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SUPPORTING INFORMATION

Facile Preparation of Pyrimidinediones and Thioacrylamides by Reductive Functionalization of Amides

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Instrumentation

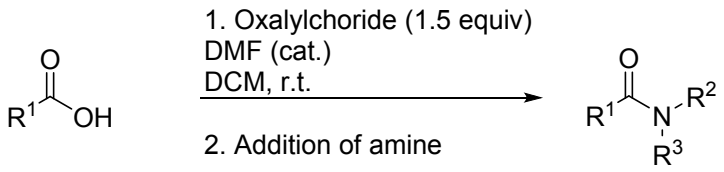
Characterizations were made by ^{1}H and ^{13}C NMR spectroscopy. NMR spectra (1D and 2D) were recorded at Bruker 400 (^{1}H) and 100 MHz (^{13}C) and were referenced internally with $CDCl_3$ (δH 7.26, δC 77.16 ppm) and $(CD_3)_2SO$ (δH 2.50, δC 39.52 ppm). High temperature NMR were recorded at Bruker 500 (^{1}H) and 125 MHz (^{13}C) and were referenced internally with $(CD_3)_2SO$ (δH 2.50, δC 39.52 ppm). High resolution mass spectroscopy (HRMS) was performed on Bruker microTOF/ESI masspectrometer.

Material

Unless otherwise noted, materials were purchased from commercial suppliers and were used without purification. $Mo(CO)_6$, sublimed 99.9+% was purchased from Sigma-Aldrich and used as received.

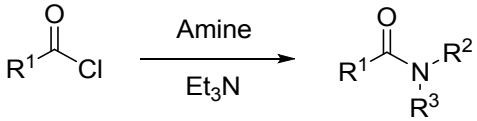
Preparation of Amides

Method A:[1]



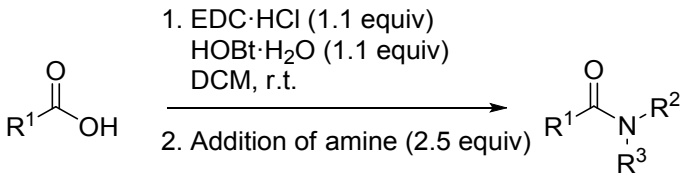
Carboxylic acid was suspended in dichloromethane and a few drops of DMF in a round bottom flask fitted with rubber septa. The reaction vessel was connected to a manifold with a flow of nitrogen and oxalylchloride (1.5 equiv) was slowly added. Upon completion of gas evolution amine (1.5 equiv) was added slowly and the reaction was stirred until completion (checked with TLC). The crude reaction mixture was extracted three times with HCl (1M) and three times with KOH (2M) and the organic phase was dried using anhydrous sodium sulphate. The solvent was evaporated under reduced pressure and the crude amide products were purified using either manual flash column chromatography or on an ISCO Combiflash using EtOAc and pentane as eluent.

Method B:[2]



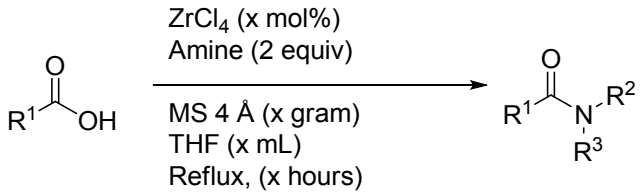
Amine and Et_3N (1.2 equiv) were dissolved in dichloromethane and commercially available acid chloride (1.2 equiv) was slowly added at r.t. The reaction was followed by TLC and upon completion extracted with HCl (1M) and KOH (2M) three times each. The organic phase was dried using sodium sulphate and concentrated under reduced pressure. The crude amide products were purified using either manual flash column chromatography or on an ISCO Combiflash using EtOAc and pentane as eluent.

Method C:[3]



Carboxylic acid was suspended in dichloromethane and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl) (1.1 equiv) was added followed by 1-hydroxybenzotriazole hydrate (HOBt·H_2O) (1.1 equiv). After 5 minutes the amine (2.5 equiv) was added dropwise and the reaction was allowed to stir overnight. An aqueous solution of citric acid (10 wt%) was added and the reaction was stirred for 30 min before the crude was filtered off. The crude reaction mixture was extracted three times with aqueous solution of citric acid (10 wt%), three times with saturated aqueous solution of $NaHCO_3$ three times with KOH (2M) and the organic phase was dried using anhydrous sodium sulphate. The solvent was evaporated under reduced pressure and the crude amide products were purified using either manual flash column chromatography or on an ISCO Combiflash using EtOAc and pentane as eluent.

Method D:[4]



Carboxylic acid, $ZrCl_4$ and molecular sieves (4 Å) were added to a round bottom flask which was fitted with a condenser and a septa. The atmosphere was exchanged to N_2 and THF was added through the septa. The reaction was heated to 70 °C and amine was added. The reaction was stirred for 24 h and the allowed to cool to r.t. The crude reaction was filtered through a pad of silica eluted with ethyl acetate : Et_3N (200 : 1). The solvent was removed under reduced pressure and if required further purification was performed using ISCO Combiflash using EtOAc and pentane as eluent.

General Procedure for the Formation of Enamines

Amide (0.5 mmol) and $Mo(CO)_6$ (0.0027 g, 0.01 mmol) were added to an oven dried 10 mL microwave tube equipped with a magnetic stirring bar. To the sealed tube, dry ethyl acetate (0.5 mL, 1M) was added and the atmosphere was exchanged to N_2 via the septa. The reaction mixture was heated at 80 °C for 10 minutes to activate the catalyst followed by exchange of the atmosphere into N_2 again and was then allowed to reach the optimized reaction temperature (see Table S1). TMDS (0.75 mmol, 0.13 mL) was added and the reaction was run the required amount of time and the ^{1}H NMR yield were determined by using 1,3,5-trimethoxybenzene as internal standard.

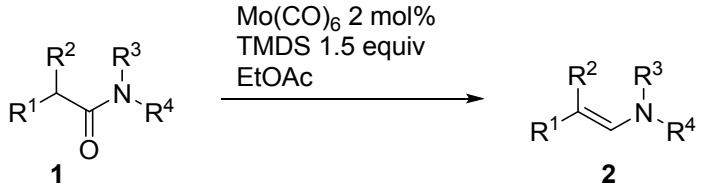
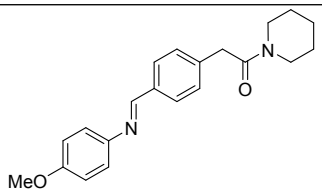
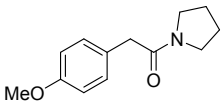
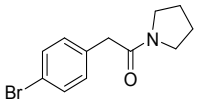
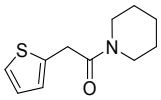
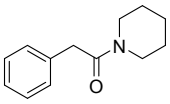
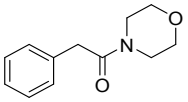
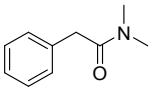


Table S1. Optimized conditions of the enamine formation for different amides.[a]

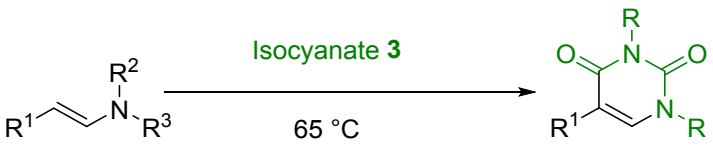
Entry	Amide	Temp [°C]	Time [h]	^{1}H NMR yield of enamine [%][b]
1	**1a**	65	0.5	>95
2	**1b**	65	1	>95
3	**1c**	65	3	>95
4	**1d**	80	2	70
5[c]	**1e**	65	2	85 (full conv.)
6[c]	**1f**	65	2.5	>95
7	**1g**	65	1	>95
8	**1h**	40	5	89

9	**1i**		65	4	>95
10	**1j**		65	1	>95
11	**1k**		65	3	>95
12	**1l**		65	3	>95
13	**1m**		65	1	>95
14	**1n**		65	3	>95
15	**1o**		65	1	>95

[a] $Mo(CO)_6$ (2 mol%), amide **1** (0.5 mmol), dried EtOAc (0.5 mL, 1M), TMDS (1.5 equiv), reaction temperature 65 °C. [b] Determined by ^1H NMR with 1,3,5-trimethoxy benzene as internal standard. [c] $Mo(CO)_6$ (5 mol%) was used.

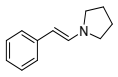
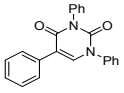
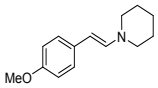
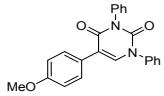
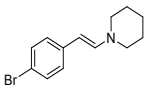
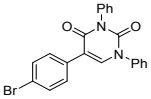
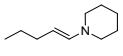
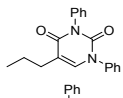
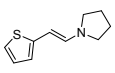
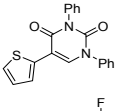
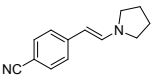
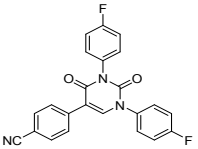
General Procedure for the Formation of 1,3-Disubstituted Pyrimidines 4

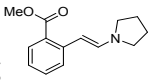
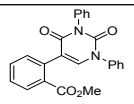
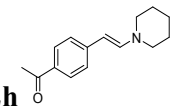
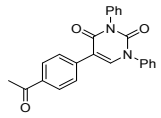
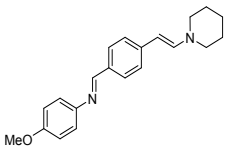
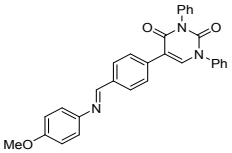
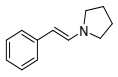
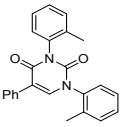
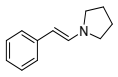
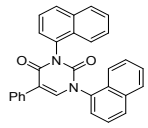
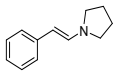
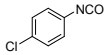
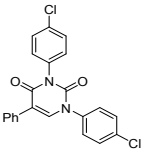
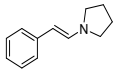
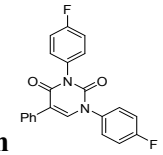
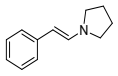
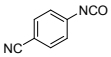
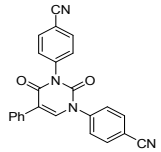
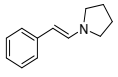
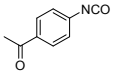
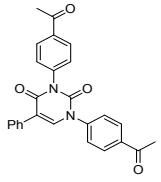
Amide (1.0 mmol) and $Mo(CO)_6$ (0.0054 g, 0.02 mmol) were added to an oven dried 10 mL microwave tube equipped with a magnetic stirring bar. To the sealed tube, dry ethyl acetate (1.0 mL, 1M) was added and the atmosphere was exchanged to N_2 via the septa. The reaction mixture was heated at 80 °C for 10 minutes to activate the catalyst followed by exchange of the atmosphere into N_2 again and was then allowed to reach the optimized reaction temperature (see Table S1). TMDS (1.5 mmol, 0.26 mL) was added and the reaction was run the required amount of time to form the corresponding enamine. To the crude reaction isocyanate **3** (2.2 equiv) was added. The reaction was stirred at 65 °C for 4 h and then cooled. Pentane was added to the reaction crude and the mixture was cleaned by removal and replacement of the pentane 10 times. The resulting residue was pure 1,3-disubstituted pyrimidine without need for further purification.



2 **4**

Table S2. Optimized conditions of the cyclization of enamines with different isocyanates to form 1,3-disubstituted pyrimidines.[a]

Entry	Enamine	Isocyanate	1,3-disubstituted pyrimidine	Isolated yield [%]
1	**2a** 	**3a** 	**4a** 	75
2	**2b** 	**3a** 	**4b** 	92
3	**2c** 	**3a** 	**4c** 	76
4	**2d** 	**3a** 	**4d** 	57
5	**2e** 	**3a** 	**4e** 	85
6[b]	**2f** 	**3e** 	**4f** 	85

7[c]	**2g** 	**3a** 	**4g** 	64
8[c]	**2h** 	**3a** 	**4h** 	71
9[c,d]	**2i** 	**3a** 	**4i** 	76
10	**2a** 	**3b** 	**4j** 	40
11[c]	**2a** 	**3c** 	**4k** 	83
12[d]	**2a** 	**3d** 	**4l** 	75
13	**2a** 	**3e** 	**4m** 	94
14[c,d]	**2a** 	**3f** 	**4n** 	86
15	**2a** 	**3g** 	**4o** 	84

[a] Isocyanate (2.2 equiv) was added to the *in situ* formed enamine from catalysis at 65 °C and left to react for 4 h, isolation performed on 1 mmol scale. [b] Isocyanate (3.5 equiv), 72 h. [c] Isolation was performed on 0.5 mmol scale. [d] 16 h. [e] Isocyanate (3.0 equiv) was used and the reaction was left at 65 °C overnight.

General Procedure for the Formation of Acryl Thioamides 6

Amide (1.0 mmol) and $Mo(CO)_6$ (0.0054 g, 0.02 mmol) were added to an oven dried 10 mL microwave tube equipped with a magnetic stirring bar. To the sealed tube, dry ethyl acetate (1.0 mL, 1M) was added and the atmosphere was exchanged to N_2 via the septa. The reaction mixture was heated at 80 °C for 10 minutes to activate the catalyst followed by exchange of the atmosphere into N_2 again and was then allowed to reach the optimized reaction temperature (see Table S1). TMDS (1.5 mmol, 0.26 mL) was added and the reaction was run the required amount of time to form the corresponding enamine. To the crude reaction isothiocyanate **5** (1.1 mmol, 1.1 equiv) was added. The reaction was stirred at 65 °C for 16 h and then cooled. Pentane was added to the reaction crude and the mixture was cleaned by removal and replacement of the pentane 10 times. The resulting residue was pure acryl thioamide without need for further purification.

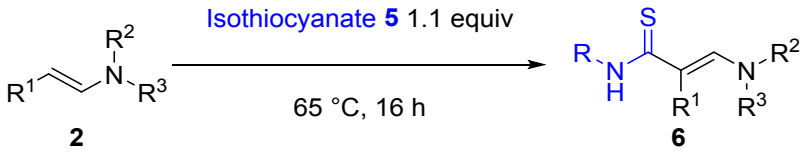
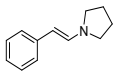
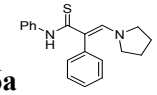
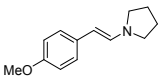
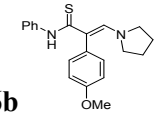
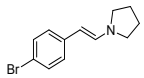
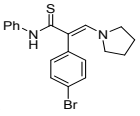
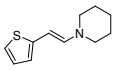
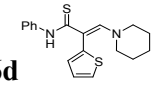
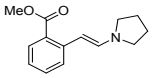
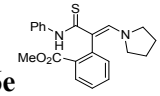
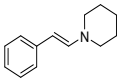
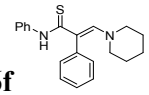
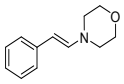
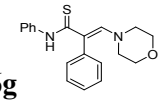
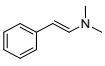
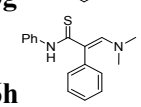
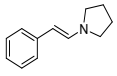
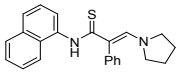
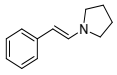
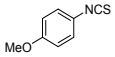
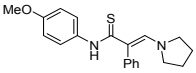
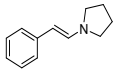
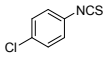
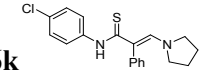
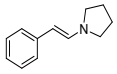
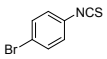
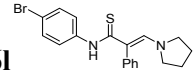
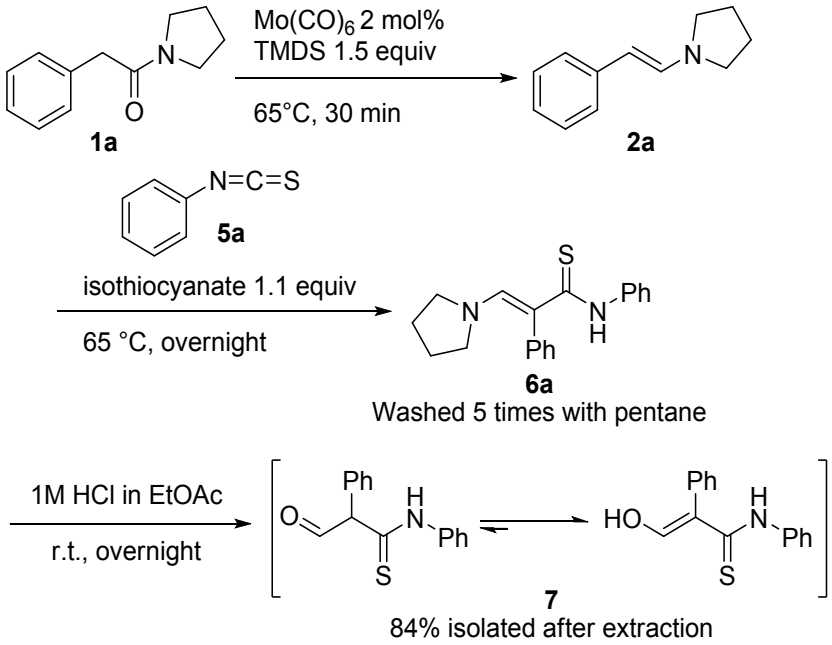


Table S3. Optimized conditions of the cyclization of enamines with different isothiocyanates to form acryl thioamides.[a]

Entry	Enamine	Isothiocyanate	Acryl thioamide	Isolated yield [%]
1	**2a** 	**5a** 	**6a** 	94
2	**2j** 	**5a** 	**6b** 	94
3	**2k** 	**5a** 	**6c** 	75
4	**2l** 	**5a** 	**6d** 	60
5	**2g** 	**5a** 	**6e** 	89
6	**2m** 	**5a** 	**6f** 	67
7	**2n** 	**5a** 	**6g** 	39
8	**2o** 	**5a** 	**6h** 	71
9	**2a** 	**5b** 	**6i** 	83
10	**2a** 	**5c** 	**6j** 	82
11	**2a** 	**5d** 	**6k** 	94
12	**2a** 	**5e** 	**6l** 	97

[a] Isothiocyanate (1.1 equiv) was added to the *in situ* formed enamine from catalysis at 65 °C and left to react for 16 h, isolation performed on 1 mmol scale.

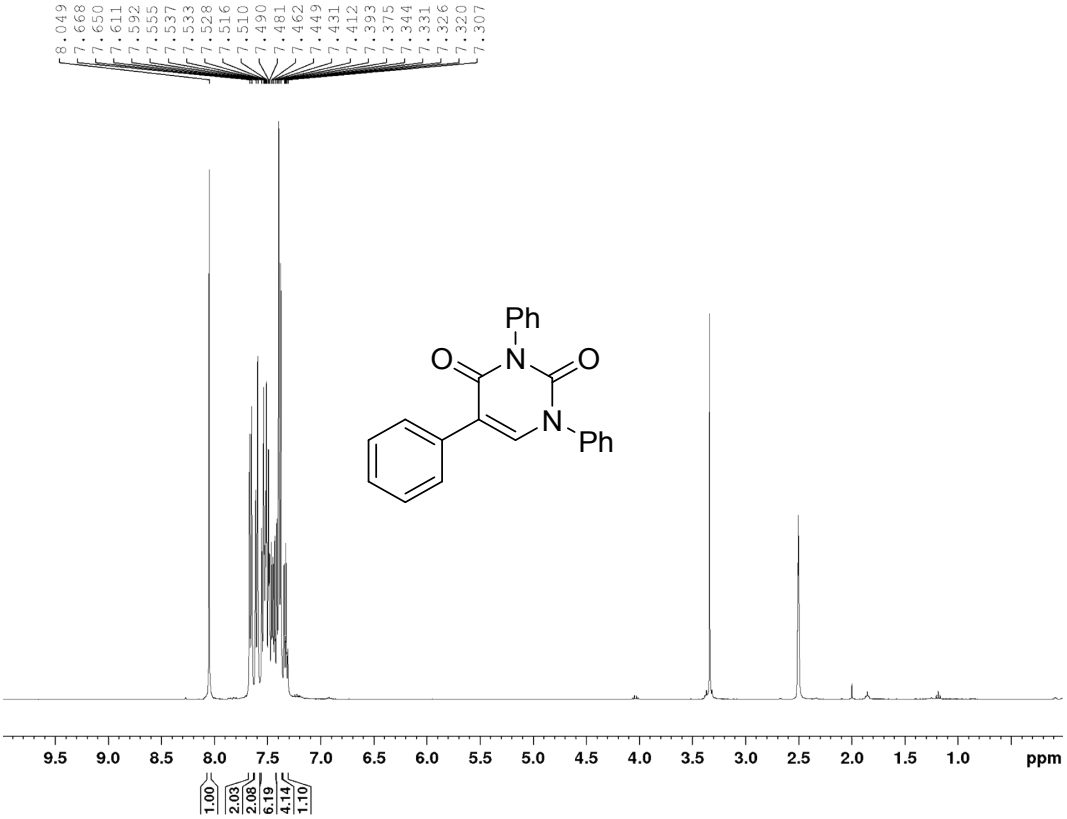
Procedure for the Formation of Aldehyde 7



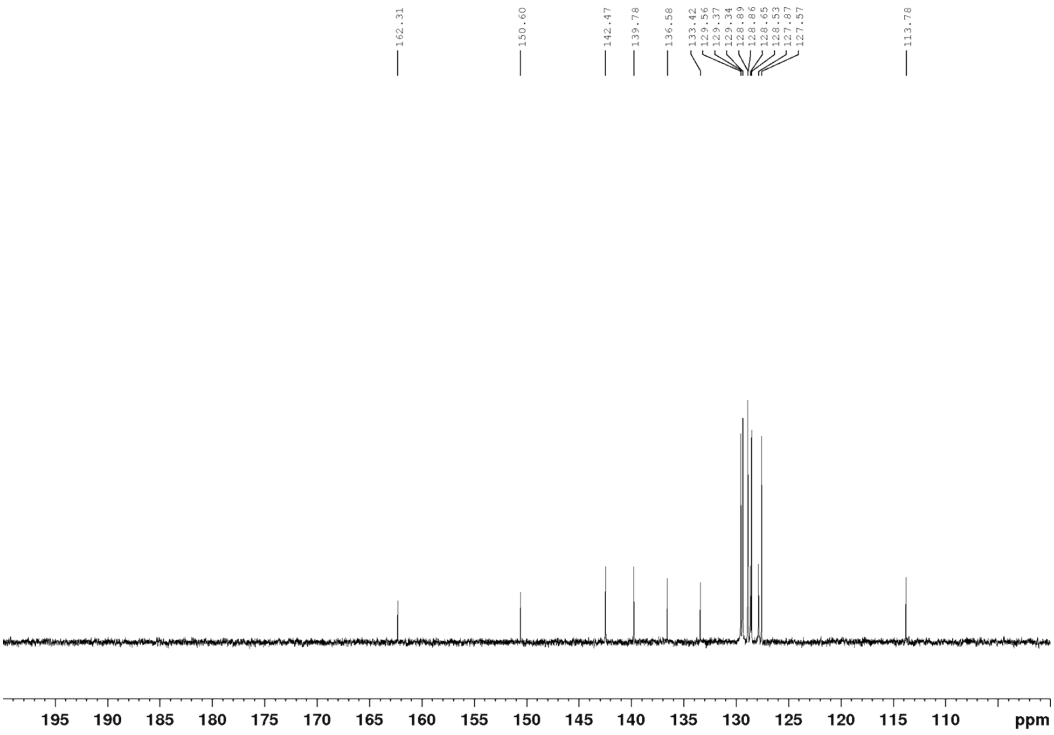
Amide **1a** (1 mmol) and $Mo(CO)_6$ (0.0054 g, 0.02 mmol) were added to an oven dried 10 mL microwave tube equipped with a magnetic stirring bar. To the sealed tube, dry ethyl acetate (1 mL, 1M) was added and the atmosphere was exchanged to N_2 via the septa. The reaction mixture was heated at 80 °C for 10 minutes to activate the catalyst followed by exchange of the atmosphere into N_2 again and was then allowed to reach 65 °C. TMDS (1.5 mmol, 0.26 mL) was added and the reaction was run for 30 min followed by addition of isothiocyanate **5a** (1.1 mmol, 0.13 mL). The reaction was stirred at 65 °C overnight and then cooled. Pentane was added to the reaction crude and the mixture was cleaned by removal and replacement of the pentane 5 times. The resulting residue was dissolved in EtOAc (2 mL) and 1M HCl (aq) (7 mL) was added to the solution which was then stirred at r.t. overnight. The mixture was dissolved in DCM followed by extraction (3 × 10 mL DCM), dried over anhydrous Na_2SO_4 and concentrated into a dark brown solid (214 mg, 84% yield). In $CDCl_3$ only the enol form of the aldehyde **7** was observed.[5] **^{1}H-NMR** (400 MHz, ($CDCl_3$): δ = 14.42 (d, *J* = 13.04 Hz, 1H), 8.11 (s, 1H), 7.53 – 7.43 (m, 3H), 7.43 – 7.37 (m, 7H), 7.32 – 7.26 (m, 1H); **^{13}C-NMR** (100 MHz, ($CDCl_3$): δ = 190.8, 163.0, 137.1, 135.4, 131.1, 129.7, 129.0, 128.8, 127.4, 125.4, 116.0; **HRMS** (ESI, m/z) calcd. for $C_{15}H_{13}NOSNa^+$ $[M + Na]^+$ 278.0621, found 278.0610; Mp 148.4 °C;

Determination of the Structure of 1,3-Disubstituted Pyrimidine 4a by 2D NMR Experiments

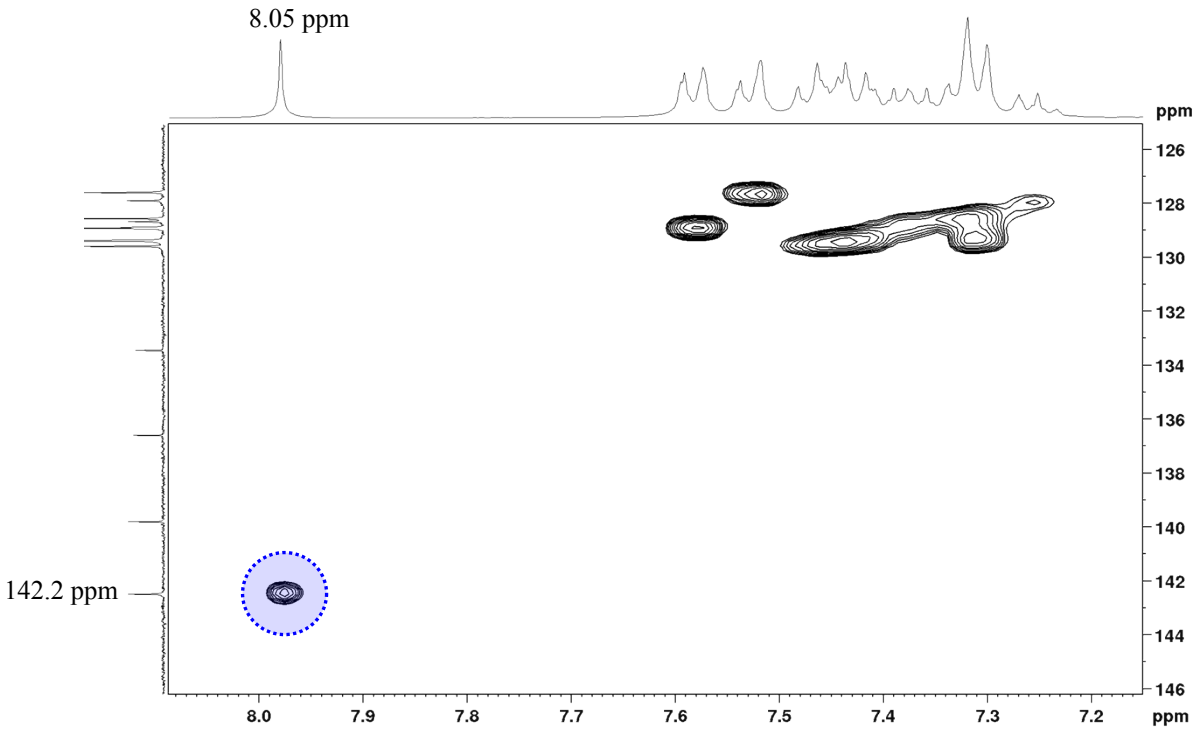
^{1}H NMR:



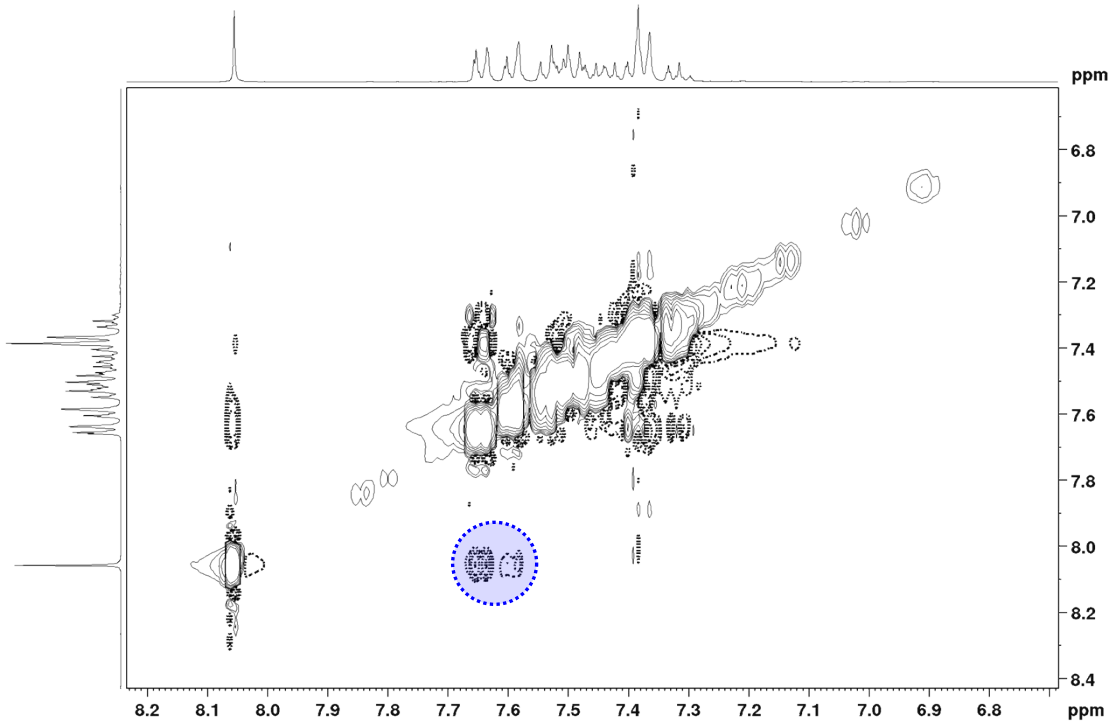
^{13}C NMR:



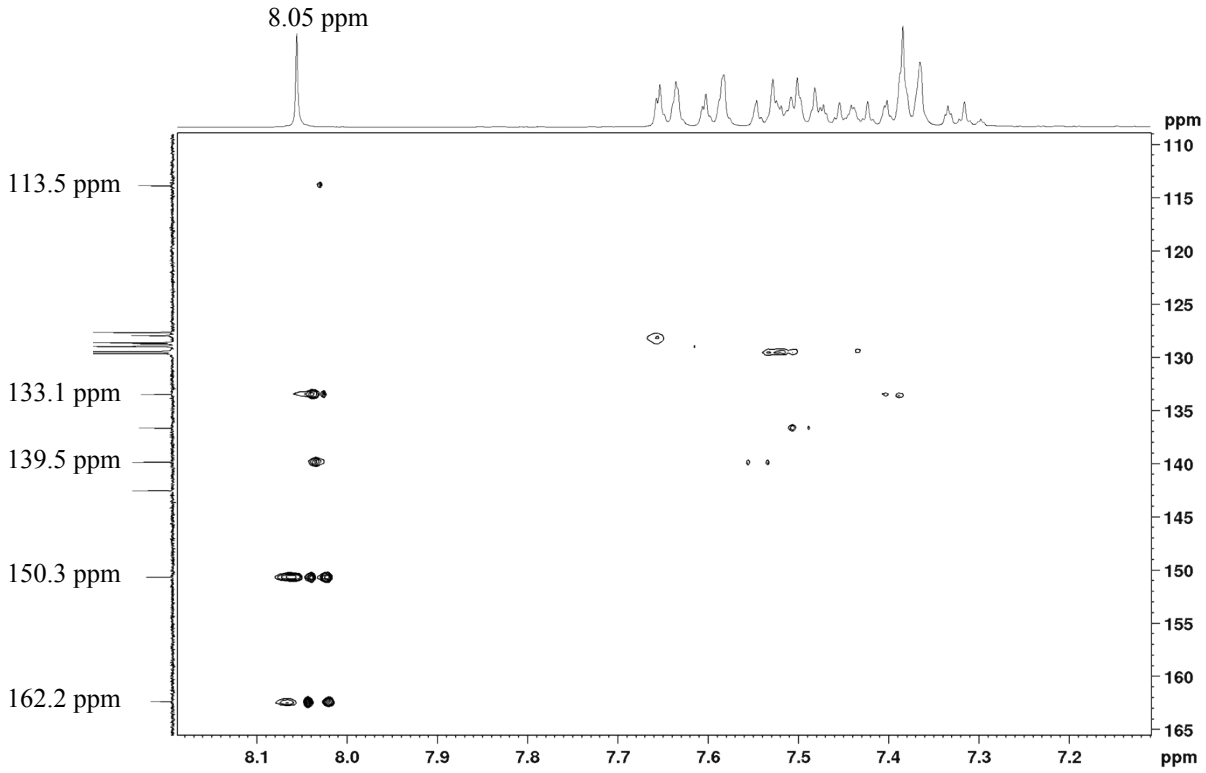
2D NMR – HSQC:

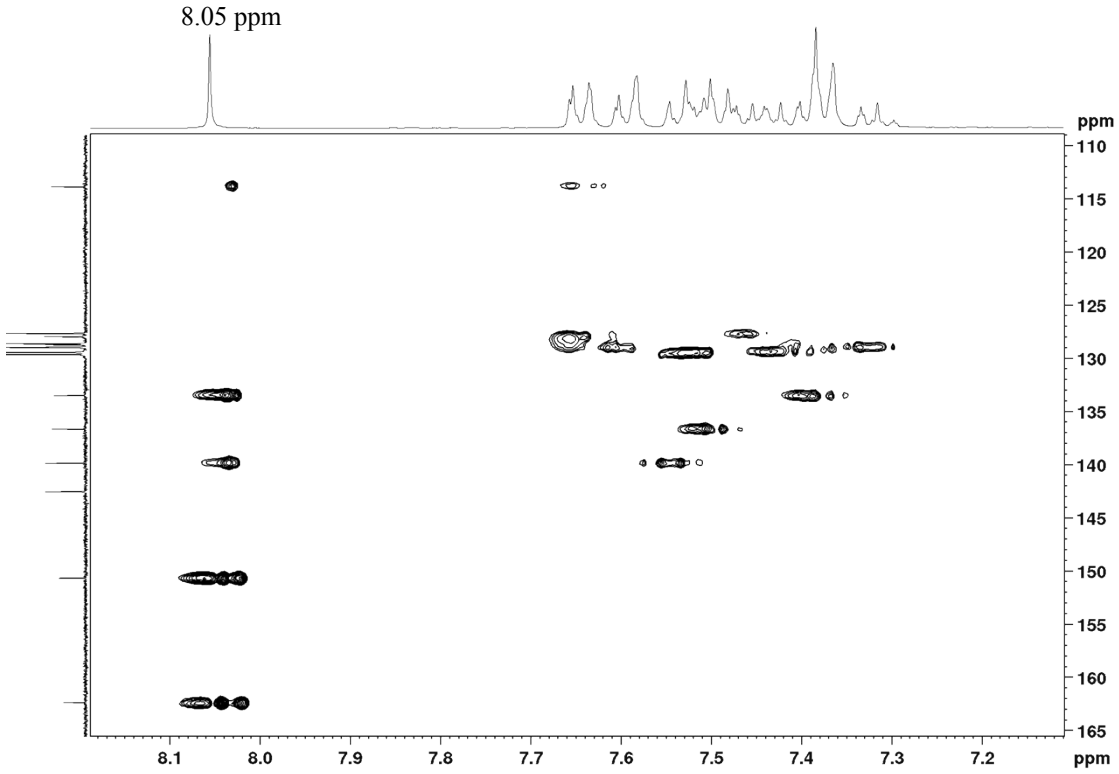


2D NMR – NOESY:



2D NMR – HMBC:


8.05 ppm
113.5 ppm
133.1 ppm
139.5 ppm
150.3 ppm
162.2 ppm
ppm
110
115
120
125
130
135
140
145
150
155
160
165
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm

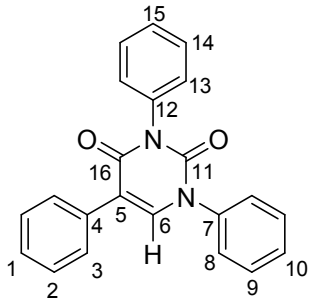

8.05 ppm
ppm
110
115
120
125
130
135
140
145
150
155
160
165
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm

Analysis and assignment of structure for 4a (Tables S4 and S5):

From the HSQC experiment we could determine that there is a $^{1}J_{C,H}$ correlation between the proton at 8.05 ppm and the carbon at 142.2 ppm (marked), which would indicate that this proton and carbon is the CH moiety in the pyrimidine structure (H6/C6). From this experiment we could also determine that the carbons at 162.2, 150.3, 139.5, 136.3, 133.1, 113.5 ppm are quaternary carbons.

From the NOESY experiment we could see that there is a correlation between the CH proton at 8.05 ppm and the two aromatic protons at 7.67 – 7.65 ppm (marked), which could be an indication that these are the *ortho* protons on the aromatic rings (H3 and H9).

From the HMBC experiment we could see that there is a strong correlation between the proton at 8.05 ppm (H6) and the following carbons; 162.2 (CO), 150.3 (CO), 139.5 (Q, Ar), 133.1 (Q, Ar) and 113.5 (Q, unsaturated carbon, C5). The two carbons at 162.2 and 150.3 ppm we assumed most likely to be the carbonyls (C16/C11) since they are quaternary carbons and are not connected to the aromatic protons. The 9 carbons in the region 130-127 ppm are close to the aromatic protons and are most likely the aromatic carbons, furthermore the peaks at 139.5, 136.3, 133.1 and 113.5 ppm are quaternary aromatic carbons.



Proposed structure of **4a**

Table S4. Collected data for **4a** obtained by 2D NMR.

Carbon	Proton attached	Type	^{1}H Short correlation (HSQC)	^{1}H Long correlation (HMBC)
162.2	-	Q	-	8.05
150.3	-	Q	-	8.05
142.2	1H, 8.05	CH in pyrimidine	8.05	8.05
139.5	-	Q	-	8.05 Aromatic CH (m, 7.55 – 7.45 ppm)
136.3	-	Q	-	Some aromatic protons Not close to CH pyrimidine
133.1	-	Q	-	8.05 Some aromatic protons
130-127 in total 9 carbons	Aromatic area	CH and C aromatic carbons	-	Aromatic CH (m, 7.67 – 7.65 ppm) Aromatic CH (m, 7.55 – 7.45 ppm) Only close to aromatic protons Not close to CH pyrimidine
113.5	-	Q	-	8.05 Aromatic CH (m, 7.67 – 7.65 ppm)

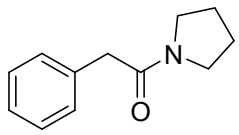
Table S5. Assignment of compound **4a**.

Carbon	Proton attached	Type	Carbon	Proton
162.2	-	Q, CO	C16/C11	-
150.3	-	Q, CO	C16/C11	-
142.2	1H, 8.05	CH in pyrimidine	C6	H6
139.5	-	Q, Ar	C4/C7	-
136.3	-	Q, Ar	C12	-
133.1	-	Q, Ar	C7/C4	-
130-127 in total 9 carbons	Aromatic area	CH and C	Aromatic carbons and protons	
113.5	-	Q, Ar	C5	-

Compound Characterization

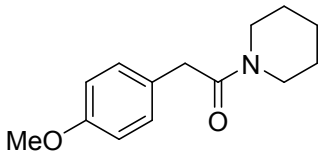
Amides:

2-phenyl-1-(pyrrolidin-1-yl)ethan-1-one (1a)



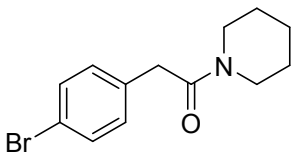
2-Phenylacetyl chloride (40 mmol, 5.3 mL) was subjected to method B (amine; pyrrolidine, 1.2 equiv) to give the corresponding amide as a yellow solid in 92% yield (36.9 mmol, 6.97 g). Spectral data is in agreement with published data.[6]

2-(4-methoxyphenyl)-1-(piperidin-1-yl)ethan-1-one (1b)



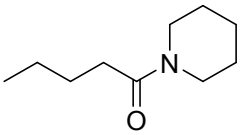
2-(4-methoxyphenyl)acetic acid (40 mmol, 6.65 g) was subjected to method A (amine; piperidine 1.5 equiv) to give the corresponding amide as an pale yellow oil in 69% yield (27.6 mmol, 9.57 g). Spectral data is in agreement with published data.[7]

2-(4-bromophenyl)-1-(piperidin-1-yl)ethan-1-one (1c)



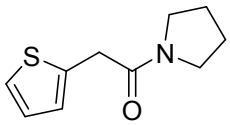
2-(4-bromophenyl)acetic acid (20 mmol, 4.3 g) was subjected to method A to give the corresponding amide as a white solid in 40% yield (8 mmol, 2.09 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.45 – 7.41 (m, 2H), 7.15 – 7.10 (m, 2H), 3.66 (s, 2H), 3.59 – 3.54 (m, 2H), 3.39 – 3.33 (m, 2H), 1.63 – 1.56 (m, 2H), 1.55 – 1.48 (m, 2H), 1.42 – 1.35 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 168.8, 134.6, 131.9, 130.6, 120.7, 47.4, 43.1, 40.5, 26.4, 25.6, 24.5; **HRMS** (ESI, m/z) calcd. for $C_{13}H_{16}BrNONa^+$ $[M + Na]^+$ 304.0307, found 304.0323.

1-(piperidin-1-yl)pentan-1-one (1d)



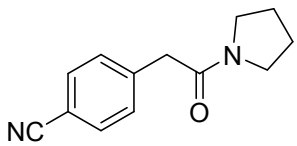
Valeroyl chloride (20 mmol, 2.4 mL) was subjected to method D (amine; piperidine 1.1 equiv) to give the corresponding amide as an pale yellow oil in 80% yield (16 mmol, 2.7 g). Spectral data is in agreement with published data.[8]

1-(pyrrolidin-1-yl)-2-(thiophen-2-yl)ethanone (1e)



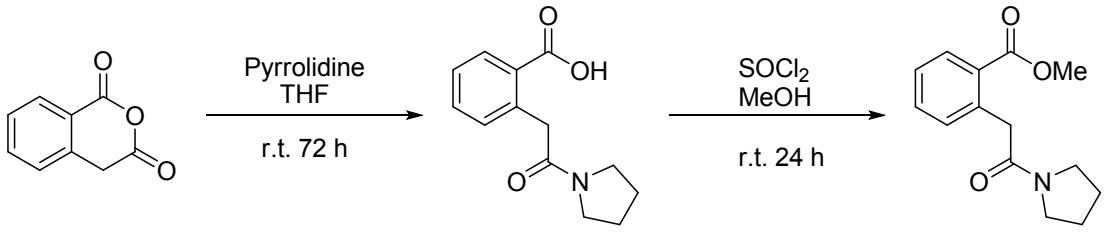
2-(thiophen-2-yl)acetic acid (40 mmol, 5.68 g) was subjected to method C (amine; pyrrolidine) to give the corresponding amide as an yellow oil in 28% yield (11 mmol, 2.09 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.20 – 7.13 (m, 1H), 6.95 – 6.89 (m, 2H), 3.82 (s, 2H), 3.52 – 3.44 (m, 4H), 1.98 – 1.89 (m, 2H), 1.88 – 1.81 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 168.3, 136.5, 126.7, 126.0, 124.7, 46.9, 46.0, 36.4, 26.2, 42.4. **HRMS** (ESI, m/z) calcd. for $C_{10}H_{13}NOSNa^+$ $[M + Na]^+$ 218.0610, found 218.0604.

4-(2-oxo-2-(pyrrolidin-1-yl)ethyl)benzonitrile (1f)



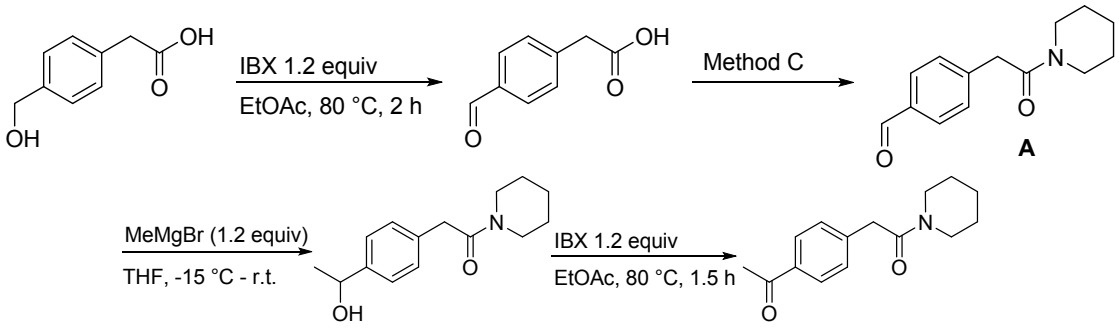
2-(4-cyanophenyl)acetic acid (27 mmol, 4.35g) was subjected to method C (amide; pyrrolidine 2.5 equiv) to give the corresponding amide as an off-white solid in 79% yield (21.3 mmol, 4.56 g). Spectral data is in agreement with published data.[9]

methyl 2-(2-oxo-2-(pyrrolidin-1-yl)ethyl)benzoate (1g)



Isochromane-1,3-dione (13 mmol, 2.15 g) was dissolved in THF (20 mL) and pyrrolidine (1 equiv, 1.06 mL) was added. The reaction was stirred at r.t. for 72 h and then extracted with DCM and HCl (2M). The organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the carboxylic acid as an orange solid (2.96 g). The crude product, 2-(2-oxo-2-(pyrrolidin-1-yl)ethyl)benzoic acid (2.33 g, 9.4 mmol), was reacted with $SOCl_2$ (1.75 equiv) in MeOH (20 mL) at r.t. for 24 h. The crude reaction was concentrated under reduced pressure. The residue was dissolved in DCM and extracted with KOH (2M, checked that the water phase was basic). The organic phase was dried over Na_2SO_4 and concentrated under vacuum and then purified by column chromatography to yield **1g** as pale brown solid in 68% yield (1.6 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 7.79, 1.33 Hz, 1H), 7.46 (dt, *J* = 7.54, 1.41 Hz, 1H), 7.32 (dt, *J* = 7.62, 1.23 Hz, 1H), 7.25 (d, *J* = 7.40 Hz, 1H), 4.02 (s, 2H), 3.82 (s, 3H), 3.53 (t, *J* = 6.81 Hz, 2H), 3.48 (t, J = 6.86 Hz, 2 H), 1.98 (qv, *J* = 6.70 Hz, 2H), 1.86 (qv, *J* = 6.70 Hz, 2H); **^{13}C-NMR** (100 MHz, CDCl3): δ = 169.3, 167.7, 137.4, 132.2, 132.0, 130.8, 130.0, 126.8, 52.0, 46.6, 45.8, 40.6, 26.2, 24.5; **HRMS** (ESI, m/z) calcd. for $C_{14}H_{17}NO_3Na^+$ $[M + Na]^+$ 270.1101, found 270.1089.

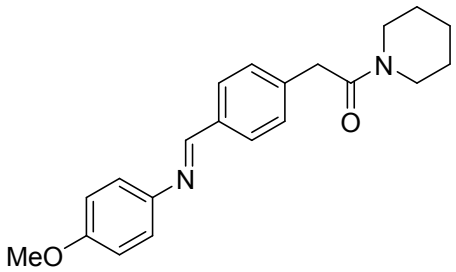
2-(4-acetylphenyl)-1-(piperidin-1-yl)ethan-1-one (1h)



To a stirred solution of 4-(hydroxymethyl)phenylacetic acid (18 mmol, 3.0 g) in dry ethyl acetate (50 mL) at 80 °C 2-iodoxybenzoic acid (IBX, 21.4 mmol, 6.0 g) was added portion wise. The reaction was allowed to stir for 2 h at 80 °C. The reaction mixture was cooled to r.t. and the precipitate was filtered off using a glass filter funnel and washed with ethyl acetate (3 × 30 mL). The ethyl acetate solution was concentrated under reduced pressure yielding target (4-formyl-phenyl)-acetic acid as a white solid. (4-formyl-phenyl)-acetic acid (18 mmol, 3.0 g) was subjected to method C (amine; piperidine 2 equiv) without additional purification to give the corresponding amide as off-white solid in 77% yield (13.8 mmol, 2.9 g). The aldehyde amide **A** (10 mmol, 2.3 g) was dissolved in dry THF (80 mL) and the reaction was cooled to -15 °C while stirring. A solution of MeMgBr (3M in Et_2O, 4 mL) was added dropwise to a stirring solution of the amide at -15 °C. After the addition the reaction mixture was allowed to warm to r.t. and stirred for 1 h. Saturated solution of NH_4Cl was added to the reaction mixture and allowed to stir for 15 min. The alcohol product was extracted with DCM (3 × 50 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure to give the corresponding alcohol containing compound in quantitative yield as a white solid. The compound was used in the oxidation step without purification. To a stirred solution of alcohol substituted amide (10 mmol, 2.46 g) in dry ethyl acetate (50 mL) at 80 °C, 2-iodoxybenzoic acid (IBX, 12 mmol, 3.36 g) was added portion wise. The reaction was allowed to stir for 2 h at 80 °C. The reaction mixture was cooled to r.t. and the precipitate was filtered off using a glass filter funnel and washed with ethyl acetate (3 × 30 mL). Ethyl acetate solution was concentrated under reduced pressure and was purified by column chromatography to give target amide **1h** as a pale brown solid in 76% yield (1.86 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.93 – 7.88 (m, 2H), 7.37 – 7.33 (m, 2H), 3.77 (*s*, 2H), 3.59 – 3.54 (m, 2H), 3.39 – 3.34 (m, 2H), 2.58 (s, 3H), 1.62 – 1.49 (m, 4H), 1.41

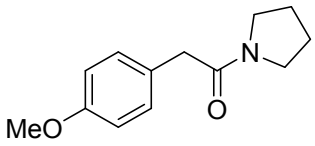
– 1.34 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 197.9, 168.5, 141.1, 135.8, 129.1, 128.8, 47.3, 43.1, 41.1, 26.7, 26.4, 25.6, 24.5; **HRMS** (ESI, m/z) calcd. for $C_{15}H_{19}NO_2Na^+$ $[M + Na]^+$ 268.1308, found 268.1303.

(*E*)-2-(4-(((4-methoxyphenyl)imino)methyl)phenyl)-1-(piperidin-1-yl)ethan-1-one (1i)



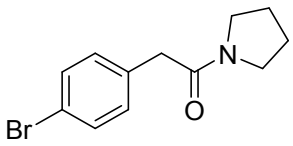
Amide **A** from the synthesis of amide **1h** (4.3 mmol, 1.0 g) and *p*-anisidine (4.3 mmol, 0.57 g) were stirred in ethanol (15 mL) for 16 h at r.t. The solvent was removed under reduced pressure to yield **1i** as an off-white solid in quantitative yield (4.3 mmol, 1.45 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.46 (s, 1H), 7.86 – 7.82 (m, 2H), 7.37 – 7.34 (m, 2H), 7.25 – 7.20 (m, 2H), 6.95 – 6.90 (m, 2H), 3.83 (s, 3H), 3.78 (s, 2H), 3.60 – 3.55 (m, 2H), 3.39 – 3.35 (m, 2H), 1.62 – 1.49 (m, 4H), 1.39 – 1.32 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 168.9, 158.4, 158.2, 145.0, 138.8, 135.2, 129.2, 129.1, 122.3, 114.5, 55.7, 47.4, 43.1, 41.4, 26.4, 25.6, 24.5; **HRMS** (ESI, m/z) calcd. for $C_{21}H_{24}N_2O_2Na^+$ $[M + Na]^+$ 359.1730, found 359.1736.

2-(4-methoxyphenyl)-1-(pyrrolidin-1-yl)ethanone (1j)



2-(4-methoxyphenyl)acetic acid (40 mmol, 6.64 g) was subjected to method C (amine; pyrrolidine) to give the corresponding amide as an colorless oil 48% yield (19 mmol, 4.18 g). Spectral data is in agreement with published data.[9]

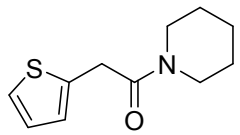
2-(4-bromophenyl)-1-(pyrrolidin-1-yl)ethanone (1k)



2-(4-bromophenyl)acetic acid (30 mmol, 6.45 g) was subjected to method A (amine; pyrrolidine, 1.5 equiv) to give the corresponding amide as an white solid 53% yield (15.8 mmol, 4.23 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.46 – 7.41 (m, 2H), 7.18 – 7.14 (m, 2H), 3.59 (s, 2H), 3.50 – 3.45 (m, 2H), 3.44 – 3.39 (m, 2H), 1.97 – 1.89 (m, 2H), 1.88 – 1.80 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 168.8, 133.9, 131.4, 130.8, 120.5,

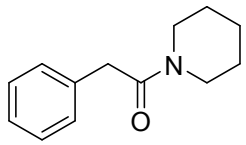
46.8, 45.9, 41.3, 26.0, 24.2. **HRMS** (ESI, m/z) calcd. for $C_{12}H_{14}NOBrNa^+$ $[M + Na]^+$ 290.0151, found 290.0154.

1-(piperidin-1-yl)-2-(thiophen-2-yl)ethan-1-one (1l)



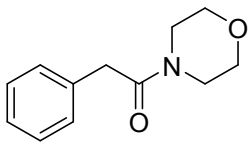
2-(thiophen-2-yl)acetic acid (10 mmol, 1.42 g) was subjected to method D ($ZrCl_4$ (20 mol%, 0.467 g), THF (80 mL), MS 4Å (5.0 g), piperidine 2.0 equiv) to give the corresponding amide as an off white solid in 78% yield (7.8 mmol, 1.64 g). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.17 – 7.15 (dd, *J* = 5.17, 1.20 Hz, 1H), 6.93 – 6.91 (m, 1H), 6.88 – 6.86 (m, 1H), 3.88 (s, 2H), 3.55 (m, 2H), 3.42 (m, 2H), 1.62 – 1.39 (m, 6H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 168.1, 136.9, 126.8, 125.9, 124.7, 47.4, 43.0, 35.3, 26.2, 25.4, 24.4; **HRMS** (ESI, m/z) calcd. for $C_{11}H_{15}NOSNa^+$ $[M + Na]^+$ 232.0767, found 232.0765.

2-phenyl-1-(piperidin-1-yl)ethan-1-one (1m)



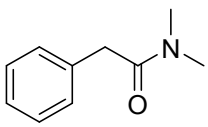
2-Phenylacetyl chloride (40 mmol, 6.4 mL) was subjected to method B (amine; piperidine, 1.15 equiv) to give the corresponding amide as an colorless oil in 83% yield (33 mmol, 6.80 g). Spectral data is in agreement with published data.[6]

1-morpholino-2-phenylethan-1-one (1n)



2-Phenylacetyl chloride (48 mmol, 6.4 mL, 1.2 equiv) was subjected to method B (amine; morpholine, 1 equiv) to give the corresponding amide as a yellow solid in 60% yield (24 mmol, 4.92 g). Spectral data is in agreement with published data.[6]

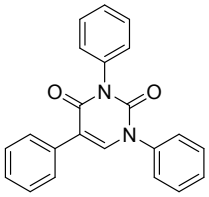
***N*,*N*-dimethyl-2-phenylacetamide (1o)**



2-Phenylacetyl chloride (40 mmol, 5.3 mL) was subjected to method B (amine; dimethylamine hydrochloride, 5 equiv) to give the corresponding amide as a yellow solid in 80% yield (32 mmol, 5.19 g). Spectral data is in agreement with published data.[10]

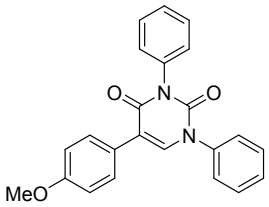
1,3-disubstituted pyrimidines:

1,3,5-triphenylpyrimidine-2,4(1*H*,3*H*)-dione (4a)



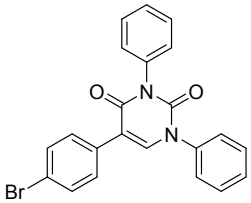
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (256 mg, 77%). **Mp** 253 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.05 (s, 1H), 7.67 – 7.65 (m, 2H), 7.67 – 7.59 (m, 2H), 7.55 – 7.45 (m, 6H), 7.41 – 7.37 (m, 4H), 7.34 – 7.31 (m, 1H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.2, 150.3, 142.2, 139.5, 136.3, 133.1, 129.3, 129.1, 129.0, 128.6, 128.5, 128.3, 128.2, 127.6, 127.3, 113.5; **IR** (KBr): 3064, 3030, 1713, 1667, 1651, 1592, 1491, 1448, 1415, 1363, 1320, 1300, 1280, 1233, 1194, 1173, 1150, 1073, 1025, 906; **HRMS** (ESI, m/z) calcd. for $C_{22}H_{16}N_2O_2Na^+$ $[M + Na]^+$ 363.1104, found 363.1095.

5-(4-methoxyphenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4b)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (312 mg, 92%). **Mp** 58 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 7.97 (s, 1H), 7.63 – 7.59 (m, 4H), 7.56 – 7.43 (m, 6H), 7.39 – 7.38 (m, 2H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.4, 159.1, 150.5, 136.5, 129.9, 129.4, 129.2, 128.7, 128.5, 127.5, 125.5, 113.9, 113.4, 55.5; **IR** (KBr): **:** 3413, 3050, 3009, 2938, 2837, 1709, 1665, 1610, 1595, 1574, 1516, 1491, 1456, 1438, 1411, 1360, 1321, 1306, 1278, 1245, 1182, 1160, 1147, 1145, 1075, 1027, 1005; **HRMS** (ESI, m/z) calcd. for $C_{23}H_{18}N_2O_3Na^+$ $[M + Na]^+$ 393.1210, found 393.1214.

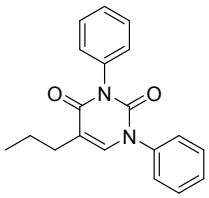
5-(4-bromophenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4c)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (316 mg, 76%). **Mp** 249 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.14 (s, 1H), 7.65 – 7.73 (m, 12H), 7.38 – 7.36 (m, 2H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.1, 150.5, 142.8, 139.7,

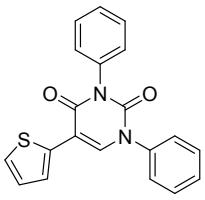
136.5, 132.7, 131.4, 130.9, 129.6, 129.4, 129.3, 128.9, 128.7, 127.6, 121.1, 112.5; **IR** (KBr): 3352, 3086, 3042, 2249, 2123, 1715, 1663, 1595, 1493, 1455, 1427, 1395, 1367, 1336, 1314, 1284, 1186, 1142, 1036, 1004; **HRMS** (ESI, m/z) calcd. for $C_{22}H_{15}BrN_2O_2Na^+$ $[M + Na]^+$ 441.0209, found 441.0204.

1,3-diphenyl-5-propylpyrimidine-2,4(1*H*,3*H*)-dione (4d)



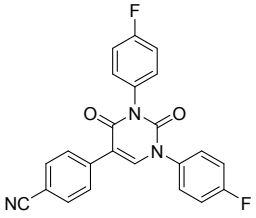
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (173 mg, 57%). **Mp** 154 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 7.69 (s, 1H), 7.50 – 7.38 (m, 8H), 7.29 – 7.27 (m, 2H), 2.28 (t, *J* = 7.45 Hz, 2H), 1.56 – 147 (m, 2H), 0.89 (t, *J* = 7.35 Hz, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 163.5, 150.8, 141.1, 139.9, 136.5, 129.6, 129.3, 128.7, 128.5, 127.4, 113.5, 29.1, 21.8, 14.1; **IR** (KBr): 3067, 2953, 2863, 1706, 1662, 1594, 1491, 1455, 1433, 1385, 1317, 1299, 1200, 1140, 1071, 1005, 929; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{18}N_2O_2Na^+$ $[M + Na]^+$ 329.1260, found 329.1268;

1,3-diphenyl-5-(thiophen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (4e)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (198 mg, 57%). **Mp** 273.2 °C (Decomposed); **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.45 (s, 1H), 7.65 – 7.63 (m, 1H), 7.60 – 7.44 (m, 9H), 7.39 – 7.37 (m, 2H), 7.08 – 7.06 (m, 1H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 161.2, 150.0, 140.0, 139.6, 136.2, 133.9, 129.5, 129.3, 129.2, 128.9, 128.7, 127.7, 126.8, 126.5, 123.6, 108.6; **IR** (KBr): 3080, 1710, 1655, 1593, 1522, 1489, 1440, 1419, 1373, 1358, 1324, 1305, 1249, 1216, 1186, 1170, 1103, 1071, 1022, 1003, 929; **HRMS** (ESI, m/z) calcd. for $C_{20}H_{14}N_2O_2SNa^+$ $[M + Na]^+$ 396.0668, found 369.0668.

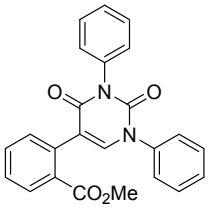
4-(1,3-bis(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)benzonitrile (4f)



Cyclization of enamine with 1-fluoro-4-isocyanatobenzene (3.5 equiv.) for 72 h yielded the 1,3-disubstituted pyrimidine **4f** after washing the crude reaction with pentane followed by diethyl

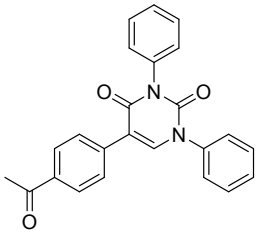
ether as a pale yellow solid (341 mg, 85% yield). **Mp** 231 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.31 (s, 1H), 7.91 – 7.82 (m, 4H), 7.66 – 7.63 (m, 2H), 7.45 – 7.31 (m, 6H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.83/160.40 (d, *J* = 246.3 Hz), 161.54, 150.12, 143.83, 138.0, 135.37 (d, *J* = 2.9 Hz), 132.03, 131.98, 130.94 (d, *J* = 8.72 Hz), 129.50 (d, *J* = 8.96 Hz), 128.91, 118.89, 115.92 (d, *J* = 23.00 Hz), 115.83 (d, *J* = 22.76 Hz), 111.41, 109.71; **IR** (KBr): 3081, 2235, 1926, 1907, 1843, 1714, 1679, 1634, 1602, 1507, 1434, 1400, 1324, 1298, 1241, 1212, 1158, 1102, 1015, 922; **HRMS** (ESI, m/z) calcd. for $C_{23}H_{13}F_2N_3O_2Na^+$ $[M + Na]^+$ 424.0868, found 424.0855;

methyl 2-(2,4-dioxo-1,3-diphenyl-1,2,3,4-tetrahydropyrimidin-5-yl)benzoate (4g)



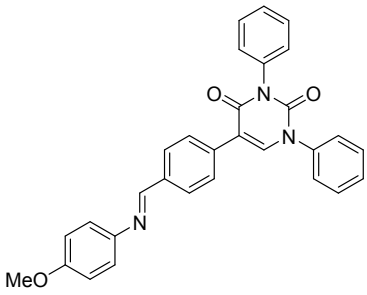
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a beige solid (253 mg, 64% yield). **Mp** 209.4 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.03 (s, 1H), 7.84 – 7.79 (m, 2H), 7.65 – 7.58 (m, 3H), 7.57 – 7.39 (m, 8H), 7.33 – 7.28 (m, 2H), 3.74 (s, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 167.4, 162.0, 150.2, 140.6, 139.1, 135.9, 132.8, 132.0, 131.2, 131.1, 129.4, 129.1, 129.0, 128.7, 128.4, 128.2, 128.1, 127.0, 115.3, 52.0; **IR** (KBr): 3416, 3348, 3050, 2965, 1951, 1711, 1674, 1592, 1571, 1481, 1448, 1415, 1364, 1317, 1262, 1190, 1134, 1088, 1074, 1047, 994, 961, 930; **HRMS** (ESI, m/z) calcd. for $C_{24}H_{18}N_2O_4Na^+$ $[M + Na]^+$ 421.1159, found 421.1170.

5-(4-acetylphenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4h)



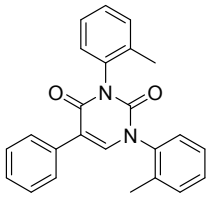
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a yellow pale solid (136 mg, 71%). **Mp** 130 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.24 (s, 1H), 7.96 (d, *J* = 8.54 Hz, 2H), 7.85 (d, *J* = 8.54 Hz, 2H), 7.62 – 7.38 (m, 10H), 2.59 (s, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.1, 150.5, 143.6, 139.7, 138.3, 136.5, 125.9, 129.6, 129.4, 129.3, 128.9, 128.8, 128.7, 128.4, 127.6, 112.6, 27.2; **IR** (KBr): 3451, 3066, 2959, 2928, 2856, 2121, 1932, 1719, 1673, 1600, 1537, 1493, 1426, 1402, 1360, 1310, 1266, 1073, 1027, 961, 909; **HRMS** (ESI, m/z) calcd. for $C_{24}H_{18}N_2O_3Na^+$ $[M + Na]^+$ 405.1210, found 405.1211.

(*E*)-5-(4-((4-methoxyphenylimino)methyl)phenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4i)



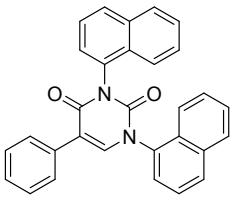
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a yellow solid (359 mg, 76%). **Mp** 168 °C (Decomposed); **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.65 (s, 1H), 8.21 (s, 1H), 7.91 (d, *J* = 8.52 Hz, 2H), 7.82 (d, *J* = 8.52 Hz, 2H), 7.32 – 7.38 (m, 11H), 7.31 (d, *J* = 8.55 Hz, 2H), 6.98 (d, *J* = 8.55 Hz, 2H), 3.77 (s, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.1, 158.3, 158.2, 150.5, 144.5, 143.1, 139.7, 136.4, 136.0, 135.6, 129.5, 129.3, 129.2, 128.9, 128.6, 128.5, 127.6, 122.8, 114.8, 112.9, 55.7; **IR** (KBr): 3412, 3353, 3064, 3043, 2986, 2937, 2905, 2834, 1886, 1713, 1665, 1622, 1607, 1557, 1492, 1427, 1406, 1369, 1310, 1290, 1245, 1196, 1176, 1107, 1062, 1025, 975, 945, 986; **HRMS** (ESI, m/z) calcd. for $C_{30}H_{23}N_3O_3Na^+$ [M + Na]$^+$ 496.1632, found 496.1634;

5-phenyl-1,3-di*o*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (4j)



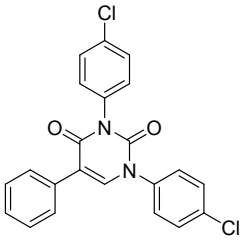
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (148 mg, 40% yield). For this compound rotamers were observed at r.t., we therefore decided to confirm this by recording ^{1}H NMR specra at higher temperature as well. **Mp** 268 °C; For this compound rotamers were observed at r.t., we therefore decided to confirm this by recording ^{1}H NMR specra at higher temperature as well, **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.02 (s, 1H), 7.66 – 7.64 (m, 2H), 7.51 – 7.49 (m, 1H), 7.42 – 7.29 (m, 10H), 2.27 and 2.24 (s, 3H, rotamers), 2.14 and 2.13 (s, 3H, rotamers); **^{1}H-NMR** (500 MHz, $(CD_3)_2SO$, 90 °C): δ = 7.89 (s, 1H), 7.70 – 7.63 (m, 2H), 7.50 – 7.45 (m, 1H), 7.43 – 7.25 (m, 10H), 2.28 (br s, 3H), 2.17 (br s, 3H) **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.0, 161.9, 149.7, 142.9, 138.7, 138.6, 136.0, 135.9, 135.7, 135.6, 135.5, 133.2, 131.4, 131.3, 131.0, 130.9, 129.7, 129.4, 129.0, 128.8, 128.63, 128.6, 128.5, 127.9, 127.6, 127.5, 127.2, 113.5, 17.8, 17.6, 17.5, 17.4 (rotamers); **IR** (KBr): 3060, 2977, 2952, 2923, 1709, 1657, 1632, 1494, 1451, 1415, 1318, 1241, 1199, 1152, 1123, 1110, 1033, 938, 914; **HRMS** (ESI, m/z) calcd. for $C_{24}H_{20}N_2O_2Na^+$ [M + Na]$^+$ 391.1405, found 391.1417;

1,3-di(naphthalen-1-yl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4k)



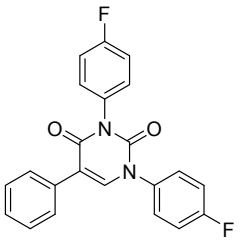
Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (365 mg, 83% yield). **Mp** 253 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.24 (s, 1H), 8.13-8.03 (m, 5H), 7.96 – 7.92 (m, 2H), 7.80 – 7.78 (m, 1H), 7.71 – 7.58 (m, 8H), 7.39 – 7.30 (m, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 162.8, 162.7, 143.6, 143.5, 130.4, 130.3, 130.0, 129.3, 129.2, 128.9, 128.8, 128.5, 127.9, 127.6, 127.4, 127.2, 126.9, 126.3, 123.3, 122.9, 122.8, 122.6; **IR** (KBr): 3060, 2219, 1714, 1666, 1600, 1503, 1450, 1417, 1368, 1318, 1241, 1176; **HRMS** (ESI, m/z) calcd. for $C_{30}H_{20}N_2O_2Na^+$ $[M + Na]^+$ 463.1417, found 463.1403.

1,3-bis(4-chlorophenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4l)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (307 mg, 75% yield). **Mp** 223 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.08 (s, 1H), 7.66 – 7.54 (m, 8H), 7.45 – 7.29 (m, 5H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 161.7, 149.9, 141.8, 138.0, 134.9, 132.9, 132.8, 132.7, 130.8, 129.0, 128.9, 128.8, 128.4, 128.1, 127.5, 113.5; **IR** (KBr): 3093, 3057, 1715, 1666, 1593, 1492, 1448, 1425, 1401, 1364, 1320, 1268, 1240, 1187, 1175, 1144, 1091, 1014; **HRMS** (ESI, m/z) calcd. for $C_{22}H_{14}Cl_2N_2O_2Na^+$ $[M + Na]^+$ 431.0325, found 431.0315.

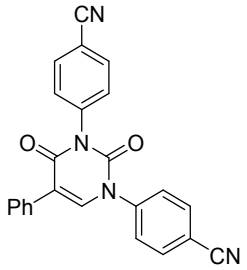
1,3-bis(4-fluorophenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4m)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a white solid (352 mg, 94%). **Mp** 264 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.06 (s, 1H), 7.66 – 7.62 (m, 4H), 7.45 – 7.30 (m, 9H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 163.1 (d, *J* = 5.67 Hz), 162.2, 160.6 (d, *J* = 5.98 Hz), 150.6, 142.4, 135.9 (d, *J* = 3.03 Hz), 132.2, 132.6 (d, *J* = 3.10 Hz), 131.3 (d, *J* = 8.67 Hz), 129.7 (d, *J* = 8.38 Hz), 128.8, 128.4, 127.8, 116.2 (d, *J* = 23.58 Hz), 116.1 (d, *J* = 23.24 Hz), 113.6; **IR** (KBr): 3068, 3027, 1713, 1665, 1601, 1508, 1449, 1423, 1407, 1363, 1311, 1285, 1241, 1225,

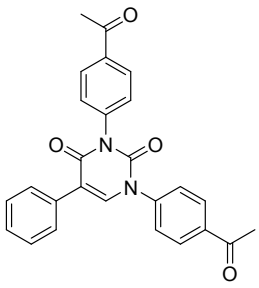
1193, 1154, 1095, 1014; **HRMS** (ESI, m/z) calcd. for $C_{22}H_{14}F_2N_2O_2Na^+$ $[M + Na]^+$ 399.0916, found 399.0935.

4,4'-(2,4-dioxo-5-phenylpyrimidine-1,3(1*H*,4*H*)diyl)dibenzonitrile (4n)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a pale brown solid (168 mg, 86%). **Mp** > 290 °C (Decomposed); **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.18 (s, 1H), 8.05 – 8.00 (m, 4H), 7.84 – 7.83 (m, 2H), 7.67 – 7.64 (m, 4H), 7.43 – 7.34 (m, 3H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 161.9, 149.9, 143.2, 141.9, 140.7, 133.7, 133.6, 133.0, 130.8, 128.9, 128.6, 128.5, 128.1, 118.9, 118.7, 114.4, 111.8, 111.5; **IR** (KBr): 3058, 2228, 1718, 1708, 1666, 1599, 1502, 1451, 1423, 1404, 1366, 1326, 1304, 1276, 1241, 1178, 1140; **HRMS** (ESI, m/z) calcd. for $C_{24}H_{14}N_4O_2Na^+$ $[M + Na]^+$ 413.1009, found 413.1024.

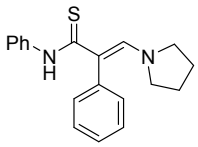
1,3-bis(4-acetylphenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4o)



Cyclization of enamine with isocyanate yielded the 1,3-disubstituted pyrimidine after washing the crude reaction with pentane as a pale yellow solid (358 mg, 84%). **Mp** 210 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.13 (s, 1H), 8.10 – 8.07 (m, 4H), 7.77 – 7.75 (m, 2H), 7.06 – 7.64 (m, 2H), 7.58 – 7.56 (m, 2H), 7.41 – 7.37 (m, 2H), 7.34 – 7.31 (m, 1H), 2.63 (s, 6H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 197.8, 197.6, 161.9, 150.1, 143.2, 141.9, 140.6, 136.9, 136.7, 133.1, 129.7, 129.4, 129.3, 128.6, 128.5, 127.9, 127.7, 114.2, 27.3, 27.2; **IR** (KBr): 3057, 1716, 1672, 1599, 1506, 1494, 1448, 1422, 1403, 1360, 1318, 1287, 1265, 1244, 1175, 1142, 1018; **HRMS** (ESI, m/z) calcd. for $C_{26}H_{20}N_2O_4Na^+$ $[M + Na]^+$ 447.1315, found 447.1331.

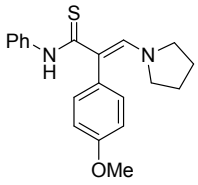
Acryl thioamides:

_N_,2-diphenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6a)



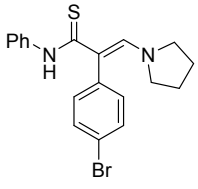
Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown/dark green solid (290 mg, 94% yield). **Mp** 150 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.60 (s, 1H), 8.35 (s, 1H), 7.44 – 7.30 (m, 5H), 7.29 – 7.21 (m, 4H), 7.11 – 7.05 (m, 1H), 3.08 – 2.93 (m, 4H), 1.73 – 1.63 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.3, 149.2, 140.8, 136.5, 132.5, 128.1, 127.9, 127.3, 124.6, 124.5, 122.4, 51.3, 24.6; **IR** (KBr): 3443, 3046, 2972, 2945, 2912, 2869, 2842, 1603, 1588, 1524, 1476, 1454, 1442, 1407, 1381, 1342, 1311, 1286, 1253, 1221, 1207, 1173, 1146, 1099, 1024, 957; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{20}N_2SNa^+$ $[M + Na]^+$ 331.1239, found 331.1224.

2-(4-methoxyphenyl)-_N_-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6b)



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown/dark green solid (318 mg, 94% yield). **Mp** 169 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.49 (s, 1H), 8.40 (s, 1H), 7.45 – 7.39 (m, 2H), 7.29 – 7.22 (m, 2H), 7.19 – 7.15 (m, 2H), 7.11 – 7.05 (m, 1H), 6.98 – 6.92 (m, 2H), 3.78 (s, 3H), 3.11 – 2.95 (m, 4H), 1.74 – 1.64 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.4, 158.5, 149.6, 140.7, 133.6, 127.9, 127.8, 124.6, 124.5, 113.6, 111.7, 55.0, 51.2, 24.6; **IR** (KBr): 3443, 3341, 2957, 2933, 2859, 2837, 1589, 1510, 1494, 1438, 1405, 1381, 1337, 1308, 1286, 1243, 1220, 1169, 1102, 1028, 970, 943; **HRMS** (ESI, m/z) calcd. for $C_{20}H_{22}N_2OSNa^+$ $[M + Na]^+$ 361.1345, found 361.1346;

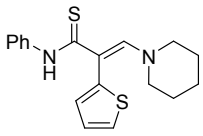
2-(4-bromophenyl)-_N_-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6c)



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown/dark yellow solid (289 mg, 75% yield **Mp** 161 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 9.05 (s, 1H), 8.25 (s, 1H), 7.53 – 7.48 (m, 2H), 7.42 – 7.37 (m, 2H), 7.29 – 7.23 (m, 2H), 7.18 – 7.14 (m, 2H), 7.12 – 7.06 (m, 1H), 3.08 – 2.93 (m, 4H), 1.76 – 1.65 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.9,

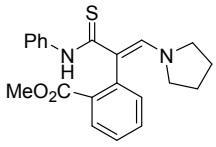
148.8, 141.1, 136.3, 134.6, 130.7, 127.8, 125.1, 124.6, 120.1, 111.2, 51.5, 24.6; **IR** (KBr): 3334, 2969, 2864, 1735, 1606, 1588, 1507, 1485, 1442, 1412, 1387, 1307, 1264, 1238, 1217, 1169, 1104, 1068, 1027, 1014, 972, 954, 942, 926, 915, 987; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{19}BrN_2SNa^+$ $[M + Na]^+$ 409.0345, found 409.0342.

***N*-phenyl-3-(piperidin-1-yl)-2-(thiophen-2-yl)prop-2-enethioamide (6d)**



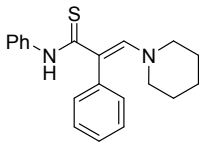
Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown foam (197 mg, 60% yield). **Mp** 147 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.74 (s, 1H), 8.36 (s, 1H), 7.73 – 7.65 (m, 1H), 7.48 – 7.38 (m, 2H), 7.32 – 7.39 (m, 2H), 7.16 – 7.08 (m, 2H), 7.05 – 7.00 (m, 1H), 3.15 – 3.07 (m, 4H), 1.55 – 1.41 (m, 6H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.6, 153.4, 140.6, 137.2, 130.3, 128.9, 127.9, 127.8, 124.9, 124.8, 100.8, 51.5, 25.8, 23.3; **IR** (KBr): 3332, 2935, 2853, 1589, 1522, 1496, 1439, 1311, 1281, 1251, 1217, 1184, 1157, 1107, 1085, 1057, 1022, 995, 919; **HRMS** (ESI, m/z) calcd. for $C_{18}H_{20}N_2S_2Na^+$ $[M + Na]^+$ 351.0960, found 351.0960.

methyl 2-(3-(phenylamino)-1-(pyrrolidin-1-yl)-3-thioxoprop-1-en-2-yl)benzoate (6e)



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown oil (325 mg, 89% yield). **Mp:** 183 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 9.05 (s, 1H), 8.12 (s, 1H), 7.77 – 7.73 (m, 1H), 7.57 – 7.52 (m, 1H), 7.44 – 7.36 (m, 4H), 7.29 – 7.23 (m, 3H), 7.11 – 7.05 (m, 1H), 3.73 (s, 3H), 3.07 – 2.87 (m, 4H), 1.77 – 1.60 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 194.2, 167.5, 147.2, 141.2, 137.4, 134.4, 133.2, 131.0, 129.3, 127.7, 127.4, 125.7, 124.8, 124.4, 112.2, 51.9, 24.7; **IR** (KBr): 3451, 2948, 2869, 1724, 1588, 1496, 1442, 1404, 1308, 1215, 1107, 1073, 913; **HRMS** (ESI, m/z) calcd. for $C_{21}H_{22}N_2O_2SNa^+$ $[M + Na]^+$ 389.1294, found 389.1281;

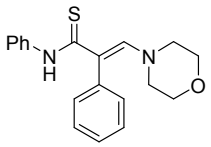
***N*,2-diphenyl-3-(piperidin-1-yl)prop-2-enethioamide (6f)**



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown solid (217 mg, 67% yield). **Mp** 136 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ =

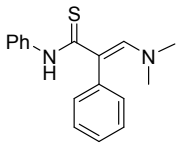
8.64 (s, 1H), 8.13 (s, 1H), 7.47 – 7.37 (m, 4H), 7.36 – 7.30 (m, 1H), 7.29 – 7.20 (m, 4H), 7.12 – 7.04 (m, 1H), 3.06 – 2.94 (m, 4H), 1.53 – 1.45 (m, 2H), 1.44 – 1.33 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.9, 151.4, 140.9, 137.1, 131.6, 128.8, 127.9, 127.4, 124.6, 111.2, 51.5, 25.5, 23.3; **IR** (KBr): 3353, 2940, 2852, 1588, 1504, 1441, 1318, 1284, 1250, 1218, 1203, 1101, 1069, 1028, 1002, 958, 938; **HRMS** (ESI, m/z) calcd. for $C_{20}H_{22}N_2SNa^+$ $[M + Na]^+$ 345.1396, found 345.1409.

3-morpholino-*N*,2-diphenylprop-2-enethioamide (6g)



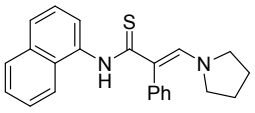
Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a dark solid (126 mg, 39% yield). **Mp**: 162 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.93 (s, 1H), 8.02 (s, 1H), 7.46 – 7.38 (m, 4H), 7.35 – 7.23 (m, 5H), 7.13 – 7.06 (m, 1H), 3.50 – 3.44 (m, 4H), 3.03 – 2.96 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 194.7, 150.4, 140.8, 136.8, 131.7, 128.8, 127.9, 127.5, 124.8, 124.7, 112.5, 65.7, 50.6; **IR** (KBr): 3446, 3349, 2961, 2888, 2851, 1605, 1591, 1530, 1497, 1439, 1315, 1275, 1235, 1211, 1105, 1023, 942; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{20}N_2OSNa^+$ $[M + Na]^+$ 347.1189, found 347.1178.

3-(dimethylamino)-*N*,2-diphenylprop-2-enethioamide (6h)



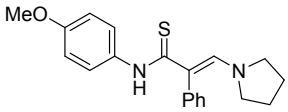
Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a brown solid (199 mg, 71% yield). **Mp** 145.2 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.70 (s, 1H), 8.13 (s, 1H), 7.47 – 7.36 (m, 4H), 7.35 – 7.31 (m, 1H), 7.29 – 7.20 (m, 4H), 7.13 – 7.05 (m, 1H), 2.68 (br s, 6H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.9, 152.7, 140.9, 136.6, 132.3, 128.4, 127.9, 127.2, 124.6, 124.5, 112.0, 42.9; **IR** (KBr): 3350, 3004, 2902, 1735, 1608, 1589, 1509, 1432, 1399, 1382, 1309, 1277, 1262, 1190, 1149, 1087, 1072, 1025, 950, 938; **HRMS** (ESI, m/z) calcd. for $C_{17}H_{18}N_2SNa^+$ $[M + Na]^+$ 305.1083, found 305.1070.

***N*-(naphthalen-1-yl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6i)**



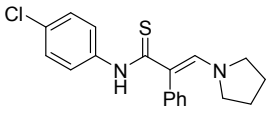
Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a dark green solid (294 mg, 83% yield). **Mp** 170 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.72 (s, 1H), 8.49 (s, 1H), 7.92 – 7.87 (m, 1H), 7.79 – 7.74 (m, 1H), 7.64 – 7.58 (m, 1H), 7.50 – 7.39 (m, 8H), 7.37 – 7.31 (m, 1H), 3.15 – 2.96 (m, 4H), 1.74 – 1.64 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 195.1, 149.6, 137.4, 136.5, 133.6, 132.7, 129.7, 128.2, 128.0, 127.4, 126.2, 125.8, 125.7, 125.3, 125.2, 123.0, 111.5, 51.2, 24.7; **IR** (KBr): 3444, 3349, 2969, 2874, 1591, 1572, 1489, 1453, 1433, 1412, 1374, 1339, 1303, 1255, 1237, 1222, 1169, 1154, 1117, 1070, 1016, 976, 958, 933, 918; **HRMS** (ESI, m/z) calcd. for $C_{23}H_{22}N_2SNa^+$ $[M + Na]^+$ 381.1396, found 381.1383.

***N*-(4-methoxyphenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6j)**



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a dark green solid (276 mg, 82% yield). **Mp** 151 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.47 (s, 1H), 8.35 (s, 1H), 7.41 – 7.30 (m, 3H), 7.29 – 7.22 (m, 4H), 6.85 – 6.79 (m, 2H), 3.71 (s, 3H), 3.05 – 2.94 (m, 4H), 1.70 – 1.64 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.4, 156.5, 149.1, 136.5, 133.8, 132.5, 128.0, 127.2, 126.4, 113.0, 111.9, 55.2, 51.2, 24.6; **IR** (KBr): 3445, 3330, 2971, 2867, 1584, 1510, 1474, 1401, 1376, 1328, 1299, 1240, 1217, 1176, 1103, 1033, 948, 929; **HRMS** (ESI, m/z) calcd. for $C_{20}H_{22}N_2OSNa^+$ $[M + Na]^+$ 361.1345, found 361.1359.

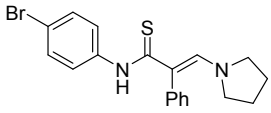
***N*-(4-chlorophenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6k)**



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a green solid (320 mg, 94% yield). **Mp** 192 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.75 (s, 1H), 8.34 (s, 1H), 7.48 – 7.43 (m, 2H), 7.40 – 7.34 (m, 2H), 7.34 – 7.27 (m, 3H), 7.26 – 7.21 (m, 2H), 3.08 – 2.89 (m, 4H), 1.73 – 1.64 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.6, 149.4, 139.9, 136.5, 132.5, 128.3, 128.0, 127.7, 127.2, 126.4, 112.5, 51.3, 24.6; **IR** (KBr): 3445, 3348, 2970, 2869, 1630, 1580, 1492, 1471, 1397, 1377, 1325, 1283, 1239, 1215, 1173, 1102, 1011, 951,

930; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{19}ClN_2SNa^+$ $[M + Na]^+$ 365.0850, found 365.0856.

***N*-(4-bromophenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6l)**



Reaction of enamine with isothiocyanate yielded the acryl thioamide after washing the crude reaction with pentane as a green solid (373 mg, 97% yield). **Mp** 196 °C; **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$): δ = 8.75 (s, 1H), 8.33 (s, 1H), 7.49 – 7.27 (m, 7H), 7.27 – 7.18 (m, 2H), 3.07 – 2.93 (m, 4H), 1.71 – 1.65 (m, 4H); **^{13}C-NMR** (100 MHz, $(CD_3)_2SO$): δ = 193.5, 149.4, 140.3, 132.5, 130.6, 128.9, 128.2, 128.0, 126.7, 116.5, 112.6, 51.3, 24.6; **IR** (KBr): 3444, 3339, 2968, 2869, 1631, 1589, 1488, 1472, 1405, 1392, 1375, 1324, 1290, 1254, 1215, 1166, 1109, 1064, 1009, 952, 929; **HRMS** (ESI, m/z) calcd. for $C_{19}H_{19}BrN_2SNa^+$ $[M + Na]^+$ 409.0345, found 409.0348;

References

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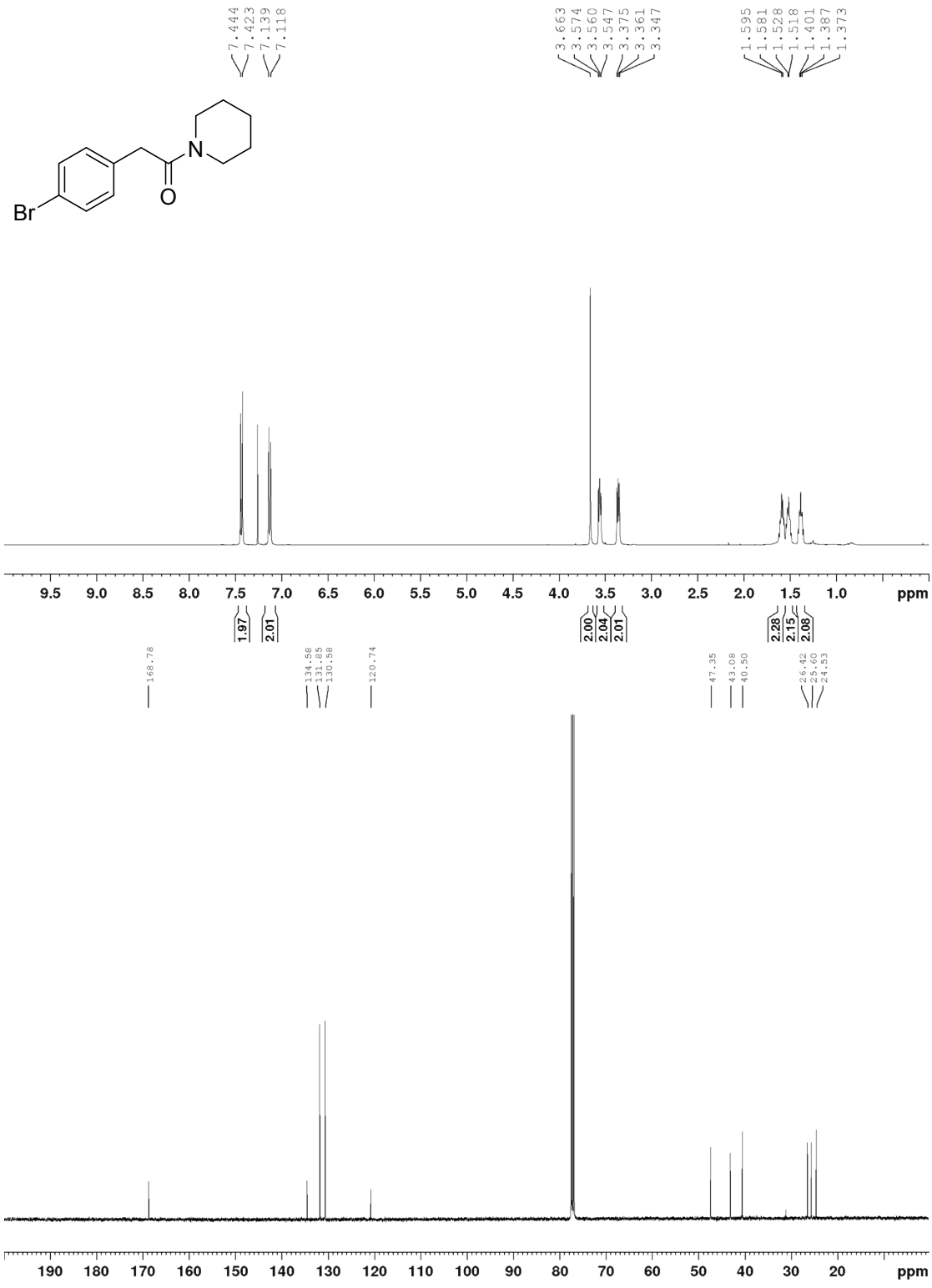
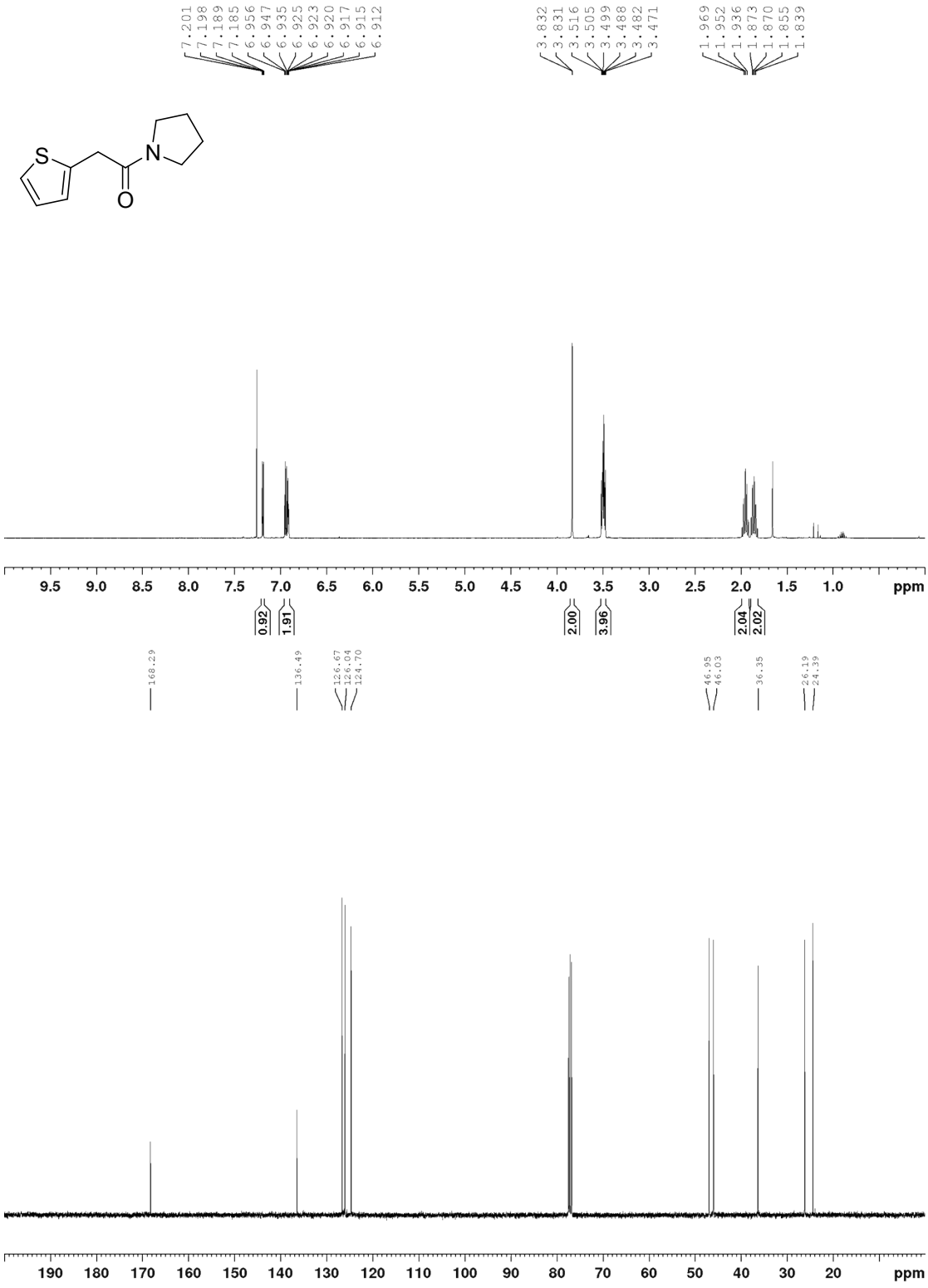
Spectroscopic Data

Amides:

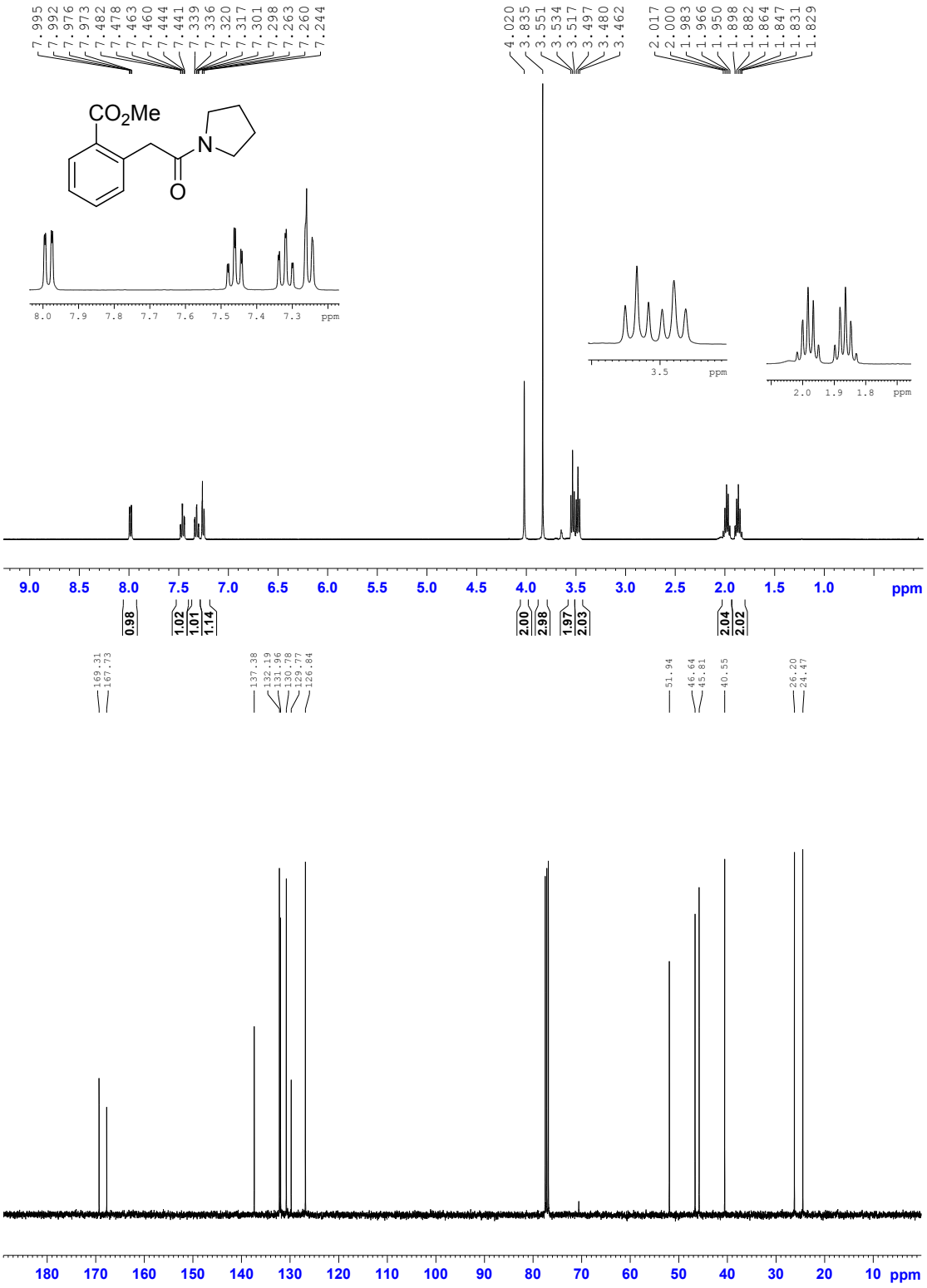
2-(4-bromophenyl)-1-(piperidin-1-yl)ethan-1-one (1c)



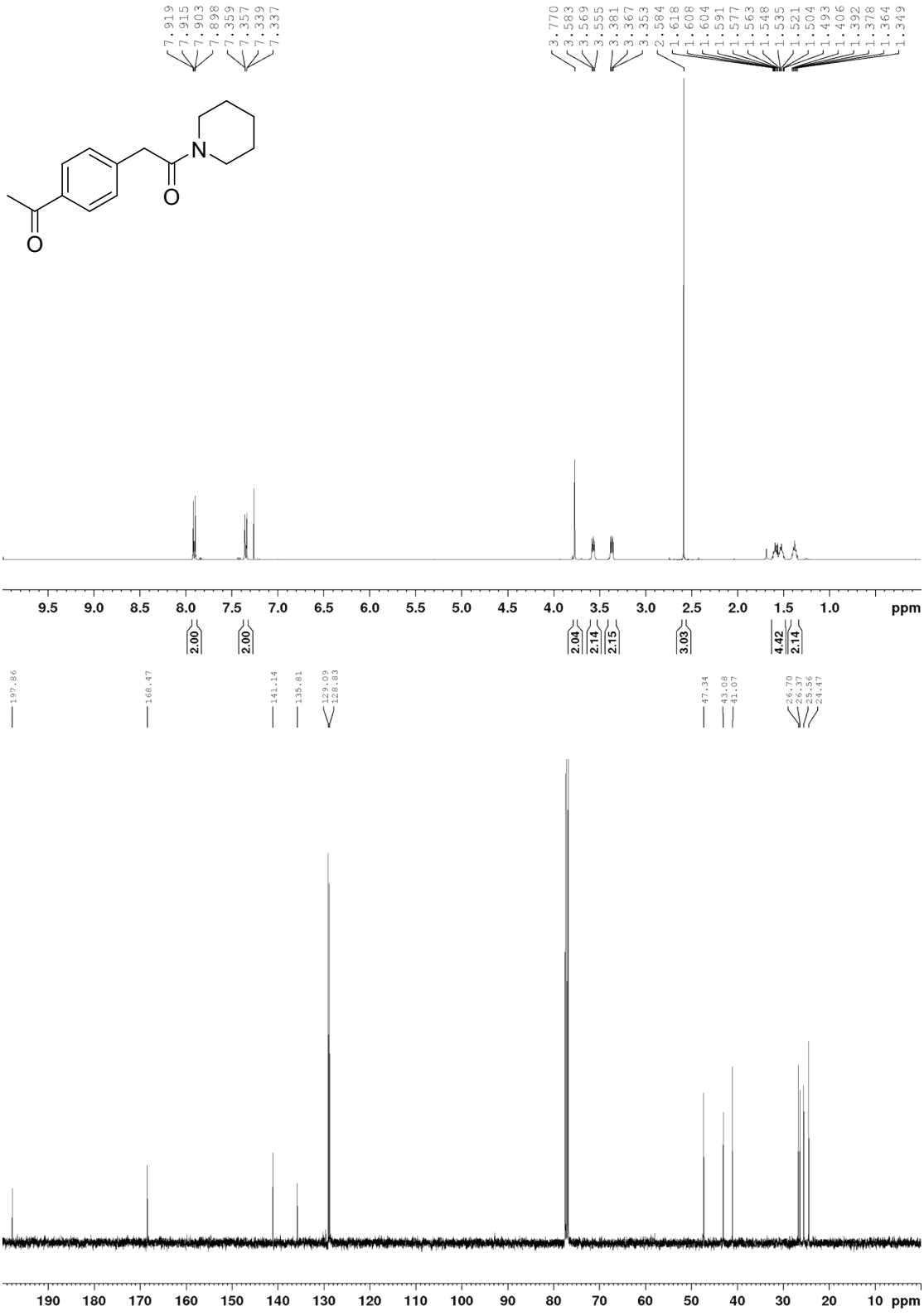
1-(pyrrolidin-1-yl)-2-(thiophen-2-yl)ethanone (1e)



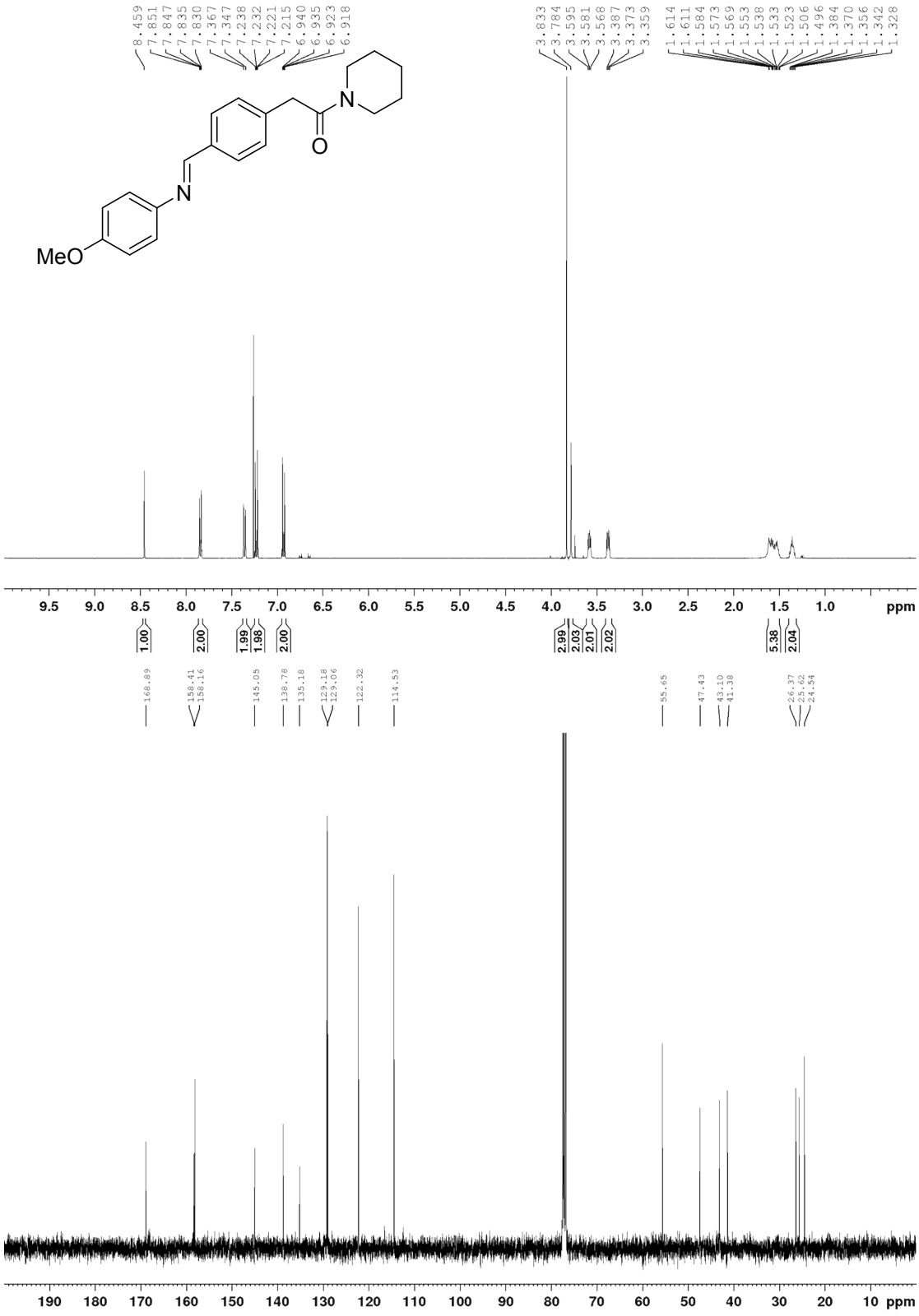
methyl 2-(2-oxo-2-(pyrrolidin-1-yl)ethyl)benzoate (1g)



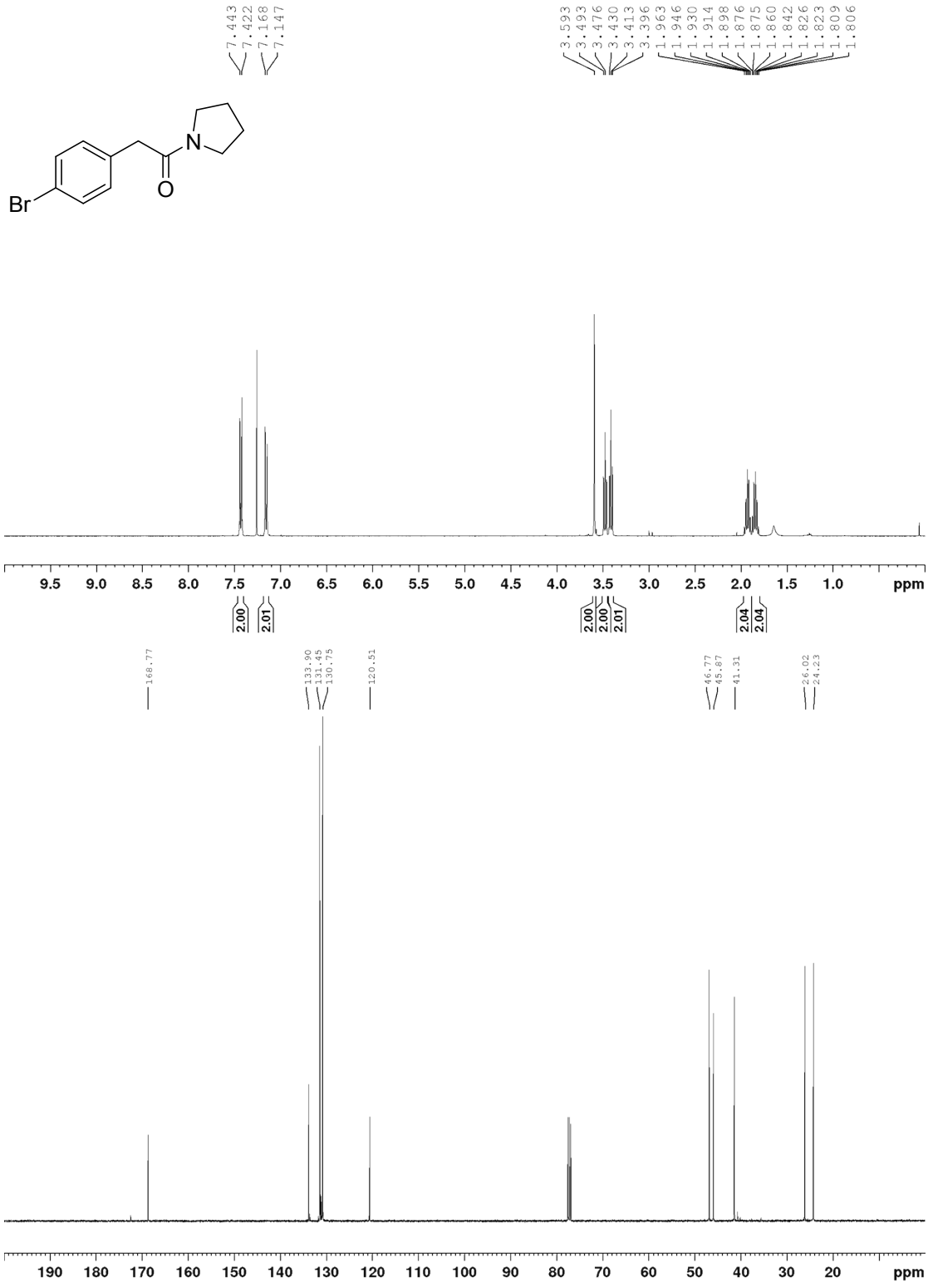
2-(4-acetylphenyl)-1-(piperidin-1-yl)ethan-1-one (1h)



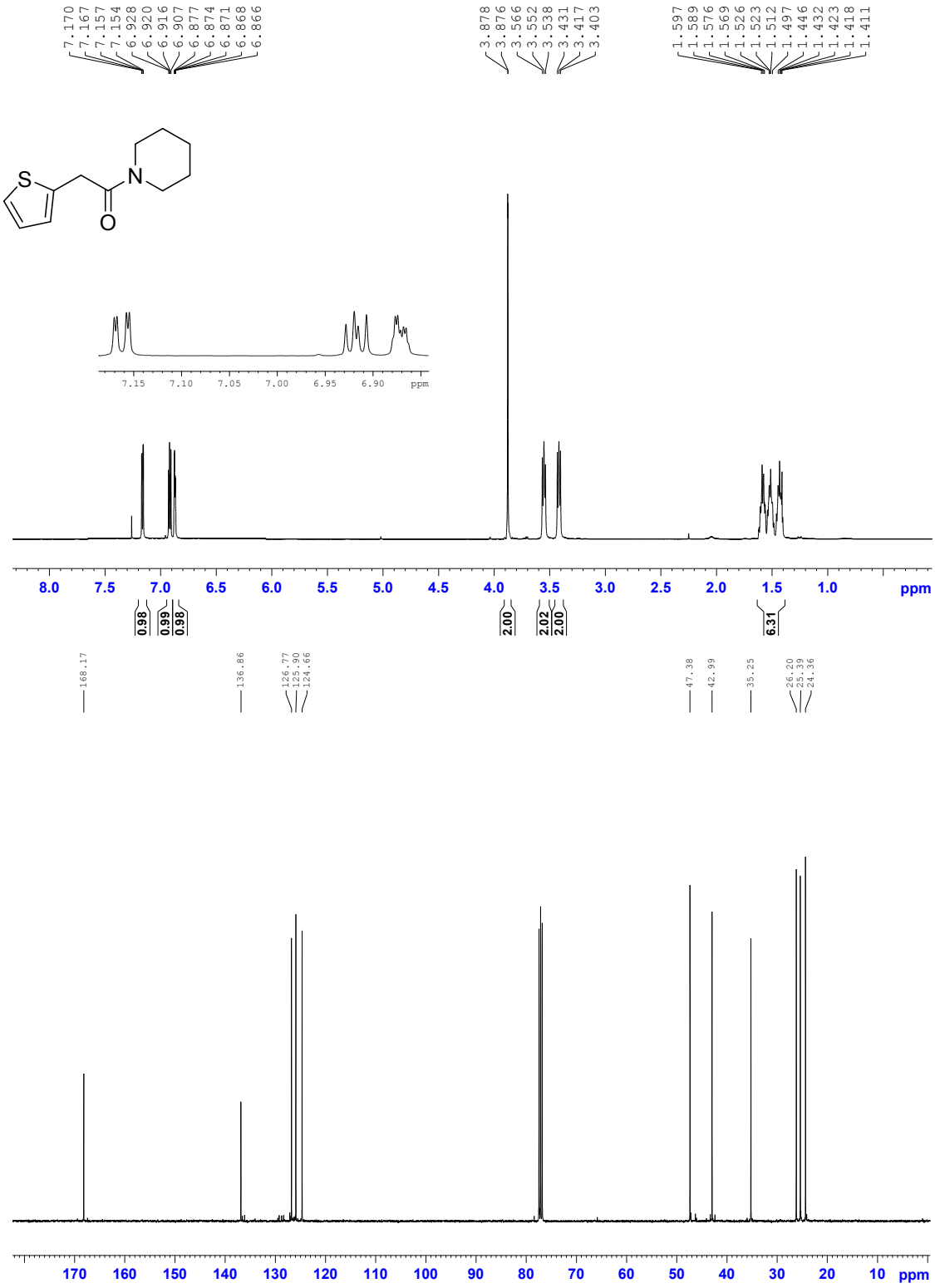
(*E*)-2-(4-(((4-methoxyphenyl)imino)methyl)phenyl)-1-(piperidin-1-yl)ethan-1-one (1i)



2-(4-bromophenyl)-1-(pyrrolidin-1-yl)ethanone (1k)



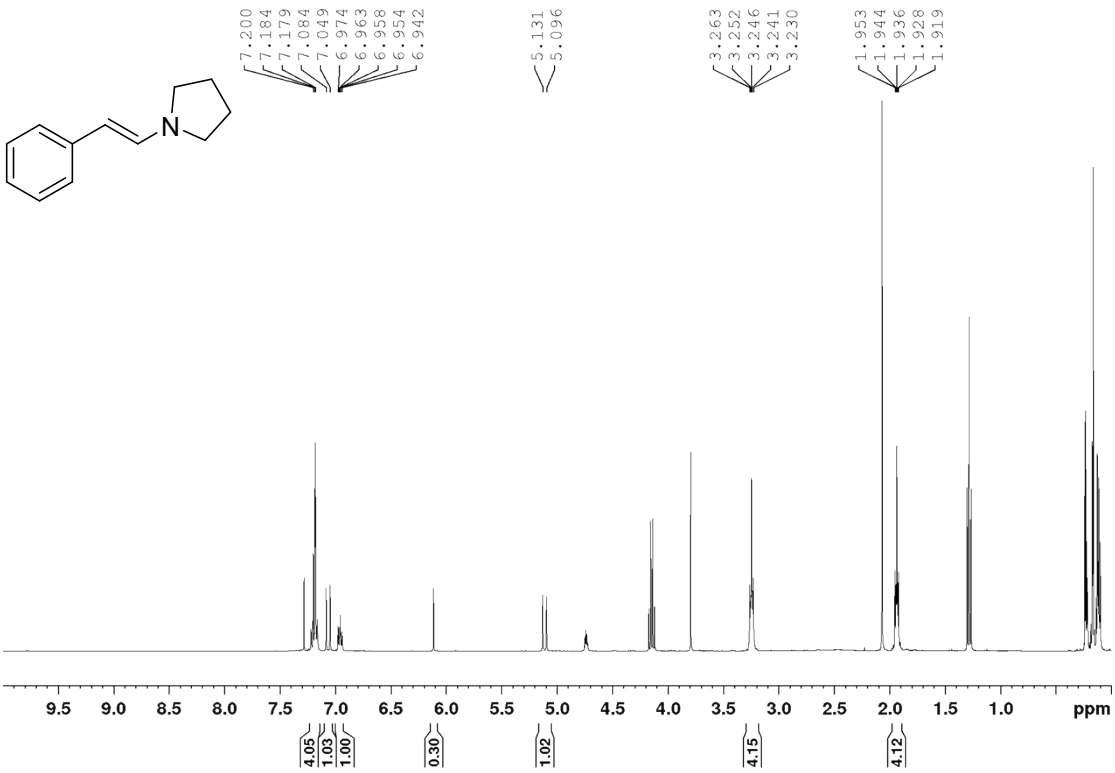
1-(piperidin-1-yl)-2-(thiophen-2-yl)ethan-1-one (1l)



Enamines:

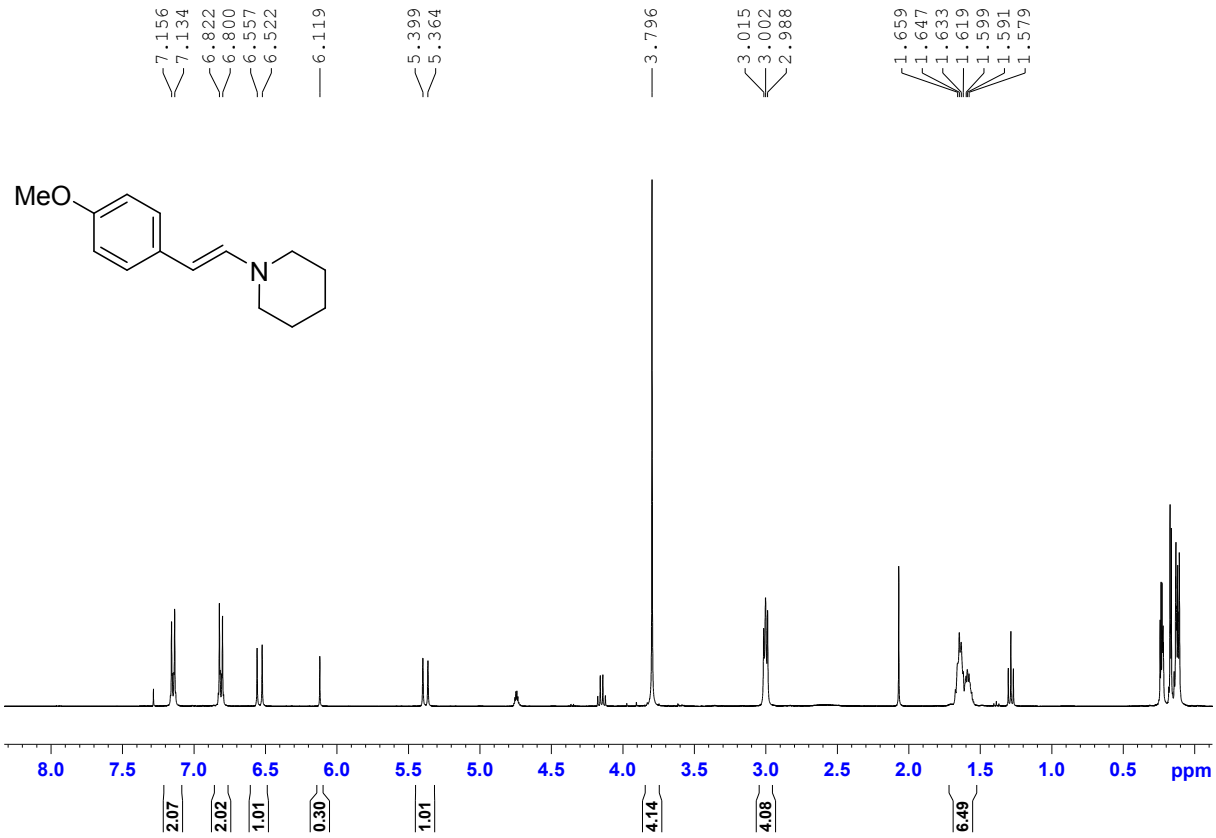
(*E*)-1-styrylpyrrolidine (2a)

Enamine formation; 30 min at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.10 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



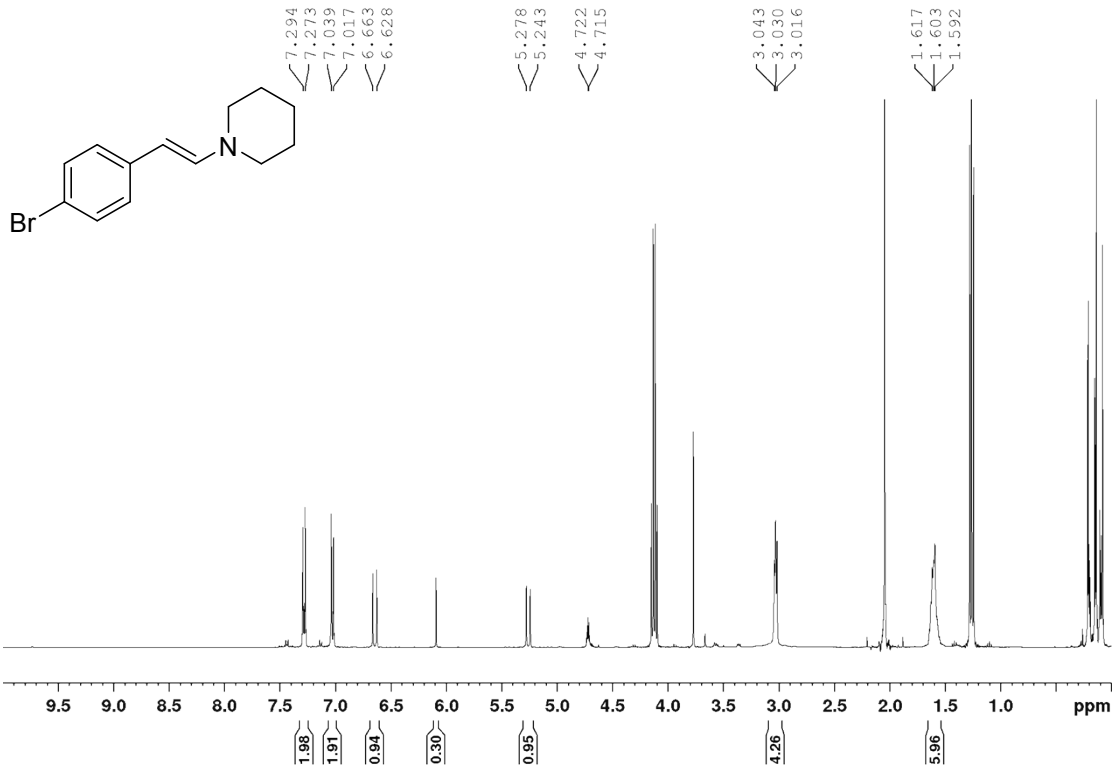
(*E*)-1-(4-methoxystyryl)piperidine (2b)

Enamine formation; 1 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.12 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



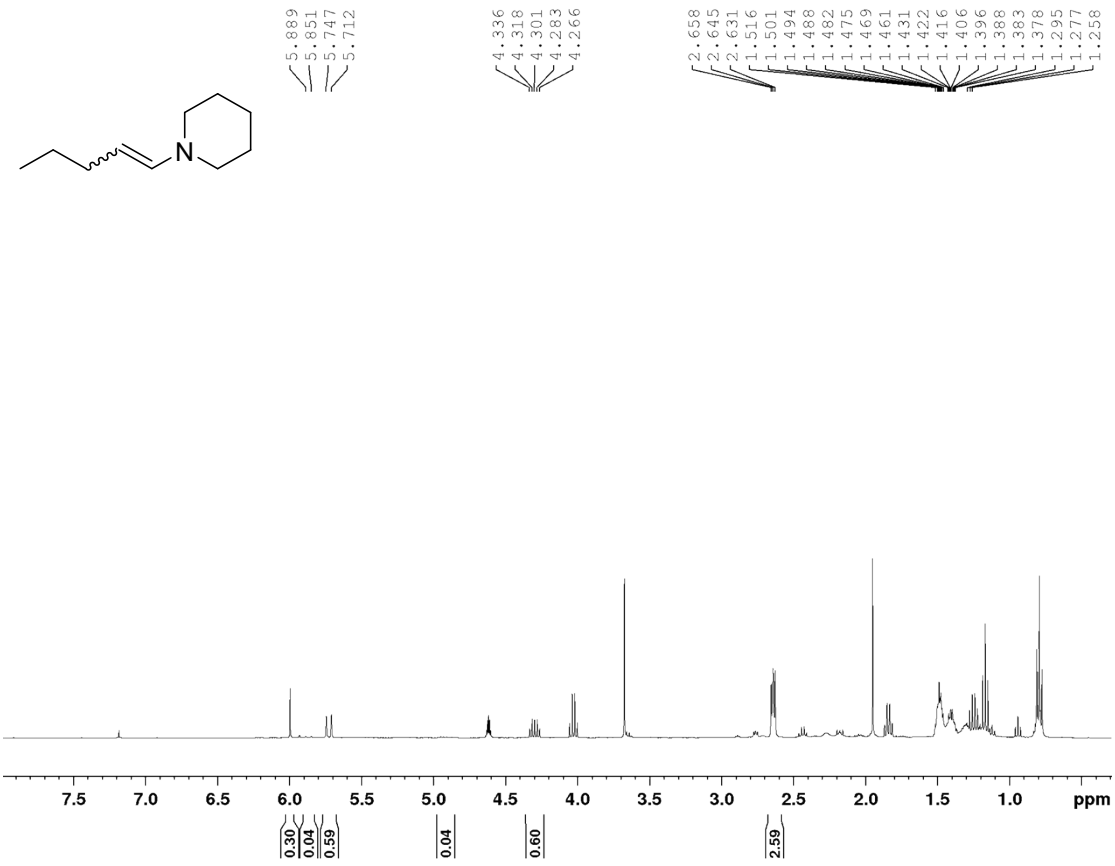
(*E*)-1-(4-bromostyryl)piperidine (2c)

Enamine formation; 3 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.11 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



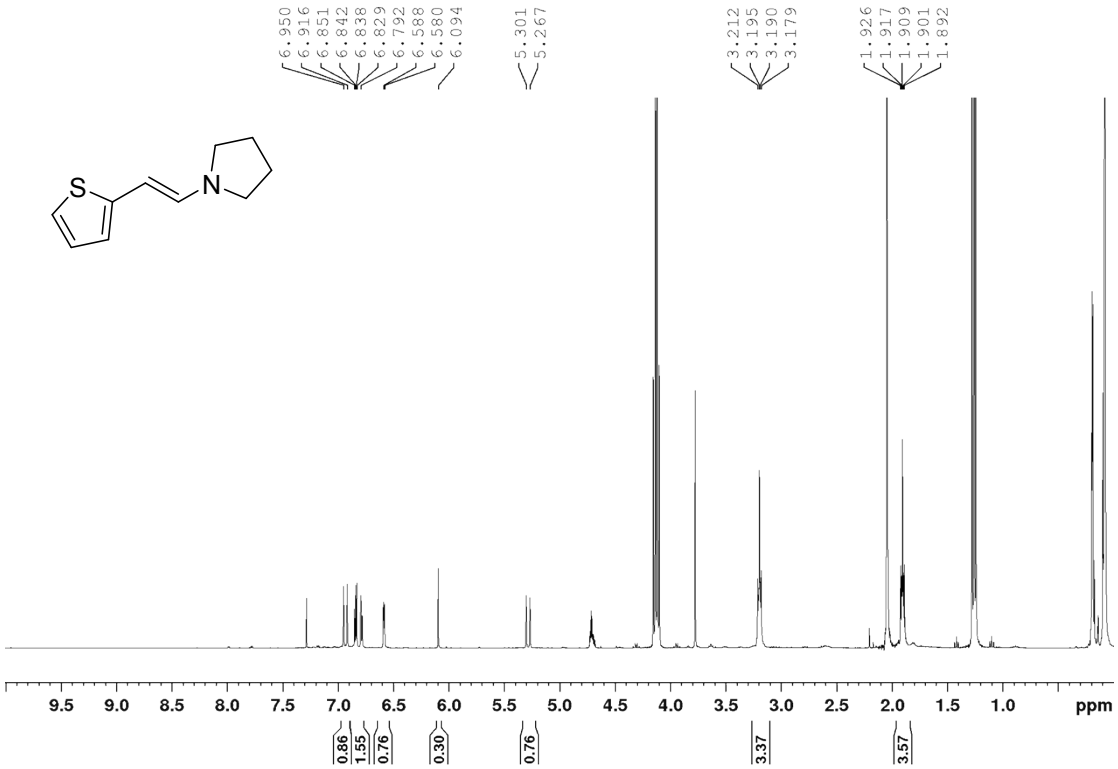
1-(pent-1-en-1-yl)piperidine (2d)

Enamine formation; 2 h at 80 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.10 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to 60%. (400 MHz, $CDCl_3$)



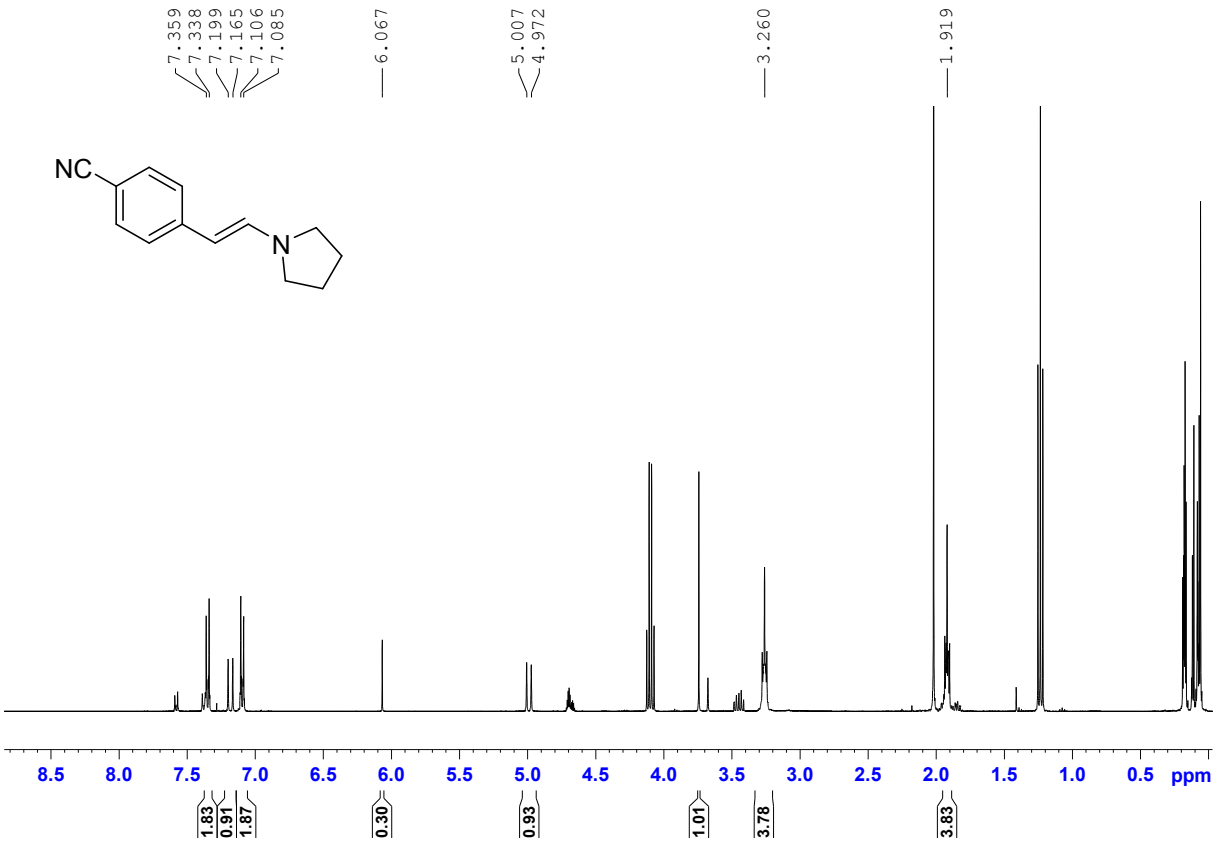
(*E*)-1-(2-(thiophen-2-yl)vinyl)pyrrolidine (2e)

Enamine formation; 2 h at 65 °C with 5 mol% $Mo(CO)_6$, 1,3,5-trimethoxybenzene (0.1 mmol / 6.09 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to 86%. (400 MHz, $CDCl_3$)



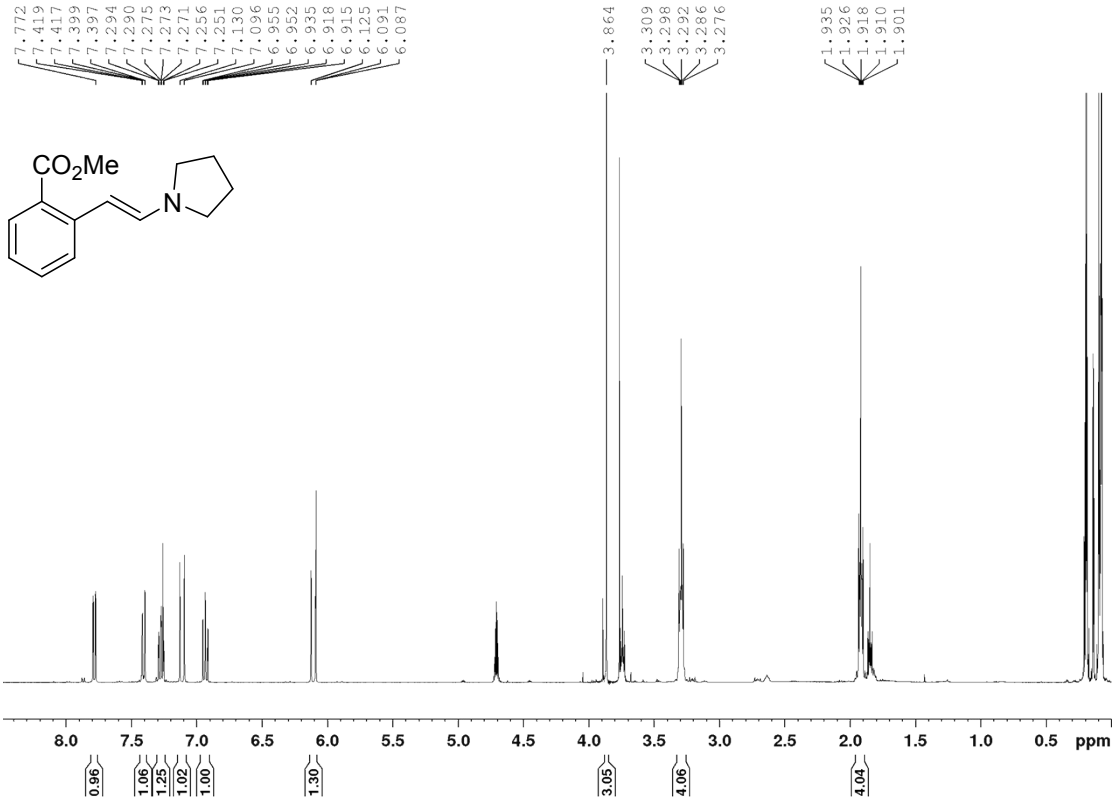
(*E*)-4-(2-(pyrrolidin-1-yl)vinyl)benzonitrile (2f)

Enamine formation; 2.5 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.07 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



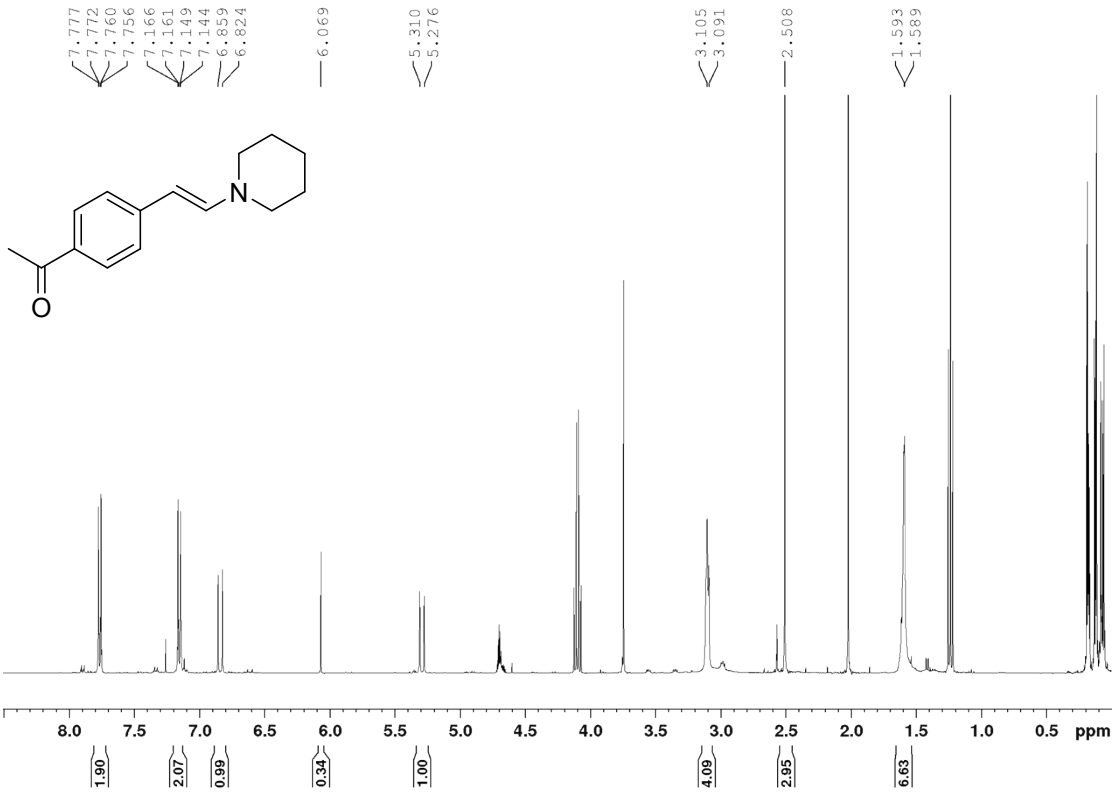
methyl (*E*)-2-(2-(pyrrolidin-1-yl)vinyl)benzoate (2g)

Enamine formation; 1 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.09 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >89%. (400 MHz, $CDCl_3$).



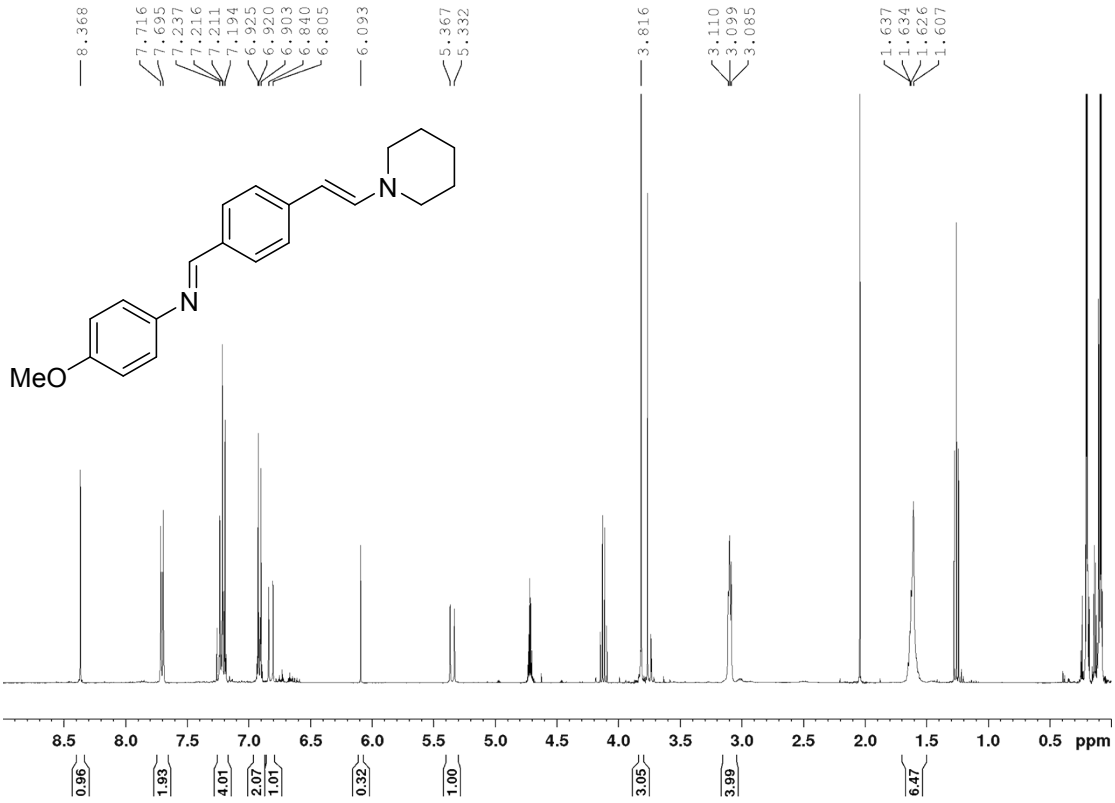
(*E*)-1-(4-(2-(piperidin-1-yl)vinyl)phenyl)ethan-1-one (2h)

Enamine formation; 5 h at 40 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.07 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to 89%. (400 MHz, $CDCl_3$)



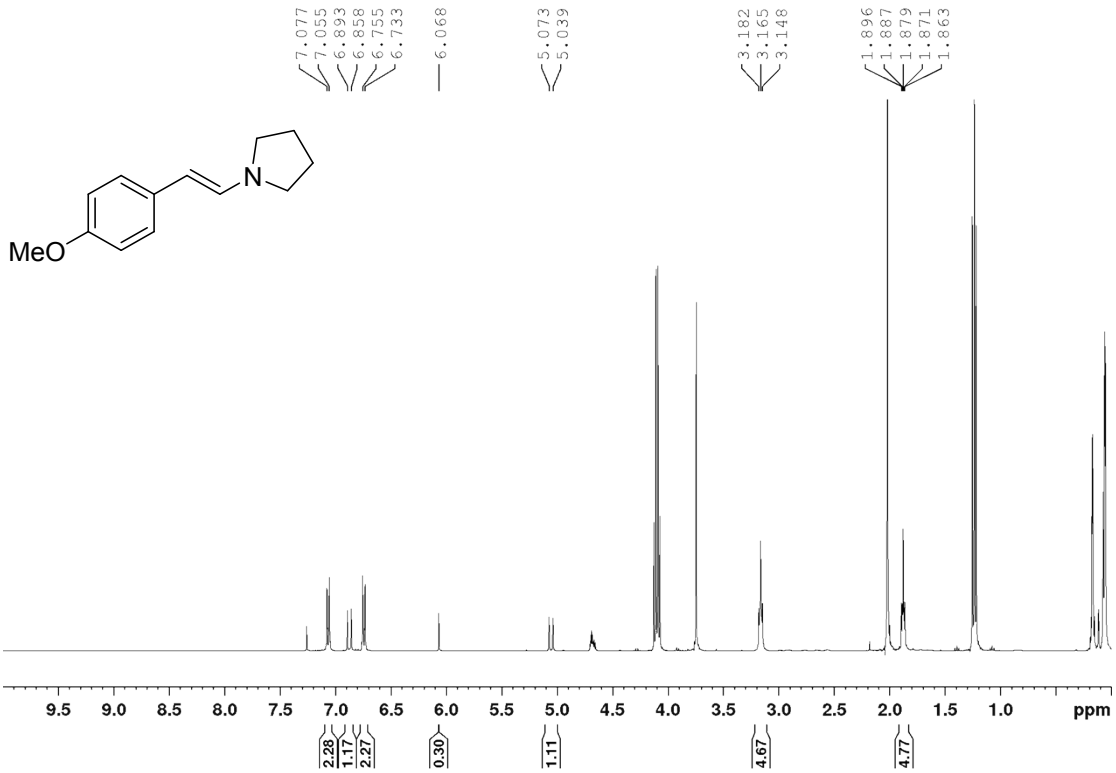
(*E*)-*N*-(4-methoxyphenyl)-1-(4-((*E*)-2-(piperidin-1-yl)vinyl)phenyl)methanimine (2i)

Enamine formation; 4 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.09 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to 94%. (400 MHz, $CDCl_3$)



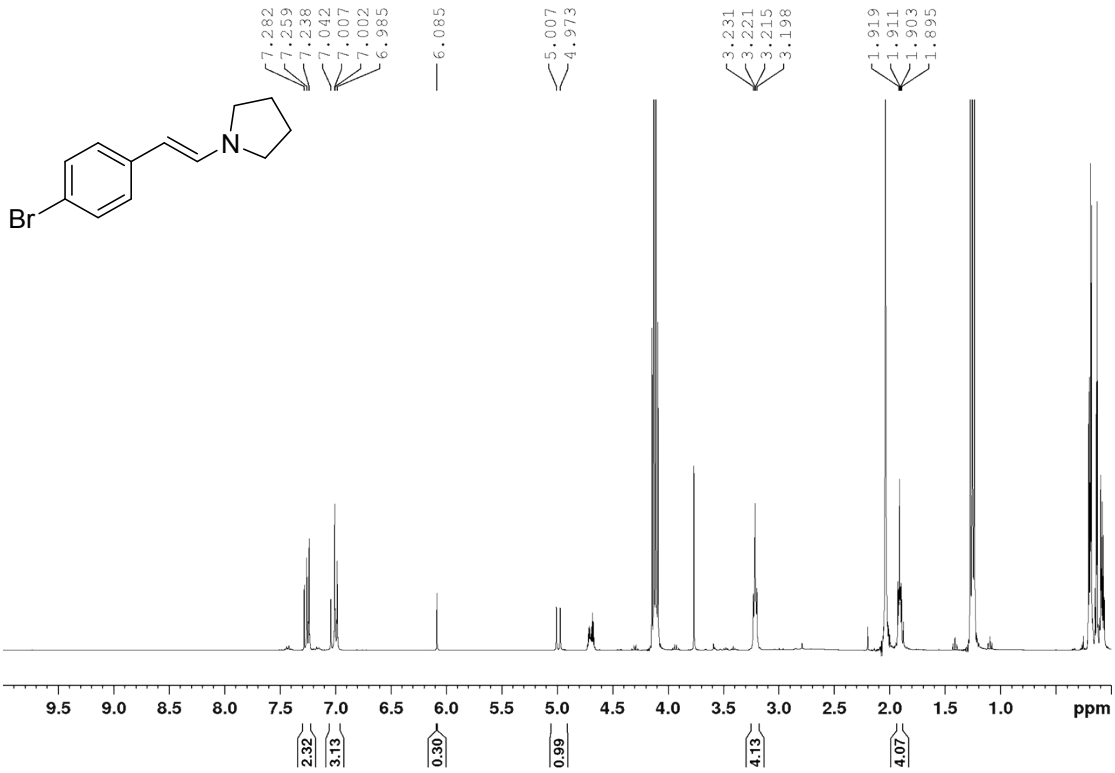
(*E*)-1-(4-methoxystyryl)pyrrolidine (2j)

Enamine formation; 1 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.07 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



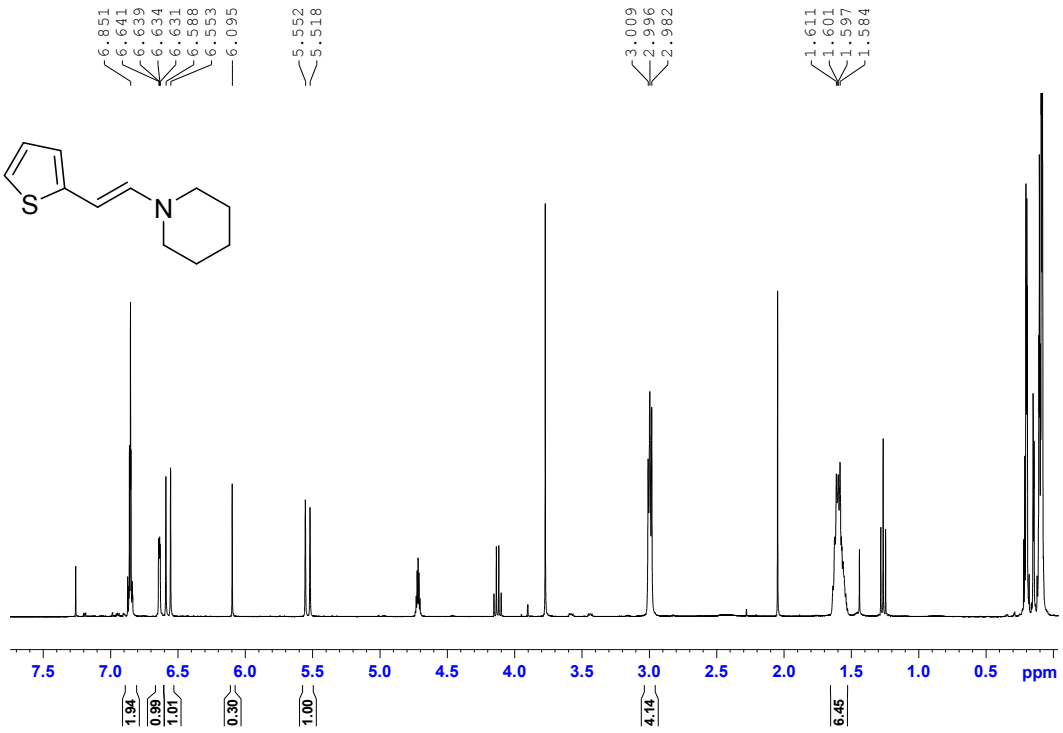
(*E*)-1-(4-bromostyryl)pyrrolidine (2k)

Enamine formation; 3 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.09 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



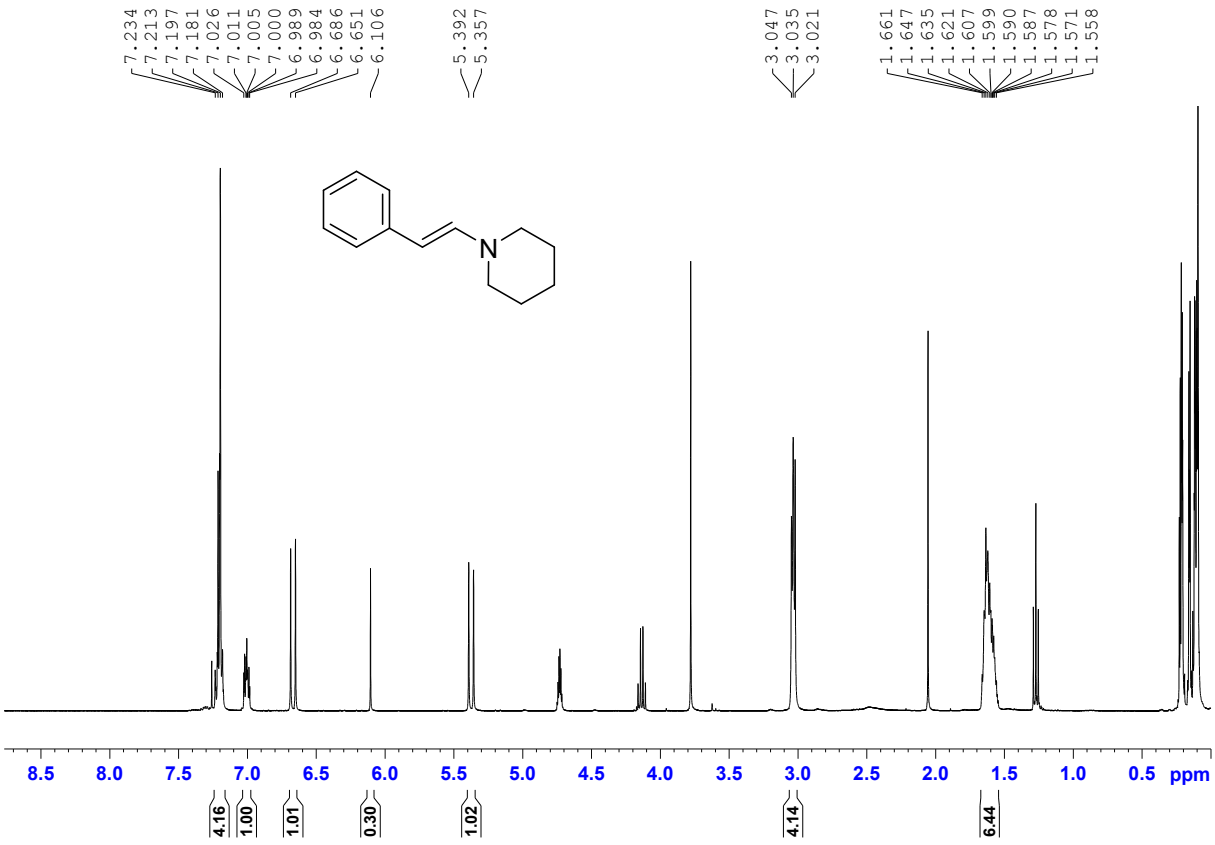
(*E*)-1-(2-(thiophen-2-yl)vinyl)piperidine (2l)

Enamine formation; 3 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.10 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



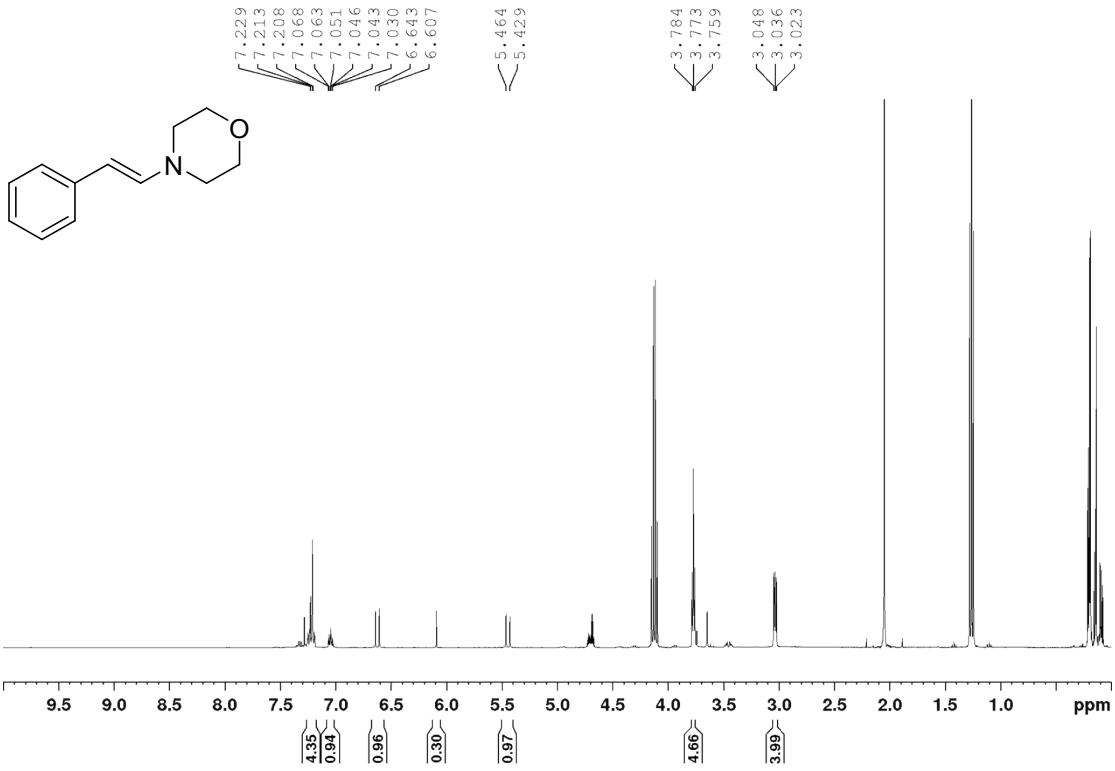
(*E*)-1-styrylpiperidine (2m)

Enamine formation; 1 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.11 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



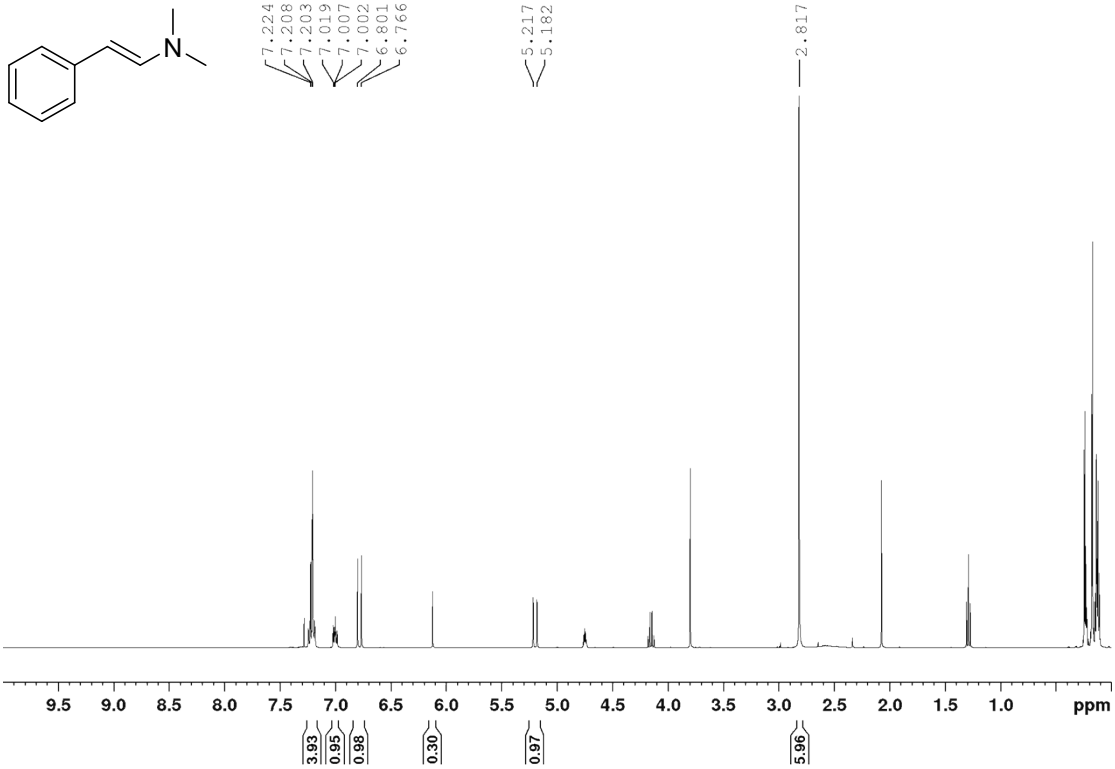
(*E*)-4-styrylmorpholine (2n)

Enamine formation; 3 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.10 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)



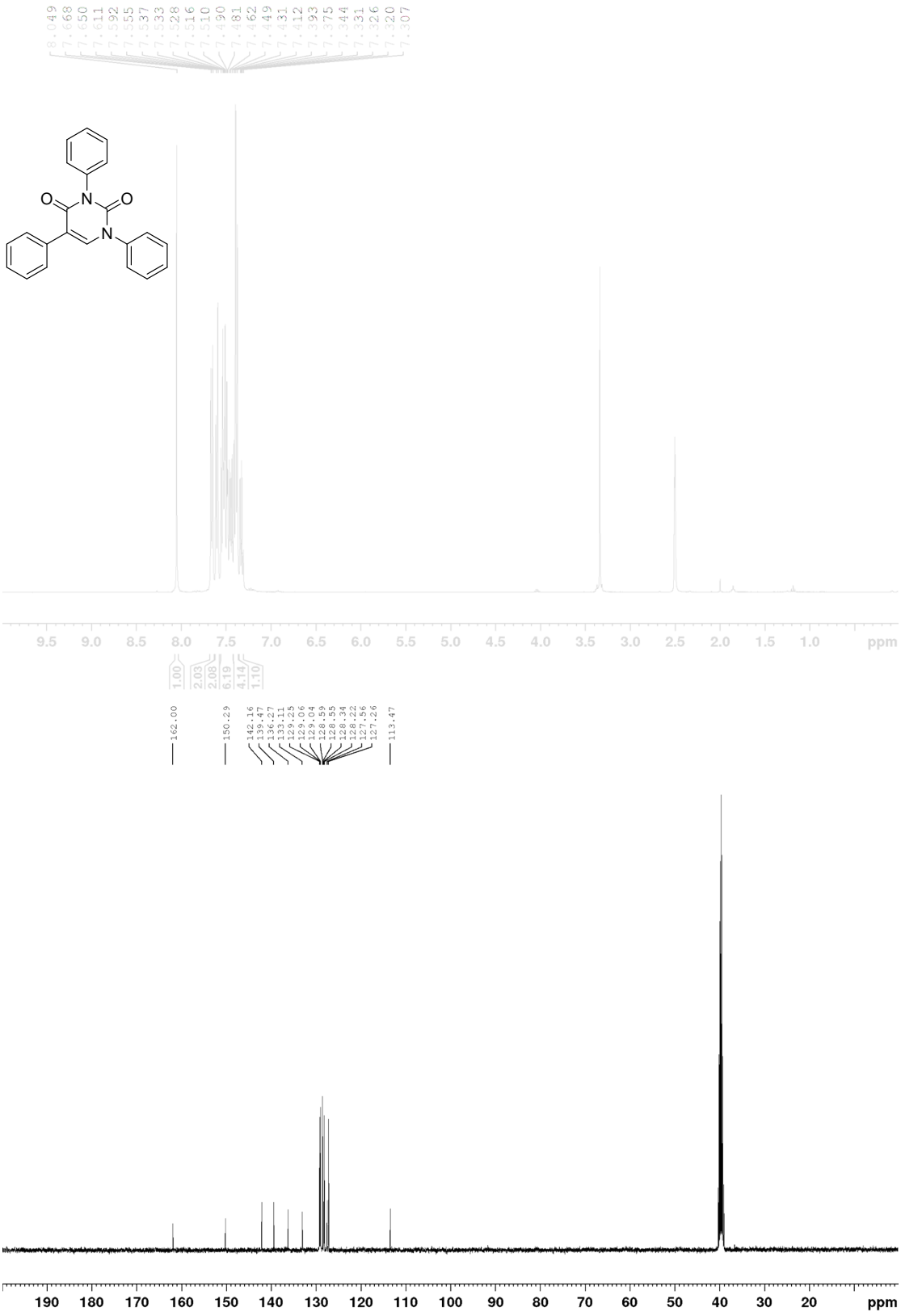
(*E*)-*N*,*N*-dimethyl-2-phenylethen-1-amine (2o)

Enamine formation; 1 h at 65 °C, 1,3,5-trimethoxybenzene (0.1 mmol / 6.10 ppm) was used as internal standard to determine the ^{1}H-NMR yield of the formed enamine to >95%. (400 MHz, $CDCl_3$)

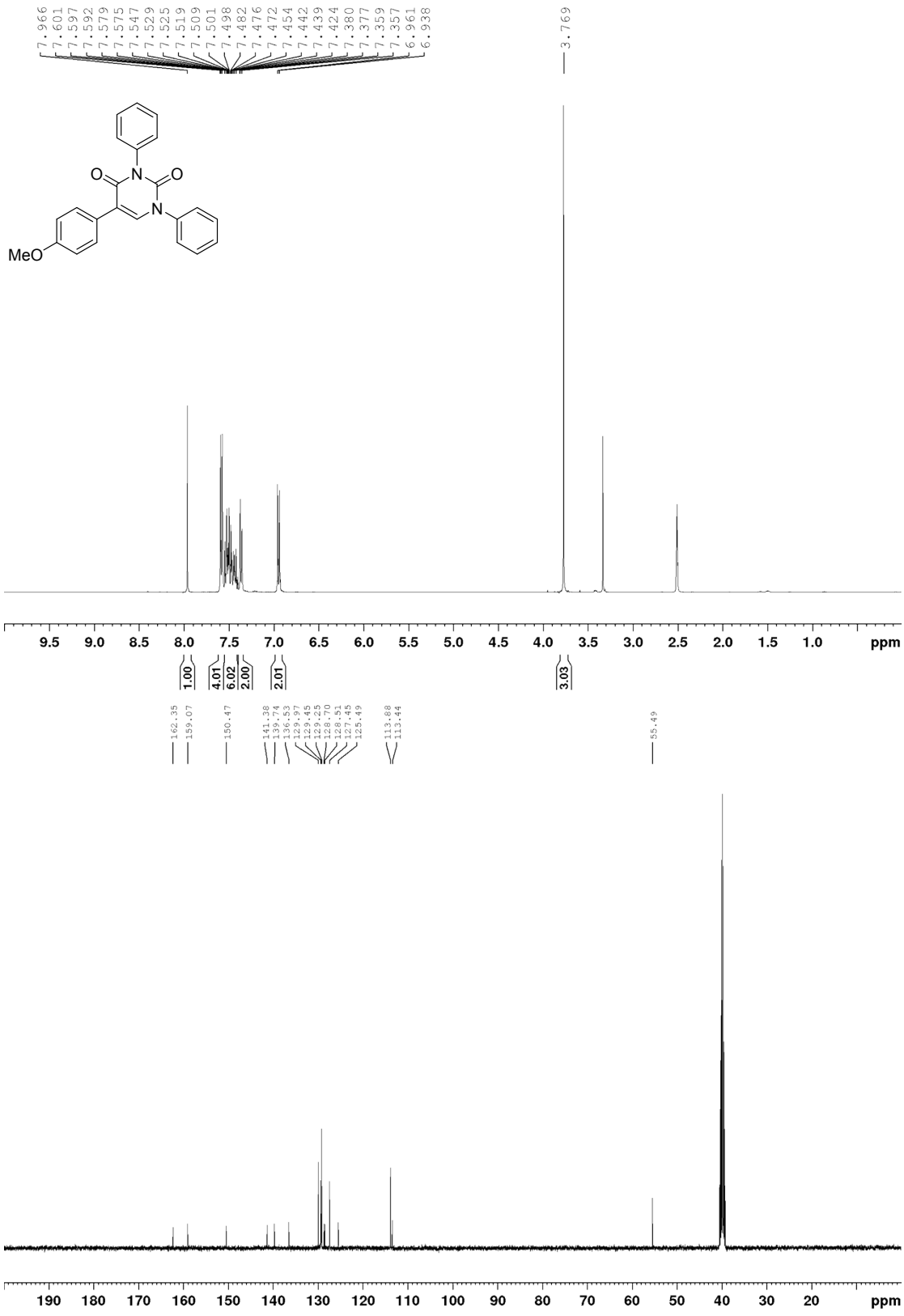


1,3-disubstituted pyrimidines:

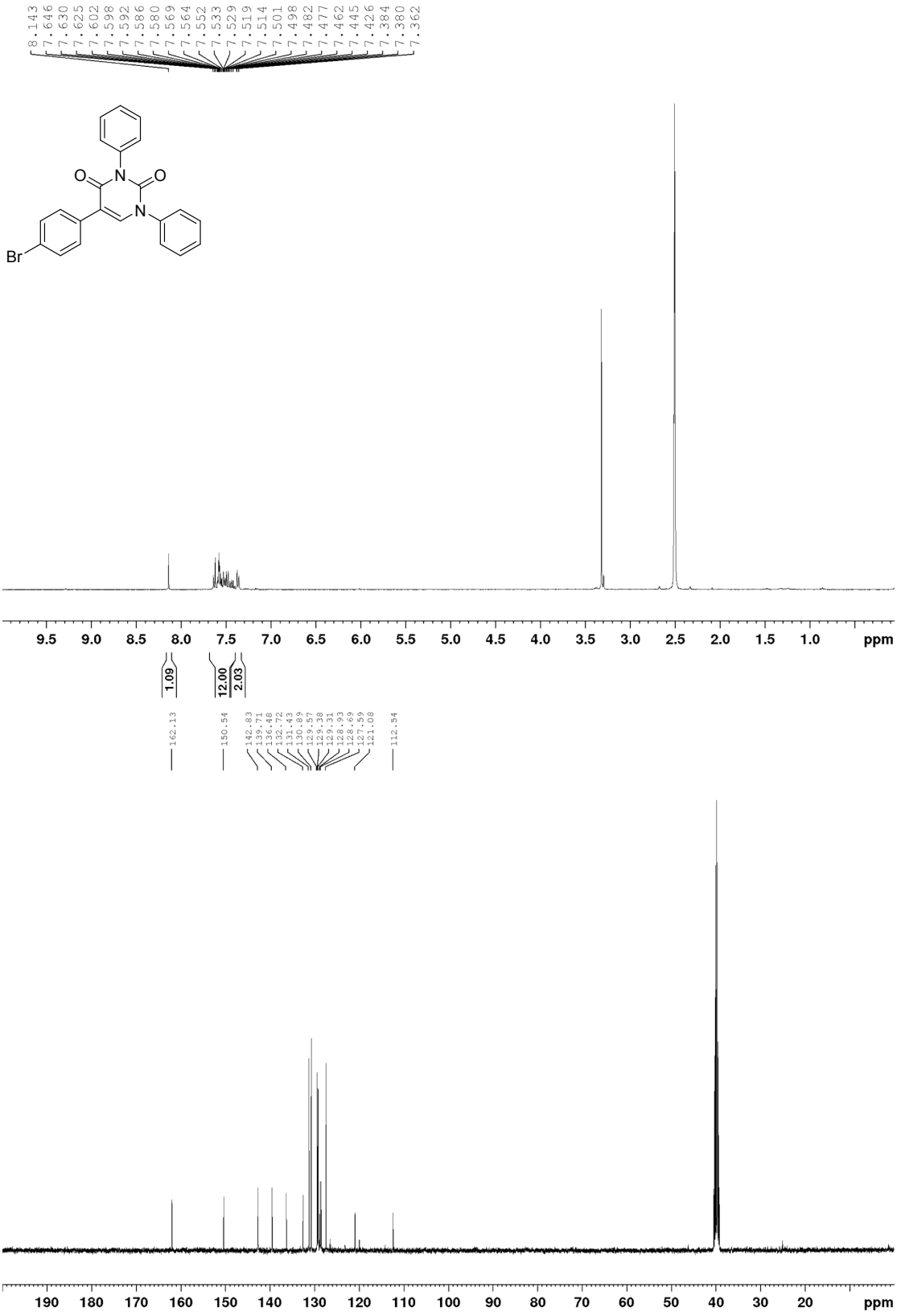
1,3,5-triphenylpyrimidine-2,4(1*H*,3*H*)-dione (4a)



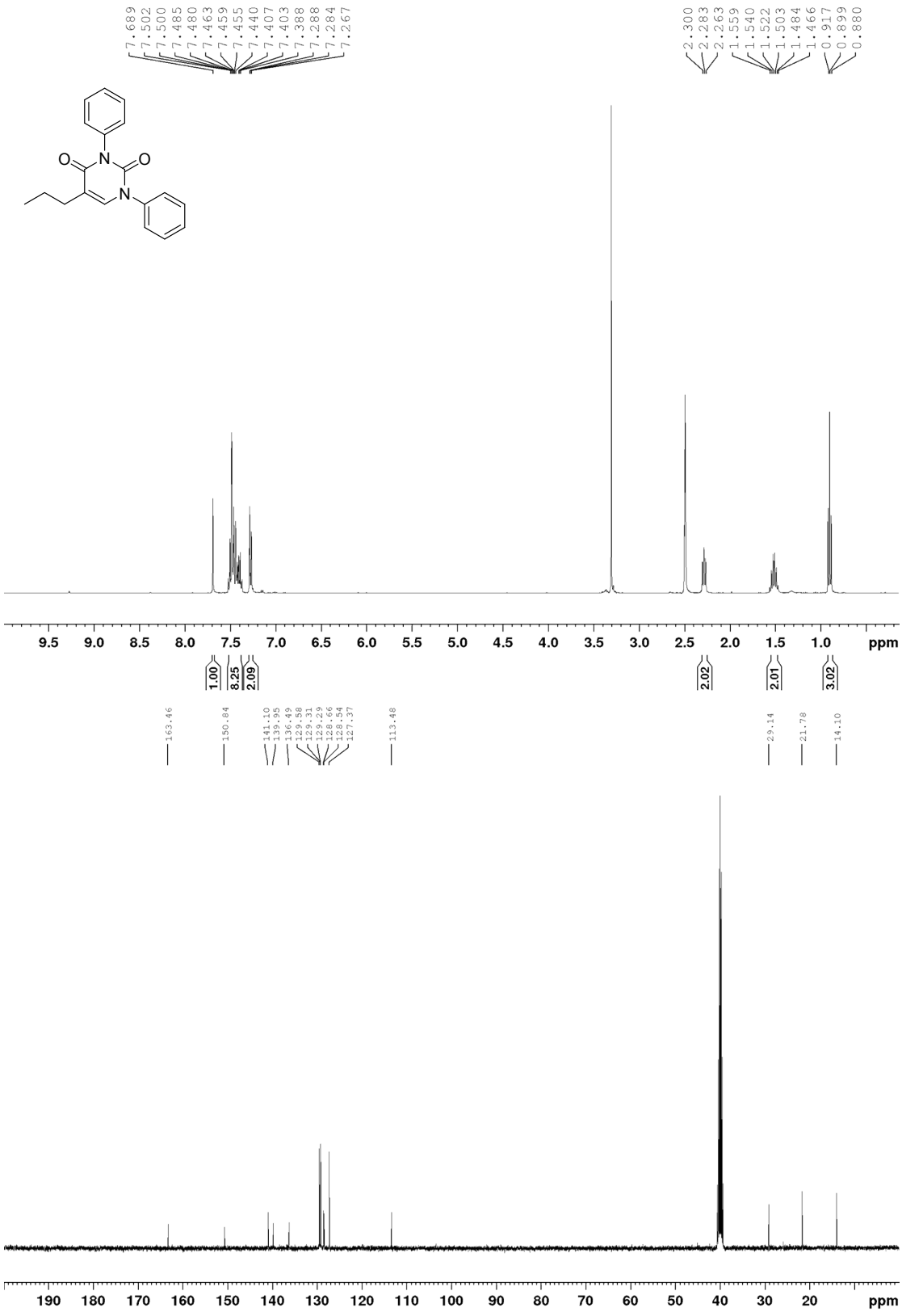
5-(4-methoxyphenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4b)



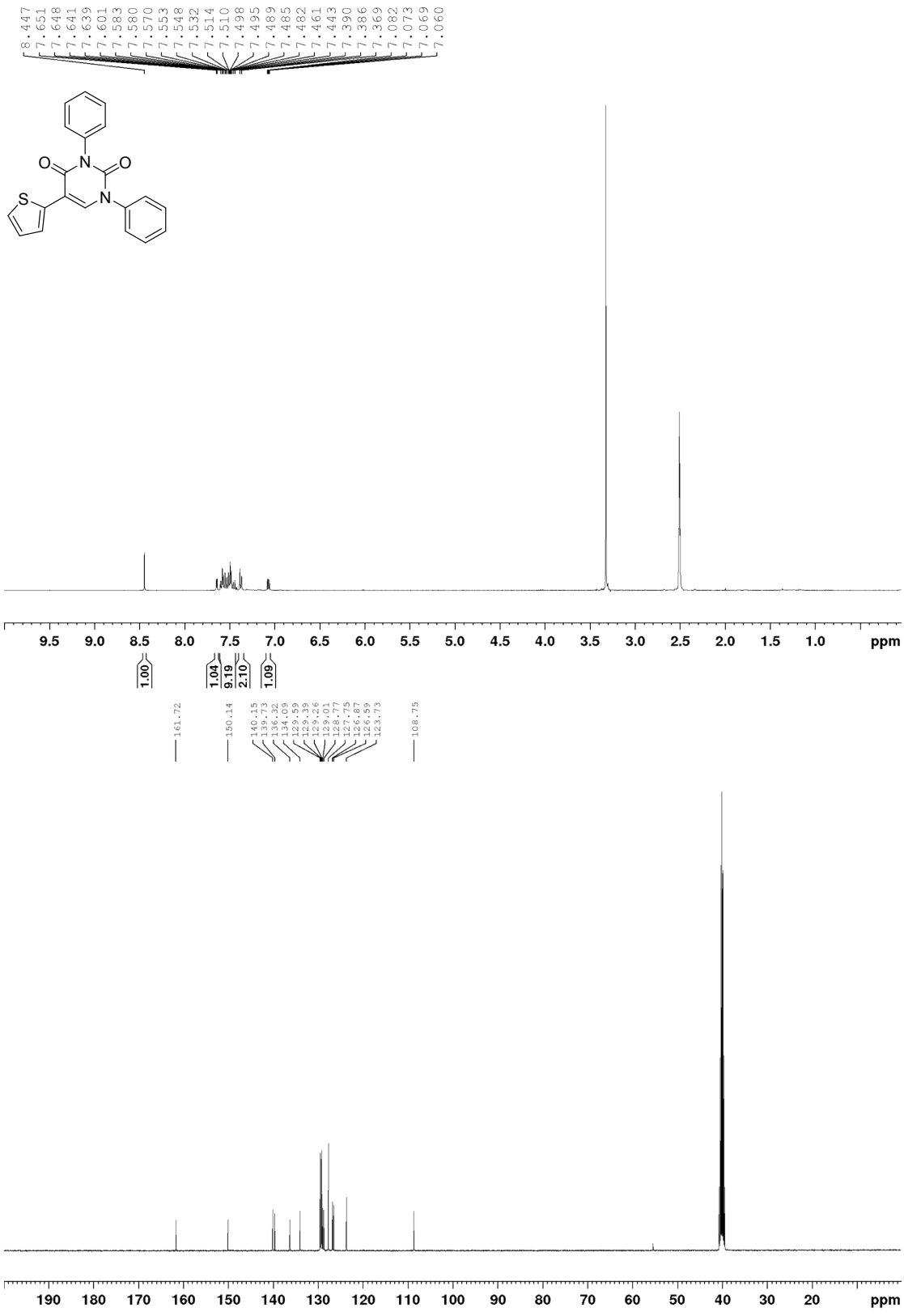
5-(4-bromophenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4c)



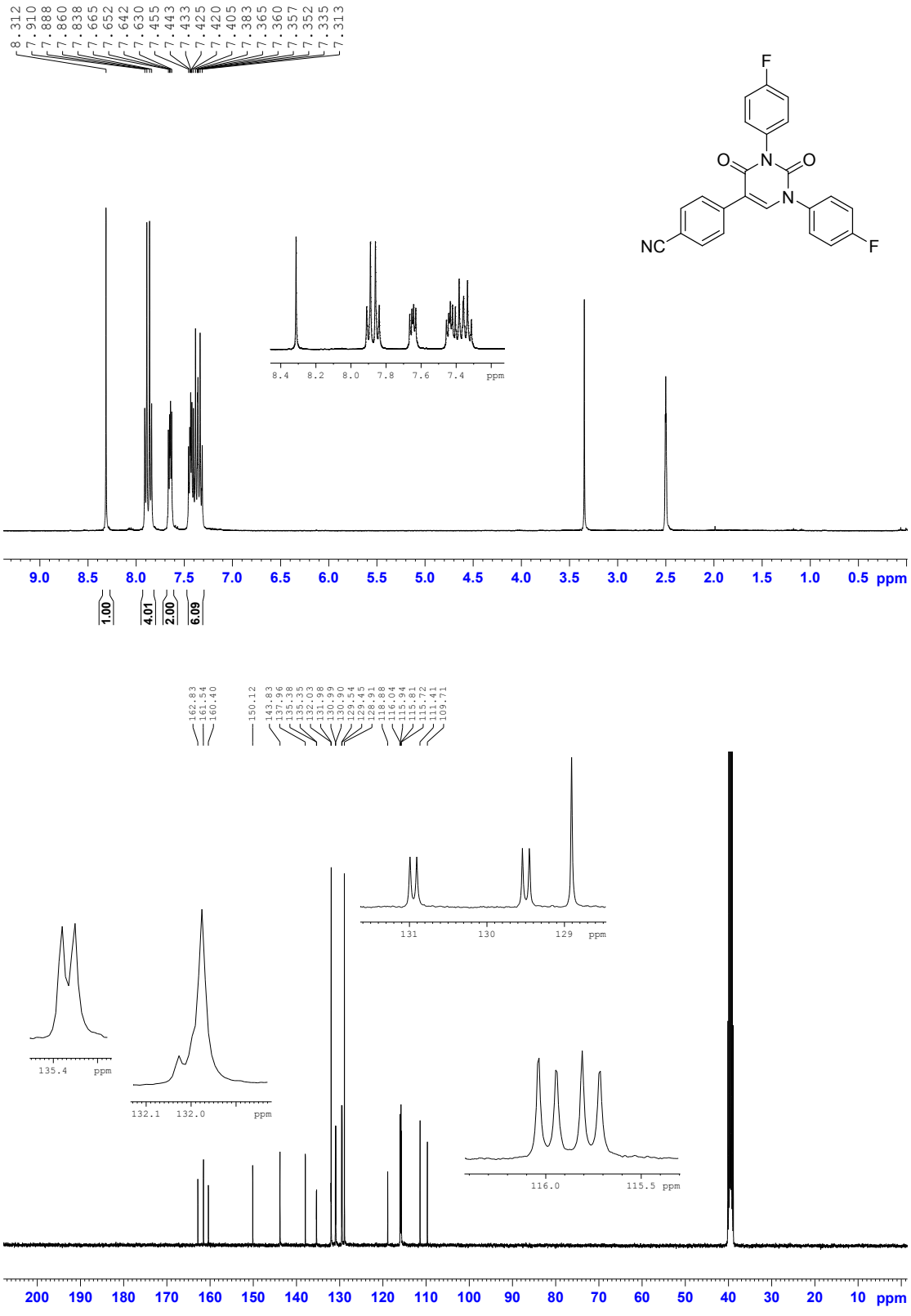
1,3-diphenyl-5-propylpyrimidine-2,4(1*H*,3*H*)-dione (4d)



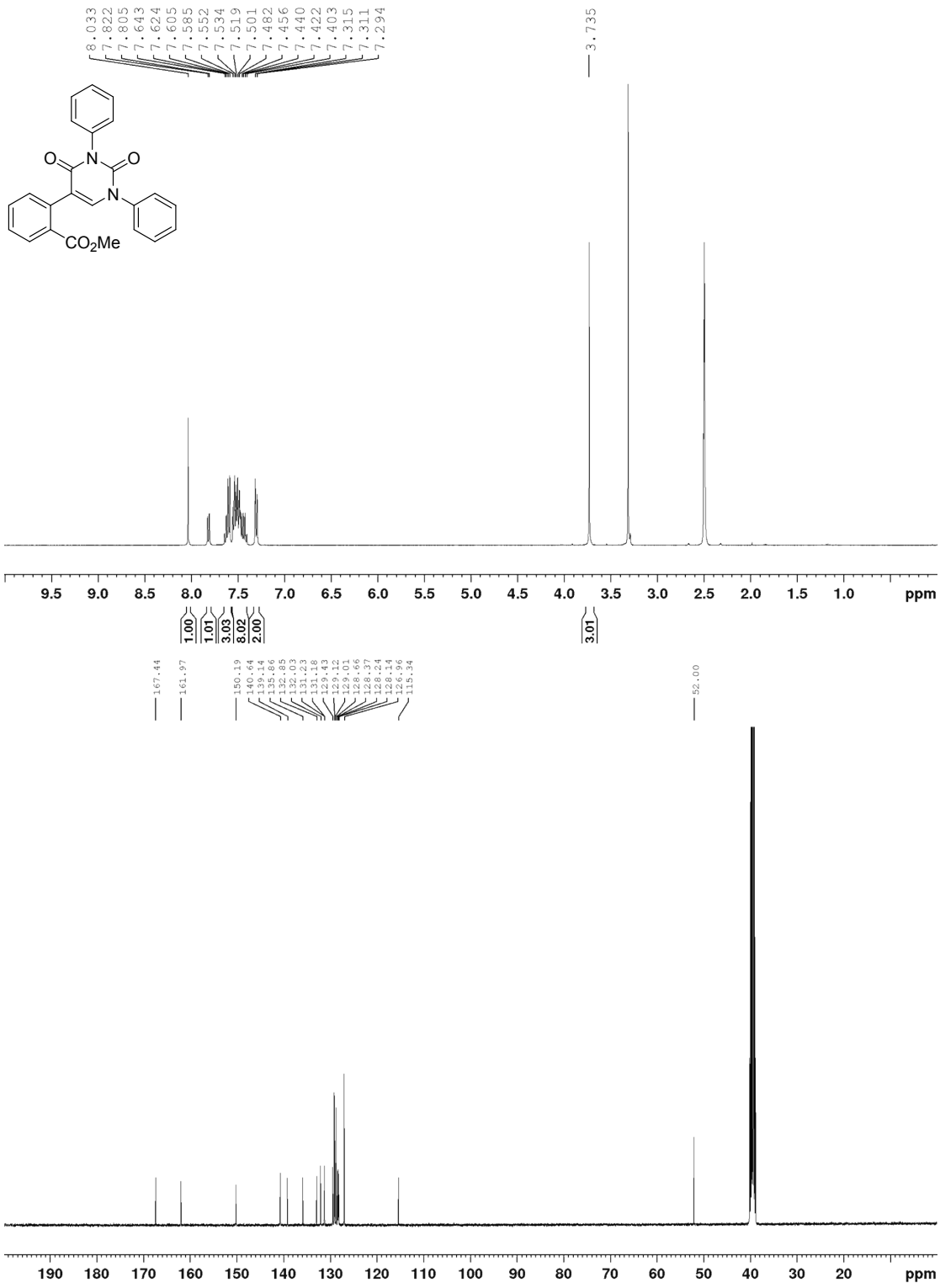
1,3-diphenyl-5-(thiophen-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (4e)



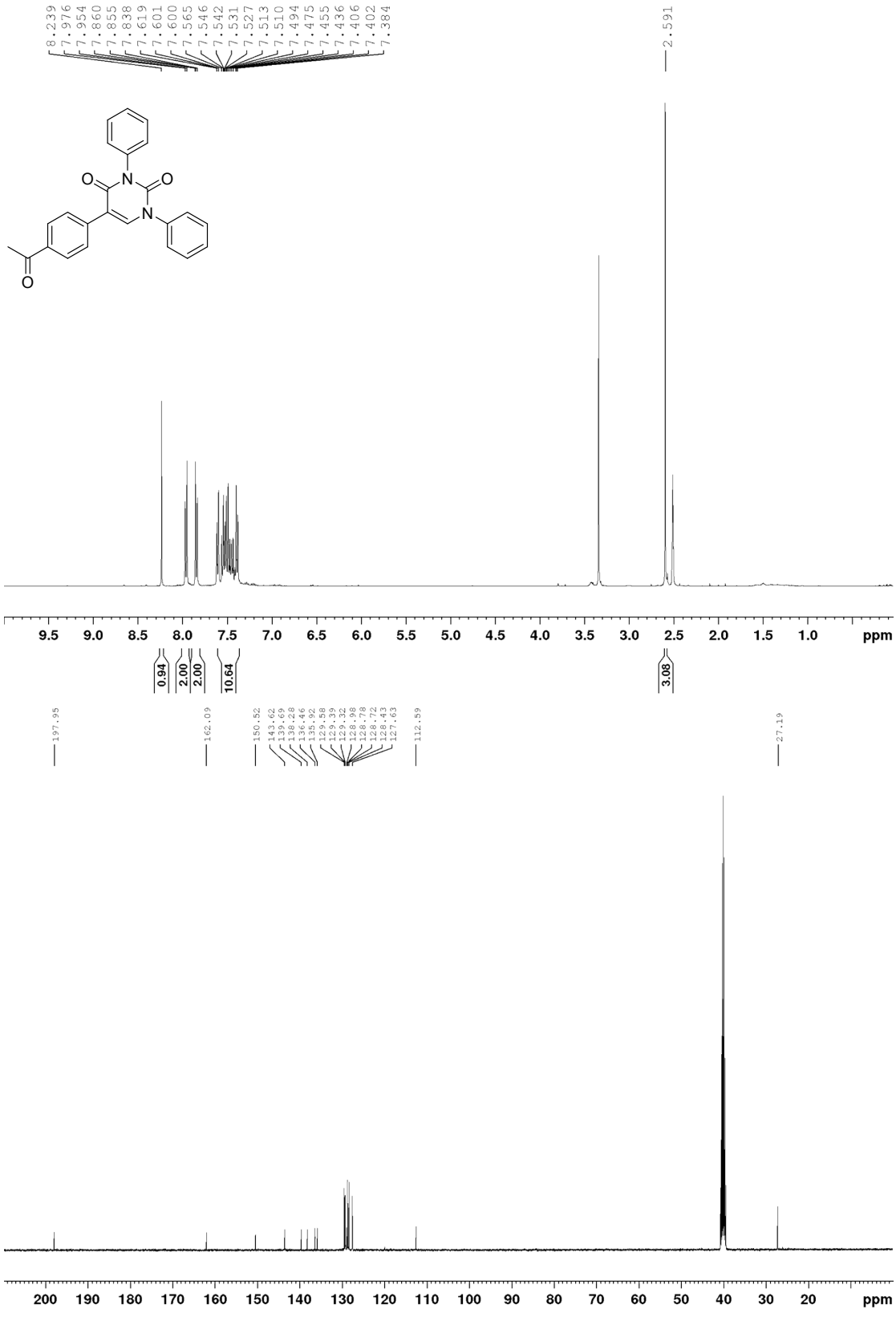
4-(1,3-bis(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)benzonitrile (4f)



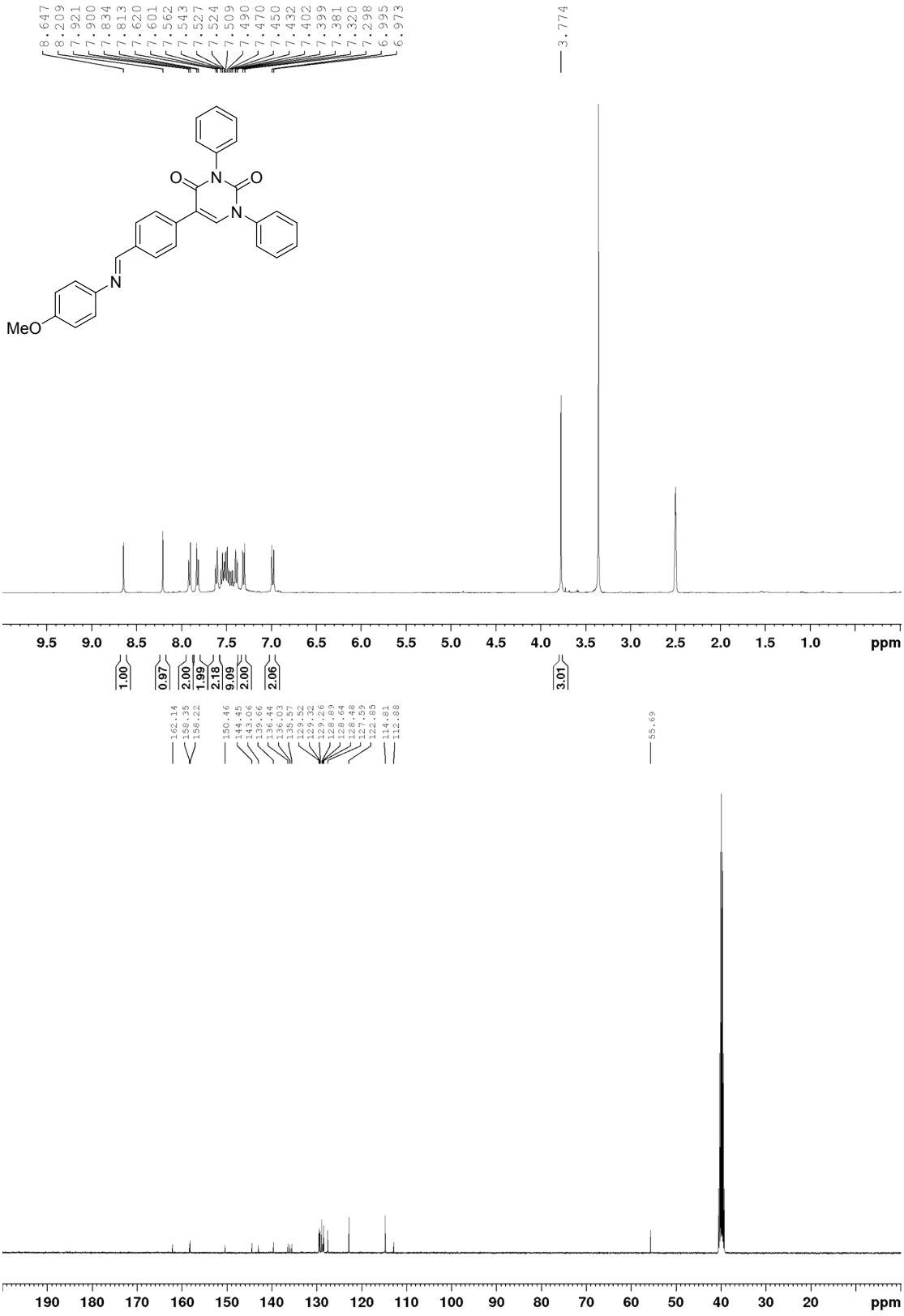
methyl 2-(2,4-dioxo-1,3-diphenyl-1,2,3,4-tetrahydropyrimidin-5-yl)benzoate (4g)



5-(4-acetylphenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4h)

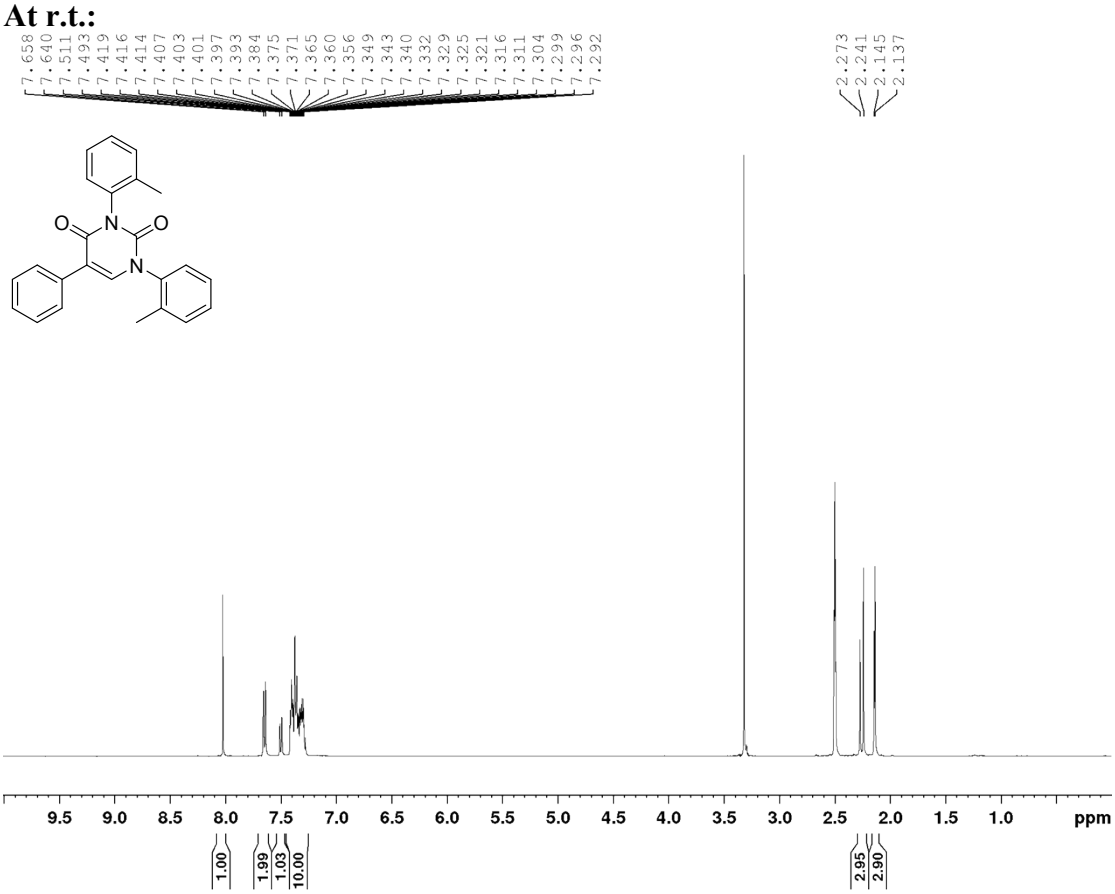


(*E*)-5-(4-((4-methoxyphenylimino)methyl)phenyl)-1,3-diphenylpyrimidine-2,4(1*H*,3*H*)-dione (4i)



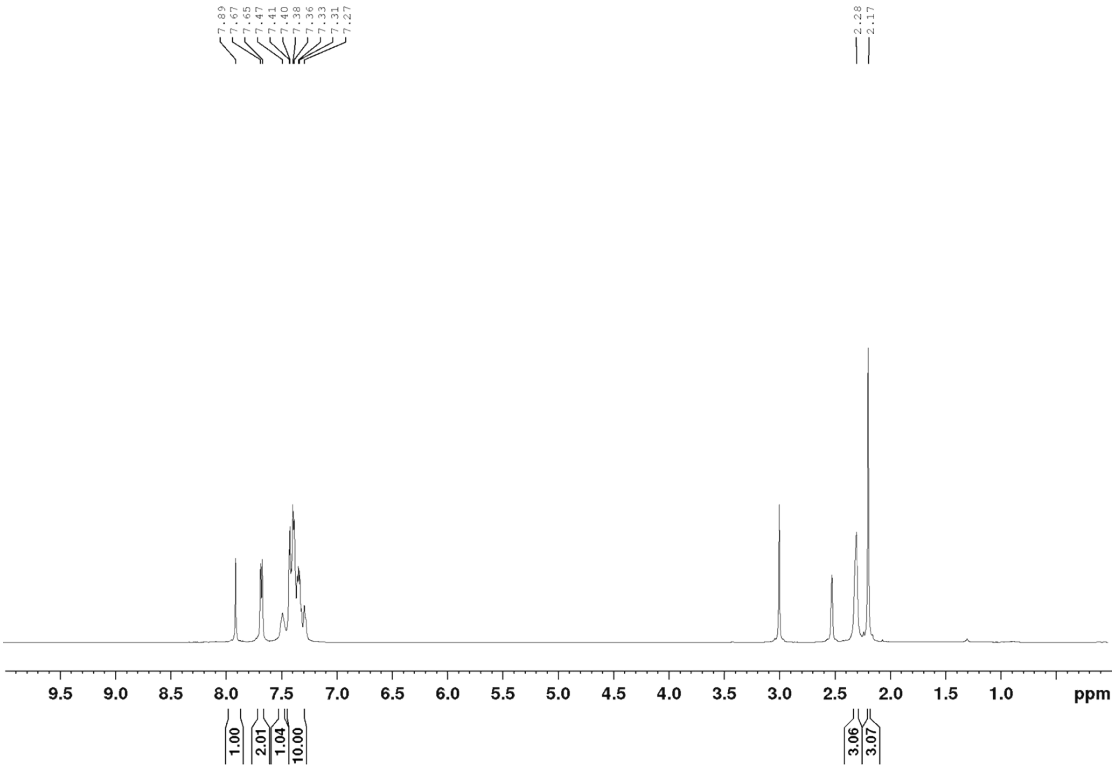
5-phenyl-1,3-di*o*-tolylpyrimidine-2,4(1*H*,3*H*)-dione (4j)

At r.t.:

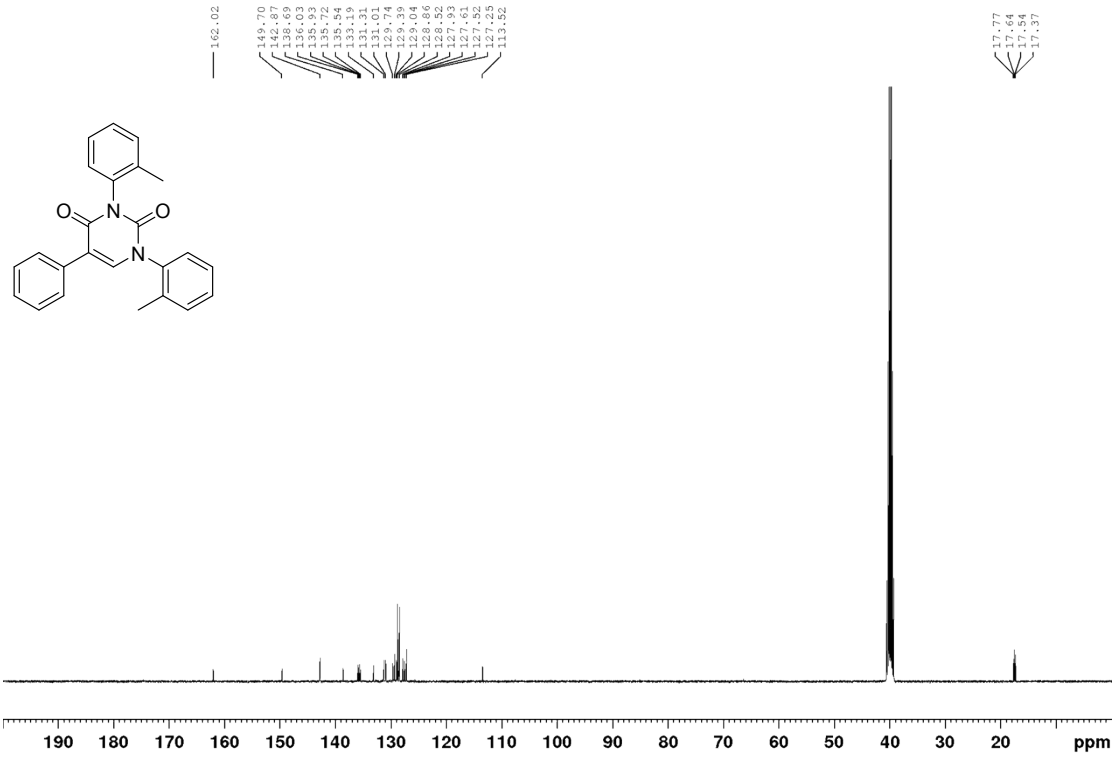


Contains rotamers.

At 90 °C:

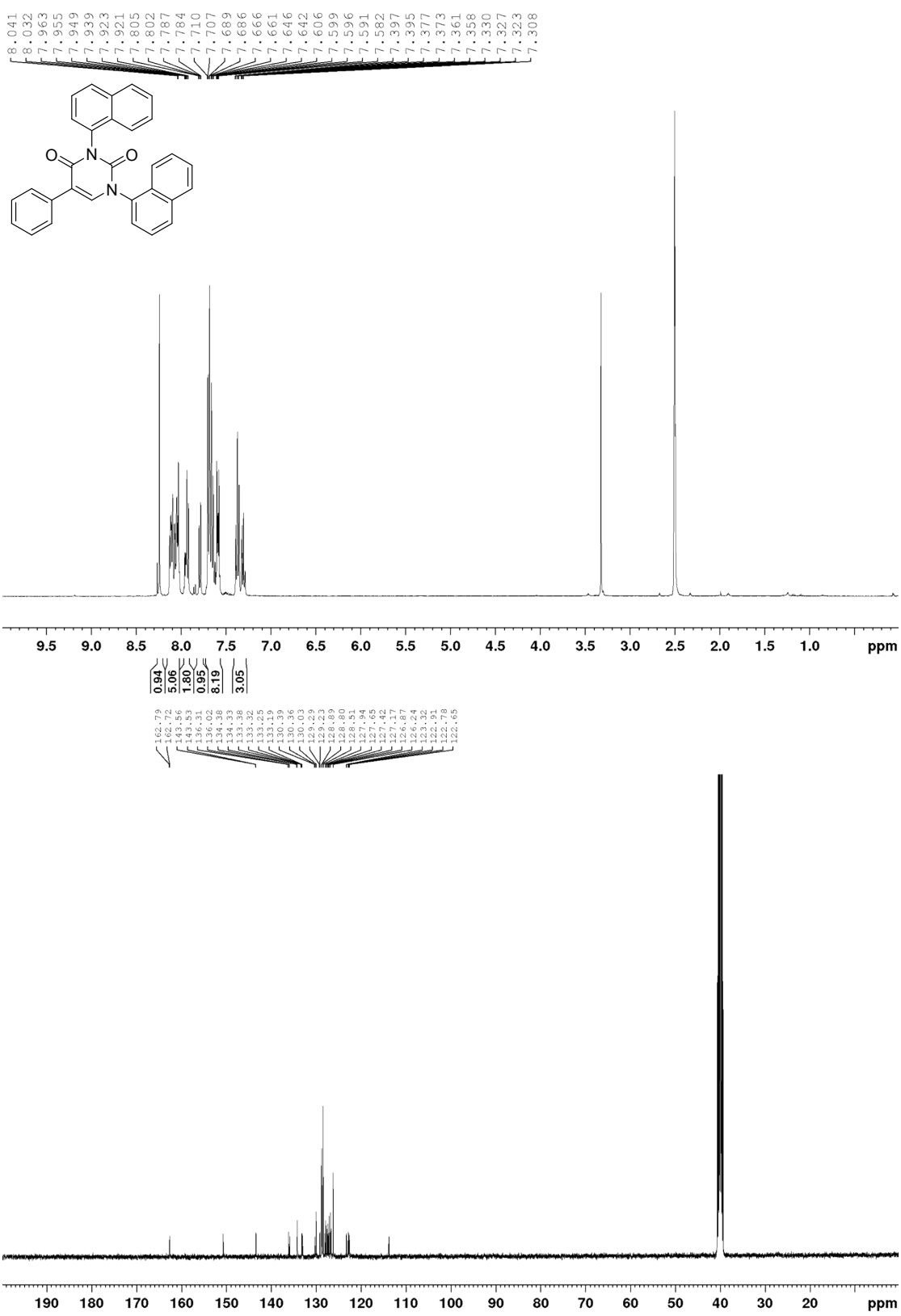


^{13}C NMR at r.t.:

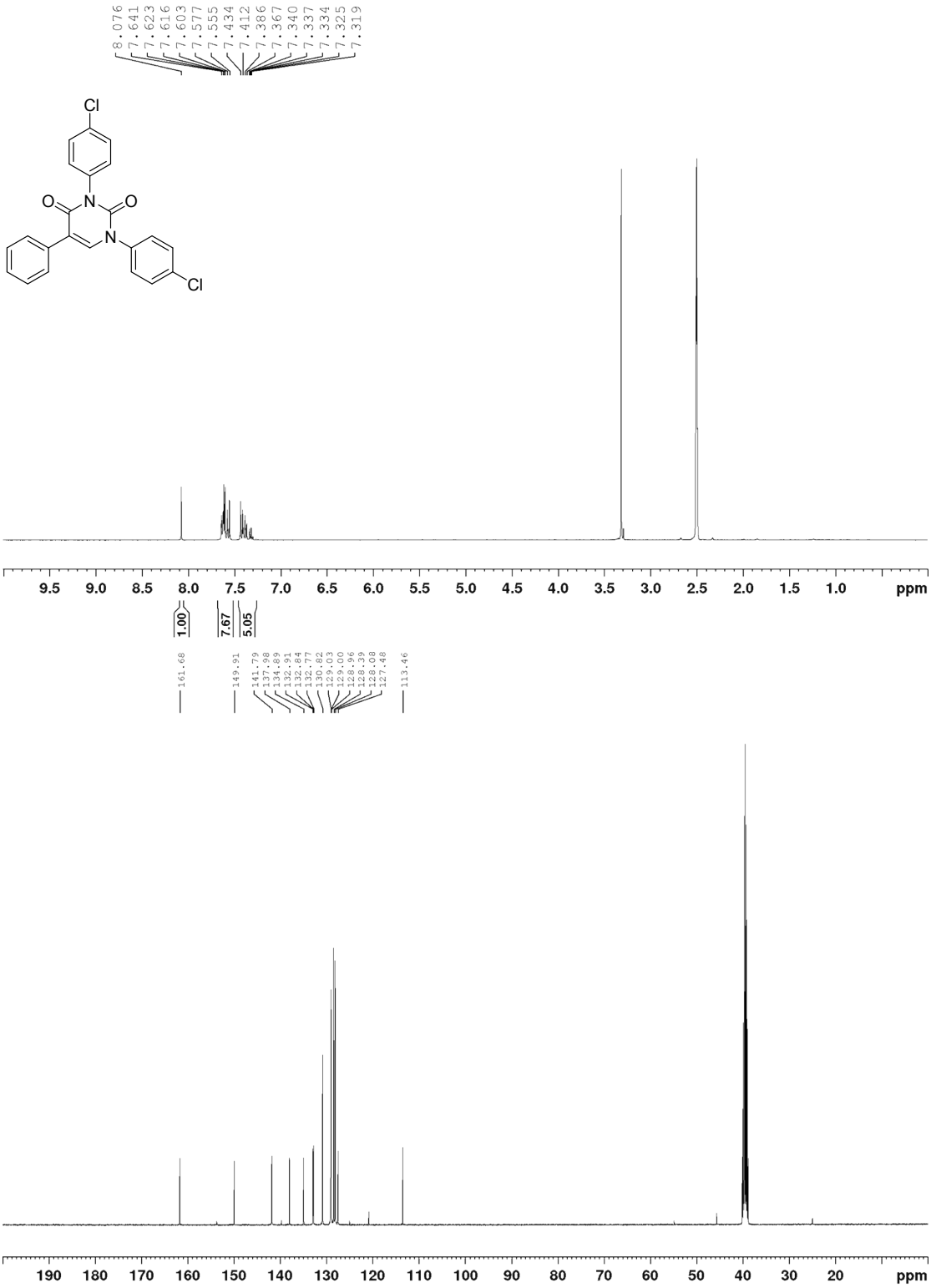


Contains rotamers.

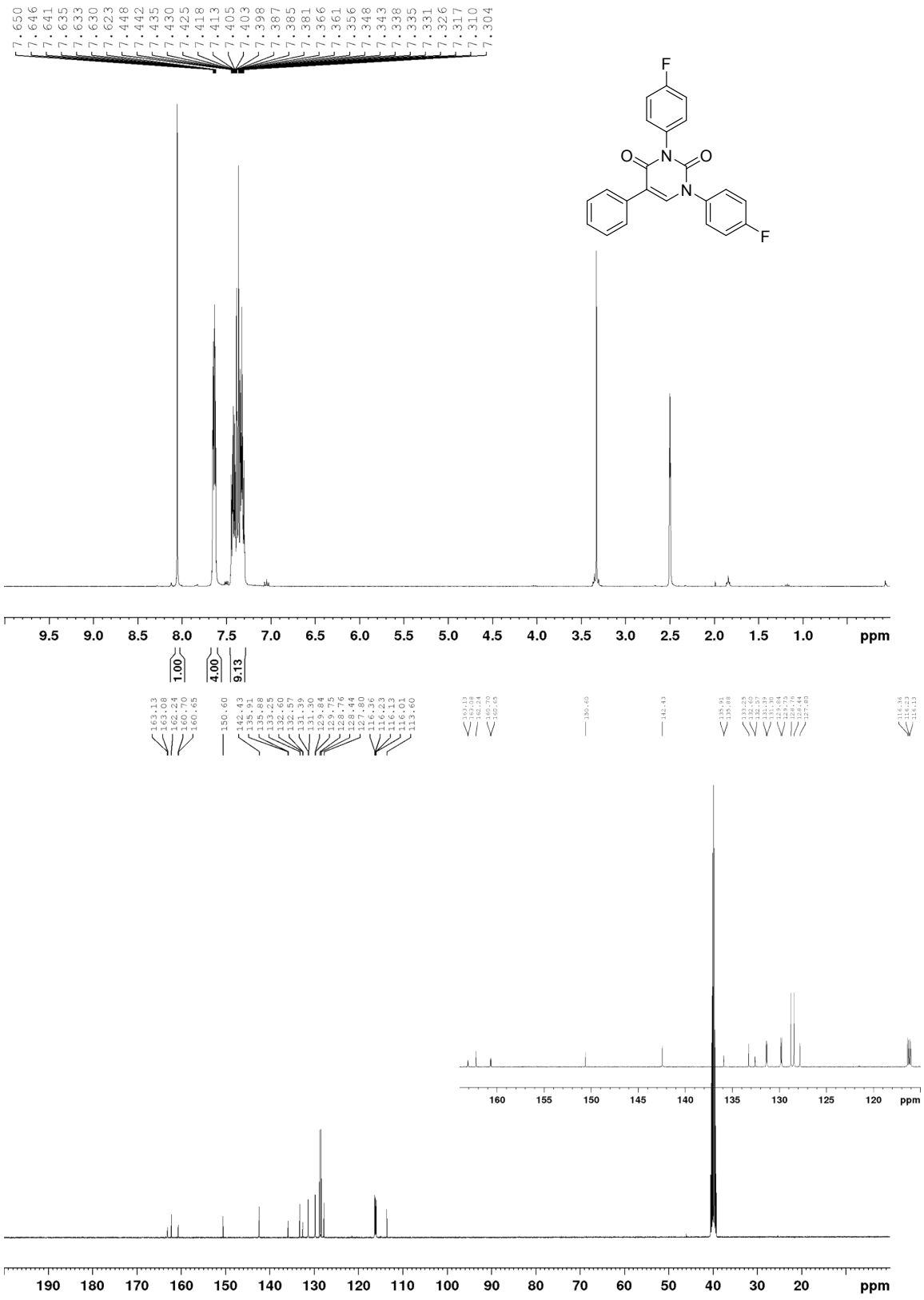
1,3-di(naphthalen-1-yl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4k)



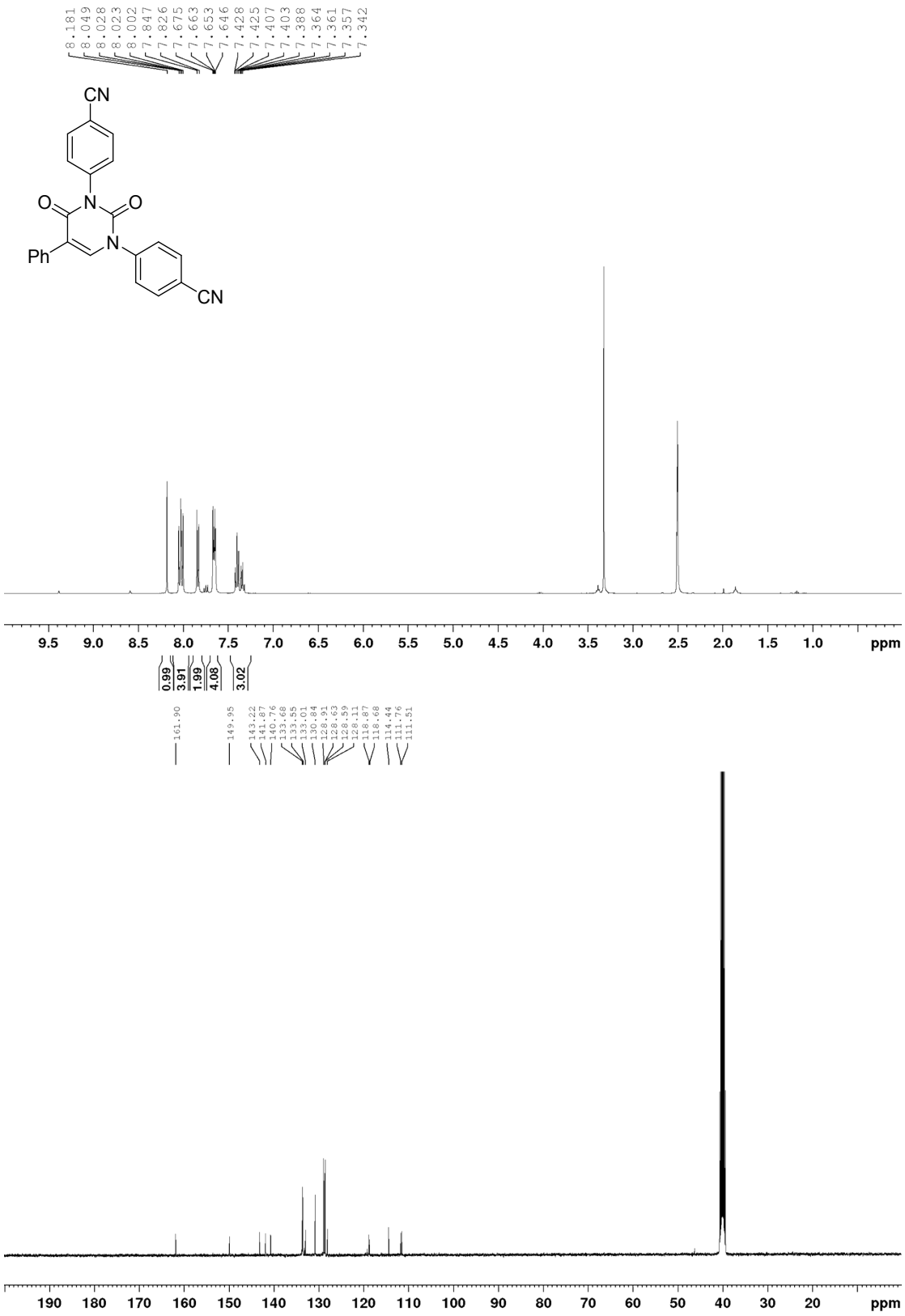
1,3-bis(4-chlorophenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4l)



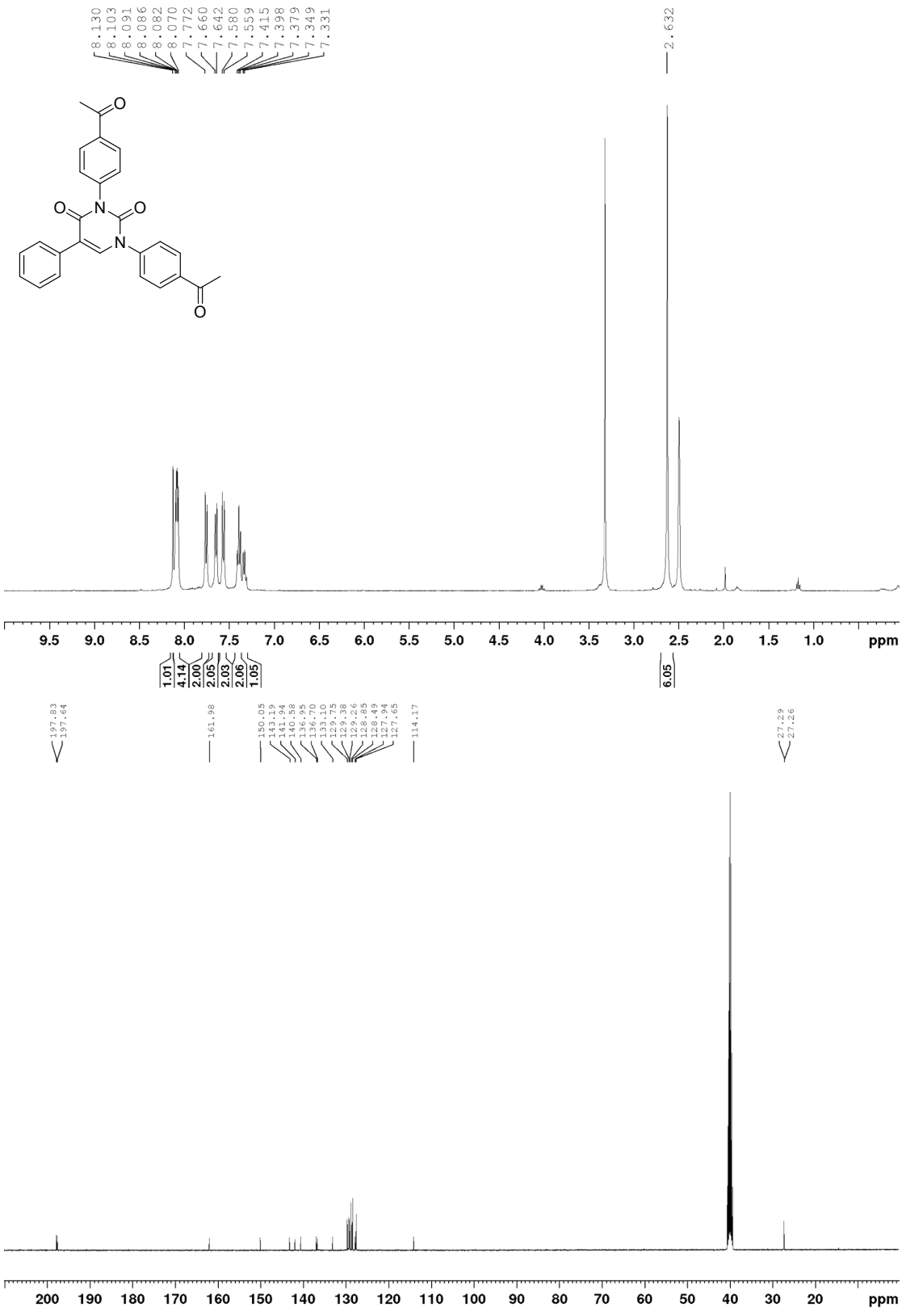
1,3-bis(4-fluorophenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4m)



4,4'-(2,4-dioxo-5-phenylpyrimidine-1,3(1*H*,4*H*)diyl)dibenzonitrile (4n)

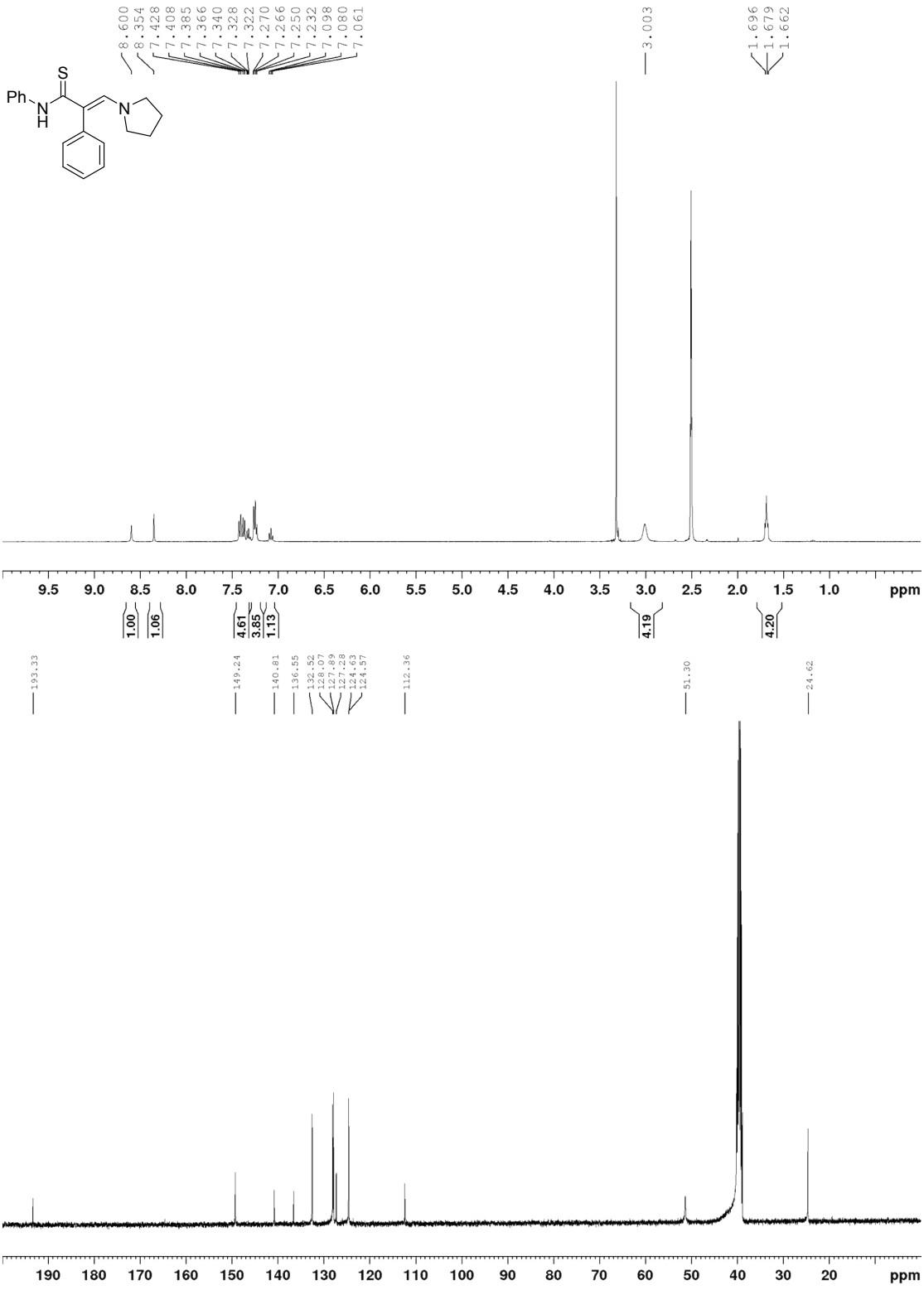


1,3-bis(4-acetylphenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-dione (4o)

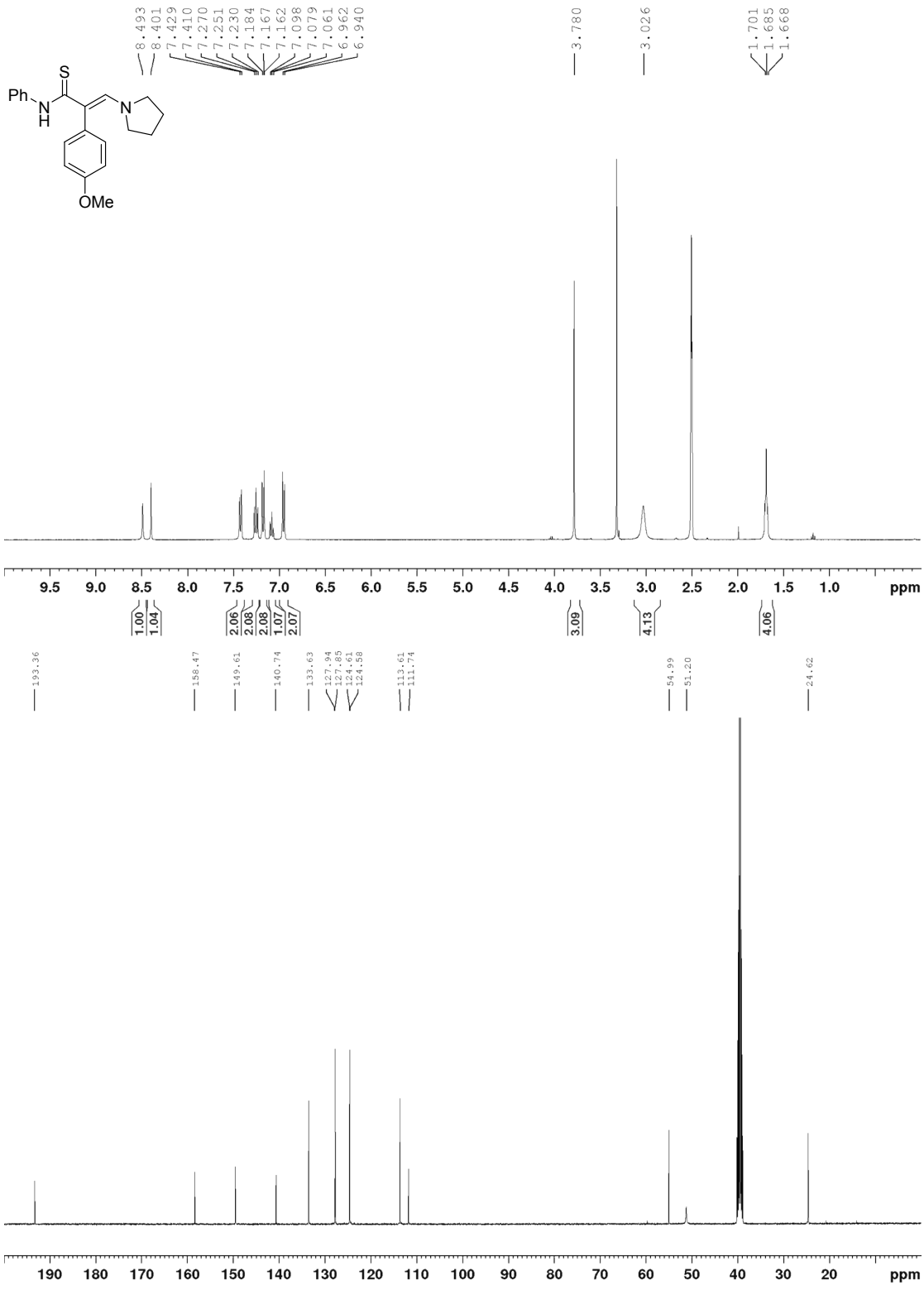


Acryl thioamides:

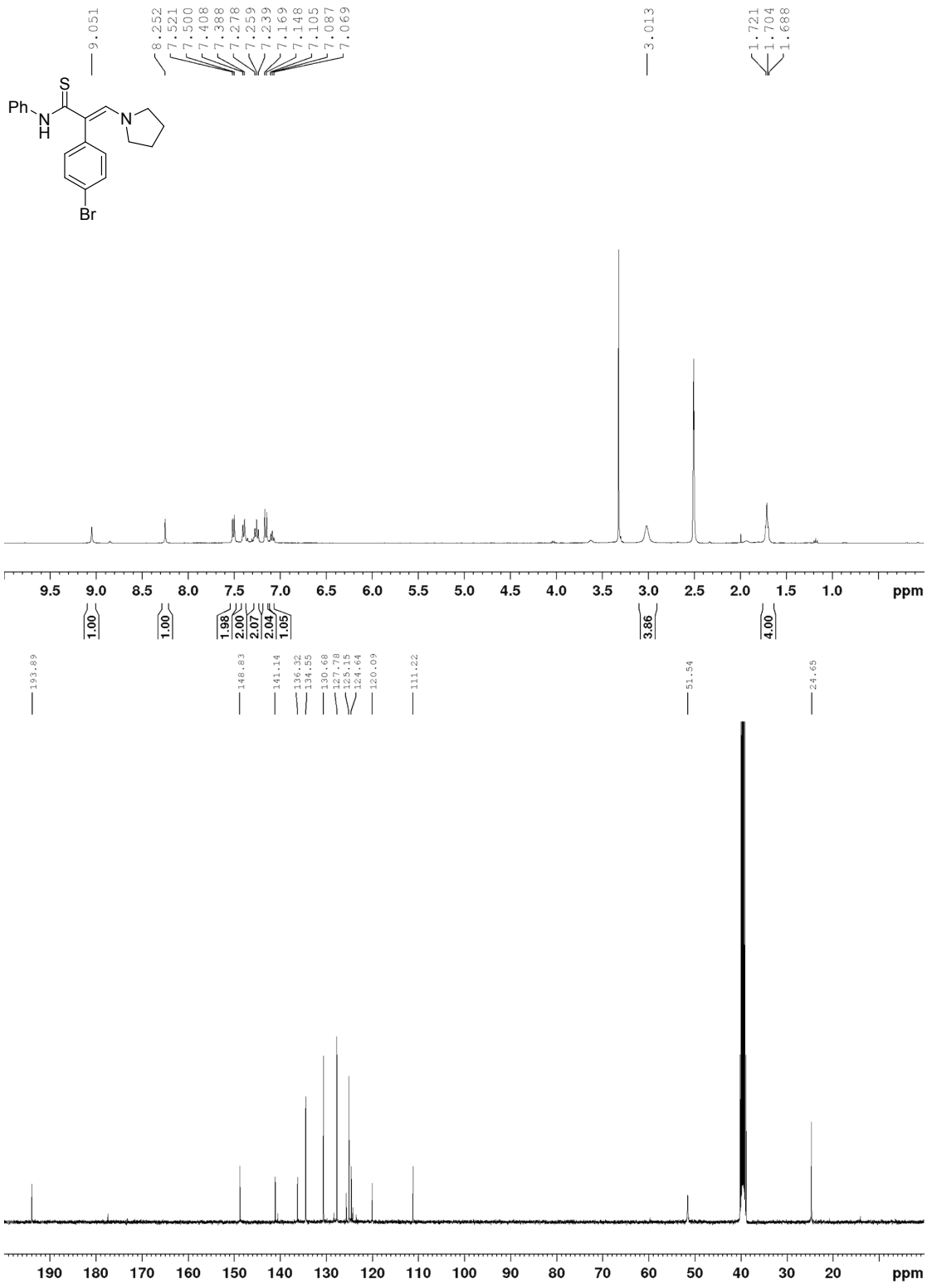
***N*,2-diphenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6a)**



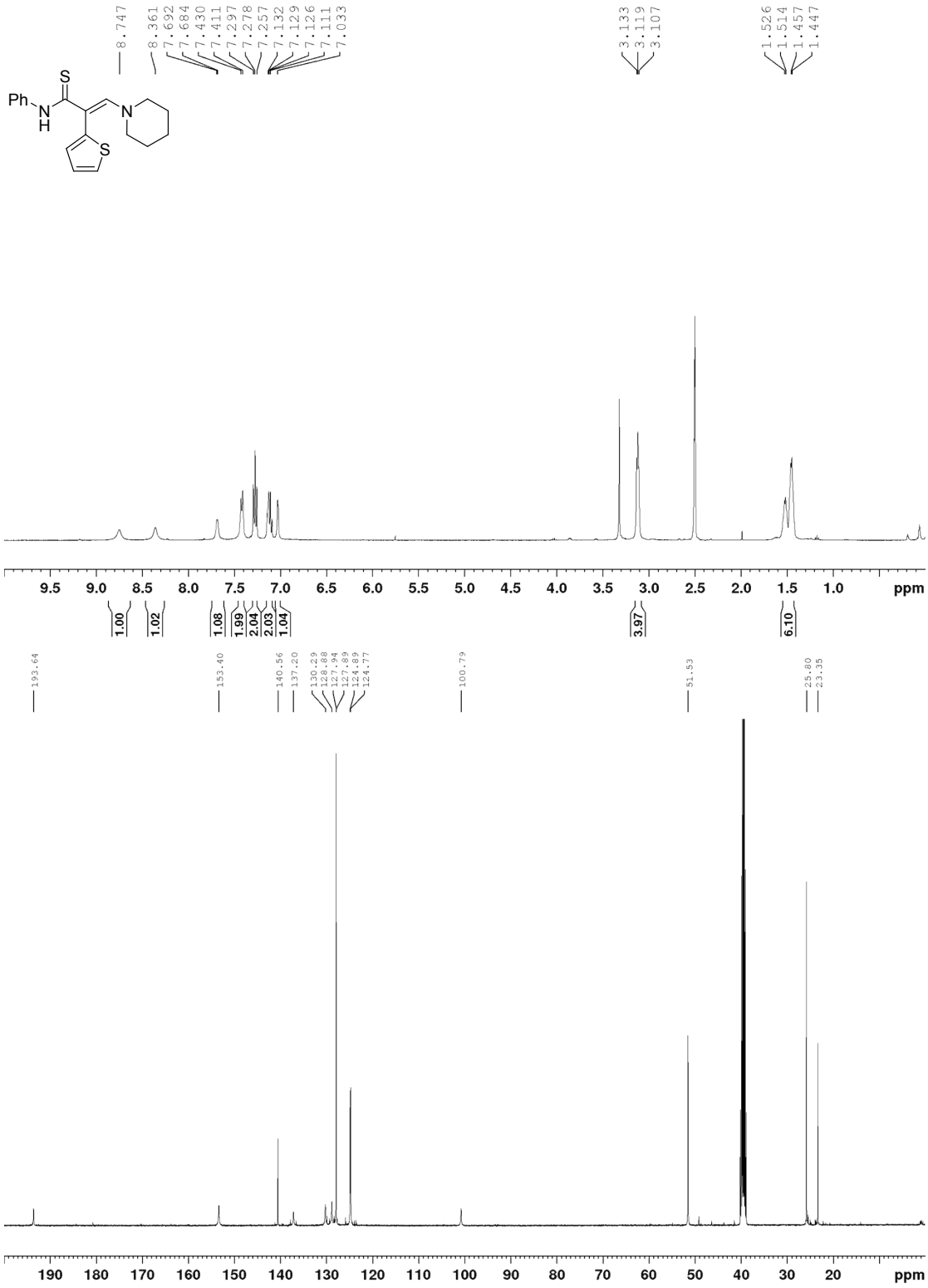
2-(4-methoxyphenyl)-*N*-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6b)



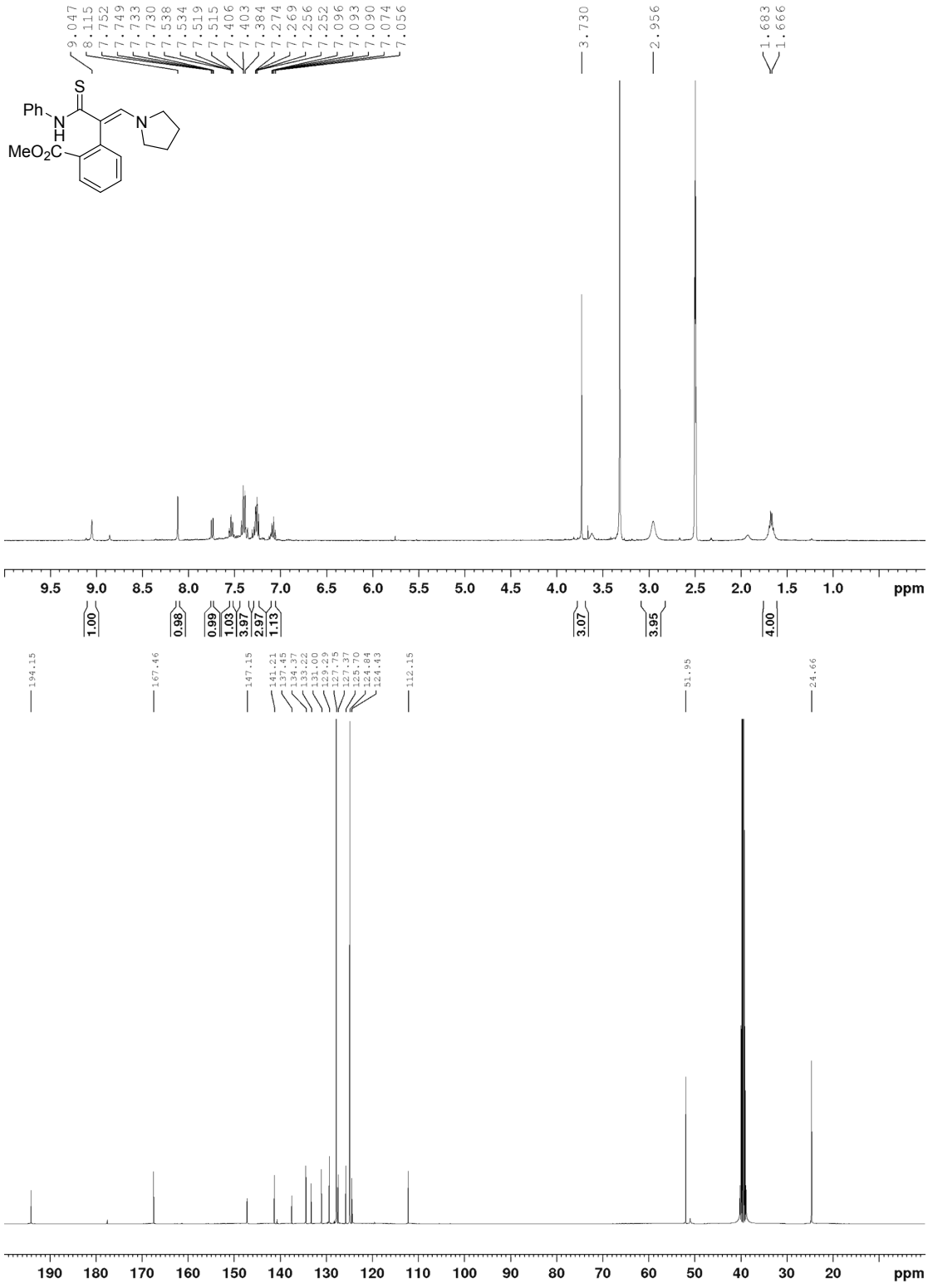
2-(4-bromophenyl)-*N*-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6c)



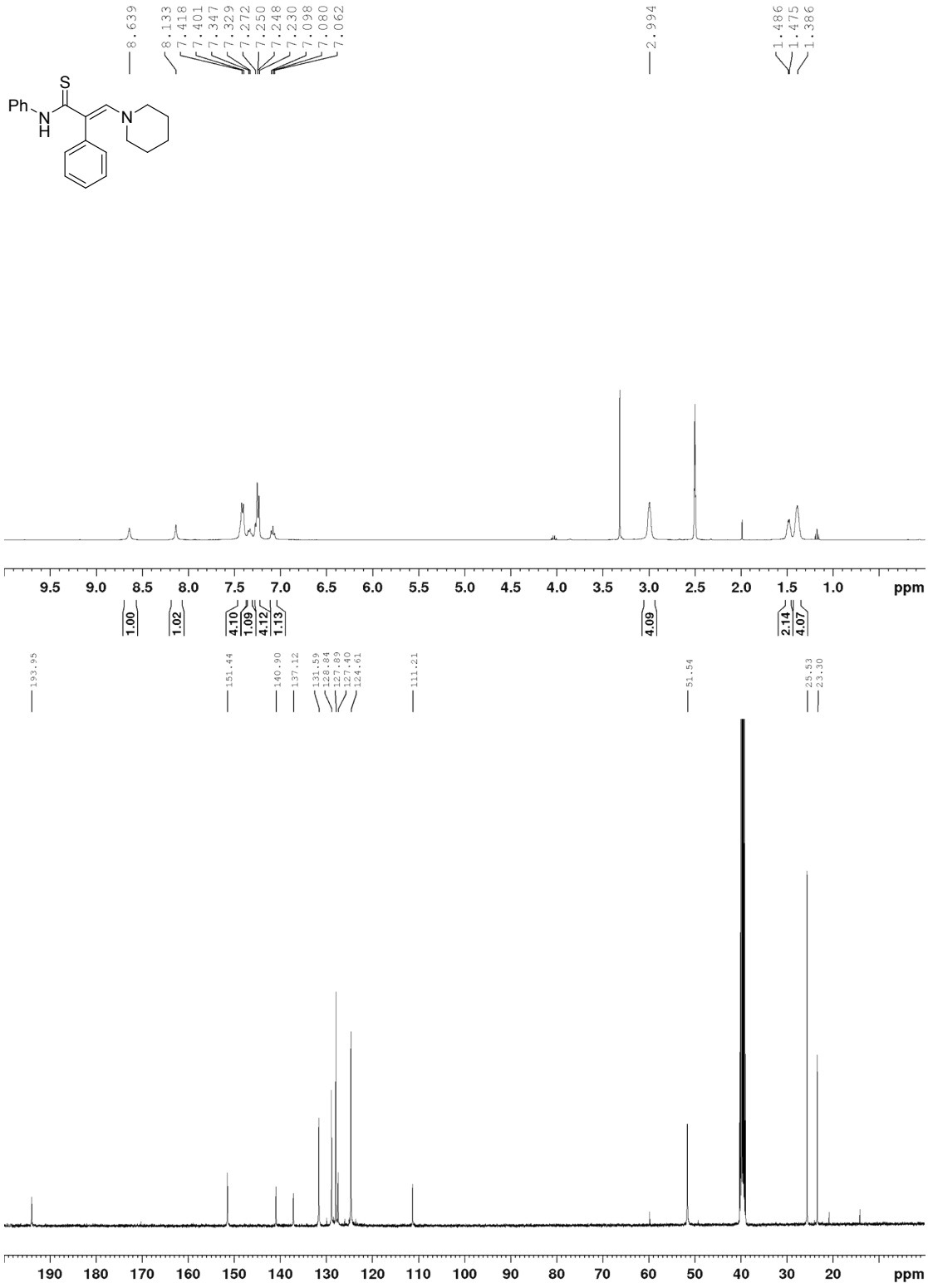
***N*-phenyl-3-(piperidin-1-yl)-2-(thiophen-2-yl)prop-2-enethioamide (6d)**



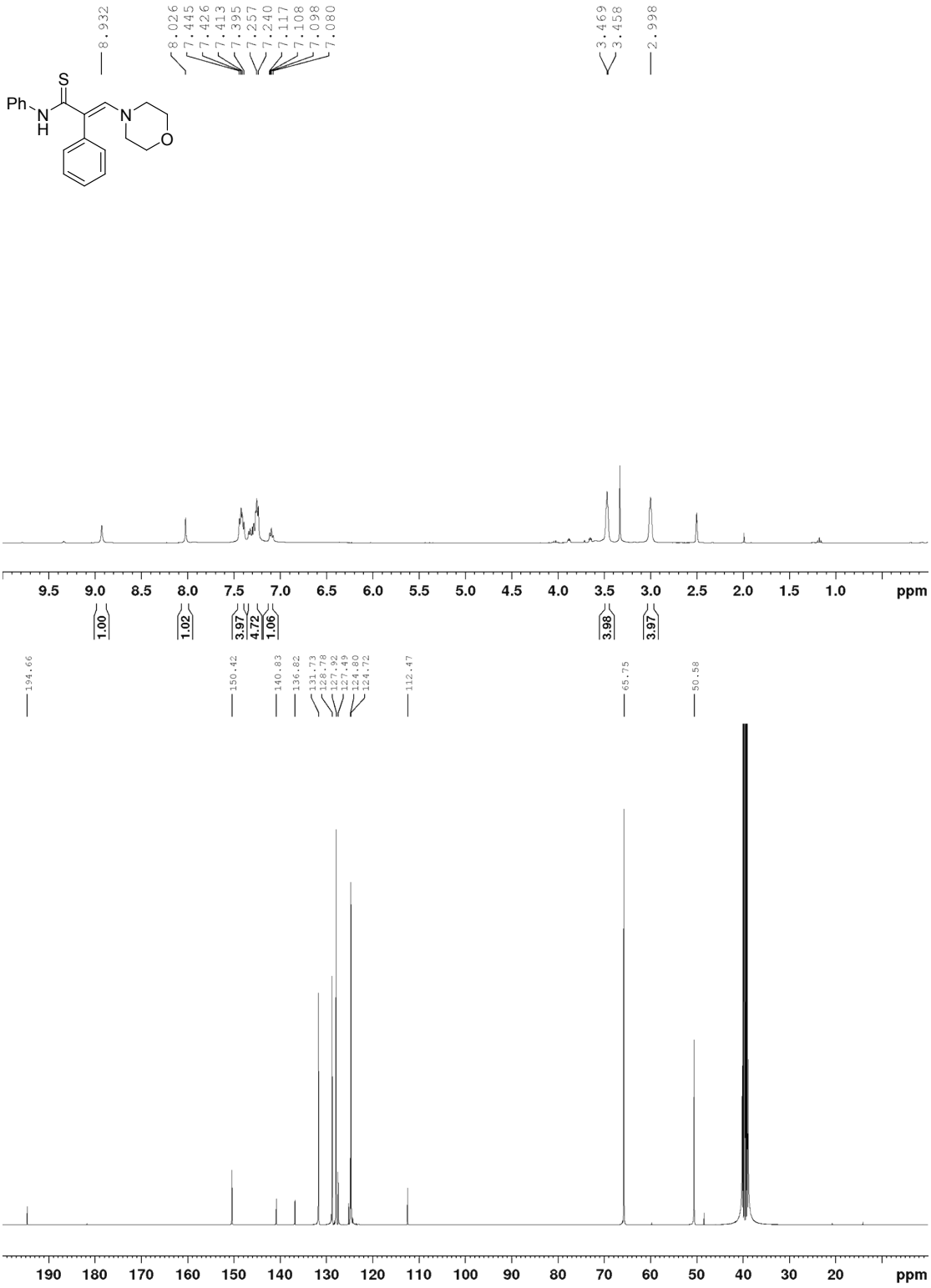
methyl 2-(3-(phenylamino)-1-(pyrrolidin-1-yl)-3-thioxoprop-1-en-2-yl)benzoate (6e)



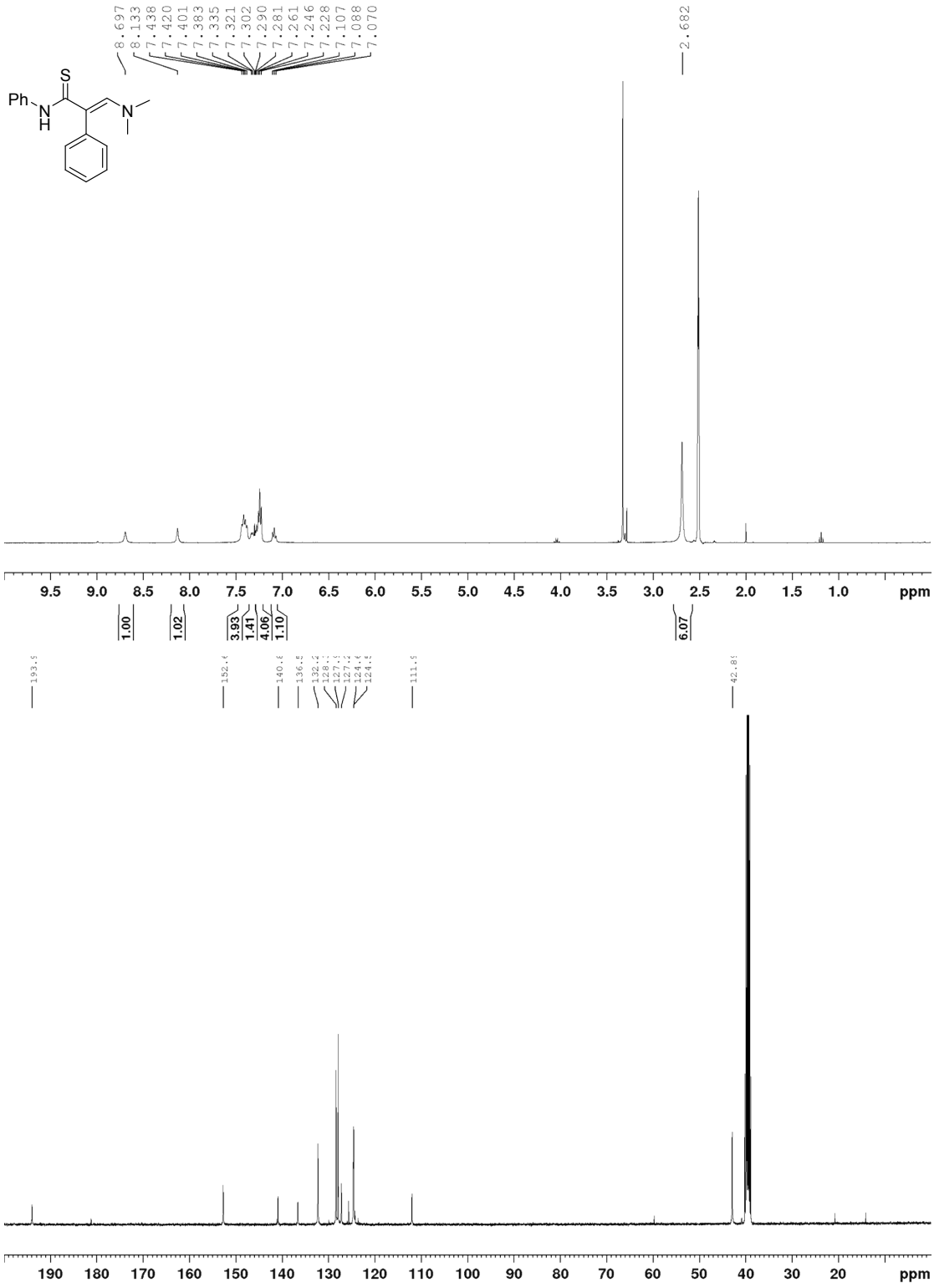
***N*,2-diphenyl-3-(piperidin-1-yl)prop-2-enethioamide (6f)**



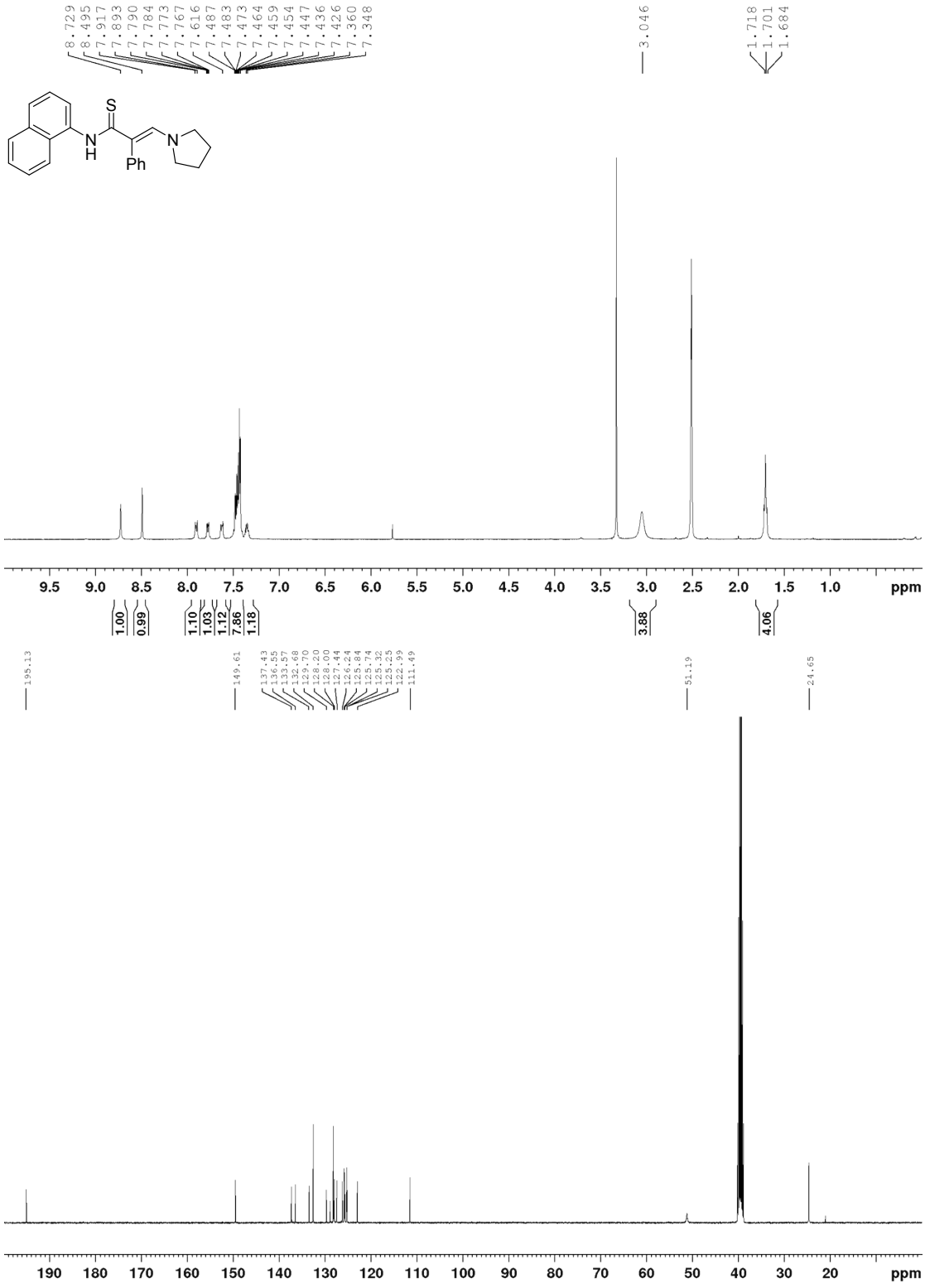
3-morpholino-*N*,2-diphenylprop-2-enethioamide (6g)



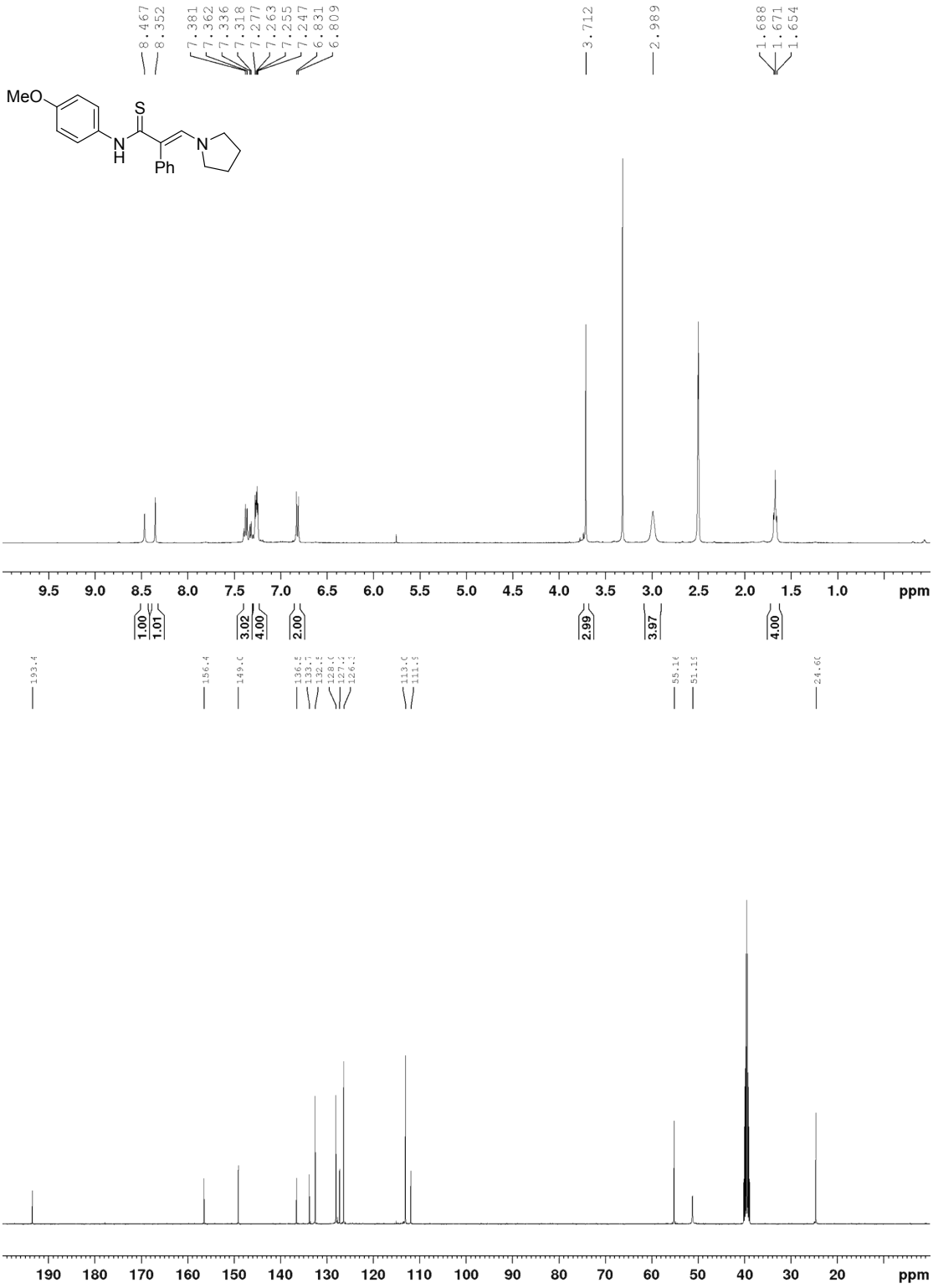
3-(dimethylamino)-*N*,2-diphenylprop-2-enethioamide (6h)



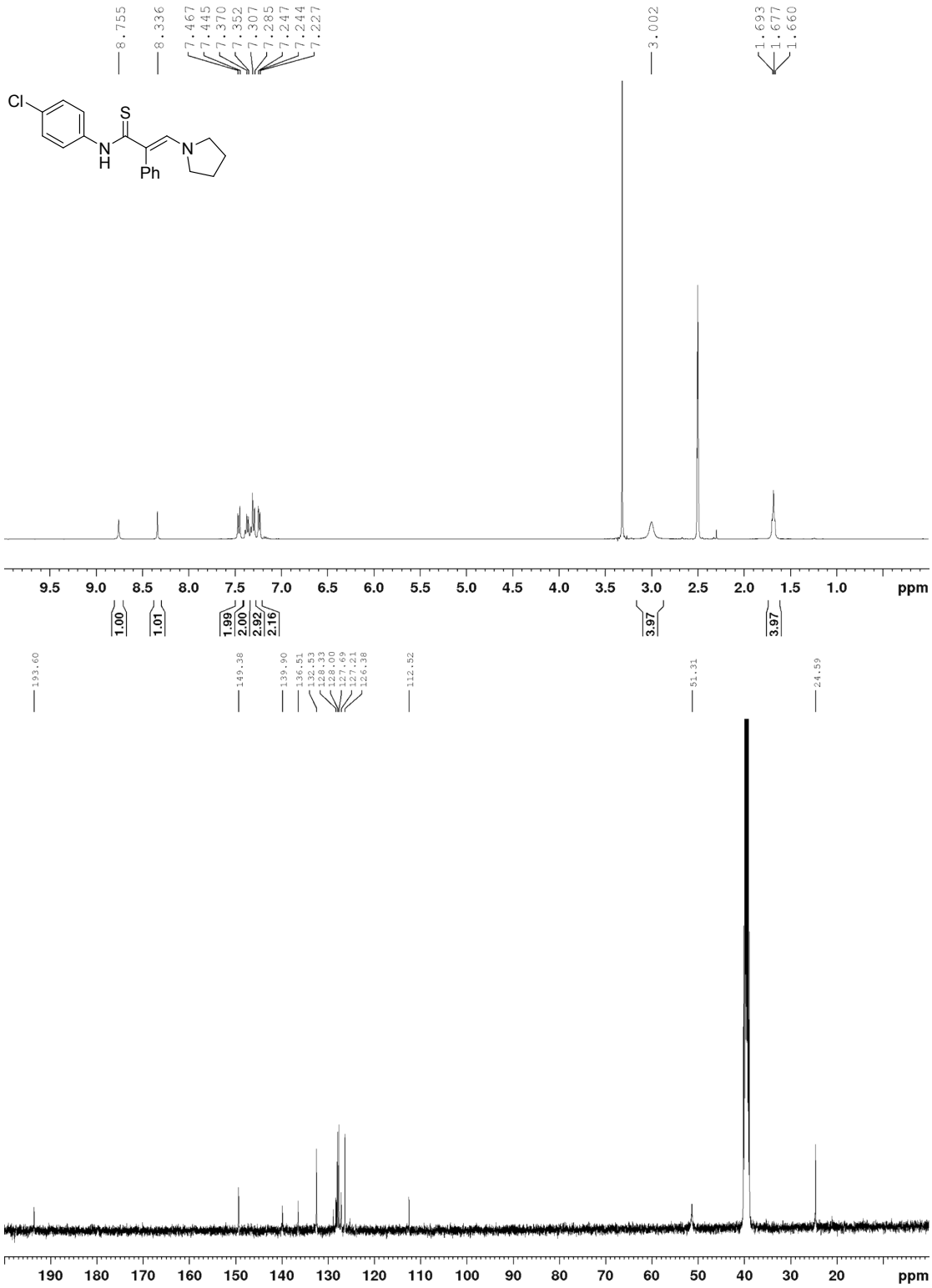
***N*-(naphthalen-1-yl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6i)**



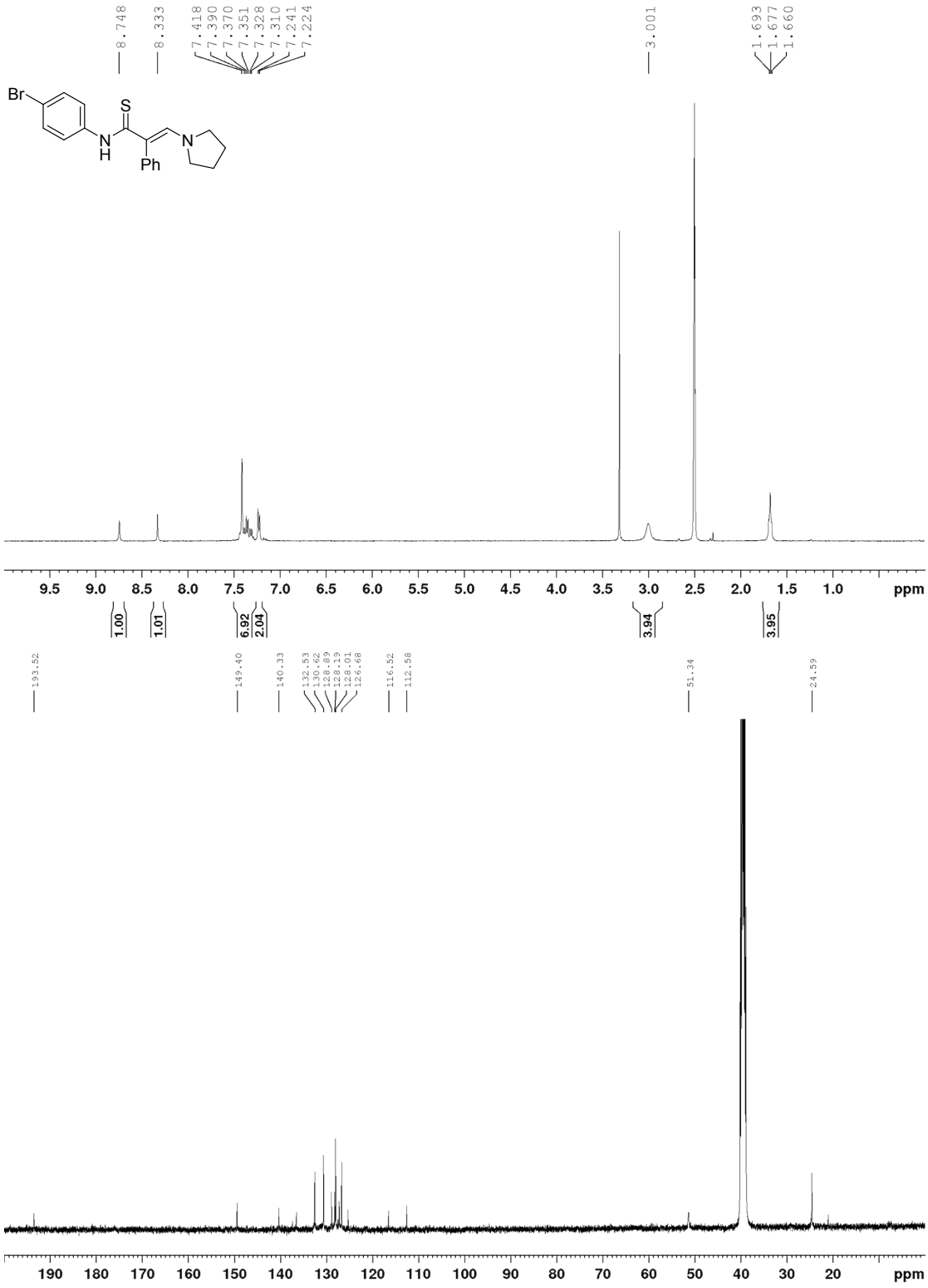
***N*-(4-methoxyphenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6j)**



***N*-(4-chlorophenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6k)**



***N*-(4-bromophenyl)-2-phenyl-3-(pyrrolidin-1-yl)prop-2-enethioamide (6l)**



Aldehyde: 3-oxo-*N*,2-diphenylpropanethioamide (7)