

**Supporting Information**  
for

**One-pot multistep mechanochemical synthesis of  
fluorinated pyrazolones**

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## General methods

<sup>1</sup>H, <sup>19</sup>F and <sup>13</sup>C NMR spectra were obtained on Bruker 400 Ultrashield<sup>TM</sup> and Bruker Ascend<sup>TM</sup> 500 MHz spectrometers with chloroform-*d* as deuterated solvent. The obtained chemical shifts;  $\delta$ , are reported in ppm and are referenced to the residual solvent signal. Spin-spin coupling constants;  $J$ , are given in Hz.

High resolution mass spectral (HRMS) data were obtained on a Thermo Scientific LTQ Orbitrap XL by the EPSRC UK National Mass Spectrometry Facility at Swansea University or on a Waters MALDI-TOF mx in Cardiff University.

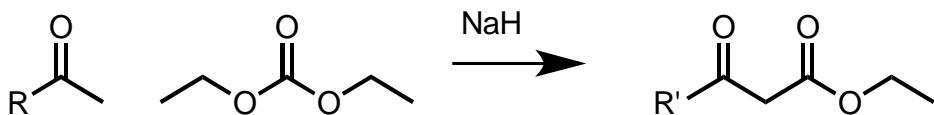
Infrared spectra were recorded on a Shimadzu IR-Affinity-1S FTIR spectrometer.

Melting points were measured using a Gallenkamp apparatus and are reported uncorrected.

The ball mill used was a Retsch MM 400 mixer mill. Unless otherwise stated, mechanochemical reactions were performed in 10 mL stainless steel jars with one stainless steel ball of mass 4 g.

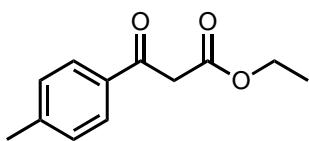
All chemicals were obtained from commercial sources and used without further purification unless stated otherwise. Dry THF was obtained from a solvent purification system. Petroleum ether refers to the 40–60 °C fraction.

## Synthesis of $\beta$ -ketoesters



### General procedure (GP1)

Following a literature procedure<sup>1</sup>: to a suspension of NaH (1.2 g, 30 mmol, 60% in mineral oil) in dry THF (10 mL) was added diethyl carbonate (4.85 mL, 40 mmol) in oven-dried glassware under N<sub>2</sub>. A solution of the corresponding ketone (10 mmol) in dry THF (5 mL) was added slowly and the reaction mixture heated under reflux for 6 hours. The reaction mixture was quenched with glacial acetic acid (1 mL) and HCl (10%, 20 mL). The aqueous phase was extracted with ethyl acetate (3  $\times$  10 mL) and the combined organic phase washed with saturated sodium hydrogen carbonate (10 mL), water (10 mL) and brine (10 mL). The combined organic phase was dried (MgSO<sub>4</sub>), filtered and the solvent removed under reduced pressure to yield the crude product. This was purified by flash column chromatography on silica gel (gradient elution EtOAc in petroleum ether (0–25%)).



### Ethyl 3-oxo-3-(*p*-tolyl)propanoate<sup>2</sup>

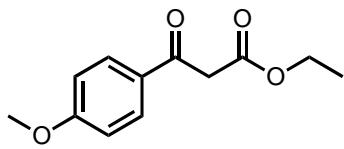
Prepared according to **GP1** with further purification by short-path distillation (190 °C, 7 mbar); 0.583 g, 2.8 mmol, 28%, yellow oil. 1:3.7 enol:keto.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  12.60 (s, enol 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.1, enol 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, enol 2H), 5.65 (s, enol 1H), 4.27 (q, *J* = 7.1 Hz, enol 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 2H), 2.44 (s, 3H), 2.41 (s, enol 3H), 1.35 (t, *J* = 7.1 Hz, enol 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>):  $\delta$  192.2, 173.4, 171.7, 167.8, 144.8, 141.8, 133.7, 130.8, 129.6, 129.4, 128.8, 126.1, 86.8, 61.6, 60.4, 46.1, 21.8, 21.6, 14.5, 14.2.

IR: 2980, 1736, 1682, 1265, 1182, 1144, 808 cm<sup>-1</sup>.

HRMS (AP+): [C<sub>12</sub>H<sub>14</sub>O<sub>3</sub> + H]<sup>+</sup> calc. 207.1021, found 207.1024.



**Ethyl 3-(4-methoxyphenyl)-3-oxopropanoate<sup>3</sup>**

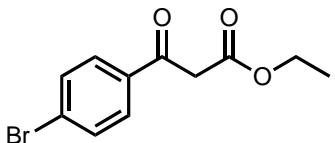
Prepared according to **GP1** with further purification by short-path distillation (200 °C, 8 mbar); 0.434 g, 2.0 mmol, 20%, colourless oil. 1:18 enol:keto.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 12.63 (s, enol 1H), 7.93 (d, *J* = 9.1 Hz, 2H), 7.74 (d, *J* = 9.1 Hz, enol 2H), 6.95 (m, 2H), 5.58 (s, enol 1H), 4.25 (q, *J* = 7.1 Hz, enol 2H), 4.22 (q, *J* = 7.1 Hz, 2H) 3.94 (s, 2H), 3.88 (s, 3H), 3.85 (s, enol 3H), 1.33 (t, *J* = 7.1 Hz, enol 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>): δ 191.1, 167.9, 164.1, 131.0, 129.3, 114.1, 61.6, 55.7, 46.0, 14.2.

IR: 2980, 1734, 1674, 1597, 1256, 1024, 843 cm<sup>-1</sup>.

HRMS (pNSI+): [C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> + H]<sup>+</sup> calc. 223.0965, found 223.0964.



**Ethyl 3-(4-bromophenyl)-3-oxopropanoate<sup>3</sup>**

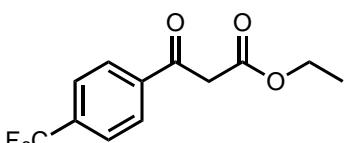
Prepared according to **GP1**; 2.395 g, 8.8 mmol, 88%, yellow oil. 1:2.2 enol:keto.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 12.56 (s, enol 1H), 7.81 (d, *J* = 8.5 Hz, 2H), 7.63 (m, 2H), 7.55 (d, *J* = 8.6 Hz, enol 2H), 5.64 (s, enol 1H), 4.30 (q, *J* = 7.3 Hz, enol 2H), 4.18 (q, *J* = 7.3 Hz, 2H), 3.95 (s, 2H), 1.33 (t, *J* = 7.1 Hz, enol 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>): δ 191.6, 173.2, 170.3, 167.3, 134.9, 132.5, 132.3, 131.9, 130.1, 129.2, 127.7, 125.9, 87.9, 61.8, 60.6, 46.1, 14.4, 14.2.

IR: 2980, 1734, 1686, 1585, 1260, 1194, 995, 800 cm<sup>-1</sup>.

HRMS (pNSI+): [C<sub>11</sub>H<sub>11</sub>O<sub>3</sub>Br + H]<sup>+</sup> calc. 270.9964, found 270.9957.



**Ethyl 3-oxo-3-(4-(trifluoromethyl)phenyl)propanoate<sup>4</sup>**

Prepared according to **GP1**; 1.701 g, 6.5 mmol, 65%, yellow oil. 3:2 enol:keto.

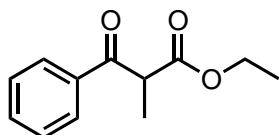
<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 12.57 (s, enol 1H), 8.06 (m, 2H), 7.88 (m, enol 2H), 7.76 (m, 2H), 7.68 (m, enol 2H), 5.72 (s, enol 1H), 4.31 (q, *J* = 7.1 Hz, enol 2H), 4.19 (q, *J* = 7.1 Hz, 2H) 4.01 (s, 2H), 1.39 (t, *J* = 7.1 Hz, enol 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

<sup>19</sup>F NMR (376 MHz; CDCl<sub>3</sub>): δ -62.9 (enol 3F), -63.2 (3F).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>):  $\delta$  191.7, 173.0, 169.5, 167.1, 138.7, 136.9, 135.0 (q, *J* = 32.7 Hz), 132.8 (q, *J* = 32.7 Hz), 129.0, 126.5, 125.9 (q, *J* = 3.7 Hz), 125.6 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 272.7 Hz), 123.6 (q, *J* = 272.7 Hz), 89.1, 61.8, 60.7, 46.2, 14.30, 14.10.

IR: 2980, 1744, 1695, 1616, 1319, 1260, 1111, 1065, 853, 802 cm<sup>-1</sup>.

HRMS (pNSI+): [C<sub>12</sub>H<sub>11</sub>F<sub>3</sub>O<sub>3</sub> + H]<sup>+</sup> calc. 261.0733, found 261.0736.



**Ethyl 2-methyl-3-oxo-3-phenylpropanoate<sup>2</sup>**

Following a literature procedure<sup>5</sup>: To a suspension of sodium hydride (0.788 g, 19.5 mmol, 60% in mineral oil) in dry THF (20 mL) was added dropwise ethyl benzoylacetate (3.75 g, 19.5 mmol). When the gas evolution stopped, methyl iodide (1.2 mL, 19.5 mmol) was added slowly. The reaction mixture was stirred for a further 20 hours at room temperature then quenched with a saturated aqueous solution of ammonium chloride (30 mL). The phases were separated and the aqueous phase further extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered and the solvent removed to yield the product as a yellow oil (4.01 g, 99%).

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.98 (d, *J* = 7.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.49-7.45 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.49 (d, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>):  $\delta$  196.0, 171.0, 136.0, 133.6, 128.84, 128.70, 61.5, 48.5, 14.1, 13.9.

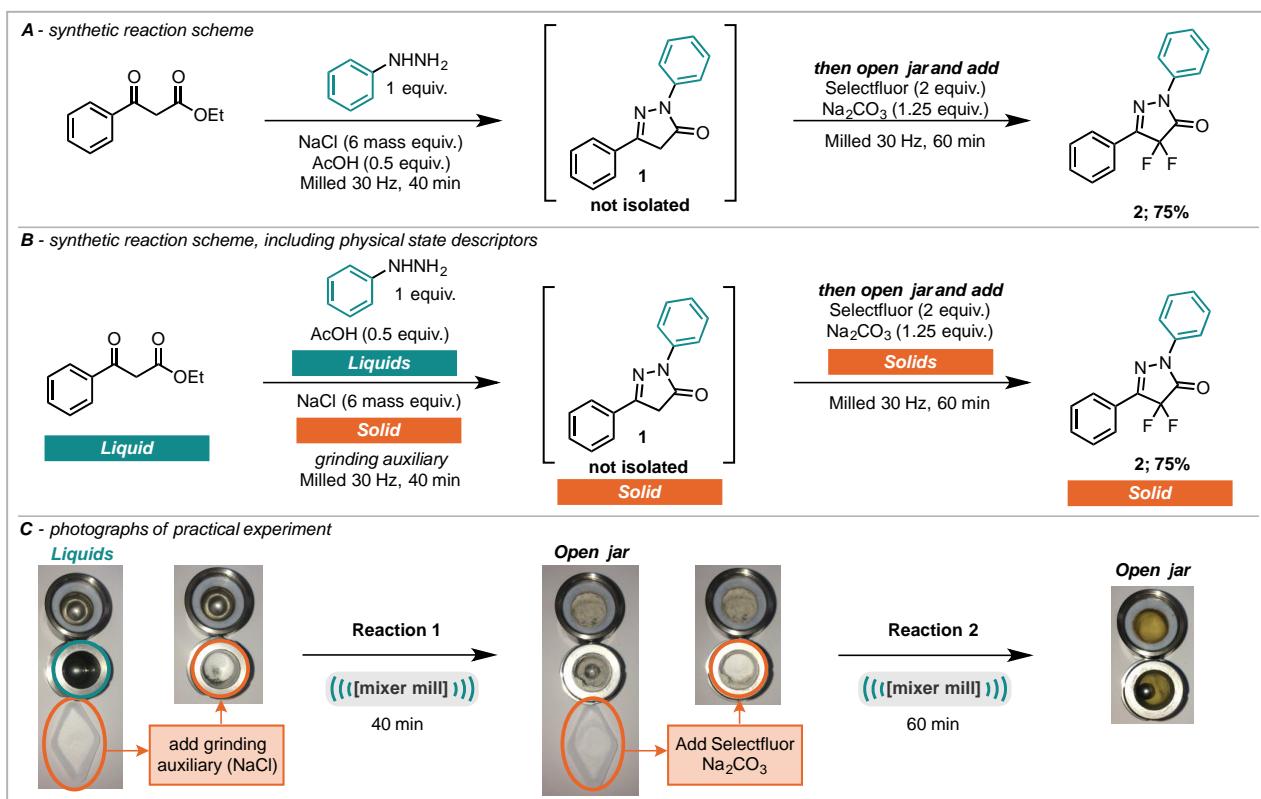
IR: 2980, 1734, 1684, 1375, 957 cm<sup>-1</sup>.

HRMS (pNSI+): [C<sub>12</sub>H<sub>14</sub>O<sub>3</sub> + H]<sup>+</sup> calc. 207.1016, found 207.1014.

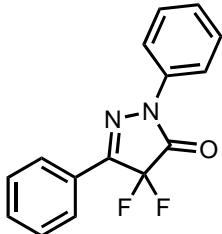
# Multistep one pot mechanochemical synthesis of fluorinated pyrazolones

## General procedure (GP2)

To a 10 mL stainless steel milling jar was added the  $\beta$ -ketoester (1 mmol), the hydrazine (1 mmol), sodium chloride (six times the total mass of reagents) and glacial acetic acid (30  $\mu$ L, 0.5 mmol). The ball was added and the mixture milled at 30 Hz for 40 minutes. Following this initial grinding period, Selectfluor (0.708 g, 2 mmol) and sodium carbonate (0.133 g, 1.25 mmol) were added to the reaction mixture. The jar was hand sealed and milled for a further 60 minutes at 30 Hz (Scheme S1). The resulting powder was transferred into a flask, washing the residue with dichloromethane (approximately 40 mL). The insoluble material was removed by filtration. The solvent was removed under reduced pressure to yield the crude product. This was purified by flash column chromatography on silica gel (gradient elution EtOAc (0–5%) in petroleum ether).



**Scheme S1:** One-pot procedure for mechanochemical synthesis of fluorinated pyrazolones.



**4,4-Difluoro-2,5-diphenyl-2,4-dihydro-3H-pyrazol-3-one, 2<sup>6</sup>**

Prepared according to **GP2**; 0.205 g, 0.75 mmol, 75%, orange powder.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.98 (m, 4H), 7.52 (m, 5H), 7.30 (t, *J* = 7.4 Hz, 1H).

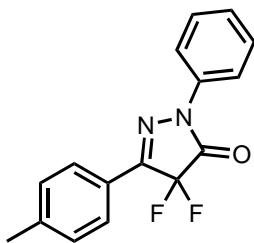
<sup>19</sup>F NMR (376 MHz; CDCl<sub>3</sub>):  $\delta$  -115.7.

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>):  $\delta$  159.3 (t, *J* = 29 Hz), 149.8 (t, *J* = 25 Hz), 136.8, 132.3, 129.33, 129.25, 126.8, 126.52, 126.37, 118.8, 109.2 (t, *J* = 265 Hz).

IR: 1736, 1491, 1410, 1179, 1101, 756, 737, 664, 631 cm<sup>-1</sup>.

HRMS (AP+): [C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>F<sub>2</sub>O + H]<sup>+</sup> calc. 273.0839, found 273.0842.

mp: 77-78 °C (ethyl acetate).



**4,4-Difluoro-2-phenyl-5-(p-tolyl)-2,4-dihydro-3H-pyrazol-3-one, 3**

Prepared according to **GP2**; 0.238 g, 0.83 mmol, 83%, Yellow powder.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.95 (d, *J* = 7.8 Hz, 2H), 7.87 (d, *J* = 7.9 Hz, 2H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.33 (m, 3H), 2.45 (s, 3H).

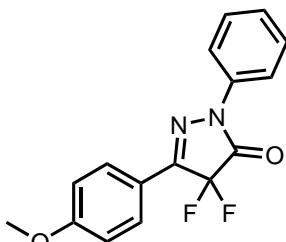
<sup>19</sup>F NMR (471 MHz; CDCl<sub>3</sub>):  $\delta$  -115.4.

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>):  $\delta$  159.3 (t, *J* = 30 Hz), 149.9 (t, *J* = 21 Hz), 143.2, 136.9, 130.1, 129.2, 126.8, 126.4, 123.7, 118.8, 109.3 (t, *J* = 258 Hz), 21.8.

IR: 1738, 1493, 1261, 1103, 743, 689 cm<sup>-1</sup>.

HRMS (AP+): [C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>F<sub>2</sub>O + H]<sup>+</sup> calc. 287.0996, found 287.0999.

mp: 112-113 °C (ethyl acetate).



**4,4-Difluoro-5-(4-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one, 4**

Prepared according to **GP2**; 0.224 g, 0.74 mmol, 74%, Yellow powder.

<sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>):  $\delta$  7.94 (m, 4H), 7.47 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 8.9 Hz, 2H), 3.89 (s, 3H).

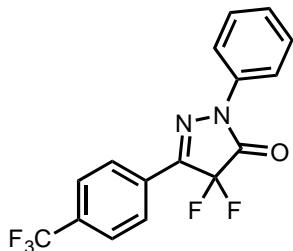
<sup>19</sup>F NMR (471 MHz; CDCl<sub>3</sub>):  $\delta$  -115.1.

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>):  $\delta$  162.9, 159.2 (t, *J* = 31 Hz), 149.7 (t, *J* = 21 Hz), 137.0, 129.2, 128.8, 126.4, 119.01, 118.86, 114.9, 109.5 (t, *J* = 258 Hz), 55.7.

IR: 1734, 1520, 1497, 1180, 1099, 833, 687  $\text{cm}^{-1}$ .

HRMS (AP+):  $[\text{C}_{16}\text{H}_{12}\text{F}_2\text{N}_2\text{O}_2 + \text{H}]^+$  calc. 303.0945, found 303.0941.

mp: 105-106  $^{\circ}\text{C}$  (ethyl acetate).



**4,4-Difluoro-2-phenyl-5-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one, 5**

Prepared according to **GP2**; 0.137 g, 0.40 mmol, 40%, Orange powder.

$^1\text{H}$  NMR (400 MHz;  $\text{CDCl}_3$ ):  $\delta$  8.10 (d,  $J = 8.4$  Hz, 2H), 7.93 (d,  $J = 8.0$  Hz, 2H), 7.79 (d,  $J = 8.4$  Hz, 2H), 7.50 (t,  $J = 8.4$  Hz, 2H), 7.32 (m, 1H).

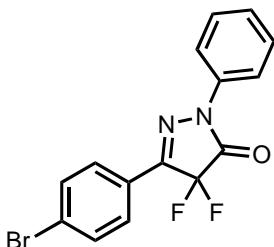
$^{19}\text{F}$  NMR (376 MHz;  $\text{CDCl}_3$ ):  $\delta$  -63.2 (3F), -116.2 (2F).

$^{13}\text{C}$  NMR (101 MHz;  $\text{CDCl}_3$ ):  $\delta$  159.1 (t,  $J = 30$  Hz), 148.5 (t,  $J = 22$  Hz), 136.6, 133.7 (q,  $J = 33$  Hz), 129.6, 129.4, 127.1, 126.9, 126.4 (q,  $J = 4$  Hz), 123.6 (q,  $J = 274$  Hz), 119.0, 108.7 (t,  $J = 259$  Hz).

IR: 1742, 1493, 1400, 1321, 1167, 1065, 1015, 934, 825, 733  $\text{cm}^{-1}$ .

HRMS (ASAP+):  $[\text{C}_{16}\text{H}_9\text{N}_2\text{F}_5\text{O} + \text{H}]^+$  calc. 341.0713, found 341.0718.

mp: 112-113  $^{\circ}\text{C}$  (ethyl acetate).



**5-(4-Bromophenyl)-4,4-difluoro-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, 6**

Prepared according to **GP2**; 0.187 g, 0.53 mmol, 53%, Yellow powder.

$^1\text{H}$  NMR (400 MHz;  $\text{CDCl}_3$ ):  $\delta$  7.92 (d,  $J$  = 8.8 Hz, 2H), 7.83 (d,  $J$  = 8.8 Hz, 2H), 7.67 (d,  $J$  = 8.8 Hz, 2H), 7.48 (m, 2H), 7.31 (t,  $J$  = 7.2 Hz, 1H).

$^{19}\text{F}$  NMR (471 MHz;  $\text{CDCl}_3$ ):  $\delta$  -115.8.

$^{13}\text{C}$  NMR (126 MHz;  $\text{CDCl}_3$ ):  $\delta$  159.1 (t,  $J$  = 30 Hz), 149.0 (t,  $J$  = 21 Hz), 136.6, 132.7, 129.3, 128.1, 127.2, 126.7, 125.2, 118.9, 108.9 (t,  $J$  = 259 Hz).

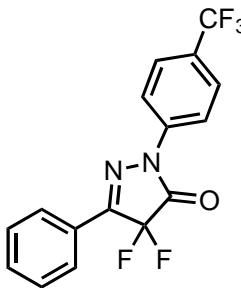
IR: 2980, 1740, 1587, 1487, 1256, 1393, 1098, 1069, 934, 745, 685  $\text{cm}^{-1}$ .

HRMS (AP+):  $[\text{C}_{15}\text{H}_9\text{N}_2\text{F}_2\text{OBr} + \text{H}]^+$  calc. 350.9945, found 350.9945.

mp: 123-124 °C (ethyl acetate).

### General Procedure 3 (GP3)

Diethyl ether (10 mL) and sodium hydroxide solution (10 mL, 0.5 M) were added to the hydrazine hydrochloride (2 mmol) and shaken until dissolved. The layers were separated and the aqueous layer further extracted with diethyl ether ( $2 \times 10$  mL). The organic phase was dried ( $\text{MgSO}_4$ ), filtered and the solvent removed to yield the hydrazine. To a 10 mL stainless steel milling jar was added ethyl benzoylacetate (0.192 g, 1 mmol), the hydrazine (1 mmol), sodium chloride (six times the total mass of reagents) and glacial acetic acid (30  $\mu\text{L}$ , 0.5 mmol). The ball was added and the mixture milled at 30 Hz for 40 minutes. Following this initial grinding period, Selectfluor (0.708 g, 2 mmol) and sodium carbonate (0.133 g, 1.25 mmol) were directly added to the reaction mixture. The jar was hand sealed and milled for a further 60 minutes at 30 Hz. The resulting powder was transferred into a flask, washing the residue with dichloromethane (about 40 mL). The insoluble material was removed by filtration. The solvent was removed under reduced pressure to yield the crude product. This was purified by flash column chromatography on silica gel (gradient elution  $\text{EtOAc}$  (0–5%) in petroleum ether).



**4,4-Difluoro-5-phenyl-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3*H*-pyrazol-3-one, 7**

Prepared according to **GP2**; 0.127 g, 0.37 mmol, 37%. Yellow powder.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 8.13 (d, *J* = 6.8 Hz, 2H), 8.00 (d, *J* = 6.0 Hz, 2H), 7.74 (d, *J* = 6.8 Hz, 2H), 7.58 (m, 3H).

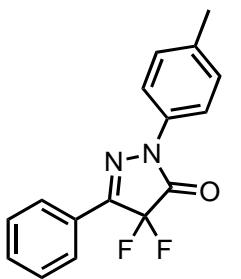
<sup>19</sup>F NMR (471 MHz; CDCl<sub>3</sub>): δ -62.3 (3F), -115.0 (2F).

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>): δ 159.5 (t, *J* = 30 Hz), 150.3 (t, *J* = 21 Hz), 139.5, 132.8, 129.5, 128.2 (q, *J* = 33 Hz), 127.0, 126.6 (q, *J* = 4 Hz), 126.0, 123.0 (q, *J* = 272 Hz), 118.4, 109.0 (t, *J* = 259 Hz).

IR: 1751, 1618, 1518, 1406, 1319, 1159, 1109, 1061, 841, 739, 687, 635, 592 cm<sup>-1</sup>.

HRMS (ASAP+): [C<sub>16</sub>H<sub>9</sub>N<sub>2</sub>F<sub>5</sub>O + H]<sup>+</sup> calc. 341.0713, found 341.0706.

mp: 84-85 °C (ethyl acetate).



**4,4-Difluoro-5-phenyl-2-(*p*-tolyl)-2,4-dihydro-3*H*-pyrazol-3-one, 8**

Prepared according to **GP3**; 0.169 g, 0.59 mmol, 59%. Brown powder.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 8.00 (d, *J* = 6.0 Hz, 2H), 7.84 (d, *J* = 6.4 Hz, 2H), 7.56 (m, 3H), 7.29 (m, 2H), 2.42 (s, 3H).

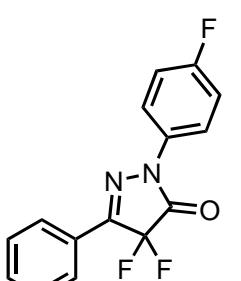
<sup>19</sup>F NMR (471 MHz; CDCl<sub>3</sub>): δ -115.8.

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>): δ 159.2 (t, *J* = 30 Hz), 149.7 (t, *J* = 21 Hz), 136.5, 135.2, 134.4, 132.3, 129.8, 129.3, 126.8, 118.9, 109.2 (t, *J* = 259 Hz), 21.2.

IR: 2980, 1754, 1512, 1402, 1256, 1067, 937, 816, 739, 664, 640, 598, 513 cm<sup>-1</sup>.

HRMS (pNSI+): [C<sub>16</sub>H<sub>12</sub>F<sub>2</sub>N<sub>2</sub>O + H]<sup>+</sup> calc. 287.0990, found 287.0992.

mp: 80-81 °C (ethyl acetate).



**4,4-Difluoro-2-(4-fluorophenyl)-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, 9**

Prepared according to **GP3**; 0.193 g, 0.67 mmol., 67%. Orange powder.

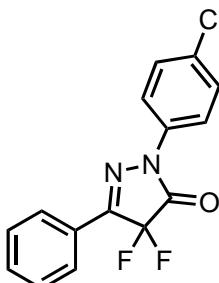
<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>): δ 7.97 - 7.92 (m, 4H), 7.56-7.51 (m, 3H), 7.19-7.14 (m, 2H).

<sup>19</sup>F NMR (376 MHz; CDCl<sub>3</sub>): δ -114.8 (1F), -115.6 (2F).

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>): δ 160.8 (d, *J* = 248 Hz), 159.1 (t, *J* = 30 Hz), 150.0 (t, *J* = 21 Hz), 132.9, 132.5, 129.4, 126.9, 126.3 (t, *J* = 2 Hz), 120.7 (d, *J* = 8 Hz), 116.1 (d, *J* = 23 Hz), 109.2 (t, *J* = 260 Hz).

IR: 2980, 1742, 1508, 1225, 1107, 1067, 831, 737, 687 cm<sup>-1</sup>.

HRMS (ASAP+):  $[C_{15}H_9N_2OF_3 + H]^+$  calc. 291.0745, found 291.0745.  
mp: 92-93 °C (ethyl acetate).



**2-(4-Chlorophenyl)-4,4-difluoro-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, 10**

Prepared according to **GP3**;

0.205 g, 0.67 mmol, 67%. Yellow powder.

$^1H$  NMR (400 MHz;  $CDCl_3$ ):  $\delta$  7.97 (d,  $J$  = 7.2 Hz, 2H), 7.91 (m, 2H), 7.53 (m, 3H), 7.44 (m, 2H).

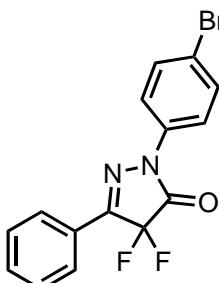
$^{19}F$  NMR (376 MHz;  $CDCl_3$ ):  $\delta$  -115.3.

$^{13}C$  NMR (101 MHz;  $CDCl_3$ ):  $\delta$  159.2 (t,  $J$  = 30 Hz), 150.1 (t,  $J$  = 21 Hz), 135.4, 132.6, 131.8, 129.40, 129.37, 126.9, 126.2 (t,  $J$  = 2 Hz), 119.9, 109.1 (t,  $J$  = 260 Hz).

IR: 1742, 1493, 1402, 1016, 1111, 737, 687  $cm^{-1}$ .

HRMS (ASAP+):  $[C_{15}H_9N_2F_2OCl + H]^+$  calc. 307.0450, found 307.0459.

mp: 79-80 °C (ethyl acetate).



**2-(4-Bromophenyl)-4,4-difluoro-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, 11**

Prepared according to **GP3**; 0.246 g, 0.70 mmol, 70%. Orange powder.

$^1H$  NMR (400 MHz;  $CDCl_3$ ):  $\delta$  7.98 (d,  $J$  = 6.8 Hz, 2H), 7.87 (d,  $J$  = 9.2 Hz, 2H), 7.58-7.52 (m, 5H).

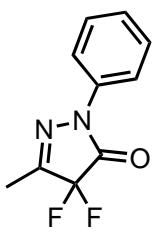
$^{19}F$  NMR (376 MHz;  $CDCl_3$ ):  $\delta$  -115.3.

$^{13}C$  NMR (101 MHz;  $CDCl_3$ ):  $\delta$  159.1 (t,  $J$  = 30 Hz), 150.1 (t,  $J$  = 21 Hz), 135.8, 132.6, 132.3, 129.4, 126.9, 126.1 (t,  $J$  = 2 Hz), 120.1, 119.6, 109.1 (t,  $J$  = 260 Hz).

IR: 1745, 1489, 1400, 1254, 1103, 739, 683  $cm^{-1}$ .

HRMS (ASAP+):  $[C_{15}H_9N_2F_2OBr + H]^+$  calc. 350.9945, found 350.9930.

mp: 79-80 °C (ethyl acetate)



**4,4-Difluoro-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one, 12<sup>7</sup>**

Prepared according to **GP2**. 0.064 g, 0.30 mmol, 30%. Red oil.

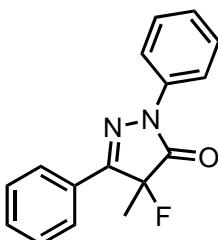
<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  7.86 (d, *J* = 7.8 Hz, 2H), 7.48-7.44 (m, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 2.32 (t, *J* = 1.3 Hz, 3H).

<sup>19</sup>F NMR (376 MHz; CDCl<sub>3</sub>):  $\delta$  -122.4.

<sup>13</sup>C NMR (101 MHz; CDCl<sub>3</sub>):  $\delta$  159.2 (t, *J* = 30 Hz), 152.0 (t, *J* = 23 Hz), 136.7, 129.2, 126.3, 118.6, 108.1 (t, *J* = 258 Hz), 11.9.

IR: 2980, 1748, 1501, 1373, 1254, 1146, 1111, 754, 731, 689, 648 cm<sup>-1</sup>.

HRMS (ASAP+): [C<sub>10</sub>H<sub>8</sub>N<sub>2</sub>OF<sub>2</sub> + H]<sup>+</sup> calc. 211.0683, found 211.0687.



**4-Fluoro-4-methyl-2,5-diphenyl-2,4-dihydro-3*H*-pyrazol-3-one, 13**

Prepared according to modified **GP2** using 1 equivalent of Selectfluor.

0.126 g, 0.47 mmol, 47%. Orange powder.

<sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>):  $\delta$  8.02-7.99 (m, 4H), 7.54-7.53 (m, 3H), 7.52-7.48 (m, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 1.91 (d, *J* = 22.4 Hz, 3H).

<sup>19</sup>F NMR (471 MHz; CDCl<sub>3</sub>):  $\delta$  -163.8 (q, *J* = 23.1 Hz).

<sup>13</sup>C NMR (126 MHz; CDCl<sub>3</sub>):  $\delta$  168.9 (d, *J* = 22 Hz), 155.8 (d, *J* = 14 Hz), 137.6, 131.4, 129.20, 129.16, 128.7 (d, *J* = 2 Hz), 126.8 (d, *J* = 2 Hz), 125.9, 119.0, 93.7 (d, *J* = 195 Hz), 21.6 (d, *J* = 27 Hz).

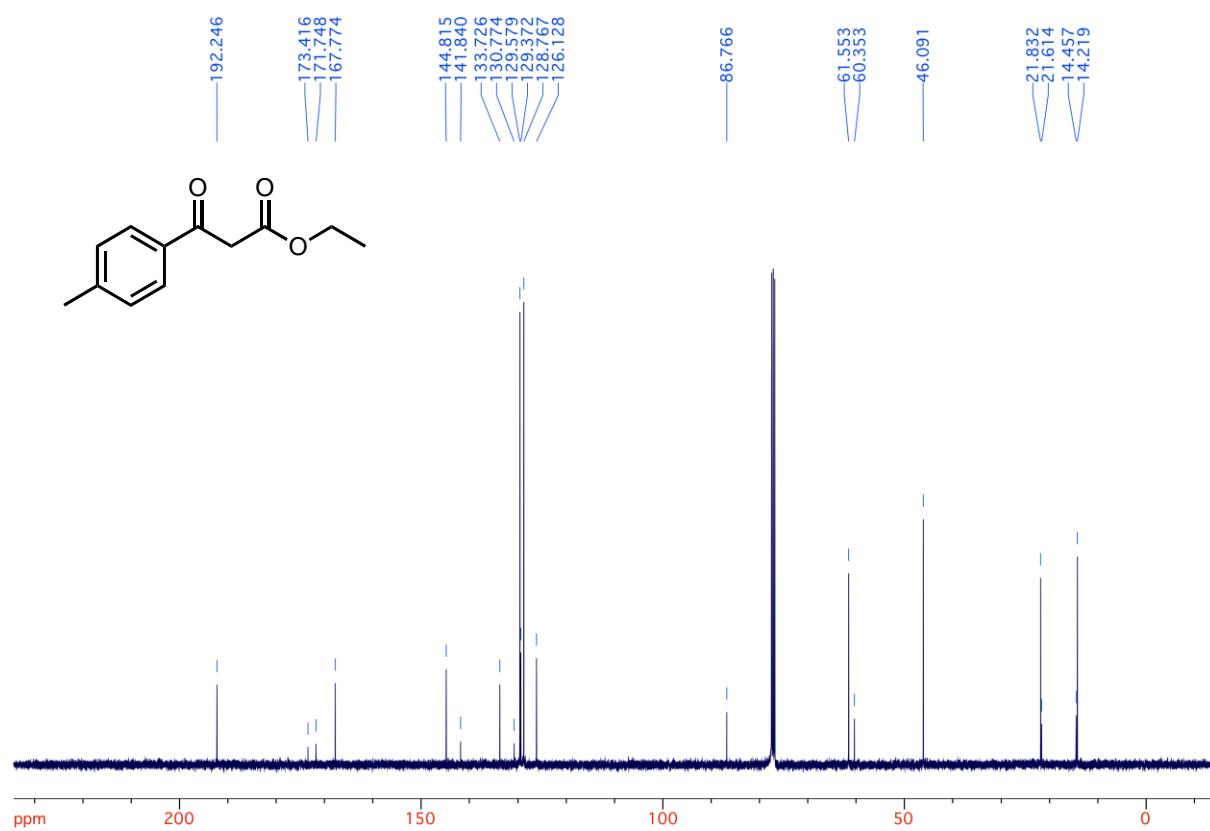
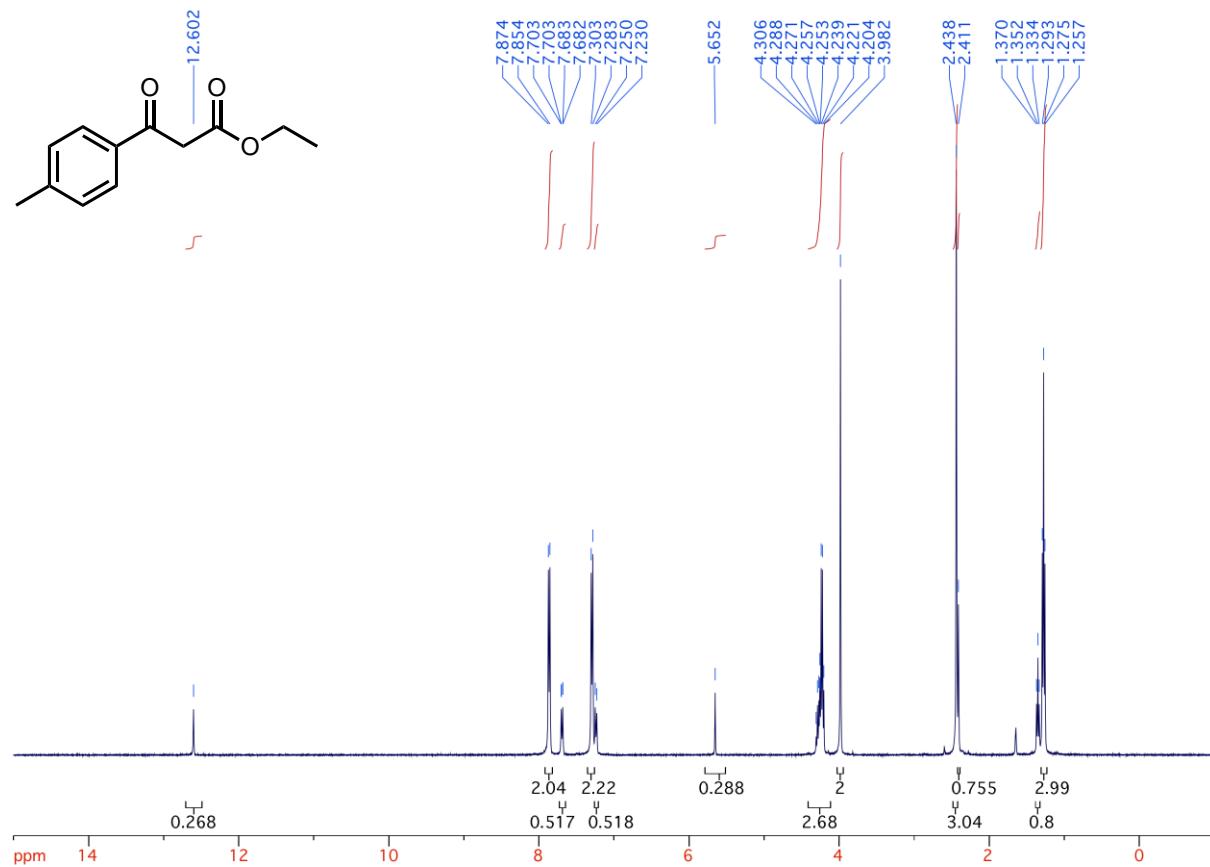
IR: 1724, 1593, 1395, 1177, 1117, 745, 683 cm<sup>-1</sup>.

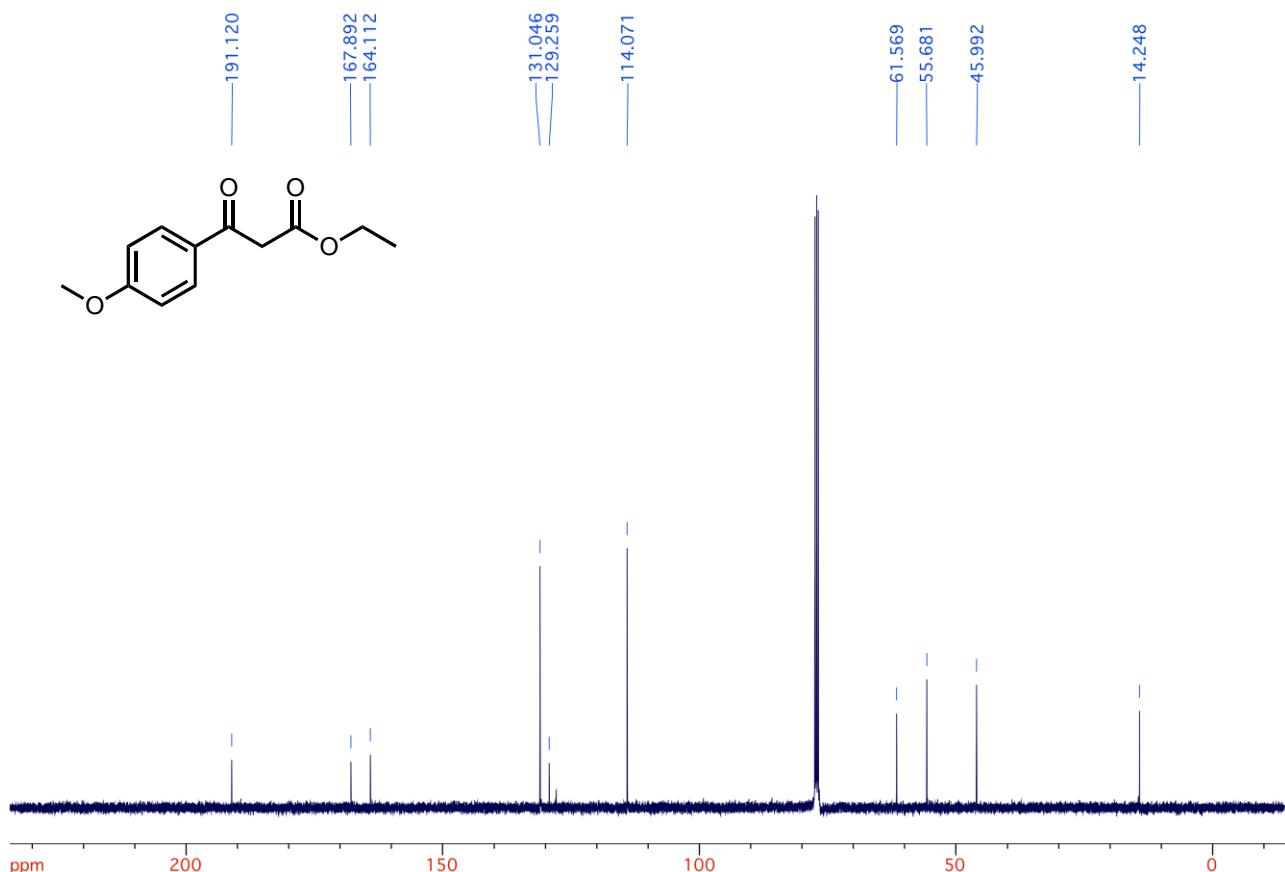
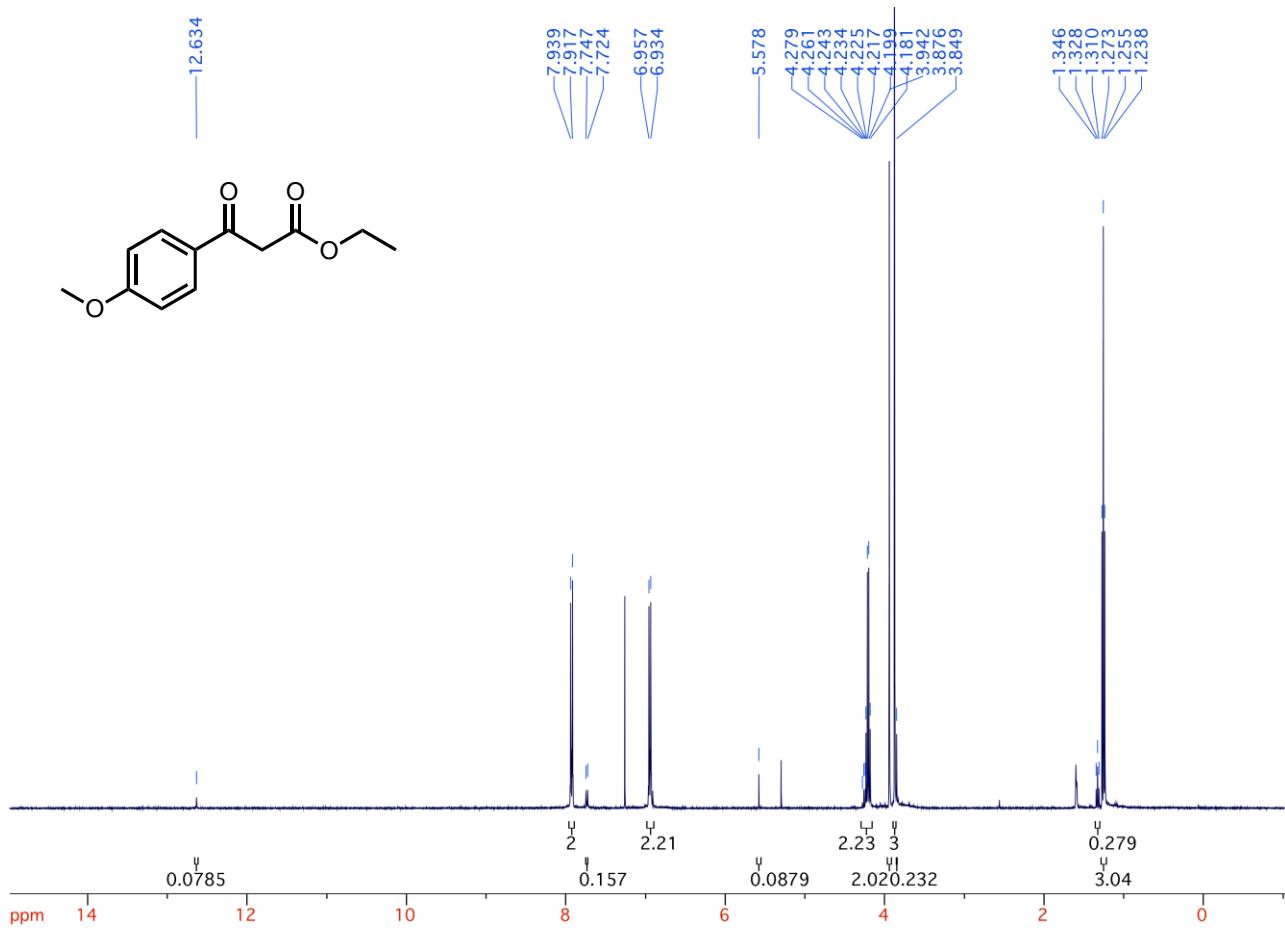
HRMS (pNSI+): [C<sub>16</sub>H<sub>13</sub>ON<sub>2</sub>F + H]<sup>+</sup> calc. 269.1085, found 269.1086.

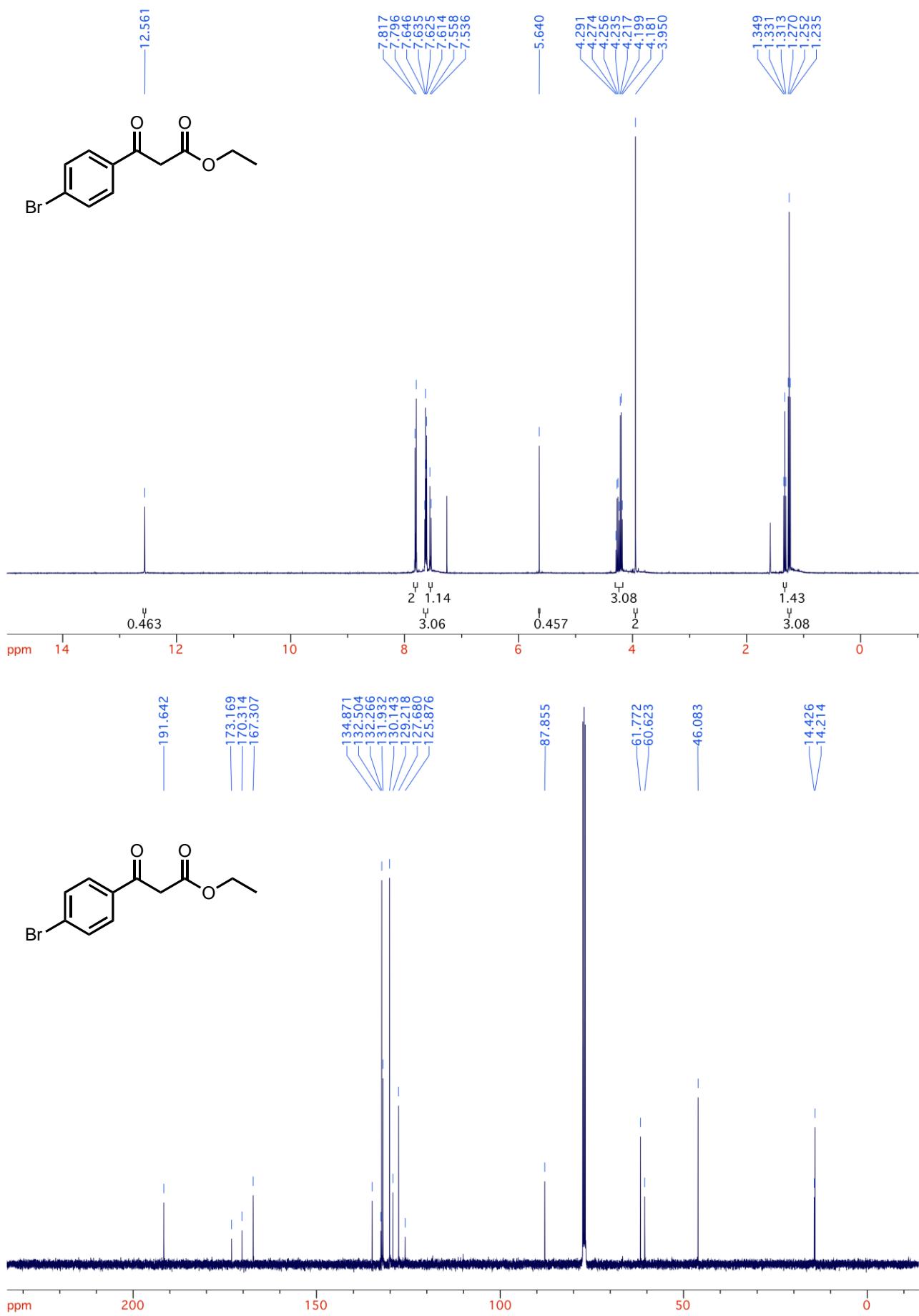
mp: 73-74 °C (ethyl acetate).

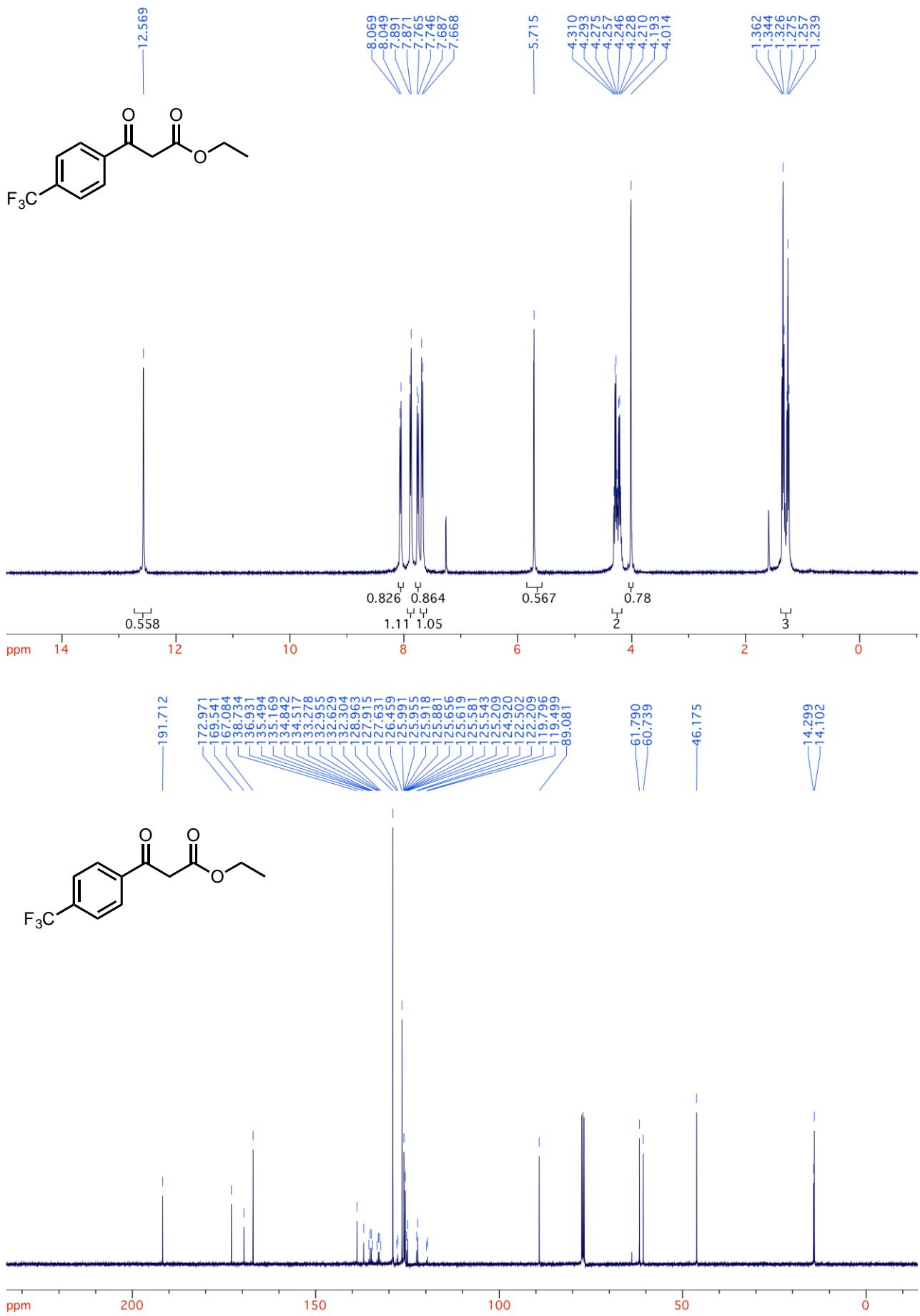
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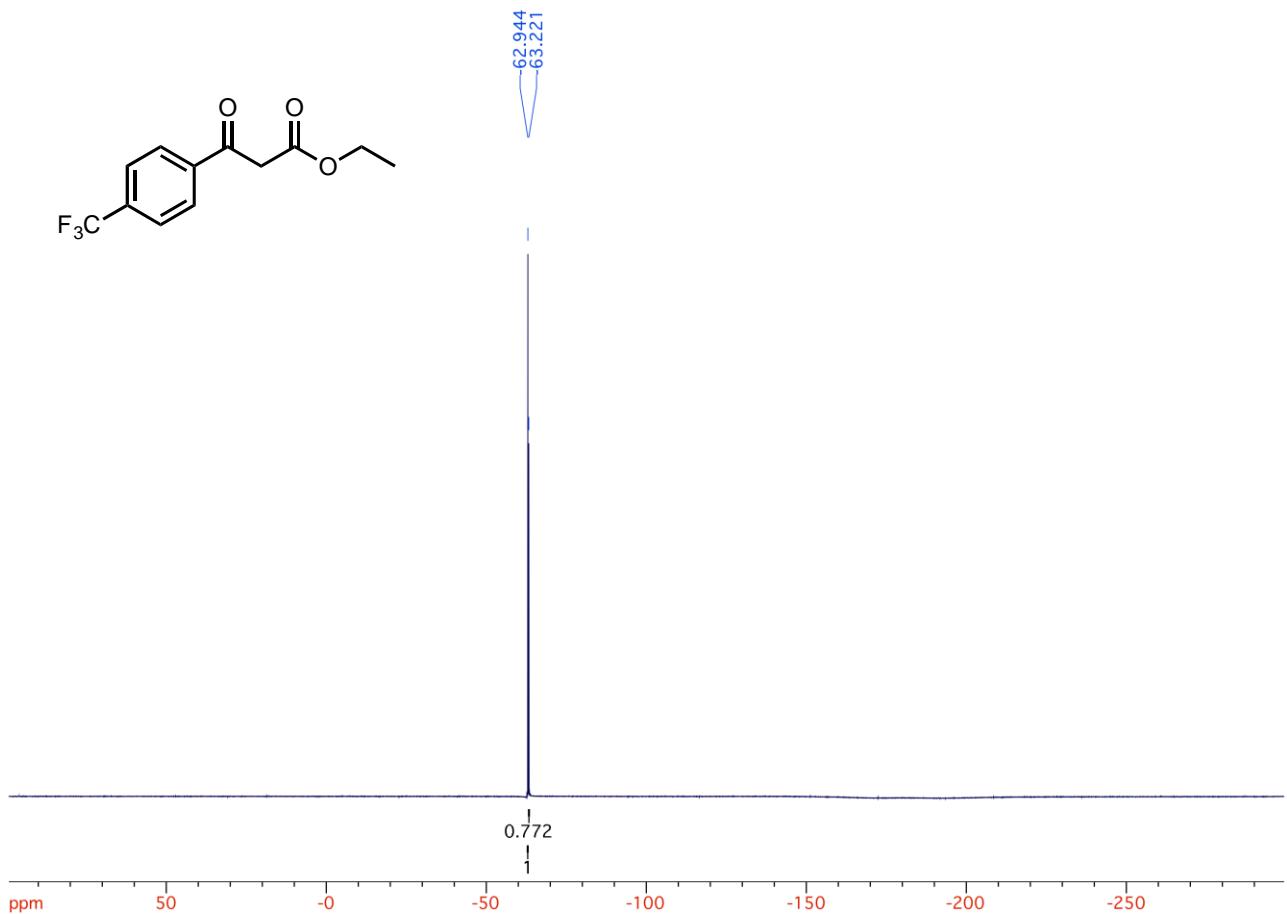
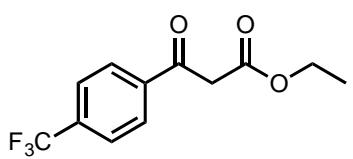
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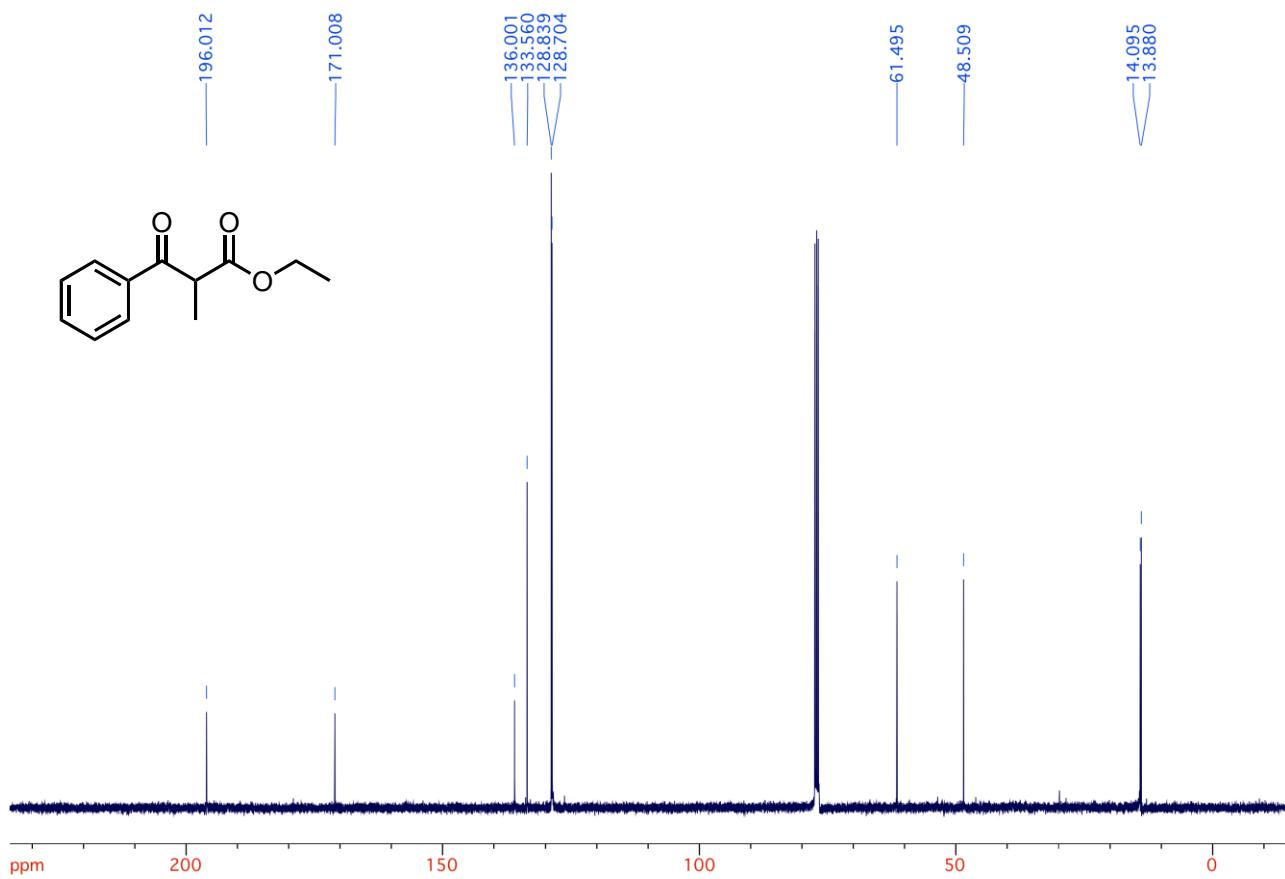
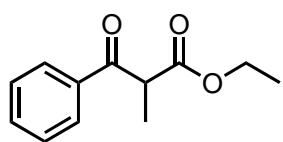
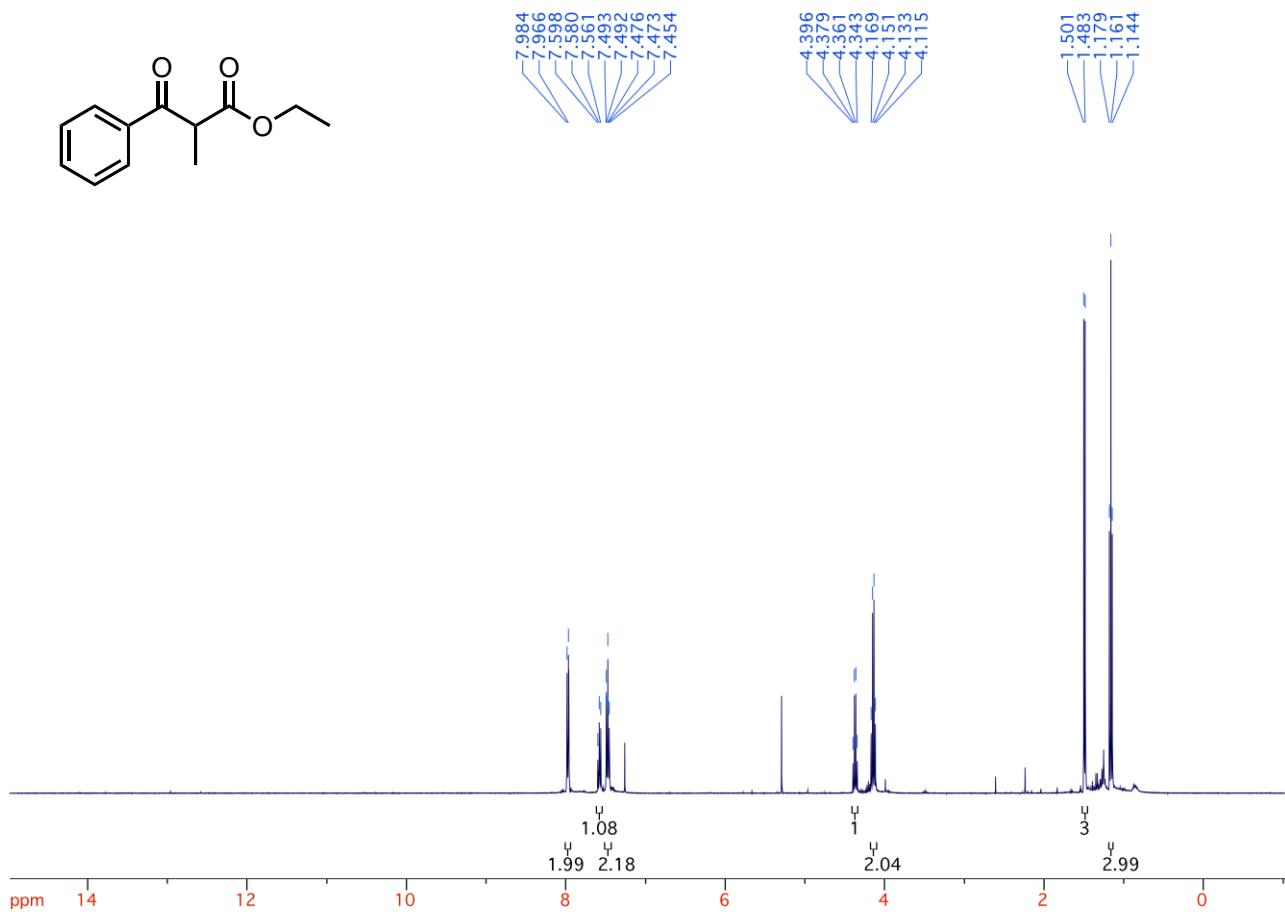
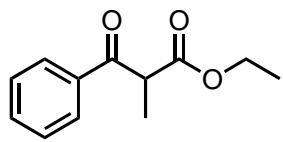




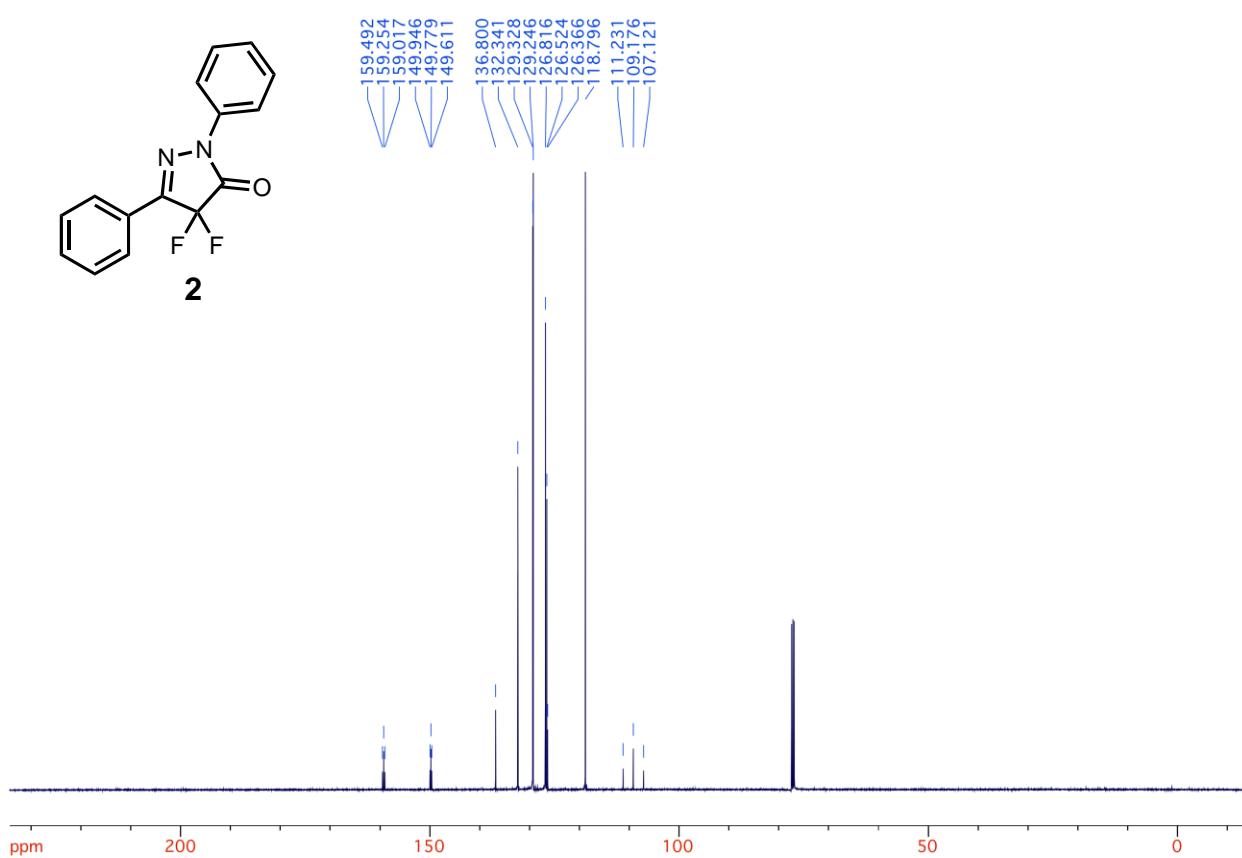
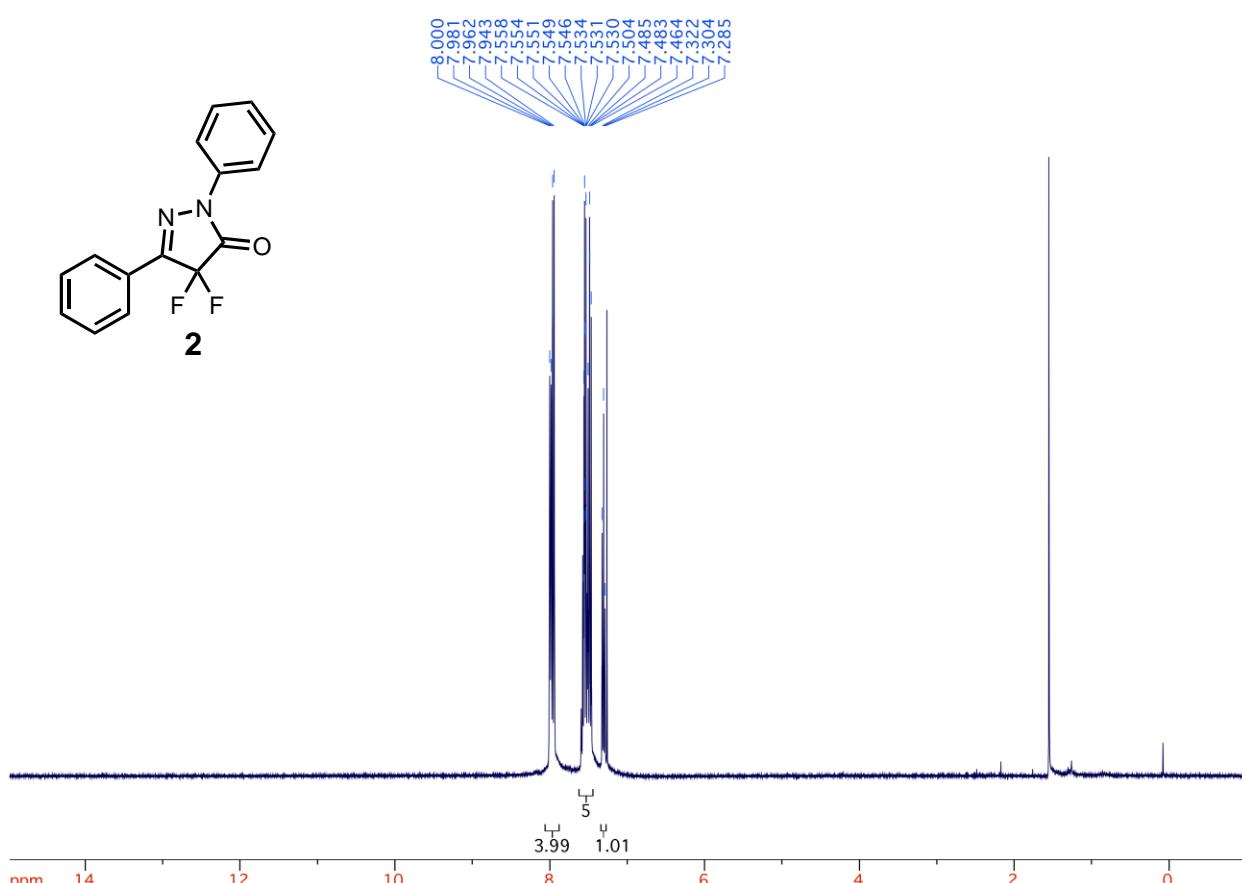


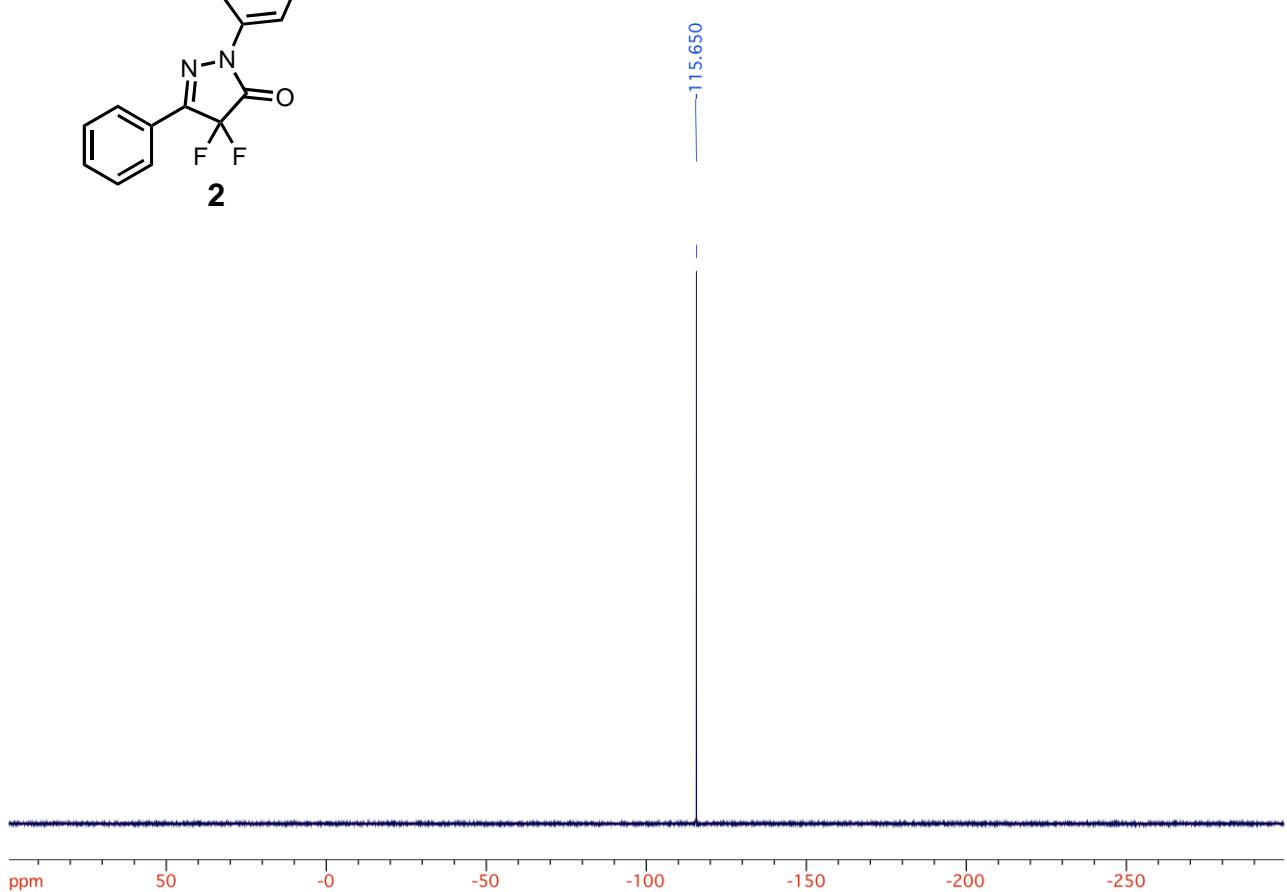
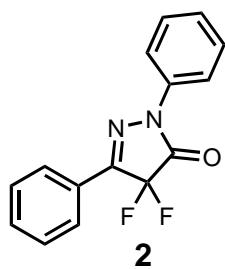


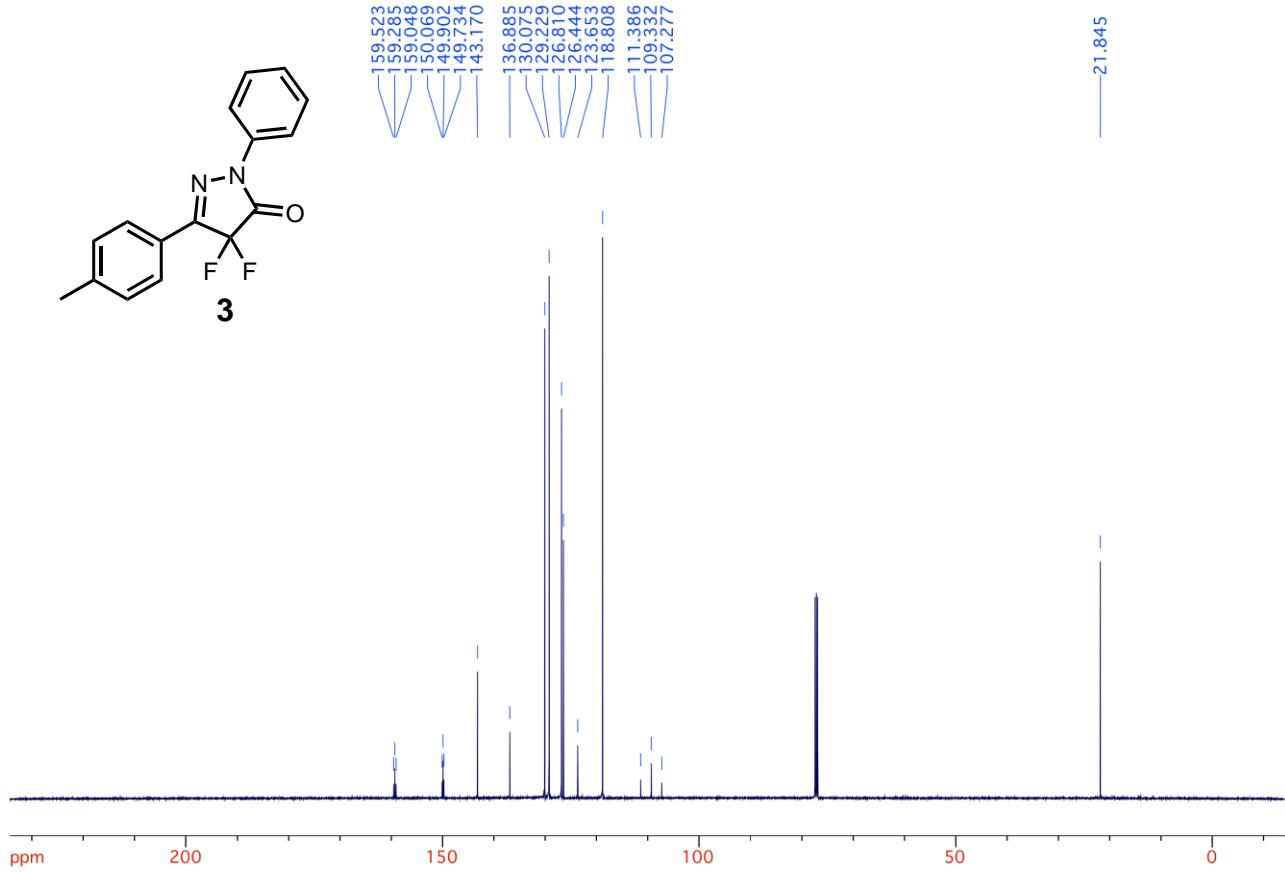
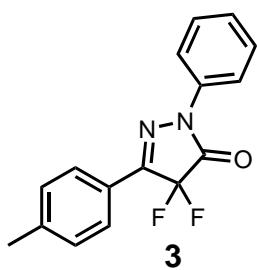
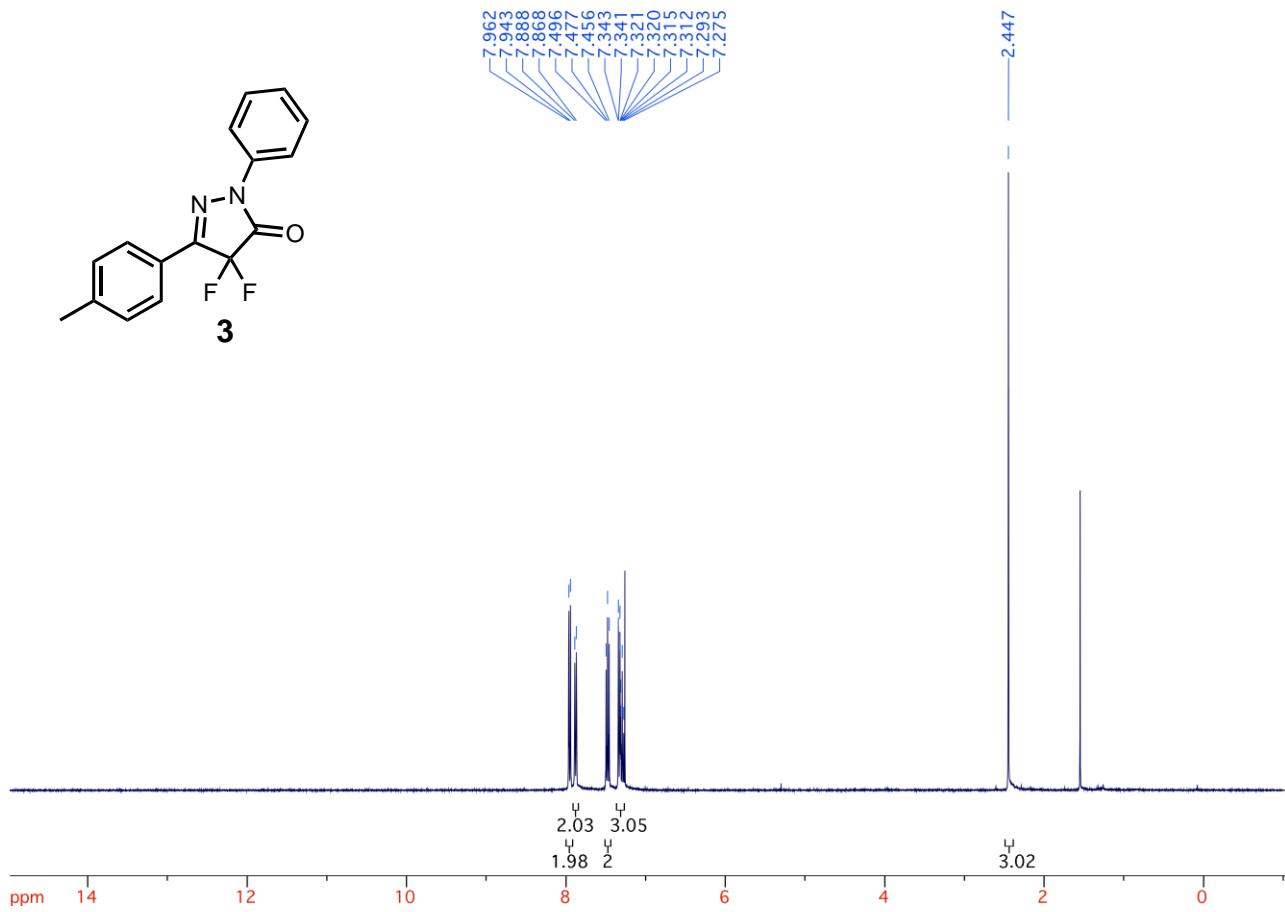
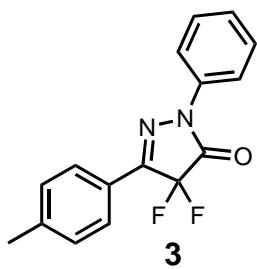


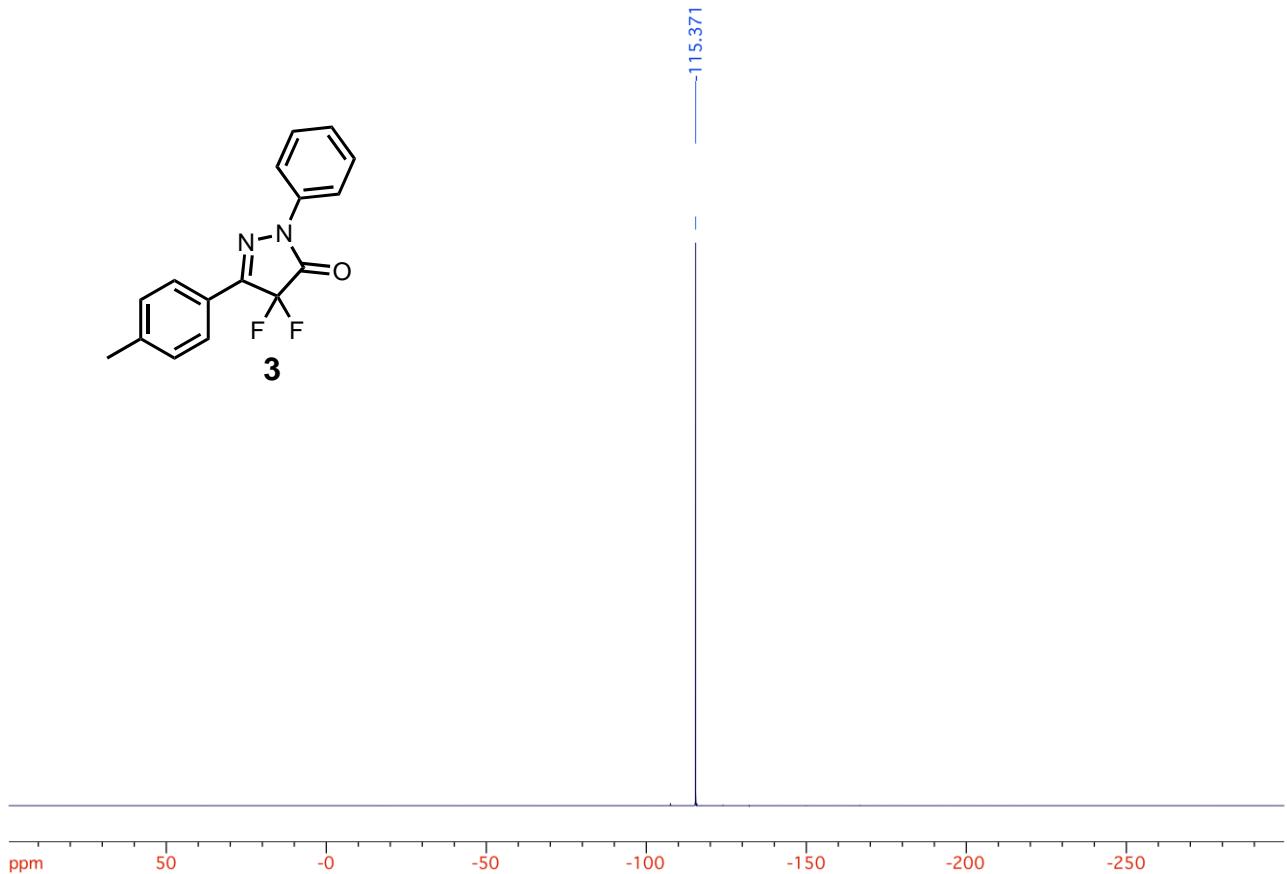
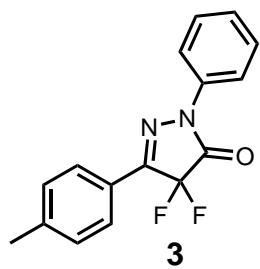


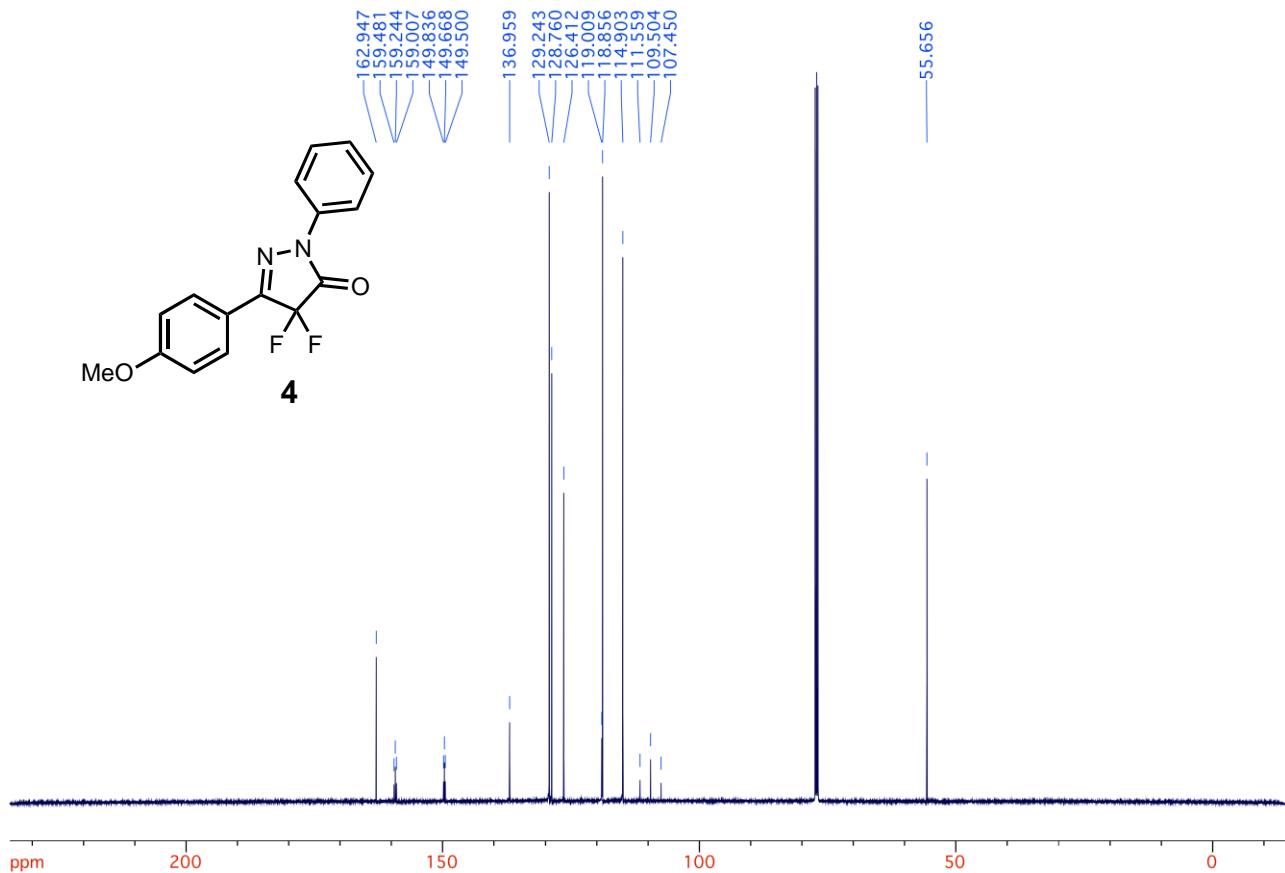
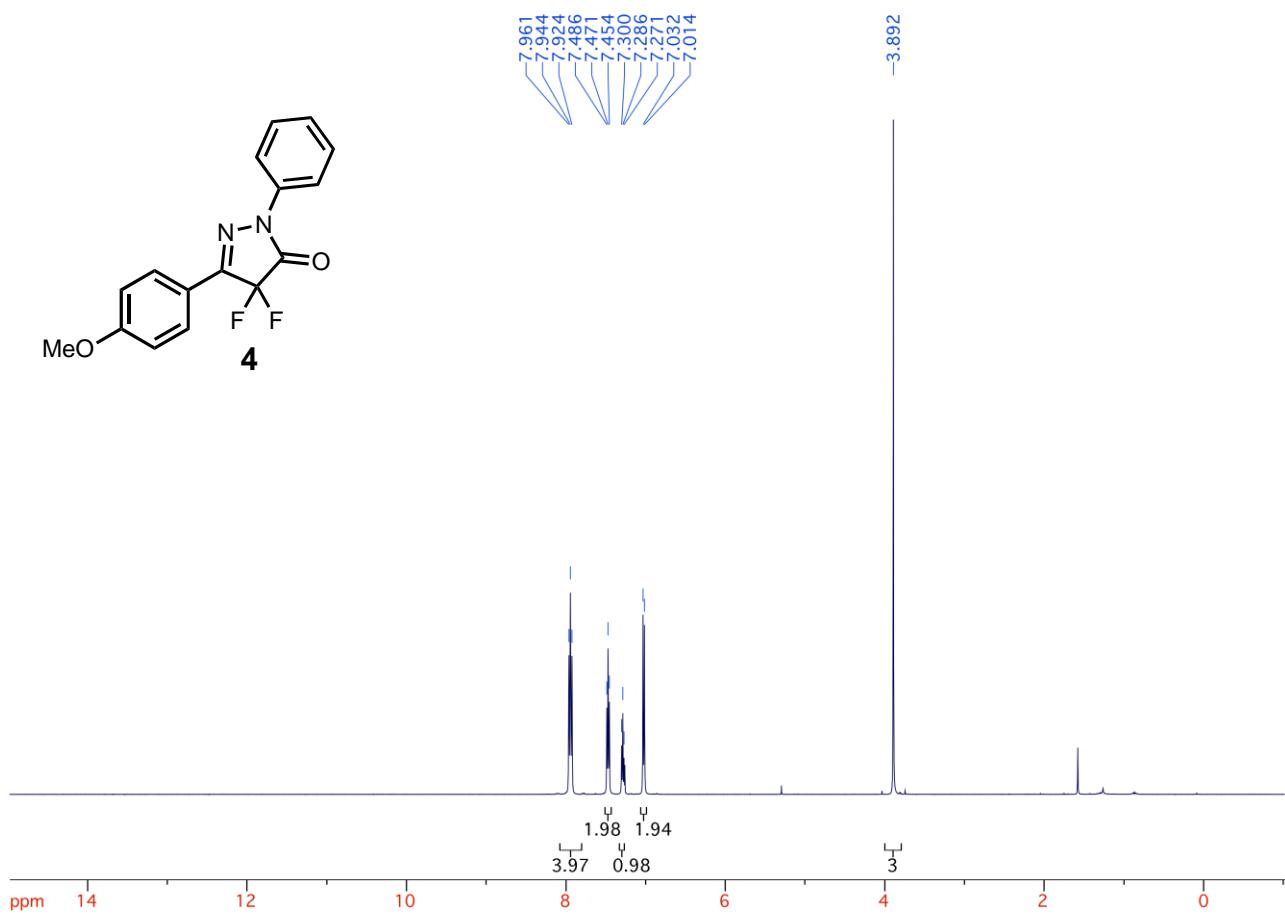
## Fluorinated pyrazolones

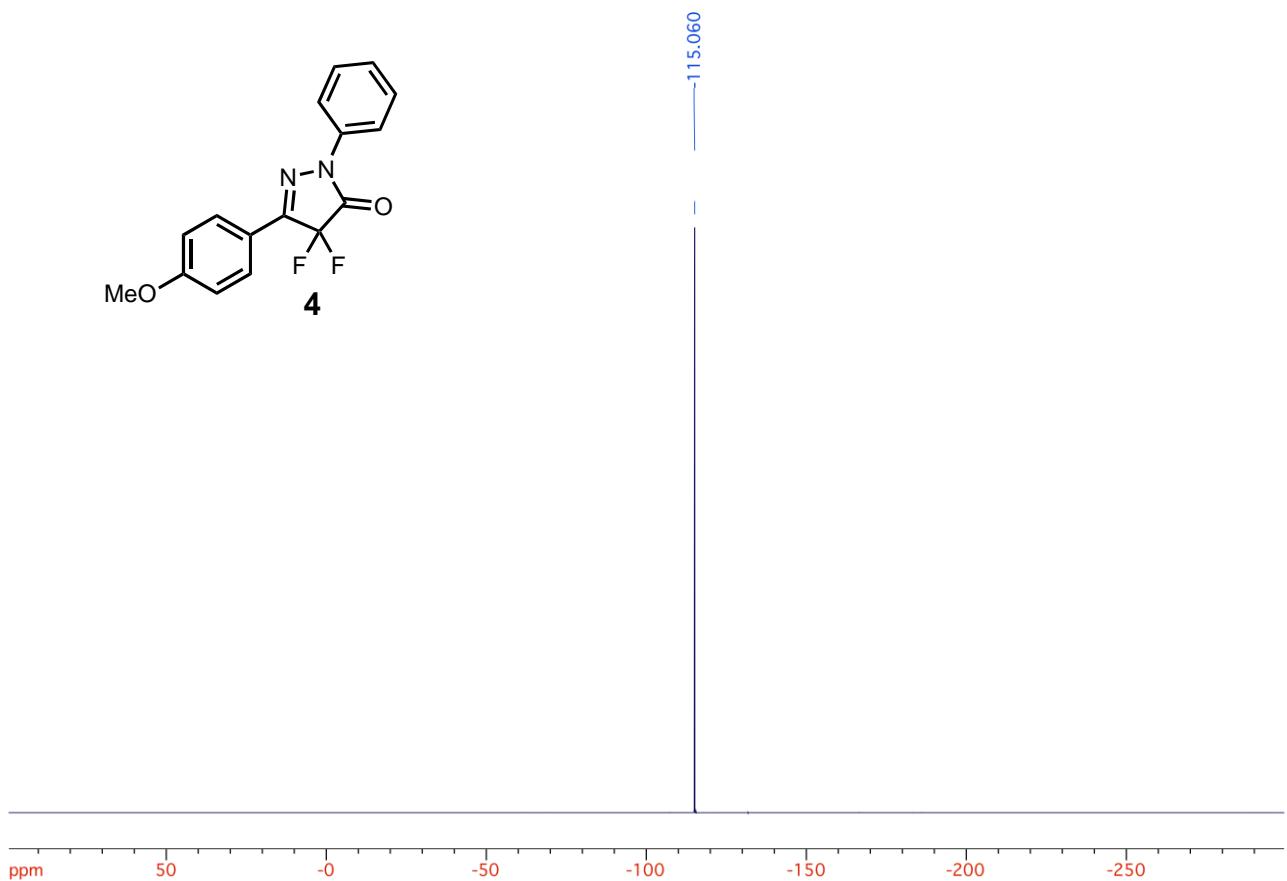
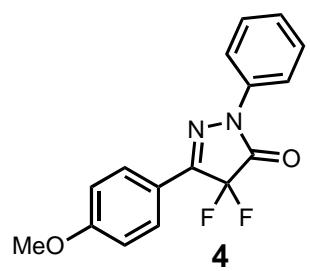


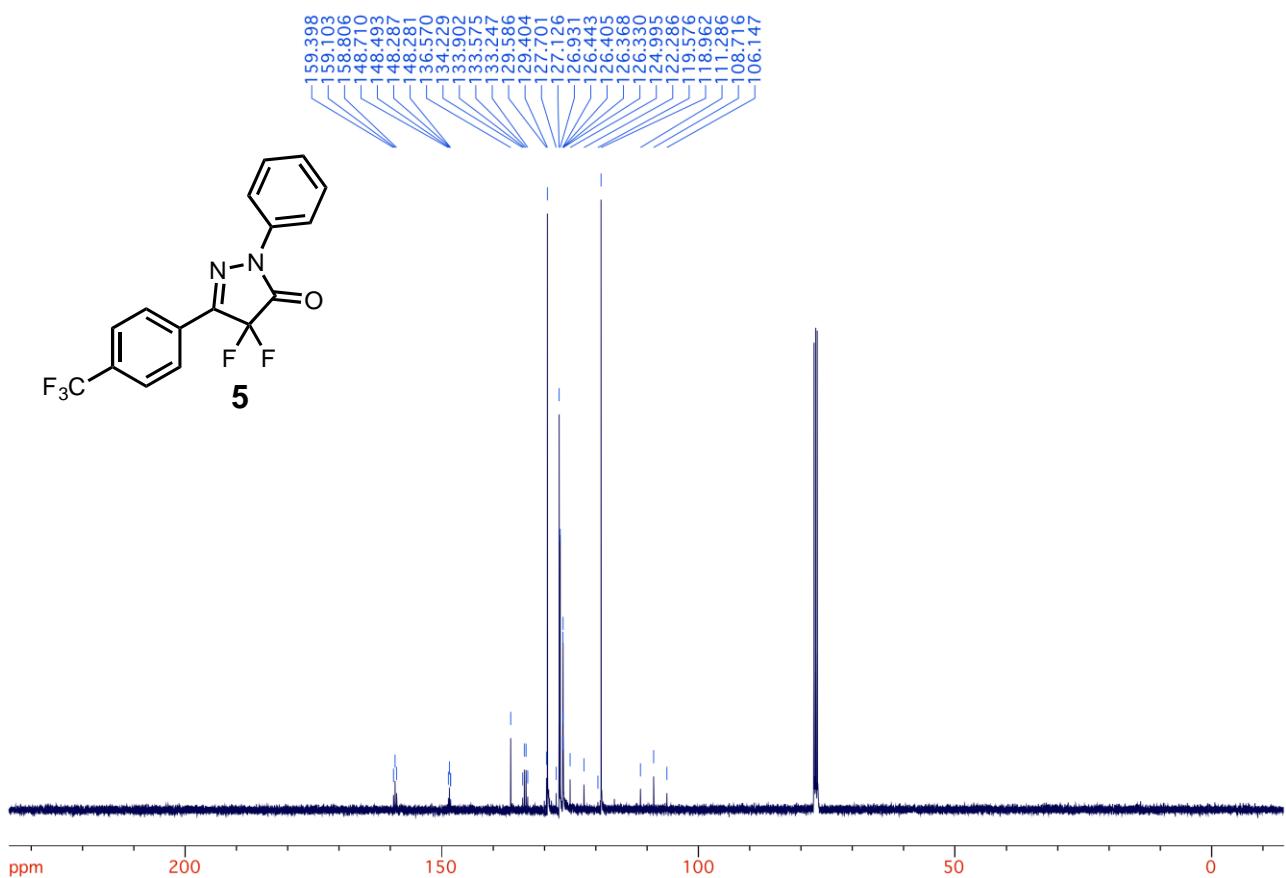
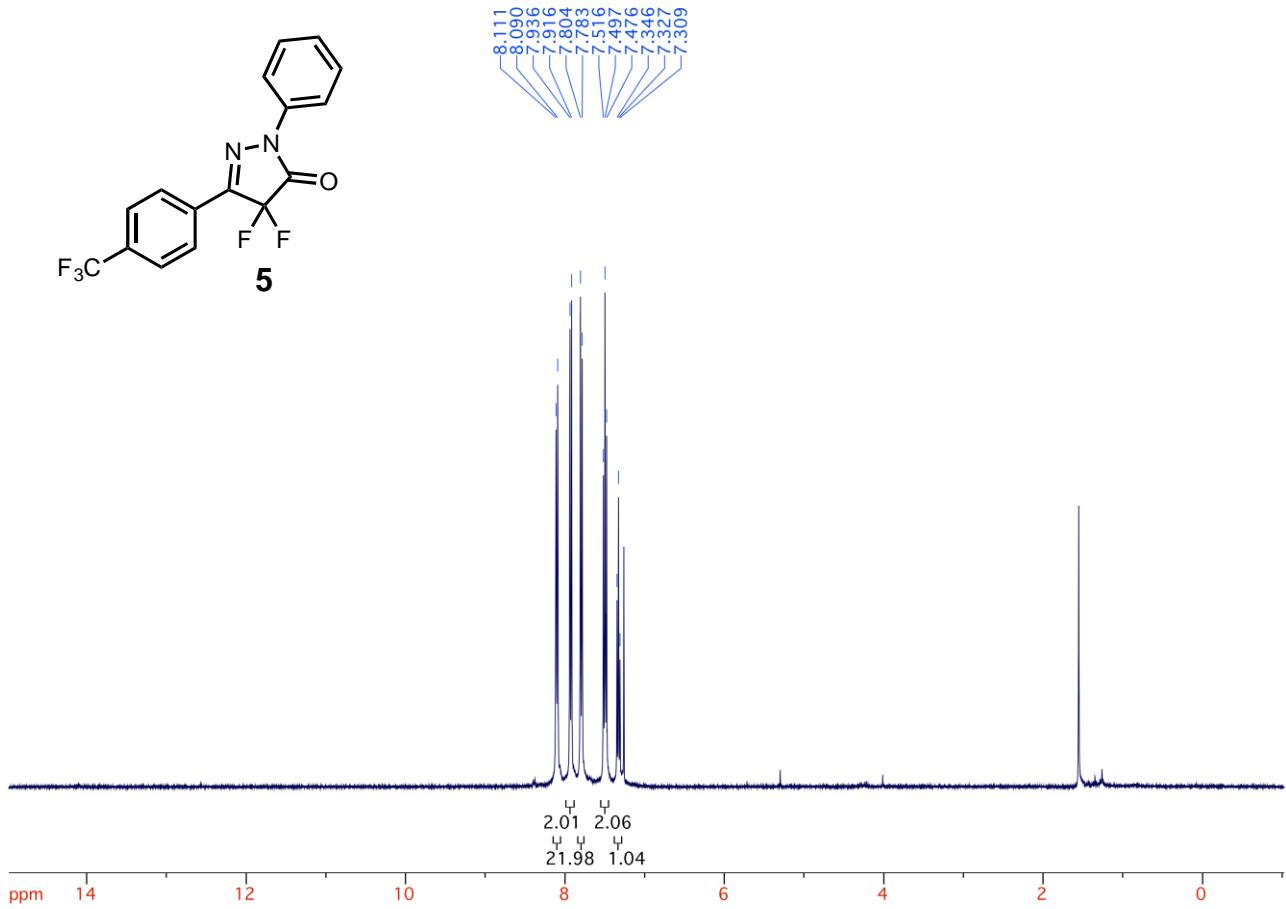


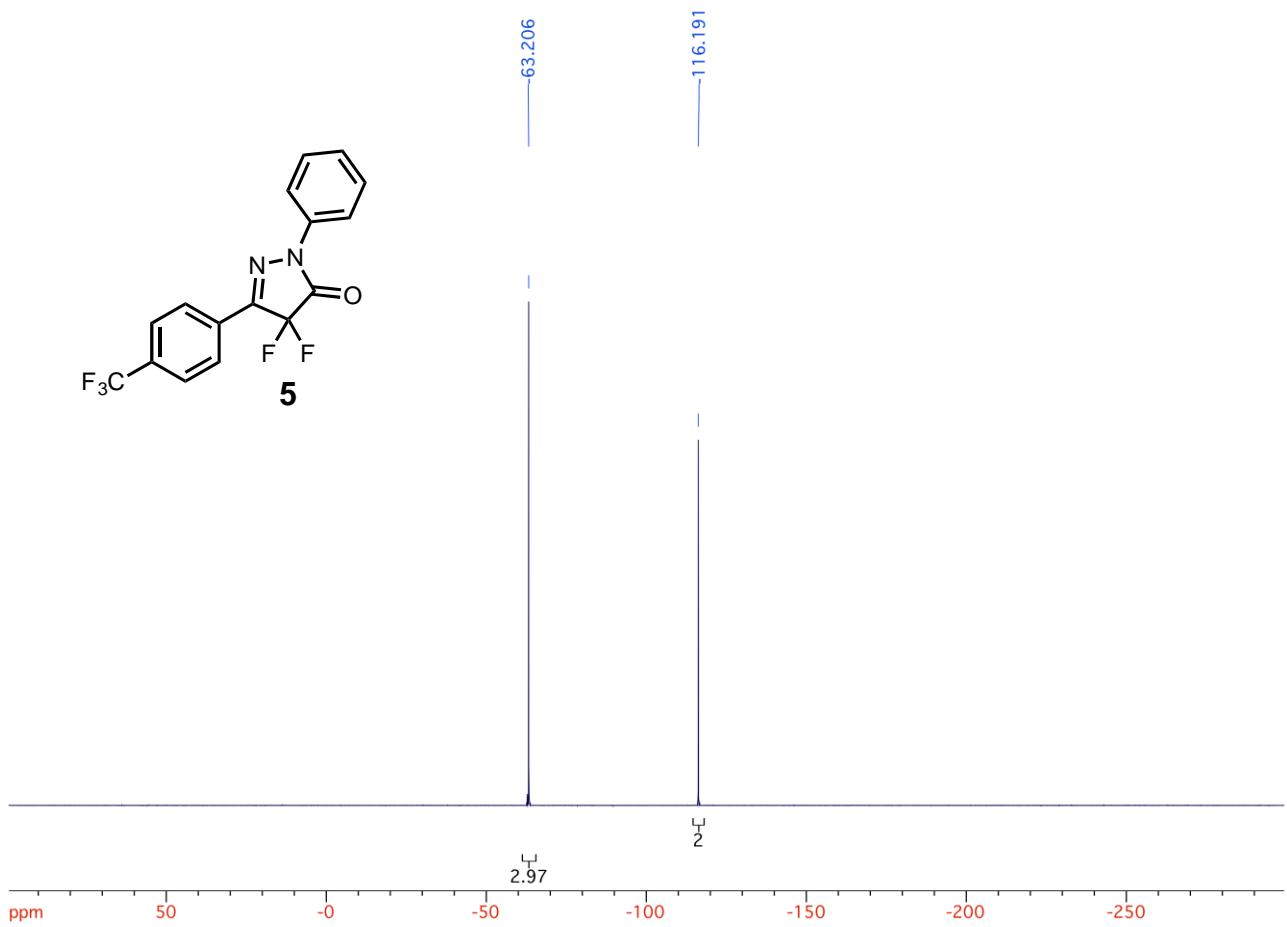
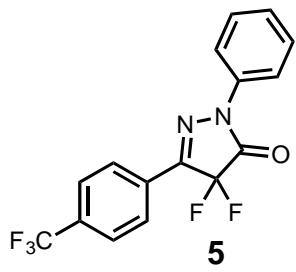


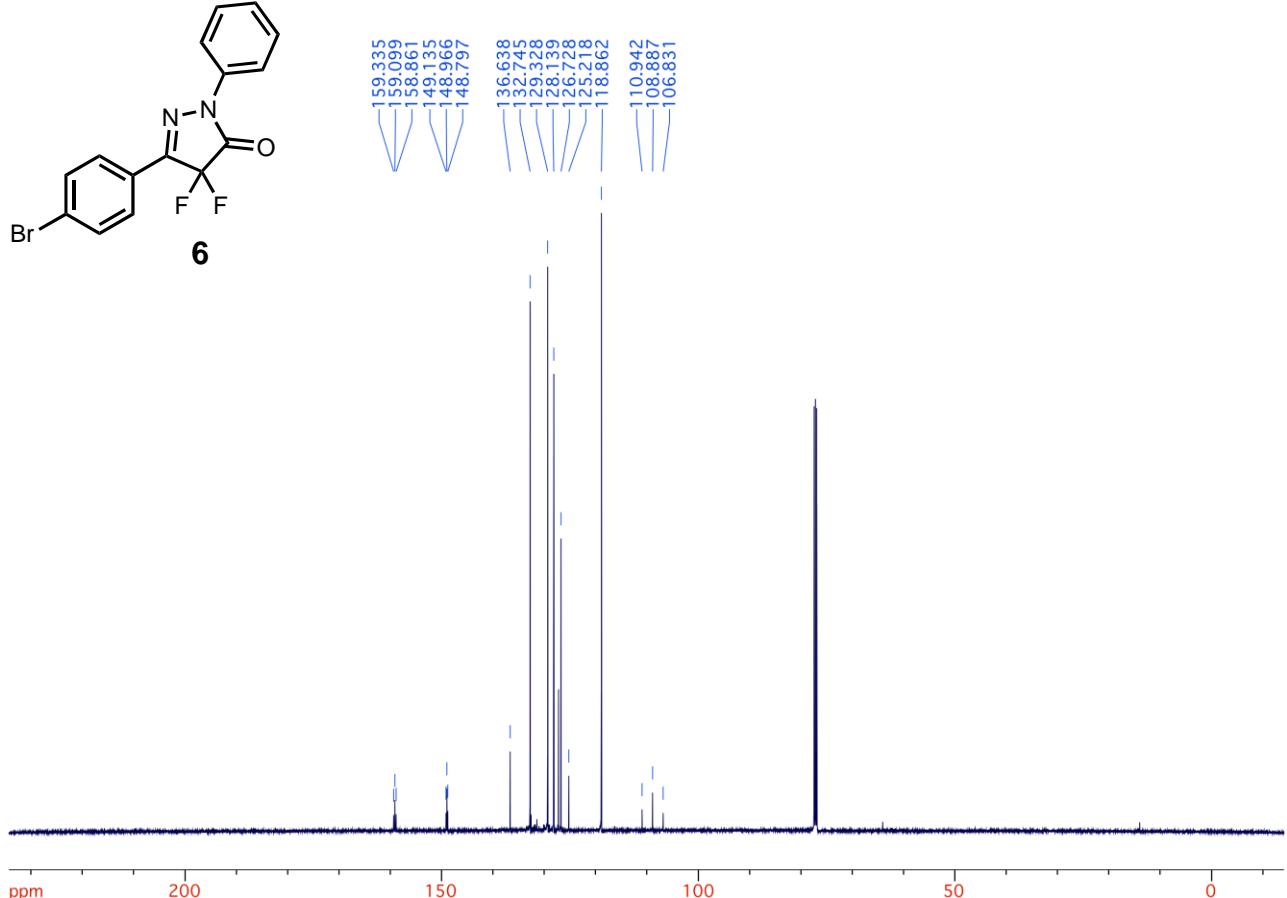
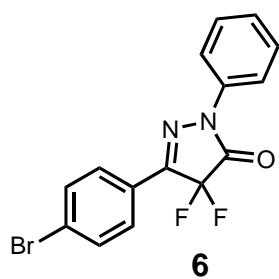
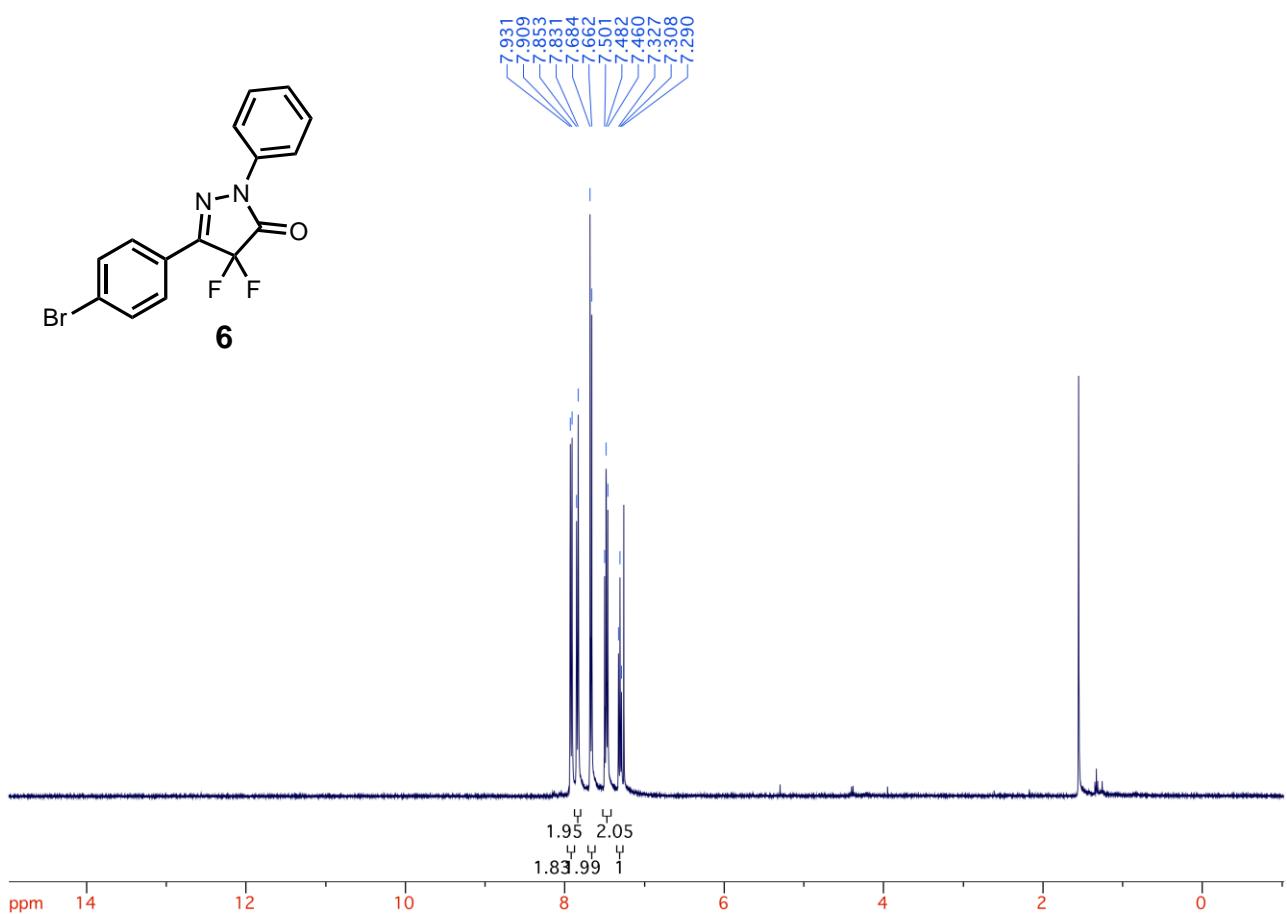
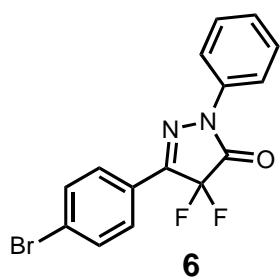


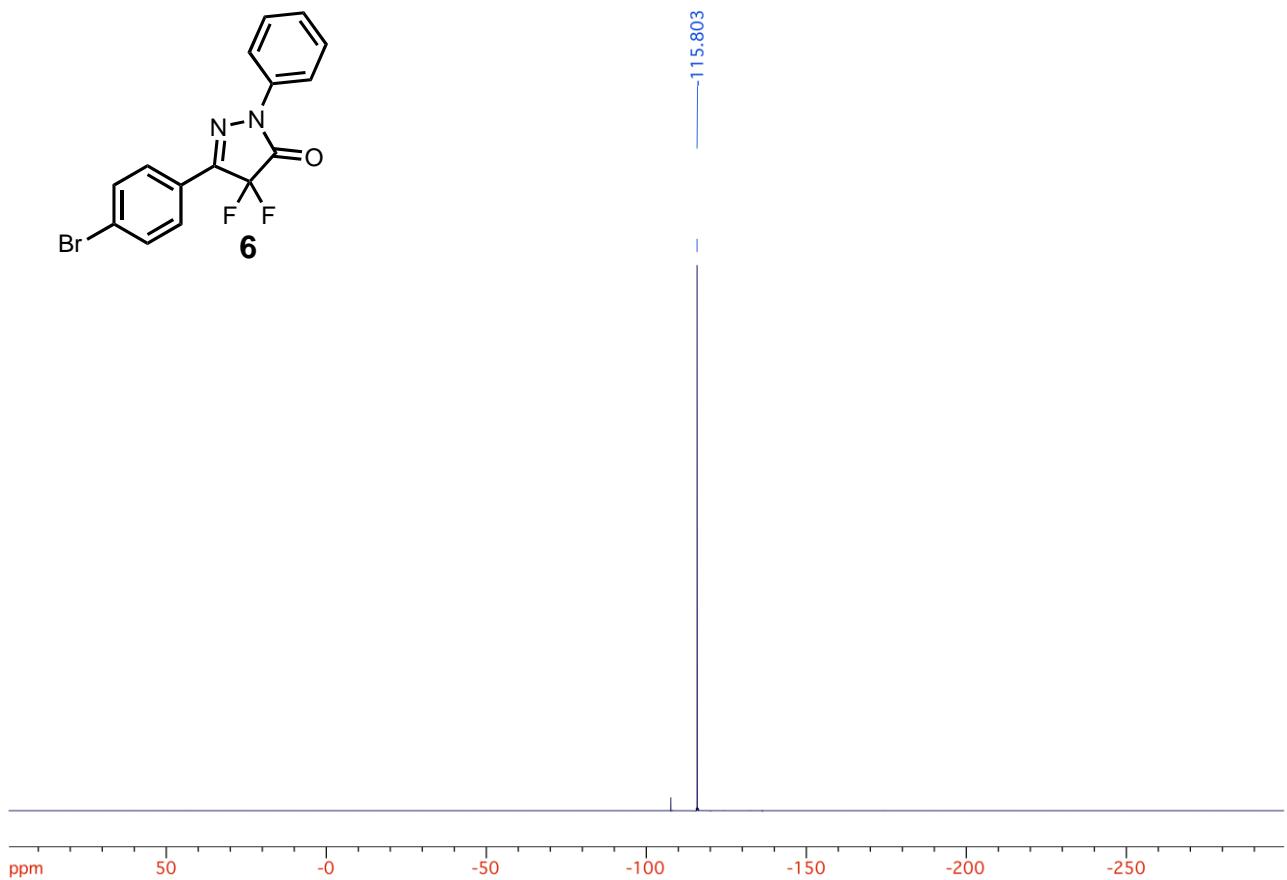
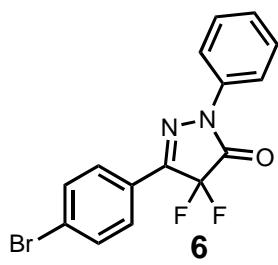


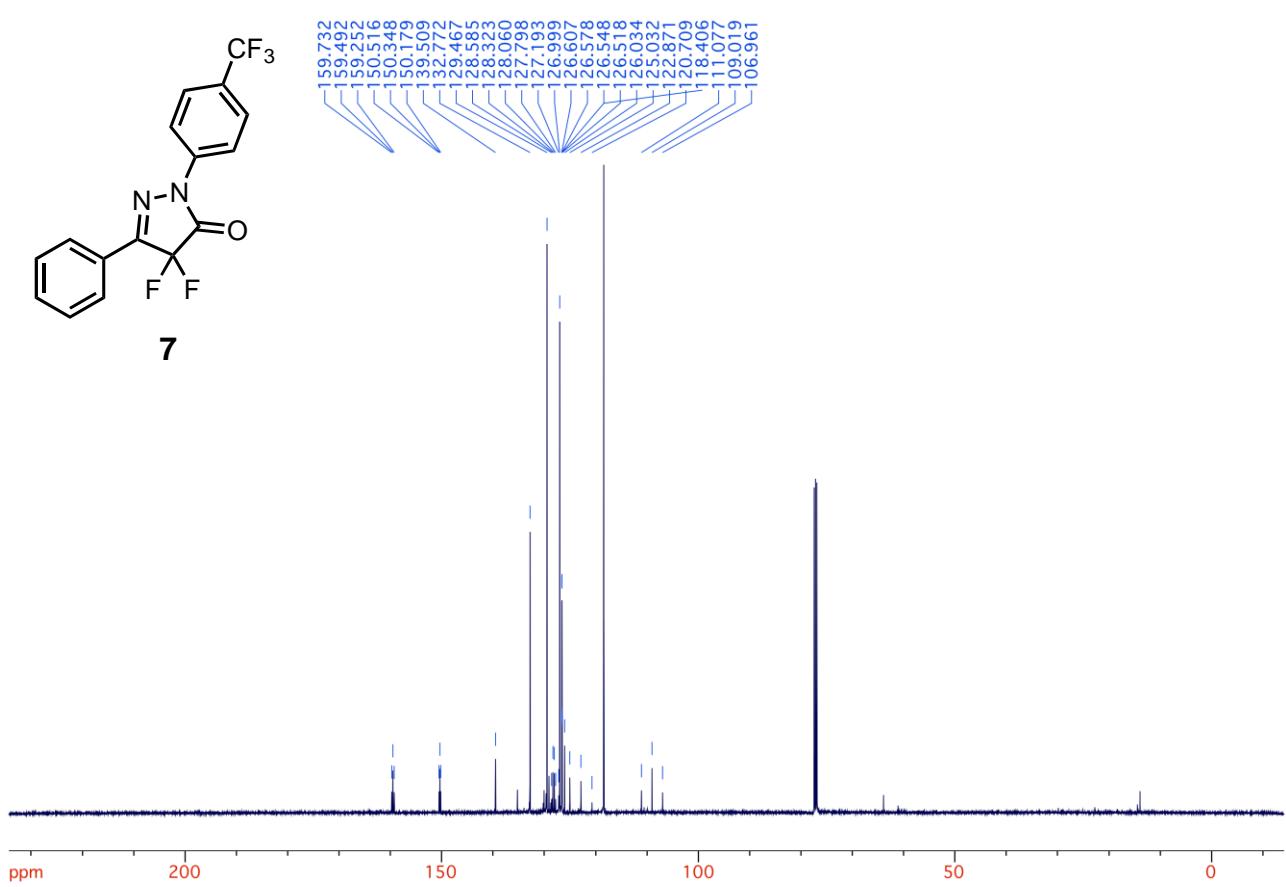
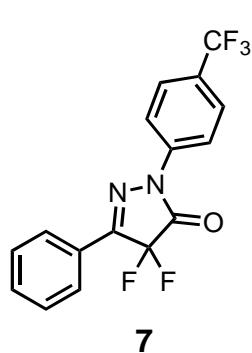
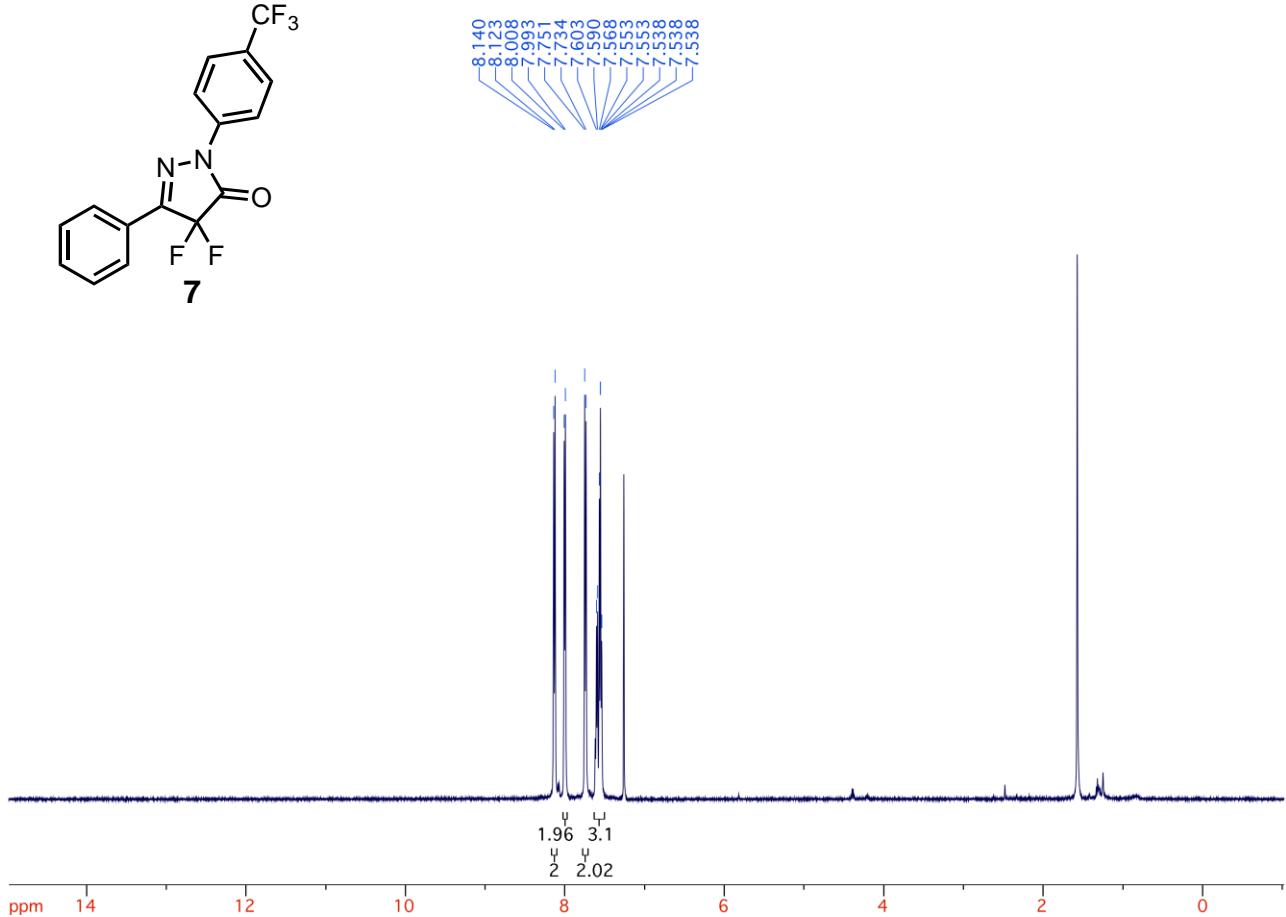
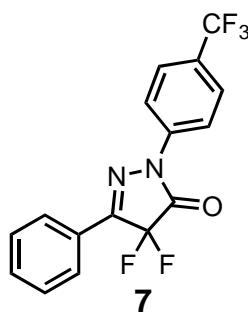


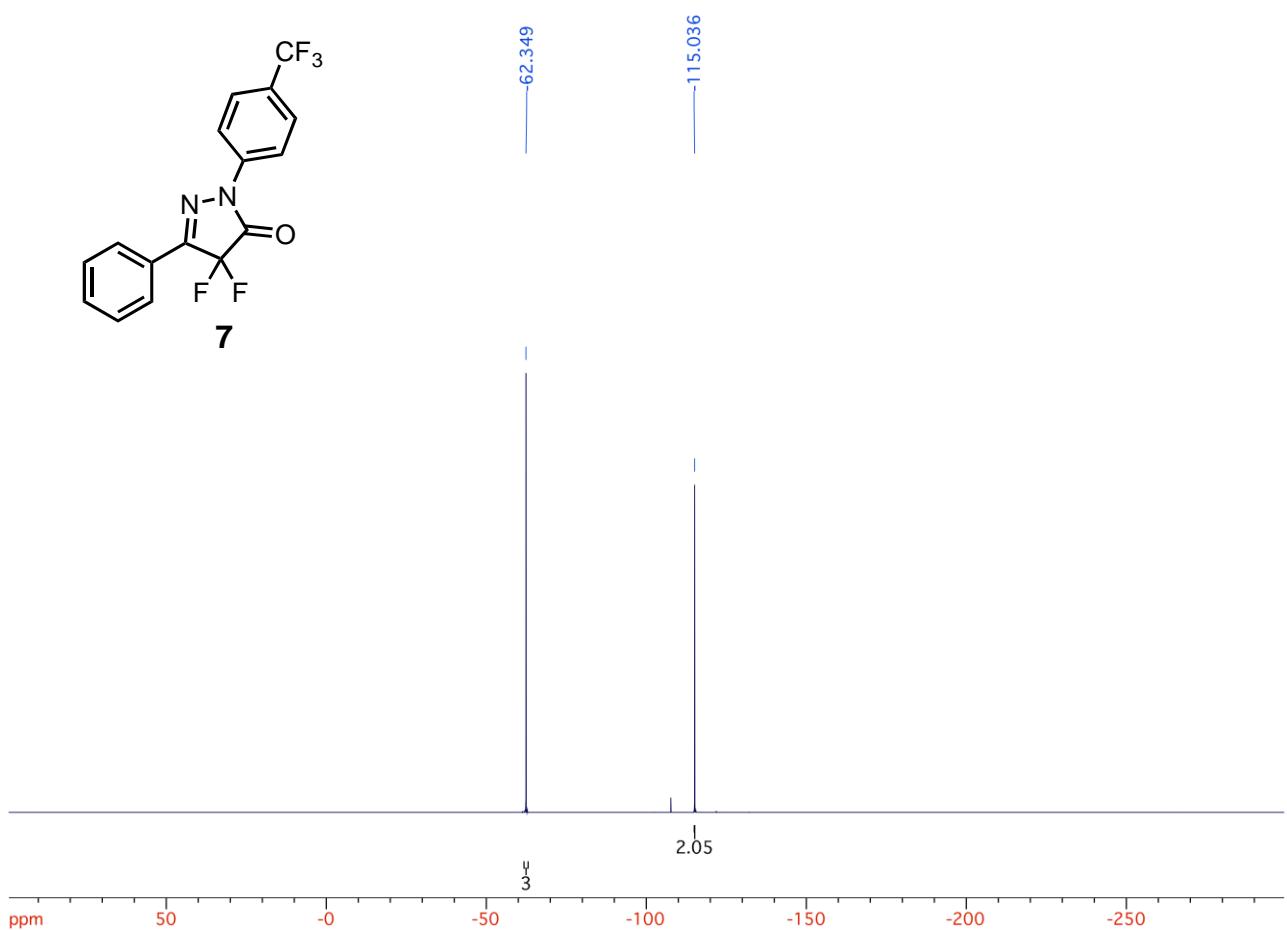
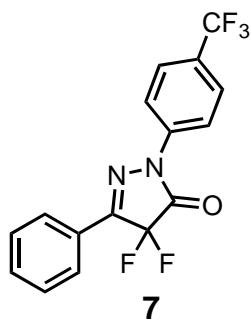


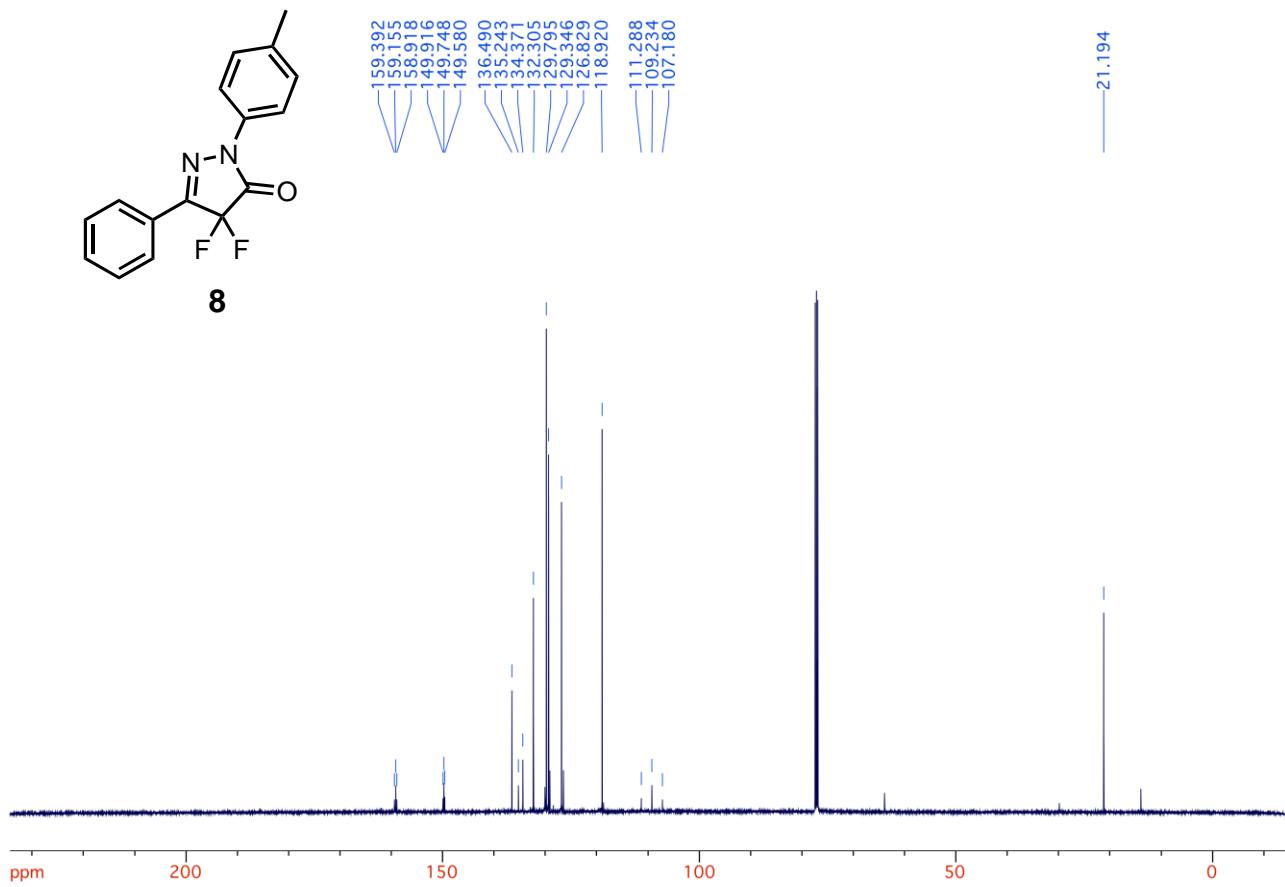
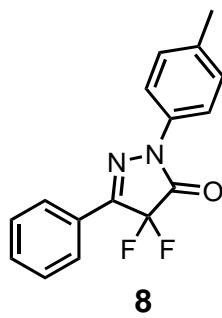
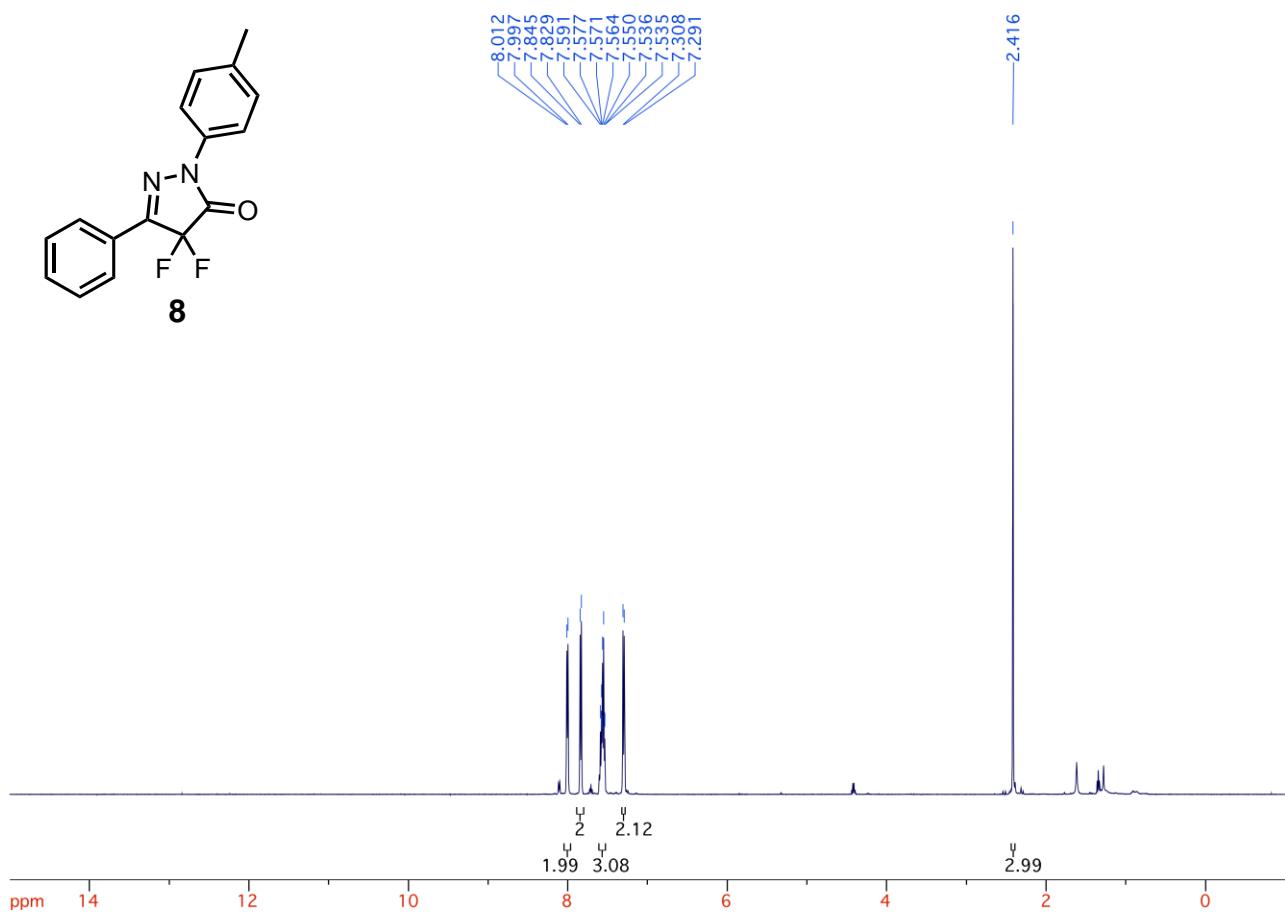
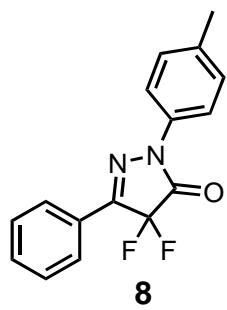


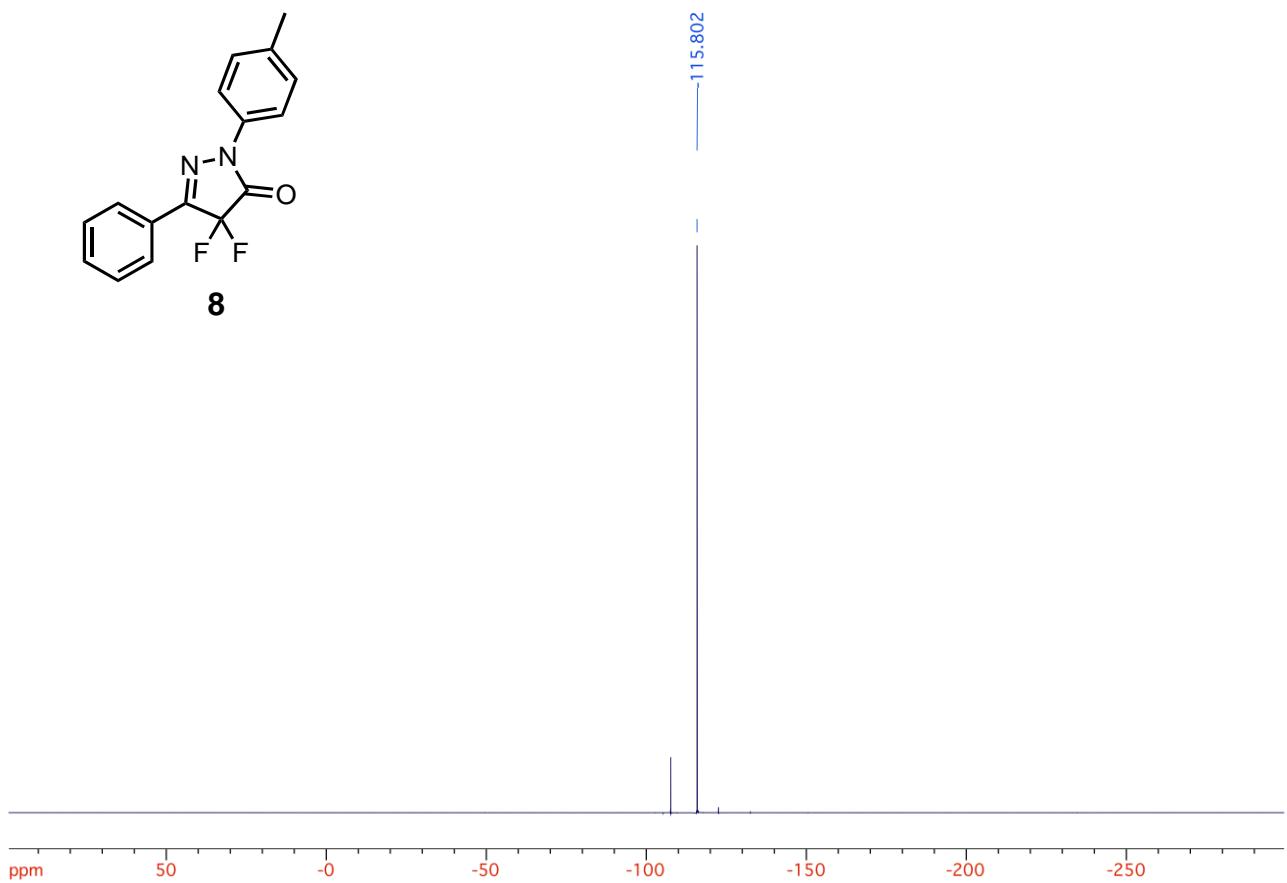
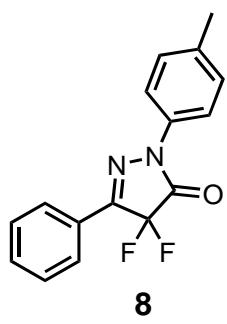


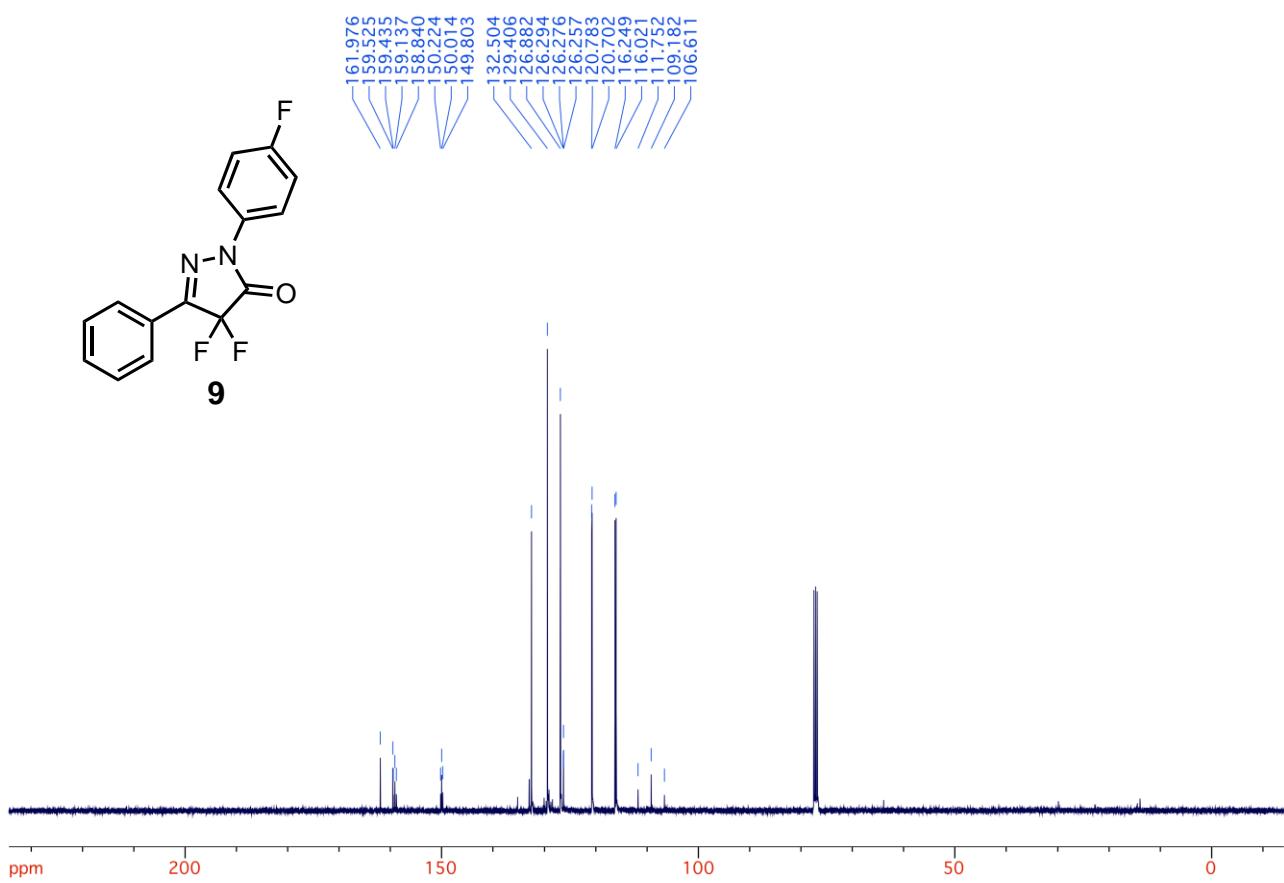
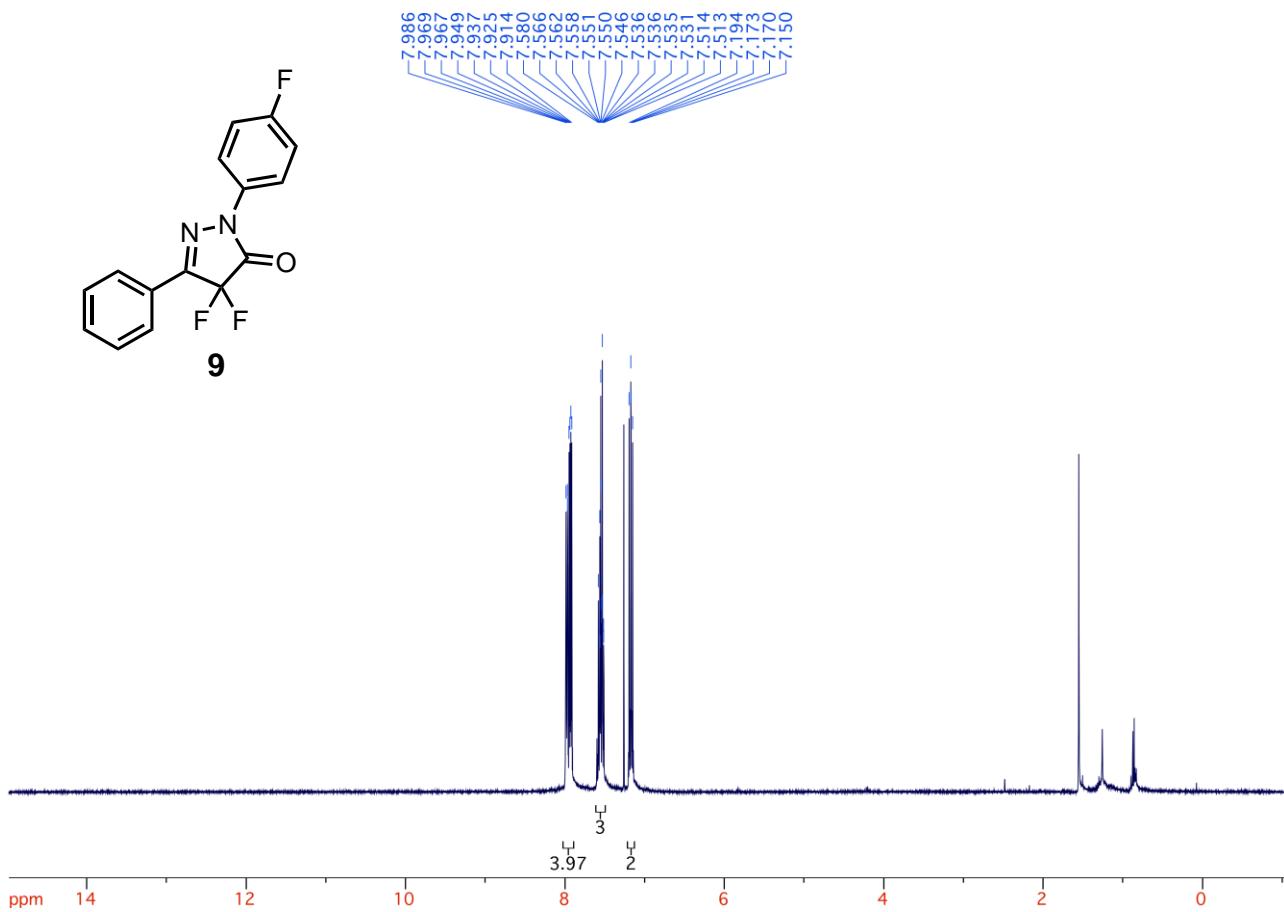


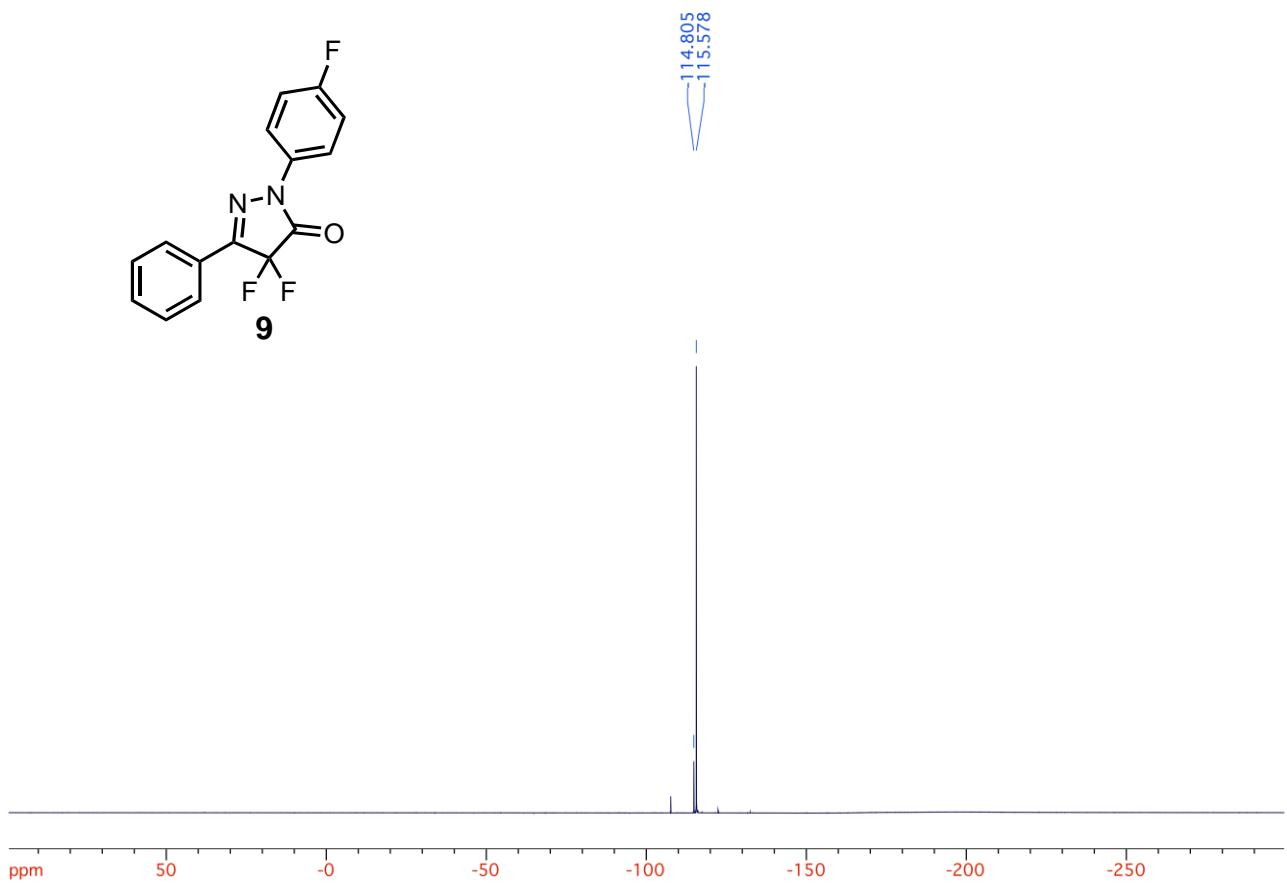
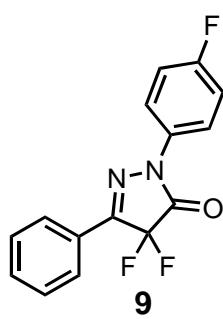


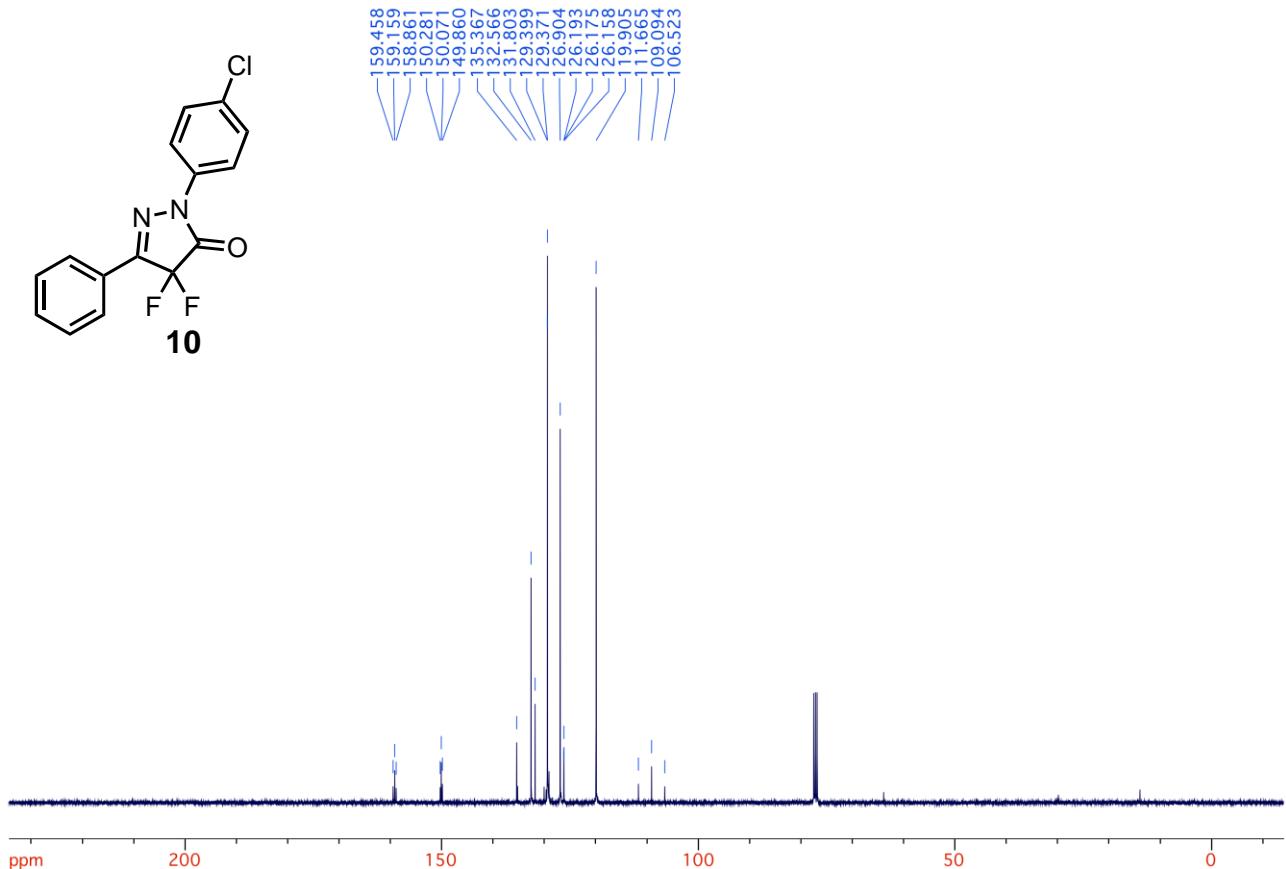
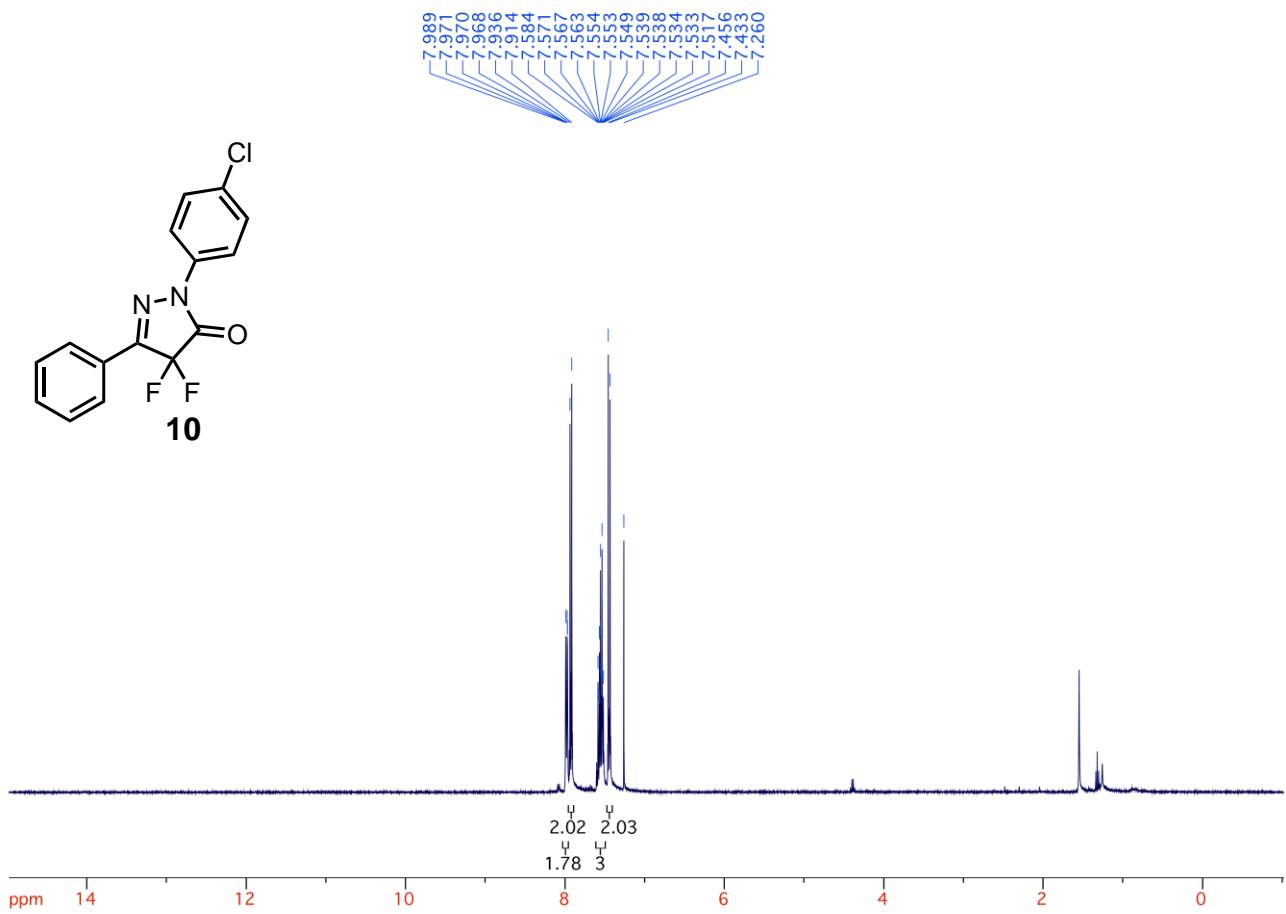


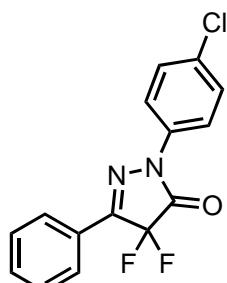




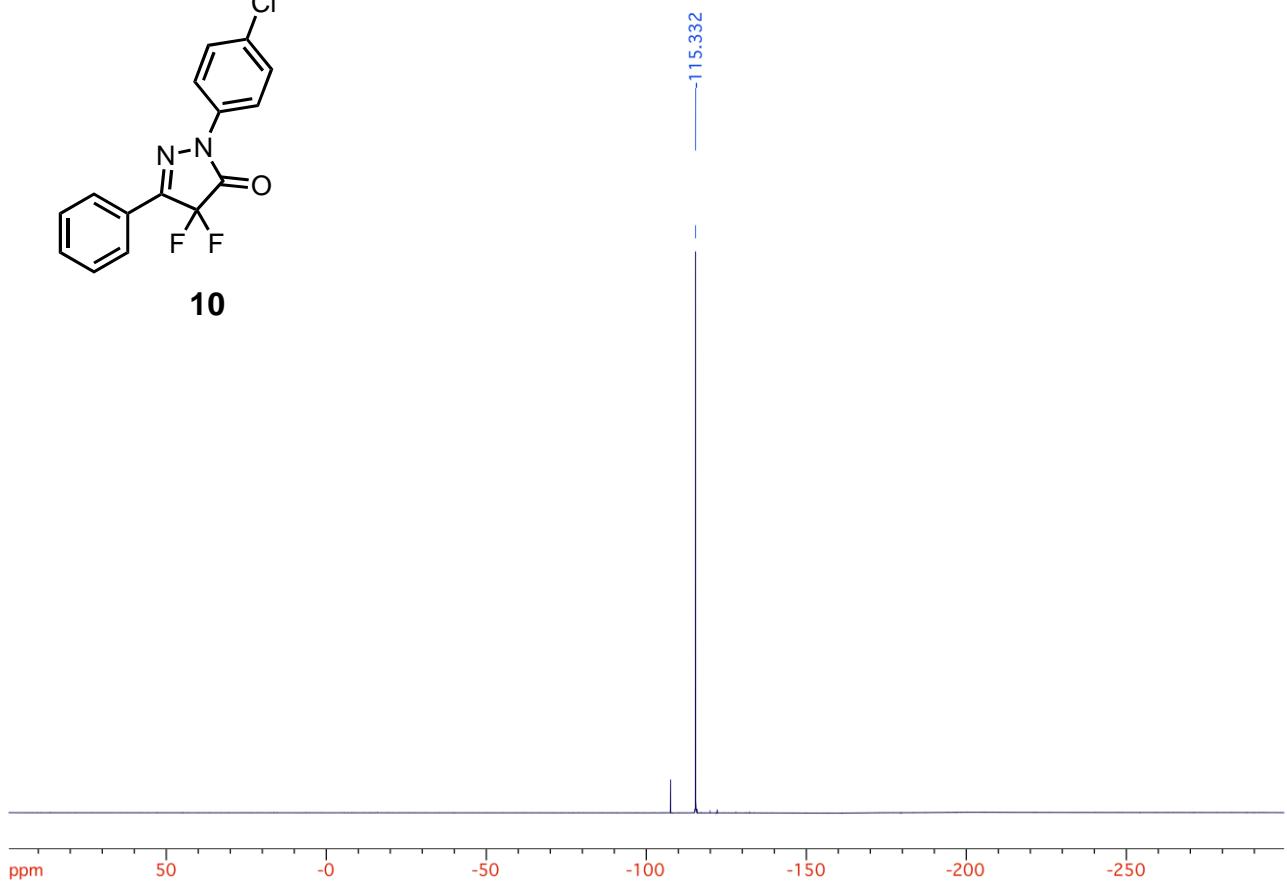


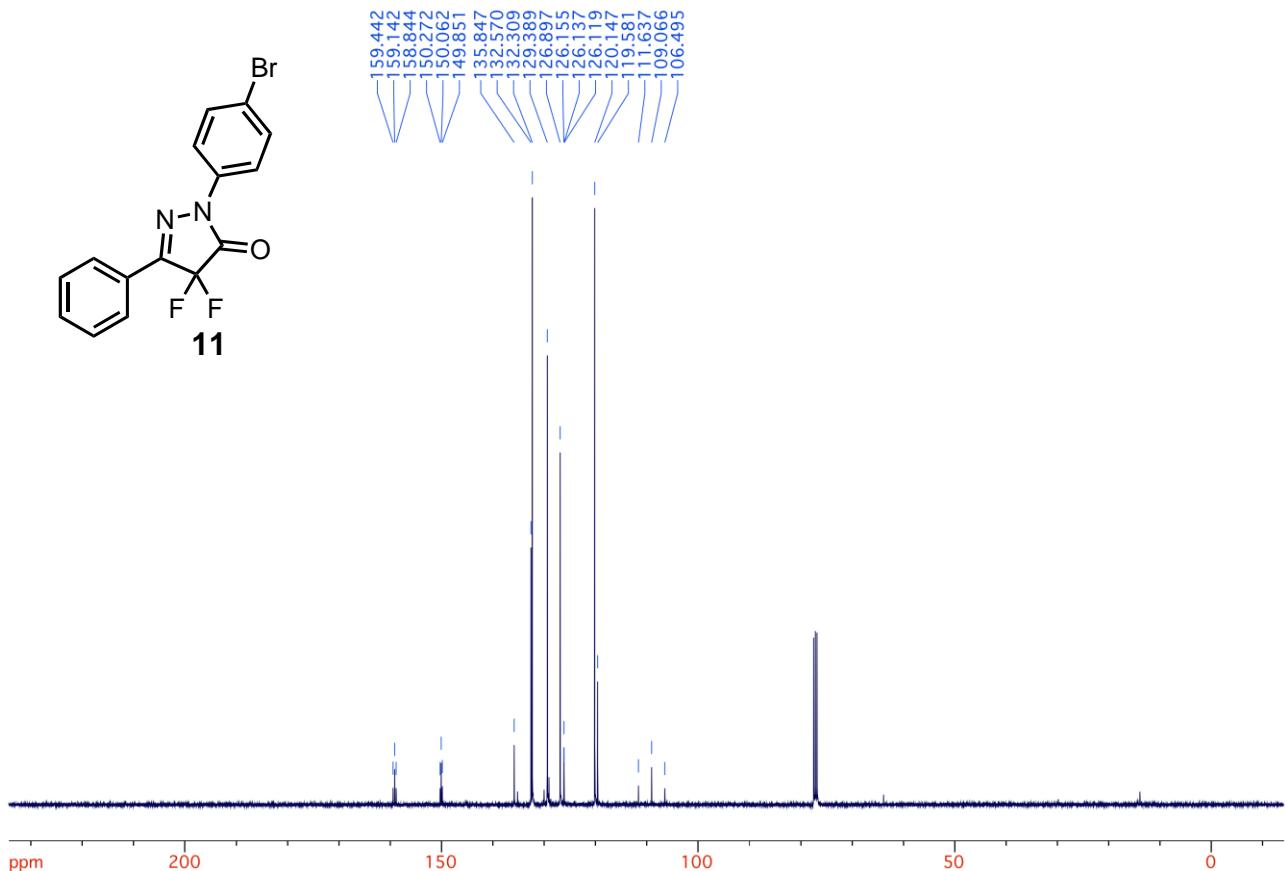
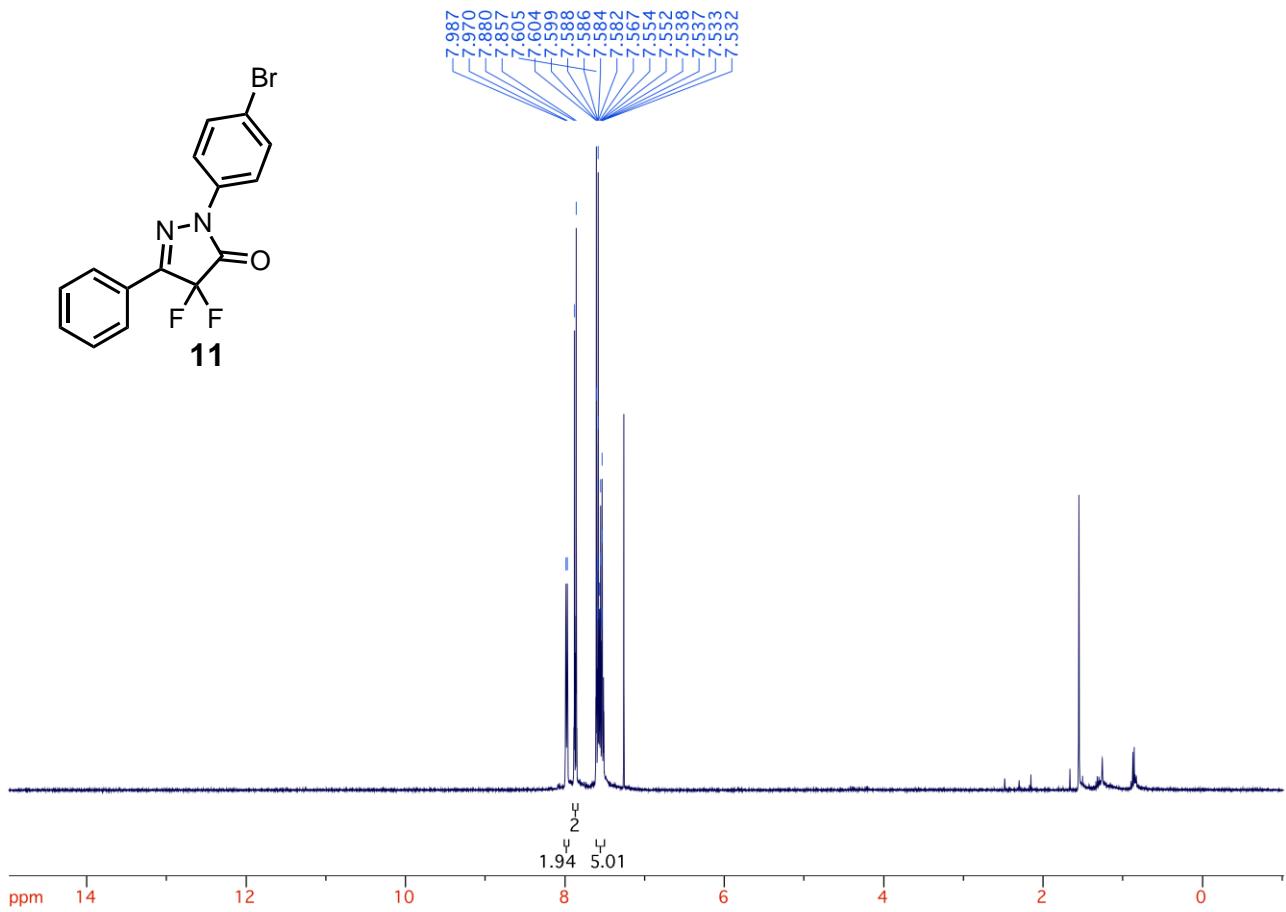


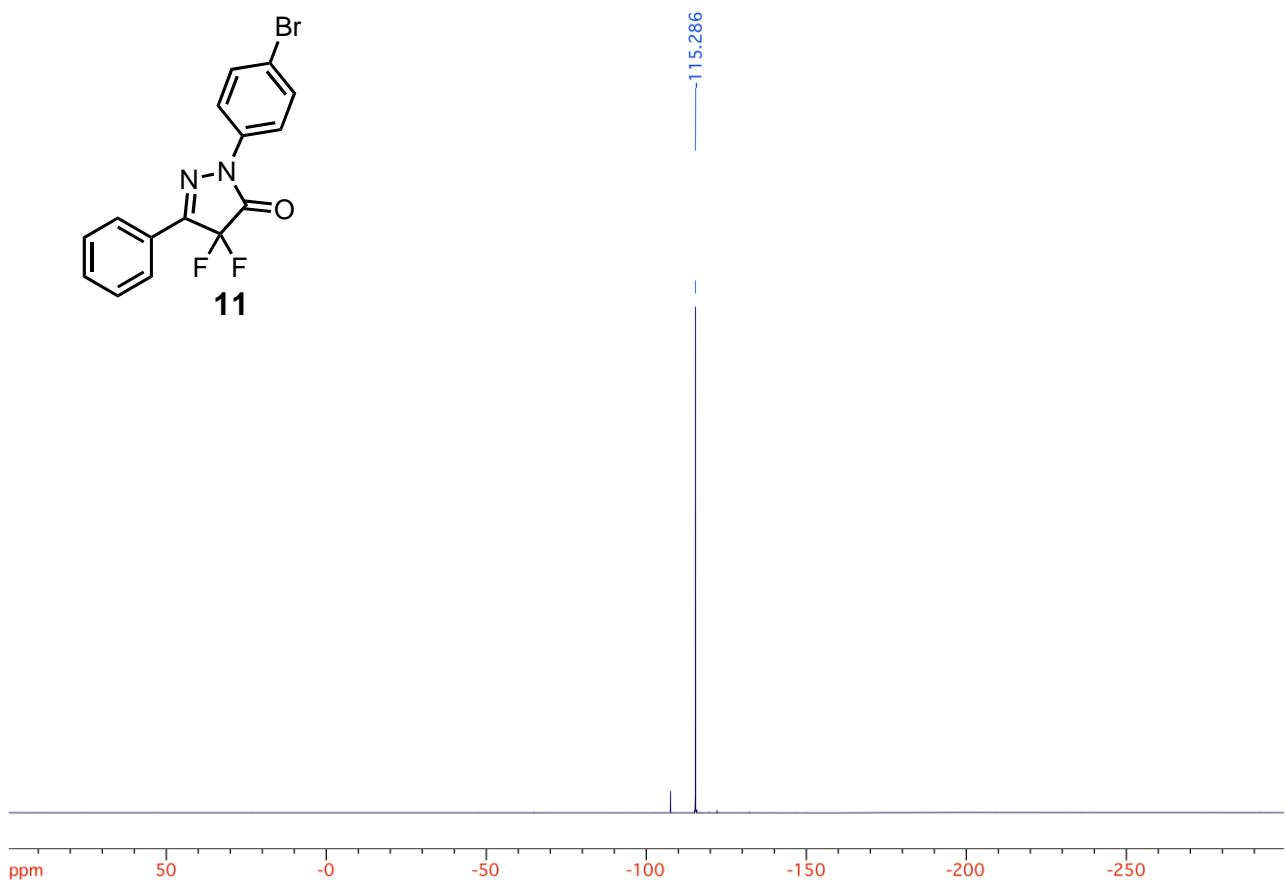
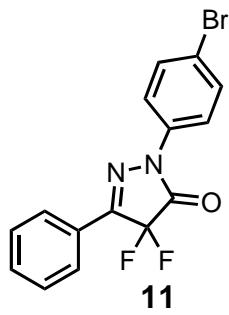


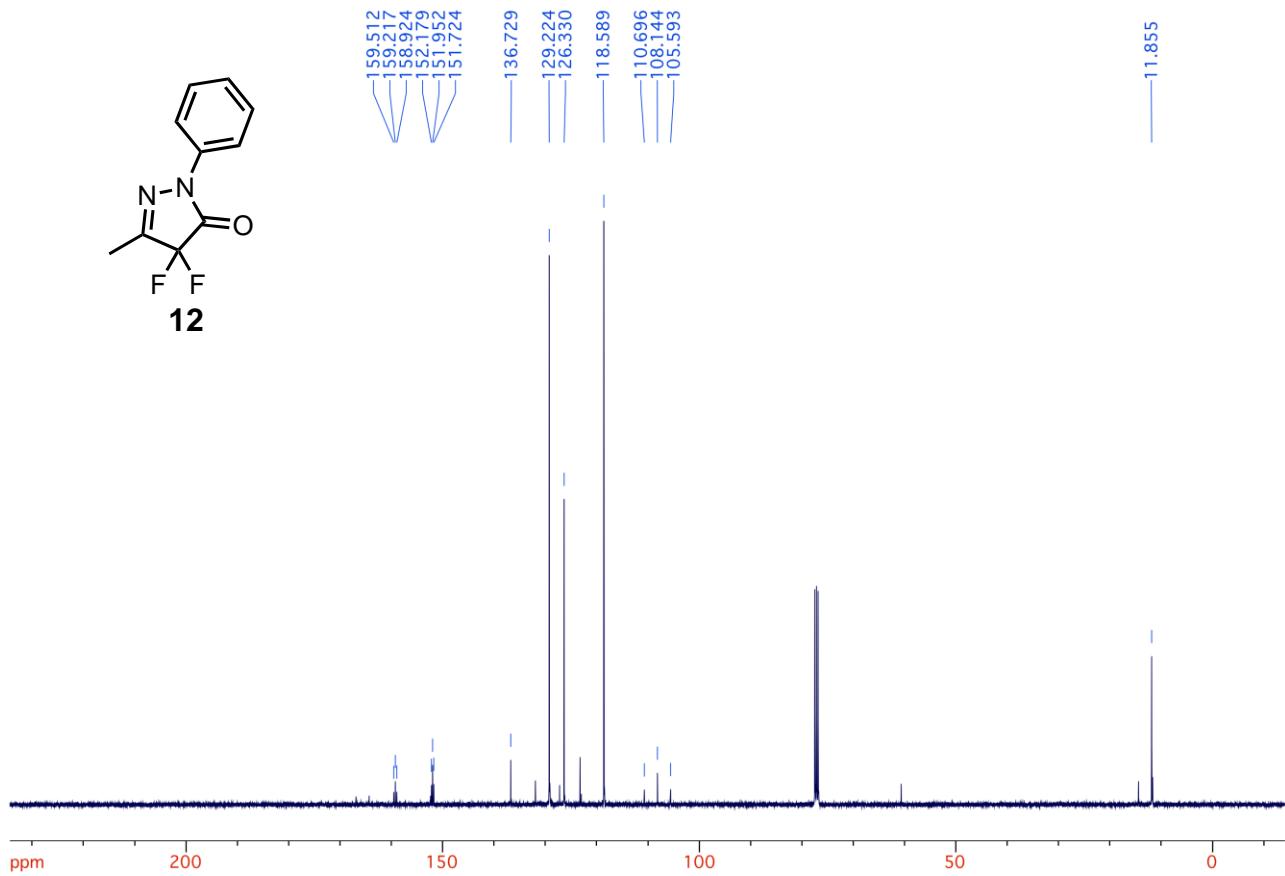
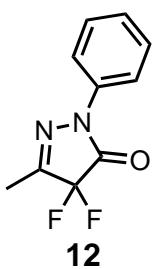
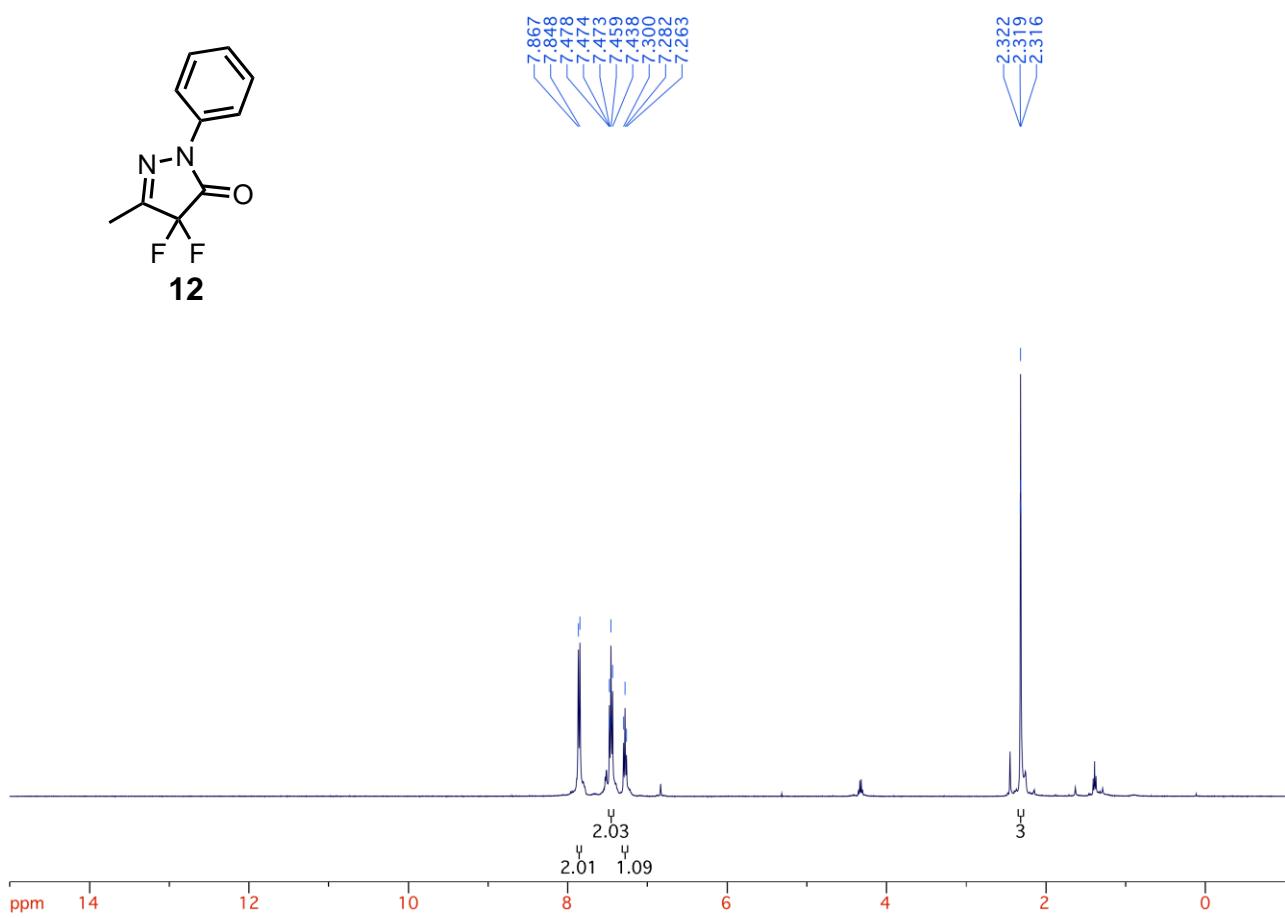
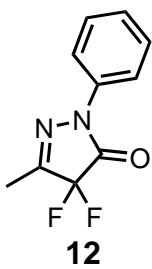


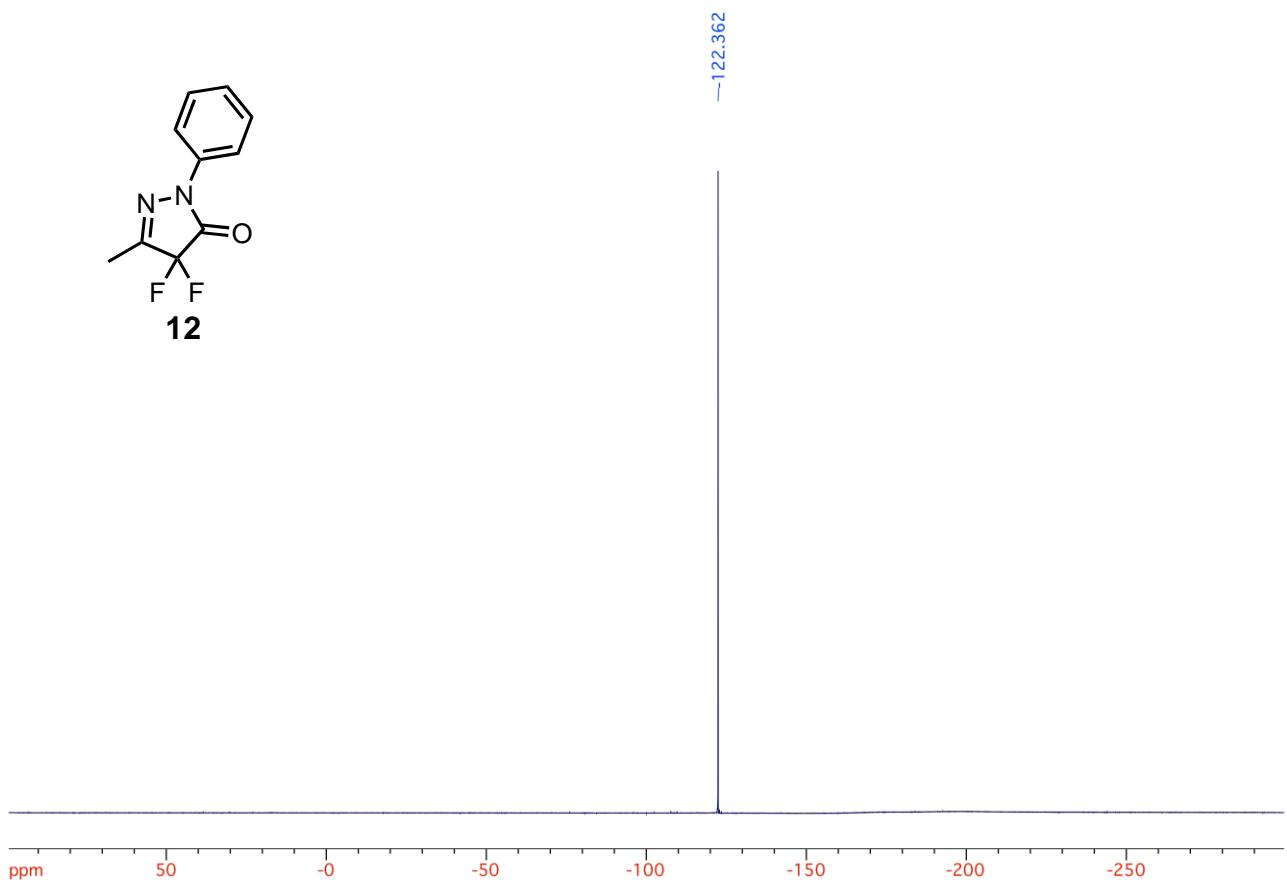
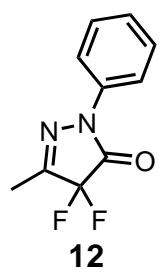
**10**





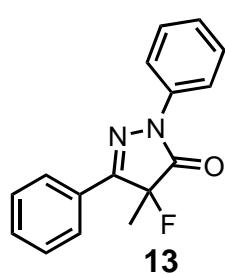
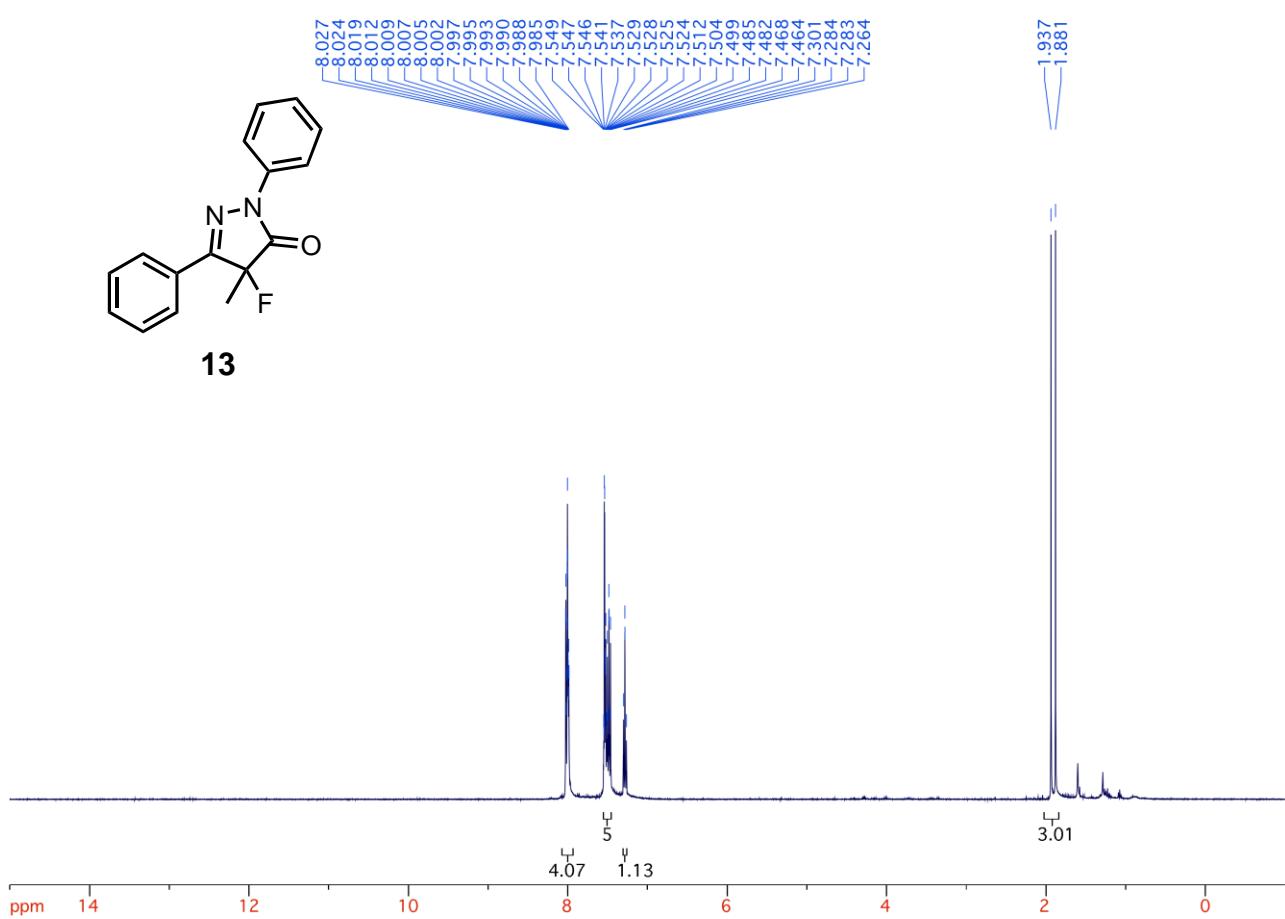




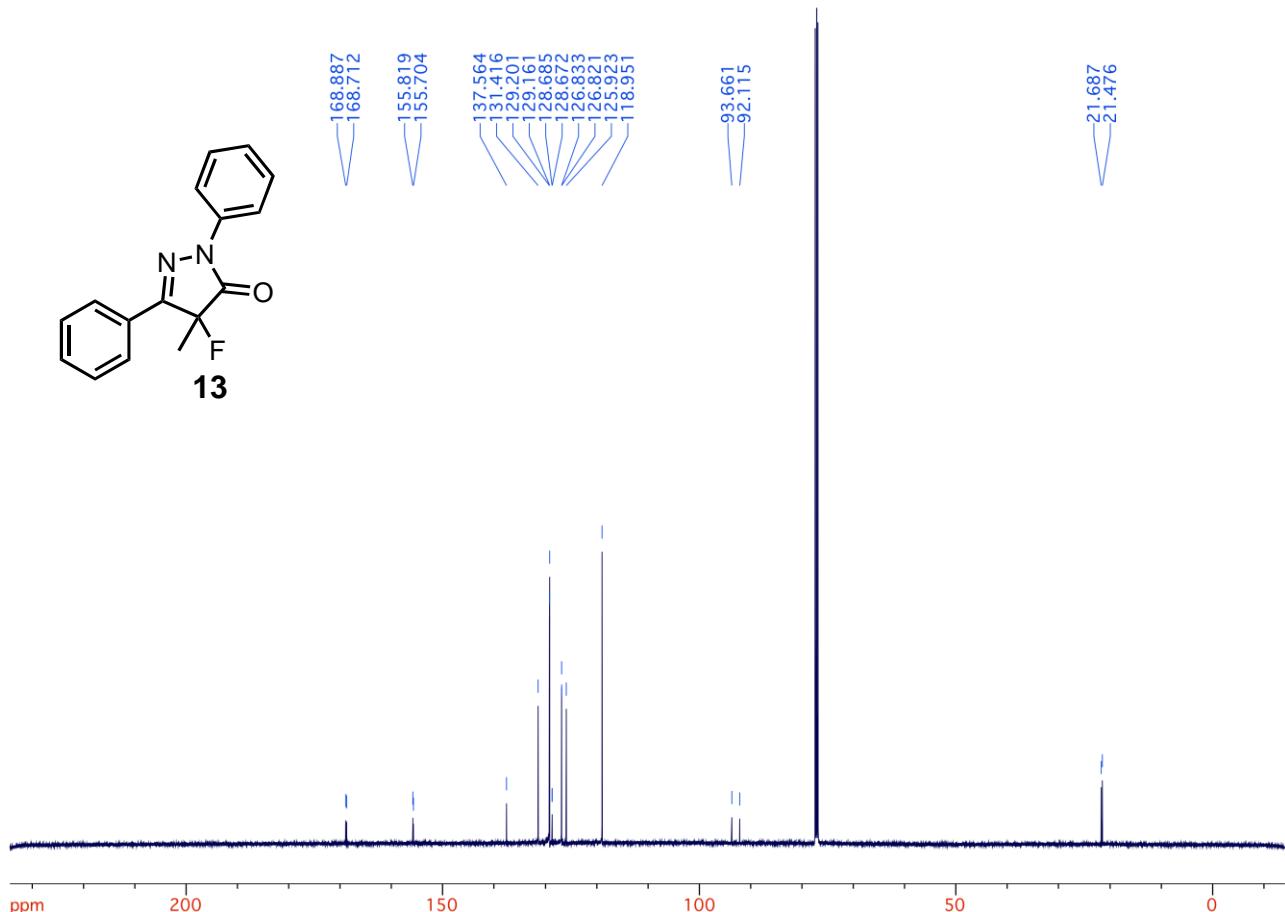


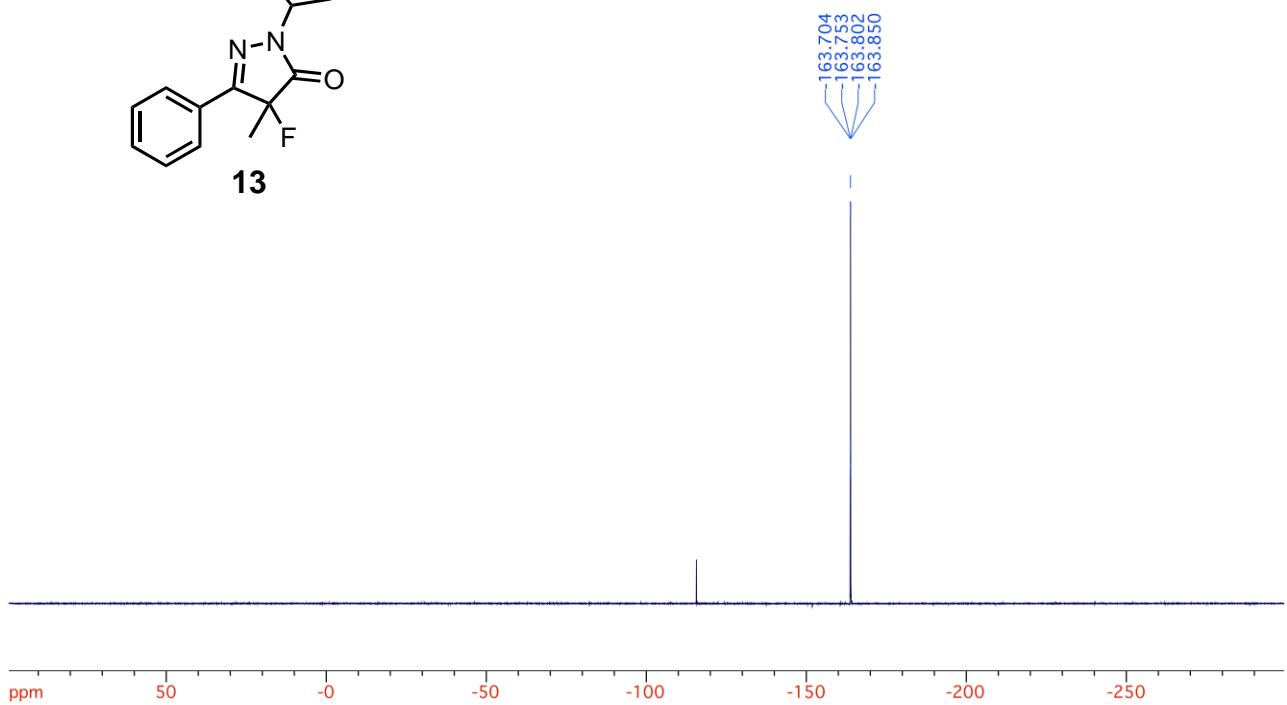
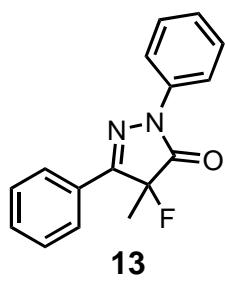


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