

## Electronic Supplementary Information

### Carboxyl group assisted isodesmic *meta*-C–H iodination of phenethylamines, benzylamines, and 2-aryl anilines

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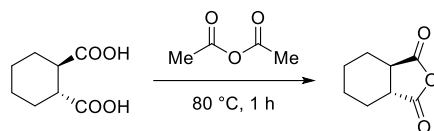
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# 1. General information

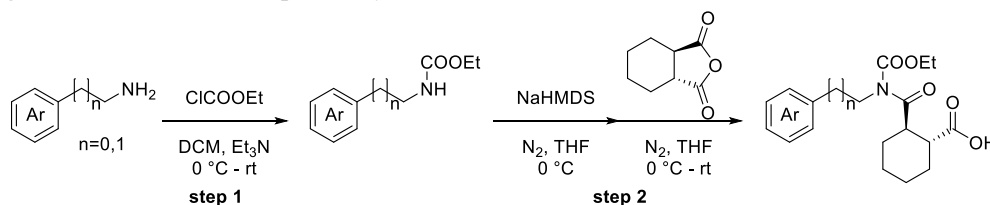
Unless otherwise noted, commercially available reagents were purchased from commercial suppliers (such as Adamas, J&K Chemical Co., Energy Chemical. etc.), and used as received. Solvents were generally dried over 4 Å molecular sieves. Hexafluoroisopropanol (HFIP) was distilled before use. The reaction vessels used for C–H functionalization were 38 mL sealed tube. Purification of products was performed by flash chromatography (FC) using silica gel or preparative thin layer chromatography or semi-preparative MPLC (medium pressure liquid chromatography).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AVANCE III spectrometer (400 MHz and 101 MHz, respectively) or a JEOL ECZ600S spectrometer (600 MHz and 151 MHz, respectively). Chemical shifts are reported parts per million (ppm) referenced to  $\text{CDCl}_3$  ( $\delta$  7.26 ppm),  $\text{DMSO-}d_6$  ( $\delta$  2.50 ppm),  $\text{CD}_3\text{OD-}d_4$  ( $\delta$  3.31 ppm), tetramethylsilane (TMS,  $\delta$  0.00 ppm) for  $^1\text{H}$  NMR;  $\text{CDCl}_3$  ( $\delta$  77.16 ppm),  $\text{DMSO-}d_6$  ( $\delta$  39.52 ppm) for  $^{13}\text{C}$  NMR. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. High-resolution mass spectra (HRMS) were obtained on an Impact II UHR-TOF mass spectrometry equipped with an ESI source from Bruker at Fujian Institute of Research on the Structure of Matter.

## 2. Experimental section

### 2.1 Preparation of substrates

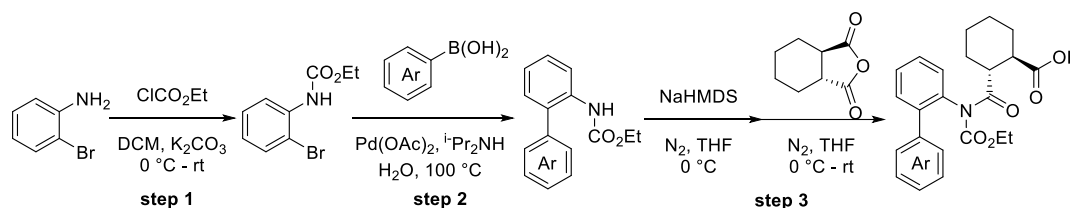


To a 100 mL round bottom flask add (1R,2R)-cyclohexane-1,2-dicarboxylic acid (5.16 g, 30 mmol), and followed by acetic anhydride (40 mL). The solution was stirred at 80 °C for 1 h. Then acetic anhydride was removed in vacuo to yield the anhydride as a white solid. The product<sup>[S1]</sup> was pure enough for the use of next step directly.



**Step 1<sup>[S2]</sup>:** The corresponding amine (1 equiv) was dissolved in  $\text{DCM}$  (0.5 M) at 0 °C. Then ethyl chloroformate (1.05 equiv) was added, and followed by  $\text{Et}_3\text{N}$  (2 equiv). The solution was kept stirring in the ice bath until the reaction was complete (monitored by TLC, about 1 hour to 12 hours). Then the reaction solution was diluted with brine and extracted three times with  $\text{DCM}$ . The combined organic layer was dried with anhydrous  $\text{Na}_2\text{SO}_4$  and the solvent was removed in vacuo. The crude product was purified via a silica gel column to afford the corresponding products (PE/EA = 10/1 to 5/1).

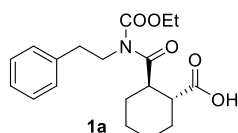
**Step 2:** The product of step 1 (1 equiv) was dissolved in anhydrous THF (0.15 M), which was then injected into a round bottom flask under N<sub>2</sub> atmosphere at 0 °C. NaHMDS (2.0 M in THF, 1.05 equiv) was added and the reaction was kept stirring for 30 min. The solution of anhydride (1 equiv, dissolved in anhydrous THF in advance) was added afterwards. After stirred for another 30 min, the solution of react mixture was diluted with H<sub>2</sub>O, acidized by 1 N HCl, and extracted three times with EA. The combined organic layer was dried over with anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed in vacuo. The crude product was purified by a silica gel column to afford the corresponding products (DCM 100 mL first, and then PE/EA = 5/1 to 3/1 with 1% of acetic acid).



**Step 1:** The corresponding amine (1 equiv) was dissolved in DCM (0.5 M) at 0 °C, then ethyl chloroformate (1.05 equiv) and K<sub>2</sub>CO<sub>3</sub> (1 equiv) was added in follow. Then remove the ice bath and keep stirring at room temperature until react completely (monitoring by silica gel plate). Then, diluted with brine and extracted three times with DCM. The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed in vacuo. The crude product was purified via a silica gel column to afford the corresponding products (PE/EA = 100/1 to 20/1).

**Step 2**<sup>[S3]</sup>: A 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with the product of step 1 (1 equiv), phenylboronic acid (1.5 equiv), Pd(OAc)<sub>2</sub> (0.25 mol%), *i*-Pr<sub>2</sub>NH (2 equiv) sequentially. Then H<sub>2</sub>O (5 mL) was added and heating the mixture to 100 °C and stirring vigorous for 2 - 4 h (until the mixture get black), The reaction mixture was diluted with brine and extracted three times with EA. The combined organic layer was dried over with anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed in vacuo. The crude product was purified by a silica gel column to afford the corresponding products (PE/EA = 10/1 to 5/1).

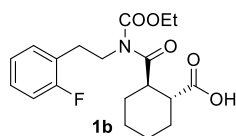
**Step 3:** The product of step 2 (1 equiv) was dissolved in anhydrous THF (0.15 M), and then, injected into a round bottom flask under N<sub>2</sub> atmosphere at 0 °C. NaHMDS (2.0 M in THF, 1.05 equiv) was added and kept stirred for 1 hour. The solution of anhydride (1 equiv, dissolved in anhydrous THF in advance) was added follow, after stirred for 30 min, the solution of react mixture was diluted with brine, acidized by 1 N HCl, and then the mixture was extracted three times with EA. The combined organic layer was dried over with Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed in vacuo. The crude product was purified by a silica gel column to afford the corresponding products (DCM 100 mL first, and then PE/EA = 10/1 to 2/1 with 1% of acetic acid)



**(1R,2R)-2-((ethoxycarbonyl)(phenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1a)**

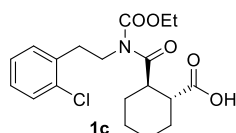
White solid, M.p.: 106.3 – 107.7 °C. Yield of last step: 35%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.23 – 7.15 (m, 3H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.95 – 3.87 (m, 2H), 3.67 (td, *J* = 11.3, 3.2 Hz, 1H), 2.89 – 2.72 (m, 3H), 2.21 – 2.04 (m, 2H), 1.86 – 1.71 (m, 2H), 1.43 – 1.12 (m, 7H). <sup>13</sup>C NMR

(101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.2, 154.2, 139.0, 129.1, 128.5, 126.4, 62.9, 46.3, 45.9, 45.5, 34.9, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>25</sub>NO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 370.1625, found 370.1626.



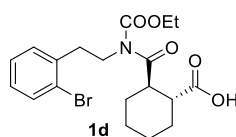
**(1R,2R)-2-((ethoxycarbonyl)(2-fluorophenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1b)**

White solid, M.p.: 104.5 – 106.0 °C. Yield of last step: 39%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.22 – 7.10 (m, 2H), 7.07 – 6.94 (m, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 4.02 – 3.88 (m, 2H), 3.67 (td, *J* = 11.4, 3.2 Hz, 1H), 2.91 – 2.75 (m, 3H), 2.21 – 2.02 (m, 2H), 1.86 – 1.71 (m, 2H), 1.42 – 1.26 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.23 – 1.08 (m, 1H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*)  $\delta$  -118.48. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  181.6, 178.2, 161.5 (d, *J*<sub>C-F</sub> = 245.3 Hz), 154.2, 131.7 (d, *J*<sub>C-F</sub> = 4.8 Hz), 128.3 (d, *J*<sub>C-F</sub> = 7.8 Hz), 125.9 (d, *J*<sub>C-F</sub> = 16.2 Hz), 124.1 (d, *J*<sub>C-F</sub> = 3.6 Hz), 115.2 (d, *J*<sub>C-F</sub> = 22.0 Hz), 62.9, 46.3, 45.4, 44.3, 29.5, 29.3, 28.3 (d, *J*<sub>C-F</sub> = 1.7 Hz), 25.7, 25.5, 14.0. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>FNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 388.1531, found 388.1531.



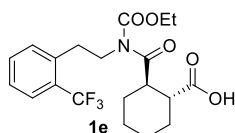
**(1R,2R)-2-((2-chlorophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1c)**

White solid, M.p.: 59.7 – 61.1 °C. Yield of last step: 48%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.34 – 7.28 (m, 1H), 7.20 – 7.09 (m, 3H), 4.04 (q, *J* = 7.1 Hz, 2H), 4.01 – 3.92 (m, 2H), 3.68 (td, *J* = 11.3, 3.2 Hz, 1H), 2.97 – 2.88 (m, 2H), 2.89 – 2.78 (m, 1H), 2.20 – 2.03 (m, 2H), 1.84 – 1.71 (m, 2H), 1.41 – 1.26 (m, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.21 – 1.11 (m, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.3, 154.2, 136.7, 134.4, 131.6, 129.4, 128.0, 126.9, 62.9, 46.2, 45.4, 43.9, 32.6, 29.5, 29.2, 25.7, 25.5, 14.1. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>ClNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 404.1235, found 404.1235.



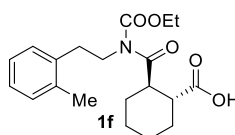
**(1R,2R)-2-((2-bromophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1d)**

Colorless sticky oil. Yield of last step: 48%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.51 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.15 (m, 2H), 7.08 – 7.02 (m, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 4.00 – 3.94 (m, 2H), 3.69 (td, *J* = 11.3, 3.2 Hz, 1H), 2.98 – 2.89 (m, 2H), 2.89 – 2.78 (m, 1H), 2.21 – 2.05 (m, 2H), 1.85 – 1.70 (m, 2H), 1.44 – 1.31 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.21 – 1.12 (m, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  181.4, 178.3, 154.2, 138.5, 132.7, 131.6, 128.2, 127.6, 124.8, 62.9, 46.3, 45.4, 44.0, 35.1, 29.6, 29.3, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>BrNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 448.0730, found 448.0728.



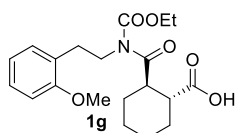
**(1R,2R)-2-((ethoxycarbonyl)(2-(trifluoromethyl)phenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1e)**

Colorless sticky oil. Yield of last step: 56%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.60 (dd,  $J = 7.9, 1.3$  Hz, 1H), 7.44 (td,  $J = 7.5, 1.3$  Hz, 1H), 7.36 (d,  $J = 7.6$  Hz, 1H), 7.28 (t,  $J = 7.6$  Hz, 1H), 4.15 – 4.04 (m, 2H), 3.92 (td,  $J = 7.7, 1.6$  Hz, 2H), 3.71 (td,  $J = 11.3, 3.2$  Hz, 1H), 3.02 – 2.88 (m, 2H), 2.88 – 2.76 (m, 1H), 2.20 – 2.05 (m, 2H), 1.86 – 1.72 (m, 2H), 1.42 – 1.27 (m, 3H), 1.27 – 1.11 (m, 4H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -59.57.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.4, 154.1, 137.6 (q,  $J_{\text{C-F}} = 1.9$  Hz), 132.4, 131.9, 128.9 (q,  $J_{\text{C-F}} = 29.7$  Hz), 126.6, 125.9 (q,  $J_{\text{C-F}} = 6.0$  Hz), 124.5 (q,  $J_{\text{C-F}} = 273.7$  Hz), 63.0, 46.2, 45.6, 45.5, 31.7, 29.5, 29.2, 25.7, 25.5, 14.0. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{24}\text{F}_3\text{NO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 438.1499, found 438.1500.



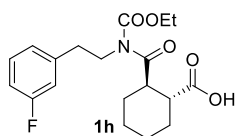
**(1R,2R)-2-((ethoxycarbonyl)(2-methylphenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1f)**

Colorless sticky oil. Yield of last step: 57%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.18 – 7.06 (m, 4H), 4.16 (q,  $J = 7.1$  Hz, 2H), 3.92 – 3.80 (m, 2H), 3.68 (td,  $J = 11.2, 3.2$  Hz, 1H), 2.90 – 2.74 (m, 3H), 2.36 (s, 3H), 2.21 – 2.07 (m, 2H), 1.87 – 1.73 (m, 2H), 1.43 – 1.17 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.2, 154.2, 137.0, 136.5, 130.2, 130.0, 126.6, 126.0, 62.9, 46.2, 45.5, 44.7, 32.3, 29.5, 29.2, 25.7, 25.5, 19.2, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{27}\text{NO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 384.1781, found 384.1781.



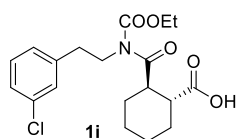
**(1R,2R)-2-((ethoxycarbonyl)(2-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1g)**

Colorless sticky oil. Yield of last step: 43%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.16 (td,  $J = 7.8, 1.8$  Hz, 1H), 7.07 (dd,  $J = 7.3, 1.7$  Hz, 1H), 6.88 – 6.78 (m, 2H), 4.11 – 4.02 (m, 2H), 4.02 – 3.86 (m, 2H), 3.81 (s, 3H), 3.66 (td,  $J = 11.4, 3.3$  Hz, 1H), 2.87 – 2.75 (m, 3H), 2.19 – 2.04 (m, 2H), 1.83 – 1.71 (m, 2H), 1.40 – 1.27 (m, 3H), 1.23 (t,  $J = 7.1$  Hz, 3H), 1.19 – 1.10 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.5, 178.2, 157.8, 154.4, 130.9, 127.7, 127.4, 120.5, 110.1, 62.6, 55.3, 46.3, 45.5, 44.3, 29.6, 29.5, 29.3, 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{27}\text{NO}_6\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 400.1731, found 400.1731.



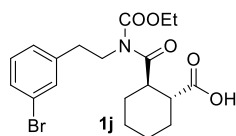
**(1*R*,2*R*)-2-((ethoxycarbonyl)(3-fluorophenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1h)**

White solid, M.p.: 63.5 – 65.3 °C. Yield of last step: 36%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.16 (m, 1H), 6.94 (dt, *J* = 7.5, 1.3 Hz, 1H), 6.92 – 6.83 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.98 – 3.82 (m, 2H), 3.65 (td, *J* = 11.3, 3.2 Hz, 1H), 2.88 – 2.69 (m, 3H), 2.20 – 2.00 (m, 2H), 1.85 – 1.69 (m, 2H), 1.40 – 1.10 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -113.72. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.7, 178.2, 162.9 (d, *J*<sub>C-F</sub> = 245.4 Hz), 154.1, 141.5 (d, *J*<sub>C-F</sub> = 7.3 Hz), 129.9 (d, *J*<sub>C-F</sub> = 8.3 Hz), 124.8 (d, *J*<sub>C-F</sub> = 2.9 Hz), 115.9 (d, *J*<sub>C-F</sub> = 20.9 Hz), 113.3 (d, *J*<sub>C-F</sub> = 20.9 Hz), 63.0, 46.3, 45.6, 45.5, 34.5 (d, *J*<sub>C-F</sub> = 3.6 Hz), 29.4, 29.2, 25.7, 25.5, 14.1. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>FNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 388.1531, found 388.1531.



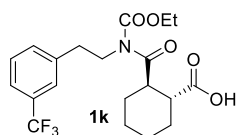
**(1*R*,2*R*)-2-((3-chlorophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1i)**

Colorless sticky oil. Yield of last step: 55%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.12 (m, 3H), 7.05 (dt, *J* = 6.6, 1.9 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.96 – 3.83 (m, 2H), 3.65 (td, *J* = 11.3, 3.2 Hz, 1H), 2.82 (td, *J* = 11.3, 3.5 Hz, 1H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.20 – 2.02 (m, 2H), 1.86 – 1.72 (m, 2H), 1.41 – 1.29 (m, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.24 – 1.10 (m, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.7, 178.2, 154.0, 141.0, 134.2, 129.7, 129.2, 127.4, 126.6, 63.0, 46.3, 45.6, 45.5, 34.5, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>ClNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 404.1235, found 404.1235.



**(1*R*,2*R*)-2-((3-bromophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1j)**

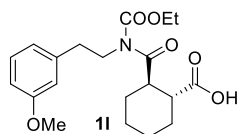
White solid, M.p.: 59.9 – 61.8 °C. Yield of last step: 48%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.30 (m, 2H), 7.16 – 7.08 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.96 – 3.83 (m, 2H), 3.65 (td, *J* = 11.3, 3.2 Hz, 1H), 2.83 (td, *J* = 11.4, 3.6 Hz, 1H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.20 – 2.03 (m, 2H), 1.86 – 1.74 (m, 2H), 1.41 – 1.09 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.7, 178.2, 154.0, 141.3, 132.1, 130.1, 129.5, 127.8, 122.5, 63.0, 46.3, 45.6, 45.5, 34.4, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>19</sub>H<sub>24</sub>BrNO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 448.0730, found 448.0729.



**(1*R*,2*R*)-2-((ethoxycarbonyl)(3-(trifluoromethyl)phenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1k)**

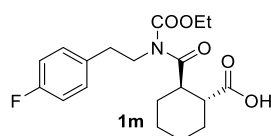
Colorless sticky oil. Yield of last step: 42%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.41 (m, 2H), 7.42 – 7.34 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.01 – 3.84 (m, 2H), 3.65 (td, *J* = 11.4, 3.2 Hz, 1H), 2.89 – 2.77 (m, 3H), 2.20 – 2.00 (m, 2H), 1.86 – 1.70 (m, 2H), 1.42 – 1.11 (m, 7H). <sup>19</sup>F NMR (376 MHz,

Chloroform-*d*)  $\delta$  -62.58.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.2, 154.0, 139.9, 132.6, 130.8 (q,  $J_{\text{C-F}} = 32.1$  Hz), 128.9, 125.8 (q,  $J_{\text{C-F}} = 3.8$  Hz), 124.3 (q,  $J_{\text{C-F}} = 272.2$  Hz), 123.3 (q,  $J_{\text{C-F}} = 3.7$  Hz), 63.0, 46.3, 45.6, 45.5, 34.6, 29.5, 29.2, 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{24}\text{F}_3\text{NO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 438.1499, found 438.1499.



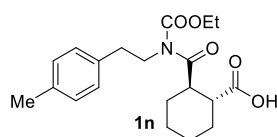
**(1R,2R)-2-((ethoxycarbonyl)(3-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1l)**

Colorless sticky oil. Yield of last step: 43%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.22 – 7.13 (m, 1H), 6.80 – 6.68 (m, 3H), 4.13 (q,  $J = 7.1$  Hz, 2H), 3.97 – 3.87 (m, 2H), 3.77 (s, 3H), 3.67 (td,  $J = 11.3, 3.2$  Hz, 1H), 2.83 (td,  $J = 11.4, 3.6$  Hz, 1H), 2.74 (t,  $J = 7.6$  Hz, 2H), 2.20 – 2.03 (m, 2H), 1.86 – 1.70 (m, 2H), 1.43 – 1.12 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.5, 178.2, 159.7, 154.2, 140.6, 129.4, 121.5, 114.5, 112.0, 62.9, 55.2, 46.2, 45.9, 45.5, 34.9, 29.5, 29.2, 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{27}\text{NO}_6\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 400.1731, found 400.1729.



**(1R,2R)-2-((ethoxycarbonyl)(4-fluorophenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1m)**

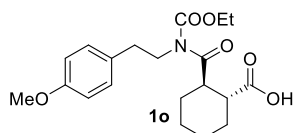
White solid, M.p.: 89.5 – 90.4°C. Yield of last step: 46%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.17 – 7.09 (m, 2H), 6.99 – 6.89 (m, 2H), 4.14 (q,  $J = 7.1$  Hz, 2H), 3.87 (td,  $J = 7.1, 2.8$  Hz, 2H), 3.65 (td,  $J = 11.3, 3.2$  Hz, 1H), 2.82 (td,  $J = 11.2, 3.4$  Hz, 1H), 2.73 (t,  $J = 7.5$  Hz, 2H), 2.20 – 2.00 (m, 2H), 1.87 – 1.70 (m, 2H), 1.43 – 1.10 (m, 7H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -116.99.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.8, 178.2, 161.7 (d,  $J_{\text{C-F}} = 243.9$  Hz), 154.1, 134.6 (d,  $J_{\text{C-F}} = 3.2$  Hz), 130.5 (d,  $J_{\text{C-F}} = 7.8$  Hz), 115.2 (d,  $J_{\text{C-F}} = 21.2$  Hz), 63.0, 46.3, 45.9, 45.5, 34.0, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{19}\text{H}_{24}\text{FNO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 388.1531, found 388.1532.



**(1R,2R)-2-((ethoxycarbonyl)(4-methylphenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1n)**

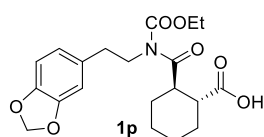
Colorless sticky oil. Yield of last step: 38%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.08 (s, 4H), 4.20 – 4.10 (m, 2H), 3.93 – 3.85 (m, 2H), 3.67 (td,  $J = 11.3, 3.2$  Hz, 1H), 2.89 – 2.79 (m, 1H), 2.78 – 2.68 (m, 2H), 2.31 (s, 3H), 2.20 – 2.04 (m, 2H), 1.85 – 1.73 (m, 2H), 1.42 – 1.12 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.6, 178.2, 154.2, 135.9, 135.8, 129.1, 129.0, 62.9, 46.3, 46.1, 45.5, 34.4, 29.5, 29.2, 25.7, 25.5, 21.1, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{27}\text{NO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 384.1781, found 384.1781.





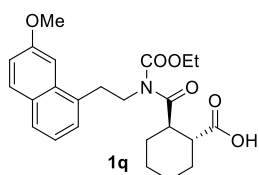
**(1R,2R)-2-((ethoxycarbonyl)(4-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylic acid (1o)**

White solid, M.p.: 76.2 – 77.3 °C. Yield of last step: 40%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.10 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.91 – 3.83 (m, 2H), 3.77 (s, 3H), 3.66 (td, *J* = 11.3, 3.2 Hz, 1H), 2.83 (td, *J* = 11.4, 3.7 Hz, 1H), 2.75 – 2.64 (m, 2H), 2.20 – 2.01 (m, 2H), 1.85 – 1.72 (m, 2H), 1.39 – 1.14 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.6, 178.2, 158.2, 154.2, 131.1, 130.1, 113.9, 62.9, 55.4, 46.3, 46.1, 45.5, 34.0, 29.5, 29.3, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>27</sub>NO<sub>6</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 400.1731, found 400.1731.



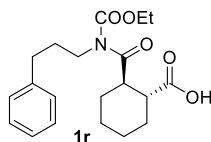
**(1R,2R)-2-((2-(benzo[d][1,3]dioxol-5-yl)ethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1p)**

Brown solid, M.p.: 72.1 – 73.6 °C. Yield of last step: 71%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 6.70 (d, *J* = 7.9 Hz, 1H), 6.68 (d, *J* = 1.6 Hz, 1H), 6.61 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.90 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.85 (td, *J* = 7.2, 2.9 Hz, 2H), 3.65 (td, *J* = 11.3, 3.2 Hz, 1H), 2.82 (td, *J* = 11.7, 3.6 Hz, 1H), 2.68 (t, *J* = 7.7 Hz, 2H), 2.18 – 2.03 (m, 2H), 1.87 – 1.71 (m, 2H), 1.41 – 1.11 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.5, 178.2, 154.2, 147.6, 146.1, 132.7, 122.0, 109.5, 108.3, 100.9, 62.9, 46.3, 46.1, 45.5, 34.6, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>NO<sub>7</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 414.1523, found 414.1523.



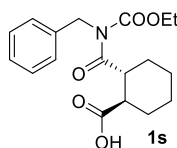
**(1R,2R)-2-((ethoxycarbonyl)(2-(7-methoxynaphthalen-1-yl)ethyl)carbamoyl)cyclohexane-1-carboxylic acid (1q)**

White solid, M.p.: 137.4 – 138.7 °C. Yield of last step: 62%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.9 Hz, 1H), 7.63 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.58 (d, *J* = 2.5 Hz, 1H), 7.26 – 7.18 (m, 2H), 7.11 (dd, *J* = 8.9, 2.4 Hz, 1H), 4.17 – 4.02 (m, 3H), 3.97 (s, 3H), 3.95 – 3.87 (m, 1H), 3.65 (td, *J* = 11.1, 3.2 Hz, 1H), 3.19 – 3.10 (m, 2H), 2.86 (td, *J* = 11.3, 3.6 Hz, 1H), 2.19 – 2.07 (m, 2H), 1.85 – 1.71 (m, 2H), 1.38 – 1.15 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.9, 178.2, 158.0, 154.2, 133.6, 133.4, 130.0, 129.2, 127.6, 127.0, 123.2, 118.3, 102.8, 63.0, 55.6, 46.5, 45.7, 45.1, 32.6, 29.5, 29.2, 25.7, 25.5, 14.0. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>24</sub>H<sub>29</sub>NO<sub>6</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 450.1887, found 450.1887.



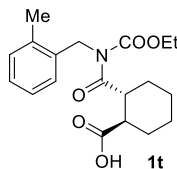
**(1R,2R)-2-((ethoxycarbonyl)(3-phenylpropyl)carbamoyl)cyclohexane-1-carboxylic acid (1r)**

Colorless sticky oil. Yield of last step: 44%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.80 – 3.60 (m, 3H), 2.82 (td, *J* = 11.3, 3.8 Hz, 1H), 2.60 (td, *J* = 7.5, 3.0 Hz, 2H), 2.17 – 2.03 (m, 2H), 1.89 – 1.73 (m, 4H), 1.40 – 1.13 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.6, 178.3, 154.3, 141.6, 128.4, 125.9, 62.9, 46.3, 45.5, 44.2, 33.2, 29.9, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>27</sub>NO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 384.1781, found 384.1781.



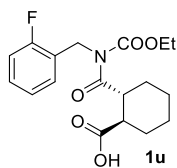
**(1R,2R)-2-(benzyl(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1s)**

Colorless sticky oil. Yield of last step: 32%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.16 (m, 5H), 5.00 – 4.86 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.82 (td, *J* = 11.3, 3.2 Hz, 1H), 2.89 (td, *J* = 11.6, 3.6 Hz, 1H), 2.23 – 2.11 (m, 2H), 1.89 – 1.75 (m, 2H), 1.46 – 1.16 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.9, 178.3, 154.2, 137.9, 128.4, 127.3, 127.1, 63.0, 47.2, 46.2, 45.5, 29.4, 29.3, 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>18</sub>H<sub>23</sub>NO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 356.1468, found 356.1468.



**(1R,2R)-2-((ethoxycarbonyl)(2-methylbenzyl)carbamoyl)cyclohexane-1-carboxylic acid (1t)**

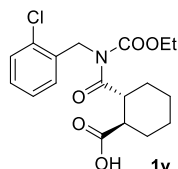
Colorless sticky oil. Yield of last step: 27%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.16 – 7.08 (m, 3H), 6.99 – 6.93 (m, 1H), 5.01 – 4.86 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.90 (td, *J* = 11.2, 3.2 Hz, 1H), 2.90 (td, *J* = 11.6, 3.5 Hz, 1H), 2.31 (s, 3H), 2.29 – 2.16 (m, 2H), 1.91 – 1.80 (m, 2H), 1.48 – 1.28 (m, 4H), 1.17 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.9, 178.1, 154.3, 135.7, 134.9, 130.1, 126.7, 126.2, 125.0, 63.1, 46.2, 45.4, 45.0, 29.6, 29.3, 25.7, 25.6, 19.2, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>19</sub>H<sub>25</sub>NO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 370.1625, found 370.1625.



**(1R,2R)-2-((ethoxycarbonyl)(2-fluorobenzyl)carbamoyl)cyclohexane-1-carboxylic acid (1u)**

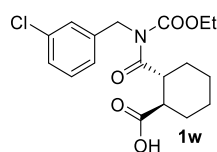
Colorless sticky oil. Yield of last step: 28%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.15 (m, 1H), 7.13 – 6.93 (m, 3H), 5.11 – 4.90 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.85 (td, *J* = 11.3, 3.2 Hz, 1H), 2.89

(td,  $J = 11.5, 3.6$  Hz, 1H), 2.27 – 2.13 (m, 2H), 1.92 – 1.75 (m, 2H), 1.46 – 1.16 (m, 7H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -119.25.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.3, 160.4 (d,  $J_{\text{C-F}} = 246.0$  Hz), 154.1, 128.6 (d,  $J_{\text{C-F}} = 8.1$  Hz), 128.4 (d,  $J_{\text{C-F}} = 4.0$  Hz), 125.0 (d,  $J_{\text{C-F}} = 14.0$  Hz), 124.3 (d,  $J_{\text{C-F}} = 3.6$  Hz), 115.1 (d,  $J_{\text{C-F}} = 21.6$  Hz), 63.2, 46.2, 45.4, 41.1 (d,  $J_{\text{C-F}} = 5.0$  Hz), 29.5, 29.3, 25.7, 25.6, 14.0. HRMS ( $m/z$ , ESI-TOF): Calcd for  $\text{C}_{18}\text{H}_{22}\text{FNO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 374.1374, found 374.1375.



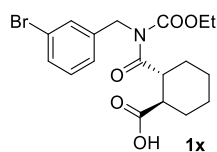
**(1R,2R)-2-((2-chlorobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1v)**

Colorless sticky oil. Yield of last step: 34%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.21 – 7.15 (m, 1H), 7.09 – 6.99 (m, 2H), 6.93 – 6.85 (m, 1H), 5.00 (d,  $J = 16.5$  Hz, 1H), 4.87 (d,  $J = 16.5$  Hz, 1H), 4.10 (q,  $J = 7.1$  Hz, 2H), 3.81 (td,  $J = 11.3, 3.2$  Hz, 1H), 2.81 (td,  $J = 11.5, 3.5$  Hz, 1H), 2.20 – 2.06 (m, 2H), 1.81 – 1.69 (m, 2H), 1.39 – 1.13 (m, 4H), 1.07 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  182.0, 178.1, 154.1, 135.1, 132.4, 129.3, 128.0, 127.0, 126.6, 63.2, 46.1, 45.4, 45.1, 29.6, 29.3, 25.7, 25.5, 14.1. HRMS ( $m/z$ , ESI-TOF): Calcd for  $\text{C}_{18}\text{H}_{22}\text{ClNO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 390.1079, found 390.1080.



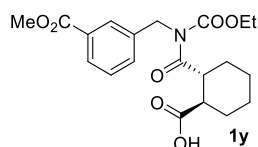
**(1R,2R)-2-((3-chlorobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1w)**

Colorless sticky oil. Yield of last step: 30%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.24 – 7.15 (m, 3H), 7.11 – 7.03 (m, 1H), 4.97 – 4.80 (m, 2H), 4.27 – 4.16 (m, 2H), 3.79 (td,  $J = 11.3, 3.1$  Hz, 1H), 2.87 (td,  $J = 11.4, 3.6$  Hz, 1H), 2.24 – 2.09 (m, 2H), 1.90 – 1.76 (m, 2H), 1.46 – 1.31 (m, 3H), 1.29 – 1.19 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 178.3, 154.0, 140.0, 134.1, 129.8, 127.8, 127.4, 125.6, 63.3, 46.8, 46.2, 45.5, 29.5, 29.3, 25.7, 25.5, 14.2. HRMS ( $m/z$ , ESI-TOF): Calcd for  $\text{C}_{18}\text{H}_{22}\text{ClNO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 390.1079, found 390.1079.



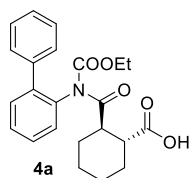
**(1R,2R)-2-((3-bromobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (1x)**

Colorless sticky oil. Yield of last step: 32%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.39 – 7.31 (m, 2H), 7.19 – 7.06 (m, 2H), 4.92 (d,  $J = 15.2$  Hz, 1H), 4.83 (d,  $J = 15.2$  Hz, 1H), 4.23 (q,  $J = 7.1$  Hz, 2H), 3.79 (td,  $J = 11.3, 3.2$  Hz, 1H), 2.87 (td,  $J = 11.5, 3.6$  Hz, 1H), 2.24 – 2.10 (m, 2H), 1.92 – 1.76 (m, 2H), 1.45 – 1.16 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.6, 178.3, 153.9, 140.3, 130.7, 130.3, 130.1, 126.0, 122.4, 63.3, 46.8, 46.2, 45.5, 29.5, 29.3, 25.7, 25.5, 14.2. HRMS ( $m/z$ , ESI-TOF): Calcd for  $\text{C}_{18}\text{H}_{22}\text{BrNO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 434.0574, found 434.0578.



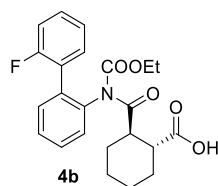
**(1R,2R)-2-((ethoxycarbonyl)(3-(methoxycarbonyl)benzyl)carbamoyl)cyclohexane-1-carboxylic acid (1y)**

Colorless sticky oil. Yield of last step: 36%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.94 – 7.84 (m, 2H), 7.39 (dt, *J* = 7.8, 1.7 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 15.2 Hz, 1H), 4.89 (d, *J* = 15.2 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 3.80 (td, *J* = 11.3, 3.2 Hz, 1H), 2.88 (td, *J* = 11.7, 3.5 Hz, 1H), 2.22 – 2.11 (m, 2H), 1.89 – 1.76 (m, 2H), 1.45 – 1.32 (m, 3H), 1.28 – 1.21 (m, 4H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 180.9, 178.3, 167.3, 154.0, 138.4, 132.1, 130.1, 128.8, 128.7, 128.5, 63.3, 52.3, 47.0, 46.4, 45.5, 29.3, 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>24</sub>NO<sub>7</sub><sup>-</sup> [M-H<sup>-</sup>] 390.1558, found 309.1559.



**(1R,2R)-2-([1,1'-biphenyl]-2-yl(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (4a)**

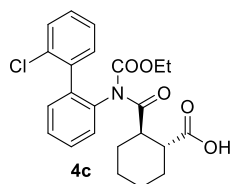
White solid, M.p.: 208.4 – 209.5 °C. Yield of last step: 50%. The two rotamers' ratio is about 78:22. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 6.06H), 7.25 – 7.16 (m, 2.01H), 7.15 – 7.10 (m, 0.69H), 7.05 – 7.01 (m, 0.20H), 4.05 – 3.93 (m, 1.71H), 3.92 – 3.79 (m, 0.52H), 3.70 (td, *J* = 11.4, 3.2 Hz, 0.78H), 2.90 – 2.74 (m, 1.00H), 2.24 – 2.09 (m, 1.24H), 1.91 – 1.77 (m, 1.94H), 1.76 – 1.67 (m, 0.80H), 1.48 – 1.20 (m, 3.66H), 1.06 (t, *J* = 7.1 Hz, 2.23H), 1.02 – 0.85 (m, 1.60H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.9, 181.7, 178.9, 178.6, 153.5, 153.1, 140.6, 140.3, 138.8, 138.3, 136.2, 136.1, 130.7, 130.2, 129.1, 128.9, 128.7, 128.65, 128.56, 128.4, 128.3, 128.12, 128.06, 127.8, 127.6, 63.00, 62.96, 46.0, 45.3, 44.9, 29.6, 29.5, 29.2, 28.6, 25.9, 25.7, 25.4, 14.1, 13.9. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>23</sub>H<sub>25</sub>NO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 418.1625, found 418.1630.



**(1R,2R)-2-((ethoxycarbonyl)(2'-fluoro-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4b)**

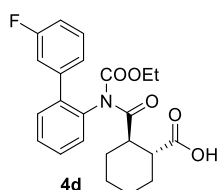
White solid, M.p.: 217.9 – 218.8 °C. Yield of last step: 33%. The two rotamers' ratio is about 84:16. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 12.26 (s, 0.92H), 7.58 – 7.32 (m, 4.02H), 7.30 – 6.99 (m, 4.00H), 4.05 – 3.70 (m, 2.19H), 3.47 (t, *J* = 12.1 Hz, 1.16H), 2.50 (s, 1.19H), 2.09 – 1.93 (m, 1.11H), 1.82 – 1.50 (m, 2.86H), 1.34 – 0.74 (m, 7.17H). <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>) δ -115.58, -116.70. <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 177.8, 176.2, 159.0 (d, *J*<sub>C-F</sub> = 245.4 Hz), 152.8, 136.8, 133.8, 131.0 (d, *J*<sub>C-F</sub> = 2.5 Hz), 130.8, 130.2 (d, *J*<sub>C-F</sub> = 8.3 Hz), 129.2, 128.8, 128.1, 125.2 (d, *J*<sub>C-F</sub> = 16.0 Hz), 124.1 (d, *J*<sub>C-F</sub> =

2.9 Hz), 115.7 (d,  $J_{C-F} = 22.0$  Hz), 62.8, 45.6, 45.2, 28.7, 28.1, 25.2, 24.9, 13.6. HRMS (m/z, ESI-TOF): Calcd for  $C_{23}H_{24}FNO_5Na^+$  [M+Na<sup>+</sup>] 436.1531, found 436.1532.



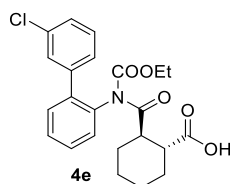
**(1R,2R)-2-((2'-chloro-[1,1'-biphenyl]-2-yl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (4c)**

White solid, M.p.: 203.9 – 205.3 °C. Yield of last step: 30%. The two rotamers' ratio is about 76:24. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.30 (m, 4.00H), 7.29 – 7.03 (m, 4.18H), 4.26 – 4.02 (m, 1.28H), 4.00 – 3.81 (m, 1.00H), 3.72 – 3.59 (m, 0.76H), 2.90 – 2.66 (m, 0.97H), 2.25 – 2.06 (m, 1.19H), 1.93 – 1.64 (m, 2.49H), 1.50 – 1.17 (m, 4.39H), 1.15 – 1.02 (m, 2.38H), 1.01 – 0.87 (m, 0.62H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 182.2, 181.7, 179.0, 178.7, 153.4, 153.1, 137.2, 137.1, 136.8, 136.5, 136.4, 135.8, 133.0, 132.6, 131.5, 131.3, 131.1, 130.7, 130.0, 129.7, 129.6, 129.5, 129.3, 129.1, 129.0, 128.7, 127.9, 127.7, 126.3, 126.0, 63.3, 63.1, 45.9, 45.8, 45.3, 44.9, 29.5, 29.1, 28.8, 28.2, 25.9, 25.7, 25.4, 25.3, 14.3, 13.9. HRMS (m/z, ESI-TOF): Calcd for  $C_{23}H_{24}ClNO_5Na^+$  [M+Na<sup>+</sup>] 452.1235, found 452.1235.



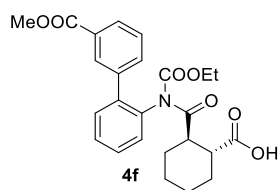
**(1R,2R)-2-((ethoxycarbonyl)(3'-fluoro-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4d)**

White solid, M.p.: 171.6 – 172.4 °C. Yield of last step: 57%. The two rotamers' ratio is about 79:21. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.33 (m, 2.24H), 7.36 – 7.25 (m, 1.78H), 7.17 – 7.10 (m, 0.80H), 7.05 – 6.96 (m, 2.27H), 6.95 – 6.89 (m, 0.91H), 4.06 – 3.87 (m, 2.23H), 3.72 (td,  $J = 11.4, 3.2$  Hz, 0.79H), 2.93 – 2.72 (m, 1.00H), 2.26 – 2.10 (m, 1.20H), 1.95 – 1.69 (m, 2.80H), 1.50 – 1.22 (m, 3.38H), 1.11 – 0.95 (m, 3.84H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -113.46, -113.50. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.74, 181.71, 178.8, 178.7, 162.6 (d,  $J_{C-F} = 245.4$  Hz), 162.5 (d,  $J_{C-F} = 246.2$  Hz), 153.4, 153.0, 141.0 (d,  $J_{C-F} = 7.9$  Hz), 140.5 (d,  $J_{C-F} = 7.7$  Hz), 139.5 (d,  $J_{C-F} = 1.4$  Hz), 139.1 (d,  $J_{C-F} = 1.9$  Hz), 136.11, 136.09, 130.5, 130.1, 130.0, 129.7 (d,  $J_{C-F} = 8.4$  Hz), 129.2, 129.1, 129.0, 128.7, 128.6, 128.5, 124.5 (d,  $J_{C-F} = 2.9$  Hz), 124.4 (d,  $J_{C-F} = 2.9$  Hz), 115.8 (d,  $J_{C-F} = 21.8$  Hz), 115.7 (d,  $J_{C-F} = 21.8$  Hz), 114.7 (d,  $J_{C-F} = 20.7$  Hz), 114.5 (d,  $J_{C-F} = 20.9$  Hz), 63.12, 63.07, 46.0, 45.3, 44.9, 29.7, 29.5, 29.1, 28.6, 25.8, 25.7, 25.4, 14.1, 13.9. HRMS (m/z, ESI-TOF): Calcd for  $C_{23}H_{24}FNO_5Na^+$  [M+Na<sup>+</sup>] 436.1531, found 436.1530.



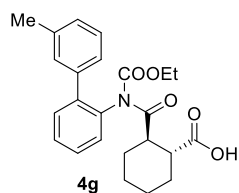
**(1*R*,2*R*)-2-((3'-chloro-[1,1'-biphenyl]-2-yl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylic acid (4e)**

White solid, M.p.: 163.8 – 164.8 °C. Yield of last step: 31%. The two rotamers' ratio is about 80:20. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.35 (m, 2.18H), 7.33 – 7.24 (m, 2.89H), 7.23 – 7.17 (m, 1.02H), 7.16 – 7.06 (m, 1.80H), 7.05 – 7.00 (m, 0.19H), 4.09 – 3.88 (m, 2.24H), 3.72 (td, *J* = 11.4, 3.2 Hz, 0.80H), 2.93 – 2.72 (m, 1.00H), 2.27 – 2.11 (m, 1.18H), 1.97 – 1.68 (m, 2.83H), 1.49 – 1.21 (m, 3.38H), 1.12 – 0.96 (m, 3.81H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.8, 181.7, 178.9, 178.8, 153.3, 153.0, 140.6, 140.2, 139.3, 139.0, 136.1, 134.0, 133.9, 130.5, 130.0, 129.8, 129.5, 129.3, 129.1, 128.95, 128.85, 128.8, 128.7, 128.6, 127.9, 127.8, 127.0, 126.8, 63.2, 63.1, 46.0, 45.2, 44.9, 29.7, 29.5, 29.1, 28.8, 25.9, 25.7, 25.4, 14.1, 14.0. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>23</sub>H<sub>24</sub>ClNO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 452.1235, found 452.1236.



**(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-(methoxycarbonyl)-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4f)**

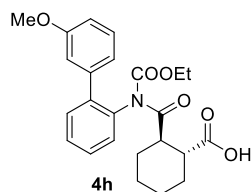
White solid, M.p.: 183.8 – 184.6 °C. Yield of last step: 35%. The two rotamers' ratio is about 79:21. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.95 (m, 0.76H), 7.95 – 7.86 (m, 1.21H), 7.47 – 7.28 (m, 5.06H), 7.19 – 7.08 (m, 0.75H), 7.07 – 7.00 (m, 0.21H), 4.04 – 3.96 (m, 1.78H), 3.95 – 3.84 (m, 3.52H), 3.68 (td, *J* = 11.4, 3.1 Hz, 0.79H), 2.90 – 2.74 (m, 1.00H), 2.24 – 2.12 (m, 1.24H), 1.89 – 1.75 (m, 2.04H), 1.73 – 1.64 (m, 0.76H), 1.47 – 1.19 (m, 3.42H), 1.06 (t, *J* = 7.1 Hz, 2.32H), 1.03 – 0.89 (m, 1.42H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.6, 181.1, 178.9, 178.7, 167.4, 166.9, 153.4, 153.0, 139.7, 139.3, 139.2, 138.8, 136.19, 136.17, 133.3, 130.8, 130.1, 129.99, 129.96, 129.8, 129.2, 129.1, 129.0, 128.9, 128.7, 128.62, 128.55, 128.3, 63.2, 63.1, 52.3, 52.2, 46.1, 45.9, 45.3, 44.8, 29.7, 29.3, 29.1, 28.7, 25.8, 25.7, 25.3, 14.0, 13.9. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>25</sub>H<sub>27</sub>NO<sub>7</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 476.1680, found 476.1679.



**(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-methyl-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4g)**

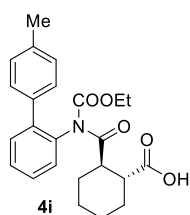
White solid, M.p.: 183.8 – 184.7 °C. Yield of last step: 43%. The two rotamers' ratio is about 82:18. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.29 (m, 2.97H), 7.28 – 7.19 (m, 1.04H), 7.17 – 7.09 (m, 1.68H), 7.08 – 6.96 (m, 2.29H), 3.97 (q, *J* = 7.1 Hz, 1.77H), 3.91 – 3.79 (m, 0.39H), 3.71 (td, *J* = 11.4, 3.1 Hz, 0.82H), 2.95 – 2.74 (m, 1.00H), 2.33 (s, 2.94H), 2.26 – 2.10 (m, 1.21H), 1.93 (dd, *J* = 12.8, 3.2 Hz, 0.82H), 1.88 – 1.69 (m, 2.00H), 1.51 – 1.23 (m, 3.36H), 1.12 – 0.92 (m, 3.77H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.6, 181.5, 178.7, 178.6, 153.5, 153.2, 140.5, 140.3, 138.6, 138.2, 137.7, 137.5, 136.1, 130.6, 130.1, 129.3, 129.0, 128.8, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 125.8, 125.7, 62.9, 62.8, 45.9,

45.2, 44.9, 29.6, 29.4, 29.1, 28.7, 25.8, 25.6, 25.3, 21.4, 21.3, 14.0, 13.8. HRMS ( $m/z$ , ESI-TOF): Calcd for  $C_{24}H_{27}NO_5Na^+$  [ $M+Na^+$ ] 432.1781, found 432.1776.



**(1R,2R)-2-((ethoxycarbonyl)(3'-methoxy-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4h)**

White solid, M.p.: 165.8 – 166.3 °C. Yield of last step: 37%. The two rotamers' ratio is about 87:13.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.40 – 7.30 (m, 3.06H), 7.27 – 7.20 (m, 1.06H), 7.15 – 7.09 (m, 0.84H), 7.04 – 6.99 (m, 0.20H), 6.87 – 6.81 (m, 1.24H), 6.80 – 6.72 (m, 1.88H), 4.09 – 3.91 (m, 2.00H), 3.80 – 3.73 (m, 3.23H), 3.73 (s, 0.87H), 2.91 – 2.72 (m, 1.00H), 2.23 – 2.11 (m, 1.27H), 1.92 – 1.66 (m, 3.04H), 1.47 – 1.20 (m, 3.31H), 1.11 – 0.92 (m, 4.00H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  181.7, 181.4, 178.8, 178.6, 159.3, 153.5, 153.2, 140.4, 140.2, 140.1, 139.7, 136.1, 130.6, 130.1, 129.4, 129.1, 128.8, 128.6, 128.5, 128.3, 128.1, 121.2, 121.1, 114.4, 113.3, 113.1, 63.0, 62.9, 55.4, 55.3, 46.01, 46.96, 45.3, 44.9, 29.7, 29.4, 29.1, 28.6, 25.8, 25.7, 25.6, 25.3, 14.1, 13.9. HRMS ( $m/z$ , ESI-TOF): Calcd for  $C_{24}H_{27}NO_6Na^+$  [ $M+Na^+$ ] 448.1731, found 448.1731.

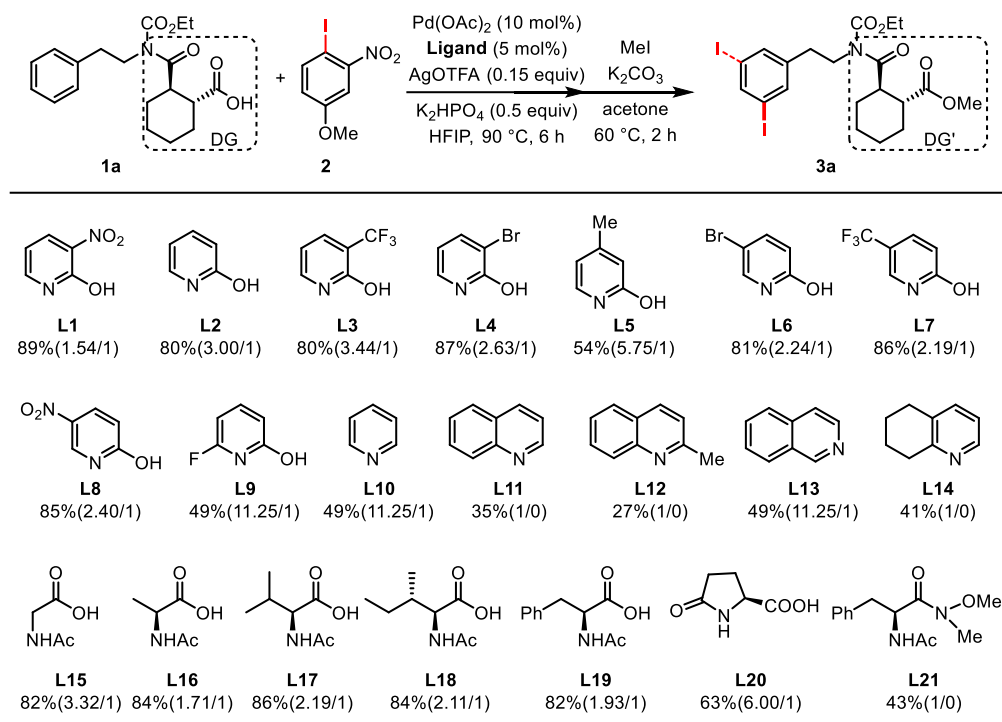


**(1R,2R)-2-((ethoxycarbonyl)(4'-methyl-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylic acid (4i)**

White solid, M.p.: 170.0 – 171.2 °C. Yield of last step: 33%. The two rotamers' ratio is about 75:25.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.42 – 7.29 (m, 3.01H), 7.20 – 7.06 (m, 4.76H), 7.03 (d,  $J = 7.3$  Hz, 0.23H), 4.06 – 3.91 (m, 1.74H), 3.91 – 3.77 (m, 0.51H), 3.71 (td,  $J = 11.4, 3.2$  Hz, 0.75H), 2.94 – 2.75 (m, 1.00H), 2.36 (s, 2.26H), 2.28 (s, 0.74H), 2.19 (dt,  $J = 11.6, 6.7$  Hz, 1.27H), 1.99 – 1.90 (m, 0.75H), 1.89 – 1.79 (m, 1.22H), 1.78 – 1.68 (m, 0.77H), 1.53 – 1.22 (m, 3.35H), 1.10 – 0.99 (m, 3.01H), 0.96 (t,  $J = 7.1$  Hz, 0.76H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  182.0, 181.7, 179.0, 178.7, 153.6, 153.1, 140.6, 140.3, 137.5, 137.3, 136.2, 136.1, 135.9, 135.4, 130.8, 130.3, 129.1, 128.9, 128.8, 128.6, 128.57, 128.52, 128.4, 128.3, 127.8, 62.95, 62.91, 46.1, 46.0, 45.3, 45.0, 29.6, 29.5, 29.2, 28.6, 25.9, 25.7, 25.4, 21.3, 21.2, 14.1, 13.9. HRMS ( $m/z$ , ESI-TOF): Calcd for  $C_{24}H_{27}NO_5Na^+$  [ $M+Na^+$ ] 432.1781, found 432.1781.

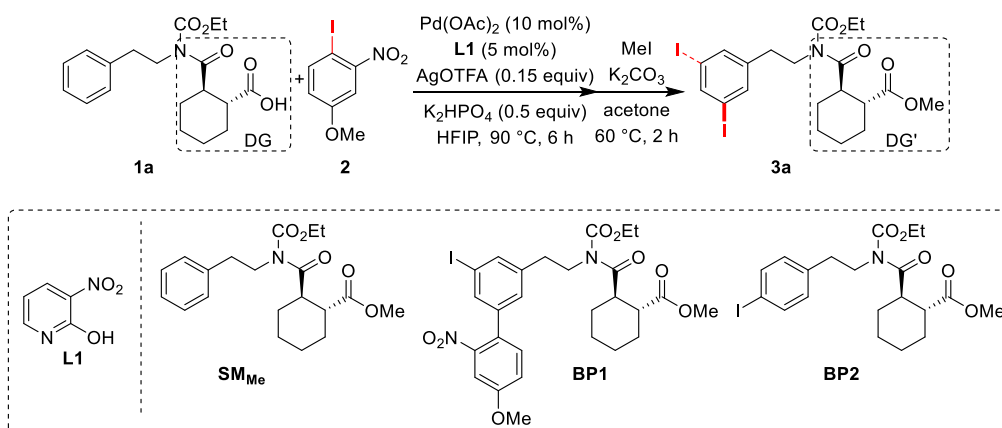
## 2.2 Optimization of the reaction conditions

Table S1 Optimization of ligands



Reaction conditions: **1a** (0.1 mmol), **2** (0.3 mmol), Pd(OAc)<sub>2</sub> (0.01 mmol), Ligand (0.005 mmol), AgOTFA (0.015 mmol), K<sub>2</sub>HPO<sub>4</sub> (0.05 mmol), HFIP (1 mL), 90 °C, 6 h; Then MeI (0.1 mL), K<sub>2</sub>CO<sub>3</sub> (0.5 mmol), acetone (2 mL), 60 °C, 2 h. Yield was determined by <sup>1</sup>H NMR with CH<sub>2</sub>Br<sub>2</sub> as internal standard, the ratio of mono/di was showed in parentheses.

Table S2 Optimization of other reaction conditions



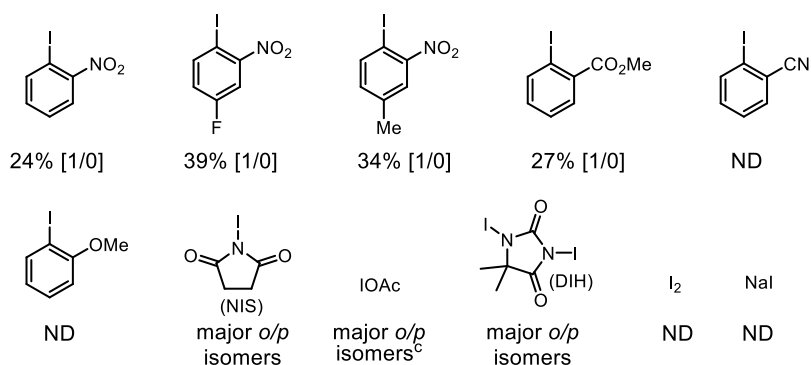
entry	deviation from standard conditions	yield (% <b>3a</b> ) [mono/di]	SM <sub>Me</sub> /BP1/BP2 (%)
<b>1</b>	none	<b>89</b> [1.54/1]	trace/4/3



entry	deviation from standard conditions	yield (% <b>, 3a</b> ) [mono/di]	SM <sub>Me</sub> /BP1/BP2 (%)
		<b>74[1.55/1]<sup>a</sup></b>	
2	without <b>L1</b>	27[27/trace]	75/trace/3
3	10 mol% of <b>L1</b>	86[2.58/1]	14/trace/4
4	15 mol% of <b>L1</b>	84[2.82/1]	15/trace/4
5	20 mol% of <b>L1</b>	80[3.44/1]	18/trace/4
6	30 mol% of <b>L1</b>	74[6.40/1]	33/trace/trace
7	without AgOTFA	76[4.43/1]	34/trace/3
8	0.05 equiv of AgOTFA	79[4.64/1]	20/trace/3
9	0.1 equiv of AgOTFA	77[3.53/1]	14/trace/3
10	0.2 equiv of AgOTFA	87[2.78/1]	15/trace/3
11	0.5 equiv of AgOTFA	84[1.47/1]	trace/6/3
12	1 equiv of AgOTFA	70[1.19/1]	0/13/7
13	2 equiv of AgOTFA	29[29/trace]	70/trace/5
14	3 equiv of AgOTFA	17[17/trace]	80/trace/3
15	AgOAc instead of AgOTFA	85[1.93/1]	4/6/3
16	Ag <sub>2</sub> CO <sub>3</sub> instead of AgOTFA	78[4.20/1]	25/trace/trace
17	without K <sub>2</sub> HPO <sub>4</sub>	67[2.94/1]	12/6/10
18	0.25 equiv of K <sub>2</sub> HPO <sub>4</sub>	88[1.44/1]	5/5/3
19	1 equiv of K <sub>2</sub> HPO <sub>4</sub>	79[5.08/1]	25/trace/2
20	K <sub>2</sub> CO <sub>3</sub> instead of K <sub>2</sub> HPO <sub>4</sub>	69[6.67/1]	31/trace/2
21	KH <sub>2</sub> PO <sub>4</sub> instead of K <sub>2</sub> HPO <sub>4</sub>	80[1.72/1]	6/8/10
22	without Pd(OAc) <sub>2</sub>	0[0/0]	100/0/0
23	70 °C instead of 90 °C	34[34/trace]	70/trace/1
24	80 °C instead of 90 °C	73[5.08/1]	30/trace/2
25	100 °C instead of 90 °C	86[2.58/1]	10/3/3
26	3 h	65[4.91/1]	30/trace/1
27	12 h	86[2.07/1]	7/4/3
<b>28</b>	<b>24 h</b>	<b>90[1/1.31]</b> <b>74[1/1.24]<sup>a</sup></b>	<b>trace/7/3</b>

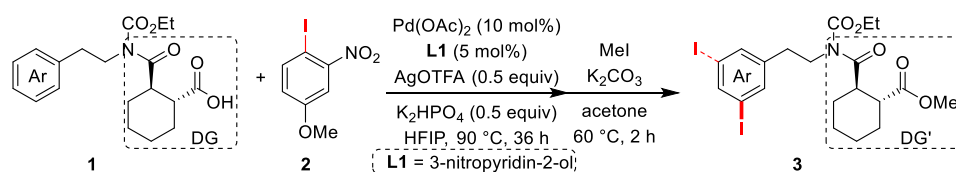
entry	deviation from standard conditions	yield (% <b>3a</b> ) [mono/di]	SM <sub>Me</sub> /BP1/BP2 (%)
29	36 h	90[1.43/1]	trace/5/3
<b>30<sup>b</sup></b>	<b>36 h</b>	<b>77[1/14.4]</b> <b>63[0/63]<sup>a</sup></b>	<b>trace/11/2</b>
31	Ar atmosphere instead of Air	84[2.00/1]	6/4/3
32	1-iodo-4-methoxy-2-nitrobenzene 2 equiv	80[3.21/1]	11/3/2
33	1-iodo-4-methoxy-2-nitrobenzene 2.5 equiv	89[2.18/1]	8/4/3

results by other iodinating reagents (3 equiv) under standard conditions:



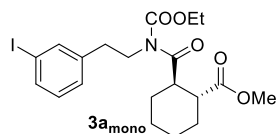
Reaction conditions: **1a** (0.1 mmol), **2** (0.3 mmol), Pd(OAc)<sub>2</sub> (0.01 mmol), **L1** (0.005 mmol), AgOTFA (0.015 mmol), K<sub>2</sub>HPO<sub>4</sub> (0.05 mmol), HFIP (1 mL), 90 °C, 6 h; Then MeI (0.1 mL), K<sub>2</sub>CO<sub>3</sub> (0.5 mmol), acetone (2 mL), 60 °C, 2 h. Yield was determined by <sup>1</sup>H NMR with CH<sub>2</sub>Br<sub>2</sub> as internal standard. <sup>a</sup>Isolated yield. <sup>b</sup>0.5 equiv of AgOTFA was used. <sup>c</sup>IOAc (from I<sub>2</sub>/PhIOAc).

## 2.3 General procedure for the synthesis of products



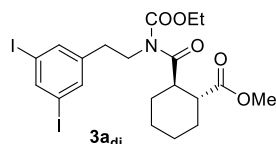
To an oven-dried 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with substrate **1** or **4** (0.1 mmol, 1 equiv), 4-iodo-3-nitroanisole (84 mg, 0.3 mmol, 3 equiv), Pd(OAc)<sub>2</sub> (2.3 mg, 0.01 mmol, 10 mol%), **L1** (3-nitropyridin-2-ol, 0.7 mg, 0.005 mmol, 5 mol%), AgOTFA (11 mg, 0.05 mmol, 0.5 equiv) and K<sub>2</sub>HPO<sub>4</sub> (8.72 mg, 0.05 mmol, 0.5 equiv) sequentially. HFIP (1 mL) was added to the mixture along the inside wall of the tube. The tube was then capped and placed into a preheated oil bath (90 °C) or hotplate (90 °C). The reaction was stirred for 36 h and cooled to room temperature. After the solvent was removed under reduced pressure, MeI (0.1 mL), K<sub>2</sub>CO<sub>3</sub> (70 mg, 0.5 mmol, 5 equiv) were added sequentially. Acetone (2 mL) was added to the mixture along the inside wall of the tube. The mixture was stirred at 60 °C for 2 h and then cooled to room temperature. The crude reaction mixture was diluted with EA (5 mL) and filtered through a short pad of Celite. The sealed tube

and Celite pad were washed with an additional 25 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by preparative thin layer chromatography using PE/EA (30/1) as the eluent to give the desired product, some products were further purified by semi-preparative MPLC (medium pressure liquid chromatography).



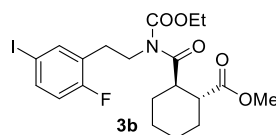
**methyl (1R,2R)-2-((ethoxycarbonyl)(3-iodophenethyl)carbamoyl)cyclohexane-1-carboxylate (3a<sub>mono</sub>)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Reaction condition 1: see table S1 entry 1; Reaction condition 2: see table S1 entry 29. Colorless sticky oil; yield 1: 22.1 mg, 45%; yield 2: 16.1 mg, 33%. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*) δ 7.56 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.7 Hz, 1H), 4.23 – 4.13 (m, 2H), 3.96 – 3.83 (m, 2H), 3.69 (td, *J* = 11.4, 3.3 Hz, 1H), 3.63 (s, 3H), 2.83 (td, *J* = 11.4, 3.7 Hz, 1H), 2.77 – 2.70 (m, 2H), 2.16 – 2.06 (m, 2H), 1.86 – 1.77 (m, 2H), 1.37 – 1.29 (m, 6H), 1.24 – 1.18 (m, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 154.1, 141.5, 138.1, 135.6, 130.3, 128.5, 94.5, 63.1, 51.9, 46.6, 45.7, 34.5, 29.7, 29.3, 25.7, 25.6, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>26</sub>INO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 510.0748, found 510.0748.



**methyl (1R,2R)-2-((3,5-diiodophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3a<sub>di</sub>)**

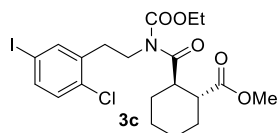
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Reaction condition 1: see table S1 entry 1; Reaction condition 2: see table S1 entry 29; Reaction condition 3: see table S1 entry 31. Colorless sticky oil; yield 1: 17.9 mg, 29%; yield 2: 24.9 mg, 41%; yield 3: 38.5 mg, 63%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.88 (t, *J* = 1.7 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 2H), 4.25 – 4.14 (m, 2H), 3.95 – 3.77 (m, 2H), 3.71 – 3.60 (m, 4H), 2.82 (td, *J* = 11.3, 4.0 Hz, 1H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.18 – 2.04 (m, 2H), 1.86 – 1.75 (m, 2H), 1.39 – 1.16 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 153.9, 143.23, 143.16, 137.5, 94.9, 63.2, 51.9, 46.5, 45.6, 45.4, 33.9, 29.7, 29.2, 25.7, 25.5, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>I<sub>2</sub>NO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 635.9714, found 635.9704.



**methyl (1R,2R)-2-((ethoxycarbonyl)(2-fluoro-5-iodophenethyl)carbamoyl)cyclohexane-1-carboxylate (3b)**

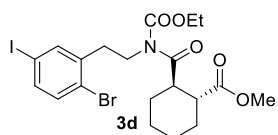
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 28.7 mg, 57%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.43 (m, 2H), 6.76 (dd, *J* = 9.5, 8.4 Hz, 1H), 4.24 – 4.07 (m, 2H), 3.98 – 3.86 (m, 2H), 3.68 (td, *J* = 11.4, 3.2 Hz, 1H), 3.62 (s, 3H), 2.87 –

2.73 (m, 3H), 2.17 – 2.03 (m, 2H), 1.87 – 1.74 (m, 2H), 1.39 – 1.12 (m, 7H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -119.57.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.4, 175.9, 161.5 (d,  $J_{\text{C-F}} = 247.2$  Hz), 154.0, 140.2 (d,  $J_{\text{C-F}} = 4.8$  Hz), 137.2 (d,  $J_{\text{C-F}} = 7.9$  Hz), 128.7 (d,  $J_{\text{C-F}} = 17.3$  Hz), 117.5 (d,  $J_{\text{C-F}} = 23.2$  Hz), 87.0 (d,  $J_{\text{C-F}} = 3.6$  Hz), 63.0, 51.8, 46.5, 45.6, 44.1, 29.7, 29.3, 28.0 (d,  $J_{\text{C-F}} = 1.9$  Hz), 25.7, 25.5, 14.1. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{25}\text{FINO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 528.0654, found 528.0648.



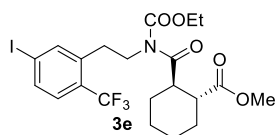
**methyl (1*R*,2*R*)-2-((2-chloro-5-iodophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3c)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 39.1 mg, 75%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.53 (d,  $J = 2.2$  Hz, 1H), 7.44 (dd,  $J = 8.3, 2.2$  Hz, 1H), 7.05 (d,  $J = 8.4$  Hz, 1H), 4.23 – 4.05 (m, 2H), 3.98 – 3.90 (m, 2H), 3.69 (td,  $J = 11.4, 3.4$  Hz, 1H), 3.63 (s, 3H), 2.93 – 2.74 (m, 3H), 2.17 – 2.04 (m, 2H), 1.86 – 1.73 (m, 2H), 1.41 – 1.16 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.5, 175.9, 154.0, 140.1, 139.1, 136.9, 134.5, 131.1, 91.5, 63.0, 51.8, 46.5, 45.6, 43.7, 32.3, 29.8, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{25}\text{ClINO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 544.0358, found 544.0352.



**methyl (1*R*,2*R*)-2-((2-bromo-5-iodophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3d)**

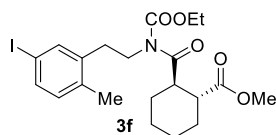
Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 44.5 mg, 79%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.54 (d,  $J = 2.2$  Hz, 1H), 7.36 (dd,  $J = 8.4, 2.2$  Hz, 1H), 7.23 (d,  $J = 8.3$  Hz, 1H), 4.19 – 4.09 (m, 2H), 3.94 (t,  $J = 7.3$  Hz, 2H), 3.69 (td,  $J = 11.4, 3.3$  Hz, 1H), 3.63 (s, 3H), 2.93 – 2.77 (m, 3H), 2.17 – 2.06 (m, 2H), 1.88 – 1.74 (m, 2H), 1.43 – 1.13 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.5, 175.9, 154.0, 140.9, 140.0, 137.2, 134.3, 124.6, 92.5, 63.0, 51.8, 46.5, 45.6, 43.7, 34.7, 29.8, 29.2, 25.7, 25.5, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{20}\text{H}_{25}\text{BrINO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 587.9853, found 587.9851.



**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(5-iodo-2-(trifluoromethyl)phenethyl)carbamoyl)cyclohexane-1-carboxylate (3e)**

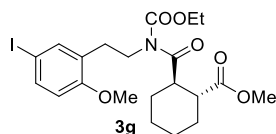
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 30.5 mg, 55%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.76 (d,  $J = 1.8$  Hz, 1H), 7.66 (dq,  $J = 8.3, 0.9$  Hz, 1H), 7.31 (d,  $J = 8.3$  Hz, 1H), 4.22 – 4.09 (m, 2H), 3.98 – 3.84 (m, 2H), 3.72 (td,  $J = 11.2, 3.2$

Hz, 1H), 3.64 (s, 3H), 2.97 – 2.81 (m, 3H), 2.20 – 2.09 (m, 2H), 1.87 – 1.74 (m, 2H), 1.38 – 1.19 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -59.86. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.6, 175.9, 154.0, 141.0, 139.7 (q, *J*<sub>C-F</sub> = 1.4 Hz), 135.9, 128.6 (q, *J*<sub>C-F</sub> = 29.8 Hz), 127.5 (q, *J*<sub>C-F</sub> = 5.4 Hz), 124.4 (q, *J*<sub>C-F</sub> = 273.7 Hz), 98.9, 63.2, 51.9, 46.5, 45.7, 45.4, 31.3, 29.7, 29.3, 25.8, 25.5, 14.1. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>25</sub>F<sub>3</sub>INO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 578.0622, found 578.0613.



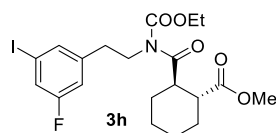
**methyl (1R,2R)-2-((ethoxycarbonyl)(5-iodo-2-methylphenethyl)carbamoyl)cyclohexane-1-carboxylate (3f)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 36.9 mg, 74%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 1.9 Hz, 1H), 7.42 (dd, *J* = 7.9, 2.0 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 4.31 – 4.14 (m, 2H), 3.89 – 3.76 (m, 2H), 3.74 – 3.59 (m, 4H), 2.83 (td, *J* = 11.3, 4.0 Hz, 1H), 2.74 (t, *J* = 7.9 Hz, 2H), 2.30 (s, 3H), 2.18 – 2.07 (m, 2H), 1.82 (d, *J* = 3.1 Hz, 2H), 1.40 – 1.28 (m, 6H), 1.23 (d, *J* = 11.5 Hz, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.5, 175.9, 154.1, 139.7, 138.6, 136.3, 135.6, 132.2, 90.9, 63.1, 51.8, 46.6, 45.7, 44.5, 32.0, 29.7, 29.3, 25.7, 25.5, 18.9, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>28</sub>INO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 524.0904, found 524.0904.



**methyl (1R,2R)-2-((ethoxycarbonyl)(5-iodo-2-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylate (3g)**

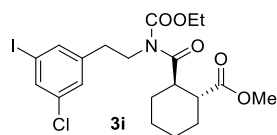
Purified by PTLC (preparative thin layer chromatography). Yellow sticky oil; yield: 39.0 mg, 75%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.36 (d, *J* = 2.3 Hz, 1H), 6.58 (d, *J* = 8.6 Hz, 1H), 4.20 – 4.05 (m, 2H), 3.98 – 3.83 (m, 2H), 3.78 (s, 3H), 3.67 (td, *J* = 11.3, 3.2 Hz, 1H), 3.62 (s, 3H), 2.92 – 2.67 (m, 3H), 2.16 – 2.02 (m, 2H), 1.86 – 1.74 (m, 2H), 1.43 – 1.14 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.3, 175.9, 157.8, 154.3, 139.2, 136.4, 130.3, 112.5, 82.6, 62.8, 55.5, 51.8, 46.5, 45.6, 44.0, 29.7, 29.3, 29.2, 25.7, 25.6, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>28</sub>INO<sub>6</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 540.0854, found 540.0855.



**methyl (1R,2R)-2-((ethoxycarbonyl)(3-fluoro-5-iodophenethyl)carbamoyl)cyclohexane-1-carboxylate (3h)**

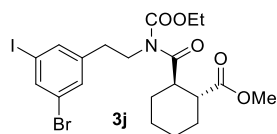
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 35.0 mg, 69%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.34 (t, *J* = 1.5 Hz, 1H), 7.30 – 7.26 (m, 1H), 6.90 (dt, *J* = 9.3, 1.9 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.98 – 3.81 (m, 2H), 3.68 (td, *J* = 11.5, 3.5 Hz, 1H), 3.64 (s, 3H), 2.83 (td, *J* = 11.4, 4.0 Hz, 1H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.17 – 2.06 (m, 2H), 1.86 –

1.74 (m, 2H), 1.37 – 1.16 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -111.24. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 162.3 (d,  $J_{C-F}$  = 251.4 Hz), 154.0, 143.3 (d,  $J_{C-F}$  = 7.4 Hz), 134.0 (d,  $J_{C-F}$  = 3.0 Hz), 122.9 (d,  $J_{C-F}$  = 23.6 Hz), 115.8 (d,  $J_{C-F}$  = 20.9 Hz), 93.5 (d,  $J_{C-F}$  = 8.5 Hz), 63.1, 51.9, 46.5, 45.7, 45.4, 34.2 (d,  $J_{C-F}$  = 3.2 Hz), 29.6, 29.2, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>FINO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 528.0654, found 528.0648.



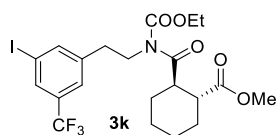
**methyl (1*R*,2*R*)-2-((3-chloro-5-iodophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3i)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 38.4 mg, 74%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.54 (t,  $J$  = 1.7 Hz, 1H), 7.43 (t,  $J$  = 1.5 Hz, 1H), 7.16 (t,  $J$  = 1.7 Hz, 1H), 4.24 – 4.14 (m, 2H), 3.97 – 3.78 (m, 2H), 3.67 (td,  $J$  = 11.4, 3.4 Hz, 1H), 3.63 (s, 3H), 2.82 (td,  $J$  = 11.3, 3.8 Hz, 1H), 2.71 (t,  $J$  = 7.6 Hz, 2H), 2.17 – 2.04 (m, 2H), 1.85 – 1.73 (m, 2H), 1.39 – 1.14 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 153.9, 142.8, 136.4, 135.1, 134.9, 128.8, 94.1, 63.1, 51.9, 46.5, 45.6, 45.4, 34.1, 29.7, 29.2, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>ClINO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 544.0358, found 544.0355.



**methyl (1*R*,2*R*)-2-((3-bromo-5-iodophenethyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3j)**

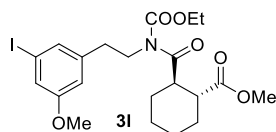
Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 41.4 mg, 73%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.69 (s, 1H), 7.48 (s, 1H), 7.31 (s, 1H), 4.25 – 4.15 (m, 2H), 3.97 – 3.79 (m, 2H), 3.72 – 3.60 (m, 4H), 2.82 (td,  $J$  = 11.3, 3.9 Hz, 1H), 2.71 (t,  $J$  = 7.6 Hz, 2H), 2.16 – 2.05 (m, 2H), 1.86 – 1.75 (m, 2H), 1.38 – 1.14 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 153.9, 143.1, 137.7, 136.9, 131.7, 122.9, 94.5, 63.2, 51.9, 46.6, 45.7, 45.4, 34.0, 29.7, 29.2, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>BrINO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 587.9853, found 587.9847.



**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(3-iodo-5-(trifluoromethyl)phenethyl)carbamoyl)cyclohexane-1-carboxylate (3k)**

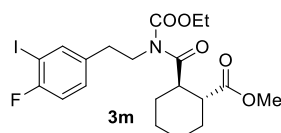
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 46.1 mg, 83%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.79 (s, 1H), 7.75 (s, 1H), 7.42 (s, 1H), 4.26 – 4.12 (m, 2H), 4.01 – 3.82 (m, 2H), 3.71 – 3.61 (m, 4H), 2.88 – 2.75 (m, 3H), 2.18 – 2.03 (m, 2H), 1.87 – 1.74 (m, 2H), 1.39 – 1.14 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -62.77. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.5, 175.9, 153.9, 142.2, 141.5, 132.44 (q,  $J_{C-F}$  = 32.5 Hz), 132.36 (q,  $J_{C-F}$  = 3.8

(Hz), 125.3 (q,  $J_{C-F} = 3.6$  Hz), 123.0 (q,  $J_{C-F} = 273.1$  Hz), 94.0, 63.2, 51.9, 46.6, 45.7, 45.4, 34.2, 29.7, 29.2, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for  $C_{20}H_{25}F_3INO_5Na^+$  [M+Na<sup>+</sup>] 578.0622, found 578.0617.



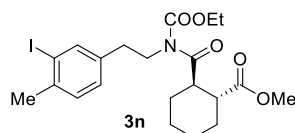
**methyl (1R,2R)-2-((ethoxycarbonyl)(3-iodo-5-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylate (3l)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 41.3 mg, 80%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.14 (t,  $J = 1.4$  Hz, 1H), 7.08 (t,  $J = 1.9$  Hz, 1H), 6.71 (t, 1H), 4.18 (q,  $J = 7.1$  Hz, 2H), 3.97 – 3.81 (m, 2H), 3.75 (s, 3H), 3.69 (td,  $J = 11.3, 3.2$  Hz, 1H), 3.63 (s, 3H), 2.83 (td,  $J = 11.3, 3.8$  Hz, 1H), 2.70 (t,  $J = 7.6$  Hz, 2H), 2.16 – 2.06 (m, 2H), 1.85 – 1.74 (m, 2H), 1.39 – 1.16 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 160.2, 154.1, 142.4, 130.5, 121.1, 114.7, 94.4, 63.1, 55.5, 51.9, 46.6, 45.7, 34.5, 29.6, 29.3, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for  $C_{21}H_{28}INO_6Na^+$  [M+Na<sup>+</sup>] 540.0854, found 540.0854.



**methyl (1R,2R)-2-((ethoxycarbonyl)(4-fluoro-3-iodophenethyl)carbamoyl)cyclohexane-1-carboxylate (3m)**

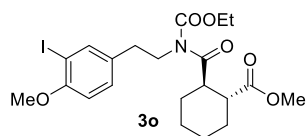
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 24.4 mg, 48%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.58 (dd,  $J = 6.0, 2.1$  Hz, 1H), 7.17 – 7.11 (m, 1H), 6.96 (t,  $J = 8.1$  Hz, 1H), 4.19 (q,  $J = 7.2$  Hz, 2H), 3.95 – 3.81 (m, 2H), 3.68 (td,  $J = 11.3, 3.2$  Hz, 1H), 3.63 (s, 3H), 2.82 (td,  $J = 11.3, 3.9$  Hz, 1H), 2.73 (t,  $J = 7.5$  Hz, 2H), 2.17 – 2.05 (m, 2H), 1.86 – 1.75 (m, 2H), 1.39 – 1.16 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -97.70. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 160.6 (d,  $J_{C-F} = 244.1$  Hz), 154.0, 139.7, 136.9 (d,  $J_{C-F} = 3.7$  Hz), 130.8 (d,  $J_{C-F} = 7.2$  Hz), 115.5 (d,  $J_{C-F} = 23.8$  Hz), 81.2 (d,  $J_{C-F} = 25.4$  Hz), 63.1, 51.9, 46.6, 45.8, 45.7, 33.6, 29.7, 29.3, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for  $C_{20}H_{25}FINO_5Na^+$  [M+Na<sup>+</sup>] 528.0654, found 528.0654.



**methyl (1R,2R)-2-((ethoxycarbonyl)(3-iodo-4-methylphenethyl)carbamoyl)cyclohexane-1-carboxylate (3n)**

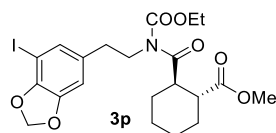
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 20.5 mg, 41%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d,  $J = 1.7$  Hz, 1H), 7.13 (d,  $J = 7.7$  Hz, 1H), 7.07 (dd,  $J = 7.7, 1.8$  Hz, 1H), 4.25 – 4.12 (m, 2H), 3.92 – 3.82 (m, 2H), 3.69 (td,  $J = 11.3, 3.2$  Hz, 1H), 3.63 (s, 3H), 2.82 (td,  $J = 11.1, 9.5, 5.6$  Hz, 1H), 2.70 (t,  $J = 7.7$  Hz, 2H), 2.37 (s, 3H), 2.16 – 2.07

(m, 2H), 1.85 – 1.75 (m, 2H), 1.39 – 1.15 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 154.1, 139.37, 139.36, 138.4, 129.7, 129.0, 101.2, 63.0, 51.8, 46.6, 45.8, 45.7, 33.8, 29.7, 29.3, 27.7, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>28</sub>INO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 524.0904, found 524.0903.



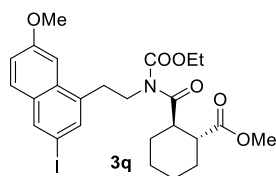
**methyl (1R,2R)-2-((ethoxycarbonyl)(3-iodo-4-methoxyphenethyl)carbamoyl)cyclohexane-1-carboxylate (3o)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 20.7 mg, 40%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 2.1 Hz, 1H), 7.13 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.93 – 3.80 (m, 5H), 3.74 – 3.63 (m, 1H), 3.63 (s, 3H), 2.82 (td, *J* = 11.2, 3.8 Hz, 1H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.17 – 2.04 (m, 2H), 1.85 – 1.75 (m, 2H), 1.39 – 1.16 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 156.8, 154.1, 139.9, 133.3, 130.2, 110.9, 85.9, 63.0, 56.5, 51.8, 46.6, 46.0, 45.7, 33.5, 29.7, 29.3, 25.7, 25.6, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>28</sub>INO<sub>6</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 540.0854, found 540.0854.



**methyl (1R,2R)-2-((ethoxycarbonyl)(2-(7-iodobenzo[d][1,3]dioxol-5-yl)ethyl)carbamoyl)cyclohexane-1-carboxylate (3p)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 29.1 mg, 55%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 6.95 (d, *J* = 1.5 Hz, 1H), 6.65 (d, *J* = 1.5 Hz, 1H), 5.97 (s, 2H), 4.27 – 4.16 (m, 2H), 3.93 – 3.75 (m, 2H), 3.68 (td, *J* = 11.3, 3.3 Hz, 1H), 3.63 (s, 3H), 2.82 (td, *J* = 11.1, 3.8 Hz, 1H), 2.66 (t, *J* = 7.7 Hz, 2H), 2.16 – 2.04 (m, 2H), 1.86 – 1.74 (m, 2H), 1.43 – 1.15 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 154.1, 148.0, 146.7, 134.9, 130.3, 109.6, 100.6, 70.5, 63.1, 51.9, 46.6, 45.9, 45.7, 34.2, 29.7, 29.3, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for C<sub>21</sub>H<sub>26</sub>INO<sub>7</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 554.0646, found 554.0646.

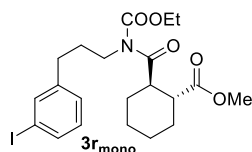


**methyl (1R,2R)-2-((ethoxycarbonyl)(2-(3-iodo-7-methoxynaphthalen-1-yl)ethyl)carbamoyl)cyclohexane-1-carboxylate (3q)**

Purified by PTLC (preparative thin layer chromatography). Yellow sticky oil; yield: 40.0 mg, 71%. <sup>1</sup>H NMR (400 MHz, Methanol-*d*<sub>4</sub>) δ 8.05 (d, *J* = 1.8 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 2.6 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.4 Hz, 1H), 4.20 – 4.02 (m, 3H), 3.98 (s, 3H), 3.94 – 3.86 (m, 1H), 3.71 – 3.61 (m, 4H), 3.17 – 3.08 (m, 2H), 2.80 (td, *J* = 11.4, 3.7 Hz, 1H), 2.19 – 2.05 (m, 2H), 1.90 – 1.76 (m, 2H), 1.43 – 1.31 (m, 3H), 1.26 – 1.15 (m, 4H). <sup>13</sup>C NMR (101 MHz, Chloroform-

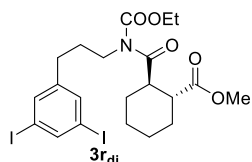


*d*)  $\delta$  178.5, 175.9, 158.5, 154.1, 136.0, 135.60, 135.57, 132.5, 130.9, 129.1, 119.3, 103.1, 87.8, 63.2, 55.7, 51.8, 46.7, 45.9, 45.0, 32.2, 29.7, 29.3, 25.7, 25.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for  $C_{25}H_{30}INO_6Na^+$  [M+Na<sup>+</sup>] 590.1010, found 590.1010.



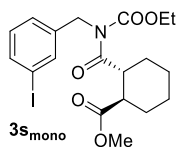
**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(3-(3-iodophenyl)propyl)carbamoyl)cyclohexane-1-carboxylate (3r<sub>mono</sub>)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 15.5 mg, 31%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.54 (t, *J* = 1.7 Hz, 1H), 7.51 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.14 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.00 (t, *J* = 7.7 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.83 – 3.71 (m, 1H), 3.73 – 3.58 (m, 5H), 2.82 (td, *J* = 11.0, 3.8 Hz, 1H), 2.54 (t, *J* = 7.9 Hz, 2H), 2.15 – 2.05 (m, 2H), 1.87 – 1.73 (m, 4H), 1.39 – 1.15 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  178.5, 175.9, 154.3, 144.3, 137.5, 135.1, 130.2, 127.8, 94.6, 63.0, 51.9, 46.6, 45.8, 44.1, 32.8, 29.8, 29.6, 29.3, 25.7, 25.5, 14.4. HRMS (m/z, ESI-TOF): Calcd for  $C_{21}H_{28}INO_5Na^+$  [M+Na<sup>+</sup>] 524.0904, found 524.0904.



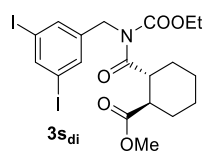
**methyl (1*R*,2*R*)-2-((3-(3,5-diiodophenyl)propyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3r<sub>di</sub>)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 17.1 mg, 27%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.86 (s, 1H), 7.50 (d, *J* = 1.4 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.83 – 3.74 (m, 1H), 3.69 – 3.61 (m, 5H), 2.82 (td, *J* = 11.2, 3.8 Hz, 1H), 2.49 (t, *J* = 8.0 Hz, 2H), 2.16 – 2.05 (m, 2H), 1.86 – 1.71 (m, 4H), 1.39 – 1.17 (m, 7H). <sup>13</sup>C NMR (101 MHz, )  $\delta$  178.6, 176.0, 154.3, 146.2, 142.7, 136.9, 94.9, 63.1, 52.0, 46.6, 45.8, 44.0, 32.4, 29.7, 29.6, 29.3, 25.7, 25.5, 14.4. HRMS (m/z, ESI-TOF): Calcd for  $C_{21}H_{27}I_2NO_5Na^+$  [M+Na<sup>+</sup>] 649.9871, found 649.9863.



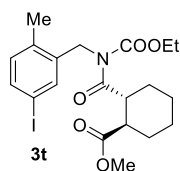
**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(3-iodobenzyl)carbamoyl)cyclohexane-1-carboxylate (3s<sub>mono</sub>)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 11.1 mg, 24%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.60 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 4.85 (q, *J* = 15.0 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.79 (td, *J* = 11.1, 3.3 Hz, 1H), 3.60 (s, 3H), 2.84 (td, *J* = 11.3, 3.8 Hz, 1H), 2.19 – 2.07 (m, 2H), 1.88 – 1.75 (m, 2H), 1.42 – 1.19 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  178.5, 175.8, 154.0, 140.4, 136.8, 136.3, 130.2, 127.0, 94.3, 63.3, 51.9, 46.7, 46.5, 45.7, 29.6, 29.3, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for  $C_{19}H_{24}INO_5Na^+$  [M+Na<sup>+</sup>] 496.0591, found 496.0588.



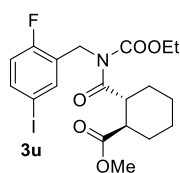
**methyl (1*R*,2*R*)-2-((3,5-diiodobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3sai)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 20.6 mg, 34%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.91 (t, *J* = 1.5 Hz, 1H), 7.56 (d, *J* = 1.6 Hz, 2H), 4.90 (d, *J* = 15.2 Hz, 1H), 4.67 (d, *J* = 15.1 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.77 (td, *J* = 11.2, 3.2 Hz, 1H), 3.64 (s, 3H), 2.84 (td, *J* = 11.2, 3.8 Hz, 1H), 2.18 – 2.08 (m, 2H), 1.86 – 1.75 (m, 2H), 1.40 – 1.20 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.5, 175.8, 153.7, 144.0, 142.1, 136.2, 94.7, 63.5, 52.1, 46.5, 46.0, 45.7, 29.6, 29.2, 25.7, 25.5, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>19</sub>H<sub>23</sub>I<sub>2</sub>NO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 621.9558, found 621.9555.



**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(5-iodo-2-methylbenzyl)carbamoyl)cyclohexane-1-carboxylate (3t)**

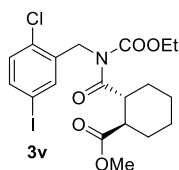
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 32.3 mg, 66%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.43 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.31 (s, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 4.84 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.87 (td, *J* = 11.2, 3.3 Hz, 1H), 3.65 (s, 3H), 2.84 (td, *J* = 11.4, 3.9 Hz, 1H), 2.27 – 2.10 (m, 5H), 1.89 – 1.78 (m, 2H), 1.44 – 1.17 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.3, 175.9, 154.1, 138.3, 135.8, 134.8, 134.3, 132.0, 91.1, 63.3, 52.1, 46.5, 45.5, 44.6, 29.7, 29.3, 25.7, 25.6, 18.9, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>26</sub>INO<sub>5</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 510.0748, found 510.0748.



**methyl (1*R*,2*R*)-2-((ethoxycarbonyl)(2-fluoro-5-iodobenzyl)carbamoyl)cyclohexane-1-carboxylate (3u)**

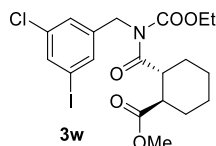
Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 21.4 mg, 44%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.43 (m, 2H), 6.76 (dd, *J* = 9.9, 8.4 Hz, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.83 (td, *J* = 11.1, 3.2 Hz, 1H), 3.66 (s, 3H), 2.85 (td, *J* = 11.3, 3.9 Hz, 1H), 2.22 – 2.09 (m, 2H), 1.88 – 1.75 (m, 2H), 1.42 – 1.18 (m, 7H). <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -120.10. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.5, 175.9, 160.5 (d, *J*<sub>C-F</sub> = 247.7 Hz), 153.8, 137.6 (d, *J*<sub>C-F</sub> = 7.9 Hz), 137.6 (d, *J*<sub>C-F</sub> = 4.0 Hz), 127.8 (d, *J*<sub>C-F</sub> = 14.9 Hz), 117.4 (d, *J*<sub>C-F</sub> = 22.9 Hz), 87.3 (d, *J*<sub>C-F</sub> = 3.4 Hz), 63.4, 52.1, 46.4, 45.6,

40.7 (d,  $J_{C-F} = 4.9$  Hz), 29.6, 29.3, 25.7, 25.5, 14.1. HRMS (m/z, ESI-TOF): Calcd for  $C_{19}H_{23}FINO_5Na^+$   $[M+Na^+]$  514.0497, found 514.0497.



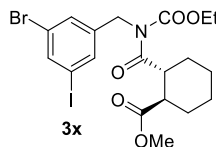
**methyl (1*R*,2*R*)-2-((2-chloro-5-iodobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3v)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 32.0 mg, 63%.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.47 (dd,  $J = 8.4, 2.1$  Hz, 1H), 7.41 (d,  $J = 2.1$  Hz, 1H), 7.04 (d,  $J = 8.2$  Hz, 1H), 5.04 (d,  $J = 16.5$  Hz, 1H), 4.89 (d,  $J = 16.5$  Hz, 1H), 4.22 (q,  $J = 7.1$  Hz, 2H), 3.89 (td,  $J = 11.2, 3.3$  Hz, 1H), 3.67 (s, 3H), 2.85 (td,  $J = 11.3, 4.0$  Hz, 1H), 2.25 – 2.09 (m, 2H), 1.89 – 1.79 (m, 2H), 1.45 – 1.16 (m, 7H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.4, 175.9, 153.8, 137.6, 137.1, 135.9, 132.6, 131.0, 91.9, 63.4, 52.2, 46.4, 45.5, 44.8, 29.6, 29.2, 25.7, 25.6, 14.1. HRMS (m/z, ESI-TOF): Calcd for  $C_{19}H_{23}ClINO_5Na^+$   $[M+Na^+]$  530.0202, found 530.0197.



**methyl (1*R*,2*R*)-2-((3-chloro-5-iodobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3w)**

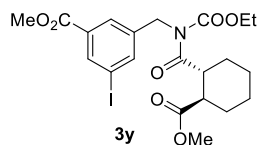
Purified by semi-preparative MPLC (medium pressure liquid chromatography). White solid, M.p.: 52.3 – 53.7 °C; yield: 25.2 mg, 50%.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.57 (t,  $J = 1.7$  Hz, 1H), 7.49 (t,  $J = 1.5$  Hz, 1H), 7.20 (t,  $J = 1.7$  Hz, 1H), 4.92 (d,  $J = 15.2$  Hz, 1H), 4.71 (d,  $J = 15.2$  Hz, 1H), 4.25 (q,  $J = 7.1$  Hz, 2H), 3.78 (td,  $J = 11.1, 3.1$  Hz, 1H), 3.63 (s, 3H), 2.84 (td,  $J = 11.1, 3.8$  Hz, 1H), 2.19 – 2.07 (m, 2H), 1.87 – 1.76 (m, 2H), 1.40 – 1.21 (m, 7H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.5, 175.8, 153.8, 141.7, 135.9, 135.1, 134.9, 127.5, 93.9, 63.5, 52.0, 46.5, 46.3, 45.7, 29.6, 29.3, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for  $C_{19}H_{23}ClINO_5Na^+$   $[M+Na^+]$  530.0202, found 530.0202.



**methyl (1*R*,2*R*)-2-((3-bromo-5-iodobenzyl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (3x)**

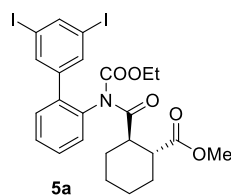
Purified by semi-preparative MPLC (medium pressure liquid chromatography). White solid, M.p.: 56.1 – 57.5 °C; yield: 27.3 mg, 50%.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.72 (s, 1H), 7.53 (s, 1H), 7.36 (s, 1H), 4.93 (d,  $J = 15.2$  Hz, 1H), 4.70 (d,  $J = 15.2$  Hz, 1H), 4.25 (q,  $J = 7.1$  Hz, 2H), 3.78 (td,  $J = 11.2, 3.2$  Hz, 1H), 3.63 (s, 3H), 2.84 (td,  $J = 11.4, 3.9$  Hz, 1H), 2.20 – 2.06 (m, 2H), 1.88 – 1.75 (m, 2H), 1.42 – 1.19 (m, 7H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.6, 175.9, 153.8, 142.0, 138.5, 135.6, 130.4,

122.9, 94.3, 63.5, 52.1, 46.5, 46.2, 45.7, 29.6, 29.3, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $C_{19}H_{23}BrINO_5Na^+$  [ $M+Na^+$ ] 573.9697, found 573.9696.



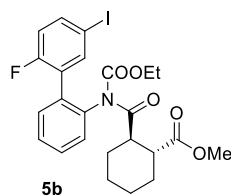
**methyl 3-(((1R,2R)-N-(ethoxycarbonyl)-2-(methoxycarbonyl)cyclohexane-1-carboxamido)methyl)-5-iodobenzoate (3y)**

Purified by semi-preparative MPLC (medium pressure liquid chromatography). Colorless sticky oil; yield: 22.4 mg, 42%.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.24 (t,  $J = 1.6$  Hz, 1H), 7.88 (t,  $J = 1.6$  Hz, 1H), 7.79 (t,  $J = 1.7$  Hz, 1H), 4.97 (d,  $J = 15.1$  Hz, 1H), 4.81 (d,  $J = 15.1$  Hz, 1H), 4.24 (q,  $J = 7.1$  Hz, 2H), 3.89 (s, 3H), 3.79 (td,  $J = 11.2, 3.2$  Hz, 1H), 3.62 (s, 3H), 2.84 (td,  $J = 11.2, 3.8$  Hz, 1H), 2.20 – 2.08 (m, 2H), 1.88 – 1.75 (m, 2H), 1.39 – 1.31 (m, 3H), 1.30 – 1.25 (m, 4H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.6, 175.9, 165.6, 153.8, 141.1, 140.5, 137.4, 131.9, 128.5, 93.9, 63.4, 52.5, 52.0, 46.5, 46.4, 45.6, 29.6, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for  $C_{21}H_{26}INO_7Na^+$  [ $M+Na^+$ ] 554.0646, found 554.0651.



**methyl (1R,2R)-2-((3',5'-diiodo-[1,1'-biphenyl]-2-yl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (5a)**

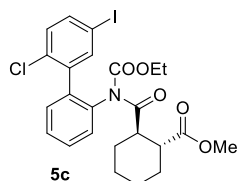
Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 38.2 mg, 58%. The two rotamers' ratio is about 92:8.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.04 (t,  $J = 1.6$  Hz, 0.1H), 8.01 (t,  $J = 1.6$  Hz, 0.83H), 7.57 (d,  $J = 1.6$  Hz, 0.19H), 7.50 (d,  $J = 1.6$  Hz, 1.73H), 7.45 – 7.35 (m, 2.06H), 7.30 – 7.25 (m, 1.11H), 7.23 – 7.17 (m, 0.91H), 4.12 – 3.92 (m, 2.04H), 3.73 (td,  $J = 11.4, 3.2$  Hz, 1.11H), 3.66 (s, 2.68H), 3.61 (s, 0.23H), 2.84 (td,  $J = 11.5, 3.9$  Hz, 0.92H), 2.66 (td,  $J = 11.5, 3.9$  Hz, 0.08H), 2.21 – 2.10 (m, 0.97H), 2.05 – 1.95 (m, 0.99H), 1.87 – 1.74 (m, 2.03H), 1.42 – 1.01 (m, 7.06H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  179.2, 175.9, 153.1, 144.2, 142.4, 137.5, 136.9, 136.3, 129.8, 129.4, 129.3, 128.6, 94.4, 63.2, 51.9, 46.4, 45.4, 29.8, 29.1, 25.7, 25.4, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for  $C_{24}H_{25}I_2NO_5Na^+$  [ $M+Na^+$ ] 683.9714, found 683.9703.



**methyl (1R,2R)-2-((ethoxycarbonyl)(2'-fluoro-5'-iodo-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylate (5b)**

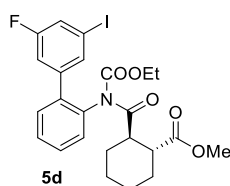
Purified by PTLC (preparative thin layer chromatography). White solid, M.p.: 163.6 – 165.4 °C; yield: 37.7 mg, 68%. The two rotamers' ratio is about 90:10.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.05 – 7.99

(m, 0.16H), 7.64 – 7.56 (m, 0.92H), 7.51 – 7.37 (m, 3.17H), 7.36 – 7.20 (m, 2.19H), 6.86 (t,  $J = 9.0$  Hz, 0.81H), 4.13 – 3.95 (m, 2.01H), 3.78 – 3.57 (m, 4.03H), 2.82 (td,  $J = 11.4, 3.8$  Hz, 0.90H), 2.73 – 2.63 (m, 0.10H), 2.19 – 2.08 (m, 0.97H), 1.98 – 1.71 (m, 3.20H), 1.42 – 1.22 (m, 3.26H), 1.18 – 1.02 (m, 3.94H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -116.0, -116.8.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  178.7, 175.9, 159.7 (d,  $J_{\text{C-F}} = 248.7$  Hz), 153.3, 146.5 (d,  $J_{\text{C-F}} = 20.0$  Hz), 139.8 (d,  $J_{\text{C-F}} = 3.0$  Hz), 138.6 (d,  $J_{\text{C-F}} = 7.9$  Hz), 136.9, 132.8, 130.7 (d,  $J_{\text{C-F}} = 20.0$  Hz), 129.6, 129.4, 128.2, 117.9 (d,  $J_{\text{C-F}} = 23.3$  Hz), 86.8 (d,  $J_{\text{C-F}} = 3.7$  Hz), 63.2, 51.9, 46.2, 45.3, 29.4, 29.1, 25.7, 25.4, 13.9. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{24}\text{H}_{25}\text{FINO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 576.0654, found 576.0650.



**methyl** **(1*R*,2*R*)-2-((2'-chloro-5'-iodo-[1,1'-biphenyl]-2-yl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (5c)**

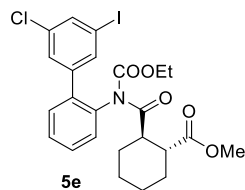
Purified by PTLC (preparative thin layer chromatography). Yellow solid, M.p.: 173.5 – 174.8 °C; yield: 39.8 mg, 70%. The two rotamers' ratio is about 71:29.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.60 – 7.53 (m, 1.04H), 7.50 – 7.37 (m, 3.04H), 7.35 – 7.30 (m, 1.00H), 7.28 – 7.22 (m, 1.02H), 7.18 – 7.12 (m, 0.95H), 4.21 (q,  $J = 7.1$  Hz, 0.45H), 4.15 – 4.06 (m, 0.75H), 3.95 – 3.84 (m, 1.04H), 3.75 – 3.59 (m, 4.10H), 2.86 (td,  $J = 11.5, 4.0$  Hz, 0.71H), 2.69 (td,  $J = 11.5, 3.7$  Hz, 0.29H), 2.20 – 2.12 (m, 0.71H), 2.11 – 2.05 (m, 0.29H), 1.95 – 1.87 (m, 0.72H), 1.86 – 1.72 (m, 1.47H), 1.62 – 1.54 (m, 0.3H), 1.43 – 1.18 (m, 5.63H), 1.10 (t,  $J = 7.1$  Hz, 2.21H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  179.2, 179.0, 177.1, 175.9, 153.6, 153.2, 139.6, 139.5, 139.2, 138.7, 138.3, 137.8, 136.5, 136.0, 135.9, 134.2, 133.2, 131.6, 131.3, 131.0, 130.8, 129.7, 129.6, 129.4, 128.0, 127.9, 91.2, 90.4, 63.4, 63.3, 51.9, 51.8, 46.2, 46.0, 45.4, 45.0, 29.8, 29.1, 28.6, 25.7, 25.6, 25.5, 25.3, 14.5, 13.9. HRMS (*m/z*, ESI-TOF): Calcd for  $\text{C}_{24}\text{H}_{25}\text{ClINO}_5\text{Na}^+$  [ $\text{M}+\text{Na}^+$ ] 592.0358, found 592.0358.



**methyl** **(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-fluoro-5'-iodo-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylate (5d)**

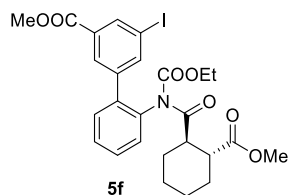
Purified by PTLC (preparative thin layer chromatography). White solid, M.p.: 80.1 – 82.0 °C; yield: 35.8 mg, 65%. The two rotamers' ratio is about 85:15.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.47 – 7.36 (m, 3.18H), 7.34 (t,  $J = 1.4$  Hz, 0.87H), 7.31 – 7.27 (m, 1.01H), 7.24 – 7.18 (m, 0.89H), 7.02 – 6.95 (m, 0.29H), 6.90 (dt,  $J = 9.3, 1.9$  Hz, 0.79H), 4.11 – 3.93 (m, 2.09H), 3.73 (td,  $J = 11.4, 3.2$  Hz, 0.99H), 3.66 (s, 2.53H), 3.62 (s, 0.46H), 2.82 (td,  $J = 11.4, 3.9$  Hz, 0.85H), 2.71 (td,  $J = 11.5, 3.5$  Hz, 0.15H), 2.22 – 2.03 (m, 1.15H), 2.03 – 1.90 (m, 0.87H), 1.86 – 1.73 (m, 2.01H), 1.42 – 1.24 (m, 3.23H), 1.18 – 1.01 (m, 3.99H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -110.45, -111.08.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  179.1, 175.9, 162.0 (d,  $J_{\text{C-F}} = 252.0$  Hz), 153.2, 142.4 (d,  $J_{\text{C-F}} = 8.1$  Hz), 137.8 (d,  $J_{\text{C-F}} = 2.0$  Hz), 136.3, 133.5 (d,  $J_{\text{C-F}} = 3.2$  Hz), 129.8, 129.38, 129.36, 128.6, 123.9 (d,  $J_{\text{C-F}} = 23.5$  Hz), 115.6 (d,  $J_{\text{C-F}}$

$-F = 21.8$  Hz), 93.2 (d,  $J_{C-F} = 8.5$  Hz), 63.2, 51.9, 46.3, 45.4, 29.2, 29.1, 25.7, 25.4, 14.2. HRMS (m/z, ESI-TOF): Calcd for  $C_{24}H_{25}FINO_5Na^+$  [ $M+Na^+$ ] 576.0654, found 576.0649.



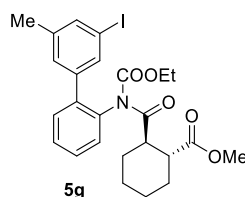
**methyl** **(1R,2R)-2-((3'-chloro-5'-iodo-[1,1'-biphenyl]-2-yl)(ethoxycarbonyl)carbamoyl)cyclohexane-1-carboxylate (5e)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 37.9 mg, 67%. The two rotamers' ratio is about 90:10.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.69 (t,  $J = 1.9$  Hz, 0.10H), 7.66 (t,  $J = 1.8$  Hz, 0.85H), 7.51 – 7.35 (m, 3.08H), 7.31 – 7.27 (m, 0.97H), 7.25 – 7.18 (m, 1.09H), 7.17 (t,  $J = 1.7$  Hz, 0.88H), 4.09 – 3.89 (m, 2.16H), 3.73 (td,  $J = 11.4, 3.2$  Hz, 0.99H), 3.66 (s, 2.63H), 3.60 (s, 0.27H), 2.84 (td,  $J = 11.3, 3.9$  Hz, 0.90H), 2.68 (td,  $J = 11.3, 3.4$  Hz, 0.10H), 2.21 – 2.09 (m, 1.03H), 2.02 – 1.92 (m, 0.93H), 1.87 – 1.73 (m, 2.05H), 1.43 – 1.21 (m, 3.26H), 1.22 – 1.02 (m, 4.08H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  179.2, 175.9, 153.1, 142.0, 137.6, 136.3, 136.1, 135.8, 134.7, 129.8, 129.4, 129.4, 128.6, 128.4, 93.7, 63.2, 51.9, 46.3, 45.4, 29.4, 29.1, 25.7, 25.4, 14.2. HRMS (m/z, ESI-TOF): Calcd for  $C_{24}H_{25}ClINO_5Na^+$  [ $M+Na^+$ ] 592.0358, found 592.0357.



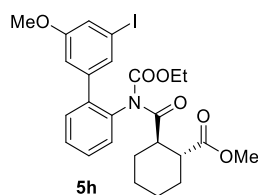
**methyl 2'-((1R,2R)-N-(ethoxycarbonyl)-2-(methoxycarbonyl)cyclohexane-1-carboxamido)-5-iodo-[1,1'-biphenyl]-3-carboxylate (5f)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 39.0 mg, 66%. The two rotamers' ratio is about 91:9.  $^1H$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.38 – 8.30 (m, 0.96H), 7.88 (t,  $J = 1.6$  Hz, 0.15H), 7.84 (t,  $J = 1.6$  Hz, 0.85H), 7.78 (t,  $J = 1.7$  Hz, 0.12H), 7.72 (t,  $J = 1.7$  Hz, 0.88H), 7.47 – 7.37 (m, 2.05H), 7.34 – 7.28 (m, 0.99H), 7.24 – 7.17 (m, 0.89H), 4.05 – 3.92 (m, 1.99H), 3.89 (s, 2.93H), 3.76 – 3.62 (m, 3.75H), 3.51 (s, 0.22H), 2.81 (td,  $J = 11.3, 3.8$  Hz, 0.91H), 2.62 (td,  $J = 11.3, 3.9$  Hz, 0.09H), 2.19 – 2.08 (m, 1.01H), 1.95 – 1.85 (m, 0.96H), 1.83 – 1.71 (m, 1.98H), 1.39 – 1.21 (m, 3.38H), 1.16 – 1.00 (m, 3.83H).  $^{13}C$  NMR (101 MHz, Chloroform-*d*)  $\delta$  179.1, 175.9, 165.4, 153.2, 141.6, 141.0, 138.0, 137.6, 136.3, 131.8, 129.9, 129.4, 129.3, 129.2, 128.6, 93.5, 63.2, 52.5, 51.9, 46.3, 45.4, 29.4, 29.1, 25.7, 25.4, 14.1. HRMS (m/z, ESI-TOF): Calcd for  $C_{26}H_{28}INO_7Na^+$  [ $M+Na^+$ ] 616.0803, found 616.0796.



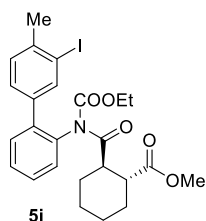
**methyl** **(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-iodo-5'-methyl-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylate (5g)**

Purified by PTLC (preparative thin layer chromatography). White solid, M.p.: 87.4 – 88.5 °C; yield: 36.5 mg, 66%. The two rotamers' ratio is about 87:13. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.51 (s, 0.13H), 7.49 (s, 0.86H), 7.42 – 7.27 (m, 4.02H), 7.21 – 7.16 (m, 0.86H), 7.08 (s, 0.13H), 7.02 – 6.94 (m, 0.98H), 4.06 – 3.89 (m, 2.22H), 3.72 (td, *J* = 11.4, 3.2 Hz, 1.03H), 3.67 (s, 2.60H), 3.61 (s, 0.35H), 2.83 (td, *J* = 11.4, 3.8 Hz, 0.87H), 2.73 (td, *J* = 11.4, 3.7 Hz, 0.13H), 2.38 (s, 0.32H), 2.27 (s, 2.674H), 2.20 – 2.04 (m, 1.18H), 2.02 – 1.94 (m, 0.87H), 1.87 – 1.71 (m, 2.07H), 1.41 – 1.26 (m, 3.16H), 1.18 – 0.99 (m, 4.00H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 179.1, 175.9, 153.3, 140.6, 139.9, 139.0, 137.2, 136.3, 134.6, 130.0, 129.2, 128.9, 128.8, 128.5, 94.0, 63.0, 51.9, 46.3, 45.4, 29.3, 29.1, 25.7, 25.4, 21.0, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>25</sub>H<sub>28</sub>INO<sub>5</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 572.0904, found 572.0900.



**methyl** **(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-iodo-5'-methoxy-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylate (5h)**

Purified by PTLC (preparative thin layer chromatography). Pale yellow sticky oil; yield: 36.3 mg, 64%. The two rotamers' ratio is about 88:12. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.34 (m, 2.02H), 7.33 – 7.27 (m, 0.98H), 7.24 – 7.15 (m, 2.01H), 7.12 (s, 0.83H), 6.79 (s, 0.12H), 6.71 (s, 0.84H), 4.07 – 3.97 (m, 1.92H), 3.79 (s, 0.36H), 3.70 (d, *J* = 35.2 Hz, 6.19H), 3.57 (s, 0.29H), 2.81 (td, *J* = 11.4, 3.8 Hz, 0.88H), 2.68 (td, *J* = 11.5, 3.7 Hz, 0.12H), 2.21 – 2.07 (m, 1.01H), 2.01 – 1.91 (m, 0.90H), 1.87 – 1.72 (m, 2.02H), 1.41 – 1.25 (m, 3.16H), 1.20 – 1.01 (m, 3.95H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 179.0, 175.9, 159.8, 153.3, 141.7, 138.8, 136.3, 129.9, 129.2, 128.9, 128.5, 122.1, 114.6, 93.9, 63.1, 55.6, 51.9, 46.3, 45.4, 29.3, 29.2, 25.7, 25.4, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>25</sub>H<sub>28</sub>INO<sub>6</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 588.0854, found 588.0851.

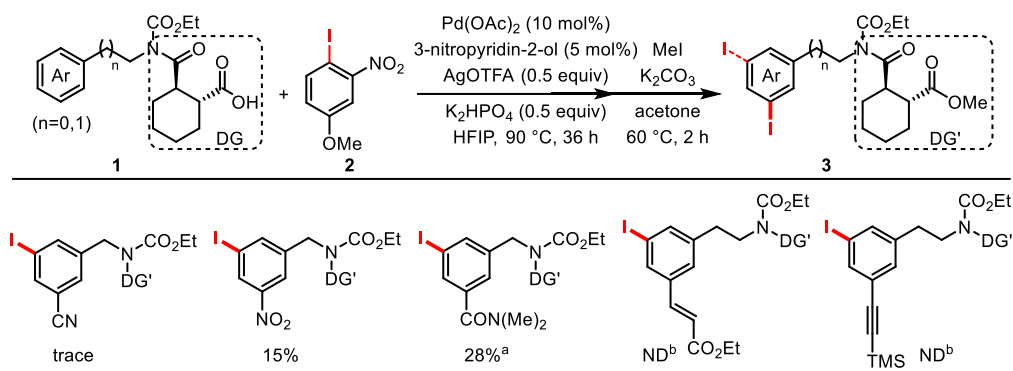


**methyl** **(1*R*,2*R*)-2-((ethoxycarbonyl)(3'-iodo-4'-methyl-[1,1'-biphenyl]-2-yl)carbamoyl)cyclohexane-1-carboxylate (5i)**

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 26.0 mg, 47%. The two rotamers' ratio is about 83:17. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 1.8 Hz, 0.14H), 7.64 (d, *J* = 1.7 Hz, 0.77H), 7.42 – 7.33 (m, 2.15H), 7.33 – 7.27 (m, 0.98H), 7.22 – 7.14 (m, 1.83H), 7.08 (dd, *J* = 7.8, 1.8 Hz, 0.83H), 7.03 – 6.98 (m, 0.17H), 4.05 – 3.90 (m, 2.18H), 3.77 – 3.64 (m, 3.44H), 3.63 (s, 0.45H), 2.88 – 2.72 (m, 1.05H), 2.50 – 2.36 (m, 2.97H), 2.20 – 2.05 (m, 1.17H), 2.02 – 1.94 (m, 0.83H), 1.86 – 1.73 (m, 1.99H), 1.42 – 1.23 (m, 3.27H), 1.17 – 0.97 (m, 3.96H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 179.1, 175.9, 153.4, 140.7, 138.7, 138.1, 136.4, 130.1, 129.3, 129.2, 128.7, 128.6, 128.5,

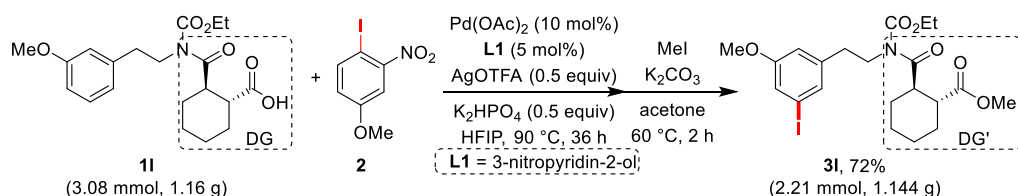
100.8, 63.1, 51.9, 46.3, 45.5, 29.3, 29.2, 27.9, 25.7, 25.4, 14.2. HRMS ( $m/z$ , ESI-TOF): Calcd for  $C_{25}H_{28}INO_5Na^+$  [ $M+Na^+$ ] 572.0904, found 572.0903.

## 2.4 Unsuccessful substrates



Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), Pd(OAc)<sub>2</sub> (0.01 mmol), 3-nitropyridin-2-ol (0.005 mmol), AgOTFA (0.05 mmol), K<sub>2</sub>HPO<sub>4</sub> (0.05 mmol), HFIP (1.0 mL), 90 °C, 36 h; Then MeI (0.1 mL), K<sub>2</sub>CO<sub>3</sub> (0.5 mmol), acetone (2.0 mL), 60 °C, 2 h. <sup>a</sup>15% unknown iodinated product was detected. <sup>b</sup>most starting material decomposed.

## 2.5 Gram-scale synthesis

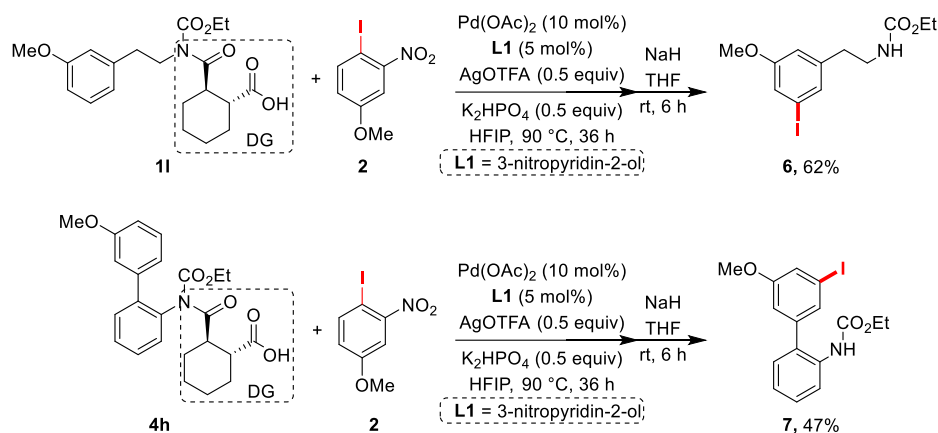


To an oven-dried 120 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with **11** (1.16 g, 3.08 mmol, 1 equiv), 4-iodo-3-nitroanisole (2.57 g, 9.24 mmol, 3 equiv), Pd(OAc)<sub>2</sub> (70 mg, 0.31 mmol, 10 mol%), **L1** (3-nitropyridin-2-ol, 21.6 mg, 0.15 mmol, 5 mol%), AgOTFA (339 mg, 1.54 mmol, 0.5 equiv) and K<sub>2</sub>HPO<sub>4</sub> (268 mg, 1.54 mmol, 0.5 equiv) sequentially. HFIP (30 mL) was added to the mixture along the inside wall of the tube. The tube was then capped and placed into a preheated oil bath (90 °C). The reaction was stirred for 36 h and cooled to room temperature. After the solvent was removed under reduced pressure, MeI (2 mL, 30.8 mmol, 10 equiv), K<sub>2</sub>CO<sub>3</sub> (2.1 g, 15.4 mmol, 5 equiv) were added sequentially. Acetone (45 mL) was added to the mixture along the inside wall of the tube. The mixture was stirred at 60 °C for 2 h and then cooled to room temperature. The crude reaction mixture was diluted with EA (20 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 150 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by flash silica gel chromatography using PE/EA (40/1 to 20/1) as the eluent to give the desired product (**31**).

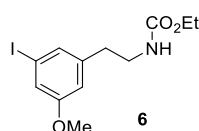


## 2.6 Removal of Directing Group (DG)

### 2.6.1 Hydrolysis DG by a one-pot protocol:

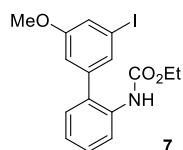


To an oven-dried 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with substrate **11** or **4h** (0.2 mmol, 1 equiv), 4-iodo-3-nitroanisole (168 mg, 0.6 mmol, 3 equiv), Pd(OAc)<sub>2</sub> (4.5 mg, 0.02 mmol, 10 mol%), **L1** (3-nitropyridin-2-ol, 1.4 mg, 0.01 mmol, 5 mol%), AgOTFA (22 mg, 0.1 mmol, 0.5 equiv) and K<sub>2</sub>HPO<sub>4</sub> (17.4 mg, 0.1 mmol, 0.5 equiv) sequentially. HFIP (2 mL) was added to the mixture along the inside wall of the tube. The tube was then capped and placed into a preheated oil bath (90 °C) or hotplate (90 °C). The reaction was stirred for 36 h and cooled to room temperature. Then the volatile matter was removed under reduced pressure, NaH (as a 60% dispersion in mineral oil, 1 mmol, 5 equiv) was added, THF (3 mL) was charged follow and stirred at room temperature for another 6 h, The crude reaction mixture was diluted with EA (5 mL) and filtered through a short pad of silica gel. The sealed tube and silica gel pad were washed with an additional 25 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by preparative thin layer chromatography using PE/EA (15/1) as the eluent to give the desired product.



#### ethyl (3-iodo-5-methoxyphenethyl)carbamate (**6**)

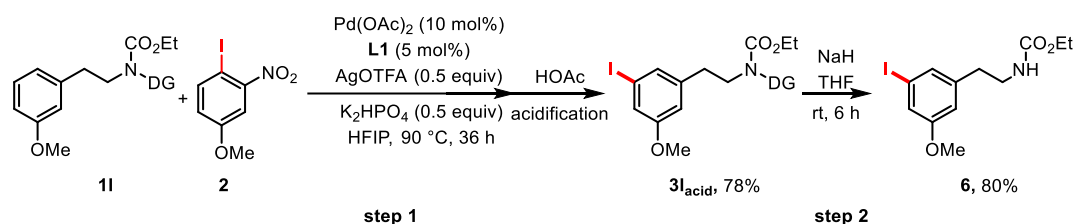
Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 43.4 mg, 62%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.12 (s, 1H), 7.09 (s, 1H), 6.67 (s, 1H), 4.76 (s, 1H), 4.09 (q,  $J = 7.2$  Hz, 2H), 3.75 (s, 3H), 3.38 (q,  $J = 6.8$  Hz, 2H), 2.71 (t,  $J = 7.1$  Hz, 2H), 1.22 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  160.3, 156.7, 142.3, 130.3, 121.1, 114.6, 94.6, 60.9, 55.5, 41.9, 35.8, 14.7. HRMS (m/z, ESI-TOF): Calcd for C<sub>12</sub>H<sub>16</sub>INO<sub>3</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 372.0067, found 372.0067.



#### ethyl (3'-iodo-5'-methoxy-[1,1'-biphenyl]-2-yl)carbamate (**7**)

Purified by PTLC (preparative thin layer chromatography). Colorless sticky oil; yield: 37.1 mg, 47%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.36 (td, *J* = 8.0, 1.7 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.85 (s, 1H), 6.55 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 160.4, 153.7, 141.2, 134.9, 130.6, 129.9, 129.1, 123.5, 122.8, 120.4 – 119.8 (m), 114.8, 95.2, 61.4, 55.7, 14.7. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>16</sub>H<sub>16</sub>INO<sub>3</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 420.0067, found 420.0067.

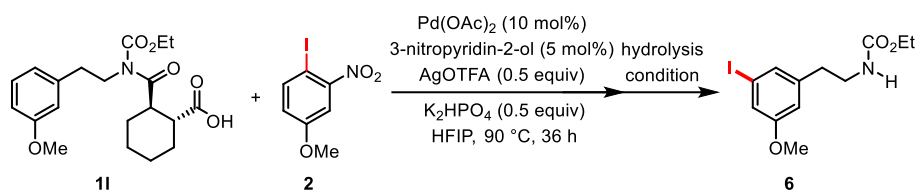
### 2.6.2 Hydrolysis by a stepwise protocol:



**Step 1:** To an oven-dried 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with substrate **11** (0.1 mmol, 1 equiv), 4-iodo-3-nitroanisole (84 mg, 0.3 mmol, 3 equiv), Pd(OAc)<sub>2</sub> (2.3 mg, 0.01 mmol, 10 mol%), **L1** (3-nitropyridin-2-ol, 0.7 mg, 0.005 mmol, 5 mol%), AgOTFA (11 mg, 0.05 mmol, 0.5 equiv) and K<sub>2</sub>HPO<sub>4</sub> (8.72 mg, 0.05 mmol, 0.5 equiv) sequentially. HFIP (1 mL) was added to the mixture along the inside wall of the tube. The tube was then capped and placed into a preheated hotplate (90 °C). The reaction was stirred for 36 h and cooled to room temperature. Then, acidize by HOAc (50 μl) with stirred for another 10 min. The crude reaction mixture was diluted with EA (5 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 25 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by preparative thin layer chromatography using PE/EA (5/1 and 0.5% of HOAc) as the eluent to give the desired product **3<sub>acid</sub>**. Brown sticky oil; yield: 39.3 mg, 78%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.12 (s, 1H), 7.08 (s, 1H), 6.68 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.94 – 3.80 (m, 2H), 3.74 (s, 3H), 3.65 (td, *J* = 11.3, 3.2 Hz, 1H), 2.82 (td, *J* = 11.4, 3.6 Hz, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.22 – 2.03 (m, 2H), 1.87 – 1.73 (m, 2H), 1.40 – 1.24 (m, 6H), 1.22 – 1.11 (m, 1H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 181.5, 178.2, 160.2, 154.0, 142.3, 130.5, 121.2, 114.5, 94.4, 63.1, 55.5, 46.3, 45.6, 45.4, 34.4, 29.5, 29.2, 25.7, 25.5, 14.2. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>20</sub>H<sub>25</sub>INO<sub>6</sub><sup>-</sup> [*M*-H<sup>+</sup>] 502.0732, found 502.0738.

**Step 2:** To an oven-dried 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with **3<sub>acid</sub>** (0.066 mmol, 1 equiv), NaH (as a 60% dispersion in mineral oil, 0.33 mmol, 5 equiv) was added, THF (1.5 mL) was charged follow and stirred at room temperature for 6 h, The crude reaction mixture was diluted with EA (5 mL) and filtered through a short pad of silica gel. The sealed tube and silica gel pad were washed with an additional 25 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by preparative thin layer chromatography using PE/EA (15/1) as the eluent to give the desired product **6** (18.5 mg, 80%).

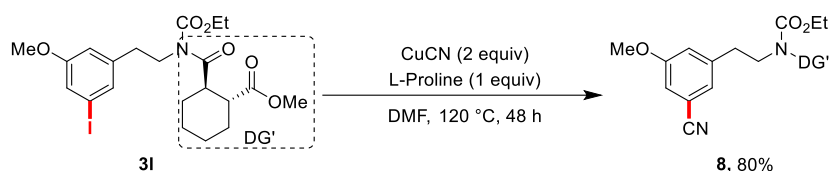
### 2.6.3 Other hydrolysis conditions by one-pot protocol:



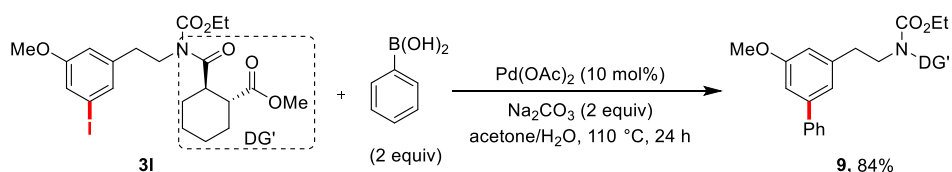
entry	acid or base	solvent	T	<i>t</i>	<b>6</b> (%)
1	K <sub>2</sub> CO <sub>3</sub>	THF	rt	6 h	ND
2	KOH	THF	rt	6 h	34
3	KOH	MeOH	110 °C	24 h	trace
4	conc. HCl	MeOH	110 °C	24 h	40

The experimental procedures were similar to **2.6.1**, entry 4 should alkalization before filtration. Yield was determined by <sup>1</sup>H NMR with CH<sub>2</sub>Br<sub>2</sub> as internal standard. ND = no product detected.

## 2.7 Further elaborations

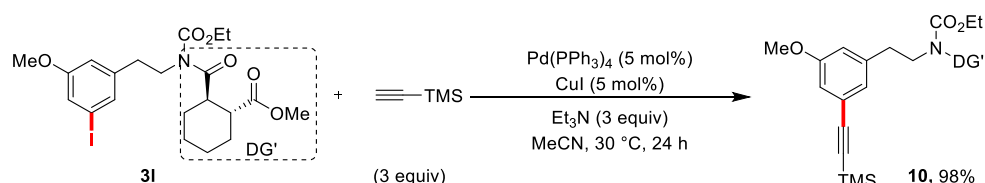


To an oven-dried 38 mL sealed tube equipped with a magnetic stir bar was charged with **31** (51.7 mg, 0.1 mmol), CuCN (17.9 mg, 0.2 mmol), L-Proline (11.5 mg, 0.1 mmol) and DMF (1 mL). Then the tube was capped and placed into a preheated hotplate (120 °C). The reaction was stirred for 48 h and cooled to room temperature. The mixture was filtered through a short pad of Celite. The filtrate was concentrated under vacuum. Afterwards, the residue was purified by preparative thin layer chromatography using PE/EA (10/1) as the eluent to afford **8**. Colorless sticky oil; yield: 33.3 mg, 80%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.09 (s, 1H), 6.99 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.82 (m, 2H), 3.81 (s, 3H), 3.67 (td, *J* = 11.4, 3.2 Hz, 1H), 3.63 (s, 3H), 2.87 – 2.70 (m, 3H), 2.19 – 2.02 (m, 2H), 1.88 – 1.72 (m, 2H), 1.37 – 1.17 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 159.9, 153.9, 142.2, 125.1, 120.0, 118.9, 115.1, 113.1, 63.1, 55.7, 51.8, 46.5, 45.6, 45.4, 34.5, 29.6, 29.2, 25.7, 25.5, 14.3. HRMS (*m/z*, ESI-TOF): Calcd for C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub>Na<sup>+</sup> [*M*+Na<sup>+</sup>] 439.1840, found 439.1842.



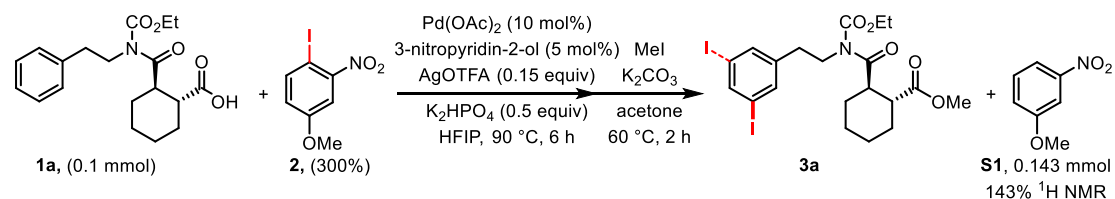
To an oven-dried Schlenk tube equipped with a magnetic stir bar was charged with **31** (51.7 mg, 0.1 mmol), benzoic acid (25 mg, 0.2 mmol), Pd(OAc)<sub>2</sub> (2.2 mg, 0.01 mmol) and Na<sub>2</sub>CO<sub>3</sub> (21.2 mg, 0.2 mmol) under Ar atmosphere. Then acetone/H<sub>2</sub>O (0.5 mL/0.5 mL) was added and the reaction was heated at 110 °C for 24 h. After cooled to room temperature, the mixture was diluted with H<sub>2</sub>O (5 mL) and the aqueous phase was extracted with EA (5 mL × 3). The combined organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated under reduced pressure. Afterwards, the residue was purified by preparative thin layer chromatography using PE/EA (10/1) as the eluent to afford **9**. Colorless sticky oil; yield: 39.2 mg,

84%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.03 (s, 1H), 6.98 (s, 1H), 6.77 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.98 (hept, *J* = 6.9, 6.4 Hz, 2H), 3.85 (s, 3H), 3.73 (td, *J* = 11.2, 3.2 Hz, 1H), 3.64 (s, 3H), 2.85 (q, *J* = 7.7 Hz, 3H), 2.13 (t, *J* = 6.8 Hz, 2H), 1.87 – 1.74 (m, 2H), 1.40 – 1.21 (m, 7H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 160.1, 154.2, 142.9, 141.1, 141.0, 128.8, 127.5, 127.3, 120.6, 113.4, 111.1, 63.0, 55.4, 51.8, 46.6, 46.0, 45.7, 35.1, 29.6, 29.3, 25.7, 25.5, 14.2. HRMS (m/z, ESI-TOF): Calcd for C<sub>27</sub>H<sub>33</sub>NO<sub>6</sub>Na<sup>+</sup> [M+Na<sup>+</sup>] 490.2200, found 490.2206.



To an oven-dried Schlenk tube equipped with a magnetic stir bar was charged with **31** (51.7 mg, 0.1 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (5.8 mg, 0.005 mmol) and CuI (1.0 mg, 0.005 mmol) under Ar atmosphere. Then anhydrous MeCN (1 mL), Et<sub>3</sub>N (42 μL, 0.3 mmol) and trimethylsilylacetylene (42 μL, 0.3 mmol) was added sequentially to the mixture. The reaction was stirred at 30 °C for 24 h. The mixture was filtered through a short pad of Celite and the filtrate was concentrated under vacuum. Afterwards, the residue was purified by preparative thin layer chromatography using PE/EA (10/1) as the eluent to afford **10**. Colorless sticky oil; yield: 47.6 mg, 98%. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 6.92 (s, 1H), 6.82 (s, 1H), 6.71 (s, 1H), 4.23 – 4.11 (m, 2H), 3.95 – 3.82 (m, 2H), 3.76 (s, 3H), 3.68 (td, *J* = 11.2, 3.2 Hz, 1H), 3.62 (s, 3H), 2.82 (td, *J* = 11.3, 3.8 Hz, 1H), 2.71 (t, *J* = 7.7 Hz, 2H), 2.10 (dd, *J* = 10.5, 5.1 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.38 – 1.18 (m, 7H), 0.23 (s, 9H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 178.4, 175.9, 159.4, 154.1, 140.5, 125.3, 124.0, 116.2, 114.6, 105.1, 93.9, 63.0, 55.4, 51.8, 46.5, 45.7, 45.7, 34.6, 29.6, 29.3, 25.7, 25.5, 14.2, 0.1. HRMS (m/z, ESI-TOF): Calcd for C<sub>26</sub>H<sub>37</sub>NO<sub>6</sub>SiNa<sup>+</sup> [M+Na<sup>+</sup>] 510.2282, found 510.2281.

## 2.8 The reduced (C–I → C–H) by-product from iodinating reagents



To an oven-dried 38 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with substrate **1a** (0.1 mmol, 1 equiv), 4-iodo-3-nitroanisole (84 mg, 0.3 mmol, 3 equiv), Pd(OAc)<sub>2</sub> (2.3 mg, 0.01 mmol, 10 mol%), **L1** (3-nitropyridin-2-ol, 0.7 mg, 0.005 mmol, 5 mol%), AgOTFA (11 mg, 0.05 mmol, 0.5 equiv) and K<sub>2</sub>HPO<sub>4</sub> (8.72 mg, 0.05 mmol, 0.5 equiv) sequentially. HFIP (1 mL) was added to the mixture along the inside wall of the tube. The tube was then capped and placed into a preheated hotplate (90 °C). The reaction was stirred for 36 h and cooled to room temperature. After the solvent was removed under reduced pressure, MeI (0.1 mL), K<sub>2</sub>CO<sub>3</sub> (70 mg, 0.5 mmol, 5 equiv) were added sequentially. Acetone (2 mL) was added to the mixture along the inside wall of the tube. The mixture was stirred at 60 °C for 2 h and then cooled to room temperature. The crude reaction mixture was diluted with EA (5 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad

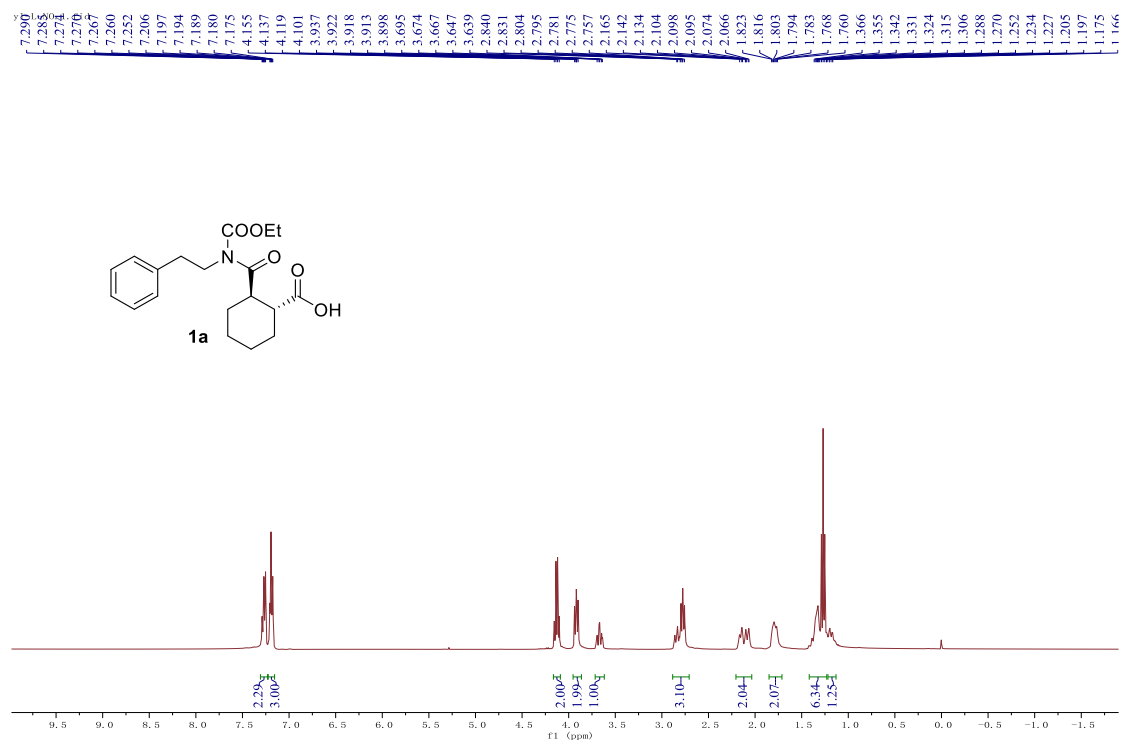
were washed with an additional 25 mL of EA. The filtrate was concentrated in vacuo, and the resulting residue was purified by preparative thin layer chromatography using PE/EA (30/1) as the eluent to give product **S1**. Yellow sticky oil; yield: 15mg, 98% (part of **S1** might be removed in vacuo). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.73 (t, *J* = 2.3 Hz, 1H), 7.43 (t, *J* = 8.2 Hz, 1H), 7.23 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.89 (s, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 160.2, 149.3, 130.1, 121.5, 115.9, 108.2, 56.0. The data are consistent with reference<sup>[S4]</sup>.

## 2.9 References

- [S1] A. Berkessel, K. Glaubitz, J. Lex, Enantiomerically Pure β-Amino Acids: A Convenient Access to Both Enantiomers of trans-2-Aminocyclohexanecarboxylic Acid, *Eur. J. Org. Chem.* **2002**, 2948-2952.
- [S2] S. S. Kinderman, M. M. Wekking, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. Rutjes, Catalytic *N*-sulfonyliminium ion-mediated cyclizations to alpha-vinyl-substituted isoquinolines and beta-carbolines and applications in metathesis, *J. Org. Chem.*, 2005, **70**, 5519-5527.
- [S3] C. Liu, Y. Zhang, N. Liu, J. Qiu, A simple and efficient approach for the palladium-catalyzed ligand-free Suzuki reaction in water, *Green Chem.*, 2012, **14**, 2999-3003.
- [S4] H. Yang, Y. Li, M. Jiang, J. Wang, H. Fu, General copper-catalyzed transformations of functional groups from arylboronic acids in water, *Chem. Eur. J.*, 2011, **17**, 5652-5660.

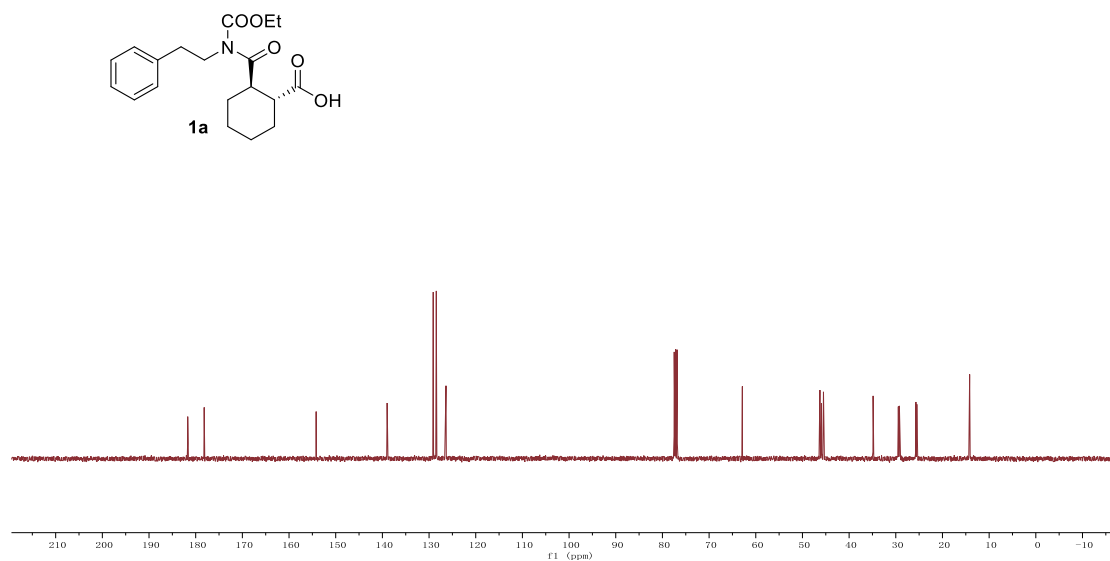
### 3. NMR spectra of compounds

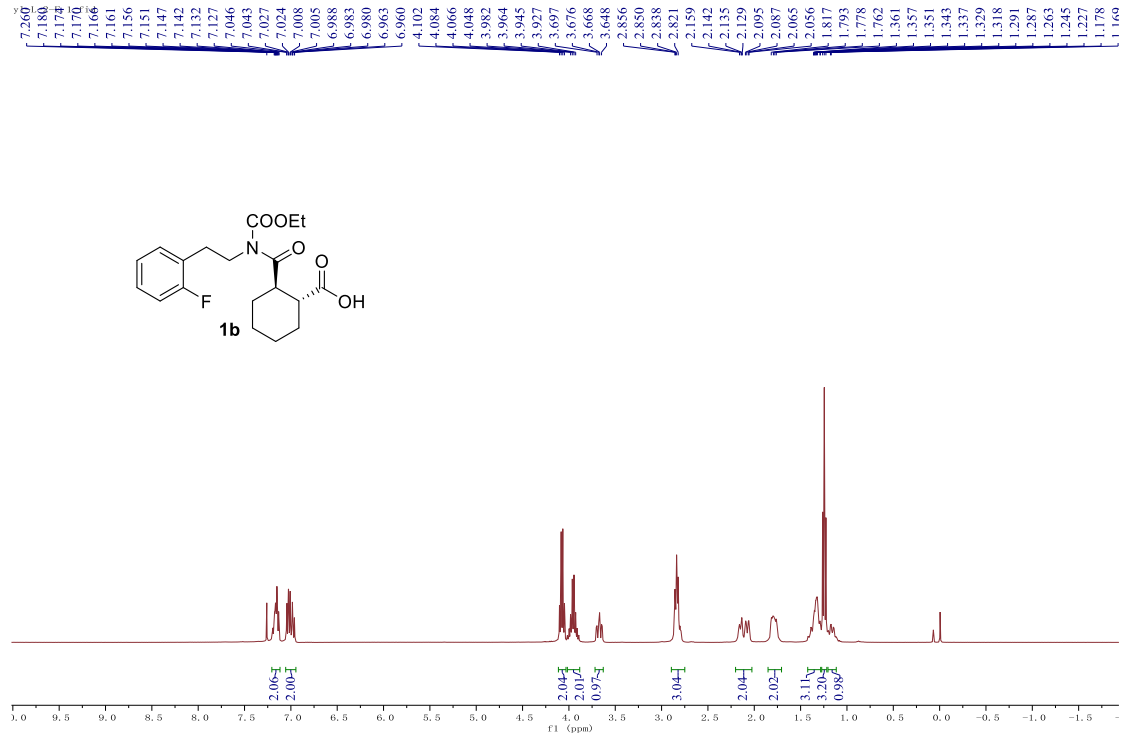
#### 3.1 NMR spectra of substrates



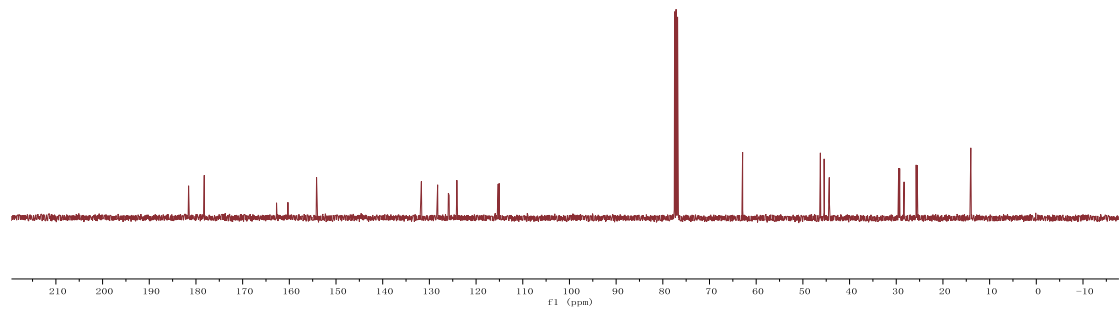
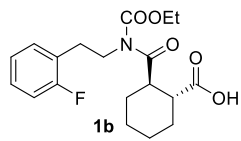
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128.450  
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77.478  
77.160  
76.842  
62.877  
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45.494  
34.860  
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25.491  
14.174

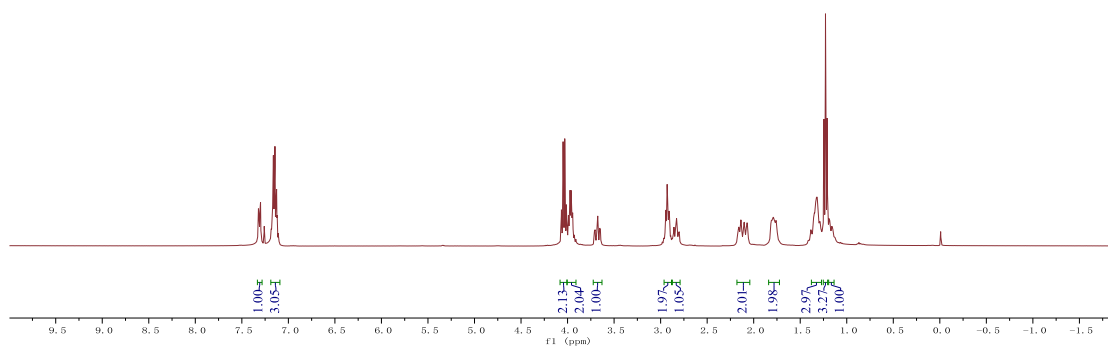
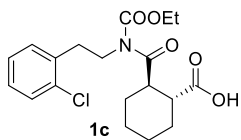




y1-L-2-F. 4. f14

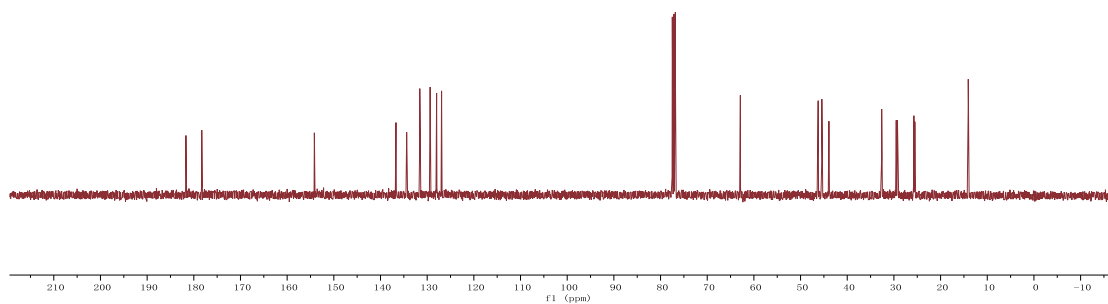
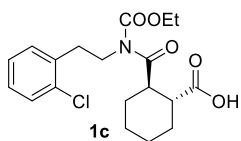


7.332  
7.316  
7.313  
7.306  
7.292  
7.259  
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7.161  
7.150  
7.144  
7.135  
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4.030  
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3.980  
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2.069  
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1.789  
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1.759  
1.751  
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1.336  
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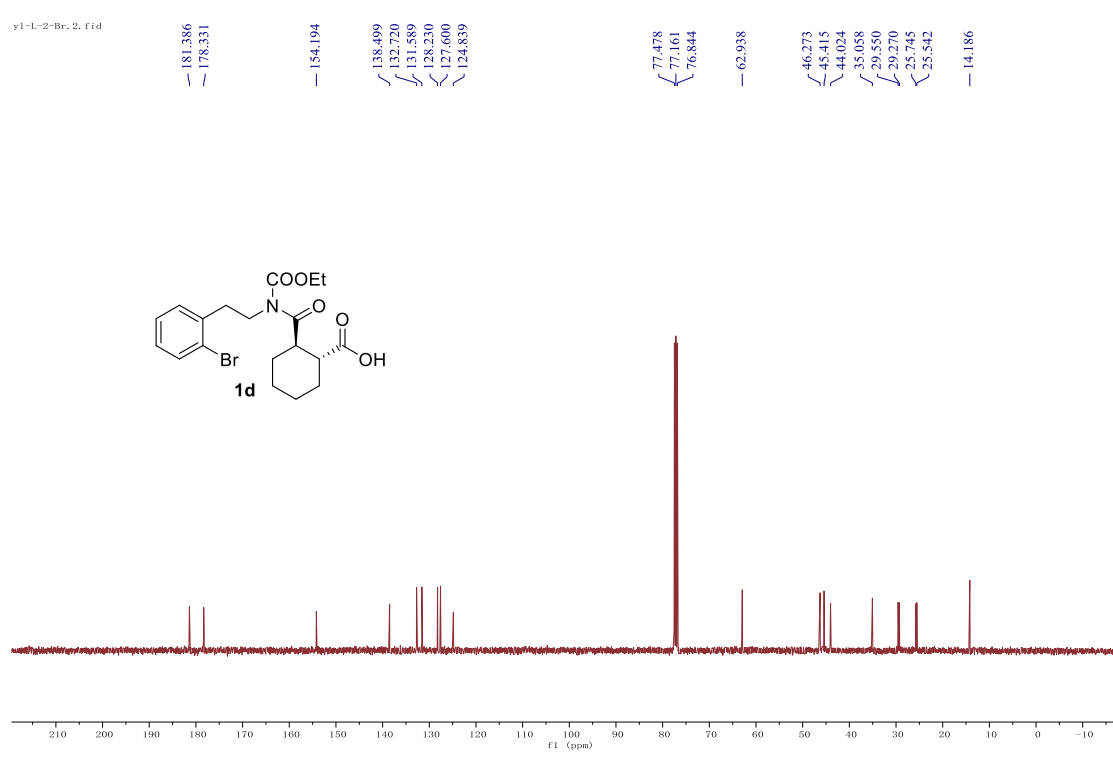
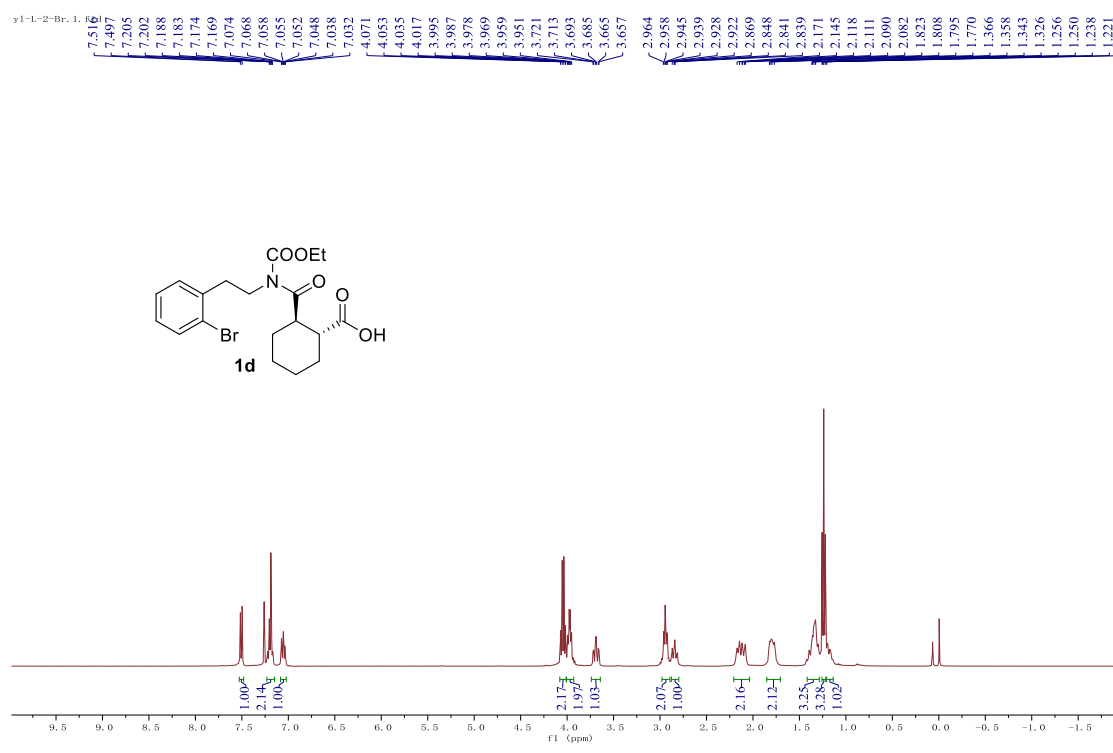


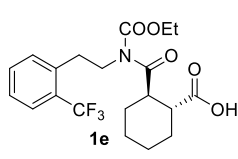
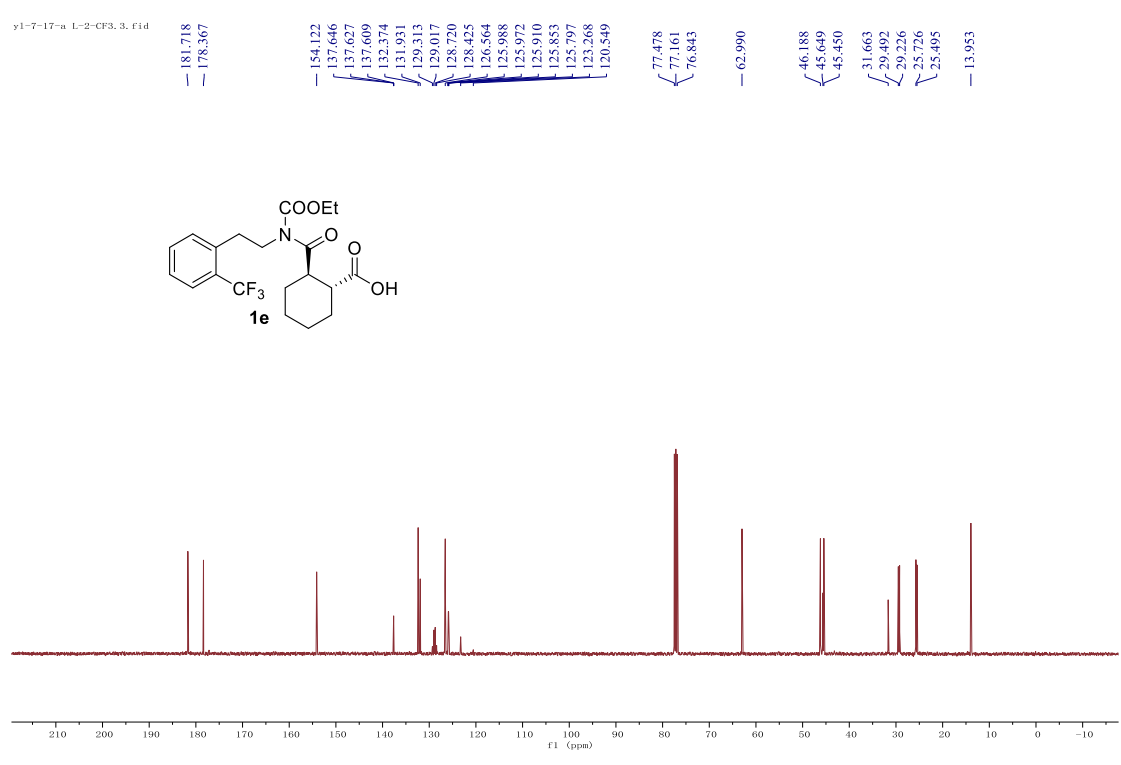
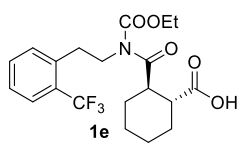
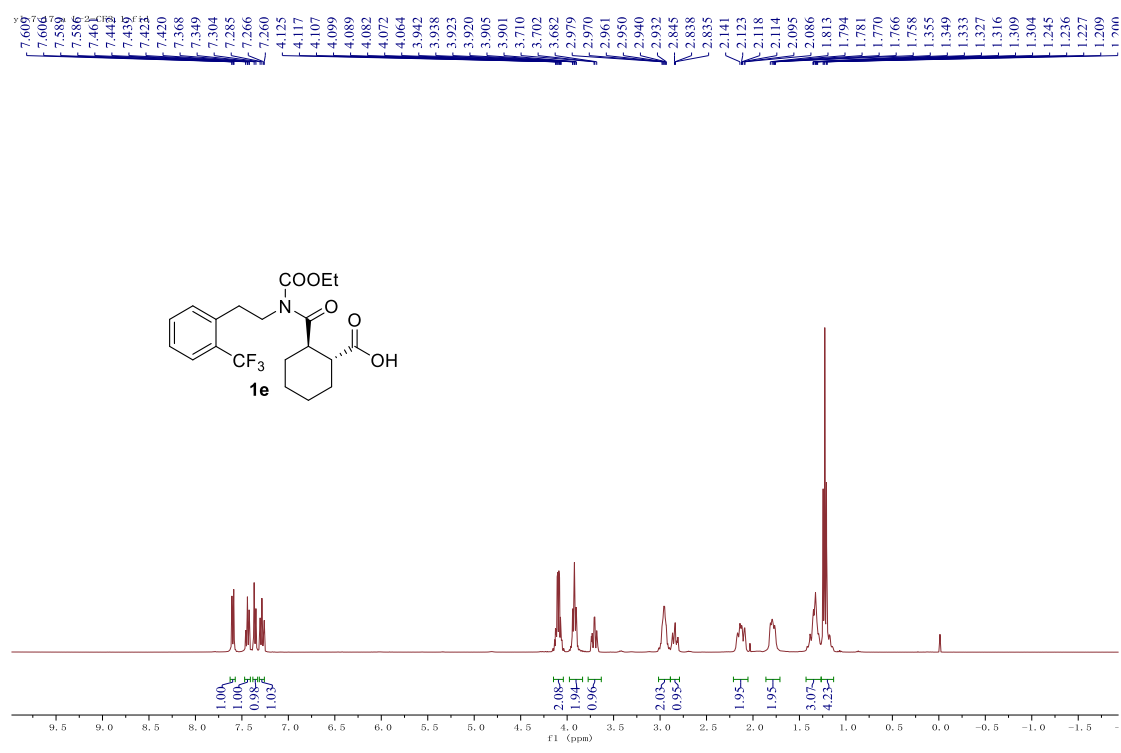
y1-L-2-C1.2, Fid

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62.898  
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45.442  
43.924  
32.617  
29.501  
29.246  
25.719  
25.513  
14.069

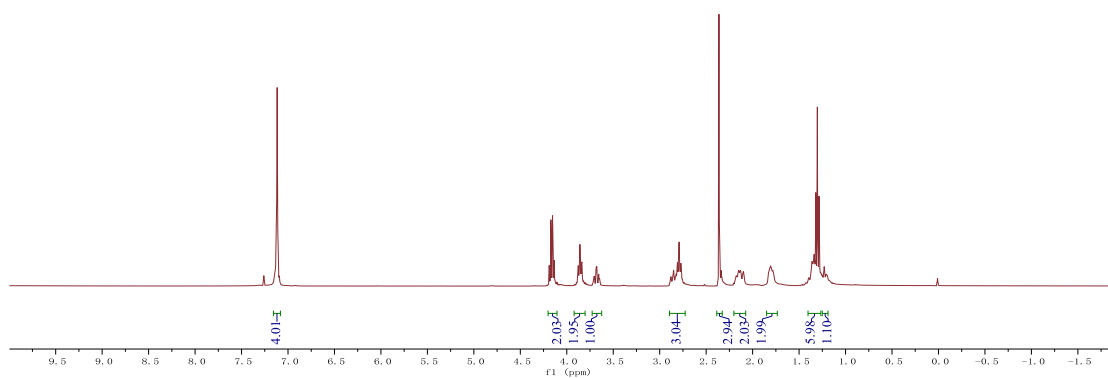
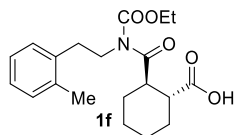






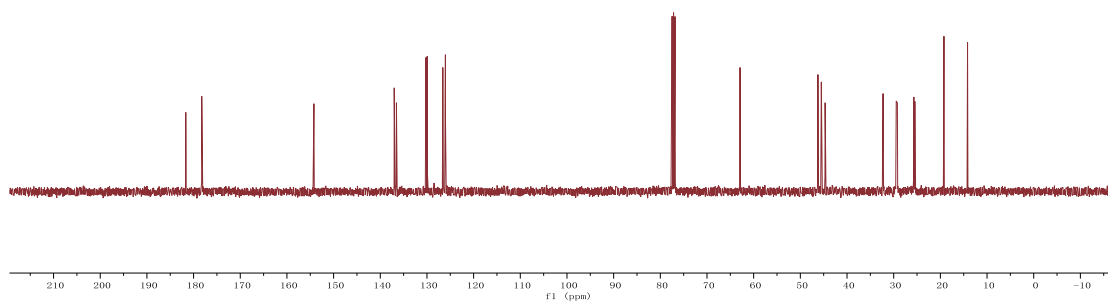
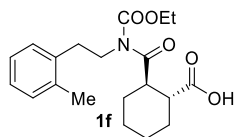


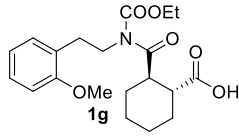
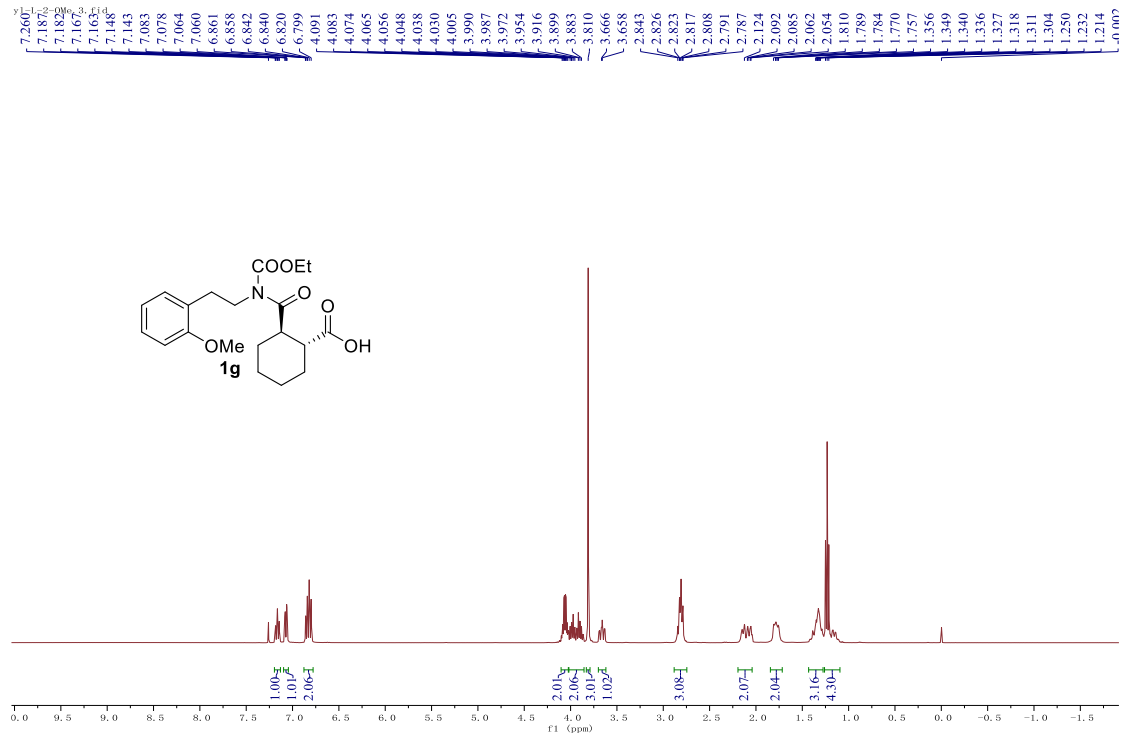
7.145  
7.140  
7.137  
7.134  
7.132  
7.116  
7.108  
7.104  
4.189  
4.171  
4.153  
3.881  
3.876  
3.867  
3.859  
3.851  
3.842  
3.837  
3.685  
3.677  
3.657  
2.859  
2.851  
2.848  
2.822  
2.813  
2.808  
2.800  
2.791  
2.783  
2.775  
2.769  
2.362  
2.355  
2.338  
2.156  
2.152  
2.145  
2.133  
2.126  
2.106  
2.098  
1.831  
1.825  
1.816  
1.804  
1.781  
1.773  
1.366  
1.362  
1.338  
1.321  
1.303  
1.286  
1.286  
1.277  
1.267  
1.258  
1.248  
1.237  
1.230  
1.212  
1.206  
1.197



y1-L-2-Me. 2. Fid

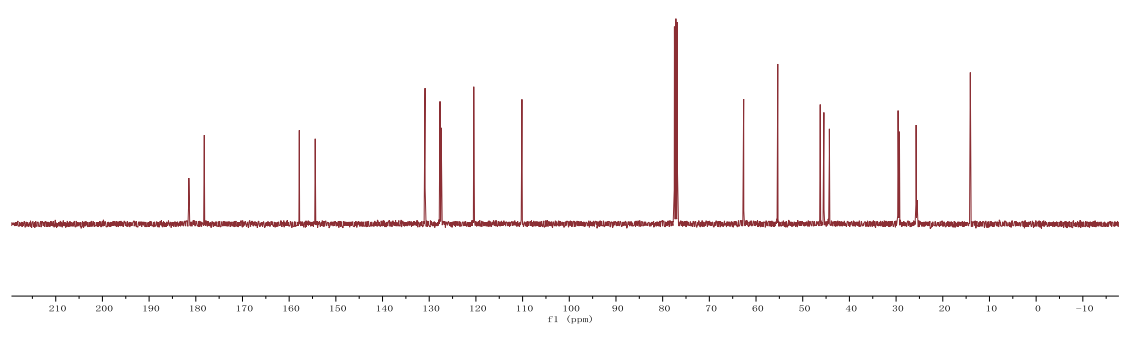
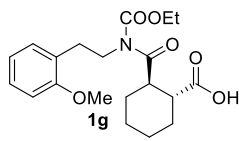
181.672  
178.248  
154.216  
137.012  
136.538  
130.219  
129.955  
126.600  
126.047  
77.479  
77.161  
76.842  
62.919  
46.228  
45.507  
44.690  
32.277  
29.451  
29.207  
25.678  
25.463  
19.228  
14.176

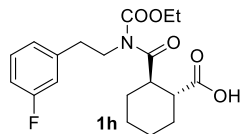
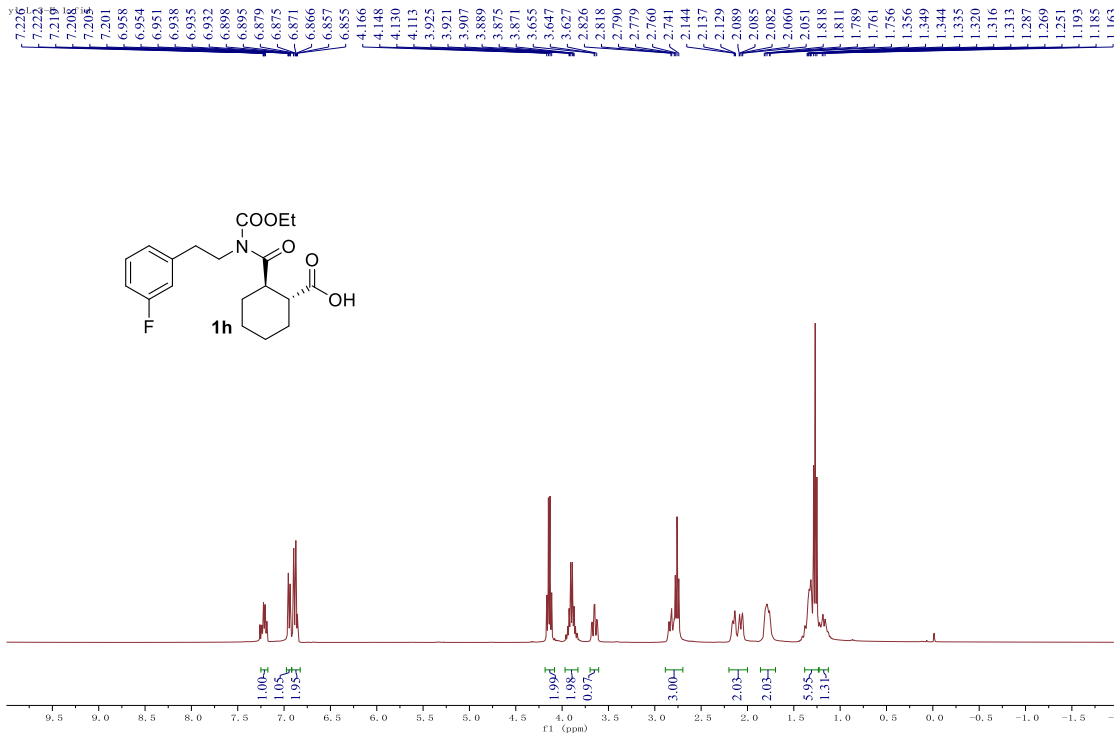




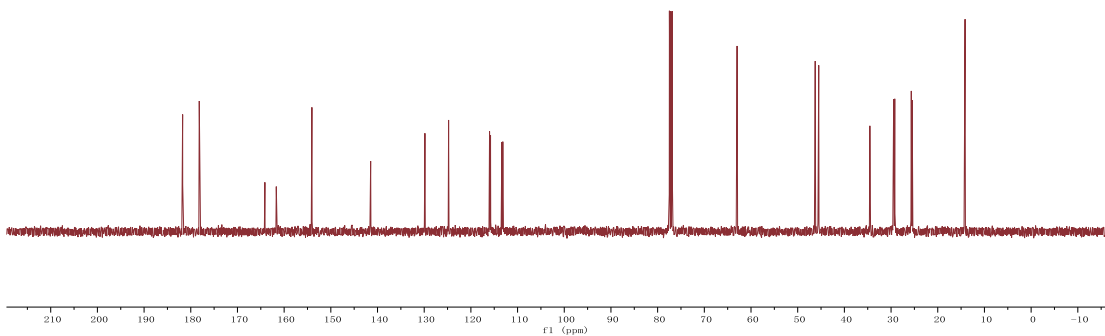
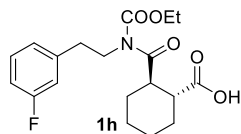
y1-L-2-OMe\_4.fid

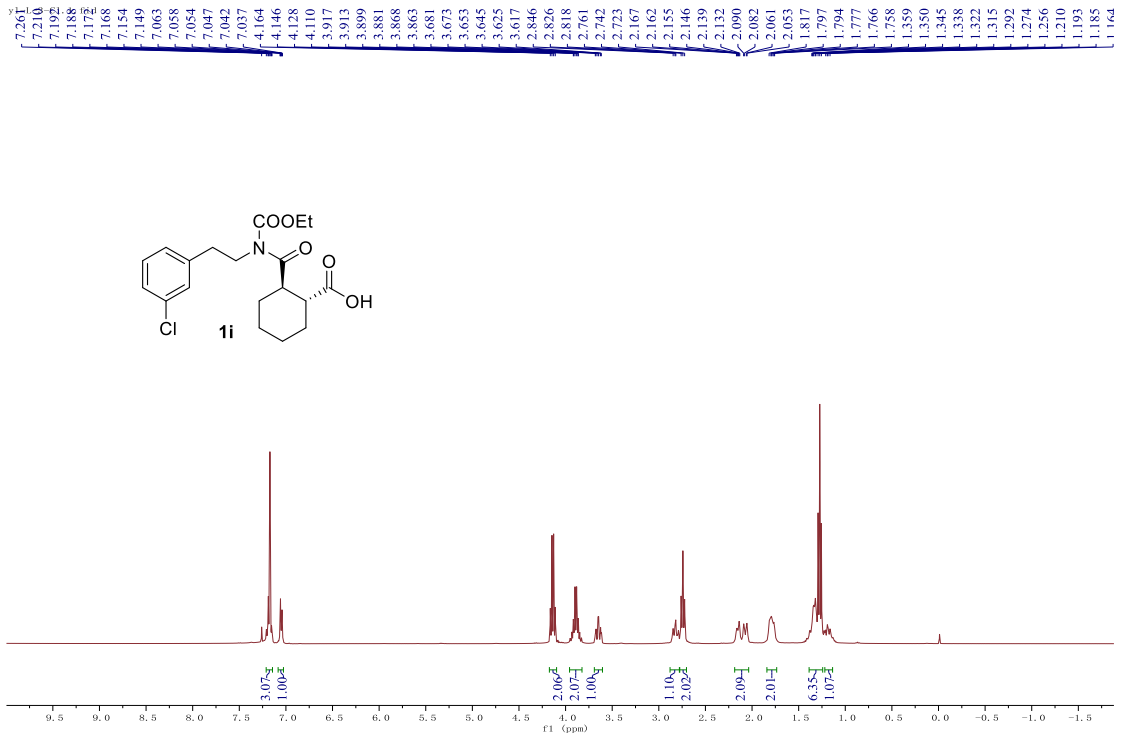
- 181.486
- 178.183
- 157.831
- 154.421
- 130.896
- 127.690
- 127.444
- 120.455
- 110.137
- 77.478
- 77.160
- 76.843
- 62.648
- 55.340
- 46.252
- 45.466
- 44.290
- 29.573
- 29.492
- 29.285
- 25.713
- 25.534
- 14.101



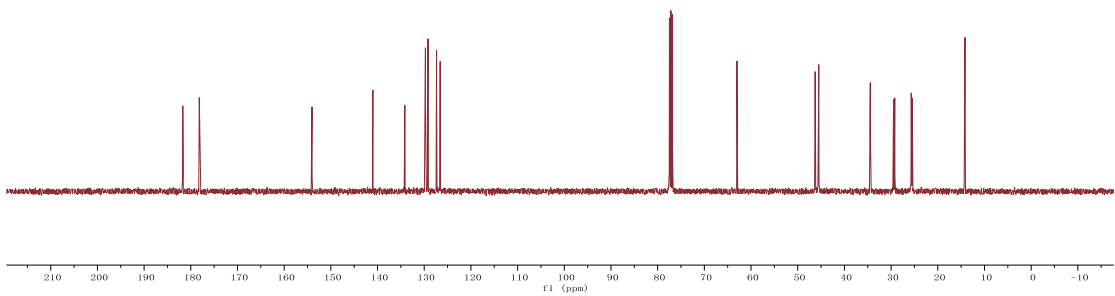
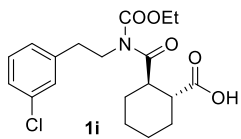


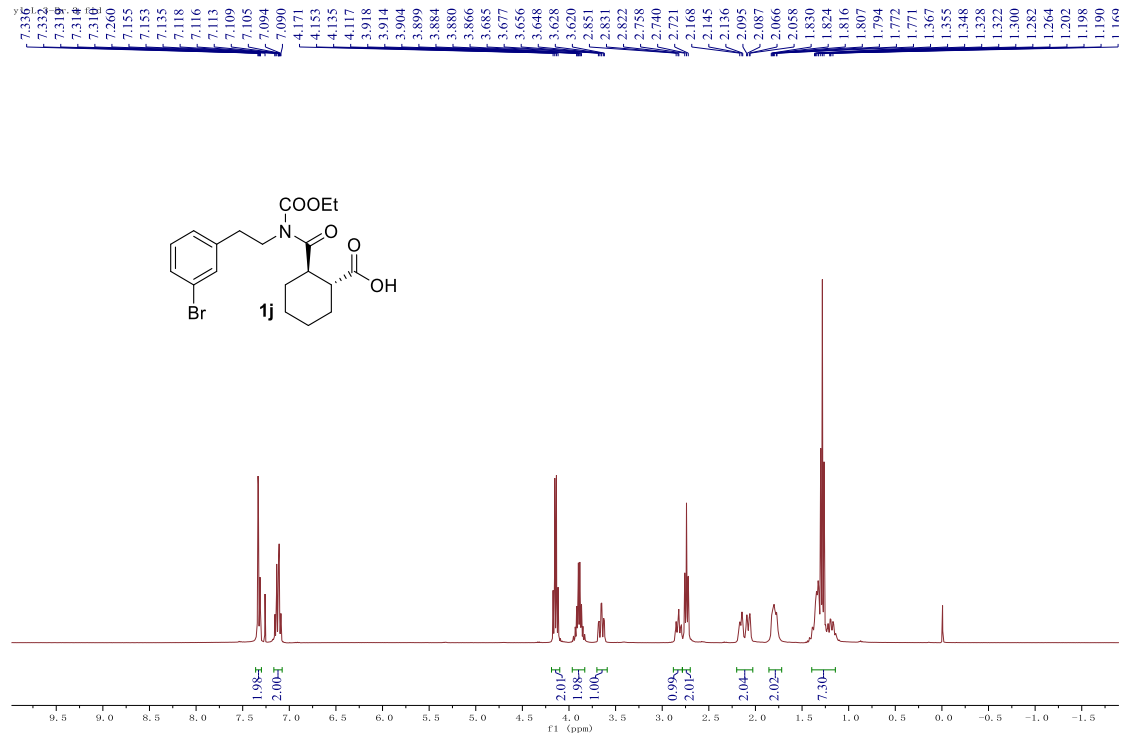
y1-L-3-F. 3. f14





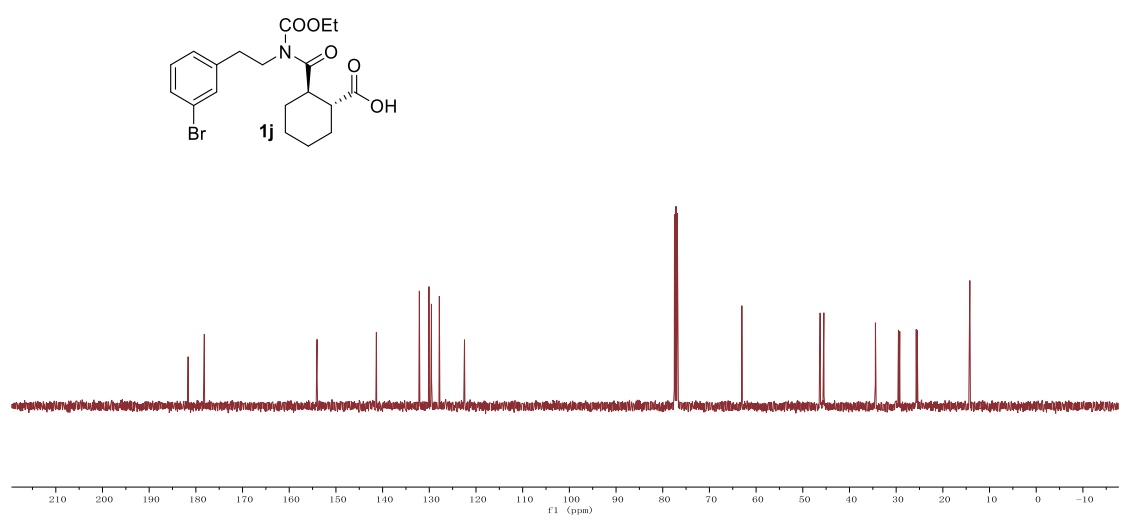
y1-L-3-C1.2.fid

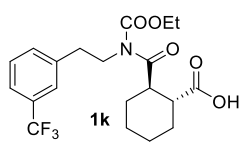
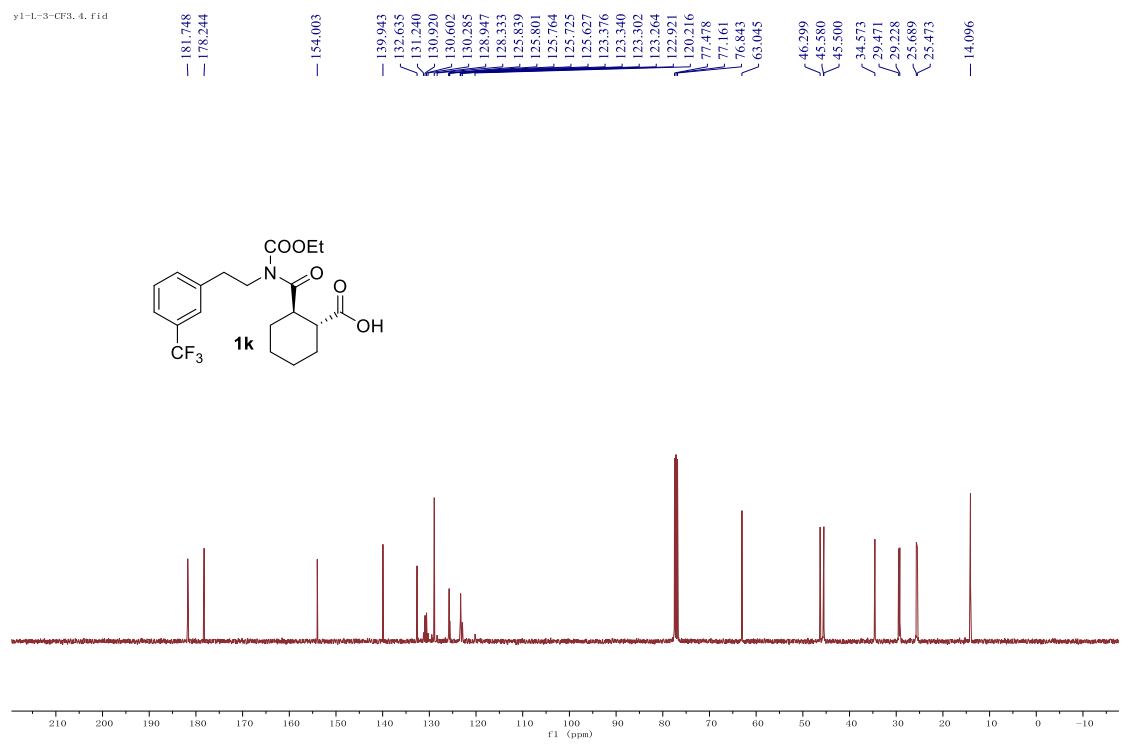
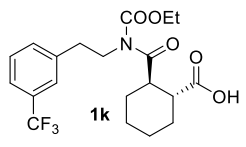
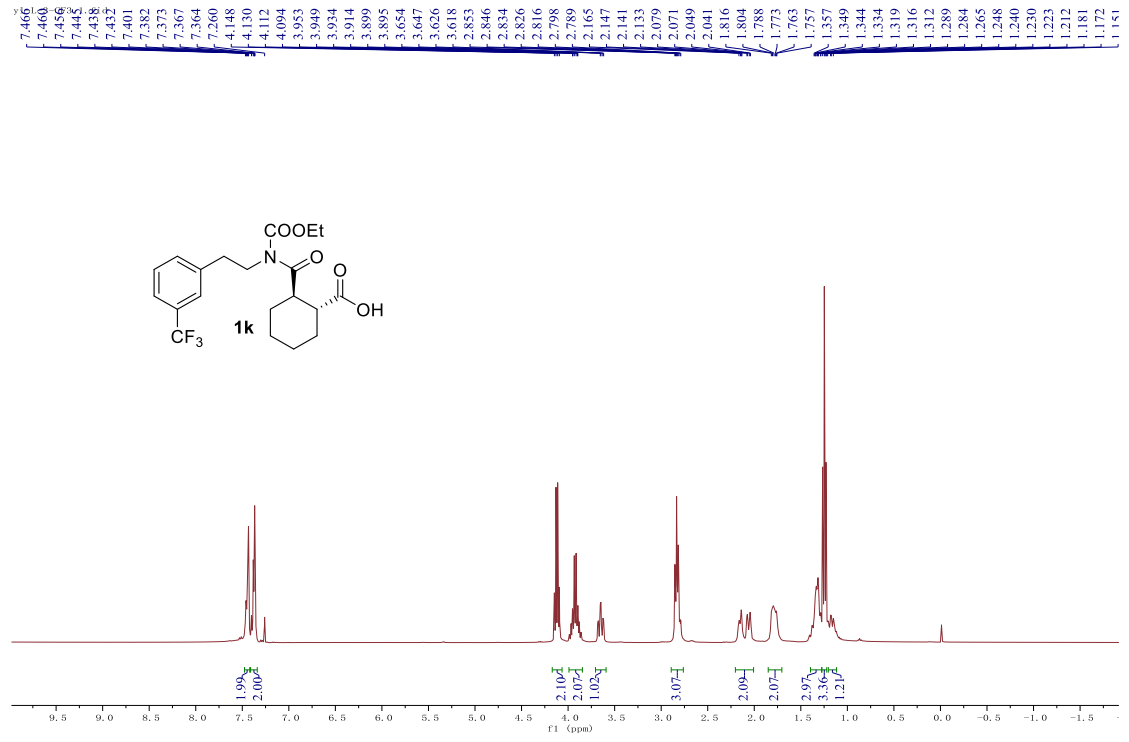




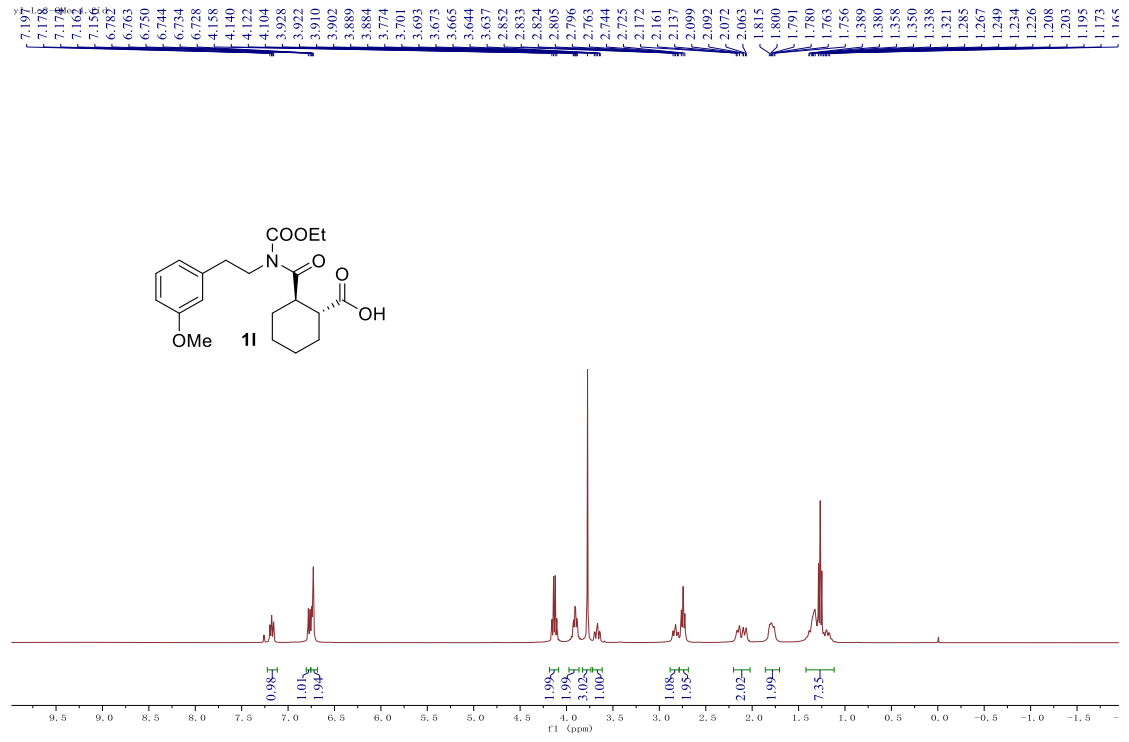
y1-L-3-Br. 2. f1d

- 181.666
- 178.188
- 154.039
- 141.329
- 132.124
- 130.073
- 129.538
- 127.848
- 122.459
- 77.478
- 77.160
- 76.843
- 63.048
- 46.288
- 45.617
- 45.483
- 34.441
- 29.506
- 29.228
- 25.698
- 25.503
- 14.218



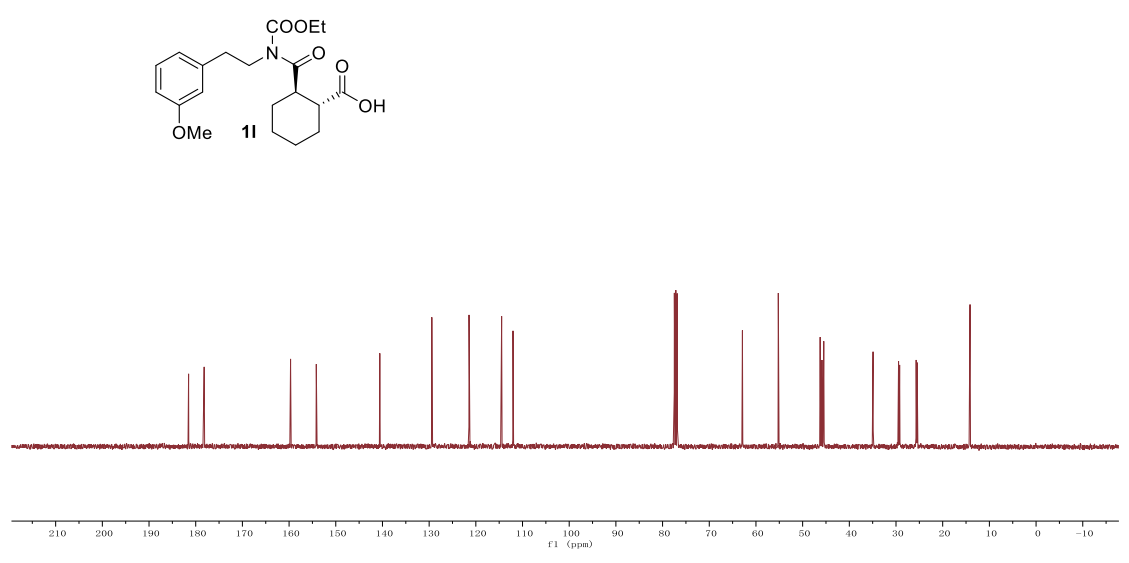


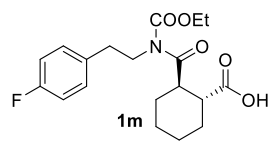
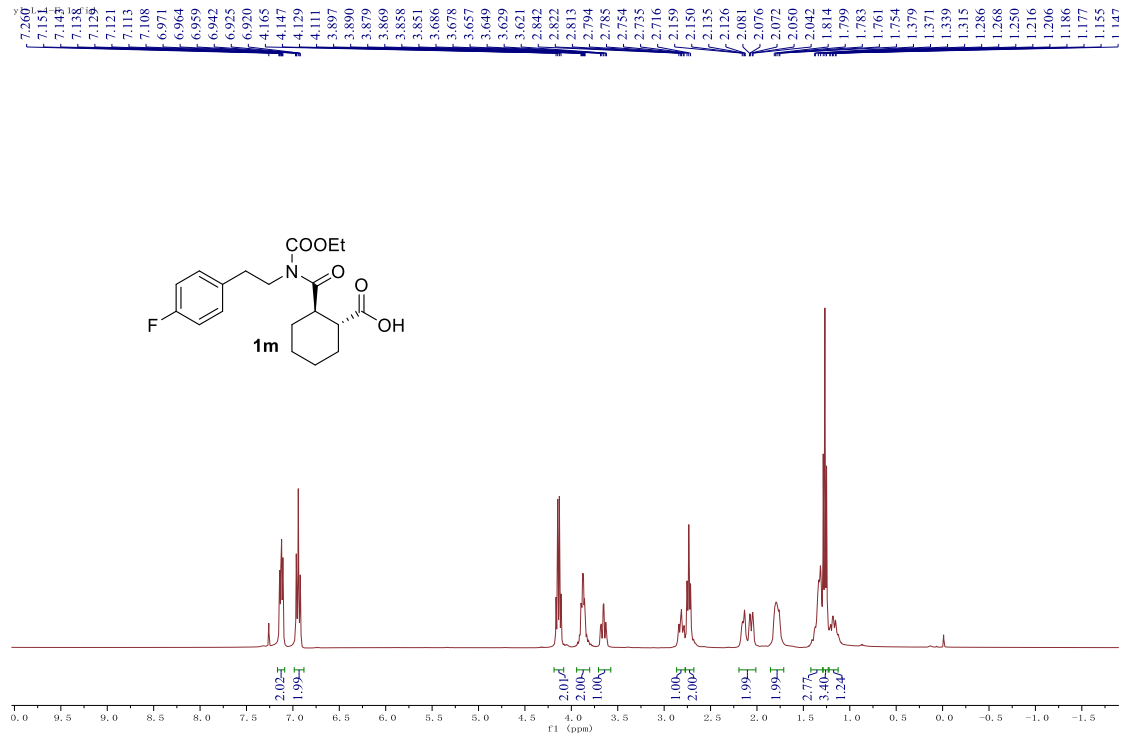




y1-L-3-OMe. 3. fid

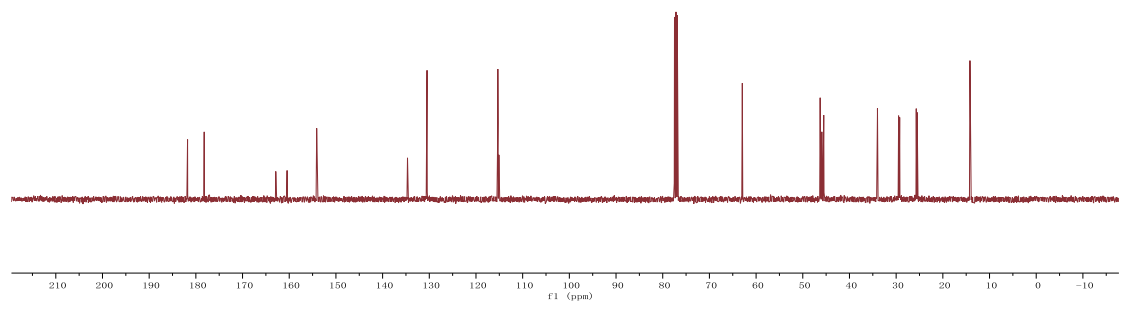
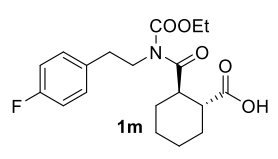
- 181.524
- 178.191
- 159.683
- 154.174
- 140.566
- 129.424
- 121.455
- 114.471
- 112.039
- 77.479
- 77.161
- 76.843
- 62.898
- 55.216
- 46.247
- 45.864
- 45.473
- 34.914
- 29.454
- 29.221
- 25.681
- 25.478
- 14.142

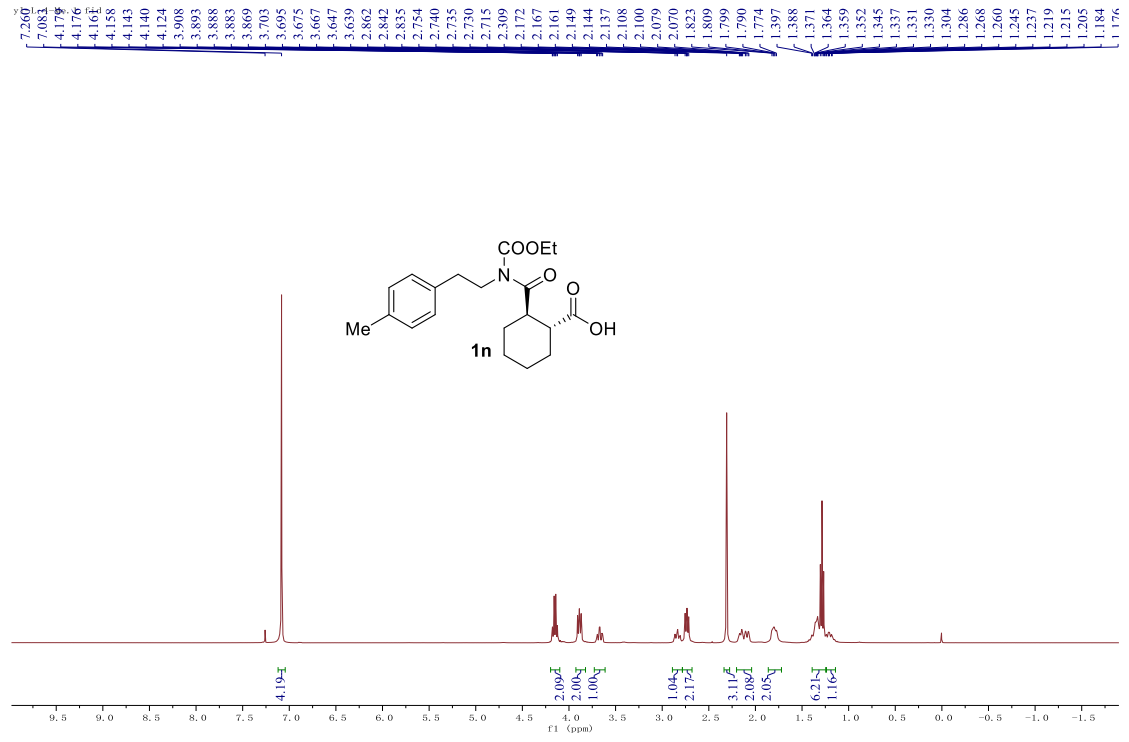




y1-L-4-F. 3. f1d

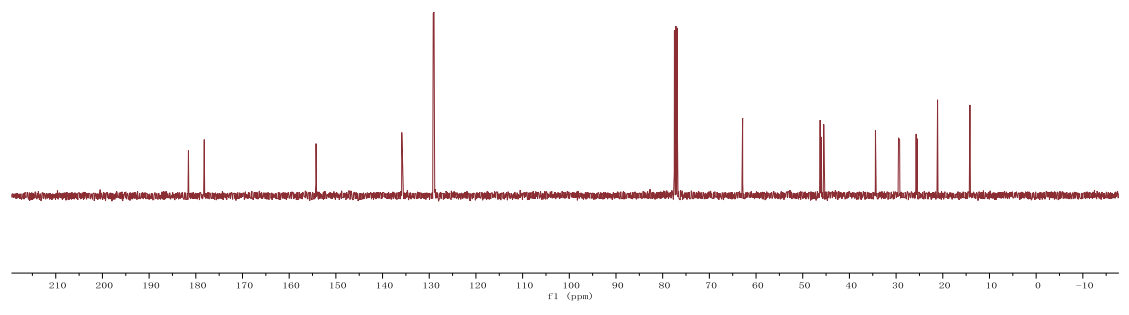
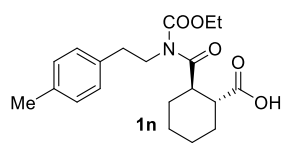
- 181.781
- 178.212
- 162.883
- 160.458
- 154.118
- 134.665
- 134.633
- 130.361
- 130.484
- 115.314
- 115.104
- 77.478
- 77.160
- 76.842
- 62.953
- 46.278
- 45.917
- 45.508
- 34.002
- 29.473
- 29.243
- 25.695
- 25.493
- 14.191



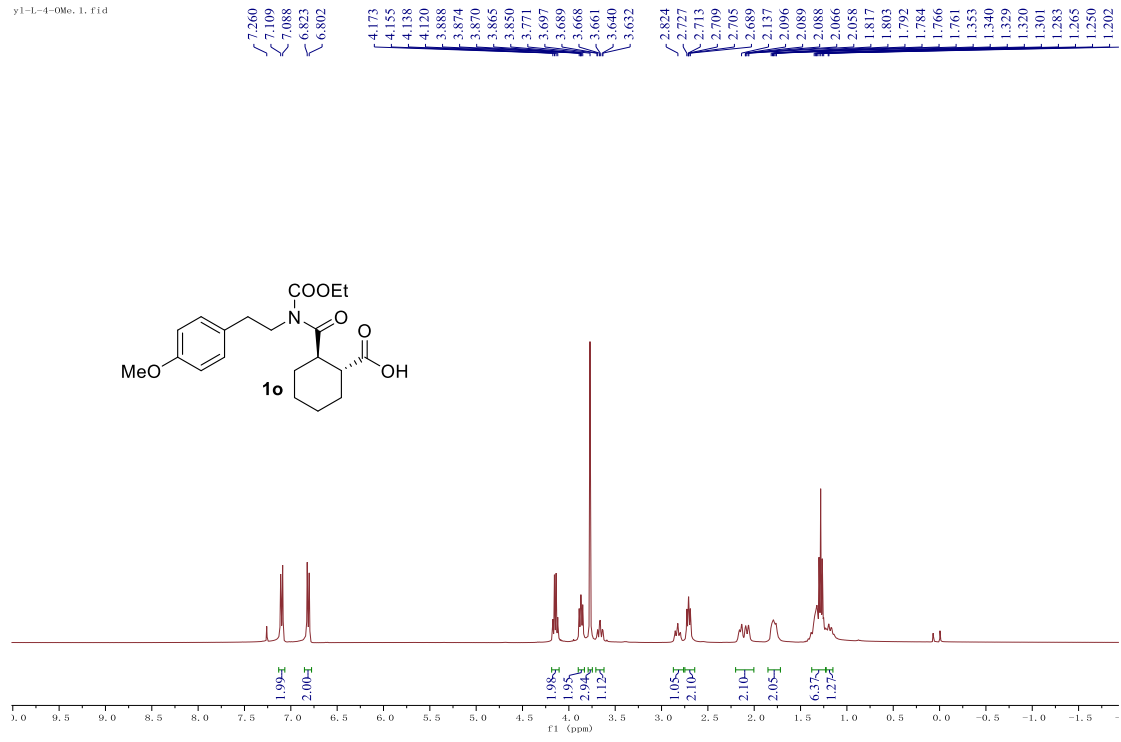


y1-L-4-Me, 2, f1d

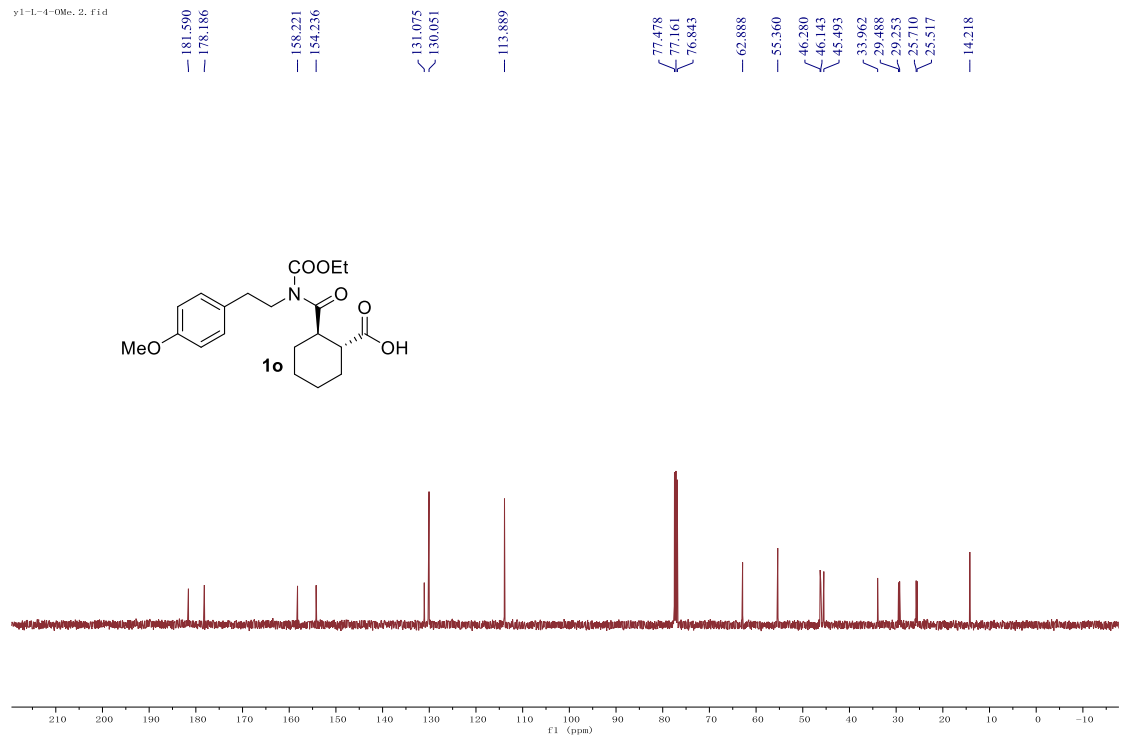
- 181.575
- 178.190
- 154.241
- 135.879
- 135.836
- 129.143
- 128.973
- 77.479
- 77.160
- 76.842
- 62.875
- 46.274
- 46.074
- 45.501
- 34.421
- 29.481
- 29.248
- 25.709
- 25.512
- 21.122
- 14.188

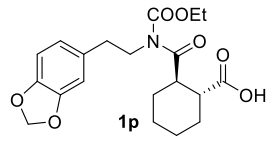
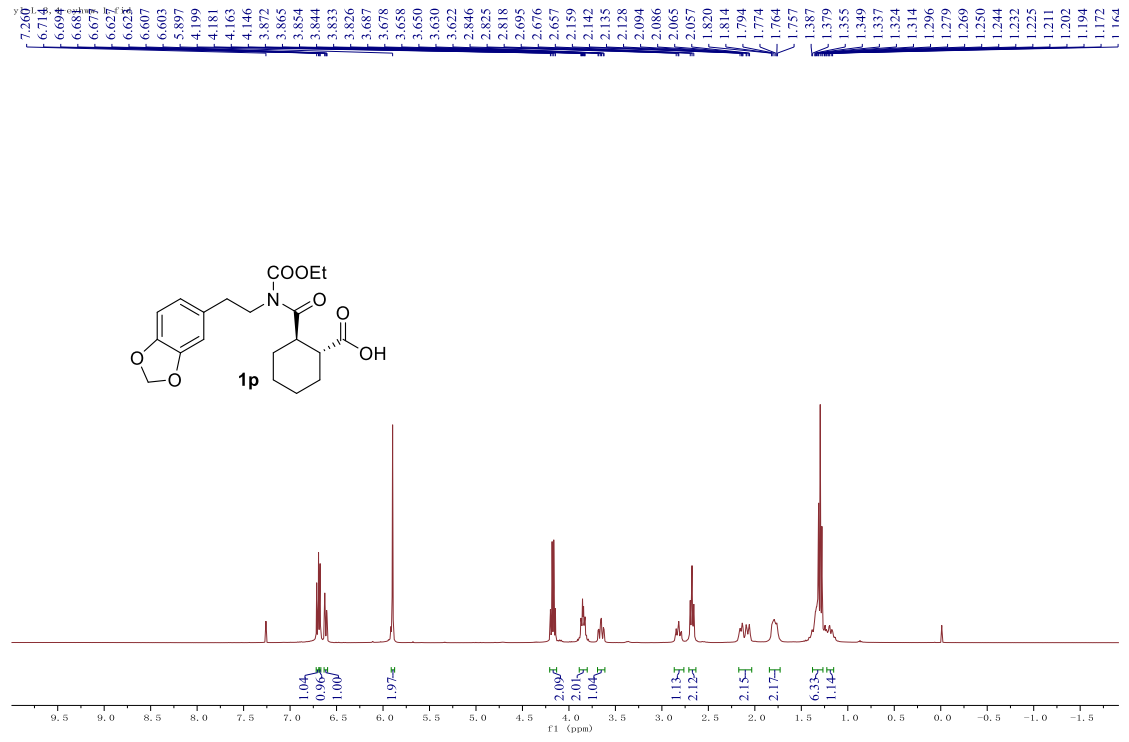


y1-L-4-OMe. 1. fid



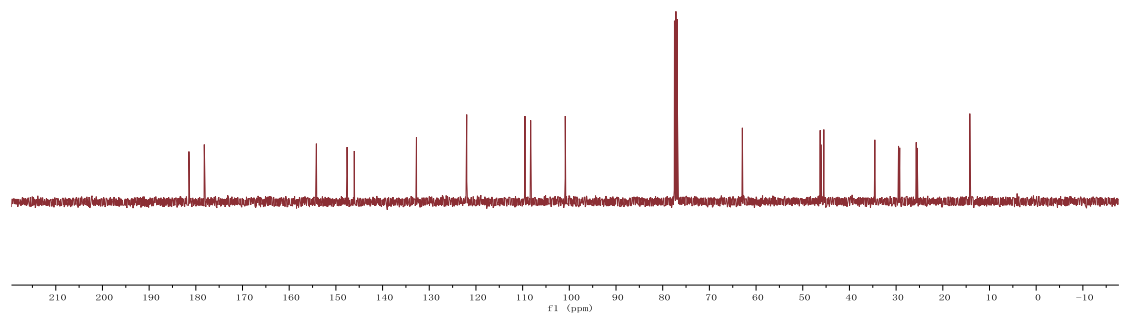
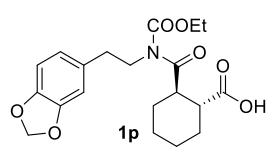
y1-L-4-OMe. 2. fid

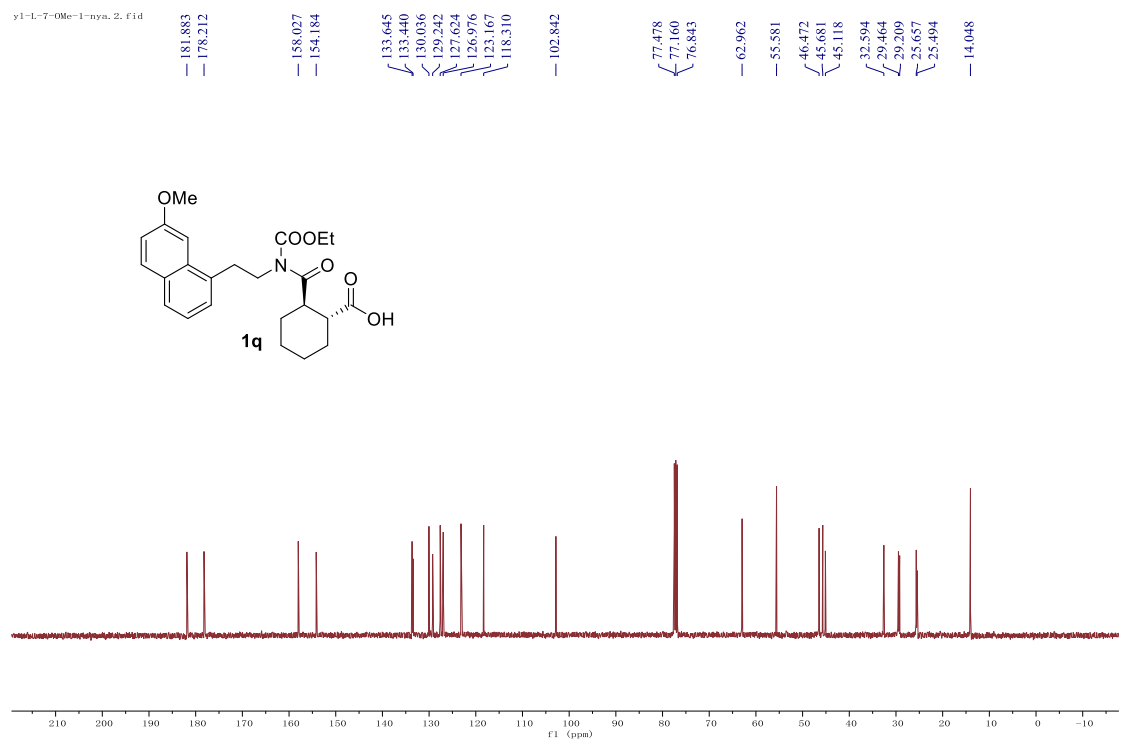
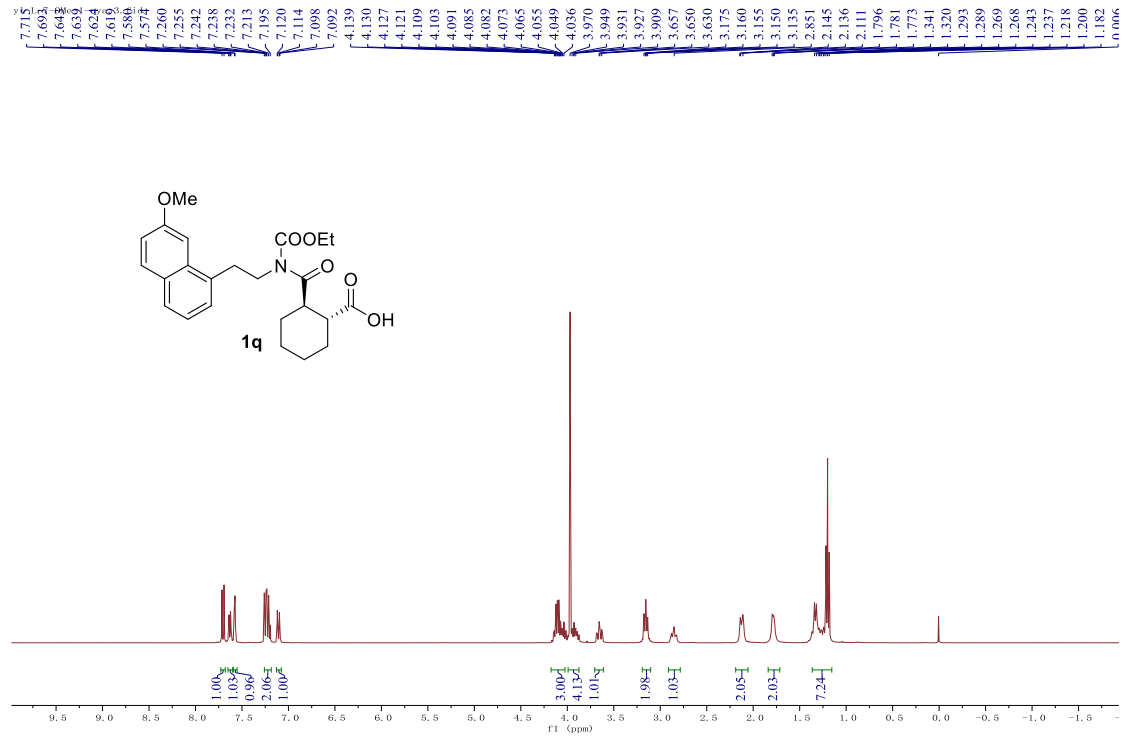




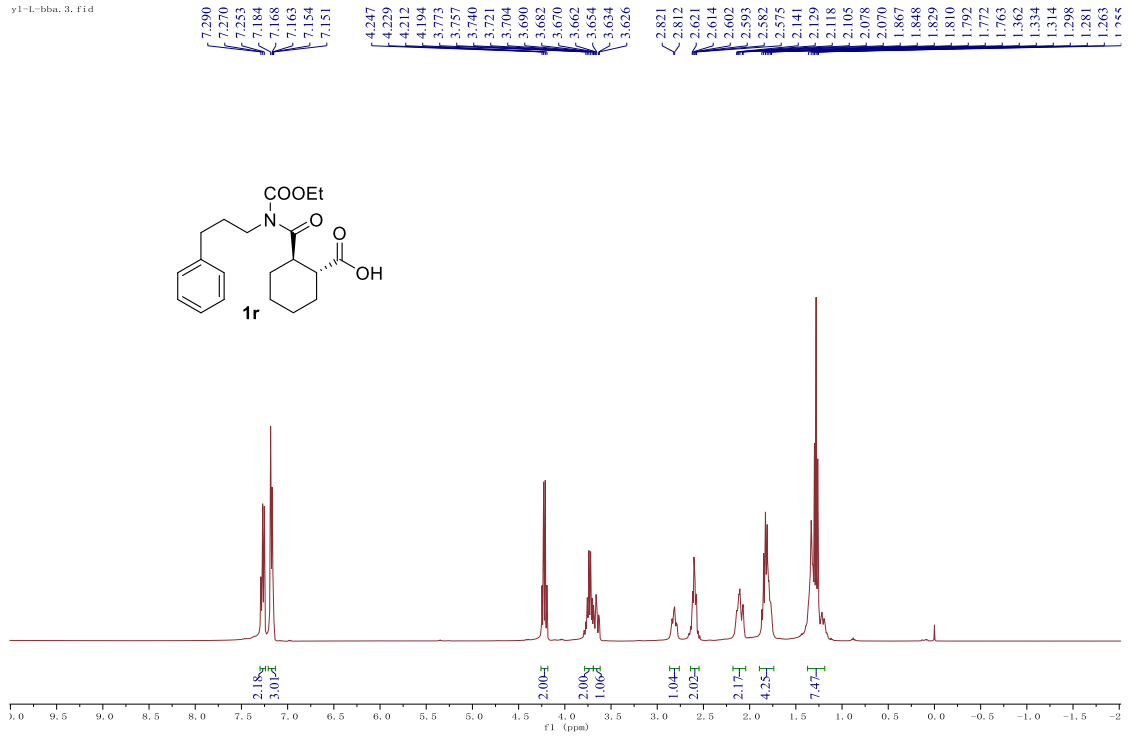
y1-L-3,4-eyhw.2.fid

- 181.478
- 178.192
- 154.178
- 147.609
- 146.066
- 132.738
- 121.975
- 109.498
- 108.278
- 100.872
- 77.477
- 77.160
- 76.842
- 62.941
- 46.270
- 46.103
- 45.483
- 34.556
- 29.482
- 29.228
- 25.695
- 25.498
- 14.216

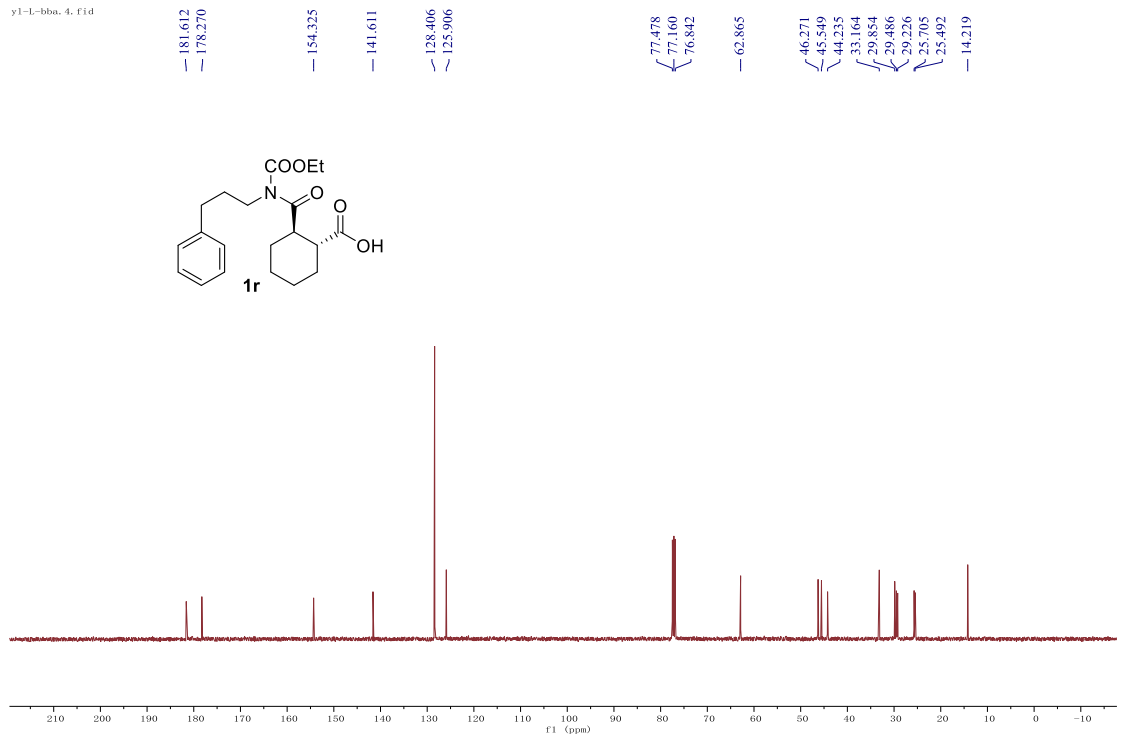


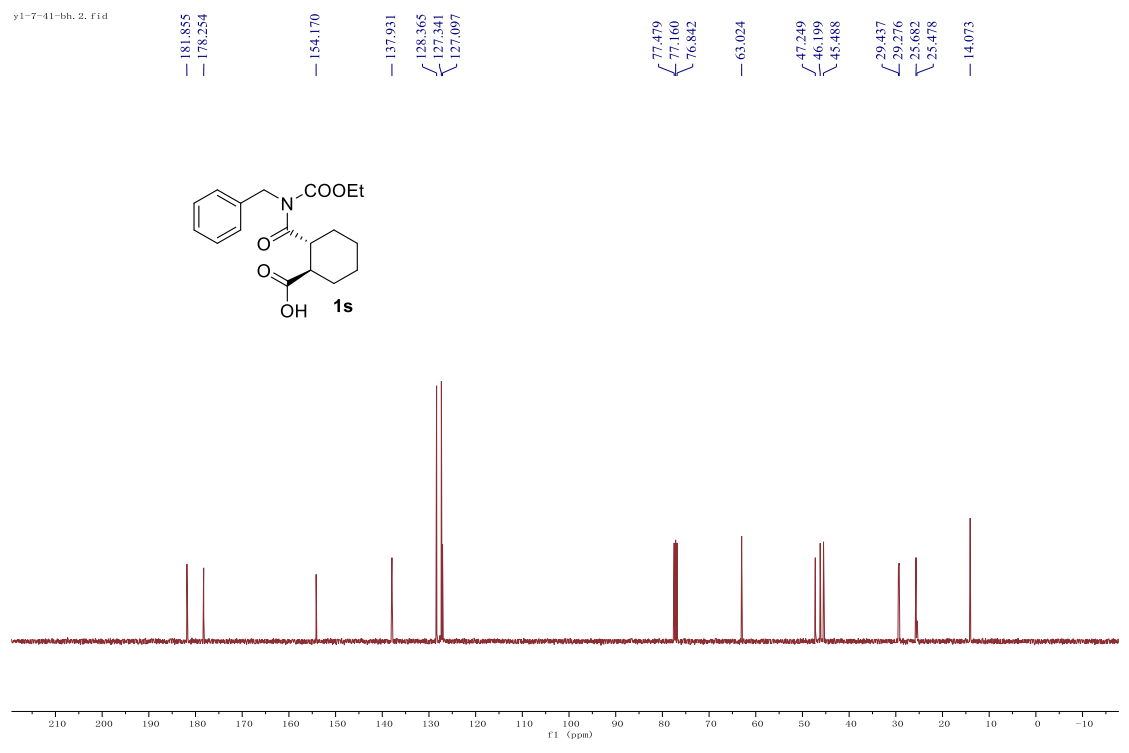
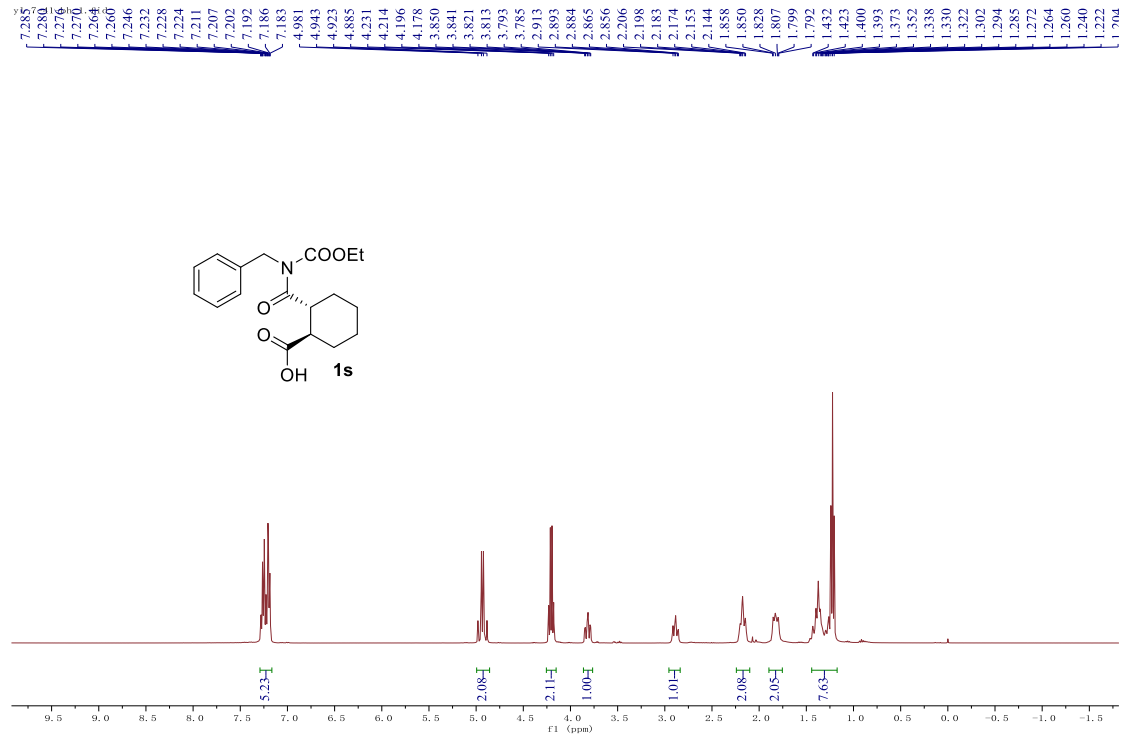


y1-l-bba. 3. f1d

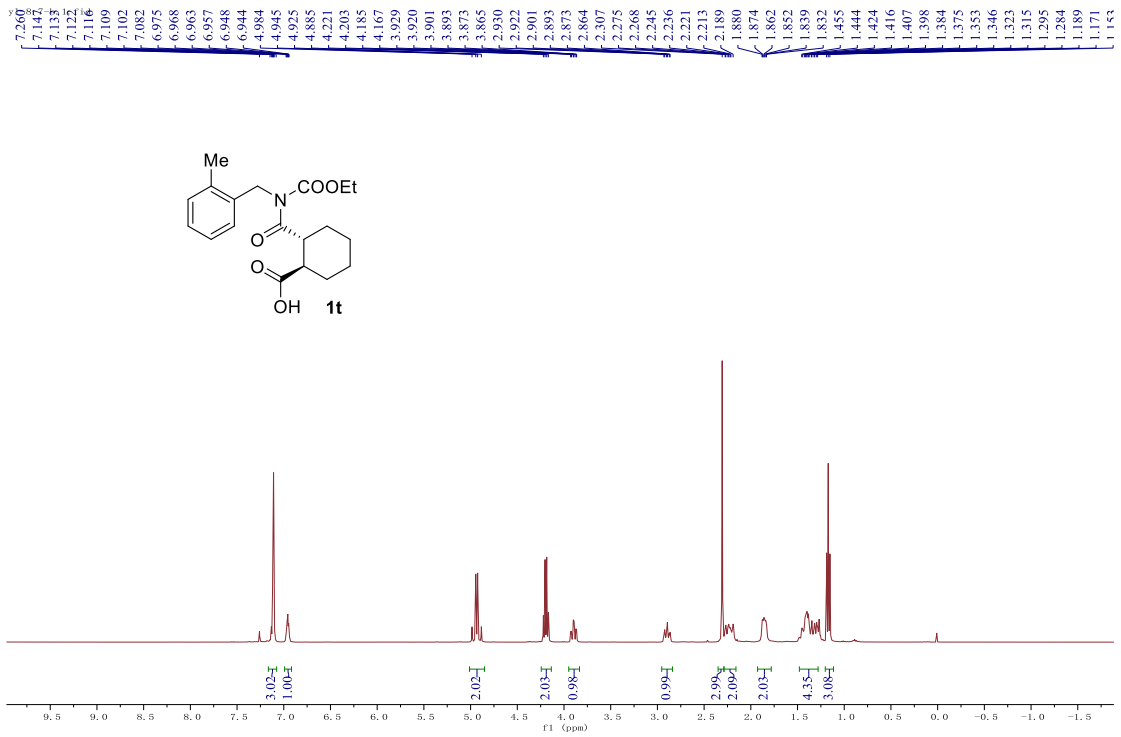


y1-l-bba. 4. f1d

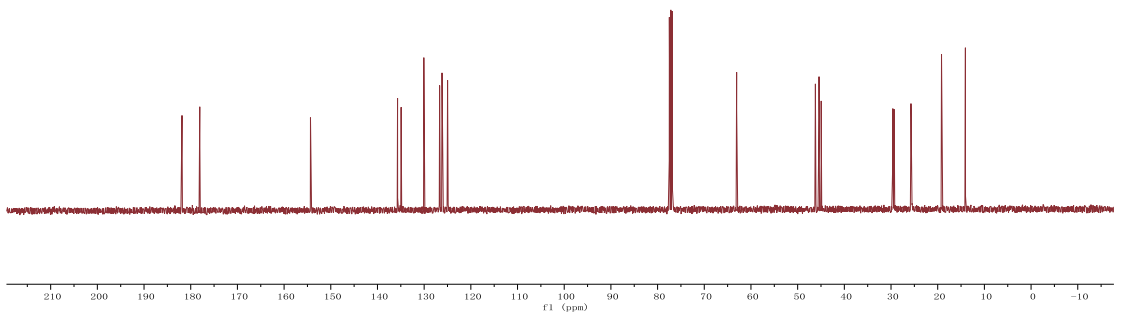
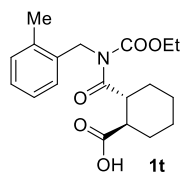


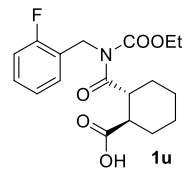
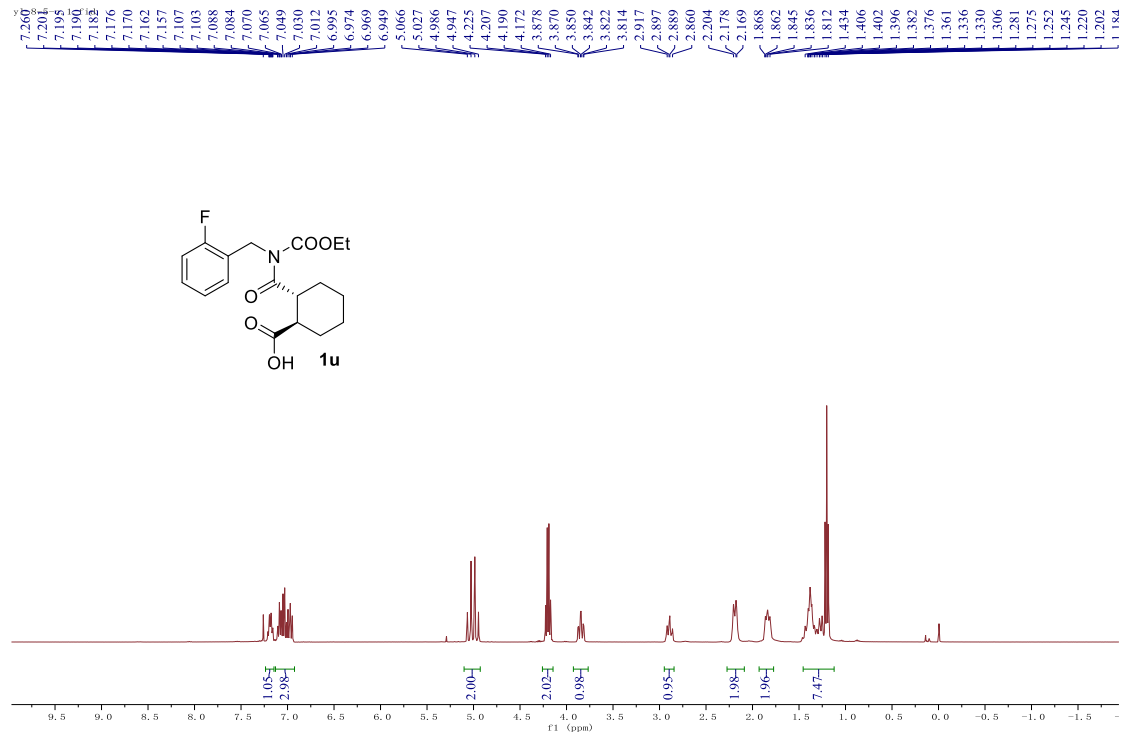






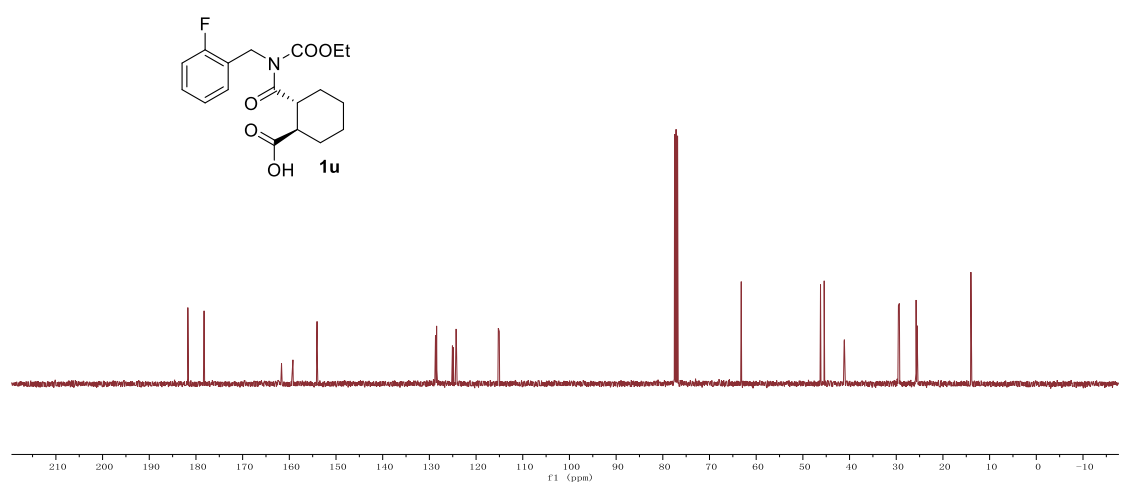
y1-8-7-b. 2. f1d

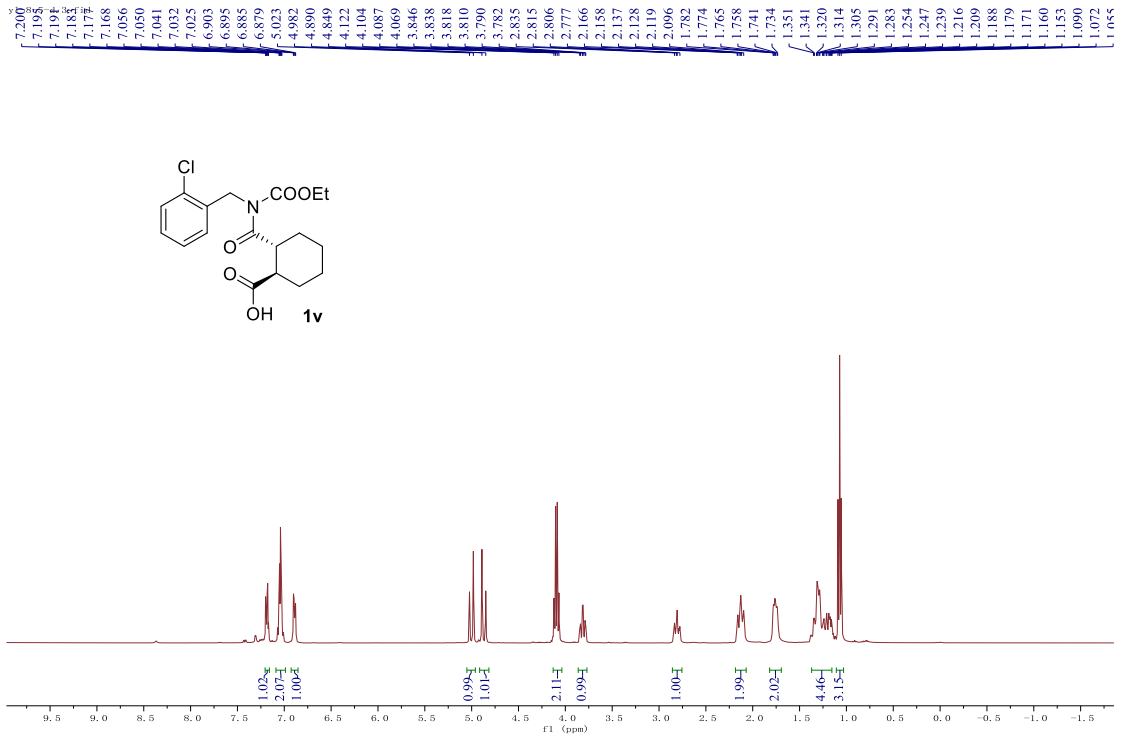




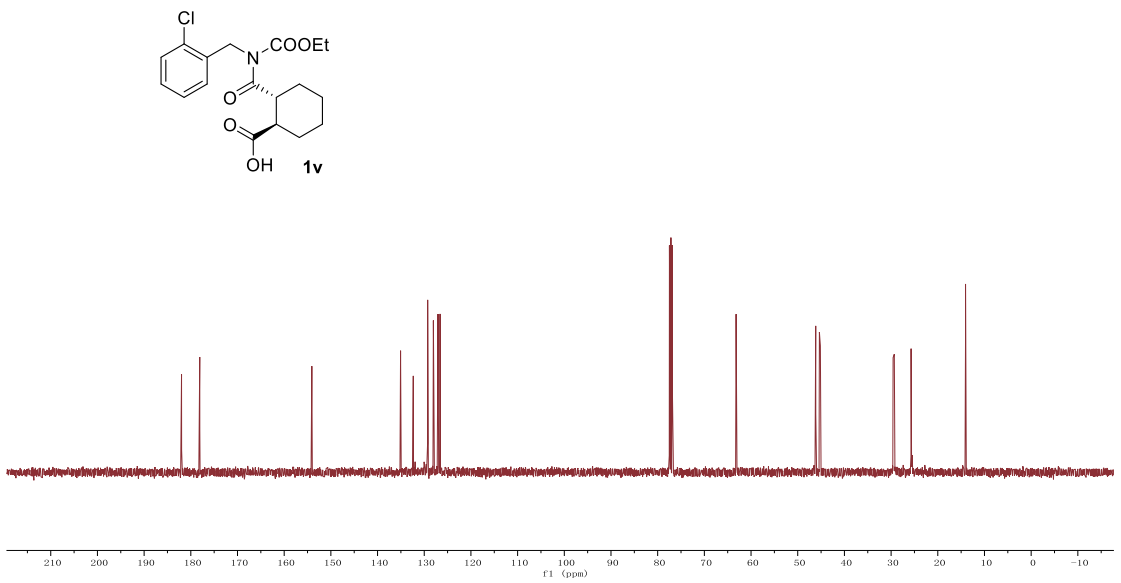
y1-8-5-c. 3. f14

- 181.738
- 178.258
- 161.672
- 159.227
- 154.058
- 128.688
- 128.607
- 128.451
- 128.411
- 125.061
- 124.921
- 124.289
- 124.254
- 115.238
- 115.023
- 77.478
- 77.160
- 76.843
- 63.198
- 46.221
- 45.432
- 41.158
- 41.108
- 29.534
- 29.333
- 25.748
- 25.553
- 14.012

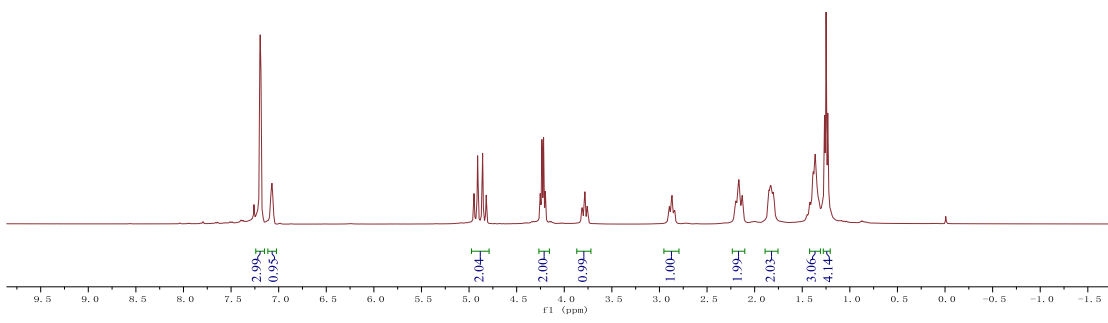
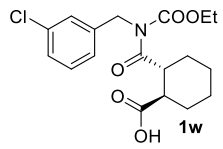




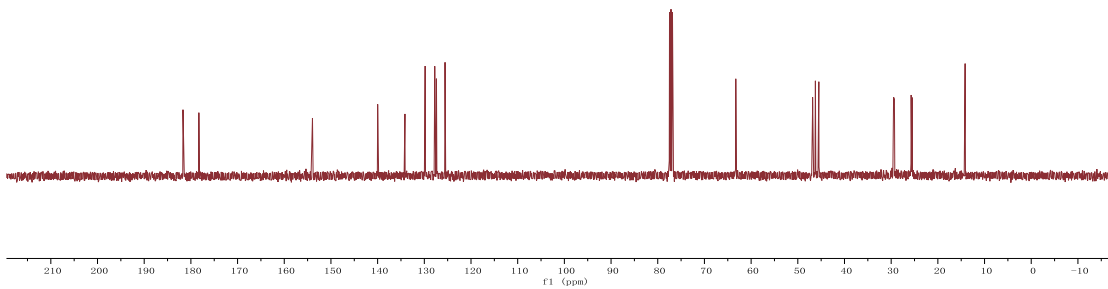
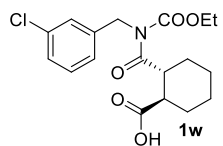
y1-8-5-d.4.f14

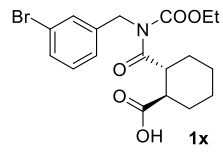
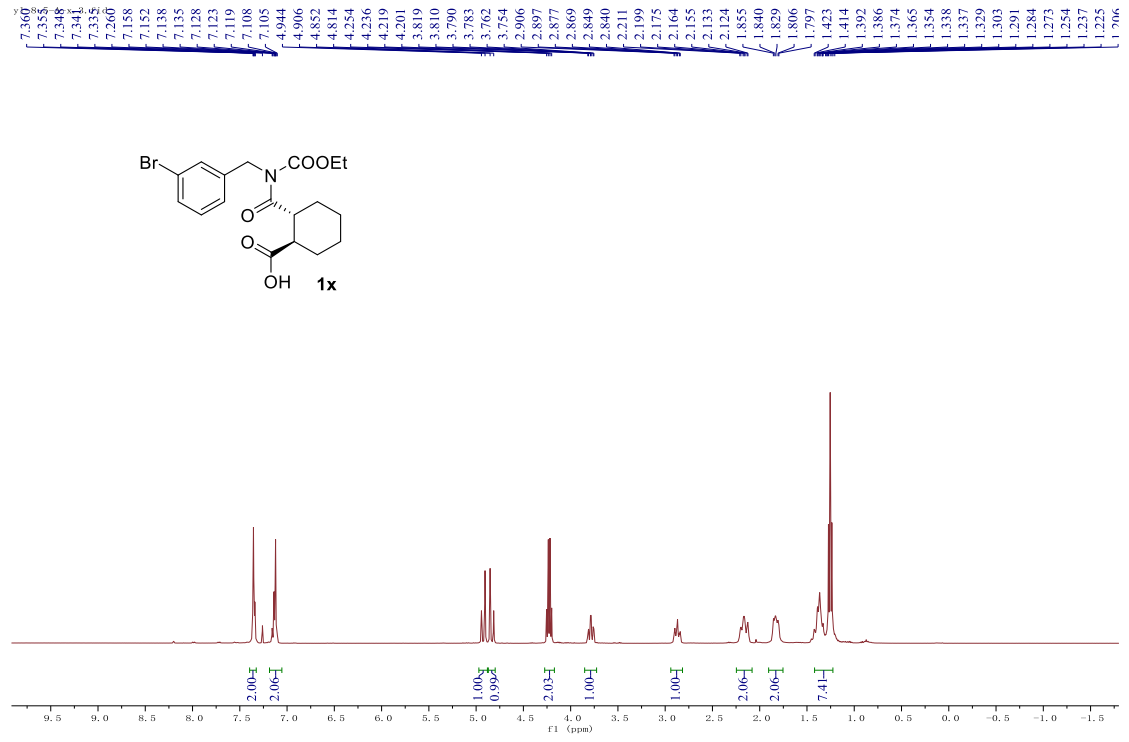


y1-7-36-a. 6. f1d



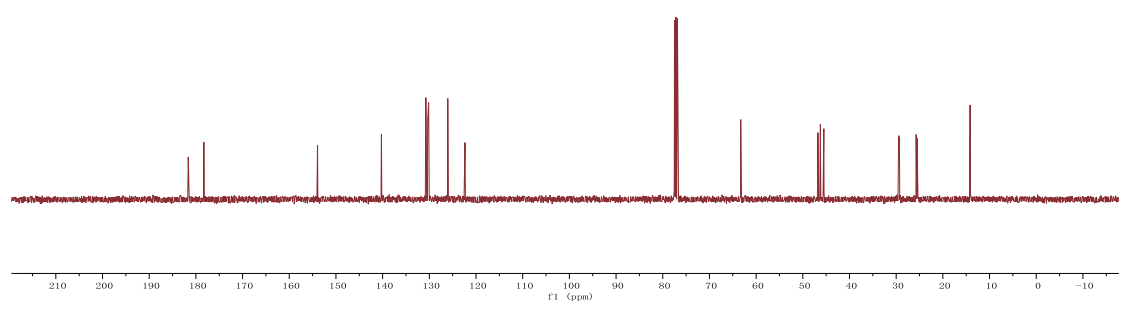
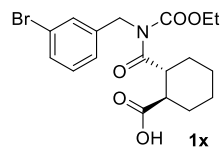
y1-7-36-a. 7. f1d

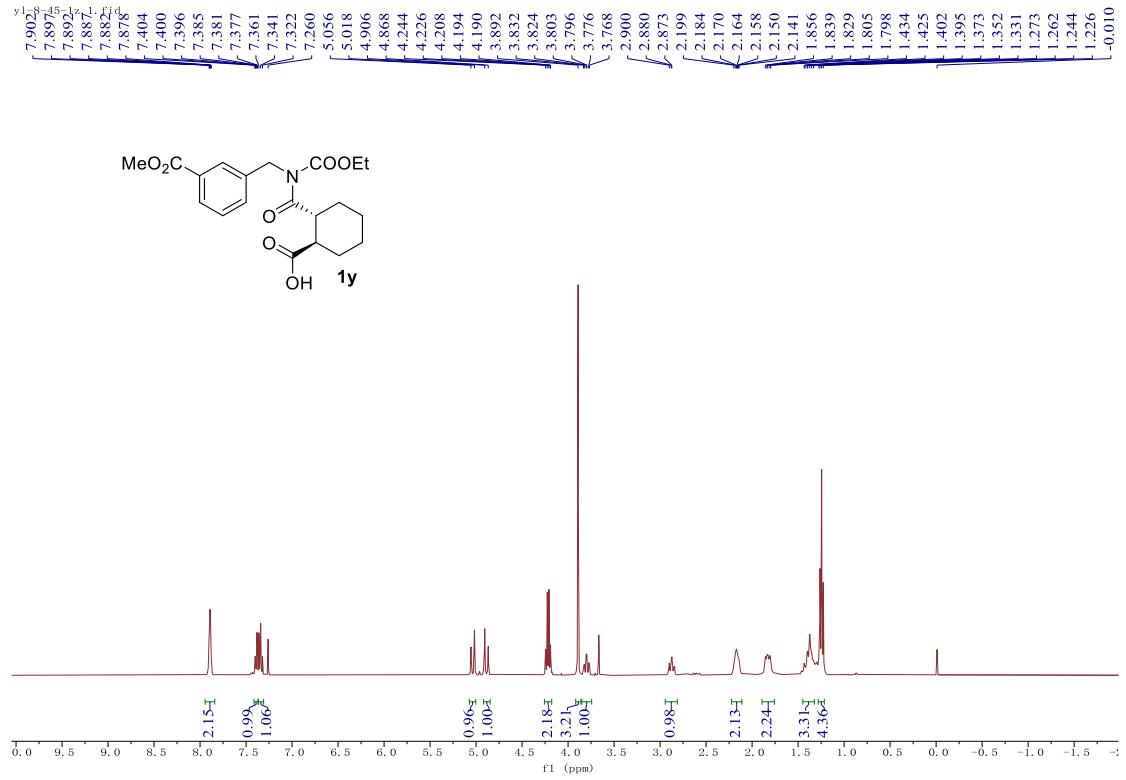




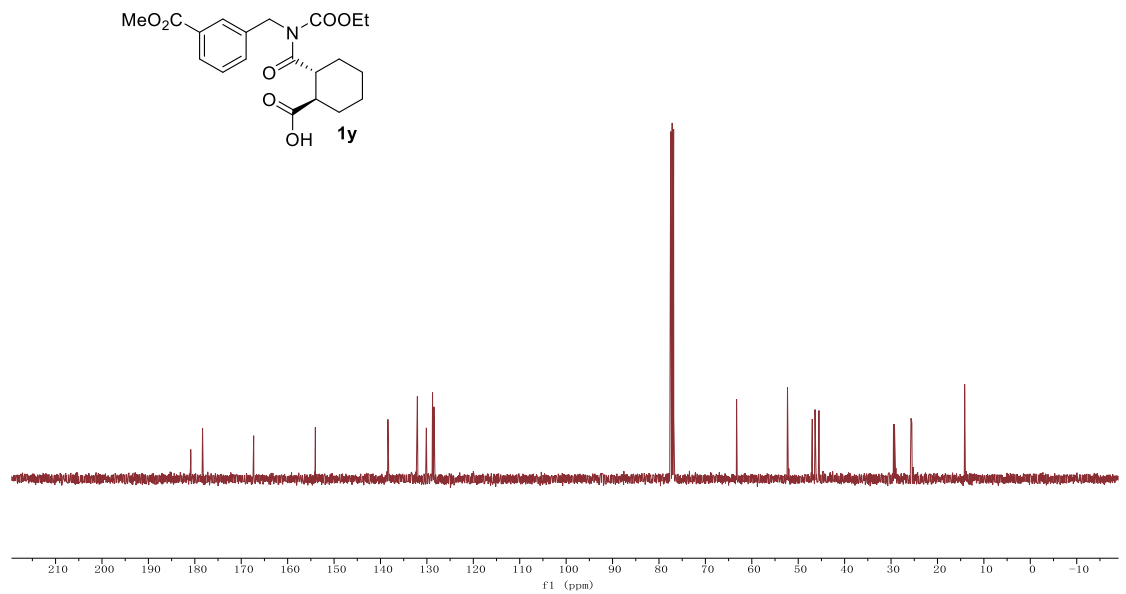
y1-8-5-A-x, 4, f1d

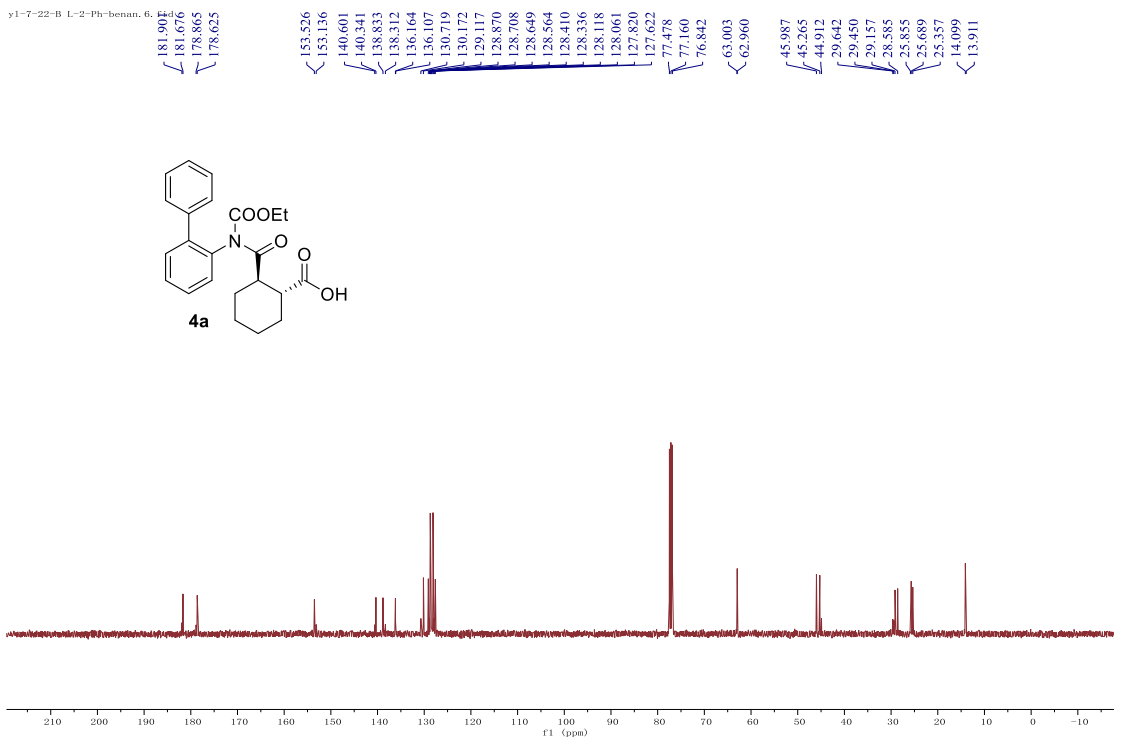
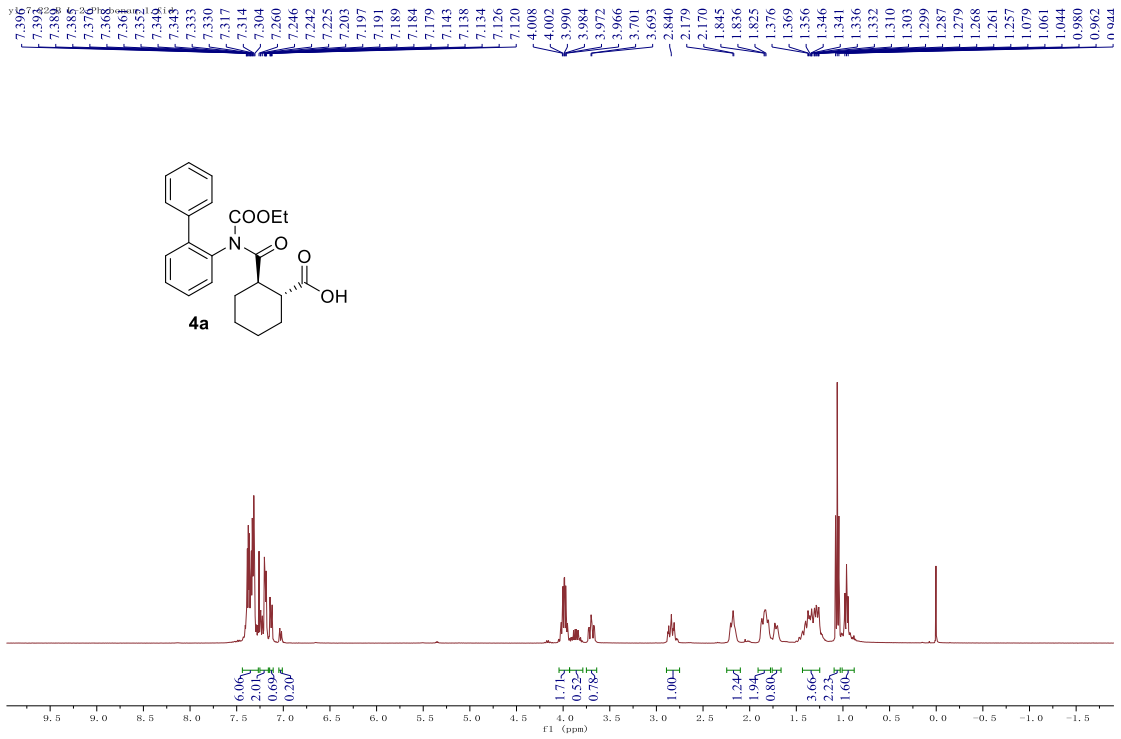
- 181.639
- 178.291
- 153.941
- 140.255
- 130.745
- 130.347
- 130.142
- 126.045
- 122.358
- 77.478
- 77.160
- 76.843
- 63.295
- 46.760
- 46.234
- 45.491
- 29.473
- 29.311
- 25.718
- 25.517
- 14.168



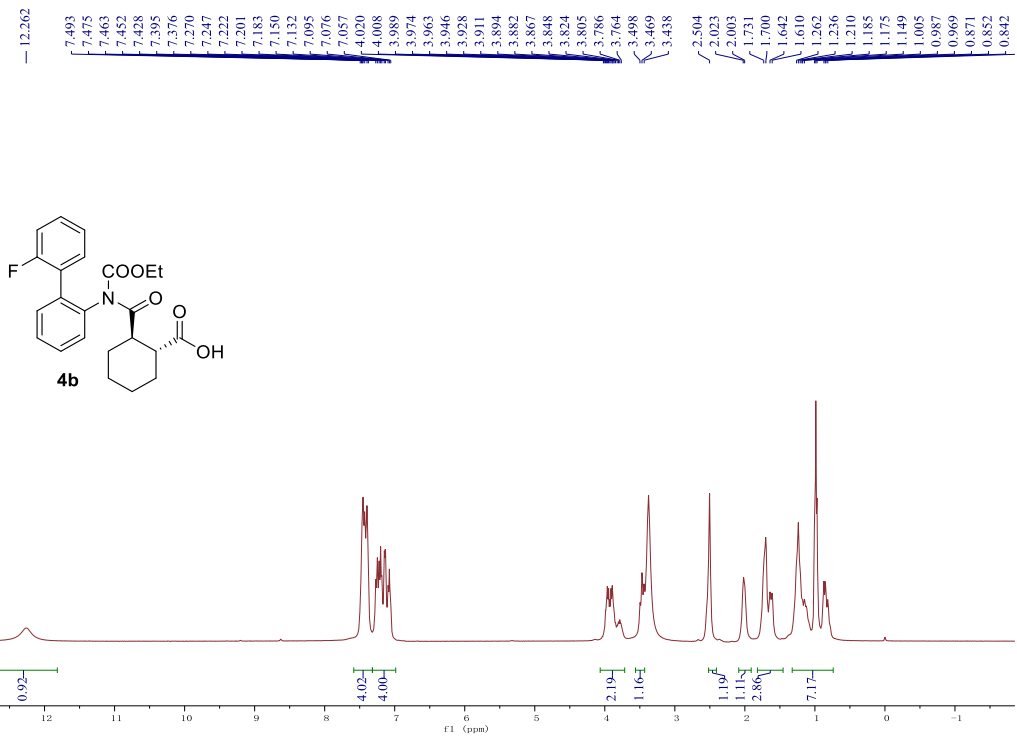


y1-8-45-1z.2. Fid

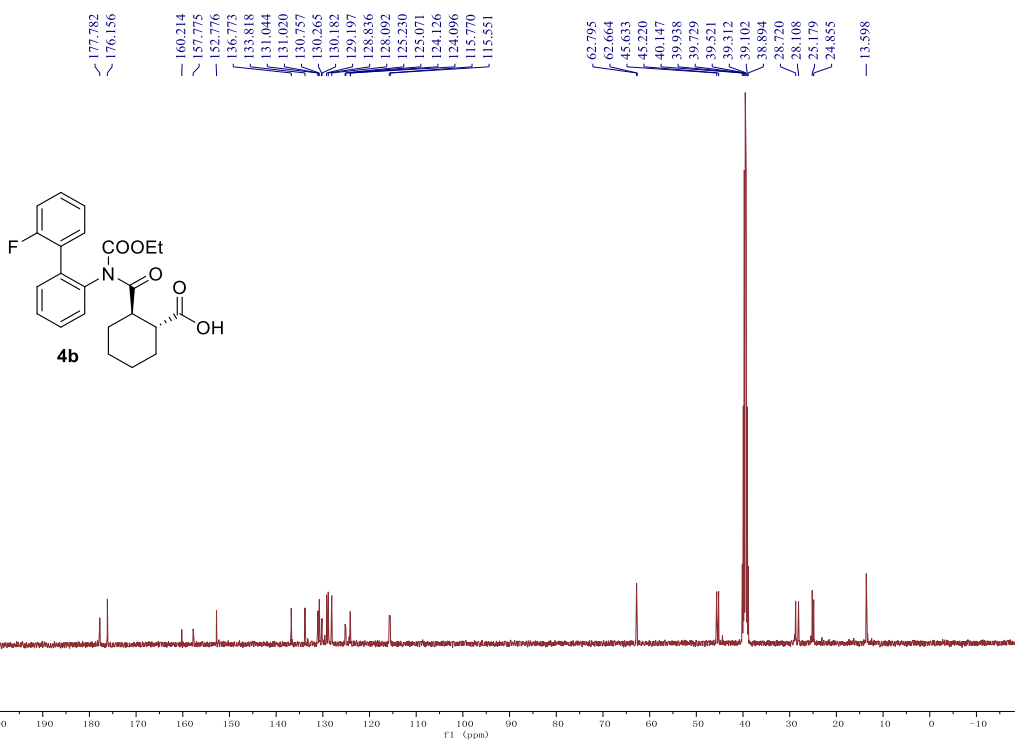




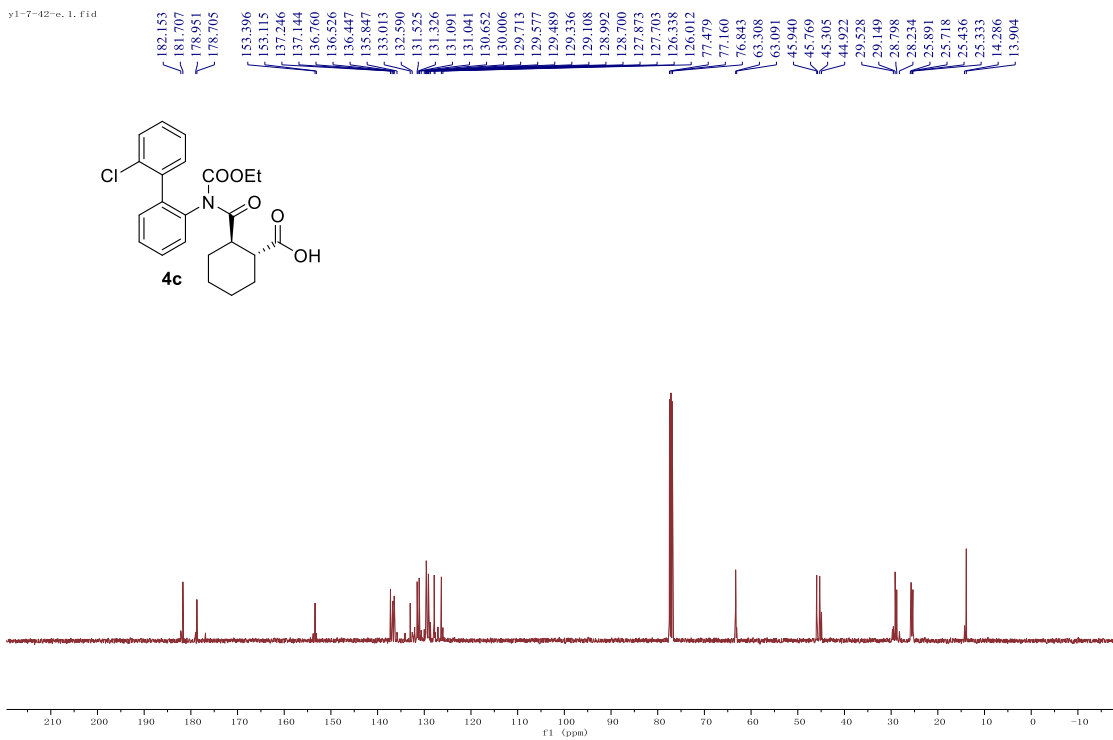
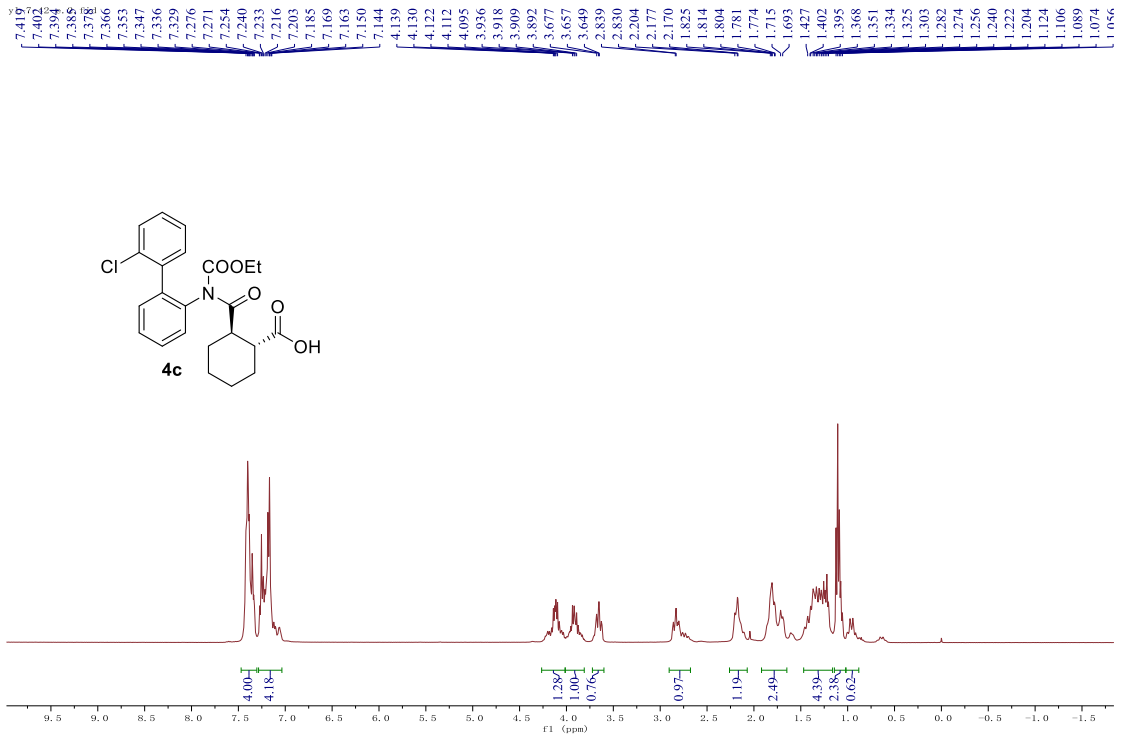
y1-7-50-c. 6. f1d

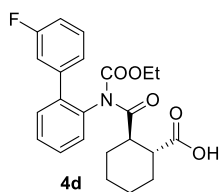
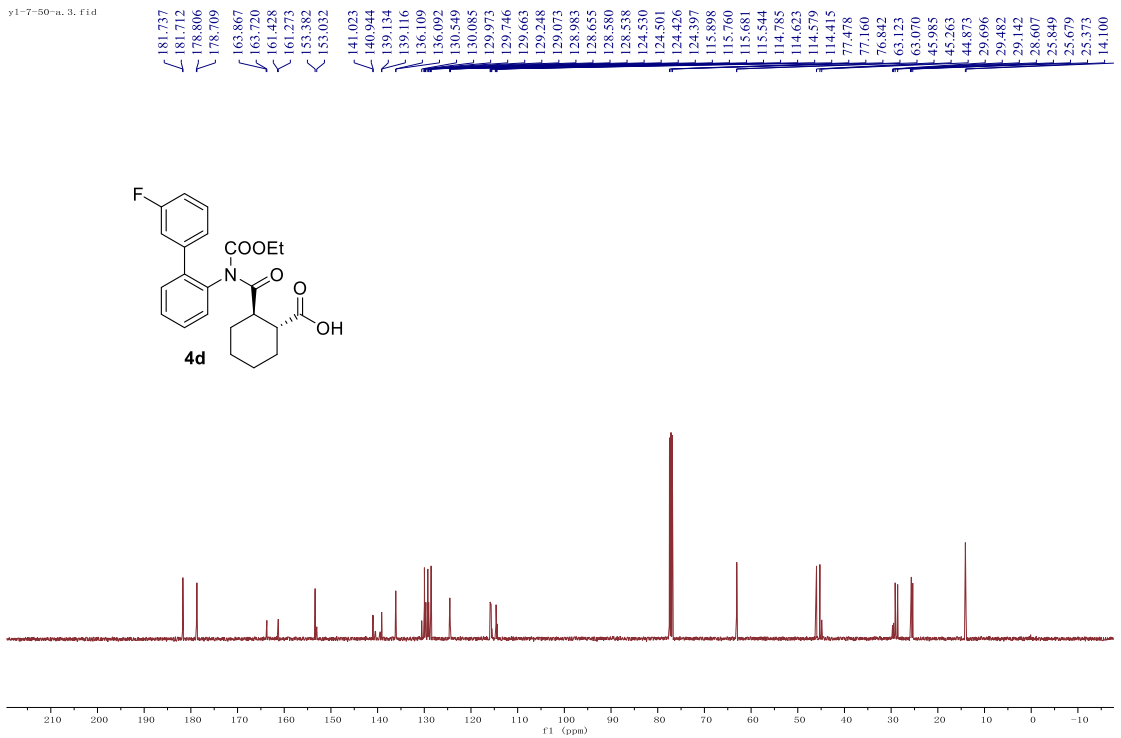
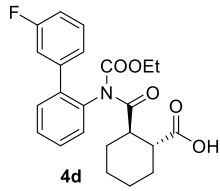
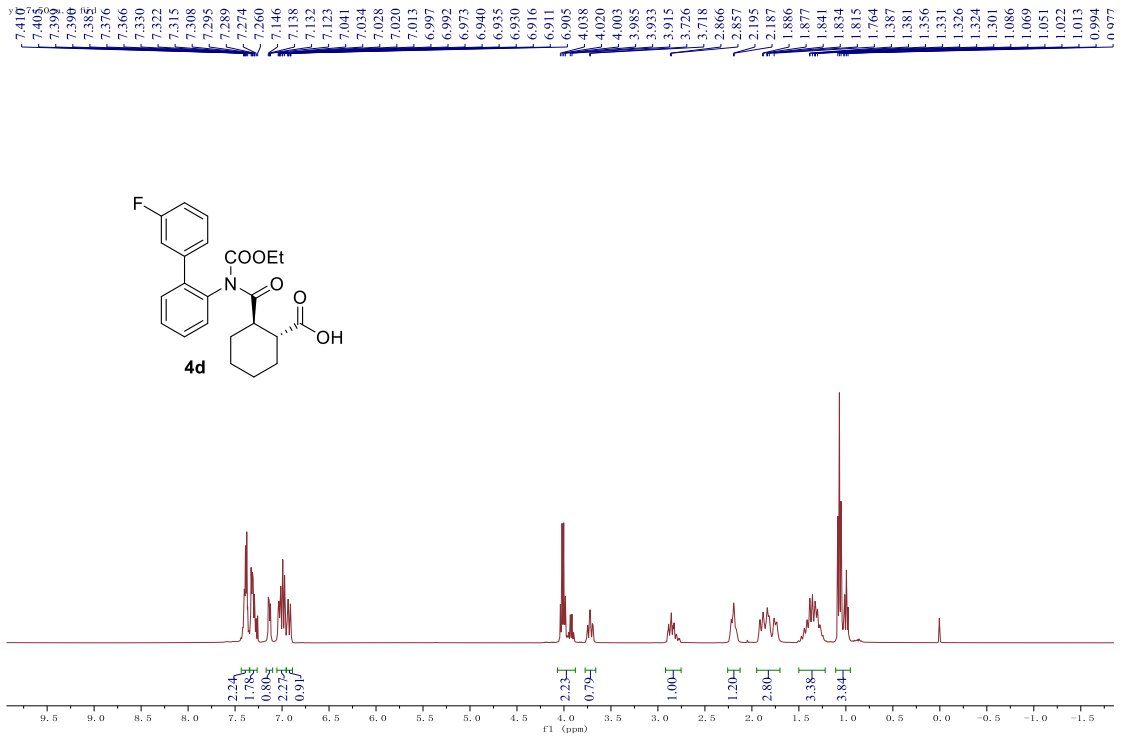


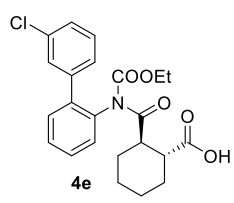
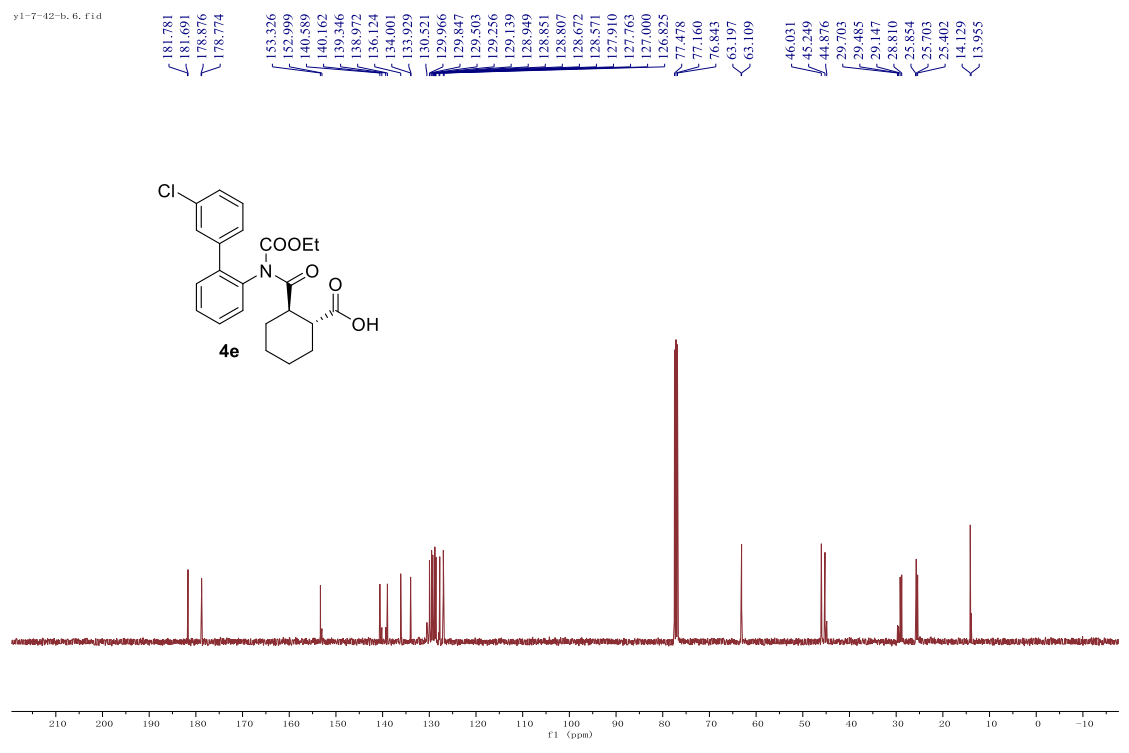
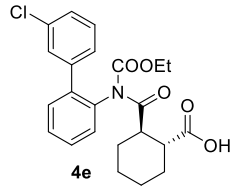
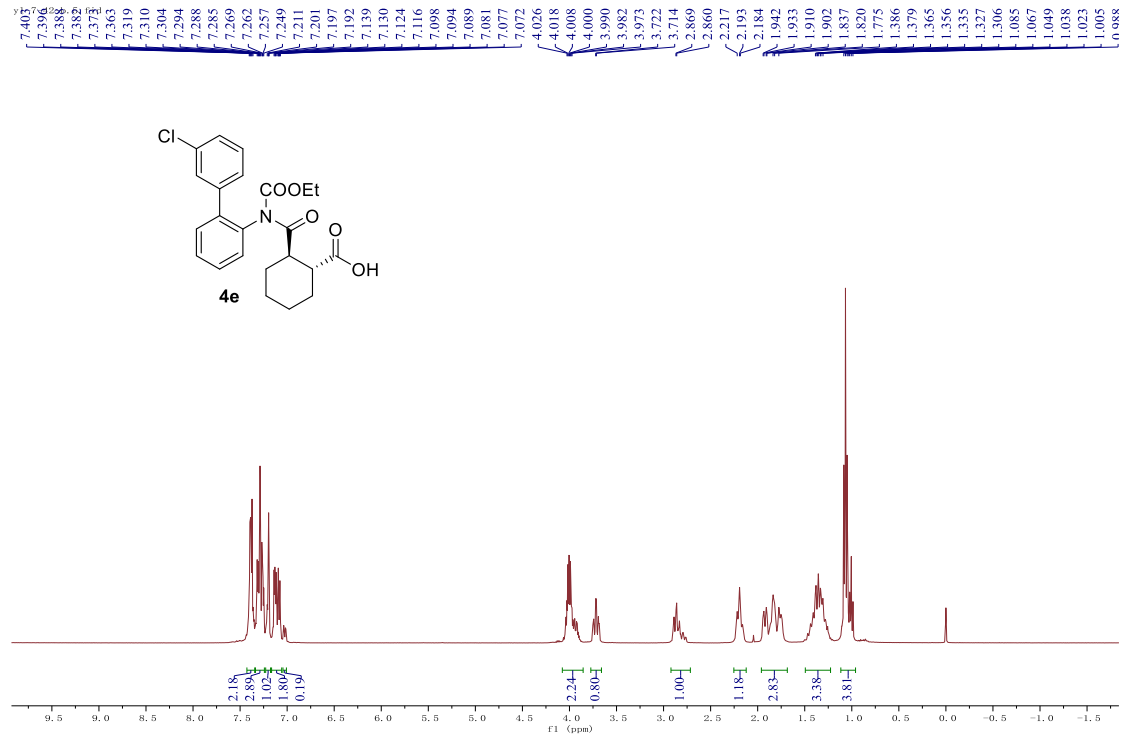
y1-7-50-c. 8. f1d

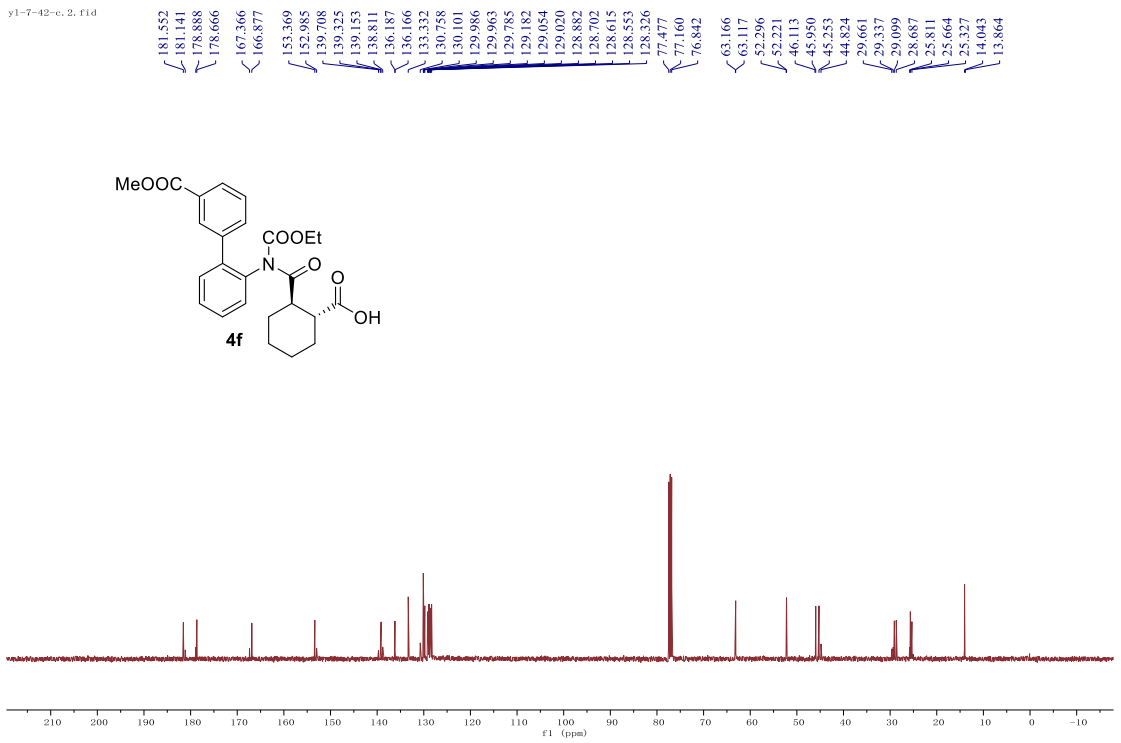
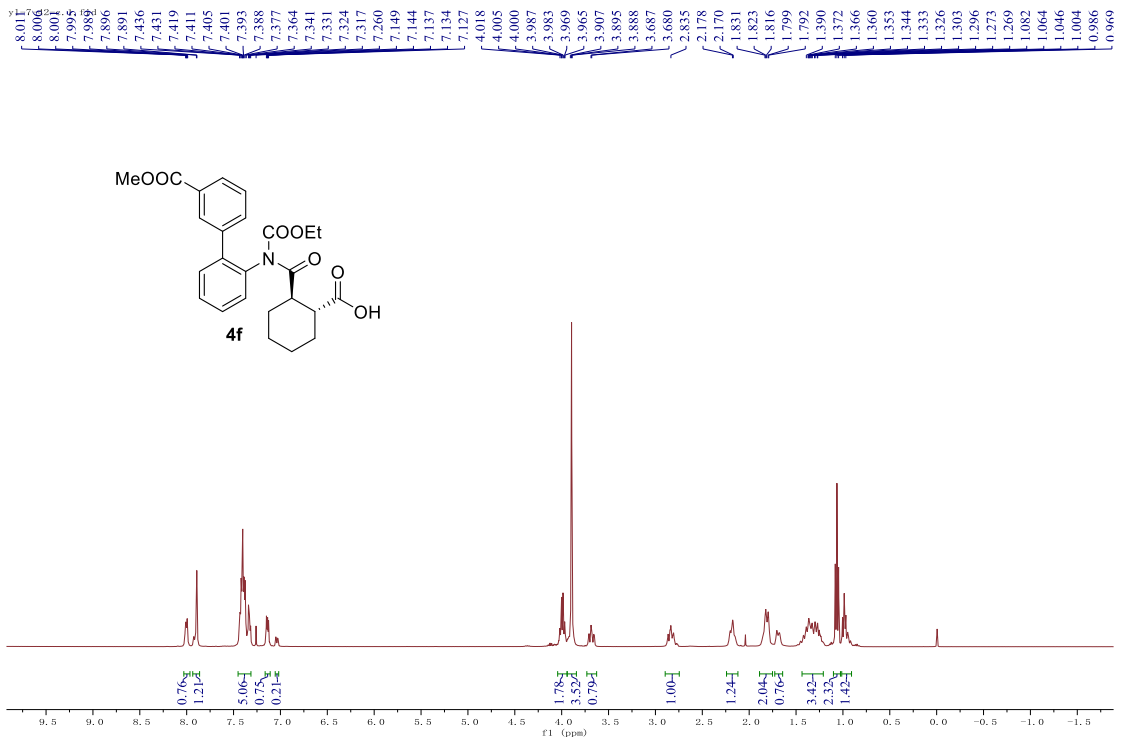


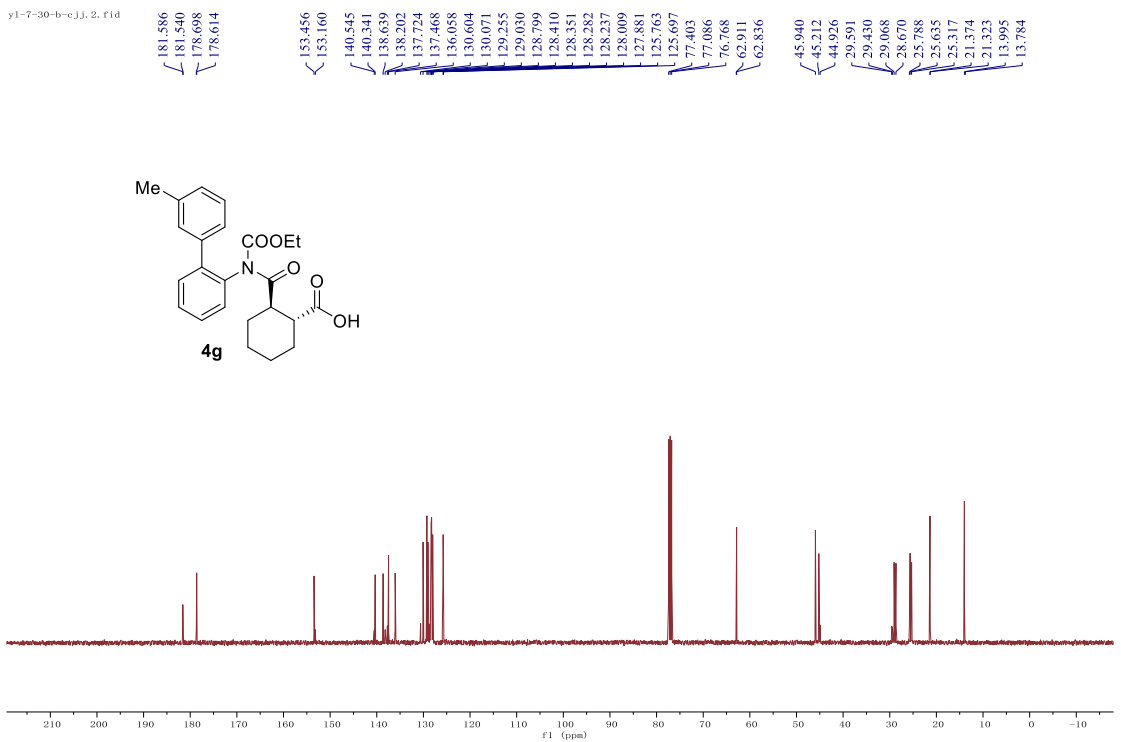
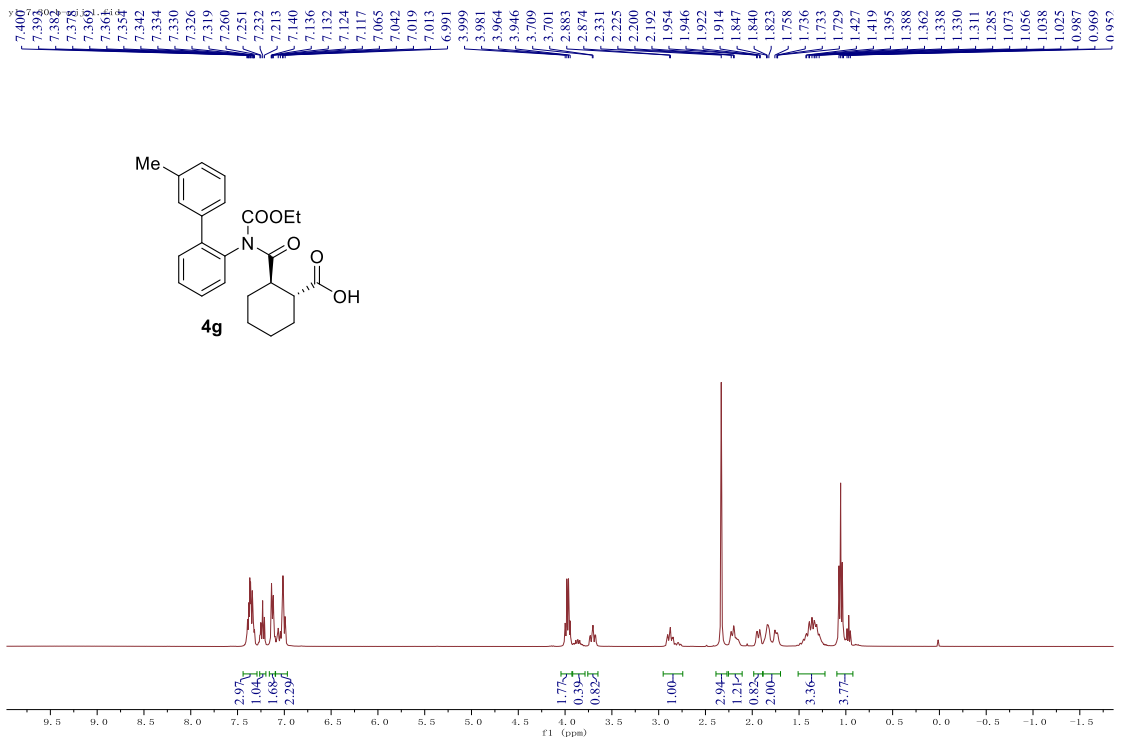


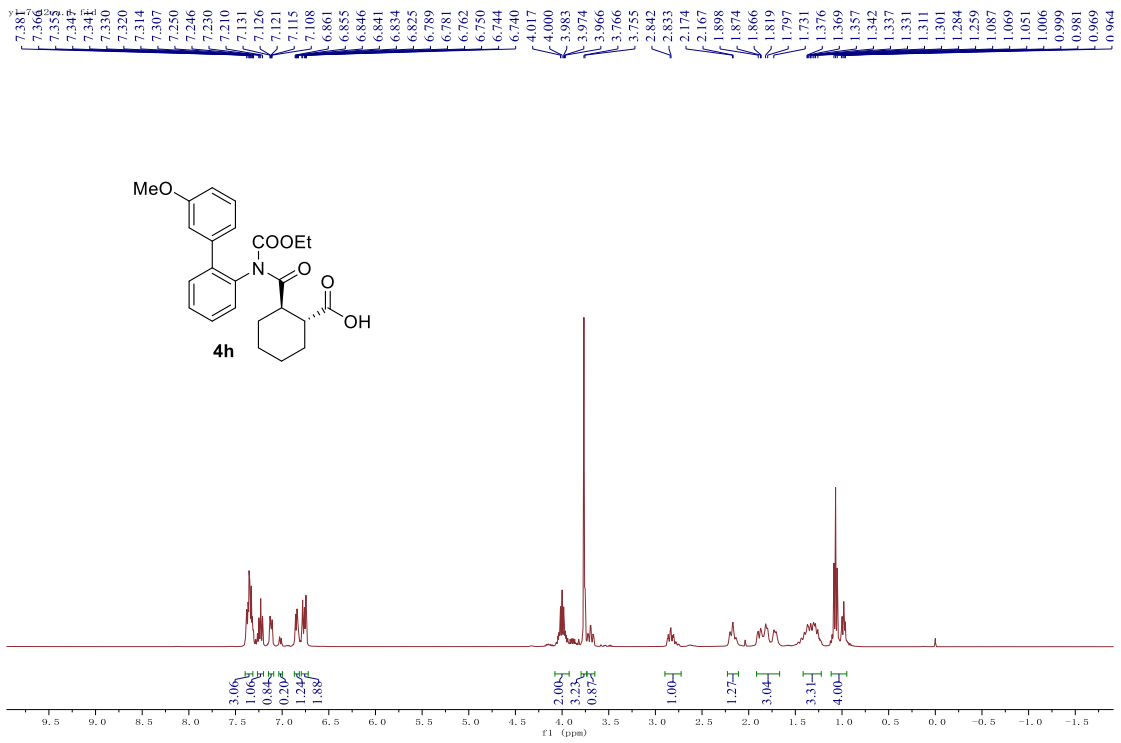




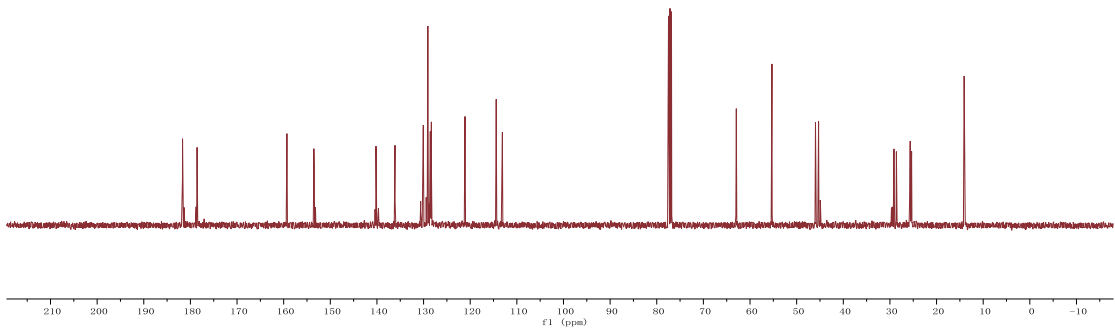
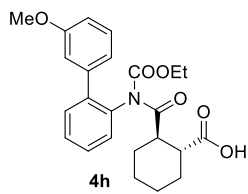


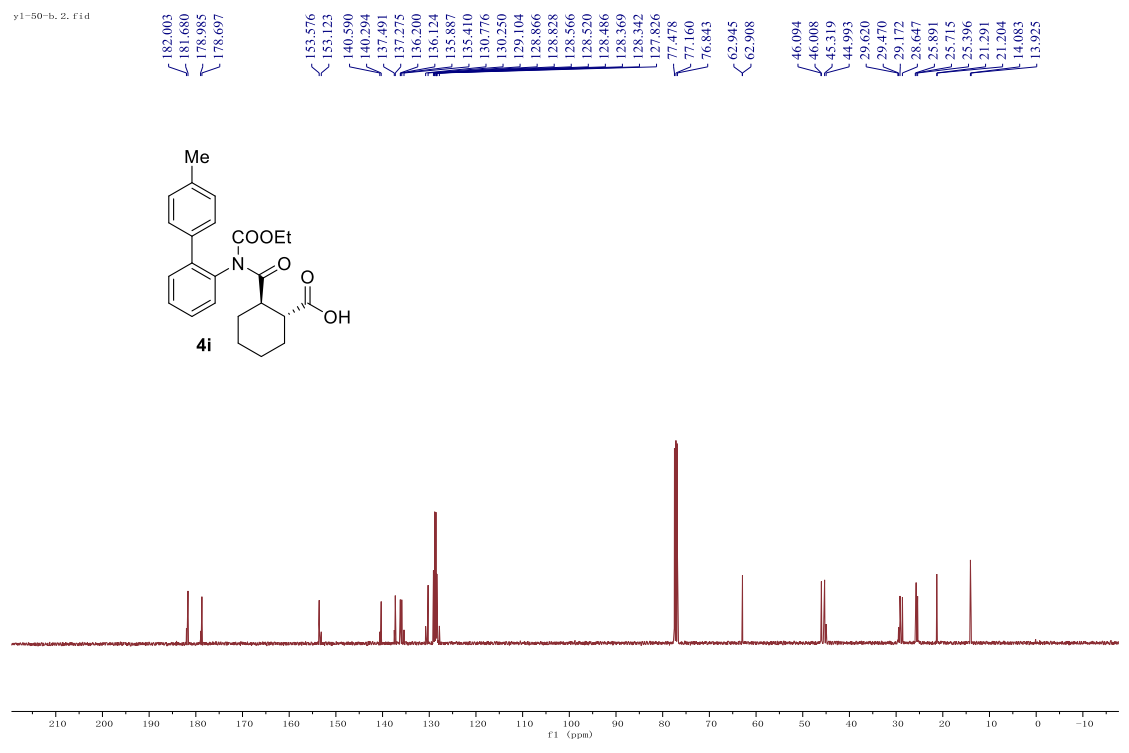
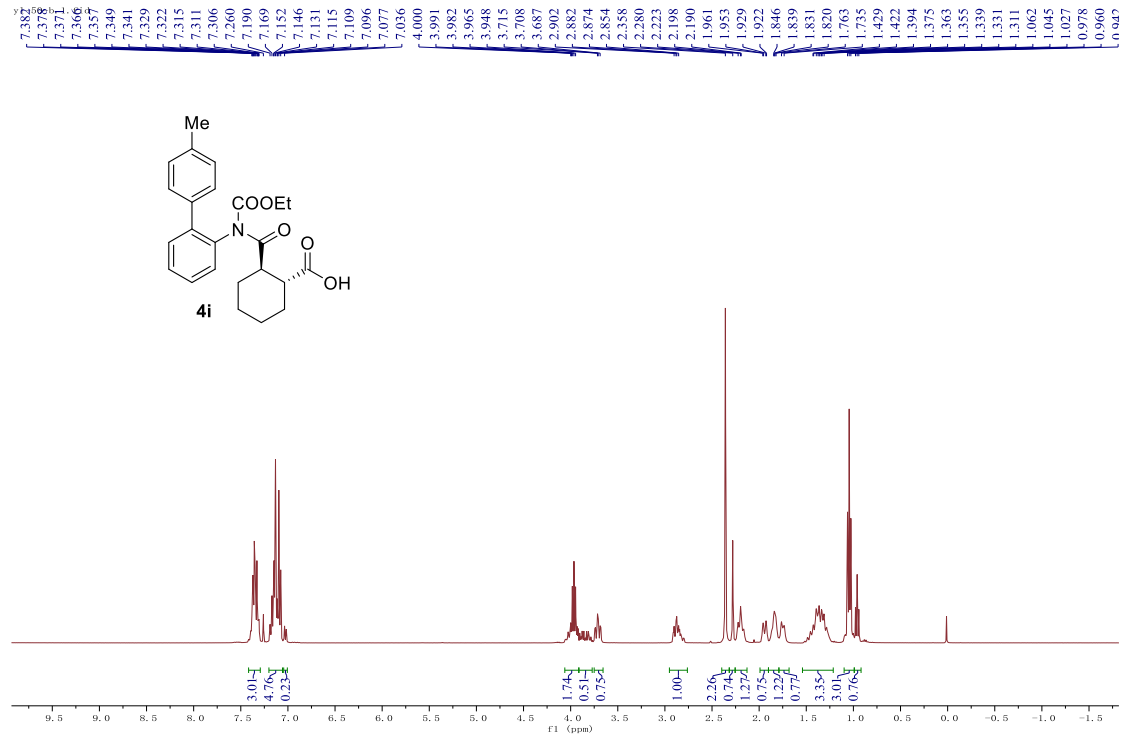




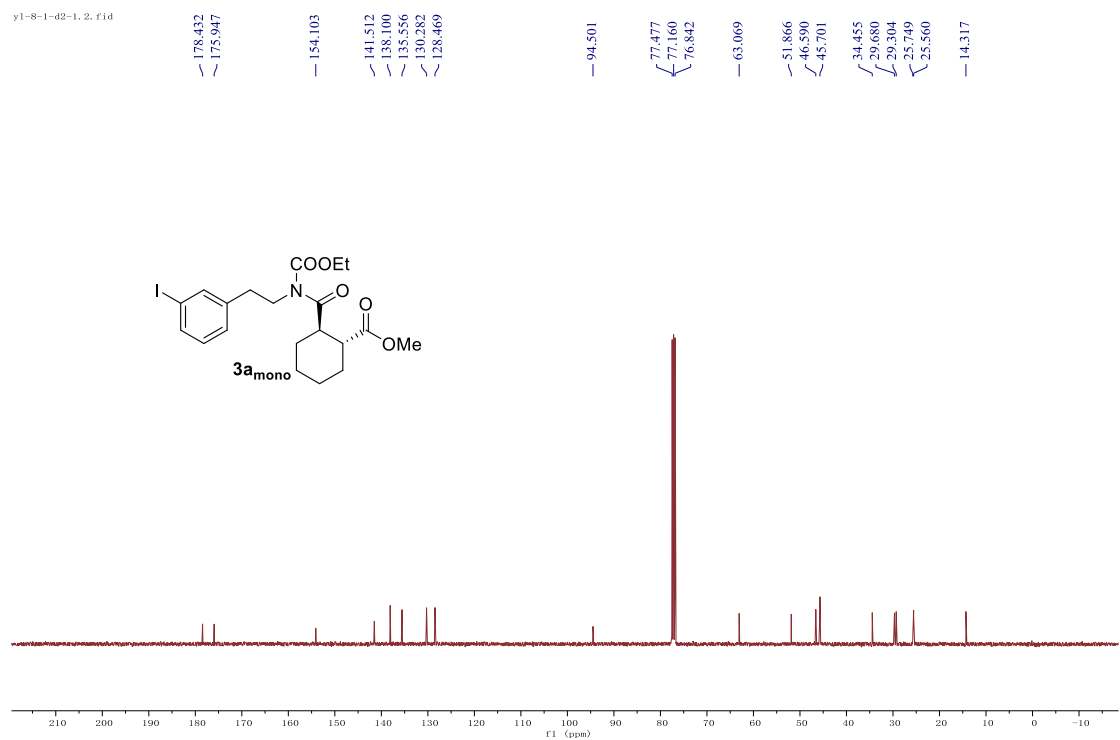
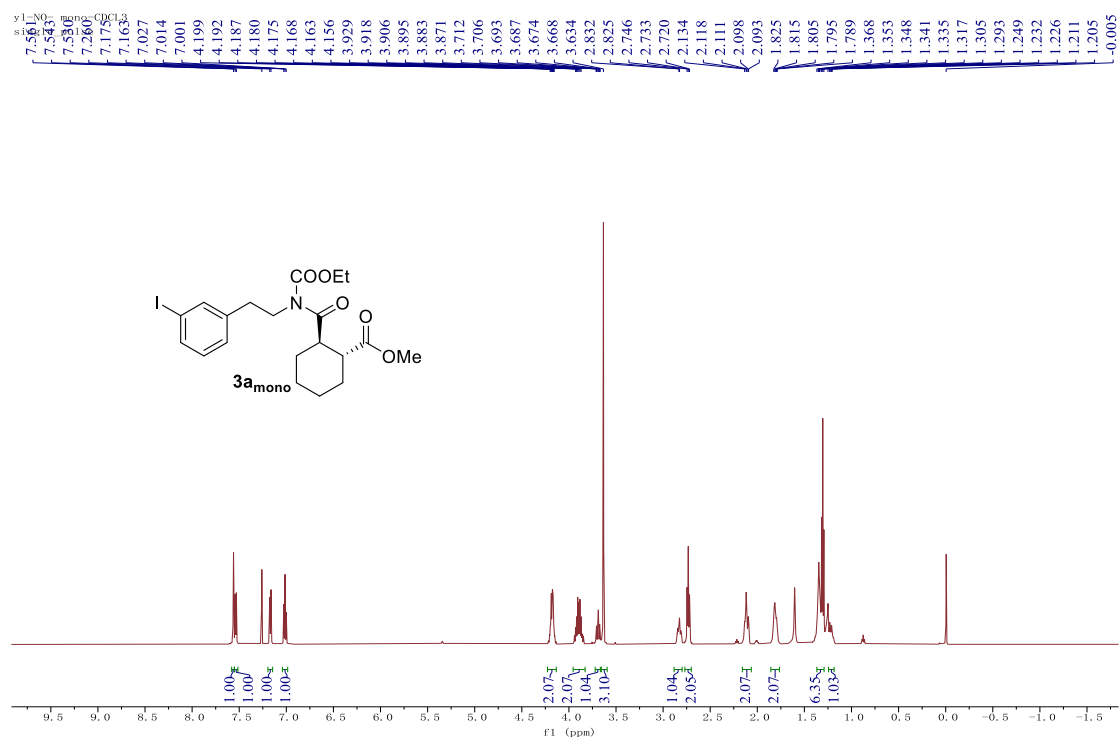


y1-7-42-a. 2. f1.d





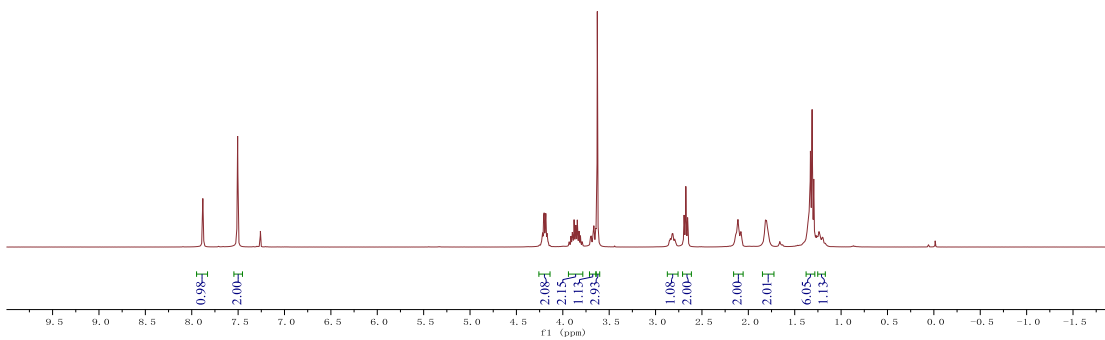
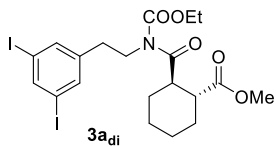
## 3.2 NMR spectra of products





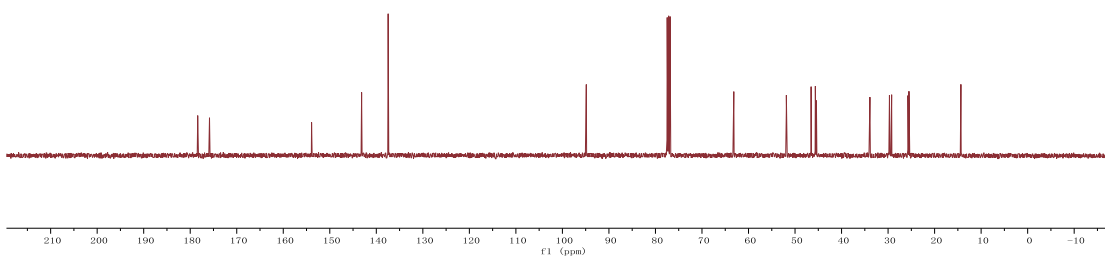
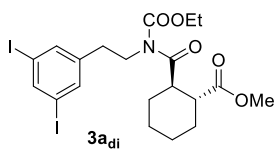
y1-NO-d1. 1. F10

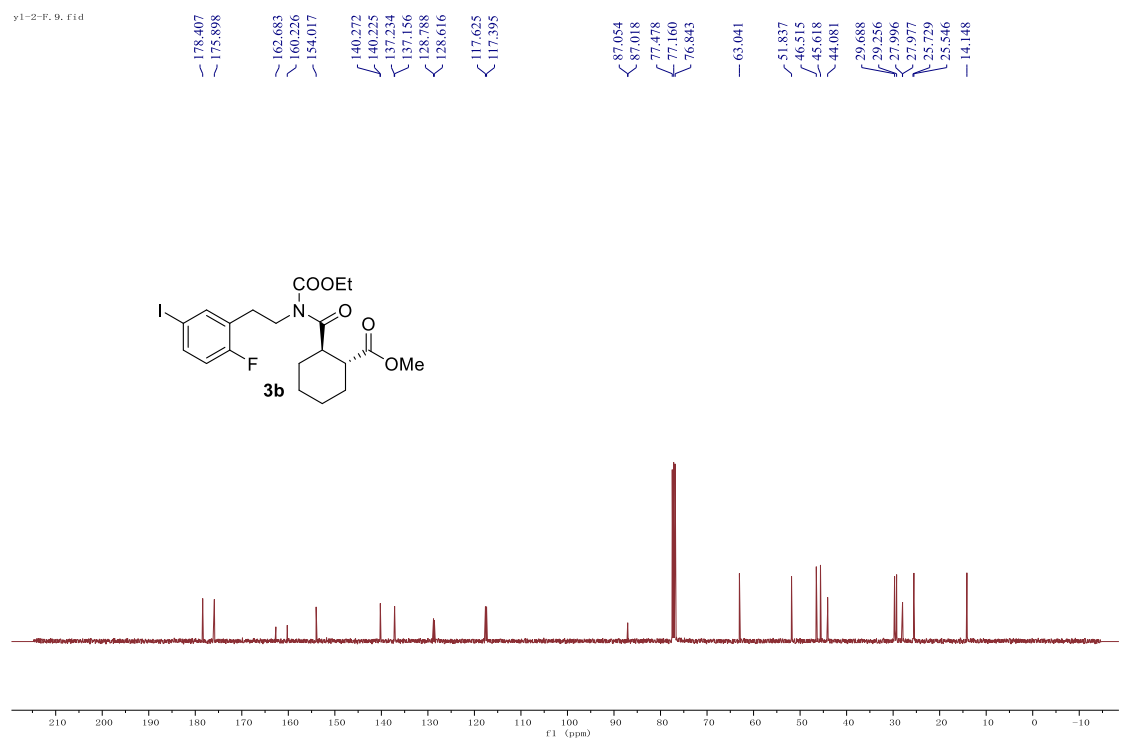
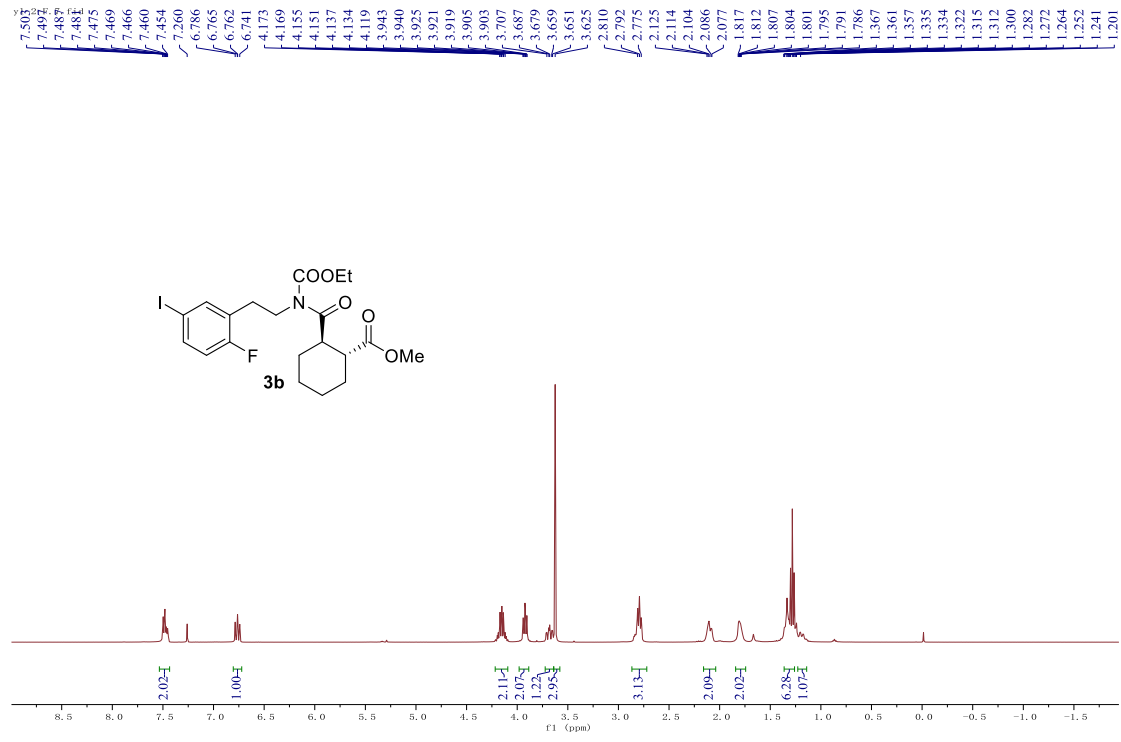
7.885  
7.881  
7.877  
7.508  
7.504  
7.260  
4.225  
4.218  
4.207  
4.201  
4.189  
4.183  
4.171  
4.165  
3.931  
3.912  
3.908  
3.893  
3.878  
3.863  
3.859  
3.844  
3.825  
3.810  
3.791  
3.701  
3.693  
3.673  
3.665  
3.650  
3.643  
3.628  
2.822  
2.813  
2.692  
2.673  
2.655  
2.134  
2.111  
2.086  
2.078  
1.824  
1.816  
1.804  
1.789  
1.370  
1.370  
1.363  
1.358  
1.354  
1.338  
1.330  
1.294  
1.272  
1.239  
1.234  
1.226  
1.203

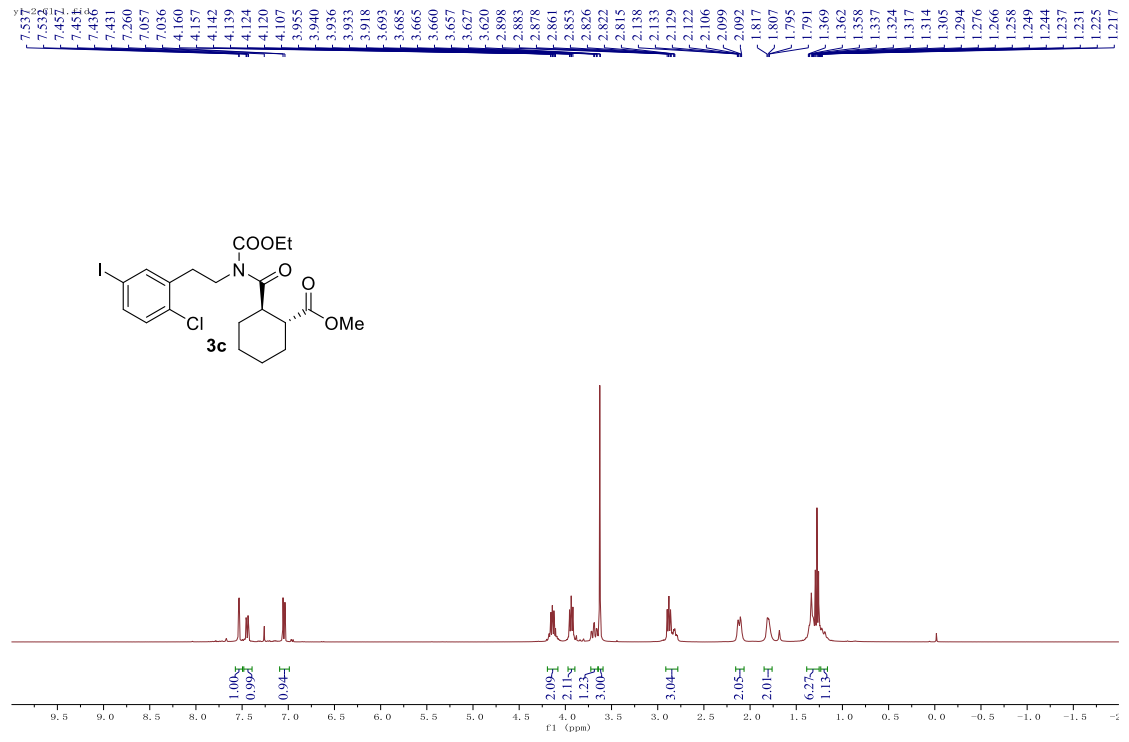


y1-NO-d1. 2. F10

178.386  
175.857  
153.913  
143.229  
143.161  
137.455  
94.866  
77.479  
77.160  
76.842  
63.159  
51.867  
46.542  
45.634  
45.406  
33.902  
29.703  
29.234  
25.714  
25.514  
14.347

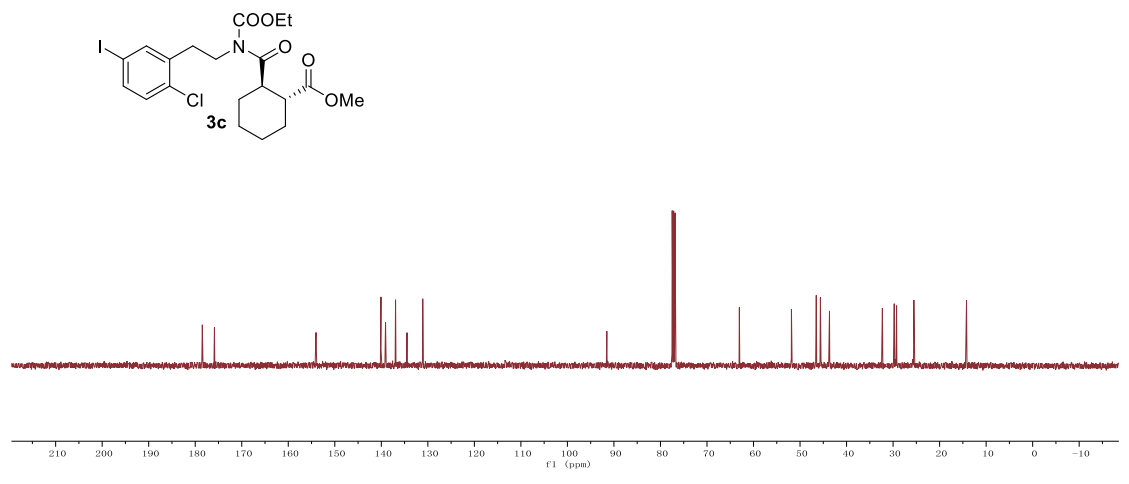






y1-2-Cl.2.fid

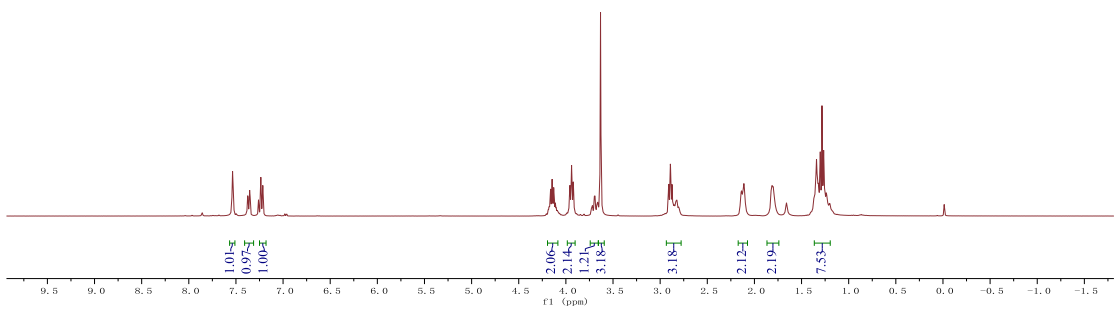
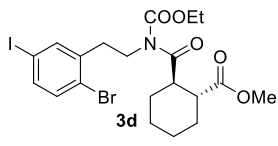
- ~ 178.477
- ~ 175.870
- 154.035
- ~ 140.072
- ~ 139.092
- ~ 136.940
- ~ 134.480
- ~ 131.093
- 91.531
- ~ 77.479
- ~ 77.161
- ~ 76.843
- 63.041
- ~ 51.846
- ~ 46.514
- ~ 45.620
- ~ 43.670
- ~ 32.300
- ~ 29.754
- ~ 29.244
- ~ 25.727
- ~ 25.529
- 14.213



y1-2-Br. 3. fid

7.538  
7.533  
7.377  
7.372  
7.356  
7.351  
7.260  
7.236  
7.215

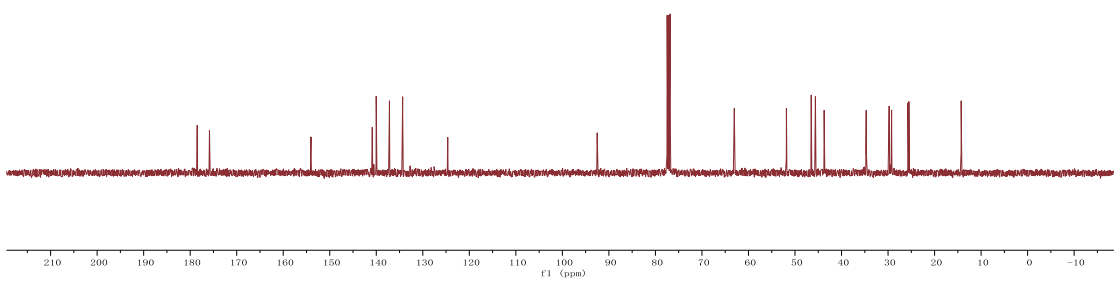
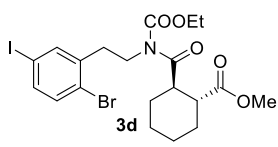
4.162  
4.146  
4.129  
4.111  
3.958  
3.940  
3.921  
3.727  
3.718  
3.698  
3.690  
3.670  
3.662  
3.653  
2.910  
2.892  
2.873  
2.860  
2.851  
2.832  
2.822  
2.805  
2.795  
2.145  
2.135  
2.111  
1.821  
1.813  
1.799  
1.367  
1.321  
1.301  
1.283  
1.266  
1.255  
1.251  
1.236  
1.205  
1.197

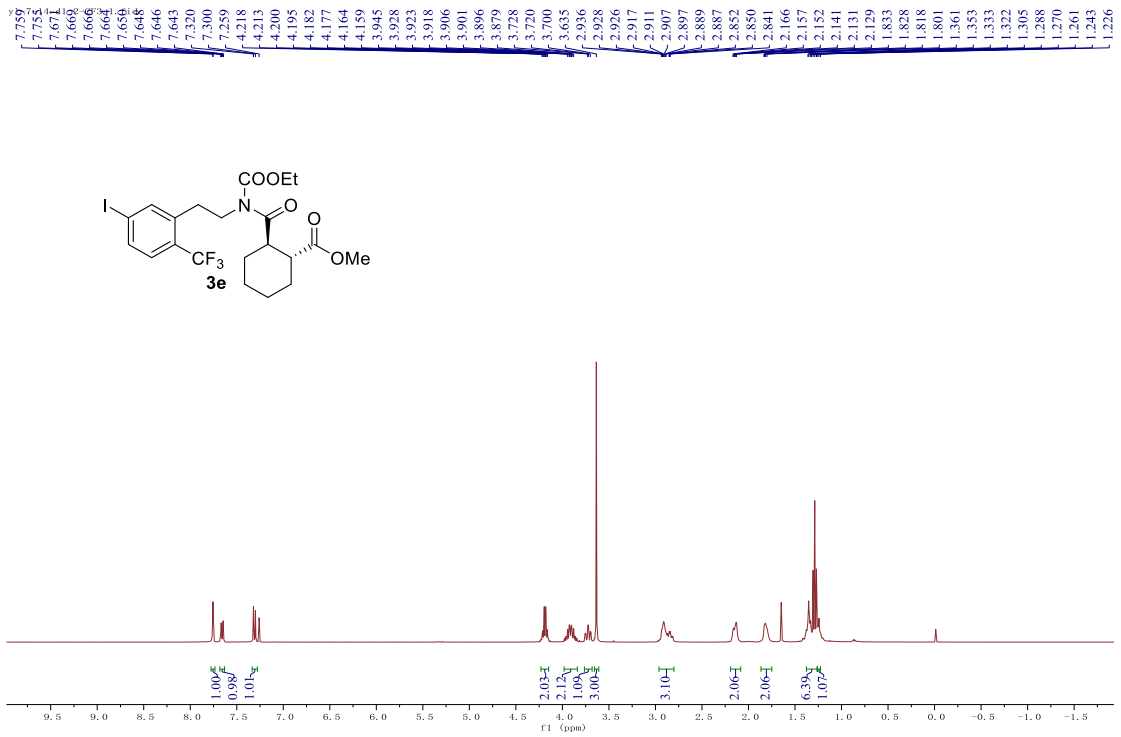


y1-2-Br. 2. fid

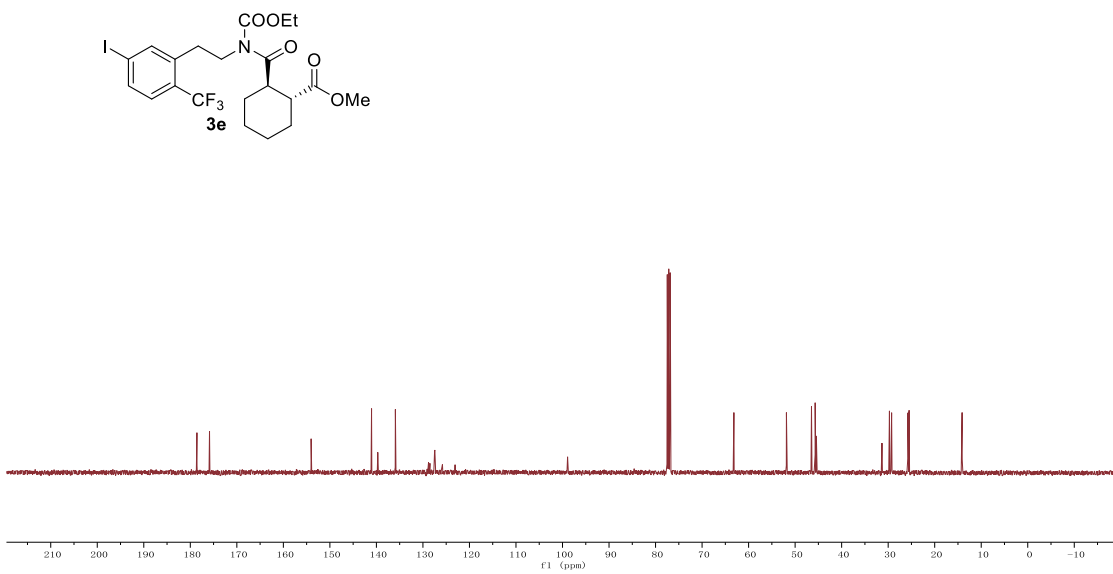
178.489  
175.856  
154.031  
140.866  
140.016  
137.165  
134.329  
124.638

92.521  
77.479  
77.161  
76.842  
63.045  
51.848  
46.509  
45.615  
43.735  
34.694  
29.764  
29.235  
25.721  
25.517  
14.283

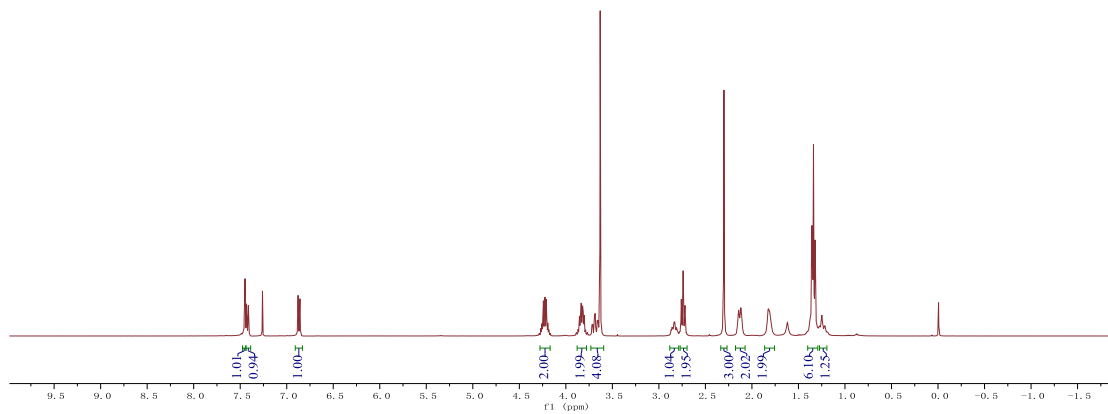
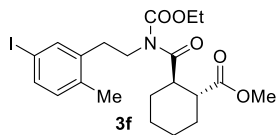




y1-7-14-d1 2-CF3, 3, fid

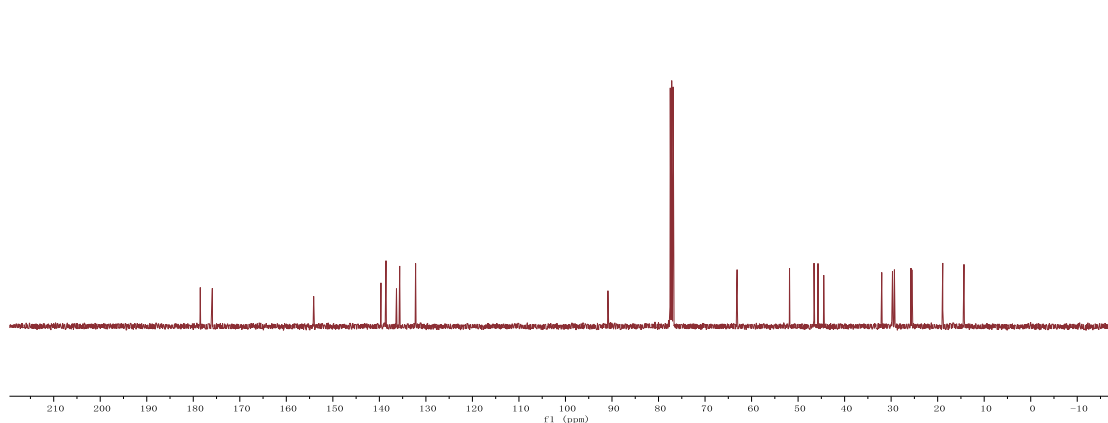
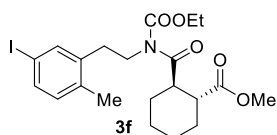


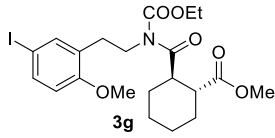
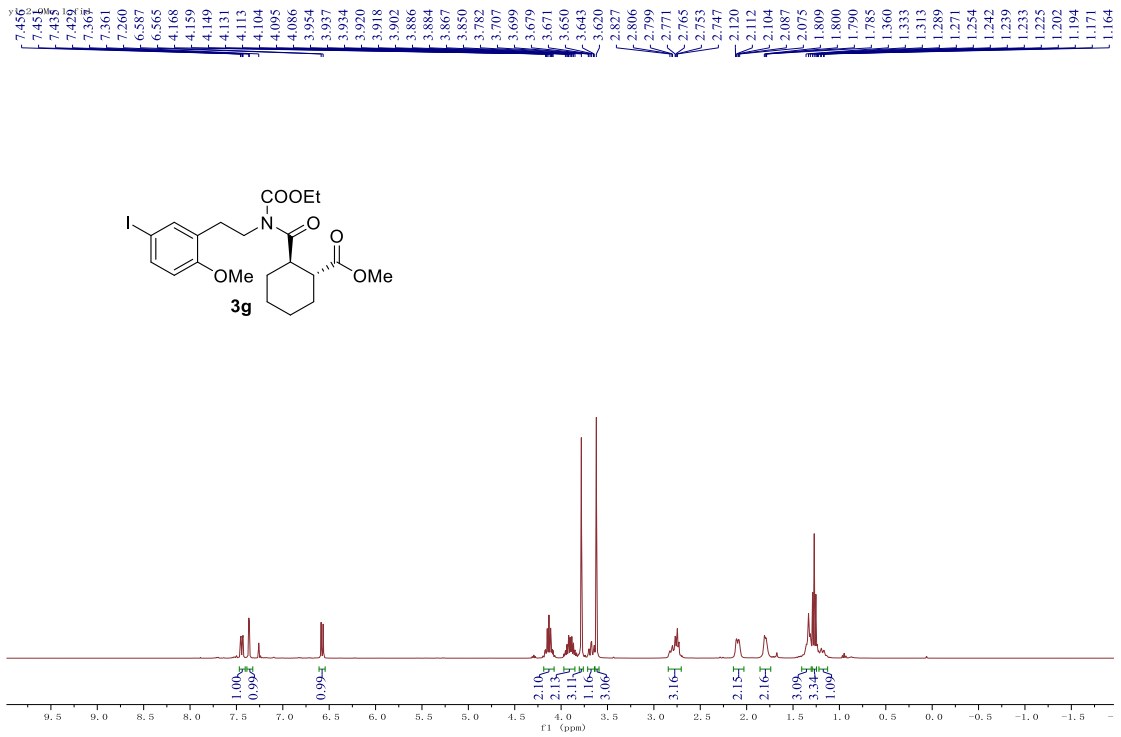
7.457  
7.448  
7.434  
7.428  
7.413  
7.408  
7.260  
6.878  
6.858  
4.267  
4.259  
4.247  
4.241  
4.229  
4.223  
4.212  
4.205  
4.194  
4.185  
3.854  
3.847  
3.842  
3.836  
3.833  
3.823  
3.820  
3.813  
3.803  
3.720  
3.711  
3.691  
3.683  
3.663  
3.655  
3.650  
3.631  
2.857  
2.839  
2.829  
2.811  
2.801  
2.759  
2.740  
2.720  
2.301  
2.148  
2.141  
2.120  
2.113  
1.829  
1.821  
1.810  
1.373  
1.356  
1.348  
1.338  
1.321  
1.321  
1.306  
1.299  
1.280  
1.273  
1.248  
1.219  
1.212



y1-7-6-a 2Me. 3. F1d

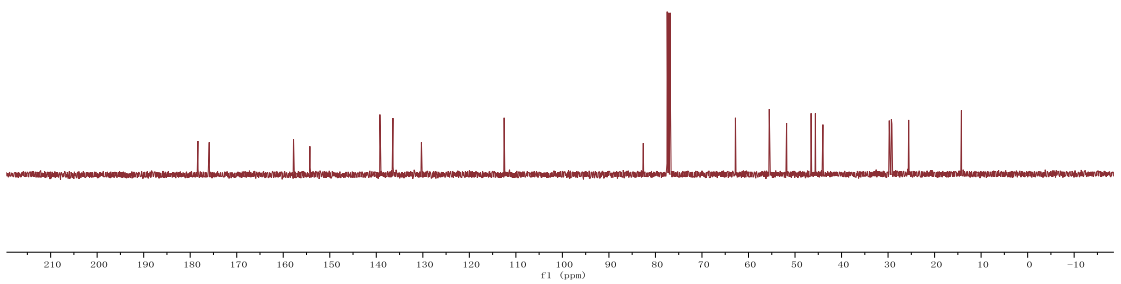
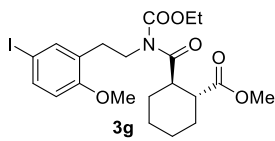
178.496  
175.905  
154.125  
139.662  
138.574  
136.323  
135.633  
132.214  
90.871  
77.477  
77.160  
76.843  
63.111  
51.841  
46.578  
45.722  
44.484  
32.018  
29.711  
29.296  
25.739  
25.537  
18.908  
14.341

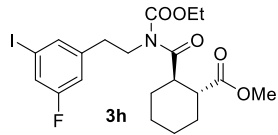
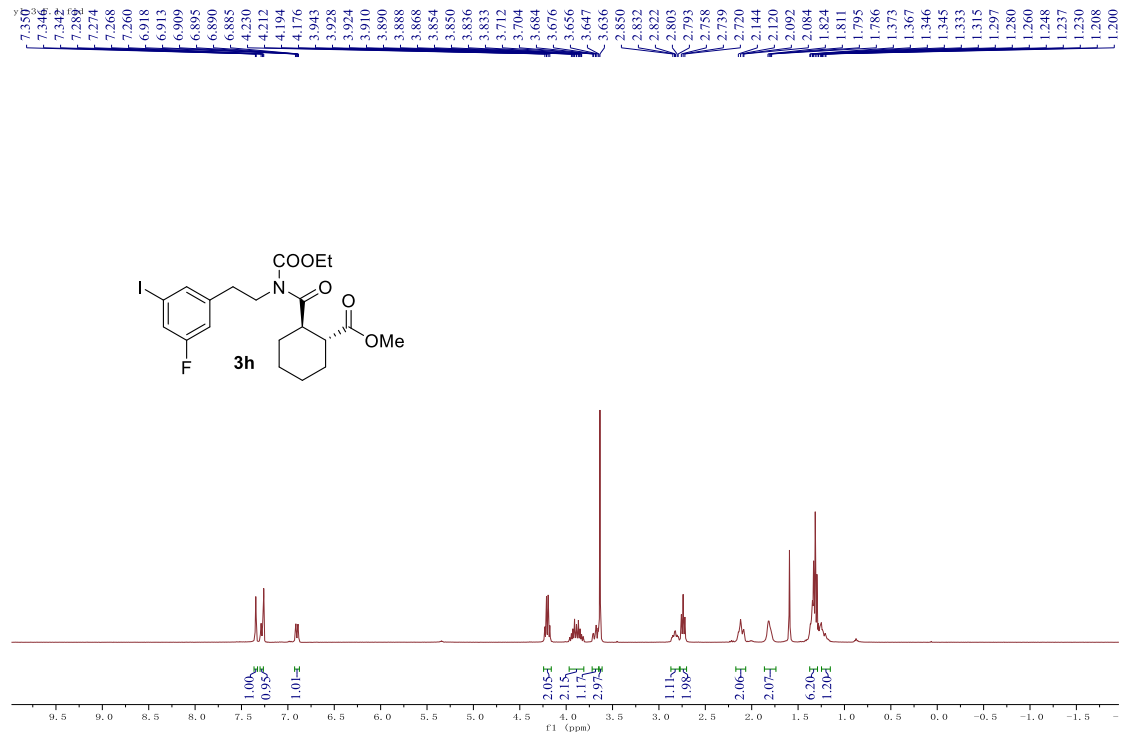




y1-2-OMe.2. Fid

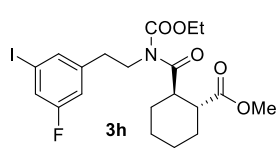
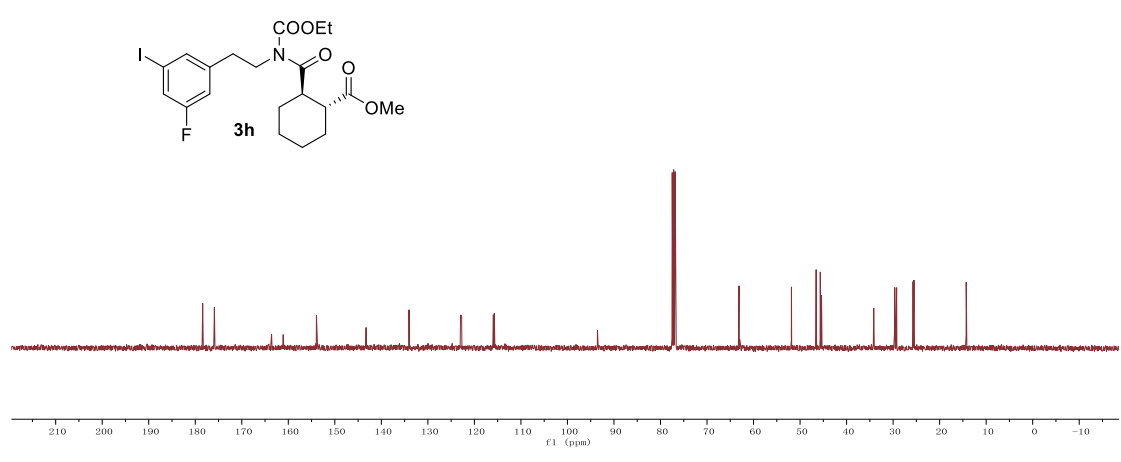
178.335  
175.911  
157.793  
154.271  
139.221  
136.415  
130.302  
112.520  
82.617  
77.478  
77.160  
76.842  
62.806  
55.532  
51.810  
46.543  
45.621  
44.002  
29.740  
29.295  
29.174  
25.720  
25.570  
14.231



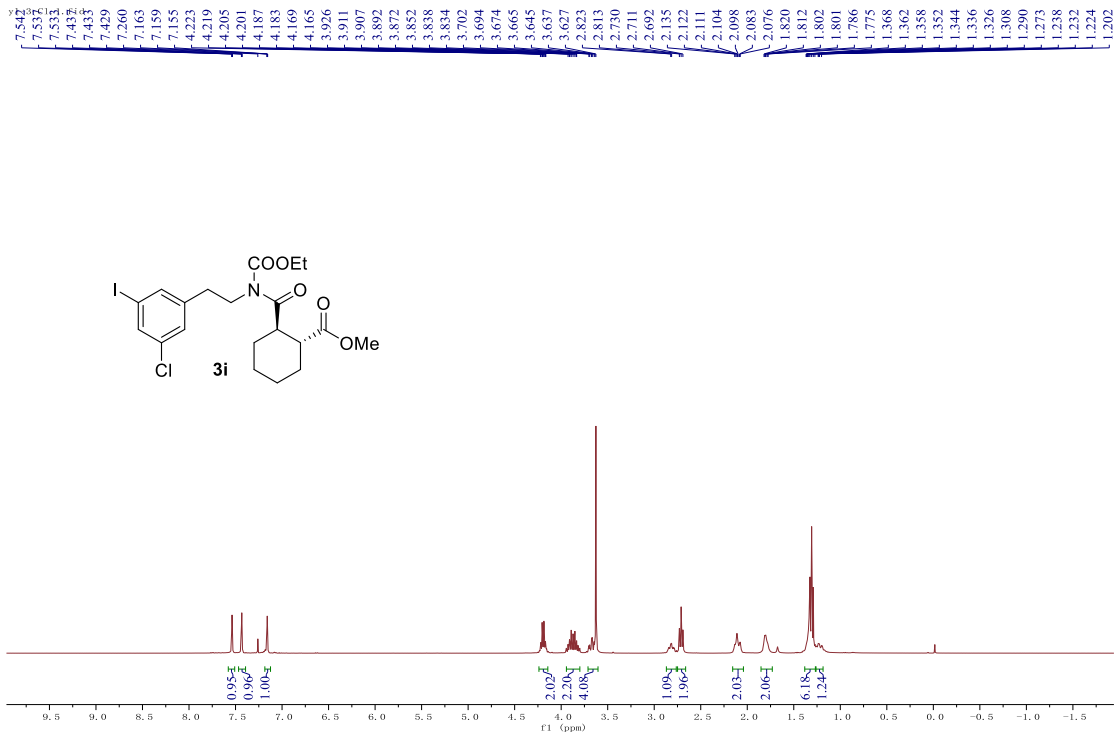


y1-6-43-e1 3-F: 2, f1d

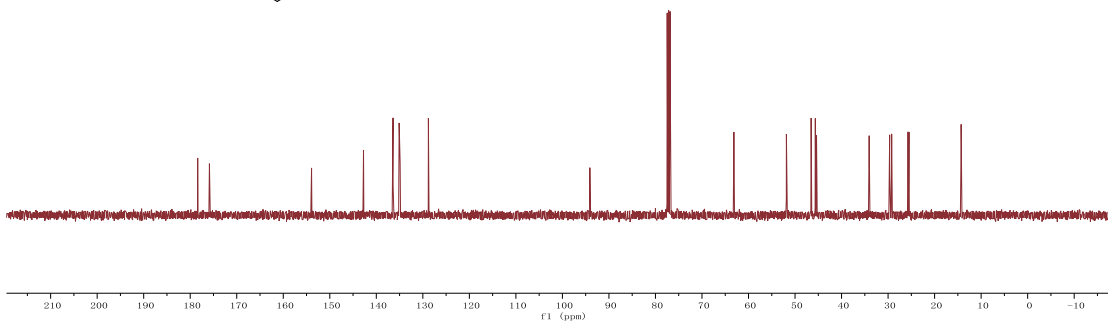
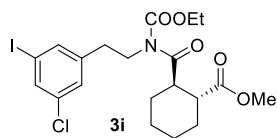
- ~ 178.403
- ~ 175.885
- ~ 163.597
- ~ 161.098
- ~ 153.951
- ~ 143.318
- ~ 143.244
- ~ 134.055
- ~ 134.026
- ~ 122.976
- ~ 122.742
- ~ 115.921
- ~ 115.713
- ~ 93.549
- ~ 93.465
- ~ 77.478
- ~ 77.161
- ~ 76.842
- ~ 63.126
- ~ 51.852
- ~ 46.342
- ~ 45.681
- ~ 45.656
- ~ 45.389
- ~ 34.159
- ~ 34.151
- ~ 29.644
- ~ 29.586
- ~ 29.240
- ~ 25.714
- ~ 25.513
- ~ 14.290



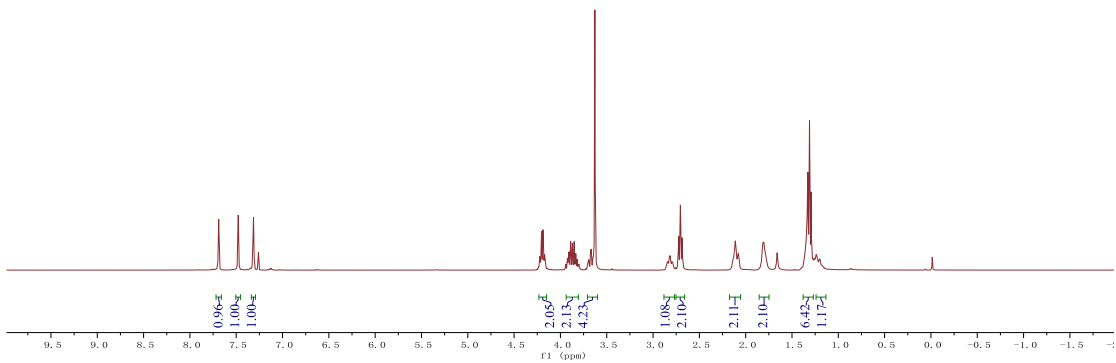
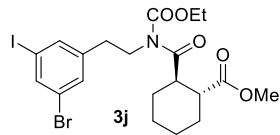




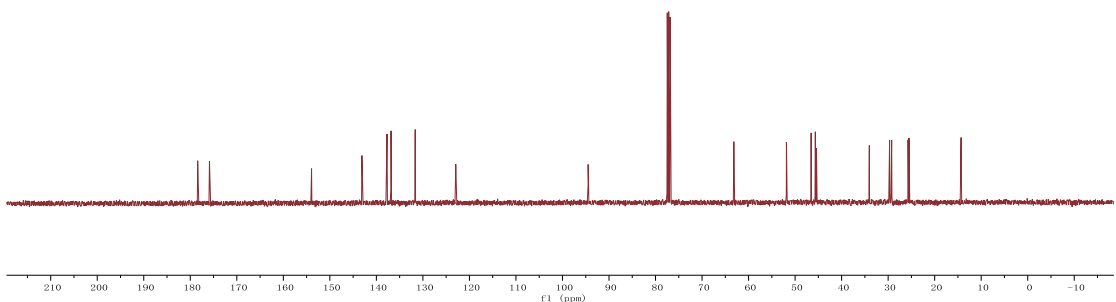
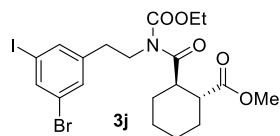
y1-3-Cl.4.fid

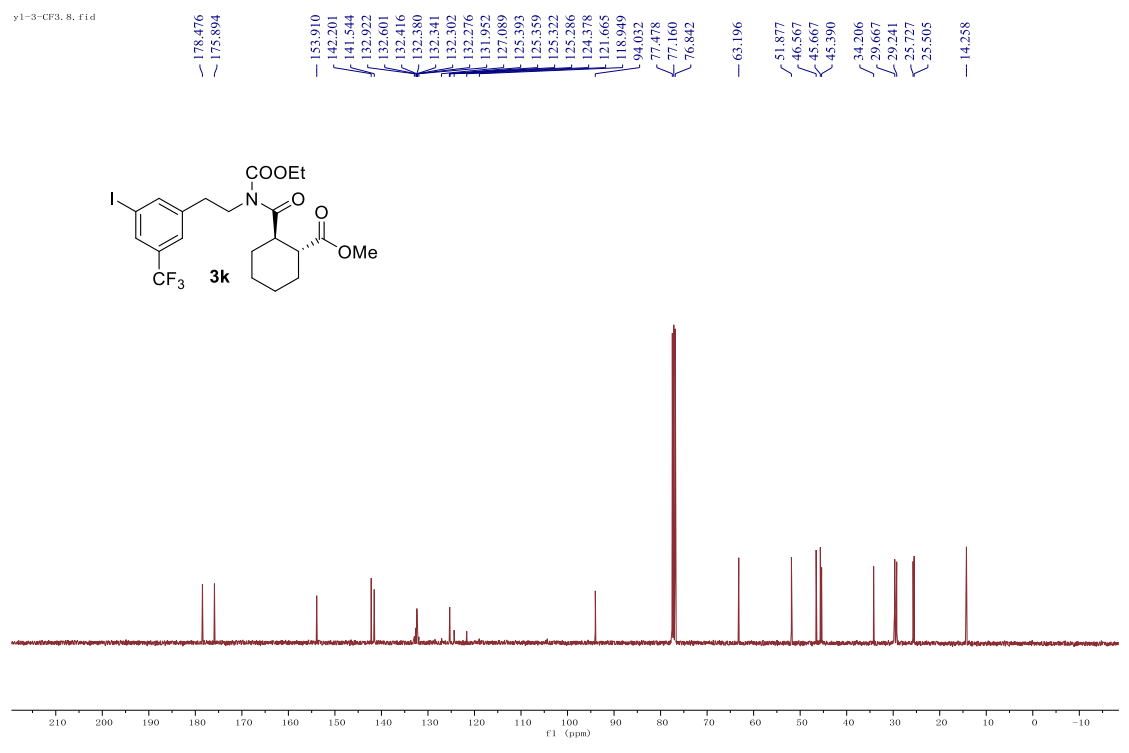
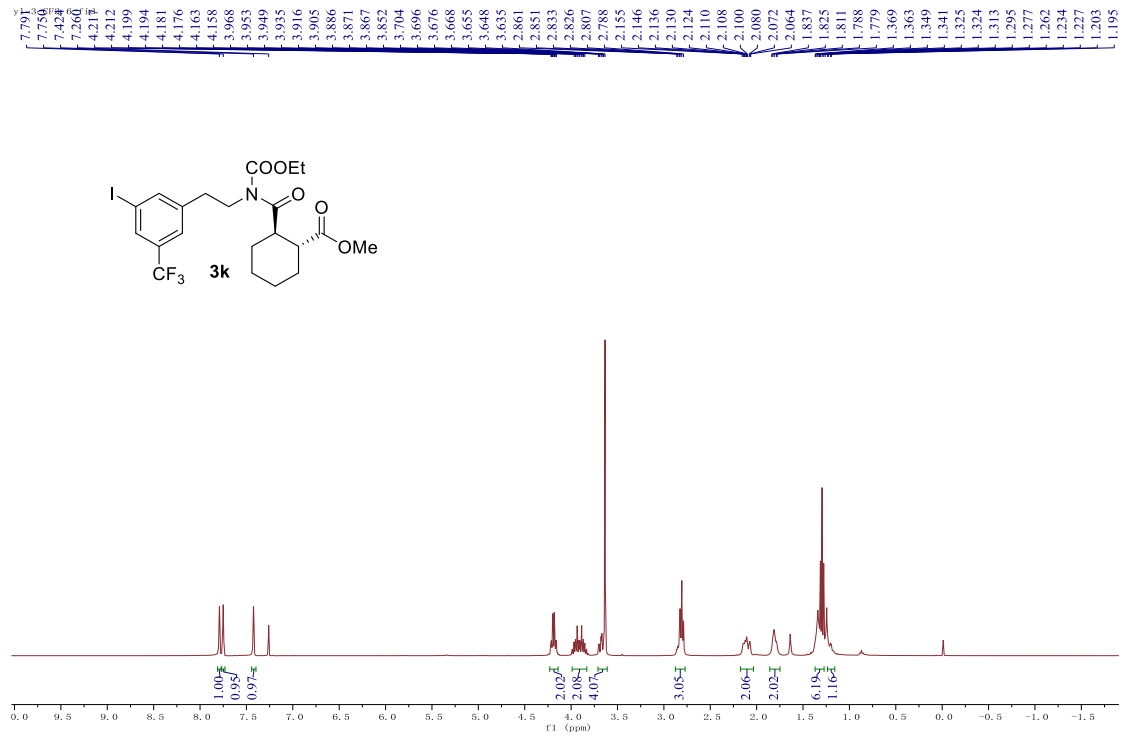


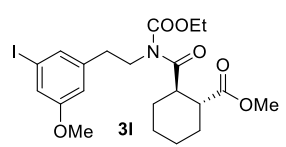
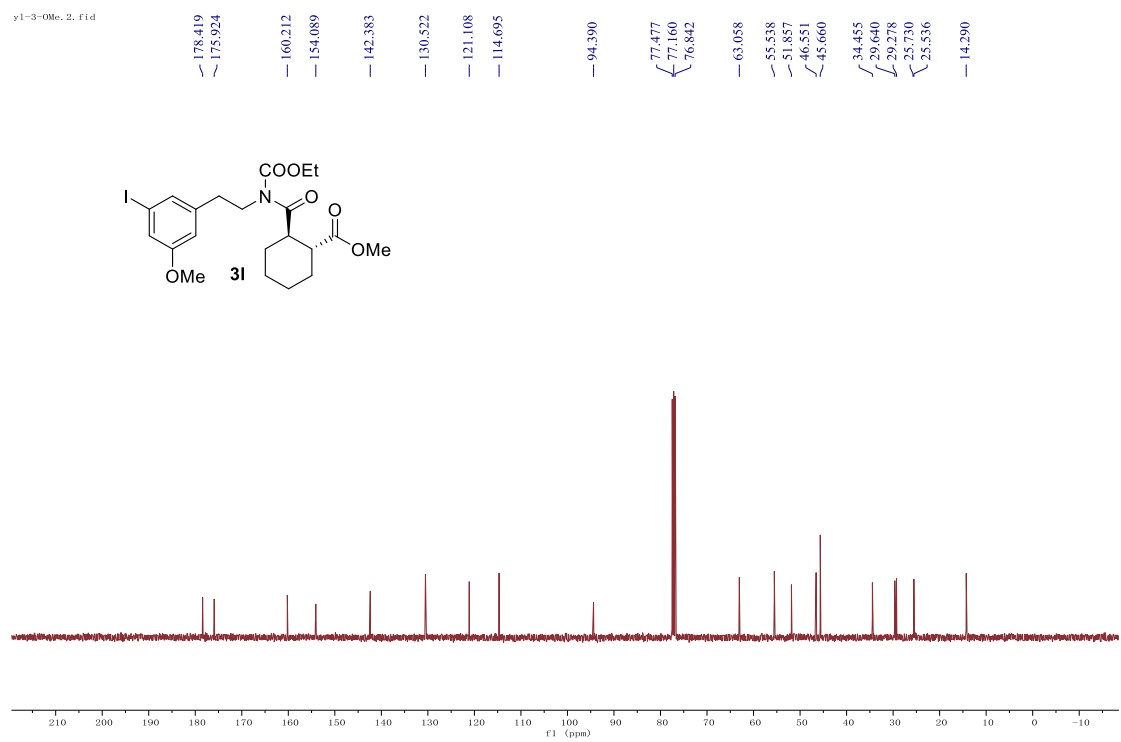
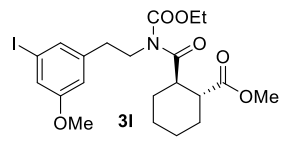
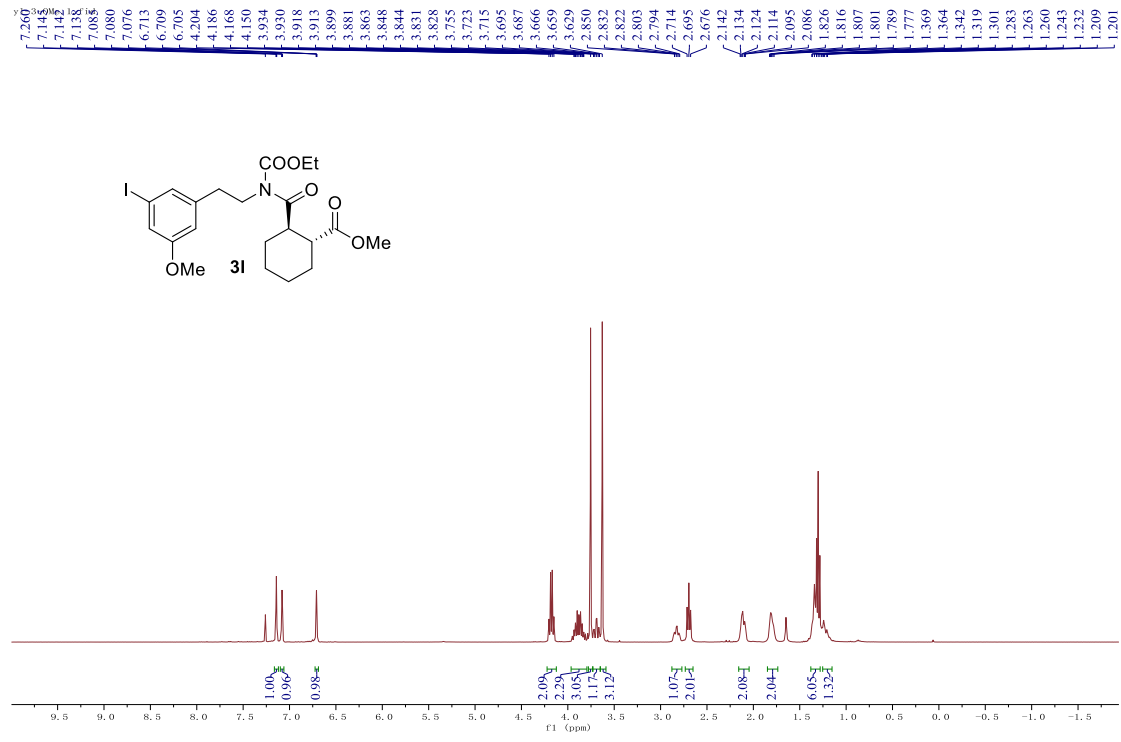
y1-3-Br\_6.fid

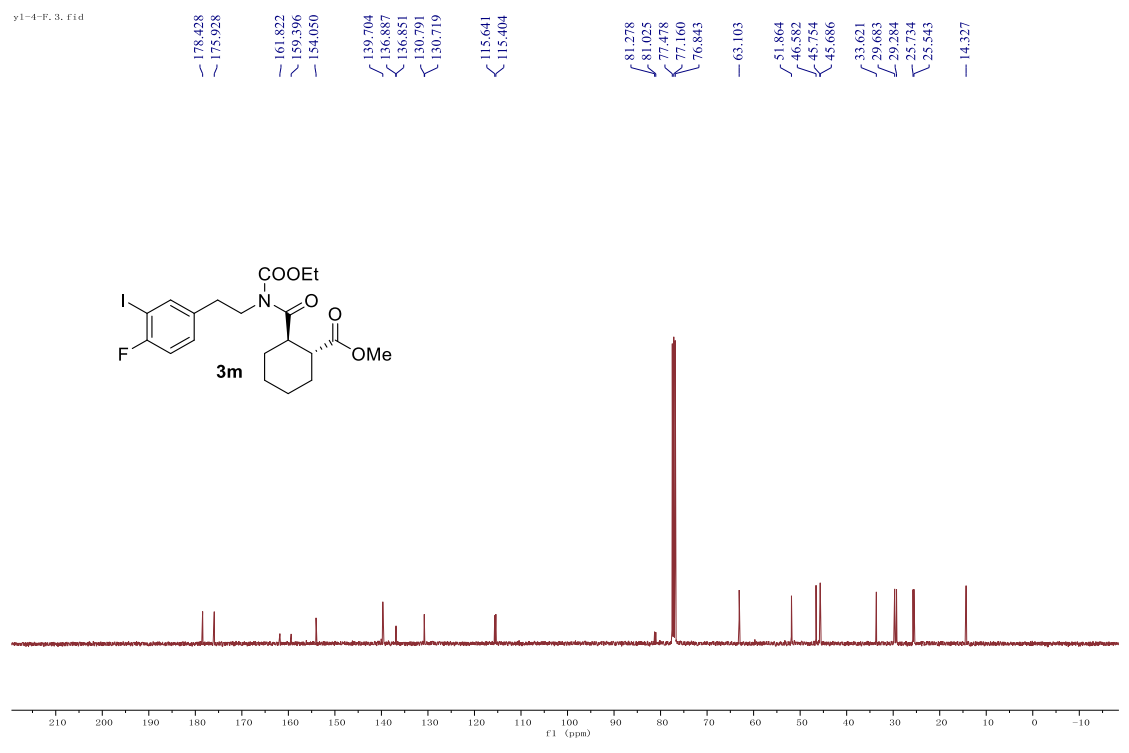
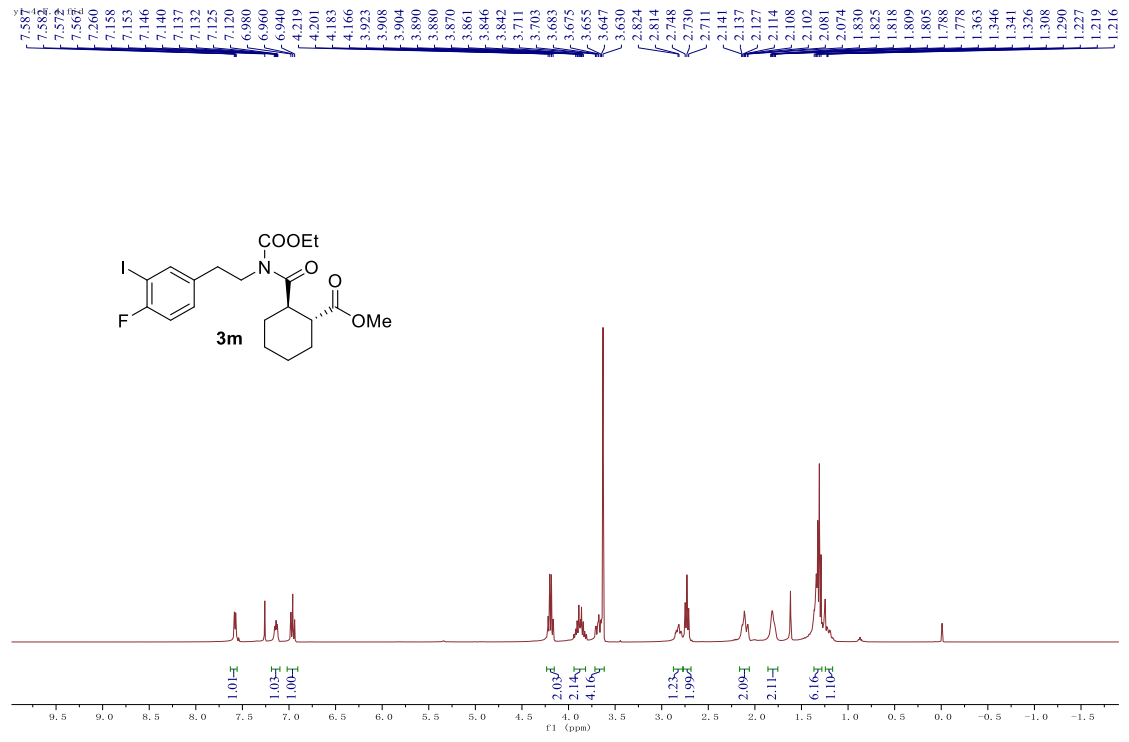


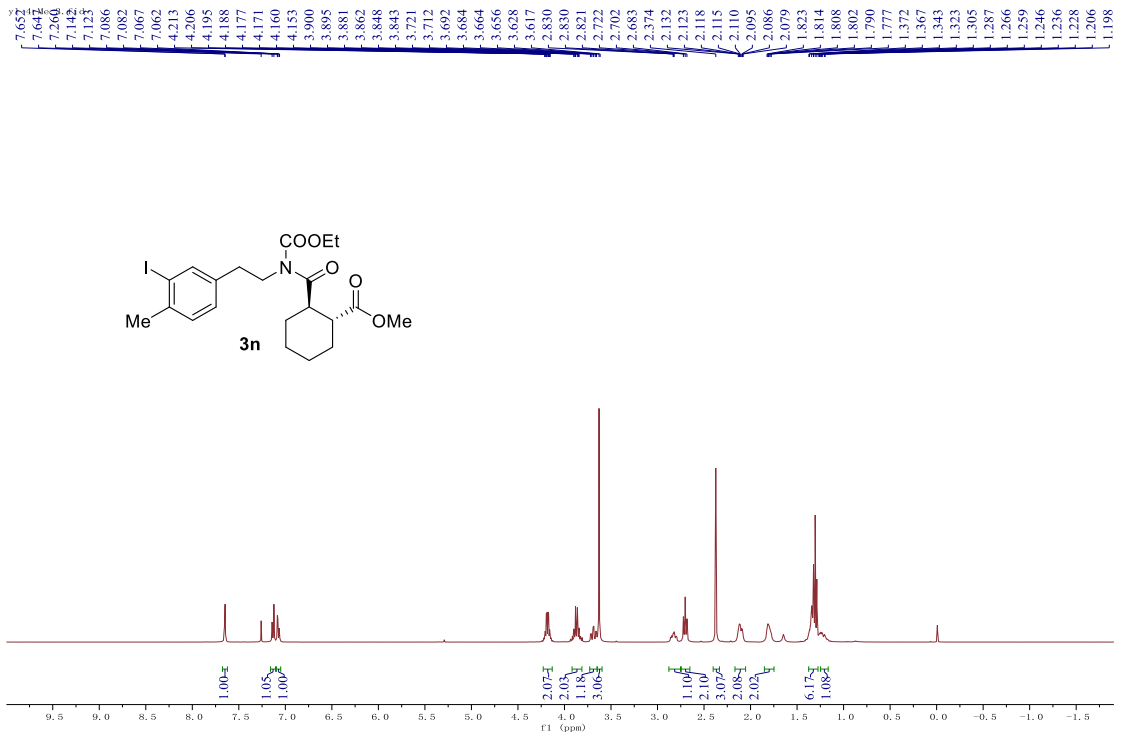
y1-3-Br\_7.fid



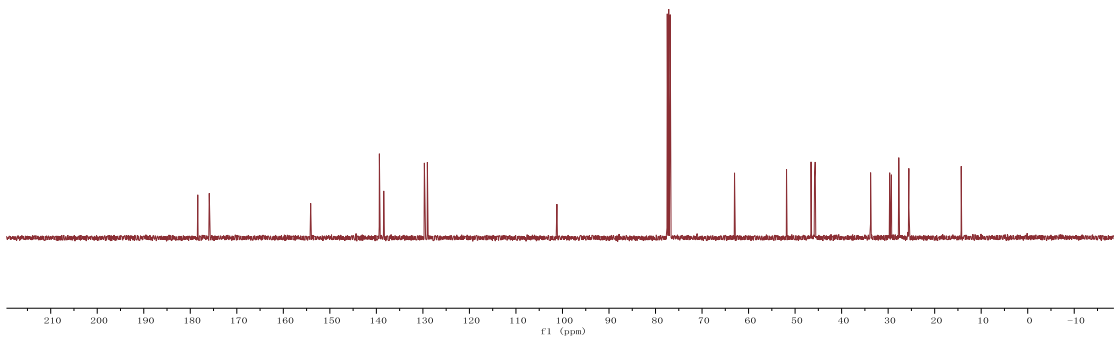
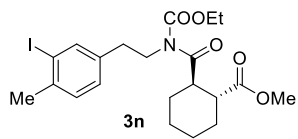




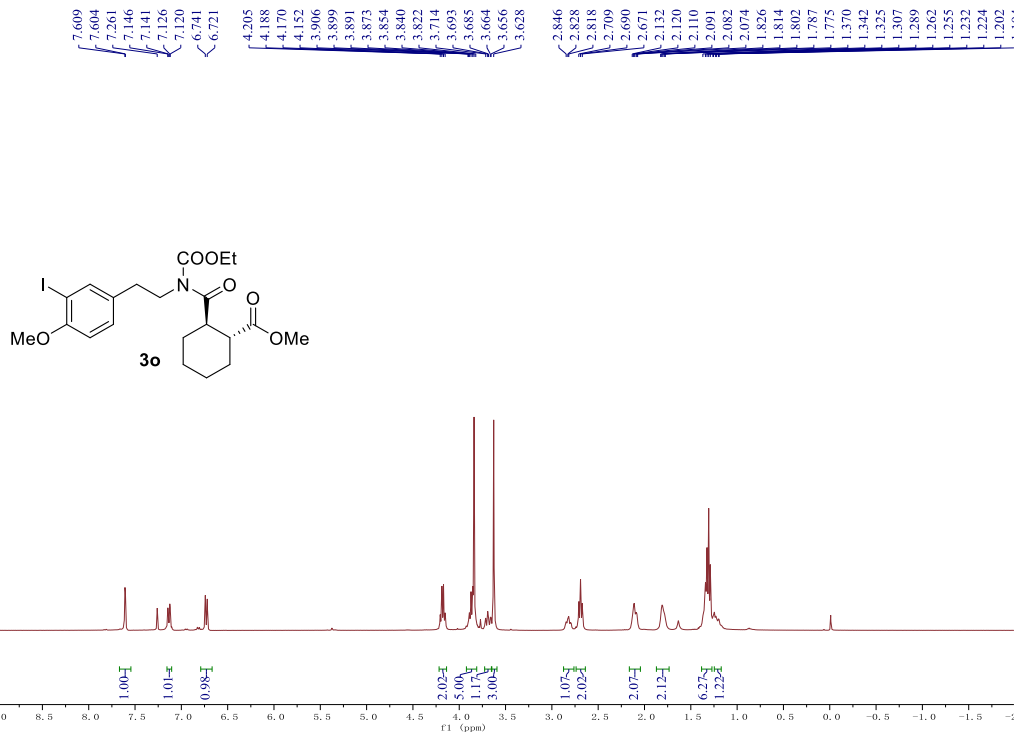




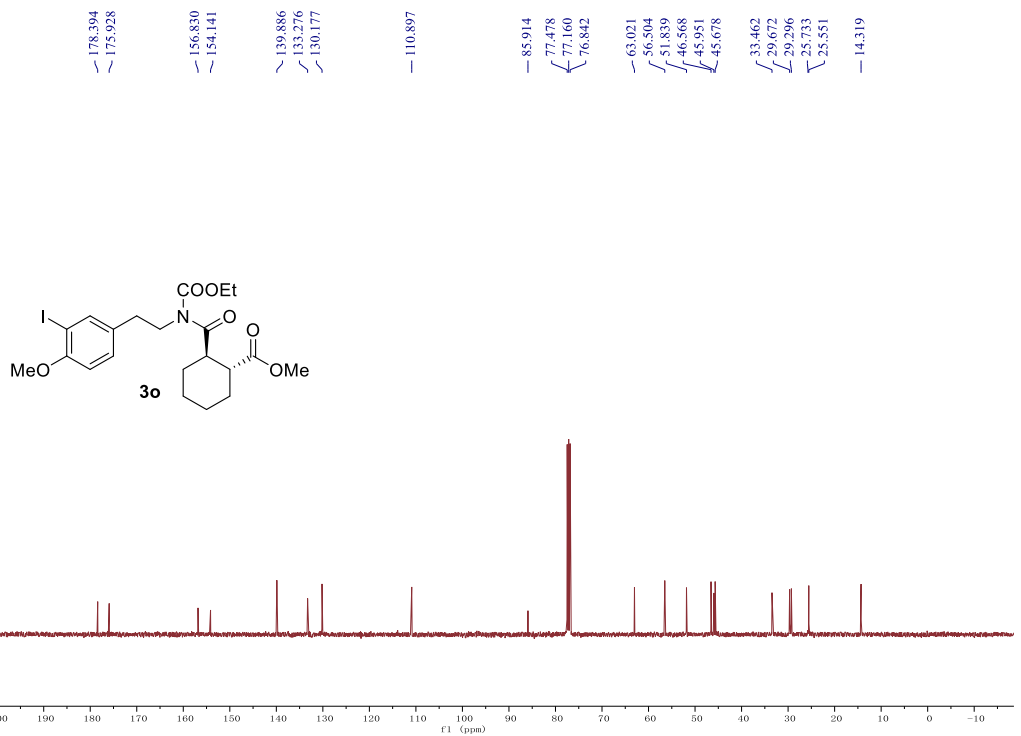
y1-4-Me, 4. fid

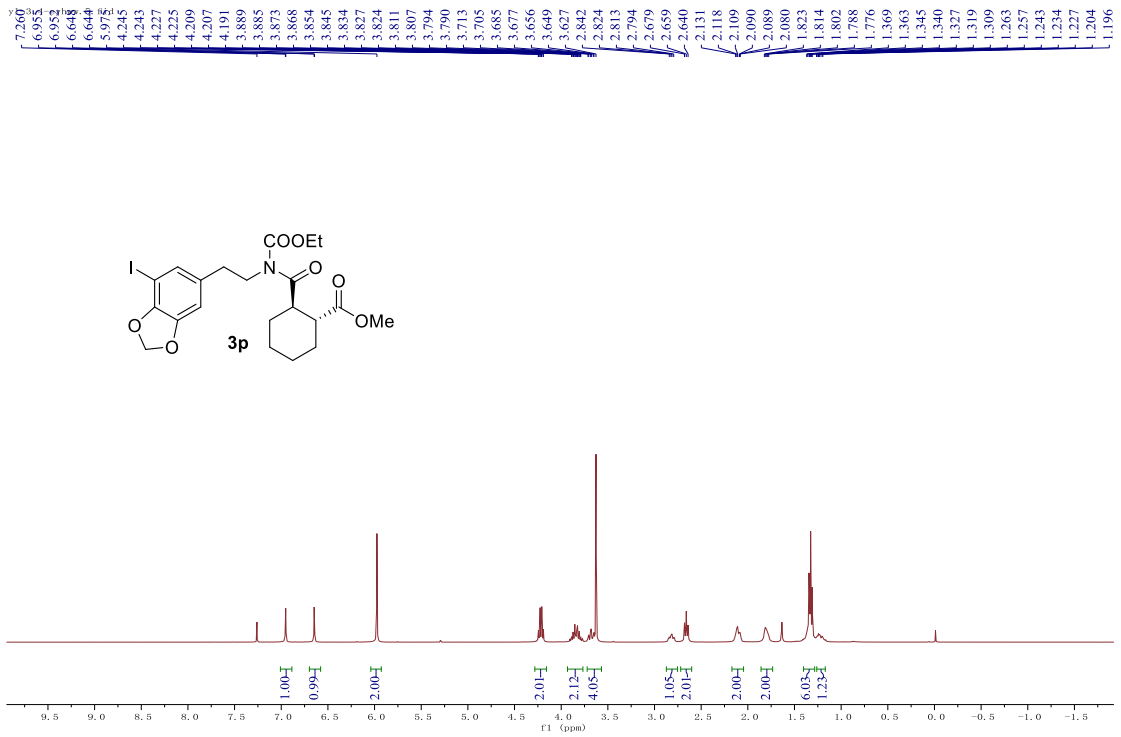


y1-4-OMe.3.fid

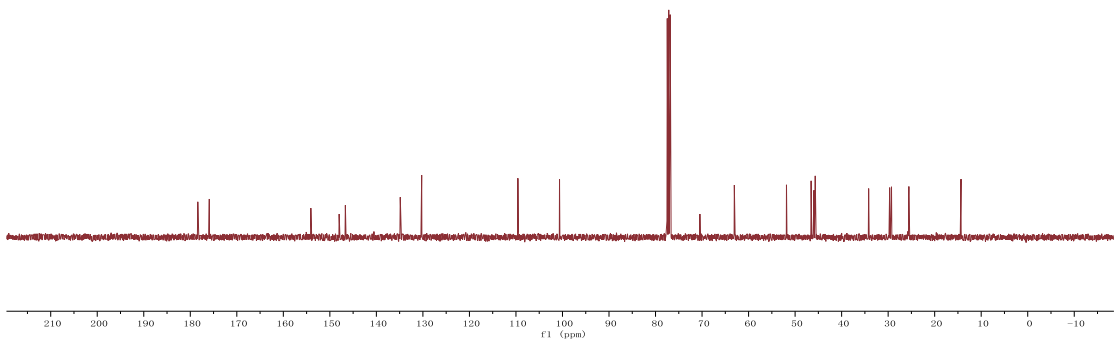
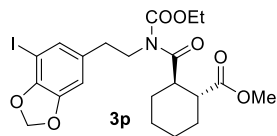


y1-4-OMe.4.fid

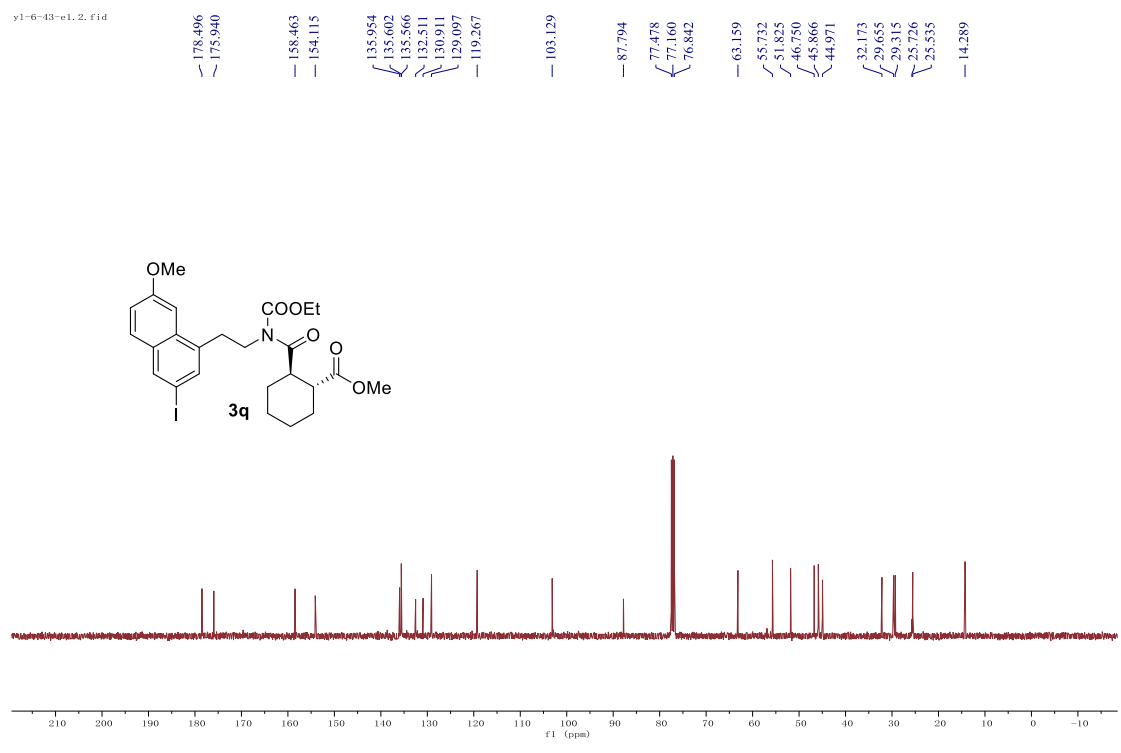
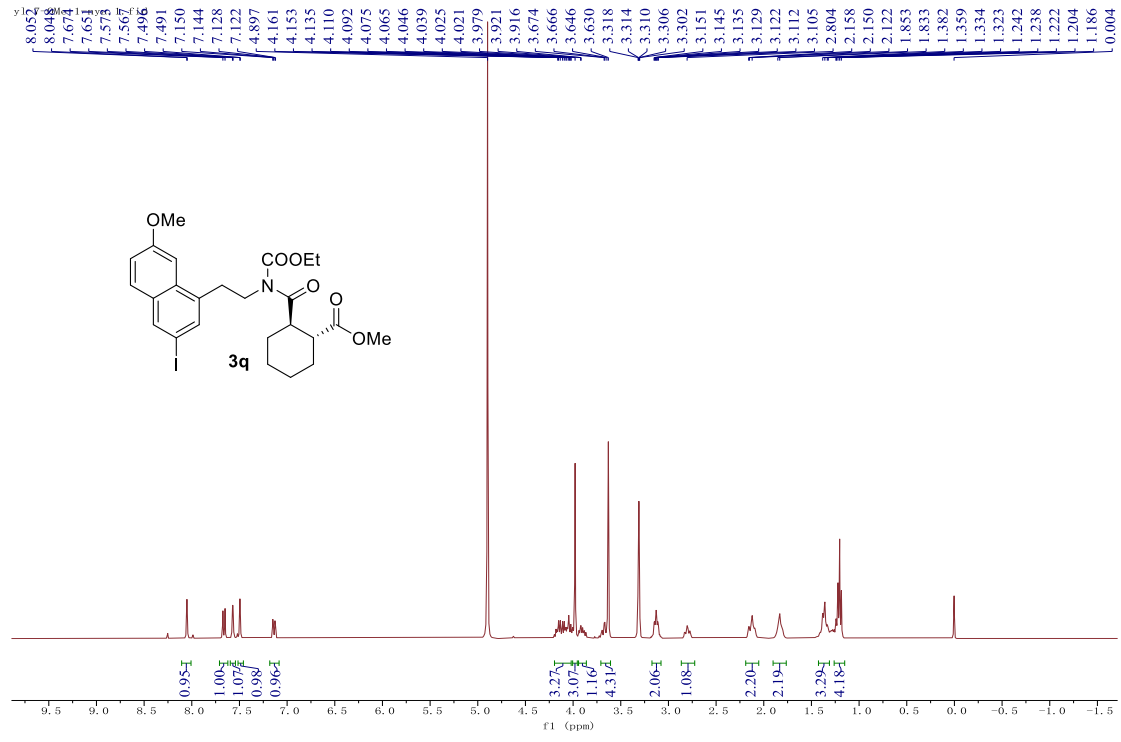


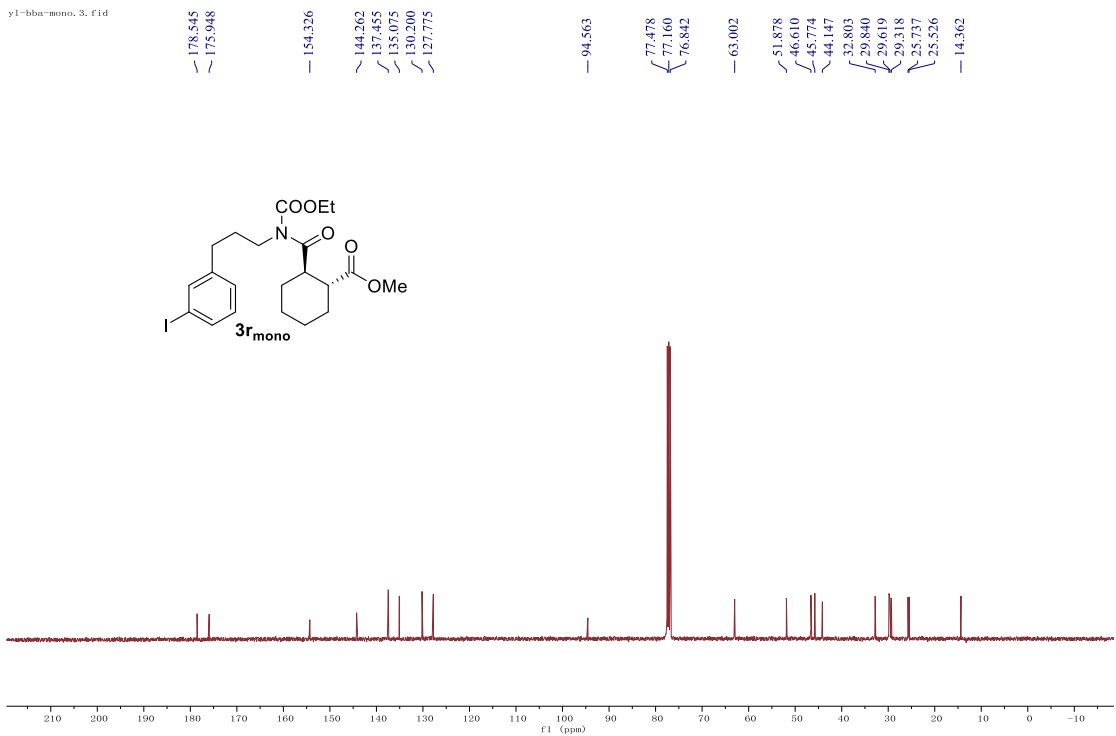
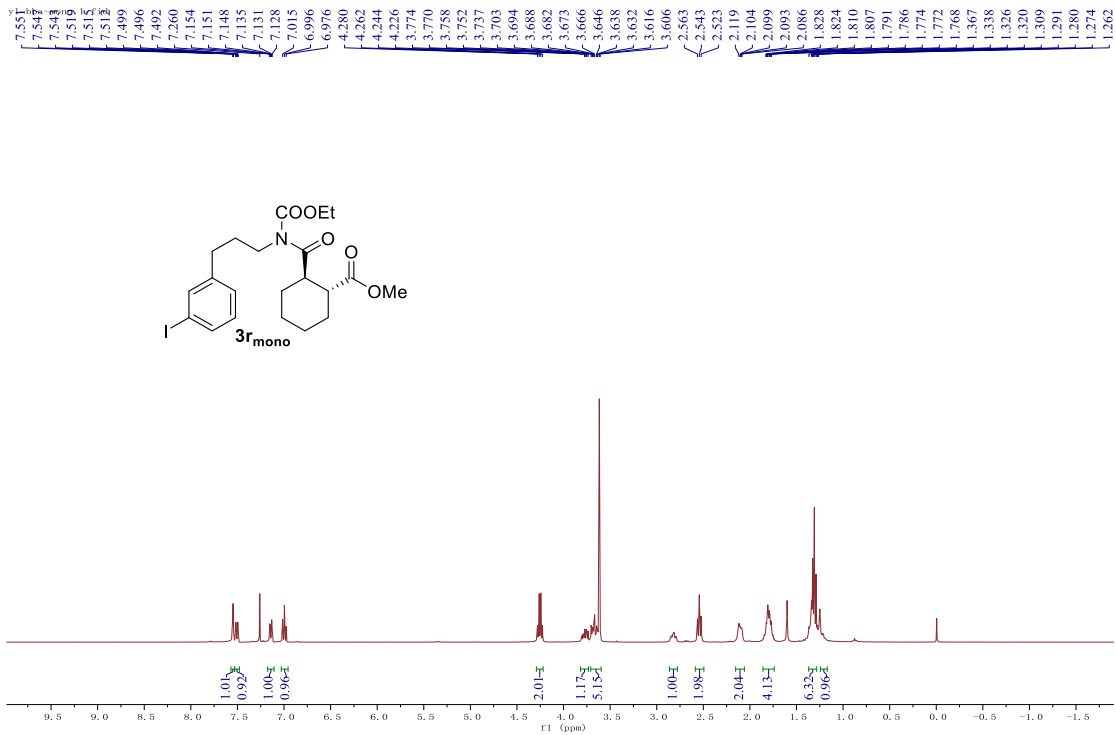


y1-3,4-eyhww\_6\_F1d

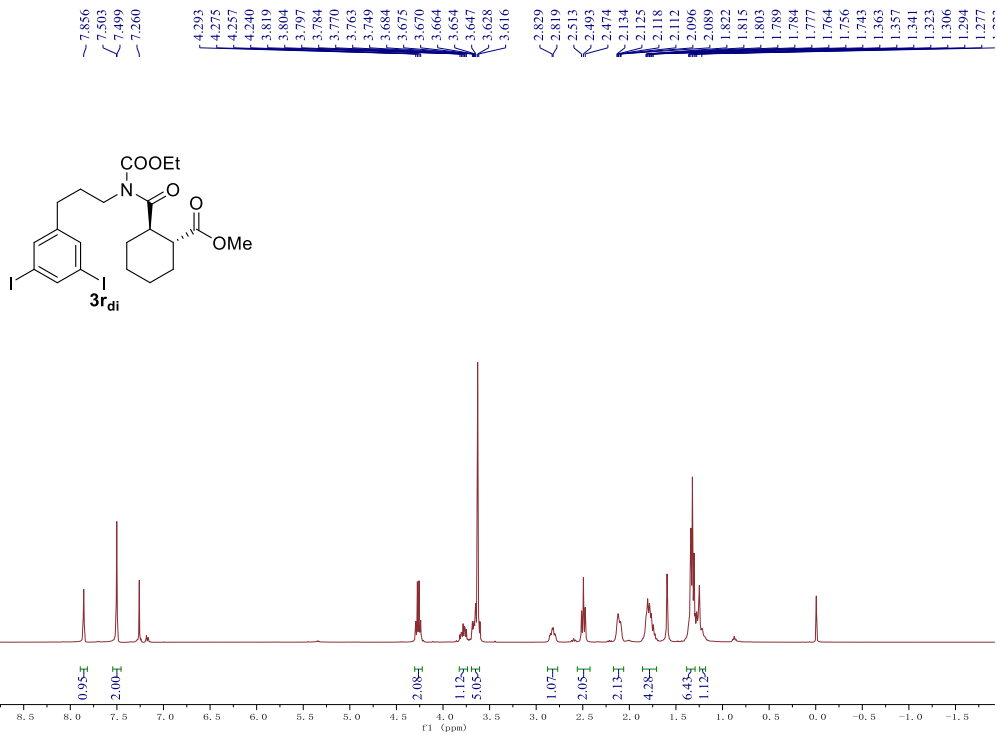




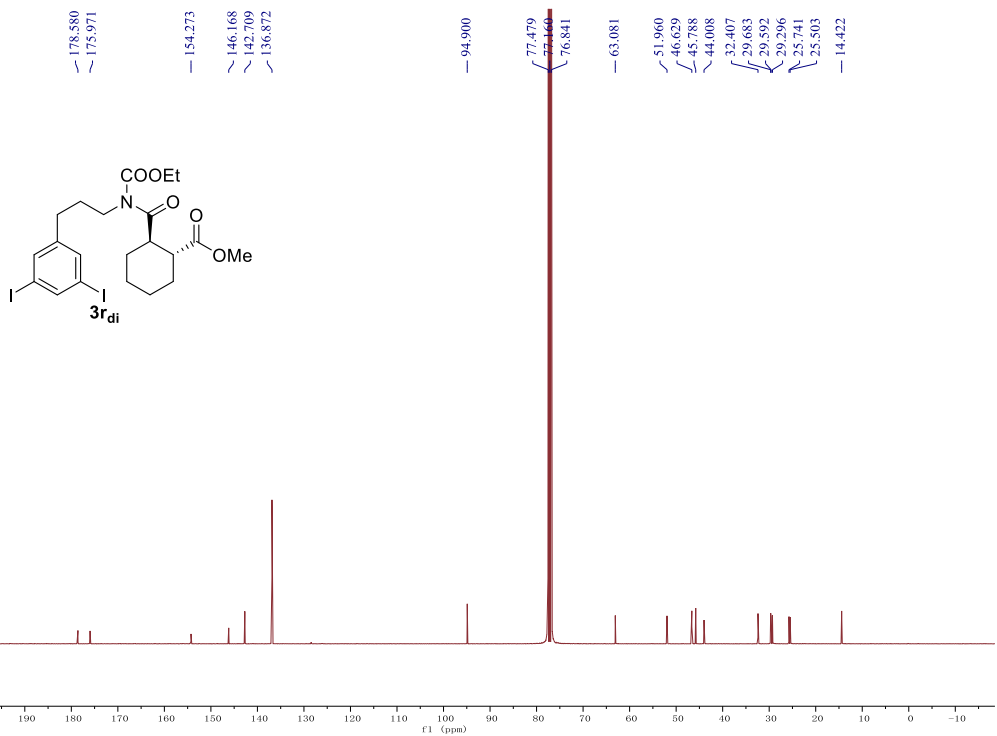




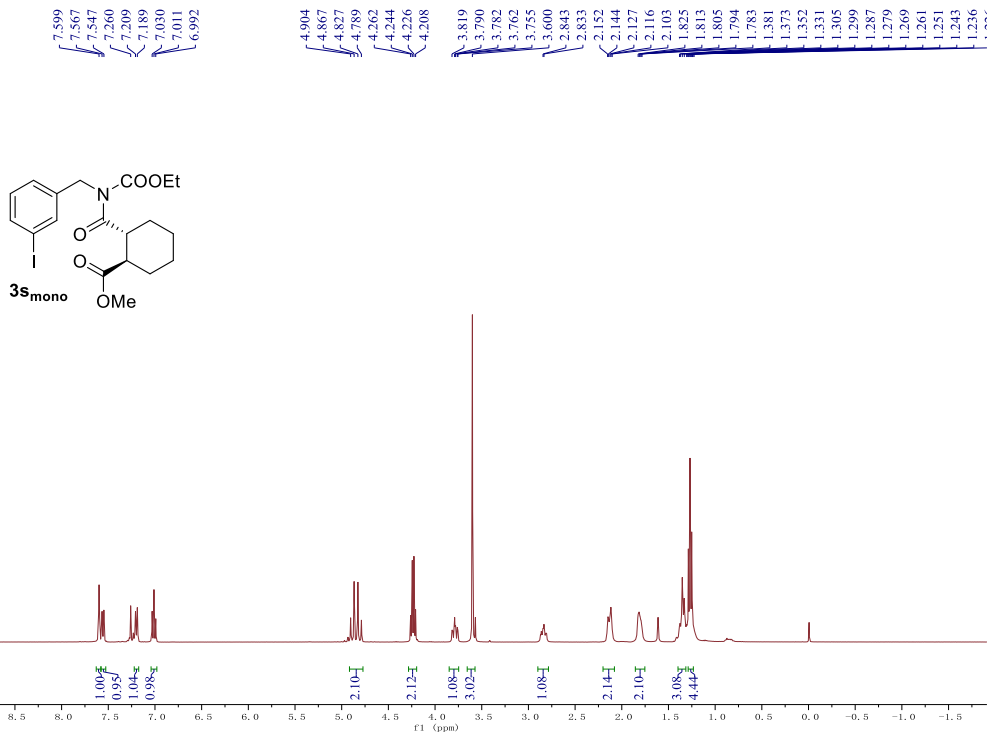
y1-bba-di.3.fid



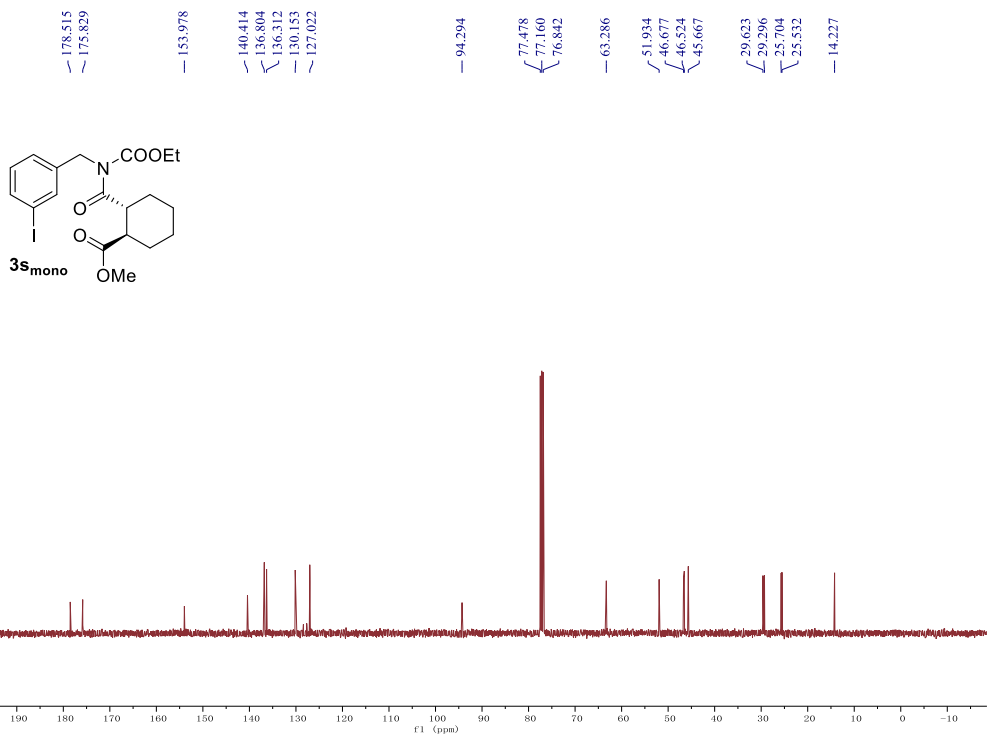
y1-bba-di.2.fid



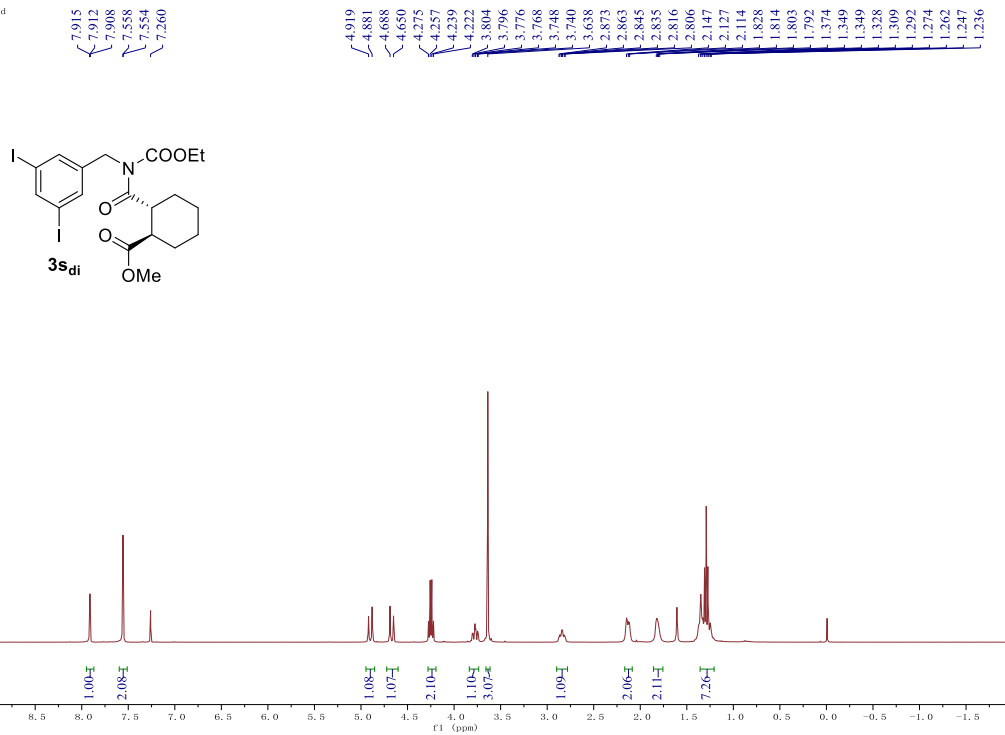
y1-7-44-cl-3.1.Fid



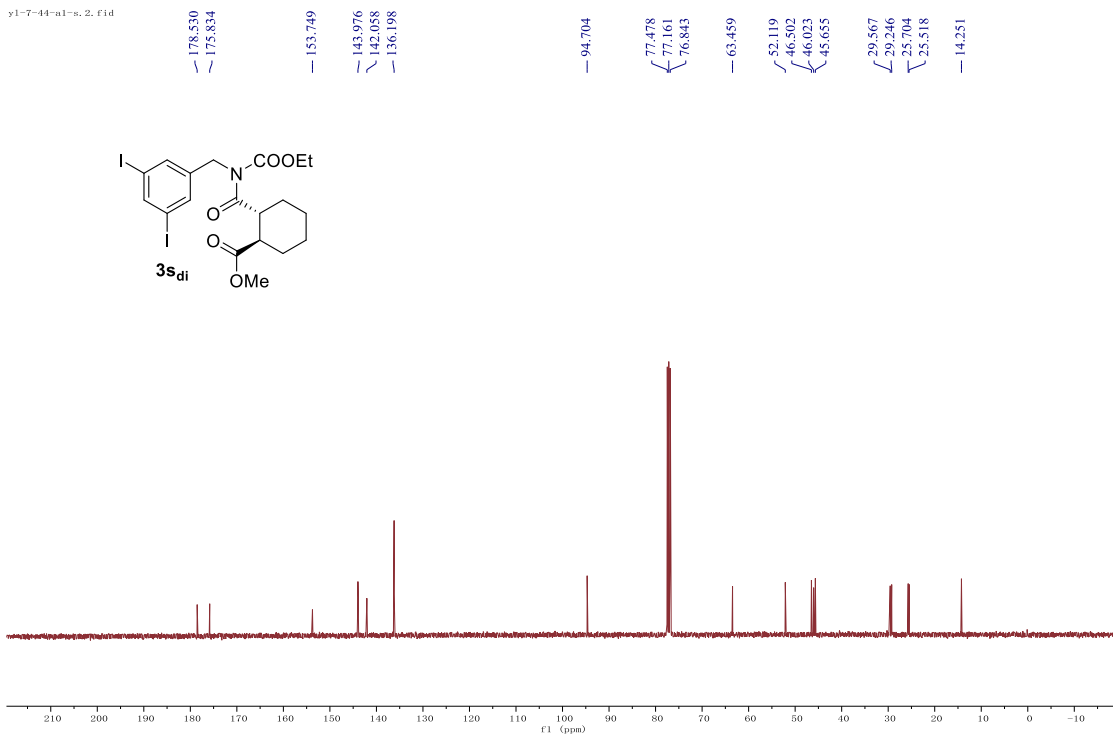
y1-7-44-cl-3.2.Fid



y1-7-44-a1-s. 1. F1d



y1-7-44-a1-s. 2. F1d

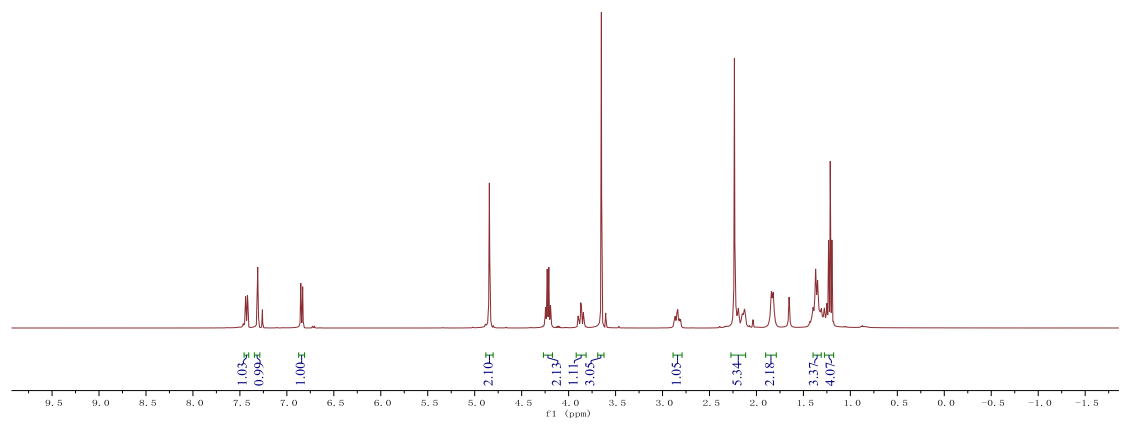
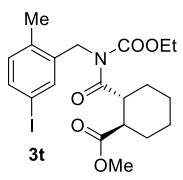


y1-8-12-an1.1.fid

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7.260  
6.852  
6.832

4.844  
4.246  
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4.211  
4.193  
3.899  
3.891  
3.871  
3.863  
3.843  
3.835  
3.651

2.866  
2.847  
2.837  
2.249  
2.235  
2.203  
2.192  
2.151  
2.137  
2.127  
2.119  
1.853  
1.840  
1.821  
1.805  
1.398  
1.370  
1.349  
1.338  
1.326  
1.313  
1.307  
1.277  
1.268  
1.249  
1.232  
1.214  
1.197



y1-8-12-an1.2.fid

178.291  
175.897  
154.073

138.257  
135.814  
134.822  
134.338  
132.009

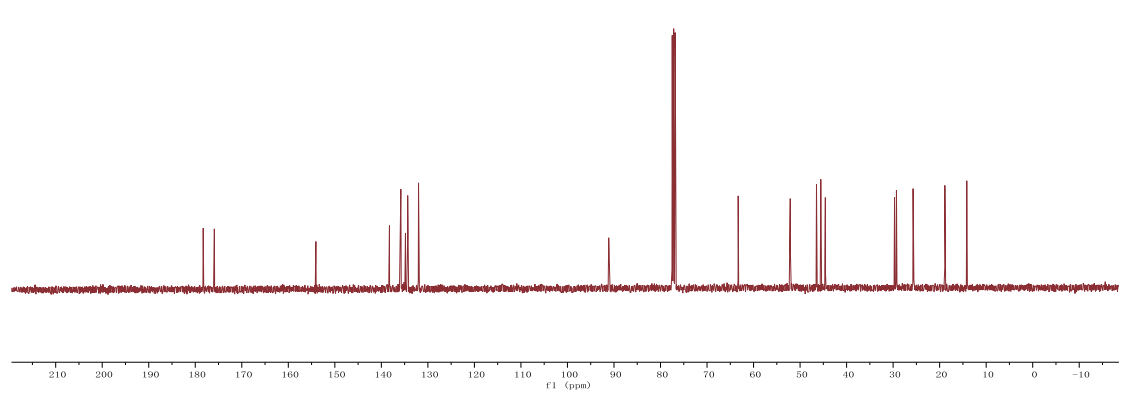
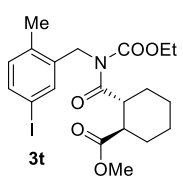
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77.478  
77.160  
76.842

63.300

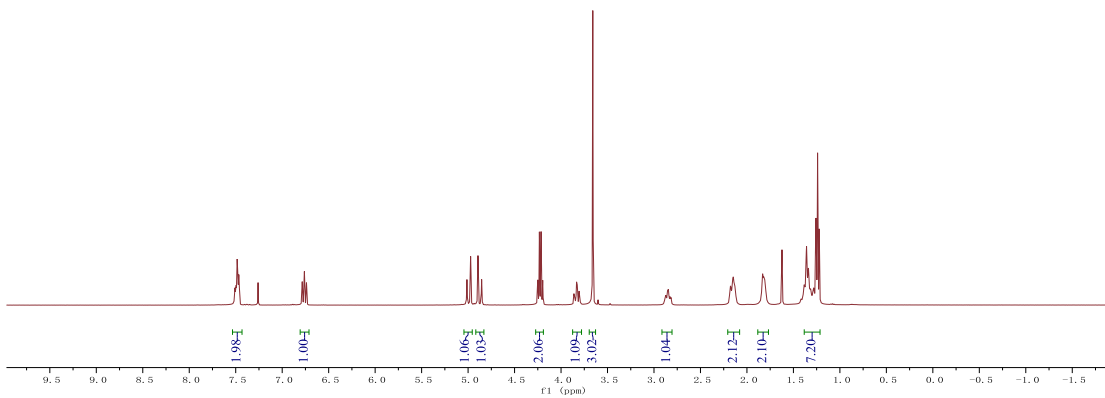
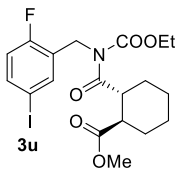
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25.709  
25.591  
18.880  
14.167



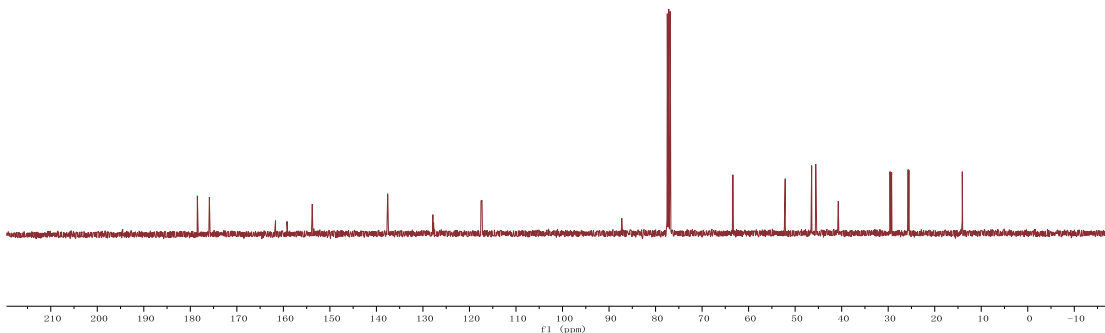
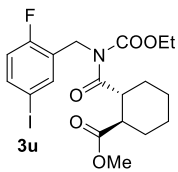
y1-8-12-b1-s. 2. F1d

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7.496  
7.485  
7.475  
7.467  
7.462  
7.260  
6.785  
6.764  
6.760  
6.739  
5.012  
4.973  
4.894  
4.854  
4.251  
4.233  
4.215  
4.197  
3.862  
3.853  
3.833  
3.825  
3.805  
3.798  
3.658  
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2.855  
2.844  
2.826  
2.816  
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2.155  
2.146  
2.130  
2.118  
1.833  
1.821  
1.808  
1.418  
1.417  
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1.281  
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1.222

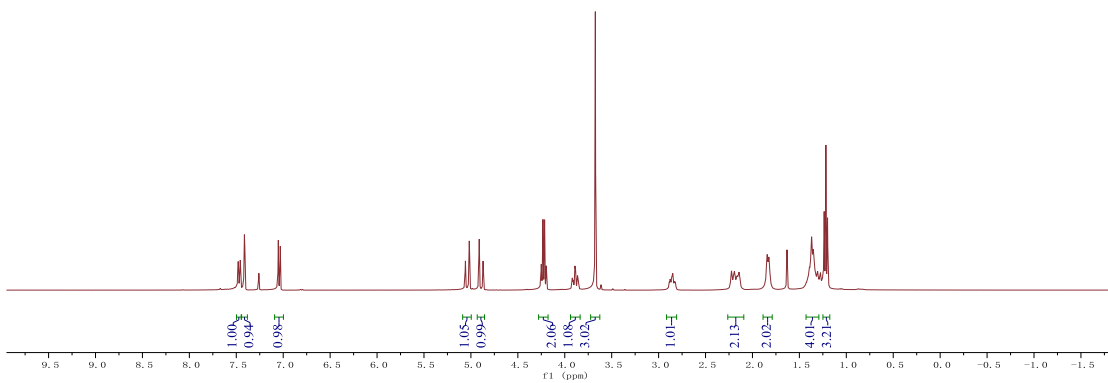
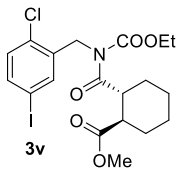


y1-8-12-b1-s. 4. F1d

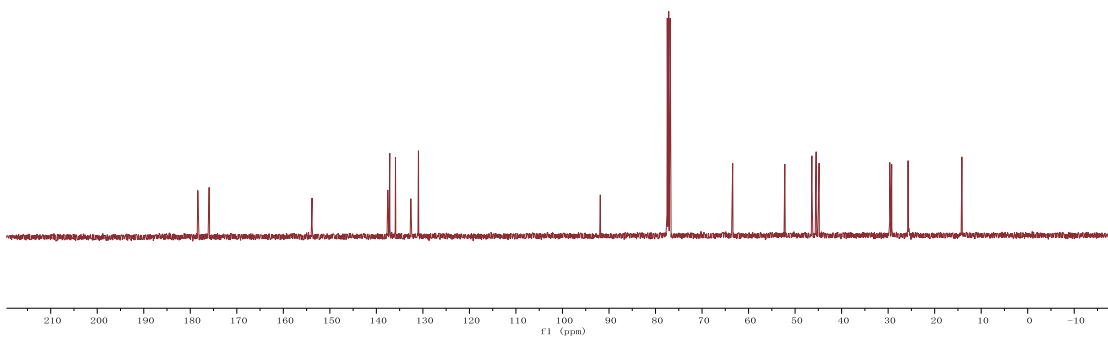
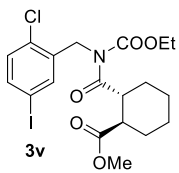
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137.581  
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127.716  
117.526  
117.298  
87.305  
87.271  
77.478  
77.160  
76.842  
63.387  
52.134  
46.448  
45.572  
40.725  
40.676  
29.597  
29.261  
25.719  
25.547  
14.077



y1-8-12-cl.3.fid



y1-8-12-cl.4.fid

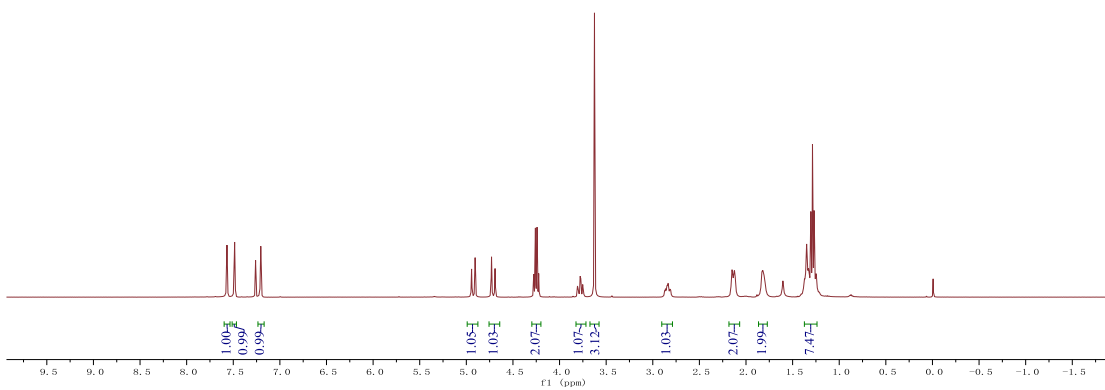
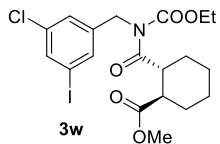




y1-7-37-b1.4.fid

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7.563  
7.489  
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7.482  
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7.209  
7.205  
7.201

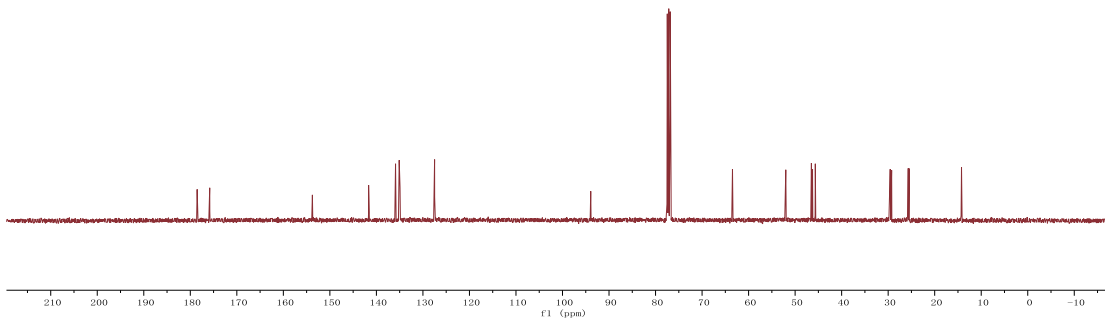
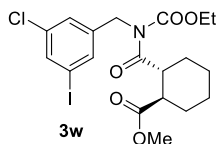
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4.692  
4.277  
4.259  
4.241  
4.224  
3.808  
3.799  
3.780  
3.772  
3.752  
3.744  
3.625  
2.873  
2.863  
2.845  
2.835  
2.816  
2.807  
2.149  
2.125  
2.118  
2.110  
1.829  
1.821  
1.817  
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1.318  
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1.287  
1.269  
1.247



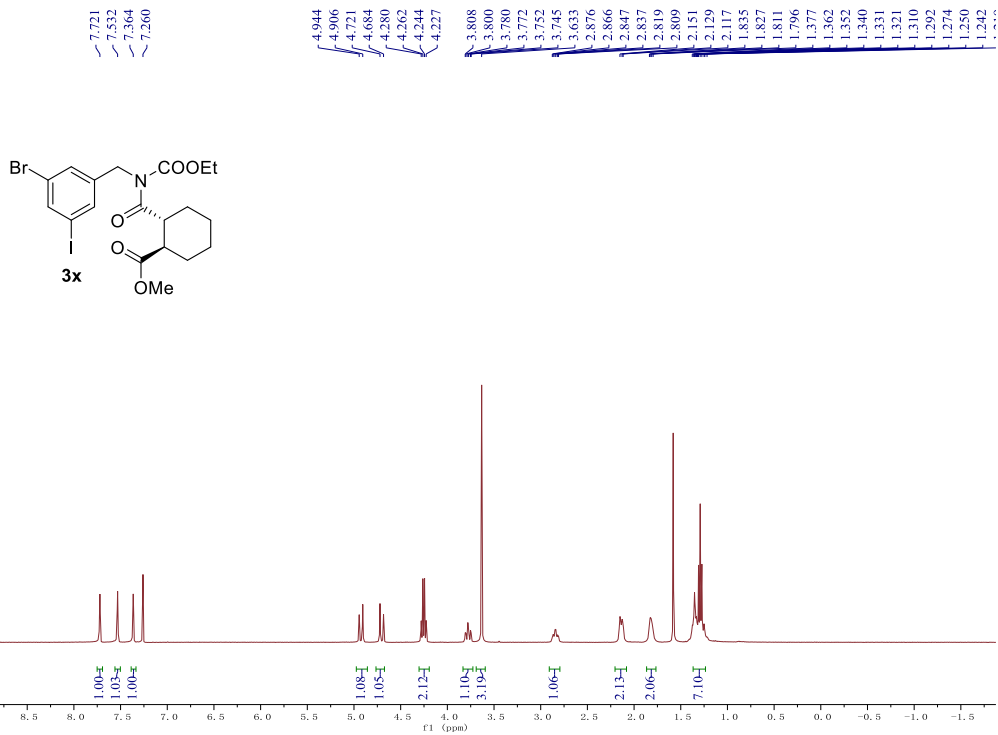
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127.490

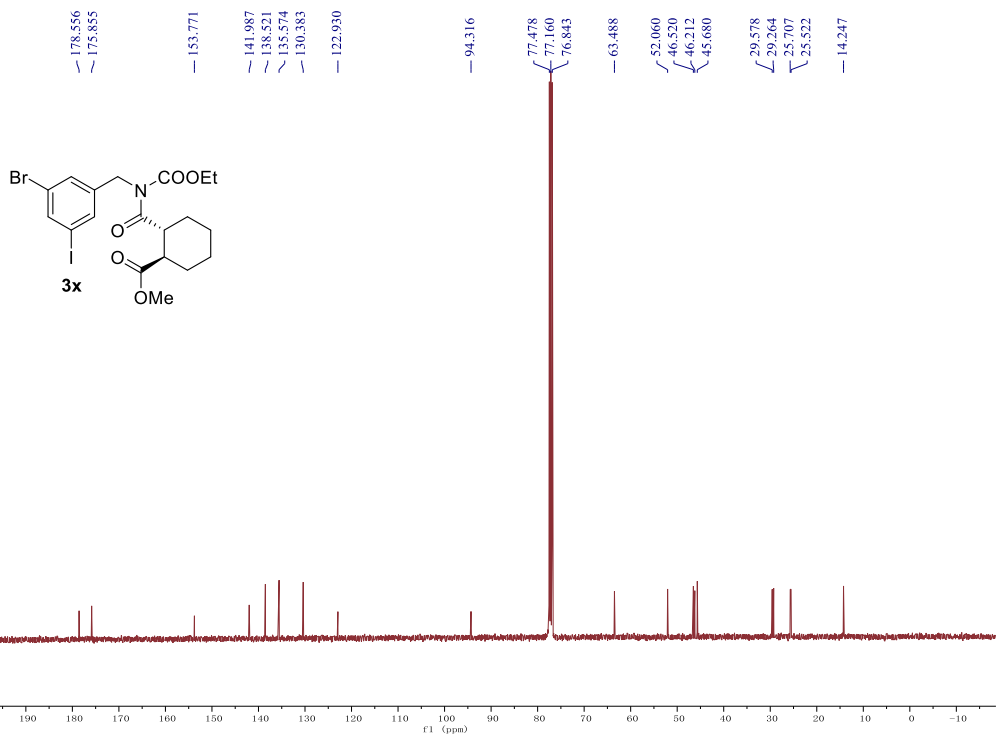
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25.505  
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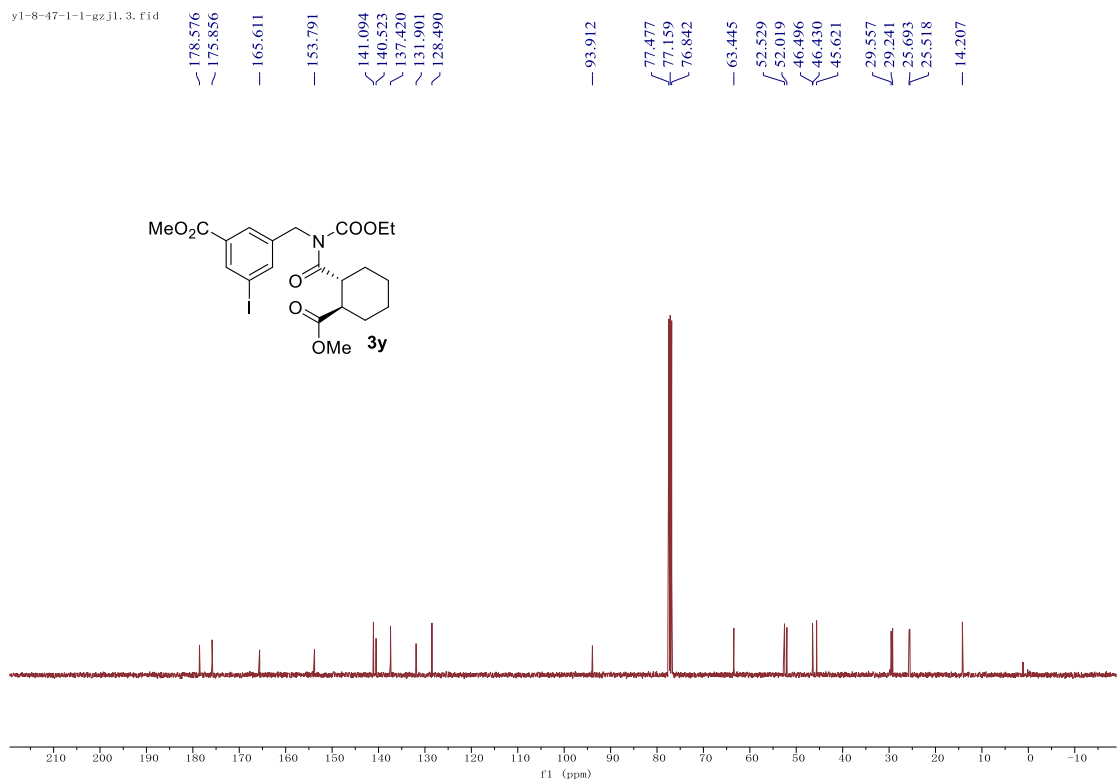
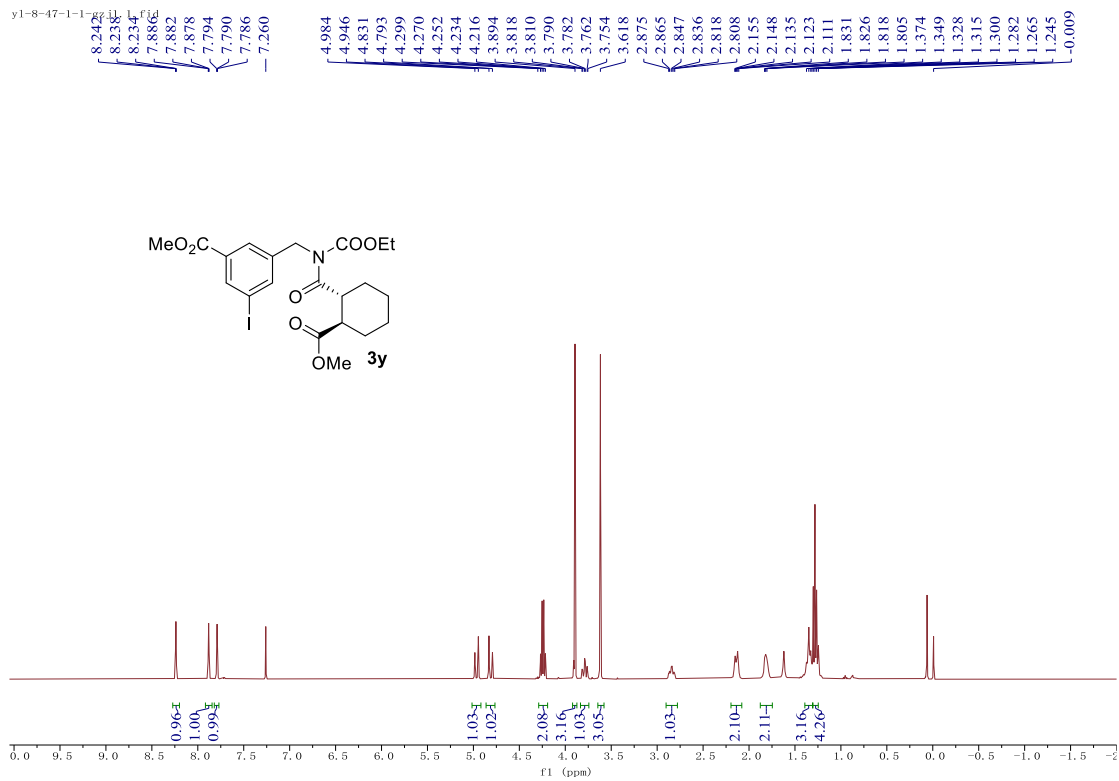


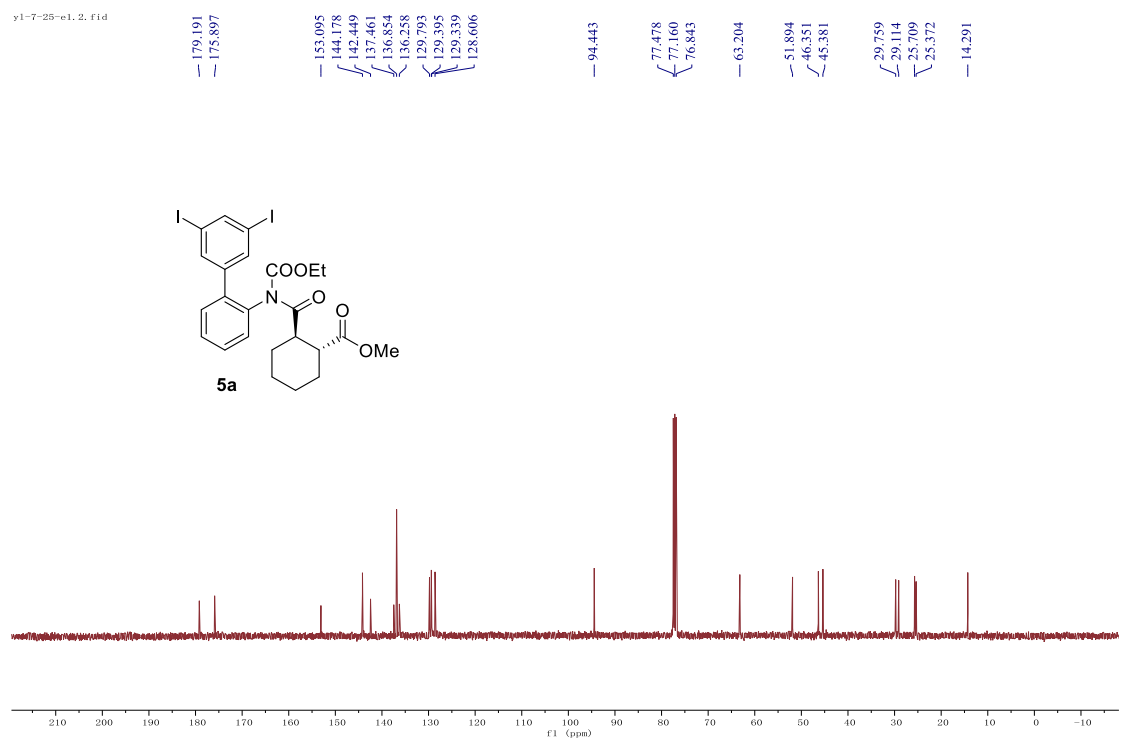
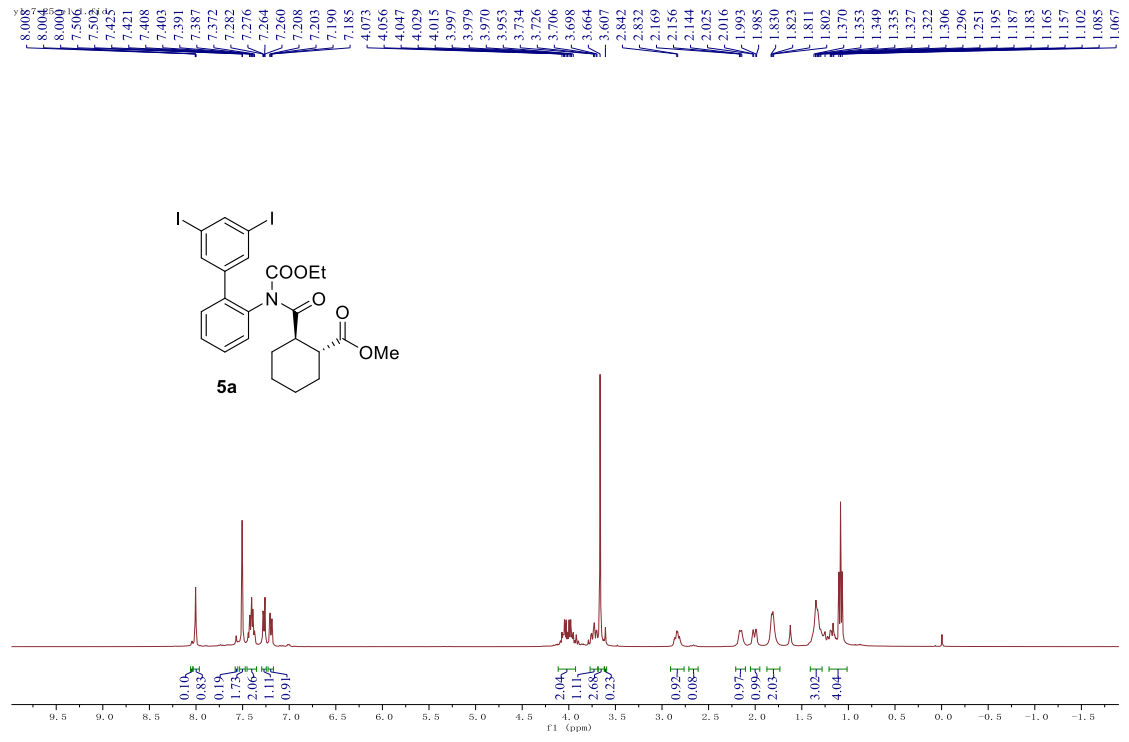
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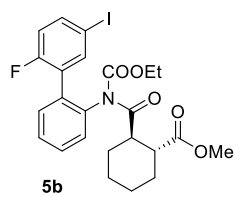
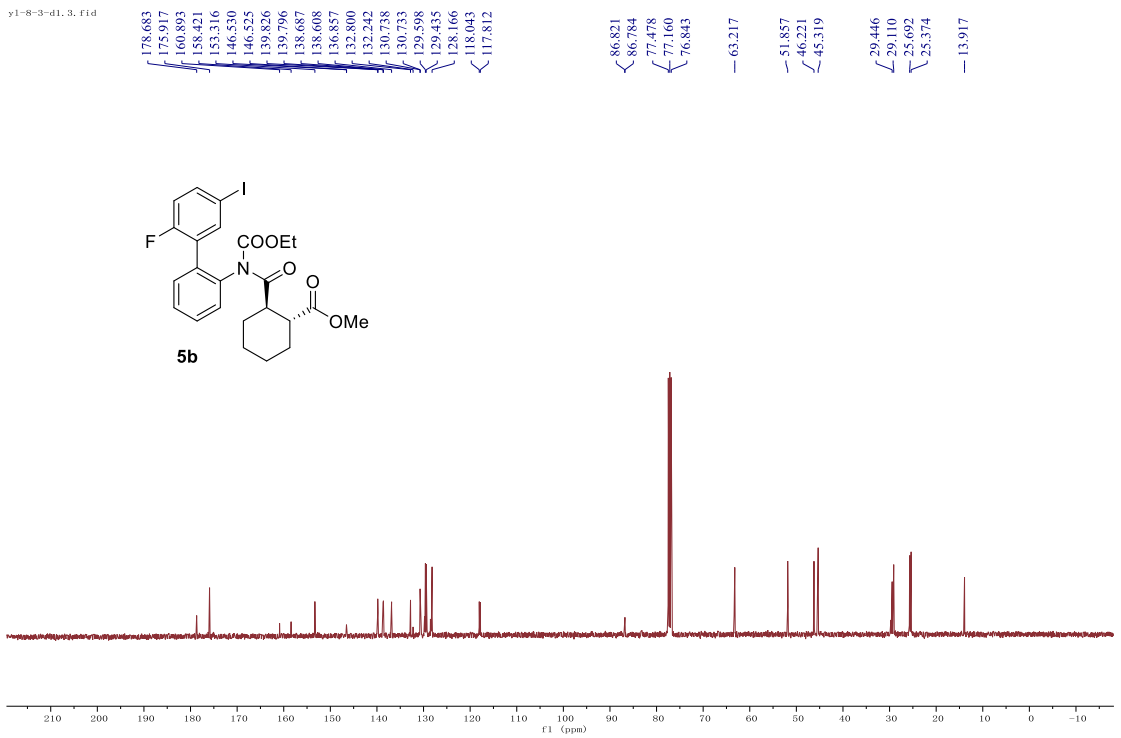
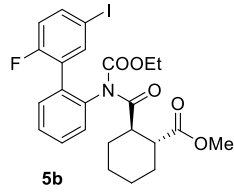
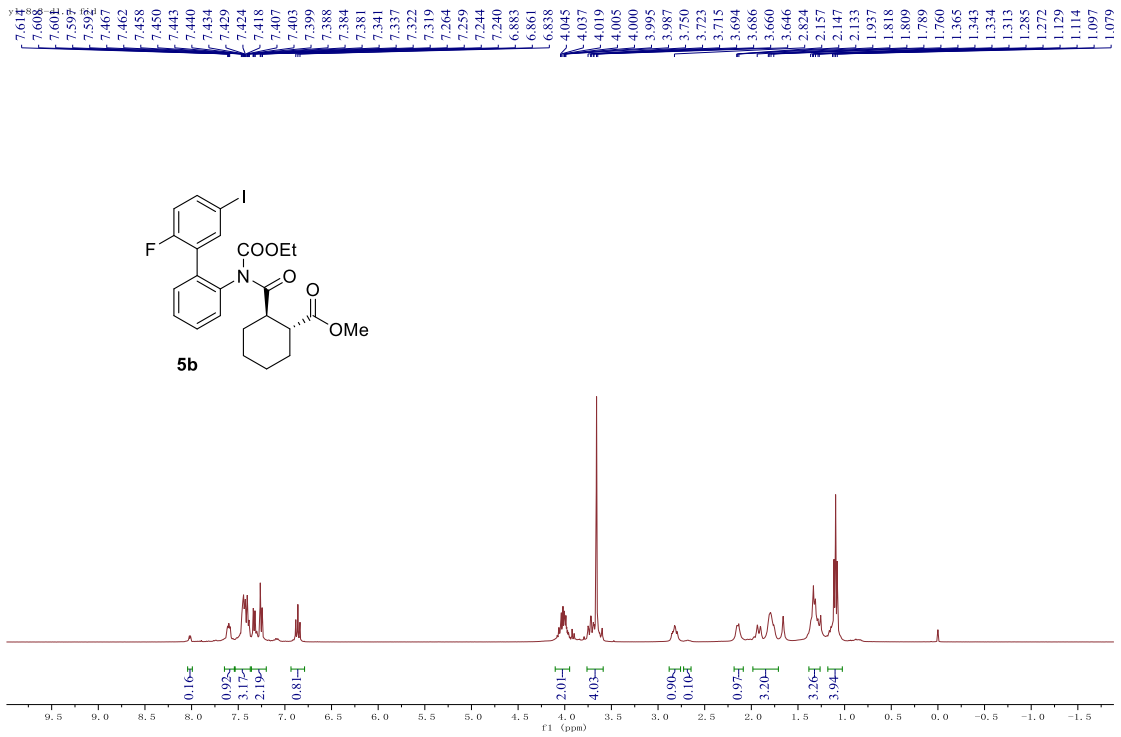


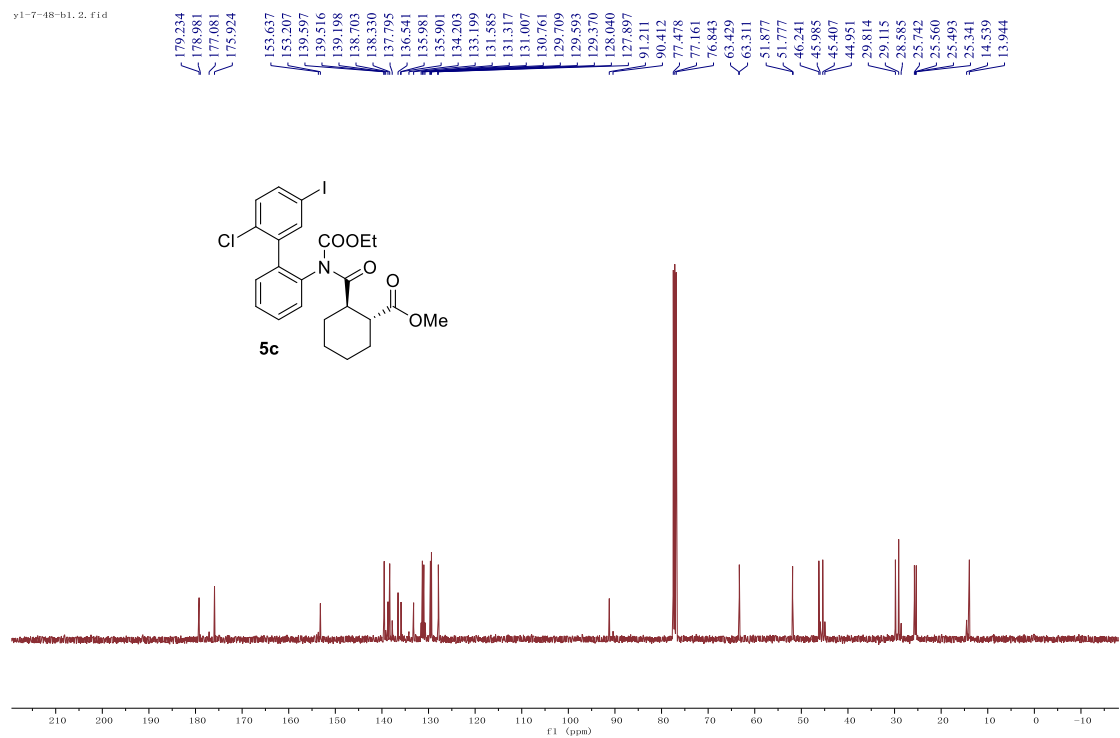
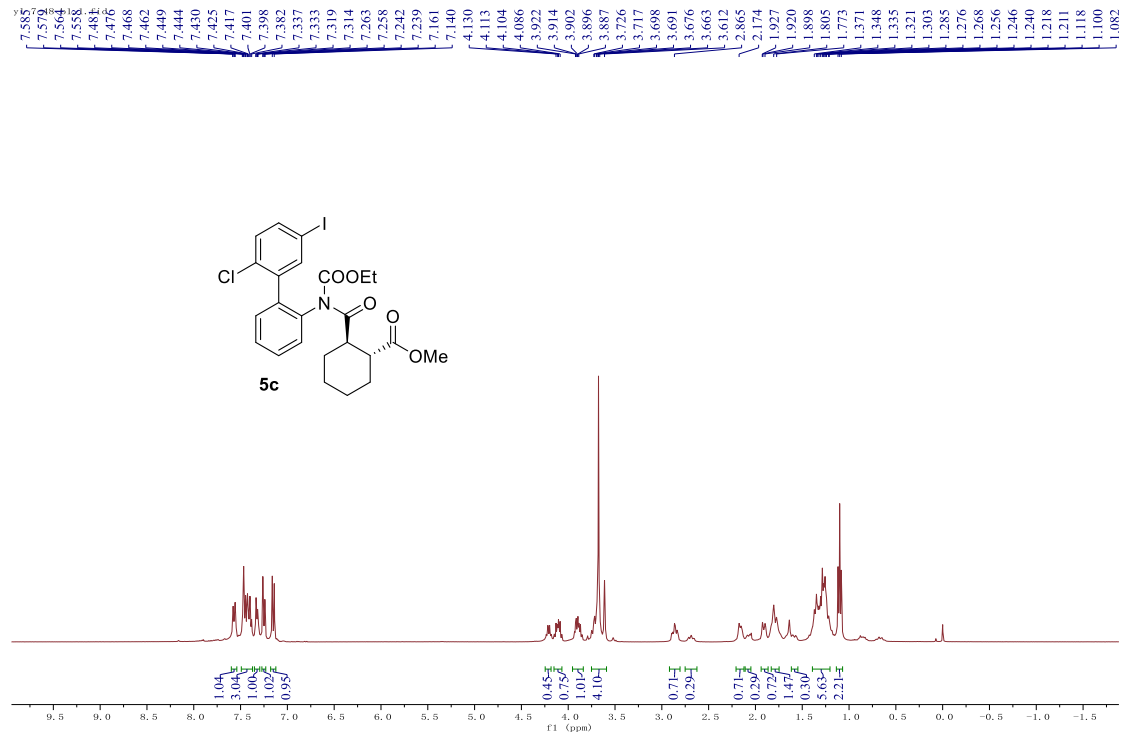
y1-8-12-41.4.fid



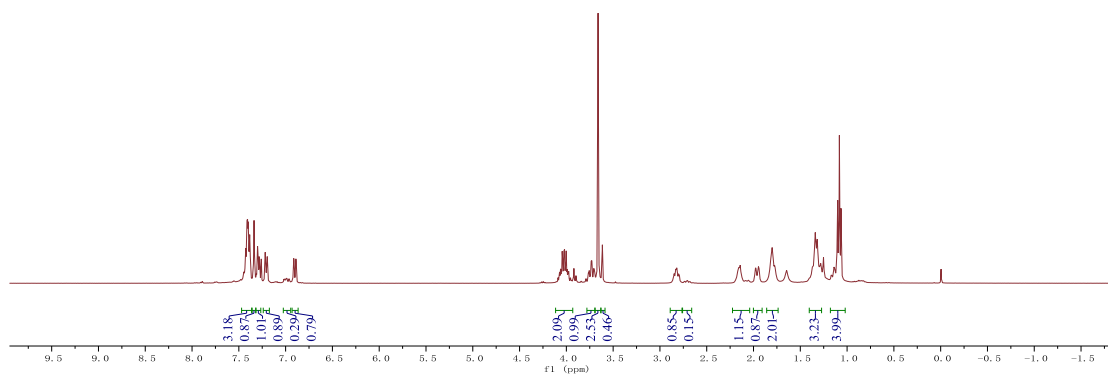
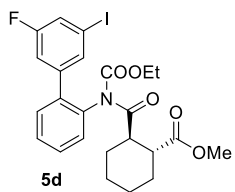






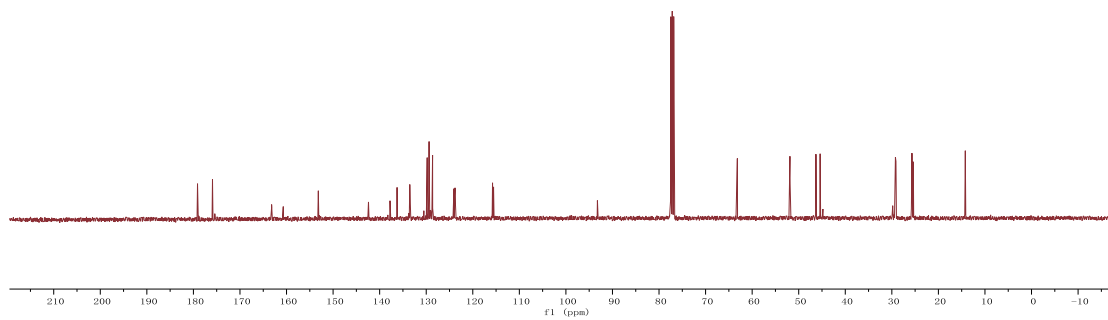
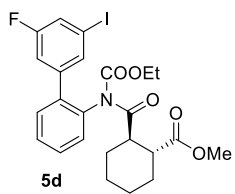


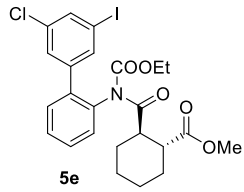
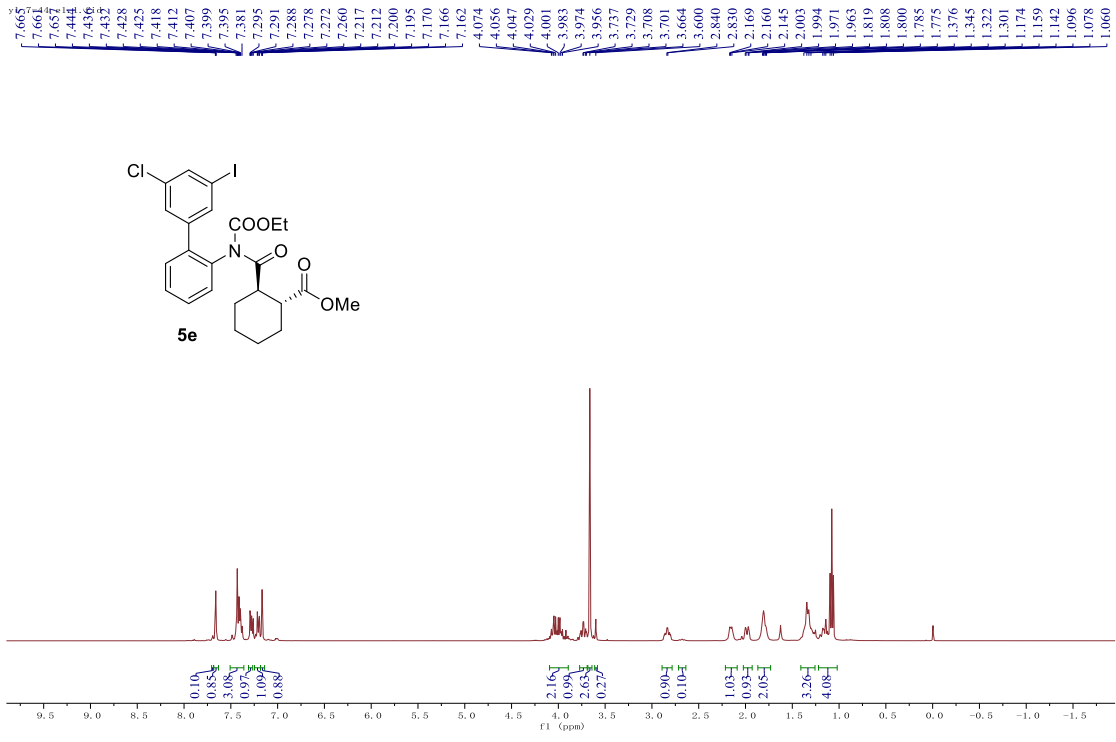
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7.300  
7.294  
7.283  
7.277  
7.260  
7.219  
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7.202  
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6.913  
6.909  
6.895  
6.890  
6.885  
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4.027  
4.019  
4.009  
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1.816  
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1.340  
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1.073  
1.065



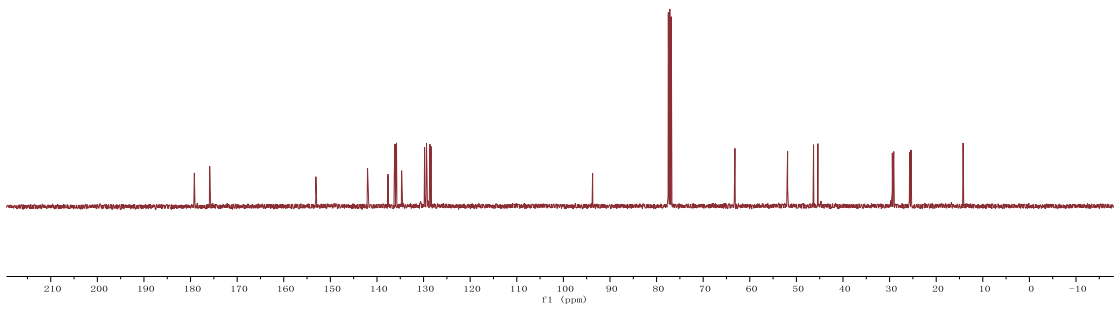
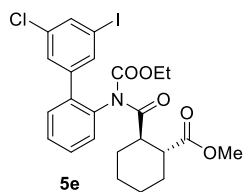
y1-8-3-a1.3.fid

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137.776  
137.756  
136.259  
133.524  
133.492  
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123.808  
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115.539  
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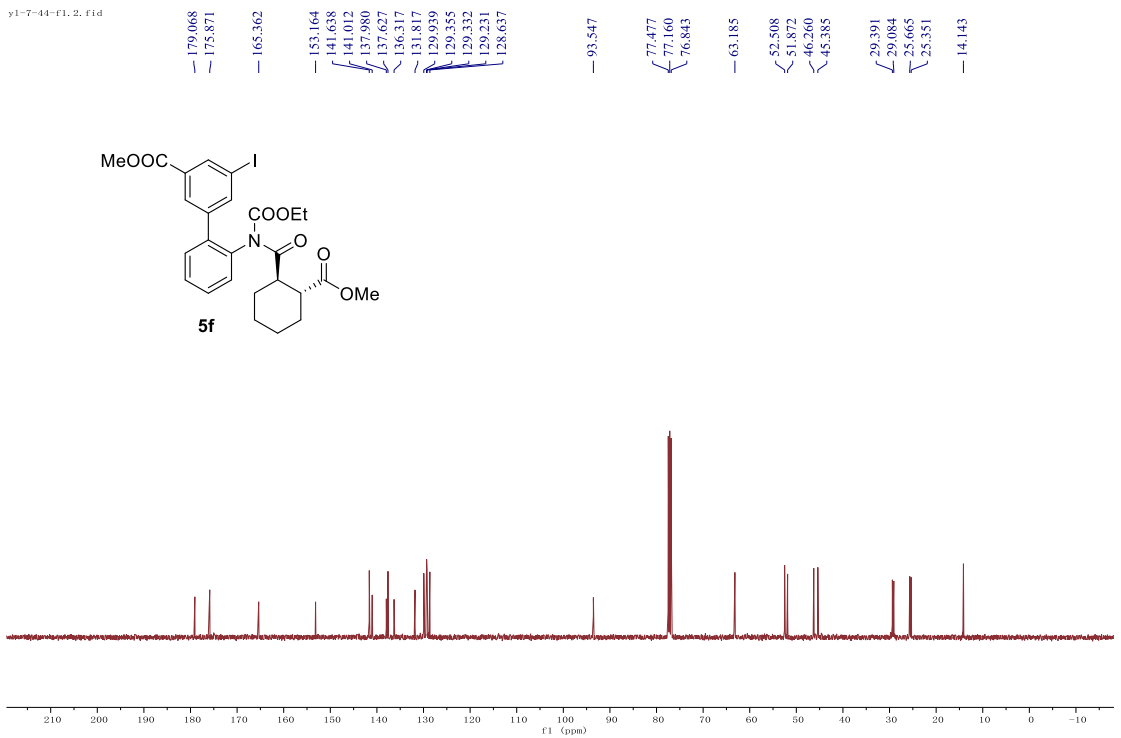
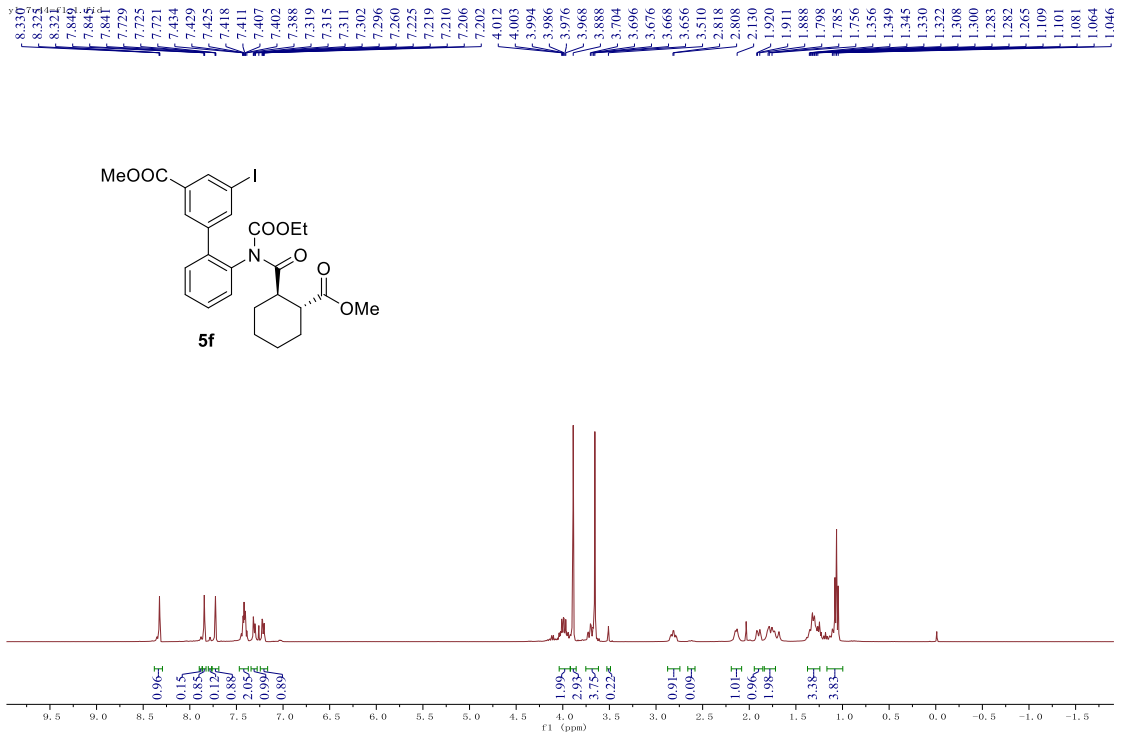


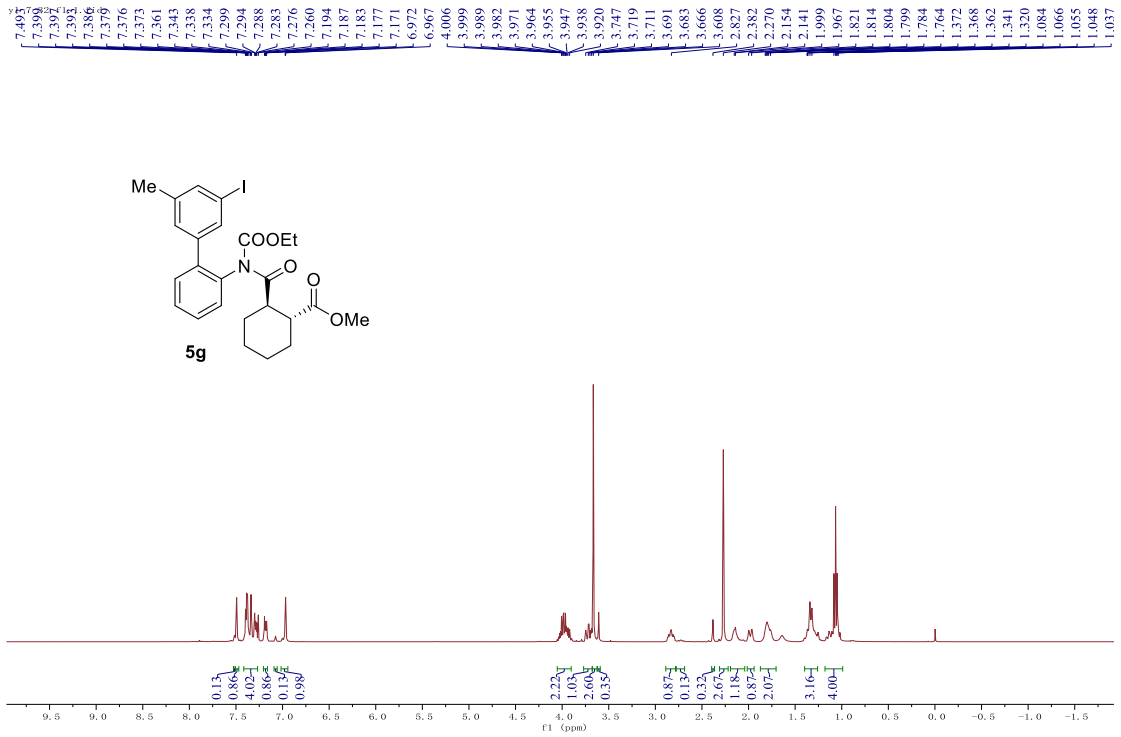


y1-7-44-e1.2.fid

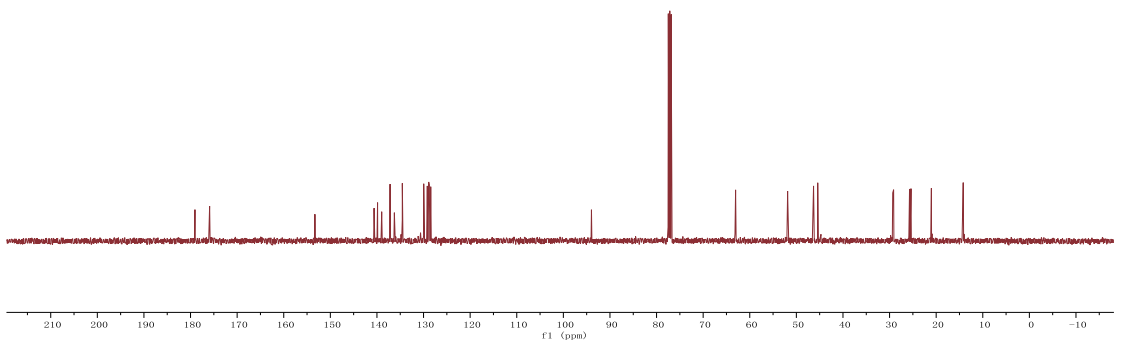
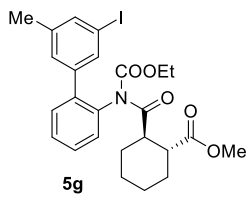


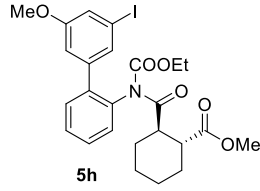
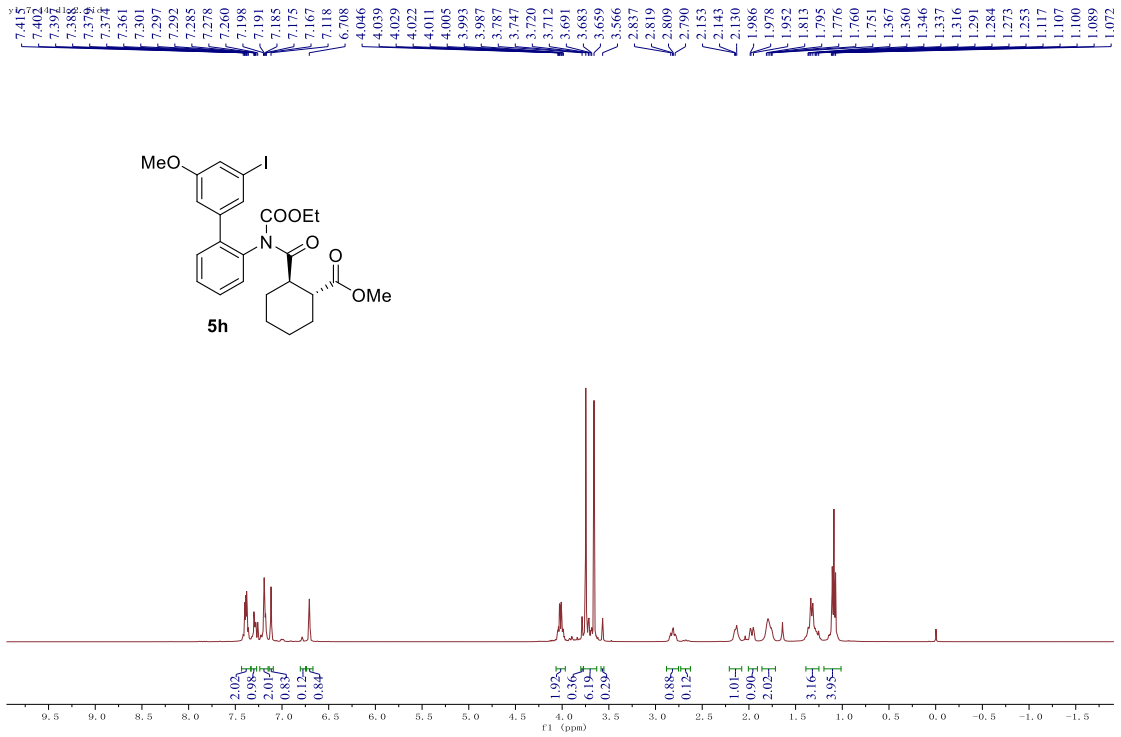




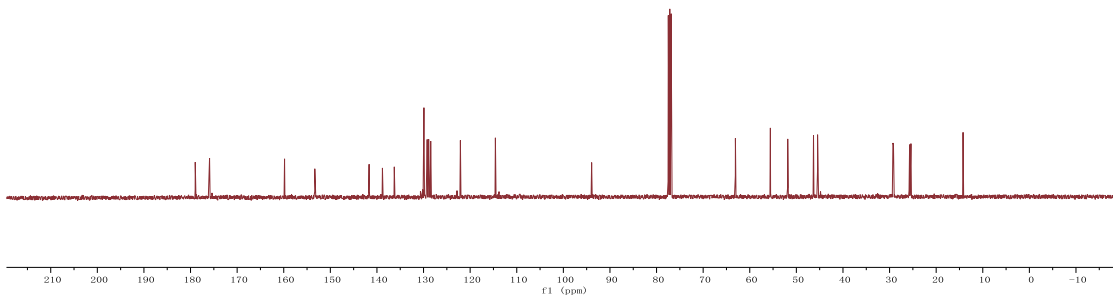
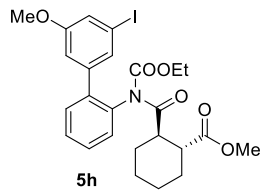


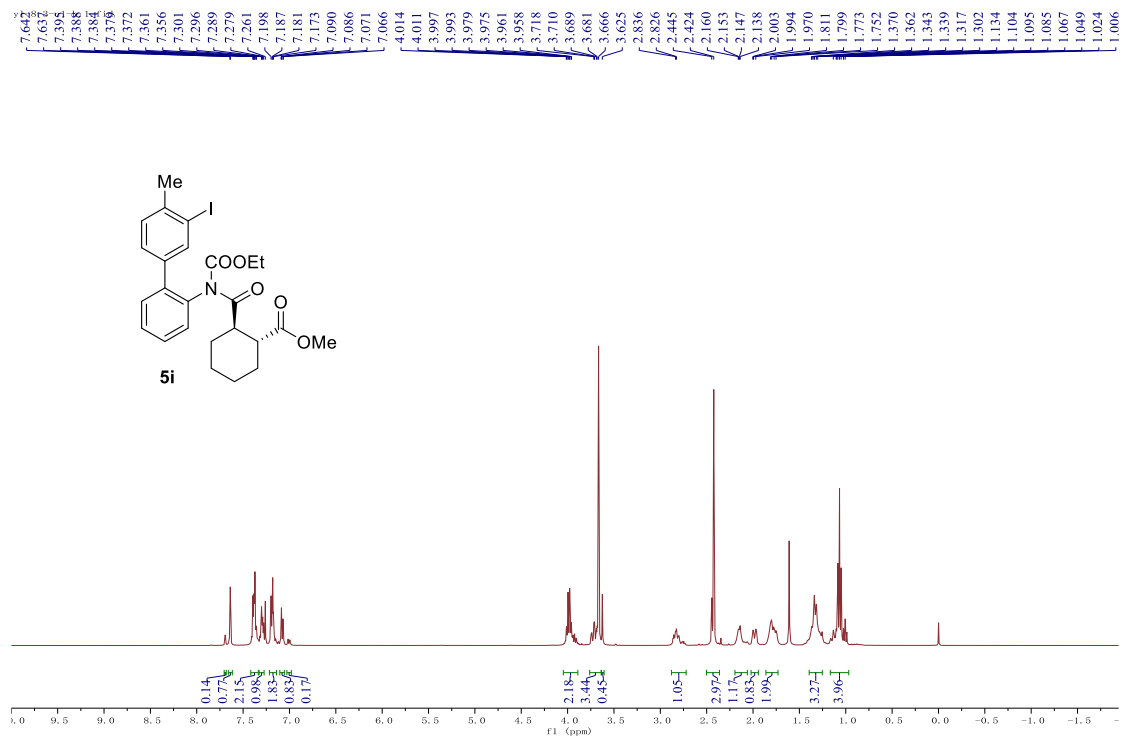
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y1-7-44-d1.1.fid





y1-8-3-e1-h, 2, f1d

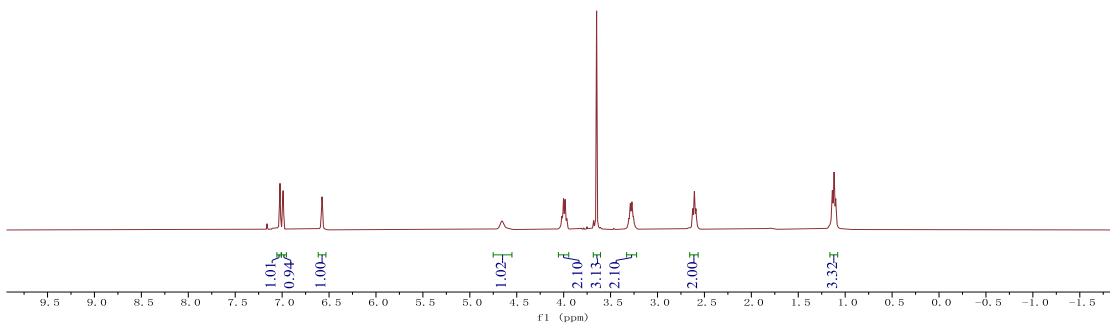
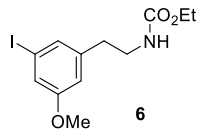


y1-8-20-a yjx-1.1.fid

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3.306  
3.289  
3.272  
3.256  
2.625  
2.608  
2.590

1.137  
1.118  
1.100



y1-8-20-a yjx-1.2.fid

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156.673

142.286

130.274

121.072

114.590

94.642

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77.160  
76.843

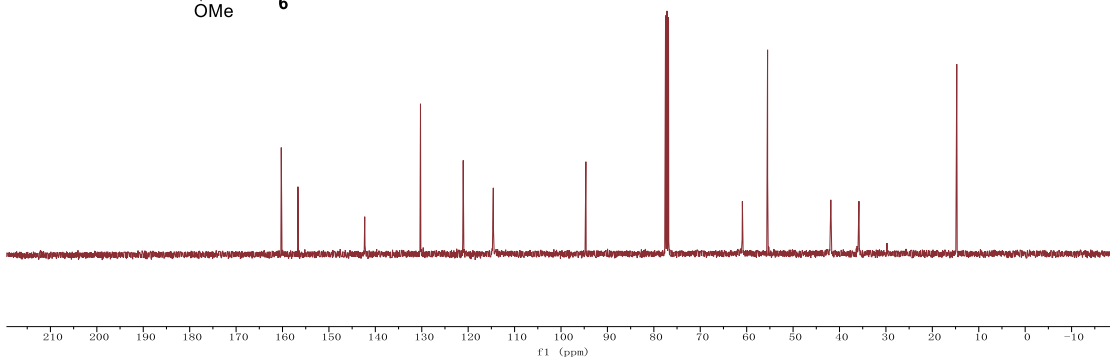
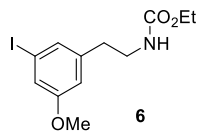
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55.494

41.871

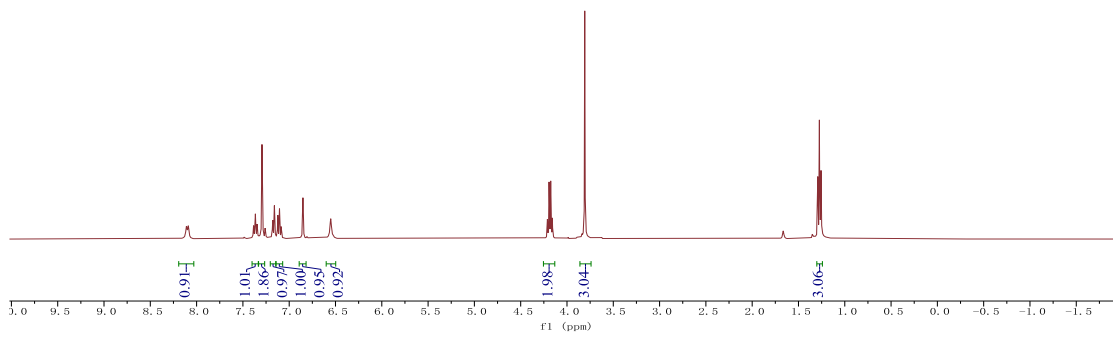
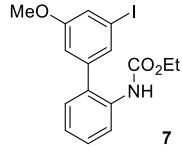
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14.736



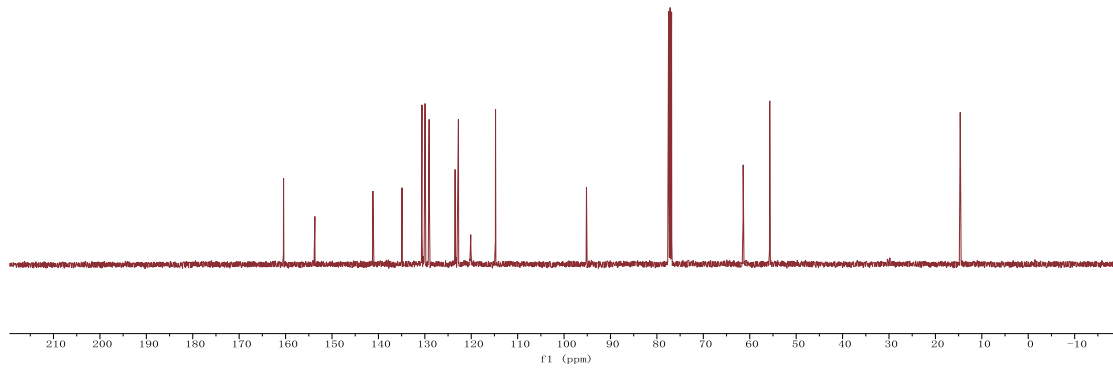
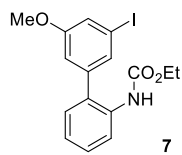
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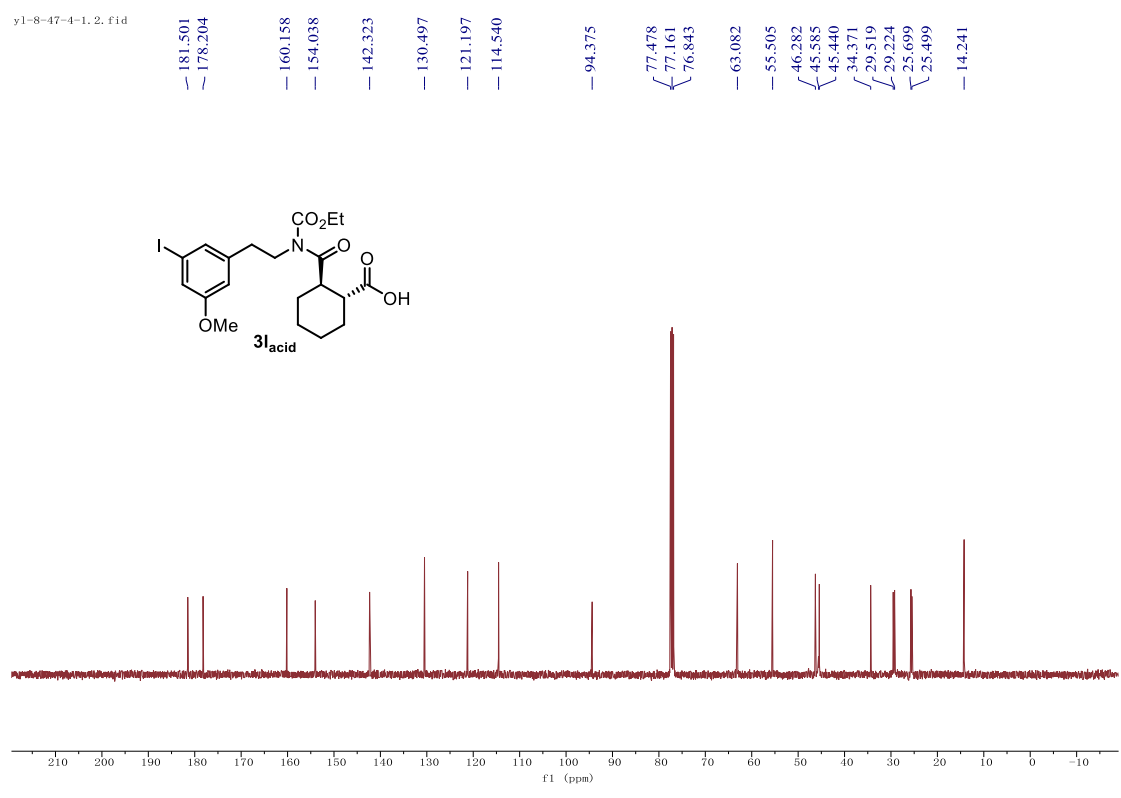
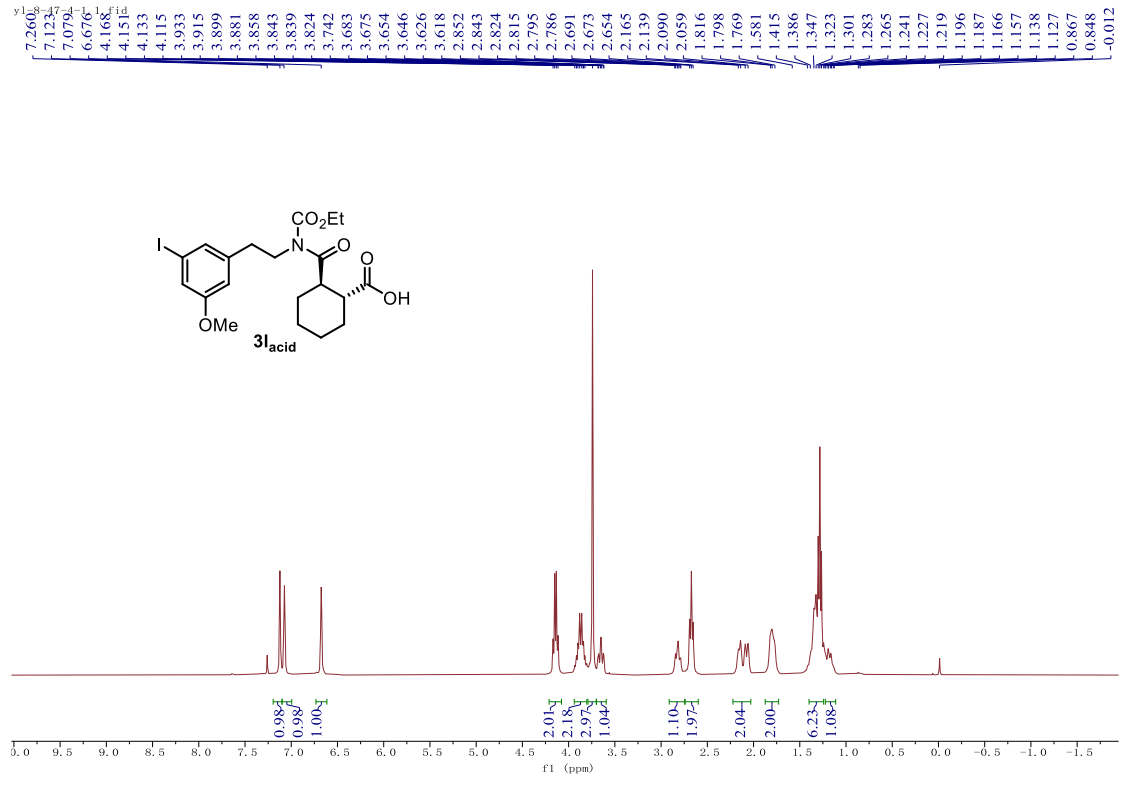
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7.178  
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7.086  
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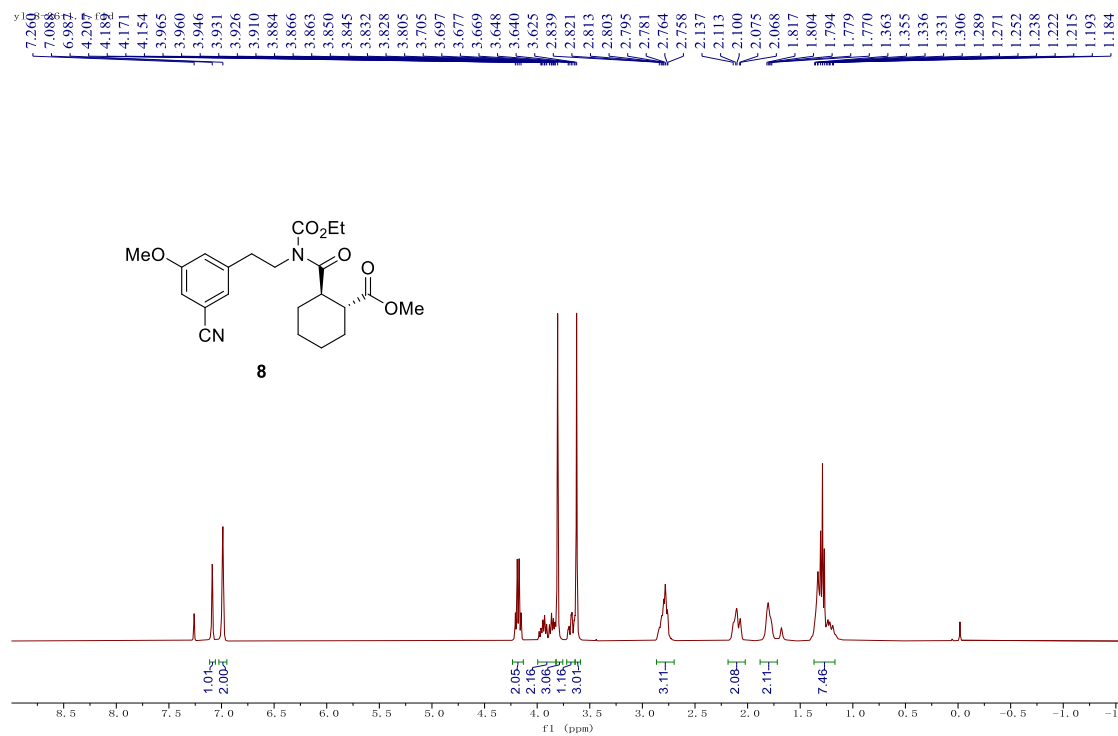


y1-8-21-a. 2. fid

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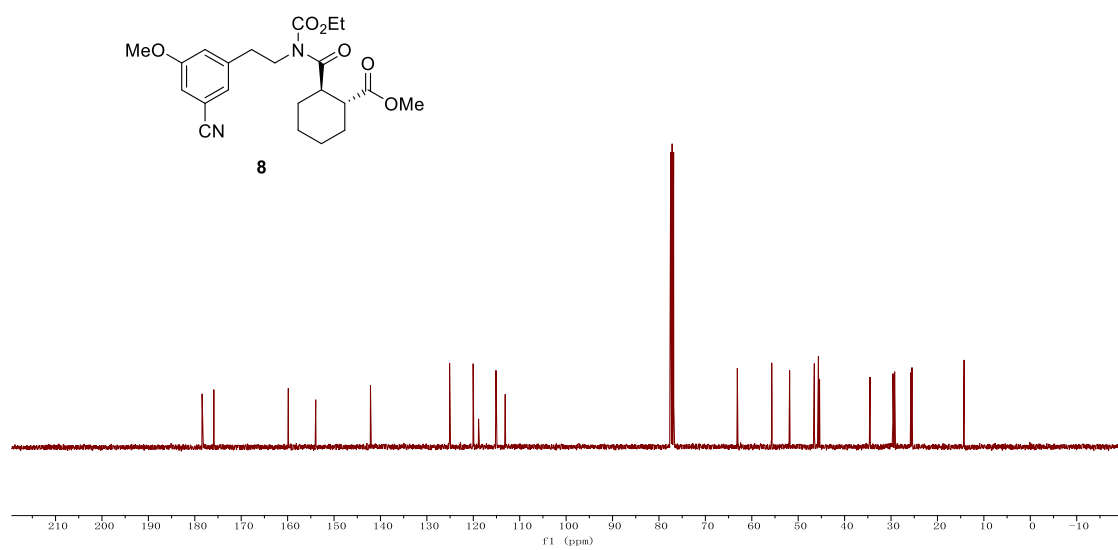




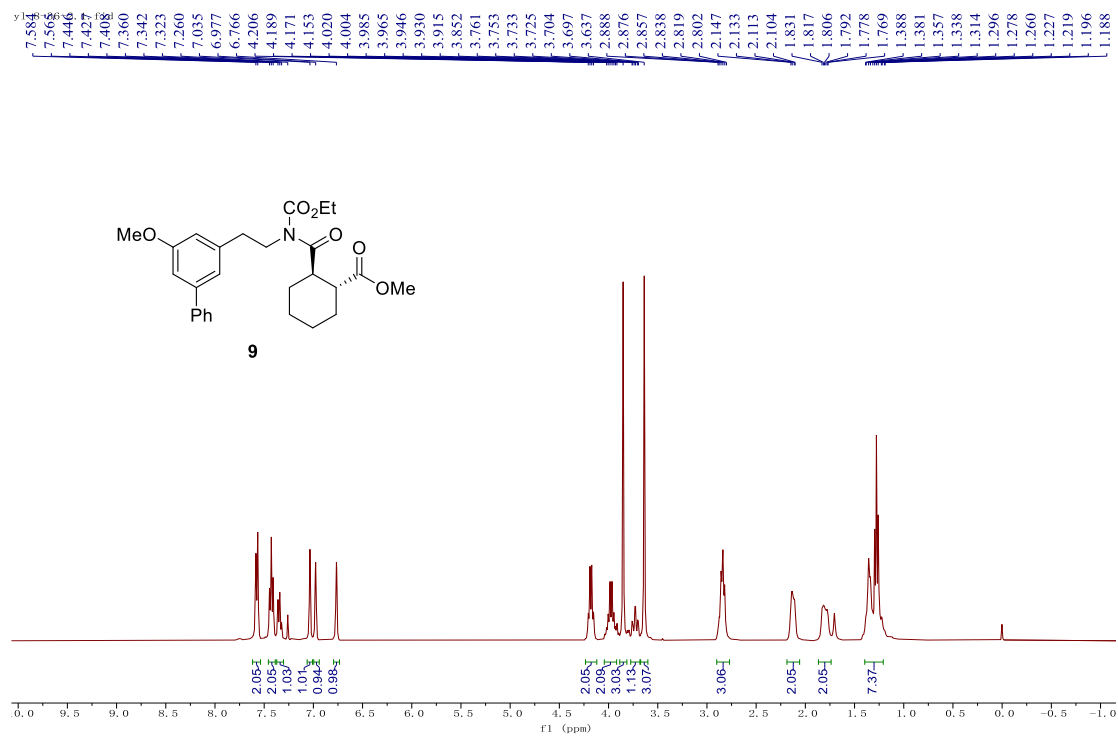


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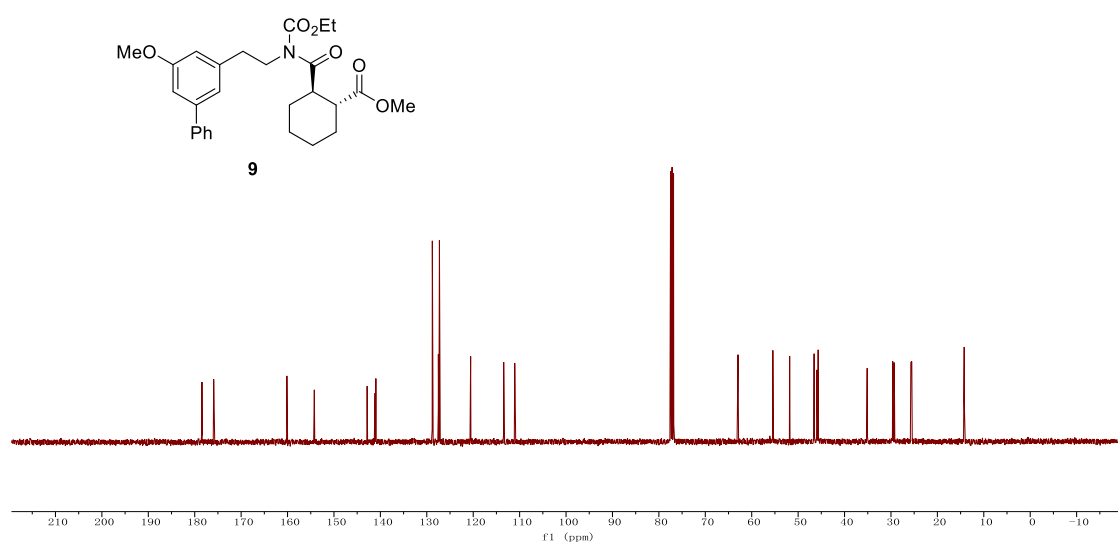
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113.123  
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45.406  
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29.587  
29.226  
25.702  
25.491  
14.261

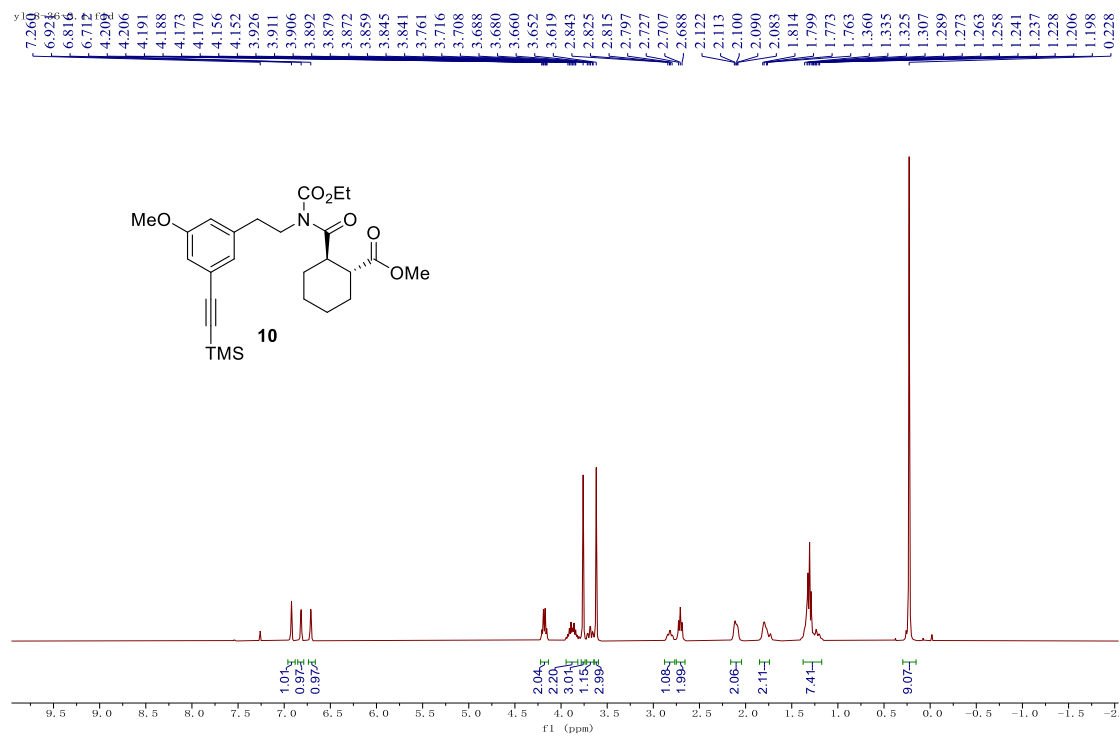






y1-8-36-2.2.f1d





y1-8-36-3.2.f1d

178.367  
175.894  
159.407  
154.121  
140.514  
125.349  
124.004  
116.182  
114.570  
105.077  
93.861  
77.479  
77.160  
76.843  
62.999  
55.403  
51.813  
46.532  
45.693  
45.660  
34.644  
29.593  
29.271  
25.712  
25.529  
14.235  
0.061

