Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

One pot transamidation of N-pivaloyl activated amides with anilines in the absence of catalyst, base, and additive

*Ida Angel Priya Samuel Rajan and Saravanakumar Rajendran**

Chemistry Division, Vellore Institute of Technology Chennai campus, Vandalur-Kelambakkam road, Chennai – 600127, Tamil Nadu, India.

*Corresponding Author & E-mail id: *sar.org@gmail.com* & *Saravanakumar.r@vit.ac.in*

Table of Contents

1. Materials and methods

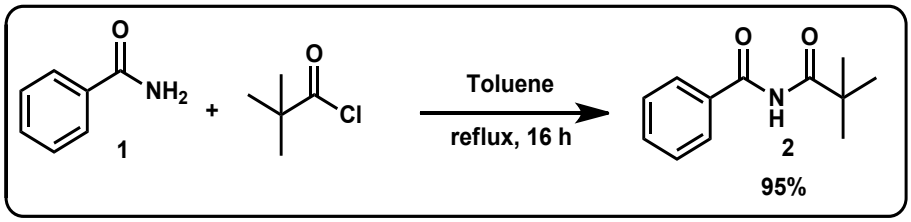
Materials

All commercially obtained reagents/solvents were used as received; chemicals were purchased from Spectrochem®, SRL®, Acros Organics®, RANKEM®, Fisher Scientific®, and used as received without further purification. Unless stated otherwise, reactions were conducted in oven-dried glassware and under normal atmospheric conditions. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz spectrometer operating with the ^{13}C resonance frequency of 100 MHz and proton resonance frequency of 400 MHz. Data from the ^{1}H NMR spectroscopy are reported as chemical shift (δ ppm) with the corresponding integration values. Coupling constants (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s (singlet), br (broad), d (doublet), t (triplet), q (quartet) and m (multiplet). Data from ^{13}C NMR spectra are reported in terms of chemical shift (δ ppm). High-resolution mass spectra were recorded on Electrospray Ionization mode on WATERS- XEVO G2-XS-QToS mass spectrometer in positive (ESI+) ion mode. Mass spectra were recorded on Perkin Elmer Clarus 600/Shimadzu QP2020 GC-MS spectrometer in EI mode. Melting points were recorded with REMI DDMS 2545. The instrument is calibrated with benzoic acid before the measurement.

Abbreviation used in this supporting information

DCM – Dichloromethane
DMF – Dimethyl formamide
THF – Tetrahydrofuran
TEA – Triethyl amine
EtOAc – Ethyl acetate
RT – Room temperature

Synthesis of N-pivaloyl benzamide



To a stirred solution of benzamide (1 g, 8.23 mmol), in 20 mL of toluene at room temperature, pivaloyl chloride (991 mg, 8.23mmol) was added dropwise. After addition, the reaction mixture was refluxed for 16 h. Progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)]. After completion, the reaction mixture was washed with 5% $NaHCO_3$ solution (2 x 50 mL) and water (1 x 50 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The obtained crude mixture was washed with hexane (10 mL) to get pure product as half-white solid in 1.60 g (95 % yield).

Physical Characteristics: **Colour and appearance**: Half-white solid

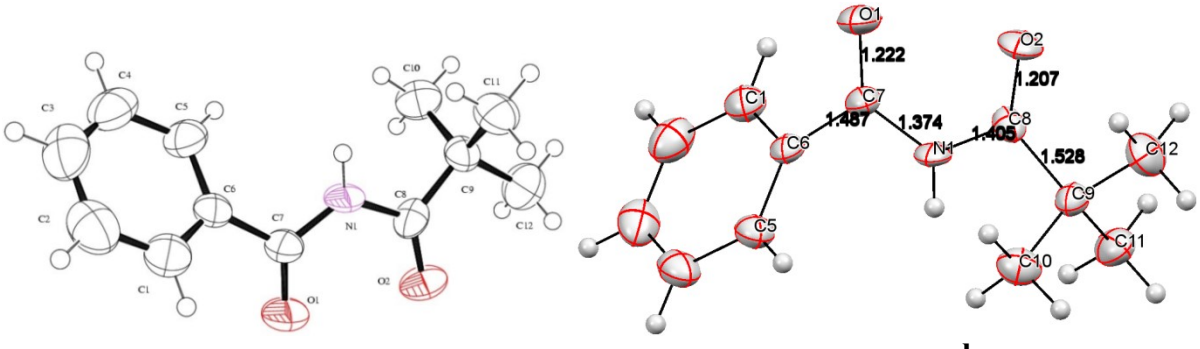
M.pt: 127 °C – 129 °C (Lit. m.pt = 126 °C – 127 °C)[1]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.24 (9H, s), 7.51 (2H, t, *J* = 8 Hz), 7.61 (1H, t, *J* = 8 Hz), 7.71 (2H, t, *J* = 8 Hz), 10.41 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 26.8, 128.7, 128.8, 132.7, 135.1, 168.52, 177.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 205.05.

Single crystal X-ray structure of *N*-pivaloyl benzamide

A toluene solution of *N*-pivaloyl benzamide was slowly evaporated at ambient condition to obtain single crystals suitable for X-ray analysis.



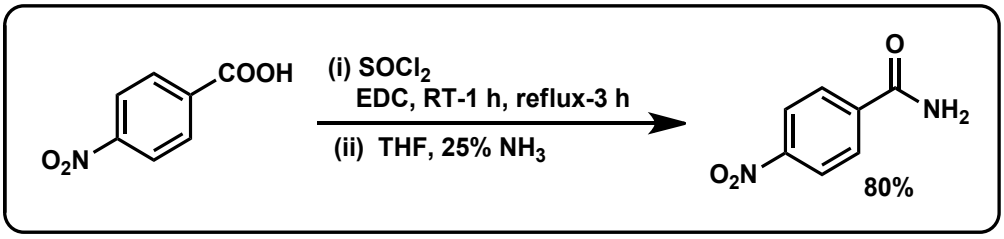
a **b**

Figure S1: Single crystal X-ray structure of *N*-pivaloyl benzamide a) ORTEP diagram; b) ellipsoid style. Bond distance: Ph(O)C7-N1 - 1.374 Å, ^{t}Bu(O)C8-N1 - 1.405 Å, PhC7=O1 - 1.222 Å, ^{t}BuC8=O2 - 1.207 Å.

General Procedure: Synthesis of benzamides and cinnamamides

To a solution of substituted benzoic acid or cinnamic acid in ethylene dichloride at RT, thionyl chloride was added slowly and the reaction mixture was stirred for 1 hour at room temperature and then refluxed for 3 hours. Excess thionyl chloride was distilled off. Without further purification the crude product was taken to next step. To a cold (5 ºC) aq. ammonia solution, the prepared acid chloride in THF was added dropwise and stirred vigorously at RT for 3 h. The obtained solid is filtered, washed with water and dried.

Synthesis of 4-nitrobenzamide



The general procedure stated above was followed. 4-Nitro benzoic acid (500 mg, 2.99 mmol), thionyl chloride (0.65 mL, 8.97 mmol), 25% of ammonia solution (4 mL, 59.8 mmol). Pure product was obtained as white solid in 397 mg (80% yield).

Physical Characteristics:

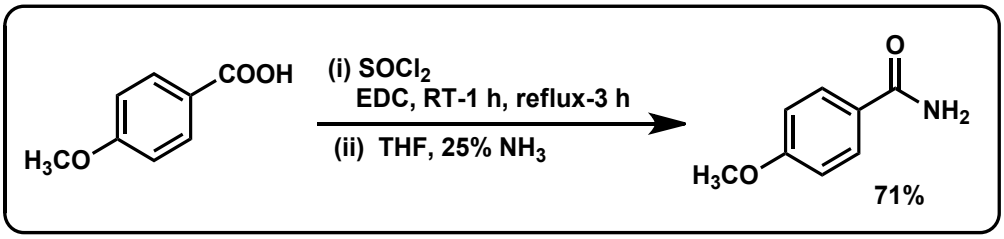
Colour and appearance: White solid

M.pt: 200 °C – 201 °C (Lit. m.pt = 196 °C – 198 °C)[2]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.74 (1H, br, s), 8.09 (2H, d, *J* = 12 Hz), 8.30 (3H, d, *J* = 12 Hz). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 123.9, 129.3, 140.4, 149.5, 166.7. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 166.05

Synthesis of 4-methoxybenzamide



The general procedure stated above was followed. 4-Methoxy benzoic acid (500 mg, 3.28 mmol), thionyl chloride (0.70 mL, 9.86 mmol), 25% of ammonia solution (4.5 mL 65.6 mmol). Pure product was obtained as white solid in 351 mg (71% yield).

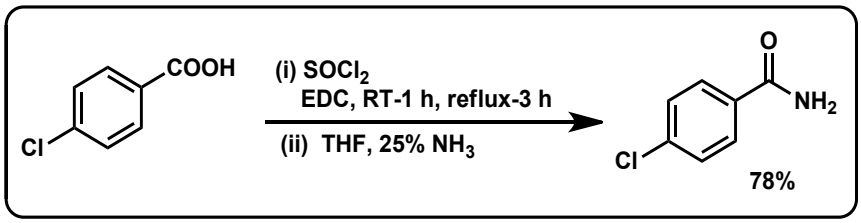
Physical Characteristics:

Colour and appearance: White solid

M.pt: 165 °C – 166 °C (Lit. m.pt = 165 °C – 167 °C)[3]

Spectral data: **^{1}H NMR**: (400 MHz, DMSO-d_6) δ: 3.80 (3H, s), 6.97 (2H, d, *J* = 12 Hz), 7.19 (1H, s), 7.85 (3H, d, *J* = 8 Hz). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 55.7, 113.8, 126.9, 129.8, 162.0, 167.9. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 151.10

Synthesis of 4-chlorobenzamide



The general procedure stated above was followed. 4-Chloro benzoic acid (500 mg, 3.20 mmol), thionyl chloride (0.69 mL, 9.61 mmol), 25% of ammonia solution (4.3 mL 64.0 mmol). Pure product was obtained as white solid in 387 mg (78% yield).

Physical Characteristics:

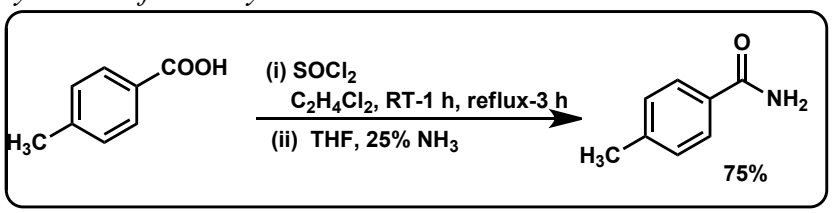
Colour and appearance: White solid

M.pt: 175 °C – 176 °C (Lit. m.pt = 178 °C – 180 °C)[2]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.47 (1H, br, s), 7.52 (2H, d, *J* = 12 Hz), 7.89 (2H, d, *J* = 8 Hz), 8.06 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 128.7, 129.8, 133.4, 136.5, 167.3. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 155.05.

Synthesis of 4-methylbenzamide



The general procedure stated above was followed. 4-Methyl benzoic acid (500 mg, 3.67 mmol), thionyl chloride (0.79 mL, 11.01 mmol), 25% of ammonia solution (5.0 mL 73.4 mmol). Pure product was obtained as white solid in 372 mg (75% yield).

Physical Characteristics:

Colour and appearance: White solid

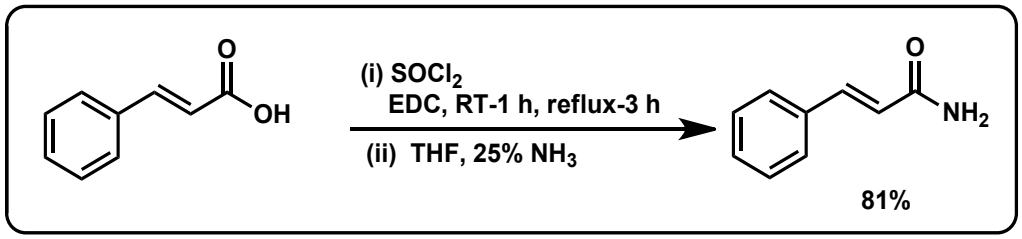
M.pt: 160 °C – 163 °C (Lit. m.pt = 159 °C – 160 °C)[4]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.34 (3H, s), 7.25 (3H, d, *J* = 8 Hz), 7.77 (2H, d, *J* = 8 Hz), 7.91 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 21.3, 127.9, 129.2, 131.8, 141.6, 168.

GC-MS (EI$^+$) *m/z*: $[M]^+$ 135.05.

Synthesis of cinnamic amide



The general procedure stated above was followed. Cinnamicacid (500 mg, 3.37 mmol), thionyl chloride (0.73 mL, 10.1 mmol), 25% of ammonia solution (4.6 mL, 67.4 mmol). Pure product was obtained as white solid in 401 mg (81% yield).

Physical Characteristics:

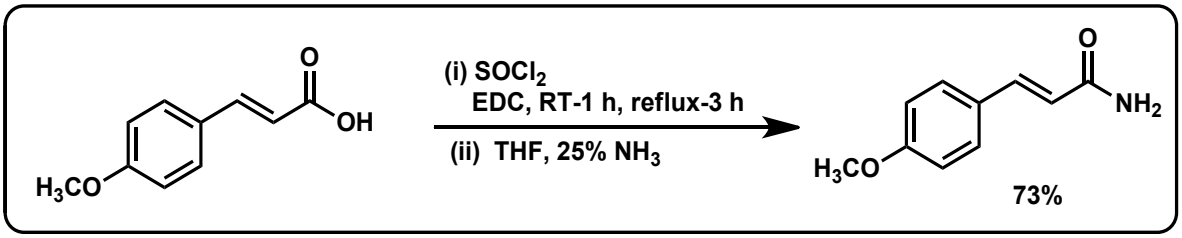
Colour and appearance: White solid

M.pt: 148 °C – 150 °C (Lit. m.pt = 145 °C – 146 °C)[5]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 6.64 (1H, d, *J* = 16 Hz), 7.14 (1H, br, s), 7.35- 7.46 (4H, m), 7.56 (3H, d, *J* = 8 Hz). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 127.5, 132.7, 134.1, 134.6, 140.0, 144.4, 172.0. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 147.00

Synthesis of 4-methoxycinnamic amide



The general procedure stated above was followed. 4-Methoxy cinnamicacid (500 mg, 2.80 mmol), thionyl chloride (0.61 mL, 8.41 mmol), 25% of ammonia solution (3.8 mL 56.0 mmol). Pure product was obtained as half-white solid in 361 mg (73% yield).

Physical Characteristics:

Colour and appearance: Half-white solid

M.pt: 198 °C – 199 °C (Lit. m.pt = 195 °C – 200 °C) [6]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.69 (3H, s), 6.37 (1H, d, *J* = 16 Hz), 6.89 (3H, t, *J* = 8 Hz), 7.27 (1H, d, *J* = 16 Hz), 7.40 (3H, t, *J* = 8 Hz). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 60.4, 119.5, 124.9, 132.6, 134.3, 144.1, 165.5, 172.2. **GC-MS (EI$^+$) *m/z***: $[M]^+$177.10

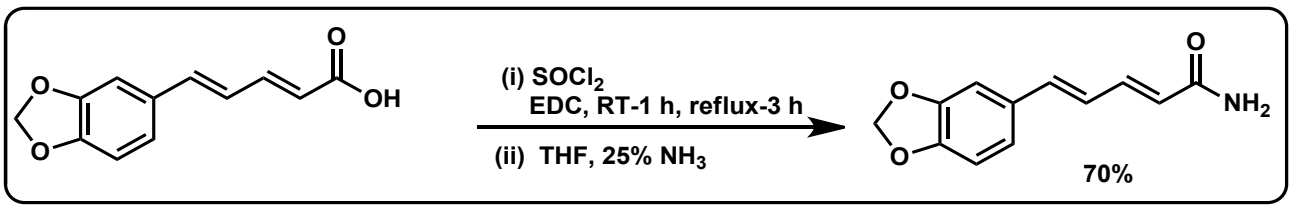
Synthesis of piperic amide

Synthesis of piperic acid from piperine

A literature reported procedure was followed for synthesis of piperic acid from piperine.[6]

To a cold solution of piperic acid in DCM at 0 °C, thionyl chloride was added slowly, the reaction mixture was stirred for 1 hour at room temperature and then refluxed for 3 hours. Excess thionyl chloride was distilled off. Without further purification the crude product was taken to next step.

To a cold solution (5 ºC) of aq. ammonia, the prepared acid chloride in THF was added dropwise and stirred vigorously at RT for 3 h. The obtained solid was filtered, washed with water and dried.



The general procedure stated above was followed. Piperic acid (500 mg, 2.29 mmol), thionyl

chloride (0.49 mL, 6.88 mmol), 25% of ammonia solution (3 mL 45.8 mmol). Pure product was obtained as brown solid in 348 mg (70% yield).

Physical Characteristics:

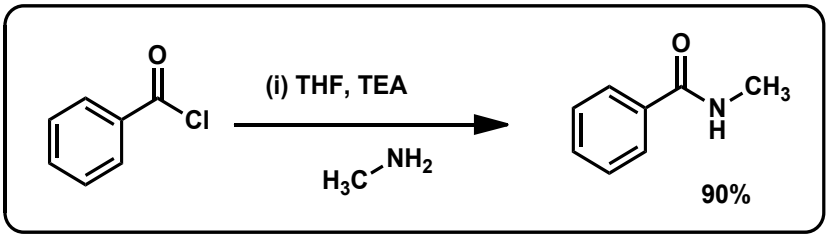
Colour and appearance: Brown Solid

M.pt: 189 °C – 191 °C

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 6.04 -6.09 (3H, m), 6.86- 6.91 (3H, m), 6.95- 7.01 (2H, m), 7.14 (1H, dd, J = 12 Hz, J = 4 Hz), 7.25 (1H, s), 7.48 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 101.7, 106.1, 108.9, 123.0, 125.0, 125.7, 131.2, 138.3, 140.3, 148.1, 148.3, 167.5. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 217.10.

Synthesis of N-methyl benzamide



To a cold solution of *N*-methyl amine (166 mg, 5.35 mmol), triethylamine (541 mg, 5.35 mmol) in THF, benzoyl chloride (500 mg, 3.57 mmol) added dropwise and stirred vigorously at RT for 8 h. After completion, the reaction mixture was washed with 5% HCl solution, 5% $NaHCO_3$ solution and water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography as a half white solid in 443 mg (90% yield).

Physical Characteristics:

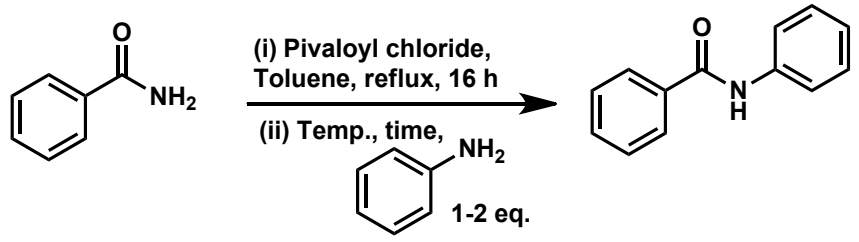
Colour and appearance: Half white solid

M.pt: 84°C – 87 °C (Lit. m.pt = 81 °C – 83 °C)[7]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.76 (3H, d, J = 4 Hz), 7.40- 7.48 (3H, m), 7.81 (2H, d, J = 8 Hz), 8.40 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 26.2, 127.0, 128.2, 131.0, 134.5, 166.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 135.10.

Table 1: Reaction optimization for aryl amines



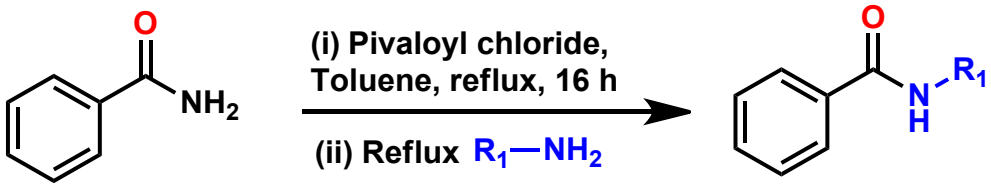
S. No	Equivalence (aniline)	Temperature (°C)	Time (h)	Yield (%)
1	1	RT	24	No reaction
		60	24	
		80	24	
		Reflux	24	Trace
2	2	RT	24	Trace
		60	24	Trace
		80	24	32
		Reflux	1	97

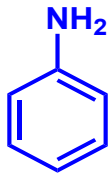
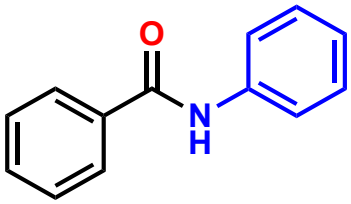
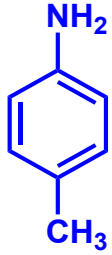
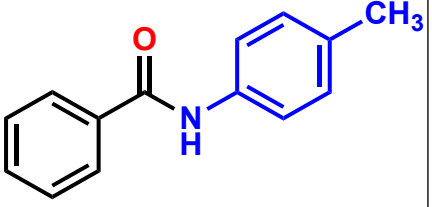
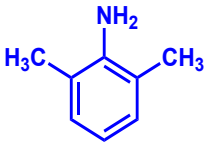
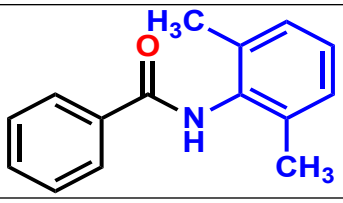
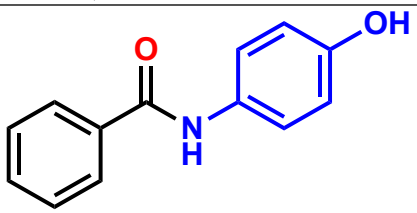
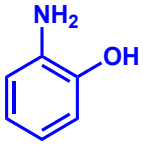
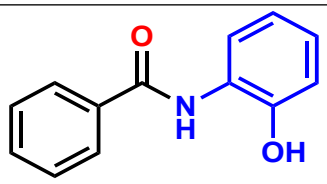
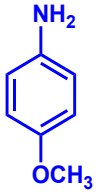
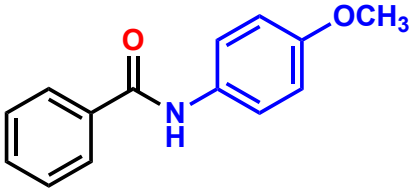
General procedure-A: Transamidation of benzamide with various arylamines

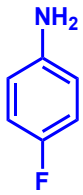
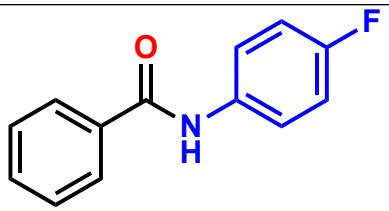
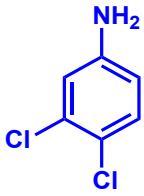
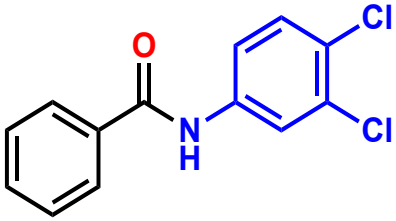
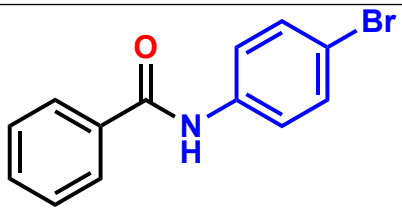
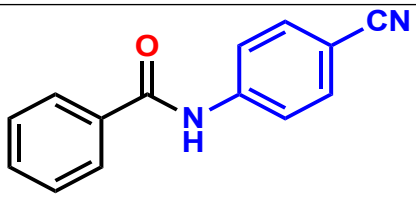
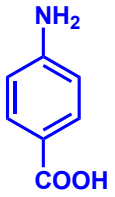
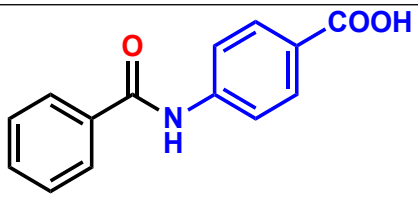
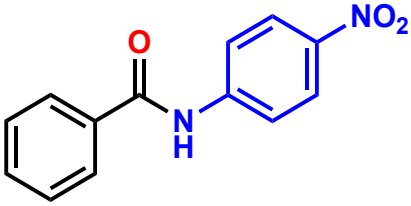
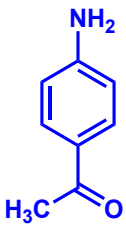
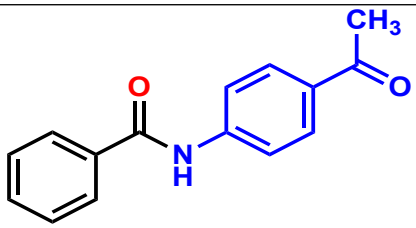
To a stirred solution of benzamide (1 eq.), in toluene (5 mL) at room temperature, pivaloyl chloride (1 eq.), was added dropwise. After addition, the reaction mixture was refluxed for 16 h. The reaction mixture was cooled down to room temperature. Without further purification the crude product was taken to next step.

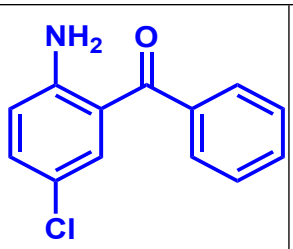
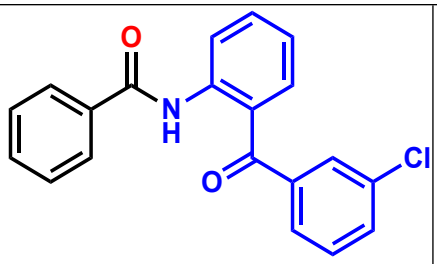
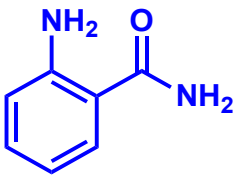
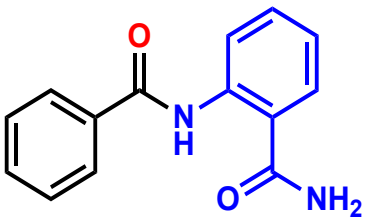
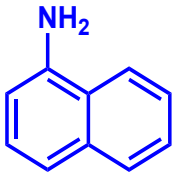
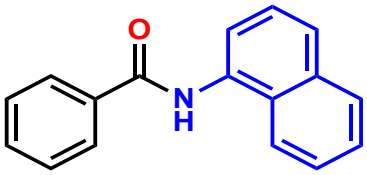
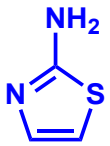
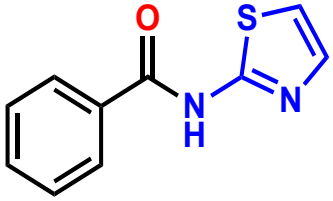
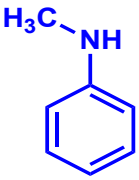
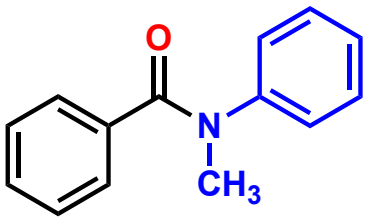
To the above synthesized imide in toluene, aryl amine (2 eq.), was added and refluxed. Progress of the reaction was monitored by TLC. Starting material consumed within 1- 8 h with all the tested amines. After completion, the reaction mixture was washed with 5% HCl solution, 5% $NaHCO_3$ solution and water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography.

Table 2: Transamidation of benzamide with aryl amines

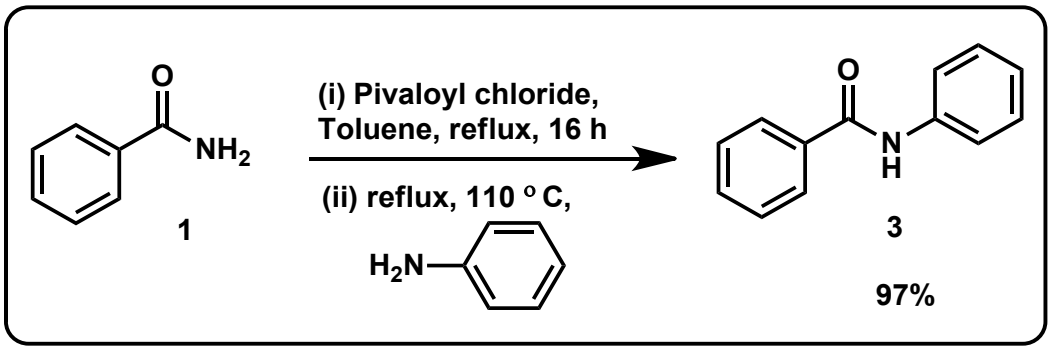


S.No	Amine	Product	Yield (%)	Time (h)
1.			**97**	**1**
2.			**90**	**1**
3.			**80**	**7**
4.			**79**	**2.5**
5.			**77**	**3**
6.			**87**	**1**

7.			**89**	**2**
8.			**80**	**2.5**
9.			**86**	**2**
10.			**62**	**6**
11.			**86**	**1.5**
12.			**59**	**5**
13.			**68**	**5**

14.			**80**	**8**
15.			**60**	5
16.			**82**	**3**
17.			**84**	**2**
18.			**64**	**6**

Transamidation of benzamide with aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), aniline (153.6 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale brown solid in 157 mg (97% yield).

Physical Characteristics:

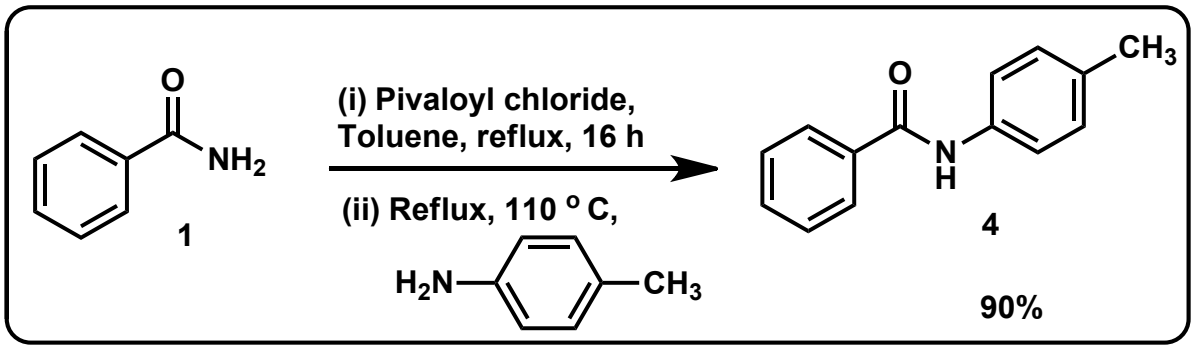
Colour and appearance: Pale brown solid

M.pt:166 °C –167 °C (Lit. M.pt = 165 °C –167 °C) [8]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.11 (1H, t, *J* = 8 Hz), 7.36 (2H, t, *J* = 4 Hz), 7.54-7.60 (3H, m), 7.79 (2H, d, *J* = 8 Hz), 7.96 (2H, d, *J* = 8 Hz), 10.26 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 120.8, 124.1, 128.1, 128.8, 129.0, 132.0, 135.4, 139.6, 166.0. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 197.10

Transamidation of benzamide with 4-methyl aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-methyl aniline (176.5 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 156 mg (90% yield).

Physical Characteristics:

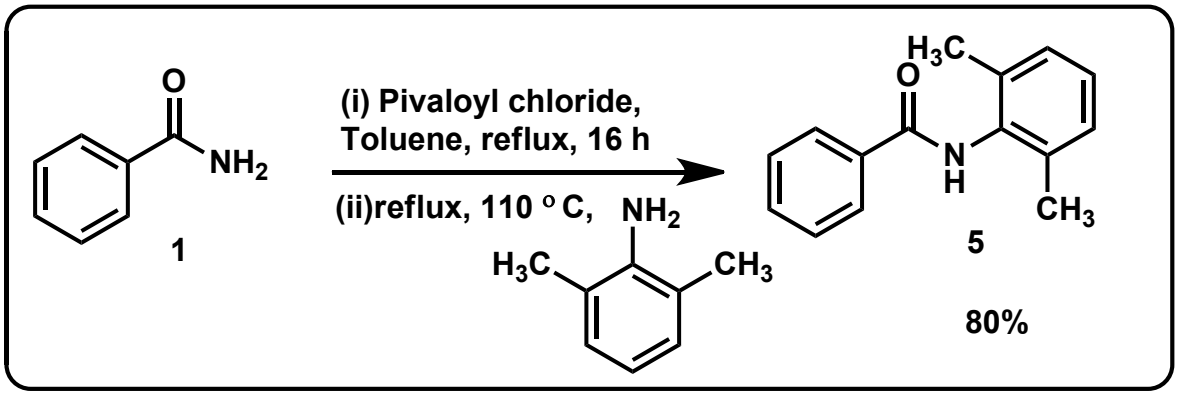
Colour and appearance: Half-white solid

M.pt: 157 °C – 158 °C (Lit. M.pt = 158 °C) [9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (3H, s), 7.14 (2H, d, *J* = 12 Hz), 7.43 (2H, t, *J* = 8Hz), 7.50-7.53 (3H, m), 7.84 (2H, d, *J* = 8 Hz), 8.01 (1H, br, s) **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 20.9, 120.4, 127.0, 128.7, 129.5, 131.7, 134.2, 135.0, 135.4, 165.8. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 211.10

Transamidation of benzamide with 2,6 dimethyl aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 2,6 dimethylaniline (199.9 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale brown solid in 148 mg (80 % yield).

Physical Characteristics:

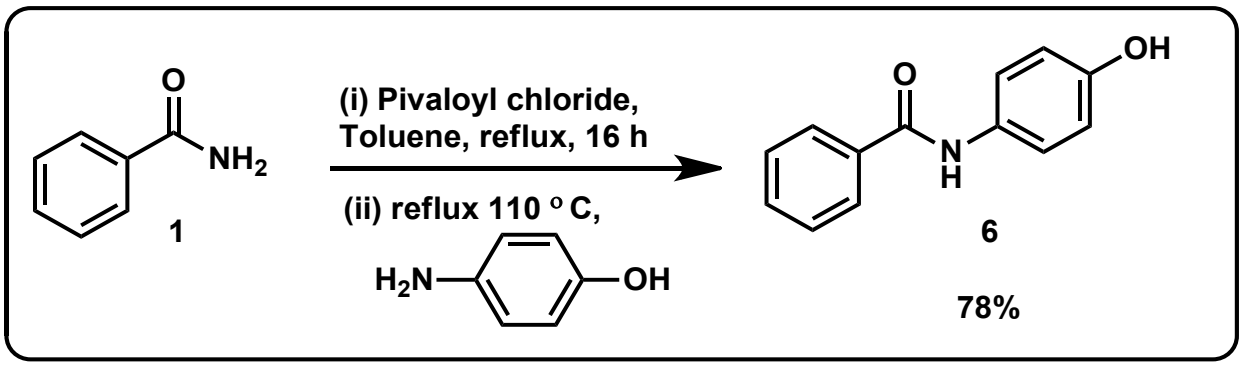
Colour and appearance: Pale brown solid

m.pt: 167 °C –169 °C (Lit. M.pt = 168 °C – 169 °C) [10]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.20 (6H, s), 7.14 (3H, s), 7.52-7.62 (3H, m), 8.02 (2H, d, *J* = 8 Hz) 9.79 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 18.5, 127.1, 127.9, 128.2, 128.9, 131.9, 134.8, 135.8, 136.1, 165.5. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 225.10

Transamidation of benzamide with 4-hydroxy aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-hydroxy aniline (179.8 mg, 1.65 mmol). Pure product was

obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 137 mg (78% yield).

Physical Characteristics:

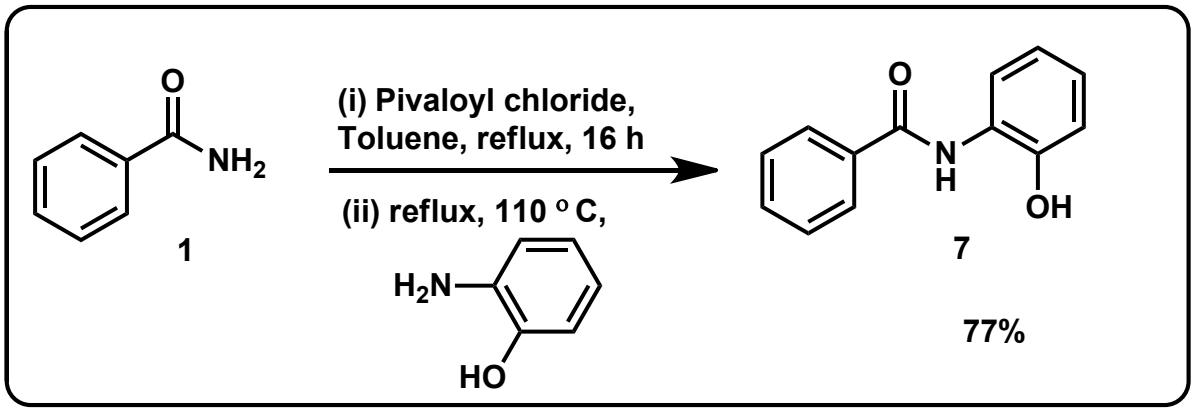
Colour and appearance: Half white solid

M.pt: 208 °C – 209 °C (Lit. M.pt = 207 °C –209 °C) [11]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.80 (2H, d, *J* = 8 Hz), 7.54 -7.62 (5H, m), 7.98 (2H, d, *J* = 4 Hz), 9.32 (1H, br, s), 10.07 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 120.1, 127.5, 132.7, 133.5, 135.9, 136.4, 140.3, 158.9, 170.1. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 213.15

Transamidation of benzamide with 2-hydroxy aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 2-hydroxy aniline (180.0 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as brown solid in 135 mg (77% yield).

Physical Characteristics:

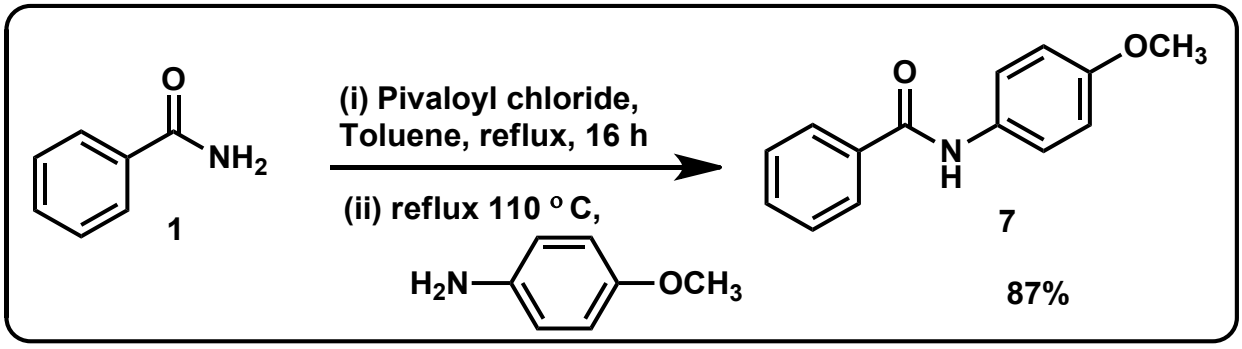
Colour and appearance: Brown solid

M.pt: 166 °C – 167 °C (Lit. M.pt = 167 °C) [12]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.90 (1H, t, *J* = 8 Hz), 6.97- 7.00 (1H, m), 7.10 (1H, t, *J* = 8Hz), 7.57- 7.64 (2H, m), 7.65-7.68 (1H, m), 7.74 (1H, d, *J* = 8 Hz), 8.03 (2H, d, *J* = 8Hz), 9.57 (1H, s), 9.81 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 116.4, 119.5, 124.6, 126.1, 126.3, 127.9, 129.0, 132.1, 134.8, 149.8, 165.7. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 213.10

Transamidation of benzamide with 4-methoxy aniline



The general procedure-A state above was followed for transamidation. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-methoxy aniline (203.1mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) light brown solid in 163 mg (87% yield).

Physical Characteristics:

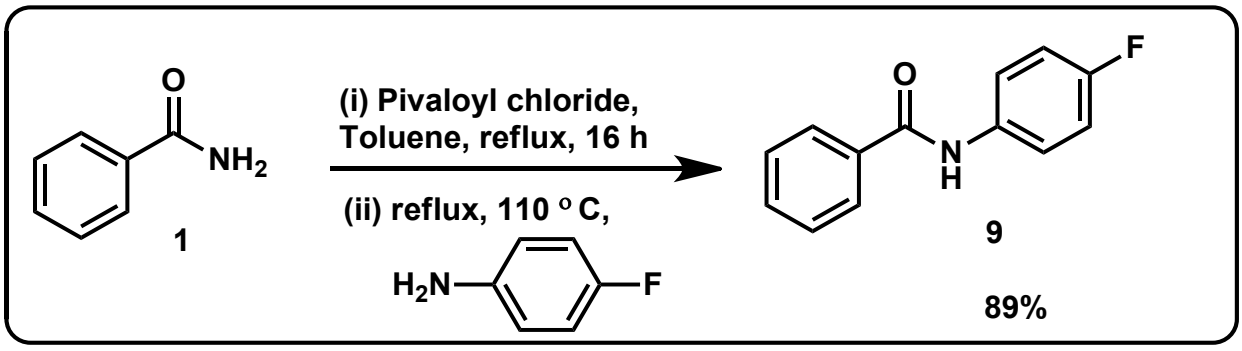
Colour and appearance: Light brown solid

M.pt: 155 °C – 156.5 °C (Lit. M.pt = 155 °C – 156 °C)[8]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.81 (3H, s), 6.90 (2H, d, *J* = 12 Hz), 7.44-7.55 (5H, m,) 7.85 (3H, d, *J* = 4 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 55.5, 114.2, 122.2, 127.0, 128.7, 131.0, 131.7, 135.0, 156.6, 165.7. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 227.10

Transamidation of benzamide with 4- fluoro aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-fluoro aniline (183.3mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 157 mg (89 % yield).

Physical Characteristics:

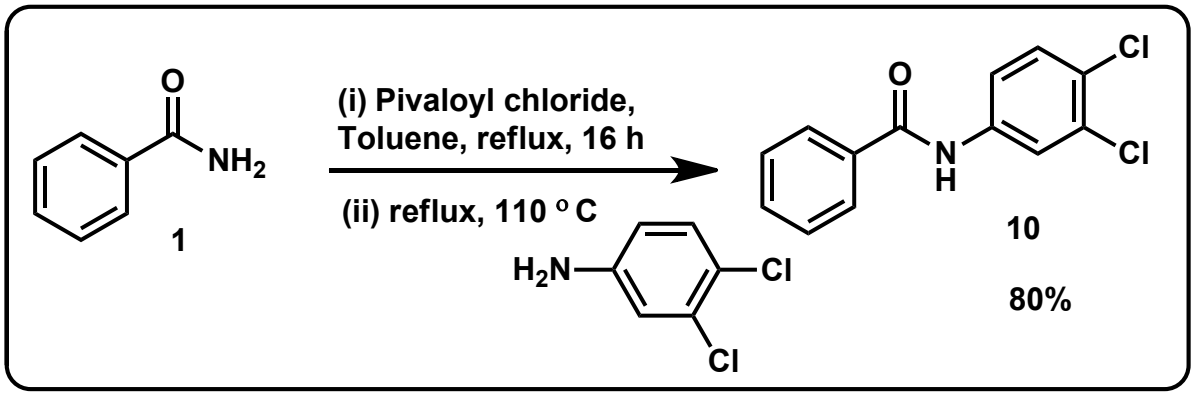
Colour and appearance: White solid

M.pt: 175 °C – 177 °C (Lit. M.pt = 175 °C – 176 °C)[13]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.20 (2H, t, *J* = 8 Hz), 7.52-7.60 (3H, m), 7.78-7.81 (2H, m), 7.96 (2H, d, *J* = 4 Hz), 10.31 (1H, s) **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 115.5, 115.7, 122.6, 122.7, 128.0, 128.8, 132.0, 135.2, 135.9, 136.0, 157.5, 159.6, 165.9. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 215.10

Transamidation of benzamide with 4-chloro aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-chloro aniline (267.3mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale-yellow solid in 175 mg (80% yield).

Physical Characteristics:

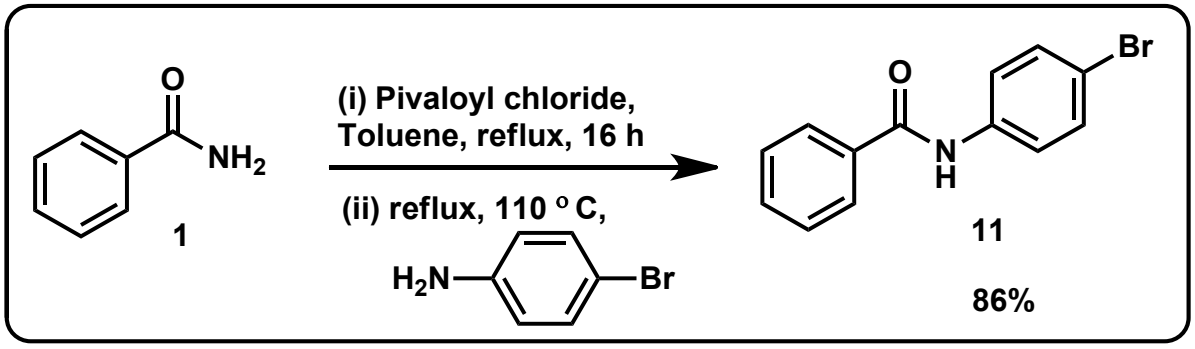
Colour and appearance: Pale-yellow solid

M.pt. 145 °C - 147 °C (Lit. M.pt.145 °C - 146 °C)[14]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.53-7.57 (2H, m), 7.60-7.64 (2H, m), 7.77 (1H, d, *J* = 8 Hz), 7.95-7.97 (2H, m), 8.17 (1H, br, s), 10.50 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 120.6, 121.8, 125.5, 128.1, 128.9, 131.0, 131.3, 132.4, 134.8, 139.8, 166.3. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 266.05.

Transamidation of benzamide with 4-Bromo aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-bromo aniline (283.8 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 195 mg (86% yield).

Physical Characteristics:

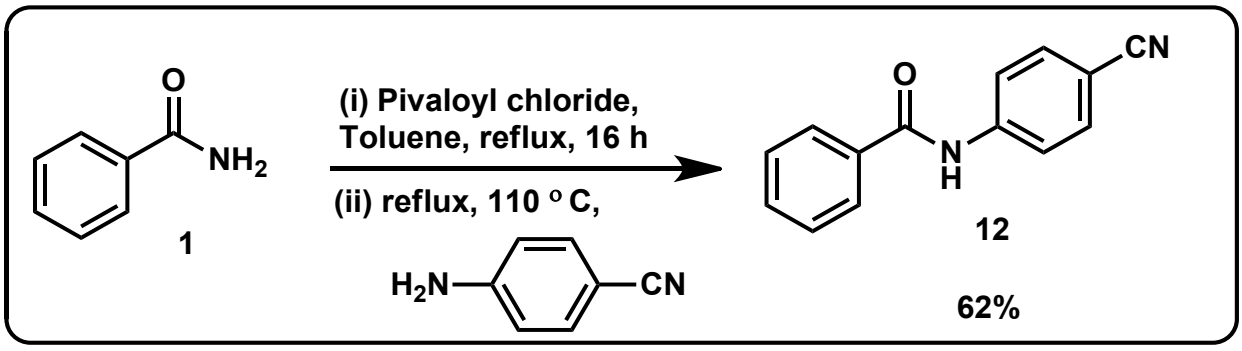
Colour and appearance: Half-white solid

M.pt: 202 °C – 204 °C (Lit. M.pt = 203 °C – 204 °C)[13]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47-7.51 (4H, m), 7.54-7.59 (3H, m), 7.81 (1H, br, s), 7.85-7.87 (2H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 117.1, 121.7, 127.0, 128.9, 132.1, 134.6, 137.0, 165.6. **GC-MS (EI^{+}) *m/z***: $[M-H]^{+}$ 275.05

Transamidation of benzamide with p-aminobenzonitrile



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), *p*-aminobenzonitrile (194.7mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 115 mg (62% yield).

Physical Characteristics:

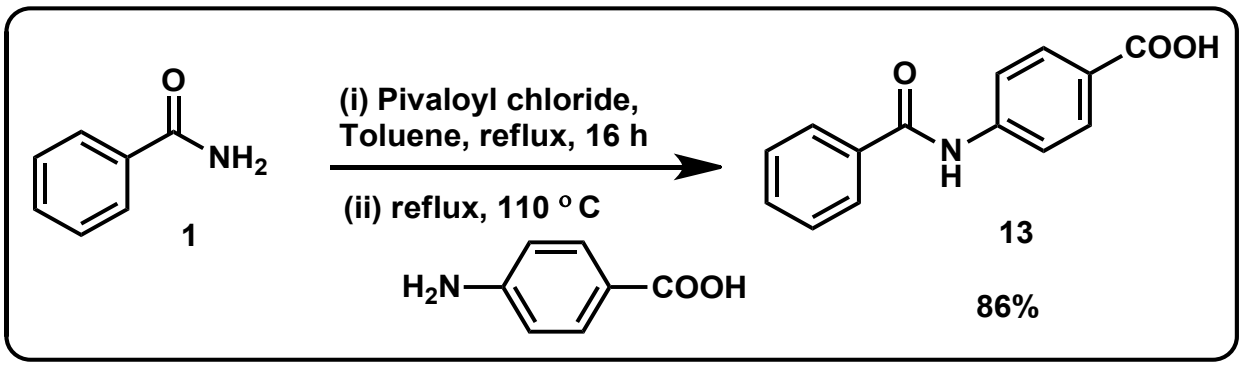
Colour and appearance: Half white solid

M.pt: 167 °C –169 °C (Lit. M.pt = 165 °C – 167 °C)[15]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.54- 7.63 (3H, m), 7.82 (2H, d, *J* = 8 Hz), 7.95-8.02 (4H, m), 10.66 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 105.8, 119.5, 120.6, 128.3, 128.9, 132.5, 133.5, 134.8, 143.9, 166.6. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 222.10

Transamidation of benzamide with 4-amino benzoic acid



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-amino benzoicacid (226.2mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 171 mg (86% yield).

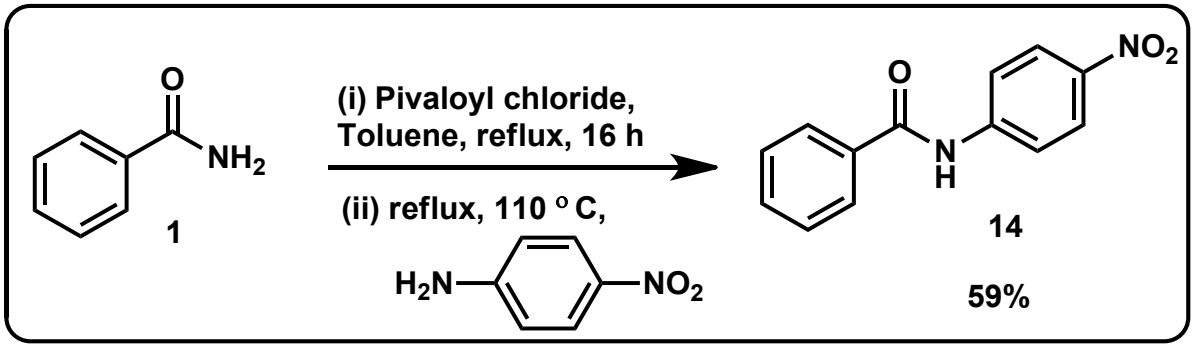
Physical Characteristics:

Colour and appearance: White solid

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.53-7.57 (2H, m), 7.60-7.64 (1H, m), 7.92-7.98 (6H, m), 10.54 (1H, s), 12.74 (1H, br, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 119.9, 125.9, 128.2, 128.9, 130.7, 132.3, 135.2, 143.7, 166.4, 167.4. **HRMS (ESI-MS)** *m/z*: Calculated for $C_{14}H_{12}NO_3$ $[M+H]^{+}$ 242.0817, found: 242.0825.

Transamidation of benzamide with 4-Nitro aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-nitro aniline (227.8mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as yellow solid in 117 mg (59% yield).

Physical Characteristics:

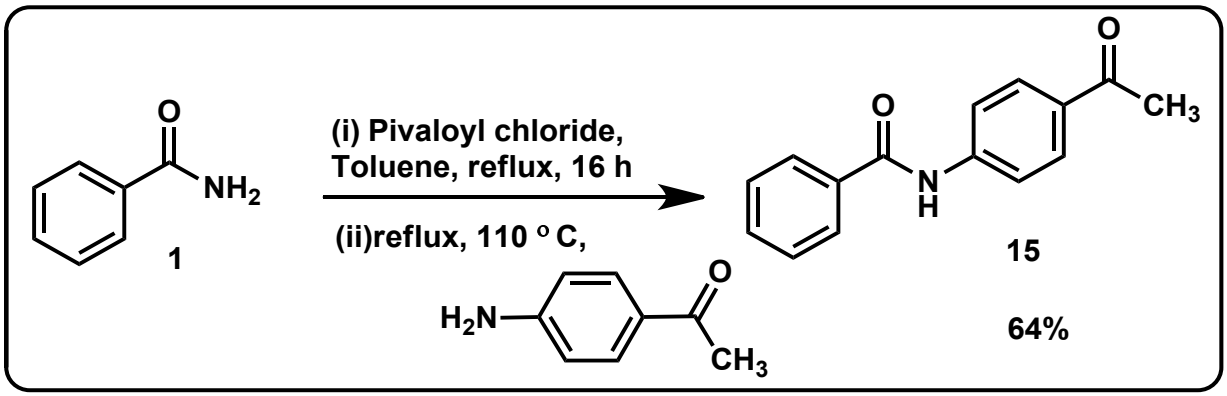
Colour and appearance: Yellow solid

M.pt: 202 °C –203 °C (Lit. M.pt = 201 °C –202 °C)[15]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.60 -7.62 (2H, m),7.64-7.69 (1H, m), 8.04 (2H, d, *J* = 8 Hz), 8.13 (2H, d, *J* = 12 Hz), 8.32 (2H, d, *J* = 12 Hz), 10.87 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 125.0, 130.0, 133.1, 133.7, 137.4, 139.4, 147.7, 150.7, 171.5. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 242.10

Transamidation of benzamide with 4-amino-acetophenone



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 4-amino-acetophenone (222.9 mg, 1.65 mmol). Pure product was

obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 126 mg (64% yield).

Physical Characteristics:

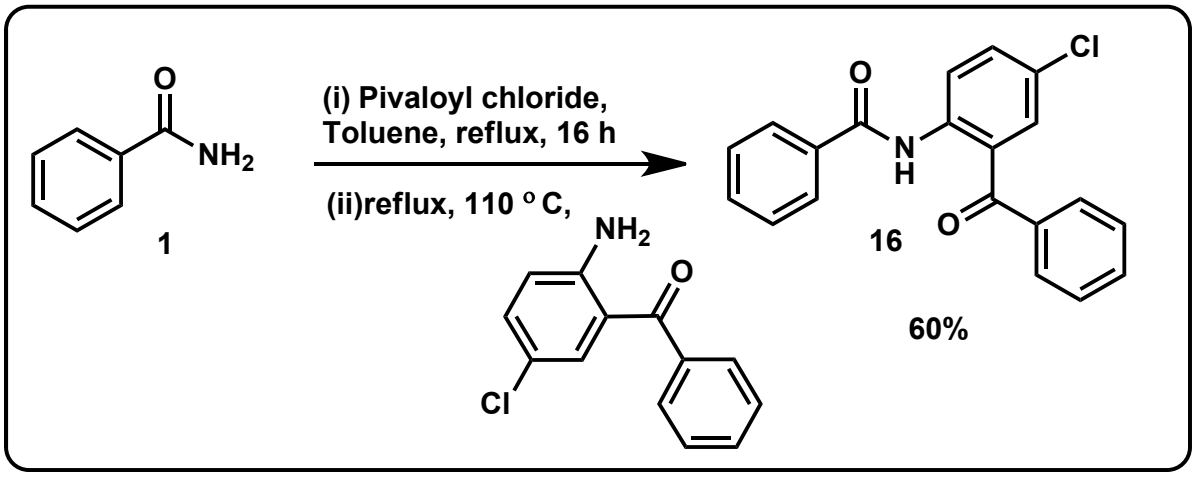
Colour and appearance: White solid

m.pt: 203 °C – 205 °C (Lit. M.pt = 200 °C) [16]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.55 (3H, s), 7.55 (2H, t, *J* = 8 Hz), 7.61- 7.64 (1H, m), 7.94- 7.99 (6H, m), 10.57 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 26.9, 119.9, 128.2, 128.9, 129.7, 132.3, 132.4, 135.0, 144.0, 166.5, 197.1. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 239.05

Transamidation of benzamide with 2-amino-5-chloro benzophenone



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 2-amino-5-chloro benzophenone (382.2 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as yellow solid in 166 mg (60% yield).

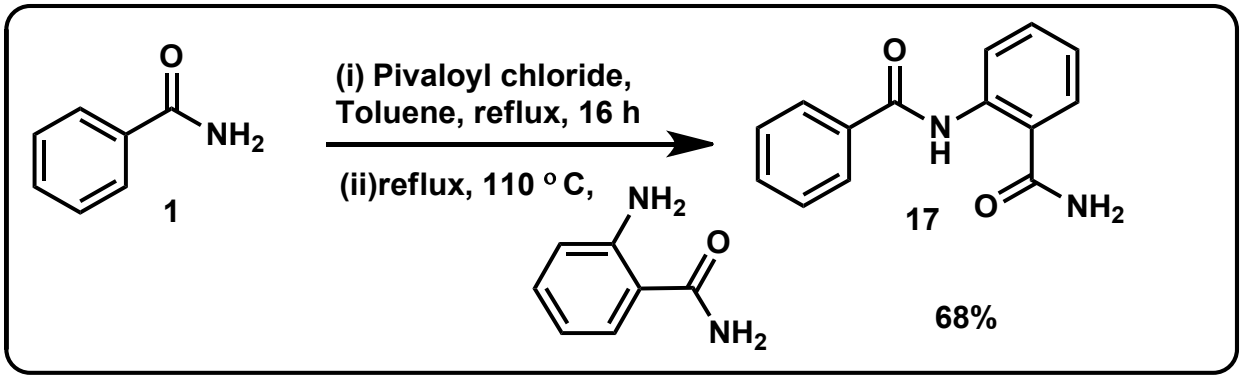
Physical Characteristics:

Colour and appearance: Yellow solid

m.pt: 112 °C –114 °C

^{1}H NMR: (400 MHz, $CDCl_3$) δ: 7.42- 7.58 (8H, m), 7.65 (2H, d, *J* = 8 Hz), 7.96 (2H, d, *J* = 8 Hz), 8.80 (1H, d, *J* = 8 Hz), 11.70 (1H, s). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 123.0, 124.4, 127.3, 127.4, 128.6, 128.9, 132.2, 132.9, 133.1, 134.2, 134.3, 138.0, 139.6, 165.7, 199.0. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 335.00

Transamidation of benzamide with 2-amino-benzamide



The general procedure-A state above was followed for transamidation. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 2-amino-benzamide (224.6 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 134 mg (68% yield).

Physical Characteristics:

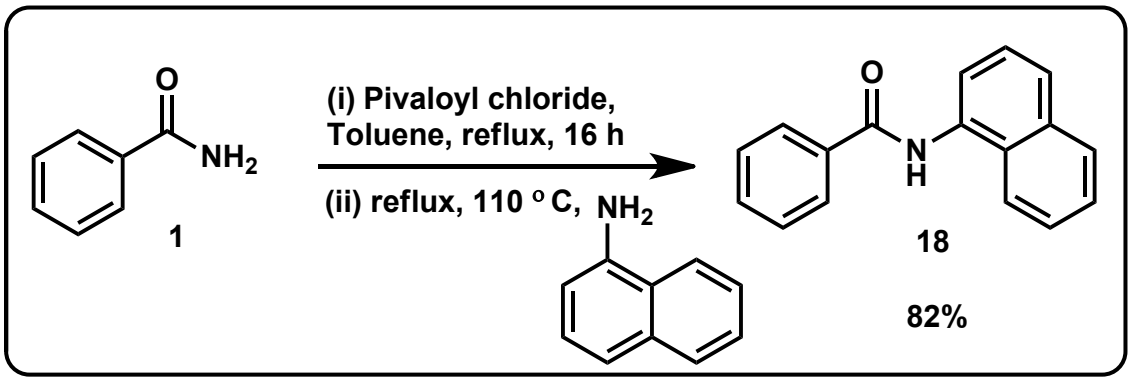
Colour and appearance: White solid

m.pt: 215 °C –217 °C (Lit. M.pt = 218 °C – 219 °C) [17]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.19 (1H, t, *J* = 8 Hz), 7.56-7.66 (4H, m), 7.86 -7.96 (4H, m), 8.44 (1H, s), 8.71(1H, d, *J* = 8 Hz), 12.95 (1H, s).**^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 119.6, 120.5, 123.1, 127.4, 129.2, 129.4, 132.5, 133.0, 135.0, 140.5, 164.9, 171.6. **HRMS (ESI-MS)** *m/z*: Calculated for $C_{14}H_{12}N_2O_2Na$ $[M+Na]^+$ 263.0796, found: 263.0824.

Transamidation of benzamide with α- naphthyl amine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), *α*- naphthyl amine (236.2 mg, 1.65 mmol). Pure product was

obtained after column chromatography (Hexane: EtOAc (80:20)) as pale-purple solid in 167 mg (82% yield).

Physical Characteristics:

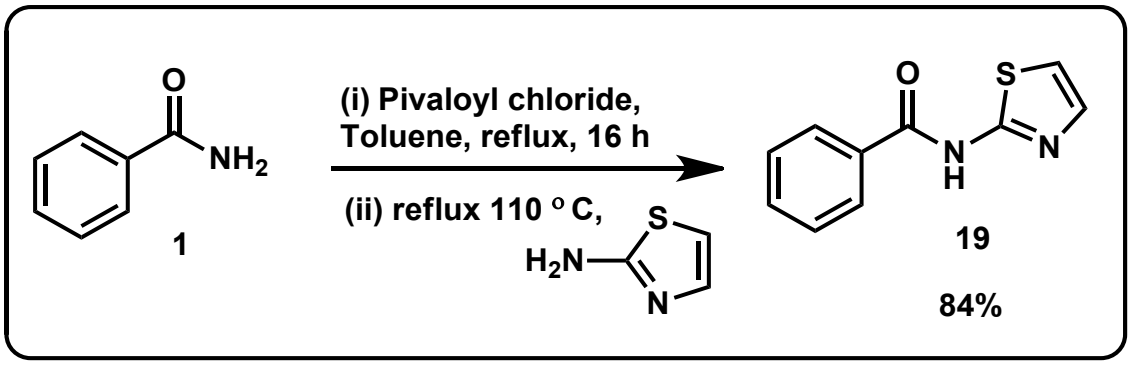
Colour and appearance: Pale-purple solid

M.pt: 171°C – 172 °C (Lit. M.pt = 170 °C –171 °C) [14]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 7.53- 7.65 (7 H, m), 7.87 (1H, d, *J* = 8 Hz), 7.98- 8.02 (2H, m), 8.12 (2H, d, *J* = 8 Hz), 10.46 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 123.8, 124.4, 126.0, 126.4, 126.5, 126.7, 128.5, 128.9, 129.7, 132.1, 134.2, 134.3, 134.9, 166.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 247. 15.

Transamidation of benzamide with 2-amino thiazole



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), 2-amino thiazole (165.1 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as brown solid in 141 mg (84% yield).

Physical Characteristics:

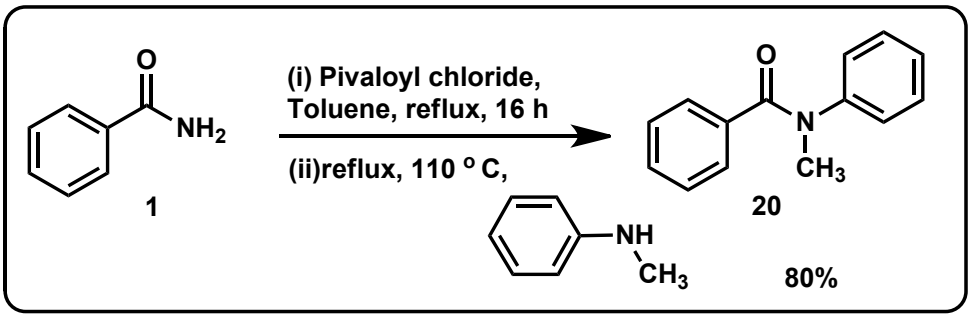
Colour and appearance: Brown solid

M.pt: 140 °C – 142 °C (Lit. M.pt = 140 °C – 141 °C)[18]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.29 (1H, d, *J* = 4 Hz), 7.53-7.57 (3H, m), 7.62-7.66 (1H, m), 8.10 (2H, d, *J* = 8 Hz), 12.63 (1H, br, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 114.3, 128.6, 129.0, 132.6, 133.0, 138.0, 159.2, 165.5. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 204.05

Transamidation of benzamide with N-methyl aniline



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), *N*-methyl aniline (176.7mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as colourless liquid in 139 mg (80% yield).

Physical Characteristics:

Colour and appearance: Colourless liquid

Spectral data:

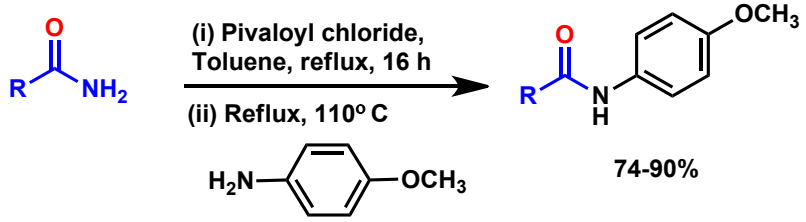
^{1}H NMR: (400 MHz, $CDCl_3$) δ: 3.42 (3H, s), 6.97 (2H, d, *J* = 8 Hz), 7.02- 7.09 (3H, m), 7.13, (3H, t, *J* = 8 Hz), 7.26 (2H, d, *J* = 8 Hz). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 38.3, 126.4, 126.8, 127.6, 128.6, 129.1, 129.5, 135.9, 144.8, 170.5. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 211.10

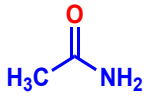
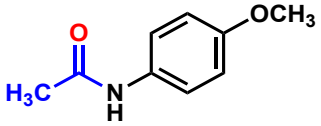
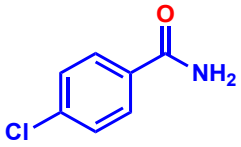
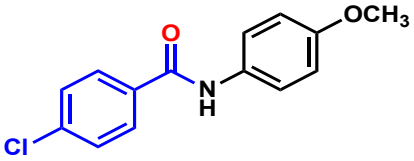
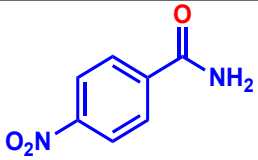
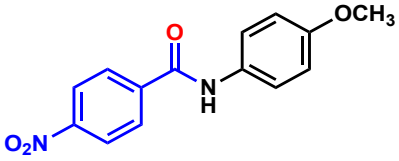
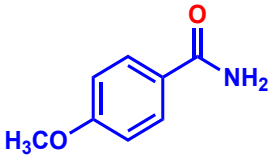
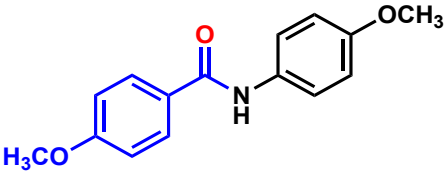
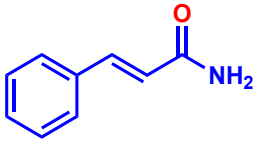
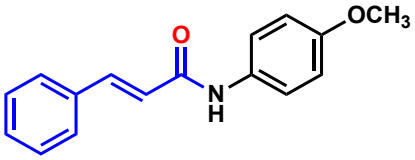
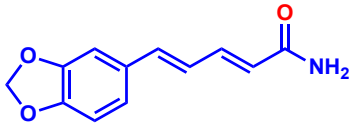
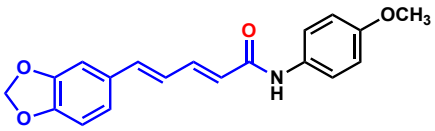
General procedure-B: Transamidation of various amides with 4-methoxy aniline

To a stirred solution of various amides (1 eq.), in toluene (5 mL) at room temperature, pivaloyl chloride (1 eq.), was added dropwise. After addition the reaction mixture was refluxed for 16 h. The reaction mixture was cooled down to room temperature. Without further purification the crude product was taken to next step.

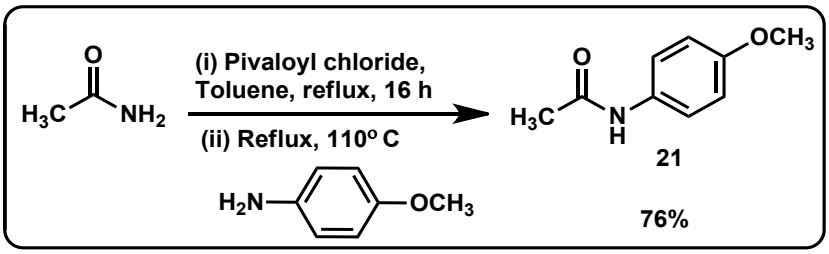
To the above synthesized imide in toluene, 4-methoxy aniline (2 eq.), was added and refluxed. Progress of the reaction was monitored by TLC. Starting material consumed in 1 h - 4 h with 4-methoxy aniline. After completion, the reaction mixture was washed with 5%HCl solution, 5% $NaHCO_3$ solution, water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography.

Table 3: Transamidation of various amides with 4-methoxy aniline



S.No	Amide	Product	Yield %	Time h
1.			**76**	**2**
2.			**82**	**2**
3.			**90**	**1**
4.			**74**	**4**
5.			**76**	**2**
6.			**82**	**2**

Transamidation of acetamide with 4-methoxy aniline



The general procedure-B stated above was followed. Acetamide (100 mg, 1.69 mmol), pivaloyl chloride (203 mg, 1.69mmol),4-methoxy aniline (416 mg, 3.38 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 212 mg (76% yield).

Physical Characteristics:

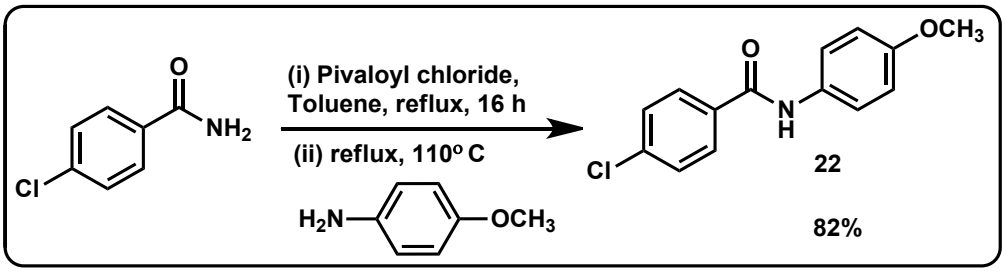
Colour and appearance: Half- white solid

M.pt: 128 °C – 130 °C (Lit. m.pt = 126 °C – 128 °C)[9]

Spectral data:

^{1}H NMR: (400 MHz, $CDCl_3$) δ: 2.05 (3H, s), 3.69 (3H, s), 6.74 (2H, d, *J* = 12 Hz), 7.32 (2H, d, *J* = 12 Hz), 8.08 (1H, s). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 24.0, 55.4,114.0, 122.0, 131.2, 156.3, 168.8. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 165.10

Transamidation of 4-chloro benzamide with 4-methoxy aniline



The general procedure-B stated above was followed. 4-chlorobenzamide (100 mg, 0.64 mmol), pivaloyl chloride (77 mg, 0.64mmol), 4-methoxy aniline (157.6 mg, 01.28 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 136 mg (82% yield).

Physical Characteristics:

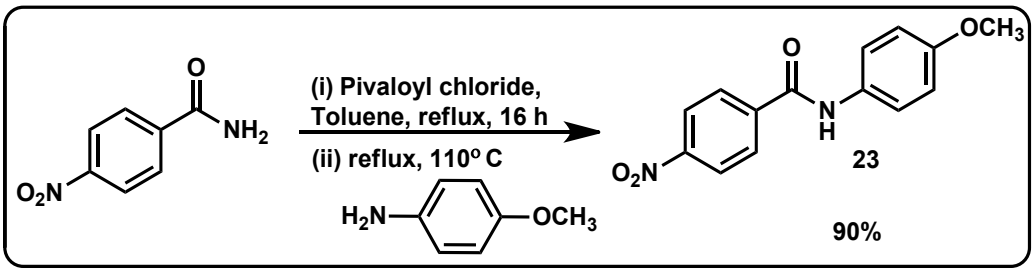
Colour and appearance: Half- white Solid

M.pt: 205 °C – 206 °C (Lit. m.pt = 209 °C – 210 °C)[19]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.75 (3H, s), 6.93 (2H, d, *J* = 12 Hz), 7.59 (2H, d, *J* = 12 Hz), 7.66 (2H, d, *J* = 12 Hz), 7.97 (2H, d, *J* = 12 Hz), 10.20 (1H, s).**^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 55.6, 114.2, 122.5, 128.8, 129.9, 132.4, 134.1, 136.6, 156.1, 164.4. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 261.05.

Transamidation of 4-nitro benzamide with 4-methoxy aniline



The general procedure-B stated above was followed. 4-Nitrobenzamide (100 mg, 0.60 mmol), pivaloyl chloride (72 mg, 0.60mmol), 4-methoxy aniline (147.8 mg, 1.20 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as green solid in 147 mg (90% yield).

Physical Characteristics:

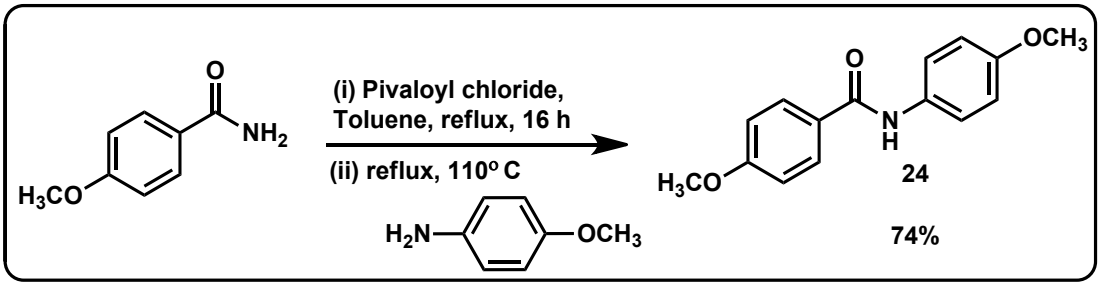
Colour and appearance: Green solid

M.pt: 194 °C – 196 °C (Lit. m.pt = 196 °C – 197 °C)[20]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.76 (3H, s), 6.96 (2H, d, *J* = 8 Hz), 7.77 (2H, d, *J* = 12 Hz), 8.17 (2H, d, *J* = 12 Hz), 8.37 (2H, d, *J* = 8 Hz), 10.46 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 55.6, 114.3, 122.5, 124.0, 129.5, 132.1, 141.1, 149.5, 156.3, 163.8. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 271.10

Transamidation of 4-methoxybenzamide with 4-methoxy aniline



The general procedure-B stated above was followed. 4-Methoxybenzamide (100 mg, 0.66 mmol), pivaloyl chloride (79.5 mg, 0.66mmol), 4-methoxy aniline (162.6 mg, 1.32 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 125 mg (74% yield).

Physical Characteristics:

Colour and appearance: Half white solid

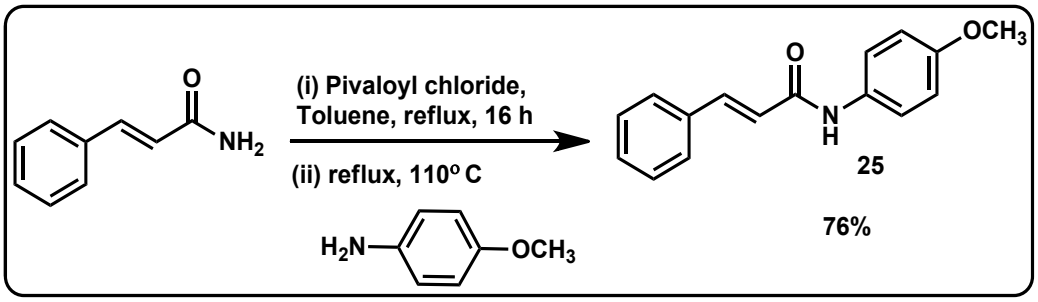
M.pt: 199 °C – 200 °C (Lit. m.pt = 201 °C – 203 °C)[21]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.74 (3H, s), 3.84 (3H, s), 6.92 (2H, d, *J* = 8 Hz), 7.05 (2H, d, *J* = 8 Hz), 7.66 (2H, d, *J* = 8 Hz), 7.95 (2H, d, *J* = 8 Hz), 9.97 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 55.6, 55.8, 114.0, 114.1, 122.4, 127.5, 129.9, 132.8, 155.8, 162.2, 164.9.

GC-MS (EI$^+$) *m/z*: $[M]^+$ 257.00

Transamidation of cinnamic amide with 4-methoxy aniline



The general procedure-B stated above was followed. Cinnamic amide (100 mg, 0.67 mmol), pivaloyl chloride (80.7 mg, 0.67mmol) 4-methoxy aniline (165.0 mg, 1.34 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as light brown solid in 128 mg (76% yield).

Physical Characteristics:

Colour and appearance: Light brown solid

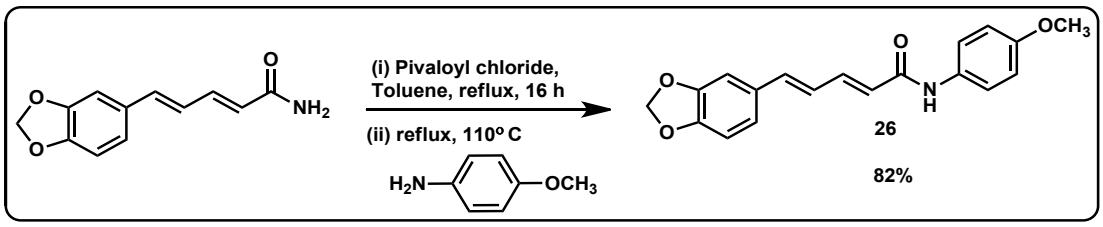
M.pt: 158 °C – 160 °C (Lit. m.pt = 156 °C – 157 °C)[22]

Spectral data:

^{1}H NMR: (400 MHz, $CDCl_3$) δ: 3.77 (3H, s), 6.64 (1H, d, *J* = 12 Hz), 6.85 (2H, d, *J* = 8 Hz), 7.33 (3H, d, *J* = 8 Hz), 7.45 (2H, d, *J* = 4 Hz), 7.57 (2H, d, *J* = 8 Hz), 7.73 (1H, d, *J* = 12 Hz),

8.17 (1H, s). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 55.4, 114.2, 121.1, 122.0, 127.9, 128.8, 129.8, 131.3, 134.7, 141.8, 156.5, 164.2. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 253.15

Transamidation of piperic amide with 4-methoxy aniline



The general procedure-B stated above was followed. Piperic amide (100 mg, 0.46 mmol), pivaloyl chloride (55 mg, 0.46 mmol), 4-methoxy aniline (113.3 mg, 0.92 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale-yellow solid in 128 mg (82% yield).

Physical Characteristics:

Colour and appearance: Pale yellow solid

M.pt: 200 °C – 201 °C

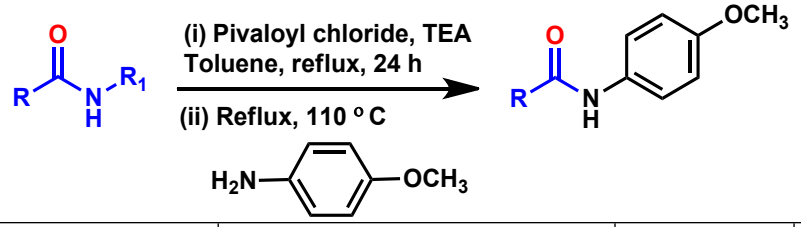
Spectral data:

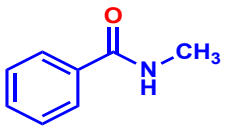
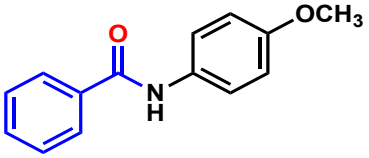
^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.67 (3H, s), 5.99 (2H, s), 6.21 (1H, d, *J* = 16 Hz), 6.82-6.98 (6H, m), 7.23 (2H, t, *J* = 12 Hz), 7.54 (2H, d, *J* = 8 Hz), 9.92 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 60.3, 106.5, 110.9, 113.6, 119.1, 125.8, 128.0, 129.7, 130.3, 136.0, 137.7, 143.7, 145.7, 153.1, 160.4, 168.6. **HRMS (ESI-MS)** *m/z*: Calculated for $C_{19}H_{18}NO_4$ $[M+H]^+$ 324.1235, found: 324.1246.

General procedure C: Transamidation of *N*-methyl-*N*-pivaloylbenzamide with 4-methoxy aniline

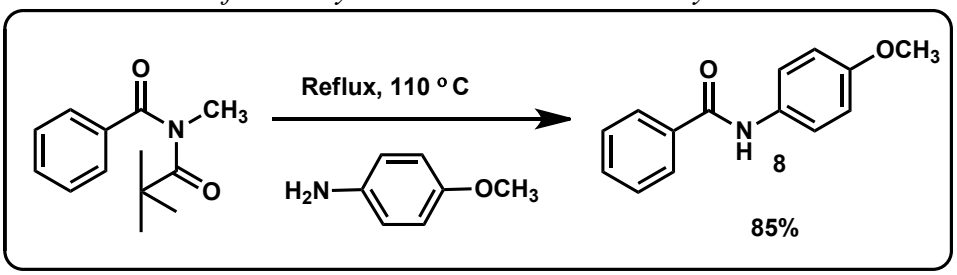
To the *N*-methyl-*N*-pivaloylbenzamide in toluene, 4-methoxy aniline (2 eq.), was added and refluxed. Progress of the reaction was monitored by TLC. Starting material consumed in 1h - 1.5h. After completion, the reaction mixture was washed with 5%HCl solution, 5% $NaHCO_3$ solution, water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography.

Table 4: Transamidation of secondary amides with 4-methoxy aniline



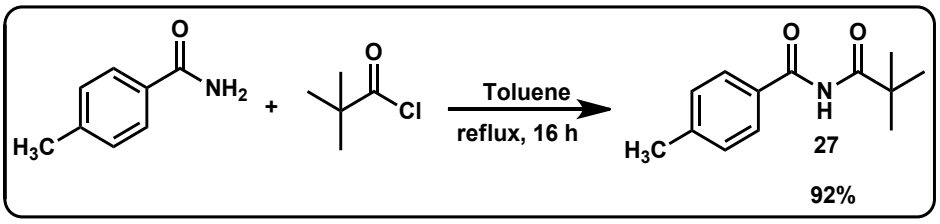
S.No	Amide	Product	Yield (%)	Time (h)
1.			85	1

Transamidation of N-methyl benzamide with 4-methoxy aniline



The general procedure-C stated above was followed. *N*-methyl-*N*-pivaloylbenzamide (100 mg, 0.45 mmol), 4-methoxy aniline (110 mg, 0.90 mmol). Pure product was obtained after column chromatography half white solid in 142 mg (85% yield).

Synthesis of 4-methyl N-pivaloyl benzamide



To a stirred solution of 4- methyl benzamide (250 g, 1.84 mmol), in 10 mL of toluene at room temperature, pivaloyl chloride (222 mg, 1.84 mmol) was added dropwise. After addition, the reaction mixture was refluxed for 16 h. Progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)]. After completion, the reaction mixture was washed with 5% $NaHCO_3$ solution and water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced

pressure. Pure product was obtained after column chromatography as white solid 371 mg (85% yield).

Spectral data:

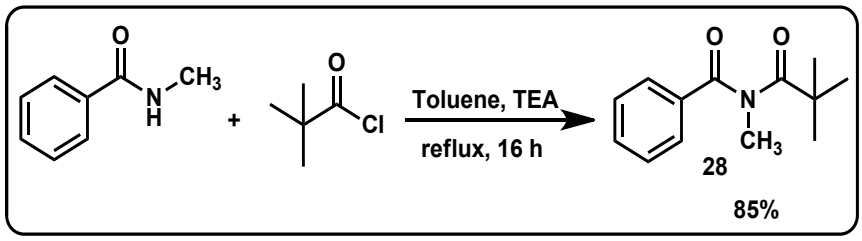
Physical Characteristics:

Colour and appearance: White solid

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 1.22 (9H, s), 2.38 (3H, s), 7.31 (2H, d, *J* = 8 Hz), 7.62 (2H, d, *J* = 8 Hz), 10.29 (1H, s).

^{13}C NMR: (100 MHz, DMSO-d_6) δ: 21.5, 26.8, 129.0, 129.3, 132.1, 143.1, 168.2, 177.6.

Synthesis of N-methyl N-pivaloyl benzamide



To a stirred solution of *N*-methyl benzamide (250 g, 1.84 mmol), triethylamine (371mg, 3.68 mmol) in 10 mL of toluene at room temperature, pivaloyl chloride (222 mg, 1.84 mmol) was added dropwise. After addition, the reaction mixture was heated upto 80 C for 24 h. Progress of the reaction was monitored by TLC [hexane-EtOAc (8:2)]. After completion, the reaction mixture was washed with with 5% HCl solution, 5% $NaHCO_3$ solution and water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography as white solid 342 mg (85% yield).

Colour and appearance: Half-White solid

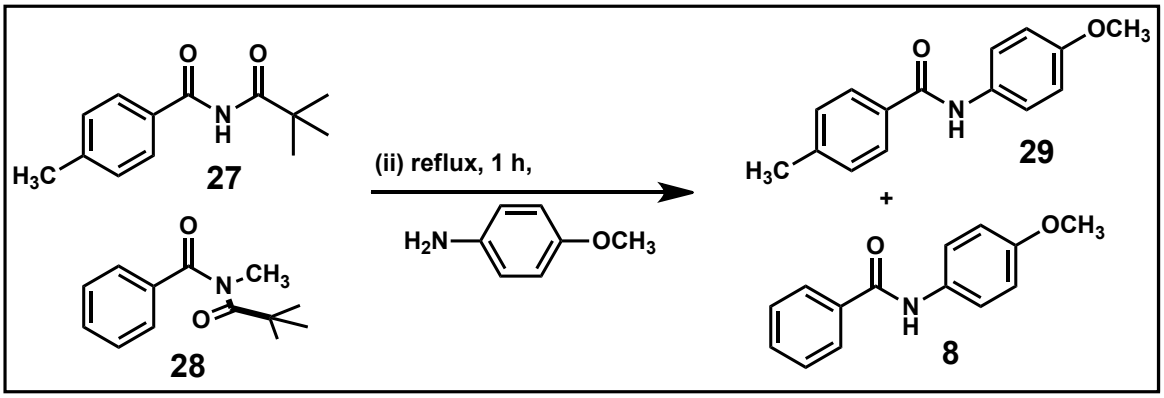
Spectral data:

H NMR: (400 MHz, DMSO-d_6) δ: 1.26 (9H, s), 3.08 (3H, s), 7.51 (2H, t, *J* = 8 Hz), 7.58 – 7.62 (1H, m), 7.67 (2H, t, *J* = 4 Hz).

^{13}C NMR: (100 MHz, DMSO-d_6) δ: 28.4, 35.0, 42.5, 129.0, 129.2, 132.7, 134.8, 174.9, 186.1.

Competitive study

N-pivaloyl activated secondary amide Vs tertiary amide



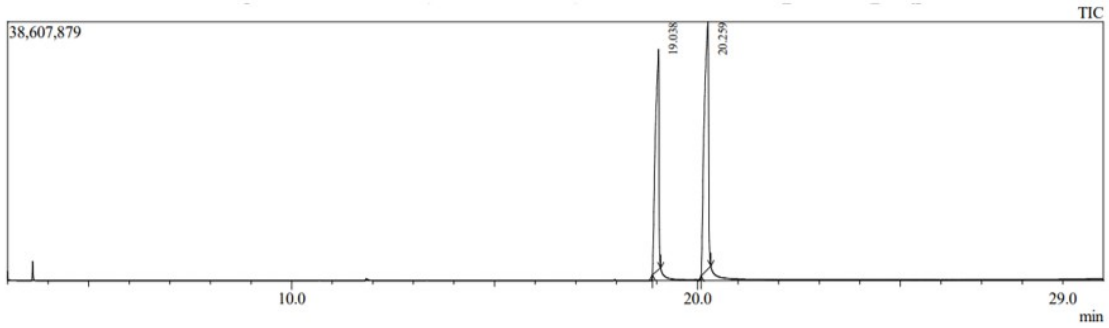
To a stirred solution of 4-methyl benzamide (50 mg, 0.228 mmol, 0.5 eq.), and *N*- methyl benzamide (50 mg, 0.228 mmol, 0.5 eq.) in toluene (3 mL). To the above mixture p-anisidine (56.3 mg, 0.456 mmol, 2 eq.) was added, the reaction mixture was refluxed for 1 h. After completion, the reaction mixture was washed with 5% HCl solution to remove excess amine and a small filtration column was performed to remove the by-products. The resulted crude reaction mixture was characterized by ^{1}H NMR.

<u>^{1}H NMR Spectral data of the selectivity reaction I</u>

29- ^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.38 (3H, s), 3.74 (3H, s), 6.92 (2H, d, *J* = 4 Hz), 7.32 (2H, d, *J* = 8 Hz), 7.66 (2H, d, *J* = 4 Hz), 7.86 (2H, d, *J* = 8 Hz), 10.05 (1H, s).

8- ^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.75 (2.6 H, s), 6.94 (1.6 H, d, *J* = 4 Hz), 7.50 – 7.60 (2.4 H, m), 7.69 (1.6 H, d, *J* = 4 Hz), 7.94 (1.6 H, d, *J* = 4 Hz), 10.14 (0.7 H, s).

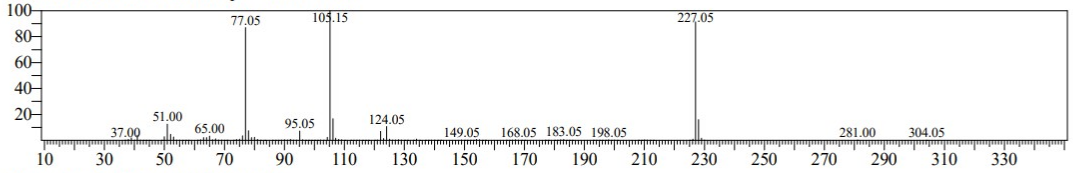
GC-MS spectra of competitive reaction between primary Vs secondary amide against anisidine



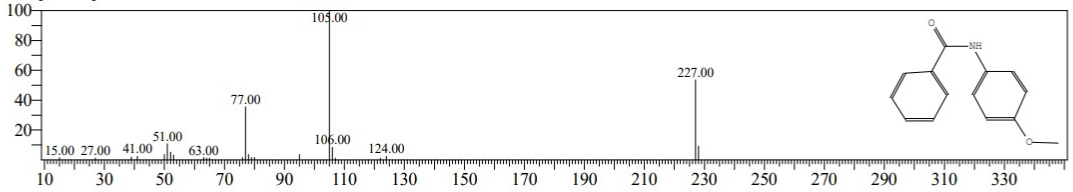
Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	19.038	18.890	19.095	198057233	42.46	32864509	47.15	6.03		
2	20.259	20.090	20.330	268424058	57.54	36838961	52.85	7.29		

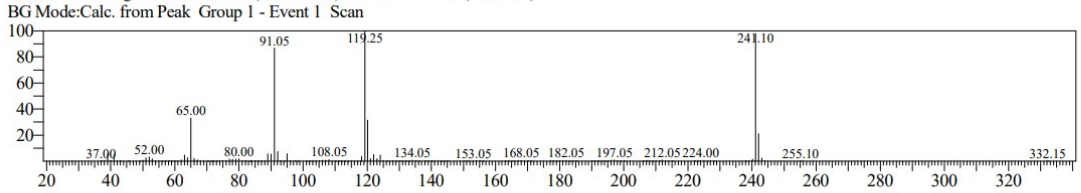
Library
<< Target >>
Line#:1 R.Time:19.040(Scan#:3209) MassPeaks:142
RawMode:Averaged 19.035-19.045(3208-3210) BasePeak:105.15(7696208)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



Hit#:1 Entry:99092 Library:NIST17.lib
SI:87 Formula:C14H13NO2 CAS:7472-54-0 MolWeight:227 RetIndex:2056
CompName:p-Benzanisidide



<< Target >>
Line#:2 R.Time:20.260(Scan#:3453) MassPeaks:165
RawMode:Averaged 20.255-20.265(3452-3454) BasePeak:119.25(7723085)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan



Hit#:1 Entry:113337 Library:NIST17.lib
SI:82 Formula:C15H15NO2 CAS:0-00-0 MolWeight:241 RetIndex:2169
CompName:Benzamide, N-(4-methoxyphenyl)-3-methyl-

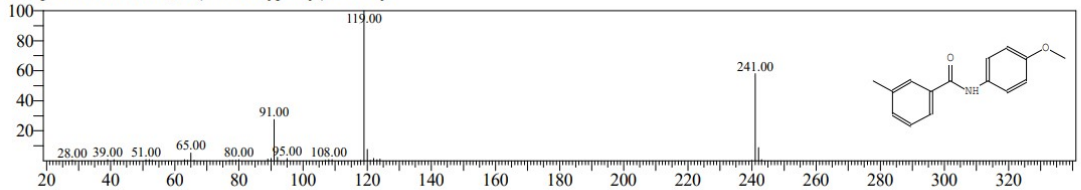


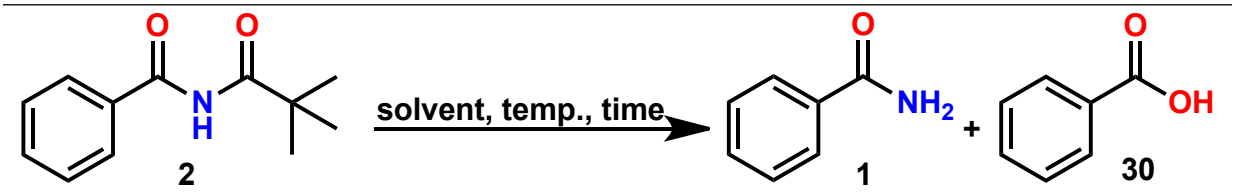
Figure S2: Chromatogram and mass spectra of competitive study.

Stability of *N*-pivaloyl benzamide

(i) **General procedure for stability studies:** To solution of *N*-pivaloyl benzamide (0.12 mmol, 1.0 eq.) in CH_3CN (10 mL) water or acid as indicated was added at room temperature, and the reaction was stirred vigorously at a given temperature. After the indicated time, progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)].

(ii) **General procedure for solvent stability studies.** The *N*-pivaloyl benzamide (0.12 mmol, 1.0 eq.) was dissolved in an DMSO (5mL), and the solution was stirred vigorously at a given temperature. After the indicated time, progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)].

Table 5: Stability of *N*-pivaloyl benzamide under various conditions



S.No	Solvent (eq.)	temp (°C)	time (h)	Yield (%)
1.	H_2O (5 eq.)	RT, 80, 100	24	0
2.	con.HCl (2 eq.)	RT	24	0
3.	con.HCl (2 eq.)	a) 80	3	70
		b) 100	1	95
4.	DMSO (excess)	RT, 80, 100	24	0

Reference

1 C. Mei, Y. Hu and W. Lu, *Synthesis*, 2018, **50**, 2999–3005.
2 D. D. Sanz Sharley and J. M. J. Williams, *Tetrahedron Letters*, 2017, **58**, 4090–4093.
3 M. Rezaei, K. Amani and K. Darvishi, *Catalysis Communications*, 2017, **91**, 38–42.
4 A. Poeschl and D. M. Mountford, *Org. Biomol. Chem.*, 2014, **12**, 7150–7158.
5 S. Sobhani, Z. M. Falatooni, S. Asadi and M. Honarmand, *Catal Lett*, 2016, **146**, 255–268.
6 R. Azadi and Z. Motamedpoor, *LOC*, 2018, **15**, 801–804.
7 Y. Wang, Z. Wu, Q. Li, B. Zhu and L. Yu, *Catal. Sci. Technol.*, 2017, **7**, 3747–3757.
8 C. A. D. Caiuby, M. P. de Jesus and A. C. B. Burtoloso, *J. Org. Chem.*, 2020, **85**, 7433–7445.
9 C. Li, M. Wang, X. Lu, L. Zhang, J. Jiang and L. Zhang, *ACS Sustainable Chem. Eng.*, 2020, **8**, 4353–4361.
10 A. Mishra, S. Singh and V. Srivastava, *Asian Journal of Organic Chemistry*, 2018, **7**, 1600–1604.
11 J.-E. Won, H.-K. Kim, J.-J. Kim, H.-S. Yim, M.-J. Kim, S.-B. Kang, H.-A. Chung, S.-G. Lee and Y.-J. Yoon, *Tetrahedron*, 2007, **63**, 12720–12730.
12 P. K. Sahu, P. K. Sahu, R. Gupta, M. Messali, S. M. Almutairi, P. L. Sahu and D. D. Agarwal, *ACS Omega*, 2018, **3**, 18976–18983.
13 S. A. Rzhevskiy, A. A. Ageshina, G. A. Chesnokov, P. S. Gribanov, M. A. Topchiy, M. S. Nechaev and A. F. Asachenko, *RSC Adv.*, 2019, **9**, 1536–1540.
14 J.-S. Li, Y. Xue, P.-Y. Li, Z.-W. Li, C.-H. Lu, W.-D. Liu, H.-L. Pang, D.-H. Liu, M.-S. Lin, B.-B. Luo and W. Jiang, *Res Chem Intermed*, 2015, **41**, 2235–2247.
15 R. Otsuka, K. Maruhashi and T. Ohwada, *Synthesis*, 2018, **50**, 2041–2057.
16 S. Das, S. Ray, A. B. Ghosh, P. K. Samanta, S. Samanta, B. Adhikary and P. Biswas, *Applied Organometallic Chemistry*, 2018, **32**, e4199.
17 P. C. S. Costa, M. R. O. Barsottini, M. L. L. Vieira, B. A. Pires, J. S. Evangelista, A. C. M. Zeri, A. F. Z. Nascimento, J. S. Silva, M. F. Carazzolle, G. A. G. Pereira, M. L. Sforça, P. C. M. L. Miranda and S. A. Rocco, *Journal of Molecular Structure*, 2020, **1208**, 127903.
18 M. Gergely and L. Kollár, *Tetrahedron*, 2018, **74**, 2030–2040.
19 W. K. Su, Y. Zhang, J. J. Li and P. Li, *Organic Preparations and Procedures International*, 2008, **40**, 543–550.
20 B. Nammalwar, N. P. Muddala, F. M. Watts and R. A. Bunce, *Tetrahedron*, 2015, **71**, 9101–9111.
21 Y. Gao, J. Liu, Z. Li, T. Guo, S. Xu, H. Zhu, F. Wei, S. Chen, H. Gebru and K. Guo, *J. Org. Chem.*, 2018, **83**, 2040–2049.
22 A. D. Kosal, E. E. Wilson and B. L. Ashfeld, *Angewandte Chemie International Edition*, 2012, **51**, 12036–12040.

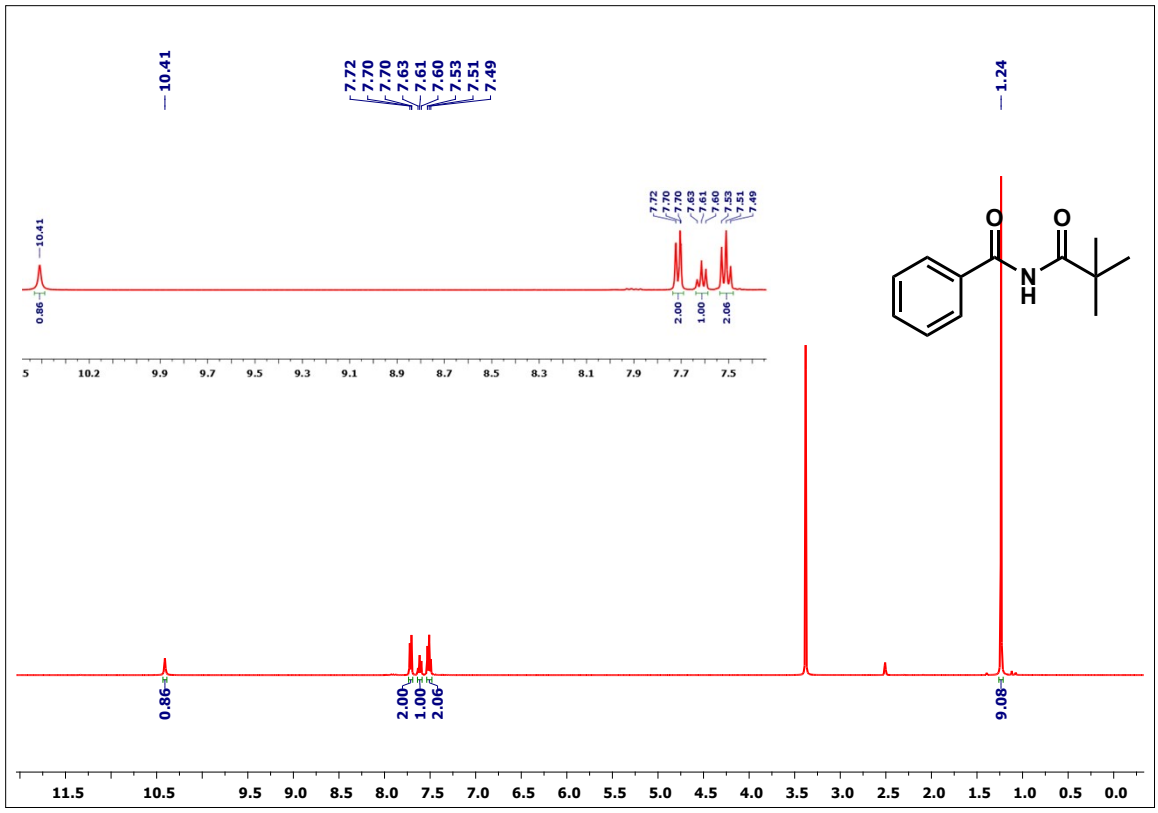


Figure S3: 400 MHz ^{1}H NMR spectrum of *N*-pivaloyl benzamide **1** in DMSO-d$_6$

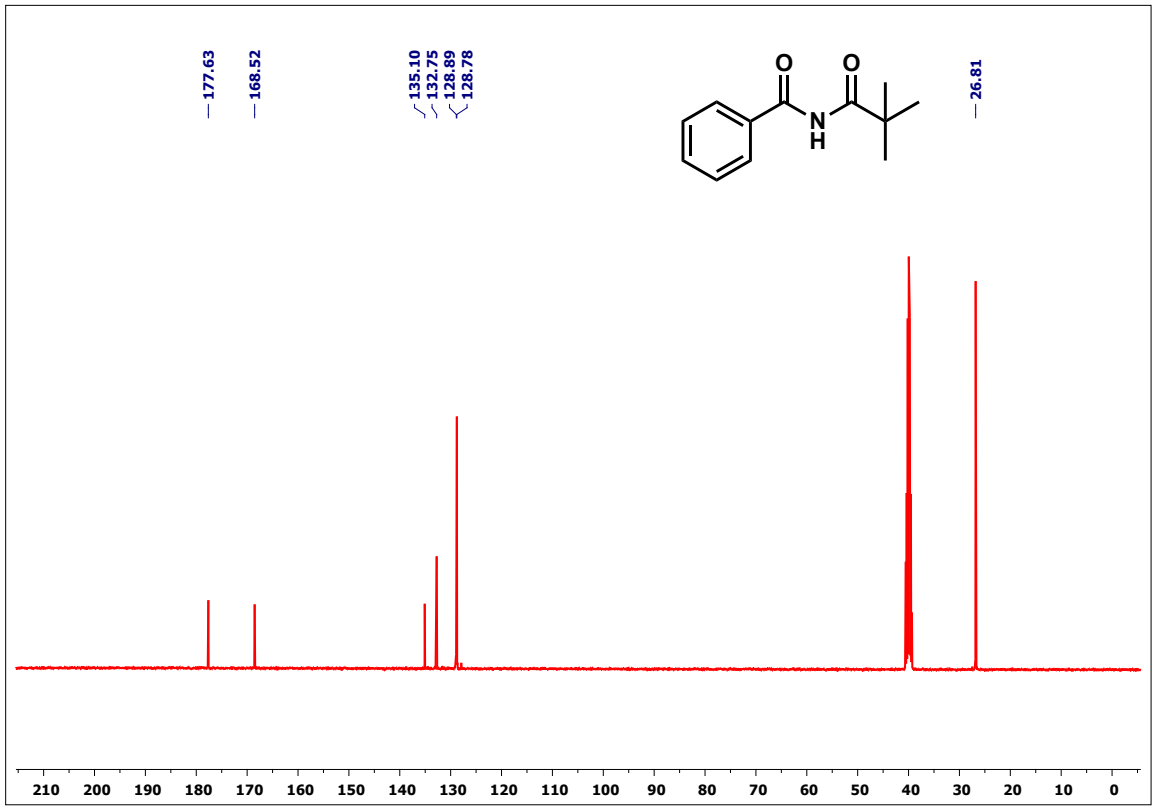


Figure S4: 100 MHz ^{13}C NMR spectrum of *N*-pivaloyl benzamide **1** in DMSO-d$_6$

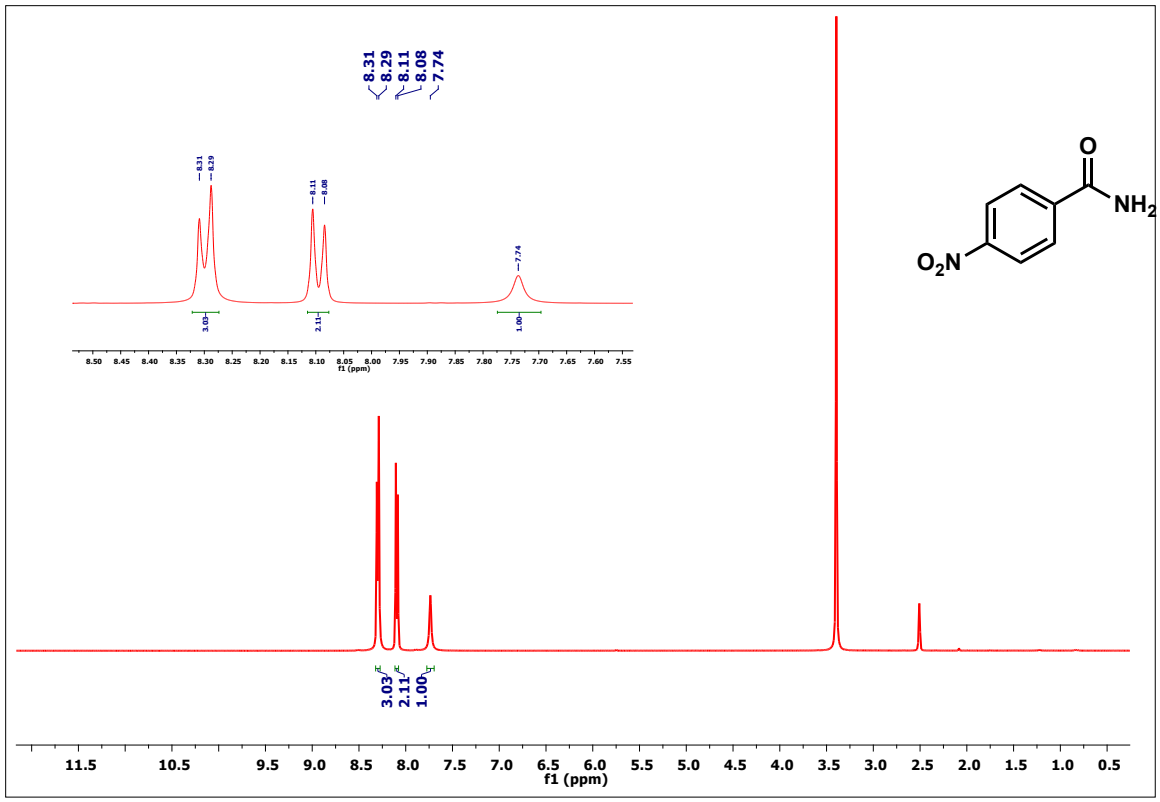


Figure S5: 400 MHz ^{1}H NMR spectrum of 4-nitro benzamide in DMSO-d_6

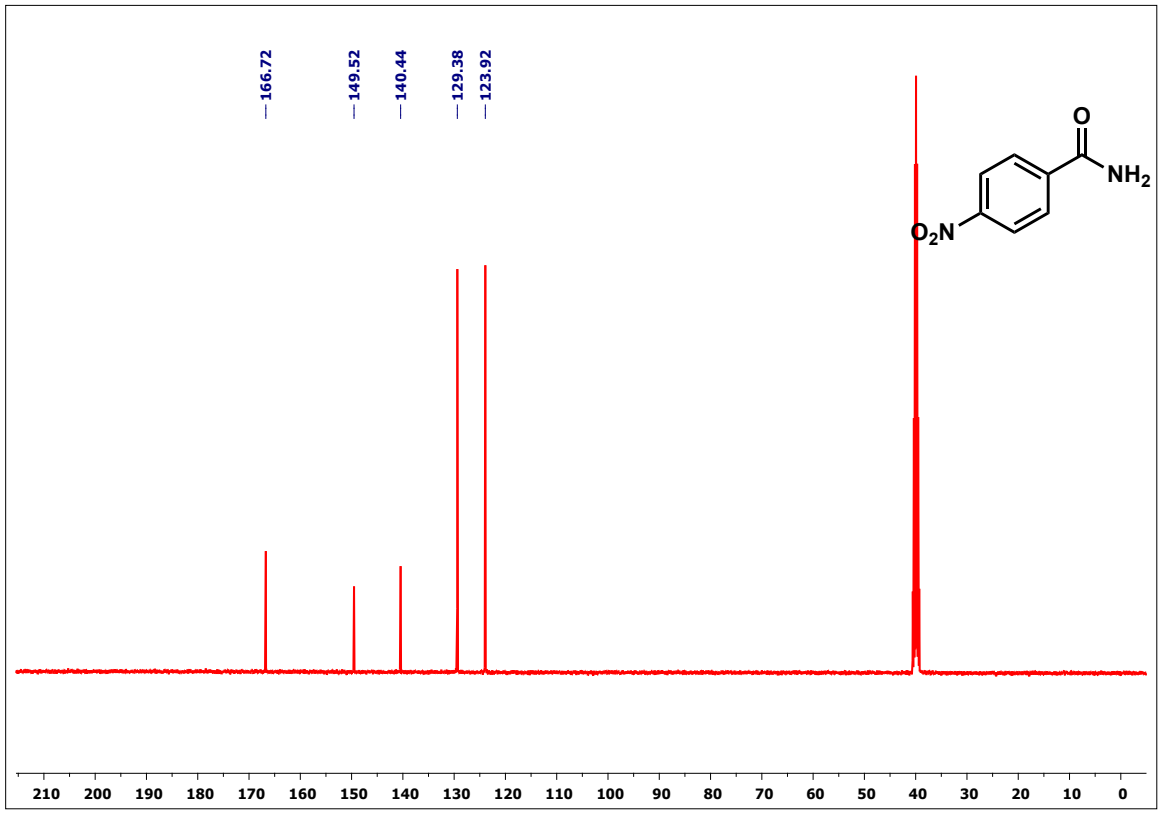


Figure S6: 100 MHz ^{13}C NMR spectrum of 4- nitro benzamide in DMSO-d_6

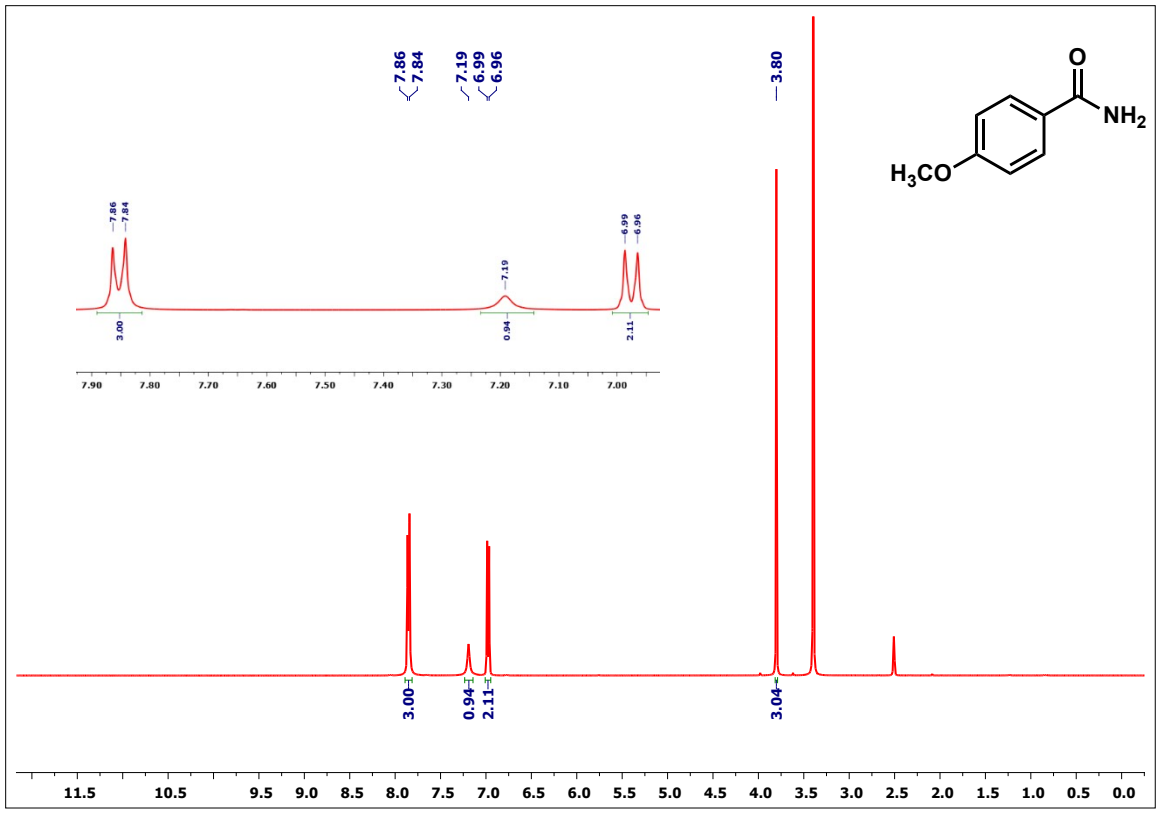


Figure S7: 400 MHz ^{1}H NMR spectrum of 4-methoxy benzamide in DMSO-d_6

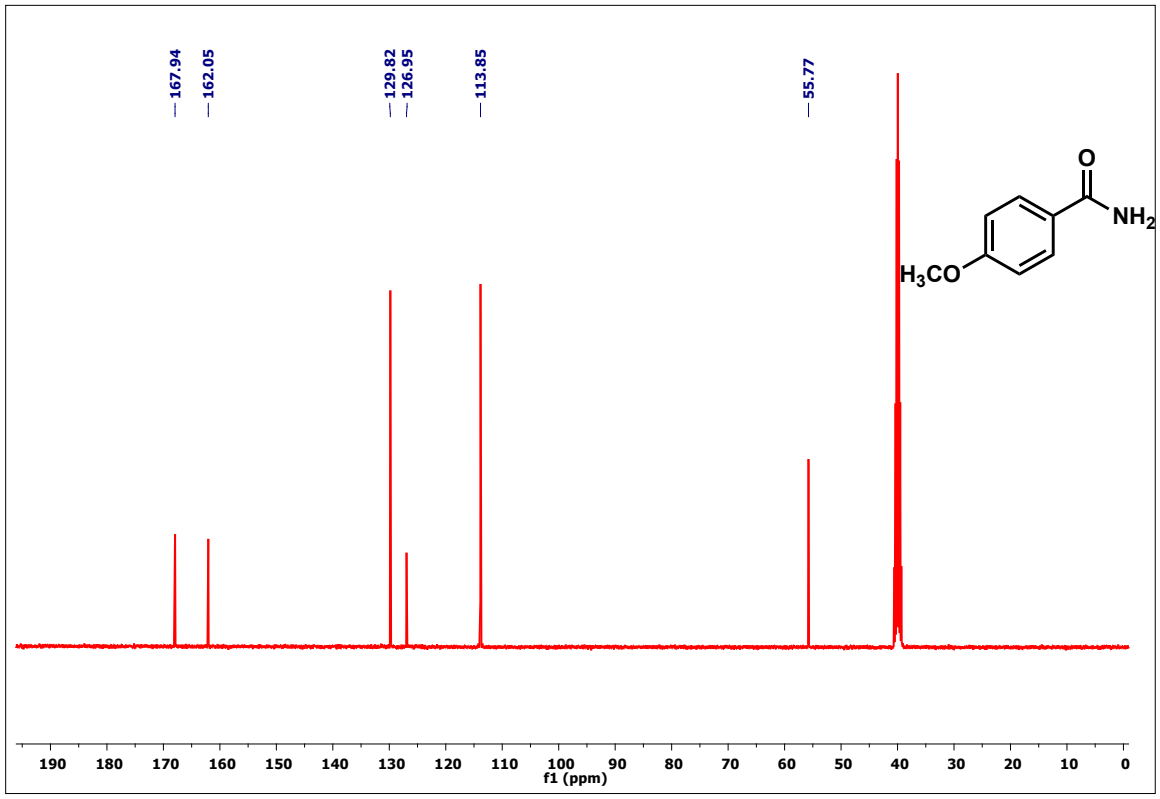


Figure S8: 100 MHz ^{13}C NMR spectrum of 4-methoxy benzamide in DMSO-d_6

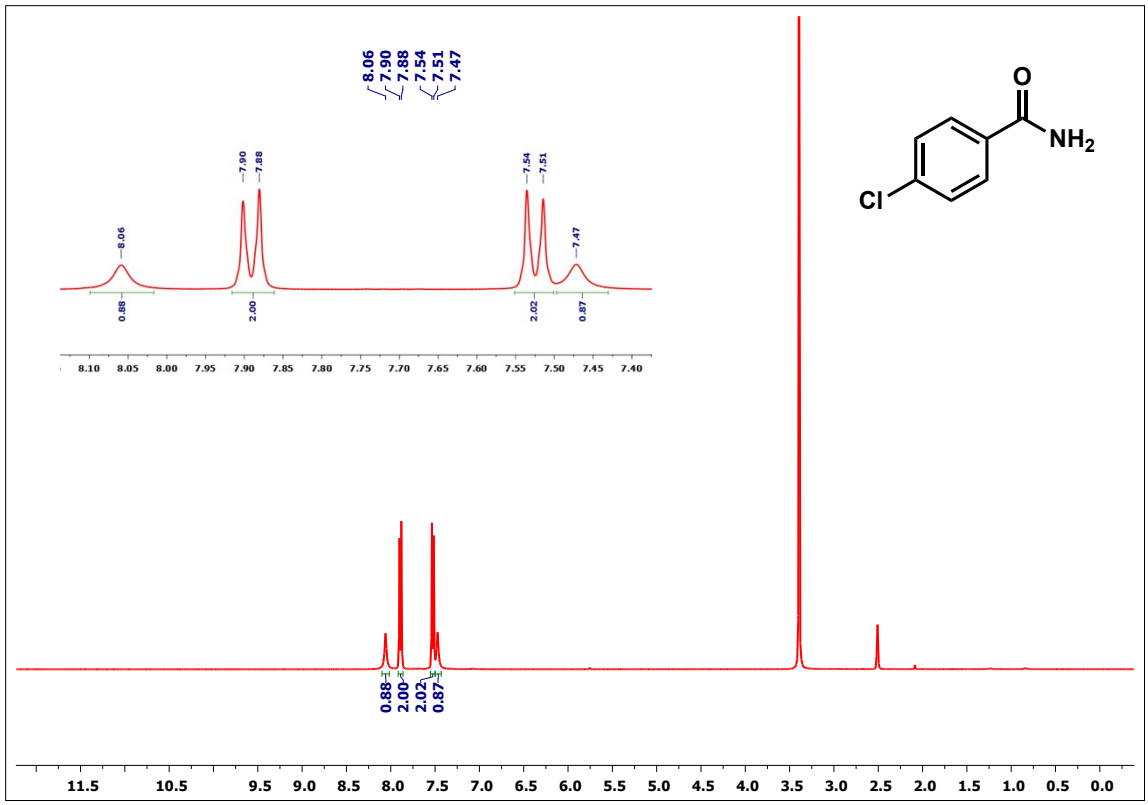


Figure S9: 400 MHz ^{1}H NMR spectrum of 4-chloro benzamide in DMSO-d_6

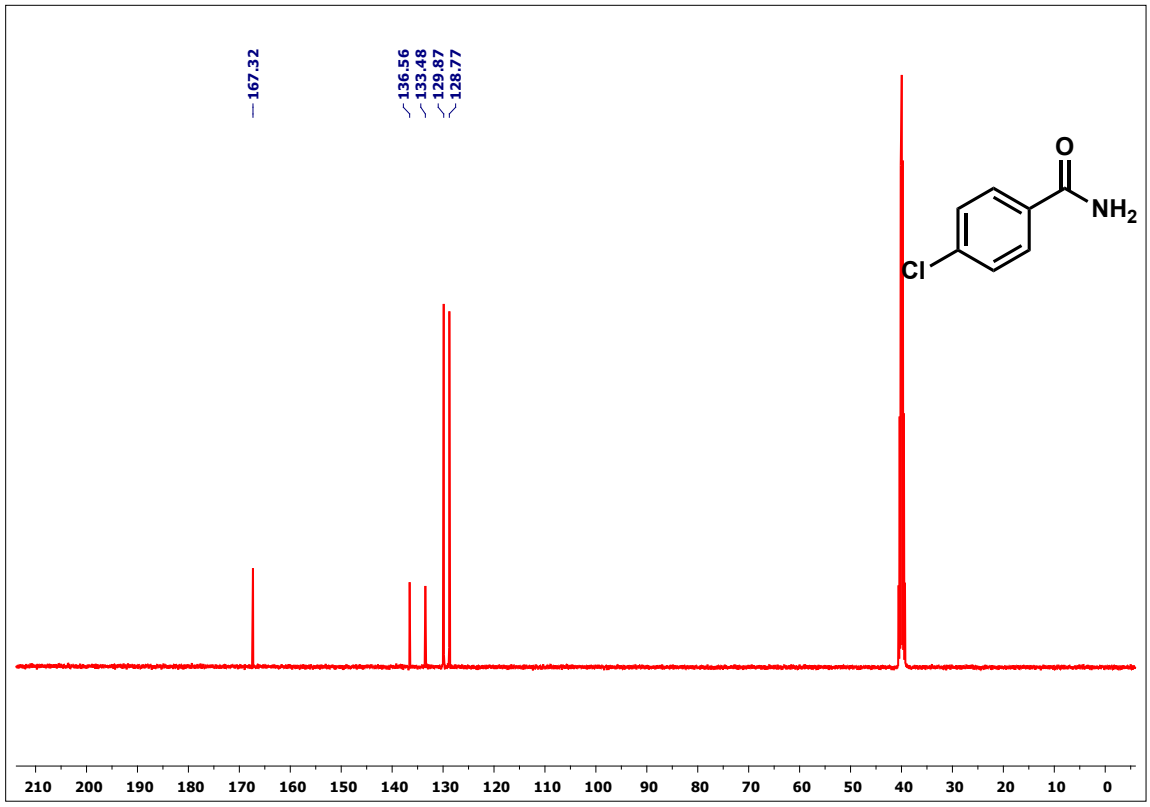


Figure S10: 100 MHz ^{13}C NMR spectrum of 4-chloro benzamide in DMSO-d_6

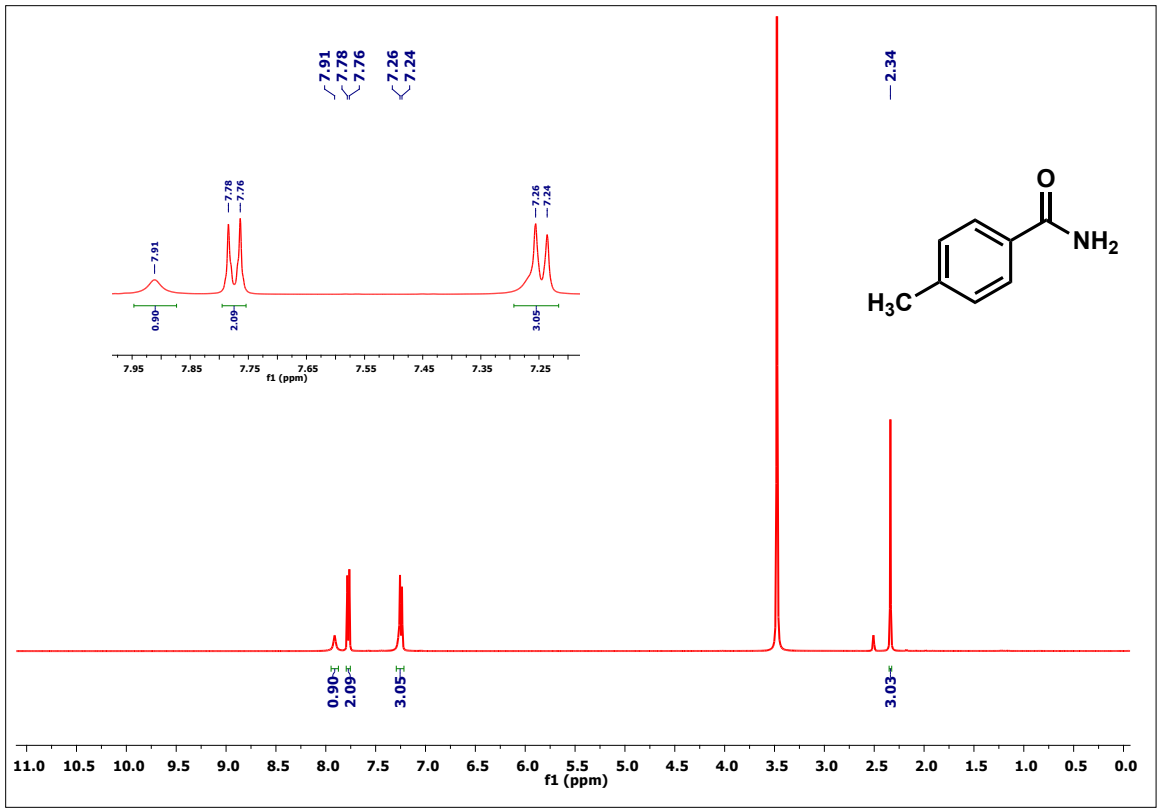


Figure S11: 400 MHz ^{1}H NMR spectrum of 4-methyl benzamide in DMSO-d_6

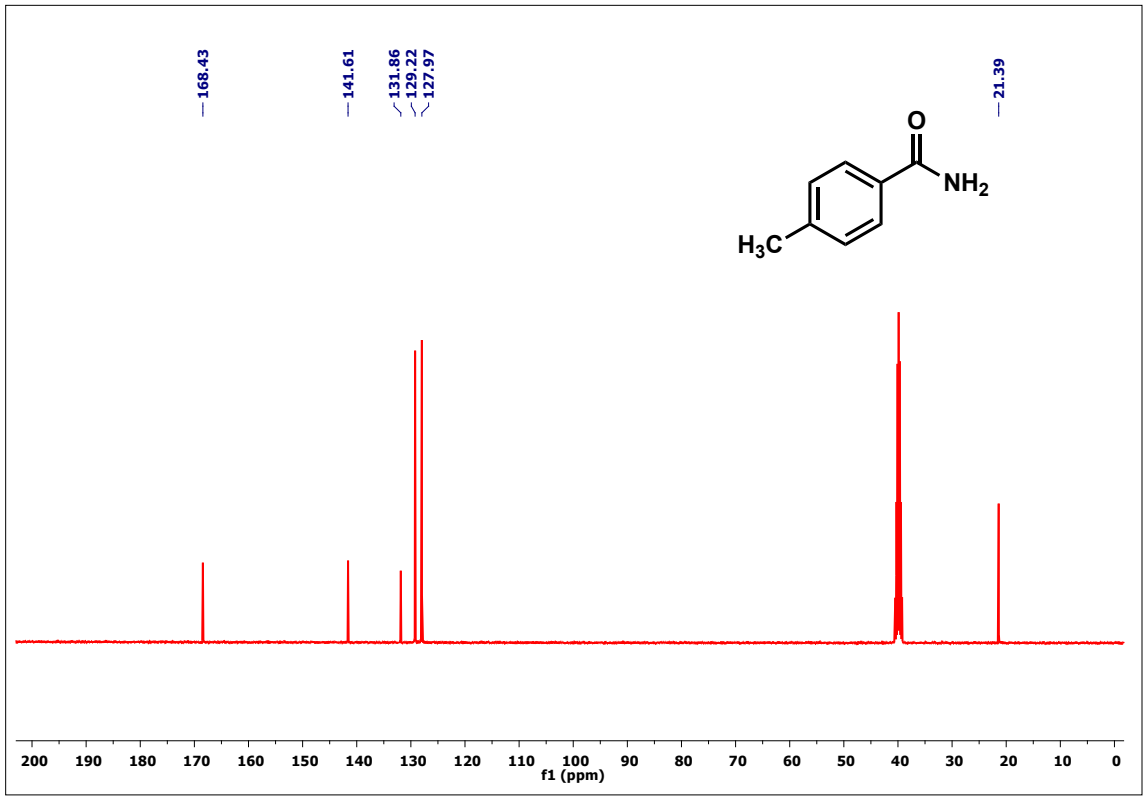


Figure S12: 100 MHz ^{13}C NMR spectrum of 4-methyl benzamide in DMSO-d_6

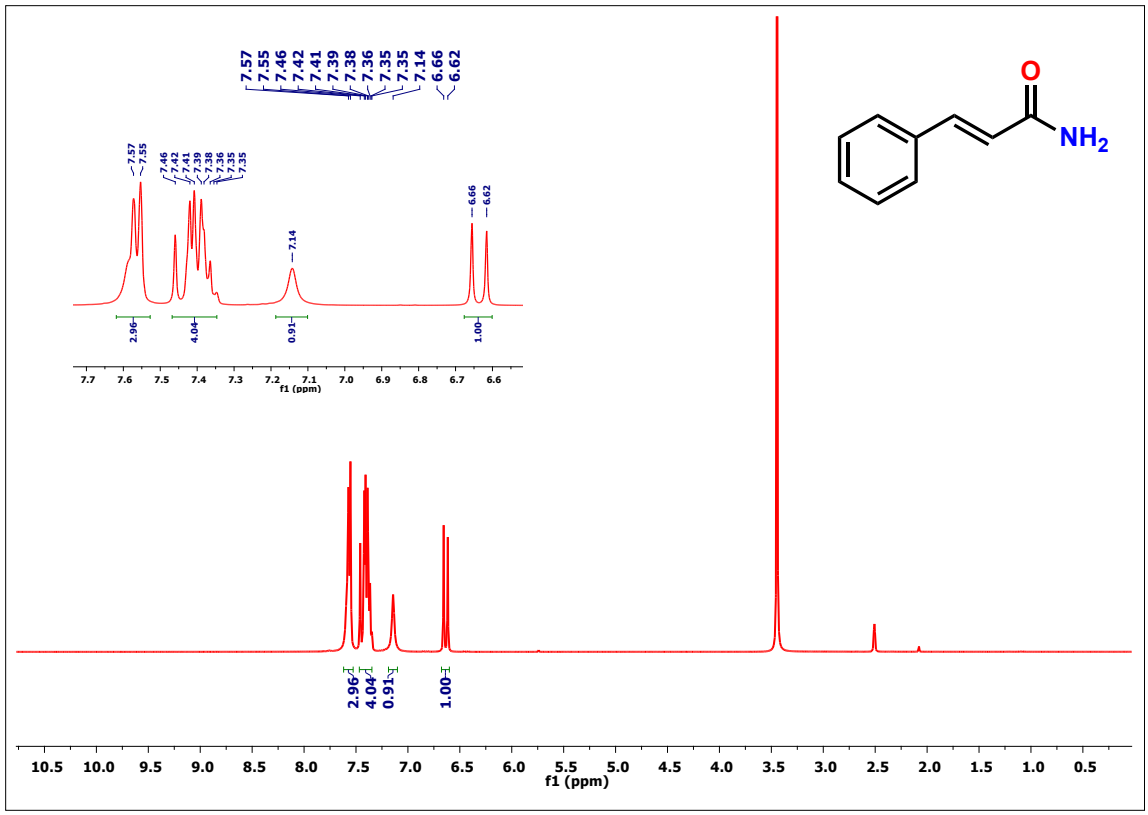


Figure S13: 400 MHz ^{1}H NMR spectrum of cinnamamide in DMSO-d_6

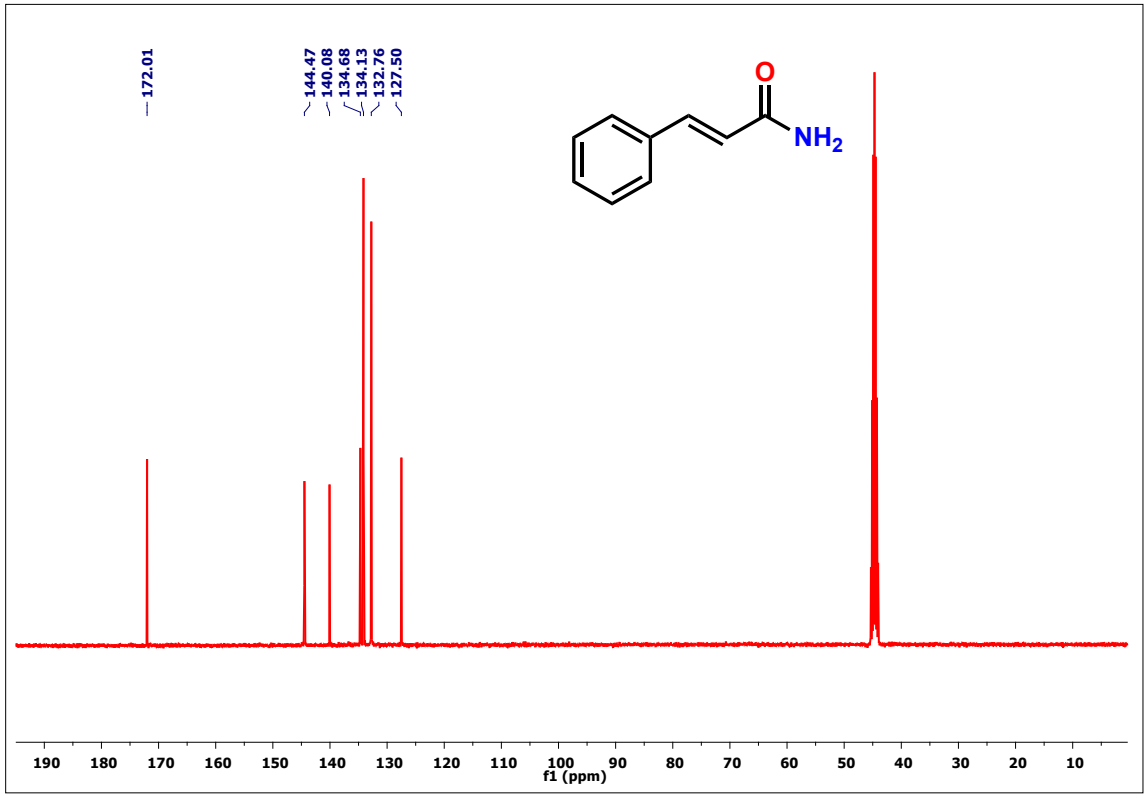


Figure S14: 100 MHz ^{13}C NMR spectrum of cinnamamide in DMSO-d_6

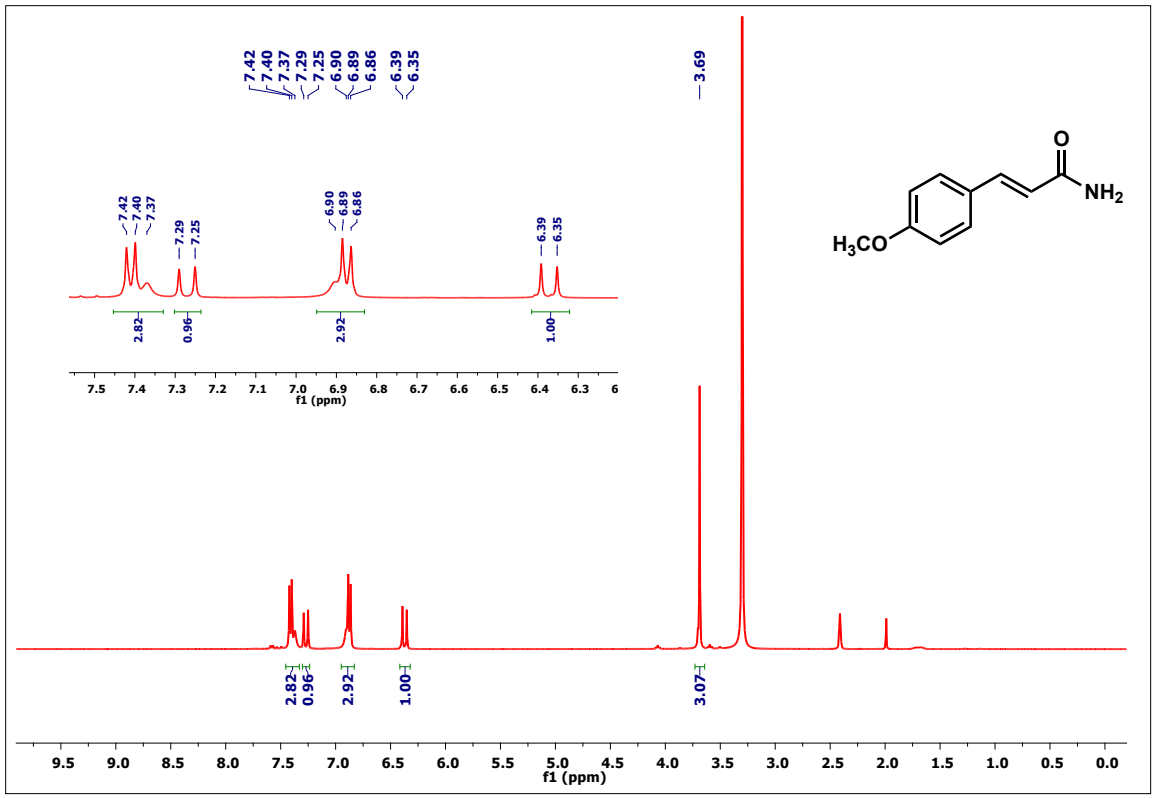


Figure S15: 400 MHz ^{1}H NMR spectrum of 4-methoxy cinnamamide in DMSO-d_6

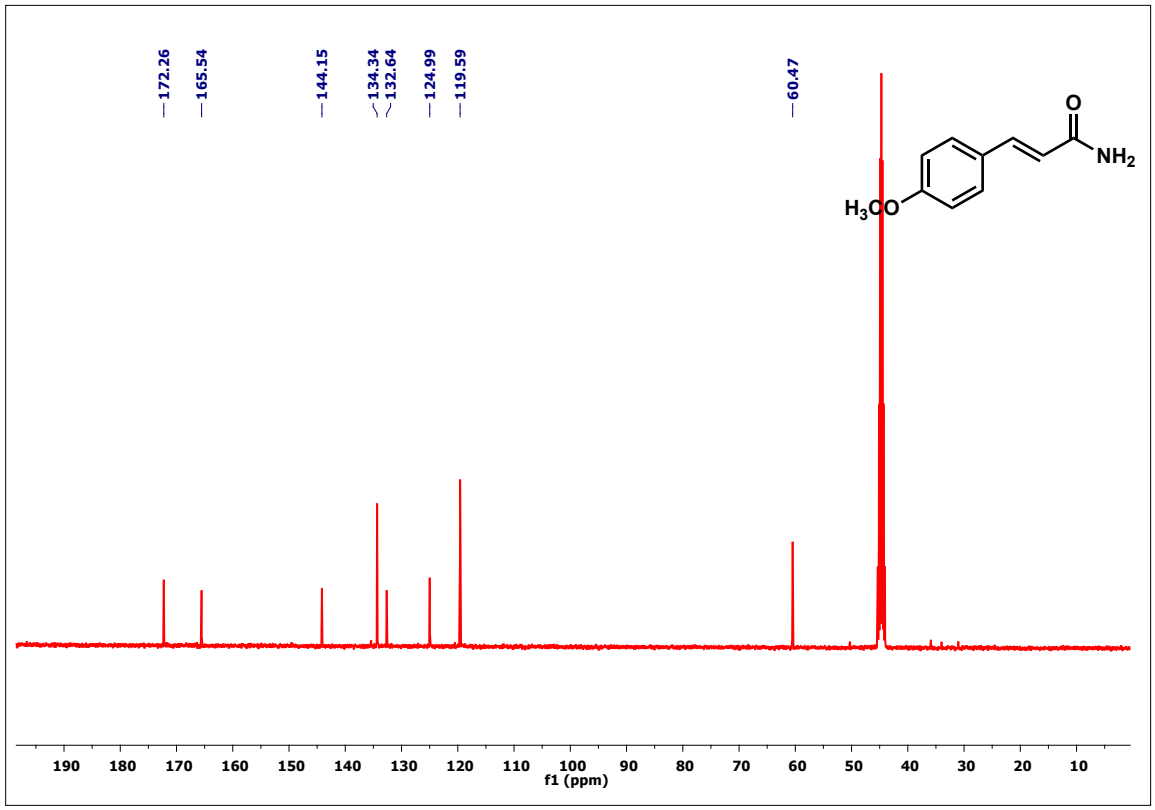


Figure S16: 100 MHz ^{13}C NMR spectrum of 4-methoxy cinnamamide in DMSO-d_6

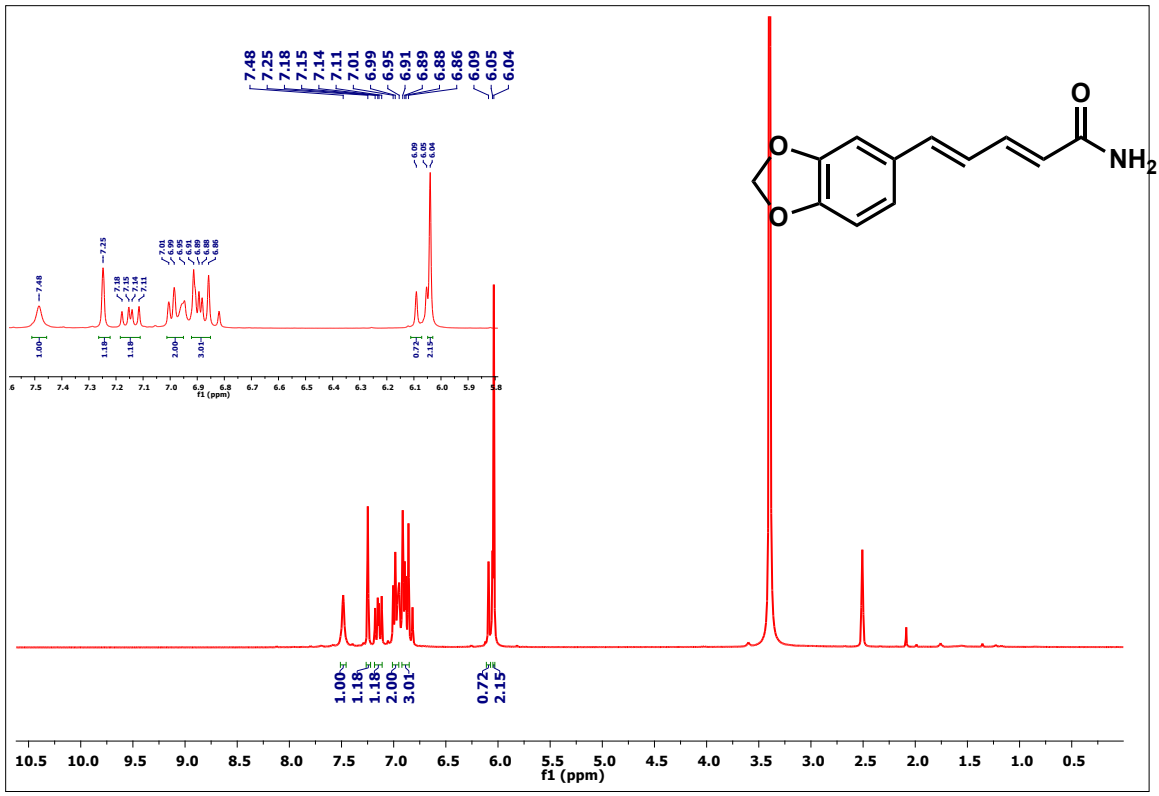


Figure S17: 400 MHz ^{1}H NMR spectrum of pipericamide in DMSO-d_6

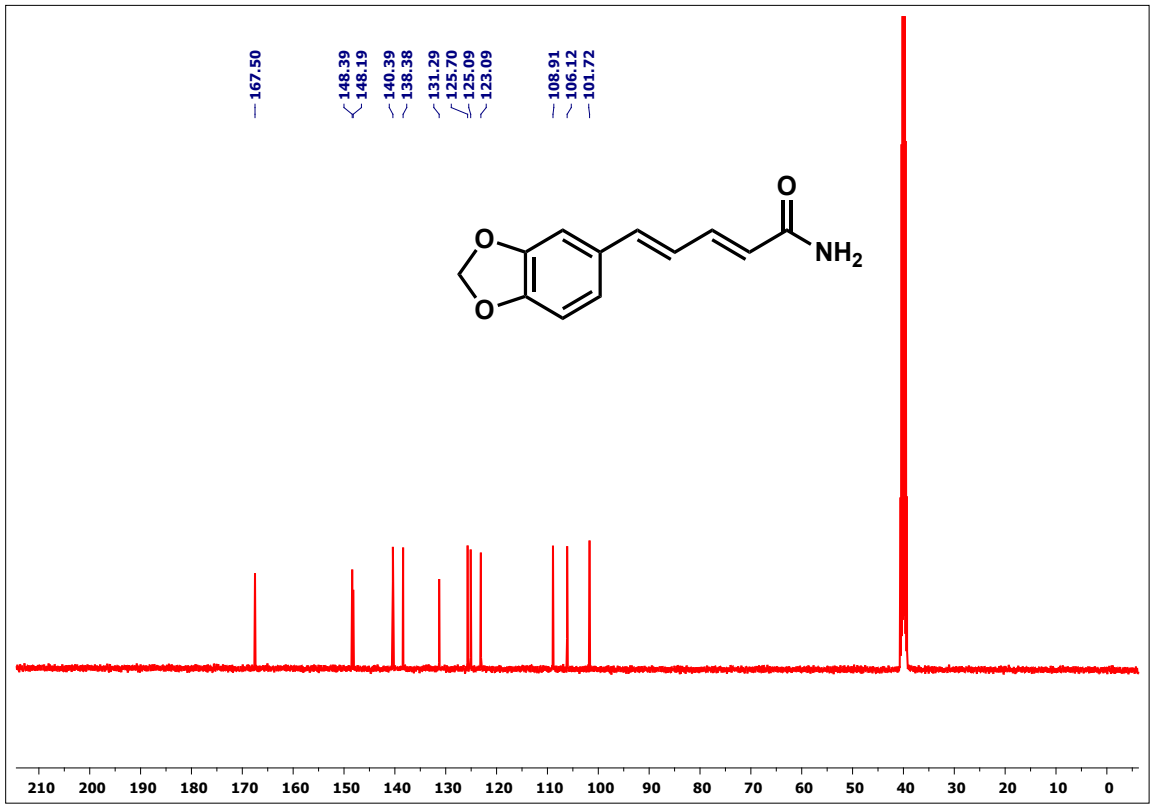


Figure S18: 100 MHz ^{13}C NMR spectrum of pipericamide in DMSO-d_6

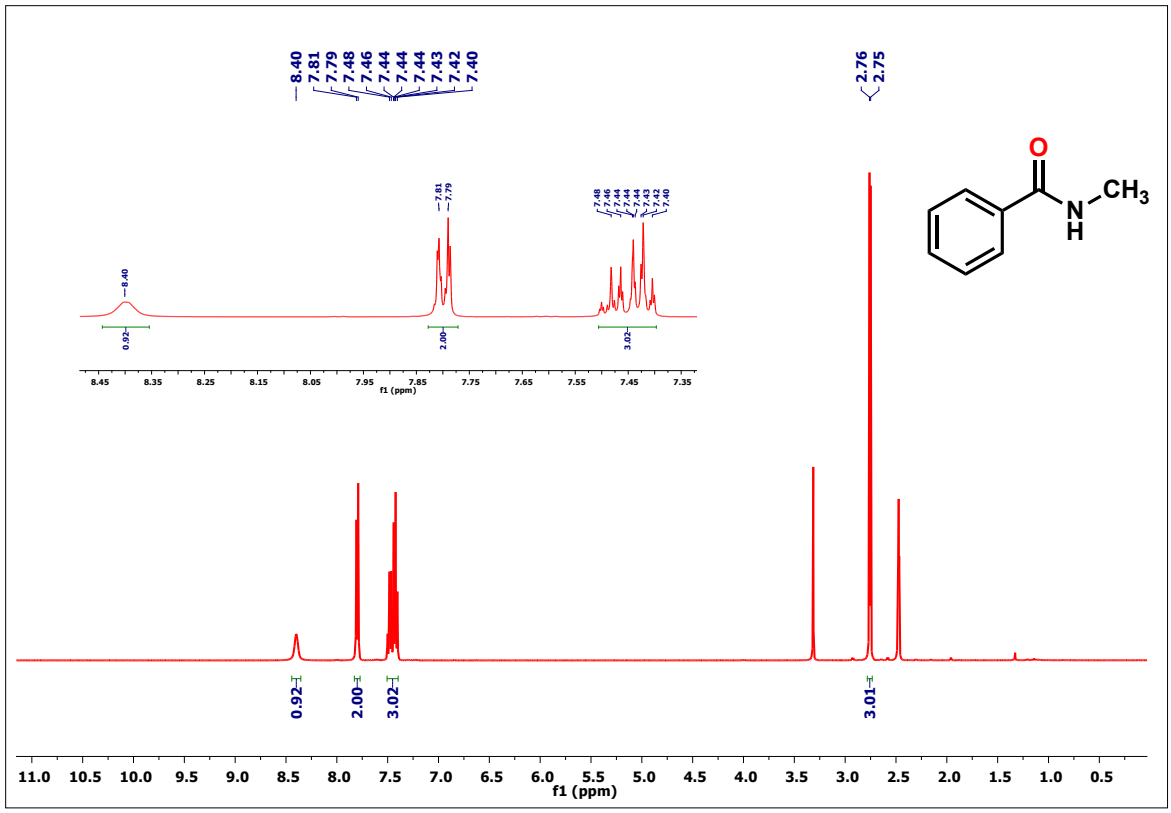


Figure S19: 400 MHz ^{1}H NMR spectrum of *N*-methyl benzamide in DMSO-d$_6$

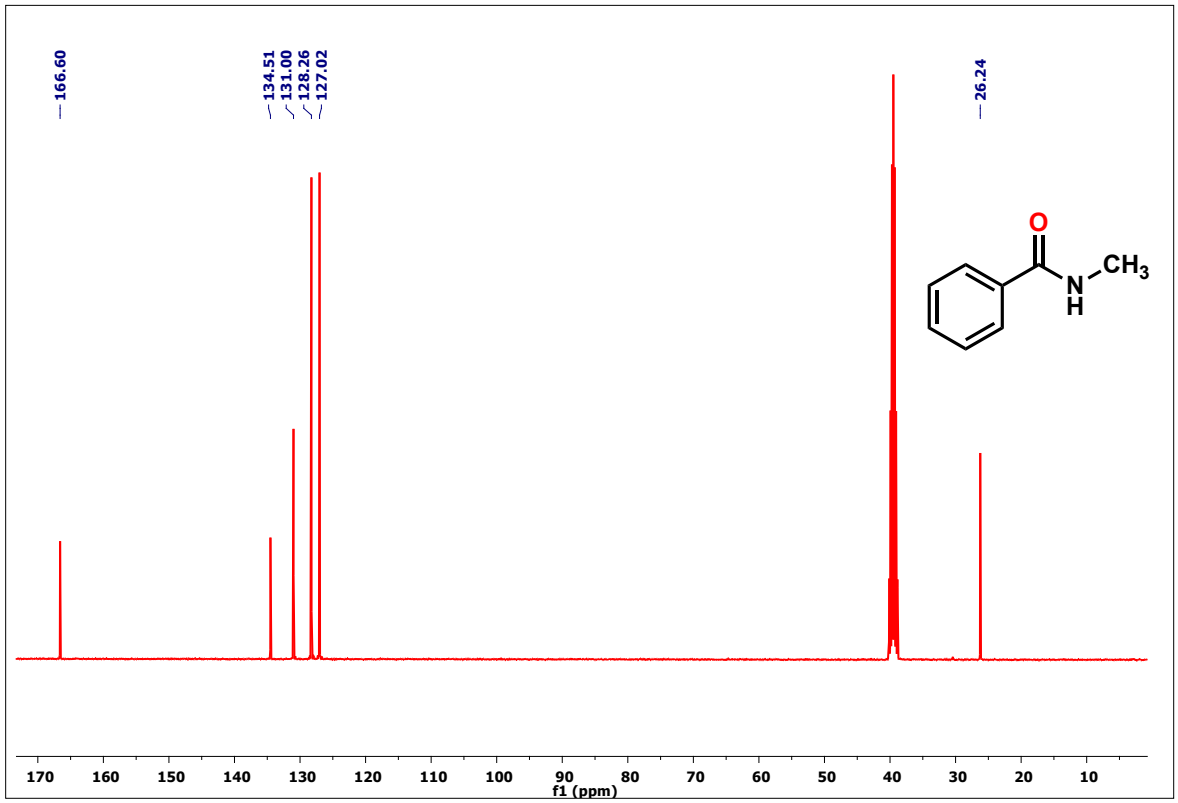


Figure S20: 100 MHz ^{13}C NMR spectrum of *N*-methyl benzamide in DMSO-d$_6$

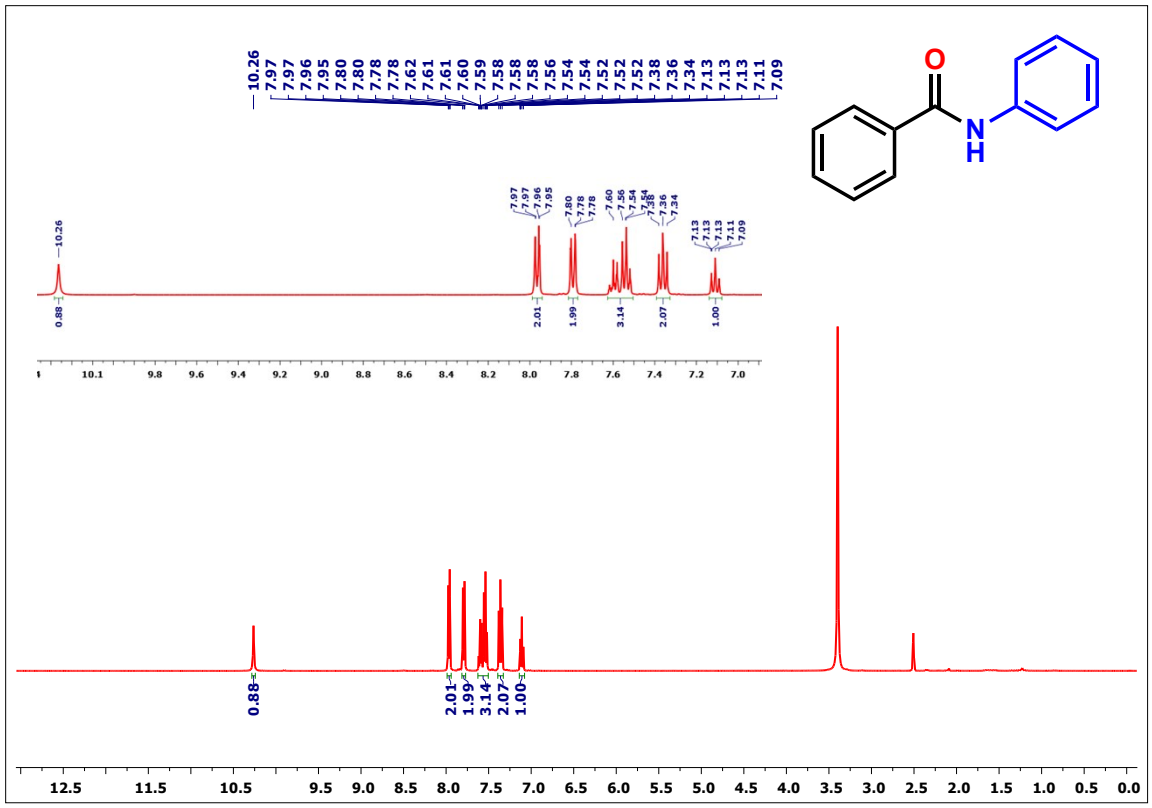


Figure S21: 400 MHz ^{1}H NMR spectrum of **3** in DMSO-d_6

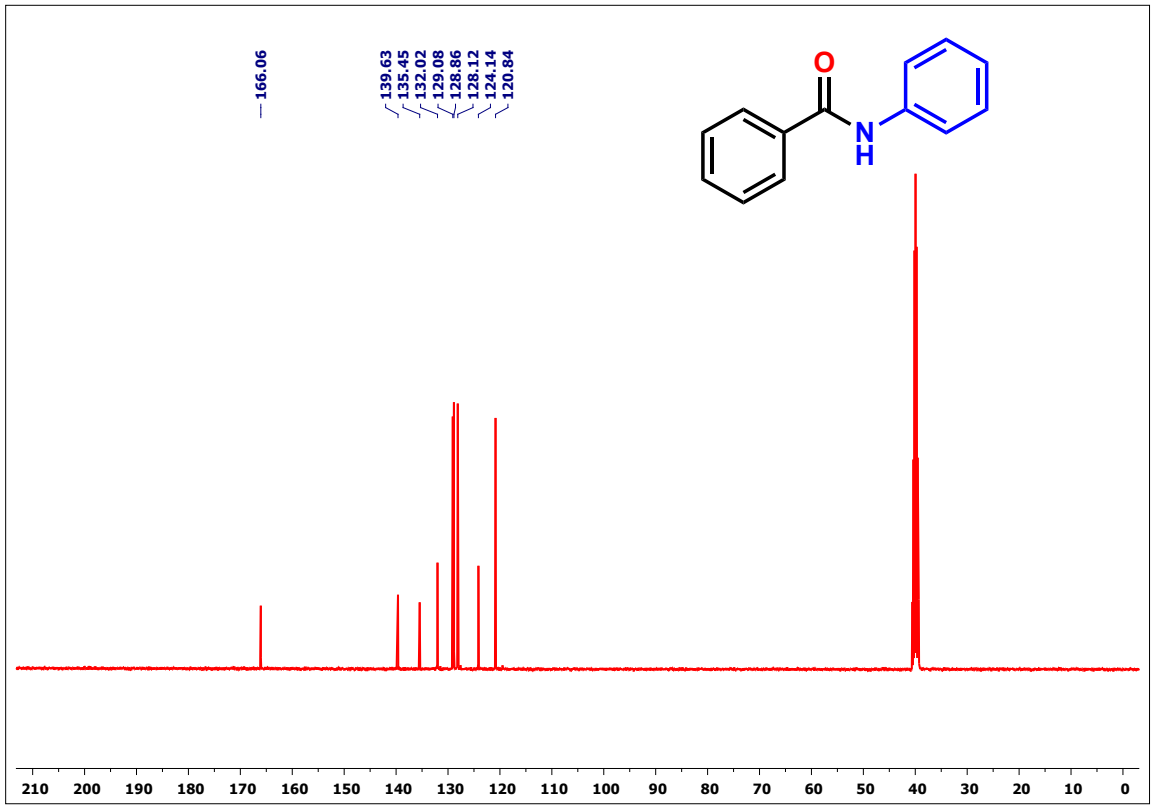


Figure S22: 100 MHz ^{13}C NMR spectrum of **3** in DMSO-d_6

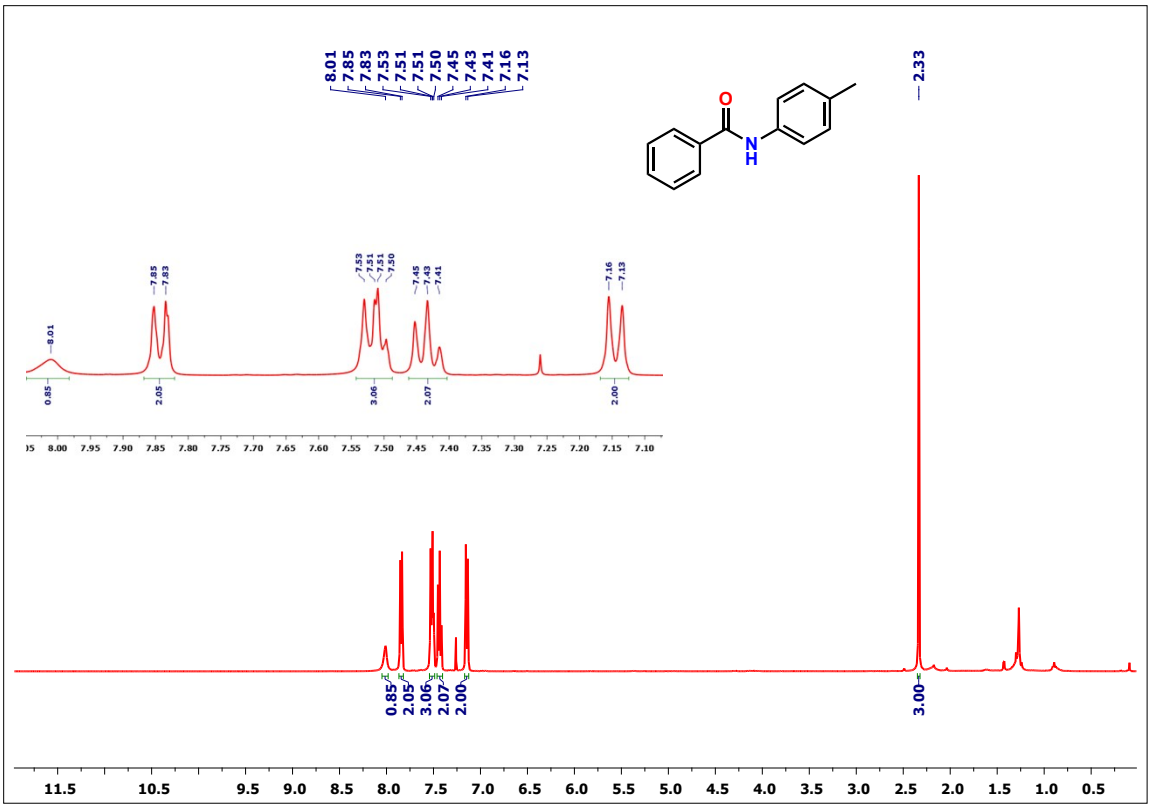


Figure S23: 400 MHz ^{1}H NMR spectrum of **4** in DMSO-d$_6$

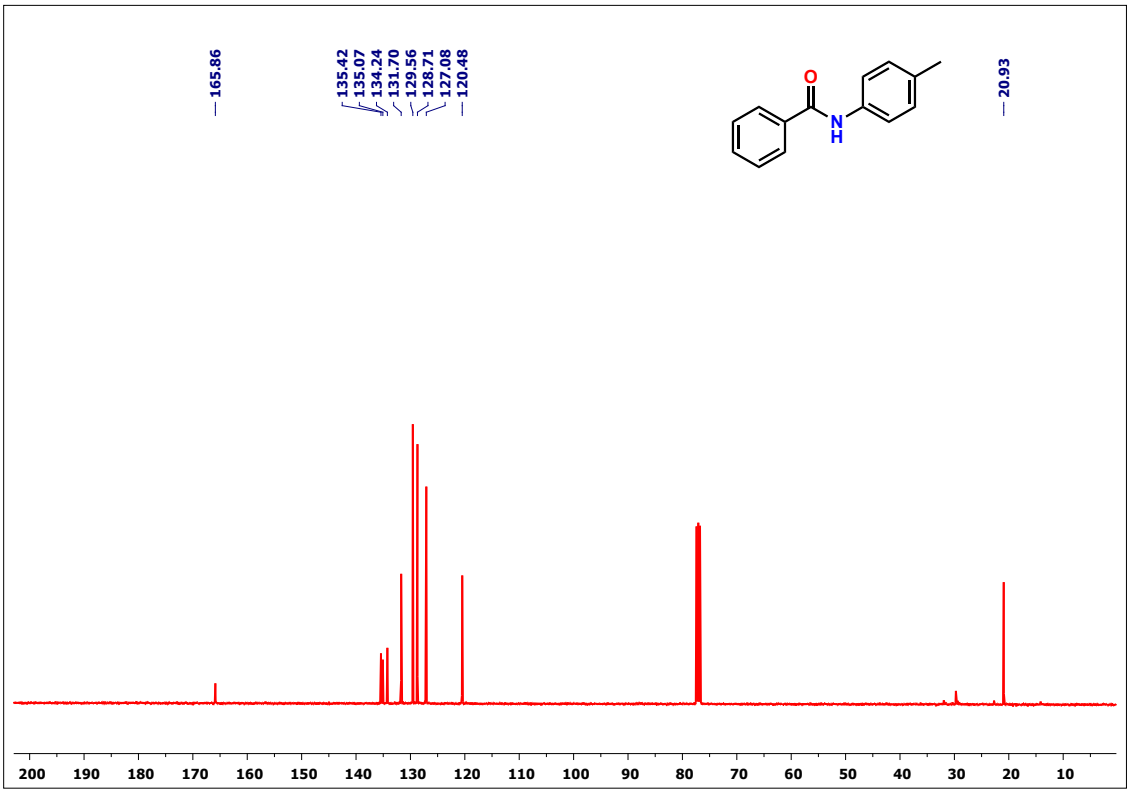


Figure S24: 100 MHz ^{13}C NMR spectrum of **4** in DMSO-d$_6$

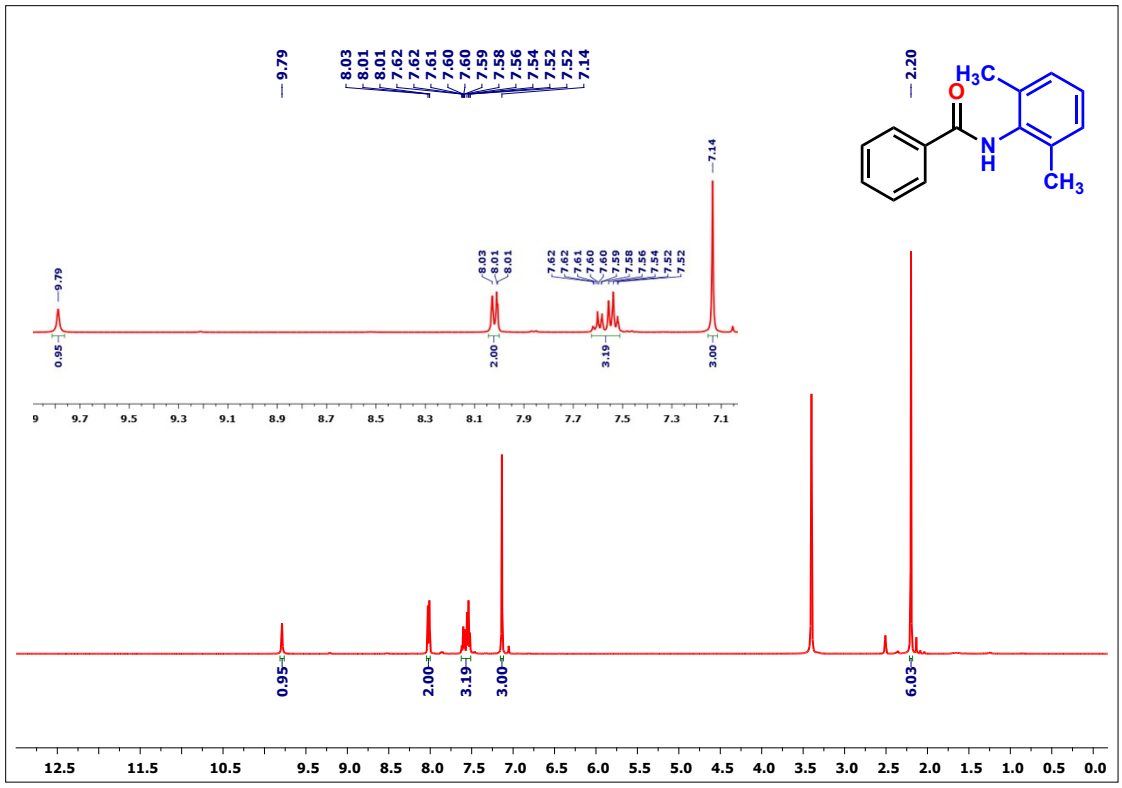


Figure S25: 400 MHz ^{1}H NMR spectrum of **5** in DMSO-d_6

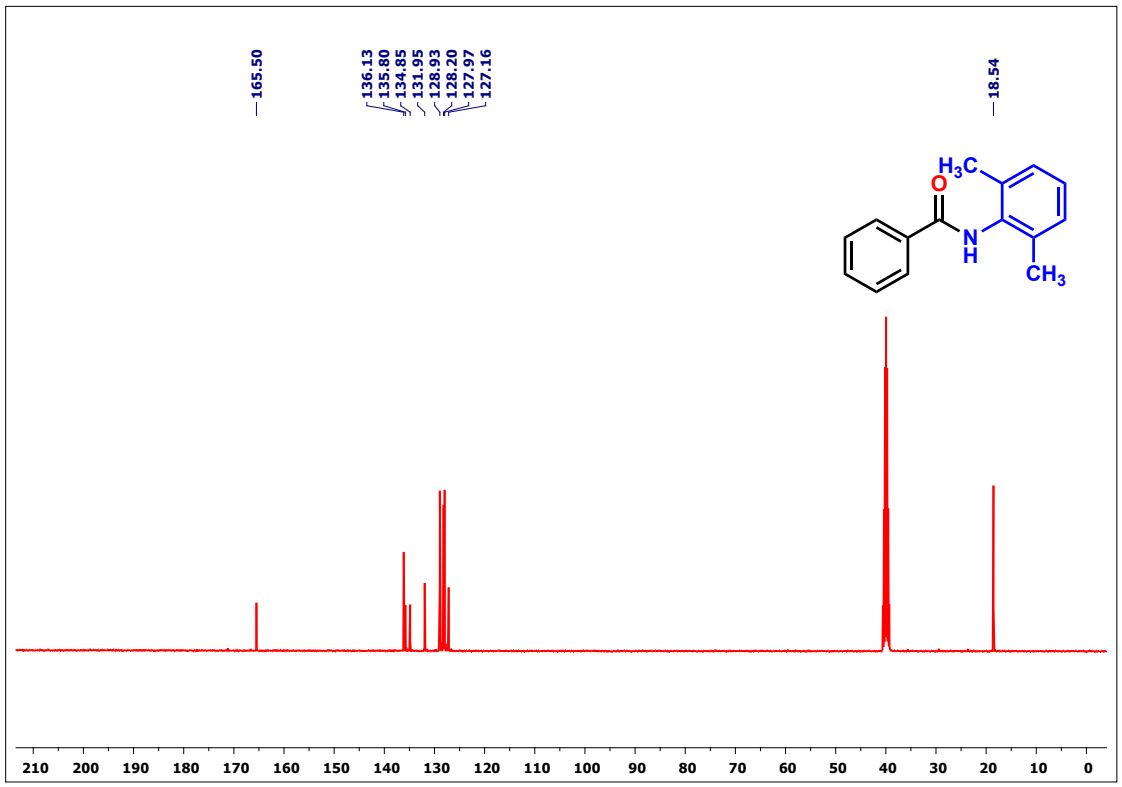


Figure S26: 100 MHz ^{13}C NMR spectrum of **5** in DMSO-d_6

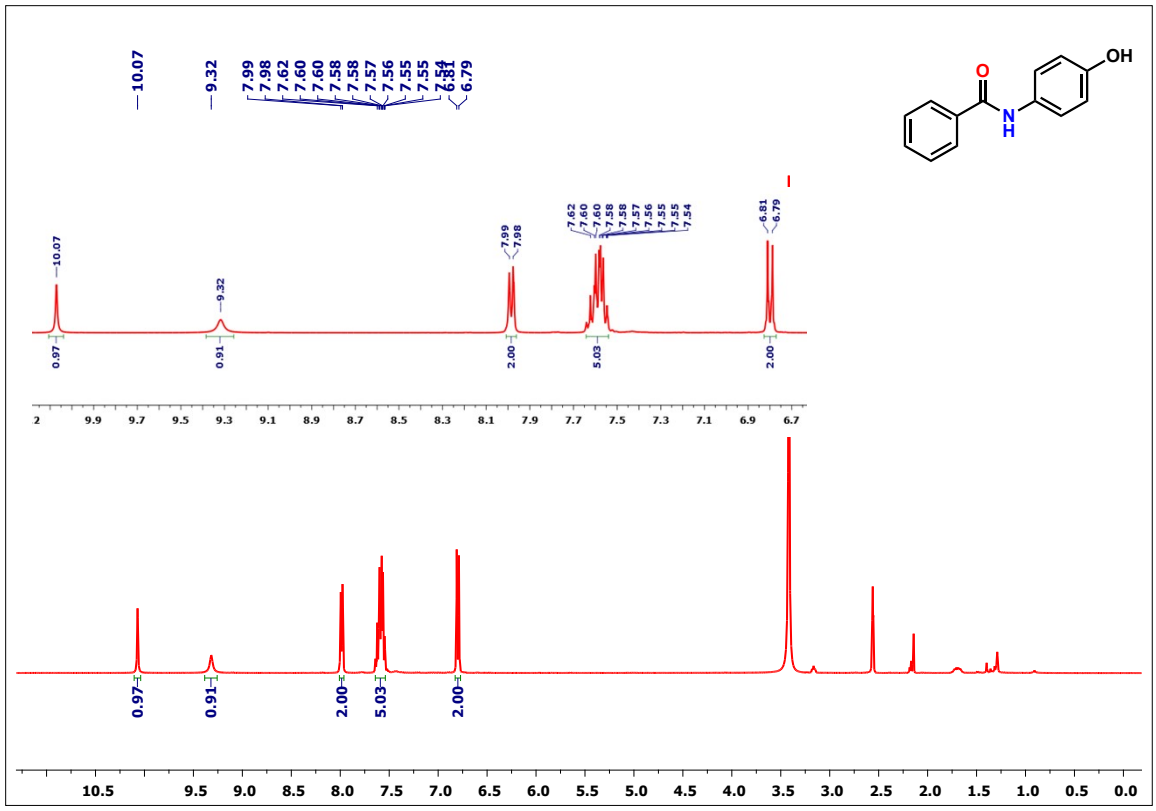


Figure S27: 400 MHz ^{1}H NMR spectrum of **6** in DMSO-d$_6$

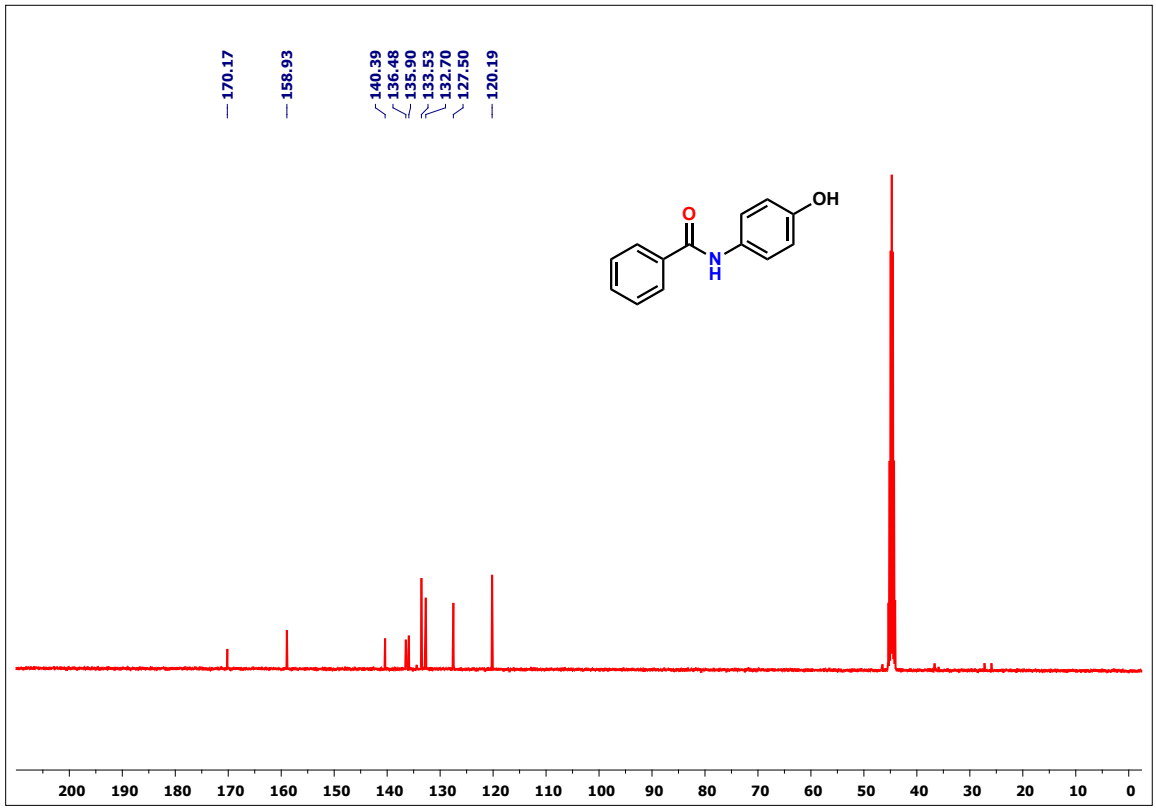


Figure S28: 100 MHz ^{13}C NMR spectrum of **6** in DMSO-d$_6$

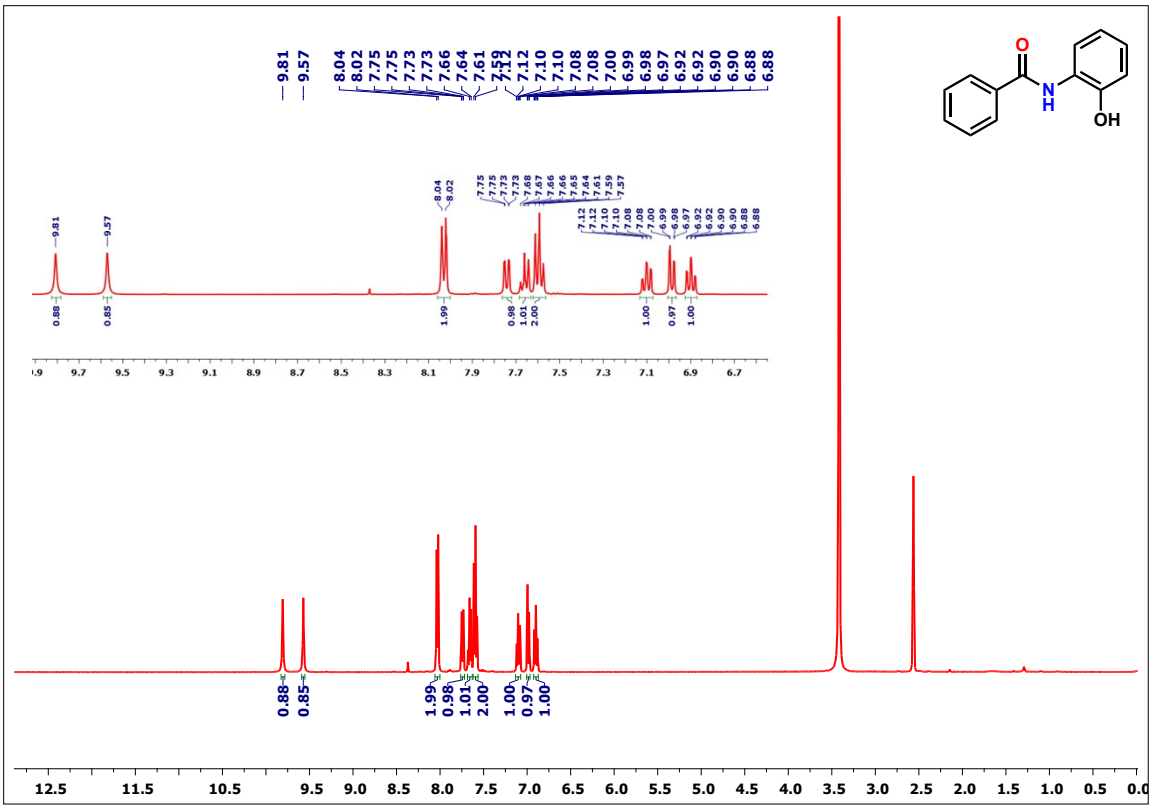


Figure S29: 400 MHz ^{1}H NMR spectrum of **7** in DMSO-d$_6$

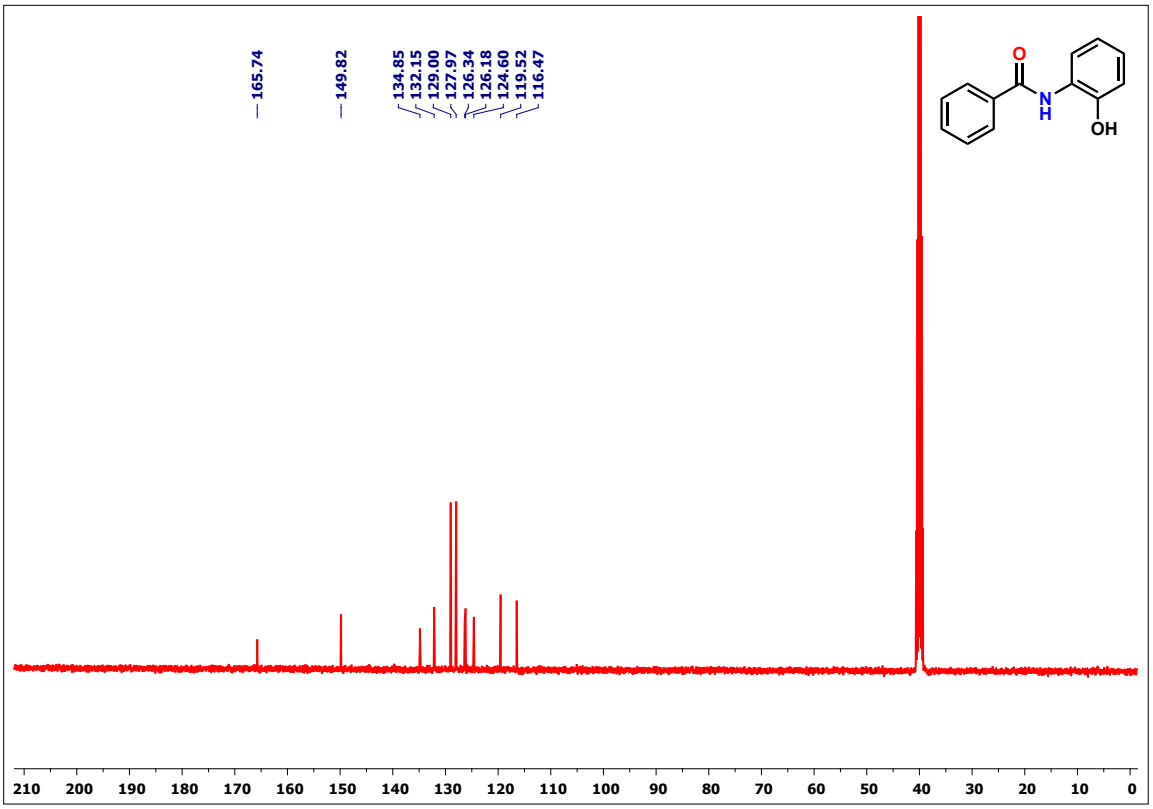


Figure S30: 100 MHz ^{13}C NMR spectrum of **7** in DMSO-d$_6$

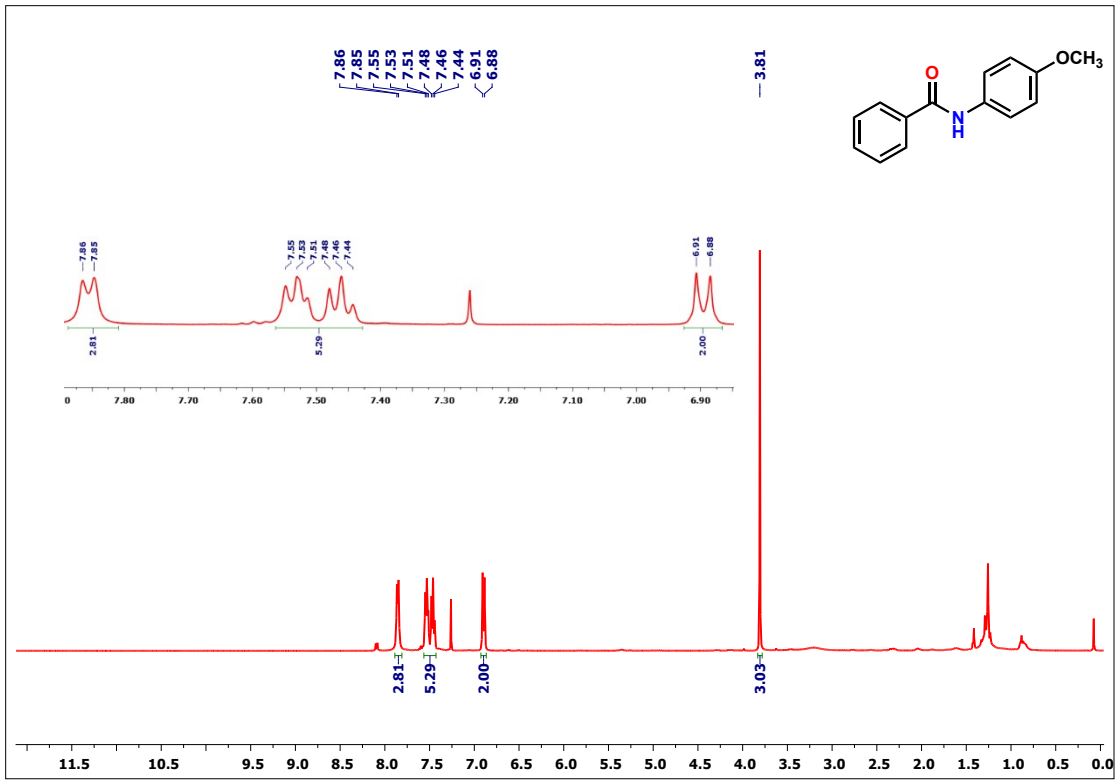


Figure S31: 400 MHz ^{1}H NMR spectrum of **8** in DMSO-d$_6$

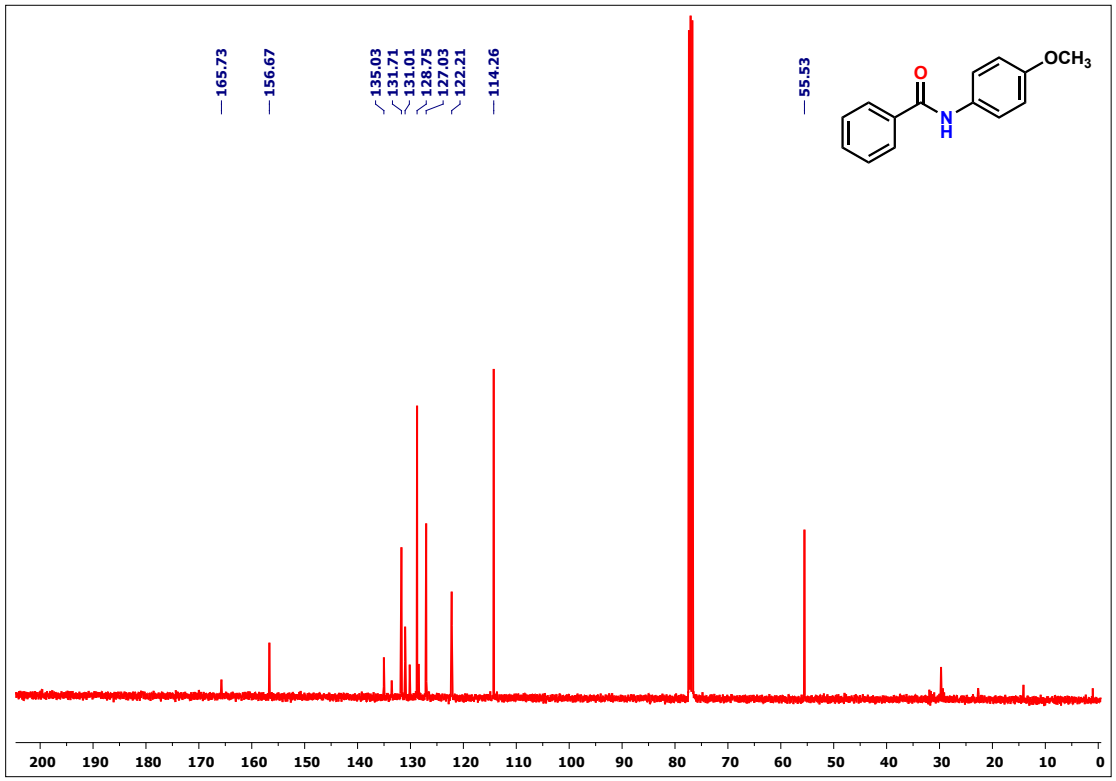


Figure S32: 100 MHz ^{13}C NMR spectrum of **8** in DMSO-d$_6$

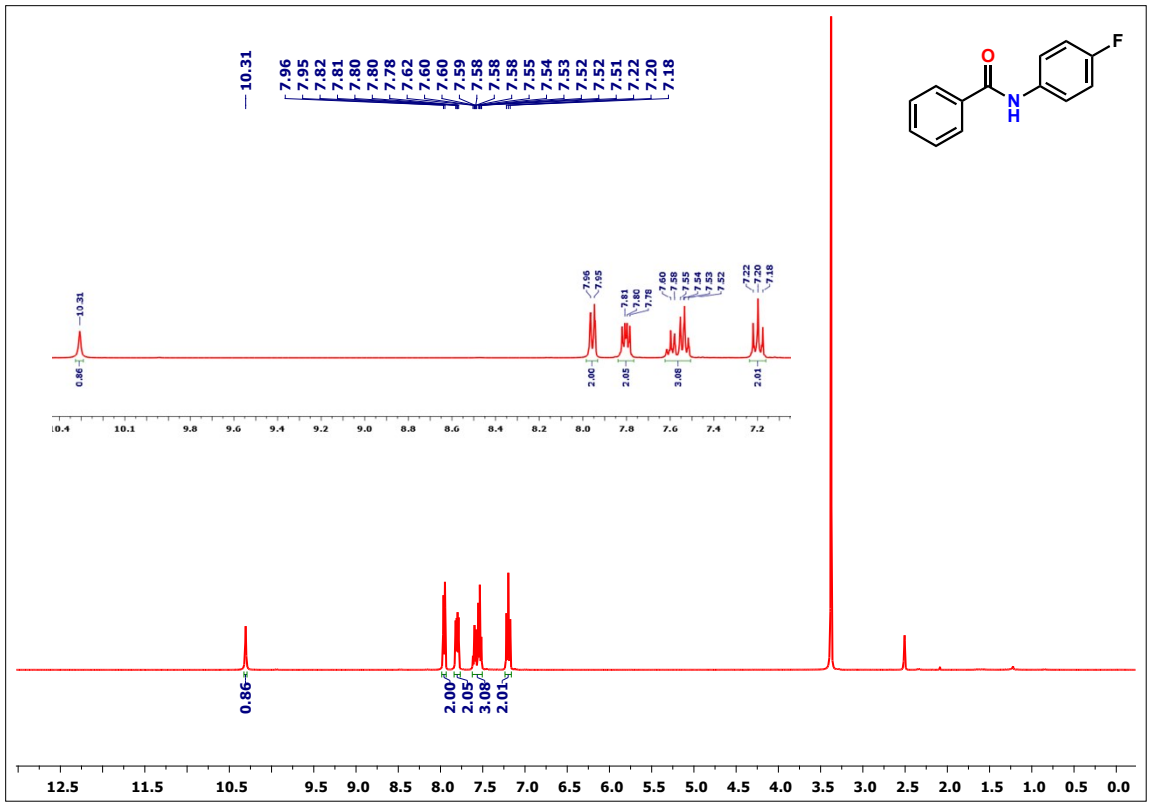


Figure S33: 400 MHz ^{1}H NMR spectrum of **9** in DMSO-d_6

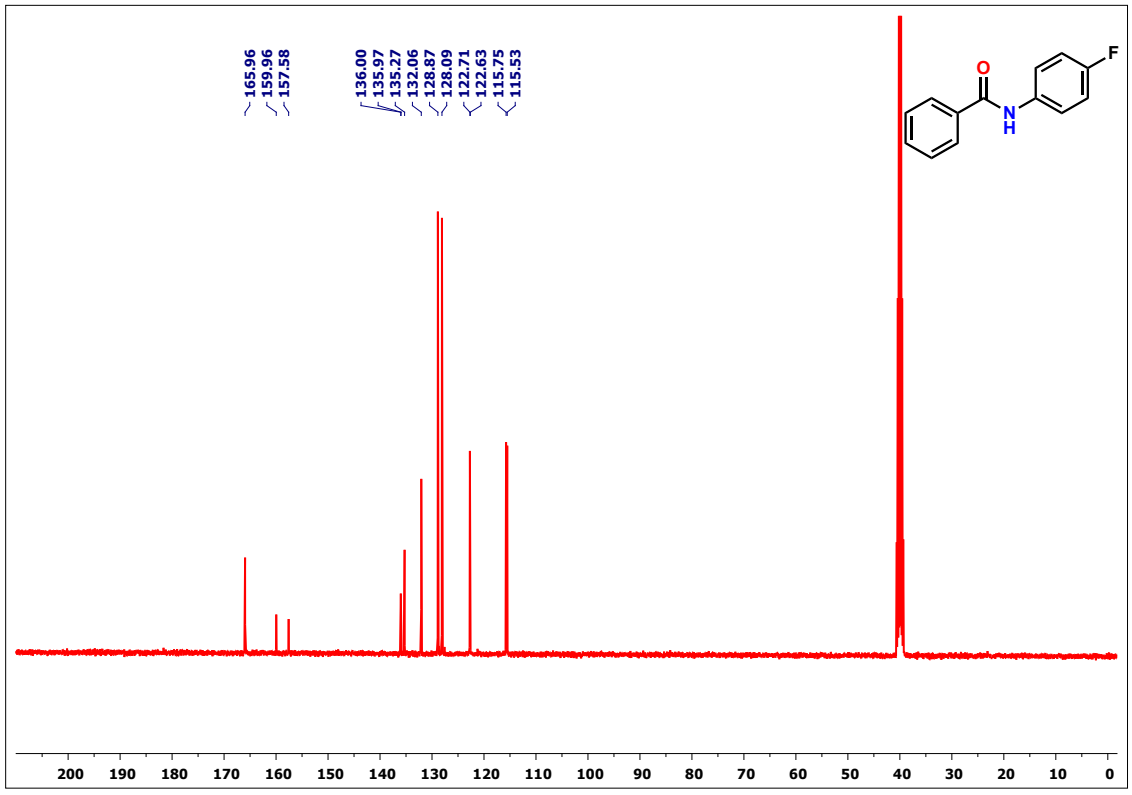


Figure S34: 100 MHz ^{13}C NMR spectrum of **9** in DMSO-d_6

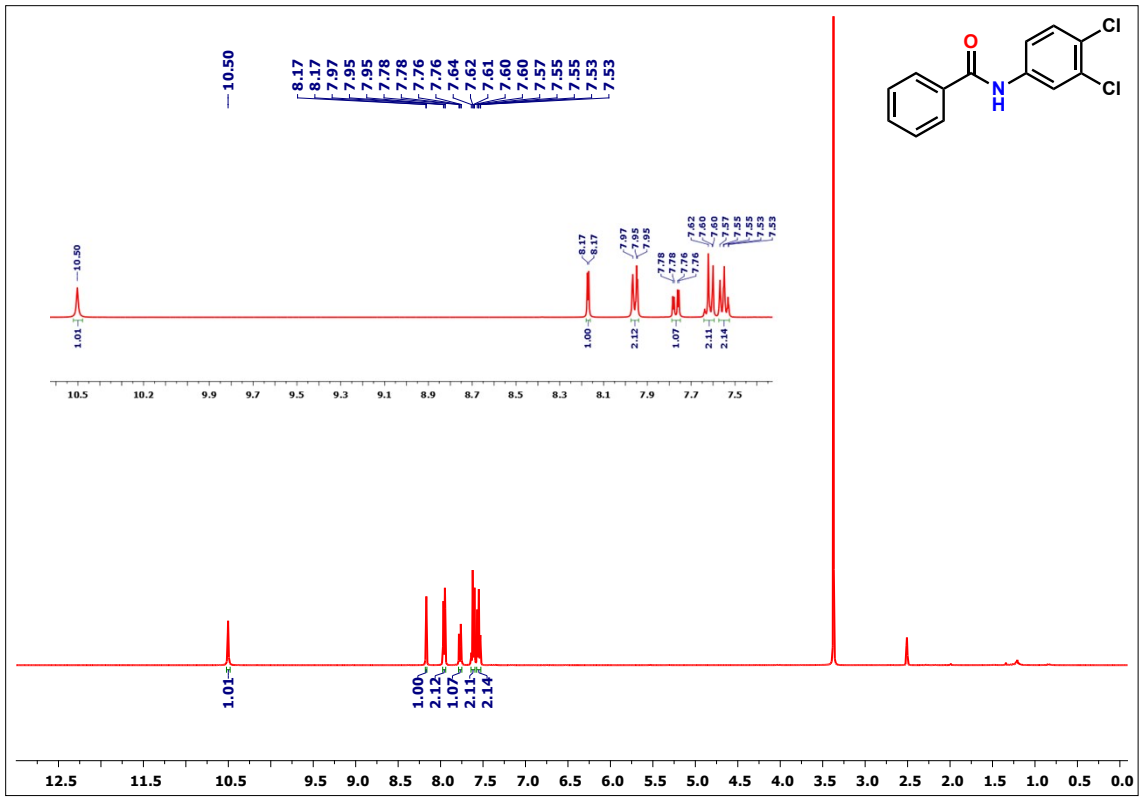


Figure S35: 400 MHz ^{1}H NMR spectrum of **10** in DMSO-d_6

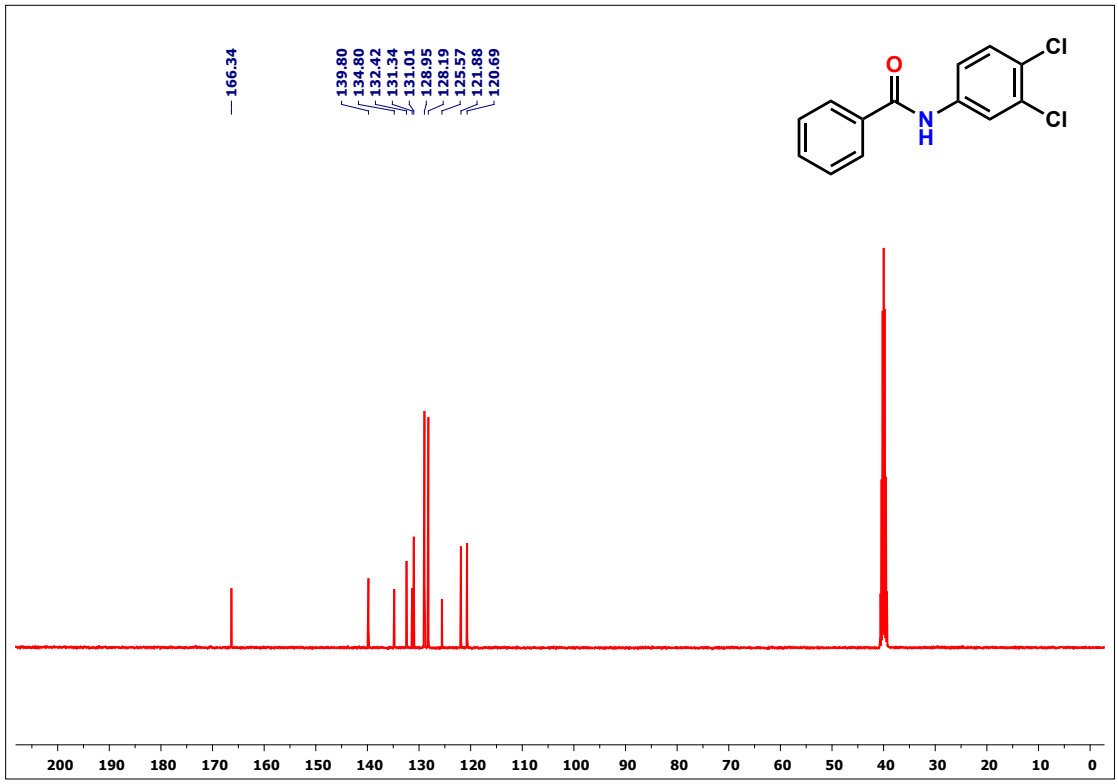


Figure S36: 100 MHz ^{13}C NMR spectrum of **10** in DMSO-d_6

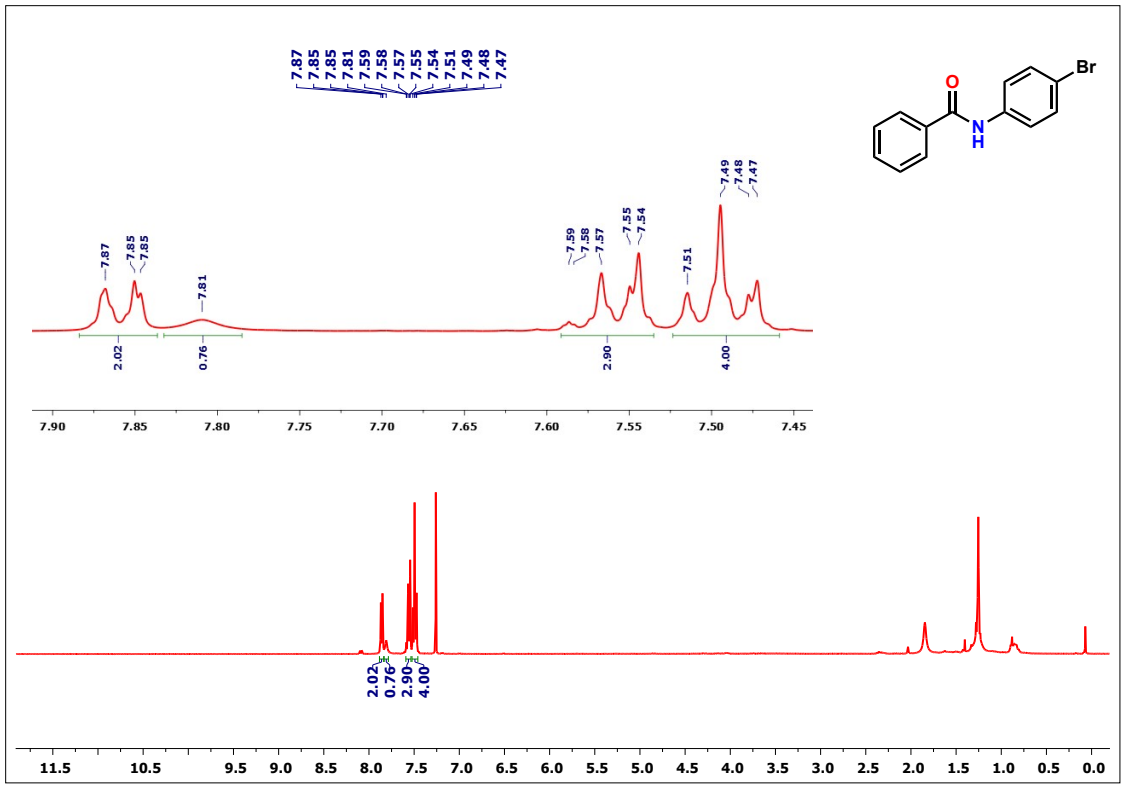


Figure S37: 400 MHz ^{1}H NMR spectrum of **11** in DMSO-d_6

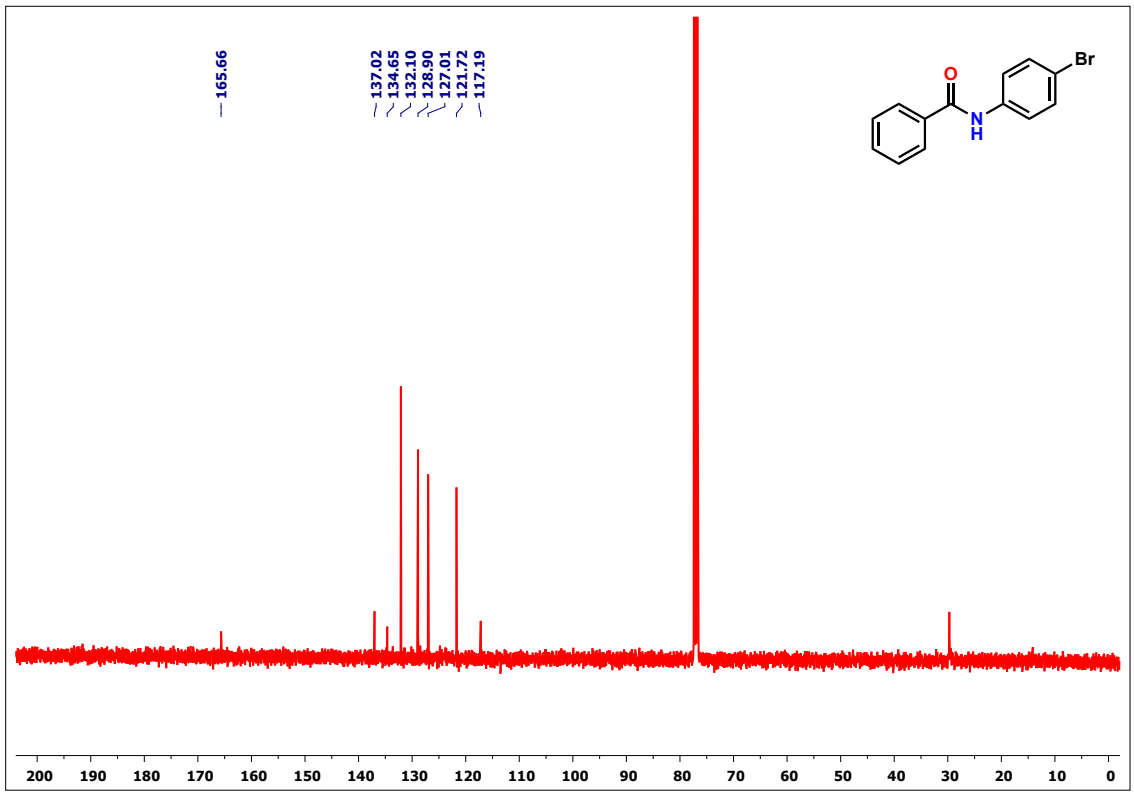


Figure S38: 100 MHz ^{13}C NMR spectrum of **11** in DMSO-d_6

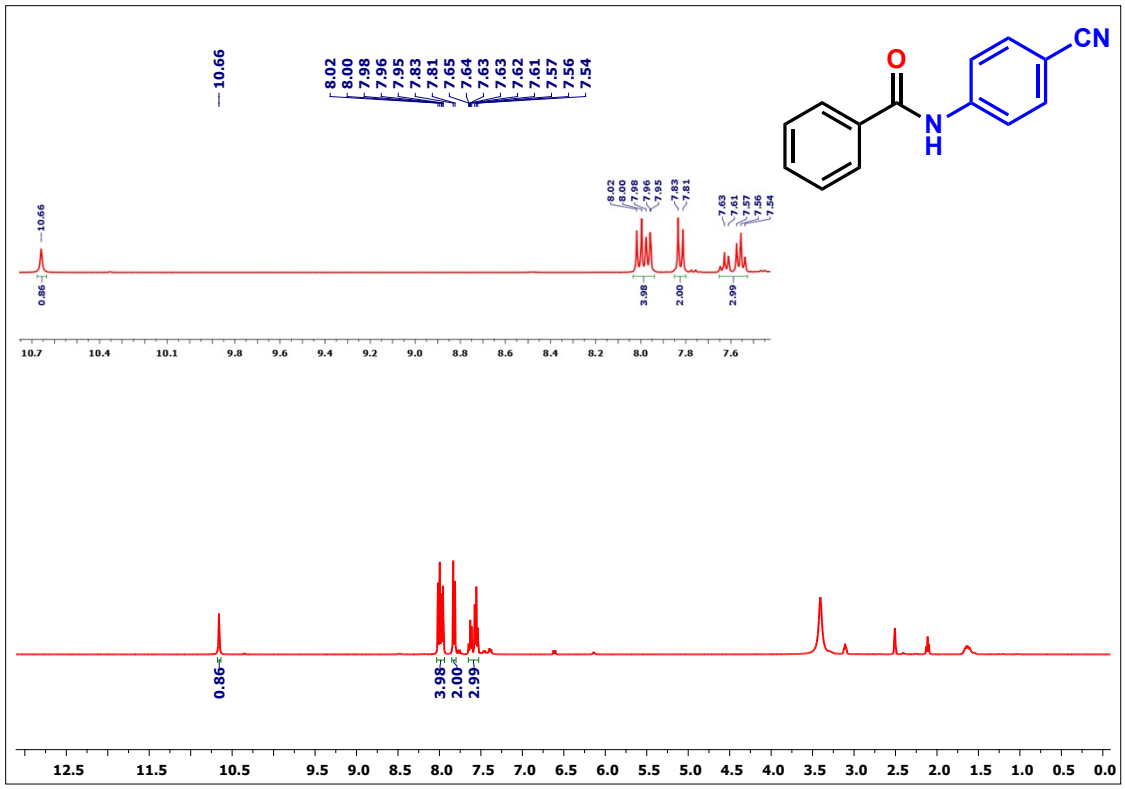


Figure S39: 400 MHz ^{1}H NMR spectrum of **12** in DMSO-d$_6$

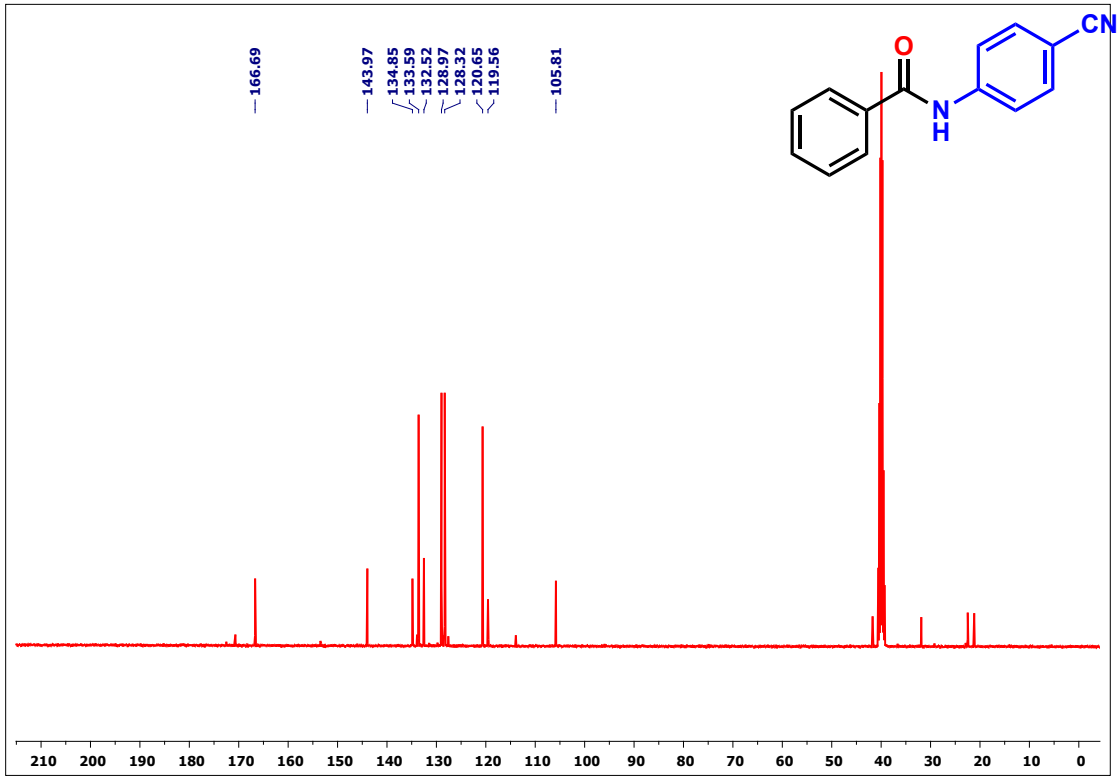


Figure S40: 100 MHz ^{13}C NMR spectrum of **12** in DMSO-d$_6$

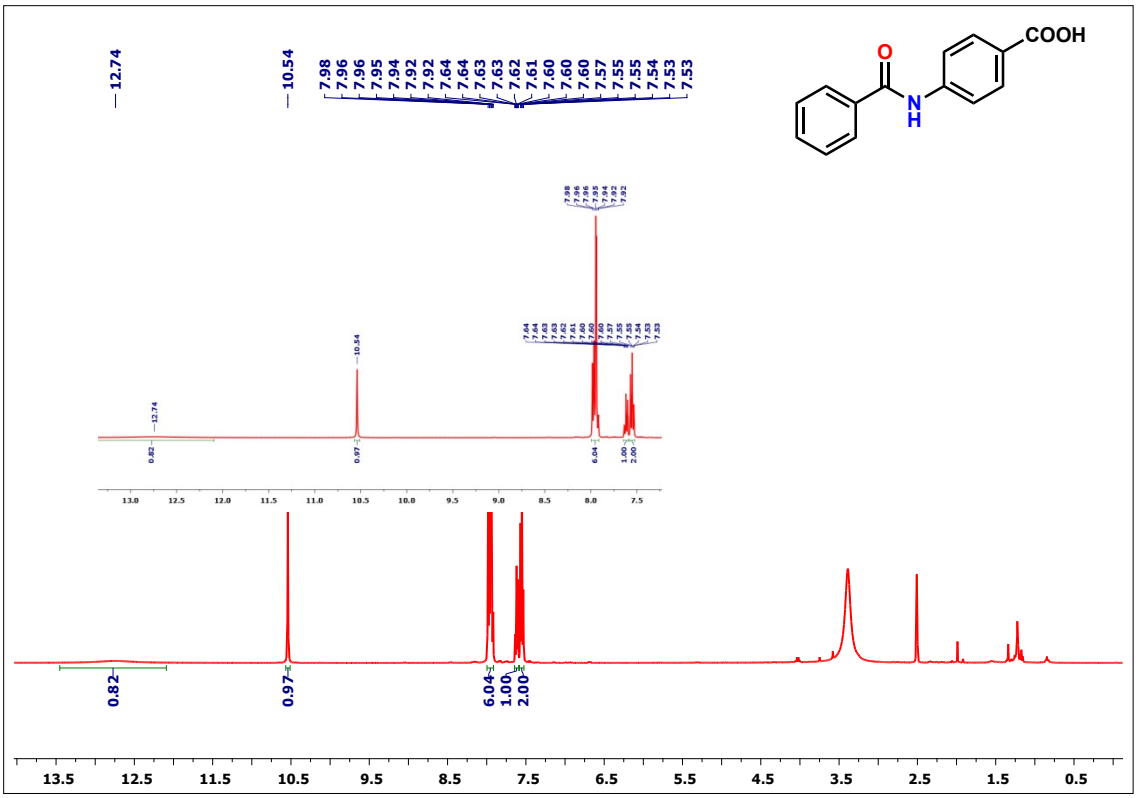


Figure S41: 400 MHz ^{1}H NMR spectrum of **13** in DMSO-d_6

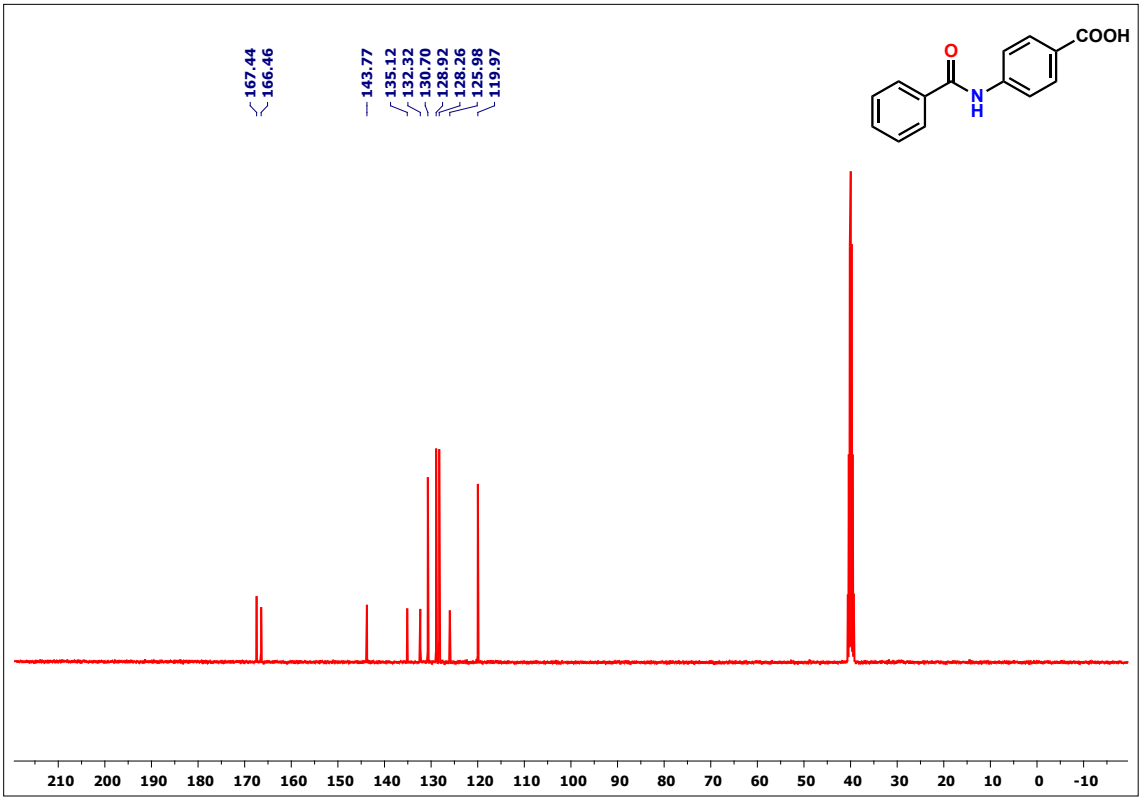


Figure S42: 100 MHz ^{13}C NMR spectrum of **13** in DMSO-d_6

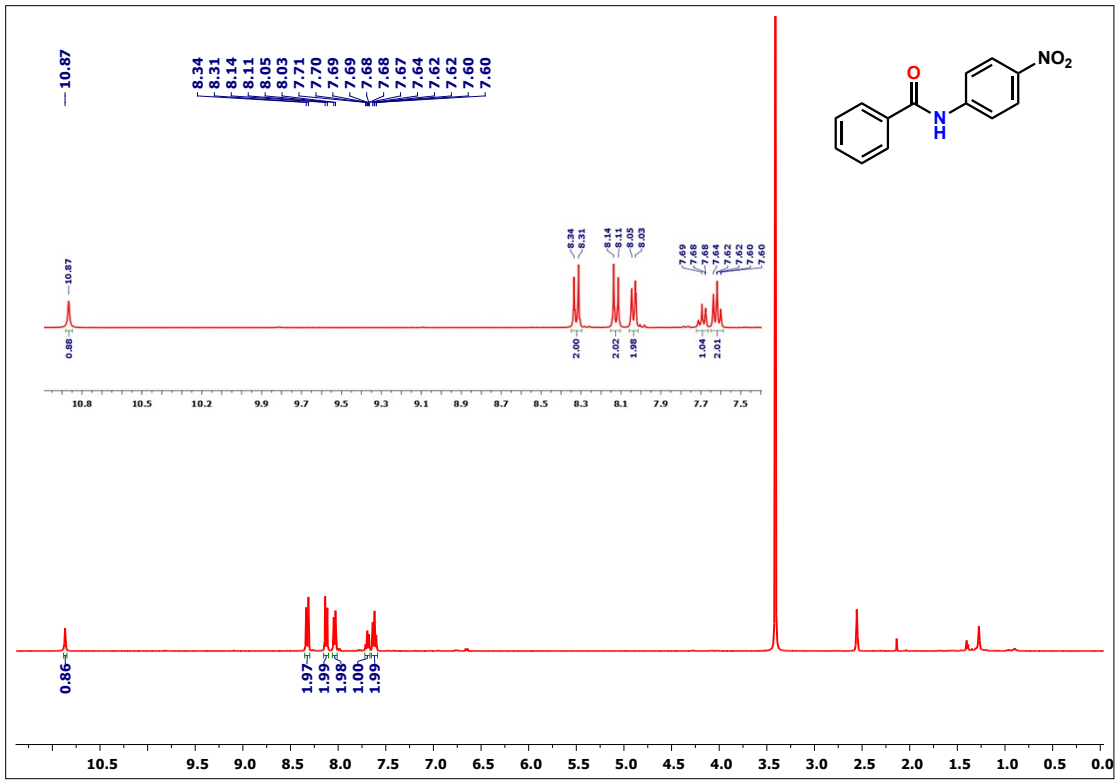


Figure S43: 400 MHz ^{1}H NMR spectrum of **14** in DMSO-d_6

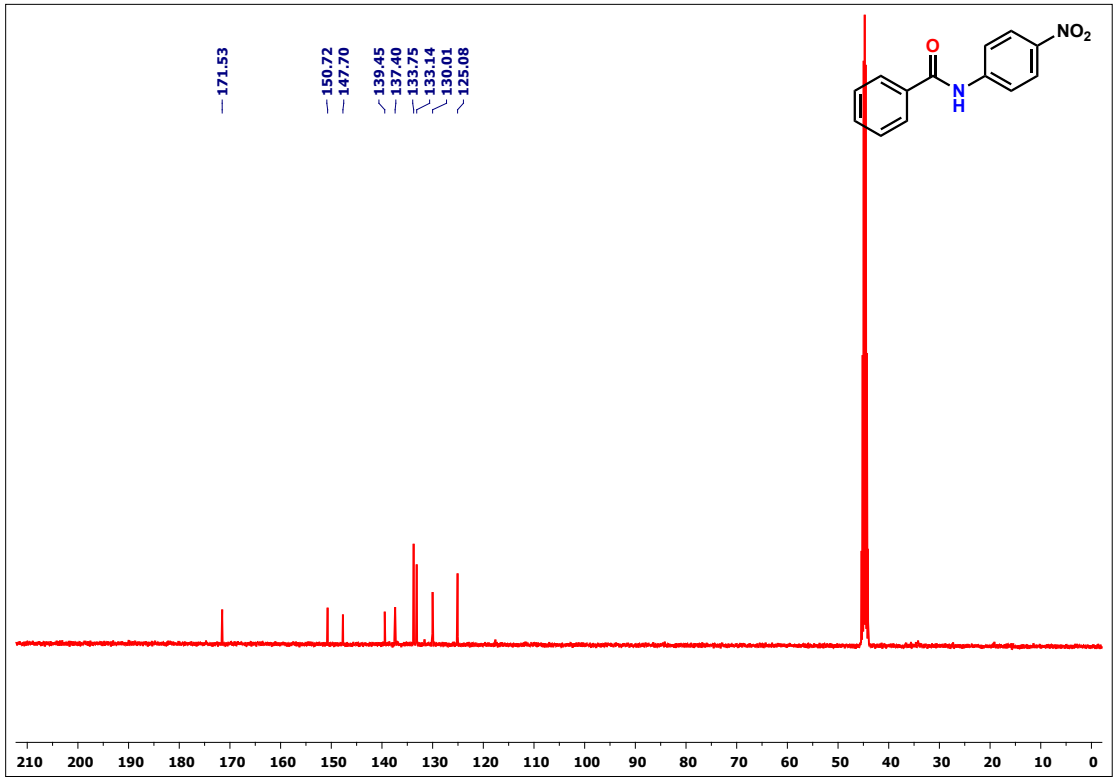


Figure S44: 100 MHz ^{13}C NMR spectrum of **14** in DMSO-d_6

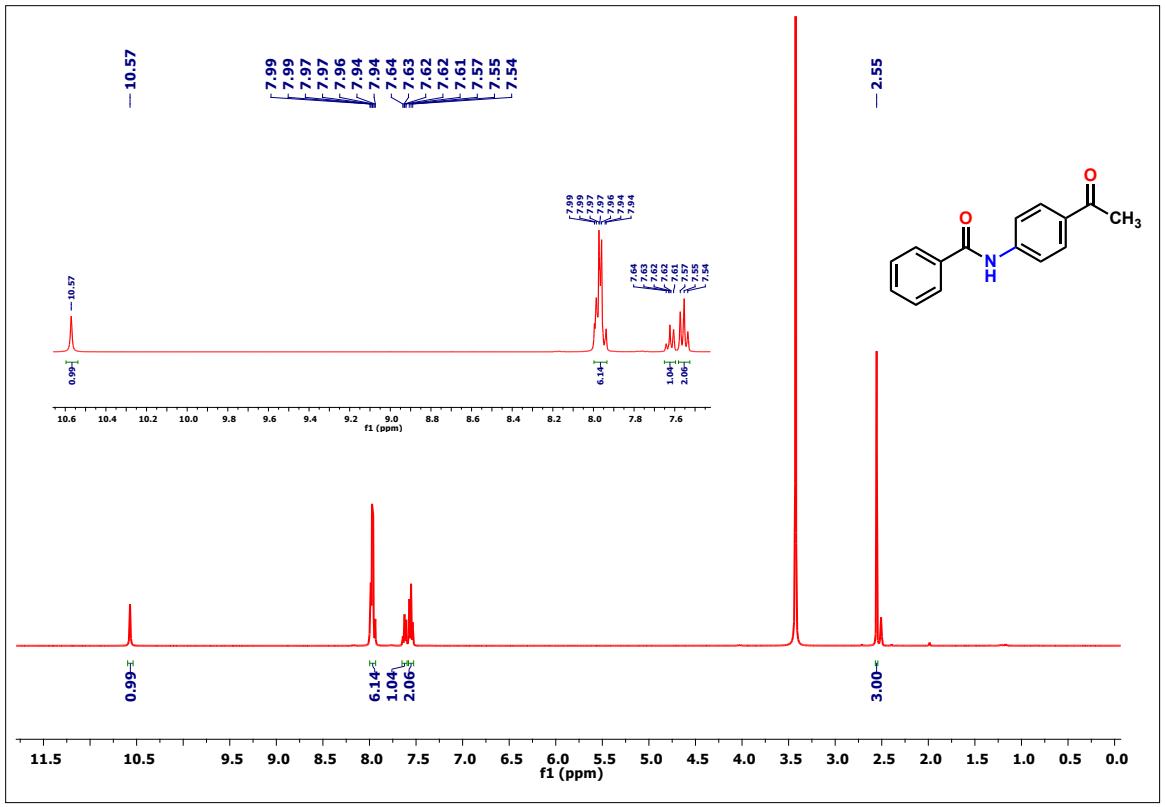


Figure S45: 400 MHz ^{1}H NMR spectrum of **15** in DMSO-d_6

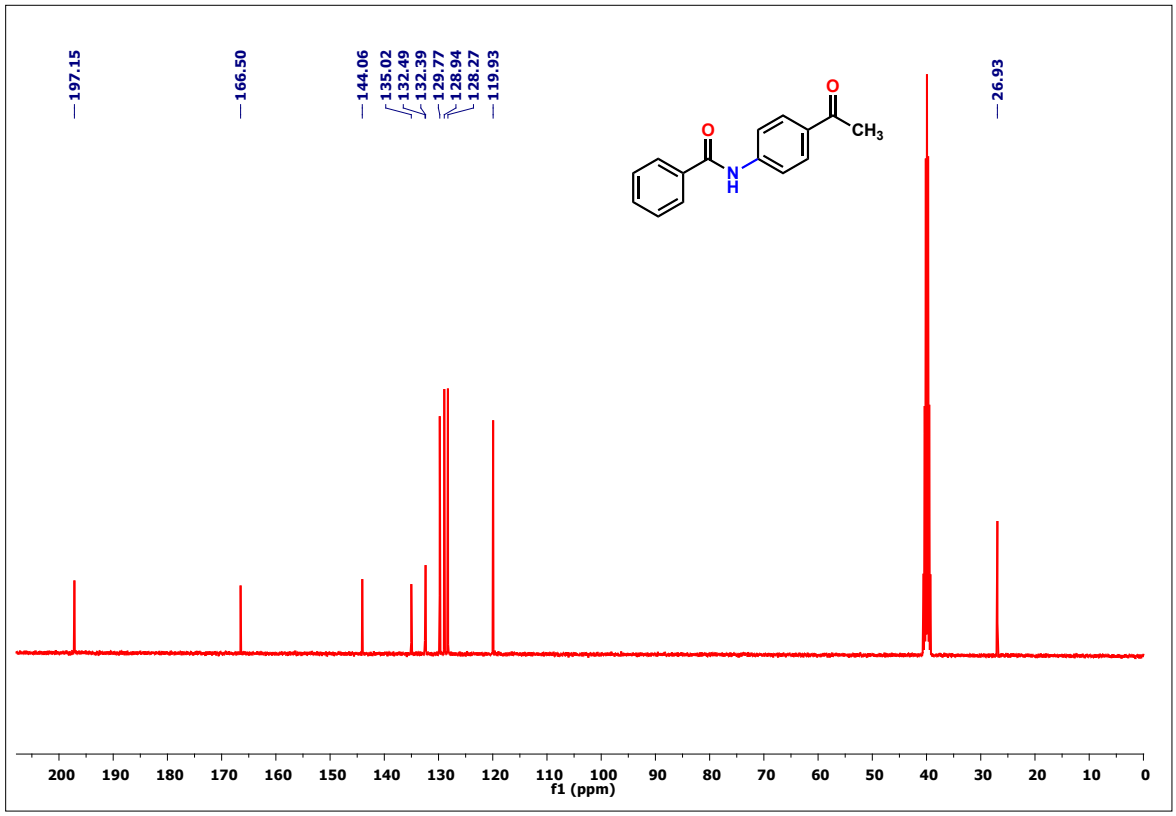


Figure S46: 100 MHz ^{13}C NMR spectrum of **15** in DMSO-d_6

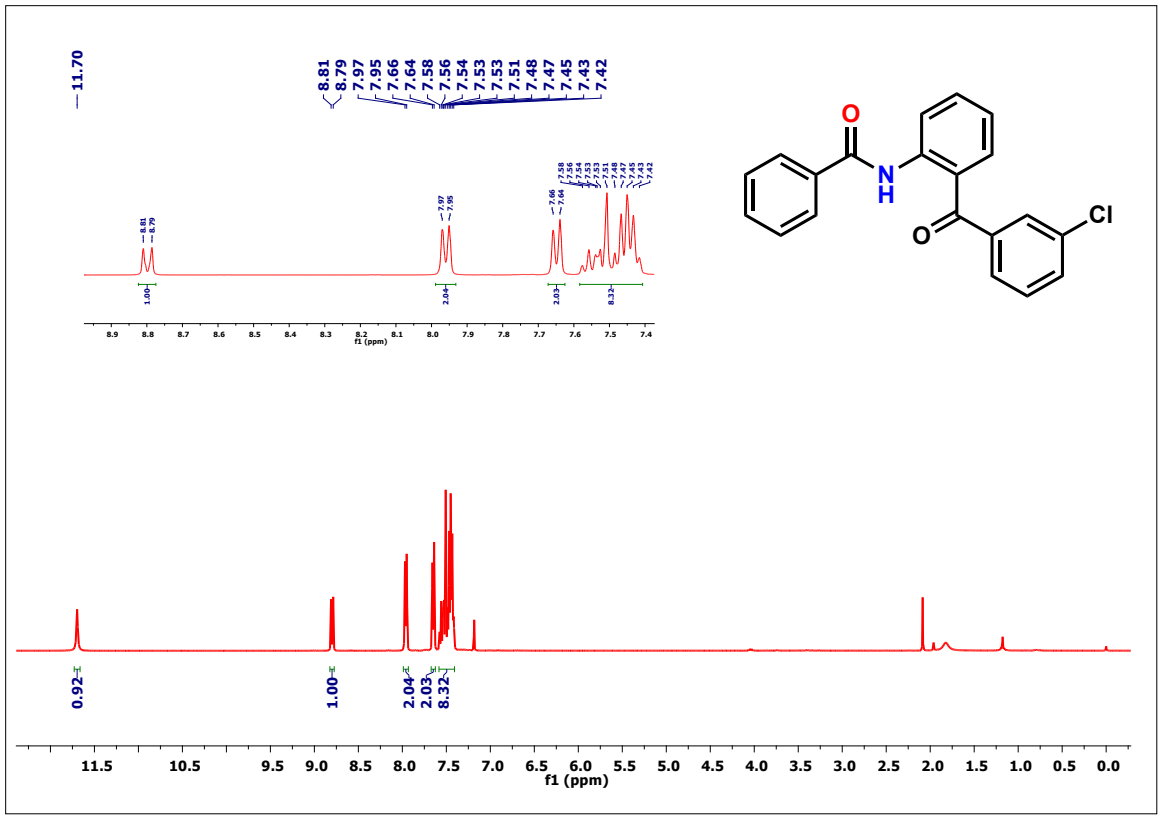


Figure S47: 400 MHz ^{1}H NMR spectrum of **16** in $CDCl_3$

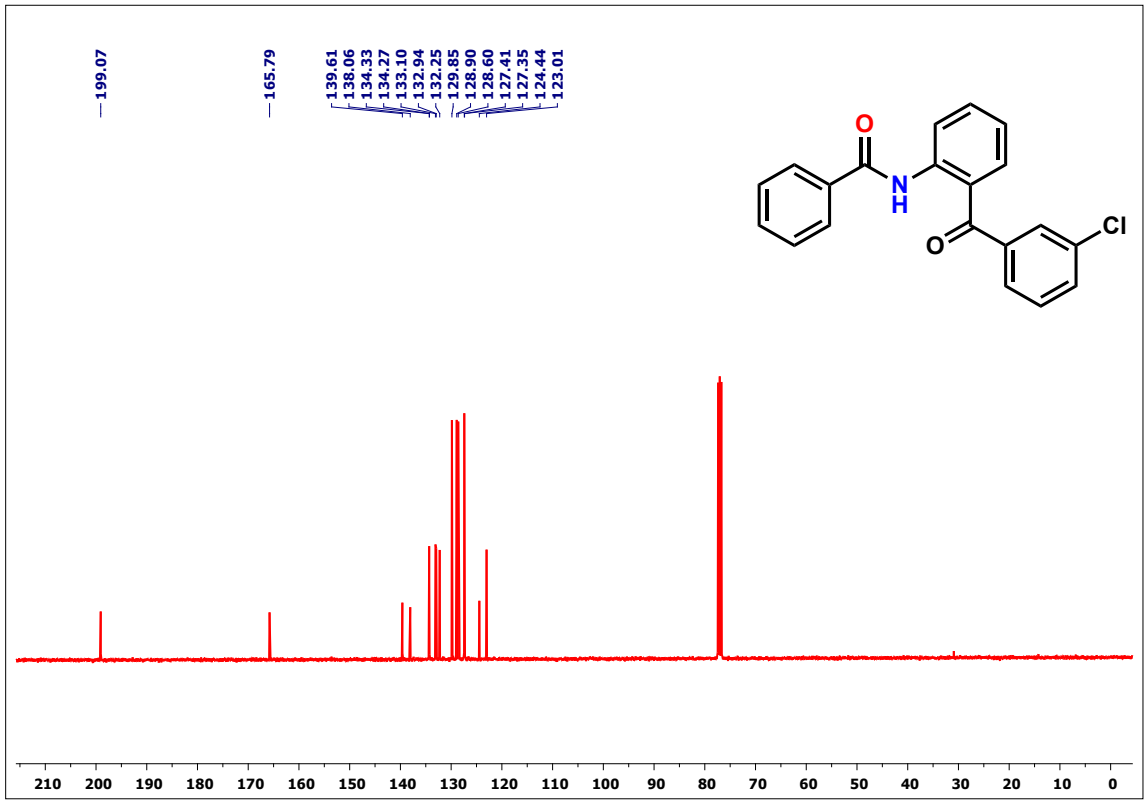


Figure S48: 100 MHz ^{13}C NMR spectrum of **16** in $CDCl_3$

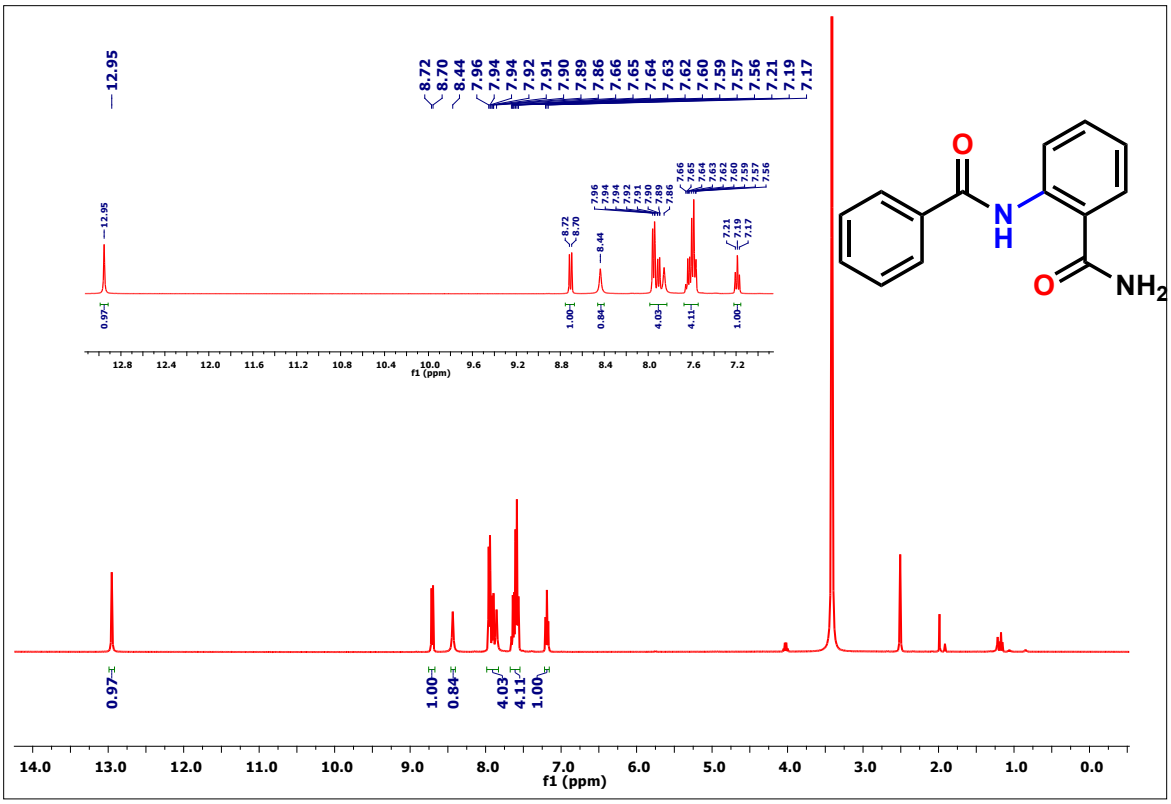


Figure S49: 400 MHz ^{1}H NMR spectrum of **17** in DMSO-d_6

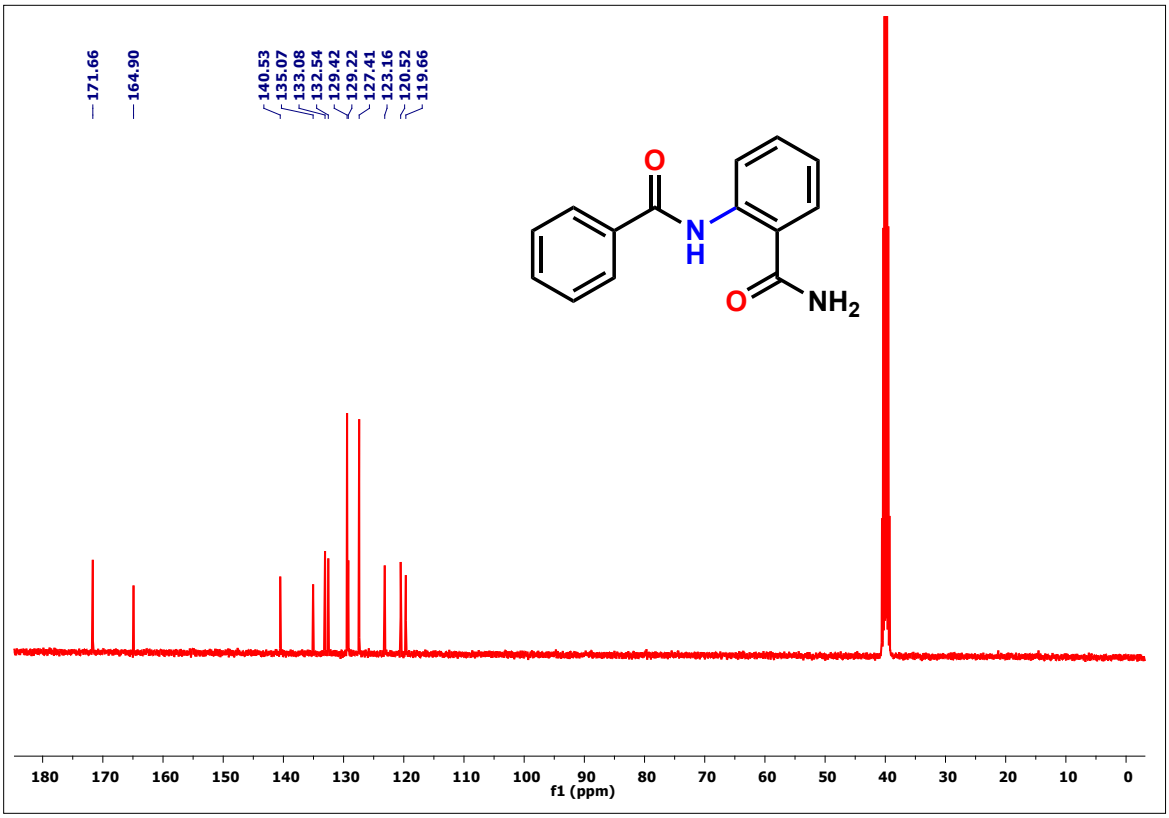


Figure S50: 100 MHz ^{13}C NMR spectrum of **17** in DMSO-d_6

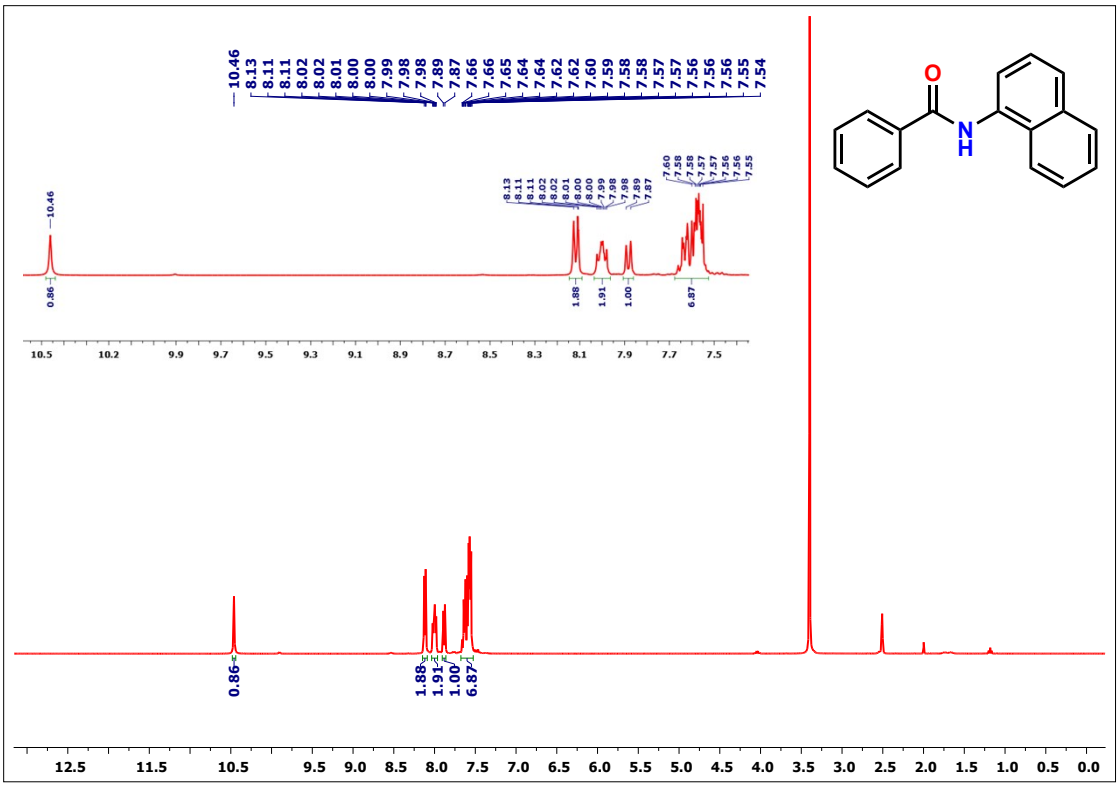


Figure S51: 400 MHz ^{1}H NMR spectrum of **18** in DMSO-d_6

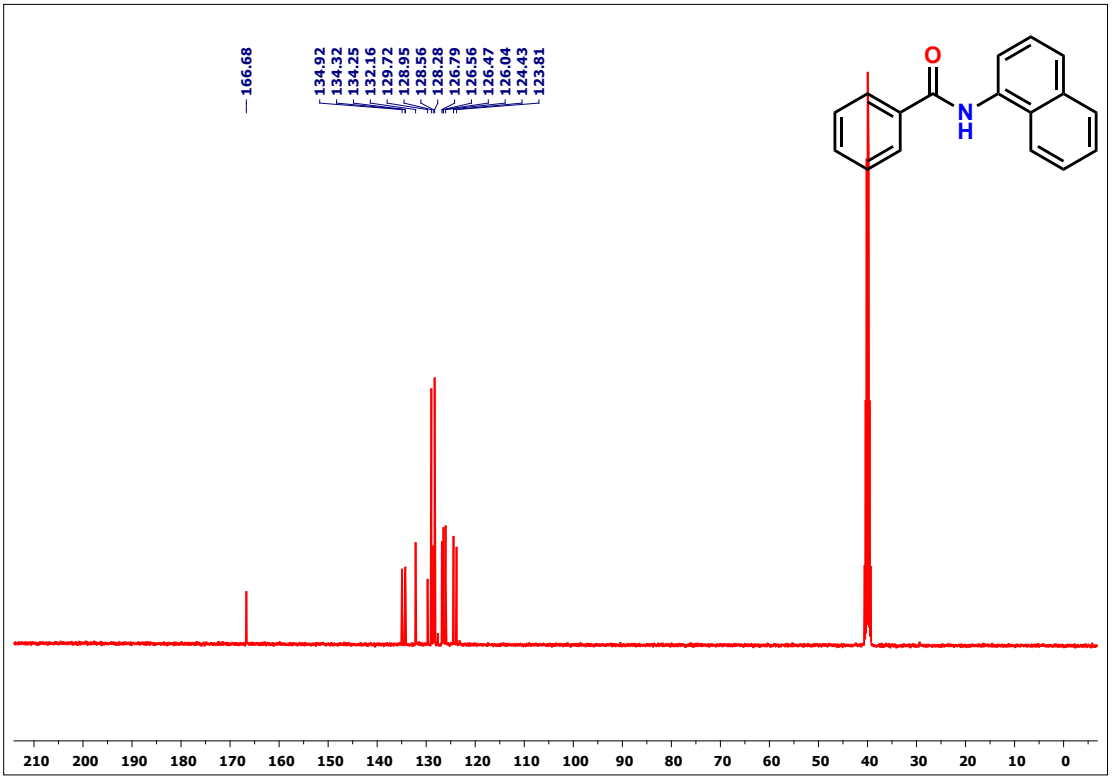


Figure S52: 100 MHz ^{13}C NMR spectrum of **18** in DMSO-d_6

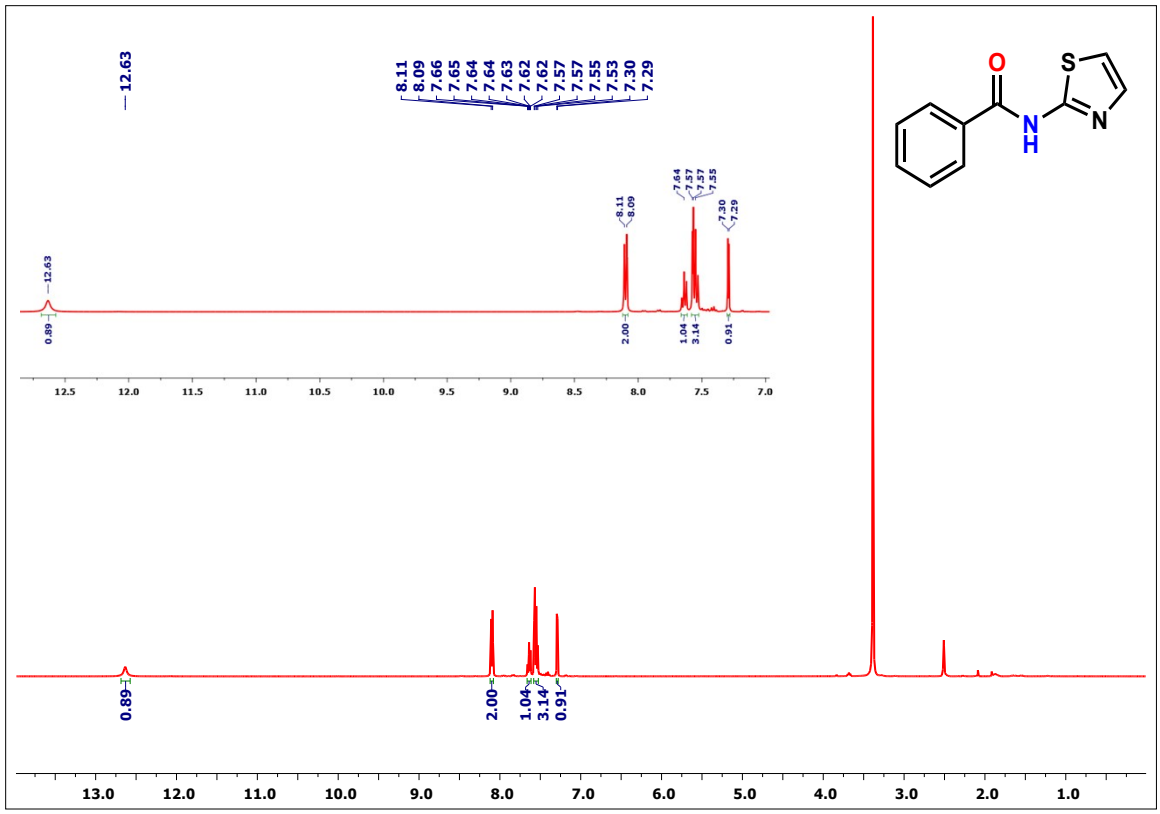


Figure S53: 400 MHz ^{1}H NMR spectrum of **19** in DMSO-d_6

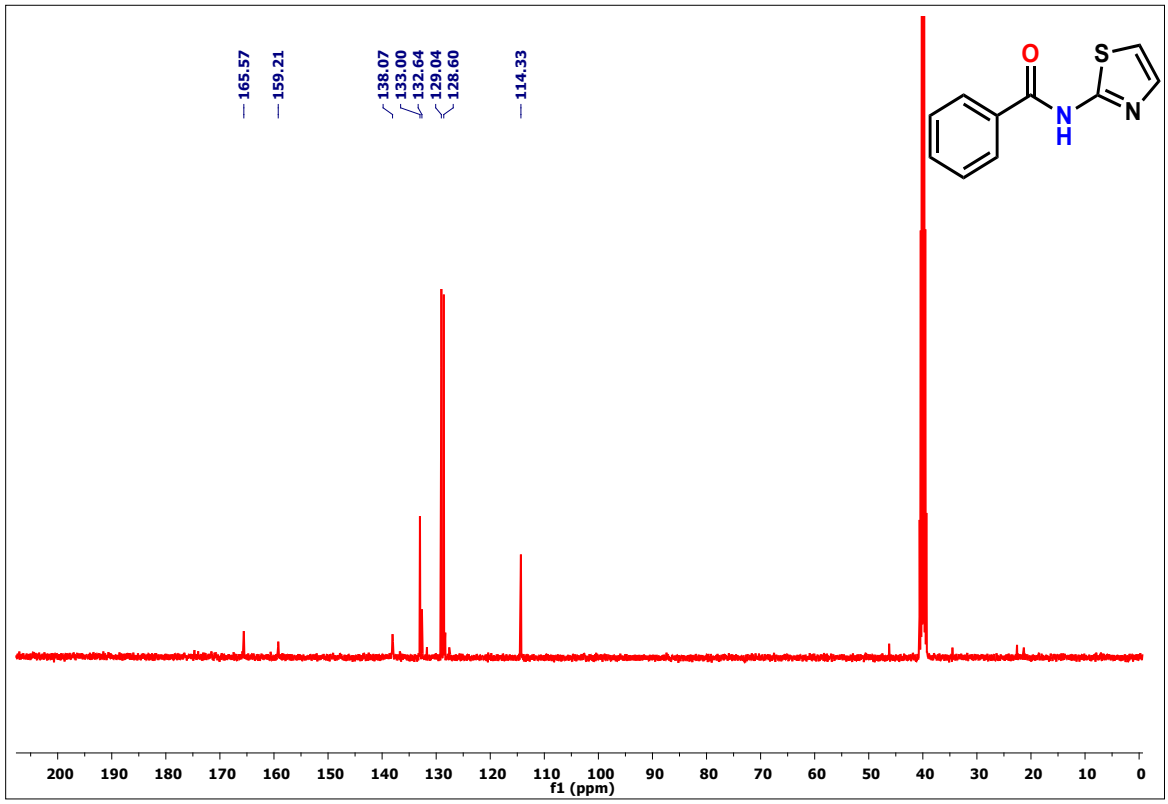


Figure S54: 100 MHz ^{13}C NMR spectrum of **19** in DMSO-d_6

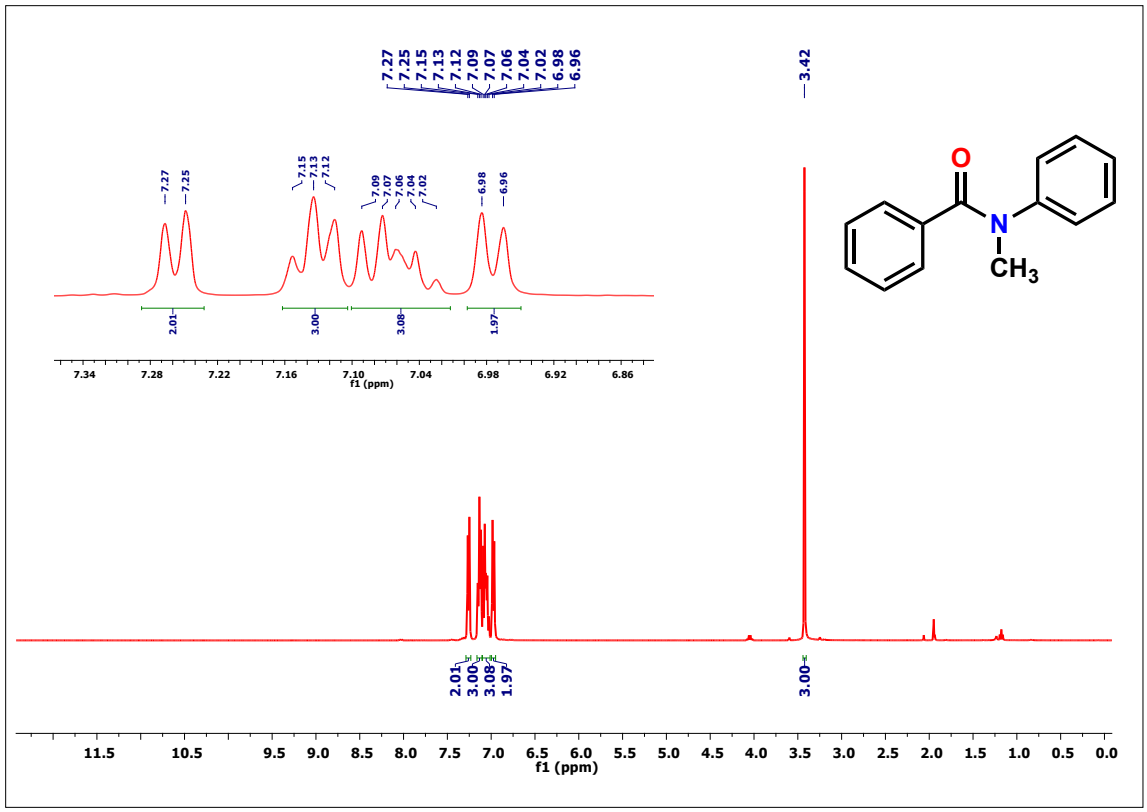


Figure S55: 400 MHz ^{1}H NMR spectrum of **20** in $CDCl_3$

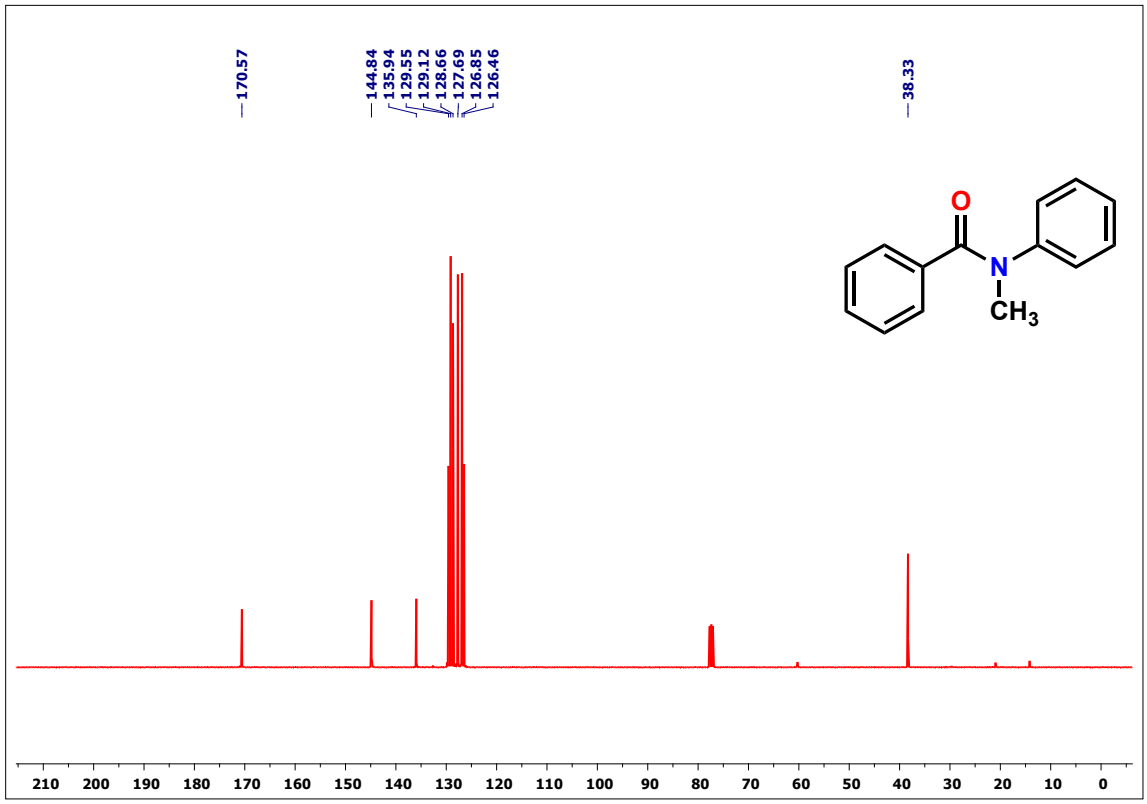


Figure S56: 100 MHz ^{13}C NMR spectrum of **20** in $CDCl_3$

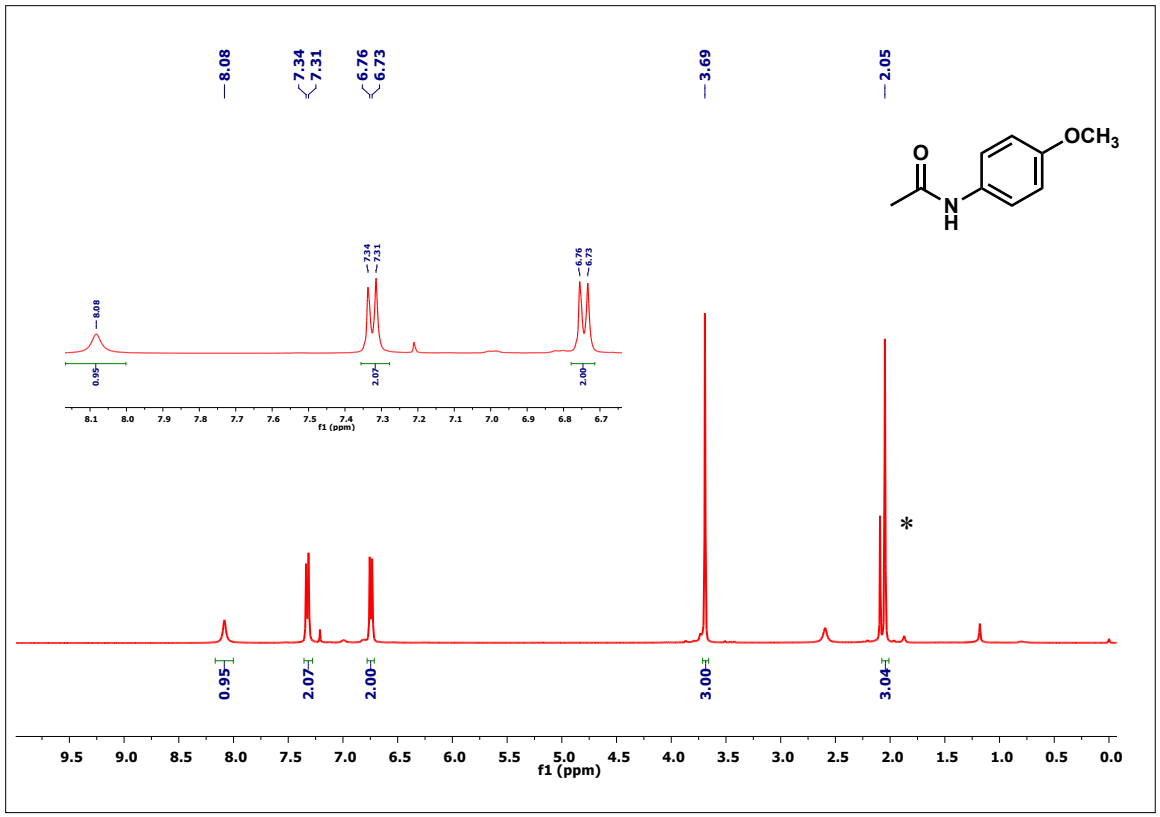


Figure S57: 400 MHz ^{1}H NMR spectrum of **21** in $CDCl_3$

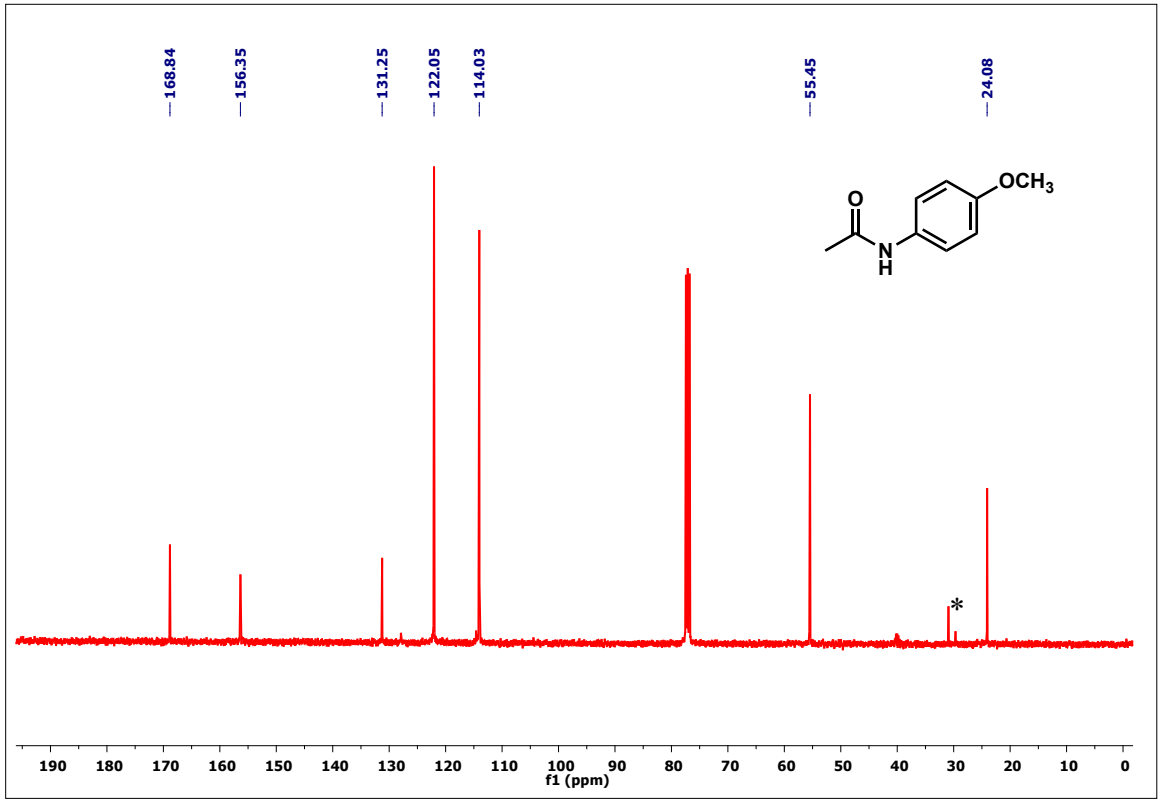


Figure S58: 100 MHz ^{13}C NMR spectrum of **21** in $CDCl_3$

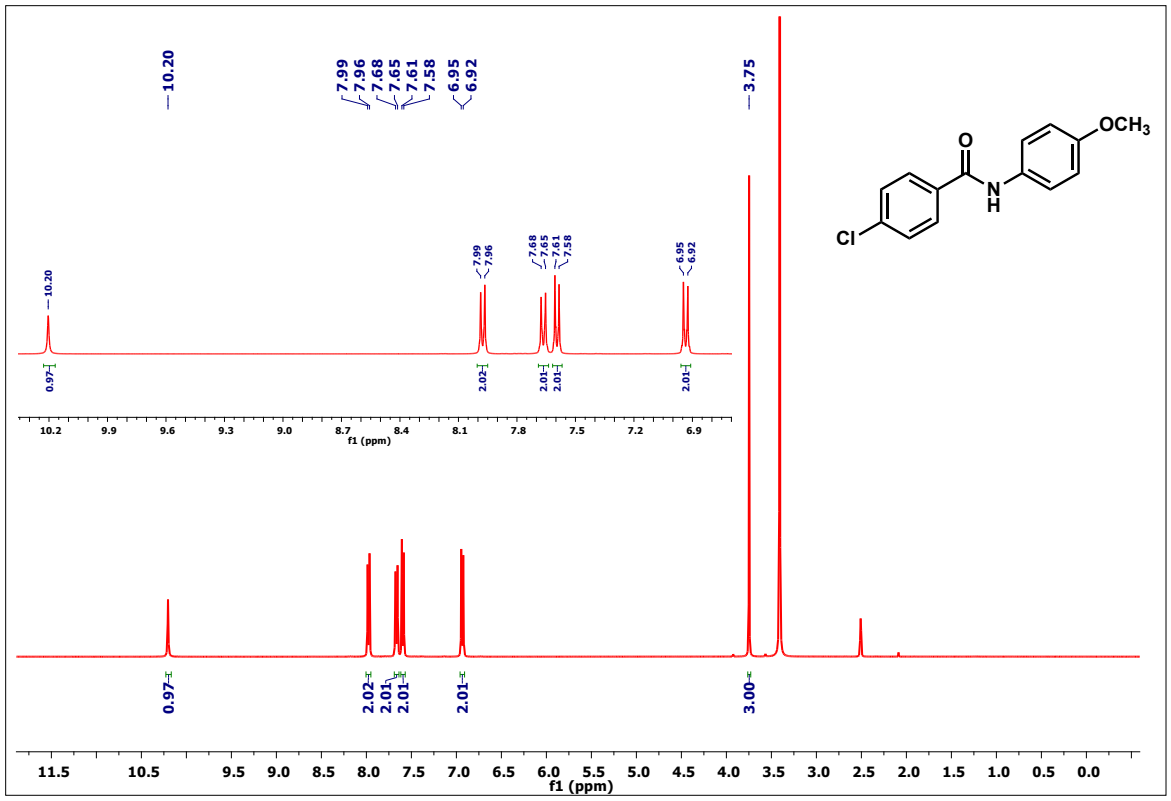


Figure S59: 400 MHz ^{1}H NMR spectrum of **22** in DMSO-d_6

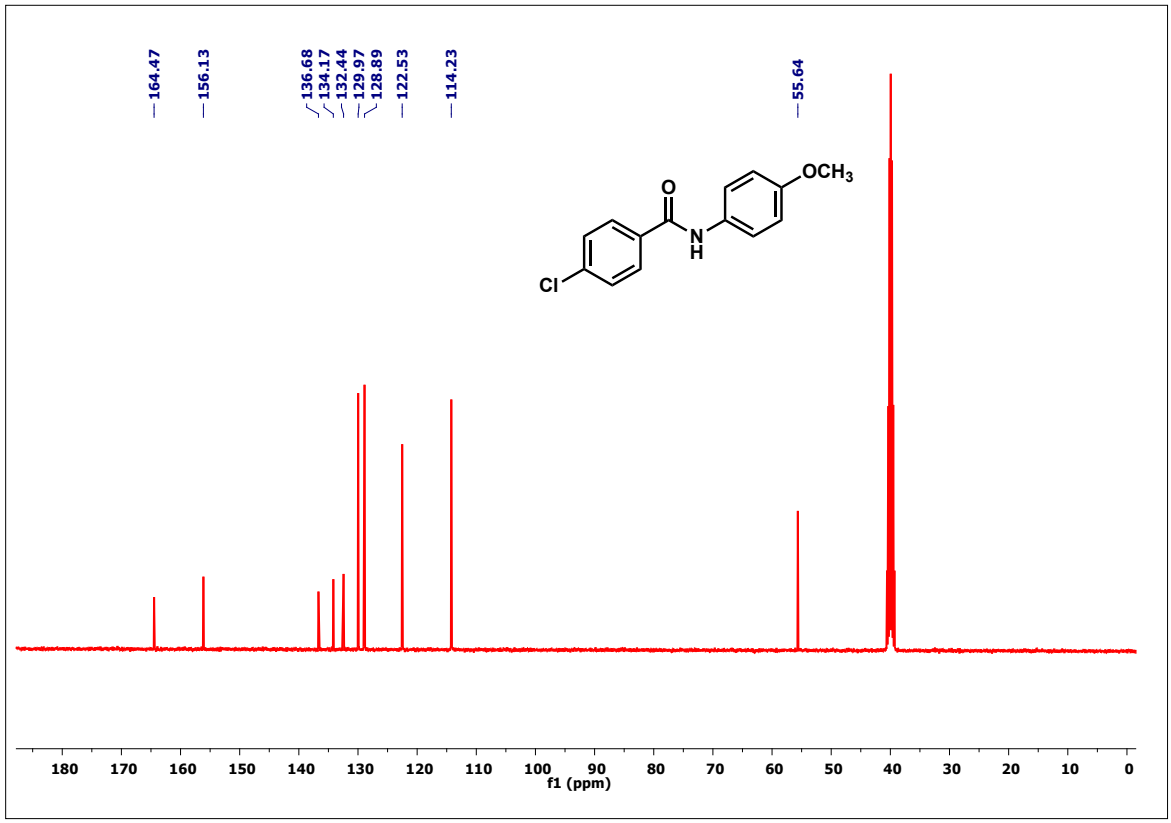


Figure S60: 100 MHz ^{13}C NMR spectrum of **22** in DMSO-d_6

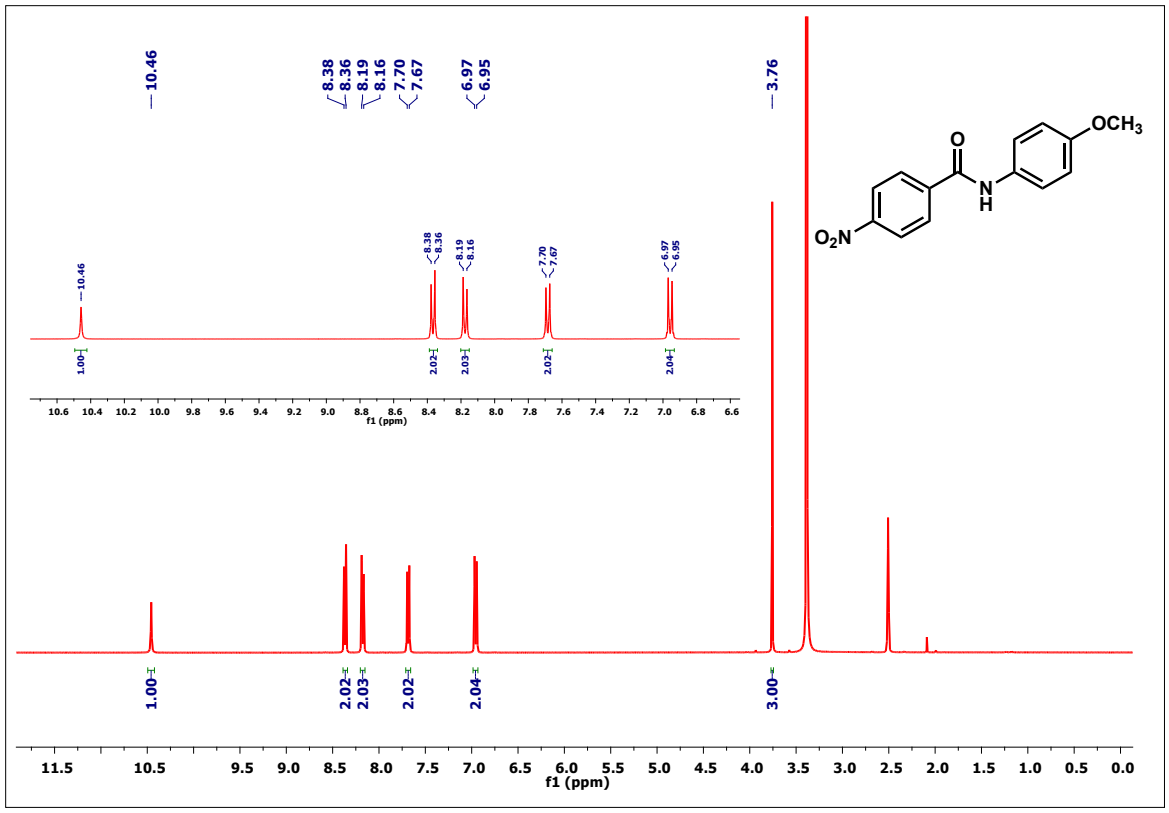


Figure S61: 400 MHz ^{1}H NMR spectrum of **23** in DMSO-d_6

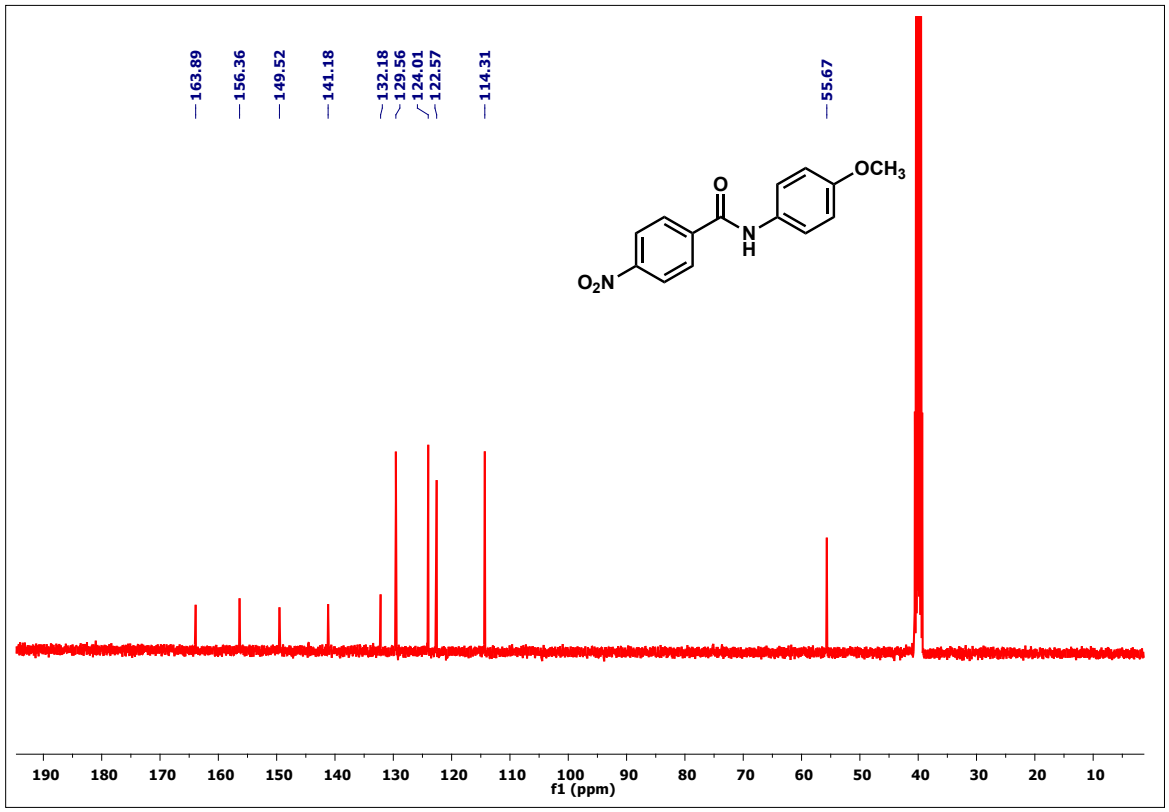


Figure S62: 100 MHz ^{13}C NMR spectrum of **23** in DMSO-d_6

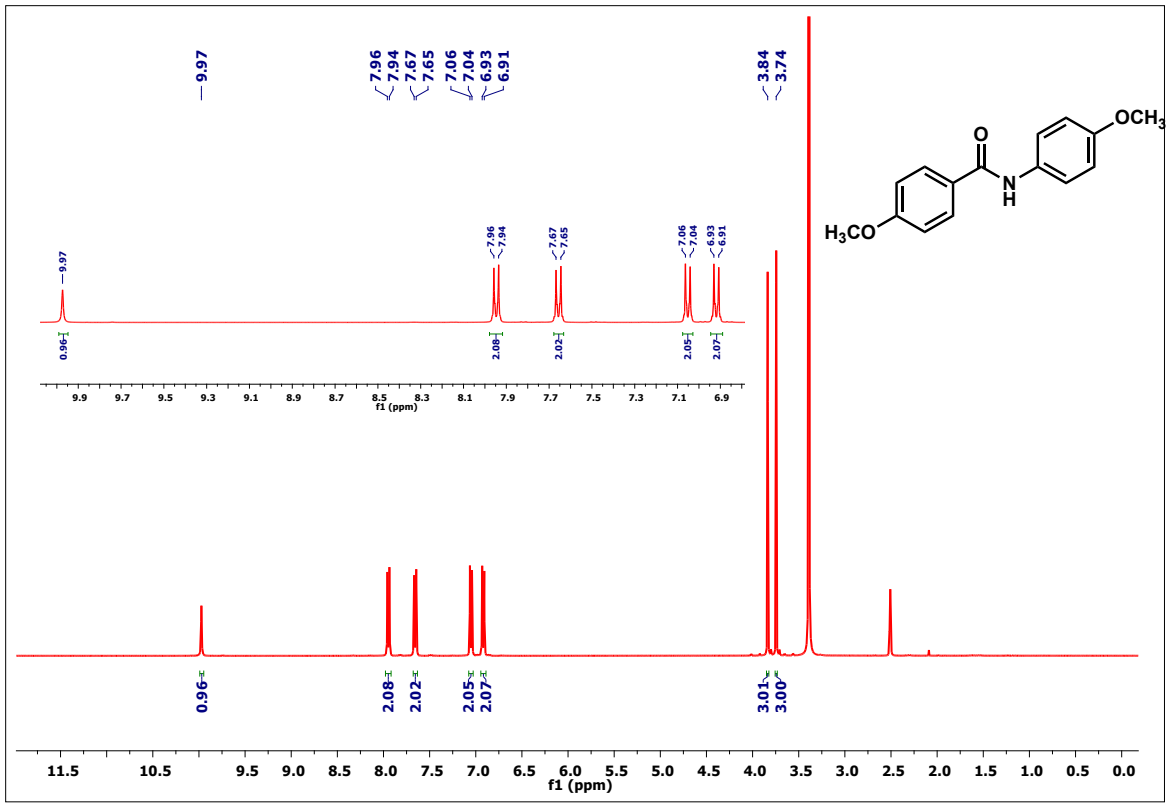


Figure S63: 400 MHz ^{1}H NMR spectrum of **24** in DMSO-d_6

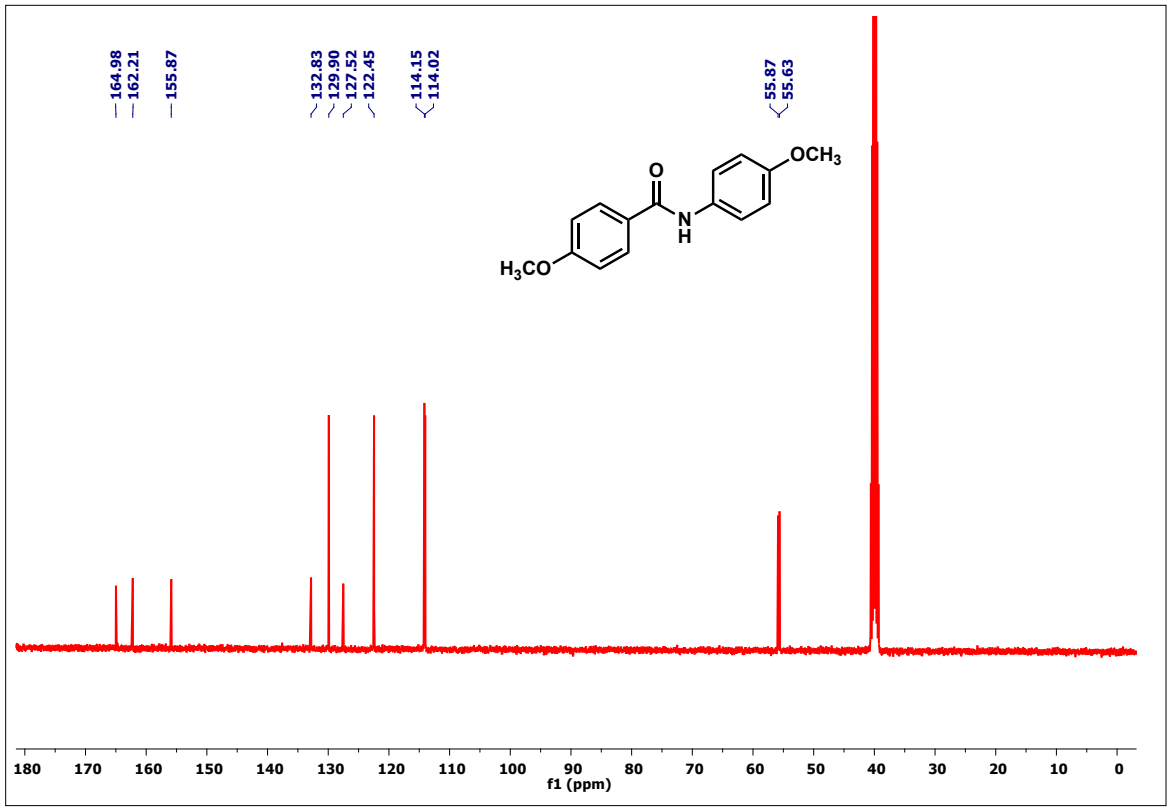


Figure S64: 100 MHz ^{13}C NMR spectrum of **24** in DMSO-d_6

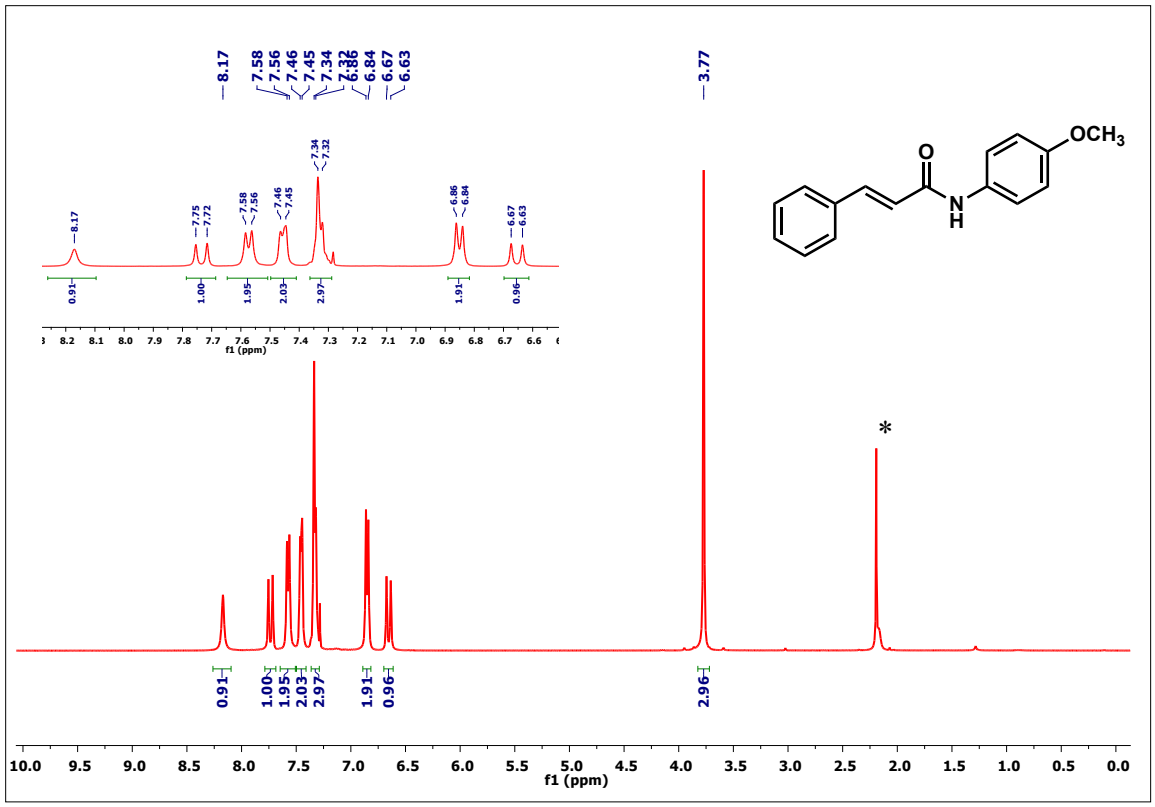


Figure S65: 400 MHz ^{1}H NMR spectrum of **25** in $CDCl_3$

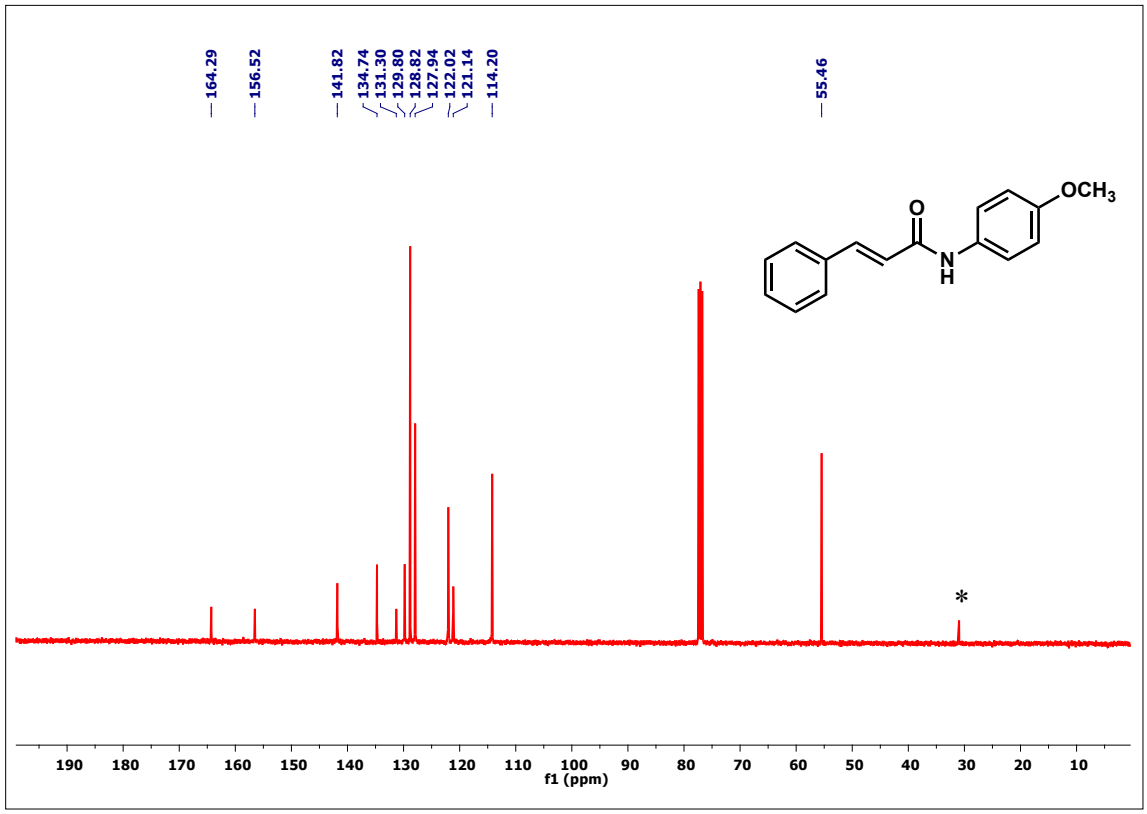


Figure S66: 100 MHz ^{13}C NMR spectrum of **25** in $CDCl_3$

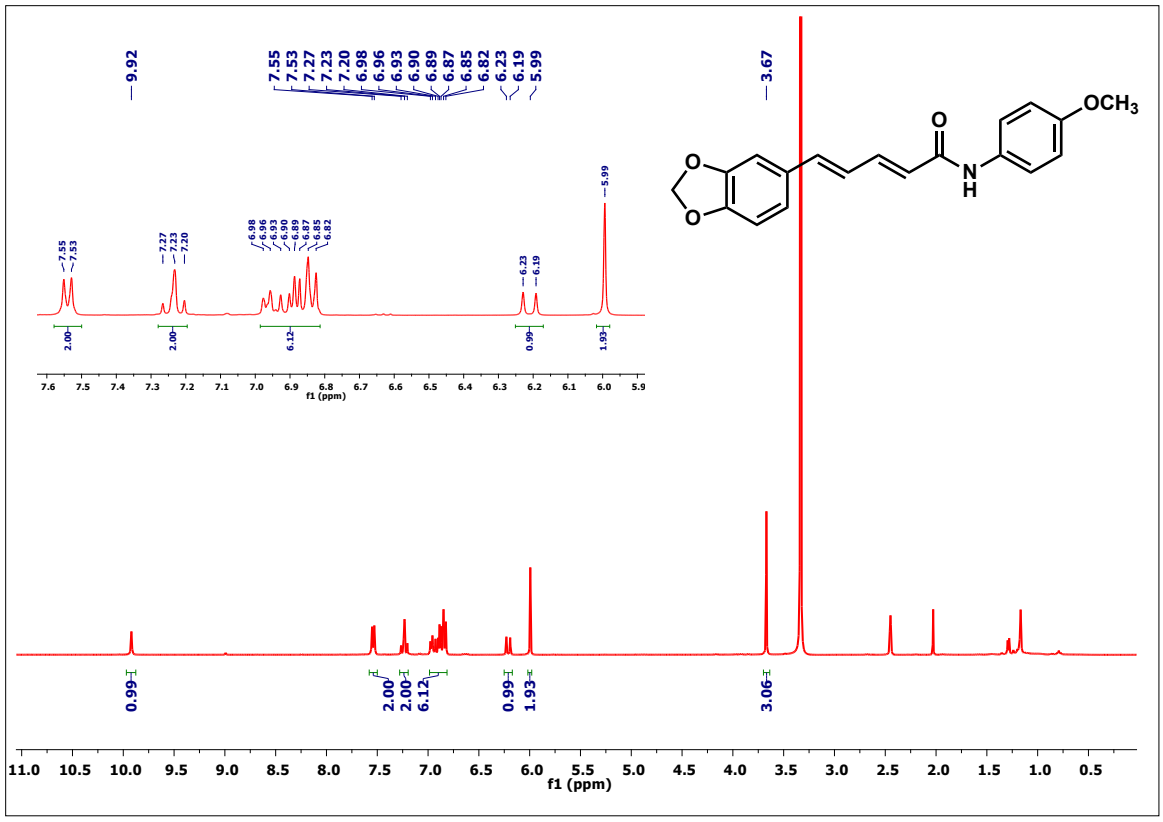


Figure S67: 400 MHz ^{1}H NMR spectrum of **26** DMSO-d_6

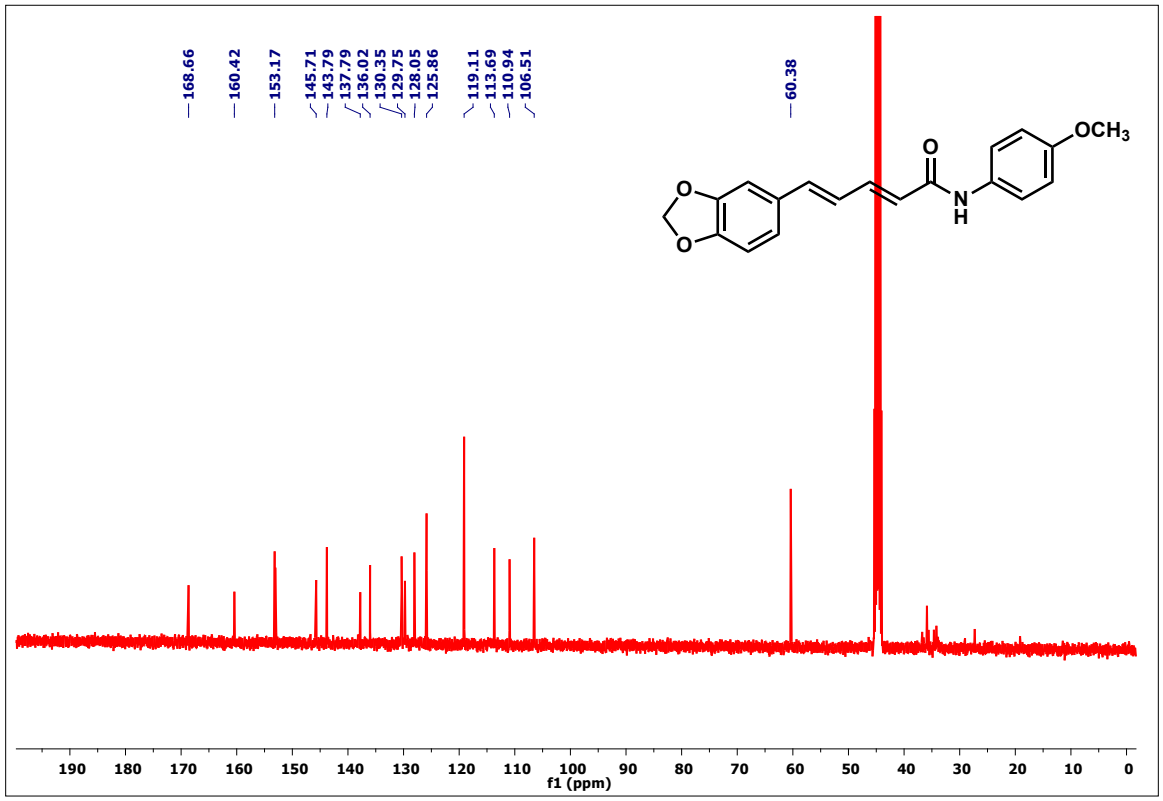


Figure S68: 100 MHz ^{13}C NMR spectrum of **26** DMSO-d_6

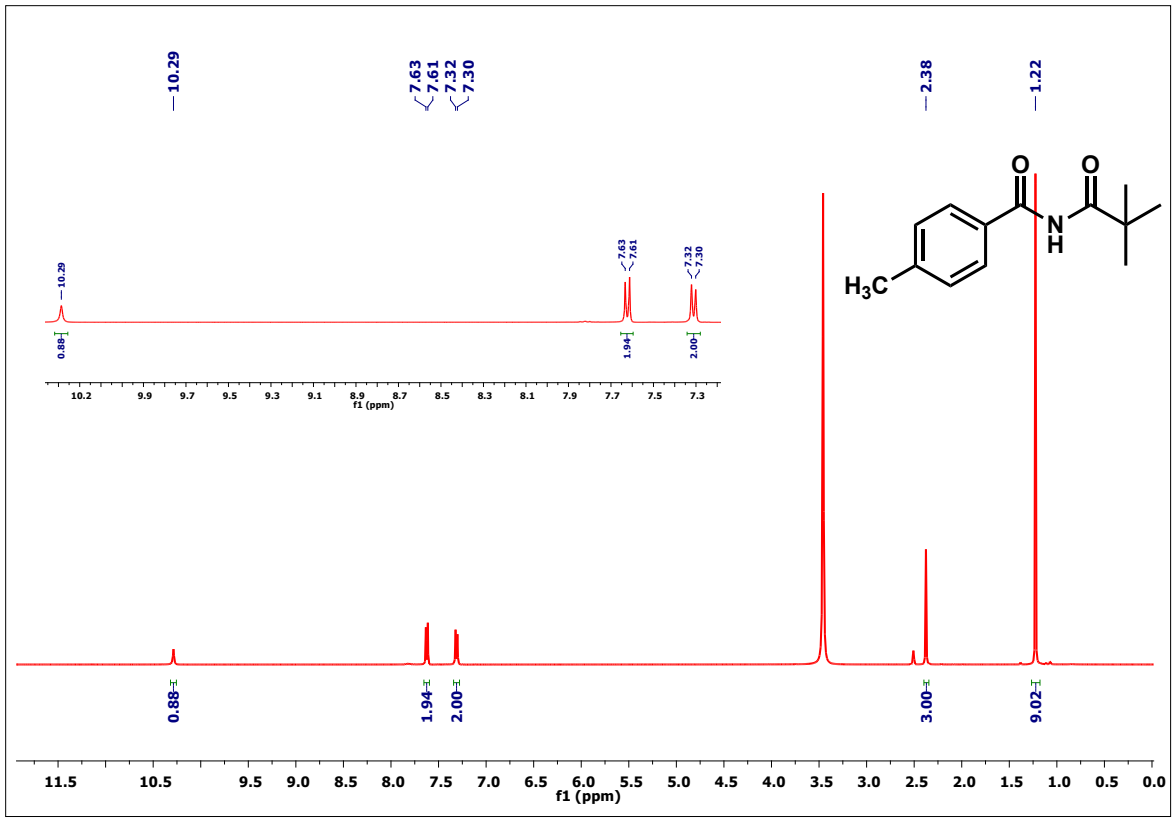


Figure S69: 400 MHz ^{1}H NMR spectrum of **27** in DMSO-d_6

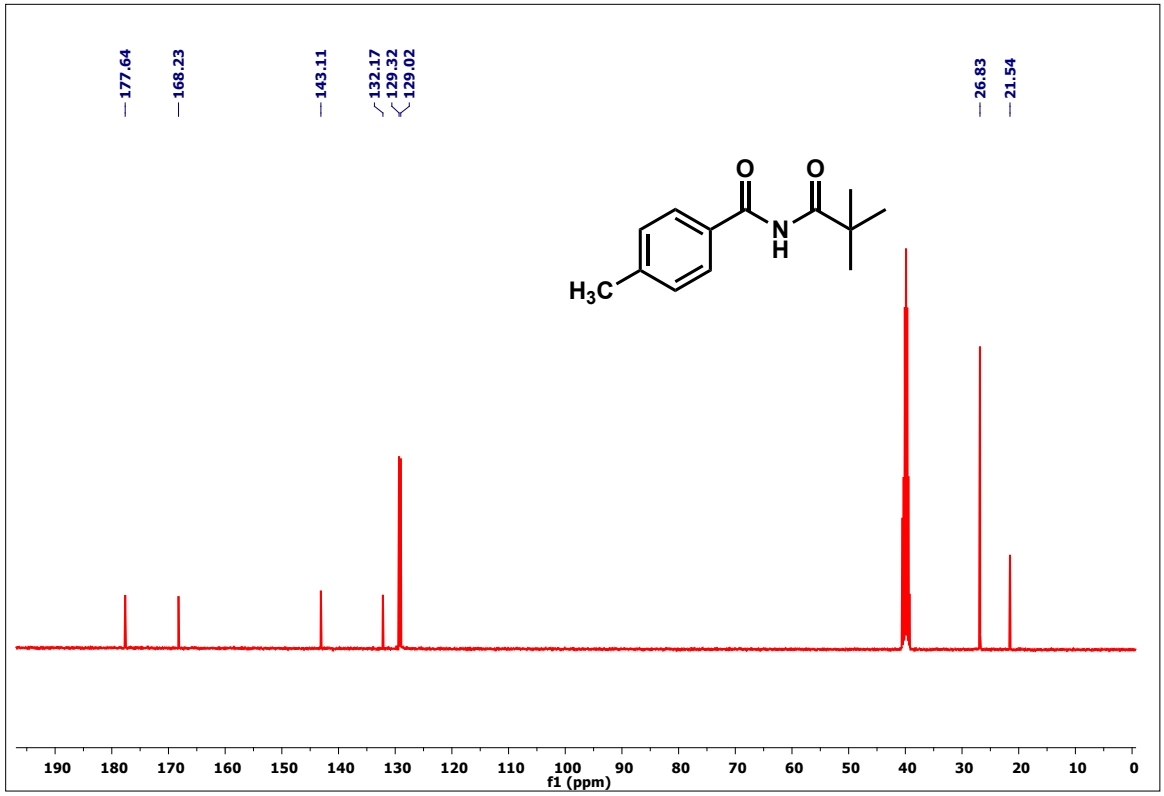


Figure S70: 100 MHz ^{13}C NMR spectrum of **27** in DMSO-d_6

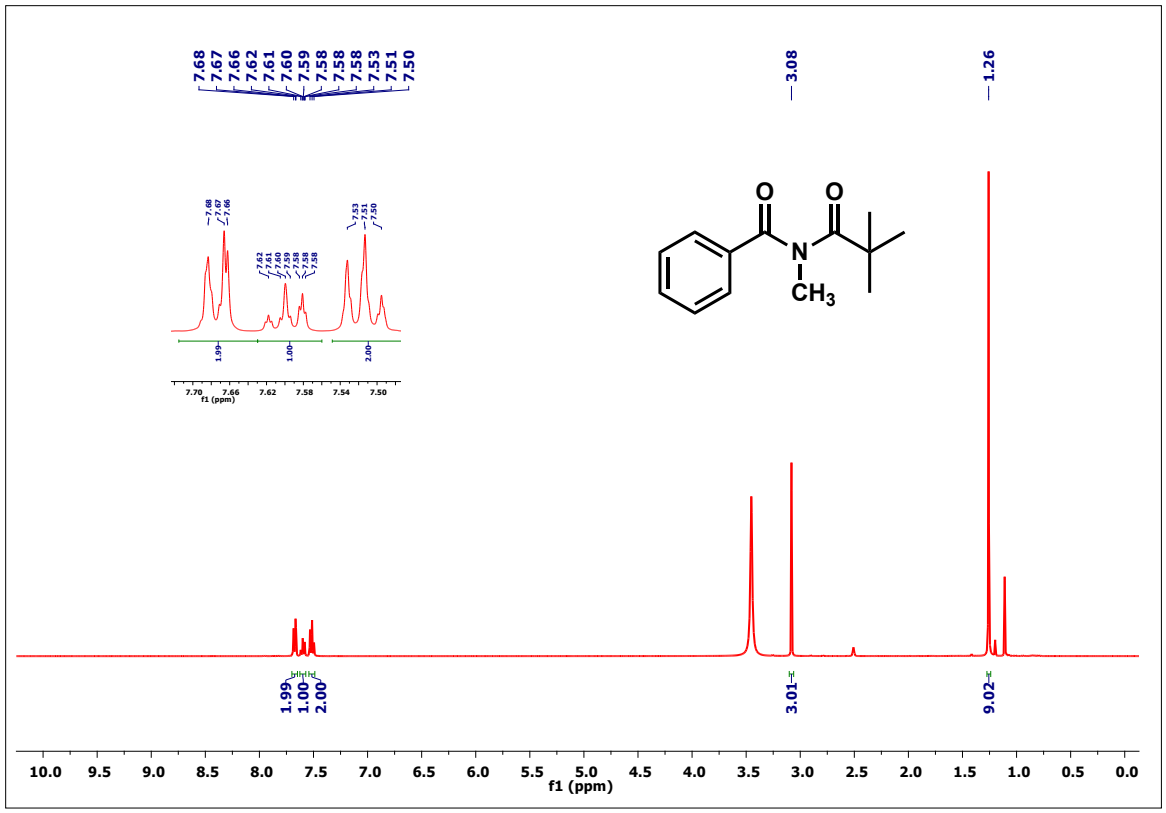


Figure S71: 400 MHz ^{1}H NMR spectrum of **28** in DMSO-d_6

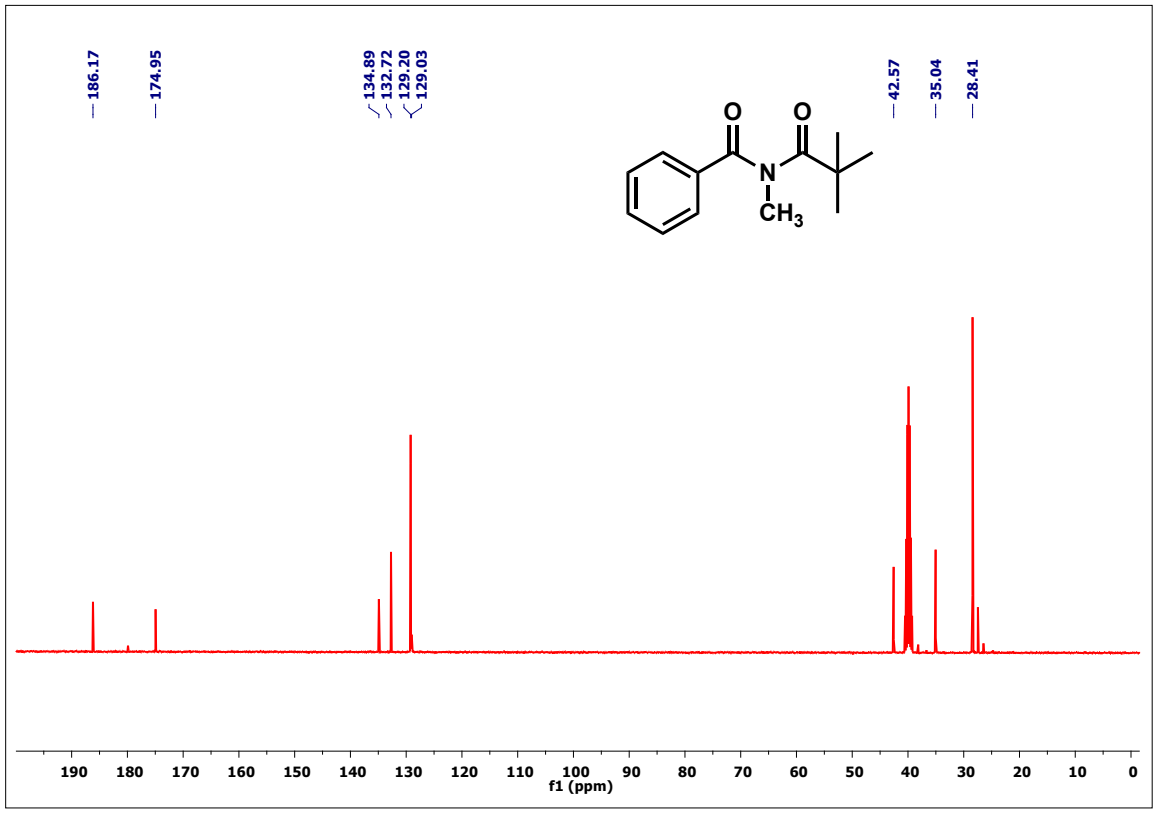


Figure S72: 100 MHz ^{13}C NMR spectrum of **28** in DMSO-d_6

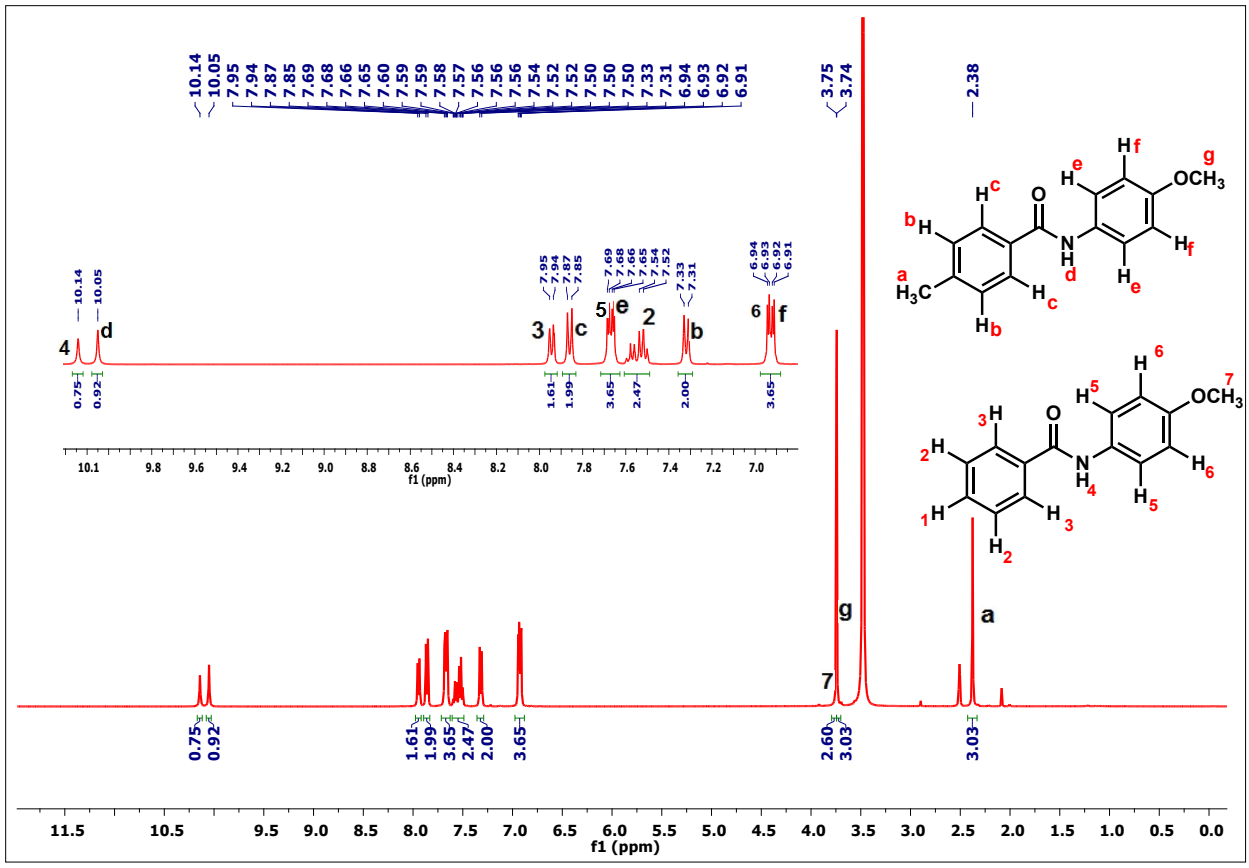


Figure S73: 400 MHz ^{1}H NMR spectrum in DMSO-d_6 of competitive study