

## Supporting Information

### A Continuous Flow Synthesis of [1.1.1]Propellane Enabling Rapid Access to Bicyclo[1.1.1]pentane Derivatives

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## 1. Materials and Methods

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Fluorochem or Sigma Aldrich and used as received.

$^1\text{H}$ -NMR spectra were recorded on 400 MHz, 500 MHz and 600 MHz instruments and are reported relative to residual solvent:  $\text{CDCl}_3$  ( $\delta$  7.26 ppm).  $^{13}\text{C}$ -NMR spectra were recorded on the same instruments (100, 125 and 150 MHz) and are reported relative to  $\text{CHCl}_3$  ( $\delta$  77.16 ppm).  $^{19}\text{F}$ -NMR were recorded on a 400 and 500 MHz (376 and 470 MHz) spectrometer.

Data for  $^1\text{H}$ -NMR are reported as follows: chemical shift ( $\delta$ / ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, sept = septet, m = multiplet. Data for  $^{13}\text{C}$ -NMR are reported in terms of chemical shift ( $\delta$ / ppm) and multiplicity (C, CH,  $\text{CH}_2$  or  $\text{CH}_3$ ). COSY, HSQC and HMBC experiments were used in the structural assignment.

IR spectra were obtained by use of a Bruker Platinum spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal) .

High-resolution mass spectrometry was performed using the indicated techniques on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine-enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass.

Photochemical experiments were performed on a Vapourtec E-series system with the UV150 photoreactor that is equipped with a medium-pressure Hg lamp (75-150 W) and used in combination with a low pass filter (emission spectra shown below).

Continuous flow experiments were performed using Chemyx Inc Fusion 100 syringe pumps in combination with a PolarBear Plus system. Flow reactor consisted of 1/8" PFA tubing combined with a stainless-steel T-piece mixer, followed by a Teflon helical static mixer.

## 2. General Experimental Procedures.

### 2.1 Synthesis of [1.1.1]propellane

#### Tricyclo[1.1.1.0]pentane ([1.1.1]propellane) (2)



Chemical Formula: C<sub>5</sub>H<sub>6</sub>  
Exact Mass: 66.0470

#### General procedure A (batch):<sup>1</sup>

Under N<sub>2</sub> atmosphere, 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane (3.00 g, 10.1 mmol) was dissolved in pentane (10 mL) and cooled to -78 °C. A solution of MeLi in Et<sub>2</sub>O (1.6 M, 14 mL, 2.2 equiv.) was added dropwise over 15 minutes with vigorous stirring. The mixture was maintained at this temperature for a further 15 minutes before warming to 0 °C and stirring for a further 2 hours. The volatile materials were then transferred to a collection flask cooled to -78 °C under reduced pressure. The resulting solution containing [1.1.1]propellane was quantified by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as internal standard.

#### General procedure B (flow):

1,1-dibromo-2,2-bis(chloromethyl)cyclopropane (**A**) (594 mg, 2 mmol) was dissolved in pentane (10 mL). MeLi (**B**) (2.65 mL, 4.24 mmol, 2.1 equiv.) was transferred to a flame-dried flask under N<sub>2</sub> atmosphere and diluted with freshly distilled Et<sub>2</sub>O (7.35 mL, final conc. 0.42 M). The flow system was flushed with a dilute solution of MeLi (0.16 M, 5 mL) prior to introducing reagents. **A** and **B** were injected at a flow rate of 0.566 mL min<sup>-1</sup> (combined flow: 1.132 mL min<sup>-1</sup>, 6 min residence time) and combined in a T-piece mixer at -15 °C. Cooling was achieved using Polar Bear Plus system, alternatively a salt-ice bath maintained at -15 °C was sufficient. The resulting solution was collected in a cooled flask (0 °C) and washed with water. The resulting organic phase was separated and used for subsequent reaction without further purification. The concentration of the resulting [1.1.1]propellane solution was determined by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as an internal standard.

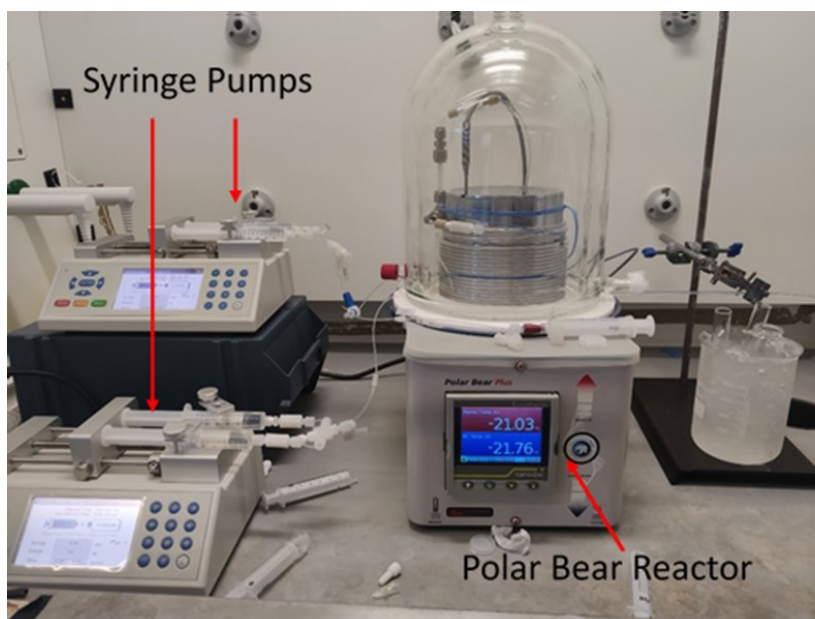
### 2.2 Synthesis of chloro-oxoacetates.

Oxalyl chloride (0.51 mL, 6 mmol) was diluted with CH<sub>2</sub>Cl<sub>2</sub> (1 mL) and cooled to 0 °C. A solution of alcohol (3 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was added **dropwise** while stirring. The mixture was stirred for 20 minutes before allowing to warm to room temperature for a further 2 hours. Solvent and excess oxalyl chloride were evaporated *in vacuo* yielding a colourless liquid. The material obtained was used for subsequent reactions without further purification.

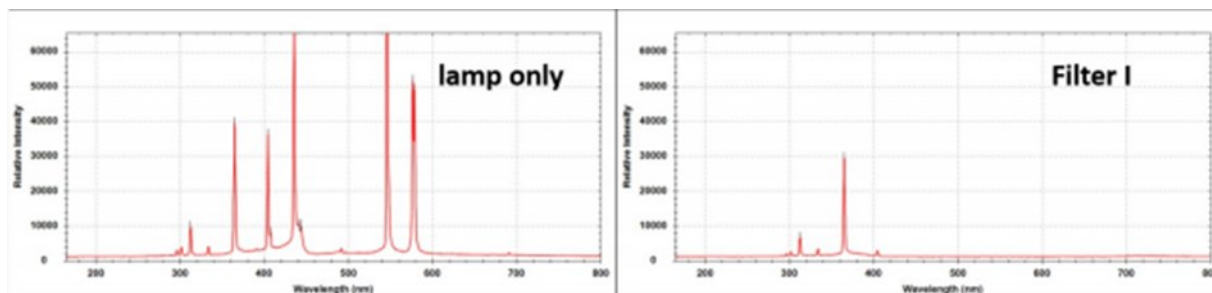
### 2.3 Synthesis of BCP amides.

To a solution of [1.1.1]propellane (2 mL, 0.17 M, 0.34 mmol) was added 2-chloro-2-oxoacetate (0.34 mmol) and acetone (1 drop). The mixture was pumped through a Vapourtec E-Series UV-150 photochemical reactor (medium pressure Hg-lamp (90 W), 10 mL reactor volume) at a flow rate of 2 mL min<sup>-1</sup> (5 min residence time). 4-Fluoroaniline (32 μL, 0.34 mmol) and triethylamine (47 μL, 0.34 mmol) were added to the resulting output solution. The mixture was stirred for 2 hours at room temperature. The mixture was acidified using HCl (1 M) and extracted with EtOAc. Solvent was evaporated *in vacuo* and the resulting residue was purified by flash chromatography.

**Flow reaction set-up:**



**UV-Vis spectra of medium-pressure Hg-lamp and effect of low-pass filter used:**



### 3. Reaction Optimisation.

#### 3.1 Flow synthesis of [1.1.1]propellane.

Table 1. Solvent optimisation.

Entry	MeLi Equiv.	Residence Time (min)	Solvent	NMR Yield (%)
1	2.1	3.8	Et <sub>2</sub> O	27
2	2.1	3.8	THF	11
3	2.1	3.8	Pentane	27
4	2.4	3.8	MeTHF	29

Reaction conditions: **A** (0.4 M) was combined with MeLi (**B**) (1.38 M in Et<sub>2</sub>O) at -10°C. The reaction material was collected in a test tube containing water (0°C) and the resulting organic phase was separated. [1.1.1]Propellane was quantified by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as internal standard. Stoichiometry was controlled by adjusting the flow rates of **A** and **B**.

Table 2. Steady state study.

Entry	A conc. (M)	B conc. (M)	MeLi (B) Equiv.	Residence time (min)	Reactor volumes to reach steady state
5	0.4	1.6	2.1 <sup>a</sup>	3	2
6	0.5	1.05	2.1	4	1
7	0.18	0.4	2.2	6	2
8	0.18	0.4	2.2	3	2
9	0.18	0.4	2.2	9	2.5

<sup>a</sup>Stoichiometry controlled using flow rate.

#### 3.2 Synthesis of BCP acyl chlorides.

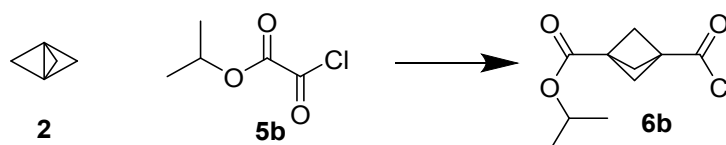


Table 3. Stoichiometry optimisation.

Entry	5b: 2	Concentration (M)	NMR Yield (%)
10	1.2: 1	0.26	15
11	1.2:1	0.13	14
12	3:1	0.27	1
13	1:1	0.16	34
14	1:2	0.16	19
15	1:3	0.16	3

Reaction conditions: **5b** was added to a solution of [1.1.1]propellane. The mixture was passed through the photochemical reactor (5 min residence time, 90 W, gold light filter). Solvent was evaporated *in vacuo* and the residue was quantified by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as internal standard.

**Table 4.** Co-solvent study.

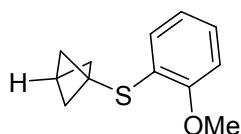
Entry	Co-solvent	NMR Yield (%)
16	Acetonitrile	1
17	DMF	14
18	DMSO	1
19	Acetone	0
20	DCM	0
21	THF	10
22	EtOAc	22

Reaction conditions: **5b** (0.23 mmol) was added to a solution of [1.1.1]propellane (1 mL, 0.23 M, 0.23 mmol). The mixture was diluted with co-solvent (1 mL) and passed through the photochemical reactor (10 min residence time, 90 W, gold light filter). Solvent was evaporated *in vacuo* and the residue was quantified by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as internal standard.

**Table 5.** Photosensitiser study.

Entry	Additive	Equivalents	NMR Yield (%)
23	Acetone	0.2	28
24	Acetone	0.5	34
25	Acetone	1	29
26	Acetone	5	21
27	Acetone	10	15
28	Benzophenone	0.2	11
29	Benzophenone	0.5	19
30	Benzophenone	1	26
31	Benzophenone	2	11
32	Benzophenone	3	13
33	Acetophenone	0.2	15
34	Acetophenone	0.5	7
35	Acetophenone	1	7
36	Pinacolone	0.2	12
37	Pinacolone	0.5	19
38	Pinacolone	1	10

Reaction conditions: Additive and **5b** (0.2 mmol) was added to a solution of [1.1.1]propellane (1 mL, 0.2 M, 0.2 mmol). The mixture was passed through the photochemical reactor (5 min residence time, 90 W, gold light filter). Solvent was evaporated *in vacuo* and the residue was quantified by <sup>1</sup>H-NMR using 1,3,5-trimethoxybenzene as internal standard.



## 4. Spectroscopic Data.

Chemical Formula: C<sub>12</sub>H<sub>14</sub>OS  
Exact Mass: 206.0765

### Bicyclo[1.1.1]pentan-1-yl(2-methoxyphenyl)sulfane (3):<sup>2</sup>

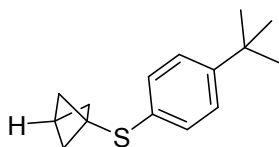
Yield: 88% (50 mg, 0.24 mmol).

Appearance: colourless liquid.

**<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)** δ/ppm 7.47 (dd, *J* = 7.6 Hz, 1.7 Hz, 1H), 7.26 (m, 1H), 6.89 (m, 2H) 3.86 (s, 3H), 2.69 (s, 1H), 1.96 (s, 6H). **<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)** δ/ppm 158.9 (C), 135.1 (CH), 129.0 (CH), 122.1 (CS), 120.7 (CH), 110.8 (CH), 55.6 (CH<sub>3</sub>), 54.1 (3CH<sub>2</sub>), 45.2 (CS), 28.6 (CH).

[1.1.1]Propellane (synthesised either by general procedure **A** or **B**) (0.275 mmol) was transferred to a flame dried flask under N<sub>2</sub> atmosphere. 4-Methoxybenzenethiol (67 μL, 0.55 mmol) was added while stirring. The mixture was stirred at room temperature for 1 hour. The mixture was washed with NaOH (1 M). The resulting organic phase was washed with water followed by brine. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and solvent was evaporated *in vacuo*. The yellow residue was purified by flash chromatography (25% EtOAc in hexanes, R<sub>f</sub>: 0.3) to yield a colourless liquid (50 mg, 88%).

### Bicyclo[1.1.1]pentan-1-yl(4-(*tert*-butyl)phenyl)sulfane (4):<sup>2</sup>



Yield: 83% (53 mg, 0.23 mmol).

Appearance: colourless liquid.

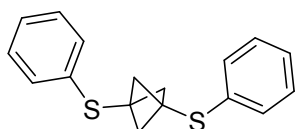
**HR-MS (QTOF)** m/z: [M]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>20</sub>S<sup>+</sup> 232.1286; found 232.1285.

Chemical Formula: C<sub>15</sub>H<sub>20</sub>S  
Exact Mass: 232.1286

**<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)** δ/ppm 7.38 - 7.35 (m, 2H), 7.33 - 7.29 (m, 2H), 2.71 (s, 1H), 1.94 (s, 6H), 1.31 (s, 9H). **<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)** δ/ppm 150.5 (C), 133.2 (2 CH), 130.4 (C), 125.7 (CH), 53.9 (3 CH<sub>2</sub>), 45.7 (C), 34.5 (C), 31.3 (3 CH<sub>3</sub>), 28.6 (CH).

[1.1.1]Propellane (synthesised either by general procedure **A** or **B**) (0.275 mmol) was transferred to a flame dried flask under N<sub>2</sub> atmosphere. 4-(*Tert*-butyl)benzenethiol (51 μL, 0.296 mmol) was added while stirring. The mixture was stirred at room temperature for 1 hour. The mixture was washed with NaOH (1 M). The resulting organic phase was washed with water followed by brine. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and solvent was evaporated *in vacuo*. The yellow residue was purified by flash chromatography (5% EtOAc in hexanes) to yield a colourless liquid (53 mg, 83%).

### 1,3-Bis(phenylthiol)bicyclo[1.1.1]pentane (5):<sup>3</sup>



Yield: 95% (249 mg, 0.88 mmol)

Appearance: white solid

Chemical Formula: C<sub>17</sub>H<sub>16</sub>S<sub>2</sub>  
Exact Mass: 284.0693

**<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)** δ/ppm 7.43 – 7.40 (m, 4H), 7.31 - 7.27 (m, 6H), 2.03 (s, 6H). **<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)** δ/ppm 134.0 (4CH), 133.3 (2C), 129.0 (4CH), 128.1 (2CH), 57.5 (3CH<sub>2</sub>), 42.7 (2C).

To a solution of [1.1.1]propellane synthesised by general procedure **B** (4 mL, 0.23 M, 0.92 mmol) was added diphenyl disulfide (606 mg, 2.78 mmol). The mixture was pumped through a Vapourtec E-Series UV-150 photochemical reactor (medium-pressure Hg lamp at 90 W, 10 mL reactor volume) at a flow rate of 1 mL min<sup>-1</sup> (10 min residence time). The solvent was evaporated *in vacuo* and the resulting residue was purified by flash chromatography.

### 1,3-Diiodobicyclo[1.1.1]pentane (6):<sup>4</sup>



Chemical Formula: C<sub>5</sub>H<sub>6</sub>I<sub>2</sub>  
Exact Mass: 319.8559

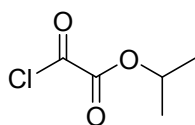
Yield: 59% (982 mg, 3.07 mmol).

Appearance: off-white solid.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ/ppm 2.67 (s, 6H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ/ppm: 68.3 (3CH<sub>2</sub>), -1.6 (C).

Iodine (1.3 g, 5.1 mmol) was added slowly to a stirring solution of [1.1.1]propellane (synthesised by general procedure B) until a dark red colour persisted. The mixture was stirred for a further 1 hour before washing with sat. sodium thiosulfate solution. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and solvent was evaporated *in vacuo*. The residue was triturated from cold EtOAc yielding an off-white solid (982 mg, 59%).

#### Isopropyl 2-chloro-2-oxoacetate (7a):



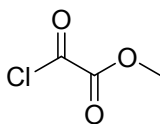
Chemical Formula: C<sub>5</sub>H<sub>7</sub>ClO<sub>3</sub>  
Exact Mass: 150.0084

Yield: 80% (360 mg, 2.39 mmol).

Appearance: colourless liquid.

<sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>) δ/ppm 5.19 (sept, *J* = 6.2 Hz, 1H), 1.39 (d, *J* = 6.3 Hz, 6H). <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>) δ/ppm: 161.6 (C), 155.4 (C), 74.2 (CH), 21.6 (2CH<sub>3</sub>).

#### Methyl 2-chloro-2-oxoacetate (7b):



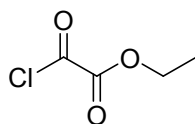
Chemical Formula: C<sub>3</sub>H<sub>3</sub>ClO<sub>3</sub>  
Exact Mass: 121.9771

Yield: 72% (269 mg, 2.20 mmol).

Appearance: colourless liquid.

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ/ppm 3.99 (s, 3H). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>) δ/ppm: 161.0 (C), 156.3 (C), 55.1 (CH<sub>3</sub>).

#### Ethyl 2-chloro-2-oxoacetate (7c):



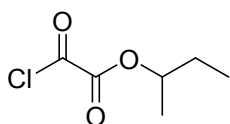
Chemical Formula: C<sub>4</sub>H<sub>5</sub>ClO<sub>3</sub>  
Exact Mass: 135.9927

Yield: 81% (331 mg, 2.42 mmol).

Appearance: pale yellow liquid.

<sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>) δ/ppm 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (d, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>) δ/ppm: 161.3 (C), 155.8 (C), 65.2 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>).

#### Sec-butyl 2-chloro-2-oxoacetate (7d):



Chemical Formula: C<sub>6</sub>H<sub>9</sub>ClO<sub>3</sub>  
Exact Mass: 164.0240

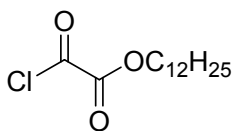
Yield: 94% (463 mg, 2.81 mmol).

Appearance: colourless liquid.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ/ppm 5.03 (sext, *J* = 6.3 Hz, 1H), 1.81-1.66 (m, 2H), 1.36 (d, *J* = 6.3 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ/ppm: 161.5 (C), 155.6 (C), 78.8 (CH), 28.6 (CH<sub>2</sub>), 19.2 (CH<sub>3</sub>), 9.6 (CH<sub>3</sub>).

#### Dodecyl 2-chloro-2-oxoacetate (7e):



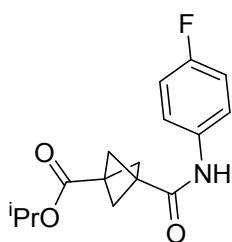


Chemical Formula: C<sub>14</sub>H<sub>25</sub>ClO<sub>3</sub>  
Exact Mass: 276.1492

Yield: quantitative (829 mg, 2.99 mmol).  
Appearance: colourless liquid.

<sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>) δ/ppm 4.36 (t, *J* = 6.8 Hz, 2H), 1.76 (p, *J* = 6.8 Hz, 2H), 1.42-1.37 (m, 2H), 1.33-1.23 (m, 16H), 0.88 (t, *J* = 6.9 Hz, 3H). <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>) δ/ppm: 161.3 (C), 156.0 (C), 69.25 (CH<sub>2</sub>), 32.0 (CH<sub>2</sub>), 29.8 (2CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.54 (CH<sub>2</sub>), 29.47 (CH<sub>2</sub>), 29.2 (CH<sub>2</sub>), 28.3 (CH<sub>2</sub>), 25.7 (CH<sub>2</sub>), 22.8 (CH<sub>2</sub>), 14.3 (CH<sub>3</sub>).

### Isopropyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9a):



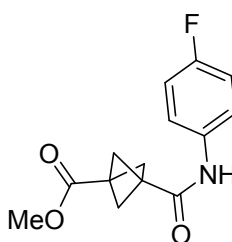
Chemical Formula: C<sub>16</sub>H<sub>18</sub>FNO<sub>3</sub>  
Exact Mass: 291.1271

Yield: 48% (47 mg, 0.16 mmol).  
Appearance: pale yellow solid.

HR-MS (QTOF) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>18</sub>O<sub>3</sub>FNa<sup>+</sup> 314.1168; Found 314.1183.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ/ppm 7.50-7.47 (m, 2H), 7.16 (br s, NH), 7.04-6.99 (m, 2H), 5.01 (sept, *J* = 6.2 Hz, 1H), 2.35 (s, 6H), 1.25 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ/ppm 169.0 (C), 167.4 (C), 159.7 (d, *J* = 243 Hz, CF), 133.4 (d, *J* = 3 Hz, C), 121.7 (d, *J* = 8 Hz, 2CH), 115.9 (d, *J* = 22 Hz, 2CH), 68.6 (CH), 52.4 (3CH<sub>2</sub>), 39.9 (C), 37.2 (C), 21.9 (2CH<sub>3</sub>). <sup>19</sup>F-NMR (376 MHz, CDCl<sub>3</sub>) δ/ppm -117.5 (m). IR (neat): ν/cm<sup>-1</sup>: 3291 (br w), 2979 (w), 1721 (m), 1651 (m), 1613 (m), 1508 (s), 1408 (m), 1309 (m), 1208 (s), 1149 (s), 1068 (m), 822 (s), 519 (m).

### Methyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9b):



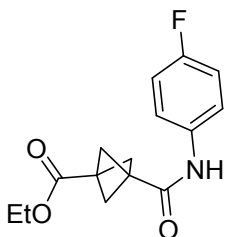
Chemical Formula: C<sub>14</sub>H<sub>14</sub>FNO<sub>3</sub>  
Exact Mass: 263.0958

Yield: 18% (15 mg, 57 μmol).  
Appearance: pale yellow solid.

HR-MS (QTOF) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>14</sub>FNO<sub>3</sub><sup>+</sup> 264.1030; Found 264.1034.

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ/ppm 7.50 – 7.47 (m, 2H), 7.13 (br s, NH), 7.05 – 6.99 (m, 2H), 3.72 (s, 3H), 2.38 (s, 6H). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>) δ/ppm 169.7 (C), 167.2 (C), 159.5 (d, *J* = 243 Hz, CF), 133.4 (d, *J* = 3 Hz, C), 121.8 (d, *J* = 8 Hz, 2CH), 115.9 (d, *J* = 22, 2CH), 52.6 (3CH<sub>2</sub>), 52.1 (CH<sub>3</sub>), 40.1 (C), 36.9 (C). <sup>19</sup>F-NMR (376 MHz, CDCl<sub>3</sub>) δ/ppm -117.5 (m). IR (neat): ν/cm<sup>-1</sup>: 3288 (br w), 2958 (w), 1722 (m), 1651 (s), 1614 (m), 1539 (m), 1506 (s), 1408 (m), 1314 (s), 1213 (s), 1156 (m), 1044 (m), 821 (s), 519 (m).

### Ethyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9c):



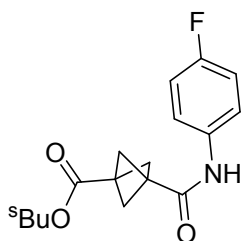
Chemical Formula:  $C_{15}H_{16}FNO_3$   
Exact Mass: 277.1114

Yield: 33% (31 mg, 0.11 mmol)  
Appearance: pale yellow solid

**HR-MS** (QTOF)  $m/z$ :  $[M+H]^+$  Calcd for  $C_{15}H_{17}FNO_3^+$  278.1187; Found 278.1192.

**$^1H$ -NMR** (500 MHz,  $CDCl_3$ )  $\delta$ /ppm 7.50-7.47 (m, 2H), 7.15 (br s, NH), 7.03-7.00 (m, 2H), 4.16 (q,  $J = 7.2$  Hz, 2H), 2.37 (s, 6H), 1.28 (t,  $J = 7.1$  Hz, 3H).  **$^{13}C$ -NMR** (125 MHz,  $CDCl_3$ )  $\delta$ /ppm 169.4 (C), 167.1 (C), 159.5 (d,  $J = 243$  Hz, CF), 133.4 (d,  $J = 3$  Hz, C), 121.8 (d,  $J = 22$  Hz, 2CH), 115.9 (d,  $J = 22$  Hz, 2CH), 61.1 ( $CH_2$ ), 52.5 (3  $CH_2$ ), 40.0 (C), 37.0 (C), 14.3 ( $CH_3$ ).  **$^{19}F$ -NMR** (376 MHz,  $CDCl_3$ )  $\delta$ /ppm -117.5 (m). **IR (neat)**:  $\nu/cm^{-1}$ : 3329 (br w), 3052 (w), 1722 (s), 1650 (s), 1613 (m), 1505 (s), 1374 (m), 1210 (s), 1010 (m), 809 (s).

### Sec-butyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9d):



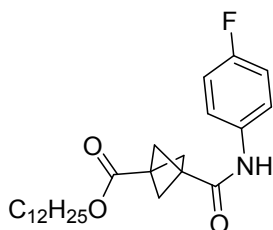
Chemical Formula:  $C_{17}H_{20}FNO_3$   
Exact Mass: 305.1427

Yield: 38% (39 mg, 0.13 mmol).  
Appearance: pale yellow solid.

**HR-MS** (QTOF)  $m/z$ :  $[M+H]^+$  Calcd for  $C_{17}H_{21}FNO_3^+$  306.1500; Found 306.1502.

**$^1H$ -NMR** (500 MHz,  $CDCl_3$ )  $\delta$ /ppm 7.49 (dd,  $J = 8.9, 4.8$  Hz, 2H), 7.17 (br s, NH), 7.02 (t,  $J = 8.7$  Hz, 2H), 4.85 (sext,  $J = 6.3$  Hz, 1H), 2.36 (s, 6H), 1.60 (m, 2H), 1.22 (d,  $J = 6.3$  Hz, 3H), 0.89 (t,  $J = 7.5$  Hz, 3H).  **$^{13}C$ -NMR** (125 MHz,  $CDCl_3$ )  $\delta$ /ppm 169.1 (C), 167.4 (C), 159.7 (d,  $J = 243$  Hz, CF), 133.4 (d,  $J = 3$  Hz, C), 121.7 (d,  $J = 8$  Hz, 2CH), 115.9 (d,  $J = 22$  Hz, 2CH), 73.0 (CH), 52.5 (3 $CH_2$ ), 40.0 (C), 37.17 (C), 28.9 ( $CH_2$ ), 19.6 ( $CH_3$ ), 9.7 ( $CH_3$ ).  **$^{19}F$ -NMR** (376 MHz,  $CDCl_3$ )  $\delta$ /ppm -117.5 (m). **IR (neat)**:  $\nu/cm^{-1}$ : 3280 (br w), 2978 (w), 1719 (m), 1650 (m), 1532 (m), 1507 (s), 1407 (m), 1311 (m), 1278 (m), 1173 (s), 1036 (m), 825 (s), 518 (m).

### Dodecyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9e):



Chemical Formula:  $C_{25}H_{36}FNO_3$   
Exact Mass: 417.2679

Yield: 30% (43 mg, 0.10 mmol).  
Appearance: off-white solid

**HR-MS** (QTOF)  $m/z$ :  $[M+H]^+$  Calcd for  $C_{25}H_{37}FNO_3^+$  418.2752; Found 418.2755.

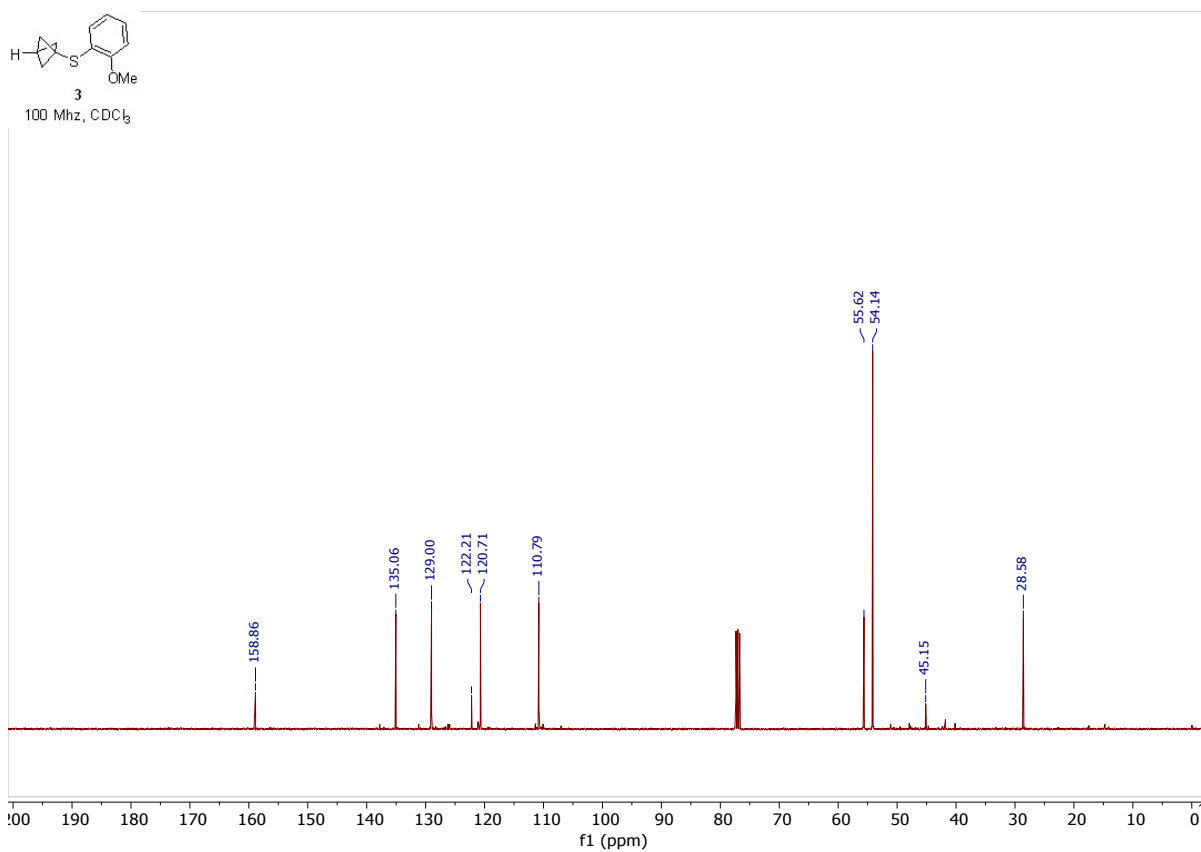
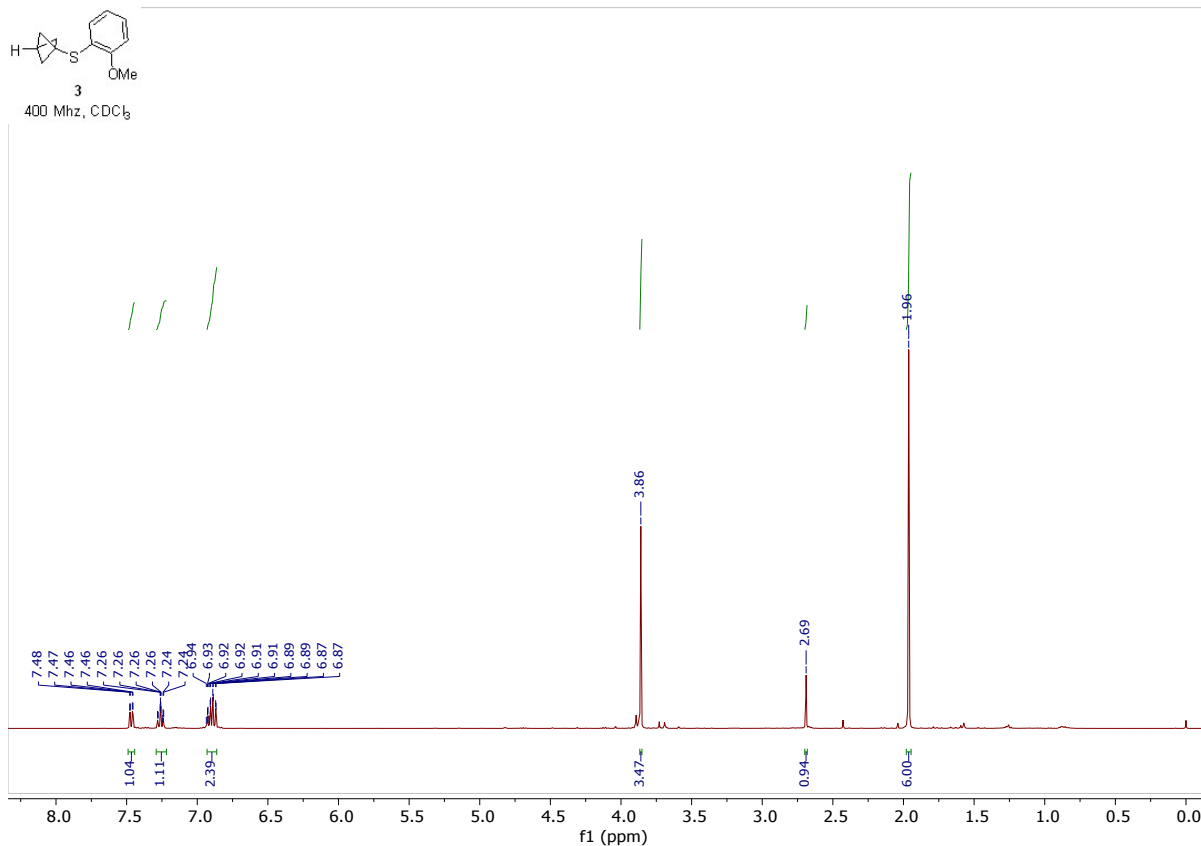
**$^1H$ -NMR** (500 MHz,  $CDCl_3$ )  $\delta$ /ppm 7.51 - 7.46 (m, 2H), 7.16 (br s, NH), 7.04-6.99 (m, 2H), 4.09 (t,  $J = 6.8$  Hz, 2H), 2.37 (s, 6H), 1.64 (pent,  $J = 5.7$  Hz, 2H), 1.29 (m, 18H), 0.88 (t,  $J = 5.7$  Hz, 3H).  **$^{13}C$ -NMR** (125 MHz,  $CDCl_3$ )  $\delta$ /ppm 169.5 (C), 167.3 (C), 159.7 (d,  $J = 243$  Hz, CF), 133.4 (d,  $J = 3$  Hz, C), 121.7 (d,  $J = 8$  Hz, 2CH), 115.9 (d,  $J = 22$  Hz, 2CH), 65.3 ( $CH_2$ ), 52.5 (3  $CH_2$ ), 40.0 (C), 37.0 (C), 32.1 ( $CH_2$ ), 29.79 ( $CH_2$ ), 29.77 ( $CH_2$ ), 29.71 ( $CH_2$ ), 29.65 (2  $CH_2$ ), 29.5 ( $CH_2$ ), 29.4 ( $CH_2$ ), 28.6 ( $CH_2$ ), 26.0 ( $CH_2$ ), 22.8 ( $CH_2$ ), 14.3 ( $CH_3$ ).  **$^{19}F$ -NMR** (376 MHz,  $CDCl_3$ )  $\delta$ /ppm -117.5 (m). **IR (neat)**:  $\nu/cm^{-1}$ : 3312 (w, br), 2916 (m), 2847 (m), 1720 (s), 1651 (s), 1537 (s), 1507 (s), 1408 (m), 1277 (m), 1210 (s), 832 (m).

## 5. References:

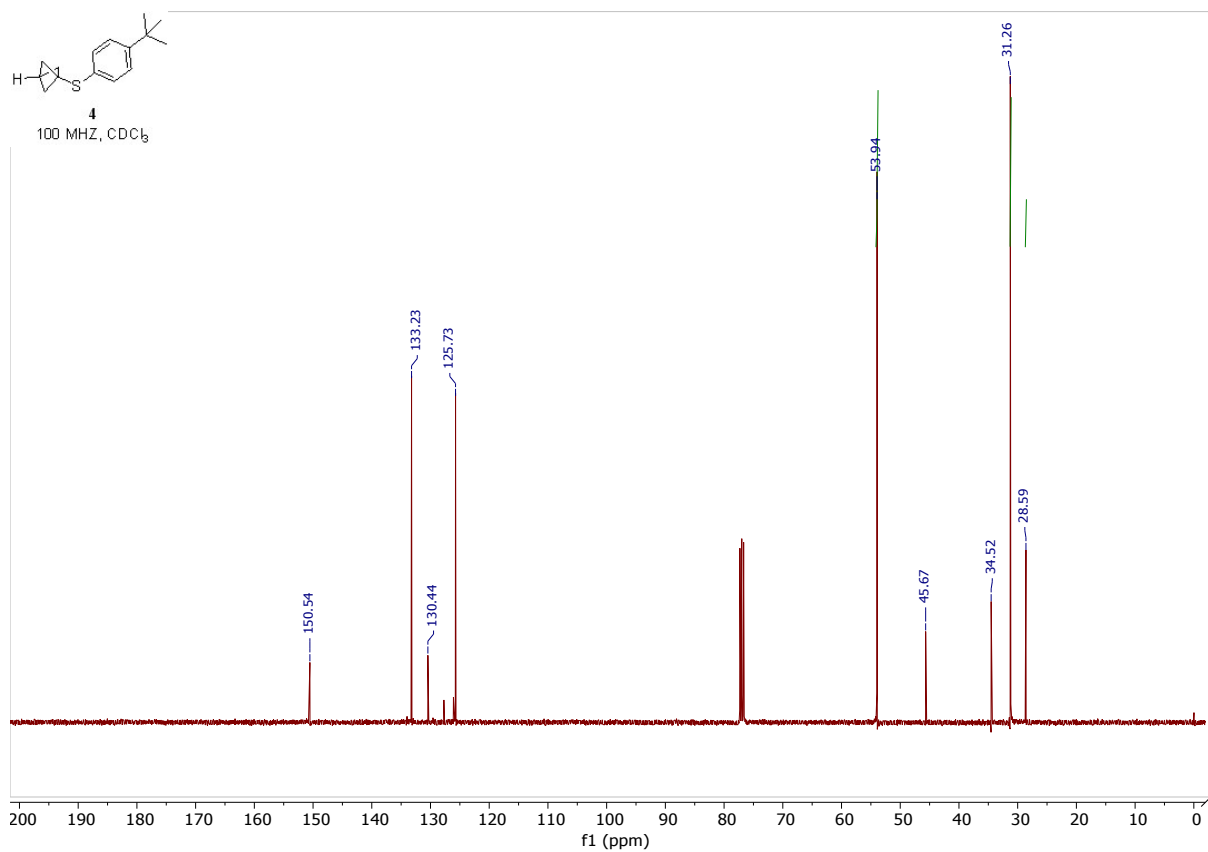
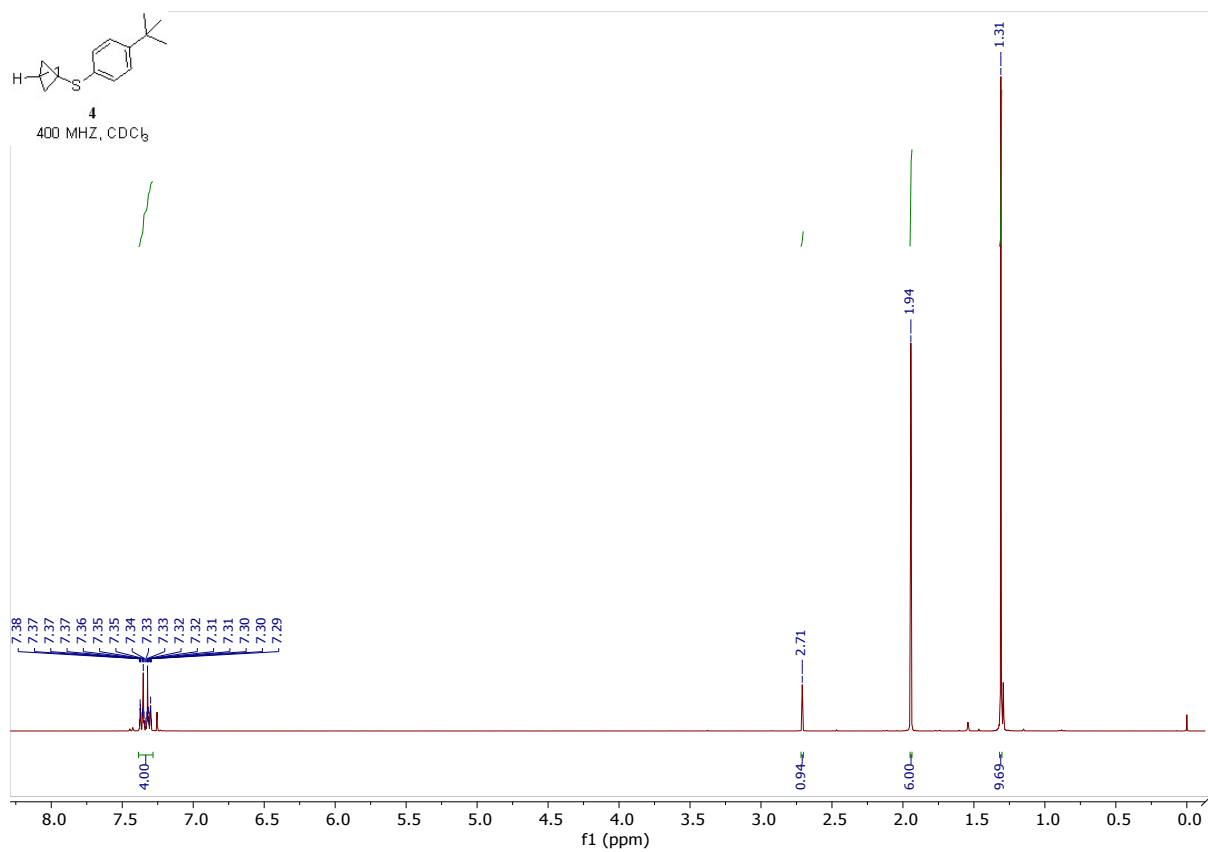
1. K. R. Mandanaro, W. P. Dailey, *Org. Synth.*, **1998**, 75, 98.
2. R. M. Bär, S. Kirschner, M. Nieger, S. Bräse, *Chem. Eur. J.*, **2018**, 24, 1373.
3. R. M. Bär, G. Heinrich, M. Nieger, O. Fuhr, S. Bräse, *Beilstein J. Org. Chem.* **2019**, 15, 1172.
4. K. B. Wiberg, S. T. Waddell, *J. Am. Chem. Soc.*, **1990**, 112, 2194.

## 6. Copies of NMR Spectra

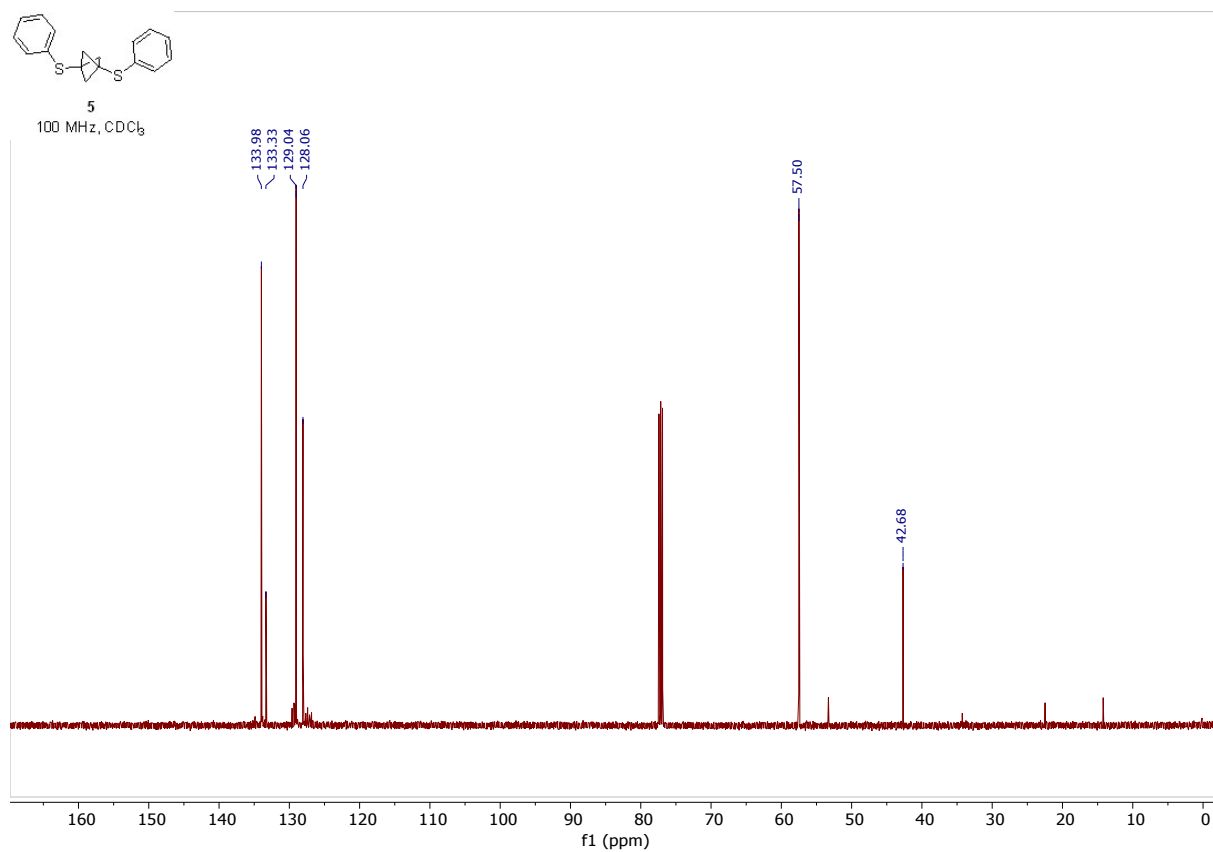
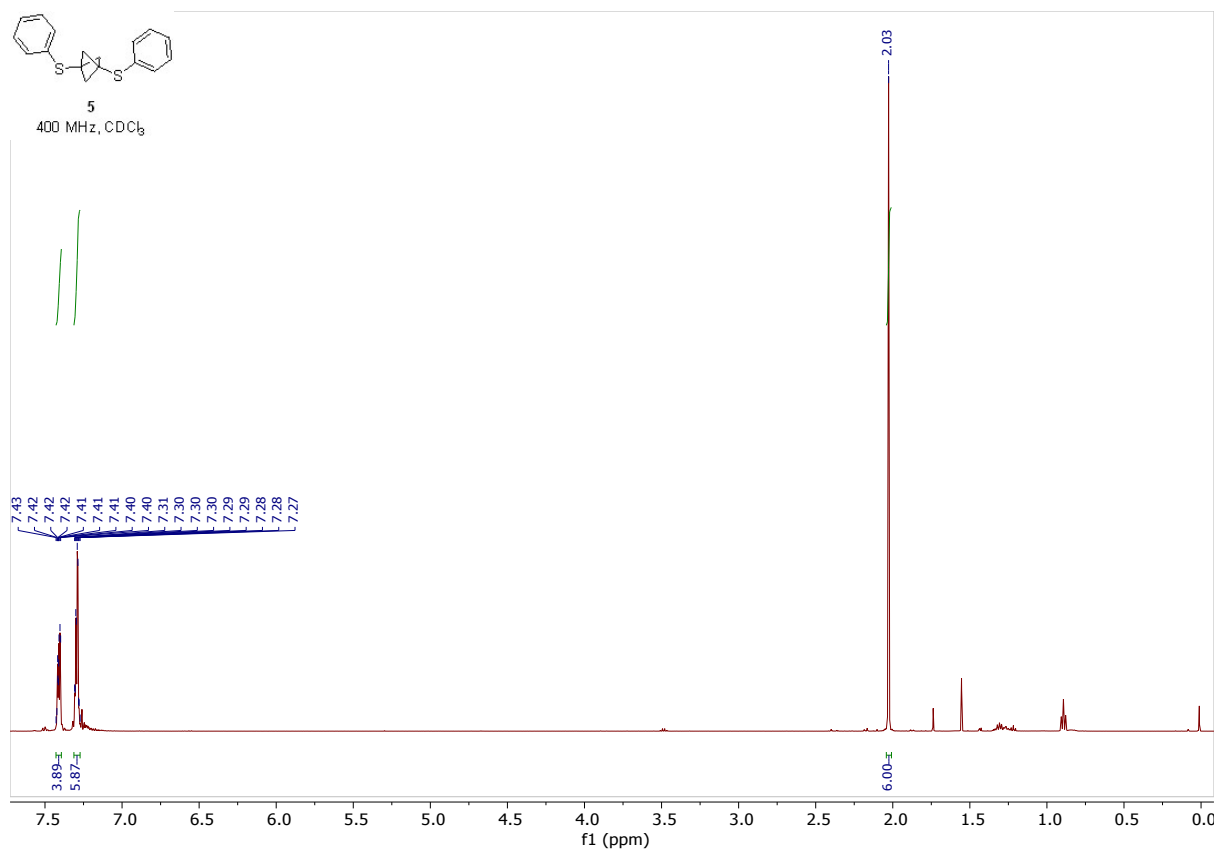
### Bicyclo[1.1.1]pentan-1-yl(2-methoxyphenyl)sulfane (3):



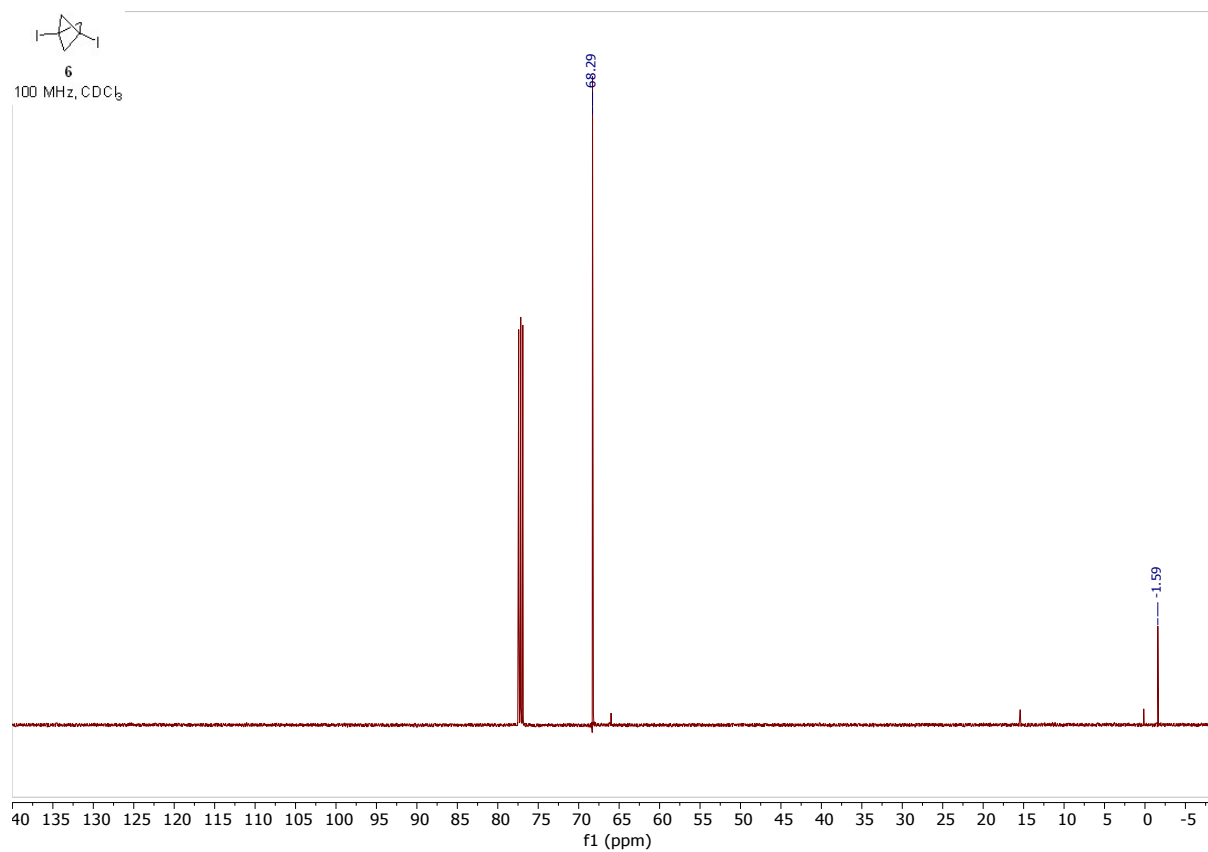
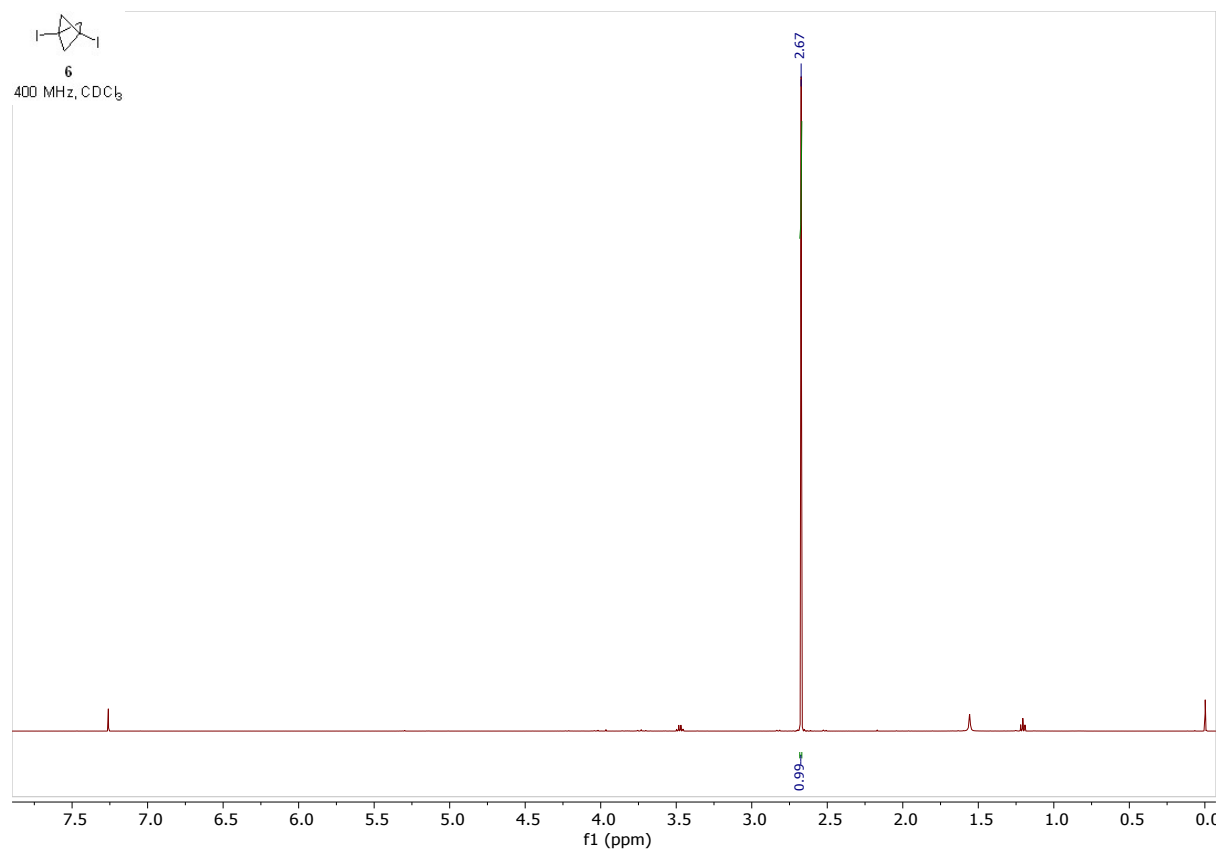
**Bicyclo[1.1.1]pentan-1-yl(4-(*tert*-butyl)phenyl)sulfane (4):**



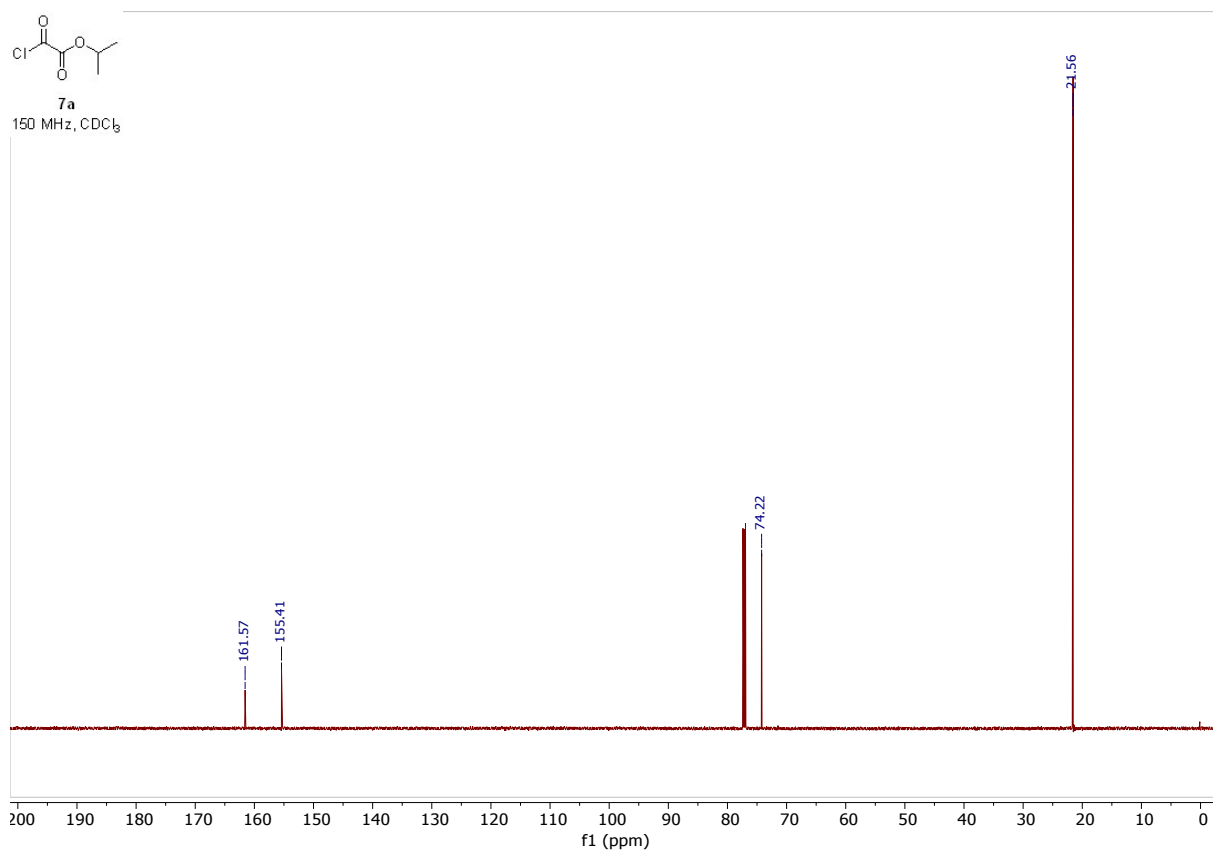
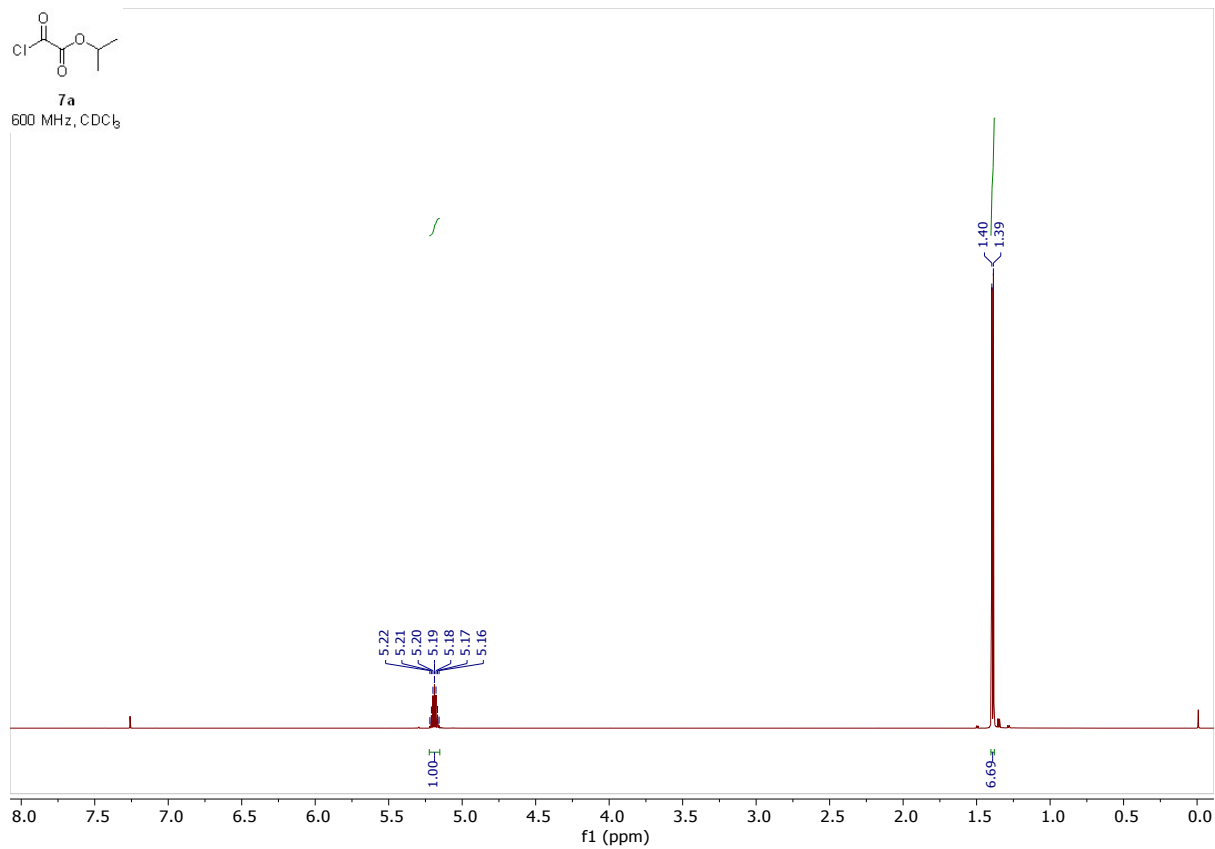
### 1,3-Bis(phenylthiol)bicyclo[1.1.1]pentane (5):



### 1,3-Diiodobicyclo[1.1.1]pentane (6):



### Isopropyl 2-chloro-2-oxoacetate (7a):



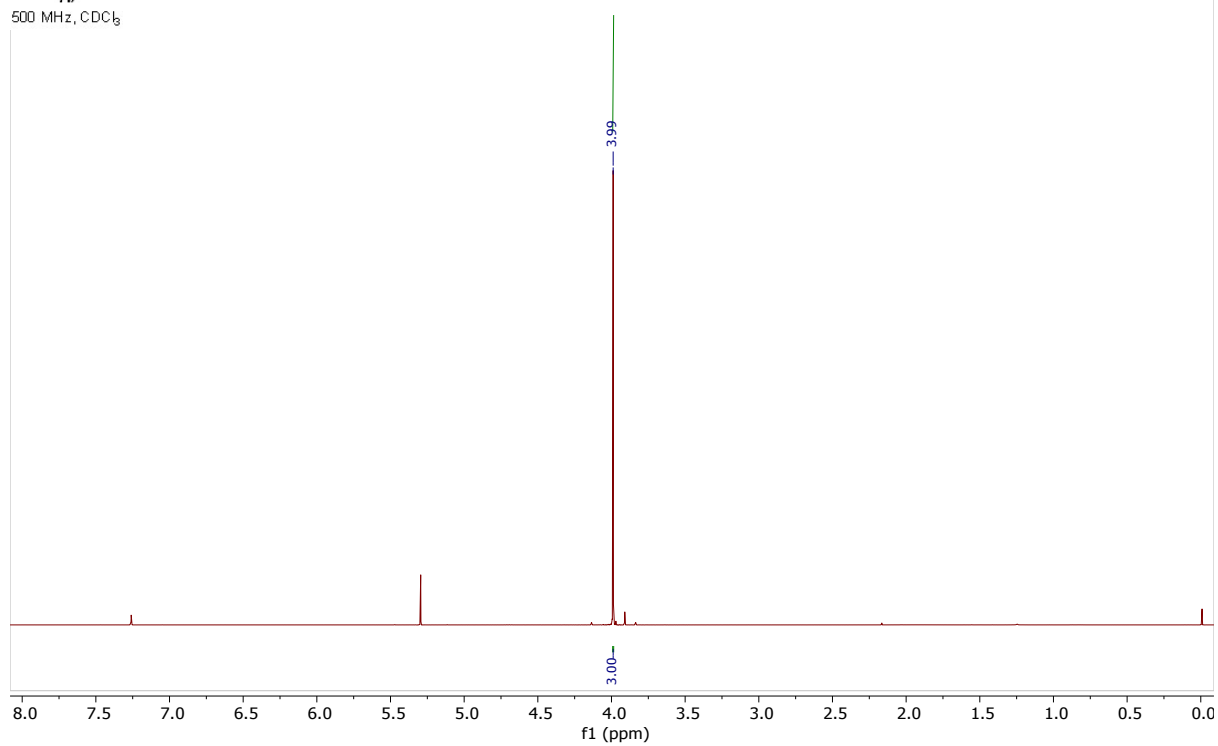


### Methyl 2-chloro-2-oxoacetate (7b):



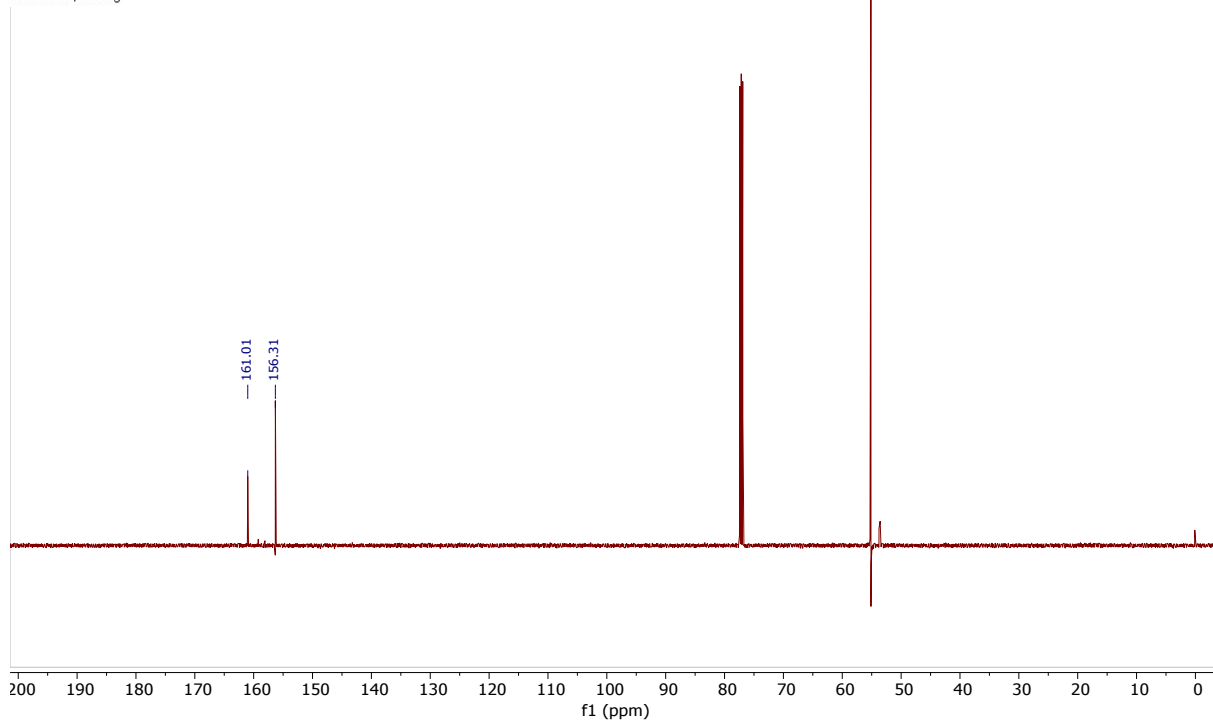
**7b**

500 MHz, CDCl<sub>3</sub>

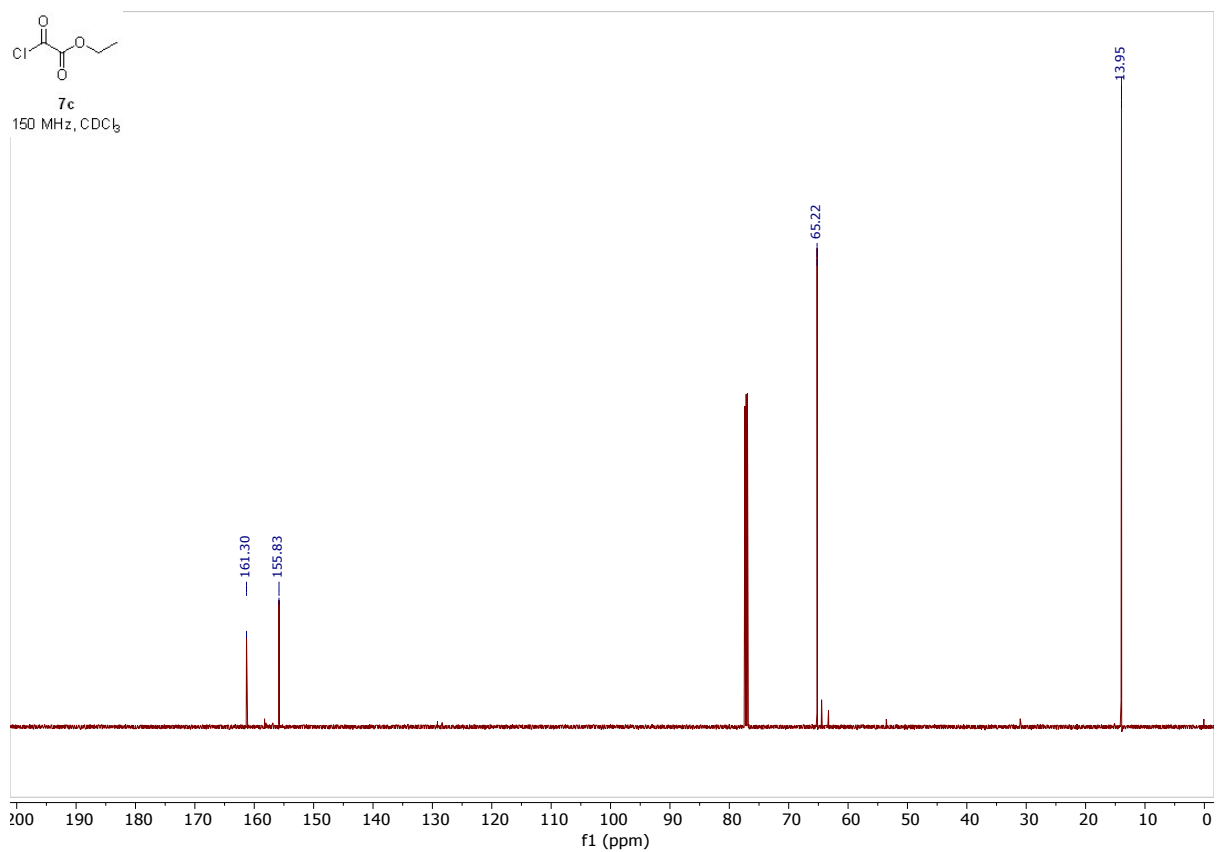
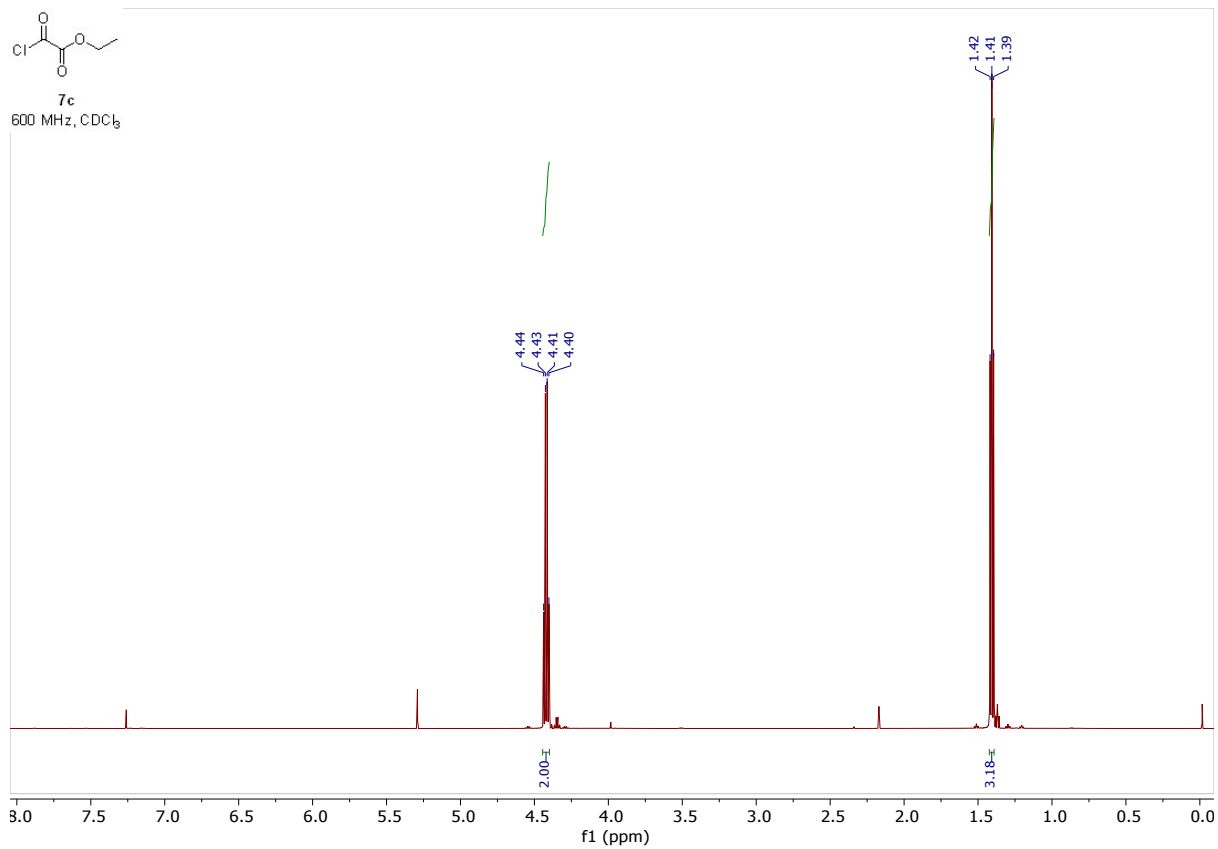


**7b**

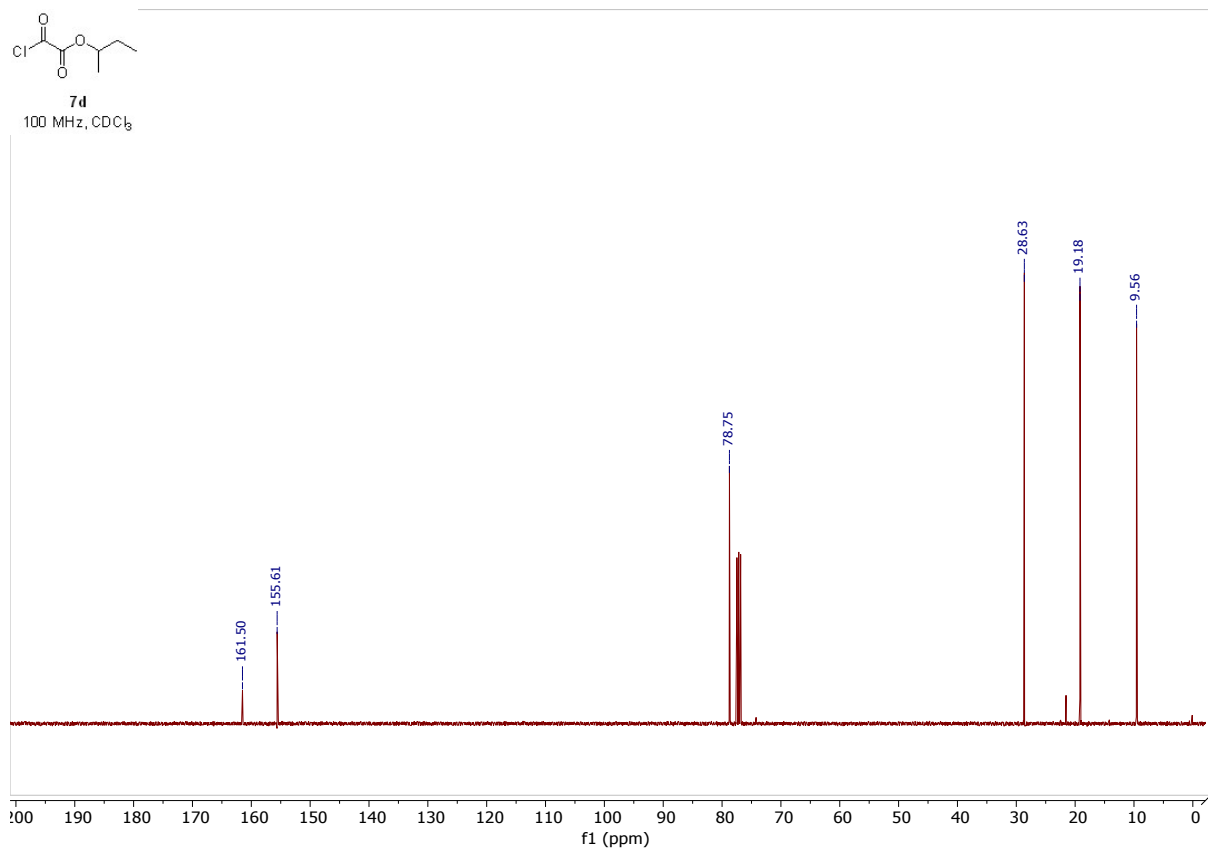
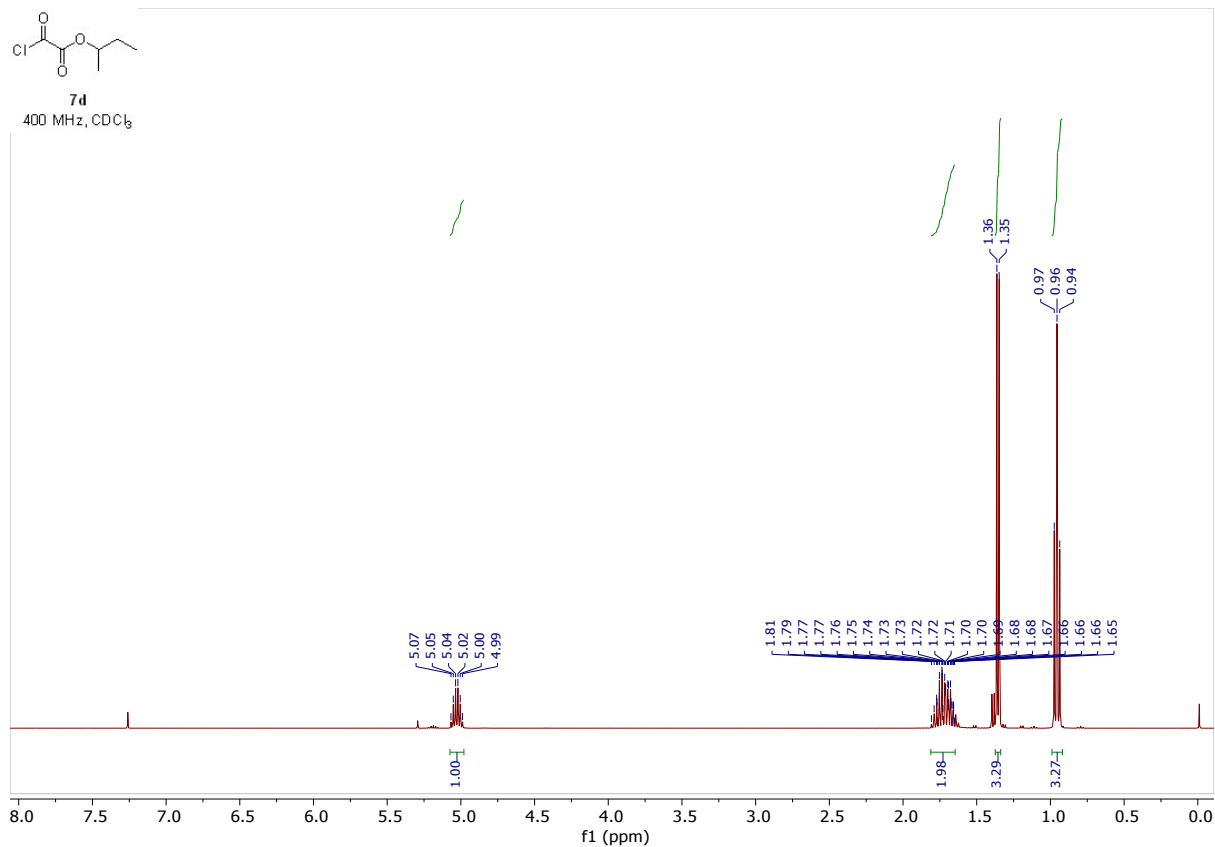
125 MHz, CDCl<sub>3</sub>



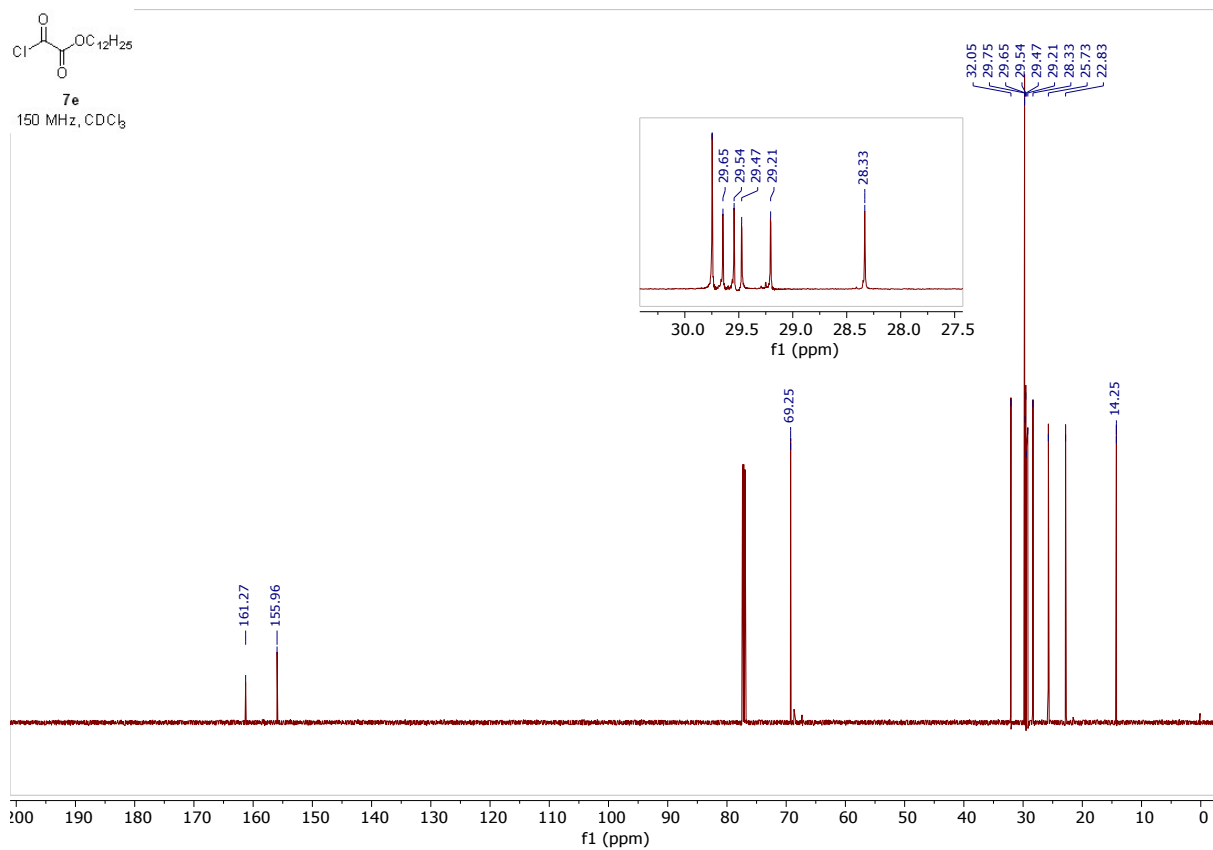
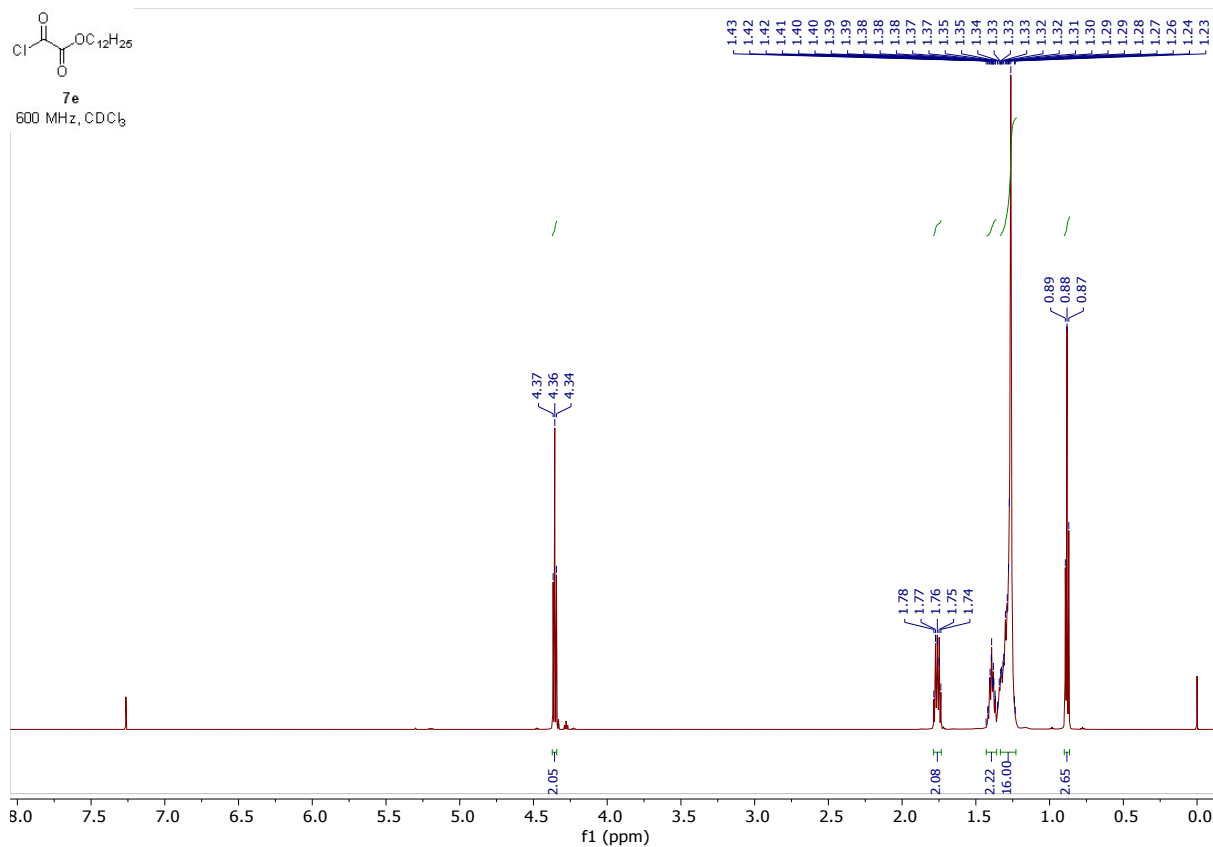
### Ethyl 2-chloro-2-oxoacetate (7c):



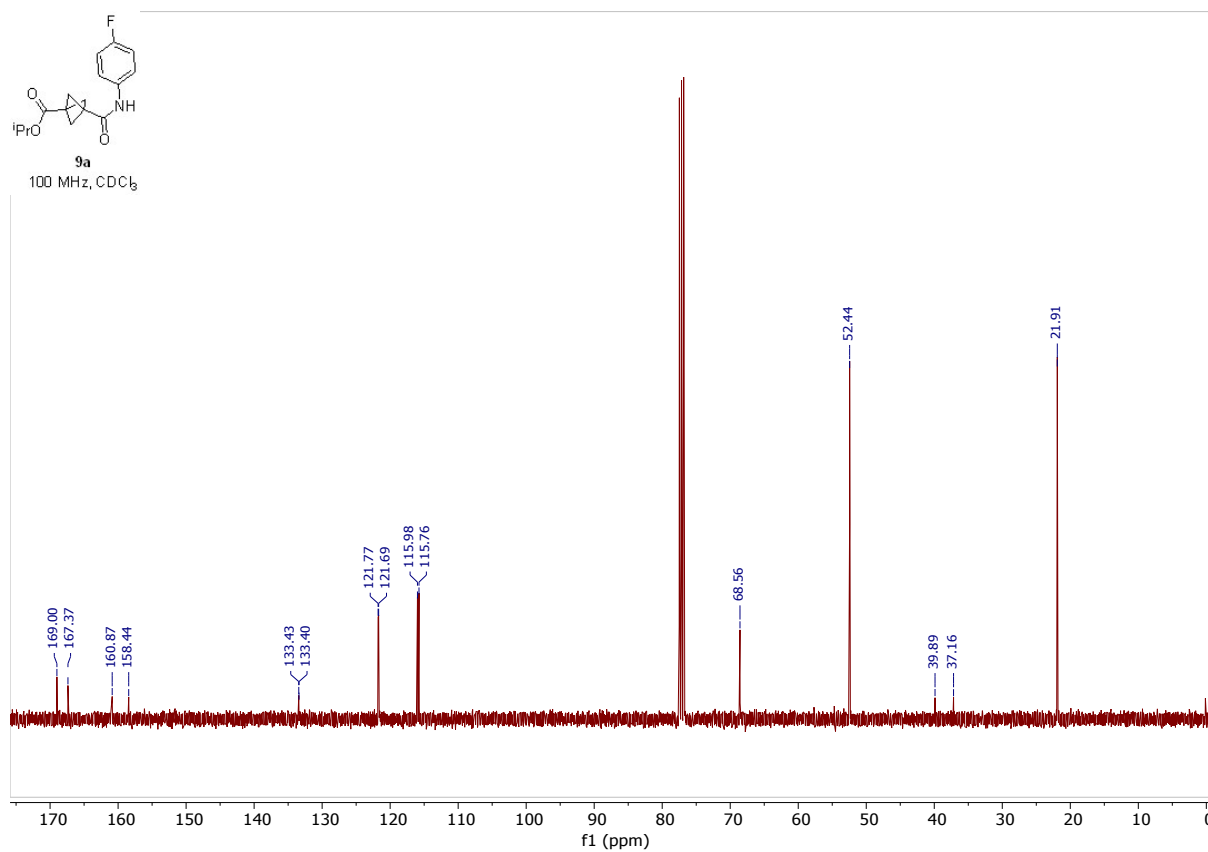
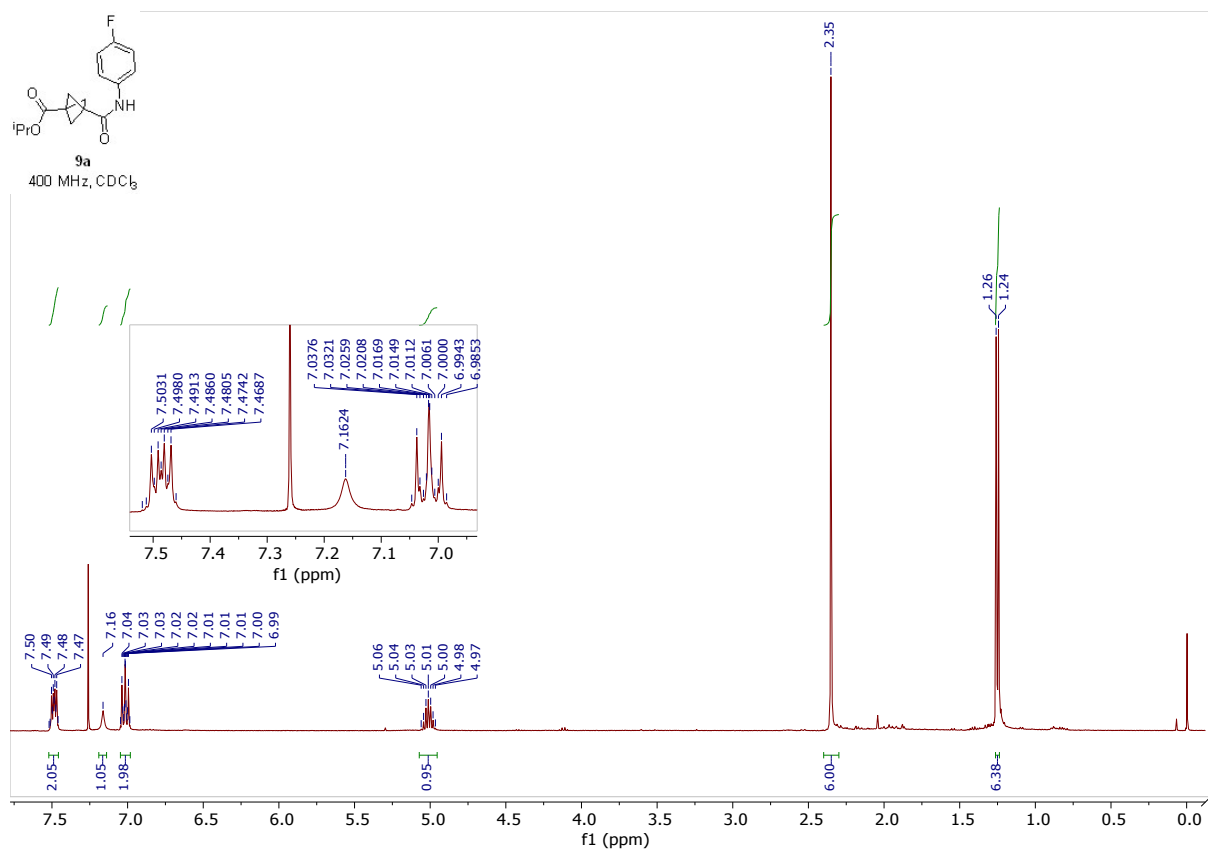
### Sec-butyl 2-chloro-2-oxoacetate (7d):

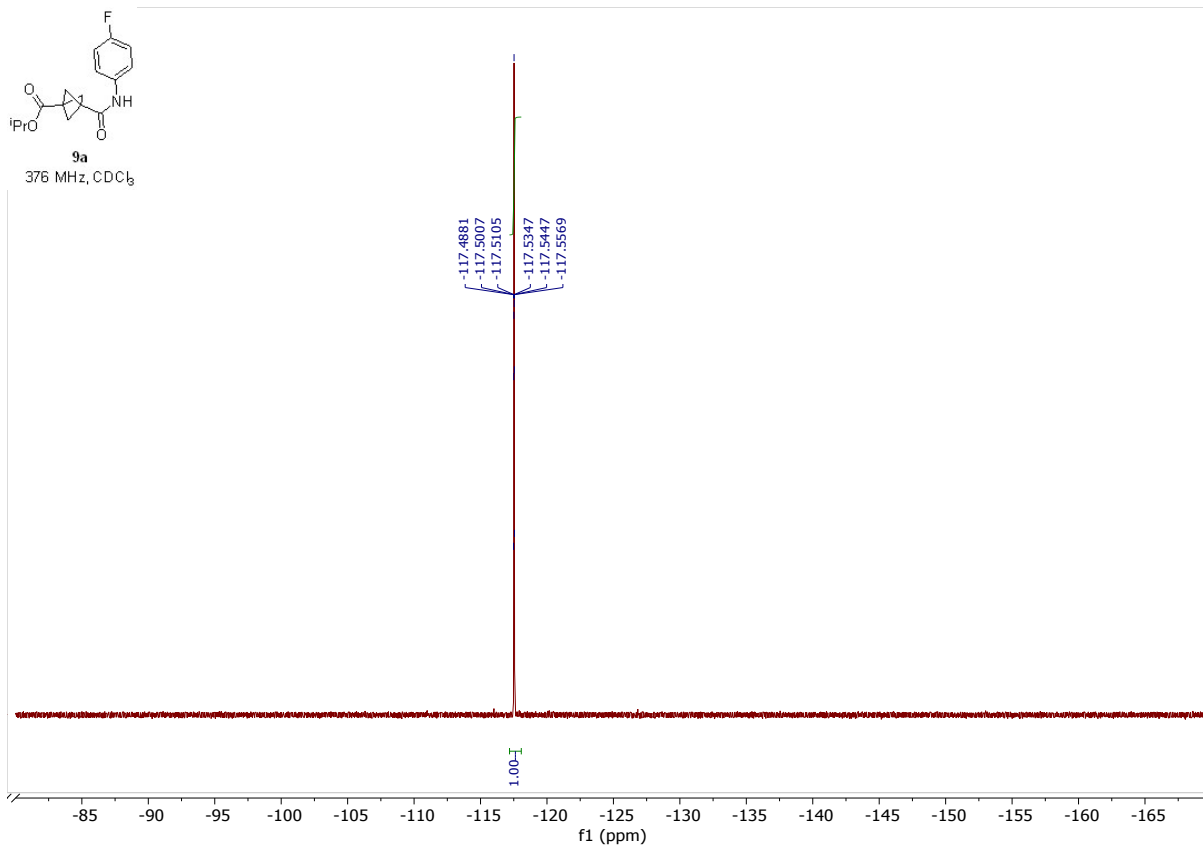


### Dodecyl 2-chloro-2-oxoacetate (7e):

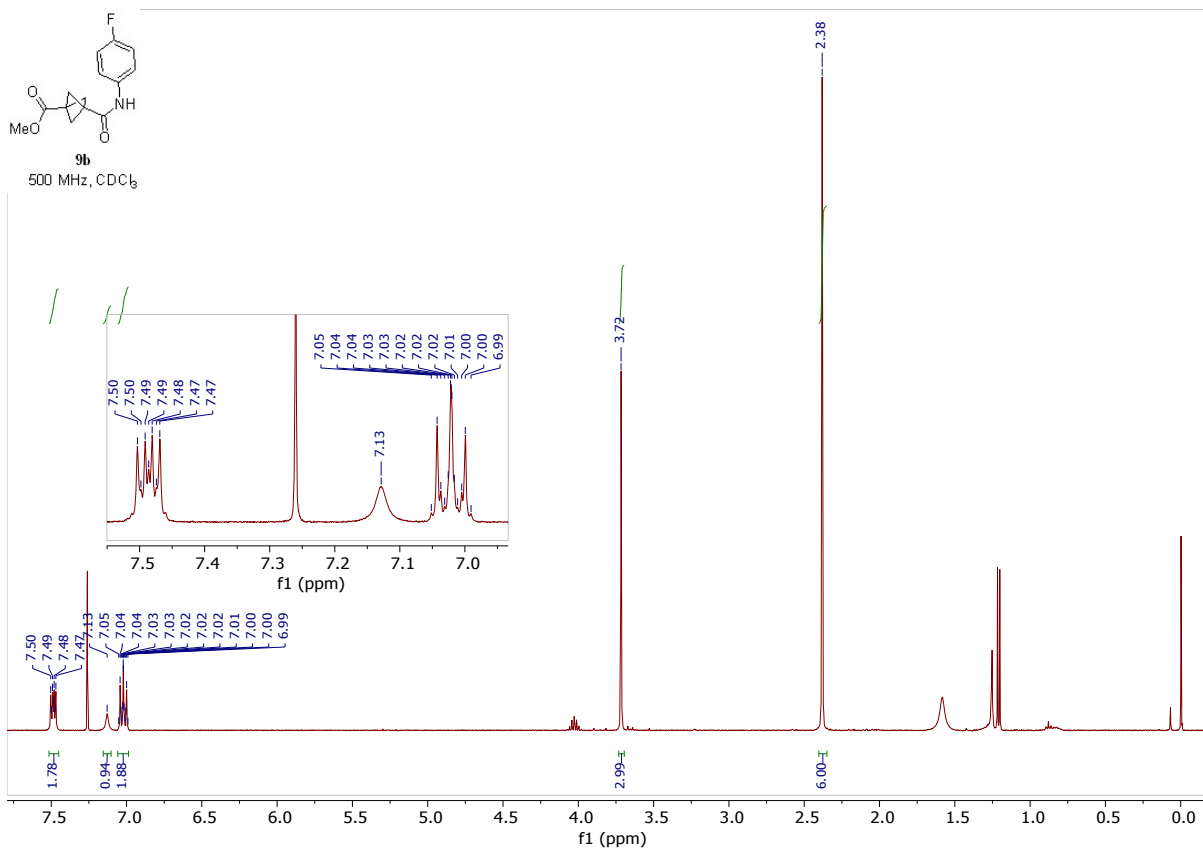


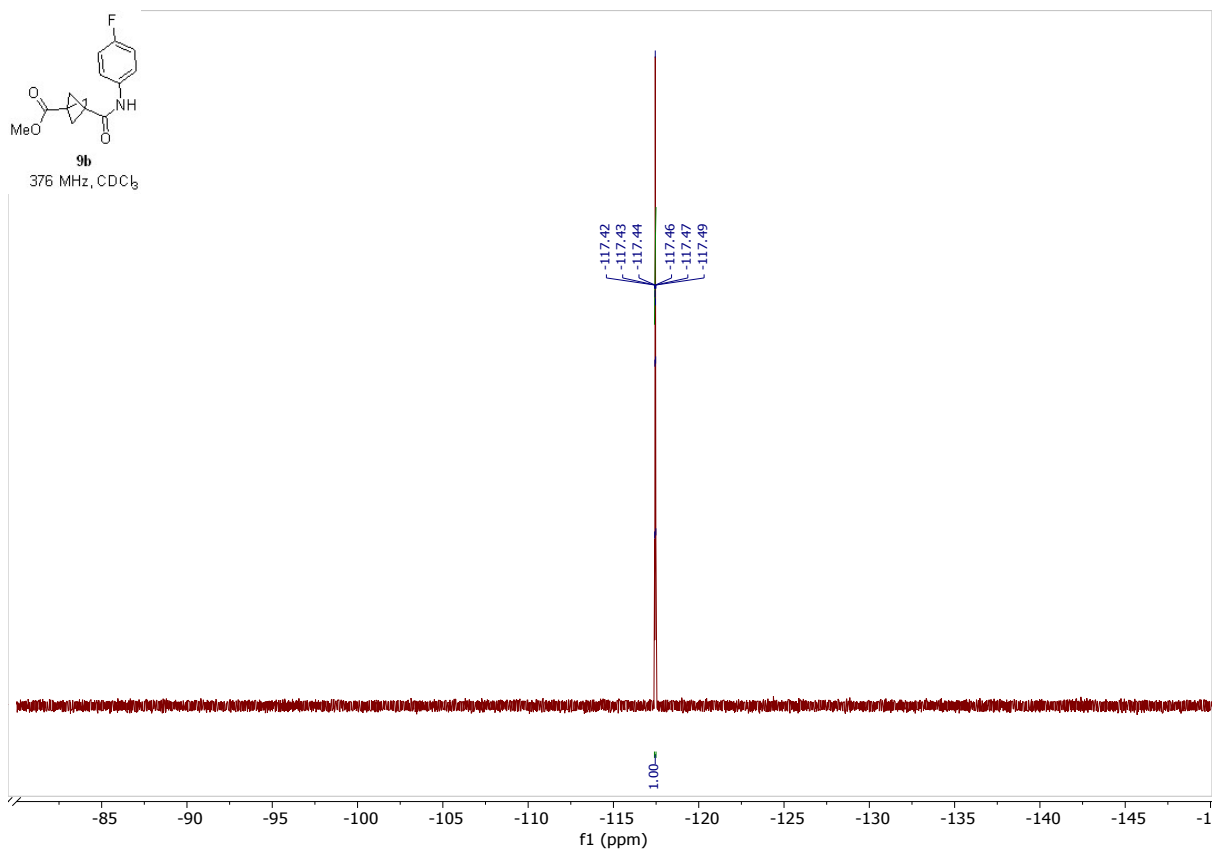
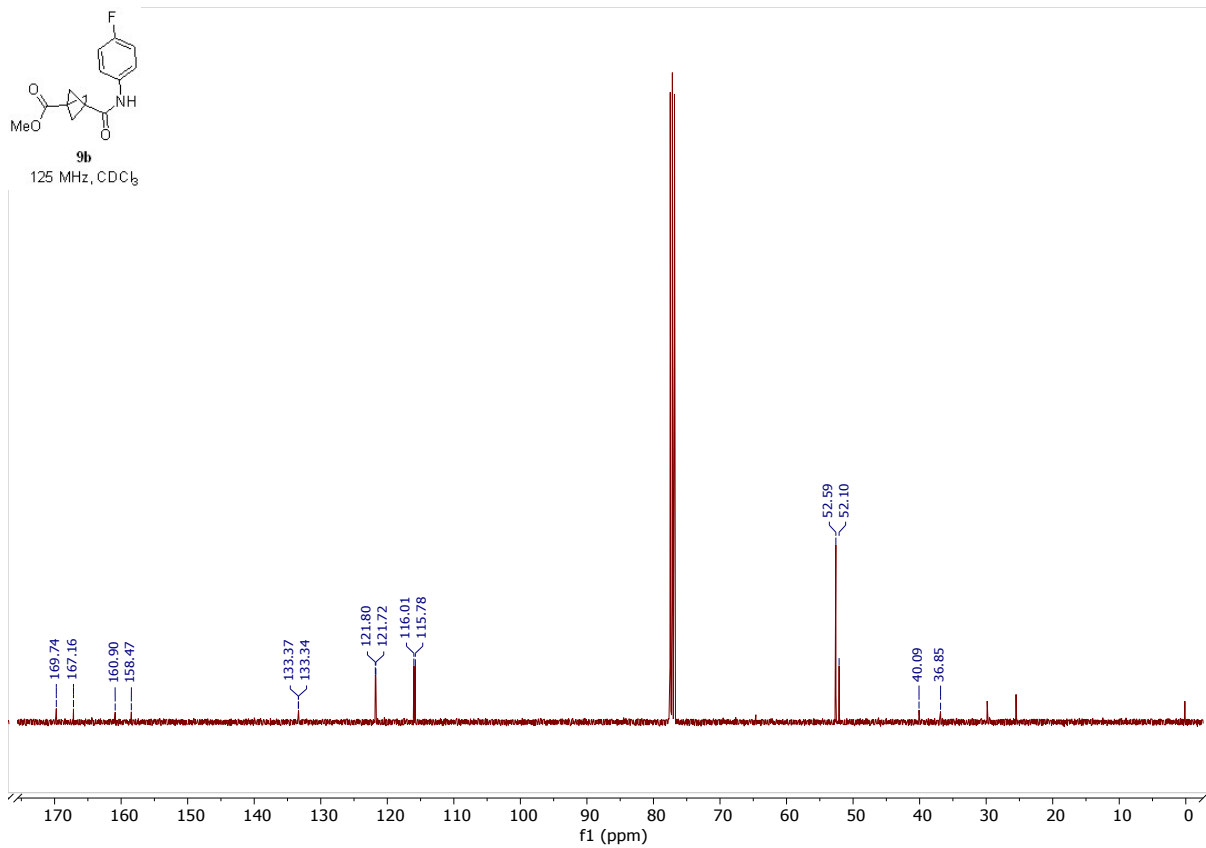
### Isopropyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9a):



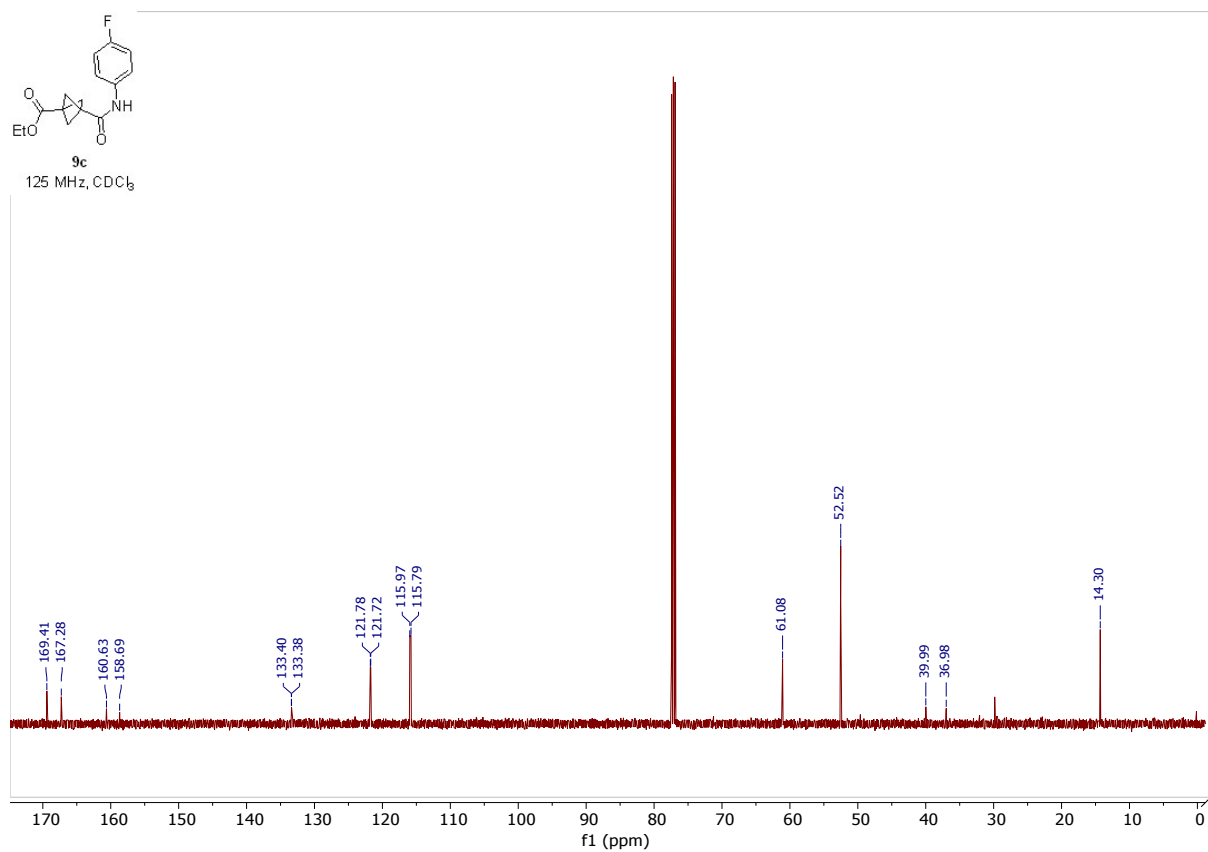
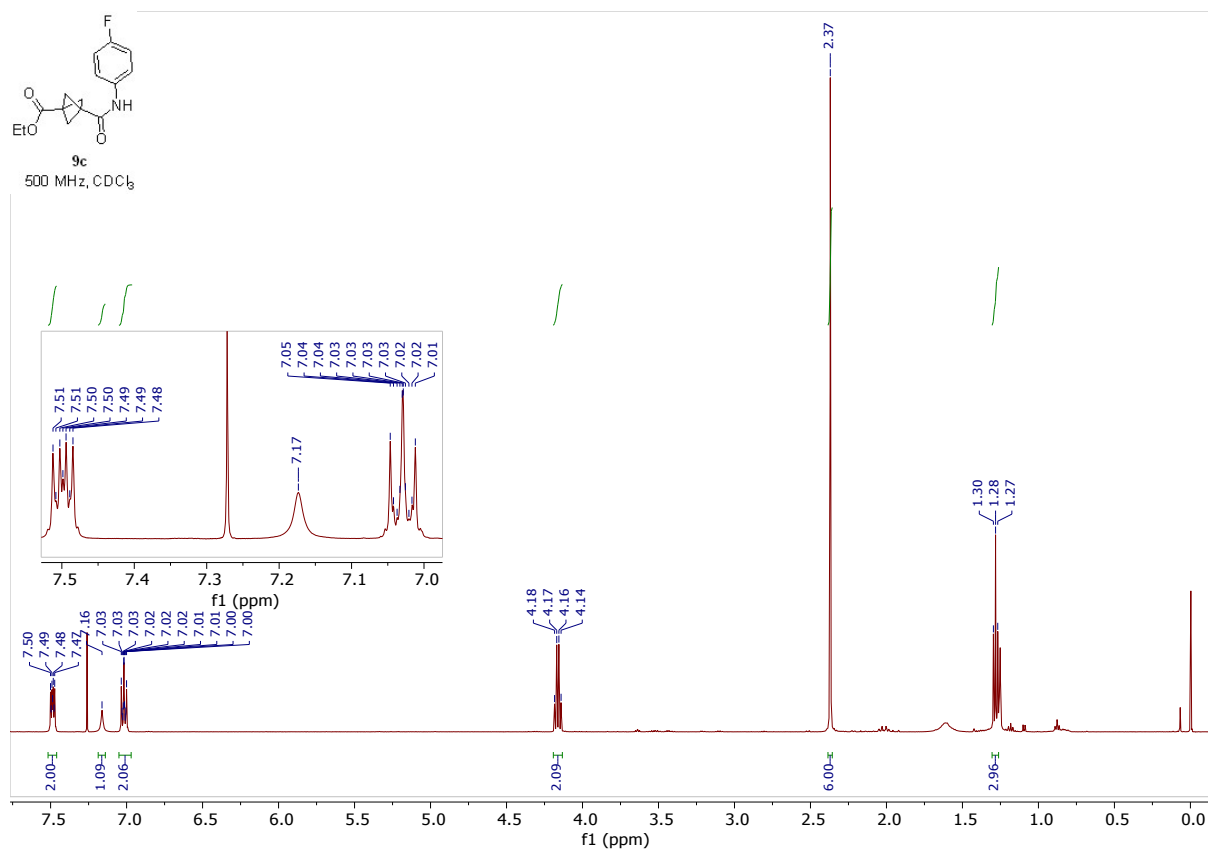


**Methyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9b):**

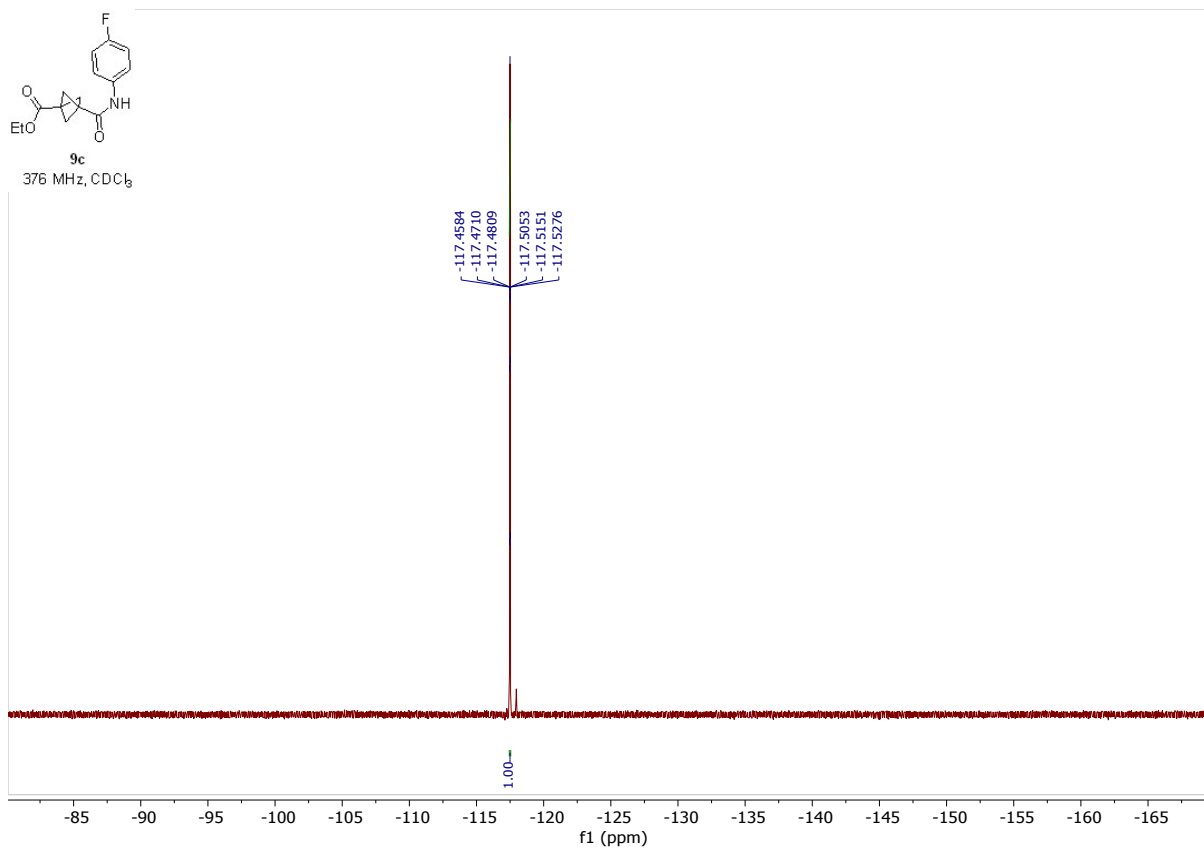




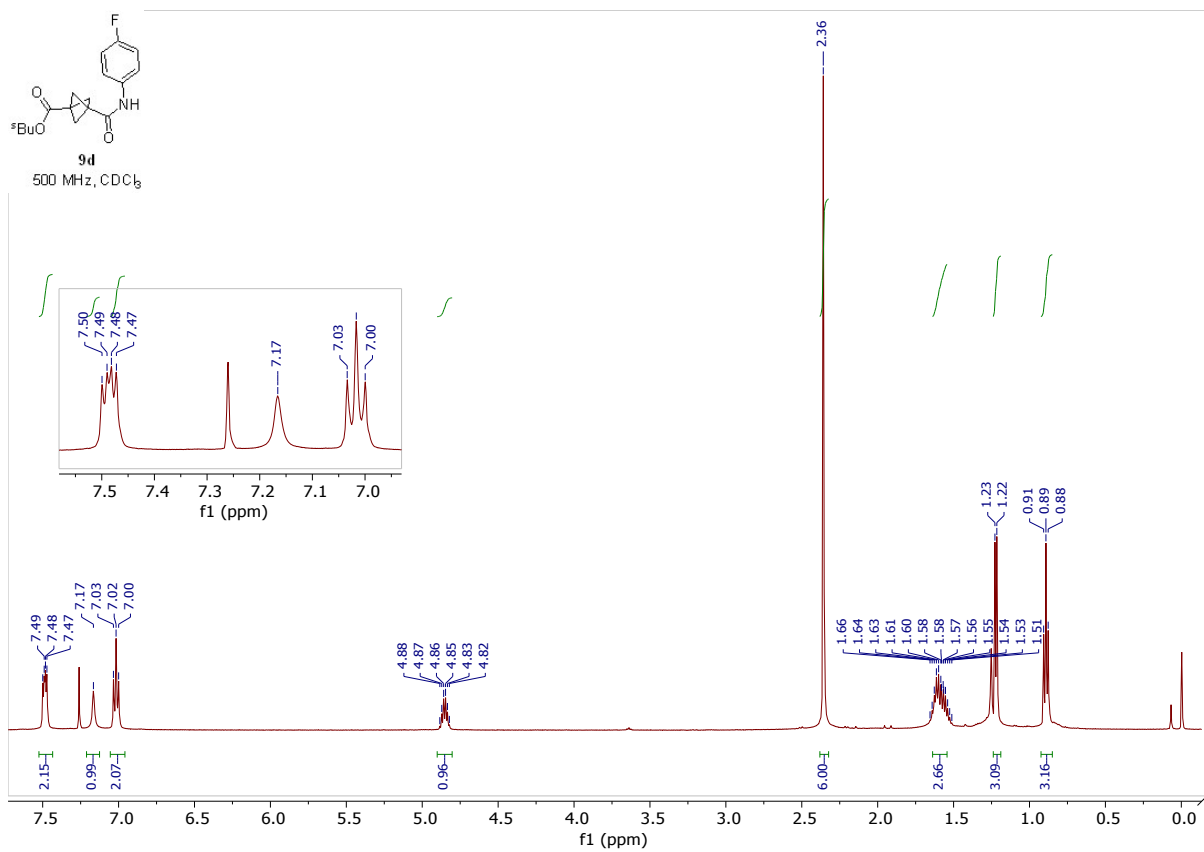
**Ethyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9c):**

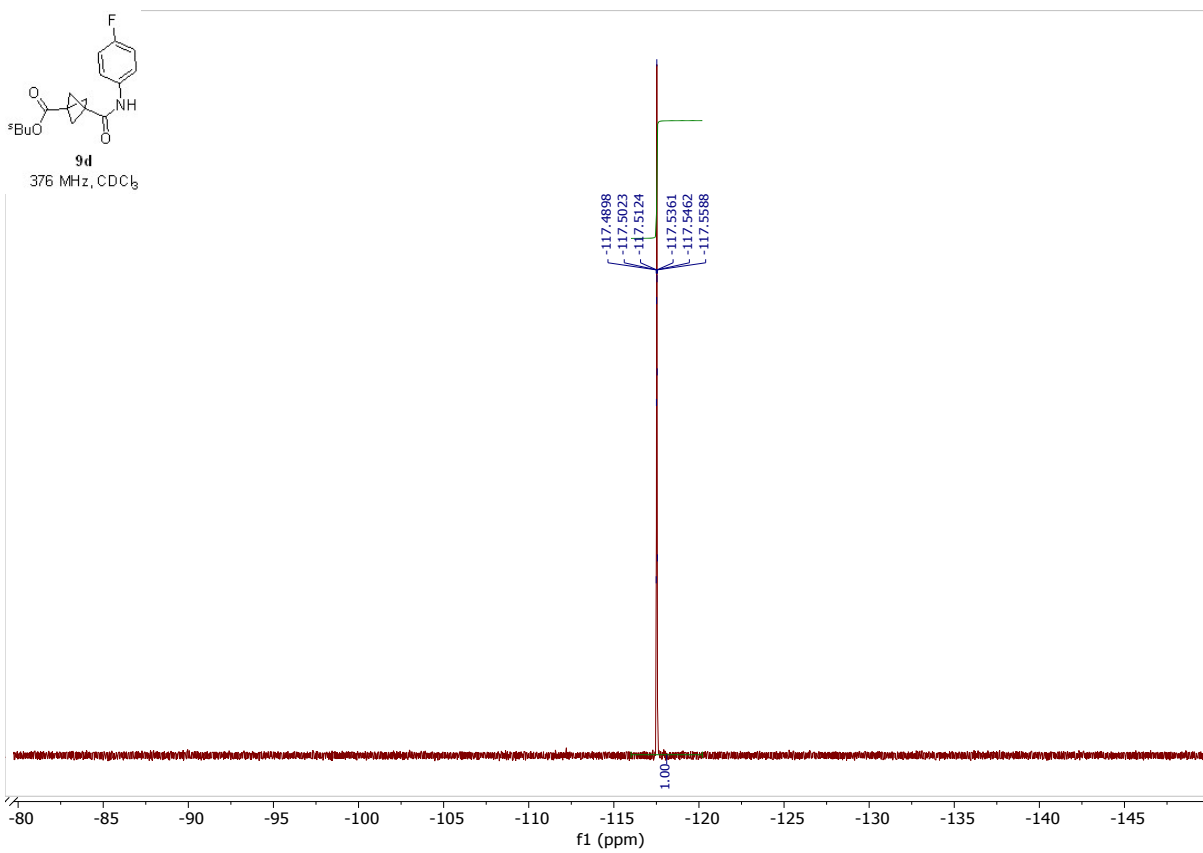
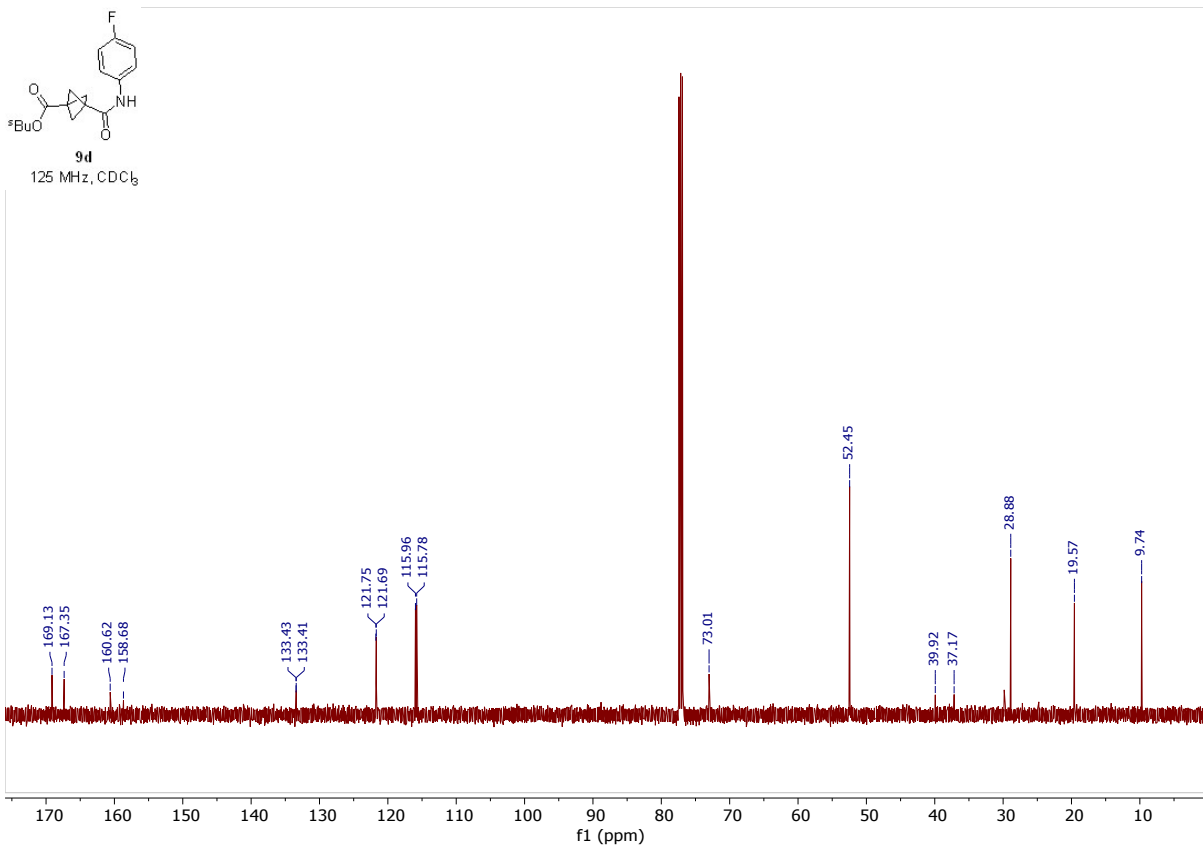






**Sec-butyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9d):**





Dodecyl 3-((4-fluorophenyl)carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate (9e):

