

Pd-Catalysed β -Selective C(sp³)-H Arylation of Simple Amides

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1. General

Unless otherwise stated, all experiments were carried out under air atmosphere. The reagents and solvents were purchased from commercial suppliers and used without further purification unless noted. ^1H NMR and ^{13}C NMR spectra were obtained on a Bruker AVANCE III 500 instrument in CDCl_3 using TMS as an internal standard, operating at 500 MHz and 126 MHz, respectively. Chemical shifts (δ) are expressed in ppm and coupling constants J are given in Hz. For CDCl_3 or $\text{DMSO}-d_6$ solutions the chemical shifts are reported as parts per million (ppm) to residual protium or carbon of the solvents; CHCl_3 δH (7.26 ppm) and CDCl_3 δC (77.03 ppm); DMSO δH (2.51 ppm) and $\text{DMSO}-d_6$ δC (39.52 ppm). ^{19}F NMR were recorded on a Bruker AVANCE III or Ascend400. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, m = multiplet, br = broad resonance. GC experiments were carried out using Agilent 7890B GC. GC-MS experiments that used dodecane as an internal standard were performed with a Thermo DSQ II, Trace GC Ultra. High resolution mass spectra (HRMS (ESI-TOF)) were obtained on an Agilent 6545 Q-TOF LC-MS spectrometer equipped with an ESI source.

2. Experimental section

2.1. Preparation of substrates

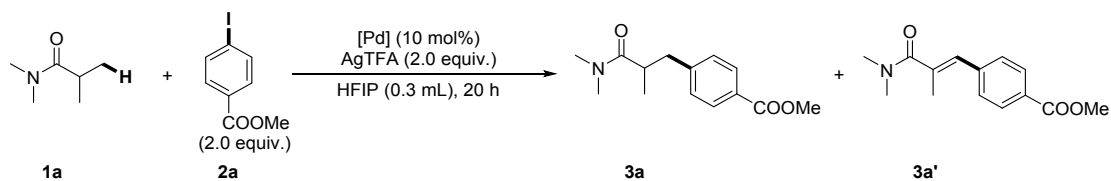
A. The substrates **1** were prepared following the literature procedure^{1,2}

To a stirring solution of isobutyryl chloride (5 mmol) in DCM (20 mL) was added the corresponding amine $\text{R}_1\text{R}_2\text{NH}$ or $\text{R}_1\text{R}_2\text{NH}\cdot\text{HCl}$ (5.5 mmol) and aqueous solution of K_2CO_3 (10 mL, 1M) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 6 h. Upon completion, the resulting mixture was separated, and the aqueous layer was extracted with DCM (3 × 20 mL). The combined organic layers was washed with brine, dried over anhydrous MgSO_4 , filtered, and concentrated in *vacuo*. The crude residue was purified by flash chromatography to afford substrate **1**.

This method also can be used for the synthesis of corresponding substrates **1**.

2.2. Optimization of reaction conditions

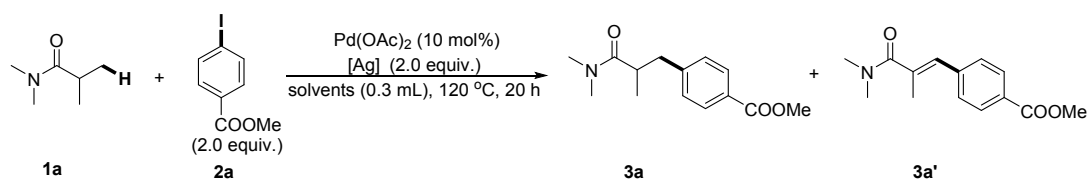
Table S1. Screening of temperatures and catalysts^a



^a Entry	[T/°C]	[Pd]	Yield of 3a/3a' (%) ^b
1	80	Pd(OAc) ₂	44
2	50	Pd(OAc) ₂	11
3	110	Pd(OAc) ₂	55/7
4 ^c	110	Pd(OAc) ₂	57/7
5	120	Pd(OAc)₂	65/8
6	130	Pd(OAc) ₂	54
7	140	Pd(OAc) ₂	52
8	120	PdCl ₂	53/7
9	120	Pd(TFA) ₂	44/6
10	120	Pd(dba) ₂	23
11	120	Pd(PPh ₃) ₄	40/7
12	120	[Pd(Cl)(C ₃ H ₅) ₂]	30/13
13	120	Pd(dppf)Cl ₂	7
14	120	PdCl ₂ (CH ₃ CN) ₂	7/10
15	120	PdCl ₂ (cod)	26/13

^aReaction conditions: **1a** (0.1 mmol), methyl 4-iodobenzoate (2.0 equiv.), [Pd] (10 mol%), AgTFA (2.0 equiv.), HFIP (0.3 mL) were added to a test tube, the mixture was stirred at indicated temperature for 20 h. ^bGC-MS analysis using dodecane as an internal standard. ^cReaction for 48 h.

Table S2. Screening of solvents and Ag salts^a



^a Entry	[Ag]	Solvents	Yield of 3a/3a' (%) ^b
1	AgTFA	HFIP	65/8
2	AgTFA	toluene	trace
3	AgTFA	DMF	trace
4	AgTFA	DCE	32
5	AgTFA	1,4-dioxane	trace
6	AgTFA	CH ₃ NO ₂	30
7	AgTFA	CH ₃ CN	n.r
8	AgTFA	TAA	25
9	AgNO ₃	HFIP	52/10
10	AgNO ₂	HFIP	43/3
11	Ag(CF ₃ SO ₃)	HFIP	47/2
12	Ag ₃ PO ₄	HFIP	8
13	Ag ₂ CO ₃	HFIP	5
14	Ag ₂ SO ₄	HFIP	15
15	AgBF ₄	HFIP	54/2
16	AgSbF ₆	HFIP	60/10
17 ^c	AgSbF ₆	HFIP	63/19
18	AgOAc	HFIP	9

^aReaction condition: **1a** (0.1 mmol), methyl 4-iodobenzoate (2.0 equiv.), Pd(OAc)₂ (10 mol%), Ag salts (2.0 equiv.), solvents (0.3 mL), the mixture was stirred at 120 °C for 20 h. ^bGC-MS analysis using dodecane as an internal standard. ^cReaction for 48 h.

2.3. General conditions for the arylation substrate scope research

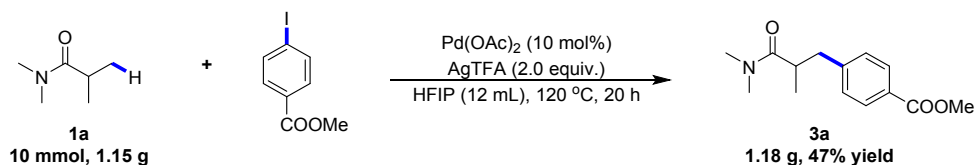
Conditions A: In a 10 mL test tube equipped with a stir bar, amide **1** (0.2 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 10 mol%), AgTFA (88.4 mg, 0.4 mmol, 2.0 equiv.), aryl iodide (0.4 mmol, 2.0 equiv.) and HFIP (0.6 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was purified by silica gel chromatography to afford the desired products **3**.

Conditions B: In a 10 mL test tube equipped with a stir bar, amide **1** (0.2 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 10 mol%), AgSbF₆ (137.5 mg, 0.4 mmol, 2.0 equiv.), aryl iodide (0.4 mmol, 2.0 equiv.) and HFIP (0.6 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was purified by silica gel chromatography to afford the desired products **3**.

3k-3p were prepared according to the procedure under **conditions B**. **3s** was prepared at 80 °C.

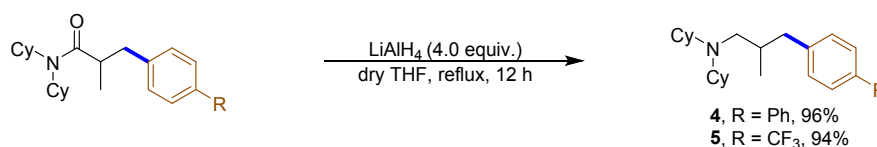
2.4. Synthetic applications

A. Gram-scale reaction



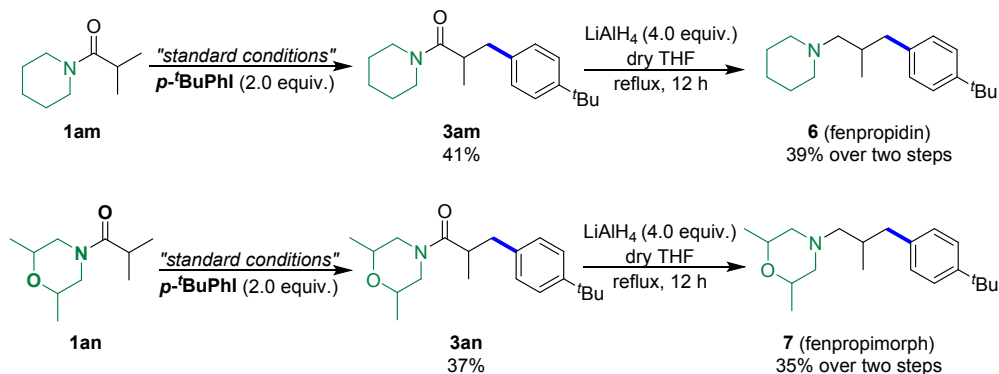
In a 100 mL test tube equipped with a stir bar, **1a** (10.0 mmol), Pd(OAc)₂ (224.5 mg, 1.0 mmol, 10 mol%), AgTFA (4.4 g, 20.0 mmol, 2.0 equiv.), methyl 4-iodobenzoate (5.2 g, 20.0 mmol, 2.0 equiv.), and HFIP (12 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was purified by silica gel chromatography to afford the desired product **3a**.

B. Reduction of arylation products



The reduction procedure was conducted according to the literature³. To a Schlenk tube (10 mL) was added corresponding amide (0.1 mmol), LiAlH₄ (15.2 mg, 0.4 mmol), and dry THF (2.0 mL). The tube was sealed with a Teflon-lined screw cap, refrigerated with liquid nitrogen, evacuated the air and filled with nitrogen by the Schlenk line for 3 times. Then the tube was refluxed for 12 h under stirring. Next, the tube was allowed to cool to room temperature. The solvent was then removed in *vacuo* and the residue was purified through flash column chromatography on silica gel (petroleum ether/EtOAc/MeOH = 1:1:0.1) to give the corresponding products.

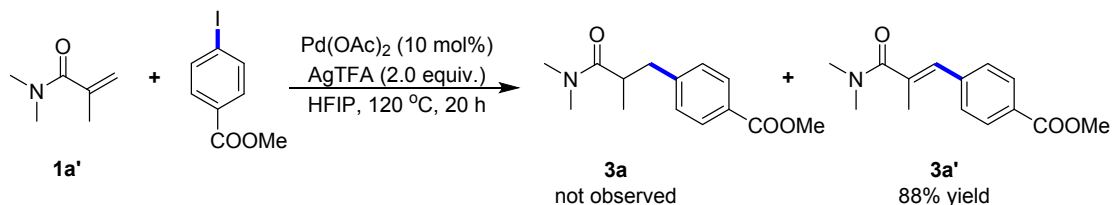
C. Direct synthesis of fungicide fenpropidin and fenpropimorph



The products **6** and **7** were prepared by the same process described above.

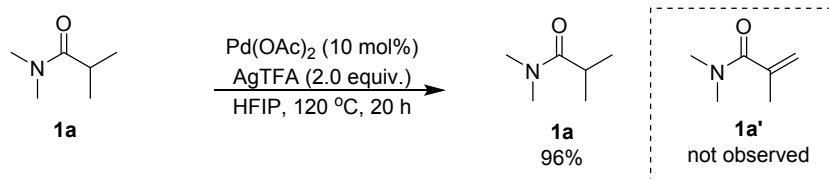
2.5. Mechanistic studies

A. Attempted reaction with olefin **1a'**



In a 10 mL test tube equipped with a stir bar, amide **1a'** (0.2 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 10 mol%), AgTFA (88.4 mg, 0.4 mmol, 2.0 equiv.), methyl 4-iodobenzoate (104.8 mg, 0.4 mmol, 2.0 equiv.) and HFIP (0.6 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was purified by silica gel chromatography to afford the products **3a'**.

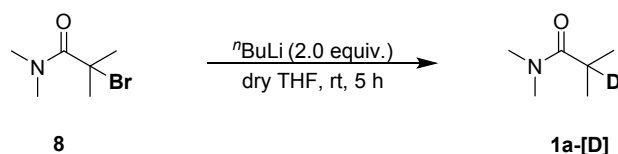
B. Control experiment without aryl iodide



In a 10 mL test tube equipped with a stir bar, amide **1a** (0.1 mmol), Pd(OAc)₂ (2.25 mg, 0.01 mmol, 10 mol%), AgTFA (44.2 mg, 0.2 mmol, 2.0 equiv.), and HFIP (0.3 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was diluted with EtOAc, washed with water, and the organic layer was filtered and subject to the GC-MS analysis.

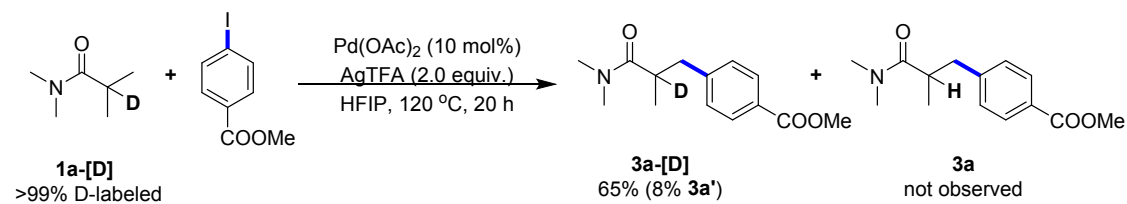
The GC-MS spectrum showed no formation of the β-H elimination product N,N-Dimethylmethacrylamide (**1a'**), indicated that the aryl iodides might play a significant role in the desaturation process.⁴

C. Deuterium-labeling experiment

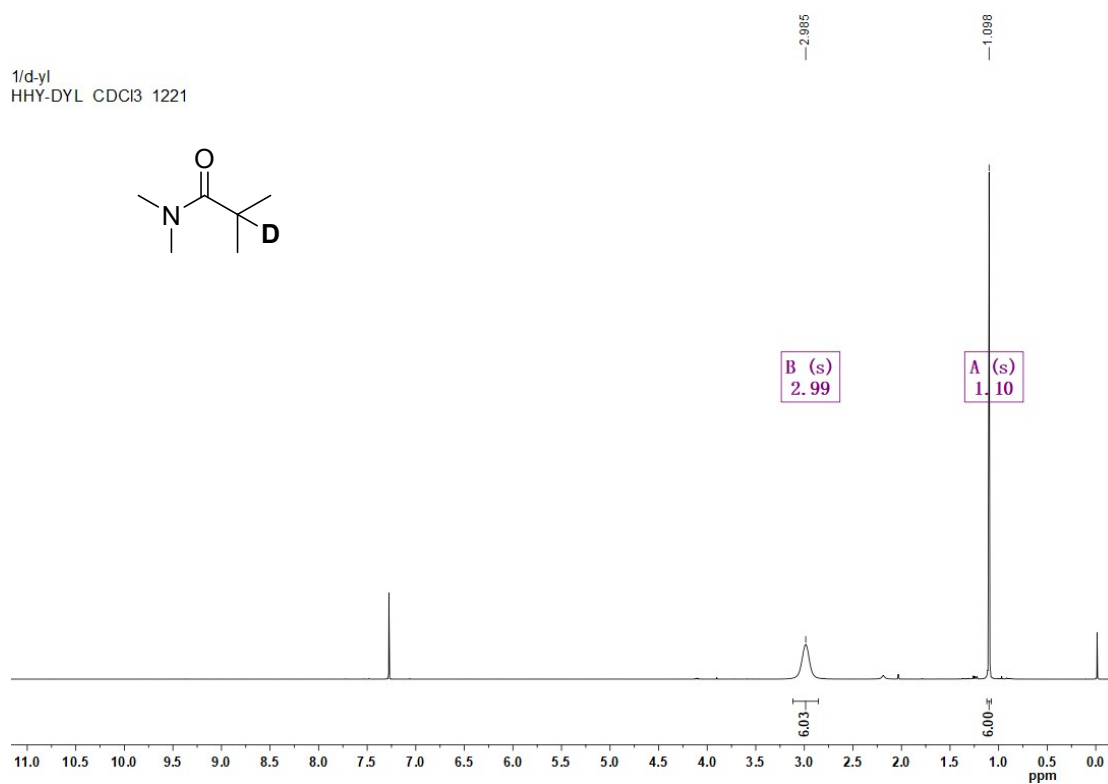


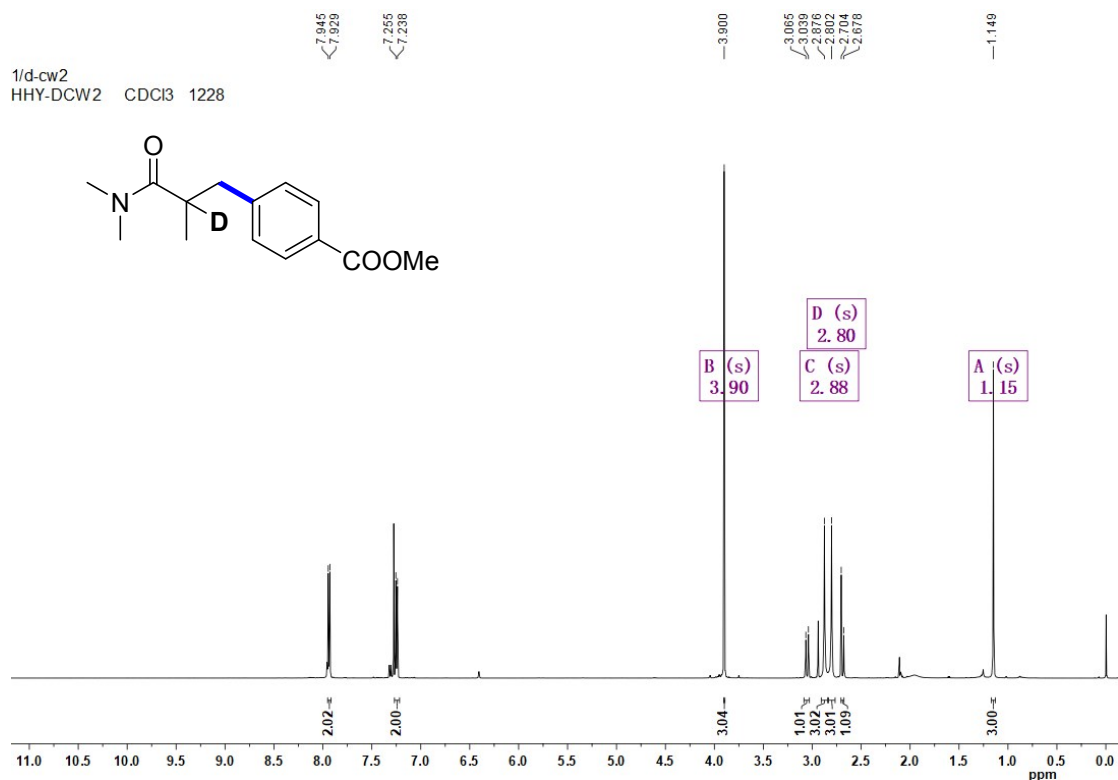
To a dried and degassed Schlenk round bottom flask was charged with **8** (970 mg, 5.0 mmol, 1.0 equiv.) and anhydrous THF (15 mL). After cooling down the resulting mixture to -78 °C, ⁿBuLi (10 mmol, 2.0 equiv.) was added dropwise, and the mixture was allowed to warm to room temperature and stirred for 5.0 h. The reaction was quenched by dropwise addition of D₂O (4.0 equiv.) at -78 °C. After warmed to room temperature, the reaction was stirred for another 3 h. The resulting mixture was extracted with

Et₂O (3 × 30 mL), dried with Na₂SO₄, and evaporated in *vacuo*. Upon completion, the residue was purified by silica gel chromatography to afford the desired product **1a-[D]**.

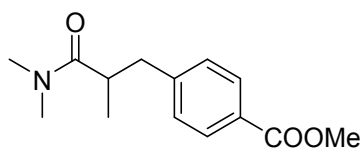


In a 10 mL test tube equipped with a stir bar, amide **1a-[D]** (0.2 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 10 mol%), AgTFA (88.4 mg, 0.4 mmol, 2.0 equiv.), methyl 4-iodobenzoate (104.8 mg, 0.4 mmol, 2.0 equiv.) and HFIP (0.6 mL) were added successively. Then the tube was sealed and heated at 120 °C for 20 h under stirring. Upon completion, the residue was purified by silica gel chromatography to afford the desired product **3a-[D]**.

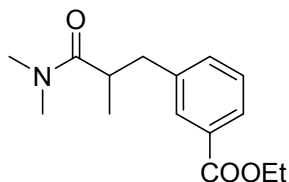




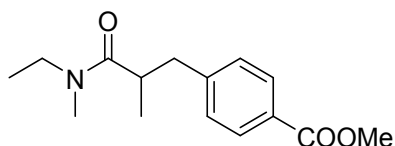
3. Characterization of products



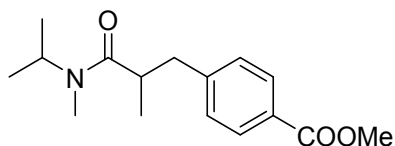
Methyl 4-(3-(dimethylamino)-2-methyl-3-oxopropyl)benzoate (3a): Colorless oil (60%, mono-diarylation = 13:1, 29.9 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.95$ (d, $J = 8.3$ Hz, 2H), 7.26 (d, $J = 8.3$ Hz, 2H), 3.91 (s, 3H), 3.12-2.98 (m, 2H), 2.89 (s, 3H), 2.82 (s, 3H), 2.75-2.68 (m, 1H), 1.17 (d, $J = 6.6$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.4$, 167.1, 145.8, 129.6 (2C), 129.0 (2C), 128.2, 52.0, 40.4, 37.7, 37.1, 35.7, 17.7 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{14}\text{H}_{19}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 272.1257, found: 272.1264.



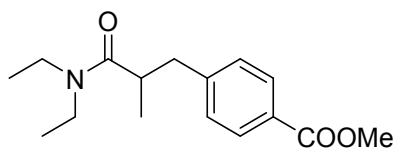
Ethyl 3-(3-(dimethylamino)-2-methyl-3-oxopropyl)benzoate (3b): Colorless oil (42%, mono-diarylation = 32:1, 22.1 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.91$ -7.86 (m, 2H), 7.39-7.32 (m, 2H), 4.38 (q, $J = 7.1$ Hz, 2H), 3.11-2.98 (m, 2H), 2.89 (s, 3H), 2.84 (s, 3H), 2.73-2.69 (m, 1H), 1.40 (t, $J = 7.1$ Hz, 3H), 1.15 (d, $J = 6.5$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.5$, 166.7, 140.5, 133.7, 130.5, 129.8, 128.3, 127.4, 60.9, 40.1, 37.7, 37.1, 35.6, 17.5, 14.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{15}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 286.1414; found: 286.1428.



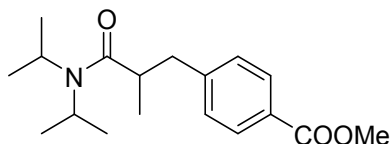
Methyl 4-(3-(ethyl(methyl)amino)-2-methyl-3-oxopropyl)benzoate (3c) (1.0:0.97 mixture of rotamers): Colorless oil (43%, mono-:di-arylation = 32:1, 22.6 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3 , mixture of rotamers): $\delta = 7.96\text{-}7.93$ (m, 2H), 7.27-7.24 (m, 2H), 3.91 (s, 3H), 3.49-3.22 (m, 1H), 3.19-2.91 (m, 3H), 2.86 (s, 3H), 2.74-2.66 (m, 1H), 1.19-1.01 (m, 3H), 0.95 (t, $J = 7.2$ Hz, 3H) ppm; major: $^{13}\text{C NMR}$ (126 MHz, CDCl_3 , mixture of rotamers): $\delta = 175.1$, 167.1, 145.9, 129.6 (2C), 129.1 (2C), 128.2, 52.0, 42.6, 40.4, 37.8, 33.1, 17.7, 12.2 ppm; minor: $^1\text{H NMR}$ (500 MHz, CDCl_3 , mixture of rotamers): $\delta = 7.96\text{-}7.93$ (m, 2H), 7.27-7.24 (m, 2H), 3.91 (s, 3H), 3.49-3.22 (m, 1H), 3.19-2.91 (m, 3H), 2.77 (s, 3H), 2.74-2.66 (m, 1H), 1.18 (dd, $J_1 = 10.5$ Hz, $J_2 = 6.7$ Hz, 3H), 1.00 (t, $J = 7.1$ Hz, 3H) ppm; minor: $^{13}\text{C NMR}$ (126 MHz, CDCl_3 , mixture of rotamers): $\delta = 174.8$, 167.1, 145.9, 129.6 (2C), 129.1 (2C), 128.2, 52.0, 44.2, 40.6, 37.8, 34.6, 18.4, 13.9 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{15}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 286.1414 found: 286.1420.



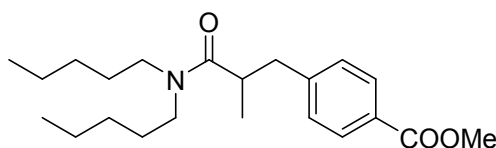
Methyl 4-(3-(isopropyl(methyl)amino)-2-methyl-3-oxopropyl)benzoate (3d) (1.0:0.77 mixture of rotamers): Colorless oil (52%, mono-:di-arylation = 32:1, 28.8 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (dd, $J_1 = 8.3$ Hz, $J_2 = 1.9$ Hz, 2H), 7.26 (dt, $J_1 = 8.2$ Hz, $J_2 = 4.1$ Hz, 2H), 4.06-3.91 (m, 4H), 3.13-2.92 (m, 2H), 2.73-2.59 (m, 4H), 1.17 (dd, $J_1 = 8.8$ Hz, $J_2 = 6.6$ Hz, 3H), 1.03 (d, $J = 6.8$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.8$, 167.1, 145.9, 129.6 (2C), 129.1 (2C), 128.1, 52.0, 43.8, 40.5, 38.3, 28.0, 20.4, 19.4, 17.8 ppm; minor: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (dd, $J_1 = 8.3$ Hz, $J_2 = 1.9$ Hz, 2H), 7.26 (dt, $J_1 = 8.2$ Hz, $J_2 = 4.1$ Hz, 2H), 4.06-3.91 (m, 4H), 3.13-2.92 (m, 2H), 2.73-2.59 (m, 4H), 1.17 (dd, $J_1 = 8.8$ Hz, $J_2 = 6.6$ Hz, 3H), 1.13 (d, $J = 6.6$ Hz, 3H), 0.83 (d, $J = 6.6$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.8$, 167.1, 146.0, 129.6 (2C), 129.1 (2C), 128.1, 52.0, 47.6, 40.7, 37.8, 26.0, 20.7, 19.3, 18.5 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{16}\text{H}_{23}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 300.1570, found: 300.1577.



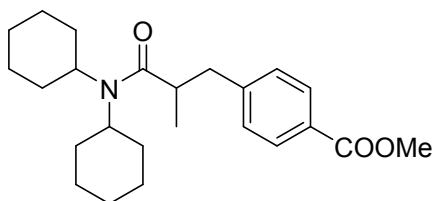
Methyl 4-(3-(diethylamino)-2-methyl-3-oxopropyl)benzoate (3e): Colorless oil (46%, mono-:di-arylation = 32:1, 25.5 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 9.5$ Hz, 2H), 3.91 (s, 3H), 3.42-3.35 (m, 1H), 3.26-3.19 (m, 1H), 3.13-3.05 (m, 3H), 2.92-2.85 (m, 1H), 2.70 (dd, $J_1 = 5.5$ Hz, $J_2 = 13$ Hz, 1H), 1.20 (d, $J = 6.5$ Hz, 3H), 1.03 (t, $J = 7.0$ Hz, 3H), 0.96 (t, $J = 7.0$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.6$, 167.1, 145.9, 129.6 (2C), 129.2 (2C), 128.1, 52.0, 41.8, 40.7 (d, $J = 22.2$ Hz, 2C), 38.0, 18.5, 14.7, 13.0 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{16}\text{H}_{23}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 300.1570, found: 300.1577.



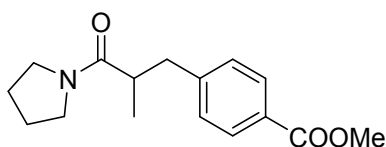
Methyl 4-(3-(diisopropylamino)-2-methyl-3-oxopropyl)benzoate (3f): Solid (60%, mono-diarylation = 19:1, 36.6 mg); $R_f = 0.58$ (petroleum ether-EtOAc = 3:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.91$ (d, $J = 7.9$ Hz, 2H), 7.25 (d, $J = 7.9$ Hz, 2H), 3.88-3.82 (m, 5H), 3.11 (dd, $J_1 = 13.1$ Hz, $J_2 = 8.8$ Hz, 1H), 2.93-2.86 (m, 1H), 2.64 (dd, $J_1 = 13.1$ Hz, $J_2 = 5.6$ Hz, 1H), 1.31 (d, $J = 6.7$ Hz, 3H), 1.22 (d, $J = 6.8$ Hz, 3H), 1.14 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.7$ Hz, 3H), 0.85 (s, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.3, 167.1, 146.1, 129.5$ (2C), 129.2 (2C), 127.9, 51.9, 447.8, 45.7, 40.6, 39.0, 21.3, 21.0, 20.7, 20.5, 18.5 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{18}\text{H}_{27}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 328.1883, found: 328.1891.



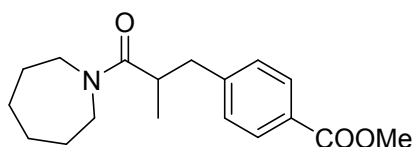
Methyl 4-(3-(dipentylamino)-2-methyl-3-oxopropyl)benzoate (3g) (1.0:0.46 mixture of rotamers): Solid (70%, 50.6 mg); $R_f = 0.58$ (petroleum ether-EtOAc = 3:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.93$ -7.92 (m, 2H), 7.28-7.24 (m, 2H), 3.90 (s, 3H), 3.29-3.01 (m, 6H), 2.68 (dd, $J_1 = 5.5$ Hz, $J_2 = 13$ Hz, 1H), 1.43-1.11 (m, 13H), 0.91-0.83 (m, 7H), 0.76-0.70 (m, 1H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3 , mixture of rotamers): $\delta = 174.9, 167.1, 145.9, 129.6$ (2C), 129.1 (2C), 128.1, 51.9, 47.8, 46.4, 40.7, 38.0, 29.2, 29.1, 28.9, 27.4, 22.4, 22.3, 18.6, 14.0, 13.9 ppm; minor: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ -7.92 (m, 2H), 7.28-7.24 (m, 2H), 3.90 (s, 3H), 3.29-3.01 (m, 6H), 2.68 (dd, $J_1 = 5.5$ Hz, $J_2 = 13$ Hz, 1H), 1.43-1.11 (m, 13H), 0.91-0.83 (m, 7H), 0.76-0.70 (m, 1H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.4, 167.1, 145.9, 129.6$ (2C), 129.2 (2C), 128.1, 51.7, 47.6, 46.2, 40.6, 38.0, 29.2, 29.1, 28.9, 27.4, 22.4, 22.3, 16.7, 11.4, 11.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{35}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 384.2509, found: 384.2518.



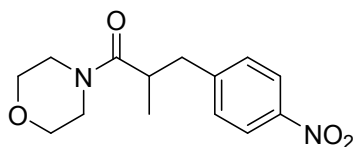
Methyl 4-(3-(dicyclohexylamino)-2-methyl-3-oxopropyl)benzoate (3h): Colorless oil (79%, mono-diarylation = 24:1, 60.8 mg); $R_f = 0.37$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (d, $J = 8.3$ Hz, 2H), 7.26 (d, $J = 8.3$ Hz, 2H), 3.90 (s, 3H), 3.35 (s, 1H), 3.13-3.05 (m, 1H), 2.98-2.88 (m, 1H), 2.66 (dd, $J_1 = 13.1$ Hz, $J_2 = 5.5$ Hz, 1H), 2.59-2.42 (m, 1H), 1.82-0.97 (m, 23H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3) $\delta = 174.4, 167.1, 146.1, 129.5$ (2C), 129.2 (2C), 128.0, 57.8, 56.1, 51.9, 40.8, 38.8, 31.7, 31.3, 30.2, 30.0, 26.6 (2C), 26.1 (2C), 25.4, 25.2, 18.7 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{24}\text{H}_{35}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 408.2509, found: 408.2517.



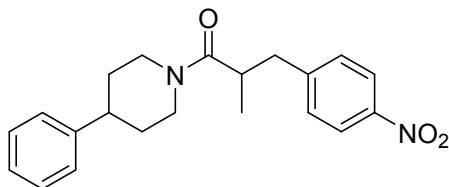
Methyl 4-(2-methyl-3-oxo-3-(pyrrolidin-1-yl)propyl)benzoate (3i) (1.0:0.37 mixture of rotamers): Solid (49%, 27.0 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.2$ Hz, 2H), 3.91 (s, 3H), 3.50-3.27 (m, 3H), 3.06 (dd, $J_1 = 13.0$ Hz, $J_2 = 8.6$ Hz, 1H), 2.98 (dt, $J_1 = 9.9$ Hz, $J_2 = 7.1$ Hz, 1H), 2.88-2.76 (m, 1H), 2.72-2.62 (m, 1H), 1.88-1.63 (m, 4H), 1.18 (d, $J = 6.7$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.0$, 166.9, 145.4, 129.7 (2C), 129.1 (2C), 128.4, 66.9, 66.5, 52.1, 46.0, 42.1, 40.5, 37.1, 18.1 ppm; minor: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.94$ (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.2$ Hz, 2H), 3.91 (s, 3H), 3.50-3.27 (m, 3H), 3.06 (dd, $J_1 = 13.0$ Hz, $J_2 = 8.6$ Hz, 1H), 2.98 (dt, $J_1 = 9.9$ Hz, $J_2 = 7.1$ Hz, 1H), 2.88-2.76 (m, 1H), 2.72-2.62 (m, 1H), 1.88-1.63 (m, 4H), 1.13 (d, $J = 6.8$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.9$, 166.6, 145.5, 129.8 (2C), 129.2 (2C), 128.4, 66.9, 66.5, 52.1, 45.6, 42.1, 37.5, 35.3, 17.2 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{16}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 298.1414, found: 298.1424.



Methyl 4-(3-(azepan-1-yl)-2-methyl-3-oxopropyl)benzoate (3j): Colorless oil (54%, 32.7 mg); $R_f = 0.49$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.93$ (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 3.90 (s, 3H), 3.63-3.58 (m, 1H), 3.33-3.27 (m, 2H), 3.22-3.16 (m, 1H), 3.14-3.10 (m, 1H), 2.97-2.90 (m, 1H), 2.67 (dd, $J_1 = 5.5$ Hz, $J_2 = 13$ Hz, 1H), 1.66-1.53 (m, 3H), 1.47-1.33 (m, 3H), 1.32-1.21 (m, 2H), 1.18 (d, $J = 6.5$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.9$, 167.1, 146.0, 129.5 (2C), 129.2 (2C), 128.0, 52.0, 47.7, 46.2, 40.5, 38.1, 29.3, 27.6, 26.5, 26.4, 18.4 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 326.1727, found: 326.1735.

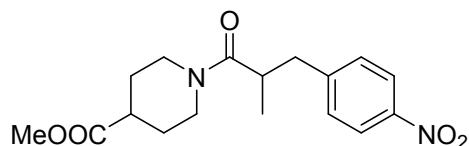


2-Methyl-1-morpholino-3-(4-nitrophenyl)propan-1-one (3k): Colorless oil (61%, 33.9 mg); $R_f = 0.38$ (petroleum ether-EtOAc = 1:2); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 8.15$ (d, $J = 8.7$ Hz, 2H), 7.36 (d, $J = 8.7$ Hz, 2H), 3.68-3.50 (m, 5H), 3.46-3.23 (m, 3H), 3.18 (dd, $J_1 = 13.3$ Hz, $J_2 = 8.5$ Hz, 1H), 3.04-2.94 (m, 1H), 2.79 (dd, $J_1 = 13.4$ Hz, $J_2 = 6.0$ Hz, 1H), 1.21 (d, $J = 6.8$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.5$, 147.9, 146.7, 129.9 (2C), 123.6 (2C), 66.9, 66.6, 46.0, 42.2, 39.9, 37.2, 18.1 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 301.1159; found: 301.1162.

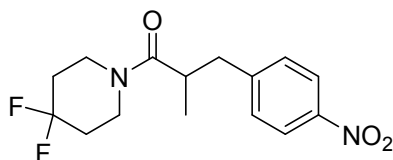


2-Methyl-3-(4-nitrophenyl)-1-(4-phenylpiperidin-1-yl)propan-1-one (3l) (1.0:0.86 mixture of rotamers): Colorless oil (40%, 28.2 mg); $R_f = 0.46$ (petroleum ether-EtOAc = 1:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 8.17$ (dd, $J_1 = 17.0$ Hz, $J_2 = 8.2$ Hz, 2H), 7.40 (dd, $J_1 = 29.2$ Hz, $J_2 = 8.3$ Hz, 2H), 7.31 (dd, $J_1 = 13.4$ Hz, $J_2 = 5.6$ Hz, 2H), 7.25-7.16 (m, 2H), 6.96 (d, $J = 7.5$ Hz, 1H), 4.77 (d, $J = 11.7$ Hz, 1H), 3.92 (t, $J = 13.8$ Hz, 1H), 3.21 (q, $J = 10.0$ Hz, 1H), 3.07 (dd, $J_1 = 22.2$ Hz, $J_2 = 9.4$ Hz, 3H), 2.73-2.53 (m, 2H), 2.00-1.51 (m, 4H), 1.25 (d, $J = 6.7$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.1$, 148.4, 146.6, 144.7, 130.1, 129.9, 128.6 (2C), 126.6, 126.5, 126.4, 123.6 (2C), 46.4, 42.9,

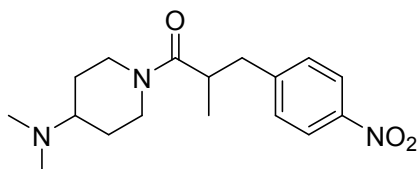
42.5, 40.4, 37.5, 33.9, 33.2, 18.3 ppm; minor: ^1H NMR (500 MHz, CDCl_3): δ = 8.17 (dd, J_1 = 17.0 Hz, J_2 = 8.2 Hz, 2H), 7.40 (dd, J_1 = 29.2 Hz, J_2 = 8.3 Hz, 2H), 7.31 (dd, J_1 = 13.4 Hz, J_2 = 5.6 Hz, 2H), 7.25-7.16 (m, 2H), 6.96 (d, J = 7.5 Hz, 1H), 4.77 (d, J = 11.7 Hz, 1H), 3.92 (t, J = 13.8 Hz, 1H), 3.21 (q, J = 10.0 Hz, 1H), 2.94-2.76 (m, 3H), 2.73-2.53 (m, 2H), 2.00-1.51 (m, 4H), 1.25 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 173.2, 148.4, 146.6, 144.7, 130.1, 129.9, 128.6 (2C), 126.6, 126.5, 126.4, 123.6 (2C), 46.1, 42.7, 42.5, 40.0, 37.4, 34.2, 32.7, 18.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 375.1679; found: 375.1683.



Methyl 1-(2-methyl-3-(4-nitrophenyl)propanoyl)piperidine-4-carboxylate (3m) (1.0:0.85 mixture of rotamers): Colorless oil (46%, 30.7 mg); R_f = 0.41 (petroleum ether-EtOAc = 2:1); major: ^1H NMR (500 MHz, CDCl_3): δ = 8.14 (t, J = 8.1 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 4.39 (dd, J_1 = 38.1 Hz, J_2 = 13.5 Hz, 1H), 3.78-3.71 (m, 1H), 3.70 (s, 3H), 3.23-3.11 (m, 1H), 3.10-2.87 (m, 2H), 2.83-2.65 (m, 2H), 2.48 (qd, J_1 = 11.0 Hz, J_2 = 7.0 Hz, 1H), 1.93-1.73 (m, 2H), 1.69-1.53 (m, 1H), 1.40-1.30 (m, 1H), 1.19 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 174.2, 173.2, 148.1, 146.7, 129.9 (2C), 123.6 (2C), 51.9, 44.9, 41.4, 40.9, 40.2, 37.4, 28.6, 28.0, 18.3 ppm; minor: ^1H NMR (500 MHz, CDCl_3): δ = 8.14 (t, J = 8.1 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 4.39 (dd, J_1 = 38.1 Hz, J_2 = 13.5 Hz, 1H), 3.78-3.71 (m, 1H), 3.65 (s, 3H), 3.23-3.11 (m, 1H), 3.10-2.87 (m, 2H), 2.83-2.65 (m, 2H), 2.48 (qd, J_1 = 11.0 Hz, J_2 = 7.0 Hz, 1H), 1.93-1.73 (m, 2H), 1.69-1.53 (m, 1H), 1.40-1.30 (m, 1H), 1.19 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 174.5, 173.2, 148.2, 146.6, 129.9 (2C), 123.5 (2C), 51.9, 44.6, 41.2, 40.7, 30.0, 37.4, 28.4, 27.9, 18.1 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ 357.1421; found: 357.1427.

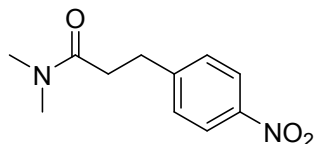


1-(4,4-difluoropiperidin-1-yl)-2-methyl-3-(4-nitrophenyl)propan-1-one (3n): Colorless oil (64%, 39.9 mg); R_f = 0.49 (petroleum ether-EtOAc = 1:1); ^1H NMR (500 MHz, CDCl_3): δ = 8.15 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 3.70 (dt, J_1 = 19.9 Hz, J_2 = 6.0 Hz, 2H), 3.55-3.44 (m, 2H), 3.19 (dd, J_1 = 13.3 Hz, J_2 = 8.5 Hz, 1H), 3.08-2.98 (m, 1H), 2.79 (dd, J_1 = 13.3 Hz, J_2 = 5.9 Hz, 1H), 2.05-1.73 (m, 4H), 1.22 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 173.4, 147.9, 146.8, 129.9 (2C), 123.7 (2C), 101.0 (t, J = 248.1 Hz), 42.3 (t, J = 7.4 Hz), 39.9, 38.9 (t, J = 8.3 Hz), 37.6, 29.7 (2C), 18.2 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{15}\text{H}_{18}\text{F}_2\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 335.1178; found: 335.1181.

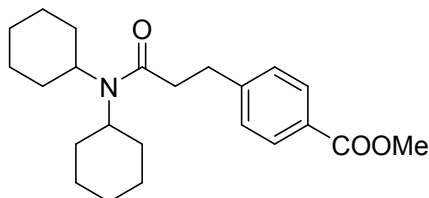


1-(4-(dimethylamino)piperidin-1-yl)-2-methyl-3-(4-nitrophenyl)propan-1-one (3o) (1:0.86 mixture of rotamers): Colorless oil (63%, 40.2 mg); R_f = 0.36 (EtOAc-MeOH = 1:1); major: ^1H NMR (500 MHz, CDCl_3): δ = 8.14 (d, J = 6.4 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 4.73 (d, J = 13.7 Hz, 1H), 3.90 (d, J = 14.6 Hz, 1H), 3.40 (s, 1H), 3.22-2.96 (m, 3H), 2.90-2.74 (m, 2H), 2.53 (s, 3H), 2.41 (s, 3H),

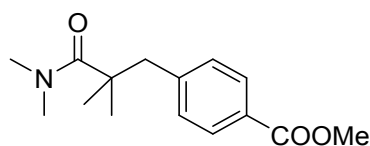
2.17-1.86 (m, 3H), 1.53-1.48 (m, 1H), 1.20 (d, $J = 6.8$ Hz, 3H).ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 173.2, 146.7, 130.1, 123.5$ (4C), 62.4, 44.3, 40.4, 40.0, 37.5, 29.7 (2C), 27.9, 26.4, 18.1 ppm; minor: ^1H NMR (500 MHz, CDCl_3): $\delta = 8.14$ (d, $J = 6.4$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 4.73 (d, $J = 13.7$ Hz, 1H), 3.90 (d, $J = 14.6$ Hz, 1H), 3.40 (s, 1H), 3.22-2.96 (m, 3H), 2.90-2.74 (m, 2H), 2.53 (s, 3H), 2.41 (s, 3H), 2.17-1.86 (m, 3H), 1.53-1.48 (m, 1H), 1.20 (d, $J = 6.8$ Hz, 3H). ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 173.2, 146.7, 129.9, 123.5$ (4C), 62.6, 44.1, 40.5, 39.9, 37.4, 29.7 (2C), 28.5, 26.2, 18.2 ppm; HRMS (ESI-TOF): calcd. $[\text{M}+\text{Na}]^+ \text{C}_{17}\text{H}_{25}\text{N}_3\text{O}_3\text{Na}$ 342.1788; found: 342.1793.



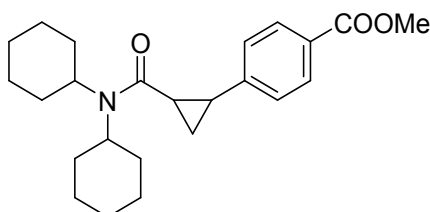
N,N-dimethyl-3-(4-nitrophenyl)propanamide (3p): Colorless oil (41%, 18.2 mg); $R_f = 0.32$ (petroleum ether-EtOAc = 1:2); ^1H NMR (500 MHz, CDCl_3): $\delta = 8.14$ (d, $J = 8.7$ Hz, 2H), 7.40 (d, $J = 8.8$ Hz, 2H), 3.09 (t, $J = 7.5$ Hz, 2H), 2.96 (d, $J = 9.8$ Hz, 6H), 2.66 (t, $J = 7.5$ Hz, 2H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 171.1, 149.5, 146.5, 129.3$ (2C), 123.6 (2C), 37.1, 35.5, 34.2, 30.9 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 245.0897; found: 245.0902.



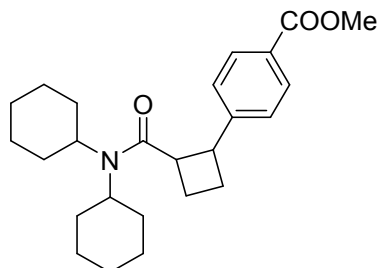
Methyl 4-(3-(dicyclohexylamino)-2-methyl-3-oxopropyl)benzoate (3q): Colorless oil (63%, 46.7 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); ^1H NMR (500 MHz, CDCl_3): $\delta = 7.97$ (d, $J = 8.3$ Hz, 2H), 7.30 (d, $J = 8.2$ Hz, 2H), 3.91 (s, 3H), 3.39 (s, 1H), 3.06-2.97 (m, 2H), 2.64-2.43 (m, 3H), 1.78 (s, 4H), 1.59 (d, $J = 10.7$ Hz, 4H), 1.46 (d, $J = 10.7$ Hz, 4H), 1.29-1.04 (m, 8H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 170.5, 167.1, 147.4, 129.8$ (2C), 128.6 (2C), 128.0, 57.8, 56.0, 52.0, 36.5, 31.7, 31.4 (2C), 30.2 (2C), 26.7 (2C), 26.0 (2C), 25.4, 25.2 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{33}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 394.2353, found: 394.2354.



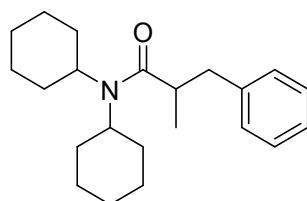
Methyl 4-(3-(dimethylamino)-2,2-dimethyl-3-oxopropyl)benzoate (3r): Colorless oil (87%, mono:di-arylation = 10:1, 45.7 mg); $R_f = 0.32$ (petroleum ether-EtOAc = 1:1); ^1H NMR (500 MHz, CDCl_3): $\delta = 7.94$ (d, $J = 8.3$ Hz, 2H), 7.20 (d, $J = 8.3$ Hz, 2H), 3.91 (s, 3H), 3.05 (s, 6H), 1.68 (s, 2H), 1.29 (s, 6H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 176.1, 167.1, 143.9, 130.2$ (2C), 129.3 (2C), 128.4, 52.0, 46.2, 43.6, 38.6 (2C), 26.5 (2C). HRMS (ESI-TOF): calcd. $\text{C}_{15}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 286.1414, found: 286.1425.



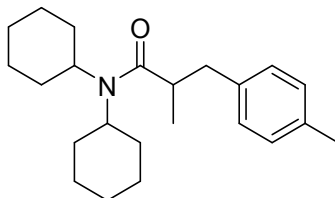
Methyl 4-(2-(dicyclohexylcarbamoyl)cyclopropyl)benzoate (3s): Solid (73%, 55.9 mg); $R_f = 0.45$ (petroleum ether-EtOAc = 3:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.89$ (d, $J = 7.0$ Hz, 2H), 7.20 (d, $J = 8.5$ Hz, 2H), 2.46 - 2.41 (m, 3H), 2.24 - 2.13 (m, 1H), 1.87 - 1.80 (m, 1H), 1.74 - 1.62 (m, 8H), 1.38 - 1.25 (m, 7H), 1.20 - 0.98 (m, 6H), 0.90 - 0.86 (m, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.0$, 167.1 , 166.9 , 143.9 , 129.2 (2C), 127.9 , 127.2 , 57.6 , 55.9 , 52.0 , 31.6 , 31.2 , 29.8 , 26.6 , 26.5 , 26.0 , 25.9 , 25.3 , 25.2 , 24.3 , 22.6 , 14.1 , 11.7 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{24}\text{H}_{33}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 406.2353, found: 406.2359.



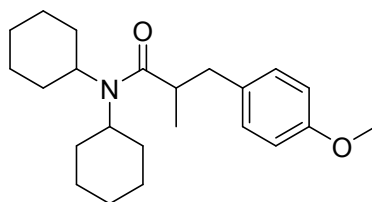
Methyl 4-(2-(dicyclohexylcarbamoyl)cyclobutyl)benzoate (3t): Solid (43%, 34.1 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.93$ (d, $J = 8.3$ Hz, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 3.90 (s, 4H), 3.56 (td, $J_1 = 8.9$ Hz, $J_2 = 5.2$ Hz, 1H), 2.93 - 2.82 (m, 1H), 2.78 - 2.72 (m, 1H), 2.66 - 2.44 (m, 2H), 2.42 - 2.24 (m, 3H), 2.12 (dq, $J_1 = 11.6$ Hz, $J_2 = 8.5$ Hz, 1H), 1.76 - 1.67 (m, 3H), 1.59 - 1.45 (m, 4H), 1.37 - 0.88 (m, 11H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 170.5$, 167.1 , 147.3 , 129.4 (2C), 128.5 , 128.4 (2C), 57.4 , 55.9 , 52.0 , 44.1 , 43.9 , 31.3 , 30.2 , 30.0 , 29.6 , 27.1 , 26.7 , 26.6 , 26.1 , 25.9 , 25.4 , 25.2 , 20.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{25}\text{H}_{35}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 420.2509; found: 420.2518.



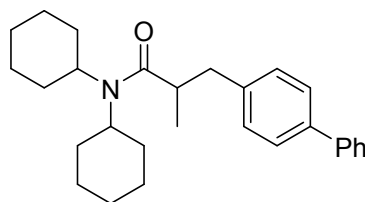
N,N-dicyclohexyl-2-methyl-3-phenylpropanamide (3u): Solid (47%, mono-:di-arylation = 10:1, 30.7 mg); $R_f = 0.63$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.30$ - 7.22 (m, 2H), 7.19 (d, $J = 7.3$ Hz, 3H), 3.36 (s, 1H), 3.06 - 2.86 (m, 2H), 2.62 (dd, $J_1 = 12.9$ Hz, $J_2 = 5.9$ Hz, 1H), 2.51 (s, 1H), 1.83 - 1.10 (m, 23H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.1$, 140.5 , 129.1 (2C), 128.2 (2C), 126.0 , 57.5 , 56.2 , 41.0 , 39.2 , 31.8 , 30.9 , 30.2 , 30.1 , 26.7 (2C), 26.1 (2C), 25.5 , 25.3 , 18.5 . HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{33}\text{NONa}$ $[\text{M}+\text{Na}]^+$ 350.2454, found: 350.2459.



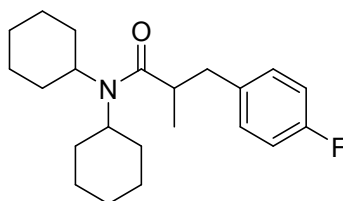
N,N-dicyclohexyl-2-methyl-3-(p-tolyl)propanamide (3v): Solid (51%, mono-:di-arylation = 24:1, 34.8 mg); $R_f = 0.63$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.07$ (s, 4H), 3.36 (s, 1H), 2.91 (ddd, $J_1 = 34.0$ Hz, $J_2 = 13.4$ Hz, $J_3 = 7.7$ Hz, 2H), 2.63 - 2.47 (m, 2H), 2.31 (s, 3H), 1.77 - 1.00 (m, 23H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.0$, 137.4 , 135.4 , 129.0 (2C), 128.9 (2C), 57.7 , 56.2 , 40.5 , 39.1 , 31.6 , 31.0 , 30.2 , 30.1 , 26.7 (2C), 26.1 (2C), 25.5 , 25.3 , 21.0 , 18.4 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{35}\text{NONa}$ $[\text{M}+\text{Na}]^+$ 364.2611, found: 364.2618.



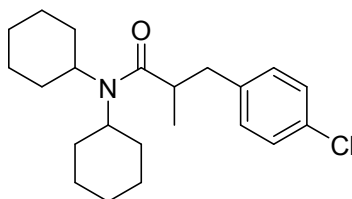
N,N-dicyclohexyl-3-(4-methoxyphenyl)-2-methylpropanamide (3w): Solid (52%, 37.1 mg); $R_f = 0.60$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.11$ (d, $J = 7.9$ Hz, 2H), 6.81 (d, $J = 7.9$ Hz, 2H), 3.79-3.78 (m, 3H), 3.38 (s, 1H), 3.07-2.81 (m, 2H), 2.67-2.42 (m, 2H), 1.90-1.54 (m, 8H), 1.50-0.97 (m, 15H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 175.0, 158.0, 132.7, 130.1$ (2C), 113.6 (2C), 57.8, 56.2, 55.3, 40.1, 39.0, 31.7, 31.1, 30.2, 30.1, 26.7 (2C), 26.2 (2C), 25.5, 25.3, 18.4 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{35}\text{NO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 380.2560; found: 380.2567.



3-([1,1'-Biphenyl]-4-yl)-N,N-dicyclohexyl-2-methylpropanamide (3x): Solid (50%, 40.3 mg); $R_f = 0.57$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.60$ -7.56 (m, 2H), 7.51 (d, $J = 8.2$ Hz, 2H), 7.47-7.42 (m, 2H), 7.35 (tt, $J_1 = 6.9$ Hz, $J_2 = 1.2$ Hz, 1H), 7.28 (d, $J = 8.1$ Hz, 2H), 3.37 (s, 1H), 3.12-2.93 (m, 2H), 2.73-2.50 (m, 2H), 1.84-1.57 (m, 8H), 1.48-1.05 (m, 15H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.4, 141.1, 139.6, 139.1, 129.6$ (2C), 128.7 (2C), 127.0, 126.9 (4C), 57.6, 56.1, 40.7, 38.9, 31.7, 31.1, 30.2, 30.1, 26.7 (2C), 26.1 (2C), 25.5, 25.3, 18.7 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{28}\text{H}_{37}\text{NO}$ Na $[\text{M}+\text{Na}]^+$ 426.2767; found: 426.2780.

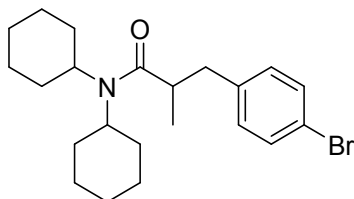


N,N-dicyclohexyl-3-(4-fluorophenyl)-2-methylpropanamide (3y): Solid (65%, 44.9 mg); $R_f = 0.50$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.14$ (dd, $J_1 = 8.4$ Hz, $J_2 = 5.6$ Hz, 2H), 6.94 (t, $J = 8.7$ Hz, 2H), 3.35 (s, 1H), 3.08-2.82 (m, 2H), 2.69-2.38 (m, 2H), 1.88-1.52 (m, 8H), 1.49-0.84 (m, 15H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.9, 161.5$ (d, $J = 243.4$ Hz), 136.3-136.2 (m), 130.6 (d, $J = 7.7$ Hz, 2C), 114.8 (d, $J = 21.2$ Hz, 2C), 57.8, 56.3, 40.1, 39.2, 31.7, 31.2, 30.3, 30.1, 26.7 (2C), 26.1 (2C), 25.5, 25.3, 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{32}\text{FNONa}$ $[\text{M}+\text{Na}]^+$ 368.2360, found: 368.2370.

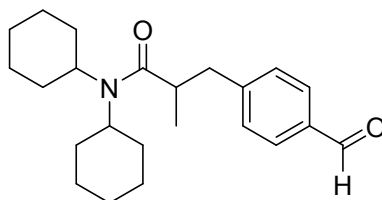


3-(4-Chlorophenyl)-N,N-dicyclohexyl-2-methylpropanamide (3z): Solid (76%, 54.9 mg); $R_f = 0.45$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.23$ (d, $J = 7.7$ Hz, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 3.34 (s, 1H), 3.01 (dd, $J_1 = 22.9$ Hz, $J_2 = 15.2$ Hz, 3H), 2.63-2.41 (m, 2H), 1.96-0.76 (m,

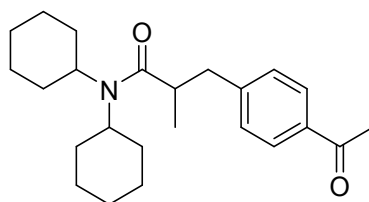
22H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 174.7, 139.0, 131.8, 130.5 (2C), 128.2 (2C), 57.7, 56.2, 40.2, 38.9, 31.6, 31.2, 30.2, 30.0, 26.6 (2C), 26.1 (2C), 25.5, 25.2, 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{32}\text{ClNO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 384.2065, found: 384.2073.



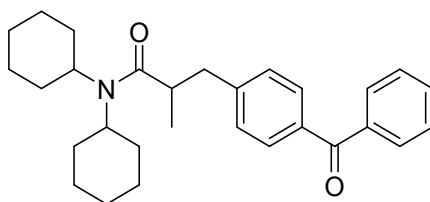
3-(4-Bromophenyl)-N,N-dicyclohexyl-2-methylpropanamide (3aa): Solid (76%, 61.6 mg); R_f = 0.50 (petroleum ether-EtOAc = 7:1); ^1H NMR (500 MHz, CDCl_3): δ = 7.38 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 3.33 (s, 1H), 2.98 (dd, J_1 = 13.1 Hz, J_2 = 8.6 Hz, 1H), 2.93-2.82 (m, 1H), 2.56 (dd, J_1 = 13.1 Hz, J_2 = 5.5 Hz, 1H), 2.48 (s, 1H), 1.76 (q, J_1 = 15.2 Hz, J_2 = 13.6 Hz, 5H), 1.63-1.60 (m, 3H), 1.48-1.40 (m, 3H), 1.26-1.02 (m, 12H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 175.0, 139.6, 131.2 (2C), 131.0 (2C), 119.9, 57.8, 56.2, 40.3, 39.0, 31.7, 31.6, 30.2, 30.1, 26.7 (2C), 26.1 (2C), 25.5, 25.3, 18.7 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{32}\text{BrNO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 428.1559; found: 428.1551.



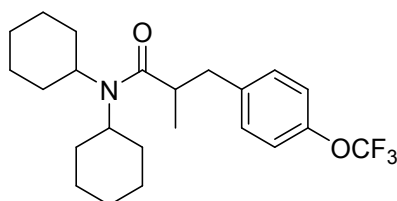
N,N-dicyclohexyl-3-(4-formylphenyl)-2-methylpropanamide (3ab): Solid (47%, 33.4 mg); R_f = 0.31 (petroleum ether-EtOAc = 7:1); ^1H NMR (500 MHz, CDCl_3): δ = 9.97 (d, J = 1.9 Hz, 1H), 7.79 (dd, J_1 = 8.1 Hz, J_2 = 1.8 Hz, 2H), 7.36 (dd, J_1 = 8.1 Hz, J_2 = 1.6 Hz, 2H), 3.35 (s, 1H), 3.14 (dd, J_1 = 13.0 Hz, J_2 = 9.0 Hz, 1H), 2.94 (dt, J_1 = 8.8 Hz, J_2 = 6.3 Hz, 1H), 2.69 (dd, J_1 = 13.1 Hz, J_2 = 5.5 Hz, 1H), 2.47 (s, 1H), 1.75-1.40 (m, 10H), 1.27-0.99 (m, 13H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 192.0, 169.7, 148.2, 134.7, 129.9 (2C), 129.8 (2C), 57.8, 56.4, 41.0, 38.8, 31.6, 31.2, 30.2, 30.0, 26.6 (2C), 26.1 (2C), 25.4, 25.2, 18.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{33}\text{NO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 378.2404, found: 378.2415.



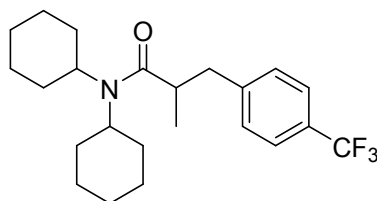
3-(4-Acetylphenyl)-N,N-dicyclohexyl-2-methylpropanamide (3ac): Solid (53%, 39.1 mg); R_f = 0.42 (petroleum ether-EtOAc = 3:1); ^1H NMR (500 MHz, CDCl_3): δ = 7.83 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 3.31 (s, 1H), 3.08-3.04 (m, 1H), 2.90 (q, J_1 = 7.2 Hz, J_2 = 6.3 Hz, 1H), 2.65-2.61 (m, 1H), 2.54-2.44 (m, 4H), 1.71-0.98 (m, 23H) ppm; ^{13}C NMR (126 MHz, CDCl_3): δ = 197.7, 174.2, 146.3, 135.1, 129.3 (2C), 128.2 (2C), 57.7, 56.1, 40.7, 38.6, 31.5, 31.0, 30.1, 29.9, 26.5, 26.4 (2C), 26.0 (2C), 25.3, 25.1, 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{24}\text{H}_{35}\text{NO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 392.2560; found: 392.2577.



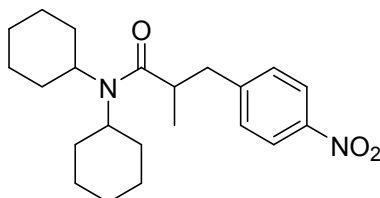
3-(4-Benzoylphenyl)-N,N-dicyclohexyl-2-methylpropanamide (3ad): Solid (42%, 36.2 mg); $R_f = 0.57$ (petroleum ether-EtOAc = 3:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.80\text{-}7.74$ (m, 2H), 7.73 (d, $J = 8.2$ Hz, 2H), 7.61-7.57 (m, 1H), 7.48 (t, $J = 7.7$ Hz, 2H), 7.33-7.30 (m, 2H), 3.39 (s, 1H), 3.13 (dd, $J_1 = 13.0$ Hz, $J_2 = 8.8$ Hz, 1H), 3.02-2.91 (m, 1H), 2.70 (dd, $J_1 = 13.0$ Hz, $J_2 = 5.6$ Hz, 1H), 2.49 (s, 1H), 1.74 (s, 5H), 1.61 (t, $J = 15.7$ Hz, 3H), 1.53-1.40 (m, 2H), 1.29-1.03 (m, 13H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3) $\delta = 196.4, 174.5, 145.8, 137.9, 135.4, 132.2, 130.2$ (2C), 129.9 (2C), 129.1 (2C), 128.2 (2C), 57.9, 56.4, 40.8, 38.9, 31.6, 31.1, 30.2, 30.1, 26.6 (2C), 26.1 (2C), 25.4, 25.2, 18.8 ppm; HRMS (ESI-TOF) m/z : calcd. for $\text{C}_{29}\text{H}_{37}\text{NO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 454.2717; found: 454.2738.



N,N-dicyclohexyl-2-methyl-3-(4-(trifluoromethoxy)phenyl)propanamide (3ae): Solid (70%, mono-:di-arylation = 6:1, 57.5 mg); $R_f = 0.50$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.21$ (d, $J = 8.3$ Hz, 2H), 7.10 (d, $J = 8.1$ Hz, 2H), 3.31 (s, 1H), 3.09-2.99 (m, 1H), 2.90 (td, $J_1 = 10.7$ Hz, $J_2 = 8.8$ Hz, $J_3 = 6.4$ Hz, 1H), 2.68-2.39 (m, 2H), 1.85-1.34 (m, 10H), 1.30-0.82 (m, 13H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.5, 147.6, 139.4, 130.5$ (2C), 120.8 (2C), 120.5 (q, $J = 257.2$ Hz), 57.8, 56.2, 40.3, 39.0, 31.7, 31.0, 30.2, 30.0, 26.6 (2C), 26.1 (2C), 25.5, 25.2, 18.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{32}\text{F}_3\text{NO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 434.2277, found: 434.2296.

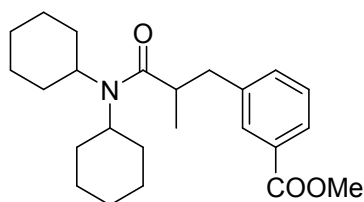


N,N-dicyclohexyl-2-methyl-3-(4-(trifluoromethyl)phenyl)propanamide (3af): Solid (73%, mono-:di-arylation = 7:1, 57.7 mg); $R_f = 0.51$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.51$ (d, $J = 7.9$ Hz, 2H), 7.30 (d, $J = 7.9$ Hz, 2H), 3.29 (s, 1H), 3.09 (dd, $J_1 = 13.1$ Hz, $J_2 = 9.0$ Hz, 1H), 2.98-2.86 (m, 1H), 2.67 (dd, $J_1 = 13.1$ Hz, $J_2 = 5.5$ Hz, 1H), 2.47 (s, 1H), 1.91-1.59 (m, 8H), 1.46-0.91 (m, 15H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.4, 144.8, 129.5$ (2C), 128.5 (q, $J = 32.3$ Hz), 125.1 (q, $J = 3.8$ Hz), 124.3 (q, $J = 272.2$ Hz), 57.8, 56.3, 40.7, 38.9, 31.6, 31.1, 30.2, 30.0, 26.6, 26.1 (2C), 26.0 (2C), 25.4, 25.2, 18.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{32}\text{F}_3\text{NONa}$ $[\text{M}+\text{Na}]^+$ 418.2328, found: 418.2349.

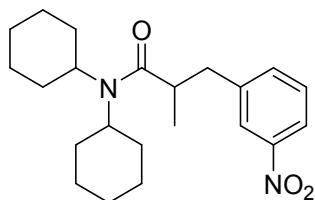


N,N-dicyclohexyl-2-methyl-3-(4-nitrophenyl)propanamide (3ag): Solid (63%, 46.9 mg); $R_f = 0.30$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 8.07\text{-}7.96$ (m, 2H), 7.34 (d, $J = 8.2$ Hz, 2H), 3.35 (s, 1H), 3.14 (dd, $J_1 = 13.4$ Hz, $J_2 = 9.3$ Hz, 1H), 2.99-2.88 (m, 1H), 2.67 (dd, $J_1 = 13.4$ Hz, $J_2 = 5.0$ Hz, 1H), 2.40 (d, $J = 41.9$ Hz, 1H), 1.80-1.01 (m, 23H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.7, 148.6, 146.4, 129.9$ (2C), 123.3 (2C), 57.8, 56.2, 40.4, 38.8, 31.5, 31.2, 30.1, 29.9, 26.5 (2C), 26.0 (2C), 25.3, 25.1, 18.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 395.2305; found:

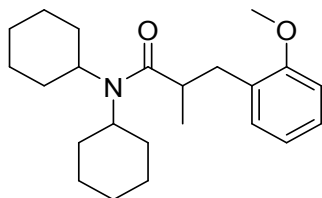
395.2322.



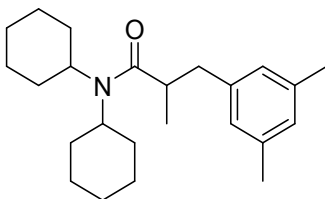
Methyl 3-(3-(dicyclohexylamino)-2-methyl-3-oxopropyl)benzoate (3ah): Solid (74%, mono-diarylation = 32:1, 56.9 mg); $R_f = 0.51$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.89\text{--}7.82$ (m, 2H), 7.37 (d, $J = 7.6$ Hz, 1H), 7.31 (t, $J = 7.6$ Hz, 1H), 3.88 (d, $J = 0.8$ Hz, 3H), 3.35 (s, 1H), 3.06 (t, $J = 11.0$ Hz, 1H), 2.93 (h, $J = 6.2$ Hz, 1H), 2.65 (dd, $J_1 = 13.1$ Hz, $J_2 = 5.5$ Hz, 1H), 2.46 (s, 1H), 1.91-1.51 (m, 7H), 1.46-0.81 (m, 16H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 174.4, 167.1, 140.9, 134.0, 130.0, 130.0, 128.2, 127.3, 57.7, 56.2, 51.9, 40.6, 38.8, 31.6, 31.0, 30.2, 29.9, 26.6$ (2C), 26.0 (2C), 25.4, 25.2, 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{24}\text{H}_{35}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 408.2509, found: 408.2528.



N,N-dicyclohexyl-2-methyl-3-(3-nitrophenyl)propanamide (3ai): Solid (79%, 58.8 mg); $R_f = 0.49$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 8.07\text{--}7.96$ (m, 2H), 7.50 (d, $J = 7.6$ Hz, 1H), 7.38 (t, $J = 7.8$ Hz, 1H), 3.35 (s, 1H), 3.14 (dd, $J_1 = 13.4$ Hz, $J_2 = 9.3$ Hz, 1H), 2.99-2.88 (m, 1H), 2.67 (dd, $J_1 = 13.4$ Hz, $J_2 = 5.0$ Hz, 1H), 2.40 (d, $J = 41.9$ Hz, 1H), 1.82-1.33 (m, 10H), 1.30-0.91 (m, 13H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 173.7, 148.0, 142.6, 135.6, 128.9, 123.5, 121.0, 57.7, 56.2, 40.0, 38.6, 31.5, 31.2, 30.1, 29.8, 26.5$ (2C), 25.9 (2C), 25.3, 25.1, 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 395.2305; found: 395.2324.

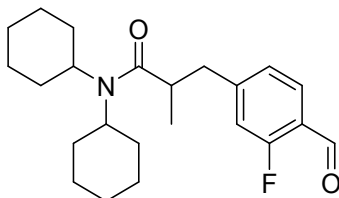


N,N-dicyclohexyl-3-(2-methoxyphenyl)-2-methylpropanamide (3aj): Solid (41%, 29.3 mg); $R_f = 0.31$ (petroleum ether-EtOAc = 10:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.22\text{--}7.11$ (m, 2H), 6.90-6.83 (m, 2H), 3.86 (s, 3H), 3.14-3.08 (m, 1H), 2.88 (s, 1H), 2.69 (s, 1H), 2.52 (s, 1H), 1.86-1.03 (m, 24H).ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 172.5, 157.4, 131.7, 128.3, 127.4$ (2C), 120.3 (2C), 109.8, 57.4, 56.1, 55.1, 36.1, 31.7, 30.3, 30.1, 26.7 (2C), 26.1 (2C), 25.5, 25.3, 18.1 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{36}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 358.2741; found: 358.2731.

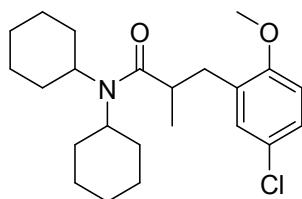


N,N-dicyclohexyl-3-(3,5-dimethylphenyl)-2-methylpropanamide (3ak): Colorless oil (40%, mono-diarylation = 19:1), 28.4 mg); $R_f = 0.51$ (petroleum ether-EtOAc = 7:1); $^1\text{H NMR}$ (500 MHz, CDCl_3):

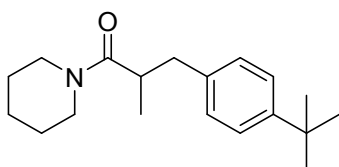
$\delta = 6.81$ (s, 3H), 3.37 (s, 1H), 2.92 (d, $J = 5.9$ Hz, 2H), 2.56 (q, $J_1 = 8.3$ Hz, $J_2 = 7.3$ Hz, 2H), 2.27 (s, 6H), 1.87-1.39 (m, 10H), 1.30-0.84 (m, 13H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 175.0$, 140.2, 137.4 (2C), 127.4, 126.9 (2C), 57.7, 56.2, 40.9, 38.8, 31.6, 30.9, 30.0, 29.8, 26.6 (2C), 26.0 (2C), 25.4, 25.2, 21.1 (2C), 18.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{24}\text{H}_{37}\text{NONa}$ $[\text{M}+\text{Na}]^+$ 378.2767; found: 378.2775.



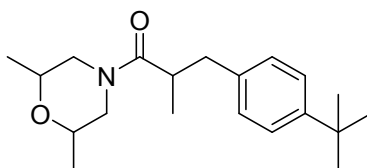
N,N-dicyclohexyl-3-(3-fluoro-4-formylphenyl)-2-methylpropanamide (3al): Solid (51%, 38.0 mg); $R_f = 0.51$ (petroleum ether-EtOAc = 3:1); ^1H NMR (500 MHz, CDCl_3): $\delta = 10.29$ (s, 1H), 7.75 (t, $J = 7.6$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 1H), 7.04-6.98 (m, 1H), 3.35 (s, 1H), 3.13 (dd, $J_1 = 13.1$ Hz, $J_2 = 9.1$ Hz, 1H), 3.00-2.86 (m, 1H), 2.64 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.2$ Hz, 1H), 2.45 (s, 1H), 1.83-1.52 (m, 8H), 1.49-0.98 (m, 15H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 186.9$ (d, $J = 6.3$ Hz), 173.8, 164.6 (d, $J = 258.8$ Hz), 151.1, 128.4 (d, $J = 2.3$ Hz), 125.5, 122.2 (d, $J = 8.1$ Hz), 117.0 (d, $J = 20.5$ Hz), 57.8, 56.3, 40.7, 38.6, 31.5, 31.3, 30.2, 30.0, 26.6 (2C), 26.1 (2C), 25.4, 25.2, 18.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{32}\text{FNO}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 396.2309; found: 396.2318.



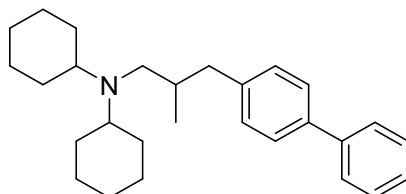
3-(5-chloro-2-methoxyphenyl)-N,N-dicyclohexyl-2-methylpropanamide (3am): Solid (72%, 56.3 mg); $R_f = 0.35$ (petroleum ether-EtOAc = 10:1); ^1H NMR (500 MHz, CDCl_3): $\delta = 7.14$ -7.07 (m, 2H), 6.73 (d, $J = 8.6$ Hz, 1H), 3.82 (s, 3H), 3.42 (s, 1H), 3.06-3.01 (m, 1H), 2.87-2.77 (m, 1H), 2.58 (m, 2H), 1.84-0.96 (m, 23H) ppm; ^{13}C NMR (126 MHz, CDCl_3): $\delta = 175.2$, 156.0, 131.2 (2C), 130.3, 126.9 (2C), 125.1, 110.9, 57.6, 56.2, 55.4, 31.7, 31.0, 30.3, 30.1, 26.7 (2C), 26.1 (2C), 25.5, 25.3, 18.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{35}\text{ClNO}_2$ $[\text{M}+\text{H}]^+$ 392.2351; found: 392.2338.



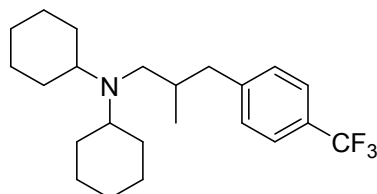
3-(4-(tert-Butyl)phenyl)-2-methyl-1-(piperidin-1-yl)propan-1-one (3an): Colorless oil (41%, mono-di-arylation = 10:1, 23.6 mg); $R_f = 0.38$ (petroleum ether-EtOAc = 4:1); ^1H NMR (500 MHz, CDCl_3) $\delta = 7.30$ (d, $J = 8.3$ Hz, 2H), 7.12 (d, $J = 8.2$ Hz, 2H), 3.76 (dd, $J_1 = 13.0$ Hz, $J_2 = 6.2$ Hz, 1H), 3.30 (qt, $J_1 = 10.6$ Hz, $J_2 = 5.0$ Hz, 2H), 3.24-3.19 (m, 1H), 3.09-2.92 (m, 2H), 2.67-2.61 (m, 1H), 1.78 (s, 1H), 1.53-1.49 (m, 2H), 1.40-1.34 (m, 2H), 1.31 (s, 9H), 1.16 (d, $J = 6.5$ Hz, 3H), 1.01-0.92 (m, 1H) ppm; ^{13}C NMR (126 MHz, CDCl_3) $\delta = 174.2$, 148.9, 137.2, 128.7 (2C), 125.1 (2C), 46.6, 42.9, 40.2, 37.4, 34.3, 31.4 (3C), 26.2, 25.5, 24.5, 17.9 ppm; HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd. for $\text{C}_{19}\text{H}_{29}\text{NONa}$ 310.2141; found: 310.2147.



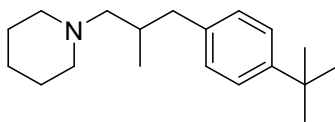
3-(4-(tert-Butyl)phenyl)-1-(2,6-dimethylmorpholino)-2-methylpropan-1-one (3ao) (1.0:0.55 mixture of rotamers): Colorless oil (37%, mono-:di-arylation = 12:1, 23.5 mg); $R_f = 0.38$ (petroleum ether-EtOAc = 4:1); major: $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 7.30$ (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 8.2$ Hz, 2H), 4.47 (d, $J = 13.2$ Hz, 1H), 3.57-2.51 (m, 6H), 2.31-2.15 (m, 2H), 1.30 (s, 9H), 1.21 (d, $J = 6.5$ Hz, 3H), 1.12 (d, $J = 6.2$ Hz, 3H), 0.94 (d, $J = 6.2$ Hz, 3H).ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3) $\delta = 174.0, 149.4, 137.0, 128.8$ (2C), 125.3 (2C), 71.7, 71.1, 51.3, 47.2, 40.8, 37.5, 34.4, 31.4 (3C), 18.7, 18.5, 18.0 ppm; minor: $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 7.30$ (d, $J = 8.4$ Hz, 2H), 7.09 (d, $J = 7.9$ Hz, 2H), 4.47 (d, $J = 13.2$ Hz, 1H), 3.57-2.51 (m, 6H), 2.31-2.15 (m, 2H), 1.31 (s, 9H), 1.18 (d, $J = 2.7$ Hz, 3H), 1.17 (d, $J = 2.9$ Hz, 3H), 1.12 (d, $J = 6.2$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3) $\delta = 174.5, 149.2, 136.8, 128.7$ (2C), 125.2 (2C), 71.9, 71.1, 50.9, 47.0, 39.9, 37.6, 34.4, 31.4 (3C), 18.7, 18.3, 18.0 ppm; HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd. for $\text{C}_{20}\text{H}_{31}\text{NO}_2\text{Na}$ 340.2247; found: 340.2251.



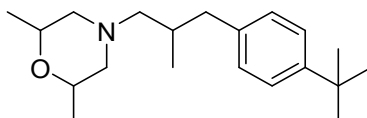
N-(3-([1,1'-biphenyl]-4-yl)-2-methylpropyl)-N-cyclohexylcyclohexanamine (4): Colorless oil (96%, 37.3 mg); $R_f = 0.58$ (petroleum ether-EtOAc = 10:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.61$ (d, $J = 7.3$ Hz, 2H), 7.53 (d, $J = 8.1$ Hz, 2H), 7.45 (t, $J = 7.7$ Hz, 2H), 7.34 (t, $J = 7.4$ Hz, 1H), 7.25 (d, $J = 7.8$ Hz, 2H), 3.06 (d, $J = 9.6$ Hz, 1H), 2.48 (d, $J = 39.6$ Hz, 4H), 2.10 (t, $J = 11.5$ Hz, 1H), 1.69 (dd, $J_1 = 62.8$ Hz, $J_2 = 17.3$ Hz, 9H), 1.27 (d, $J = 16.5$ Hz, 10H), 1.13-1.05 (m, 2H), 0.84 (d, $J = 6.6$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 141.7, 141.3, 138.3, 129.5$ (2C), 128.7 (2C), 126.9 (2C), 126.9, 126.8 (2C), 58.1, 52.9, 41.1, 35.4, 32.4 (2C), 32.1 (2C), 29.7, 26.8 (2C), 26.7 (2C), 26.4 (2C), 17.8 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{28}\text{H}_{40}\text{N}$ $[\text{M}+\text{H}]^+$ 390.3155; found: 390.3160.



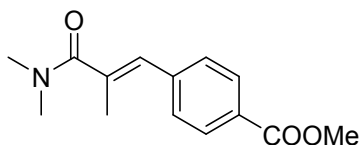
N-cyclohexyl-N-(2-methyl-3-(4-(trifluoromethyl)phenyl)propyl)cyclohexanamine (5): Colorless oil (94%, 35.8 mg); $R_f = 0.56$ (petroleum ether-EtOAc = 10:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.53$ (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.2$ Hz, 2H), 3.10 (d, $J = 15.8$ Hz, 1H), 2.54-2.32 (m, 4H), 2.14-2.02 (m, 1H), 1.78-1.56 (m, 10H), 1.28-1.17 (m, 8H), 1.07 (dd, $J_1 = 16.9$ Hz, $J_2 = 7.8$ Hz, 2H), 0.93-0.83 (m, 1H), 0.78 (d, $J = 6.2$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 146.9, 129.4$ (2C), 127.9 (q, $J = 6.1$ Hz), 125.0 (q, $J = 3.9$ Hz), 124.5 (q, $J = 271.6$ Hz, 2C), 58.1, 52.8, 41.3, 35.5, 32.5 (2C), 32.0 (2C), 29.7, 26.8 (2C), 26.7 (2C), 26.4 (2C), 17.6 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{23}\text{H}_{35}\text{F}_3\text{N}$ $[\text{M}+\text{H}]^+$ 382.2716; found: 382.2721.



1-(3-(4-(tert-Butyl)phenyl)-2-methylpropyl)piperidine (6): Colorless oil (39%, 10.6 mg); $R_f = 0.51$ (EtOAc-MeOH = 4:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.30$ (d, $J = 8.3$ Hz, 2H), 7.10 (d, $J = 8.2$ Hz, 2H), 2.80 (dd, $J_1 = 13.5$ Hz, $J_2 = 4.8$ Hz, 1H), 2.43-2.26 (m, 5H), 2.23-2.19 (m, 2H), 1.99 (dq, $J_1 = 13.6$ Hz, $J_2 = 6.9$ Hz, 1H), 1.61 (p, $J = 5.5$ Hz, 4H), 1.45 (d, $J = 5.4$ Hz, 2H), 1.33 (s, 9H), 0.87 (d, $J = 6.6$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 148.3, 138.2, 128.9$ (2C), 124.9 (2C), 65.8, 55.0 (2C), 40.9, 34.3, 32.4, 31.5 (3C), 29.7, 26.0, 24.6, 18.3 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{19}\text{H}_{32}\text{N}$ $[\text{M}+\text{H}]^+$ 274.2529; found: 274.2536.



4-(3-(4-(tert-Butyl)phenyl)-2-methylpropyl)-2,6-dimethylmorpholine (7): Colorless oil (35%, 10.6 mg); $R_f = 0.41$ (petroleum ether-EtOAc = 1:5); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.31$ (d, $J = 8.3$ Hz, 2H), 7.10 (d, $J = 8.3$ Hz, 2H), 3.77 (s, 2H), 2.76 (dd, $J_1 = 13.4$ Hz, $J_2 = 4.9$ Hz, 3H), 2.50-1.99 (m, 5H), 1.74 (s, 1H), 1.33 (s, 9H), 1.17 (d, $J = 1.4$ Hz, 3H), 1.16 (d, $J = 1.4$ Hz, 3H), 0.91 (d, $J = 6.6$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 148.6, 128.8$ (2C), 125.0 (2C), 111.5, 71.3, 64.8, 40.9, 34.3, 31.9, 31.4 (2C), 30.3, 29.7 (2C), 29.3, 22.7, 19.1, 14.1 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{20}\text{H}_{34}\text{NO}$ $[\text{M}+\text{H}]^+$ 304.2635; found: 304.2641.

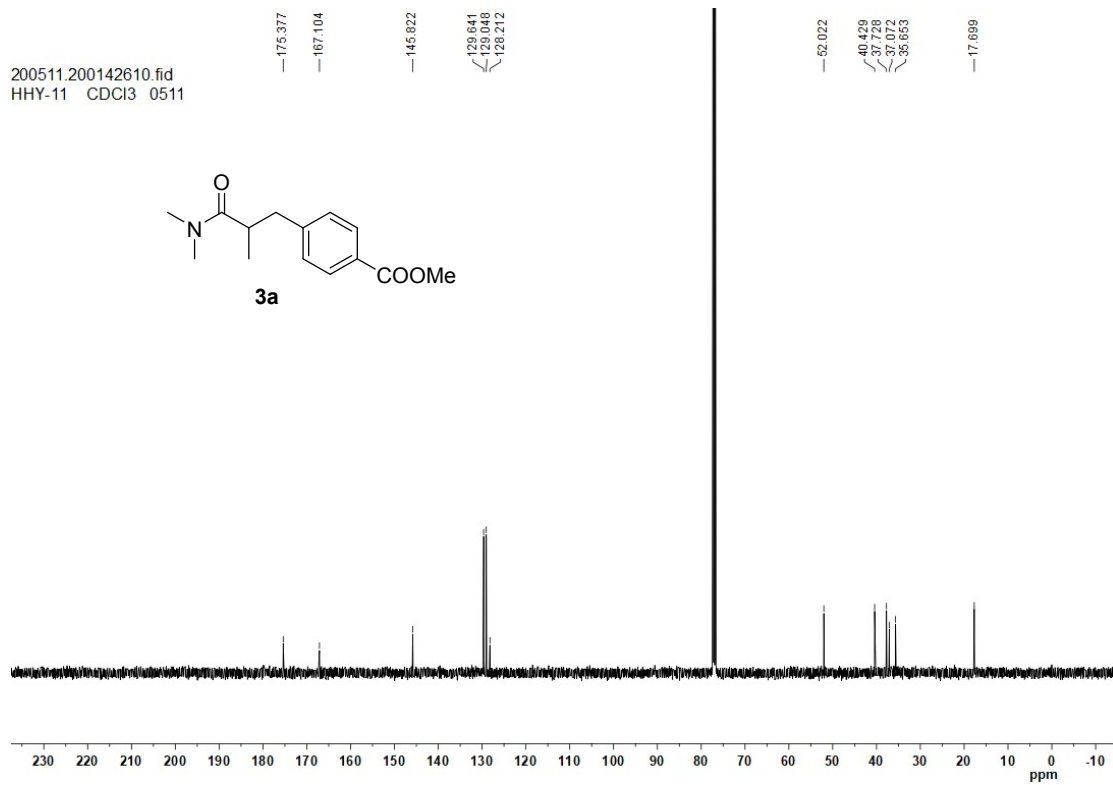
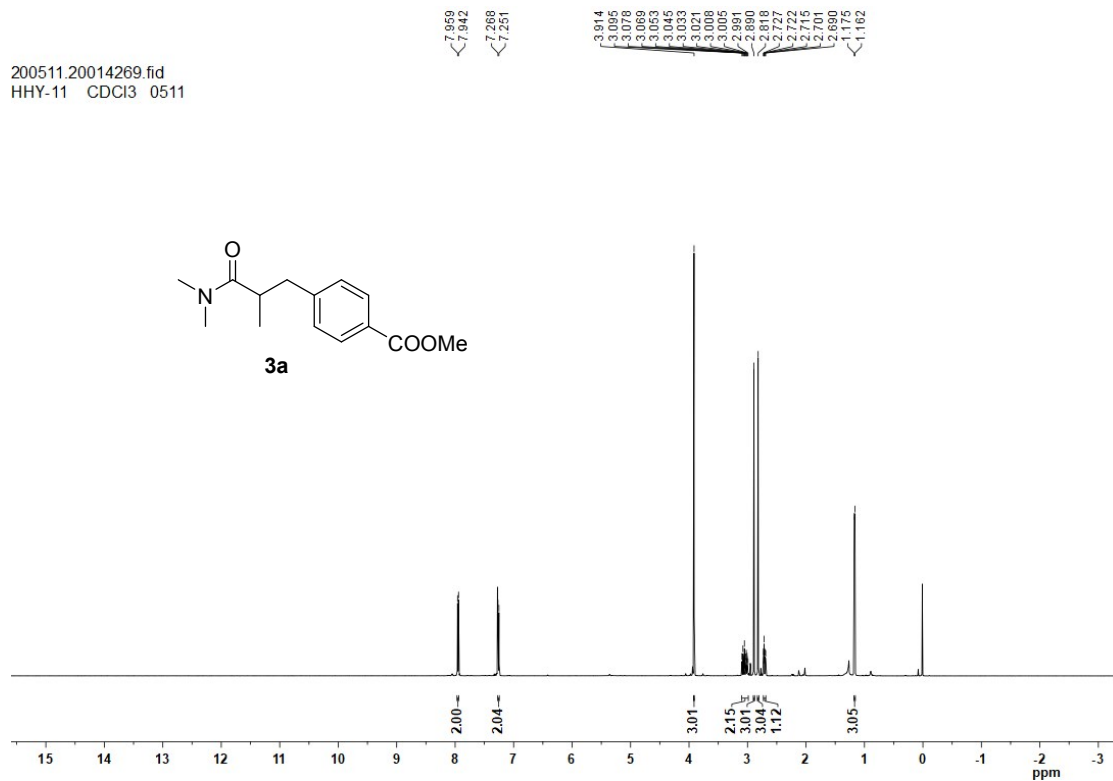


Methyl (E)-4-(3-(dimethylamino)-2-methyl-3-oxoprop-1-en-1-yl)benzoate (3a¹): Solid (88%, 43.5 mg); $R_f = 0.33$ (petroleum ether-EtOAc = 1:1); $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.95$ (d, $J = 8.4$ Hz, 2H), 7.31 (d, $J = 8.3$ Hz, 2H), 6.40 (s, 1H), 3.90 (s, 3H), 2.94 (s, 3H), 2.70 (s, 3H), 2.11 (d, $J = 1.5$ Hz, 3H) ppm; $^{13}\text{C NMR}$ (126 MHz, CDCl_3): $\delta = 171.6, 166.8, 140.6, 135.7, 129.8$ (2C), 128.9 (2C), 127.3, 126.6, 52.1, 37.0, 34.2, 22.1 ppm; HRMS (ESI-TOF): calcd. $\text{C}_{14}\text{H}_{17}\text{NO}_3$ $[\text{M}+\text{Na}]^+$ 270.1101; found: 270.1107.

4. References

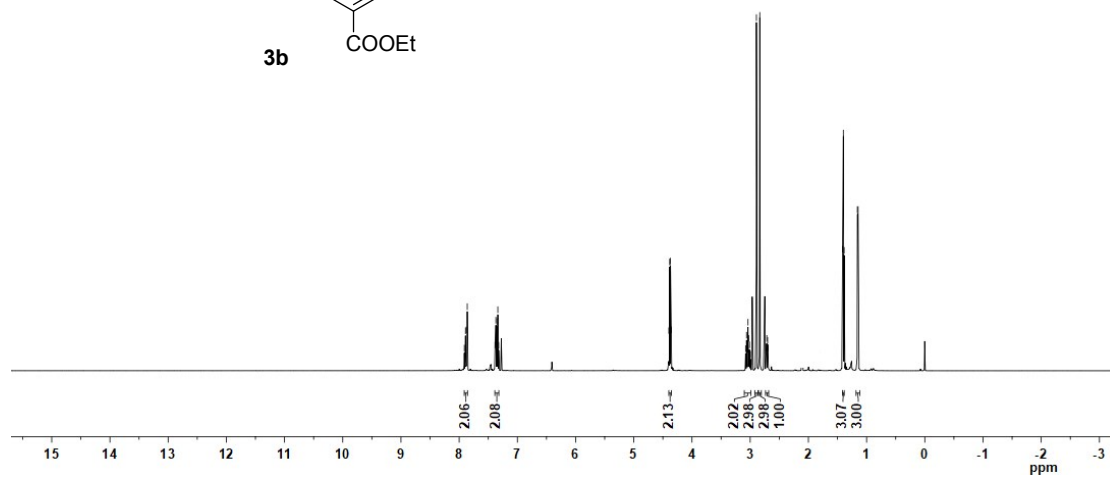
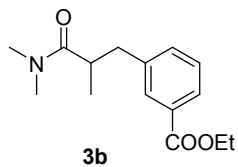
1. Mao, Y.-J., Lou, S.-J., Hao, H.-Y. and Xu, D.-Q. *Angew. Chem. Int. Ed.* 2018, **57**, 14085.
2. Park, H., Li, Y., and Yu, J.-Q. *Angew. Chem. Int. Ed.* 2019, **58**, 11424.
3. Yang, W.-J., Ling, B., Hu, B.-W., Yin, H.-L., Mao, J.-Y and Walsh, P. J. *Angew. Chem. Int. Ed.* 2020, **59**, 161.
4. a) Chen, M. Liu, F. and Dong, G. *Angew. Chem. Int. Ed.*, 2018, **57**, 3815; b) Deng, Y. Gong, He, W. J. and Yu, J.-Q. *Angew. Chem. Int. Ed.*, 2014, **53**, 6692.

5. NMR Spectra



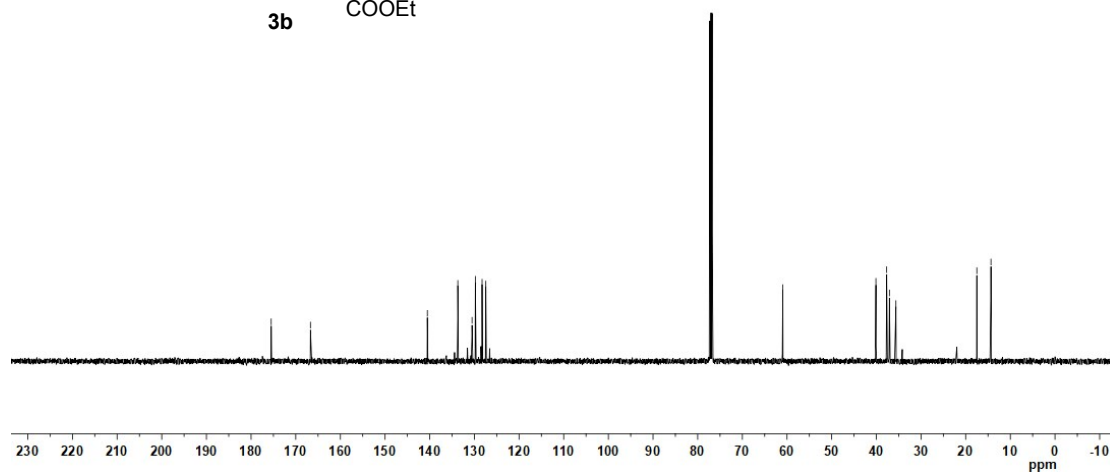
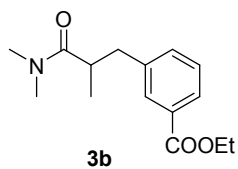
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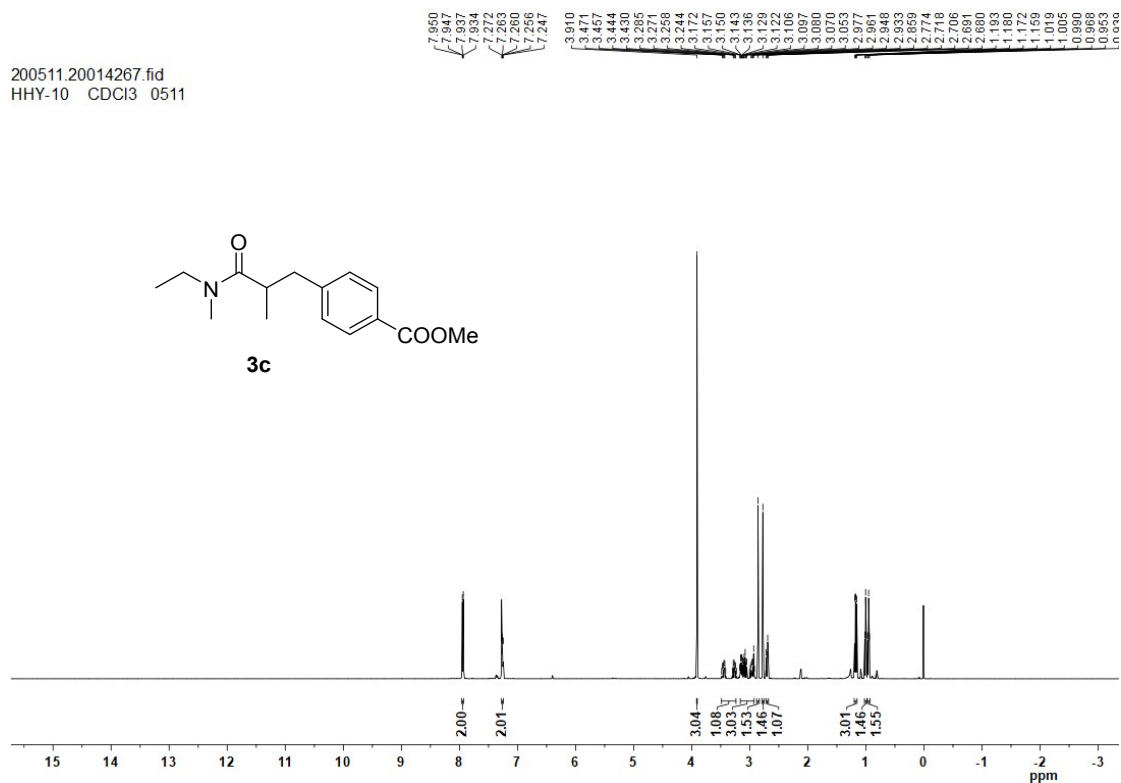


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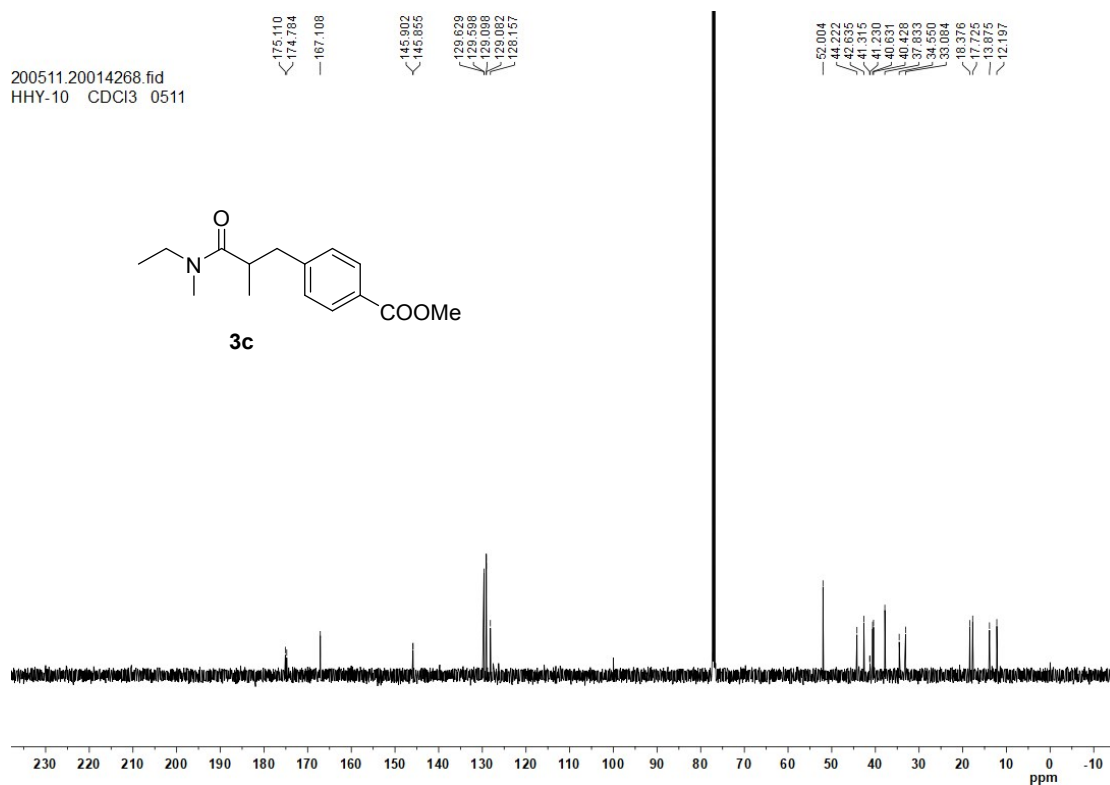
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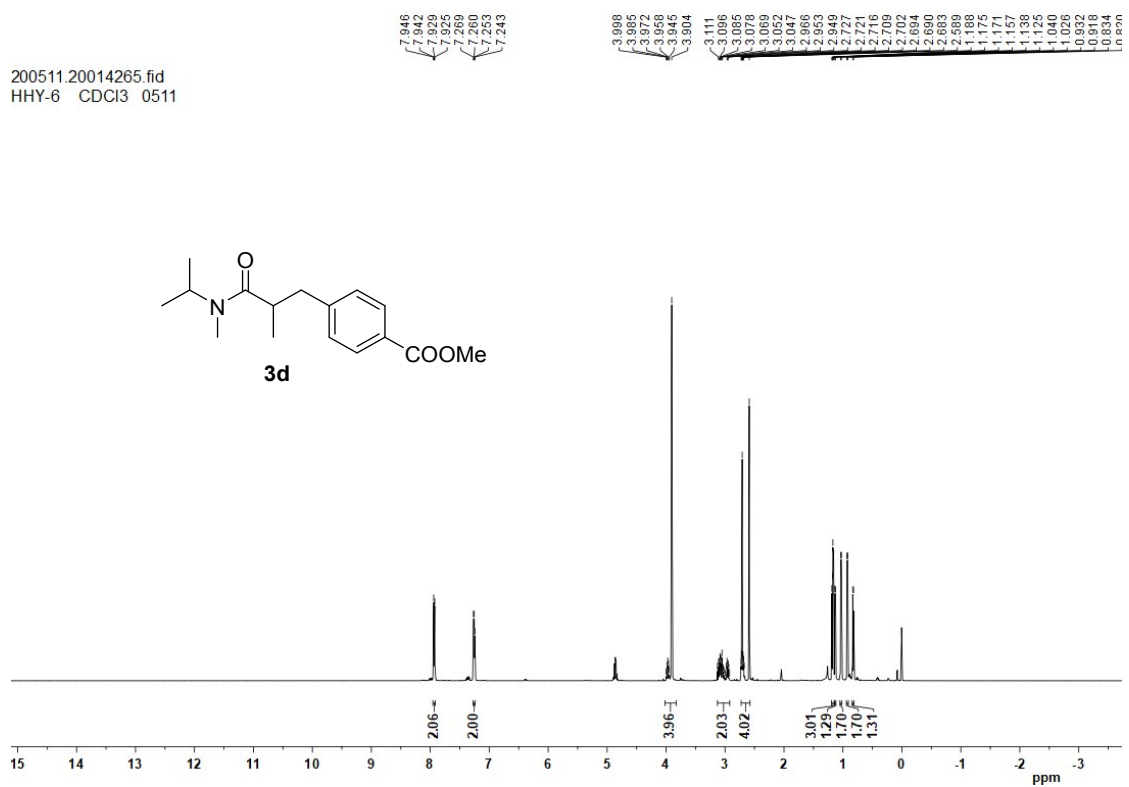
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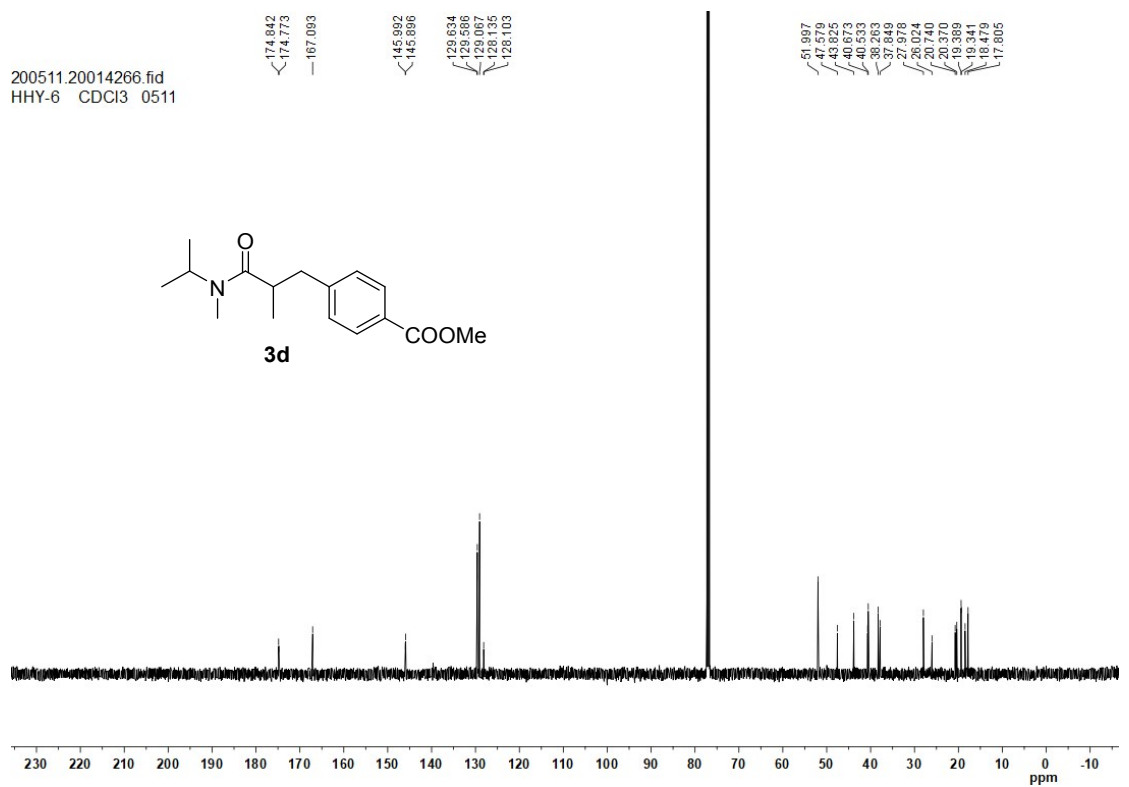
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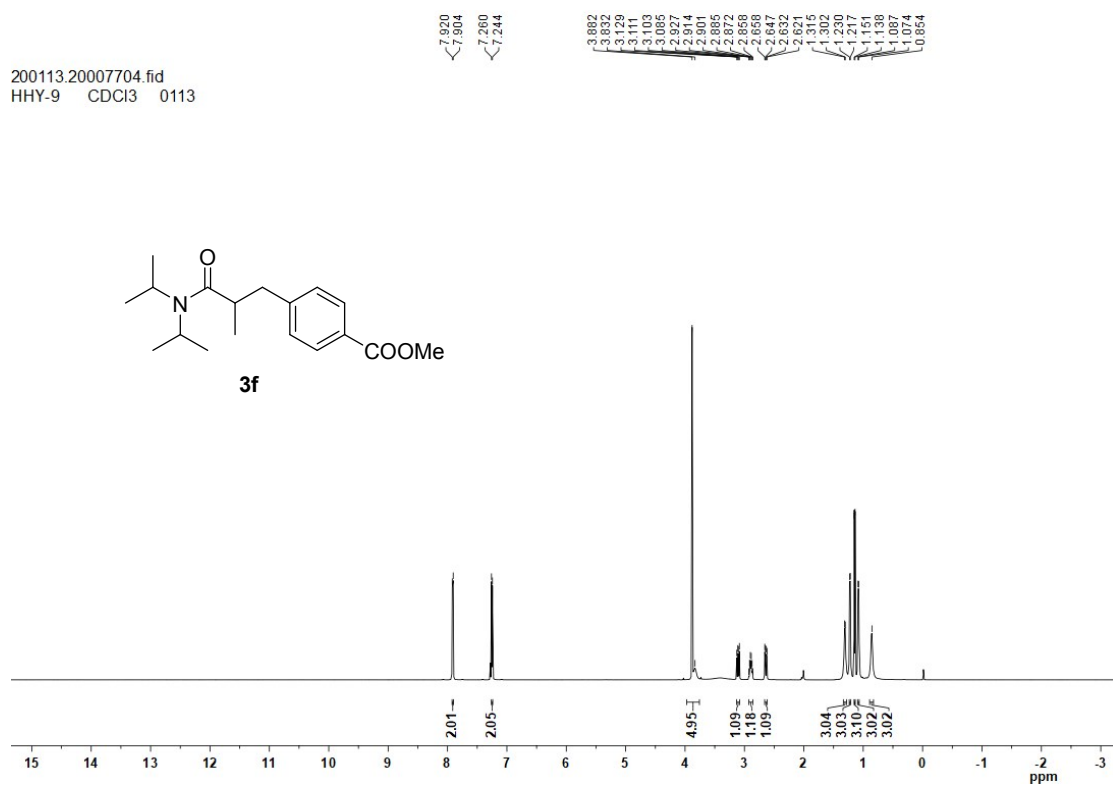
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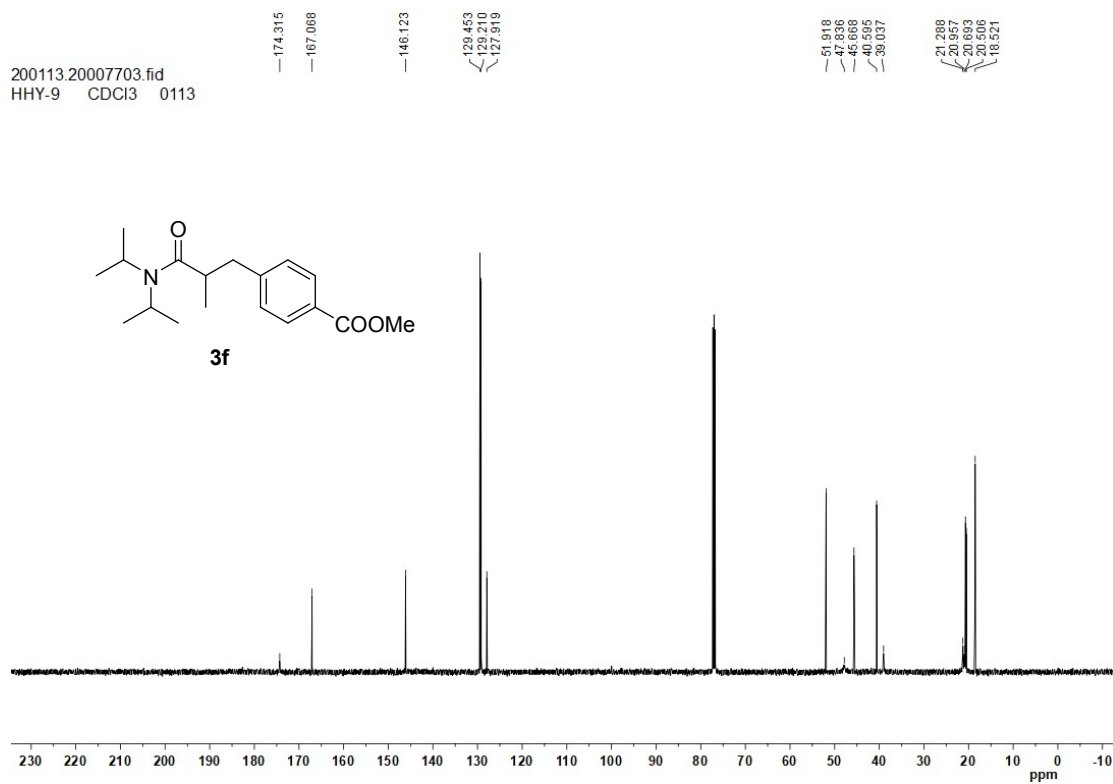
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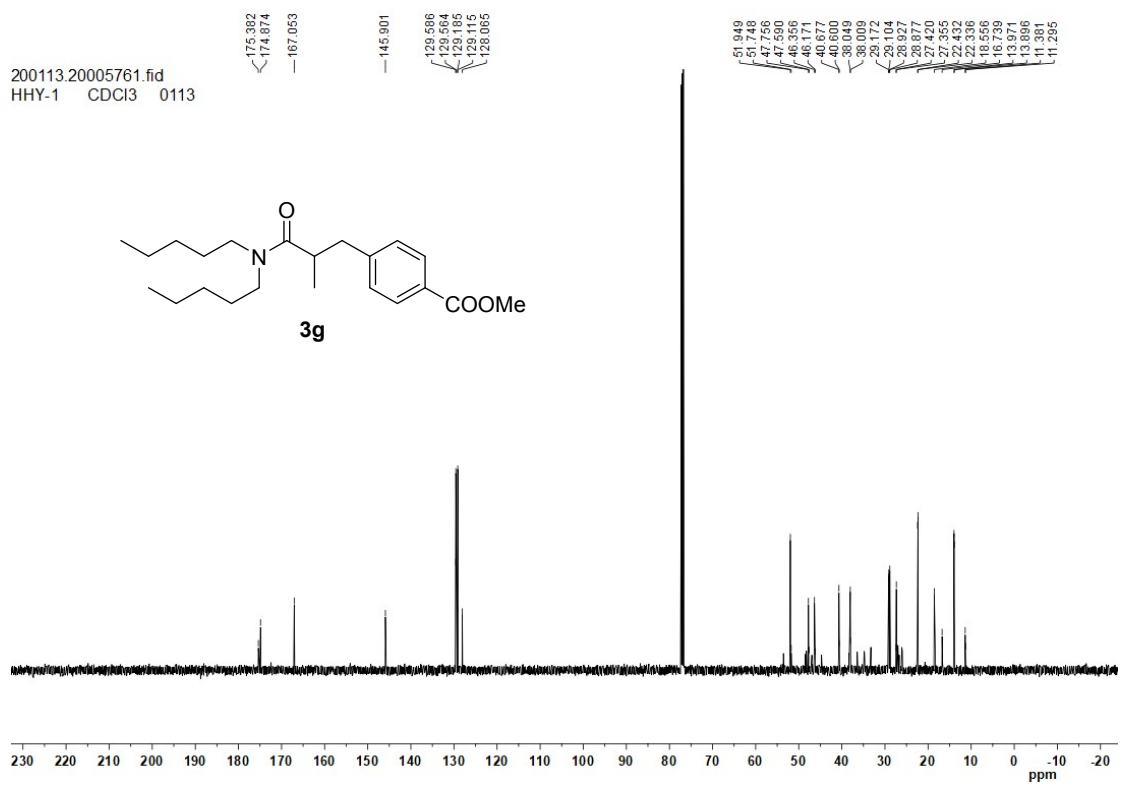
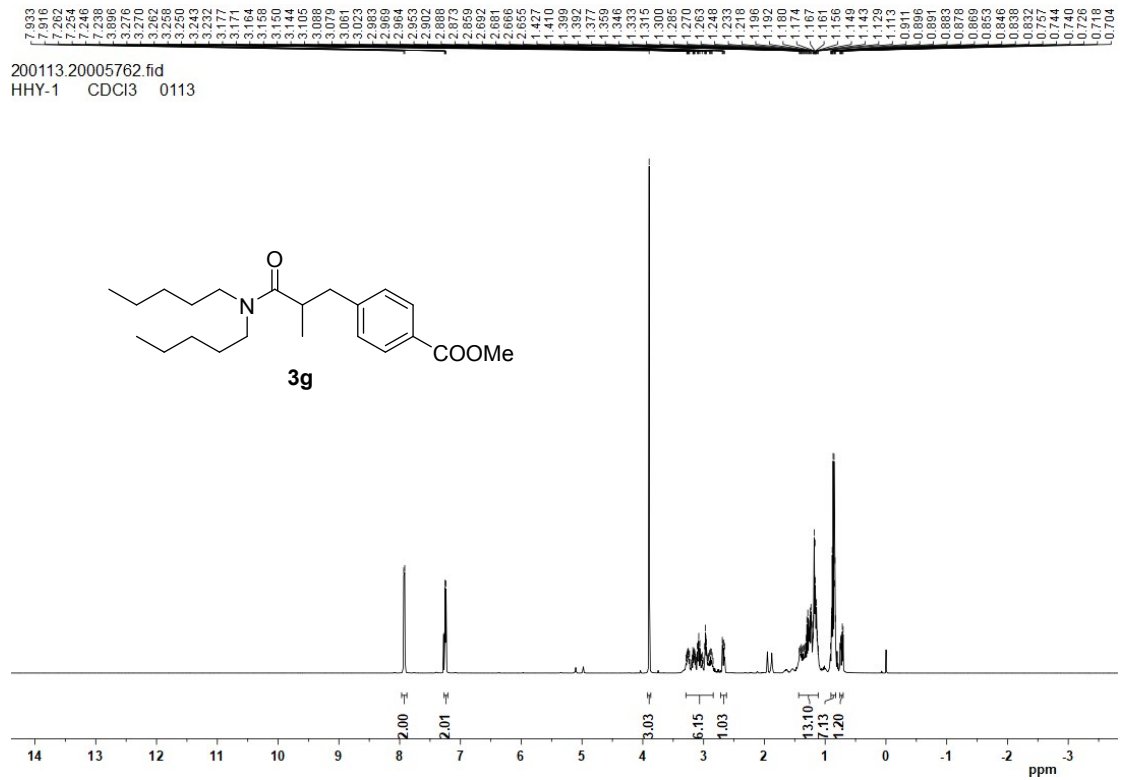


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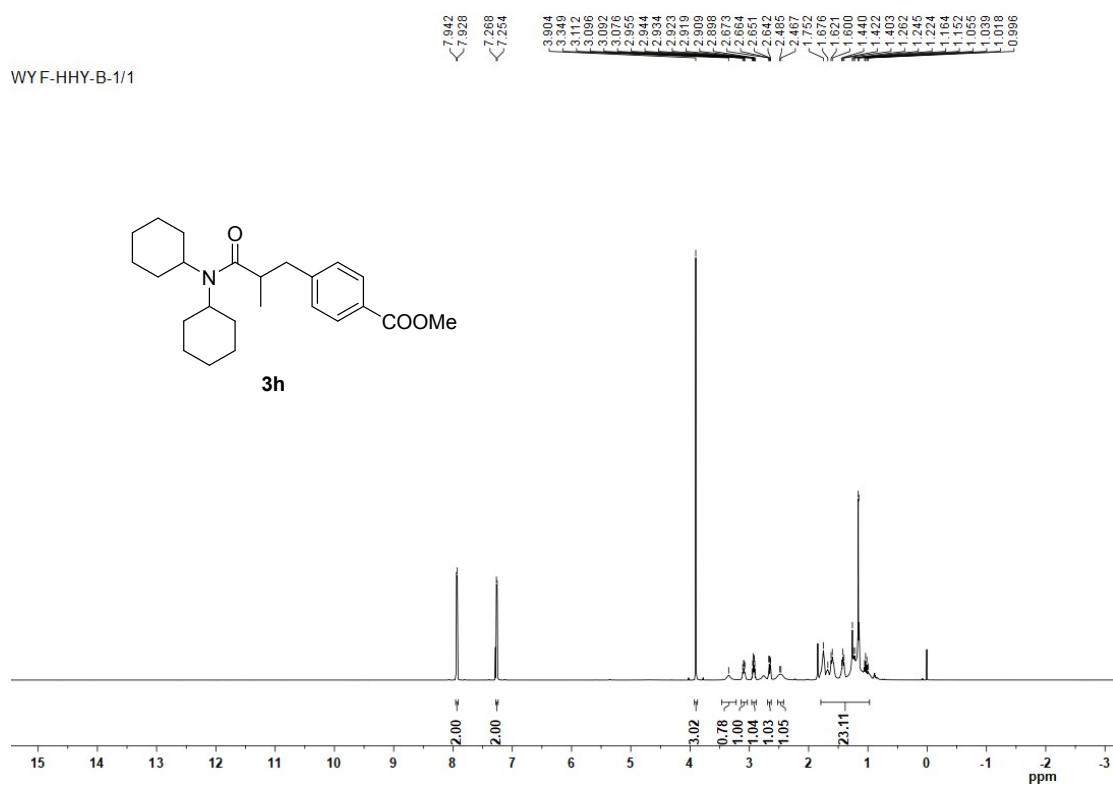


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HHY-9 CDCl3 0113



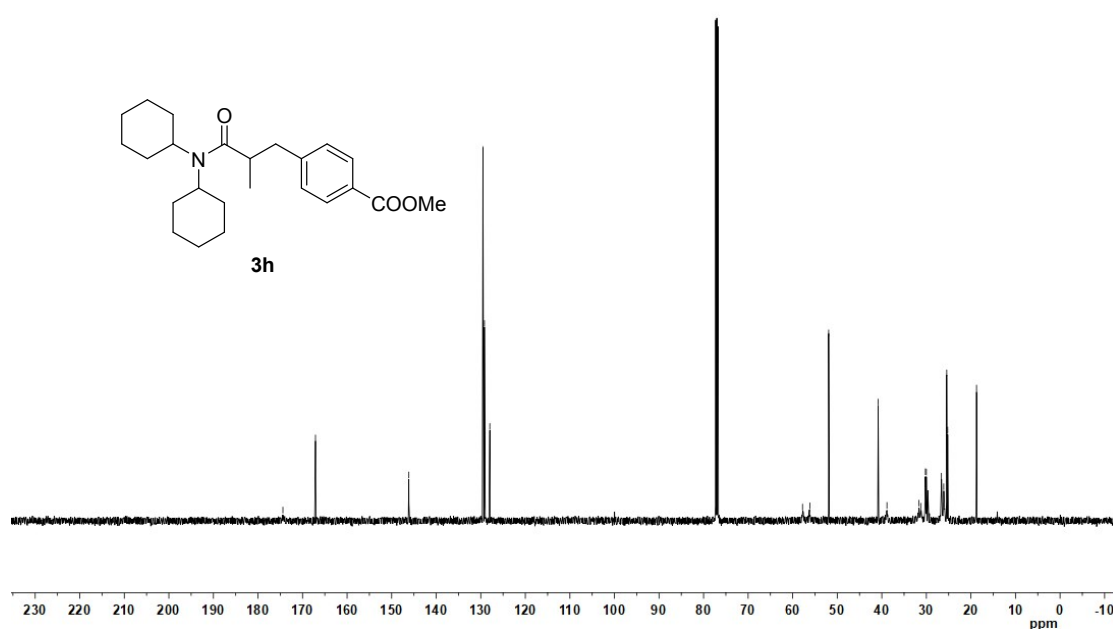


WYF-HHY-B-1/1



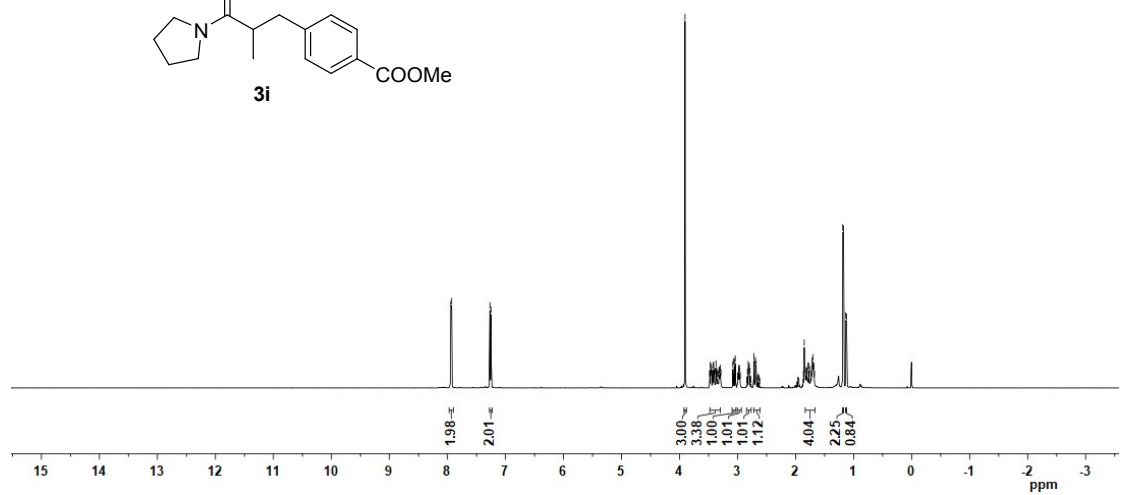
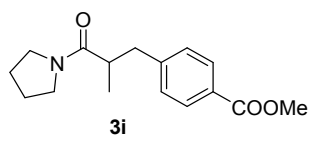
174.406, 167.097, 146.147, 128.512, 128.176, 127.974, 57.794, 56.144, 51.930, 40.818, 38.846, 31.883, 31.072, 30.217, 29.889, 26.622, 26.107, 25.431, 25.214, 16.742.

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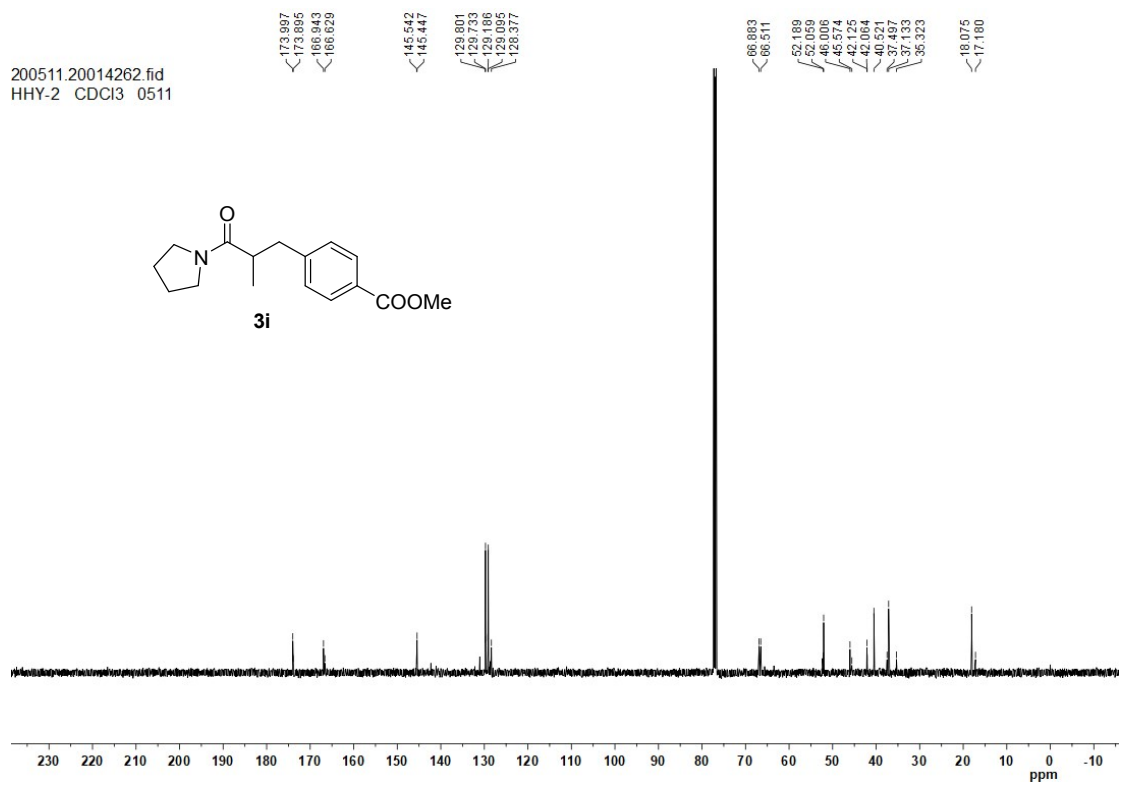
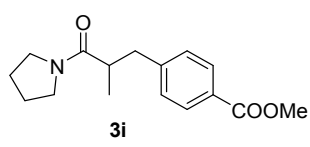


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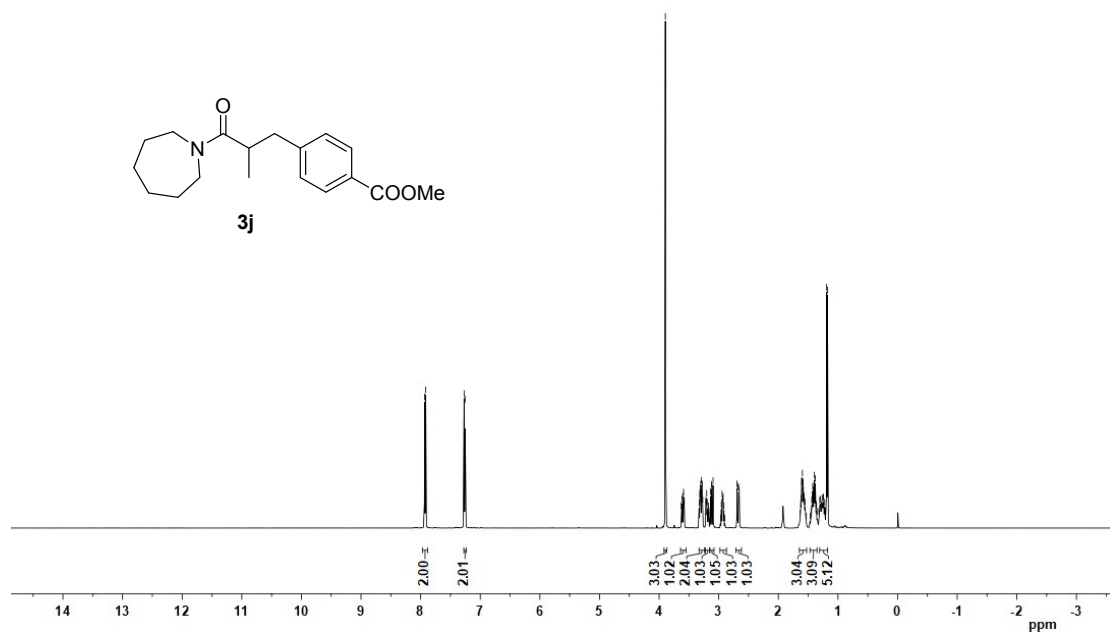
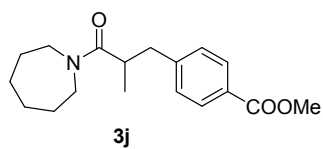
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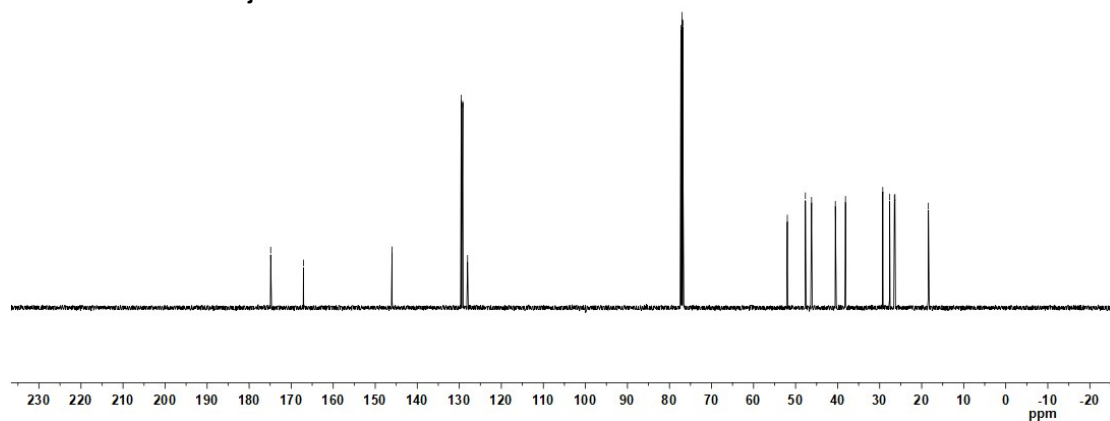
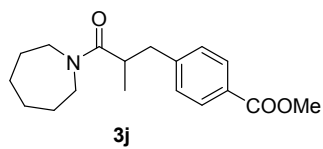
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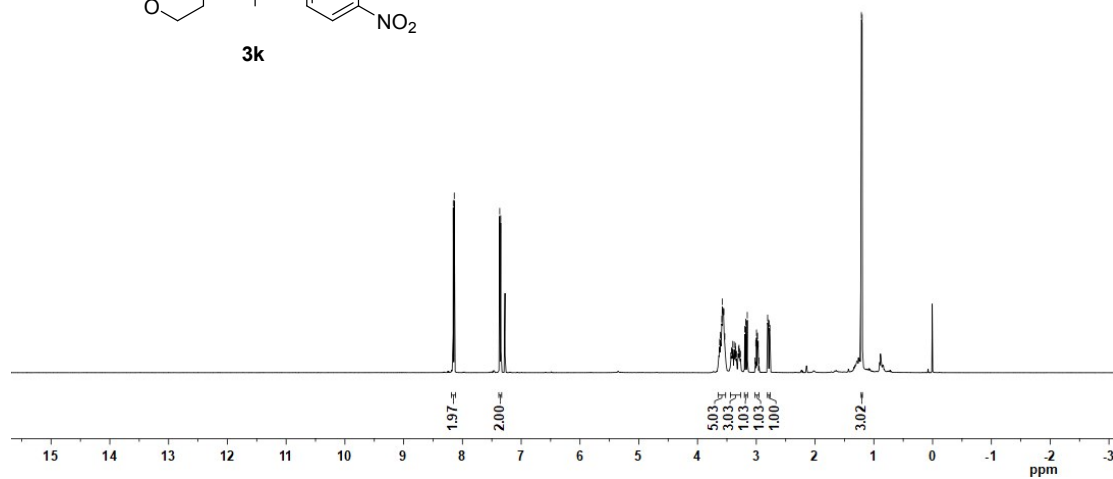
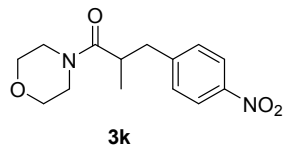


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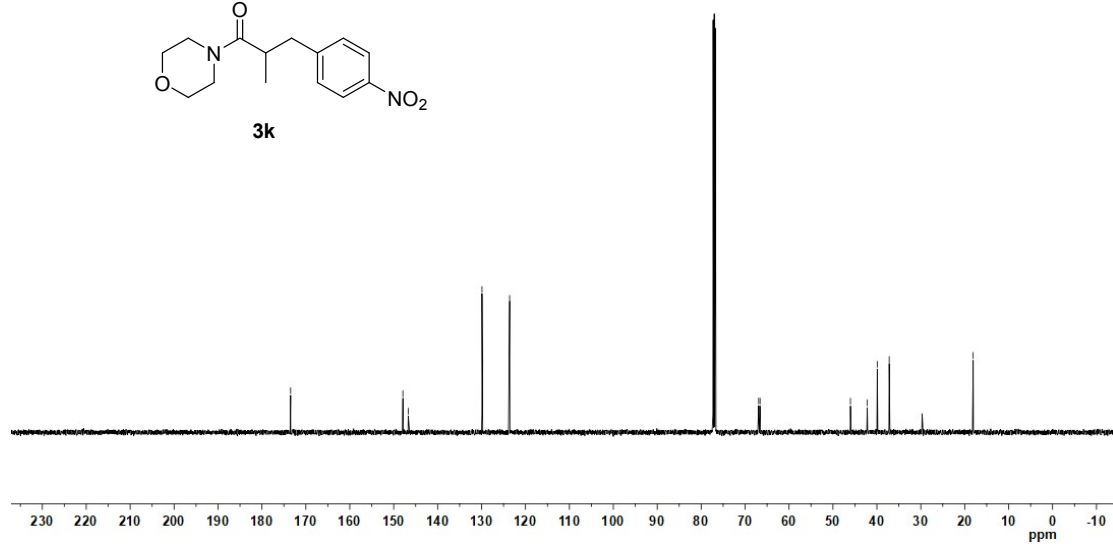
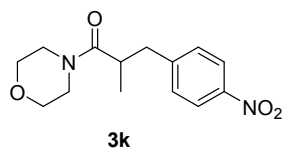
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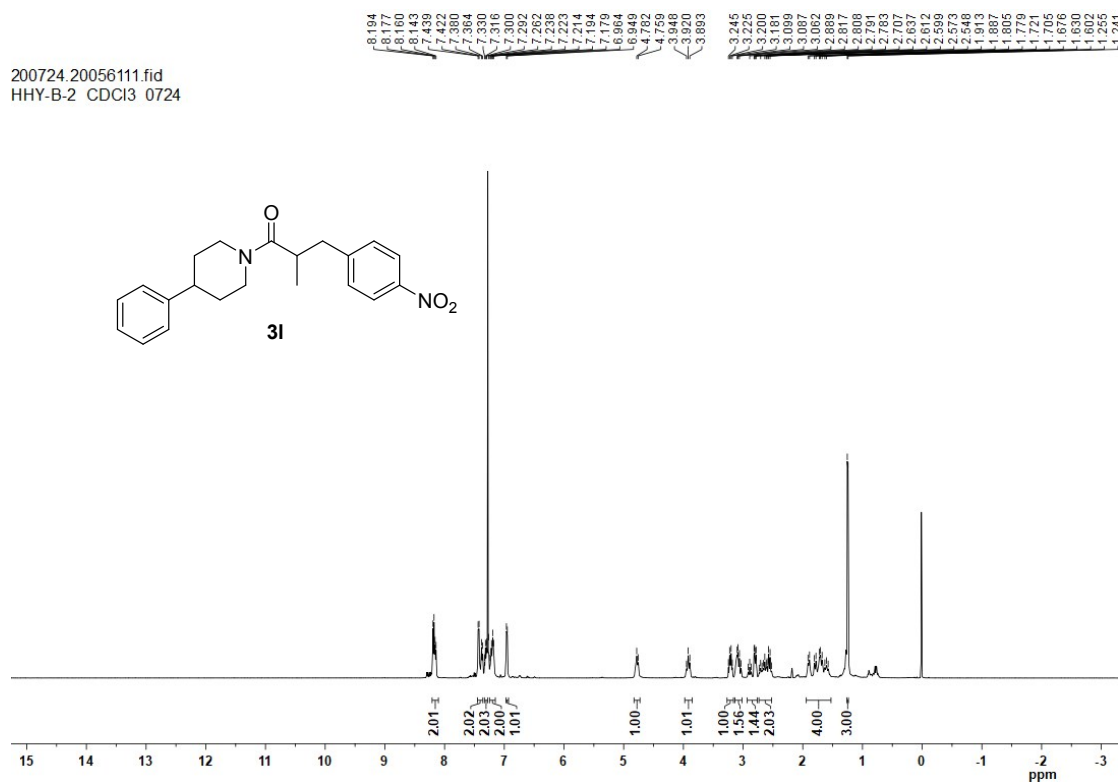


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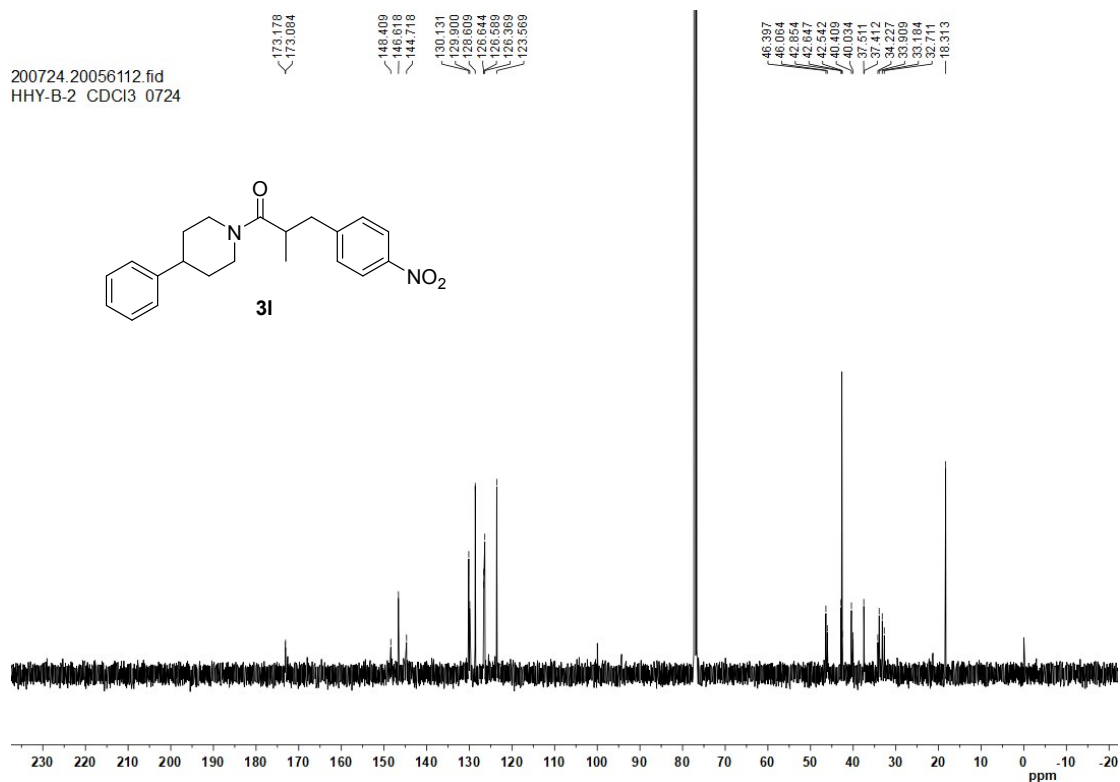
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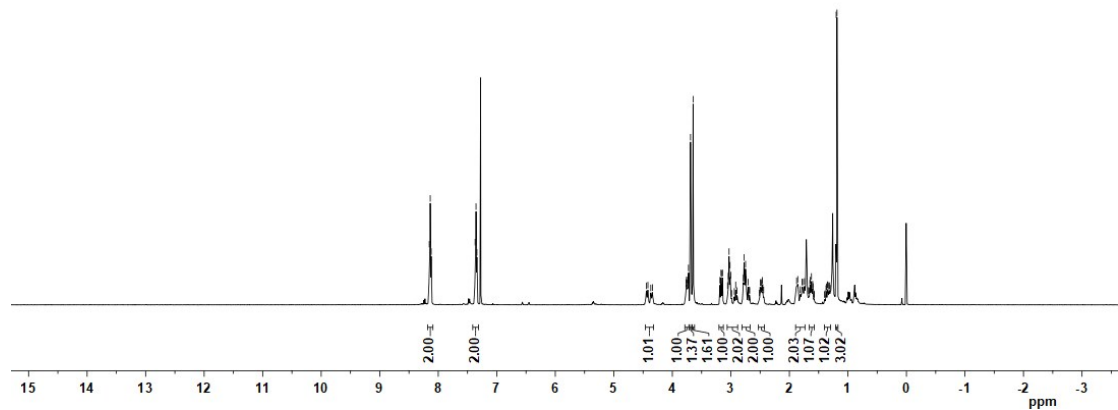
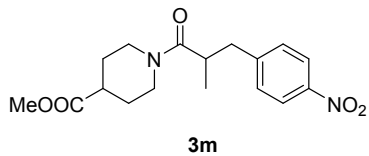


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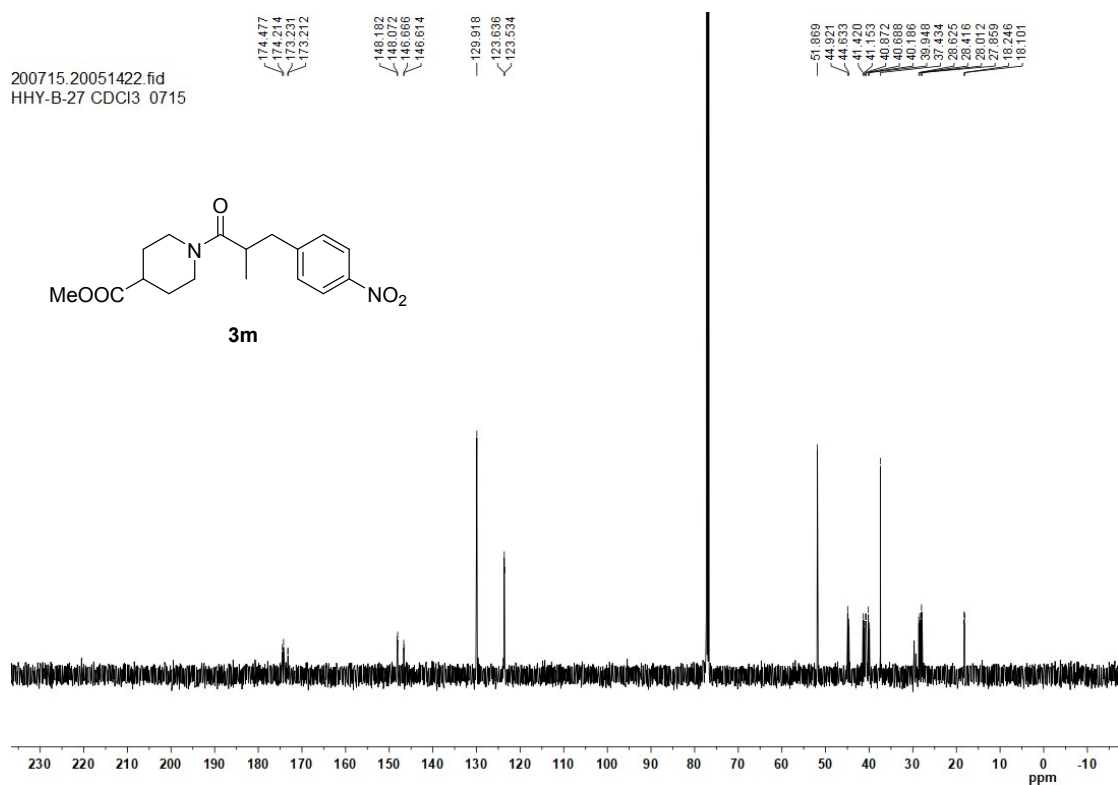
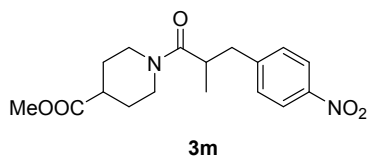


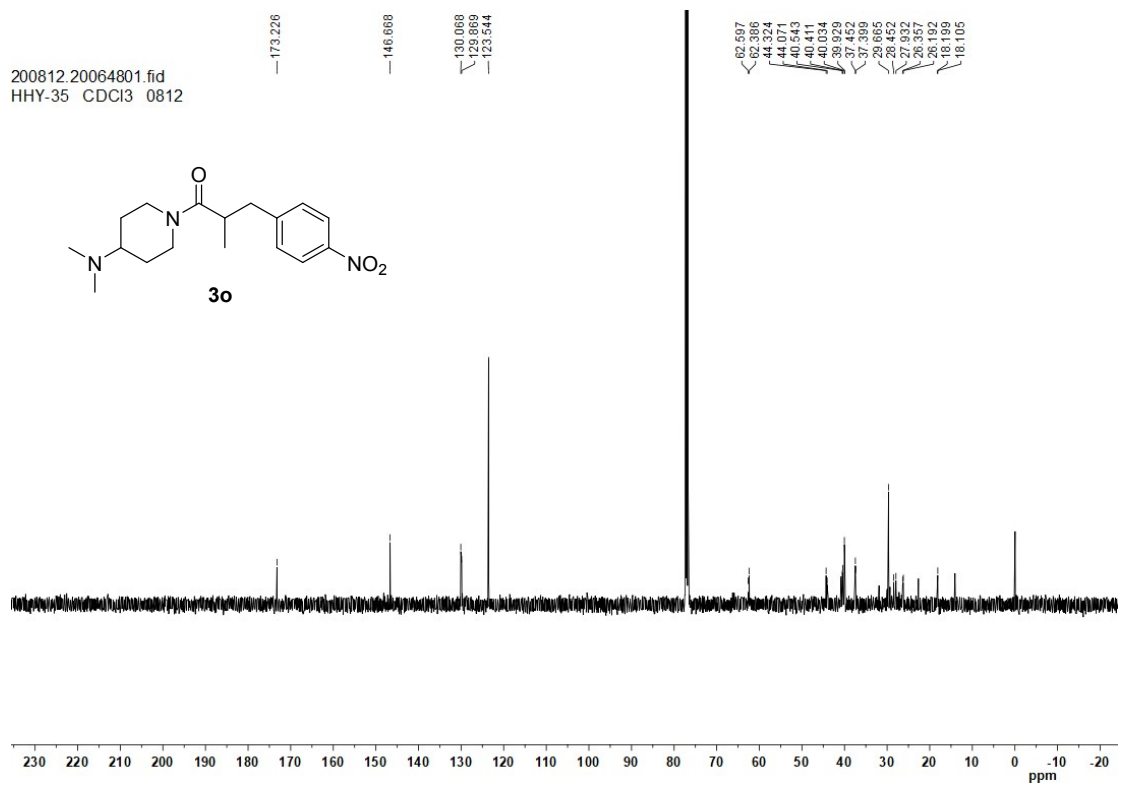
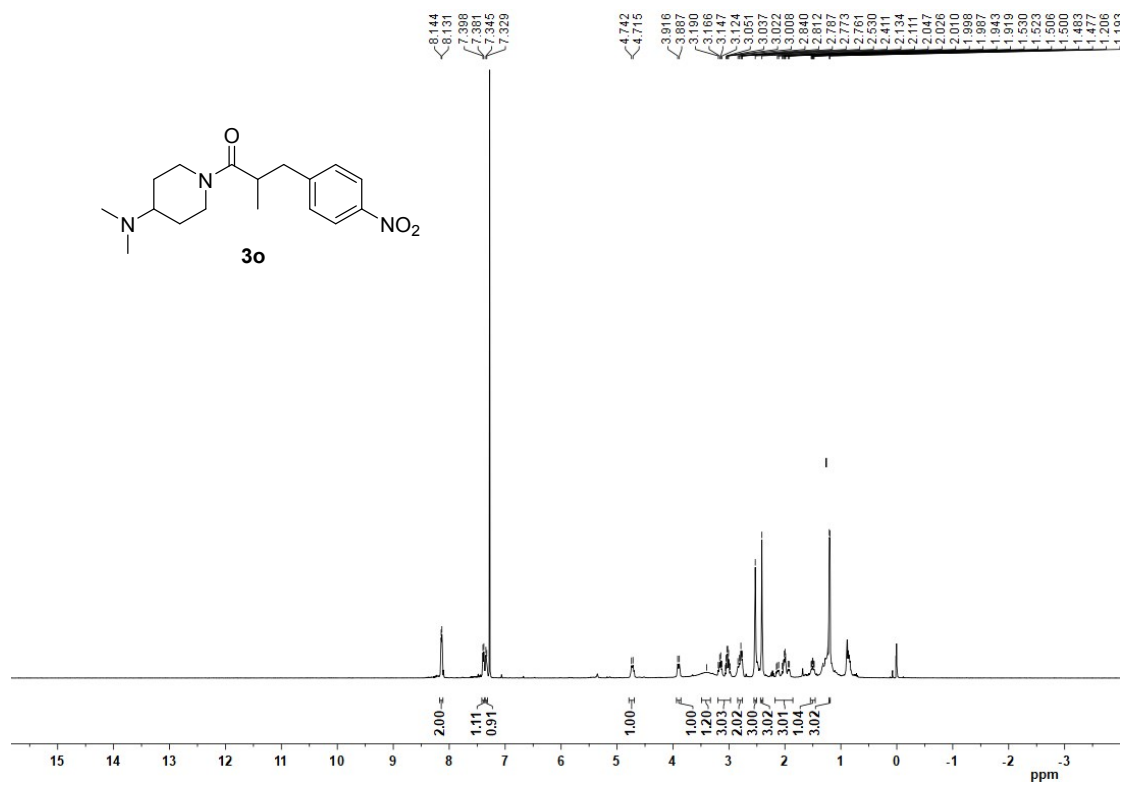
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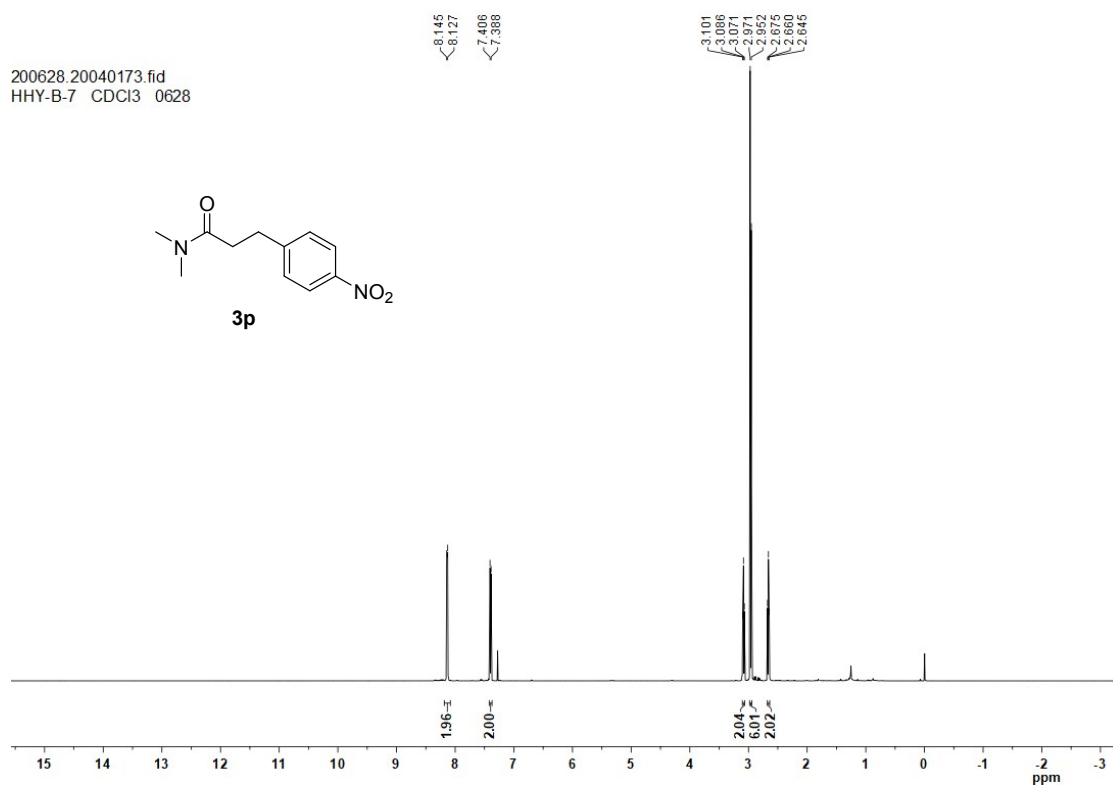
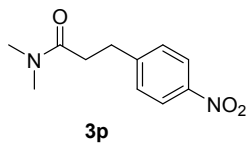


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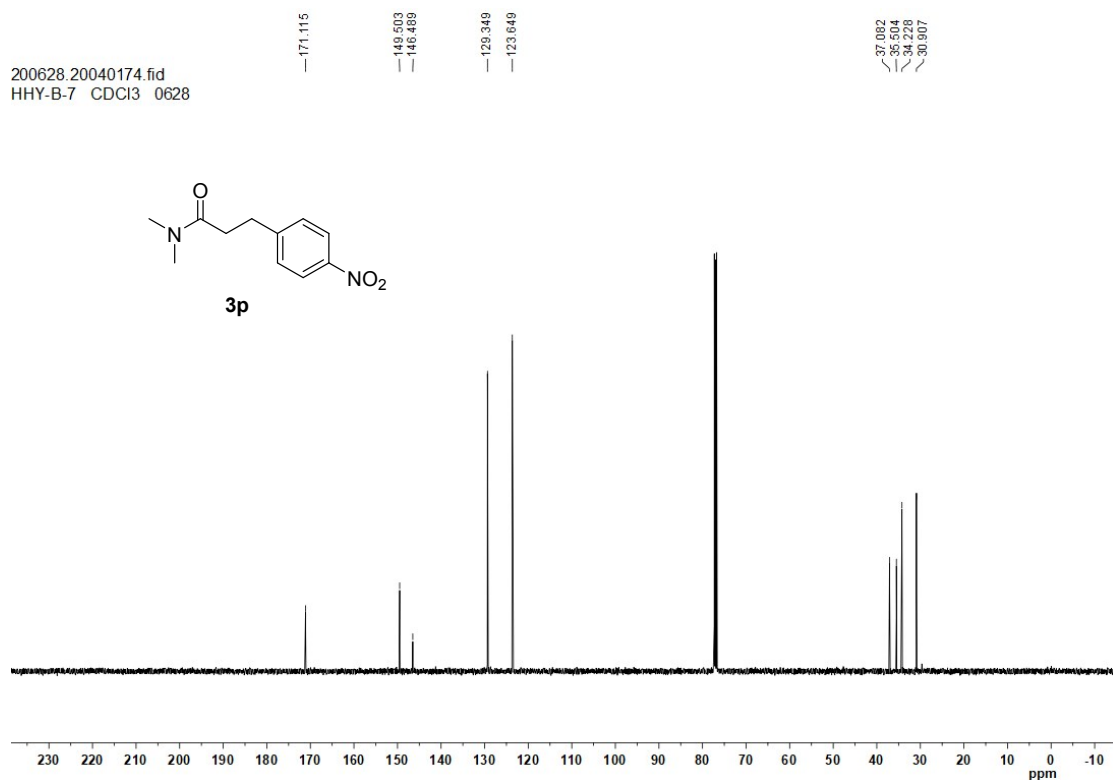
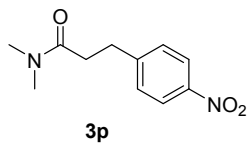




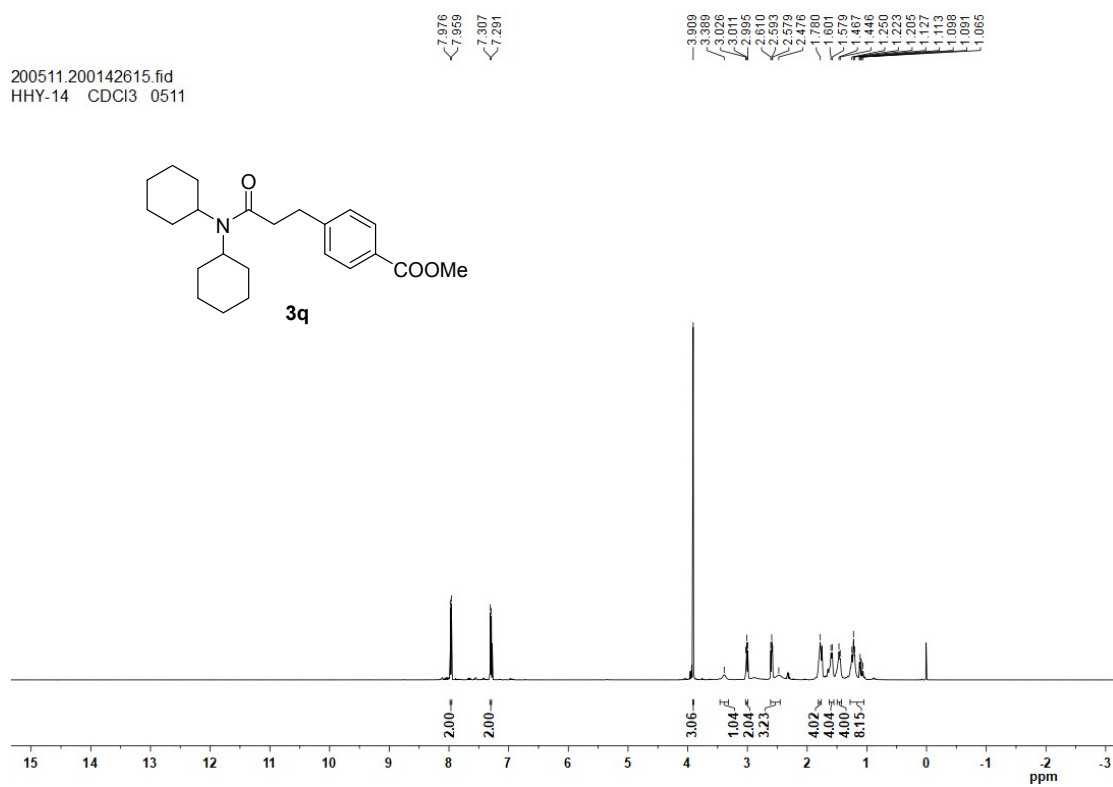
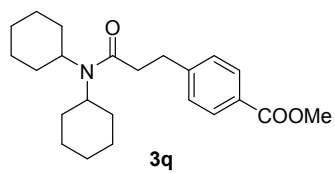
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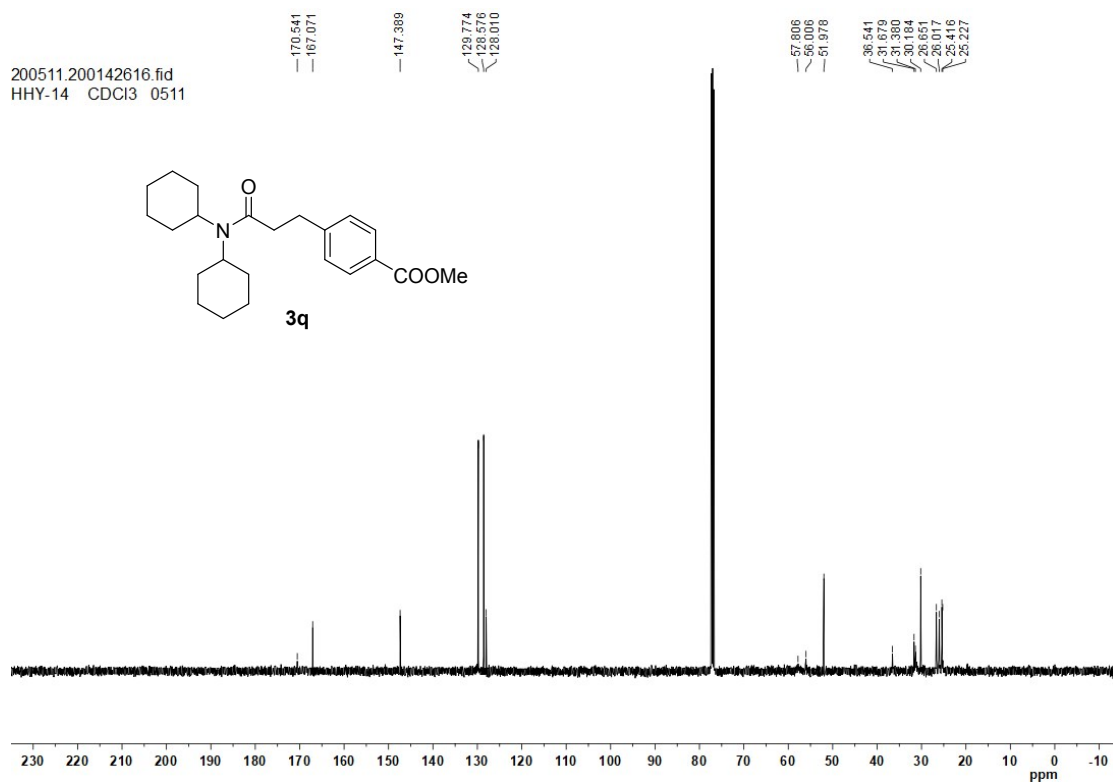
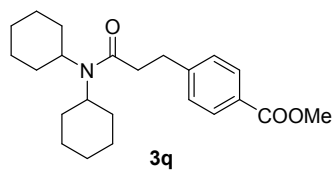
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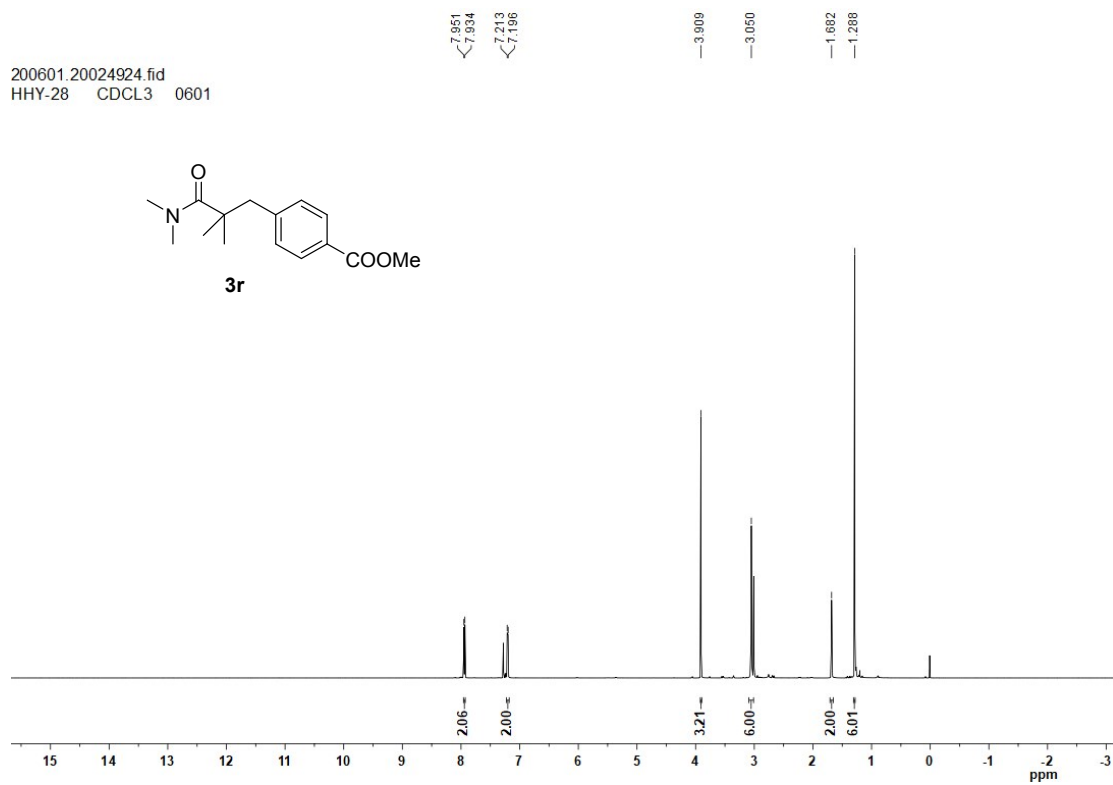
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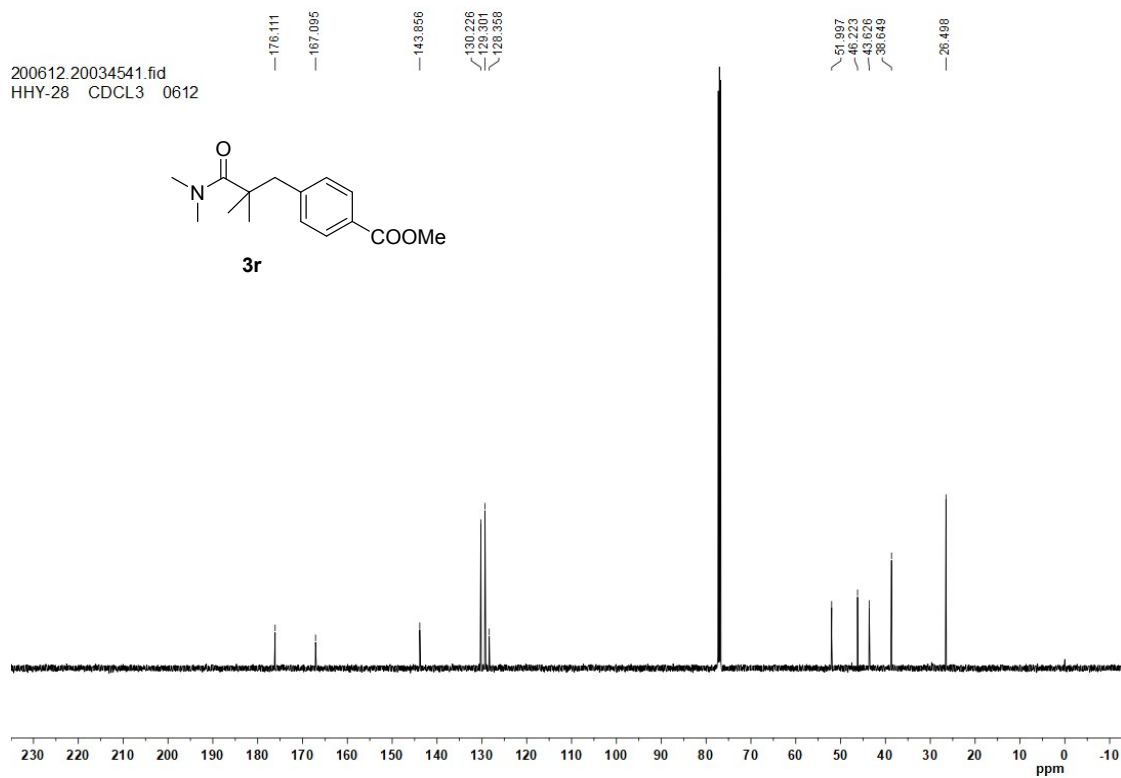
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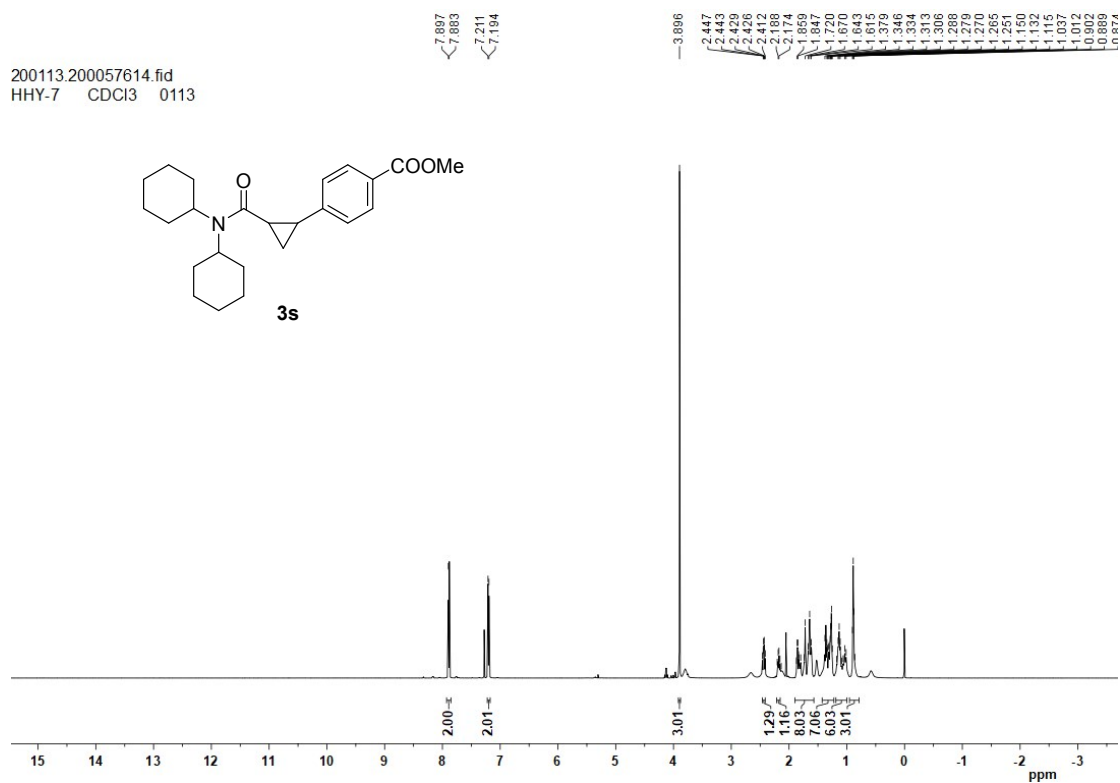
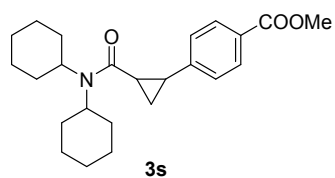
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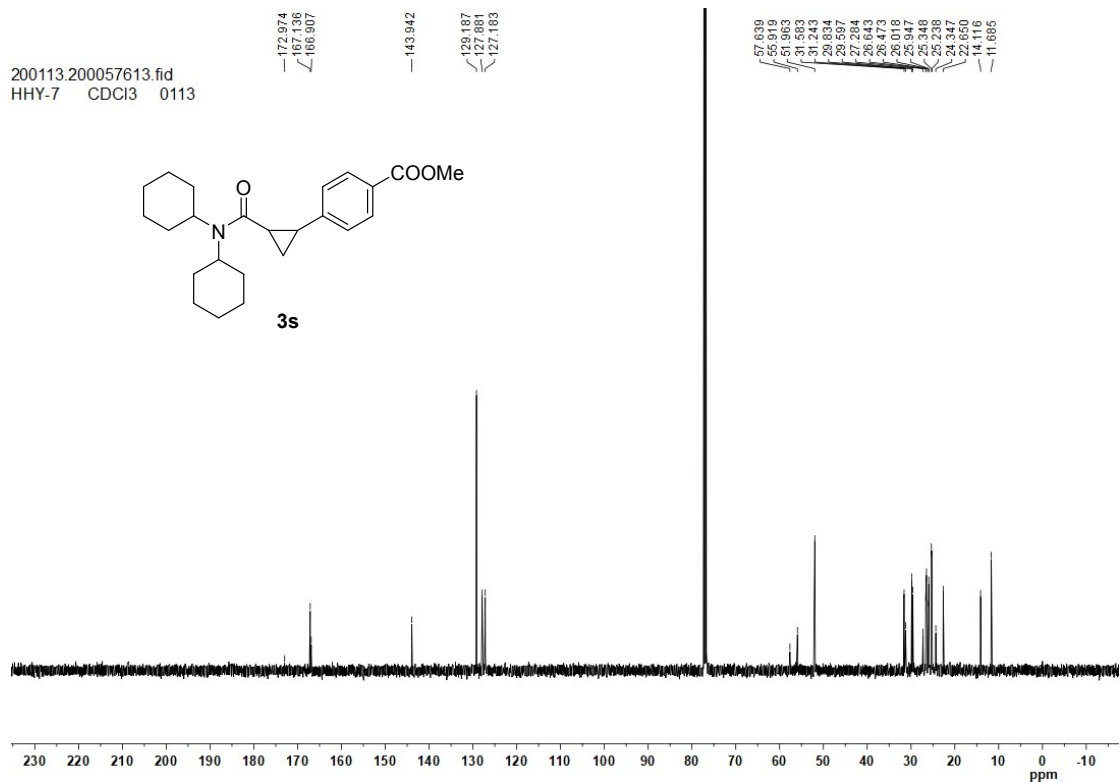
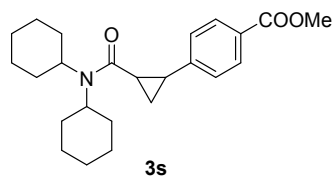
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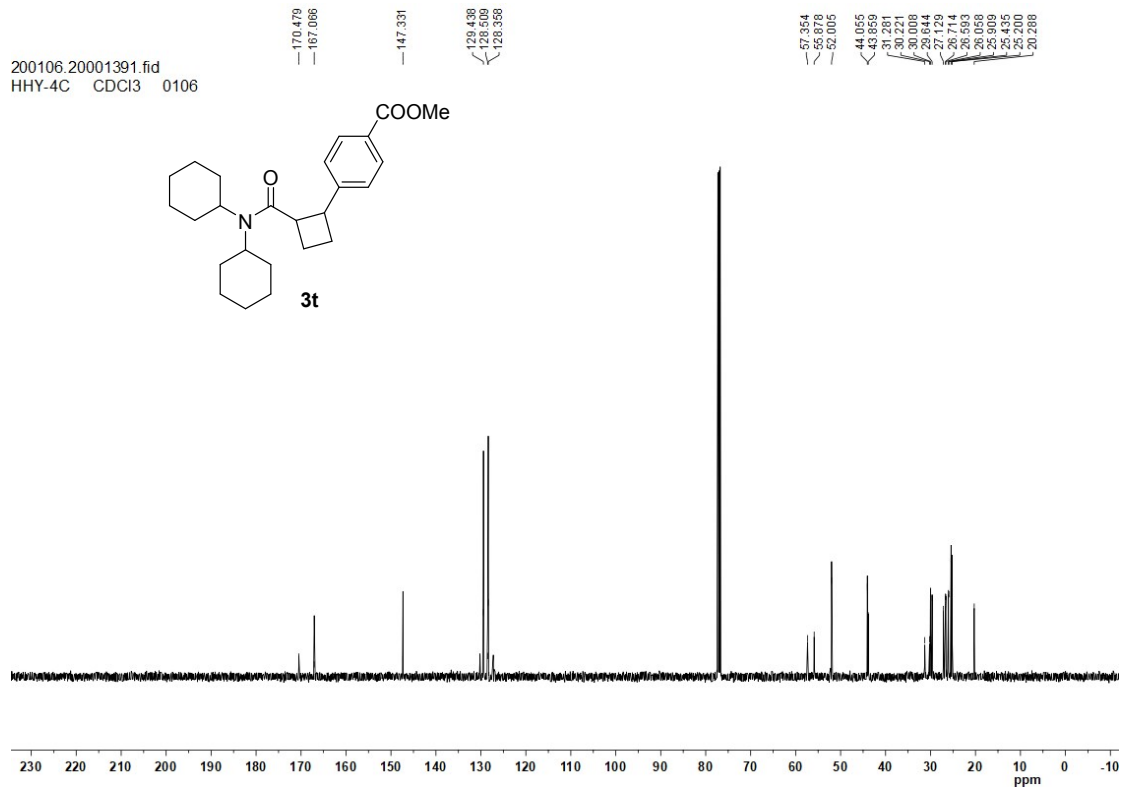
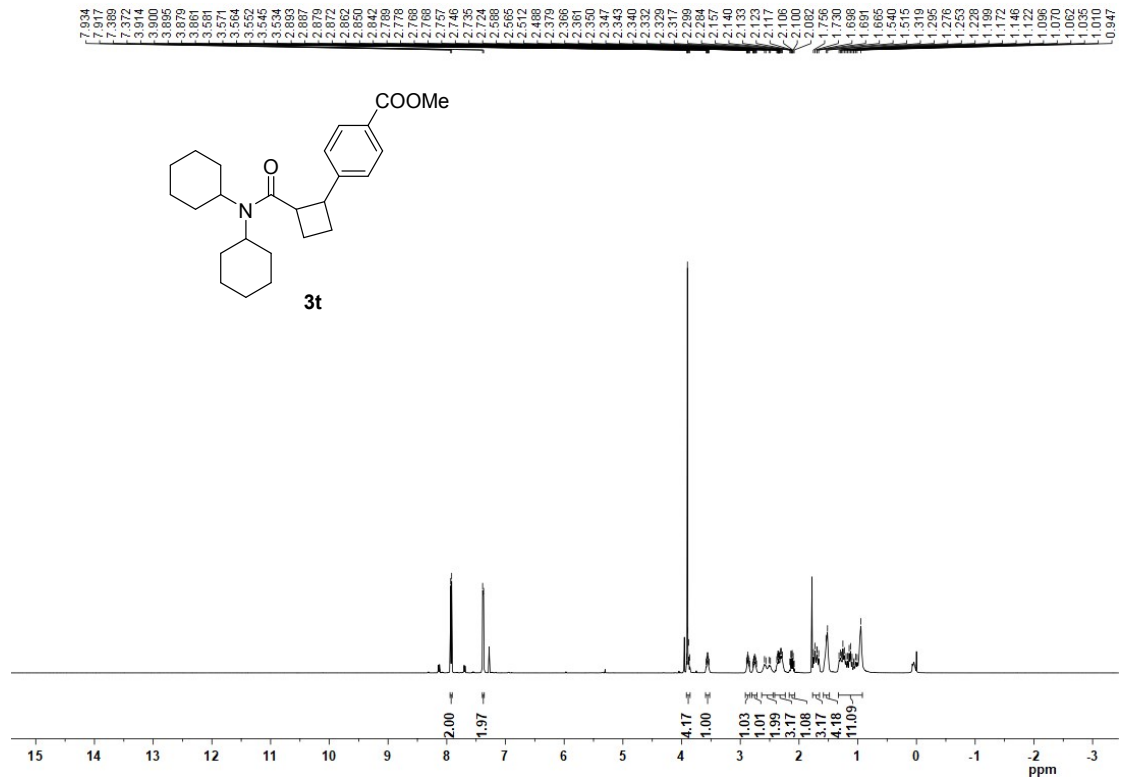


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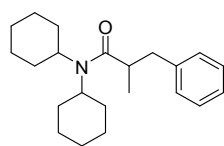


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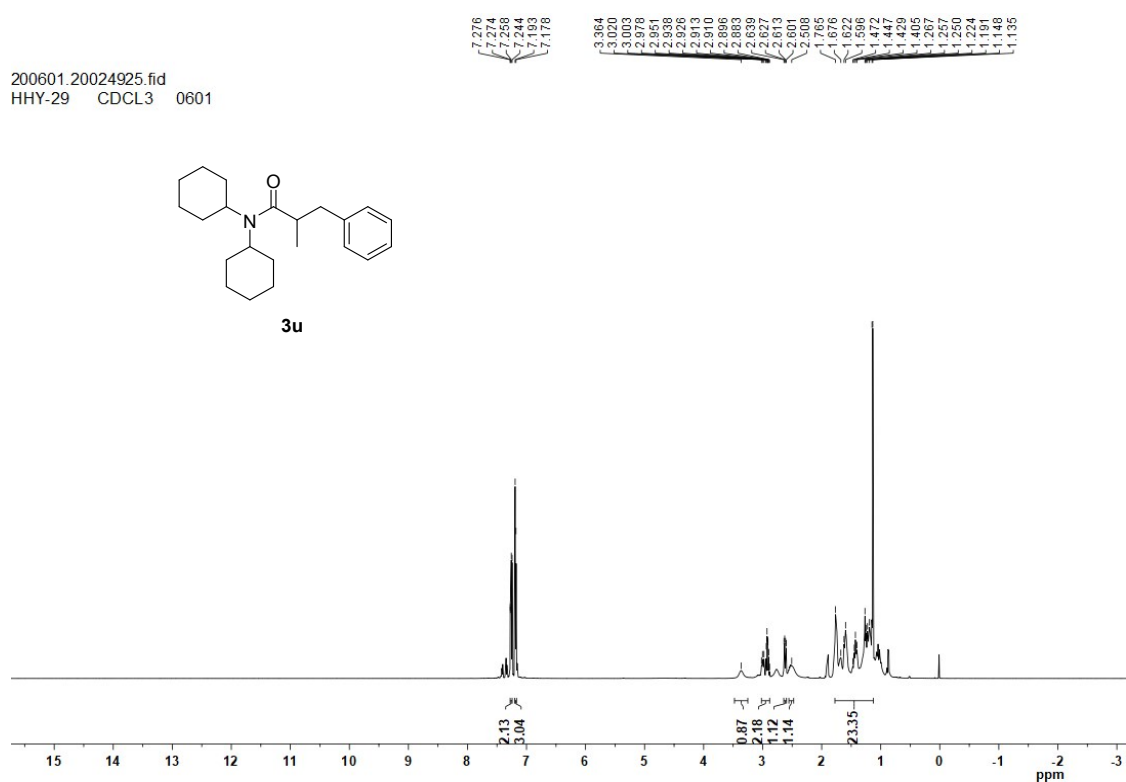




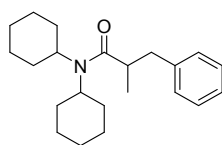
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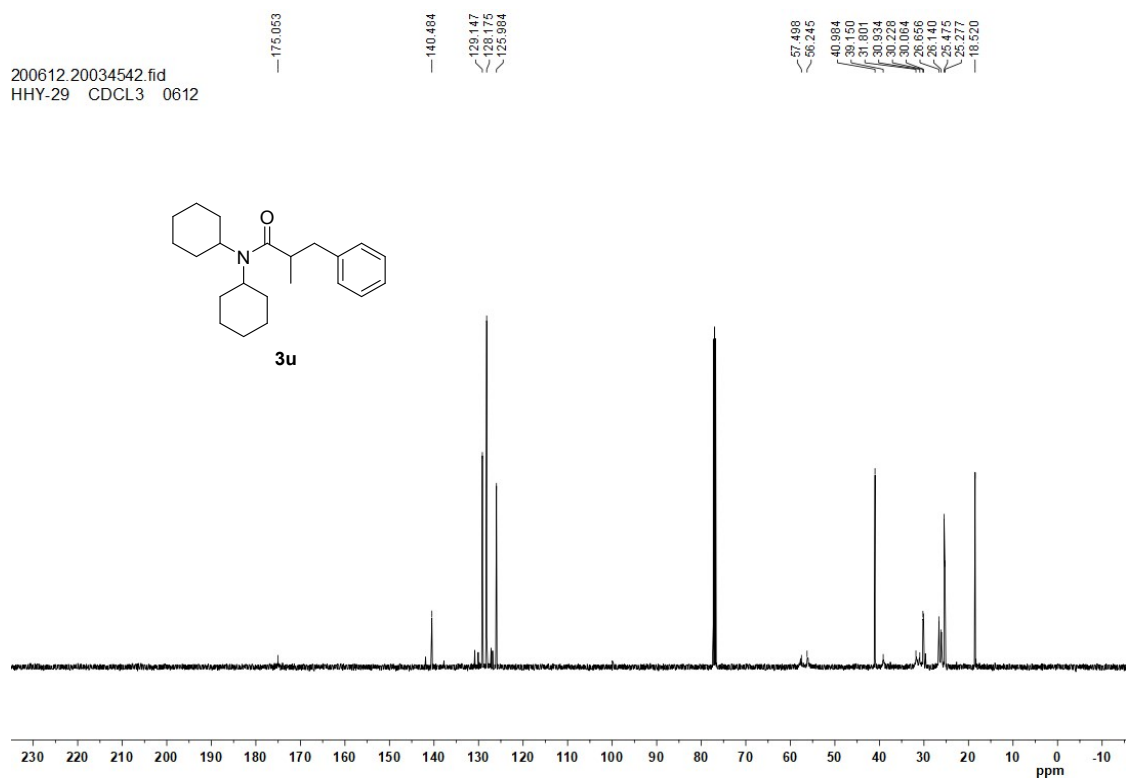
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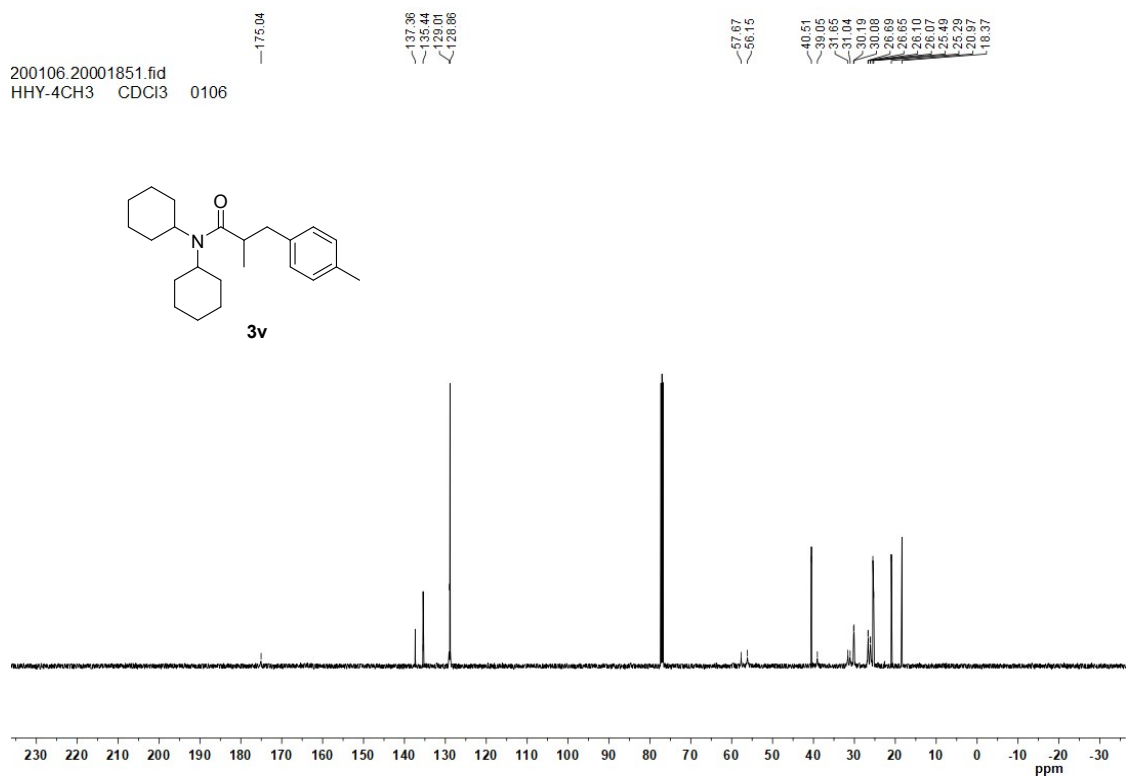
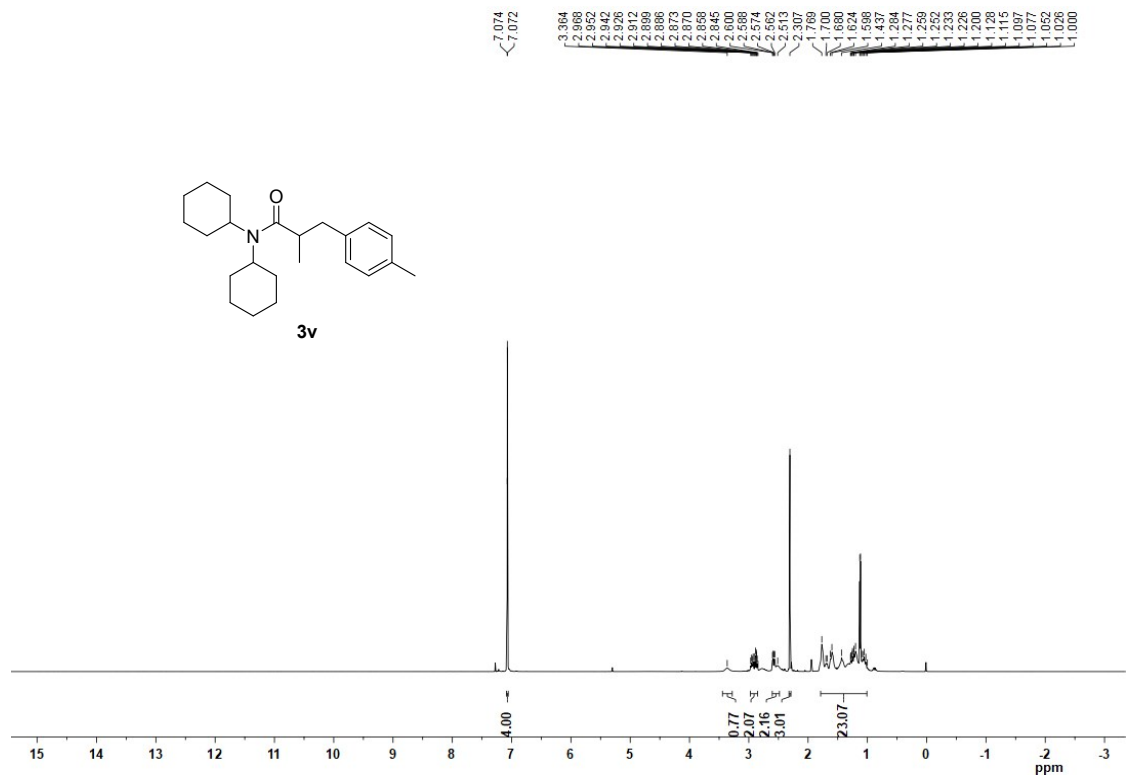


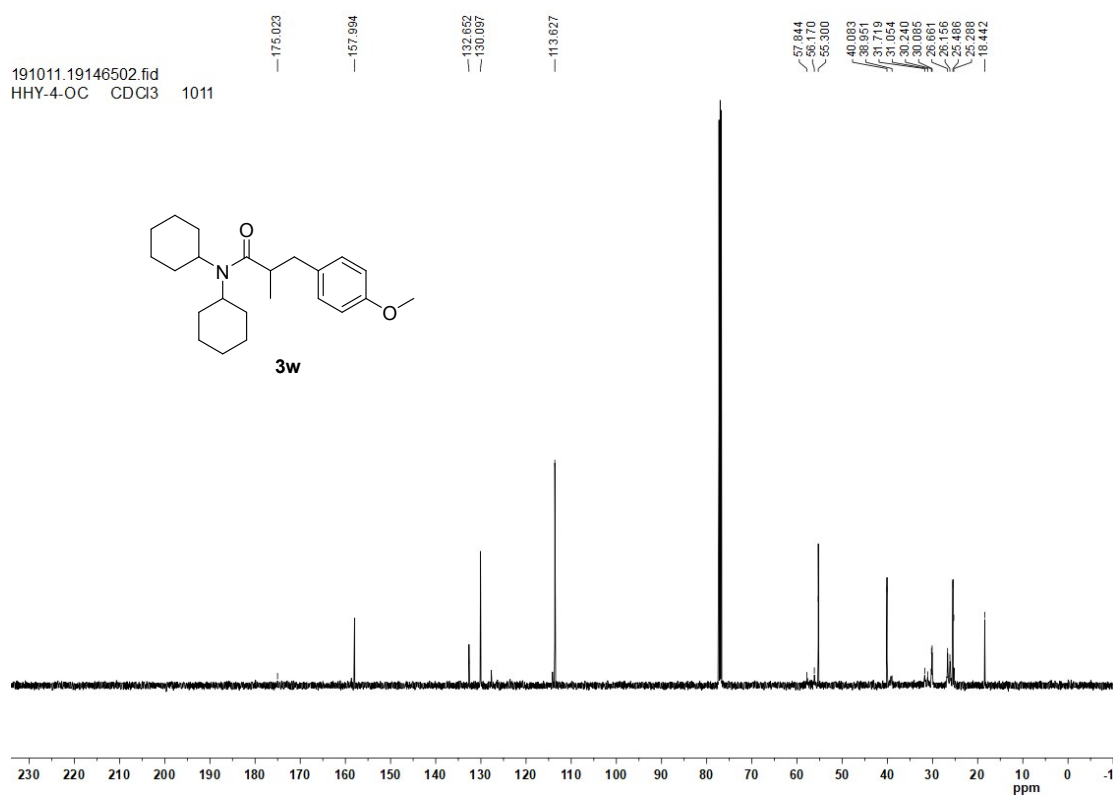
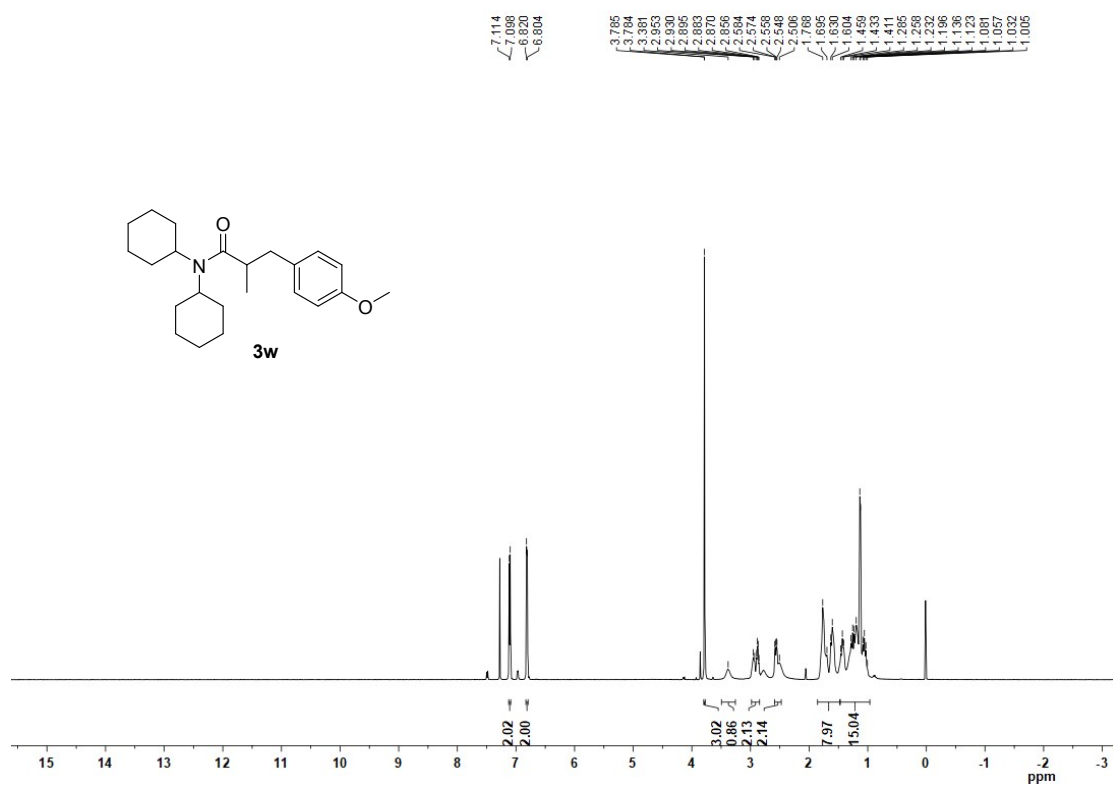
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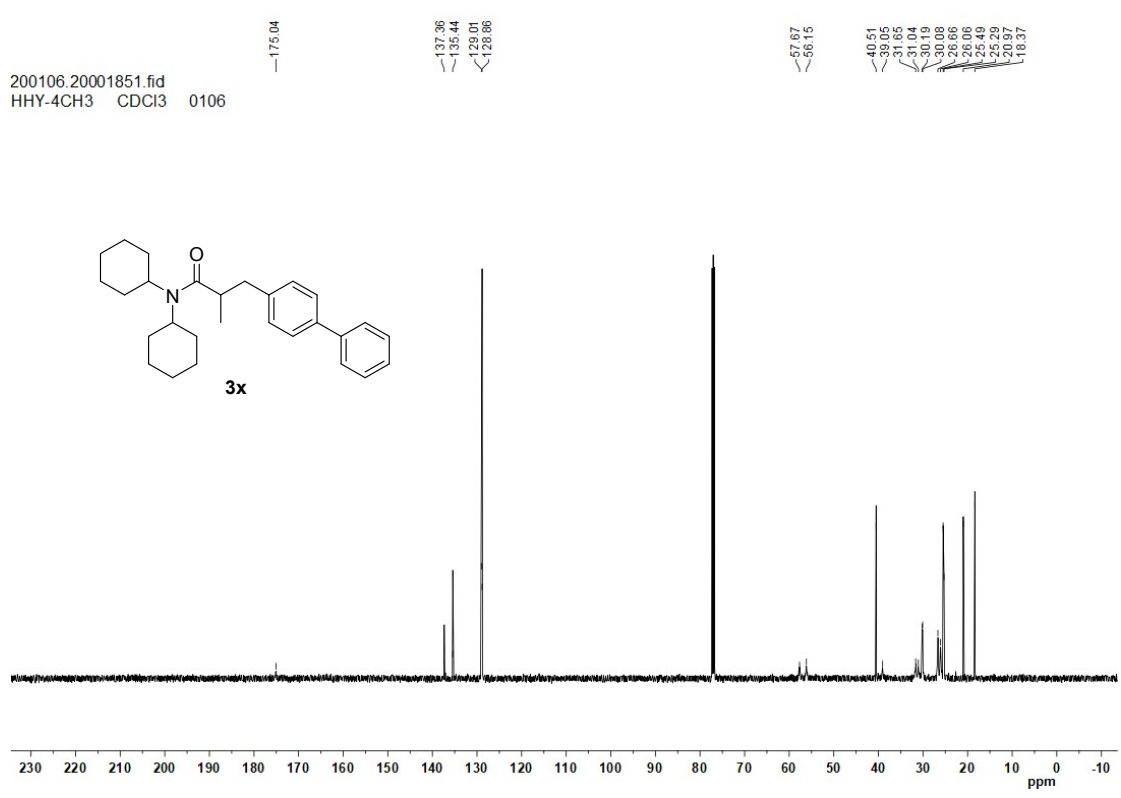
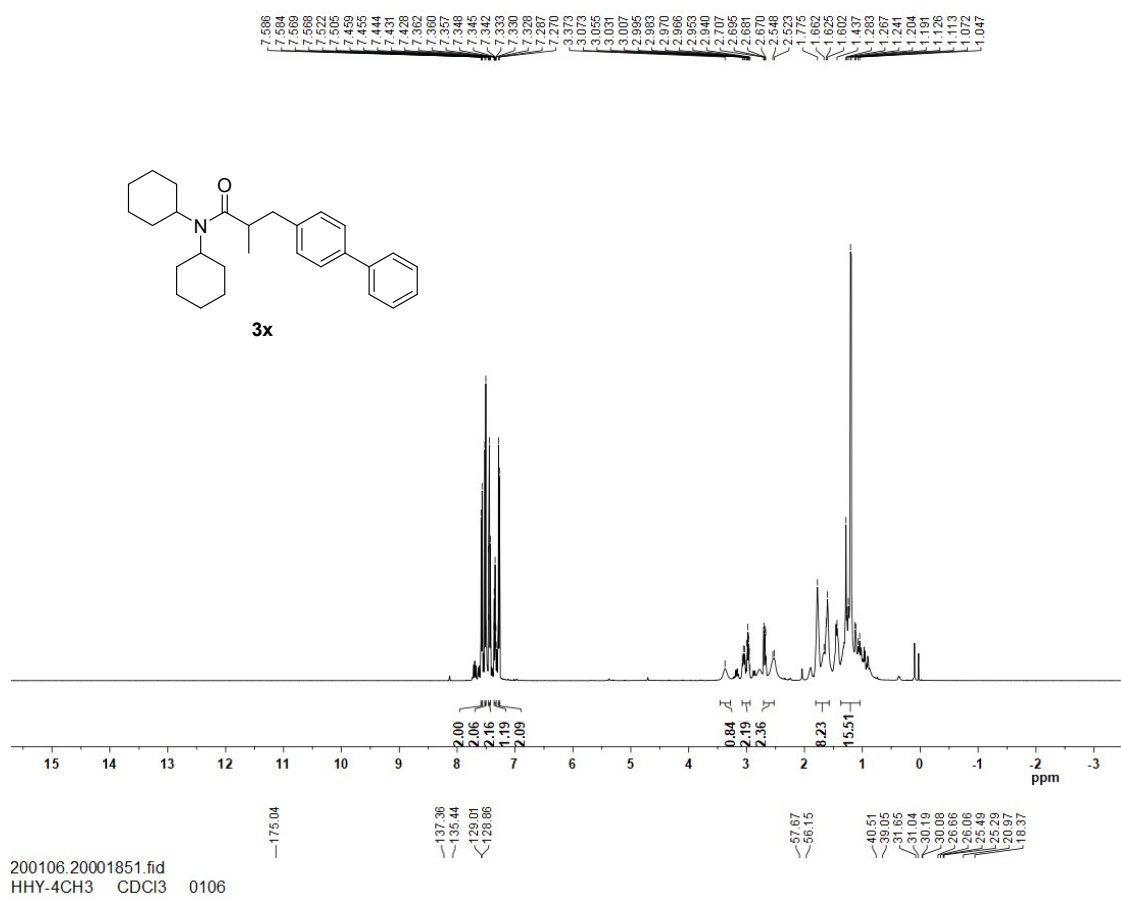


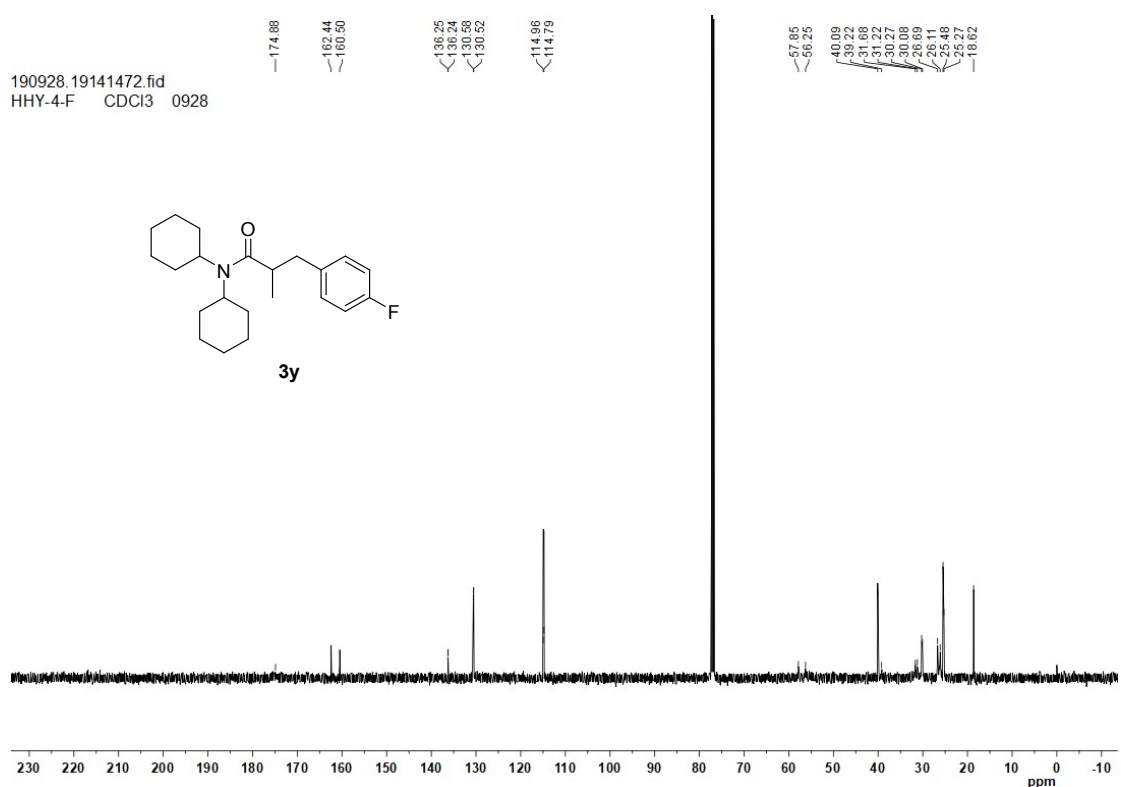
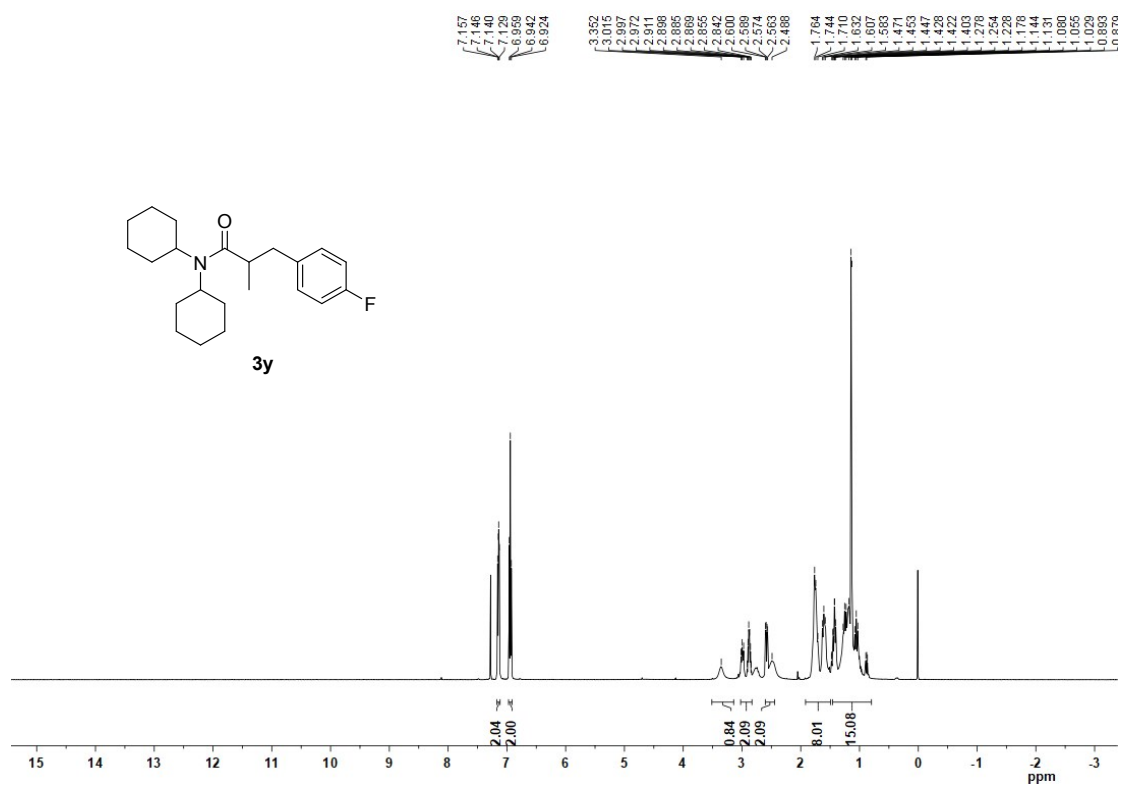
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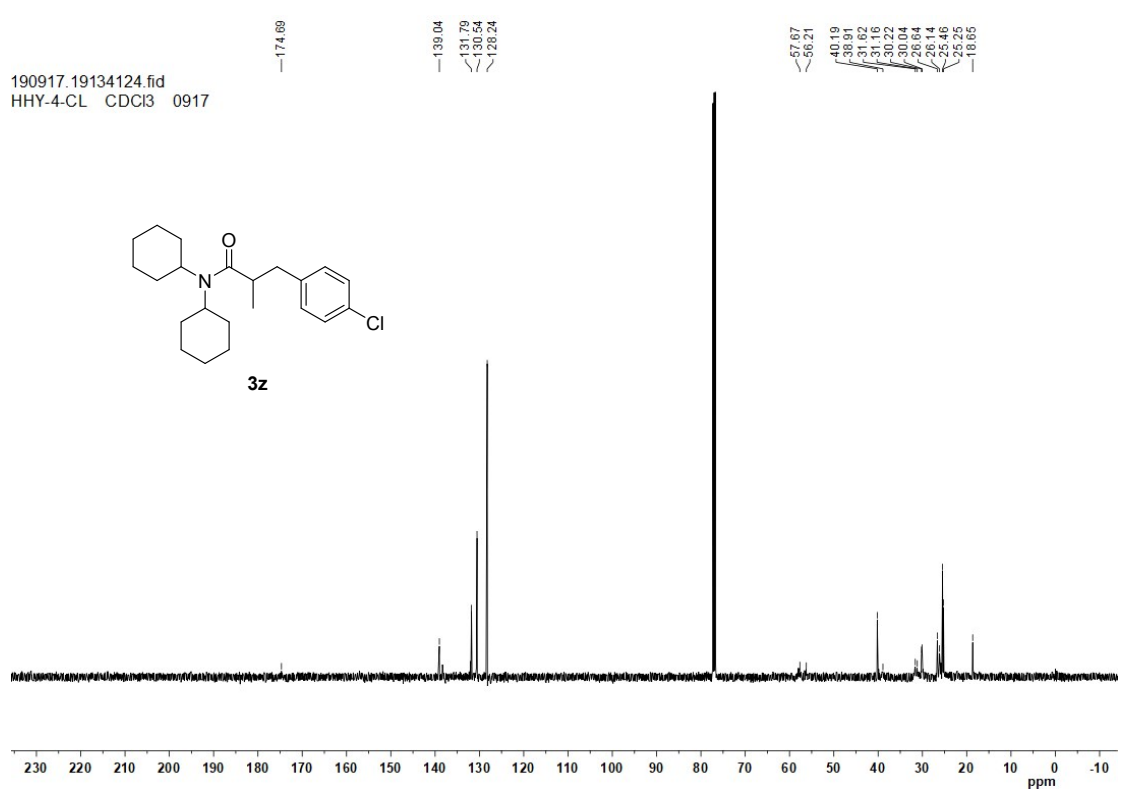
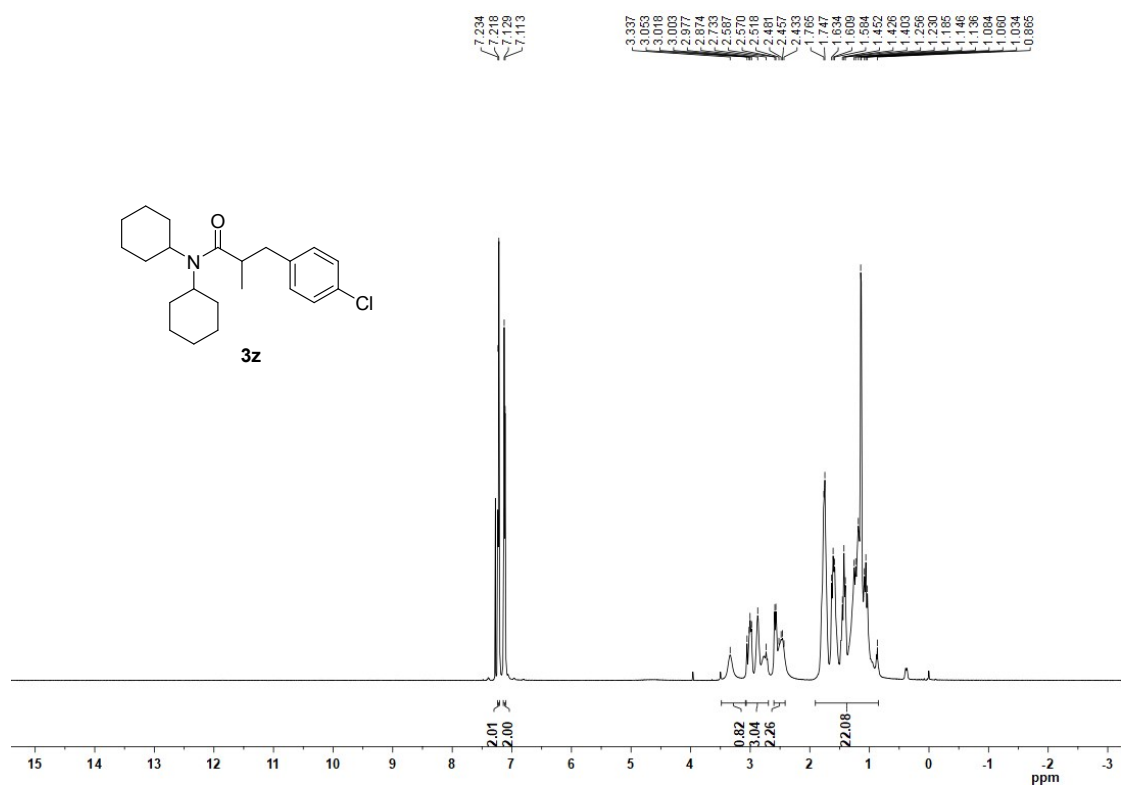


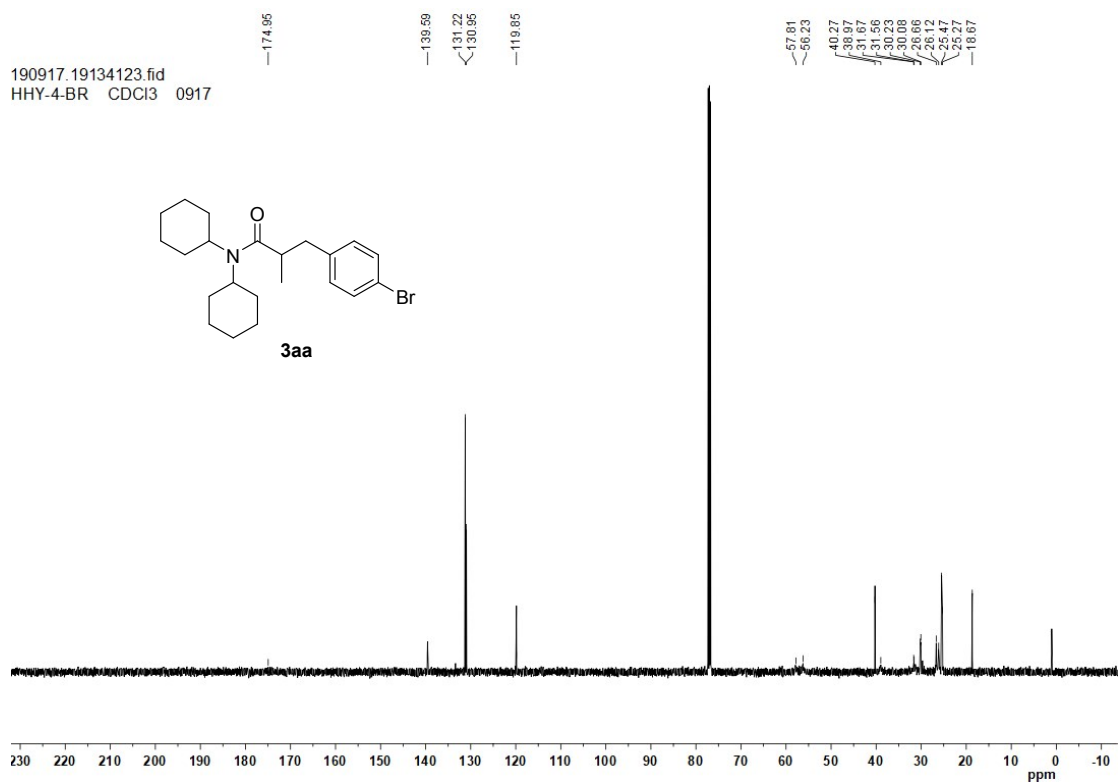
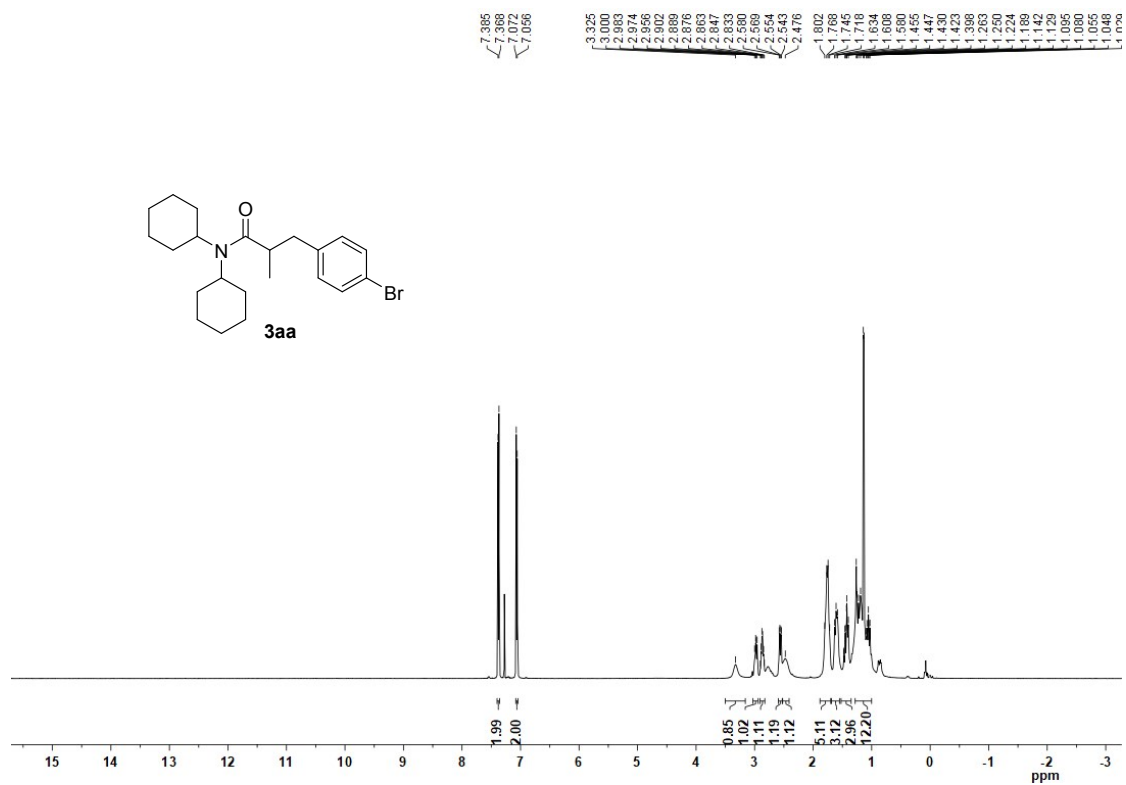


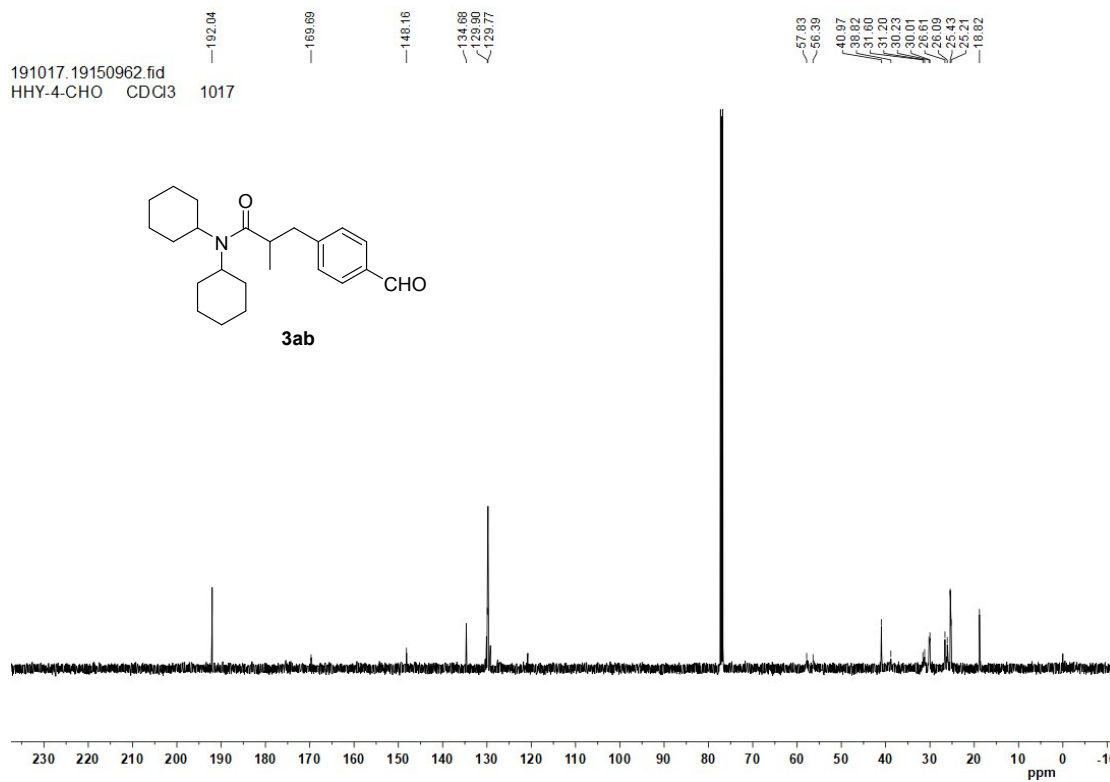
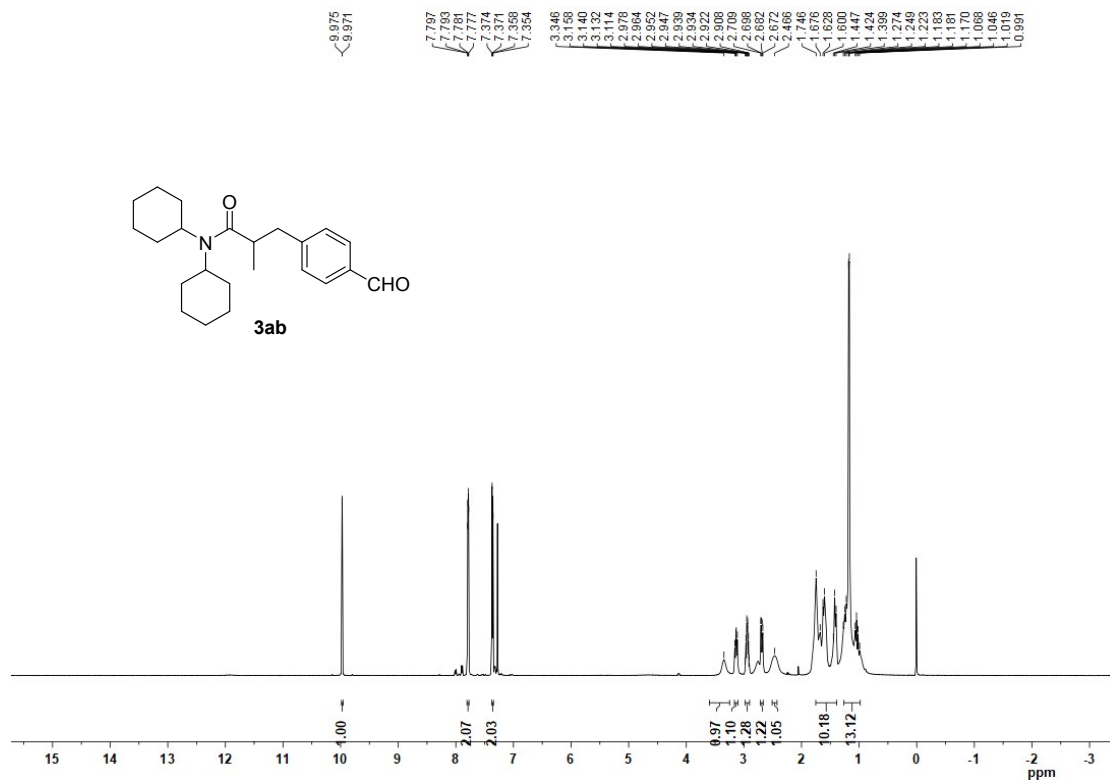




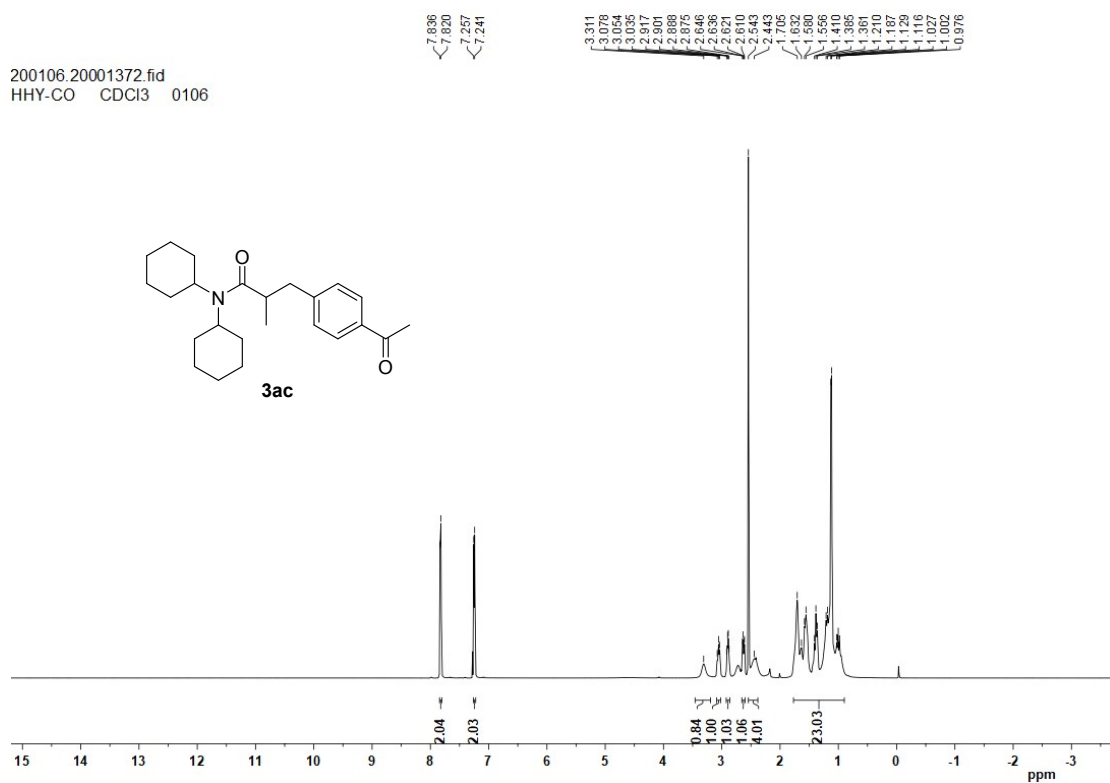




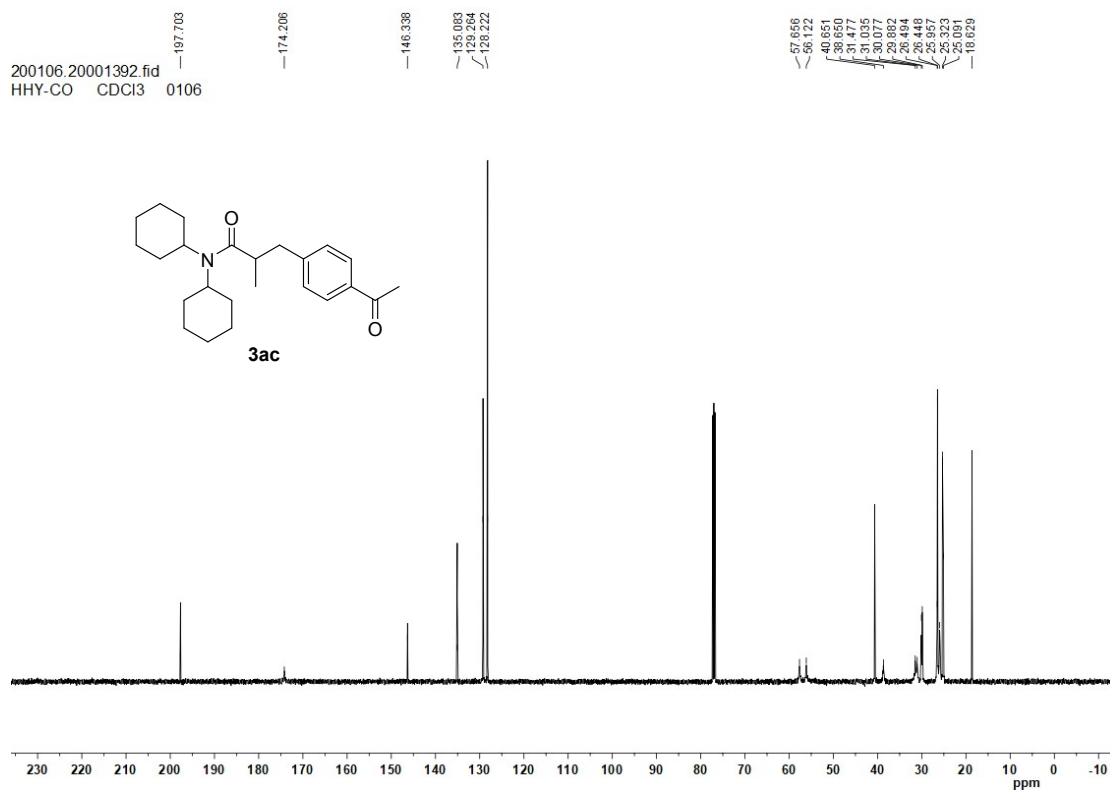


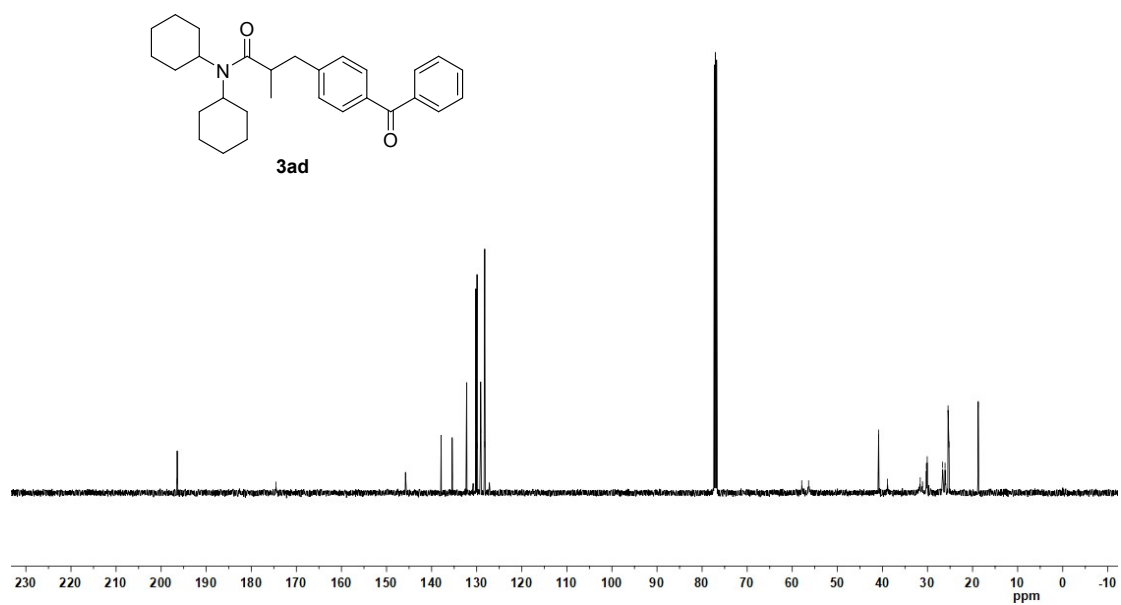
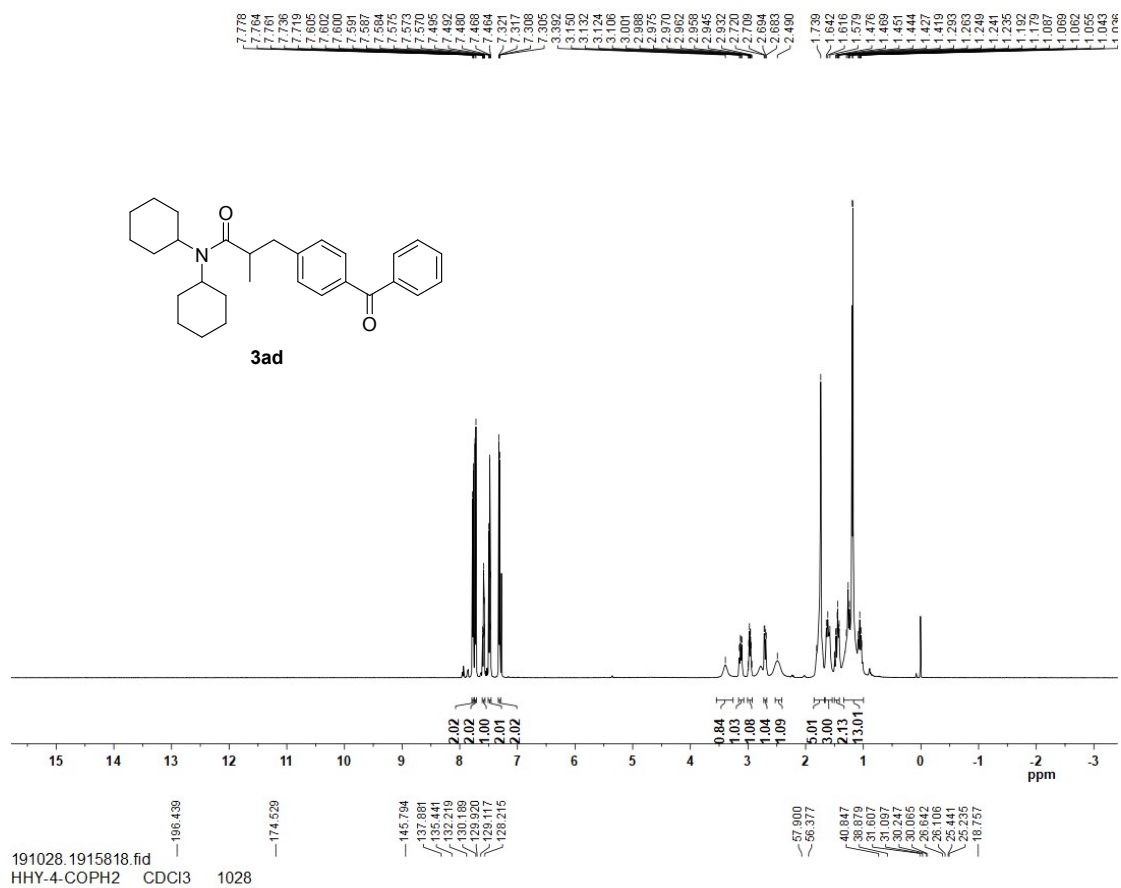


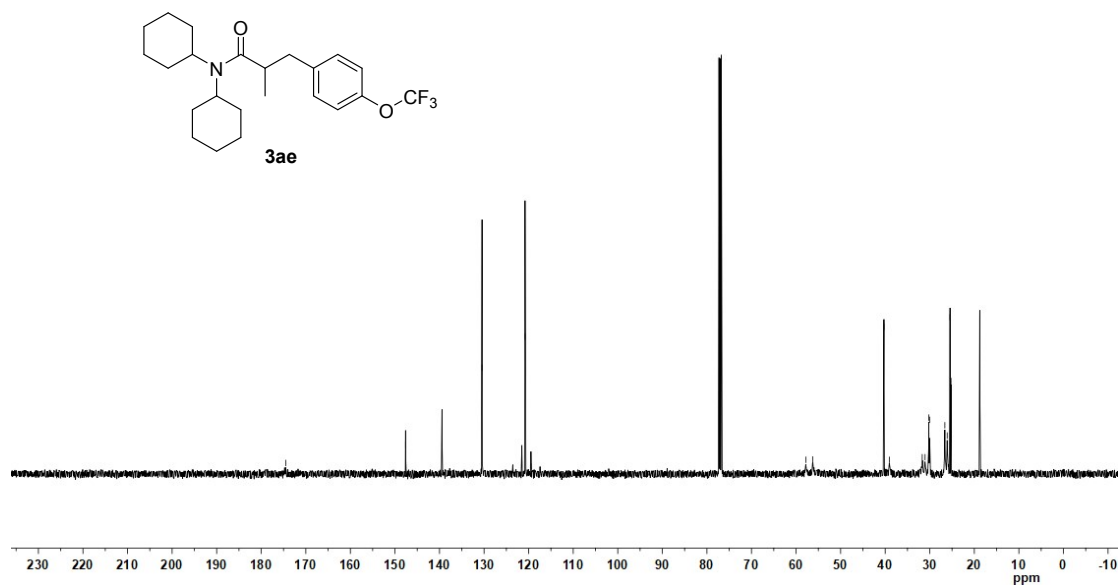
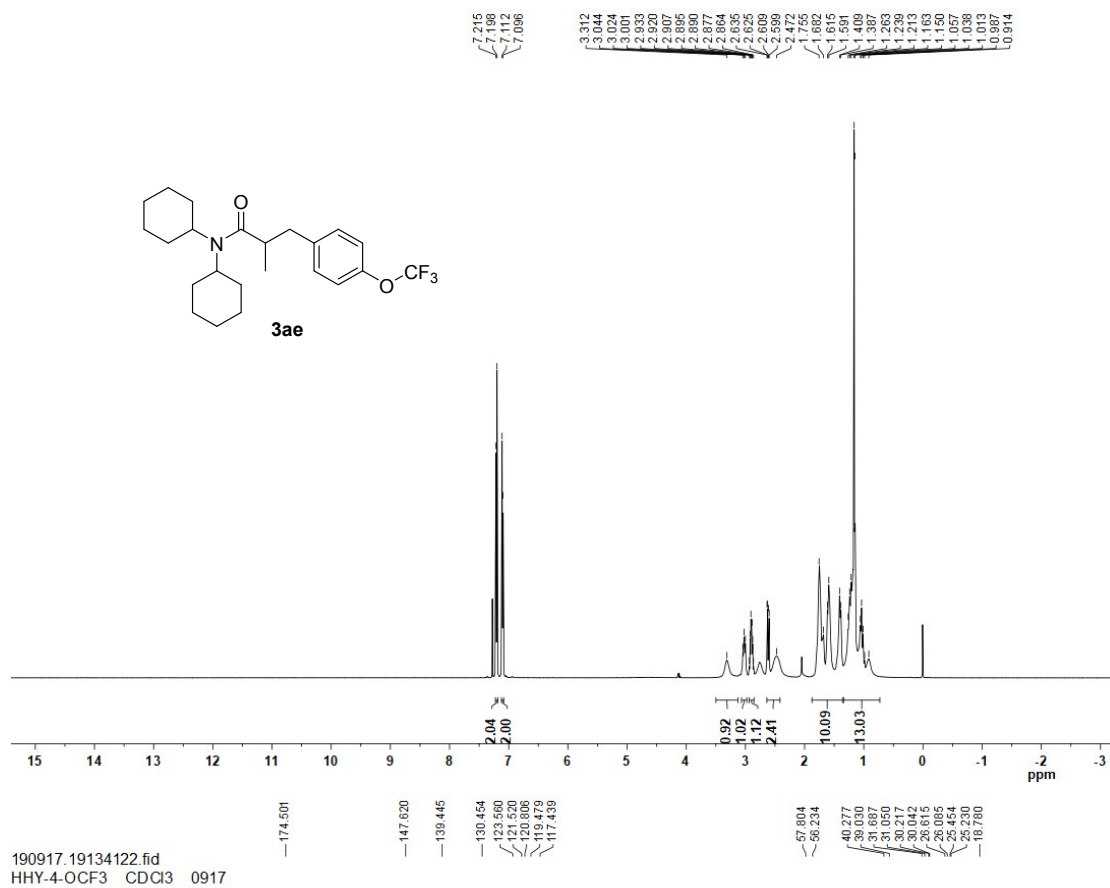
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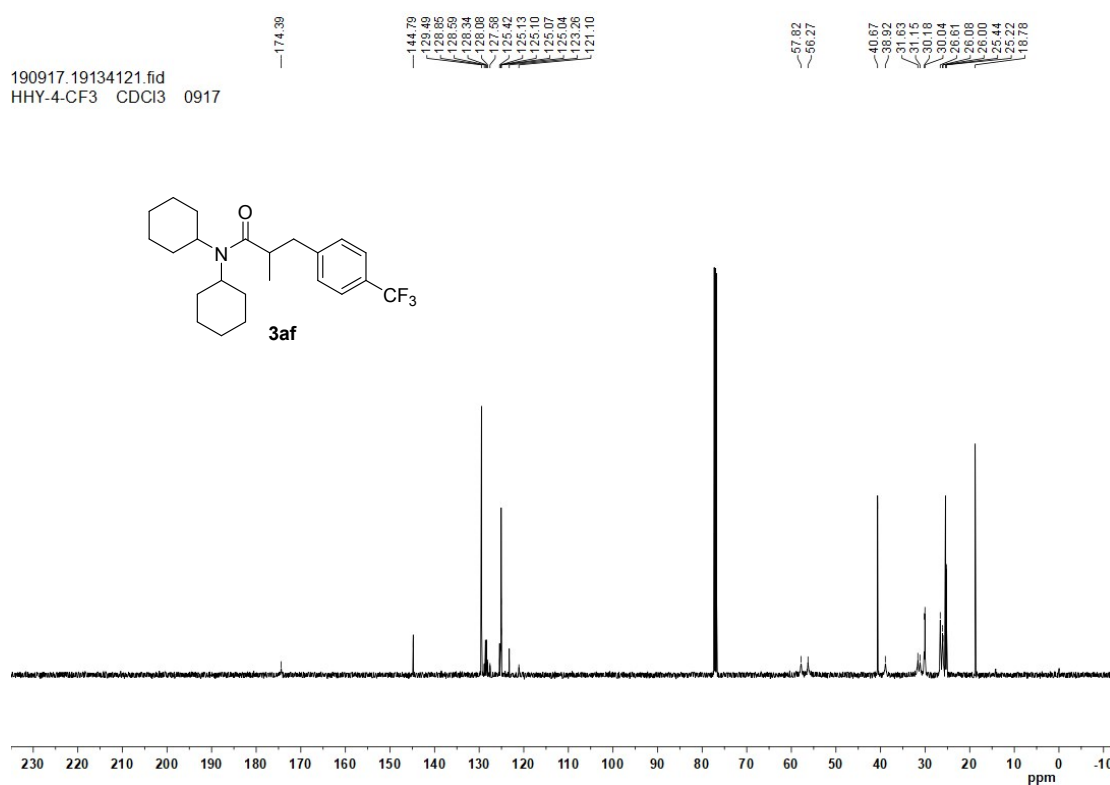
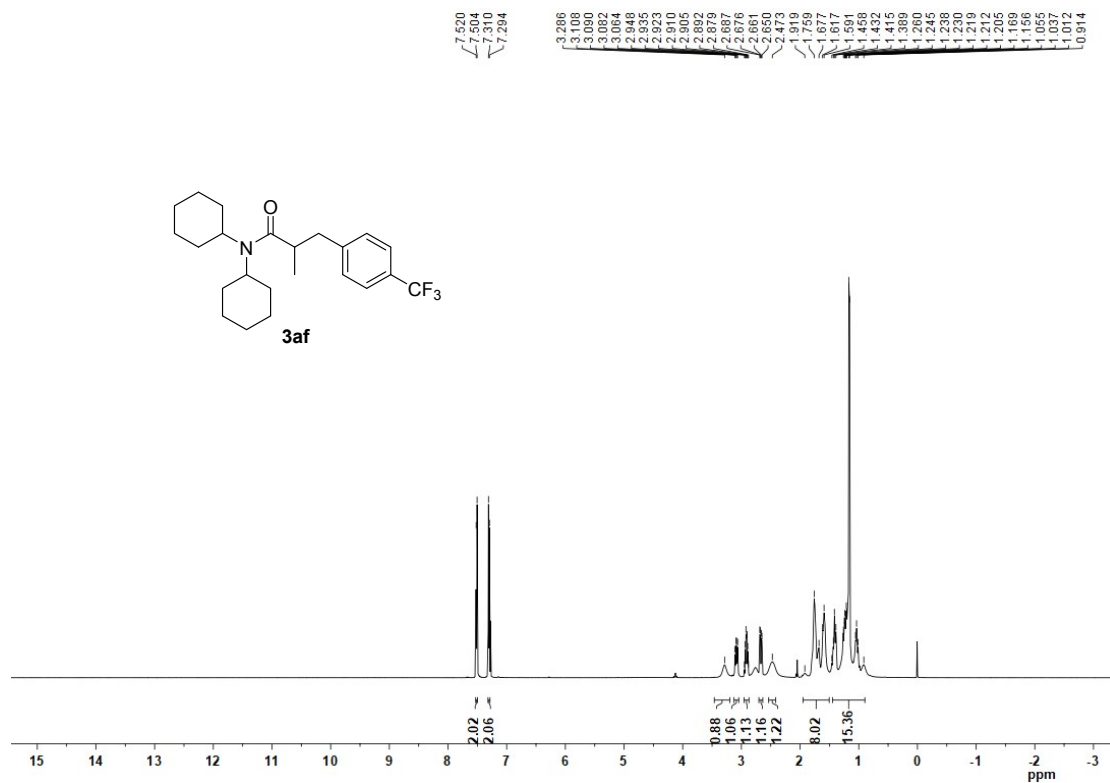


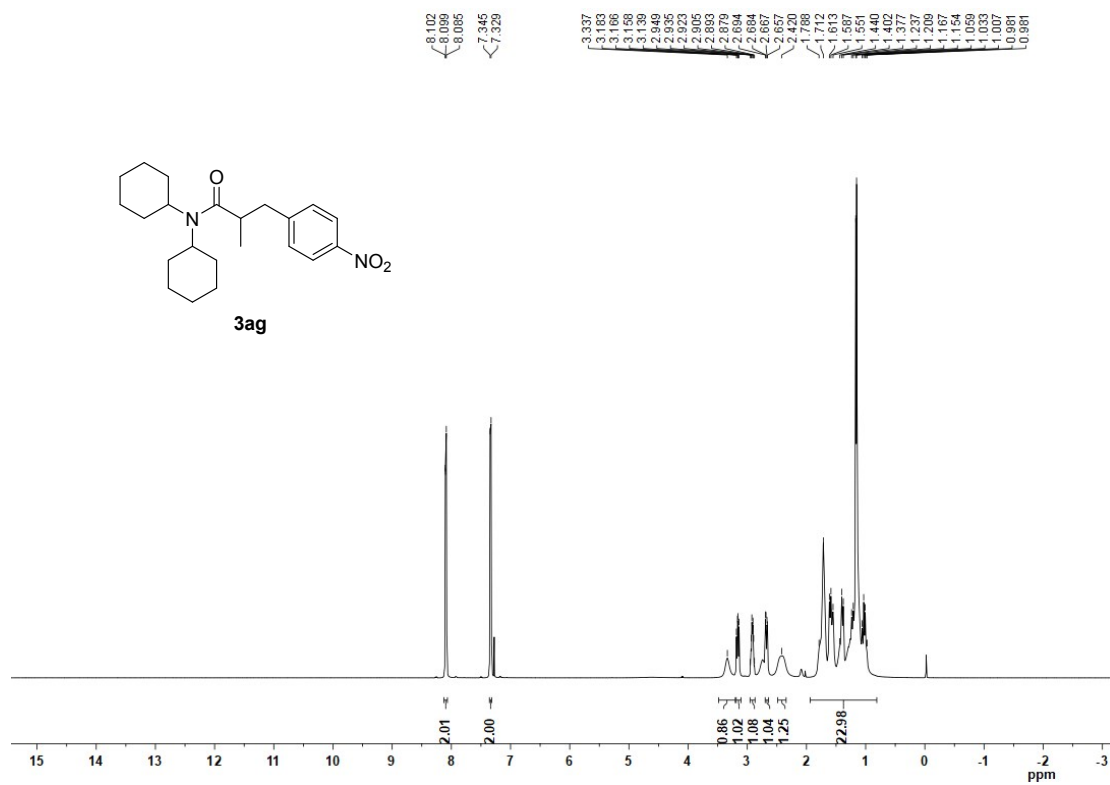
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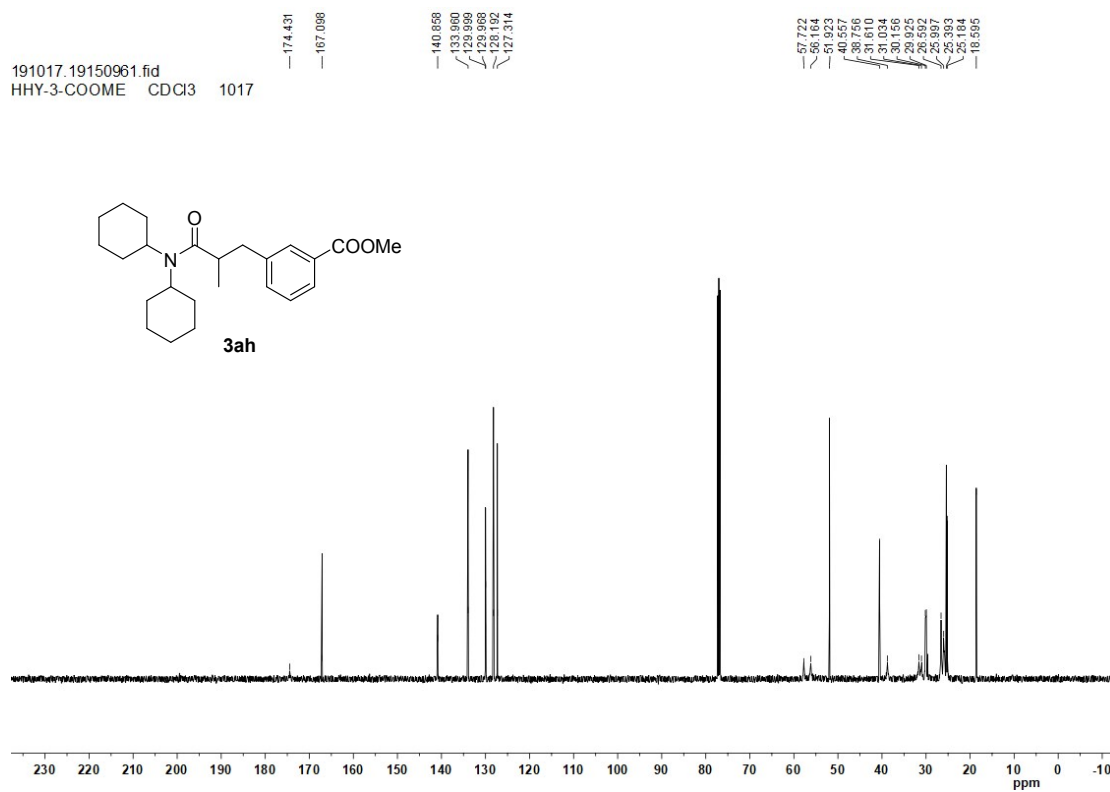
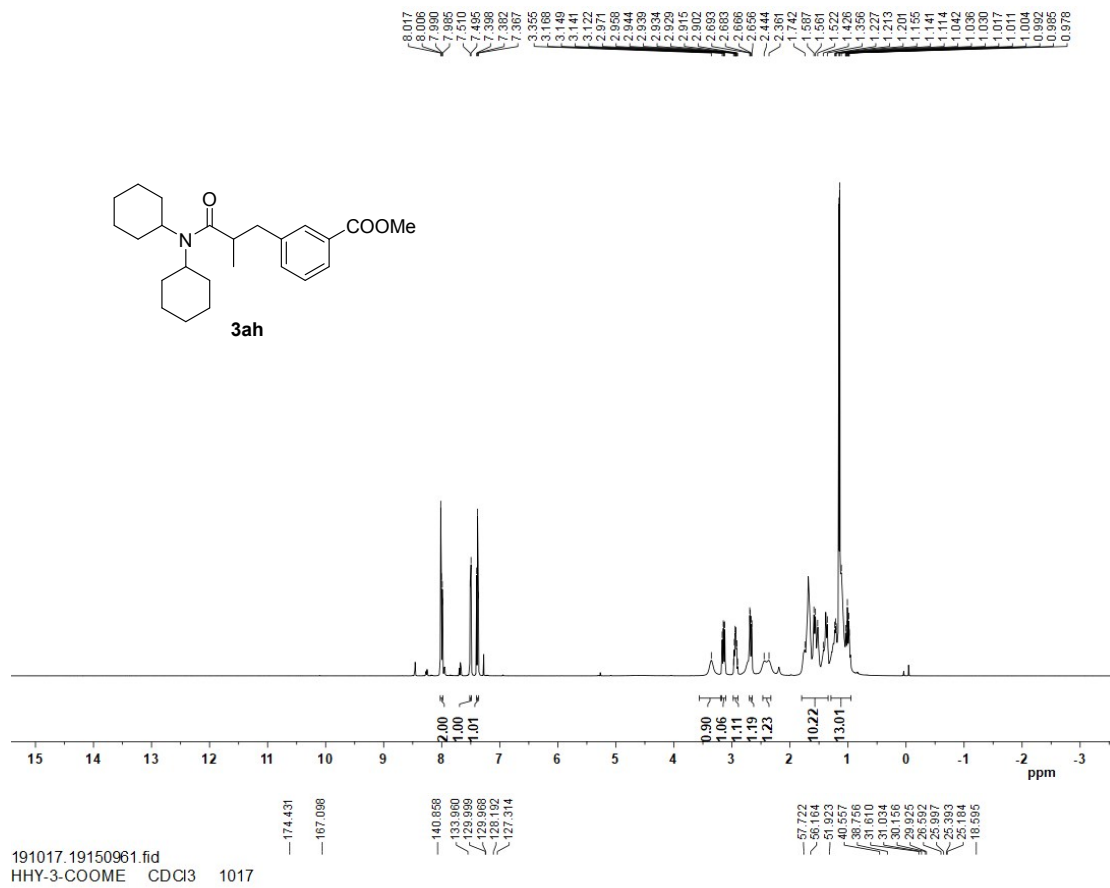


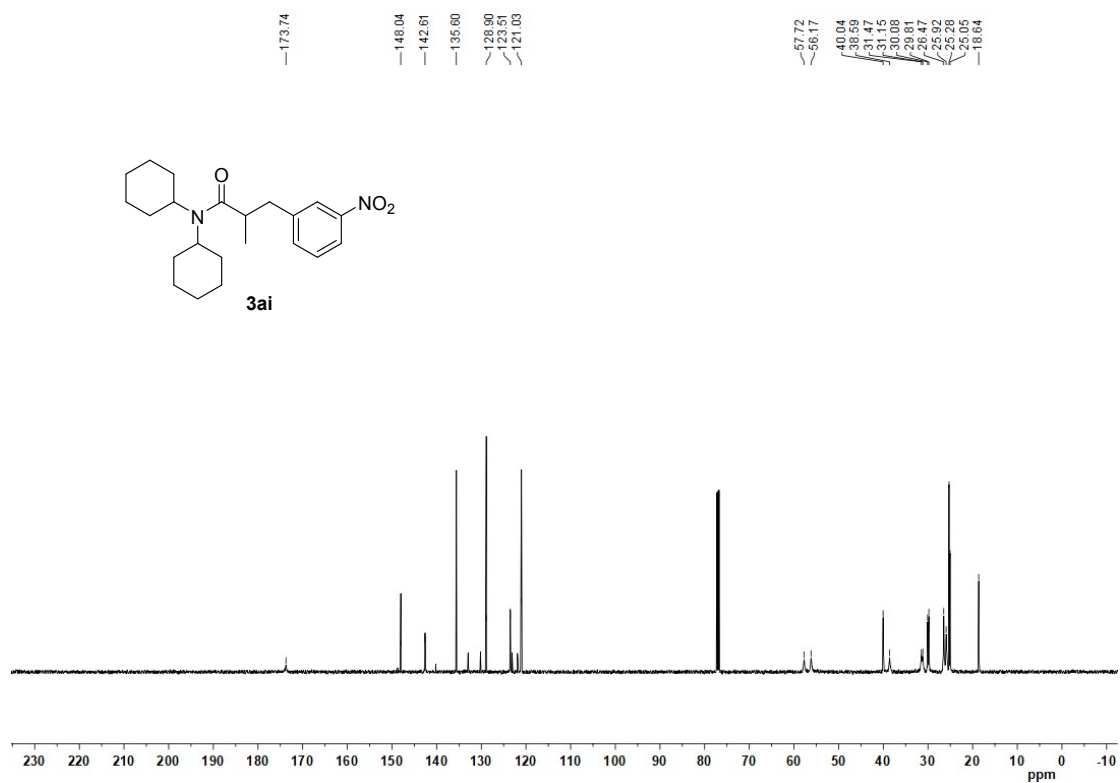
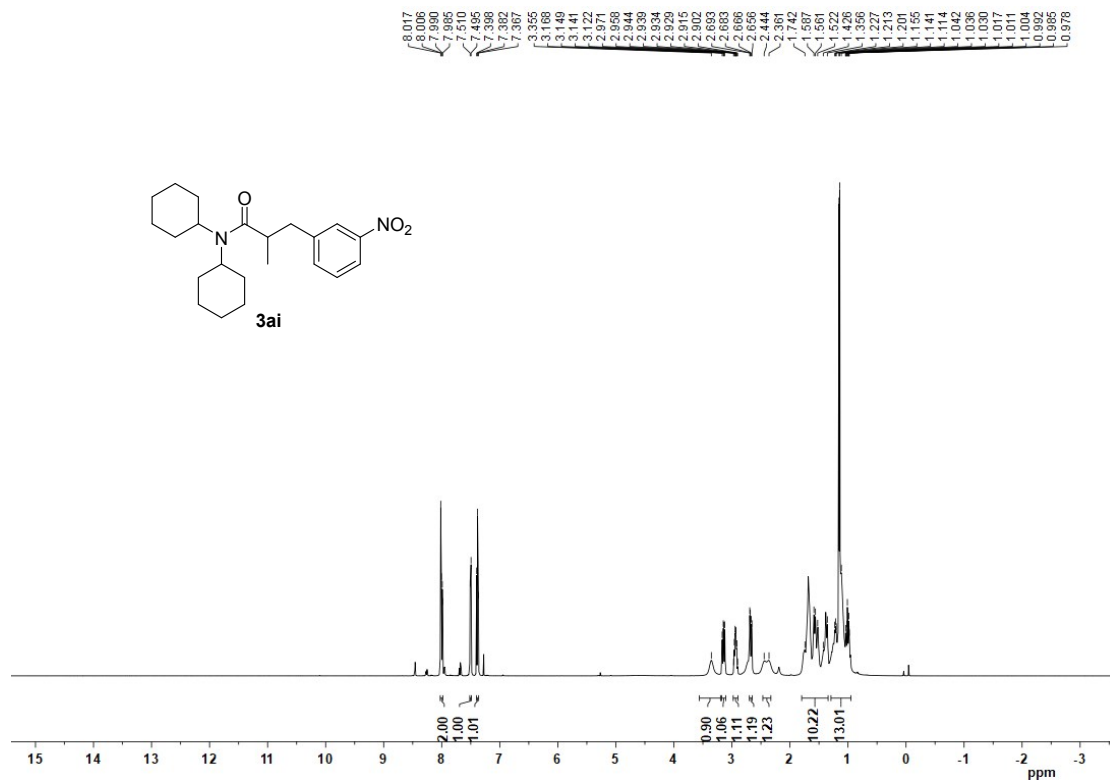




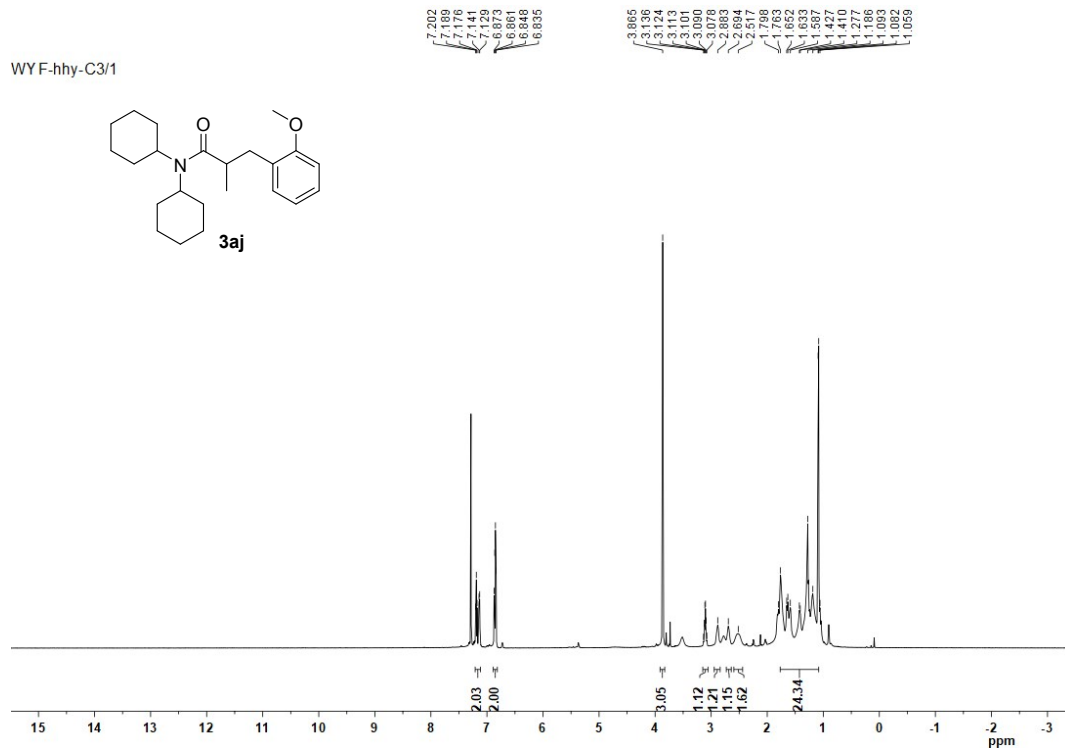
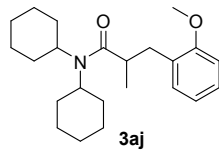




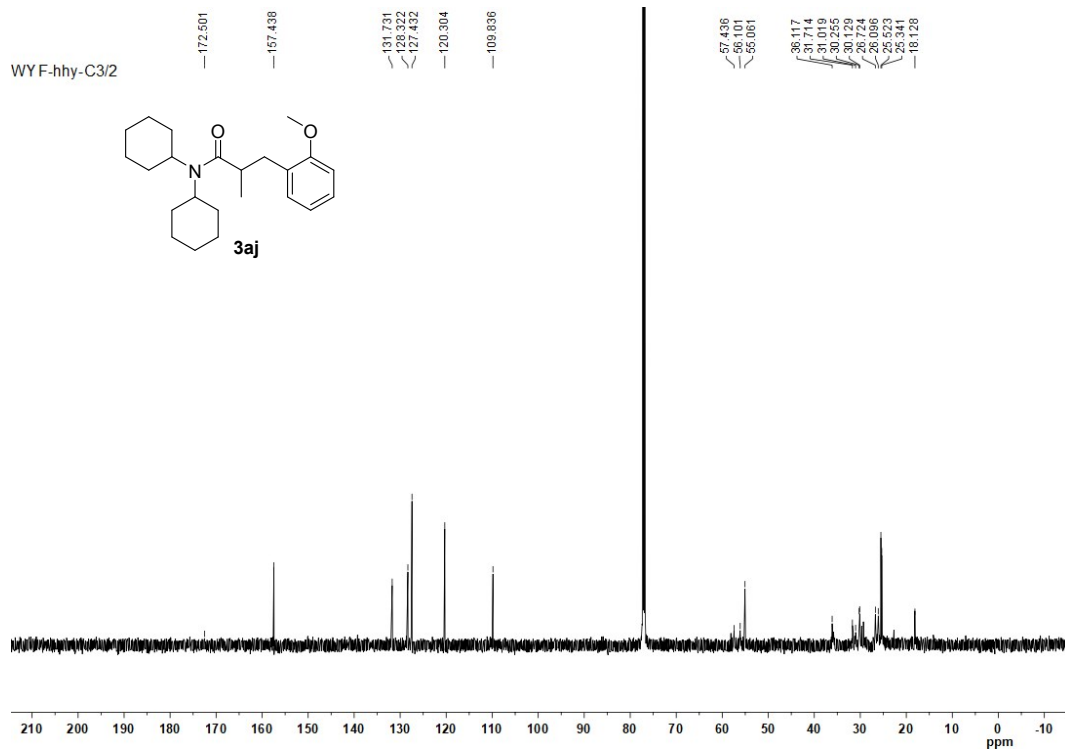
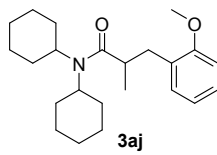


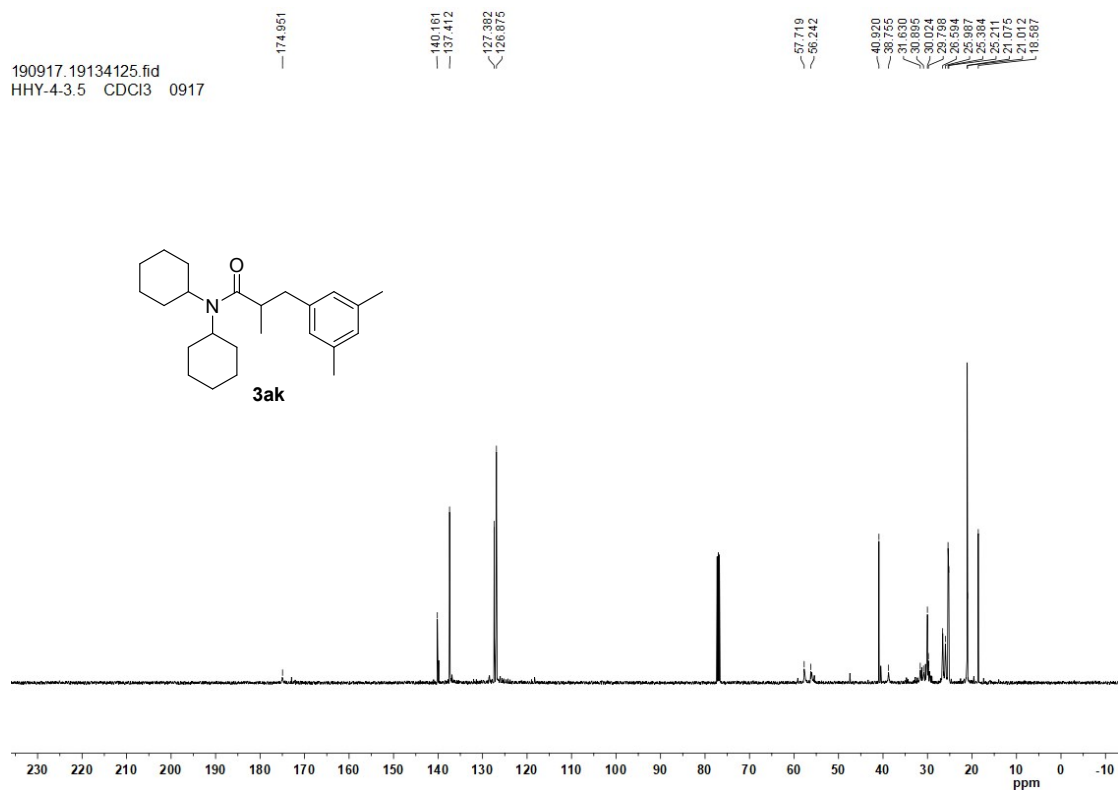
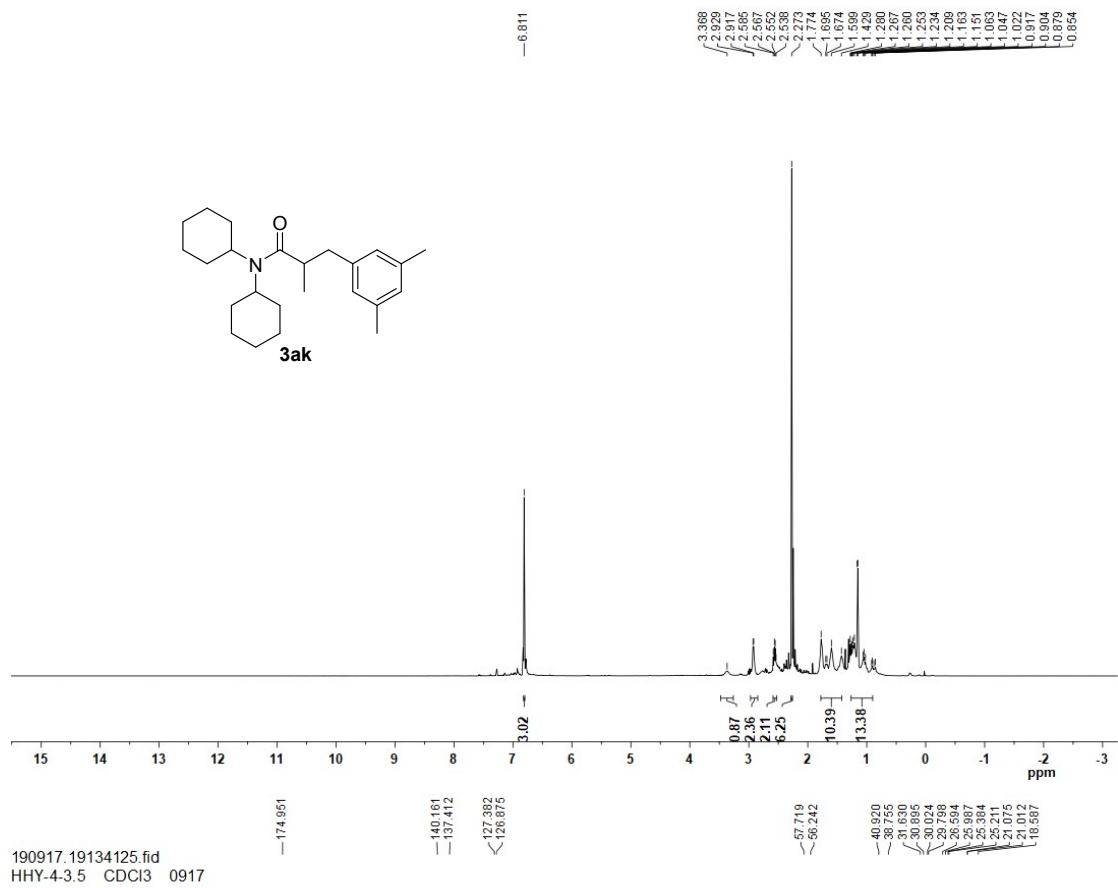


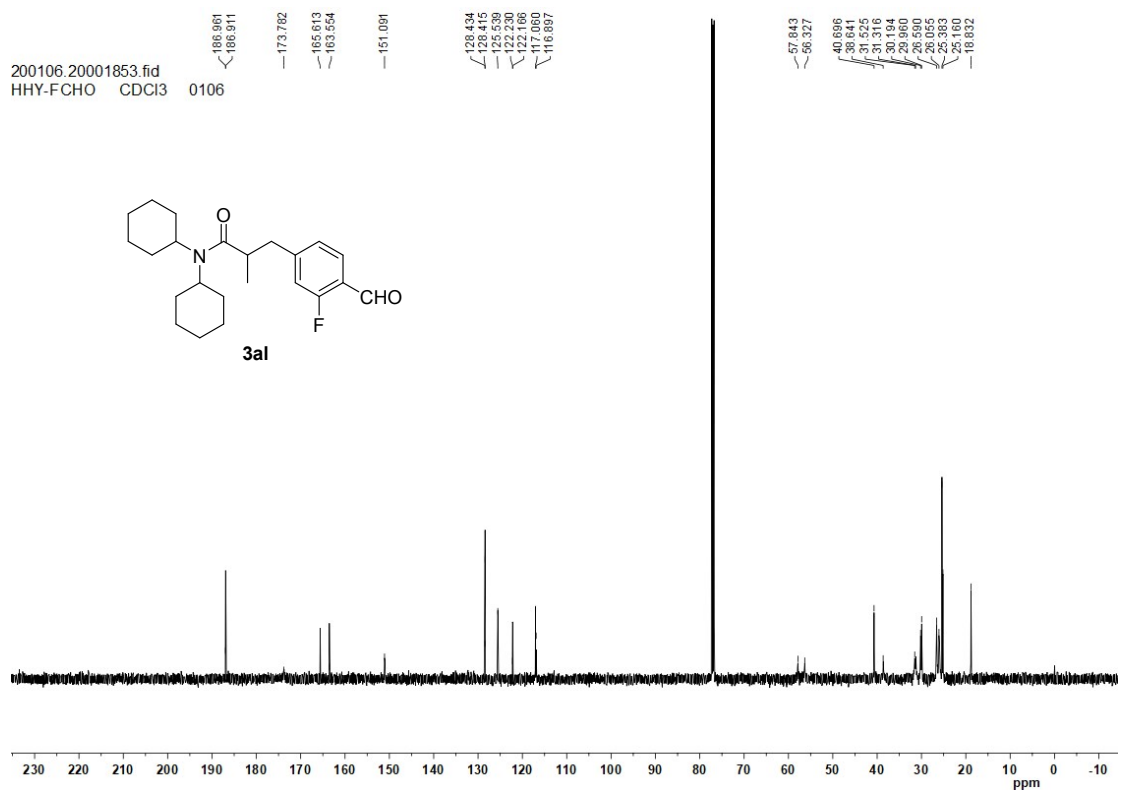
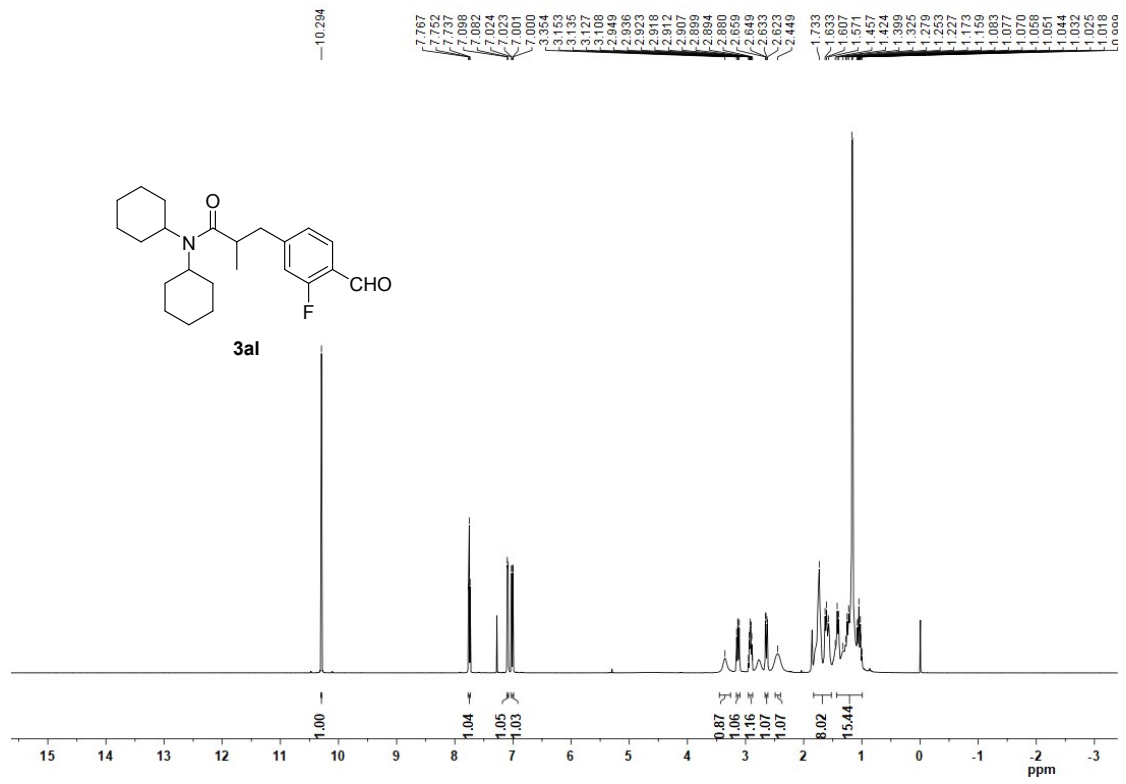
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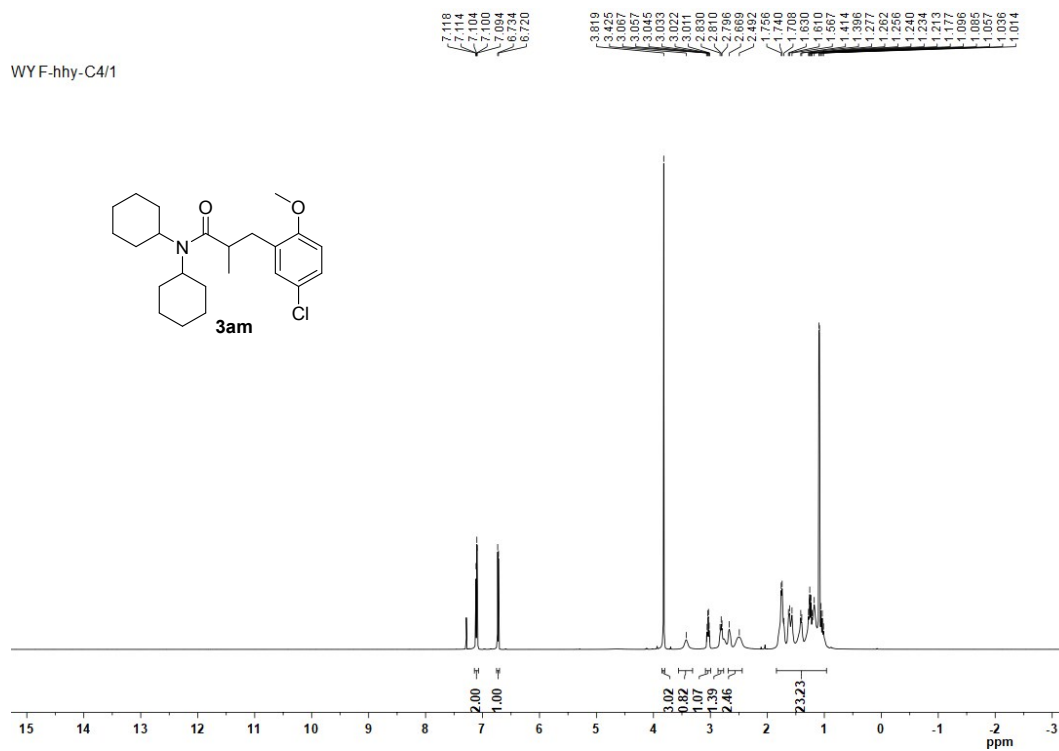
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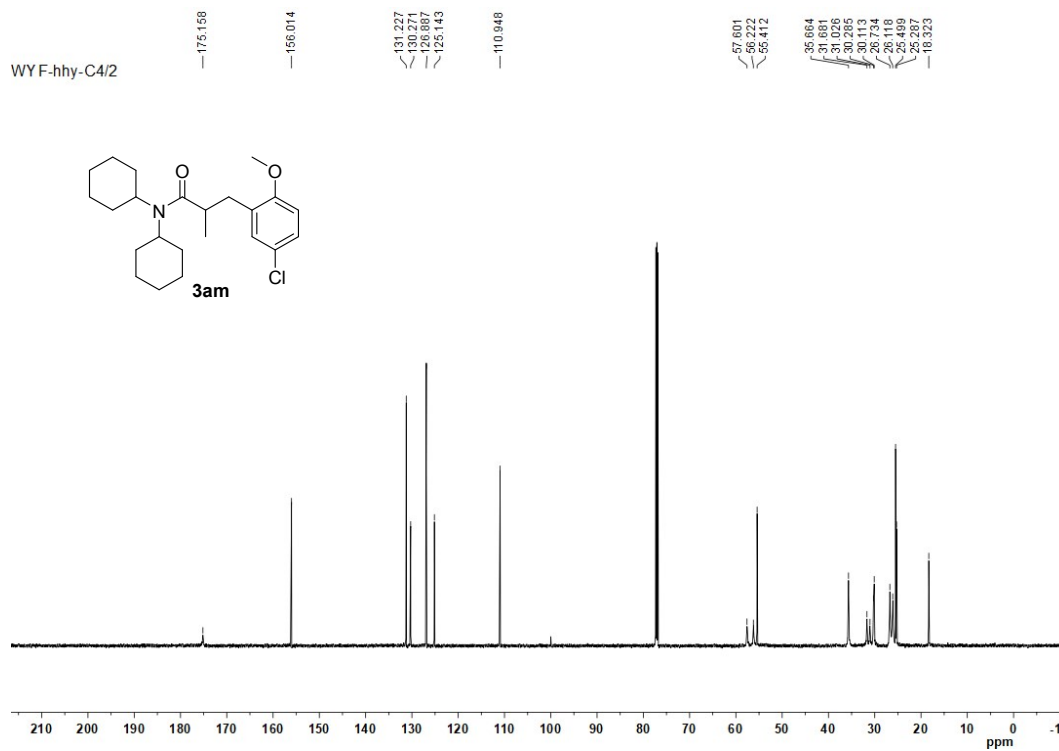




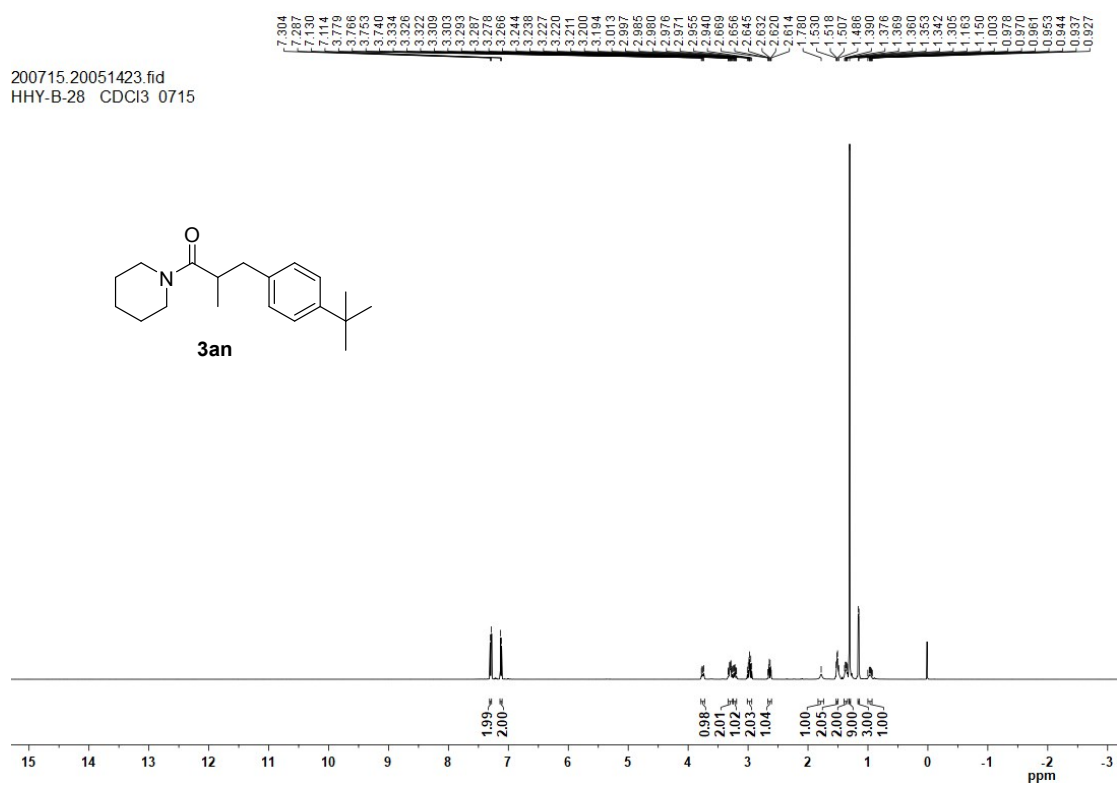
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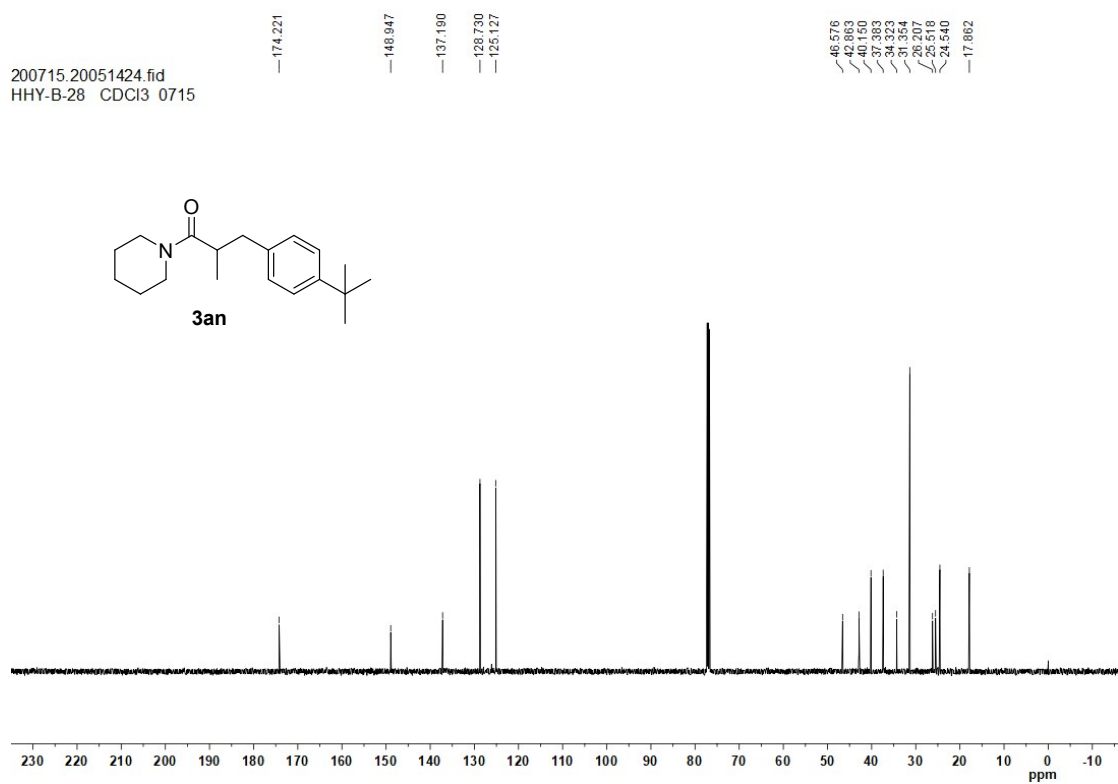
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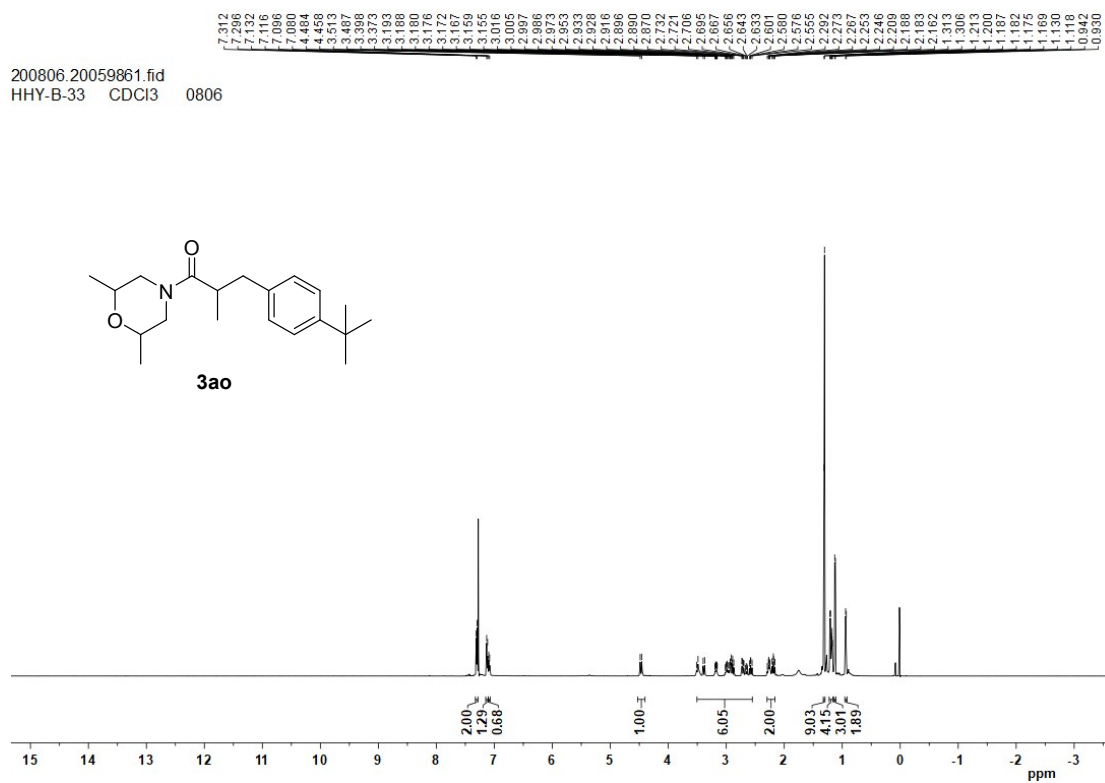
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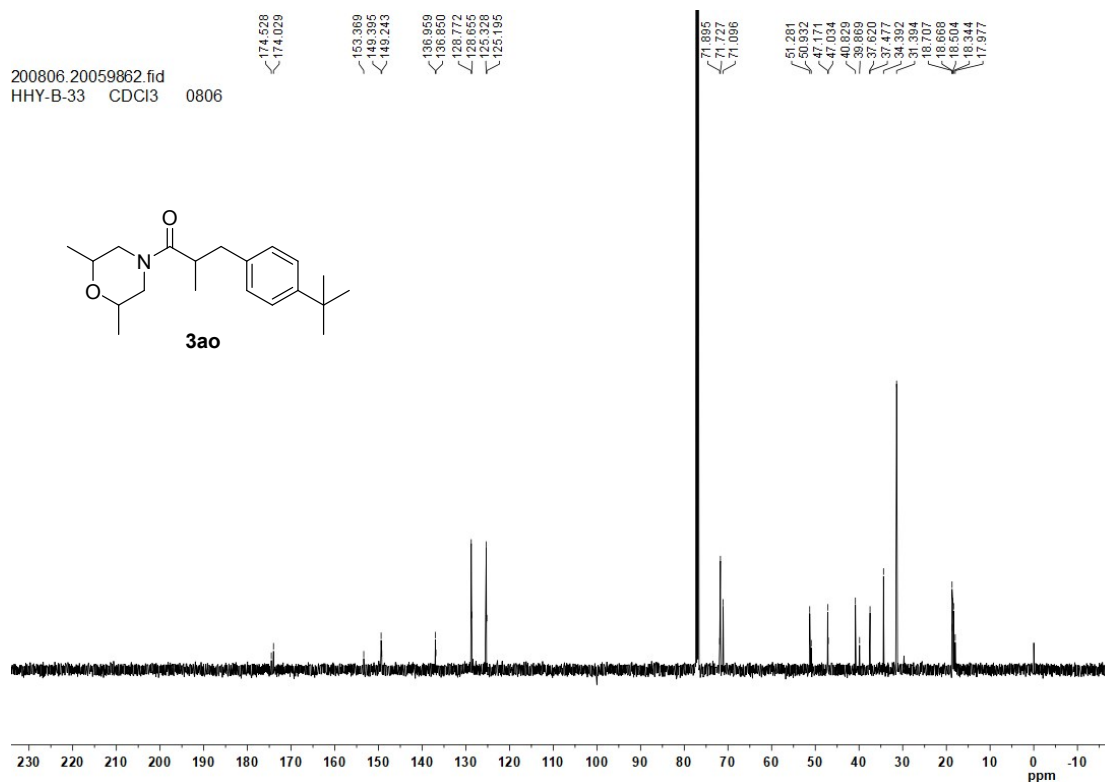
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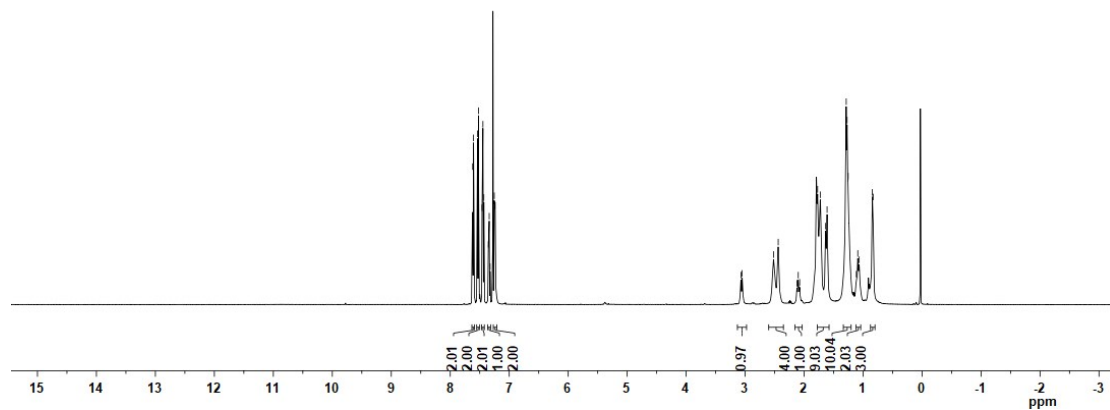
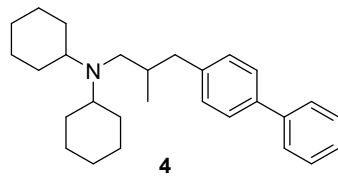
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7.431
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7.254
7.238

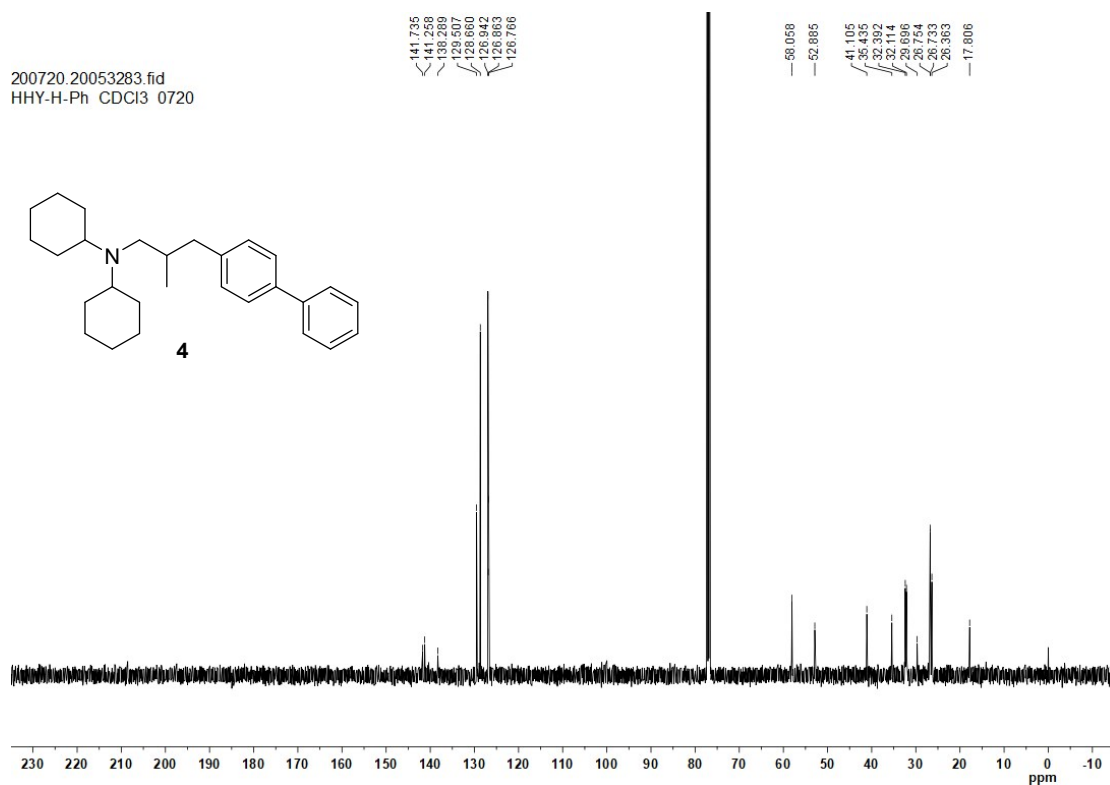
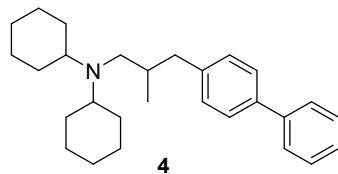
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3.051
2.518
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1.114
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0.650



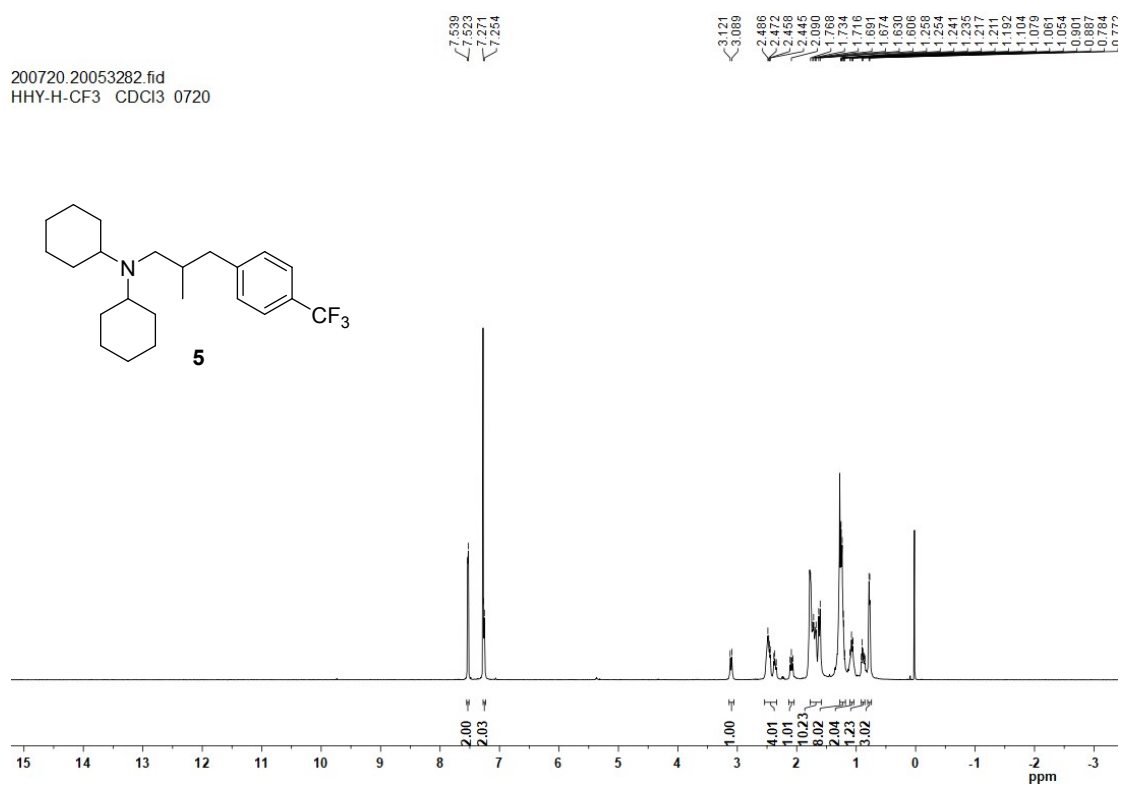
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126.766

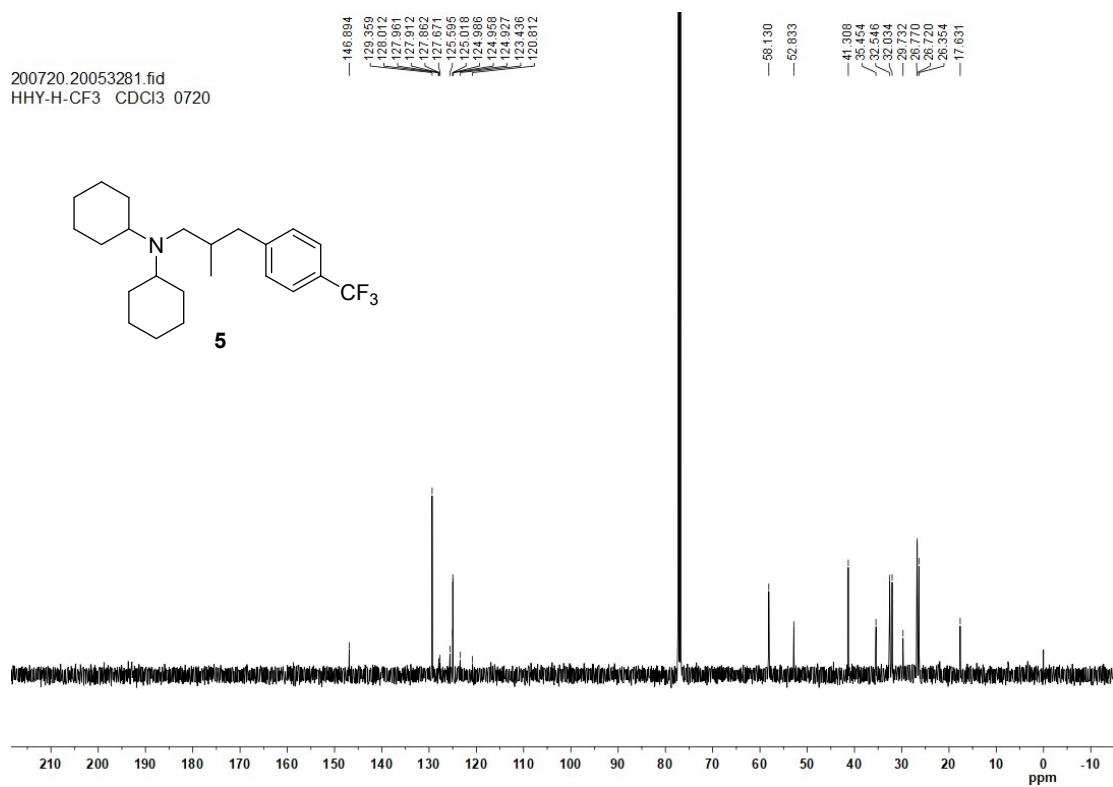
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26.303
17.806



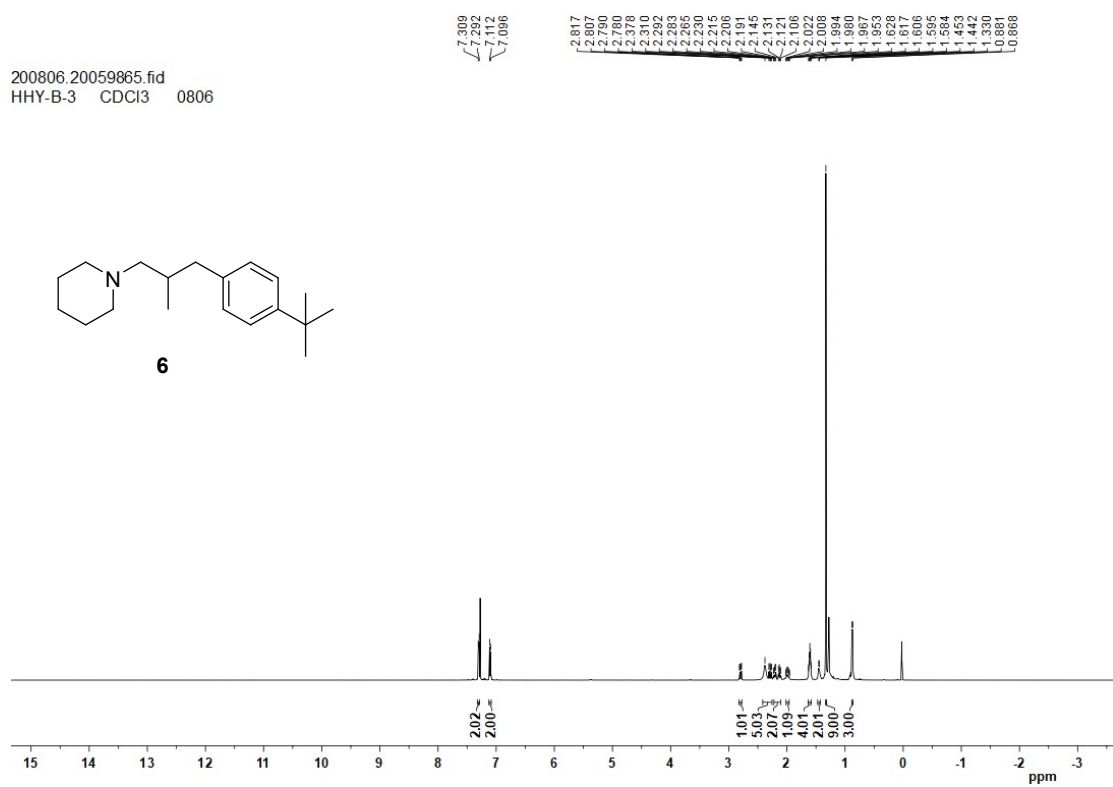
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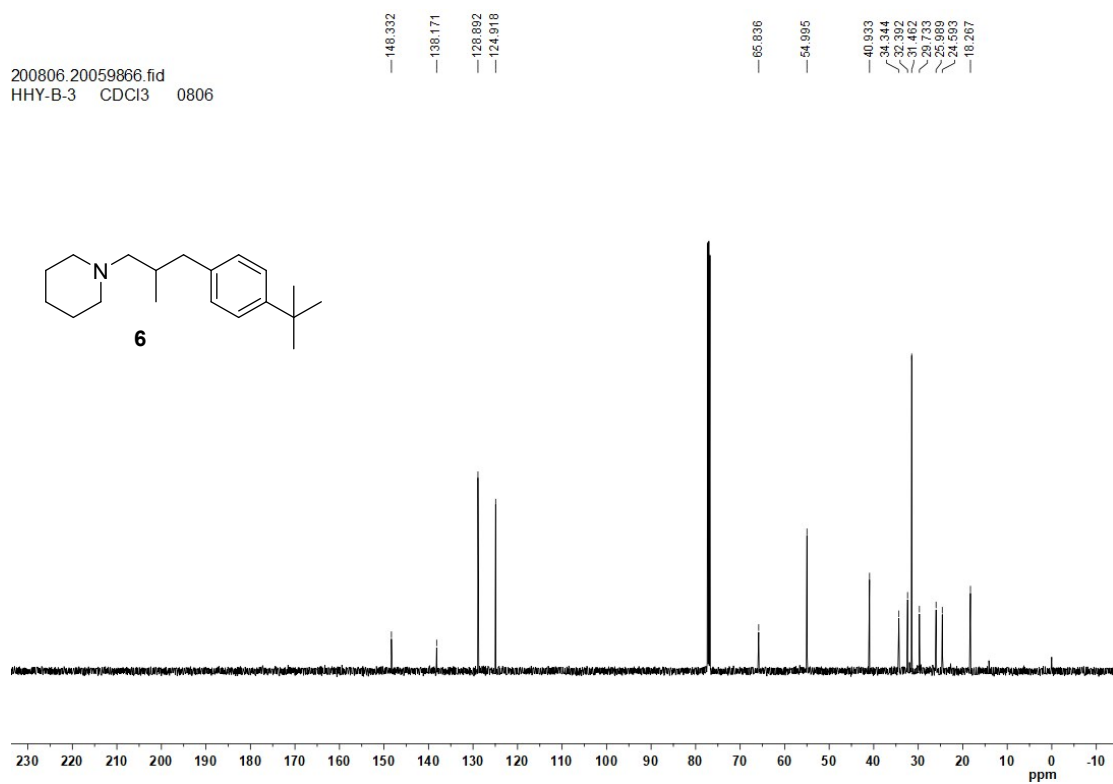
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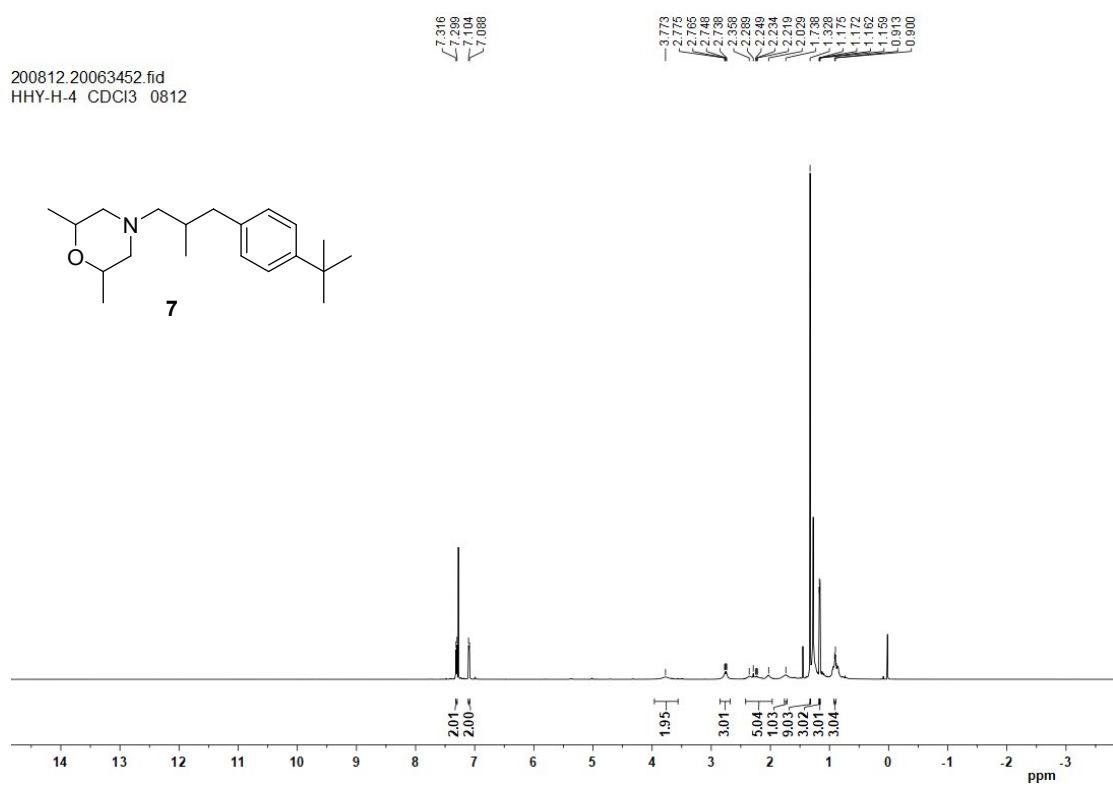
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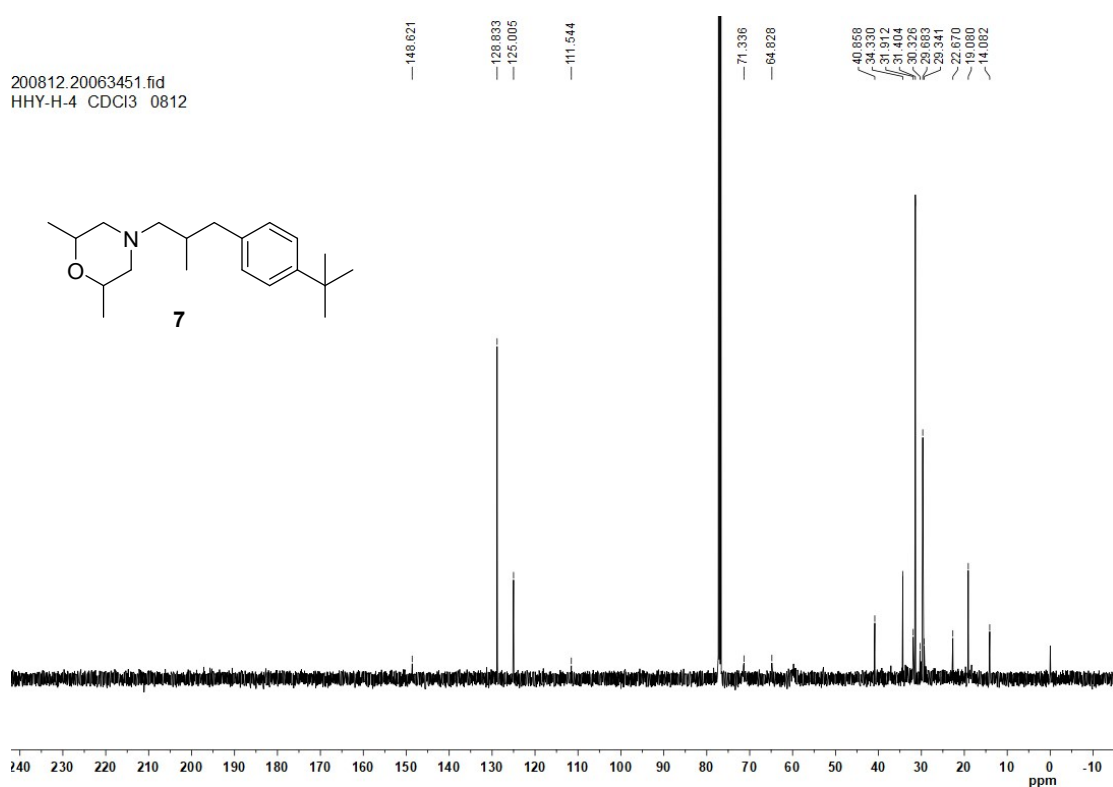
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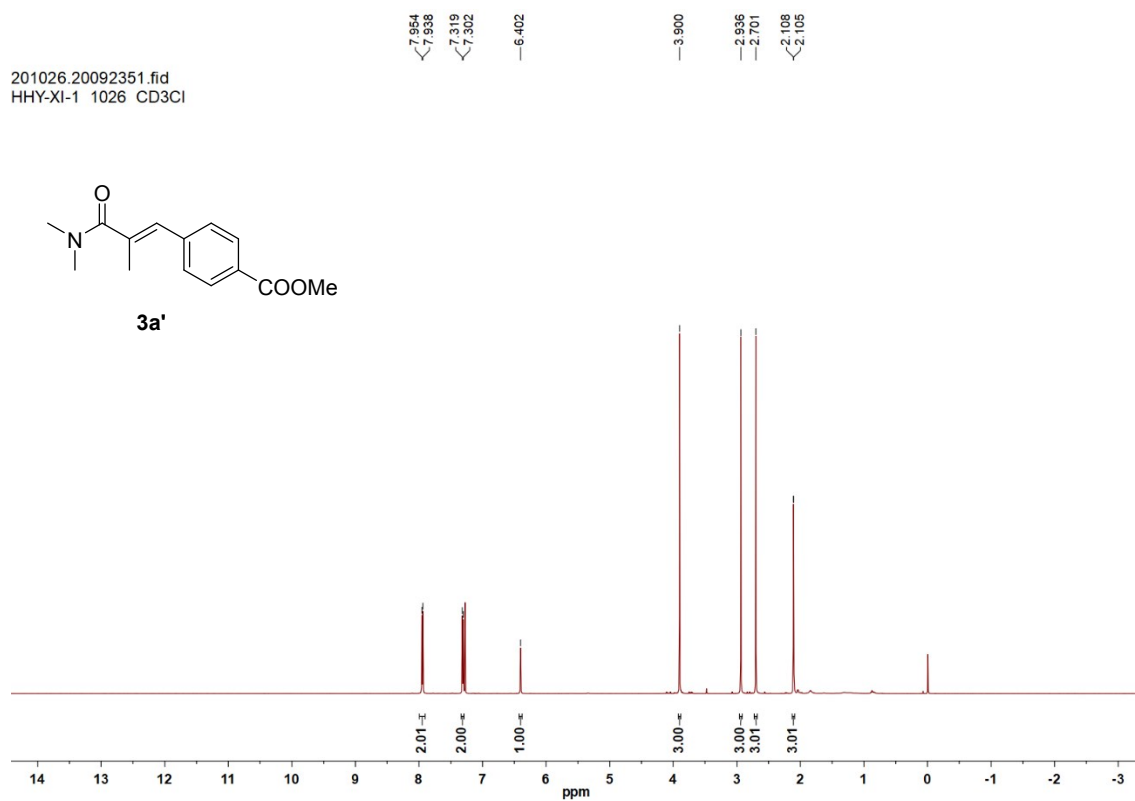
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201026.20092351.fid
HHY-XI-1 1026 CD3Cl



201026.20092352.fid
HHY-XI-1 1026 CD3Cl

