Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Amidic Resonance not a Barrier for Transamidation of N-Pivaloyl Activated Amides:

Catalyst, Base and Additive Free Conditions

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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

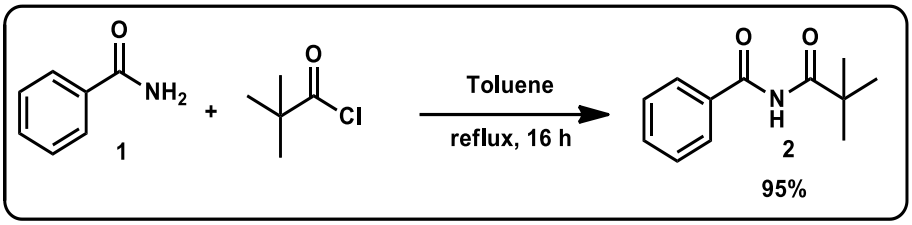
THF – Tetrahydrofuran

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]

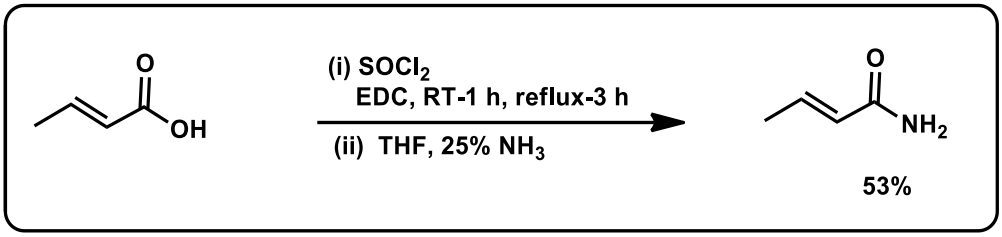
Spectral data:

^{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.

General Procedure: Synthesis of aliphaticamides, 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 crotonicamide



The general procedure stated above was followed. Crotonicacid (500 mg, 5.74 mmol), thionyl chloride (1.25 mL, 17.2 mmol), 25% of ammonia solution (8 mL, 114.8 mmol). Pure product was obtained as half-white solid in 258 mg (53% yield).

Physical Characteristics:

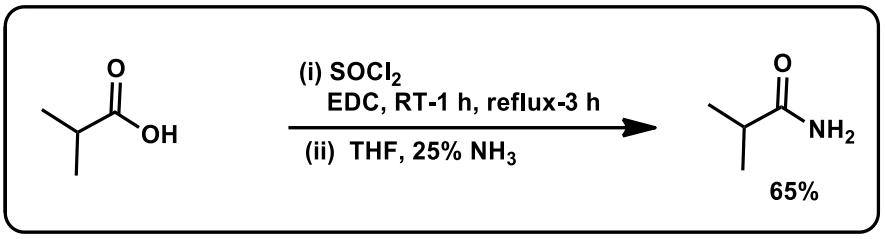
Colour and appearance: halfwhite solid

M.pt: 130 °C – 135 °C

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 1.75 (3H, d, *J* = 8 Hz), 5.88 (1H, d, *J* = 16 Hz), 6.56 – 6.65 (1H, m), 6.85 (1H, s), 7.36 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ: 17.7, 126.2, 139.0, 167.4. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 85.05.

Synthesis of isobutamide



The general procedure stated above was followed. isobutyric (500 mg, 5.68 mmol), thionyl chloride (1.25 mL, 17.2 mmol), 25% of ammonia solution (8 mL, 113.8 mmol). Pure product was obtained as white solid in 321 mg (65% yield).

Physical Characteristics:

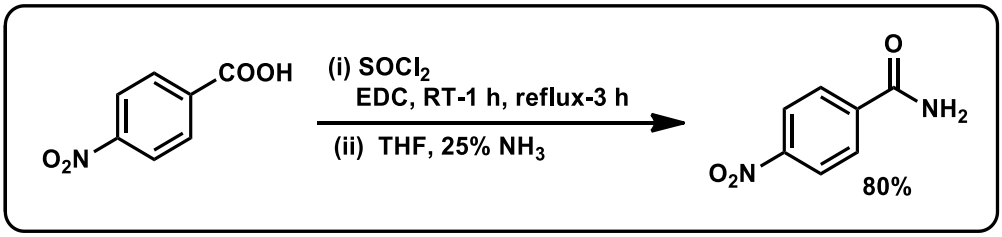
Colour and appearance: white solid

M.pt: 126 °C – 130 °C

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 0.98 (6H, d, *J* = 8 Hz), 2.27 – 2.37 (1H, m), 6.64 (1H, s), 7.22 (1H, s). **^{13}C NMR**: (100 MHz, DMSO-d_6) δ:19.9, 34.1, 179.2. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 87.05

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:

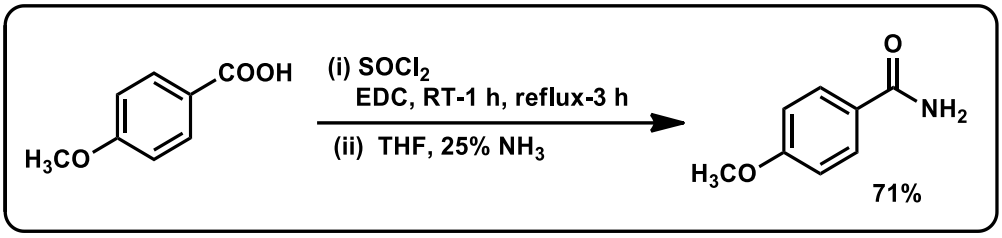
Colour and appearance: White solid

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).

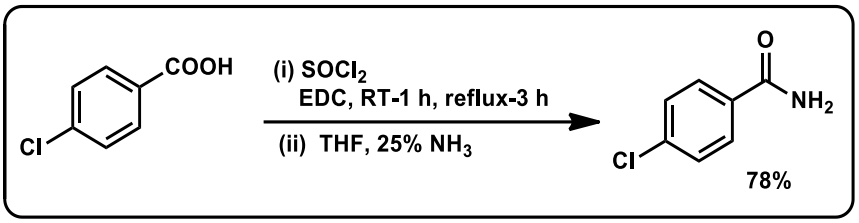
Physical Characteristics:

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:

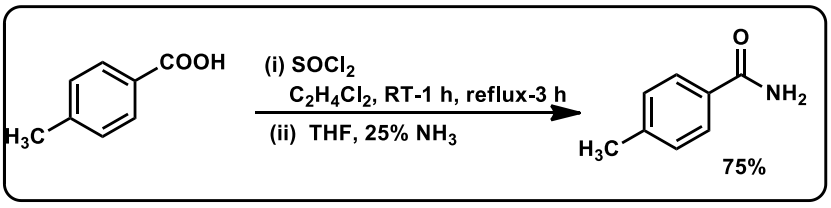
Colour and appearance: White solid

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

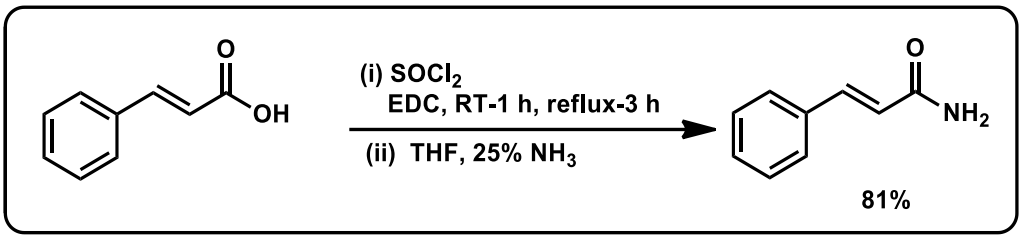
M.pt: 160 °C – 163 °C (Lit. m.pt = 159 °C – 160 °C)[4]

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:

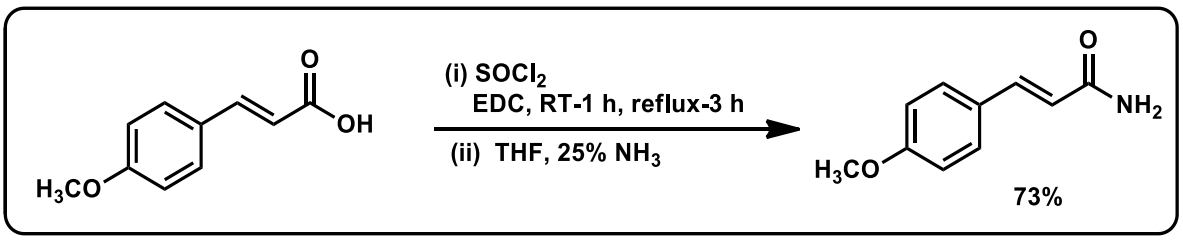
Colour and appearance: White solid

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

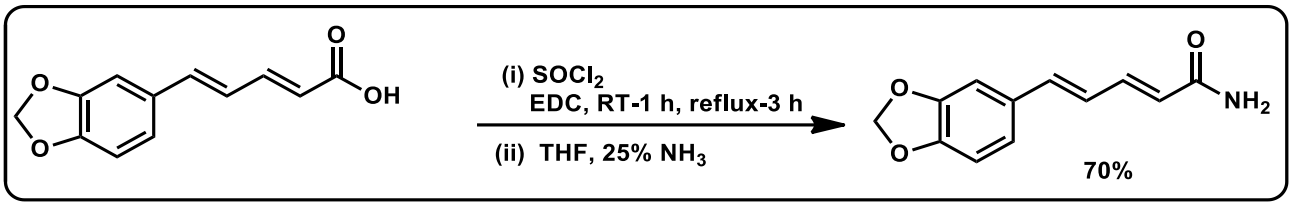
Synthesis of piperic amide

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:

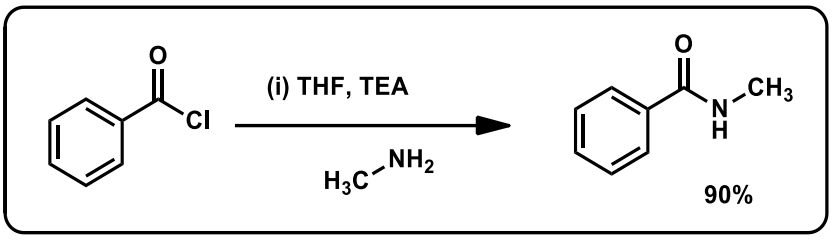
Colour and appearance: Brown Solid

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

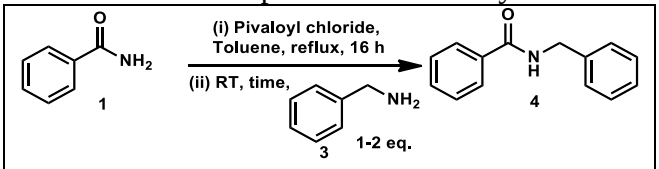
M.pt: 84°C – 87 °C (Lit. m.pt = 81 °C – 83 °C)[7]

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 alkyl amines



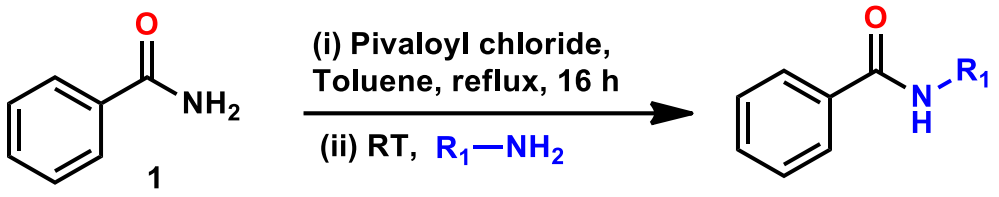
S. No	Equivalence (amine)	Time	Yield (%)
1	1	1 h	No reaction
2	2	15 min	64
		30 min	95

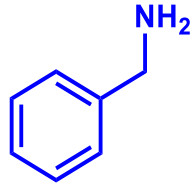
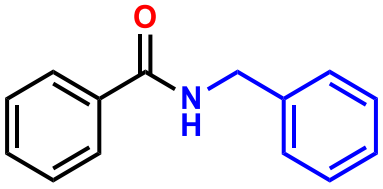
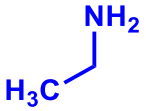
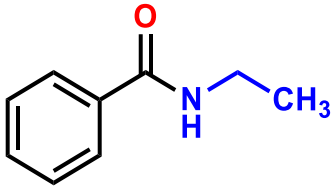
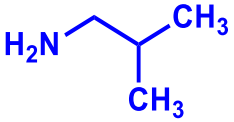
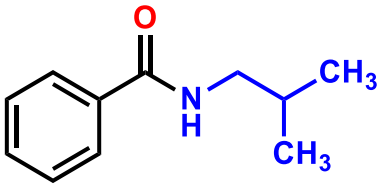
General procedure-A: Transamidation of benzamide with alkyl amines

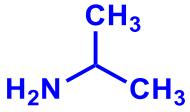
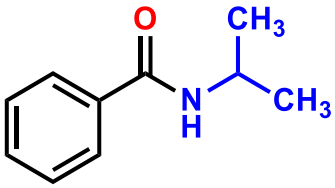
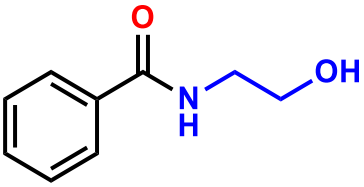
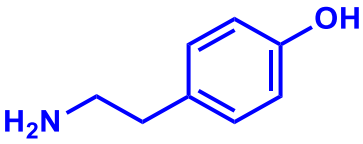
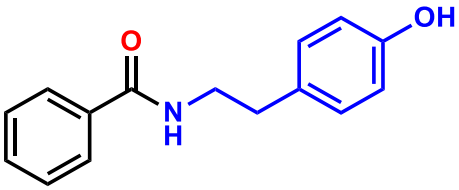
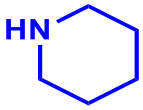
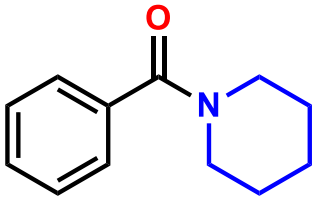
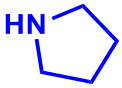
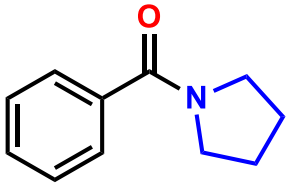
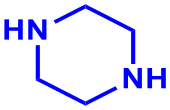
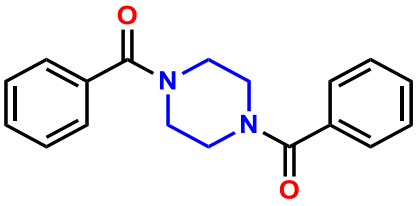
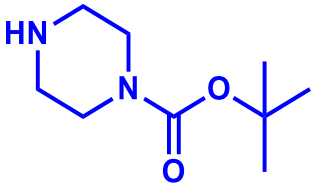
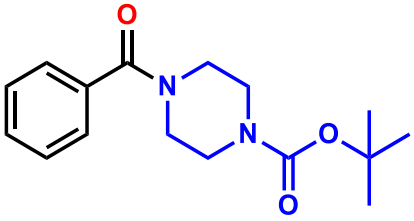
To a stirred solution of benzamide (1 eq.), in toluene (5 mL) at room temperature, pivaloyl chloride (1 eq.), was added dropwise. After addition, the reaction mixture was refluxed for 16 h. The reaction mixture was cooled down to room temperature. Without further purification the crude product was taken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

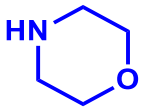
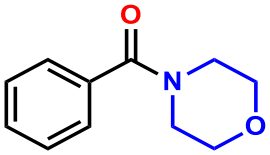
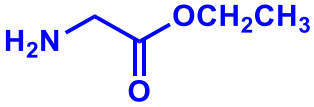
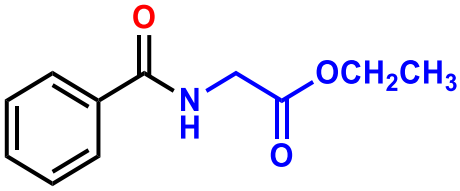
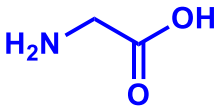
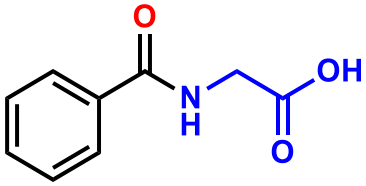
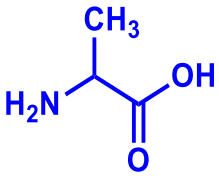
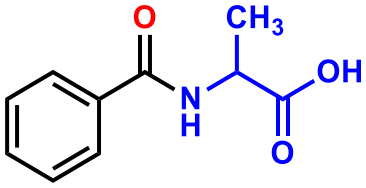
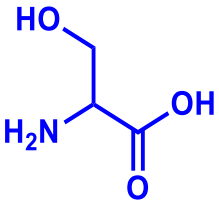
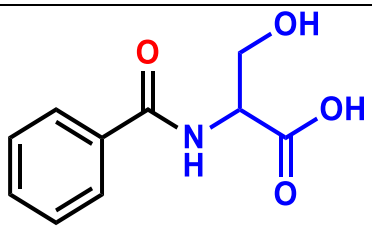
To the above synthesized imide in toluene, alkyl amine (2 eq.) was added and stirred at room temperature. Progress of the reaction was monitored by TLC. Starting material consumed within 30 min - 4 h with all the tested amines. After completion, the reaction mixture was washed with 5% HCl solution, 5% $NaHCO_3$ 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 alkyl amines

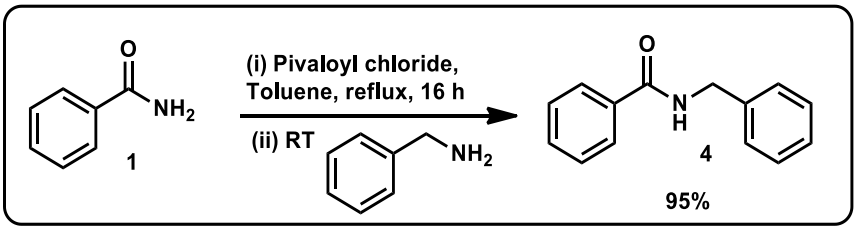


S.no	Amine	Product	Yield	Time
1.			**95**	**30 min**
2.			**96**	**30 min**
3.			**90**	**30 min**

4.			**82**	**1h**
5.			**88**	**30 min**
6.			**79**	**30 min**
7.			**90**	**1h**
8.			**90**	**1h**
9.			**73**	**4h**
11.			**87**	**1h**

12.			**89**	**1h**
13.			**86**	**45 min**
14.			**70**	**1h**
15.			**67**	**2h**
16.			**60**	**2h**

Transamidation of benzamide with benzylamine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), benzylamine (176 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 165 mg (95%).

Physical Characteristics:

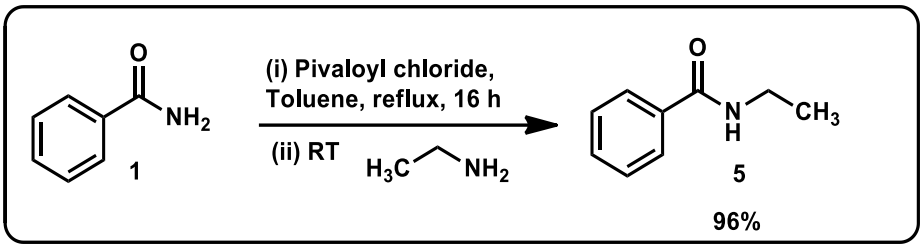
Colour and appearance: Half-white solid

M.pt: 103 °C – 105 °C (Lit. m.pt = 104 °C – 105 °C)[8]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.65 (2H, d, *J* = 8 Hz), 7.29-7.36 (4H, m), 7.43 (2H, t, *J* = 8 Hz), 7.48-7.52 (1H, m), 7.79 (2H, d, *J* = 8 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 44.1, 126.7, 126.9, 127.6, 127.9, 128.6, 128.8, 131.5, 134.3, 138.1, 167.3. **GC-MS (EI$^+$) *m/z***: (M^+): 211.00.

Transamidation of benzamide with Ethylamine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), ethylamine (106 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale-yellow solid in 118 mg (96% yield).

Physical Characteristics:

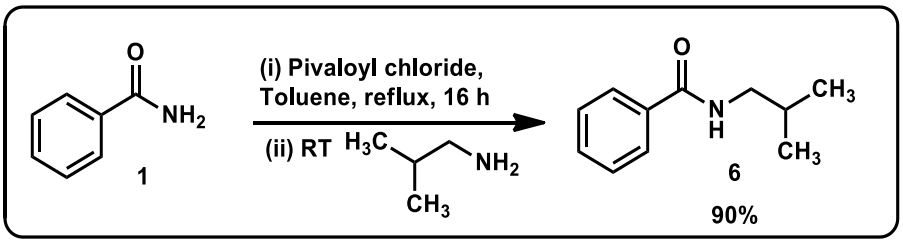
Colour and appearance: Pale-yellow solid

M.pt: 66 °C – 69 °C (Lit. m.pt = 71 °C – 72 °C)[9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (3H, t, *J* = 8 Hz), 3.47 (2H, d, *J* = 4 Hz), 6.42 (1H, br, s), 7.38-7.41 (2H, m), 7.45-7.49 (1H, m) 7.76 (2H, d, *J* = 8 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 10.1, 14.8, 35.0, 126.9, 128.5, 131.3, 134.6, 167.6. **GC-MS (EI$^+$) *m/z***: (M^+): 149.10

Transamidation of benzamide with isobutyl amine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), isobutylamine (120 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as pale-yellow solid in 131 mg (90%).

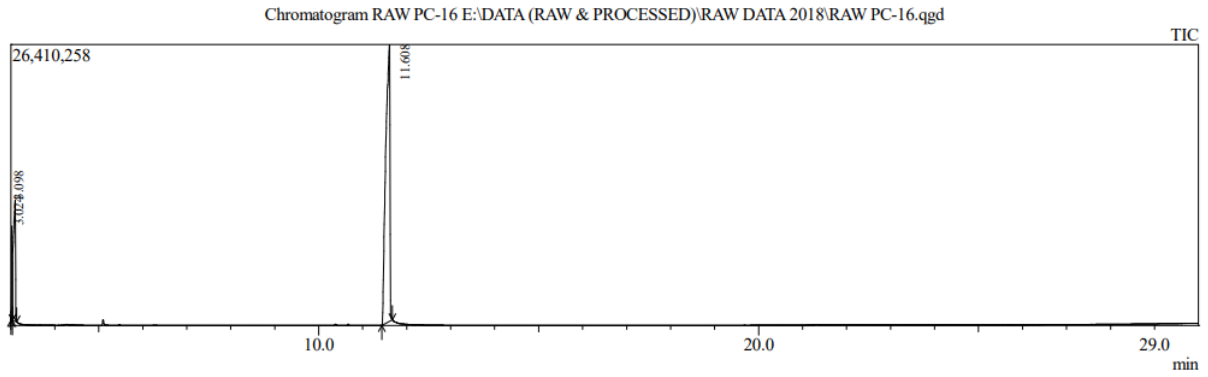
Physical Characteristics:

Colour and appearance: Pale yellow solid

M.pt: 54 °C – 55 °C (Lit. m.pt = 56 °C – 58 °C)[10]

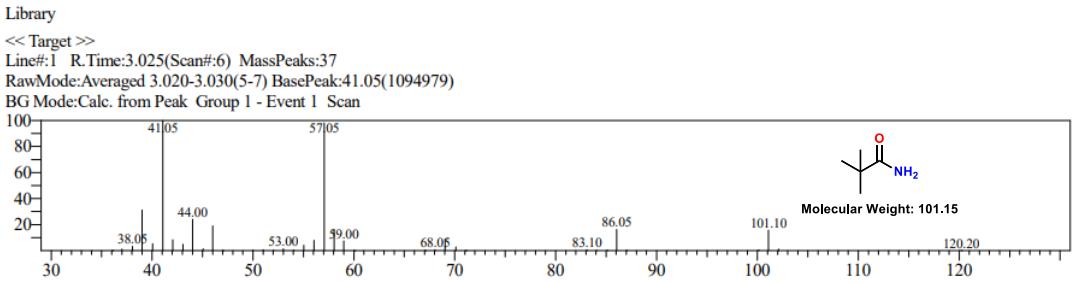
Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 0.89 (6H, d, *J* = 8 Hz), 1.82-1.89 (1H, m), 3.09 (2H, t, *J* = 8 Hz), 7.43-7.53 (3H, m), 7.85 (2H, d, *J* = 8Hz), 8.46 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 20.6, 28.5, 47.1, 127.6, 128.6, 131.4, 135.2, 166.7. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 177.10



Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	3.024	3.005	3.035	9724197	4.44	8858850	19.15	1.10		
2	3.098	3.035	3.135	38423239	17.53	11382433	24.61	3.38	V	
3	11.608	11.435	11.675	171007034	78.03	26011752	56.24	6.57		
				219154470	100.00	46253035	100.00			



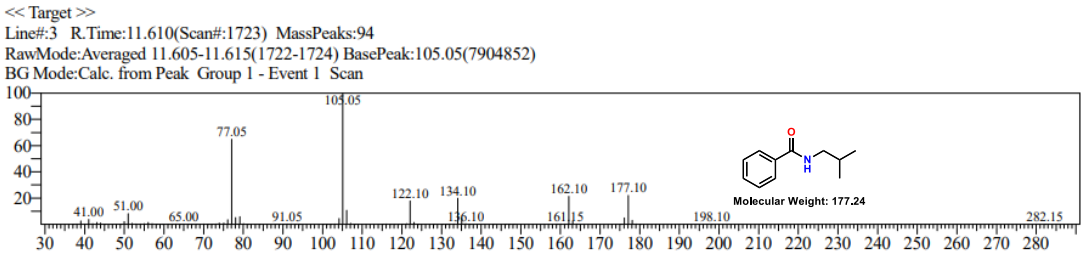
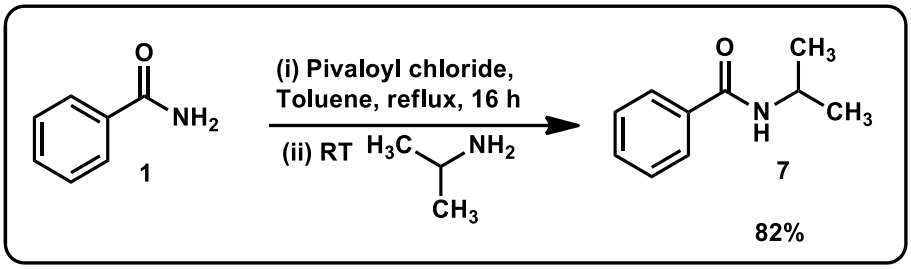


Figure S1: Chromatogram and mass spectra of pivalic amide and transamidation product (**6**)

Transamidation of benzamide with iso-propyl amine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), isopropylamine (97.5mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 110 mg (82% yield).

Physical Characteristics:

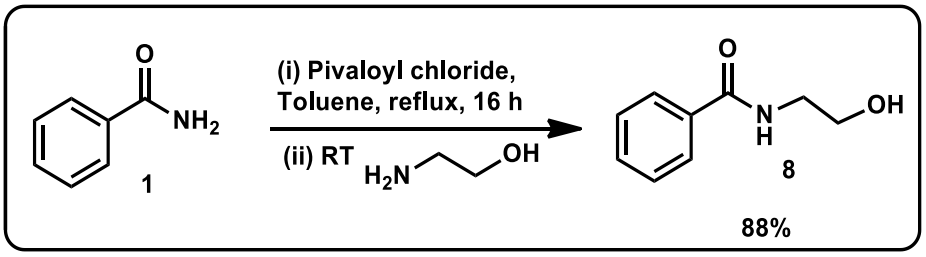
Colour and appearance: White solid

M.pt: 97 °C – 98 °C (Lit. m.pt = 97 °C – 99 °C)[11]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.17 (6H, d, *J* = 8 Hz), 4.08 -4.13 (1H, m), 7.43-7.53 (3H, m), 7.84 (2H, d, *J* = 4 Hz), 8.22 (1H, d, *J* = 8 Hz).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 22.7, 41.4, 127.6, 128.5, 131.3, 135.3, 165.8. **GC-MS (EI$^+$)** ***m/z***: $[M]^+$ 163.10

Transamidation of benzamide with ethanol amine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), ethanol amine (100 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 119 mg (88% yield).

Physical Characteristics:

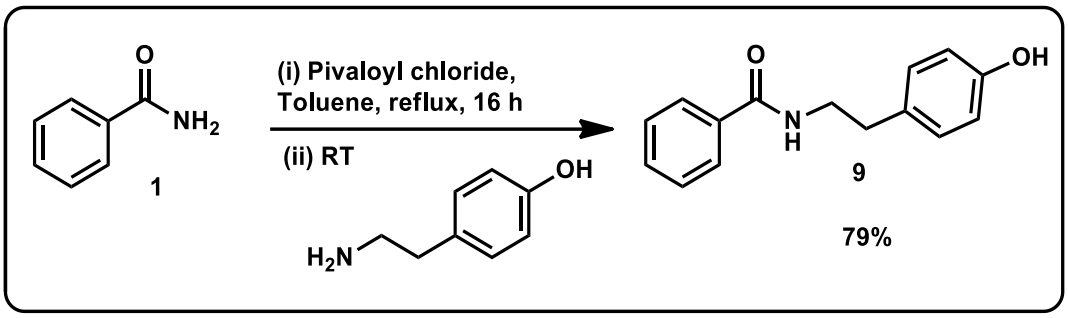
Colour and appearance: White Solid

M.pt: 60 °C – 63 °C (Lit. m.pt = 60 °C – 62 °C)[12]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.33- 3.37 (2H, m), 3.51-3.55 (2H, m), 4.78 (1H, t, *J* = 8 Hz), 7.44- 7.53 (3H, m), 7.86 (2H, d, *J* = 8 Hz), 8.44 (1H, t, *J* = 8 Hz).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 42.6, 60.2, 127.6, 128.6, 131.5, 134.9, 166.8. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 165.10

Transamidation of benzamide with tyramine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), tyramine (226.3 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as light brown solid in 157 mg (79 % yield).

Physical Characteristics:

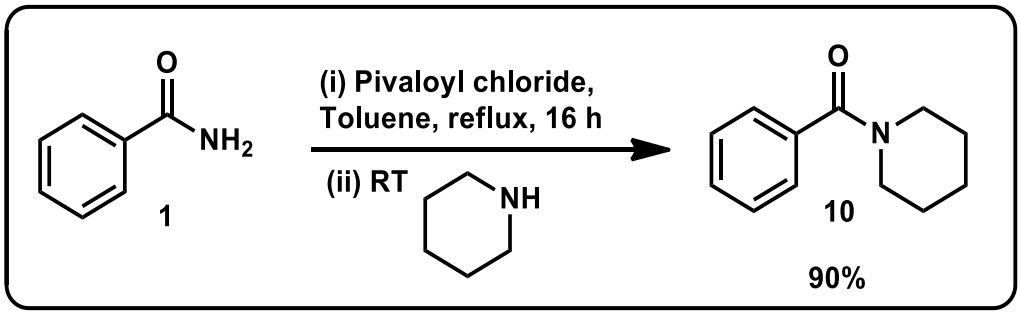
Colour and appearance: Light brown solid

M.pt: 155 °C – 156 °C (Lit. m.pt = 158 °C – 159 °C) [13]

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.73 (2H, t, *J* = 8 Hz), 6.79 (2H, d, *J* = 8 Hz), 7.03, (2H, d, *J* = 8 Hz), 7.43-7.52 (3H, m), 7.82 (2H, d, *J* = 8 Hz), 8.53 (1H, t, *J* = 8 Hz), 9.21 (1H, s).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 34.7, 41.7, 115.5, 127.5, 128.7, 129.9, 131.5, 135.1, 156.0, 166.6. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 241.00

Transamidation of benzamide with piperidine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), piperidine (140 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as yellow liquid in 143 mg (90% yield).

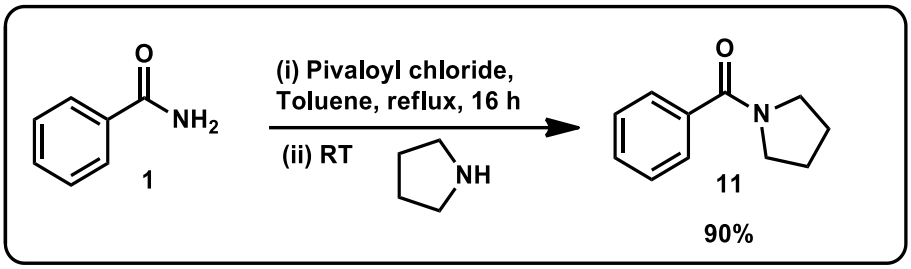
Physical Characteristics:

Colour and appearance: Yellow liquid

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.43 -1.60 (6H, m), 3.25 (2H, br, s), 3.58 (2H, s), 7.34- 7.38 (2H, m), 7.43 (3H, t, *J* = 4 Hz).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 24.5, 25.7, 26.4, 42.7, 48.4, 127.0, 128.8, 129.6, 137.0, 169.3. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 189.15

Transamidation of benzamide with pyrrolidine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), pyrrolidine (117 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as colourless liquid in130 mg (90% yield).

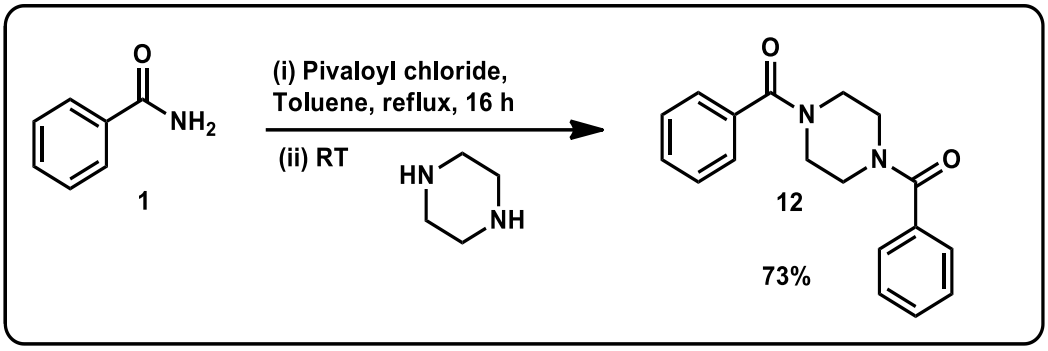
Physical Characteristics:

Colour and appearance: Colourless liquid

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.76- 1.89 (4H, m), 3.35 (2H, t, *J* = 8 Hz), 3.46 (2H, t, *J* = 8 Hz), 7.43 (3H, d, *J* = 8 Hz), 7.49- 7.51 (2H, m).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 24.3, 26.4, 46.3, 49.3, 127.4, 128.6, 130.1, 137.7, 168.7. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 175.10

Transamidation of benzamide with Piperazine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), Piperazine (142.0 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 177 mg (73% yield).

Physical Characteristics:

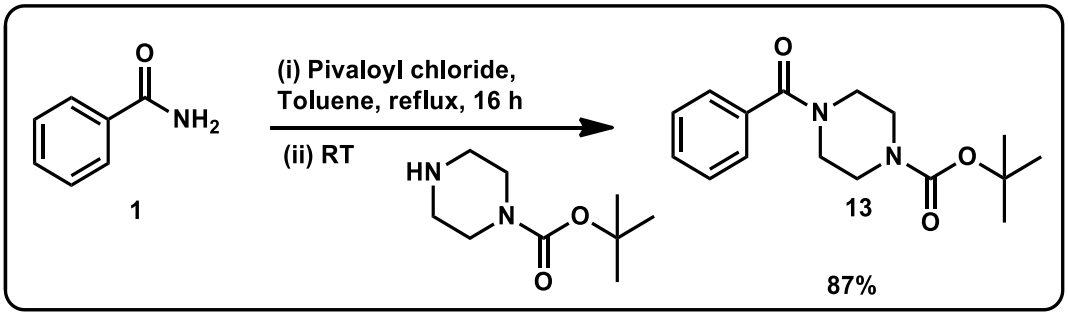
Colour and appearance: White solid

M.pt: 195 °C – 197 °C (Lit. m.pt = 196 °C – 197 °C)[14]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.49- 3.63 (8H, m), 7.34 (10H, s). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 127.0, 128.6, 130.1, 135.1, 170.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 294.00

Transamidation of benzamide with Boc-piperazine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), Boc-piperazine (307.3 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 208 mg (87% yield).

Physical Characteristics:

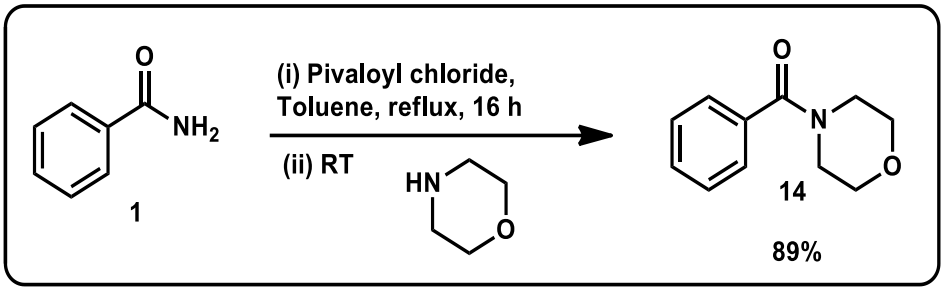
Colour and appearance: White Solid

M.pt: 107 °C – 109 °C (Lit. m.pt = 107 °C – 108 °C)[15]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.39 (9H, s), 3.35-3.65 (8H, m), 7.33 (5H, t, *J* = 8 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 28.3, 80.3, 127.0, 128.5, 129.8, 135.4, 154.5, 170.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 290.10.

Transamidation of benzamide with Morpholine



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), Morpholine (143 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as Pale-yellow Liquid in 140 mg (89% yield).

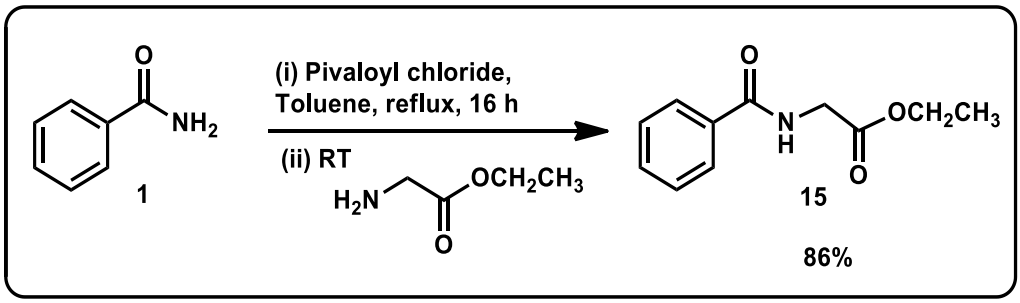
Physical Characteristics:

Colour and appearance: Pale yellow Liquid

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.34-3.39 (8H, m), 7.39 – 7.46 (5H, m). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 66.5, 127.4, 128.9, 129.8, 130.1, 131.1, 135.9, 169.6. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 191.00

Transamidation of benzamide with glysine ethyl ester



The general procedure-A stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), glysine ethyl ester (170.1 mg, 1.65 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 147 mg (86% yield).

Physical Characteristics:

Colour and appearance: White Solid

M.pt: 61 °C – 62 °C (Lit. m.pt = 62 °C)[16]

Spectral data:

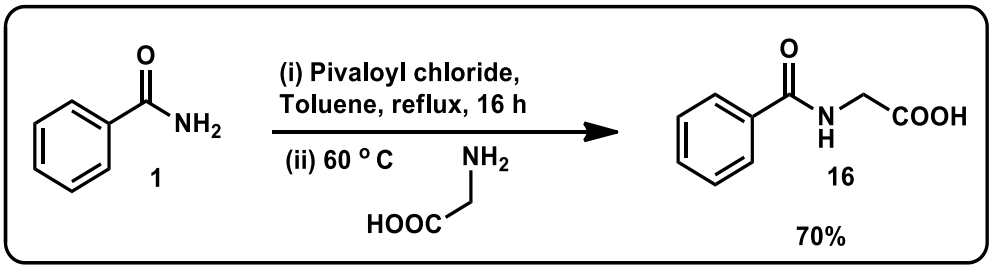
^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.21 (3H, t, *J* = 8 Hz), 4.02 (2H, d, *J* = 4 Hz), 4.10-4.15 (2H, m), 7.47-7.58 (3H, m), 7.89 (2H, d, *J* = 8 Hz), 8.95 (1H, s).**^{13}C NMR** (100 MHz, DMSO-d_6) δ: 14.5, 41.7, 55.3, 60.9, 127.7, 128.8, 131.9, 134.1, 167.1, 170.3. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 207.00

General procedure-B: *Synthesis of N-benzoyl glycine and N-benzoyl alanine*

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 a solution of amino acid (2 eq.), in water (5 eq.), TEA (2 eq.), was added and stirred at room temperature for 15 min. To this, the above synthesized imide in toluene was added dropwise at room temperature and heated to 60 ºC. Progress of the reaction was monitored by TLC. Starting material consumed within 2 h. After completion, the reaction mixture was washed with 5% HCl 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.

Transamidation of benzamide with glycine



The general procedure-B stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), glycine (123.8 mg, 1.65 mmol), water (74 mg, 4.12 mmol), triethylamine (166 mg, 1.65mmol) Pure product was obtained after column chromatography (Chloroform:methanol (90:10)) as white solid in 103 mg (70% yield).

Physical Characteristics:

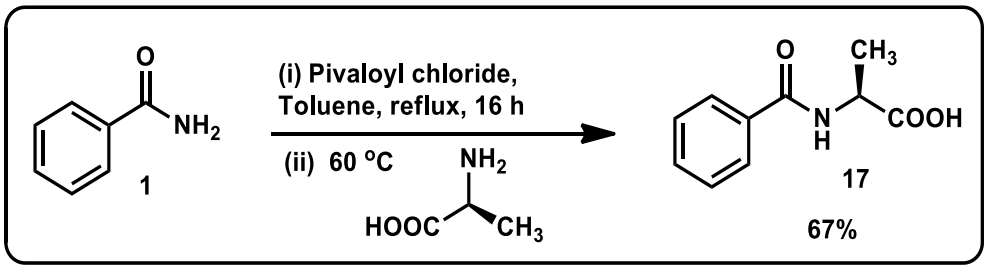
Colour and appearance: White solid

M.pt: 188 °C -189 °C

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.93 (2H, d, *J* = 8 Hz), 7.49 (2H, t, *J* = 8 Hz), 7.55 (1H, t, *J* = 8 Hz), 7.87 (2H, d, *J* = 8 Hz), 8.84 (1H, t, *J* = 8 Hz). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 41.6, 127.6, 128.8, 131.9, 134.2, 166.9, 171.8. **HRMS (ESI-MS)** *m/z*: Calculated for $C_9H_9NO_3Na$ $[M+Na]^+$ 202.0480, found: 202.0481.

Transamidation of benzamide with alanine



The general procedure-B stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), alanine (146.9 mg, 1.65 mmol), water (74 mg, 4.12 mmol), triethylamine (166 mg, 1.65mmol). Pure product was obtained after column chromatography (Chloroform:methanol (90:10)) as white solid in 106 mg (67% yield).

Physical Characteristics:

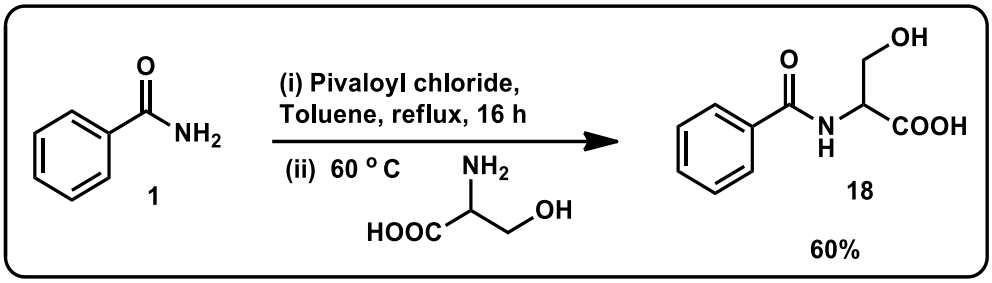
Colour and appearance: White Solid

M.pt: 137 °C – 139 °C

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.40 (3H, d, *J* = 8 Hz), 4.39-4.46 (1H, m), 7.48 (2H, t, *J* = 8 Hz), 7.55 (1H, t, *J* = 8 Hz), 7.89 (2H, d, *J* = 8 Hz), 8.66 (1H, d, *J* = 4 Hz). **^{13}C NMR** (100 MHz DMSO-d_6) δ: 17.3, 48.6, 127.8, 128.7, 131.8, 134.3, 166.6, 174.6. **HRMS (ESI-MS)** *m/z*: Calculated for $C_{10}H_{11}NO_3Na$ $[M+Na]^+$ 216.0636, found: 216.0638.

Transamidation of benzamide with serine



The general procedure-B stated above was followed. Benzamide (100 mg, 0.825 mmol), pivaloyl chloride (99 mg, 0.825mmol), serine (173.2 mg, 1.65 mmol), water (74 mg, 4.12 mmol), triethylamine (166 mg, 1.65mmol). Pure product was obtained after column chromatography (Chloroform:methanol (90:10)) as white solid in 103 mg (60% yield).

Physical Characteristics:

Colour and appearance: White Solid

M.pt: 147 °C – 149 °C

Spectral data:

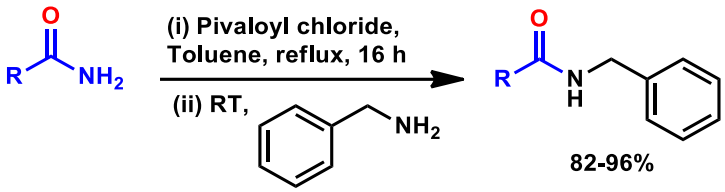
^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.77 (2H, d, *J* = 8 Hz), 4.42-4.47 (1H, m), 7.44 -7.53 (3H, m), 7.86 (2H, t, *J* = 8 Hz), 8.37 (1H, d, *J* = 8 Hz). **^{13}C NMR** (100 MHz DMSO-d_6) δ: 55.6, 61.2, 127.3, 128.3, 131.4, 133.9, 166.3, 171.9. **HRMS (ESI-MS)** *m/z*: Calculated for $C_{10}H_{11}NO_3Na$ $[M+Na]^+$ 232.0685, found: 232.0550.

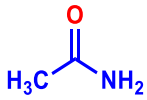
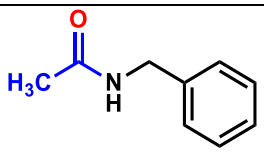
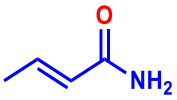
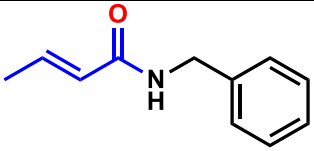
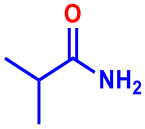
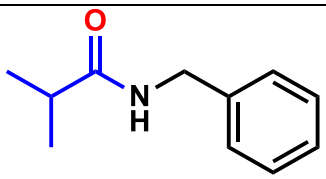
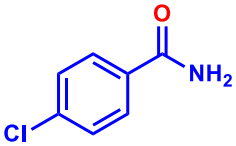
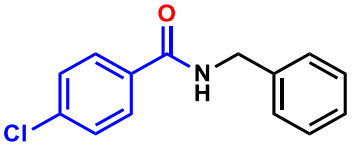
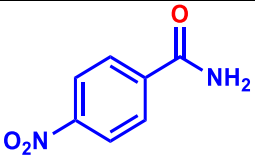
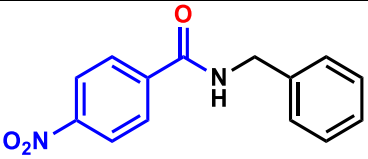
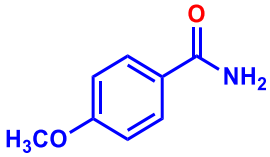
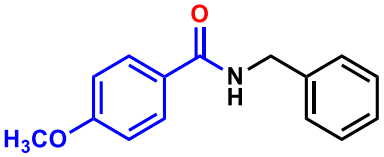
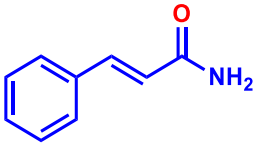
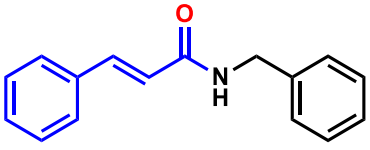
General procedure-C: Transamidation of various amides with *N*-benzyl amine

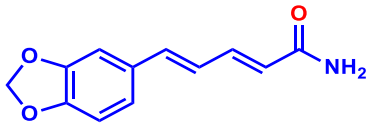
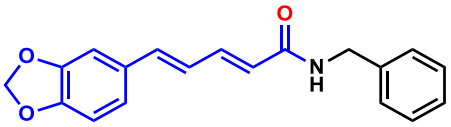
To a stirred solution of various amides (1 eq.), in toluene (5 mL) at room temperature, pivaloyl chloride (1 eq.), was added dropwise. After addition the reaction mixture was refluxed for 16 h. The reaction mixture was cooled down to room temperature. Without further purification the crude product was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

To the above synthesized imide in toluene, benzyl amine (2 eq.), was added and stirred at room temperature. Progress of the reaction was monitored by TLC. Starting material consumed in 30 min - 2 h with benzyl amine. 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

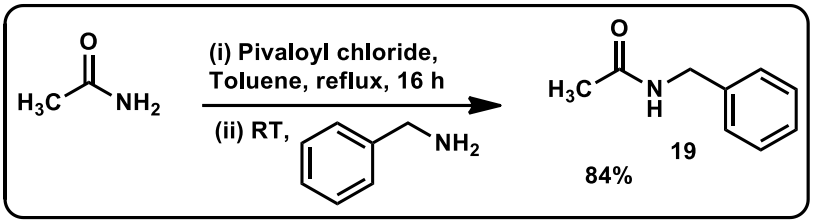
Table 3: Transamidation of various amides with benzyl amine



S.NO	Amide	Product	Yield%	Time
1.			**84**	**30 min**
2.			**73**	**1.5h**
3.			**68**	**1.5h**
4.			**87**	**45 min**
5.			**96**	**30 min**
6.			**82**	**2h**
7.			**89**	**1h**

8.			**93**	**1h**

Transamidation of Acetamide with benzyl amine



The general procedure-C stated above was followed. Acetamide (100 mg, 1.69 mmol), pivaloyl chloride (203 mg, 1.69mmol), benzylamine (361 mg, 3.38 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 211 mg (84% yield).

Physical Characteristics:

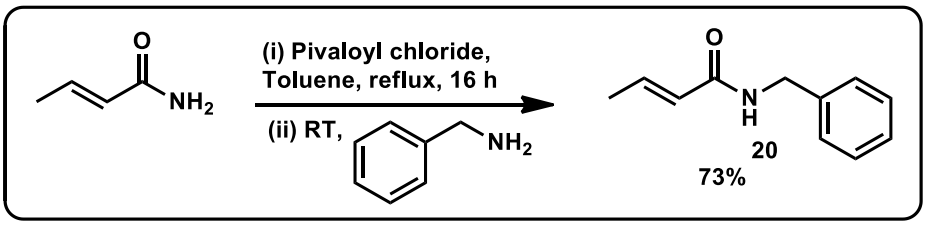
Colour and appearance: White solid

M.pt: 62 °C – 65 °C (Lit. m.pt = 67 °C – 68 °C) [9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.89 (3H, s), 4.28 (2H, d, *J* = 4 Hz), 6.40 (1H, s), 7.16 - 7.25 (5H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 23.0, 43.6, 127.4, 127.7, 128.6, 138.2, 170.4. **GC-MS (EI^{+}) *m/z***: (M^{+}): 149.10

Transamidation of Crotonicamide with benzyl amine



The general procedure-C stated above was followed. Crotonicamide (100 mg, 1.13 mmol), pivaloyl chloride (136 mg, 1.13mmol), benzylamine (241 mg, 2.26 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as Half-white solid in 144 mg (73% yield).

Physical Characteristics:

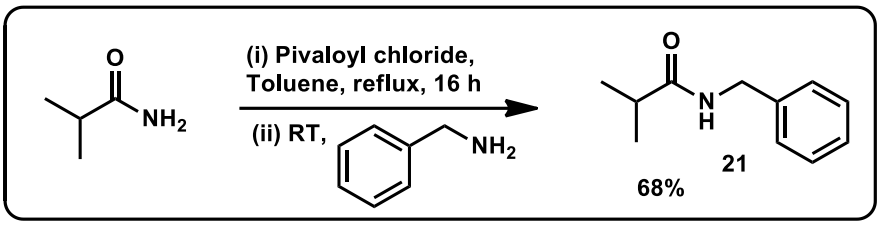
Colour and appearance: Half-White solid

M.pt: 114 °C – 116 °C

Spectral data:

^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.79 (3H, d, *J* = 4 Hz), 4.33 (2H, d, *J* = 8 Hz), 5.98 (1H, d, *J* = 16 Hz), 6.63 – 6.72 (1H, m), 7.24 – 7.26 (3H, m), 7.30 – 7.33 (2H, m), 8.42 (1H, s). **^{13}C NMR** (100 MHz, DMSO-d_6) δ: 17.8, 42.5, 126.0, 127.2, 127.7, 128.7, 138.8, 139.9, 165.9. **GC-MS (EI$^+$) *m/z***: (M^+): 175.00.

Transamidation of isobutricamide with benzyl amine



The general procedure-C stated above was followed. isobutricamide (100 mg, 1.14 mmol), pivaloyl chloride (140 mg, 1.14mmol), benzylamine (245 mg, 2.28 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 137 mg (68% yield).

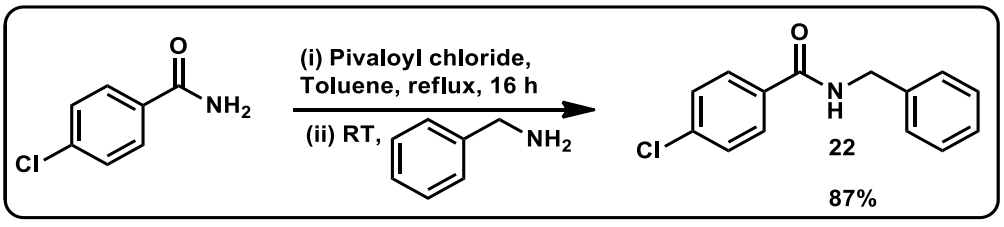
Physical Characteristics:

Colour and appearance: White solid

M.pt: 82 °C – 85 °C (Lit. m.pt = 84 °C – 86 °C) [37]

H NMR: (400 MHz, $CDCl_3$) δ: 1.11 (3H, d, *J* = 4 Hz). 2.29-2.36 (1H, m), 3.35 (2H, *d*, *J* = 8 Hz), 5.86 (1H, s, br), 7.18 – 7.21(3H, m), 7.25 (2H, *t*, *J* = 8 Hz).**^{13}C NMR:** (100 MHz $CDCl_3$) δ: 19.6, 35.6, 43.5, 127.4, 127.7, 128.7, 138.4, 177.0. **GC-MS (EI$^+$) *m/z***: (M^+): 178.10.

Transamidation of 4-chloro benzamide with benzyl amine



The general procedure-C stated above was followed. 4-chlorobenzamide (100 mg, 0.64 mmol), pivaloyl chloride (77 mg, 0.64mmol), benzylamine (137 mg, 1.28 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 136 mg (87% yield).

Physical Characteristics:

Colour and appearance: Half white solid

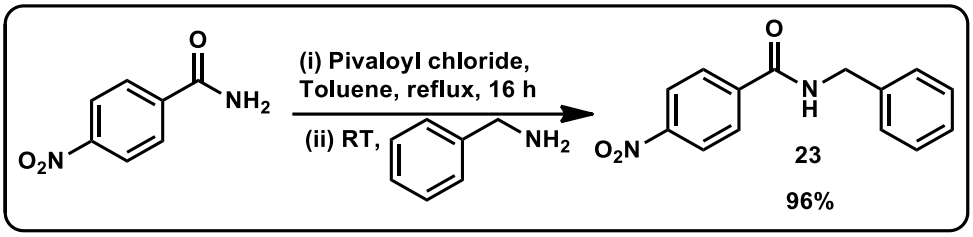
M.pt: 160 °C –162 °C (Lit. M.pt = 159 °C – 161 °C) [17]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 4.49 (2H, d, *J* = 4 Hz), 7.22 – 7.28 (1H, m), 7.33 (4H, t, *J* = 4 Hz), 7.55 (2H, d, *J* = 12 Hz), 7.92 (2H, d, *J* = 8 Hz), 9.14 (1H, t, *J* = 12 Hz). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 43.1, 127.2, 127.7, 128.7, 128.8, 129.6, 133.5, 136.5, 139.9, 165.6.

GC-MS (EI$^+$) *m/z*: $[M]^+$ 245.05

Transamidation of 4-nitro benzamide with benzyl amine



The general procedure-C stated above was followed. 4-Nitrobenzamide (100 mg, 0.60 mmol), pivaloyl chloride (72 mg, 0.60mmol), benzylamine (141 mg, 1.32 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as yellow solid in 147 mg (96% yield).

Physical Characteristics:

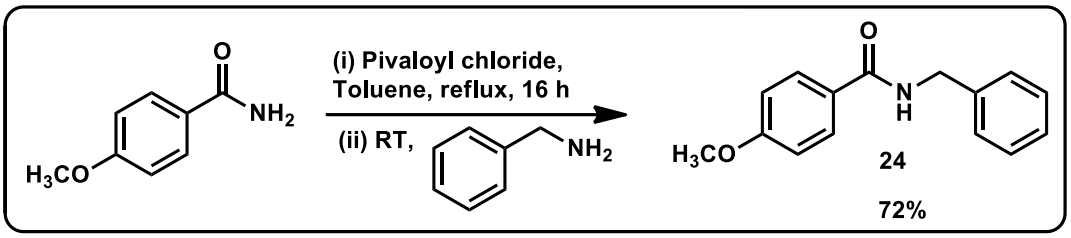
Colour and appearance: Yellow solid

M.pt: 140 °C –142 °C (Lit. M.pt = 138 °C -140 °C) [18]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 4.52 (2H, d, *J* = 8 Hz), 7.23-7.29 (1H, m), 7.34 (4H, d, *J* = 4 Hz), 8.13 (2H, d, *J* = 8 Hz), 8.33 (2H, d, *J* = 8 Hz), 9.39 (1H, t, *J* = 4 Hz). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 43.3, 124.0, 127.3, 127.7, 128.8, 129.2, 139.5, 140.4, 149.5, 165.1. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 256.10

Transamidation of 4-methoxybenzamide with benzyl amine



The general procedure-C stated above was followed. 4-Methoxybenzamide (100 mg, 0.66 mmol), pivaloyl chloride (79.5 mg, 0.66mmol), benzylamine (141 mg, 1.32 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as half-white solid in 114 mg (72% yield).

Physical Characteristics:

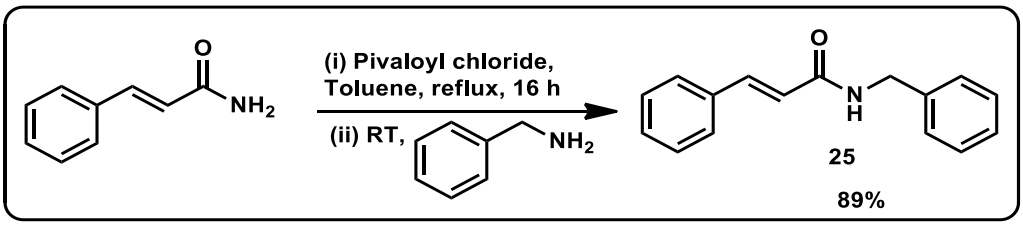
Colour and appearance: Half white solid

M.pt: 125 °C –127 °C (Lit. M.pt = 122 °C) [19]

Spectral data:

^{1}H NMR: (400 MHz, DMSO-d_6) δ: 3.81 (3H, s), 4.47 (2H, d, *J* = 8 Hz), 7.01 (2H, d, *J* = 8 Hz), 7.21-7.27 (1H, m), 7.32 (4H, t, *J* = 8 Hz), 7.88 (2H, d, *J* = 12 Hz), 8.91 (1H, t, *J* = 4 Hz). **^{13}C NMR:** (100 MHz, DMSO-d_6) δ: 42.9, 55.8, 113.9, 126.9, 127.1, 127.6, 128.7, 129.5, 140.3, 162.0, 166.1. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 241.10

Transamidation of cinnamic-amide with benzyl amine



The general procedure-C stated above was followed. Cinnamic amide (100 mg, 0.67 mmol), pivaloyl chloride (80 mg, 0.67mmol), benzylamine (143 mg, 1.34 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 141 mg (89% yield).

Physical Characteristics:

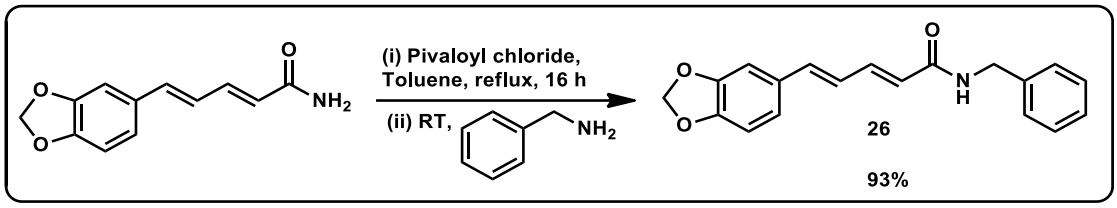
Colour and appearance: White solid

M.pt: 96 °C – 98 °C (Lit. m.pt = 98 °C – 99 °C)[9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.57 (2H, d, *J* = 8 Hz), 6.29 (1H, s), 6.48 (2H, d, *J* = 16 Hz), 7.28-7.37 (8H, m), 7.49-7.51 (2H, m), 7.69 (2H, d, *J* = 16 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 43.8, 120.5, 127.5, 127.8, 128.7, 128.8, 128.9, 129.7, 134.7, 138.2, 141.3, 165.9. **GC-MS (EI$^+$) *m/z***: (M^+): 237.00.

Transamidation of piperic-amide with benzyl amine



The general procedure-C stated above was followed. piperic amide (100 mg, 0.46 mmol), pivaloyl chloride (55 mg, 0.46mmol), benzylamine (98 mg, 0.92 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 131 mg (93% yield).

Physical Characteristics:

Colour and appearance: White solid

M.pt: 155 °C – 158 °C (Lit. m.pt = 162 °C – 163 °C)[9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.47 (1H, d, *J* = 4 Hz), 5.90 (2H, s), 6.57-6.63 (1H, m), 6.99-6.73 (2H, m), 6.82 (2H, d, *J* = 8 Hz), 7.19-7.29 (6H, m), 7.35 (1H, dd, *J* = 12 Hz, *J* = 8 Hz).
^{13}C NMR (100 MHz, $CDCl_3$) δ: 43.8, 101.3, 105.7, 108.5, 122.4, 122.7, 124.5, 127.6, 127.9, 128.7, 130.7, 138.1, 139.4, 141.8, 148.2, 148.3, 166.1. **GC-MS (EI$^+$) *m/z***: (M^+): 307.15

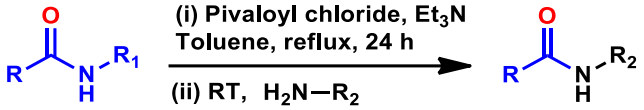
General procedure D: Transamidation of Secondary amides with alkylamine

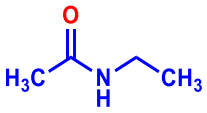
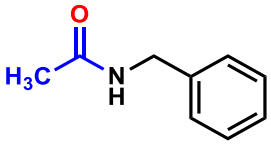
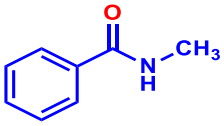
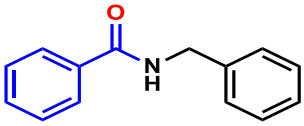
To a stirred solution of various amides (1 eq.), triethylamine (2 eq.), in toluene (5 mL) at room temperature, pivaloyl chloride (1 eq.), was added dropwise. After addition the reaction mixture was heated up to 80˚C for 24 h. The reaction mixture was cooled down to room temperature.

To the above synthesized imide in toluene, alkyl amine (2 eq.), was added and stirred at room temperature. Progress of the reaction was monitored by TLC. Starting material consumed in 30 min. After completion, the reaction mixture was washed with 5% HCl solution, 5% $NaHCO_3$

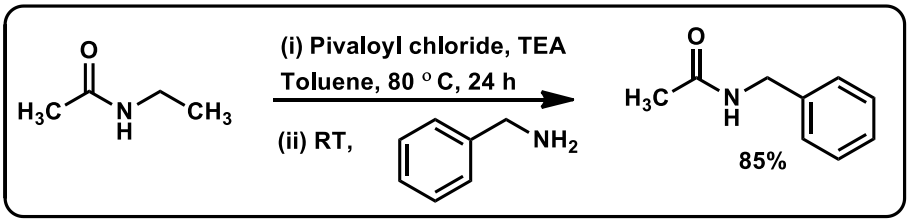
solution, water. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. Pure product was obtained after column chromatography.

Table 4: Transamidation of secondary amides with alkyl amines



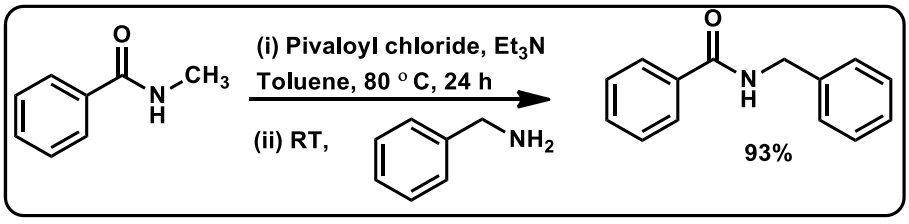
S.NO	Amide	Product	Yield%	Time (min.)
1.			**85**	**30**
2.			**93**	**30**

Transamidation of N-ethyl acetamide with benzylamine



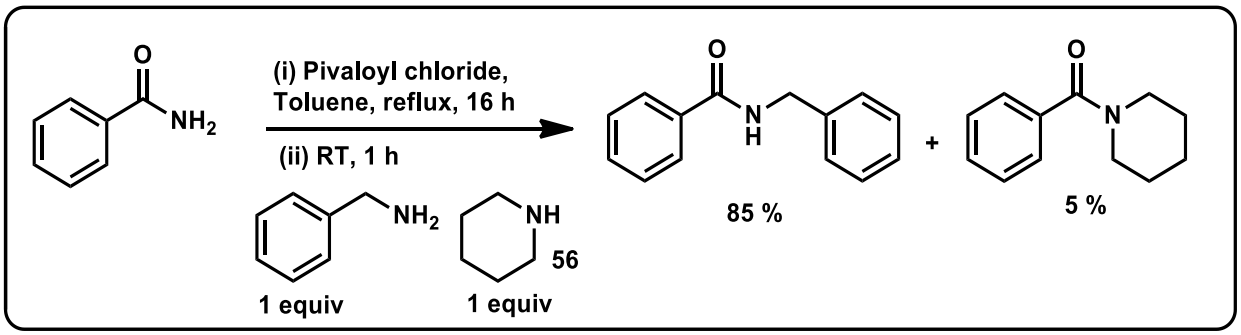
The general procedure-D stated above was followed. *N*- ethyl acetamide (100 mg, 1.14 mmol), pivaloyl chloride (138 mg, 1.14 mmol), triethylamine (230 mg, 2.29 mmol), benzylamine (245 mg, 2.29 mmol). Pure product was obtained after column chromatography white solid in 144 mg (85% yield).

Transamidation of N-methyl benzamide with benzylamine



The general procedure-D stated above was followed. *N*- methyl benzamide (100 mg, 0.74 mmol), pivaloyl chloride (89 mg, 0.74 mmol), triethylamine (149 mg, 1.48 mmol), benzylamine (79.1 mg, 1.48 mmol). Pure product was obtained after column chromatography half white solid in 145 mg (93% yield).

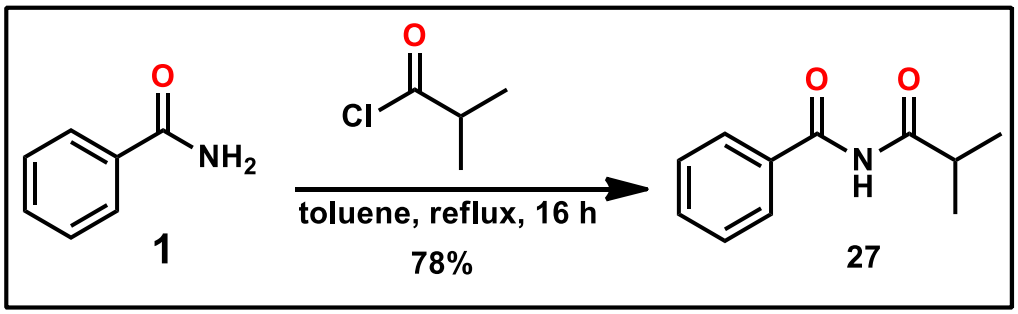
Competitive study- Primary vs secondary amine



To a stirred solution of benzamide (200 mg, 1.65 mmol, 1 eq.), in toluene at room temperature, pivaloyl chloride (198 mg, 1.65 mmol, 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, an equimolar mixture of benzylamine (176 mg, 1.65 mmol, 1 equiv.) and piperidine (140 mg, 1.65 mmol, 1 equiv) was added and stirred at room temperature. Progress of the reaction was monitored by TLC. 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. The crude mass was column purified to get pure benzyl amine transamidation product in 295 mg (85%) and piperidine transamidation product in 16 mg (5%).

Synthesis of *N*-isobutyrylbenzamide



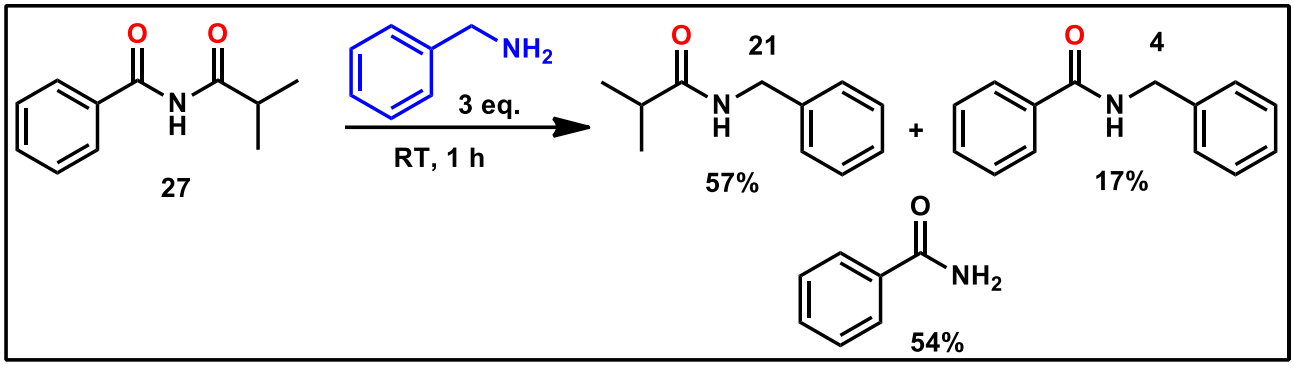
To a stirred solution of benzamide (500 mg, 4.13 mmol), in 15 mL of toluene at room temperature, pivaloyl chloride (497 mg, 4.13mmol) was added dropwise. After addition, the reaction mixture was refluxed for 16 h. Progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)]. After completion, the 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 527 mg (67 % yield).

Physical Characteristics: Colour and appearance: White solid

M.pt: 152 °C – 153 °C (Lit. m.pt = 151 °C – 152 °C)[1]

H NMR: (400 MHz, DMSO-d_6): δ: 1.11 (6H, d, *J* = 8 Hz), 3.05- 3.15 (1H, m), 7.51 (2H, *t*, *J* = 8 Hz), 7.62 (1H, *t*, *J* = 8 Hz), 7.88 (2H, d, *J* = 8 Hz), 10.86 (1H, s). **^{13}C NMR:** (100 MHz, DMSO-d_6): δ: 19.3, 35.0, 128.7, 128.8, 133.0,134.1, 166.9, 178.3. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 191.10.

Transamidation of *N*-isobutyrylbenzamide with benzylamine



In oven dried round bottom flask *N*-isobutyrylbenzamide (200 mg, 1.04mmol) was taken in which benzylamine (333.8 mg, 3.12 mmol) was added and stirred at room temperature for 1 h. Progress of the reaction was monitored by TLC [hexane-EtOAc (7:3)]. After completion, the reaction mixture was washed with 5% HCl solution (2 x 25 mL), 5% $NaHCO_3$ solution (2 x 25 mL) and water (1 x 25 mL). 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 **60** (105mg, 57%) and white solid **61** (37 mg, 17%).

26-Physical Characteristics: Colour and appearance: White solid

M.pt: 82 °C – 85 °C (Lit. m.pt = 84 °C – 86 °C) [37]

H NMR: (400 MHz, $CDCl_3$) δ: 1.11 (3H, d, *J* = 4 Hz). 2.29-2.36 (1H, m), 3.35 (2H, *d*, *J* = 8 Hz), 5.86 (1H, s, br), 7.18 – 7.21(3H, m), 7.25 (2H, *t*, *J* = 8 Hz).**^{13}C NMR:** (100 MHz $CDCl_3$) δ: 19.6, 35.6, 43.5, 127.4, 127.7, 128.7, 138.4, 177.0. **GC-MS (EI$^+$) *m/z***: (M^+): 178.10.

4-Physical Characteristics:

Colour and appearance: Half-white solid

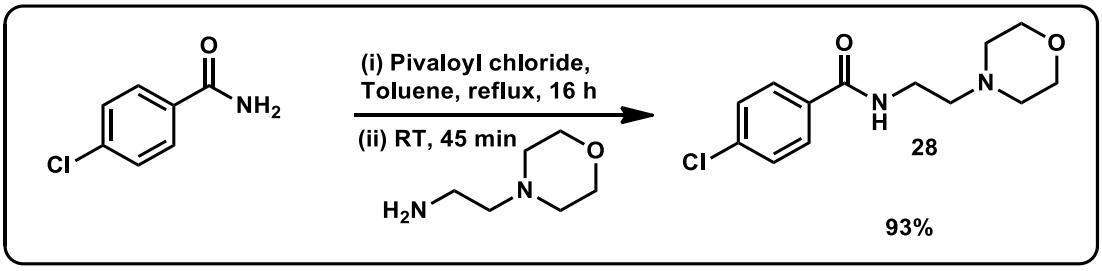
M.pt: 103 °C – 105 °C (Lit. m.pt = 104 °C – 105 °C)[8]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.65 (2H, d, *J* = 8 Hz), 7.29-7.36 (4H, m), 7.43 (2H, t, *J* = 8 Hz), 7.48-7.52 (1H, m), 7.79 (2H, d, *J* = 8 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 44.1, 126.7, 126.9, 127.6, 127.9, 128.6, 128.8, 131.5, 134.3, 138.1, 167.3. **GC-MS (EI$^+$) *m/z***: (M^+): 211.00.

Synthesis of moclobemide

Transamidation of 4-chloro benzamide with 4-(2-aminoethyl) morpholine



The general procedure-A stated above was followed. 4-Chlorobenzamide (100 mg, 0.64 mmol), pivaloyl chloride (77 mg, 0.64 mmol), 4-(2-aminoethyl) morpholine (166 mg, 1.28 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as yellow solid in 159 mg (93% yield).

Physical Characteristics:

Colour and appearance: Yellow solid

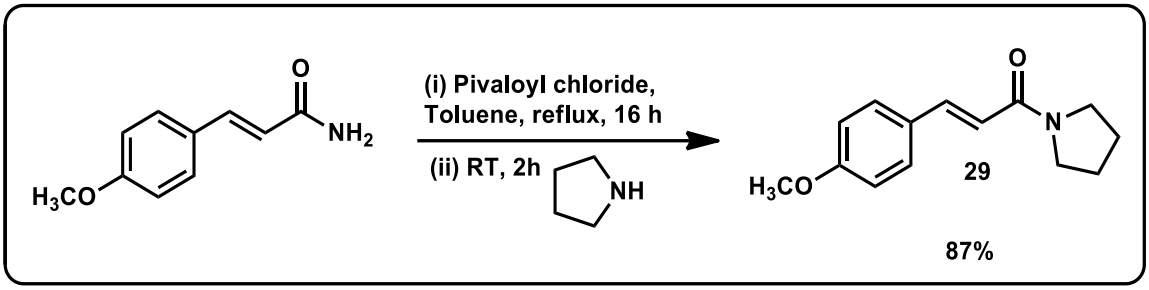
M.pt: 132 °C – 133 °C (Lit. m.pt = 136.1 °C – 136.7 °C)[35]

Spectral data:

^{1}H NMR: (400 MHz, $CDCl_3$) δ: 2.47 (4H, s), 2.56 (2H, t, *J* = 8 Hz), 3.47-3.51 (2H, m), 3.67 (4H, t, *J* = 8 Hz), 6.82 (1H, s), 7.34 (2H, d, *J* = 8 Hz), 7.66 (2H, d, *J* = 8 Hz). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 36.0, 53.3, 56.9, 66.8, 128.4, 128.8, 132.9, 137.6, 166.3. **GC-MS (EI$^+$) *m/z***: $[M]^+$ 268.15

Synthesis of Natural product

Synthesis of Piperlotine-A



The general procedure-A stated above was followed. 4-methoxy cinnamicamide (100 mg, 0.56), pivaloyl chloride (67 mg, 0.56 mmol), pyrrolidine (80 mg, 1.12 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as Light brown Solid in 112 mg (87% yield).

Physical Characteristics:

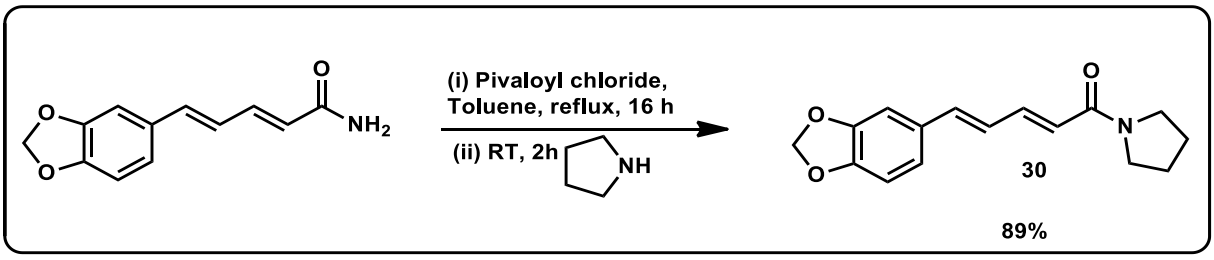
Colour and appearance: Light brown Solid

M.pt: 114 °C – 115 °C (Lit. m.pt = 115 °C – 116 °C)[36]

Spectral data:

^{1}H NMR: (400 MHz, $CDCl_3$) δ: 1.93 (4H, s), 3.58 (4H, d, *J* = 4 Hz), 3.81 (3H, s), 6.59 (1H, d, *J* = 16 Hz), 6.88 (2H, d, *J* = 8 Hz), 7.47 (2H, d, *J* = 8 Hz), 7.65 (1H, d, *J* = 16 Hz). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ: 55.3, 114.2, 116.3, 128.0, 129.3, 141.4, 160.8, 165.0. **GC-MS (EI^{+}) *m/z***: $[M]^{+}$ 231.10

Synthesis of Piperylin



General procedure-A stated above was followed. Piperic amide (100 mg, 0.46 mmol), pivaloyl chloride (55 mg, 0.46mmol), pyrrolidine (65 mg, 0.92 mmol). Pure product was obtained after column chromatography (Hexane: EtOAc (80:20)) as white solid in 110 mg (89% yield).

Physical Characteristics:

Colour and appearance: White solid

M.pt: 140 °C – 142 °C (Lit. m.pt = 145 °C – 147 °C) [9]

Spectral data:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.94 (4H, br, s), 3.56-3.59 (4H, m), 5.97 (2H, s), 6.24 (2H, d, *J* = 16 Hz), 6.70-6.84 (3H, m), 6.90 (2H, d, *J* = 8 Hz), 7.52 (2H, dd, *J* = 16 Hz, *J* = 4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.5, 101.3, 105.7, 108.5, 120.5, 122.8, 125.0, 130.9, 139.4, 142.8, 148.2, 148.3, 165.1. **GC-MS (EI$^+$) *m/z***: (M^+): 271.20.

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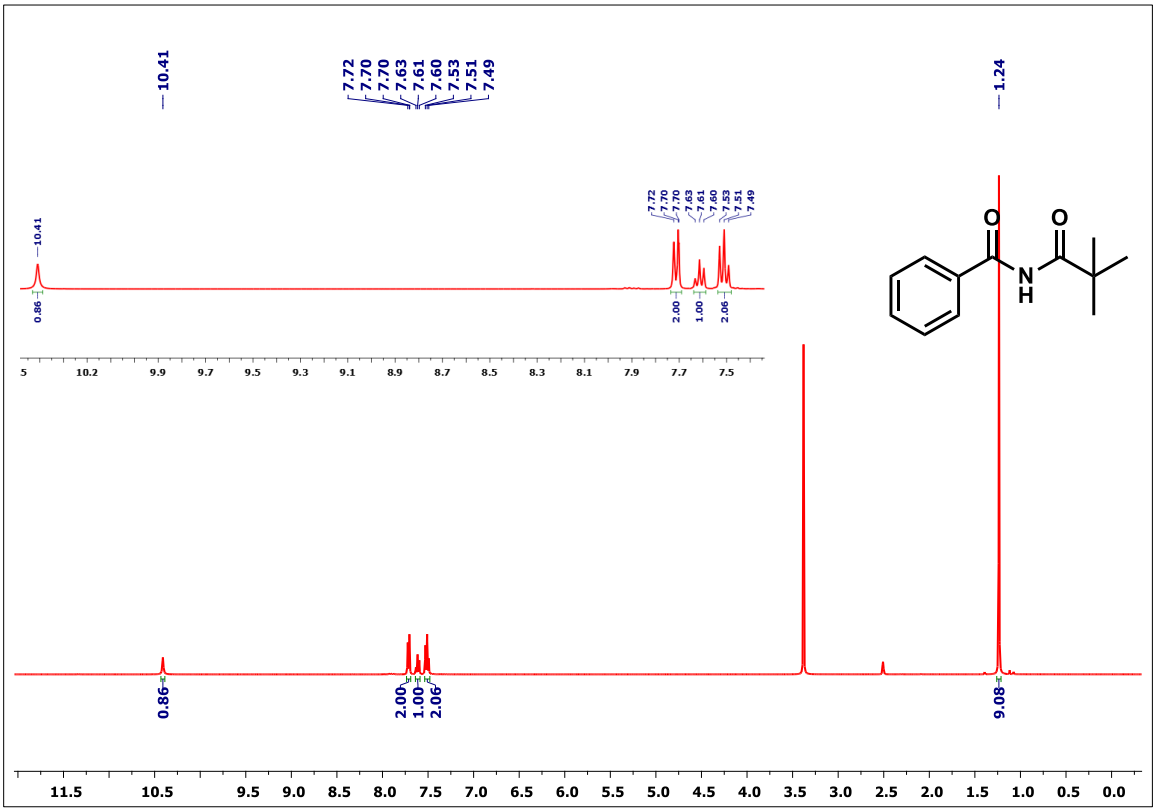

Figure S2: 400 MHz ^{1}H NMR spectrum of *N*-pivaloyl benzamide **1** in DMSO-d_6

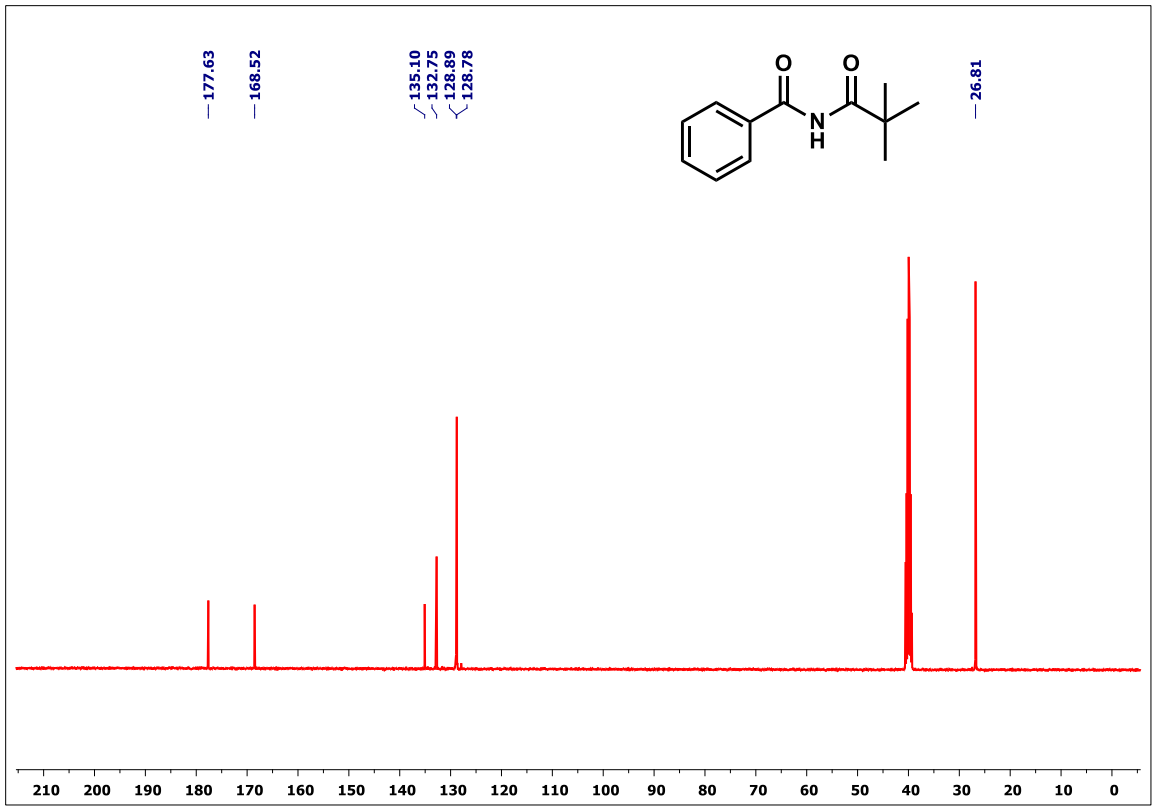

Figure S3: 100 MHz ^{13}C NMR spectrum of *N*-pivaloyl benzamide **1** in DMSO-d$_6$

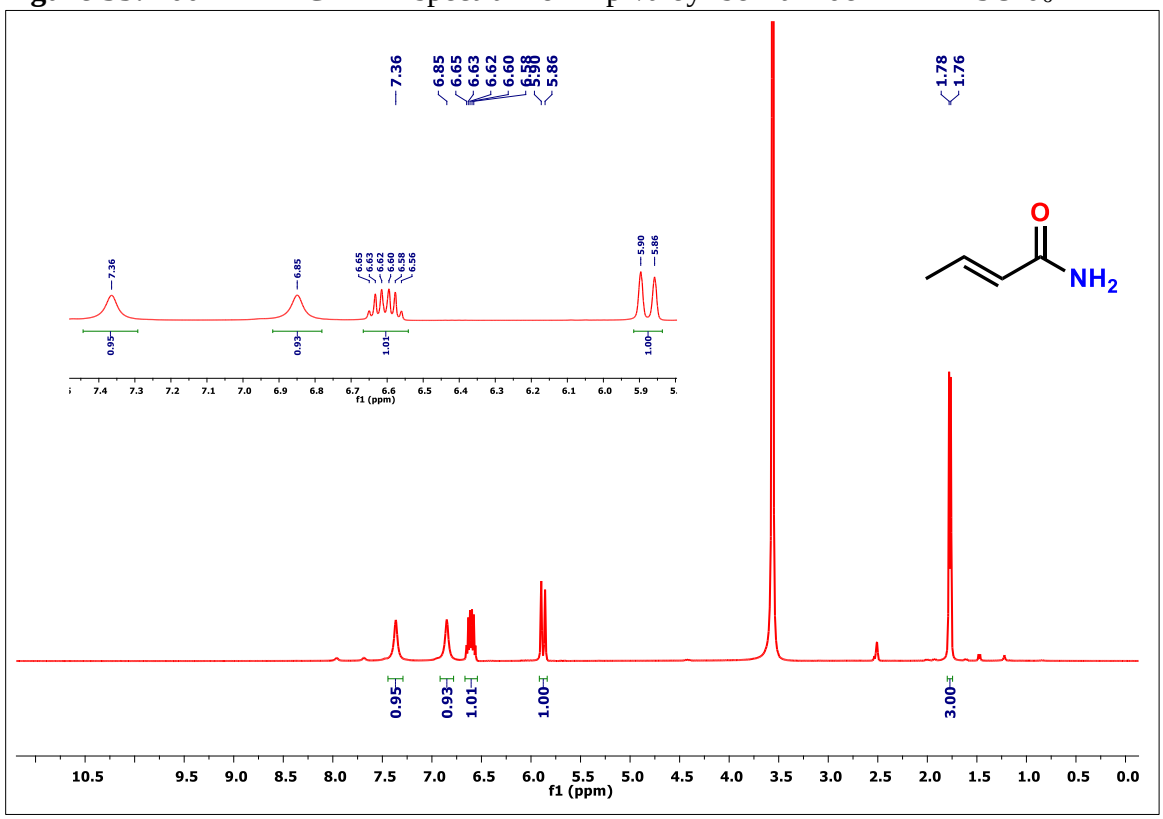

Figure S4: 400 MHz ^{1}H NMR spectrum of crotonicamide in DMSO-d$_6$

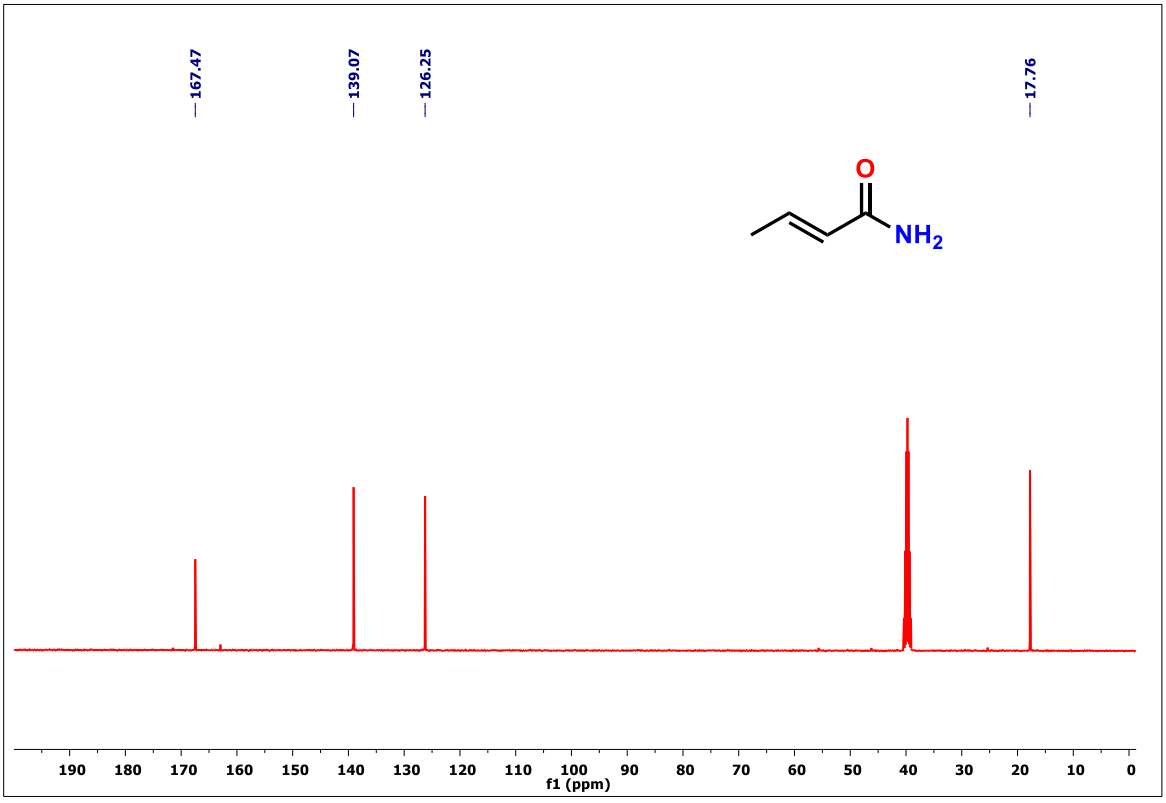

Figure S5: 400 MHz ^{1}H NMR spectrum of crotonicamide in DMSO-d_6

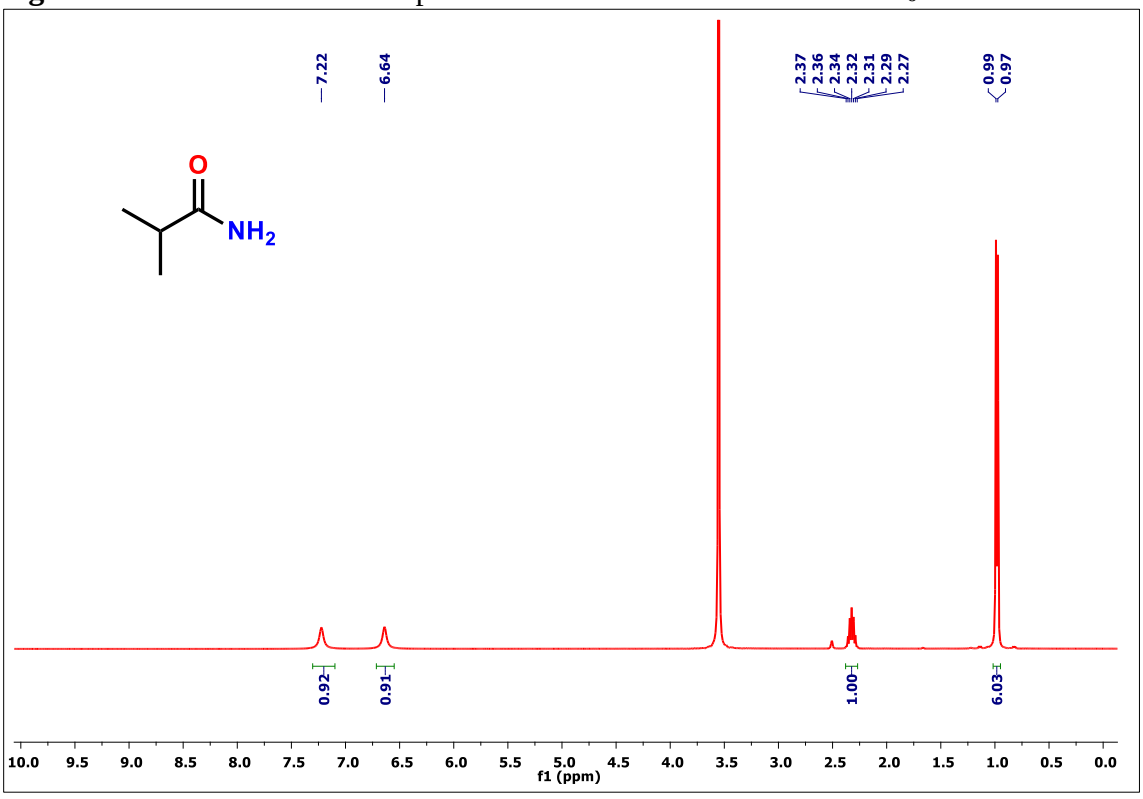

Figure S6: 400 MHz ^{1}H NMR spectrum of isobutyricamide in DMSO-d_6

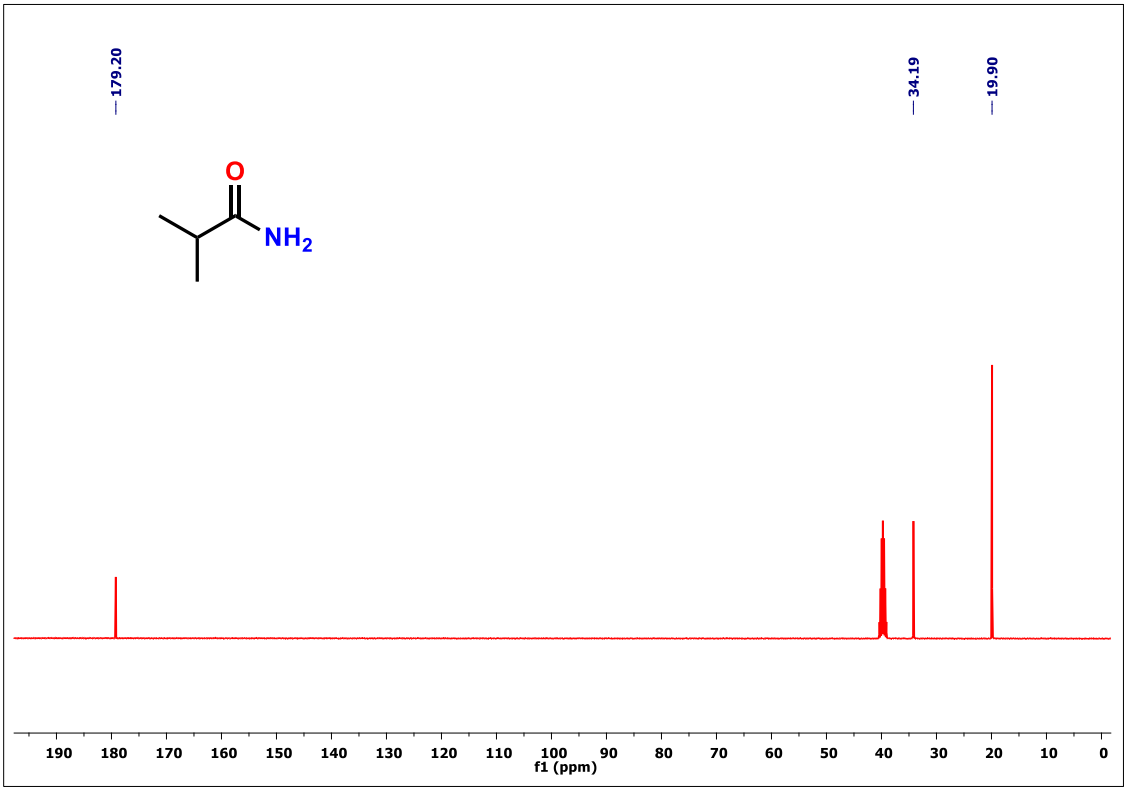

Figure S7: 400 MHz ^{1}H NMR spectrum of isobutyric amide in DMSO-d$_6$

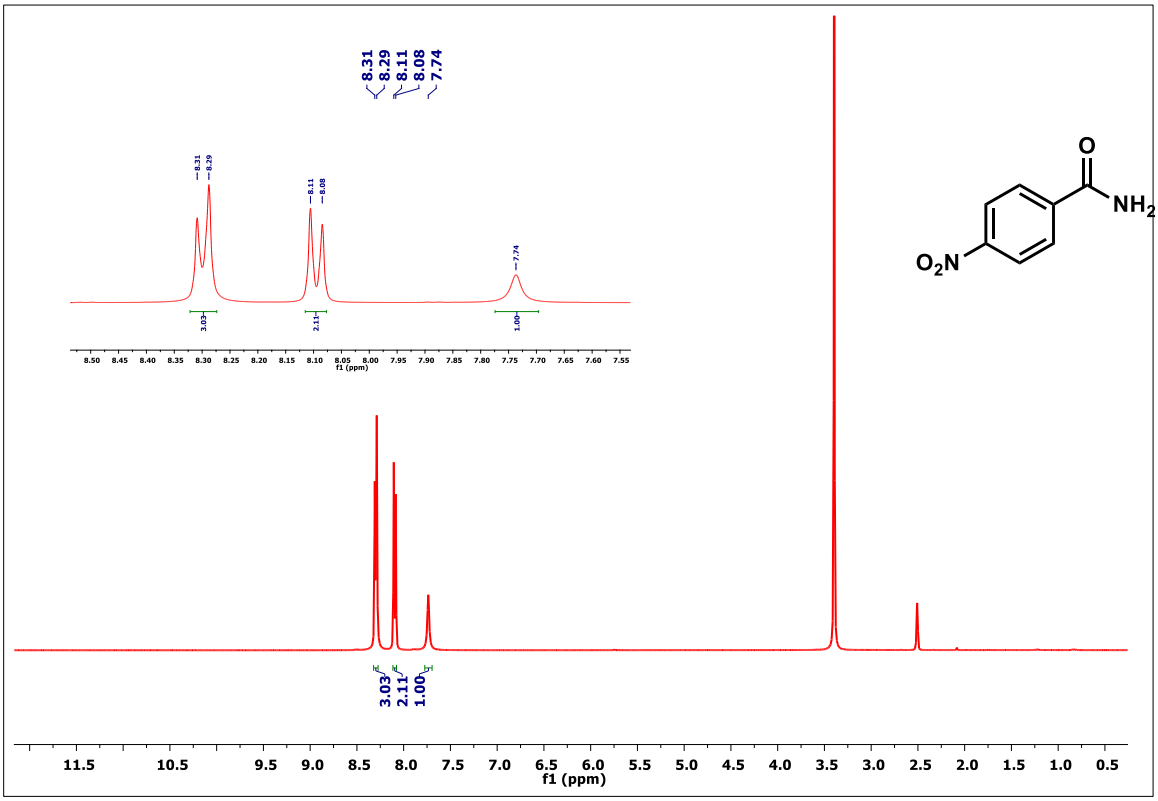

Figure S8: 400 MHz ^{1}H NMR spectrum of 4-nitro benzamide in DMSO-d_6

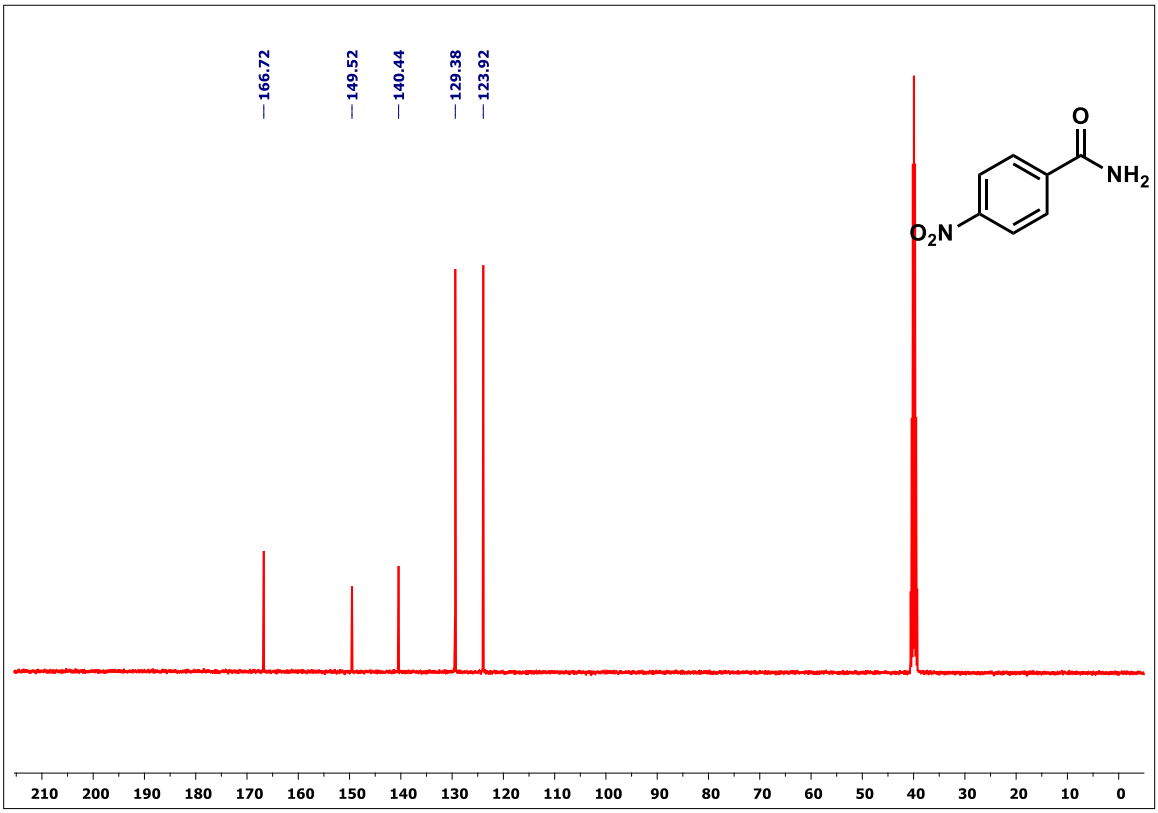

Figure S9: 100 MHz ^{13}C NMR spectrum of 4- nitro benzamide in DMSO-d_6

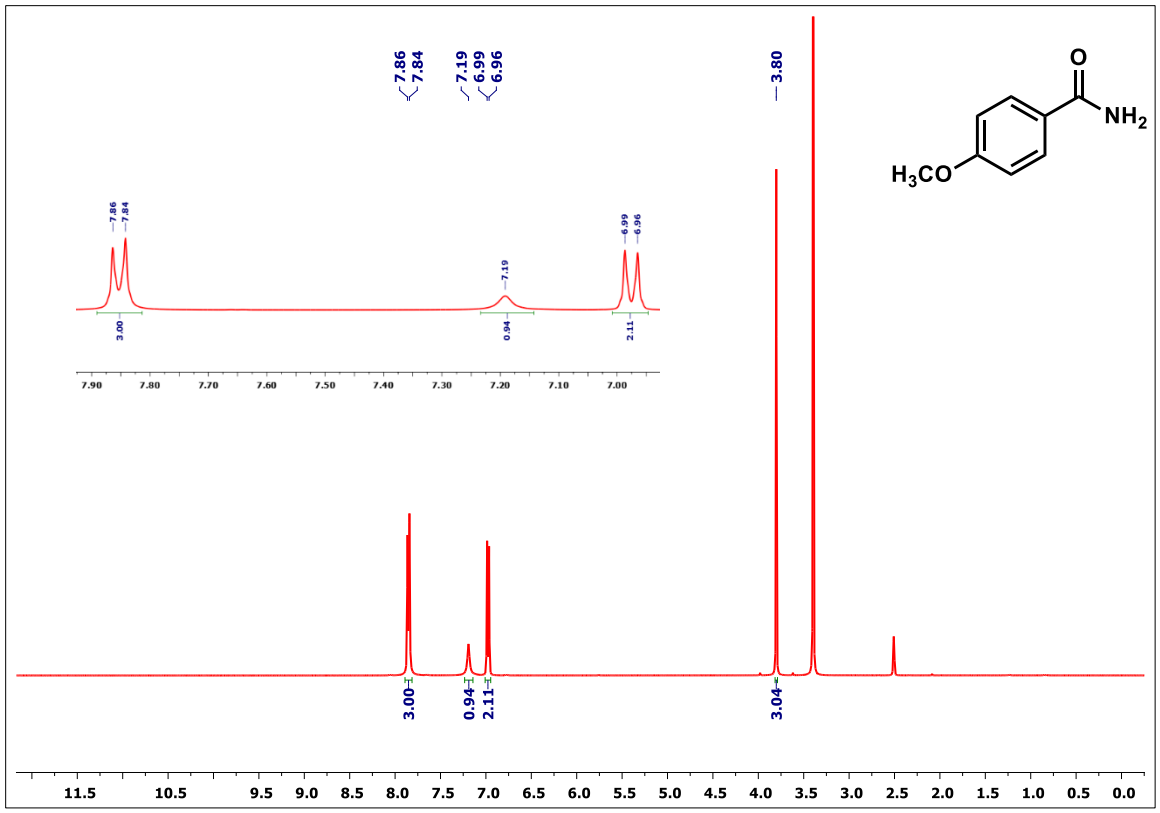

Figure S10: 400 MHz ^{1}H NMR spectrum of 4-methoxy benzamide in DMSO-d_6

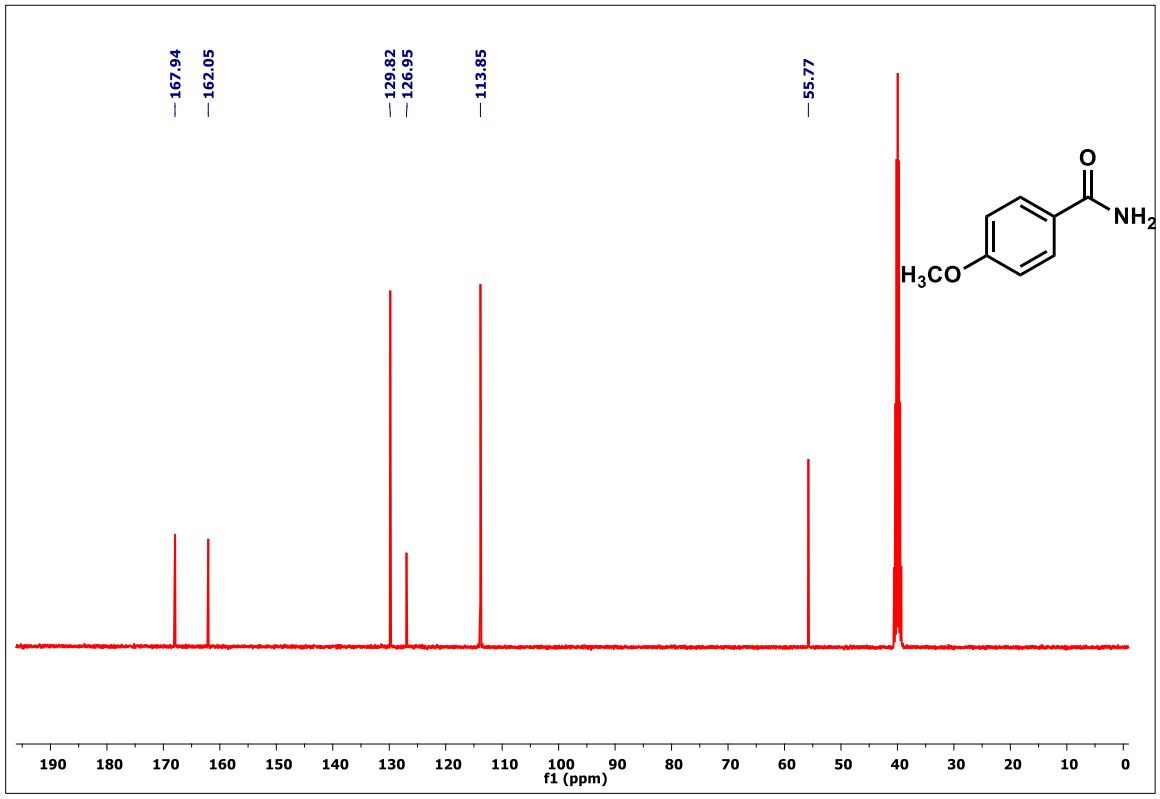

Figure S11: 100 MHz ^{13}C NMR spectrum of 4-methoxy benzamide in DMSO-d_6

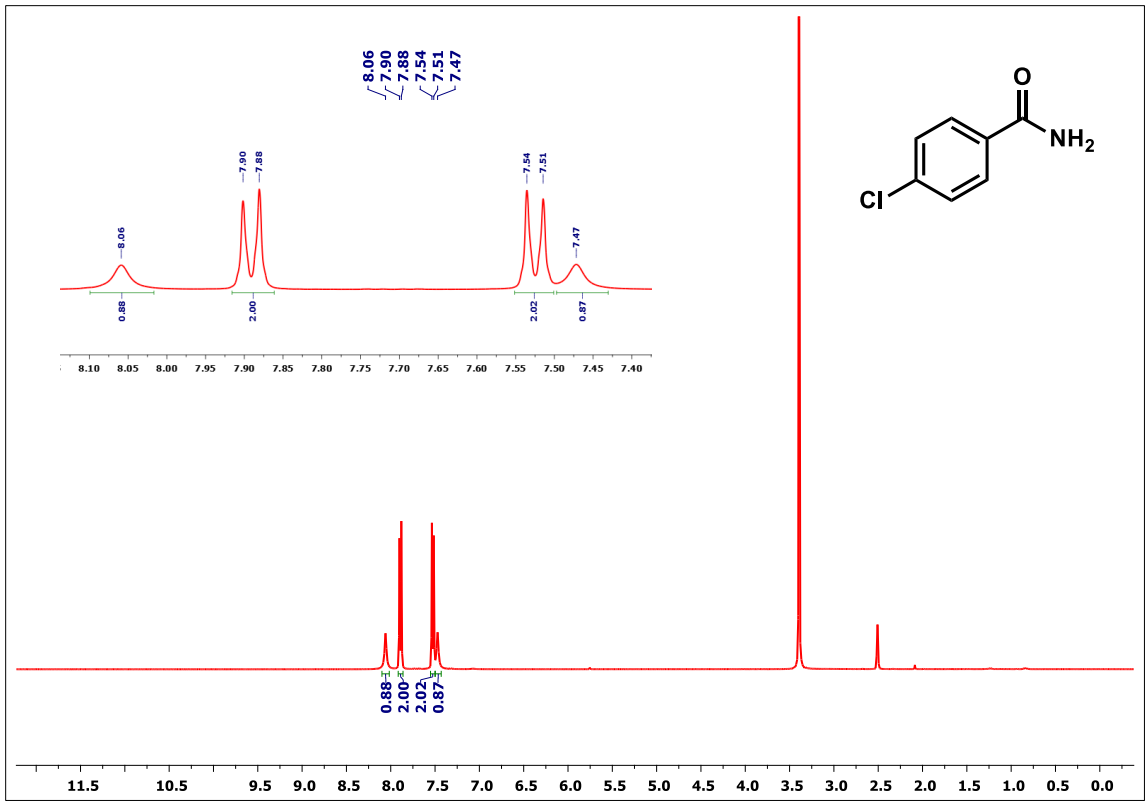

Figure S12: 400 MHz ^{1}H NMR spectrum of 4-chloro benzamide in DMSO-d_6

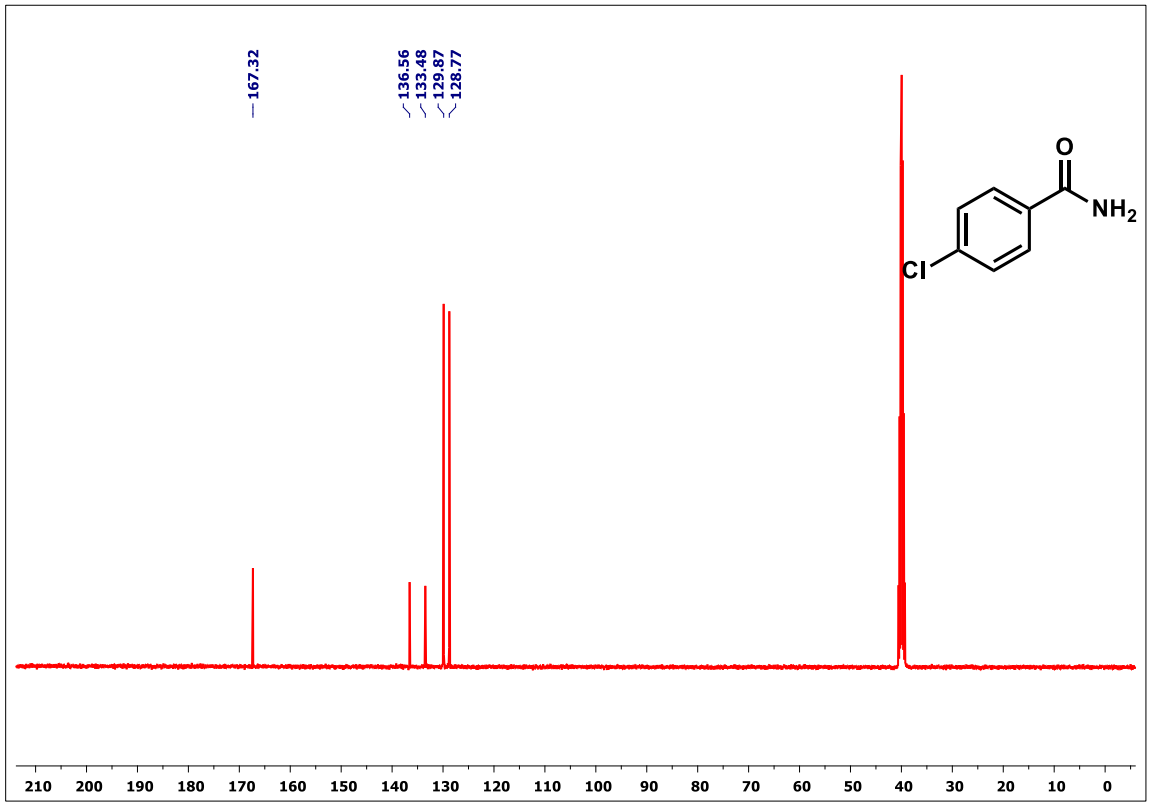

Figure S13: 100 MHz ^{13}C NMR spectrum of 4-chloro benzamide in DMSO-d_6

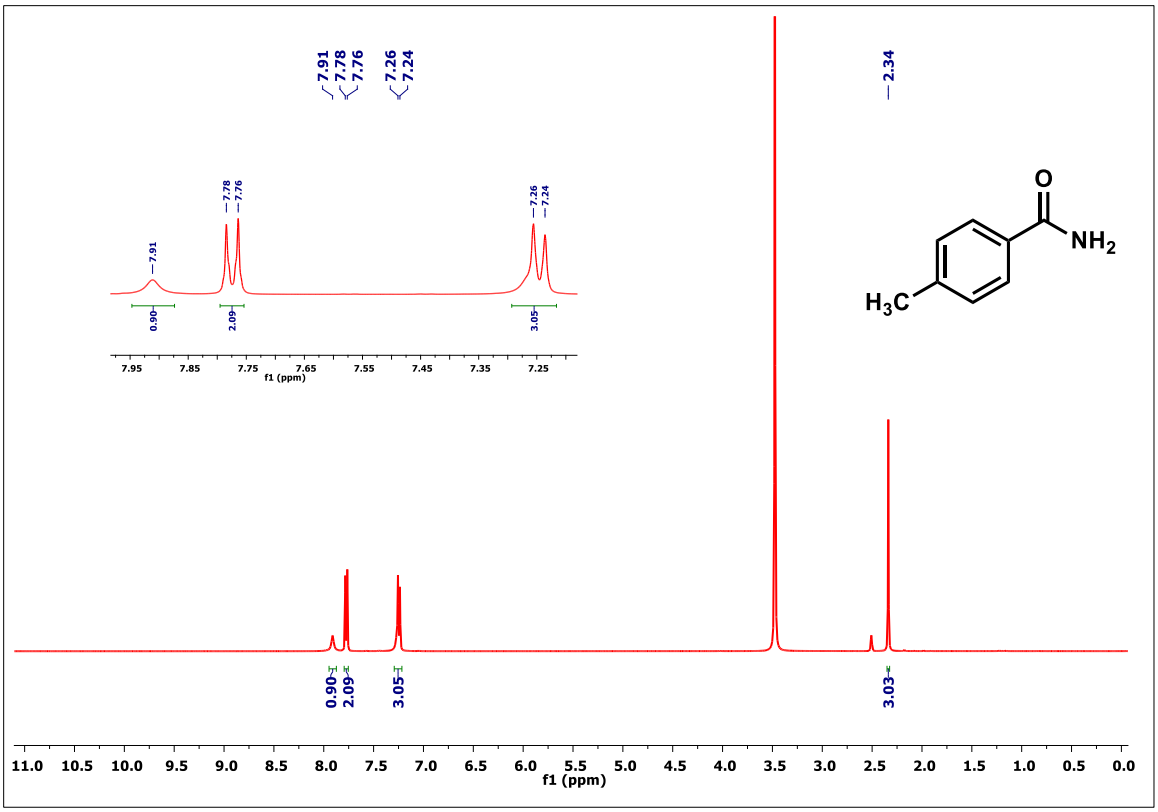

Figure S14: 400 MHz ^{1}H NMR spectrum of 4-methyl benzamide in DMSO-d_6

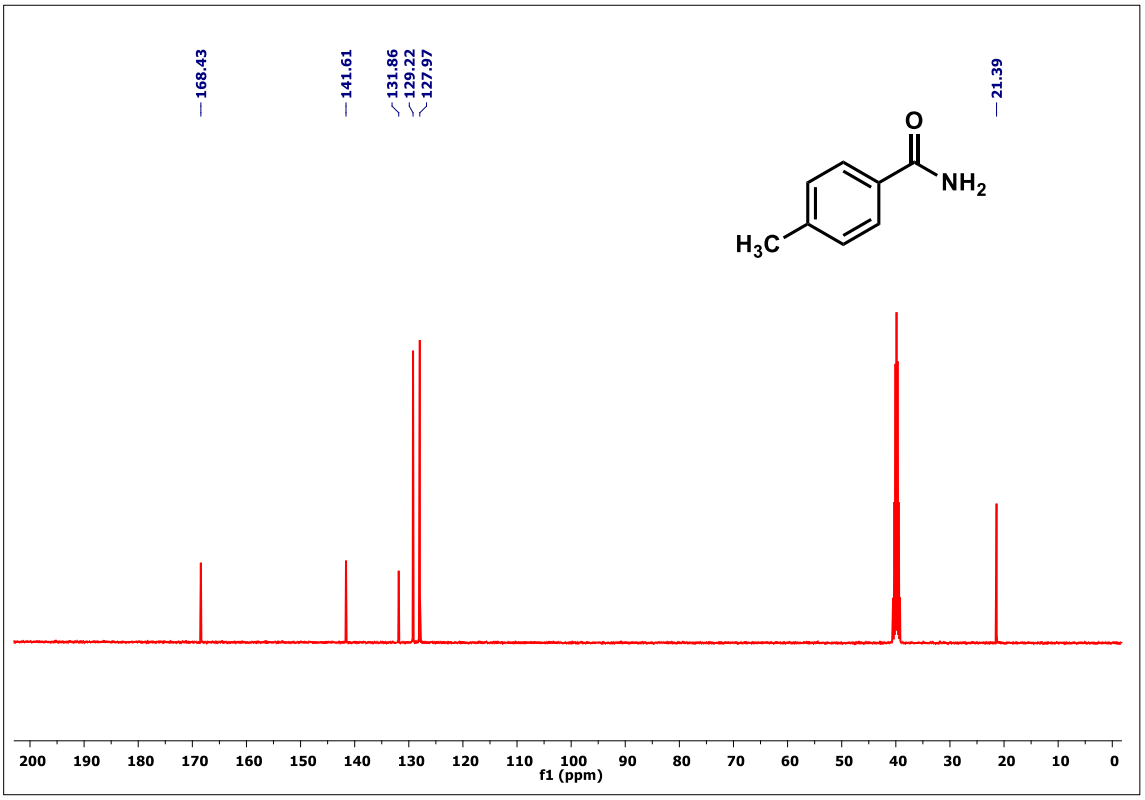

Figure S15: 100 MHz ^{13}C NMR spectrum of 4-methyl benzamide in DMSO-d_6

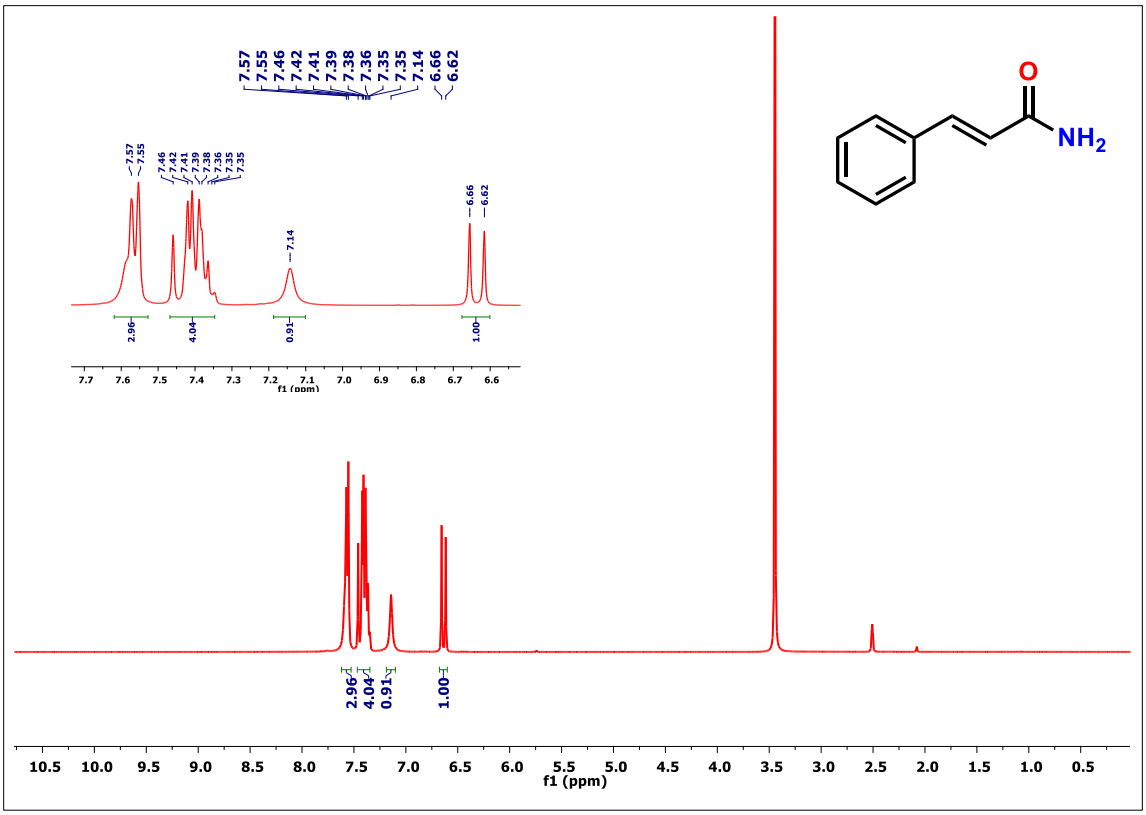

Figure S16: 400 MHz ^{1}H NMR spectrum of cinnamamide in DMSO-d$_6$

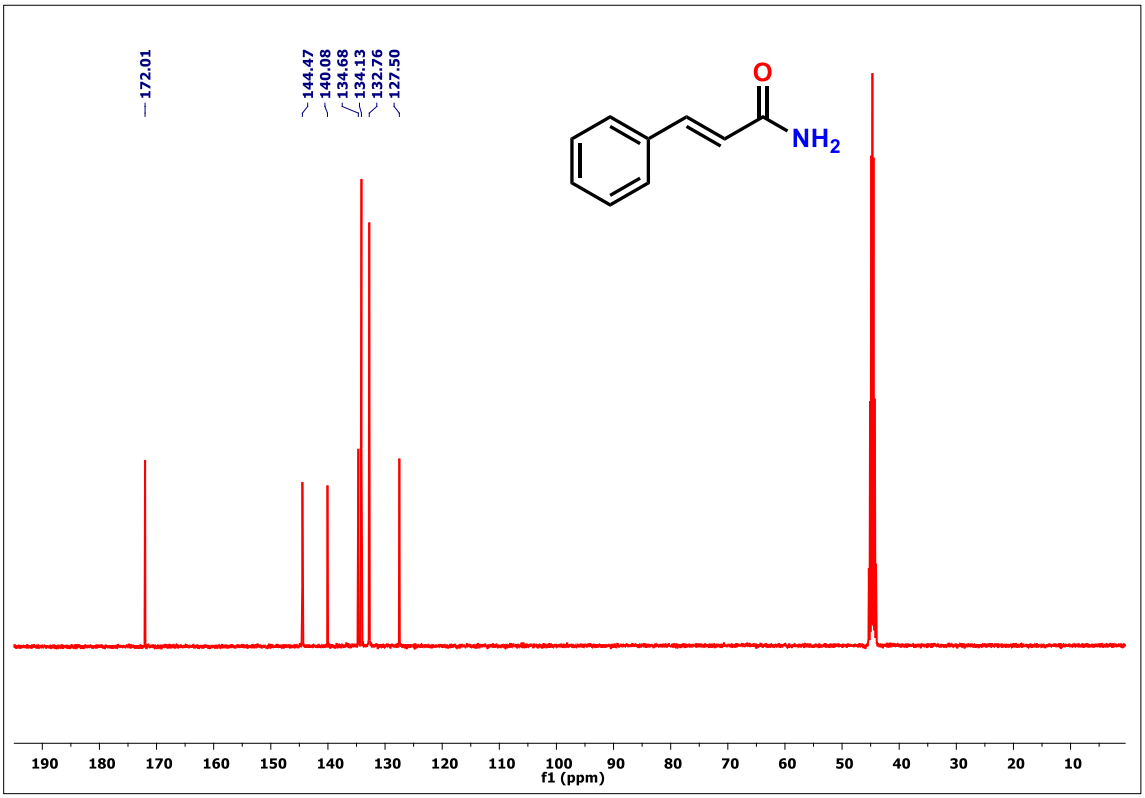

Figure S17: 100 MHz ^{13}C NMR spectrum of cinnamamide in DMSO-d$_6$

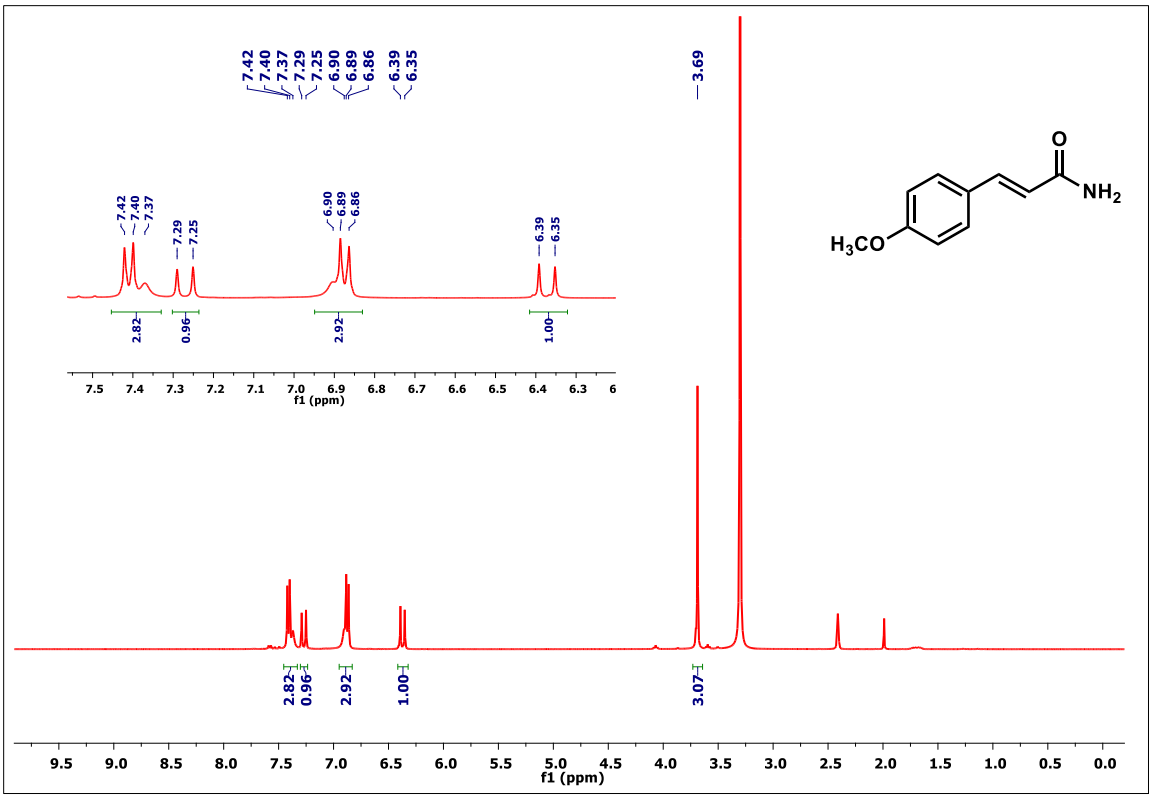

Figure S18: 400 MHz ^{1}H NMR spectrum of 4-methoxy cinnamamide in DMSO-d_6

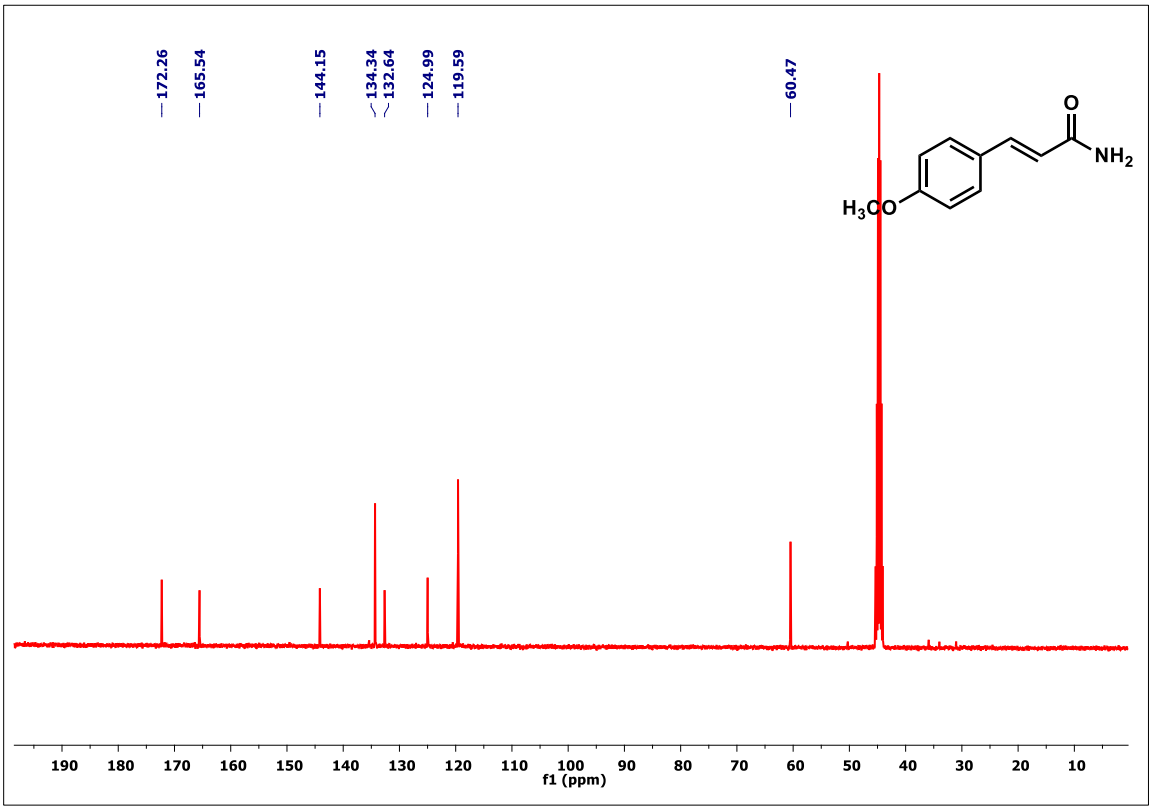

Figure S19: 100 MHz ^{13}C NMR spectrum of 4-methoxy cinnamamide in DMSO-d_6

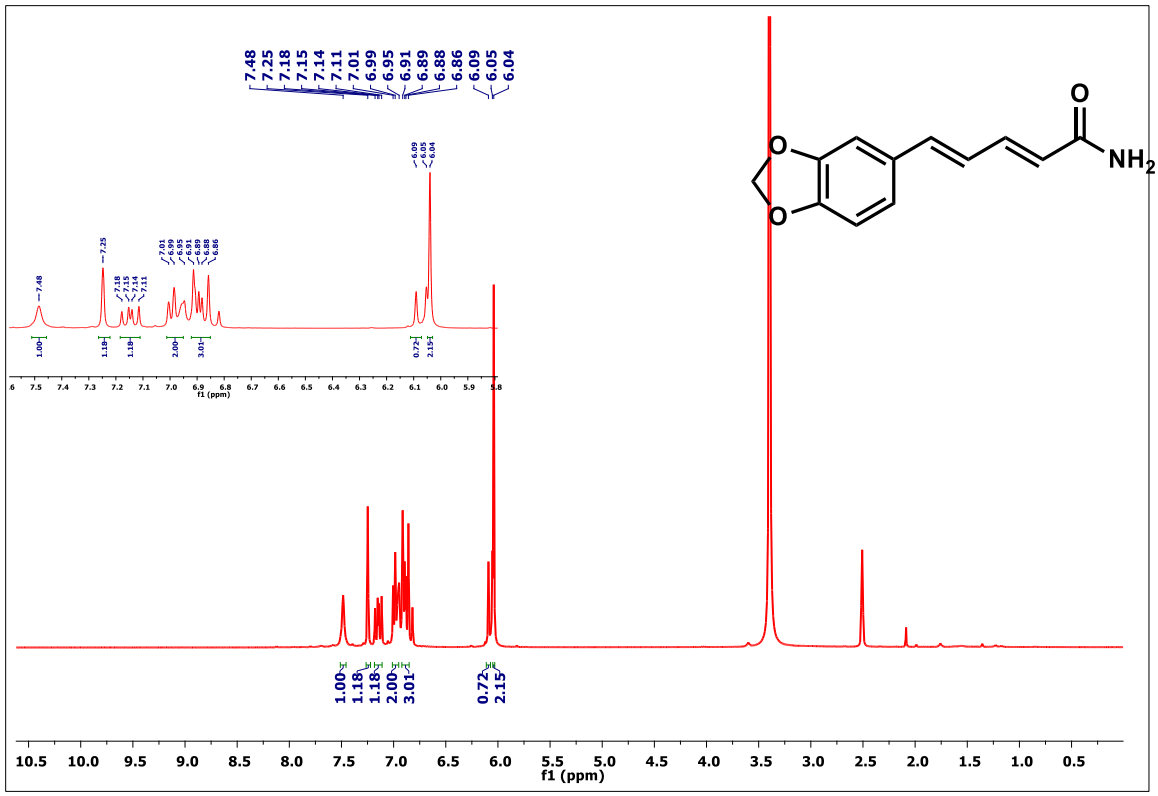

Figure S20: 400 MHz ^{1}H NMR spectrum of pipericamide in DMSO-d_6

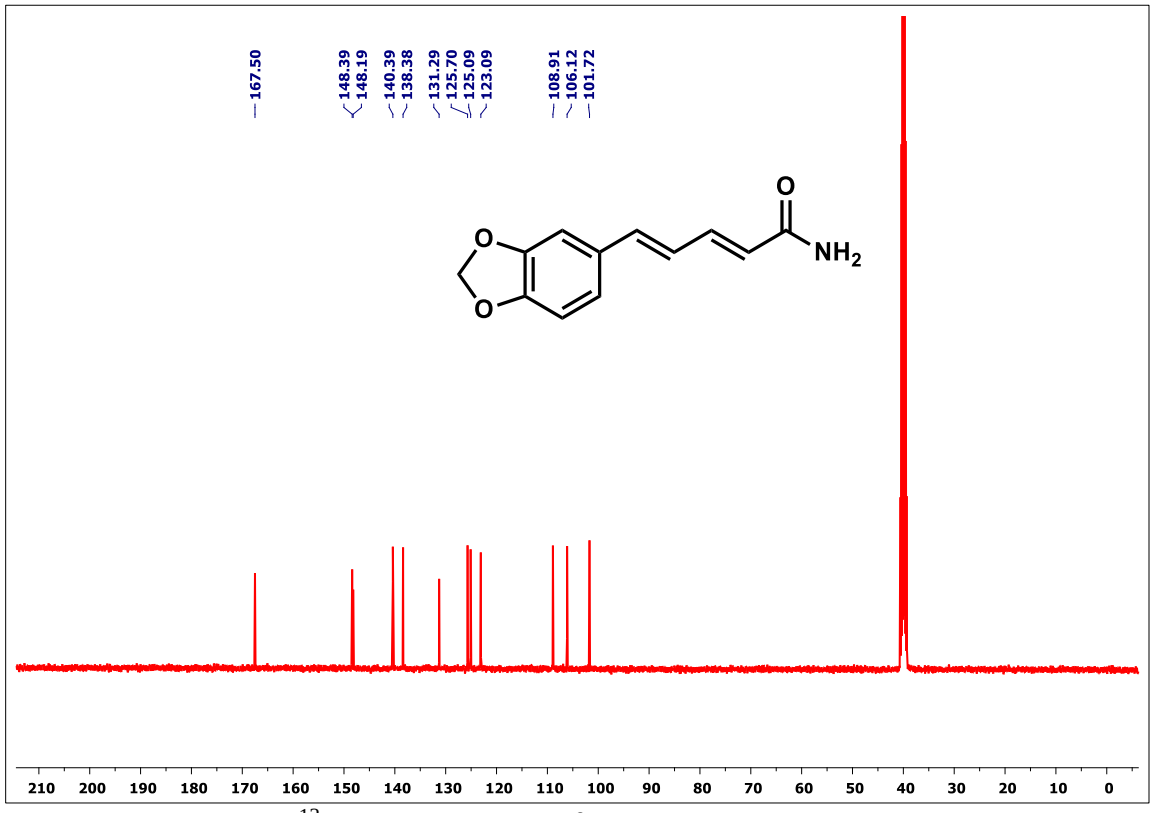

Figure S21: 100 MHz ^{13}C NMR spectrum of pipericamide in DMSO-d_6

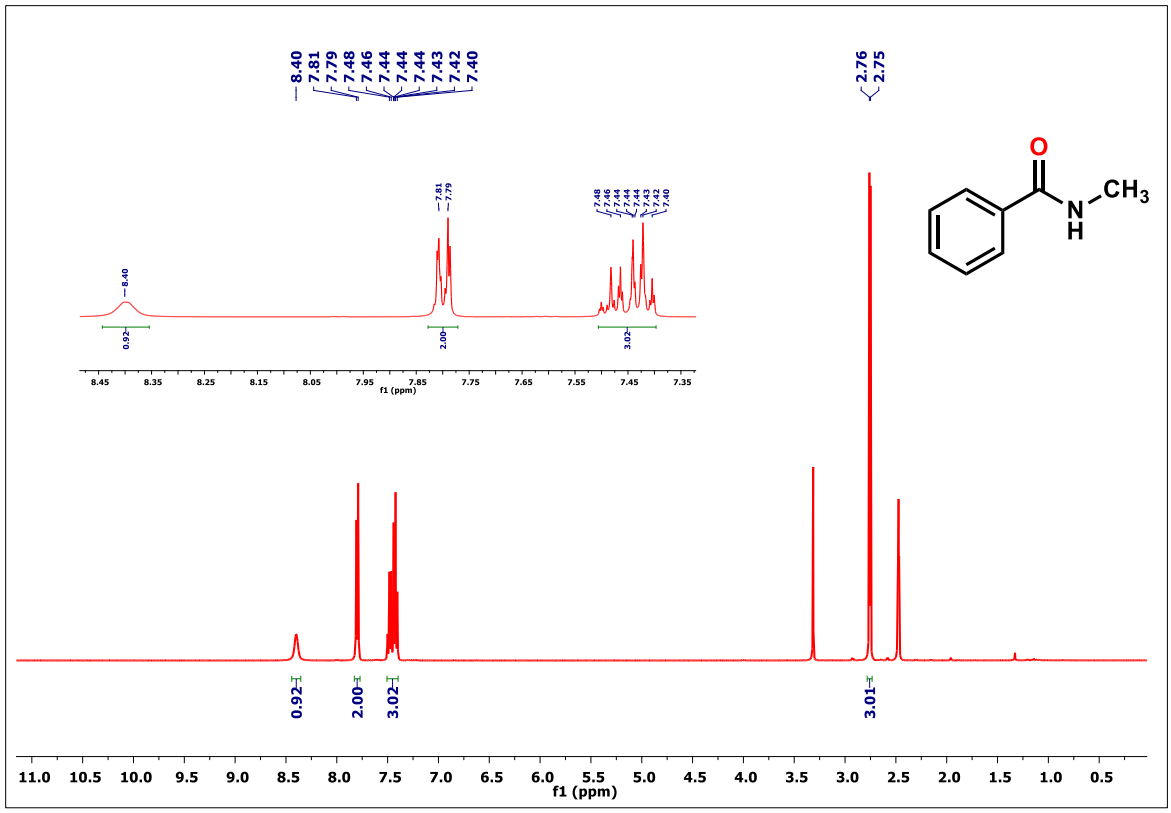

Figure S22: 400 MHz ^{1}H NMR spectrum of *N*-methyl benzamide in DMSO-d$_6$

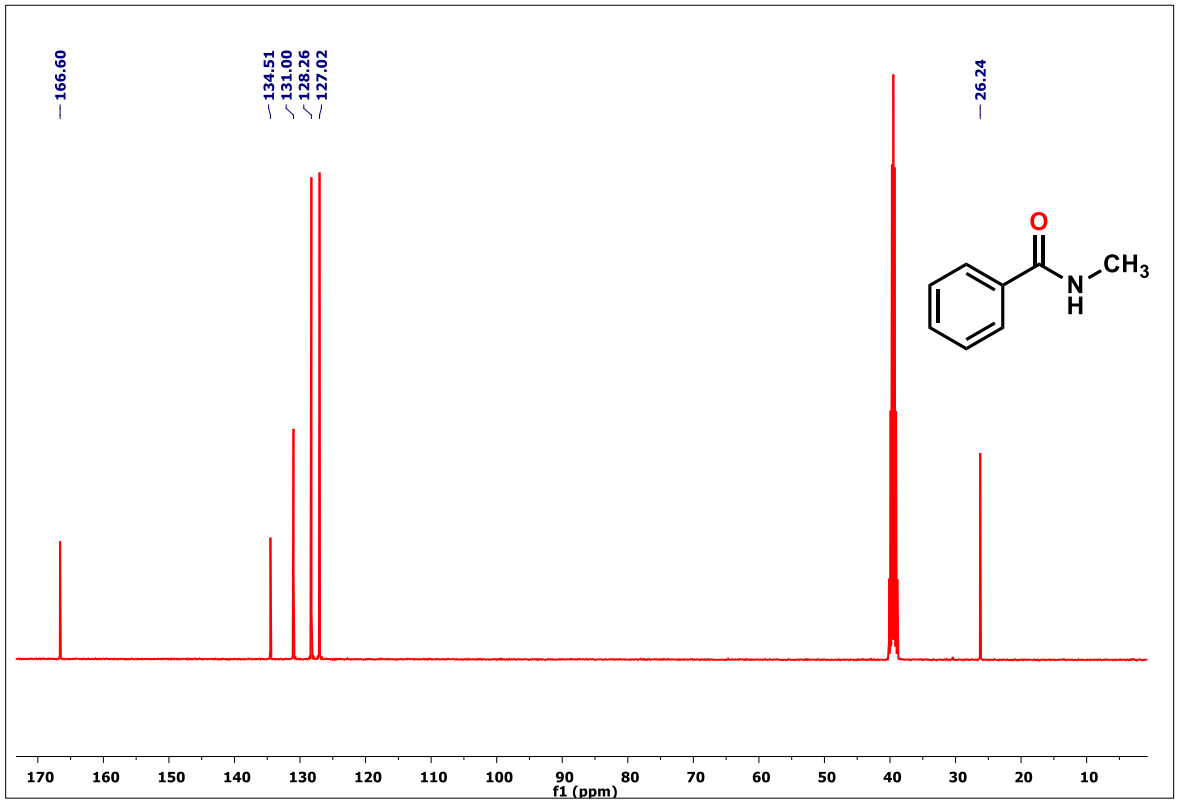

Figure S23: 100 MHz ^{13}C NMR spectrum of *N*-methyl benzamide in DMSO-d$_6$

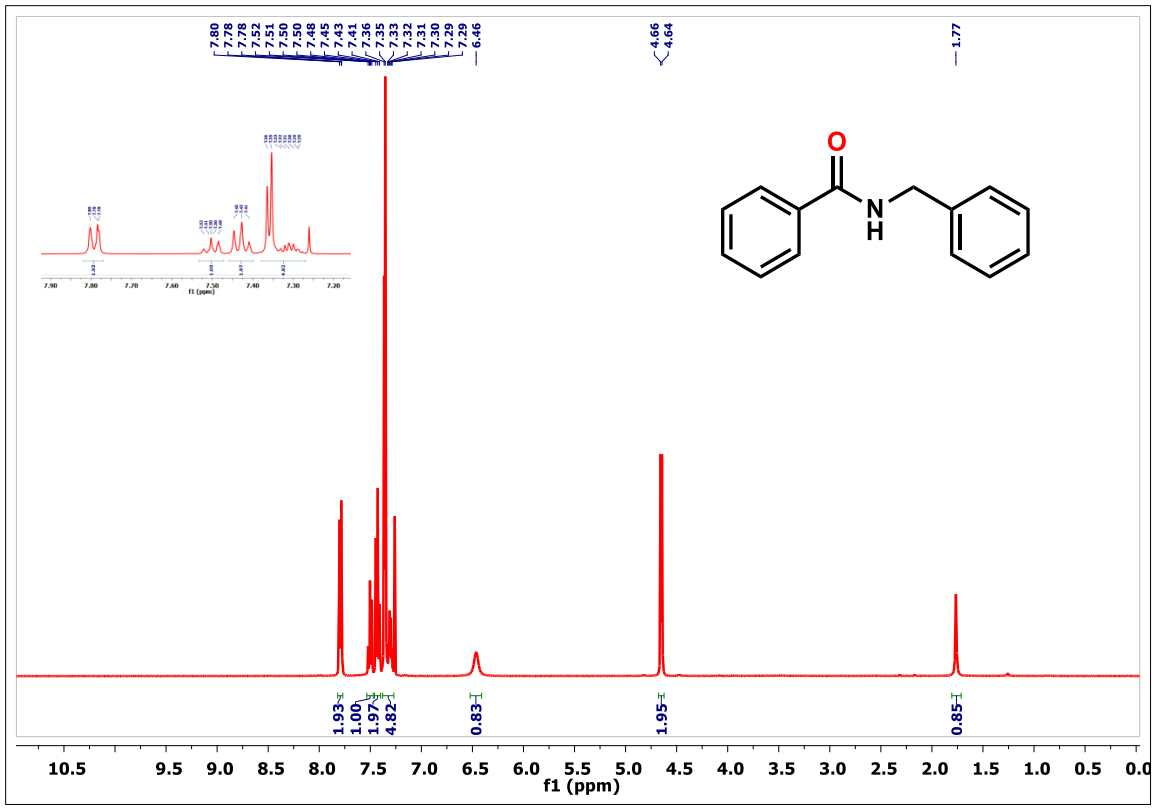

Figure S24: 400 MHz ^{1}H NMR spectrum of **4** in $CDCl_3$

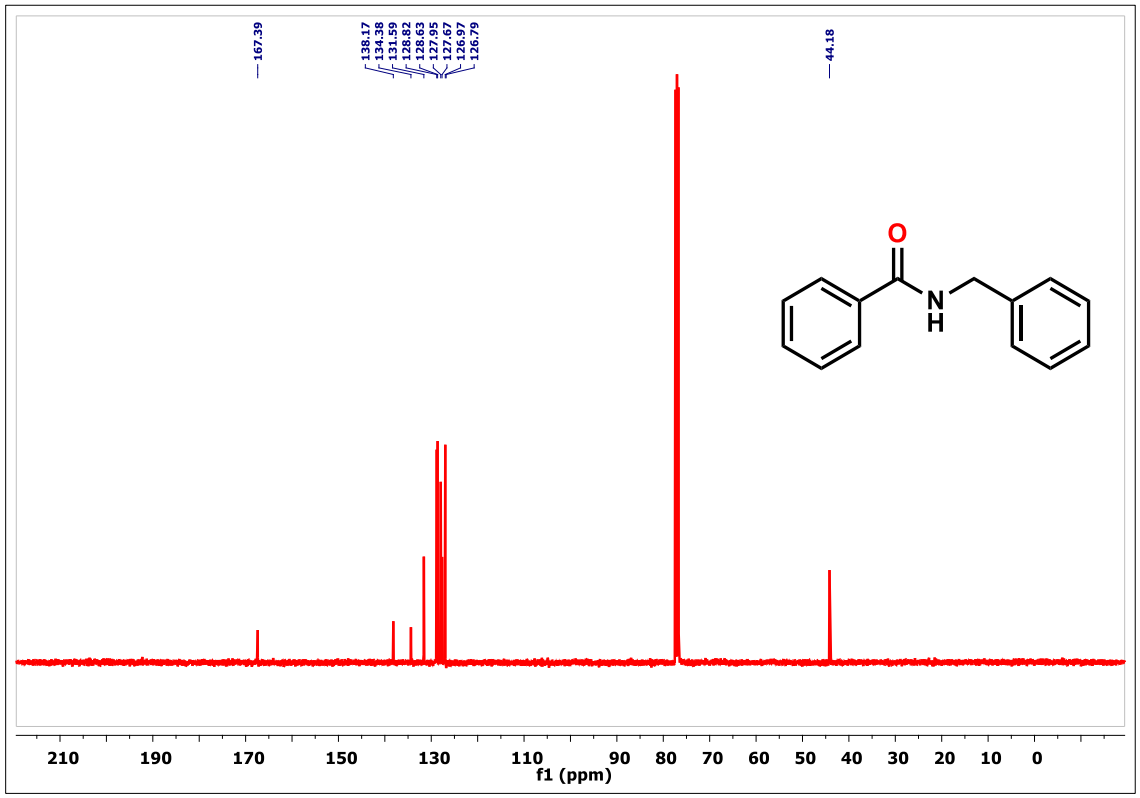

Figure S25: 100 MHz ^{13}C NMR spectrum of **4** in $CDCl_3$

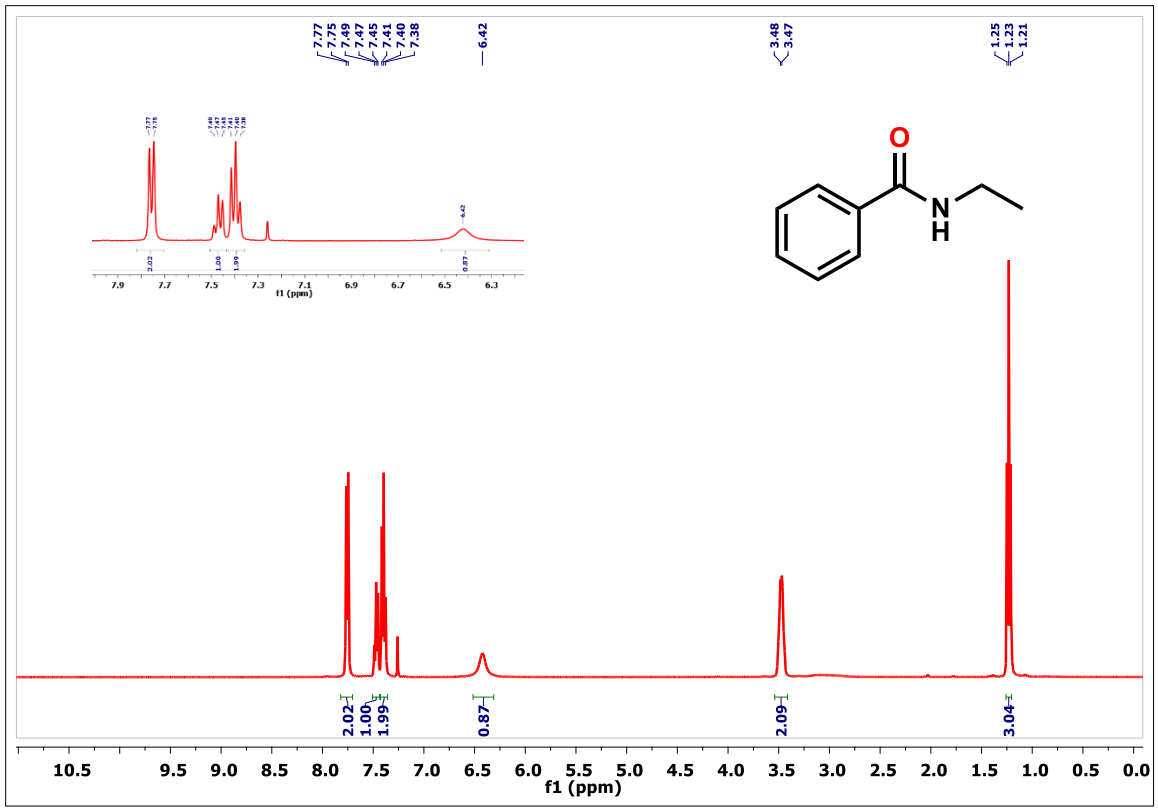

Figure S26: 400 MHz ^{1}H NMR spectrum of **5** in $CDCl_3$

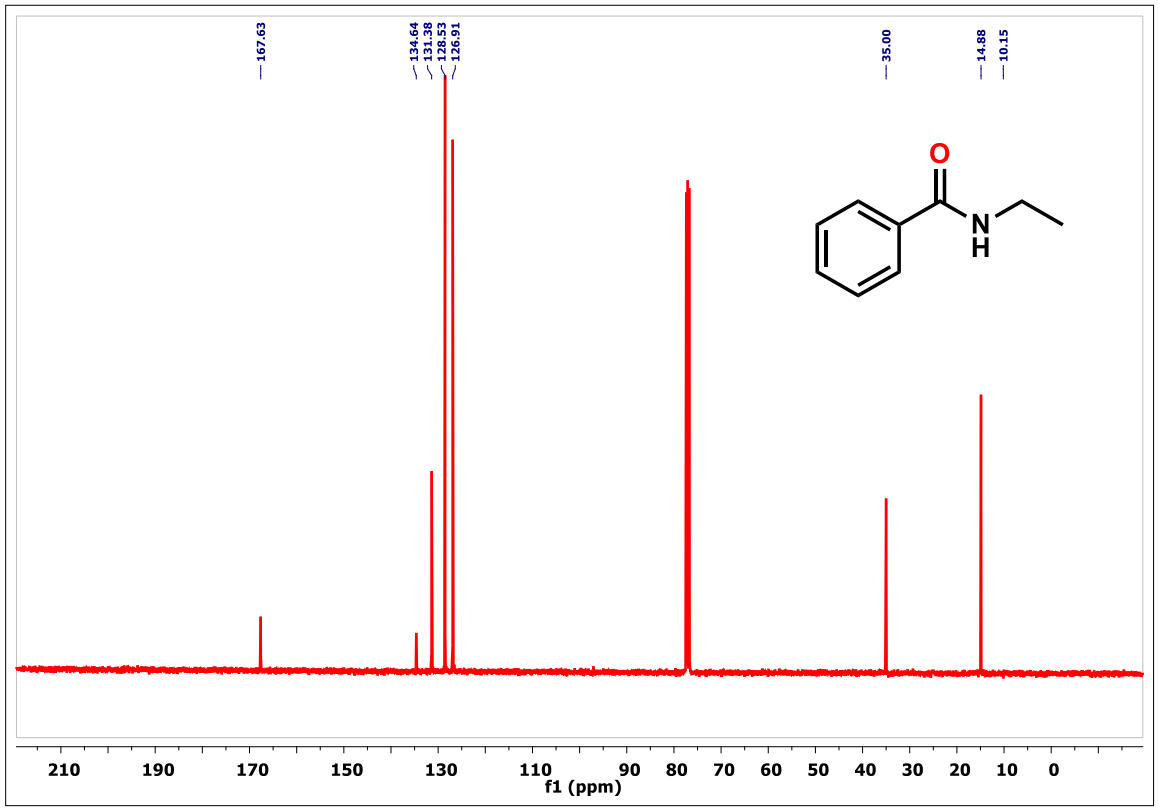

Figure S27: 100 MHz ^{13}C NMR spectrum of **5** in $CDCl_3$

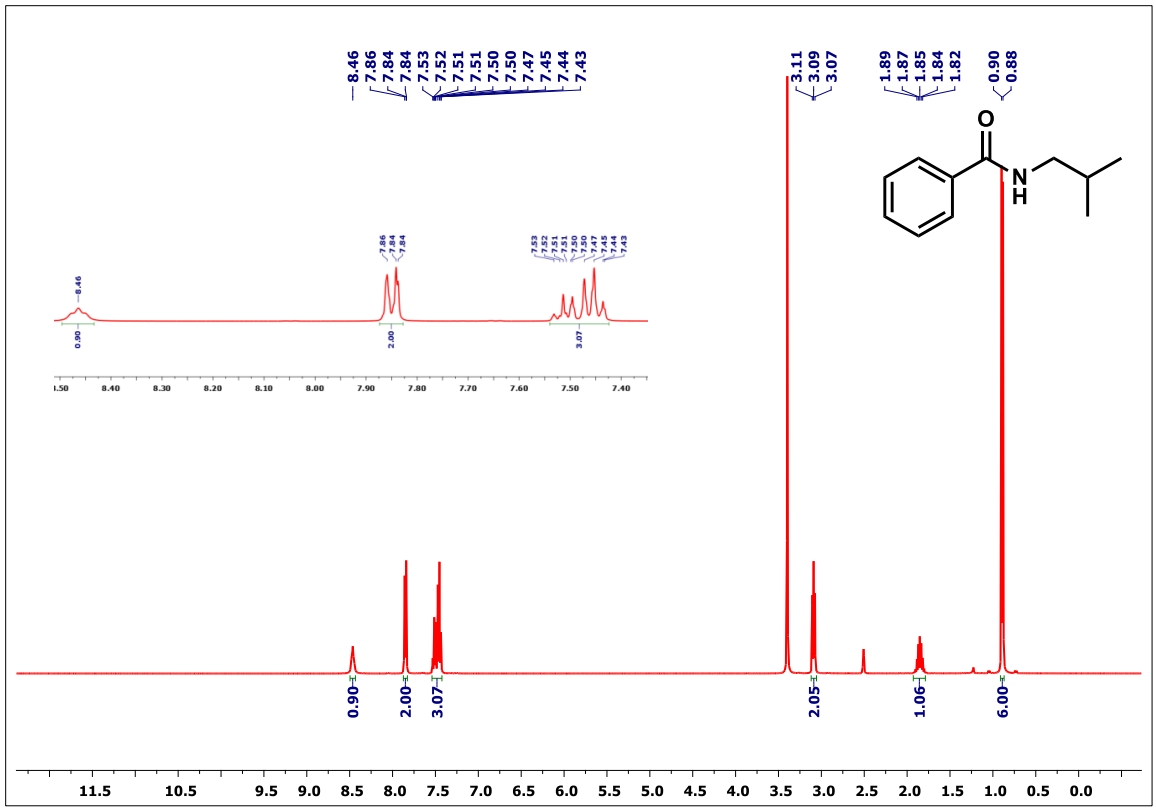

Figure S28: 400 MHz ^{1}H NMR spectrum of **6** in DMSO-d_6

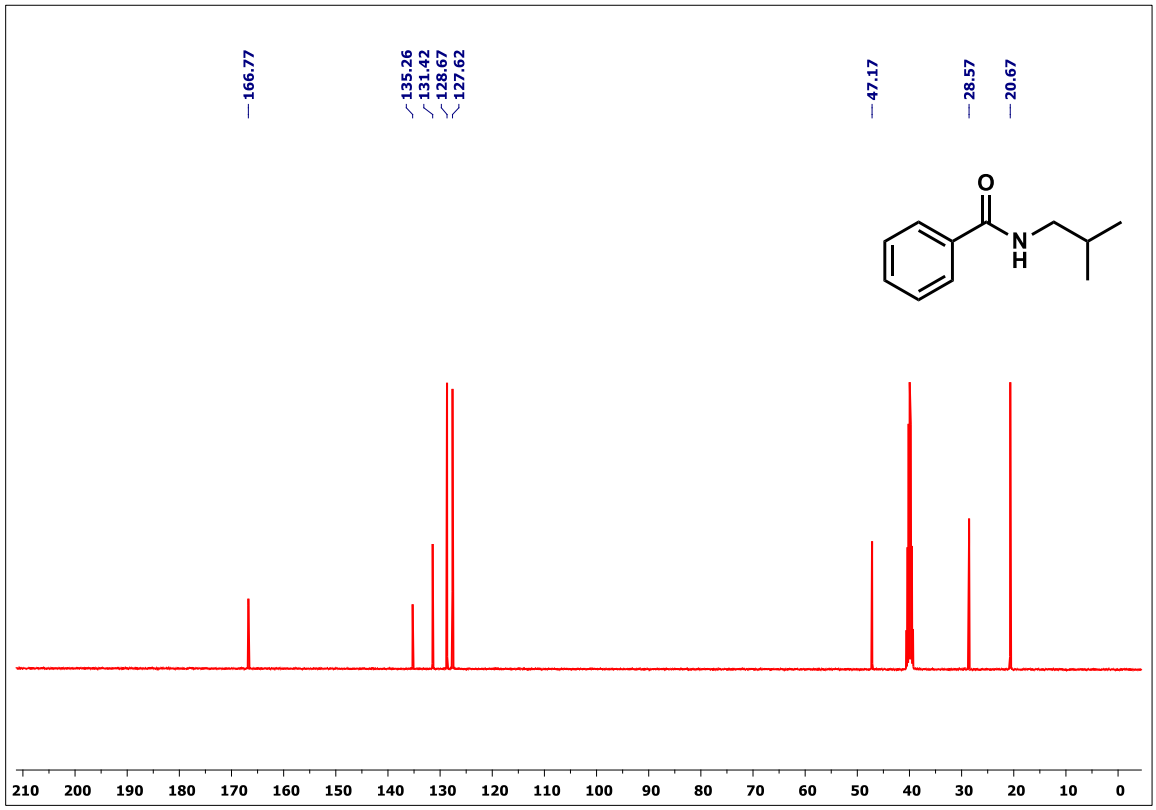

Figure S29: 100 MHz ^{13}C NMR spectrum of **6** in DMSO-d_6

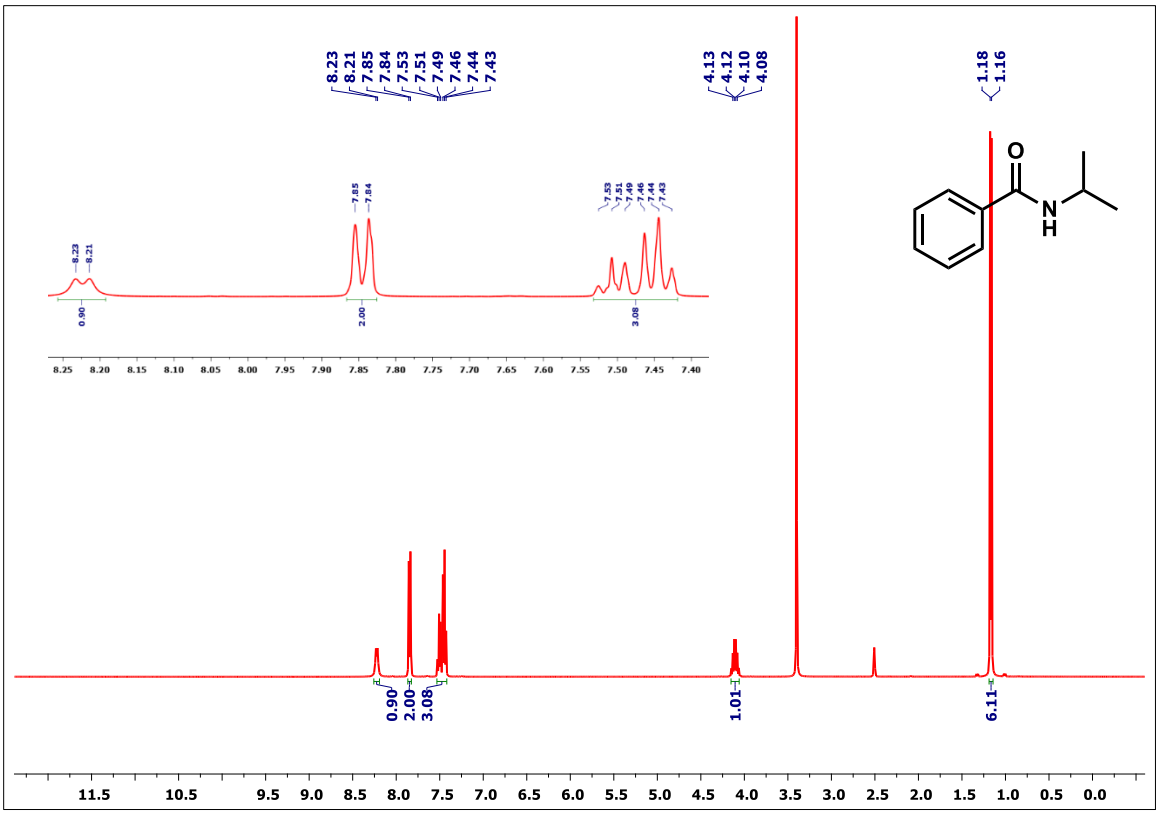

Figure S30: 400 MHz ^{1}H NMR spectrum of **7** in DMSO-d_6

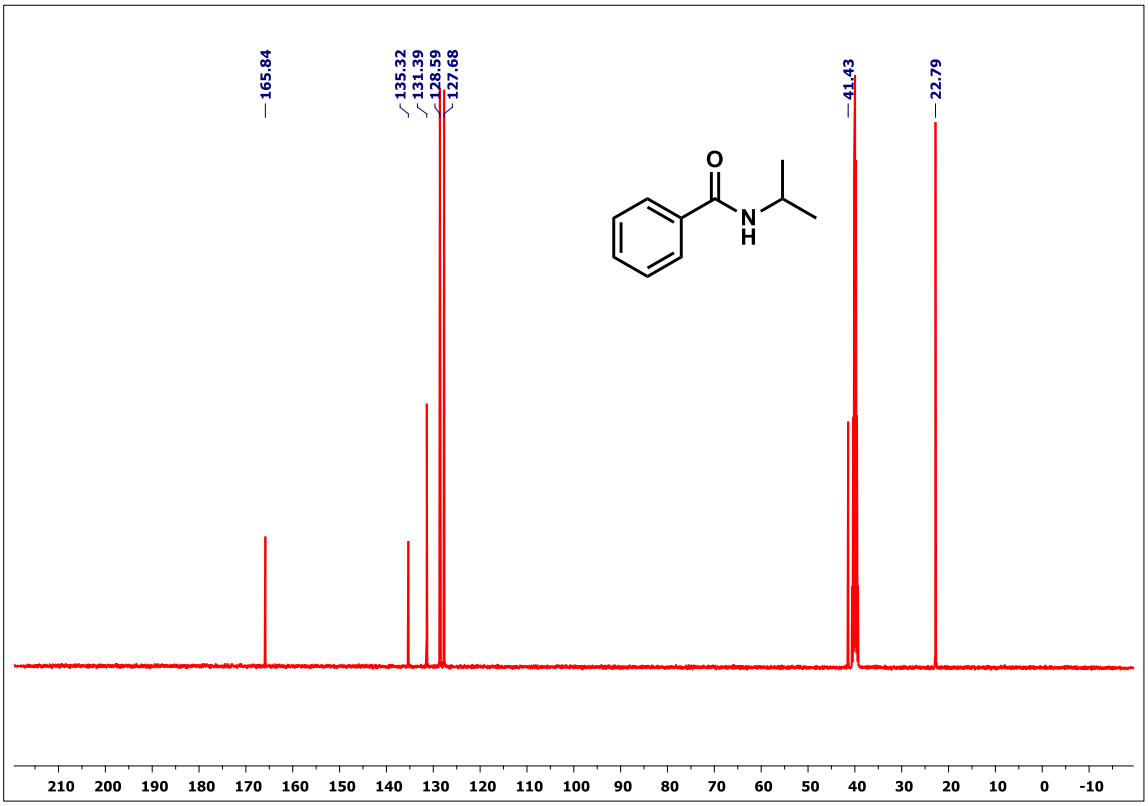

Figure S31: 100 MHz ^{13}C NMR spectrum of **7** in DMSO-d_6

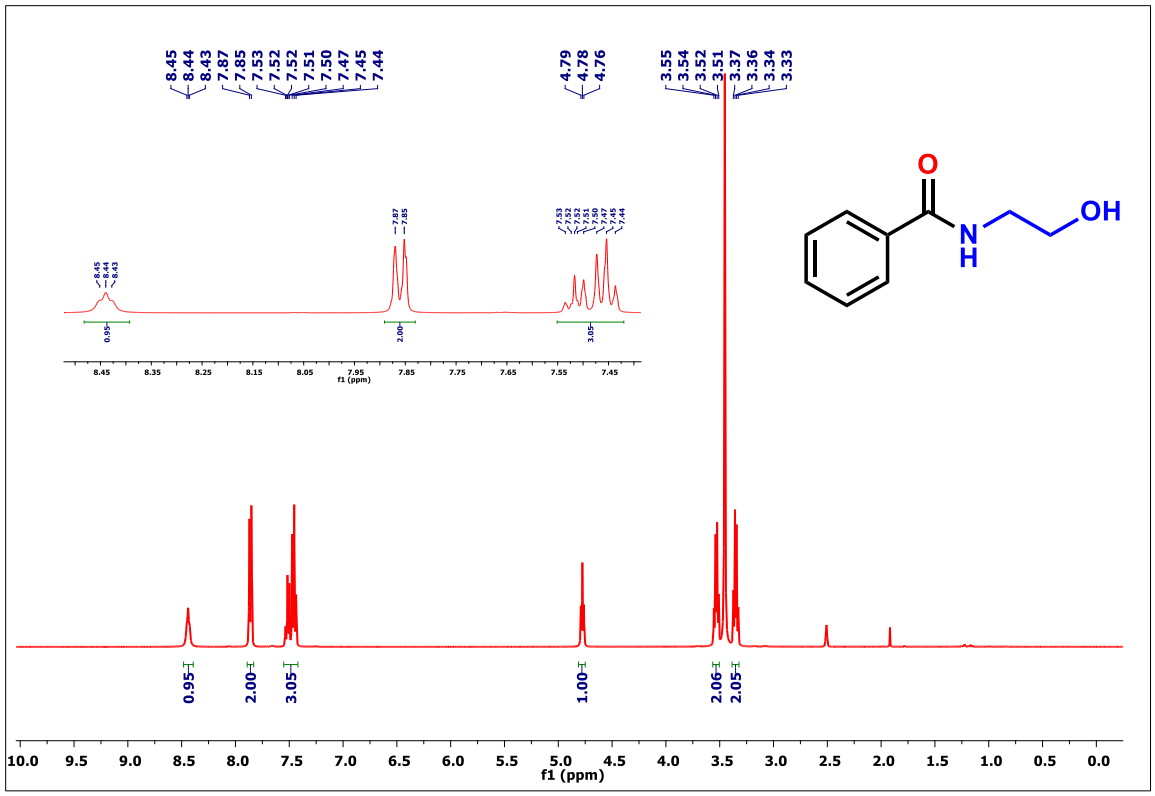

Figure S32: 400 MHz ^{1}H NMR spectrum of **8** in DMSO-d$_6$

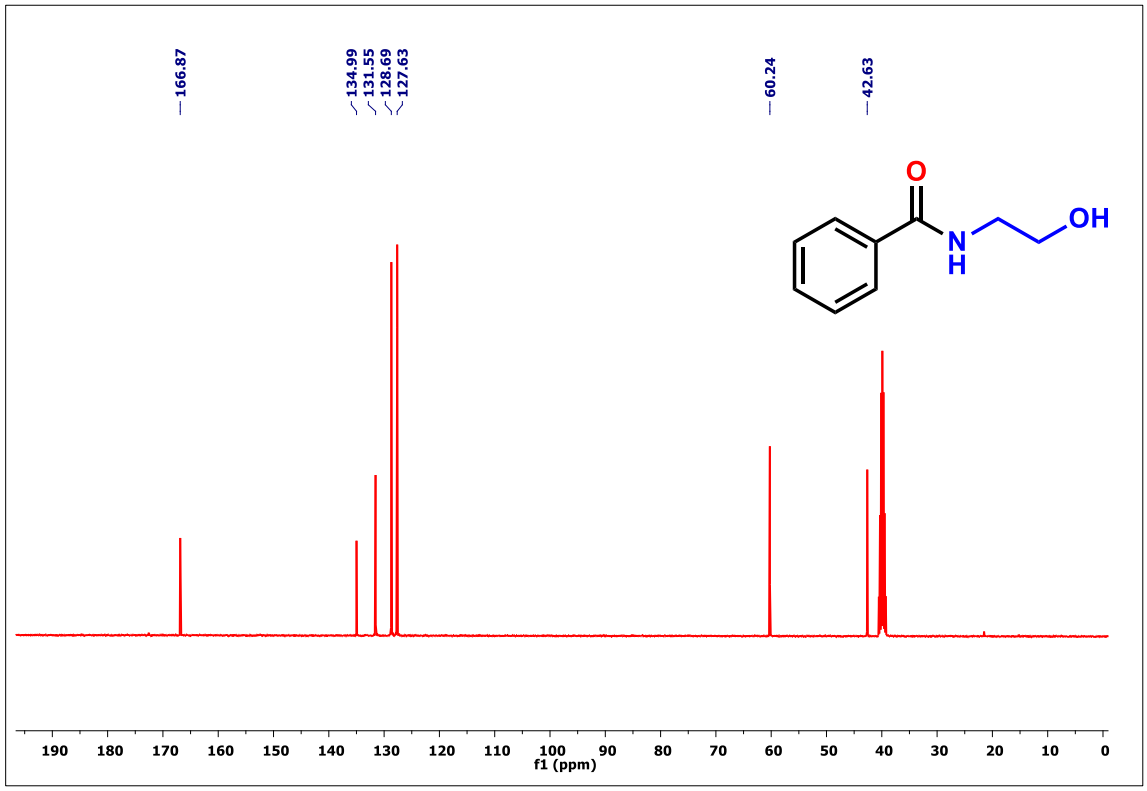

Figure S33: 100 MHz ^{13}C NMR spectrum of **8** in DMSO-d$_6$

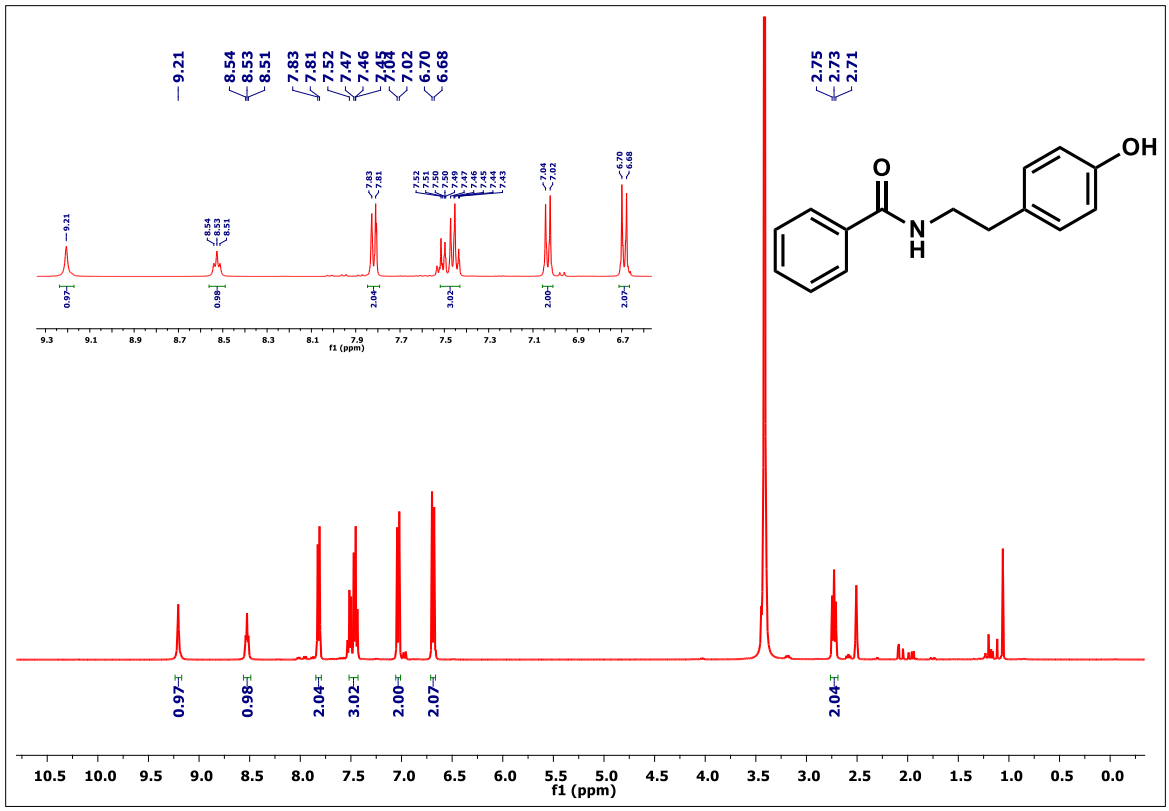

Figure S34: 400 MHz ^{1}H NMR spectrum of **9** in DMSO-d$_6$

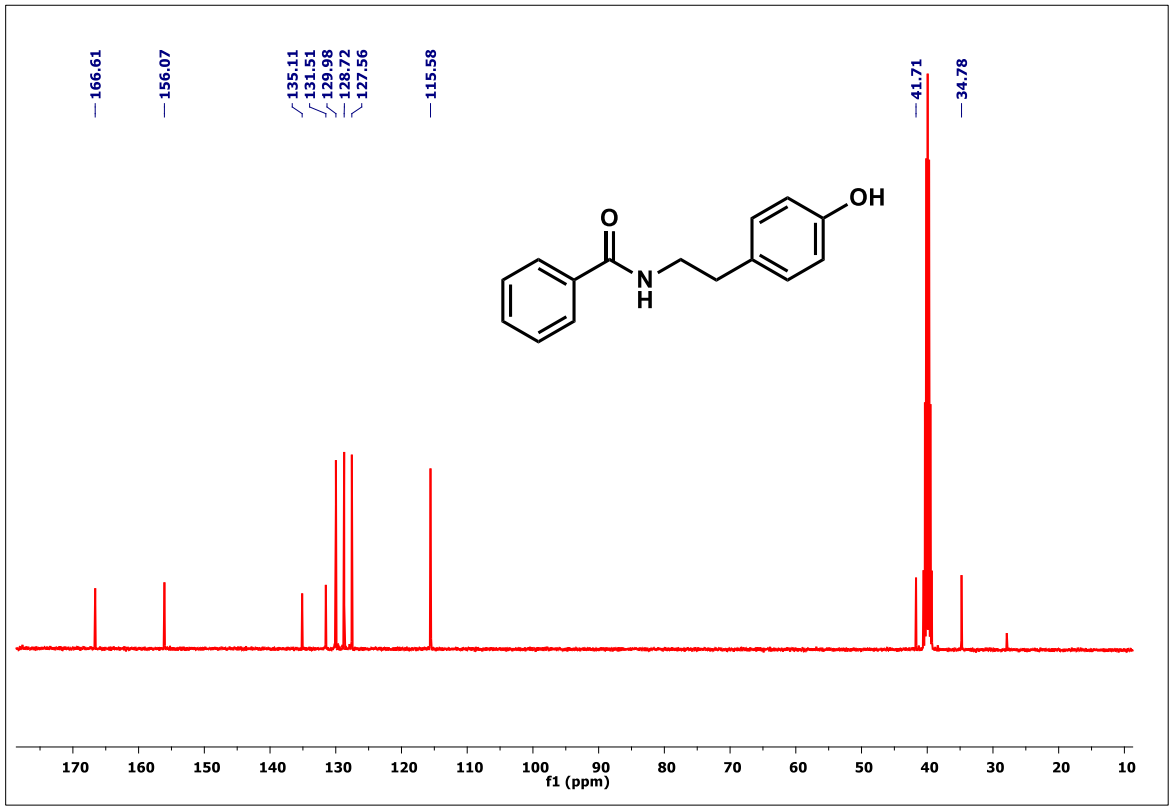

Figure S35: 100 MHz ^{13}C NMR spectrum of **9** in DMSO-d$_6$

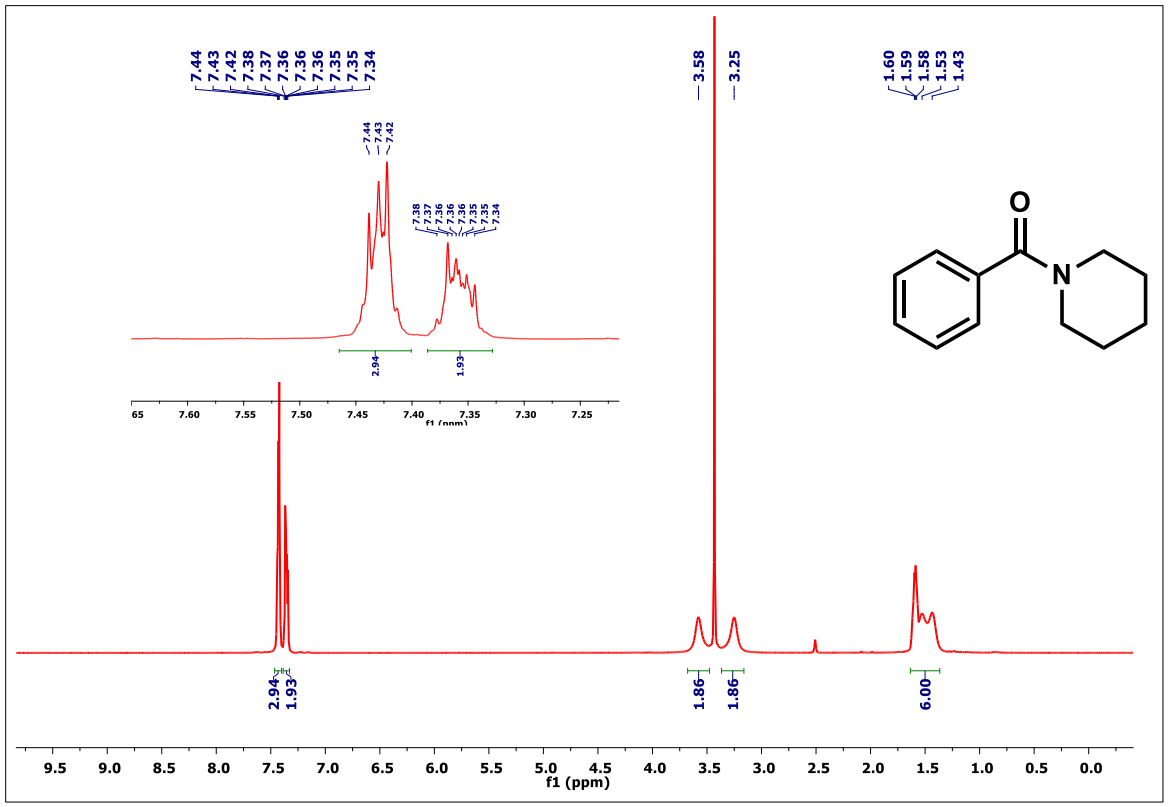

Figure S36: 400 MHz ^{1}H NMR spectrum of **10** in DMSO-d_6

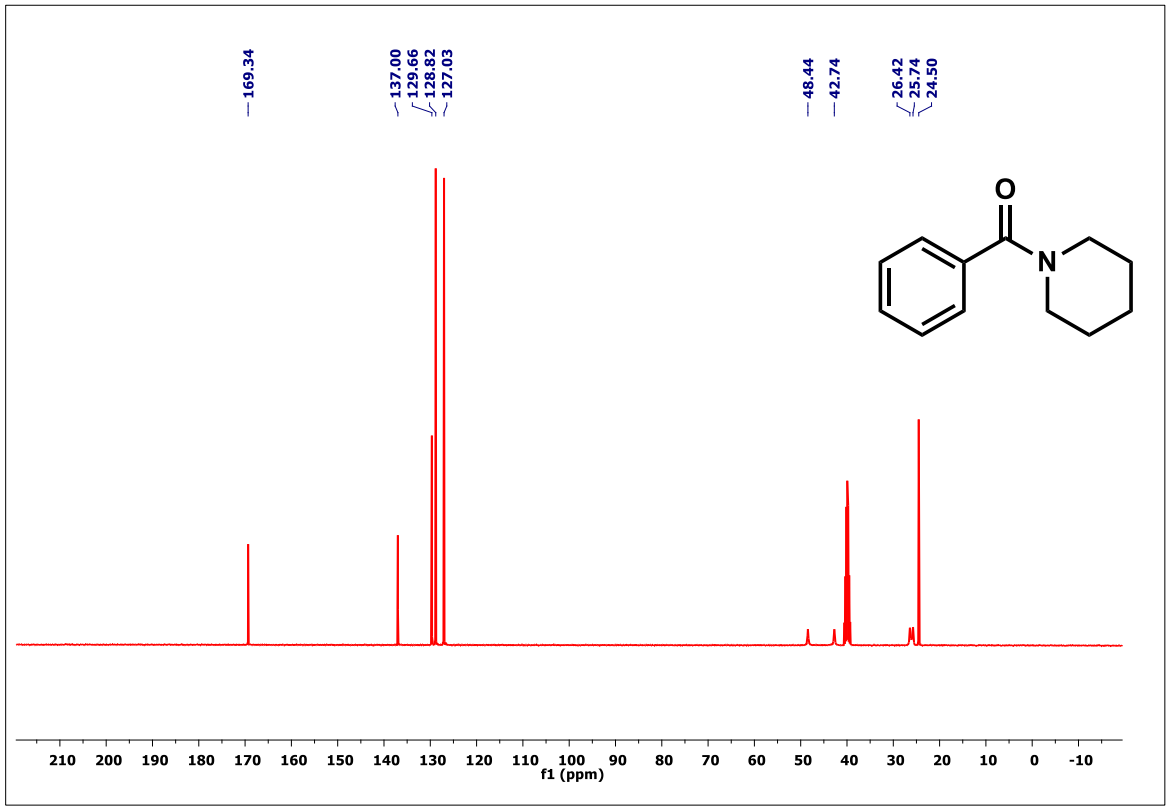

Figure S37: 100 MHz ^{13}C NMR spectrum of **10** in DMSO-d_6

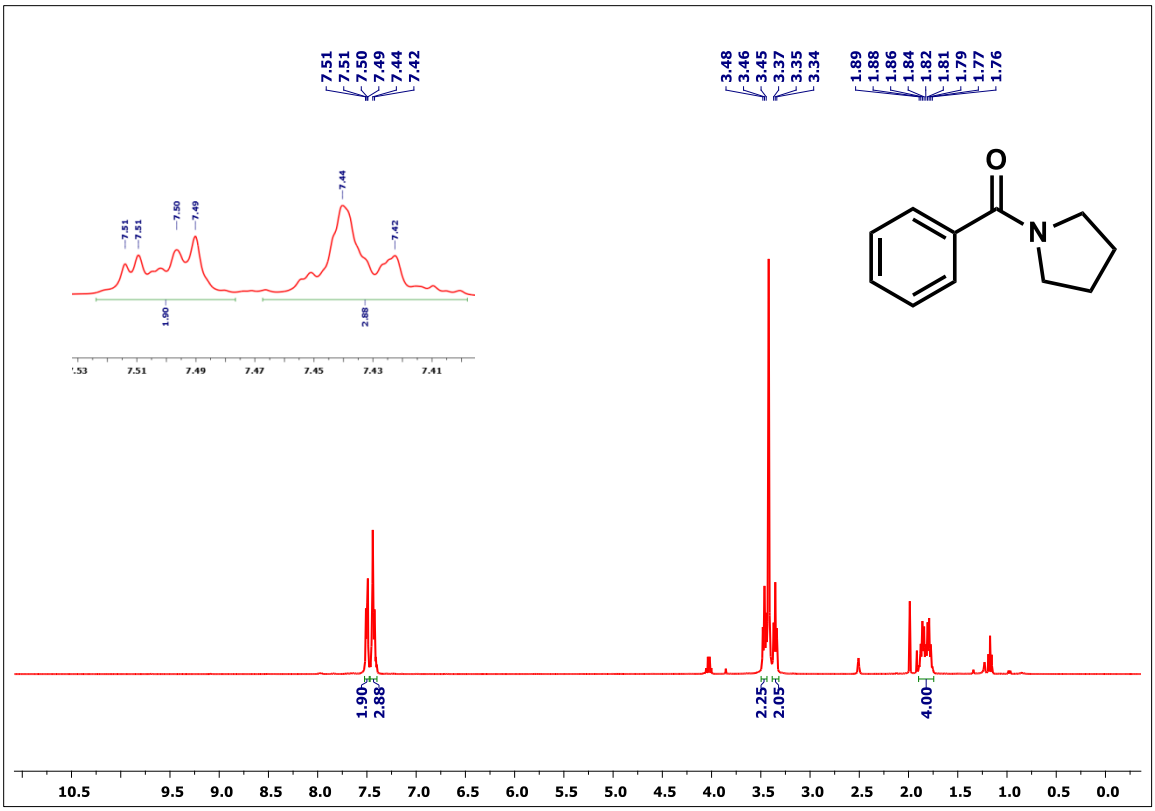

Figure S38: 400 MHz ^{1}H NMR spectrum of **11** in DMSO-d_6

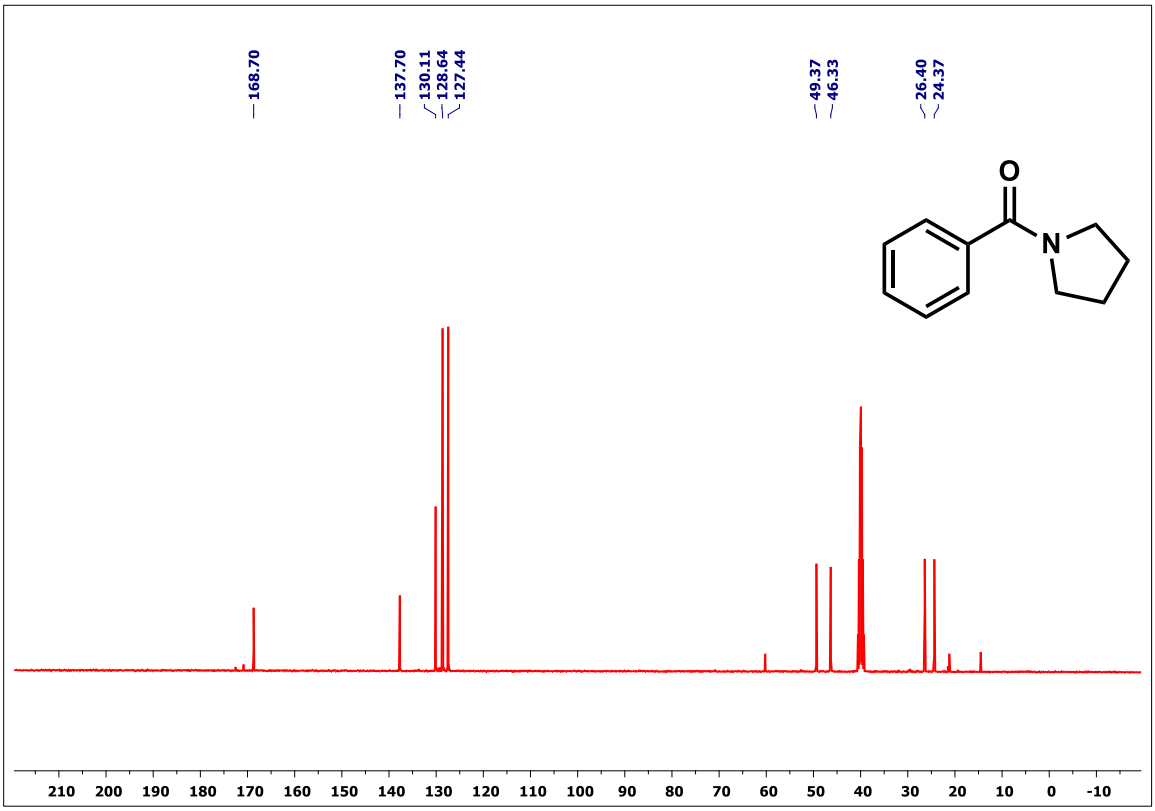

Figure S40: 100 MHz ^{13}C NMR spectrum of **11** in DMSO-d_6

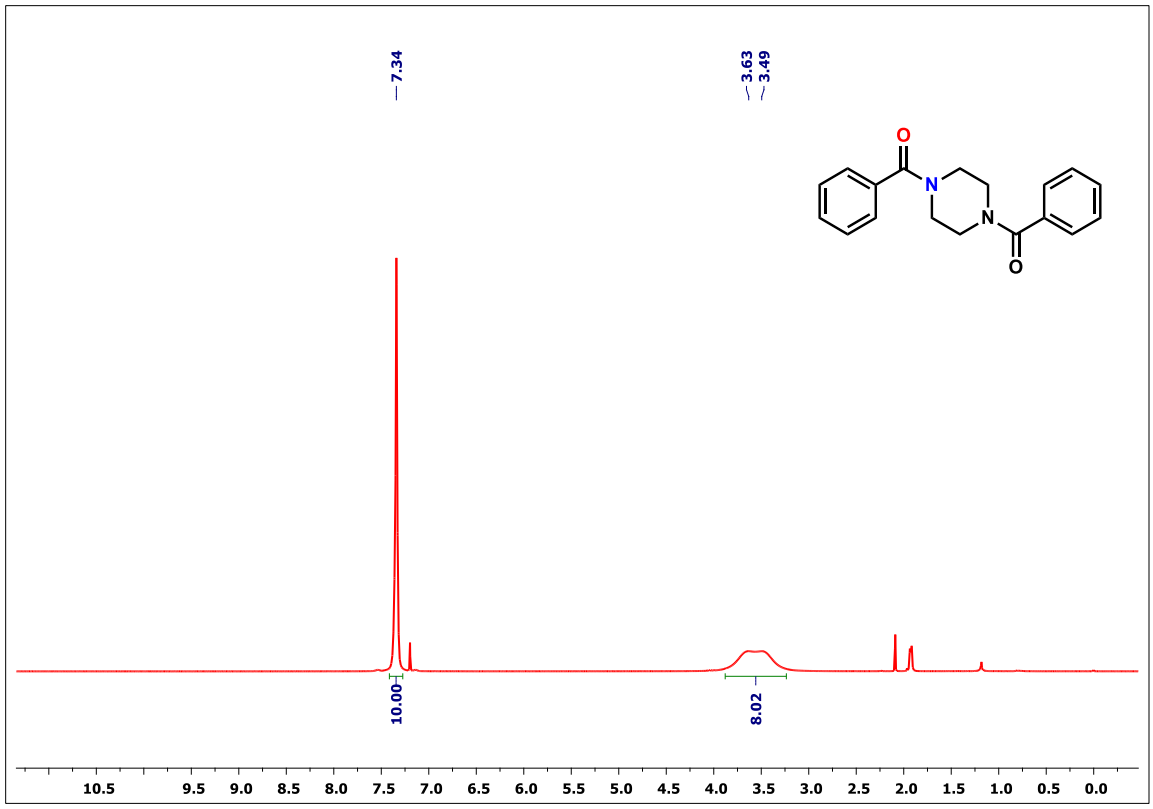

Figure S41: 400 MHz ^{1}H NMR spectrum of **12** in $CDCl_3$

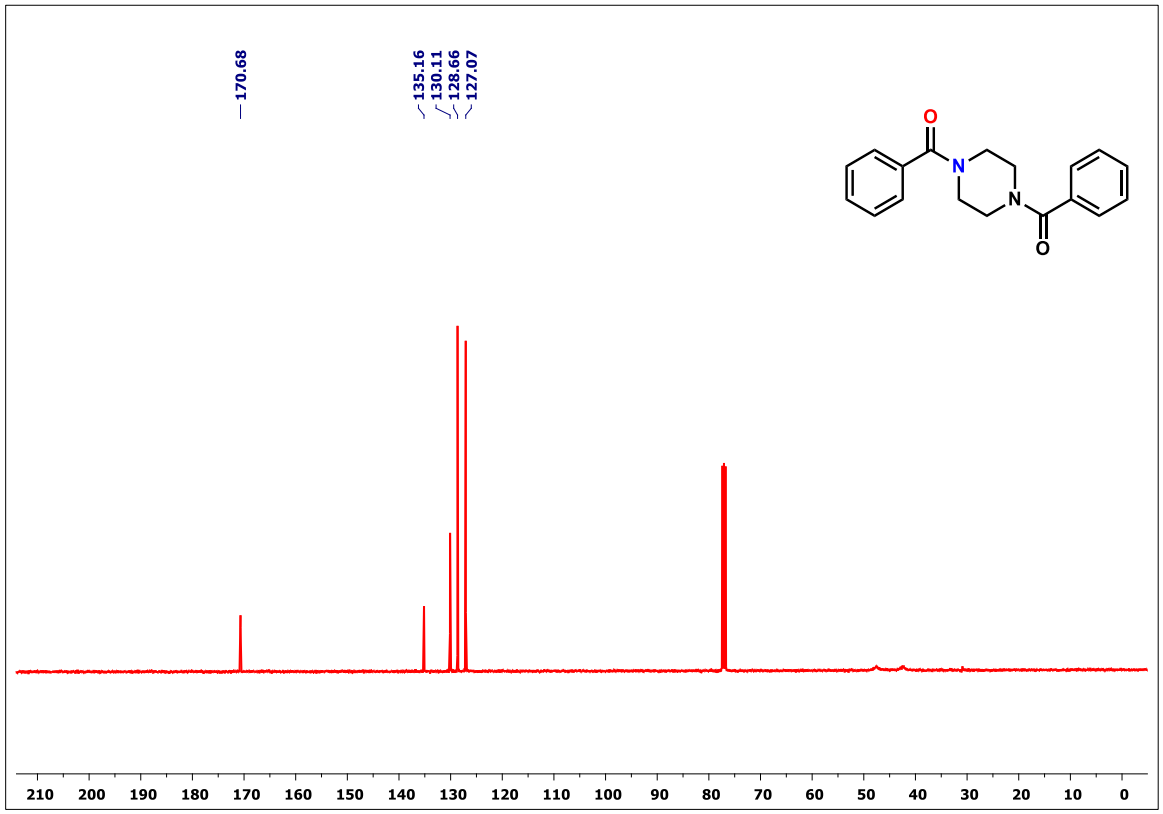

Figure S42: 100 MHz ^{13}C NMR spectrum of **12** in $CDCl_3$

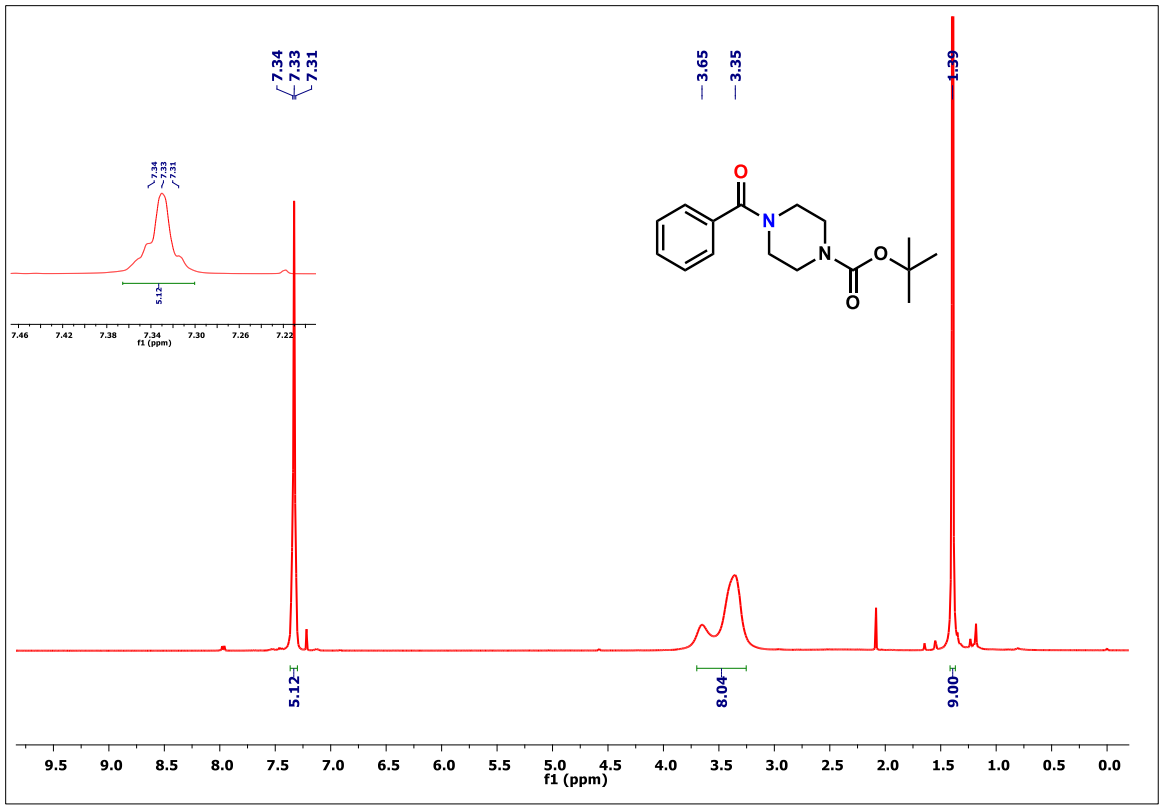

Figure S43: 400 MHz ^{1}H NMR spectrum of **13** in $CDCl_3$

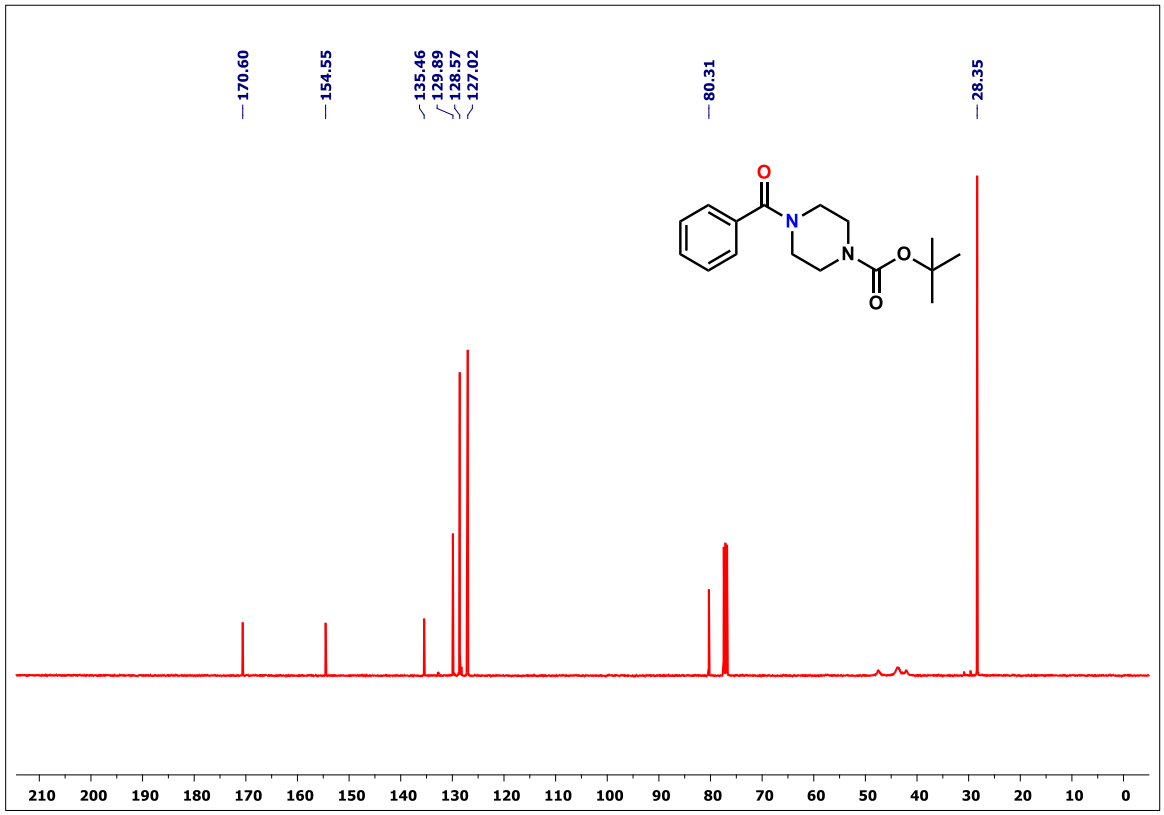

Figure S44: 100 MHz ^{13}C NMR spectrum of **13** in $CDCl_3$

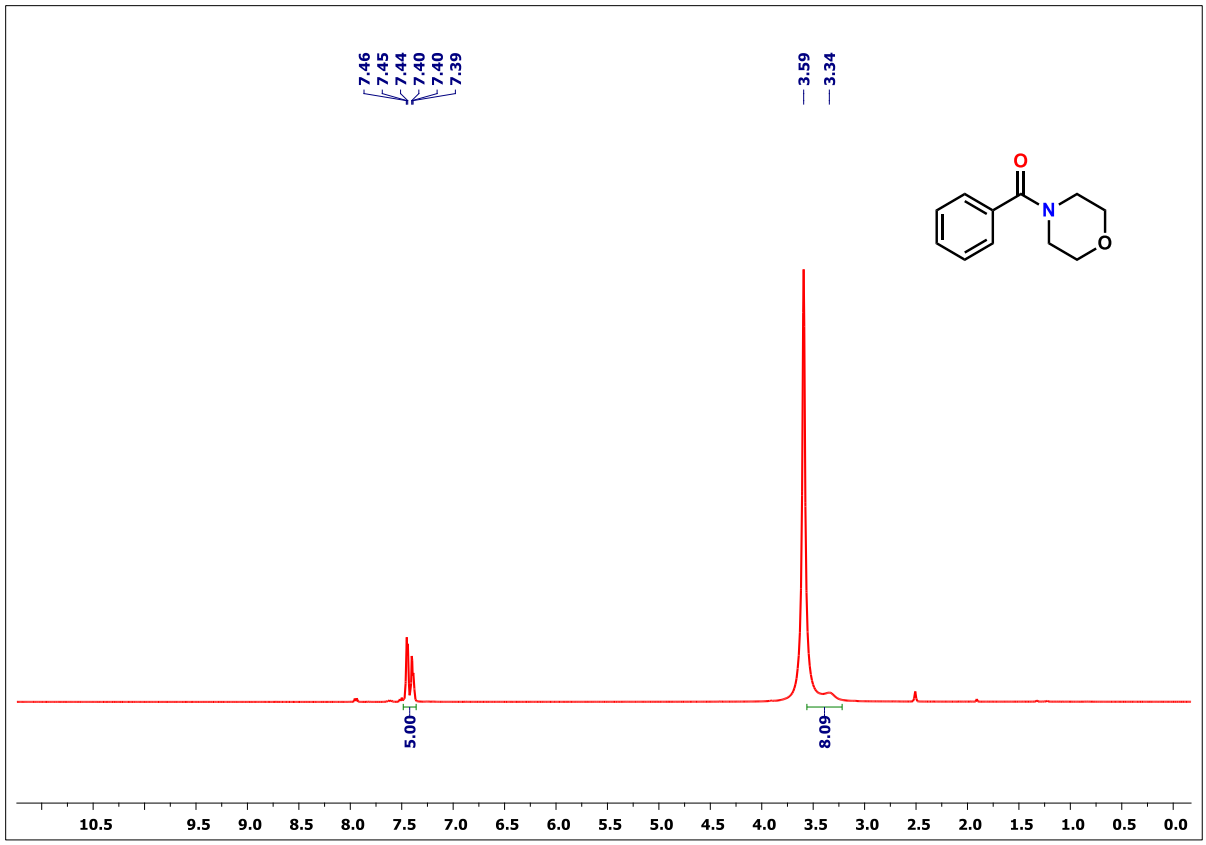

Figure S45: 400 MHz ^{1}H NMR spectrum of **14** in $CDCl_3$

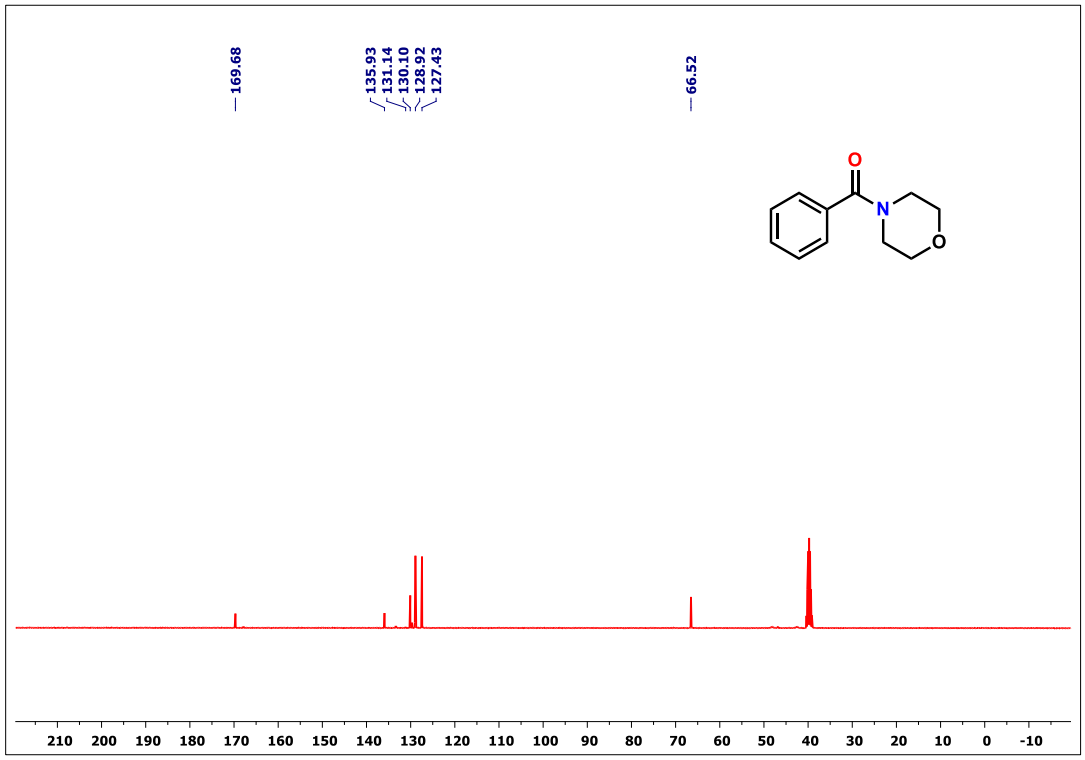

Figure S46: 100 MHz ^{13}C NMR spectrum of **14** in $CDCl_3$

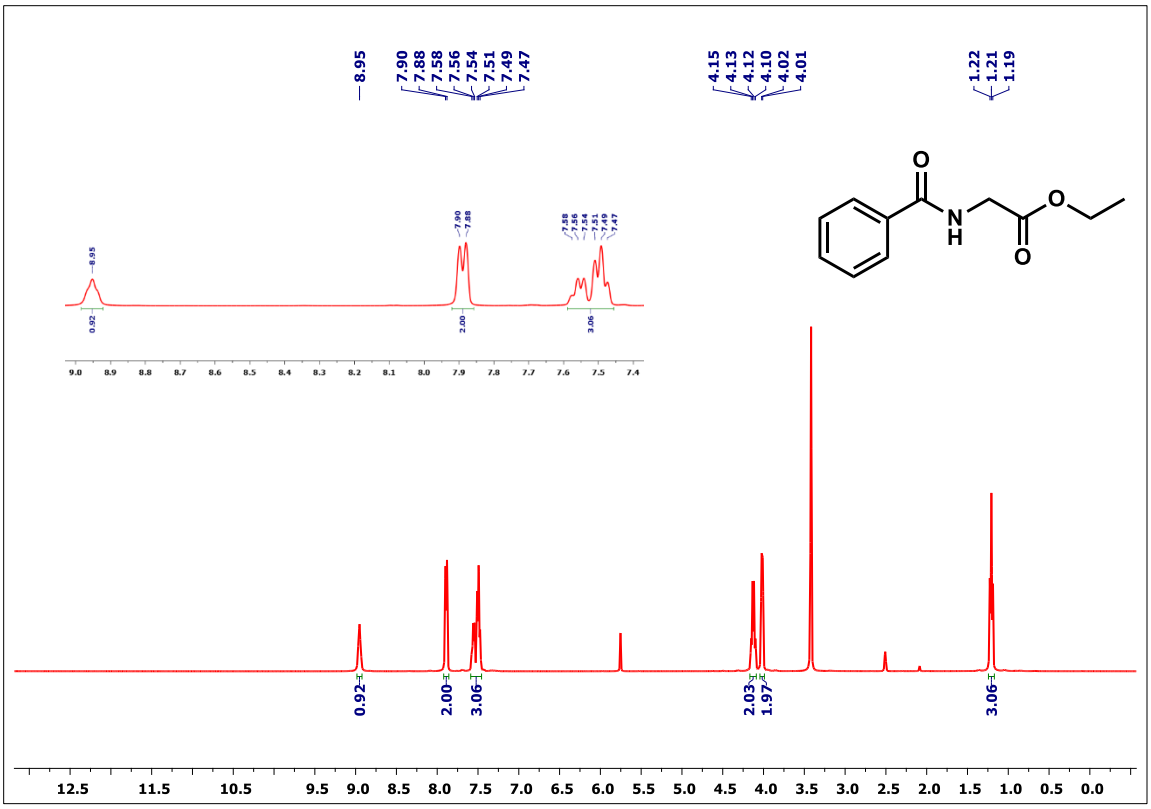

Figure S47: 400 MHz ^{1}H NMR spectrum of **15** in DMSO-d_6

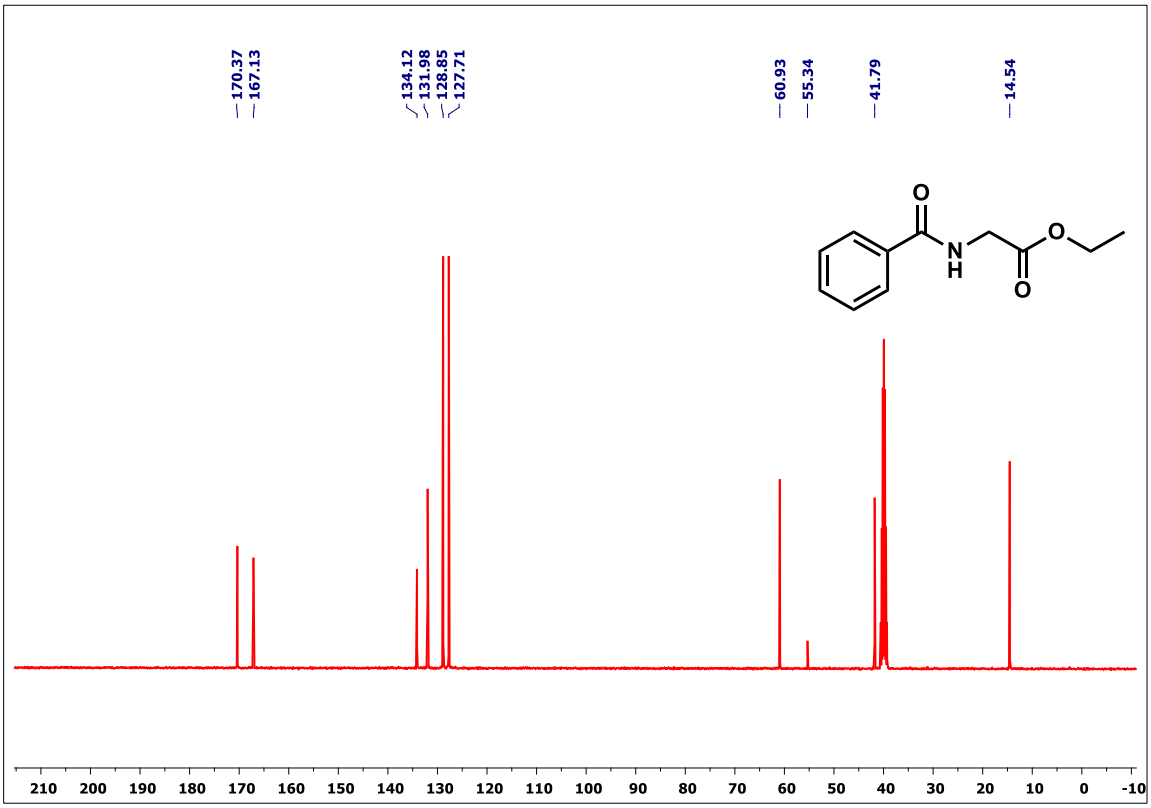

Figure S48: 100 MHz ^{13}C NMR spectrum of **15** in DMSO-d_6

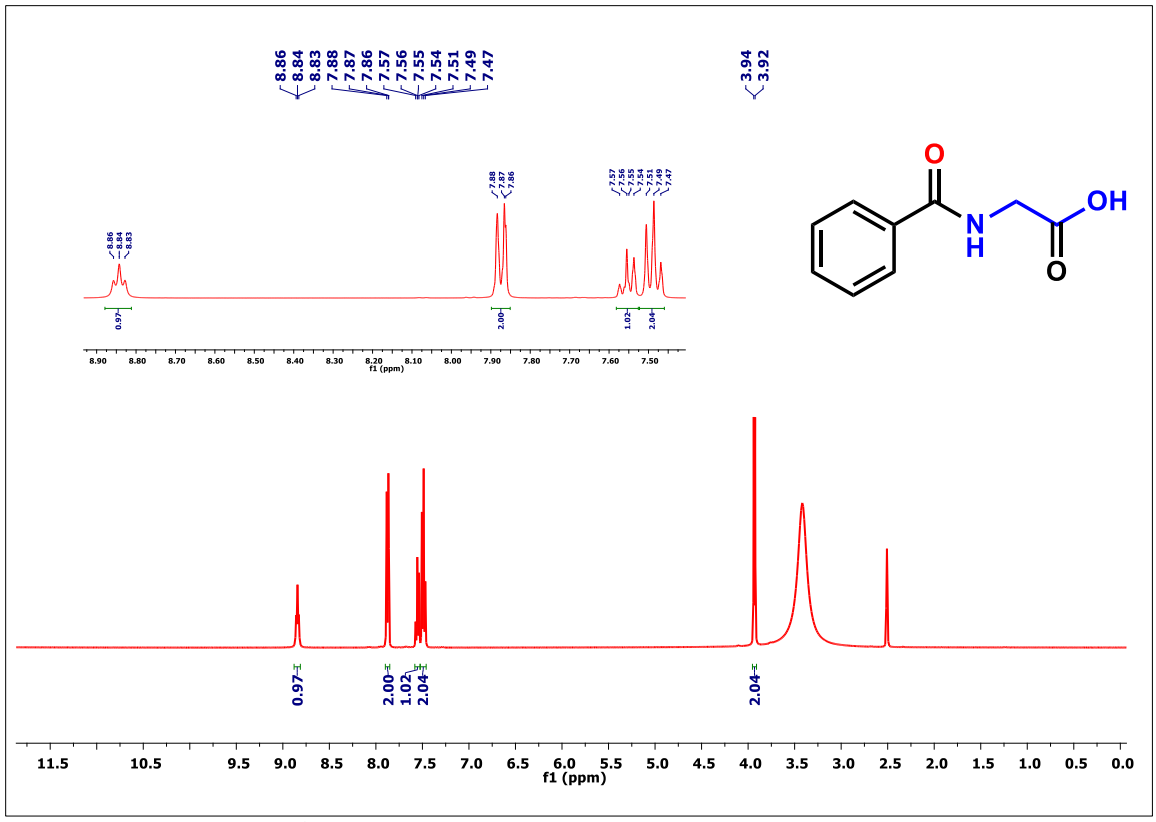

Figure S49: 400 MHz ^{1}H NMR spectrum of **16** in DMSO-d$_6$

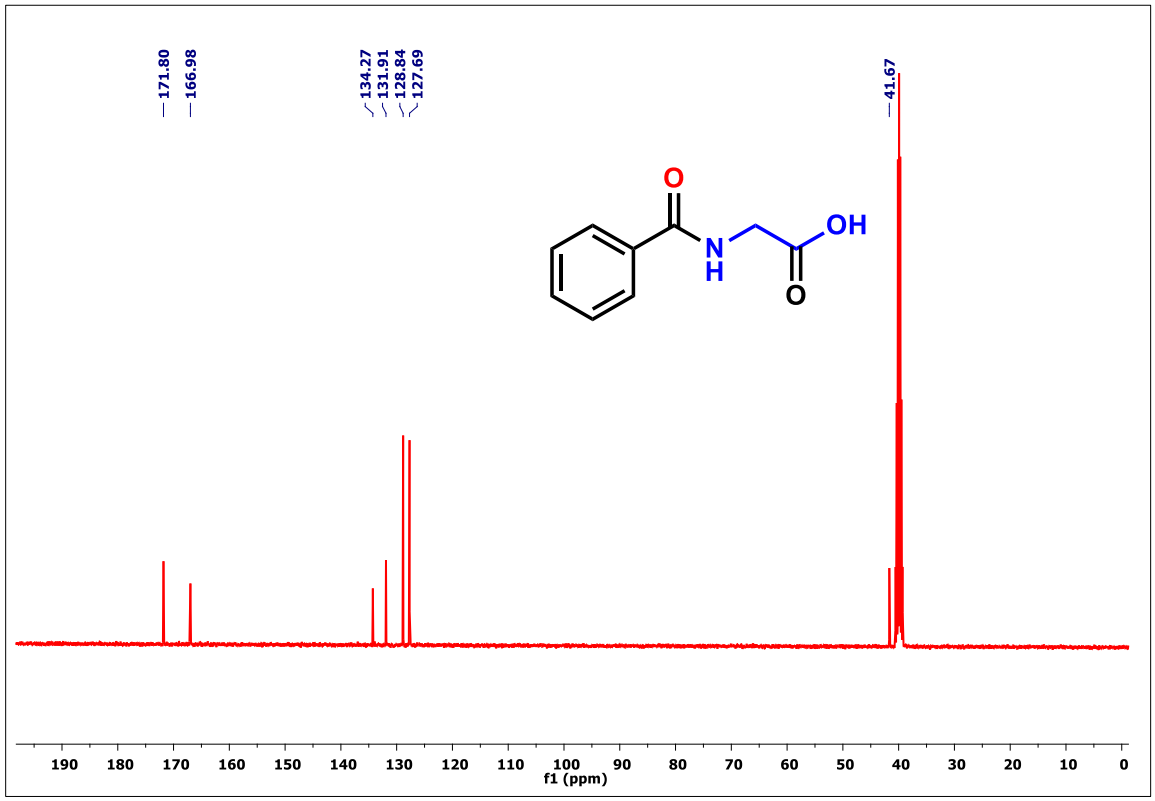

Figure S50: 100 MHz ^{13}C NMR spectrum of **16** in DMSO-d$_6$

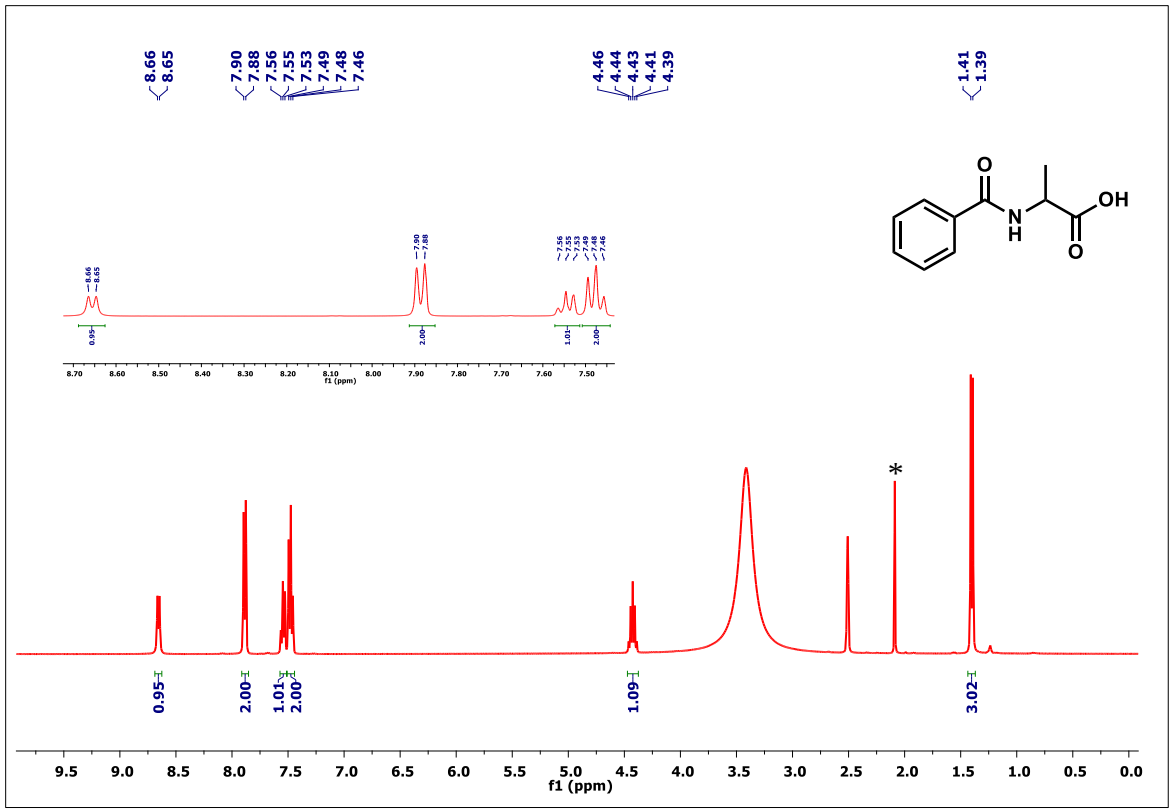

Figure S51: 400 MHz ^{1}H NMR spectrum of **17** in DMSO-d_6. *acetone

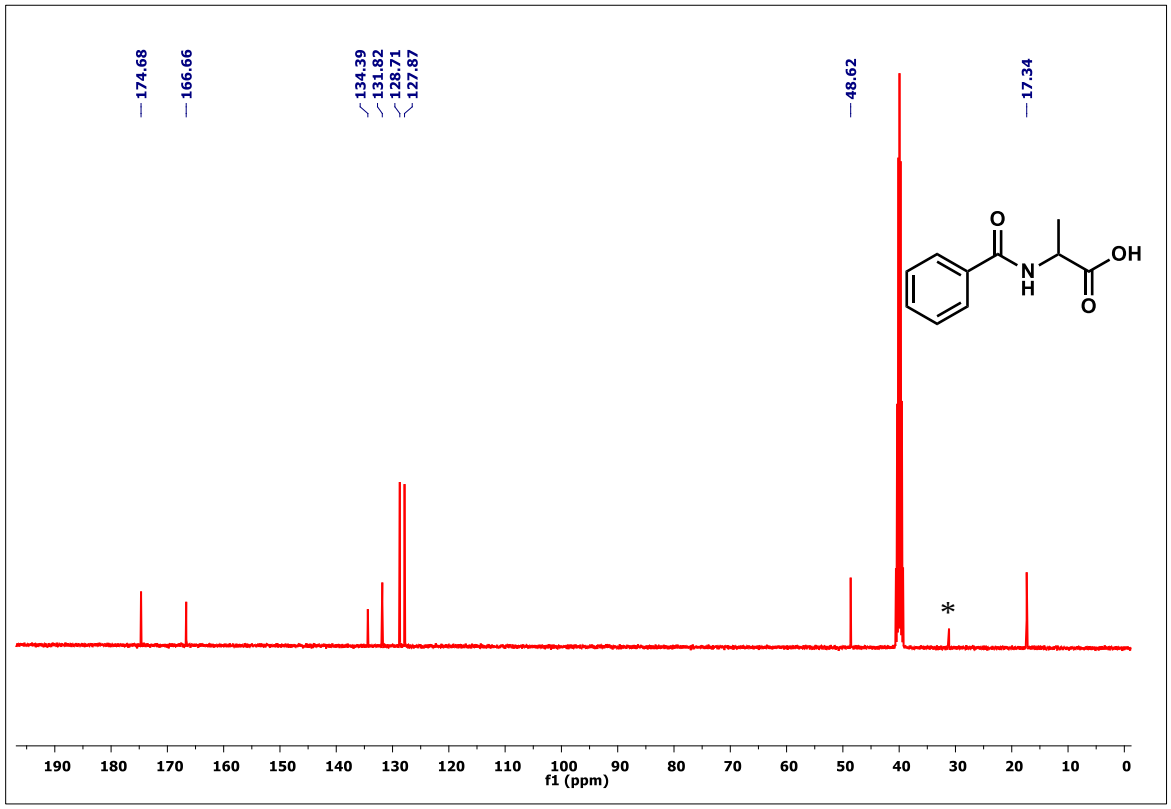

Figure S52: 100 MHz ^{13}C NMR spectrum of **17** in DMSO-d_6. *acetone

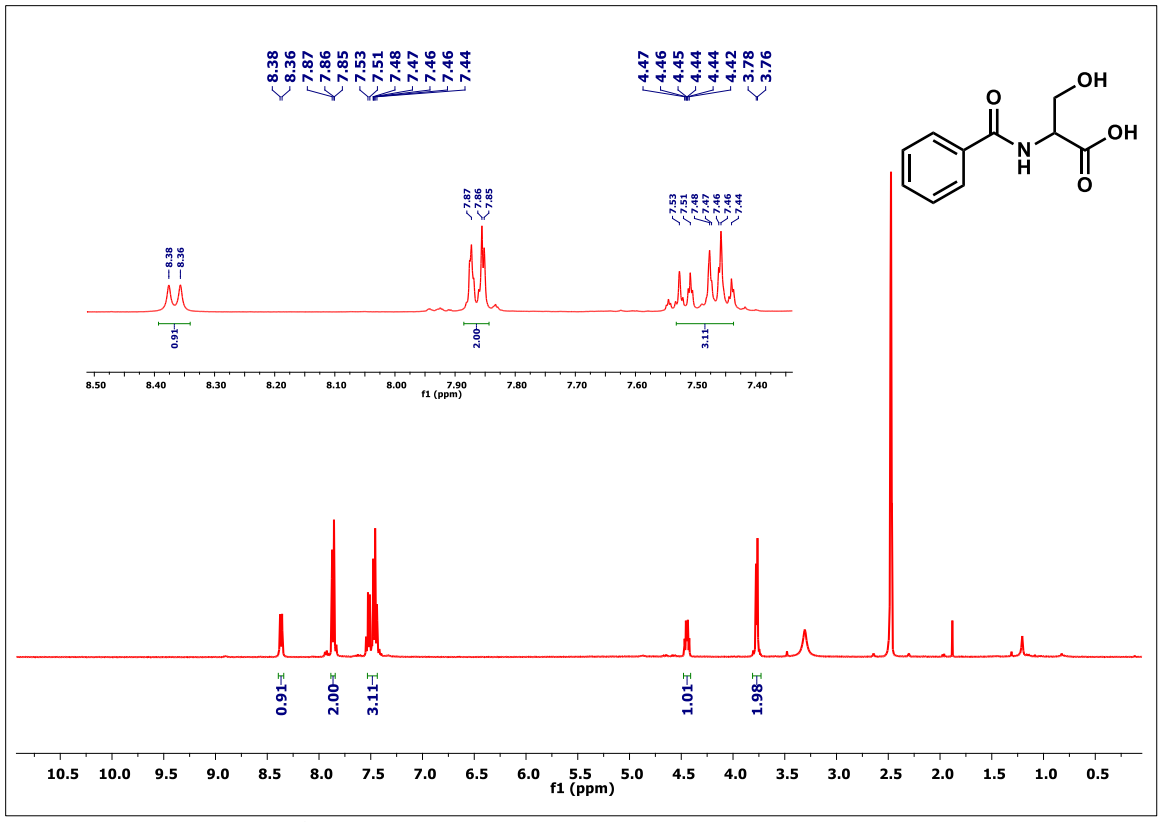

Figure S53: 400 MHz ^{1}H NMR spectrum of **18** in DMSO-d_6

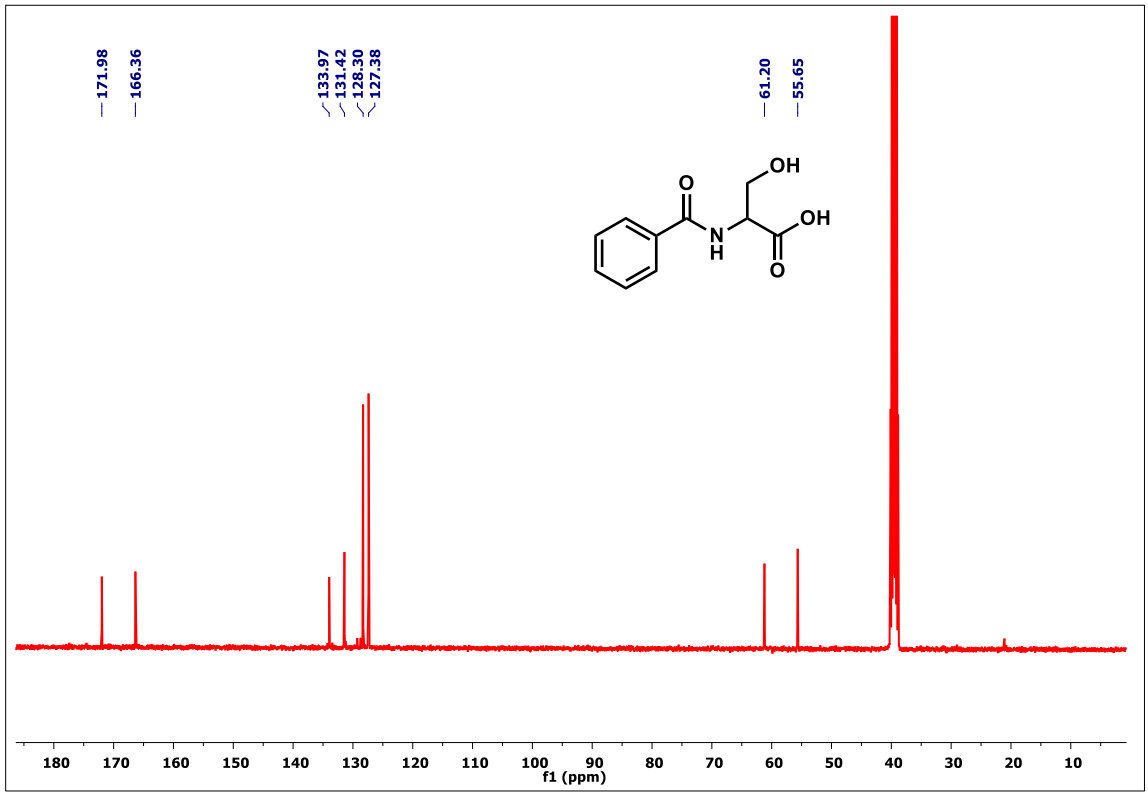

Figure S54: 100 MHz ^{13}C NMR spectrum of **18** in DMSO-d_6

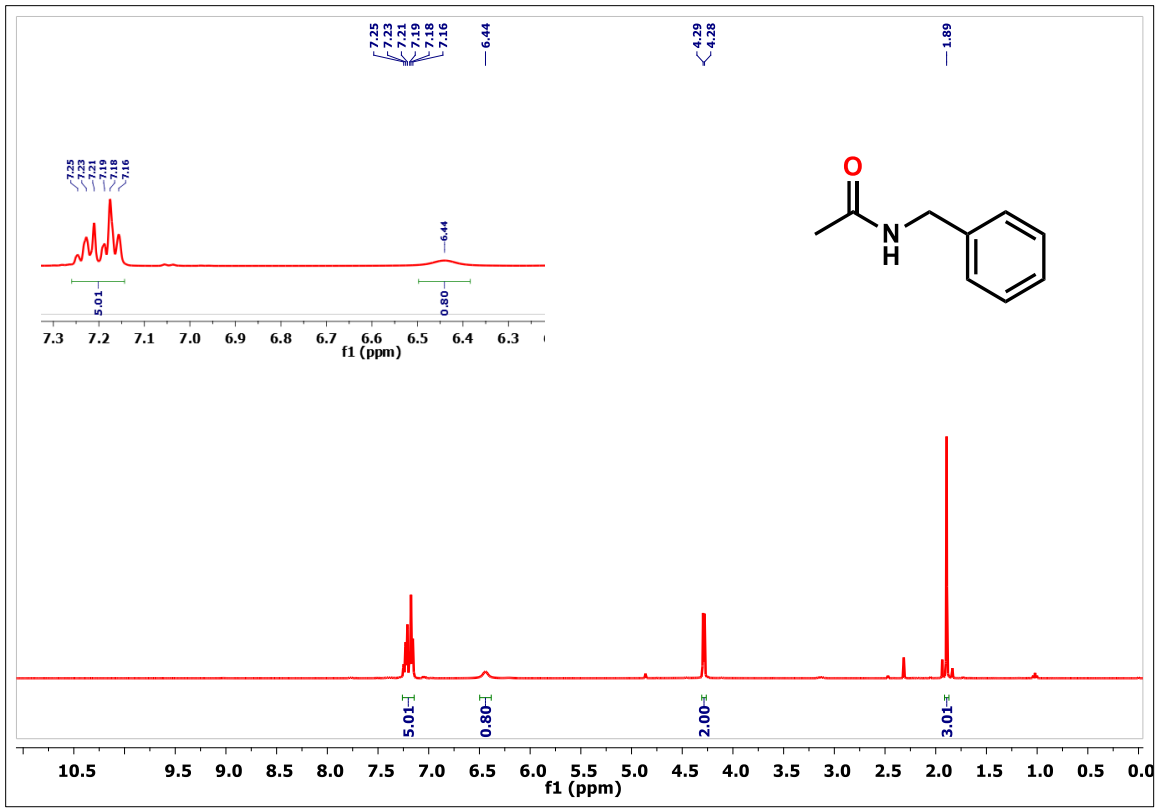

Figure S55: 400 MHz ^{1}H NMR spectrum of **19** in $CDCl_3$

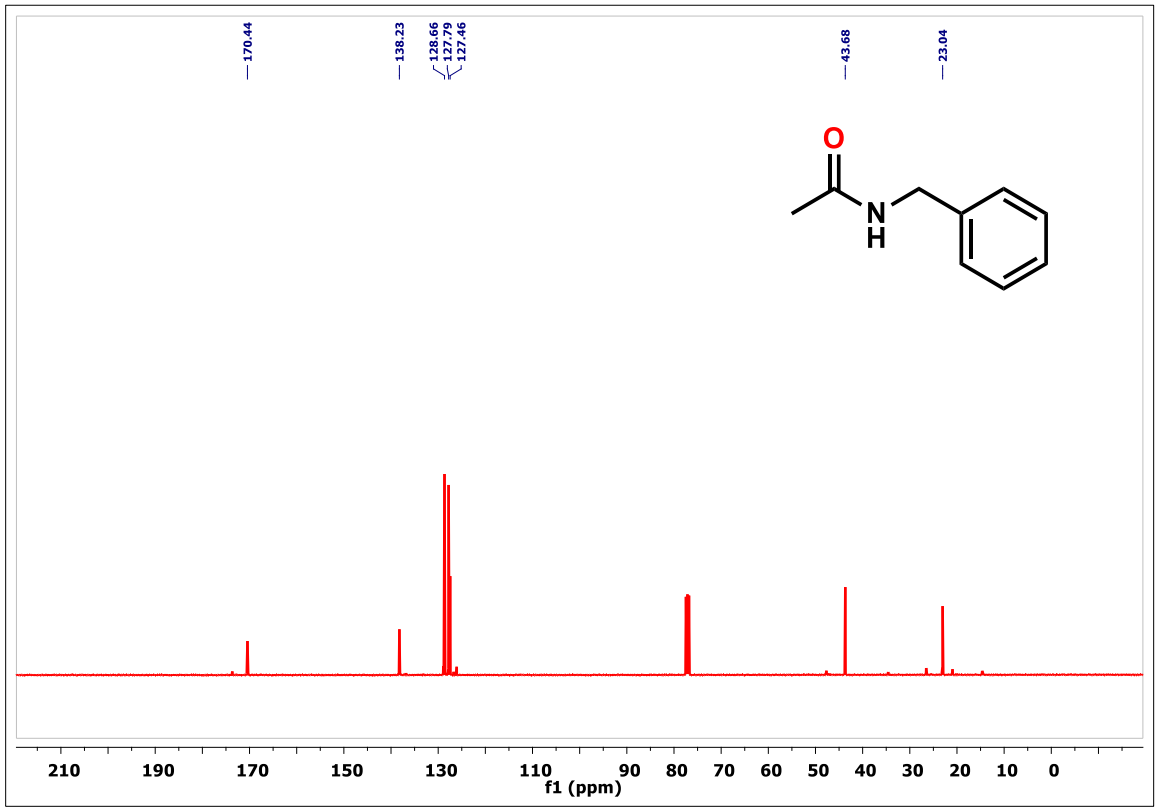

Figure S56: 100 MHz ^{13}C NMR spectrum of **19** in $CDCl_3$

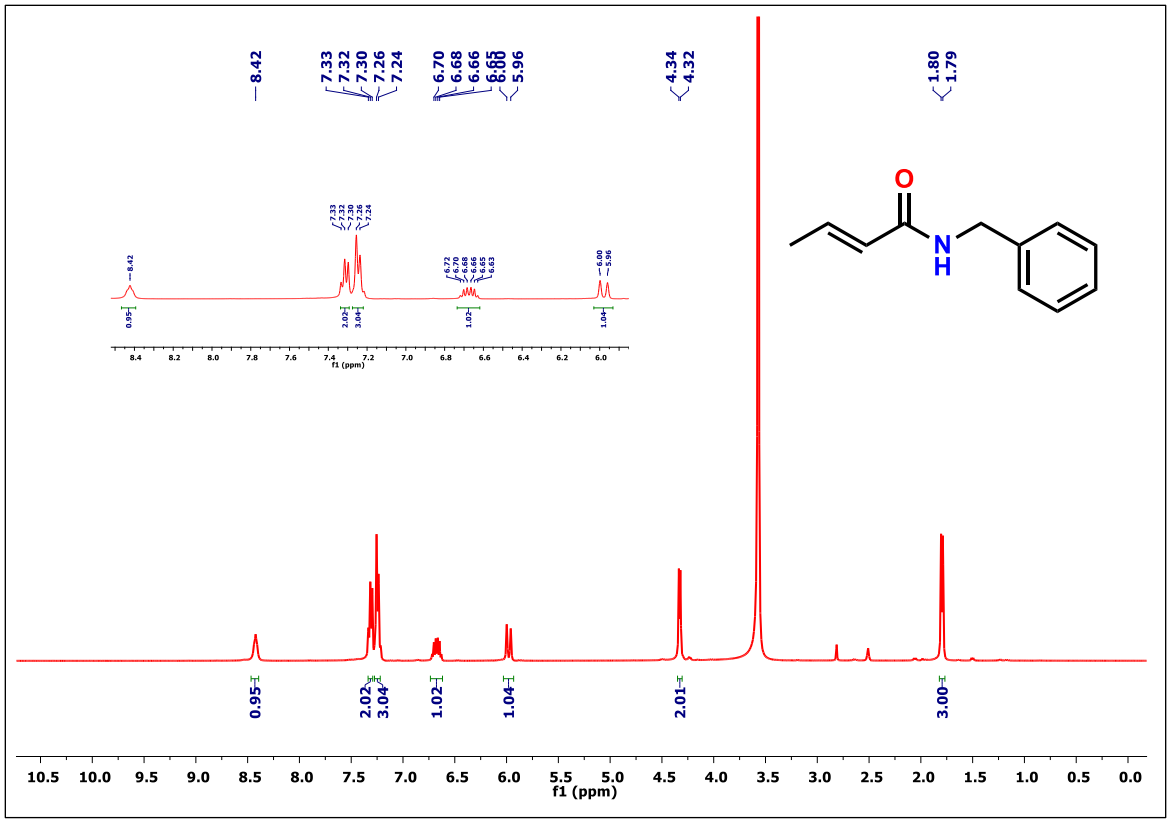

Figure S57: 100 MHz ^{13}C NMR spectrum of **20** in DMSO-d_6

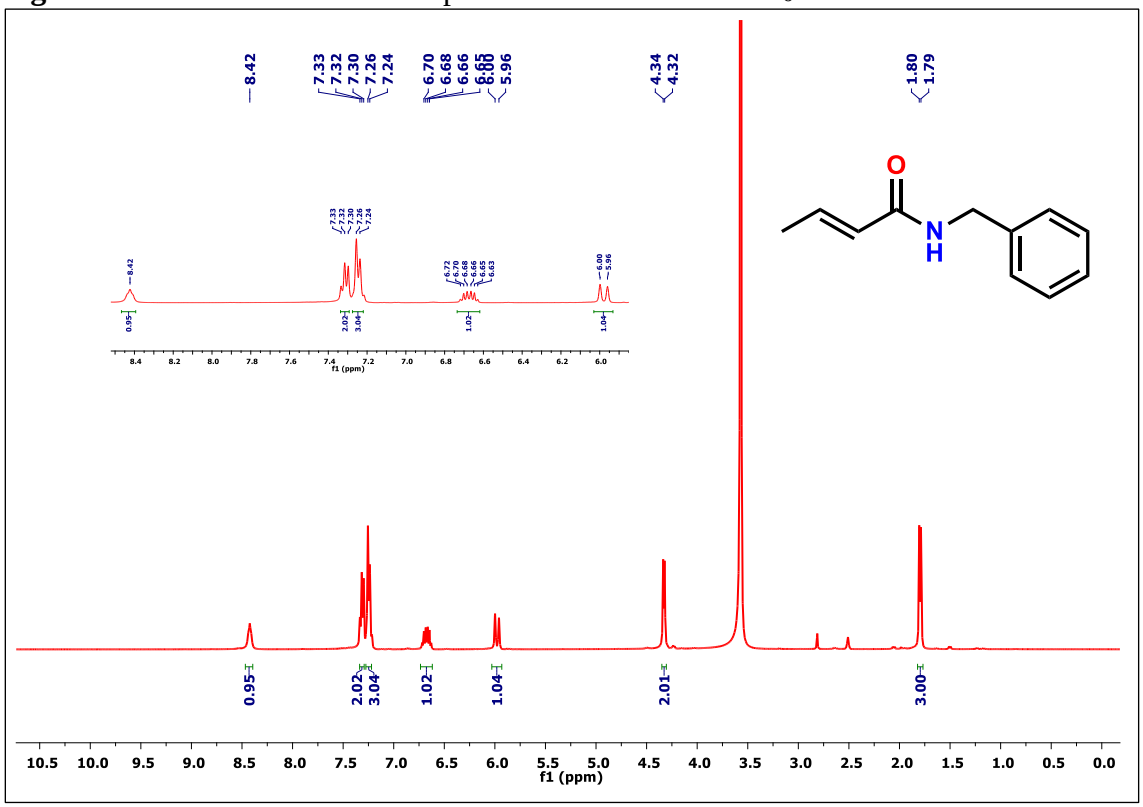

Figure S58: 100 MHz ^{13}C NMR spectrum of **20** in DMSO-d_6

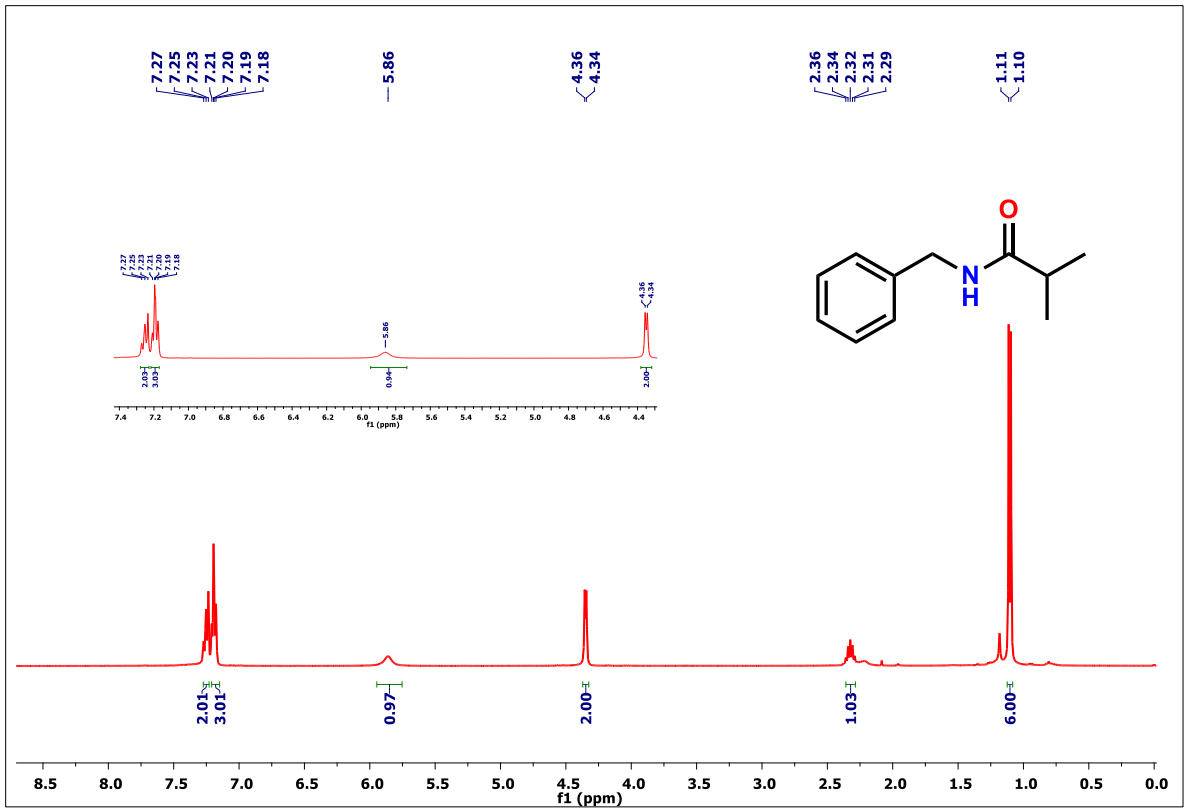

Figure S59: 400 MHz ^{1}H NMR spectrum of **21** in $CDCl_3$

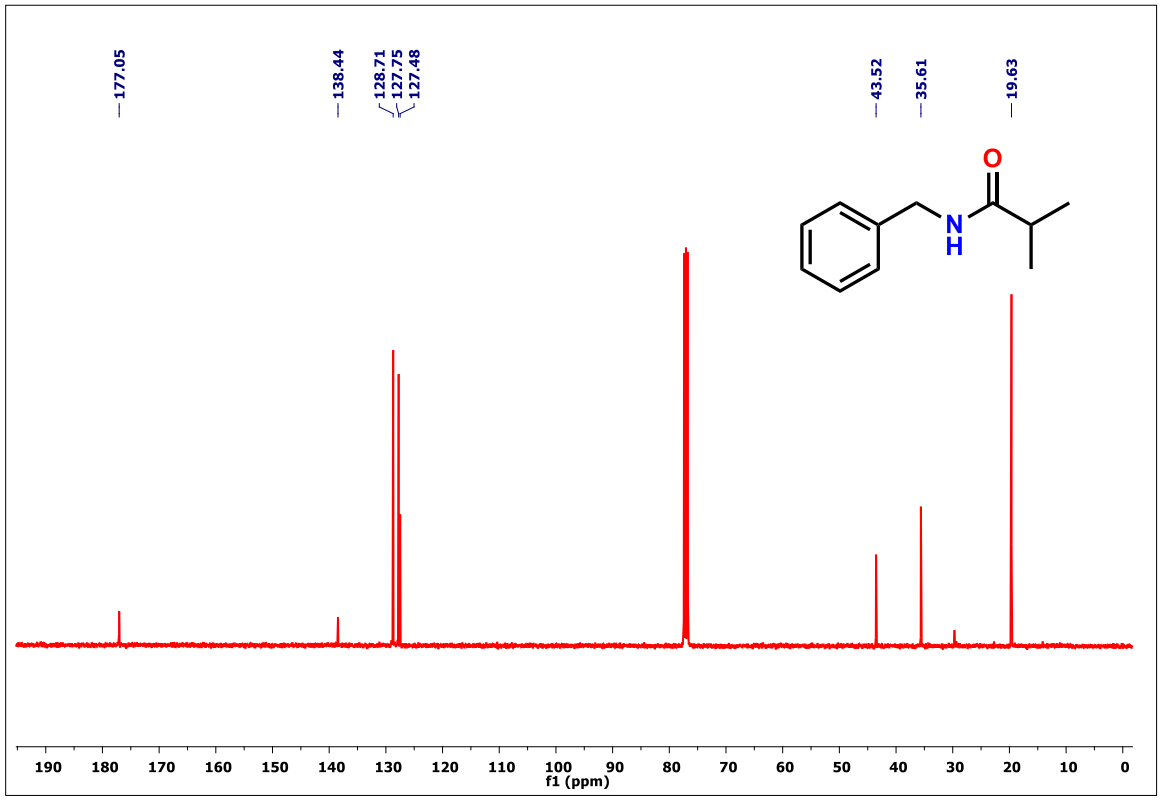

Figure S60: 100 MHz ^{13}C NMR spectrum of **21** in $CDCl_3$

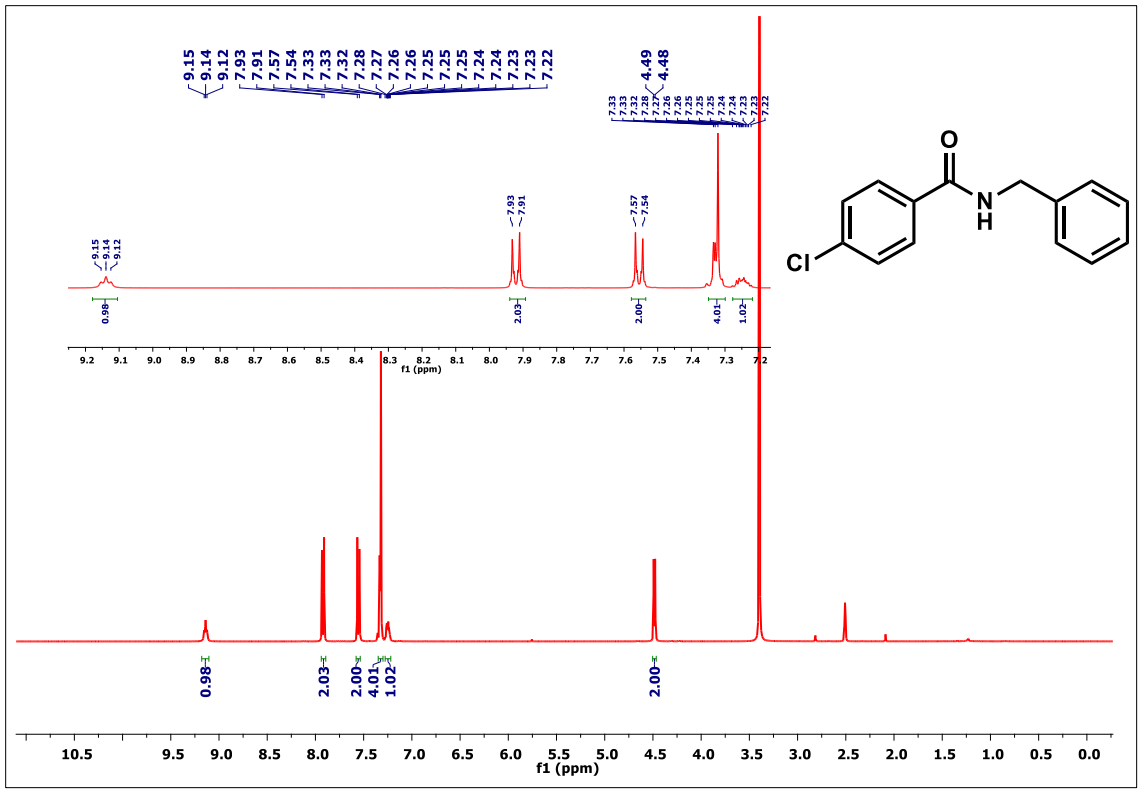

Figure S61: 400 MHz ^{1}H NMR spectrum of **22** in DMSO-d_6

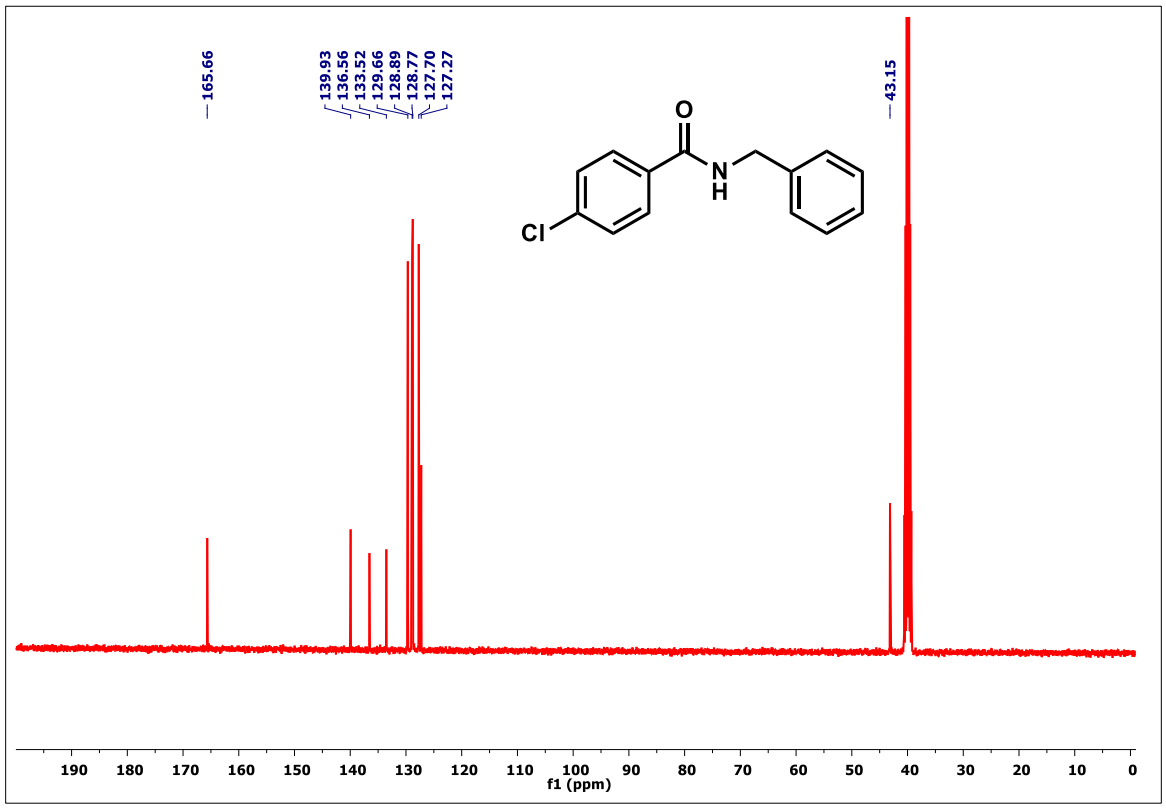

Figure S62: 100 MHz ^{13}C NMR spectrum of **22** in DMSO-d_6

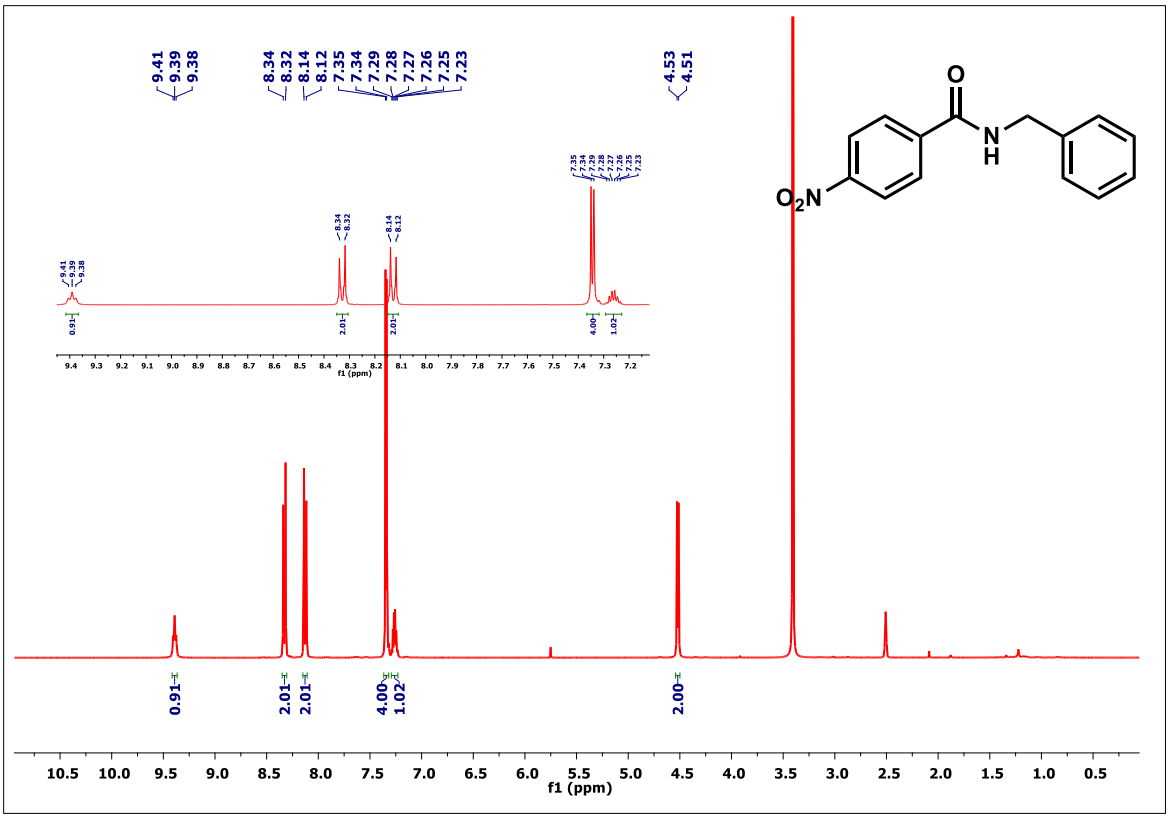

Figure S63: 400 MHz ^{1}H NMR spectrum of **23** in DMSO-d$_6$

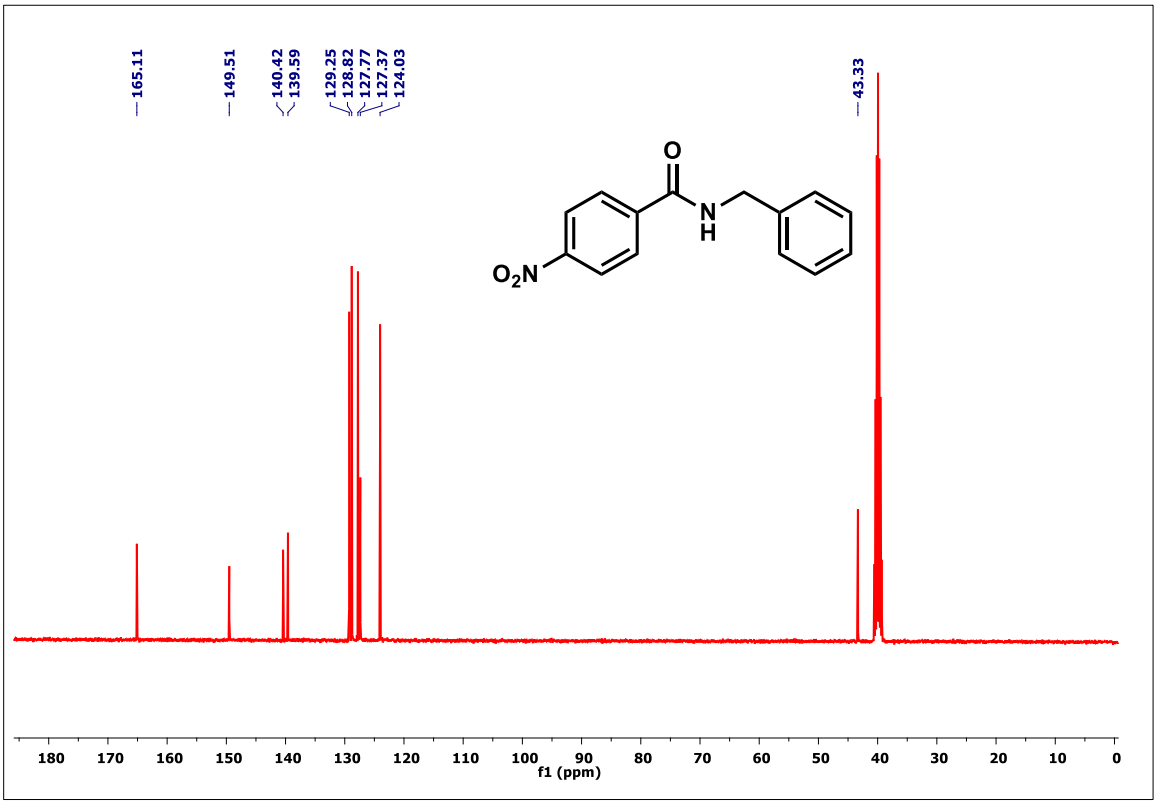

Figure S64: 100 MHz ^{13}C NMR spectrum of **23** in DMSO-d$_6$

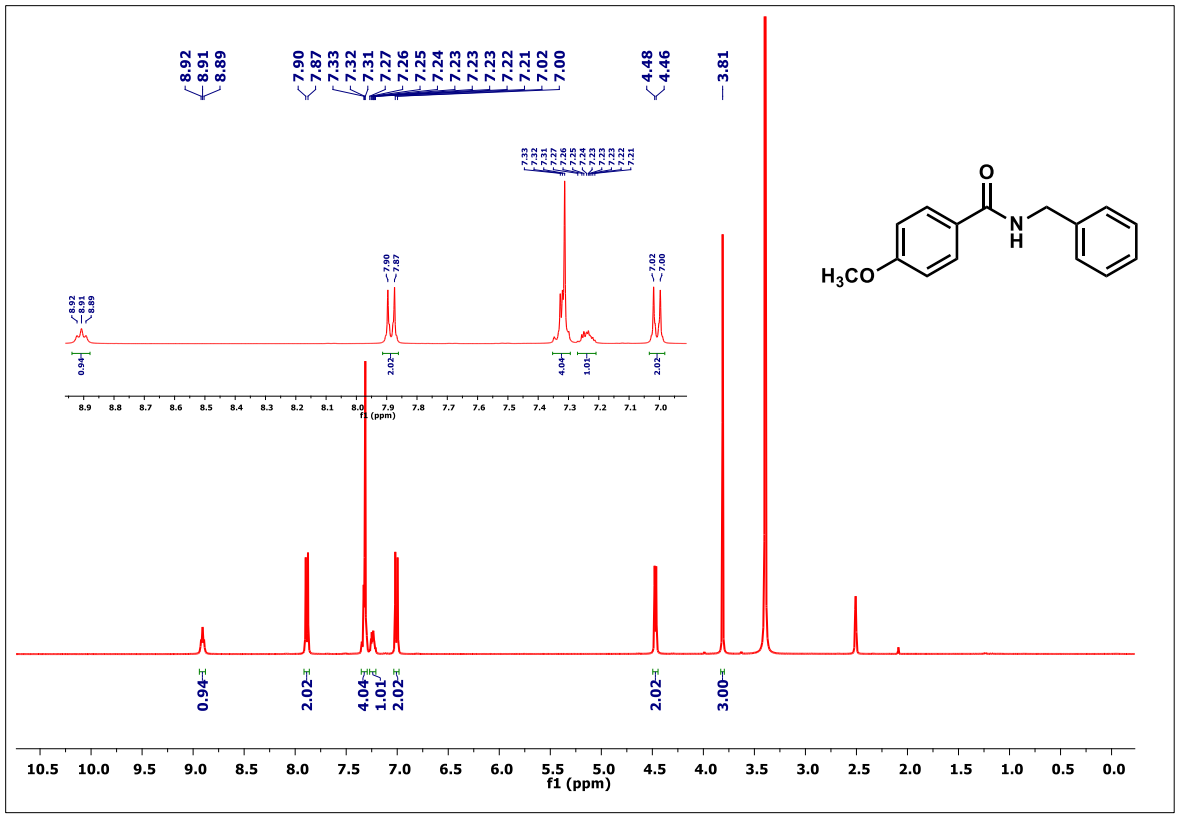

Figure S65: 400 MHz ^{1}H NMR spectrum of **24** in DMSO-d_6

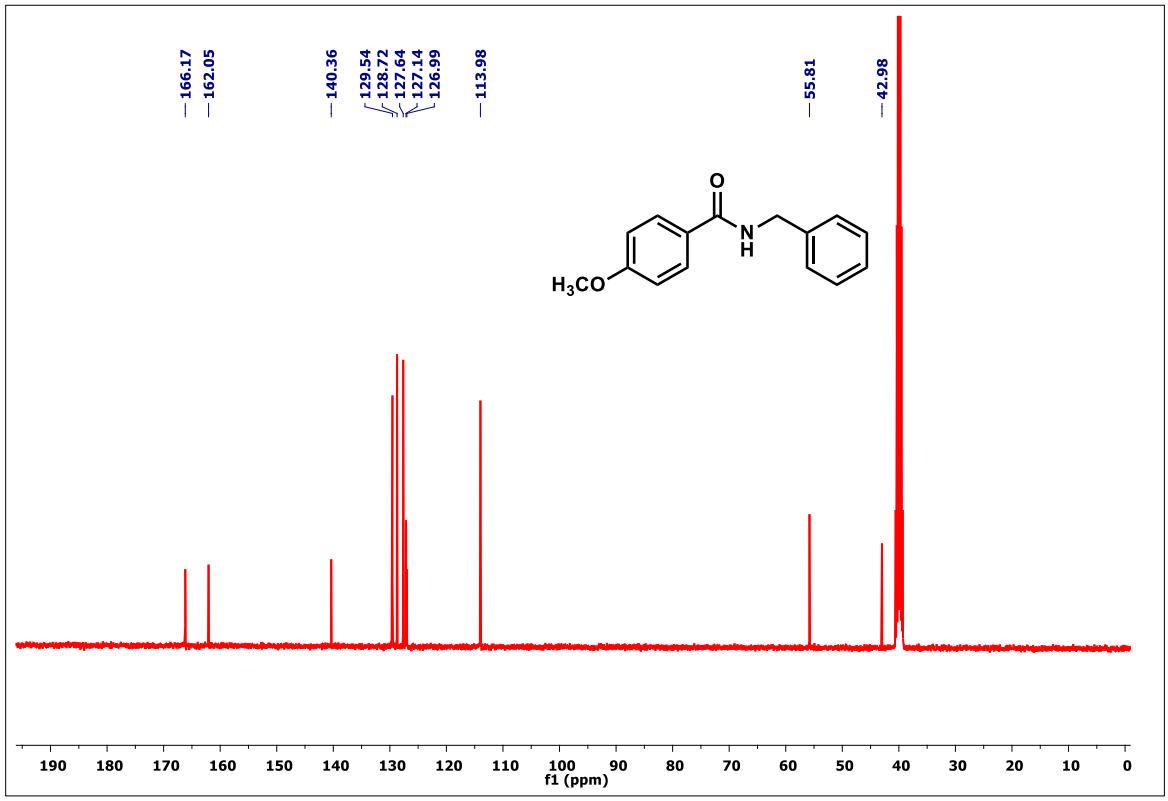

Figure S66: 100 MHz ^{13}C NMR spectrum of **24** in DMSO-d_6

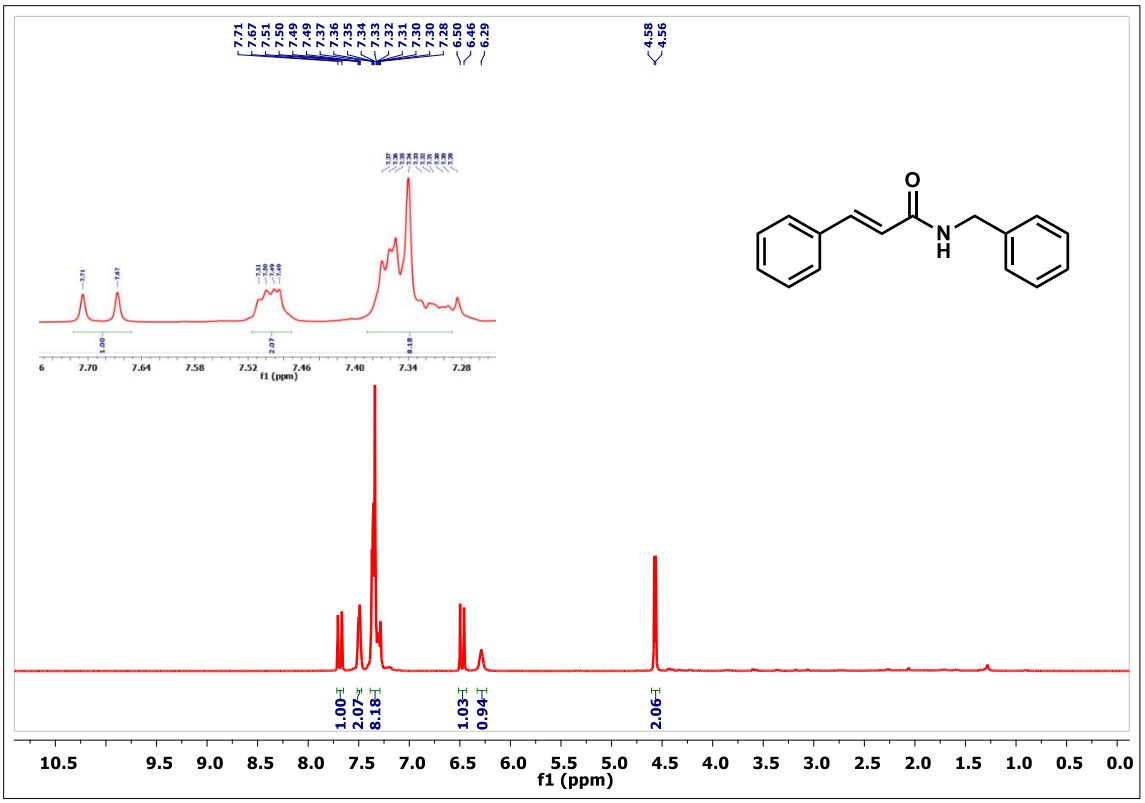

Figure S67: 400 MHz ^{1}H NMR spectrum of **25** in $CDCl_3$

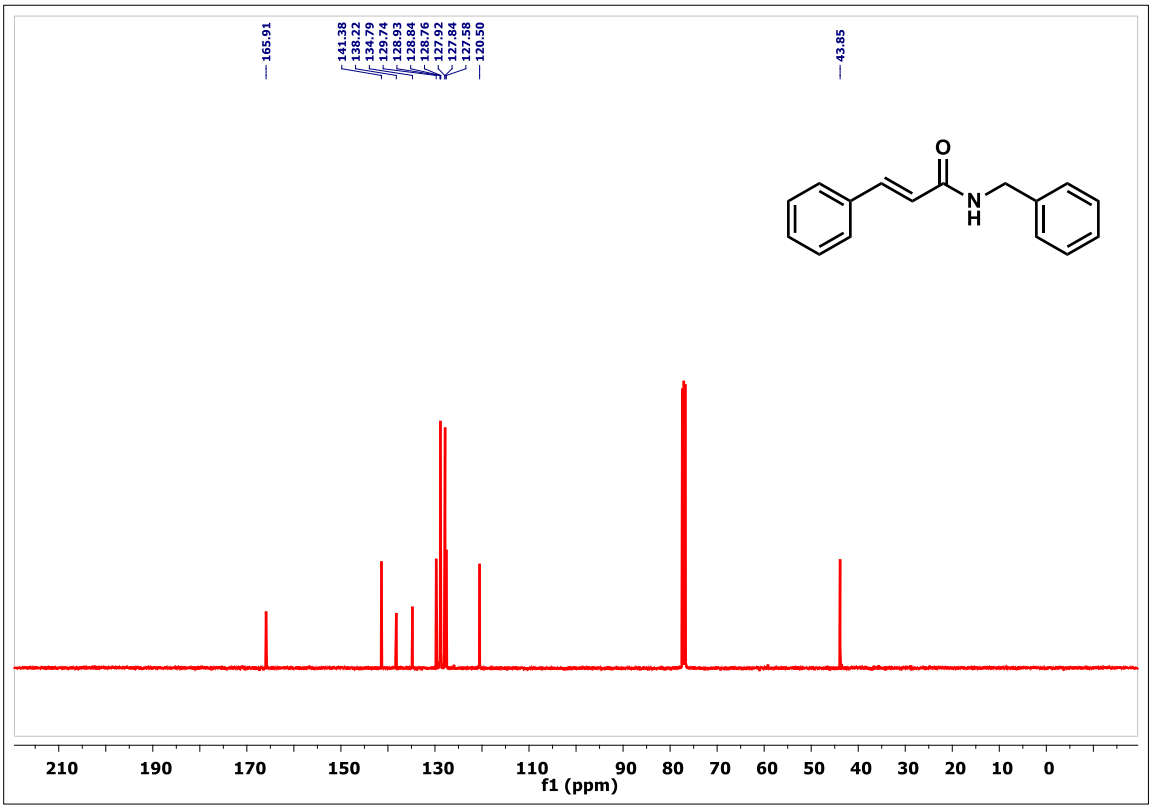

Figure S68: 100 MHz ^{13}C NMR spectrum of **25** in $CDCl_3$

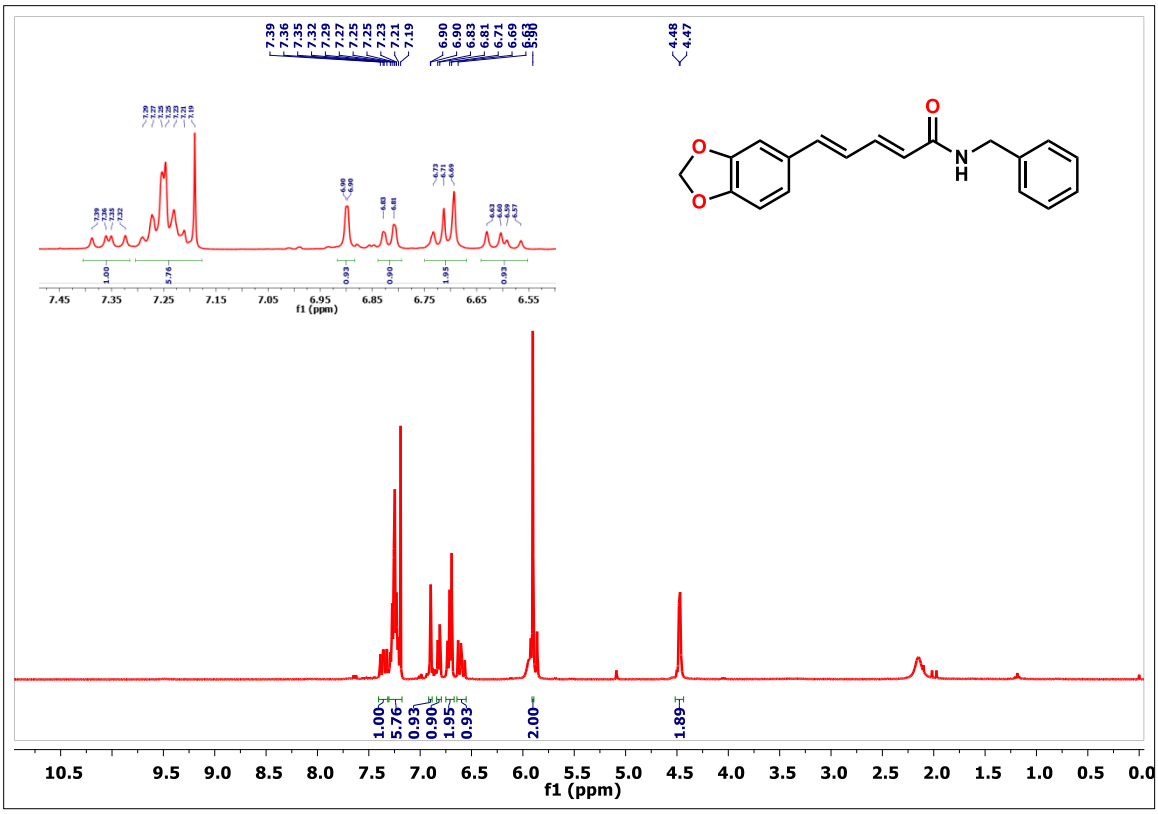

Figure S69: 400 MHz ^{1}H NMR spectrum of **26** in $CDCl_3$

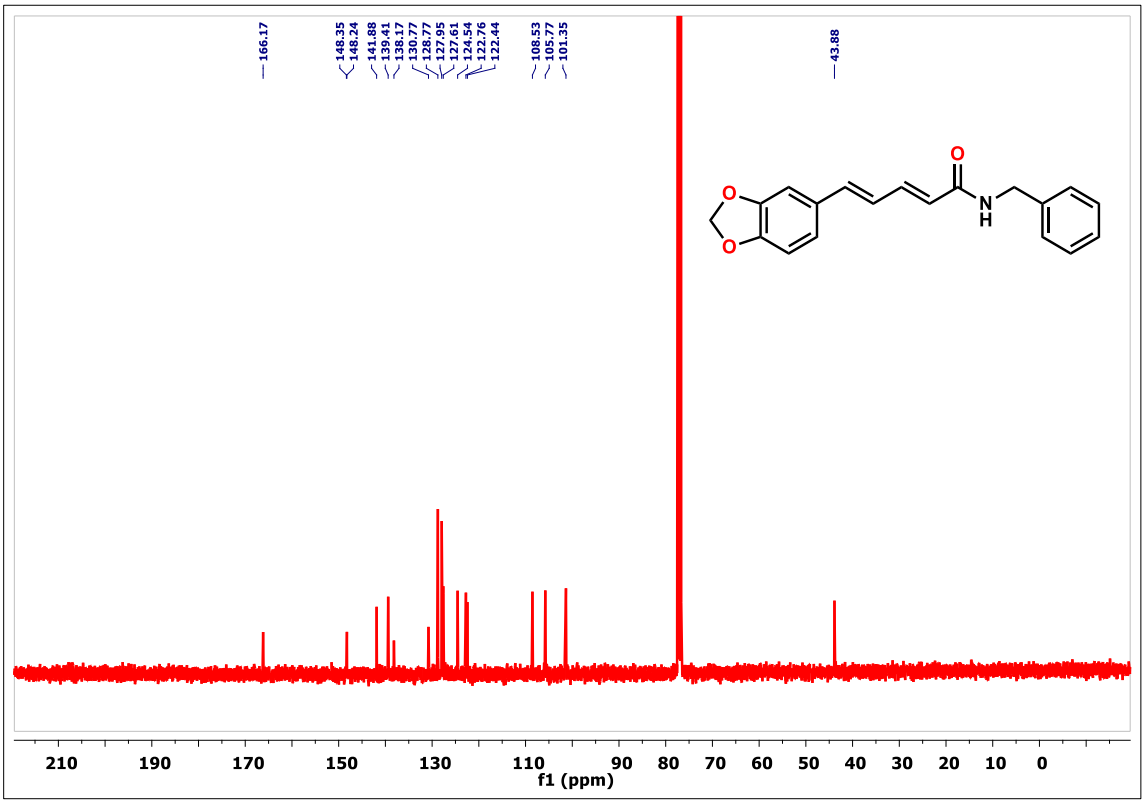

Figure S70: 100 MHz ^{13}C NMR spectrum of **26** in $CDCl_3$

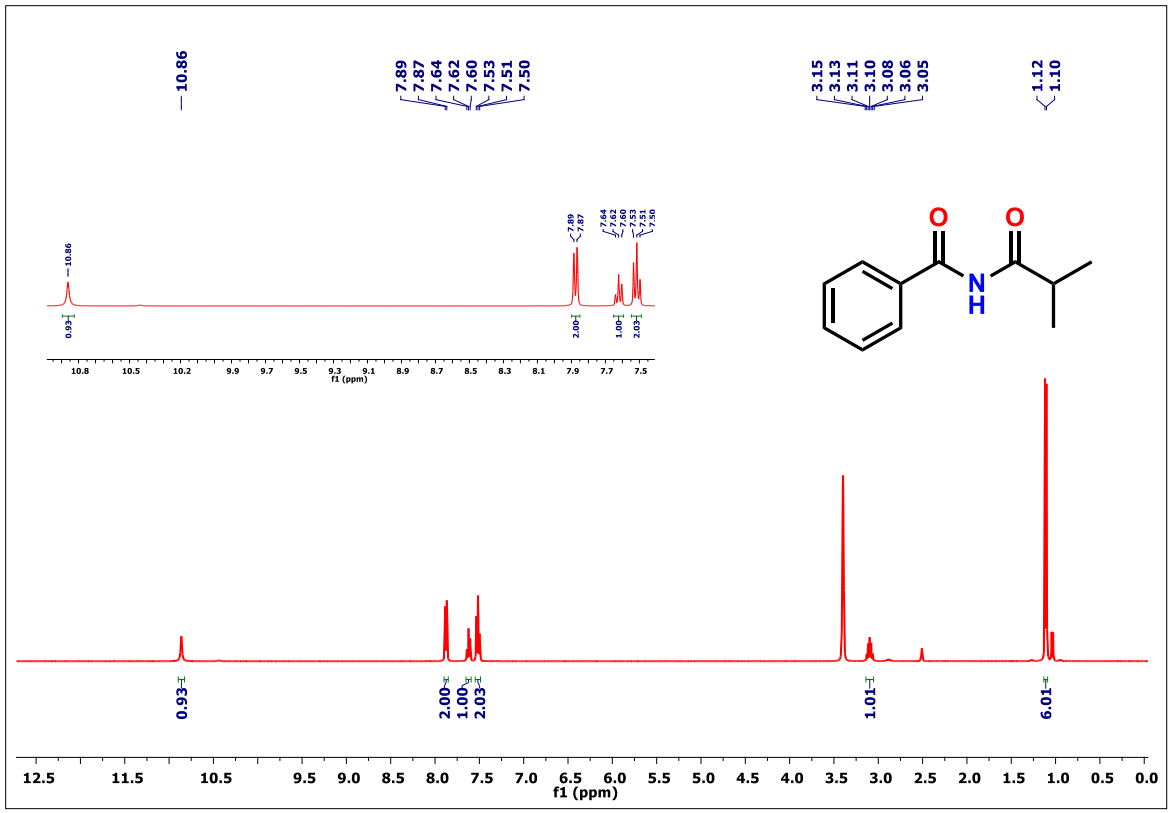

Figure S71: 400 MHz ^{1}H NMR spectrum of **27** in DMSO-d$_6$

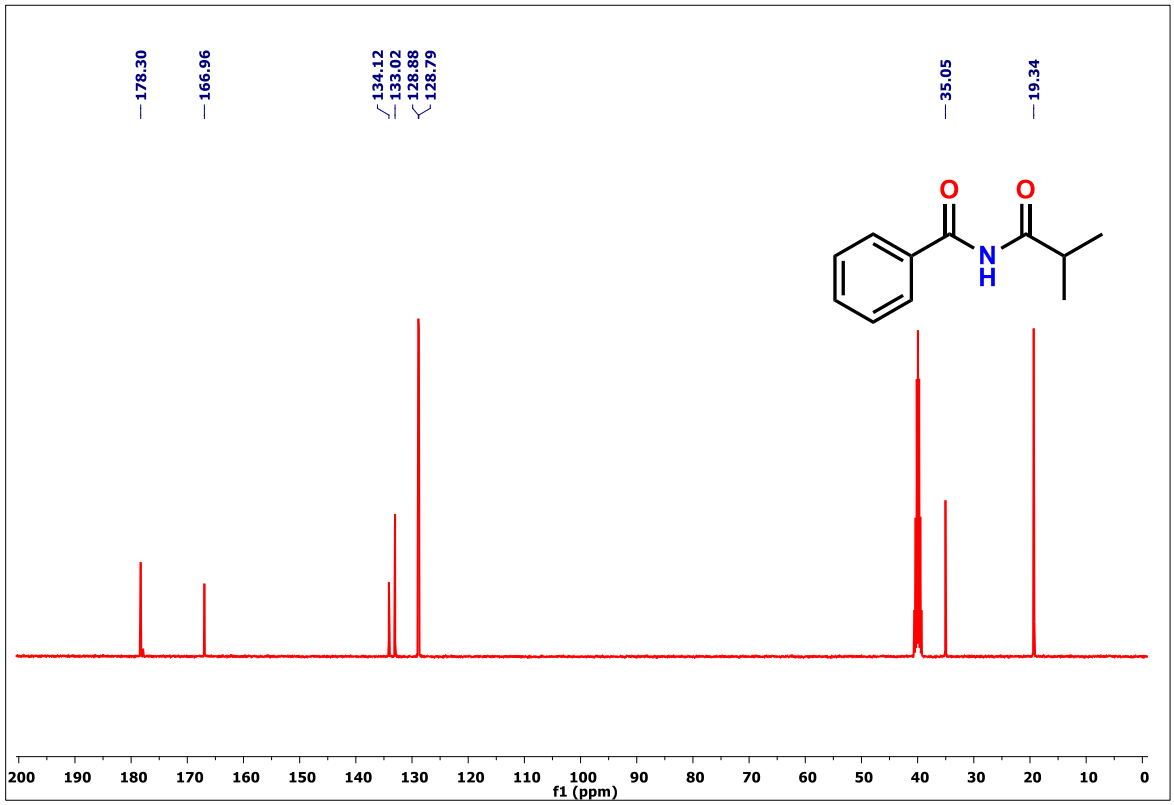

Figure S72: 100 MHz ^{13}C NMR spectrum of **27** in DMSO-d$_6$

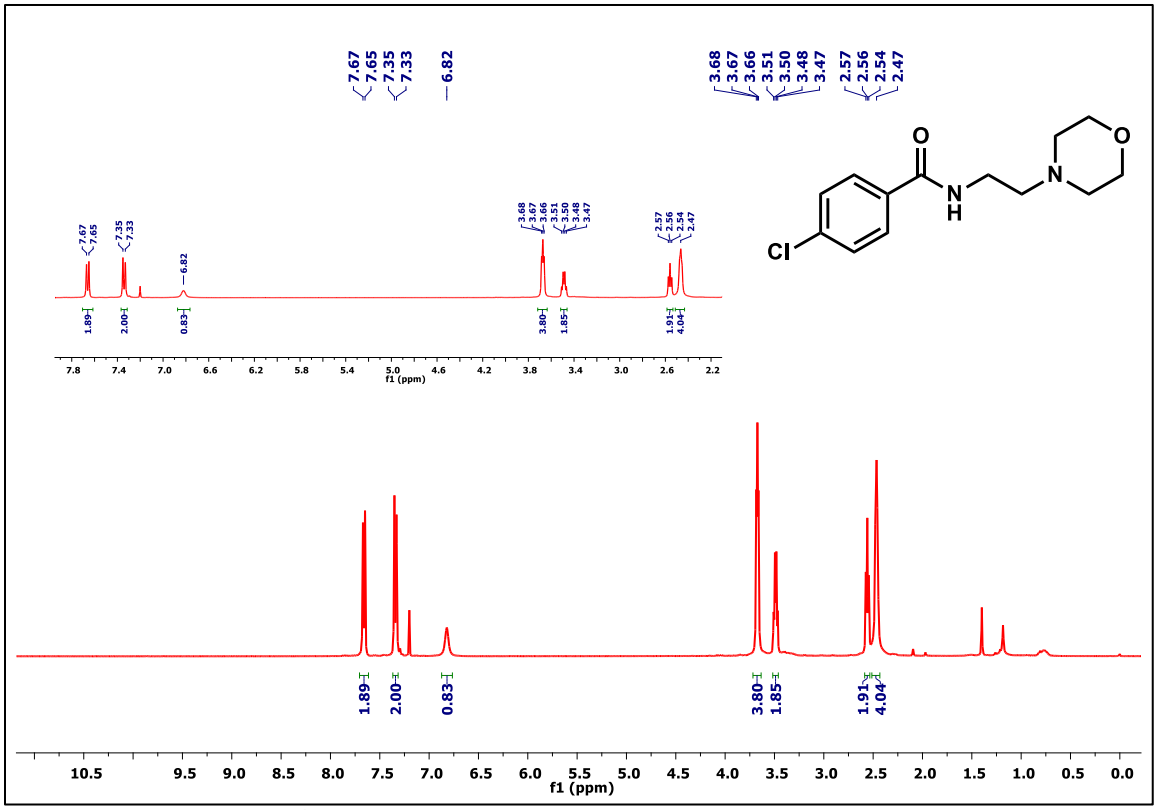

Figure S73: 400 MHz ^{1}H NMR spectrum of **28** in $CDCl_3$

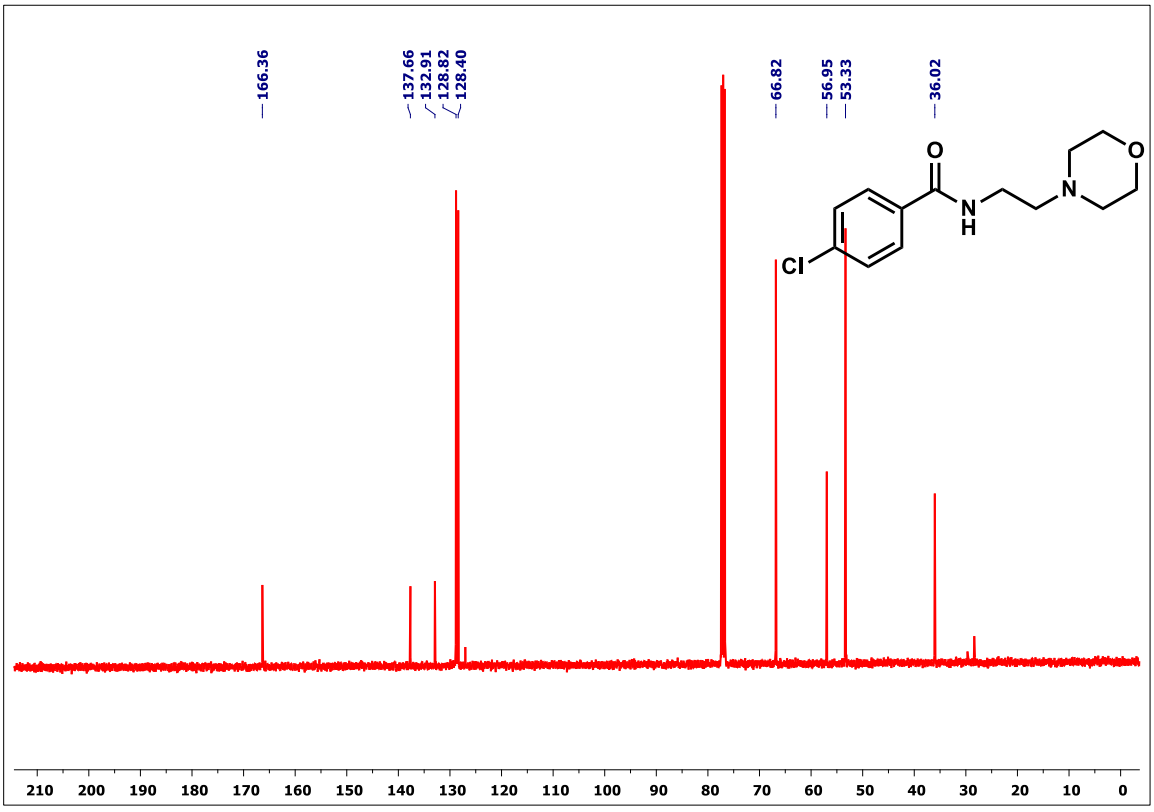

Figure S74: 100 MHz ^{13}C NMR spectrum of **28** in $CDCl_3$

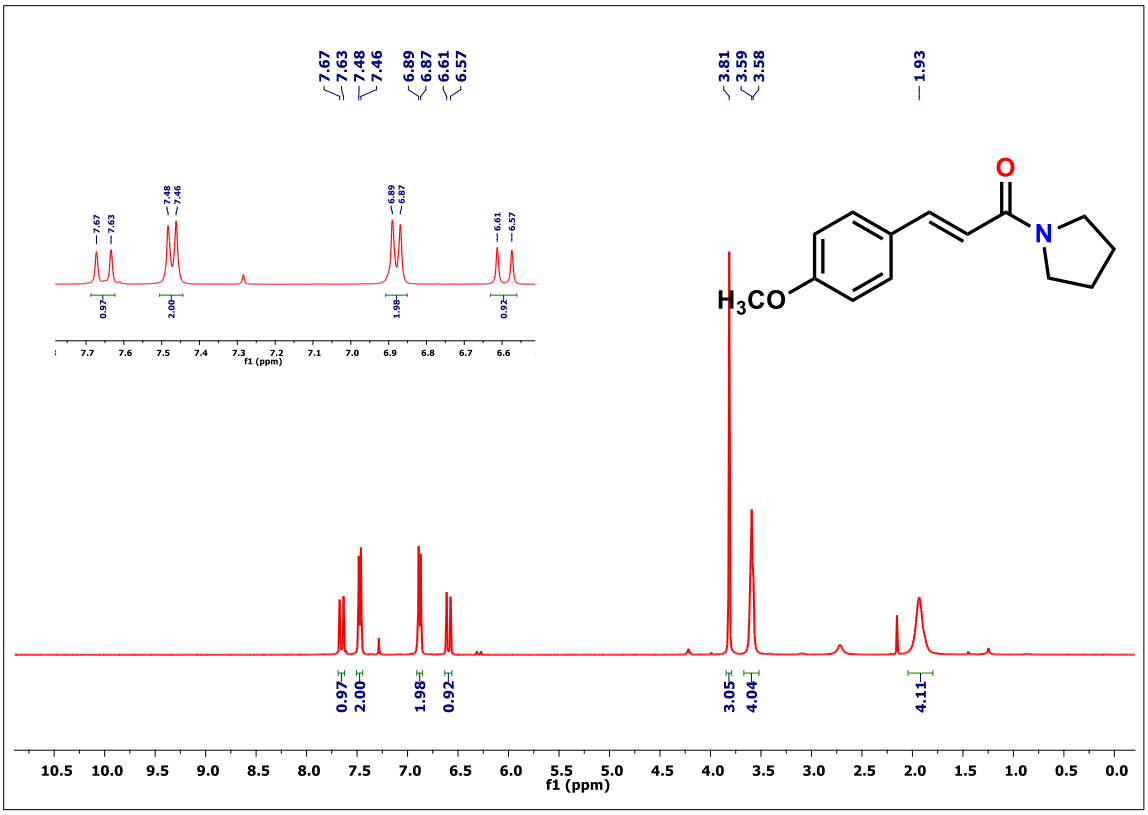

Figure S75: 400 MHz ^{1}H NMR spectrum of **29** in $CDCl_3$

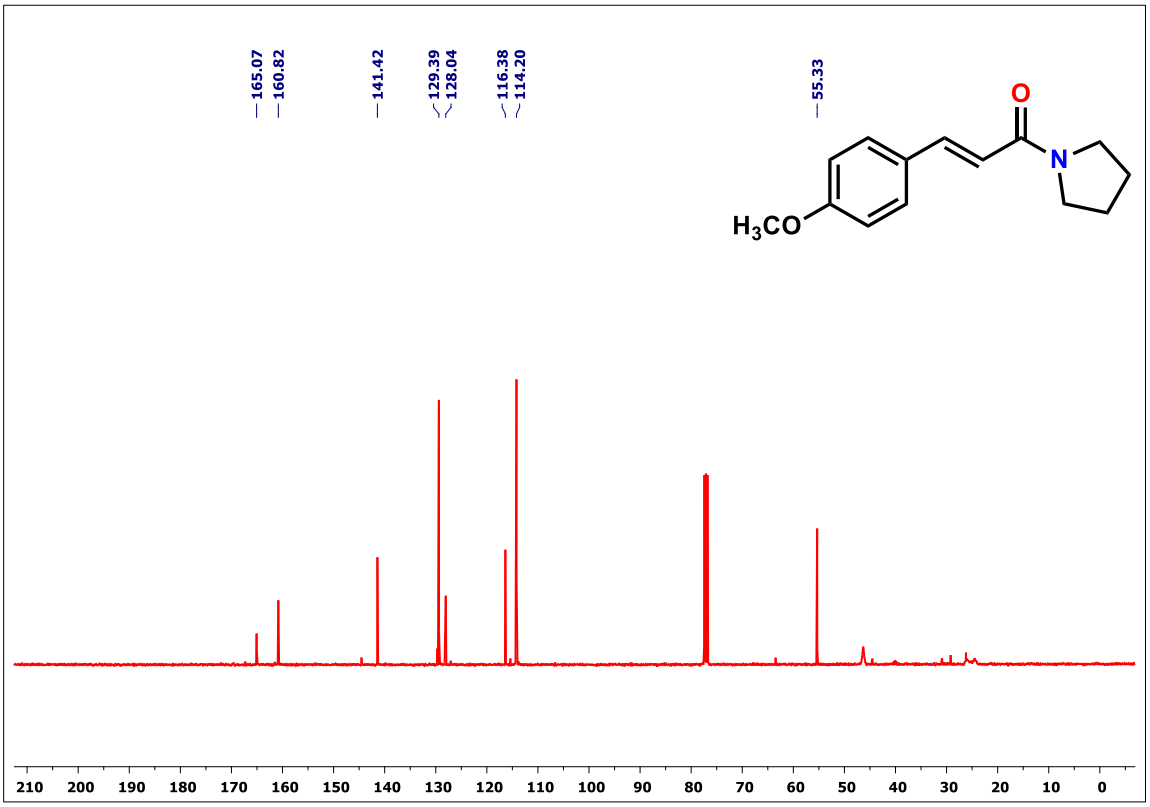

Figure S76: 100 MHz ^{13}C NMR spectrum of **29** in $CDCl_3$

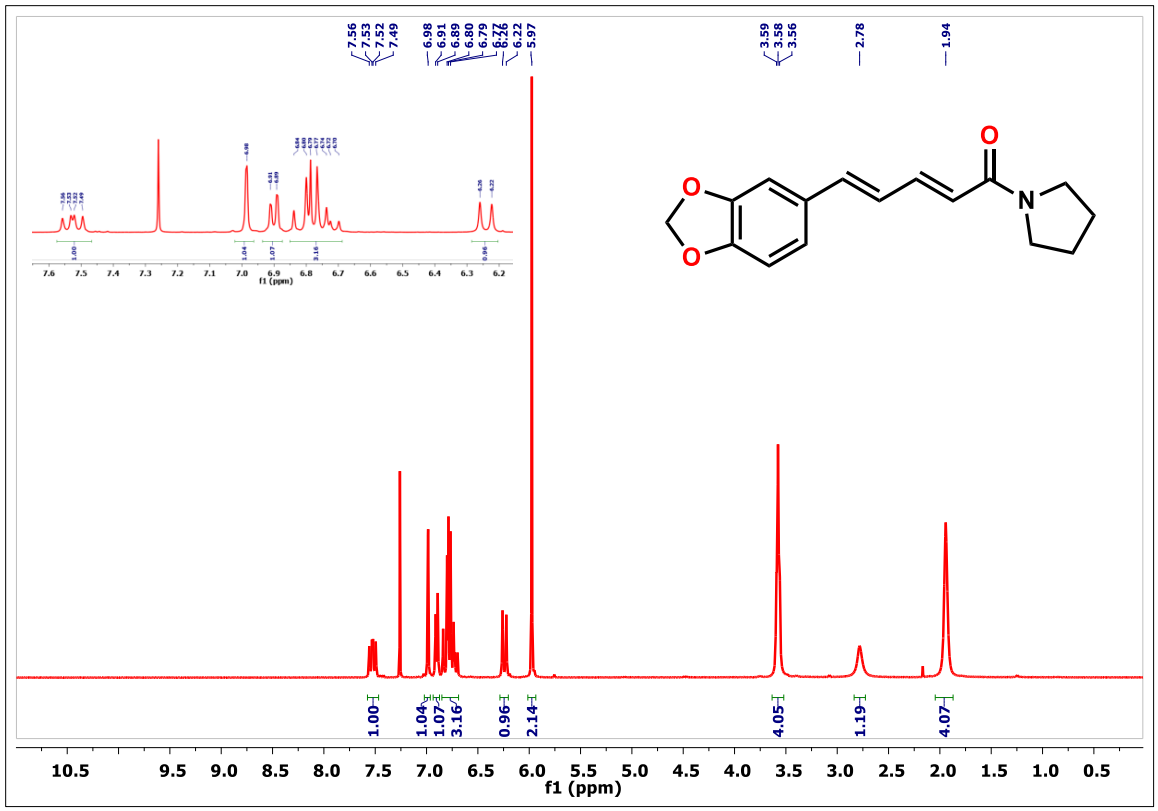

Figure S77: 400 MHz ^{1}H NMR spectrum of **30** in $CDCl_3$

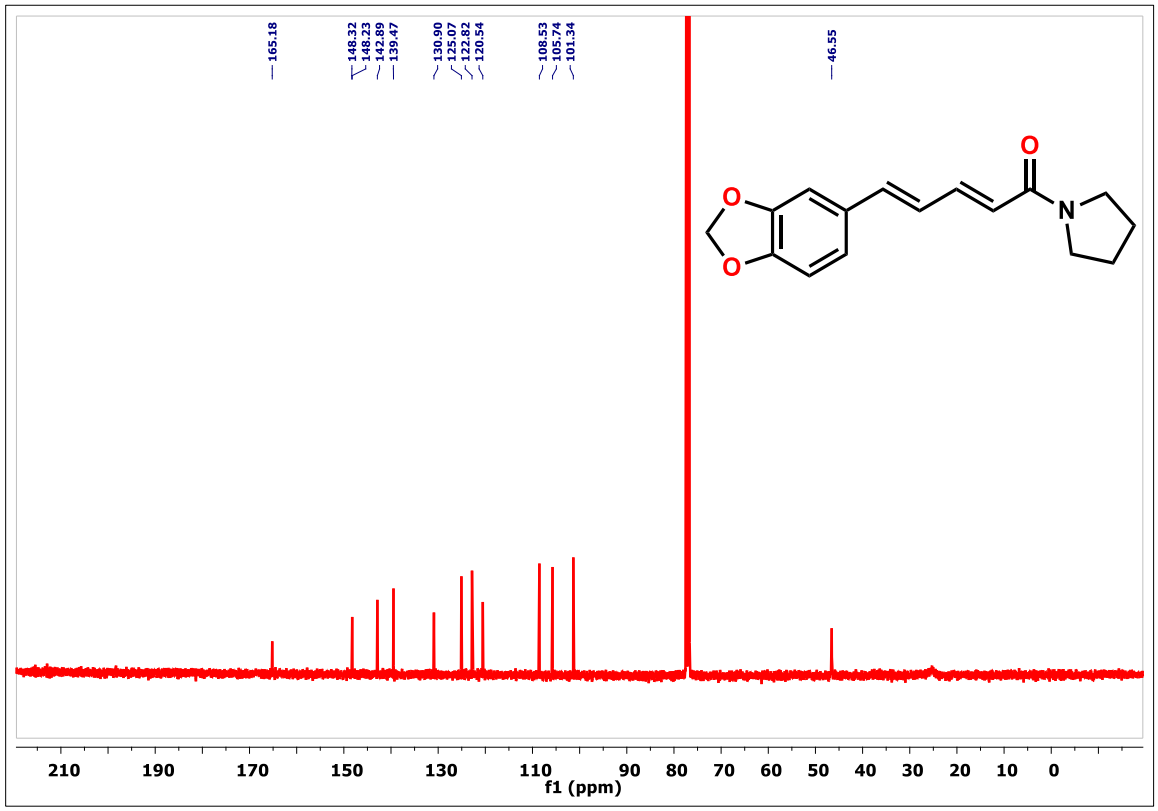

Figure S78: 100 MHz ^{13}C NMR spectrum of **30** in $CDCl_3$