

## Organophotocatalytic dehydrogenative preparation of amides directly from alcohols

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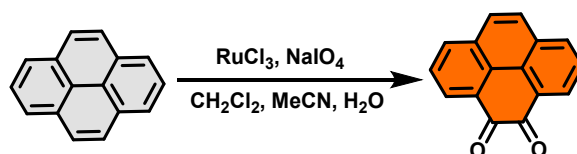
## 1. General information

All starting materials used in this study were procured from commercial suppliers and were used without further purification. Potassium tert-butoxide, potassium hydroxide, sodium hydroxide and other bases were purchased from Avra Synthesis Pvt. Ltd., India. Alcohol and amines were purchased from Sigma, Alfa Aesar, TCI, Avra Synthesis and used without any purification. The glassware was dried overnight in a 120 °C oven prior to their use. Pyrene,  $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$  were purchased from Sigma Aldrich. Solvents such as acetonitrile, toluene and dichloromethane were purchased from the commercial suppliers (Finar Chemicals). Toluene was dried by heating over sodium using benzophenone as an indicator. For thin layer chromatography (TLC), aluminum foil (from Merck) coated with silica and fluorescent indicator 254 nm was used. Column chromatography was performed using SD Fine silica gel 60-120 mesh using a gradient of hexane and ethyl acetate/ diethyl ether as mobile phase.

*Analytical Information:* All isolated compounds were characterized by  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR spectroscopies and ESI-mass spectrometry.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a 400 MHz Bruker Biospin Advance III FT-NMR spectrometer. NMR shifts are reported as delta ( $\delta$ ) units in parts per million (ppm) and coupling constants ( $J$ ) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Chemical shifts ( $\delta$ ) are quoted to the nearest 0.01 ppm relative to the residual protons in  $\text{CDCl}_3$  ( $\delta$  7.26 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in  $\text{CDCl}_3$  ( $\delta$  77.1 ppm). UV-Vis was recorded using Varian Cary 60 (Agilent Technologies) spectrophotometer. The total volume in the cuvette was fixed at 1 ml and a cuvette of path length 1 cm was used. The photochemical reactions were conducted with eplite 50 W blue LED (455 nm). The reaction tube was kept 7-8 cm away from the light source.

## 2. General synthetic procedure of 4,5-pyrenedione (PD)<sup>1</sup>

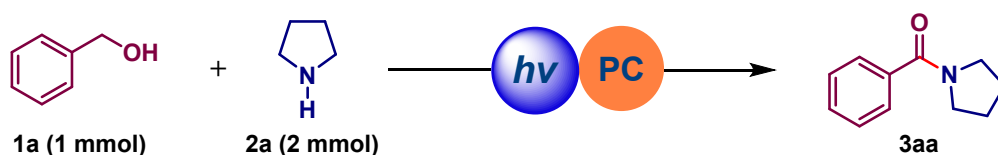
To a solution of dichloromethane (40 mL), acetonitrile (40 mL), and water 25 mL, pyrene (2 g, 10 mmol) was added followed by ruthenium (III) chloride hydrate (0.2 g, 0.96 mmol). The reaction mixture was cooled to 0 °C. To this reaction mixture sodium periodate (10 g, 47 mmol) was added portion-wise. The reaction temperature was kept at 0 °C for 10-15 min and then warmed to room temperature. The dark green suspension was stirred overnight. The reaction mixture was extracted with water-dichloromethane mixture. The organic layer was washed with water (3×100 mL) and dried over sodium sulphate. The solvent was dried in-vacuo and the residue was purified by column chromatography using petroleum ether/dichloromethane (60-100%) as eluent to afford pure 4,5-pyrenedione (964 mg) as bright orange solid in 42% yield, mp: 305-307 °C.



## 3. Systematic Optimization:

### a) Optimizing the photocatalyst loading:

Benzyl alcohol (**1a**, 1 mmol) and pyrrolidine (**2a**, 2 mmol) in 2 mL of toluene in a 20 mL vial was charged with different amounts of the photocatalyst 4,5-pyrenedione (**PD**) in the presence of 0.5 equivalents of potassium *tert*-butoxide (KO<sup>t</sup>Bu) under blue LED light source. The reaction mixture was kept under an oxygen-filled balloon. The desired amide product phenyl-1-pyrrolidinylmethanone (**3aa**) was obtained at the maximum yield with 8 mol% of the catalyst loading (see the table below).

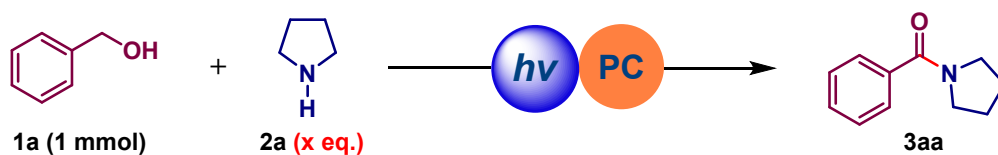


Condition: PD (x mol%), O<sub>2</sub> balloon, KO<sup>t</sup>Bu (0.5 eq), toluene (2 mL), blue LED (50 W), 24 h

Entry	Amount of PD (mol%)	Yield of <b>3aa</b> (%)
1	4	53
2	5	55
3	6	61
4	7	62
5	8	66
6	9	66
7	10	65

### b) Optimizing the amount of the amine:

After having the optimum photocatalyst loading, we varied the equivalents of amine required for this reaction. When the analogous reaction mixture (see section 3a) was charged with different equivalents of the amine, optimum product yield was obtained with 1.5 equivalents of the amine.

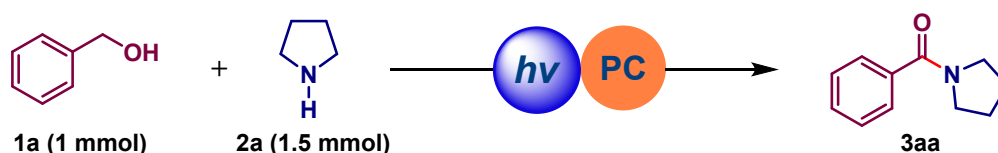


Condition: PD (8 mol%), O<sub>2</sub> balloon, KO<sup>t</sup>Bu (0.5 eq), toluene (2 mL), blue LED (50 W), 24 h

Entry	Amount of amine (eq.)	Yield of <b>3aa</b> (%)
1	1	39
2	1.2	52
3	1.5	73
4	2	66

### c) Optimizing the base required:

We proceeded with 8 mol% of **PD** and 1.5 equivalents of pyrrolidine loading to optimize the suitable base required for the reaction. While performing this reaction under identical conditions with various other bases, we found the reaction worked best with  $\text{KO}^t\text{Bu}$ . Other base like  $\text{NaO}^t\text{Bu}$  also yielded some product but the efficiency is much less compared to  $\text{KO}^t\text{Bu}$ .<sup>2,3</sup>

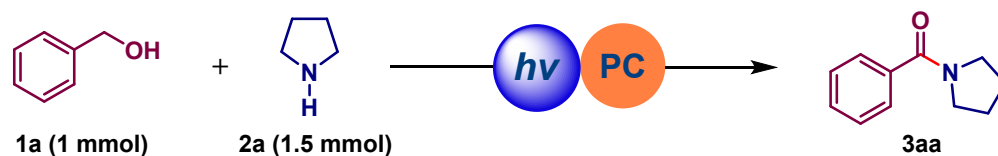


Condition: **PD** (8 mol%),  $\text{O}_2$  balloon, **base** (0.5 eq), toluene (2 mL), blue LED (50 W), 24 h

Entry	Base (0.5 equiv)	Yield of <b>3aa</b> (%)
1	$\text{NEt}_3$	n.r
2	KOH	n.r
3	NaOH	n.r
<b>4</b>	<b><math>\text{KO}^t\text{Bu}</math></b>	<b>73</b>
5	$\text{Na}_2\text{CO}_3$	n.r
6	$\text{K}_2\text{CO}_3$	n.r
7	DIPEA	n.r
8	$\text{NaO}^t\text{Bu}$	23

### d) Optimizing the base loading:

We then targeted to evaluate the amount of base loading to achieve the maximum product yield. The reaction does not take place without the base. Carrying out the reaction with different base loading suggested 30 mol% of  $\text{KO}^t\text{Bu}$  is ideal for secondary amine substrates. Please note that for primary amine substrates, 50 mol% base loading was deemed optimal.

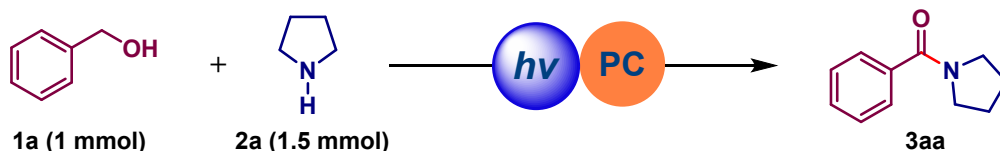


Condition: **PD** (8 mol%),  $\text{O}_2$  balloon,  $\text{KO}^t\text{Bu}$  (x eq.), toluene (2 mL), blue LED (50 W), 24 h

Entry	Base loading (equiv)	Yield of <b>3aa</b> (%)
1	0	0
2	0.2	73
<b>3</b>	<b>0.3</b>	<b>81</b>
4	0.4	76
5	0.5	73

### e) Solvent screening:

After establishing these optimum conditions, we explored the dependence of solvent on the reaction outcome. While studying the reaction in different solvents, we found decent yields in acetonitrile and xylene, however toluene proved to be the best.

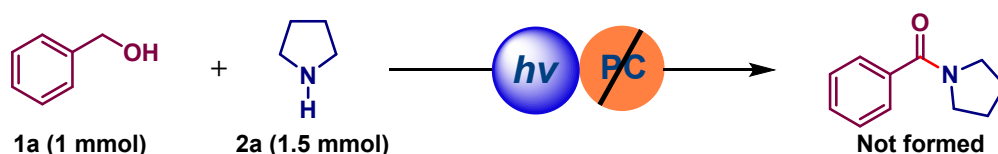


Condition: PD (8 mol%), O<sub>2</sub> balloon, KO<sup>t</sup>Bu (0.3 eq.), solvent (2 mL), blue LED (50 W), 24 h

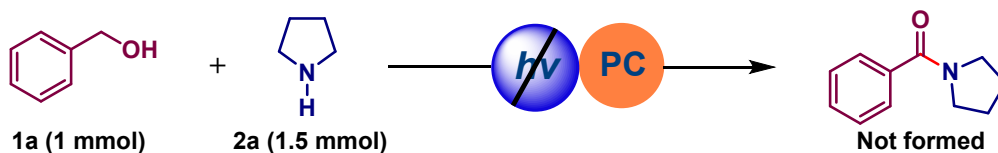
Entry	Solvent	Yield (%)
1	DMF	n.r.
2	THF	trace
3	MeCN	33
4	DMSO	n.r.
5	Xylene	77
6	Toluene	81

### f) Understanding the role of the photocatalyst and blue light:

When the reaction was performed in the absence of photocatalyst (PD) keeping other optimized conditions identical, no product formation was observed. The same was true when we eliminated the blue light source from the optimized reaction condition. These experiments clearly indicate that both PD and blue light source are indispensable for the reaction to take place.



Condition: O<sub>2</sub> balloon, KO<sup>t</sup>Bu (0.3 eq), toluene (2 mL), blue LED (50 W), 24 h



Condition: PD (8 mol%), O<sub>2</sub> balloon, KO<sup>t</sup>Bu (0.3 eq), toluene (2 mL), 24 h

## 4. General Procedure

In a typical reaction, a 20 mL vial was charged with PD (8 mol%), KO<sup>t</sup>Bu (30 mol%), alcohol (1 mmol), amine (1.5 mmol) in 2 mL toluene. The reaction mixture was allowed to stir under the light irradiation from eplite 50 W blue LED (455 nm) and the reaction tube was kept 7-8 cm away from the light source. The reaction flask was placed under an oxygen-filled balloon and stirred for 24 h. After completion of the reaction, the reaction mixture was concentrated *in vacuo*. The residue was purified by column

chromatography using hexane:ethyl acetate as eluent to afford pure products. Amides were fully characterized by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopies.

### 5. ICP-MS Analysis for used $\text{KO}^t\text{Bu}$ to detect any trace metal contamination.

The ICP-MS analysis was conducted in an iCAP RQ instrument. The contents of transition metal elements (Pd, Fe, Co, Ni and Cu) were found to be less than detection limit (0.1 ppm).

Entry	Metals	contents (in ppm)
1	Palladium	ND
2	Iron	0.165
3	Cobalt	ND
4	Nickel	ND
5	Copper	ND

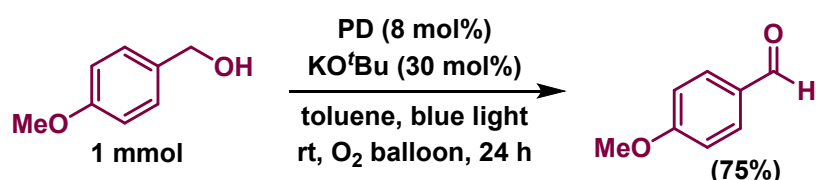
ND: Not detected

Additionally,  $\text{KO}^t\text{Bu}$  from different commercial sources such as Alfa Aesar, Sigma Aldrich, TCI were used in a new set of glassware. In all cases, the yield of the reaction was reproducible. These results strongly suggest that the reaction is not catalyzed by the adventitious presence of transition metals.

### 6. Mechanistic investigations

#### a) Photocatalyzed alcohol dehydrogenation:

A 20 mL vial tube was charged with 8 mol% of PD,  $\text{KO}^t\text{Bu}$  (0.3 mmol), and 4-methoxy benzyl alcohol (1 mmol) in 2 mL toluene. The reaction mixture was stirred under blue light irradiation for 24 h while the reaction flask was kept under an oxygen-filled balloon. Upon completion, the reaction mixture was dried and analyzed by  $^1\text{H}$  NMR spectroscopy, through which the yield was also determined. It is found that 75% of 4-methoxy benzaldehyde formed after 24 h under the given photochemical condition.



#### Analytical data for 4-methoxybenzaldehyde<sup>4</sup>:

*Appearance:* Light yellow liquid

*Eluent:* Hexane

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.98 (s, 1H), 7.85 (d,  $J = 8.8$  Hz, 2H), 7.02 (d,  $J = 8.7$  Hz, 2H), 3.91 (s, 3H) ppm.

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  190.2, 164.1, 131.4, 129.5, 113.9, 55.0 ppm.

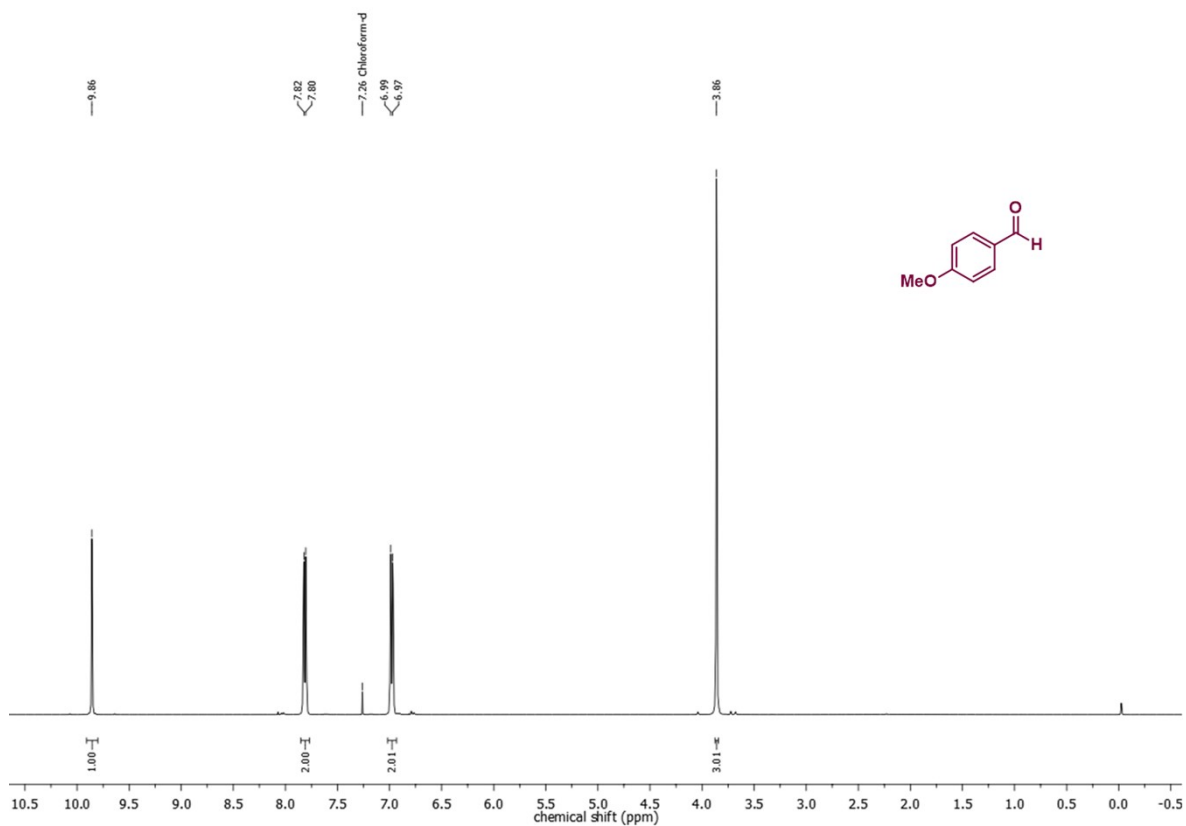


Figure 1:  $^1\text{H}$  NMR spectrum of 4-methoxybenzaldehyde in  $\text{CDCl}_3$ .

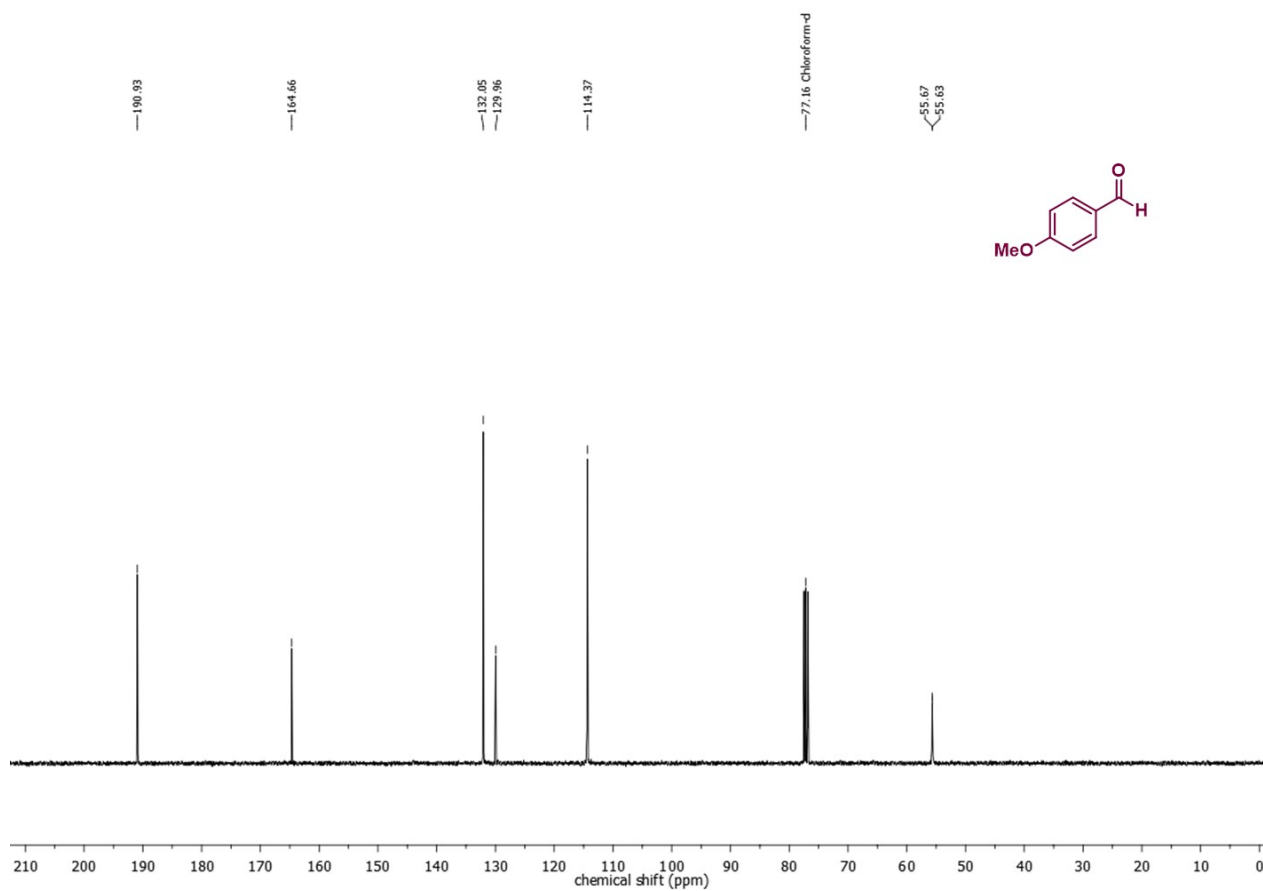
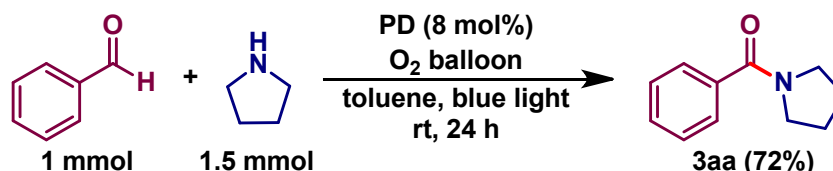


Figure 2:  $^{13}\text{C}$  NMR spectrum of 4-methoxybenzaldehyde in  $\text{CDCl}_3$ .

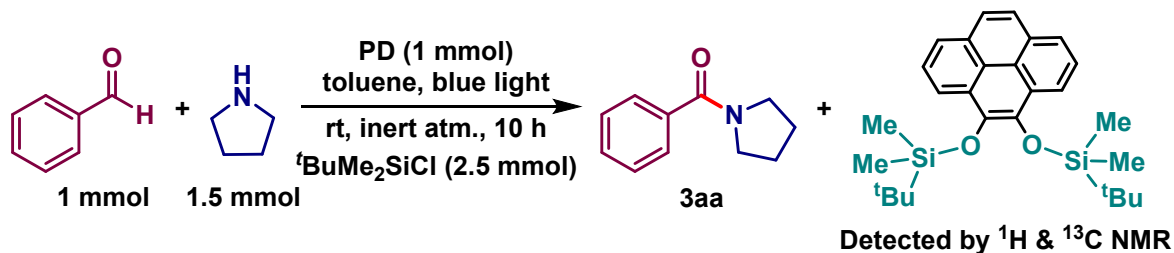
**b) Formation of amide in the absence of KO<sup>t</sup>Bu, when started from aldehyde stage:**

A 20 mL vial tube was charged with 8 mol% of PD, 1.5 mmol of pyrrolidine, and 1 mmol of benzaldehyde in 2 mL toluene. The reaction mixture was stirred under blue light irradiation for 24 h while the reaction flask was kept under an oxygen-filled balloon. Upon completion, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography using hexane : ethyl acetate as eluent to afford pure product **3aa** (72% yield).



**c) Trapping of fully reduced PD:**

A 25 mL Schlenk flask was charged with PD (1 mmol), benzaldehyde (1 mmol), pyrrolidine (1.5 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl) (2.5 mmol) in 10 mL dry toluene under inert conditions. The reaction mixture was stirred for 10 h under a 50 W blue LED light. Upon completion, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography using hexane:ethyl acetate as eluent to afford the silyl ether protected catechol form of PD. The isolated product was characterized by <sup>1</sup>H & <sup>13</sup>C NMR spectroscopies.



**Analytical data for 4,5-bis(*tert*-butyldimethylsiloxy)-pyrene<sup>5</sup>:**

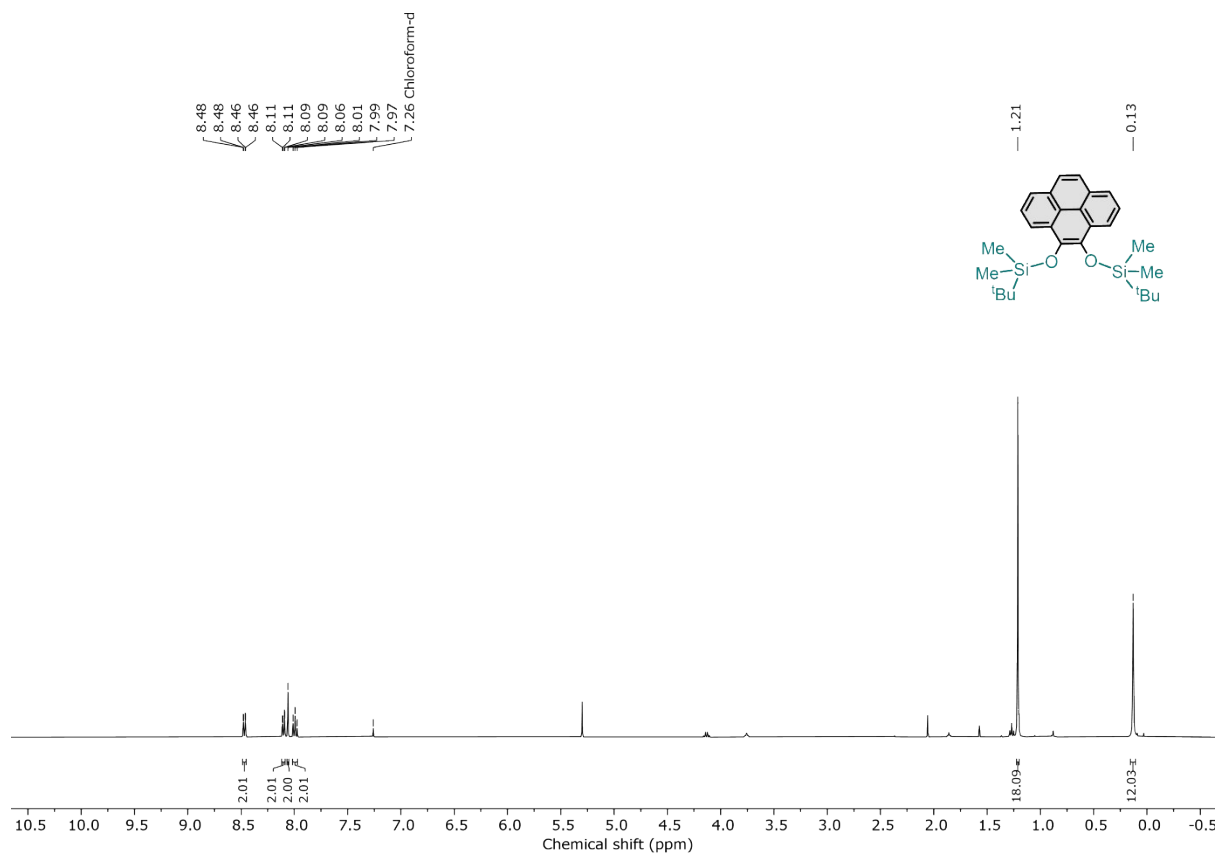
*Appearance*: Light yellow powder

*Eluent*: 1:49 mixture of EtOAc and hexane

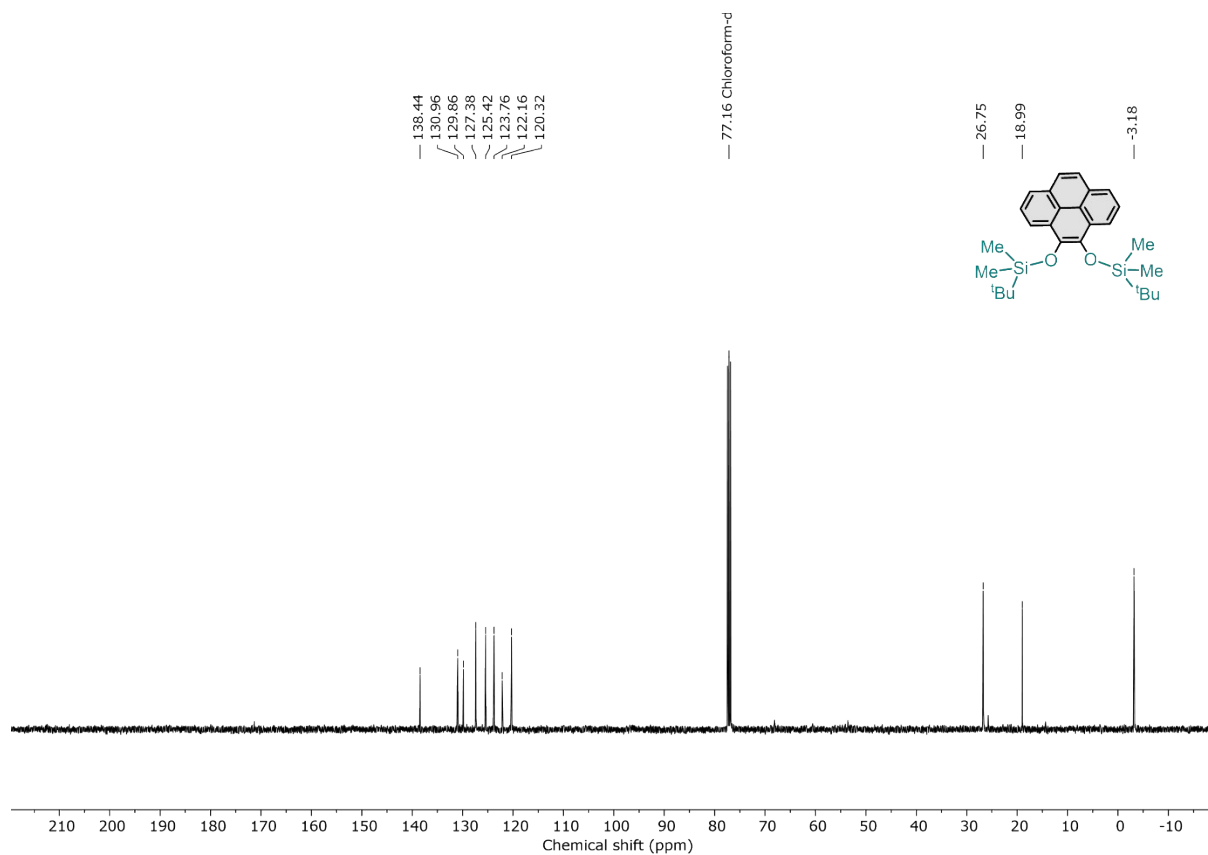
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.47 (dd, *J* = 7.9, 1.2 Hz, 2H), 8.10 (dd, *J* = 7.6, 1.1 Hz, 2H), 8.06 (s, 2H), 7.99 (t, *J* = 7.7 Hz, 2H), 1.21 (s, 18H), 0.13 (s, 12H) ppm.

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 138.4, 131.0, 129.9, 127.4, 125.4, 123.8, 122.2, 120.3, 26.8, 19.0, -3.18 ppm.





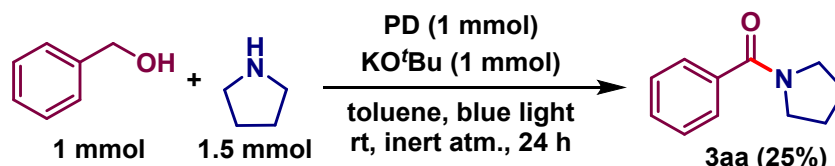
**Figure 3:**  $^1\text{H}$  NMR spectrum of 4,5-bis(*tert*-butyldimethylsiloxy)-pyrene in  $\text{CDCl}_3$ .



**Figure 4:**  $^{13}\text{C}$  NMR spectrum of 4,5-bis(*tert*-butyldimethylsiloxy)-pyrene in  $\text{CDCl}_3$ .

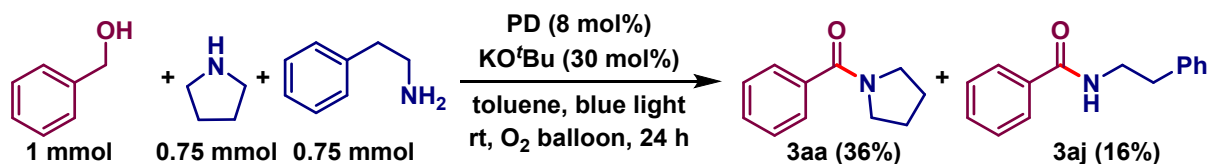
**d) Formation of amide in the absence of O<sub>2</sub>:**

A 25 mL Schlenk flask was charged with PD (1 mmol), KO<sup>t</sup>Bu (1 mmol), benzyl alcohol (1 mmol) and pyrrolidine (1.5 mmol) in 10 mL dry toluene under inert condition. The reaction mixture was stirred for 24 h under blue LED light. Upon completion, the reaction mixture was concentrated in vacuo and the residue was purified by column chromatography using hexane:ethyl acetate as eluent to afford the pure product **3aa**.



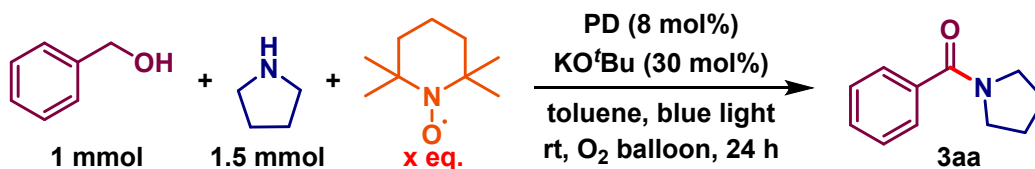
**e) Intermolecular competition reaction:**

A 20 mL vial tube was charged with 8 mol% of PD, 1 mmol of benzyl alcohol, 0.75 mmol of pyrrolidine, 0.75 mmol of 2-phenylethanamine and 30 mol% of KO<sup>t</sup>Bu in 2 mL toluene. The reaction mixture was allowed to stir under blue light irradiation for 24 h under O<sub>2</sub>-filled balloon. Upon completion, the reaction was concentrated in vacuo and the residue was purified by column chromatography using hexane:ethyl acetate as eluent to afford the pure products (**3aa** and **3aj**).



**f) Procedure for radical quenching experiment:**

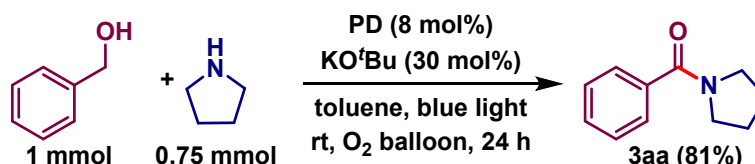
In a typical reaction, 20 mL vial was charged with PD (8 mol%), KO<sup>t</sup>Bu (30 mol%), benzyl alcohol (1 mmol), pyrrolidine (1.5 mmol) and varying equivalents of TEMPO dissolved in 2 mL toluene. The reaction mixture was stirred for 24 h under blue LED light, under O<sub>2</sub> balloon keeping the identical conditions to optimized protocol. The yield of the reaction decreased drastically with the addition of TEMPO, as probed by GC-MS analysis.



Entry	Amounts of TEMPO added (eq.)	Yield (%)
1	0.5	8%
2	1	n.r.

**g) Experiment with a new stirring bead and new reaction flask**

In a typical reaction, 20 mL vial was charged with PD (8 mol%), KO<sup>t</sup>Bu (30 mol%), benzyl alcohol (1 mmol), pyrrolidine (1.5 mmol) dissolved in 2 mL toluene. The reaction was performed in a new flask with a fresh magnetic bead. The reaction flask was kept under an oxygen-filled balloon. The reaction mixture was stirred for 24 h under blue LED light. The desired product **3aa** was formed in 81% yield.

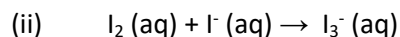
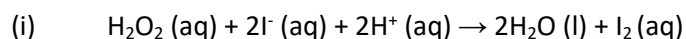


**h) Gram-scale synthesis of 3aa**

In a typical reaction, a 100 mL round bottomed flask was charged with PD (8 mol%), KO<sup>t</sup>Bu (30 mol%), alcohol (7 mmol), amine (10.5 mmol) in 10 mL toluene. The reaction mixture was allowed to stir under eplite 50 W blue LED (455 nm) and the reaction tube was kept 7-8 cm away from the light source. The reaction flask was placed under an oxygen-filled balloon and stirred for 24 h. After completion of the reaction, the reaction mixture was concentrated *in vacuo*. The desired product **3aa** was formed in 48% yield.

## 7. Detection of H<sub>2</sub>O<sub>2</sub> produced during the reaction

In the case of amide formation, the appearance of H<sub>2</sub>O<sub>2</sub> in the reaction mixture was analyzed by UV-vis spectroscopy using the iodometric assay based on the peak of I<sub>3</sub><sup>-</sup> at λ<sub>max</sub> around 350 nm (ε = 26000 M<sup>-1</sup>cm<sup>-1</sup>) upon reaction with KI. A 20 mL glass vial was charged with 4-methoxybenzyl alcohol (1 mmol), pyrrolidine (1.5 mmol), KO<sup>t</sup>Bu (30 mol%), PD (8 mol%) in 2 mL dry toluene and was closed with rubber septum. The resulting solution was kept under oxygen-filled balloon. The reaction mixture was allowed to stir for 12 h under blue LED light. The reaction mixture was then extracted in 10 mL of water and a few drops of dilute H<sub>2</sub>SO<sub>4</sub> (pH = 2) were added to stop further oxidation. After that, 1 mL of a 10% solution of KI and 2-3 drops of a 3% solution of ammonium molybdate was added. The produced H<sub>2</sub>O<sub>2</sub> oxidizes I<sup>-</sup> to I<sub>2</sub>, which reacts with an excess of I<sup>-</sup> to form I<sub>3</sub><sup>-</sup>. The chemical reactions are as follows<sup>6,7</sup>:



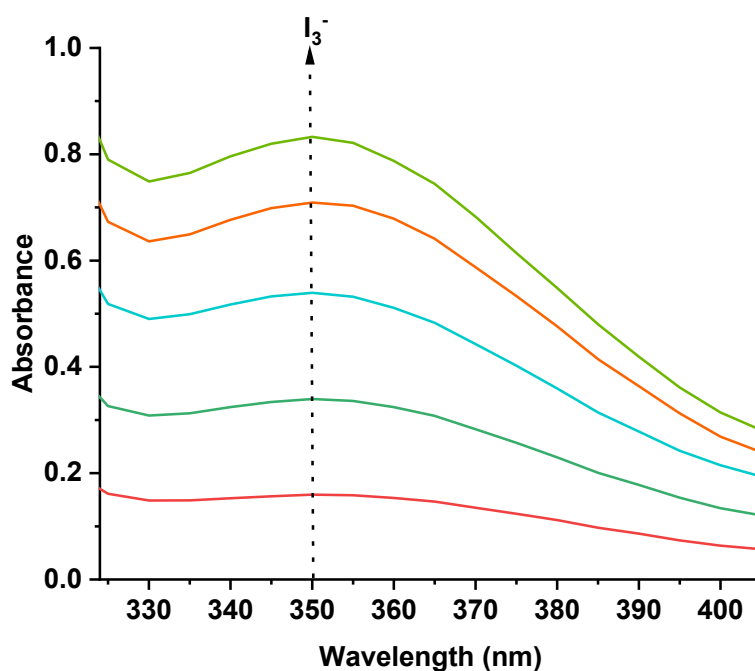


Figure 5: UV-Visible spectrum of  $I_3^-$  ion formation in the presence of  $H_2O_2$ .

### 8. Greenness of the reaction

Following the guidelines of green chemistry-

- Our used solvent is toluene which is an acceptable solvent.
- We used simple organic molecule as a catalyst which is under green flag.
- After reaction completion we only need to evaporate the reaction mixture which is under green flag.
- We are doing room temperature photochemical reaction which is also under green flag.

### Atom Economy (AE) - (*Chem. Soc. Rev.*, 2012, **41**, 1437-1451)

Atom economy of the reaction was calculated as the percentage of reactants converted into products.

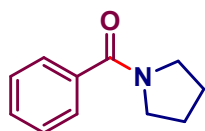
$$\begin{aligned}
 AE &= \frac{\text{Molecular weight of product}}{\text{Total molecular weight of reactants}} \times 100 \\
 &= \frac{175.23}{108.14 + 71.12} \times 100 \\
 &= \frac{175.23}{179.26} \times 100 \\
 &= 97.75
 \end{aligned}$$

### Reaction Mass Efficiency (RME) -

Reaction Mass Efficiency measures the efficiency with which reactant mass ends up in the desired product, usually expressed as a percentage. It takes into account both atom economy and chemical yield. (Yield of product **3aa** is 81%)

$$\begin{aligned} RME &= \frac{\text{Mass of isolated product}}{\text{Total mass of reactants}} \times 100 \\ &= \frac{141.93}{108.14 + 106.68} \times 100 \\ &= \frac{141.93}{214.82} \times 100 \\ &= 66.06 \end{aligned}$$

### 9. Analytical data for synthesized products



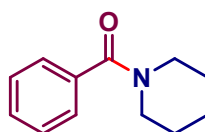
#### Phenyl(pyrrolidin-1-yl)methanone (**3aa**)<sup>8</sup>:

**Appearance:** Colorless oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.46 – 7.41 (m, 2H), 7.35 – 7.29 (m, 3H), 3.57 (t, *J* = 7.0 Hz, 2H), 3.34 (t, *J* = 6.6 Hz, 2H), 1.93 – 1.83 (m, 2H), 1.82 – 1.73 (m, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.6, 137.1, 129.7, 128.1, 126.9, 49.5, 46.1, 26.3, 24.3 ppm.



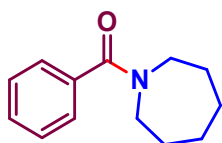
#### Phenyl(1-piperidinyl)methanone(**3ab**)<sup>8</sup>:

**Appearance:** Colorless oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.30 (dd, *J* = 3.2, 2.1 Hz, 5H), 3.63 (brs, 2H), 3.25 (brs, 2H), 1.58 (brs, 4H), 1.42 (brs, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 170.1, 136.3, 129.2, 128.2, 126.6, 48.6, 42.9, 26.4, 25.5, 24.4 ppm.



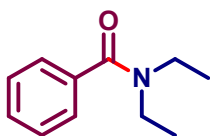
**Azepan-1-yl(phenyl)methanone(3ac)<sup>9</sup>:**

**Appearance:** Pale yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.35 – 7.31 (m, 5H), 3.63 (t, *J* = 5.9 Hz, 2H), 3.31 (t, *J* = 5.6 Hz, 2H), 1.79 (p, *J* = 5.9 Hz, 2H), 1.60 – 1.53 (m, 6H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 171.5, 137.5, 129.0, 128.3, 126.4, 49.7, 46.2, 29.4, 27.8, 27.2, 26.4 ppm.



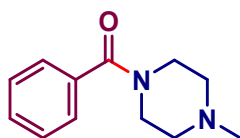
**N,N-Diethylbenzamide (3ad)<sup>10</sup>:**

**Appearance:** Brown oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.31 (s, 5H), 3.48 (brs, 2H), 3.18 (brs, 2H), 1.18 (s, 3H), 1.03 (s, 3H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 171.2, 137.2, 129.0, 128.3, 126.1, 43.2, 39.1, 14.1, 12.8 ppm.



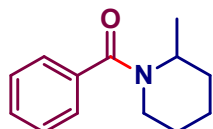
**1-Benzoyl-4-methylpiperazine(3ae)<sup>9</sup>:**

**Appearance:** Pale yellow oil

**Eluent:** 1:5 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.39 (s, 5H), 3.79 (br s, 2H), 3.43 (br s, 2H), 2.48 (br s, 2H), 2.30 (br s, 5H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 170.5, 135.9, 130.0, 128.6, 127.1, 55.4, 54.8, 47.7, 46.2, 42.1 ppm.



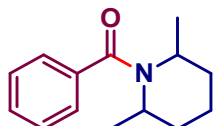
**(2-Methylpiperidin-1-yl)(phenyl)methanone(3af)<sup>11</sup>:**

**Appearance:** Colorless powder

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.36-7.35 (m, 5H), 5.07-3.45 (m, 2H), 2.97 (brs, 1H), 1.70-1.42 (m, 6H), 1.22 (d, *J* = 6.9 Hz, 3H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 170.0, 136.6, 128.7, 128.0, 125.9, 29.9, 25.6, 18.5, 15.7 ppm.



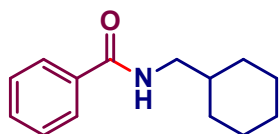
**(2,6-Dimethylpiperidin-1-yl)(phenyl)methanone(3ag)<sup>12</sup>:**

**Appearance:** White solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.32 – 7.29 (m, 3H), 7.28 – 7.26 (m, 2H), 4.38 (s, 2H), 1.84 – 1.74 (m, 1H), 1.65 – 1.56 (m, 2H), 1.51 – 1.43 (m, 3H), 1.20 (d, *J* = 6.3 Hz, 6H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 171.0, 137.5, 128.3, 128.1, 125.5, 29.8, 20.8, 13.8 ppm.



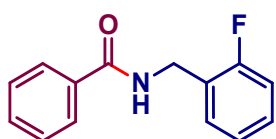
***N*-(Cyclohexylmethyl)benzamide (3ah)<sup>13</sup>:**

**Appearance:** White solid

**Eluent:** 1:4 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.78–7.75 (m, 2H), 7.45 – 7.40 (m, 1H), 7.37 – 7.32 (m, 2H), 6.78 (s, 1H), 3.23 (t, *J* = 1.7 Hz, 2H), 1.74 – 1.61 (m, 5H), 1.58– 1.49 (m, 1H), 1.23–1.09 (m, 3H), 0.97 – 0.87 (m, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.7, 134.9, 131.2, 128.4, 127.0, 46.2, 38.0, 30.9, 26.4, 25.8 ppm.



***N*-(2-Fluorobenzyl)benzamide (3ai)<sup>10</sup>:**

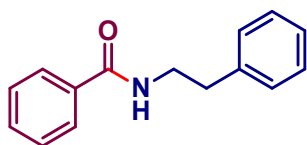
**Appearance:** White solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.81 (d, *J* = 7.0 Hz, 2H), 7.49 – 7.39 (m, 1H), 7.30 (t, *J* = 7.0 Hz, 3H), 7.24 – 7.14 (m, 1H), 7.06 – 6.91 (m, 2H), 4.59 (d, *J* = 6.1 Hz, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.8, 161.8 (d, *J*<sub>C-F</sub> = 243 Hz), 133.9, 131.2, 129.5, 128.8 (d, *J*<sub>C-F</sub> = 8 Hz), 128.2, 127.1, 125.3 (d, *J*<sub>C-F</sub> = 14 Hz), 124.0 (d, *J*<sub>C-F</sub> = 4 Hz), 115.1 (d, *J*<sub>C-F</sub> = 21 Hz), 37.4 (d, *J*<sub>C-F</sub> = 4 Hz) ppm.

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -118.8



***N*-Phenethylbenzamide (3aj)<sup>14</sup>:**

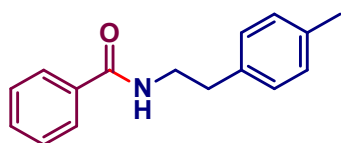
**Appearance:** Colorless solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.70 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.32 (t, *J* = 1.1 Hz, 2H), 7.24 (t, *J* = 1.3 Hz, 3H), 6.36 (s, 1H), 3.70 (td, *J* = 7.0, 5.8 Hz, 2H), 2.93 (t, *J* = 7.0 Hz, 2H) ppm.



$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.6, 139.0, 134.7, 131.4, 128.9, 128.8, 128.6, 126.9, 126.7, 41.3, 35.8 ppm.



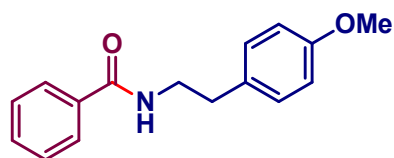
**N-(4-Methylphenethyl)benzamide (3ak)<sup>15</sup>:**

**Appearance:** Pale white powder

**Eluent:** 1:3 mixture of EtOAc and hexane

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.73 (d,  $J = 7.2$  Hz, 2H), 7.47 (t,  $J = 7.3$  Hz, 1H), 7.38 (t,  $J = 1.2$  Hz, 2H), 7.12 (s, 4H), 6.58 (s, 1H), 3.68 (q,  $J = 5.8$  Hz, 2H), 2.88 (t,  $J = 7.1$  Hz, 2H), 2.34 (s, 3H) ppm.

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.6, 136.1, 135.8, 134.7, 131.4, 129.4, 128.7, 128.5, 126.9, 41.3, 35.3, 21.1 ppm.



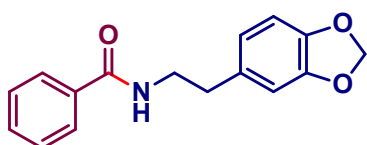
**N-(4-Methoxyphenethyl)benzamide (3al)<sup>16</sup>:**

**Appearance:** Off white solid

**Eluent:** 1:3 mixture of EtOAc and hexane

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.70 (d,  $J = 7.2$  Hz, 2H), 7.48 (tt,  $J = 7.3, 1.4$  Hz, 1H), 7.40 (t,  $J = 7.6$  Hz, 2H), 7.15 (d,  $J = 8.5$  Hz, 2H), 6.86 (d,  $J = 8.7$  Hz, 2H), 6.24 (s, 1H), 3.79 (s, 3H) 3.70–3.65 (m, 2H), 2.87 (t,  $J = 6.9$  Hz, 2H) ppm.

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.6, 158.4, 134.8, 131.5, 131.0, 129.9, 128.7, 126.9, 114.2, 55.4, 41.4, 34.9 ppm.



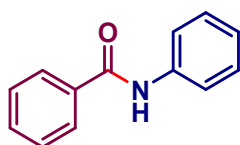
**N-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)benzamide (3am)<sup>17</sup>:**

**Appearance:** White solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.70 (d, *J* = 7.0 Hz, 2H), 7.48 (t, *J* = 7.0 Hz, 1H), 7.40 (t, *J* = 7 Hz, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 1.7 Hz, 1H), 6.66 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.29 (brs, 1H), 5.93 (s, 2H), 3.65 (q, *J* = 5.8 Hz, 2H), 2.83 (t, *J* = 6.9 Hz, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.6, 148.0, 146.3, 134.7, 132.7, 131.5, 128.7, 126.9, 121.8, 109.2, 108.5, 101.0, 41.4, 35.5 ppm.



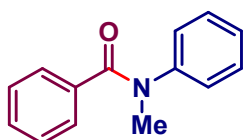
**N-Phenylbenzamide (3an)<sup>11</sup>:**

**Appearance:** White solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.91 – 7.84 (m, 3H), 7.67 – 7.63 (m, 2H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.49 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.37 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.16 (s, 1H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 165.9, 138.0, 135.1, 132.0, 129.3, 128.9, 127.1, 124.7, 120.3 ppm.



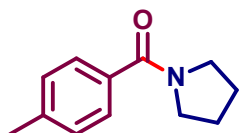
**N-Methyl-N-phenylbenzamide (3ao)<sup>11</sup>:**

**Appearance:** Pale yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.27 (d, *J* = 6.9 Hz, 2H), 7.18-7.13 (m, 3H), 7.11-7.04 (m, 3H), 6.99 (d, *J* = 7.1 Hz, 2H), 3.44 (s, 3H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 170.4, 144.6, 135.7, 129.4, 128.9, 128.5, 127.5, 126.7, 126.3, 38.2 ppm.



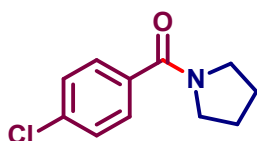
**Pyrrolidin-1-yl(p-tolyl)methanone (3ba)<sup>18</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>):** δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 3.64 (t, *J* = 7.0 Hz, 2H), 3.44 (t, *J* = 6.6 Hz, 2H), 2.37 (s, 3H), 1.99 – 1.91 (m, 2H), 1.89 – 1.83 (m, 2H).

**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>):** δ 170.0, 143.9, 134.3, 130.2, 129.2, 128.9, 127.3, 49.8, 46.4, 29.8, 26.5, 24.6, 21.5 ppm.



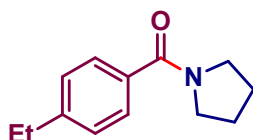
**(4-Chlorophenyl)(pyrrolidin-1-yl)methanone (3ca)<sup>19</sup>:**

**Appearance:** Colorless oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>):** δ 7.37 – 7.29 (m, 2H), 7.24 – 7.20 (m, 2H), 3.47 (t, *J* = 6.9 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 1.84 – 1.76 (m, 2H), 1.73 (q, *J* = 6.5, 5.9 Hz, 2H).

**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>):** δ 168.6, 135.8, 135.5, 128.7, 128.5, 49.6, 46.3, 26.4, 24.4 ppm.



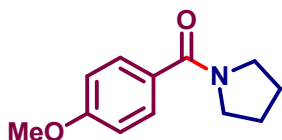
**(4-Ethylphenyl)(pyrrolidin-1-yl)methanone (3da)<sup>20</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.43 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 3.62 (t, *J* = 7.0 Hz, 2H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.95-1.90 (m, 2H), 1.88-1.83 (m, 2H), 1.22 (t, *J* = 7.6 Hz, 3H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.9, 146.3, 134.6, 127.7, 127.4, 49.8, 46.3, 28.8, 26.5, 24.6, 15.5 ppm.



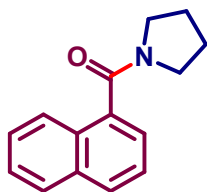
**(4-Methoxyphenyl)(pyrrolidin-1-yl)methanone (3ea)<sup>21</sup>:**

**Appearance:** Colorless oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>):** δ 7.47-7.51 (m, 2H), 6.89-6.85 (m, 2H), 3.80 (s, 3H), 3.61 (t, *J* = 6.9 Hz, 2H), 3.45 (t, *J* = 6.5 Hz, 2H), 1.96-1.89 (m, 2H), 1.87-1.81 (m, 2H) ppm.

**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>):** δ 169.5, 160.8, 129.4, 129.2, 113.5, 55.4, 49.9, 46.4, 26.6, 24.5 ppm.



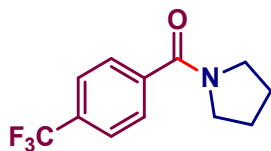
**Naphthalen-1-yl(pyrrolidin-1-yl)methanone (3fa)<sup>22</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.89–7.83 (m, 3H), 7.54 – 7.43 (m, 4H), 3.79 (t, *J* = 7.1 Hz, 2H), 3.11 (t, *J* = 6.8 Hz, 2H), 2.01 – 1.97 (m, 2H), 1.85 – 1.78 (m, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.3, 135.9, 133.6, 129.3, 129.2, 128.5, 127.0, 126.4, 125.3, 125.0, 123.8, 48.6, 45.7, 26.1, 24.7 ppm.



**Pyrrolidin-1-yl(4-(trifluoromethyl)phenyl)methanone (3ga)<sup>22</sup>:**

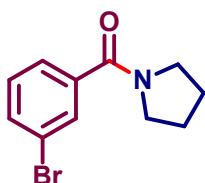
**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.70 – 7.59 (m, 4H), 3.66 (t, *J* = 7.0 Hz, 2H), 3.39 (t, *J* = 6.6 Hz, 2H), 2.02 – 1.95 (m, 2H), 1.93 – 1.86 (m, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 168.4, 140.8, 131.8 (q, *J*<sub>C-F</sub> = 33 Hz), 127.6, 125.5 (q, *J*<sub>C-F</sub> = 4 Hz), 122.4 (t, *J*<sub>C-F</sub> = 270 Hz), 49.6, 46.4, 26.5, 24.5 ppm.

**<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):** δ -62.9



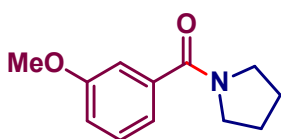
**(3-Bromophenyl)(pyrrolidin-1-yl)methanone (3ha)<sup>23</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.62 (t, *J* = 1.5 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.42 – 7.39 (m, 1H), 7.26 – 7.24 (m, 1H), 3.60 (t, *J* = 6.9 Hz, 2H), 3.38 (t, *J* = 6.6 Hz, 2H), 1.95 – 1.84 (m, 4H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 168.0, 139.2, 132.9, 130.2, 130.0, 125.7, 122.4, 49.6, 46.3, 26.4, 24.5 ppm.



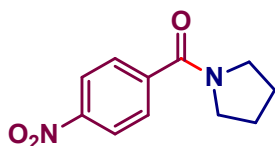
**(3-Methoxyphenyl)(pyrrolidin-1-yl)methanone (3ia)<sup>24</sup>:**

**Appearance:** Colorless oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.28 (t, *J* = 7.9 Hz, 1H), 7.07-7.03 (m, 2H), 6.94 (m, 1H), 3.80 (s, 3H), 3.62 (t, *J* = 6.8 Hz, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 1.96-1.92 (m, 2H), 1.86-1.83 (m, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.5, 159.4, 138.4, 129.3, 119.2, 115.7, 112.3, 55.3, 55.3, 49.6, 46.1, 26.3, 24.4 ppm.



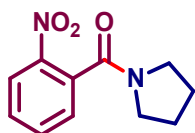
**(4-Nitrophenyl)(pyrrolidin-1-yl)methanone (3ja)<sup>25</sup>:**

**Appearance:** Yellow solid

**Eluent:** 1:6 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.21 – 8.18 (m, 2H), 7.64 – 7.61 (m, 2H), 3.59 (t, *J* = 3.5 Hz, 1H), 3.32 (t, *J* = 1.7 Hz, 1H), 1.95 – 1.84 (m, 4H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.3, 148.3, 143.1, 128.1, 123.6, 49.4, 46.3, 26.3, 24.3 ppm.



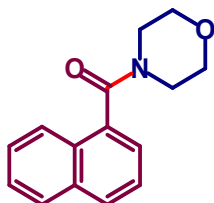
**(2-Nitrophenyl)(pyrrolidin-1-yl)methanone (3ka)<sup>26</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>):** δ 8.15 (d, *J* = 8.3 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 3.68 (t, *J* = 6.9 Hz, 2H), 3.12 (t, *J* = 6.7 Hz, 2H), 2.01-1.94 (m, 2H), 1.92-1.85 (m, 2H) ppm.

**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>):** δ 166.4, 145.0, 134.6, 134.1, 129.8, 128.2, 124.7, 48.3, 45.9, 25.9, 24.6 ppm.



**Morpholino(naphthalen-1-yl)methanone (3fp)<sup>27</sup>:**

**Appearance:** Brown oil

**Eluent:** 1:2 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.92 – 7.81 (m, 3H), 7.57 – 7.46 (m, 3H), 7.42 (d, *J* = 8.4 Hz, 1H), 4.03 (d, *J* = 17.7 Hz, 1H), 3.93 – 3.81 (m, 3H), 3.52 (s, 2H), 3.20 (t, *J* = 9.0 Hz, 2H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.6, 133.7, 133.6, 129.6, 129.5, 128.6, 127.3, 126.7, 125.3, 124.7, 124.0, 67.2, 67.1, 47.7, 42.3 ppm.



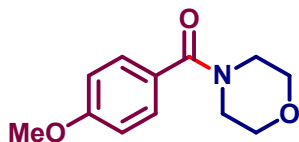
**(4-Chlorophenyl)(morpholino)methanone (3cp)<sup>27</sup>:**

**Appearance:** Light brown solid

**Eluent:** 1:2 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.38 (q, *J* = 8.7 Hz, 4H), 3.59 (d, *J* = 113.8 Hz, 8H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.5, 136.1, 133.7, 129.0, 128.8, 66.8, 48.5 ppm. Two aliphatic carbon resonances did not show up.



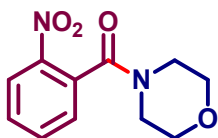
**(4-Methoxyphenyl)(morpholino)methanone (3ep)<sup>28</sup>:**

**Appearance:** Colorless liquid

**Eluent:** 1:1.5 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.40 – 7.35 (m, 2H), 6.93 – 6.88 (m, 2H), 3.83 (s, 3H), 3.74 – 3.57 (m, 8H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 170.6, 161.0, 129.3, 127.4, 113.9, 67.1, 55.5, 55.5, 29.1 ppm.



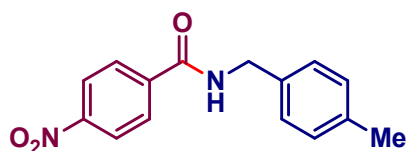
**Morpholino(2-nitrophenyl)methanone (3kp)<sup>29</sup>:**

**Appearance:** Pale orange oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.18 (d, *J* = 8.2 Hz, 1H), 7.71 (td, *J* = 7.5, 1.0 Hz, 1H), 7.57 (ddd, *J* = 8.8, 7.5, 1.5 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.2 Hz, 1H), 3.88-3.78 (m, 4H), 3.62-3.60 (m, 2H), 3.21 (t, *J* = 4.9 Hz, 2H) ppm.

**<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):** δ 166.7, 145.5, 134.7, 132.5, 130.1, 128.1, 124.9, 66.5, 66.4, 47.3, 42.3 ppm.



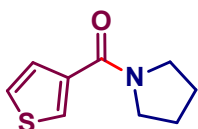
**N-(4-Methylbenzyl)-4-nitrobenzamide (3lq)<sup>30</sup>:**

**Appearance:** Yellow solid

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.67 (s, 1H), 4.59 (d, *J* = 5.6 Hz, 2H), 2.34 (s, 3H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 165.4, 149.7, 140.1, 137.8, 134.5, 129.7, 128.3, 128.1, 123.9, 44.3, 21.3 ppm.



**Pyrrolidin-1-yl(thiophen-3-yl)methanone (3pa)<sup>22</sup>:**

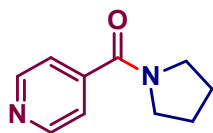
**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane



**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.66 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.37 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.30 (dd, *J* = 5.0, 2.9 Hz, 1H), 3.61 (dt, *J* = 16.0, 6.6 Hz, 4H), 1.97 – 1.90 (m, 4H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 164.6, 138.1, 127.4, 125.4, 49.5, 49.3, 46.7.



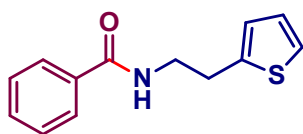
**Pyridin-4-yl(pyrrolidin-1-yl)methanone (3qa)<sup>22</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:2.5 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.59 – 8.58 (m, 2H), 7.29 – 7.28 (m, 2H), 3.53 (t, *J* = 6.9 Hz, 2H), 3.28 (t, *J* = 6.6 Hz, 2H), 1.91 – 1.77 (m, 4H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.0, 150.0, 144.4, 121.1, 49.1, 46.1, 26.2, 24.2 ppm.



**N-(2-(thiophen-2-yl)ethyl)benzamide (3ar)<sup>24</sup>:**

**Appearance:** White solid

**Eluent:** 1:4 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.77 – 7.75 (m, 2H), 7.47–7.43 (m, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.12 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.06 (s, 1H), 6.92 (dd, *J* = 5.2, 3.4 Hz, 1H), 6.82 (dd, *J* = 3.4, 1.2 Hz, 1H), 3.66 (q, *J* = 5.8 Hz, 2H), 3.11 (t, *J* = 6.7 Hz, 2H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 167.7, 141.3, 134.4, 131.3, 128.4, 127.0, 126.9, 125.3, 123.8, 41.4, 29.8 ppm.



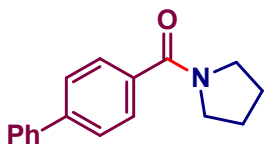
**(1-methyl-1H-pyrrol-2-yl)(pyrrolidin-1-yl)methanone (3ra)<sup>31</sup>:**

**Appearance:** Yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 6.68 (t, *J* = 2.1 Hz, 1H), 6.51 (dd, *J* = 3.9, 1.7 Hz, 1H), 6.08 (dd, *J* = 3.9, 2.6 Hz, 1H), 3.87 (s, 3H), 3.71 – 3.57 (m, 4H), 1.94 – 1.88 (m, 4H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 162.1, 126.8, 126.3, 113.6, 106.7, 49.7, 46.4, 36.7, 26.7, 24.3.



**[1,1'-biphenyl]-4-yl(pyrrolidin-1-yl)methanone (3sa)<sup>17</sup>:**

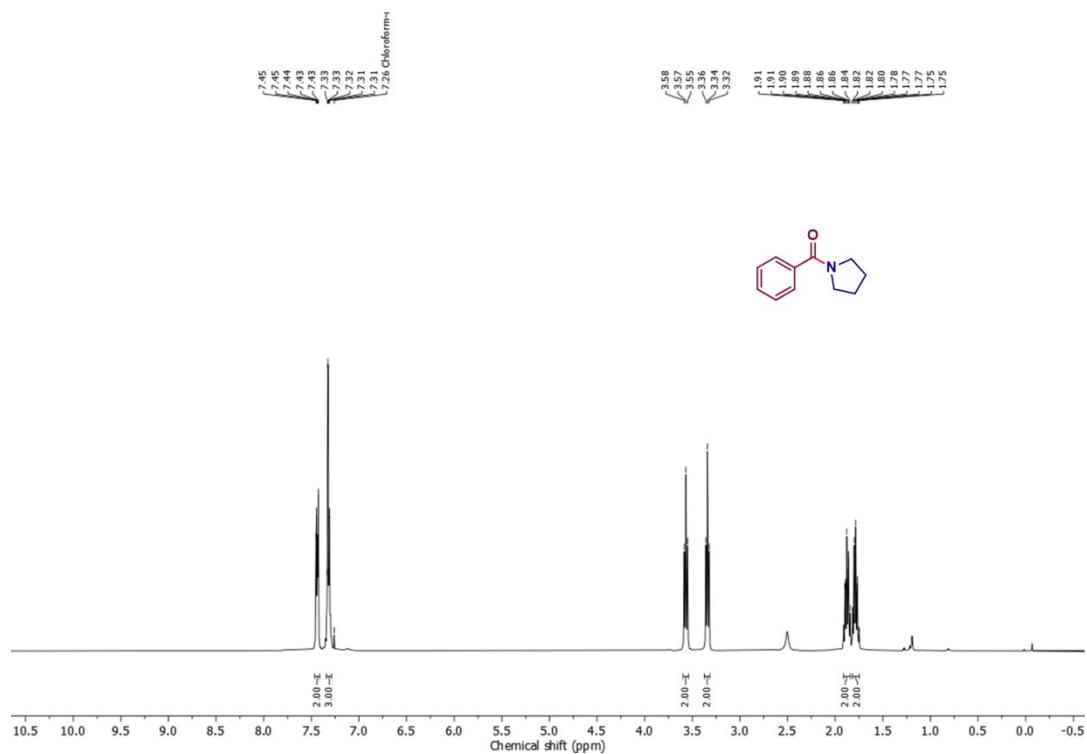
**Appearance:** Light yellow oil

**Eluent:** 1:3 mixture of EtOAc and hexane

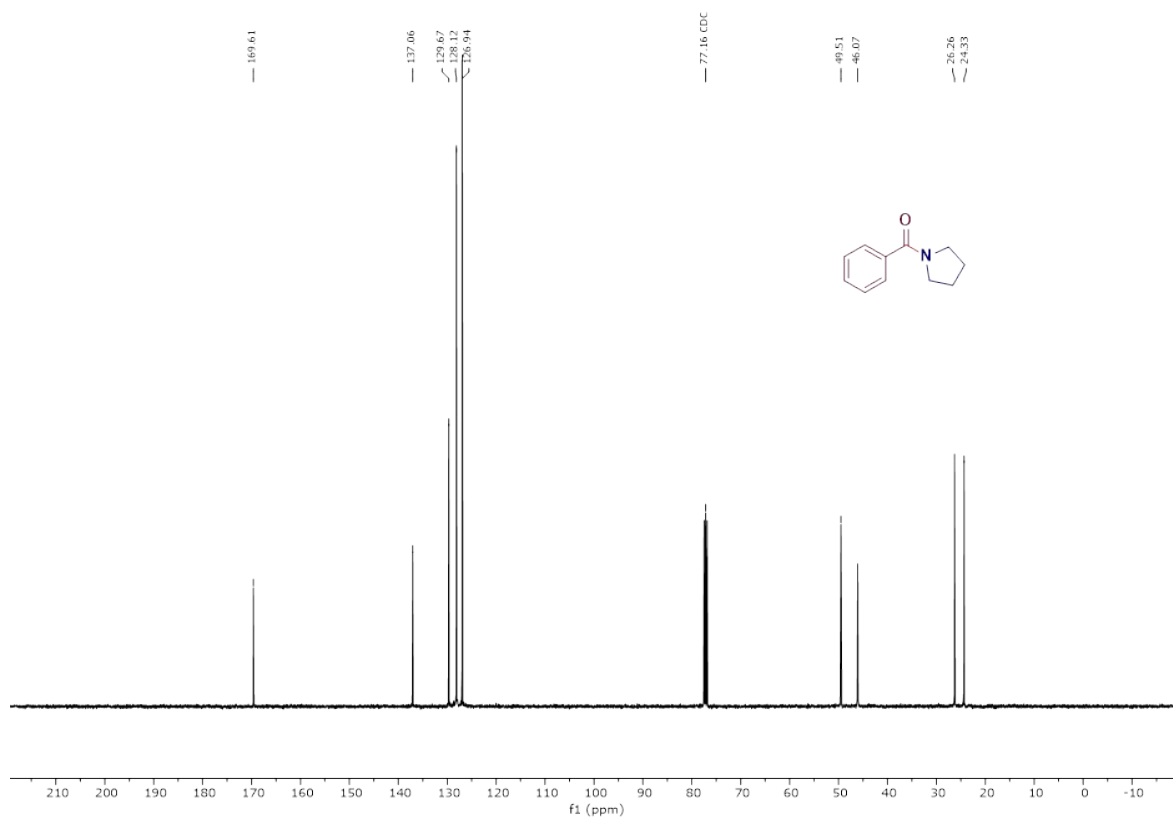
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 7.63–7.58 (m, 6H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 3.67 (t, *J* = 7.0 Hz, 2H), 3.49 (t, *J* = 6.6 Hz, 2H), 2.00–1.85 (m, 4H) ppm.

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ 169.6, 142.7, 140.4, 136.0, 129.0, 127.8, 127.8, 127.2, 127.0, 49.8, 46.4, 26.5, 24.6 ppm.

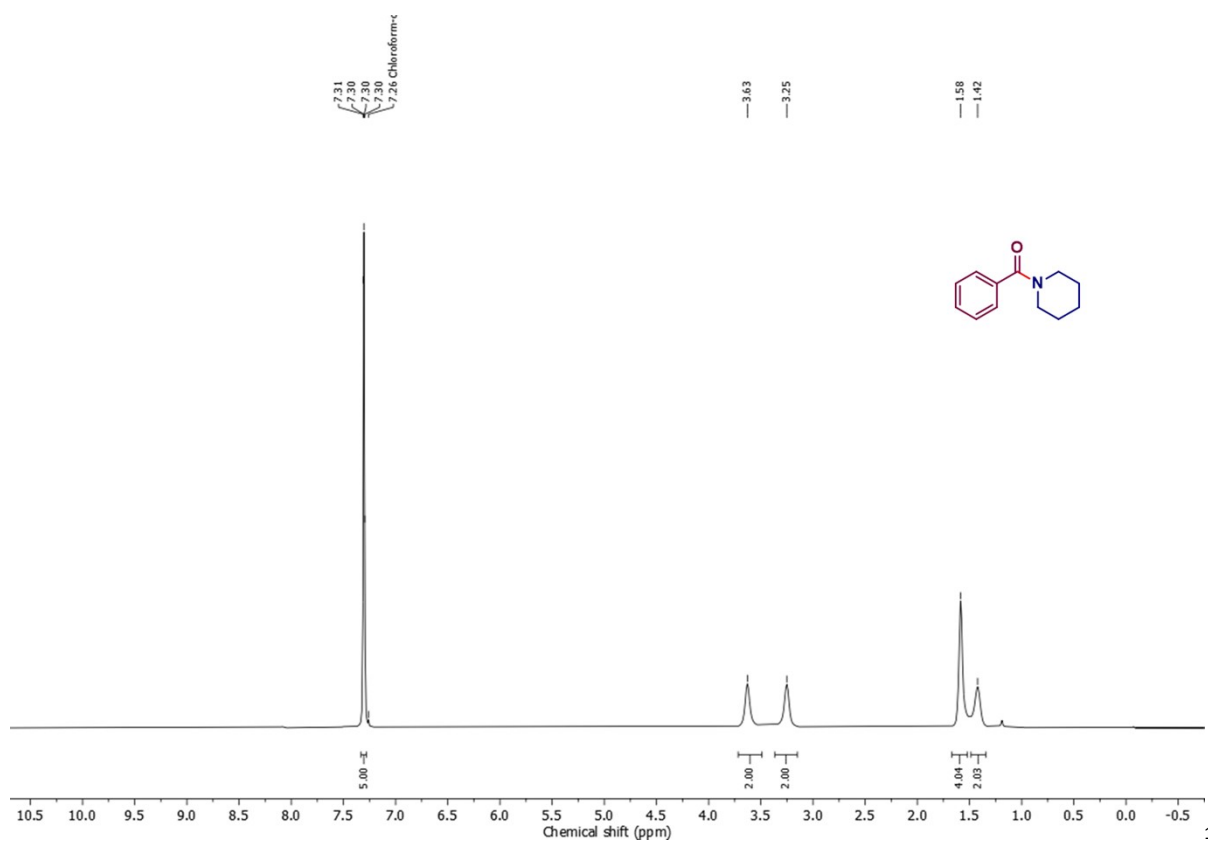
10.  $^1\text{H}$ ,  $^{13}\text{C}$  NMR spectra for synthesized compounds



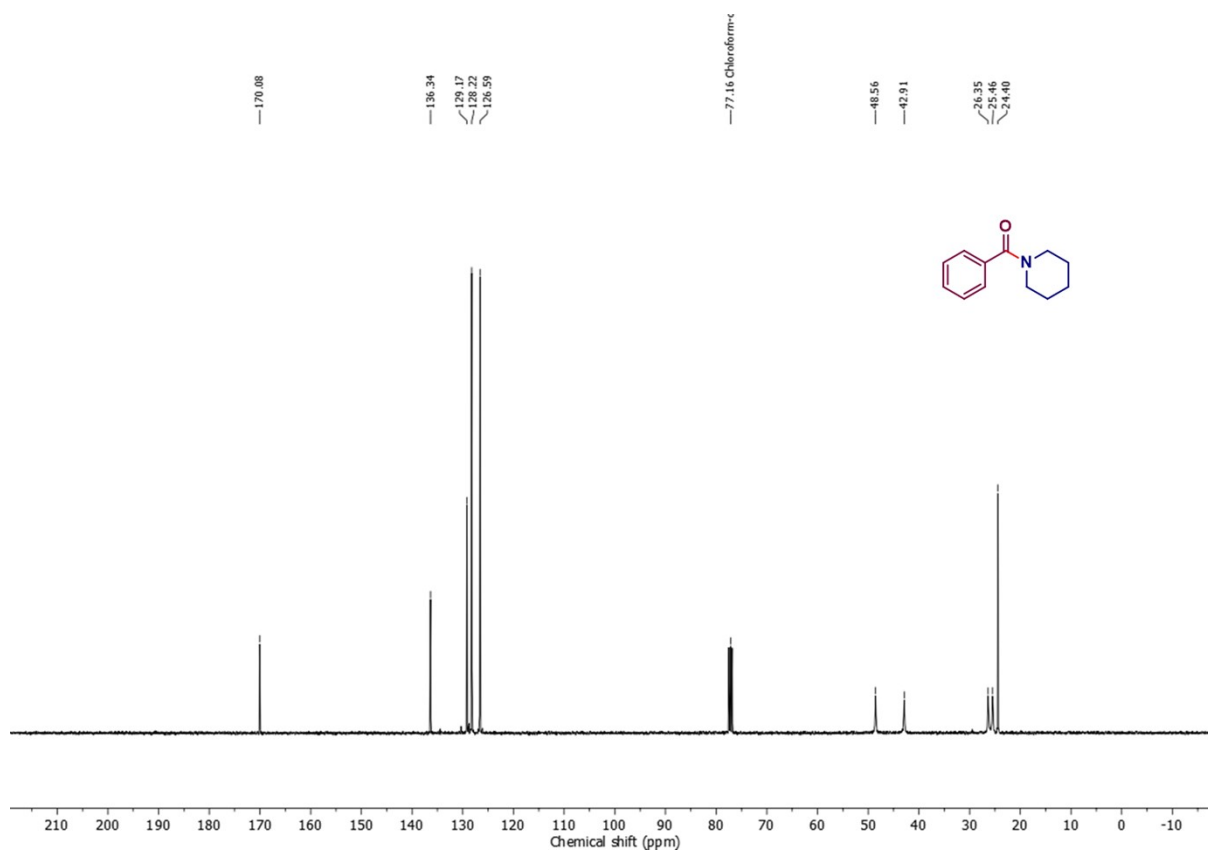
$^1\text{H}$  NMR spectrum (400 MHz) of **3aa** in  $\text{CDCl}_3$ .



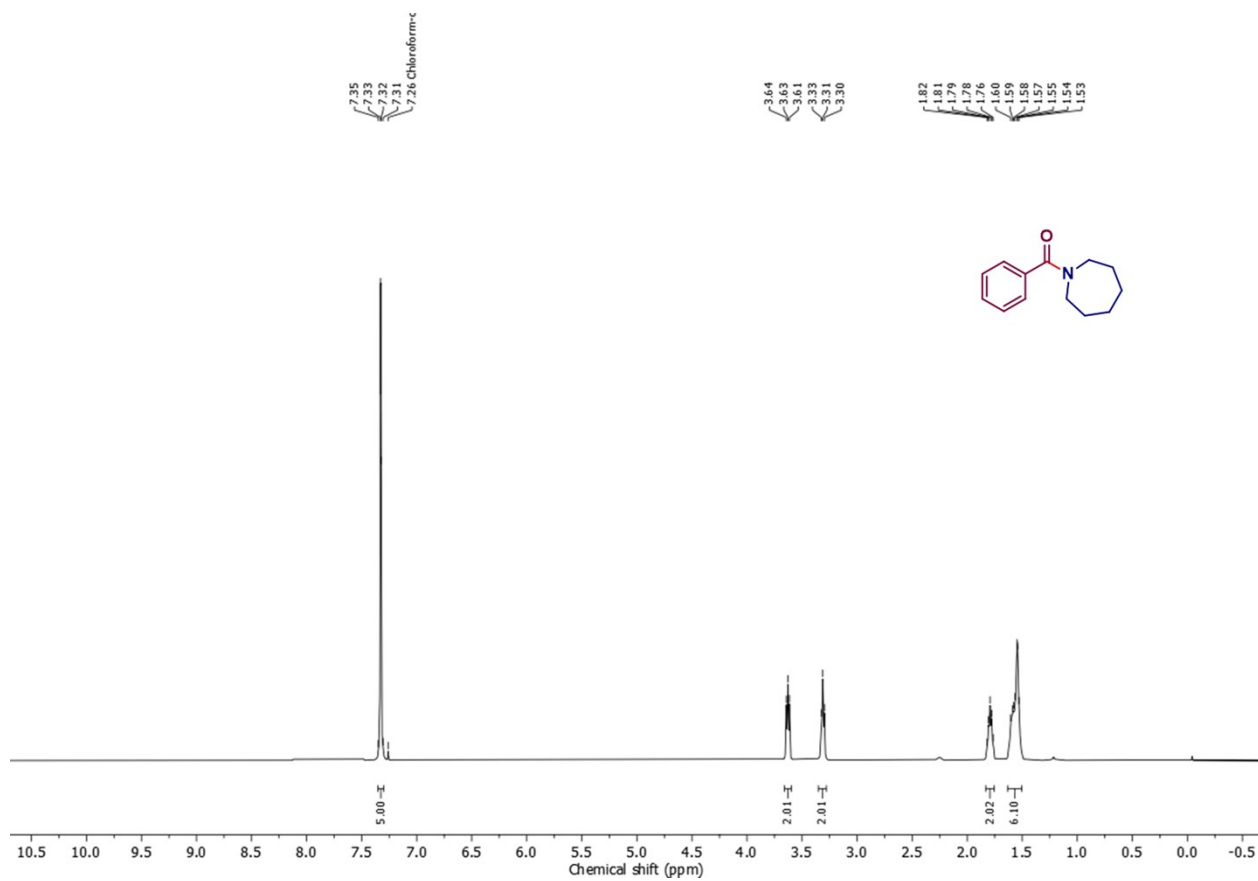
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3aa** in  $\text{CDCl}_3$ .



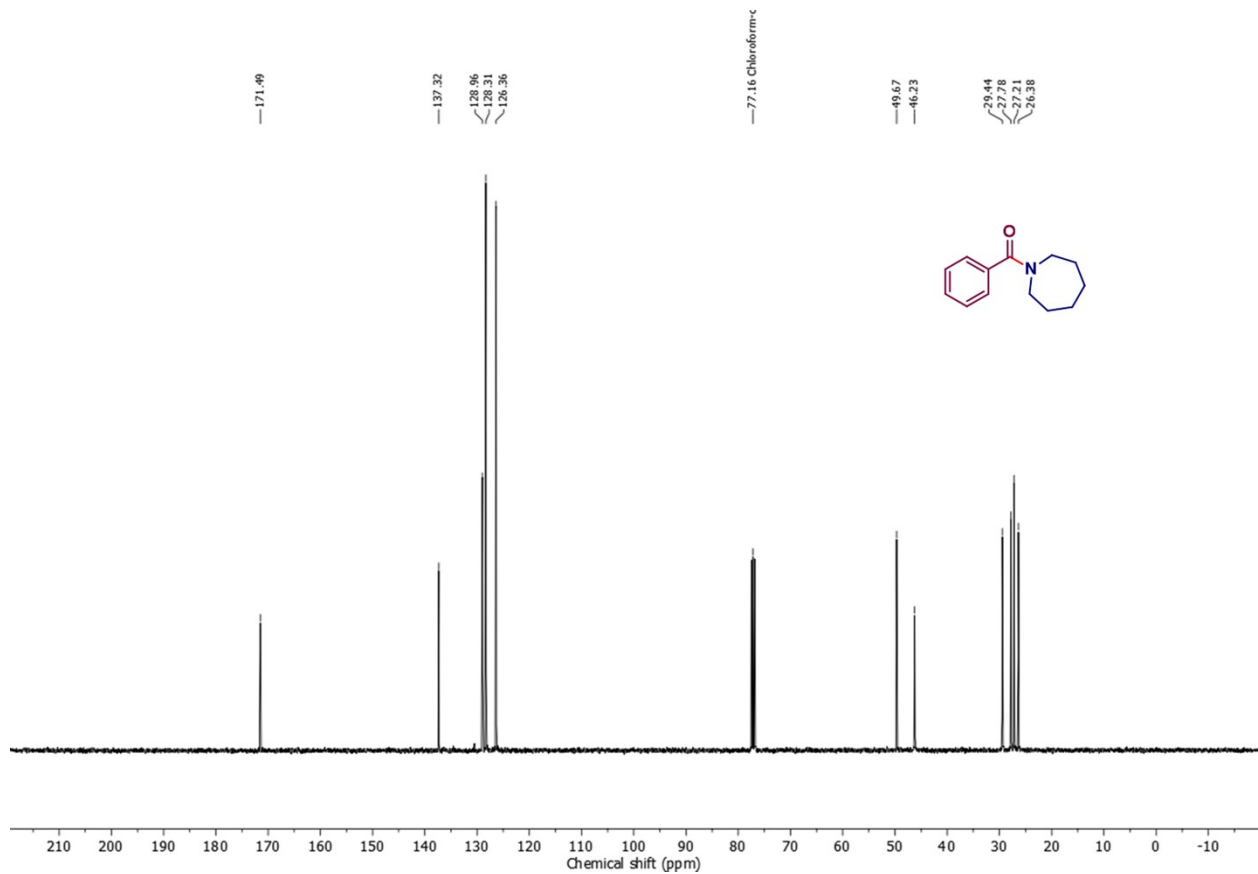
<sup>1</sup>H NMR spectrum (400 MHz) of **3ab** in CDCl<sub>3</sub>.



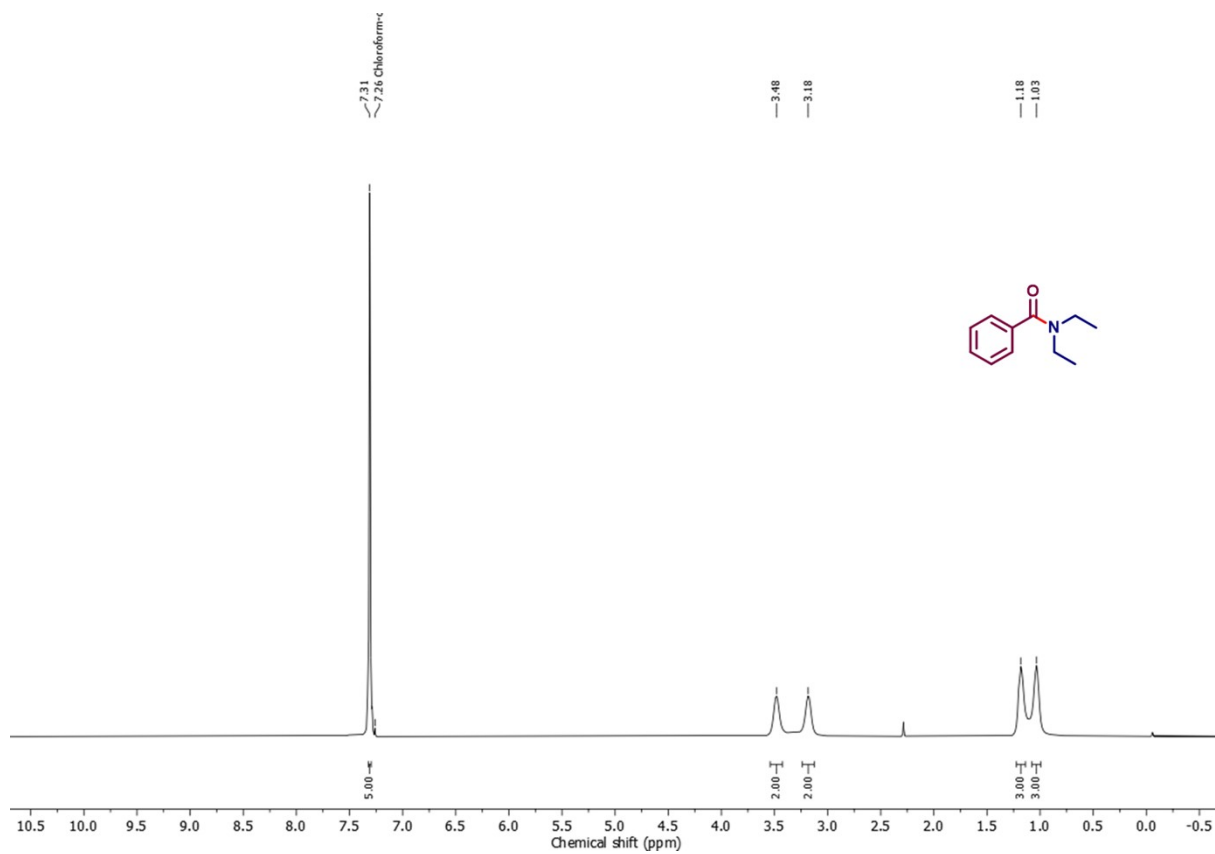
<sup>13</sup>C NMR spectrum (100 MHz) of **3ab** in CDCl<sub>3</sub>.



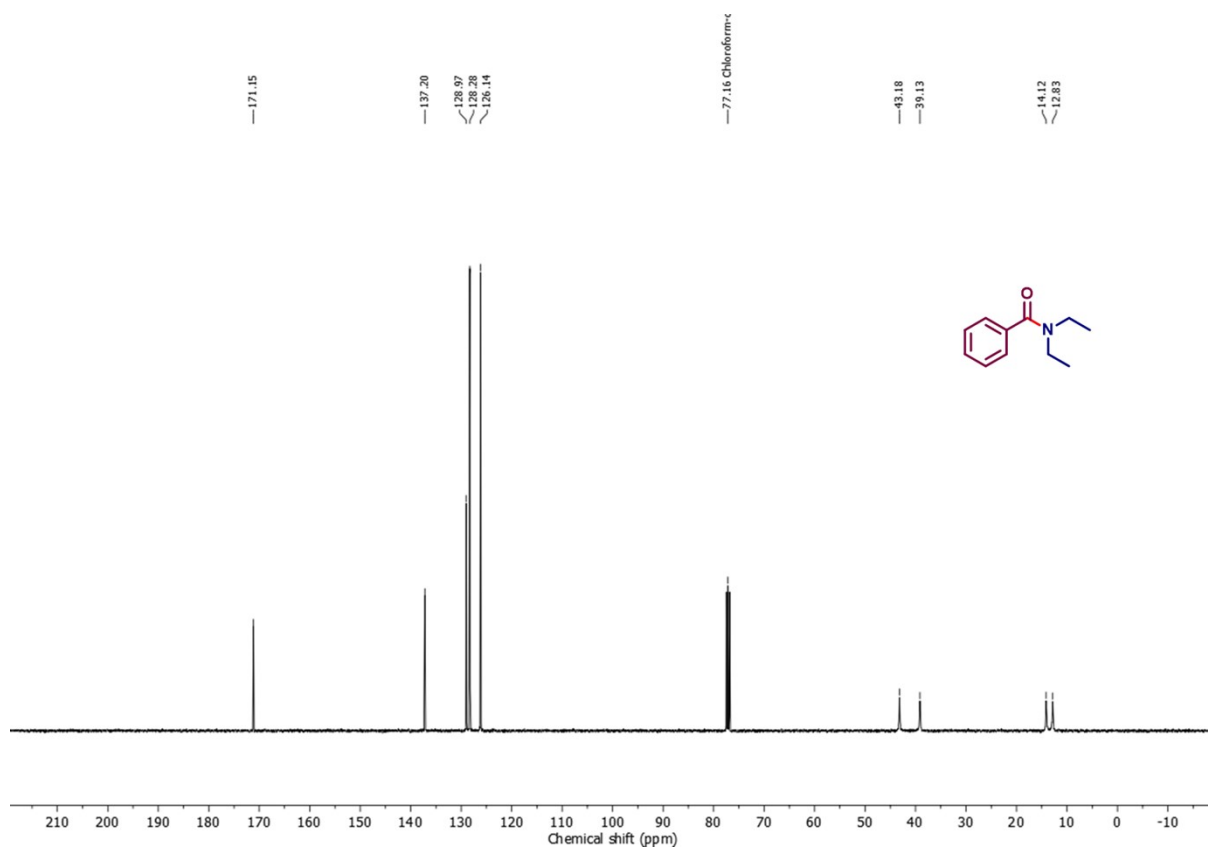
$^1\text{H}$  NMR spectrum (400 MHz) of **3ac** in  $\text{CDCl}_3$ .



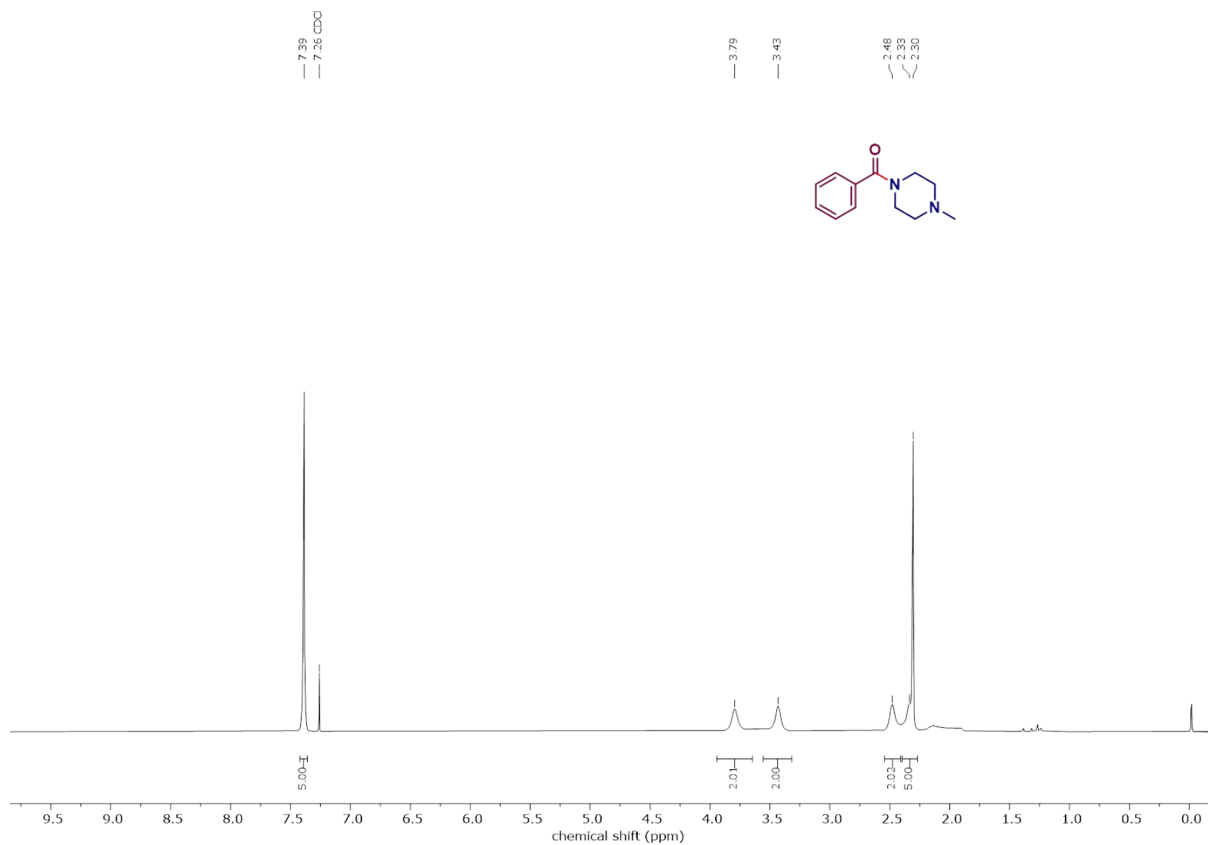
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ac** in  $\text{CDCl}_3$ .



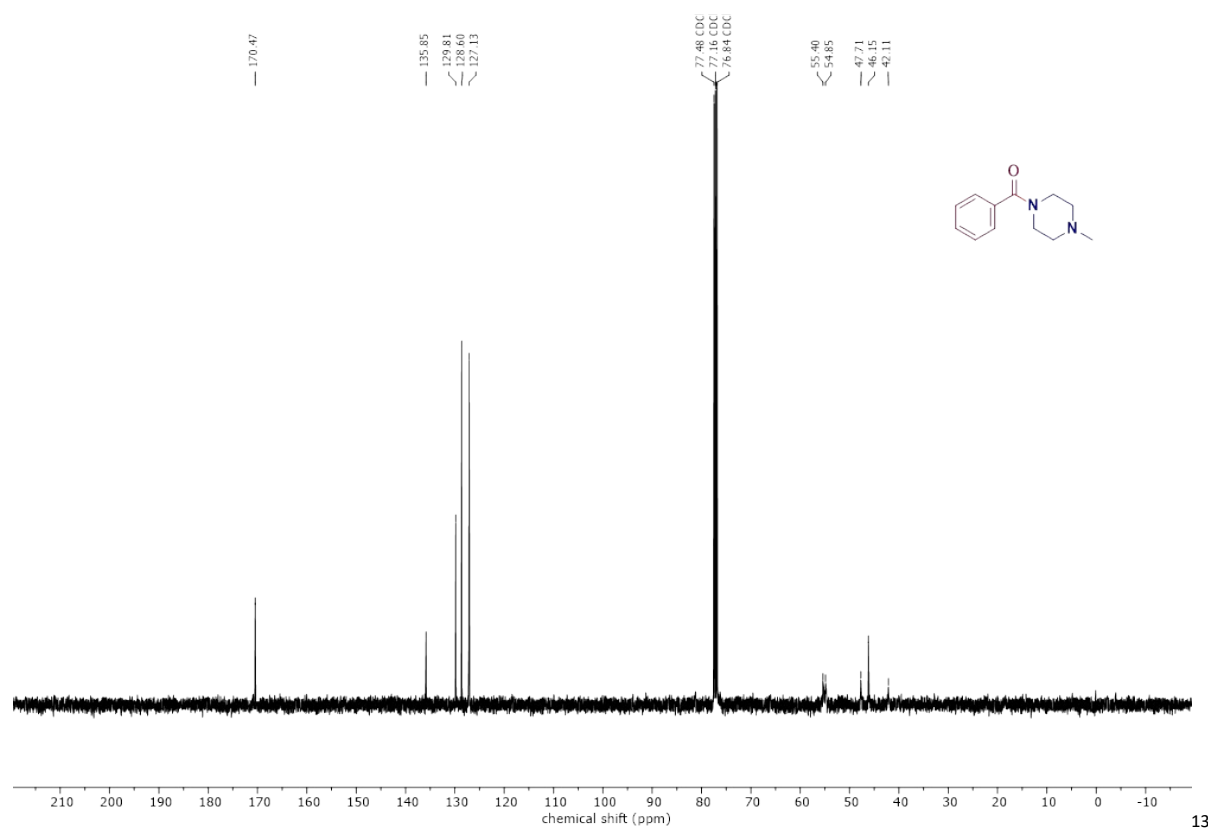
$^1\text{H}$  NMR spectrum (400 MHz) of **3ad** in  $\text{CDCl}_3$ .



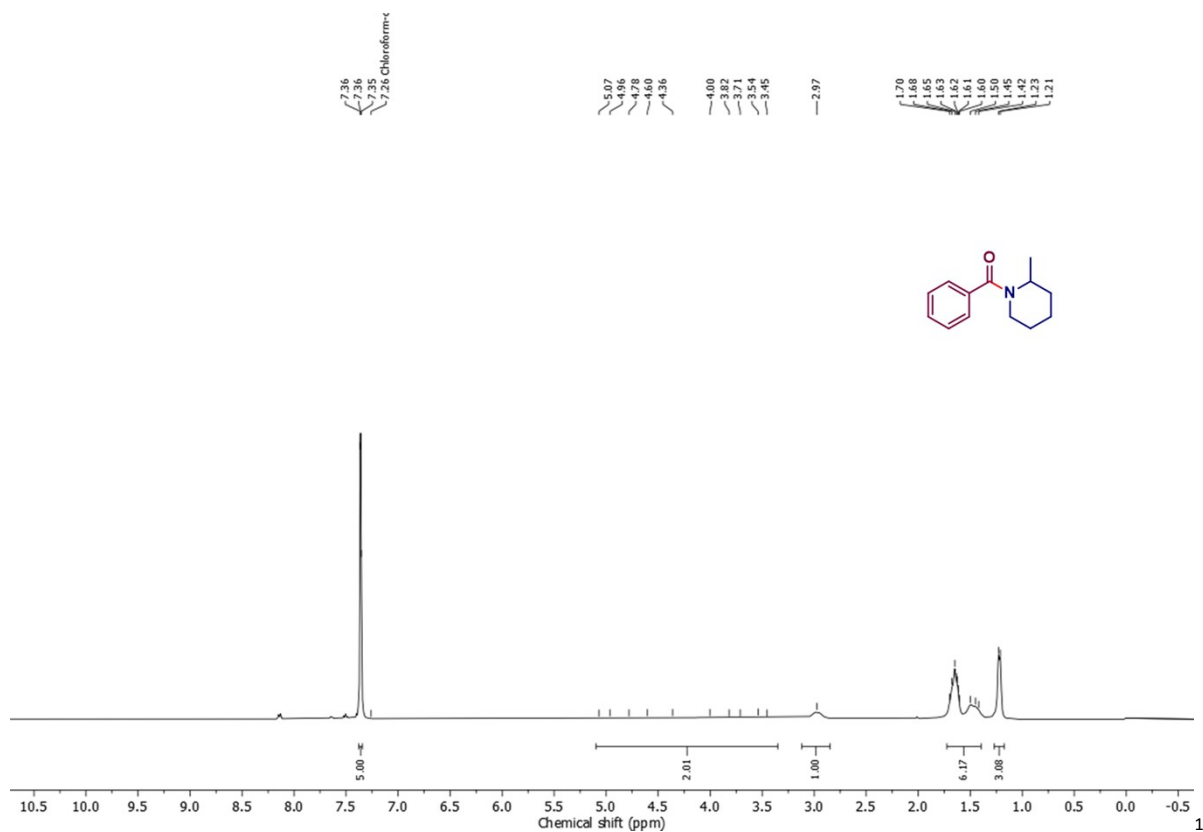
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ad** in  $\text{CDCl}_3$ .



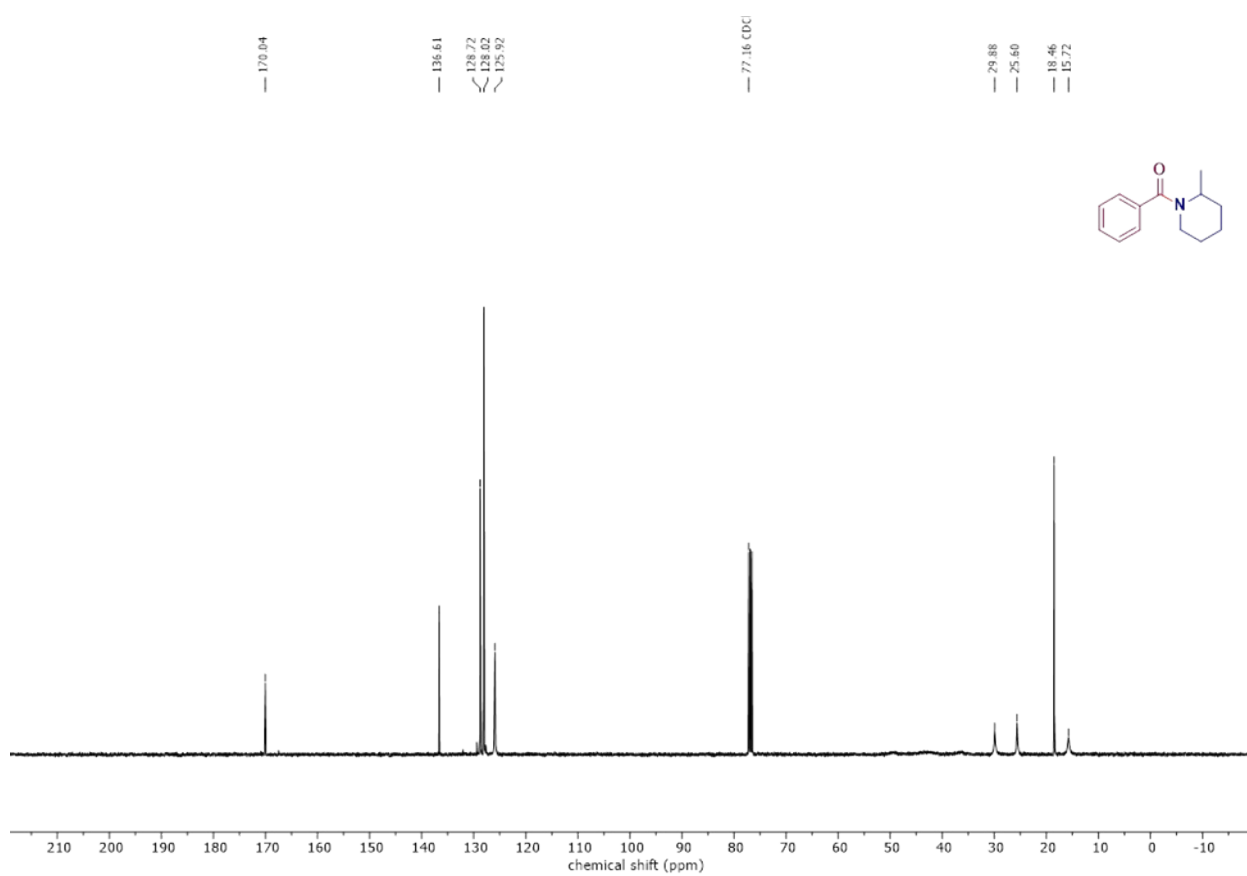
<sup>1</sup>H NMR spectrum (400 MHz) of **3ae** in CDCl<sub>3</sub>.



<sup>13</sup>C NMR spectrum (100 MHz) of **3ae** in CDCl<sub>3</sub>.

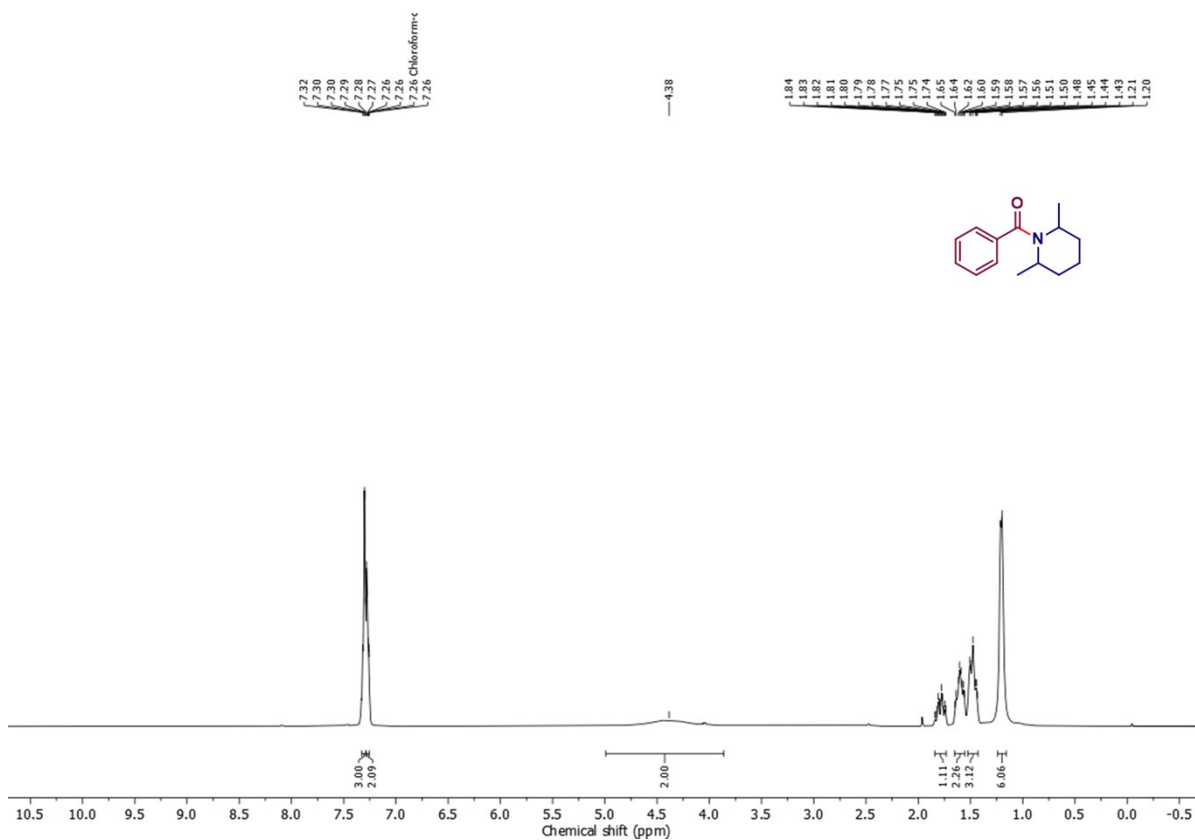


<sup>1</sup>H NMR spectrum (400 MHz) of **3af** in CDCl<sub>3</sub>.

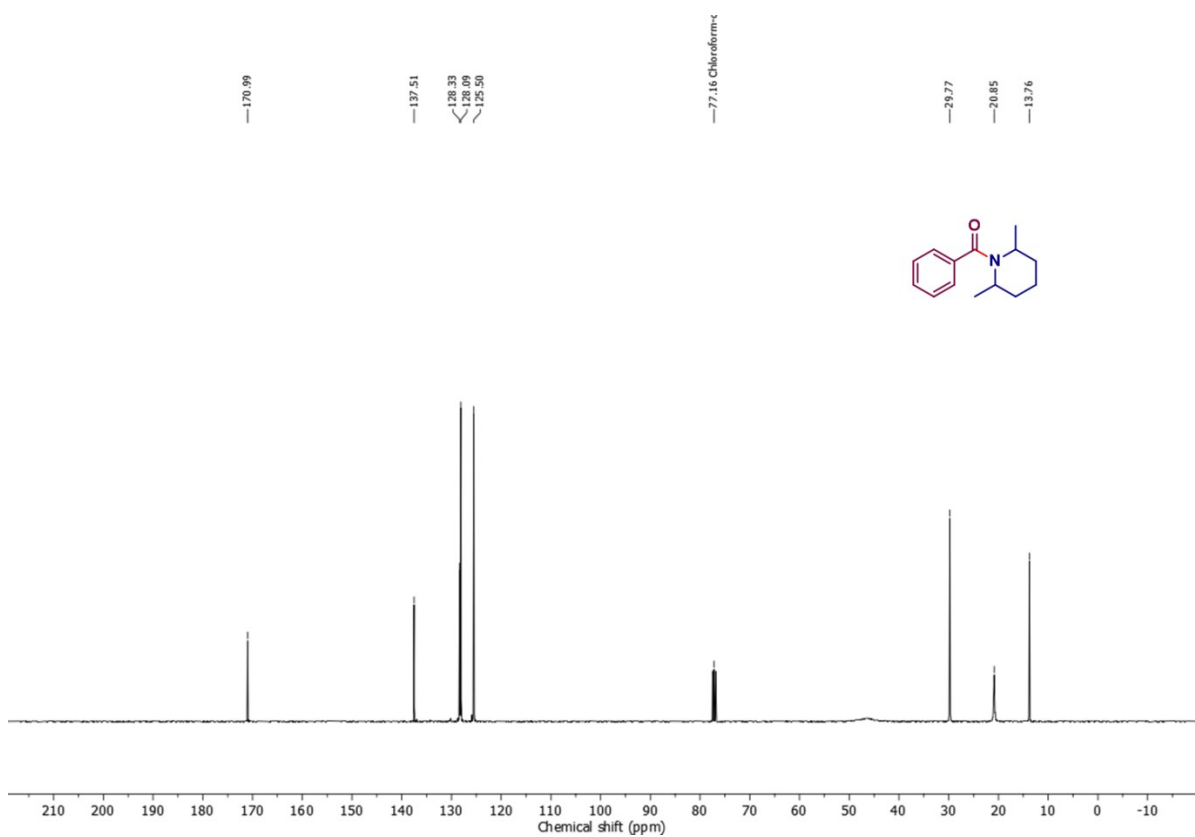


<sup>13</sup>C NMR spectrum (100 MHz) of **3af** in CDCl<sub>3</sub>.

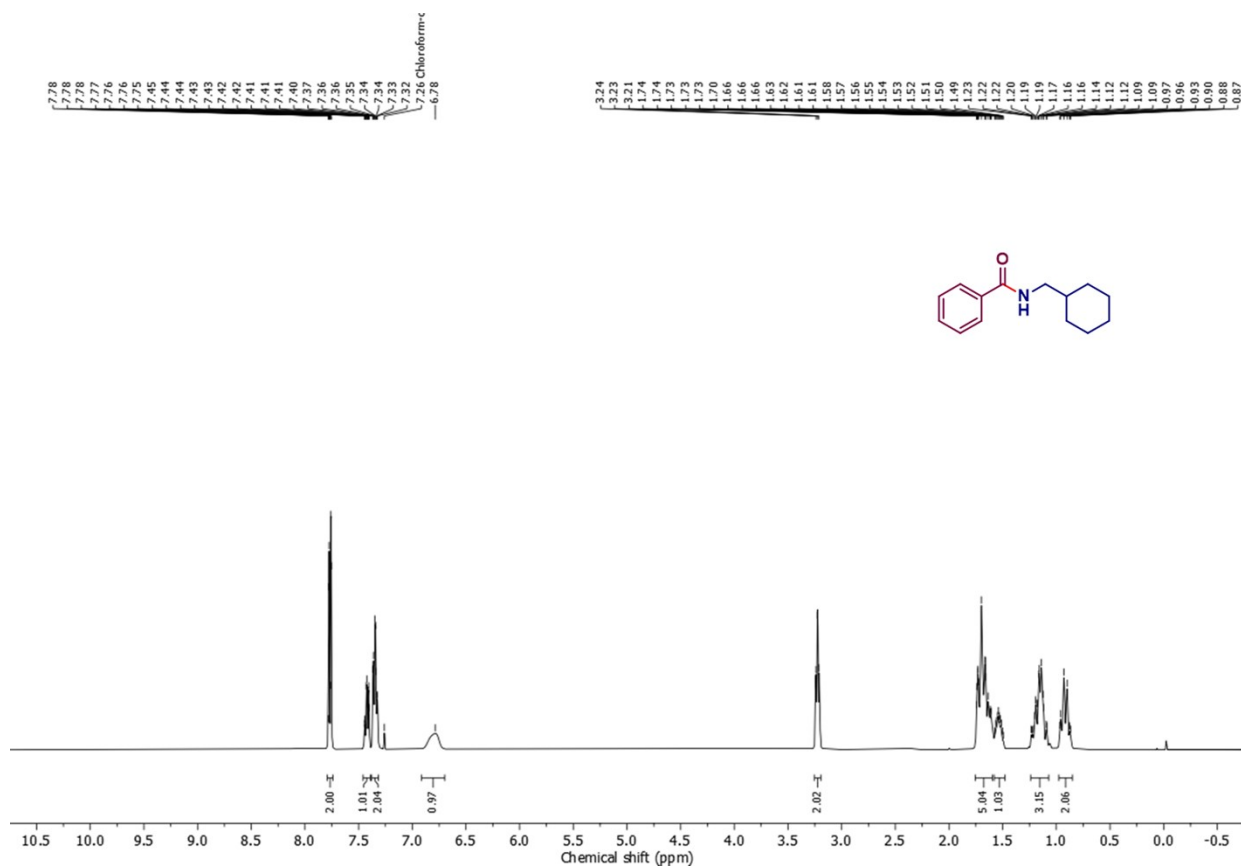




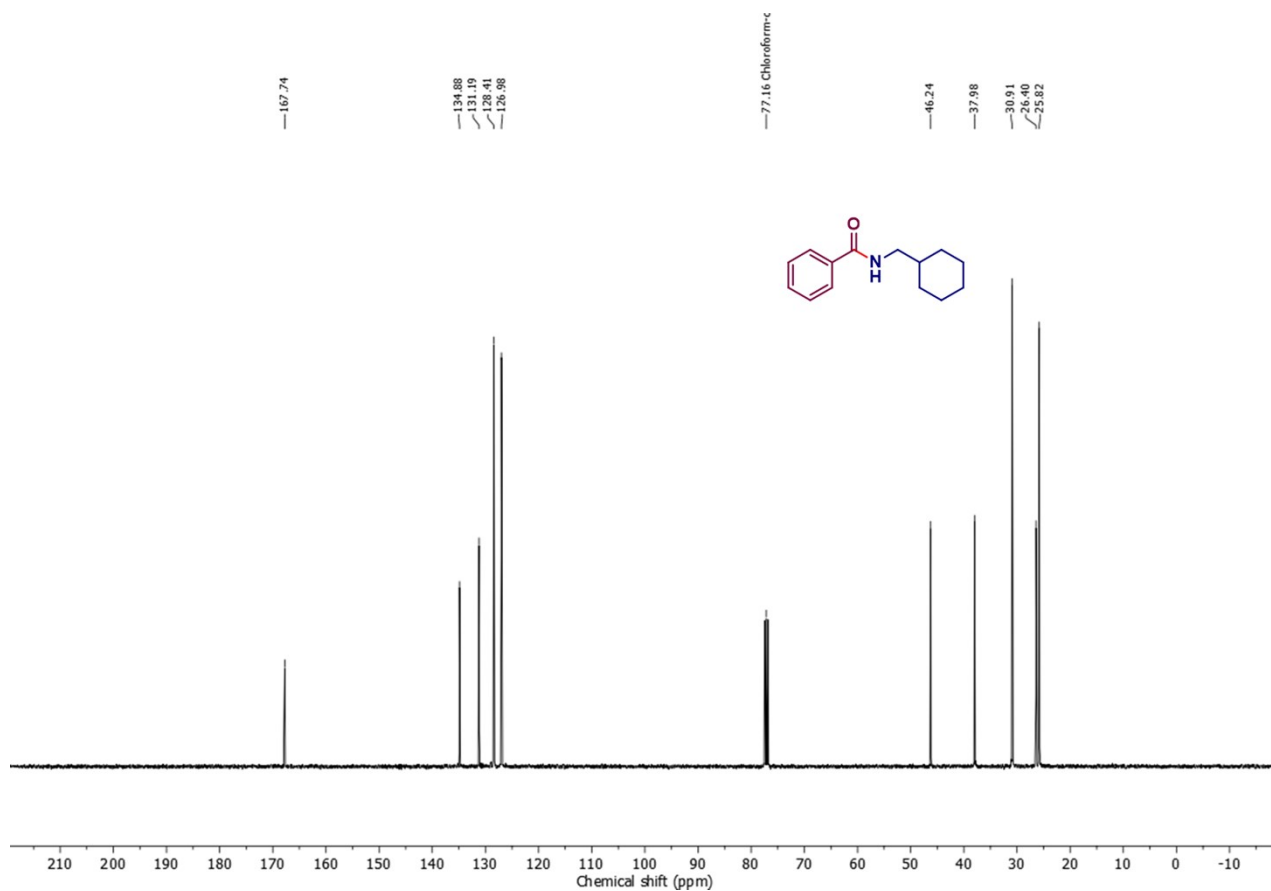
<sup>1</sup>H NMR spectrum (400 MHz) of **3ag** in CDCl<sub>3</sub>.



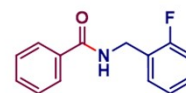
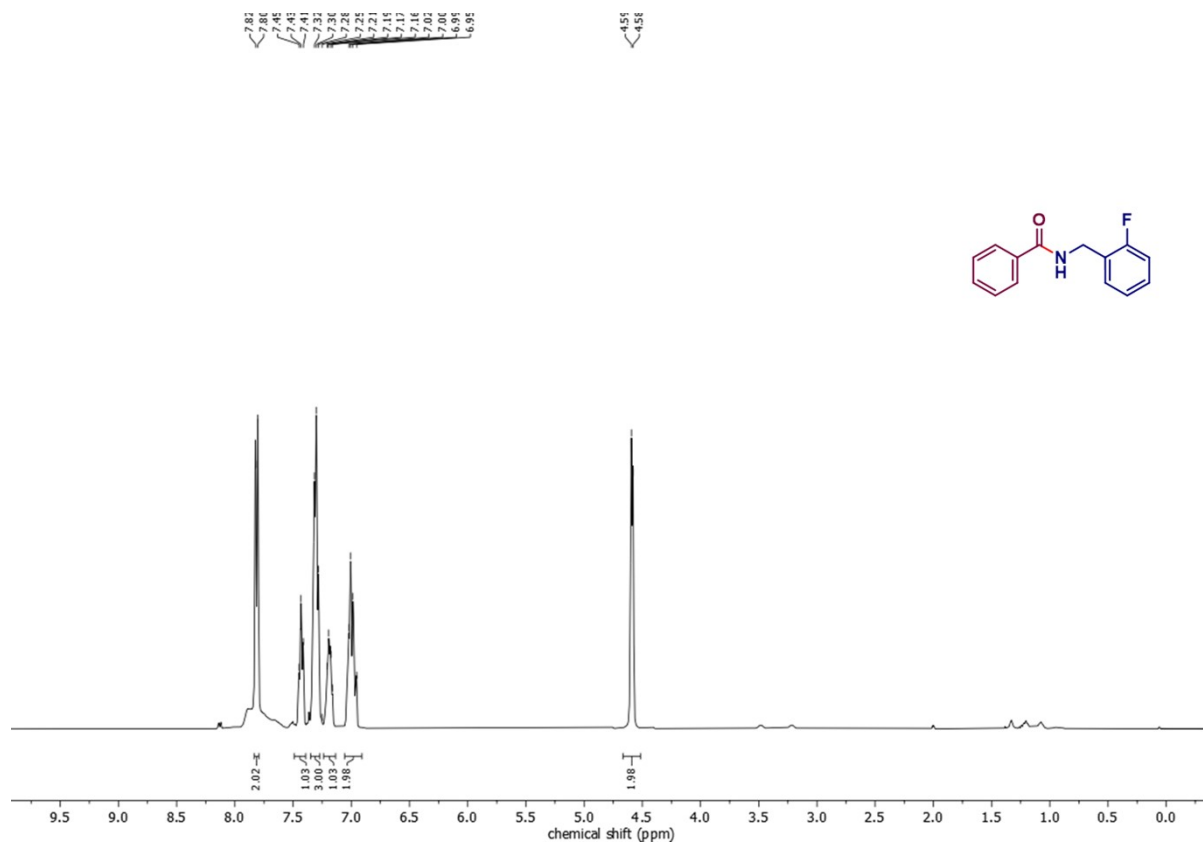
<sup>13</sup>C NMR spectrum (100 MHz) of **3ag** in CDCl<sub>3</sub>.



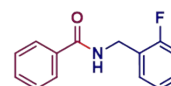
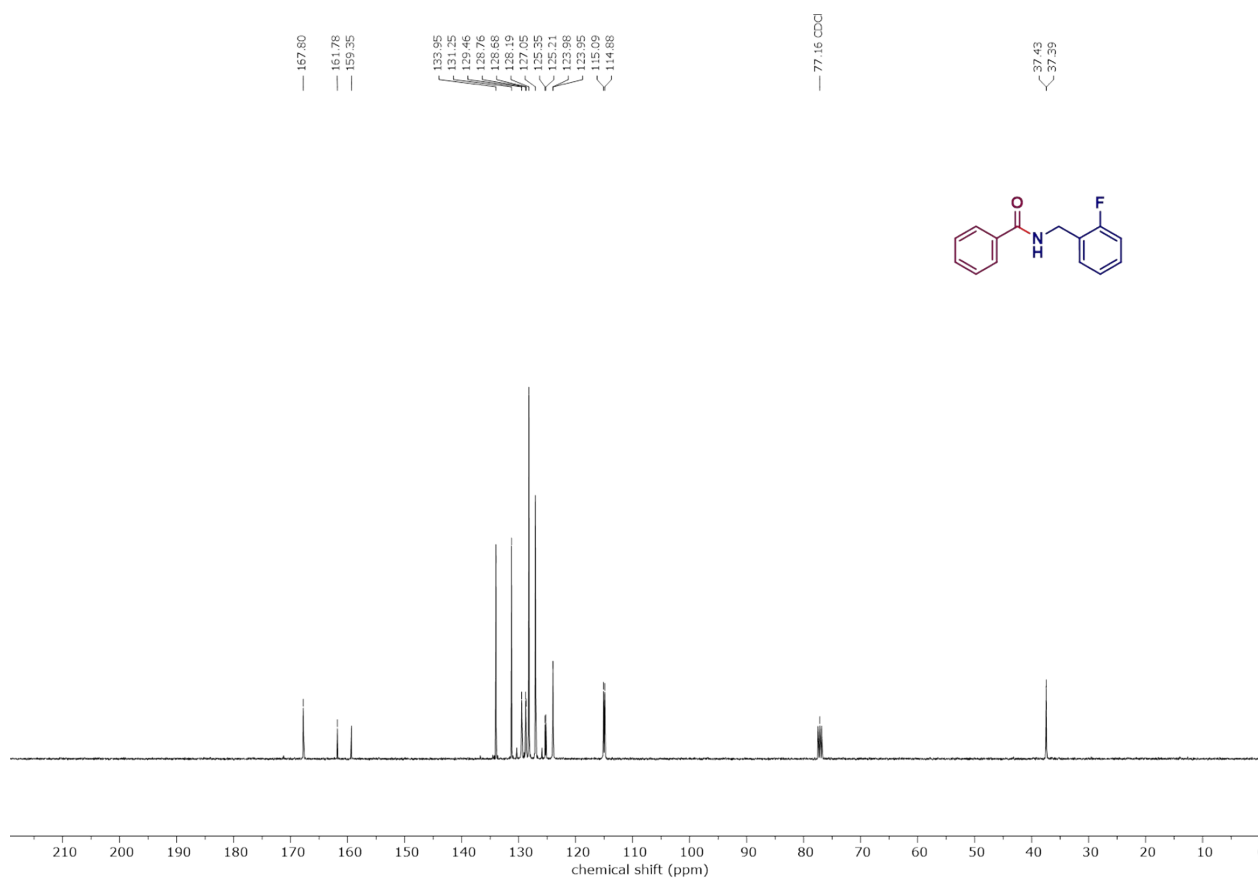
$^1\text{H}$  NMR spectrum (400 MHz) of **3ah** in  $\text{CDCl}_3$ .



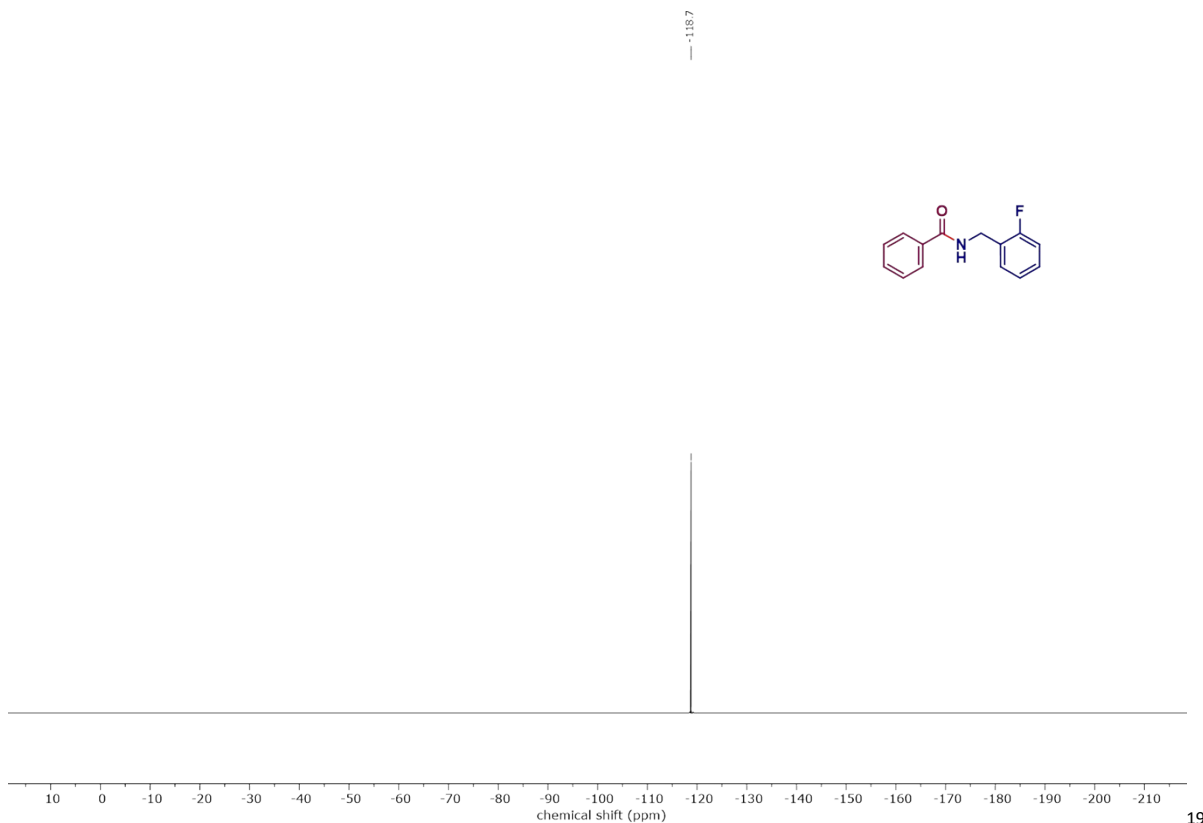
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ah** in  $\text{CDCl}_3$ .



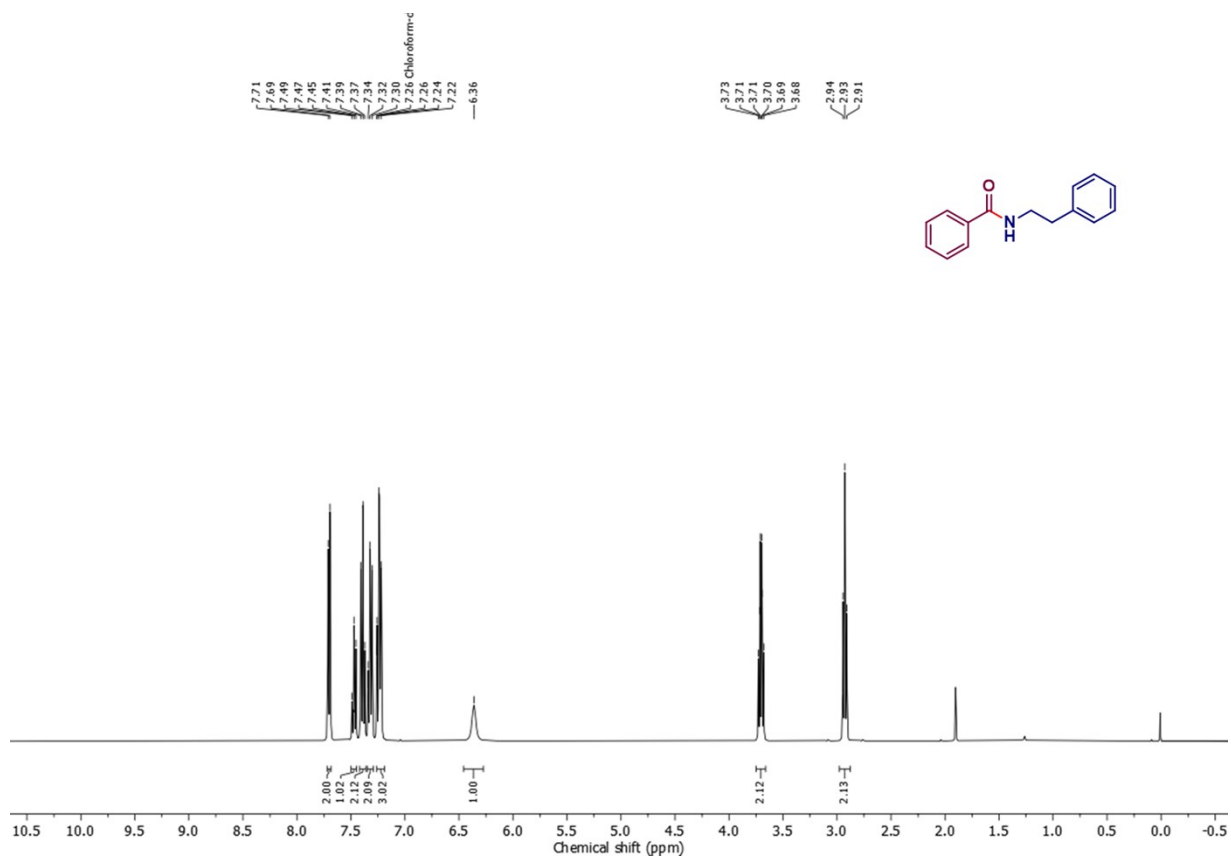
<sup>1</sup>H NMR spectrum (400 MHz) of **3ai** in CDCl<sub>3</sub>.



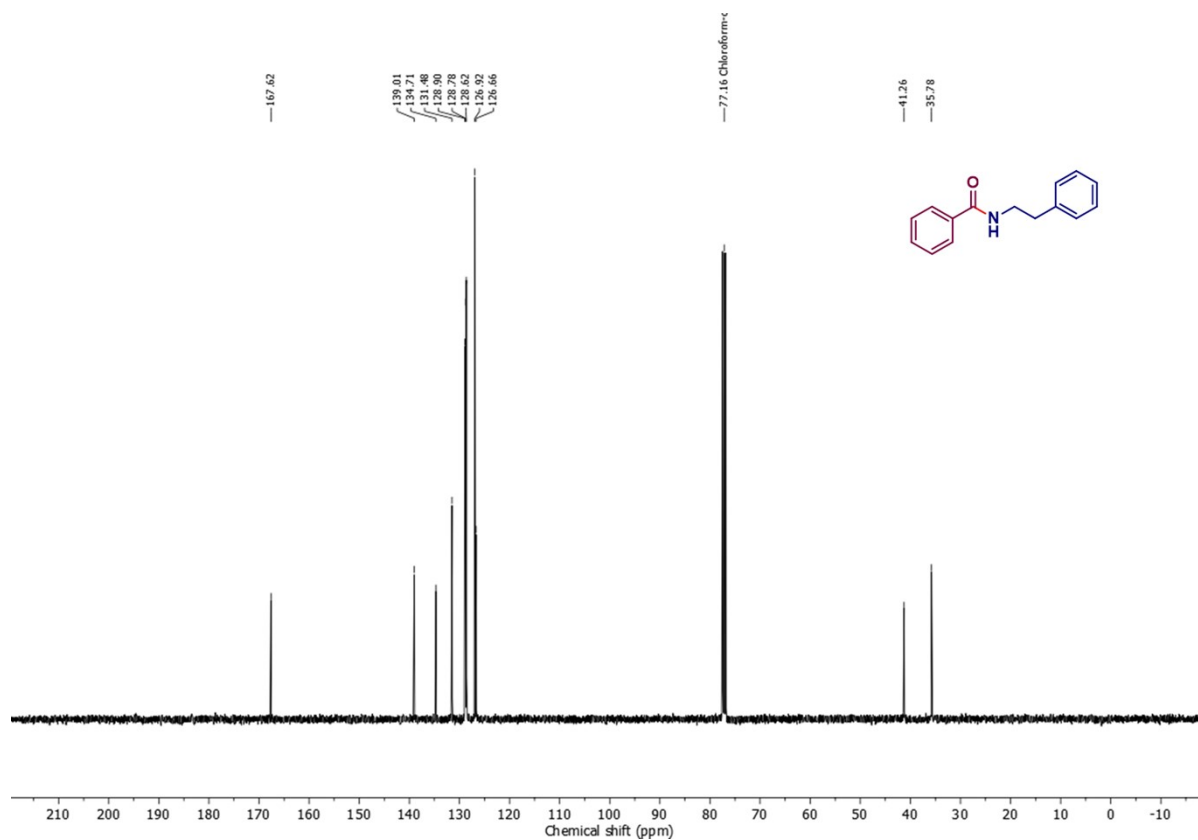
<sup>13</sup>C NMR spectrum (100 MHz) of **3ai** in CDCl<sub>3</sub>.



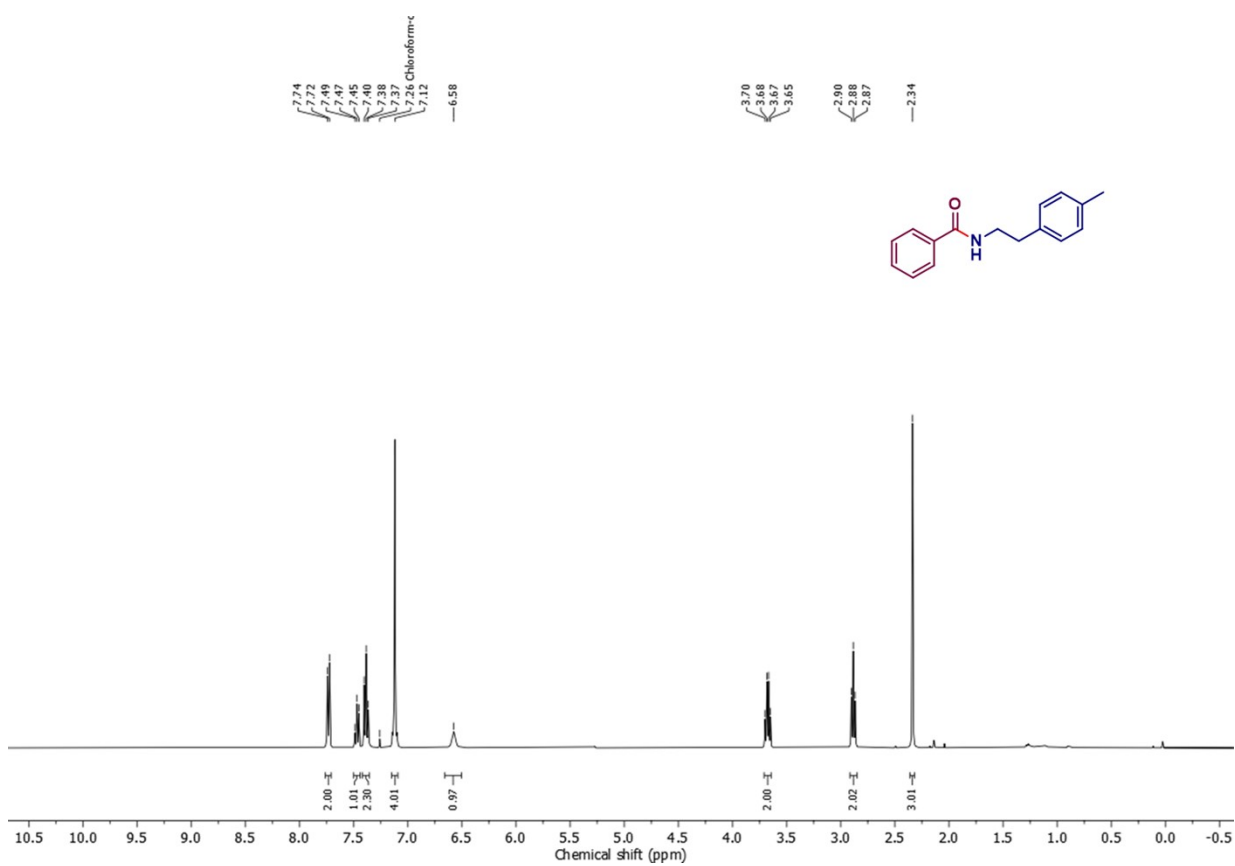
F NMR spectrum (376 MHz) of **3ai** in CDCl<sub>3</sub>.



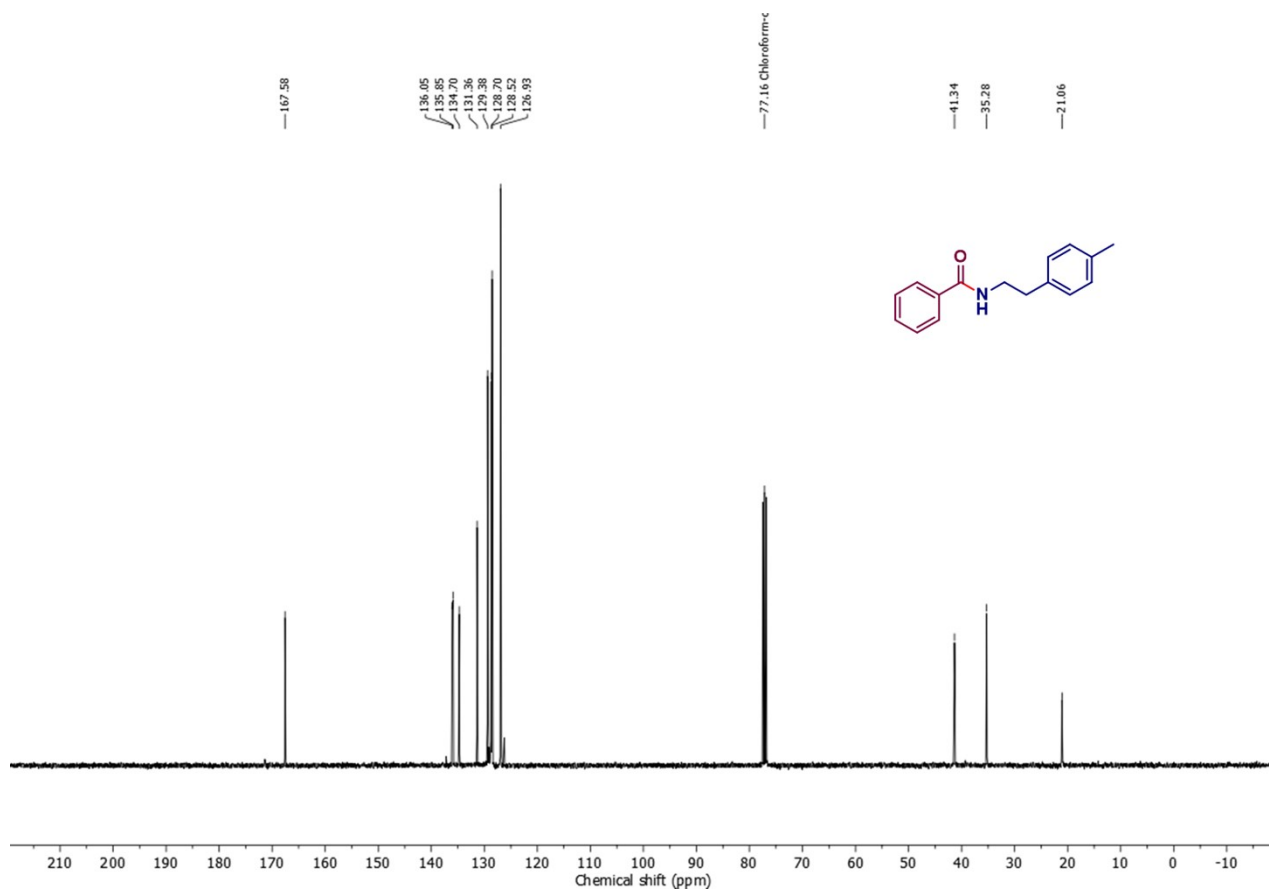
<sup>1</sup>H NMR spectrum (400 MHz) of **3aj** in CDCl<sub>3</sub>.



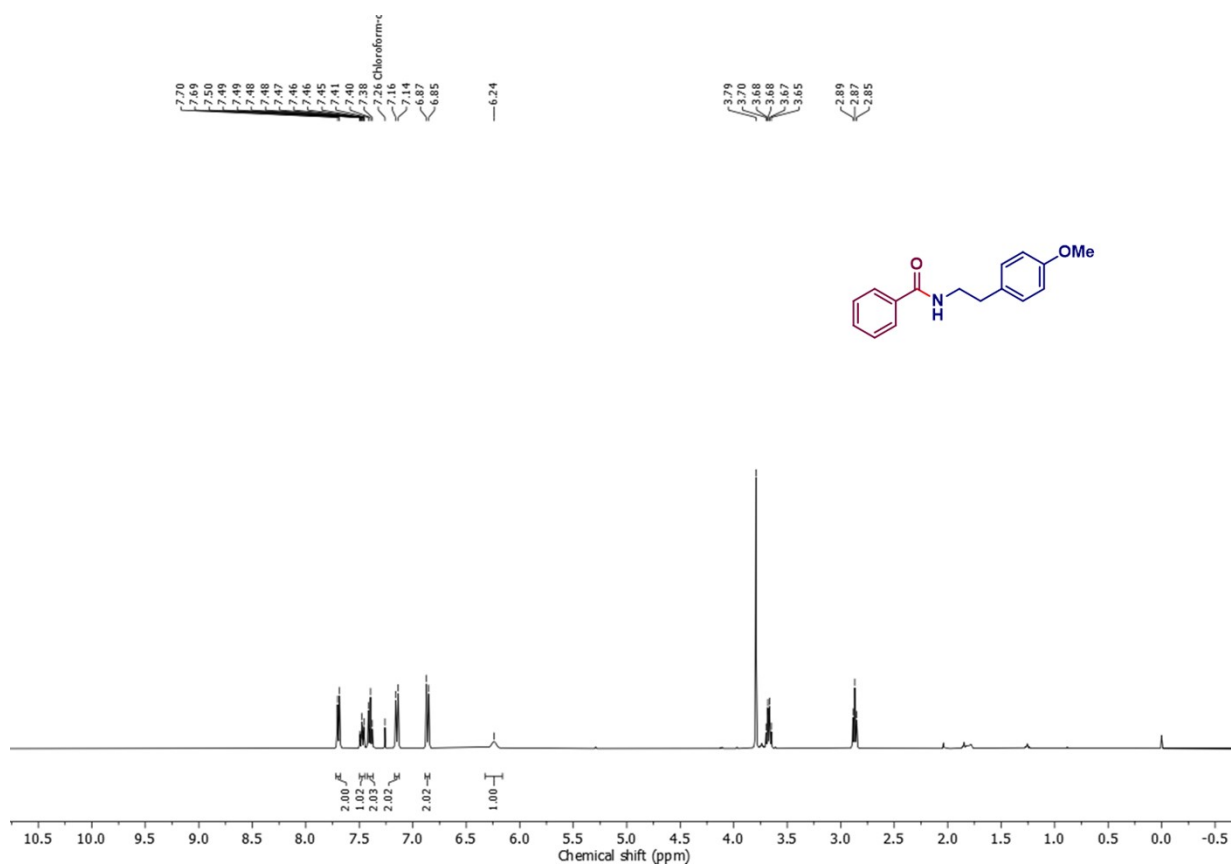
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3aj** in  $\text{CDCl}_3$ .



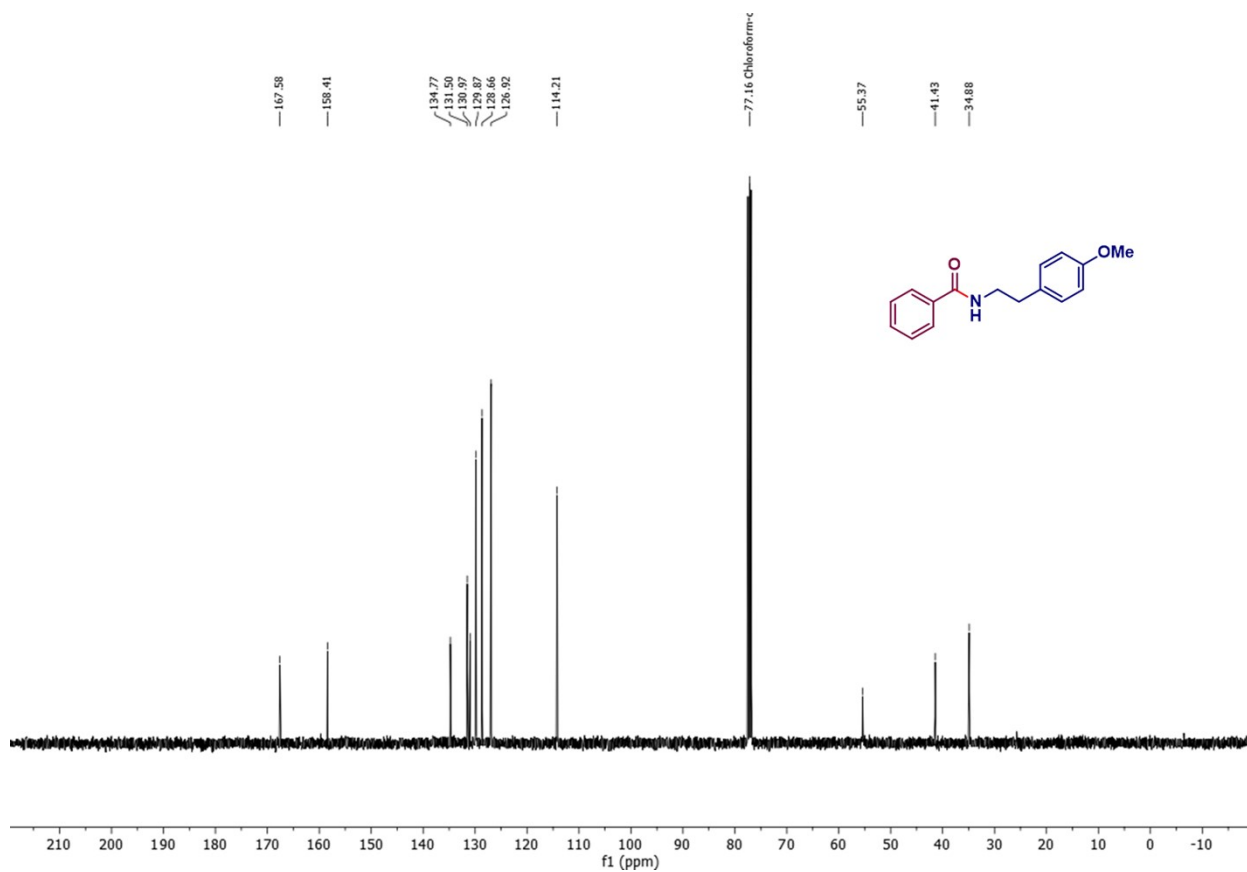
$^1\text{H}$  NMR spectrum (400 MHz) of **3ak** in  $\text{CDCl}_3$ .



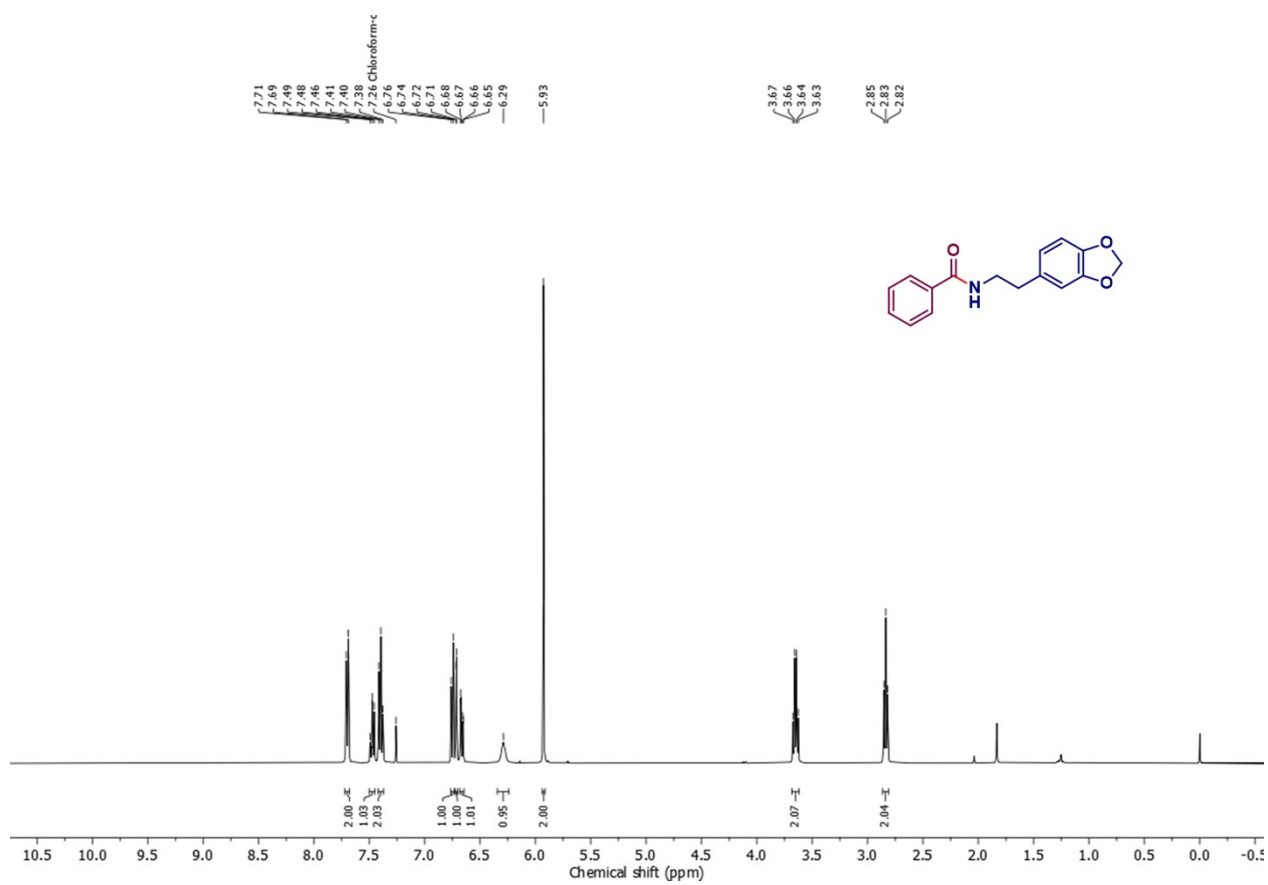
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ak** in  $\text{CDCl}_3$ .



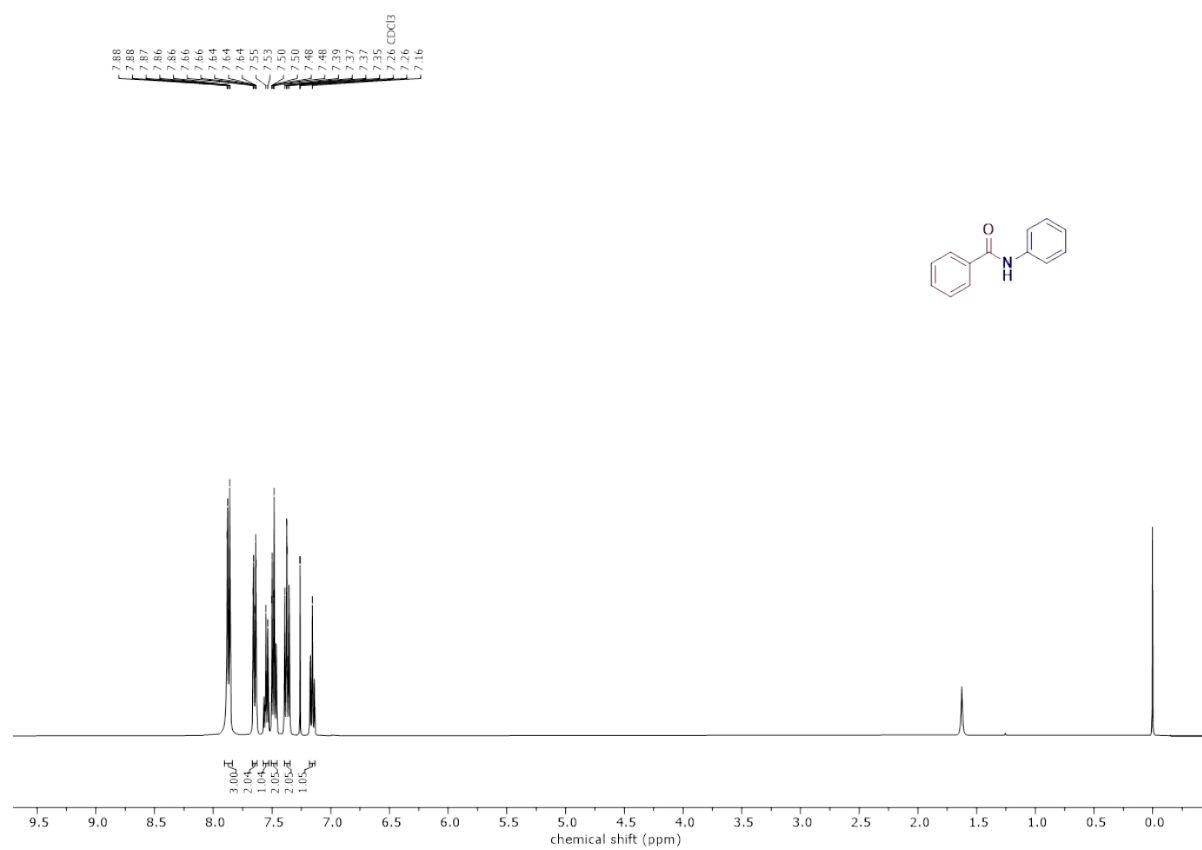
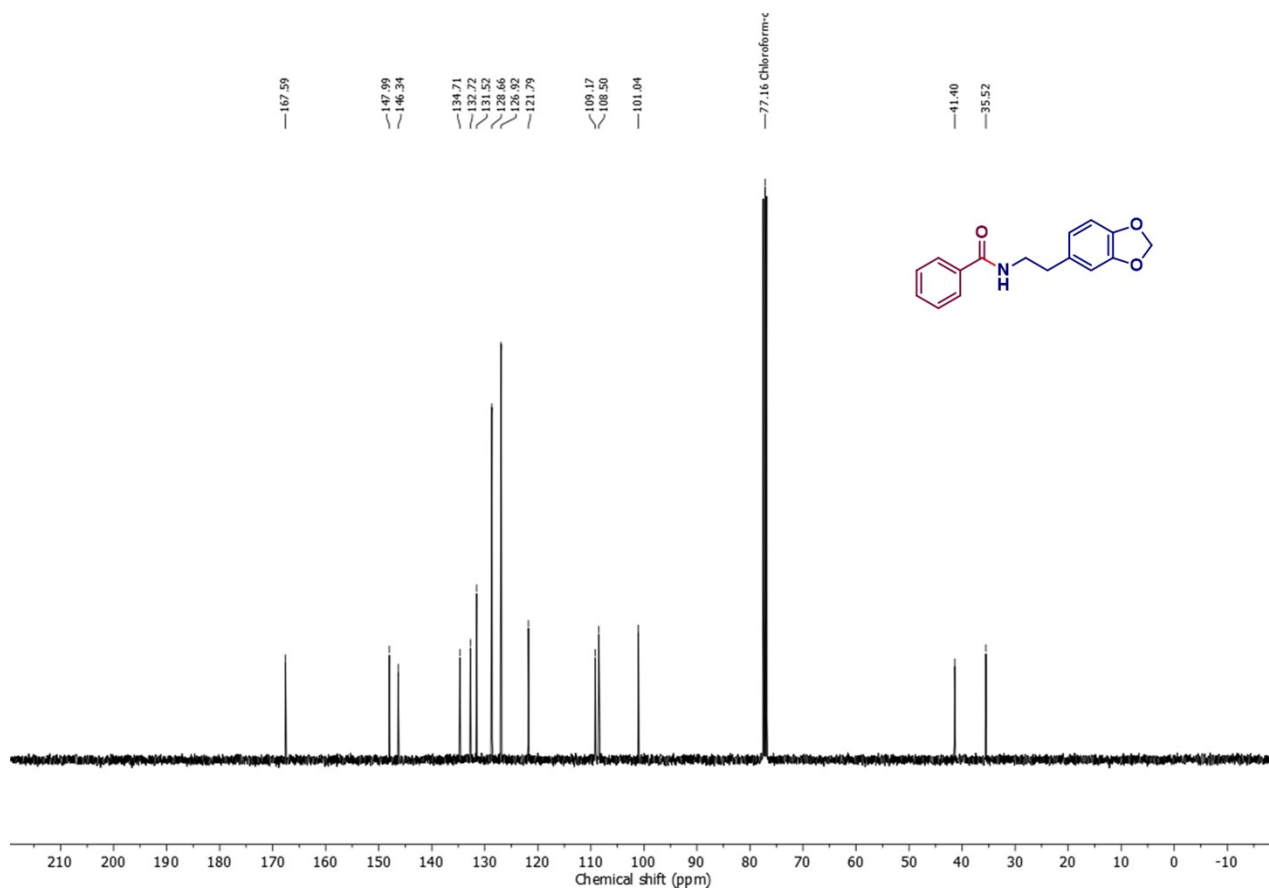
$^1\text{H}$  NMR spectrum (400 MHz) of **3al** in  $\text{CDCl}_3$ .



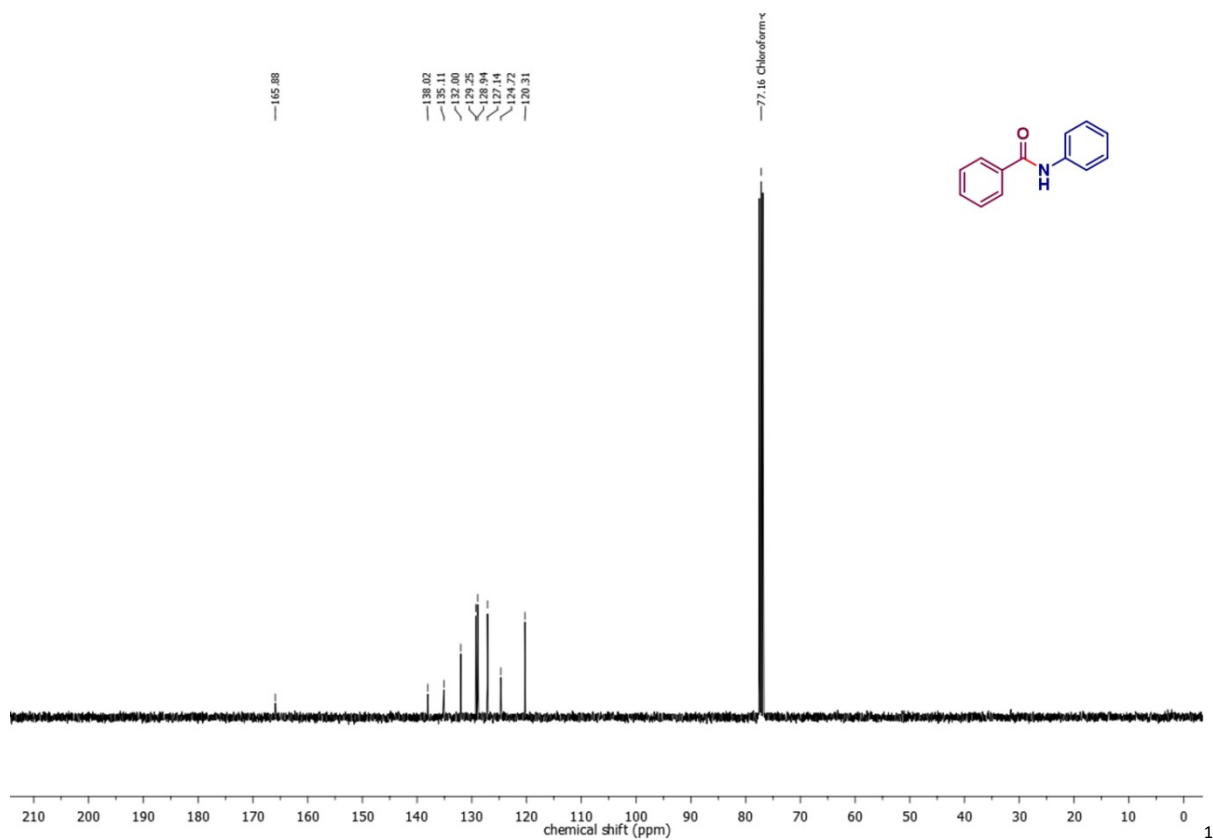
<sup>13</sup>C NMR spectrum (100 MHz) of **3al** in CDCl<sub>3</sub>.



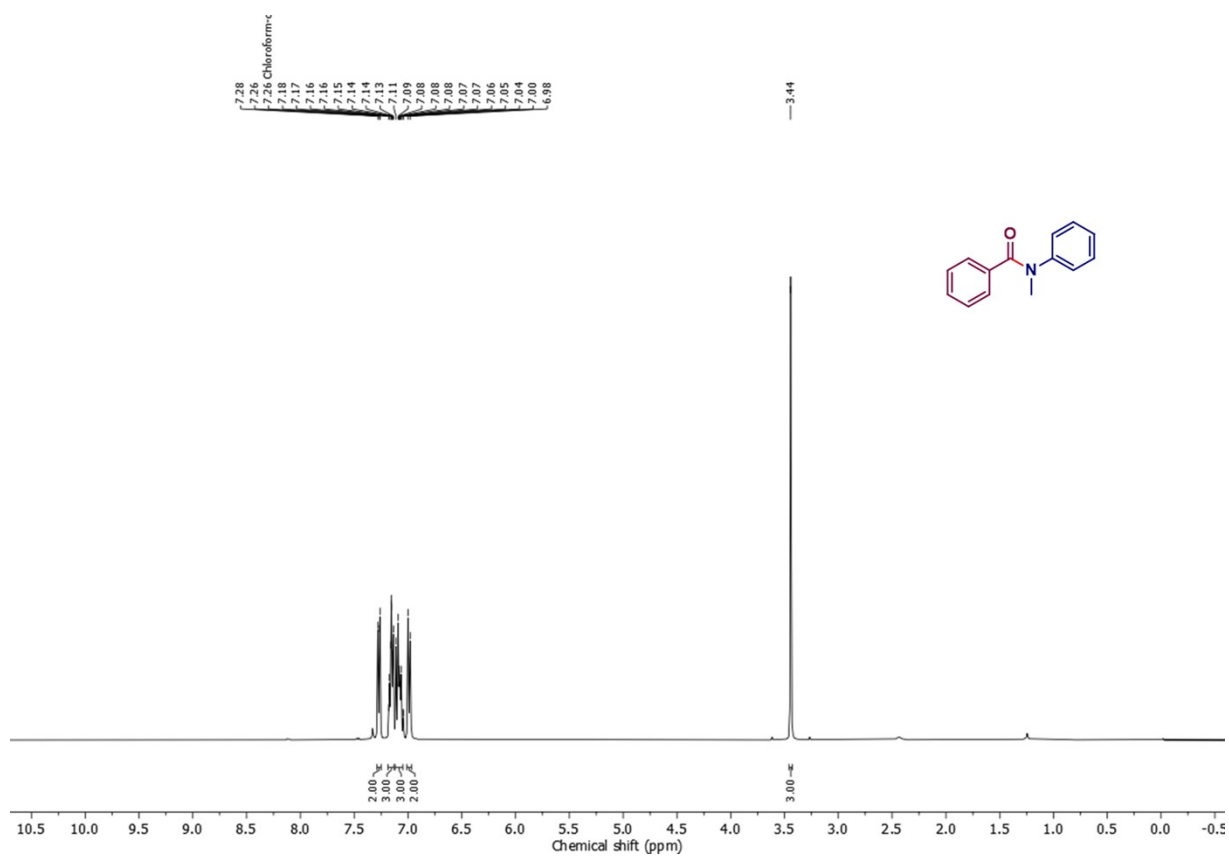
<sup>1</sup>H NMR spectrum (400 MHz) of **3am** in CDCl<sub>3</sub>.



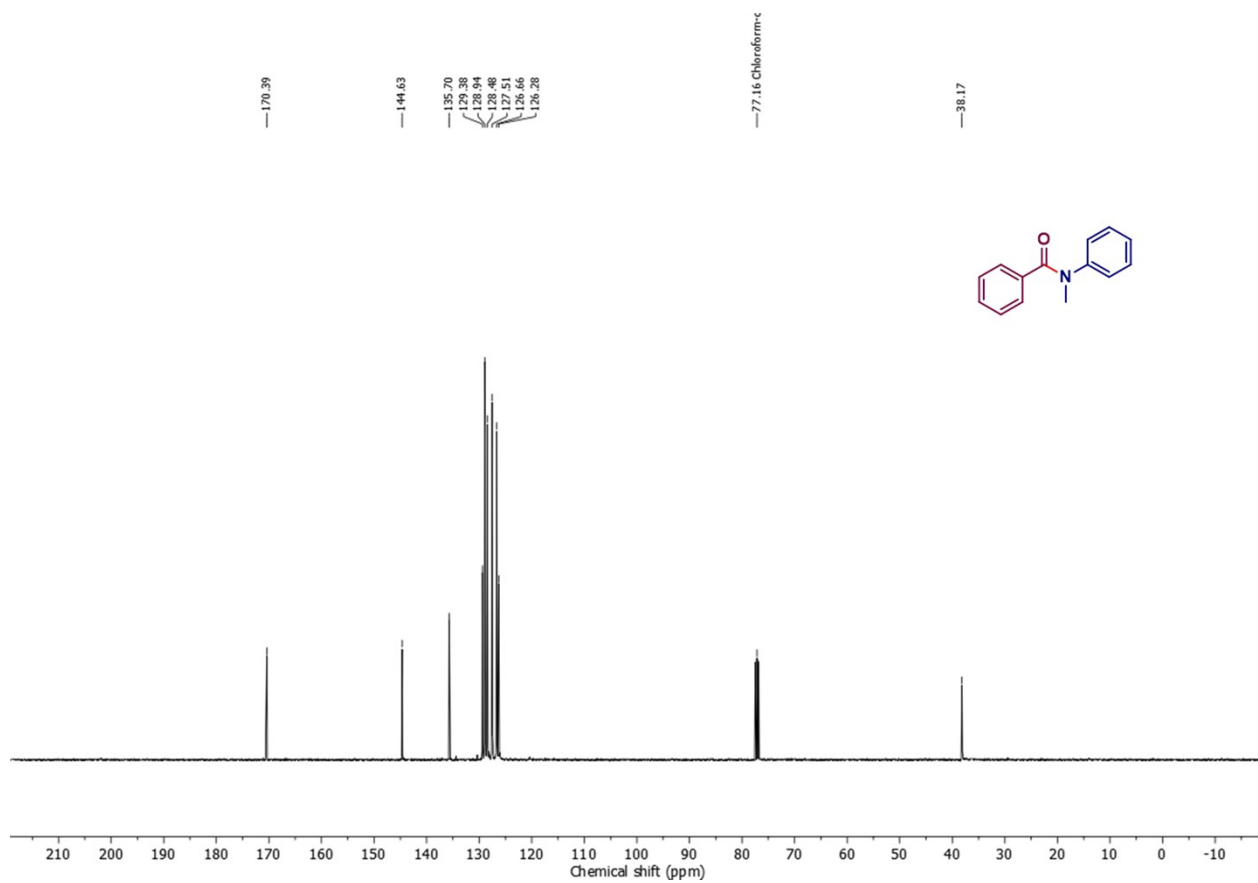




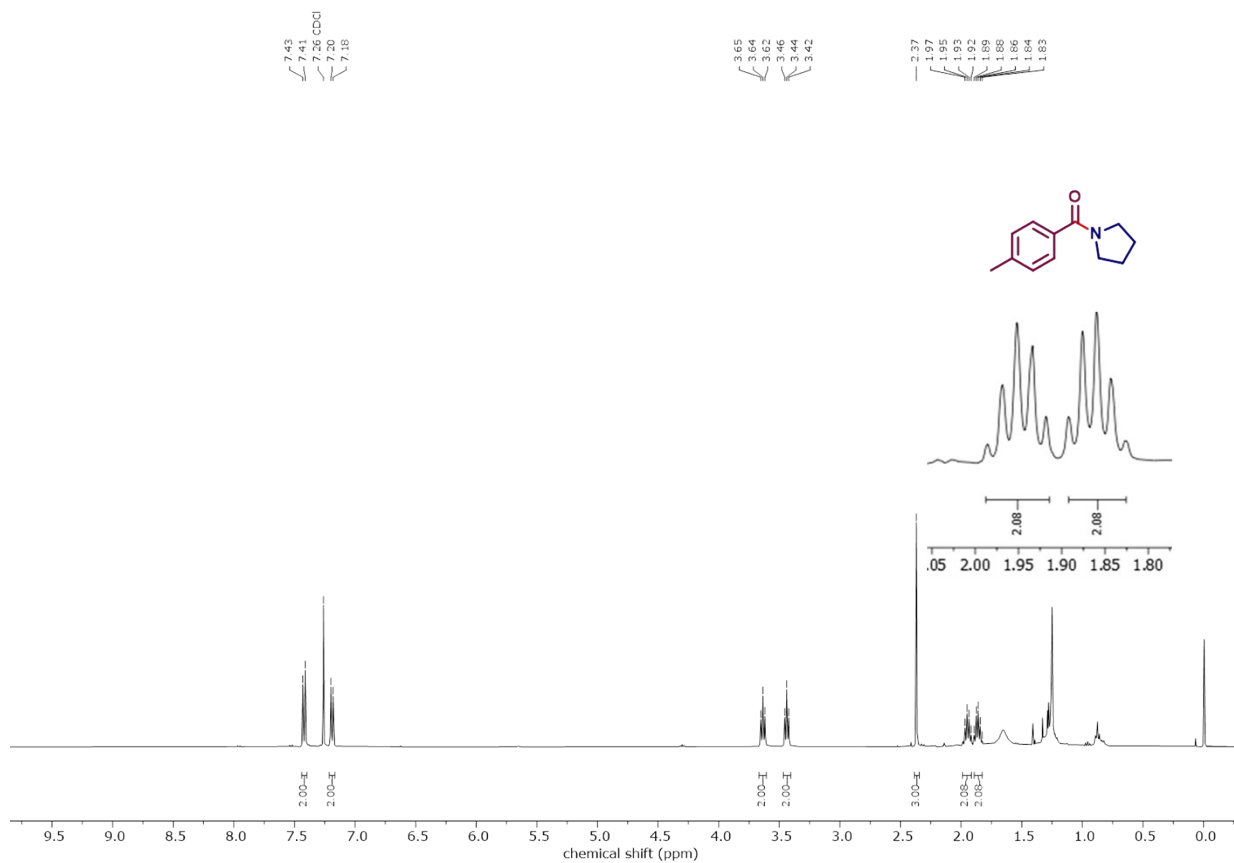
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3an** in  $\text{CDCl}_3$ .



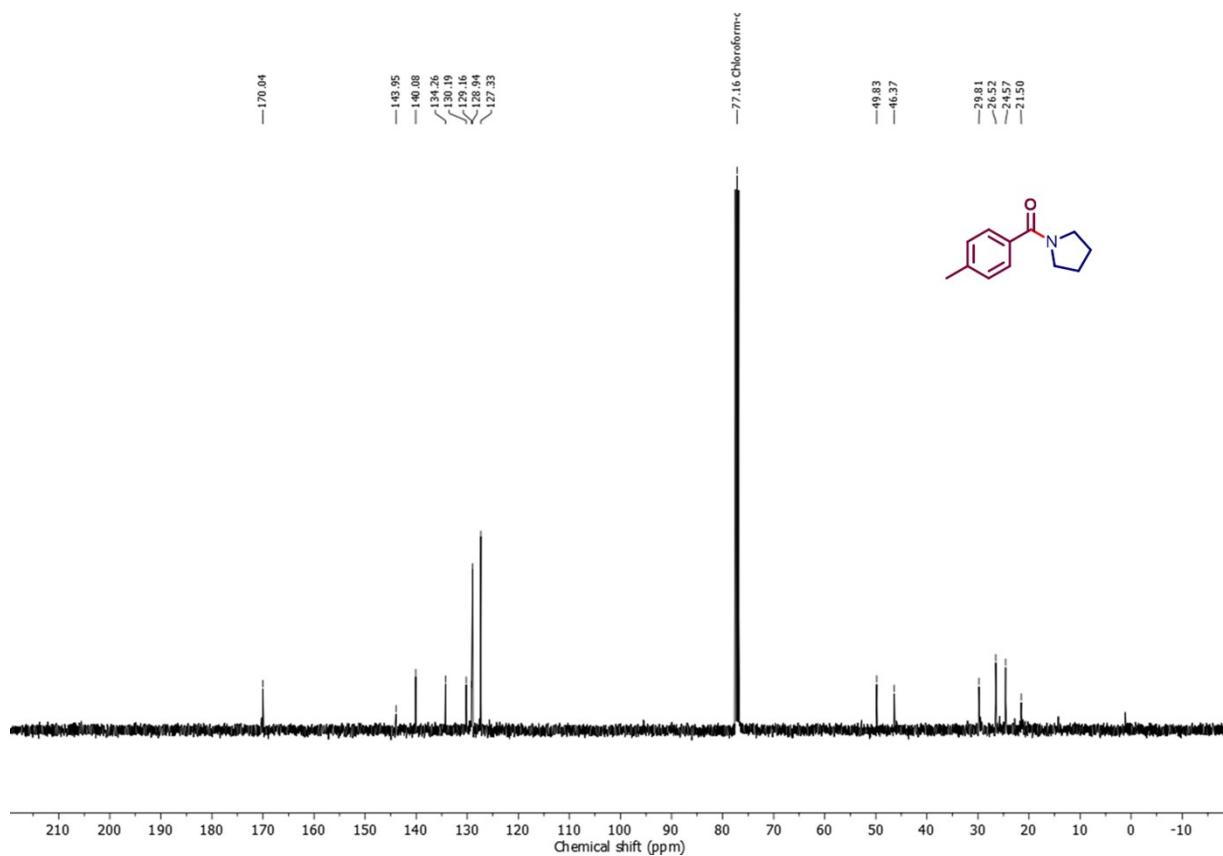
$^1\text{H}$  NMR spectrum (400 MHz) of **3ao** in  $\text{CDCl}_3$ .



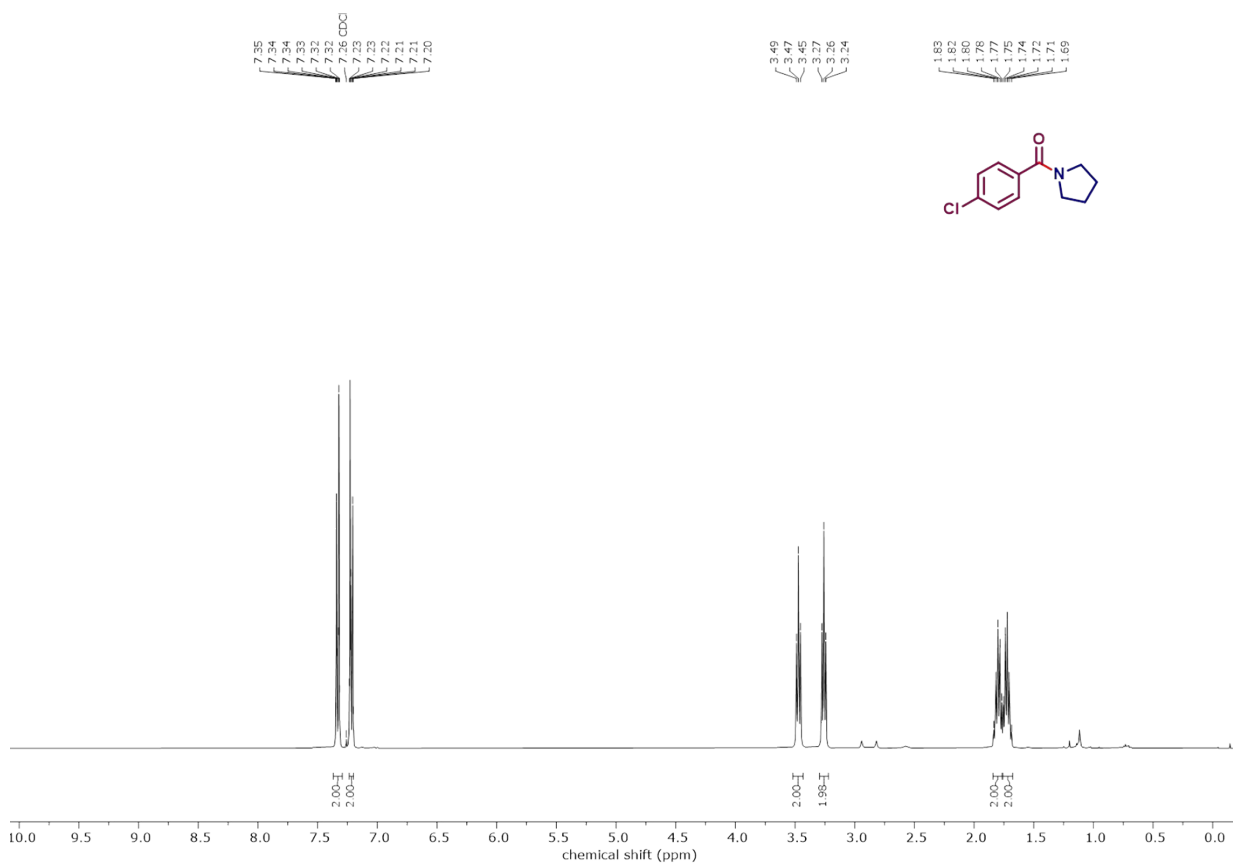
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ao** in  $\text{CDCl}_3$ .



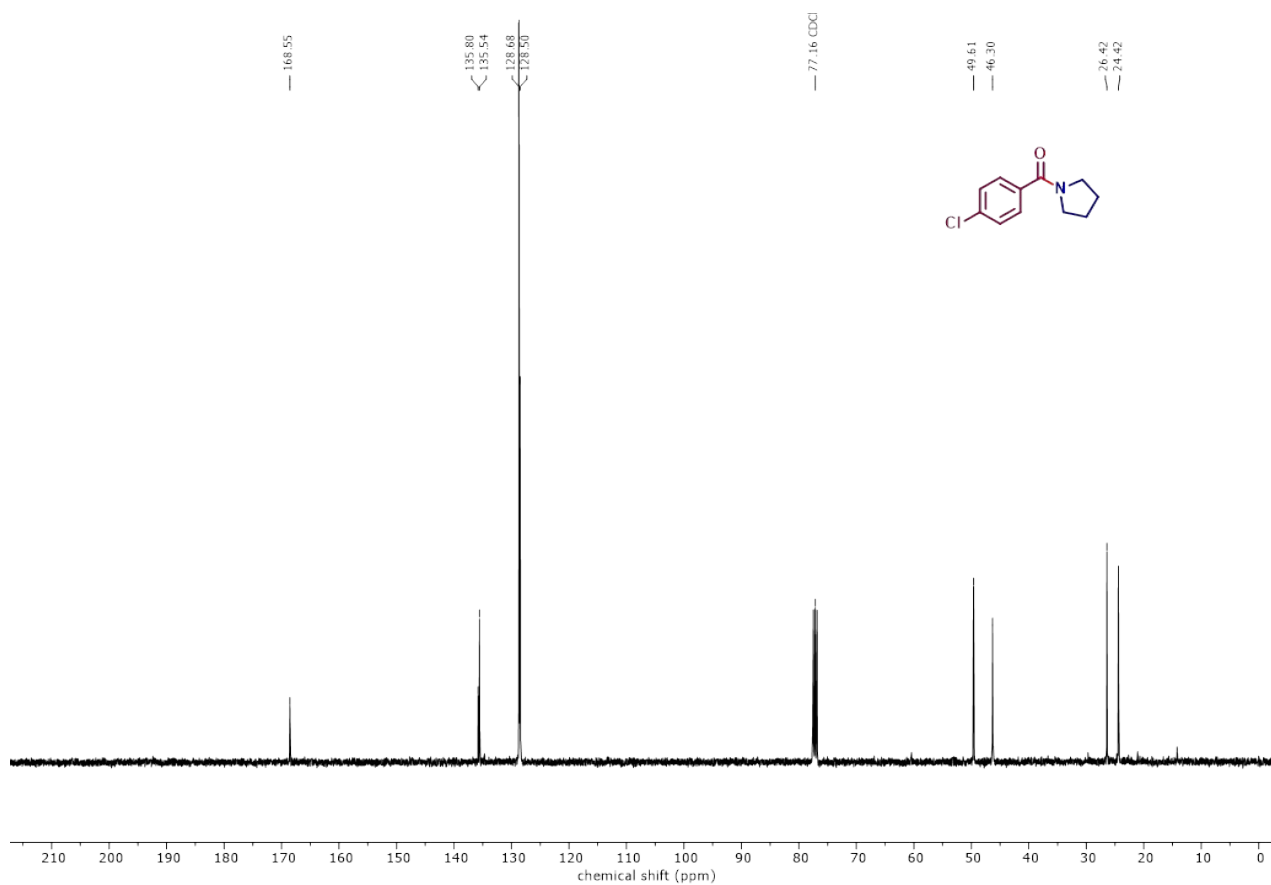
$^1\text{H}$  NMR spectrum (400 MHz) of **3ba** in  $\text{CDCl}_3$ .



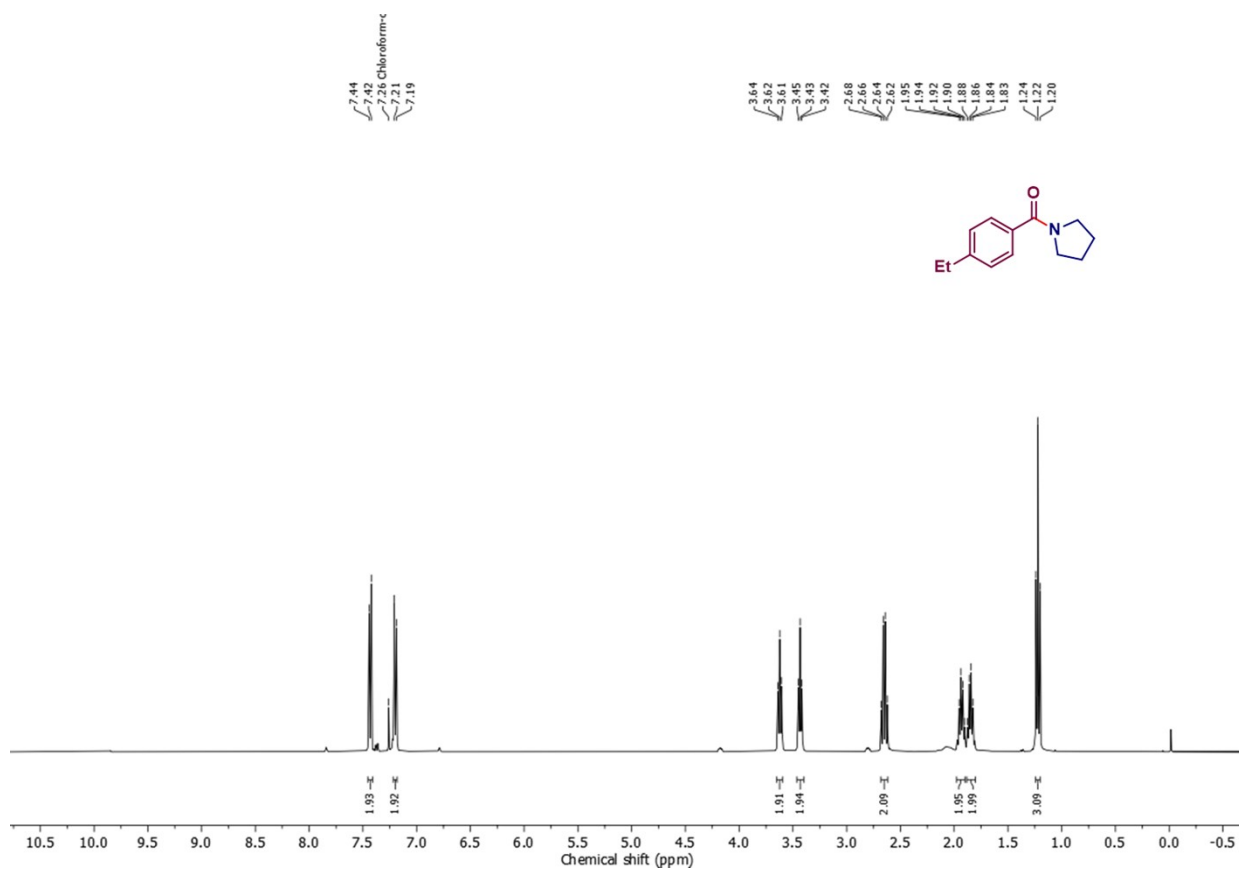
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ba** in  $\text{CDCl}_3$ .



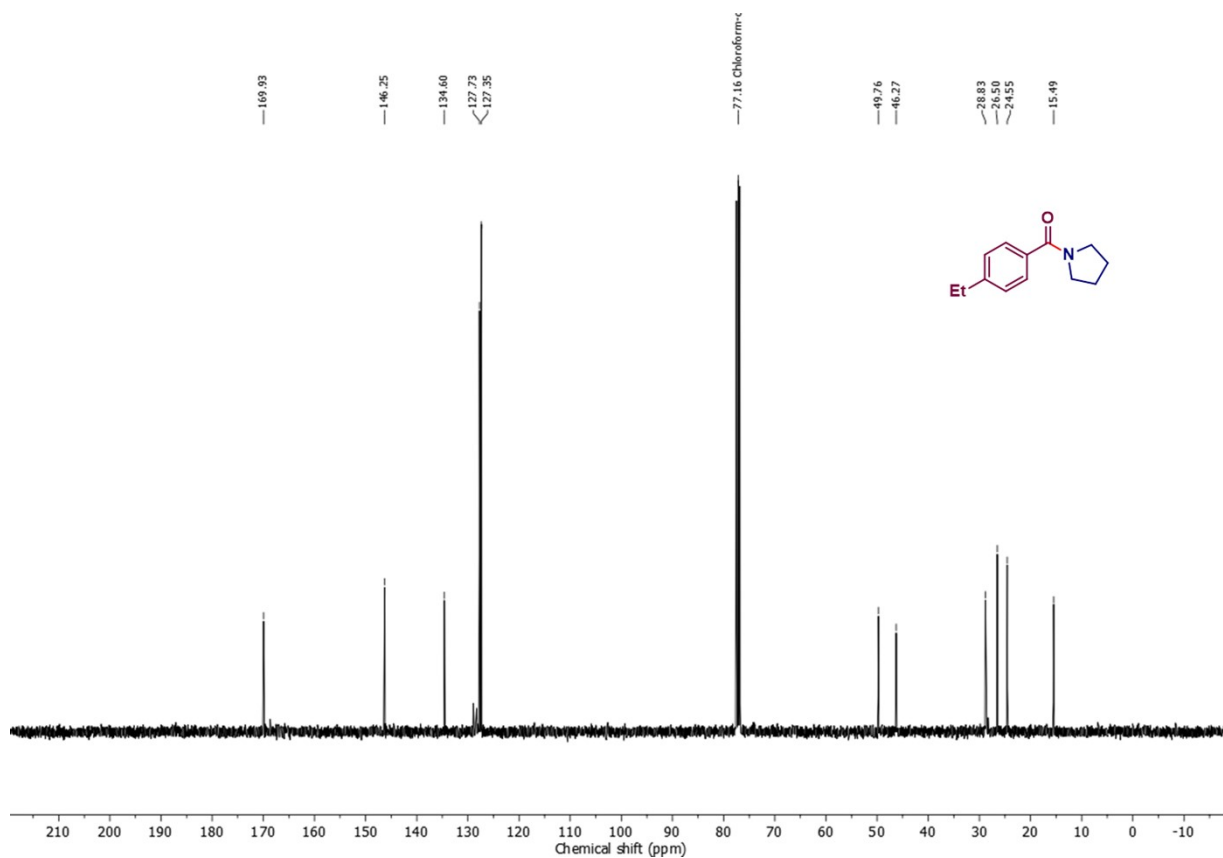
$^1\text{H}$  NMR spectrum (400 MHz) of **3ca** in  $\text{CDCl}_3$ .



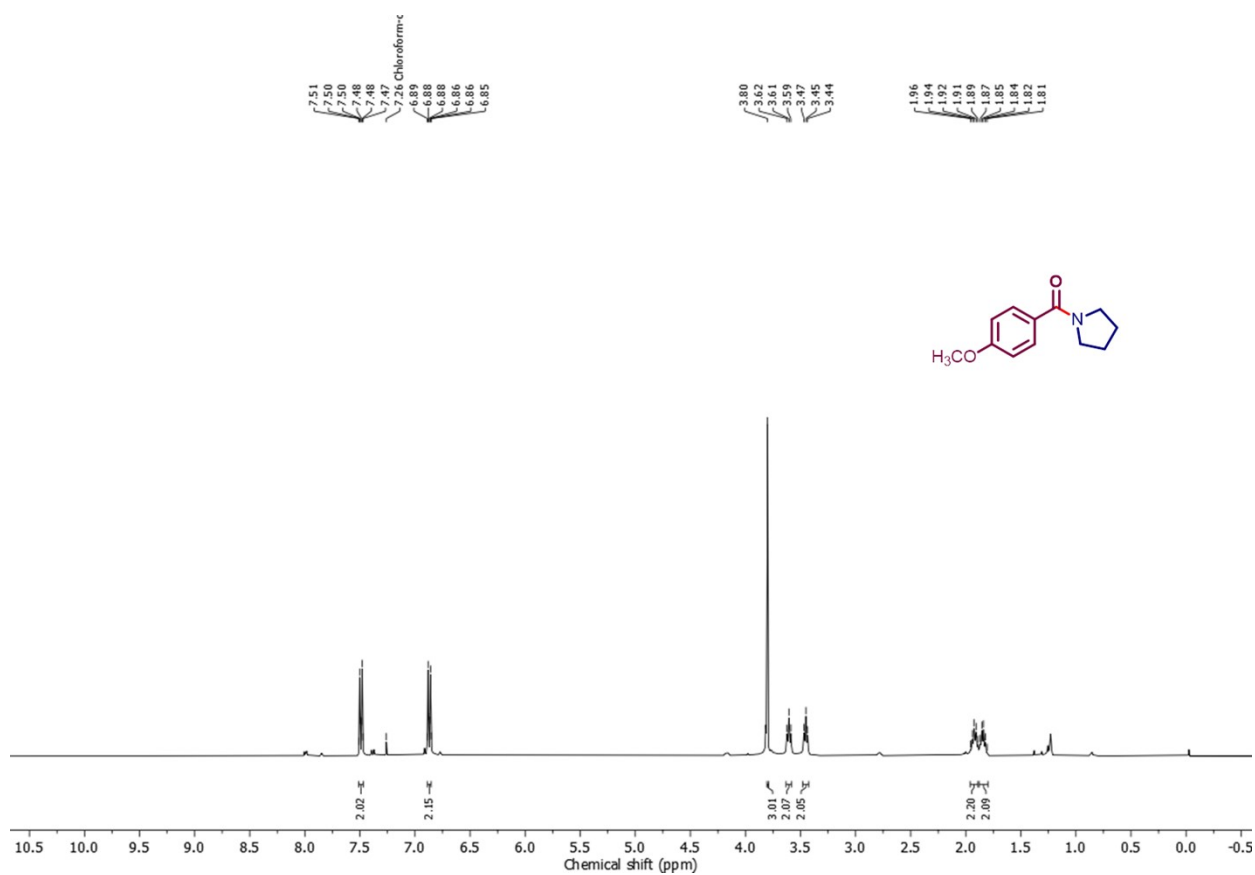
<sup>13</sup>C NMR spectrum (100 MHz) of **3ca** in CDCl<sub>3</sub>.



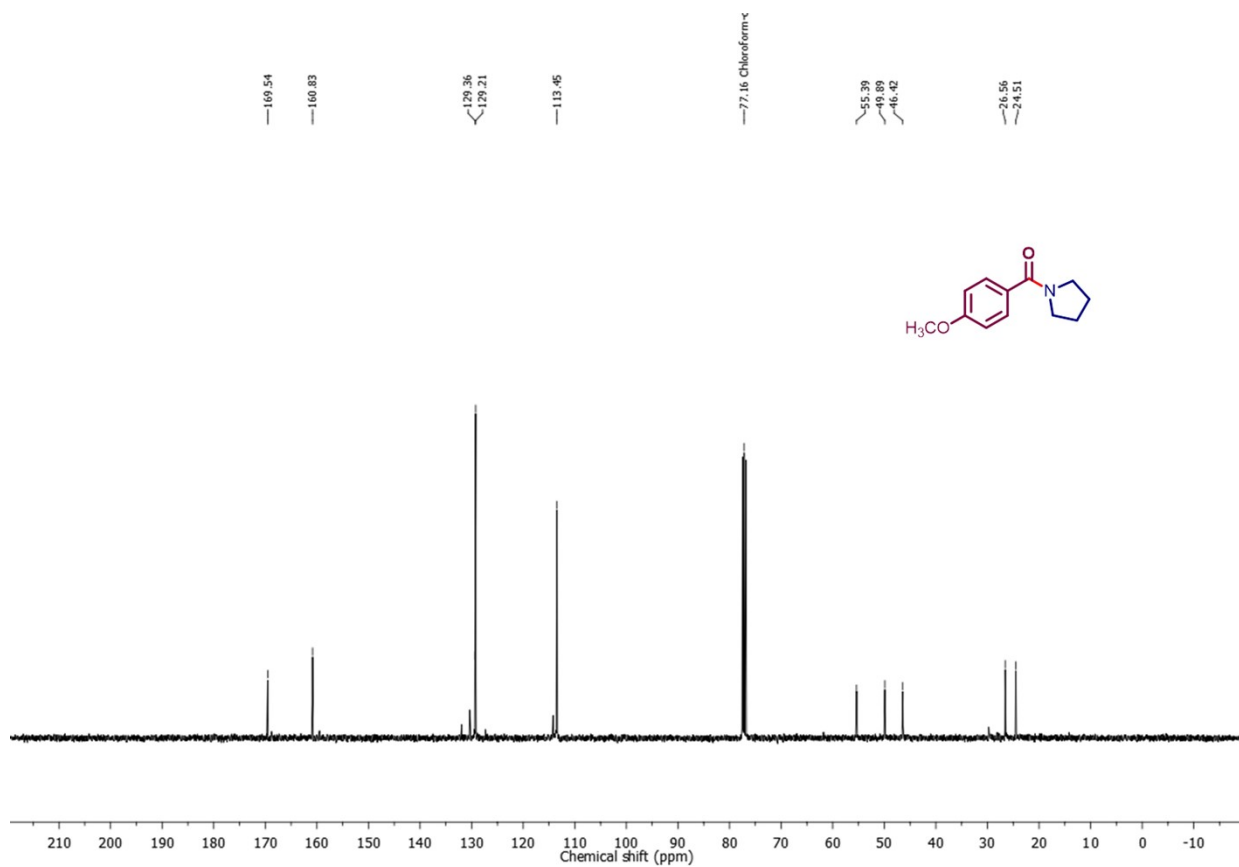
<sup>1</sup>H NMR spectrum (400 MHz) of **3da** in CDCl<sub>3</sub>.



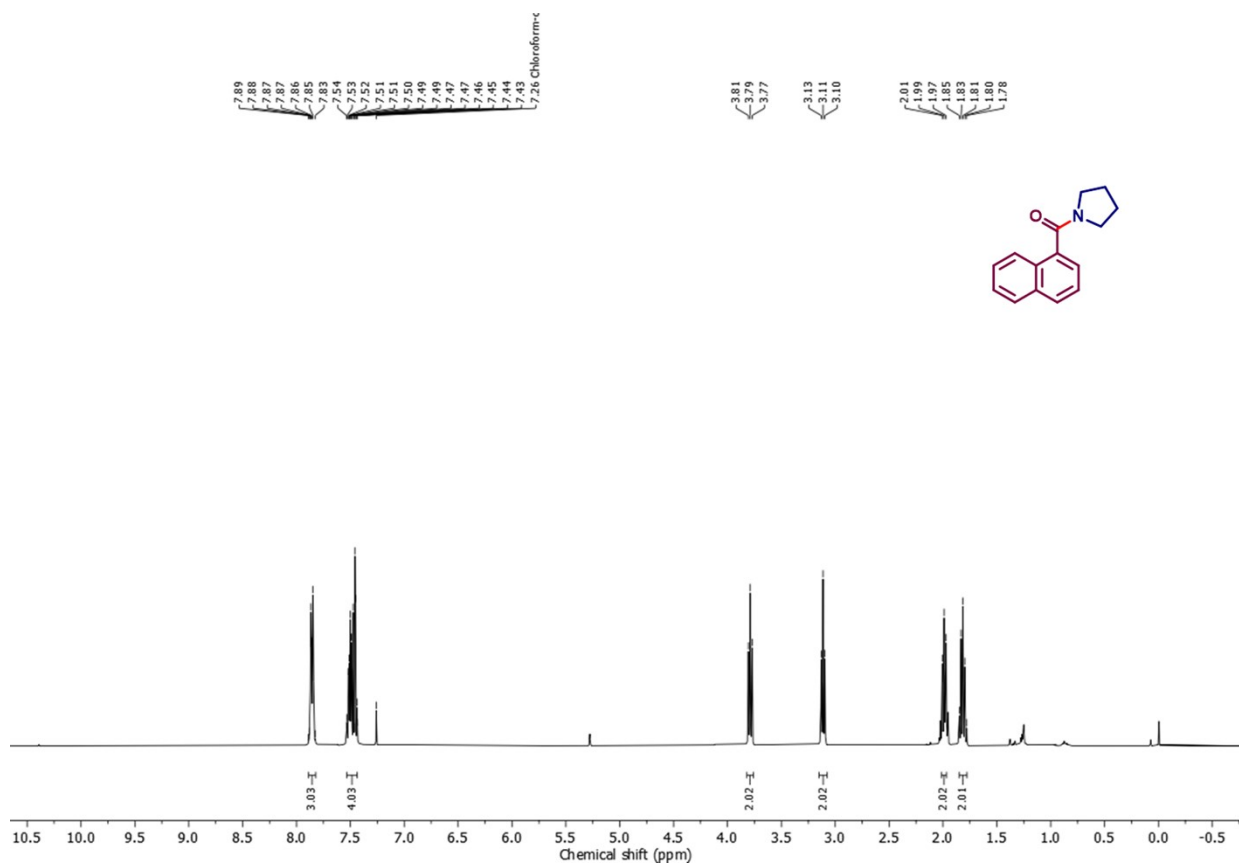
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3da** in  $\text{CDCl}_3$ .



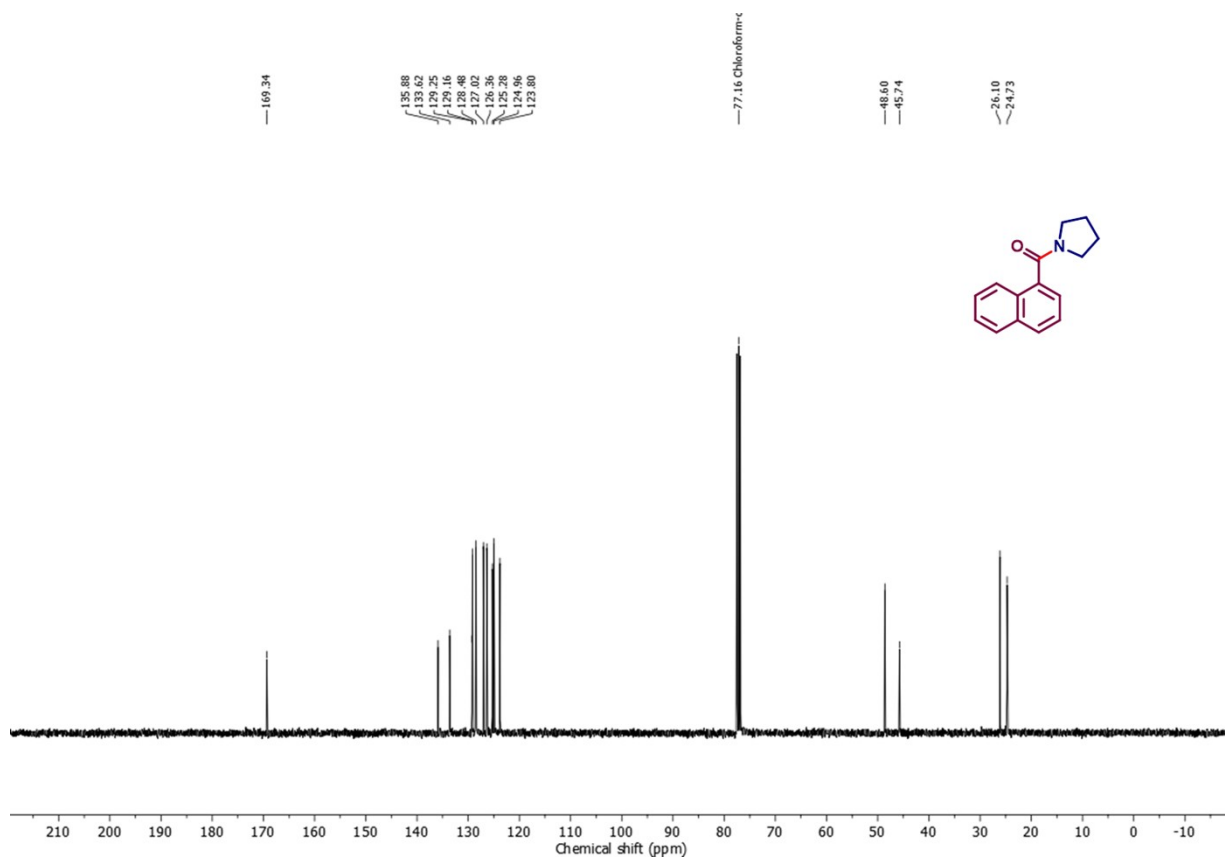
$^1\text{H}$  NMR spectrum (400 MHz) of **3ea** in  $\text{CDCl}_3$ .



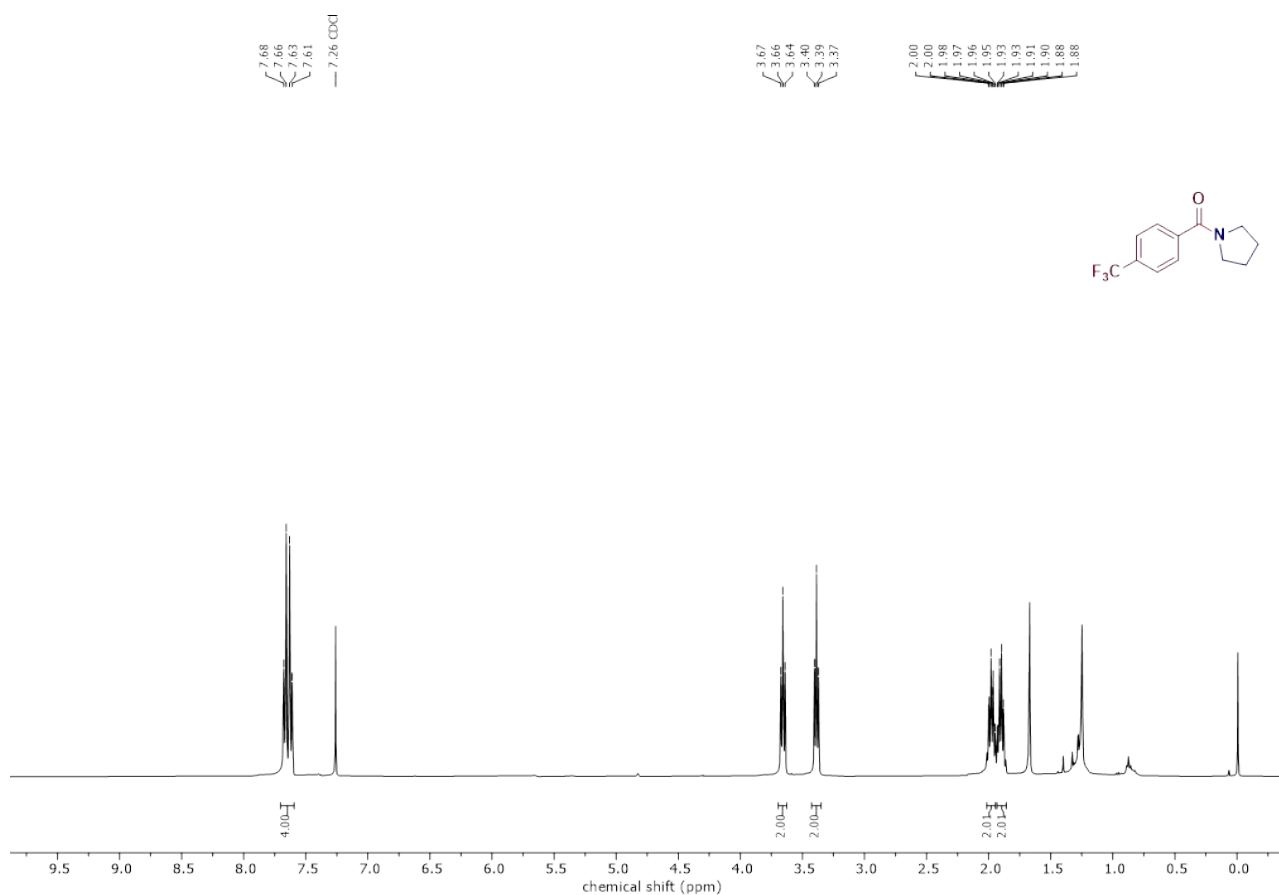
<sup>13</sup>C NMR spectrum (100 MHz) of **3ea** in CDCl<sub>3</sub>.



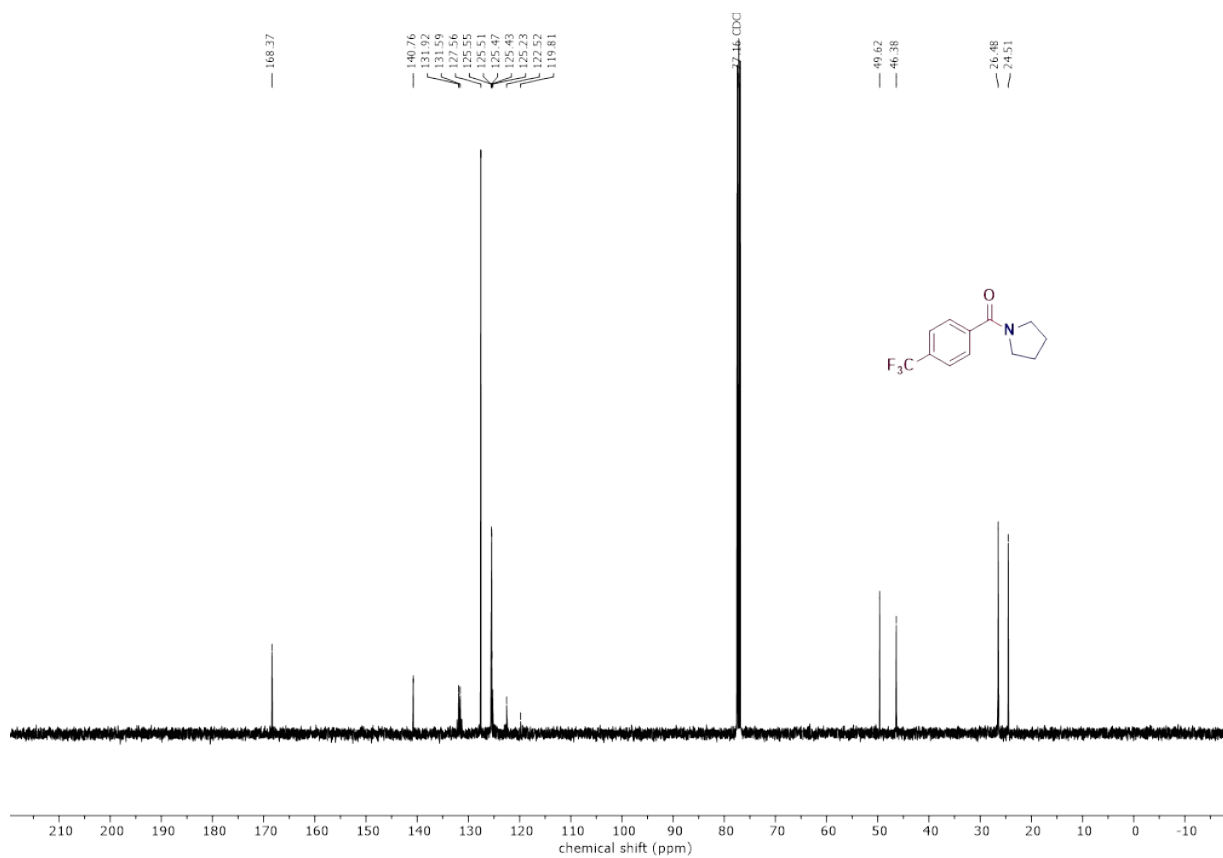
<sup>1</sup>H NMR spectrum (400 MHz) of **3fa** in CDCl<sub>3</sub>.



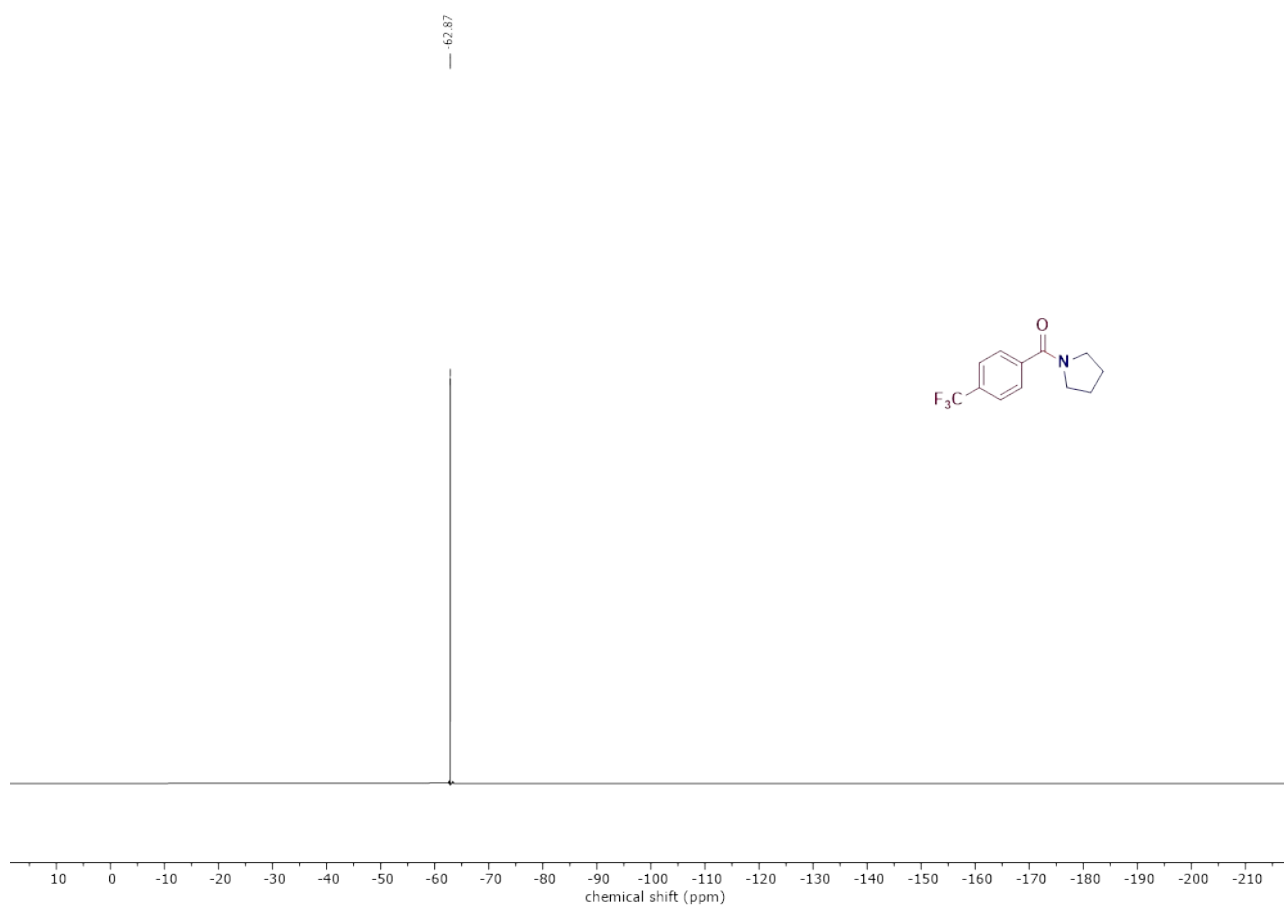
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3fa** in  $\text{CDCl}_3$ .



$^1\text{H}$  NMR spectrum (400 MHz) of **3ga** in  $\text{CDCl}_3$ .

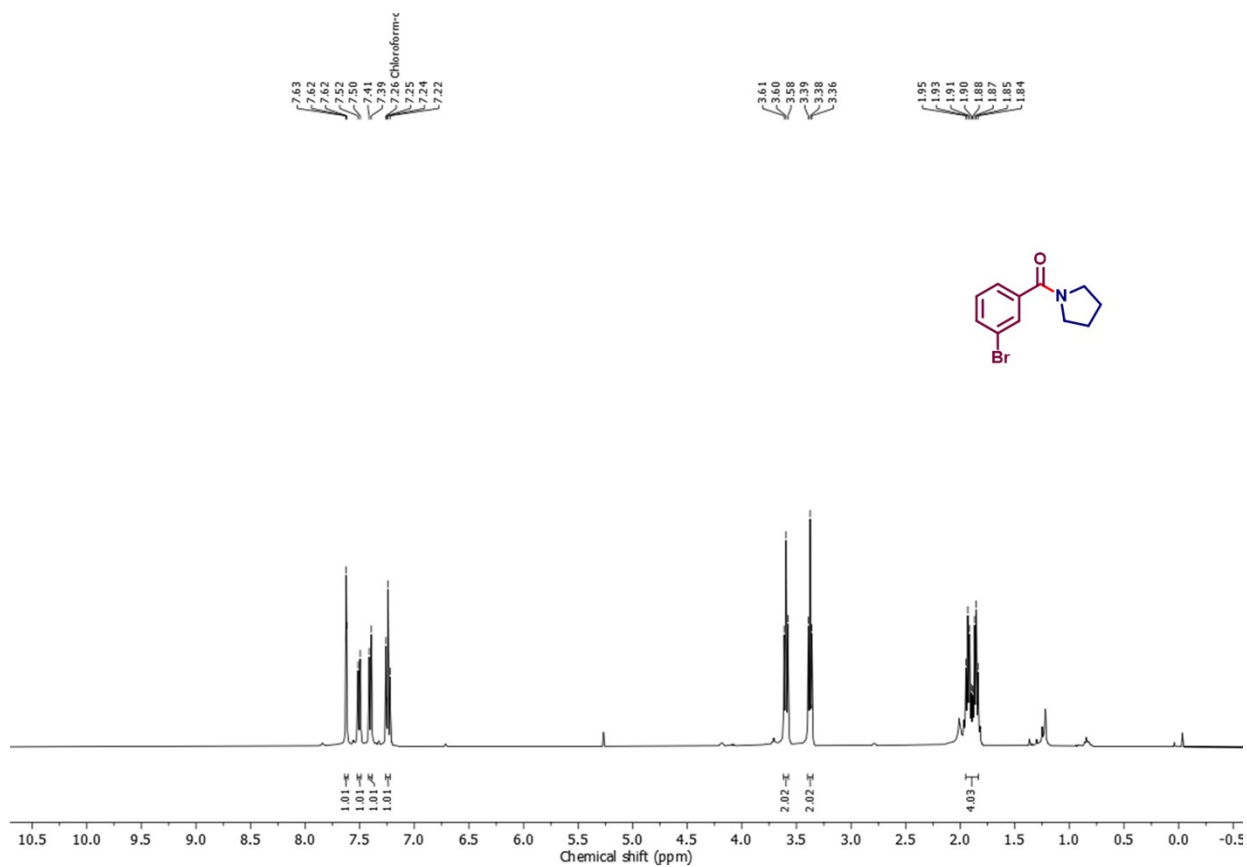


<sup>13</sup>C NMR spectrum (100 MHz) of **3ga** in CDCl<sub>3</sub>.

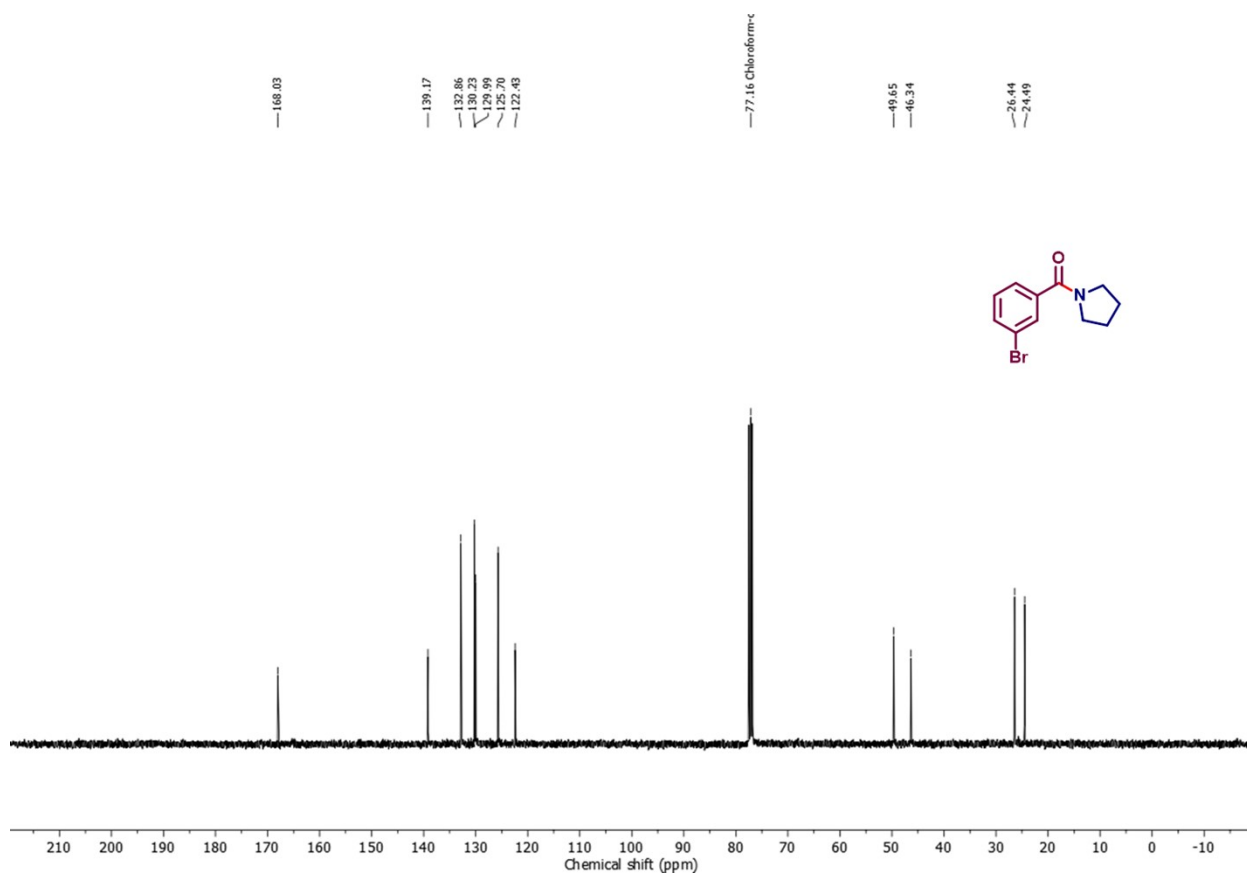


<sup>19</sup>F NMR spectrum (376 MHz) of **3ga** in CDCl<sub>3</sub>.

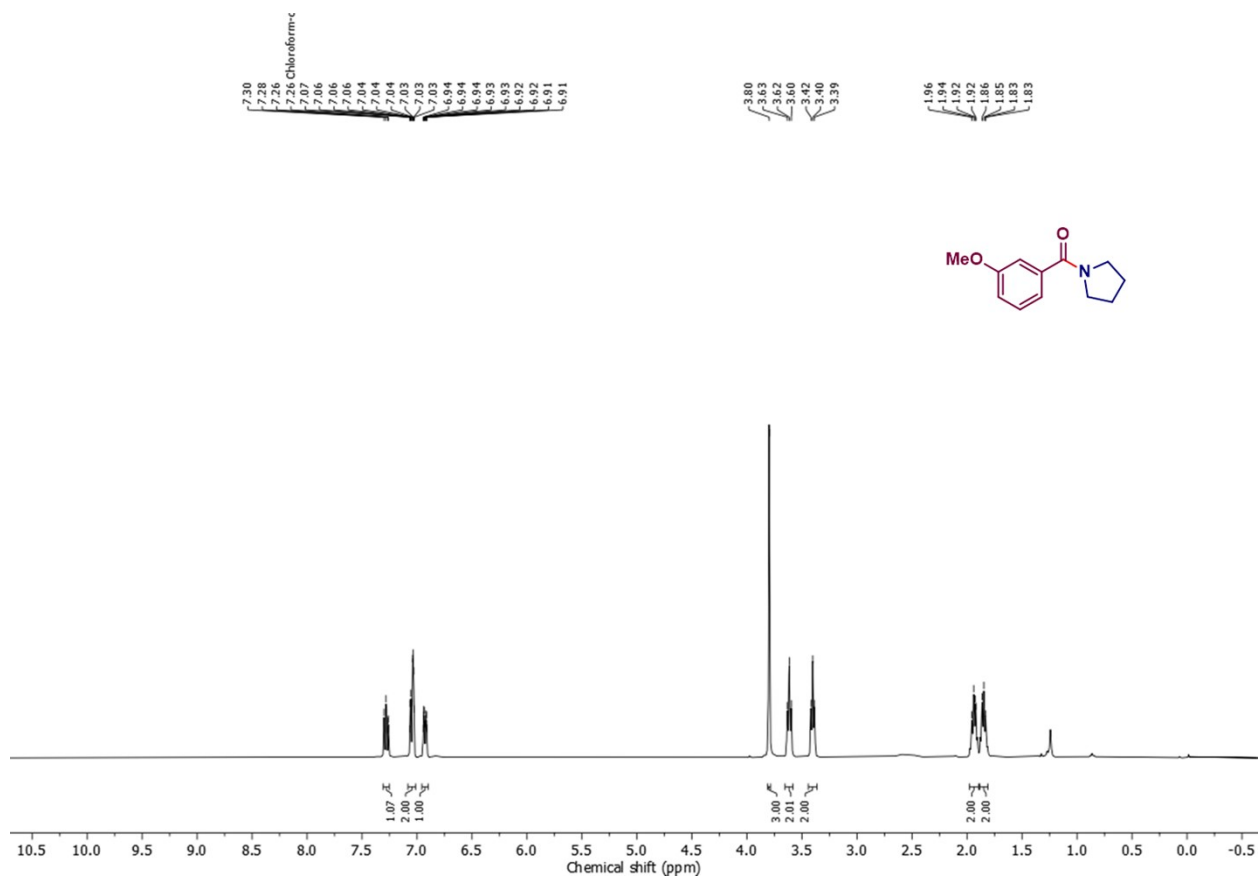




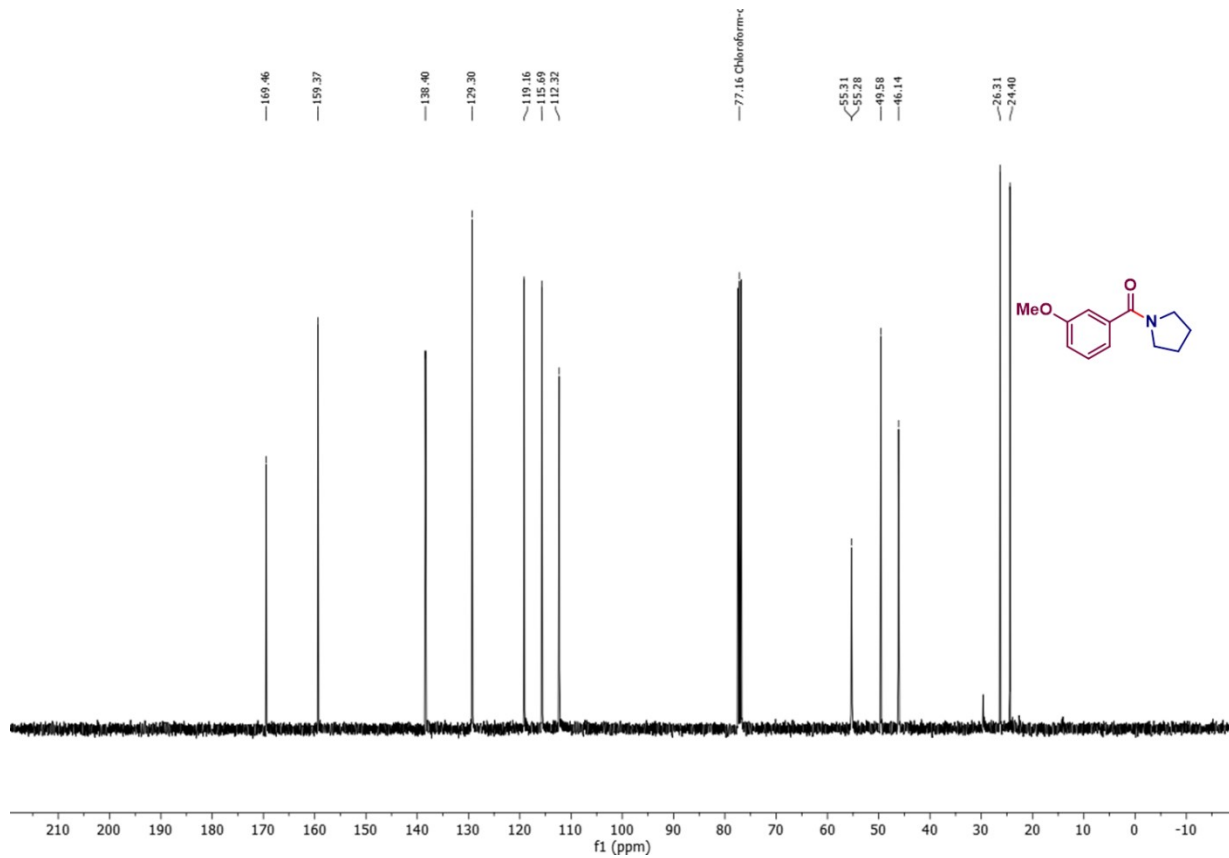
<sup>1</sup>H NMR spectrum (400 MHz) of **3ha** in CDCl<sub>3</sub>.



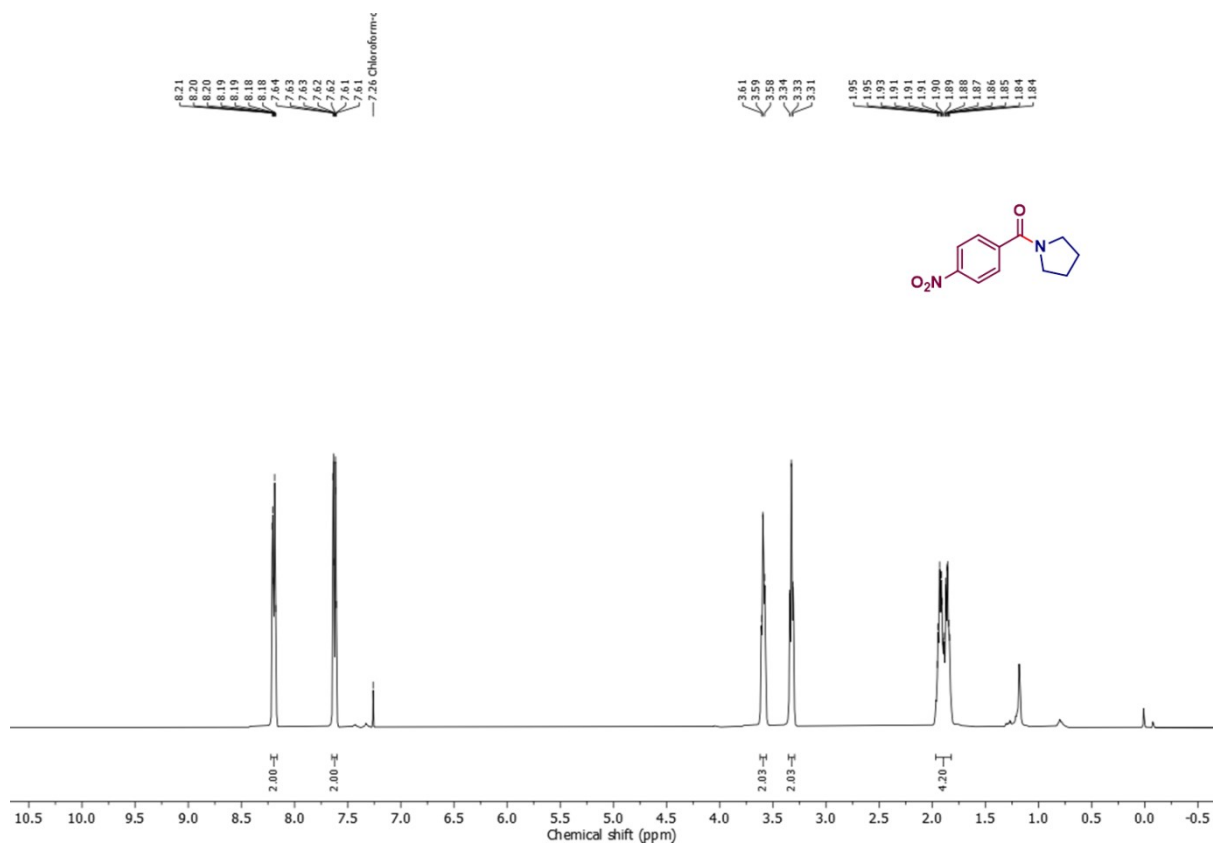
<sup>13</sup>C NMR spectrum (100 MHz) of **3ha** in CDCl<sub>3</sub>.



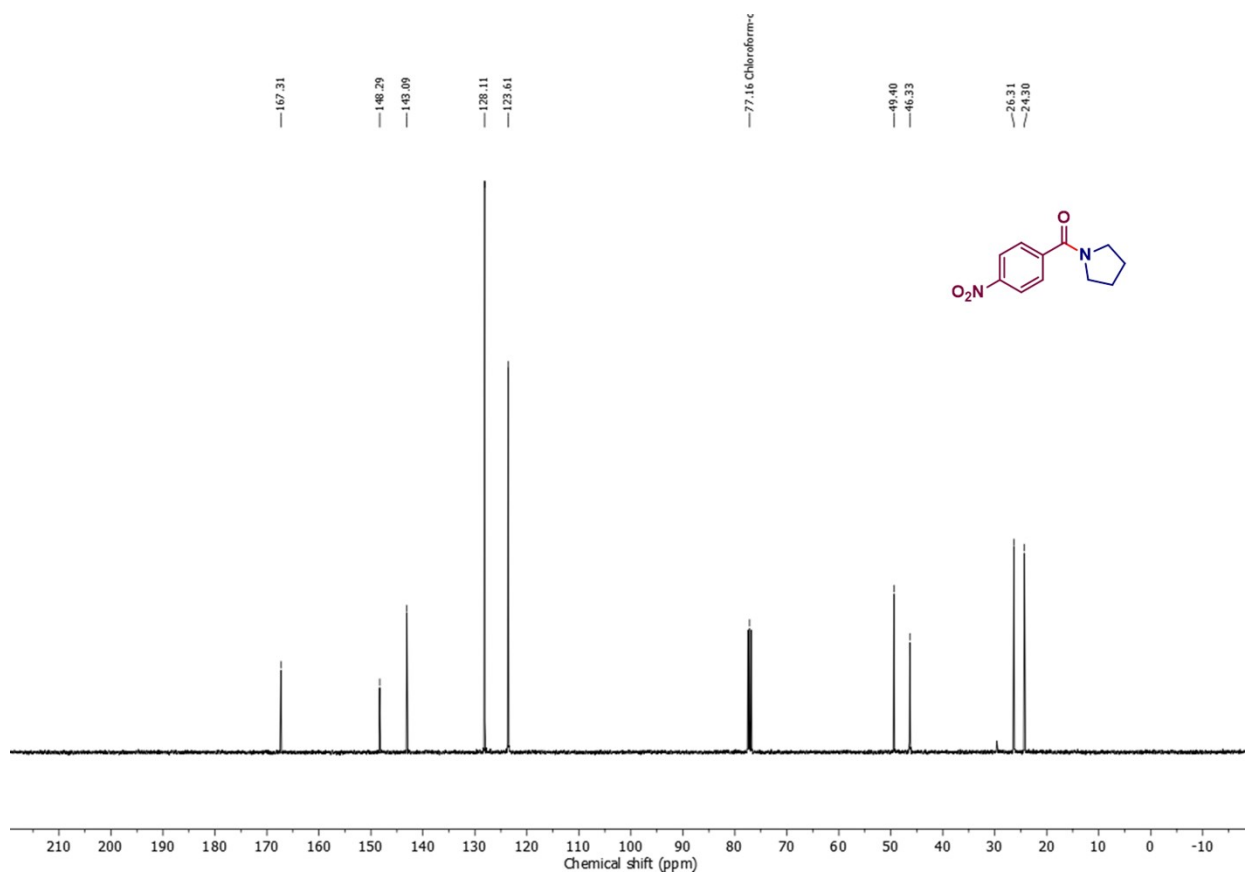
<sup>1</sup>H NMR spectrum (400 MHz) of **3ia** in CDCl<sub>3</sub>.



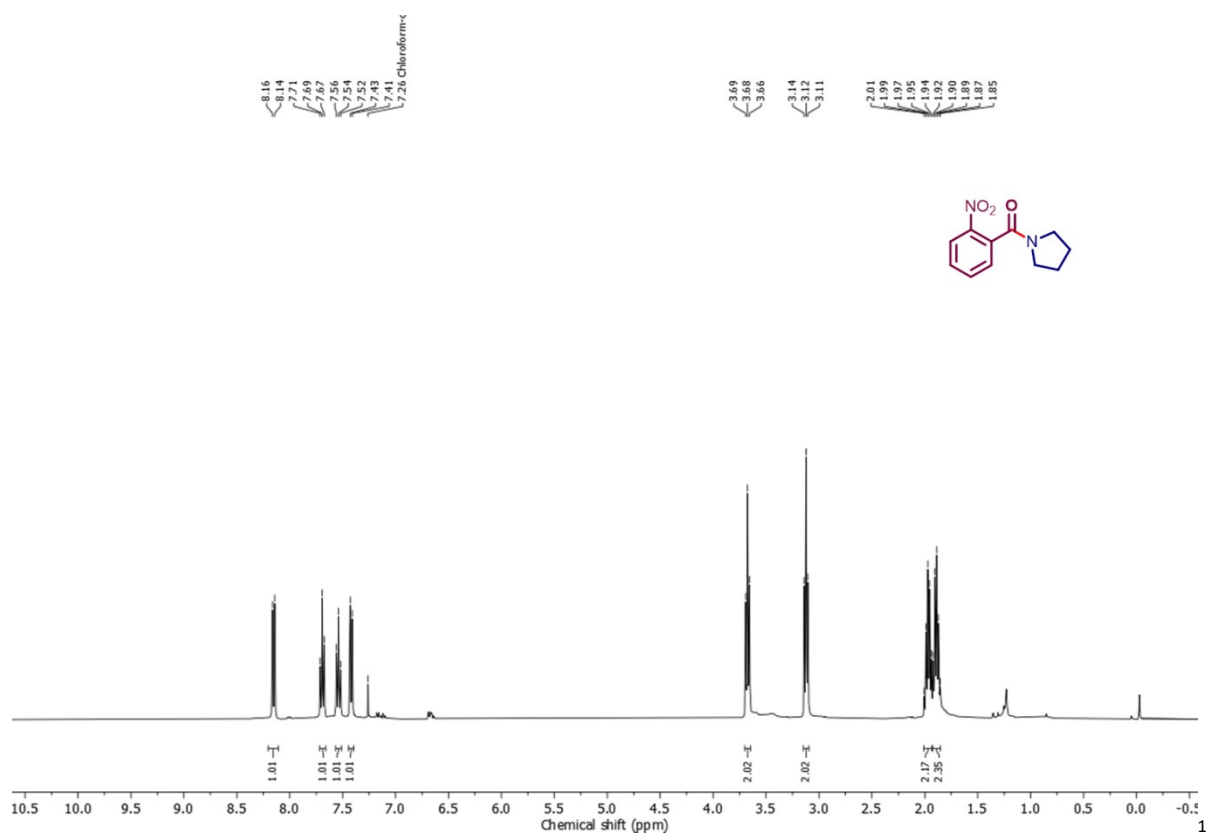
<sup>13</sup>C NMR spectrum (100 MHz) of **3ia** in CDCl<sub>3</sub>.



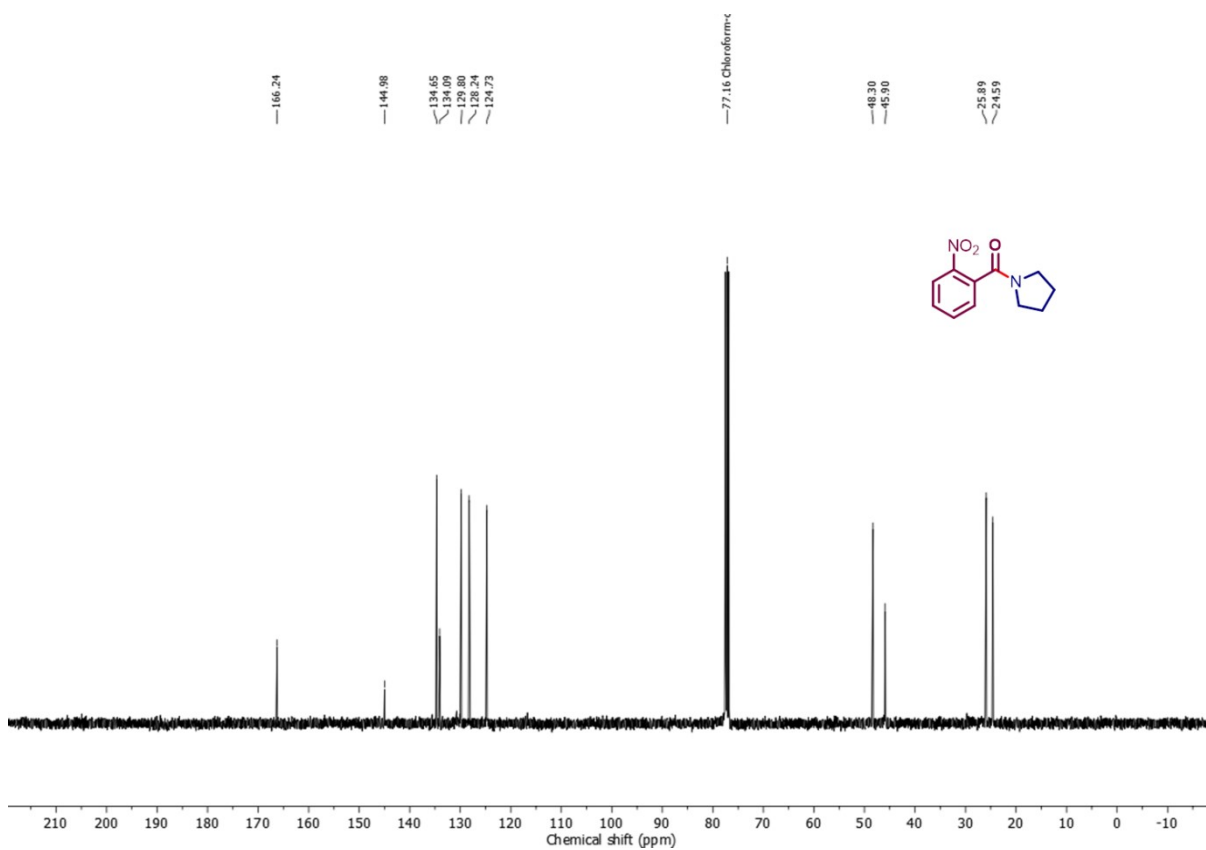
<sup>1</sup>H NMR spectrum (400 MHz) of **3ja** in CDCl<sub>3</sub>.



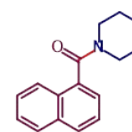
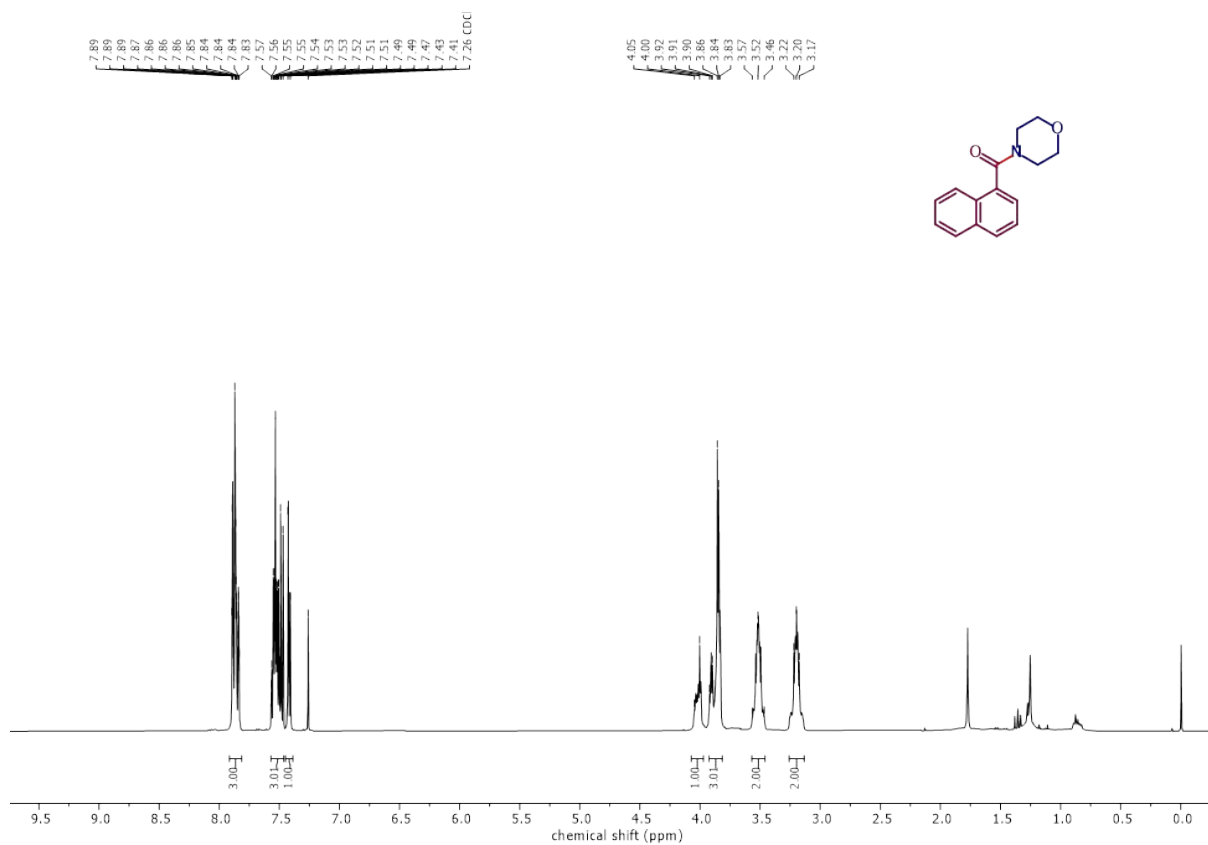
<sup>13</sup>C NMR spectrum (100 MHz) of **3ja** in CDCl<sub>3</sub>.



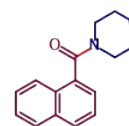
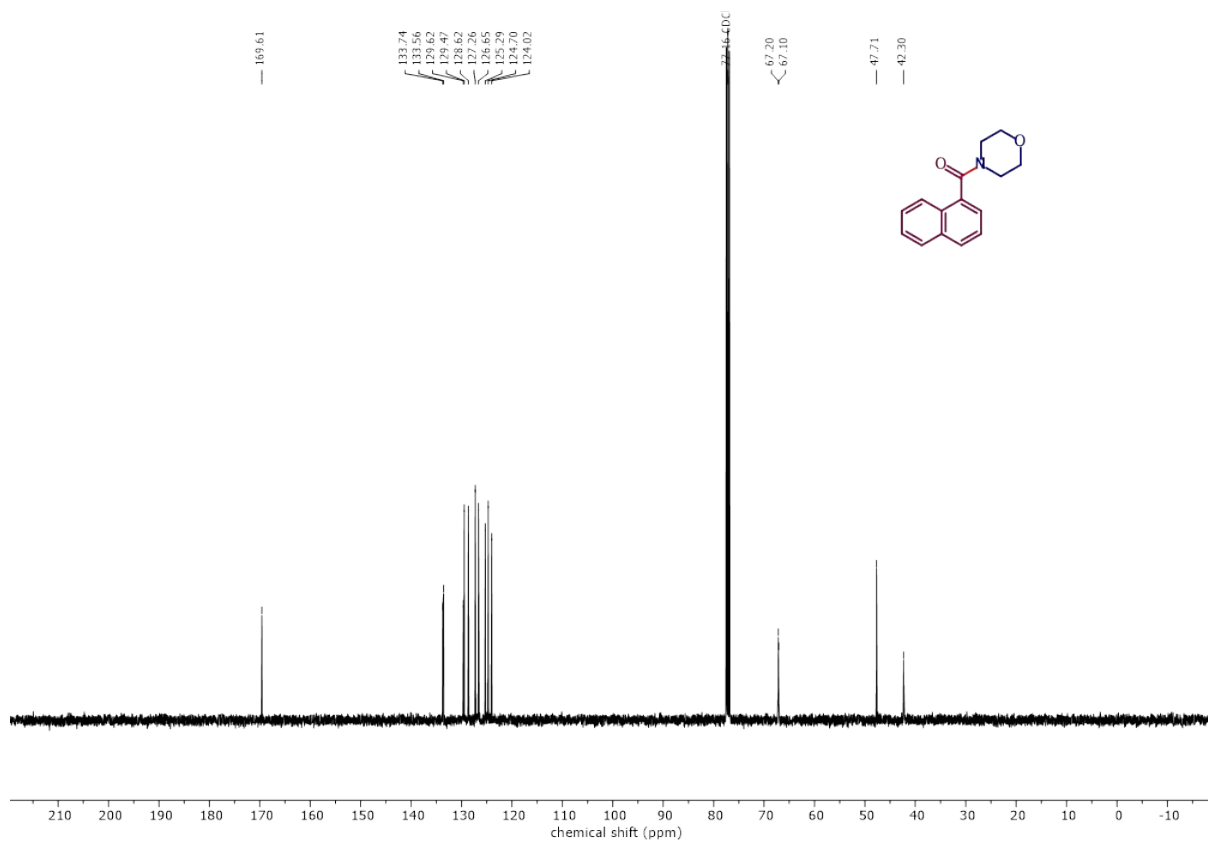
$^1\text{H}$  NMR spectrum (400 MHz) of **3ka** in  $\text{CDCl}_3$ .



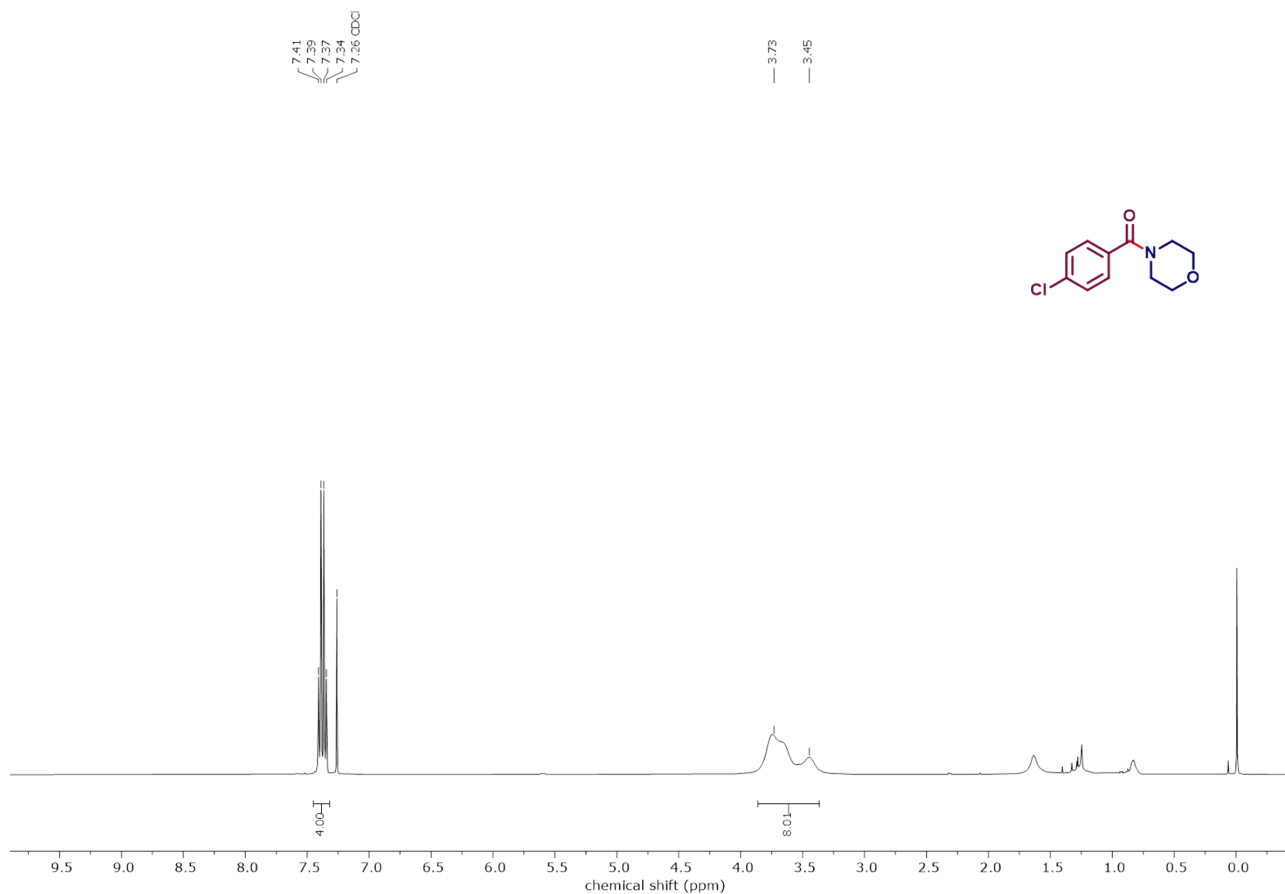
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ka** in  $\text{CDCl}_3$ .



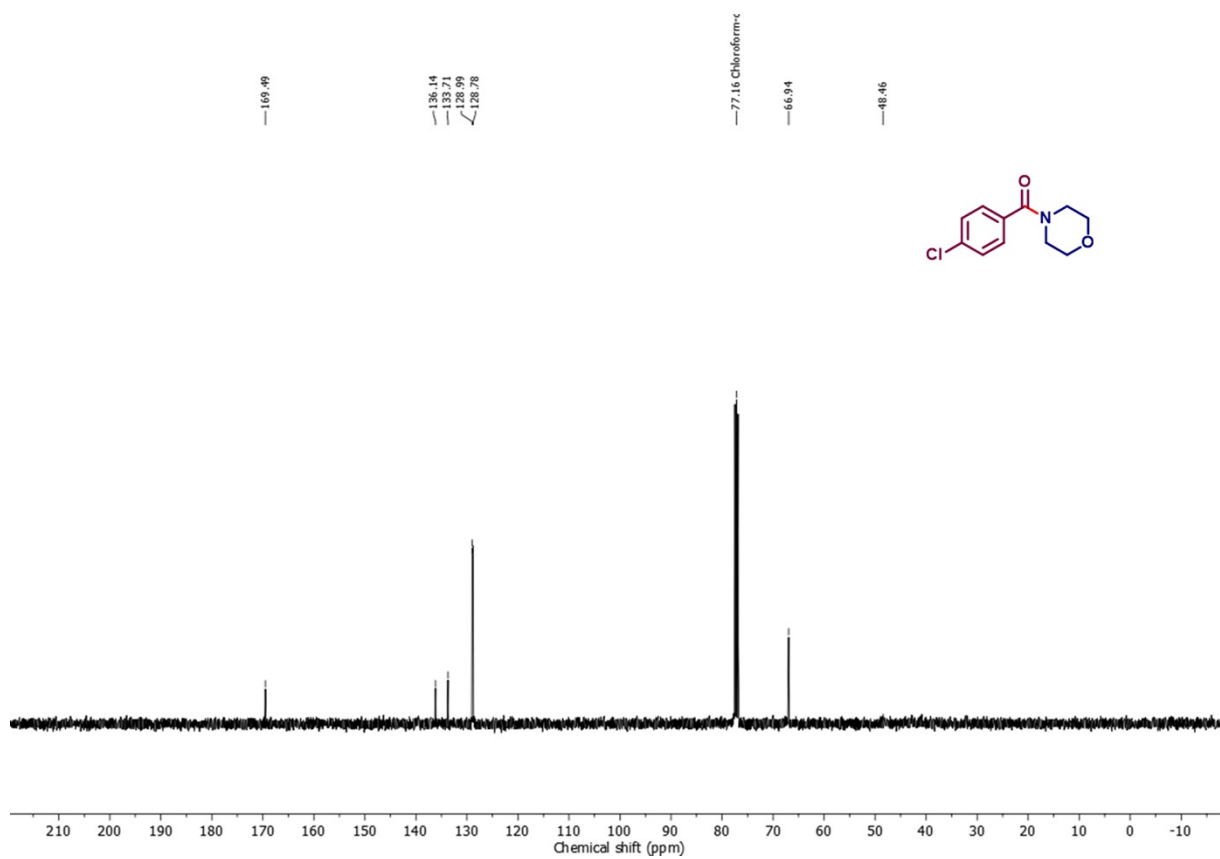
<sup>1</sup>H NMR spectrum (400 MHz) of **3fp** in CDCl<sub>3</sub>.



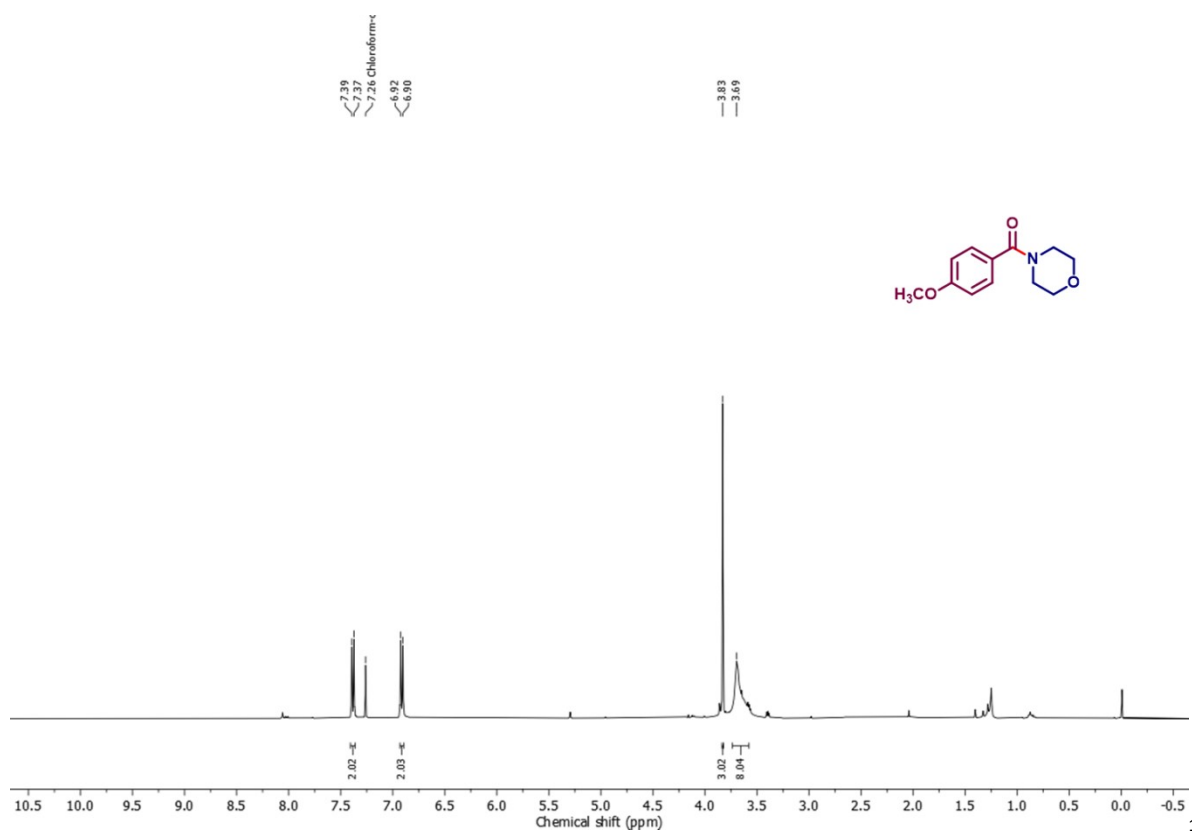
<sup>13</sup>C NMR spectrum (100 MHz) of **3fp** in CDCl<sub>3</sub>.



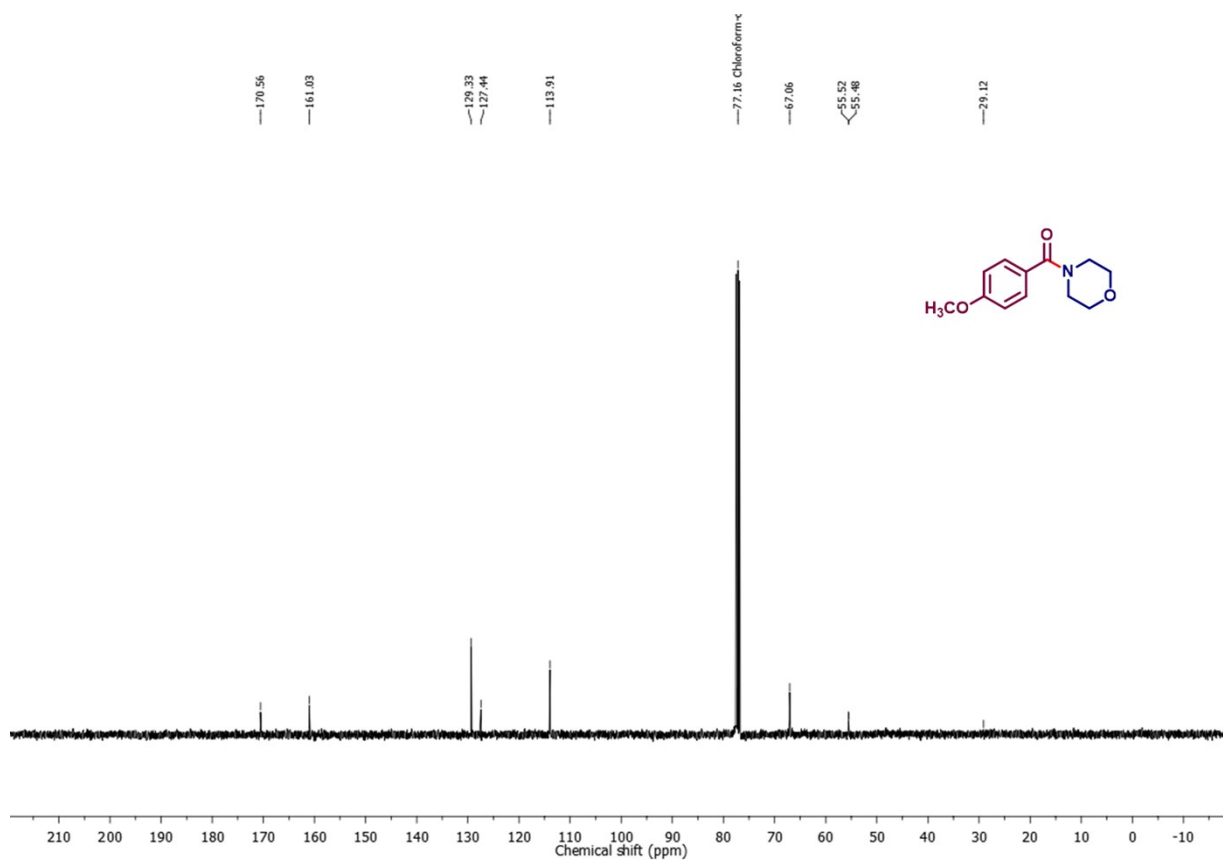
$^1\text{H}$  NMR spectrum (400 MHz) of **3cp** in  $\text{CDCl}_3$ .



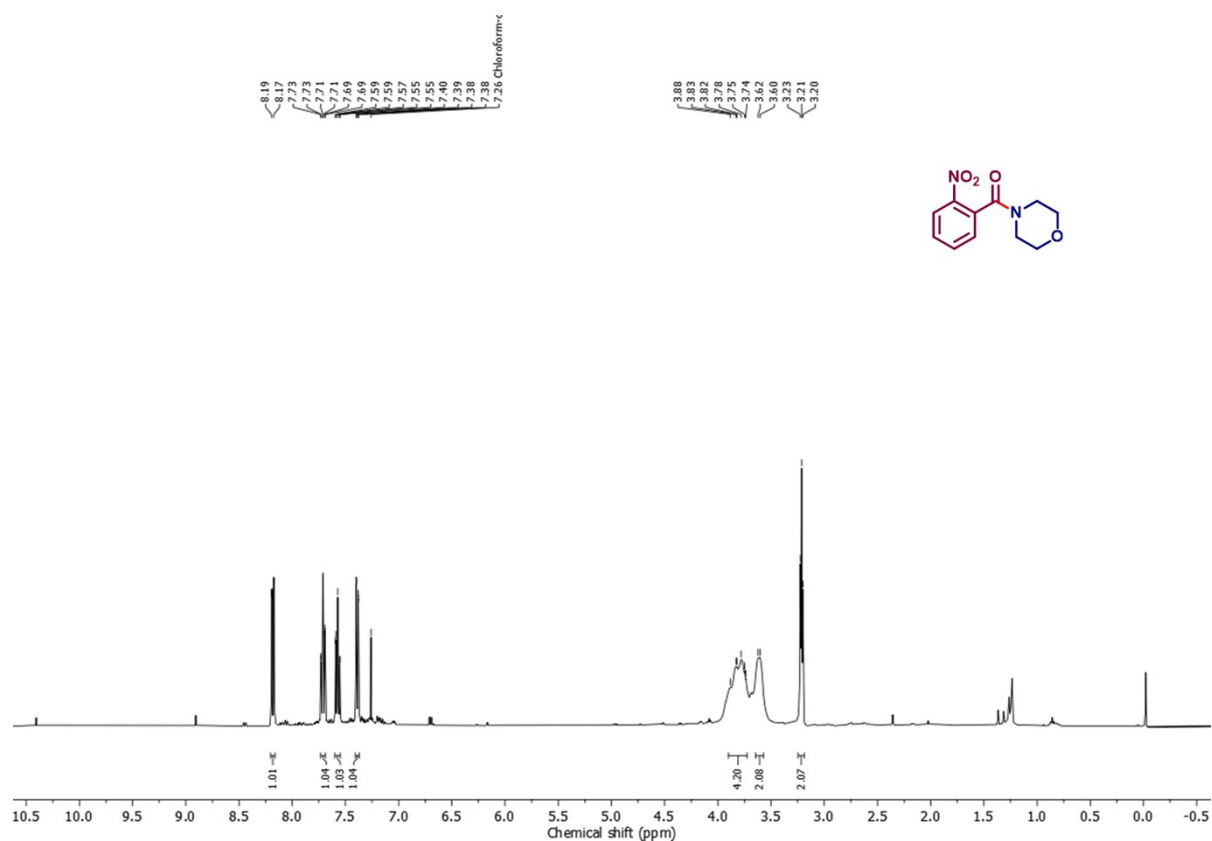
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3cp** in  $\text{CDCl}_3$ .



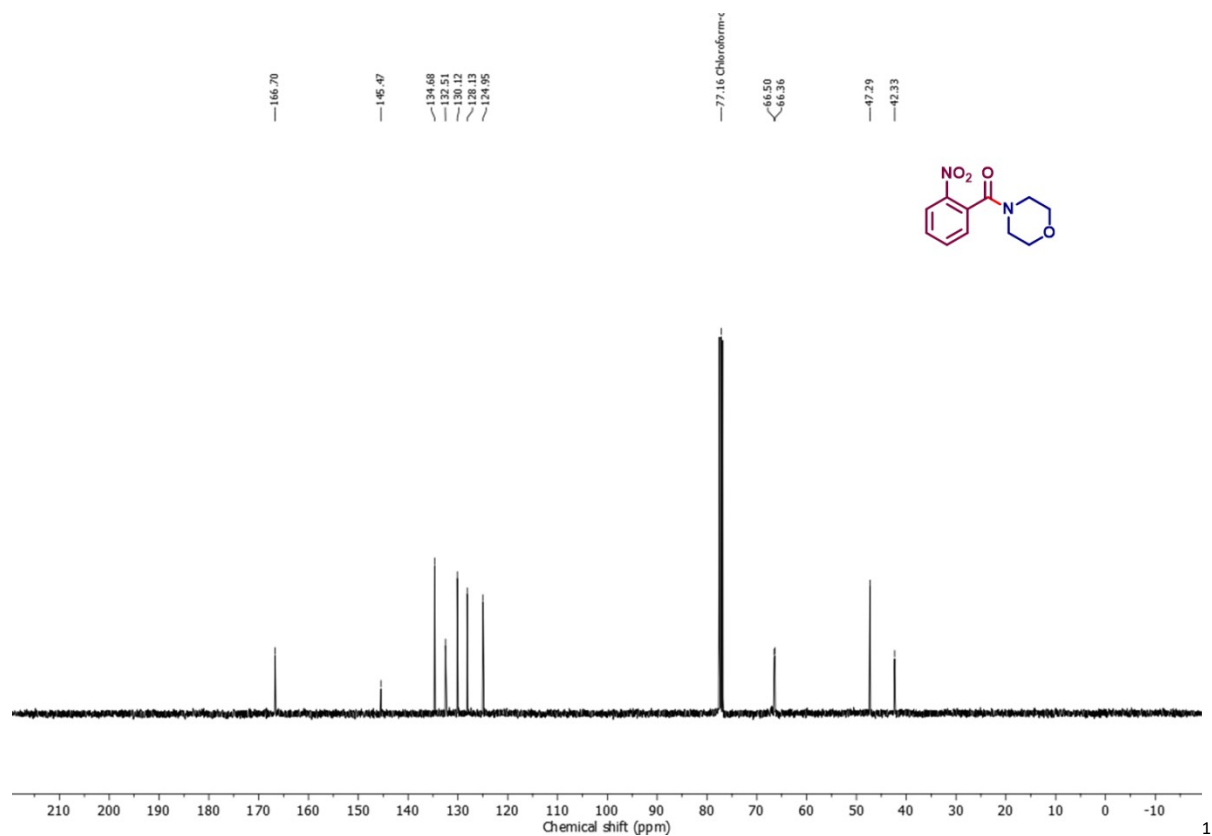
$^1\text{H}$  NMR spectrum (400 MHz) of **3ep** in  $\text{CDCl}_3$ .



$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ep** in  $\text{CDCl}_3$ .

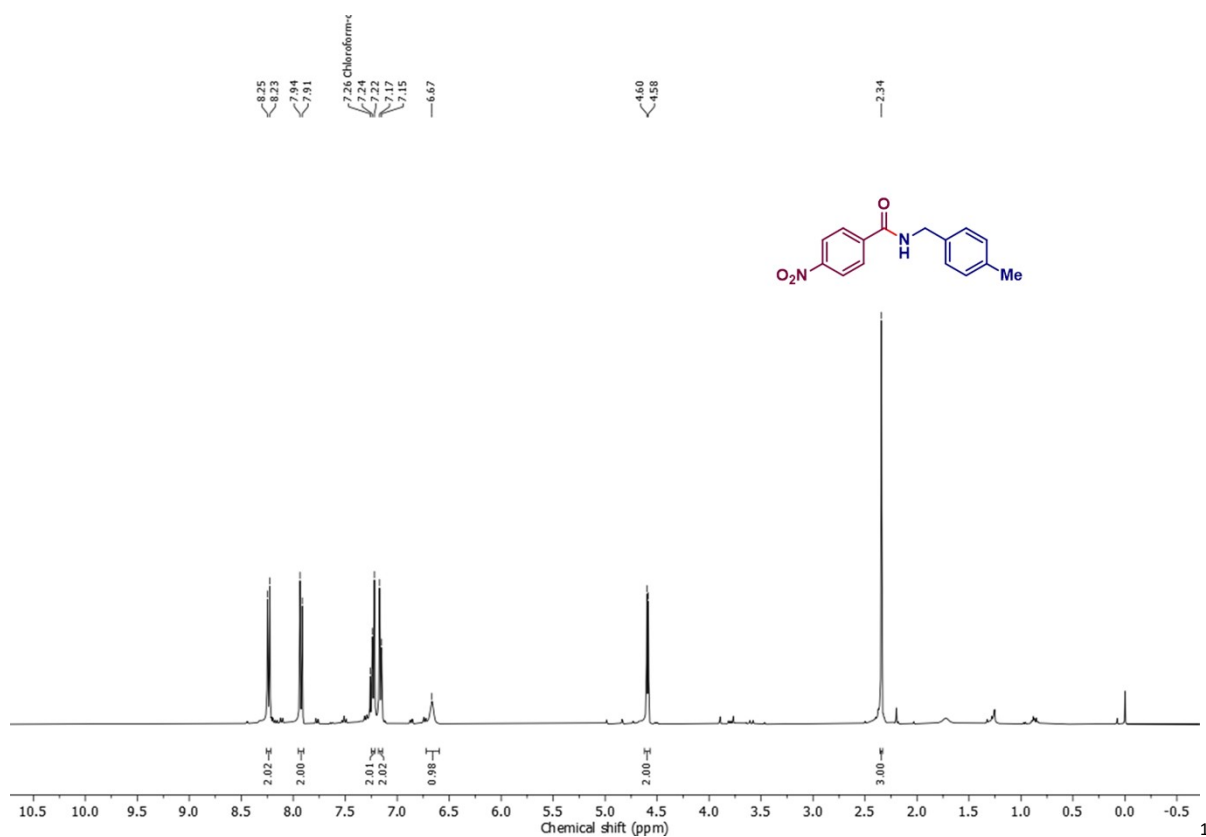


<sup>1</sup>H NMR spectrum (400 MHz) of **3kp** in CDCl<sub>3</sub>.

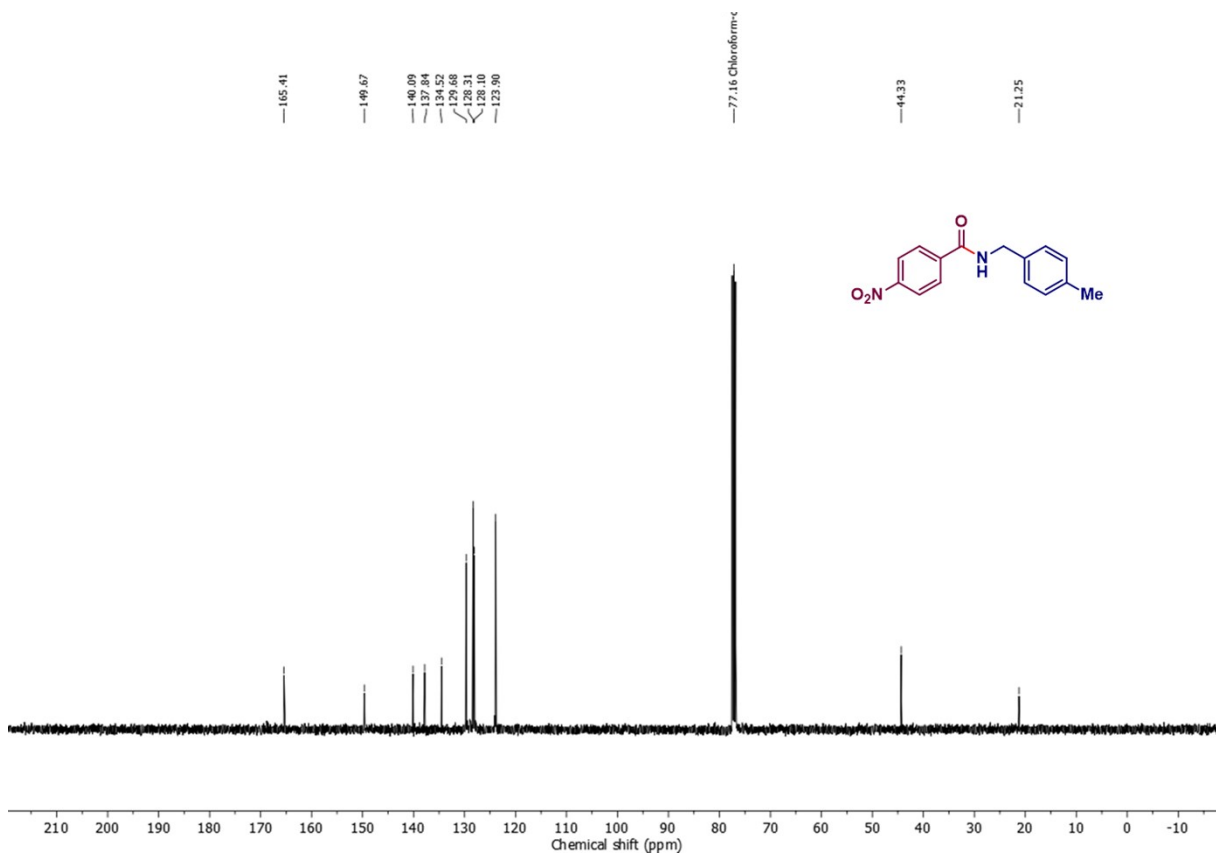


<sup>13</sup>C NMR spectrum (100 MHz) of **3kp** in CDCl<sub>3</sub>.

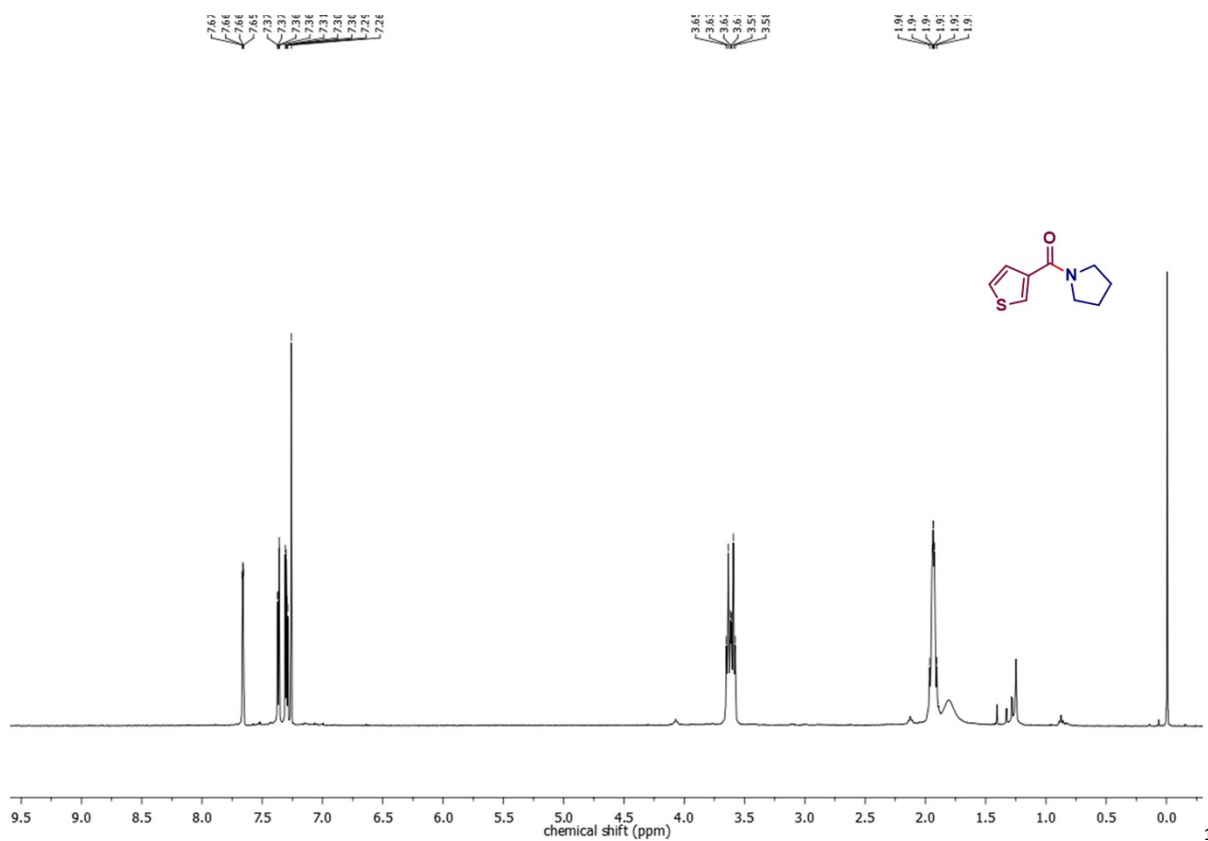




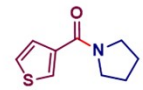
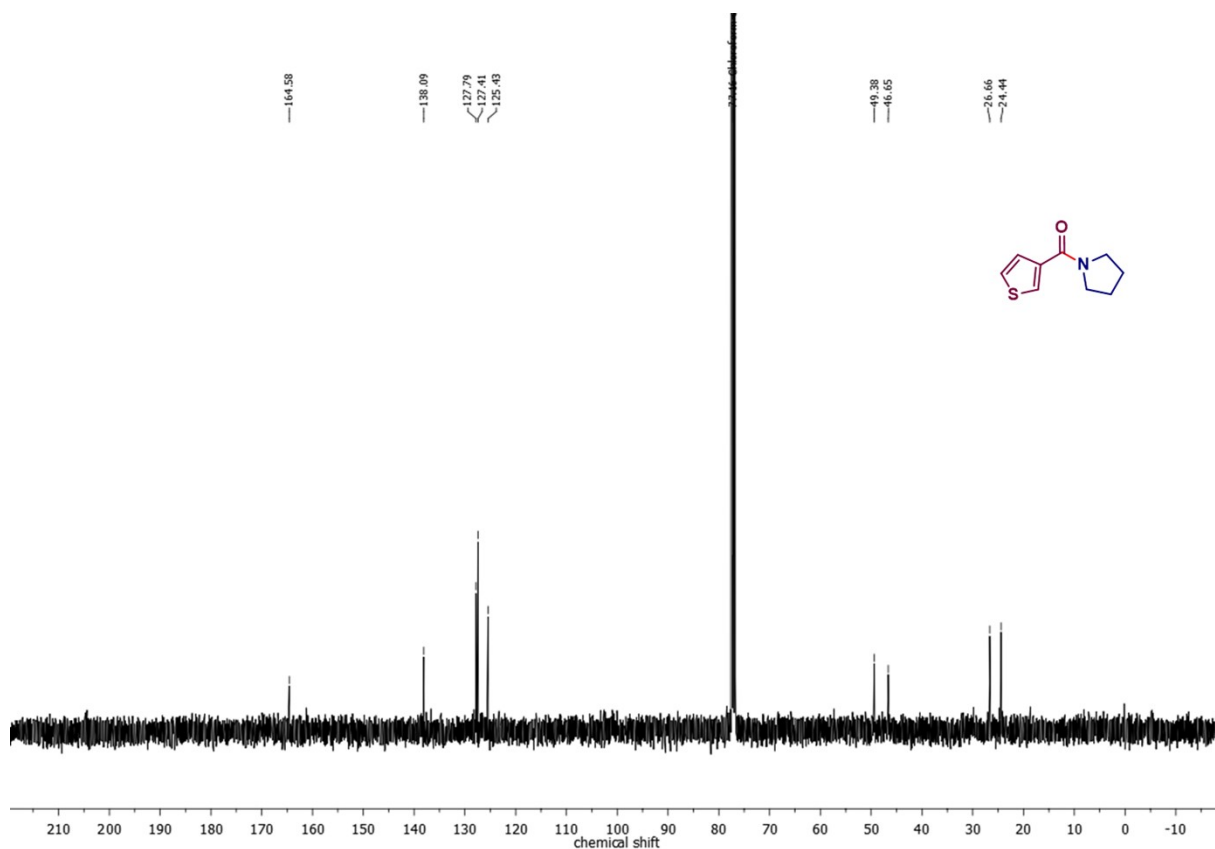
<sup>1</sup>H NMR spectrum (400 MHz) of **31q** in CDCl<sub>3</sub>.



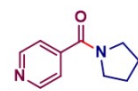
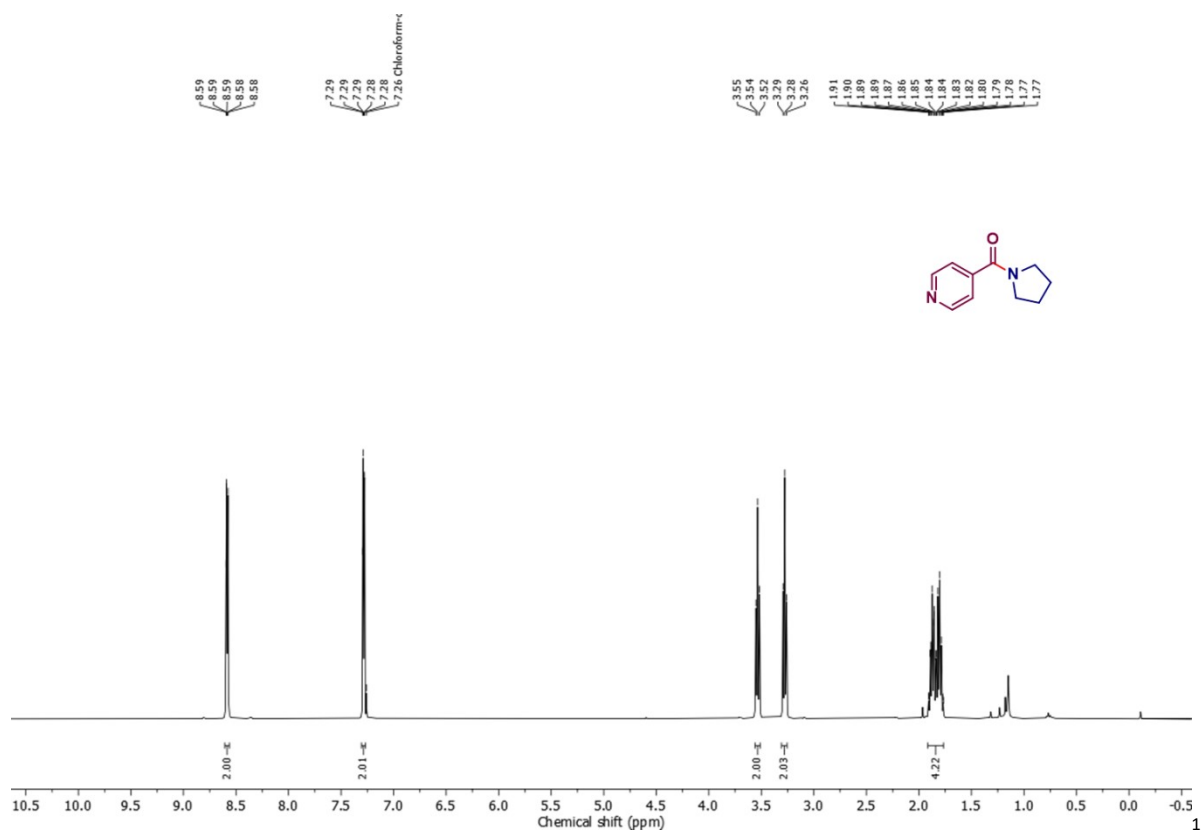
<sup>13</sup>C NMR spectrum (100 MHz) of **31q** in CDCl<sub>3</sub>.



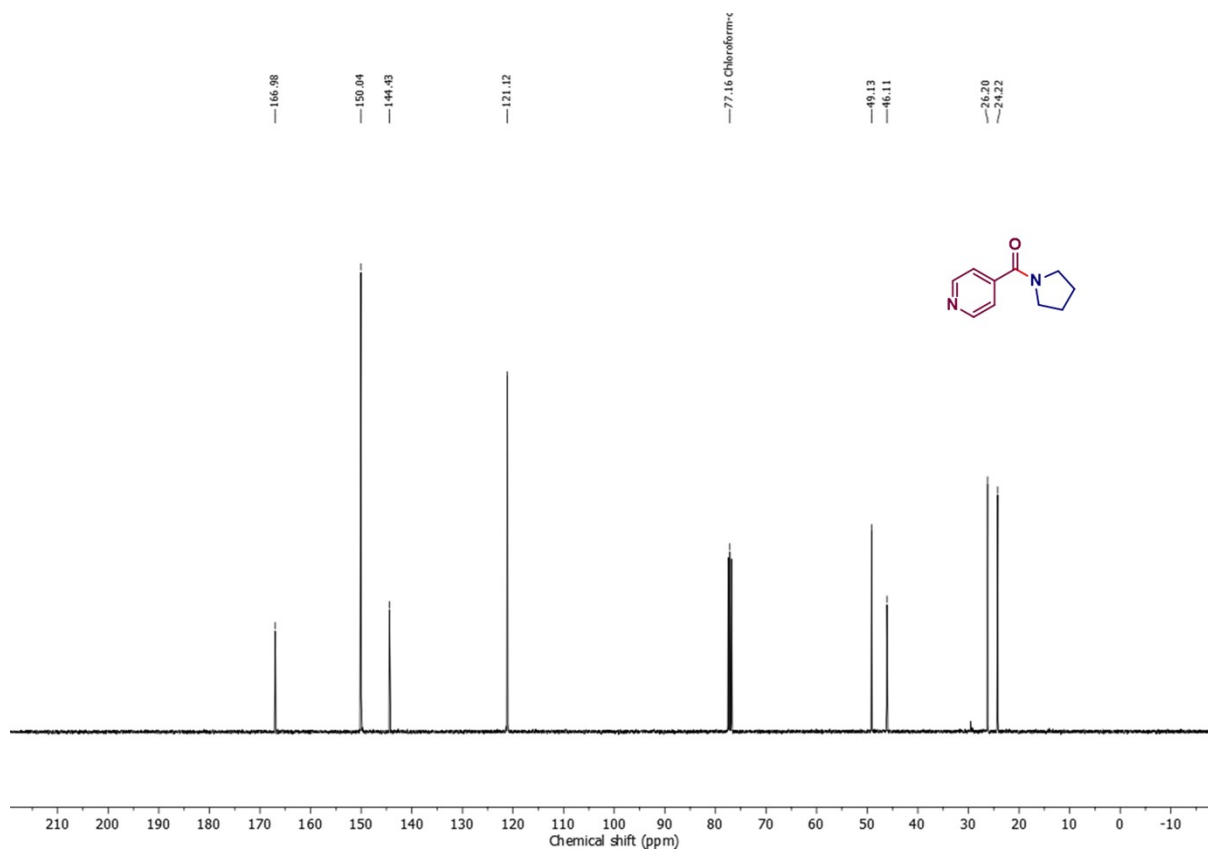
$^1\text{H}$  NMR spectrum (400 MHz) of **3pa** in  $\text{CDCl}_3$ .



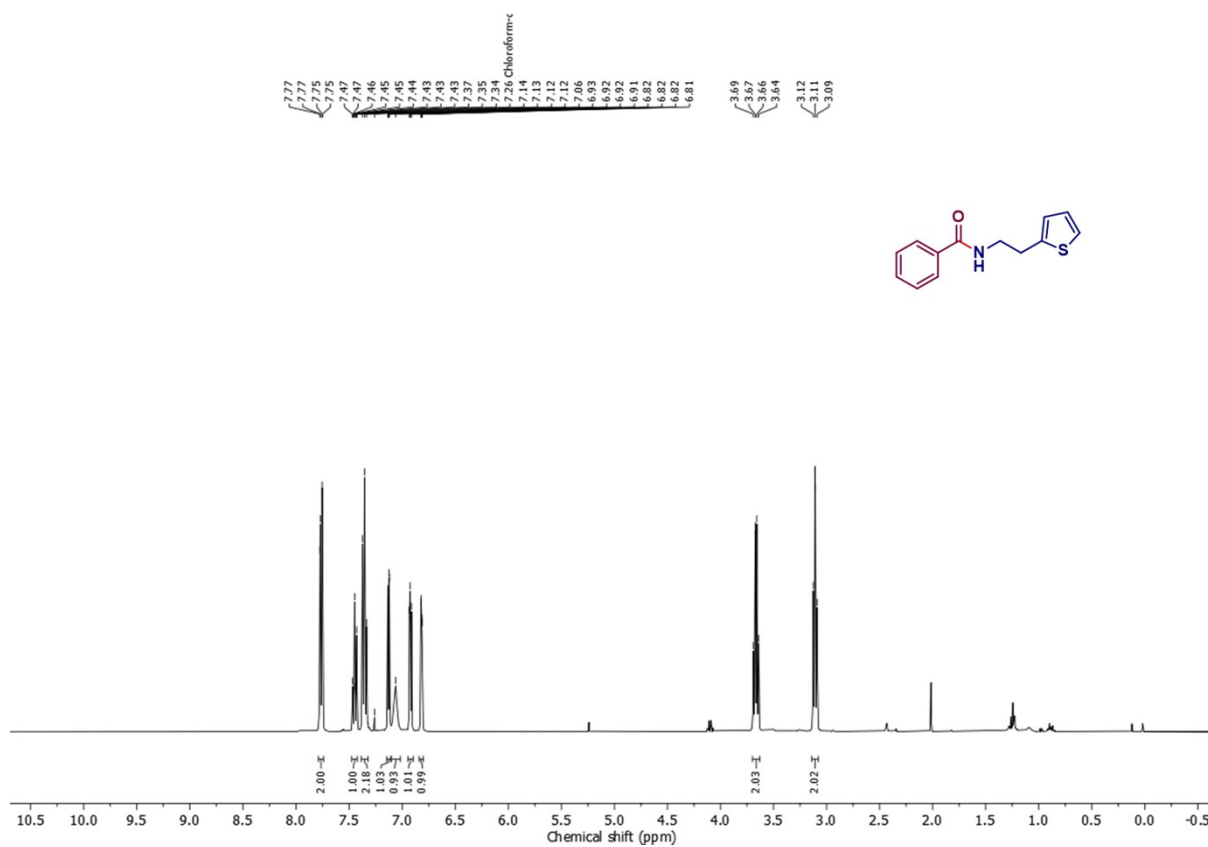
<sup>13</sup>C NMR spectrum (100 MHz) of **3pa** in CDCl<sub>3</sub>.



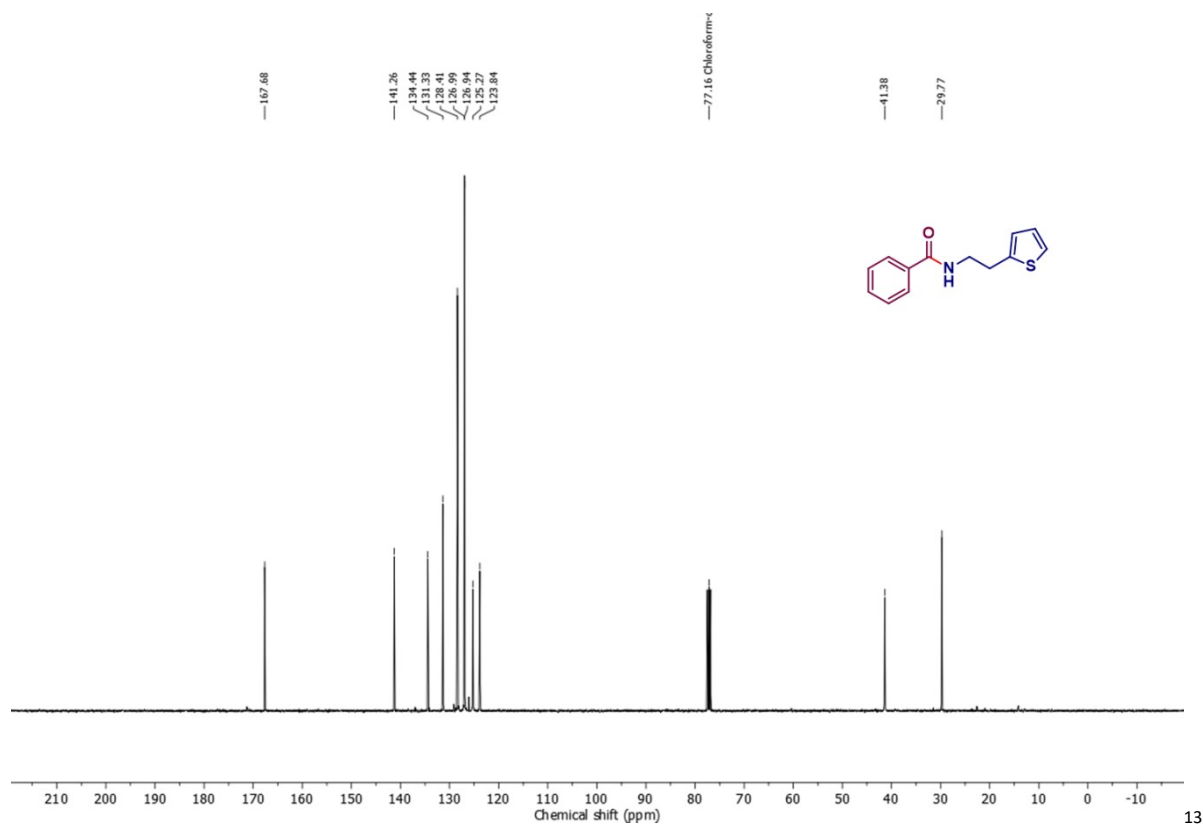
<sup>1</sup>H NMR spectrum (400 MHz) of **3qa** in CDCl<sub>3</sub>.



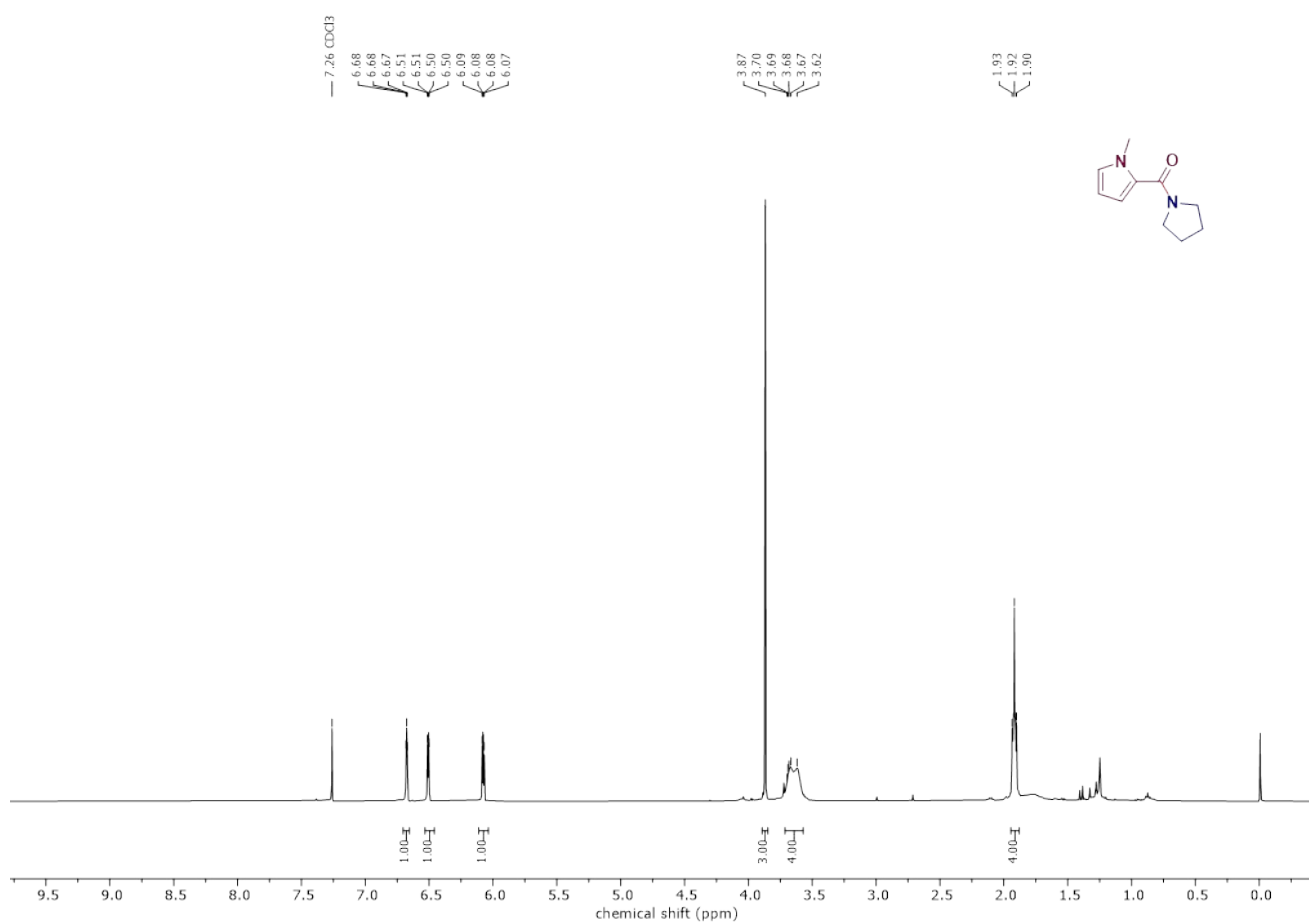
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3qa** in  $\text{CDCl}_3$ .



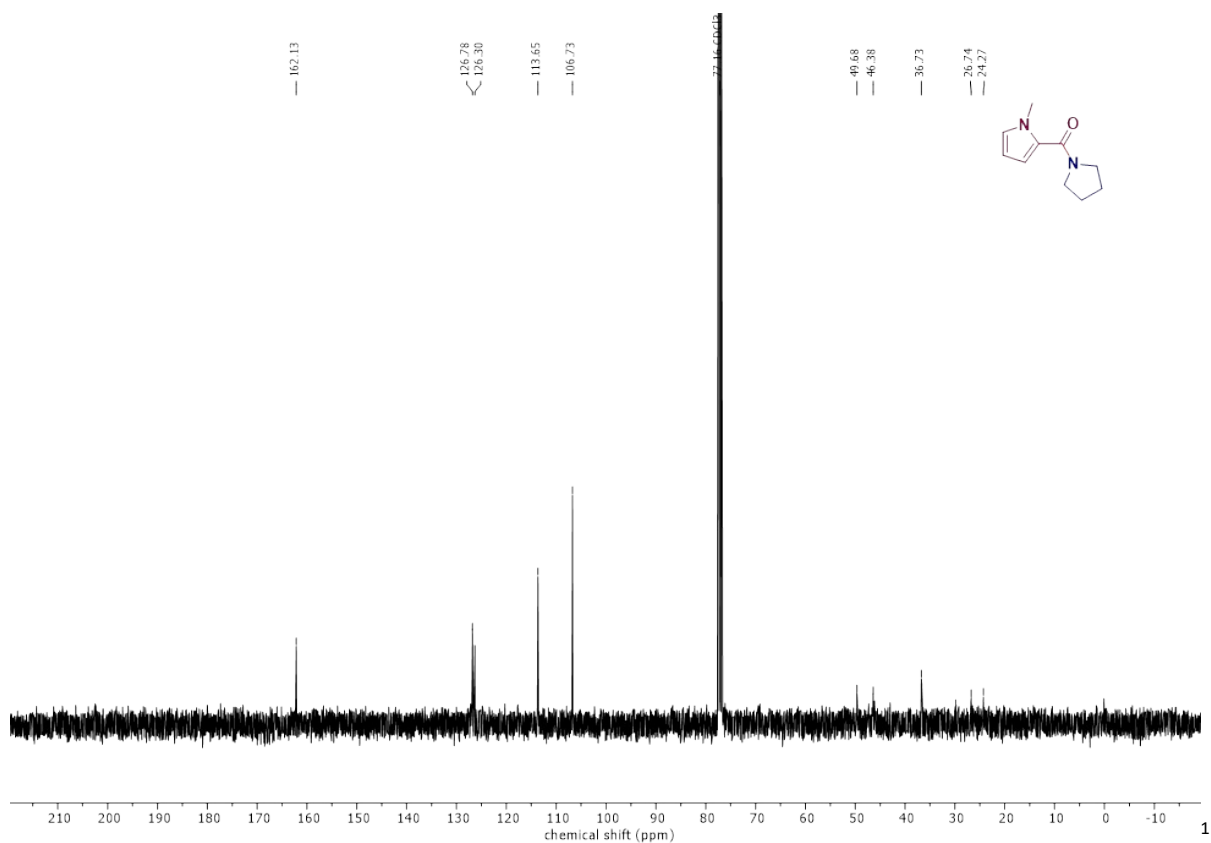
$^1\text{H}$  NMR spectrum (400 MHz) of **3ar** in  $\text{CDCl}_3$ .



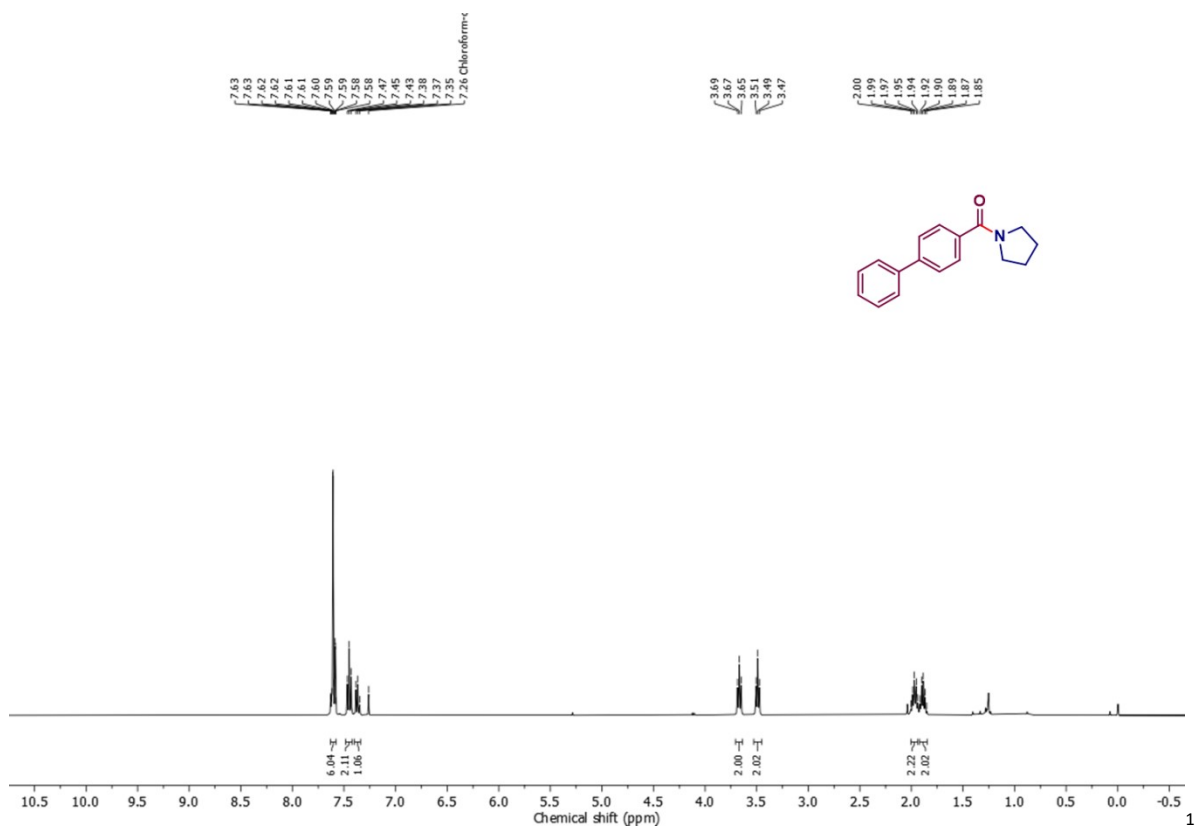
$^{13}\text{C}$  NMR spectrum (100 MHz) of **3ar** in  $\text{CDCl}_3$ .



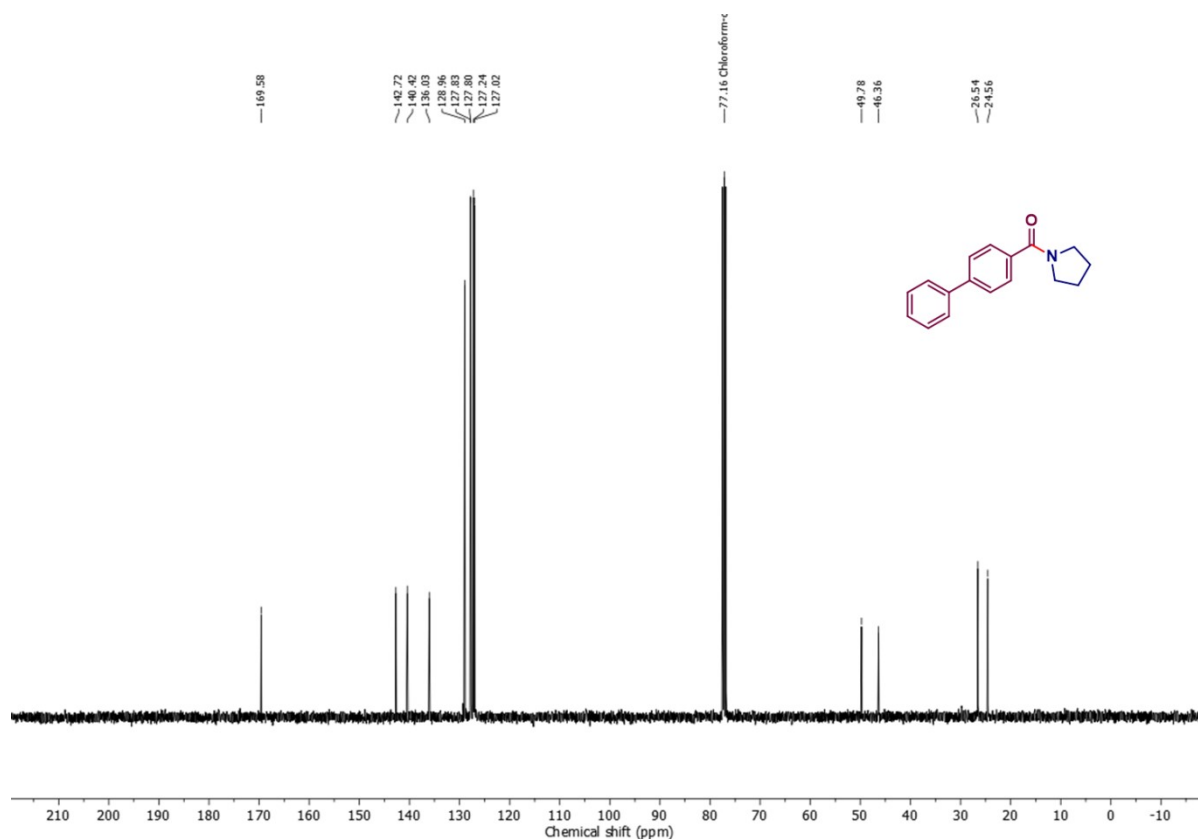
$^1\text{H}$  NMR spectrum (400 MHz) of **3ra** in  $\text{CDCl}_3$ .



<sup>13</sup>C NMR spectrum (100 MHz) of **3ra** in CDCl<sub>3</sub>.



<sup>1</sup>H NMR spectrum (400 MHz) of **3sa** in CDCl<sub>3</sub>.



$^{13}\text{C}$  NMR spectrum (100 MHz) of **3sa** in  $\text{CDCl}_3$ .

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