Supporting Information

Divergent Synthesis of Pyrrole Carboxamides from Pyrrole Carboxaldehydes and Formamides /Amines via Oxidative Amidation Involving Pyrrole Acyl Radicals

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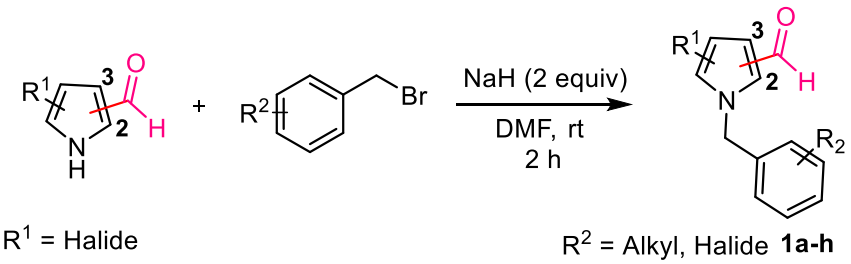
1. GENERAL CONSIDERATION

Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. The glassware to be used in the reaction was thoroughly washed and dried in an oven and the experiments were carried out with the required precautions. Reactions were monitored by TLC, which was performed with 0.2 mm Merck pre-coated silica gel 60 F254 Aluminium sheets. TLC plates were visualized with UV light and column chromatography was performed using silica gel (60-120, 100-200, or 230-400 mesh). New compounds were characterized by melting point, ^{1}H NMR, ^{13}C NMR, IR, and HRMS data. High-Resolution Mass Spectra (HRMS) were obtained using the Electron spin ionization (ESI) technique and as a TOF mass analyzer. All melting points were taken using a melting point apparatus equipped with a calibrated thermometer and are uncorrected. ^{1}H and ^{13}C spectra were recorded on Jeol 500, 600 MHz, and 125, 150 MHz NMR spectrometers in $CDCl_3$ and DMSO-d_6 with residual undeuterated solvent ($CDCl_3$: 7.26/7.00) using Me_3SiCl as an internal standard. Chemical shifts (δ) are given in ppm and *J* values are given in Hz, pattern was designated as s, singlet; bs, broad singlet; d, doublet; dd, doublet of doublet; dt, triplet of doublet; t, triplet; m, multiplet.

2. EXPERIMENTATION SECTION

(i) Representative procedure for *N*-benzylation of substituted pyrrole-2-carboxaldehyde (1a-1n)[1]

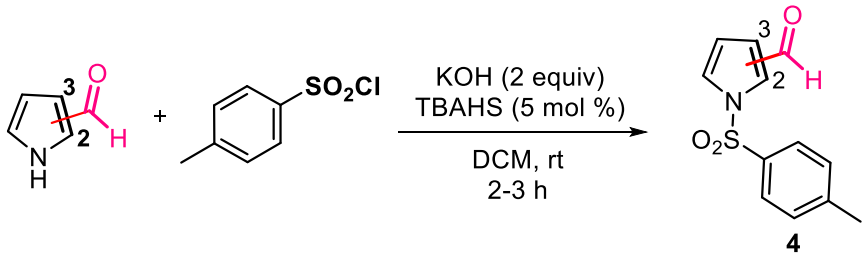


R^1 = Halide

R^2 = Alkyl, Halide **1a-h**

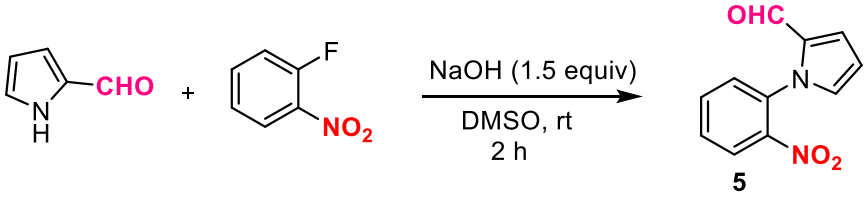
Following a literature protocol[1], a dried round bottom flask equipped with a magnetic stirrer bar was charged with substituted pyrrole-2-carboxaldehyde (1 mmol) and anhydrous DMF (3 mL) under inert condition. The reaction mixture was cooled down to 0 ºC and NaH (2 mmol) was added slowly. The benzyl bromide (1.1 mmol) was then added dropwise to the above reaction mixture and continued the stirring for 2 h. After completion of the reaction, the reaction mixture was quenched with cold water (10 mL) and extracted with EtOAc (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was triturated with pentane and dried to obtain the corresponding *N*-alkylated heterocycle **1a-n** in 96-98% yield.

(ii) Representative procedure for *N*-sulfonylation of pyrroles (4)[2]



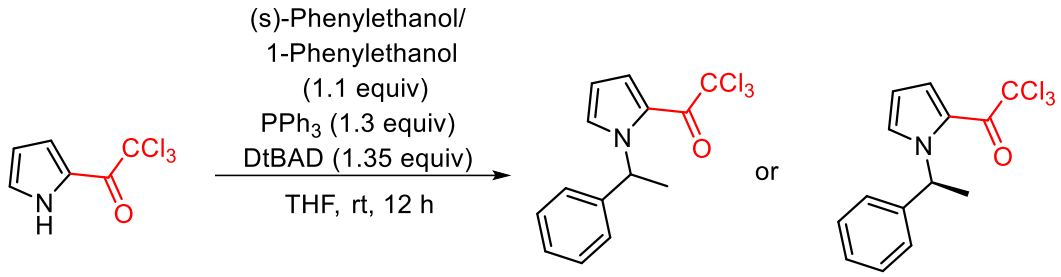
Following a literature procedure[3], to a stirred solution of substituted pyrrole-2-carboxaldehyde (0.5 mmol) in dichloromethane (2.5 mL) was added KOH (1 mmol) followed by addition of tetrabutylammonium hydrogensulfate (TBAHS) (0.025 mmol) and the resulting reaction mixture was allowed to stir at room temperature for 10 min. Further, a solution of 2-nitrobenzene sulfonyl chloride (0.6 mmol) in dichloromethane (1.0 mL) was added dropwise to the reaction mixture and stirred at room temperature until all the starting material was consumed. Water (10 mL) was then added and the aqueous layer was extracted with DCM (20 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by column chromatography [silica, EtOAc/hexanes = 1/9] which gave the desired *N*-sulfonylated pyrroles **4a** and **8a** in good yields of about 92% and 90% respectively.

(iii) Representative procedure for *N*-arylation of substituted pyrrole-2-carboxaldehyde (5)[3]



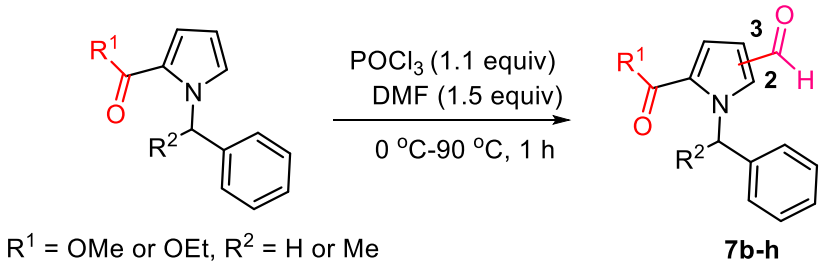
To a stirred solution of substituted pyrrole-2-carboxaldehyde (1 mmol) in DMSO (1 mL), NaOH (1.5 mmol) and 1-fluoro-2-nitrobenzene derivatives (1.1 mmol) were added slowly. The reaction mixture was then stirred vigorously for 2 h at room temperature. After completion of the reaction, as monitored by TLC, the reaction mixture was diluted with saturated brine solution and extracted with EtOAc (20 mL × 3). The organic layer was combined and dried over anhydrous sodium sulfate (Na_2SO_4). Finally, the solvent was evaporated under reduced pressure to obtain the desired product **5**. The crude products were triturated with pentane and DCM to get the analytically pure **5** in 99 % yield.

(iv) Representative procedure for mitsunobu reaction of 2-trichloroacetylpyrrole[4]



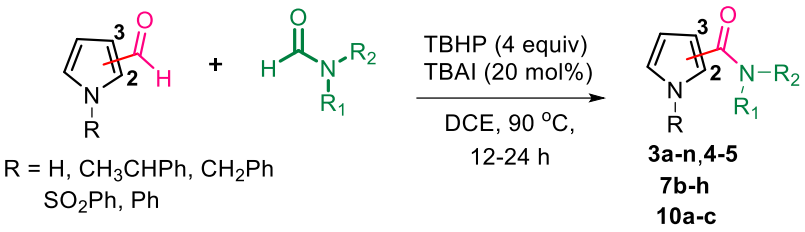
Following a literature procedure[4], an oven-dried round bottom flask equipped with a magnetic stir bar was charged with pyrrole substrate (1 mmol) and triphenylphosphine (1.3 equiv), following which nitrogen was flushed three times, and anhydrous THF (3 mL) was added. Then, (S)- phenyl ethanol/1-phenyl ethanol (1.1 equiv) dissolved in anhydrous THF (2 mL) was added dropwise under a nitrogen atmosphere. Then, Di-tert-butylazodicarboxylate (DtBAD) (1.35 equiv) dissolved in anhydrous THF (2 mL) was added under a nitrogen atmosphere. Then, the reaction was allowed to continue overnight. After that, diethyl ether was added and the reaction mixture was stirred for 1 hr which was then filtered and the filtrate was concentrated under reduced pressure followed by chromatography [silica, EtOAc-hexanes = 0.1:9.9 ~ 0.5:9.5] gave corresponding *N*-alkylated pyrrole in good yield.

(v) Representative procedure for formylation of substituted pyrroles (7b-7h)[5]



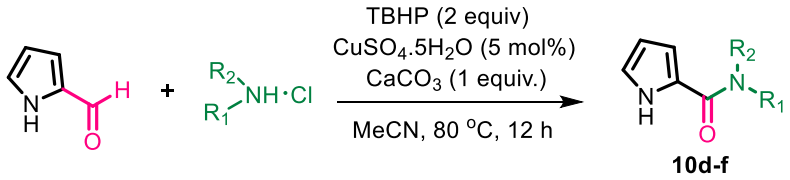
The Vilsmeier reagent was prepared by adding $POCl_3$ (5.0 mmol) dropwise to ice-cold dry DMF (5 mL) under stirring. The mixture was then stirred for 10-15 min at 0 °C. To the above Vilsmeier reagent was added substituted pyrrole (1.0 mmol) as a solution in DCE (5.0 mL). Then the mixture was allowed to warm to 100 °C and was stirred for 1.0 h. After the starting material was consumed (monitored by TLC), the reaction mixture was poured into saturated sodium chloride aqueous (50 mL). The mixture was extracted with dichloromethane (3 × 20 mL), and the combined organic phase was washed with water (3 × 20 mL), dried over MgSO4, filtered, and concentrated in a vacuum. The crude product was triturated and washed with pentane to give the desired product.

(vi) General procedures for amides (3a-3n), (4,5), (7b-7h), (10a-10c)



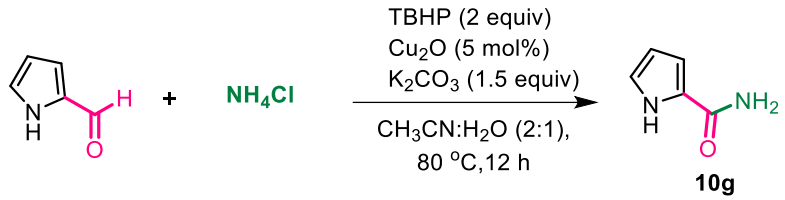
The aldehyde (0.5 mmol), *N*,*N*-disubstituted formamide (2.5 mmol), Bu_4NI (0.1 mmol, 20 mol%), TBHP (2.9 mmol, 0.4 mL of a 70% aqueous solution), and dichloroethane (2.0 mL) were added to a test tube in air. The reaction mixture was heated in an oil bath at 90 °C for 12-24 h and was quenched with a saturated solution of Na_2SO_3, for removal of excess TBHP. The mixture was extracted with dichloromethane (3 × 20 mL), and the combined organic phase was washed with water (3 × 20 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, Ethyl acetate: Hexanes = 4:6 to 8:2) to give the desired product.

(vii) General procedure for the oxidative amidation of aldehydes with primary amine hydrochloride salts (10d-10f)



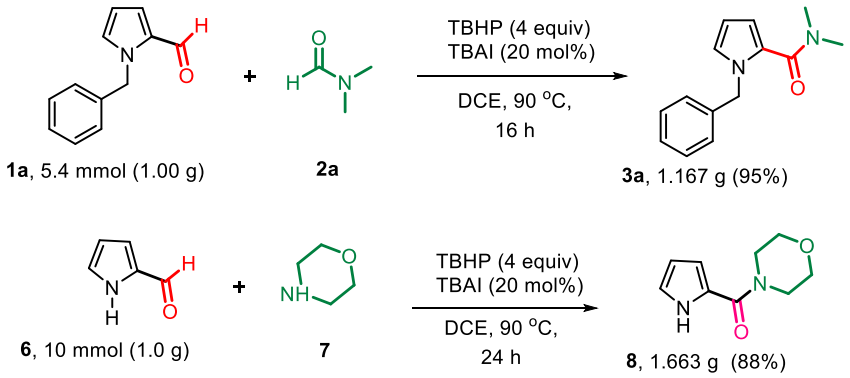
To a mixture of $CuSO_4 \cdot 5H_2O$ (12.5 mg, 0.05 mmol, 5.0 mol %), primary amine hydrochloride salt 2 (1.2 mmol, 1.2 equiv), and $CaCO_3$ (110 mg, 1.1 mmol, 1.1 equiv) in acetonitrile (0.2 mL) were added aldehyde1 (1 mmol, 1 equiv) and TBHP (70 wt % in H2O, 0.16 mL, 1.1 mmol,1.1 equiv) under argon atmosphere at room temperature. The reaction vessel was capped and allowed to stir at room temperature overnight. The volatiles were removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, Ethyl acetate: Hexanes = 6:4 to 8:2) to obtain the amide product. All secondary amides were identified by full spectroscopic characterization and comparison with literature or analogous literature data.

(viii) General procedure for the conversion of aldehydes to primary amides (10g)



To a mixture of Cu_2O (7 mg, 0.05 mmol, 5.0 mol %), NH_4Cl (134 mg, 2.5 mmol, 2.5 equiv), and K_2CO_3 (207 mg, 1.5 mmol, 1.5 equiv) in acetonitrile (0.2 mL) and water (0.1 mL) were added an aldehyde 1 (1 mmol, 1 equiv) and TBHP (70 wt % in H_2O, 0.22 mL, 1.5 equiv) under argon atmosphere at room temperature. The reaction vessel was capped and allowed to stir for 4 h at 80 °C. The reaction mixture was then concentrated and purified by silica gel column chromatography (silica gel, Ethyl acetate: Hexanes = 9:1)to provide the corresponding primary amide

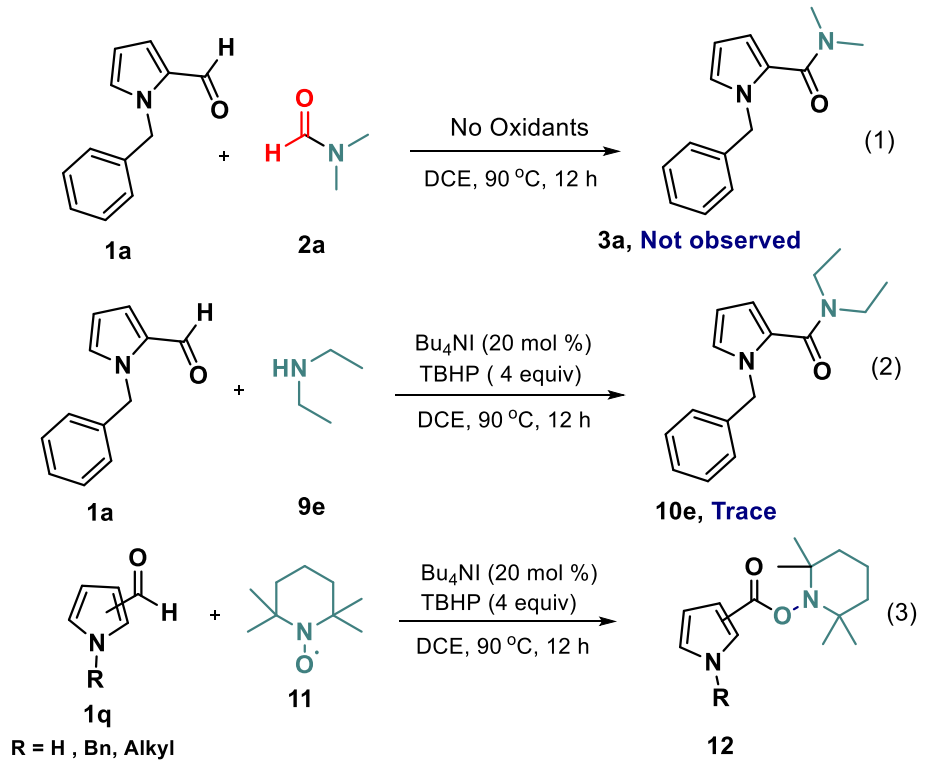
(ix) General procedure for the scale up reactions



To a clean dried test tube was added aldehyde (5.4 mmol/10 mmol), *N*,*N*-disubstituted formamide (27 mmol/50 mmol), Bu_4NI (1 mmol/ 2 mmol), TBHP (21.6 mmol/40 mmol, 4.32 mL/8 mL of a 70% aqueous solution), and dichloroethane (21.6 mL). The reaction mixture was heated in an oil bath at 90 °C for 12-24 h and was quenched with a saturated solution of Na_2SO_3 (for removal of excess TBHP) and extracted with ethyl acetate. The organic solvent was removed under vacuum and purification by chromatography (silica gel) afforded the desired product.

(x) Peripheral discussion on reaction mechanism

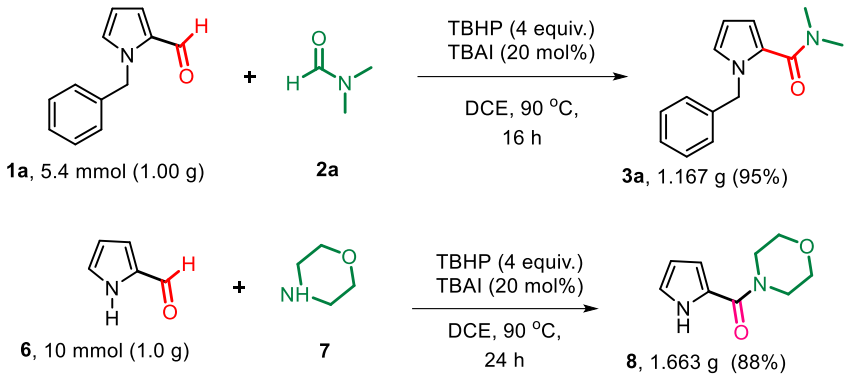
The possible reaction pathway for the reaction is shown in the scheme no. 5 mentioned in the manuscript. Some control experiments were carried out in order to get basic insights into the reaction mechanism. Initially the reaction was attempted with *N*-benzylated pyrrole-2-carboxaldehyde (**1a**) and *N,N* dimethylformamide (DMF) in the absence of oxidant and heated with dichloroethane as solvent under 90 ^{o}C, however, desired product formation could not be seen. Next, the reaction was tried with (**1a**) and dimethylamine (**9e**) under standard reaction conditions, but desired product formation could not be seen due to the inability of dimethyl amine to form *N* centered radical and this suggests that along with acyl radical *N* centered radical is needed to form corresponding amide (**10e**). Furthermore, pyrrole acyl radical was trapped with TEMPO as a radical scavenger forming the corresponding pyrrole acyl radical adducts and this experiment suggests the reaction proceeds via a radical pathway. On gaining confidence with these control experiments, the plausible mechanism is proposed in the paper.



Scheme 1 Control experiments

(xi) Calculation of Process Mass Intensity (PMI)

The PMI of the oxidative amidation is calculated by considering the reaction below.



Process Mass Intensity (PMI)

$$PMI = \frac{\text{Total mass used in the process step (Kg/g)}}{\text{Mass of product (Kg/g)}}$$

$$\mathbf{PMI_1} = \frac{\text{1.00gm (wt. of } \mathbf{1a}\text{) + 1.971gm (wt. of DMF) + 398.52 gm (wt. of } {}^{n}Bu_4NI\text{) + 1.987 gm (wt. of TBHP) + 26.25 gm (wt. of DCE)}}{\text{1.167gm (wt. of product formed)}}$$

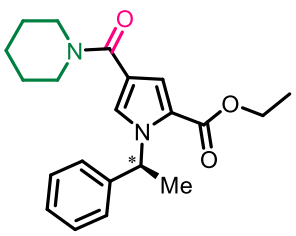
= **30.65 gm/gm**

$$\mathbf{PMI_2} = \frac{\text{1.00gm (wt. of } \mathbf{6}\text{) + 4.578gm (wt. of } \mathbf{7}\text{) + 738 gm (wt. of } {}^{n}Bu_4NI\text{) + 3.680 gm (wt. of TBHP) + 26.25 gm (wt. of DCE)}}{\text{1.25gm (wt. of product formed)}}$$

= **18.325 gm/gm**

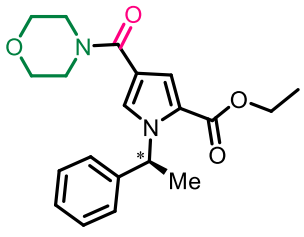
(xii) Specific Rotation

The specific rotation of the (R) isomer of molecules (**7g**) and (**7h**) were recorded on Rudolf Polarimeter, Model-Autopol-V at wavelength- 365nm.



7h

$[\alpha]_D$ = -190

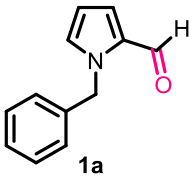


7i

$[\alpha]_D$ = -202

3. CHARACTERIZATION DATA

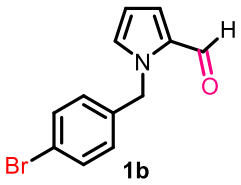
1-Benzyl-1*H*-Pyrrole-2-carbaldehyde (1a)[1]



1a

Brown oily liquid (185 mg, 99%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.56 (s, 1H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.26 (dd, *J* = 6.4, 4.1 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 2H), 6.97 (d, *J* = 3.3 Hz, 2H), 6.27 (t, *J* = 3.1 Hz, 1H), 5.56 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 179.6, 137.6, 131.5, 128.8, 127.8, 127.3, 124.9, 110.2, 52.0.

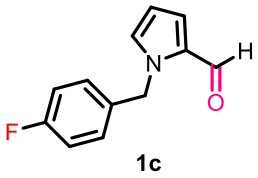
1-(4-Bromobenzyl-1*H*-Pyrrole-2-carbaldehyde (1b)[1]



1b

White solid (254 mg, 97%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.52 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 6.98 (dd, *J* = 18.3, 5.2 Hz, 4H), 6.27 (s, 1H), 5.49 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 179.6, 131.9, 131.46, 129.0, 125.1, 121.7, 110.4, 51.4.

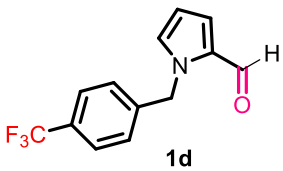
1-(4-Fluorobenzyl-1*H*-Pyrrole-2-carbaldehyde (1c)[1]



1c

Yellow oily liquid (198 mg, 98%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.54 (s, 1H), 7.32 – 7.19 (m, 1H), 6.96 – 6.89 (m, 2H), 6.78 (d, *J* = 9.6 Hz, 1H), 6.31 – 6.27 (m, 1H), 5.54 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 179.6, 164.0, 162.1, 140.31 (d, 3*J*C−F = 7.3 Hz), 131.55 (d, 2*J*C−F = 5.2 Hz), 130.31 (d, 3*J*C−F = 8.4 Hz), 125.1, 122.75 (d, 4*J*C−F = 3.1 Hz), 114.69 (d, 2*J*C−F = 21.2 Hz), 114.0 (d, 2*J*C−F = 22.1 Hz), 110.4, 51.5.

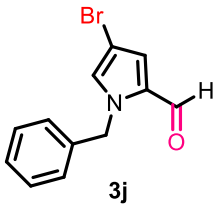
1-(4-Trifluorobenzyl-1*H*-Pyrrole-2-carbaldehyde (1d)[1]



1d

Yellow oily liquid (253 mg, 98%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.54 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.37 (s, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 3.6 Hz, 2H), 6.34 – 6.28 (m, 1H), 5.60 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 179.6, 138.7, 131.5, 130.5, 129.3, 125.2, 124.6 (d, 4*J*C−F = 3.3 Hz), 123.8 (d, 4*J*C−F = 3.4 Hz), 110.6, 51.5.

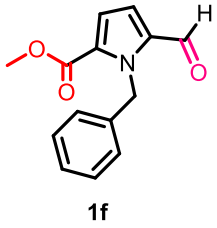
1-Benzyl-4-bromo-1*H*-Pyrrole-2-carbaldehyde (1e)[6]



3j

Pink solid (256 mg, 98%); NMR (600 MHz, $CDCl_3$-d_6) δ 9.49 (s, 1H), 7.34 – 7.31 (m), 7.30 – 7.28 (m), 7.16 (dd, *J* = 5.0, 3.3 Hz), 6.93 (d, *J* = 1.8 Hz), 6.93 – 6.91 (m), 5.51 (s). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 179.1, 136.6, 131.7, 130.5, 128.9, 128.2, 127.6, 125.4 97.4, 52.3.

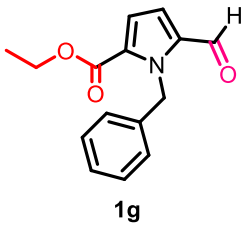
Methyl-1-benzyl-5-formyl-1*H*-Pyrrole-2-carbaldehyde (**1f**)



1f

Orange oily liquid (238 mg, 98%); NMR (600 MHz, $CDCl_3$-d_6) δ 9.72 (s, 1H), 7.27 – 7.24 (m, 1H), 7.24 – 7.23 (m, 1H), 7.21 – 7.18 (m, 1H), 7.04 (d, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 4.3 Hz, 1H), 6.95 (d, *J* = 4.2 Hz, 1H), 6.11 (s, 2H), 3.82 (s, 3H). NMR (151 MHz, $CDCl_3$-d_6) δ 181.1, 161.1, 138.1, 135.3, 129.5, 128.5, 127.3, 126.5, 122.5, 117.6, 51.9, 49.3. HRMS (ESI) m/z calcd for $C_{14}H_{13}NO_3$, $[M+1]^+$ 244.0974, found $[M+H]^+$ 244.0976.

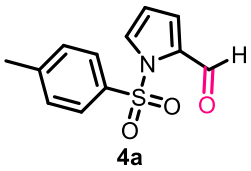
Ethyl-1-benzyl-5-formyl-1*H*-Pyrrole-2-carbaldehyde (**19**)



1g

Brown oily liquid (251 mg, 98%); NMR (600 MHz,) δ 9.72 (s, 1H), 7.28 – 7.24 (m, 2H), 7.22 – 7.18 (m,1H), 7.07 (d, *J* = 4.5 Hz, 1H), 7.03 (d, *J* = 4.3 Hz, 1H), 6.95 (d, *J* = 4.5 Hz, 1H), 6.13 (s, 1H), 4.29 (q, *J* = 7.3 Hz, 2H), 1.32 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$-d_6)δ 181.1, 160.7, 138.2, 135.3, 129.9, 129.5, 128.7, 128.5, 128.5, 128.2, 127.2, 126.6, 122.5, 61.0, 49.3, 14.2. HRMS (ESI) m/z calcd for $C_{15}H_{15}NO_3$, $[M+1]^+$ 258.1130, found $[M+H]^+$ 258.1135.

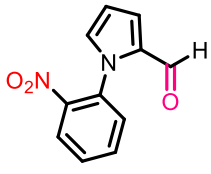
1-(Phenylsulfonyl)-1*H*-Pyrrole-2-carbaldehyde (4)[7]



4a

white solid (223 mg, 95%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.96 (s, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.61 (s, 1H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.15 (s, 1H), 6.39 (s, 1H), 2.41 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 179.0, 146.0, 135.2, 133.5, 130.2, 129.5, 127.5, 124.5, 112.4, 21.7.

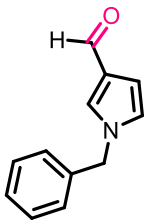
1-(2-nitrophenyl)-1*H*-Pyrrole-2carbaldehyde (5)



5'

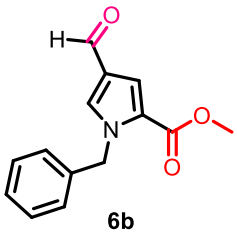
Yellow solid (213 mg, 99%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.48 (s, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 2.3 Hz, 1H), 7.00 (s, 1H), 6.51 – 6.44 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 178.8, 145.9, 133.7, 133.6, 132.7, 131.2, 129.8, 129.6, 125.3, 124.9, 111.7. HRMS (ESI) m/z calcd for $C_{11}H_8N_2O_3$, $[M+1]^+$ 217.0613, found $[M+H]^+$ 217.0610.

1-Benzyl-1*H*-Pyrrole-3-carbaldehyde (6a)[8]



Brown oily liquid (181 mg, 98%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.68 (s, 1H), 7.36 – 7.26 (m, 4H), 7.13 (d, *J* = 7.0 Hz, 2H), 6.70 – 6.65 (m, 1H), 6.62 (s, 1H), 5.04 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 185.5, 129.5, 129.1, 128.4, 127.5, 126.8, 123.9, 108.5, 54.0.

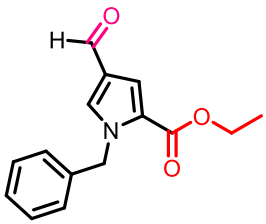
Methyl-1-benzyl-4-formyl-1*H*-Pyrrole-2-carboxylate (6b)[9]



6b

Yellow solid (238 mg, 98%); ^{1}H NMR (600 MHz,) δ 9.75 (s,1H), 7.43 (d, *J* = 1.9 Hz, 1H), 7.40 (d, *J* = 1.9 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.31 – 7.29 (m, 1H), 7.17 – 7.12 (m, 2H), 5.57 (s, 2H), 3.80 (s, 3H). ^{13}C NMR.NMR (151 MHz, $CDCl_3$-d_6) δ 185.3, 161.1, 136.3, 133.1, 129.0, 128.2, 127.5, 125.1, 124.4, 118.0, 53.0, 51.7.

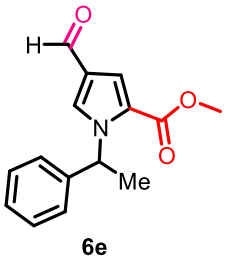
Ethyl-1-benzyl-4-formyl-1*H*-Pyrrole-2-carboxylate (6d)[10]



6d

Light brown oily liquid (251 mg, 98%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 9.73 (s, 1H), 7.41 (dd, *J* = 7.2, 1.9 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 2H), 5.56 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). NMR (151 MHz, $CDCl_3$-d_6) δ 185.4, 160.7, 136.4, 133.2, 129.0, 128.5, 128.2, 127.4, 127.0, 125.0, 124.7, 117.8, 60.6, 53.0, 14.3.

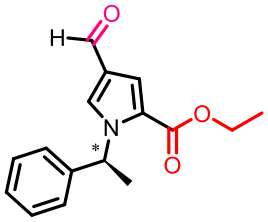
Methyl-4-Formyl-1-(1-phenylethyl)-1*H*-Pyrrole-2-carboxylate (6e)



6e

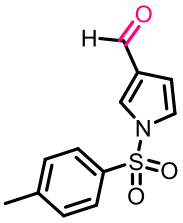
Orange solid (251 mg, 98%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.75 (s, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 2H), 6.57 (q, *J* = 7.1 Hz, 1H), 3.79 (s, 3H), 1.82 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 185.4, 161.1, 141.2, 130.1, 128.9, 128.0, 126.4, 125.0, 124.4, 118.3, 77.3, 77.1, 76.8, 56.6, 51.6, 29.7, 22.1. HRMS (ESI) m/z calcd for $C_{15}H_{15}NO_3$, $[M+1]^+$ 258.1130, found $[M+H]^+$ 258.1135.

Ethyl-4-Formyl-1-(1-phenylethyl)-1*H*-Pyrrole-2-carboxylate (6f)



6g

Brown solid (265 mg, 98%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 9.74 (s), 7.56 (d, *J* = 1.8 Hz), 7.41 (d, *J* = 1.8 Hz), 7.32 (dd, *J* = 10.3, 4.6 Hz), 7.26 (dd, *J* = 9.1, 7.1 Hz), 7.17 (d, *J* = 7.4 Hz), 6.57 (q, *J* = 7.0 Hz), 4.24 (dd, *J* = 13.2, 7.1 Hz), 1.81 (d, *J* = 7.1 Hz), 1.30 (t, *J* = 7.1 Hz). NMR (151 MHz, $CDCl_3$-d_6) δ 185.52, 160.74, 141.31, 130.19, 128.92, 128.06, 124.97, 124.84, 118.20, 77.37, 77.15, 76.94, 60.61, 56.58, 22.16, 14.32. HRMS (ESI) m/z calcd for $C_{16}H_{17}NO_3$, $[M+1]^+$ 271.1208, found $[M+H]^+$ 271.1206.

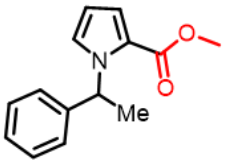


8a

1-(Phenylsulfonyl)-1*H*-Pyrrole-3-carbaldehyde (8)[11]

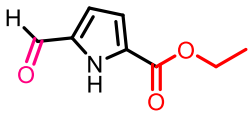
White solid (236 mg, 95%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.79 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.76 (s, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 2.7 Hz, 1H), 6.71 – 6.62 (m, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 185.2, 146.3, 134.9, 130.5, 129.6, 128.1, 127.4, 122.4, 110.9, 21.8.

Ethyl-(1-phenylethyl)-1*H*-Pyrrole-2-carboxylate (6f)[6]



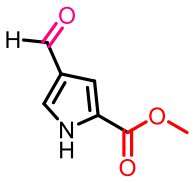
Brown oily liquid (160 mg, 70 %); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.30 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 2.9 Hz, 1H), 6.60 (q, *J* = 7.1 Hz, 1H), 6.19 (t, *J* = 3.2 Hz, 1H), 3.77 (s, 1H), 1.81 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 161.6, 143.0, 128.6, 127.4, 126.2, 125.5, 122.1, 118.5, 108.5, 55.4, 51.0, 22.2.

Ethyl-5-Formyl-1H-pyrrole-2-carboxylate[5]



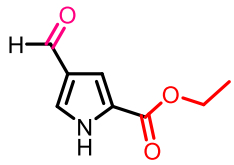
Orange solid (100 mg, 60 %); ^{1}H NMR (NMR (600 MHz, $CDCl_3$-d_6) δ 10.12 (s), 9.65 (s), 6.98 – 6.83 (m), 4.36 (q, *J* = 7.1 Hz), 1.36 (t, *J* = 7.1 Hz). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 180.5, 160.4, 134.4, 128.7, 119.8, 115.6, 61.4, 14.3.

Methyl-4-Formyl-1H-pyrrole-2-carboxylate[5]



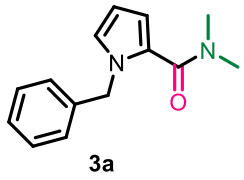
Orange solid (61 mg, 40 %); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 9.98 (s, 1H), 9.84 (s, 1H), 7.61 – 7.49 (m, 1H), 7.31 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 185.7, 161.4, 128.6, 127.6, 124.8, 114.3, 77.3, 77.1, 76.8, 52.1.

Ethyl-4-Formyl-1H-pyrrole-2-carboxylate[5]



White solid (67 mg, 60 %); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 10.26 (s, 1H), 9.83 (s, 1H), 7.57 (dd, *J* = 3.3, 1.5 Hz, 1H), 7.33 – 7.28 (m, 1H), 4.39 – 4.28 (m,2H), 1.36 (t, *J* = 7.1 Hz, 3H). NMR (151 MHz, $CDCl_3$-d_6) δ 185.8, 158.7, 128.7, 127.5, 125.2, 114.3, 61.2, 14.3.

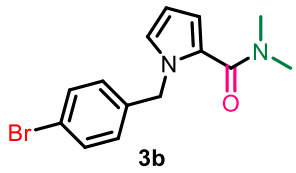
Benzyl-*N,N*-dimethyl-1*H*-Pyrrole-2-carboxamide (**3a**)[12]



3a

Pink oil (43 mg, 95%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.27 (d, *J* = 7.4 Hz, 2H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 2H), 6.77 (s, 1H), 6.40 – 6.35 (m, 1H), 6.15 – 6.09 (m, 1H), 5.34 (s, 2H), 3.00 (s, 3H), 2.94 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 164.15, 138.58, 128.41, 127.27, 126.89, 125.26, 125.09, 113.14, 107.01, 77.33, 77.12, 76.91, 51.58, 51.32, 39.60, 35.15. Rotameric methyl carbons detected under specified parameters: sample temperature -20 ^{o}C, relaxation delay; 8 sec, scans 512, Flip angle: 90 degree, X points:16348, IR (KBr, cm-1): 1634; HRMS (ESI) m/z calcd for $C_{14}H_{16}N_2O$ $[M+Na]^+$ 251.1160, found 251.1158.

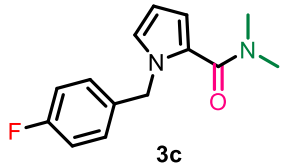
1-(4-Bromobenzyl)-*N,N*-dimethyl-1*H*-Pyrrole-2-carboxamide (**3b**)



3b

Pink oil (56 mg, 90%);^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.38 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 2.1 Hz, 1H), 6.38 (dd, *J* = 3.7, 1.5 Hz, 1H), 6.15 – 6.09 (m, 1H), 5.29 (s, 2H), 3.01 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ) 164.19, 137.89, 131.66, 128.91, 125.38, 121.33, 113.62, 107.49, 51.04, Methyl signals of rotameric carbons[13] around 39 and 35 not visible, but broad singlet of 6H present in ^{1}H, IR (KBr, cm-1): 1616; HRMS (ESI) m/z calcd for $C_{14}H_{15}BrN_2O$ $[M+Na]^+$ 329.0265, found $[M+Na]^+$ 329.0267.

1-(4-Fluorobenzyl)-*N,N*-dimethyl-1*H*-Pyrrole-2-carboxamide (**3c**):

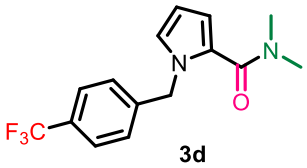


3c

Pink oil (44 mg, 89%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.23 – 7.19 (m, 1H), 6.91 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 6.77 – 6.72 (m, 2H), 6.39 (d, *J* = 3.8 Hz, 1H), 6.15 – 6.11 (m, 1H), 5.34 (s, 2H), 3.00 (s, 5H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 164.2, 162.0, 141.4, 130.0, 125.4, 122.6, 114.3 (d, 2*J*C−F = 21.3 Hz), 113.9(d, 2*J*C−F = 22.1 Hz), 113.5, 107.5, 51.1, Methyl signals of rotameric carbons around 39 and 39 visible as a broad hump,

broad singlet of 6H present in ^{1}H, IR (KBr, cm-1): 1614; HRMS (ESI) m/z calcd for $C_{14}H_{15}FN_2O$ [M+Na]$^{+}$ 269.1066, found [M+Na]$^{+}$ 269.1068.

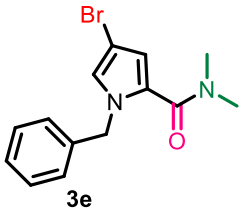
1-(4-(Trifluoromethyl)benzyl)-*N*,*N*-dimethyl-1*H*-Pyrrole-2-carboxamide (3d)



3d

Pink oil (55 mg, 93%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.48 (d, *J* = 6.7 Hz, 1H), 7.40 (dd, *J* = 9.2, 5.1 Hz, 1H), 7.29 (s, 2H), 6.81 – 6.73 (m, 1H), 6.40 (td, *J* = 3.7, 1.8 Hz, 1H), 6.15 (m,1H), 5.41 (s, 2H), 2.99 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 164.1, 139.9, 130.6, 129.0, 125.3, 124.3, 123.7, 113.7, 107.6, 51.2, Methyl signals of rotameric carbons around 40 not visible, but broad singlet of 6H present in ^{1}H, IR (KBr, cm^{-1}): 1611; HRMS (ESI) m/z calcd for $C_{15}H_{15}F_3N_2O$ [M+Na]$^{+}$ 319.1034, found [M+Na]$^{+}$ 319.1041.

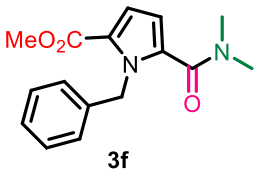
1-Benzyl-4-bromo-*N*,*N*-dimethyl-1*H*-Pyrrole-2-carboxamide (3e)



3e

Pink solid (52 mg, 85%); MP 80 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.29 (t, *J* = 7.2 Hz, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.1 Hz, 2H), 6.74 (d, *J* = 1.5 Hz, 1H), 6.32 (d, *J* = 1.5 Hz, 1H), 5.25 (s, 2H), 2.95 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 163.1, 137.7, 128.7, 127.8, 127.5, 127.2, 126.2, 124.4, 114.5, 113.1, 107.1, 94.7, 51.9, Methyl signals of rotameric carbons visible as two broad hump around 39 and 35 and broad singlet of 6H present in ^{1}H, IR (KBr, cm^{-1}): 1605; HRMS (ESI) m/z calcd for $C_{14}H_{15}BrN_2O$ [M+Na]$^{+}$ 329.0265, found [M+Na]$^{+}$ 329.0278.

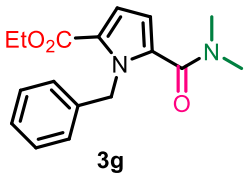
Methyl-1-benzyl-5-(dimethylcarbamoyl)-1*H*-Pyrrole-2-Carboxylate (3f)



3f

Transparent oil (47 mg, 82%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.24 – 7.20 (m, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.3 Hz, 2H), 6.93 (d, *J* = 4.0 Hz, 1H), 6.20 (d, *J* = 4.1 Hz, 1H), 5.80 (s, 2H), 3.78 (s, 3H), 2.89 (s, 3H), 2.62 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ NMR (151 MHz,) δ 163.9, 161.4, 138.7, 133.05, 128.4, 127.3, 127.1, 123.7, 116.9, 110.4, 51.4, 48.7, 38.8, 34.9. IR (KBr, cm^{-1}): 1628; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_2O_3$ [M+Na]$^{+}$ 309.1215, found [M+Na]$^{+}$ 309.1235.

Ethyl-1-benzyl-5-(dimethylcarbamoyl)-1*H*-Pyrrole-2-Carboxylate (3g)

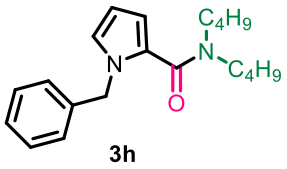


3g

Transparent oil (48 mg, 80%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.36 – 7.33 (m, 1H), 7.23 – 7.20 (m, 2H), 7.05 (d, *J* = 7.1 Hz, 2H), 6.95 (d, *J* = 4.0 Hz, 1H), 6.21 (d, *J* = 4.0 Hz, 1H), 5.81 (s, 2H), 4.24 (dq, *J* = 14.8, 7.2

Hz, 2H), 2.90 (s, 3H), 2.64 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 164.0, 161.1, 138.8, 136.2, 132.8, 128.4, 127.1, 127.1, 124.2, 116.8, 110.4, 65.9, 60.3, 48.8, 38.9, 34.9. IR (KBr, cm^{-1}): 1629; HRMS (ESI) m/z calcd for $C_{17}H_{20}N_2O_3$, [M+1] 301.1552, found [M+1] 301.1549, $[M+Na]^+$ 323.1723, found $[M+Na]^+$ 323.1367.

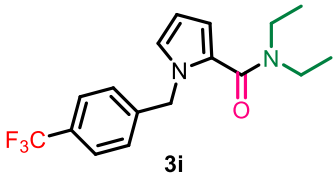
1-Benzyl-*N*,*N*-dibutyl-1*H*-Pyrrole-2-Carboxamide (**3h**)



3h

Pink oil (53 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.27 – 7.25 (m, 1H), 7.23 (s, 1H), 7.20 (dd, *J* = 6.4, 3.8 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 2.0 Hz, 1H), 6.35 – 6.26 (m, 1H), 6.15 – 6.05 (m, 1H), 5.30 (s, 2H), 3.32 – 3.24 (m, 4H), 1.38 (s, 4H), 1.19 (s, 4H), 0.85 (s, H).^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 164.2, 138.6, 128.5, 127.4, 127.3, 126.1, 125.0, 111.6, 106.9, 51.6, 29.7, 26.5, 20.1, 13.9. IR (KBr, cm^{-1}): 1629; HRMS (ESI) m/z calcd for $C_{20}H_{28}N_2O$, $[M+1]^+$ 313.2280, found $[M+H]^+$ 313.2284.

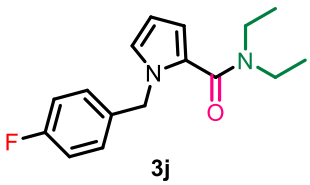
***N*,*N*-diethyl-1-(4-(trifluoromethyl)benzyl)-1*H*-Pyrrole-2-Carboxamide** (**3i**)



3i

Pink oil (58 mg, 90%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.46 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.27 (t, *J* = 9.1 Hz, 2H), 6.81 (s, 1H), 6.36 (d, *J* = 2.9 Hz, 1H), 6.13 (s, 1H), 5.37 (s, 2H), 3.38 – 3.25 (m, 4H), 0.99 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 164.1, 139.9, 130.6 (d, 2*J*C−F = 1.2 Hz), 129.0, 125.3 (d, 3*J*C−F = 12.1 Hz), 124.3 (d, 4*J*C−F = 3.9 Hz), 123.7 (d, 4*J*C−F = 3.7 Hz), 113.7, 107.6, 51.1. δ 163.6, 139.9, 130.7, 129.0, 125.7, 124.3, 123.8, 111.9, 107.3, 77.3, 77.1, 76.8, 51.3, 29.7, 15.0. IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{17}H_{19}F_3N_2O$, $[M+H]^+$ 325.1527, found $[M+H]^+$ 325.1540.

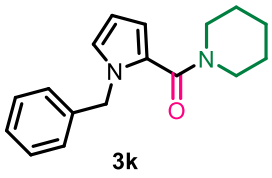
***N*,*N*-diethyl-1-(4-fluoromethyl)benzyl)-1*H*-Pyrrole-2-Carboxamide** (**3j**)



3j

Pink oil (47 mg, 85%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.24 – 7.17 (m, 1H), 6.93 – 6.84 (m, 2H), 6.79 (dt, *J* = 4.0, 2.0 Hz, 1H), 6.75 (d, *J* = 9.7 Hz, 1H), 6.35 (dd, *J* = 3.7, 1.6 Hz, 3H), 6.11 (dd, *J* = 3.7, 2.7 Hz, 4H), 5.31 (s, 2H), 3.35 (q, *J* = 7.1 Hz, 4H), 1.03 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 163.9, 162.3, 141.4 (d, 3*J*C−F = 7.0 Hz), 130.1 (d, 3*J*C−F = 8.2 Hz), 126.1, 125.6 (d, 1*J*C−F = 124.4 Hz), 114.36 (dd, 2*J*C−F *J* = 25.0, 22.1 Hz), 111.7, 107.2, 51.3. IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{16}H_{19}FN_2O$, $[M+H]^+$ 297.137 2*J*C−F 9, found $[M+H]^+$ 297.1382.

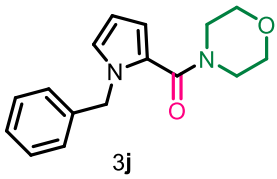
1-Benzyl-1*H*-Pyrrol-2-yl)(piperidin-1-yl)methanone (3k)



3k

Yellow oil (48 mg, 89%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.37 (s, 1H), 7.24 (s, 1H), 7.20 (dd, *J* = 8.4, 6.2 Hz, 2H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.80 – 6.78 (m, 1H), 6.27 (dd, *J* = 3.7, 1.6 Hz, 1H), 6.09 (dd, *J* = 3.5, 2.9 Hz, 1H), 5.30 (s, 2H), 3.51 – 3.46 (m, 4H), 1.56 – 1.51 (m, 4H), 1.38 – 1.29 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 163.1, 138.7, 128.5, 127.4, 125.7, 125.1, 112.2, 106.9, 51.6, 48.0, 26.5, 26.0, 24.7. IR (KBr, cm^{-1}): 1672; HRMS (ESI) m/z calcd for $C_{17}H_{20}N_2O$, $[M+H]^+$ 269.1654, found $[M+H]^+$ 269.1650.

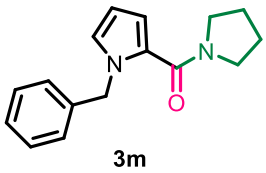
1-Benzyl-1*H*-Pyrrol-2-yl)(morpholino)methanone (3l)



3j

Pink oil (43 mg, 80%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.29 – 7.25 (m, 2H), 7.25 – 7.22 (m, 1H), 7.07 (d, *J* = 7.0 Hz, 2H), 6.86 – 6.83 (m, 1H), 6.29 – 6.27 (m, 1H), 6.11 (dd, *J* = 3.7, 2.7 Hz, 1H), 5.31 (s, 2H), 3.58 – 3.53 (m, 4H), 3.36 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6 δ 163.2, 138.6, 128.6, 127.7, 127.3, 125.8, 124.6, 113.0, 107.1, 77.3, 77.1, 76.9, 66.8, 53.6, 51.7. IR (KBr, cm^{-1}): 1616; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_2O2$, $[M+H]^+$ 271.1447, found $[M+H]^+$ 271.1444.

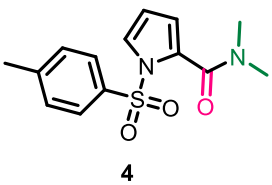
1-Benzyl-1*H*-Pyrrol-2-yl)(pyrrolidin-1-yl)methanone (3m)



3m

Brown solid (40 mg, 79%); MP 120 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.27 – 7.25 (m, 1H), 7.24 (s, 1H), 7.20 (dd, *J* = 8.4, 6.2 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 2H), 6.77 – 6.74 (m, 1H), 6.47 (dd, *J* = 3.8, 1.6 Hz, 1H), 6.11 (dd, *J* = 3.7, 2.7 Hz, 1H), 5.43 (s, 2H), 3.48 (t, *J* = 6.2 Hz, 4H), 1.78 (d, *J* = 41.2 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6)δ 162.4, 139.0, 128.4, 127.2, 126.6, 125.5, 113.3, 107.1, 77.3, 77.1, 76.9, 51.8, 49.5, 46.0. IR (KBr, cm^{-1}): 1614; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_2O$, $[M+H]^+$ 255.1497, found $[M+H]^+$ 255.1499.

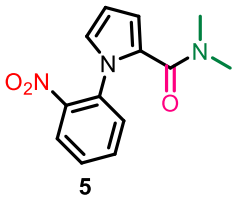
***N*,*N*-diethyl-(1-phenylsulfone)-1*H*-Pyrrole-2-Carboxamide (4)**



4

Brown solid (44 mg, 75%); MP 107 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.20 – 7.16 (m, 1H), 6.25 (s, 1H), 6.23 (t, *J* = 3.1 Hz, 1H), 3.10 (s, 3H), 2.96 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 163.6, 145.3, 135.5, 129.8, 128.7, 127.9, 127.5, 122.4, 113.6, 112.2, 39.1, 35.2, 21.7. IR (KBr, cm^{-1}1619; HRMS (ESI) m/z calcd for $C_{14}H_{16}N_2O_3S$, $[M+Na]^+$ 315.0779, found $[M+Na]^+$ 315.0790.

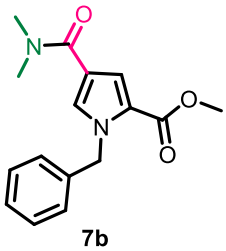
***N,N*-dimethyl-(2-nitrophenyl)-1*H*-Pyrrole-2-Carboxamide (5)**



5

Brown oily liquid (45 mg, 87%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.94 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.70 – 7.61 (m, 1H), 7.50 (ddd, *J* = 15.7, 8.0, 1.3 Hz, 2H), 6.86 – 6.78 (m, 1H), 6.55 (dd, *J* = 3.8, 1.6 Hz, 1H), 6.37 – 6.30 (m, 1H), 3.28 (s, 3H), 2.93(s. 3H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 162.91, 146.0, 134.6, 133.4, 129.7, 128.5, 127.5, 126.2, 125.7, 124.8, 114.4, 109.2, Methyl signals of rotameric carbons around 39 and 35 not visible, but broad singlet of 6H present in ^{1}H; IR (KBr, cm^{-1}): 1619; HRMS (ESI) m/z calcd for $C_{13}H_{13}N_3O3$, $[M+H]^+$ 260.1035, found $[M+H]^+$ 260.1041.

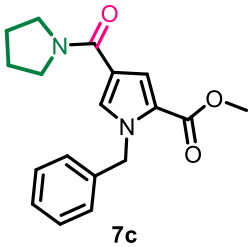
Methyl-1-benzyl-4-(dimethylcarbamoyl)-1*H*-Pyrrole-2-Carboxylate (7b)



7b

White solid (46 mg, 80%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.36 – 7.27 (m, 4H), 7.14 (dd, *J* = 9.1, 4.5 Hz, 3H), 5.53 (s, 2H), 3.77 (s, 3H), 3.18 (s, 3H), 3.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 166.0, 161.3, 137.1, 131.5, 128.8, 127.8, 127.3, 121.9, 118.7, 118.3, 77.3, 77.1, 76.8, 52.5, 51.4, 42.0. IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_2O_3$, $[M+H]^+$ 287.1396, found $[M+H]^+$ 287.1401.

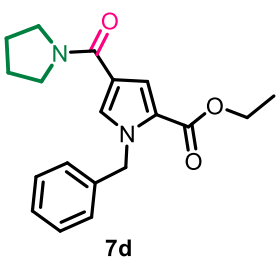
Methyl-1-benzyl-4-(morpholine-4-carbamoyl)-1*H*-Pyrrole-2-Carboxylate (7c)



7c

Light brown solid (49 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) NMR (600 MHz,) NMR (600 MHz,) δ 7.43 (d, *J* = 1.9 Hz, 1H), 7.29 (dd, *J* = 8.0, 6.5 Hz, 2H), 7.25 (d, *J* = 3.4 Hz, 2H), 5.54 (s, 2H), 3.77 (s, 3H), 3.64 (s, 4H), 1.92 (d, *J* = 1.5 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 163.6, 161.4, 137.3, 132.2, 128.9, 127.9, 127.3, 122.2, 119.9, 118.2, 77.4, 77.2, 77.0, 52.6, 51.5, 47.0, 26.8. IR (KBr, cm^{-1}): 1698; HRMS (ESI) m/z calcd for $C_{18}H_{20}N_2O_3$, $[M+H]^+$ 313.1552, found $[M+H]^+$ 313.1557, $[M+Na]^+$ 335.1372, found $[M+Na]^+$ 335.1379.

Ethyl-1-benzyl-4-(pyrrolidine-1-carbonyl)-1*H*-Pyrrole-2-Carboxylate (7d)

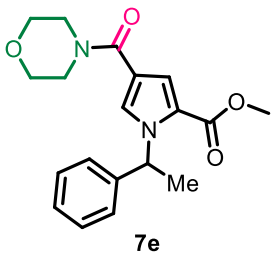


7d

White solid (51 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 7.40 (d, *J* = 1.3 Hz, 1H), 7.28 (td, *J* = 6.6, 1.5 Hz, 3H), 7.23 (dd, *J* = 6.0, 3.5 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 2H), 5.53 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.69 (t, *J* = 6.4 Hz, 2H), 3.61 (t, *J* = 6.4 Hz, 2H), 1.98 – 1.92 (m, 2H), 1.90 – 1.84 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, NMR (151 MHz,) δ 163.7, 161.0, 137.4, 132.0, 128.8, 127.87, 127.2, 122.5, 119.8, 118.2, 77.4,

77.2, 77.0, 60.3, 52.6, 48.6, 46.9, 29.8, 26.8, 24.2, 14.4. δ IR (KBr, cm^{-1}): 1655; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_3$, $[M+H]^+$ 327.1709, found $[M+H]^+$ 327.1723.

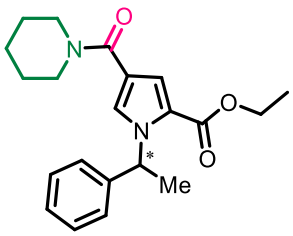
Methyl-4-(morpholine-4-carbonyl)-1-(1-phenylethyl)-1*H*-Pyrrole-2-Carboxylate (**7e**)



7e

White solid (53 mg, 78%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.40 (s, 1H), 7.31 (d, *J* = 6.9 Hz, 2H), 7.25 (s, 1H), 7.17 (d, *J* = 7.3 Hz, 2H), 7.03 (s, 1H), 6.52 (dd, *J* = 13.6, 6.7 Hz, 1H), 3.77 (s, 3H), 3.74 – 3.67 (m, 8H), 1.80 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 166.0, 161.3, 137.1, 131.5, 128.8, 127.8, 127.3, 121.9, 118.7, 118.3, 77.3, 77.1, 76.8, 52.5, 51.4, 29.7. IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_4$, $[M+H]^+$ 343.1658, found $[M+H]^+$ 343.1659.

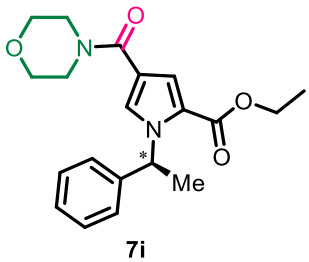
(R)-Ethyl-1-(1-phenylethyl)-4-(piperidine-1-carbonyl)-1*H*-Pyrrole-2-Carboxylate (**7h**)



7h

White solid (57 mg, 80%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.35 (s), 7.29 (t, *J* = 7.4 Hz), 7.23 (d, *J* = 7.1 Hz), 7.15 (d, *J* = 7.4 Hz), 7.06 (s), 6.52 (q, *J* = 6.9 Hz), 4.22 (dt, *J* = 10.3, 3.3 Hz), 3.62 (s), 1.79 (d, *J* = 7.0 Hz), 1.66 (d, *J* = 4.7 Hz), 1.58 (s), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 165.2, 160.9, 142.1, 128.7, 127.8, 127.6, 126.4, 122.2, 118.6, 117.8, 77.3, 77.1, 76.9, 60.2, 56.0, 48.0, 24.7, 22.2, 14.4. IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{21}H_{26}N_2O_3$, $[M+H]^+$ 355.2022, found $[M+H]^+$ 355.2017.

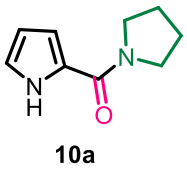
R-Ethyl-4-(morpholine-4-carbonyl)-1-(1-phenyl-1-ethyl)-1*H*-Pyrrole-2-Carboxylate (**7i**)



7i

White solid 61 (mg, 08%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.38 (s, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.25 (d, *J* = 3.7 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.04 (s, 1H), 6.53 (q, *J* = 7.0 Hz, 1H), 4.29 – 4.15 (m, 2H), 3.71 (dd, *J* = 10.9, 7.5 Hz, 8H), 1.80 (d, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 166.0, 161.3, 137.1, 131.5, 128.8, 127.8, 127.3, 121.9, 118.7, 118.3, 77.6, 77.1, 76.8, 52.5, 51.4, 42.0; IR (KBr, cm^{-1}): 1610; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_4$, $[M+H]^+$ 357.1814, found $[M+H]^+$ 357.1852.

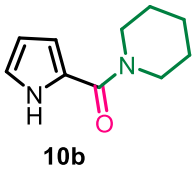
(1*H*-Pyrrol-2-yl)(pyrrolidine-1-yl)methanone (10a)[13]



10a

White solid (24 mg, 80 %); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 10.13 (s, 1H), 6.98 – 6.87 (m, 1H), 6.58 (t, *J* = 1.8 Hz, 1H), 6.40 – 6.20 (m, 1H), 3.70 (dt, *J* = 38.6, 6.7 Hz, 4H), 2.08 – 1.76 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) ^{3}C NMR (126 MHz, $CDCl_3$-d_6) δ 160.53, 126.21, 121.05, 112.01, 109.78, 77.41, 77.15, 76.90, 47.97, 47.08, 26.73, 24.04.

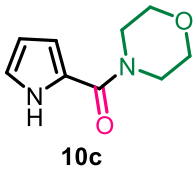
Piperidin-1-yl(1*H*-Pyrrol-2-yl)methanone (10b)[13]



10b

White solid (30 mg, 85%);^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 10.11 (s, 1H), 6.88 (td, *J* = 2.7, 1.4 Hz, 1H), 6.50 (ddd, *J* = 3.7, 2.6, 1.3 Hz, 1H), 6.21 (dt, *J* = 3.6, 2.7 Hz, 1H), 3.76 (s, 4H), 1.90 – 1.40 (m, 7H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 161.87, 124.98, 120.88, 111.81, 109.17, 77.41, 77.15, 76.90, 26.21, 24.81.

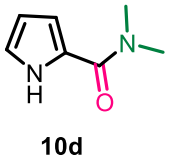
Morpholino(1*H*-Pyrrol-2-yl)methanone (10c)[13]



10c

White solid (32 mg, 88%);^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 10.35 (s, 1H), 6.89 (td, *J* = 2.6, 1.1 Hz, 1H), 6.61 – 6.31 (m, 1H), 6.21 (dd, *J* = 6.2, 2.6 Hz, 1H), 3.85 (d, *J* = 4.2 Hz, 4H), 3.77 – 3.54 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 162.18, 124.20, 121.54, 112.32, 109.41, 77.43, 77.17, 76.92, 66.95.

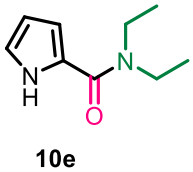
***N,N*-Dimethyl-1*H*-pyrrole-2-carboxamide (10d)[13]**



10d

Brown solid (23 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 11.37 (s, 1H), 6.83 (s, 1H), 6.50 (s, 1H), 6.08 (dd, *J* = 5.6, 2.4 Hz, 1H), 3.06 (s, 6H).). ^{13}C NMR (126 MHz) δ 158.6, 121.2, 116.9, 108.7, 105.8.

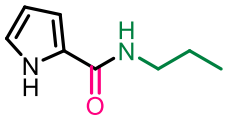
***N,N*-Diethyl-1*H*-pyrrole-2-carboxamide (10e)[14]**



10e

Brown solid (29 mg, 88%);^{1}H NMR (500 MHz, DMSO-d6) δ 11.35 (s, 1H), 6.82 (s, 1H), 6.41 (d, *J* = 2.6 Hz, 1H), 6.08 (d, *J* = 3.3 Hz, 1H), 3.33 (dt, *J* = 29.3, 14.6 Hz, 4H), 1.13 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.6, 125.1, 121.4, 111.2, 109.1, 14.1, 8.2.

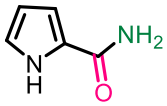
***N*-Propyl-1*H*-pyrrole-2-carboxamide (10f)[15]**



10f

Brown oily liquid (25 mg, 82%); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.27 (s, 1H), 7.85 (t, *J* = 5.4 Hz, 1H), 6.73 (td, *J* = 2.6, 1.5 Hz, 1H), 6.65 (ddd, *J* = 3.7, 2.5, 1.5 Hz, 1H), 5.97 (dt, *J* = 3.5, 2.4 Hz, 1H), 3.07 (dd, *J* = 13.7, 6.3 Hz, 2H), 1.44 – 1.36 (m, 2H), 0.79 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.1, 127.0, 121.5, 110.0, 108.9, 40.7, 40.1, 40.0, 39.9, 23.2, 11.9.

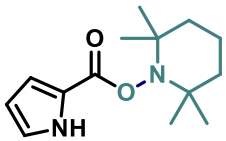
1H-Pyrrole-2-carboxamide (10g)[16]



10g

White solid (15 mg, 70%); ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.30 (s, 1H), 7.38 (s, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.65 (s, 1H), 6.01 – 5.90 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.70, 127.61, 122.73, 111.98, 109.88.

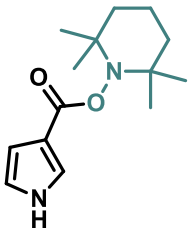
2,2,6,6-Tetramethylpiperidin-1-yl-1H-Pyrrole-2-carboxylate (11a)



12a

Brown solid (40 mg, 80%); MP 150 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 9.67 (s, 1H), 6.98 (t, *J* = 27.6 Hz, 2H), 6.25 (d, *J* = 3.2 Hz, 1H), 1.59 (dddd, *J* = 41.6, 35.6, 12.7, 4.6 Hz, 6H), 1.23 (d, *J* = 8.1 Hz, 6H), 1.09 (d, *J* = 9.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 162.3, 123.6, 121.3, 114.7, 110.2, 77.4, 77.1, 76.9, 60.4, 39.1, 32.0, 29.7, 20.7, 17.0 .IR (KBr, cm^{-1}): 1725; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_4$, $[M+H]^+$ 251.1760, found $[M+H]^+$ 251.1763.

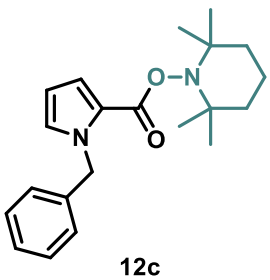
2,2,6,6-Tetramethylpiperidin-1-yl-1H-Pyrrole-3-carboxylate (12b)



12b

Light brown solid (30 mg, 60%); MP 230 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6) δ 11.42 (s, 1H), 7.40 (dd, *J* = 2.9, 1.6 Hz, 1H), 6.80 (dd, *J* = 4.6, 2.4 Hz, 1H), 6.41 (dd, *J* = 4.0, 2.5 Hz, 1H), 1.72 – 1.29 (m, 6H), 1.13 (s, 6H), 0.93 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ 164.6, 123.7, 119.9, 113.9, 109.2, 59.8, 40.3, 40.1, 40.0, 39.8, 39.7, 39.2, 32.1, 20.8, 17.1. IR (KBr, cm^{-1}): 1715; HRMS (ESI) m/z calcd for $C_{14}H_{22}N_2O_2$, $[M+H]^+$ 251.1760, found $[M+H]^+$ 251.1770.

2,2,6,6-Tetramethylpiperidin-1-yl 1-benzyl-1*H*-Pyrrole-2-carboxylate (12c)

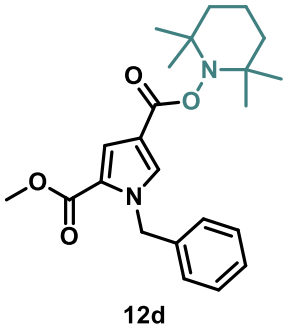


12c

Brown solid (61 mg, 90%); MP 90 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.23 (d, *J* = 7.1 Hz, 2H), 7.20 (d, *J* = 6.9 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 7.03 – 6.99 (m, 1H), 6.94 (d, *J* = 1.4 Hz, 1H), 6.17 (d, *J* = 2.4 Hz, 1H), 5.55 (s, 2H), 1.69 (d, *J* = 12.4 Hz, 2H), 1.52 (d, *J* = 12.4 Hz, 2H), 1.40 (d, *J* = 15.3 Hz, 2H), 1.18 (s, 6H), 0.99 (s, 6H). ^{13}C NMR (126

MHz, $CDCl_3$-d_6)) δ 161.58, 138.23, 129.04, 128.52, 127.46, 120.68, 117.42, 108.28, 77.41, 77.16, 76.90, 60.25, 52.24, 39.13, 31.86, 20.76, 17.10. IR (KBr, cm^{-1}): 1722; HRMS (ESI) m/z calcd for $C_{21}H_{29}N_2O_2$, $[M+H]^+$ 341.2229, found $[M+H]^+$ 341.2229.

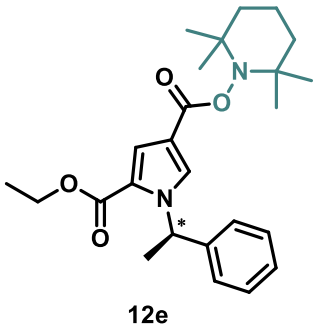
2-Methyl 4-(2,2,6,6-Tetramethylpiperidin-1-yl) 1-benzyl -1*H*-Pyrrole-2,4-dicarboxylate (12d)



12d

Brown solid (60 mg, 75%); MP 103 °C ; ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 7.51 (s, 1H), 7.38 (s, 1H), 7.31 (dd, *J* = 15.7, 8.6 Hz, 1H), 7.26 (d, *J* = 12.3 Hz, 3H), 7.16 (d, *J* = 7.3 Hz, 2H), 5.56 (s, 2H), 3.80 (s, 3H), 1.71 – 1.38 (m, 6H), 1.22 (s, 6H), 1.09 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$-d_6) δ 163.9, 161.1, 136.8, 132.6, 128.9, 128.0, 127.3, 123.0, 118.9, 114.4, 77.3, 77.1, 76.8, 60.3, 52.8, 51.5, 39.0, 32.0, 20.8, 17.0. IR (KBr, cm^{-1}): 1715; HRMS (ESI) m/z calcd for $C_{23}H_{30}N_2O_4$, $[M+H]^+$ 399.2284, found $[M+H]^+$ 399.2287.

2-Ethyl 4-(2,2,6,6-Tetramethylpiperidin-1-yl)1-(1-phenyl-1-ethyl)-1*H*-Pyrrole-2,4-dicarboxylate (12e)



12e

Light brown solid (64 mg, 75%); MP 100 °C; ^{1}H NMR (600 MHz,) δ 7.65 (d, *J* = 1.8 Hz, 1H), 7.37 (d, *J* = 1.7 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.23 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 2H), 6.56 (q, *J* = 7.0 Hz, 1H), 4.25 (dd, *J* = 7.0, 4.1 Hz, 2H), 1.81 (d, *J* = 7.1 Hz, 3H), 1.72 – 1.41 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.24 (d, *J* = 13.3 Hz, 6H), 1.10 (d, *J* = 2.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$-d_6) δ NMR (151 MHz,) δ 165.0, 161.5, 142.5, 130.4, 129.6, 128.6, 127.1, 124.3, 119.5, 115.0, 78.3, 78.1, 77.9, 61.1, 57.2, 39.8, 32.8, 30.5, 23.5, 23.0, 21.6, 17.8, 15.2. IR (KBr, cm^{-1}): 1715; HRMS (ESI) m/z calcd for $C_{25}H_{34}N_2O_4$, $[M+H]^+$ 427.2597, found $[M+H]^+$ 427.2600.

4. COMPUTATIONAL DETAILS

Radical philicities were calculated as previously described[17] using the hybrid functional B3LYP[18] with the triple-basis set 6-311+G(d,p) in the gas phase. The calculations were performed with Gaussian16.[19]

The global electrophilicity index ω was derived from vertical ionization potentials (IP) and electron affinities (EA) at the B3LYP/6-311+G(d,p) level of theory using the following equation:

$$IP = E(\text{Cation}) - E(\text{Radical}) \quad \text{(eq. S1)}$$

$$EA = E(\text{Radical}) - E(\text{Anion}) \quad \text{(eq. S2)}$$

$$\mu = -\frac{IP + EA}{2} \quad \text{(eq. S3)}$$

$$\eta = IP - EA \quad \text{(eq. S4)}$$

$$\omega = \frac{\mu^2}{2\eta} \quad \text{(eq. S5)}$$

N-Benzyl pyrrole 2-acyl radical

E(Radical) –593.368588887 hartree
E(Cation) –593.093629193 hartree
E(Anion) –593.375752569 hartree

Cartesian Coordinates Radical (B3LYP):

C	-1.04595	-1.77383	-0.00313
C	-2.22907	-2.03943	-0.68436
N	-1.05719	-0.48650	0.42246
C	-2.25359	0.10518	0.02214
C	-2.98949	-0.86078	-0.67025
H	-0.19960	-2.41321	0.19319
H	-2.49461	-2.98263	-1.13586
H	-3.96286	-0.69502	-1.10466
C	-2.55707	1.47111	0.33050
O	-3.51511	2.13353	0.06998
C	0.00286	0.16147	1.20428
C	1.34613	0.17817	0.50507
H	0.08744	-0.34458	2.16946
H	-0.34472	1.17912	1.39725
C	2.48187	-0.31415	1.15111
C	3.73016	-0.26876	0.52917
C	3.85144	0.26700	-0.74994
C	2.72041	0.75875	-1.40368
C	1.47721	0.71611	-0.78034
H	0.60206	1.09858	-1.29476
H	4.81936	0.30153	-1.23686
H	2.80878	1.17834	-2.39946
H	2.39277	-0.73482	2.14785
H	4.60296	-0.65509	1.04338

N-Benzyl pyrrole 3-acyl radical

E(Radical) –593.367593614 hartree
E(Cation) –593.095920127 hartree
E(Anion) –593.360902230 hartree

Cartesian Coordinates Radical (B3LYP):

C	-1.08500	-0.68988	1.17314
C	-2.35058	-0.17900	1.26386
N	-0.74850	-0.80385	-0.16850
C	-1.78851	-0.36889	-0.92747
C	-2.81288	0.03231	-0.07978
H	-2.90193	0.02698	2.16717
C	-4.08248	0.55364	-0.53432
O	-5.02921	0.92576	0.08642
C	0.52497	-1.31156	-0.67560
C	1.72196	-0.44829	-0.31993
H	0.42279	-1.38760	-1.76140
H	0.67515	-2.32680	-0.29849
C	2.92714	-1.05213	0.04543
C	4.05339	-0.27853	0.32449
C	3.98123	1.11011	0.24717
C	2.77874	1.72031	-0.11002
C	1.65642	0.94646	-0.39310
H	0.72283	1.42929	-0.66066
H	4.85353	1.71431	0.46863
H	2.71420	2.80102	-0.16675
H	2.98785	-2.13384	0.11464
H	4.98169	-0.76109	0.60858
H	-1.74802	-0.37265	-2.00526
H	-0.38133	-0.97612	1.93850

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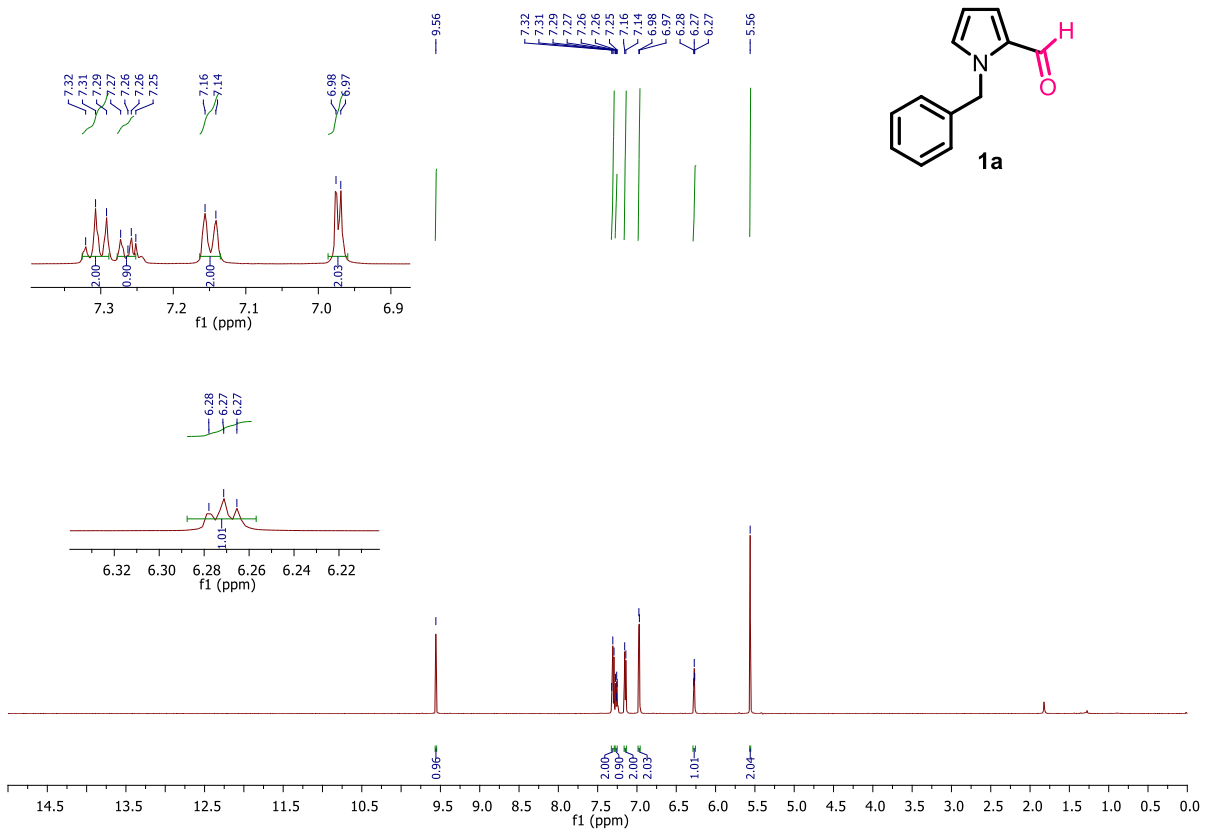
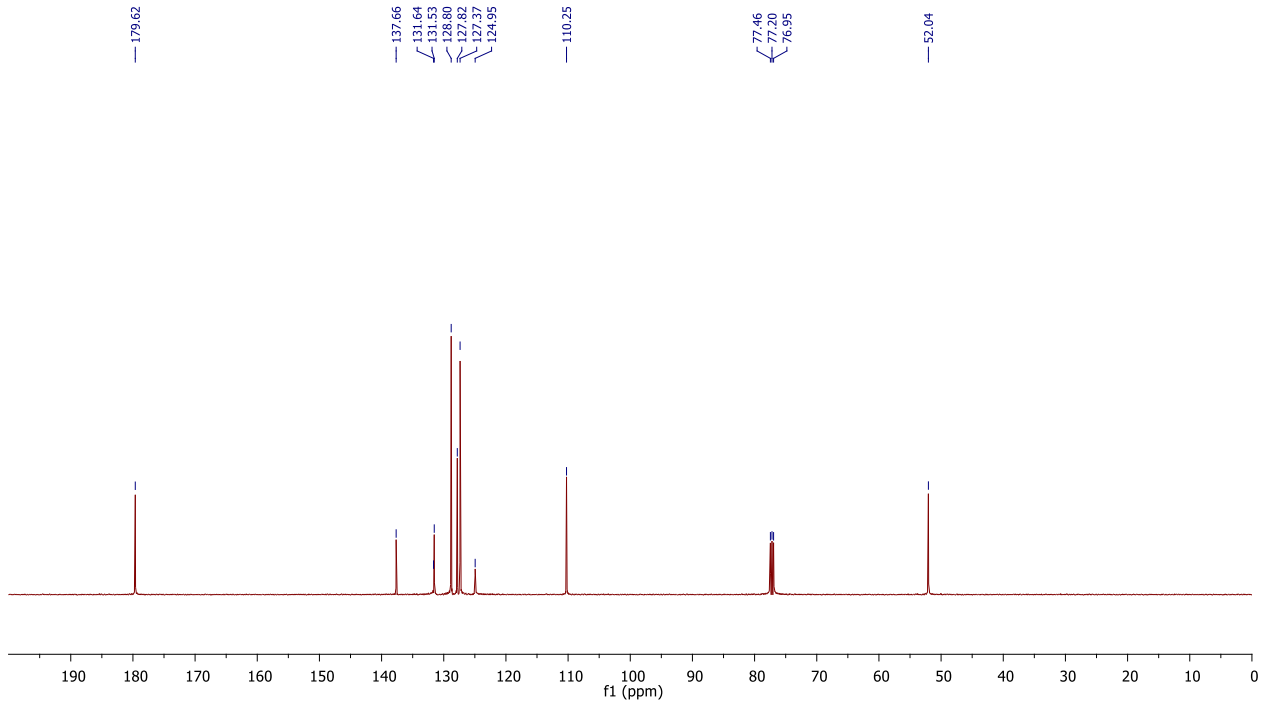
6a. ^{1}H and ^{13}C Spectra of Substrates

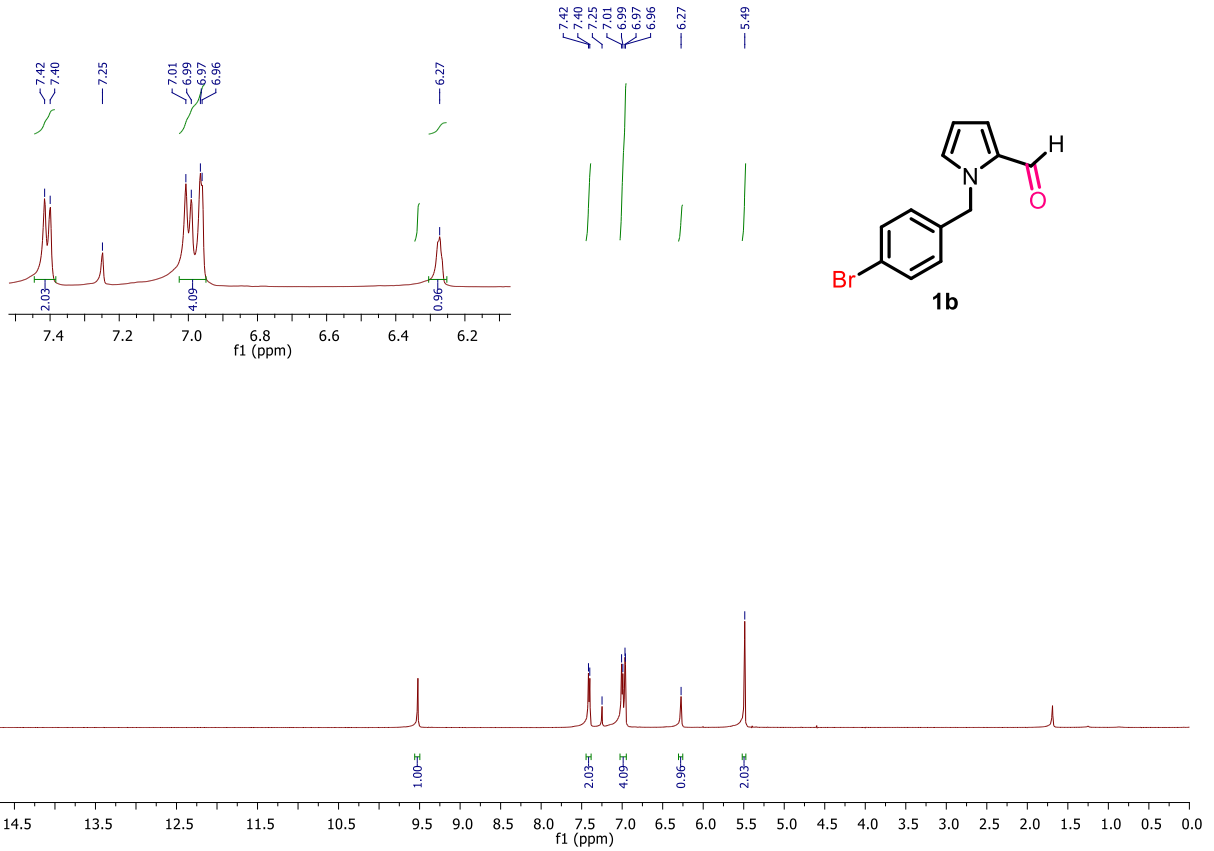
1a ^{1}H NMR ($CDCl_3$)



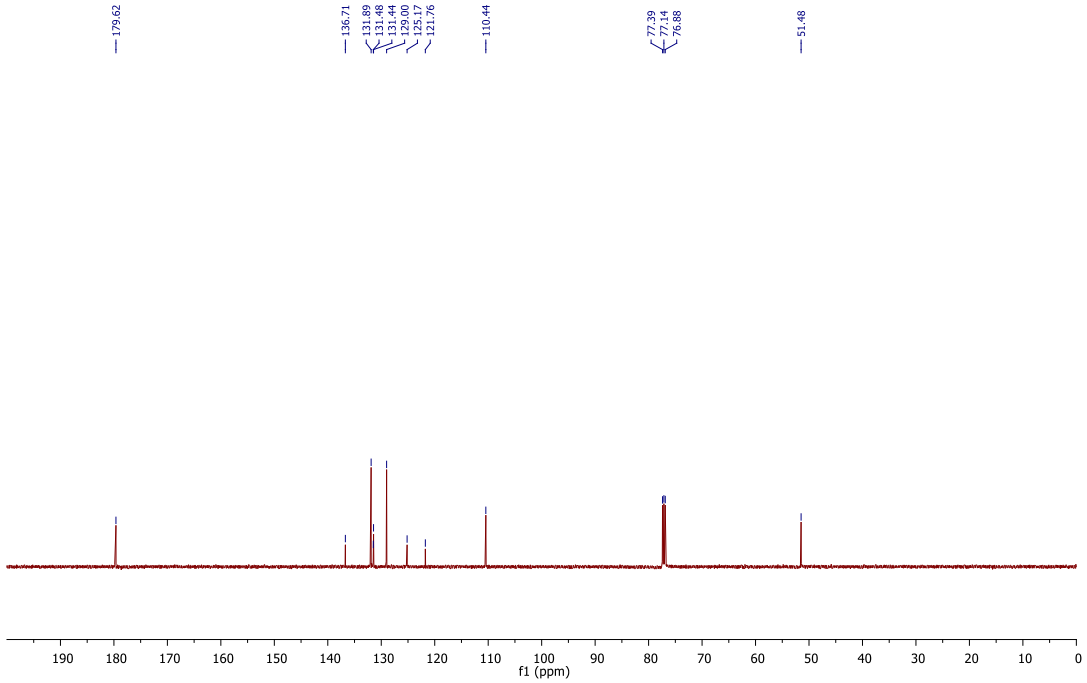
^{13}C{1H} NMR ($CDCl_3$)



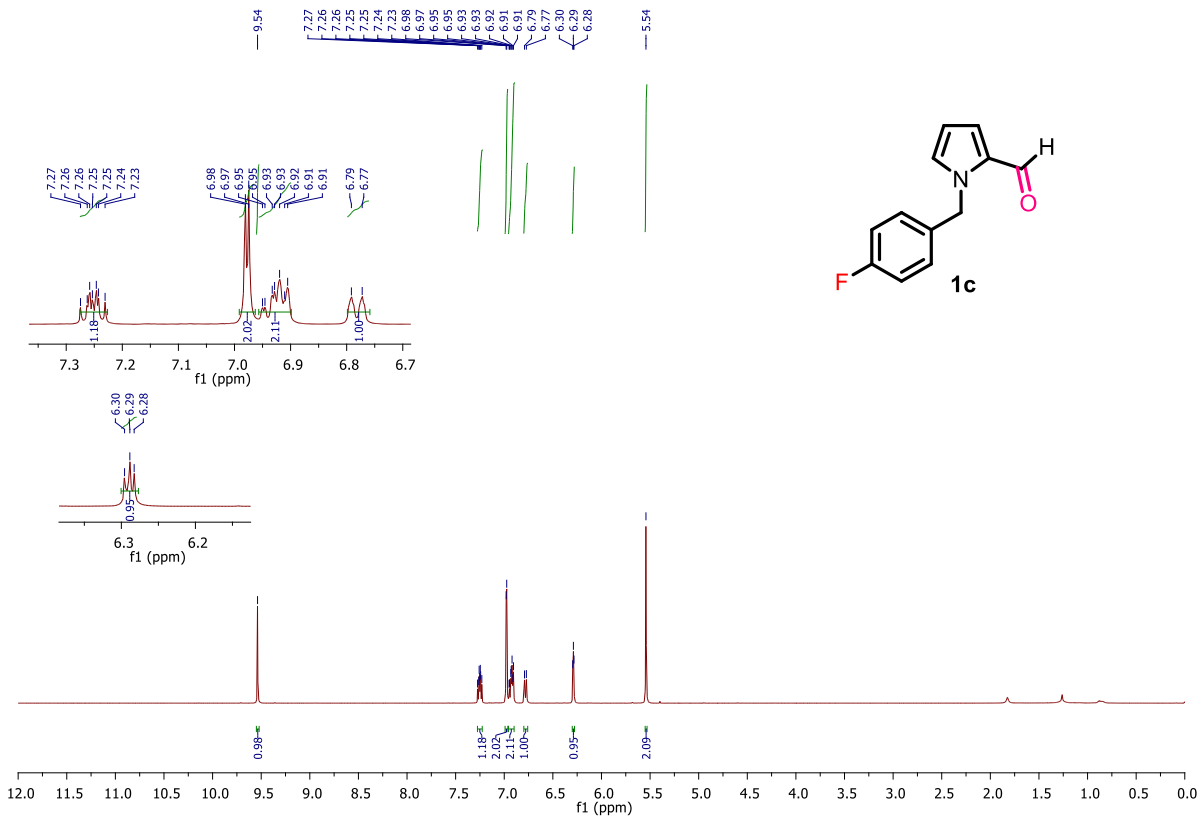
1b ^{1}H NMR ($CDCl_3$)



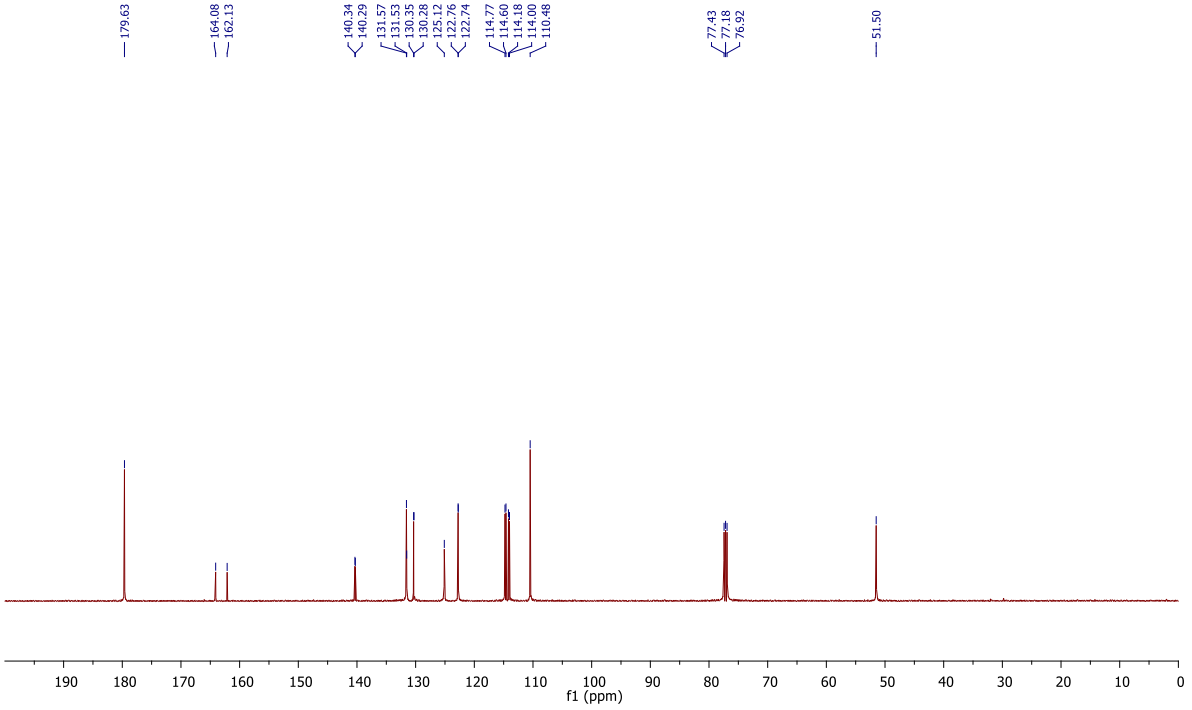
^{13}C{1H} NMR ($CDCl_3$)



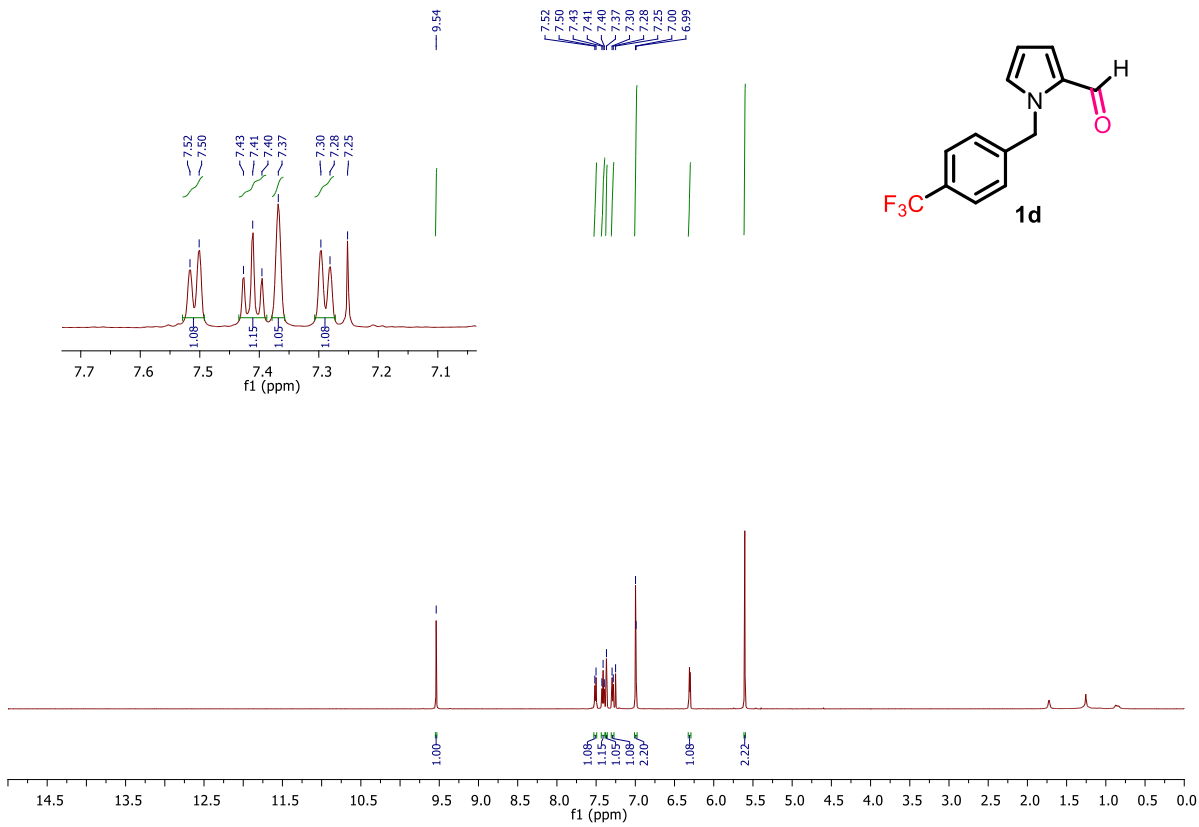
1c ^{1}H NMR ($CDCl_3$)



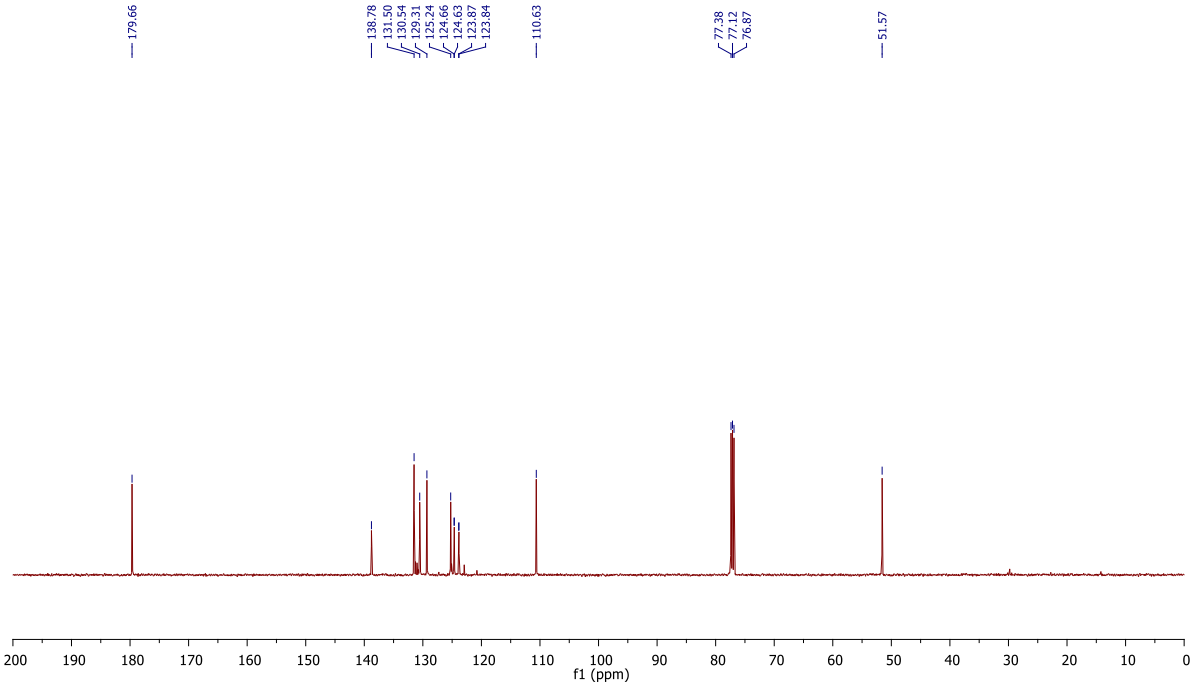
^{13}C{1H} NMR ($CDCl_3$)



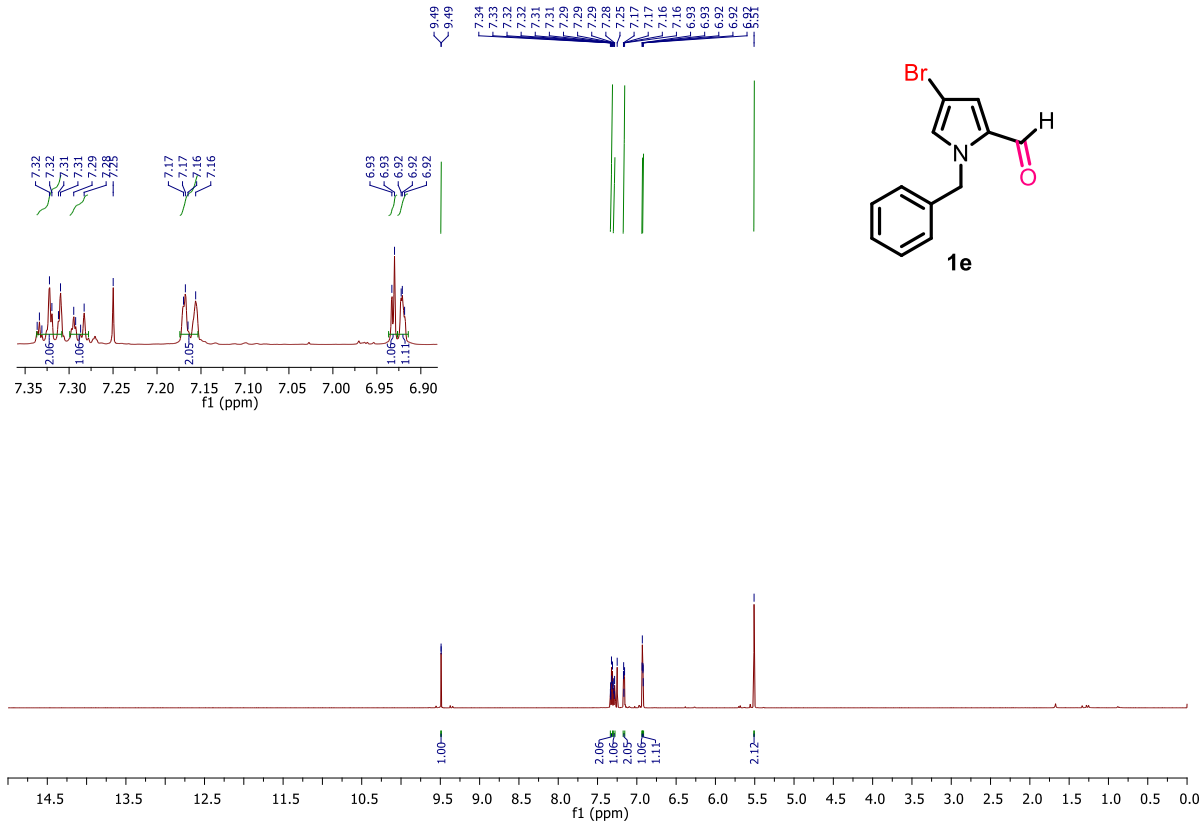
1d ^{1}H NMR ($CDCl_3$)



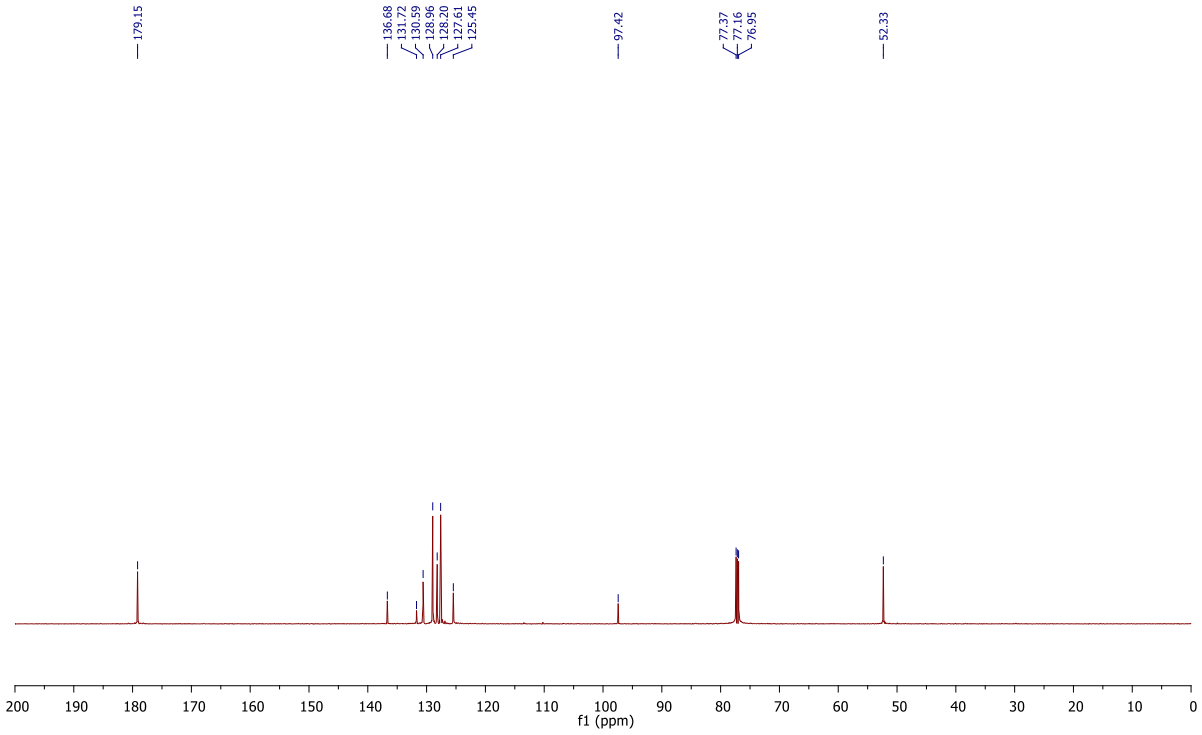
^{13}C{1H} NMR ($CDCl_3$)



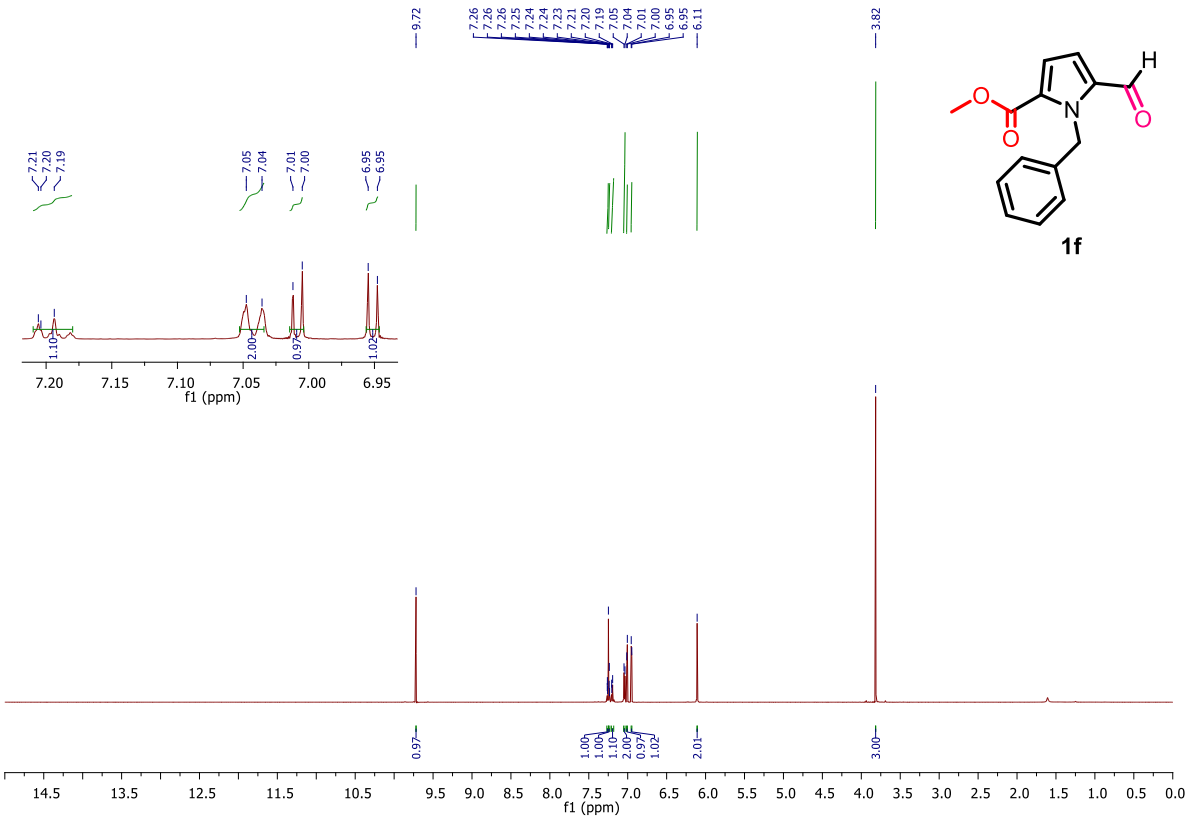
1e ^{1}H NMR ($CDCl_3$)



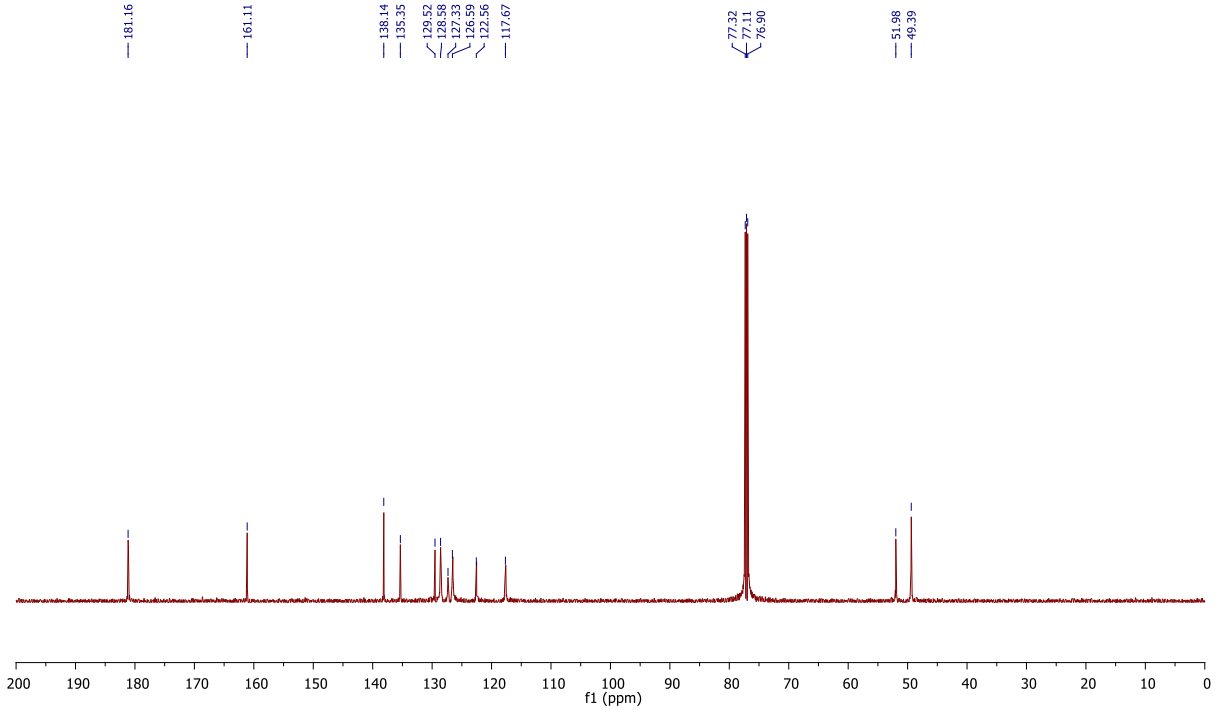
^{13}C{1H} NMR ($CDCl_3$)



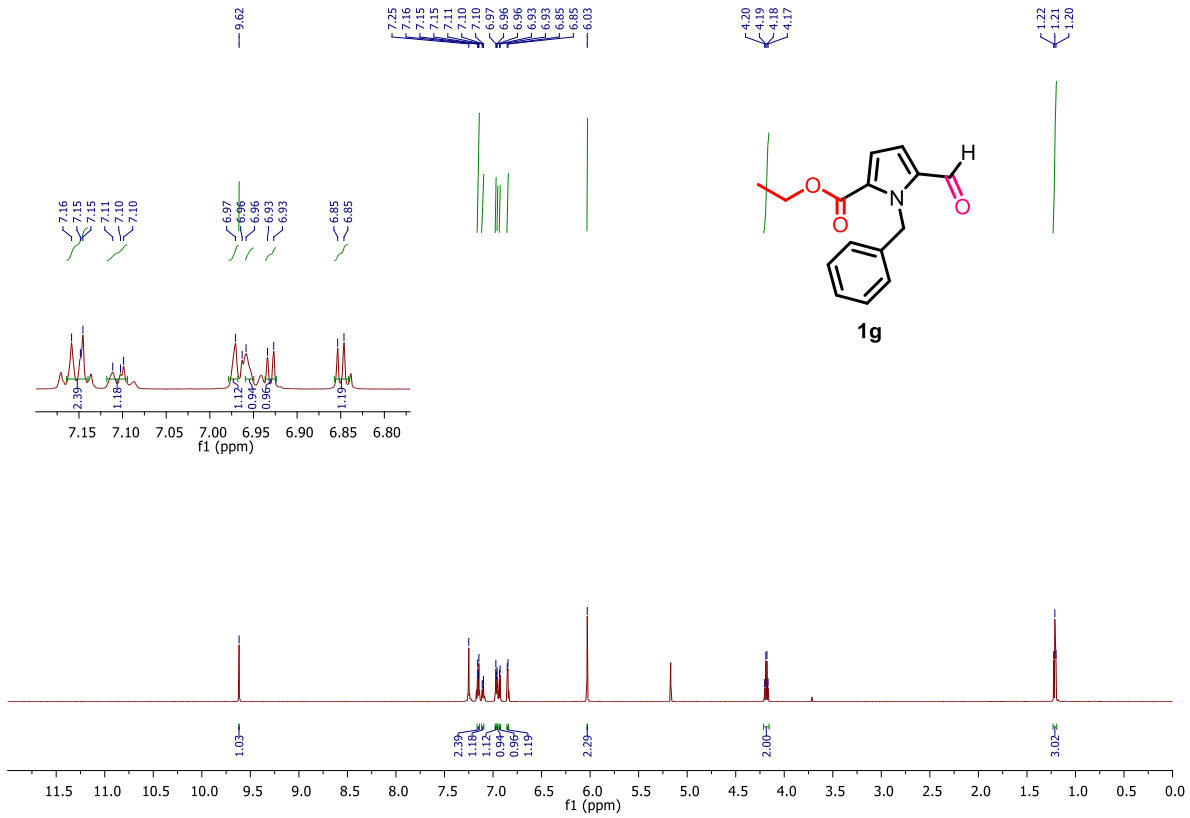
1f ^{1}H NMR ($CDCl_3$)



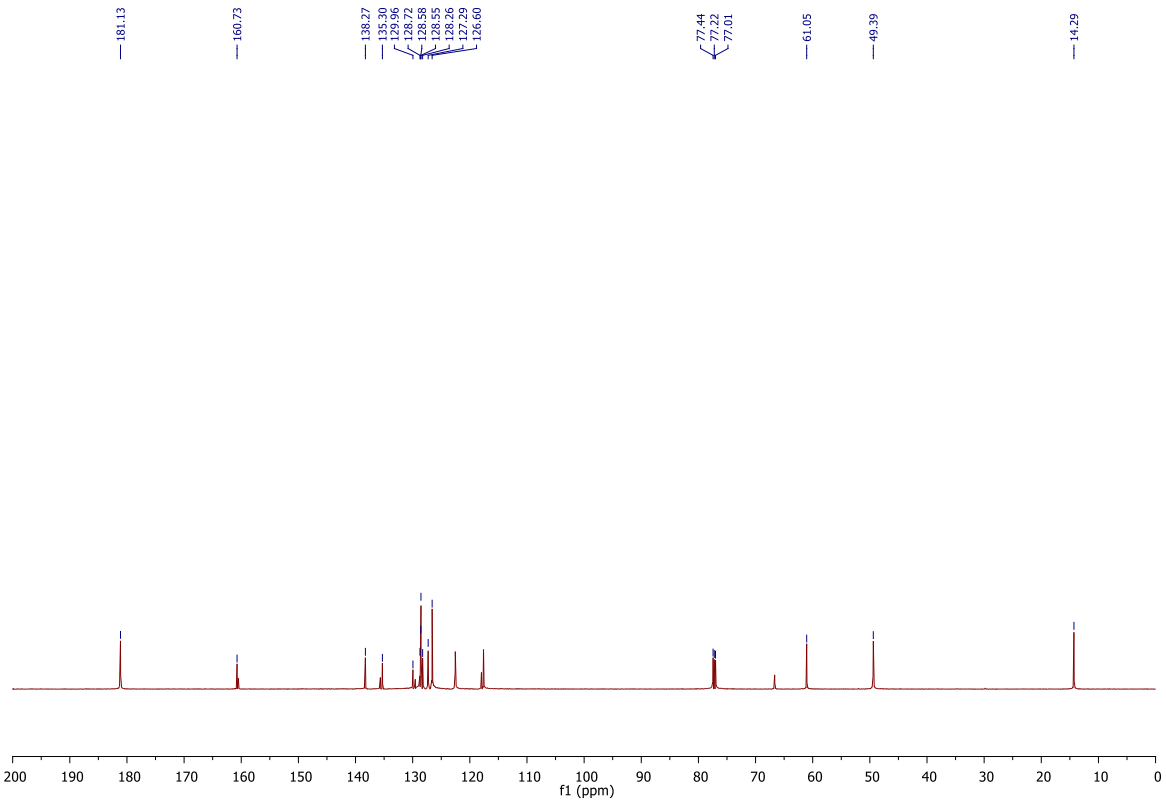
^{13}C{1H} NMR ($CDCl_3$)



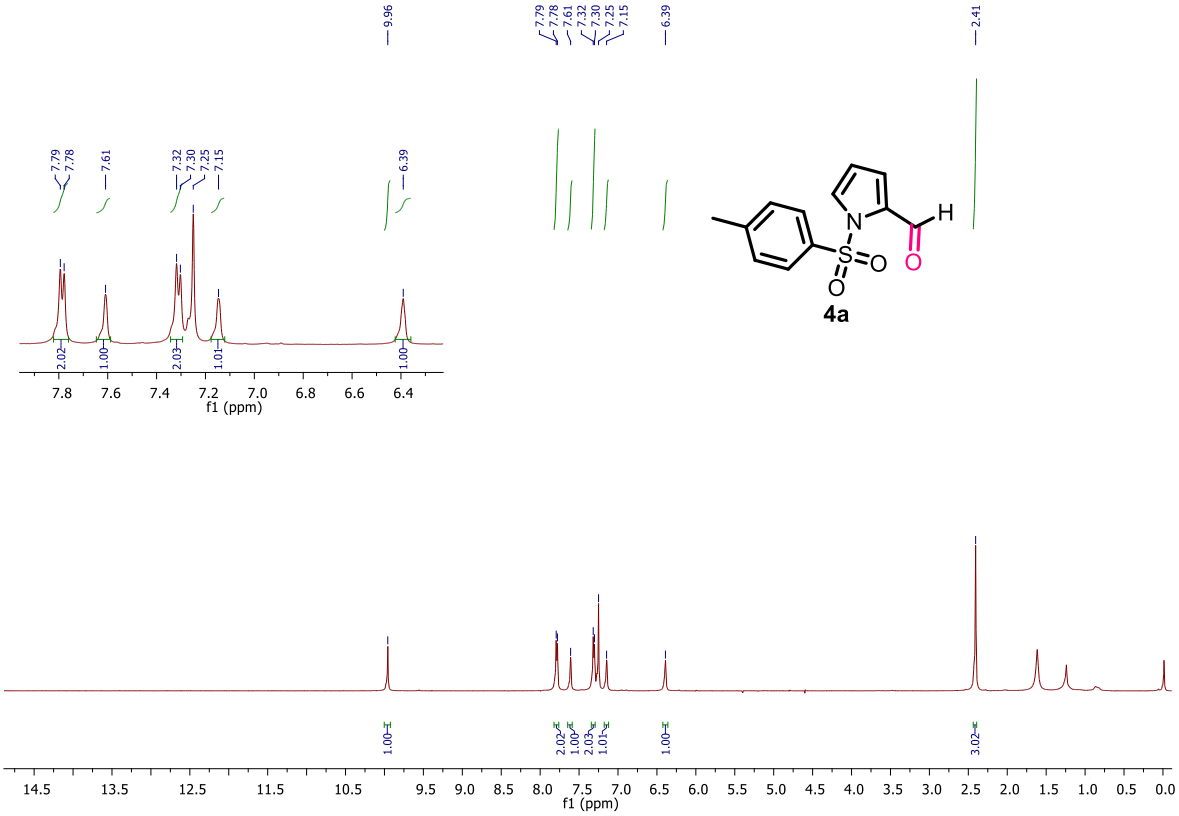
1g ^{1}H NMR ($CDCl_3$)



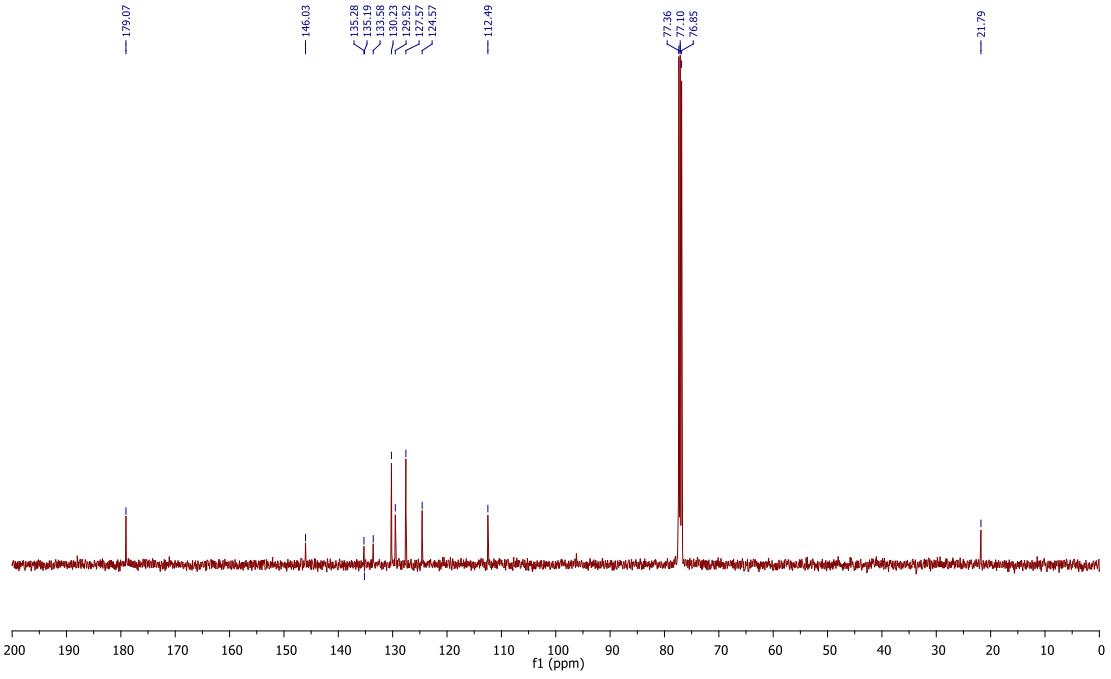
^{13}C{1H} NMR ($CDCl_3$)



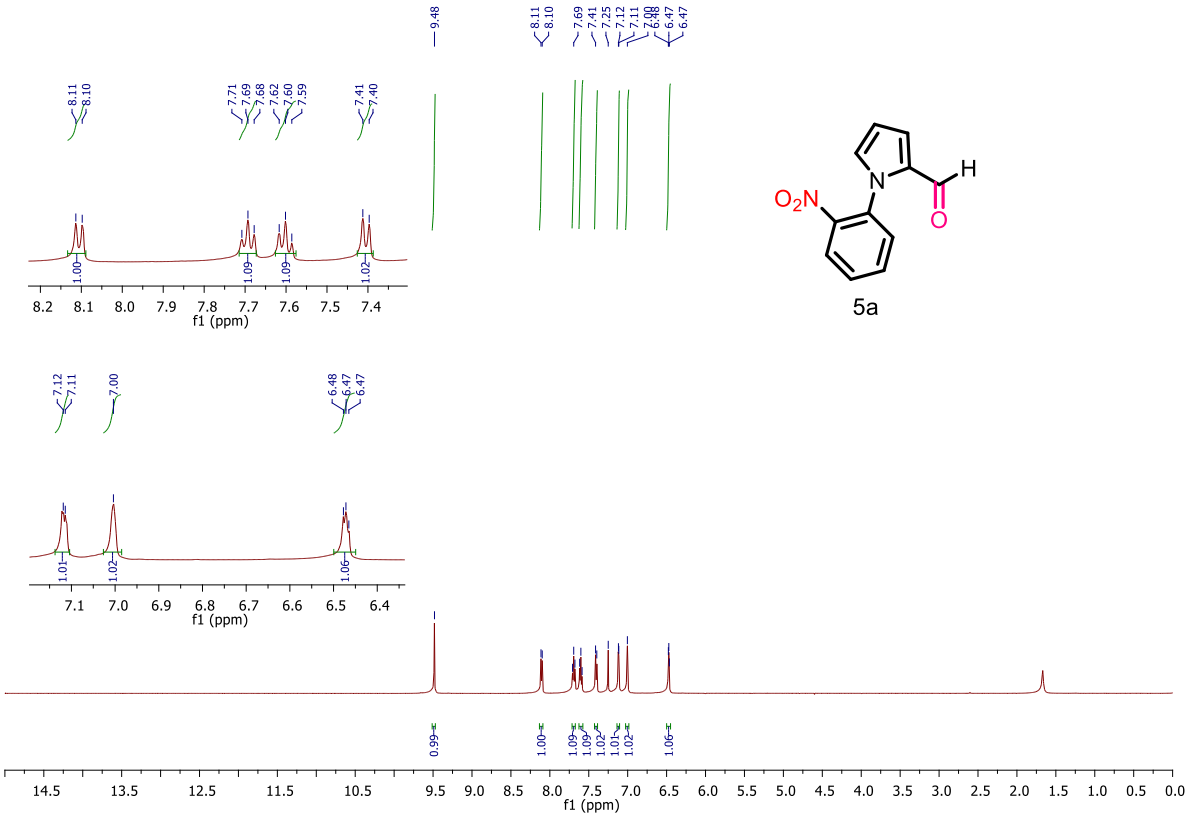
4a ^{1}H NMR ($CDCl_3$)



^{13}C{1H} NMR ($CDCl_3$)

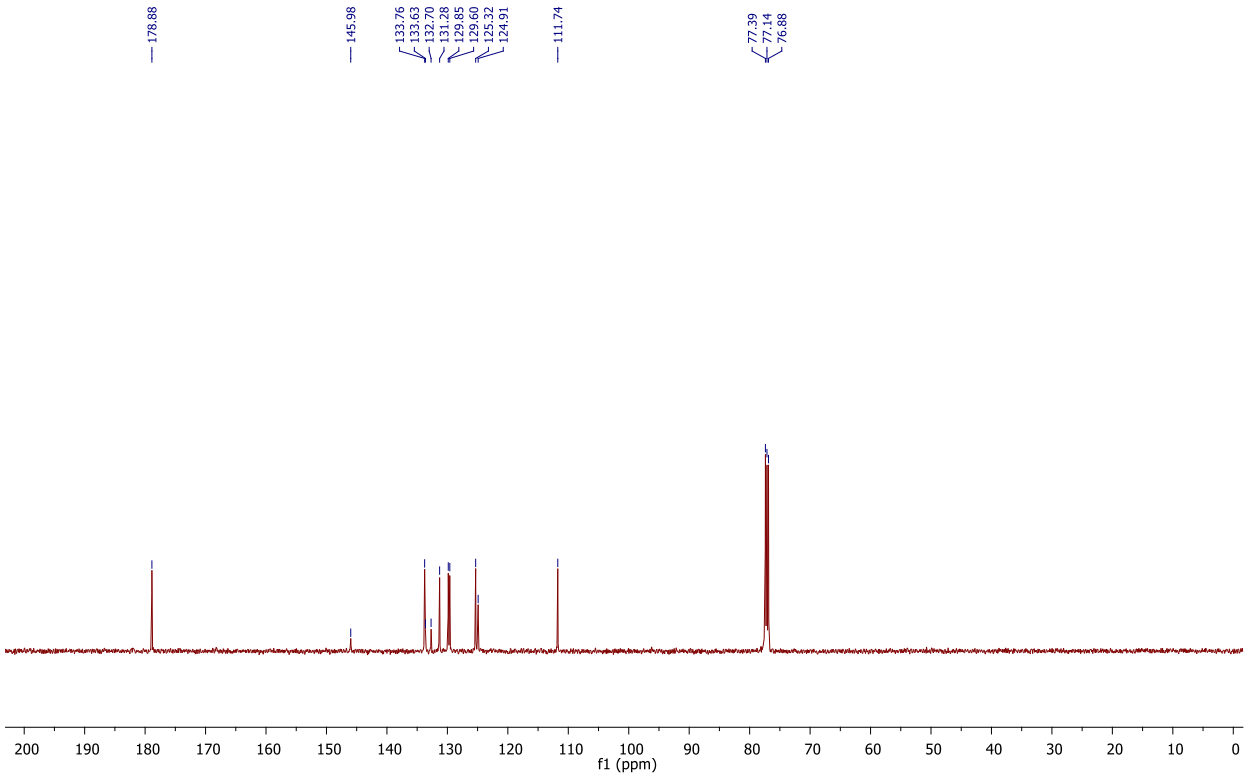


5a ^{1}H NMR ($CDCl_3$)

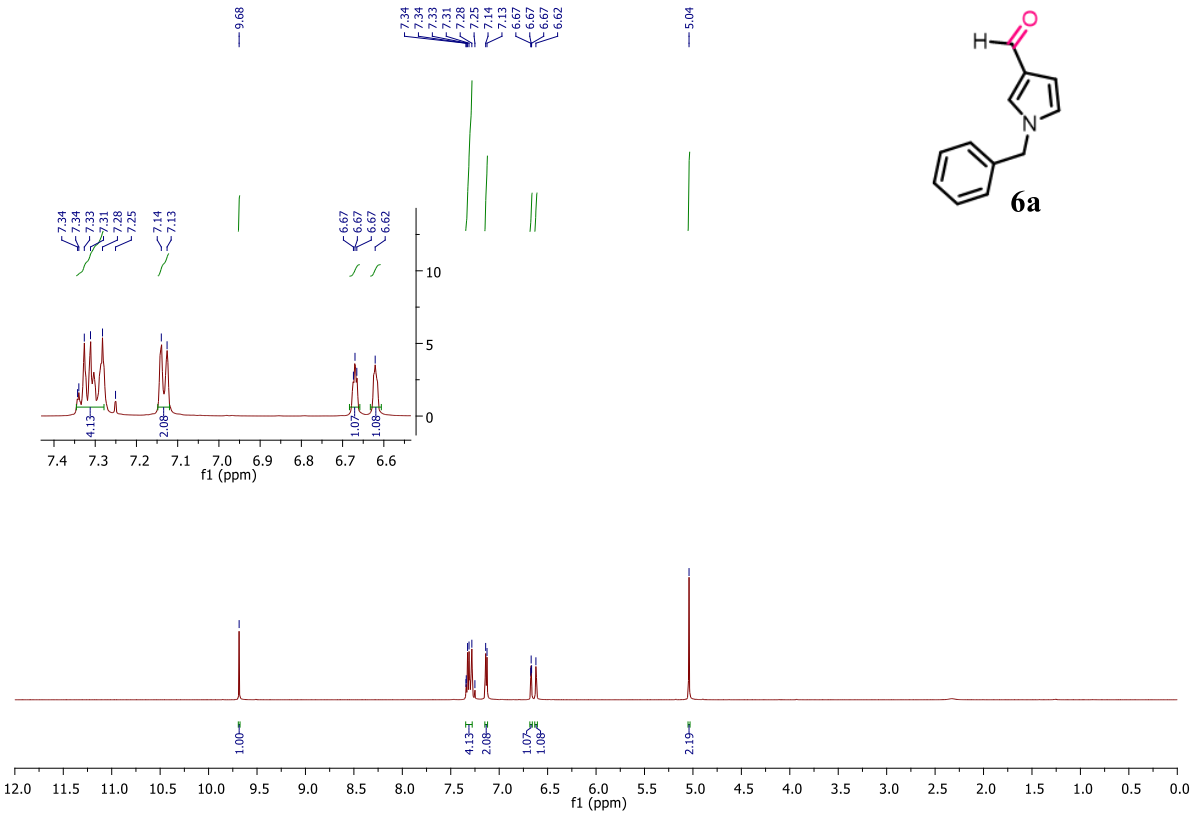


5a

^{13}C{1H} NMR ($CDCl_3$)

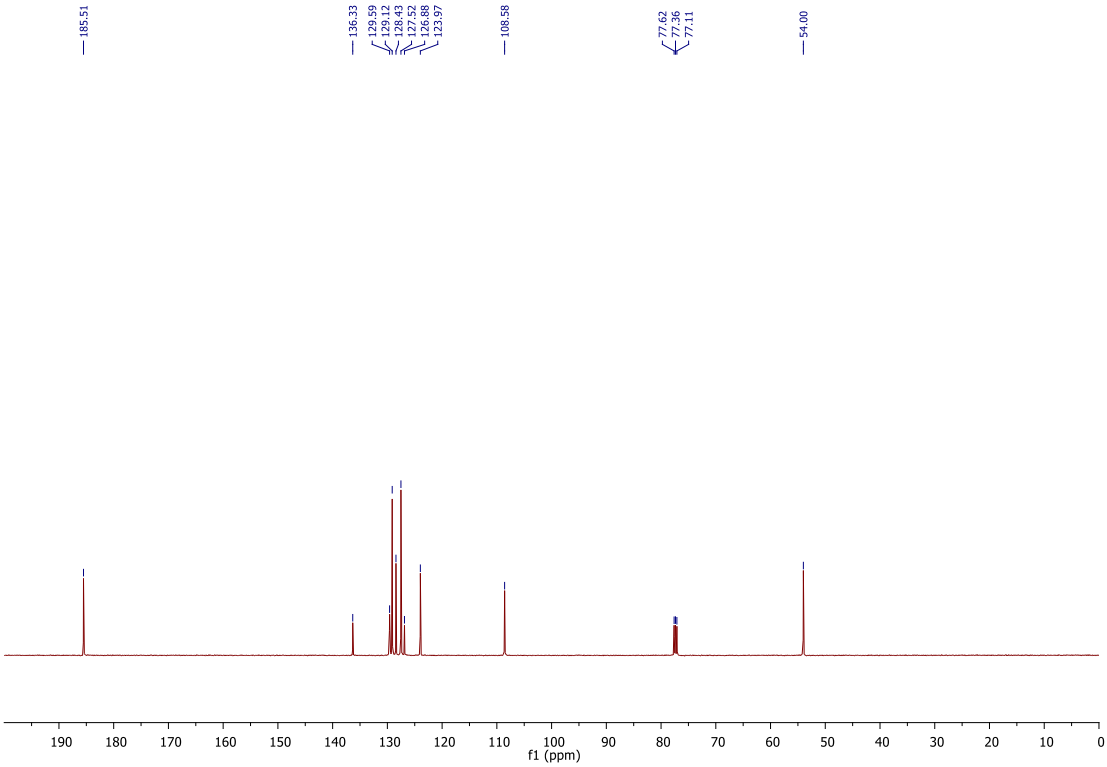


6a ^{1}H NMR ($CDCl_3$)

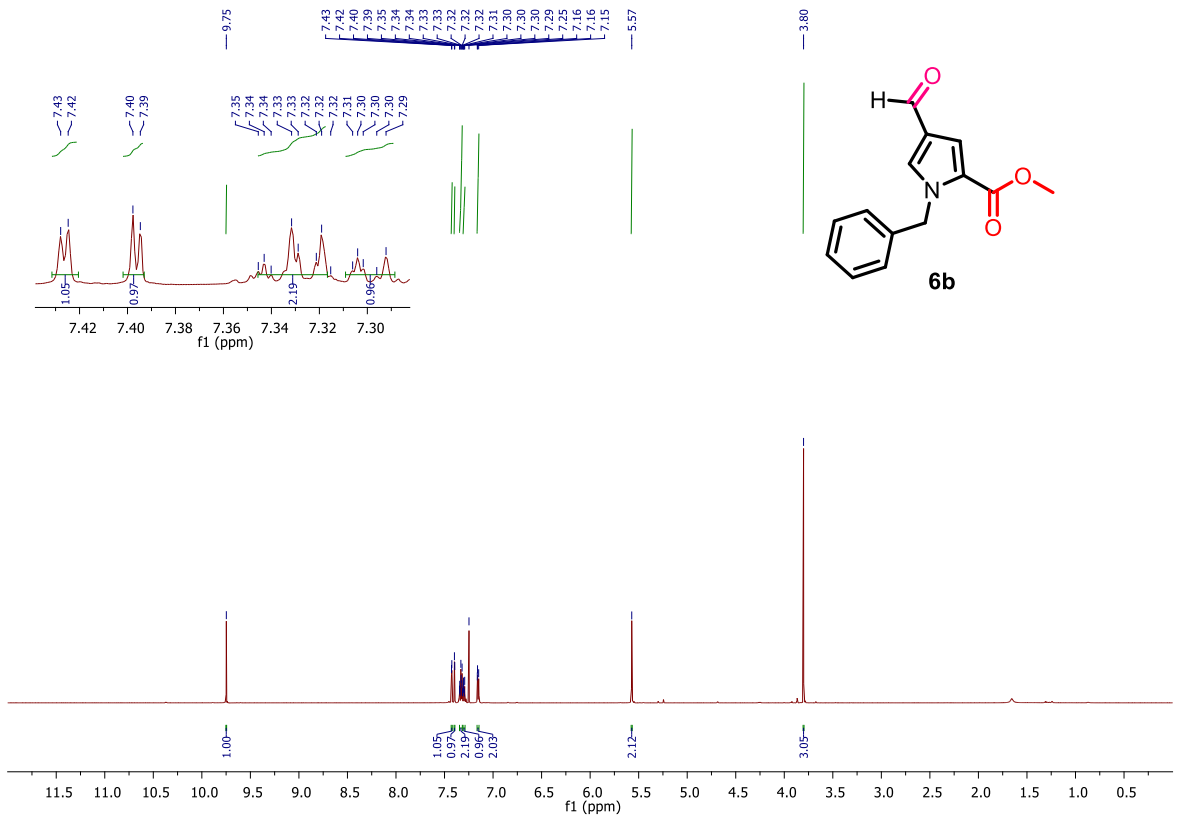


6a

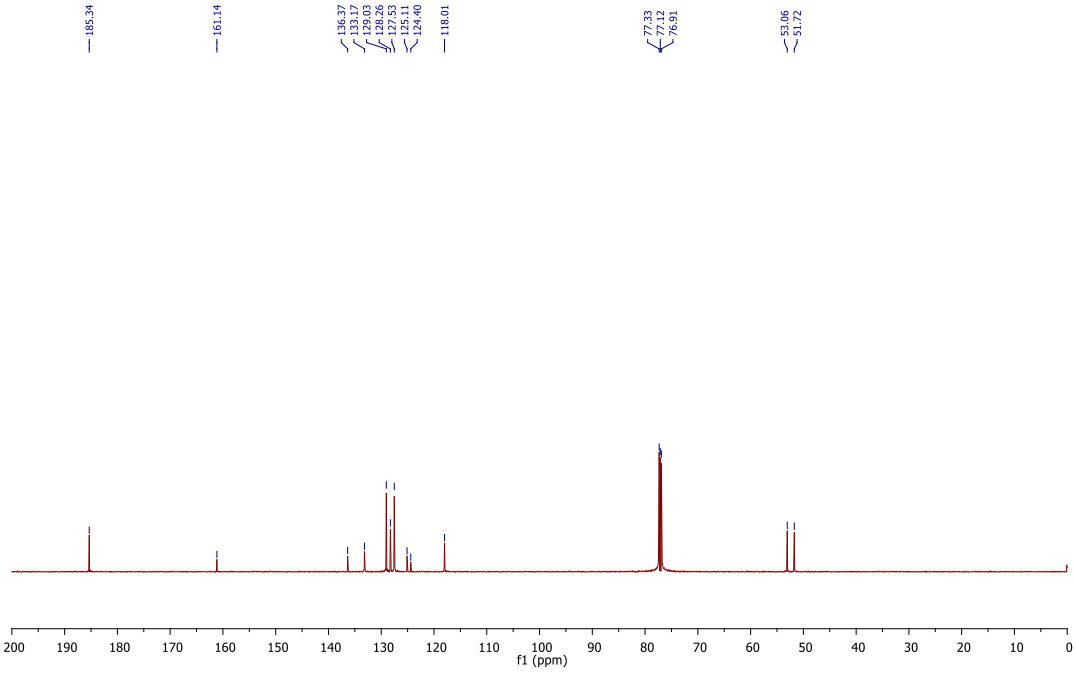
^{1}H NMR ($CDCl_3$)



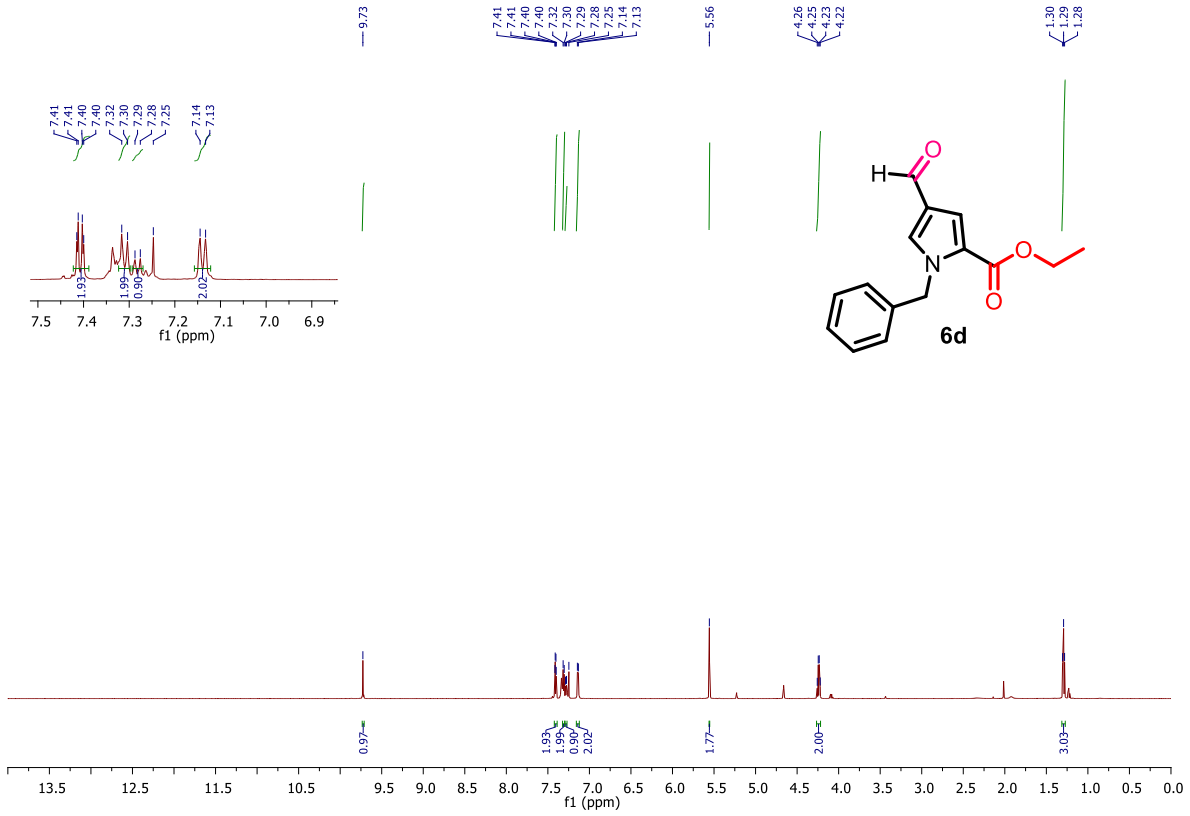
6b ^{1}H NMR ($CDCl_3$)



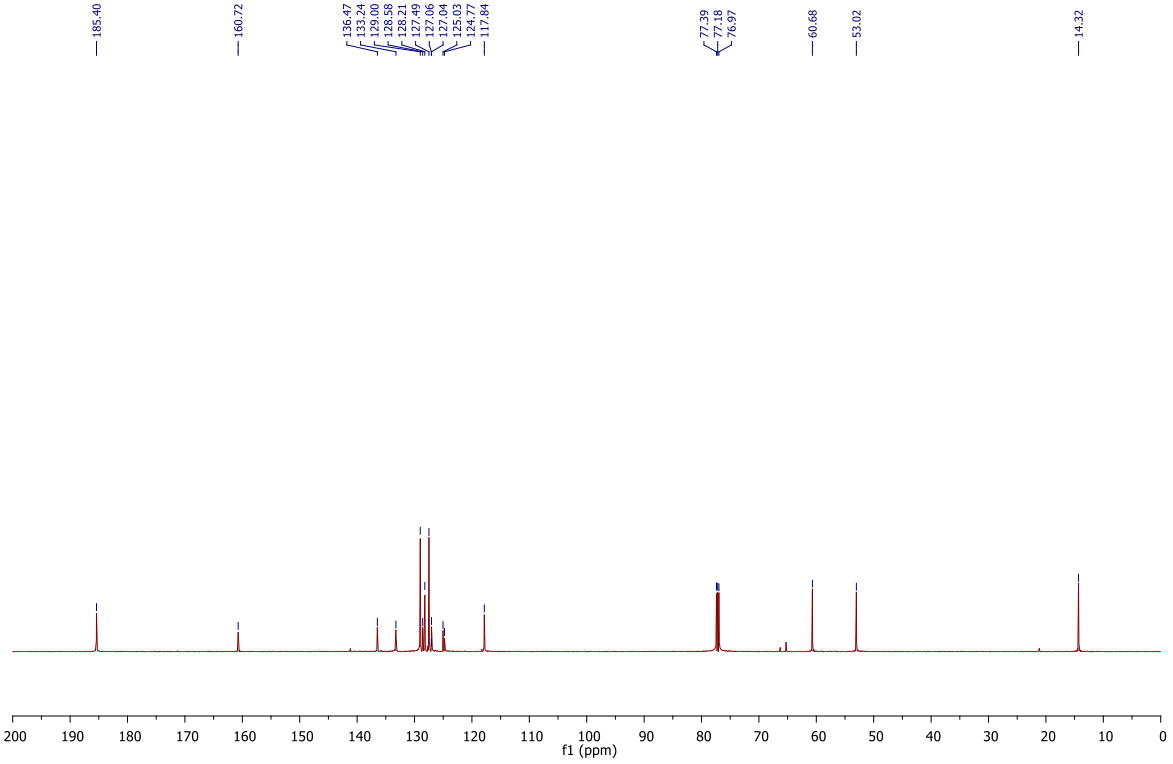
^{13}C{1H} NMR ($CDCl_3$)



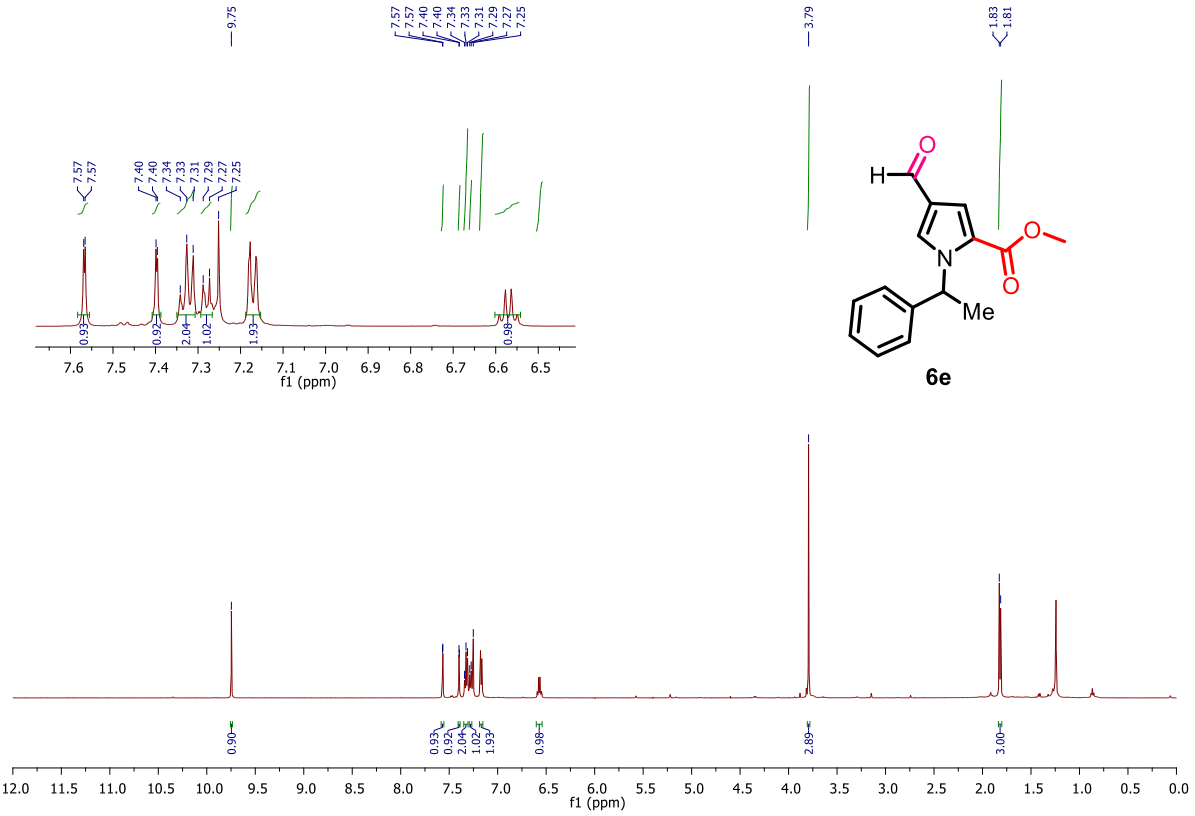
6d ^{1}H NMR ($CDCl_3$)



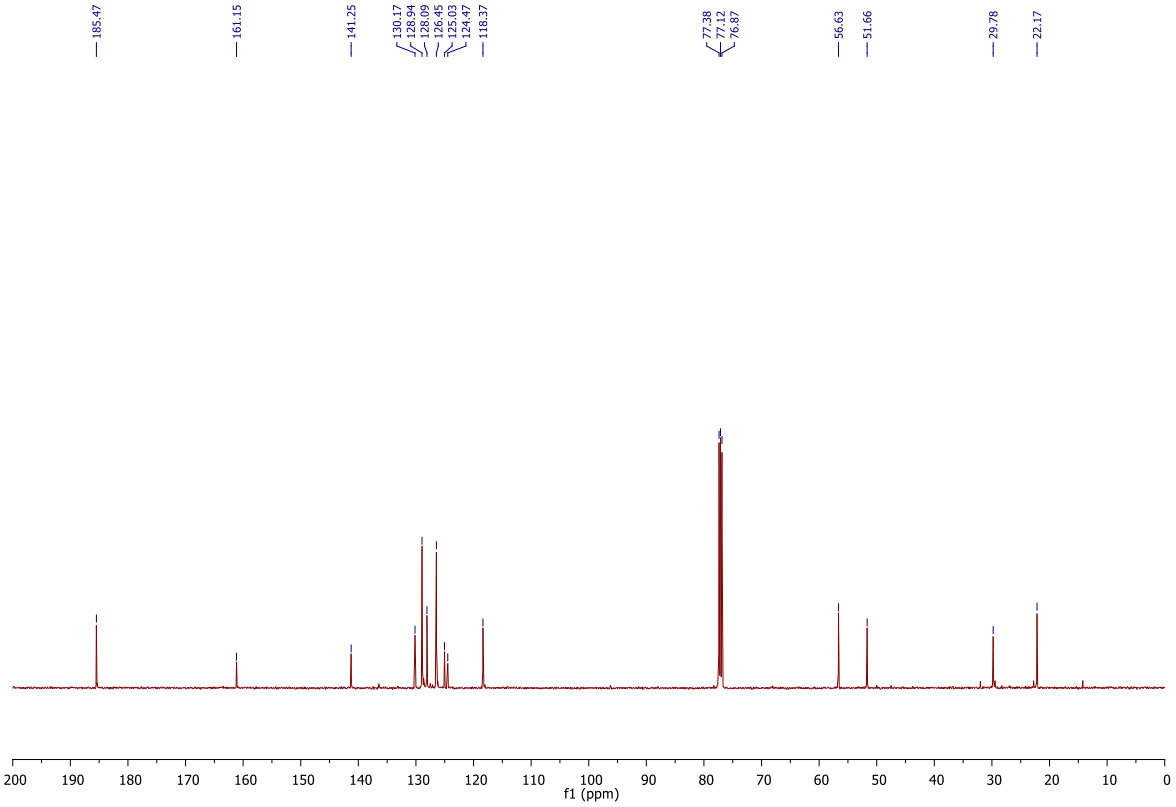
^{13}C{1H} NMR ($CDCl_3$)



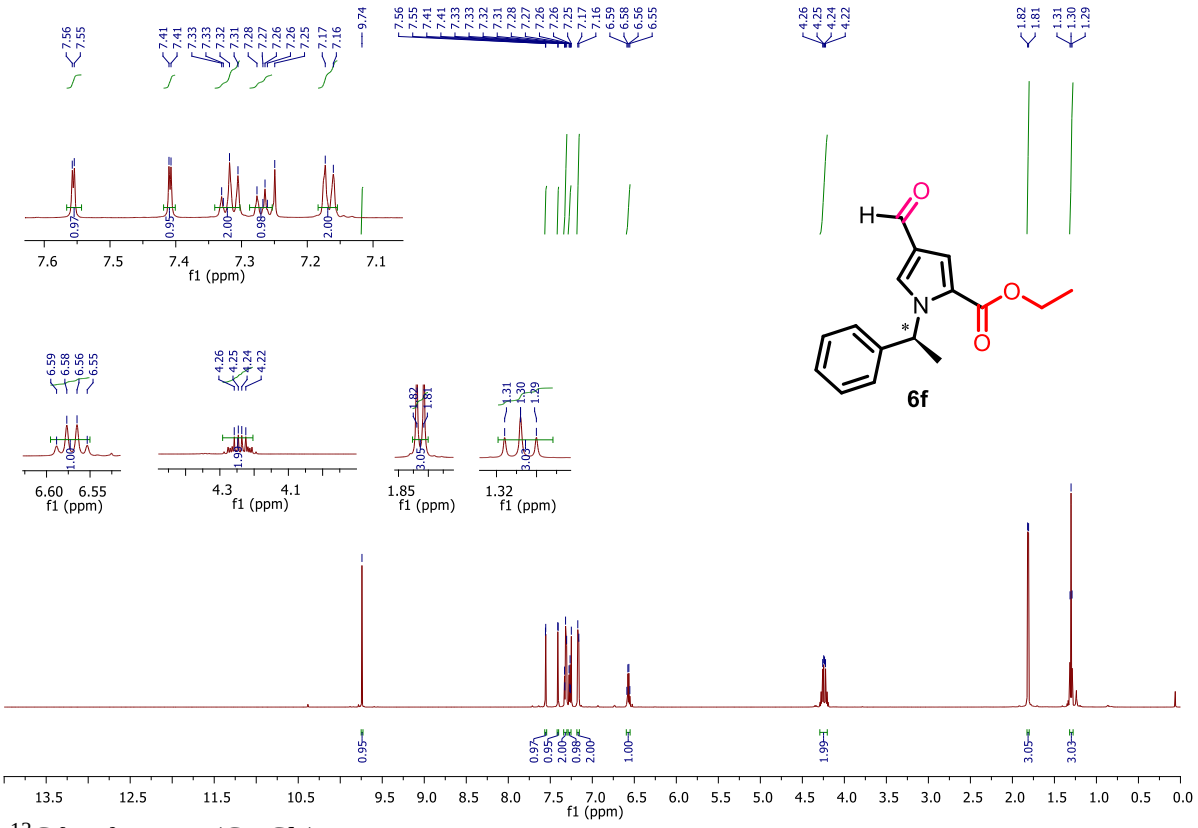
6e ^{1}H NMR ($CDCl_3$)



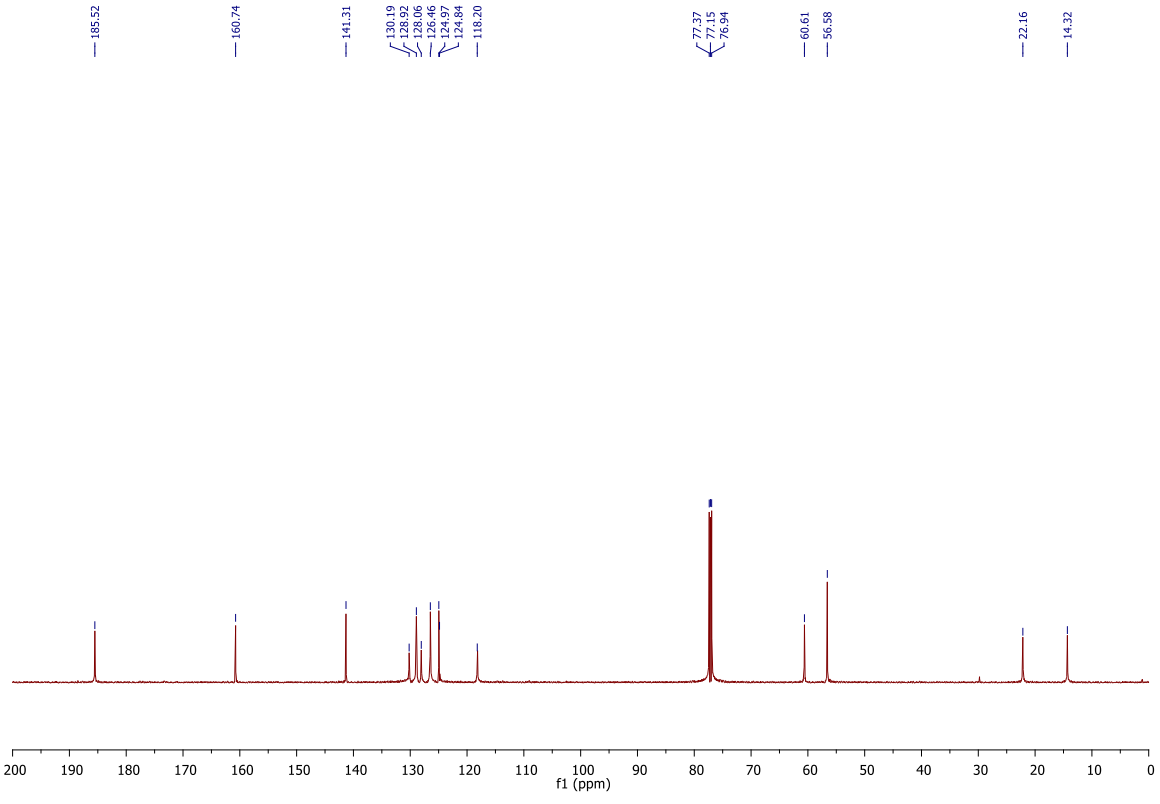
^{13}C{1H} NMR ($CDCl_3$)



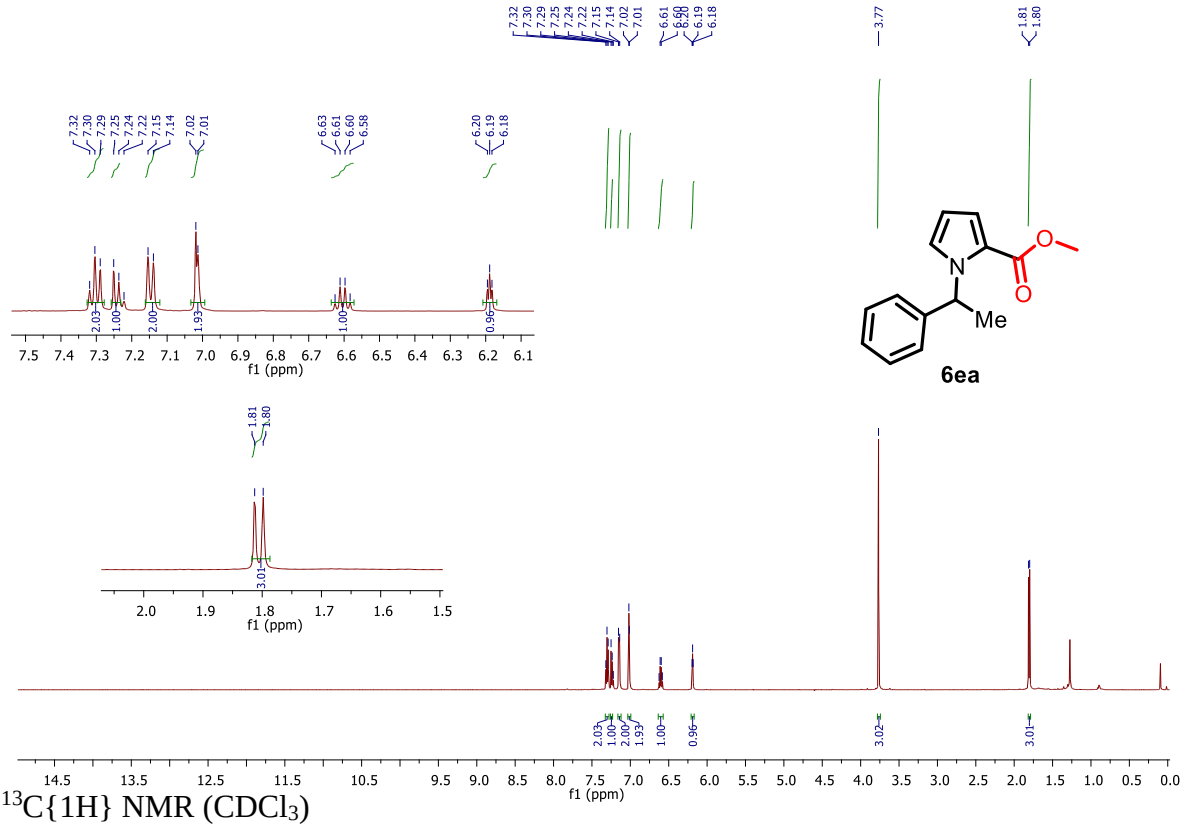
6f ^{1}H NMR ($CDCl_3$)



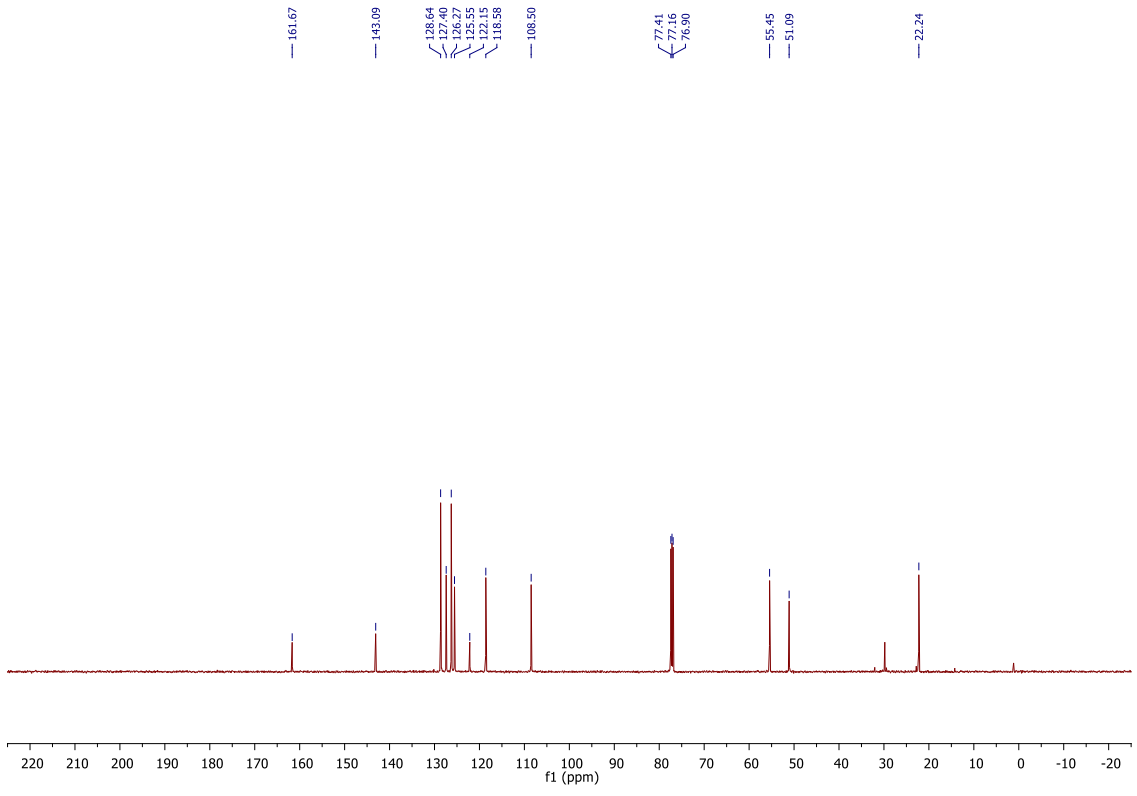
^{13}C{1H} NMR ($CDCl_3$)



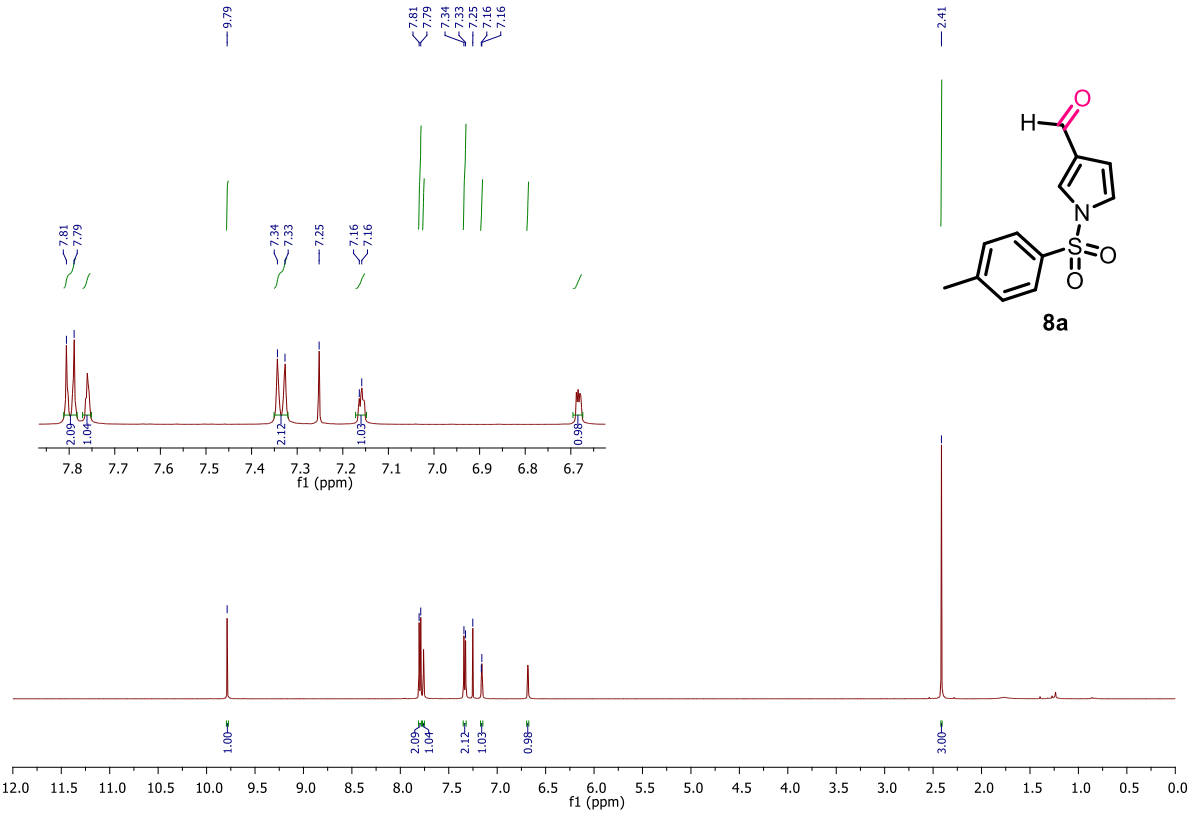
6ea ^{1}H NMR ($CDCl_3$)



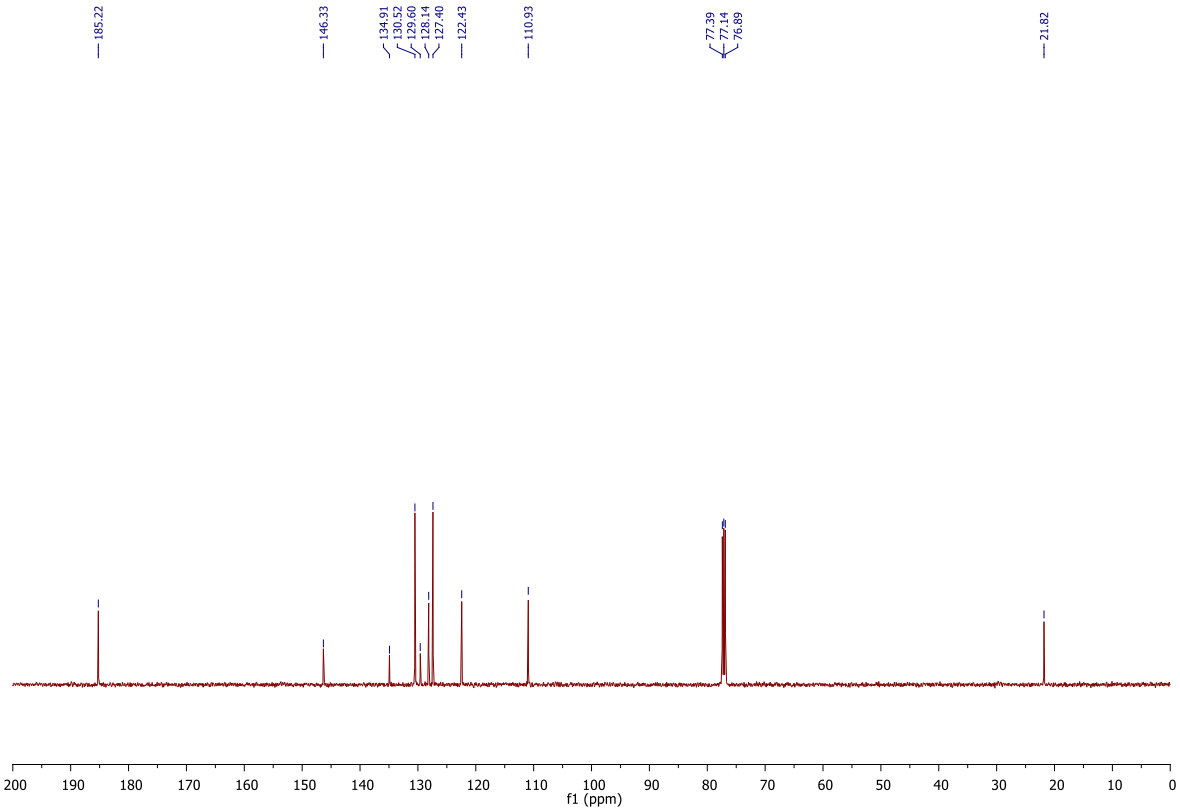
^{13}C{1H} NMR ($CDCl_3$)



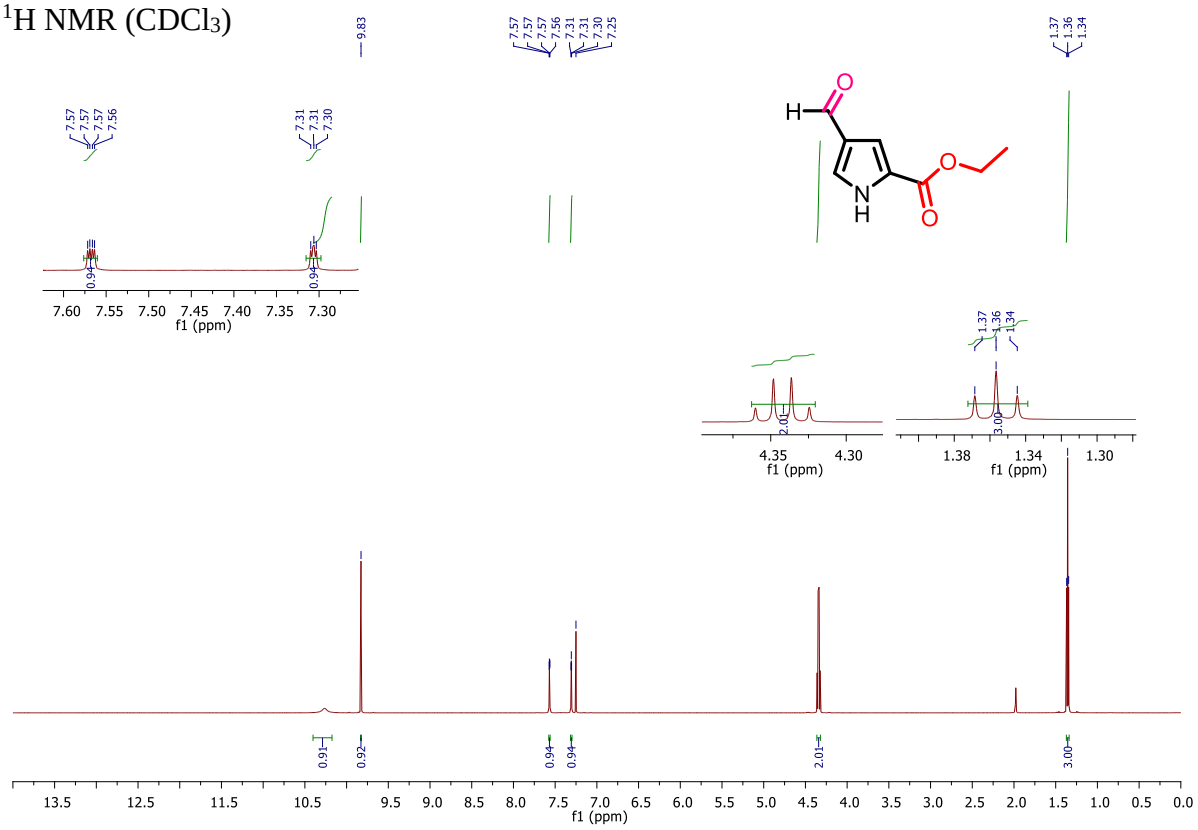
8a ^{1}H NMR ($CDCl_3$)



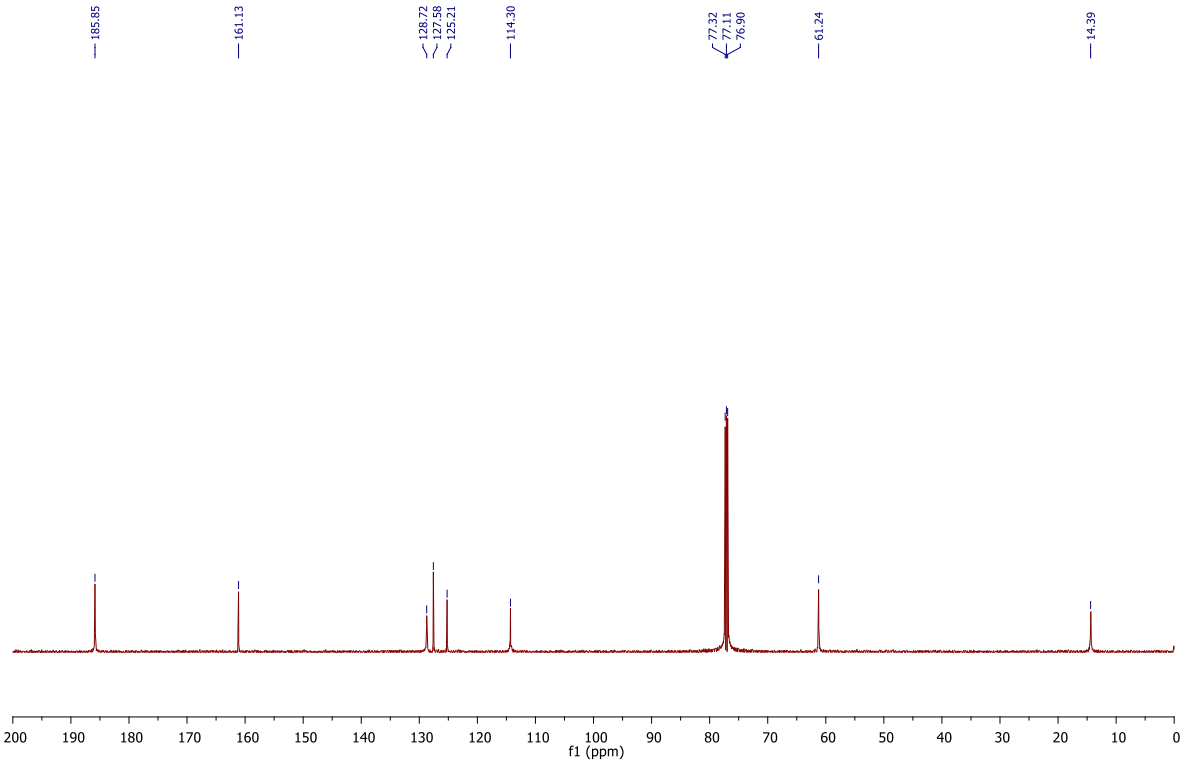
^{13}C{1H} NMR ($CDCl_3$)



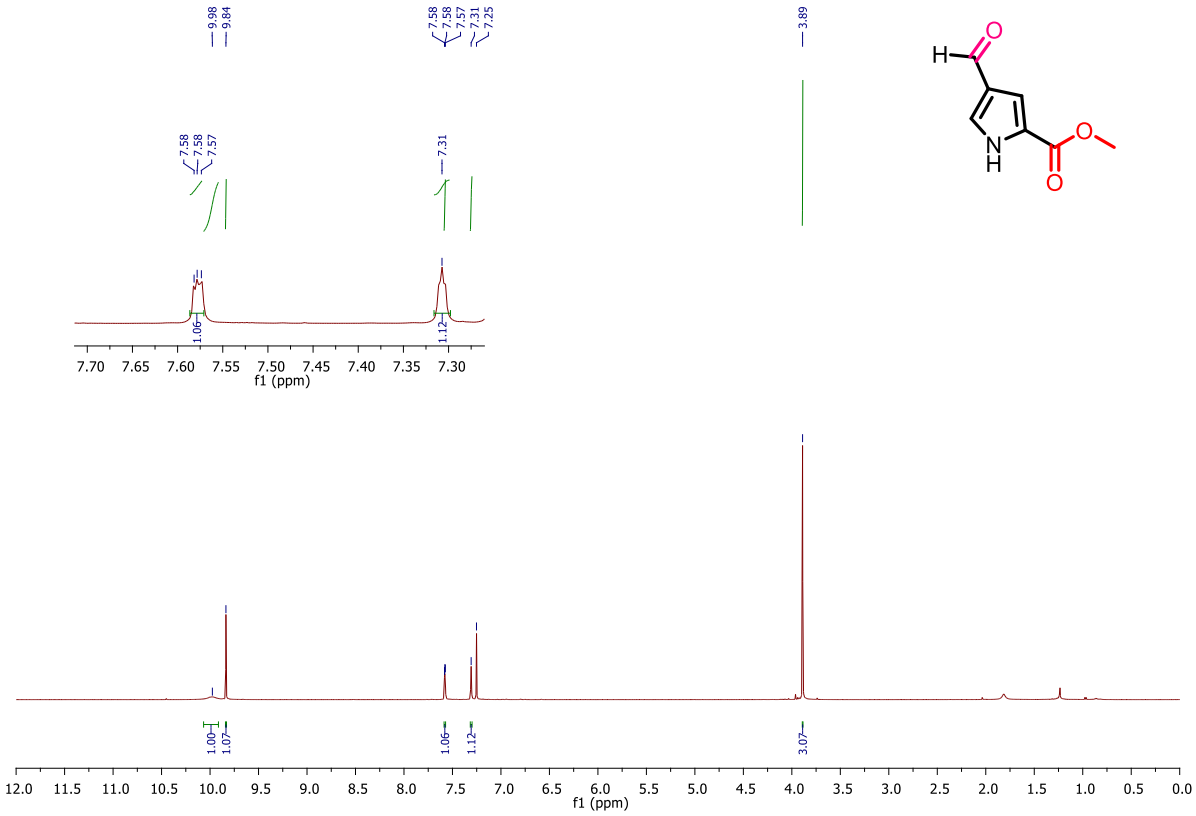
^{1}H NMR ($CDCl_3$)



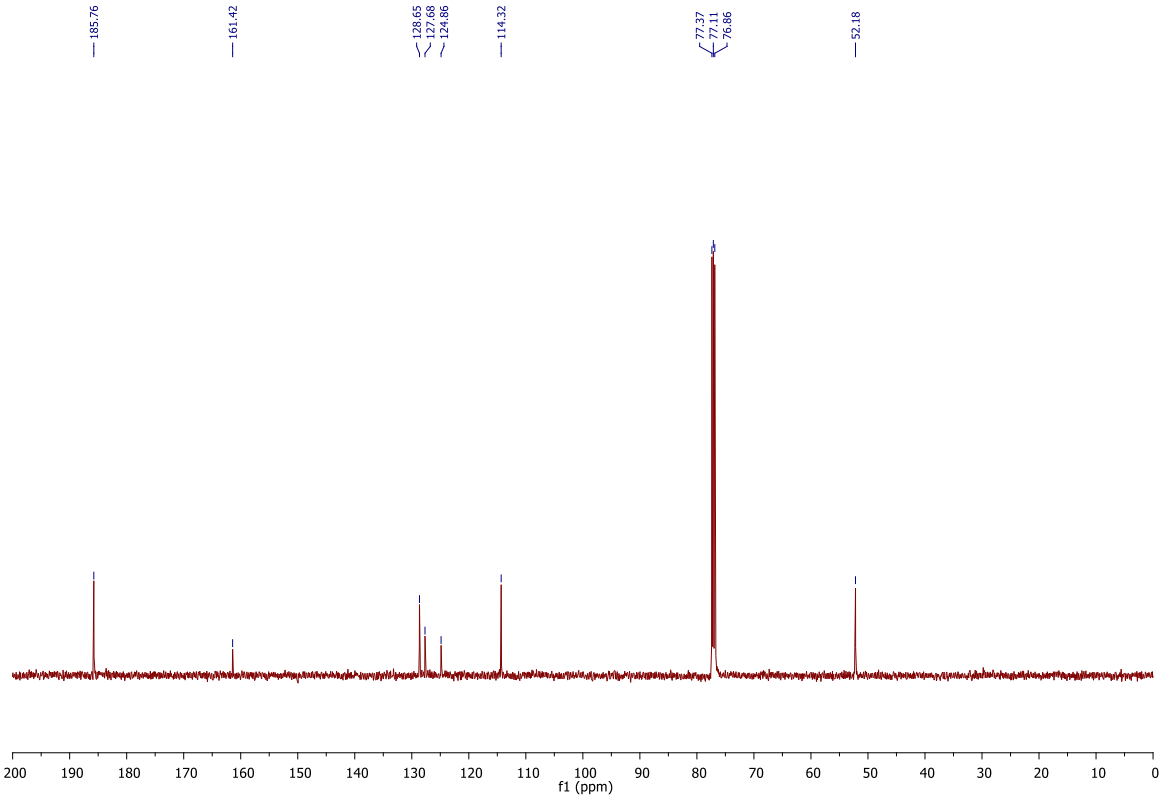
^{13}C{1H} NMR ($CDCl_3$)



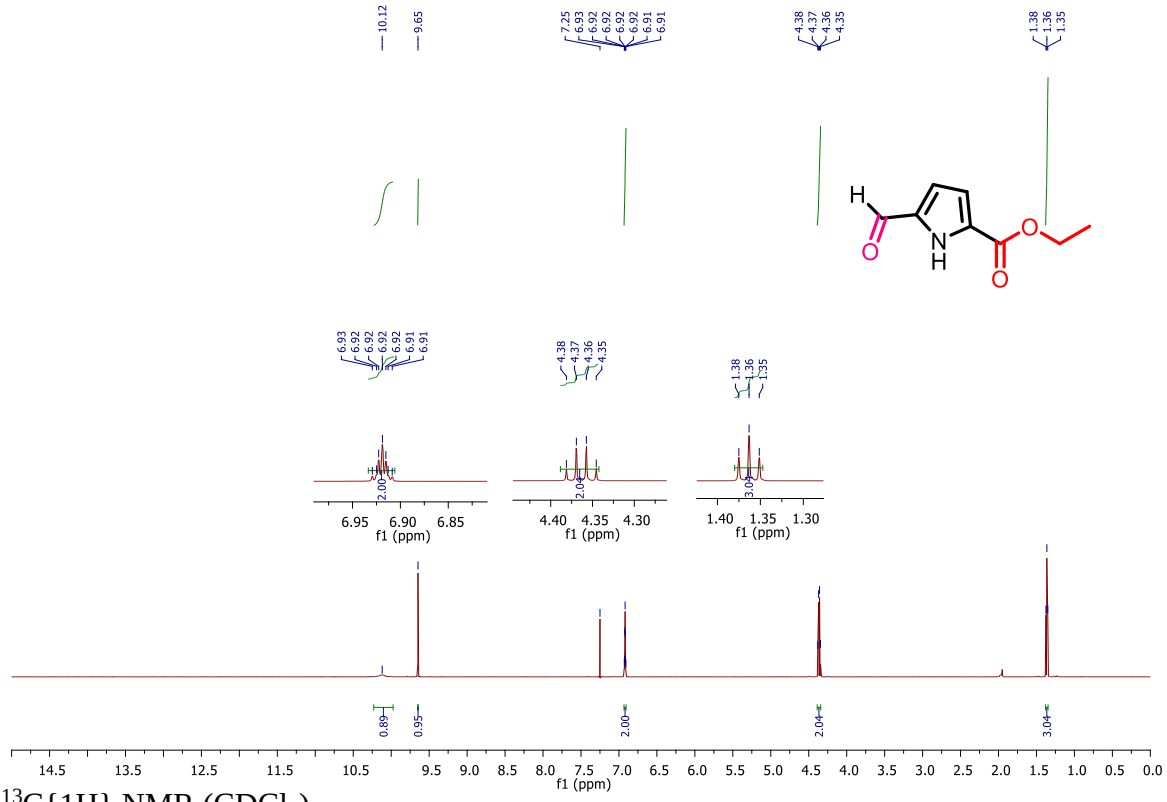
^{1}H NMR ($CDCl_3$)



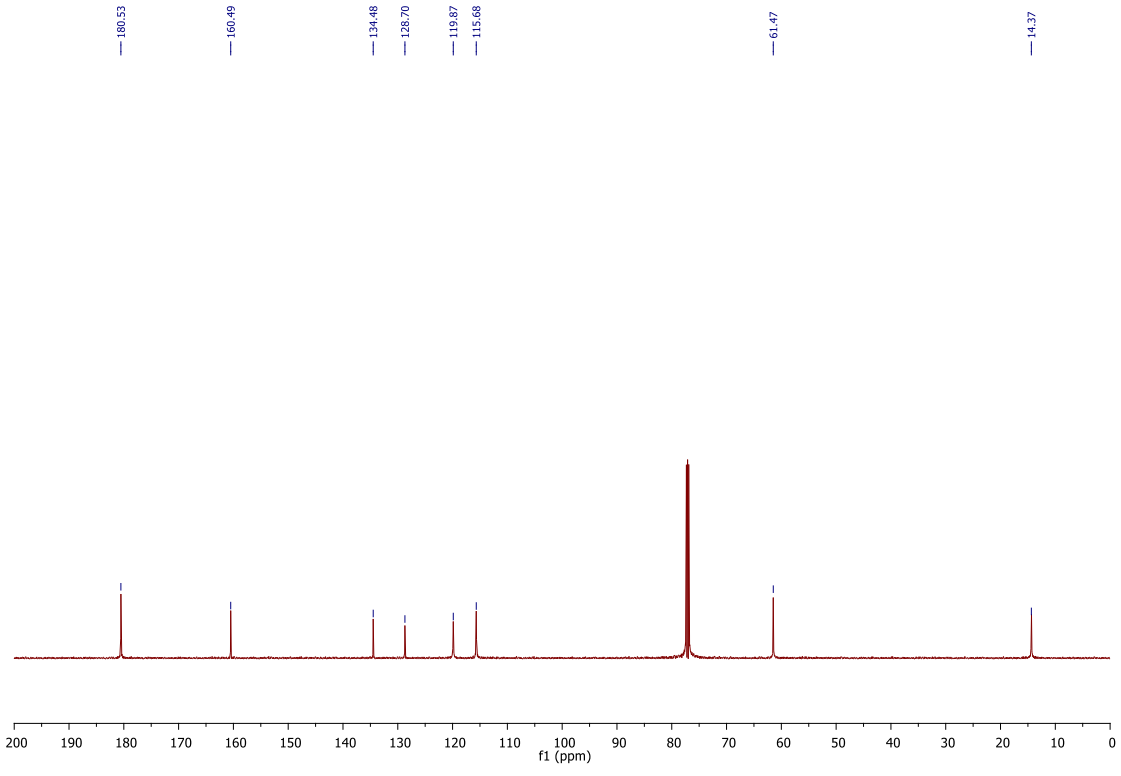
^{13}C{1H} NMR ($CDCl_3$)



^{1}H NMR ($CDCl_3$)

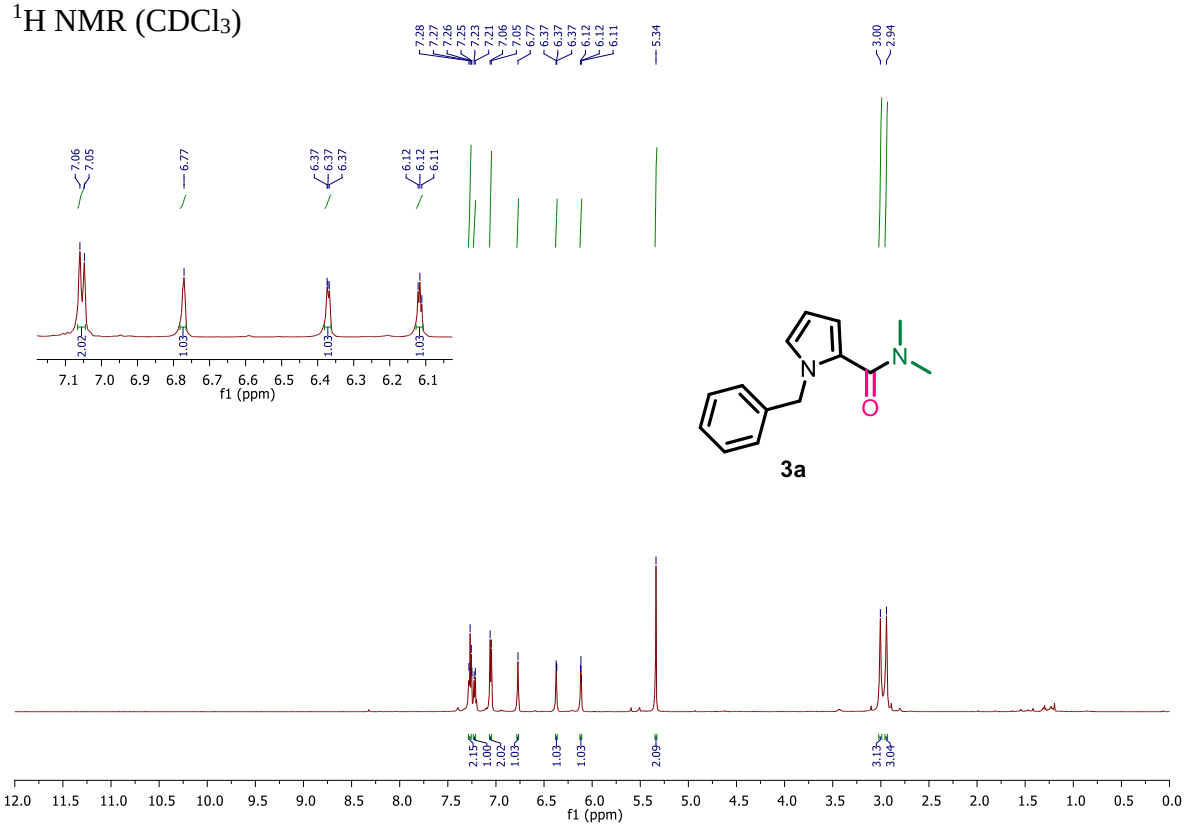


^{13}C{1H} NMR ($CDCl_3$)

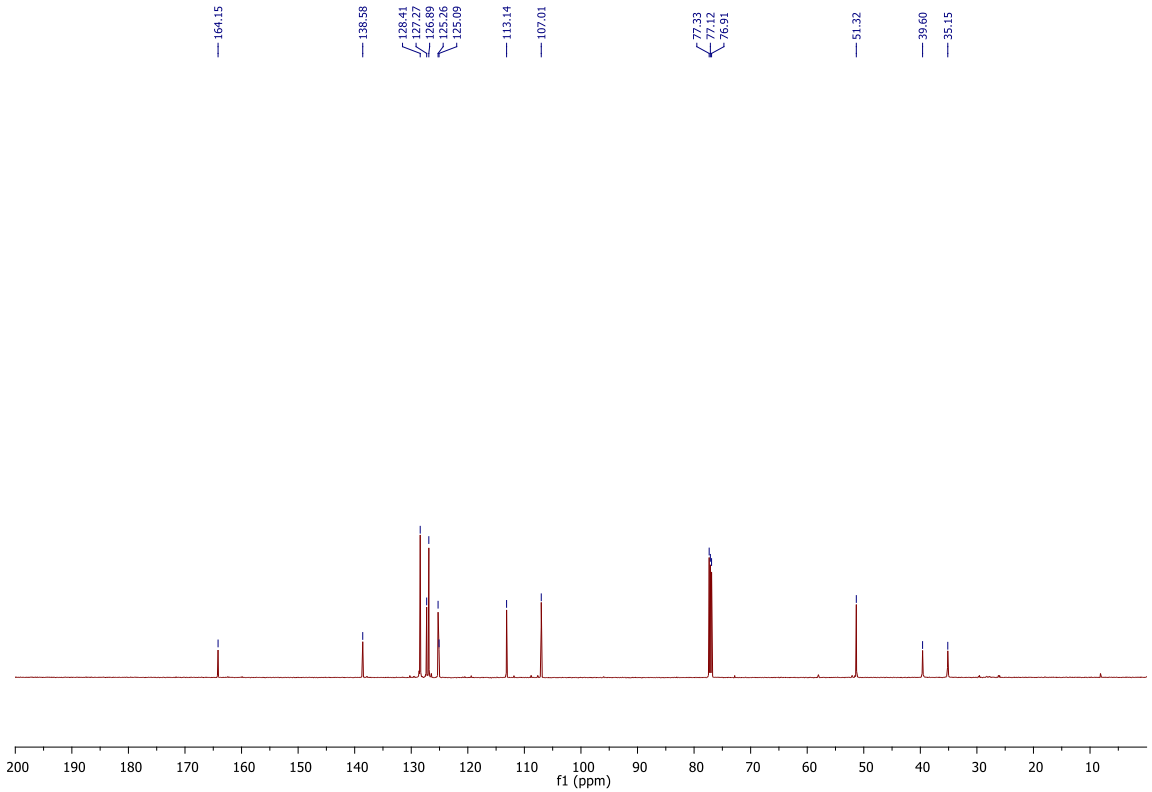


6b. ^{1}H and ^{13}C Spectra of Pyrrole Amides

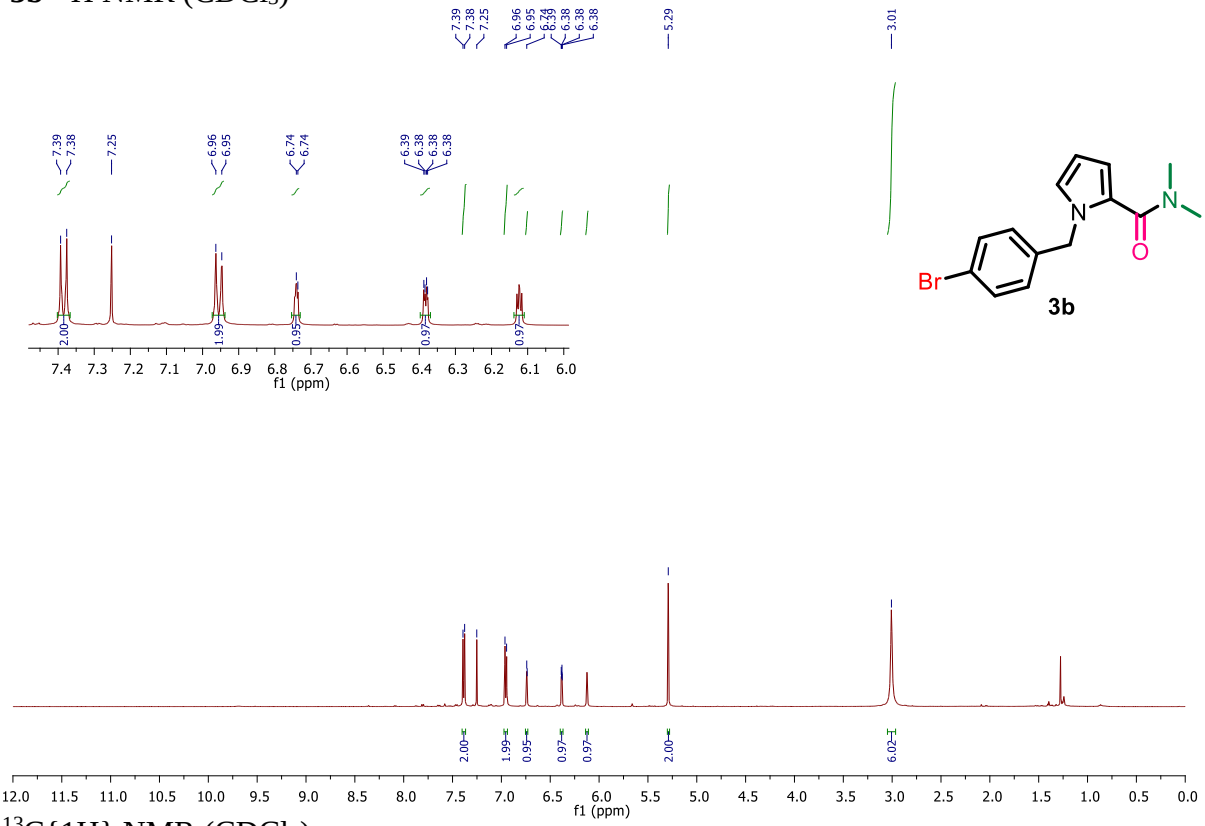
3a ^{1}H NMR ($CDCl_3$)



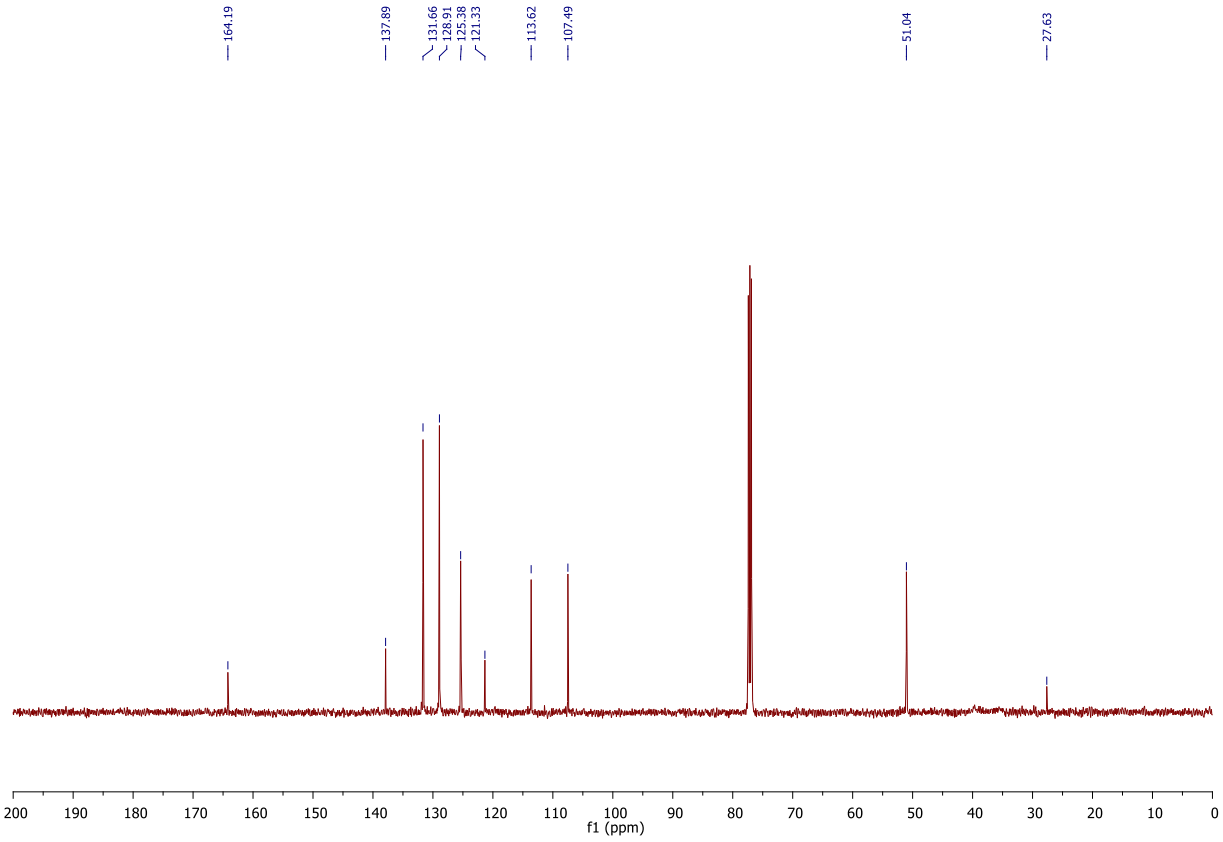
$^{13}C\{1H\}$ NMR ($CDCl_3$)



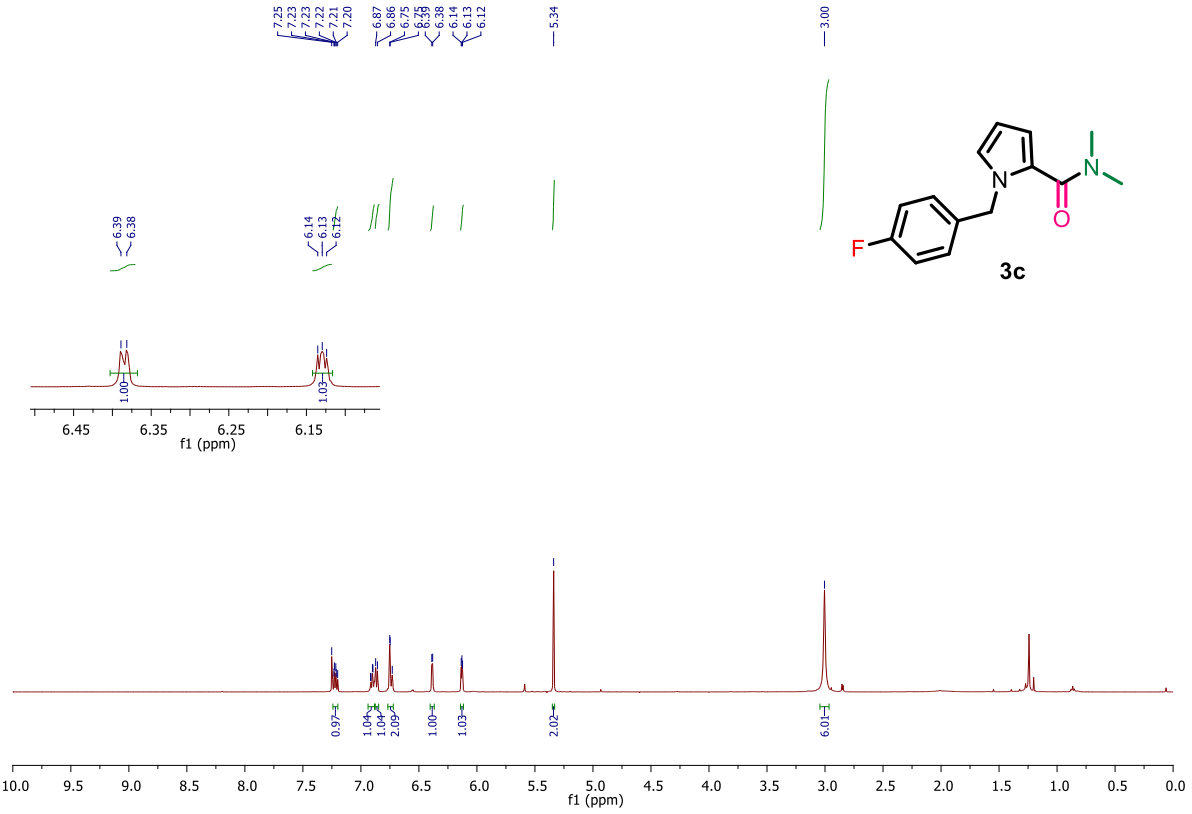
3b ^{1}H NMR ($CDCl_3$)



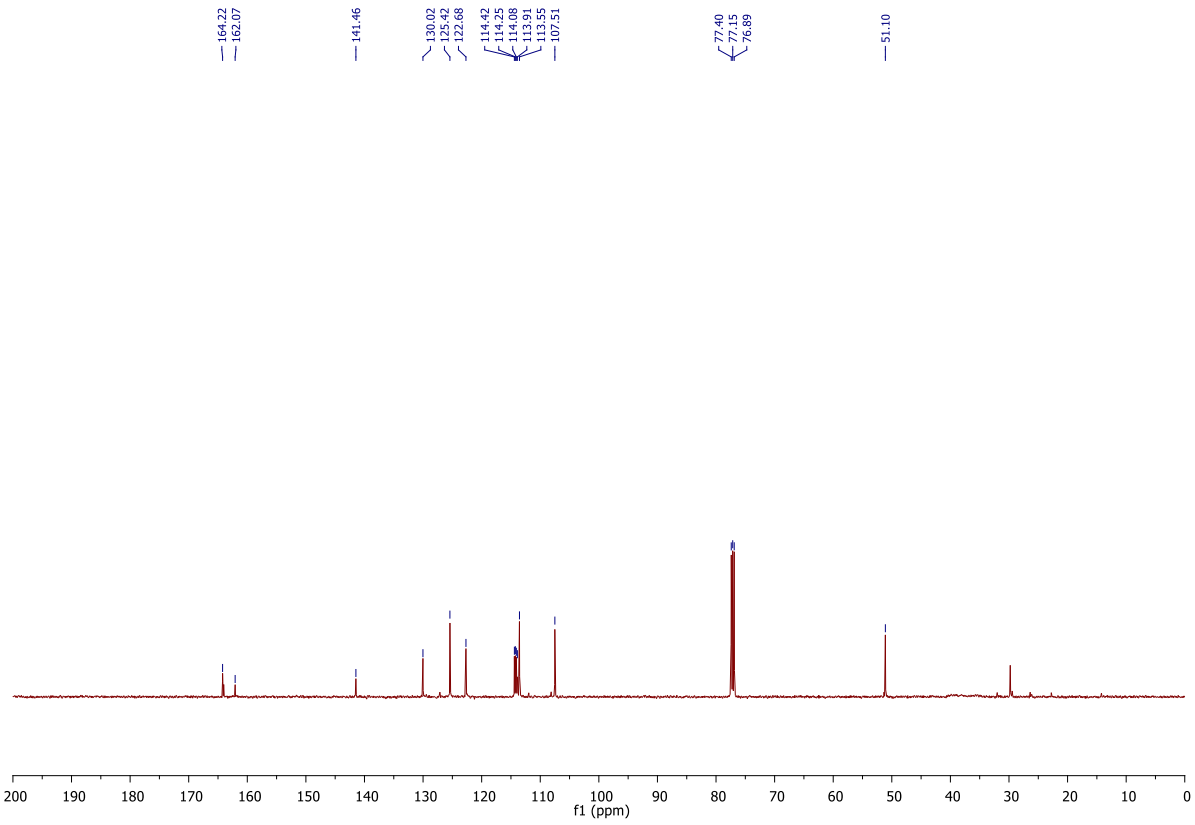
^{13}C{1H} NMR ($CDCl_3$)



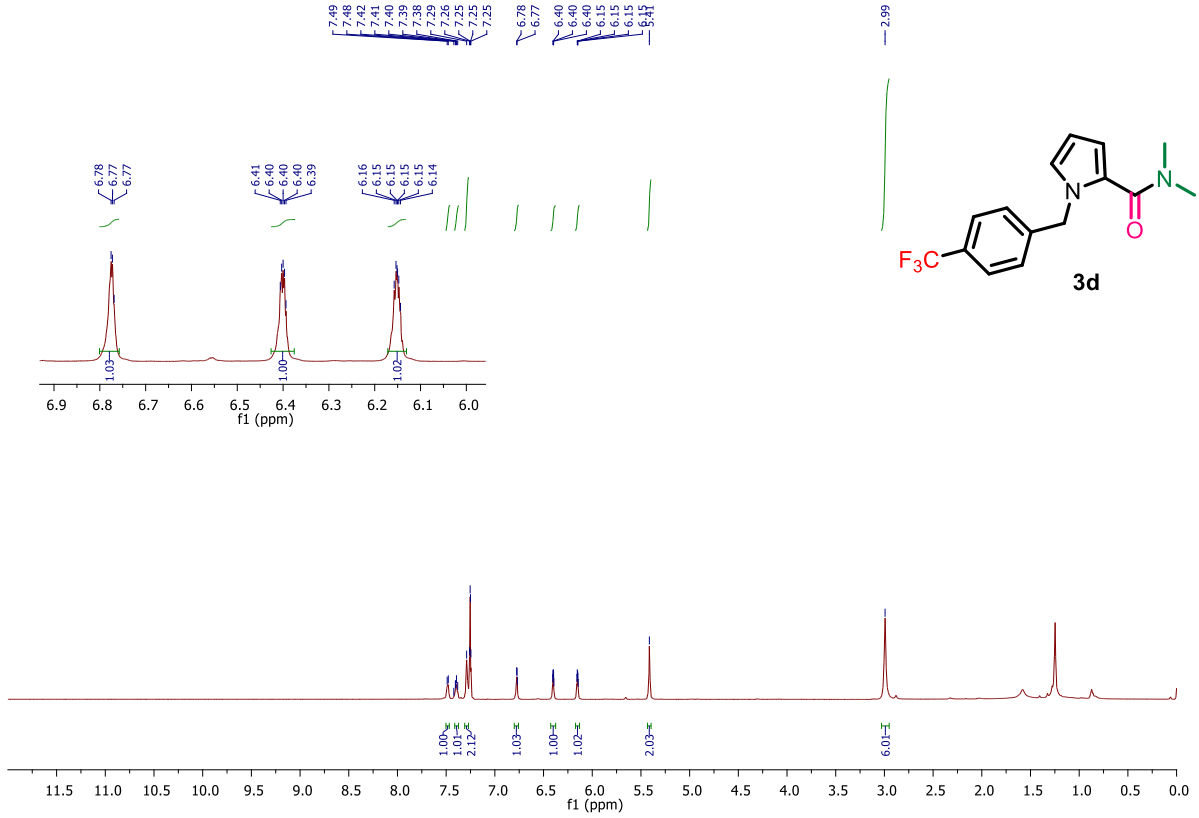
3c ^{1}H NMR ($CDCl_3$)



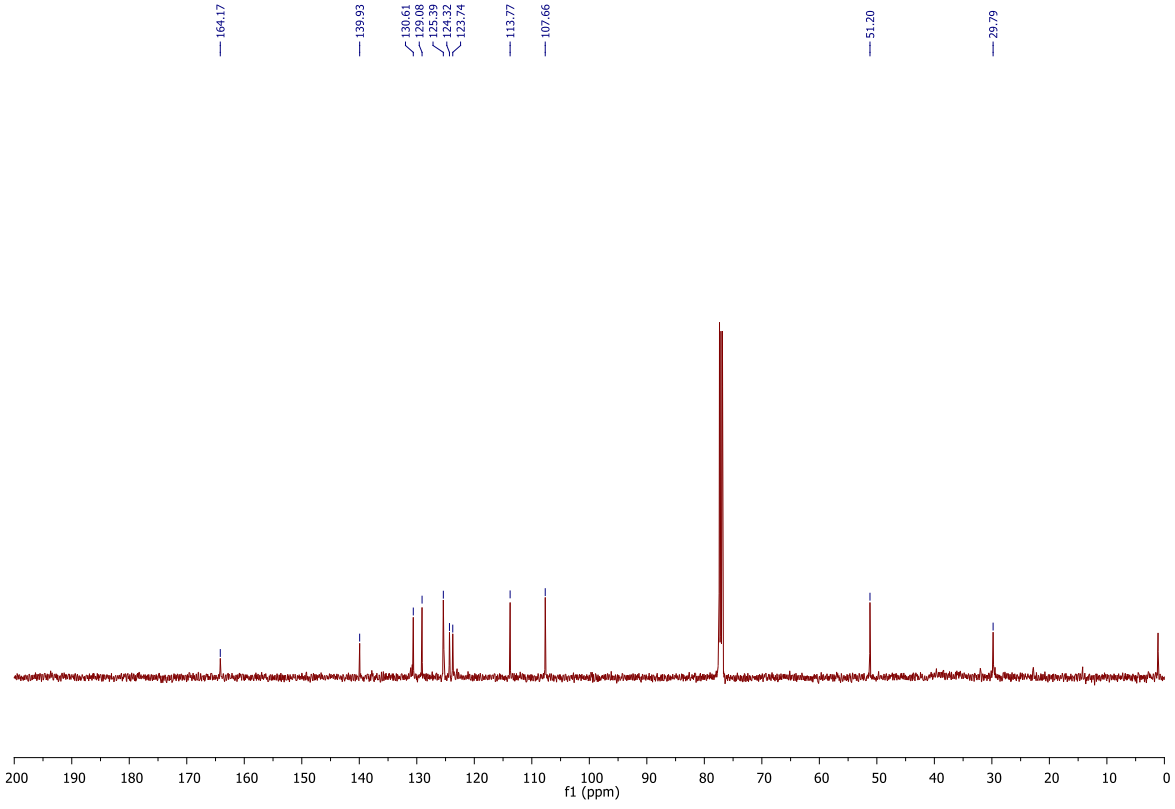
^{13}C{1H} NMR ($CDCl_3$)



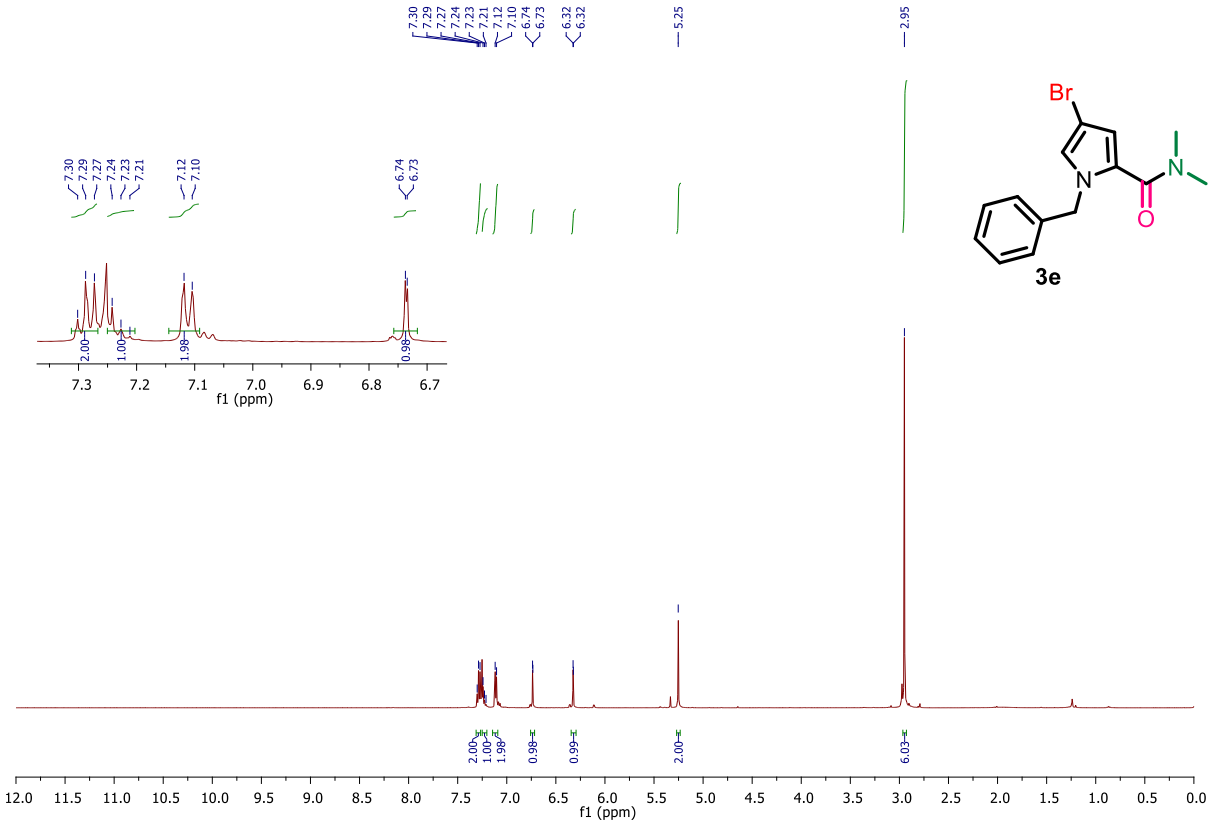
3d ^{1}H NMR ($CDCl_3$)



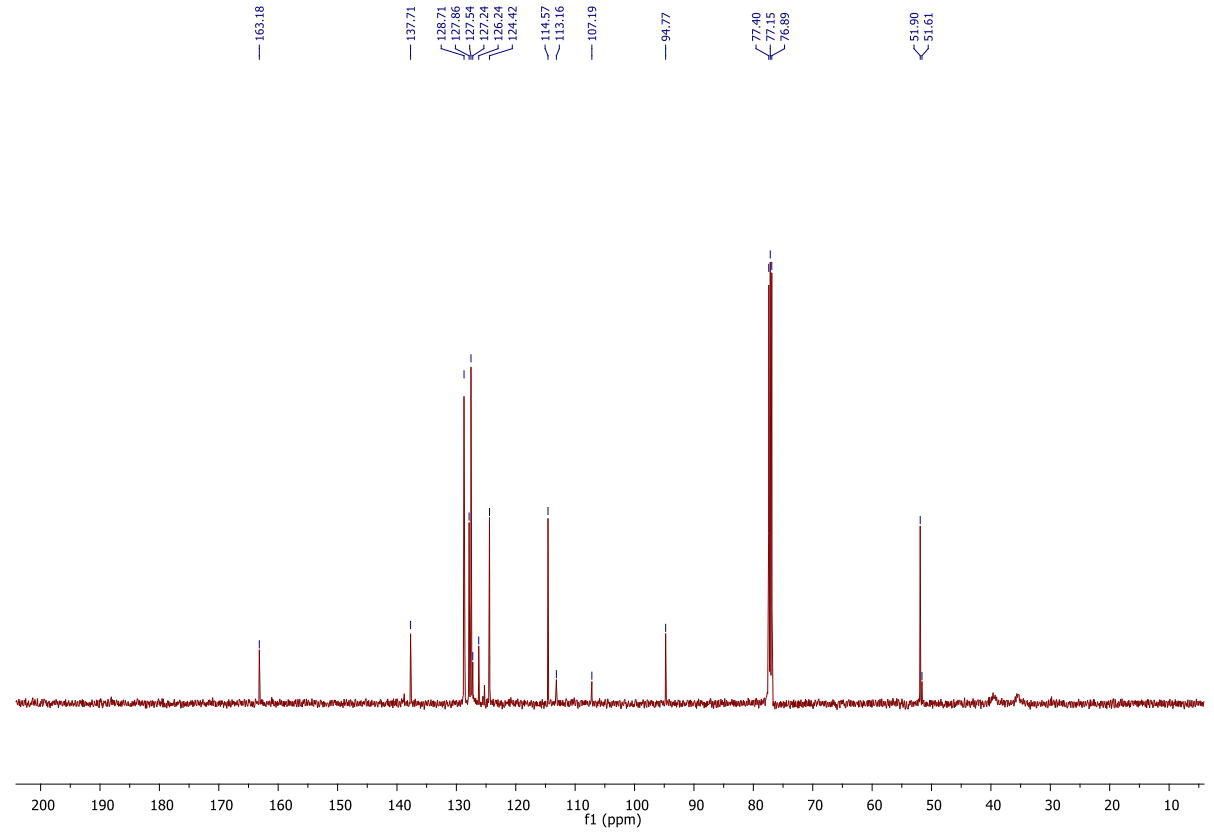
^{13}C{1H} NMR ($CDCl_3$)



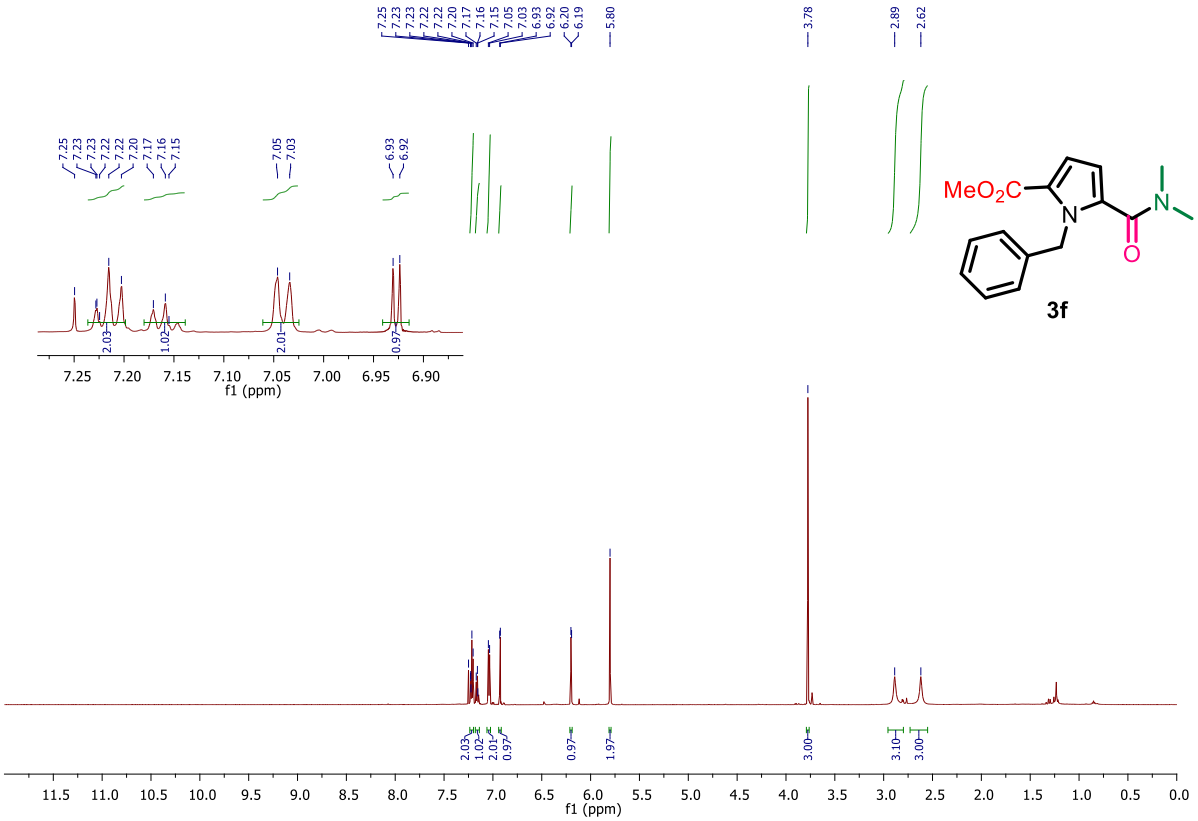
3e ^{1}H NMR ($CDCl_3$)



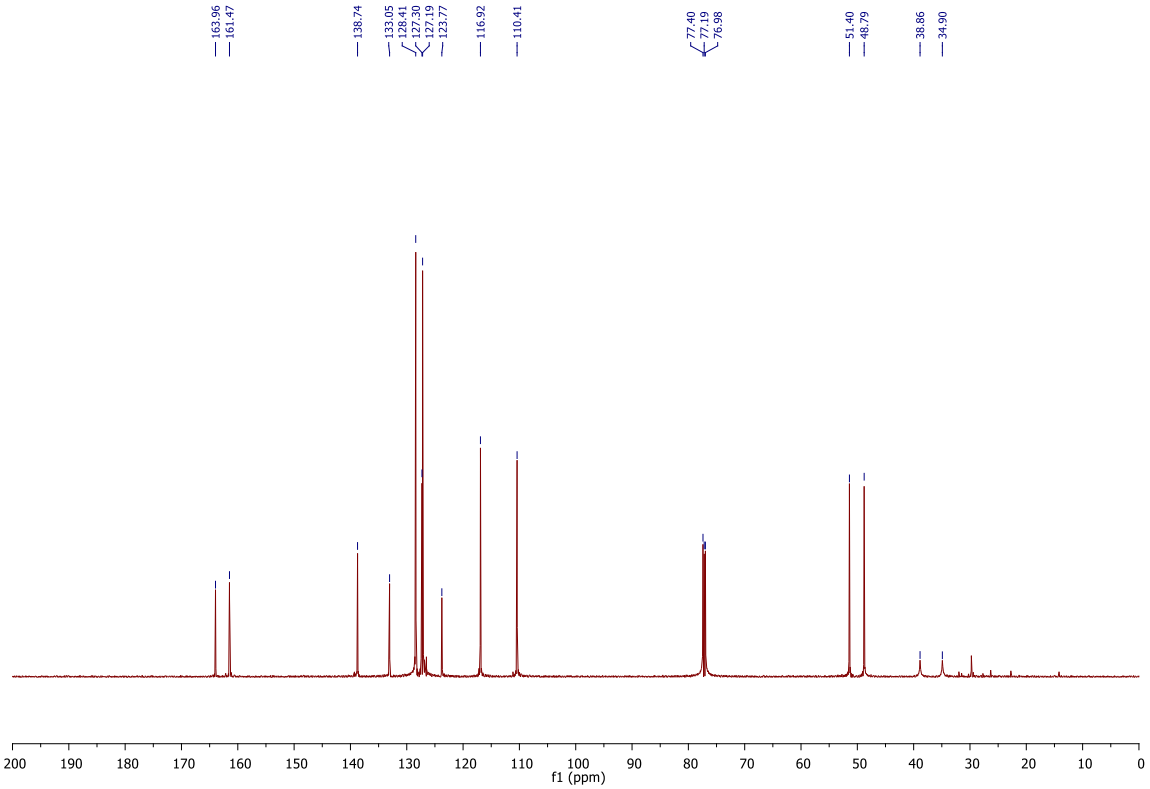
^{13}C{1H} NMR ($CDCl_3$)



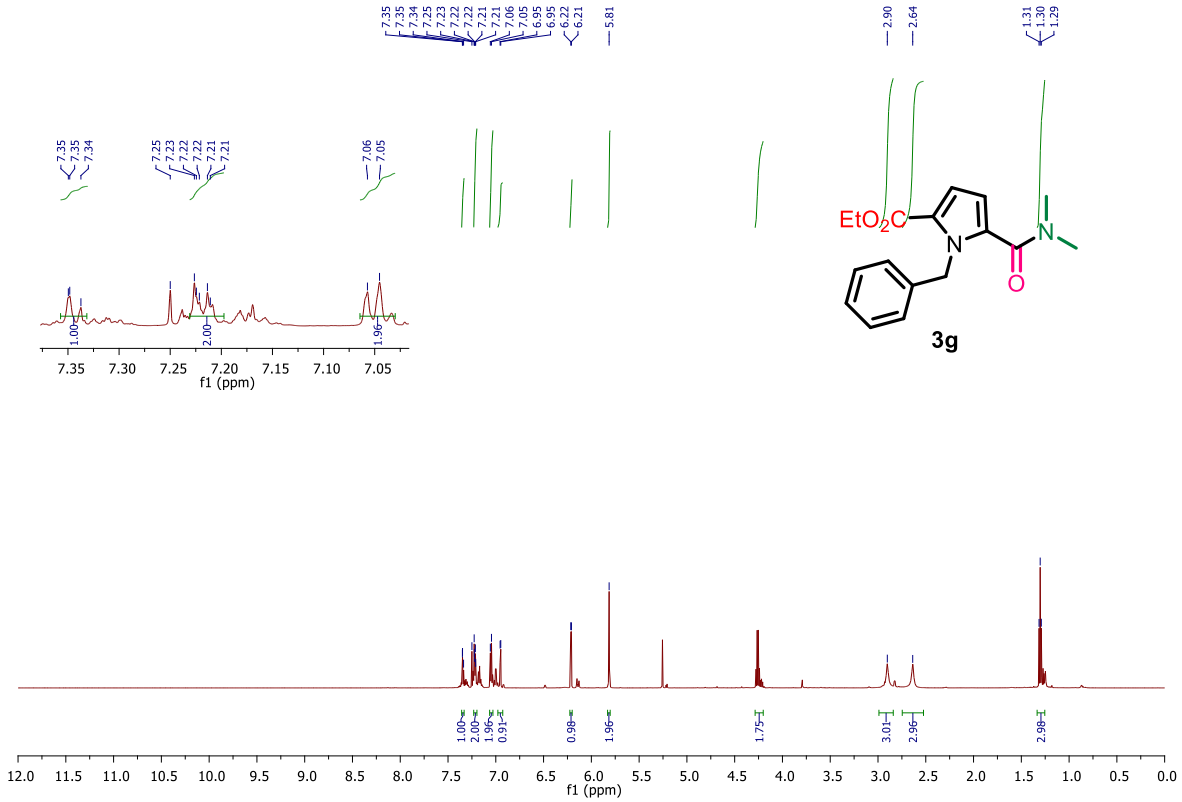
3f ^{1}H NMR ($CDCl_3$)



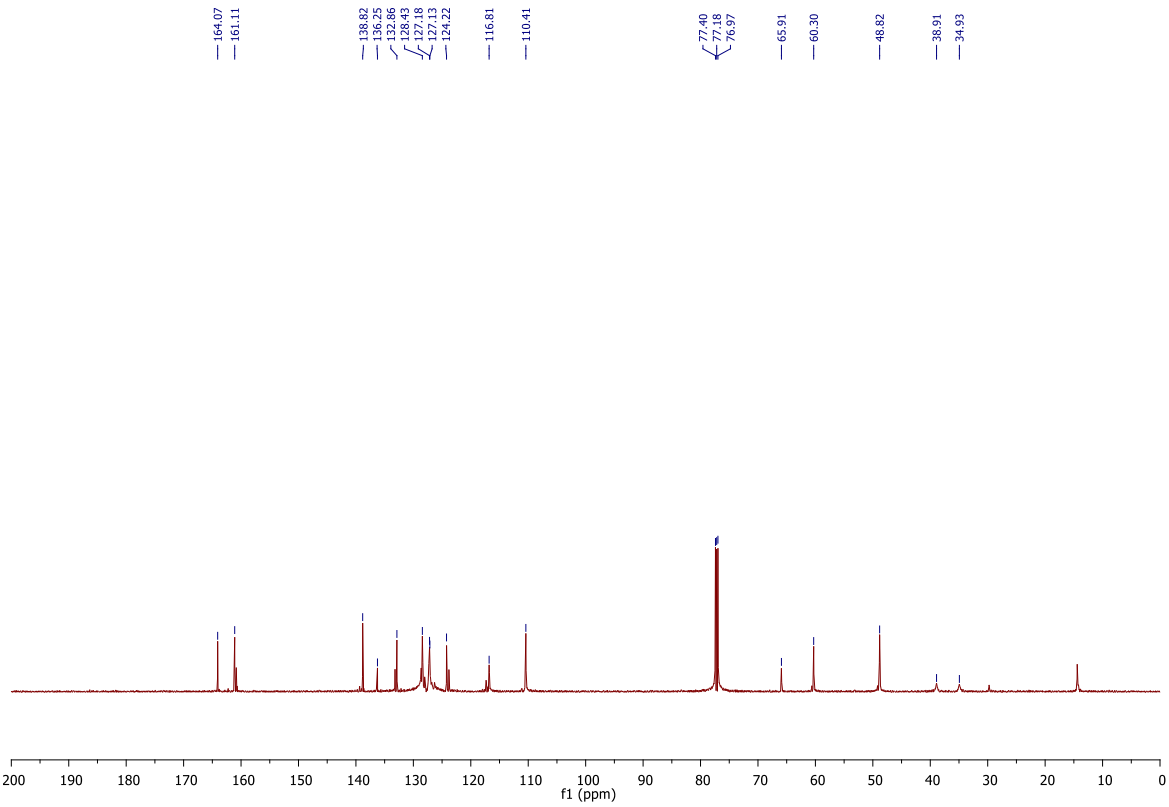
^{13}C{1H} NMR ($CDCl_3$)



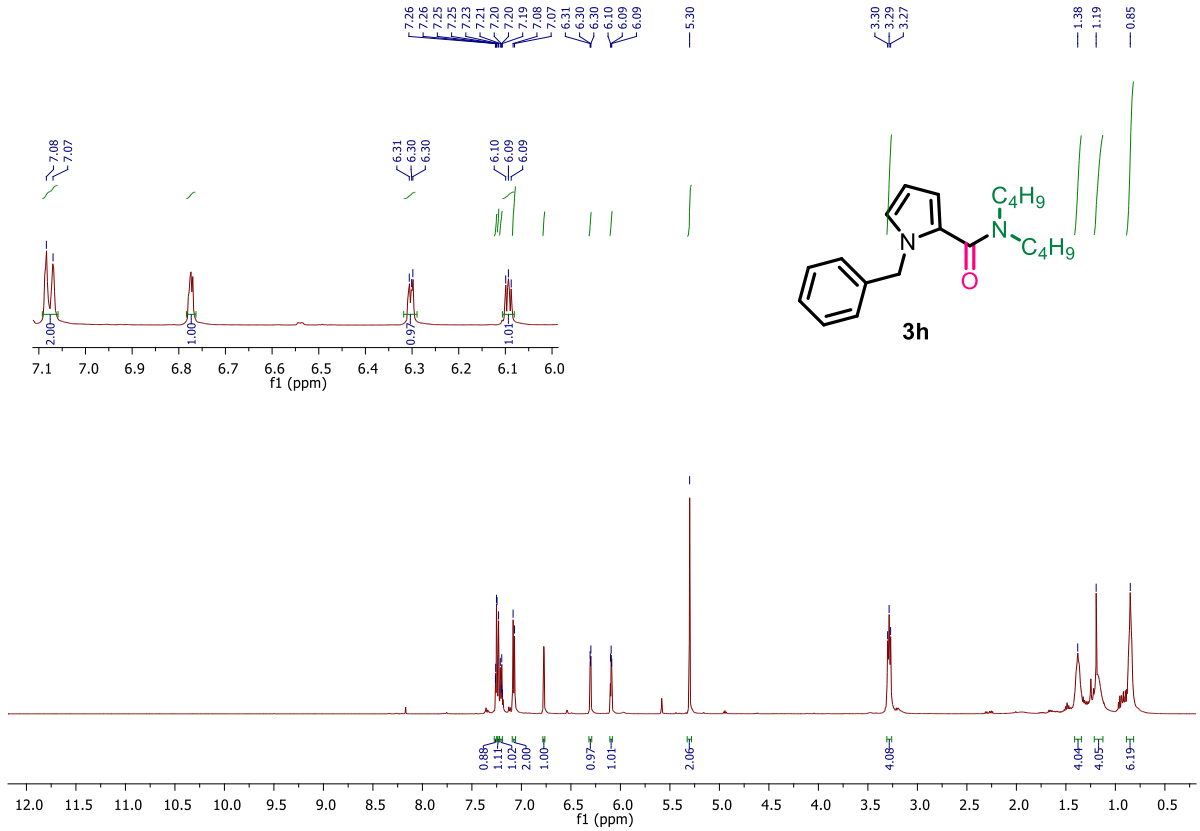
3g ^{1}H NMR ($CDCl_3$)



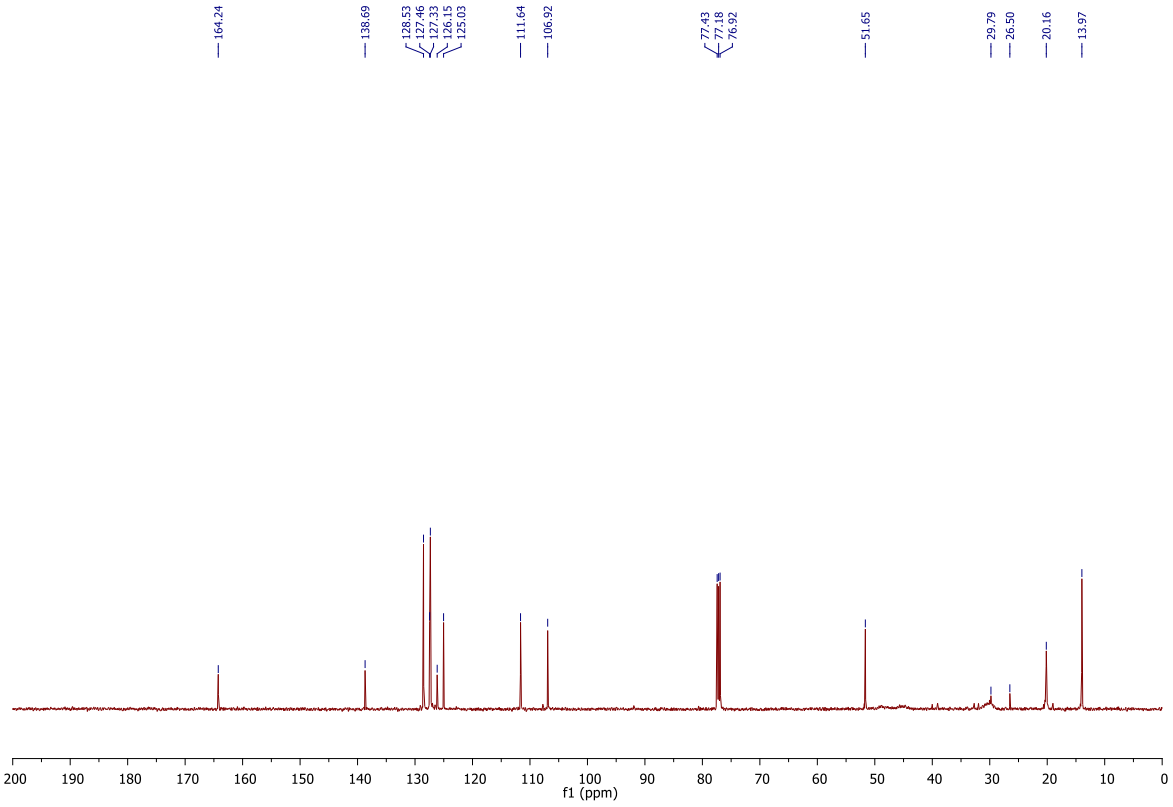
^{13}C{1H} NMR ($CDCl_3$)



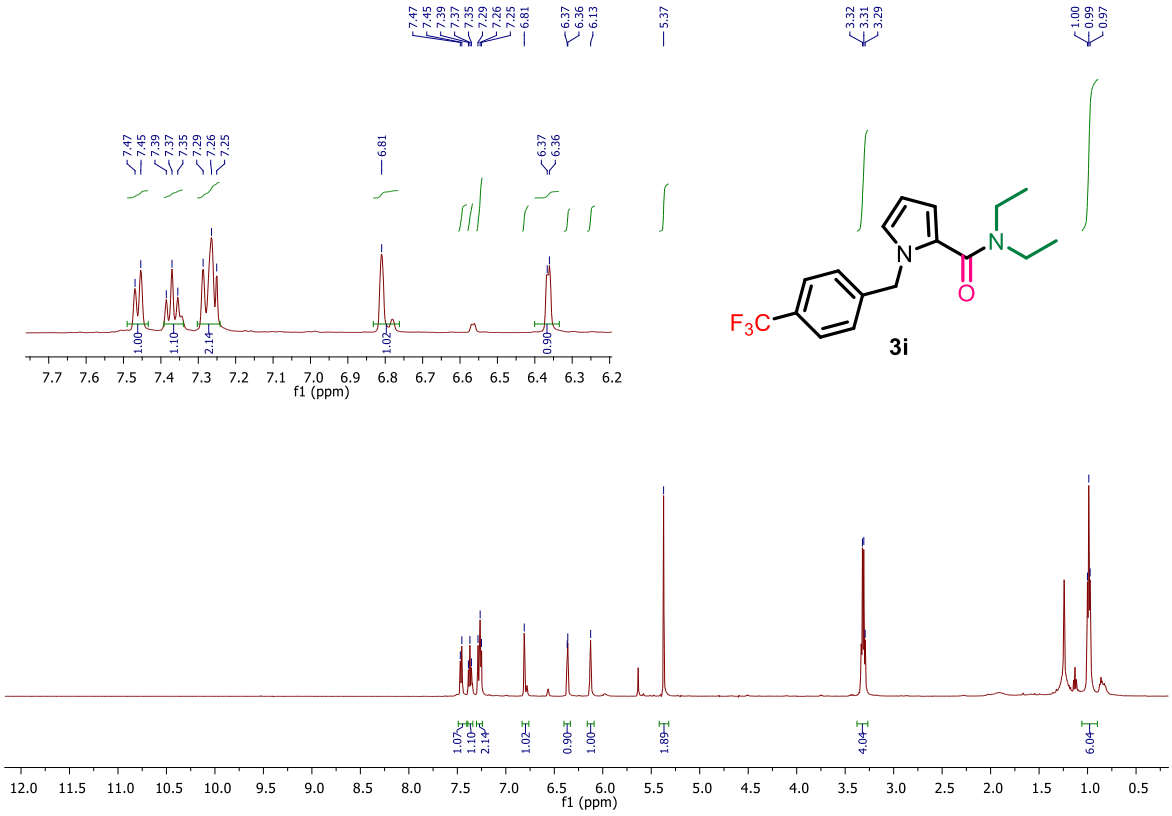
3h ^{1}H NMR ($CDCl_3$)



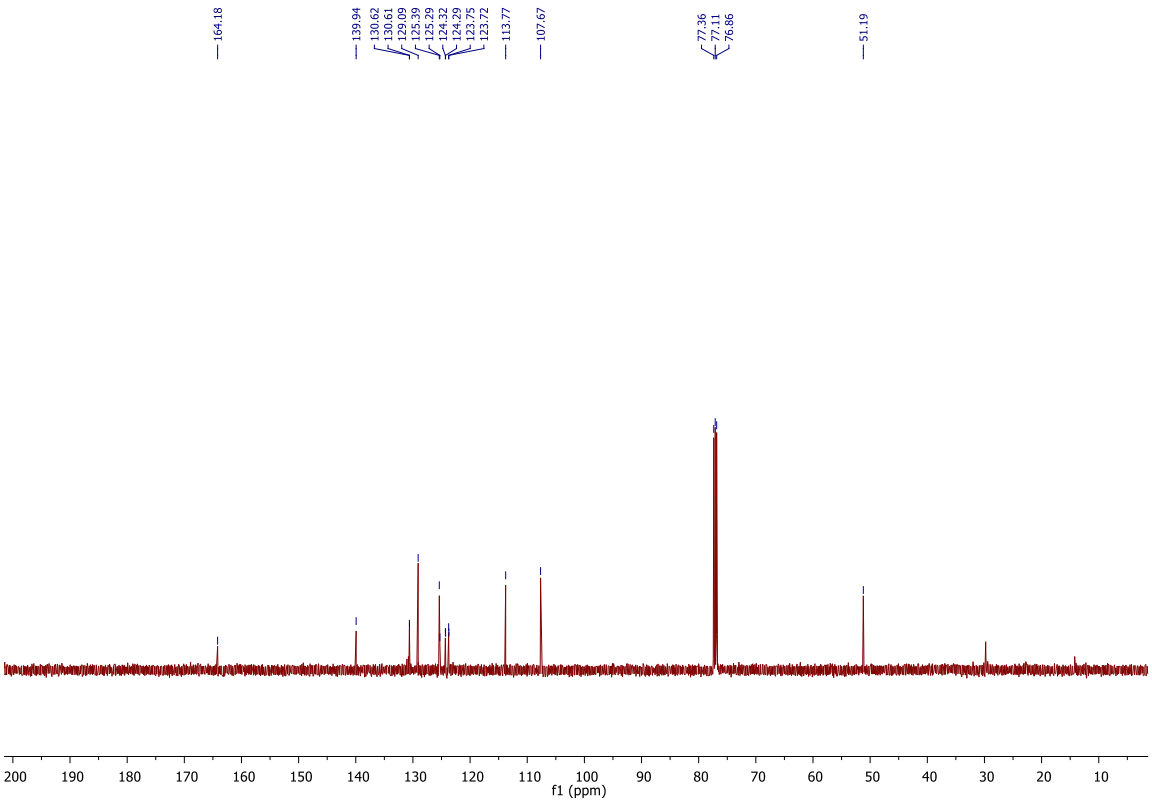
^{13}C{1H} NMR ($CDCl_3$)



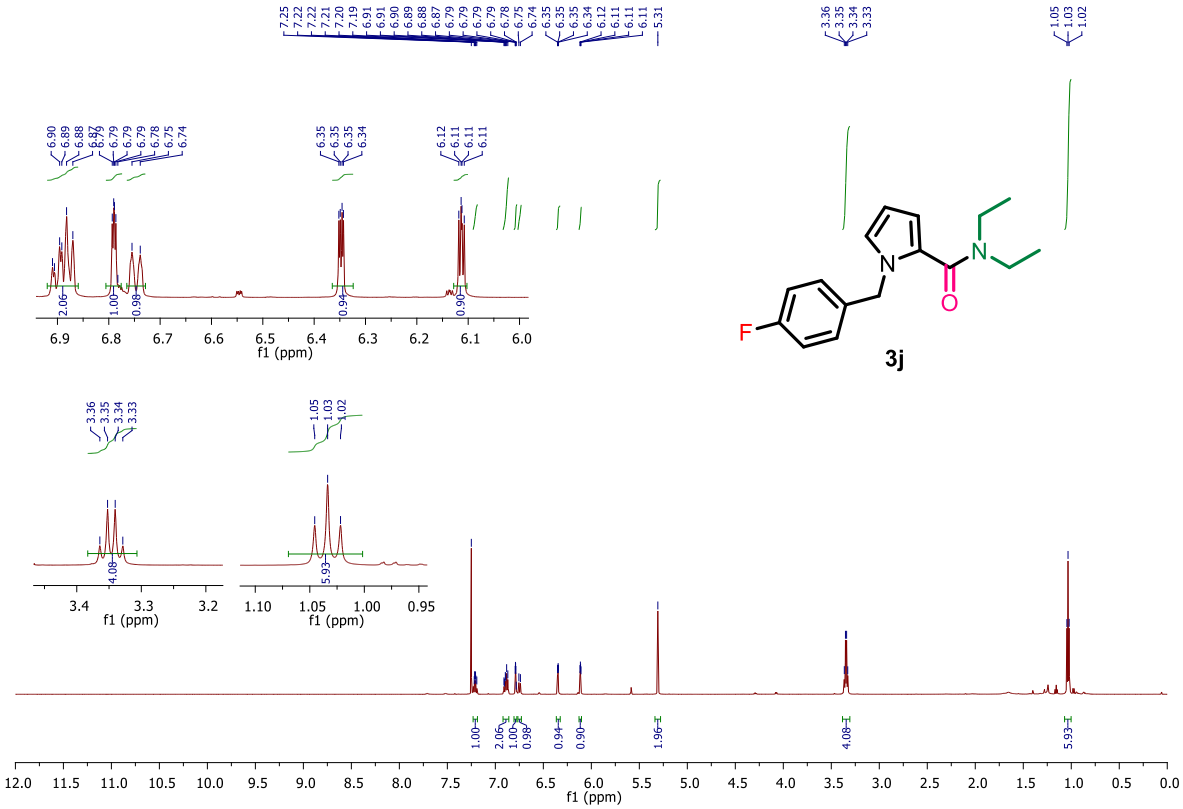
3i ^{1}H NMR ($CDCl_3$)



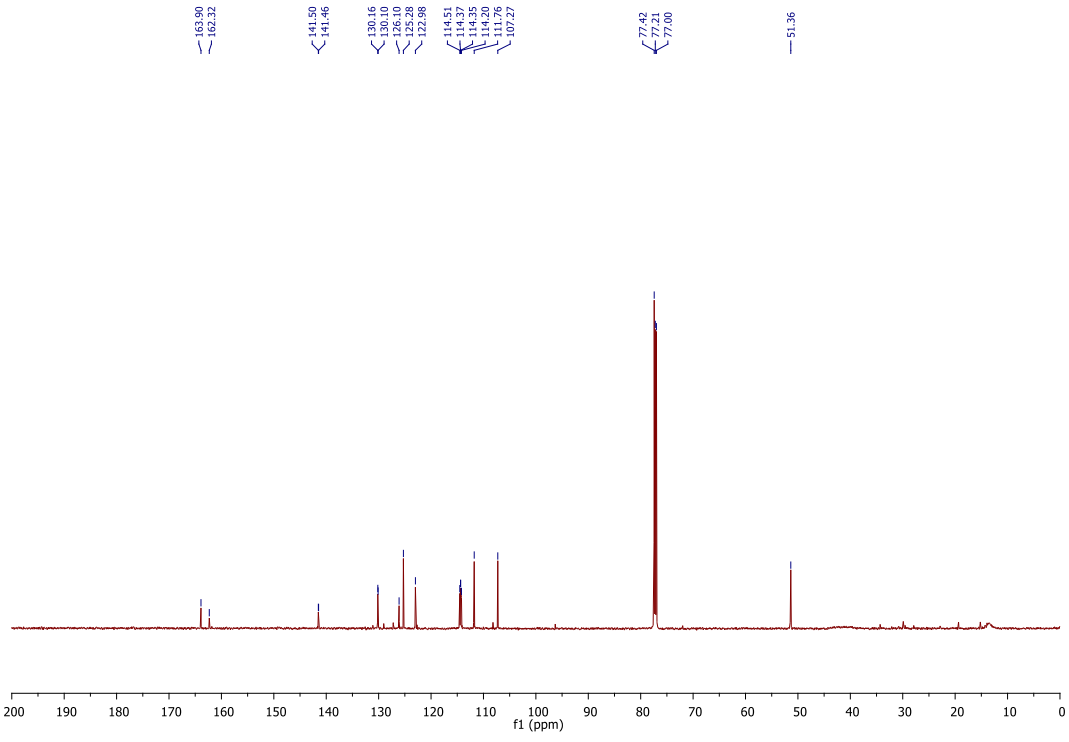
^{13}C{1H} NMR ($CDCl_3$)



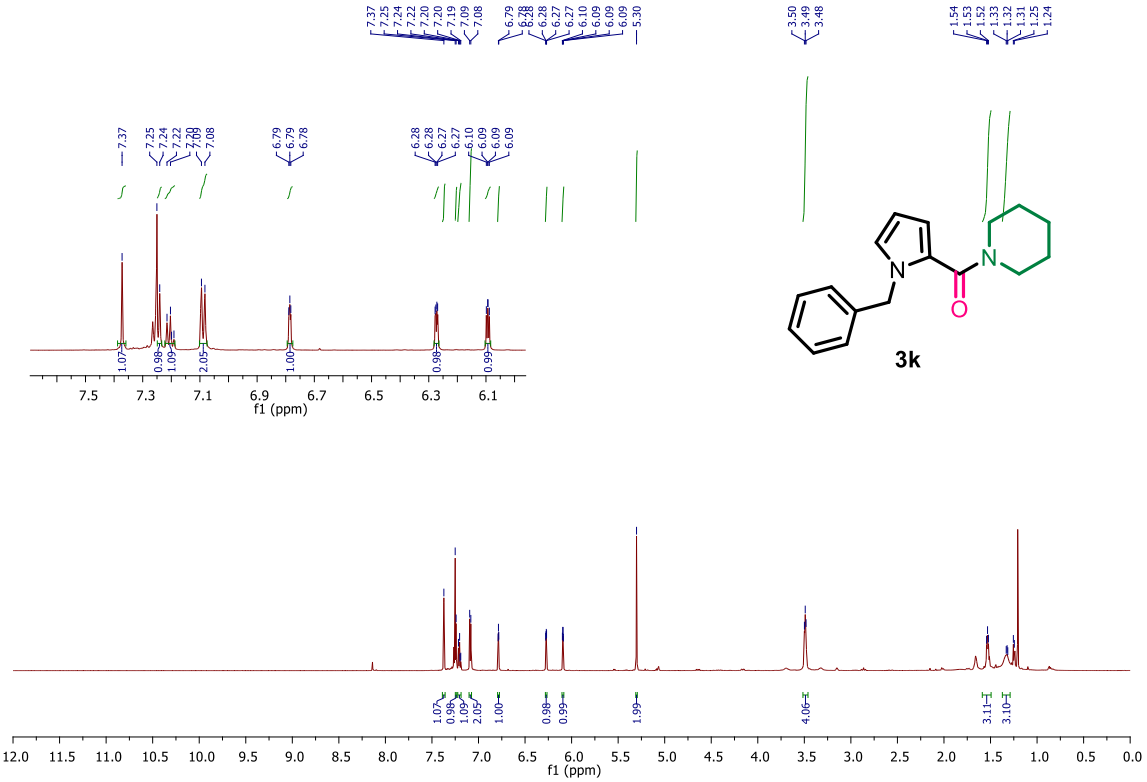
3j ^{1}H NMR ($CDCl_3$)



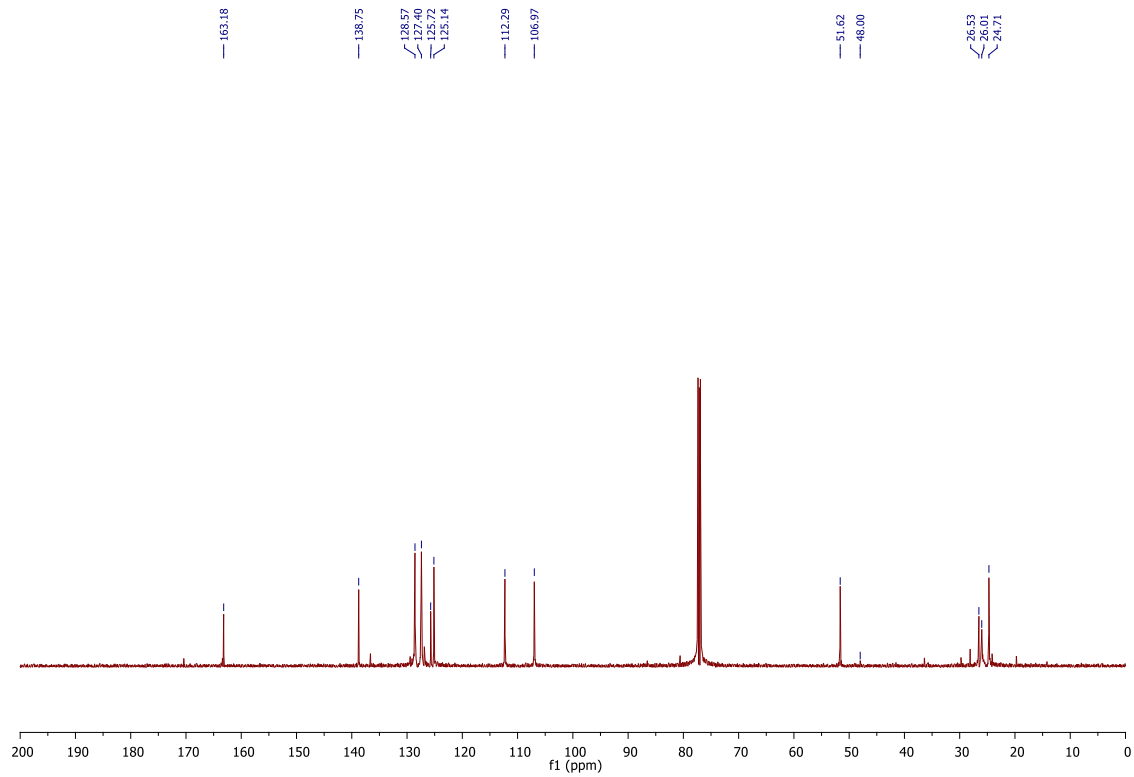
^{13}C{1H} NMR ($CDCl_3$)



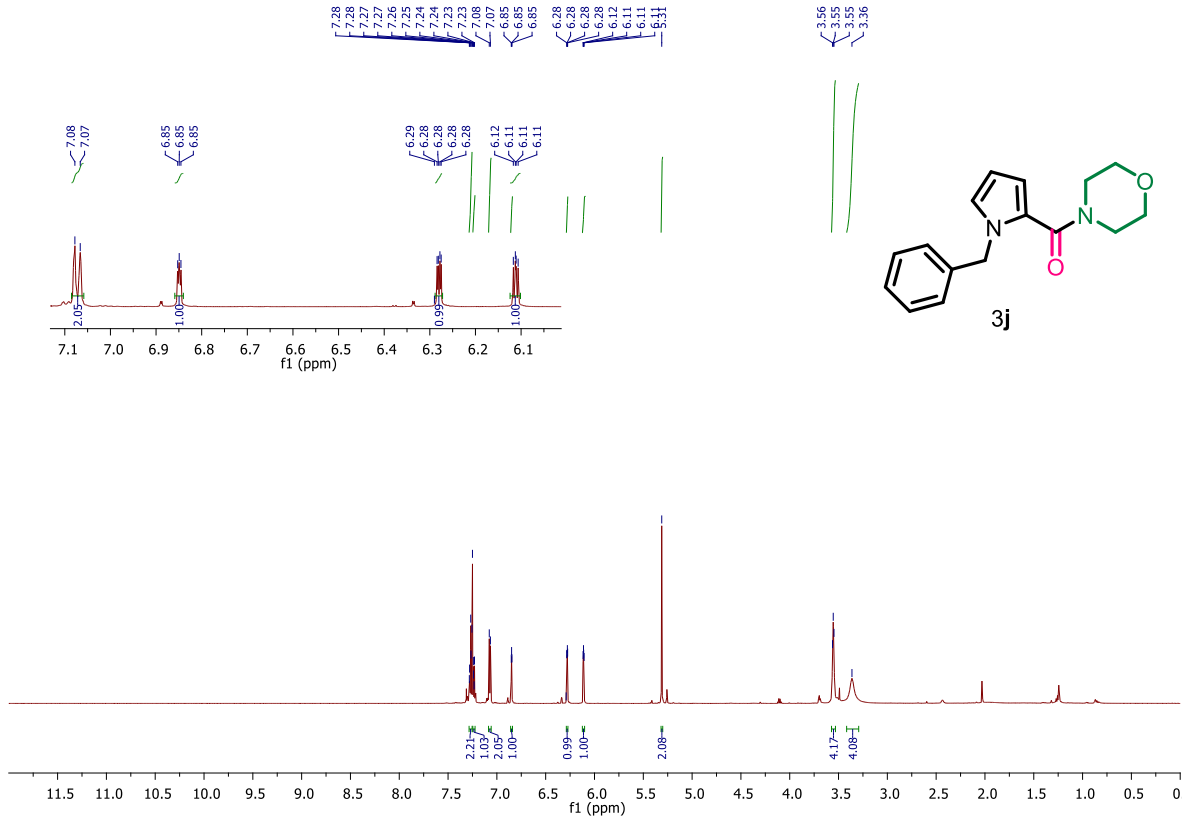
3k ^{1}H NMR ($CDCl_3$)



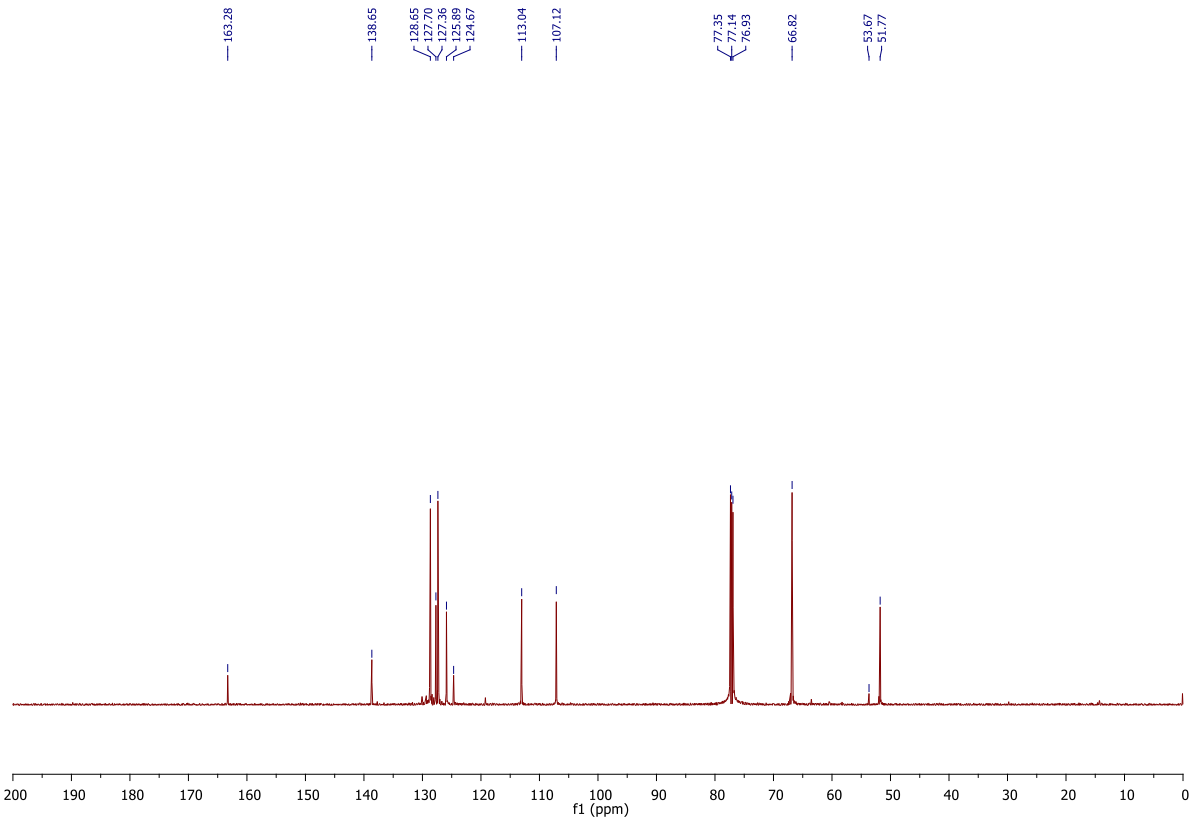
^{13}C{1H} NMR ($CDCl_3$)



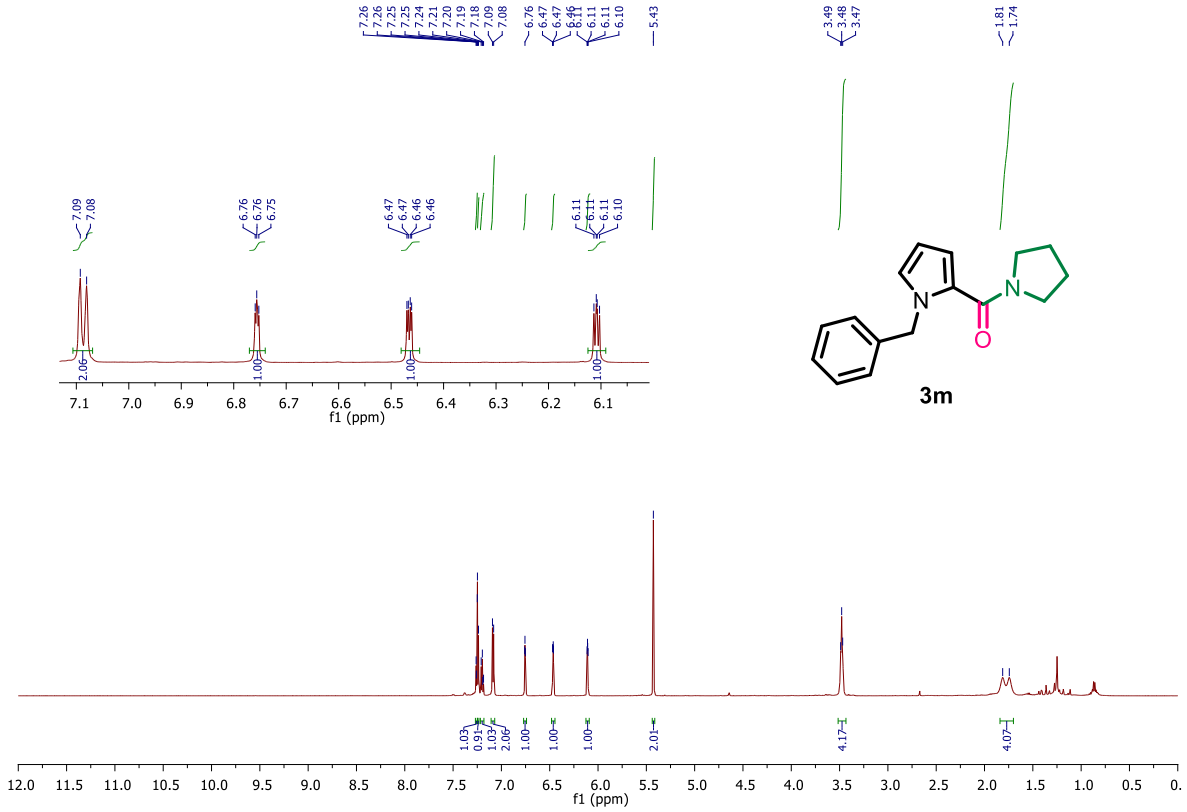
3l ^{1}H NMR ($CDCl_3$)



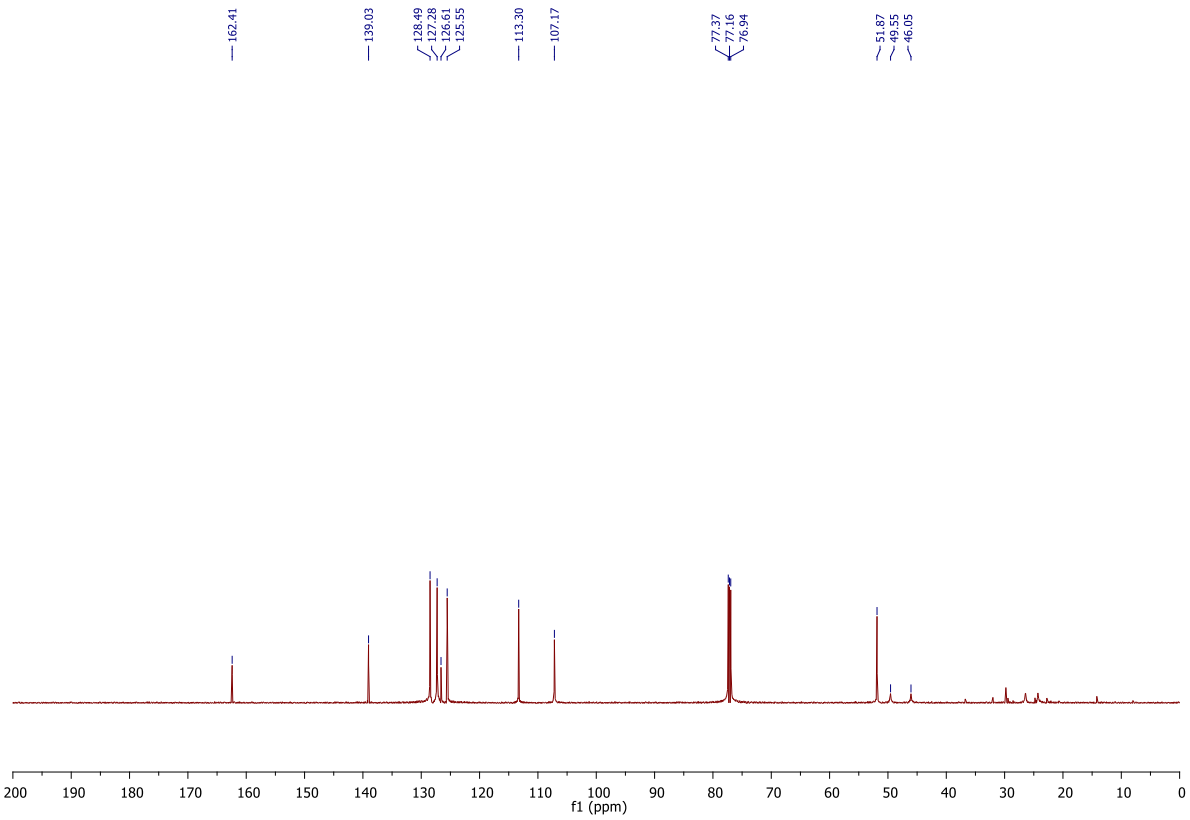
^{13}C{1H} NMR ($CDCl_3$)



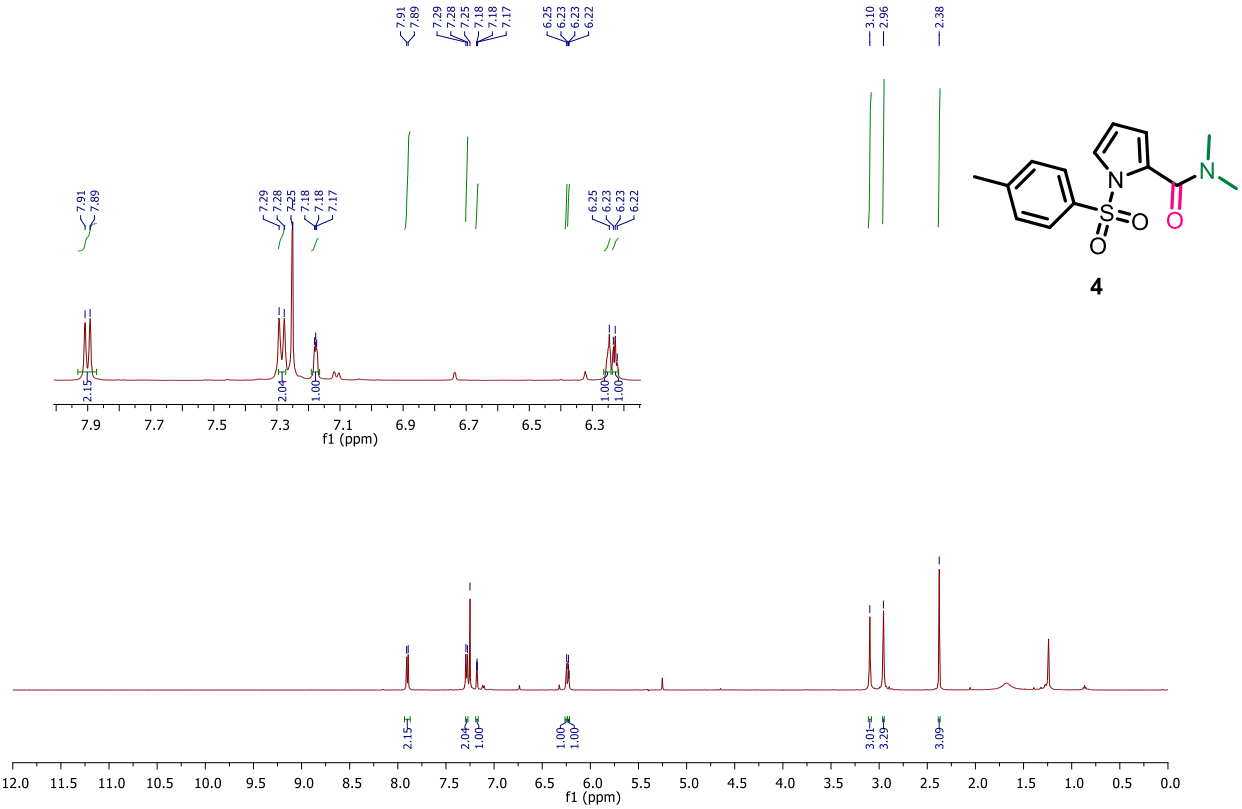
3m ^{1}H NMR ($CDCl_3$)



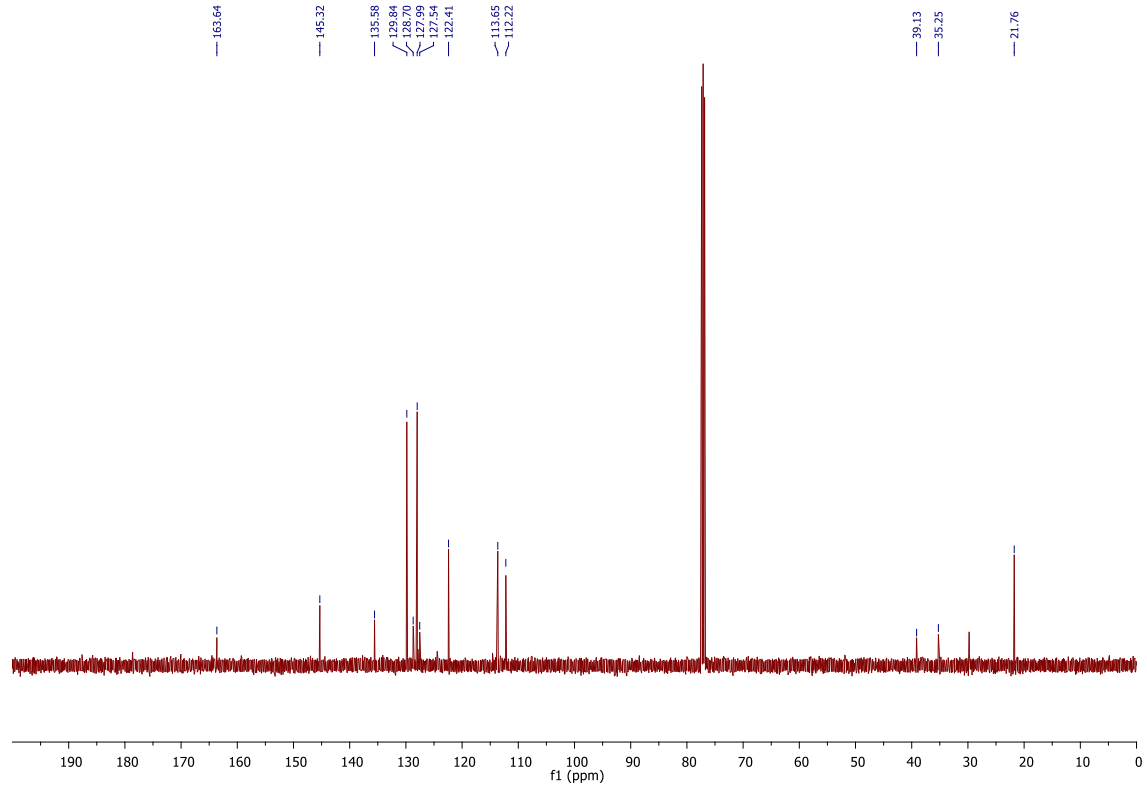
^{13}C{1H} NMR ($CDCl_3$)



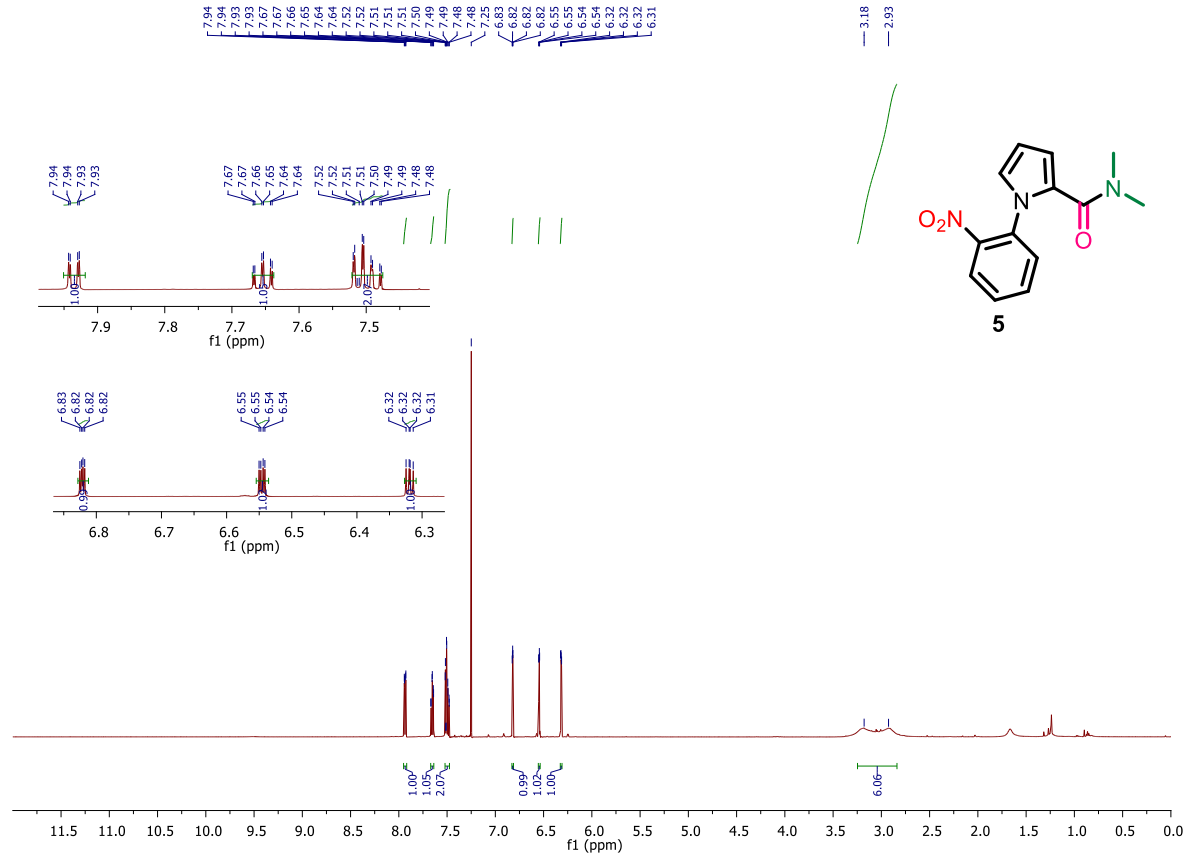
4 ^{1}H NMR ($CDCl_3$)



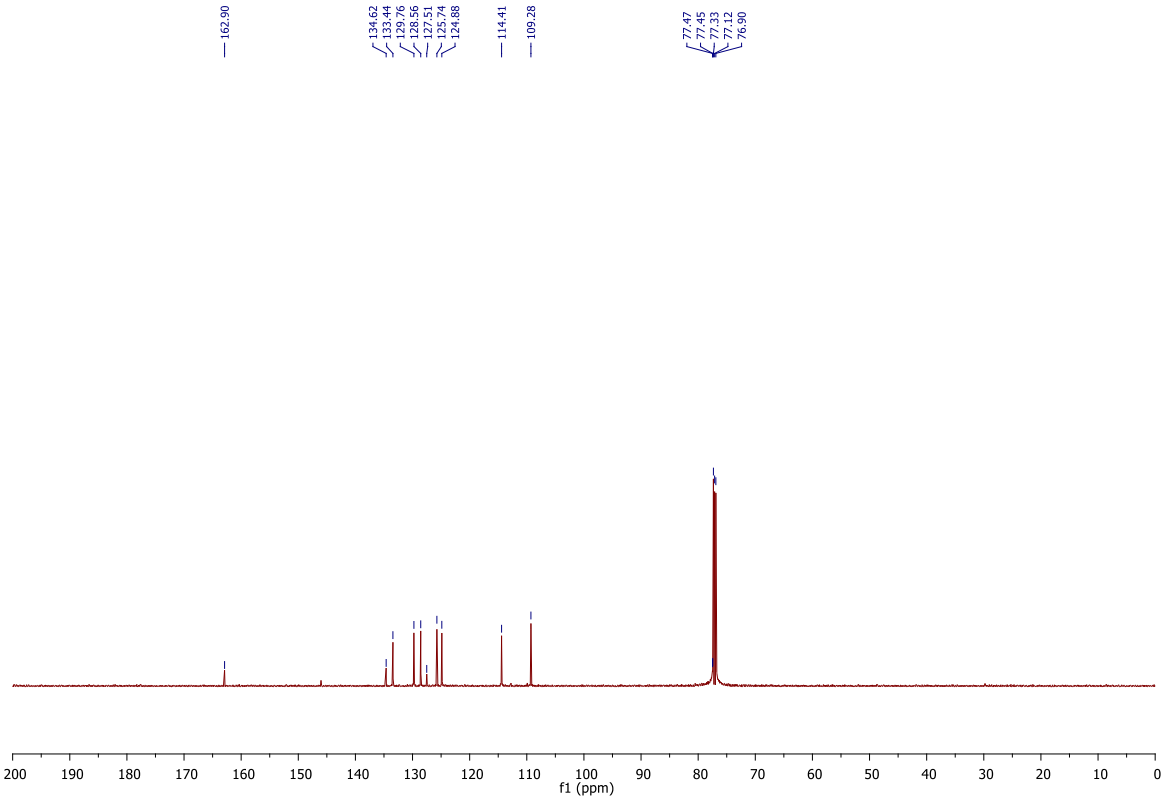
^{13}C{1H} NMR ($CDCl_3$)



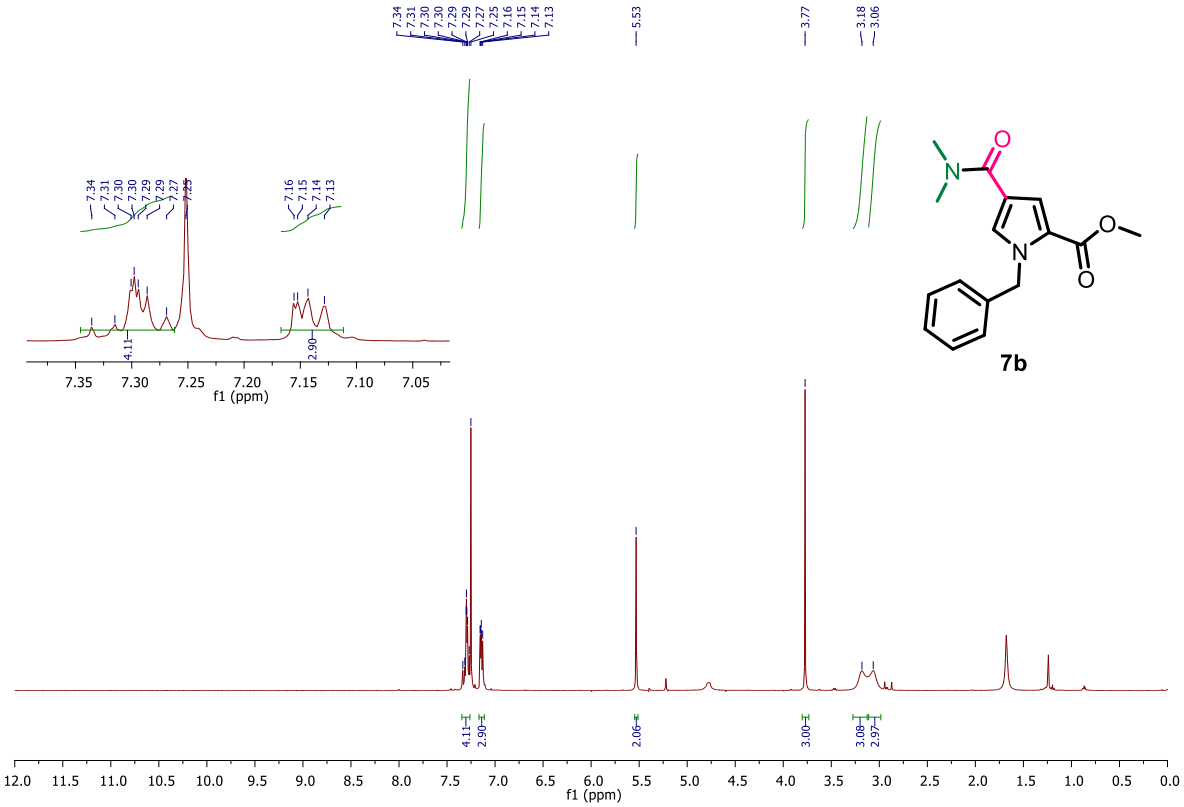
5 ^{1}H NMR ($CDCl_3$)



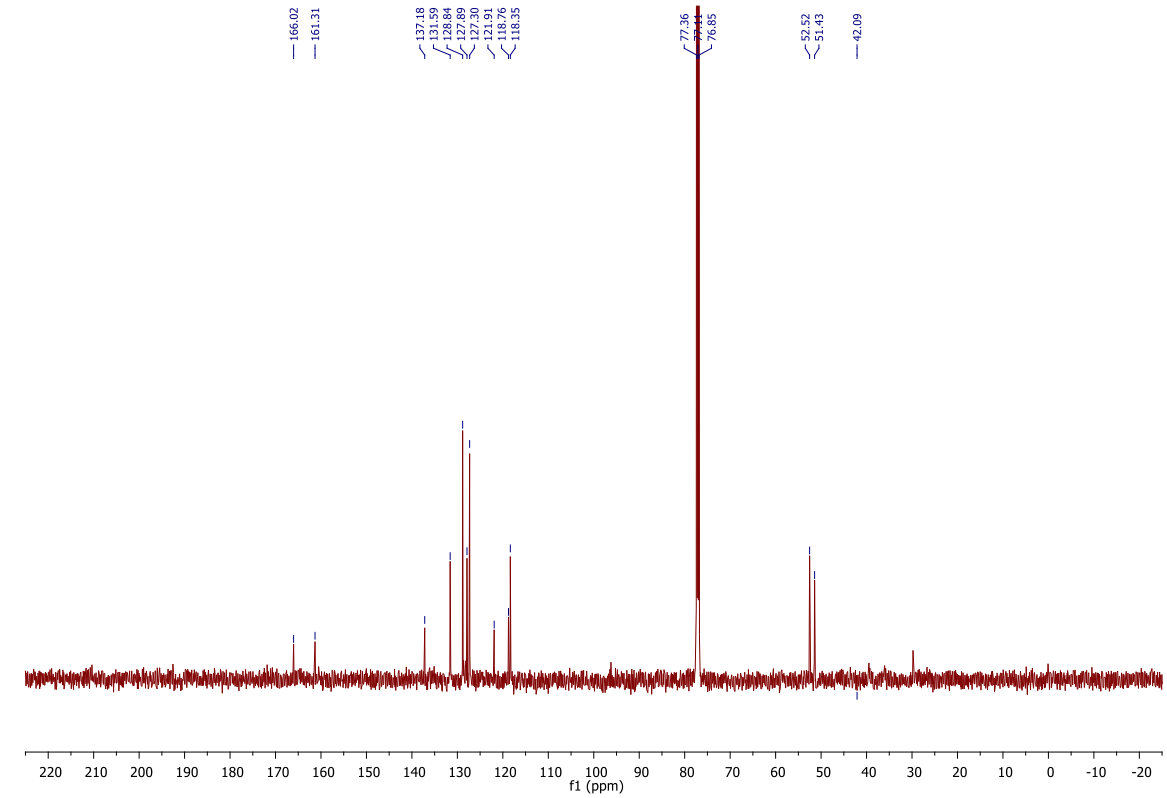
^{13}C{1H} NMR ($CDCl_3$)



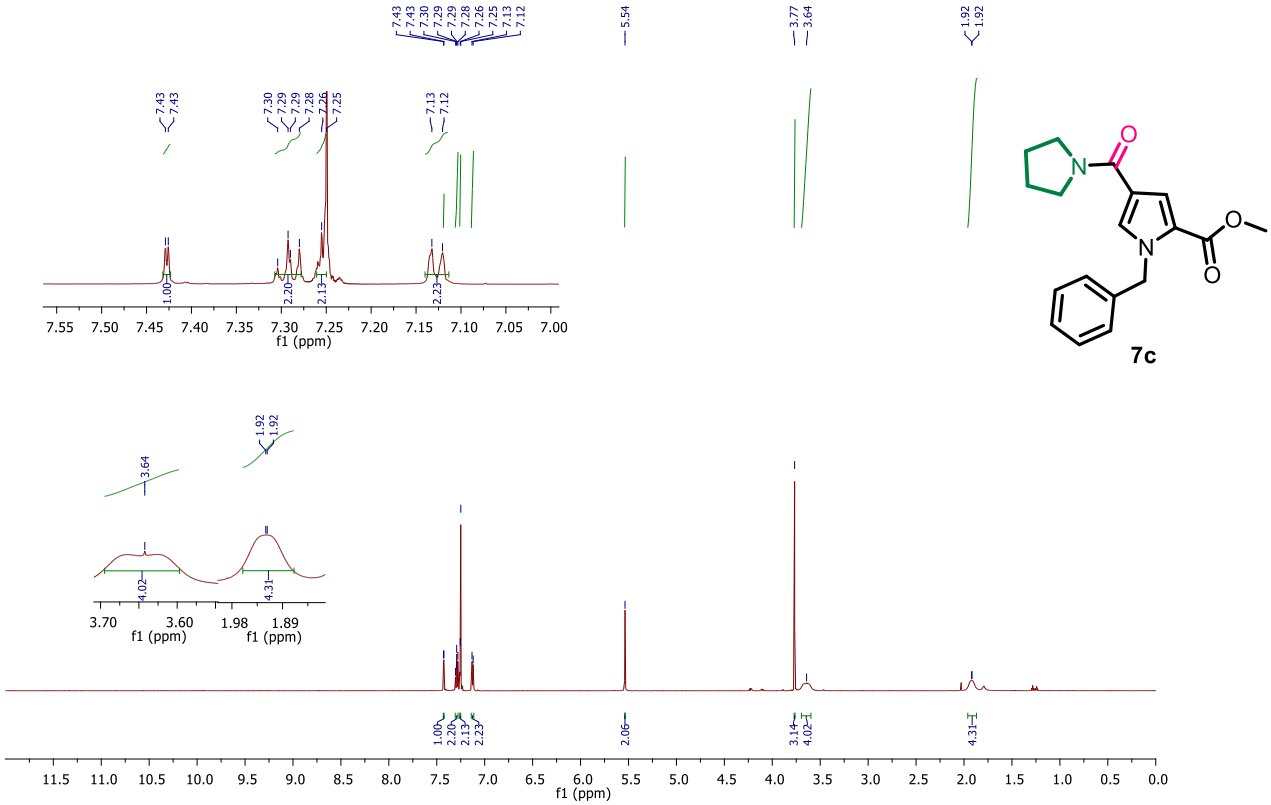
7b ^{1}H NMR ($CDCl_3$)



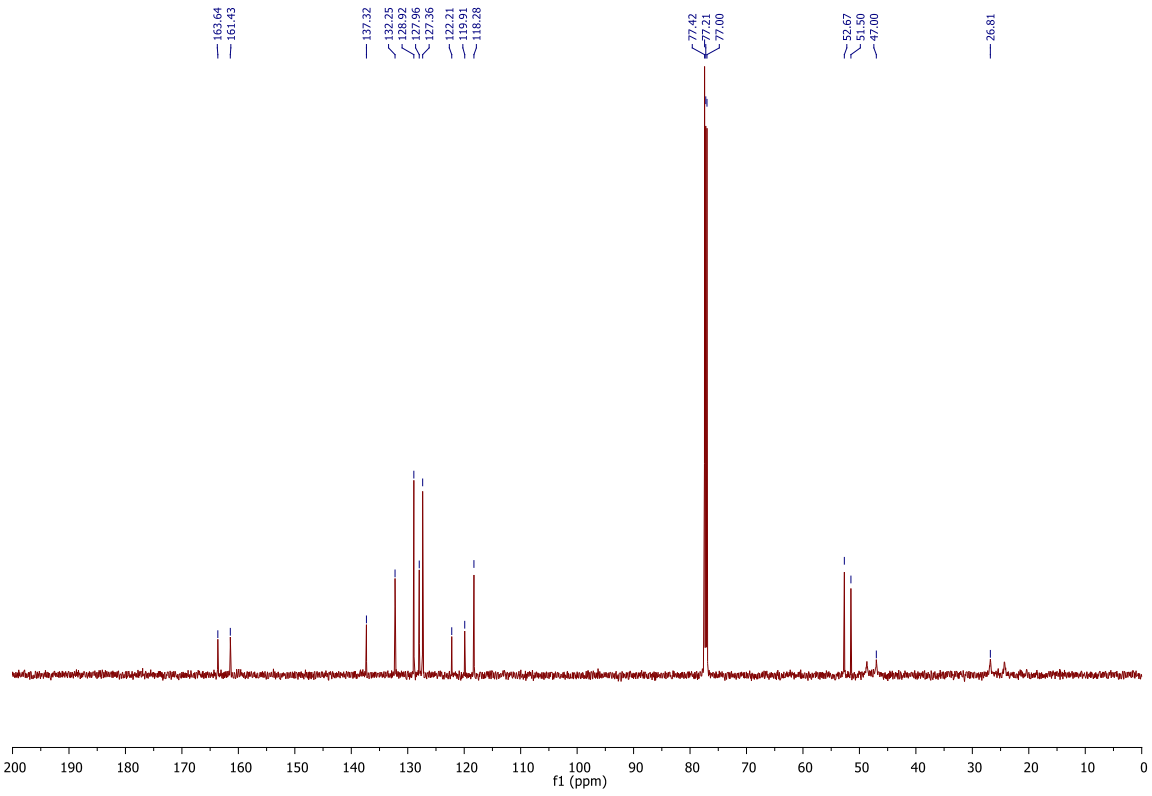
^{13}C{1H} NMR ($CDCl_3$)



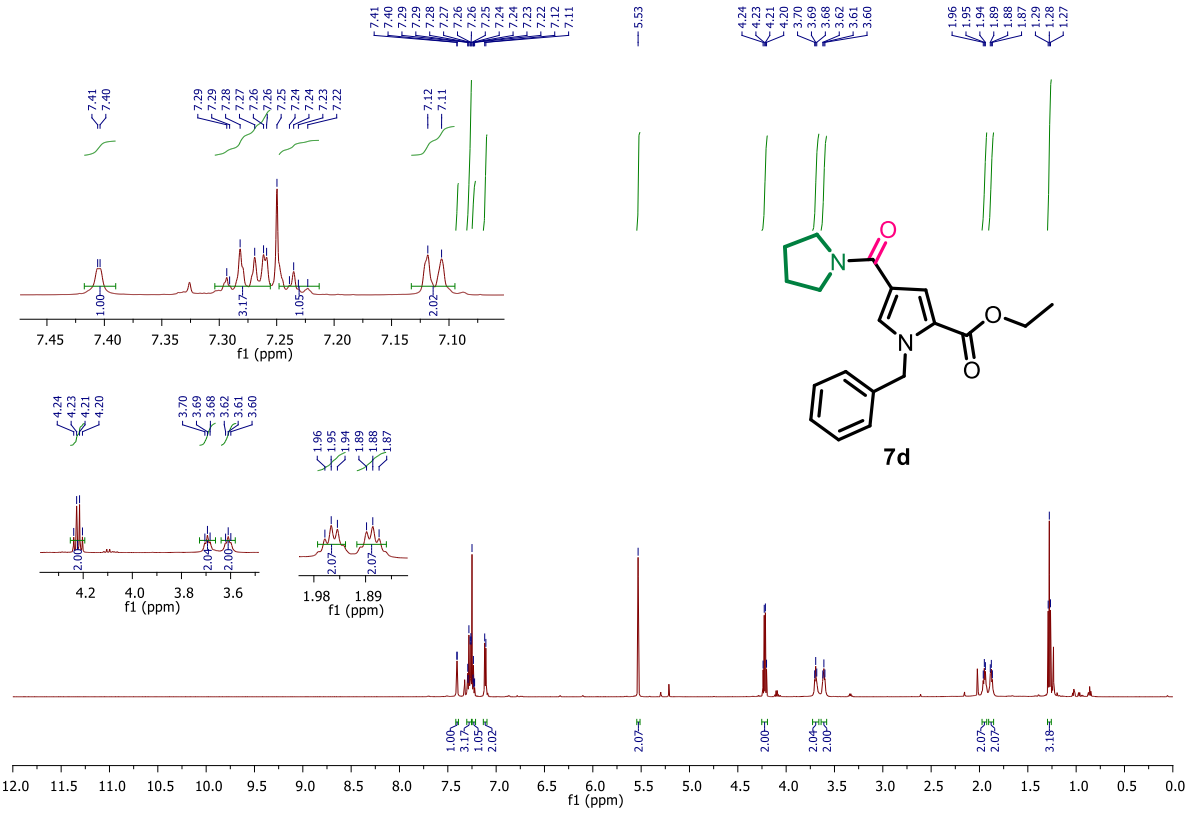
7c ^{1}H NMR ($CDCl_3$)



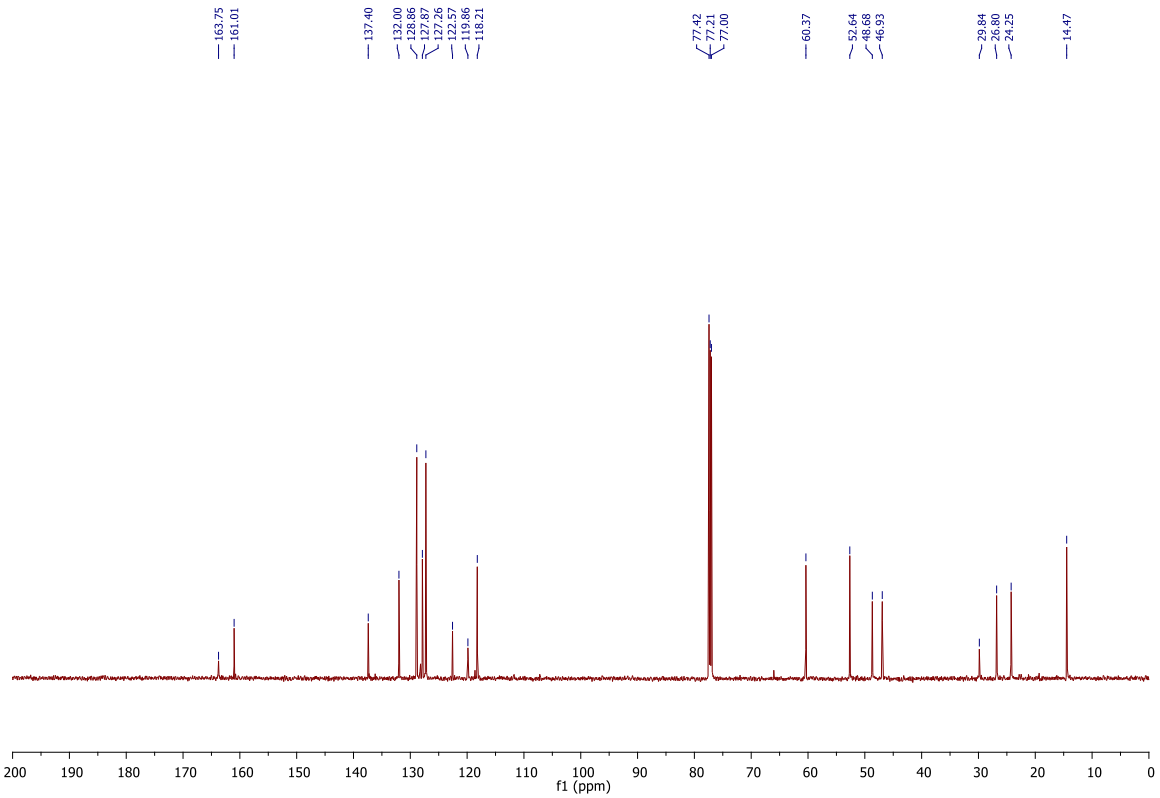
^{13}C{1H} NMR ($CDCl_3$)



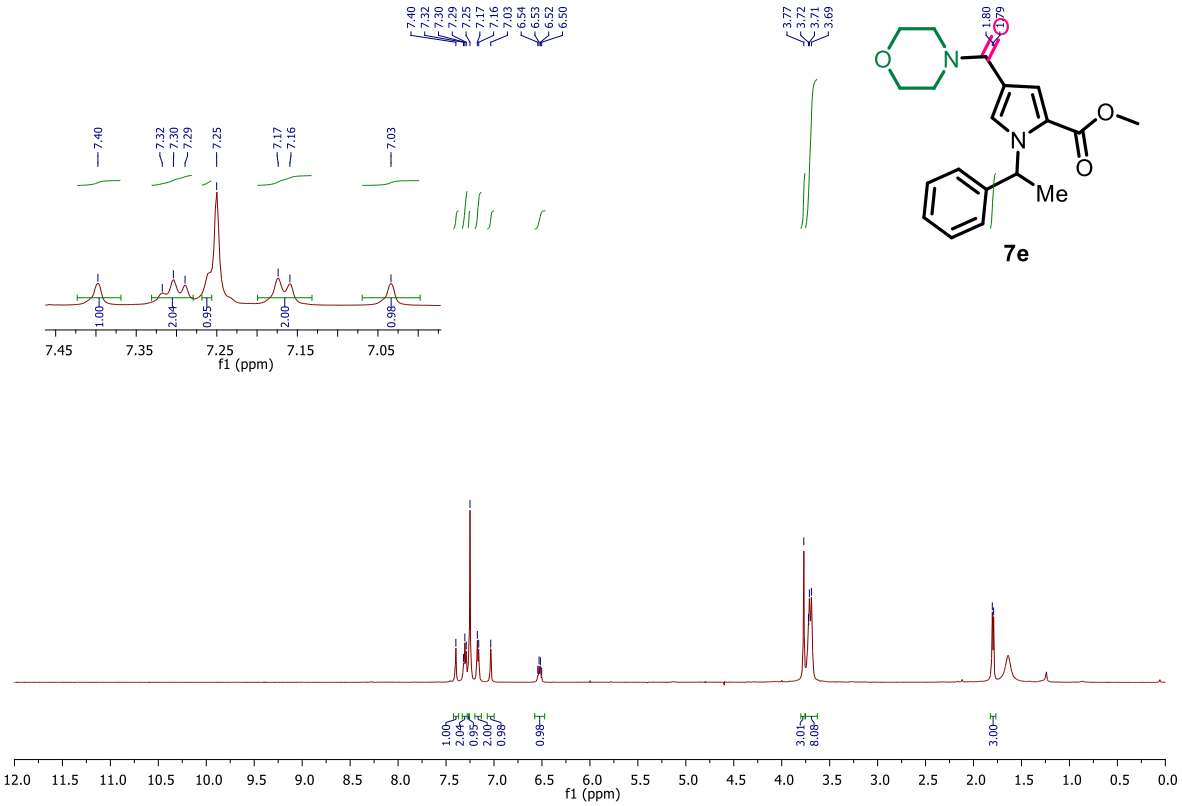
7d ^{1}H NMR ($CDCl_3$)



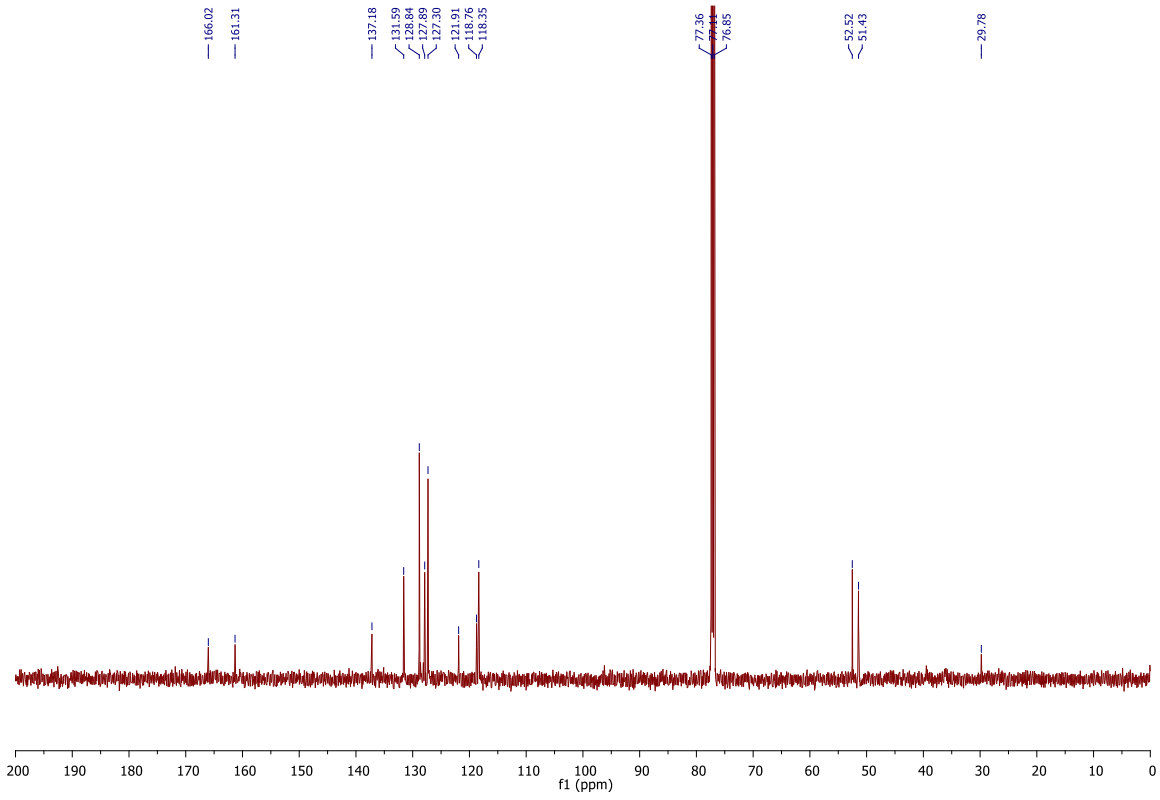
^{13}C{1H} NMR ($CDCl_3$)



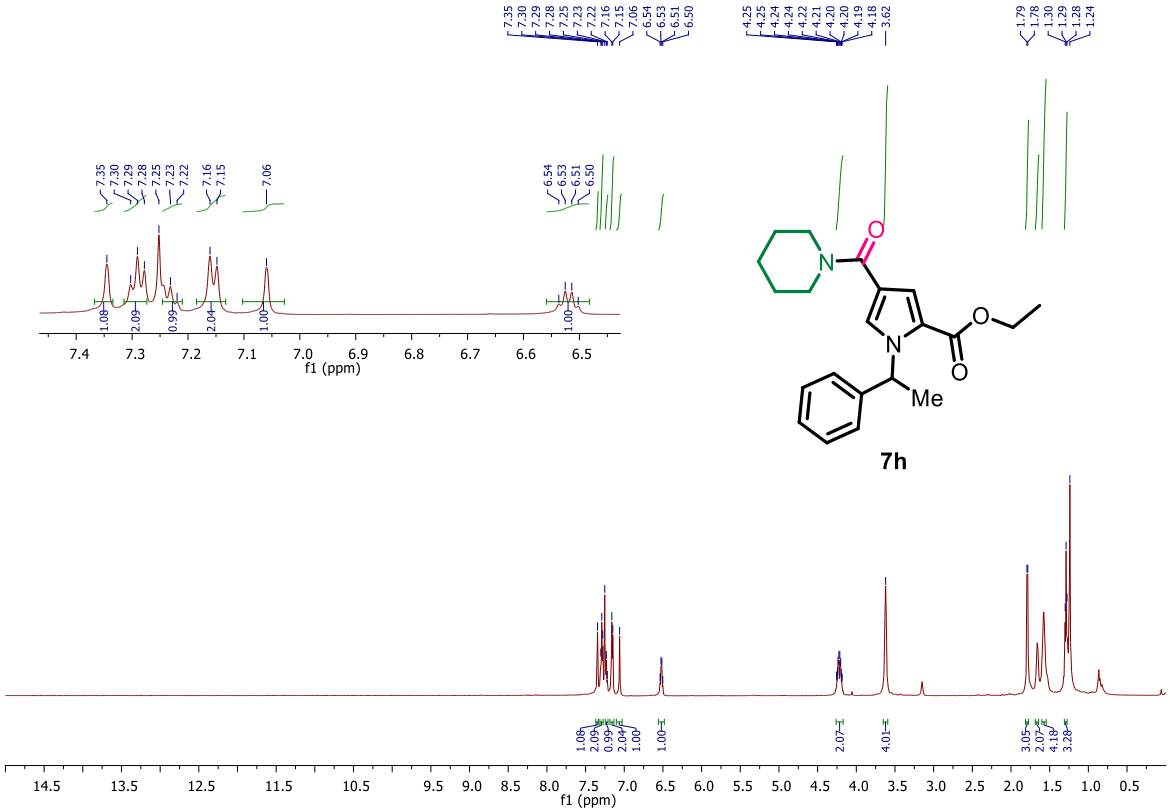
7e ^{1}H NMR ($CDCl_3$)



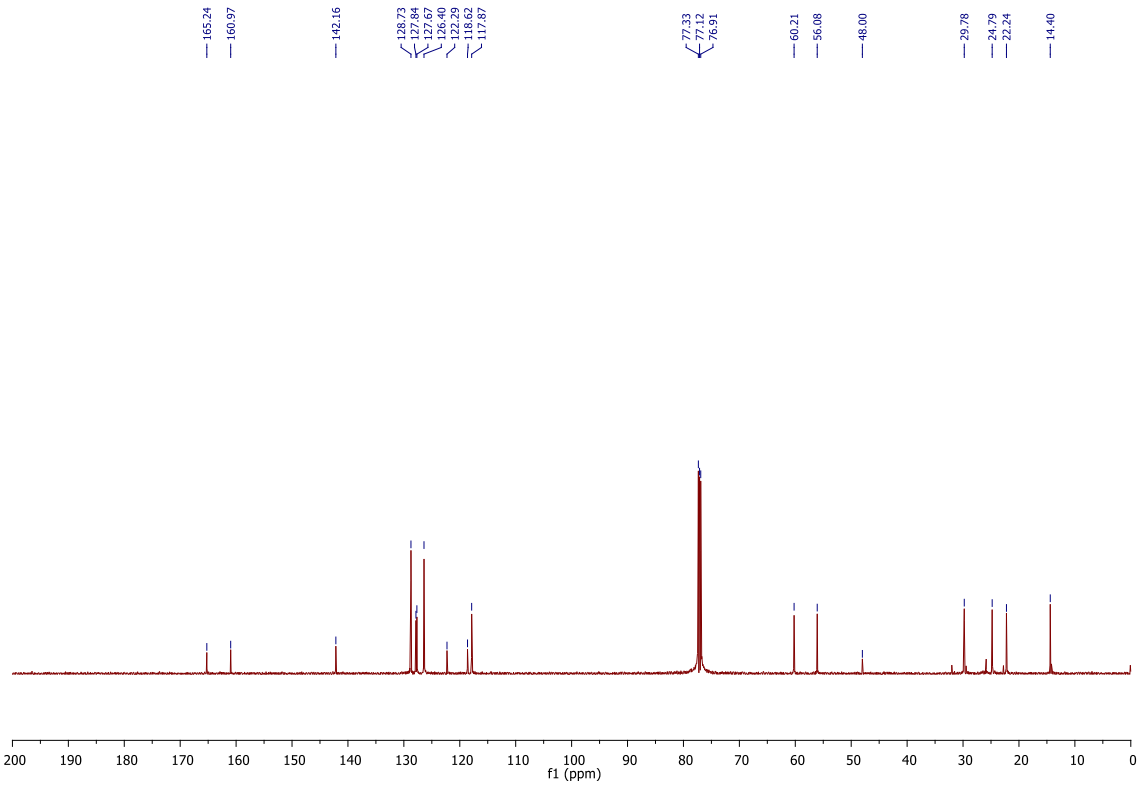
^{13}C{1H} NMR ($CDCl_3$)



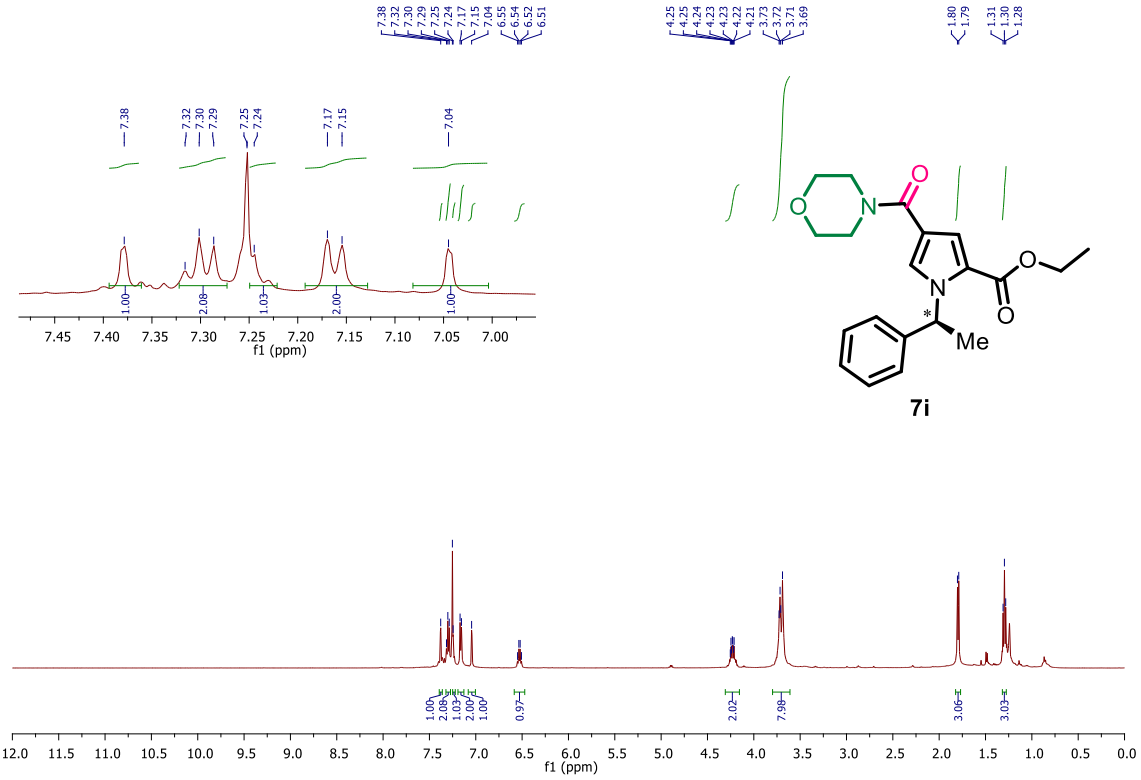
7h ^{1}H NMR ($CDCl_3$)



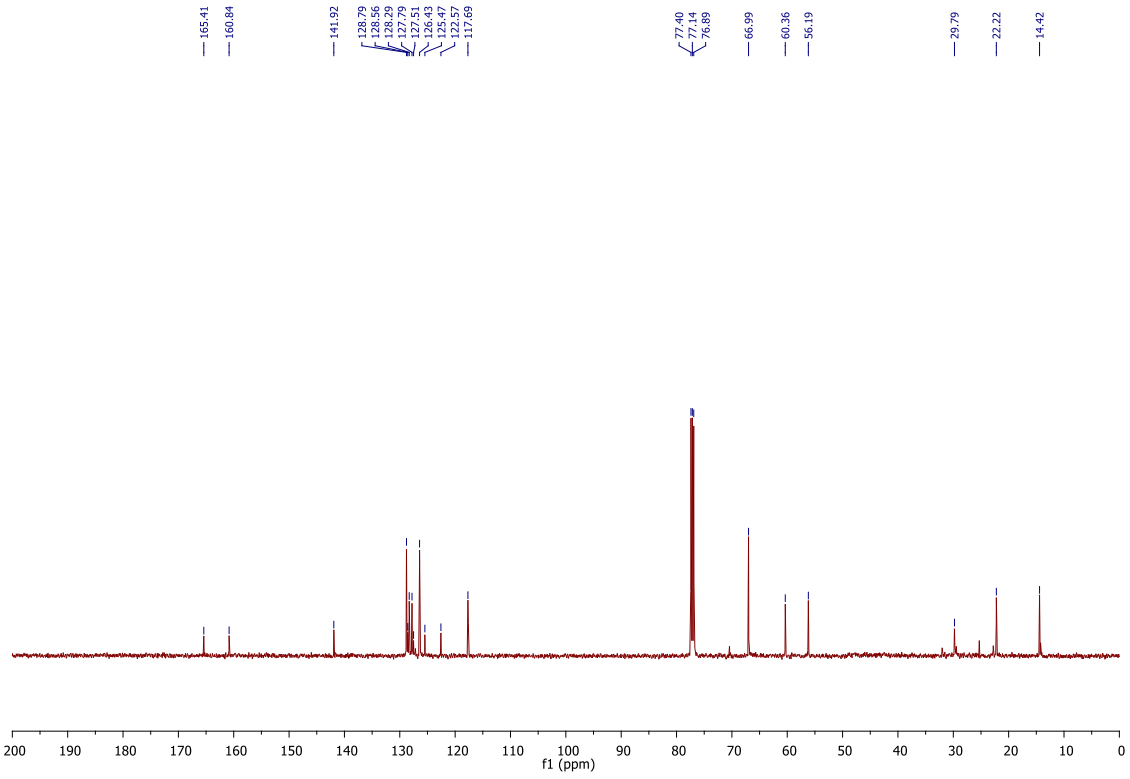
^{13}C{1H} NMR ($CDCl_3$)



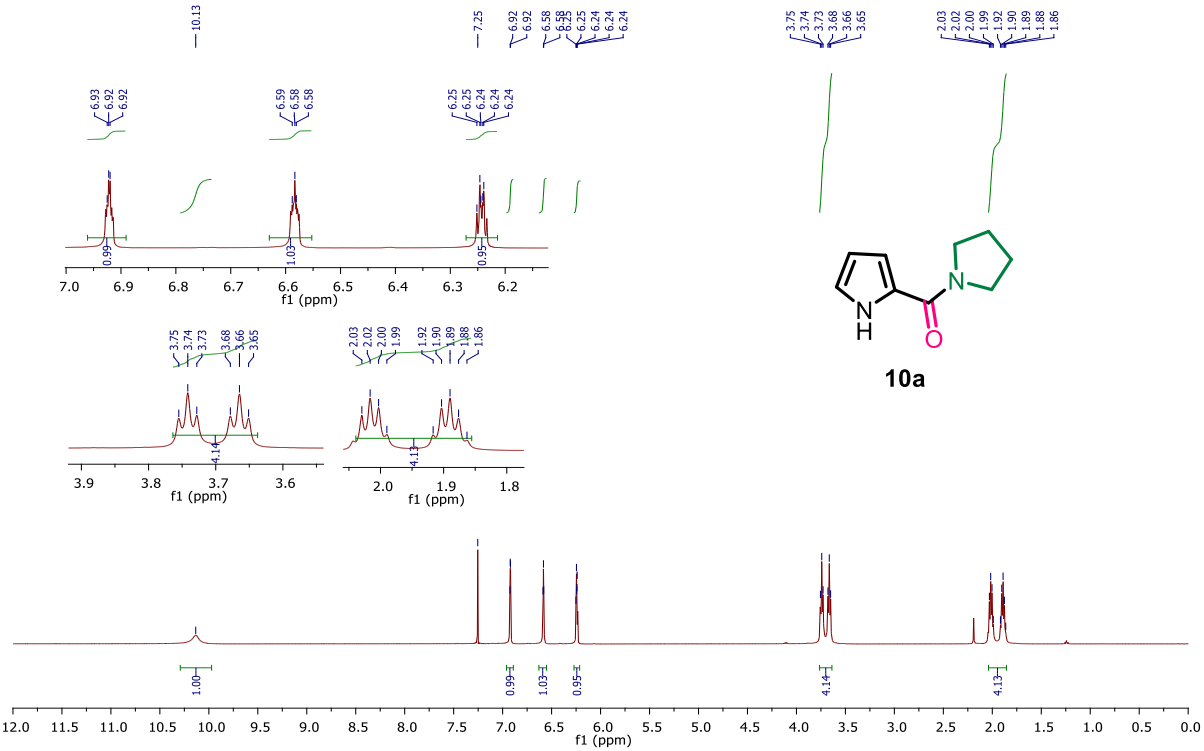
7i ^{1}H NMR ($CDCl_3$)



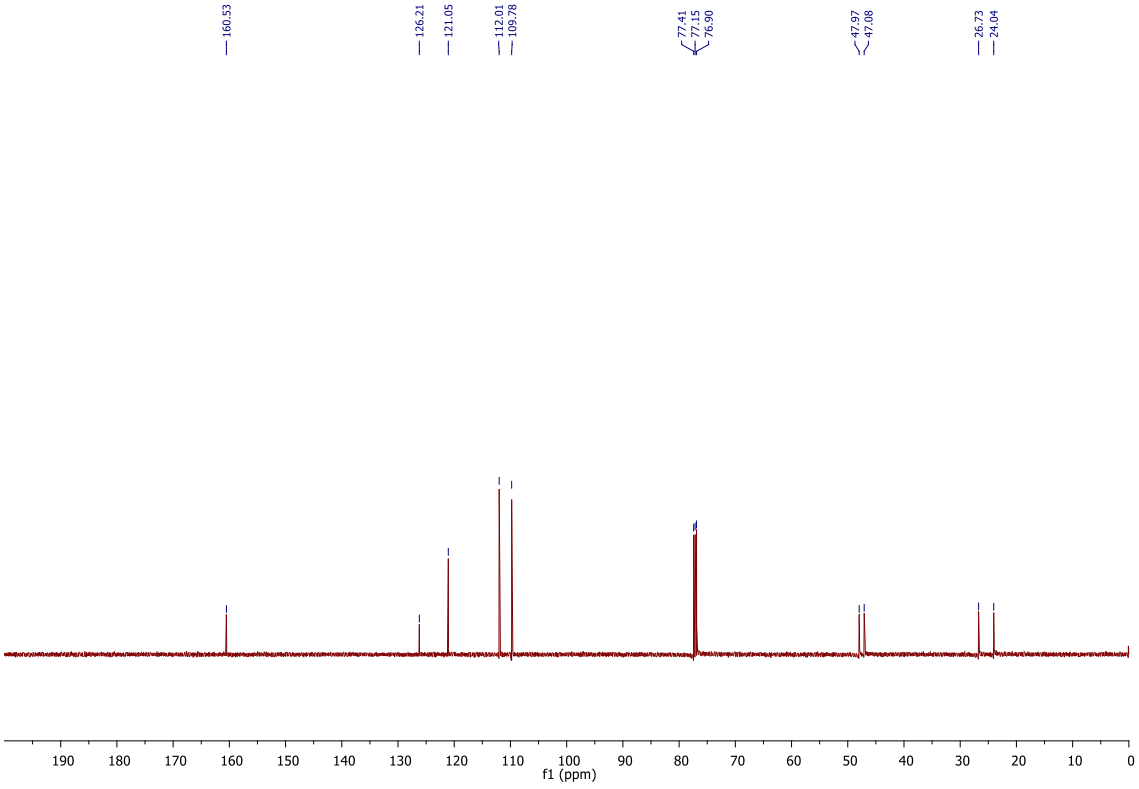
^{13}C{1H} NMR ($CDCl_3$)



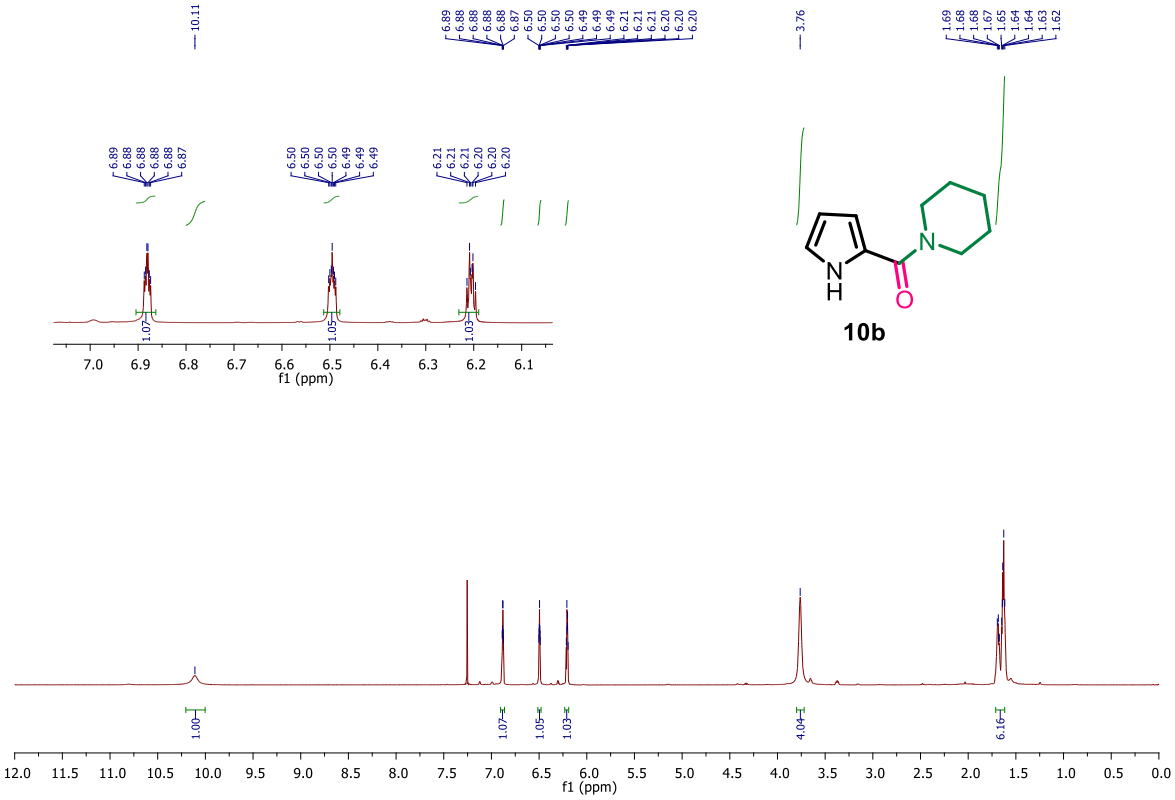
10a ^{1}H NMR ($CDCl_3$)



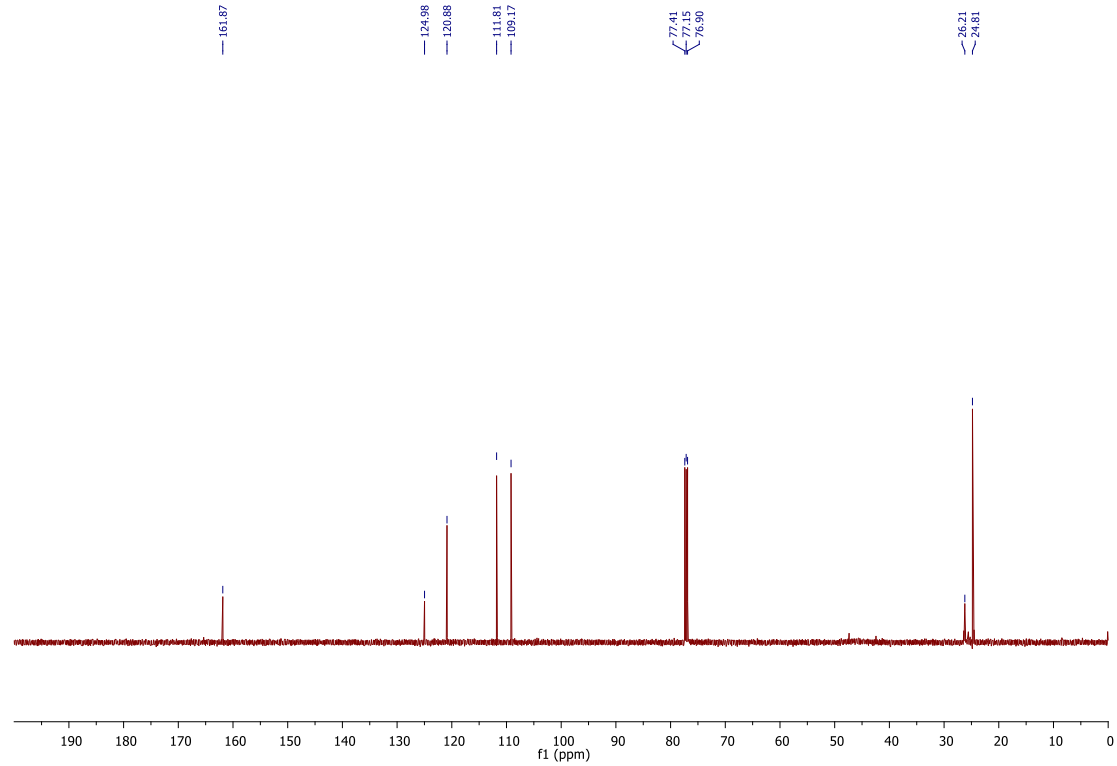
^{13}C{1H} NMR ($CDCl_3$)



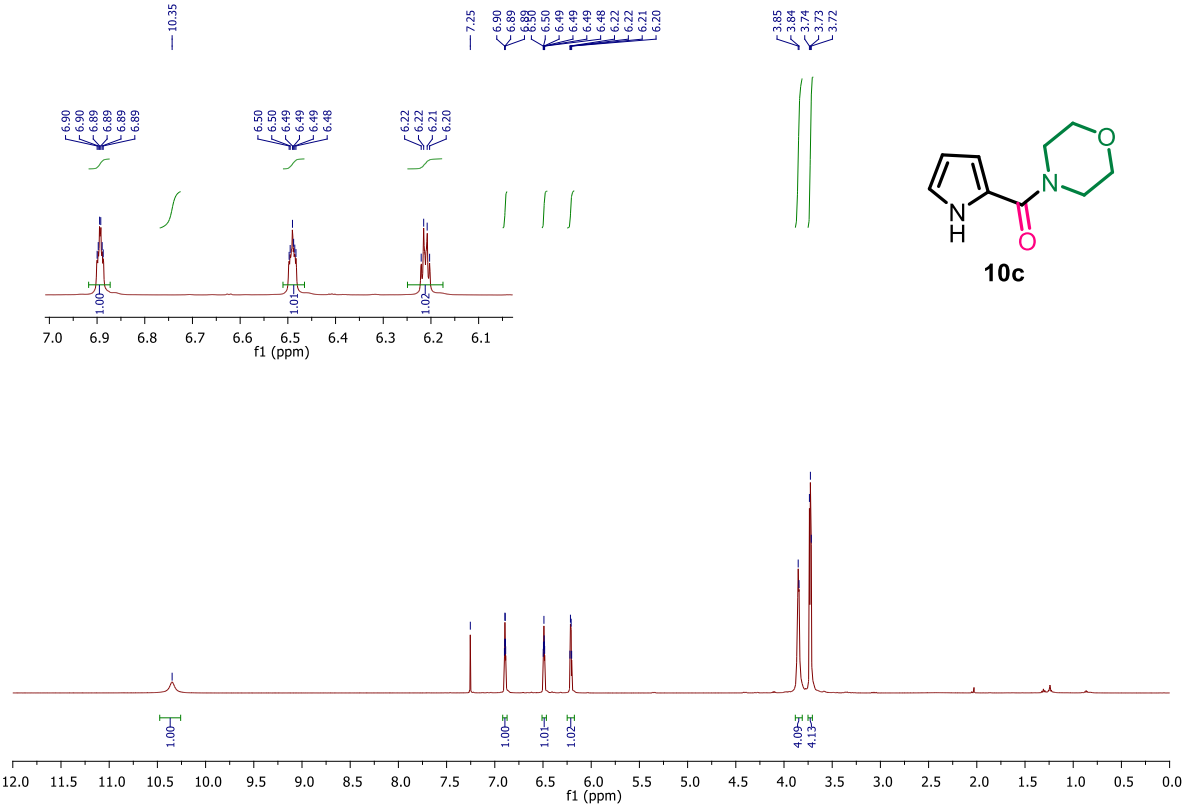
10b ^{1}H NMR ($CDCl_3$)



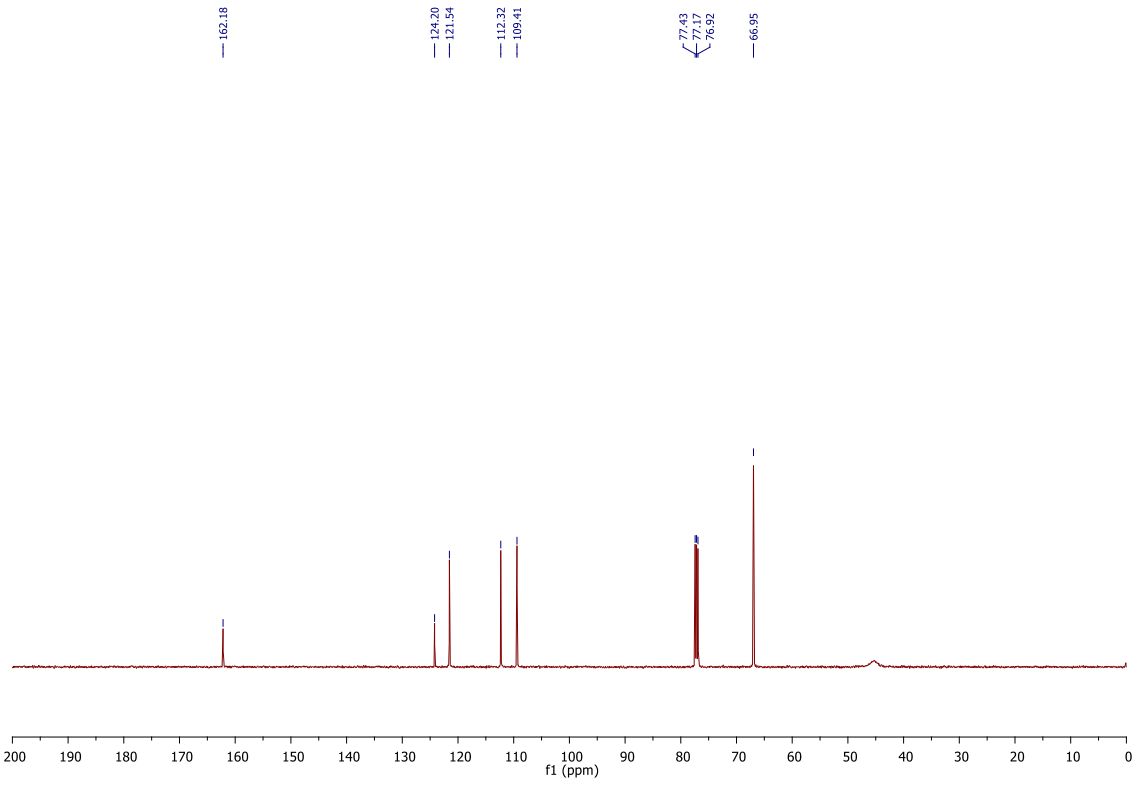
^{13}C{1H} NMR ($CDCl_3$)



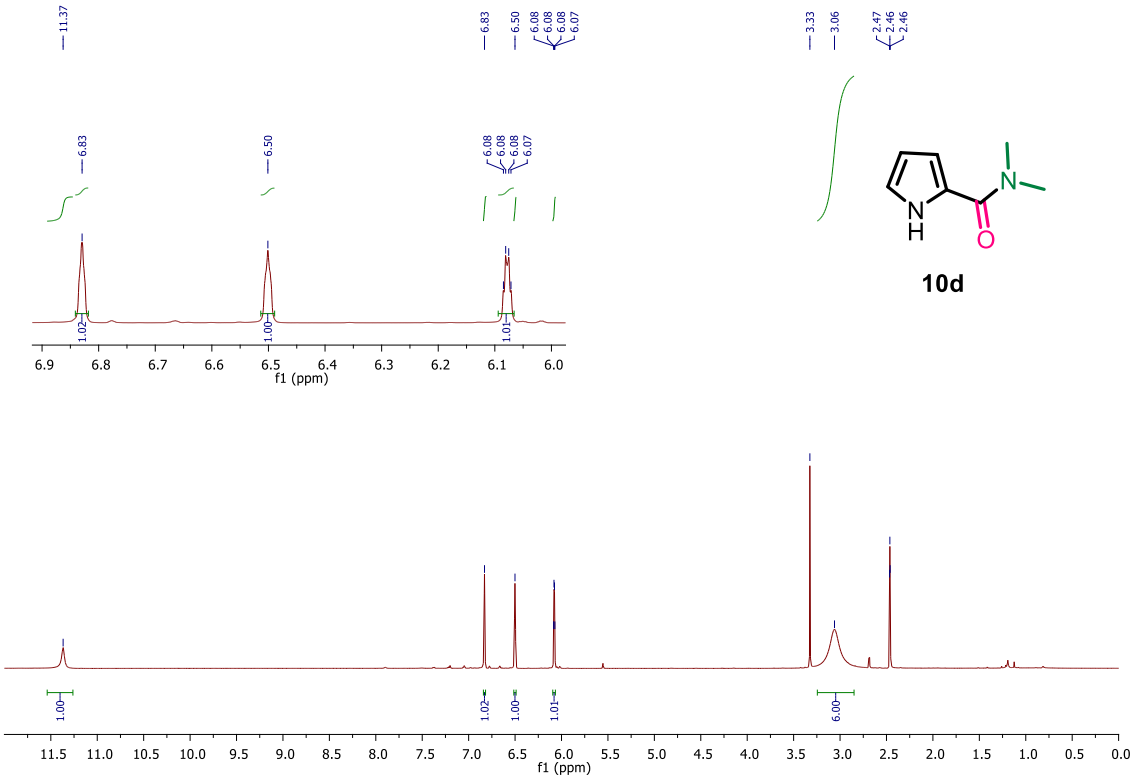
10c ^{1}H NMR ($CDCl_3$)



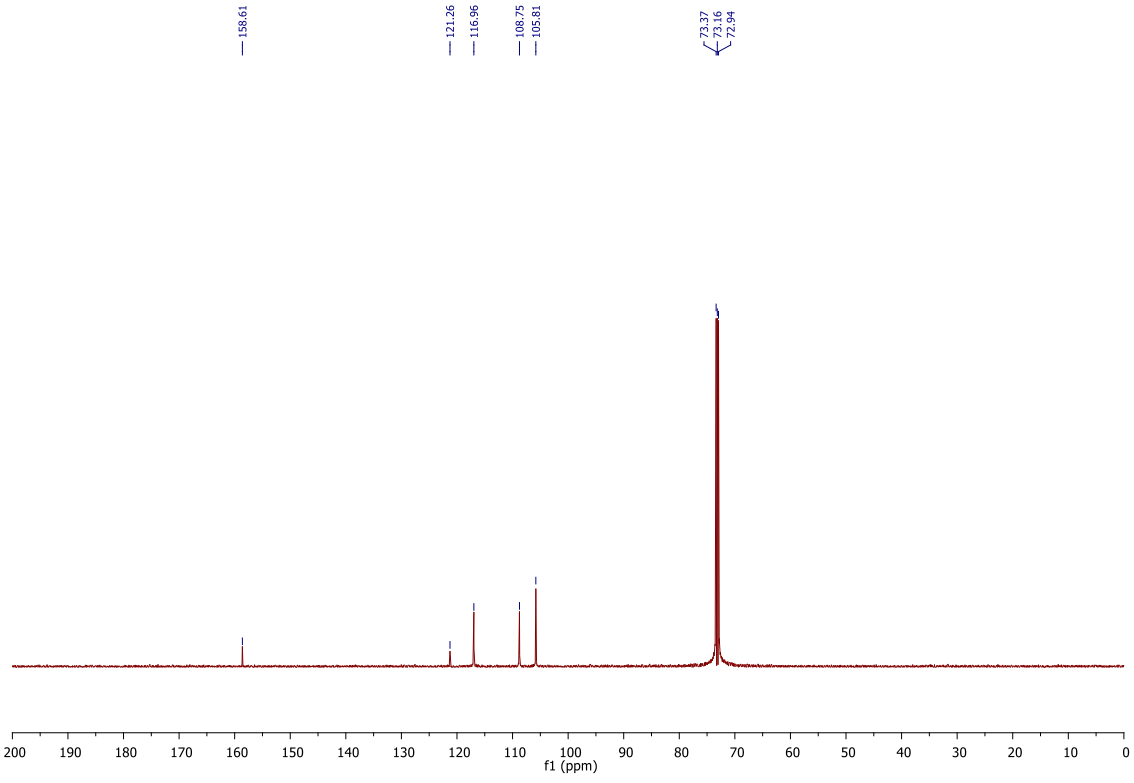
^{13}C{1H} NMR ($CDCl_3$)



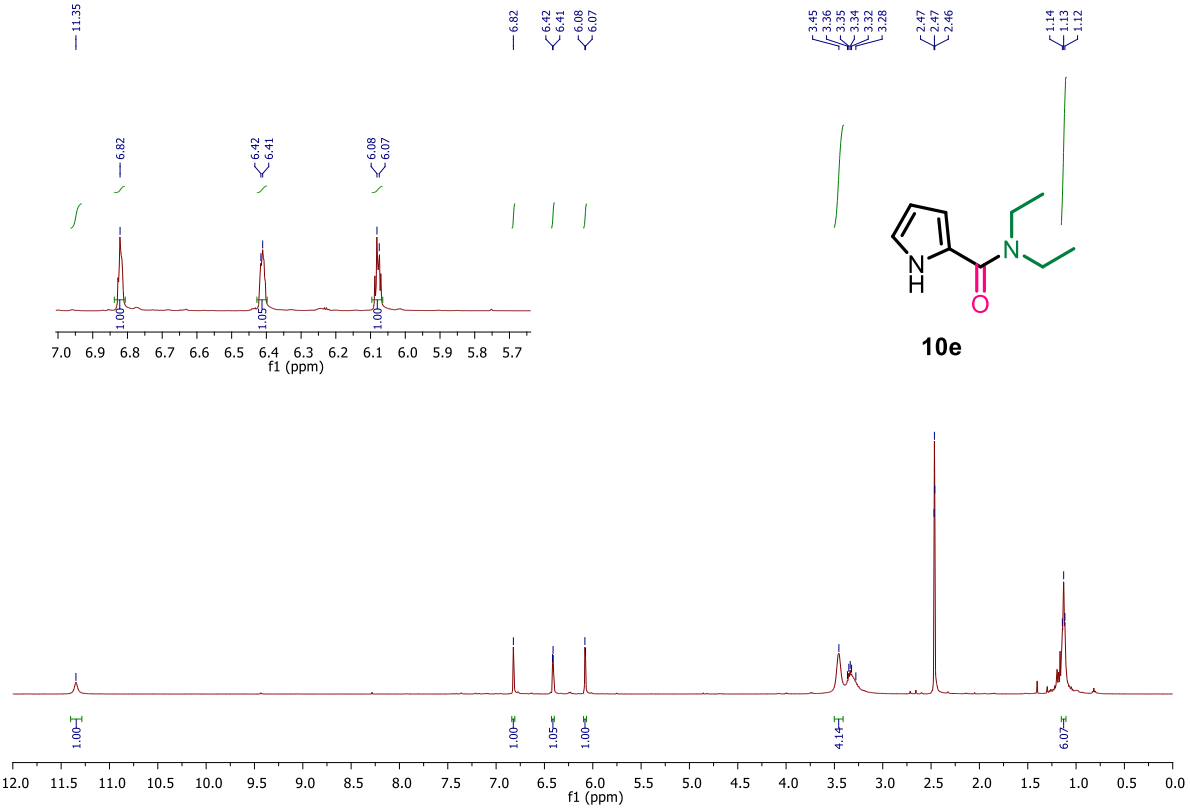
10d ^{1}H NMR ($CDCl_3$)



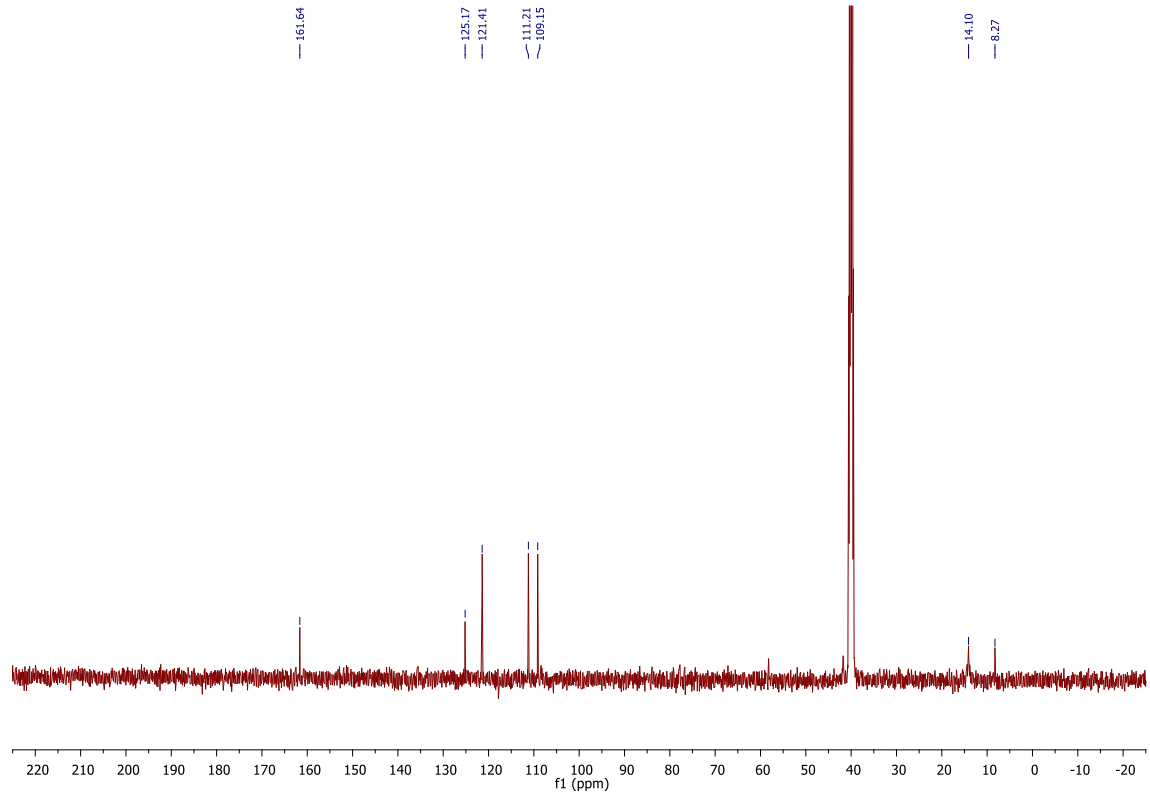
^{13}C{1H} NMR ($CDCl_3$)



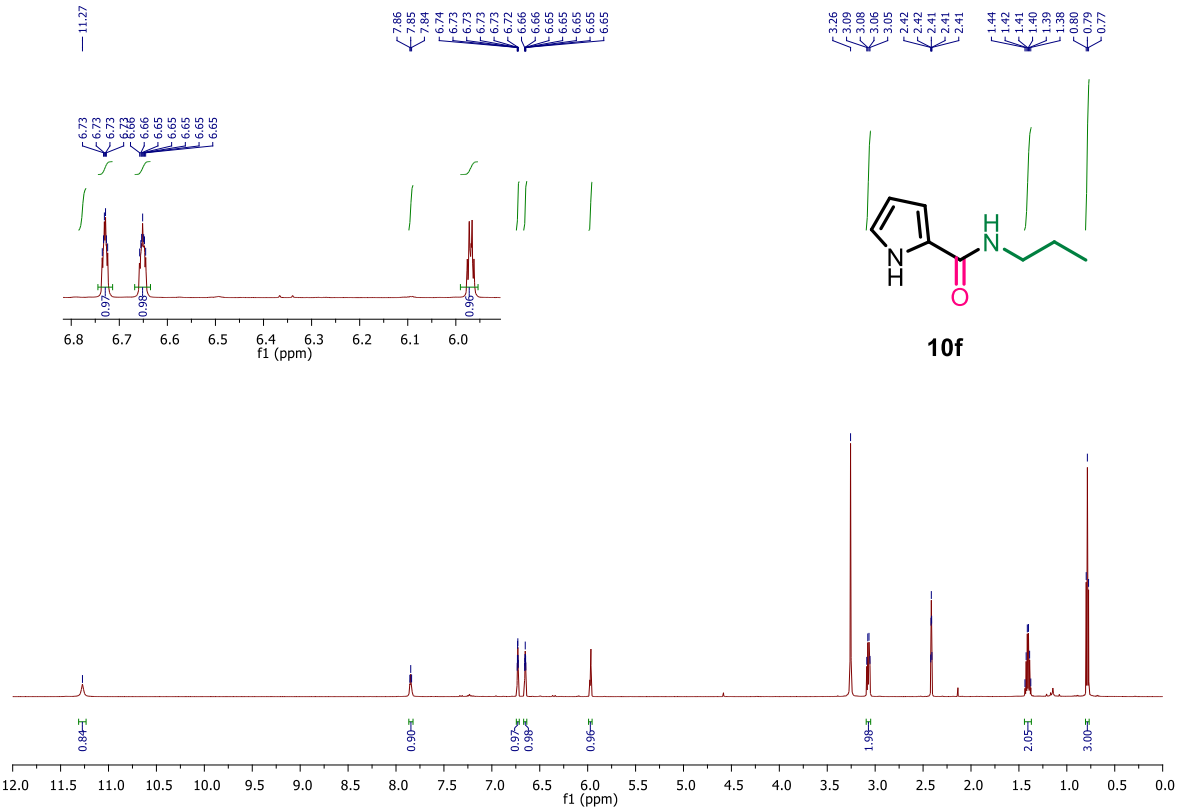
10e ^{1}H NMR ($CDCl_3$)



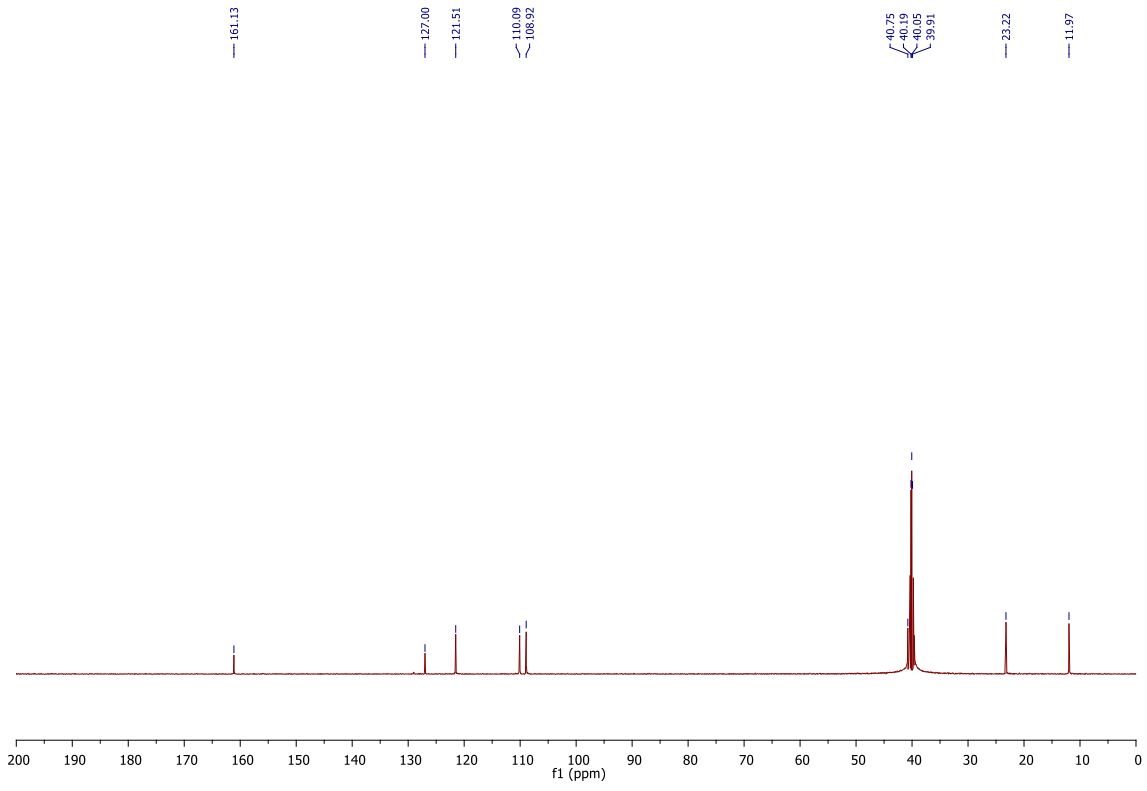
^{13}C{1H} NMR ($CDCl_3$)



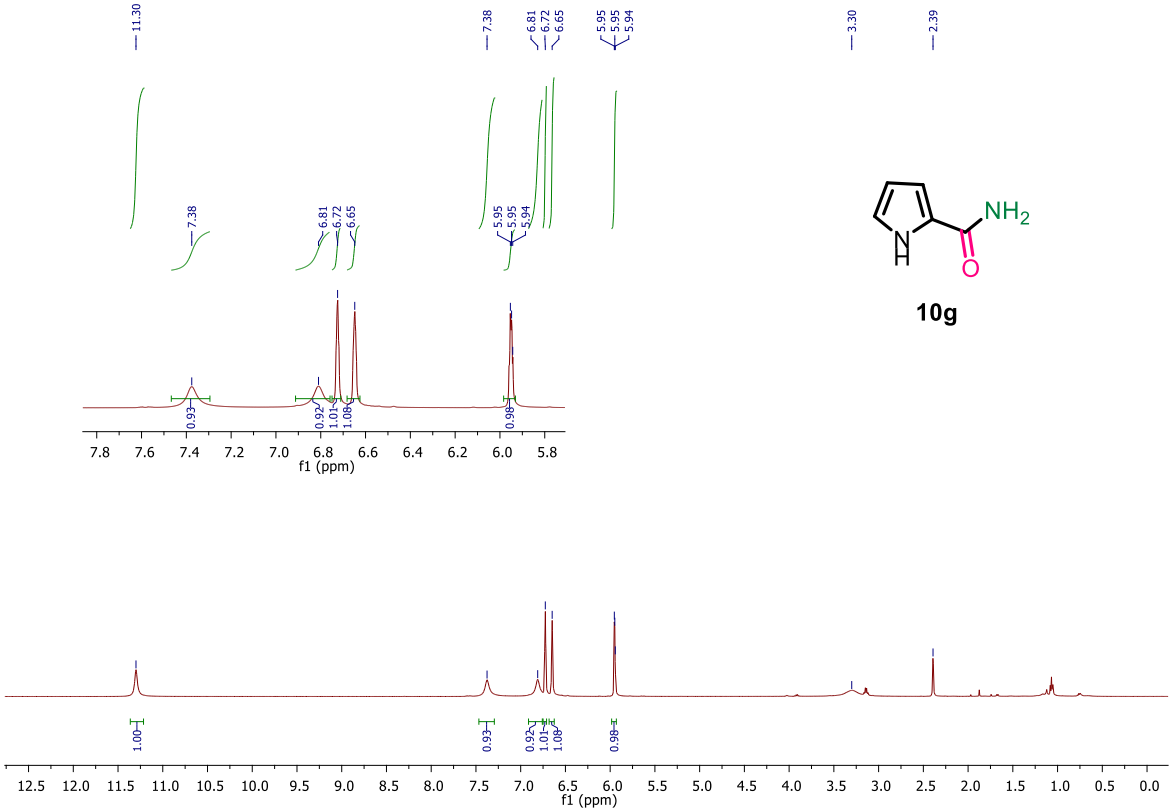
10f ^{1}H NMR ($CDCl_3$)



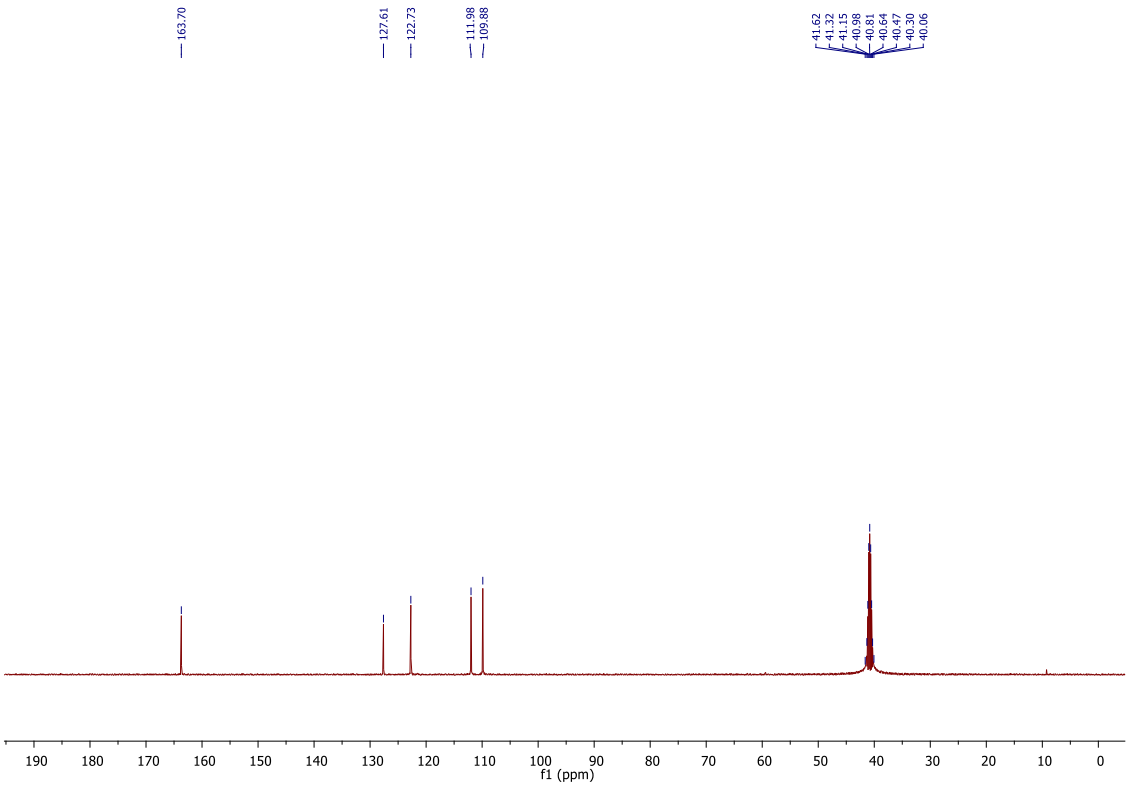
^{13}C{1H} NMR ($CDCl_3$)



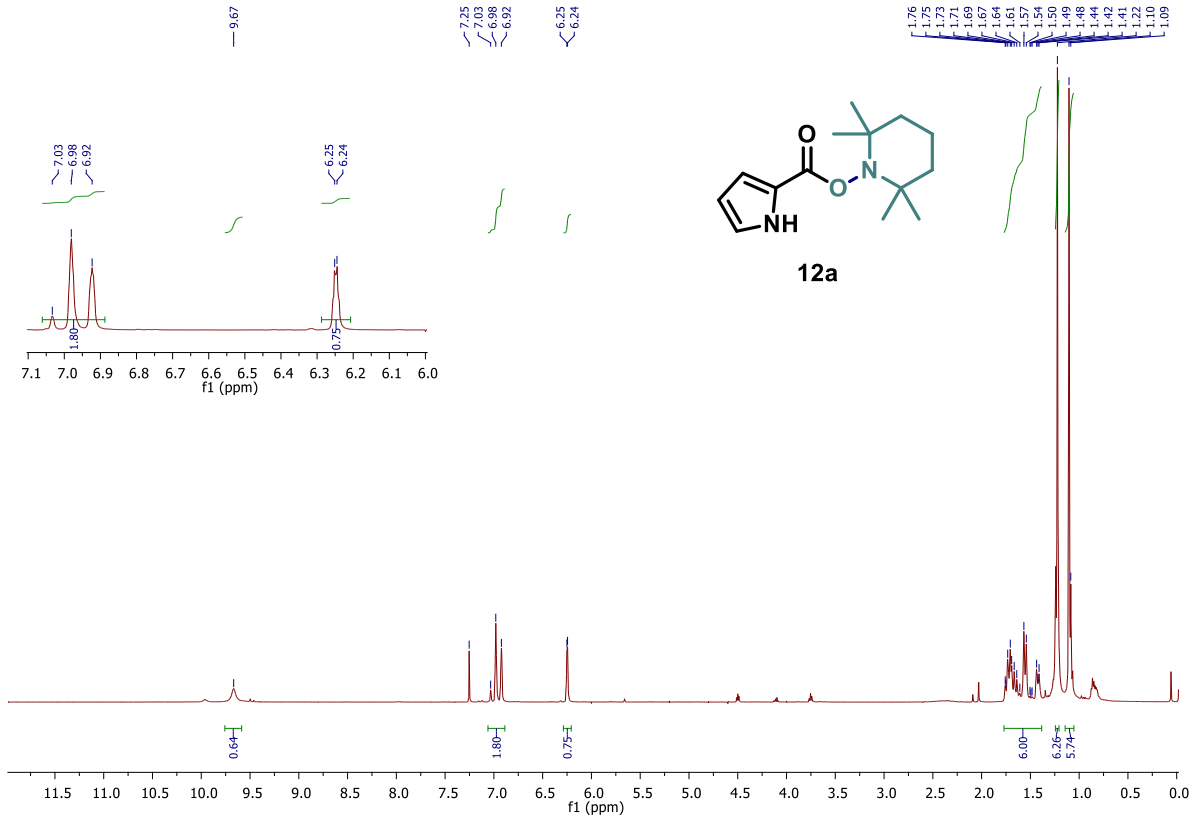
10g ^{1}H NMR ($CDCl_3$)



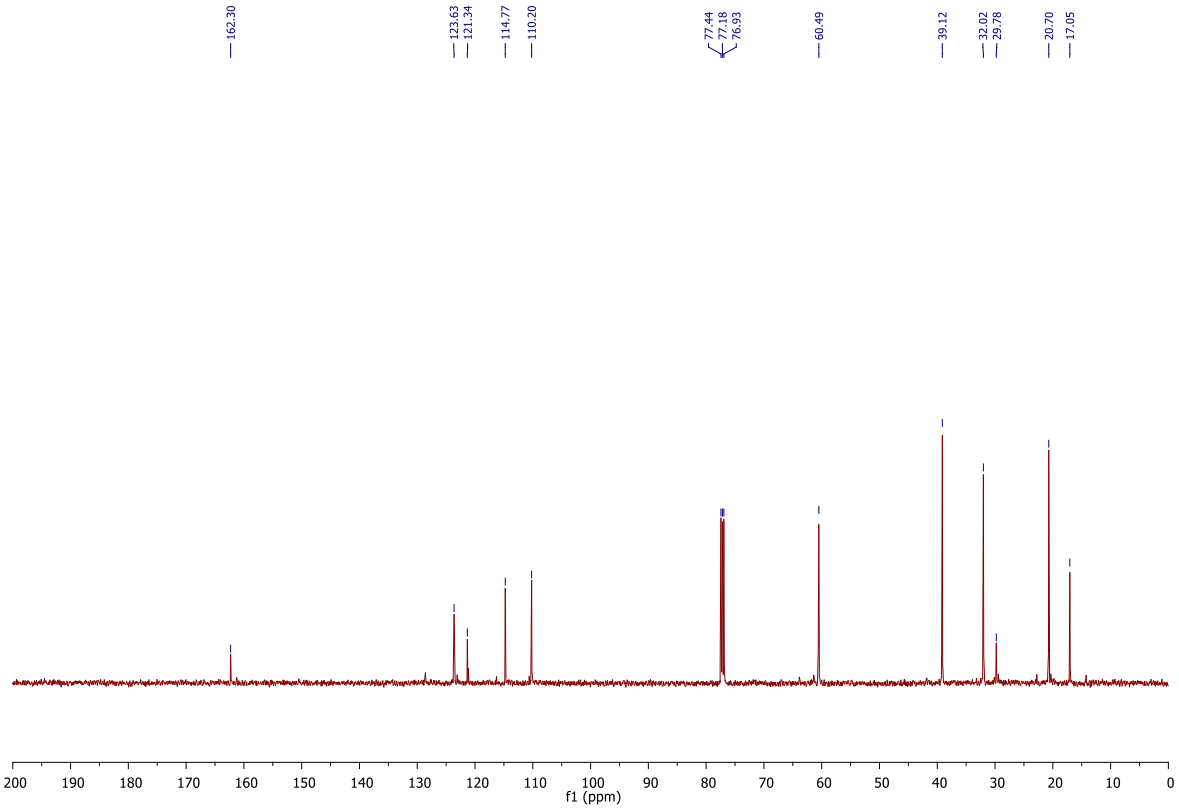
^{13}C{1H} NMR ($CDCl_3$)



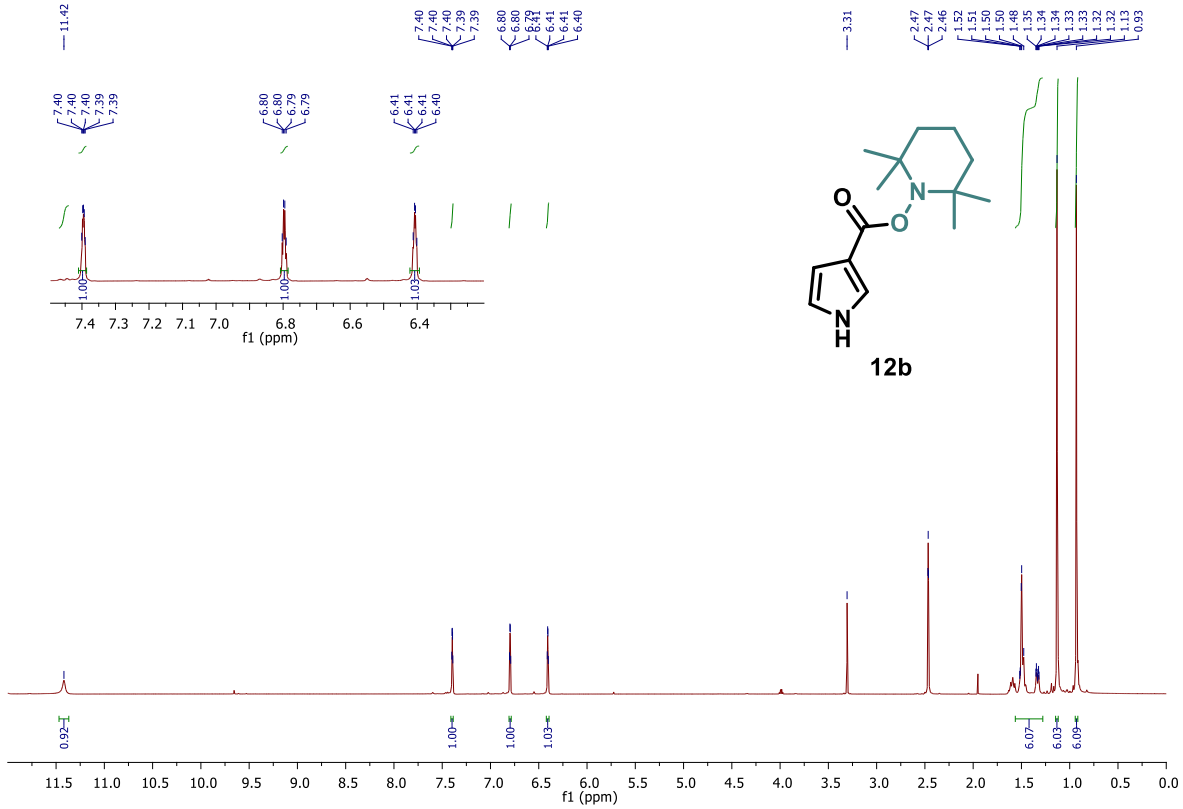
12a ^{1}H NMR ($CDCl_3$)



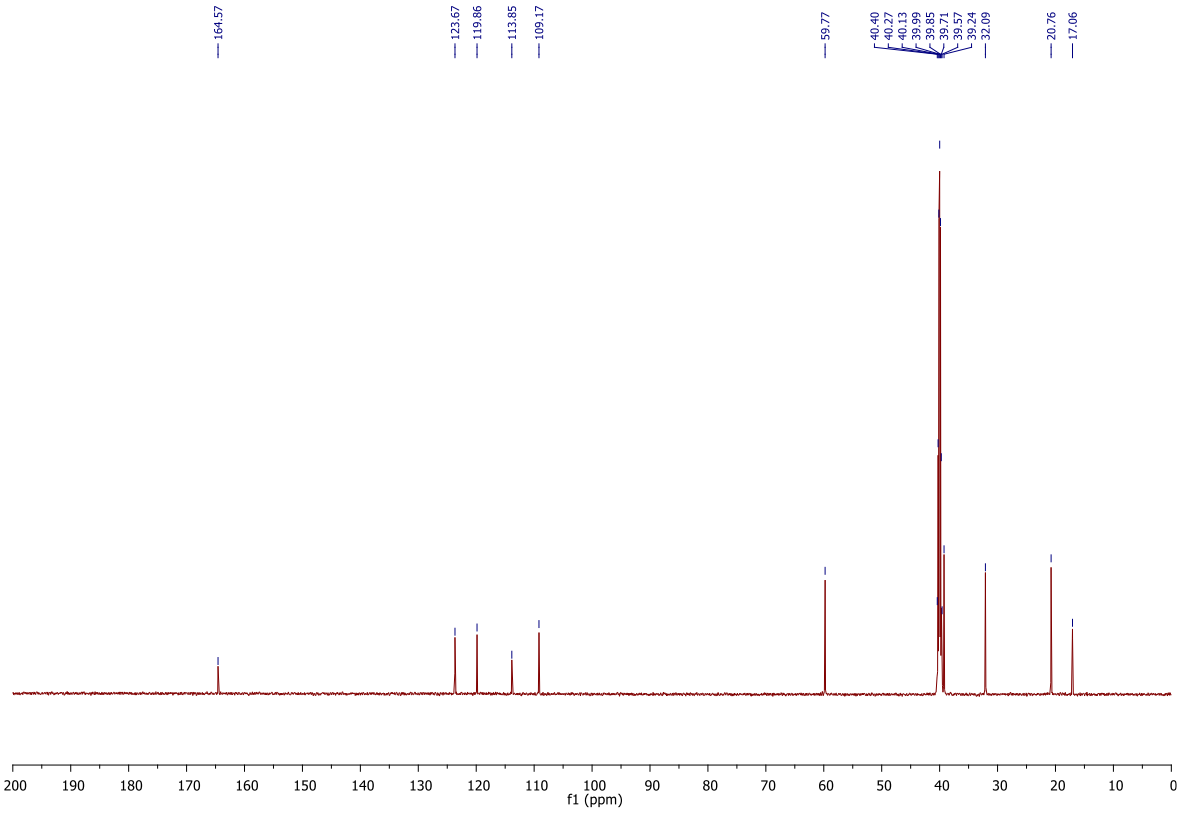
^{13}C{1H} NMR ($CDCl_3$)



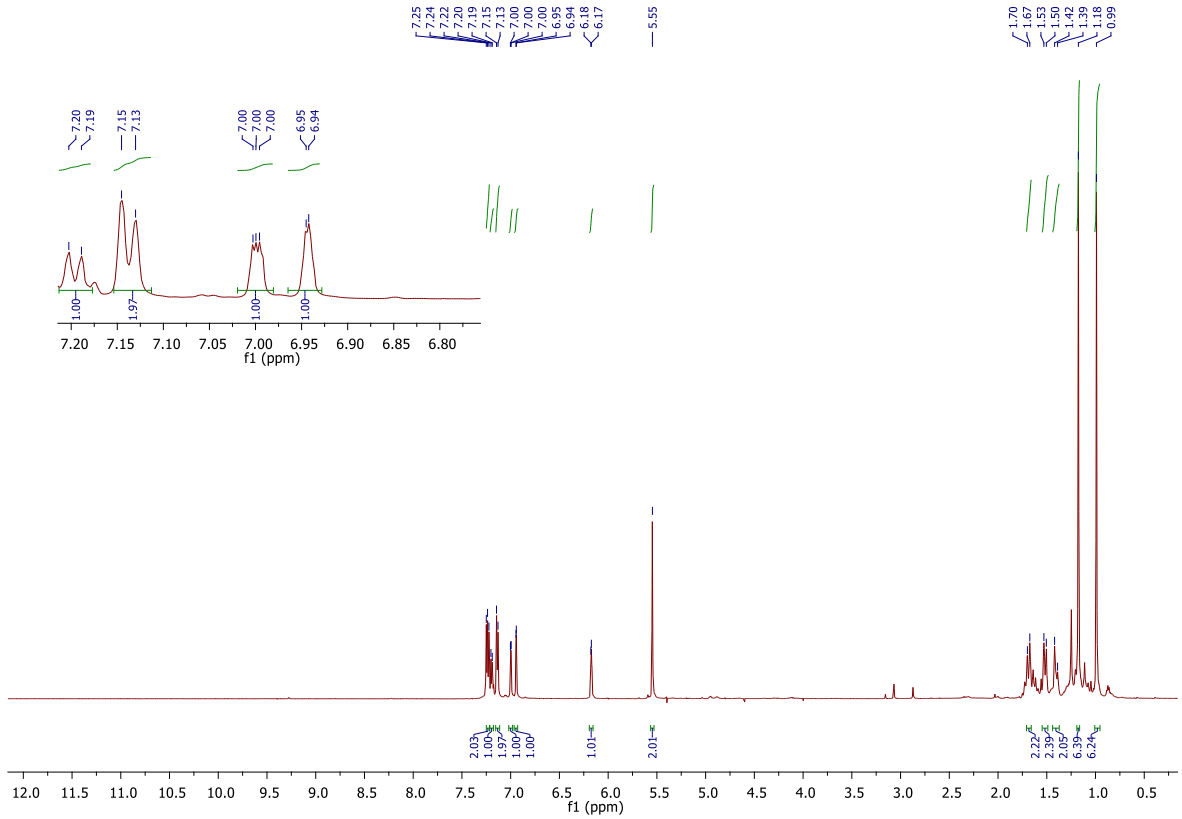
12b ^{1}H NMR ($CDCl_3$)



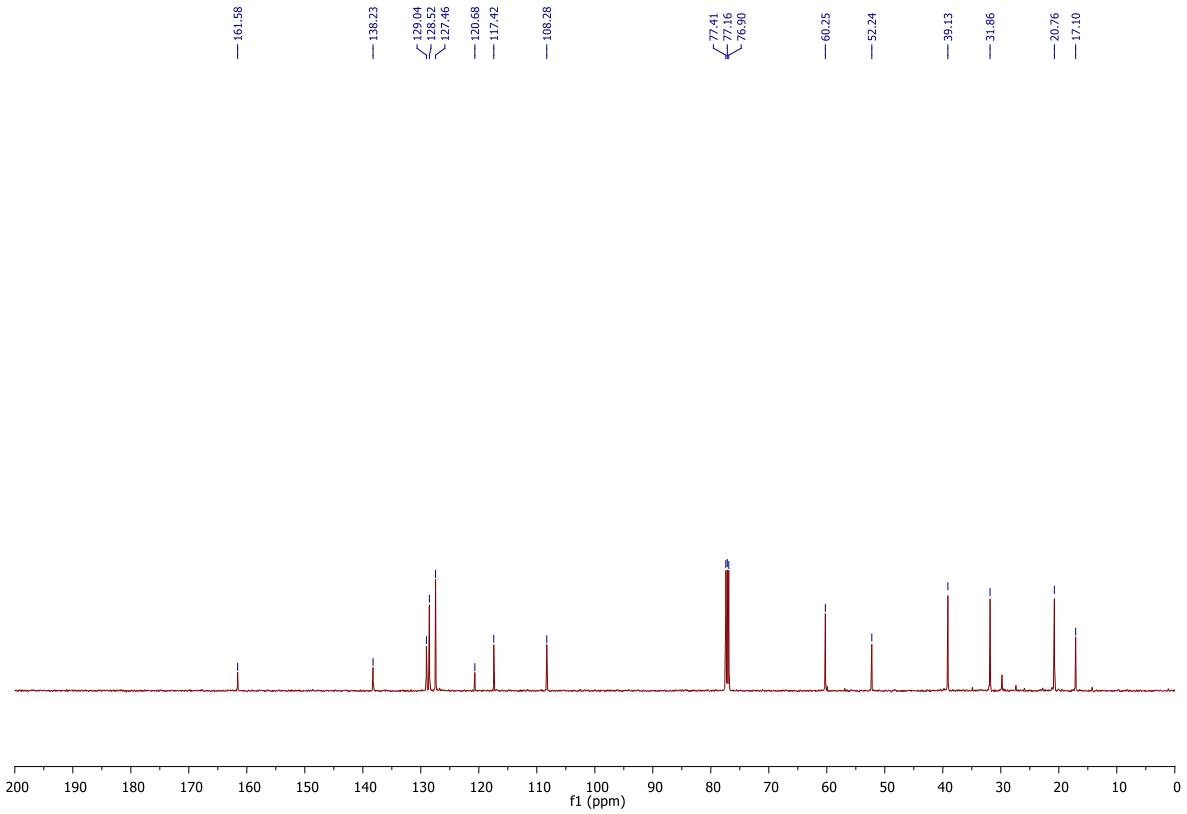
^{13}C{1H} NMR ($CDCl_3$)



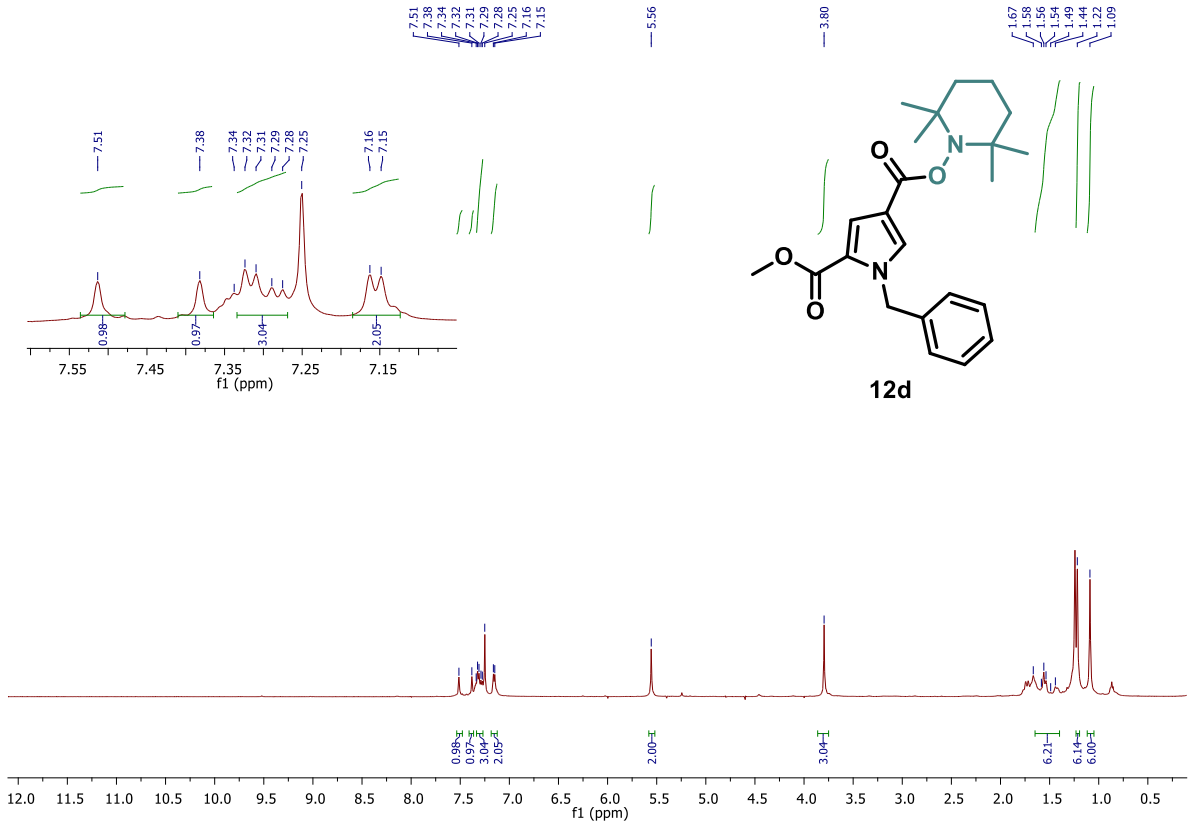
12c ^{1}H NMR ($CDCl_3$)



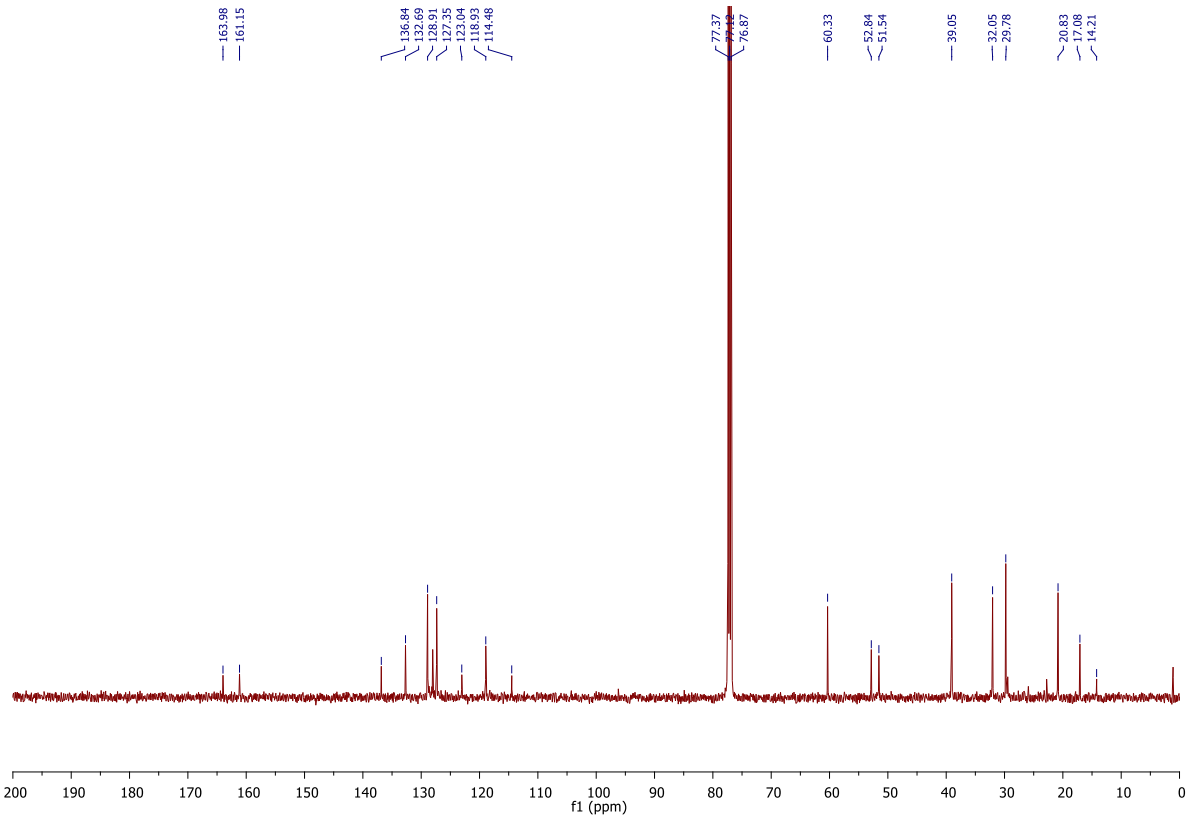
^{13}C{1H} NMR ($CDCl_3$)



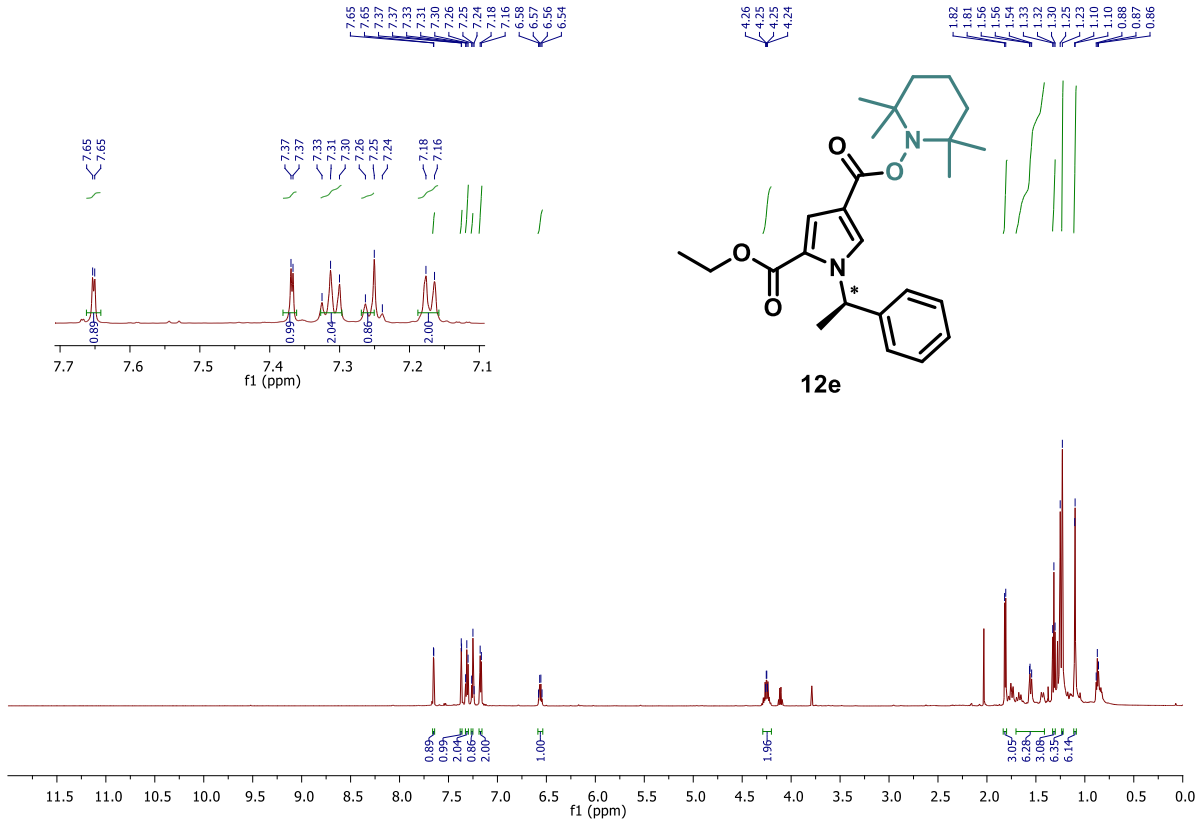
12d ^{1}H NMR ($CDCl_3$)



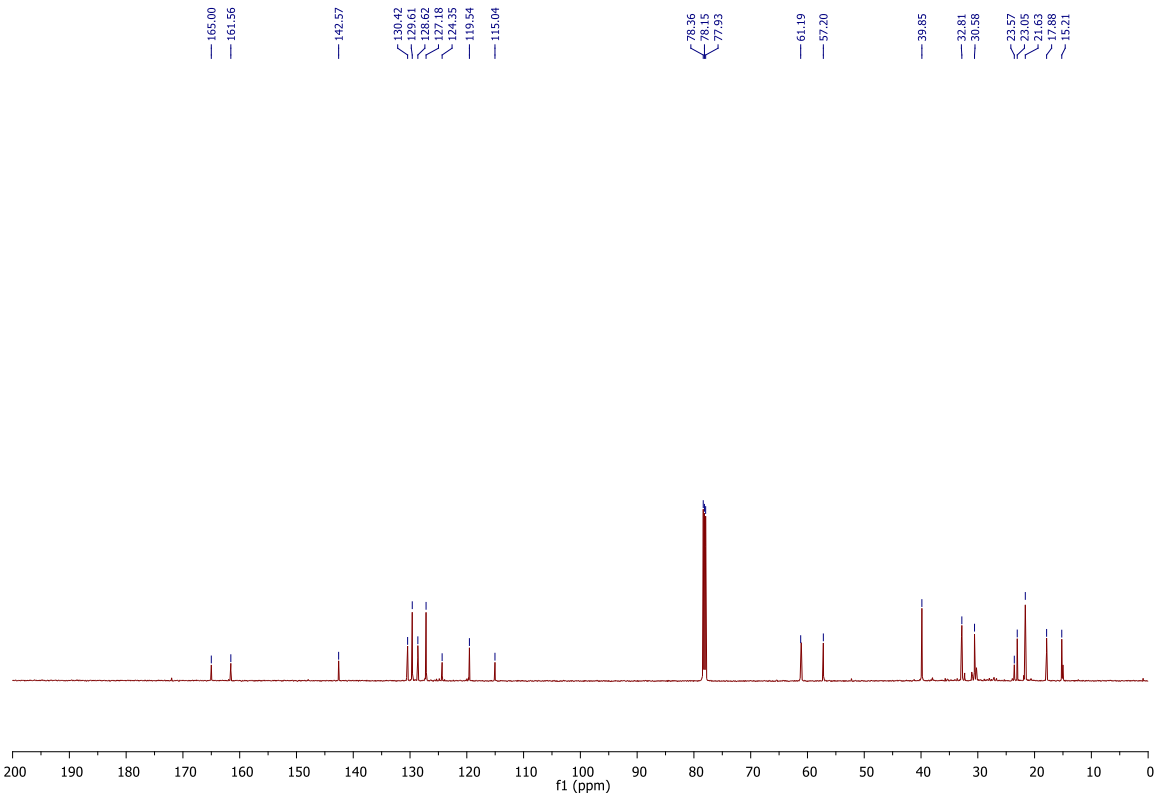
^{13}C{1H} NMR ($CDCl_3$)



12e ^{1}H NMR ($CDCl_3$)



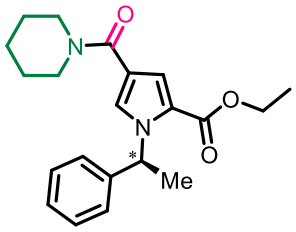
^{13}C{1H} NMR ($CDCl_3$)



7. HPLC Spectra

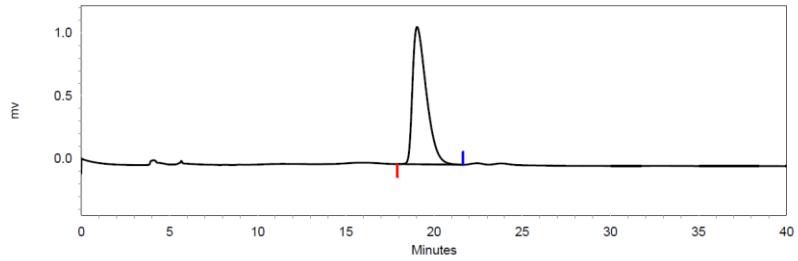
Chiral HPLC Specifications

Chiral HPLC performed with chiracel OD-H column (4.6 mm x 250 mm, Daicel Chemical, Japan) $t_{(s)}$ = 9.8 min; $t_{(R)}$ = 10.7 min (n-hexane/2-propanol/ (95:5). Flow rate of 1 mL/min.



7h

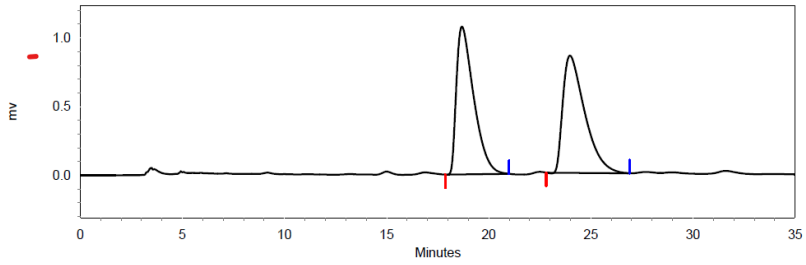
(a) HPLC Chromatogram of (R)-Ethyl-1-(1-phenylethyl)-4-(piperidine-1-carbonyl)-1*H*-Pyrrole-2-Carboxylate (7h)



Detector A (270nm)

Retention Time	Area	Area Percent
19.042	59398100	100.00
Totals	59398100	100.00

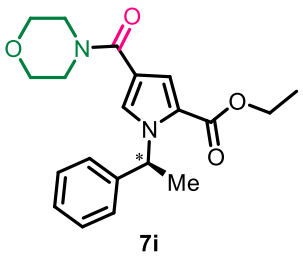
(b) HPLC Chromatogram of Ethyl-1-(1-phenylethyl)-4-(piperidine-1-carbonyl)-1*H*-Pyrrole-2-Carboxylate (7f)



Detector A (270nm)

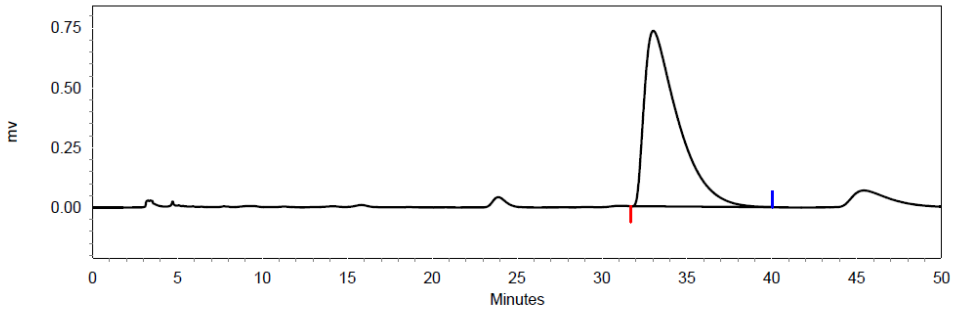
Retention Time	Area	Area Percent
18.683	63487803	49.98
23.975	63526136	50.02
Totals	127013939	100.00

Chiral HPLC performed with chiracel OD-H column (4.6 mm x 250 mm, Daicel Chemical, Japan) $t_{(s)}$ = 9.8 min; $t_{(R)}$ = 10.7 min (n-hexane/2-propanol/ (95:2). Flow rate of 1 mL/min.



7i

(a) HPLC Chromatogram of R-Ethyl-4-(morpholine-4-carbonyl)-1-(1-phenyl-1-ethyl)-1*H*-Pyrrole-2-Carboxylate (7i)

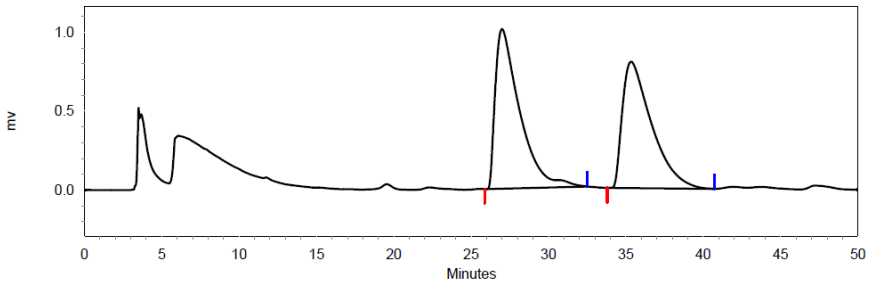


Detector A (270nm)

Retention Time	Area	Area Percent
33.025	101105474	100.00

Totals	101105474	100.00

(a) HPLC Chromatogram of Ethyl-4-(morpholine-4-carbonyl)-1-(1-phenyl-1-ethyl)-1*H*-Pyrrole-2-Carboxylate (7g)



Detector A (270nm)

Retention Time	Area	Area Percent
26.992	111224422	51.40
35.333	105153651	48.60

Totals	216378073	100.00