SUPPLEMENTARY INFORMATION FILE

C-ALKYLATION OF *N*-ALKYLAMIDES WITH STYRENES IN AIR AND SCALE-UP USING A MICROWAVE FLOW REACTOR

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S1. GENERAL EXPERIMENTAL INFORMATION

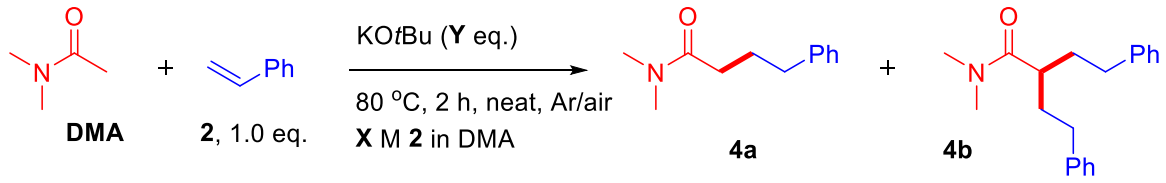
Unless specified otherwise, batch reactions were carried out under an inert (Ar) atmosphere. Cryogenic conditions (-78 ^{o}C) were achieved using dry ice/acetone baths. Temperatures of 0 ^{o}C were obtained by means of an ice bath. 'Room temperature' (rt) indicates temperatures in the range of 20-25 ^{o}C.

For purposes of thin layer chromatography (TLC), Silica gel 60N Aluminium plates were uise, with UV light ($\lambda = 254$ nm) used for visualization and/or cerium molybdate stain as the developing agent. Purification was achieved by column chromatography, using Silica gel N-60, particle size 40-100 μm (Kanto Chemical Co., Inc.). In some cases, purification was achieved using a Shimadzu recycling preparative HPLC system (LC-20AR column, YMC-GPC T-2000), using $CHCl_3$ as eluent (Flow rate = 5.0 mL/min) and following by a UV detector ($\lambda = 254$ nm).

Removal of solvents (*in vacuo*) was achieved using rotary evaporators. For NMR spectroscopy, chloroform-d (D, 99.8% + 0.03v/v% TMS, KANTO Chemical Co., Inc.) was used. ^{1}H, ^{19}F were measured on a JEOL JNM-ECX-500 spectrometer at 500 and 470 MHz, respectively. ^{13}C NMR spectra were recorded on a JEOL JNM-ECX-500 spectrometer at 125 MHz. Reference values for residual solvents were taken as δ = 7.27 ($CDCl_3$) for ^{1}H NMR; δ = 77.00 ppm ($CDCl_3$) for ^{13}C NMR. Multiplicities for coupled signals were denoted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, apt. = apparent and dd = double doublet *etc.* Coupling constants (*J*) are given in Hz and are uncorrected. Where appropriate, COSY, DEPT, HSQC and HMBC experiments were carried out to aid assignment. Infra-red spectra were measured on a SHIMADZU IRPrestige-21 and only diagnostic absorptions are listed. ESI-MS data were taken on a Thermo SCIENTIFIC ACCELA Exactive liquid chromatography-mass spectrometer (LC-MS). All solvents and reagents were purchased from Wako Pure Chemical Industries Ltd., Tokyo Chemical Industry Co., Ltd. (TCI) or Sigma-Aldrich and were used as supplied or purified using standard techniques.[1]

S2. Reaction Optimization for DMA

S2.1 Effect of Concentration, KO*t*Bu Equivalents and Air

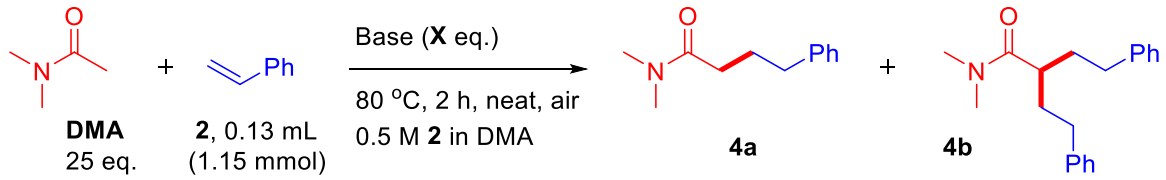


Entry	Concentration in DMA (X M of 2)	KO*t*Bu (Y eq.)	Atmosphere	Yield (%)[a] 4a	4b	Ratio 4a : 4b
1	0.50	0.2	air	1	0	-
2	1.90	0.6	Ar	39	51	1 : 1.31
3	0.50	0.6	Ar	77	15	1 : 0.19
4	0.50	0.6	air	71	16	1 : 0.23
5	0.50	1.5	Ar	80	18	1 : 0.23
6[b]	0.50	1.5	air	72	21	1 : 0.29
7	0.23	1.5	air	75	11	1 : 0.15
8[c]	26.8	1.5[d]	air	36	28	1 : 0.78
9	0.50	3.0	Ar	58	14	1 : 0.24
10	0.50	3.0	air	63	16	1 : 0.25

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Average of 3 replicates. [c]Reaction conducted using 1.15 mmol DMA in styrene (3.3 mL, 25 eq.) as the solvent. [d]Relative to DMA as the limiting reagent.

Results show that: 0.2 eq. KO*t*Bu gives no reaction whereas 0.6 eq. gives full conversion in 2 h. Selectivity for monoadduct **4a** increases as concentration of **2** in DMA decreases. The reaction proceeds in air as well as Ar atmosphere in comparable conversion and **4a** : **4b** selectivity. 0.6 eq. and 1.5 eq. of KO*t*Bu give comparable conversion and **4a** : **4b** selectivity whilst 3.0 eq. of KO*t*Bu gives inferior conversion. Using styrene as solvent and DMA as the limiting reagent promotes bisadduct **4b** but monoadduct **4a** is still the major component.

S2.2 EFFECT OF BASE

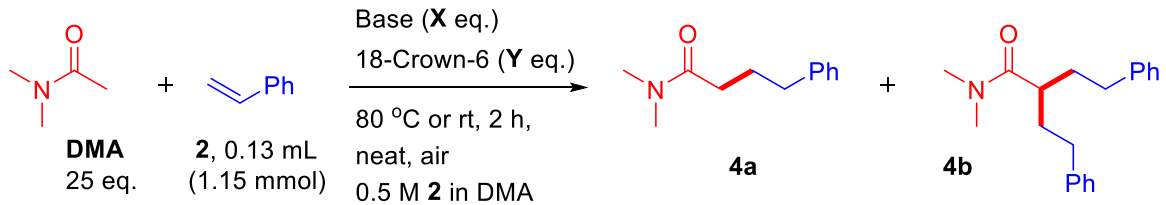


Entry	Base (X eq.)	Yield (%)[a] 4a	4b	Ratio 4a : 4b
1[b]	KO*t*Bu (3.0 eq.)	63	16	1 : 0.25
2[c]	KO*t*Bu (1.5 eq.)	72	21	1 : 0.29
3	KO*t*Am (3.0 eq.)	68	18	1 : 0.26
4	KHMDS (1.5 eq.)	80	18	1 : 0.23
5	NaHMDS (1.5 eq.)	75	16	1 : 0.21
6	KOH (1.5 eq.)	74	16	1 : 0.22
7	NaO*t*Bu (3.0 eq.)	3	0	-
8	NaO*t*Bu (1.5 eq.)	4	0	-
9	KF (1.5 eq.)	0	0	-
10	K_2CO_3 (1.5 eq.)	0	0	-
11	DABCO (3.0 eq.)	0	0	-
12	DBU (3.0 eq.)	0	0	-

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Table **S2.1**, entry 10 shown for comparison. [c]Table **S2.1**, entry 6 shown for comparison.

Results show that: KO*t*Bu, KO*t*Am, KHMDS, NaHMDS and KOH all give comparable conversion and **4a** : **4b** selectivity after 2 h. Weaker bases NaO*t*Bu, KF, K_2CO_3 give trace conversion or no reaction. Organic bases DABCO and DBU give no reaction.

S2.3 Effect of Temperature and 18-Crown-6 Additive

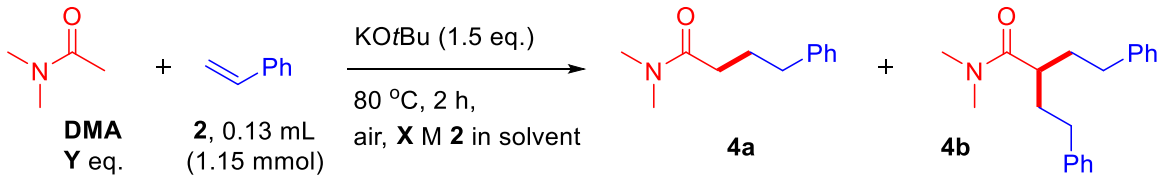


Entry	Base (X eq.)	18-Crown-6 (Y eq.)	Temp. (°C)	Yield (%)[a] 4a	4b	Ratio 4a : 4b
1[b]	KO*t*Bu (1.5 eq.)	0.0	80	72	21	1 : 0.29
2	KO*t*Bu (1.5 eq.)	0.0	rt	23	2	1 : 0.09
3	KO*t*Bu (3.0 eq.)	0.0	rt	15	2	1 : 1.13
4	KO*t*Bu (1.5 eq.)	1.0	80	48	36	1 : 0.75
5	KO*t*Bu (1.5 eq.)	1.0	rt	39	45	1 : 1.15
6	KO*t*Bu (0.0 eq.)	1.0	80	0	0	-
7[c]	NaO*t*Bu (1.5 eq.)	0.0	80	4	0	-
8	NaO*t*Bu (1.5 eq.)	1.0	80	65	9	1 : 0.14
9	NaO*t*Bu (1.5 eq.)	1.0	rt	0	0	-

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Table **S2.1**, entry 6 shown for comparison. [c]Table **S2.2**, entry 8 shown for comparison.

Results show that: Using KO*t*Bu only, the reaction proceeds at room temperature after 2 h but is sluggish (similarly to Table S1, an increased loading of 3.0 eq. KO*t*Bu gives inferior conversion). Use of 18-crown-6 additive significantly decreases selectivity for monoadduct **4a** (a control reaction with 18-crown-6 in the absence of KO*t*Bu gives no reaction). Whilst NaO*t*Bu only gives no reaction, the combination of NaO*t*Bu with 18-crown-6 additive successfully promotes the reaction at 80 °C, but not at rt (moreover, this combination appears more soluble than reactions involving KO*t*Bu only, KO*t*Bu + 18-crown-6 or NaO*t*Bu only).

S2.4 Effect of Other Solvents

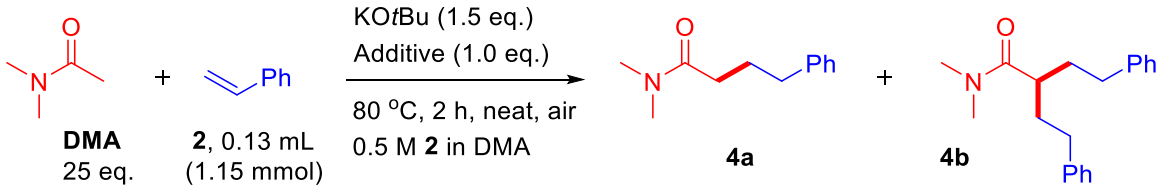


Entry	Solvent (X M)	DMA (Y eq.)	Temp. (°C)	Yield (%)[a] 4a	4b	Ratio 4a : 4b
1[b]	DMA (0.5 M **2**)	25.0	80	72	21	1 : 0.29
2	*t*BuOH (0.35 M **2**)	15.0	80	0	0	-
3	DMSO (0.35 M **2**)	15.0	80	29	0	-

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Table **S2.1**, entry 6 shown for comparison.

Results show that: Protic solvent *t*BuOH completely prevents the desired reaction. The reaction proceeds in DMSO as solvent but is sluggish.

S2.5 Effect of Darkness, Radical Trapping or Protic Agents



Entry	Additive	Yield (%)[a] 4a	4b	Ratio 4a : 4b
1[b]	-	72	21	1 : 0.29
2[c]	-	68	18	1 : 0.26
3[d,e]	- (in the dark)	73	21	1 : 0.29
4[e]	TEMPO	64	15	1 : 0.23
5[e]	Galvinoxyl radical	0	0	-
6[e]	BHT	4	0	-
7	EtOH[f]	3	0	-

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Table **S2.1**, entry 6 shown for comparison. [c]Repeat of Table **S2.1**, entry 6 conditions; average of two replicates; reactions were run side-by-side with reactions using radical traps as an additive (entry 4,5,6). [d]Reaction carried out with seclusion of ambient light, average of two replicates. [e]Average of two replicates. [f]10 eq. of EtOH was employed.

Results show that: Seclusion of ambient light does not affect the reaction. Radical trap TEMPO does not result in significant inhibition of the reaction, suggesting a radical mechanism is unlikely. Galvinoxyl radical completely inhibits the reaction but no radical-trapped products (structures **S1** or **S2**) were

detected by mass spectrometry, thus it cannot be concluded that a radical mechanism is operative. Protic additives BHT (1.0 eq.) or EtOH (10.0 eq.) prevent the desired reaction.

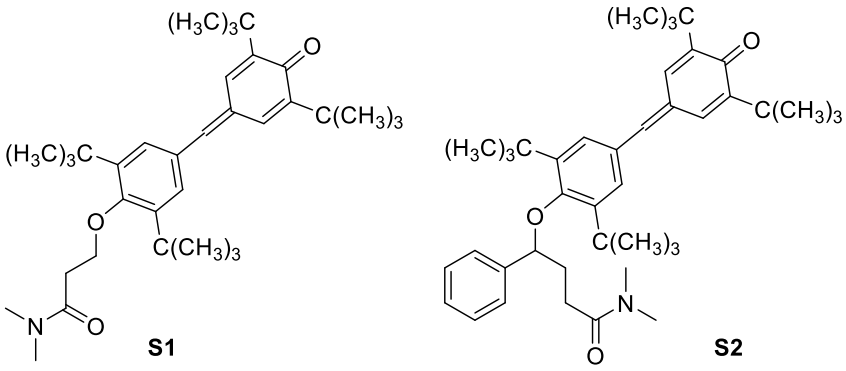
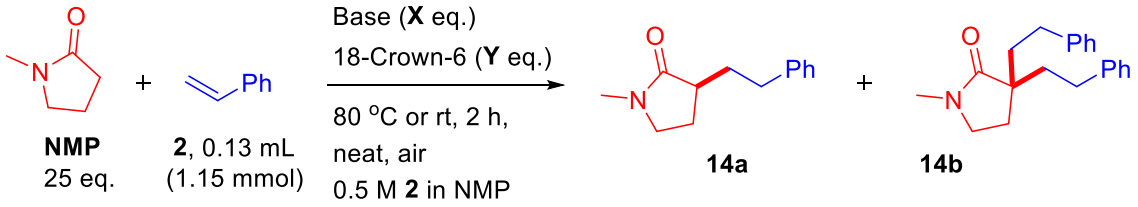


Fig. S1. Galvinoxyl radical-trapped products which were not detected by mass spectrometry.

S3. Reaction Optimization for NMP

S3.1 Effect of Temperature and 18-Crown-6 Additive



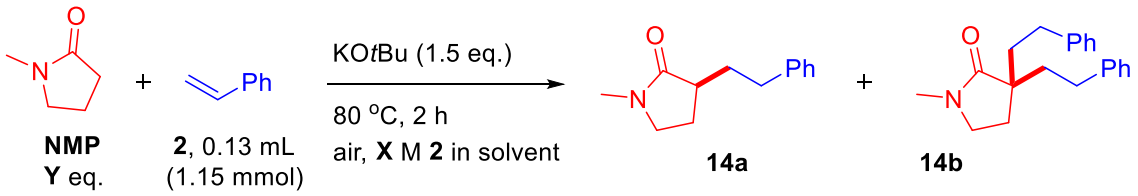
Entry	Base (X eq.)	18-Crown-6 (Y eq.)	Temp. (°C)	Yield (%)[a] 14a	14b	Ratio 14a : 14b
1	KO*t*Bu (1.5 eq.)	0.0	80	87	11	1 : 0.13
2	KO*t*Bu (1.5 eq.)	0.0	rt	79	15	1 : 0.19
3	KO*t*Bu (1.5 eq.)	1.5	80	80	17	1 : 0.21
4	KO*t*Bu (1.5 eq.)	1.5	rt	71	26	1 : 0.37
5	NaO*t*Bu (1.5 eq.)	0.0	80	0	0	-
6	NaO*t*Bu (1.5 eq.)	1.5	80	88	10	1 : 0.11
7	NaO*t*Bu (1.5 eq.)	1.5	rt	0	0	-
8	NaO*t*Bu (1.5 eq.)	0.3	80	90	8	1 : 0.09
9	NaO*t*Bu (0.3 eq.)	0.3	80	20	0	-
10	NaO*t*Bu (0.15 eq.)	0.15	80	0	0	-
11	NaO*t*Bu (0.6 eq.)	0.6	80	85	9	1 : 0.11

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard.

Results show that: Reactions of NMP give greater monoadduct selectivity compared to reactions of DMA. Using KO*t*Bu only, the reaction proceeds at room temperature after 2 h. Use of 18-crown-6 additive decreases selectivity for monoadduct **14a**. Selectivity is even lower if the reaction is conducted

at rt in the presence of 18-crown-6 additive. Whilst NaO*t*Bu only gives no reaction, the combination of NaO*t*Bu with 18-crown-6 additive successfully promotes the reaction at 80 °C, but not at rt (moreover, this combination appears more soluble than reactions involving KO*t*Bu only, KO*t*Bu + 18-crown-6 or NaO*t*Bu only). The reaction is equally effective using 1.5 eq. NaO*t*Bu and only 0.3 eq. of 18-crown-6 (although solubility appears is inferior compared to when 18-crown-6 and NaO*t*Bu are equimolar). Decreasing the loading of NaO*t*Bu below 0.6 eq. is detrimental to the reaction. Entry 11 shows the optimal conditions for high conversion at the lowest NaO*t*Bu and 18-crown-6 loading, which were explored in continuous flow (Section S7).

S3.2 Effect of Other Solvents



NMP **Y** eq. + **2**, 0.13 mL (1.15 mmol) → **14a** + **14b**

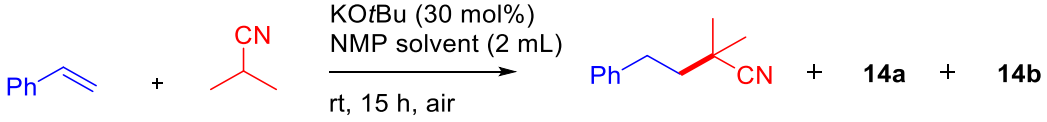
Entry	Solvent (X M)	NMP (Y eq.)	Temp. (°C)	Yield (%)[a] 14a	14b	Ratio 14a : 14b
1[b]	NMP (0.5 M **2**)	25.0	80	87	11	1 : 0.13
2[c]	DMSO (0.35 M **2**)	15.0	80	78	10	1 : 0.13
3	DMSO (0.25 M **2**)	3.0	80	39	19	1 : 0.49

[a]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [b]Table **S3.1**, entry 1 shown for comparison. [c]Average of two replicates.

S4. Unsuccessful Styrenes and Amide Partners

S4.1 Investigation of Isobutyronitrile Under Previously Reported Conditions

This reaction was conducted according to a literature procedure.[2] Yields quoted are ^{1}H NMR yields, see Section 5 for example calculation.



2 (1.3 eq.) (210 mg) + **S6**, (1.0 eq.) (104 mg) → **S18** + **14a** + **14b**

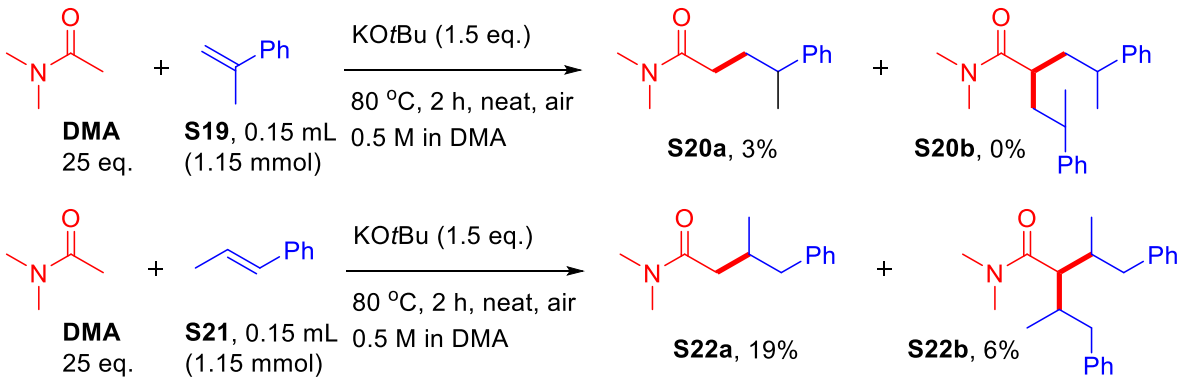
	S18	**14a**	**14b**
Yields (Knochel):	80%	N.D.	N.D.
Yields (Herein):	81%	26%*	0%

*Based on **2** as limiting reagent

In comparison to the reaction of isobutyrionitrile **S6** under conditions employed herein (Table **S2.1**, entry 6, using isobutyrionitrile as solvent and where NMP was not employed), which gave no reaction, the reaction reported by Knochel[2] was successfully reproduced. In addition to **S18**, NMP monoadduct **14a** was detected. This reveals that the presence of NMP is essential to promote the reaction of **S6**. Furthermore, NMP allows successful reaction with only 0.3 eq. KO*t*Bu yet studies herein (Table **S2.1**, entry 1) show that catalytic use of base is detrimental to reaction conversion in the case of DMA.

S4.2 Investigation of Alkyl-substituted Styrenes

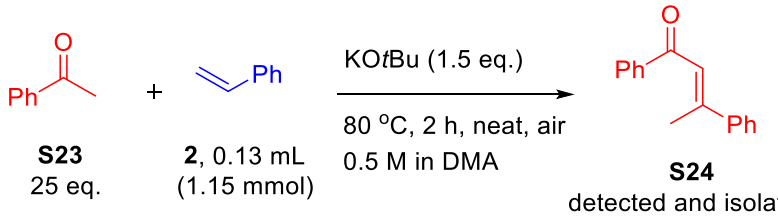
Reactions conducted according to General Procedure **A** (see Section 9 for details). Yields quoted are ^{1}H NMR yields, see Section 5 for an example calculation.



Both α-methylstyrene **S19** and β-methylstyrene **S21** reacted poorly, but surprisingly, α-methylstyrene **S19** gave less conversion. Since the styrenes are expected to be similarly electron-rich, this comparison reveals that the reaction is sensitive to sterics and particularly at the α-position.

S4.3 Investigation of Acetophenone

Reactions conducted according to General Procedure **A** (see Section 9 for details).



When acetophenone **S23** was employed, the desired product(s) were not detected and instead dypnone was detected by ^{1}H NMR of the crude reaction products, which presumably formed through the well-precedented Aldol condensation reaction.[3] The identity of dypnone **S24** was confirmed by isolation:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03-7.41 (m, 10H), 7.19 (s, 1H), 2.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 155.3, 143.0, 139.6, 132.8, 129.4, 128.8 (2 x C), 128.5, 126.7, 122.2, 19.0. ^{1}H and ^{13}C NMR data are consistent with the literature.[4]

S5. REPRESENTATIVE CALCULATIONS OF NMR YIELDS

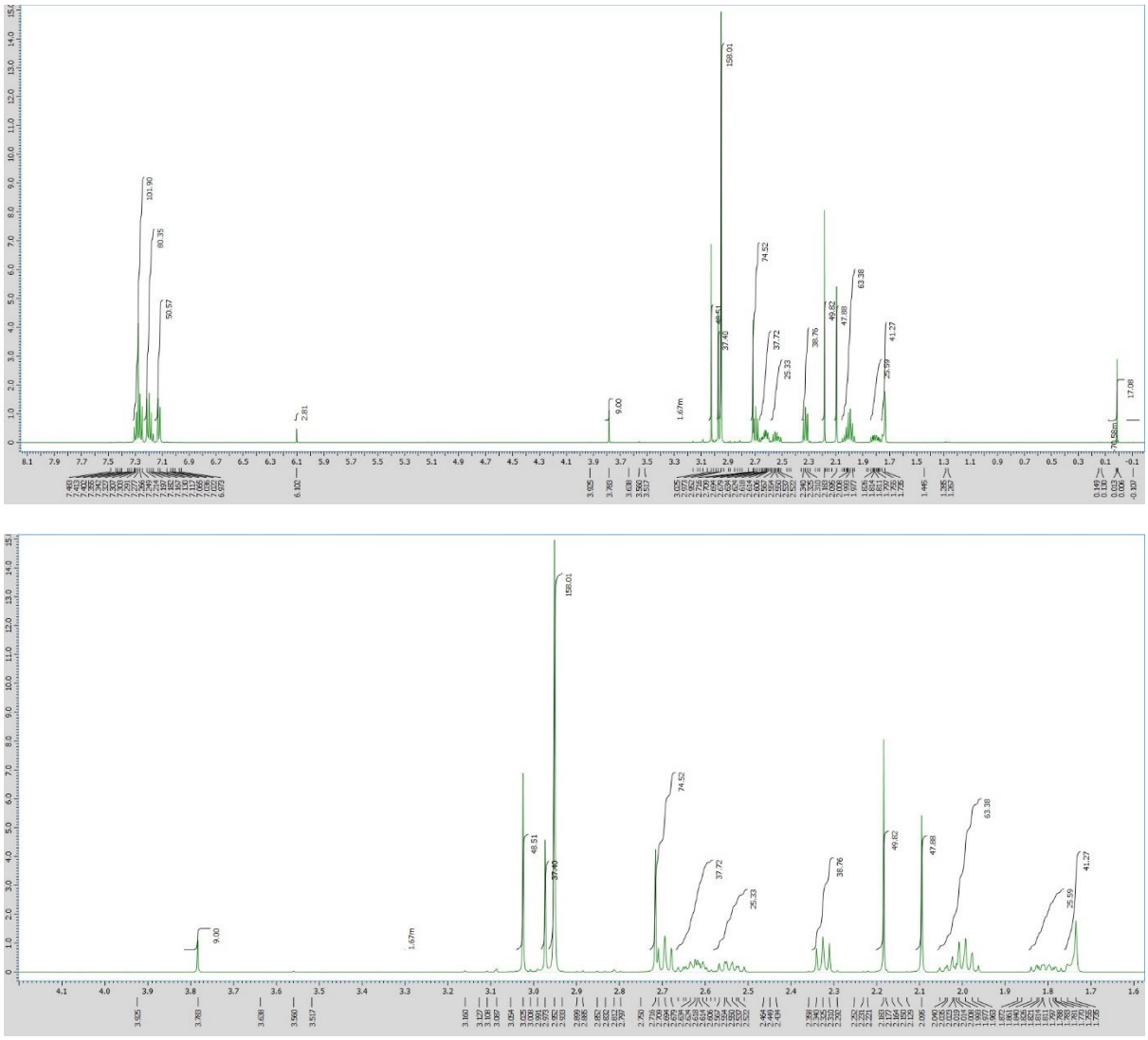


Fig. S4. Top: ^{1}H NMR ($CDCl_3$) spectra for the reaction depicted in Table 1, entry 1 of the manuscript (Table S2.1, entry 2 herein). Bottom: Expansion of the aliphatic region of the same spectrum.

To the crude reaction mixture (Table 1, entry 1 of the manuscript, Table 2.1, entry 2 herein), 2 mol% 1,3,5-trimethoxybenzene (3.9 mg, 23.0 μmol) was added. The integration of the peak at 3.78 ppm (1,3,5-trimethoxybenzene ArO-C**H**$_3$ protons) was set to 9 units. The integration of the unobstructed peak at 2.33 ppm (t, 2H) revealed a 39% yield of **4a** according to the following calculation:

$$\frac{38.76\ (integral)}{2\ (no.H\ atoms)} \times 2\ (mol\%\ of\ internal\ standard) = 39\%$$

The integration of the unobstructed peak at 1.81 ppm (m, 2H) revealed a 51% yield of **4b** according to the following calculation:

$$\frac{25.59\ (integral)}{2\ (no.H\ atoms)} \times 2\ (mol\%\ internal\ standard) \times 2\ (2\ eq.styrenes\ needed\ to\ form\ product) = 51\%$$

The isolated yields after chromatography (25-75% EtOAc/Hexane) were: **4a**, 36% and **4b**, 47%. ^{1}H NMR and isolated yields are in good agreement, which validates the NMR yield method.

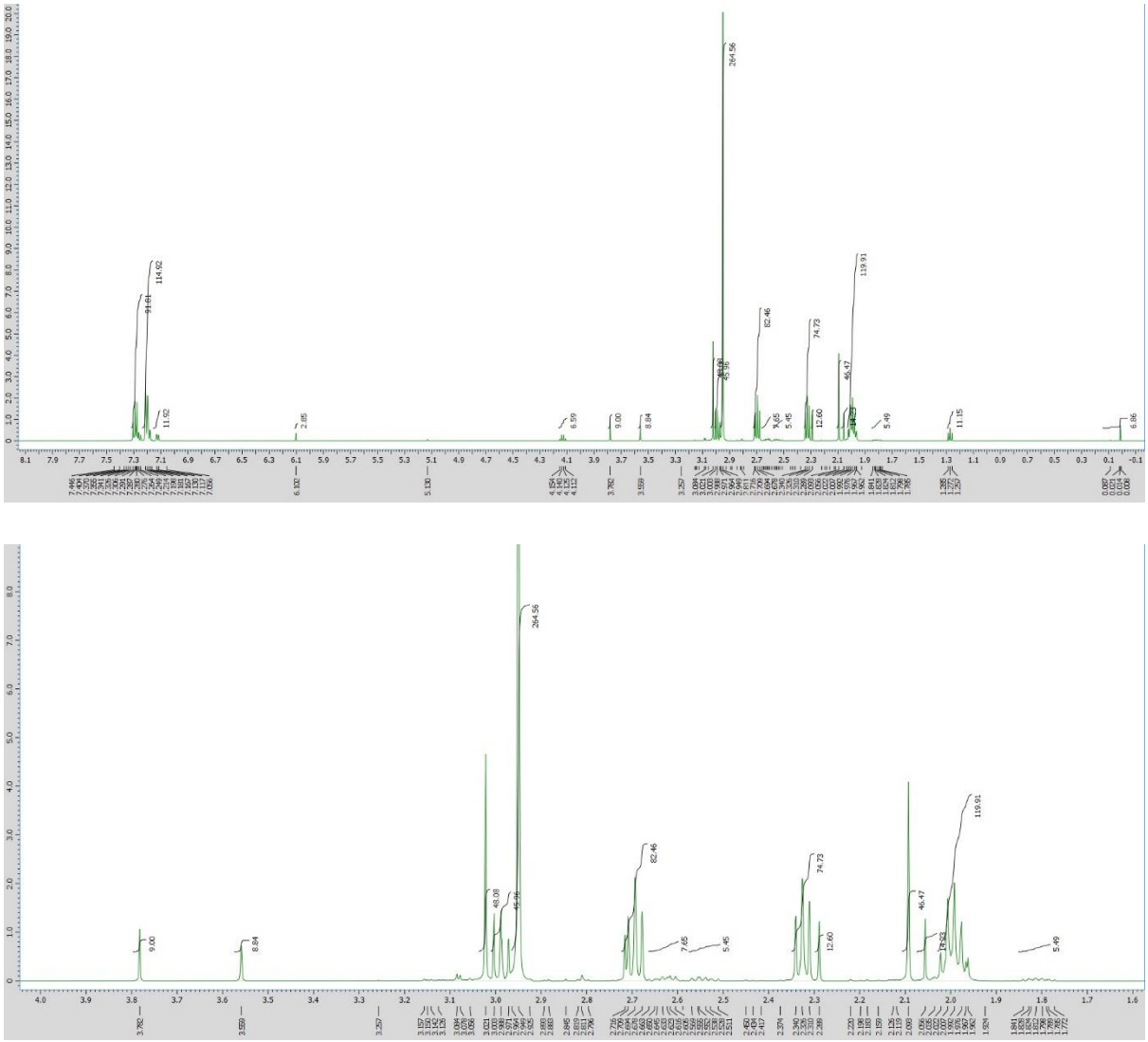


Fig. S5. Top: ^{1}H NMR ($CDCl_3$) spectra for the reaction depicted in Table 1, entry 7 of the manuscript (Table S2.1, entry 7 herein). Bottom: Expansion of the aliphatic region of the same spectrum.

To the crude reaction mixture (Table 1, entry 7 of the manuscript and Table S2.1, entry 7 herein), 2 mol% 1,3,5-trimethoxybenzene (3.9 mg, 23.0 μmol) was added. The integration of the peak at 3.78 ppm (1,3,5-trimethoxybenzene ArO-C**H**$_3$ protons) was set to 9 units. The integration of the unobstructed peak at 2.33 ppm (t, 2H) revealed a 75% yield of **4a** according to the calculation described above:

$$\frac{74.73}{2} \times 2 \ = 75\%$$

The integration of the unobstructed peak at 1.81 ppm (m, 2H) revealed a 51% yield of **4b** according to the following calculation:

$$\frac{5.49}{2} \times 2 \ \times 2 \ = 11\%$$

The isolated yields after chromatography (25-75% EtOAc/Hexane) were: **4a**, 77% and **4b**, 7%. ^{1}H NMR and isolated yields are in good agreement, which validates the NMR yield method.

S6. Details of the Microwave Flow Reactor and Reactor Tubes

Details of the MW flow reactor, designed by SAIDA FDS Inc. and employed herein have been described in previous reports.[5,6] The reactor consists of a MW generator, a resonant cavity (8 cm x 8 cm x 20 cm), a helical tubular borosilicate glass tube reactor (channel o.d. 6.0 mm, channel i.d. 3.6 mm, coil o.d. 20.0 mm, internal volume in the resonant cavity: 6.2 mL), a pumping system and a power controller. The MW generator is a solid-state device which generates a uniform electromagnetic field within the resonant cavity. The tuning of the irradiation frequency used a technology which adjusts the frequency for detected electric power in the resonator to be maximized. The device output is up to 200 W in the 2.4 - 2.5 GHz frequency range. Irradiation power, reflected power, internal reactor exit temperature (a thermocouple is set at the exit of the helical tube reactor) and reaction mixture pressure are monitored and controlled in real time. A back-pressure regulator (BPR, rated to 3.0 MPa), fitted after the helical tube reactor, maintains the reaction mixture pressure.

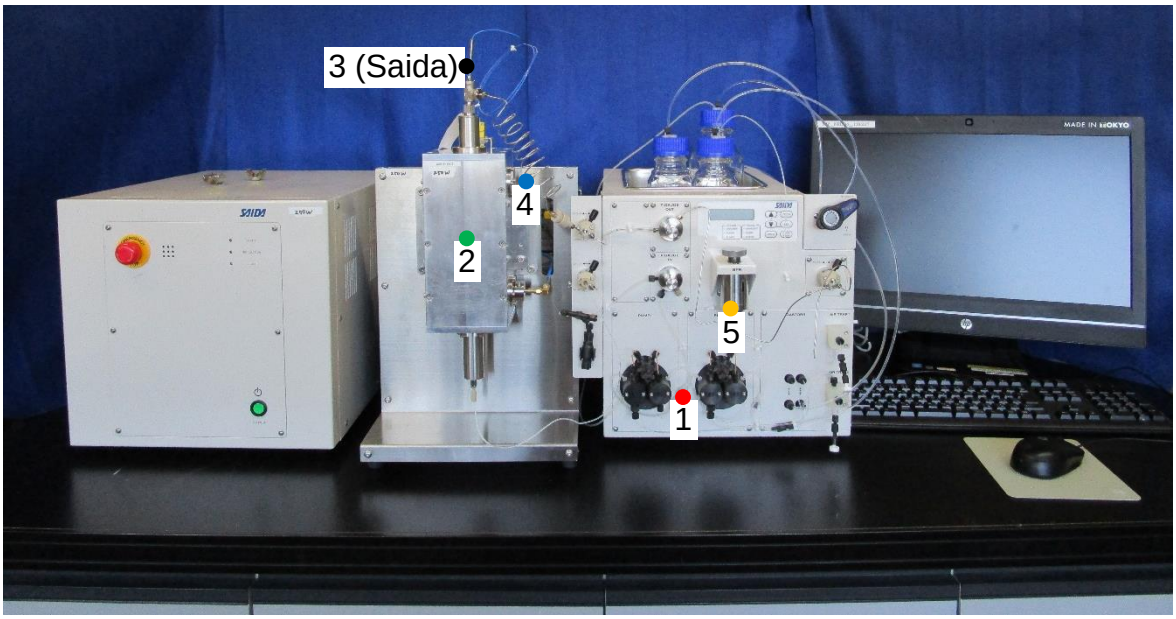


Fig. S6. Assembled 250 W MW flow reactor consisting of 1) pump unit, 2) 250 W MW cavity, 3) Reactor exit temperature probe 'Saida', 4) Cooling coil, 5) Adjustable Back Pressure Regulator (BPR). Note that the model used in the study herein used a 200 W MW cavity.

S7. SCALE-UP OF *C*-ALKYLATION REACTION IN CONTINUOUS FLOW

S7.1 GENERAL EXPERIMENTAL

Prior to conducting any reaction, the flow rate was set and actual flow rate measured using solvent only to ensure consistency. All residence times (R_T) quoted are calculated from the actual measured flow rate, not the set flow rate. The adjustable back pressure regulator (BPR) was opened fully during operation and reactor exit temperature (as measured by the 'Saida' temperature probe) was never allowed to exceed 200 °C (the reactor was always operated below the boiling point of the reaction solvent).

General Procedure 3. The specified amounts of NaO*t*Bu and 18-crown-6 were dissolved in NMP, sealed under an Ar atmosphere (Ar funnel) and sonicated for ~10 min. A known volume of styrene was injected to prepare the desired concentration of styrene in NMP, the resultant mixture sealed under an Ar atmosphere (Ar funnel) and sonicated until clear from particles (~10 min). The unfiltered solution was then stirred under an Ar atmosphere (Ar balloon) and passed through the microwave flow reactor at the specified flow rate, heating to the specified temperature (by adjusting the applied MW power until stable temperature was reached). This temperature was that measured by the 'Saida' temperature probe at the reactor tube exit. Once stable temperature had been reached, reaction mixture was discarded to waste until >1 residence time had passed, then samples were collected. The actual flow rate was measured again upon reaching stable temperature. For NMR yields (shown in Table 2 of the manuscript), an aliquot of reaction mixture of known volume and concentration was collected and immediately quenched with MeOH of equivalent volume. The resultant mixture was subjected to EtOAc/H_2O work up (according to **Procedure A**, see Section S9), was concentrated to dryness *in vacuo* and 1,3,5-trimethoxybenzene (10 mol%, based on initial styrene concentration and hence based on the maximum theoretical no. mol of product) was added. The sample was dissolved in $CDCl_3$ and yield determined by ^{1}H NMR (see Section S5 for example calculations).

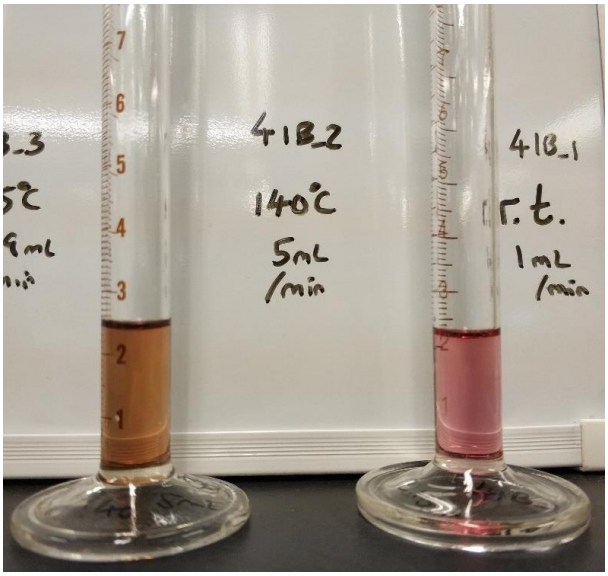
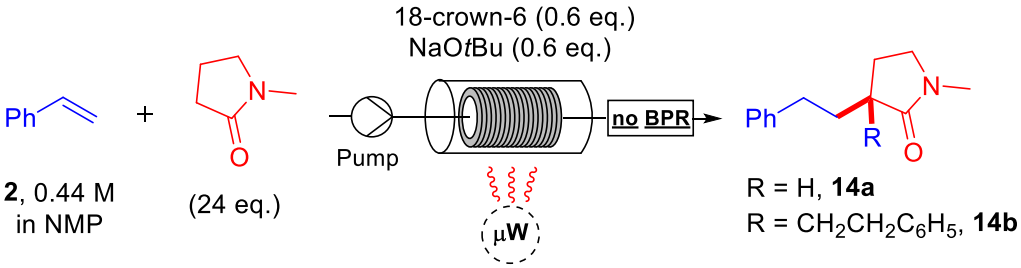


Fig. S7. Color differences in a reaction mixture (0.22 M) processed at rt (purple) *vs*. 140 °C (brown).

S7.2 Full Results for the Scale-up in Flow



Entry	Conc. 2	Flow Rate	R_T[a]	Temp.[b]	Yield (%)[c,d]		Productivity (g/h)[e]	
	(M)	(mL/min)	(min)	(°C)	14a	14b	14a	14b
1	0.11	1.05	5.9	100	50	11	0.70	0.23
2	0.11	0.80	7.8	140	73	22	0.78	0.35
3	0.22	0.93	6.7	100	85	11	2.09	0.41
4	0.22	1.80	3.4	100	84	11	4.02	0.80
5	0.22	2.00	3.1	140	86	12	4.57	0.97
6	0.44	2.05	3.0	rt	0	0	-	-
7	0.44	2.05	3.0	140	87	8	9.49	1.32
8	0.44	10.80	0.6	140	38	3	21.84	2.61
9	0.44	11.20	0.6	180	82	7	48.87	6.31
10	0.44	16.70	0.4	180	73 [70]	7 [3]	64.86	9.40
11	0.44	20.00	0.3	175*	61	5	65.12	8.07

[a]R_T, residence time, calculated from measured reactor volume and measured flow rate and quoted to the nearest single decimal place. [b]Reaction temperature measured at the reactor tube exit upon reaching steady-state. [c]Yields determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol%) as an internal standard. [d]Isolated yields in parentheses; 5.17 g of **14a** and 0.32 g of **14b** isolated after employing entry 10 conditions for 5.0 min. [e]Flow productivities are calculated from NMR yield and flow rate.

*Under the conditions of entry 11, when the R_T was 0.3 min, the yields of **14a** and **14b** decreased and the 200 W MW cavity was not powerful enough to sustain a reaction temperature of 180 °C.

S7.3 Example Productivity Calculation

$$\mathbf{14a}\ (gh^{-1}) = [\mathbf{14a}]\ (M) \times \frac{volume}{hour}\ (Lh^{-1}) \times M.W.\ (gmol^{-1})$$

Where: $[\mathbf{14a}]\ (M) = [\mathbf{2}](M) \times \frac{\%yield}{100}$

For Table S10.2, entry 10, the productivities of **14a** and **14b** (g/h) are calculated as shown below.

For **14a**: $\mathbf{14a}\ (gh^{-1}) = \left(0.4362 \times \frac{73}{100}\right) \times (0.0167 \times 60) \times 203.3 = 64.86\ gh^{-1}$

Similarly, for **14b**: $\mathbf{14b}\ (gh^{-1}) = \left(0.4362 \times \frac{7}{100}\right) \times (0.0167 \times 60) \times 307.4 = 9.40\ gh^{-1}$

S7.4 Multigram-scale Flow Reaction and Isolation

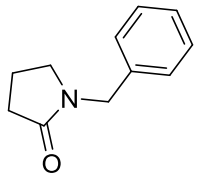
According to **General Procedure 3**, a reaction mixture (0.44 M styrene in NMP) was prepared using

NaO*t*Bu (4.12 g), 18-crown-6 (11.12 g), NMP (163 mL) and styrene (8.20 mL). Prior to processing, the reaction mixture appeared purple/red in color (Figure S8). At the desired temperature of 180 ^{o}C and at R_T = 0.4 min, 2.35 mL was collected (dark brown solution), immediately quenched with ~2 mL MeOH (color changed to pale brown) and was washed into a separatory funnel with EtOAc (20 mL) and H_2O (10 mL). The layers were separated and the aqueous layer extracted with further EtOAc (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a colorless oil, to which 1,3,5-trimethoxybenzene (17.3 mg, 10 mol%) was added. The sample was dissolved in $CDCl_3$ and yields of **14a** (73%) and **14b** (7%) were determined by ^{1}H NMR. A further 83.5 mL was collected over a period of 5 min, immediately quenched with ~85 mL MeOH (color changed to pale brown) and was washed into a separatory funnel with EtOAc (300 mL) and H_2O (150 mL). The layers were separated and the aqueous layer extracted with further EtOAc (3 x 300 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a pale brown oil, which was purified by column chromatography (25 - 75% EtOAc/Hexane) to afford **14a** (5.17 g, 70%) and **14b** (0.32 g, 3%). Isolated yields were in good agreement with the NMR yields.

Fig. S8. Unfiltered reaction mixture passed through the flow reactor: 0.44 M styrene in NMP with 0.6 eq. NaO*t*Bu and 0.6 eq. 18-crown-6).

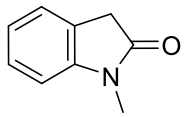
S8. SYNTHESIS OF *N*-ALKYLAMIDES

N-benzylpyrrolidin-2-one (S1)



Prepared according to a literature procedure.[7] A flame-dried flask was charged with sodium hydride (2.90 g, 72.3 mmol, 60% in oil) and anhydrous THF (63 mL). The mixture was cooled to 0 °C under Ar. After stirring for 15 min, a solution of 2-pyrrolidinone (5.0 mL, 65.8 mmol) in dry THF (63 mL) was added. After stirring for 30 min at 0 °C, benzyl bromide (7.75 mL, 65.8 mmol) was added carefully, dropwise over 30 min. The reaction was allowed to warm to rt and was stirred for 3 h, before concentrating *in vacuo* and partitioning between $CHCl_3$ (200 mL) and H_2O (200 mL). The layers were separated and organic layer washed with H_2O (3 x 100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a pale brown oil. Purification by column chromatography (50% EtOAc/Hexane) gave **S1** as a pale yellow oil (8.85 g, 77%); IR ν_{max} (neat) 2974 - 2874 (C-H), 1678 (C=O), 1605 (Ar), 1495 (Ar), 1422, 1360, 1285, 1261, 1223, 1204 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.0 Hz, 2H), 7.30 - 7.24 (m, 3H), 4.46 (s, 2H), 3.27 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 8.0 Hz, 2H), 2.00 (quint, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 136.6, 128.7, 128.1, 127.5, 46.6 (2 x C), 30.9, 17.7; HRMS (ESI^+) *m/z* calculated for $C_{11}H_{14}NO$ ($[M+H]^+$), 176.1075; Found 176.1074. ^1H and ^{13}C NMR data are consistent with the literature.[8]

N-methylindolin-2-one (S2)



Prepared according to a literature procedure.[9] A suspension of NaH (2.0 g, 50.0 mmol, 60% in oil) and Xylenes (100.0 mL) was heated at 130 °C. After 15 min, 2-oxindole (6.66 g, 50.0 mmol) was added carefully, portionwise over 5 min (evolution of gas was observed). The resultant suspension was heated to reflux for 1 h. Me_2SO_4 (4.75 mL, 50.0 mmol) was added carefully, dropwise. The suspension evolved gas during the addition, then became clear and orange. After refluxing for 1 h, the reaction was cooled to rt overnight. NaOH (15%) (15 mL) was added and the reaction mixture was stirred at rt for 2 h, before adding EtOAc (100 mL). The organic layer was washed with H_2O (2 x 100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (40% EtOAc/Hexane) gave **S2** as a pale yellow microcrystalline solid (4.49 g, 61%); m.p. 88-89 °C (lit. 87-88 °C[10]); IR ν_{max} (neat) 3063 - 2920 (C-H), 1695 (C=O), 1611 (Ar), 1495 (Ar), 1464, 1449, 1423, 1368, 1348, 1314, 1265, 1250, 1213 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.49 (s, 2H), 3.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 145.0,

127.7, 124.3, 124.1, 122.2, 107.9, 35.6, 26.0; HRMS (ESI$^+$) *m/z* calculated for $C_9H_{10}NO$ ([M+H]$^+$), 148.0762; Found 148.0768. ^{1}H and ^{13}C NMR data are consistent with the literature.[9,10]

S9. General Procedure for *C*-alkylation Reaction of *N*-alkylamides

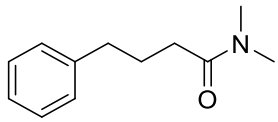
Procedure A. An oven-dried reaction vessel equipped with a stirrer bar was charged with KO*t*Bu (385 mg, 3.45 mmol, 0.6 eq.), DMA (2.50 mL, 4.5 eq.) and styrene (0.70 mL, 6.06 mmol, 1.0 eq.). A pale yellow color developed. The reaction vessel was bubbled with Ar for 5 min, sealed and stirred at 80 ^{o}C for 2 h. A pale brown color developed after heating. After cooling to rt, the reaction mixture was quenched with H_2O (~1 mL) and washed into a separatory funnel with EtOAc (20 mL) and H_2O (10 mL). The layers were separated and the aqueous layer extracted with further EtOAc (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a colorless oil, to which 1,3,5-trimethoxybenzene (19.3 mg, 2 mol%) was added. ^{1}H NMR revealed a 39% yield of **4a** and a 51% yield of **4b**. Purification by column chromatography (25 - 75% EtOAc/Hexane) gave **4a** (412.3 mg, 36%) as a colorless oil and **4b** (416.8 mg, 47%) as a colorless oil (Table 1, entry 1 of the manuscript and Table **S2.1**, entry 2 herein).

General Procedure B. Alternatively, the reaction was carried out using styrene (1.15 mmol), KO*t*Bu (1.5 eq.) and amide (25 eq.) and was sealed under air (Table 1, entry 4 of the manuscript and Table S2.1, entry 6 herein). Following work up (according to **Procedure A**), 1,3,5-trimethoxybenzene (19.3 mg, 10 mol%) was added, ^{1}H NMR revealed a 72% yield of **4a** and a 21% yield of **4b** (average of 3 replicates). These conditions were employed as standard operating conditions for the substrate scope investigation.

General Procedure C. Alternatively, the reaction was carried out using styrene (1.15 mmol), KO*t*Bu (1.5 eq.) and amide (15 eq.) in DMSO (0.35 M styrene in DMSO) and was sealed under air (Table S3.2, entry 2 herein). Following work up (according to **Procedure A**), 1,3,5-trimethoxybenzene (19.3 mg, 10 mol%) was added, ^{1}H NMR revealed a 78% yield of **14a** and a 10% yield of **14b**.

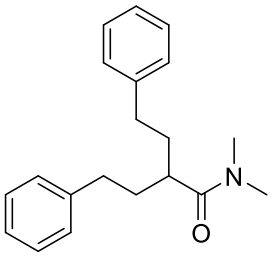
S10. Data for Compounds

***N*,*N*-dimethyl-4-phenylbutanamide (4a)**



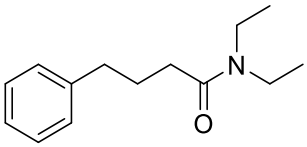
Prepared according to **Procedure A**. Colorless oil (412.3 mg, 36%); IR ν_{max} (neat) 3024 - 2860 (C-H), 1639 (C=O), 1495 (Ar), 1454, 1396, 1263 cm^{-1} ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 2H), 7.21 - 7.18 (m, 3H), 2.95 (s, 6H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.32 (t, *J* = 7.5 Hz, 2H), 2.00 (quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 141.8, 128.5, 128.3, 125.8, 37.2, 35.3 (2 x C), 32.4, 26.5; HRMS (ESI$^+$) *m/z* calculated for $C_{12}H_{18}NO$ ([M+H]$^+$), 192.1388; Found 192.1389. ^{1}H and ^{13}C NMR data are consistent with the literature.[11]

***N*,*N*-dimethyl-2-phenethyl-4-phenylbutanamide (4b)**



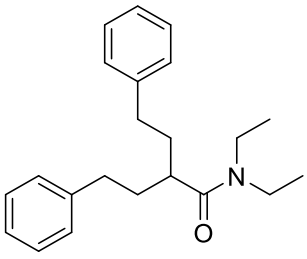
Prepared according to **Procedure A** and isolated from the reaction above. Colorless oil (416.8 mg, 47%); IR ν_{max} (neat) 3024 - 2869 (C-H), 1638 (C=O), 1603 (Ar), 1495 (Ar), 1454, 1416, 1396, 1354, 1339, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 - 7.25 (m, 4H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 7.5 Hz, 4H), 2.97 (s, 3H), 2.71 (s, 3H), 2.66 - 2.50 (m, 5H), 2.04 - 1.99 (m, 2H), 1.83 - 1.78 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 141.8, 128.4, 128.3, 125.8, 39.0, 36.9, 35.6, 34.0, 33.4; HRMS (ESI^+) *m/z* calculated for $C_{20}H_{26}NO$ ($[M+H]^+$), 296.2014; Found 296.2016.

***N*,*N*-diethyl-4-phenylbutanamide (5a)**



Prepared according to **General Procedure B.** Colorless oil (191.6 mg, 76%); IR ν_{max} (neat) 3024 - 2874 (C-H), 1636 (C=O), 1603 (Ar), 1477, 1452, 1427, 1379, 1362, 1346, 1308, 1260, 1221 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 2H), 7.21 - 7.18 (m, 3H), 3.37 (q, *J* = 7.0 Hz, 2H), 3.25 (q, *J* = 7.0 Hz, 2H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.31 (t, *J* = 7.0 Hz, 2H), 2.00 (apt. quint, *J* = 7.5 Hz, 2H), 1.12 (apt. dt, *J* = 7.5, 3.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 141.9, 128.5, 128.3, 125.8, 41.9, 40.0, 35.3, 32.2, 26.8, 14.3, 13.1; HRMS (ESI^+) *m/z* calculated for $C_{14}H_{22}NO$ ($[M+H]^+$), 220.1701; Found 220.1700. ^{1}H and ^{13}C NMR data are consistent with the literature.[12]

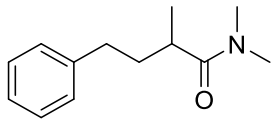
***N*,*N*-diethyl-2-phenethyl-4-phenylbutanamide (5b)**



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (18.5 mg, 10%); IR ν_{max} (neat) 3024 - 2857 (C-H), 1632 (C=O), 1603 (Ar), 1495 (Ar), 1479, 1454, 1429, 1379, 1362, 1260, 1219 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 - 7.26 (m, 4H), 7.20 - 7.14 (m, 6H), 3.38 (q, *J* = 7.5 Hz, 2H), 3.05 (q, *J* = 7.5 Hz, 2H), 2.67 - 2.54 (m, 5H), 2.04 - 1.97 (m, 2H), 1.89 - 1.81 (m, 2H),

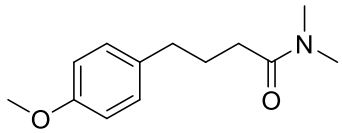
1.15 (t, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 141.9, 128.4, 128.3, 125.8, 41.6, 40.3, 39.4, 34.2, 33.5, 14.7, 13.1; HRMS (ESI$^+$) *m/z* calculated for $C_{22}H_{30}NO$ ([M+H]$^+$), 324.2327; Found 324.2322.

_N_,_N_-2-trimethyl-4-phenylbutanamide (6a)



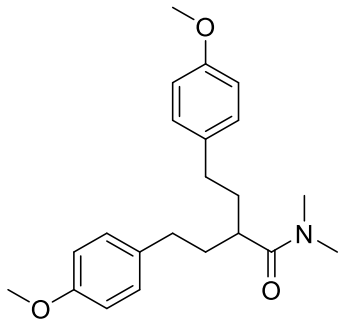
Prepared according to **General Procedure B.** Colorless oil (220.5 mg, 93%); IR ν_{max} (neat) 2967 - 2866 (C-H), 1638 (C=O), 1495 (Ar), 1454, 1412, 1396, 1373, 1331, 1260 cm^{-1} ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.8 Hz, 2H), 7.20 - 7.15 (m, 3H), 2.96 (s, 3H), 2.91 (s, 3H), 2.70 - 2.53 (m, 3H), 2.10 - 2.00 (m, 1H), 1.72 - 1.64 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 141.9, 128.4, 128.3, 125.8, 37.0, 35.6, 35.4, 34.5, 33.4, 17.4; HRMS (ESI$^+$) *m/z* calculated for $C_{13}H_{20}NO$ ([M+H]$^+$), 206.1545; Found 206.1547.

4-(4-methoxyphenyl)-_N_,_N_-dimethylbutanamide (7a)



Prepared according to **General Procedure B.** Colorless oil (119.0 mg, 45%); IR ν_{max} (neat) 2932 - 2835 (C-H), 1639 (C=O), 1611 (Ar), 1510 (Ar), 1456, 1396, 1300, 1242 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 2.95 (s, 6H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.95 (quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 157.8, 133.9, 129.3, 113.7, 55.2, 37.2, 35.3, 34.4, 32.4, 26.7; HRMS (ESI$^+$) *m/z* calculated for $C_{13}H_{20}NO_2$ ([M+H]$^+$), 222.1494; Found 222.1497.

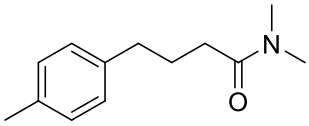
2-(4-methoxyphenethyl)-4-(4-methoxyphenyl)-_N,N_-dimethylbutanamide (7b)



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (2.5 mg, 1%); IR ν_{max} (neat) 2860 (C-H), 1647 (C=O), 1612 (Ar), 1512 (Ar), 1503, 1462, 1454, 1443, 1400, 1300, 1261, 1250 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.7 Hz, 4H), 6.81 (d, *J* = 8.7 Hz, 4H),

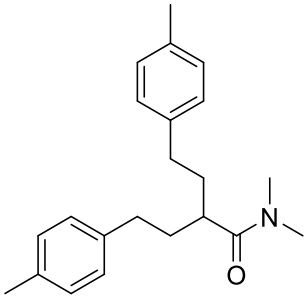
3.79 (s, 6H), 2.96 (s, 3H), 2.73 (s, 3H), 2.59 - 2.53 (m, 3H), 2.50 - 2.44 (m, 2H), 2.00 - 1.92 (m, 2H), 1.78 - 1.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 157.7, 133.8, 129.2, 113.7, 55.2, 38.9, 37.0, 35.6, 34.2, 32.4; HRMS (ESI$^+$) *m/z* calculated for $C_{22}H_{30}NO_3$ ([M+H]$^+$), 356.2226; Found 356.2233.

_N_,_N_-dimethyl-4-(_p_-tolyl)butanamide (8a)



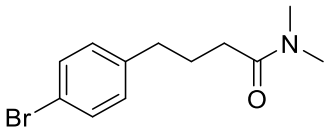
Prepared according to **General Procedure B.** Colorless oil (175.9 mg, 75%); IR ν_{max} (neat) 2913 - 1862 (C-H), 1641 (C=O), 1514 (Ar), 1495, 1454, 1395, 1265 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (apt. s, 4H), 2.95 (s, 6H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.34 - 2.29 (m, 5H), 1.96 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 138.7, 135.2, 129.0, 128.3, 37.1, 35.3, 34.8, 32.4, 26.6, 20.9; HRMS (ESI$^+$) *m/z* calculated for $C_{13}H_{20}NO$ ([M+H]$^+$), 206.1545; Found 206.1544.

_N_,_N_-dimethyl-2-(4-methylphenethyl)-4-(_p_-tolyl)butanamide (8b)



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (26.0 mg, 14%); IR ν_{max} (neat) 2920 - 2859 (C-H), 1639 (C=O), 1514 (Ar), 1454, 1396, 1260, cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.5 Hz, 4H), 7.01 (d, *J* = 7.5 Hz, 4H), 2.98 (s, 3H), 2.77 (s, 3H), 2.65 - 2.55 (m, 3H), 2.53 - 1.45 (m, 2H), 2.32 (s, 6H), 2.03 - 1.96 (m, 2H), 1.80 - 1.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 138.7, 135.2, 129.0, 128.3, 39.2, 37.1, 35.7, 34.2, 33.0, 21.0; HRMS (ESI$^+$) *m/z* calculated for $C_{22}H_{30}NO$ ([M+H]$^+$), 324.2327; Found 324.2330.

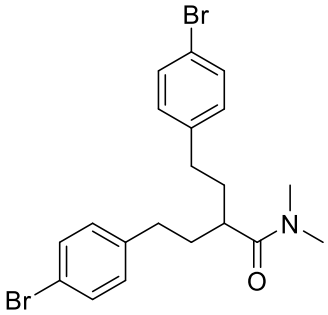
4-(4-bromophenyl)-_N_,_N_-dimethylbutanamide (9a)



Prepared according to **General Procedure B.** Colorless oil (121.6 mg, 39%); IR ν_{max} (neat) 2932 - 2864 (C-H), 1638 (C=O), 1487 (Ar), 1456, 1396, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 2.95 (2 x s, 2 x 3H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.95

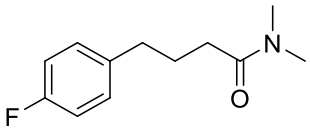
(quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 140.8, 131.3, 130.2, 119.6, 37.2, 35.4, 34.7, 32.2, 26.3; HRMS (ESI$^+$) *m/z* calculated for $C_{12}H_{17}BrNO$ ([M+H]$^+$), 270.0494; Found 270.0488.

2-(4-bromophenethyl)-4-(4-bromophenyl)-*N*,*N*-dimethylbutanamide (9b)



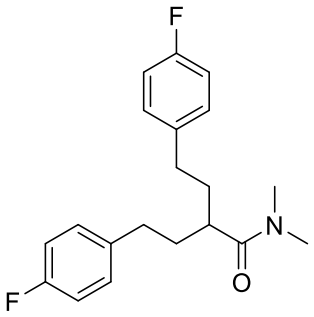
Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (43.2 mg, 8%); IR ν_{max} (neat) 2926 - 2859 (C-H), 1638 (C=O), 1487 (Ar), 1456, 1398, 1354, 1339, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.0 Hz, 4H), 7.00 (d, *J* = 8.0 Hz, 4H), 2.97 (s, 3H), 2.78 (s, 3H), 2.62 - 2.53 (m, 3H), 2.52 - 2.45 (m, 2H), 2.03 - 1.95 (m, 2H), 1.78 - 1.70 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 140.6, 131.4, 130.1, 119.7, 39.1, 37.1, 35.7, 33.8, 32.8; HRMS (ESI$^+$) *m/z* calculated for $C_{20}H_{24}Br_2NO$ ([M+H]$^+$), 452.0225; Found 452.0223.

4-(4-fluorophenyl)-*N*,*N*-dimethylbutanamide (10a)



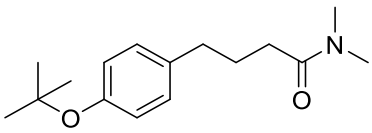
Prepared according to **General Procedure B.** Colorless oil (114.3 mg, 44%); IR ν_{max} (neat) 2932 - 2862 (C-H), 1638 (C=O), 1601 (Ar), 1508 (Ar), 1491, 1456, 1396, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 8.0, 5.0 Hz, 2H), 6.95 (apt. t, *J* = 8.5 Hz, 2H), 2.94 (s, 6H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.94 (quint, *J* = 7.5 Hz, 2H); ^{19}F NMR (470 MHz, $CDCl_3$) δ -117.7 (sept, *J* = 4.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 162.2 (d, *J* = 242.0 Hz), 137.4 (d, *J* = 2.4 Hz), 129.7 (d, *J* = 7.1 Hz), 115.1 (d, *J* = 21.5 Hz), 37.1, 35.3, 34.4, 32.2, 26.6; HRMS (ESI$^+$) *m/z* calculated for $C_{12}H_{17}FNO$ ([M+H]$^+$), 210.1294; Found 210.1293.

2-(4-fluorophenethyl)-4-(4-fluorophenyl)-*N*,*N*-dimethylbutanamide (10b)



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (6.9 mg, 4%); IR ν_{max} (neat) 2922 - 2860 (C-H), 1638 (C=O), 1601 (Ar), 1508 (Ar), 1454, 1433, 1416, 1398, 1354, 1339, 1260, 1219 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (apt. t, *J* = 6.8 Hz, 4H), 6.95 (apt. t, *J* = 8.8 Hz, 4H), 2.97 (s, 3H), 2.76 (s, 3H), 2.63 - 2.48 (m, 5H), 2.03 - 1.95 (m, 2H), 1.80 - 1.72 (m, 2H); ^{19}F NMR (470 MHz, $CDCl_3$) δ -117.4 (sept, *J* = 3.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1, 162.2 (d, *J* = 242.0 Hz), 137.3 (d, *J* = 3.6 Hz), 129.7 (d, *J* = 8.3 Hz), 115.1 (d, *J* = 21.5 Hz), 39.0, 37.0, 35.7, 34.1, 32.6, 29.7; HRMS (ESI^+) *m/z* calculated for $C_{20}H_{24}F_2NO$ ($[M+H]^+$), 332.1826; Found 332.1825.

4-(4-(*tert*-butoxy)phenyl)-*N*,*N*-dimethylbutanamide (S3)



During the isolation of compounds **10a** and **10b**, compound **S3** was also isolated. Colorless oil (7.9 mg, 2%); IR ν_{max} (neat) 2974 - 2866 (C-H), 1643 (C=O), 1609 (Ar), 1504 (Ar), 1476, 1454, 1396, 1364, 1260, 1233 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 2.94 (s, 3H), 2.93 (s, 3H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.96 (quint, *J* = 7.5 Hz, 2H), 1.33 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 153.3, 136.7, 128.8, 124.1, 37.2, 35.4, 34.6, 32.4, 28.8, 26.6; HRMS (ESI^+) *m/z* calculated for $C_{16}H_{26}NO_2$ ($[M+H]^+$), 264.1964; Found 264.1964.

Compound **S3** was detected in the crude reaction mixture (5% by ^{1}H NMR), together with **10a** (74%) and **10b** (17%). Presumably, **S3** formed *via* S_NAr reaction of KO*t*Bu with 4-fluorostyrene prior to reaction of the styrene with DMA (or, reaction with **10a**), see Figure S9. Only one regioisomer of **S3** (*para*-disubstituted) was observed, ruling against a pathway involving benzyne formation followed by addition of KO*t*Bu[13] (which would afford a 1:1 mixture of regioisomers). The similar polarities of **10a** and **S3** meant that multiple chromatographic separations were required and the isolated yield of **10a** (44%) was significantly lower than the ^{1}H NMR yield (74%).

The *tert*-butoxide *para*-substituted product was not detected in the reaction of NMP with 4-fluorostyrene in which **21a** (87%) and **21b** (12%) accounted for 99% of the mass balance. In line with control reactions, which show that the reaction of NMP + styrene at rt (Table S3.1, entry 2) gives higher conversion than

the reaction of DMA + styrene at rt (Table S2.3, entry 2), NMP is presumably more reactive than DMA and in that case the desired reaction outcompetes the S_NAr process.

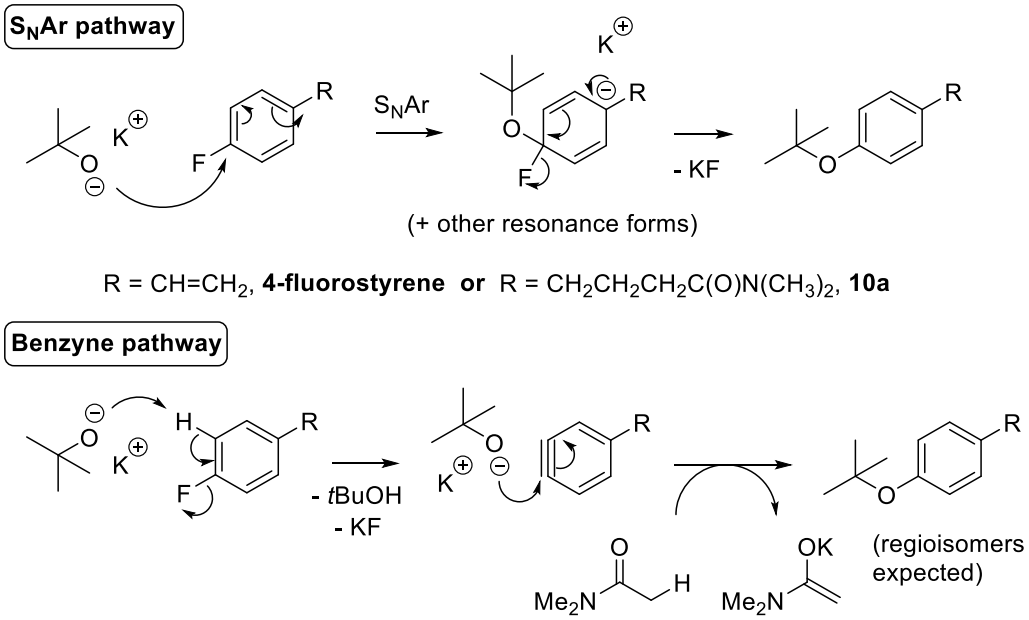
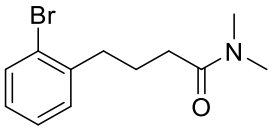


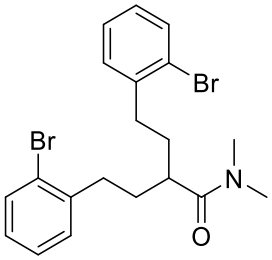
Fig. S9 Rationalization of formation of by-product **S3**.

4-(2-bromophenyl)-*N*,*N*-dimethylbutanamide (11a)



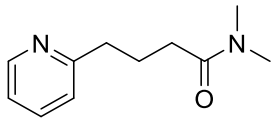
Prepared according to **General Procedure B.** Colorless oil (90.3 mg, 39%); IR ν_{max} (neat) 2933 - 2866 (C-H), 1639 (C=O), 1489 (Ar), 1470, 1456, 1439, 1396, 1354, 1263 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 1H), 7.27 - 7.22 (m, 2H), 7.06 (dt, *J* = 6.5, 1.5 Hz, 1H), 2.98 (s, 3H), 2.95 (s, 3H), 2.81 (t, *J* = 7.5 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.98 (quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 141.1, 132.7, 130.4, 127.6, 127.4, 124.5, 37.2, 35.4, 35.3, 32.5, 25.1; HRMS (ESI^+) *m/z* calculated for $C_{12}H_{17}BrNO$ ($[M+H]^+$), 270.0494; Found 270.0497.

2-(2-bromophenethyl)-4-(2-bromophenyl)-*N*,*N*-dimethylbutanamide (11b)



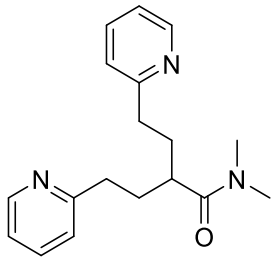
Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (37.0 mg, 7%); IR ν_{max} (neat) 2930 - 2860 (C-H), 1638 (C=O), 1566 (Ar), 1489 (Ar), 1470, 1454, 1437, 1416, 1396, 1354, 1339, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.0 Hz, 2H), 7.17 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.08 - 7.03 (m, 2H), 3.00 (s, 3H), 2.86 (s, 3H), 2.80 - 2.68 (m, 4H), 2.68 - 2.73 (m, 1H), 2.06 - 1.98 (m, 2H), 1.89 - 1.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 141.1, 132.8, 130.5, 127.6, 127.4, 124.4, 39.7, 37.0, 35.7, 33.7, 32.0; HRMS (ESI^+) *m/z* calculated for $C_{20}H_{24}Br_2NO$ ($[M+H]^+$), 452.0225; Found 452.0236.

***N,N*-dimethyl-4-(pyridin-2-yl)butanamide (12a)**



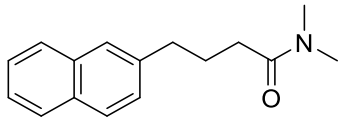
Prepared according to **General Procedure B.** Colorless oil (73.0 mg, 33%); IR ν_{max} (neat) 2930 - 2866 (C-H), 1634 (C=O), 1589 (Ar), 1586 (Ar), 1497 (Ar), 1474, 1458, 1435, 1396, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.0 Hz, 1H), 7.60 (apt. t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 7.0 Hz, 1H), 7.12 - 7.10 (m, 1H), 2.97 (s, 3H), 2.94 (s, 3H), 2.87 (t, *J* = 7.0 Hz, 2H), 2.38 (t, *J* = 7.0 Hz, 2H), 2.09 (quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 161.6, 149.1, 136.3, 122.9, 121.1, 37.7, 37.2, 35.3, 32.6, 25.1; HRMS (ESI^+) *m/z* calculated for $C_{11}H_{17}N_2O$ ($[M+H]^+$), 193.1341; Found 193.1348.

***N,N*-dimethyl-4-(pyridin-2-yl)-2-(2-(pyridin-2-yl)ethyl)butanamide (12b)**



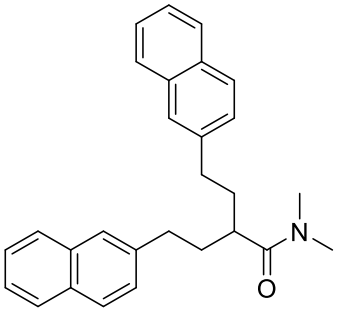
Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (1.4 mg, 0.4%); IR ν_{max} (neat) 2922 - 2855 (C-H), 1634 (C=O), 1589 (Ar), 1568 (Ar), 1474, 1433, 1398, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.5 Hz, 2H), 7.58 (apt. t, *J* = 8.0 Hz, 2H), 7.13 - 7.08 (m, 4H), 2.97 (s, 3H), 2.89 (s, 3H), 2.83 - 2.70 (m, 5H), 2.18 - 2.10 (m, 2H), 2.00 - 1.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 161.5, 149.1, 136.3, 122.8, 121.1, 39.7, 37.2, 35.8, 35.7, 32.4; HRMS (ESI^+) *m/z* calculated for $C_{18}H_{24}N_3O$ ($[M+H]^+$), 298.1919; Found 298.1922.

***N,N*-dimethyl-4-(naphthalen-2-yl)butanamide (13a)**



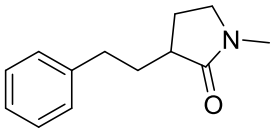
Prepared according to **General Procedure B.** Yellow solid (147.1 mg, 53%); m.p. 50-52 ^{o}C; IR ν_{max} (neat) 2953 - 2884 (C-H), 1649 (C=O), 1547 (Ar), 1504 (Ar), 1452, 1400, 1366, 1294, 1265, 1202 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 - 7.77 (m, 3H), 7.64 (s, 1H), 7.44 (quint, *J* = 6.8 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 1H), 2.95 (s, 3H), 2.94 (s, 3H), 2.86 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.09 (quint, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 139.2, 133.5, 131.9, 127.8, 127.5, 127.3, 127.2, 126.4, 125.8, 125.0, 37.0, 35.3, 35.2, 32.3, 26.2; HRMS (ESI^{+}) *m/z* calculated for $C_{16}H_{20}NO$ ([M+H]$^{+}$), 242.1545; Found 242.1541.

N,N-dimethyl-4-(naphthalen-2-yl)-2-(2-(napthalen-2-yl)ethyl)butanamide (13b)



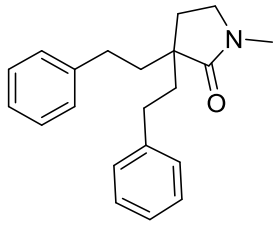
Prepared according to **General Procedure B.** Yellow oil (22.7 mg, 10%); IR ν_{max} (neat) 2880 (C-H), 1630 (C=O), 1585 (Ar), 1533 (Ar), 1506 (Ar), 1452, 1396, 1364, 1350, 1341, 1314, 1294, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 - 7.76 (m, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.66 - 7.64 (m, 2H), 7.50 (s, 2H), 7.43 - 7.39 (m, 4H), 7.25 (dd, *J* = 8.4, 1.7 Hz, 2H), 2.96 (s, 3H), 2.81 - 2.76 (m, 2H), 2.72 - 2.66 (m, 3H), 2.63 (s, 3H), 2.15 - 2.08 (m, 2H), 1.94 - 1.87 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 139.2, 133.5, 132.0, 127.9, 127.6, 127.3, 127.2, 126.5, 125.9, 125.1, 39.0, 37.0, 35.7, 33.9, 33.5; HRMS (ESI^{+}) *m/z* calculated for $C_{28}H_{30}NO$ ([M+H]$^{+}$), 396.2327; Found 396.2333.

***N*-methyl-3-phenethylpyrrolidin-2-one (14a)**



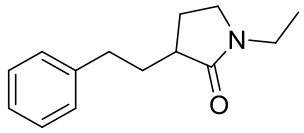
Prepared according to **General Procedure B.** Colorless oil (201.7 mg, 86%); IR ν_{max} (neat) 2924 - 2859 (C-H), 1676 (C=O), 1497, 1472, 1452, 1431, 1400, 1300, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 2H), 7.23 - 7.18 (m, 3H), 3.34 - 3.28 (m, 2H), 2.86 (s, 3H), 2.80 - 2.67 (m, 2H), 2.43 - 2.37 (m, 1H), 2.28 - 2.18 (m, 2H), 1.75 - 1.65 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 141.6, 128.5, 128.3, 125.9, 47.6, 41.0, 33.4, 33.1, 29.7, 25.0; HRMS (ESI^{+}) *m/z* calculated for $C_{13}H_{18}NO$ ([M+H]$^{+}$), 204.1388; Found 204.1385.

***N*-methyl-3,3-diphenethylpyrrolidin-2-one (14b)**



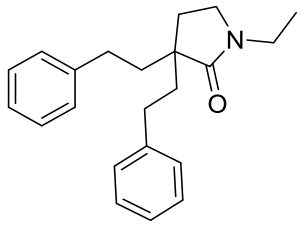
Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (13.8 mg, 4%) which crystallized overnight to give a microcrystalline white solid; m.p. 98-100 ^{o}C (101 - 102 ^{o}C[14]); IR ν_{max} (neat) 3026 - 2860 (C-H), 1670 (C=O), 1603 (Ar), 1508 (Ar), 1497, 1454, 1437, 1402, 1319, 1302, 1277 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 4H), 7.20 - 7.17 (m, 6H), 3.34 (t, *J* = 7.5 Hz, 2H), 2.90 (s, 3H), 2.67 (dt, *J* = 12.0, 6.5 Hz, 2H), 2.57 (dt, *J* = 12.0, 6.5 Hz, 2H), 2.07 (t, *J* = 7.5 Hz, 2H), 1.94 - 1.83 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 142.1, 128.4, 128.3, 125.8, 47.6, 46.6, 39.1, 30.8, 29.8, 28.5; HRMS (ESI^{+}) *m/z* calculated for $C_{21}H_{26}NO$ ([M+H]$^{+}$), 308.2014; Found 308.2019. The m.p. of **14b** is consistent with the literature.[14]

***N*-ethyl-3-phenethylpyrrolidin-2-one (15a)**



Prepared according to **General Procedure B.** Colorless oil (210.9 mg, 86%); IR ν_{max} (neat) 3024 - 2860 (C-H), 1676 (C=O), 1495 (Ar), 1454, 1429, 1356, 1300, 1273, 1231 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 2H), 7.23 - 7.17 (m, 3H), 3.38 - 3.29 (m, 4H), 2.80 - 2.67 (m, 2H), 2.43 - 2.37 (m, 1H), 2.27 - 2.18 (m, 2H), 1.74 - 1.61 (m, 2H), 1.11 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 141.6, 128.5, 128.3, 125.9, 44.6, 41.4, 37.2, 33.4, 33.0, 25.0, 12.5; HRMS (ESI^{+}) *m/z* calculated for $C_{14}H_{20}NO$ ([M+H]$^{+}$), 218.1545; Found 218.1544.

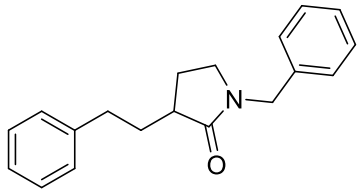
***N*-ethyl-3,3-diphenethylpyrrolidin-2-one (15b)**



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (9.9 mg, 5%); IR ν_{max} (neat) 2974 - 2866 (C-H), 1670 (C=O), 1497 (Ar), 1454, 1433, 1275, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 4H), 7.21 - 7.17 (m, 6H), 3.40 (q, *J* = 7.5 Hz, 2H), 3.35 (t, *J* = 7.0 Hz, 2H), 2.67 (dt, *J* = 12.0, 6.0 Hz, 2H), 2.58 (dt, *J* = 12.0, 6.0 Hz, 2H), 2.07 (t, *J* = 7.0 Hz, 2H), 1.95

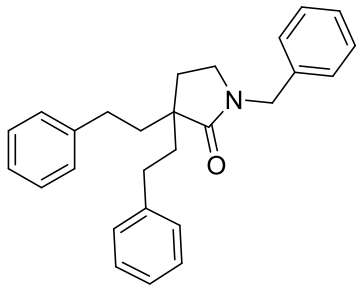
- 1.82 (m, 4H), 1.16 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 142.1, 128.4 (2 x C), 125.8, 47.9, 43.6, 39.1, 37.3, 30.7, 28.5, 12.6; HRMS (ESI$^+$) *m/z* calculated for $C_{22}H_{28}NO$ ([M+H]$^+$), 322.2171; Found 322.2173.

_N_-benzyl-3-phenethylpyrrolidin-2-one (16a)



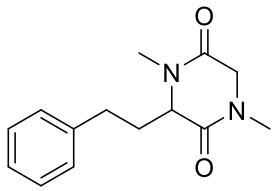
Prepared according to **General Procedure B.** Colorless oil (192.6 mg, 60%); IR ν_{max} (neat) 3026 - 2859 (C-H), 1678 (C=O), 1495 (Ar), 1452, 1425, 1300, 1260 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 - 7.21 (m, 10H), 4.54 (d, *J* = 14.5 Hz, 2H), 4.48 (d, *J* = 14.5 Hz, 2H), 3.26 - 3.17 (m, 2H), 2.86 - 2.71 (m, 2H), 2.53 - 2.47 (m, 1H), 2.37 - 2.28 (m, 1H), 2.25 - 2.18 (m, 1H), 1.78 - 1.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 141.5, 136.5, 128.6, 128.4, 128.3, 128.0, 127.4, 125.8, 46.6, 44.7, 41.1, 33.3, 33.0, 25.0; HRMS (ESI$^+$) *m/z* calculated for $C_{19}H_{22}NO$ ([M+H]$^+$), 280.1701; Found 280.1702.

_N_-benzyl-3,3-diphenethylpyrrolidin-2-one (16b)



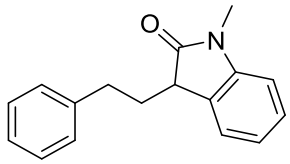
Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (3.1 mg, 1%); IR ν_{max} (neat) 3026 - 2857 (C-H), 1674 (C=O), 1495 (Ar), 1454, 1433, 1356, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 - 7.27 (m, 9H), 7.21 - 7.18 (m, 6H), 1.98 (s, 2H), 3.22 (apt. t, *J* = 5.5 Hz, 2H), 2.68 (dt, *J* = 12.0, 6.0 Hz, 2H), 2.60 (dt, *J* = 12.0, 6.0 Hz, 2H), 2.03 (t, *J* = 7.5 Hz, 2H), 1.98 - 1.86 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 142.1, 136.7, 128.7, 128.4 (2 x C), 128.2, 127.6, 125.9, 47.7, 46.8, 43.7, 39.0, 30.7, 29.7, 28.6; HRMS (ESI$^+$) *m/z* calculated for $C_{27}H_{30}NO$ ([M+H]$^+$), 384.2327; Found 384.2330.

1,4-dimethyl-3-phenethylpiperazine-2,5-dione (17a)



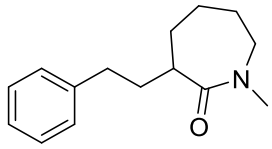
Prepared according to **General Procedure B**, using DMSO (2.5 mL) for solubility (0.5 M styrene in DMSO). Pale yellow microcrystalline solid (177.6 mg, 63%); m.p. 114 - 116 ^{o}C; IR ν_{max} (neat) 3001 - 2928 (C-H), 1647 (C=O), 1489 (Ar), 1454, 1425, 1404, 1339, 1314, 1265, 1254, 1231 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.5 Hz, 2H), 7.23 - 7.19 (m, 3H), 4.03 (d, *J* = 18.0 Hz, 1H), 3.99 - 3.97 (m, 1H), 3.88 (d, *J* = 18.0 Hz, 1H), 3.00 (s, 3H), 2.93 (s, 3H), 2.72 - 2.66 (m, 1H), 2.64 - 2.57 (m, 1H), 2.41 - 2.33 (m, 1H), 2.18 - 2.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 163.7, 139.8, 128.6, 128.3, 126.4, 61.7, 51.5, 33.4, 33.0, 32.2, 30.3; HRMS (ESI^{+}) *m/z* calculated for $C_{14}H_{19}N_2O_2$ ([M+H]$^{+}$), 247.1447; Found 247.1440.

***N*-methyl-3-phenethylindolin-2-one (18a)**



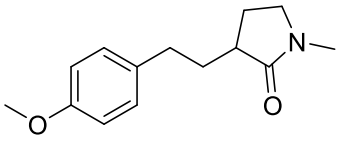
Prepared according to **General Procedure C.** Pale yellow oil (230.1 mg, 80%); IR ν_{max} (neat) 3026 - 2920 (C-H), 1703 (C=O), 1611 (Ar), 1493 (Ar), 1470, 1452, 1435, 1420, 1375, 1342, 1312, 1298, 1261, 1204 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 - 7.24 (m, 4H), 7.18 - 7.16 (m, 3H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 3.48 (t, *J* = 6.0 Hz, 1H), 3.19 (s, 3H), 2.77 - 2.70 (m, 1H), 2.69 - 2.62 (m, 1H), 2.30 - 2.22 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 144.4, 141.2, 128.9, 128.5, 128.3, 127.9, 126.0, 123.7, 122.3, 107.9, 44.9, 32.3, 31.9, 26.1; HRMS (ESI^{+}) *m/z* calculated for $C_{17}H_{18}NO$ ([M+H]$^{+}$), 252.1388; Found 252.1389. ^{1}H and ^{13}C NMR data are consistent with the literature.[15]

***N*-methyl-3-phenethylazepan-2-one (19a)**



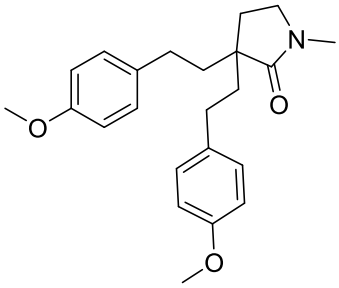
Prepared according to **General Procedure B.** Colorless oil (234.6 mg, 88%); IR ν_{max} (neat) 2922 - 2853 (C-H), 1639 (C=O), 1485 (Ar), 1454, 1429, 1396, 1332, 1263, 1215 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 - 7.26 (m, 2H), 7.21 - 7.16 (m, 2H), 3.58 (dd, *J* = 15.0, 11.5 Hz, 1H), 3.14 (dd, *J* = 15.0, 5.5 Hz, 1H), 3.01 (s, 3H), 2.77 - 2.70 (m, 1H), 2.65 - 2.58 (m, 1H), 2.53 - 2.47 (m, 1H), 2.28 - 2.20 (m, 1H), 1.95 - 1.88 (m, 1H), 1.77 - 1.64 (m, 2H), 1.62 - 1.52 (m, 2H), 1.50 - 1.35 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 142.6, 128.5, 128.2, 125.6, 50.2, 42.6, 35.7, 34.5, 34.0, 30.4, 29.0, 26.8; HRMS (ESI^{+}) *m/z* calculated for $C_{15}H_{22}NO$ ([M+H]$^{+}$), 232.1701; Found 232.1704.

3-(4-methoxyphenethyl)-1-methylpyrrolidin-2-one (20a)



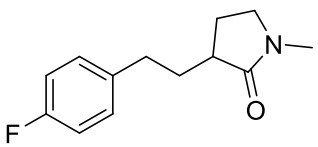
Prepared according to **General Procedure B.** Colorless oil (217.7 mg, 81%); IR ν_{max} (neat) 2934 - 2859 (C-H), 1678 (C=O), 1611 (Ar), 1510 (Ar), 1454, 1433, 1400, 1289, 1242 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 3.79 (s, 3H), 3.34 - 3.25 (m, 2H), 2.84 (s, 3H), 2.74 - 2.60 (m, 2H), 2.42 - 2.34 (m, 1H), 2.23 - 2.16 (m, 2H), 1.75 - 1.58 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6, 157.8, 133.6, 129.3, 113.7, 55.2, 47.6, 40.9, 33.3, 32.5, 29.7, 24.9; HRMS (ESI^+) *m/z* calculated for $C_{14}H_{20}NO_2$ ($[M+H]^+$), 234.1494; Found 234.1492.

3,3-bis(4-methoxyphenethyl)-1-methylpyrrolidin-2-one (20b)



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (13.8 mg, 7%); IR ν_{max} (neat) 2930 - 2833 (C-H), 1680 (C=O), 1611 (Ar), 1510 (Ar), 1454, 1441, 1400, 1300, 1244 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.0 Hz, 4H), 6.81 (d, *J* = 8.0 Hz, 4H), 3.79 (s, 6H), 3.33 (t, *J* = 7.5 Hz, 2H), 2.89 (s, 3H), 2.61 (td, *J* = 12.0, 5.5 Hz, 1H), 2.50 (td, *J* = 12.0, 5.5 Hz, 1H), 2.05 (t, *J* = 7.5 Hz, 2H), 1.90 - 1.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 157.8, 134.1, 129.2, 113.8, 55.2, 47.6, 46.7, 39.4, 29.8 (2 x C), 28.5; HRMS (ESI^+) *m/z* calculated for $C_{23}H_{30}NO_3$ ($[M+H]^+$), 368.2226; Found 368.2228.

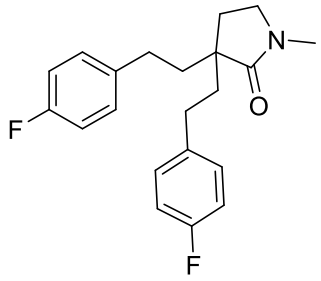
3-(4-fluorophenethyl)-1-methylpyrrolidin-2-one (21a)



Prepared according to **General Procedure B.** Colorless oil (212.2 mg, 83%); IR ν_{max} (neat) 2928 - 2860 (C-H), 1678 (C=O), 1601 (Ar), 1508 (Ar), 1471, 1454, 1431, 1400, 1298, 1271, 1260, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (apt. t, *J* = 9.0 Hz, 2H), 6.96 (apt. t, *J* = 10.0 Hz, 2H), 3.34 - 3.27 (m, 2H), 2.85 (s, 3H), 2.77 - 2.64 (m, 2H), 2.42 - 2.34 (m, 1H), 2.24 - 2.15 (m, 2H), 1.73 - 1.58 (m, 2H); ^{19}F NMR (470 MHz, $CDCl_3$) δ -117.6 (sept, *J* = 3.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 161.3 (d, *J* =

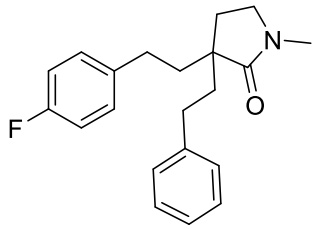
243.0 Hz), 137.2 (apt. s), 129.8 (d, *J* = 8.4 Hz), 115.1 (d, *J* = 20.3 Hz), 47.6, 40.9, 33.3, 32.6, 29.7, 24.9; HRMS (ESI$^+$) *m/z* calculated for $C_{13}H_{17}FNO$ ([M+H]$^+$), 222.1294; Found 222.1297.

3,3-bis(4-fluorophenethyl)-1-methylpyrrolidin-2-one (21b)



Prepared according to **General Procedure B** and isolated from the reaction above. Colorless oil (14.5 mg, 7%); IR ν_{max} (neat) 3001 - 2866 (C-H), 1672 (C=O), 1601 (Ar), 1508 (Ar), 1474, 1456, 1435, 1404, 1306, 1271, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (apt. t, *J* = 8.0 Hz, 4H), 6.96 (apt. t, *J* = 9.0 Hz, 4H), 3.34 (t, *J* = 7.5 Hz, 2H), 2.89 (s, 3H), 2.65 (td, *J* = 6.0, 3.0 Hz, 2H), 2.52 (td, *J* = 6.0, 3.0 Hz, 2H), 2.06 (t, *J* = 7.5 Hz, 2H), 1.90 - 1.78 (m, 4H); ^{19}F NMR (470 MHz, $CDCl_3$) δ -117.5 (sept, *J* = 4.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 161.2 (d, *J* = 242.0 Hz), 137.5 (d, *J* = 1.8 Hz), 129.6 (d, *J* = 8.4 Hz), 115.1 (d, *J* = 21.5 Hz), 47.5, 46.6, 39.3, 29.9, 29.8, 28.4; HRMS (ESI$^+$) *m/z* calculated for $C_{21}H_{24}F_2NO$ ([M+H]$^+$), 344.1826; Found 344.1823.

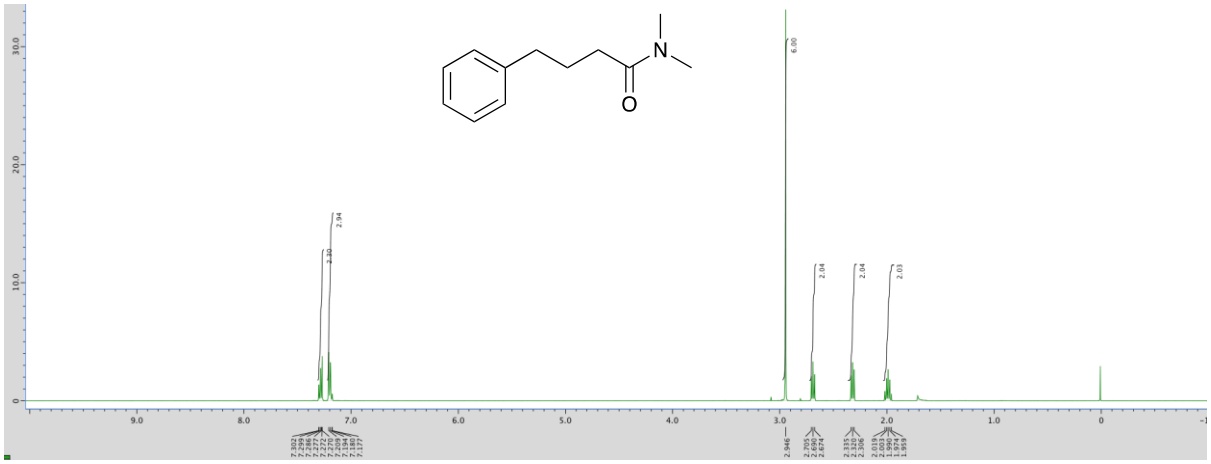
3-(4-fluorophenethyl)-1-methyl-3-phenethylpyrrolidin-2-one (23)

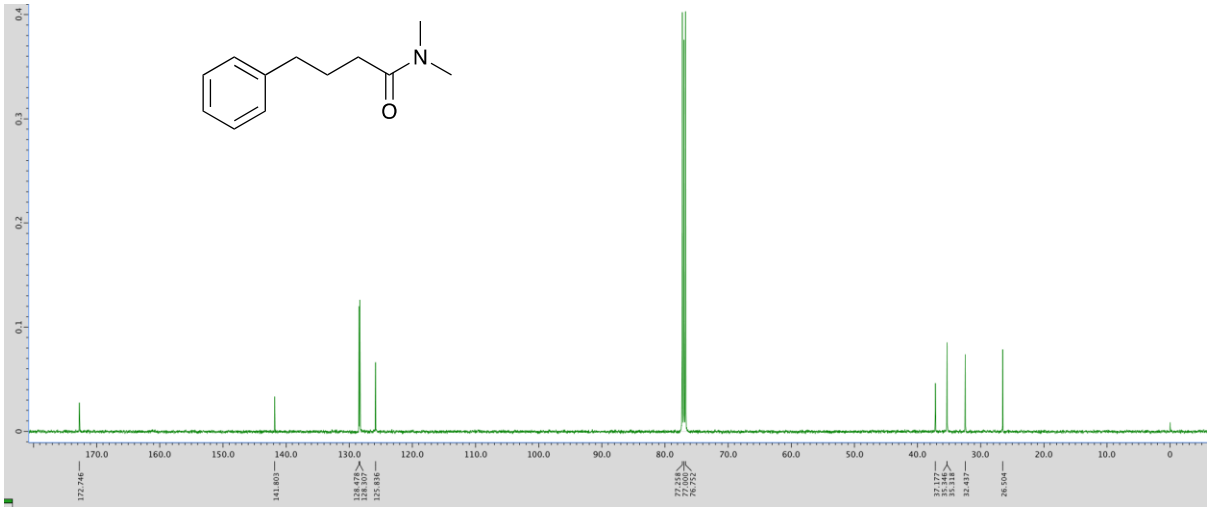


Prepared by treating compound **14a** (1.0 mmol) under **General Procedure C** using 4-fluorostyrene (0.5 mmol) and 18-crown-6 additive (1.5 eq.) but using only 2.0 eq. of amide **14a**. Yellow oil (105.8 mg, 65%); IR ν_{max} (neat) 2930 - 2864 (C-H), 1665 (C=O), 1603 (Ar), 1512 (Ar), 1474, 1454, 1437, 1404, 1302, 1271, 1225, 1215 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (apt. t, *J* = 7.8 Hz, 2H), 7.19 - 7.11 (m, 5H), 6.94 (apt. t, *J* = 8.8 Hz, 2H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.88 (s, 3H), 2.69 - 2.61 (m, 2H), 2.57 - 2.47 (m, 2H), 2.04 (td, *J* = 6.7, 1.9 Hz, 2H), 1.91 - 1.79 (m, 4H); ^{19}F NMR (470 MHz, $CDCl_3$) δ -155.8 (sept, *J* = 4.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 161.2 (d, *J* = 242.0 Hz), 141.9 (apt. s), 137.6 (d, *J* = 3.3 Hz), 129.7, 129.6, 128.3 (d, *J* = 8.4 Hz), 125.8, 115.0 (d, *J* = 20.9 Hz), 47.6, 46.6, 39.2, 39.1, 30.7, 29.9, 29.7, 28.4; HRMS (ESI$^+$) *m/z* calculated for $C_{21}H_{25}FNO$ ([M+H]$^+$), 326.1920; Found 326.1910.

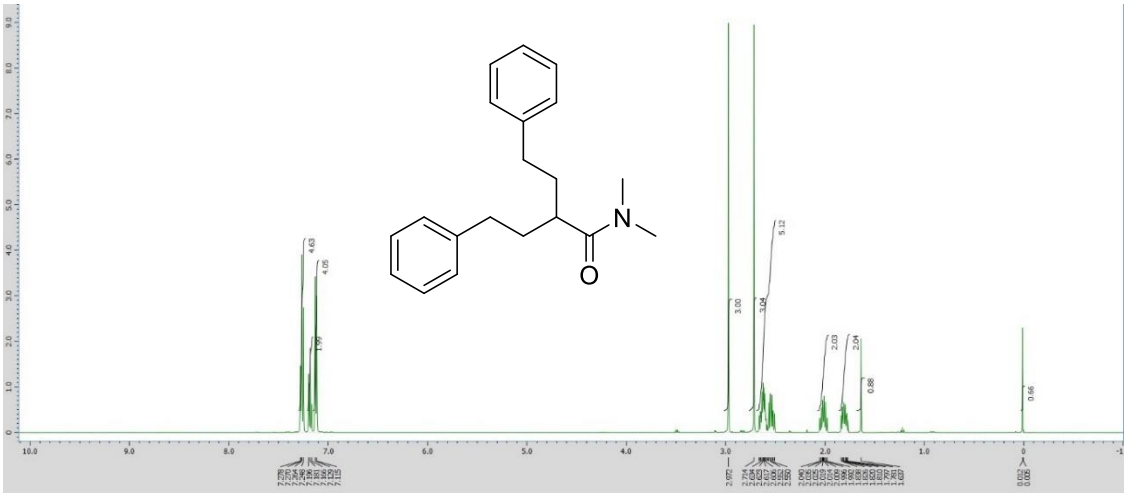
S11. NMR SPECTRA

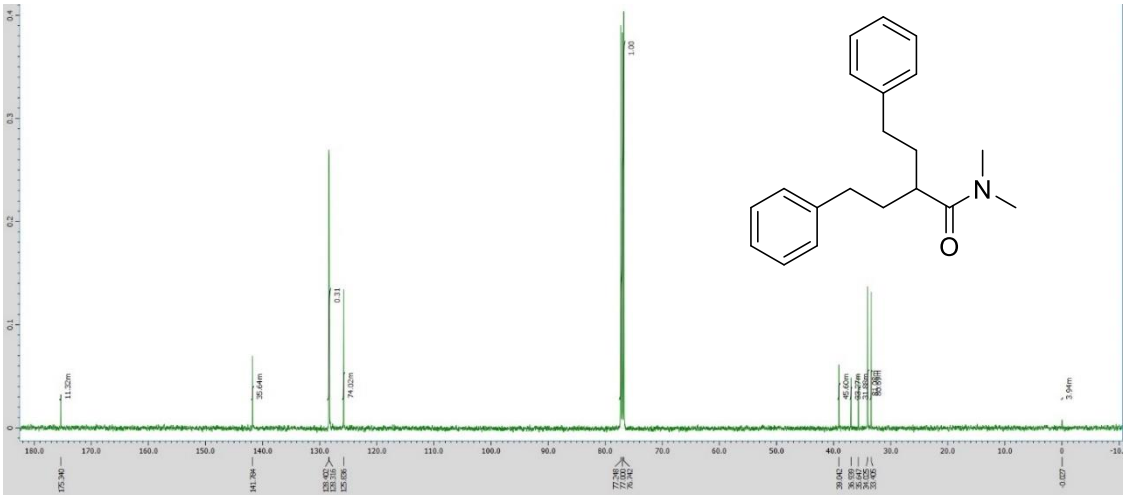
N,N-dimethyl-4-phenylbutanamide (4a)



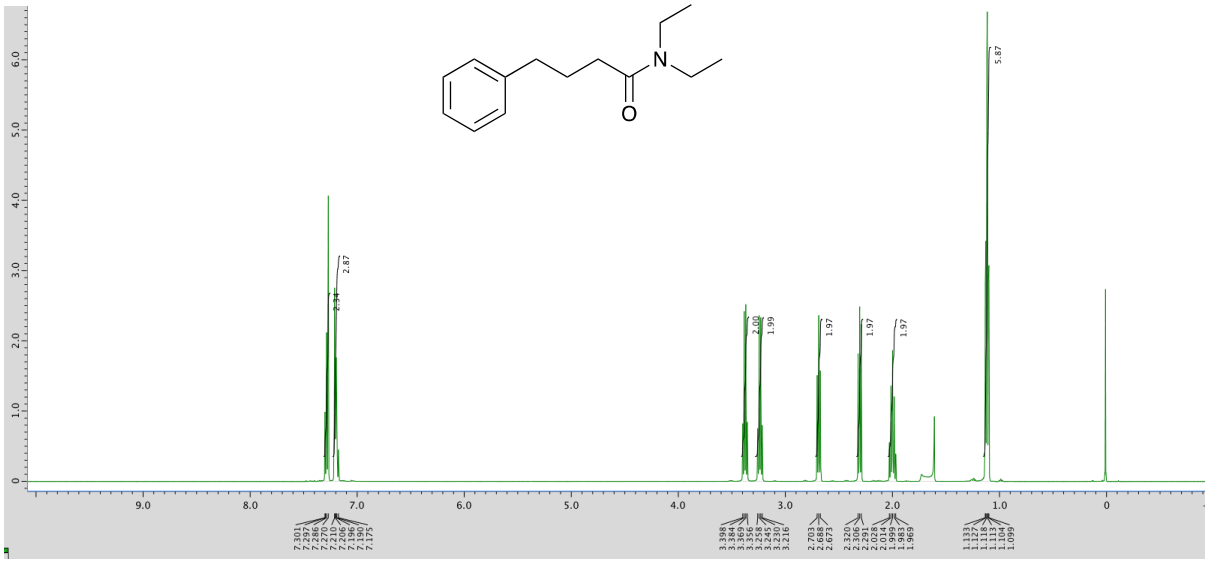


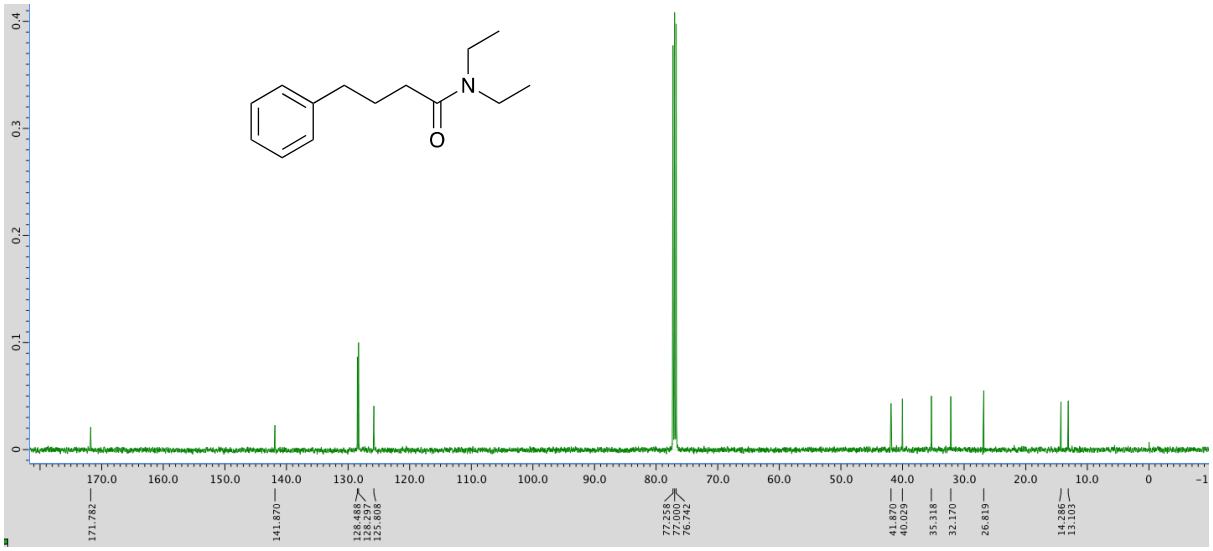
N,N-dimethyl-2-phenethyl-4-phenylbutanamide (4b)



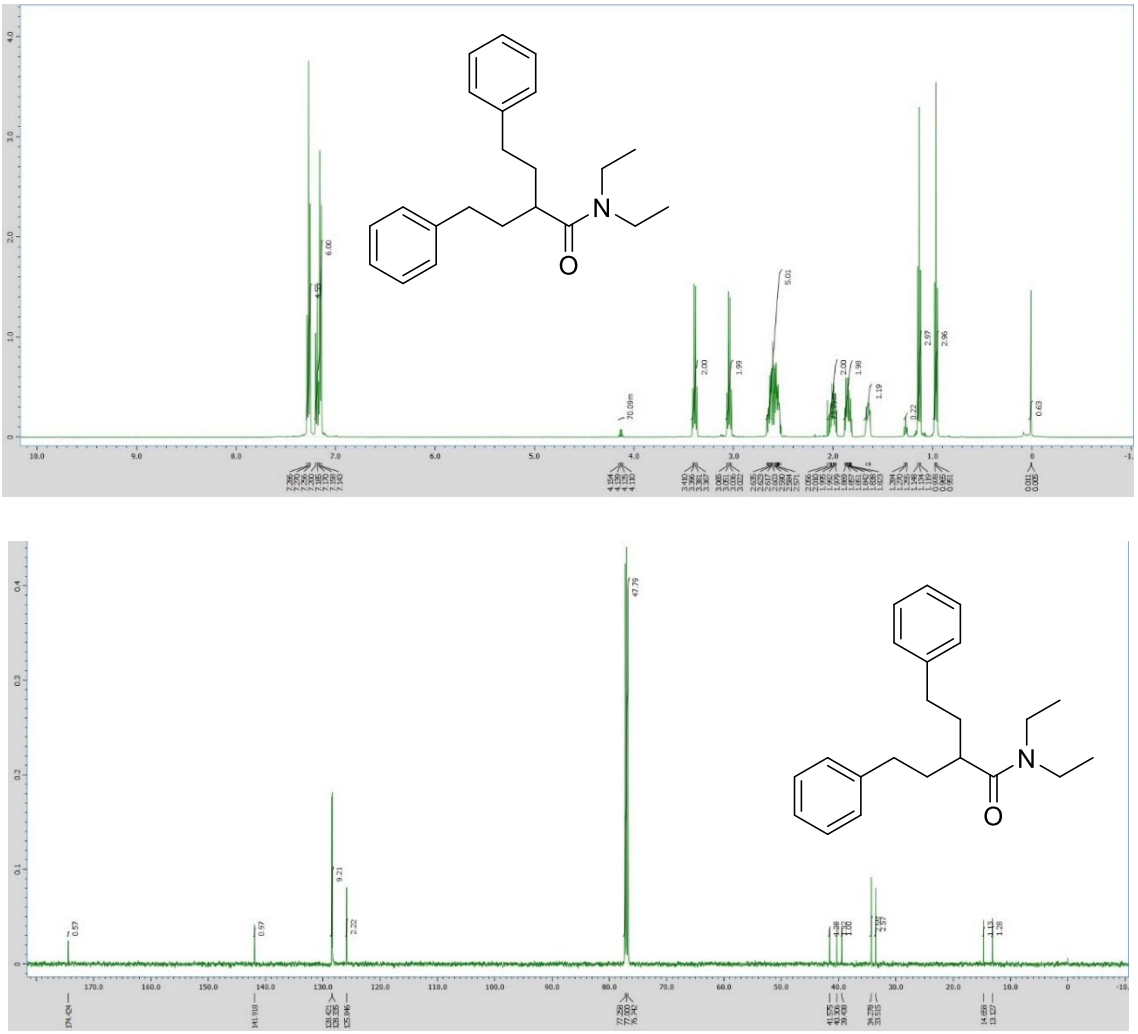


_N_,_N_-diethyl-4-phenylbutanamide (5a)

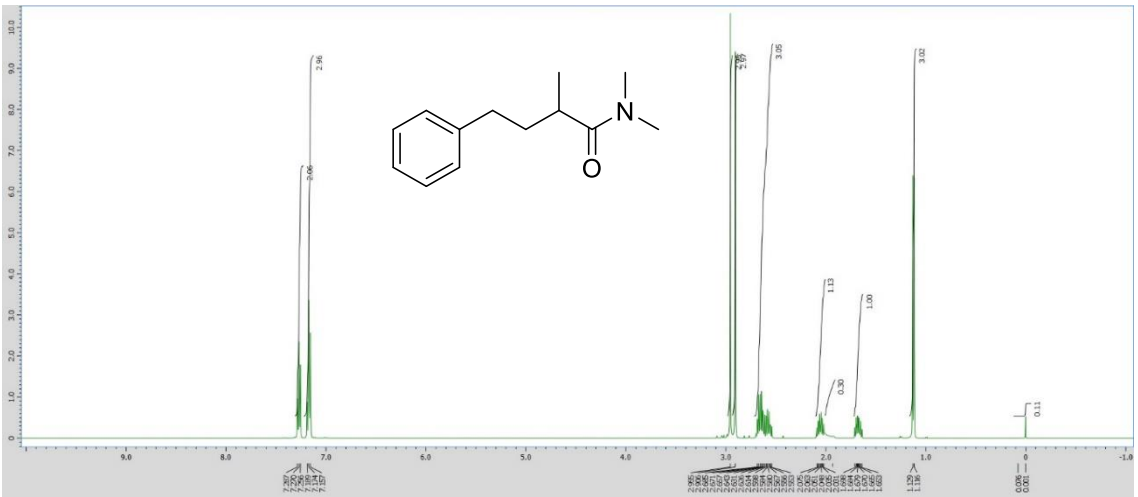


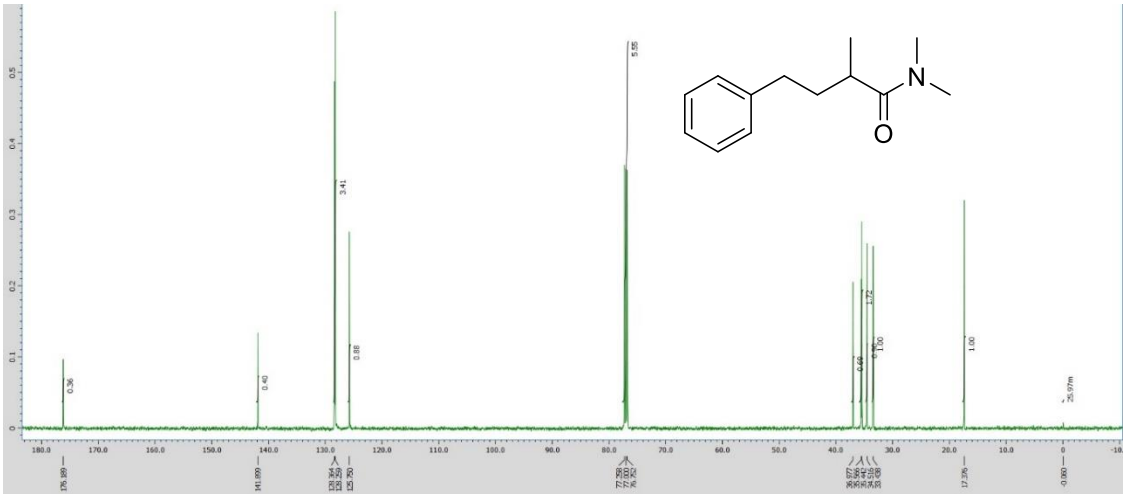


***N*,*N*-diethyl-2-phenethyl-4-phenylbutanamide (5b)**

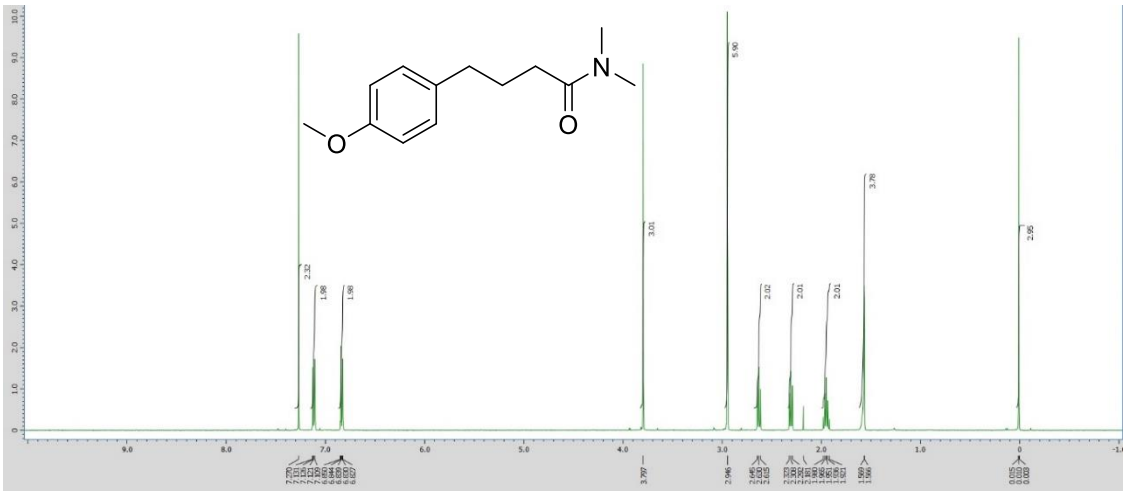


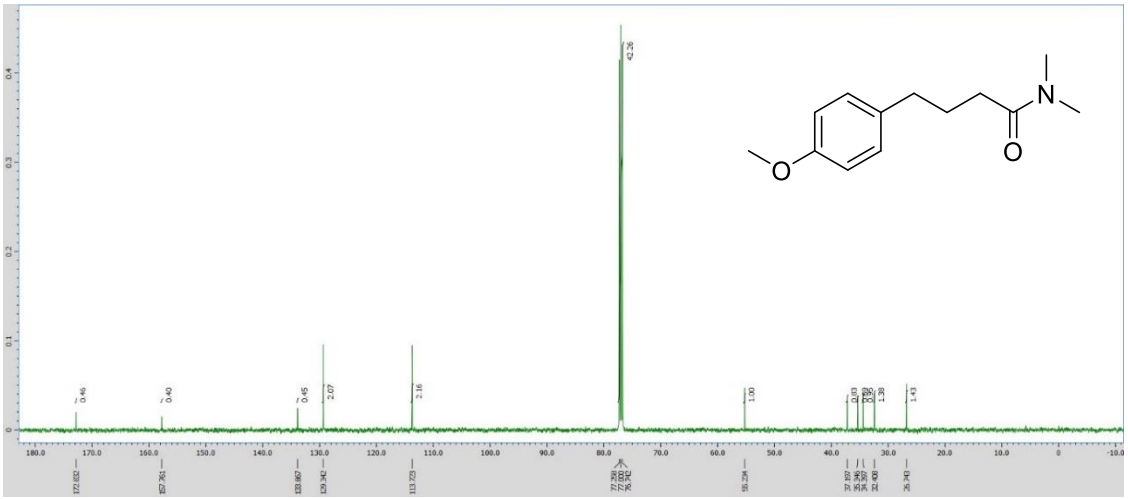
***N*,*N*-2-trimethyl-4-phenylbutanamide (6a)**



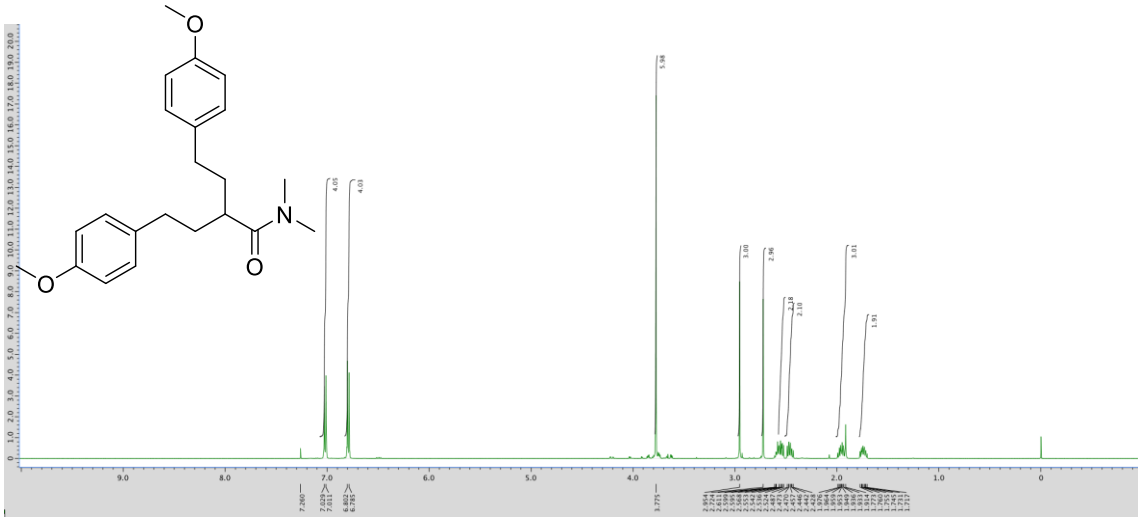


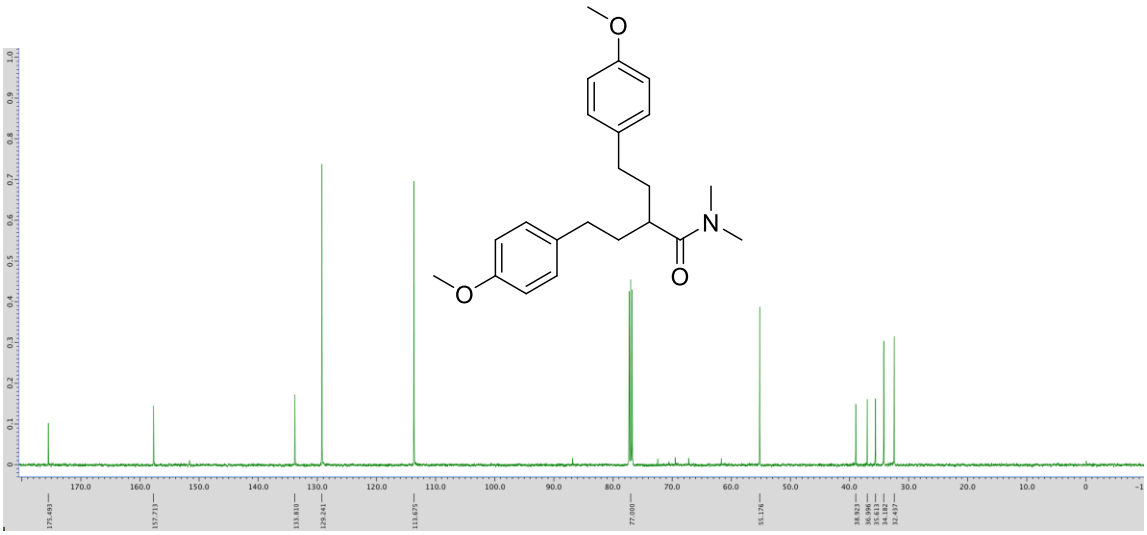
4-(4-methoxyphenyl)-*N*,*N*-dimethylbutanamide (7a)



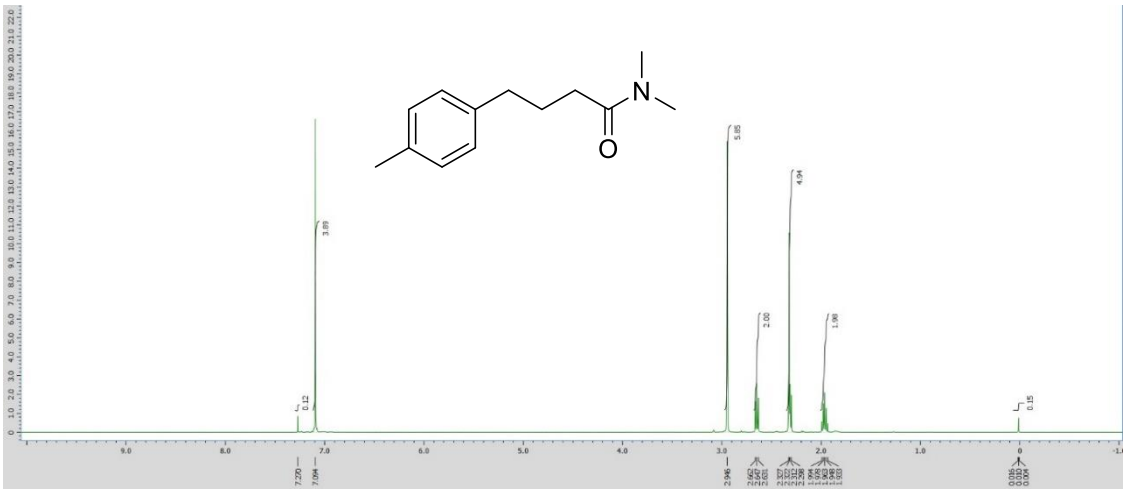


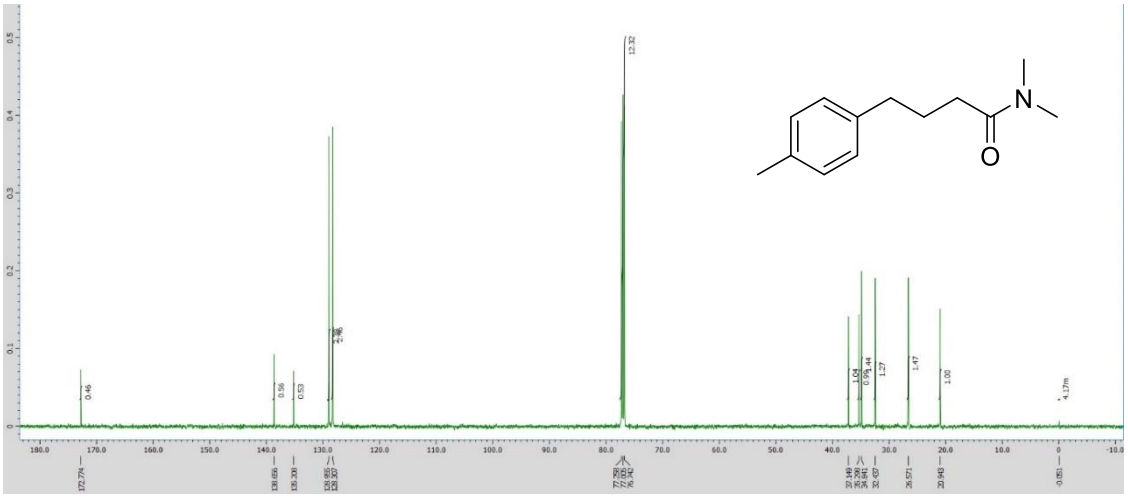
3-(4-methoxyphenethyl)-1-methylpyrrolidin-2-one (7b)



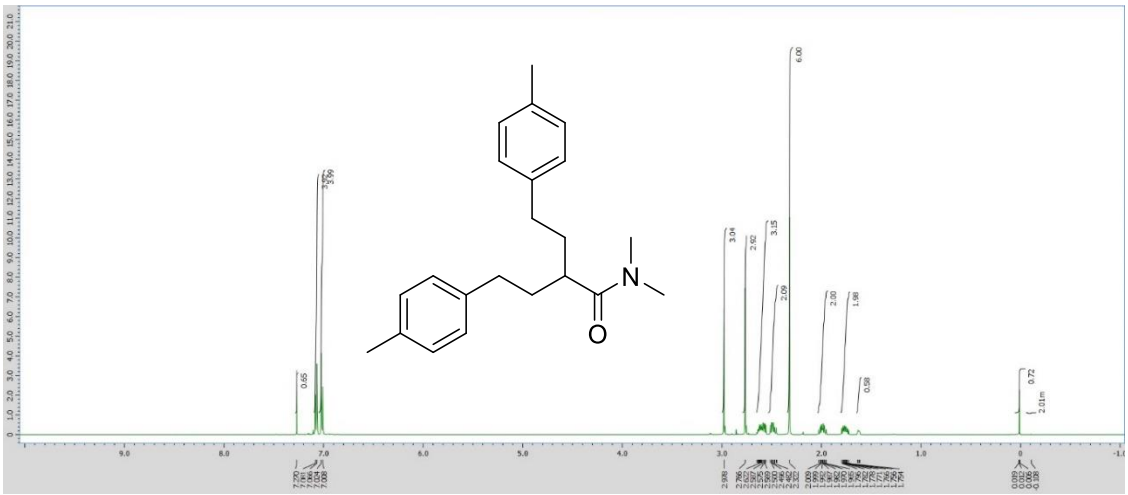


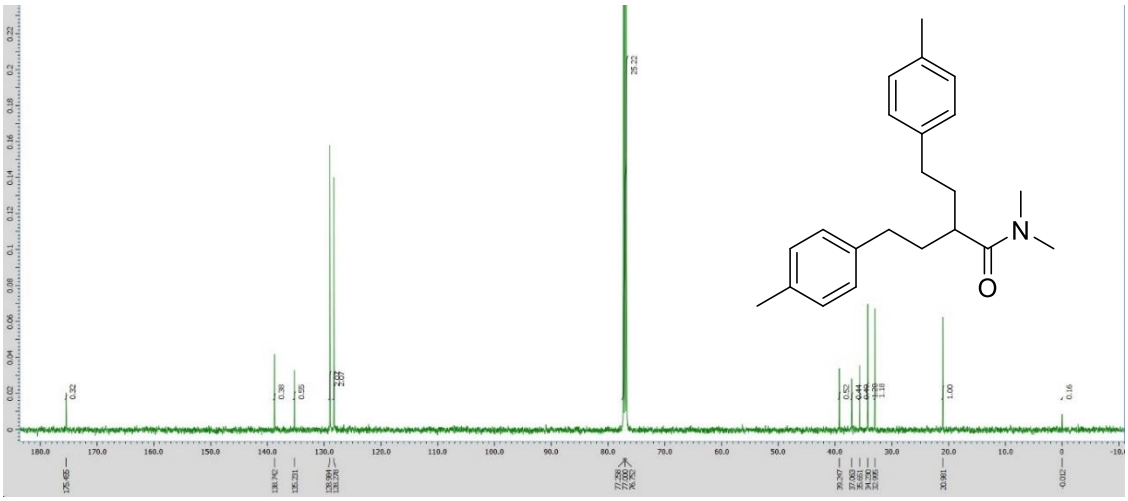
***N*,*N*-dimethyl-4-(*p*-tolyl)butanamide (8a)**



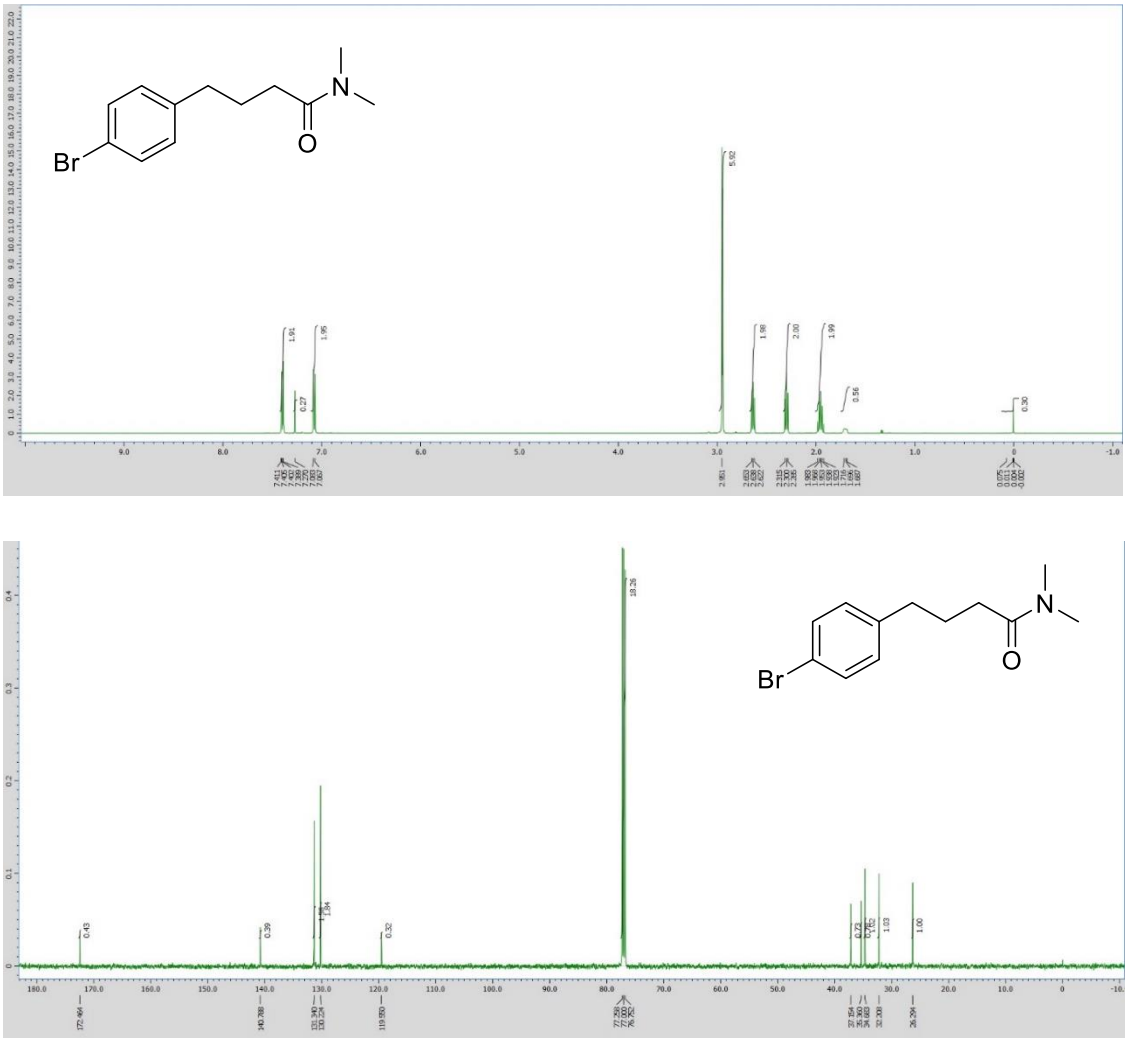


***N*,*N*-dimethyl-2-(4-methylphenethyl)-4-(*p*-tolyl)butanamide (8b)**

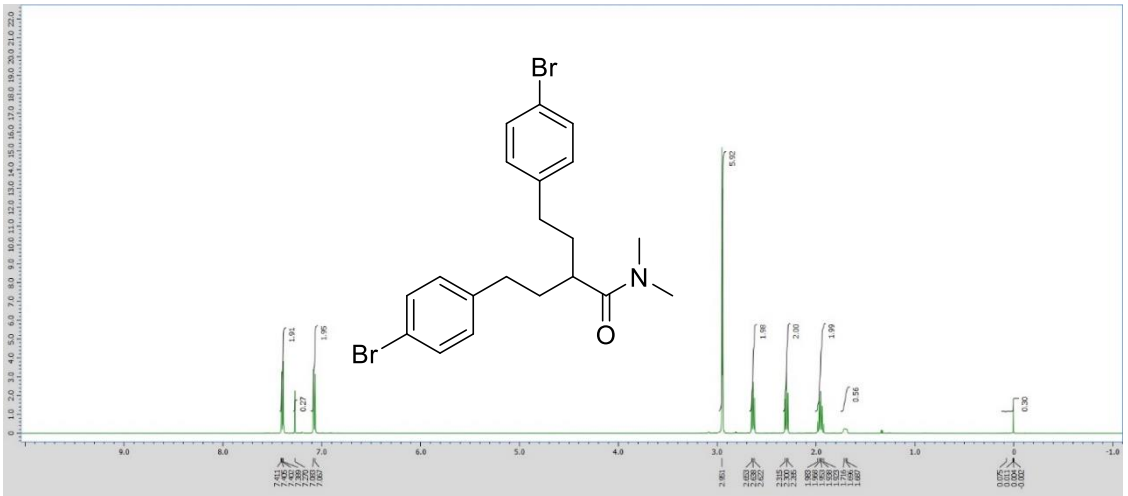


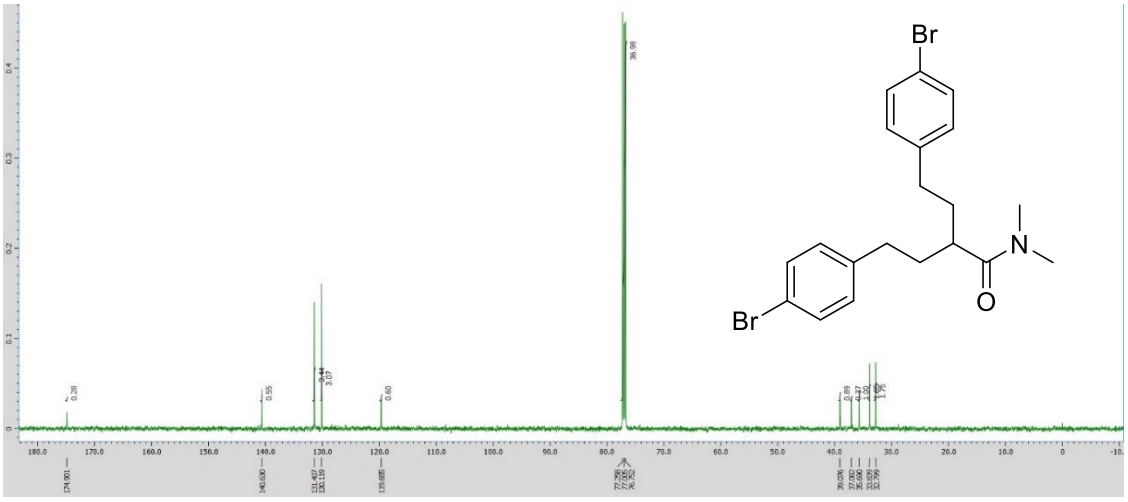


4-(4-bromophenyl)-*N*,*N*-dimethylbutanamide (9a)

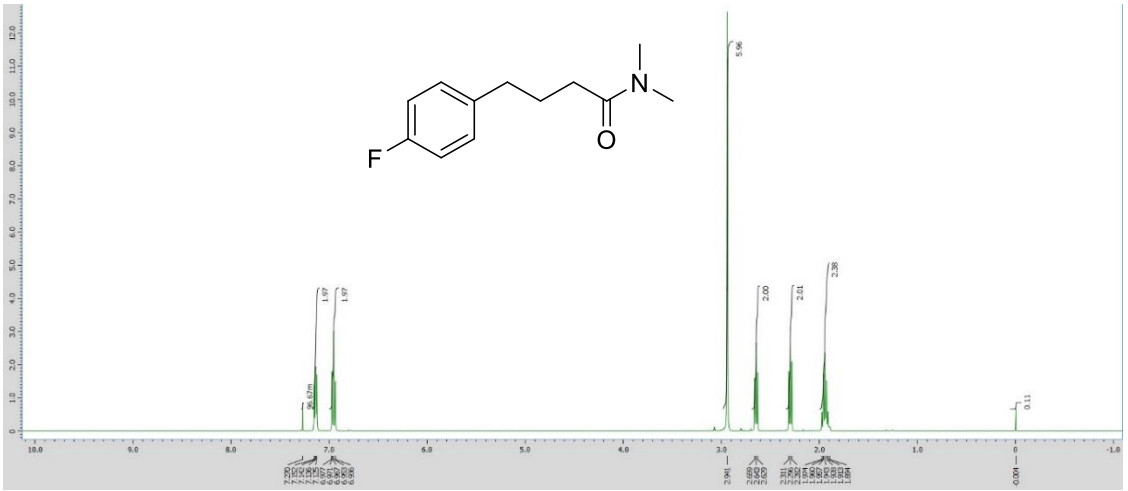


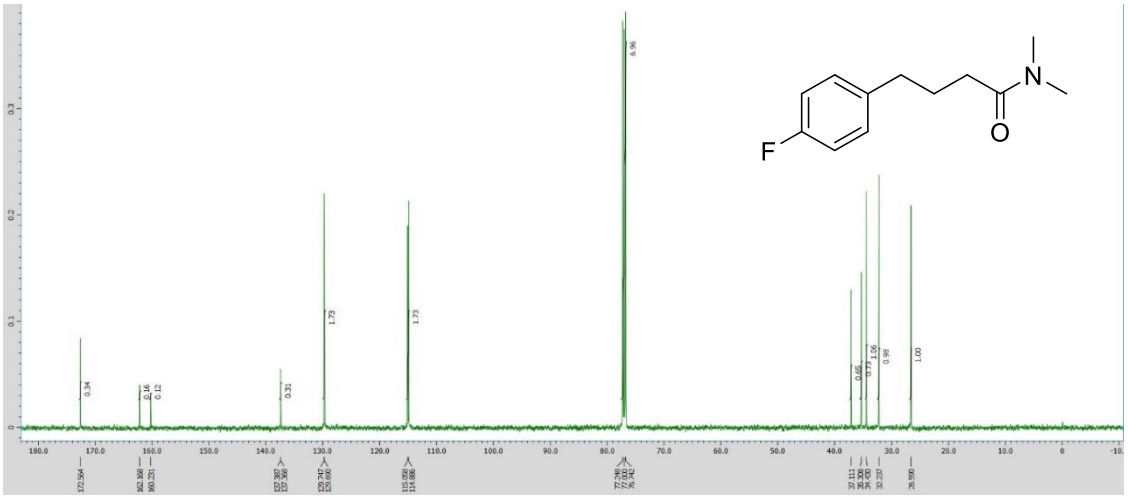
2-(4-bromophenethyl)-4-(4-bromophenyl)-*N*,*N*-dimethylbutanamide (9b)



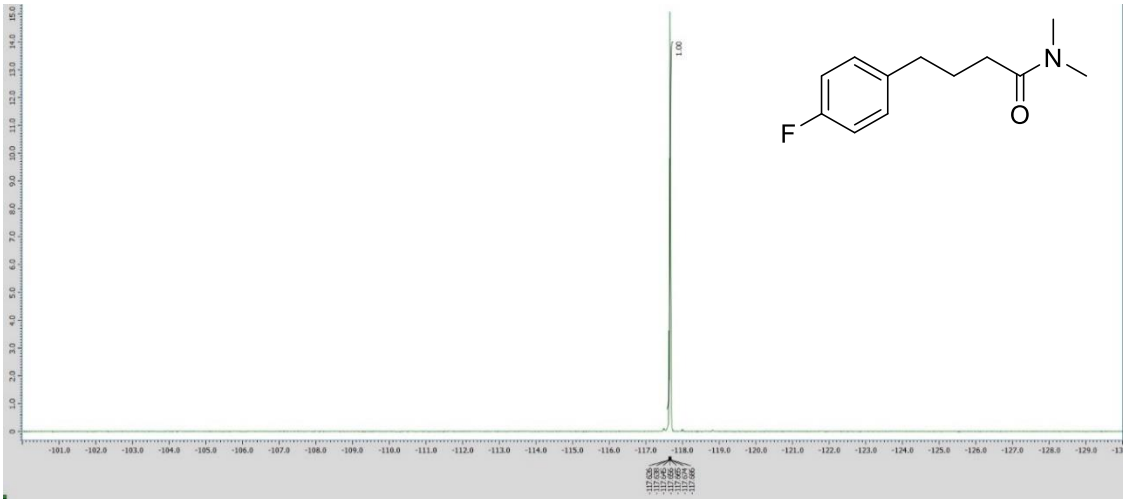


4-(4-fluorophenyl)-*N*,*N*-dimethylbutanamide (10a)

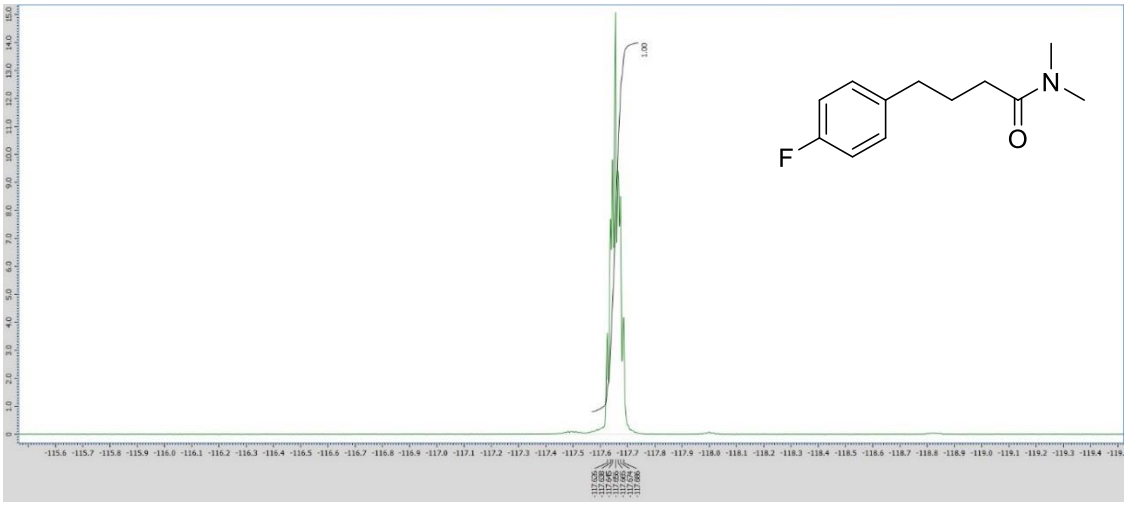




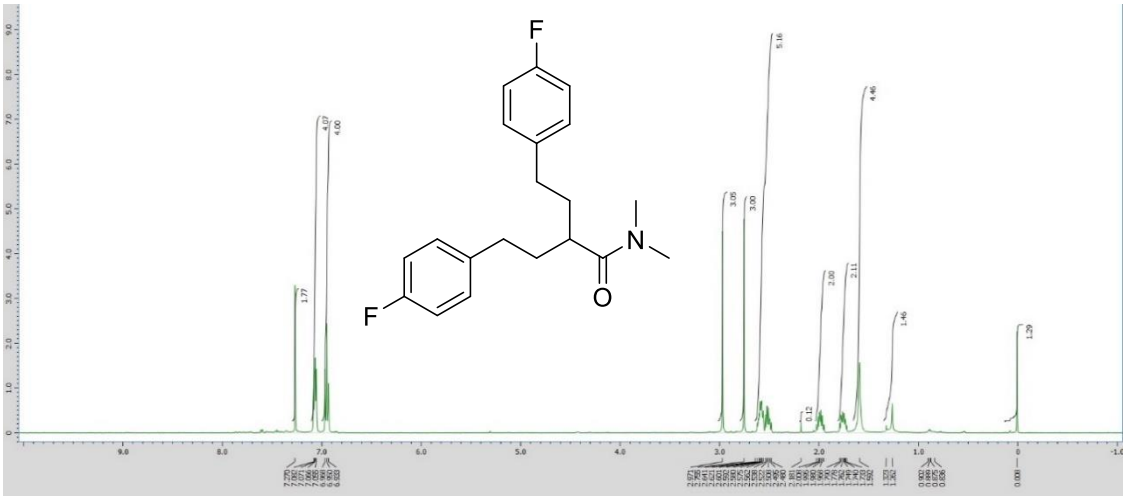
^{19}F NMR

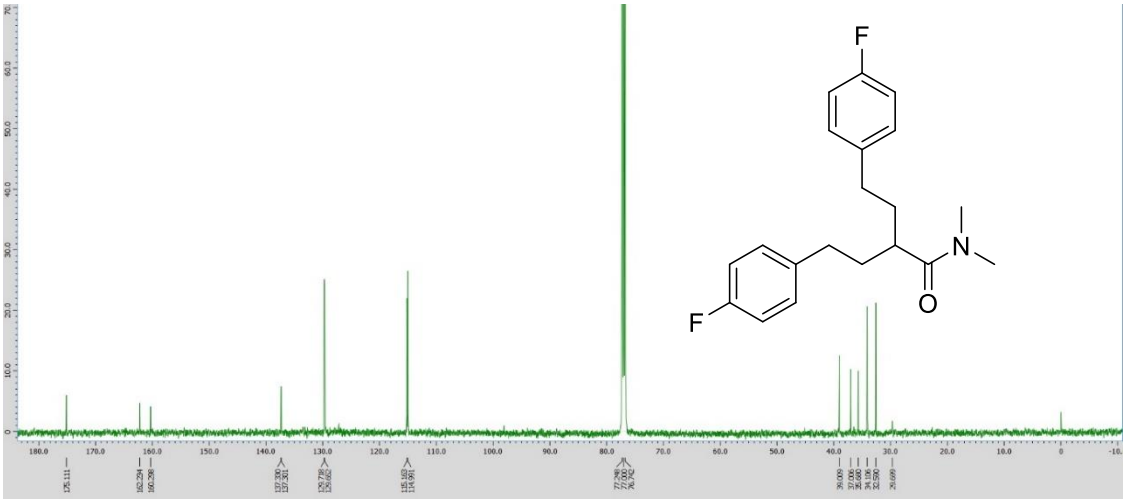


^{19}F NMR (expansion)

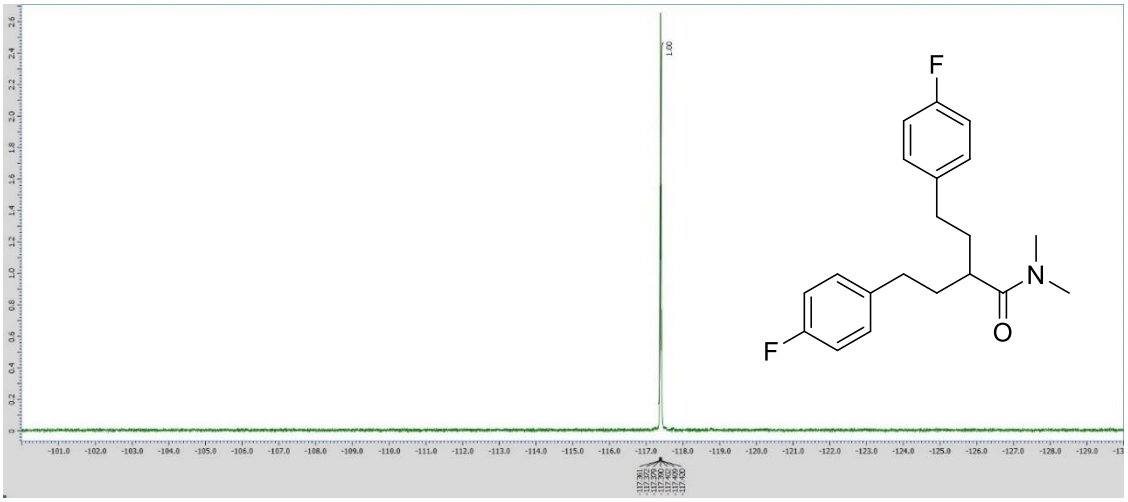


2-(4-fluorophenethyl)-4-(4-fluorophenyl)-*N*,*N*-dimethylbutanamide (10b)

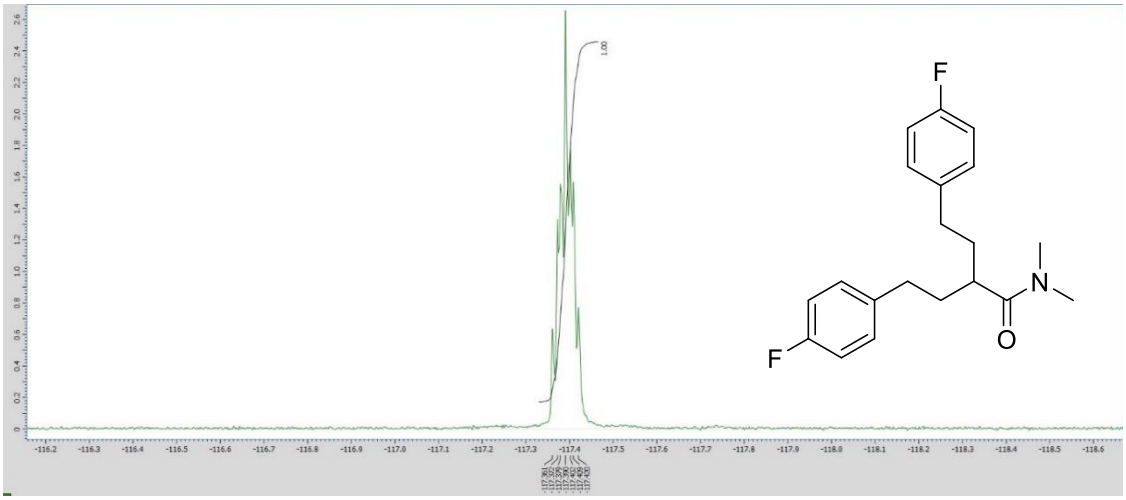




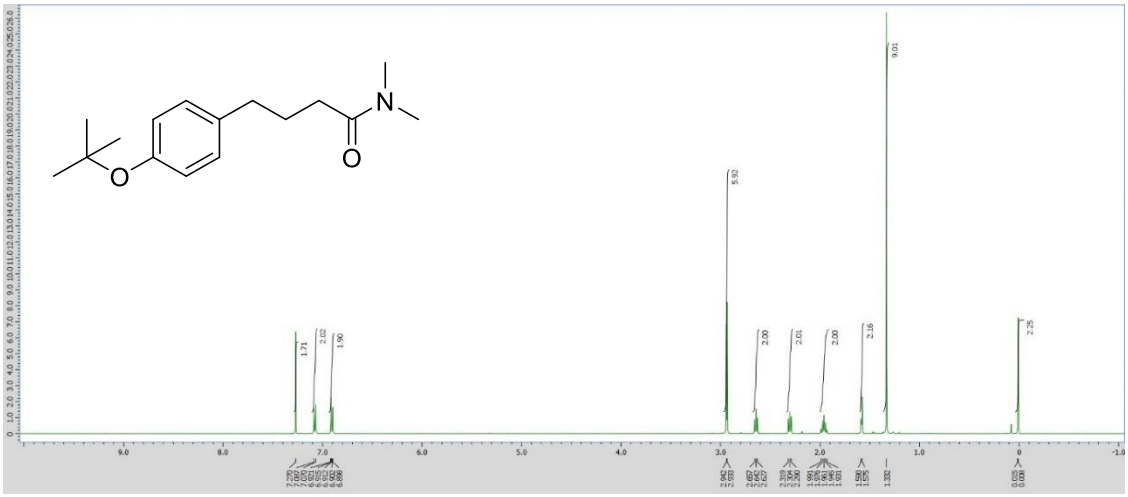
^{19}F NMR

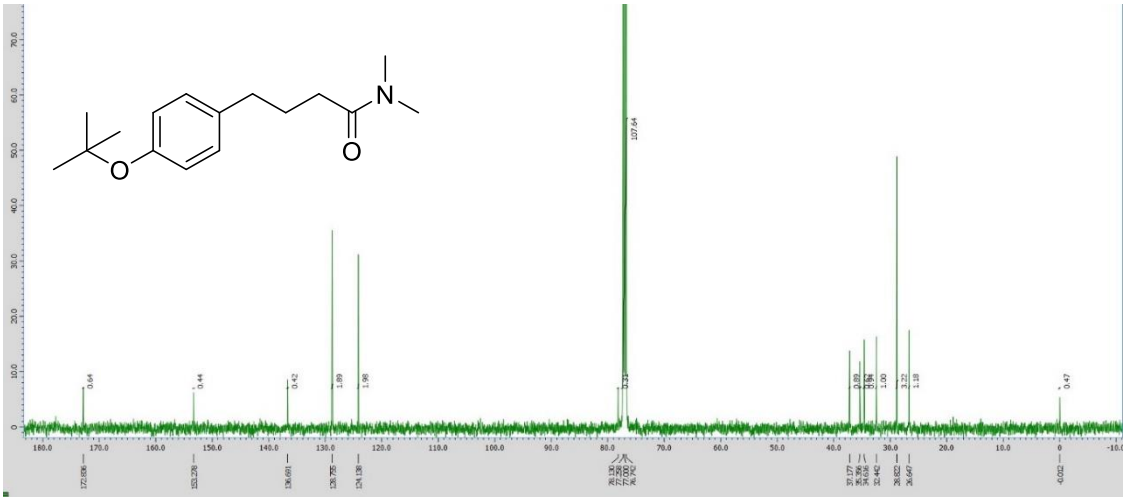


^{19}F NMR (expansion)

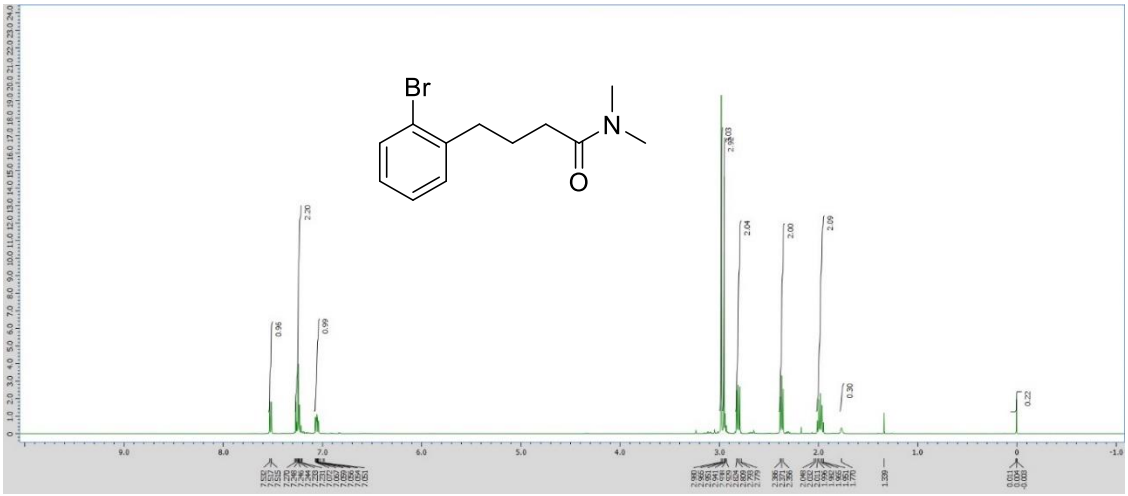


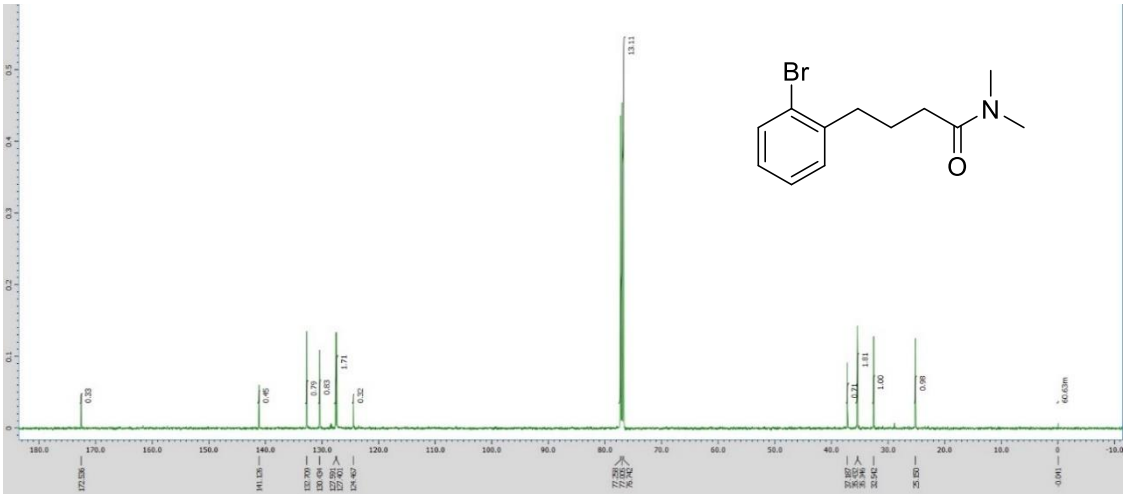
4-(4-(*tert*-butoxy)phenyl)-*N*,*N*-dimethylbutanamide (S3)



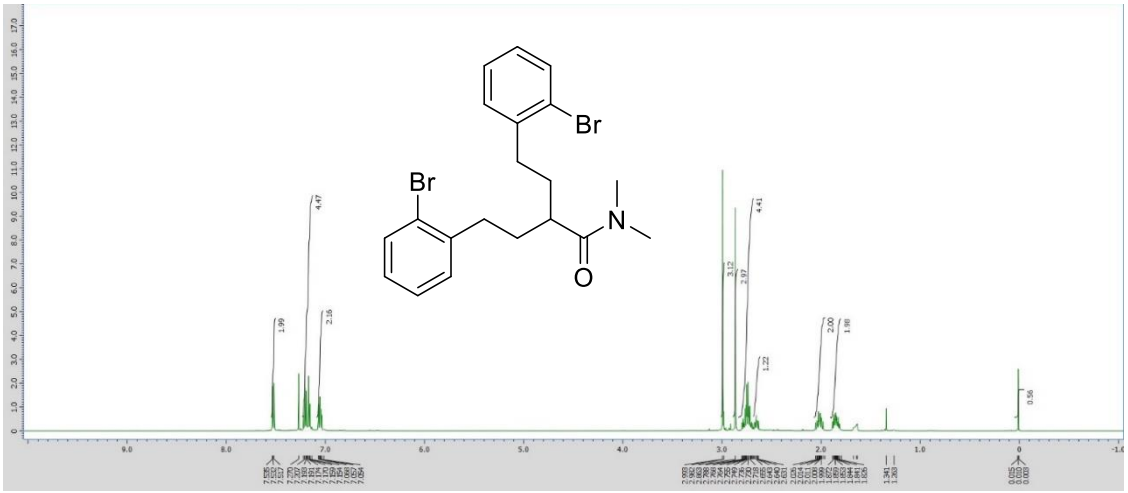


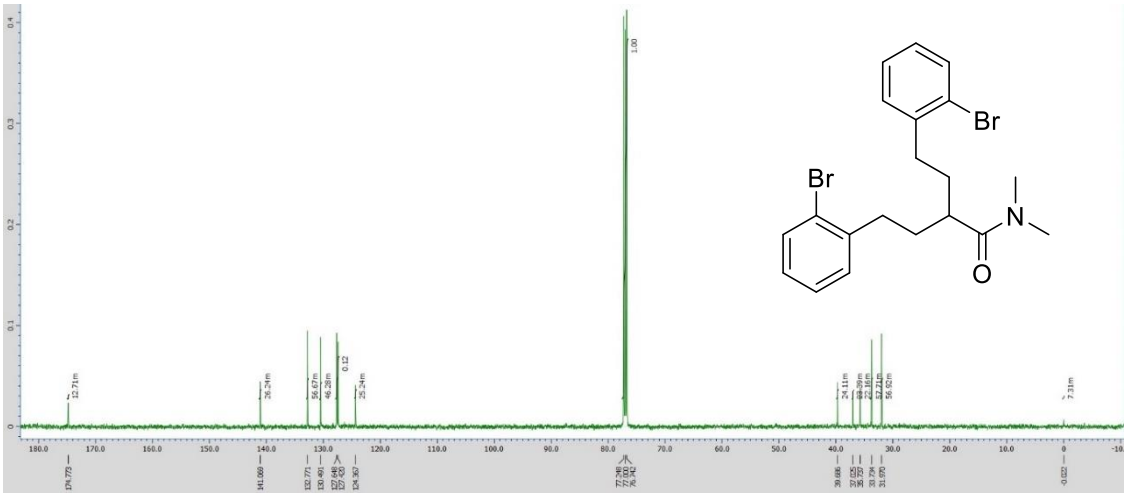
4-(2-bromophenyl)-*N*,*N*-dimethylbutanamide (11a)



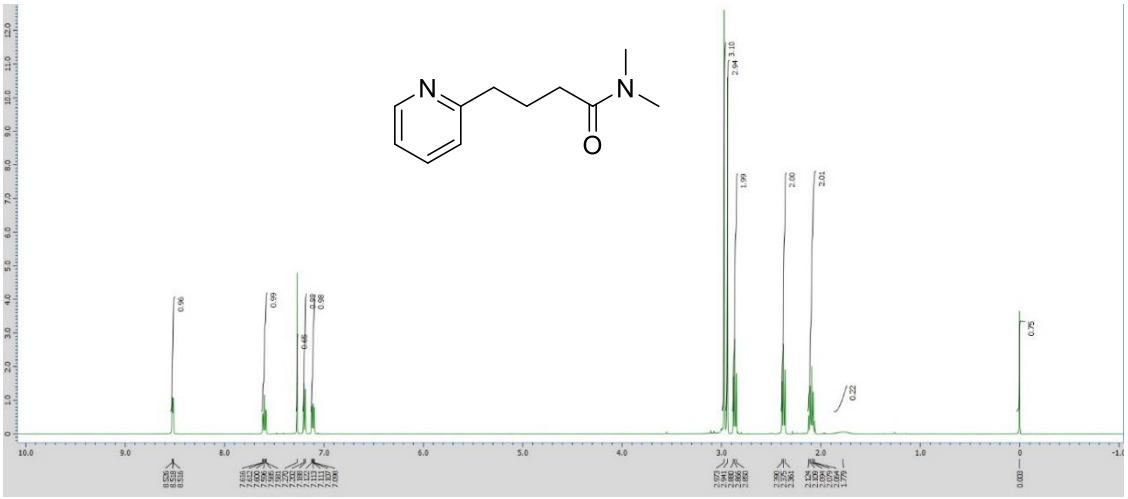


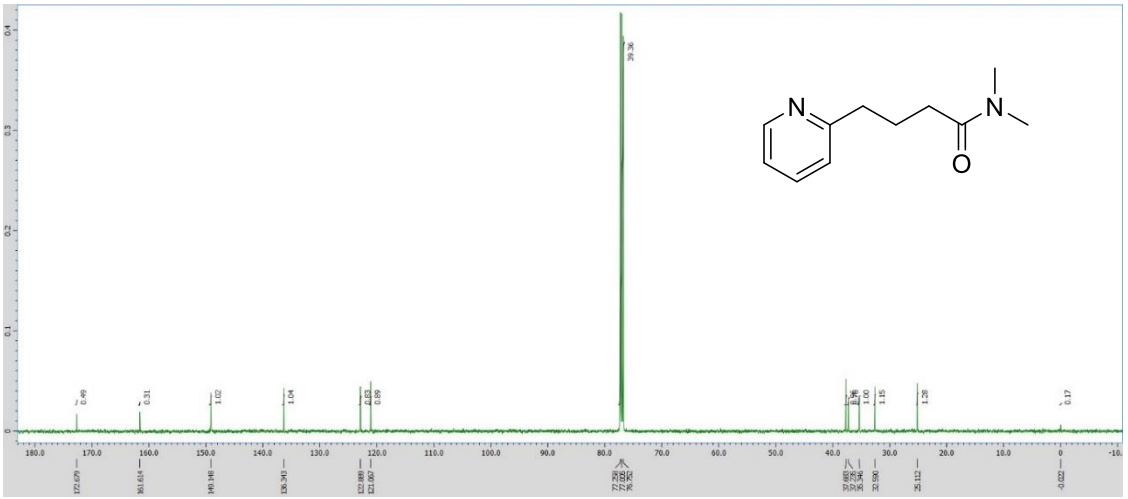
2-(2-bromophenethyl)-4-(2-bromophenyl)-*N*,*N*-dimethylbutanamide (11b)



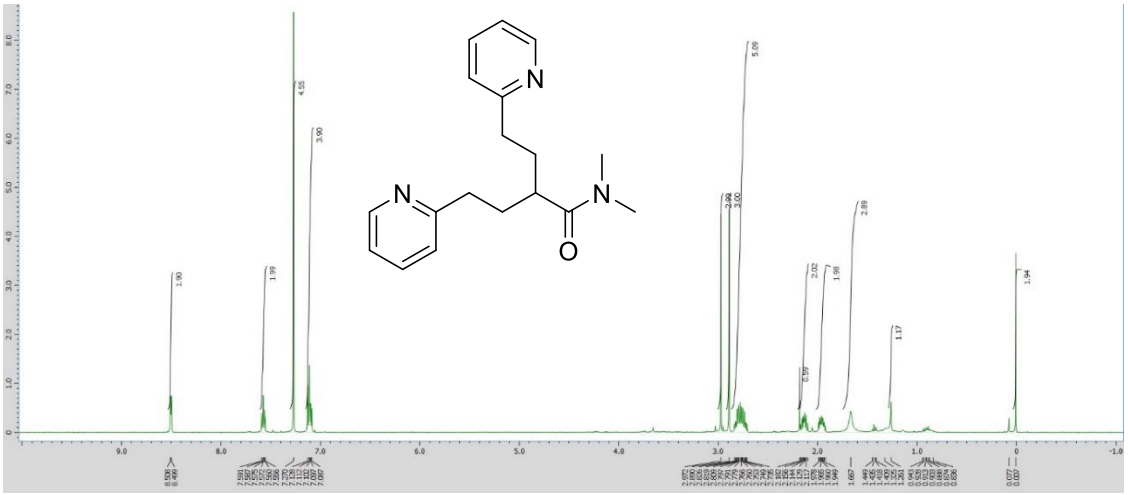


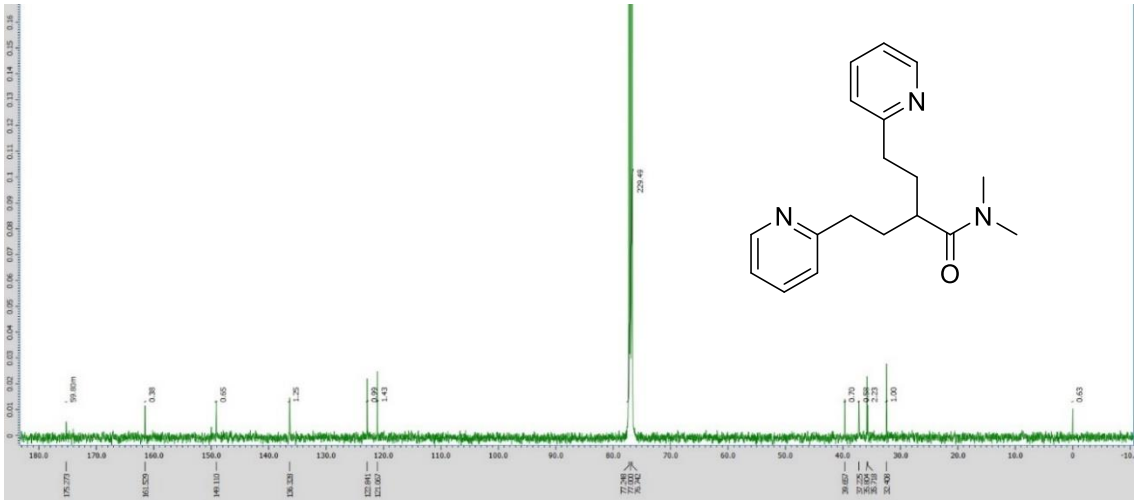
***N,N*-dimethyl-4-(pyridin-2-yl)butanamide (12a)**



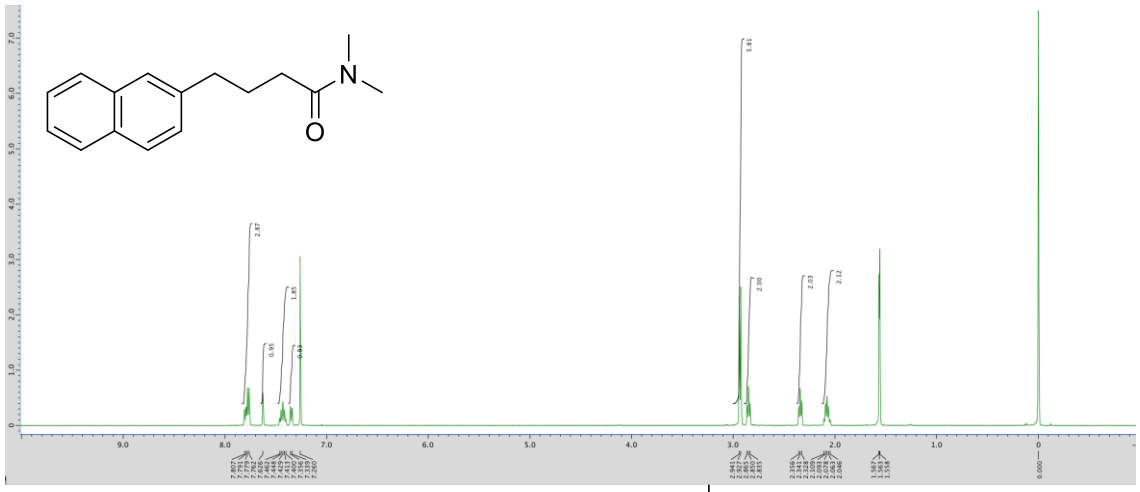


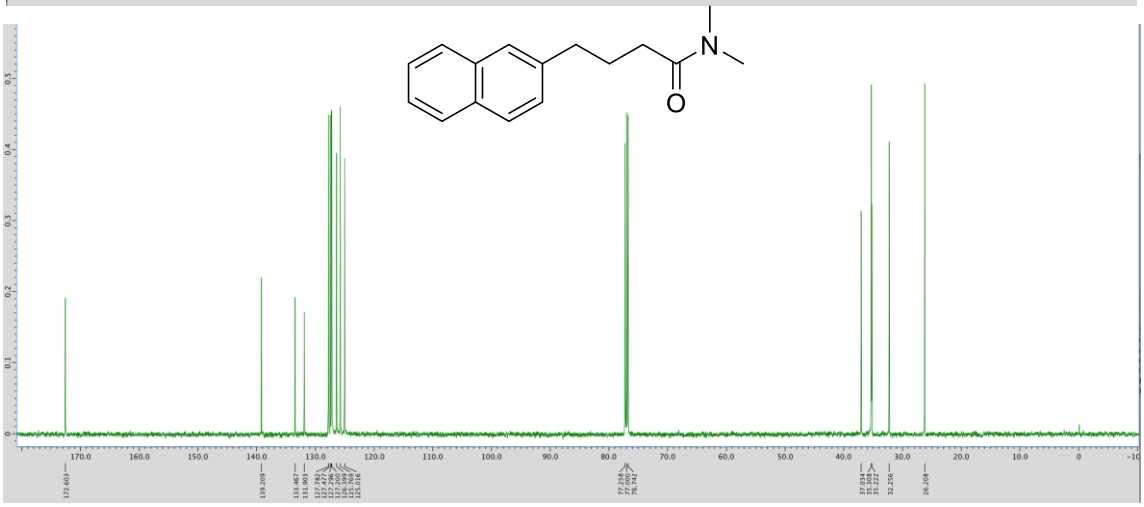
***N,N*-dimethyl-4-(pyridin-2-yl)-2-(2-(pyridin-2-yl)ethyl)butanamide (12b)**



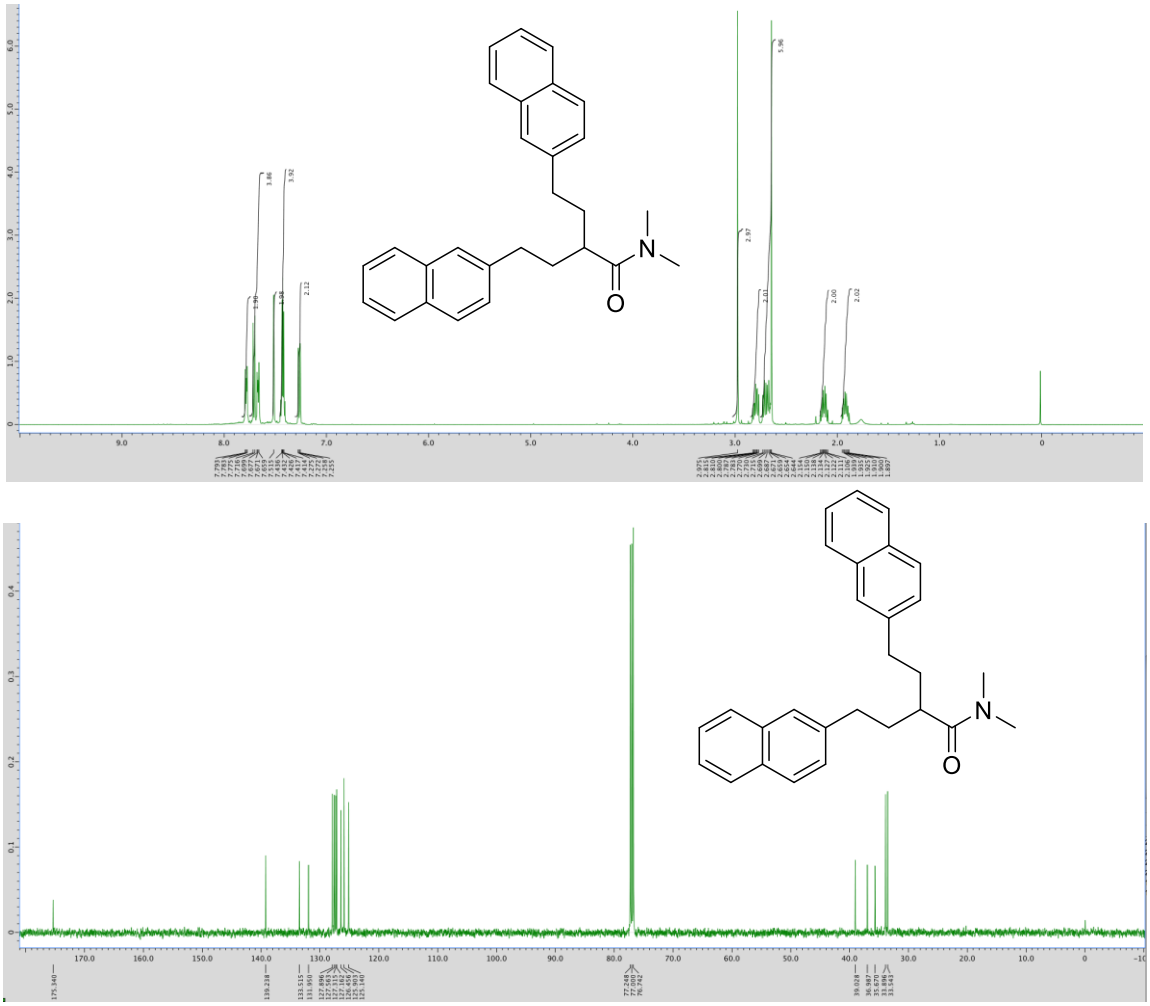


***N*,*N*-dimethyl-4-(naphthalen-2-yl)butanamide (13a)**

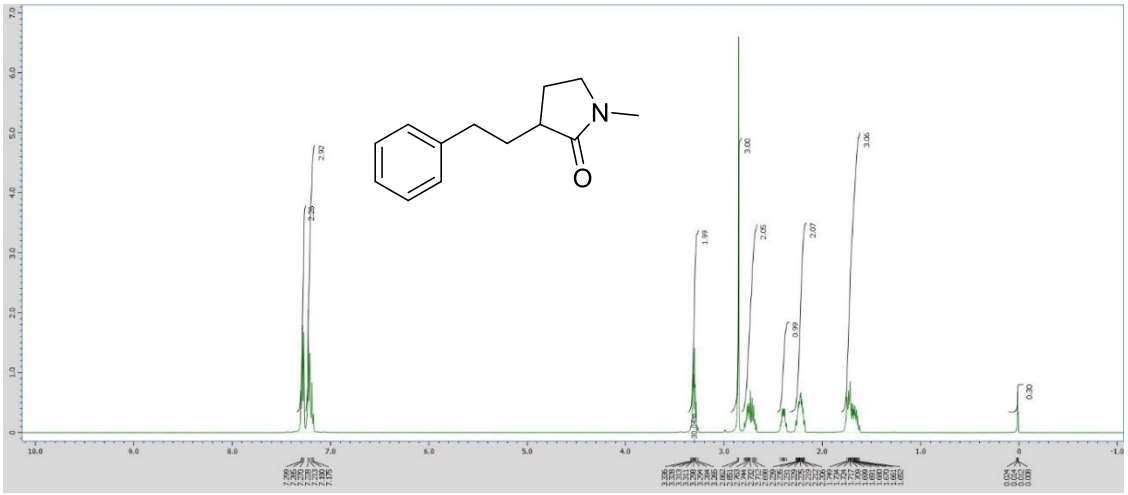


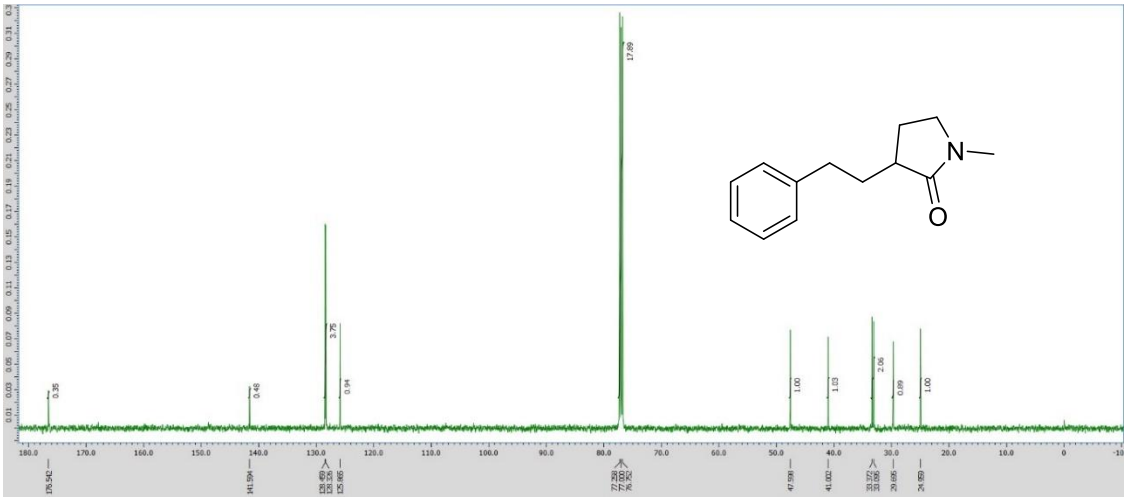


3-(4-fluorophenethyl)-1-methyl-3-phenethylpyrrolidin-2-one (13b)

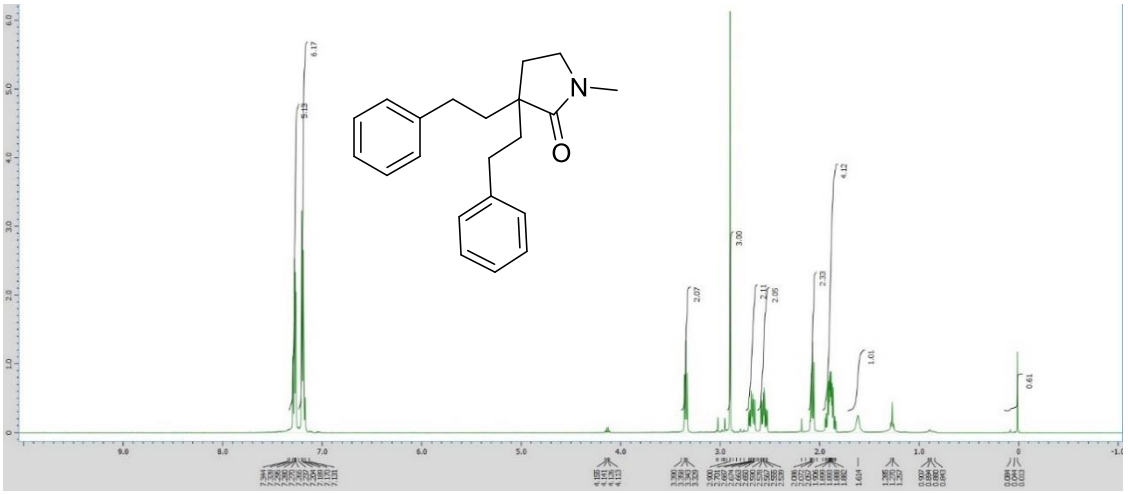


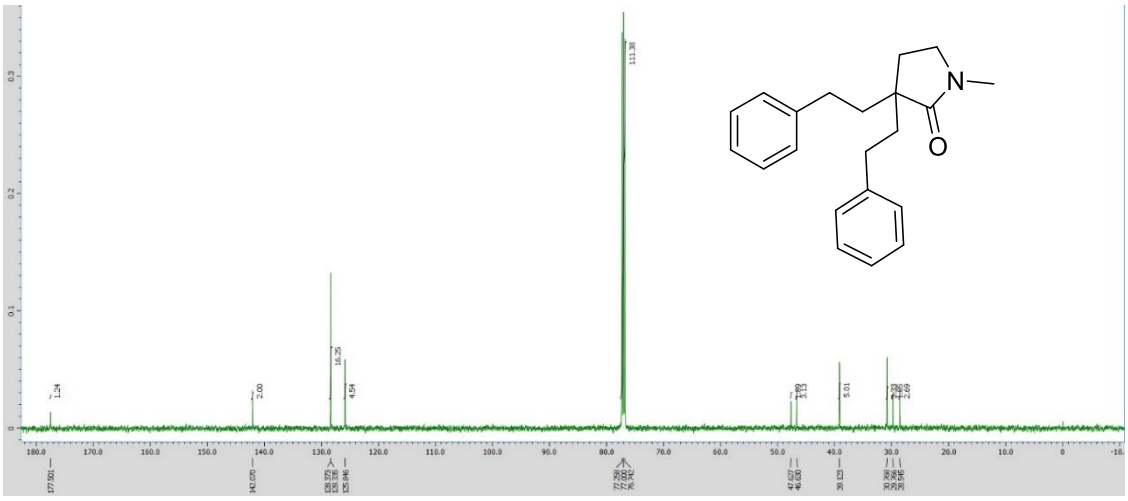
***N*-methyl-3-phenethylpyrrolidin-2-one (14a)**



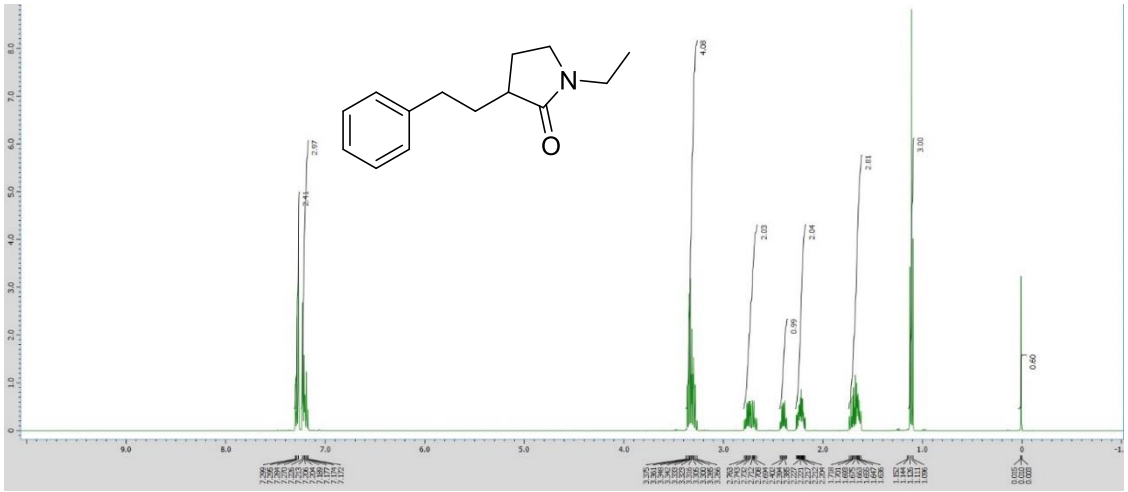


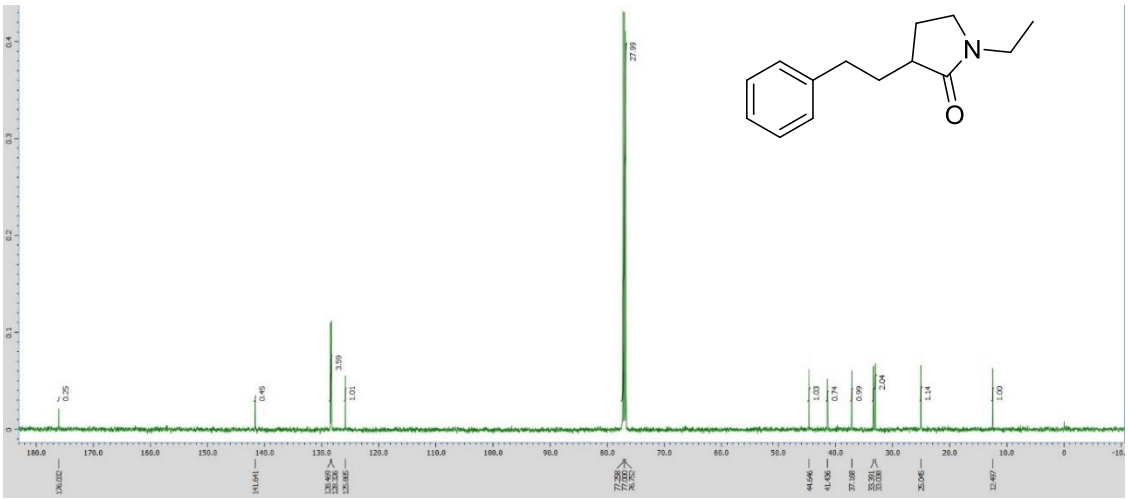
***N*-methyl-3,3-diphenethylpyrrolidin-2-one (14b)**



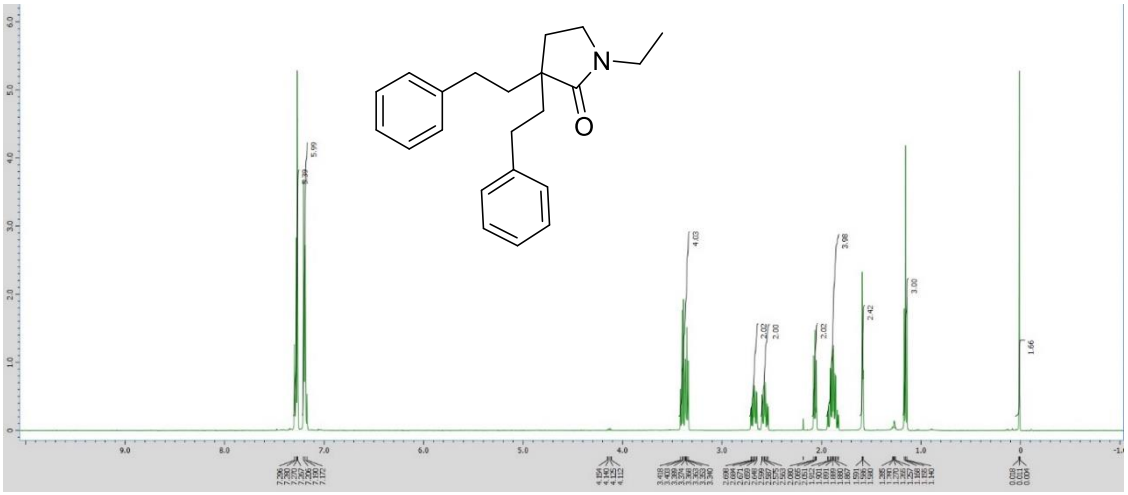


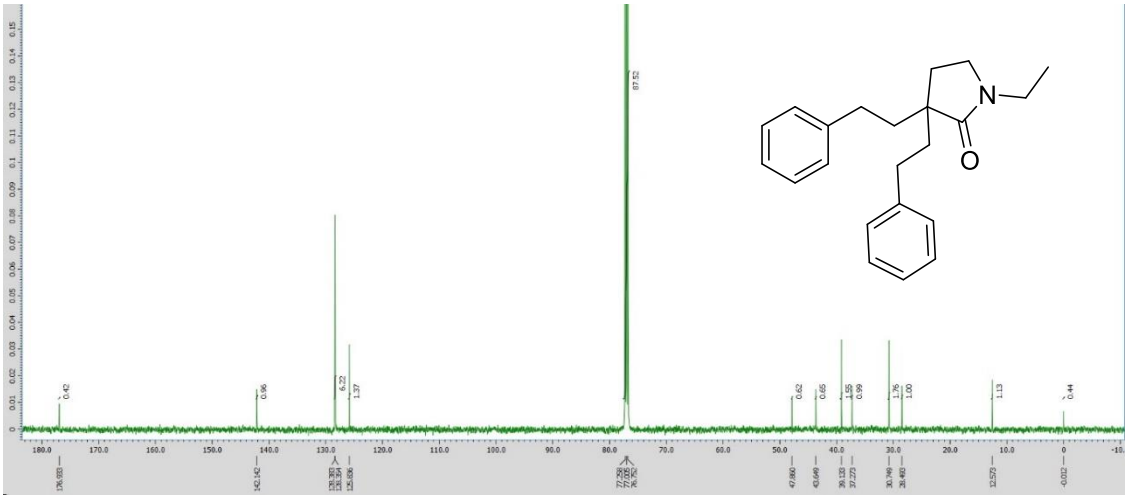
***N*-ethyl-3-phenethylpyrrolidin-2-one (15a)**



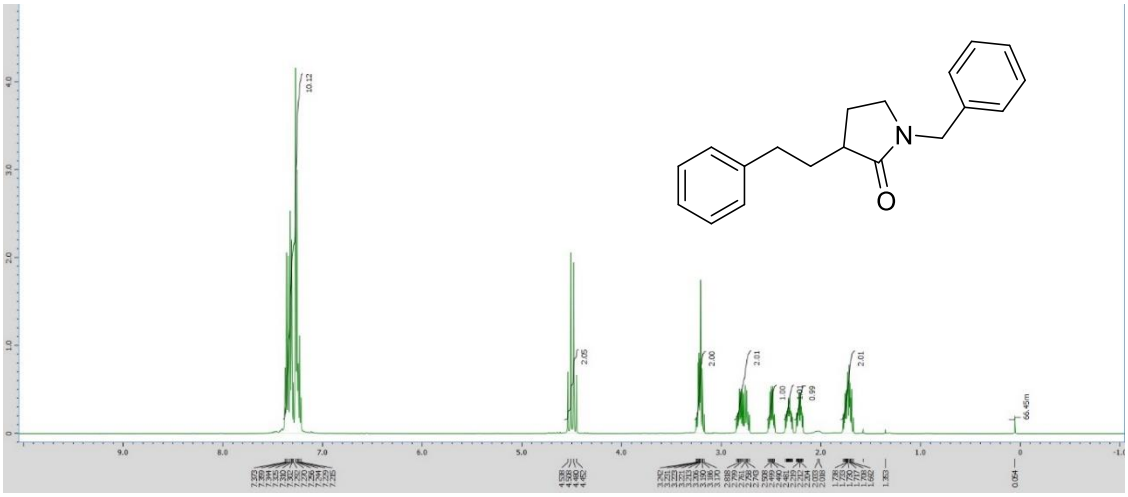


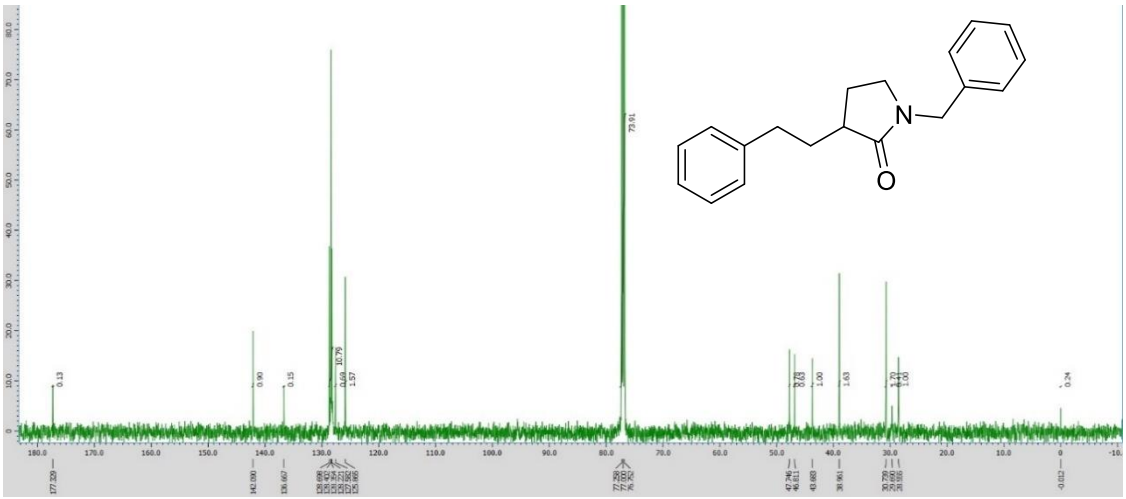
***N*-ethyl-3,3-diphenethylpyrrolidin-2-one (15b)**



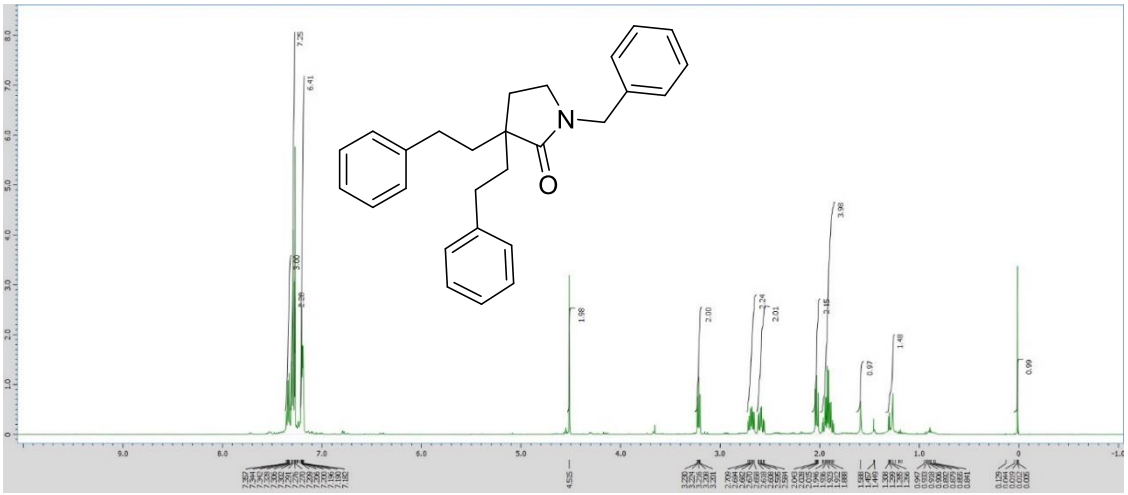


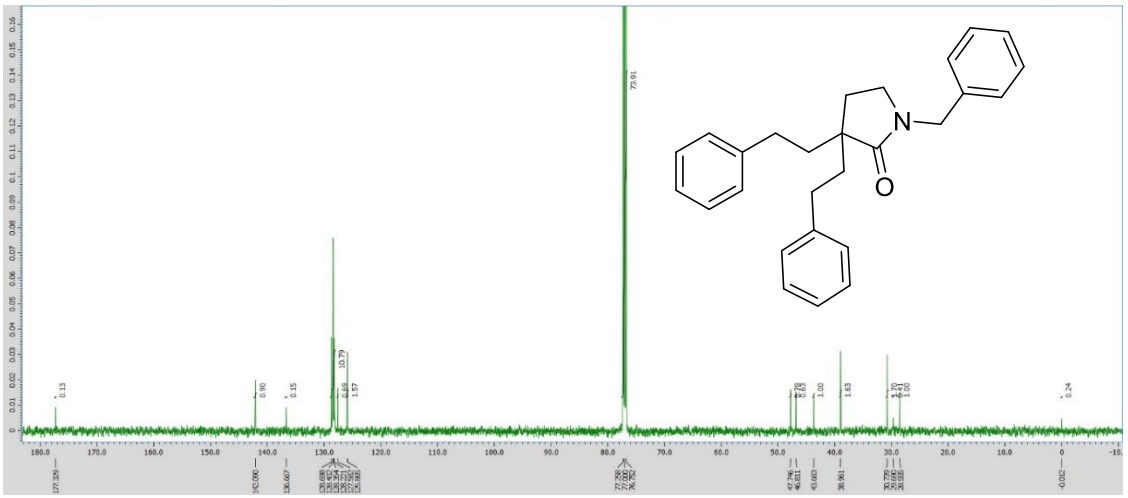
***N*-benzyl-3-phenethylpyrrolidin-2-one (16a)**



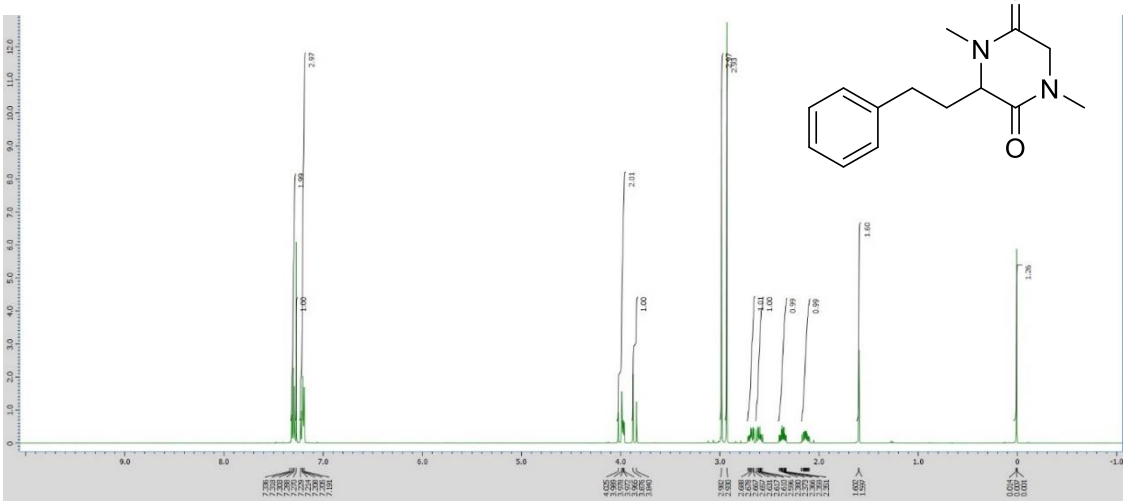


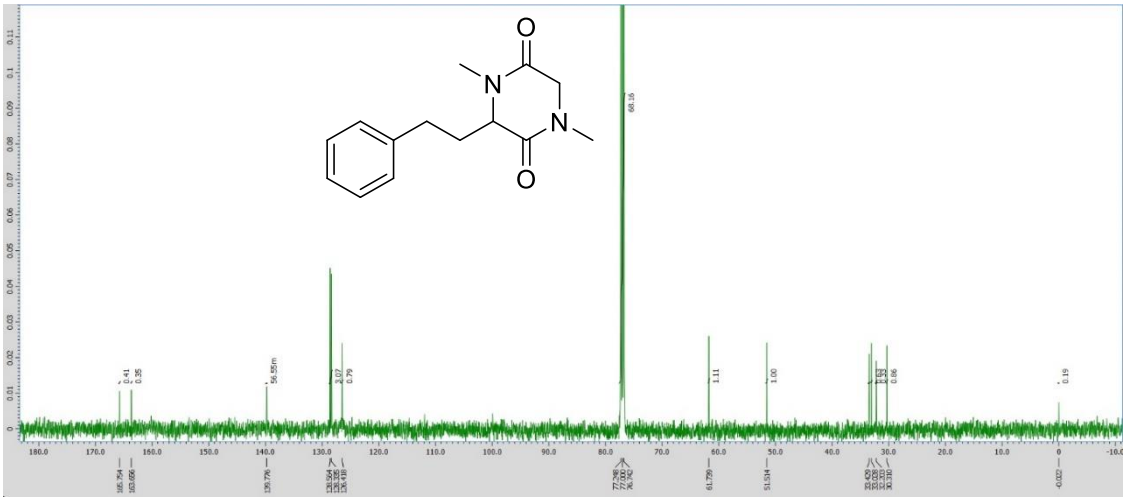
***N*-benzyl-3,3-diphenethylpyrrolidin-2-one (16b)**



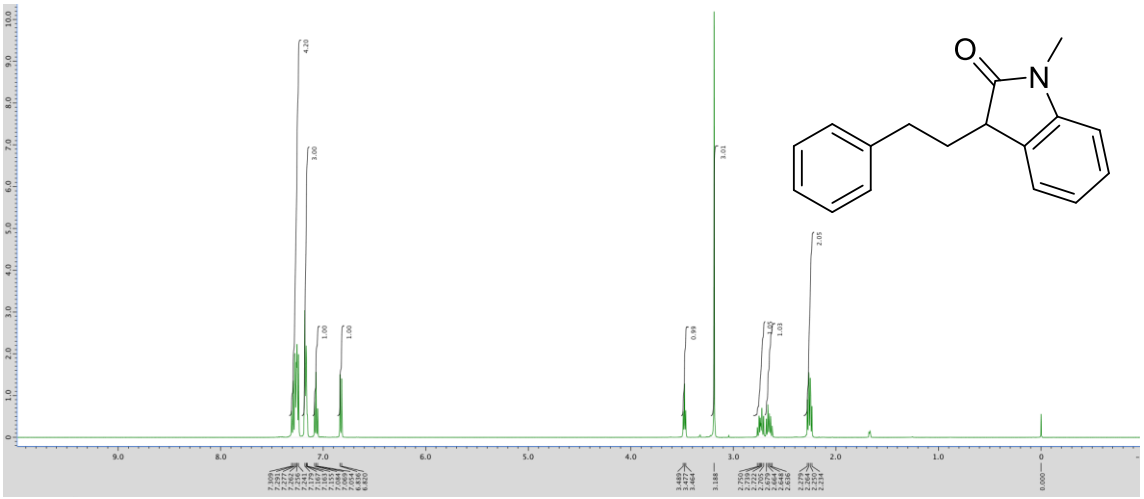


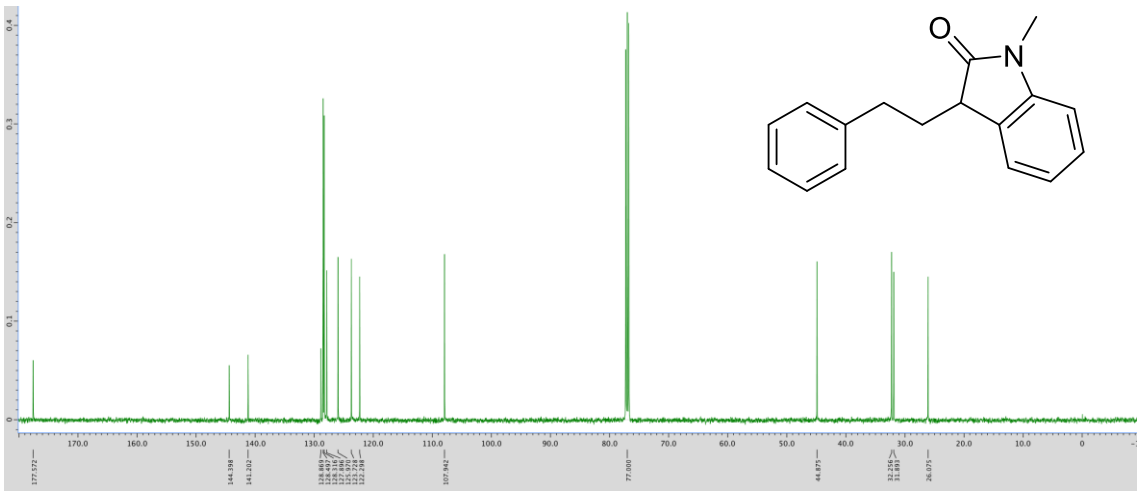
1,4-dimethyl-3-phenethylpiperazine-2,5-dione (17a)



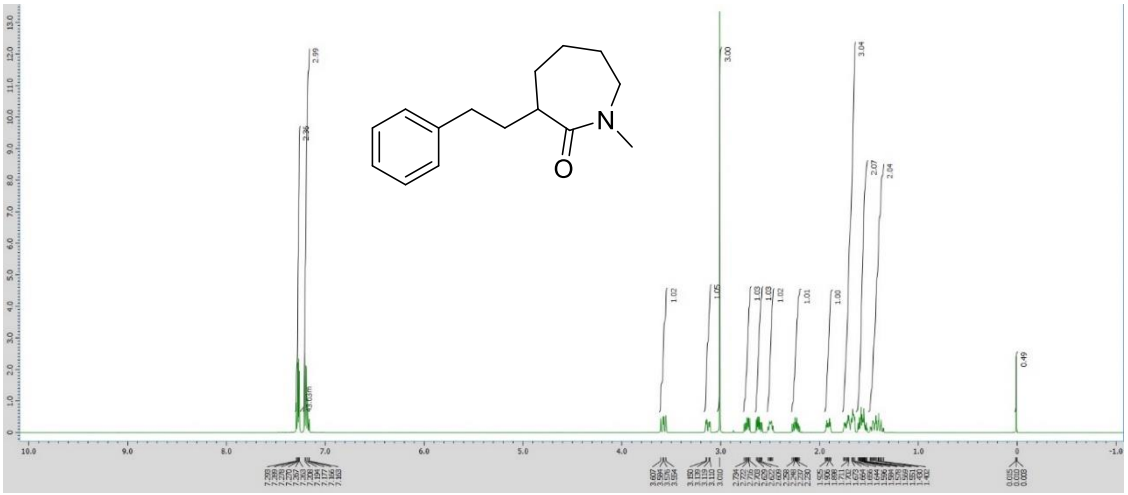


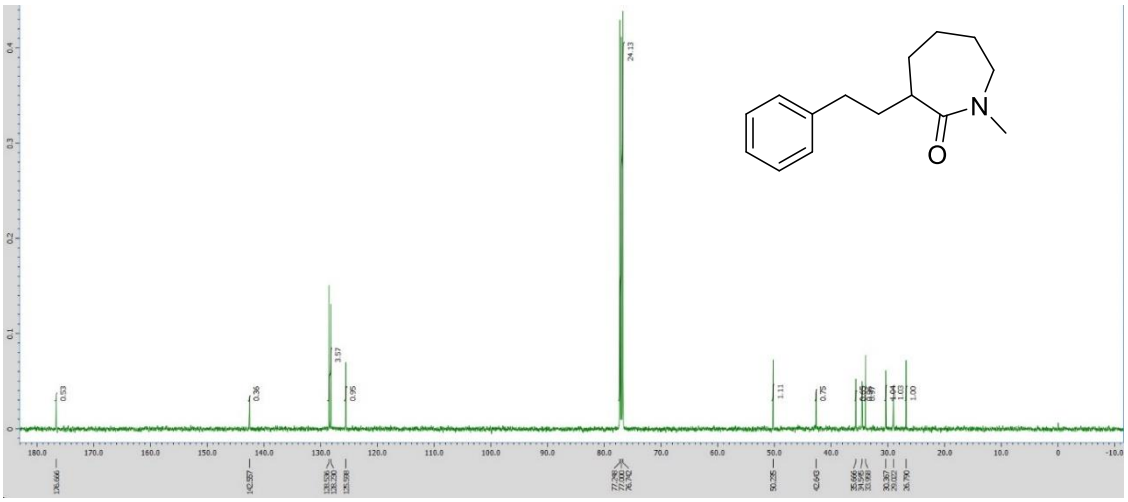
1-methyl-3-phenethylindol-2-one (18a)



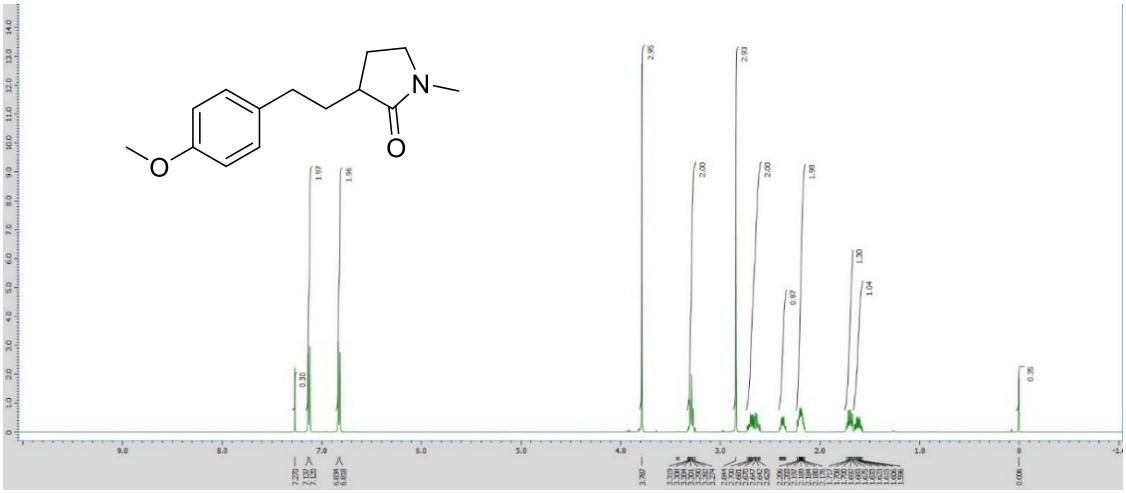


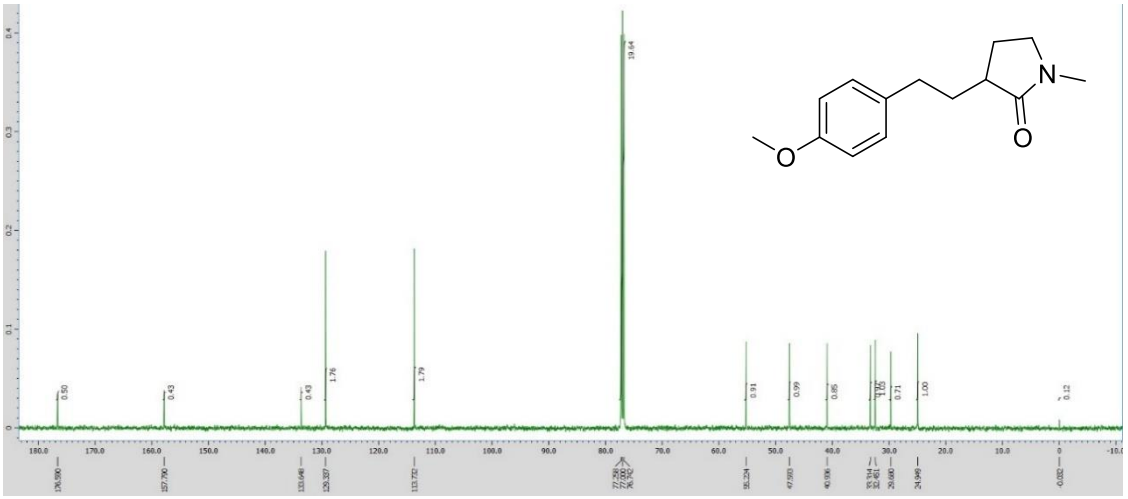
***N*-methyl-3-phenethylazepan-2-one (19a)**



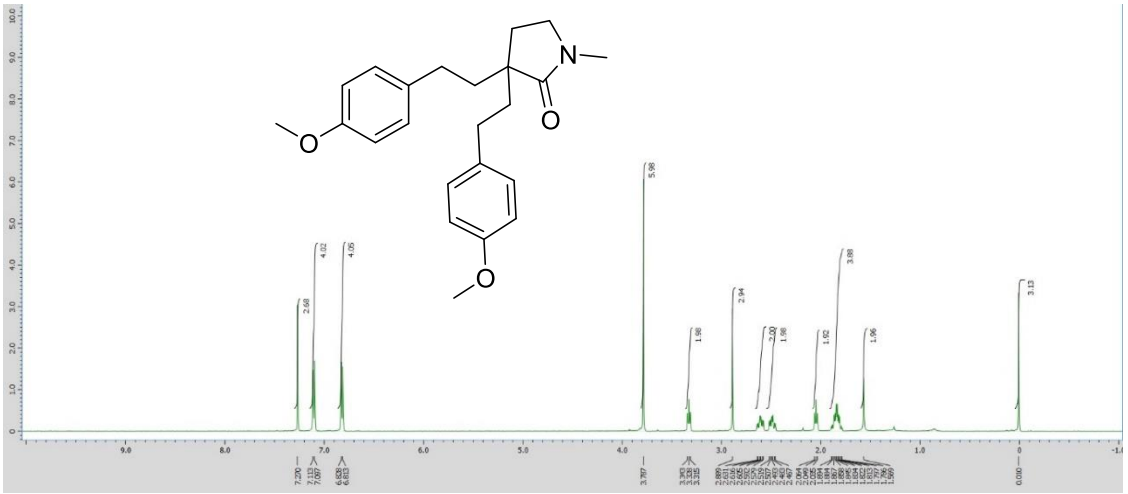


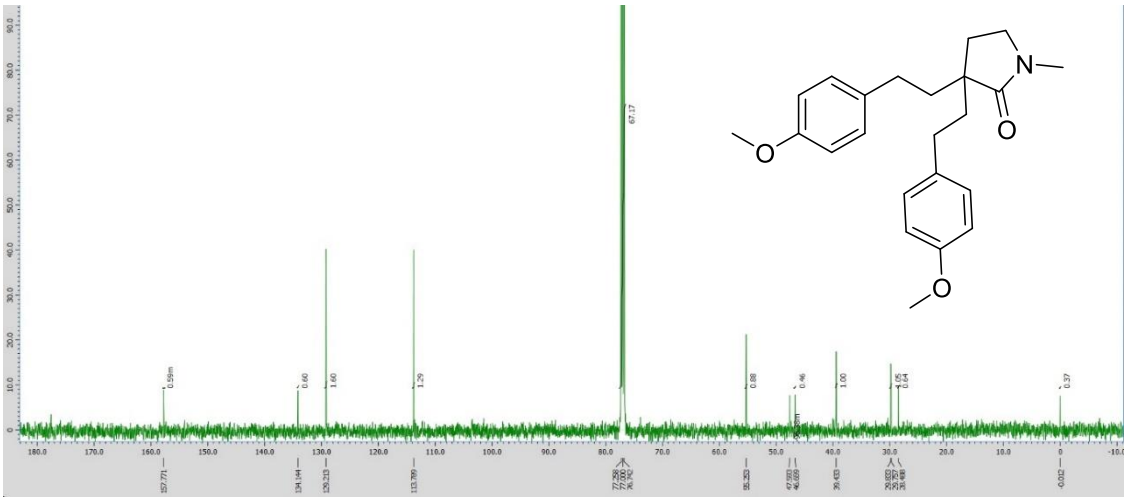
3-(4-methoxyphenethyl)-1-methylpyrrolidin-2-one (20a)



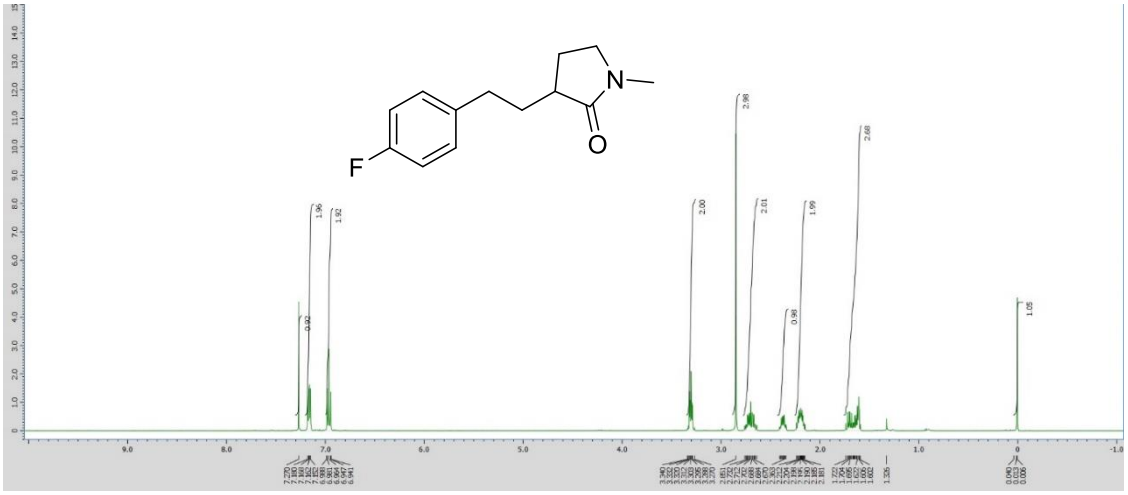


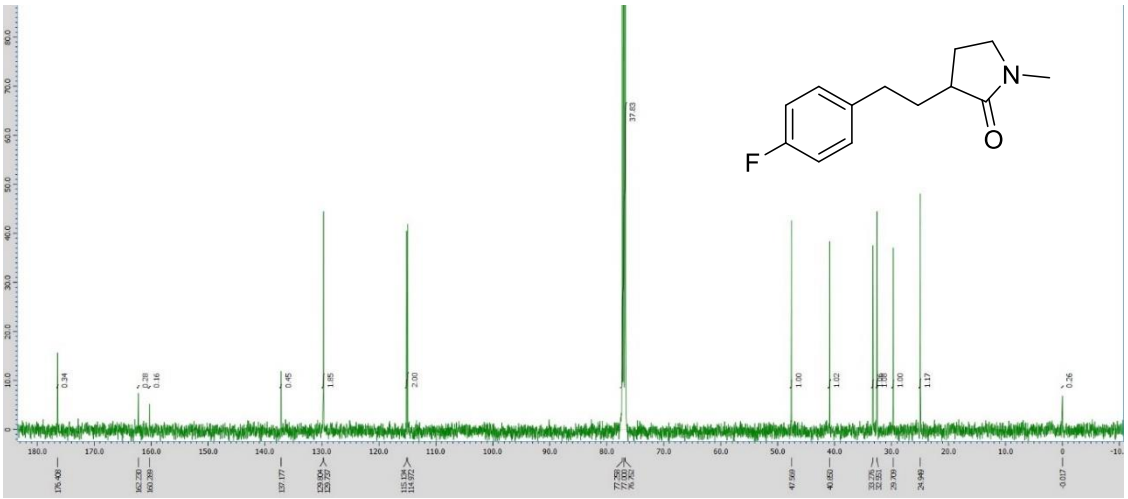
3,3-bis(4-methoxyphenethyl)-1-methylpyrrolidin-2-one (20b)



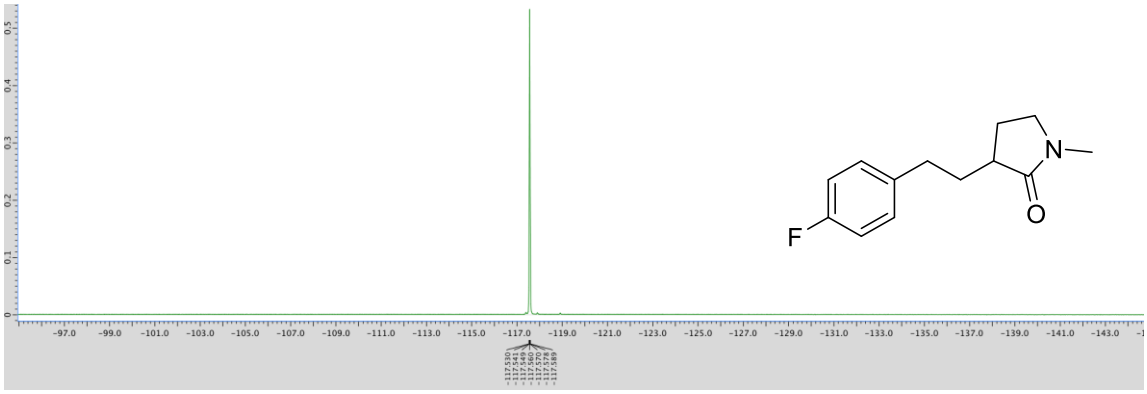


3-(4-fluorophenethyl)-1-methylpyrrolidin-2-one (21a)

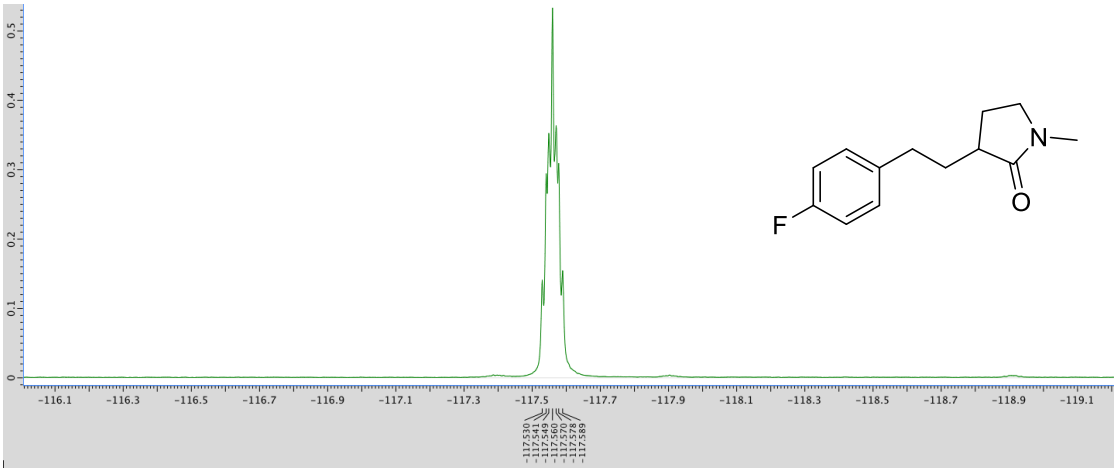




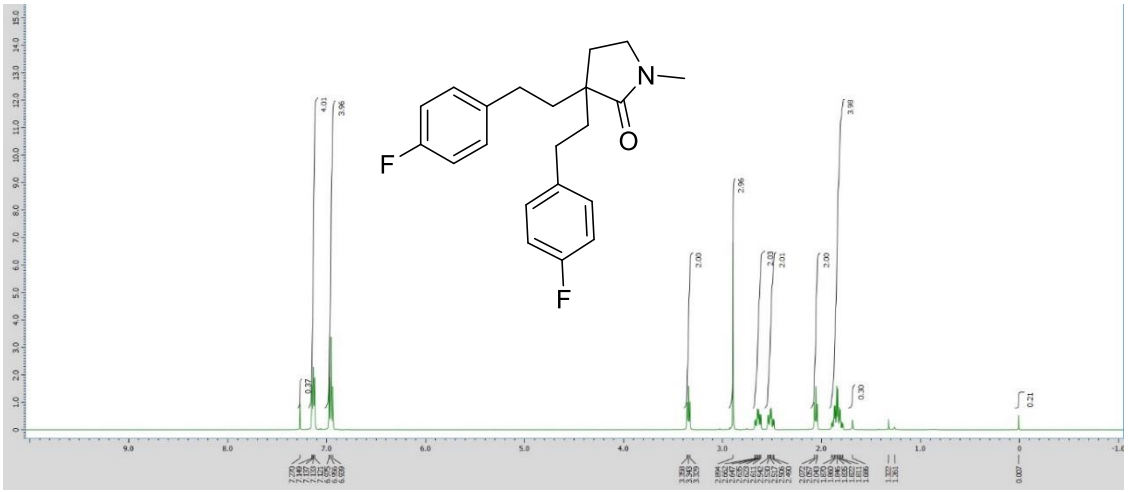
^{19}F NMR

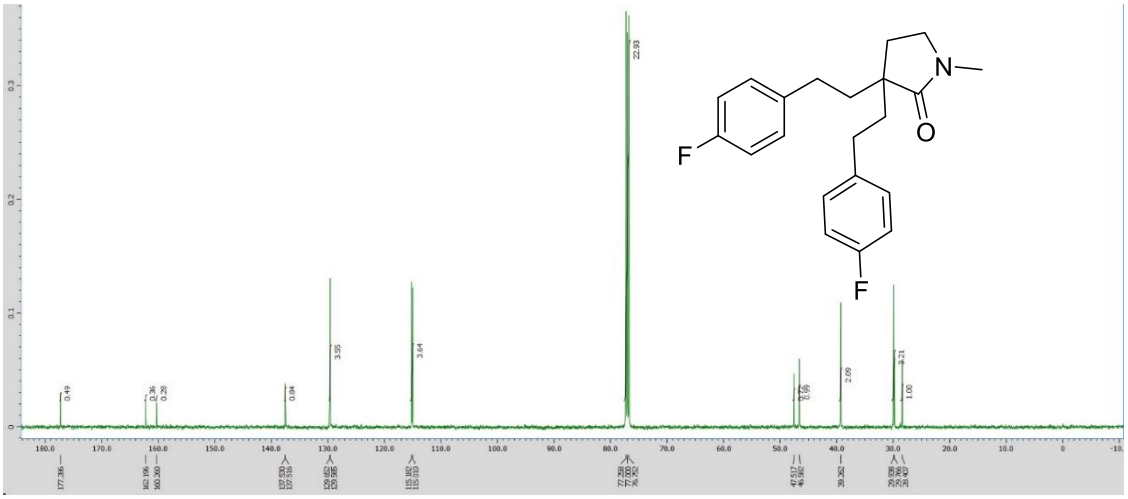


^{19}F NMR (expansion)

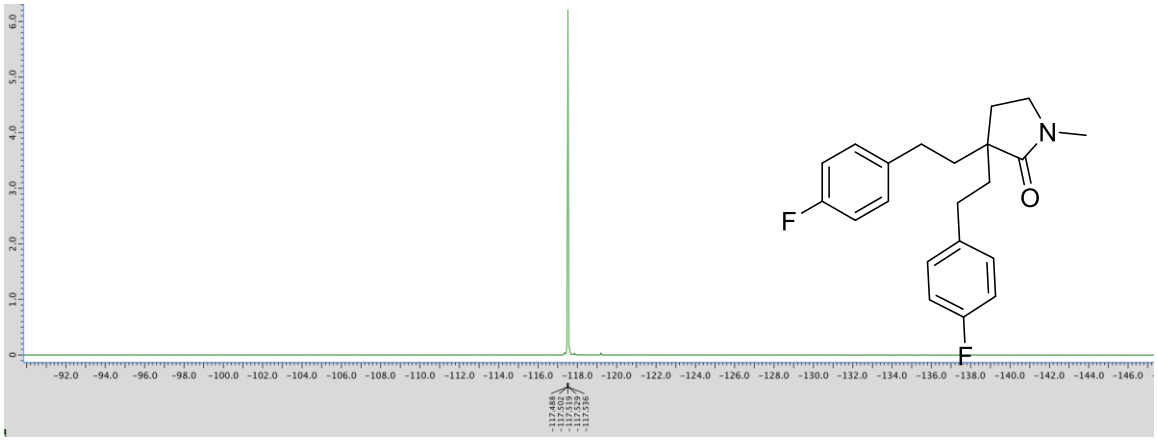


3,3-bis(4-fluorophenethyl)-1-methylpyrrolidin-2-one (21b)

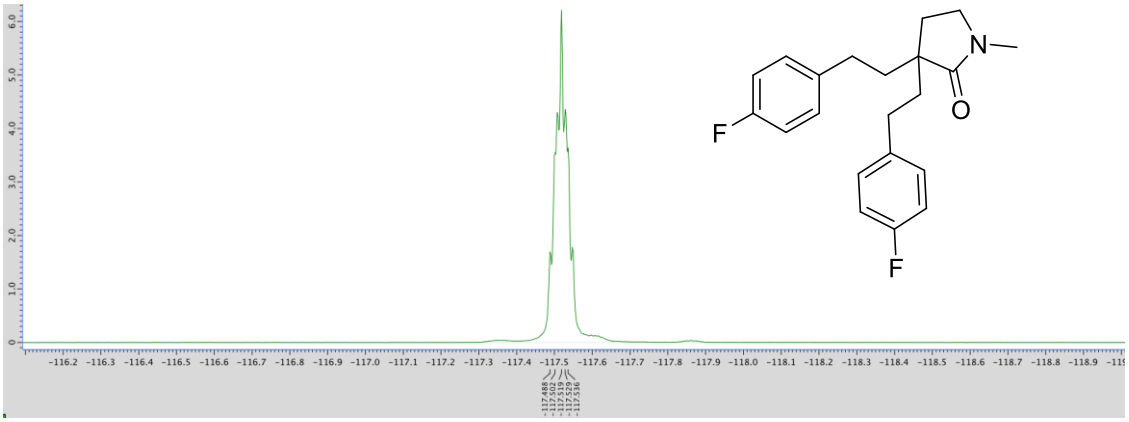




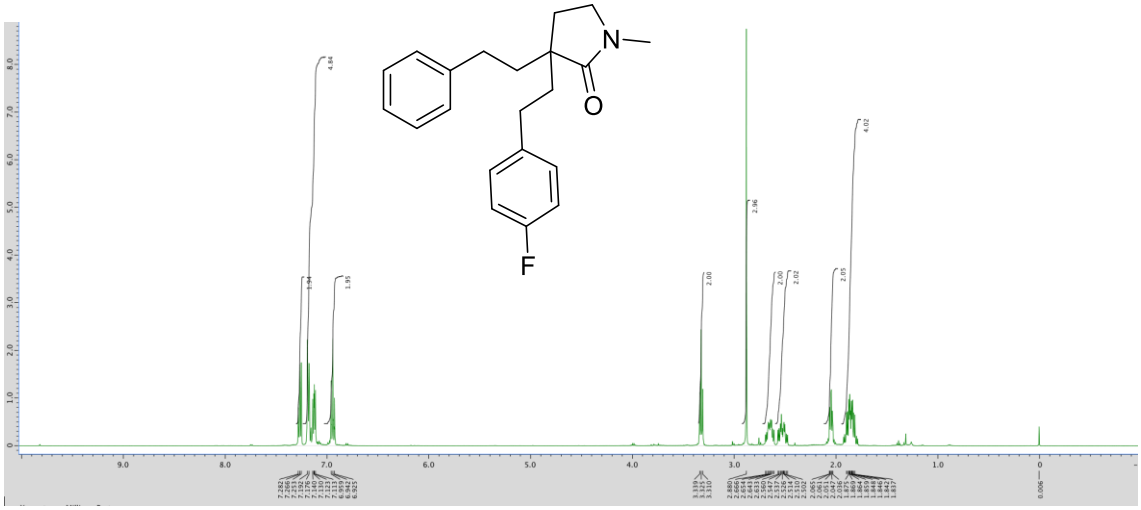
^{19}F NMR

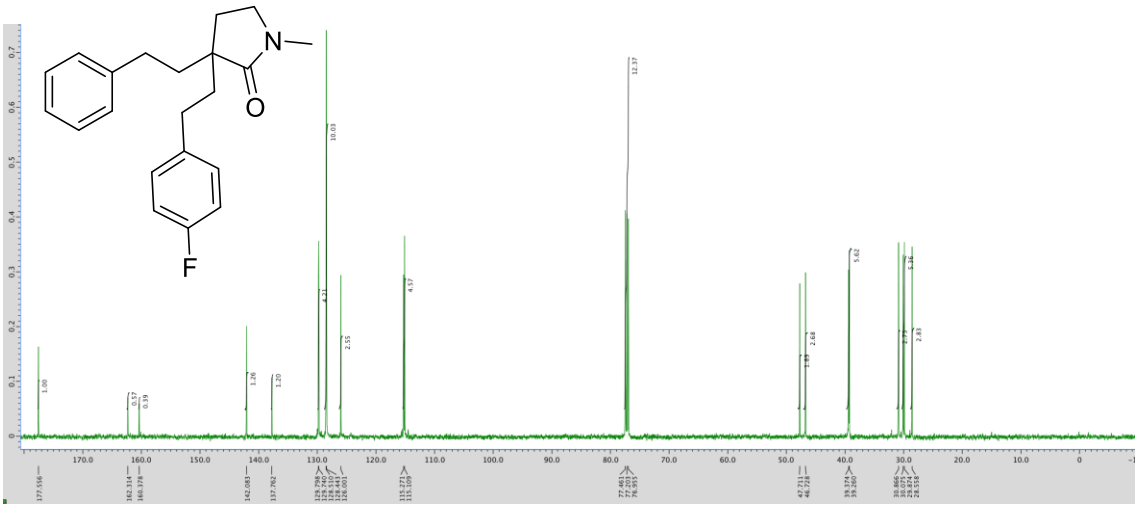


^{19}F NMR (expansion)

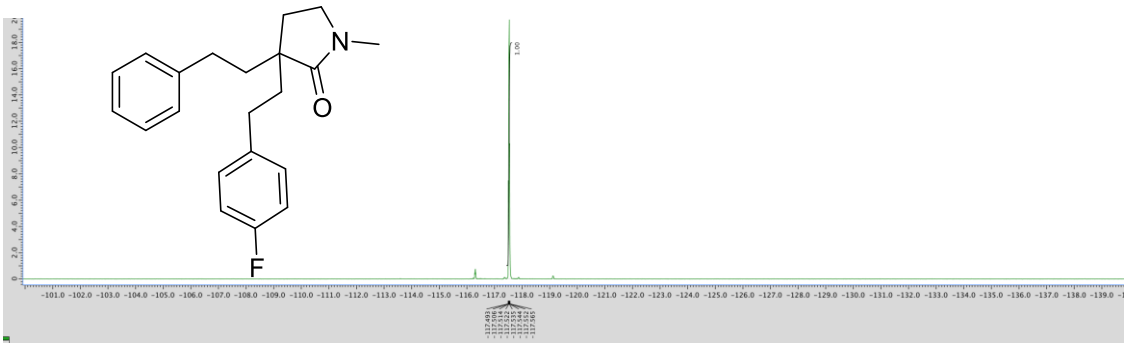


3-(4-fluorophenethyl)-1-methyl-3-phenethylpyrrolidin-2-one (23)

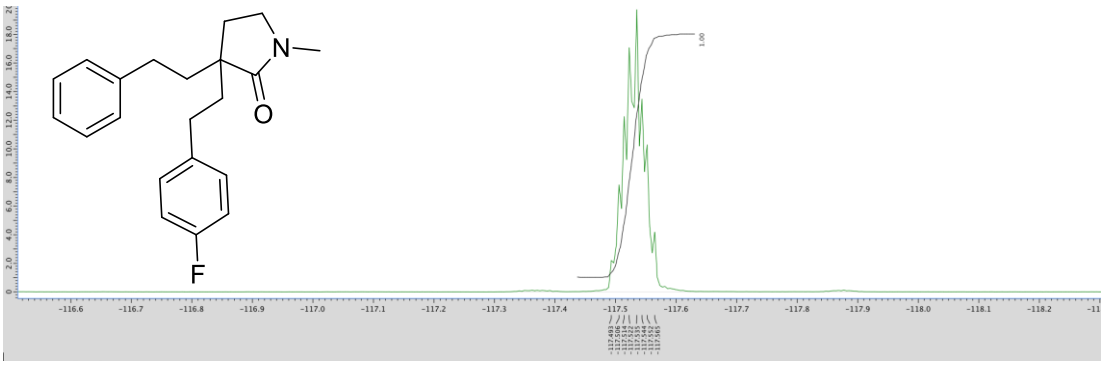




^{19}F NMR



^{19}F NMR (expansion)



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