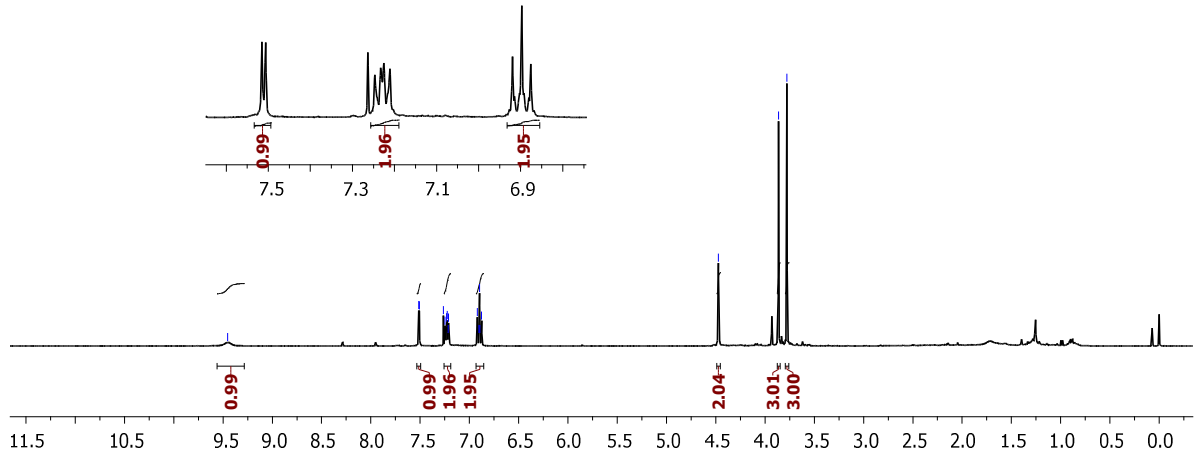
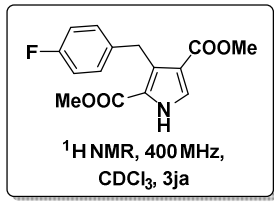


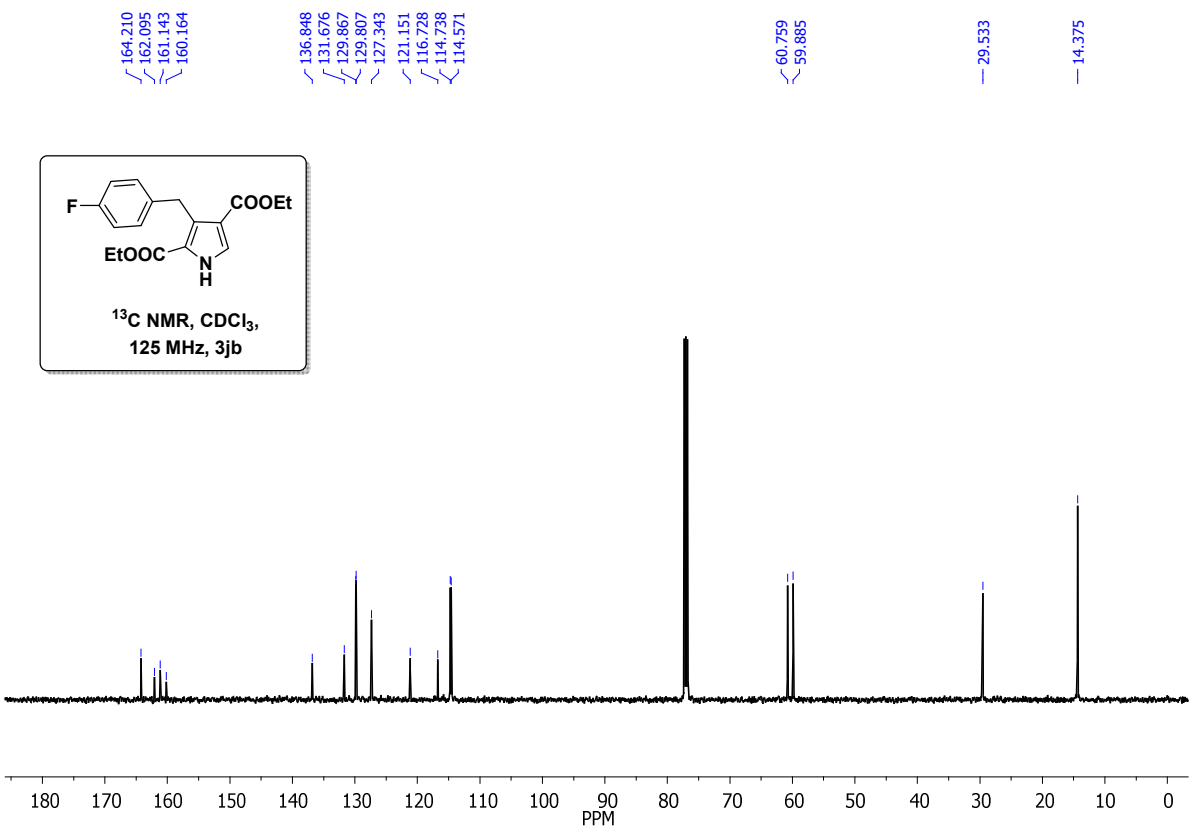
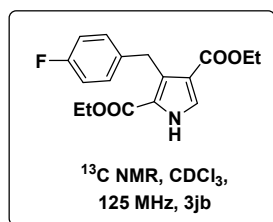
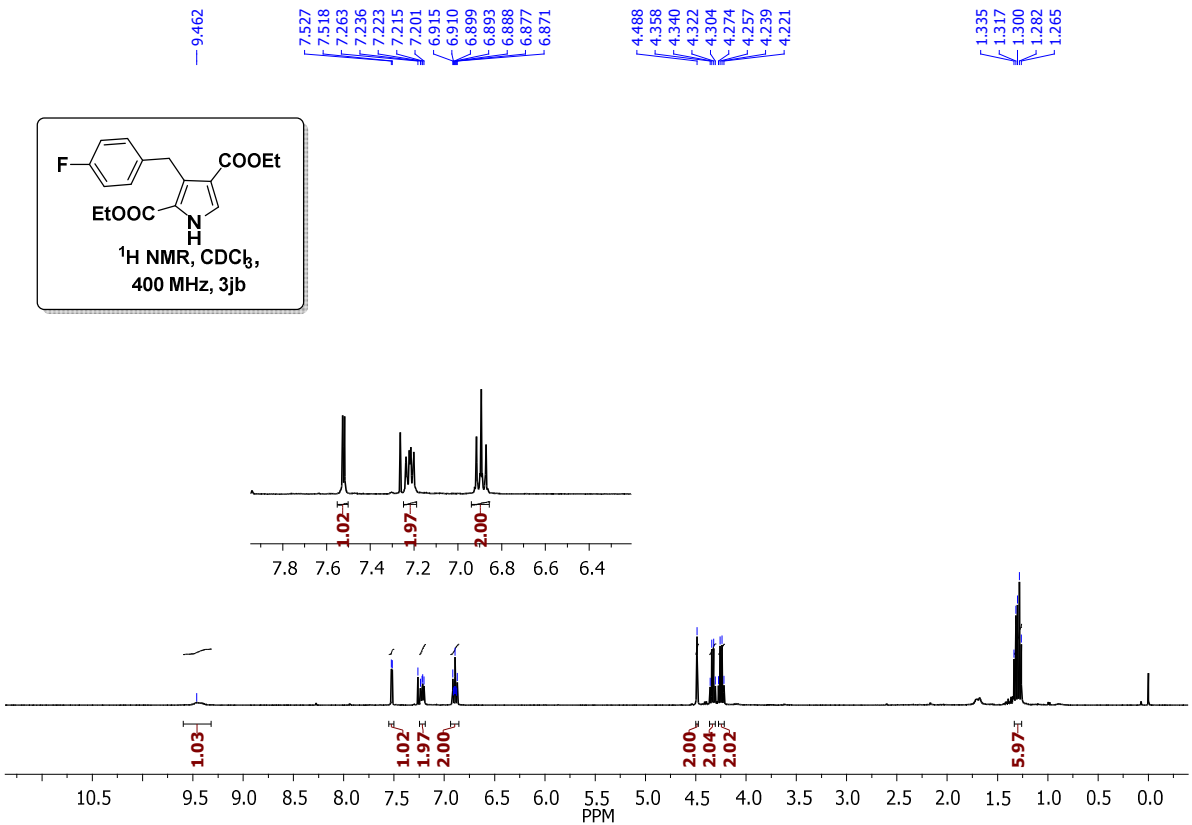
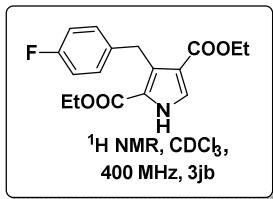
9.307
 7.458, 7.451, 7.263, 7.247, 7.072, 7.056
 1.260, 1.246, 1.231, 1.225, 1.210, 1.196

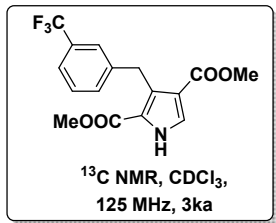
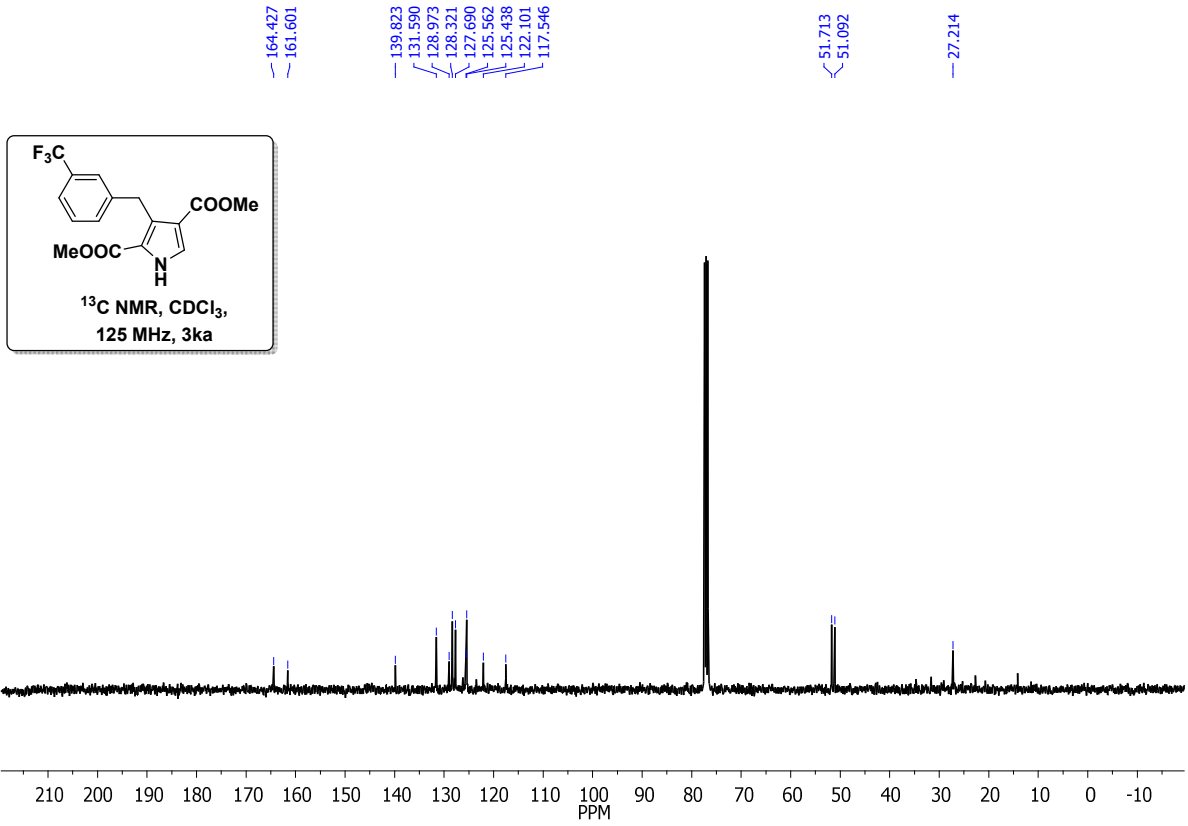
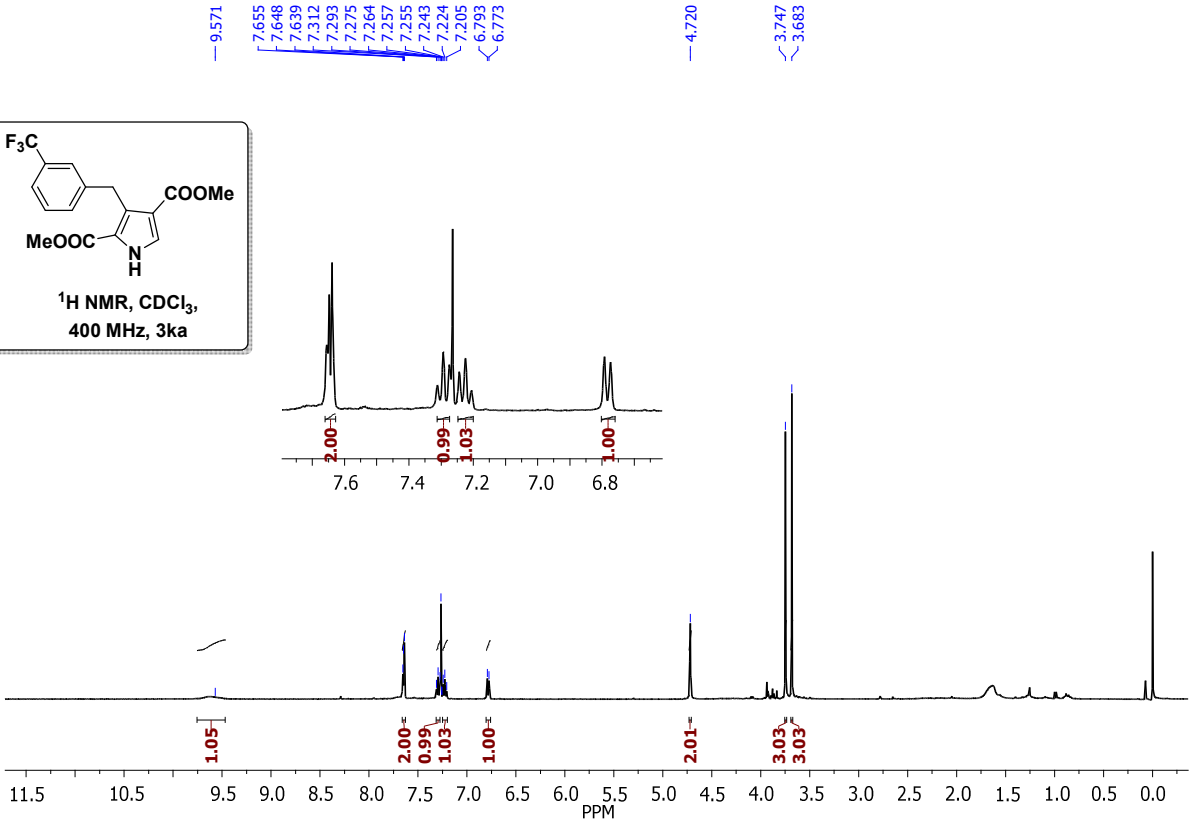
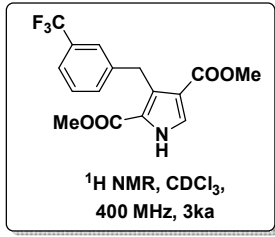


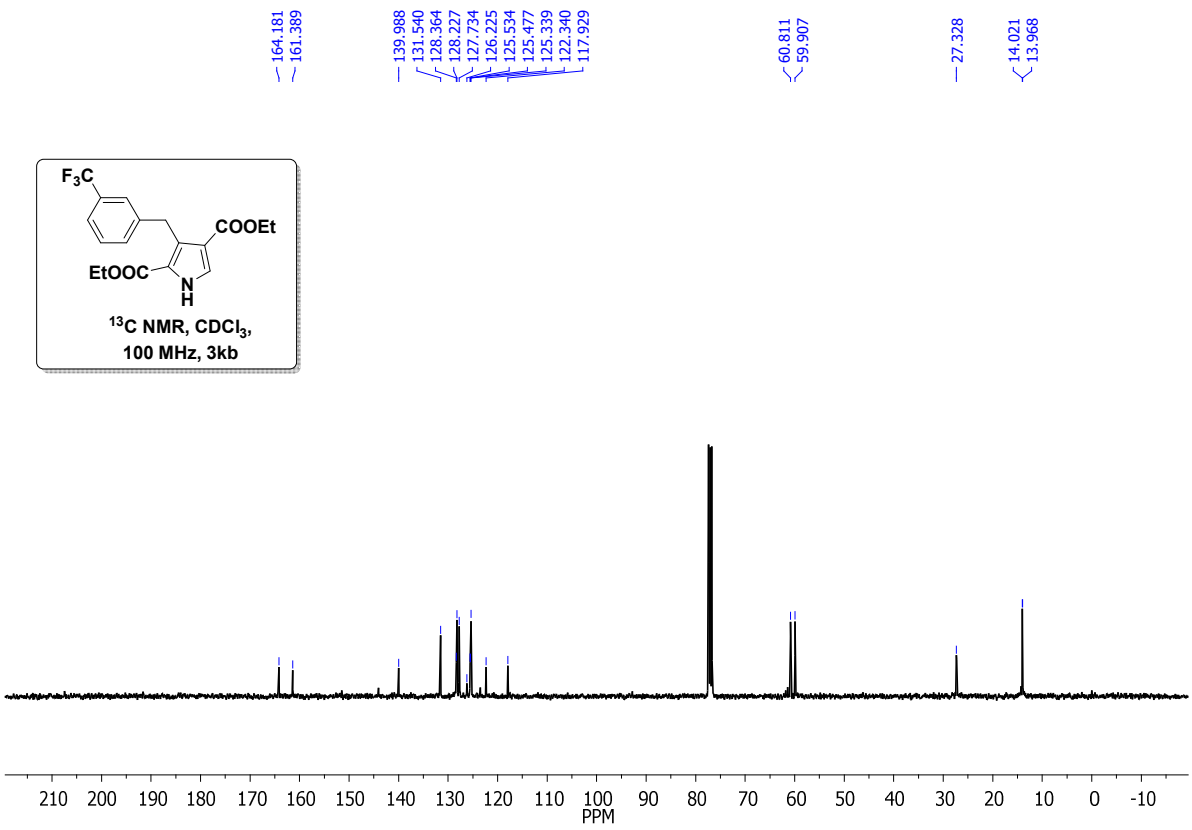
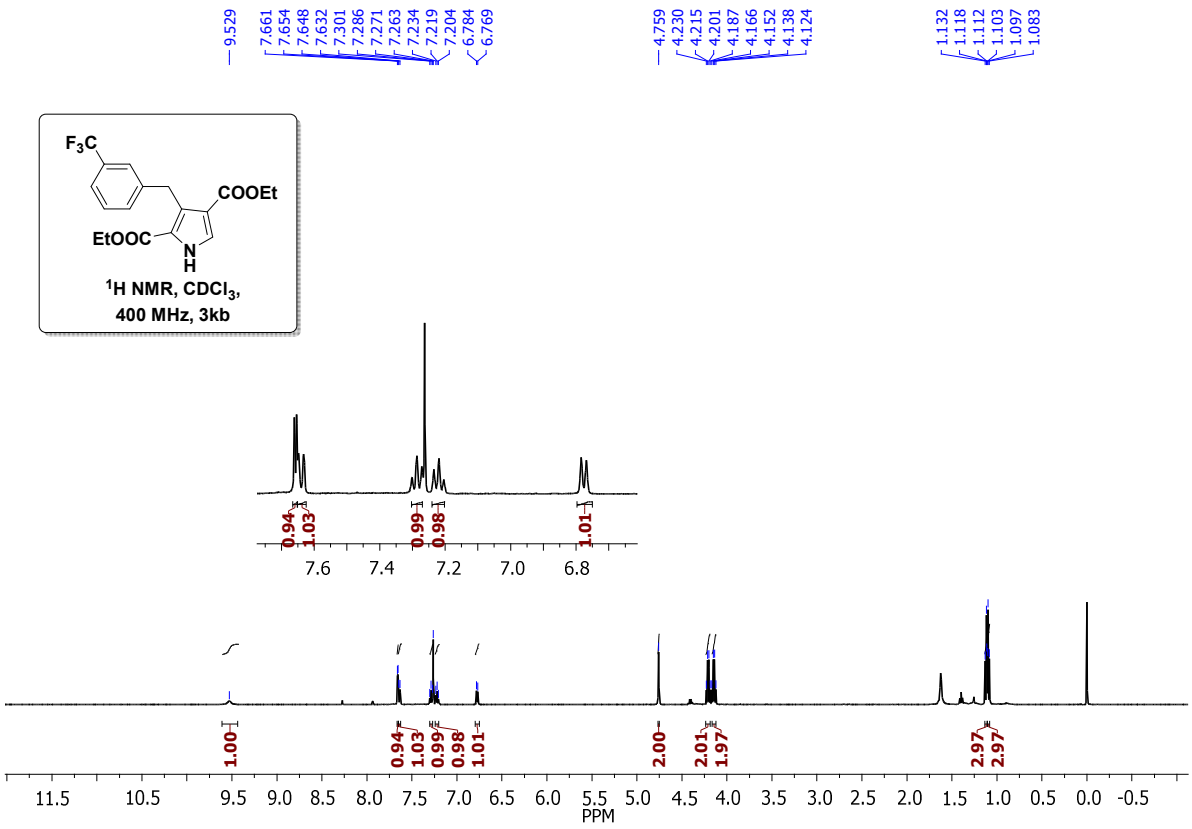
163.127, 160.069
 139.205, 130.074, 129.988, 129.270, 126.319, 120.204, 118.318, 115.743
 59.788, 58.893
 28.780
 13.353

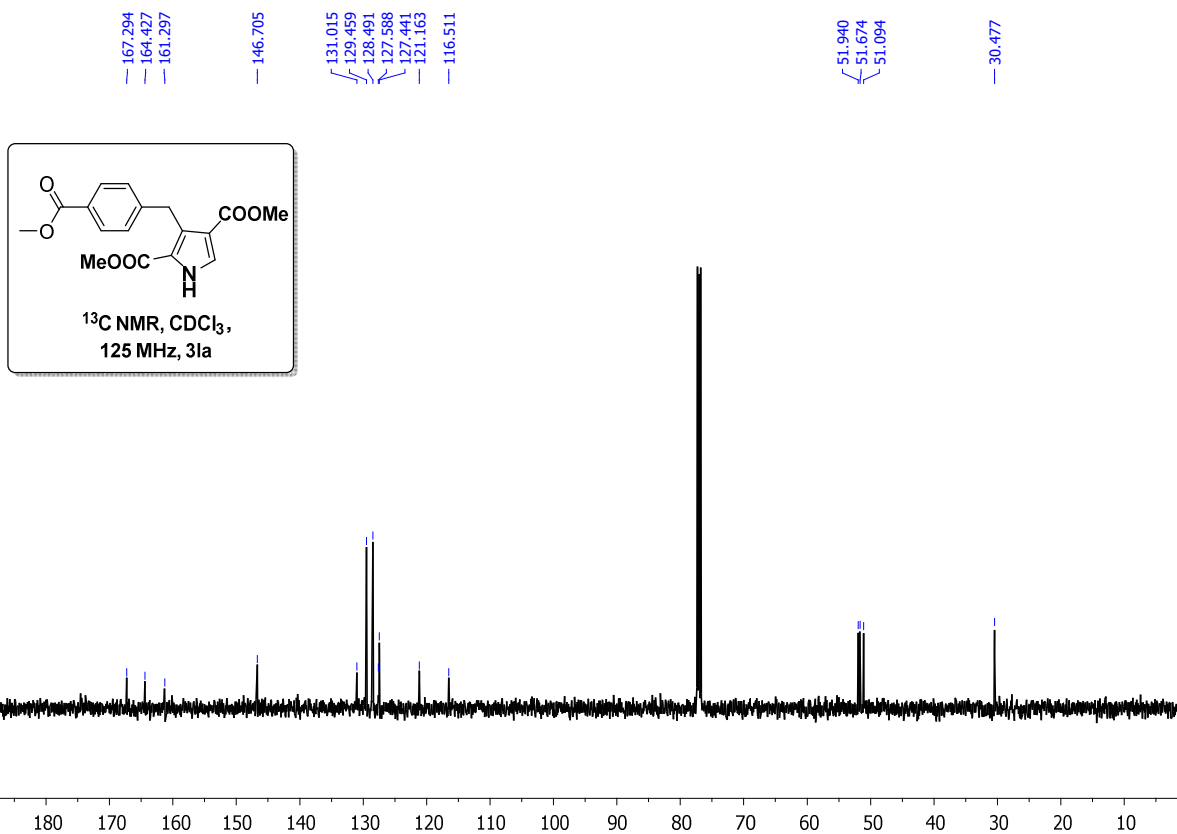
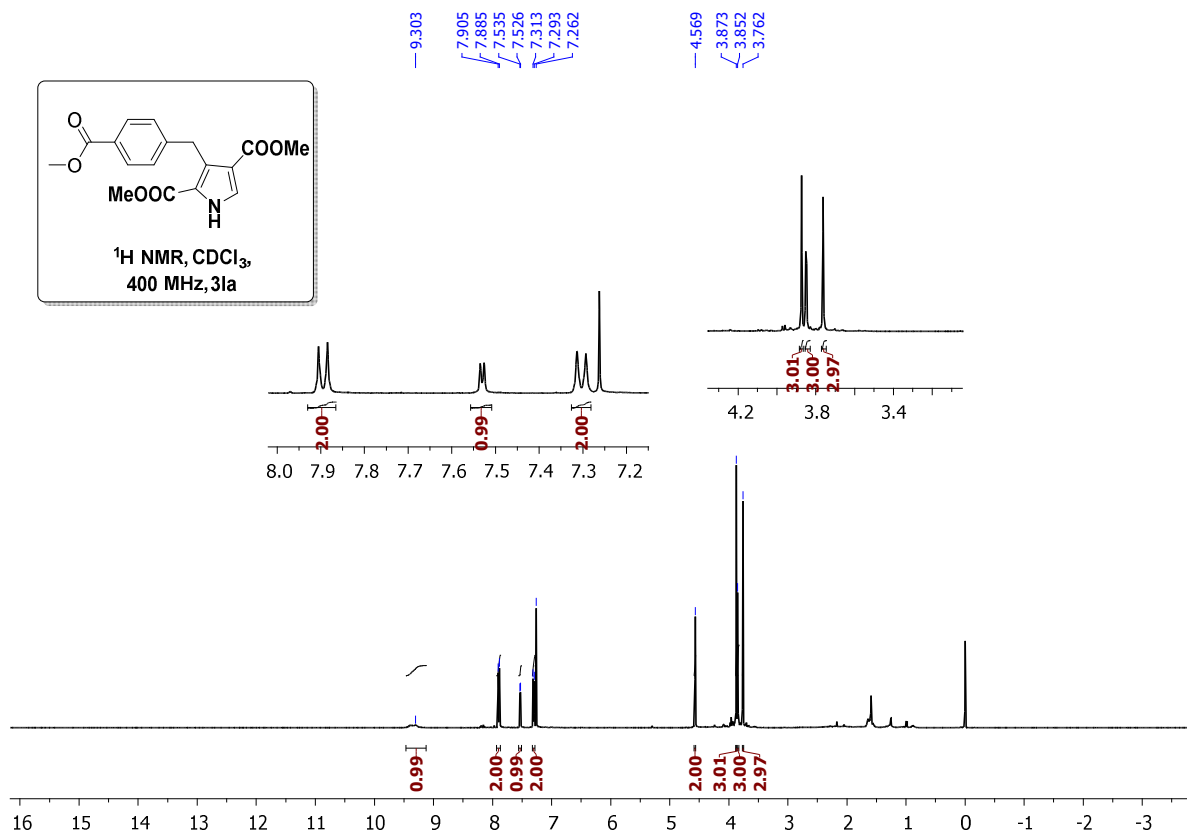
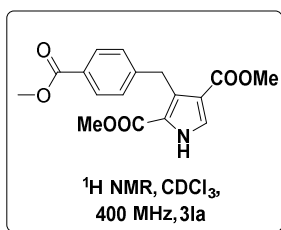


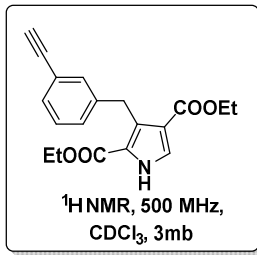




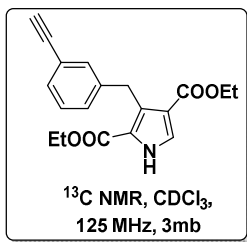
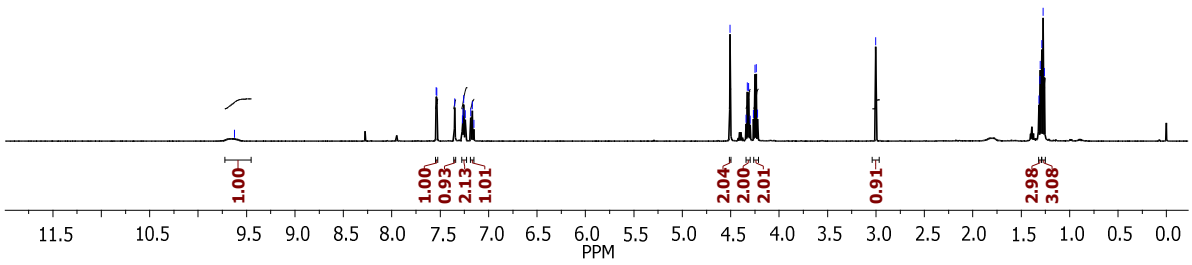
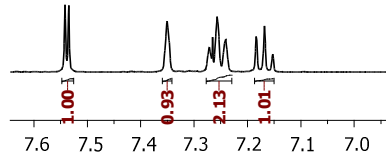




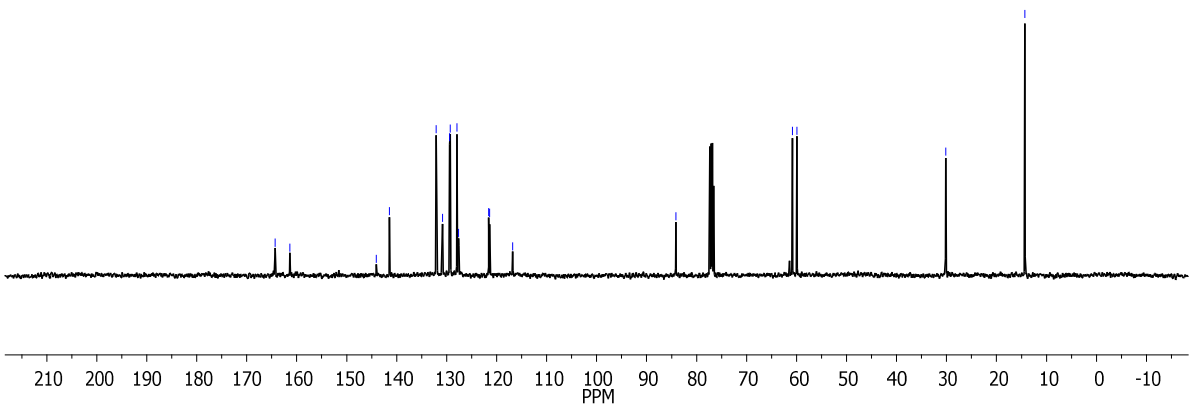


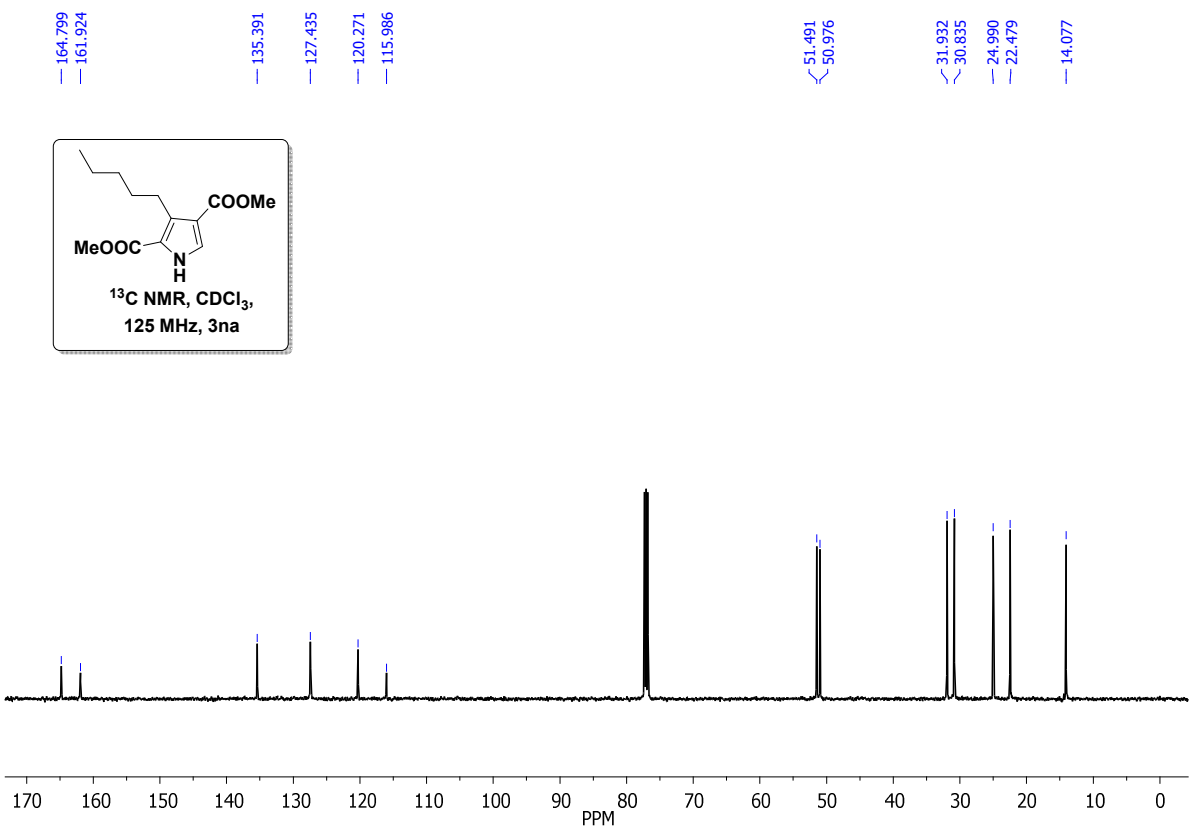
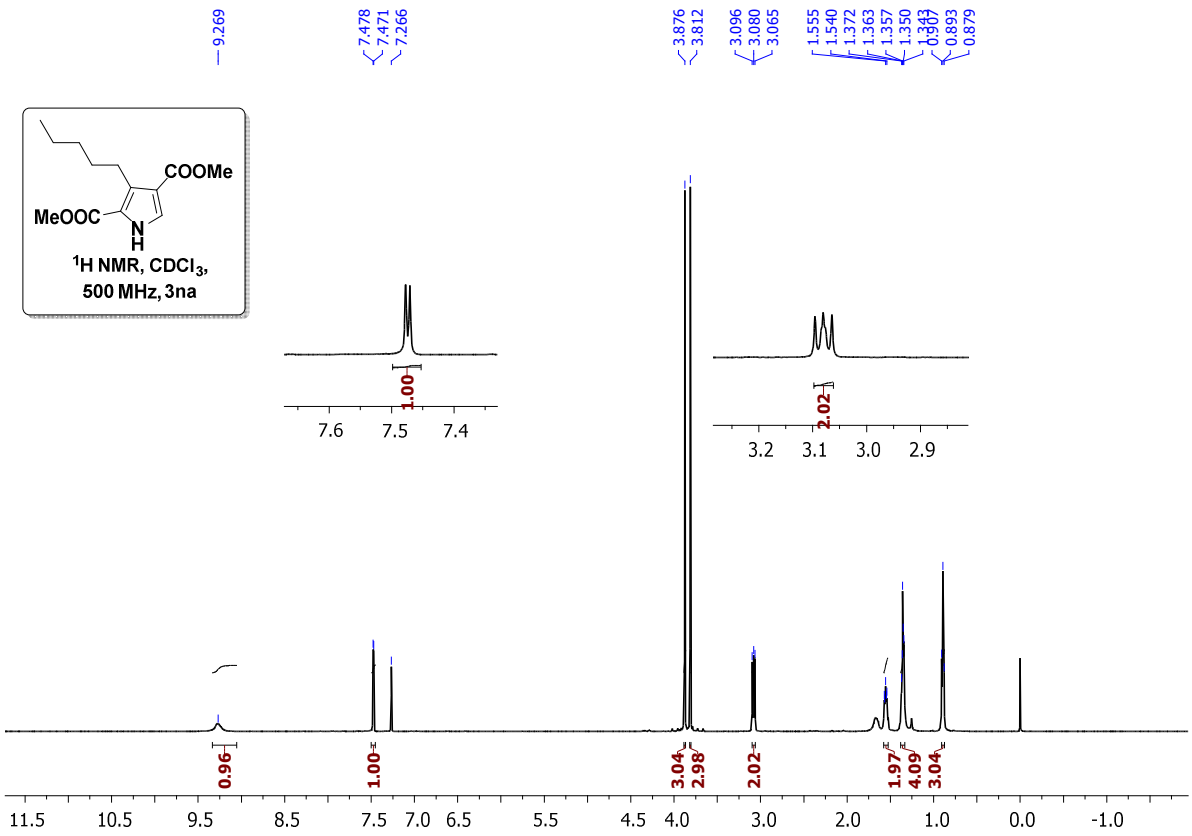


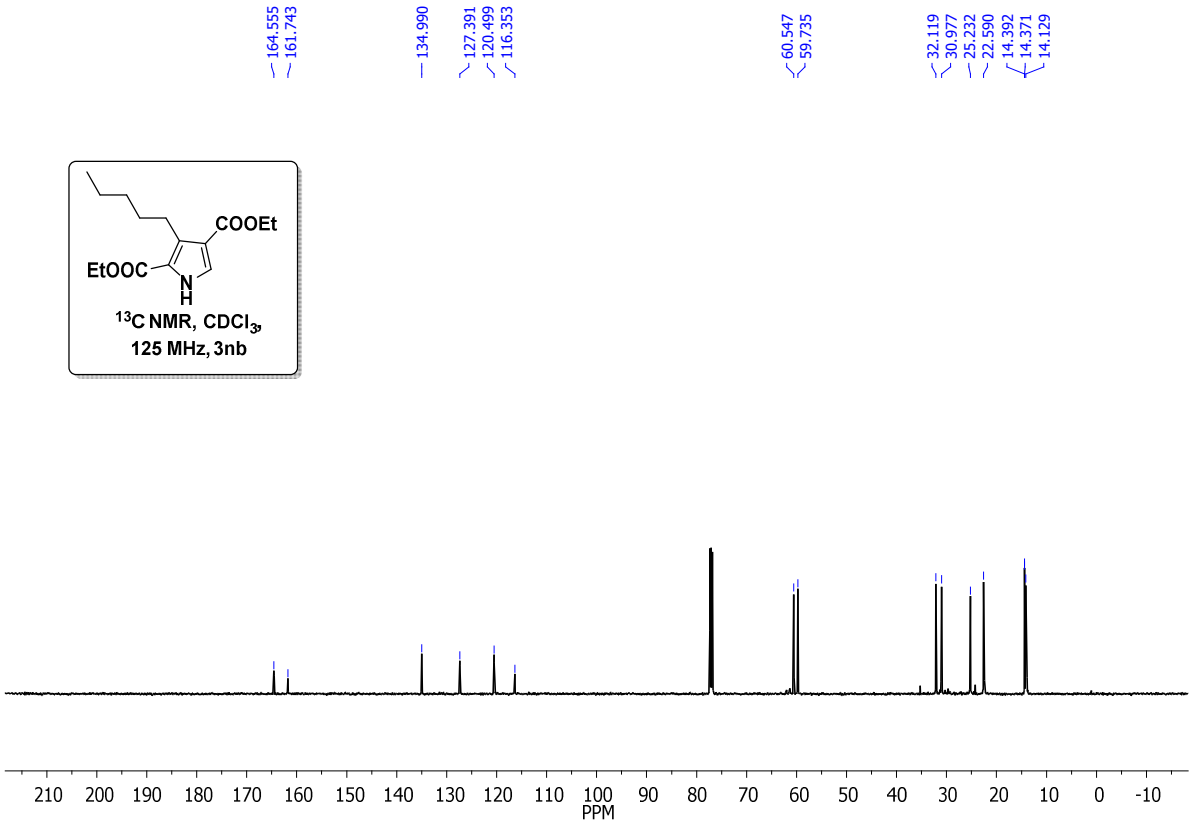
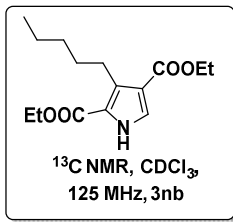
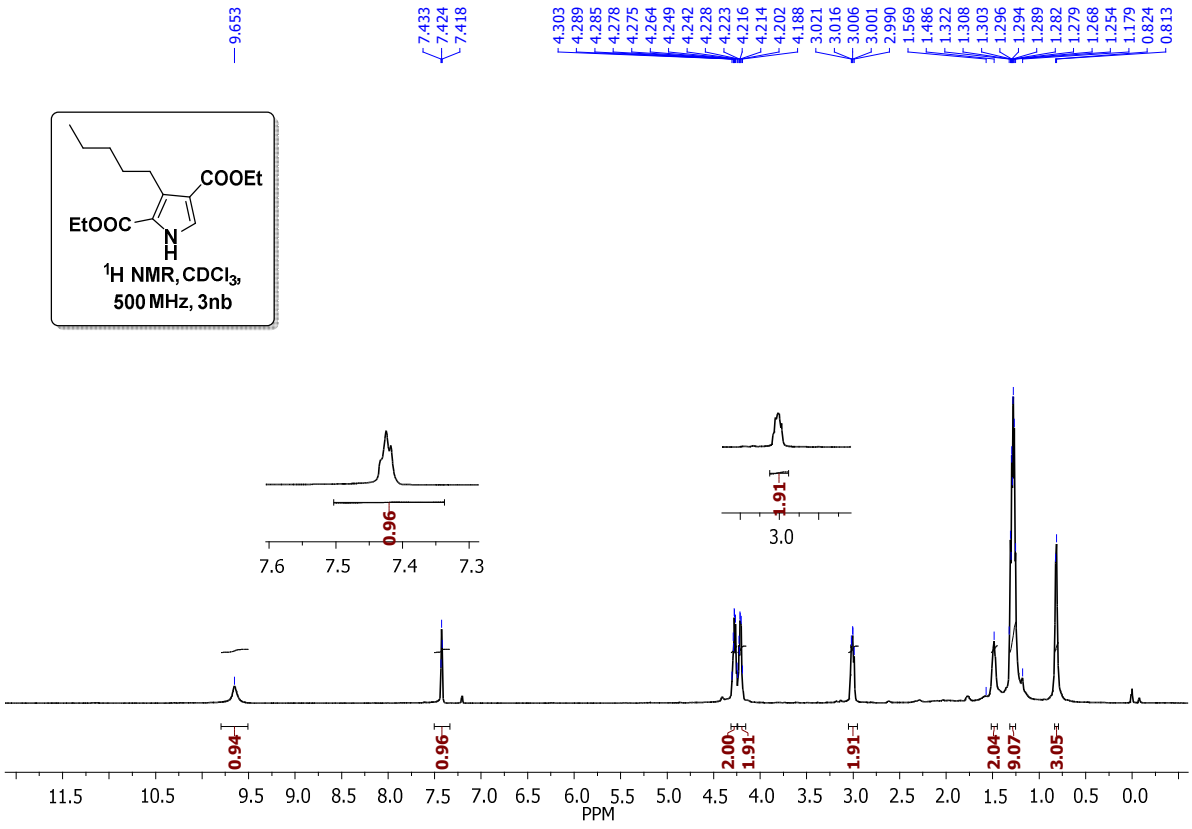
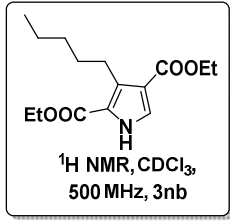
9.624
 7.542, 7.535, 7.350, 7.272, 7.265, 7.257, 7.241, 7.183, 7.168, 7.153
 4.507, 4.343, 4.328, 4.314, 4.300, 4.265, 4.250, 4.236, 4.222
 3.002
 1.318, 1.306, 1.303, 1.288, 1.274, 1.260

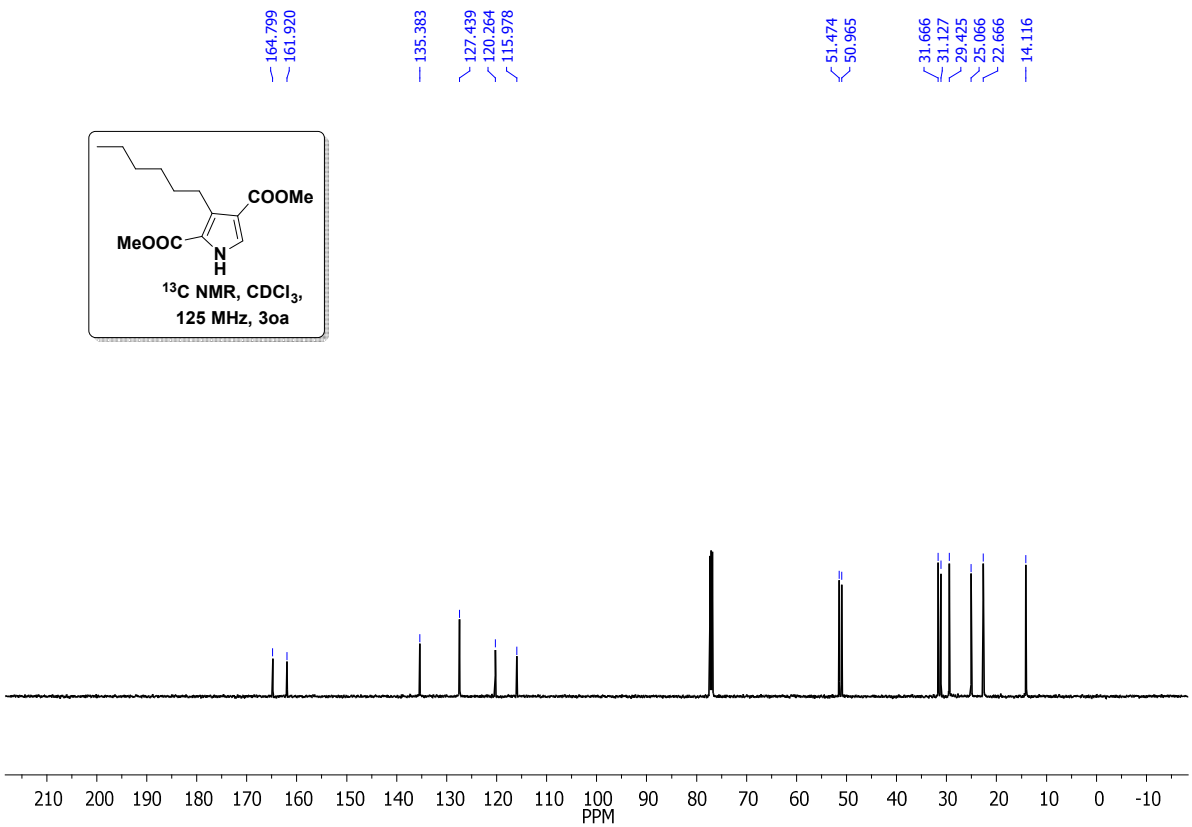
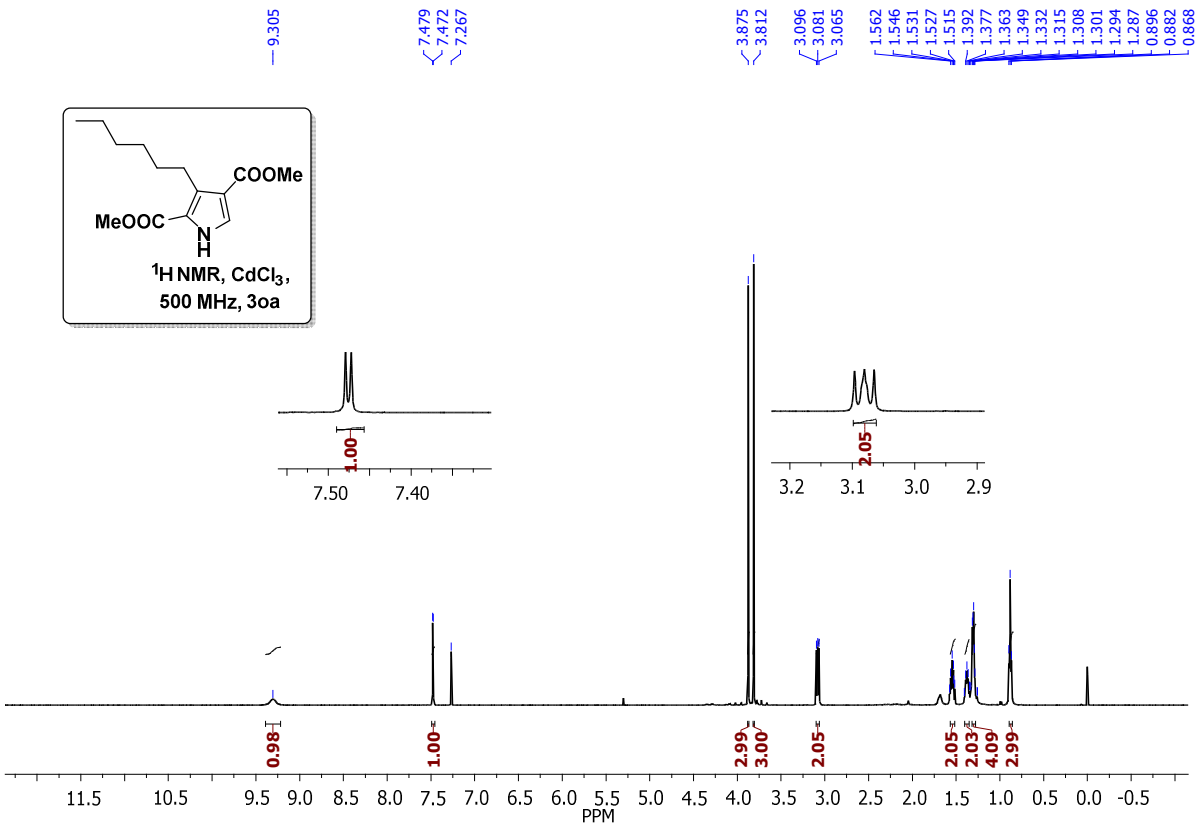


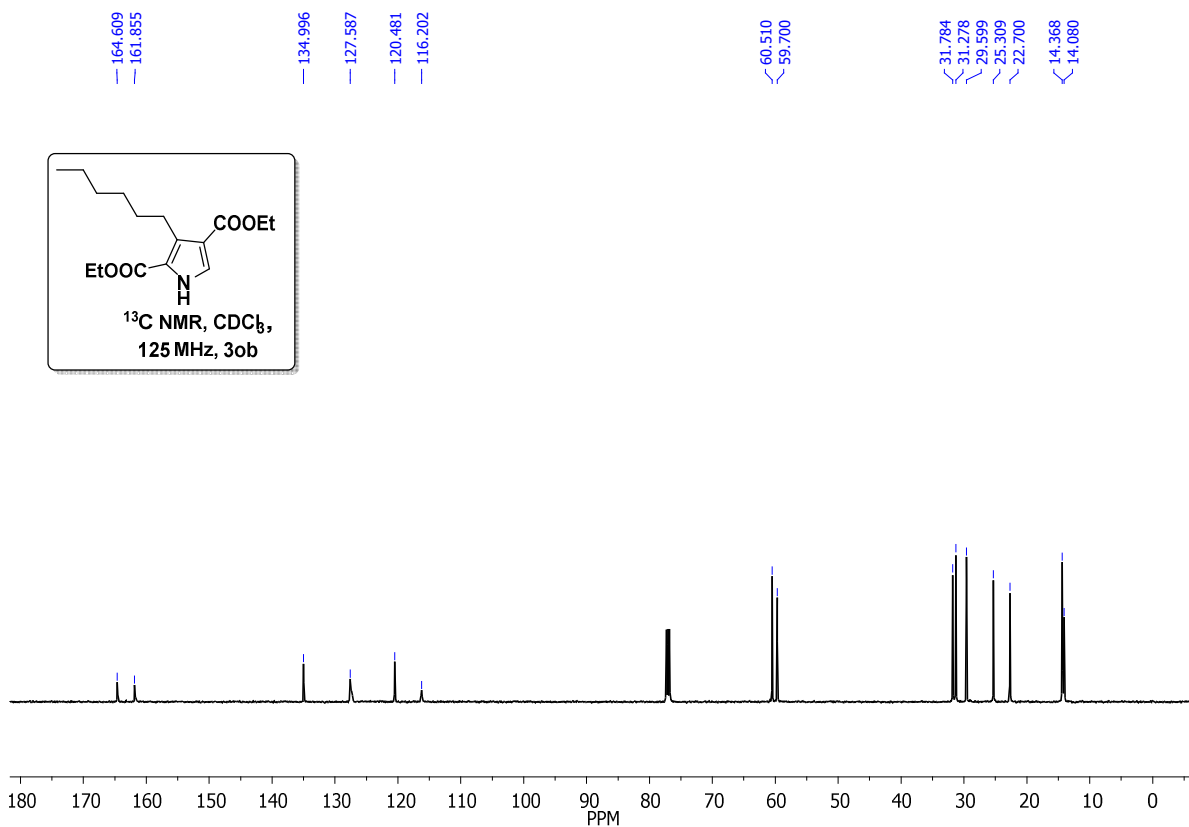
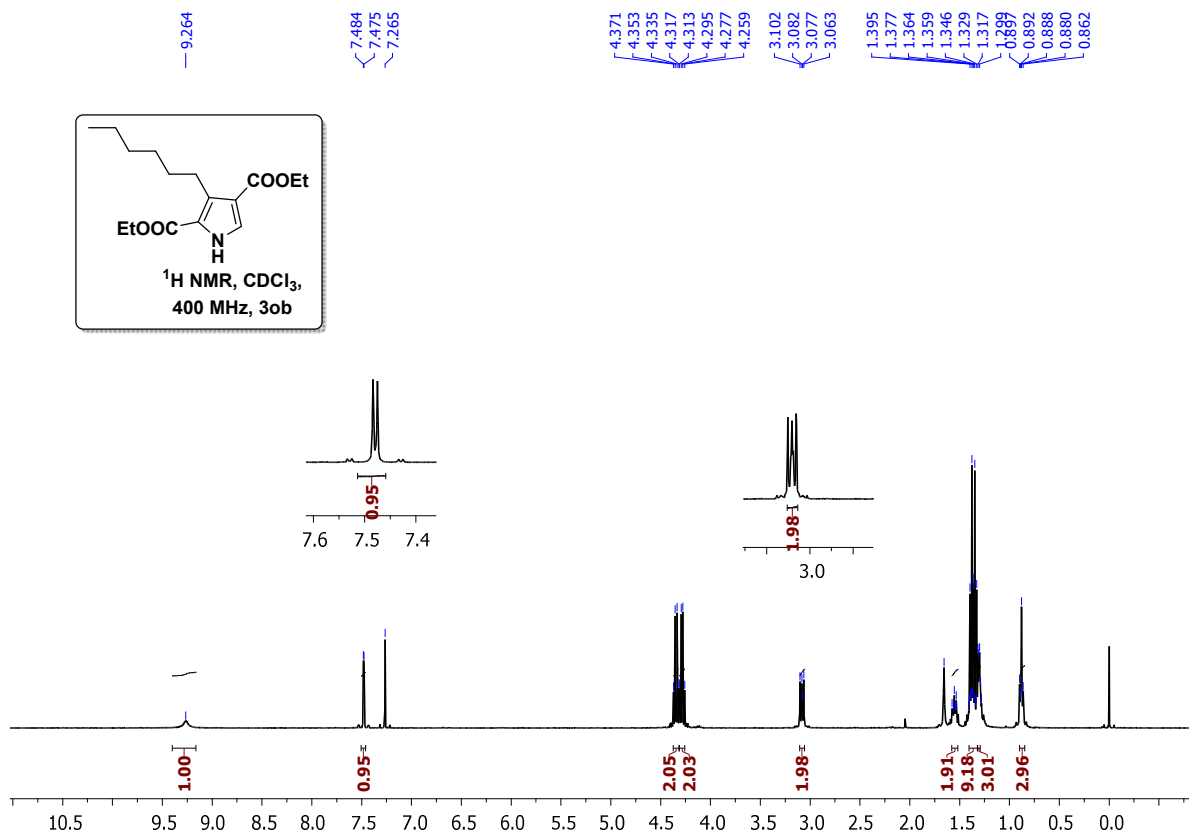
164.313, 161.371
 144.103, 141.446, 132.119, 130.800, 129.437, 129.258, 127.967, 127.638, 121.574, 121.385, 116.781
 84.165
 60.821, 59.916
 30.154
 14.338

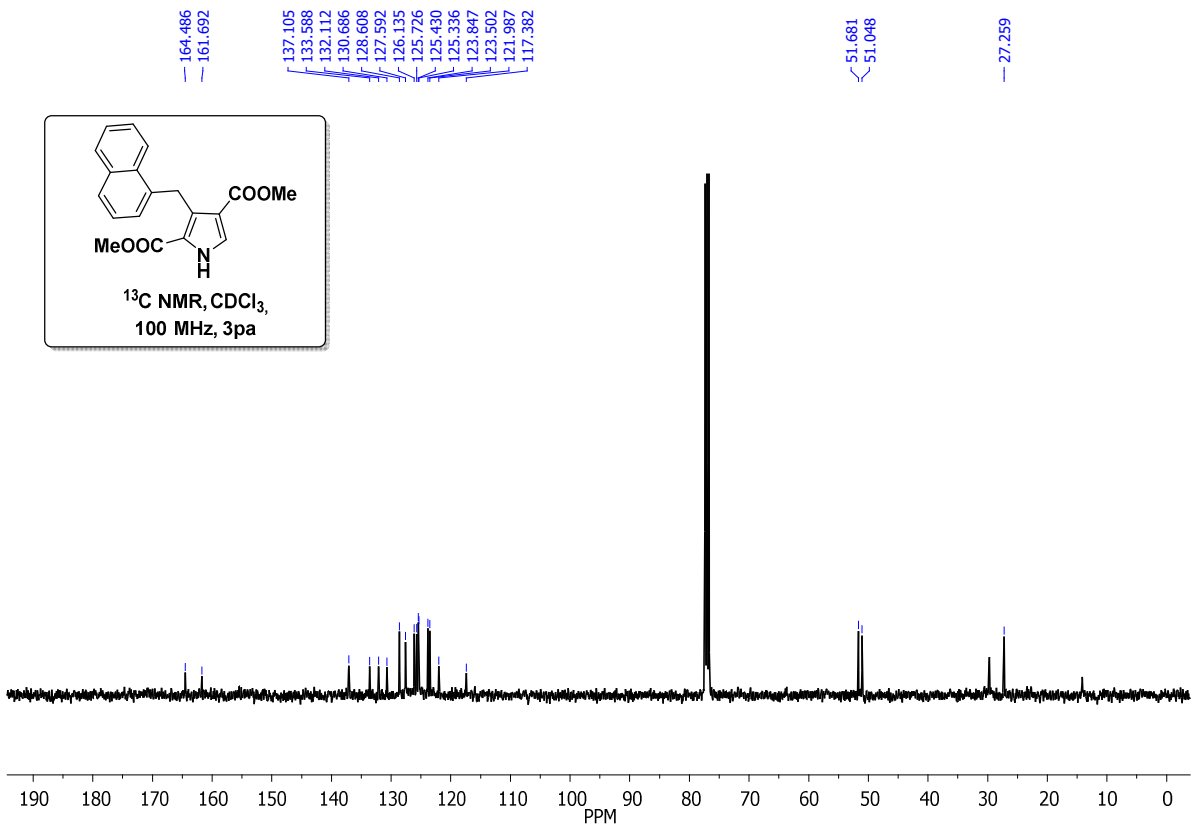
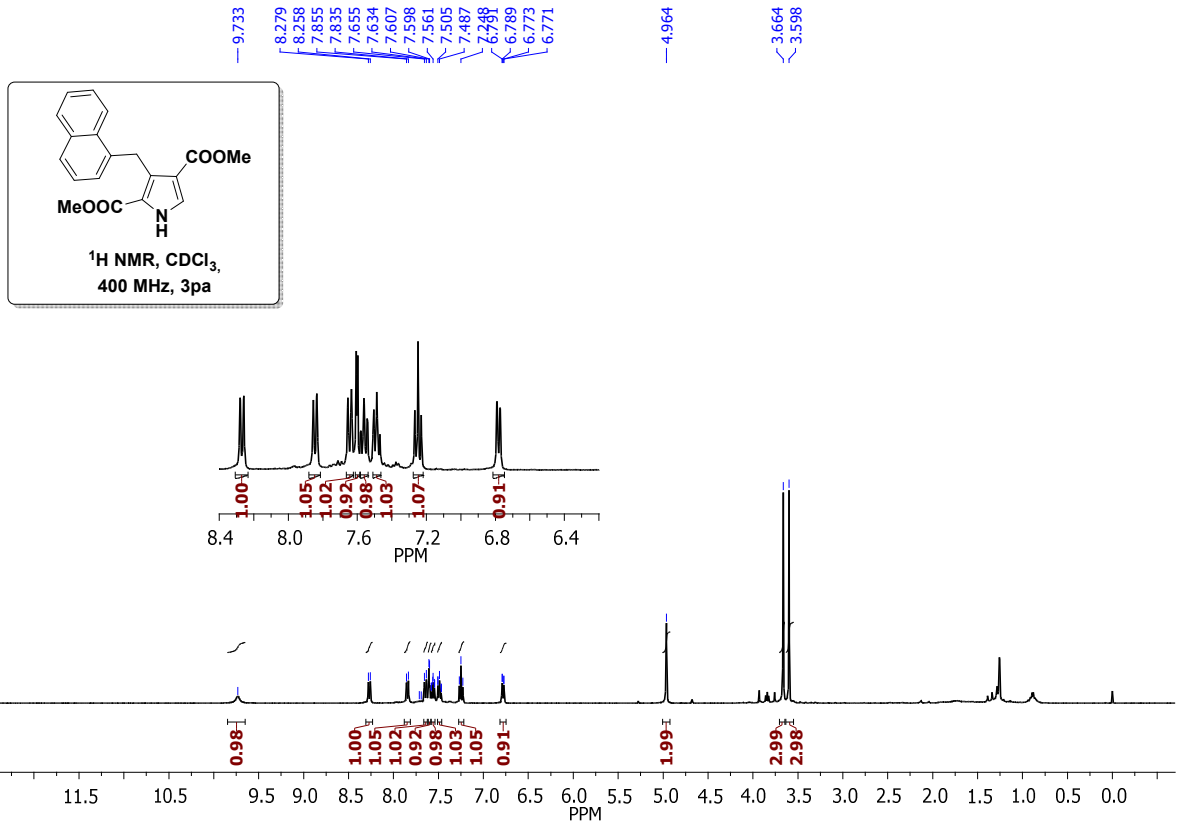


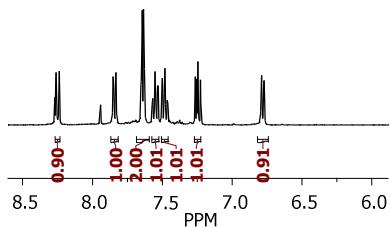
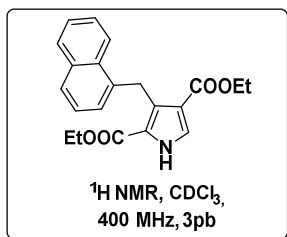








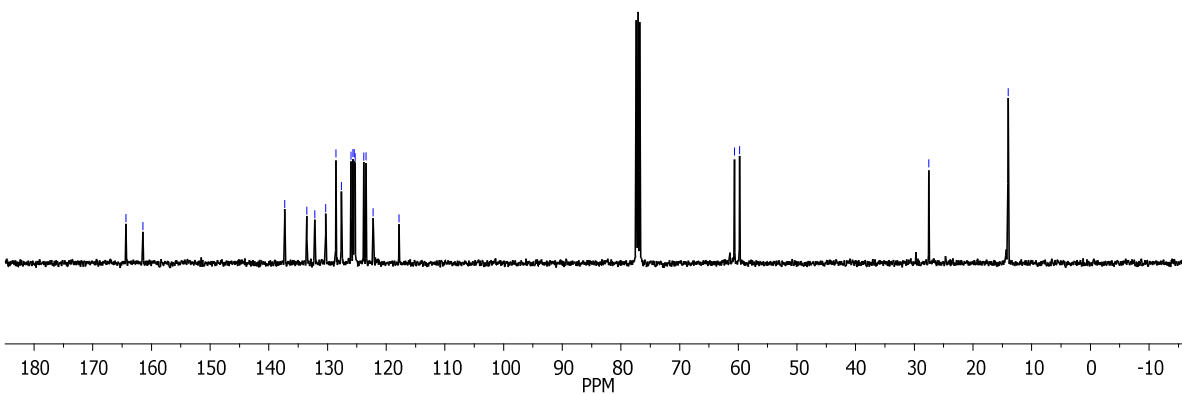
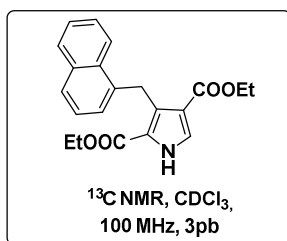
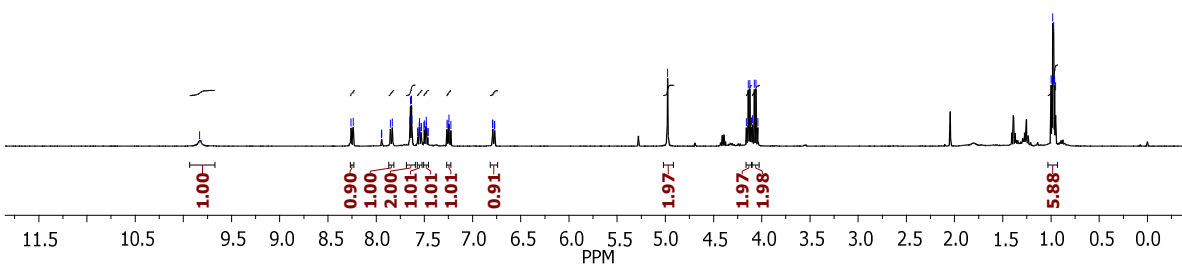




9.830
 8.259
 8.238
 7.852
 7.833
 7.649
 7.643
 7.634
 7.629
 7.551
 7.499
 7.482
 7.264
 7.254
 6.785
 6.789
 6.774
 6.771

4.976
 4.159
 4.141
 4.123
 4.106
 4.095
 4.078
 4.060
 4.042

0.999
 0.989
 0.981
 0.972
 0.963
 0.954



164.326
 161.471
 137.283
 133.530
 132.137
 130.298
 128.567
 127.617
 125.997
 125.657
 125.425
 125.285
 123.788
 123.420
 122.208
 117.806

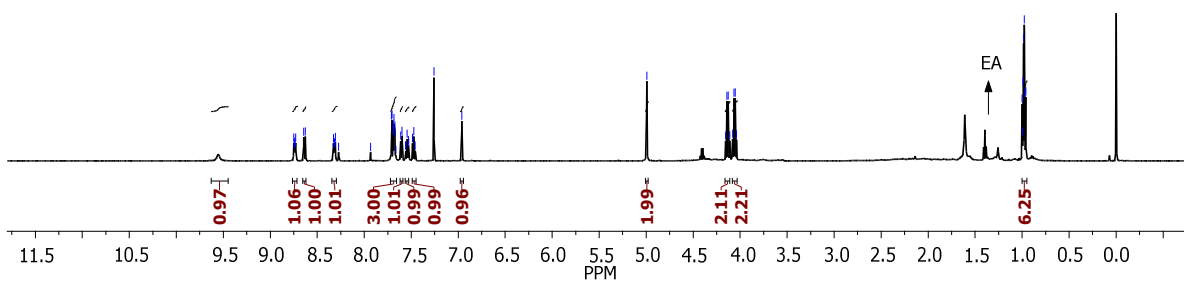
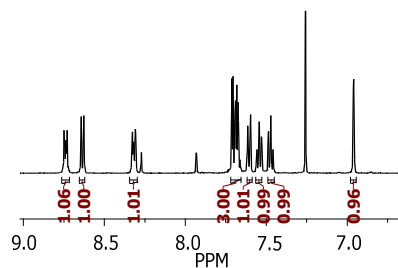
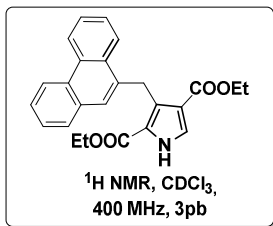
60.634
 59.787

27.543

14.010

8.748
8.745
8.738
8.735
8.729
8.643
8.627
8.327
8.322
8.318
8.311
8.308
8.272
7.932
7.712
7.705
7.693
7.690
7.682
7.675
7.672
7.613
7.598
7.560
7.558
7.544
7.530
7.527
7.487
7.485
7.471
7.458
7.258
6.994
4.155
4.140
4.126
4.112
4.080
4.066
4.052
4.037

0.999
0.996
0.990
0.985
0.976
0.971
0.961



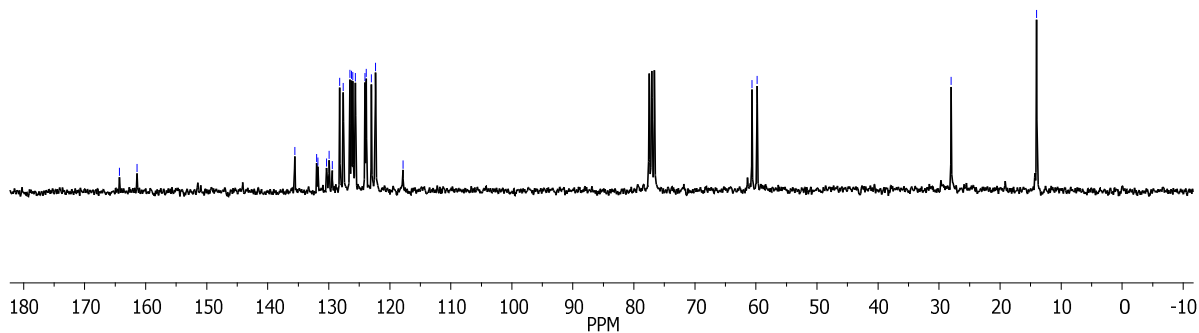
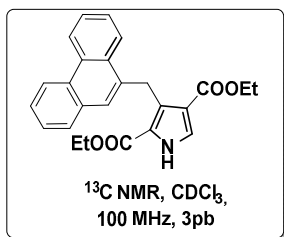
164.292
161.431

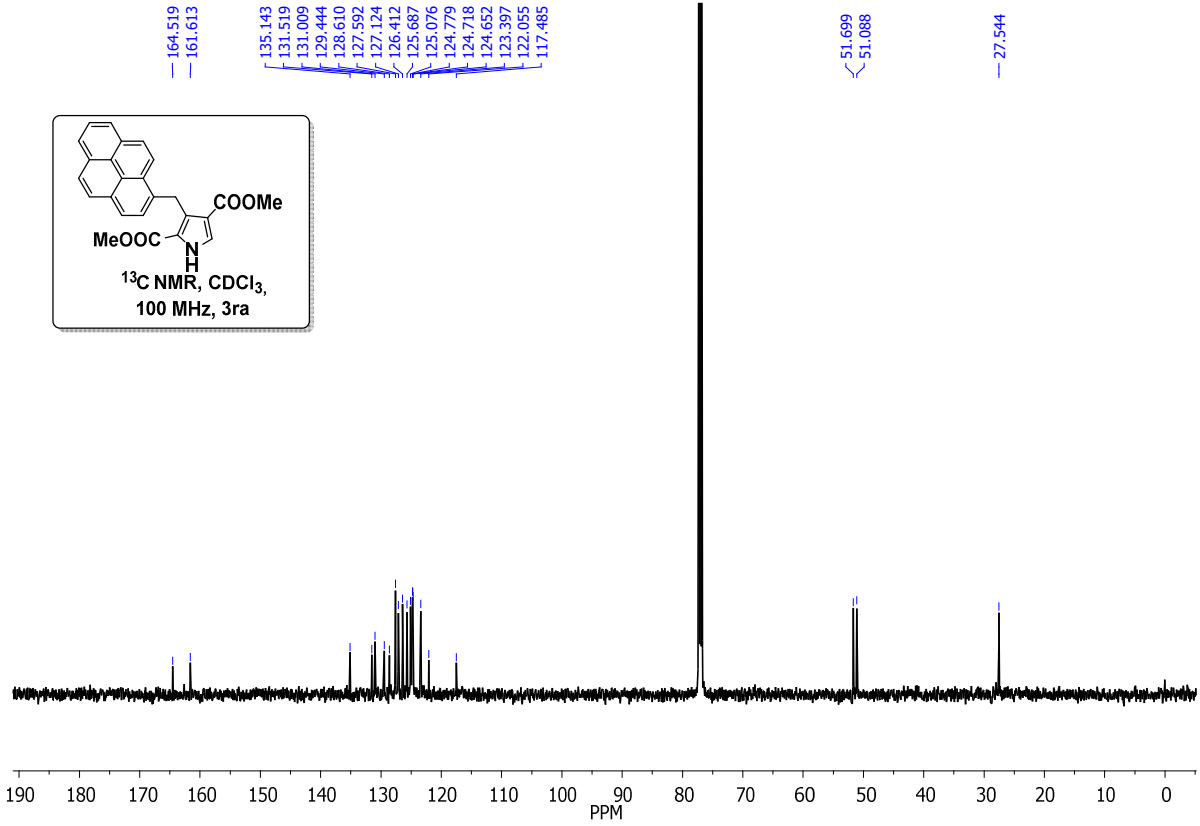
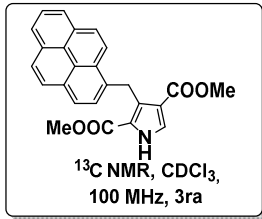
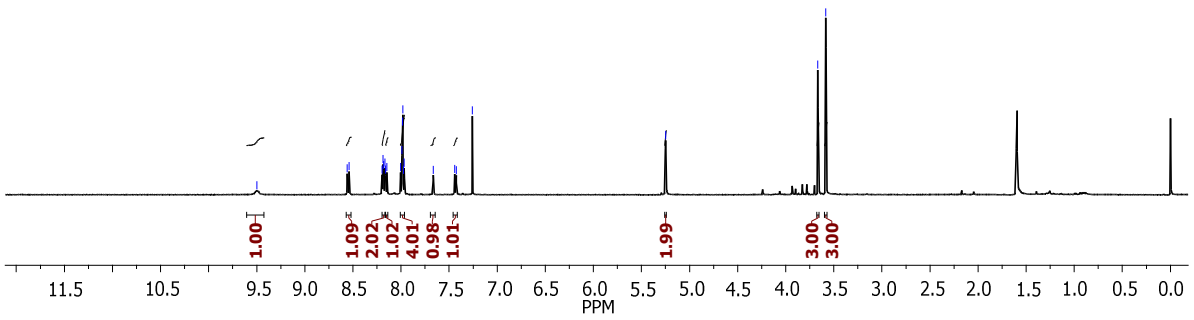
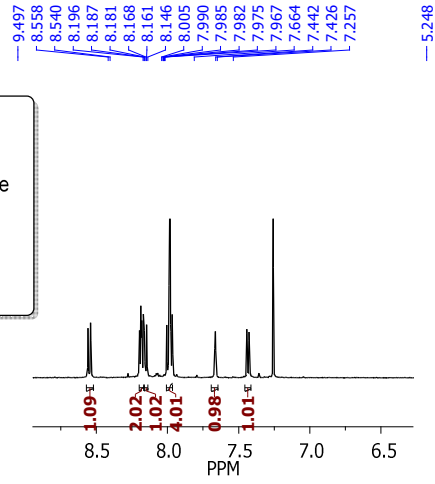
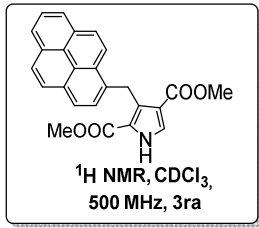
135.562
131.965
131.772
130.339
129.934
129.444
128.218
127.632
126.552
126.269
126.054
125.637
124.046
123.845
123.009
122.332
117.848

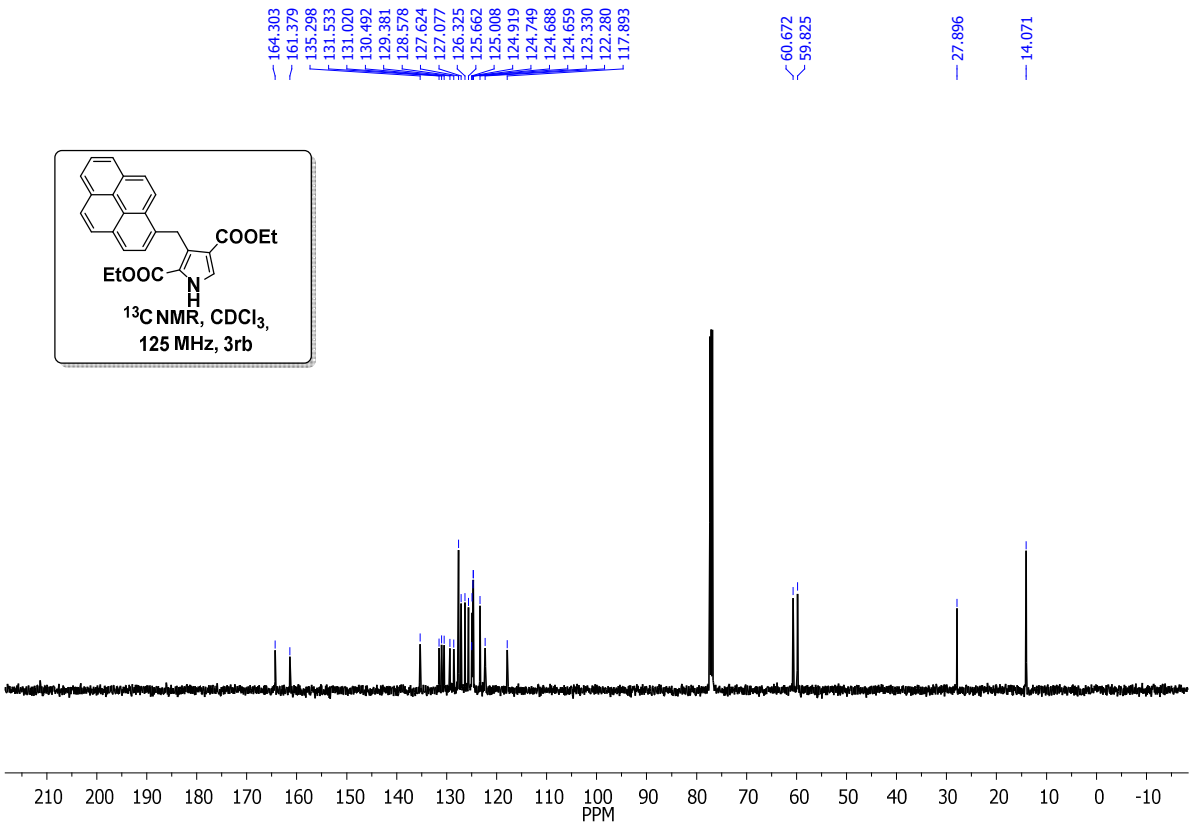
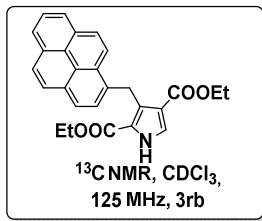
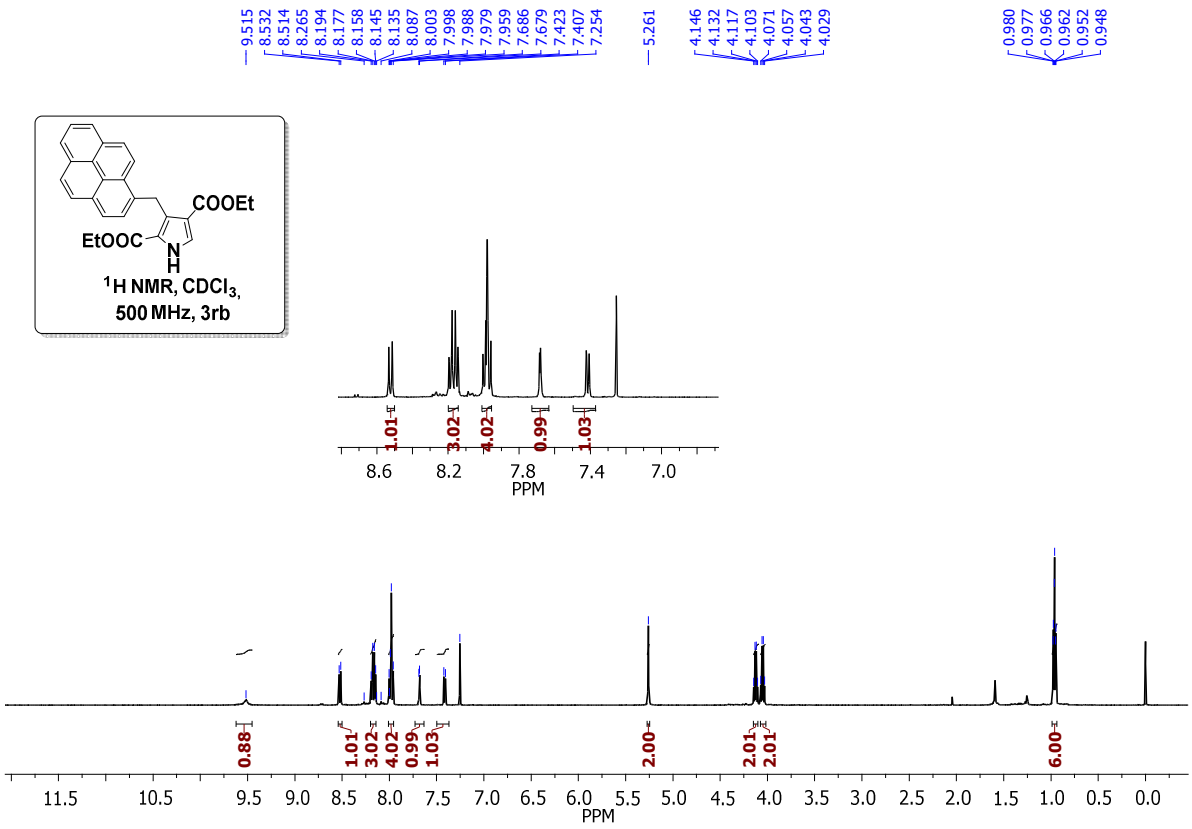
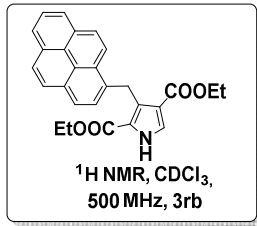
60.653
59.798

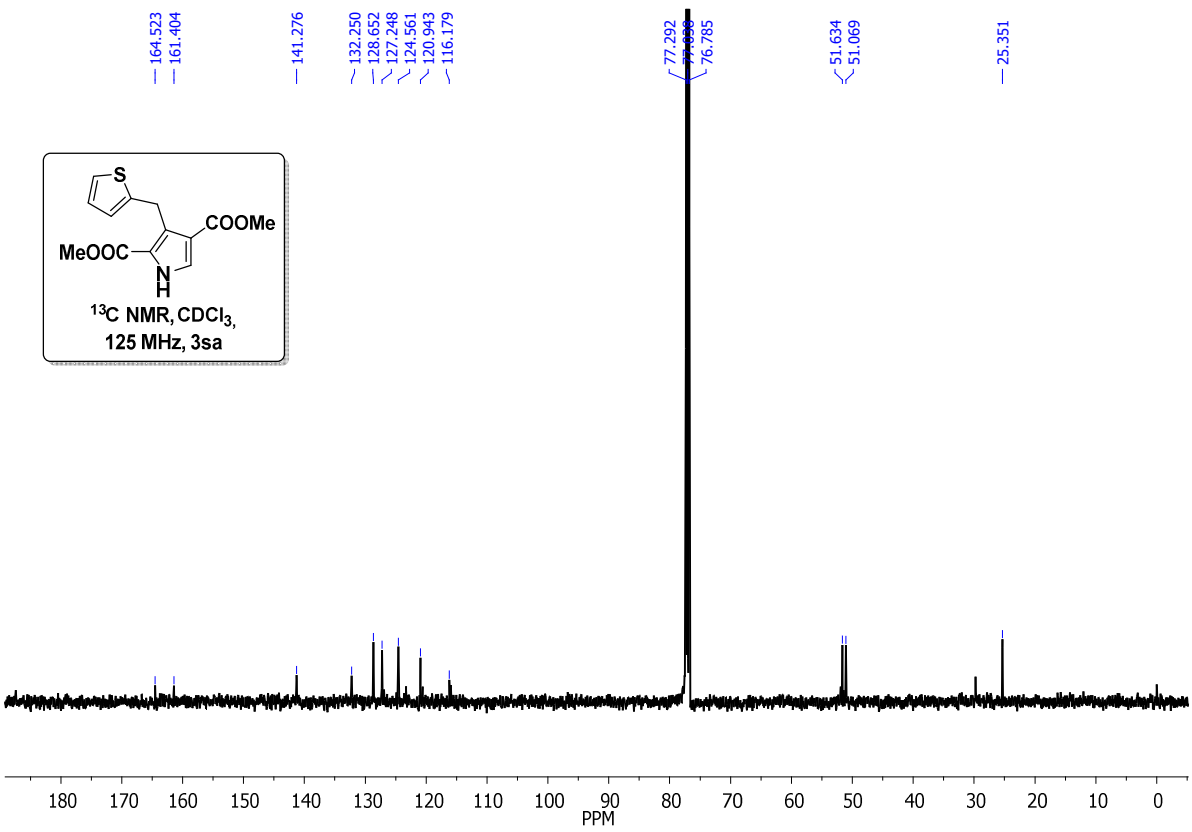
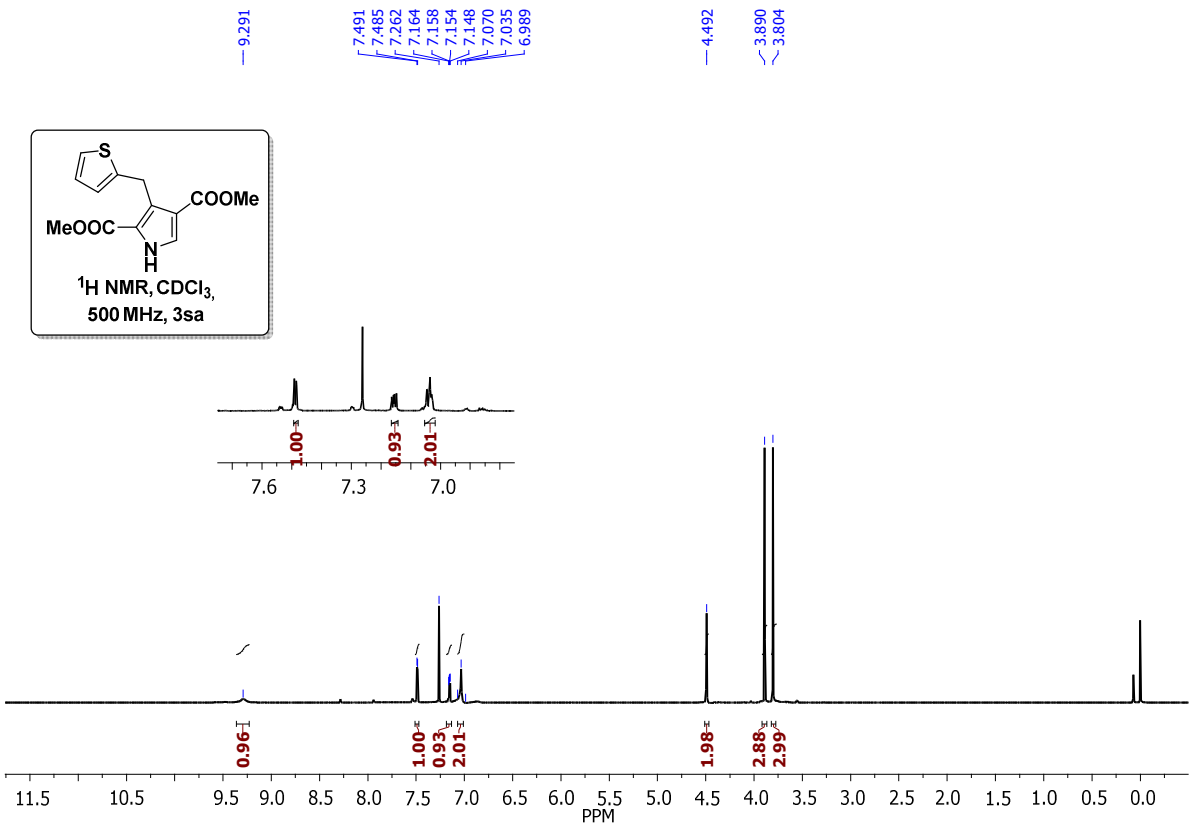
28.022

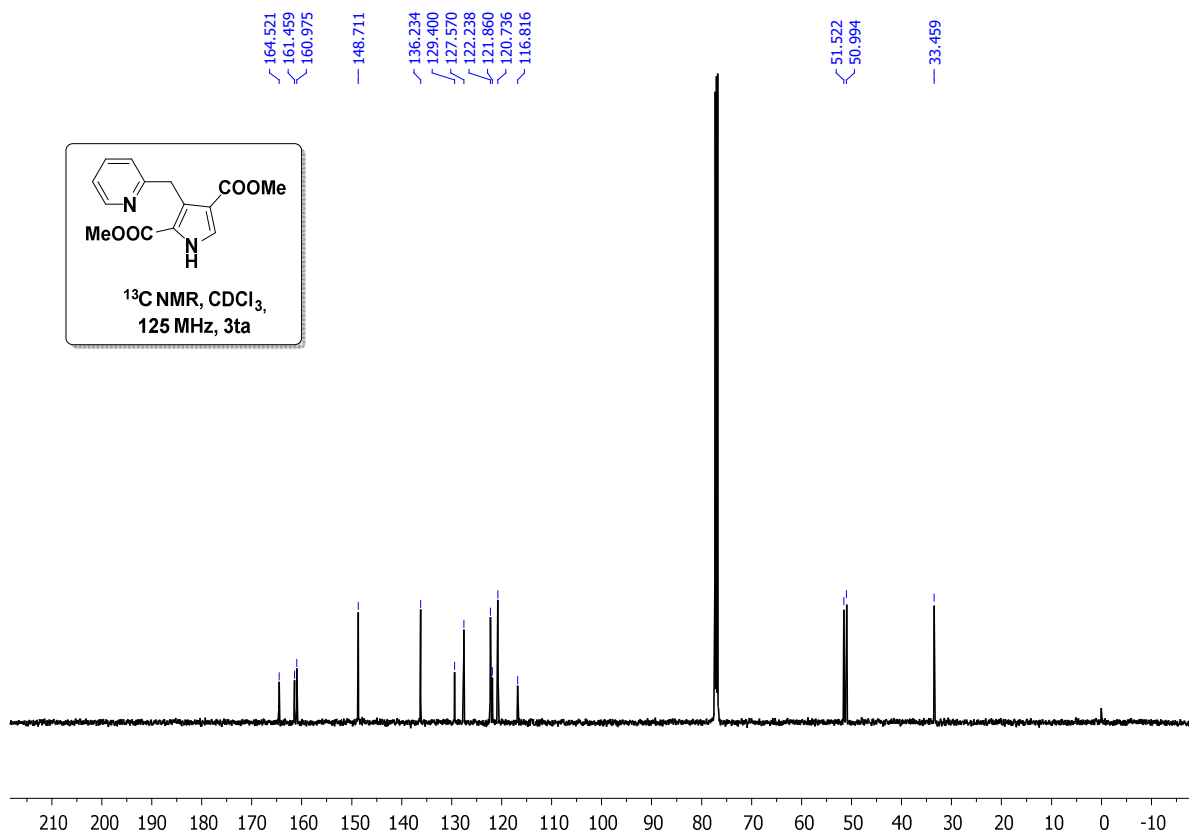
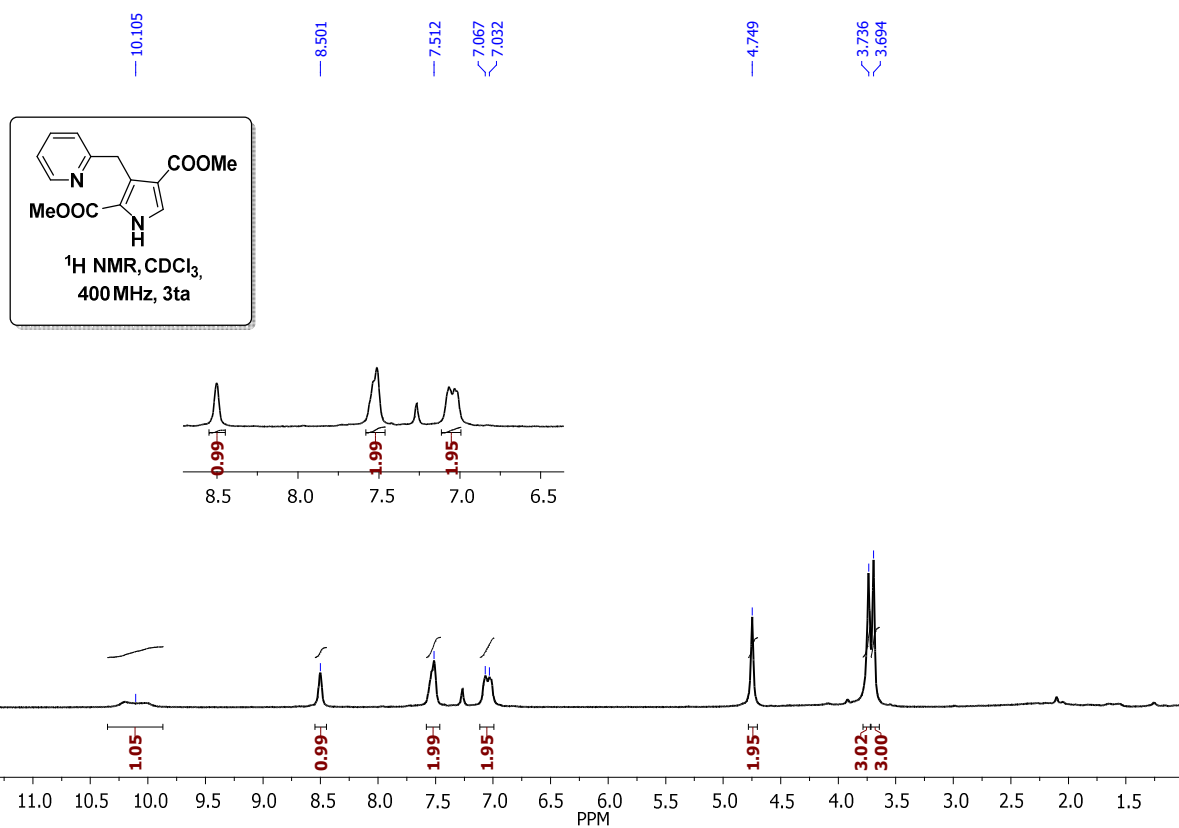
13.997

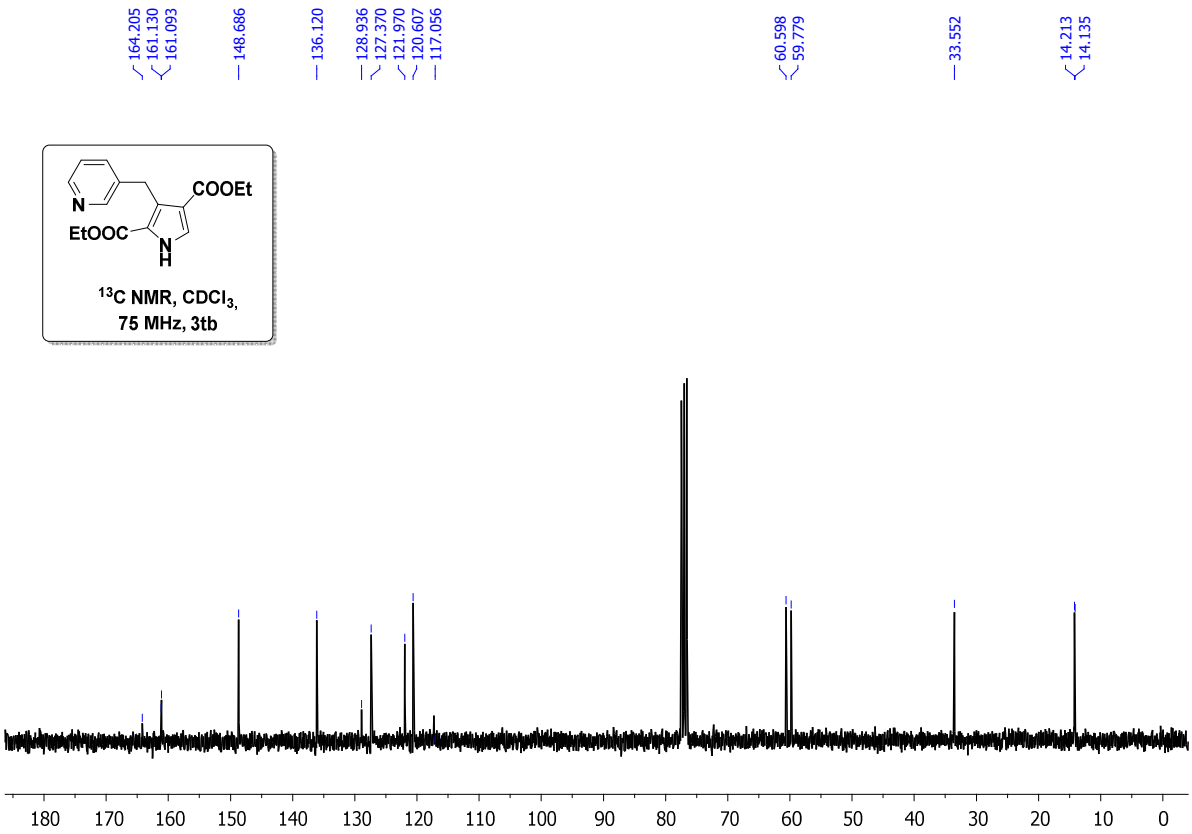
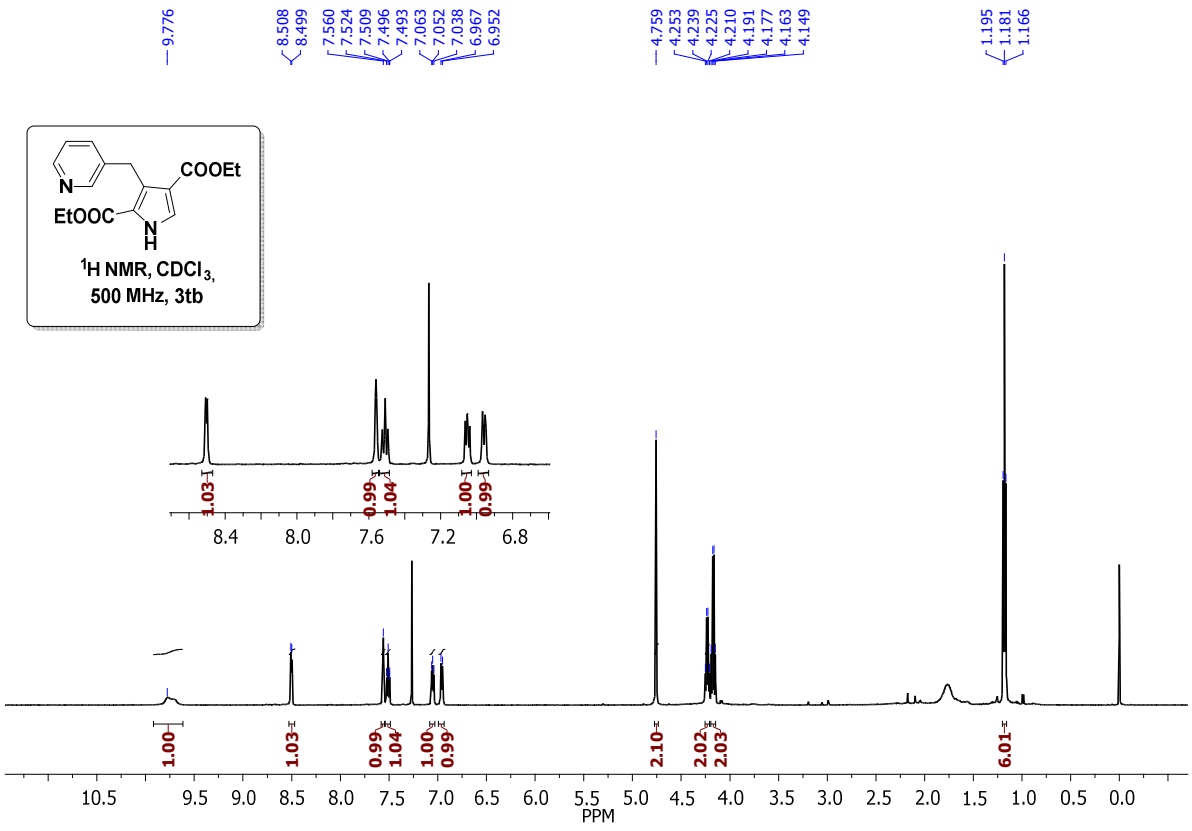


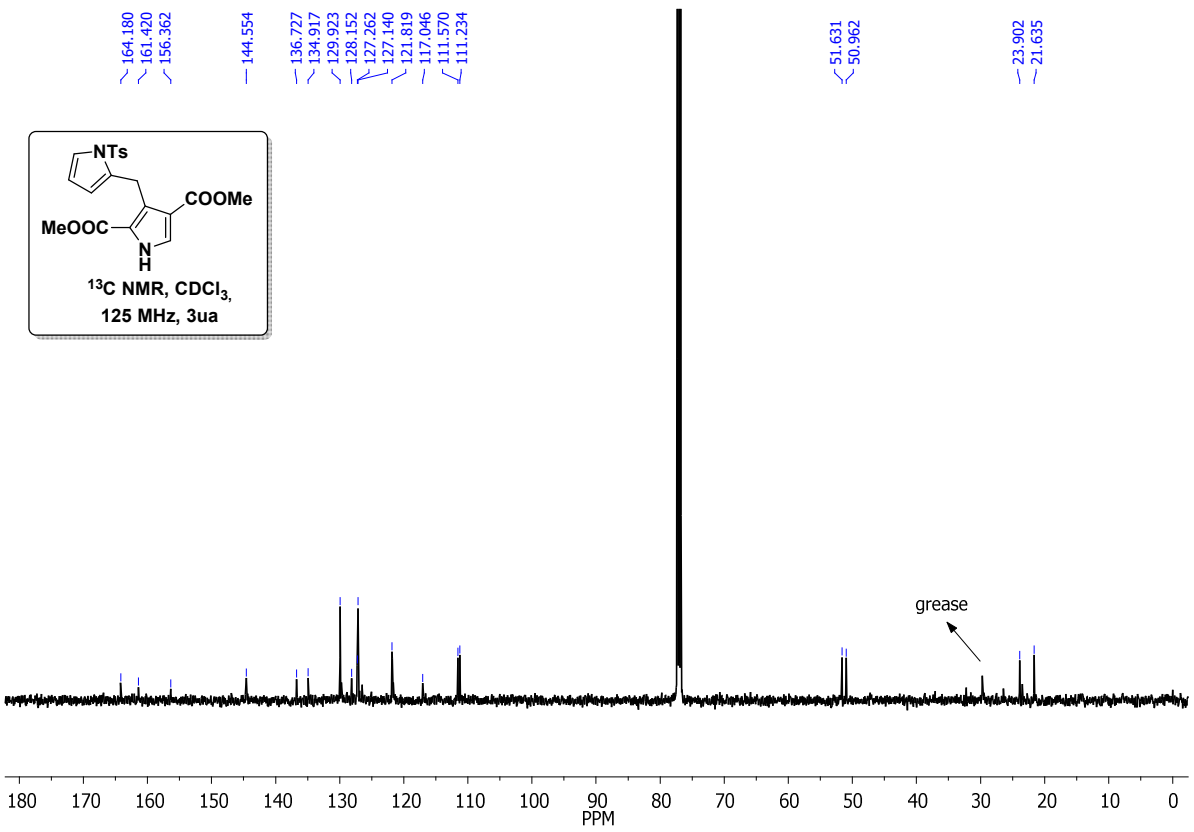
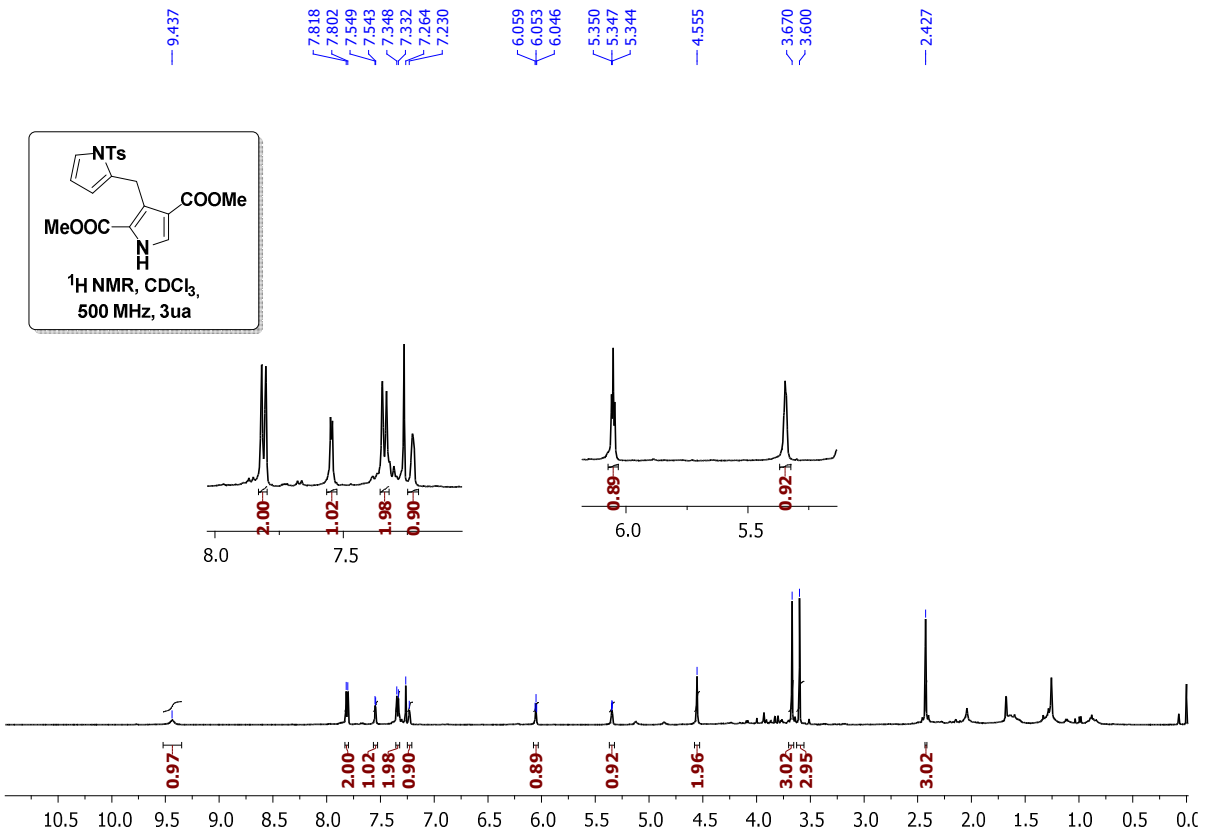


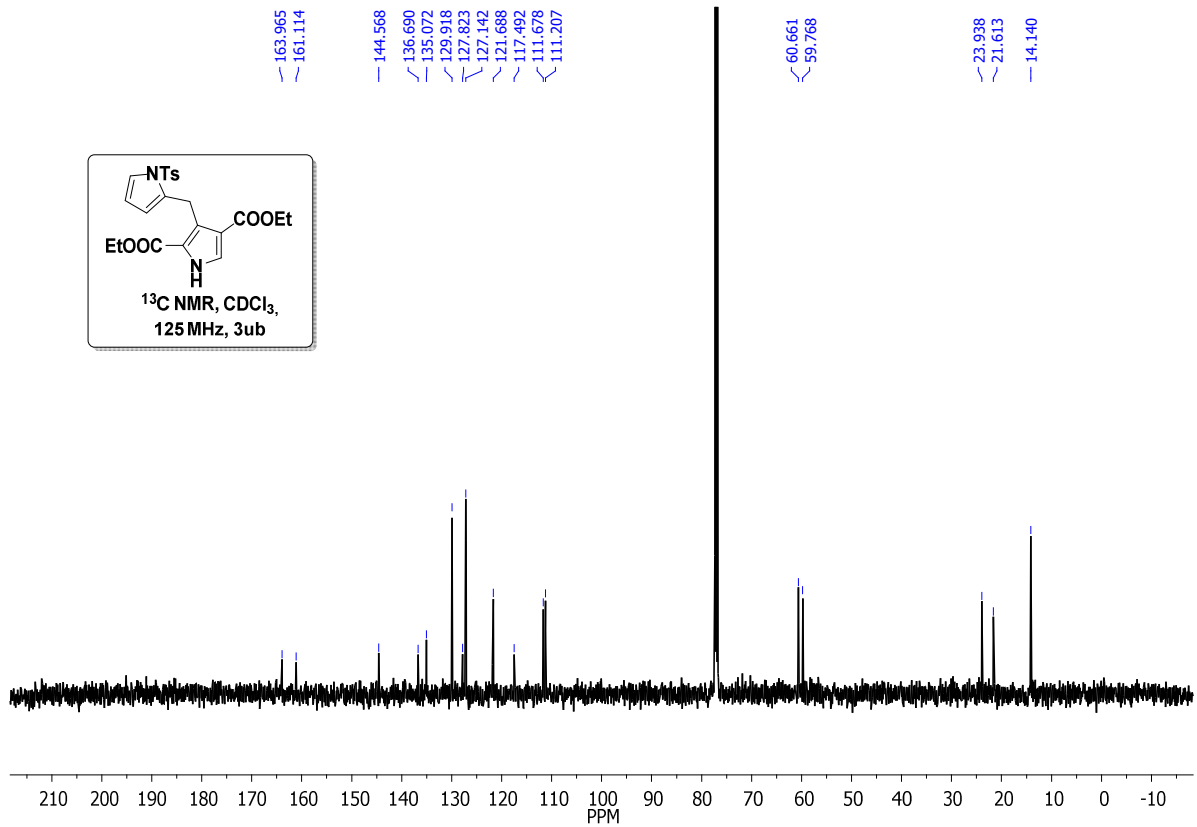
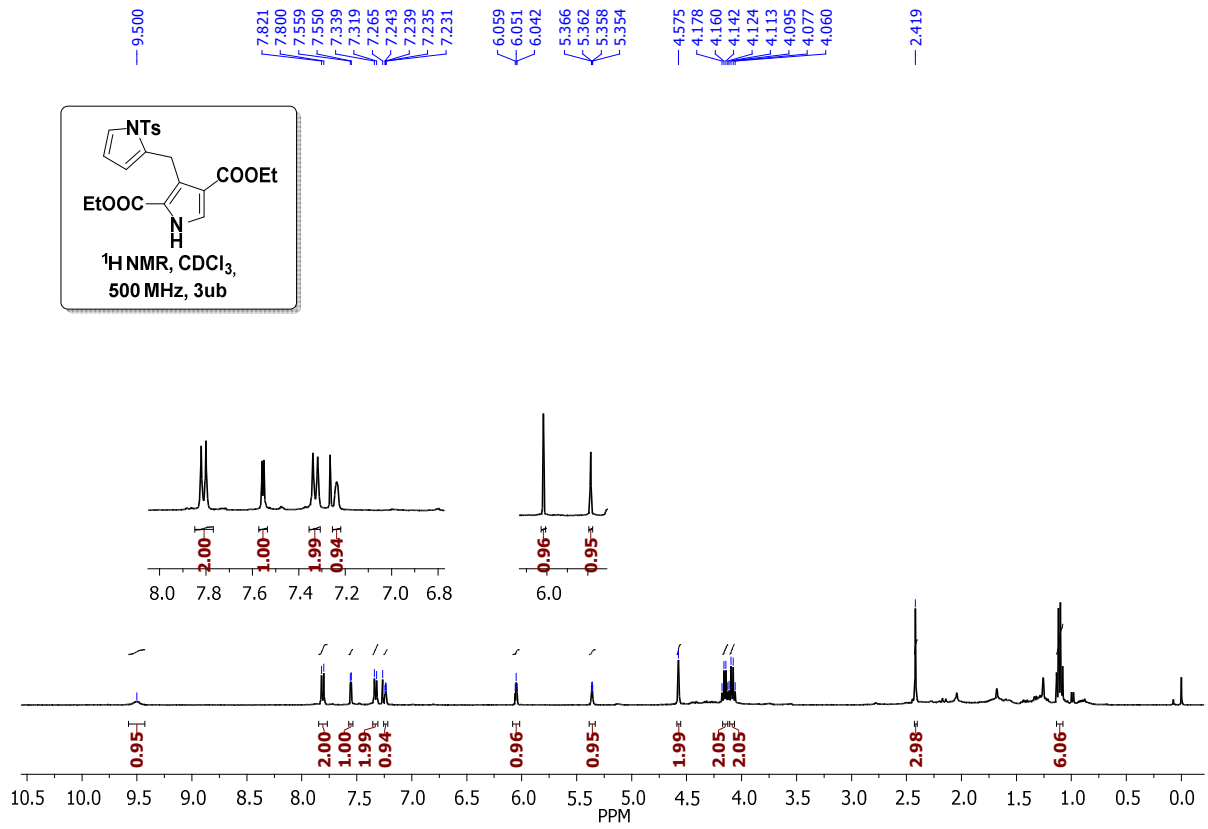


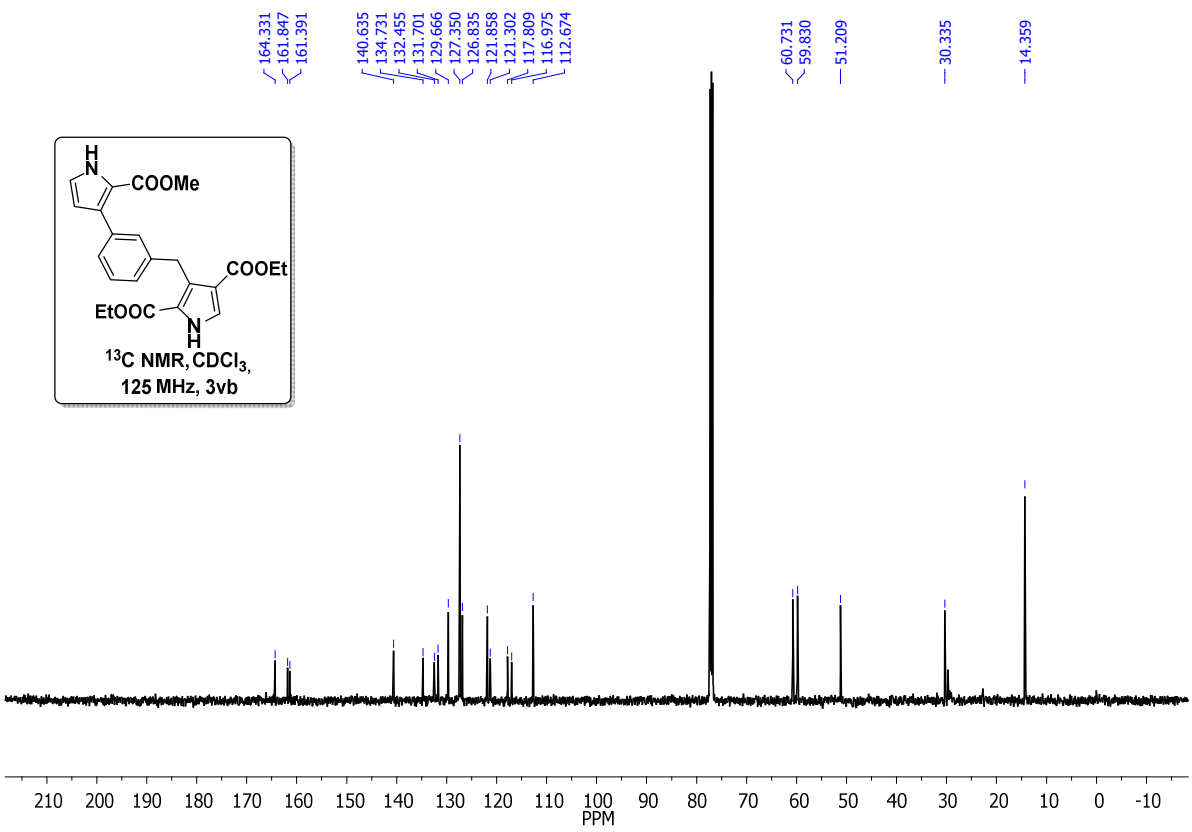
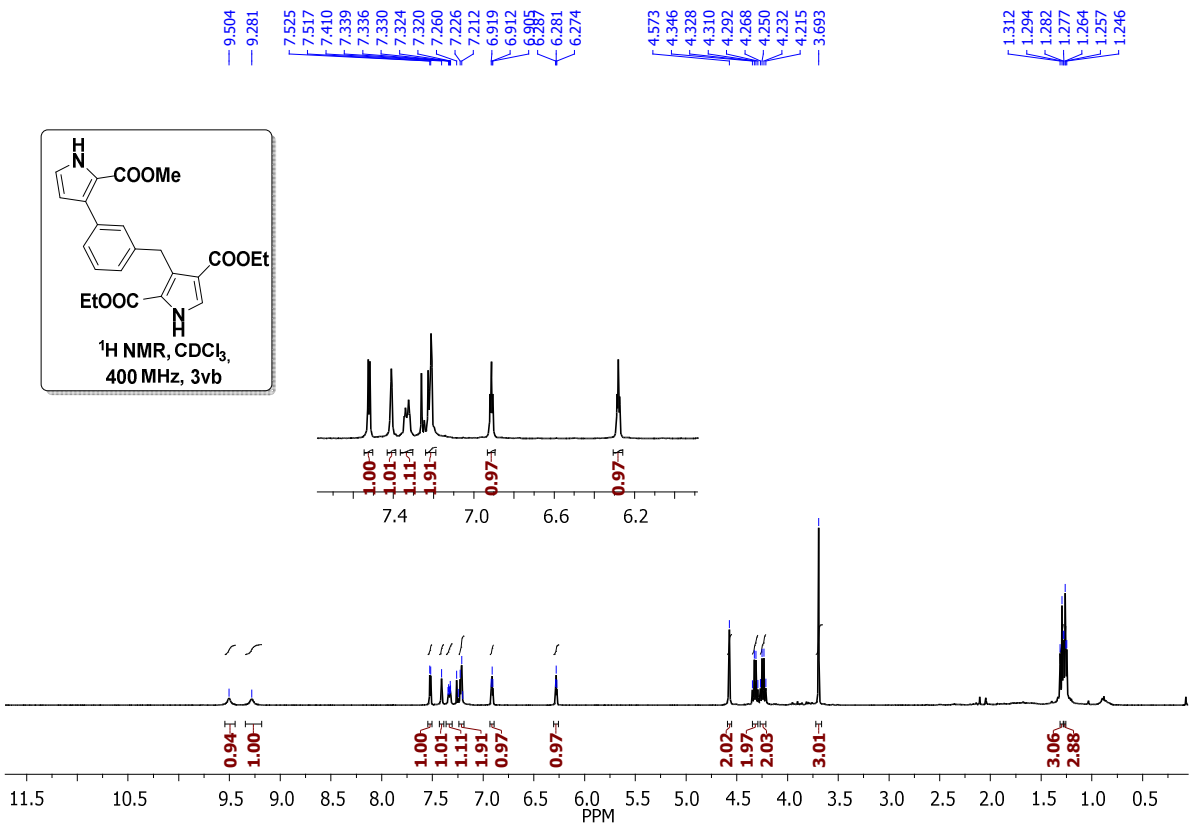












9. X-ray Data of Sample code BA-88 Compound No (3pa)

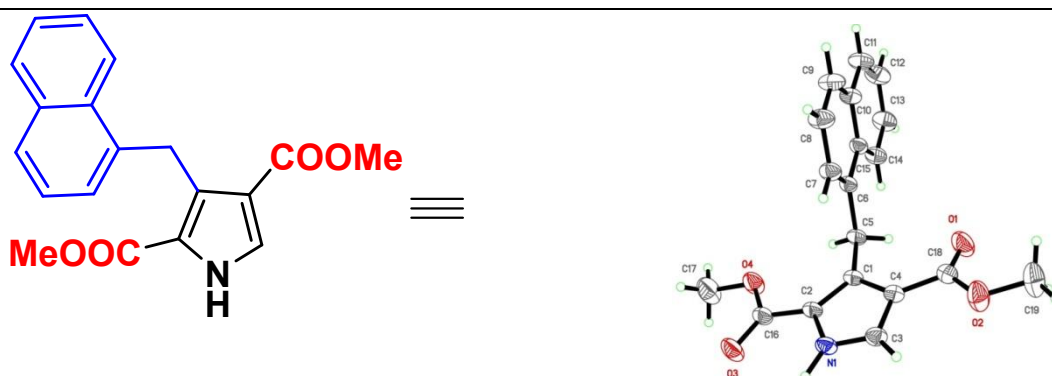


Figure ORTEP diagram of **3pa**: The molecular structure of **BA88**, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

X-ray data were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoK α radiation ($\lambda=0.71073\text{\AA}$) with ω -scan method.¹ Preliminary lattice parameters and orientation matrices were obtained from four sets of frames.

Integration and scaling of intensity data were accomplished using SAINT program.¹ The structures were solved by Direct Methods using SHELXS² and refinement was carried out by full-matrix least-squares technique using SHELXL.² Anisotropic displacement parameters were included for all non-hydrogen atoms. The hydrogen atom attached to nitrogen atom was located in a difference density map and refined isotropically. All other H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 \AA and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H or $1.2U_{\text{eq}}(\text{C})$ for other H atoms]. The methyl groups were allowed to rotate but not to tip.

Crystal Data for BA88: C₁₉H₁₇NO₄ ($M=323.33$): triclinic, space group P-1 (no. 2), $a = 8.9379(13)\text{\AA}$, $b = 10.7203(16)\text{\AA}$, $c = 11.0337(16)\text{\AA}$, $\alpha = 118.687(2)^\circ$, $\beta = 110.073(2)^\circ$, $\gamma = 93.964(2)^\circ$, $V = 835.3(2)\text{\AA}^3$, $Z = 2$, $T = 294.15\text{ K}$, $\mu(\text{MoK}\alpha) = 0.091\text{ mm}^{-1}$, $D_{\text{calc}} = 1.286\text{ g/mm}^3$, 9679 reflections measured ($4.414 \leq 2\theta \leq 56.942$), 3904 unique ($R_{\text{int}} = 0.0210$) which were used in all calculations. The final R_1 was 0.0580 ($I > 2\sigma(I)$) and wR_2 was 0.2191 (all data). CCDC 1442529 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or

from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

10. References:

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. (2015). *Acta Cryst.* C71, 3–8.
3. A. K. Morri, Y. Thummala, V. R. Doddi, *Org. Lett.* **2015**, *17*, 4640 – 4643.