Supplementary Materials for

Regio-Controllable [2+2] Benzannulation with Two Adjacent C(sp^3)–H Bonds

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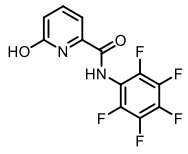
1. General Information

$Pd(OAc)_2$, $Pd(CH_3CN)_4(BF_4)_2$, Ag_2CO_3 were purchased from Strem and Sigma-Aldrich. Solvents were obtained from Sigma-Aldrich, Alfa-Aesar, and Acros, and used directly without further purification. Other reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. ^1H NMR spectra were recorded on Bruker AMX-400, Bruker AV-500, or Bruker DRX-600 instruments. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-600 and were fully decoupled by broad band proton decoupling. Chemical shifts were referenced to the appropriate residual solvent peaks. Column chromatography was performed using E. Merck silica (60, particle size 0.043–0.063 mm), and pTLC was performed on Merck silica plates (60F-254). High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). The single crystal X-ray diffraction studies were carried out on a Bruker D8 Venture Ultra diffractometer equipped with Mo K_α radiation ($\lambda = 0.71073$). Melting points were measured using a Stuart SMP50.

2. Preparation of Bidentate Amide-Pyridone Ligands



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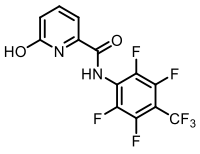

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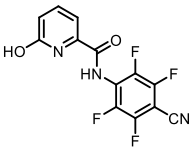

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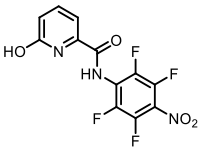

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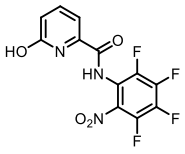

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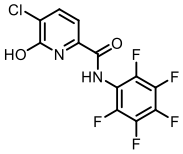

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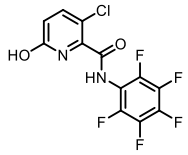

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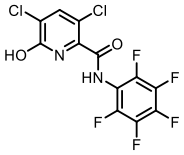

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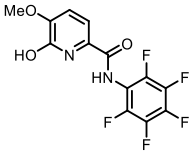

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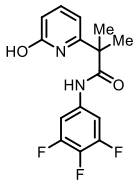

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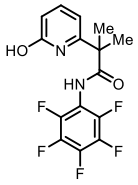

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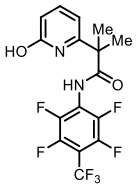

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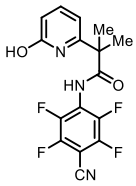

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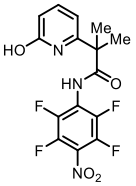

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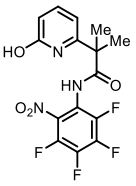

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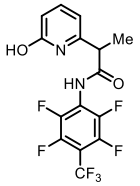

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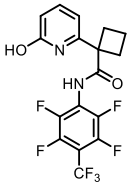

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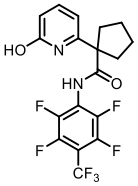

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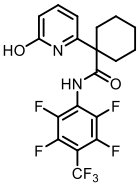

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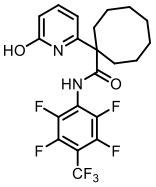

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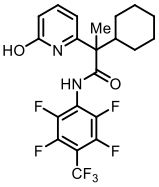

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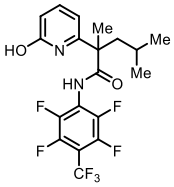

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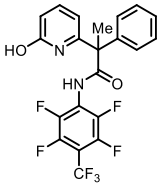

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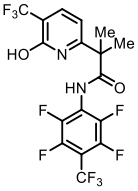

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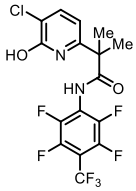

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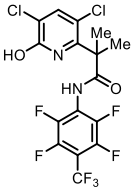
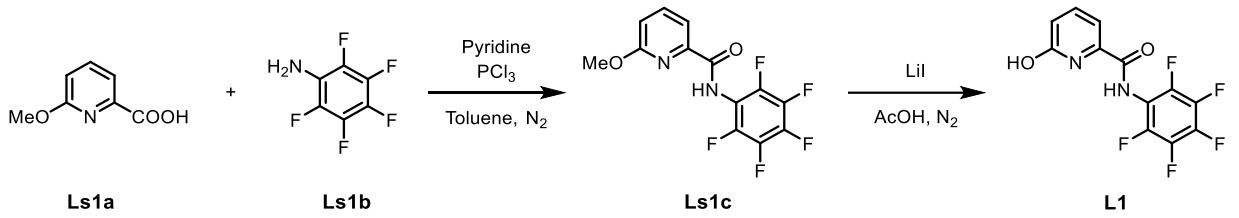


L26

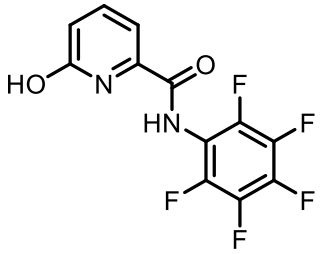
Preparation of **L1**



Ls1a **Ls1b** **Ls1c** **L1**

To a flame-dried 16 mL reaction tube **Ls1a** (2.2 mmol) and **Ls1b** (2 mmol) were added. The tube was sealed tightly, evacuated, and refilled with N_2 three times. Then anhydrous toluene (6.6 mL) was added, followed by pyridine (2 drops). Then phosphorus trichloride (1 mmol) was added dropwise while vigorously stirred at room temperature (solidification may occur in the solution if stirring is not vigorous enough). The tube was put into a 145 ^oC heating bath and stirred. Solution became clear and red solid formed at the inner surface of the tube in about 1 min. The tube was heated at 145 ^oC and stirred for 16 h (inner pressure is high). The tube was removed from the heating bath and cooled down to room temperature. The solution was poured into water (10 mL) and extracted by EtOAc (10 mL x 3). The organic phase was washed by *conc.* brine (10 mL x 3) and dried by anhydrous Na_2SO_4. The dried organic phase was passed through a pad of silica gel and washed by EtOAc (30 mL). The solvent was removed by a rotavapor, and **Ls1b** was removed by blowing with compressed air under room temperature if there is any. **Ls1c** was obtained as a white solid and used in the next step without further purification.

To a 16 mL reaction tube **Ls1c** (1 mmol) and LiI (5 mmol) were added, followed by 2 mL AcOH. The tube was sealed, evacuated, and refilled with N_2 three times. The tube was put into a 110 ^oC heating bath, heated and stirred under this temperature for 2 h. Then the tube was removed from the heating bath and cooled down to room temperature. The reaction mixture was poured into water (10 mL), and solid Na_2CO_3 was added into the solution until pH=2. The solution was extracted by EtOAc (10 mL x 3) and washed by *conc.* brine (10 mL x 3). The organic phase was dried by anhydrous Na_2SO_4 and passed through a pad of celite. The solvent was removed, and the residue was purified by flash silica gel column chromatography (2% formic acid with 10% to 50% EtOAc/hexane) to give the **L1** (82% over two steps) as a white solid.



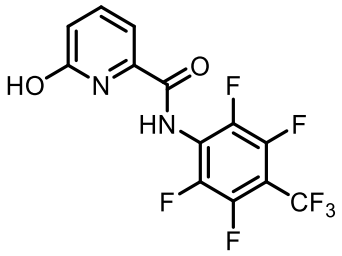
L1

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.91 (dd, J = 8.4, 7.2 Hz, 1H), 7.68 (dd, J = 7.3, 0.9 Hz, 1H), 7.01 (dd, J = 8.3, 0.8 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 163.7, 163.3, 146.7, 144.5 (dm, J = 248.0 Hz), 141.8, 140.8 (dm, J = 252.5 Hz), 138.8 (dm, J = 251.7 Hz), 115.9, 115.4, 114.1 (m). ^{19}F NMR (376 MHz, $CDCl_3$) δ -146.9 (m), -158.8 (t, J = 20.7 Hz), -164.6 (m). m.p. = 214 – 216 ^{o}C.

HRMS (ESI-TOF) Calculated for $C_{12}H_6F_5N_2O_2$ $[M+H]^+$: 305.0349, Found: 305.0350.

Preparation of **L2** to **L5**

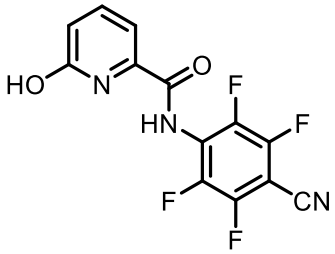
Preparation of **L2** to **L5** followed the procedure of the preparation of **L1** with corresponding aniline, and the reaction mixture was purified by flash silica gel column chromatography (2% formic acid with 10% to 50% EtOAc in hexane) to give **L2**, **L3** and **L5** as a white solid, and **L4** as a yellow solid.



L2

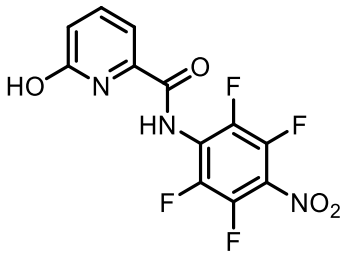
^{1}H NMR (400 MHz, Acetone-d_6) δ 10.07 (s, 1H), 7.94 (dd, J = 8.4, 7.2 Hz, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.04 (d, J = 8.3 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 163.7, 162.7, 146.6, 145.4 (dm, J = 236.0 Hz), 143.7 (dm, J = 230.7 Hz), 142.0, 122.9 (m), 122.1 (q, J = 272.4 Hz), 116.0, 115.9, 107.2 (m). ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.7 (t, J = 21.7 Hz), -143.4 (m), -145.0 (m). m.p. = 218 – 220 ^{o}C.

HRMS (ESI-TOF) Calculated for $C_{13}H_6F_7N_2O_2$ $[M+H]^+$: 355.0317, Found: 355.0319.



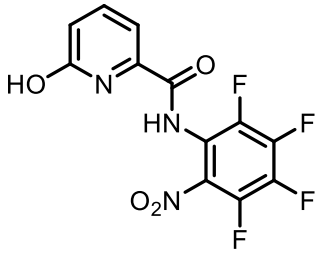
L3

^{1}H NMR (600 MHz, Acetone-d_6) δ 10.13 (s, 1H), 7.94 (dd, J = 8.3, 7.2 Hz, 1H), 7.72 (dd, J = 7.3, 0.9 Hz, 1H), 7.04 (dd, J = 8.3, 0.8 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 163.7, 162.6, 148.5 (dm, J = 257.7 Hz), 146.5, 143.3 (dm, J = 247.2 Hz), 142.0, 124.7 (m), 116.0, 115.9, 108.5, 92.1 (m). ^{19}F NMR (376 MHz, $CDCl_3$) δ -134.9 (m), -143.6 (m). m.p. = 215 – 216 °C.
HRMS (ESI-TOF) Calculated for $C_{13}H_6F_4N_3O_2$ $[M+H]^+$: 312.0396, Found: 312.0393.



L4

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.93 (dd, J = 8.4, 7.2 Hz, 1H), 7.71 (d, J = 7.3 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 163.7, 162.6, 146.3, 143.7 (ddm, J = 200.5, 14.7 Hz), 142.0 (ddm, J = 210.8, 16.8 Hz), 142.0, 128.6 (m), 123.4 (m), 116.2, 115.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -143.3 (m), -148.9 (m). m.p. = 205 – 207 °C.
HRMS (ESI-TOF) Calculated for $C_{12}H_6F_4N_3O_4$ $[M+H]^+$: 332.0294, Found: 332.0298.

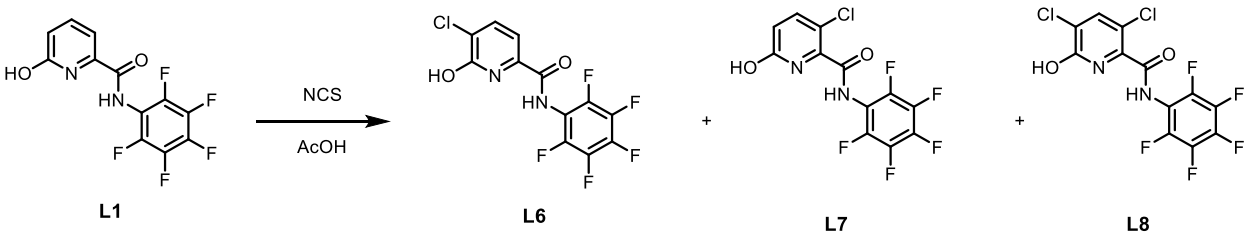


L5

^{1}H NMR (600 MHz, Acetone-d_6) δ 10.21 (s, 1H), 7.93 (dd, J = 8.3, 7.2 Hz, 1H), 7.69 (dd, J = 7.3, 0.9 Hz, 1H), 7.04 (dd, J = 8.4, 0.9 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 163.8, 163.1, 146.5, 144.3 (dm, J = 258.2 Hz), 143.7 (dm, J = 246.1 Hz), 143.1 (dm, J = 273.3 Hz), 140.0 (dm, J = 253.7 Hz), 142.1, 133.0 (m), 119.2 (dm, J = 15.4 Hz), 116.0, 115.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.1 (ddm, J = 22.0, 8.2 Hz), -147.5 (dt, J = 22.6, 7.1 Hz), -149.6 (td, J = 21.1, 5.8 Hz), -156.5 (tm, J = 21.5 Hz). m.p. = 187 – 189 °C.

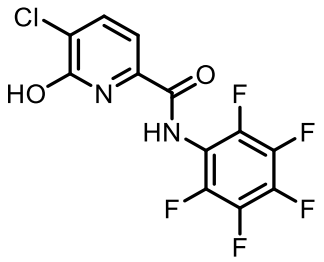
HRMS (ESI-TOF) Calculated for $C_{12}H_6F_4N_3O_4$ $[M+H]^+$: 332.0294, Found: 332.0292.

Preparation of **L6** to **L8**



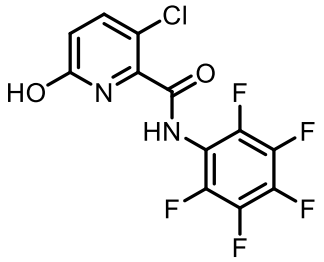
L1 **L6** **L7** **L8**

To a 16 mL reaction tube was added **L1** (1 mmol) and followed by 2 mL AcOH. *N*-chlorosuccinimide (NCS, 1.5 mmol) was added to the solution. The tube was capped and stirred at 120 °C for 16 h. After cooling down, the reaction mixture was poured into water (10 mL), and solid Na_2CO_3 was added into the solution until pH=2. The solution was extracted by EtOAc (10 mL x 3) and washed by *conc.* brine (10 mL x 3). The organic phase was dried by anhydrous Na_2SO_4 and passed through a pad of celite. The solvent was removed, and the residue was purified by dedicated silica gel column chromatography (2% formic acid with 10% to 50% EtOAc in hexane) to give the **L6** (25%), **L7** (33%) and **L8** (13%) as white solids.



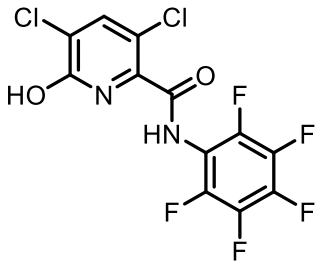
L6

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.98 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 162.3, 159.3, 144.5 (dm, J = 249.9 Hz), 143.1, 141.0 (dm, J = 251.1 Hz), 140.6, 138.8 (dm, J = 248.3 Hz), 124.8, 114.6, 113.7 (tm, J = 14.9 Hz). ^{19}F NMR (376 MHz, CD_3OD) δ -149.7 (m), -162.2 (t, J = 20.7 Hz), -168.5 (m). m.p. = 225 – 227 °C.
HRMS (ESI-TOF) Calculated for $C_{12}H_5ClF_5N_2O_2$ $[M+H]^+$: 338.9960, Found: 338.9957.



L7

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.87 (d, J = 8.8 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 161.6, 161.2, 143.5 (dm, J = 242.6 Hz), 143.1, 143.1, 139.9 (dm, J = 250.6 Hz), 137.8 (dm, J = 249.0 Hz), 121.9, 114.8, 112.8 (tm, J = 14.8 Hz).^{19}F NMR (376 MHz, CD_3OD) δ -149.3 (m), -162.5 (t, J = 20.8 Hz), -168.6 (m). m.p. = 220 – 222 °C.
HRMS (ESI-TOF) Calculated for $C_{12}H_5ClF_5N_2O_2$ $[M+H]^+$: 338.9960, Found: 338.9956.



L8

^{1}H NMR (600 MHz, Acetone-d_6) δ 8.06 (s, 1H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 162.0, 158.5, 144.4 (dm, J = 254.0 Hz), 142.4, 142.0, 141.0 (dm, J = 250.9 Hz), 138.8 (dm, J = 253.2 Hz), 122.5, 121.4, 113.6 (tm, J = 13.3 Hz). ^{19}F NMR (376 MHz, CD_3OD) δ -149.3 (m), -162.3 (*t*, J = 20.6 Hz), -168.5 (m). m.p. = 231 – 233 ºC.

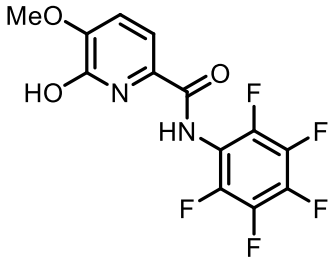
HRMS (ESI-TOF) Calculated for $C_{12}H_4Cl_2F_5N_2O_2$ $[M+H]^+$: 372.9570, Found: 372.9566.

Preparation of **L7** in large scale

Preparation of **L7** in large scale followed the procedure of the preparation of **L1** with 3-chloro-6-methoxypicolinic acid (11 mmol) and **Ls1b** (10 mmol) to give **L7** (67% over two steps) as a white solid**.**

Preparation of **L9**

Preparation of **L9** followed the procedure of the preparation of **L1** with 5,6-dimethoxypicolinic acid and **Ls1b** and purified by preparative HPLC (water/acetonitrile) to give **L9** as a white solid.

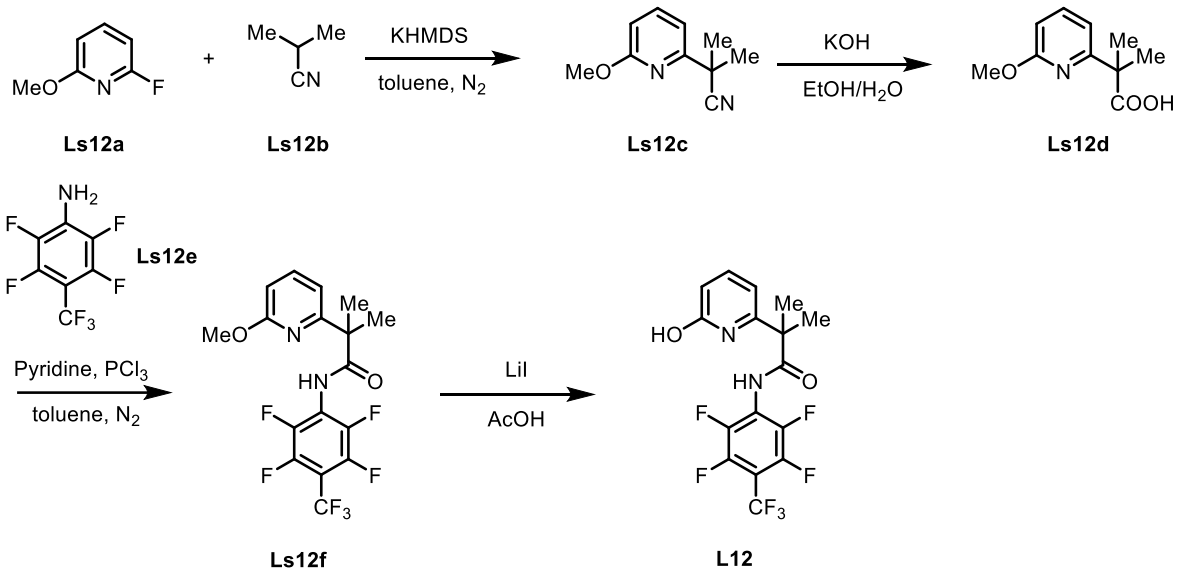


L9

^{1}H NMR (600 MHz, CD_3OD) δ 7.33 (d, J = 7.8 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 3.93 (s, 3H) ^{13}C NMR (151 MHz, CD_3OD) δ 170.1, 162.6, 158.5, 153.8, 144.9 (dm, J = 249.7 Hz), 141.5 (dm, J =

252.0 Hz), 139.2 (dm, J = 248.5 Hz), 114.8, 113.8, 112.0 (m), 56.8. ^{19}F NMR (376 MHz, Acetone-d_6) δ -149.1 (m), -162.6 (*t*, J = 19.9 Hz), -168.4 (m). m.p. = 253 – 254 °C.
HRMS (ESI-TOF) Calculated for $C_{13}H_8F_5N_2O_3$ $[M+H]^+$: 335.0455, Found: 335.0453.

Preparation of **L12**

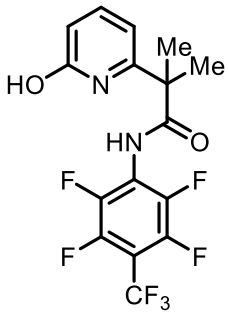


To a dry 100 mL round-bottom flask, **Ls12a** (10 mmol) was added. The flask was sealed, evacuated, and refilled by N_2 three times. Anhydrous toluene (20 mL) and **Ls12b** (10 mmol) was added to the flask, followed by dropwise addition of potassium bis(trimethylsilyl)amide (KHMDS, 11 mmol, 1.0 M in THF) at room temperature. Then the flask was put into a 50 °C heating bath, heated and stirred under this temperature for 16 h. After the completion of the reaction, the reaction mixture was cooled down and water (20 mL) was added slowly. The mixture was extracted by EtOAc (30 mL x 3) and washed by *conc.* brine (30 mL x 3). The organic phase was dried by anhydrous Na_2SO_4 and passed through a pad of silica gel. Solvent was removed from the solution by a rotavapor, and **Ls12c** was used in the next step without further purification.

Ls12c (10 mmol) was added to a 100 mL round-bottom flask. Potassium hydroxide (300 mmol) was dissolved in 30 mL water, and the solution was poured into the round-bottom flask, followed by addition of 30 mL ethanol. The flask was equipped with a condenser, and put into a 115 °C heating bath, stirred and refluxed at this temperature for 24 h or longer for substrates with bulky

side chain (up to 72 h). After completion of the reaction, the reaction mixture was cooled down, and poured into a 500 mL flask with ice inside. 22.5 mL *conc.* HCl (aq) was added carefully into the solution while shaking and there was ice inside the flask (until pH =2, diluted HCl (aq) can also be used but will introduce much water). Then the solvent was concentrated to 10 mL by a rotavapor (to remove ethanol). The aqueous solution was extracted by EtOAc (30 mL x 3), and the organic phase was washed by *conc.* brine (30 mL x 3) and dried by anhydrous Na_2SO_4. The dried organic phase was passed through a pad of silica gel, washed by 50 mL EtOAc. And solvent was removed by a rotavapor to afford **Ls12d**, which was used in the next step without purification.

Ls12d (2.2 mmol), with **Ls12e** (2 mmol), was applied to the procedure of preparation of **L1**. The reaction mixture after two steps was purified by flash silica gel column chromatography (2% formic acid with 10% to 50% EtOAc/hexane) to give the **L12** (62 % over four steps) as a white solid.



L12

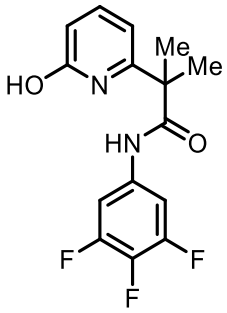
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.51 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.49 (dd, *J* = 7.2, 0.9 Hz, 1H), 6.46 (dd, *J* = 9.0, 0.9 Hz, 1H), 1.83 (s, 6H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 173.6, 164.7, 155.5, 145.3 (dm, *J* = 224.4 Hz), 143.7 (dm, *J* = 230.3 Hz), 142.0, 123.3 (tm, *J* = 14.3 Hz), 122.2 (q, *J* = 273.3 Hz), 115.3, 108.2, 106.9 (m), 49.0, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8, -143.8, -145.6. m.p. = 167 – 168 ^{o}C.

HRMS (ESI-TOF) Calculated for $C_{16}H_{12}F_7N_2O_2$ $[M+H]^+$: 397.0787, Found: 397.0779.

Preparation of **L10**, **L11, L13** to **L15**

Preparation of **L10**, **L11, L13** to **L15** followed the procedure of preparation of **L12** with corresponding aniline and the reaction mixture was purified by flash silica gel column

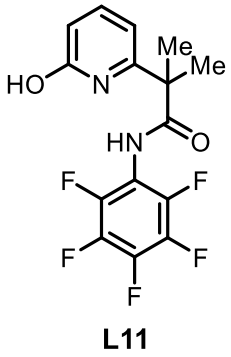
chromatography (2% formic acid with 10% to 50% EtOAc/hexane) to give **L10**, **L11, L13** to **L15** as a white solid.



L10

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.57 (dd, *J* = 9.0, 7.2 Hz, 1H), 7.35 (dd, *J* = 9.6, 6.2 Hz, 2H), 6.57 (dd, *J* = 9.0, 0.9 Hz, 1H), 6.49 (dd, *J* = 7.2, 1.0 Hz, 1H), 1.78 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1, 165.4, 151.0 (dm, *J* = 252.1 Hz), 150.8, 143.0, 136.5 (dm, *J* = 241.6 Hz), 134.2 (m), 118.0, 106.0, 104.7 (dd, *J* = 20.9, 5.5 Hz), 47.4, 24.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ -134.15 (d, *J* = 21.0 Hz), -166.00 (t, *J* = 21.0 Hz). m.p. = 187 – 189 ^{o}C.

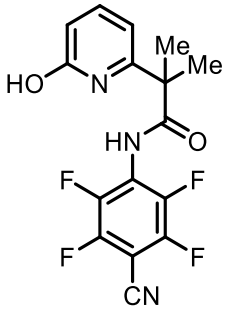
HRMS (ESI-TOF) Calculated for $C_{15}H_{14}F_3N_2O_2$ $[M+H]^+$: 311.1007, Found: 311.1007.



L11

^{1}H NMR (600 MHz, $CDCl_3$) δ 12.61 (s, 1H), 9.15 (s, 1H), 7.47 (dd, *J* = 9.1, 7.2 Hz, 1H), 6.45 (dd, *J* = 7.2, 1.0 Hz, 1H), 6.42 (dd, *J* = 9.1, 0.9 Hz, 1H), 1.81 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.8, 165.3, 150.4, 143.3 (dm, *J* = 245.9 Hz), 142.5, 140.2 (dm, *J* = 257.1 Hz), 137.9 (dm, *J* = 242.1 Hz), 118.3, 112.5 (m), 105.9, 47.0, 24.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -145.3 (d, *J* = 21.5 Hz), -156.4 (t, *J* = 21.2 Hz), -162.6 (t, *J* = 21.5 Hz). m.p. = 173 – 175 ^{o}C.

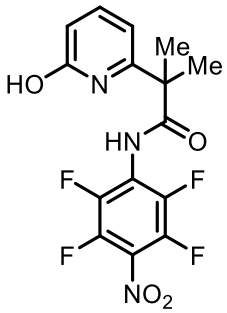
HRMS (ESI-TOF) Calculated for $C_{15}H_{12}F_5N_2O_2$ $[M+H]^+$: 347.0819, Found: 347.0817.



L13

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.53 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.51 (dd, *J* = 7.2, 0.9 Hz, 1H), 6.46 (dd, *J* = 9.0, 0.9 Hz, 1H), 1.83 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.2, 165.3, 150.1, 147.4 (dm, *J* = 261.6 Hz), 142.9, 142.2 (dm, *J* = 239.8 Hz), 123.5 (m), 118.1, 107.4, 106.5, 91.5 (m), 47.3, 24.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -133.1 (d, *J* = 12.9 Hz), -141.8 (d, *J* = 12.7 Hz). m.p. = 177 – 179 °C.

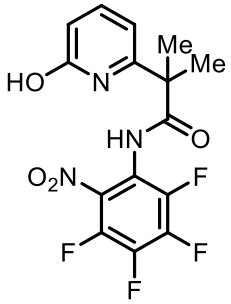
HRMS (ESI-TOF) Calculated for $C_{16}H_{12}F_4N_3O_2$ $[M+H]^+$: 354.0866, Found: 354.0864.



L14

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.54 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.51 (dd, *J* = 7.3, 0.9 Hz, 1H), 6.47 (dd, *J* = 9.0, 0.9 Hz, 1H), 1.83 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.2, 165.3, 150.1, 142.4 (dm, *J* = 246.4 Hz), 142.9, 140.7 (dm, *J* = 245.4 Hz), 128.5 (m), 121.5 (m), 118.2, 106.5, 47.3, 24.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.0 (m), -149.6 (m). m.p. = 173 – 174 °C.

HRMS (ESI-TOF) Calculated for $C_{15}H_{12}F_4N_3O_4$ $[M+H]^+$: 374.0764, Found: 374.0768.



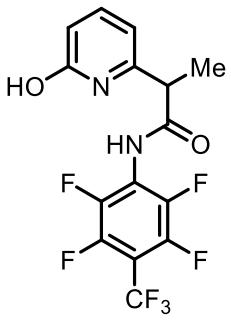
L15

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 9.1, 7.1 Hz, 1H), 6.50 (dd, *J* = 9.0, 0.9 Hz, 1H), 6.44 (dd, *J* = 7.2, 0.9 Hz, 1H), 1.77 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.8, 165.1, 149.9, 142.4, 145.0 – 137.7 (m, four carbons connected to F), 131.8, 118.2, 117.9 (m), 106.3, 47.2, 24.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -140.3 (d, *J* = 16.8 Hz), -145.7 (d, *J* = 21.1 Hz), -147.9 (t, *J* = 21.2 Hz), -154.7 (t, *J* = 21.3 Hz). m.p. = 178 – 180 °C.

HRMS (ESI-TOF) Calculated for $C_{15}H_{12}F_4N_3O_4$ $[M+H]^+$: 374.0764, Found: 374.0757.

Preparation of **L16**

Preparation of **L16** followed the procedure of preparation of **L12** with 22 mmol (2.2 eq) KHMDS and propiononitrile (10 mmol), and the reaction mixture was purified by flash silica gel column chromatography (2% formic acid with 10% to 50% EtOAc/hexane) to give **L16** as a white solid.



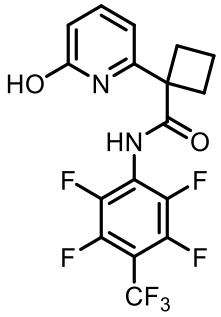
L16

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.90 (s, 1H), 7.61 (dd, *J* = 9.0, 7.1 Hz, 1H), 6.91 – 6.02 (m, 2H), 4.00 (q, *J* = 7.0 Hz, 1H), 1.65 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 165.8, 147.5, 143.9, 118.0, 106.7, 44.0, 14.6. (Signal of seven carbons on the aniline is too low to read due to poor solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.7 Hz), -143.6 (m), -145.7 (m). m.p. = 204 – 206 °C.

HRMS (ESI-TOF) Calculated for $C_{15}H_{10}F_7N_2O_2$ $[M+H]^+$: 383.0630, Found: 383.0625.

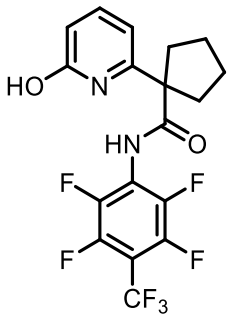
Preparation of **L17** to **L23**

Preparation of **L17** to **L23** followed the procedure of preparation of **L12** with corresponding nitriles, and the reaction mixture was purified by flash silica gel column chromatography (2% formic acid with 10% to 50% EtOAc/hexane) to give **L17** to **L23** as a white solid. Nitriles were commercially available or prepared from commercially available ketones (*1*).



L17

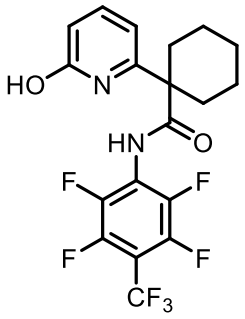
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.11 (s, 1H), 7.55 (dd, *J* = 9.1, 7.1 Hz, 1H), 6.46 (dd, *J* = 9.1, 0.9 Hz, 1H), 6.42 (dd, *J* = 7.1, 1.0 Hz, 1H), 3.34 – 2.92 (m, 2H), 2.93 – 2.51 (m, 2H), 2.11 (m, 1H), 1.97 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0, 165.8, 150.0, 143.2, 117.7, 107.0, 52.9, 32.0, 16.6. (Signal of seven carbons on the aniline is too low to read due to poor solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.7 Hz), -143.8 (m), -145.9 (m). m.p. = 227 – 229 ^{o}C.
HRMS (ESI-TOF) Calculated for $C_{17}H_{12}F_7N_2O_2$ $[M+H]^+$: 409.0787, Found: 409.0782.



L18

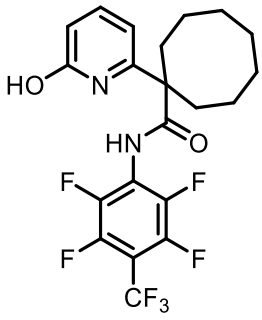
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.52 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.47 (dd, *J* = 4.4, 0.9 Hz, 1H), 6.46 (dd, *J* = 6.3, 0.9 Hz, 1H), 3.11 – 2.94 (m, 2H), 2.14 – 1.99 (m, 2H), 1.90 – 1.75 (m,

4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4, 165.5, 149.5, 143.1, 118.0, 107.5, 59.9, 34.8, 23.2. (Signal of seven carbons on the aniline is too low to read due to poor solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.7 Hz), -143.9 (m), -145.8 (m). m.p. = 207 – 209 °C.
HRMS (ESI-TOF) Calculated for $C_{18}H_{14}F_7N_2O_2$ $[M+H]^+$: 423.0944, Found: 423.0937.



L19

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.83 (s, 1H), 7.52 (dd, *J* = 9.0, 7.5 Hz, 1H), 6.48 (d, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 9.0 Hz, 1H), 2.73 (m, 2H), 1.99 (m, 2H), 1.82 – 1.70 (m, 2H), 1.70 – 1.61 (m, 2H), 1.45 – 1.27 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.2, 165.5, 149.4, 142.9, 118.1, 106.9, 51.2, 32.5, 25.3, 23.1. (Signal of seven carbons on the aniline is too low to read due to poor solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.7 Hz), -143.9 (m), -145.4 (m). m.p. = 147 – 149 °C.
HRMS (ESI-TOF) Calculated for $C_{19}H_{16}F_7N_2O_2$ $[M+H]^+$: 437.1100, Found: 437.1100.

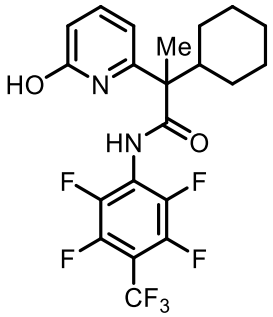


L20

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.23 (s, 1H), 7.48 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.46 (d, *J* = 6.9 Hz, 1H), 6.43 (d, *J* = 9.1 Hz, 1H), 2.58 (dd, *J* = 15.2, 8.4 Hz, 2H), 2.38 (dd, *J* = 14.9, 8.0 Hz, 2H), 1.61 (d, *J* = 54.1 Hz, 10H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1, 165.1, 149.4, 142.3, 118.2, 107.3, 55.3, 29.0, 28.3, 25.1, 22.7. (Signal of seven carbons on the aniline is too low to read due to poor

solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.8 Hz), -143.8 (m), -145.5 (m). m.p. = 156 – 158 °C.

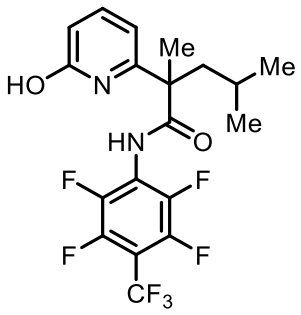
HRMS (ESI-TOF) Calculated for $C_{21}H_{20}F_7N_2O_2$ $[M+H]^+$: 465.1413, Found: 465.1416.



L21

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.69 (dd, *J* = 8.4, 7.4 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 2.46 (tt, *J* = 11.5, 3.1 Hz, 1H), 1.87 – 1.76 (m, 2H), 1.72 – 1.61 (m, 2H), 1.54 (s, 3H), 1.40 – 1.20 (m, 2H), 1.20 – 1.12 (m, 2H), 1.12 – 0.95 (m, 2H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 173.2, 163.7, 157.4, 145.3 (dm, *J* = 244.3 Hz), 143.4 (dm, *J* = 236.7 Hz), 141.7, 123.7 (m), 122.2 (q, *J* = 272.8 Hz), 112.9, 111.4, 106.4 (m), 56.5, 48.7, 29.1, 28.1, 27.8, 27.6, 27.2, 14.6. ^{19}F NMR (376 MHz, Acetone-d_6) δ -59.4 (t, *J* = 21.7 Hz), -146.7 (m), -146.9 (m). m.p. = 171 – 173 °C.

HRMS (ESI-TOF) Calculated for $C_{21}H_{20}F_7N_2O_2$ $[M+H]^+$: 465.1413, Found: 465.1413.

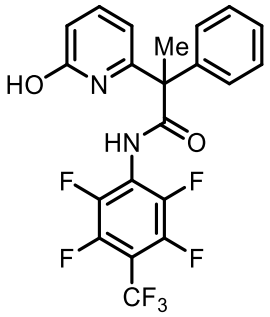


L22

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.49 (dd, *J* = 9.0, 7.2 Hz, 1H), 6.87 – 6.27 (m, 2H), 2.33 (dd, *J* = 14.3, 6.1 Hz, 1H), 2.15 (dd, *J* = 14.3, 6.1 Hz, 1H), 1.84 – 1.72 (m, 4H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.3, 164.9, 150.4, 142.5, 118.0, 106.6, 50.8, 44.7, 25.4, 24.1, 23.8, 20.5. (Signal of seven carbons on the aniline is too low

to read due to poor solubility) ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.8 (t, *J* = 21.7 Hz), -143.8 (m), -145.4 (m). m.p. = 139 – 141 °C.

HRMS (ESI-TOF) Calculated for $C_{19}H_{18}F_7N_2O_2$ $[M+H]^+$: 439.1257, Found: 439.1253.

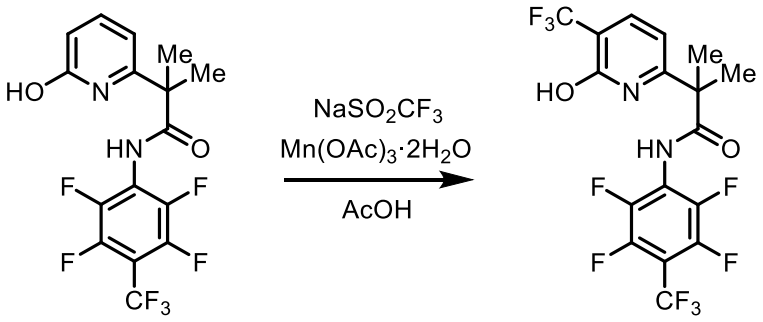


L23

^{1}H NMR (600 MHz, Acetone-d_6) δ 7.68 (q, *J* = 8.1 Hz, 1H), 7.47 – 7.35 (m, 2H), 7.36 – 7.28 (m, 1H), 7.23 (ddd, *J* = 7.8, 3.9, 1.7 Hz, 2H), 6.86 – 6.68 (m, 1H), 6.58 (t, *J* = 9.8 Hz, 1H), 2.00 (d, *J* = 3.4 Hz, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 172.2, 163.9, 156.3, 145.3, 145.3 (dm, *J* = 258.2 Hz), 143.6 (dm, *J* = 237.2 Hz), 141.9, 129.5, 128.3, 128.2, 123.2 (m), 122.2 (q, *J* = 272.5 Hz), 113.4, 112.5, 106.7 (m), 58.5, 26.0. ^{19}F NMR (376 MHz, Acetone-d_6) δ -59.4 (t, *J* = 21.7 Hz), -146.40 (m), -146.8 (m). m.p. = 163 – 165 °C.

HRMS (ESI-TOF) Calculated for $C_{21}H_{14}F_7N_2O_2$ $[M+H]^+$: 459.0944, Found: 459.0942.

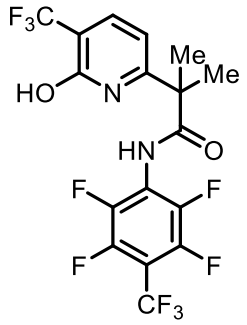
Preparation of **L24**



L12 **L24**

To a 12 mL reaction tube was added **L12** (0.1 mmol) and sodium trifluoromethanesulfinate (0.3 mmol), followed by addition of 0.1 mL AcOH. Manganese(II) acetate dihydrate (0.3 mmol) was added in batches while the reaction mixture was stirred at room temperature, followed by addition

of 0.1 mL AcOH. The reaction mixture was stirred at room temperature for 16 h. After completion, 0.2 mL H_2O was added to the reaction mixture, and the solution was extracted by EtOAc (0.2 mL x 3). Then the mixture was purified by pTLC (2% formic acid with 20% EtOAc/hexane), to afford **L24** (60 %) as a white solid.

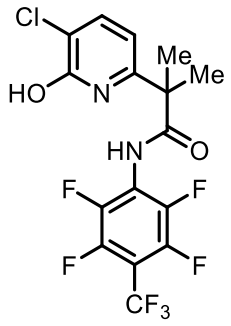


L24

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 1.87 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6, 161.8, 154.9, 144.4 (dm, *J* = 263.8 Hz), 143.0 (dm, *J* = 250.8 Hz), 141.6, 139.8, 138.3, 122.5 (q, *J* = 271.0 Hz), 120.5 (m), 118.8, 105.0, 47.5, 24.2. (Some multiplicity was not assigned due to low signal from poor solubility) ^{19}F NMR (376 MHz, CD_3OD) δ -60.3 (t, *J* = 21.7 Hz), -69.3 (s), -147.0 (m), -147.4 (m). m.p. = 190 – 192 ^{o}C.
HRMS (ESI-TOF) Calculated for $C_{17}H_{11}F_{10}N_2O_2$ $[M+H]^+$: 465.0661, Found: 465.0657.

Preparation of **L25** and **L26**

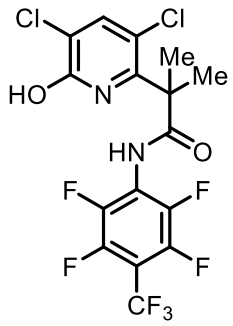
Preparation of **L25** and **L26** followed the procedure of preparation of **L6** to **L8** with **L12**, and the reaction mixture was purified by pTLC (2% formic acid with 20% EtOAc/hexane) to give **L25** and **L26** as white solids.



L25

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.25 (s, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 6.47 (d, *J* = 7.8 Hz, 1H), 1.85 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.0, 161.3, 148.8, 140.5, 124.4, 106.2, 46.5, 24.6. (Signal of seven carbons on the aniline is too low to read due to poor solubility) ^{19}F NMR (376 MHz, CD_3OD) δ -60.3 (t, *J* = 21.7 Hz), -147.0 (m), -147.4 (m). m.p. = 175 – 177 °C.

HRMS (ESI-TOF) Calculated for $C_{16}H_{11}ClF_7N_2O_2$ $[M+H]^+$: 431.0397, Found: 431.0398.



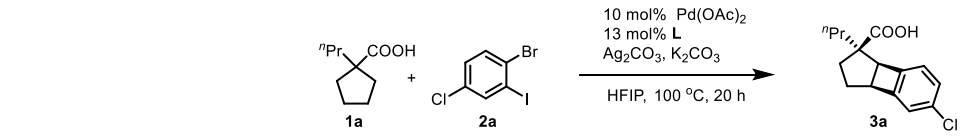
L26

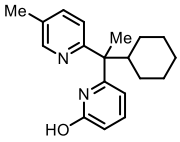
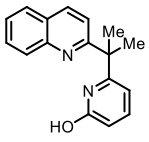
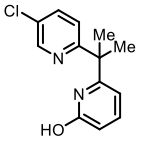
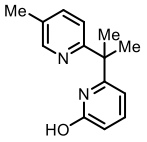
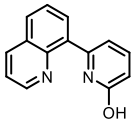
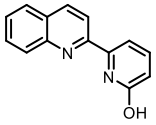
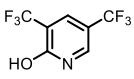
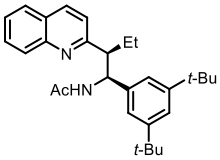
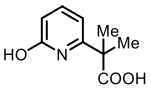
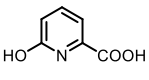
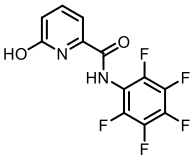
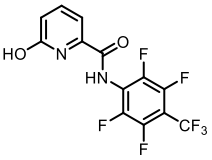
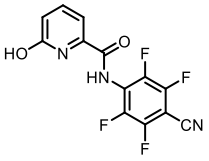
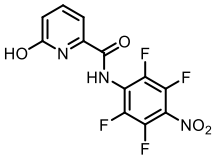
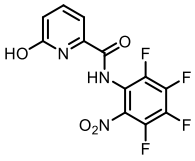
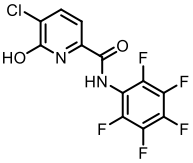
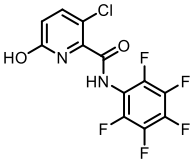
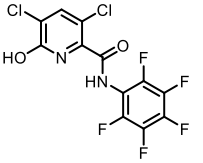
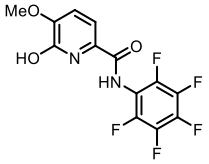
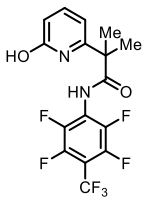
^{1}H NMR (600 MHz, Acetone-d_6) δ 7.84 (s, 1H), 1.66 (s, 6H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 173.9, 158.9, 154.2, 145.3 (dm, *J* = 259.2 Hz), 144.0 (dm, *J* = 254.2 Hz), 141.4, 123.3 (m), 121.3, 122.2 (q, *J* = 273.6 Hz), 117.3, 106.9 (m), 50.6, 25.5. ^{19}F NMR (376 MHz, CD_3OD) δ -60.3 (m), -147.2 (m), -147.2 (m). m.p. = 227 – 229 °C.

HRMS (ESI-TOF) Calculated for $C_{16}H_{10}Cl_2F_7N_2O_2$ $[M+H]^+$: 465.0008, Found: 465.0005.

3. Condition Screenings for the [2+2] Annulation Reaction

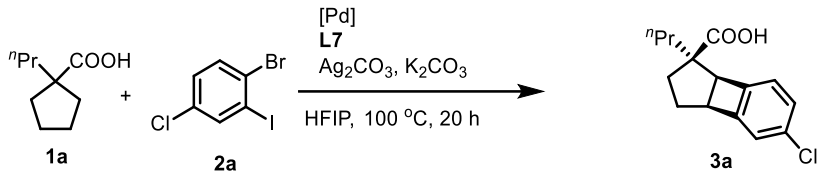
Table S1. Ligands screening for [2+2] annulation of cyclic aliphatic acid*



					
L27, 4%	**L28**, 20%	**L29**, 7%	**L30**, 7%	**L31**, 8%	**L32**, 12%
					
L33, 10%	**L34**, 17%	**L35**, 17%	**L36**, 22%	**L1**, 38%	**L2**, 44%
					
L3, 57%	**L4**, 67%	**L5**, 60%	**L6**, 14%	**L7**, 82%	**L8**, 67%
		No Ligand			
L9, 50%	**L12**, 22%	7%			

*Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), **L** (13 mol%), K_2CO_3 (2.5 equiv), Ag_2CO_3 (2.0 equiv), HFIP (1.0 mL), at 100 °C for 20 hours. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard.

Table S2. Palladium sources and loading screening for cyclic aliphatic acid*

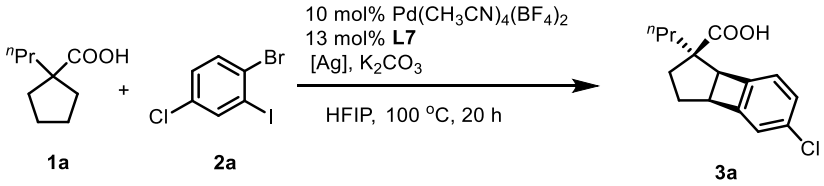


1a 2a 3a

entry	[Pd]	loading	Time (h)	yield
1	$Pd(OAc)_2$	10 mol%	20	82%
2	$Pd(CH_3CN)_2Cl_2$	10 mol%	20	84%
3	$Pd(TFA)_2$	10 mol%	20	86%
4	$Pd_2(dba)_3$	5 mol%	20	60%
5	$Pd(OPiv)_2$	10 mol%	20	86%
6	$Pd(CH_3CN)_4(BF_4)_2$	10 mol%	20	90% (90%[a])
7	$Pd(CH_3CN)_4(BF_4)_2$	5 mol%	40	84%
8	$Pd(CH_3CN)_4(BF_4)_2$	1 mol%	56	61%

*Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), **L7** (1.3 equiv to [Pd] loading), K_2CO_3 (2.5 equiv), Ag_2CO_3 (2.0 equiv), HFIP (1.0 mL), at 100 °C. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard. [a]Isolated yield.

Table S3. Silver salts screening for cyclic aliphatic acid*

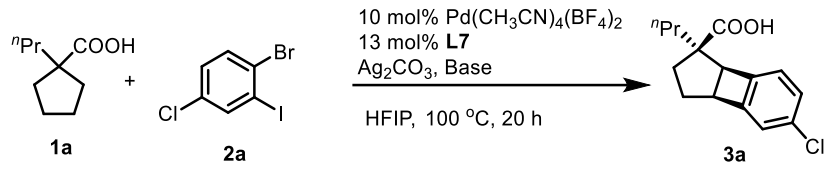


1a 2a 3a

entry	[Ag]	yield
1	Ag_2CO_3	90%
2	AgOAc	59%
3	Ag_3PO_4	65%
4	Ag_2O	63%
5	AgF	77%

*Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(CH_3CN)_4(BF_4)_2$ (10 mol%), **L7** (13 mol%), K_2CO_3 (2.5 equiv), HFIP (1.0 mL), at 100 °C for 20 hours. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard.

Table S4. Bases screening for cyclic aliphatic acid*

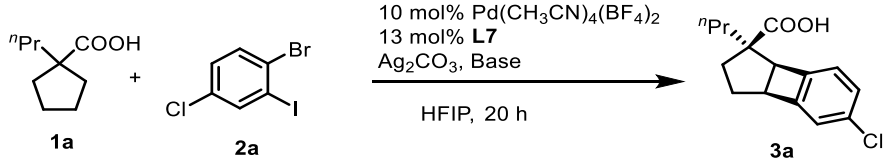


1a 2a 3a

entry	Base	yield
1	K_2CO_3	90%
2	$KHCO_3$	81%
3	KH_2PO_4	32%
4	K_3PO_4	65%
5	Na_2CO_3	67%
6	$NaHCO_3$	55%
7	NaOAc	39%
8	Cs_2CO_3	80%
9	Li_2CO_3	23%

*Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(CH_3CN)_4(BF_4)_2$ (10 mol%), **L7** (13 mol%), Ag_2CO_3 (2.0 equiv), Base (2.5 equiv), HFIP (1.0 mL), at 100 °C for 20 hours. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard.

Table S5. Temperature screening for cyclic aliphatic acid*

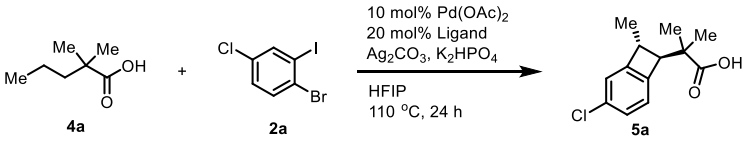


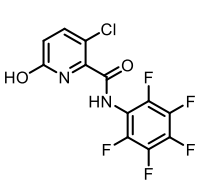
1a 2a 3a

entry	Temperature	yield
1	100 °C	90%
2	90 °C	84%
3	80 °C	77%

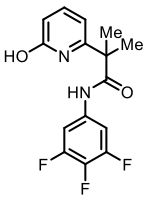
*Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(CH_3CN)_4(BF_4)_2$ (10 mol%), **L7** (13mol%), K_2CO_3 (2.5 equiv), Ag_2CO_3 (2.0 equiv), HFIP (1.0 mL), for 20 hours. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard.

Table S6. Ligands screening for [2+2] annulation of acyclic aliphatic acid*

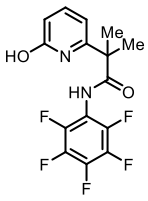




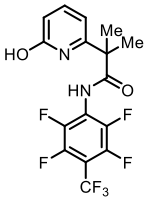
L7, 2%



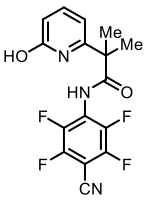
L10, 18%



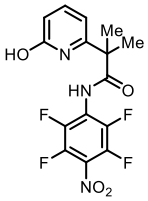
L11, 50%



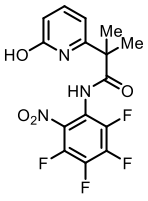
L12, 68%



L13, 43%



L14, 47%



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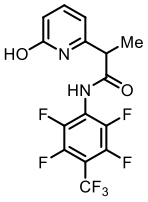

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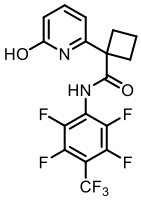

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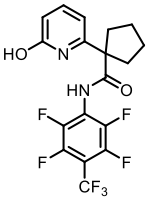

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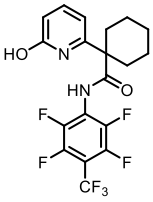

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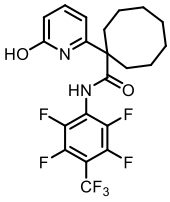

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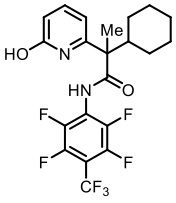

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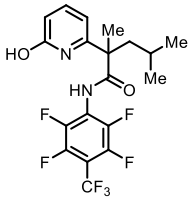

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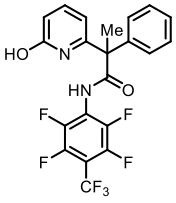

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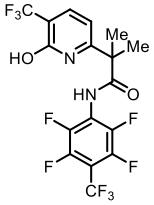

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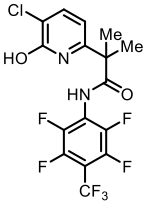

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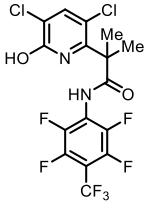

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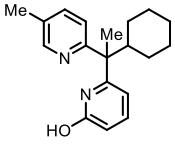
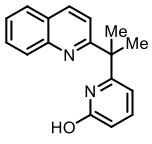
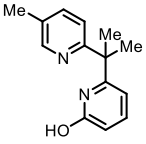


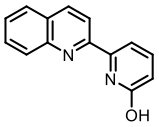
L27, 2%



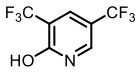
L28, 36%



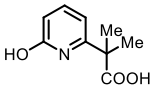
L30,2%



L32,14%



L33, N.D.



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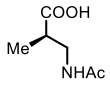
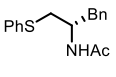
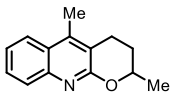


L37,10%



L38, 4%



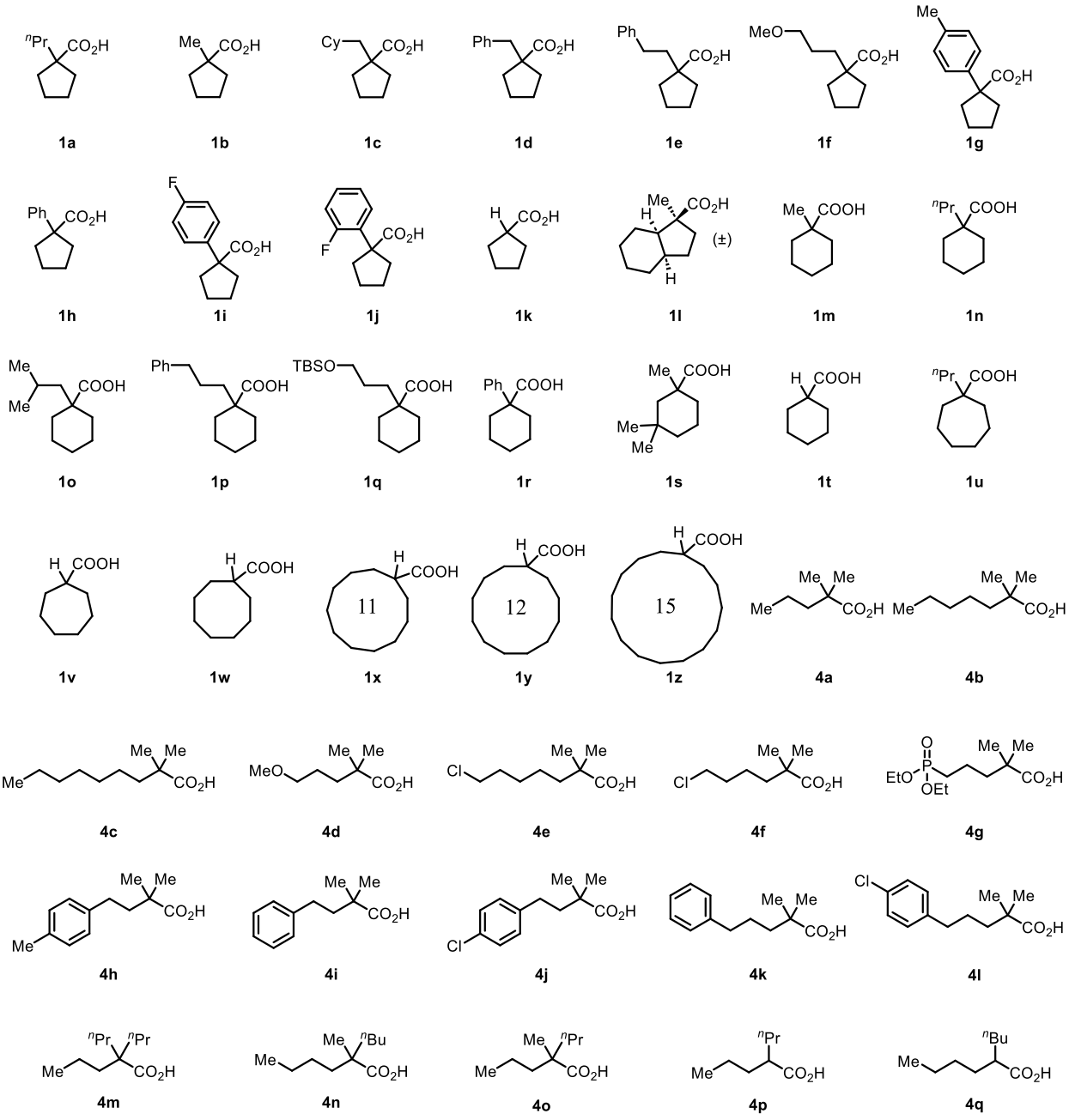
L39, 4%

No Ligand

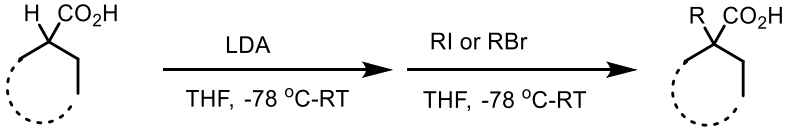
N.D.

* Reaction conditions: aliphatic acid (0.1 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol%), **L** (20 mol%), K_2HPO_4 (4.0 equiv), Ag_2CO_3 (2.0 equiv), HFIP (1.2 ml), at 110 °C for 24 hours. The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard.

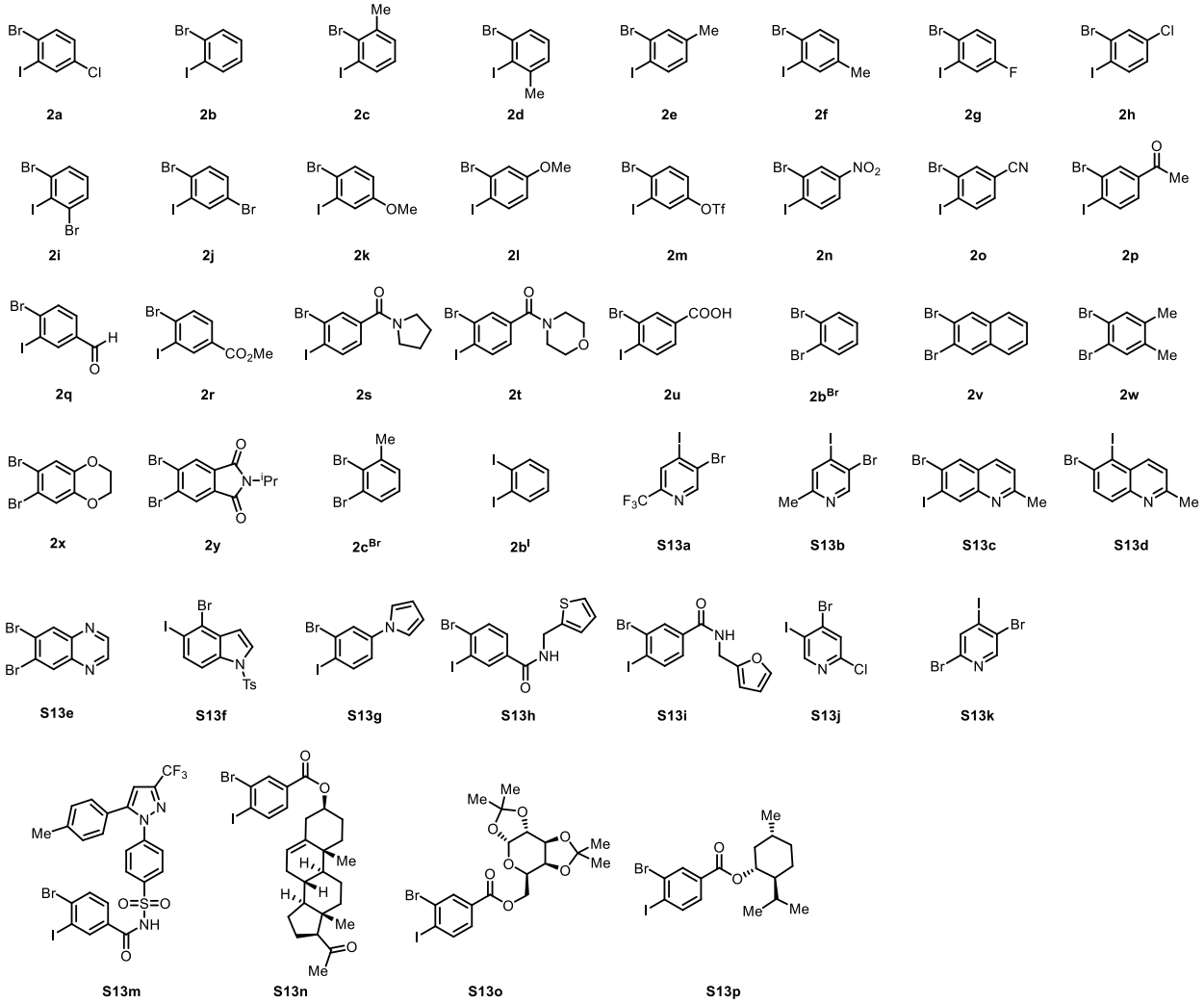
4. Preparation for the Substrates



1b, **1g-k**, **1m**, **1r-t**, **1v**, **1x-z**, **4a-c**, **4m-q** are commercially available. **1z** was prepared according to reported procedure (*31*). Other aliphatic acids were prepared by the following procedure.

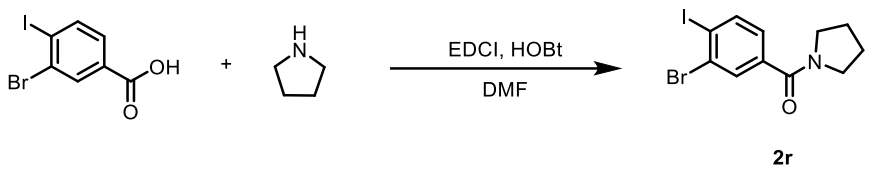


LDA (55 mmol) was added dropwise to a mixture of α-H-aliphatic acid (22 mmol) and THF (50 mL) at -78 ^{o}C, and the mixture was allowed to warm up to room temperature and stirred for 1 h. Then the reaction mixture was recooled to -78 ^{o}C and RI or RBr (22 mmol) was added dropwise. The resulting solution was allowed to warm up to room temperature and stirred overnight. After the reaction finished, the reaction mixture was quenched with 10% HCl solution and extracted with EtOAc. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product. Then purified by chromatography on silica gel to afford the desired aliphatic acid.



2a-q, **2t-w**, **2c^{Br}, 2b^{I}**, **S13b**, **S13j-k** are commercially available. **2x** (*32*), **S13a** (*33*), **S13c** (*34*), **S13d** (*34*), **S13e** (*35*) were prepared according to reported procedure.

Preparation of 2r



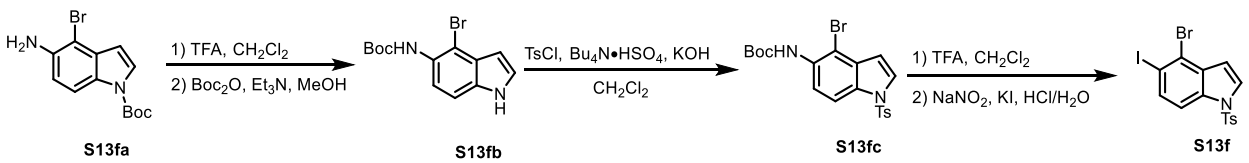
2r

To a solution of 3-bromo-4-iodobenzoic acid (3 mmol, 981 mg) in DMF (10 mL) was added *N*-(3-(((ethylimino)methylene)amino)propylidene)-*N*-methylmethanaminium chloride (EDCI, 4.5 mmol, 862 mg) and HOBt (4.5 mmol, 608 mg), then the reaction stirred at room temperature for 10 min. Thereafter, pyrrolidine (4.5 mmol, 320 mg) was added, and the mixture stirred at room temperature for 18 h. The mixture was quenched with saturated $NaHCO_3$ (10 mL), extracted with EtOAc (3 x 10 mL), washed with brine, and dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using EtOAc/hexane to afford the expected product **2r** (85% yield, 2.55 mmol, 969 mg) as white solid, m.p. = 68 – 70 ^oC. ^1H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 1.9 Hz, 1H), 7.14 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.62 (t, *J* = 7.0 Hz, 2H), 3.41 (t, *J* = 6.7 Hz, 2H), 2.00 – 1.86 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 140.4, 138.7, 131.4, 130.0, 127.1, 103.2, 49.7, 46.5, 26.5, 24.5. HRMS (ESI-TOF) Calculated for $C_{11}H_{12}BrClNO$ $[M+H]^+$: 379.9147, Found: 379.9148.

2s (white solid, 82% yield, 2.46 mmol, 974 mg, m.p. = 82 – 84 ^oC) is synthesized with the same preparation procedure of **2r** by using morpholine instead of pyrrolidine. ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 1.9 Hz, 1H), 7.03 (dd, *J* = 8.1, 1.9 Hz, 1H), 3.91 – 3.32 (brm, 8H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 140.6, 136.8, 131.3, 130.4, 126.7, 103.3, 66.9, 48.3, 42.7.

HRMS (ESI-TOF) Calculated for $C_{11}H_{12}BrClNO_2$ $[M+H]^+$: 395.9096, Found: 395.9095.

Preparation of S13f



S13fa **S13fb** **S13fc** **S13f**

To a stirred solution of **S13fa** (3.11g, 10 mmol) in CH_2Cl_2 (50 mL) was added TFA (1.46 g, 15 mmol) and the reaction was stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution, water and brine solution. The separated CH_2Cl_2 layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product for next step without further purification.

After above crude product dissolved in MeOH (50 mL), triethylamine (1.52 g, 15 mmol) and Boc_2O (2.62g, 12 mmol) were added and the mixture solution was stirred at room temperature for 6 h. The reaction solution was concentrated under reduced pressure, and the residue was partitioned with ethyl acetate (100 mL) and water (50 mL), and the organic layer was washed with a saturated sodium chloride solution. The organic layer was dried and then concentrated under reduced pressure. The residue was purified by a silica gel column to obtain **S13fb** (93% yield for two steps, 2.89 g, 9.3 mmol) as a white solid, m.p. = 108 – 110 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.86 (s, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 7.22 (t, *J* = 2.9 Hz, 1H), 6.85 (s, 1H), 6.54 (td, *J* = 2.2, 1.1 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 132.6, 129.2, 128.8, 125.5, 110.6, 103.3, 80.7, 28.5. HRMS (ESI-TOF) Calculated for $C_{13}H_{15}BrN_2O_2Na$ $[M+Na]^+$: 333.0215, Found: 333.0223.

Tetrabutylammonium hydrogen sulfate (68 mg, 0.2 mmol) was added to the solution of **S13fb** (622 mg, 2 mmol) in CH_2Cl_2 (20 mL) and the reaction mass was stirred for 5 min at room temperature. Then, potassium hydroxide powder (336 mg, 6 mmol) added to the clear solution and stirred 0 °C for 10 min. After that, TsCl (572 mg, 3 mmol) was added, and the reaction mass stirred for reaction completion at room temperature overnight. After the completion of the reaction, the mass was filtered out and washed with 20 mL of CH_2Cl_2. Further, the filtered content dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Then the residue was purified by flash chromatography on silica gel using EtOAc/hexane to obtain **S13fc** (90% yield, 838 mg, 1.8 mmol) as a white solid, m.p. = 142 – 144 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 9.1 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 3.7 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.89 (s, 1H), 6.65 (d, *J* = 4.4 Hz, 1H), 2.34 (s, 3H), 1.53 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.0, 145.4, 135.0, 132.4, 131.7, 131.0, 127.6, 127.0, 127.0, 118.1, 113.2, 109.2, 105.0, 81.2, 28.4, 21.7.

HRMS (ESI-TOF) Calculated for $C_{15}H_{14}BrN_2O_2S$ $[M\text{-}Boc+2H]^+$: 364.9959, Found: 364.9960.

To a stirred solution of **S13fc** (465 mg, 1 mmol) in CH_2Cl_2 (5 mL) was added TFA (146 mg, 1.5 mmol) and the reaction was stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution, water and brine solution. The separated CH_2Cl_2 layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product for next step without further purification.

After above crude product dissolved in in conc. HCl (2 mL) at -5 ºC, $NaNO_2$ (86 mg, 1.25 mmol) in H_2O (2 mL) was added dropwise. The resulting mixture was stirred at same temperature for 30 min. Then a solution of KI (332 mg, 2 mmol) in H_2O (2 mL) was added dropwise. The temperature was raised to room temperature slowly and the reaction mixture was stirred for 2 h. Upon completion of the reaction (monitored by TLC), 5% $Na_2S_2O_3$ solution was added. The reaction mixture was then extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, the crude product was purified by silica gel column chromatography using EtOAc/hexane to provide **S13f** (60% yield for two steps, 286 mg, 0.6 mmol) as a white solid, m.p. = 150 – 52 ºC. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 4H), 7.56 (d, *J* = 3.8 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 3.7 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.7, 135.3, 134.9, 134.3, 130.3, 127.6, 127.0, 122.5, 114.2, 110.5, 95.1, 21.8. HRMS (ESI-TOF) Calculated for $C_{15}H_{12}BrClNO_2S$ $[M+H]^+$: 475.8817, Found: 475.8811.

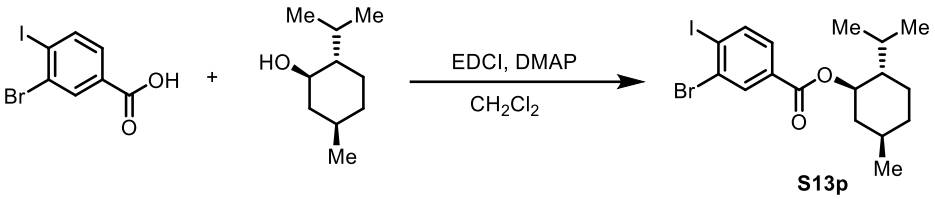
Preparation of S13g

S13g

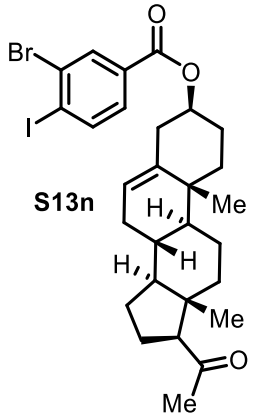
A mixture of the 3-bromo-4-iodoaniline (1.49 g, 5 mmol), 2,5-dimethoxytetrahydrofuran (661 mg, 5 mmol), acetic acid (0.35 mL), 1,2-dichloroethane (10 mL), and water (5 mL) was heated under reflux for 24 h. After removal of the solvent, the crude residue was dissolved in a mixture of water (10 mL) and CH_2Cl_2 (10 mL). The organic extract was washed with a saturated sodium carbonate solution (10 mL) and brine (10 mL). After dried over Mg_2SO_4, the solvent removed in vacuo. The resulting residue was purified by silica gel column chromatography using EtOAc/hexane to afford **S13g** (96% yield, 4.8 mmol, 1.66 g) as a yellow solid, m.p. = 63 – 65 ºC. ^{1}H NMR (600 MHz,

$CDCl_3$) δ 7.86 (d, *J* = 8.5 Hz, 1H), 7.68 (d, *J* = 2.6 Hz, 1H), 7.08 – 7.02 (m, 3H), 6.36 (q, *J* = 2.1 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.7, 141.0, 130.7, 124.4, 120.4, 119.2, 111.6, 96.3. HRMS (ESI-TOF) Calculated for $C_{10}H_8BrIN$ $[M+H]^+$: 347.8885, Found: 347.8882.

Preparation of S13p



A mixture of L-menthol (781 mg, 5 mmol), 3-bromo-4-iodobenzoic acid (1.96 g, 6 mmol), *N*-(3-(((ethylimino)methylene)amino)propylidene)-*N*-methylmethanaminium chloride (EDCI, 1.25 g, 6.5 mmol), and DMAP (122 mg, 1 mmol) in 25 mL of CH_2Cl_2 was stirred at room temperature overnight. The mixture was quenched with saturated NH_4Cl (20 mL), extracted with CH_2Cl_2 (3 x 20 mL), washed with brine, and dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the expected product **S13p** (87% yield, 2.02 g, 4.35 mmol) as a colorless oil. ^1H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 1.9 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.62 (dd, *J* = 8.2, 1.9 Hz, 1H), 4.92 (td, *J* = 10.9, 4.5 Hz, 1H), 2.11 – 2.05 (m, 1H), 1.88 (pd, *J* = 7.0, 2.9 Hz, 1H), 1.77 – 1.69 (m, 2H), 1.57 – 1.50 (m, 2H), 1.17 – 1.04 (m, 2H), 0.92 (dd, *J* = 10.2, 6.8 Hz, 7H), 0.78 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 140.5, 133.5, 132.5, 130.1, 129.1, 107.5, 75.8, 47.3, 41.0, 34.4, 31.6, 26.7, 23.7, 22.2, 20.9, 16.6.

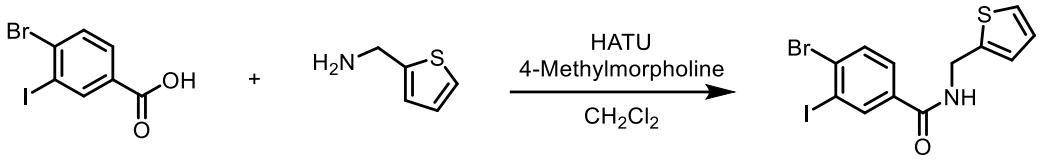


S13n (white solid, 80% yield, 2.5 g, 4.0 mmol, m.p. = 219 – 221 °C) is synthesized with the same preparation procedure of **S13p** by using dehydroepiandrosterone instead of menthol.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (t, *J* = 2.2 Hz, 1H), 7.94 (dd, *J* = 8.3, 2.8 Hz, 1H), 7.62 (dt, *J* = 8.2, 2.1 Hz, 1H), 5.42 (s, 1H), 4.89 – 4.74 (m, 1H), 2.54 (td, *J* = 9.0, 2.8 Hz, 1H), 2.48 – 2.43 (m, 2H), 2.18 (dddd, *J* = 14.2, 9.5, 7.1, 2.5 Hz, 1H), 2.13 (d, *J* = 2.2 Hz, 3H), 2.09 – 1.96 (m, 3H), 1.93 (dq, *J* = 13.4, 3.5 Hz, 1H), 1.78 – 1.58 (m, 5H), 1.55 – 1.43 (m, 3H), 1.28 – 1.14 (m, 3H), 1.08 – 1.00 (m, 4H), 0.64 (d, *J* = 2.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 209.7, 164.5, 140.5, 139.5, 133.5, 1324, 130.1, 129.1, 122.9, 107.5, 75.4, 63.8, 57.0, 50.0, 44.1, 38.9, 38.2, 37.1, 36.8, 32.0, 31.9, 31.7, 27.9, 24.6, 23.0, 21.2, 19.5, 13.4.

HRMS (ESI-TOF) Calculated for $C_{28}H_{35}BrIO_3$ $[M+H]^+$: 625.0814, Found: 625.0798.

Preparation of S13h, S13i, S13m, S13o



S13h

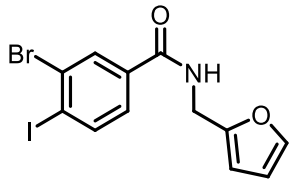
To a 40 mL vial, dihalogenbenzoic acid (2 mmol) and amine (2.5 mmol) were added, followed by 10 mL CH_2Cl_2, and stirred at room temperature for 1 min. HATU (3 mmol) and 4-methylmorpholine (4 mmol) were added sequentially. The vial was capped, and the mixture was stirred at room temperature overnight. After the reaction was finished (monitored by TLC or UPLC), the reaction mixture was passed through a pad of silica, washed by 10 mL EtOAc. The solvent in the filtrate was removed, and the mixture was purified by flash chromatography on silica gel (0% to 20% EtOAc/hexane) to afford the expected product **S13h** as a white solid (80%, 1.6 mmol, 675 mg, m.p. = 161 – 163 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 2.1 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.59 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.26 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.04 (dq, *J* = 3.5, 0.9 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.38 (s, 1H), 4.79 (dd, *J* = 5.6, 0.8 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 140.2, 138.9, 134.5, 133.8, 132.9, 128.0, 127.2, 126.7, 125.8, 101.6, 39.1.

HRMS (ESI-TOF) Calculated for $C_{12}H_{10}BrINOS$ $[M+H]^+$: 421.8711, Found: 421.8705.

Preparation of S13i

Preparation of **S13i** followed the procedure of the preparation of **S13h** with corresponding dihalogenbenzoic acid and amine, the product **S13i** was purified by flash chromatography on silica gel (20% to 50% EtOAc in hexane) as a white solid (90%, 1.8 mmol, 730 mg, m.p. = 151 – 153 ^{o}C).

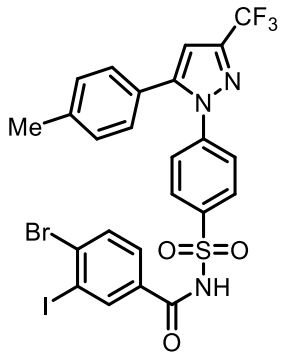


S13i

^{1}H NMR (600 MHz, Acetone-d_6) δ 8.31 (brs, 1H), 8.20 (d, *J* = 2.0 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.64 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.46 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.36 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.30 (dt, *J* = 3.2, 0.8 Hz, 1H), 4.57 (dd, *J* = 5.7, 0.8 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 150.7, 142.7, 140.7, 135.7, 131.2, 130.5, 126.7, 110.7, 108.2, 105.7, 37.3.
HRMS (ESI-TOF) Calculated for $C_{12}H_{10}BrINO_2$ $[M+H]^+$: 405.8940, Found: 405.8935.

Preparation of S13m

Preparation of **S13m** followed the procedure of the preparation of **S13h** with corresponding dihalogenbenzoic acid and Celecoxib, the product **S13m** was purified by chromatography on silica gel (0% to 3% MeOH in EtOAc) as a yellow solid (50%, 1.0 mmol, 690 mg, m.p. = 220-222 ^{o}C).

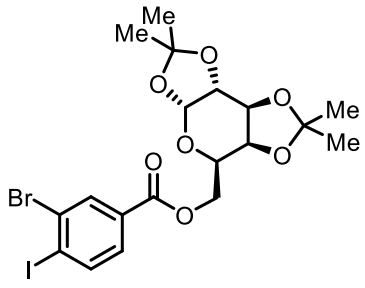


S13m

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 2.2 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.58 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.15 – 7.07 (m, 2H), 6.75 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 145.6 (q, *J* = 38.7 Hz), 144.4, 143.8, 140.2, 139.6, 137.4, 136.3, 133., 131.3, 130.0, 130.0, 128.9, 128.6, 125.7, 125.3, 120.2 (q, *J* = 269.3 Hz), 106.8, 101.9, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.1.
HRMS (ESI-TOF) Calculated for $C_{24}H_{17}BrF_3IN_3O_3S$ $[M+H]^+$: 689.9171, Found: 689.9177.

Preparation of S13o

Preparation of **S13o** followed the procedure of the preparation of **S13h** with corresponding dihalogenbenzoic acid and 1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose, the product **S13o** was purified by flash chromatography on silica gel (0% to 20% EtOAc in hexane) as sticky liquid (82%, 1.64 mmol, 933 mg).



S13o

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 1.9 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.61 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.54 (d, *J* = 4.9 Hz, 1H), 4.64 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.50 (dd, *J* = 11.6, 4.6 Hz,

1H), 4.42 (dd, *J* = 11.5, 7.6 Hz, 1H), 4.33 (dd, *J* = 5.0, 2.5 Hz, 1H), 4.29 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.19 – 4.11 (m, 1H), 1.50 (s, 3H), 1.46 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.8, 140.5, 133.5, 131.5, 130.1, 129.1, 109.8, 108.9, 107.9, 96.3, 71.1, 70.8, 70.5, 66.1, 64.6, 26.1, 26.1, 25.1, 24.6.

HRMS (ESI-TOF) Calculated for $C_{19}H_{23}BrIO_7$ $[M+H]^+$: 568.9672, Found: 568.9675.

5. General Procedure for the [2+2] Annulation

General Procedure for the [2+2] annulation of cyclic aliphatic acids and haloarenes.

In a sealed 8 mL vial equipped with a magnetic stir bar was charged with the appropriate aliphatic acid substrate (0.10 mmol), dihaloarene (0.20 mmol), Ag_2CO_3 (55.0 mg, 0.20 mmol), and K_2CO_3 (34.5 mg, 0.25 mmol). A solution of $Pd(CH_3CN)_4(BF_4)_2$ (4.4 mg, 10 mol%) and **L7** (4.4 mg, 13 mol%) in HFIP (1.0 mL) was premixed and added before the vial was briefly flushed with nitrogen. Subsequently the vial was capped and closed tightly. The reaction mixture was then stirred at the rate of 300 rpm at 100 °C for 20 h. After being allowed to cool to room temperature, the mixture was acidified with 80 μL of formic acid and stirred for 30 seconds. The mixture was passed through a pad of celite with EtOAc as the eluent to remove any insoluble precipitate. The resulting solution was concentrated, and the residual mixture was purified using pTLC or reverse phase chromatography to afford BCB products.

General Procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes.

In a sealed 12 mL reaction tube equipped with a magnetic stir bar was charged with the appropriate dihaloarene (0.30 mmol), Ag_2CO_3 (55.0 mg, 0.20 mmol), K_2HPO_4 (61.0 mg, 0.35 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol%) and **L12** (7.9 mg, 20 mol%), followed by aliphatic acid substrate (0.10 mmol) and HFIP (1.2 mL). Subsequently the tube was capped and closed tightly. The reaction mixture was then stirred at the rate of 200 rpm at 110 °C for 24 h (Stirring should be appropriate for inhibition of large precipitate formation and adhesion of solids to vial wall above the solution). After being allowed to cool to room temperature, the mixture was acidified with 80 μL of formic acid and stirred for 30 seconds. Spherical solid was crushed, and the mixture was passed through a pad of celite with EtOAc as the eluent to remove any insoluble precipitate. The resulting solutions was concentrated, and the residual mixture was purified using pTLC to afford BCB products.

Procedure for the gram scale [2+2] annulation of cyclic aliphatic acids and haloarenes.

To a 150 mL heavy wall pressure vessel with an internal thread was added $Pd(CH_3CN)_4(BF_4)_2$ (200 mg, 10 mol%), **L7** (200 mg, 13 mol%), HFIP (45 mL) and a stir bar. The reaction mixture stirred for 5 min before aliphatic acid (4.5 mmol), dihaloarene (9.0 mmol), Ag_2CO_3 (2.48

g, 9.0 mmol), and K_2CO_3 (1.55 g, 11.25 mmol) were added. Then the reaction mixture stirred at 300 rpm and 100 °C (oil bath temperature) for 20 h. The reaction mixture was then cooled to room temperature and formic acid (4.0 mL) was added, followed by filtration through a short plug of Celite®. The filtrate was then concentrated under reduced pressure. The product was purified by column chromatography (20% EtOAc/hexane + 1% formic acid). The desired product **3a** was isolated as a white solid (1.05 g, 3.96 mmol, 88% yield).

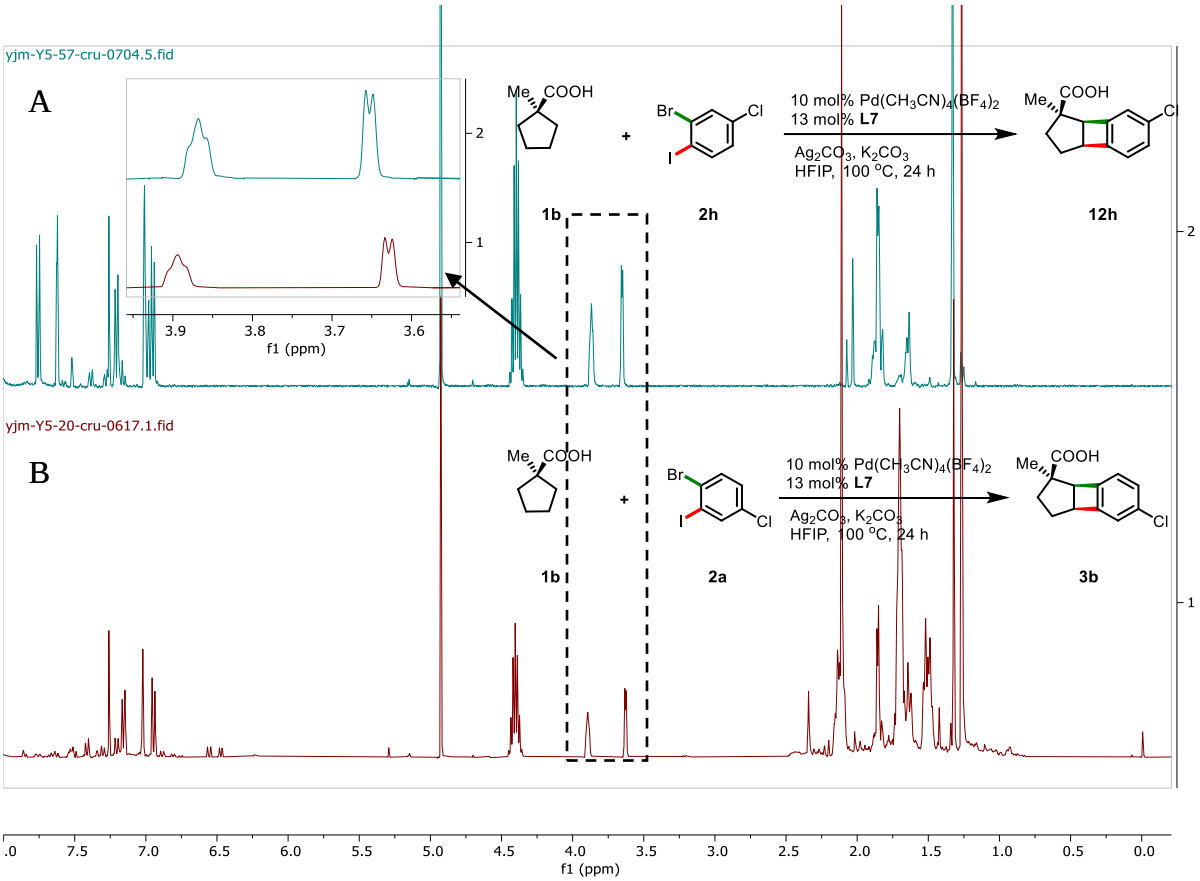
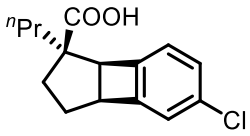


Figure S1. ^{1}H-NMR spectra evidence for the exclusive regioselectivity. (A) ^{1}H-NMR spectra of the Pd-catalyzed [2+2] annulation of **1b** and **2h** at reaction time 24 h. (B) ^{1}H-NMR spectra of the Pd-catalyzed [2+2] annulation of **1b** and **2a** at reaction time 24 h.

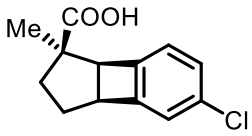
6. Characterization Data of Products Obtained from the [2+2] Annulation



3a

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3a** in 90% yield (white solid, 23.8 mg, 0.09 mmol, m.p. = 91– 93 °C).

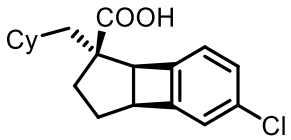
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.8 Hz, 1H), 7.03 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 3.91 – 3.85 (m, 1H), 3.67 (d, *J* = 3.7 Hz, 1H), 1.85 – 1.76 (m, 4H), 1.74 – 1.69 (m, 1H), 1.55 – 1.49 (m, 1H), 1.44 – 1.32 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.7, 147.9, 142.6, 134.0, 128.2, 124.6, 122. 7, 55.4, 54.4, 47.3, 37.6, 29.2, 26.0, 18.4, 14.6.
HRMS (ESI-TOF) Calculated for $C_{15}H_{18}ClO_2$ $[M+H]^+$: 265.0995, Found: 265.0999.



3b

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3b** in 86% yield (white solid, 20.4 mg, 0.086 mmol, m.p. = 125–128 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 7.7, 2.1 Hz, 1H), 7.04 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 3.93 – 3.87 (m, 1H), 3.64 (d, *J* = 3.9 Hz, 1H), 1.92 – 1.83 (m, 3H), 1.69 – 1.61 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 147.7, 142.6, 134.0, 128.2, 124.9, 122.7, 55.7, 49.9, 47.6, 32.4, 26.0, 22.7.
HRMS (ESI-TOF) Calculated for $C_{13}H_{14}ClO_2$ $[M+H]^+$: 237.0682, Found: 237.0679.

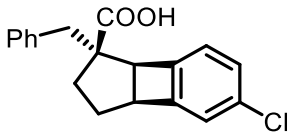


3c

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3c** in 75% yield (white solid, 23.9 mg, 0.075 mmol, m.p. = 139–141 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.07 – 7.00 (m, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.62 (d, *J* = 3.9 Hz, 1H), 1.85 – 1.72 (m, 6H), 1.72 – 1.61 (m, 4H), 1.48 – 1.40 (m, 2H), 1.32 – 1.11 (m, 3H), 1.08 – 0.93 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 147.9, 142.3, 134.1, 128.2, 124.2, 122.8, 56.6, 53.2, 47.3, 42.2, 35.3, 34.5, 33.3, 28.4, 26.54, 26.4, 26.4, 26.2.

HRMS (ESI-TOF) Calculated for $C_{19}H_{24}ClO_2$ $[M+H]^+$: 319.1465, Found: 319.1462.

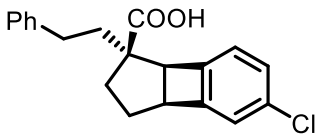


3d

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3d** in 60% yield (colorless oil, 18.7 mg, 0.06 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 3H), 7.22 – 7.16 (m, 3H), 7.06 (dt, *J* = 1.8, 0.7 Hz, 1H), 6.94 (dt, *J* = 7.8, 0.8 Hz, 1H), 3.99 (dd, *J* = 7.6, 3.7 Hz, 1H), 3.83 (d, *J* = 3.7 Hz, 1H), 3.19 (d, *J* = 13.8 Hz, 1H), 2.79 (d, *J* = 13.8 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.92 – 1.86 (m, 1H), 1.79 – 1.72 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.7, 147.8, 142.2, 137.3, 134.2, 129.8, 128.6, 128.3, 127.1, 124.4, 122.8, 55.8, 55.6, 47.6, 40.9, 28.3, 26.1.

HRMS (ESI-TOF) Calculated for $C_{19}H_{16}ClO_2$ $[M-H]^-$: 311.0839, Found: 311.0831.

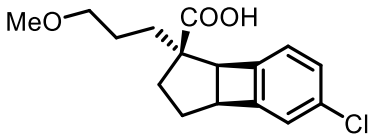


3e

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3e** in 54% yield (colorless oil, 17.6 mg, 0.054 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.24 – 7.18 (m, 3H), 7.16 (ddd, *J* = 7.7, 1.8, 0.6 Hz, 1H), 7.05 (dt, *J* = 1.6, 0.7 Hz, 1H), 6.98 (dt, *J* = 8.0, 0.8 Hz, 1H), 3.89 (dd, *J* = 6.6, 3.7 Hz, 1H), 3.73 (d, *J* = 3.7 Hz, 1H), 2.75 – 2.62 (m, 2H), 2.09 (ddd, *J* = 13.9, 12.1, 5.2 Hz, 1H), 1.94 – 1.81 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.8, 147.8, 142.3, 141.6, 134.2, 128.7, 128.5, 128.3, 126.3, 124.6, 122.8, 55.4, 54.3, 47.3, 37.2, 31.6, 29.2, 26.0.

HRMS (ESI-TOF) Calculated for $C_{20}H_{18}ClO_2$ [M-H]$^-$: 327.1152, Found: 327.1151.

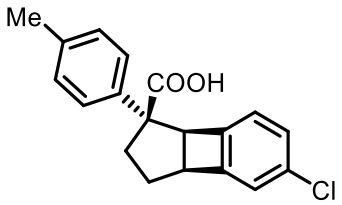


3f

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3f** in 90% yield (white solid, 26.5 mg, 0.09 mmol, m.p. = 132–135 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (d, *J* = 7.8 Hz, 1H), 7.03 (s, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.68 (d, *J* = 3.9 Hz, 1H), 3.43 (s, 2H), 3.35 (s, 3H), 1.85 – 1.75 (m, 5H), 1.71 – 1.59 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.6, 147.8, 142.5, 134.0, 128.2, 124.7, 122.7, 72.8, 58.7, 55.3, 54.0, 47.4, 31.9, 29.2, 26.0, 25.3.

HRMS (ESI-TOF) Calculated for $C_{16}H_{18}ClO_3$ [M-H]$^-$: 293.0944, Found: 293.0942.



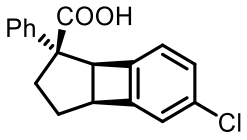
3g

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3g** in 72% yield (white solid, 22.5 mg, 0.072 mmol, m.p. = 185–187 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.06 (s, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 4.42 (d, *J* = 3.6 Hz, 1H), 3.96 (dd, *J* = 7.6, 3.7 Hz, 1H), 2.37 (s, 3H), 2.12 – 2.06 (m, 2H), 1.79 – 1.73 (m, 1H), 1.67 – 1.57 (m, 1H). ^{13}C NMR (151

MHz, $CDCl_3$) δ 179.8, 147.6, 142.1, 137.6, 137.3, 134.3, 129.6, 128.4, 126.6, 124.7, 122.7, 57.8, 53.4, 48.0, 33.3, 26.0, 21.1.

HRMS (ESI-TOF) Calculated for $C_{19}H_{16}ClO_2$ $[M-H]^-$: 311.0839, Found: 311.0835.

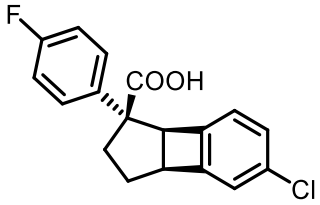


3h

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3h** in 68% yield (white solid, 20.3 mg, 0.068 mmol, m.p. = 195–197 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 2H), 7.40 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.36 – 7.30 (m, 1H), 7.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.06 – 7.08 (m, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 4.44 (d, *J* = 3.7 Hz, 1H), 3.99 (dd, *J* = 7.6, 3.7 Hz, 1H), 2.17 – 2.06 (m, 2H), 1.80 – 1.74 (m, 1H), 1.67 – 1.58 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.5, 147.6, 142.00, 140.7, 134.4, 128.9, 128.5, 127.6, 126.7, 124.6, 122.8, 58.1, 53.4, 48.1, 33.5, 25.9.

HRMS (ESI-TOF) Calculated for $C_{18}H_{14}ClO_2$ $[M-H]^-$: 297.0682, Found: 297.0677.



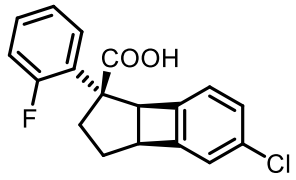
3i

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3i** in 81% yield (white solid, 25.7 mg, 0.081 mmol, m.p. = 215–217 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.19 (ddd, *J* = 7.8, 1.8, 0.6 Hz, 1H), 7.12 – 7.05 (m, 3H), 6.98 (dt, *J* = 7.9, 0.8 Hz, 1H), 4.39 (d, *J* = 3.7 Hz, 1H), 3.97 (dd, *J* = 7.6, 3.7 Hz, 1H), 2.16 – 2.03 (m, 2H), 1.81 – 1.74 (m, 1H), 1.59 (tdd, *J* = 13.3, 7.8, 6.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.5, 162.2 (d, *J* = 246.5 Hz), 147.4, 141.8, 136.2 (d, *J* = 3.3 Hz), 134.5, 128.5

(d, *J* = 14.6 Hz), 128.4, 124.6, 122.8, 115.8 (d, *J* = 21.5 Hz), 57.6, 53.5, 47.9, 33.5, 25.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.7.

HRMS (ESI-TOF) Calculated for $C_{18}H_{13}ClFO_2$ $[M-H]^-$: 315.0588, Found: 315.0579.

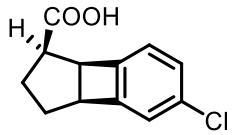


3j

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3j** in 43% yield (white solid, 13.6 mg, 0.043 mmol, m.p. = 182–185 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 2H), 7.23 (ddd, *J* = 7.8, 1.8, 0.6 Hz, 1H), 7.19 (td, *J* = 7.5, 1.3 Hz, 1H), 7.12 (ddd, *J* = 11.3, 8.2, 1.3 Hz, 1H), 7.09 – 7.07 (m, 1H), 6.97 (dt, *J* = 7.8, 0.8 Hz, 1H), 4.38 (d, *J* = 3.5 Hz, 1H), 4.08 (dd, *J* = 7.8, 3.8 Hz, 1H), 2.31 (td, *J* = 13.6, 6.5 Hz, 1H), 1.89 (dd, *J* = 12.8, 6.0 Hz, 1H), 1.85 – 1.80 (m, 1H), 1.62 – 1.52 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.7, 160.5 (d, *J* = 246.7 Hz), 146.9, 134.6, 129.6 (d, *J* = 13.6 Hz), 129.2 (d, *J* = 8.3 Hz), 128.6, 127.8 (d, *J* = 4.0 Hz), 124.6, 124.0 (d, *J* = 3.4 Hz), 122.8, 116.3, 116.1, 54.2, 53.8, 48.7, 33.1, 26.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.2.

HRMS (ESI-TOF) Calculated for $C_{18}H_{15}ClFO_2$ $[M+H]^+$: 317.0745, Found: 317.0741.



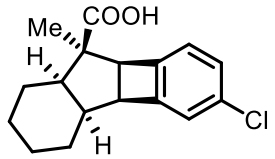
3k

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes using aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv). the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3k** in 36% yield (colorless oil, 8.0 mg, 0.036 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.03 – 7.01 (m, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 4.03 (dd, *J* = 7.4, 3.9 Hz, 1H), 3.90 (dd, *J* = 7.3, 3.8 Hz, 1H), 2.90 – 2.83 (m, 1H), 1.99

– 1.89 (m, 2H), 1.74 – 1.58 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.9, 147.6, 141.5, 134.1, 128.3, 125.2, 122.4, 48.6, 48.0, 45.7, 28.1, 26.6.

HRMS (ESI-TOF) Calculated for $C_{12}H_{12}ClO_2$ $[M+H]^+$: 223.0526, Found: 223.0522.

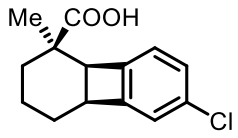


3l

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3l** in 32% yield (colorless oil, 9.3 mg, 0.032 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.03 (s, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 3.74 (d, *J* = 4.0 Hz, 1H), 3.61 (d, *J* = 4.0 Hz, 1H), 2.52 (td, *J* = 7.3, 2.1 Hz, 1H), 2.19 – 2.03 (m, 2H), 1.93 – 1.85 (m, 1H), 1.66 – 1.54 (m, 2H), 1.53 (s, 3H), 1.42 – 1.30 (m, 2H), 1.27 – 1.18 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.9, 148.6, 143.0, 133.9, 127.9, 124.7, 122.5, 57.8, 53.9, 53.3, 42.0, 30.5, 25.1, 24.4, 24.0, 23.4.

HRMS (ESI-TOF) Calculated for $C_{17}H_{20}ClO_2$ $[M+H]^+$: 291.1152, Found: 291.1143.



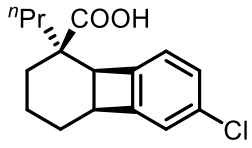
3m

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3m** in 50% yield (colorless oil, 12.5 mg, 0.05 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H), 7.07 (ddd, *J* = 1.8, 0.8, 0.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 3.75 (td, *J* = 6.1, 3.1 Hz, 1H), 3.66 (d, *J* = 5.5 Hz, 1H), 2.11 – 2.01 (m, 1H), 1.89 – 1.82 (m, 1H), 1.71 – 1.64 (m, 1H), 1.50 – 1.60 (m, 2H), 1.48 (s, 4H). ^{13}C NMR

(151 MHz, $CDCl_3$) δ 184.2, 149.9, 144.1, 133.6, 127.8, 125.0, 122.4, 47.3, 43.7, 40.8, 26.0, 25.5, 23.1, 16.1.

HRMS (ESI-TOF) Calculated for $C_{14}H_{16}ClO_2$ $[M+H]^+$: 251.0839, Found: 251.0836.

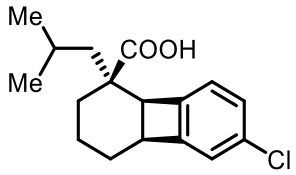


3n

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3n** in 43% yield (colorless oil, 12.0 mg, 0.043 mmol, m.p. = 125–128 °C).

^1H NMR (600 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.8 Hz, 1H), 7.06 (s, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), δ 3.72 (td, *J* = 6.2, 2.9 Hz, 1H), 3.69 (d, *J* = 5.5 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.89 – 1.80 (m, 2H), 1.80 – 1.72 (m, 1H), 1.60 (t, *J* = 7.1 Hz, 2H), 1.55 – 1.45 (m, 2H), 1.45 – 1.30 (m, 2H), 0.98 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 150.3, 143.9, 133.5, 127.8, 124.6, 122.3, 47.6, 47.2, 40.9, 40.2, 23.6, 23.3, 18.4, 16.3, 14.7.

HRMS (ESI-TOF) Calculated for $C_{16}H_{20}ClO_2$ $[M+H]^+$: 279.1152, Found: 279.1152.

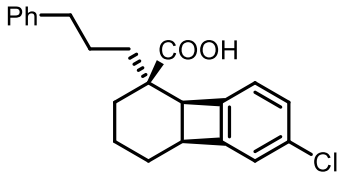


3o

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3o** in 46% yield (white solid, 13.5 mg, 0.046 mmol, m.p. = 129–131 °C).

^1H NMR (600 MHz, $CDCl_3$) δ 7.16 – 7.11 (m, 1H), 7.06 (s, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 3.74 – 3.68 (m, 1H), 3.66 (d, *J* = 5.5 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.90 – 1.76 (m, 4H), 1.66 – 1.48 (m,

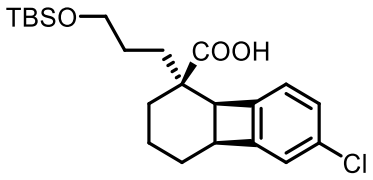
4H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 184.2, 150.5, 143.4, 133.6, 127.7, 124.4, 122.3, 48.0, 46.8, 46.0, 40.8, 25.2, 24.6, 23.5, 23.2, 22.7, 16.5.
HRMS (ESI-TOF) Calculated for $C_{17}H_{22}ClO_2$ $[M+H]^+$: 293.1308, Found: 293.1304.



3p

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3p** in 35% yield (colorless oil, 12.4 mg, 0.035 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.21 – 7.18 (m, 3H), 7.11 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 3.70 – 3.63 (m, 2H), 2.73 – 2.61 (m, 2H), 1.95 – 1.86 (m, 2H), 1.84 – 1.77 (m, 2H), 1.74 – 1.65 (m, 2H), 1.59 – 1.56 (m, 2H), 1.48 – 1.43 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.3, 150.2, 143.7, 142.0, 133.6, 128.5, 128.5, 127.8, 126.1, 124.6, 122.3, 47.5, 47.1, 40.8, 37.2, 36.2, 26.7, 23.5, 23.1, 16.2.
HRMS (ESI-TOF) Calculated for $C_{22}H_{24}ClO_2$ $[M+H]^+$: 355.1465, Found: 355.1464.



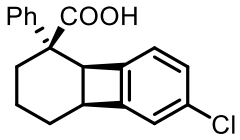
3q

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3q** in 49% yield (colorless oil, 20.0 mg, 0.049 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.12 – 7.02 (m, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 3.74 – 3.59 (m, 4H), 2.09 – 1.97 (m, 1H), 1.93 – 1.81 (m, 3H), 1.63 – 1.46 (m, 6H), 0.91

(s, 9H), 0.07 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.2, 150.3, 143.8, 133.5, 127.8, 124.7, 122.3, 63.1, 47.2, 47.1, 40.9, 34.0, 28.4, 26.1, 23.5, 23.1, 18.4, 16.1, -5.1.

HRMS (ESI-TOF) Calculated for $C_{22}H_{32}ClO_3Si$ [M-H]$^-$: 407.1809, Found: 407.1802.

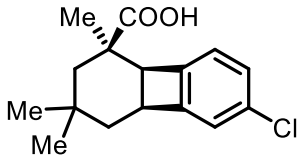


3r

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3r** in 20% yield (white solid, 6.2 mg, 0.02 mmol, m.p. = 177–179 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.30 (m, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.10 (s, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 4.59 (d, *J* = 4.1 Hz, 1H), 3.81 – 3.75 (m, 1H), 2.36 – 2.23 (m, 1H), 1.78 – 1.70 (m, 1H), 1.70 – 1.62 (m, 1H), 1.57 – 1.49 (m, 1H), 1.49 – 1.41 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.3, 150.0, 143.6, 141.1, 133.7, 128.9, 128.1, 127.5, 127.1, 124.9, 122.9, 51.5, 45.8, 41.7, 24.6, 21.9, 16.1.

HRMS (ESI-TOF) Calculated for $C_{19}H_{18}ClO_2$ [M+H]$^+$: 313.0995, Found: 313.0992.

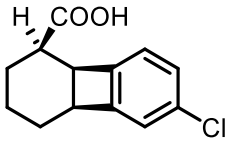


3s

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3s** in 50% yield (white solid, 13.9 mg, 0.05 mmol, m.p. = 122–124 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H), 7.11 (dt, *J* = 1.8, 1.0 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 3.79 (td, *J* = 5.8, 2.9 Hz, 1H), 3.65 (dd, *J* = 5.5, 1.0 Hz, 1H), 1.91 (dd, *J* = 15.1, 5.8 Hz, 1H), 1.84 (dd, *J* = 15.0, 2.8 Hz, 1H), 1.51 (dd, *J* = 14.5, 1.7 Hz, 1H), 1.49 (s, 3H),

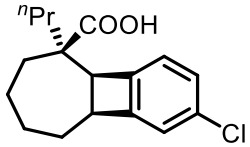
1.41 (d, *J* = 14.6 Hz, 1H), 1.03 (s, 3H), 0.74 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 150.2, 143.7, 133.5, 127.9, 125.3, 122.9, 47.3, 45.6, 41.6, 39.6, 36.8, 35.3, 35.0, 29.5, 24.6.
HRMS (ESI-TOF) Calculated for $C_{16}H_{20}ClO_2$ $[M+H]^+$: 279.1152, Found: 279.1145.



3t

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3t** in 20% yield (colorless oil, 4.7 mg, 0.02 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.20 (s, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 3.92 (t, *J* = 4.8 Hz, 1H), 3.71 (q, *J* = 4.5 Hz, 1H), 2.99 (dt, *J* = 12.9, 5.0 Hz, 1H), 1.90 – 1.76 (m, 3H), 1.56 (s, 1H), 1.46 – 1.39 (m, 1H), 1.36 – 1.29 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.4, 146.8, 146.1, 133.1, 128.3, 125.0, 123.8, 42.2, 41.2, 29.8, 23.5, 20.1, 16.7.
HRMS (ESI-TOF) Calculated for $C_{13}H_{14}ClO_2$ $[M+H]^+$: 237.0682, Found: 237.0676.

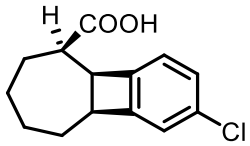


3u

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3u** in 54% yield (white solid, 15.8 mg, 0.054 mmol, m.p. = 118–120 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (ddd, *J* = 7.7, 1.8, 0.8 Hz, 1H), 7.03 (dt, *J* = 1.8, 0.9 Hz, 1H), 6.93 (dt, *J* = 7.8, 1.0 Hz, 1H), 4.01 (d, *J* = 5.5 Hz, 1H), 3.97 – 3.94 (m, 1H), 2.24 – 2.19 (m, 1H), 2.00 – 1.89 (m, 2H), 1.87 – 1.76 (m, 2H), 1.65 – 1.57 (m, 2H), 1.52 – 1.45 (m, 1H), 1.40 – 1.23 (m, 3H), 1.14 – 1.04 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 148.3, 143.5, 133.4, 127.7, 124.4, 122.4, 53.6, 52.0, 47.9, 31.0, 25.9, 25.0, 18.0, 14.8.

HRMS (ESI-TOF) Calculated for $C_{17}H_{22}ClO_2$ $[M+H]^+$: 293.1308, Found: 293.1308.

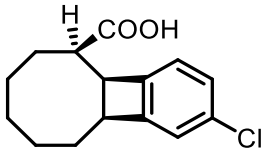


3v

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3v** in 38% yield (white solid, 9.5 mg, 0.038 mmol, m.p. = 112–114 ^oC).

^1H NMR (600 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.05 (s, 1H), 4.07 (dd, *J* = 5.9, 2.8 Hz, 1H), 3.98 – 3.92 (m, 1H), 2.82 – 2.77 (m, 1H), 2.31 – 2.24 (m, 1H), 1.93 (dd, *J* = 14.3, 5.2 Hz, 1H), 1.79 – 1.69 (m, 2H), 1.68 – 1.62 (m, 1H), 1.39 – 1.30 (m, 1H), 1.19 – 1.06 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.9, 148.6, 143.2, 133.6, 127.8, 125.8, 122.9, 48.0, 47.2, 46.6, 30.7, 29.9, 28.8, 25.5.

HRMS (ESI-TOF) Calculated for $C_{14}H_{16}ClO_2$ $[M+H]^+$: 251.0839, Found: 251.0836.

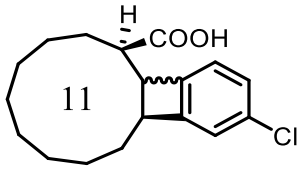


3w

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3w** in 48% yield (colorless oil, 12.7 mg, 0.048 mmol).

^1H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.05 (s, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 3.62 (dd, *J* = 11.0, 5.1 Hz, 1H), 3.57 (ddd, *J* = 12.2, 5.2, 1.9 Hz, 1H), 2.82 (td, *J* = 11.4, 3.6 Hz, 1H), 2.15 – 2.08 (m, 1H), 2.00 – 1.91 (m, 1H), 1.87 – 1.62 (m, 5H), 1.54 – 1.39 (m, 2H), 1.38 – 1.29 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 149.6, 143.0, 133.7, 128.0, 124.7, 122.1, 48.4, 47.5, 43.5, 34.6, 30.4, 29.4, 26.4, 24.9.

HRMS (ESI-TOF) Calculated for $C_{15}H_{18}ClO_2$ $[M+H]^+$: 265.0995, Found: 265.0992.

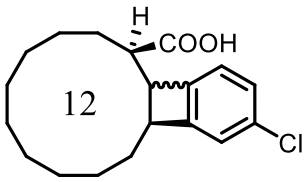


3x

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes using **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3x** in 50% yield (white solid, 15.3 mg, 0.05 mmol, d.r. = 4:1). *Trans* or *cis* stereochemistry determined based on the small $^3J_{HH}$ coupling (*trans* for 2.4 Hz, *cis* for 5.0 Hz), consistent with the relationship of hydrogens in benzocyclobutenes (*36*).

trans-**3x** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.06 – 7.03 (m, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 3.41 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.29 (dt, *J* = 11.4, 2.9 Hz, 1H), 2.65 – 2.59 (m, 1H), 2.05 – 1.99 (m, 1H), 1.95 – 1.90 (m, 2H), 1.82 – 1.35 (m, 13H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.7, 149.2, 143.8, 133.5, 127.9, 124.7, 122.2, 50.4, 49.7, 48.2, 32.3, 29.5, 28.3, 28.1, 27.1, 25.7, 25.0, 21.5.

cis-**3x** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 7.8, 2.7 Hz, 1H), 7.06 – 7.05 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 3.73 (dd, *J* = 11.2, 5.0 Hz, 1H), 3.60 (dd, *J* = 10.8, 4.9 Hz, 1H), 2.59 – 2.53 (m, 1H), 1.82 – 1.35 (m, 16H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.3, 149.5, 143.4, 133.7, 124.3, 122.3, 48.9, 47.9, 46.3, 29.4, 28.1, 27.2, 26.6, 25.2, 25.1, 23.0, 21.4, 21.0.
HRMS (ESI-TOF) Calculated for $C_{18}H_{24}ClO_2$ $[M+H]^+$: 307.1465, Found: 307.1460.



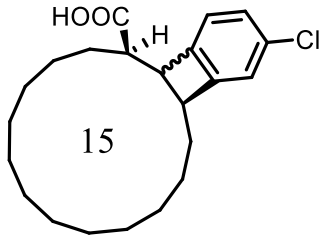
3y

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes using **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3y** in 50% yield (white solid, 16.0 mg, 0.05 mmol, d.r. = 4:1, m.p. = 121–123 °C pure *cis*-**3y** was not separable).

trans-**3y** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.05 (s, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 3.34 (dd, *J* = 11.7, 2.1 Hz, 1H), 3.24 (dd, *J* = 12.1, 4.2 Hz, 1H), 2.62 (dt, *J* = 11.9, 4.8 Hz, 1H), 1.94 (tt, *J* = 13.8, 4.7 Hz, 2H), 1.82 (tt, *J* = 13.5, 4.1 Hz, 1H), 1.75 – 1.60 (m, 4H), 1.59 – 1.17 (m, 11H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.3, 149.9, 144.8, 133.3, 127.7, 124.8, 122.4, 49.3, 48.0, 46.9, 33.6, 29.6, 27.5, 27.2, 25.9, 24.3, 23.5, 23.0, 22.9.

cis-**3y** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 – 7.13 (m, 1H), 7.05 (dt, *J* = 1.9, 1.0 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 3.70 – 3.64 (m, 1H), 3.59 (ddd, *J* = 10.4, 5.0, 2.2 Hz, 1H), 2.82 – 2.75 (m, 1H), 1.82 – 1.17 (m, 18H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.0, 149.4, 142.9, 133.8, 127.9, 124.1, 122.2, 48.6, 47.4, 44.3, 31.1, 28.3, 28.3, 28.1, 27.7, 27.6, 26.1, 23.6, 23.3.

HRMS (ESI-TOF) Calculated for $C_{19}H_{26}ClO_2$ $[M+H]^+$: 321.1621, Found: 321.1621.

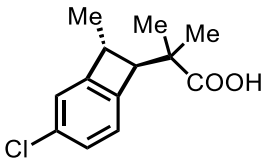


3z

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes using **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **3z** in 52% yield (white solid, 18.9 mg, 0.052 mmol, m.p. = 87–89 °C, d.r. > 10:1, cis-**3z** was too little to be collected).

trans-**3z** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.08 (s, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 3.22 (dd, *J* = 11.1, 2.6 Hz, 1H), 3.17 (td, *J* = 7.6, 2.3 Hz, 1H), 2.58 (ddd, *J* = 11.3, 6.7, 5.0 Hz, 1H), 1.88 – 1.74 (m, 3H), 1.72 – 1.66 (m, 1H), 1.61 – 1.50 (m, 4H), 1.46 – 1.29 (m, 16H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.6, 148.9, 143.5, 133.5, 127.8, 124.7, 122.8, 49.9, 49.2, 48.9, 32.2, 31.1, 27.1, 26.9, 26.8, 26.7, 26.5, 26.2, 26.1, 26.1, 25.6, 25.1.

HRMS (ESI-TOF) Calculated for $C_{22}H_{32}ClO_2$ $[M+H]^+$: 363.2091, Found: 363.2089.

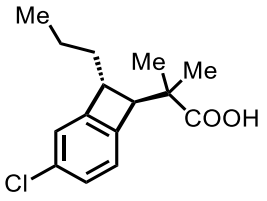


5a

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5a** in 68% yield (yellow oil, 16.2 mg, 0.068 mmol). *Trans* stereochemistry determined based on the small $^{3}J_{HH}$ coupling (2.7 Hz), consistent with the *trans* relationship of hydrogens in benzocyclobutenes (*36*).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 7.8, 2.6 Hz, 1H), 7.06 (s, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 3.36 (qd, *J* = 7.1, 2.8 Hz, 1H), 3.24 (d, *J* = 2.7 Hz, 1H), 1.39 (d, *J* = 7.1 Hz, 3H), 1.27 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.6, 150.1, 141.8, 133.5, 127.8, 125.0, 122.3, 58.08, 43.6, 40.5, 22.9, 21.9, 18.7.

HRMS (ESI-TOF) Calculated for $C_{13}H_{16}ClO_2$ $[M+H]^+$: 239.0839, Found: 239.0838.

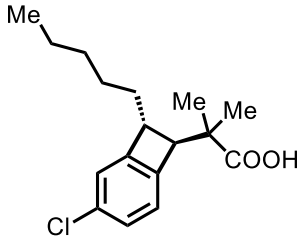


5b

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5b** in 65% yield (yellow oil, 17.3 mg, 0.065 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.09 (s, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 3.30 (d, *J* = 2.5 Hz, 1H), 3.28 (ddd, *J* = 8.8, 6.1, 2.5 Hz, 1H), 1.79 – 1.71 (m, 1H), 1.65 – 1.55 (m, 1H), 1.55 – 1.43 (m, 2H), 1.24 (s, 3H), 1.22 (s, 3H), 0.96 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 184.0, 149.5, 142.2, 133.3, 127.7, 124.9, 122.9, 56.5, 45.6, 43.6, 36.3, 22.7, 22.1, 21.5, 14.3.

HRMS (ESI-TOF) Calculated for $C_{15}H_{20}ClO_2$ $[M+H]^+$: 267.1152, Found: 267.1152.

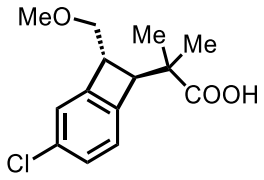


5c

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5c** in 59% yield (colorless oil, 17.4 mg, 0.059 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.09 (s, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 3.30 (d, *J* = 2.6 Hz, 1H), 3.26 (ddd, *J* = 8.9, 6.2, 2.5 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.65 – 1.56 (m, 1H), 1.51 – 1.38 (m, 2H), 1.36 – 1.29 (m, 4H), 1.24 (s, 3H), 1.21 (s, 3H), 0.93 – 0.88 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.7, 149.5, 142.2, 133.3, 127.7, 124.9, 122.9, 56.5, 45.8, 43.6, 34.0, 32.1, 28.0, 22.7, 22.7, 22.1, 14.2.

HRMS (ESI-TOF) Calculated for $C_{17}H_{24}ClO_2$ $[M+H]^+$: 295.1465, Found: 295.1463.

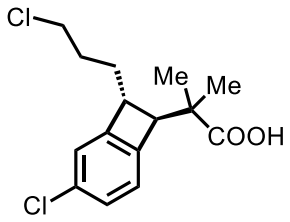


5d

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5d** in 50% yield (colorless oil, 13.4 mg, 0.05 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.14 (s, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 3.70 (dd, *J* = 8.9, 5.5 Hz, 1H), 3.58 – 3.49 (m, 2H), 3.44 (d, *J* = 3.1 Hz, 1H), 3.38 (s, 3H), 1.26 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.2, 146.7, 142.5, 133.6, 128.2, 124.8, 123.3, 74.4, 59.2, 53.6, 45.2, 43.4, 22.8, 22.1.

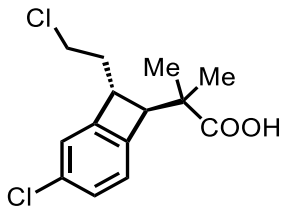
HRMS (ESI-TOF) Calculated for $C_{14}H_{18}ClO_3$ $[M+H]^+$: 269.0944, Found: 269.0938.



5e

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5e** in 55% yield (colorless oil, 16.6 mg, 0.055 mmol).

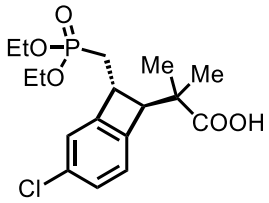
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.09 (s, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 3.57 (t, *J* = 6.4 Hz, 2H), 3.33 (d, *J* = 3.5 Hz, 1H), 3.30 (ddd, *J* = 5.5, 5.5, 2.7 Hz, 1H), 2.00 – 1.86 (m, 3H), 1.83 – 1.68 (m, 1H), 1.26 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.9, 148.5, 142.0, 133.5, 128.1, 125.0, 122.9, 56.4, 45.0, 44.9, 43.6, 31.2, 31.2, 23.0, 22.0.
HRMS (ESI-TOF) Calculated for $C_{15}H_{19}Cl_2O_2$ $[M+H]^+$: 301.0762, Found: 301.0766.



5f

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (10% EtOAc/hexane + 1% formic acid) to afford **5f** in 42% yield (colorless oil, 12.1 mg, 0.042 mmol).

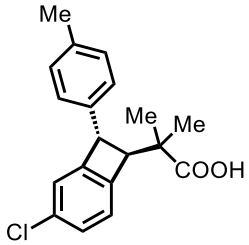
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (ddd, *J* = 7.8, 1.8, 0.7 Hz, 1H), 7.13 (dt, *J* = 1.7, 0.8 Hz, 1H), 7.06 (dt, *J* = 7.8, 0.9 Hz, 1H), 3.72 – 3.64 (m, 2H), 3.50 (ddd, *J* = 8.8, 6.3, 2.4 Hz, 1H), 3.38 (dd, *J* = 2.5, 0.9 Hz, 1H), 2.32 – 2.22 (m, 1H), 2.10 (ddt, *J* = 14.1, 8.6, 6.3 Hz, 1H), 1.28 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 177.1, 144.3, 138.8, 131.0, 125.9, 122.8, 120.9, 57.3, 45.1, 45.0, 44.6, 38.6, 25.6, 24.5.
HRMS (ESI-TOF) Calculated for $C_{14}H_{17}Cl_2O_2$ $[M+H]^+$: 287.0606, Found: 287.0606.



5g

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (50% EtOAc/hexane + 1% formic acid) to afford **5g** in 45% yield (colorless oil, 16.9 mg, 0.045 mmol).

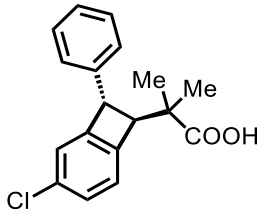
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 4.21 – 4.09 (m, 4H), 3.57 (tt, *J* = 10.8, 3.2 Hz, 1H), 3.42 (d, *J* = 2.5 Hz, 1H), 2.49 (ddd, *J* = 19.1, 15.3, 3.8 Hz, 1H), 2.07 (ddd, *J* = 17.3, 15.3, 11.1 Hz, 1H), 1.35 (dt, *J* = 12.7, 7.0 Hz, 6H), 1.31 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.8, 147.5 (d, *J* = 5.2 Hz), 141.9, 133.5, 128.4, 124.7, 124.3, 62.2 (d, *J* = 6.6 Hz), 62.0 (d, *J* = 6.9 Hz), 57.8 (d, *J* = 18.9 Hz), 43.5, 39.3 (d, *J* = 6.3 Hz), 29.5 (d, *J* = 139.3 Hz), 24.1, 21.0, 16.6, 16.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.15. HRMS (ESI-TOF) Calculated for $C_{17}H_{25}ClO_5P$ $[M+H]^+$: 375.1128, Found: 375.1123.



5h

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5h** in 45% yield (colorless oil, 14.2 mg, 0.045 mmol).

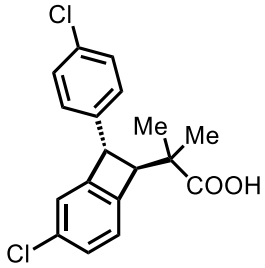
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 1H), 7.15 – 7.05 (m, 6H), 4.42 (d, *J* = 2.6 Hz, 1H), 3.55 (d, *J* = 2.6 Hz, 1H), 2.32 (s, 3H), 1.30 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.0, 147.6, 142.9, 138.4, 136.6, 133.9, 129.4, 128.4, 127.3, 125.2, 123.4, 60.5, 49.6, 43.9, 22.5, 22.5, 21.2. HRMS (ESI-TOF) Calculated for $C_{19}H_{20}ClO_2$ $[M+H]^+$: 315.1152, Found: 315.1154.



5i

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5i** in 52% yield (colorless oil, 15.6 mg, 0.052 mmol).

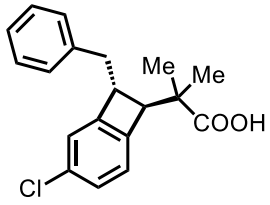
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 4H), 7.20 – 7.16 (m, 2H), 7.16 – 7.09 (m, 2H), 4.46 (d, *J* = 2.9 Hz, 1H), 3.58 (d, *J* = 2.9 Hz, 1H), 1.31 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 147.3, 142.9, 141.4, 133.9, 128.7, 128.5, 127.4, 127.0, 125.3, 123.5, 60.4, 49.9, 44.0, 22.5, 22.5.
HRMS (ESI-TOF) Calculated for $C_{18}H_{18}ClO_2$ $[M+H]^+$: 301.0995, Found: 301.0995.



5j

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5j** in 60% yield (colorless oil, 20.1 mg, 0.06 mmol).

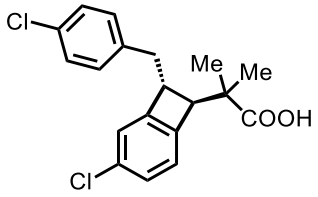
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.12 – 7.08 (m, 3H), 4.42 (d, *J* = 2.7 Hz, 1H), 3.53 (d, *J* = 2.7 Hz, 1H), 1.31 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.1, 146.9, 142.7, 139.9, 134.1, 132.8, 129.8, 128.8, 128.7, 125.3, 123.4, 60.6, 49.2, 44.0, 22.7, 22.2.
HRMS (ESI-TOF) Calculated for $C_{18}H_{15}Cl_2O_2$ $[M-H]^-$: 333.0449, Found: 333.0435.



5k

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5k** in 40% yield (colorless oil, 12.6 mg, 0.04 mmol).

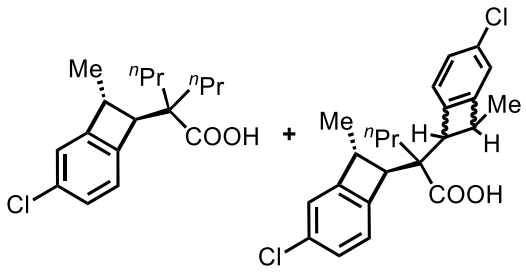
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.26 – 7.21 (m, 3H), 7.18 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.78 (s, 1H), 3.54 (td, *J* = 6.3, 3.0 Hz, 1H), 3.43 (d, *J* = 2.6 Hz, 1H), 3.12 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.88 (dd, *J* = 13.6, 9.5 Hz, 1H), 1.21 (s, 3H), 1.11 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 182.9, 148.5, 142.0, 140.2, 133.3, 129.1, 128.6, 128.1, 126.5, 125.0, 123.1, 56.2, 47.1, 43.5, 40.1, 22.7, 22.1.
HRMS (ESI-TOF) Calculated for $C_{19}H_{20}ClO_2$ $[M+H]^+$: 315.1152, Found: 315.1151.



5l

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **5l** in 30% yield (colorless oil, 10.5 mg, 0.030 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.18 (ddd, *J* = 7.9, 1.9, 0.7 Hz, 1H), 7.17 – 7.13 (m, 2H), 7.06 – 7.02 (m, 1H), 6.79 – 6.75 (m, 1H), 3.51 (ddd, *J* = 9.1, 6.2, 2.4 Hz, 1H), 3.44 – 3.36 (m, 1H), 3.09 (dd, *J* = 13.6, 6.2 Hz, 1H), 2.83 (dd, *J* = 13.6, 9.4 Hz, 1H), 1.22 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 148.1, 141.9, 138.6, 133.4, 132.3, 130.5, 128.7, 128.3, 125.0, 123.0, 56.1, 46.8, 43.5, 39.4, 22.9, 22.0.
HRMS (ESI-TOF) Calculated for $C_{19}H_{19}Cl_2O_2$ $[M+H]^+$: 349.0762, Found: 349.0751.



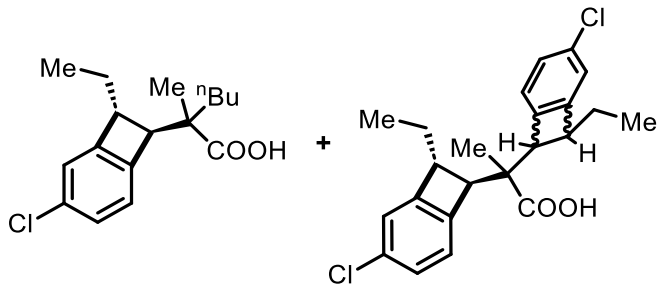
mono: 47% di: 8%

5m, 55%

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford mono-**5m** in 47% yield (colorless oil, 13.9 mg, 0.047 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (ddd, *J* = 8.0, 1.7, 0.8 Hz, 1H), 7.07 – 7.01 (m, 2H), 3.48 (qd, *J* = 7.0, 2.6 Hz, 1H), 3.28 (dd, *J* = 2.7, 0.9 Hz, 1H), 1.70 – 1.58 (m, 4H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.35 – 1.26 (m, 4H), 0.90 (td, *J* = 7.3, 3.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.4, 150.0, 142.5, 133.2, 127.7, 125.4, 122.1, 55.8, 50.9, 40.5, 36.6, 18.9, 18.1, 17.9, 17.3, 14.9, 14.8.
HRMS (ESI-TOF) Calculated for $C_{17}H_{25}ClO_2$ $[M+H]^+$: 295.1465, Found: 295.1460.

Di-BCB products were identified by ^{1}H NMR as a mixture of diastereomers, and the yield was identified by crude ^{1}H NMR using CH_2Br_2 as internal standard.



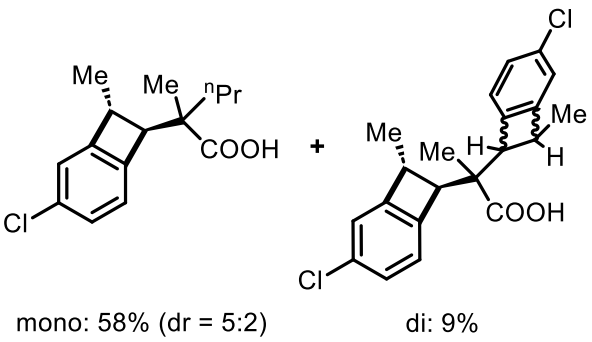
mono: 58% (dr = 5:2) di: 6%

5n, 64%

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (20% EA/hexane + 1% formic acid) to afford mono-**5n** in 58% yield (white solid, 17.1 mg, 0.058 mmol, dr = 5:2). Diastereomers were not separable by column chromatography or pTLC, ^{1}H and ^{13}C NMR data is reported as a mixture of diastereomers. Diastereomeric ratio was identified by ^{1}H NMR of the mixture of the diastereomers.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 1.37H), 7.09 (ddt, J = 6.3, 1.7, 0.8 Hz, 1.37H), 7.04 (dt, J = 7.8, 0.9 Hz, 0.37H), 7.00 – 6.96 (m, 1H), 3.35 (d, *J* = 2.2 Hz, 1H), 3.32 (d, *J* = 2.1 Hz, 0.37H), 3.24 (m, 1.37H), 1.88 – 1.73 (m, 2.74H), 1.66 – 1.45 (m, 3.11H), 1.36 – 1.26 (m, 5.11H), 1.11 (s, 3H), 1.07 (s, 1.11H), 1.06 (t, J = 7.4 Hz, 3H), 1.03 (t, J = 7.4 Hz, 1.11H), 0.96 – 0.87 (m, 4.11H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 182.4, 149.4, 149.1, 142.4, 142.0, 133.3, 133.2, 127.8, 127.7, 124.9, 124.9, 123.0, 122.8, 56.1, 55.5, 47.6, 47.4, 47.3, 47.1, 37.9, 37.0, 27.3, 27.2, 27.1, 26.8, 23.4, 23.3, 18.6, 18.2, 14.1, 14.1, 12.6, 12.5.
HRMS (ESI-TOF) Calculated for $C_{17}H_{24}ClO_2$ [M-H]$^-$: 293.1308, Found: 293.1307.

Di-BCB products were identified by ^{1}H NMR of a mixture of diastereomers, which were not separable, and the yield was identified by crude ^{1}H NMR using CH_2Br_2 as internal standard.

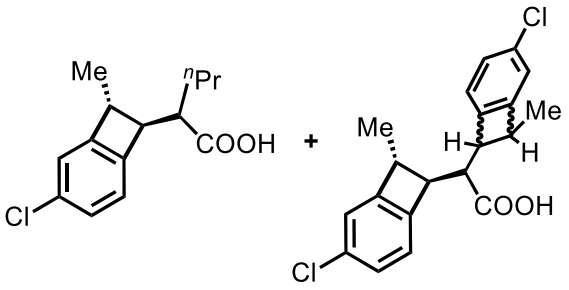


5o, 67%

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford mono-**5o** in 58% yield (colorless oil, 15.5 mg, 0.058 mmol, dr = 5:2). Diastereomers were not separable by column chromatography or pTLC, ^{1}H and ^{13}C NMR data is reported as a mixture of diastereomers. Diastereomeric ratio was identified by ^{1}H NMR of the mixture of the diastereomers.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (tdd, J = 7.9, 1.8, 0.7 Hz, 1.38H), 7.07 – 7.01 (m, 1.76H), 6.98 (dd, J = 7.8, 0.9 Hz, 1H), 3.38 (dtd, J = 9.6, 7.0, 4.3 Hz, 1.38H), 3.30 (dd, J = 2.7, 0.9 Hz, 1H), 3.26 (dd, J = 2.6, 0.9 Hz, 0.38H), 1.77 (m, 1.38H), 1.61 – 1.47 (m, 1.38H), 1.44 – 1.29 (m, 6.9H), 1.12 (s, 3H), 1.09 (s, 1.14H), 0.94 (td, J = 7.3, 5.1 Hz, 4.14H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 182.6, 150.2, 149.9, 142.1, 141.7, 133.5, 133.3, 127.8, 127.7, 125.0, 125.0, 122.4, 122.2, 57.8, 57.5, 47.7, 47.4, 40.4, 40.3, 40.1, 39.5, 18.9, 18.7, 18.6, 18.4, 18.4, 18.3, 14.7, 14.7.
HRMS (ESI-TOF) Calculated for $C_{15}H_{20}ClO_2$ [M+H]$^+$: 267.1152, Found: 267.1149.

Di-BCB products were identified by ^{1}H NMR of a mixture of diastereomers, which were not separable, and the yield was identified by crude ^{1}H NMR using CH_2Br_2 as internal standard.



mono: 42% (dr = 10:1) di:9%

5p, 51%

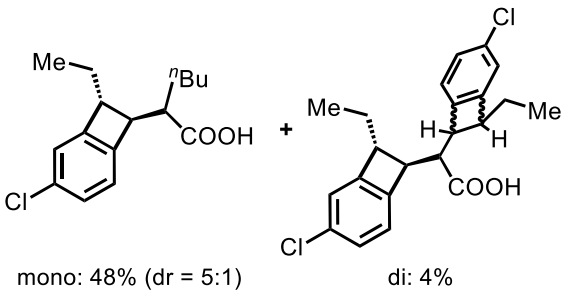
Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes with modifications: **2a** (0.35 mmol), K_2HPO_4 (0.3 mmol), HFIP (1.8 mL), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford mono-**5p** in 42% yield (colorless oil, 10.6 mg, 0.042 mmol, dr = 10:1) and di-**5p** (colorless oil, dr=10:1:0). Diastereomers were not separable by column chromatography or pTLC, ^{1}H and ^{13}C NMR data is reported as a mixture of diastereomers. Diastereomeric ratio was identified by ^{1}H NMR of the mixture of the diastereomers. Yield of di-**5p** was identified by crude ^{1}H NMR using CH_2Br_2 as internal standard.

mono-**5p**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 0.1H), 7.15 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 1H), 7.09 – 7.04 (m, 1.1H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 0.1H), 3.29 (qd, *J* = 7.0, 2.3 Hz, 0.1H), 3.24 (qd, *J* = 7.0, 2.3 Hz, 1H), 3.14 (dd, *J* = 10.0, 2.09 Hz, 0.1H), 3.11 (dd, *J* = 10.0, 2.09 Hz, 1H), 2.62 (td, *J* = 9.8, 4.0 Hz, 1.1H), 1.79 (m, 1.1H), 1.65 – 1.57 (m, 1.1H), 1.54 – 1.45 (m, 1.1H), 1.41 (d, *J* = 7.1 Hz, 3H), 1.39 – 1.33 (m, 1.4H), 0.95 (t, *J* = 7.3 Hz, 3.3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.7, 180.6, 149.9, 149.6, 143.2, 142.7, 133.7, 133.6, 127.9, 127.9, 124.8, 124.5, 122.7, 122.5, 52.2, 52.2, 49.1, 47.4, 43.9, 43.6, 33.0, 32.9, 20.7, 20.6, 18.8, 18.3, 14.5, 14.2.

HRMS (ESI-TOF) Calculated for $C_{14}H_{18}ClO_2$ $[M+H]^+$: 253.0995, Found: 253.0996.

di-**5p** (major diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (dd, J = 7.7, 1.9 Hz, 2H), 7.07 (m, 2H), 7.02 (d, J = 7.8 Hz, 2H), 3.41 (qd, J = 7.0, 2.1 Hz, 2H), 3.32 (dd, J = 8.2, 2.3 Hz, 2H), 3.05 (t, J = 8.3 Hz, 1H), 1.26 (d, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.2, 149.8, 142.1, 133.9, 128.1, 124.8, 122.6, 51.1, 50.9, 43.3, 18.5.

HRMS (ESI-TOF) Calculated for $C_{20}H_{19}Cl_2O_2$ $[M+H]^+$: 361.0762, Found: 361.0760.



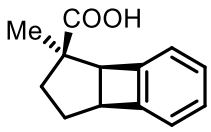
5q, 52%

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes with modifications: **2a** (0.35 mmol), K_2HPO_4 (0.3 mmol), HFIP (1.8 mL), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford mono-**5q** in 48% yield (colorless oil, 10.7 mg, 0.048 mmol, dr = 5:1). Diastereomers were not separable by column chromatography or pTLC, ^{1}H and ^{13}C NMR data is reported as a mixture of diastereomers. Diastereomeric ratio was identified by ^{1}H NMR of the mixture of the diastereomers.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 0.2H), 7.16 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 1H), 7.11 (m, 0.2H), 7.10 (m, 1H), 7.06 (dt, *J* = 7.8, 0.9 Hz, 0.2H), 6.98 (dt, *J* = 7.8, 0.9 Hz, 1H), 3.22 – 3.16 (m, 1.4H), 3.11 (ddd, *J* = 8.5, 6.5, 2.2 Hz, 1H), 2.59 (td, *J* = 9.9, 3.9 Hz, 1.2H), 1.85 – 1.62 (m, 4.8H), 1.47 – 1.30 (m, 4.8H), 1.07 (t, *J* = 7.4 Hz, 3H), 1.03 (t, *J* = 7.4 Hz, 0.6H), 0.91 (t, *J* = 7.0Hz, 3.6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.1, 179.9, 149.1, 148.7, 143.1, 143.1, 133.6, 133.5, 127.9, 127.7, 124.7, 124.4, 123.2, 123.1, 50.7, 50.5, 50.4, 50.2, 49.1, 49.0, 30.7, 30.5, 29.8, 29.6, 26.9, 26.5, 22.8, 22.7, 14.1, 14.0, 12.6, 12.5.

HRMS (ESI-TOF) Calculated for $C_{16}H_{20}ClO_2$ $[M-H]^-$: 279.1152, Found: 279.1145.

Di-BCB products were identified by ^{1}H NMR of a mixture of diastereomers, which were not separable, and the yield was identified by crude ^{1}H NMR using CH_2Br_2 as internal standard.

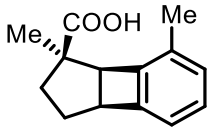


12b

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12b** in 72% yield (white solid, 14.6 mg, 0.072 mmol, m.p. = 136 – 138 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.17 (m, 2H), 7.05 (dd, *J* = 13.0, 7.2 Hz, 2H), 3.94 (dd, *J* = 8.0, 3.5 Hz, 1H), 3.71 (d, *J* = 3.9 Hz, 1H), 1.97 – 1.83 (m, 3H), 1.66 – 1.60 (m, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.2, 146.5, 144.6, 128.4, 127.6, 123.2, 122.0, 56.4, 49.9, 47.8, 32.4, 26.2, 22.9.

HRMS (ESI-TOF) Calculated for $C_{13}H_{15}O_2$ $[M+H]^+$: 203.1072, Found: 203.1069.

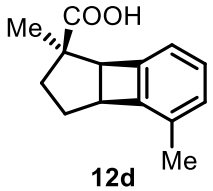


12c

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12c** in 62% yield (white solid, 13.4 mg, 0.062 mmol, m.p. = 89 – 91 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 7.1 Hz, 1H), 6.85 (d, *J* = 8.1 Hz, 1H), 3.84 (dd, *J* = 7.4, 4.0 Hz, 1H), 3.75 (d, *J* = 3.7 Hz, 1H), 2.13 (s, 3H), 2.12 – 2.07 (m, 1H), 1.91 – 1.76 (m, 2H), 1.60 – 1.53 (m, 1H), 1.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.8, 146.3, 142.0, 133.7, 128.9, 128.6, 119.0, 57.6, 49.2, 47.1, 32.6, 26.0, 22.4, 17.4.

HRMS (ESI-TOF) Calculated for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.1229, Found: 217.1228.



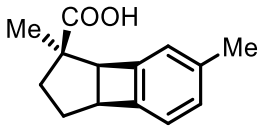
12d

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12d** in 66% yield (white solid, 14.3 mg, 0.066 mmol, m.p. = 109 – 112 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.6 Hz, 1H), 7.02 (dq, *J* = 7.8, 0.8 Hz, 1H), 6.87 (d, *J* = 6.6 Hz, 1H), 3.91 (dd, *J* = 7.4, 3.9 Hz, 1H), 3.65 (d, *J* = 3.9 Hz, 1H), 2.20 (s, 3H), 1.97 – 1.78 (m,

3H), 1.65 – 1.59 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 144.4, 144.1, 132.3, 129.1, 128.0, 120.4, 55.8, 49.7, 46.8, 32.5, 25.1, 22.9, 16.3.

HRMS (ESI-TOF) Calculated for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.1229, Found: 217.1225.

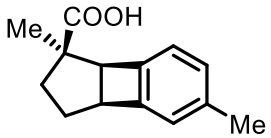


12e

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12e** in 65% yield (white solid, 14.1 mg, 0.065 mmol, m.p. = 128 – 130 ºC).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 7.4 Hz, 1H), 6.87 (s, 1H), 3.93 – 3.86 (m, 1H), 3.66 (d, *J* = 3.9 Hz, 1H), 2.28 (s, 3H), 1.97 – 1.89 (m, 1H), 1.87 – 1.81 (m, 2H), 1.65 – 1.60 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 144.5, 143.2, 137.3, 129.2, 123.8, 121.7, 56.1, 49.9, 47.2, 32.4, 26.2, 23.0, 22.2.

HRMS (ESI-TOF) Calculated for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.1229, Found: 217.1226.

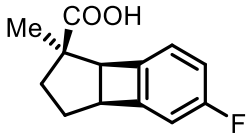


12f

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12f** in 72% yield (white solid, 15.6 mg, 0.072 mmol, m.p. = 101 – 103 ºC).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.01 (d, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.86 (s, 1H), 3.92 – 3.85 (m, 1H), 3.65 (d, *J* = 3.7 Hz, 1H), 2.33 (s, 3H), 1.96 – 1.88 (m, 1H), 1.87 – 1.81 (m, 2H), 1.64 – 1.58 (m, 1H), 1.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.7, 146.7, 141.3, 138.1, 128.4, 122.9, 122.6, 55.9, 49.9, 47.5, 32.4, 26.3, 22.8, 22.3.

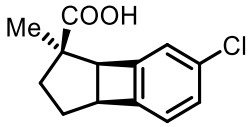
HRMS (ESI-TOF) Calculated for $C_{14}H_{15}O_2$ $[M-H]^-$: 215.1072, Found: 215.1073.



12g

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12g** in 84% yield (white solid, 18.5 mg, 0.084 mmol, m.p. = 113 – 115 °C).

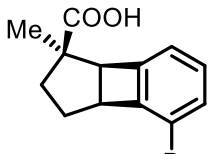
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 8.1, 4.8 Hz, 1H), 6.91 – 6.84 (m, 1H), 6.77 (dd, *J* = 7.8, 2.3 Hz, 1H), 3.88 (dd, *J* = 7.5, 3.7 Hz, 1H), 3.63 (d, *J* = 3.7 Hz, 1H), 1.93 – 1.83 (m, 3H), 1.68 – 1.61 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 163.5 (d, *J* = 244.8 Hz), 147.6 (d, *J* = 6.6 Hz), 139.6 (d, *J* = 2.8 Hz), 125.0 (d, *J* = 8.8 Hz), 115.1 (d, *J* = 23.2 Hz), 109.8 (d, *J* = 22.0 Hz), 55.4, 49.9, 47.1, 32.4, 26.0, 22.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.5.
HRMS (ESI-TOF) Calculated for $C_{13}H_{12}FO_2$ $[M-H]^-$: 219.0821, Found: 219.0820.



12h

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12h** in 92% yield (white solid, 21.8 mg, 0.092 mmol, m.p. = 195 – 197 °C).

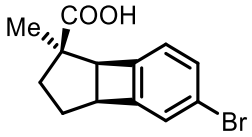
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H), 7.06 (dt, *J* = 1.8, 0.9 Hz, 1H), 6.95 (dt, *J* = 7.8, 0.8 Hz, 1H), 3.90 – 3.85 (m, 1H), 3.67 (d, *J* = 3.9 Hz, 1H), 1.94 – 1.82 (m, 3H), 1.70 – 1.62 (m, 1H), 1.35 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 145.8, 144.5, 133.4, 128.9, 124.0, 123.5, 55.8, 49.9, 47.2, 32.4, 26.1, 23.0.
HRMS (ESI-TOF) Calculated for $C_{13}H_{14}ClO_2$ $[M+H]^+$: 237.0682, Found: 237.0679.



12i

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12i** in 79% yield (white solid, 22.2 mg, 0.079 mmol, m.p. = 121 – 123 °C).

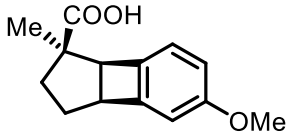
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.1 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 3.91 (dd, *J* = 6.6, 3.8 Hz, 1H), 3.67 (d, *J* = 3.7 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.93 – 1.78 (m, 2H), 1.70 – 1.63 (m, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 146.4, 145.4, 131.0, 129.7, 122.3, 115.5, 55.5, 49.7, 48.0, 32.5, 24.2, 22.9.
HRMS (ESI-TOF) Calculated for $C_{13}H_{14}BrO_2$ $[M+H]^+$: 281.0177, Found: 281.0174.



12j

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12j** in 87% yield (white solid, 24.5 mg, 0.087 mmol, m.p. = 101 – 103 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.19 (s, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 3.94 – 3.88 (m, 1H), 3.62 (d, *J* = 3.7 Hz, 1H), 1.94 – 1.83 (m, 3H), 1.68 – 1.61 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 148.0, 143.1, 131.0, 125.6, 125.3, 122.2, 55.8, 49.9, 47.8, 32.4, 26.1, 22.9.
HRMS (ESI-TOF) Calculated for $C_{13}H_{14}BrO_2$ $[M+H]^+$: 281.0177, Found: 281.0172.

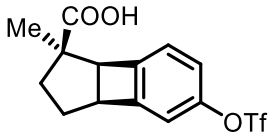


12k

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12k** in 79% yield (colorless oil, 18.4 mg, 0.079 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.95 (d, *J* = 8.1 Hz, 1H), 6.74 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 3.86 (dd, *J* = 7.5, 3.9 Hz, 1H), 3.77 (s, 3H), 3.62 (d, *J* = 3.7 Hz, 1H), 1.96 – 1.87

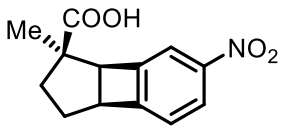
(m, 1H), 1.86 – 1.82 (m, 2H), 1.64 – 1.58 (m, 1H), 1.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.4, 160.5, 147.2, 136.1, 124.4, 114.2, 107.7, 55.5, 49.8, 47.2, 32.4, 26.0, 22.8.
HRMS (ESI-TOF) Calculated for $C_{14}H_{17}O_3$ $[M+H]^+$: 233.1178, Found: 233.1179.



12l

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12l** in 90% yield (white solid, 31.5 mg, 0.09 mmol, m.p. = 111 – 113 ºC).

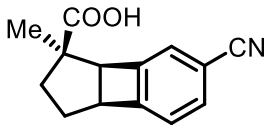
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.1 Hz, 1H), 7.07 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.99 (d, *J* = 2.3 Hz, 1H), 3.94 (dd, *J* = 6.9, 3.8 Hz, 1H), 3.68 (d, *J* = 3.7 Hz, 1H), 1.96 – 1.82 (m, 3H), 1.72 – 1.66 (m, 1H), 1.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 150.0, 148.1, 144.8, 125.6, 121.2, 115.9, 118.9 (q, *J* = 320.8 Hz), 55.6, 49.9, 47.4, 32.5, 25.9, 22.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.59.
HRMS (ESI-TOF) Calculated for $C_{14}H_{12}F_3O_5S$ $[M-H]^-$: 349.0358, Found: 349.0349.



12m

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (30% EtOAc/hexane + 1% formic acid) to afford **12m** in 85% yield (colorless oil, 21.0 mg, 0.085 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.1 Hz, 1H), 7.89 (s, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 3.99 (dd, *J* = 8.0, 3.7 Hz, 1H), 3.76 (d, *J* = 4.5 Hz, 1H), 2.02 – 1.83 (m, 3H), 1.72 (dd, *J* = 12.8, 6.5 Hz, 1H), 1.39 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.1, 154.4, 148.4, 145.6, 124.8, 122.9, 119.2, 55.7, 50.0, 48.0, 32.5, 26.0, 22.8.
HRMS (ESI-TOF) Calculated for $C_{13}H_{12}NO_4$ $[M-H]^-$: 246.0766, Found: 246.0765.

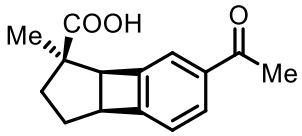


12n

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (40% EtOAc/hexane + 1% formic acid) to afford **12n** in 78% yield (white solid, 17.7 mg, 0.078 mmol, m.p. = 194 – 196 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.34 (s, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 3.98 (dd, *J* = 7.5, 3.8 Hz, 1H), 3.74 (d, *J* = 3.8 Hz, 1H), 2.00 – 1.82 (m, 3H), 1.75 – 1.69 (m, 1H), 1.38 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.6, 152.2, 145.6, 133.0, 127.2, 123.0, 119.7, 111.4, 56.1, 50.0, 48.4, 32.6, 26.0, 22.9.

HRMS (ESI-TOF) Calculated for $C_{14}H_{14}NO_2$ $[M+H]^+$: 228.1025, Found: 228.1023.

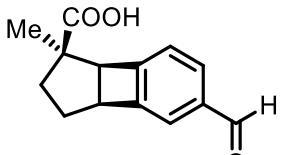


12o

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12o** in 85% yield (colorless oil, 20.8 mg, 0.085 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (ddd, *J* = 7.7, 1.5, 0.6 Hz, 1H), 7.62 (s, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 3.95 (dd, *J* = 6.9, 3.7 Hz, 1H), 3.73 (d, *J* = 4.1 Hz, 1H), 2.50 (s, 3H), 1.96 – 1.84 (m, 3H), 1.70 – 1.64 (m, 1H), 1.37 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.5, 181.9, 152.7, 145.0, 137.1, 129.3, 123.5, 122.1, 56.1, 50.0, 48.0, 32.5, 26.8, 26.1, 22.9.

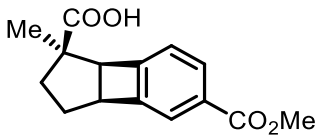
HRMS (ESI-TOF) Calculated for $C_{15}H_{17}O_3$ $[M+H]^+$: 245.1178, Found: 245.1181.



12p

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12p** in 78% yield (white solid, 18.0 mg, 0.078 mmol, m.p. = 115 – 117 ^{o}C).

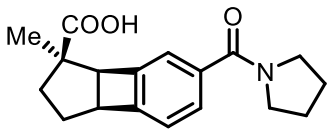
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.73 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.59 (s, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 3.99 (dd, *J* = 8.0, 3.9 Hz, 1H), 3.75 (d, *J* = 3.9 Hz, 1H), 1.98 – 1.83 (m, 3H), 1.71 – 1.65 (m, 1H), 1.38 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 192.7, 182.3, 152.5, 147.5, 137.2, 131.4, 124.0, 122.6, 56.5, 50.2, 47.5, 32.6, 26.2, 23.0.
HRMS (ESI-TOF) Calculated for $C_{14}H_{15}O_3$ $[M+H]^+$: 231.1021, Found: 231.1022.



12q

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12q** in 91% yield (white solid, 23.7 mg, 0.091 mmol, m.p. = 143 – 145 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.72 (s, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 3.95 – 3.94 (m, 1H), 3.90 (s, 3H), 3.72 (d, *J* = 3.9 Hz, 1H), 1.95 – 1.82 (m, 3H), 1.69 – 1.62 (m, 1H), 1.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 167.7, 150.3, 146.6, 130.4, 129.7, 123.3, 123.3, 56.4, 52.2, 50.1, 47.5, 32.5, 26.1, 23.0.
HRMS (ESI-TOF) Calculated for $C_{15}H_{17}O_4$ $[M+H]^+$: 261.1127, Found: 261.1128.

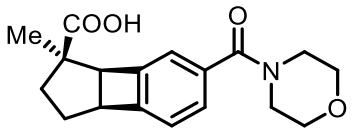


12r

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (60% EtOAc/hexane + 1% formic acid) to afford **12r** in 89% yield (white solid, 26.6 mg, 0.089 mmol, m.p. = 212 – 214 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.22 (s, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 3.93 – 3.89 (m, 1H), 3.68 (d, *J* = 3.9 Hz, 1H), 3.62 (t, *J* = 7.0 Hz, 2H), 3.38 (t, *J* = 6.7 Hz, 2H), 1.95 –

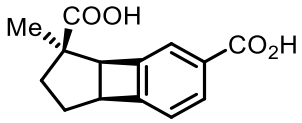
1.79 (m, 7H), 1.64 – 1.59 (m, 1H), 1.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.4, 170.8, 148.7, 144.6, 136.1, 127.5, 122.4, 121.7, 56.3, 50.0, 49.9, 47.8, 46.5, 32.6, 26.5, 26.2, 24.6, 22.8.
HRMS (ESI-TOF) Calculated for $C_{18}H_{22}NO_3$ $[M+H]^+$: 300.1600, Found: 300.1602.



12s

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (60% EtOAc/hexane + 1% formic acid) to afford **12s** in 89% yield (colorless oil, 28.1 mg, 0.089 mmol, m.p. = 106 – 108 °C).

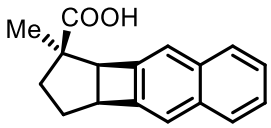
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 7.5, 2.1 Hz, 1H), 7.08 (s, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 3.95 – 3.90 (m, 1H), 3.89 – 3.21 (m, 9H), 1.91 – 1.83 (m, 3H), 1.69 – 1.60 (m, 1H), 1.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.9, 171.4, 148.8, 144.8, 134.3, 127.6, 122.3, 122.3, 67.0, 56.2, 49.9, 47.9, 32.6, 26.1, 22.8.
HRMS (ESI-TOF) Calculated for $C_{18}H_{22}NO_4$ $[M+H]^+$: 316.1549, Found: 316.1552.



12t

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (50% EtOAc/hexane + 1% formic acid) to afford **12t** in 64% yield (white solid, 15.8 mg, 0.064 mmol, m.p. = 126 – 228 °C).

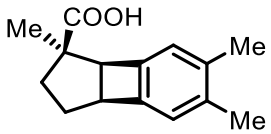
^{1}H NMR (600 MHz, CD_3CN) δ 7.96 – 7.91 (m, 1H), 7.60 (s, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 3.94 (dd, *J* = 7.9, 3.8 Hz, 1H), 3.67 (d, *J* = 3.6 Hz, 1H), 1.93 – 1.88 (m, 1H), 1.83 (dd, *J* = 13.3, 6.8 Hz, 1H), 1.71 (td, *J* = 13.1, 6.9 Hz, 1H), 1.56 (dd, *J* = 12.9, 6.6 Hz, 1H), 1.29 (s, 3H). ^{13}C NMR (151 MHz, CD_3CN) δ 177.8, 168.4, 153.9, 146.1, 131.2, 130.2, 125.1, 123.1, 56.9, 50.5, 48.8, 33.2, 26.5, 23.0.
HRMS (ESI-TOF) Calculated for $C_{14}H_{15}O_4$ $[M+H]^+$: 247.0970, Found: 247.0973.



12u

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12u** in 67% yield (white solid, 16.9 mg, 0.067 mmol, m.p. = 111 – 113 ^{o}C).

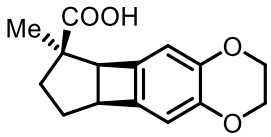
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 7.45 (s, 1H), 7.42 – 7.32 (m, 2H), 4.12 – 4.08 (m, 1H), 3.89 (d, *J* = 4.4 Hz, 1H), 2.04 – 1.91 (m, 3H), 1.71 – 1.65 (m, 1H), 1.43 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 145.4, 143.3, 134.9, 134.4, 128.6, 128.2, 125.0, 124.8, 121.5, 120.0, 56.1, 51.1, 47.6, 32.6, 27.4, 23.3.
HRMS (ESI-TOF) Calculated for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.1229, Found: 253.1225.



12v

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **12v** in 54% yield (white solid, 12.4 mg, 0.054 mmol, m.p. = 143 – 145 ^{o}C).

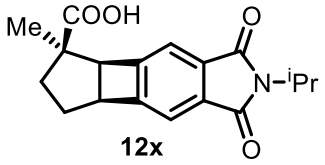
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.81 (s, 1H), 3.92 – 3.85 (m, 1H), 3.65 (d, *J* = 3.7 Hz, 1H), 2.23 (s, 3H), 2.19 (s, 3H), 1.98 – 1.91 (m, 1H), 1.84 – 1.79 (m, 2H), 1.65 – 1.58 (m, 1H), 1.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 143.8, 142.0, 136.8, 135.9, 124.2, 123.0, 56.1, 49.7, 47.4, 32.5, 26.2, 22.9, 20.5, 20.5.
HRMS (ESI-TOF) Calculated for $C_{15}H_{19}O_2$ $[M+H]^+$: 231.1385, Found: 231.1387.



12w

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (30% EtOAc/hexane + 1% formic acid) to afford **12w** in 39% yield (white solid, 10.1 mg, 0.039 mmol, m.p. = 133 – 135 °C).

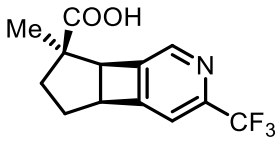
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.59 (s, 1H), 6.55 (s, 1H), 4.24 – 4.15 (m, 4H), 3.83 – 3.79 (m, 1H), 3.58 (d, *J* = 3.8 Hz, 1H), 1.97 – 1.89 (m, 1H), 1.83 – 1.76 (m, 2H), 1.65 – 1.59 (m, 1H), 1.30 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.6, 144.7, 144.0, 138.7, 136.8, 113.0, 111.4, 64.4, 64.3, 55.5, 49.8, 47.1, 32.5, 26.3, 22.9.
HRMS (ESI-TOF) Calculated for $C_{15}H_{17}O_4$ $[M+H]^+$: 261.1127, Found: 261.1126.



12x

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (50% EtOAc/hexane + 1% formic acid) to afford **12x** in 47% yield (white solid, 14.7 mg, 0.047 mmol, m.p. = 157 – 159 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.47 (s, 1H), 4.53 – 4.44 (m, 1H), 3.97 (dd, *J* = 7.7, 3.9 Hz, 1H), 3.75 (d, *J* = 4.1 Hz, 1H), 2.02 – 1.80 (m, 3H), 1.71 (dd, *J* = 13.0, 6.4 Hz, 1H), 1.46 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.5, 169.1, 169.0, 153.4, 151.4, 132.6, 131.9, 118.9, 117.2, 55.9, 50.1, 47.5, 43.0, 32.5, 26.0, 22.9, 20.3.
HRMS (ESI-TOF) Calculated for $C_{18}H_{20}NO_4$ $[M+H]^+$: 314.1392, Found: 314.1395.

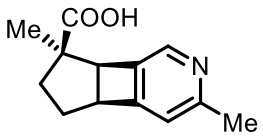


13a

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), dihaloarene (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13a** in 59% yield (white solid, 16.0 mg, 0.059 mmol, m.p. = 201 – 203 °C).

^{1}H NMR (600 MHz, CD_3OD) δ 8.26 (d, *J* = 1.4 Hz, 1H), 7.58 (d, *J* = 1.4 Hz, 1H), 4.08 (dd, *J* = 8.1, 3.7 Hz, 1H), 3.88 (d, *J* = 3.7 Hz, 1H), 2.03 (tdd, *J* = 13.4, 8.2, 6.9 Hz, 1H), 1.96 – 1.90 (m, 1H), 1.77 (td, *J* = 13.2, 6.8 Hz, 1H), 1.68 (dd, *J* = 12.8, 6.5 Hz, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, CD_3OD) δ 179.7, 160.1, 148.1 (q, *J* = 34.0 Hz), 147.0 (q, *J* = 1.7 Hz), 144.6, 123.1 (q, *J* = 273.5 Hz), 116.2 (q, *J* = 2.8 Hz). 57.8, 51.0, 50.1, 33.8, 26.2, 23.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.69.

HRMS (ESI-TOF) Calculated for $C_{13}H_{13}F_3NO_2$ $[M+H]^+$: 272.0898, Found: 272.0901.

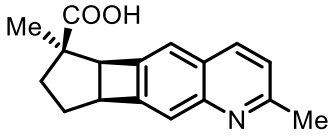


13b

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), dihaloarene (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13b** in 32% yield (white solid, 6.9 mg, 0.032 mmol, m.p. = 213 – 215 ^{o}C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (s, 1H), 6.95 (s, 1H), 4.00 – 3.95 (m, 1H), 3.81 (d, *J* = 3.7 Hz, 1H), 2.59 (s, 3H), 2.00 – 1.86 (m, 3H), 1.66 (dd, *J* = 13.5, 4.8 Hz, 1H), 1.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.5, 159.2, 156.4, 140.6, 140.0, 118.2, 56.7, 50.7, 49.3, 33.0, 26.2, 23.9, 22.7.

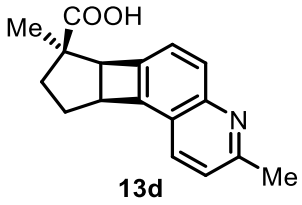
HRMS (ESI-TOF) Calculated for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1181, Found: 218.1185.



13c

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), dihaloarene (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13c** in 40% yield (colorless oil, 10.7 mg, 0.04 mmol).

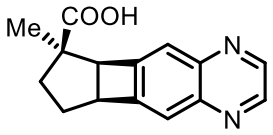
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.70 (s, 1H), 7.41 (s, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.14 – 4.09 (m, 1H), 3.89 (d, *J* = 4.2 Hz, 1H), 2.72 (s, 3H), 2.07 – 1.97 (m, 2H), 1.96 – 1.88 (m, 1H), 1.74 – 1.67 (m, 1H), 1.43 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.9, 157.5, 149.9, 148.9, 143.6, 137.2, 127.6, 121.5, 120.9, 120.6, 56.0, 51.2, 47.8, 32.8, 27.3, 24.9, 23.3. HRMS (ESI-TOF) Calculated for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338, Found: 268.1339.



13d

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), dihaloarene (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13d** in 43% yield (colorless oil, 11.5 mg, 0.043 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 9.2 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 4.20 – 4.15 (m, 1H), 3.81 (d, *J* = 3.4 Hz, 1H), 2.80 (s, 3H), 2.03 – 1.92 (m, 3H), 1.75 – 1.67 (m, 1H), 1.41 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.6, 158.0, 147.6, 142.0, 141.4, 131.3, 128.4, 125.8, 122.3, 122.3, 56.6, 48.8, 46.7, 32.9, 25.4, 24.9, 22.8. HRMS (ESI-TOF) Calculated for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338, Found: 268.1339.



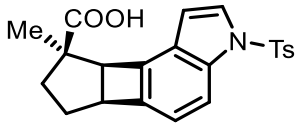
13e

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), dihaloarene (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (50% EA/hexane + 1% formic acid) to afford **13e** in 49% yield (white solid, 12.5 mg, 0.049 mmol, m.p. = 182 – 184 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (d, *J* = 1.9 Hz, 1H), 8.77 (d, *J* = 2.1 Hz, 1H), 8.10 (t, *J* = 1.1 Hz, 1H), 7.78 (t, *J* = 1.0 Hz, 1H), 4.22 – 4.15 (m, 1H), 4.01 (d, *J* = 4.3 Hz, 1H), 2.15 – 2.04 (m,

2H), 1.94 (td, *J* = 13.1, 7.2 Hz, 1H), 1.79 (dd, *J* = 13.8, 6.0 Hz, 1H), 1.47 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.2, 151.5, 150.0, 145.3, 143.8, 142.6, 141.6, 122.6, 122.0, 56.2, 51.5, 48.0, 33.2, 27.5, 23.7.

HRMS (ESI-TOF) Calculated for $C_{15}H_{15}N_2O_2$ $[M+H]^+$: 255.1134, Found: 255.1134.

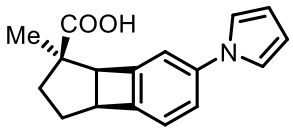


13f

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (50% EtOAc/hexane + 1% formic acid) to afford **13f** in 48% yield (white solid, 18.9 mg, 0.048 mmol, m.p. = 132 – 135 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.32 (d, *J* = 3.7 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.39 (dd, *J* = 3.7, 0.9 Hz, 1H), 3.95 – 3.91 (m, 1H), 3.80 (d, *J* = 3.6 Hz, 1H), 2.30 (s, 3H), 1.88 – 1.80 (m, 3H), 1.62 – 1.55 (m, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 145.0, 140.9, 135.9, 135.4, 135.3, 129.9, 127.2, 127.0, 126.5, 117.8, 114.0, 106.6, 56.5, 49.2, 47.8, 32.4, 25.8, 22.8, 21.7.

HRMS (ESI-TOF) Calculated for $C_{22}H_{22}NO_4S$ $[M+H]^+$: 396.1270, Found: 396.1266.

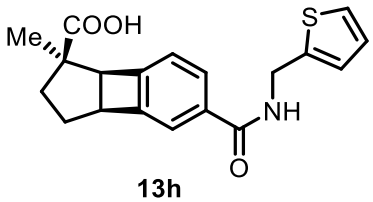


13g

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **13g** in 41% yield (white solid, 11.0 mg, 0.041 mmol, decomposed over 150 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (dddd, *J* = 7.8, 2.0, 0.7 Hz, 1H), 7.09 – 7.04 (m, 2H), 6.98 (t, *J* = 2.2 Hz, 2H), 6.28 (t, *J* = 2.1 Hz, 2H), 3.95 – 3.91 (m, 1H), 3.70 (d, *J* = 3.7 Hz, 1H), 1.99 – 1.85 (m, 3H), 1.73 – 1.60 (m, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.0, 145.6, 143.8, 140.8, 123.1, 121.8, 119.9, 116.7, 110.0, 55.8, 49.7, 47.3, 32.6, 26.2, 23.0.

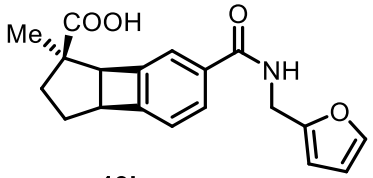
HRMS (ESI-TOF) Calculated for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338, Found: 268.1338.



13h

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (70% EtOAc/hexane + 1% formic acid) to afford **13h** in 81% yield (white solid, 27.7 mg, 0.081 mmol, m.p. = 186 – 188 °C).

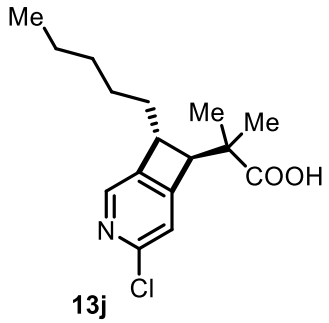
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.48 (s, 1H), 7.22 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.95 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.82 (t, *J* = 5.7 Hz, 1H), 4.80 (d, *J* = 5.7 Hz, 2H), 3.96 – 3.91 (m, 1H), 3.70 (d, *J* = 3.8 Hz, 1H), 1.91 – 1.82 (m, 3H), 1.68 – 1.60 (m, 1H), 1.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.1, 168.0, 148.9, 146.9, 141.2, 134.4, 127.1, 127.1, 126.3, 125.3, 123.4, 120.9, 56.3, 50.1, 47.7, 39.0, 32.4, 26.1, 23.0.
HRMS (ESI-TOF) Calculated for $C_{19}H_{20}NO_3S$ $[M+H]^+$: 342.1164, Found: 342.1161.



13i

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (70% EtOAc/hexane + 1% formic acid) to afford **13i** in 62% yield (colorless oil, 20.2 mg, 0.062 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.51 (s, 1H), 7.31 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.66 (t, *J* = 6.0 Hz, 1H), 6.29 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 4.54 (qd, *J* = 15.5, 5.5 Hz, 2H), 3.96 – 3.87 (m, 1H), 3.71 (d, *J* = 3.7 Hz, 1H), 1.94 – 1.82 (m, 3H), 1.63 (q, *J* = 4.7 Hz, 1H), 1.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.4, 168.2, 151.5, 150.7, 145.0, 133.8, 127.9, 122.1, 122.1, 110.6, 107.7, 56.3, 49.8, 47.9, 37.2, 32.6, 26.2, 22.7.
HRMS (ESI-TOF) Calculated for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1392, Found: 326.1396.

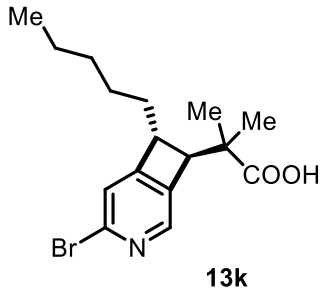


13j

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13j** in 34% yield (white solid, 10.1 mg, 0.034 mmol, m.p. = 174 – 176 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (q, *J* = 1.2 Hz, 1H), 7.10 (s, 1H), 3.44 (dd, *J* = 2.7, 0.9 Hz, 1H), 3.35 (ddd, *J* = 8.9, 6.3, 2.7 Hz, 1H), 1.78 (ddt, *J* = 13.1, 9.9, 6.3 Hz, 1H), 1.62 (dtd, *J* = 14.1, 9.4, 5.3 Hz, 1H), 1.47 – 1.40 (m, 2H), 1.36 – 1.28 (m, 4H), 1.26 (s, 3H), 1.24 (s, 3H), 0.93 – 0.86 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.2, 160.8, 149.2, 143.4, 139.9, 118.9, 56.4, 46.6, 43.37, 33.2, 31.9, 27.9, 22.9, 22.7, 22.3, 14.1.

HRMS (ESI-TOF) Calculated for $C_{16}H_{23}ClNO_2$ $[M+H]^+$: 296.1417, Found: 296.1417.

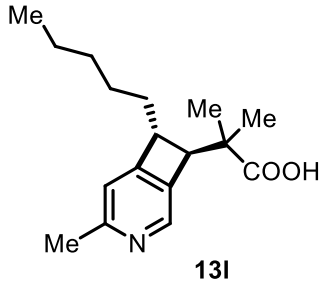


13k

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13k** in 25% yield (white solid, 8.5 mg, 0.025 mmol, m.p. = 185 – 187 °C).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.26 (s, 1H), 3.42 (d, *J* = 2.8 Hz, 1H), 3.38 – 3.34 (m, 1H), 1.83 – 1.74 (m, 1H), 1.62 (qd, *J* = 9.0, 4.8 Hz, 1H), 1.48 – 1.41 (m, 2H), 1.35 – 1.30 (m, 4H), 1.26 (s, 3H), 1.25 (s, 3H), 0.93 – 0.88 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.81, 160.39, 144.06, 140.2, 139.7, 122.7, 56.5, 46.7, 43.3, 33.2, 31.9, 28.0, 22.9, 22.7, 22.4, 14.2.

HRMS (ESI-TOF) Calculated for $C_{16}H_{23}BrNO_2$ $[M+H]^+$: 340.0912, Found: 342.0893.

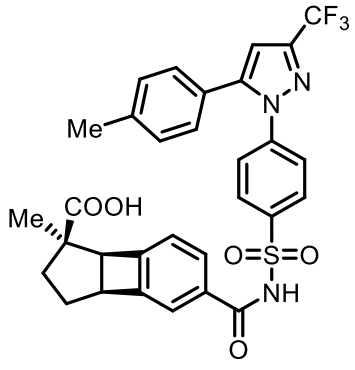


13l

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: **L28** instead of **L7**, $KHCO_3$ instead of K_2CO_3, the compound was purified by reverse phase chromatography (0%-50% MeCN/H_2O) using Biotage IsoleraTM one with Biotage SNAP C18 to afford **13l** in 47% yield (colorless oil, 12.9 mg, 0.047 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (s, 1H), 6.92 (s, 1H), 3.43 (d, *J* = 2.6 Hz, 1H), 3.30 (ddd, *J* = 9.1, 6.1, 2.5 Hz, 1H), 2.51 (s, 3H), 1.78 – 1.70 (m, 1H), 1.60 – 1.51 (m, 1H), 1.47 – 1.37 (m, 2H), 1.32 – 1.24 (m, 4H), 1.19 (s, 3H), 1.12 (s, 3H), 0.90 – 0.84 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.0, 159.9, 155.8, 141.5, 139.6, 117.9, 57.5, 46.8, 43.7, 33.5, 32.0, 28.1, 24.0, 23.3, 22.7, 22.6, 14.2.

HRMS (ESI-TOF) Calculated for $C_{17}H_{26}NO_2$ $[M+H]^+$: 276.1964, Found: 276.1964.

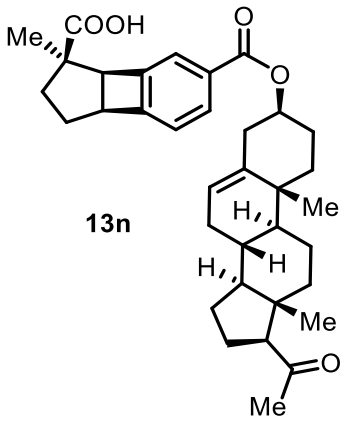


13m

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes with modifications: aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (3% MeOH in EtOAc + 1% formic acid) to afford **13m** in 41% yield (colorless oil, 25.0 mg, 0.041 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 – 8.07 (m, 2H), 7.58 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.48 – 7.40 (m, 3H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.12 – 7.07 (m, 2H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.73 (s, 1H), 3.89 (dd, *J* = 7.4, 3.9 Hz, 1H), 3.67 (d, *J* = 3.8 Hz, 1H), 2.35 (s, 3H), 1.89 – 1.70 (m, 3H), 1.60 (dd, *J* = 12.8, 6.4 Hz, 1H), 1.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.6, 165.2, 151.2, 147.2, 145.5, 144.3 (q, *J* = 38.7 Hz), 143.5, 140.0, 138.0, 131.4, 129.9, 129.9, 128.8, 127.9, 125.7, 125.3, 123.6, 121.9, 121.1 (d, *J* = 269.3 Hz), 106.6, 56.5, 50.0, 47.7, 32.5, 26.2, 26.0, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.1.

HRMS (ESI-TOF) Calculated for $C_{31}H_{27}F_3N_3O_5S$ $[M+H]^+$: 610.1624, Found: 610.1627.

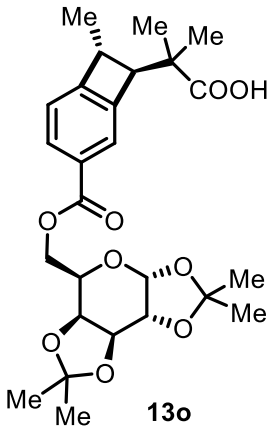


13n

Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **13n** in 86% yield (white solid, 46.8 mg, 0.086 mmol, m.p. = 217 – 221 ^{o}C). A 1:1 diastereomers were obtained as the product, d.r. was analyzed by ^{1}H NMR. Some ^{13}C peaks overlap.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.71 (s, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 5.41 – 5.36 (m, 1H), 4.85 – 4.72 (m, 1H), 3.96 – 3.92 (m, 1H), 3.71 (d, *J* = 3.8 Hz, 1H), 2.55 (t, *J* = 9.0 Hz, 1H), 2.43 (s, 2H), 2.23 – 2.16 (m, 1H), 2.14 (s, 3H), 2.07 – 1.86 (m, 7H), 1.74 – 1.57 (m, 6H), 1.53 – 1.44 (m, 3H), 1.35 (d, *J* = 0.9 Hz, 3H), 1.28 – 1.15 (m, 3H), 1.07 – 1.00 (m, 4H), 0.64 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 209.6, 164.4, 140.5, 139.5, 133.5, 132.4, 130.1, 129.1, 122.9, 107.5, 75.4, 63.8, 57.0, 50.0, 44.1, 38.9, 38.2, 37.1, 36.8, 32.0, 31.9, 31.7, 27.9, 24.6, 23.0, 21.2, 19.5, 13.4.

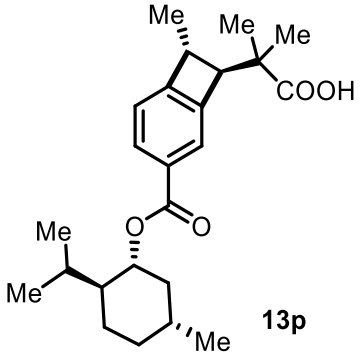
HRMS (ESI-TOF) Calculated for $C_{35}H_{45}O_5$ $[M+H]^+$: 545.3267, Found: 545.3262.



13o

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (30% EtOAc/hexane + 1% formic acid) to afford **13o** in 47% yield (colorless oil, 23.1 mg, 0.047 mmol). A 1:1 diastereomers were obtained as the product. ^{1}H NMR and ^{13}C NMR were reported as a mixture of diastereomers, d.r. was analyzed by ^{1}H NMR. Some peaks overlap.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.80 (dt, *J* = 2.3, 1.2 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 5.56 (d, *J* = 4.9 Hz, 1H), 4.65 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.51 (ddd, *J* = 16.3, 11.5, 4.8 Hz, 1H), 4.41 (ddd, *J* = 14.1, 11.5, 7.6 Hz, 1H), 4.33 (dd, *J* = 4.9, 2.5 Hz, 1H), 4.31 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.19 (ddt, *J* = 8.0, 4.7, 1.6 Hz, 1H), 3.41 (qd, *J* = 7.0, 2.5 Hz, 1H), 3.33 (dd, *J* = 2.6, 1.1 Hz, 1H), 1.51 (s, 3H), 1.47 (s, 3H), 1.40 (d, *J* = 7.0 Hz, 3H), 1.35 (s, 3H), 1. 33 (s, 3H), 1.32 (d, *J* = 3.0 Hz, 3H), 1.20 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.9, 182.8, 167.1, 167.1, 154.9, 143.9, 143.9, 130.0, 129.3, 129.3, 124.8, 121.6, 109.8, 109.0, 96.4, 71.3, 71.3, 70.9, 70.7, 66.4, 66.4, 64.0, 58.4, 58.4, 43.6, 40.9, 26.2, 26.2, 26.1, 25.1, 24.6, 23.6, 23.5, 21.6, 21.5, 18.5. HRMS (ESI-TOF) Calculated for $C_{26}H_{35}O_9$ $[M+H]^+$: 491.2281, Found: 491.2285.

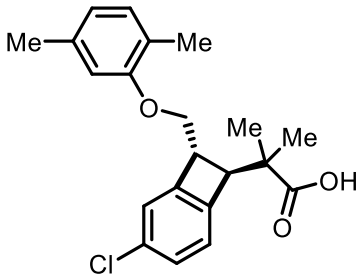


13p

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes, the compound was purified by pTLC (30% EtOAc/hexane + 1% formic acid) to afford **13p** in 42% yield (colorless oil, 16.2 mg, 0.042 mmol). A 1:1 diastereomers were obtained as the product. ^{1}H NMR and ^{13}C NMR were reported as a mixture of diastereomers, d.r. was analyzed by ^{1}H NMR. Some peaks overlap.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (ddt, *J* = 7.7, 4.2, 1.0 Hz, 1H), 7.78 (dq, *J* = 12.3, 1.1 Hz, 1H), 7.12 (dd, *J* = 7.7, 1.0 Hz, 1H), 4.92 (tdd, *J* = 10.9, 4.4, 1.5 Hz, 1H), 3.41 (qt, *J* = 7.0, 2.5 Hz, 1H), 3.34 (dd, *J* = 4.3, 2.7 Hz, 1H), 2.11 (dtd, *J* = 12.1, 4.0, 1.7 Hz, 1H), 1.95 (dqd, *J* = 16.6, 6.9, 3.5 Hz, 1H), 1.80 – 1.68 (m, 2H), 1.61 – 1.48 (m, 2H), 1.40 (d, *J* = 7.0 Hz, 3H), 1.34 (d, *J* = 7.2 Hz, 3H), 1.21 (d, *J* = 2.2 Hz, 3H), 1.17 – 1.05 (m, 2H), 0.92 (ddd, *J* = 7.1, 4.5, 2.3 Hz, 7H), 0.79 (dd, *J* = 6.9, 3.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.1, 166.8, 154.5, 143.9, 143.9, 130.2, 130.2, 129.9, 129.8, 124.7, 124.6, 121.5, 74.9, 74.8, 58.4, 58.3, 47.4, 47.4, 43.6, 43.6, 41.1, 41.1, 40.8, 40.8, 34.5, 31.6, 31.6, 26.8, 26.6, 23.9, 23.7, 23.6, 23.5, 22.2, 21.6, 21.6, 21.0, 20.9, 18.6, 16.8, 16.6.

HRMS (ESI-TOF) Calculated for $C_{24}H_{33}O_4$ $[M-H]^-$: 385.2379, Found: 385.2372.

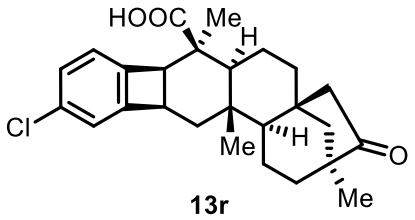


13q

Following the general procedure for the [2+2] annulation of acyclic aliphatic acids and dihaloarenes, the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **13q** in 45% yield (colorless oil, 16.2 mg, 0.045 mmol).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.7 Hz, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 4.25 (ddd, *J* = 8.1, 6.2, 1.6 Hz, 1H), 4.15 – 4.09 (m, 1H), 3.77 (t, *J* = 7.1 Hz, 1H), 3.59 – 3.55 (m, 1H), 2.30 (s, 3H), 2.18 (s, 3H), 1.31 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 156.8, 146.2, 142.5, 136.7, 133.6, 130.6, 128.5, 125.0, 123.6, 123.4, 121.2, 111.9, 69.5, 53.9, 44.9, 43.4, 22.7, 22.6, 21.5, 16.1.

HRMS (ESI-TOF) Calculated for $C_{21}H_{22}ClO_3$ [M-H]$^-$: 357.1257, Found: 357.1251.



13r

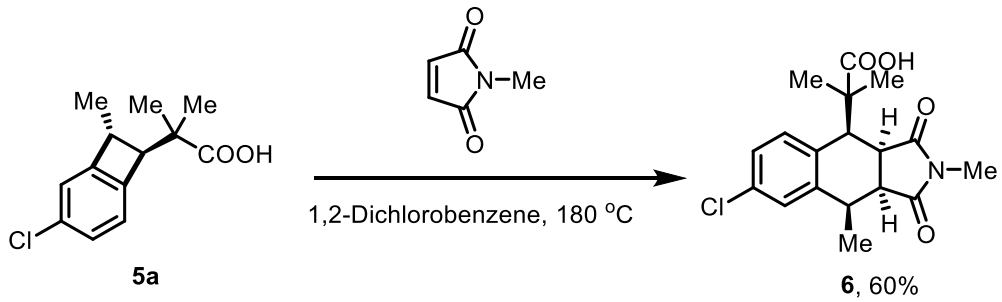
Following the general procedure for the [2+2] annulation of cyclic aliphatic acids and dihaloarenes using aliphatic acid (0.2 mmol), **2a** (0.1 mmol), K_2CO_3 (3.5 equiv), the compound was purified by pTLC (20% EtOAc/hexane + 1% formic acid) to afford **13r** in 35% yield (white solid, 14.9 mg, 0.035 mmol, m.p. = 199 – 202 ^oC).

^1H NMR (600 MHz, $CDCl_3$) δ 7.09 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.03 (s, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 3.85 – 3.81 (m, 1H), 3.56 (d, *J* = 5.7 Hz, 1H), 2.69 – 2.63 (m, 1H), 2.25 (d, *J* = 13.9 Hz, 1H), 1.84 – 1.75 (m, 3H), 1.66 – 1.62 (m, 3H), 1.58 (s, 3H), 1.54 – 1.46 (m, 3H), 1.42 – 1.37 (m, 3H), 1.21 – 1.12 (m, 2H), 0.98 (s, 3H), 0.45 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 222.4, 177.7, 150.4, 144.6, 133.7, 127.6, 123.9, 121.8, 55.4, 55.1, 54.5, 48.9, 48.6, 48.1, 47.0, 41.6, 41.3, 40.6, 39.9, 38.1, 37.3, 31.9, 23.7, 20.8, 19.9, 17.4.

HRMS (ESI-TOF) Calculated for $C_{26}H_{32}ClO_3$ [M+H]$^+$: 427.2040, Found: 427.2039.

7. Synthetic Transformations

Synthesis of 6



5a **6**, 60%

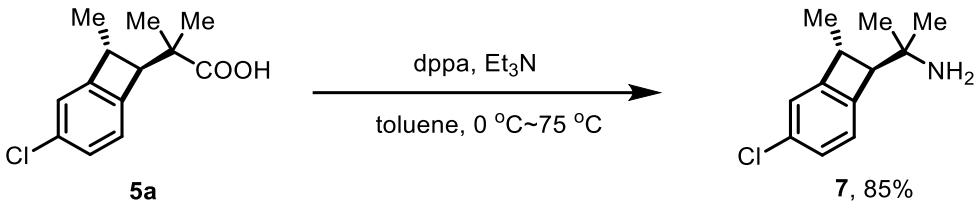
The mixture of **5a** (0.1 mmol, 23.8 mg) and *N*-methylmaleimide (0.2 mmol, 22.2 mg) in *o*-dichlorobenzene (0.3 mL) was stirred at 180 °C for 72 h. Solvent was evaporated and the residue

was purified by chromatography on silica gel using EtOAc/hexane as eluent to give the cycloaddition product **6** (60% yield, 0.06 mmol, 21.0 mg) as white solid, m.p. = 100 – 102 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 – 7.08 (m, 3H), 3.84 (s, 1H), 3.29 – 3.19 (m, 2H), 2.98 (dd, *J* = 9.1, 3.6 Hz, 1H), 2.91 (s, 3H), 1.61 (d, *J* = 7.4 Hz, 3H), 1.29 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.8, 180.1, 178.9, 141.4, 133.8, 133.2, 129.6, 129.3, 126.4, 47.1, 44.9, 43.8, 41.8, 34.1, 25.6, 25.6, 25.4, 23.2.

HRMS (ESI-TOF) Calculated for $C_{18}H_{21}ClNO_4$ $[M+H]^+$: 350.1159, Found: 350.1155.

Synthesis of 7



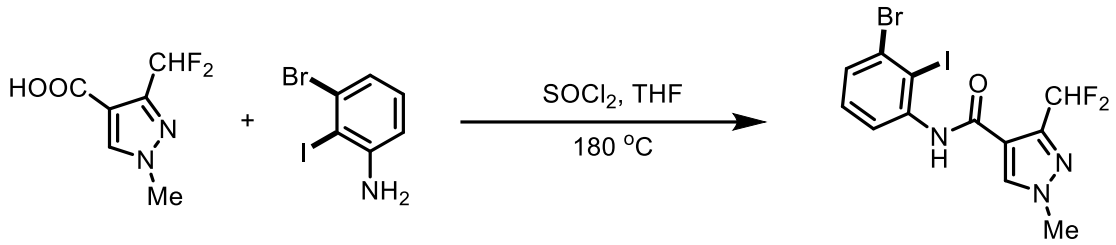
5a **7**, 85%

To a solution of **5a** (0.1 mmol, 23.8 mg) in toluene (1.0 mL), Et_3N (0.11 mmol, 11.1 mg) was added and cooled to 0 °C. To this cooled mixture was added diphenylphosphonicazide (dppa, 0.11 mmol, 30.3 mg) and the mixture was stirred at room temperature for 15 min and then heated to 75 °C for 2.5 h. Then the reaction was cooled to room temperature, quenched with water, and extracted with EtOAc. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by chromatography on silica gel using EtOAc/hexane to afford the expected product **7** (85% yield, 0.085 mmol, 17.8 mg) as colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (ddd, *J* = 7.8, 1.9, 0.9 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.06 (dt, *J* = 7.8, 1.0 Hz, 1H), 3.38 (qd, *J* = 7.1, 2.5 Hz, 1H), 3.01 (d, *J* = 2.5 Hz, 1H), 1.45 (s, 3H), 1.41 (d, *J* = 7.0 Hz, 3H), 1.40 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.0, 140.8, 134.0, 128.1, 124.6, 122.7, 61.7, 59.4, 40.8, 28.6, 28.3, 18.5.

HRMS (ESI-TOF) Calculated for $C_{12}H_{17}ClN$ $[M+H]^+$: 210.1050, Found: 210.1048.

Synthesis of 10



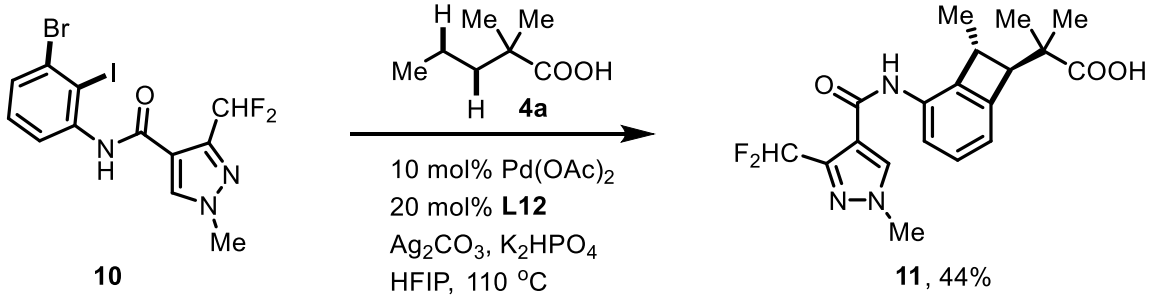
8 **9** **10**, 82%

To a dry 12 mL reaction tube charged a stir bar added **8** (0.5 mmol, 88.1 mg) and 0.5 mL thionyl chloride ($SOCl_2$). The reaction tube was capped, and put into a heating bath of 80 °C, stirred under this temperature for 1 h. After cooling down to room temperature, the cap was removed (inner pressure can be high. When scaling up, condenser with balloon is recommended). $SOCl_2$ in the reaction tube was removed by a rotavapor. Then **9** (0.6 mmol, 0.179 g) in 0.3 mL dry THF was added dropwisely into the reaction tube under room temperature. The reaction tube was capped and heated under 100 °C for 1 h. After cooling down to room temperature, water (1 mL) was added into the reaction mixture. The mixture was extracted by EtOAc (3 x 1 mL) and washed by brine (2 x 1 mL). The organic phase was combined, dried by anhydrous Na_2SO_4, and the solvent was removed by a rotavapor. The mixture was purified by a flash chromatography on silica gel (0~20% EtOAc/hexane), to afford **10** (82% yield, 0.41 mmol, 187.8 mg) as a white solid, m.p. = 211 – 213 °C.

^{1}H NMR (600 MHz, Acetone-d_6) δ 8.79 (s, 1H), 8.45 (s, 1H), 7.81 (ddd, J = 8.3, 6.3, 1.5 Hz, 1H), 7.59 (dd, J = 8.0, 1.4 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.30 (t, J = 54.1 Hz, 1H), 4.04 (s, 3H).^{13}C NMR (151 MHz, Acetone-d_6) δ 160.8, 146.5 (t, J = 24.3 Hz), 142.6, 133.7, 131.0, 131.0, 130.6, 125.0, 117.0, 111.0 (t, J = 234.3 Hz), 102.9, 40.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.0.

HRMS (ESI-TOF) Calculated for $C_{12}H_{10}BrF_2IN_3O$ $[M+H]^+$: 455.9020, Found: 455.9018.

Synthesis of 11



10 **11**, 44%

Synthesis of **11** followed general procedure for the [2+2] annulation of acyclic aliphatic acids and haloarenes with a modification: all components excepted from **10** and Ag_2CO_3 were mixed and stirred for 3 min before adding **10** and Ag_2CO_3. **11** (44% yield, 0.044 mmol, 16.6 mg) was isolated by pTLC (50% EtOAc/hexane) as a yellow solid), m.p. = 100 – 105 ^oC.

^1H NMR (600 MHz, Acetone-d_6) δ 9.07 (s, 1H), 8.32 (s, 1H), 7.35 (t, *J* = 54.3 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 7.2 Hz, 1H), 3.99 (s, 3H), 3.61 (q, *J* = 6.9 Hz, 1H), 3.21 (d, *J* = 2.4 Hz, 1H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.27 (s, 3H), 1.19 (s, 3H). ^{13}C NMR (151 MHz, Acetone-d_6) δ 178.9, 160.1, 146.5, 139.9, 133.6, 133.1, 128.5, 120.3, 120.1, 117.4, 111.1 (t, *J* = 234.3 Hz), 108.1, 59.1, 44.0, 42.7, 39.9, 23.7, 22.4, 19.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.3 (d, *J* = 102.3 Hz).

HRMS (ESI-TOF) Calculated for $C_{19}H_{22}F_2N_3O_3$ $[M+H]^+$: 378.1629, Found: 378.1632.

8. Preliminary mechanistic studies

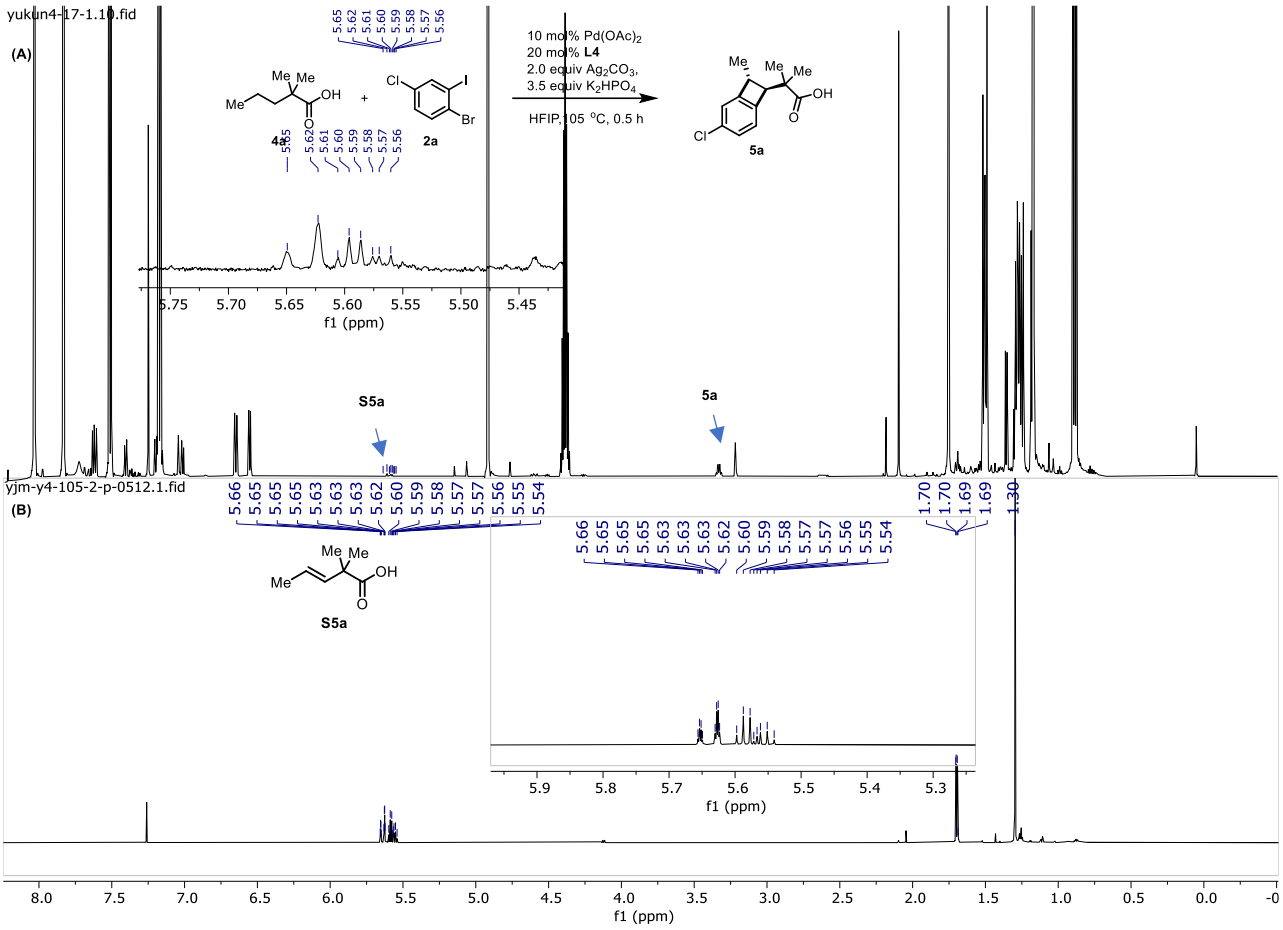


Figure S2. Monitoring experiment. (A) ^{1}H-NMR spectra of the Pd-catalyzed [2+2] annulation of **4a** and **2a** at reaction time 0.5 h. (B) ^{1}H-NMR spectra of **S5a**.

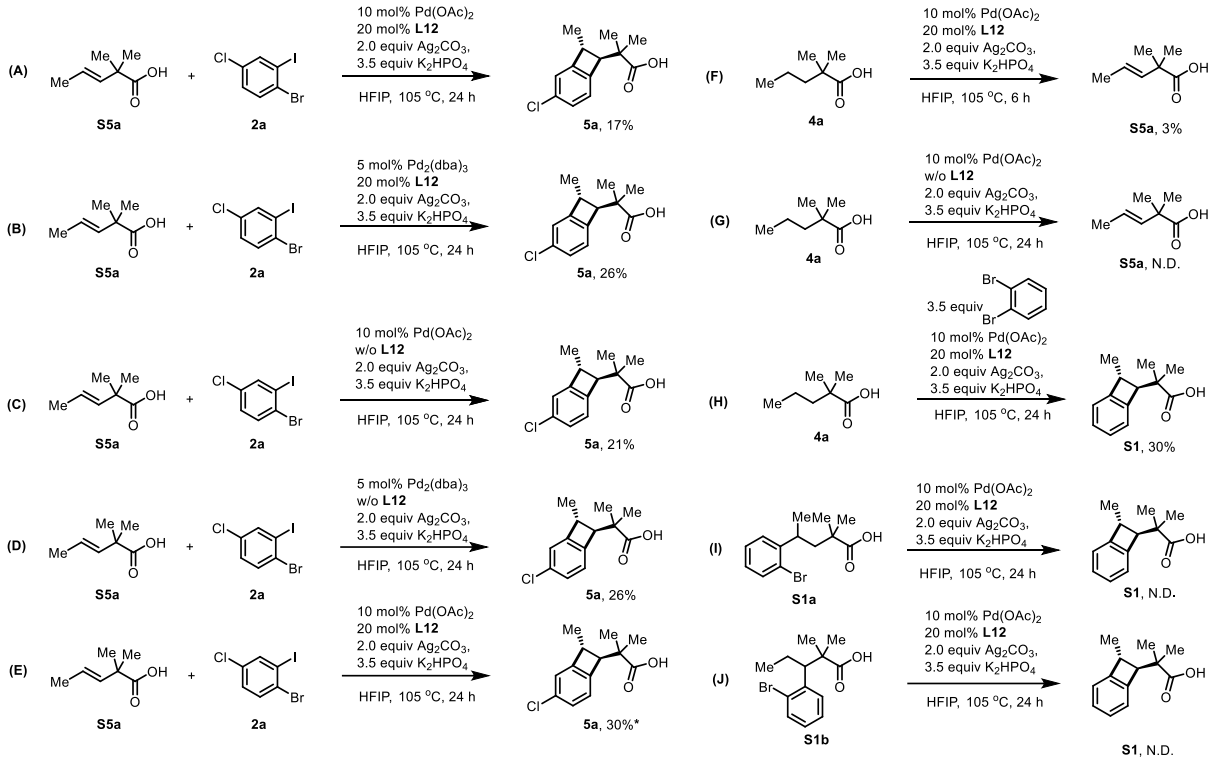


Figure S3. Control experiments. ***S5a** was added in four batches over four hours, with one-hour intervals between each addition, then reacted for 20 h.

To gain mechanistic insights of this Pd-catalyzed [2+2] annulation, the reaction of **4a** and **2a** was monitored by ^{1}H NMR. A trace of β,γ-dehydrogenation product **S5a** (<3% yield) was observed since the beginning of the reaction (Figure S2A). Next, using dehydrogenation product **S5a** as the substrate, the desired BCB product **5a** could be obtained in 17% or 26% yield with $Pd(OAc)_2$ or $Pd_2(dba)_3$ as the catalyst (Figure S3A, B). The fact that $Pd_2(dba)_3$ gave a similar yield to $Pd(OAc)_2$ with **S5a** as the substrate is consistent with the hypothesis that Pd(0) is a viable active species involved in the proposed catalytic cycle. In the absence of **L12**, the yield of **5a** was almost not affected (Figure S3C, D), indicating ligand **L12** is unessential for this process. Under the standard conditions without dihaloarene coupling partner, we observed the formation of **S5a** in 3% yield (Figure S3F), and **S5a** was not formed under the ligandless conditions (Figure S3G), indicating ligand **L12** is crucial for the dehydrogenation process. It is known that olefin products could react with Pd(II) via directed vinyl C–H activation and inhibit the catalytic reaction (*22*). We propose in situ slow formation of olefin is essential for dehydrogenation to continuously proceed and give BCB in high yields, which is supported by the fact that multi-addition of **S5a** leads to an increase in yield (Figure S3E). No desired BCB product could be observed when using β- or γ-C−H

monoarylation intermediates **S1a** and **S1b** as the substrates under the standard conditions without dihaloarene (Figure S3I, J). Taken together, these results suggest that dehydrogenation product **S5a** is the reasonable intermediate in this reaction.

Based on the above control experiments, we propose that our transformation proceeds via a Pd(II)/Pd(0)/Pd(II)/Pd(IV) catalytic cycle outlined in Fig. S4. Firstly, Pd(II) coordinates with a substrate and an amide-pyridone ligand to form **int-I** for the cleavage of γ-C−H bond, promoted by the bidentate ligand. Then, it goes through a β-hydride elimination to form **int-II** as a Pd(0) species. **Int-II** can be a resting state if there is no dihaloarene pushing it forward since the yield of dehydrogenation is very low in the absence of dihaloarene (Figure S3E). A β-C−H activation followed by β-hydride elimination with the γ-C−H bond cannot be excluded. After a ligand dissociation and an intermolecular oxidative addition of the Pd(0) into the aryl-iodo bond, **int-III** is formed as a Pd(II) species. Then, it goes through a carbopalladation to form **int-IV**. Next, we propose an intramolecular oxidative addition of the Pd(II) into the aryl-bromo bond to form **int-V** as a Pd(IV) species. Then, after a reductive elimination, the product can be obtained with a regenerated Pd(II) species. Silver salt is proposed to be a halogen scavenger, and its roles in other steps is under research. Diastereoselectivity of BCB products is proposed to be from the dehydrogenation step, in which small cyclic acids tend to form *cis*-alkene leading to *cis*-BCBs, and the acyclic acids generate *trans*-alkenes leading to *trans*-BCBs. Further studies on the reaction mechanism are under way.

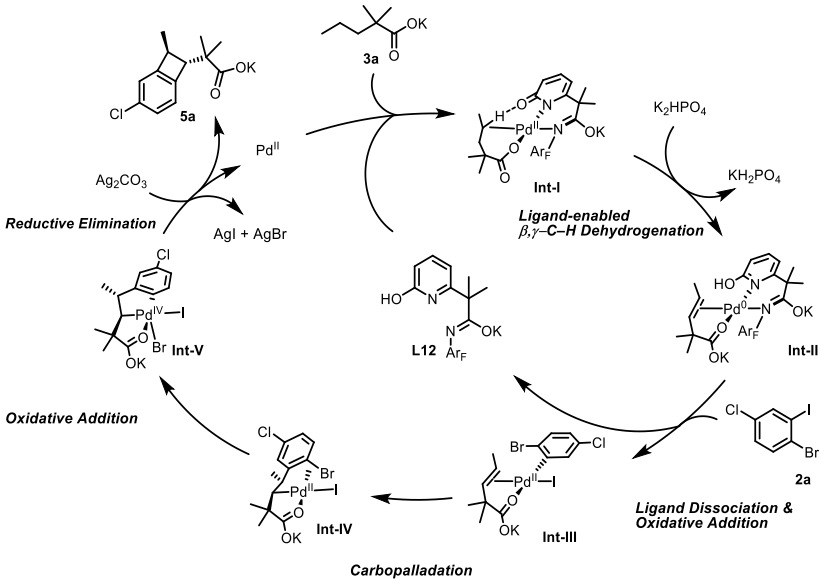
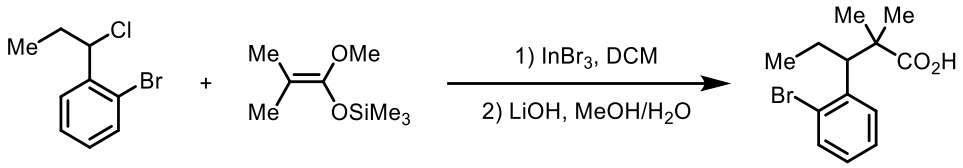


Figure S4. Proposed mechanism.

Compound **S1a** was synthesized according to the procedure below (*37*).



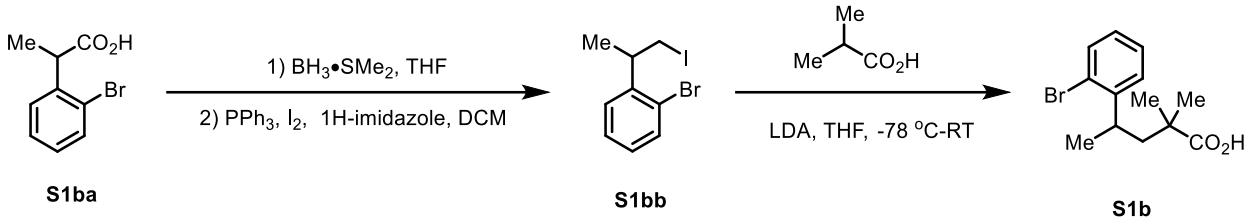
S1aa **S1a**

S1aa was synthesized according to the reported procedure (*38*). To a mixture of $InBr_3$ (0.05 mmol, 17.7 mg) and dimethylketene methyl trimethylsilyl acetal (1.5 mmol, 261 mg) in CH_2Cl_2 (1.0 mL) was added **S1aa** (1 mmol, 233 mg) under nitrogen. The reaction mixture was stirred overnight. The resulting mixture was poured into Et_2O (10 mL) and aqueous $NaHCO_3$ (10 mL). The solution was extracted with Et_2O and the organic layer was dried over $MgSO_4$. The evaporation of the solvent gave the crude product which could be used for next step without purification.

Redissolved the crude product in MeOH (10 mL) followed by adding water (5 mL) and LiOH (2 mmol, 48 mg). Then the reaction stirred at 50 °C for 18 h. The volatiles were removed in vacuo and the resulting residue was partitioned between a saturated solution of NH_4Cl and CH_2Cl_2. The aqueous phase was further extracted with CH_2Cl_2 and the combined organic layers was dried by anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using EtOAc/hexane to afford the expected product **S1a** (75% yield for two steps, 0.75 mmol, 214 mg, white solid, m.p. = 219-221 ^oC). ^1H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 1H), 7.31 – 7.24 (m, 2H), 7.09 (ddd, J = 8.8, 6.4, 2.4 Hz, 1H), 3.79 (dd, J = 11.3, 3.8 Hz, 1H), 1.84 – 1.69 (m, 2H), 1.18 (s, 3H), 1.17 (s, 3H), 0.71 (t, J = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 184.5, 140.1, 133.2, 129.2, 128.6, 128.2, 127.2, 51.3, 47.3, 25.3, 24.8, 20.0, 12.5.

HRMS (ESI-TOF) Calculated for $C_{13}H_{16}BrO_2$ $[M-H]^-$: 283.0334, Found: 283.0326.

Compound **S1b** was synthesized according to the procedure below.



S1ba **S1bb** **S1b**

To an ice-cold solution of acid **S1ba** (10 mmol, 2.29 g) in THF (100 mL), a borane dimethyl sulfide complex in THF (10 mL, 20 mmol) was added dropwise. The solution was warmed at room temperature and stirred for overnight. Then the reaction was cooled at 0 °C and quenched with MeOH (20 mL) and stirred for 10 min. The residue was dissolved in EtOAc, washed with brine, dried over Na_2SO_4 and concentrated in vacuo to obtain the alcohol as colorless oil without further purification.

A solution of triphenylphosphine (15 mmol, 3.93 g) and iodine (15 mmol, 3.81 g) in 50 mL of CH_2Cl_2 was stirred 10 min at room temperature, then treated with imidazole (25 mmol, 1.7 g), and stirred an additional 10 min. Then add the alcohol obtained in the last step in 40 mL of CH_2Cl_2 to the solution. After being left to stand overnight at room temperature, the mixture was washed with 10% aqueous sodium bisulfate, the organic layer was separated, and the aqueous layer was extracted three times with Et_2O. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel using EtOAc/hexane to afford the expected product **S1bb** (46% yield for two steps, 4.6 mmol, 1.49 g) as yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.0 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.14 – 7.08 (m, 1H), 3.52 (h, *J* = 6.9 Hz, 1H), 3.45 (dd, *J* = 9.7, 5.4 Hz, 1H), 3.30 (dd, *J* = 9.8, 7.8 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.1, 133.3, 128.5, 127.8, 127.2, 124.8, 40.5, 20.8, 13.3.

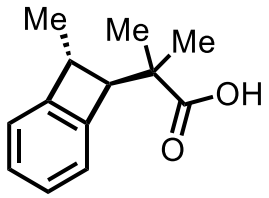
LDA solution in THF (10 mL, 5.0 mmol) was added dropwise to a mixture of isobutyric acid (2.0 mmol, 176 mg) and THF (10 mL) at -78 °C, and the mixture was allowed to warm up to room temperature and stirred for 1 h. Then the reaction mixture was recooled to -78 °C and **S1bb** (2.0 mmol, 650 mg) in THF (5 mL) was added dropwise. The resulting solution was allowed to warm up to room temperature and stirred overnight. After the reaction finished, the reaction mixture was

quenched with 10% HCl solution and extracted with EtOAc. The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product. Then purified by chromatography on silica gel to afford the desired aliphatic acid **S1b** (66% yield, 1.32 mmol, 376 mg) as white solid, m.p. = 95 – 97 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.01 (td, *J* = 7.6, 1.9 Hz, 1H), 3.44 (h, *J* = 6.9 Hz, 1H), 2.01 – 1.91 (m, 2H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.18 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 184.3, 146.5, 132.9, 128.1, 127.7, 127.6, 124.3, 47.5, 42.1, 35.3, 26.8, 24.6, 22.8.

HRMS (ESI-TOF) Calculated for $C_{13}H_{16}BrO_2$ $[M-H]^-$: 283.0334, Found: 283.0327.

Characterization of Compound **S1**.



S1

Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (p, *J* = 7.3 Hz, 3H), 7.11 (d, *J* = 7.1 Hz, 1H), 7.06 (d, *J* = 6.8 Hz, 1H), 3.41 – 3.35 (m, 1H), 3.32 (d, *J* = 2.8 Hz, 1H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.30 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.4, 149.0, 143.8, 127.8, 127.3, 123.4, 121.6, 58.8, 43.6, 40.7, 23.2, 21.7, 18.8.

HRMS (ESI-TOF) Calculated for $C_{13}H_{17}O_2$ $[M+H]^+$: 205.1229, Found: 205.1220.

9. X-Ray Crystallographic Data

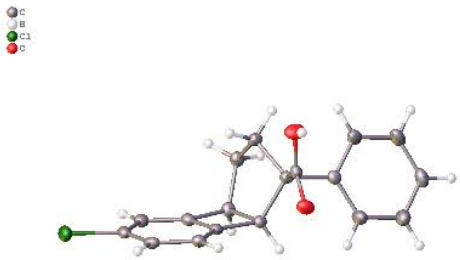


Table S7. Crystal data and structure refinement for **3h** (CCDC 2220709).

Report date	2022-11-18	
Identification code	Yu169	
Empirical formula	C18 H15 Cl O2	
Molecular formula	C18 H15 Cl O2	
Formula weight	298.75	
Temperature	100.00 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.8756(5) Å	α = 111.078(2)°.
	b = 17.3839(9) Å	β = 97.869(2)°.
	c = 19.1933(9) Å	γ = 106.461(2)°.
Volume	2841.6(2) $Å^3$	
Z	8	
Density (calculated)	1.397 Mg/m^3	
Absorption coefficient	0.270 mm^{-1}	
F(000)	1248	

Crystal size	0.25 x 0.2 x 0.16 mm^3
Crystal color, habit	colorless block
Theta range for data collection	2.439 to 26.022°.
Index ranges	-11<=h<=12, -21<=k<=21, -23<=l<=23
Reflections collected	64201
Independent reflections	11182 [R(int) = 0.0566]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6412 and 0.6090
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11182 / 0 / 761
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0398, wR2 = 0.0991
R indices (all data)	R1 = 0.0588, wR2 = 0.1095
Largest diff. peak and hole	0.327 and -0.297 $e.Å^{-3}$

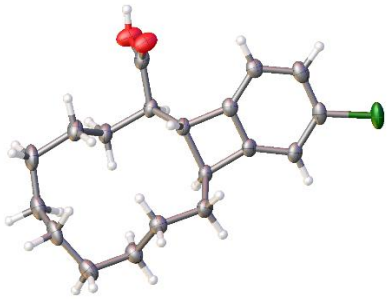


Table S8. Crystal data and structure refinement for **3x** (CCDC 2246693).

Identification code	yu227_0m_a	
Empirical formula	C19 H25 Cl O2	
Formula weight	320.84	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 43.028(5) Å	□= 90°.
	b = 8.5181(10) Å	□= 129.010(3)°.
	c = 27.957(3) Å	□ = 90°.
Volume	7962.0(16) $Å^3$	
Z	16	
Density (calculated)	1.071 Mg/m^3	
Absorption coefficient	0.196 mm^{-1}	
F(000)	2752	
Crystal size	0.1 x 0.03 x 0.03 mm^3	
Theta range for data collection	2.467 to 25.839°.	
Index ranges	-52<=h<=52, -10<=k<=10, -34<=l<=34	
Reflections collected	127299	

Independent reflections	7651 [R(int) = 0.0936]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.4903 and 0.4075
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7651 / 0 / 399
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0673, wR2 = 0.1809
R indices (all data)	R1 = 0.0852, wR2 = 0.1924
Largest diff. peak and hole	0.963 and -0.496 e.$Å^{-3}$

10. NMR Spectra

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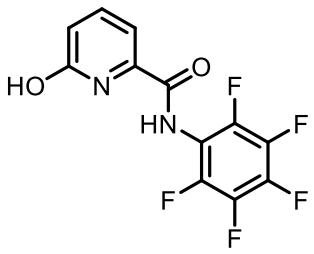

L1

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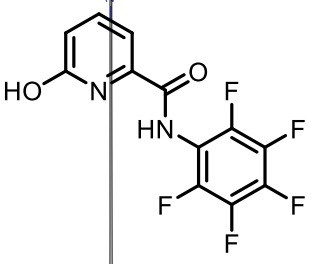
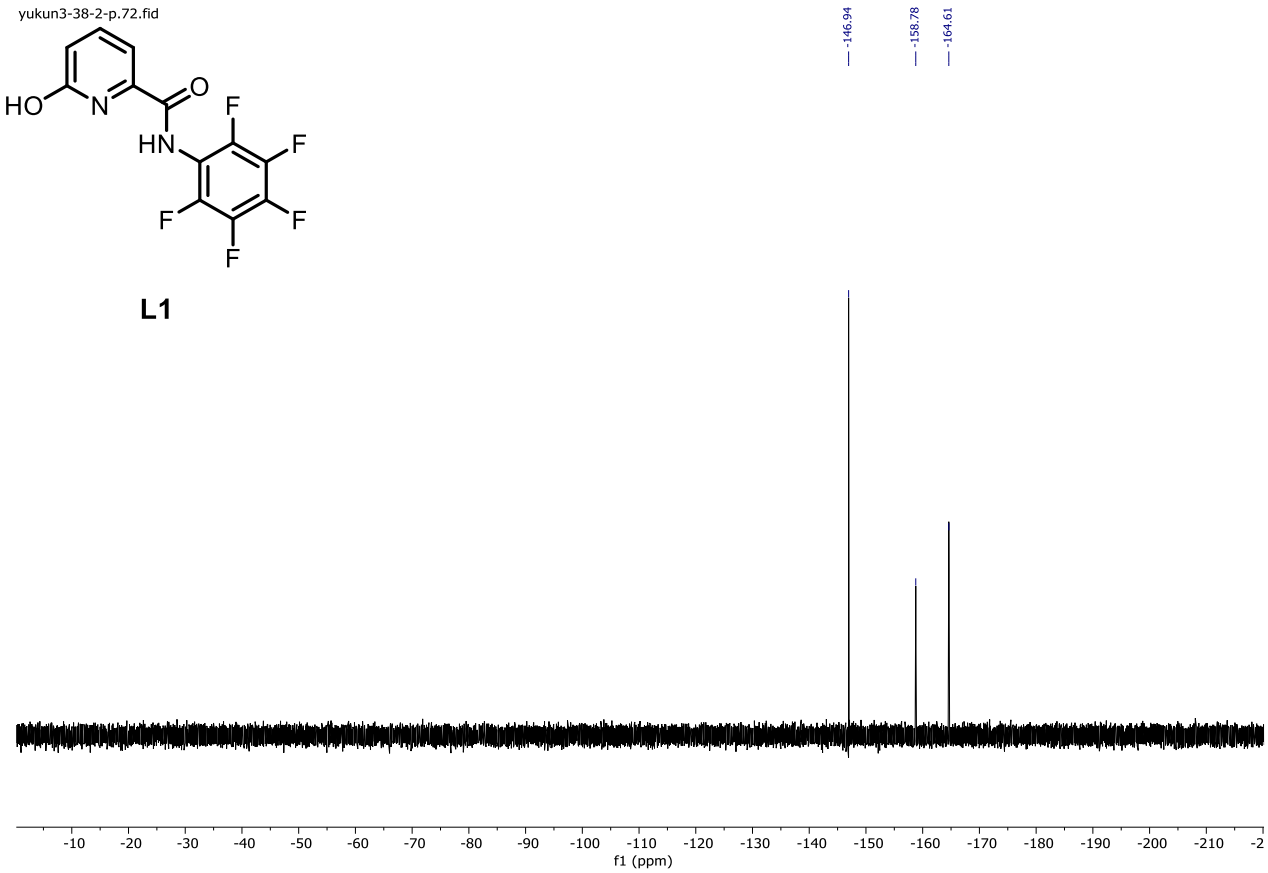


L1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O
HN
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F
F
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-158.78
-164.61
-10
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-60
-70
-80
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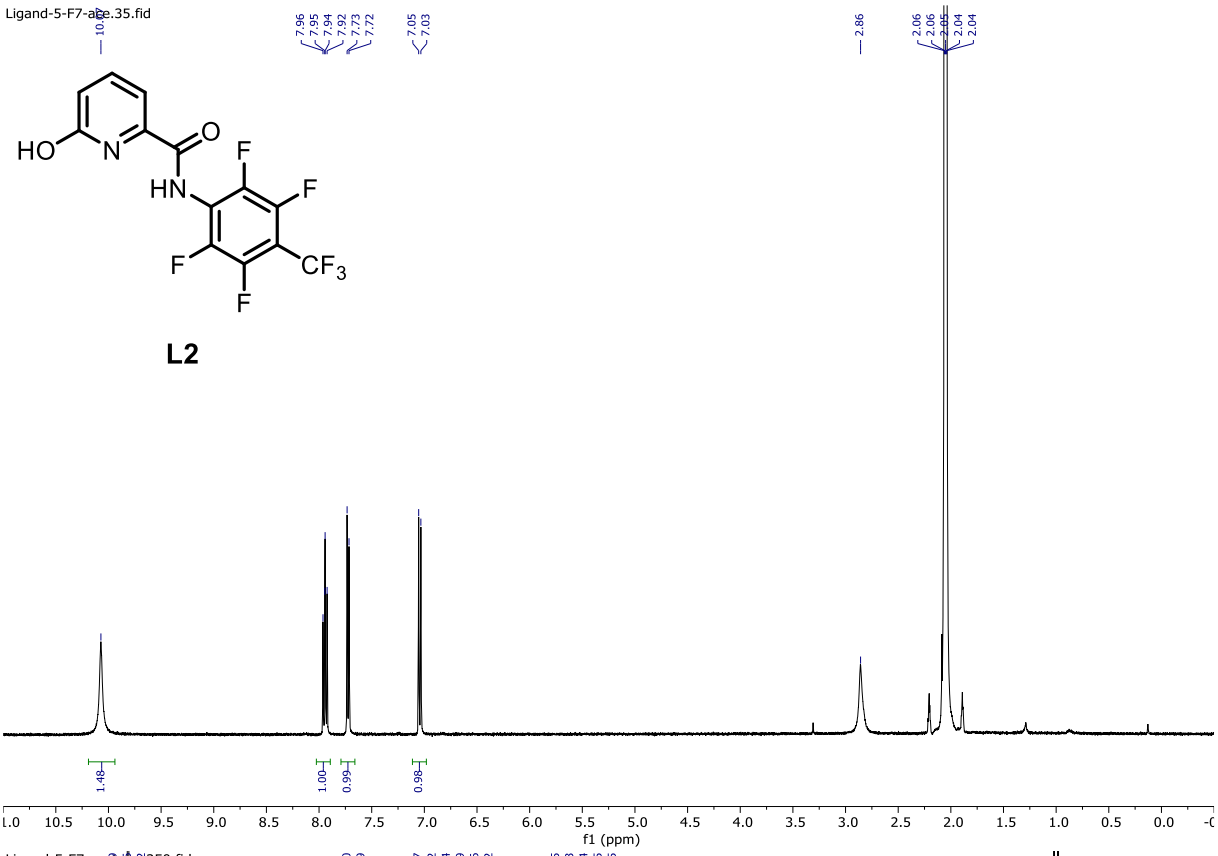
f1 (ppm)

L1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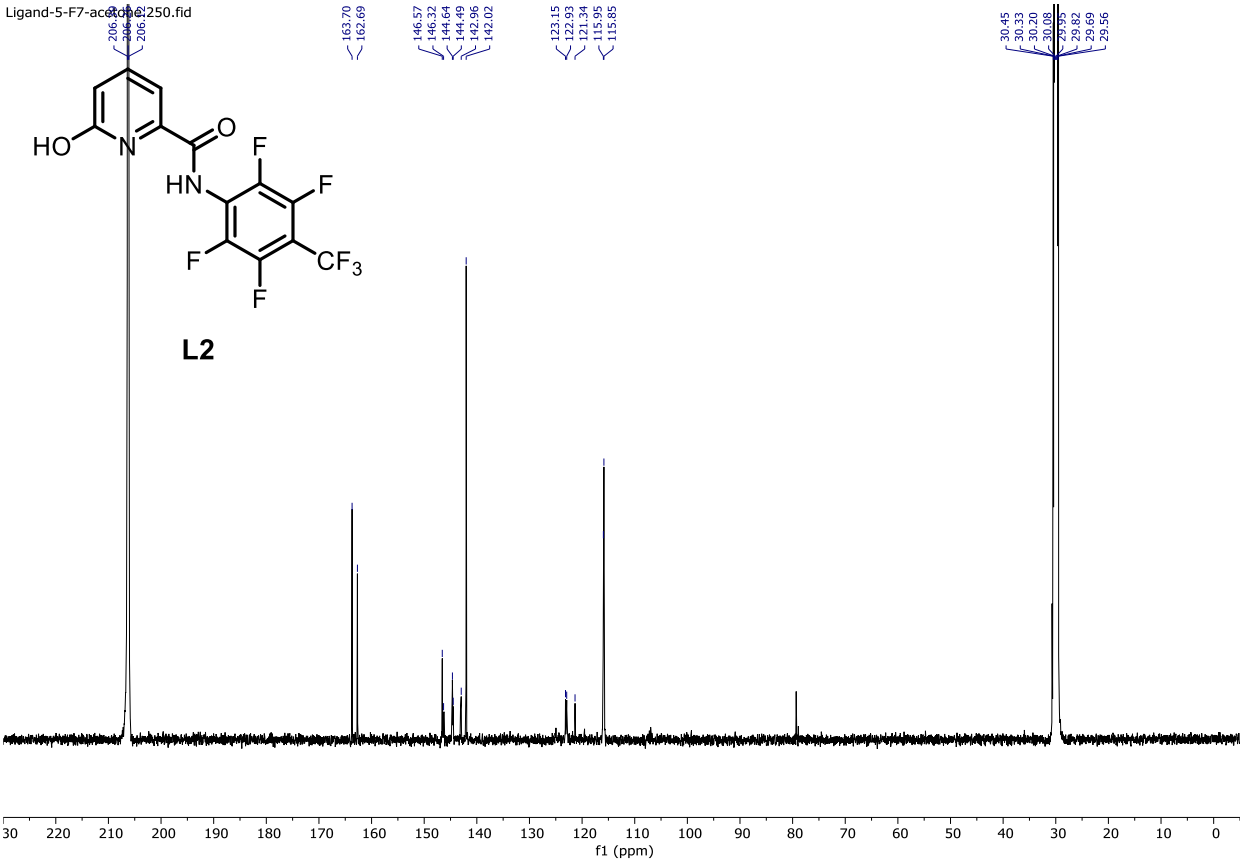
O
HN
F
F
F
F
CF3
L2
f1 (ppm)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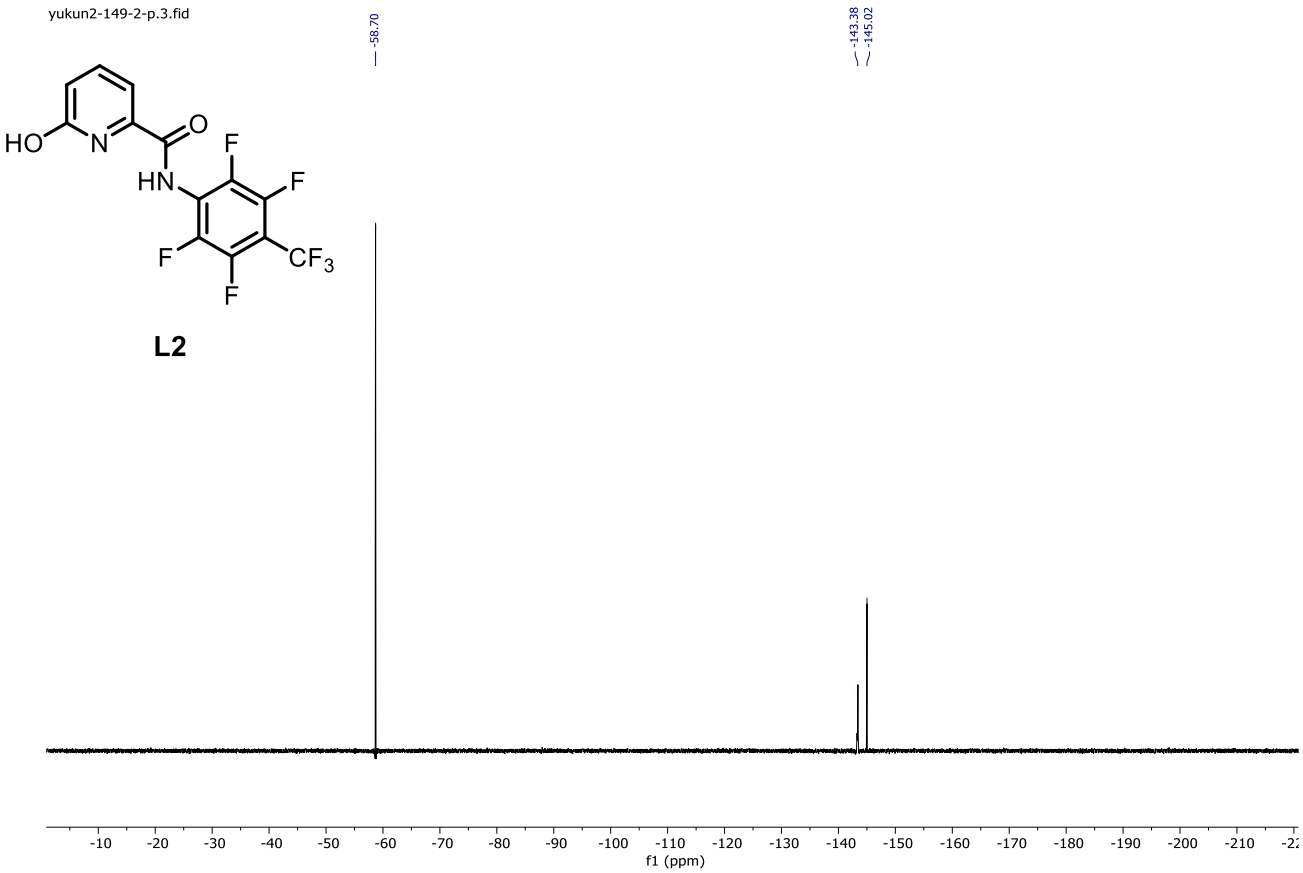
HN
F
F
F
F
CF3
L2
f1 (ppm)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HN
F
F
F
F
CF3
L2
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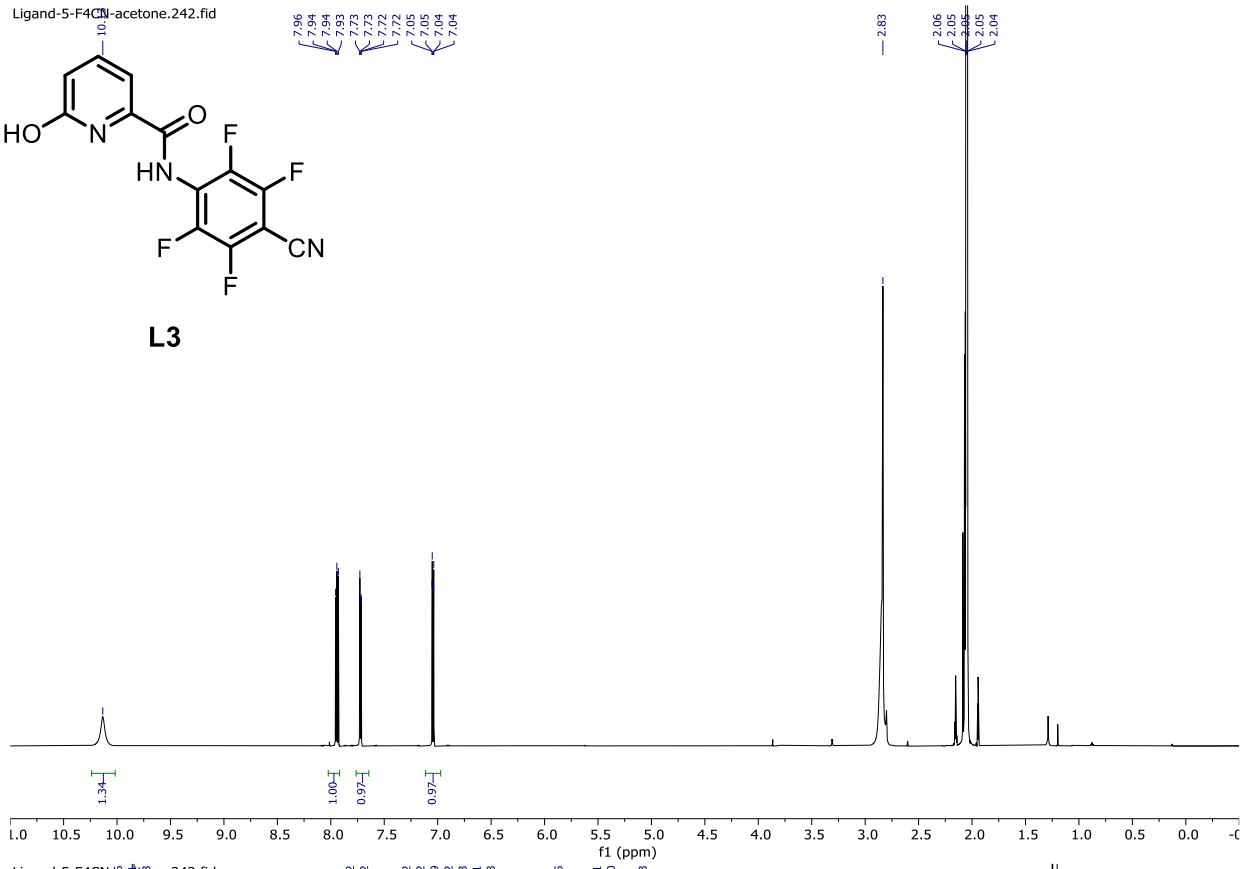
f1 (ppm)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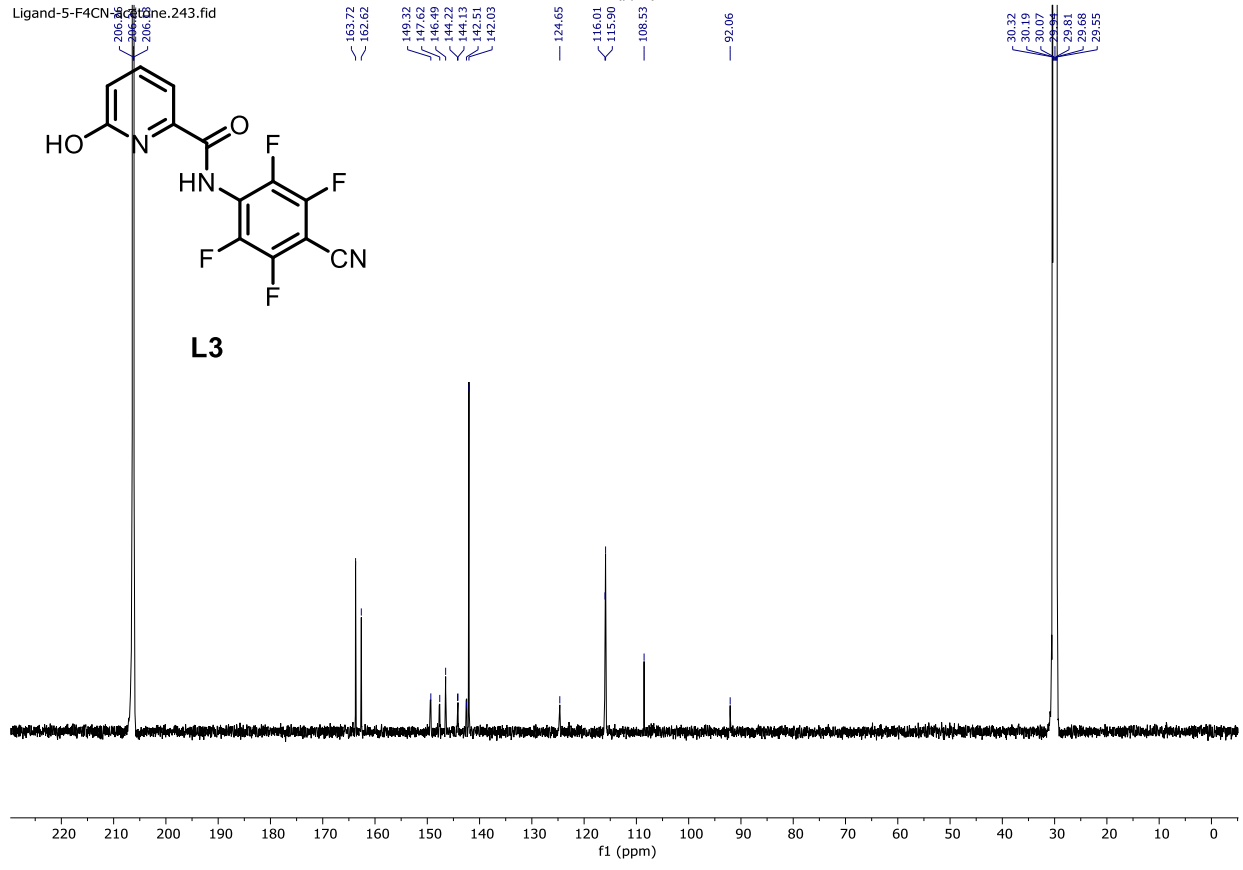
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CN
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147.62
146.49
144.22
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142.51
142.03
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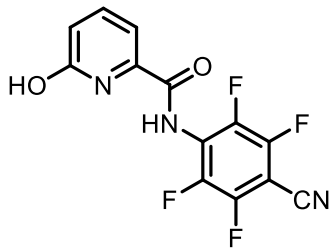

L3

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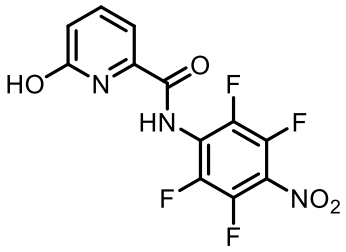

L4

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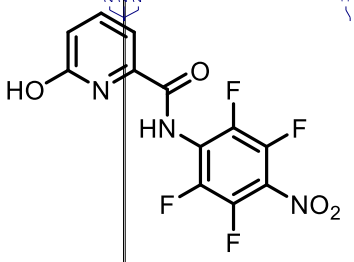

L4

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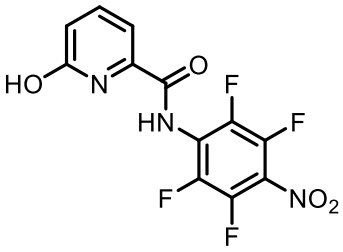
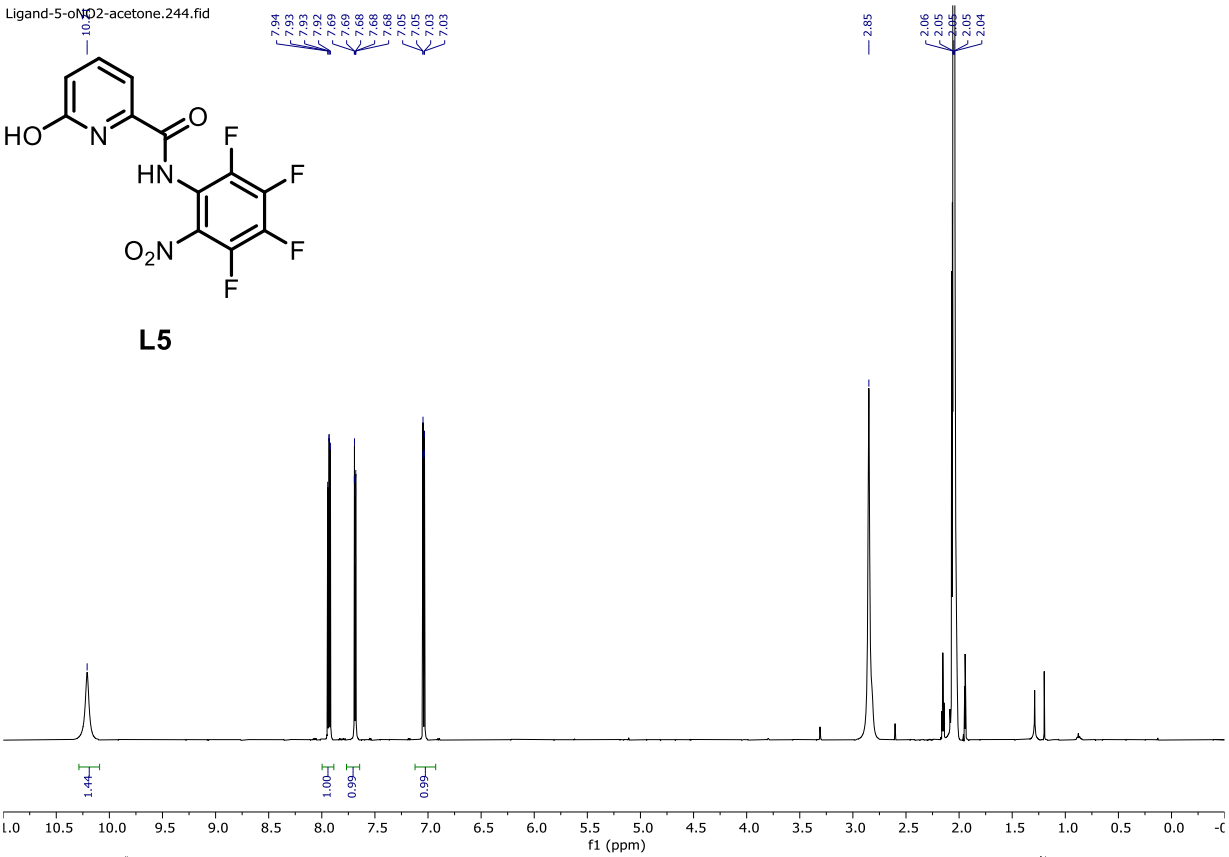


L4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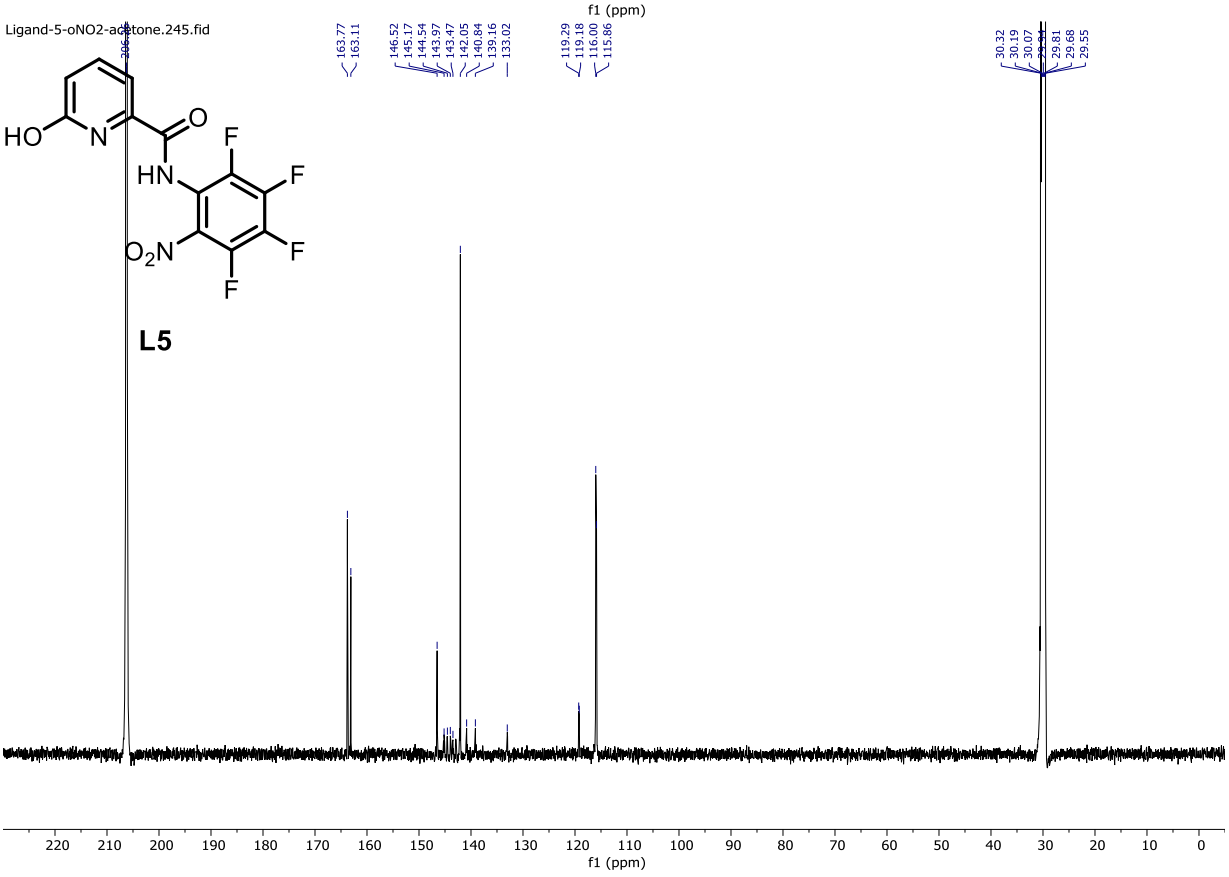
L5
f1 (ppm)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f1 (ppm)

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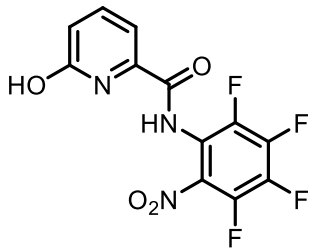
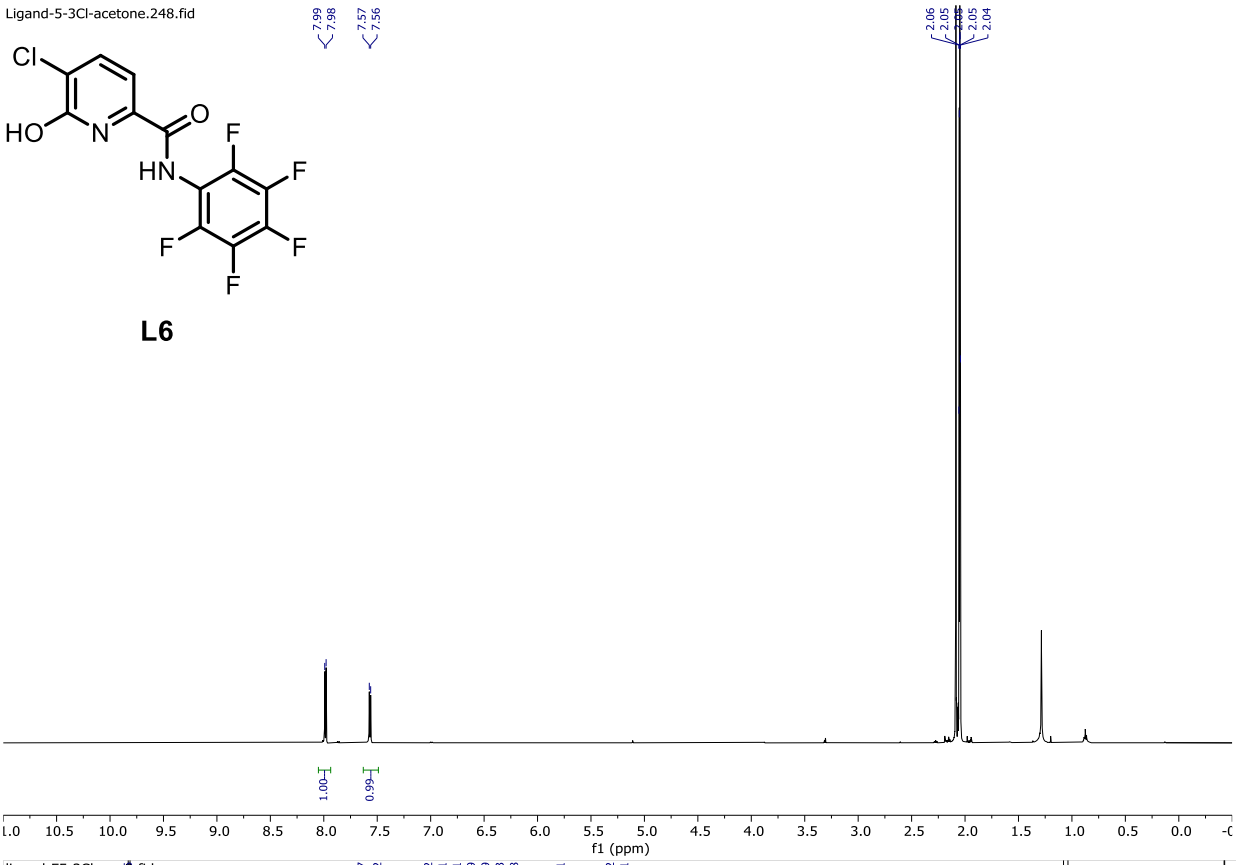


L5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F
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F
F
L6
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2.05
2.05
2.04
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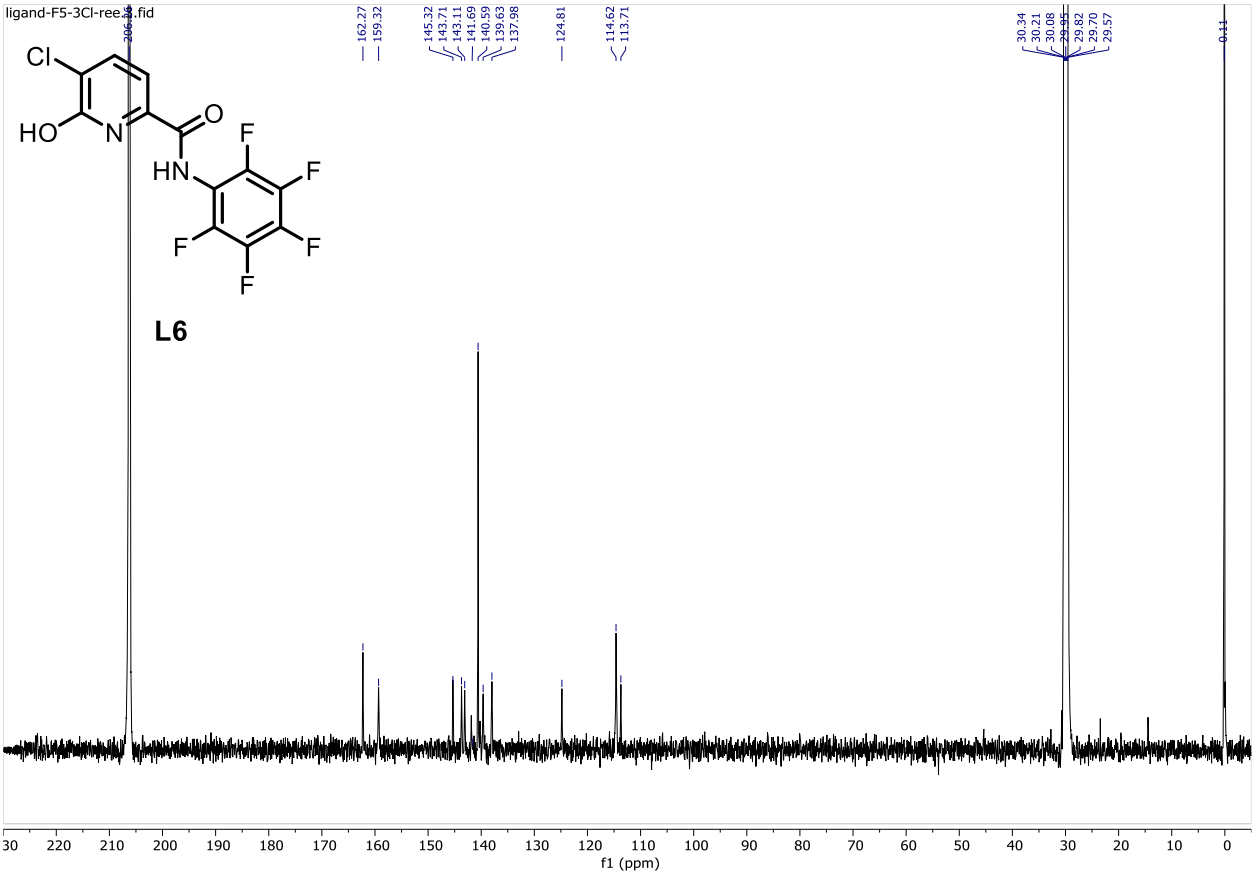
0.99
f1 (ppm)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N
O
HN
F
F
F
F
F
L6
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139.63
137.98
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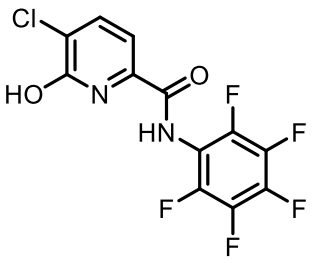
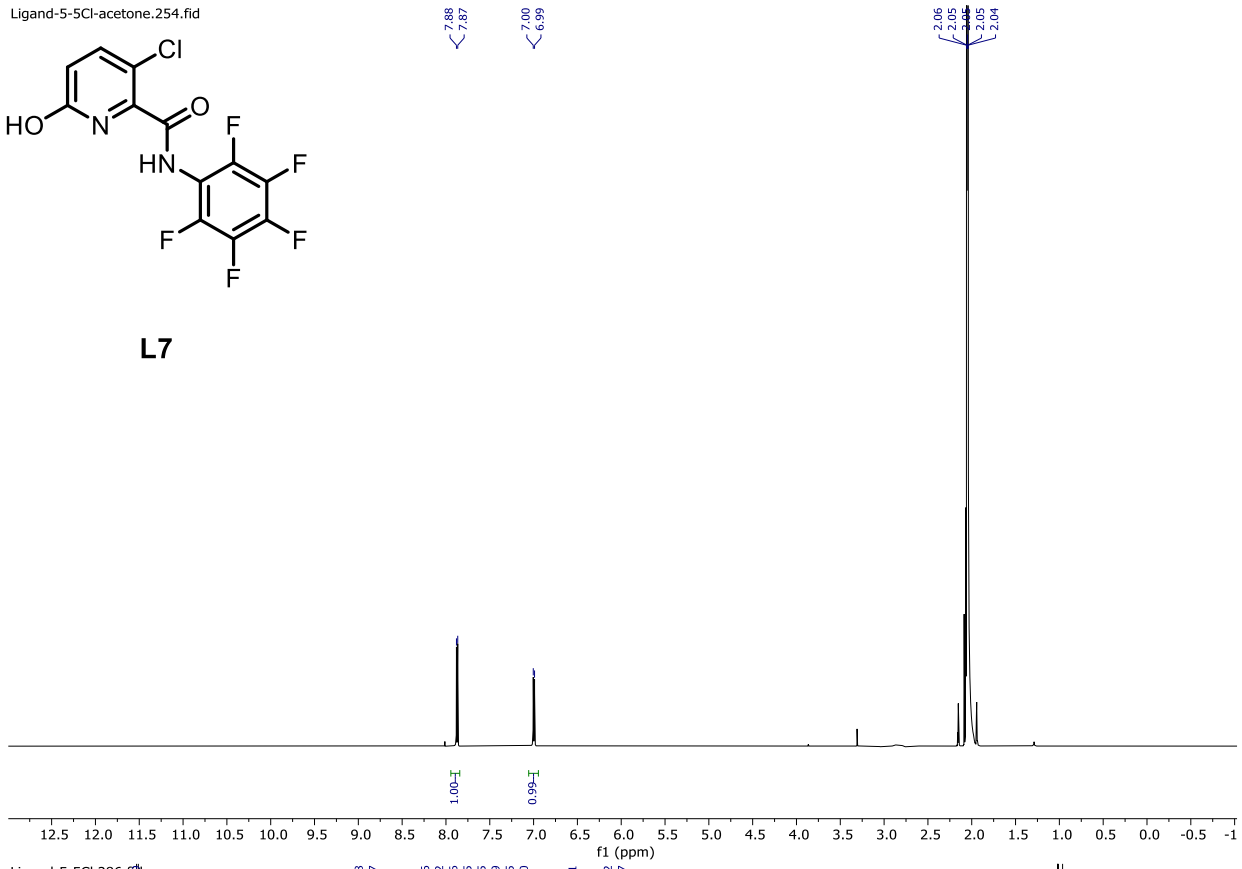
f1 (ppm)

yukun3-72-2.32.fid



L6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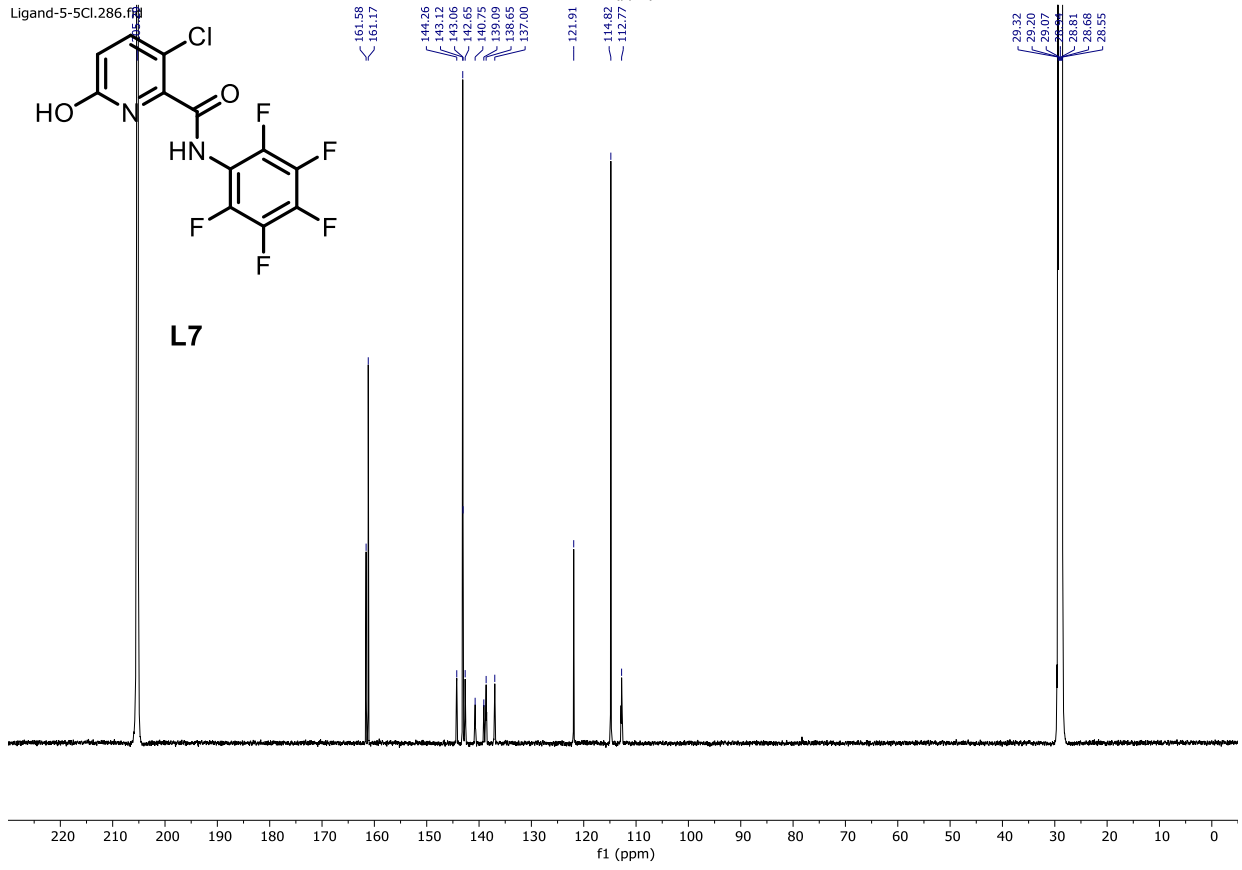
0.99
f1 (ppm)

L7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F
F
F
F
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143.06
142.65
140.75
139.09
138.65
137.00
121.91
114.82
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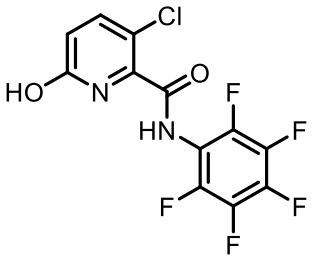
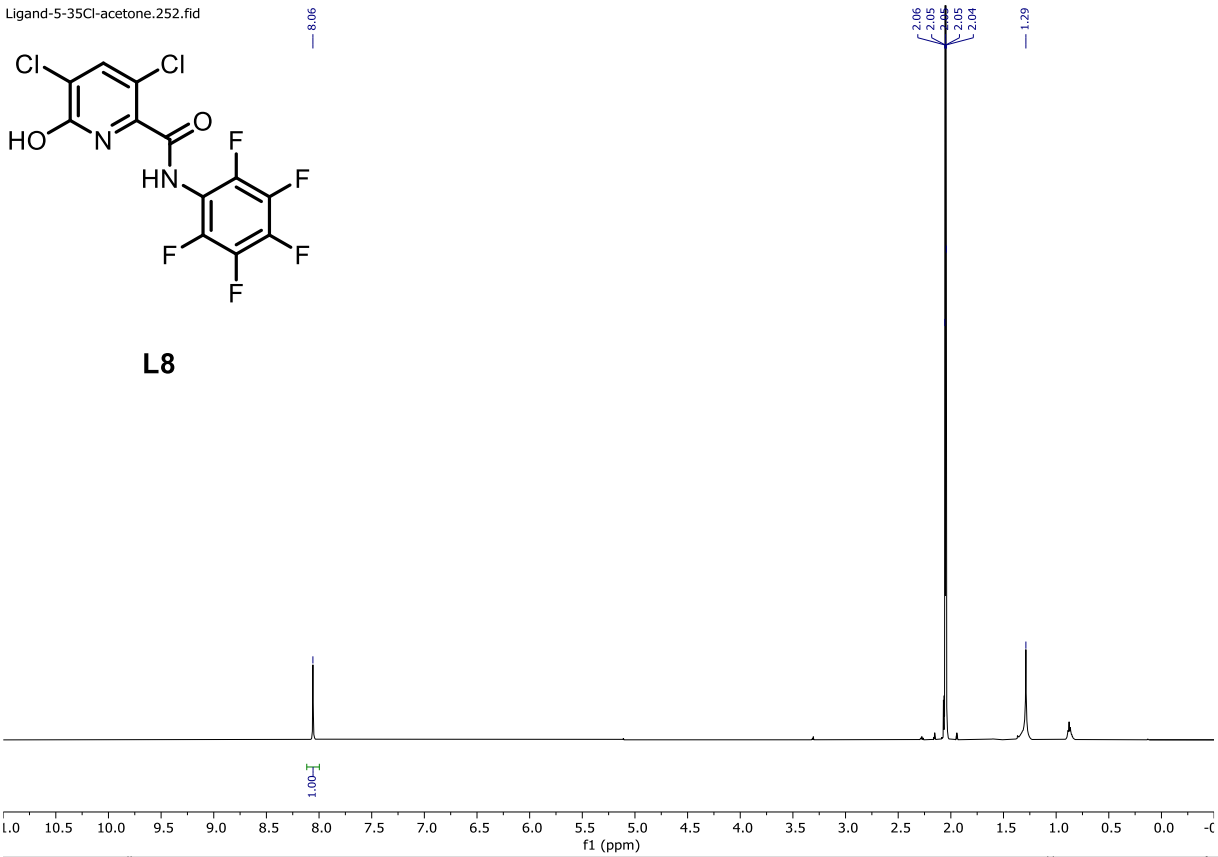
28.55
f1 (ppm)

L7

yukun3-72-3.34.fid



L7


Ligand-5-35Cl-acetone.252.fid
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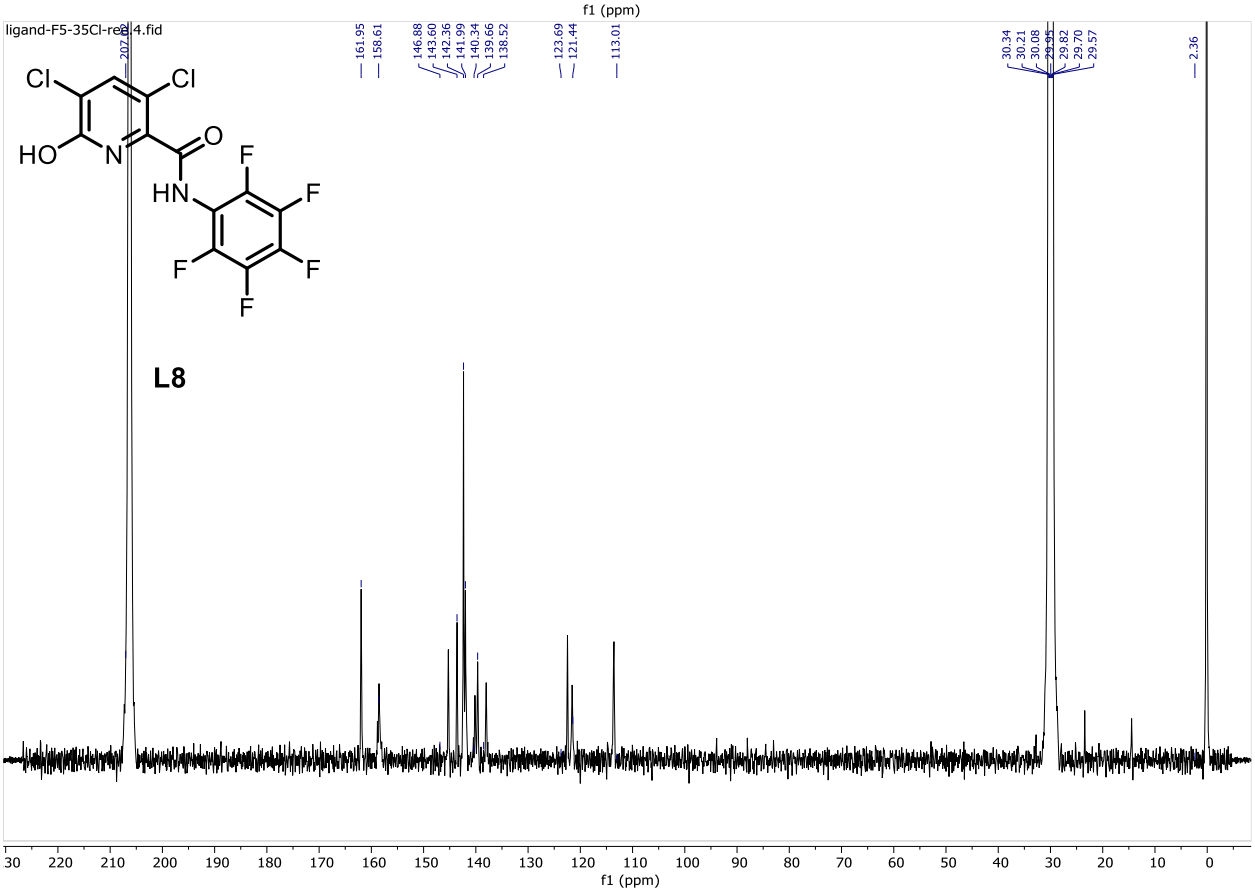
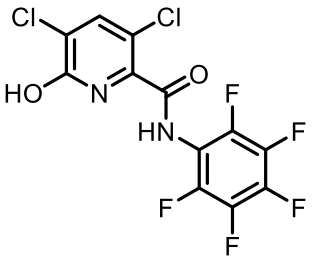
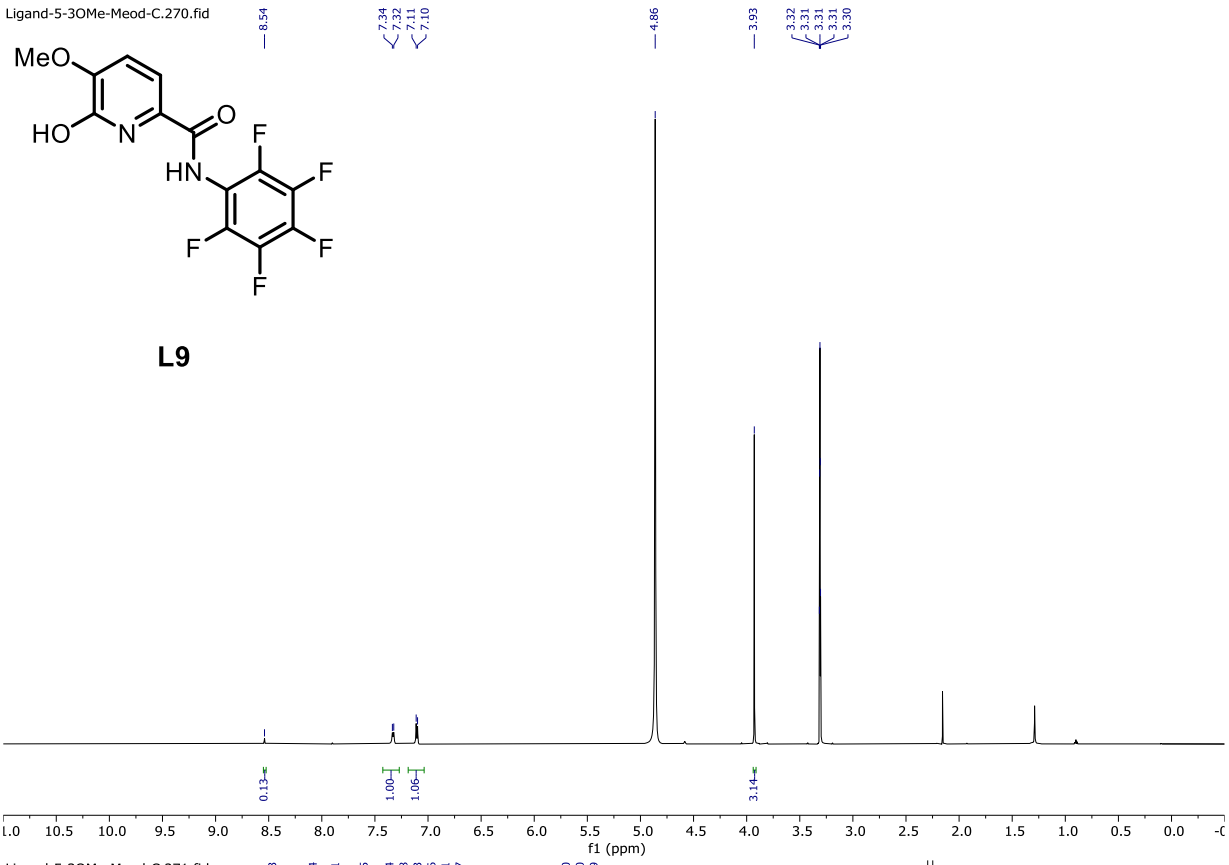
2.04
1.29
Cl
Cl
HO
N
O
HN
F
F
F
F
F
L8
1.00
f1 (ppm)


ligand-F5-35Cl-red.4.fid
161.95
158.61
146.88
143.60
142.36
141.99
140.34
139.66
138.52
123.69
121.44
113.01
30.34
30.21
30.08
29.82
29.70
29.57
2.36
Cl
Cl
HO
N
O
HN
F
F
F
F
F
L8
f1 (ppm)

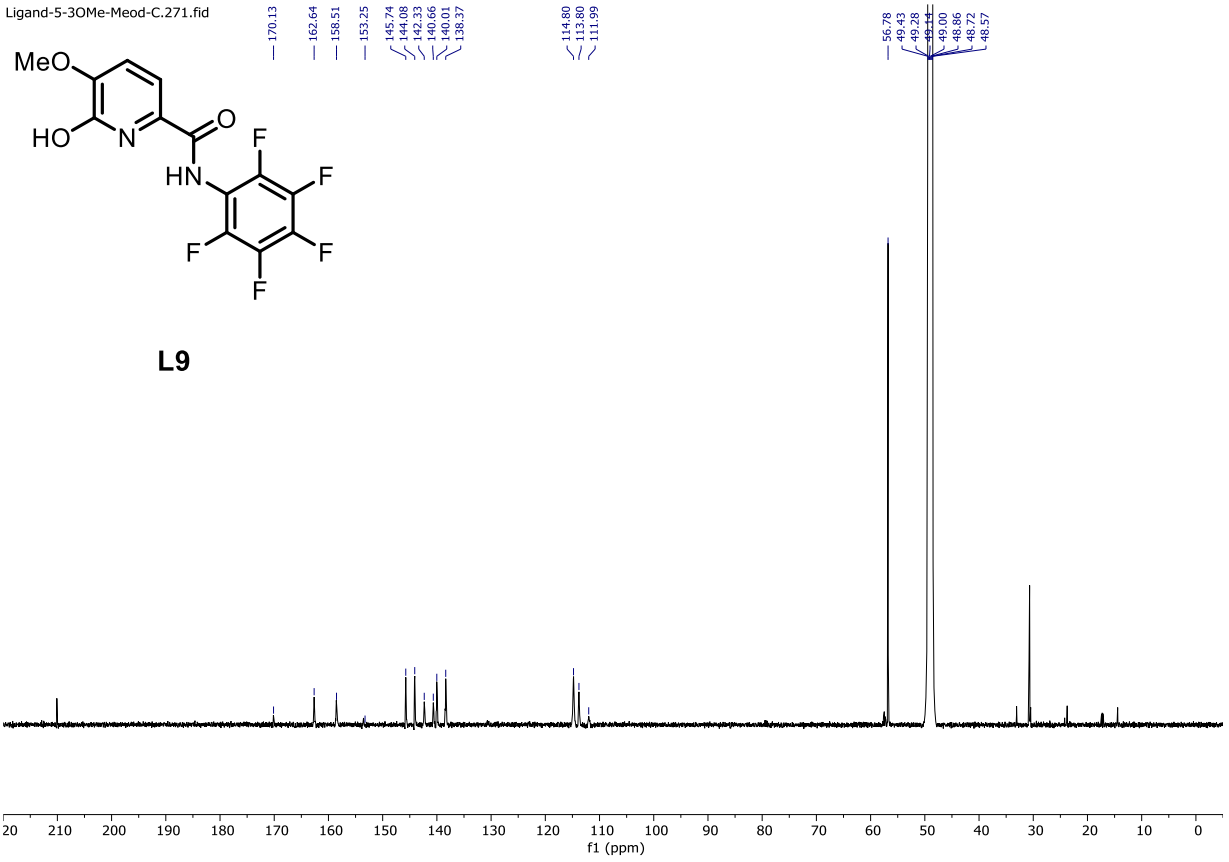
yukun3-72-1.30.fid



L8

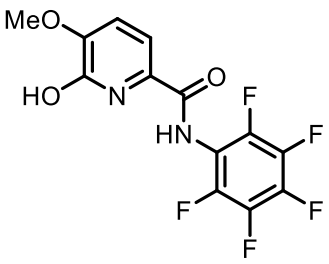

Ligand-5-3OMe-Meod-C.270.fid
8.54
7.34
7.32
7.11
7.10
4.86
3.93
3.32
3.31
3.31
3.31
3.30
MeO
HO
N
O
HN
F
F
F
F
F
0.13
1.00
1.06
3.14
f1 (ppm)

L9

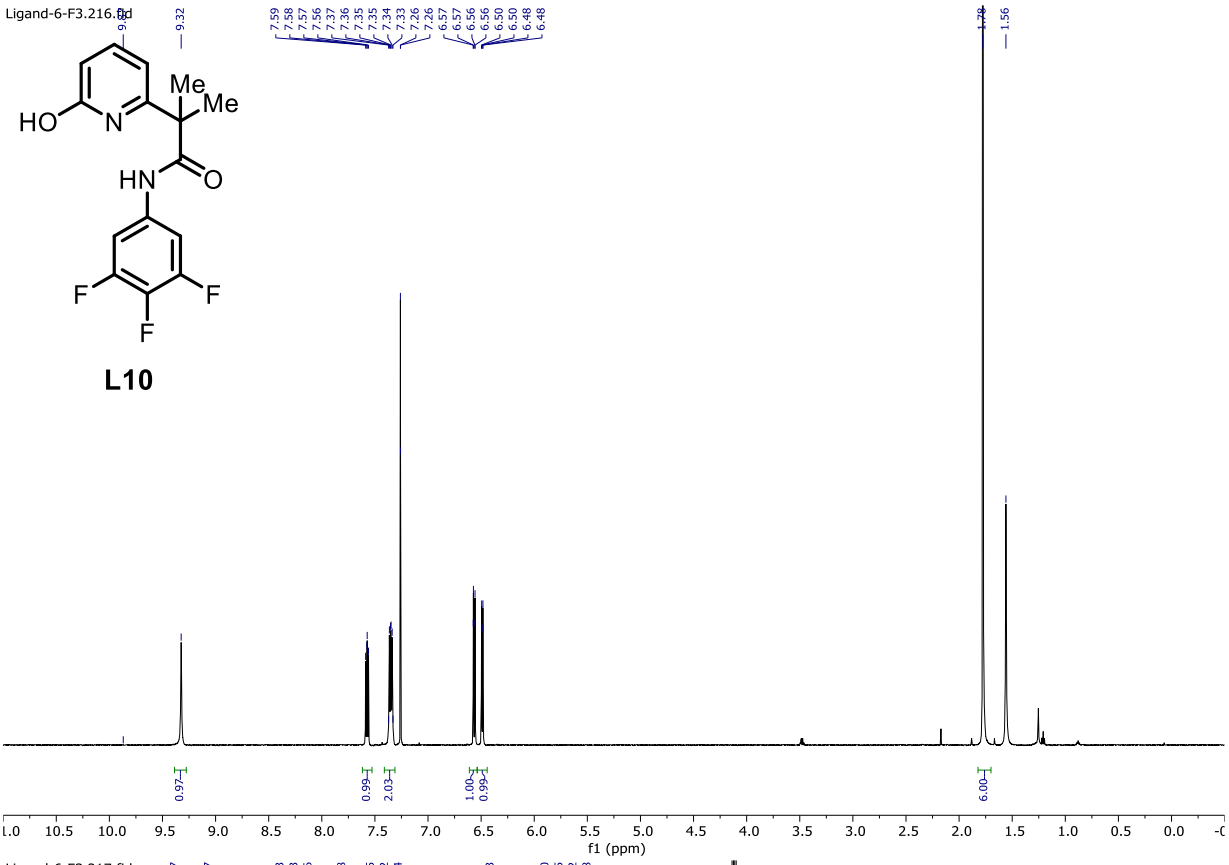

Ligand-5-3OMe-Meod-C.271.fid
170.13
162.64
158.51
153.25
145.74
144.08
142.33
140.66
140.01
138.37
114.80
113.80
111.99
56.78
49.43
49.28
49.14
49.00
48.86
48.72
48.57
MeO
HO
N
O
HN
F
F
F
F
F
f1 (ppm)

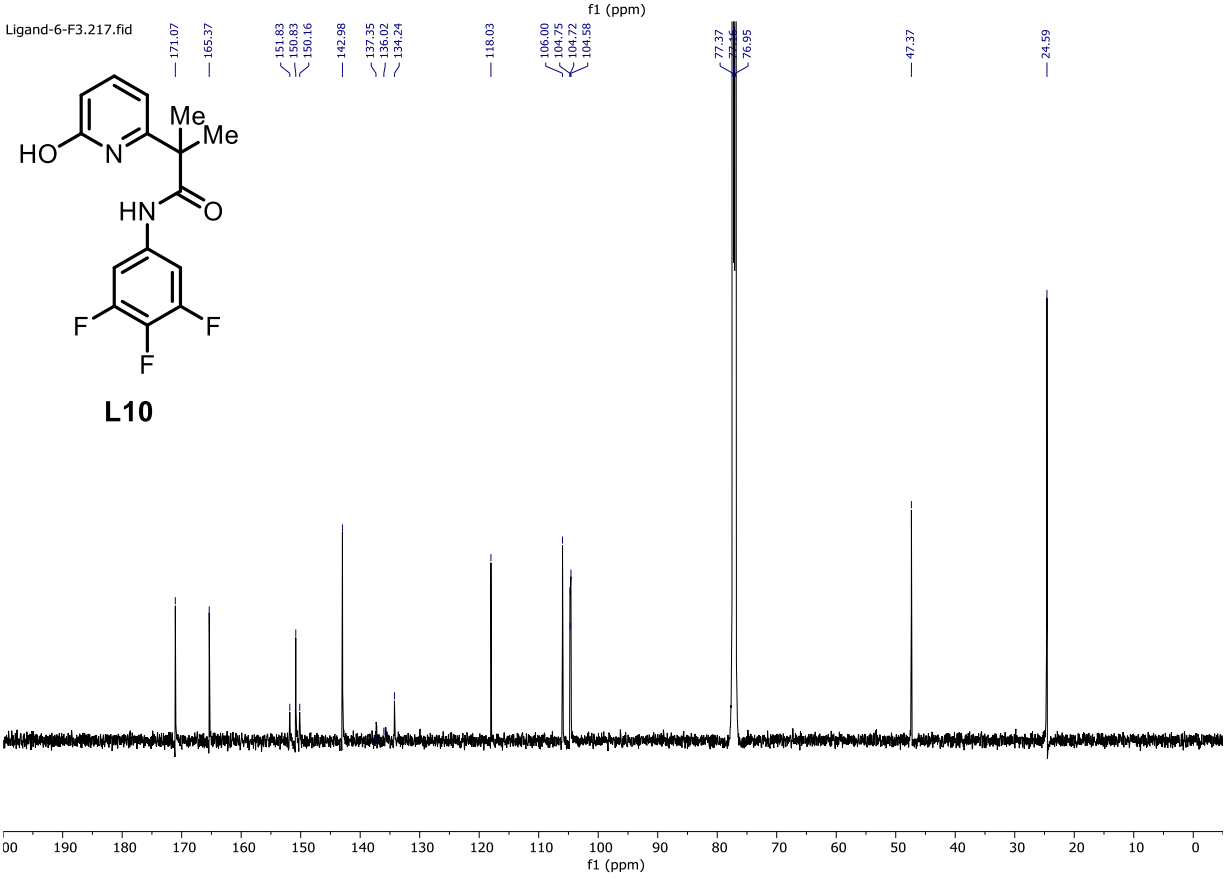
L9

Ligand-5-3OMe-acetone.148.fid

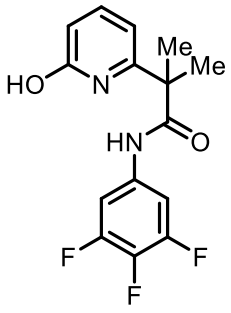


L9


Ligand-6-F3.216.fid
9.32
7.59
7.58
7.57
7.56
7.37
7.36
7.35
7.35
7.34
7.33
7.26
7.26
6.57
6.57
6.56
6.56
6.50
6.50
6.48
6.48
1.78
1.56
Me
Me
HO
N
HN
O
F
F
F
L10
0.97
0.99
2.03
1.00
0.99
6.00
f1 (ppm)

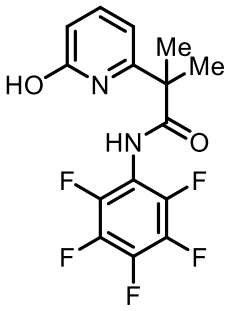

Ligand-6-F3.217.fid
171.07
165.37
151.83
150.83
150.16
142.98
137.35
136.02
134.24
118.03
106.00
104.75
104.72
104.58
77.37
77.16
76.95
47.37
24.59
Me
Me
HO
N
HN
O
F
F
F
L10
f1 (ppm)

yukun2-143-4-p.11.fid



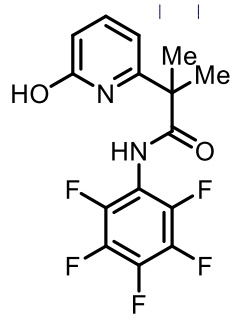
L10

Ligand-6-F5.218.fid



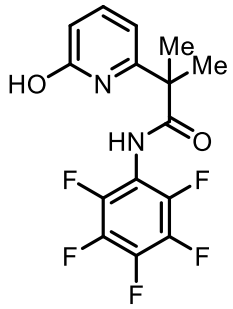
L11

Ligand-6-F5.219.fid

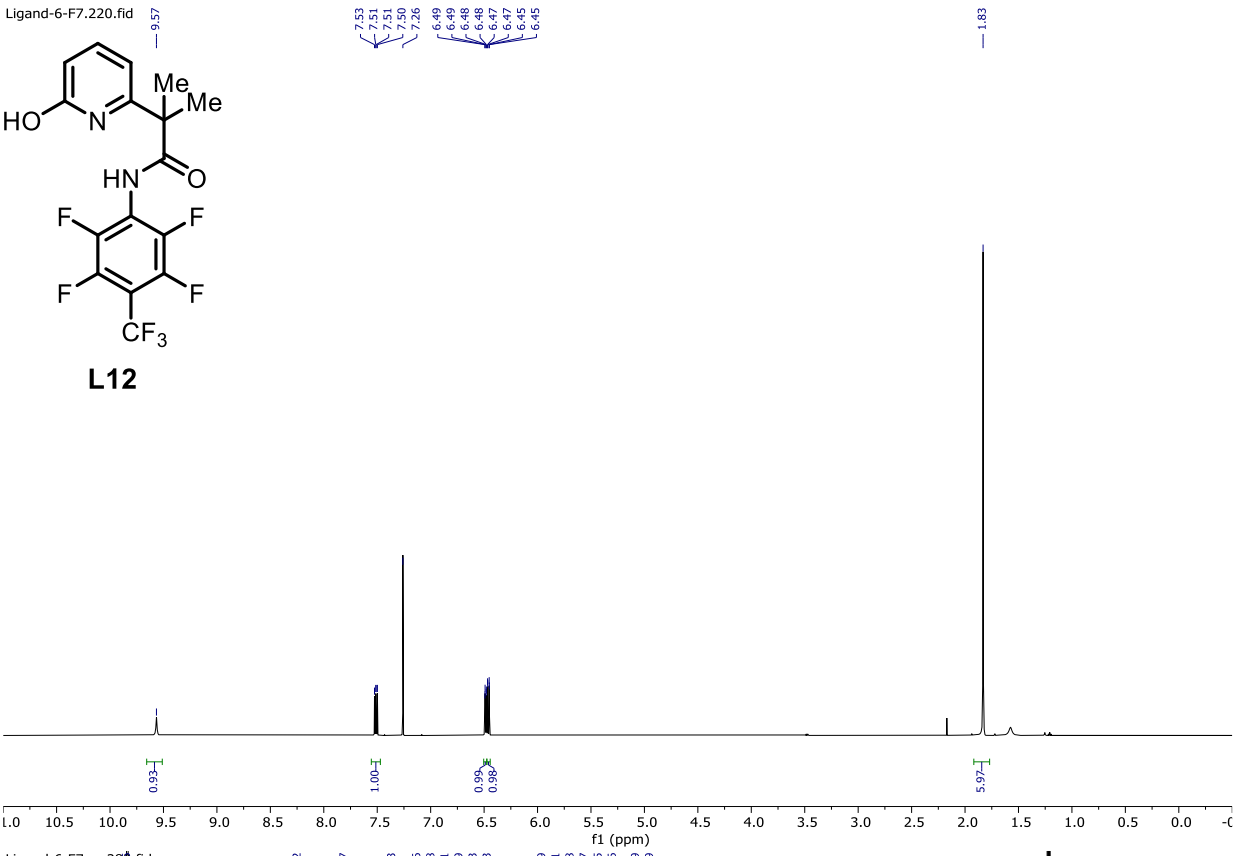


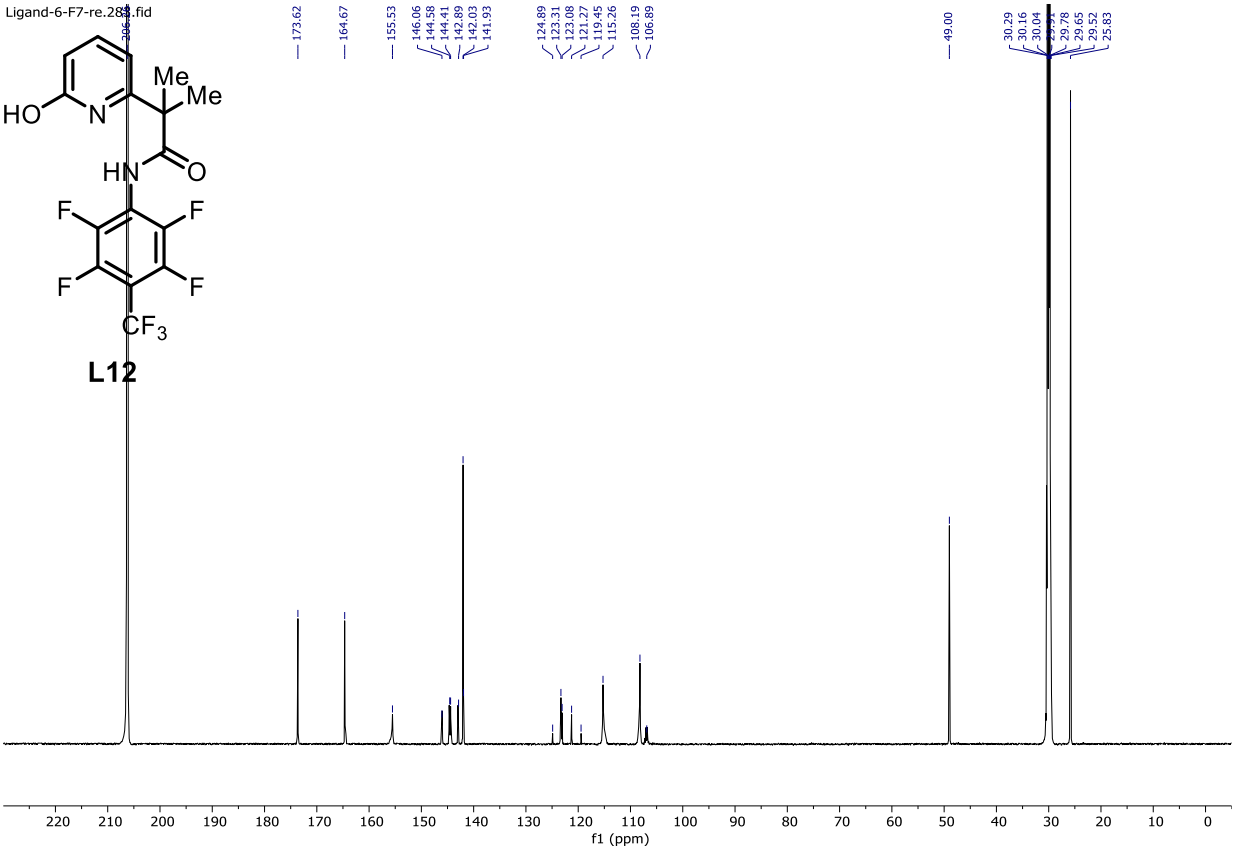
L11

yukun2-143-3-p.11.fid

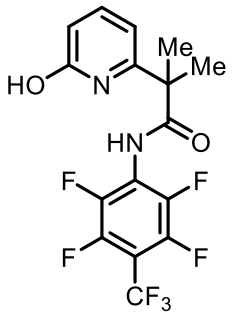


L11

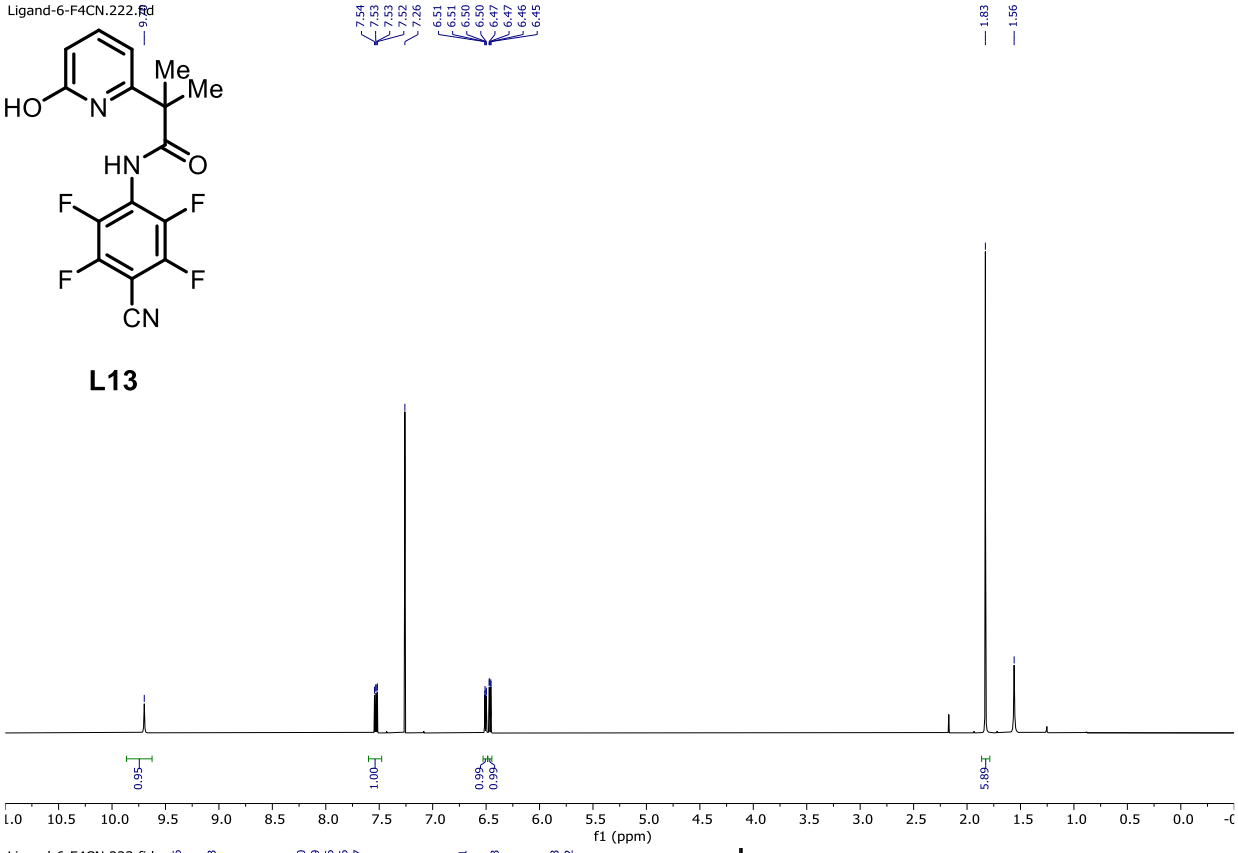

Ligand-6-F7.220.fid
9.57
7.53
7.51
7.51
7.50
7.26
6.49
6.49
6.48
6.48
6.47
6.47
6.45
6.45
1.83
Me
Me
HO
N
HN
O
F
F
F
F
CF3
L12
0.93
1.00
0.99
0.98
5.97
f1 (ppm)

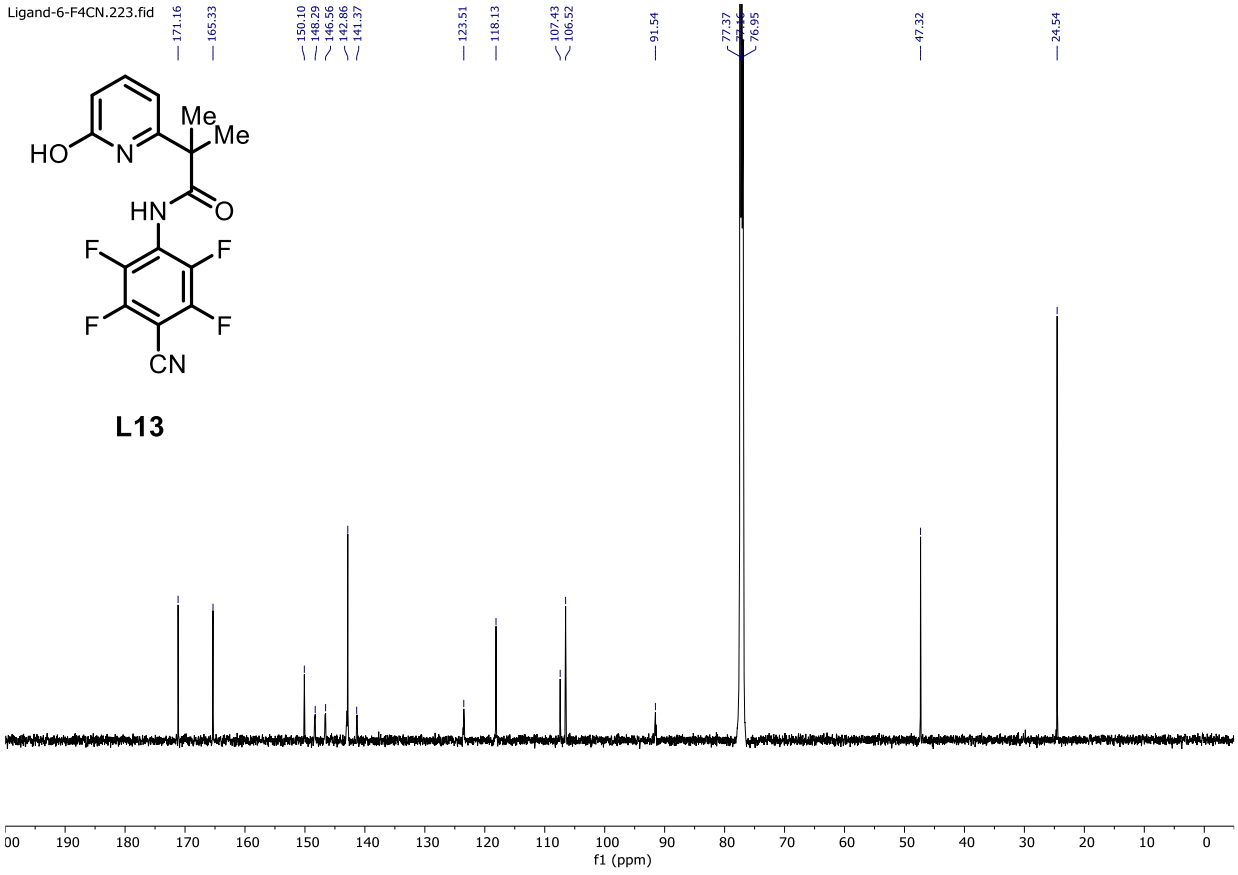

Ligand-6-F7-re.28
173.62
164.67
155.53
146.06
144.58
144.41
142.89
142.03
141.93
124.89
123.31
123.08
121.27
119.45
115.26
108.19
106.89
49.00
30.29
30.16
30.04
29.78
29.65
29.52
25.83
Me
Me
HO
N
HN
O
F
F
F
F
CF3
L12
f1 (ppm)

Ligand-6-F7-F.136.fid

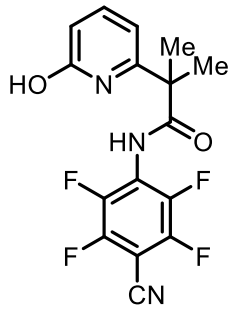


L12


Ligand-6-F4CN.222.fid
HO
N
Me
Me
HN
O
F
F
F
F
CN
L13
f1 (ppm)

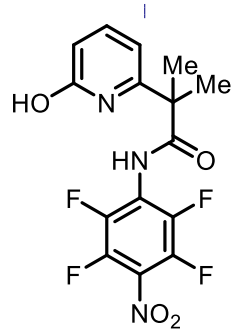

Ligand-6-F4CN.223.fid
HO
N
Me
Me
HN
O
F
F
F
F
CN
L13
f1 (ppm)

yukun2-143-1-p.11.fid



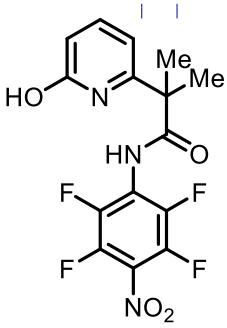
L13

Ligand-6-pNO2.224.fid



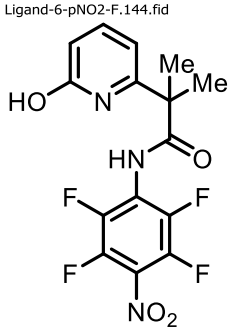
L14

Ligand-6-pNO2.225.fid



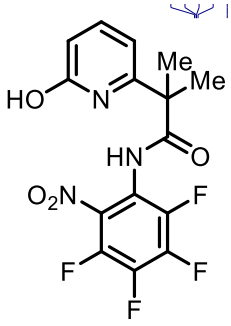
L14

Ligand-6-pNO2-F.144.fid



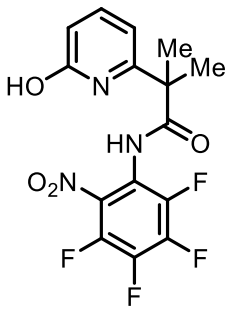
L14

Ligand-6-oNO2.226.fid



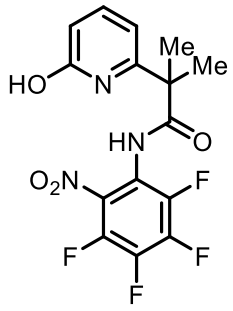
L15

Ligand-6-oNO2.227.fid

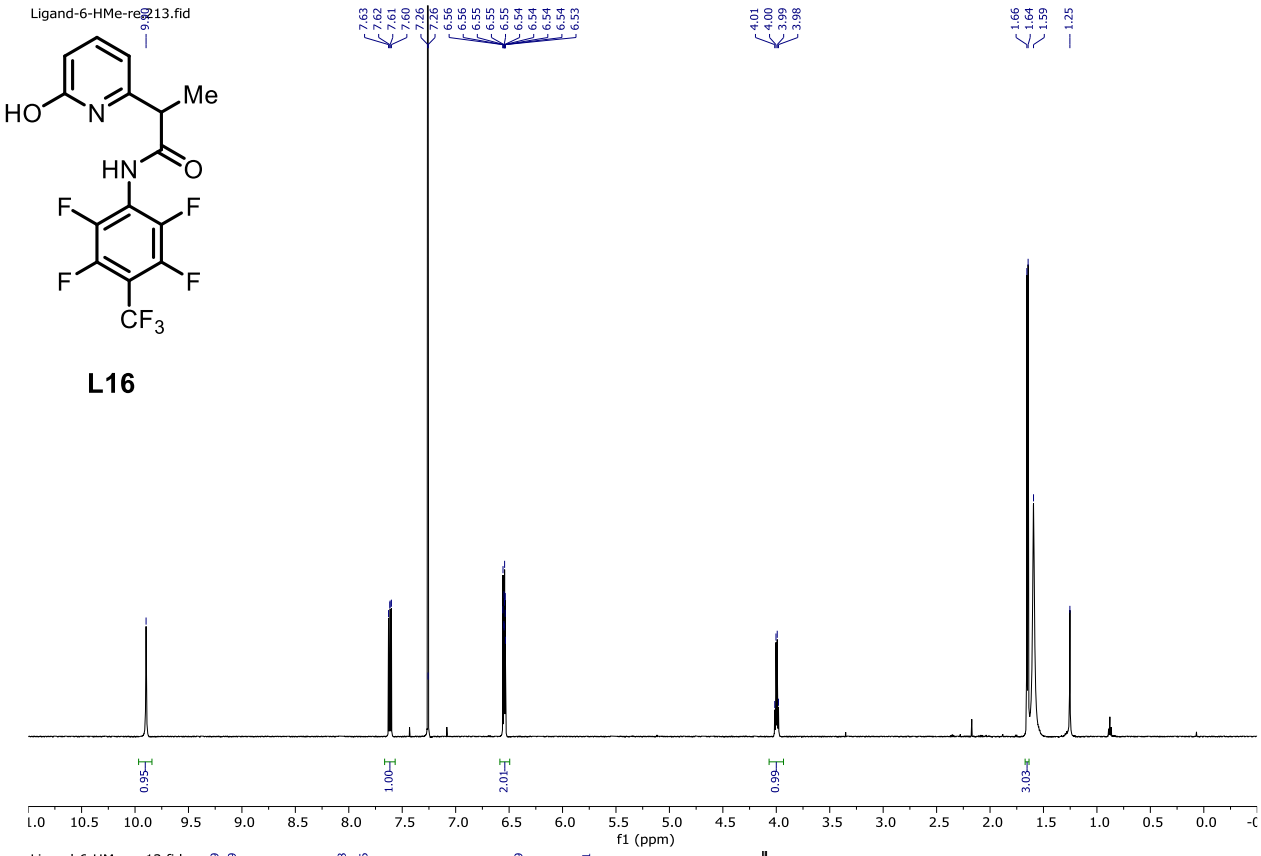


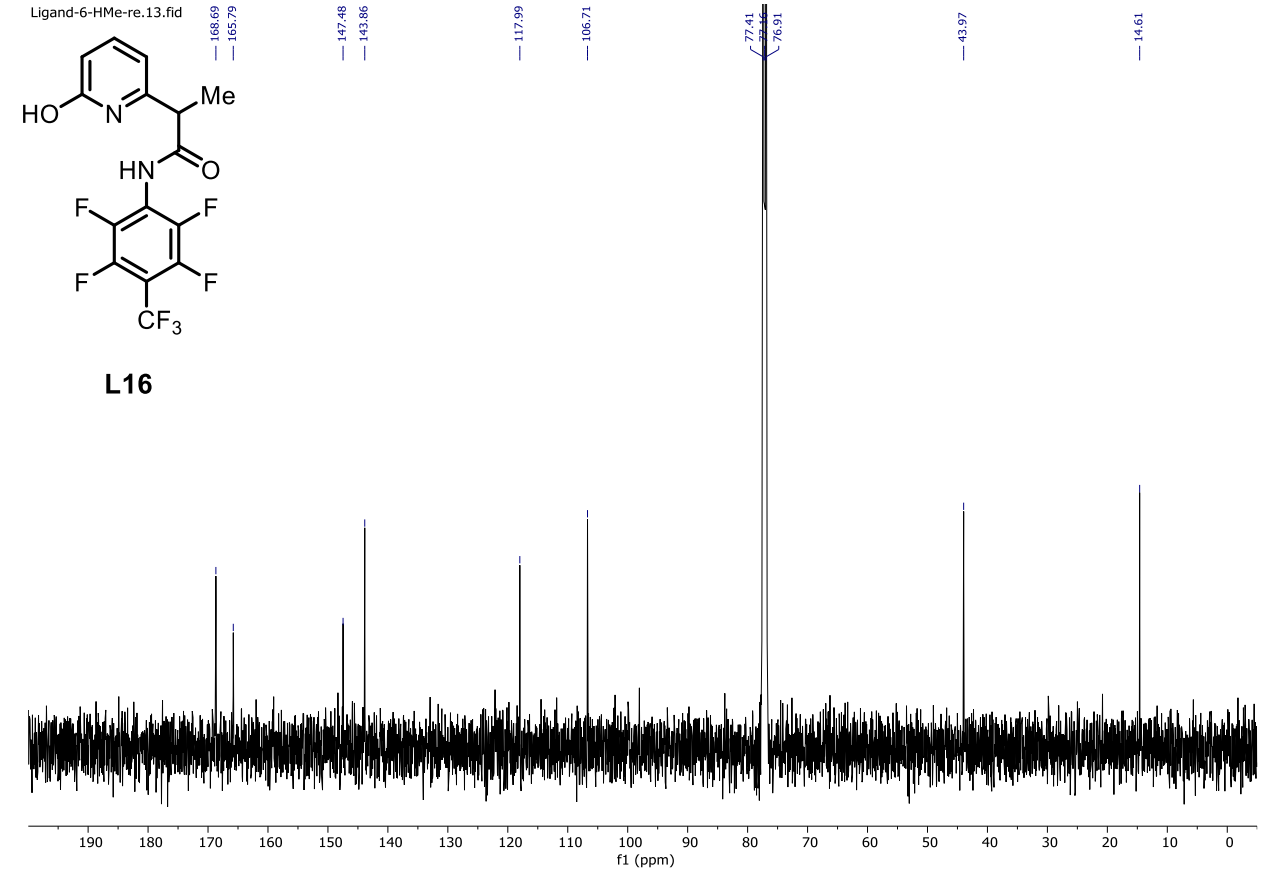
L15

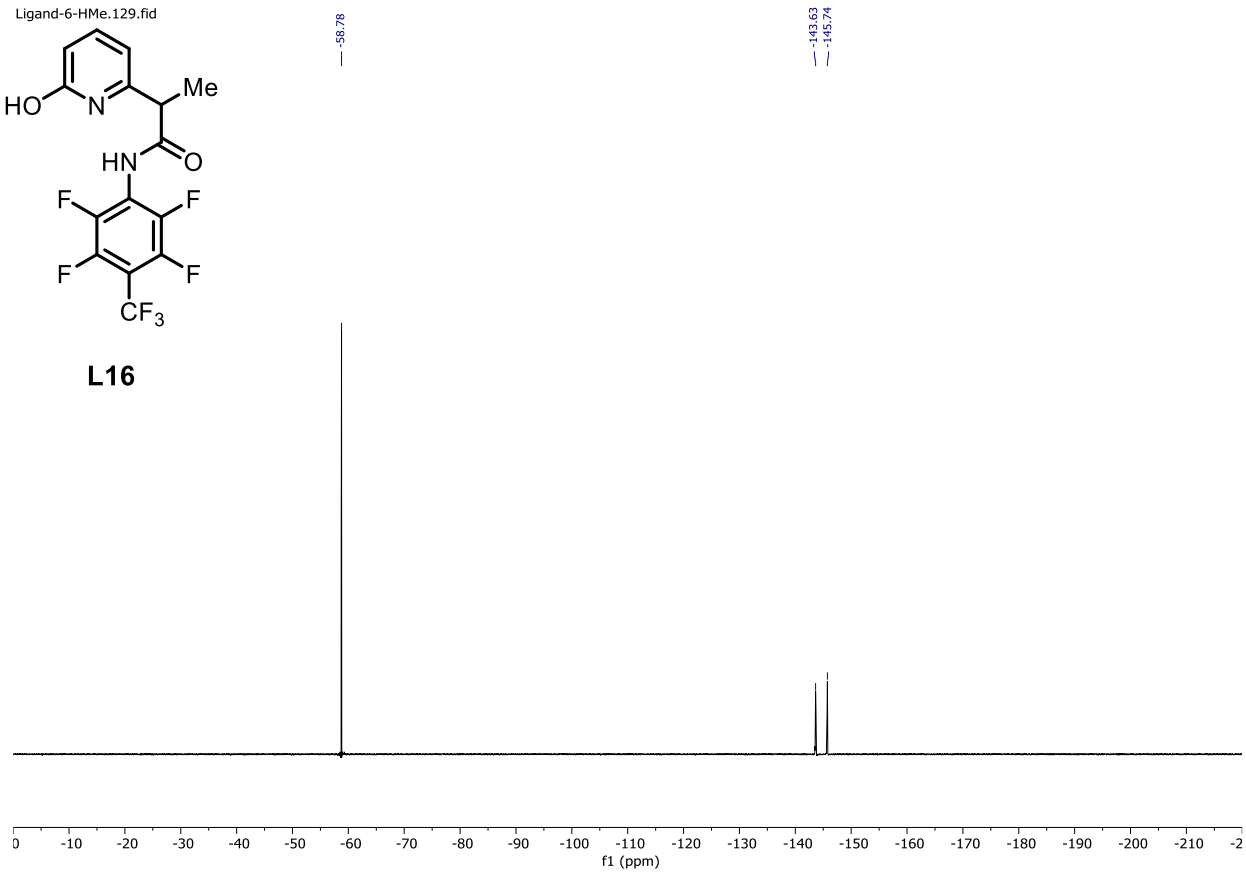
yukun2-146-2-3-p.11.fid

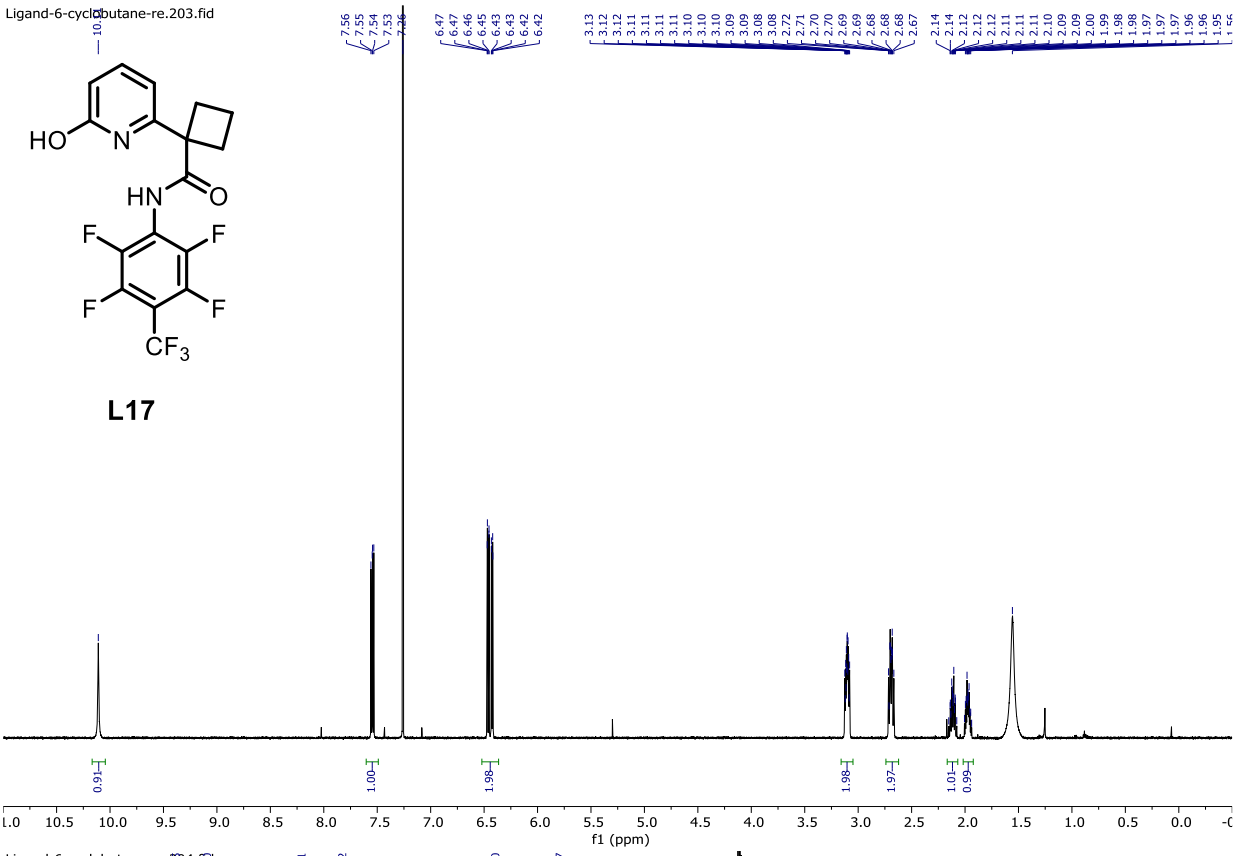


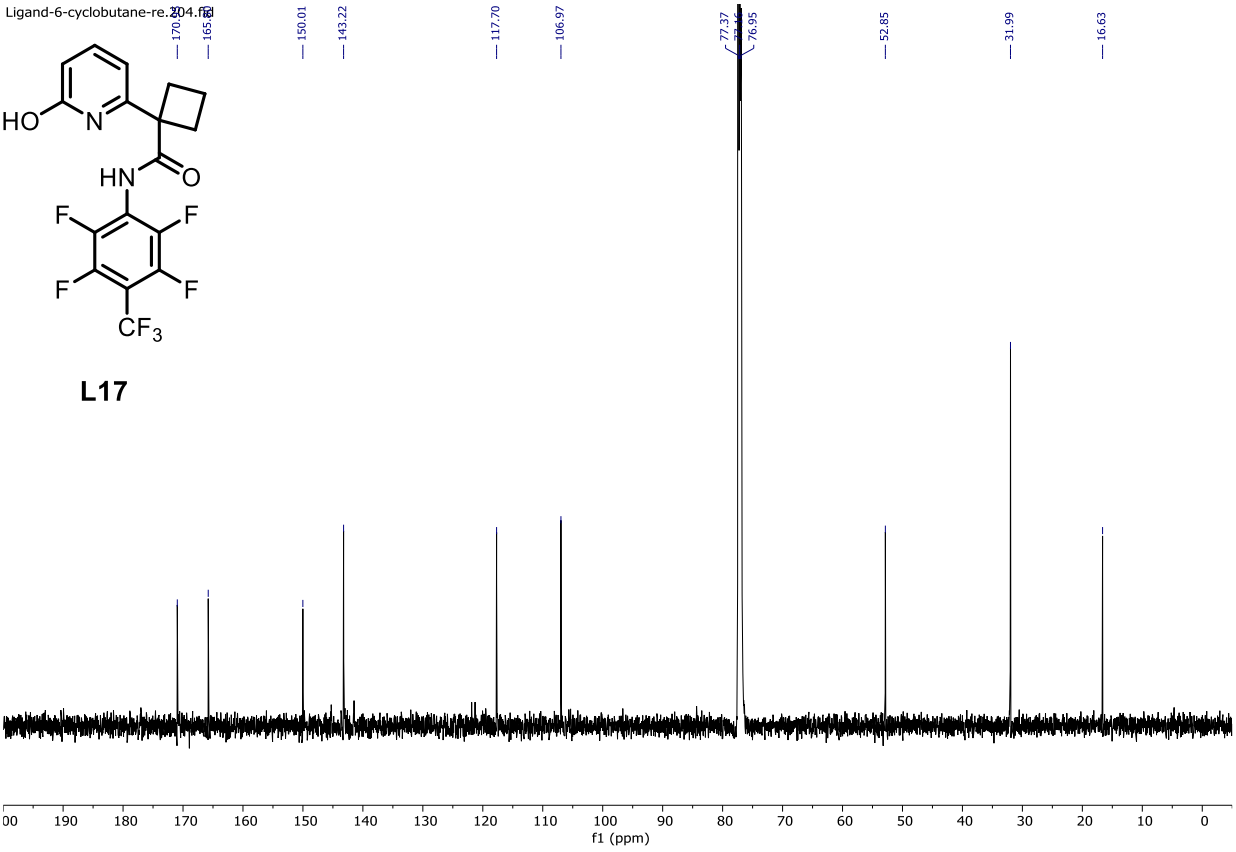
L15


Ligand-6-HMe-re.13.fid
HO
N
Me
HN
O
F
F
F
F
CF3
L16
7.63
7.62
7.61
7.60
7.26
6.56
6.55
6.55
6.55
6.54
6.54
6.54
6.54
6.53
4.01
4.00
3.99
3.98
1.66
1.64
1.59
1.25
0.95
1.00
2.01
0.99
3.03
f1 (ppm)

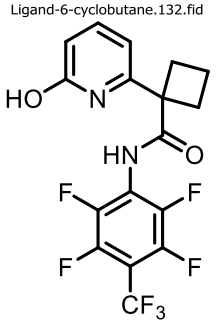

Ligand-6-HMe-re.13.fid
HO
N
Me
HN
O
F
F
F
F
CF3
L16
168.69
165.79
147.48
143.86
117.99
106.71
77.41
77.16
76.91
43.97
14.61
f1 (ppm)


Ligand-6-HMe.129.fid
-58.78
-143.63
-145.74
HO
N
Me
HN
O
F
F
F
F
CF3
L16
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

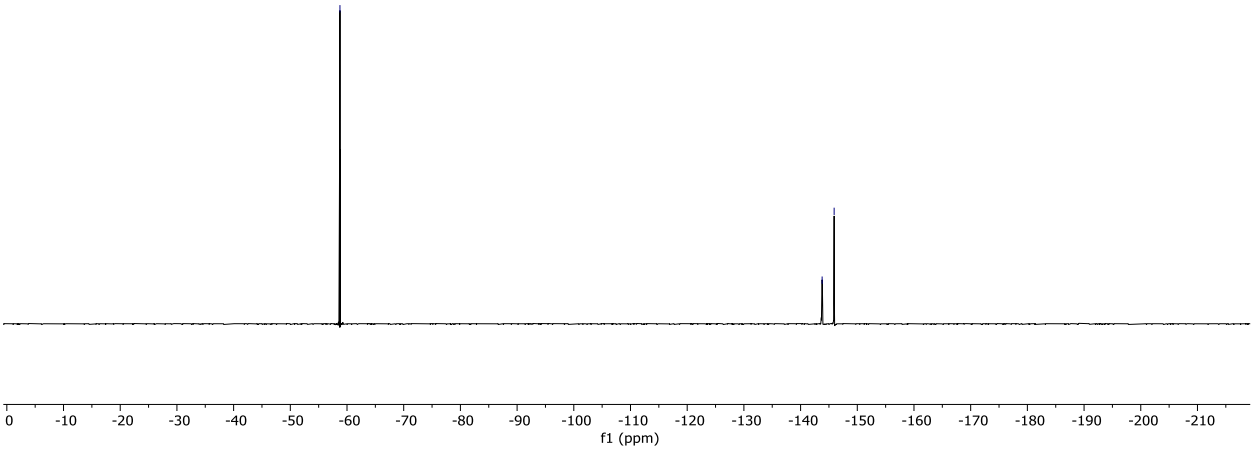

Ligand-6-cyclobutane-re.203.fid
HO
N
HN
O
F
F
F
F
CF3
L17
f1 (ppm)

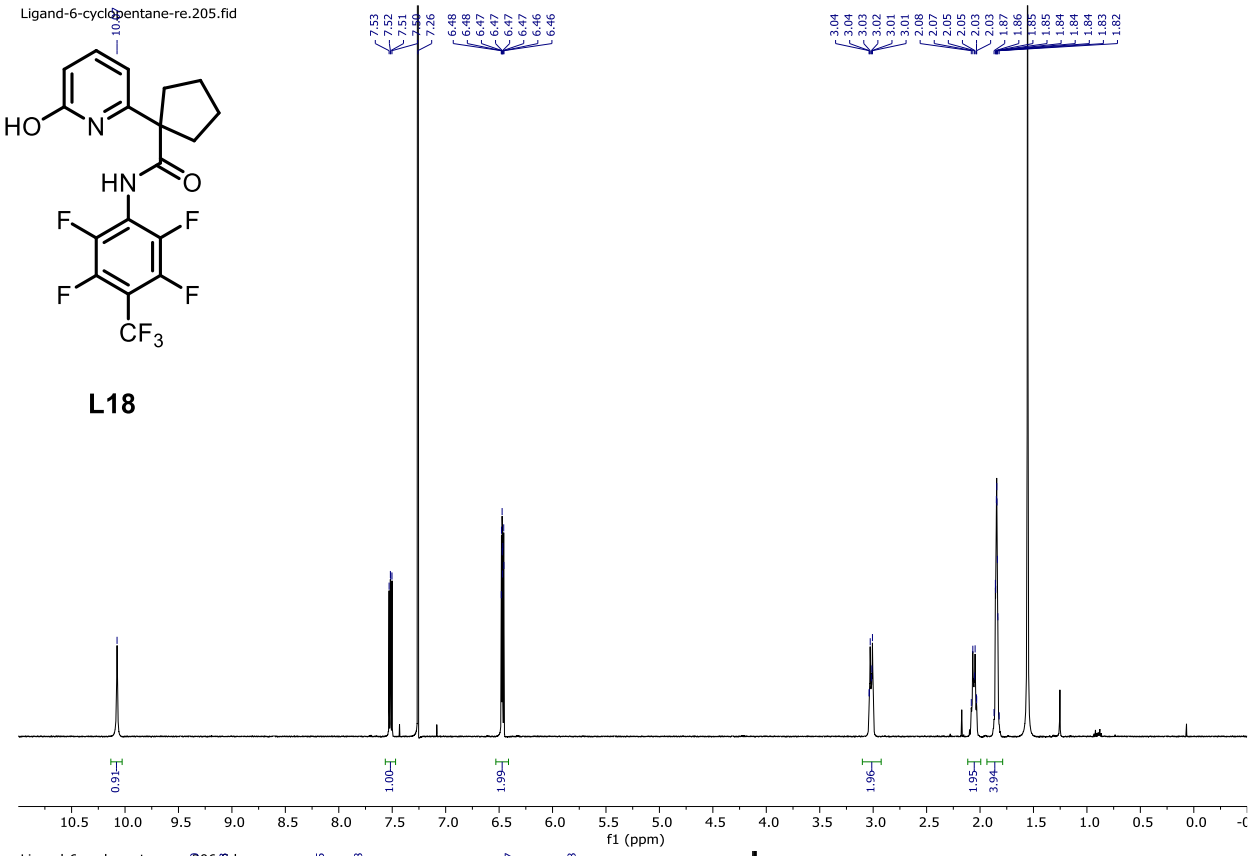

Ligand-6-cyclobutane-re.204.fid
HO
N
HN
O
F
F
F
F
CF3
L17
f1 (ppm)

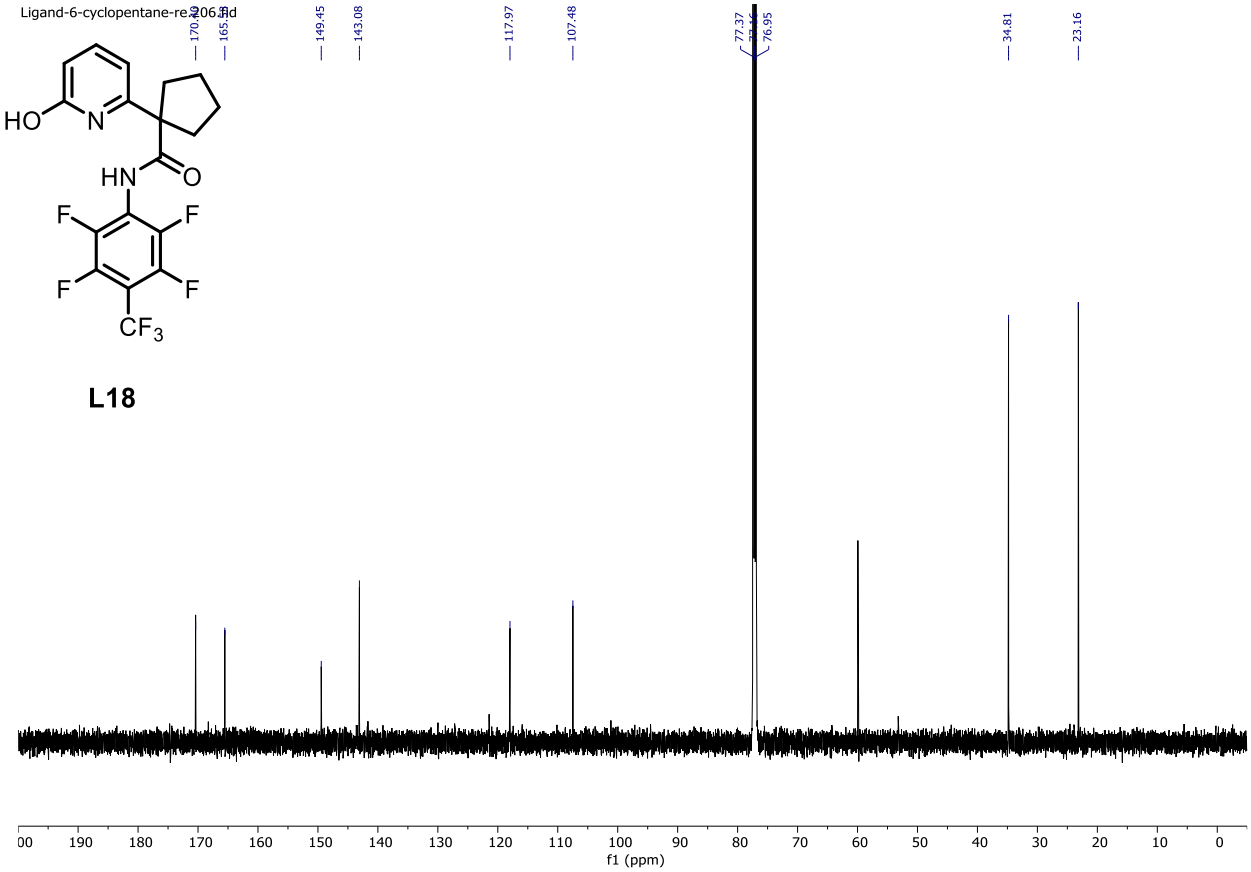
Ligand-6-cyclobutane.132.fid

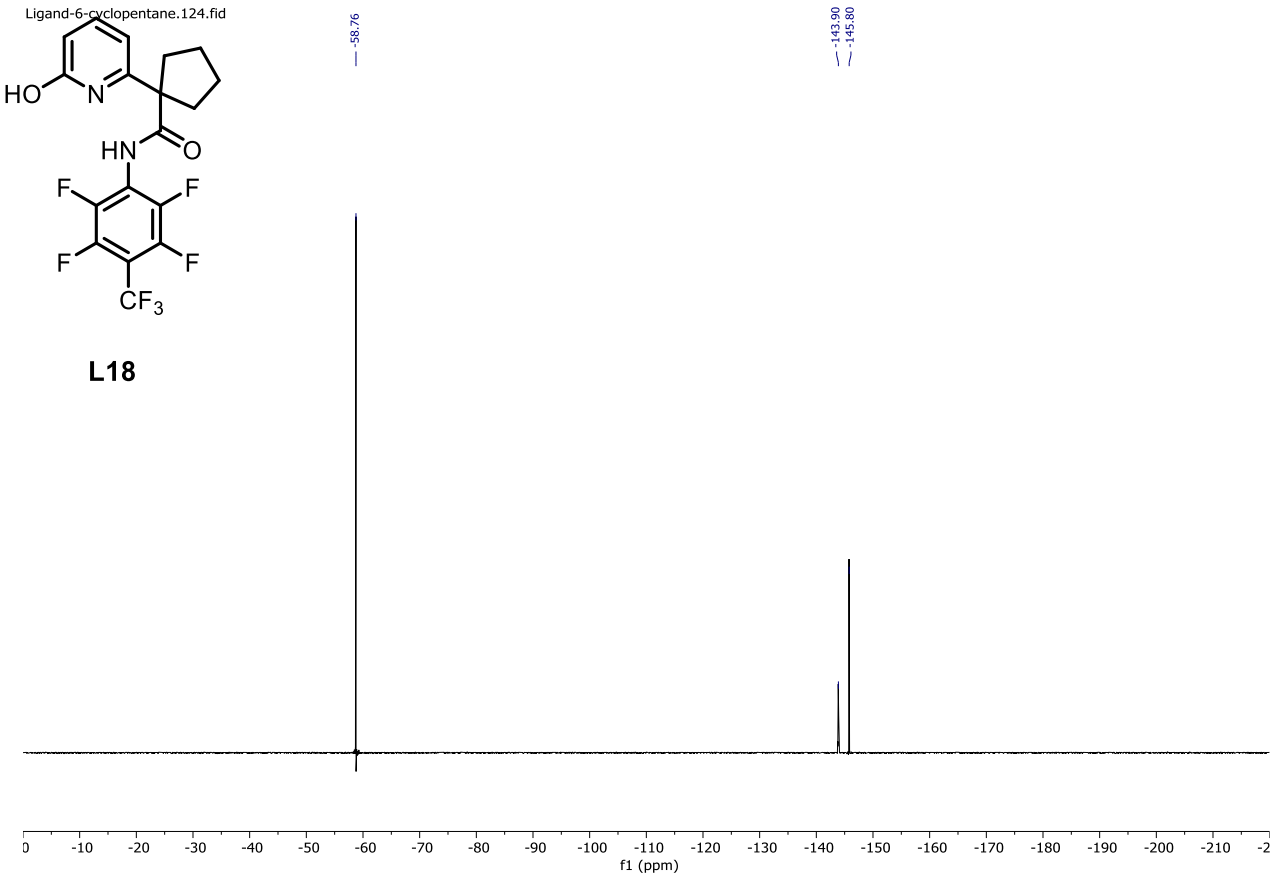


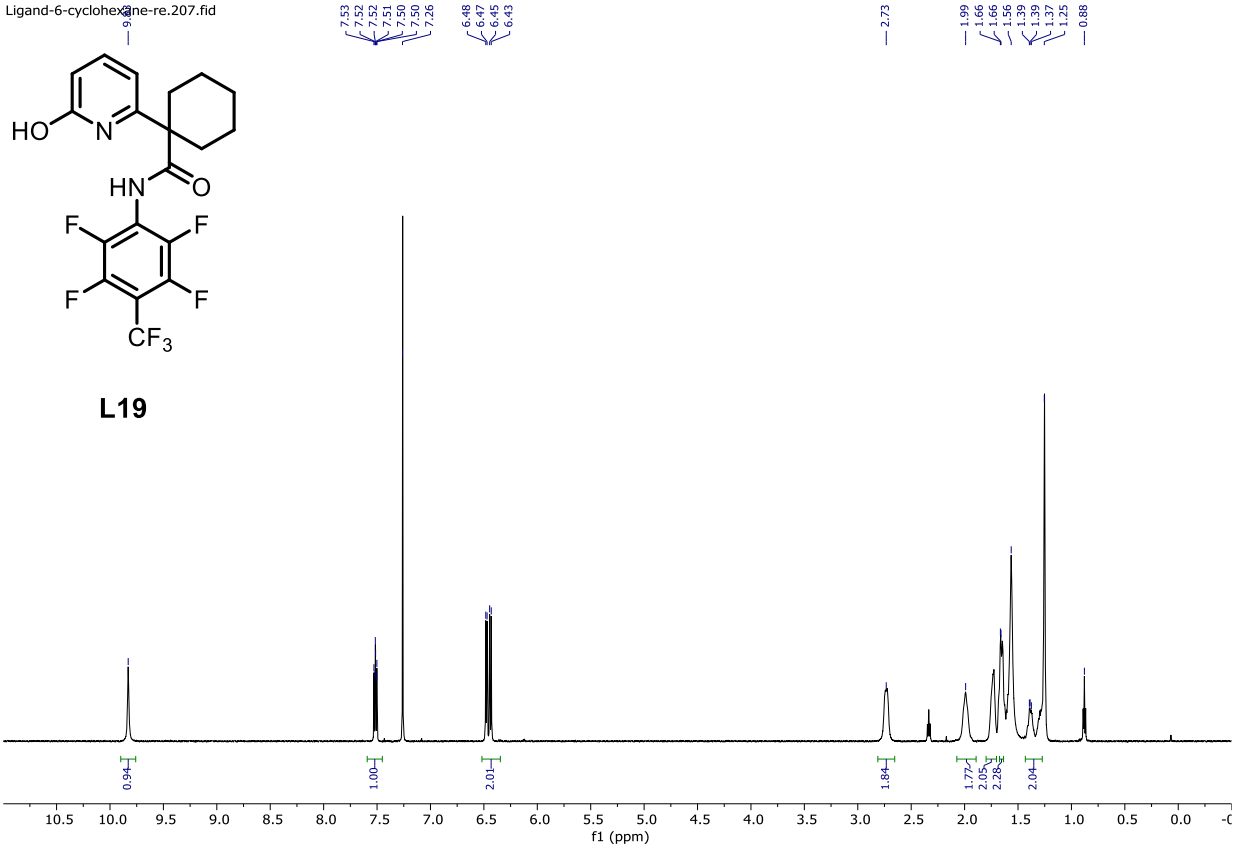
L17

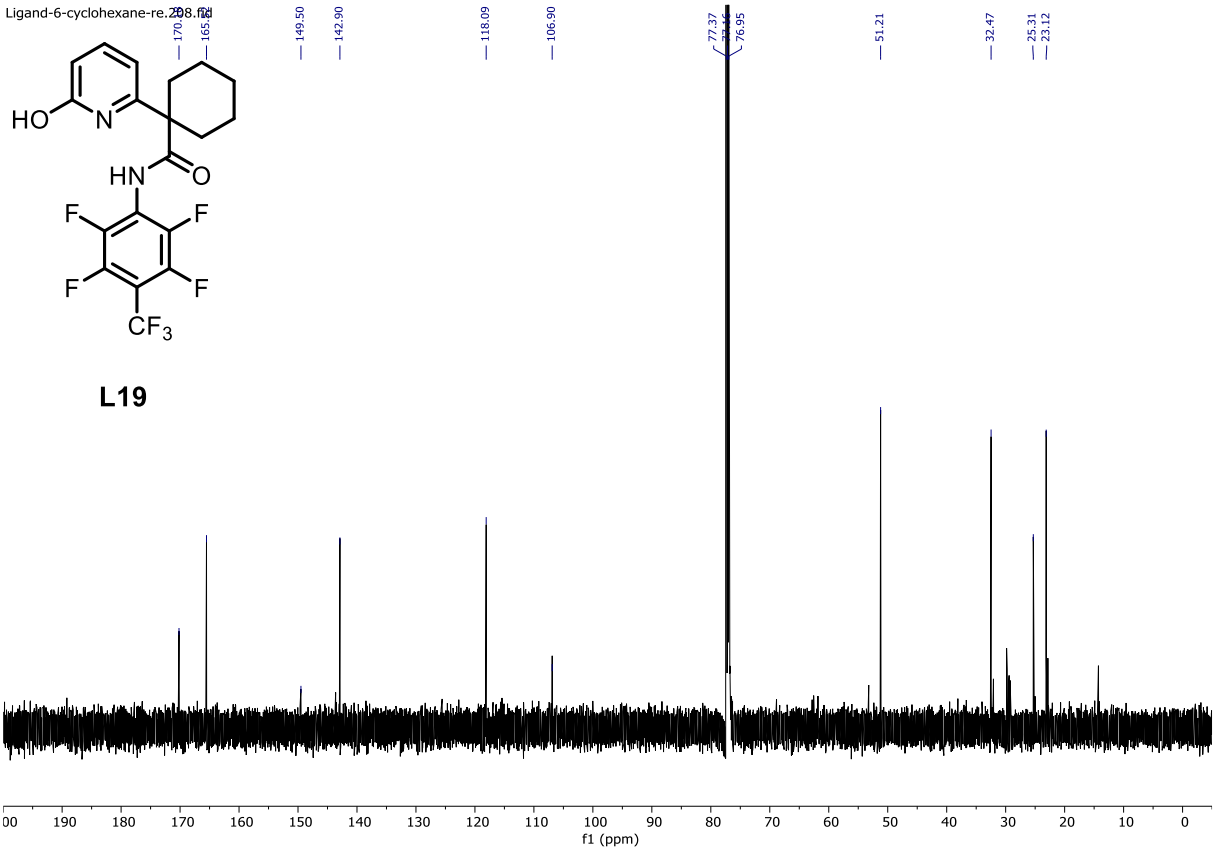



Ligand-6-cyclopentane-re.205.fid
HO
N
HN
O
F
F
F
F
CF3
L18
10.04
7.53
7.52
7.51
7.50
7.26
6.48
6.48
6.47
6.47
6.47
6.47
6.46
6.46
3.04
3.04
3.03
3.02
3.01
3.01
2.08
2.07
2.05
2.05
2.03
2.03
1.87
1.86
1.85
1.85
1.84
1.84
1.84
1.83
1.82
0.91
1.00
1.99
1.96
1.95
3.94
f1 (ppm)

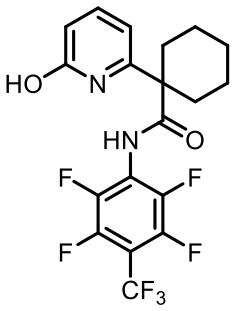

Ligand-6-cyclopentane-re.206.fid
HO
N
HN
O
F
F
F
F
CF3
L18
170.42
165.55
149.45
143.08
117.97
107.48
77.37
77.16
76.95
34.81
23.16
f1 (ppm)


Ligand-6-cyclopentane.124.fid
HO
N
HN
O
F
F
F
F
CF3
L18
-58.76
-143.90
-145.80
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

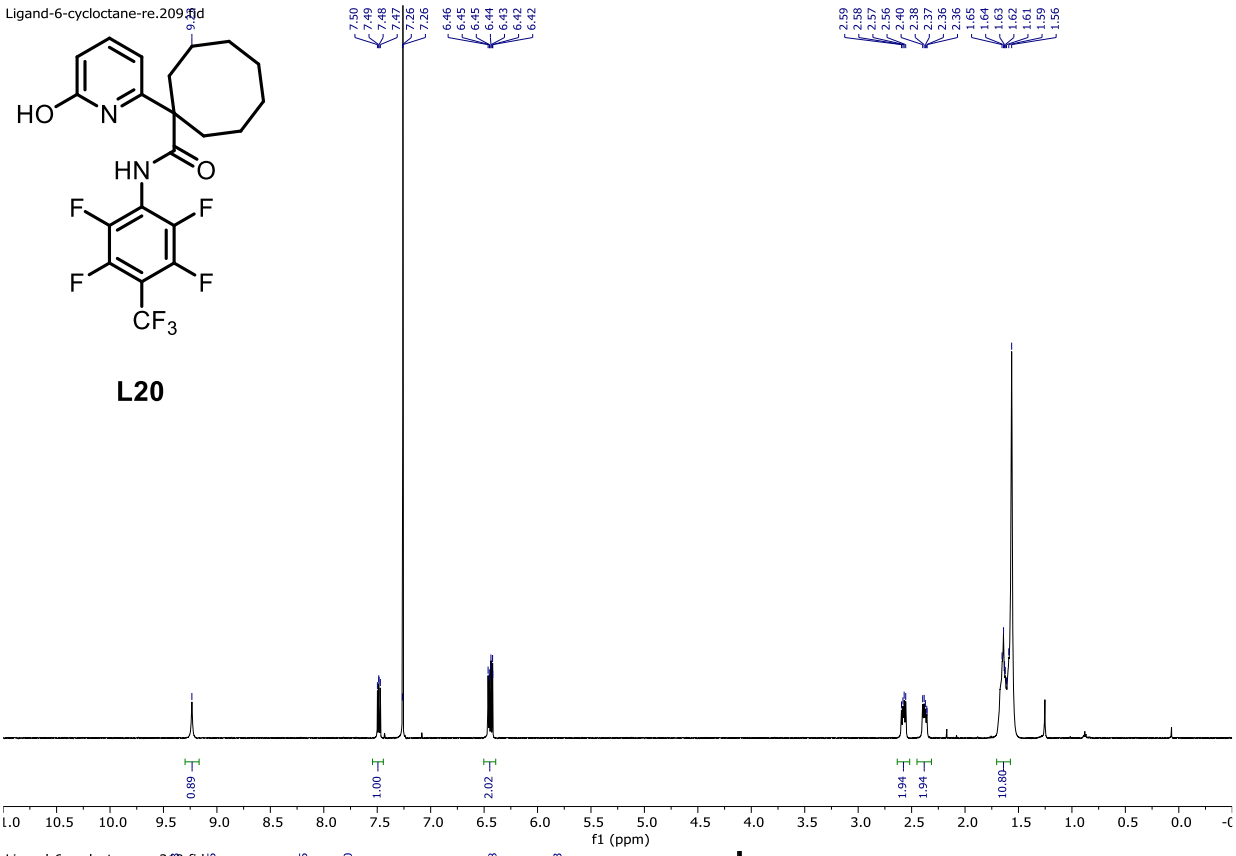

Ligand-6-cyclohexane-re.207.fid
HO
N
HN
O
F
F
F
F
CF3
L19
9.44
7.53
7.52
7.52
7.51
7.50
7.50
7.26
6.48
6.47
6.45
6.43
2.73
1.99
1.66
1.66
1.56
1.39
1.39
1.37
1.25
0.88
0.94
1.00
2.01
1.84
1.77
2.05
2.28
2.04
f1 (ppm)


Ligand-6-cyclohexane-re.208.fid
HO
N
HN
O
F
F
F
F
CF3
L19
170.28
165.52
149.50
142.90
118.09
106.90
77.37
77.16
76.95
51.21
32.47
25.31
23.12
f1 (ppm)

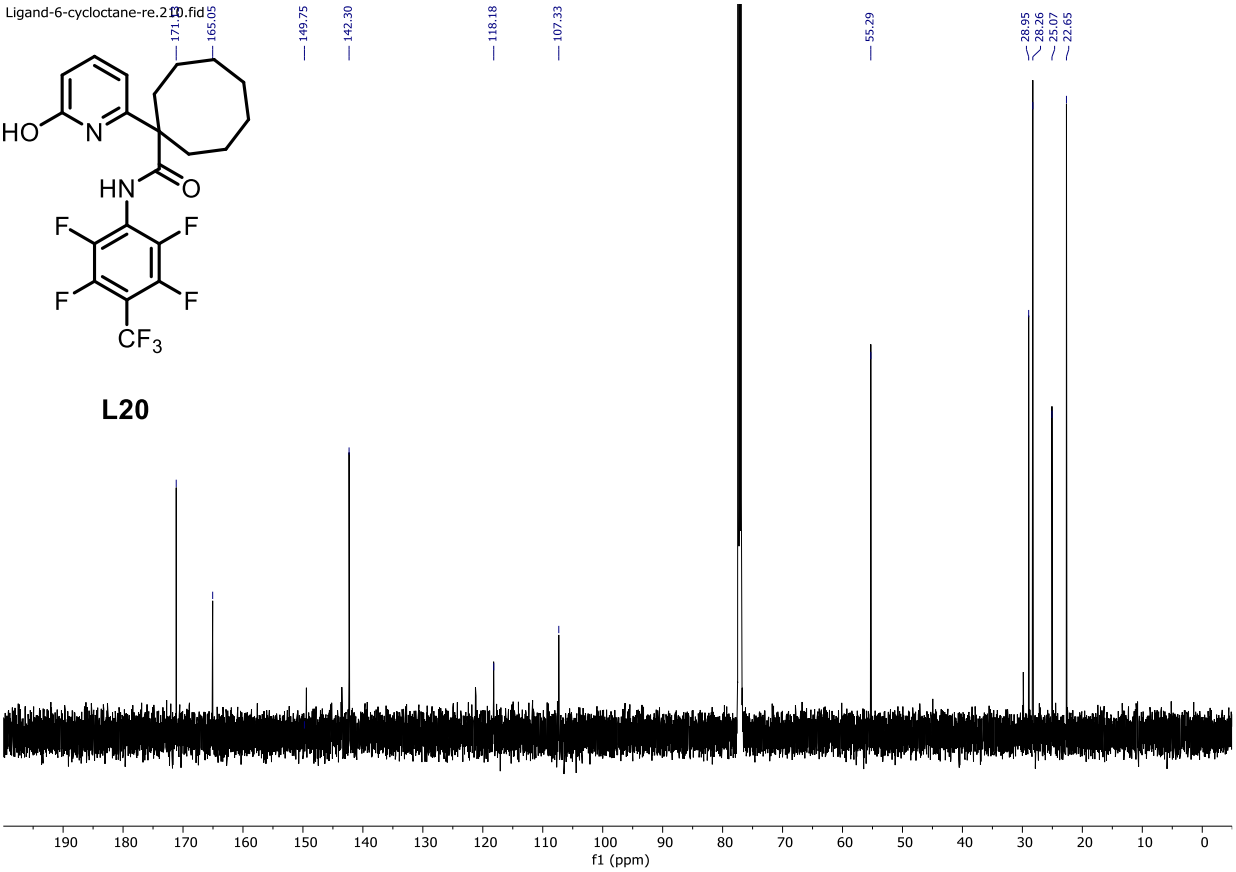
Ligand-6-cyclohexane.126.fid



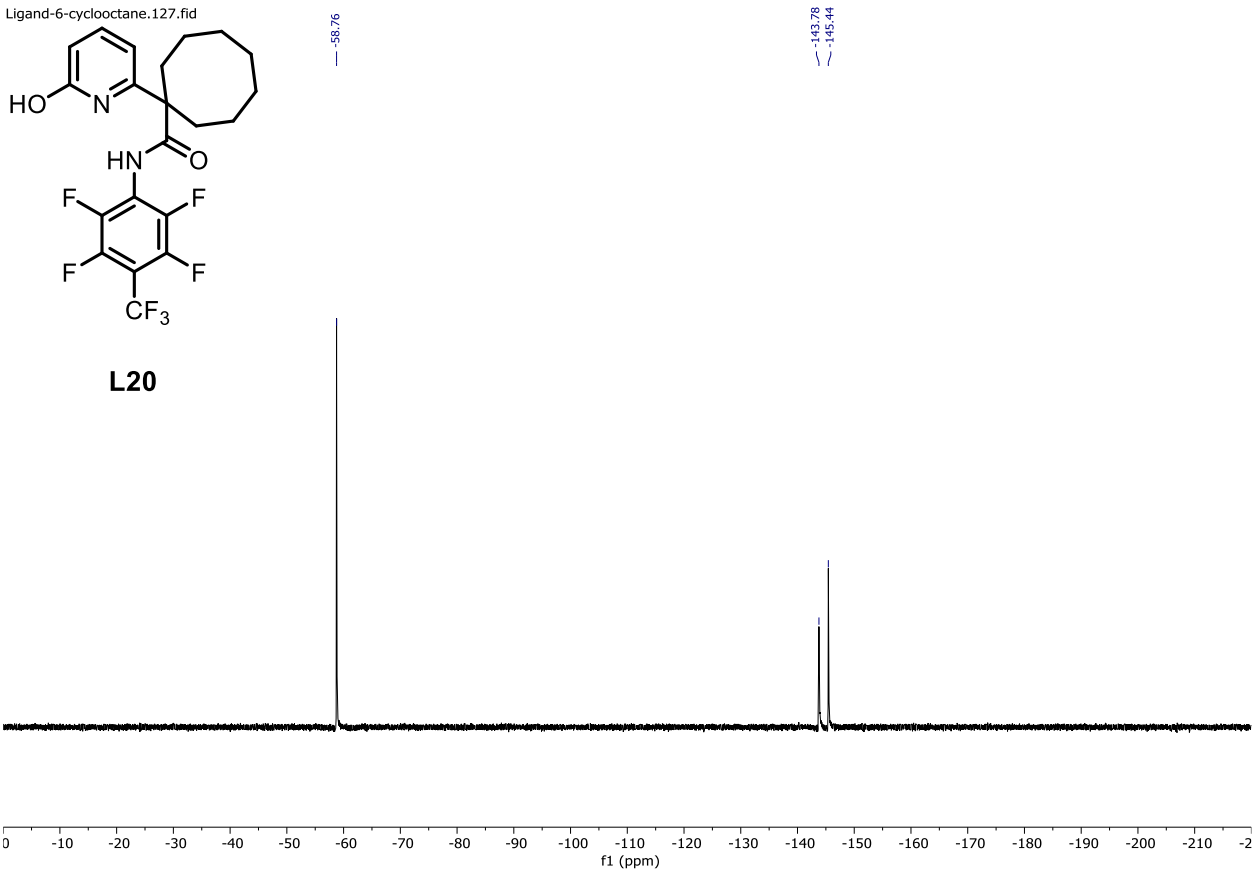
L19


Ligand-6-cycloctane-re.209.fid
HO
N
HN
O
F
F
F
F
F
CF3
7.50
7.49
7.48
7.47
7.26
6.46
6.45
6.44
6.43
6.42
2.59
2.58
2.57
2.56
2.40
2.38
2.37
2.36
1.65
1.64
1.63
1.62
1.61
1.59
1.56
0.89
1.00
2.02
1.94
1.94
10.80
f1 (ppm)

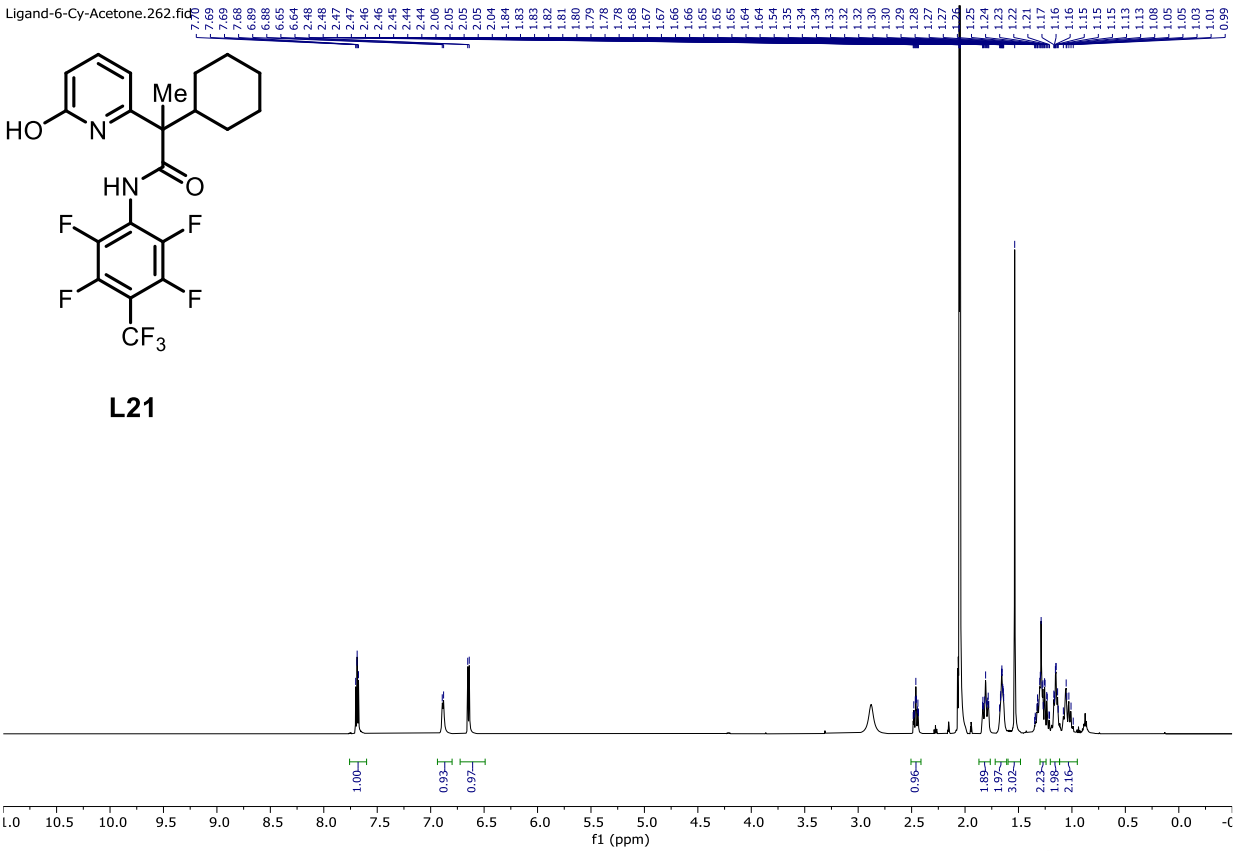
L20

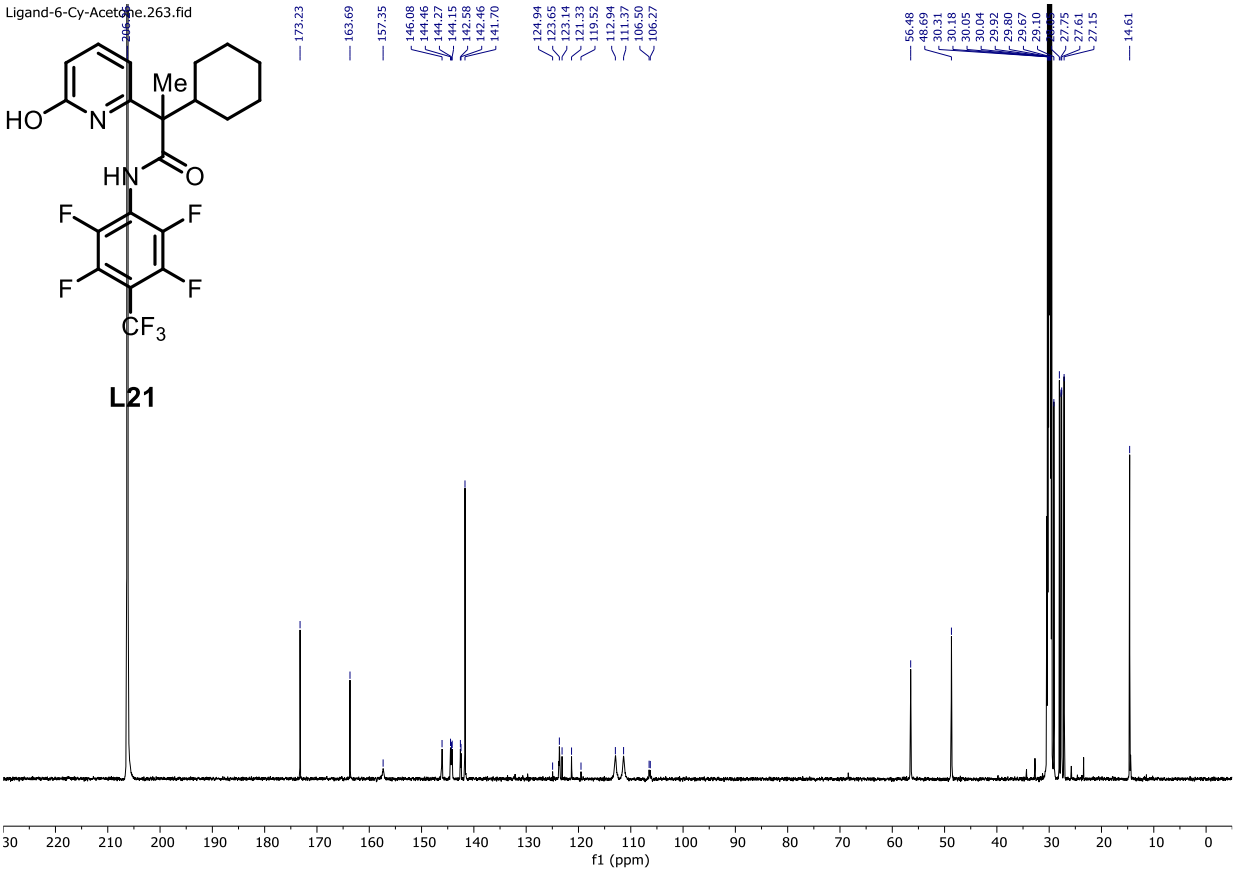

Ligand-6-cycloctane-re.210.fid
HO
N
HN
O
F
F
F
F
F
CF3
171.10
165.05
149.75
142.30
118.18
107.33
55.29
28.95
28.26
25.07
22.65
f1 (ppm)

L20

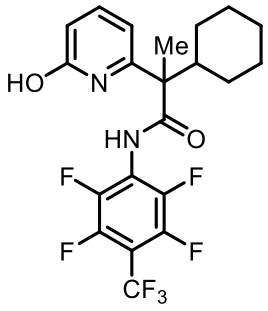

Ligand-6-cyclooctane.127.fid
-58.76
-143.78
-145.44
HO
N
HN
O
F
F
F
F
CF3
f1 (ppm)

L20

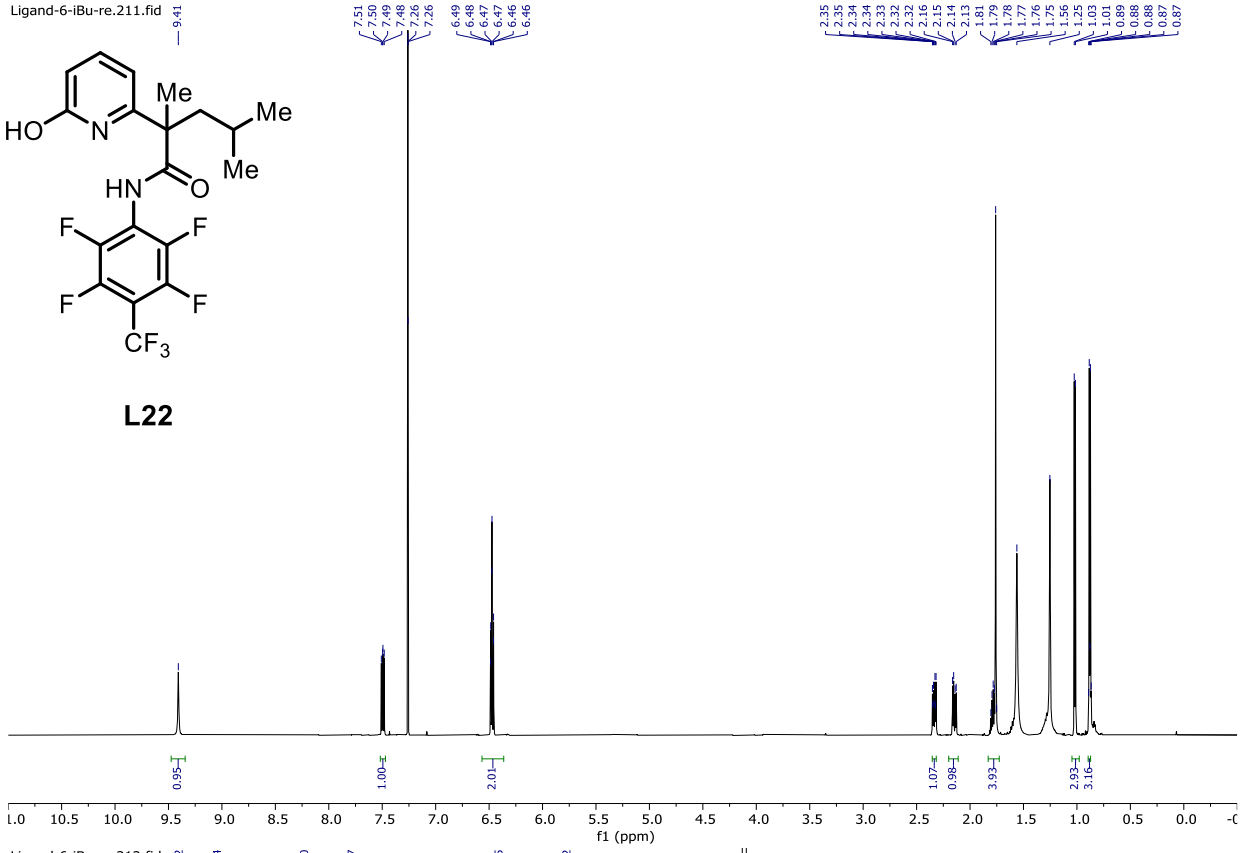

Ligand-6-Cy-Acetone.262.fid
Me
HO
N
HN
O
F
F
F
F
CF3
L21
f1 (ppm)


Ligand-6-Cy-Acetone.263.fid
Me
HO
N
HN
O
F
F
F
F
CF3
L21
f1 (ppm)

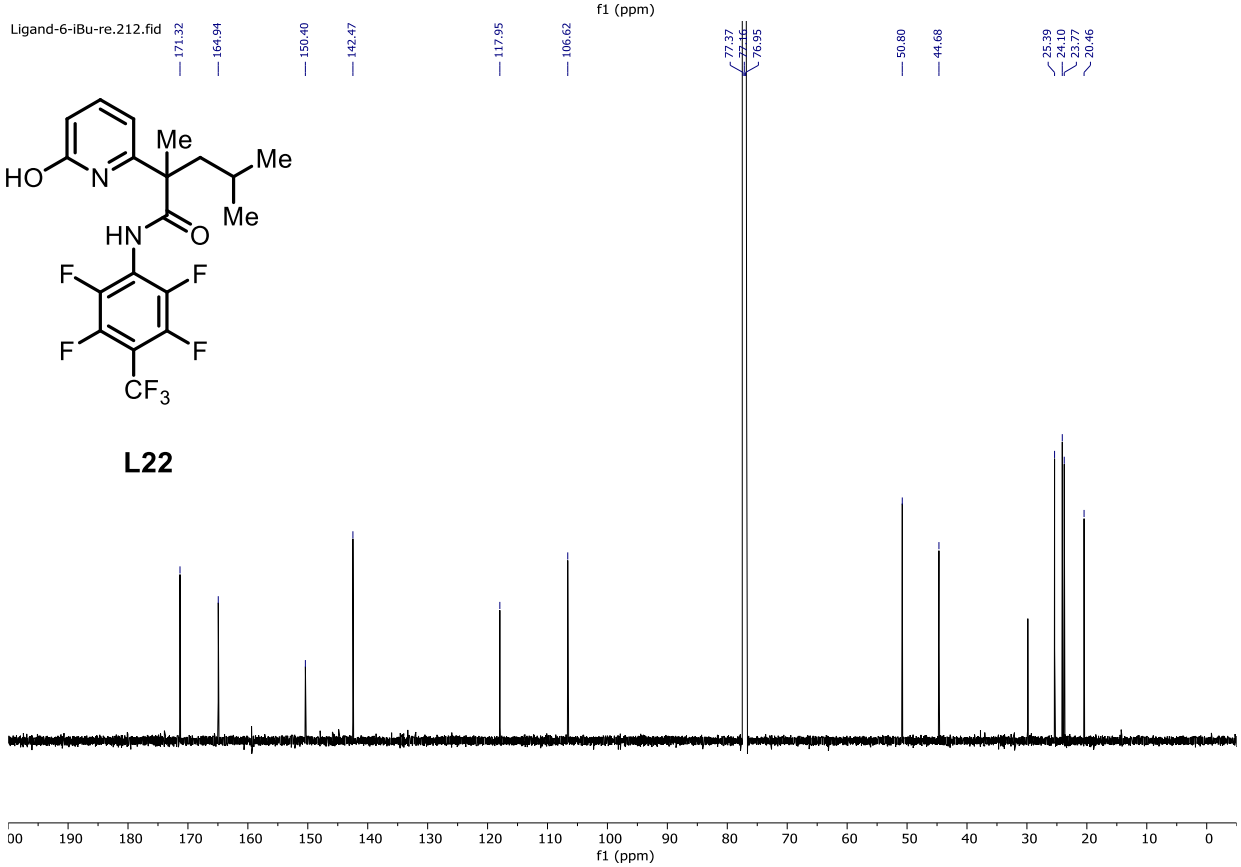
Ligand-6-Cy-acetone.149.fid



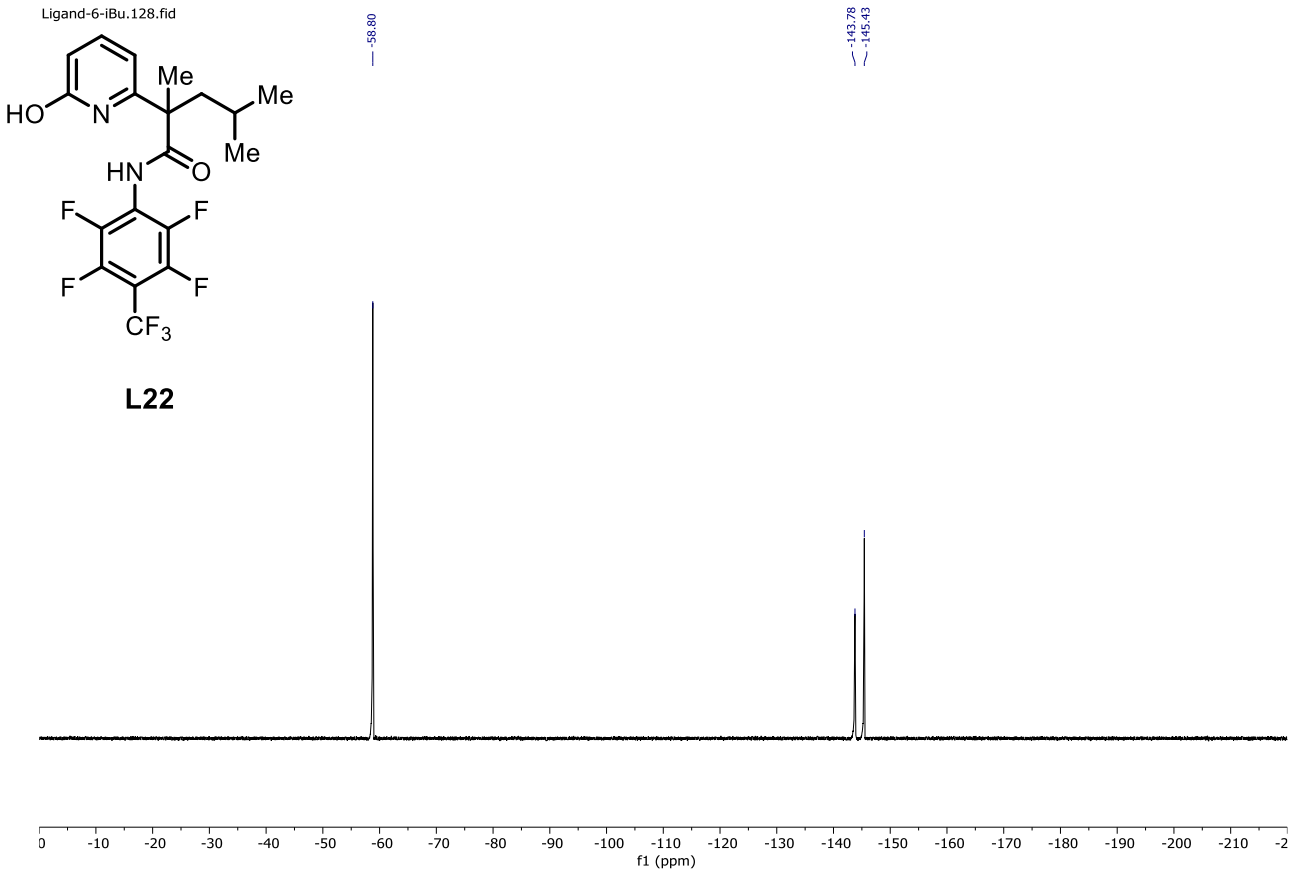
L21


Ligand-6-iBu-re.211.fid
9.41
7.51
7.50
7.49
7.48
7.26
7.26
6.49
6.48
6.47
6.47
6.46
6.46
2.35
2.35
2.34
2.34
2.33
2.32
2.32
2.16
2.15
2.14
2.13
1.81
1.79
1.78
1.77
1.76
1.75
1.56
1.25
1.03
1.01
0.89
0.88
0.88
0.87
0.87
HO
N
Me
Me
Me
HN
O
F
F
F
F
CF3
0.95
1.00
2.01
1.07
0.98
3.93
2.93
3.16
f1 (ppm)

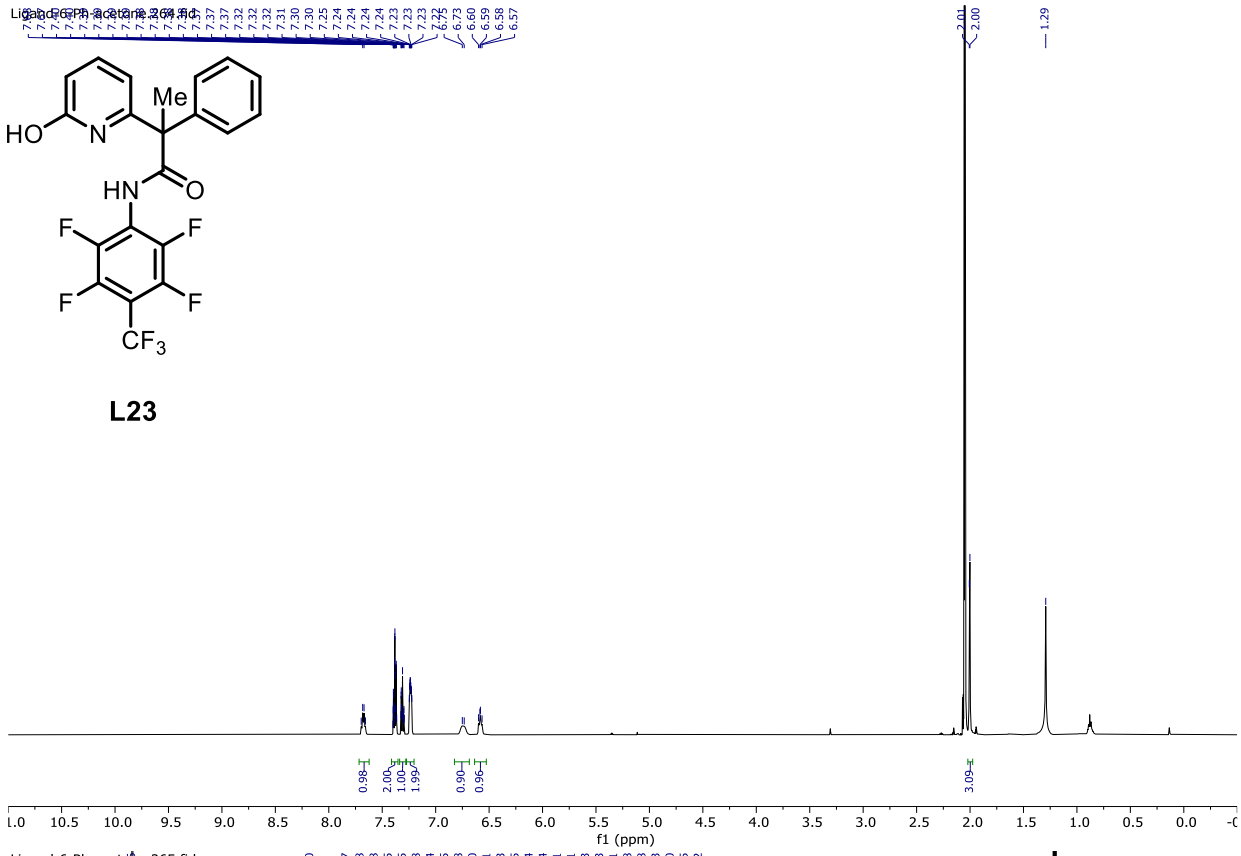
L22


Ligand-6-iBu-re.212.fid
171.32
164.94
150.40
142.47
117.95
106.62
77.37
77.16
76.95
50.80
44.68
25.39
24.10
23.77
20.46
HO
N
Me
Me
Me
HN
O
F
F
F
F
CF3
f1 (ppm)

L22

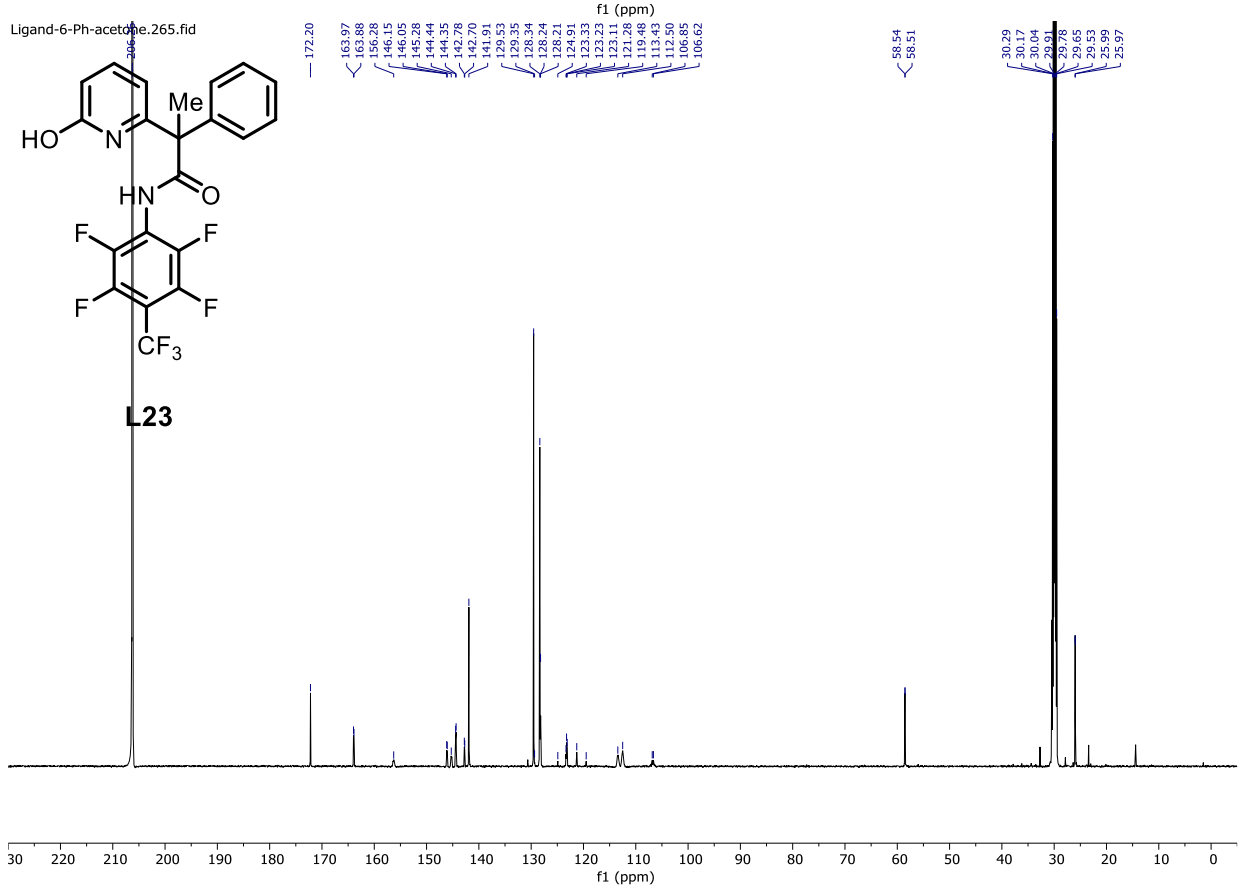

Ligand-6-iBu.128.fid
-58.80
-143.78
-145.43
HO
N
Me
Me
Me
HN
O
F
F
F
F
CF3
f1 (ppm)

L22


Me
HO
N
HN
O
F
F
F
F
CF3

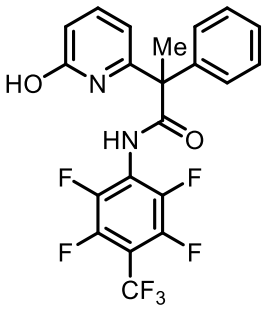
L23

f1 (ppm)


Ligand-6-Ph-acetone.265.fid
Me
HO
N
HN
O
F
F
F
F
CF3
f1 (ppm)

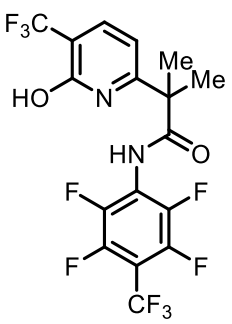
L23

Ligand-6-Ph-acetone.150.fid



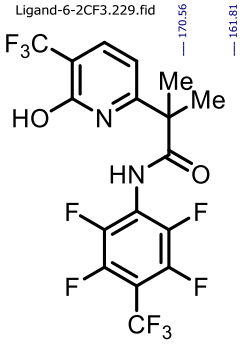
L23

Ligand-6-2CF3.228.fid

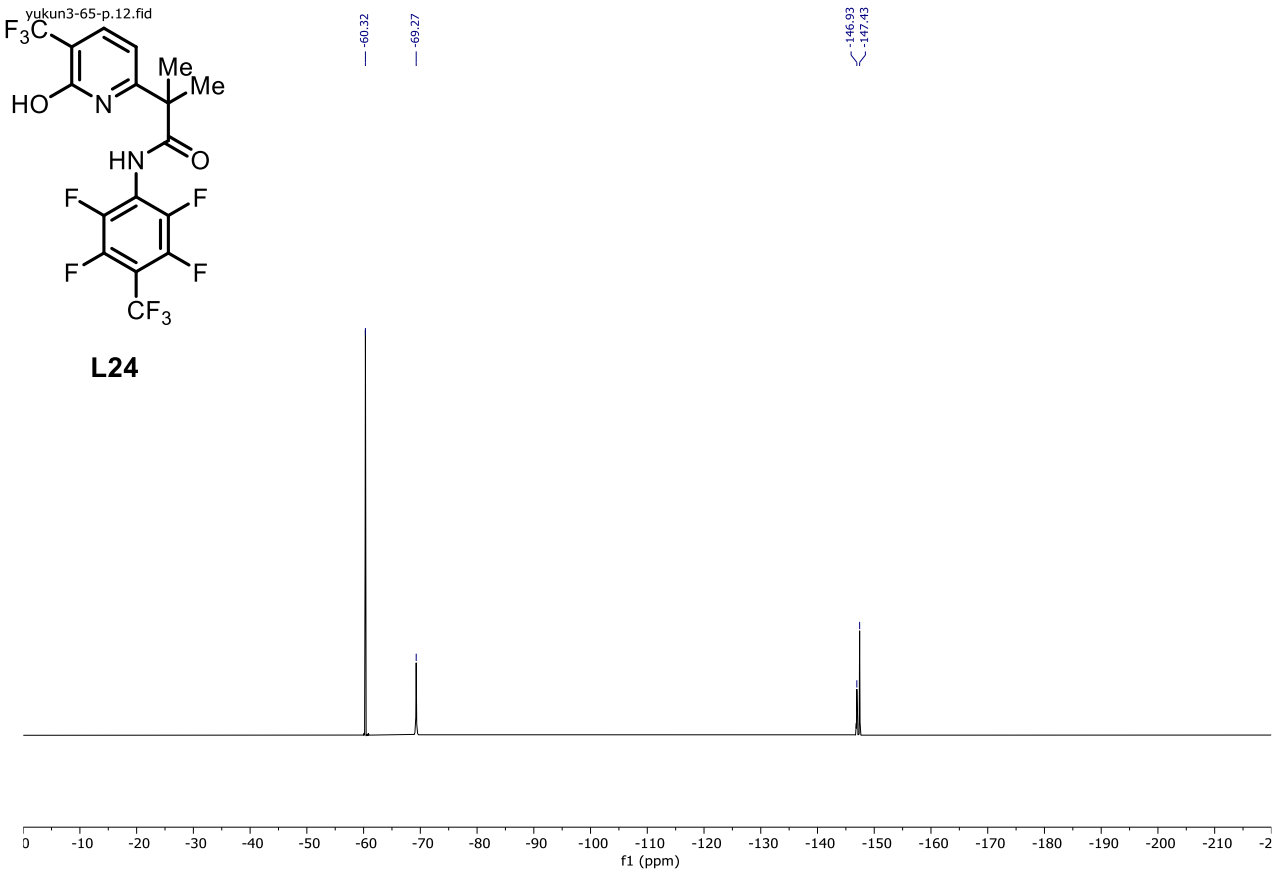


L24

Ligand-6-2CF3.229.fid

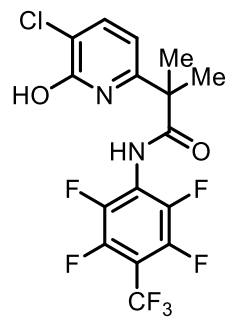


L24


yukun3-65-p.12.fid
F3C
Me
Me
HO
N
HN
O
F
F
F
F
CF3
-60.32
-69.27
-146.93
-147.43
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-2
f1 (ppm)

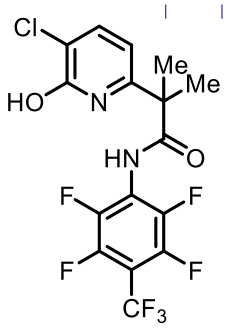
L24

Ligand-6-3Cl.230.fid



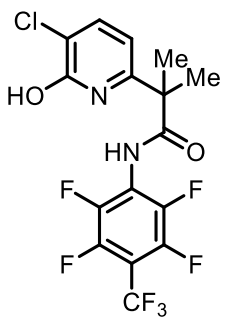
L25

Ligand-6-3Cl.231.fid



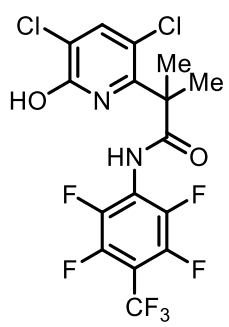
L25

yukun3-64-2.19.fid



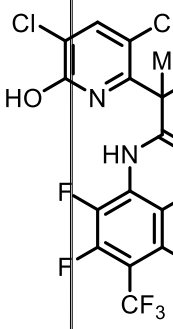
L25

Ligand-6-35Cl-acetone-re.238.fid



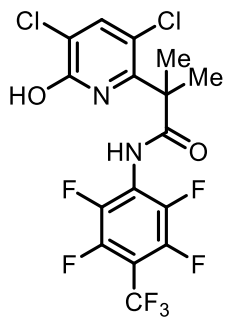
L26

Ligand-6-35Cl-acetone-re.239.fid

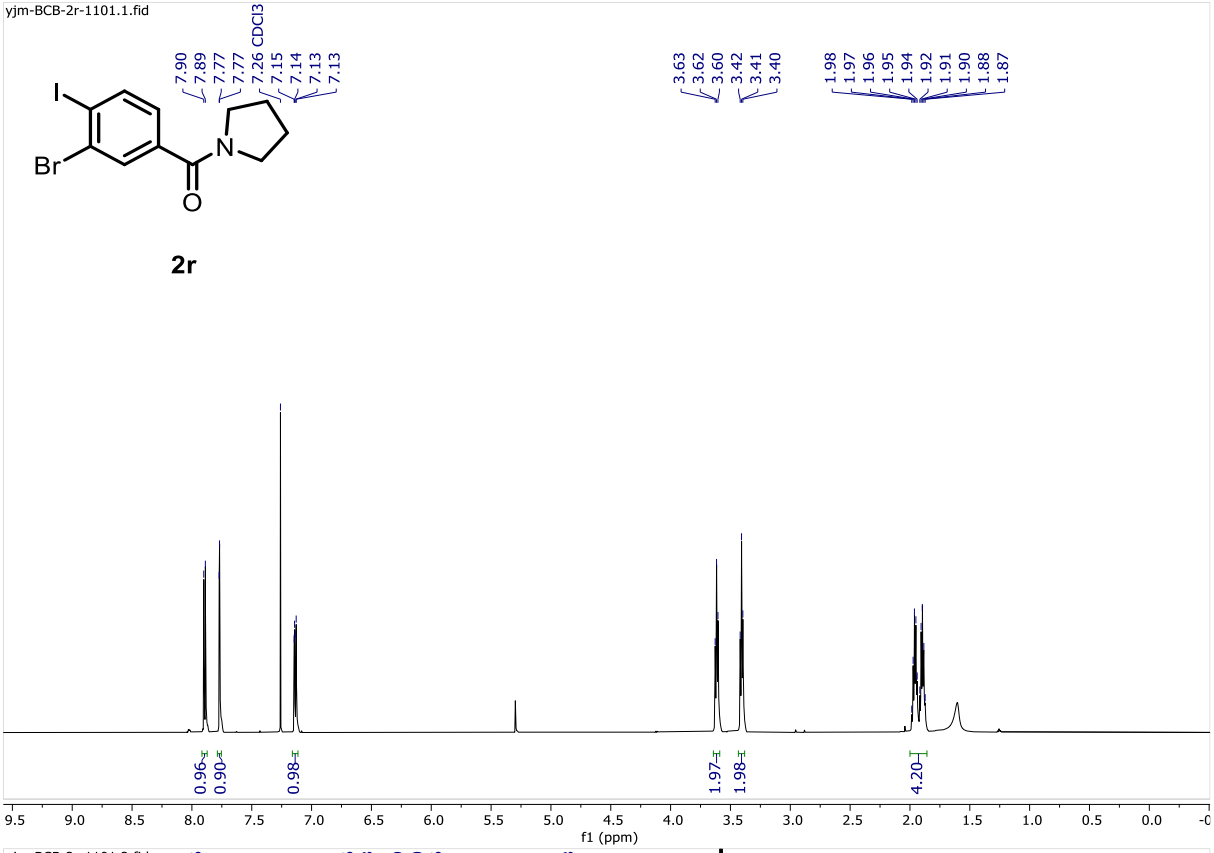


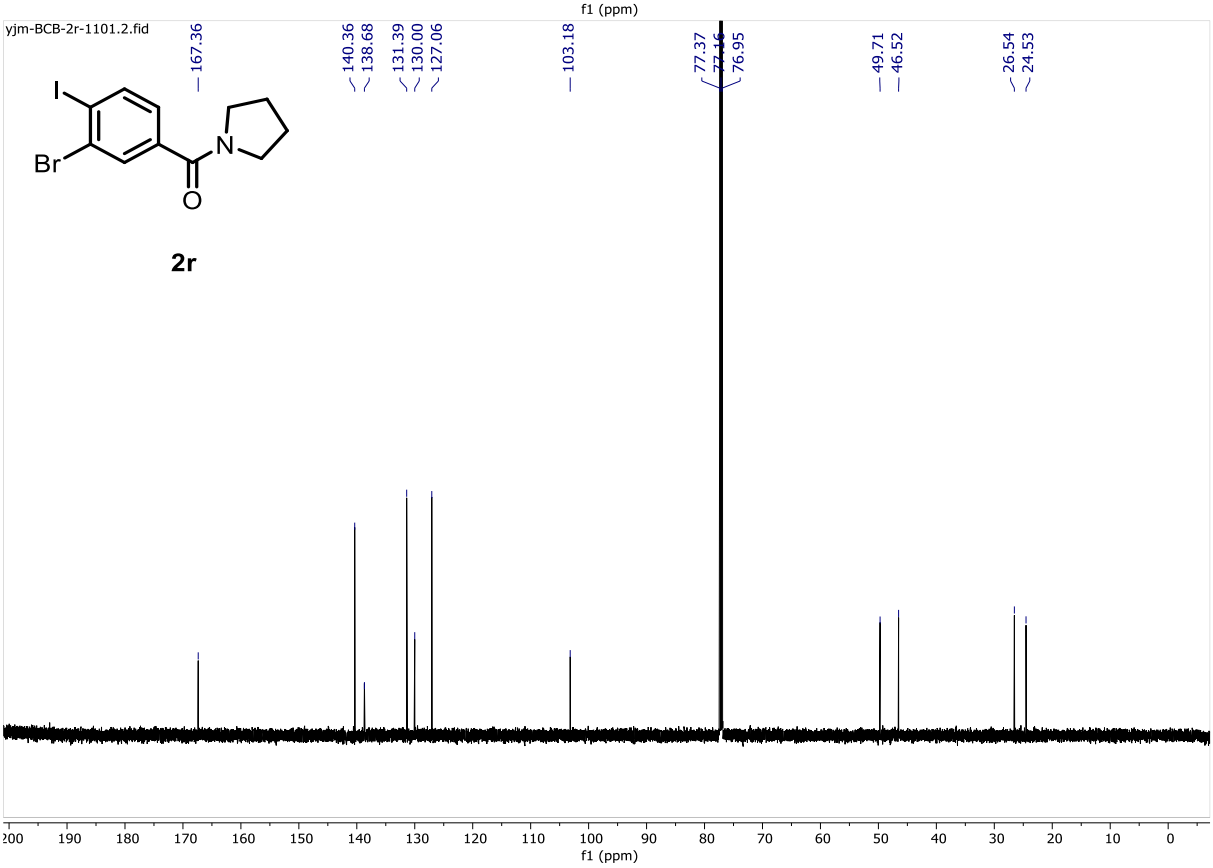
L26

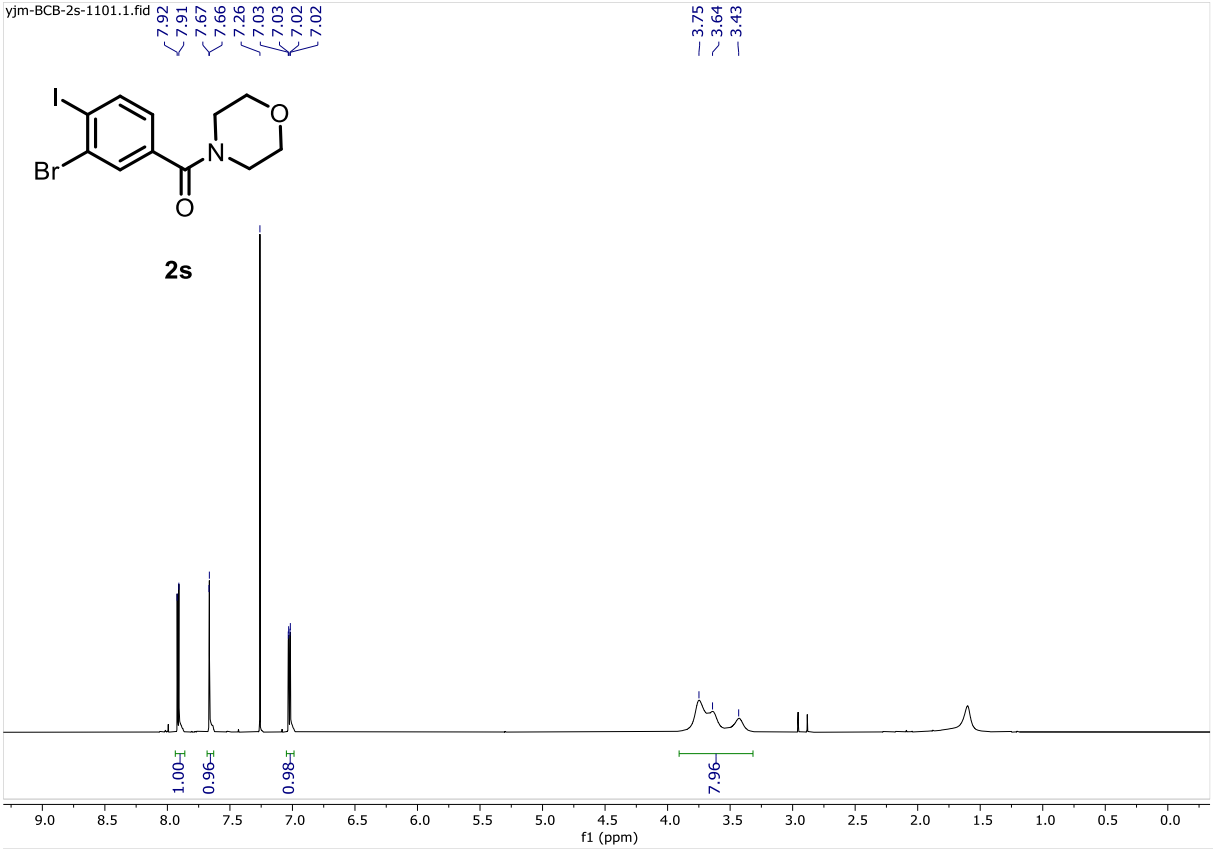
yukun3-64-1.17.fid

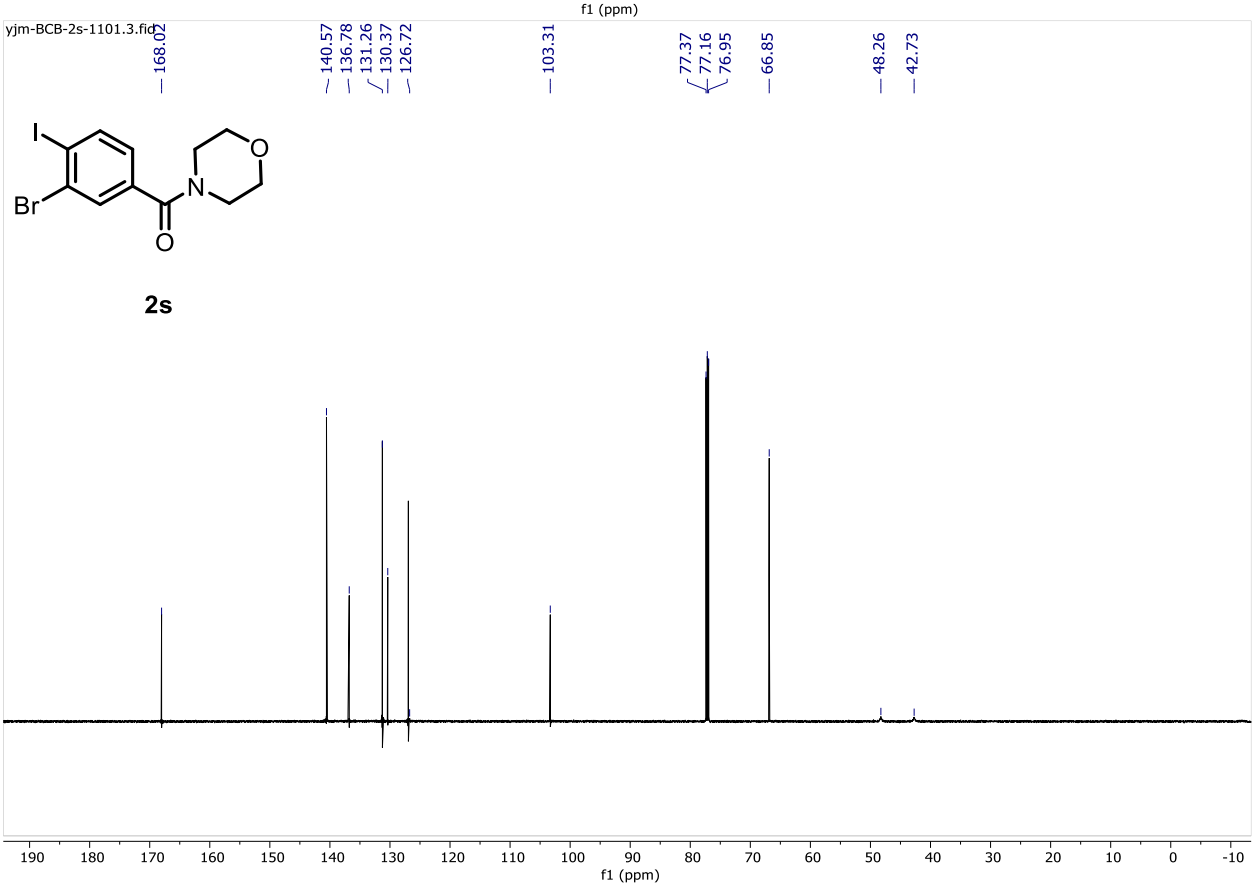


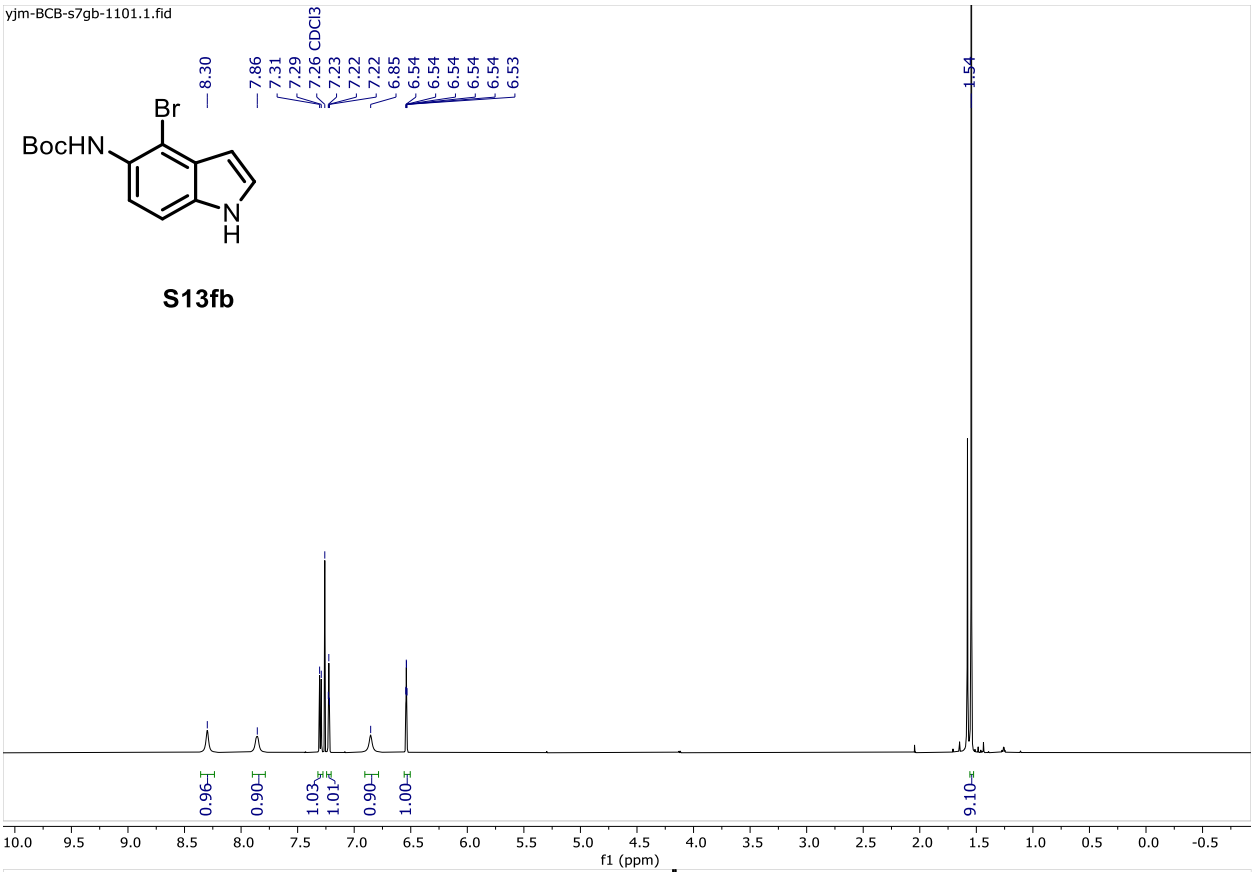
L26

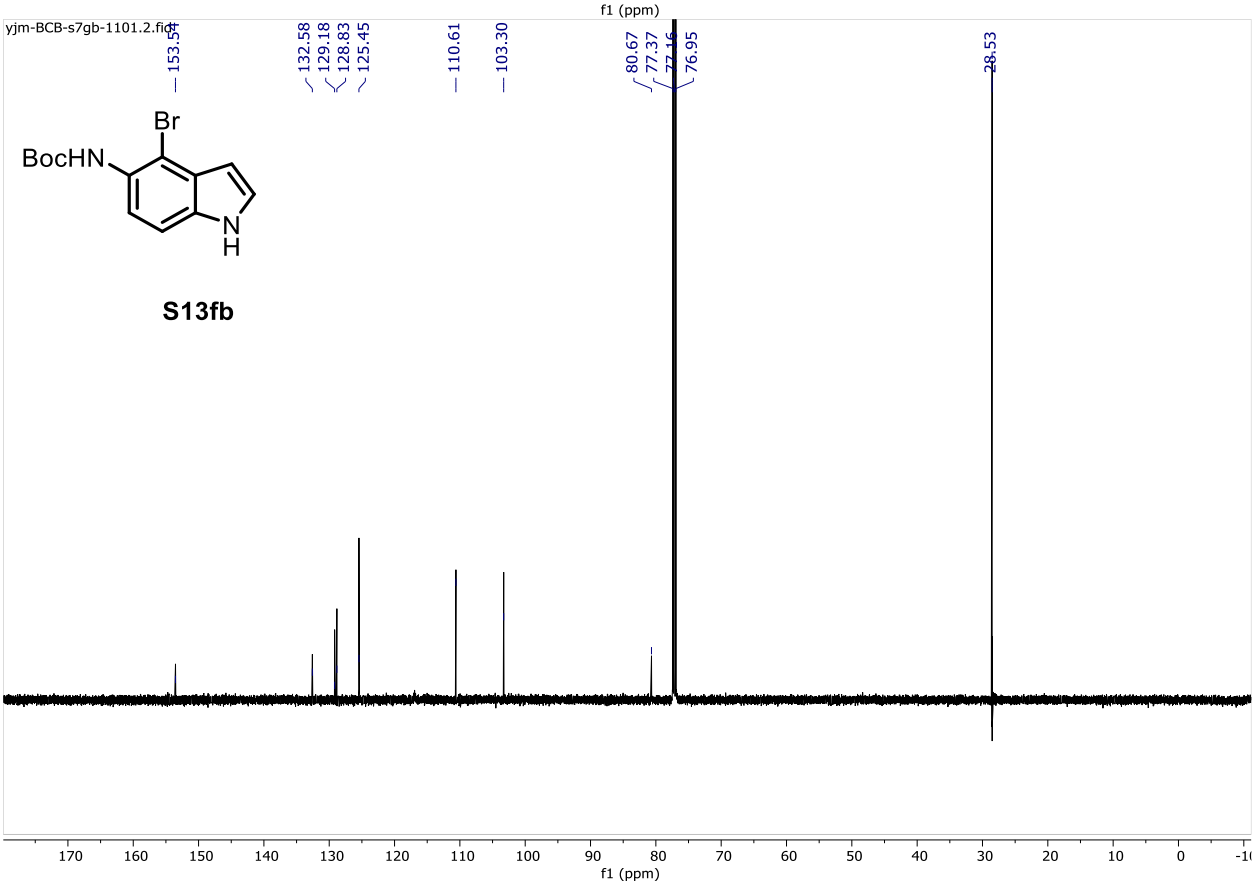

yjm-BCB-2r-1101.1.fid
7.90
7.89
7.77
7.77
7.26 CDCl3
7.15
7.14
7.13
7.13
3.63
3.62
3.60
3.42
3.41
3.40
1.98
1.97
1.96
1.95
1.94
1.92
1.91
1.90
1.88
1.87
I
Br
N
O
2r
0.96
0.90
0.98
1.97
1.98
4.20
f1 (ppm)

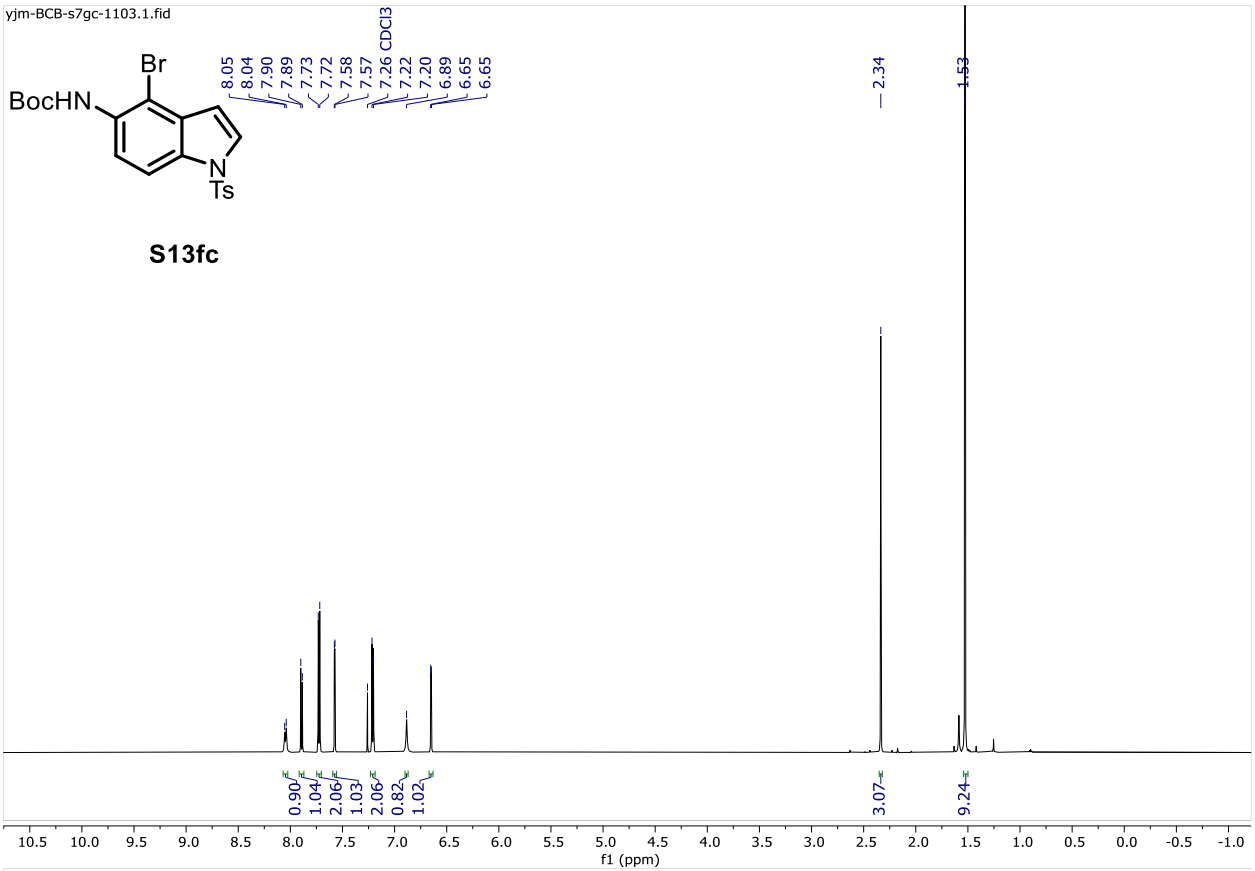

yjm-BCB-2r-1101.2.fid
167.36
140.36
138.68
131.39
130.00
127.06
103.18
77.37
77.16
76.95
49.71
46.52
26.54
24.53
I
Br
N
O
2r
f1 (ppm)


yjm-BCB-2s-1101.1.fid
7.92
7.91
7.67
7.66
7.26
7.03
7.03
7.02
7.02
3.75
3.64
3.43
I
Br
O
N
O
2s
1.00
0.96
0.98
7.96
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

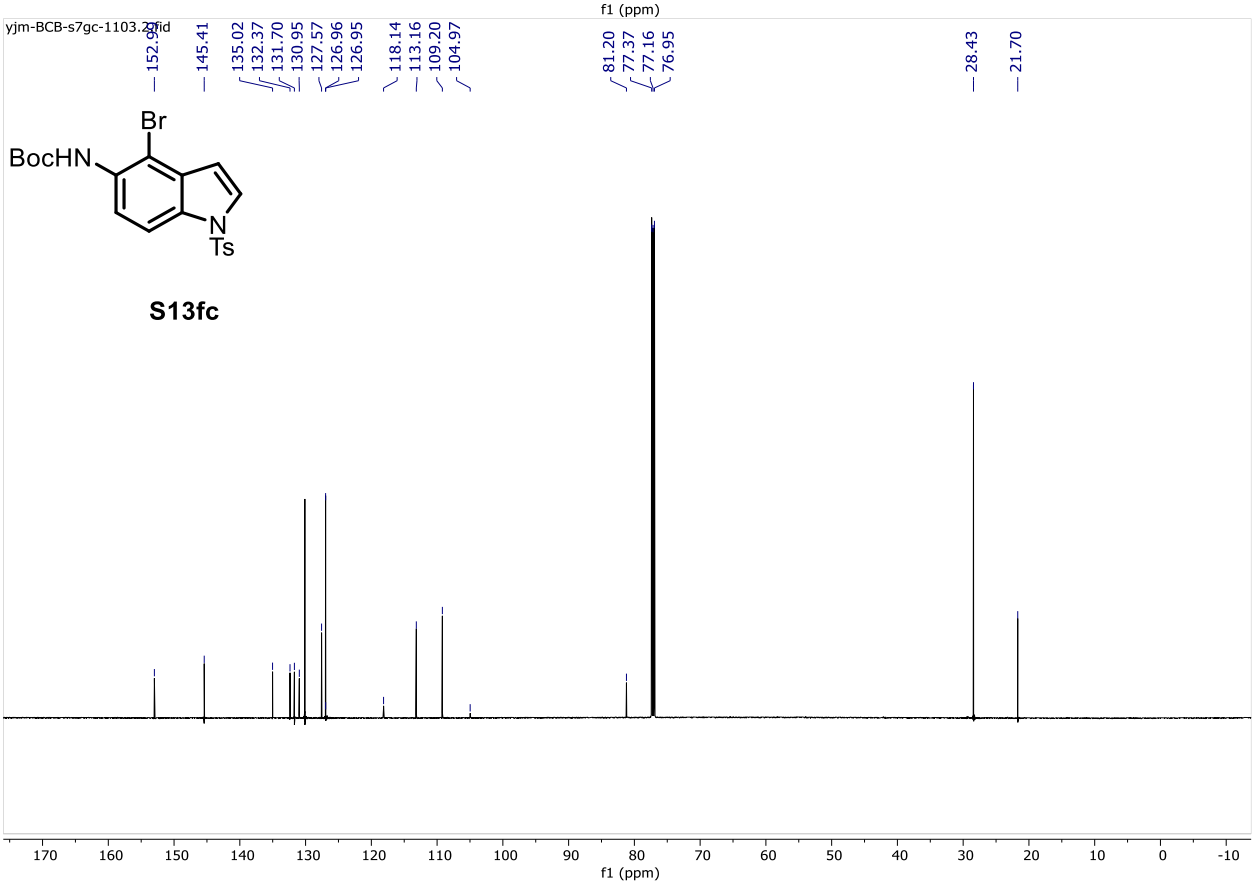

yjm-BCB-2s-1101.3.fid
168.02
140.57
136.78
131.26
130.37
126.72
103.31
77.37
77.16
76.95
66.85
48.26
42.73
I
Br
O
N
O
2s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


yjm-BCB-s7gb-1101.1.fid
8.30
7.86
7.31
7.29
7.26 CDCl3
7.23
7.22
7.22
6.85
6.54
6.54
6.54
6.54
6.54
6.53
1.54
Br
BocHN
N
H
S13fb
0.96
0.90
1.03
1.01
0.90
1.00
9.10
f1 (ppm)

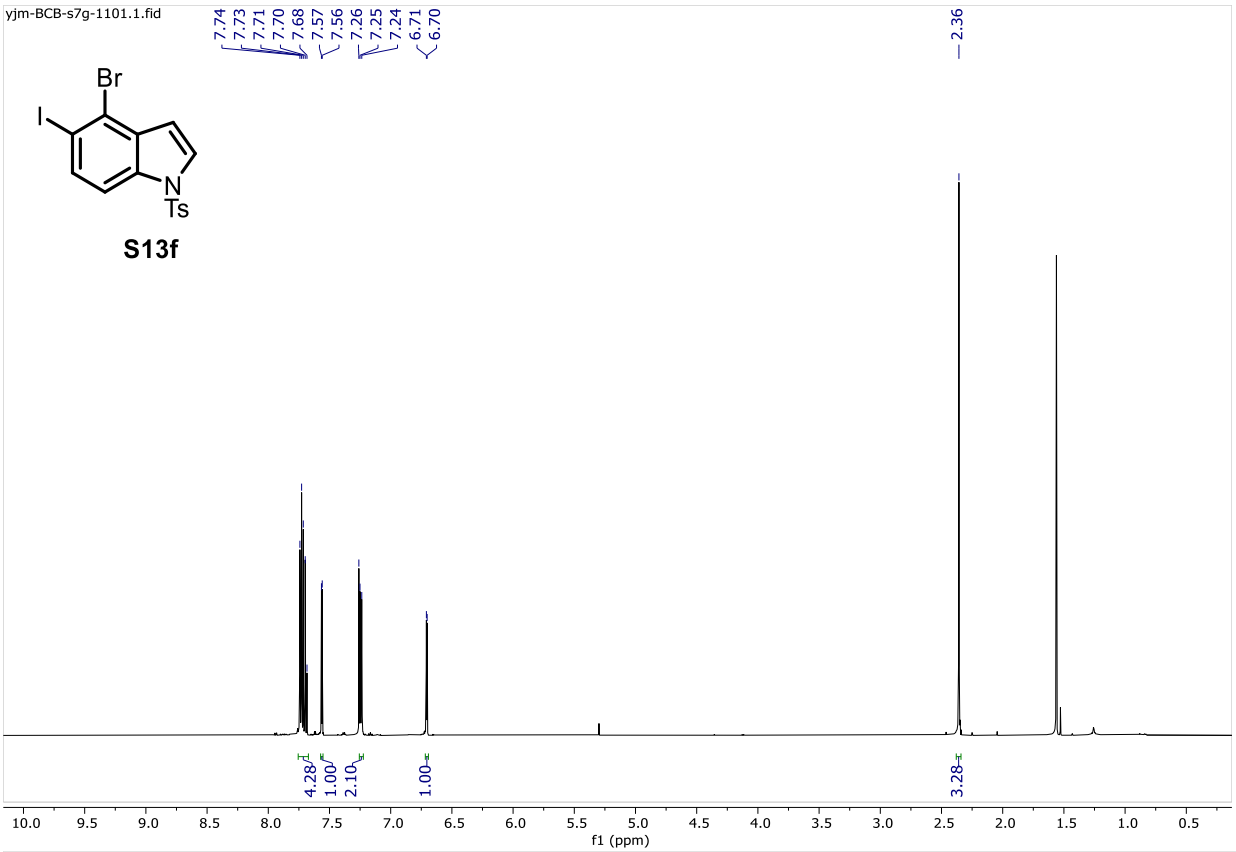

yjm-BCB-s7gb-1101.2.fid
153.54
132.58
129.18
128.83
125.45
110.61
103.30
80.67
77.37
77.16
76.95
28.53
Br
BocHN
N
H
S13fb
f1 (ppm)

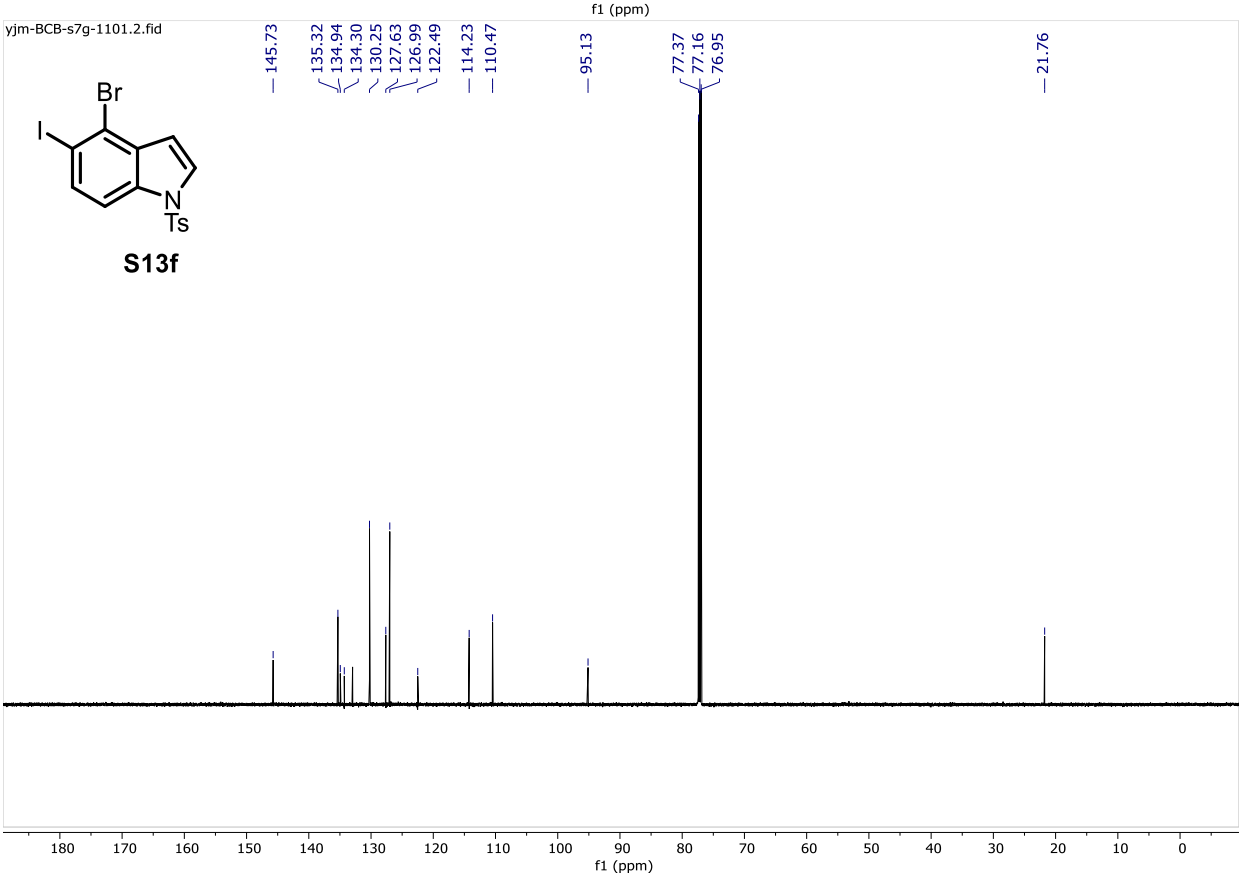

yjm-BCB-s7gc-1103.1.fid
Br
BocHN
N
Ts
8.05
8.04
7.90
7.89
7.73
7.72
7.58
7.57
7.26 CDCl3
7.22
7.20
6.89
6.65
6.65
2.34
1.53
0.90
1.04
2.06
1.03
2.06
0.82
1.02
3.07
9.24
f1 (ppm)

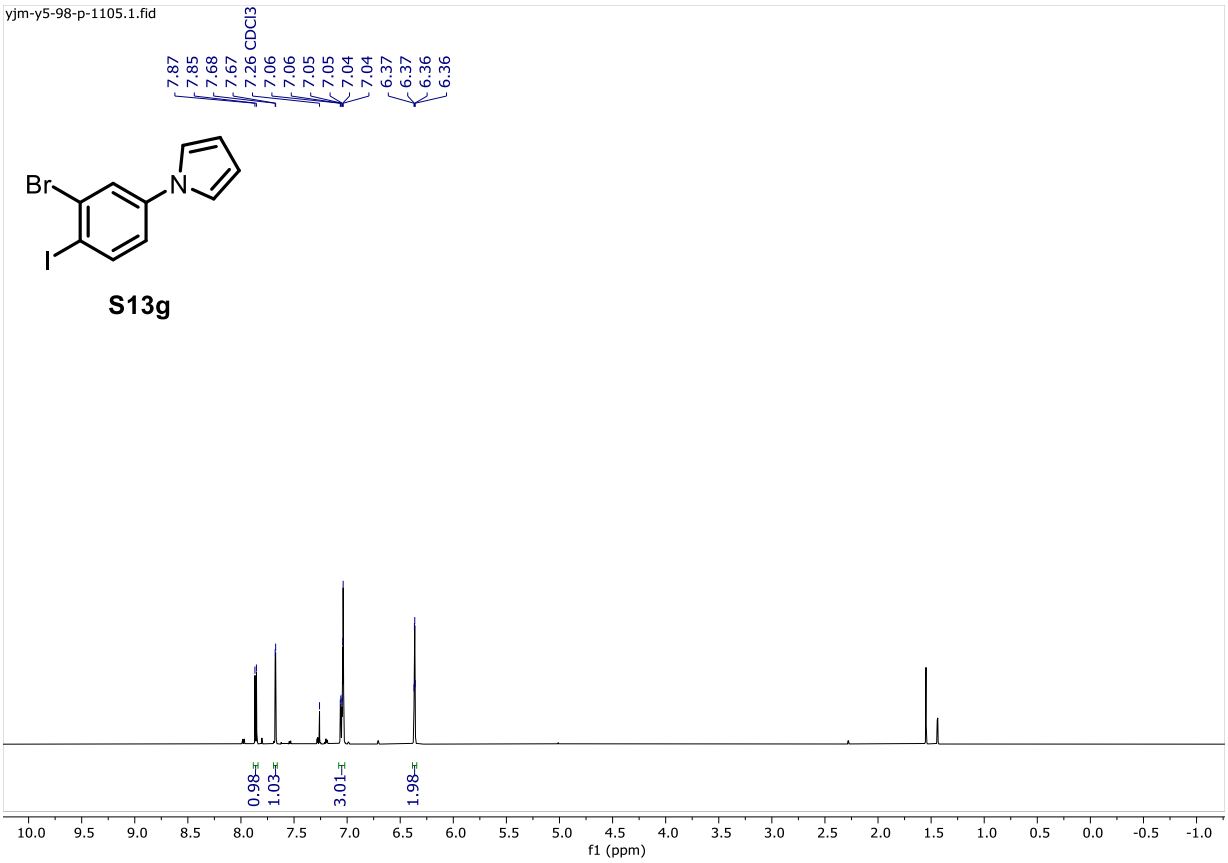
S13fc


yjm-BCB-s7gc-1103.2.fid
Br
BocHN
N
Ts
152.99
145.41
135.02
132.37
131.70
130.95
127.57
126.96
126.95
118.14
113.16
109.20
104.97
81.20
77.37
77.16
76.95
28.43
21.70
f1 (ppm)

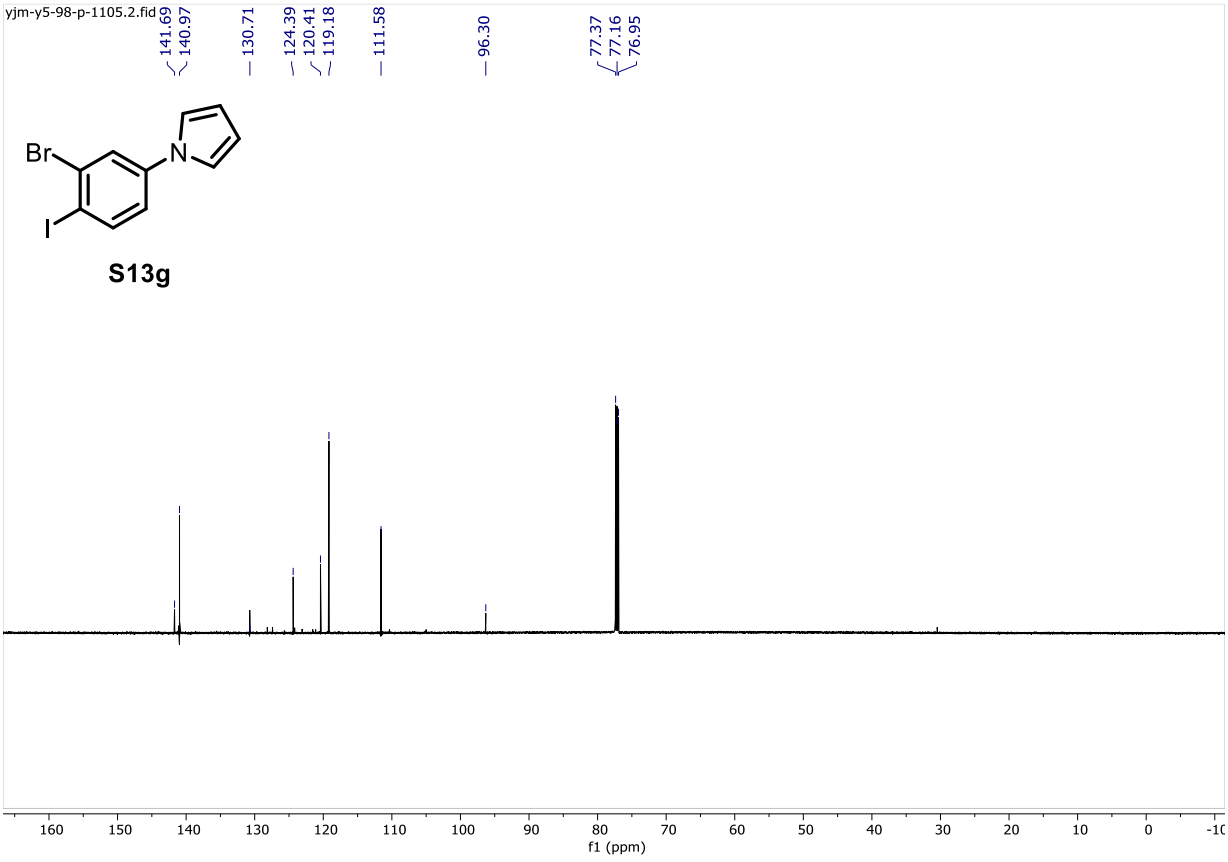
S13fc


yjm-BCB-s7g-1101.1.fid
7.74
7.73
7.71
7.70
7.68
7.57
7.56
7.26
7.25
7.24
6.71
6.70
2.36
Br
I
N
Ts
S13f
4.28
1.00
2.10
1.00
3.28
f1 (ppm)

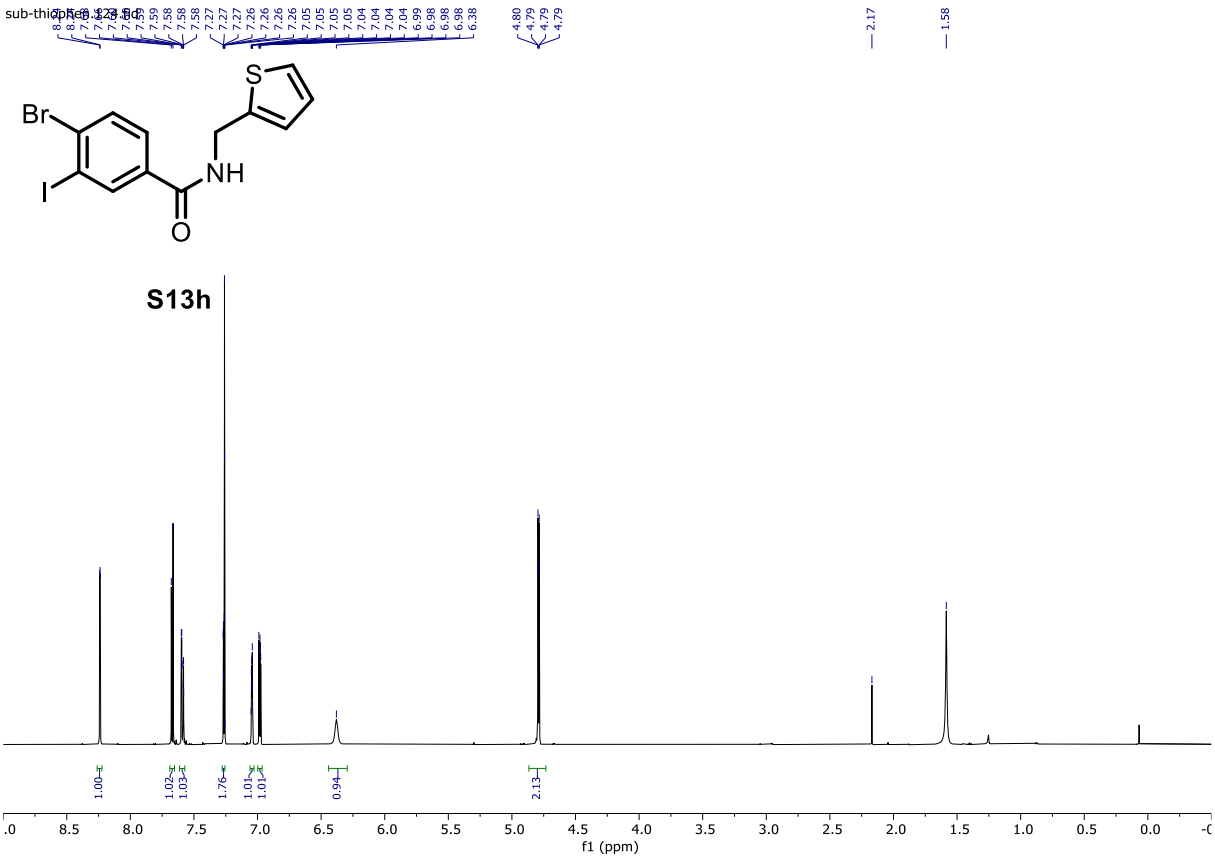

yjm-BCB-s7g-1101.2.fid
145.73
135.32
134.94
134.30
130.25
127.63
126.99
122.49
114.23
110.47
95.13
77.37
77.16
76.95
21.76
Br
I
N
Ts
S13f
f1 (ppm)

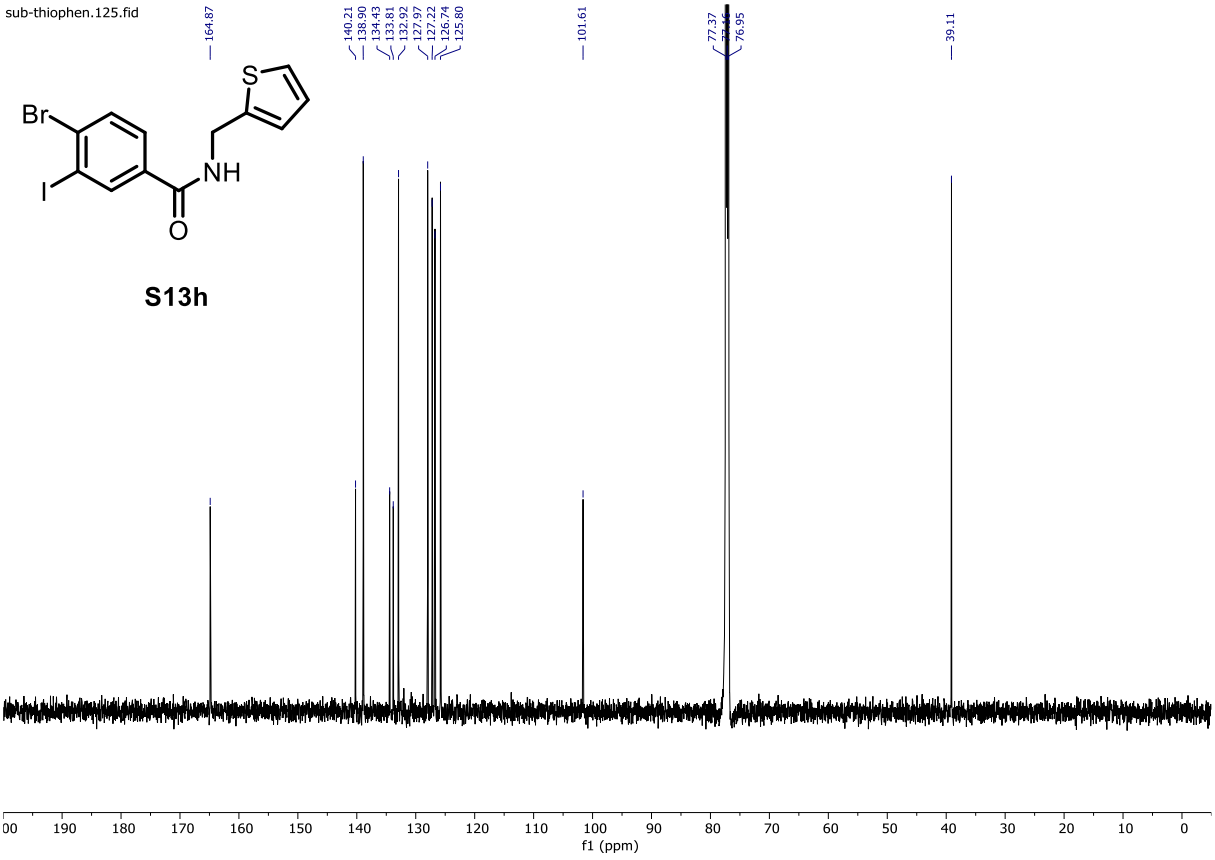

yjm-y5-98-p-1105.1.fid
7.87
7.85
7.68
7.67
7.26 CDCl3
7.06
7.06
7.05
7.05
7.04
7.04
6.37
6.37
6.36
6.36
Br
N
I
0.98
1.03
3.01
1.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

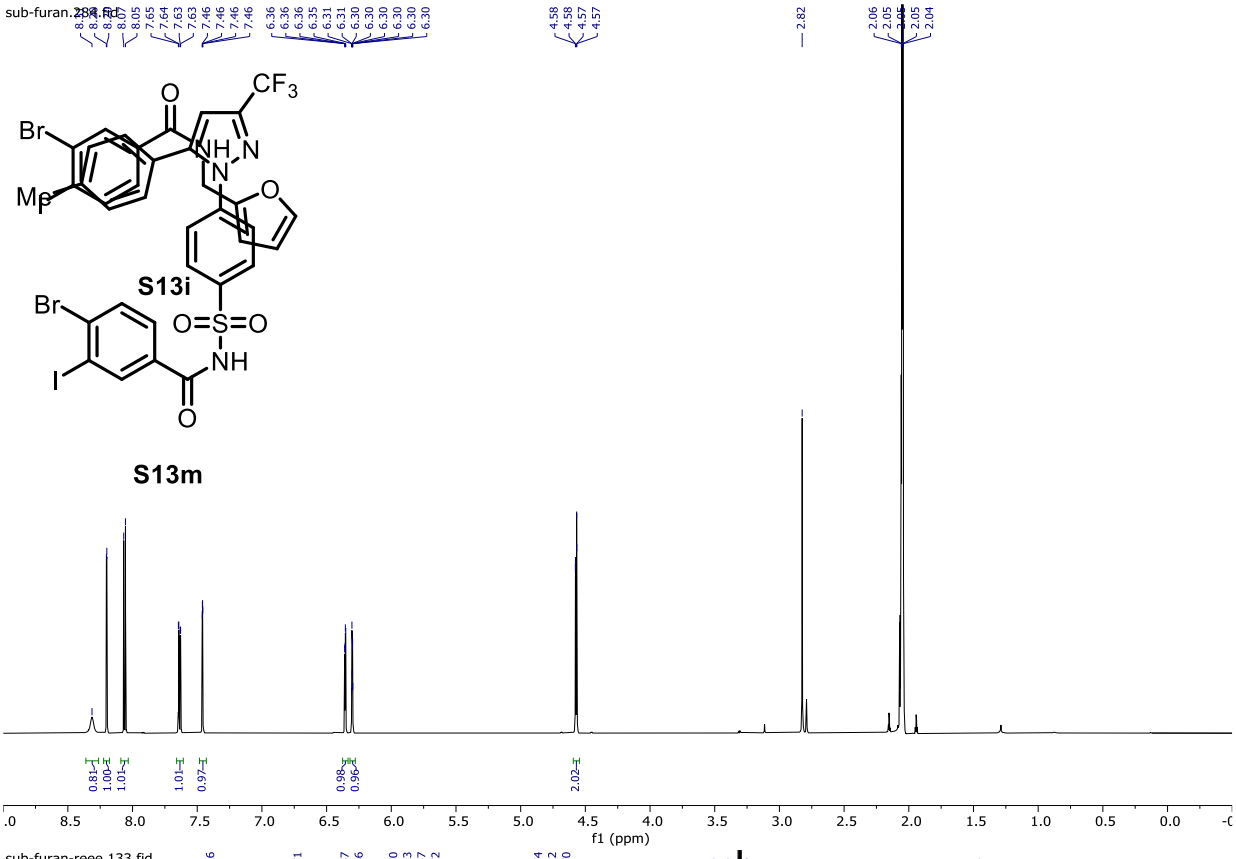
S13g

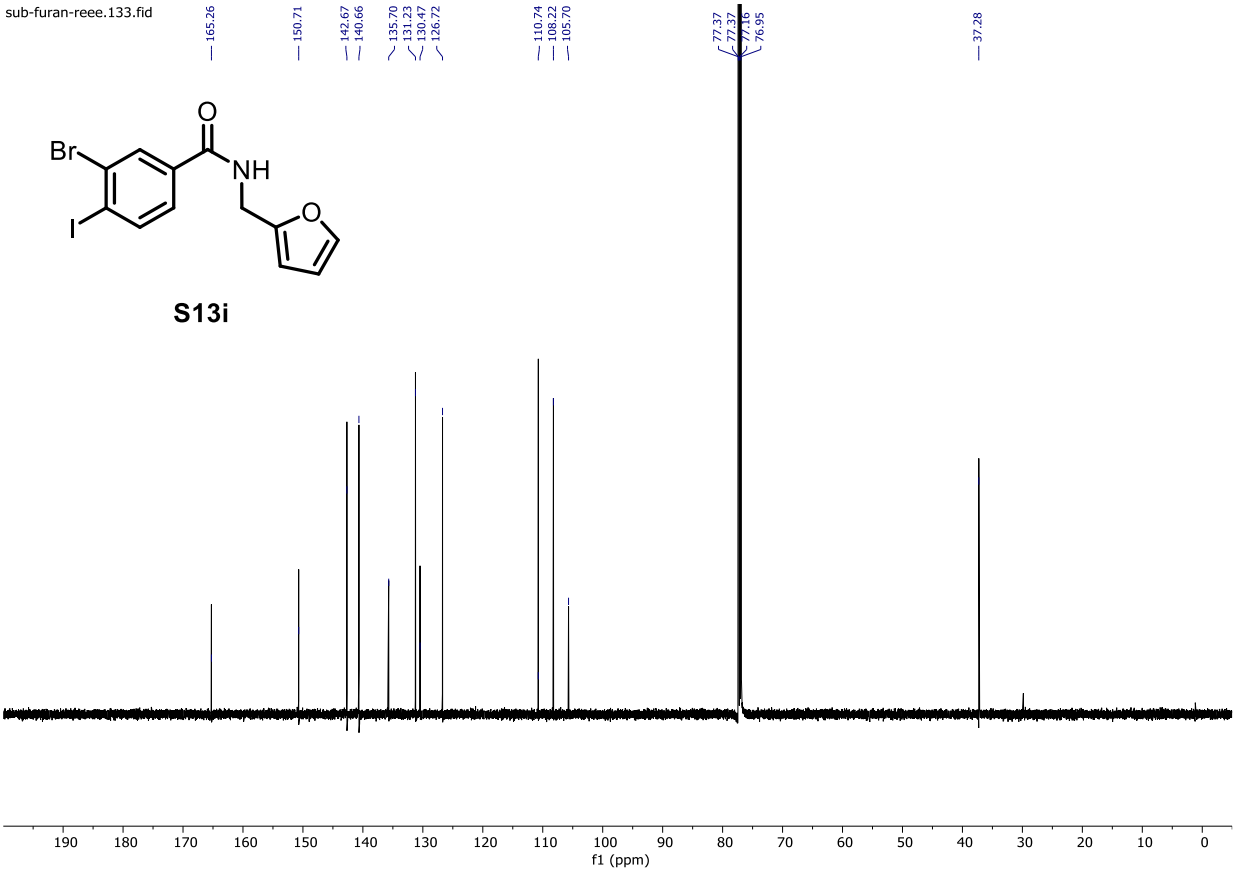

yjm-y5-98-p-1105.2.fid
141.69
140.97
130.71
124.39
120.41
119.18
111.58
96.30
77.37
77.16
76.95
Br
N
I
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

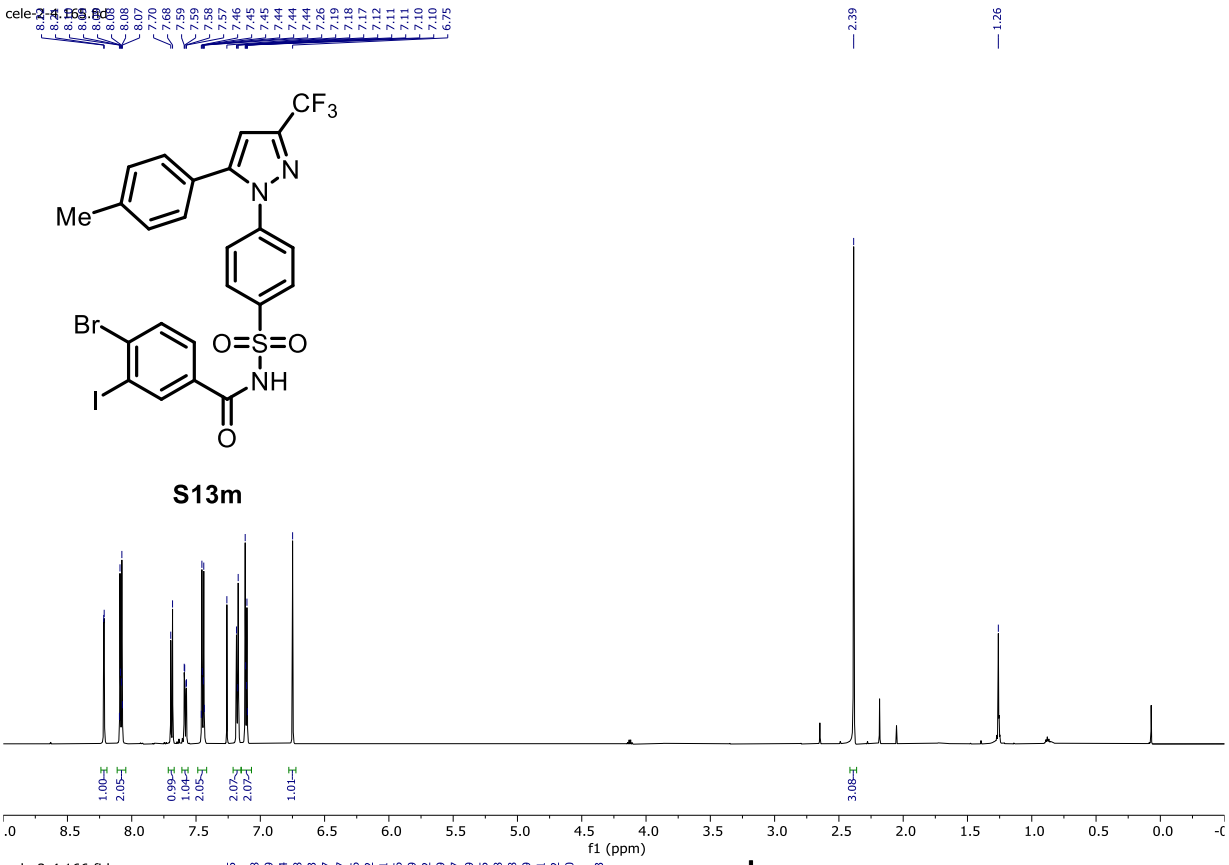
S13g


sub-thiophen.124.fid
Br
I
NH
O
S
S13h
f1 (ppm)

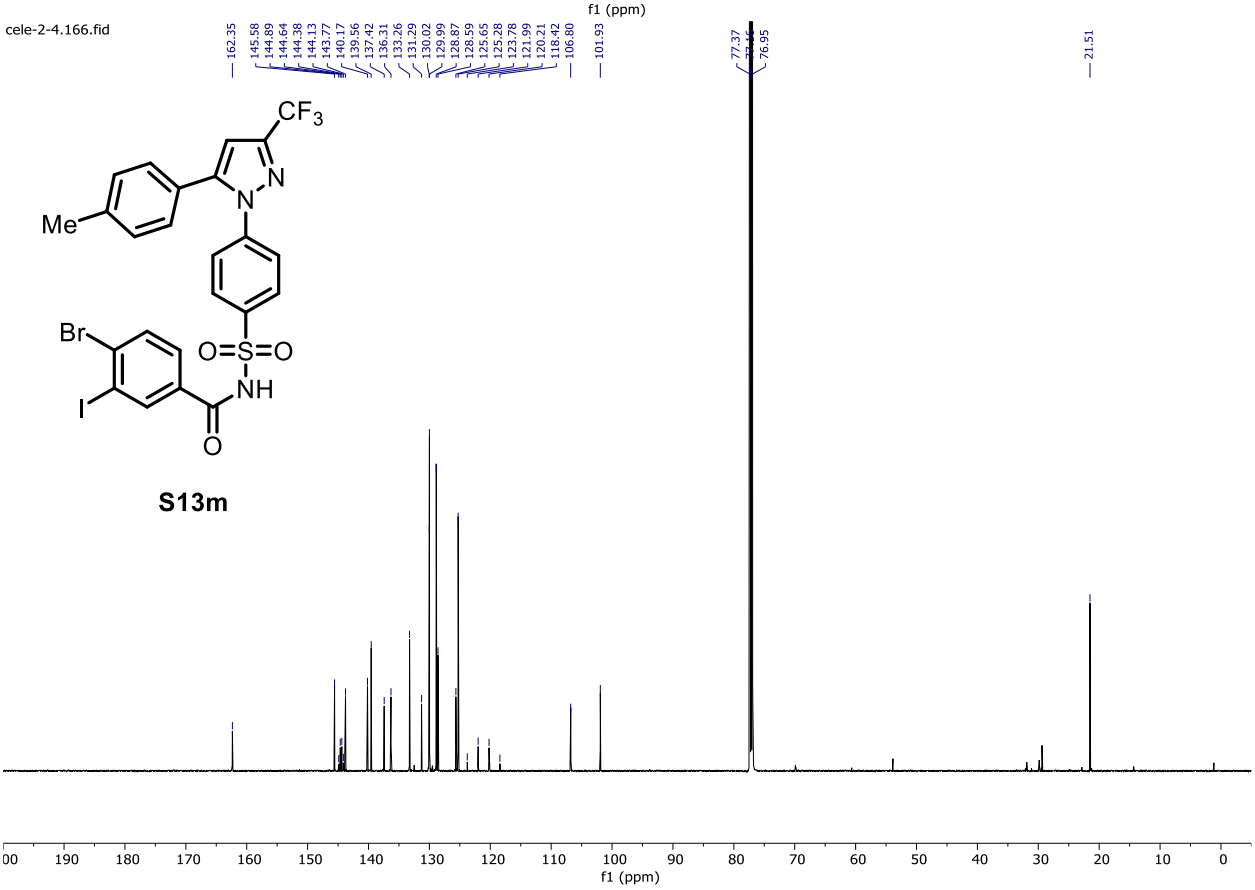

sub-thiophen.125.fid
Br
I
NH
O
S
S13h
f1 (ppm)


sub-furan.238.fid
8.24
8.07
8.05
7.65
7.64
7.63
7.46
6.36
6.35
6.31
6.30
4.58
4.57
2.82
2.06
2.05
2.04
Br
Me
O
CF3
NH
N
O
S13i
Br
I
O=S=O
NH
O
S13m
0.81
1.00
1.01
1.01
0.97
0.98
0.96
2.02
f1 (ppm)


sub-furan-reee.133.fid
165.26
150.71
142.67
140.66
135.70
131.23
130.47
126.72
110.74
108.22
105.70
77.37
77.37
77.16
76.95
37.28
Br
I
O
NH
O
S13i
f1 (ppm)

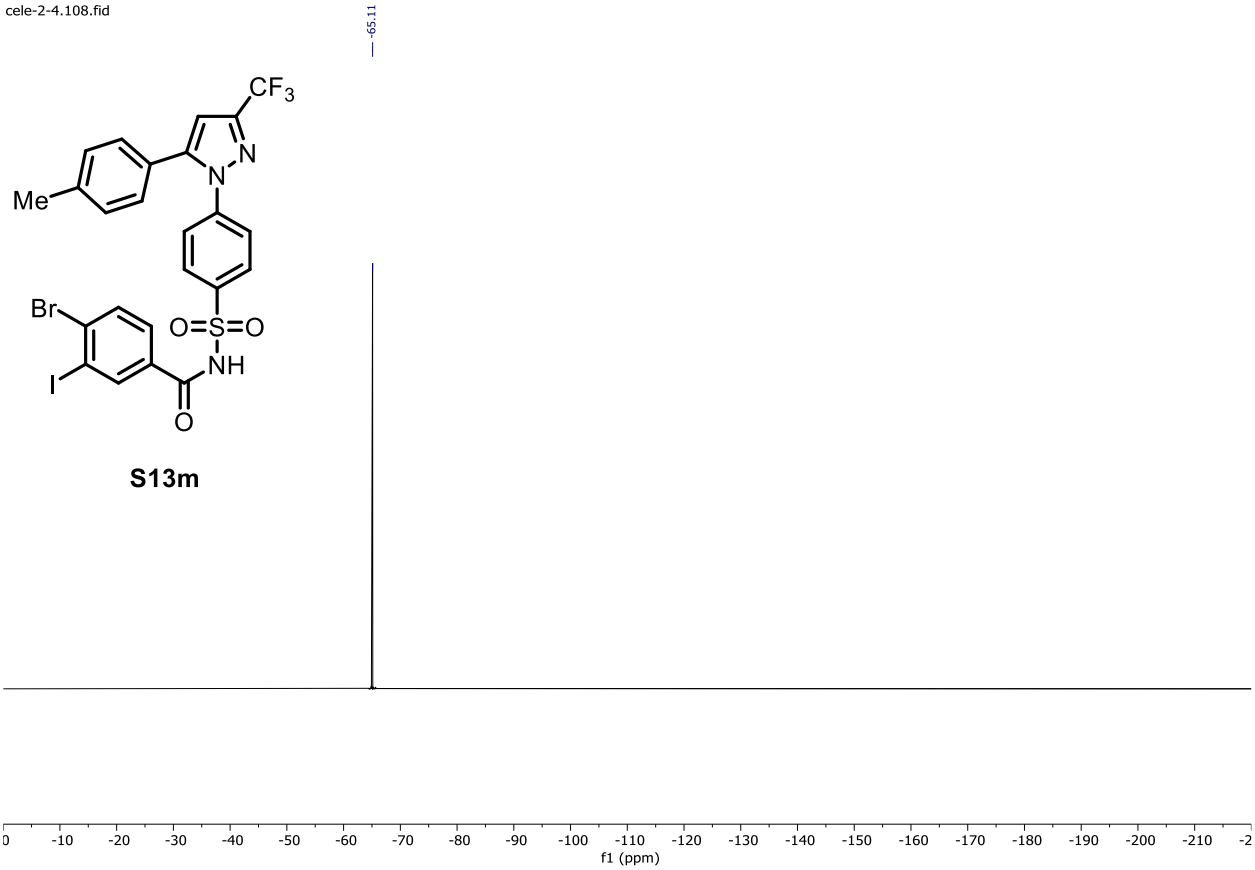

cele-2-4.166.fid
8.14 8.13 8.13 8.08 8.08 8.07 7.70 7.68 7.59 7.59 7.58 7.57 7.46 7.45 7.44 7.44 7.44 7.26 7.19 7.18 7.17 7.12 7.11 7.11 7.10 7.10 6.75
2.39
1.26
CF3
N
N
Me
Br
O=S=O
NH
I
O
1.00 2.05 0.99 1.04 2.05 2.07 2.07 1.01 3.08
f1 (ppm)

S13m

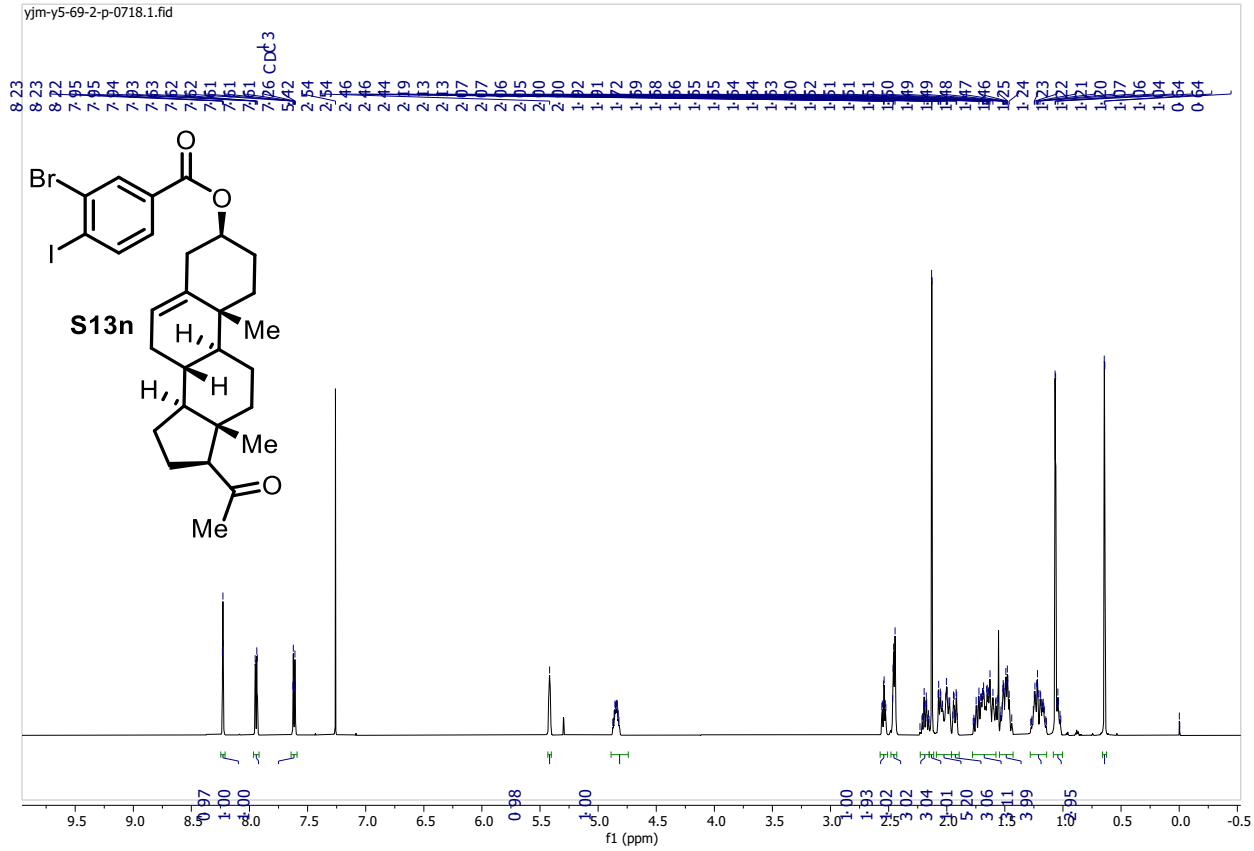

cele-2-4.166.fid
162.35 145.58 144.89 144.64 144.38 144.13 143.77 140.17 139.56 137.42 136.31 133.26 131.29 130.02 129.99 128.87 128.59 125.65 125.28 123.78 121.99 120.21 118.42 106.80 101.93 77.37 77.16 76.95 21.51
CF3
N
N
Me
Br
O=S=O
NH
I
O
f1 (ppm)

S13m

cele-2-4.108.fid



S13m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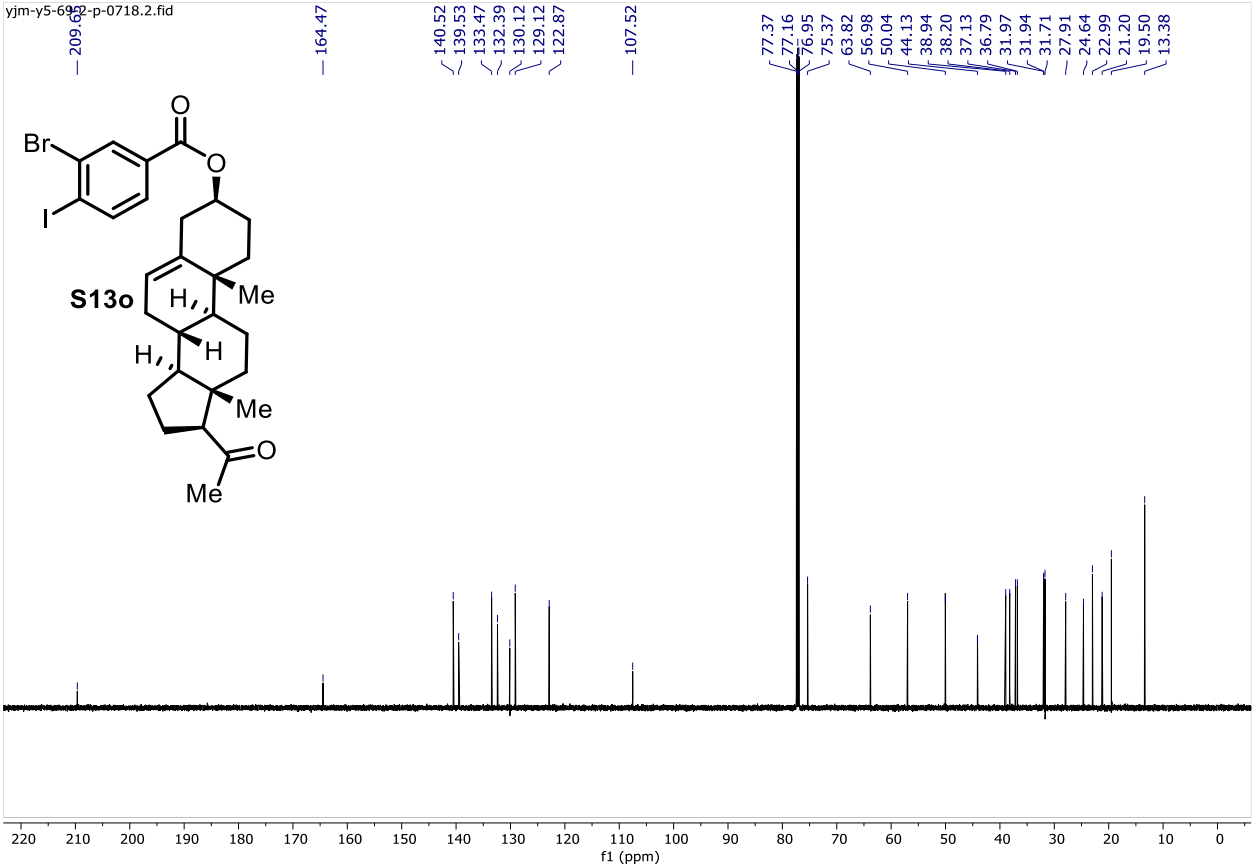
S13n
f1 (ppm)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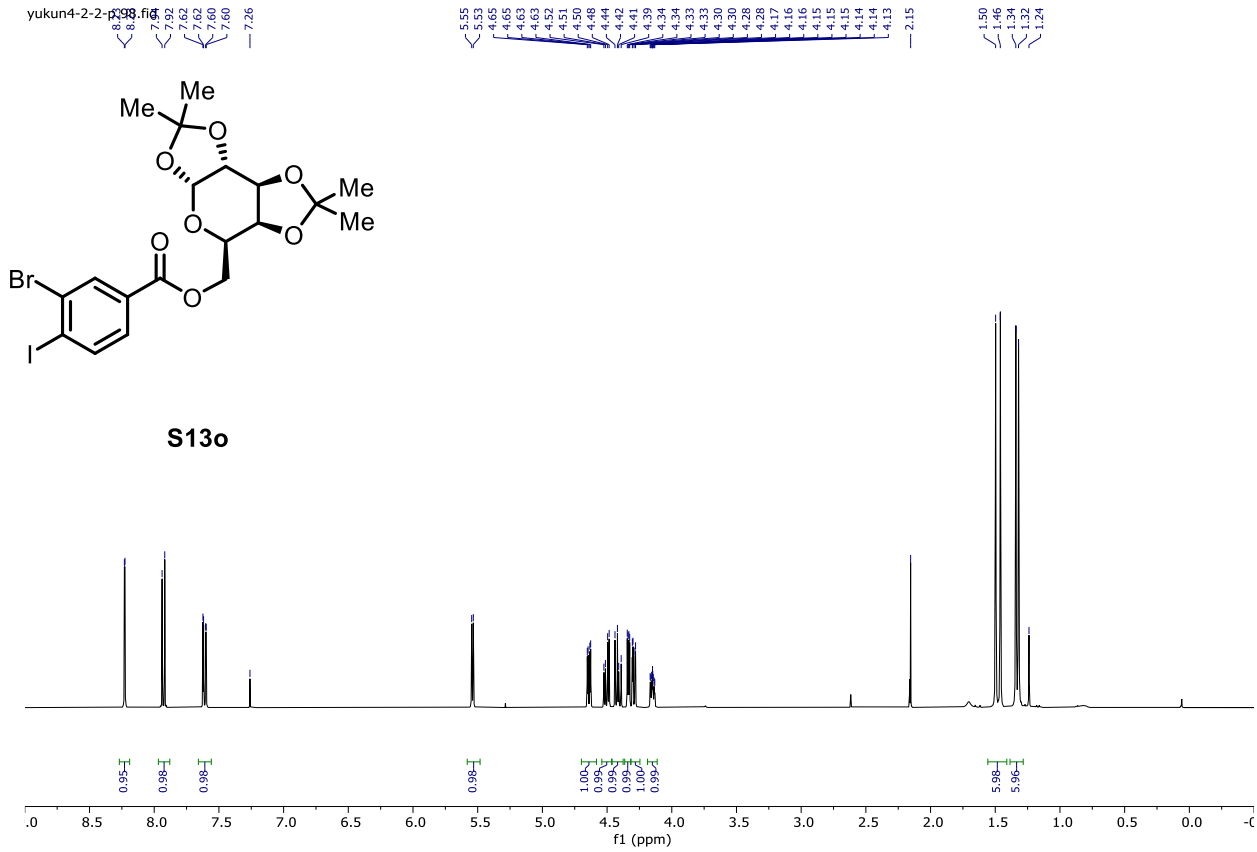
S13o
f1 (ppm)


yukun4-2-2-p98.fid
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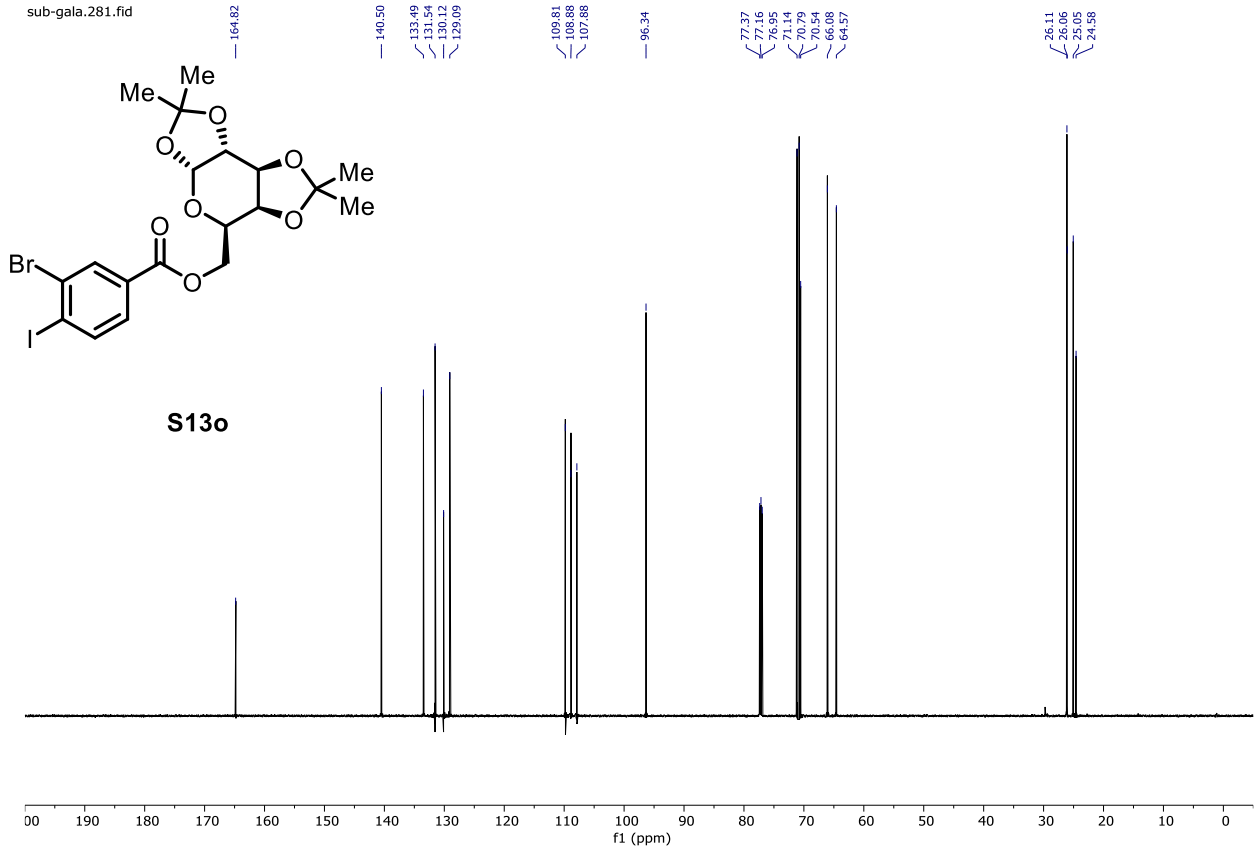
Me
O
O
O
O
Me
Me
O
O
Br
I
S13o
f1 (ppm)


sub-gala.281.fid
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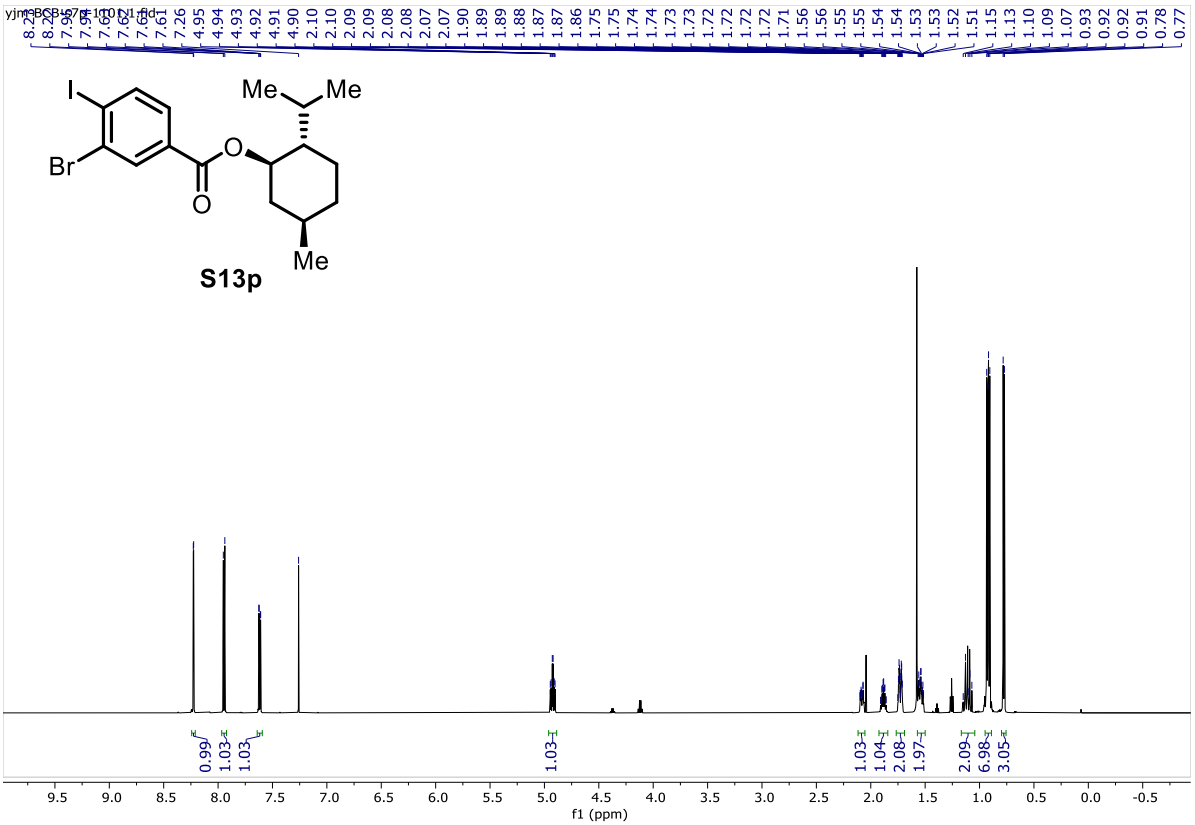
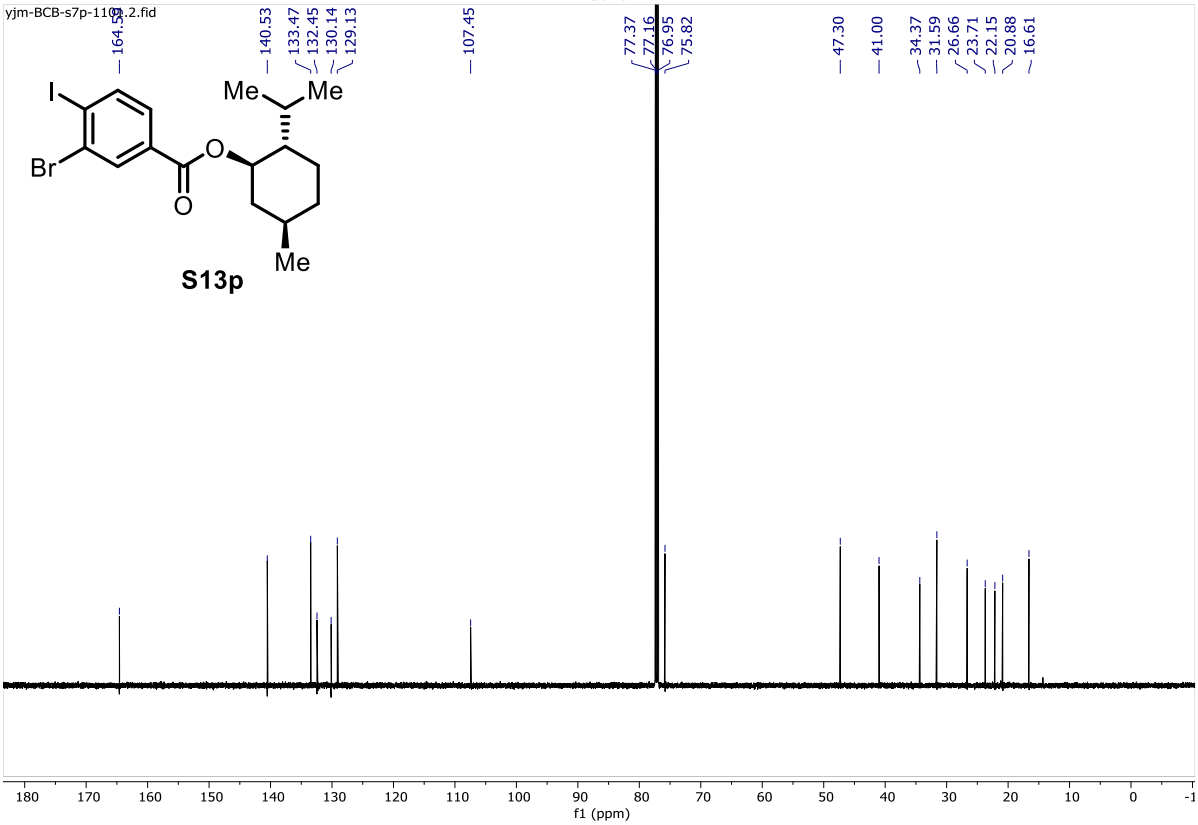
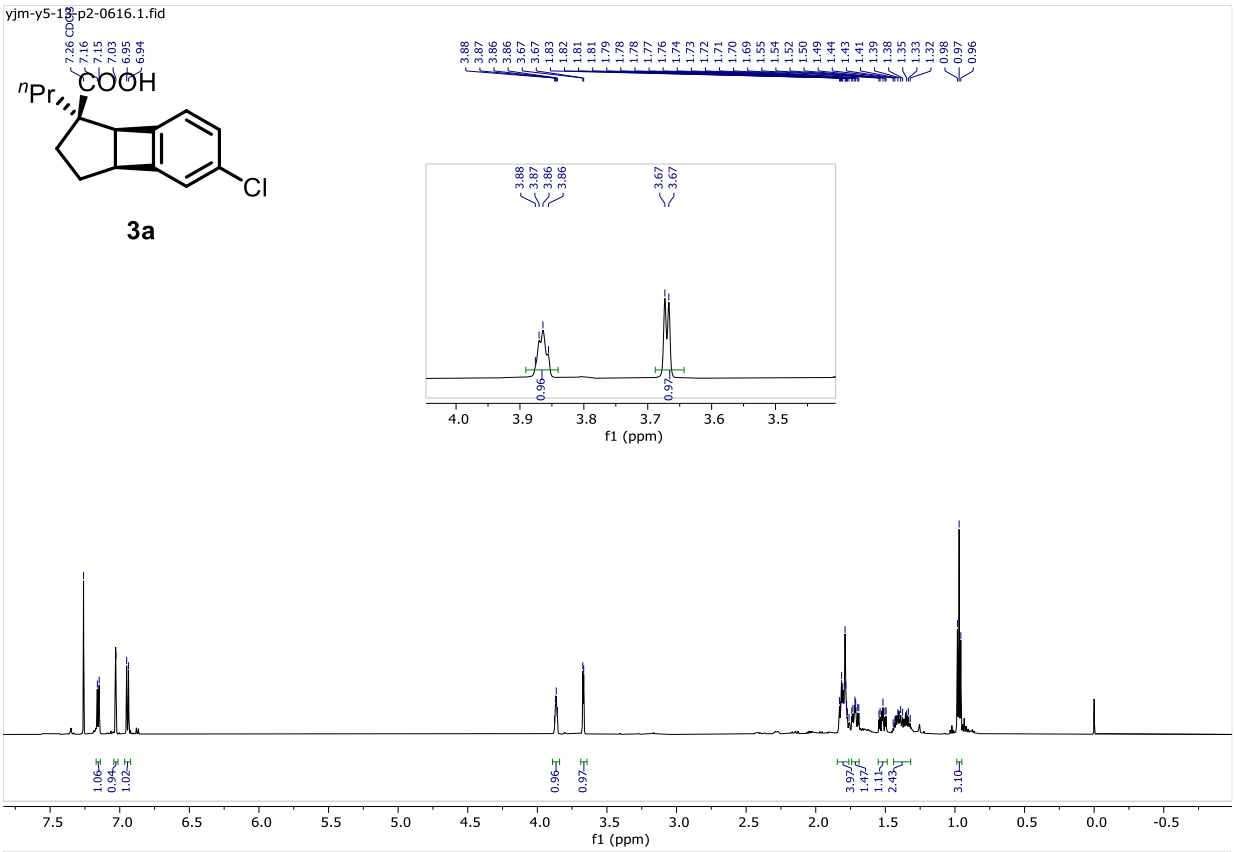
Me
O
O
O
O
Me
Me
O
O
Br
I
S13o
f1 (ppm)


yjm-BCB-s7p-1101.1.fid
I
Br
O
O
Me
Me
Me
S13p
0.99
1.03
1.03
1.03
1.03
1.04
2.08
1.97
2.09
6.98
3.05
f1 (ppm)


yjm-BCB-s7p-1101.2.fid
164.53
140.53
133.47
132.45
130.14
129.13
107.45
77.37
77.16
76.95
75.82
47.30
41.00
34.37
31.59
26.66
23.71
22.15
20.88
16.61
I
Br
O
O
Me
Me
Me
S13p
f1 (ppm)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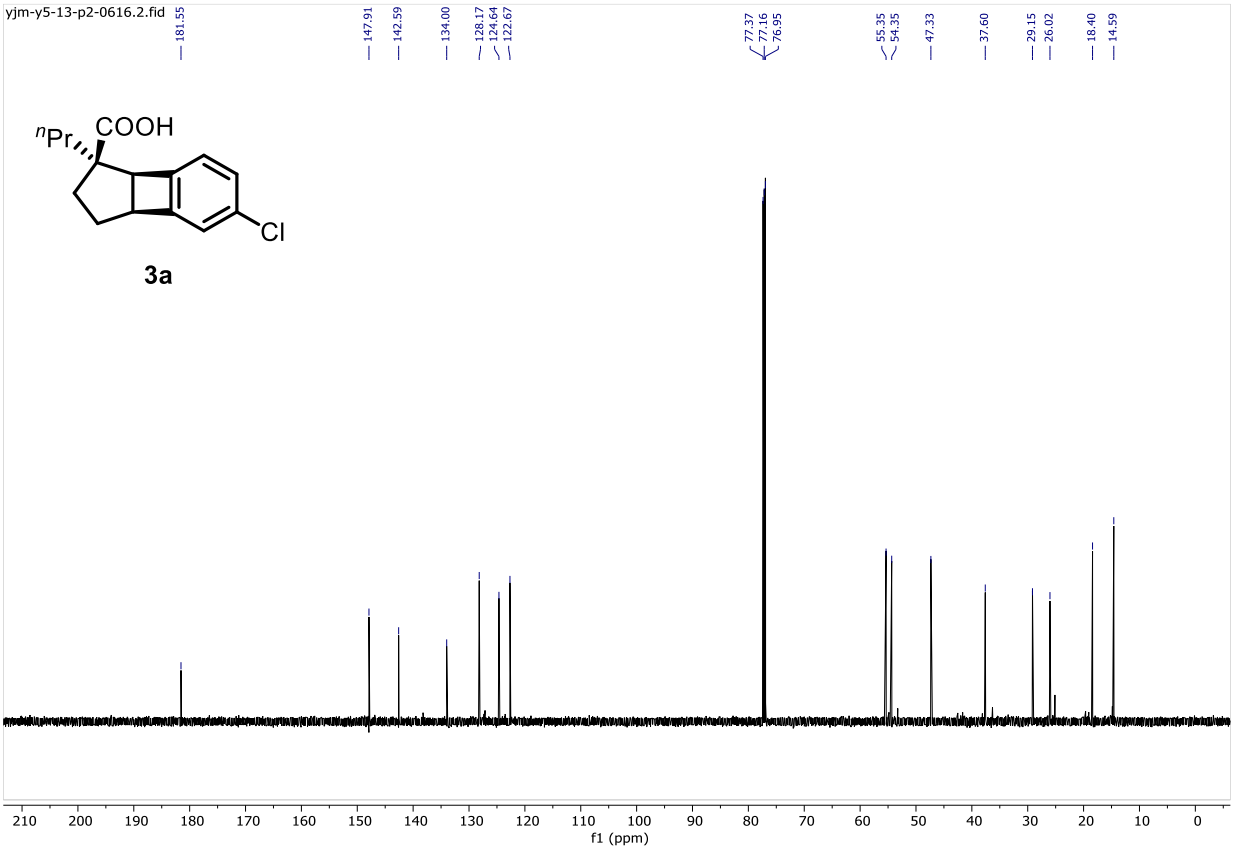
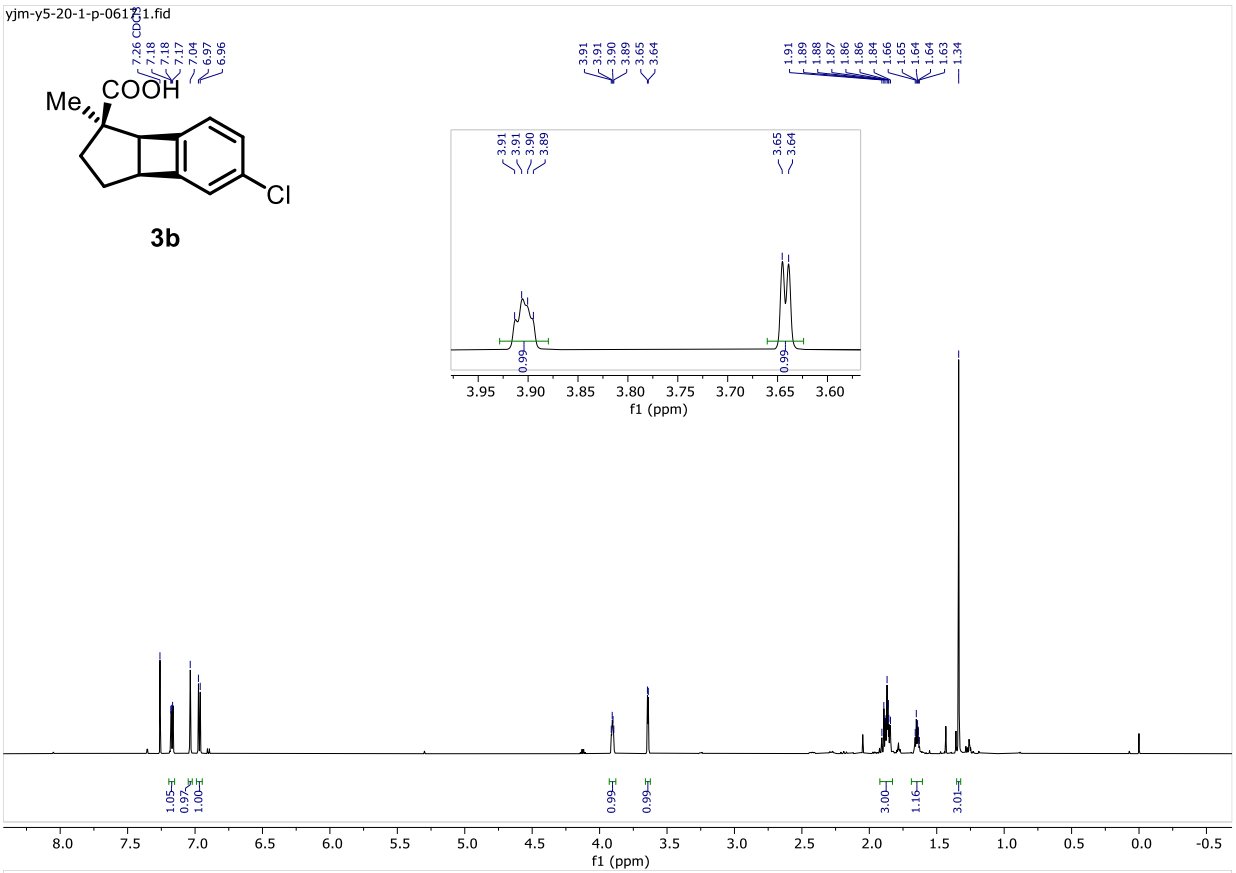
nPr
COOH
Cl
3a
f1 (ppm)


yjm-y5-13-p2-0616.2.fid
nPr
COOH
Cl
3a
f1 (ppm)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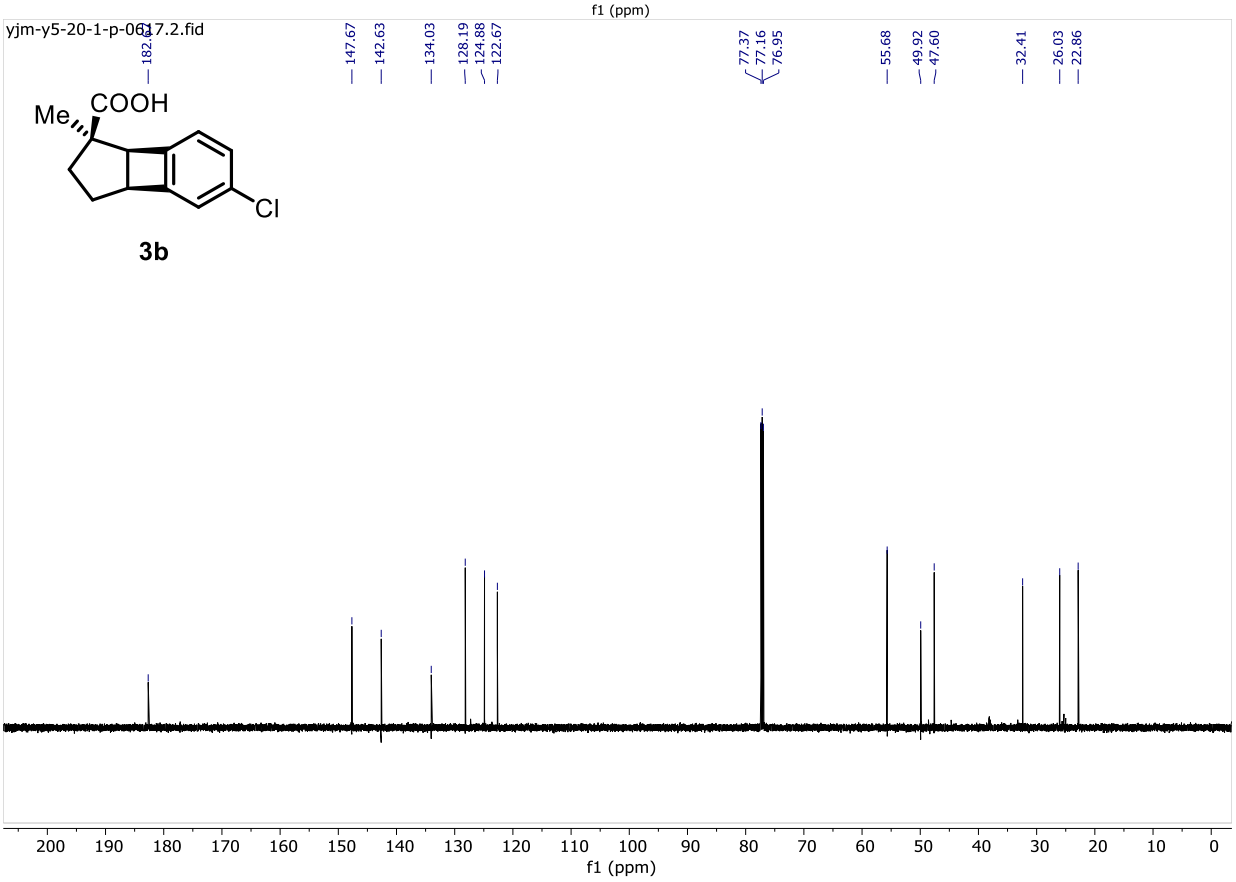
Me
COOH
Cl
3b
f1 (ppm)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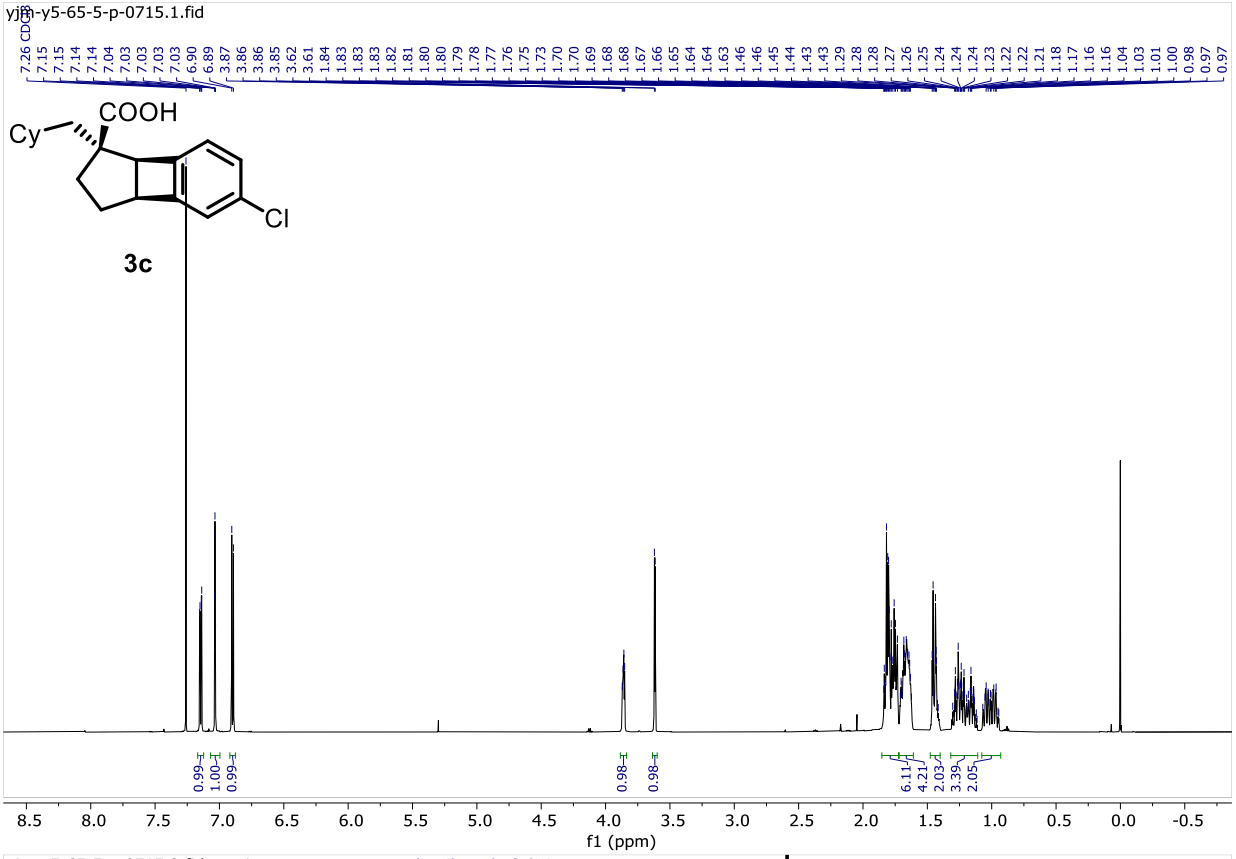
Me
COOH
Cl
3b
f1 (ppm)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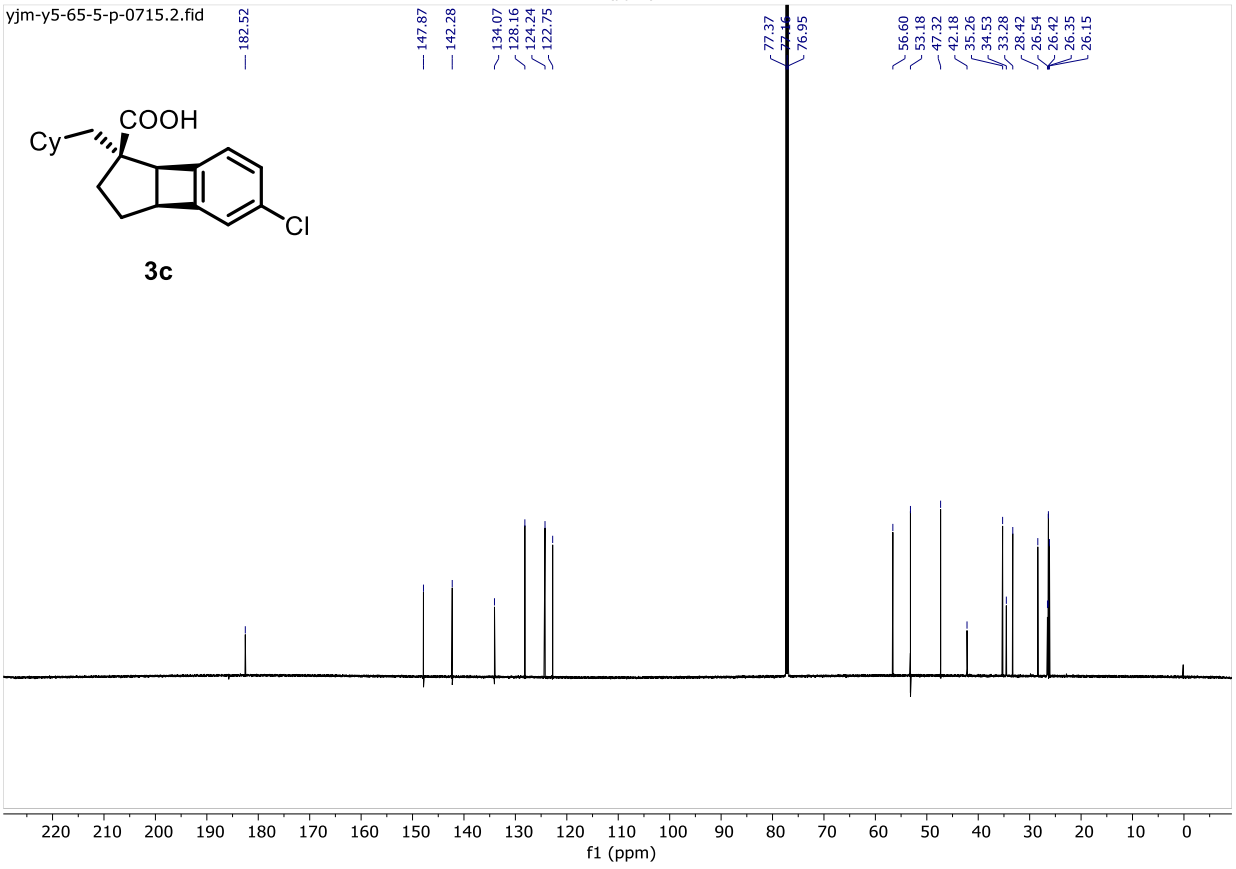
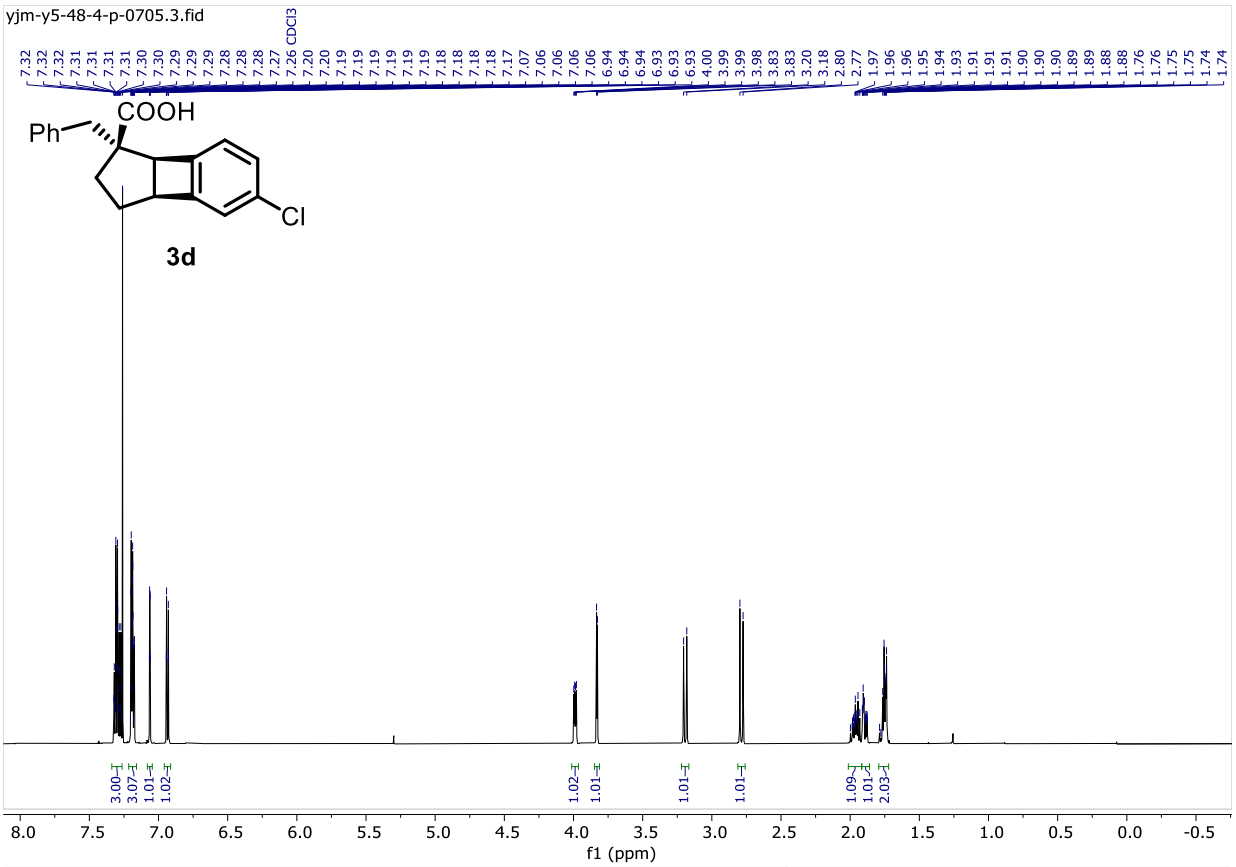
COOH
Cy
Cl
3c
f1 (ppm)


yjm-y5-65-5-p-0715.2.fid
COOH
Cy
Cl
3c
f1 (ppm)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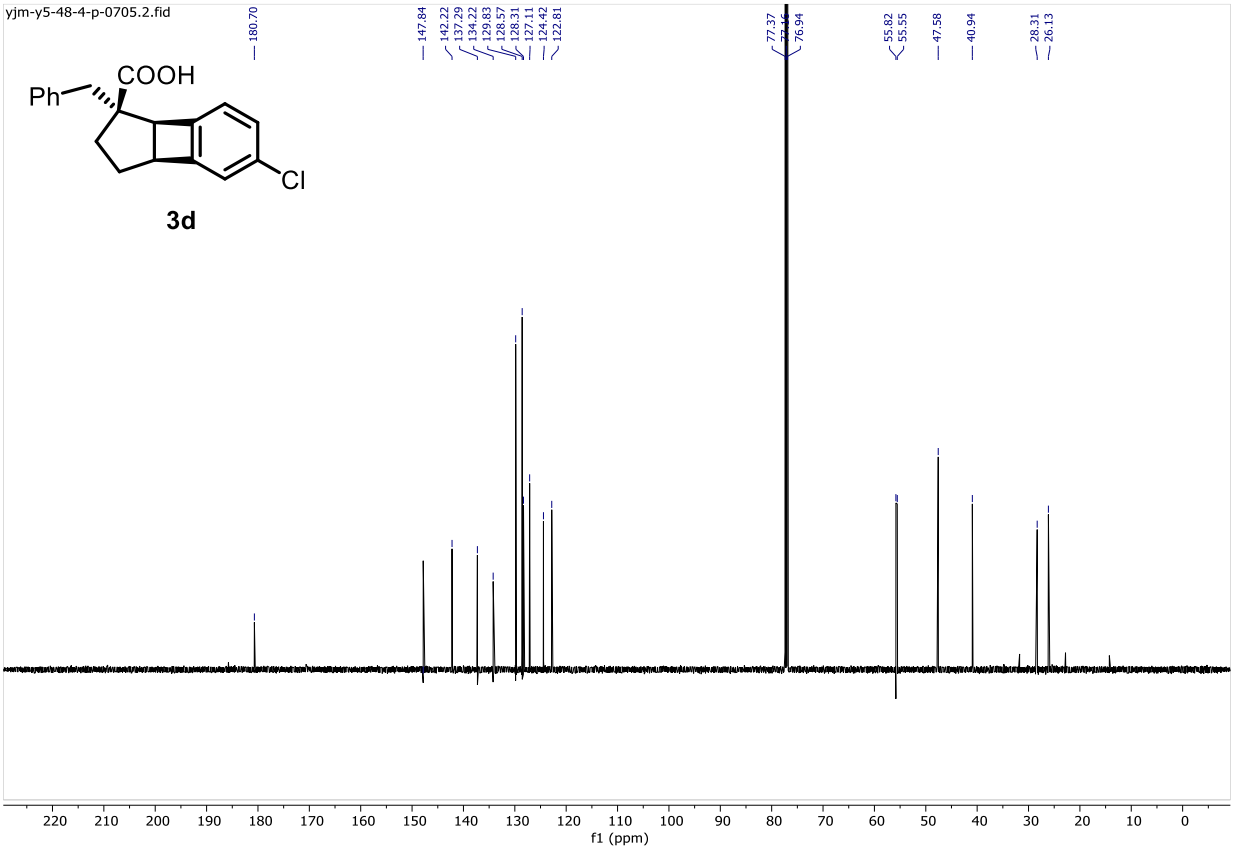
COOH
Ph
Cl
3d
f1 (ppm)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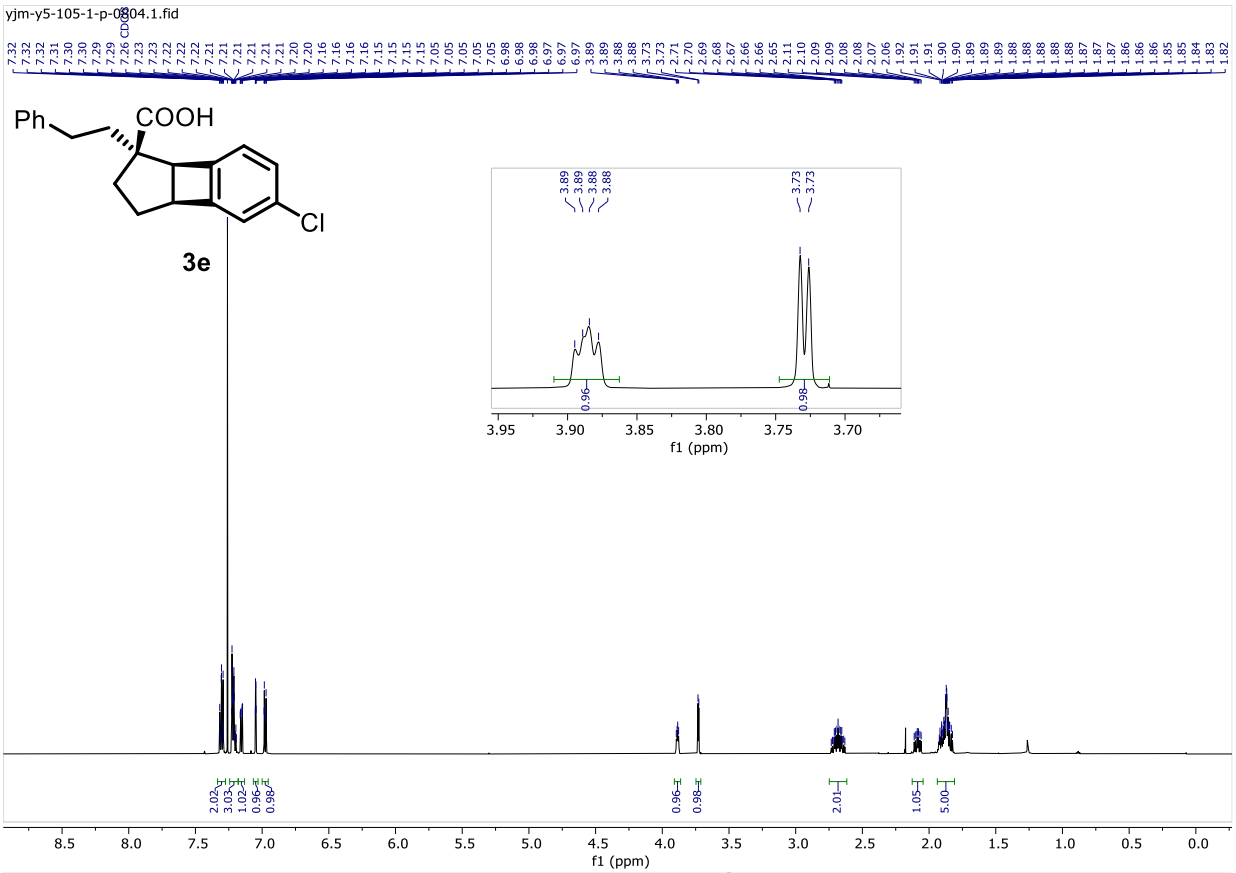
COOH
Ph
Cl
3d
f1 (ppm)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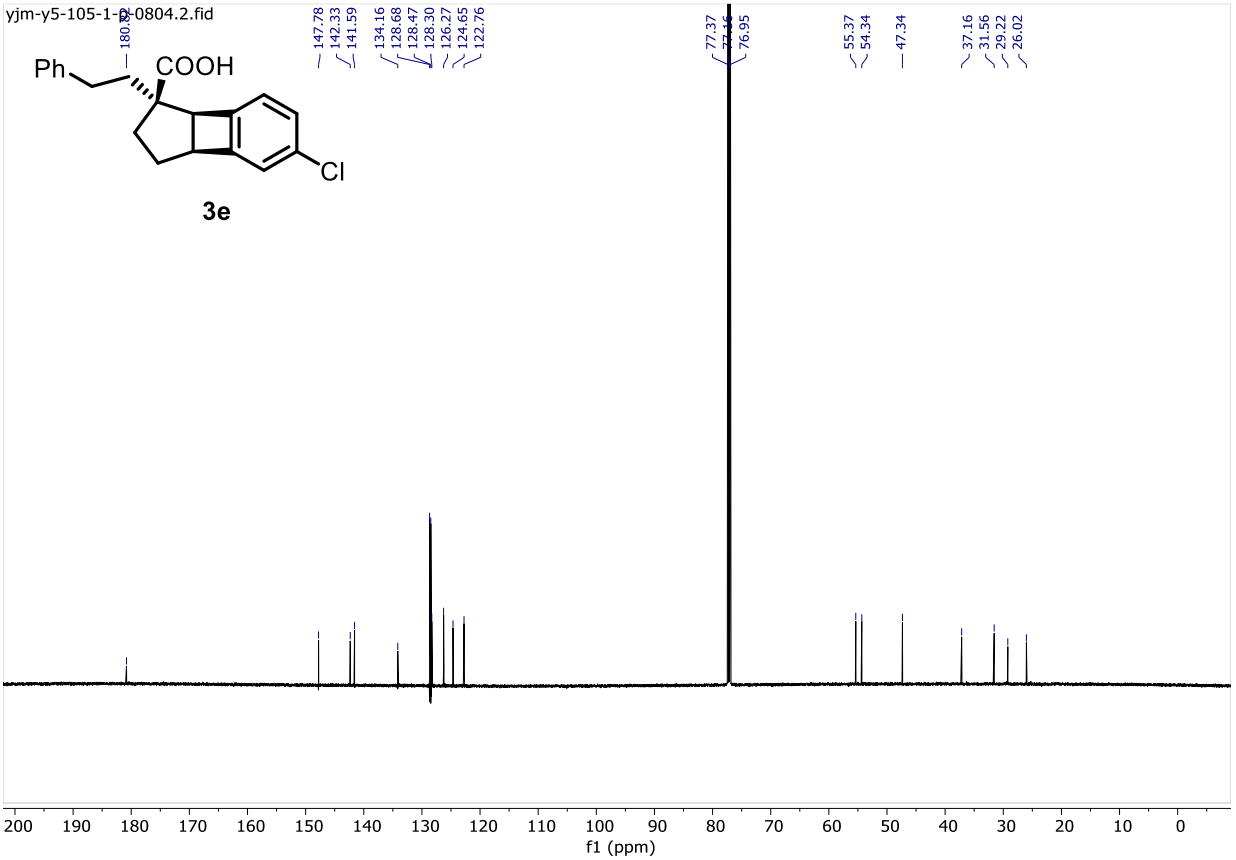
Ph
COOH
Cl
3e
f1 (ppm)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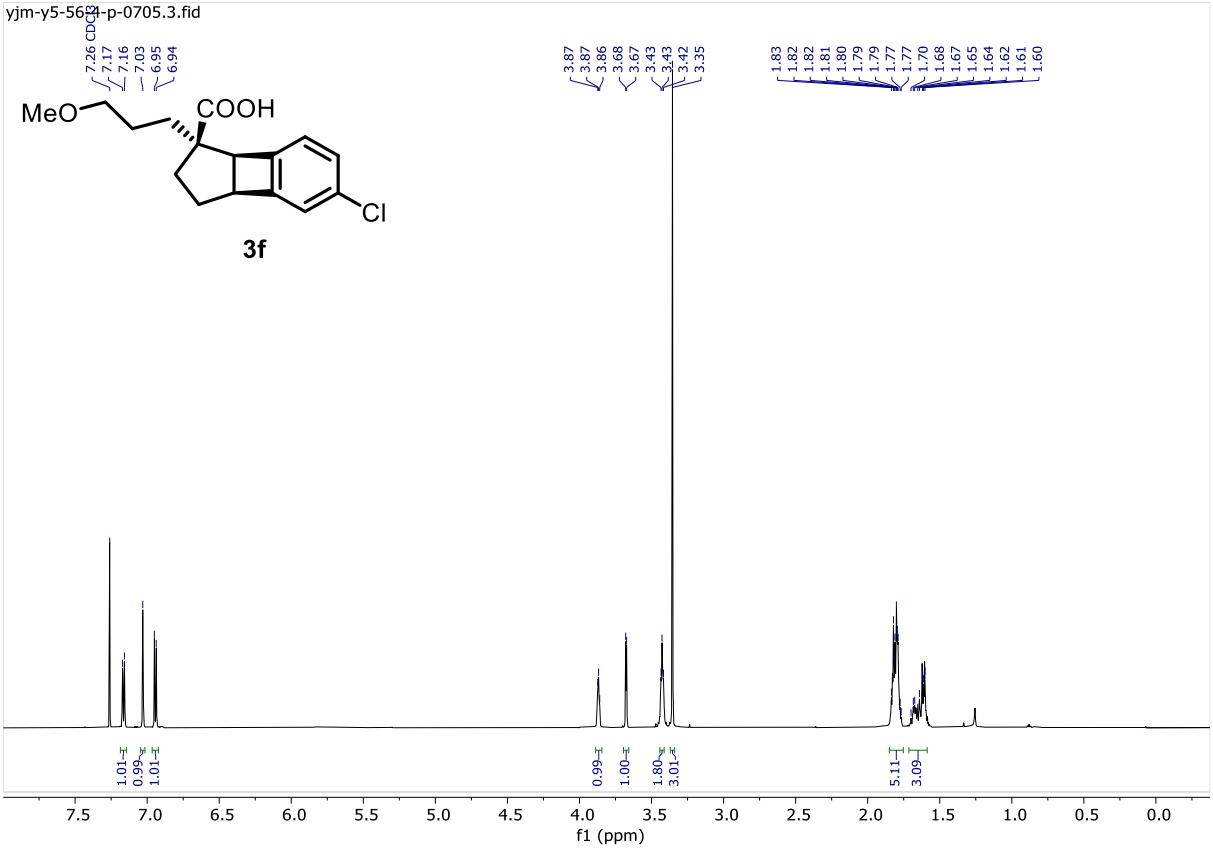
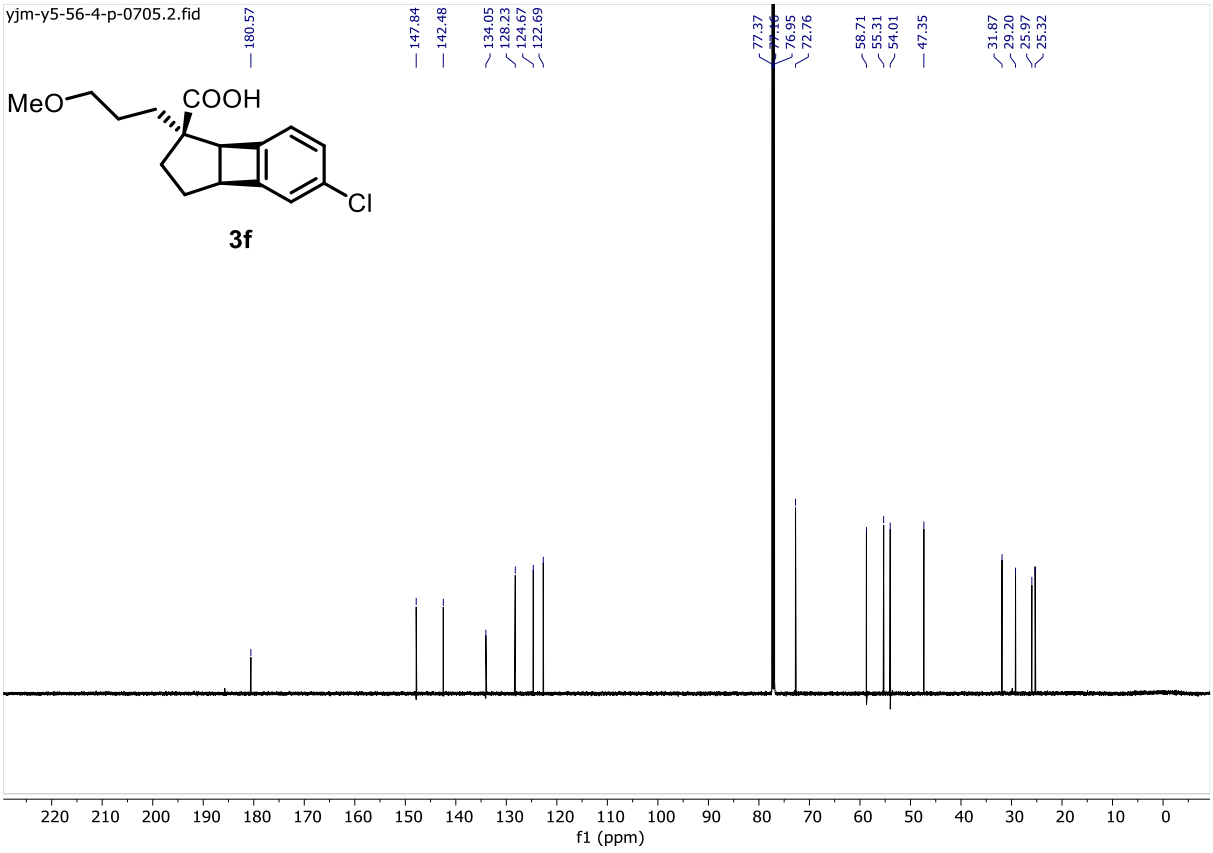
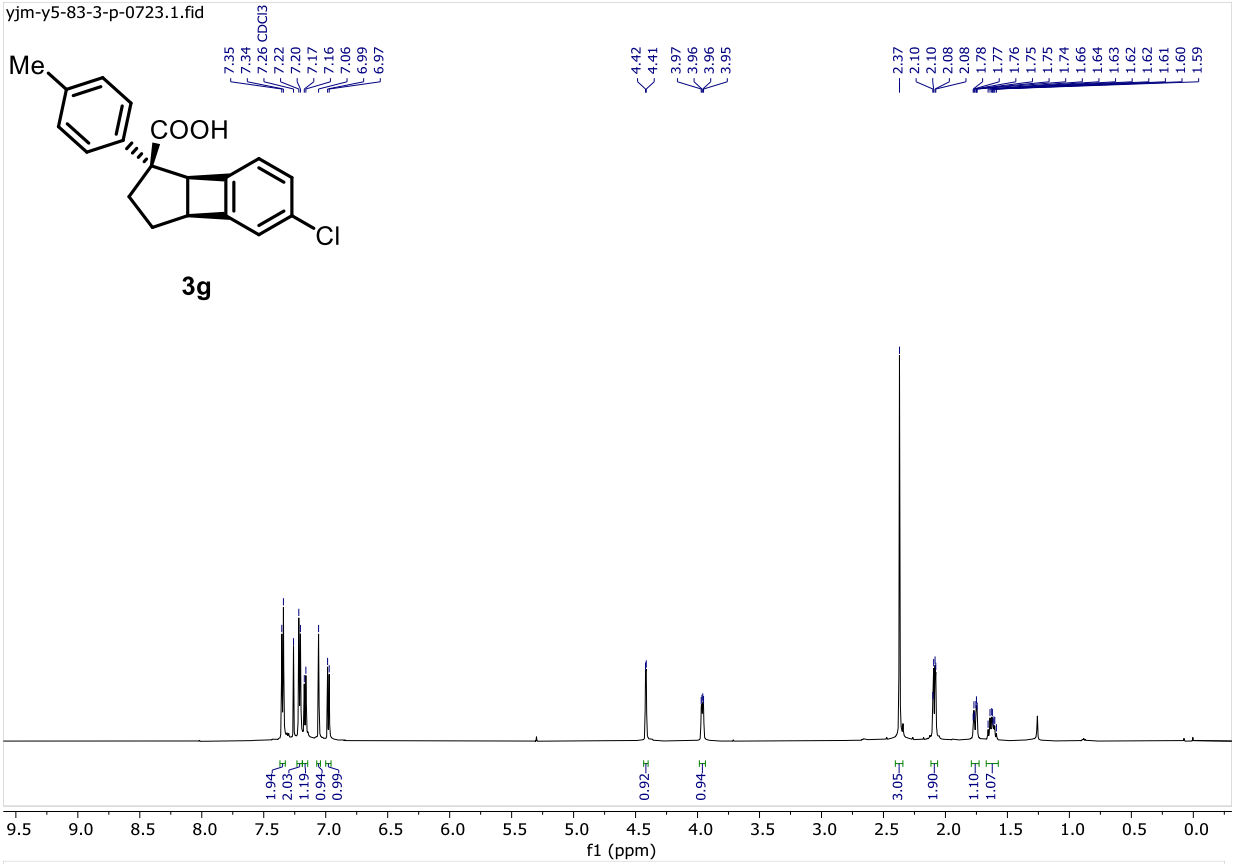
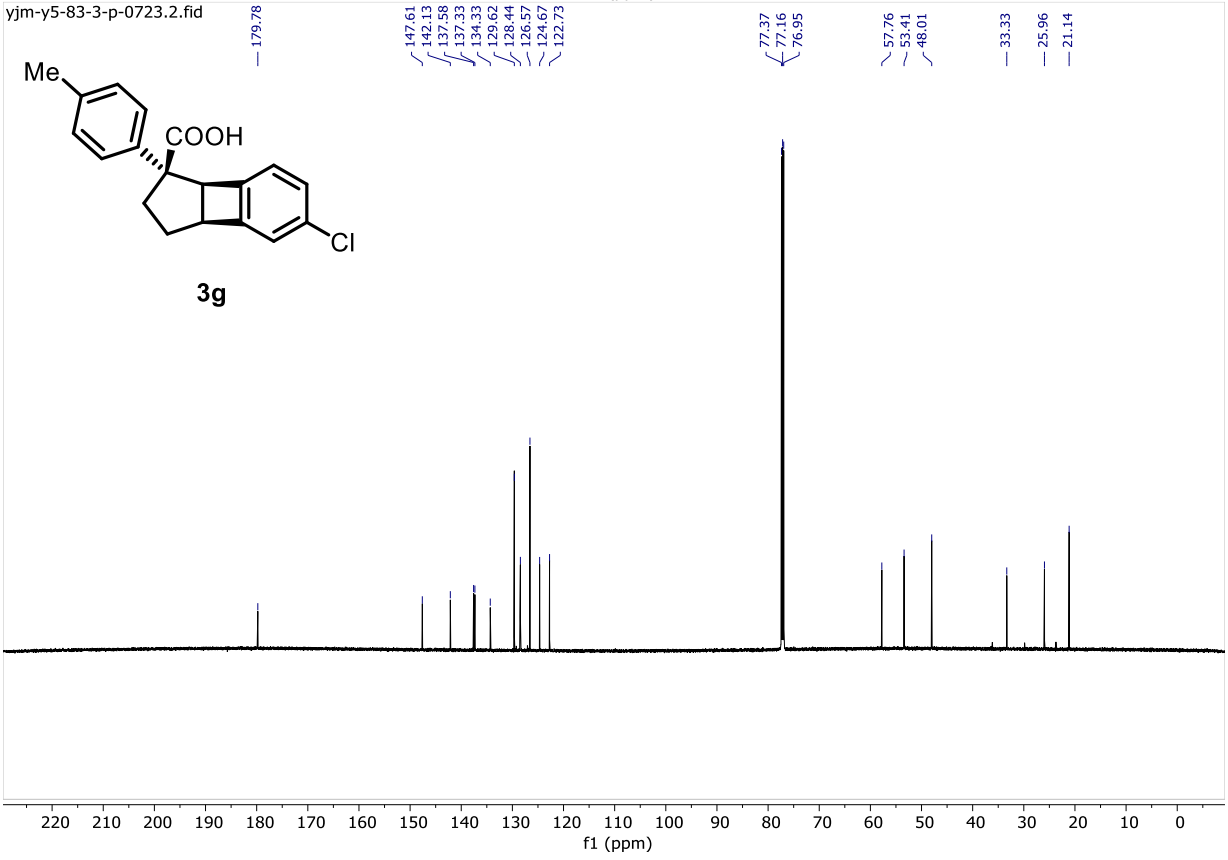
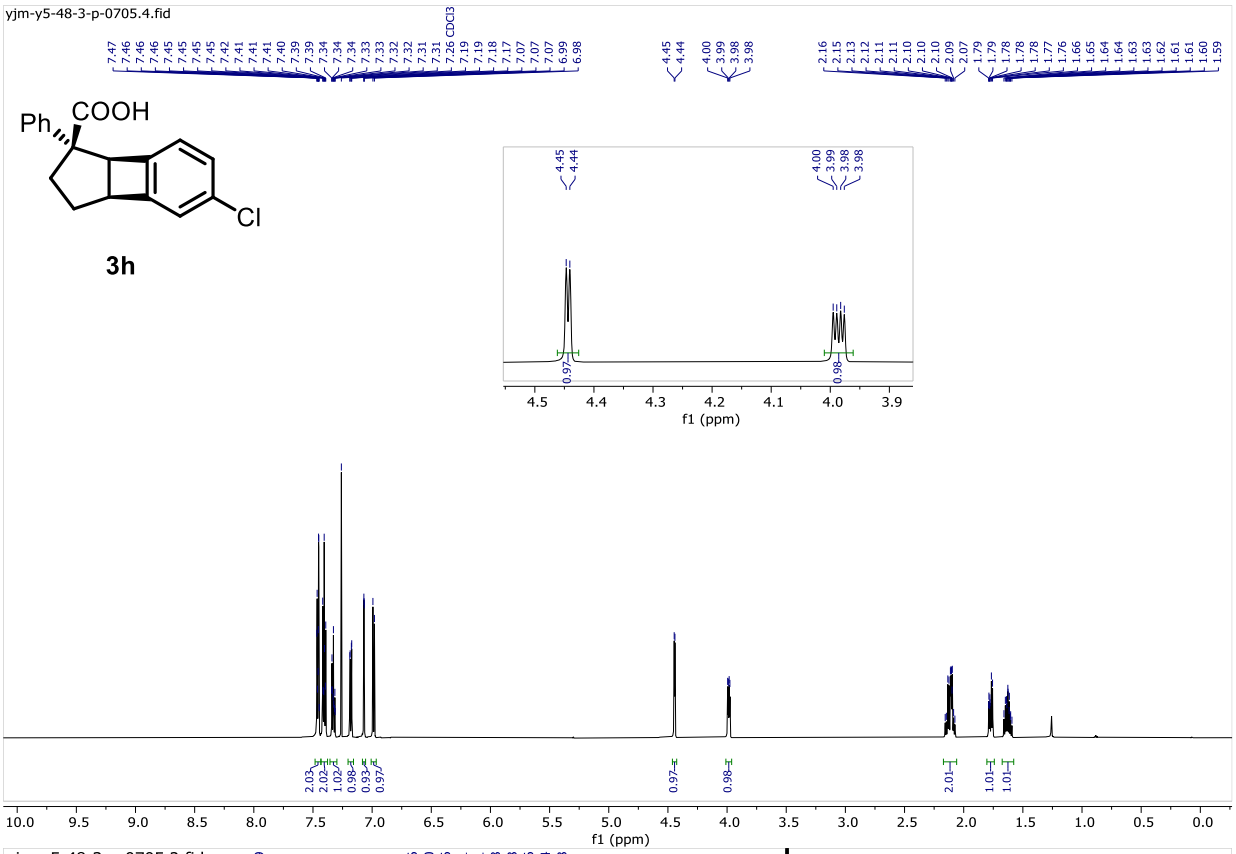
Ph
COOH
Cl
3e
f1 (ppm)


yjm-y5-56-4-p-0705.3.fid
7.26 CDCl3
7.17
7.16
7.03
6.95
6.94
3.87
3.87
3.86
3.68
3.67
3.43
3.43
3.42
3.35
1.83
1.82
1.82
1.81
1.80
1.79
1.79
1.77
1.77
1.70
1.68
1.67
1.65
1.64
1.62
1.61
1.60
MeO
COOH
Cl
3f
1.01
0.99
1.01
0.99
1.00
1.80
3.01
5.11
3.09
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


yjm-y5-56-4-p-0705.2.fid
180.57
147.84
142.48
134.05
128.23
124.67
122.69
77.37
77.16
76.95
72.76
58.71
55.31
54.01
47.35
31.87
29.20
25.97
25.32
MeO
COOH
Cl
3f
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


yjm-y5-83-3-p-0723.1.fid
Me
COOH
Cl
3g
7.35
7.34
7.26 CDCl3
7.22
7.20
7.17
7.16
7.06
6.99
6.97
4.42
4.41
3.97
3.96
3.96
3.95
2.37
2.10
2.10
2.08
2.08
1.78
1.77
1.76
1.75
1.75
1.74
1.66
1.64
1.63
1.62
1.62
1.61
1.60
1.59
1.94
2.03
1.19
0.94
0.99
0.92
0.94
3.05
1.90
1.10
1.07
f1 (ppm)


yjm-y5-83-3-p-0723.2.fid
Me
COOH
Cl
3g
179.78
147.61
142.13
137.58
137.33
134.33
129.62
128.44
126.57
124.67
122.73
77.37
77.16
76.95
57.76
53.41
48.01
33.33
25.96
21.14
f1 (ppm)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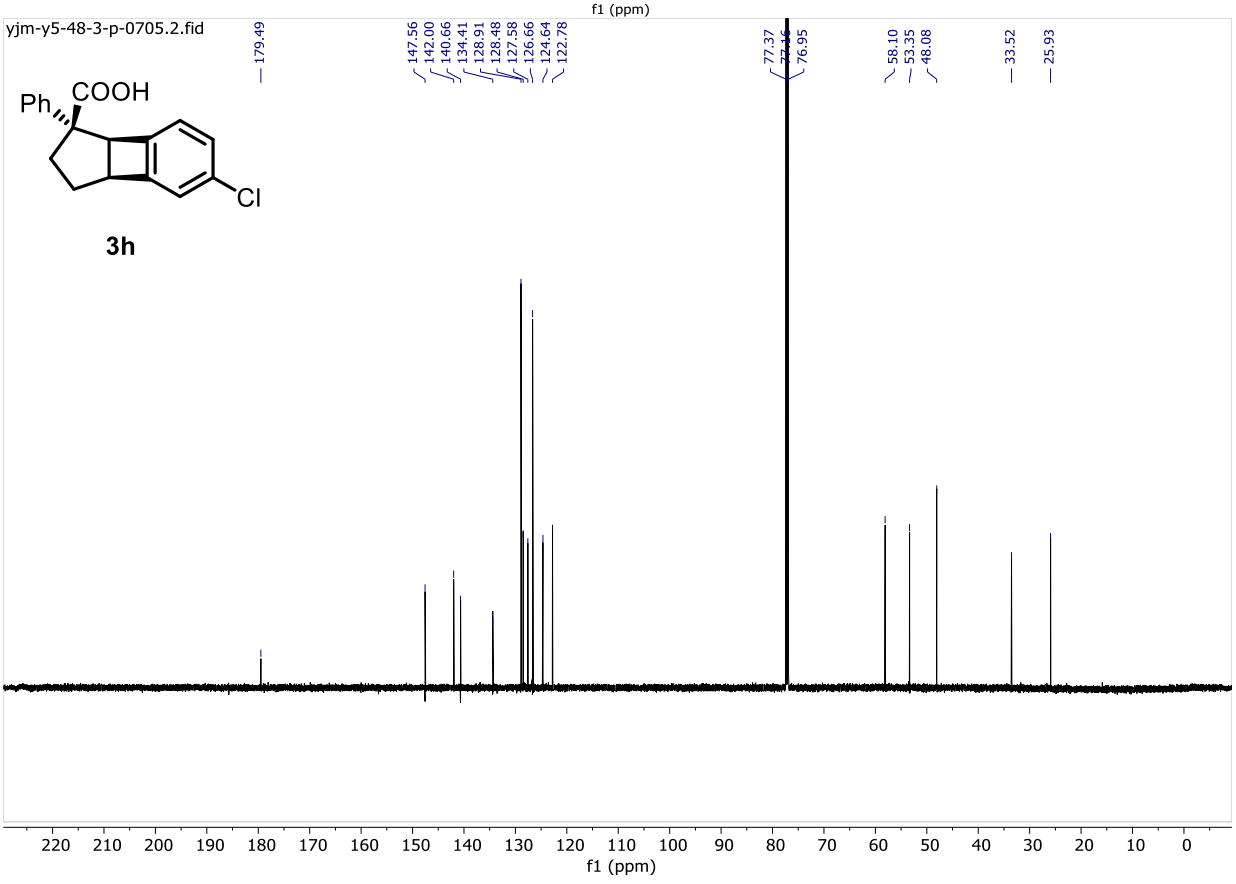
Ph
COOH
Cl
3h
f1 (ppm)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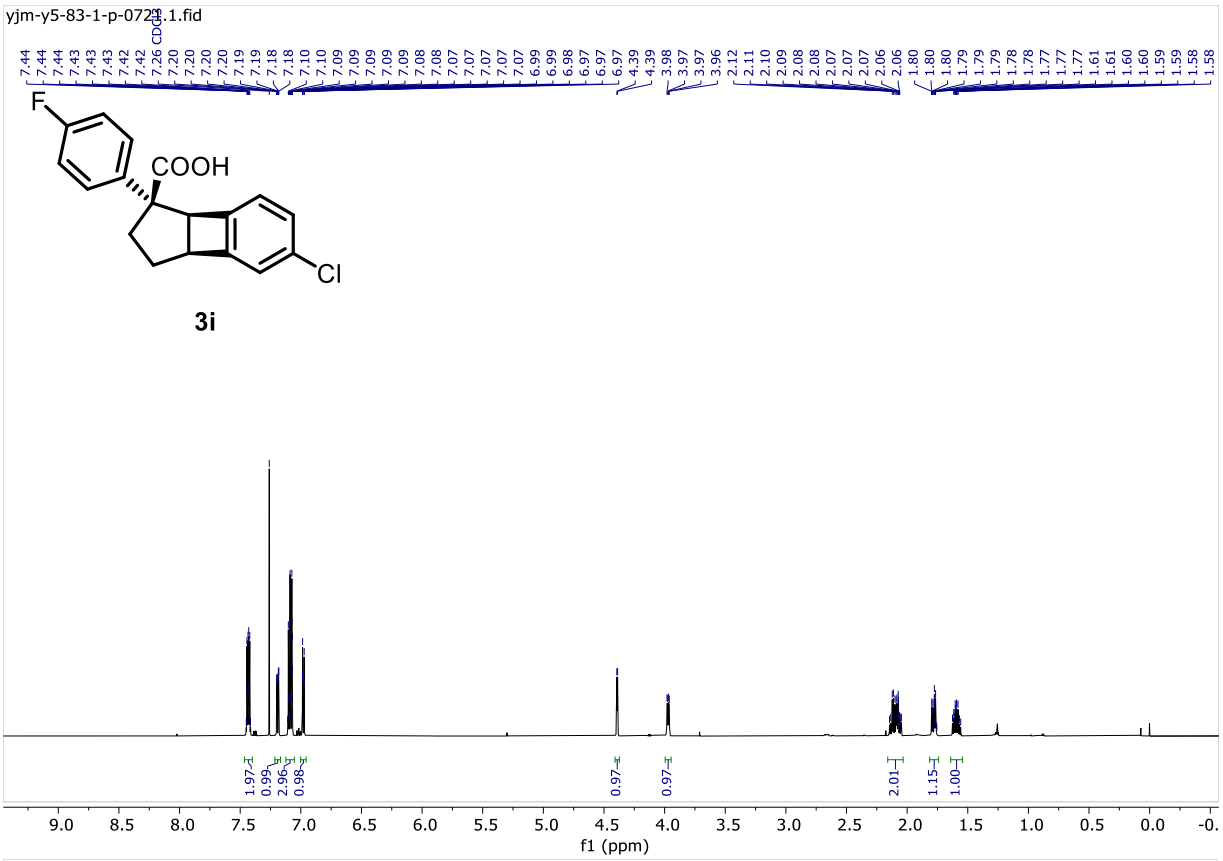
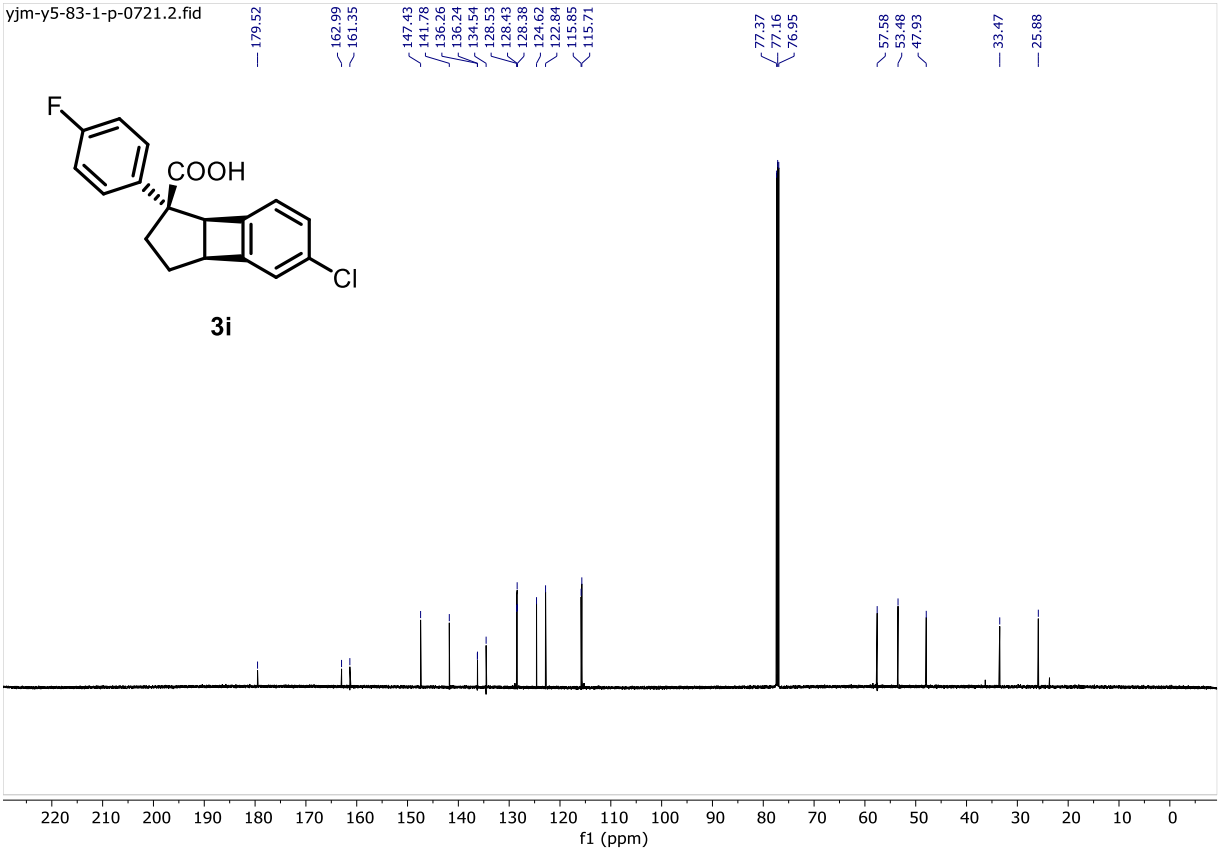
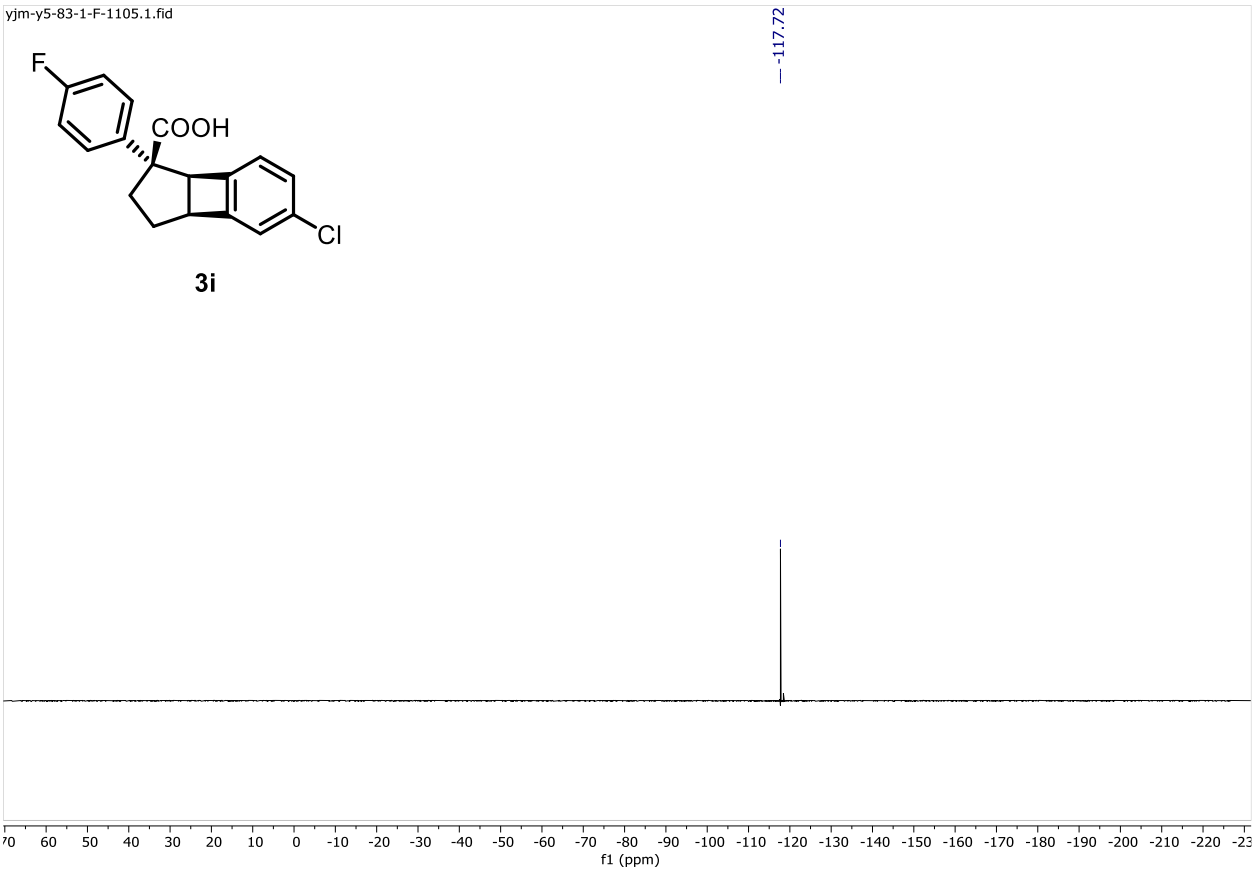
Ph
COOH
Cl
3h
f1 (ppm)


yjm-y5-83-1-p-0721.1.fid
F
COOH
Cl
3i
f1 (ppm)


yjm-y5-83-1-p-0721.2.fid
F
COOH
Cl
3i
f1 (ppm)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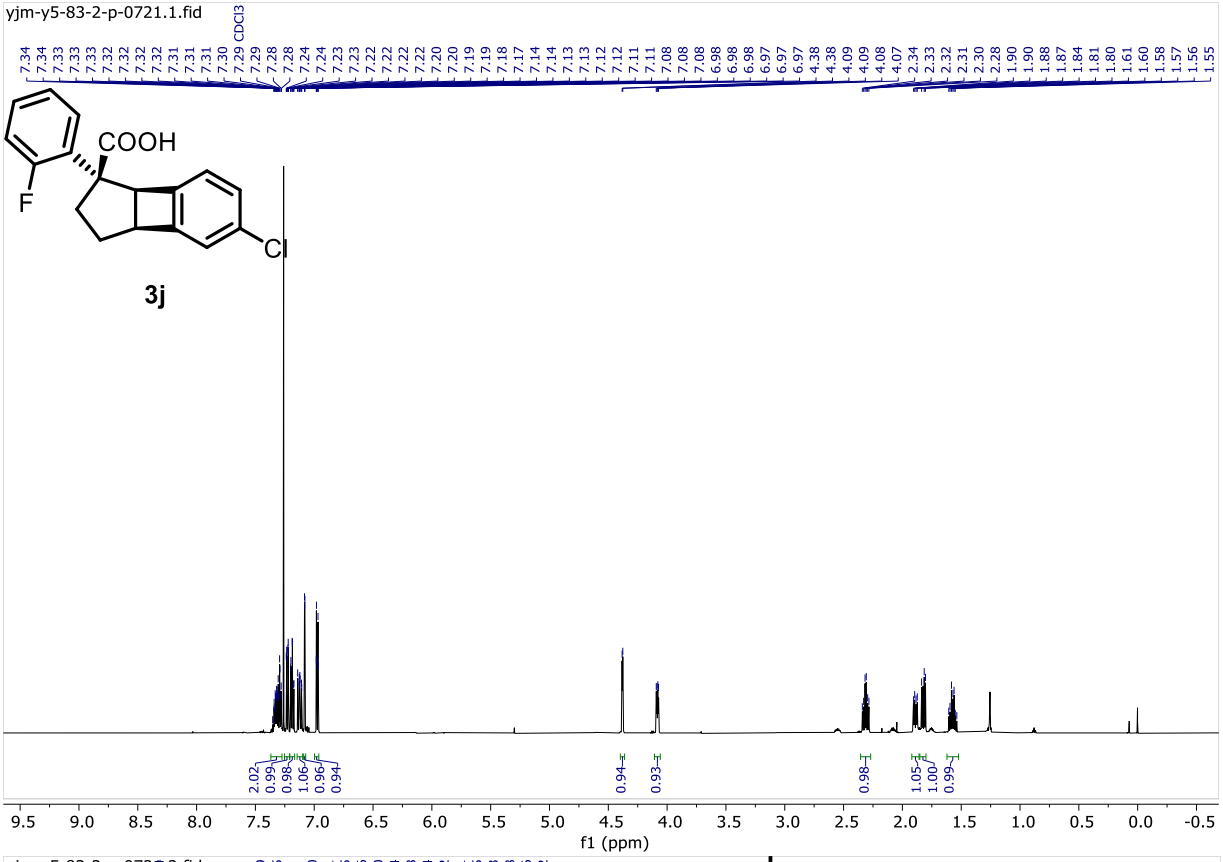
-117.72
F
COOH
Cl
3i
f1 (ppm)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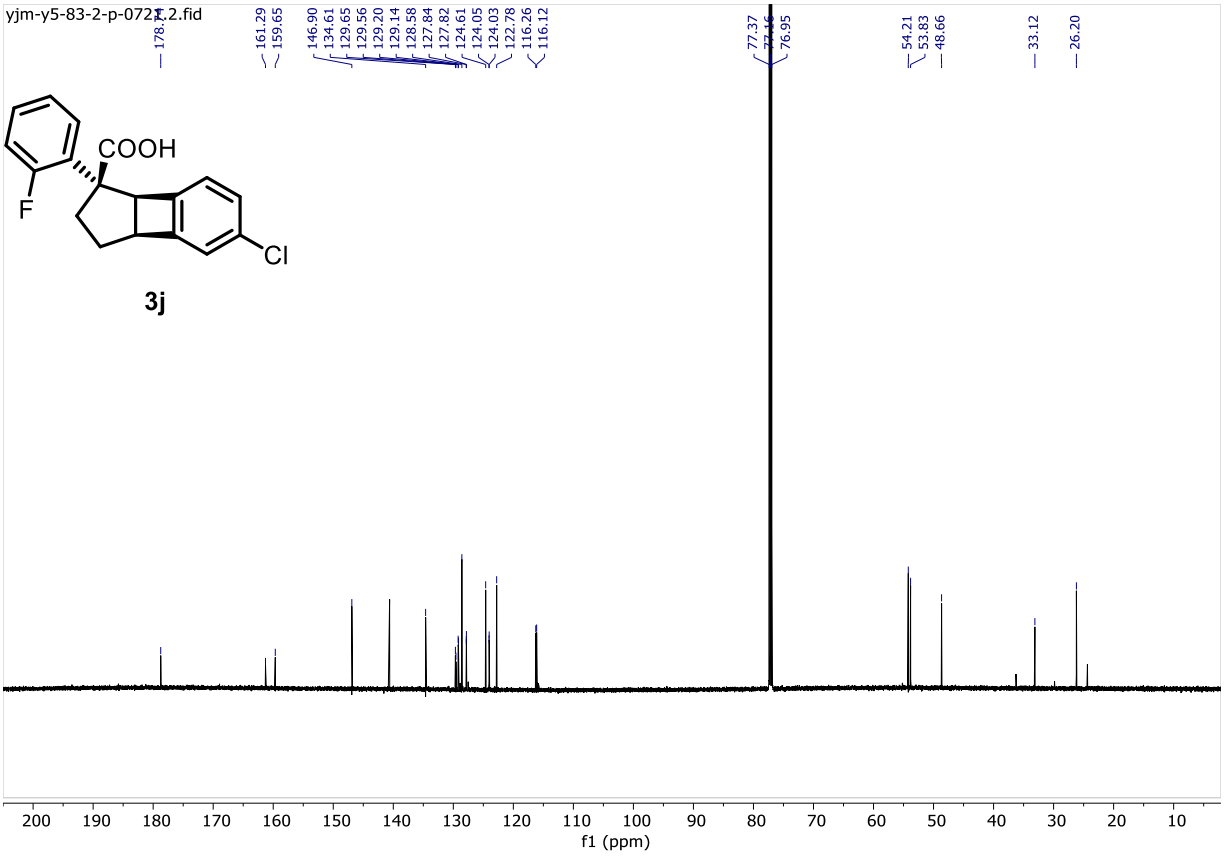
F
Cl
3j
f1 (ppm)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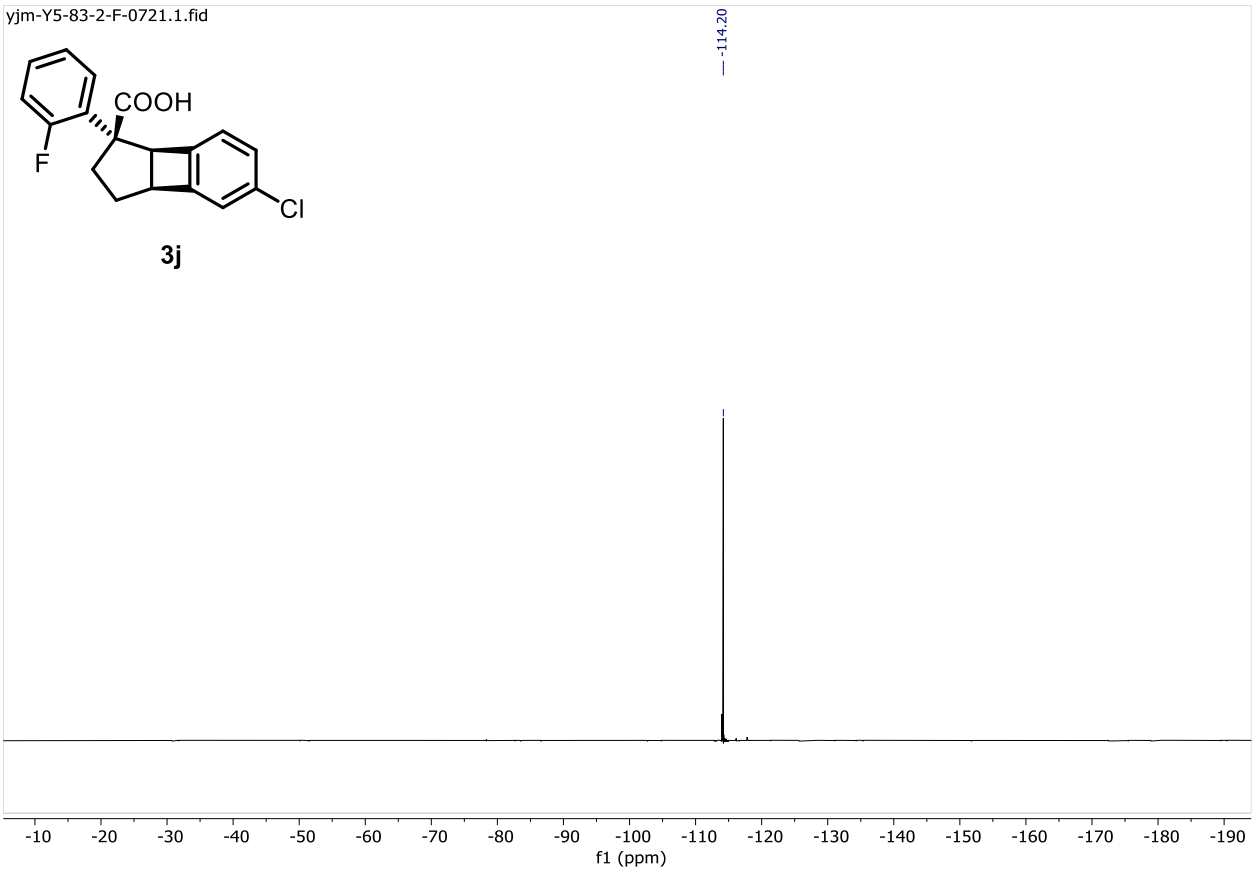
F
Cl
3j
f1 (ppm)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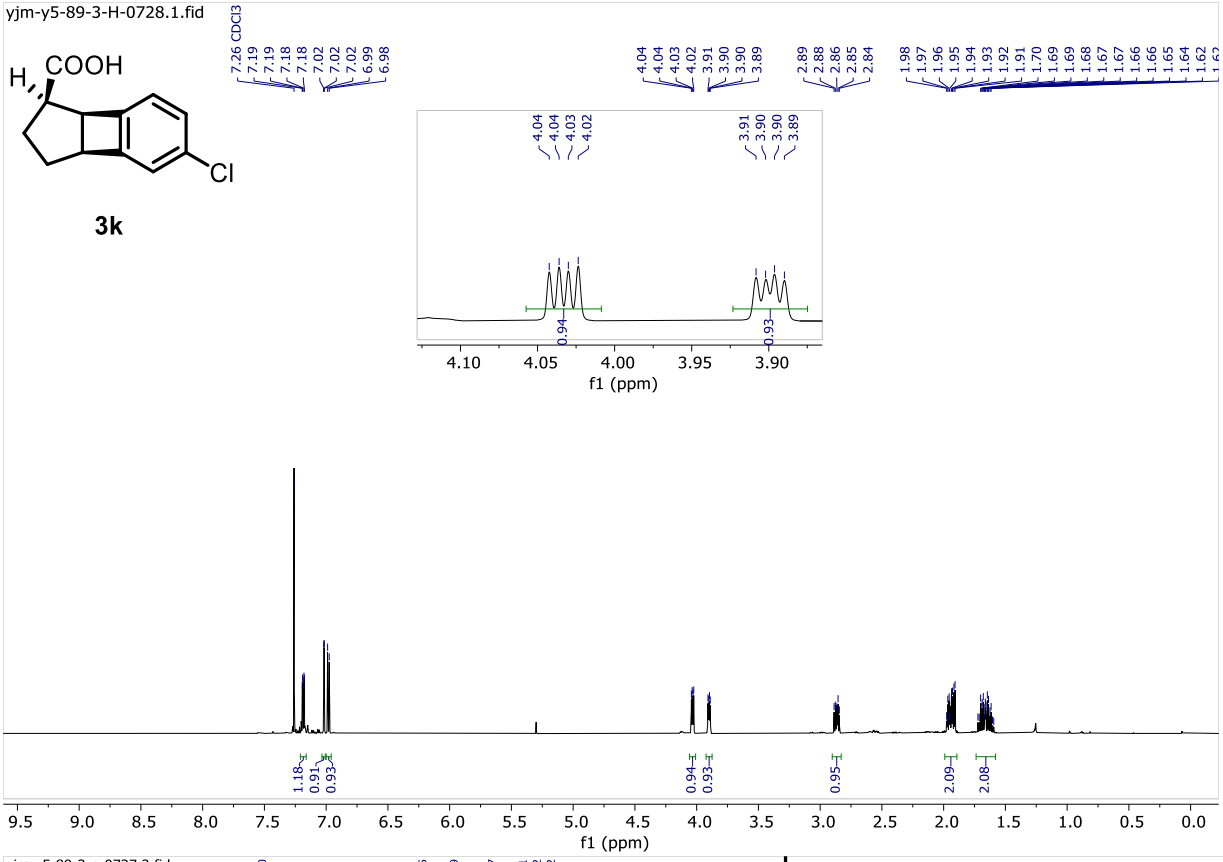
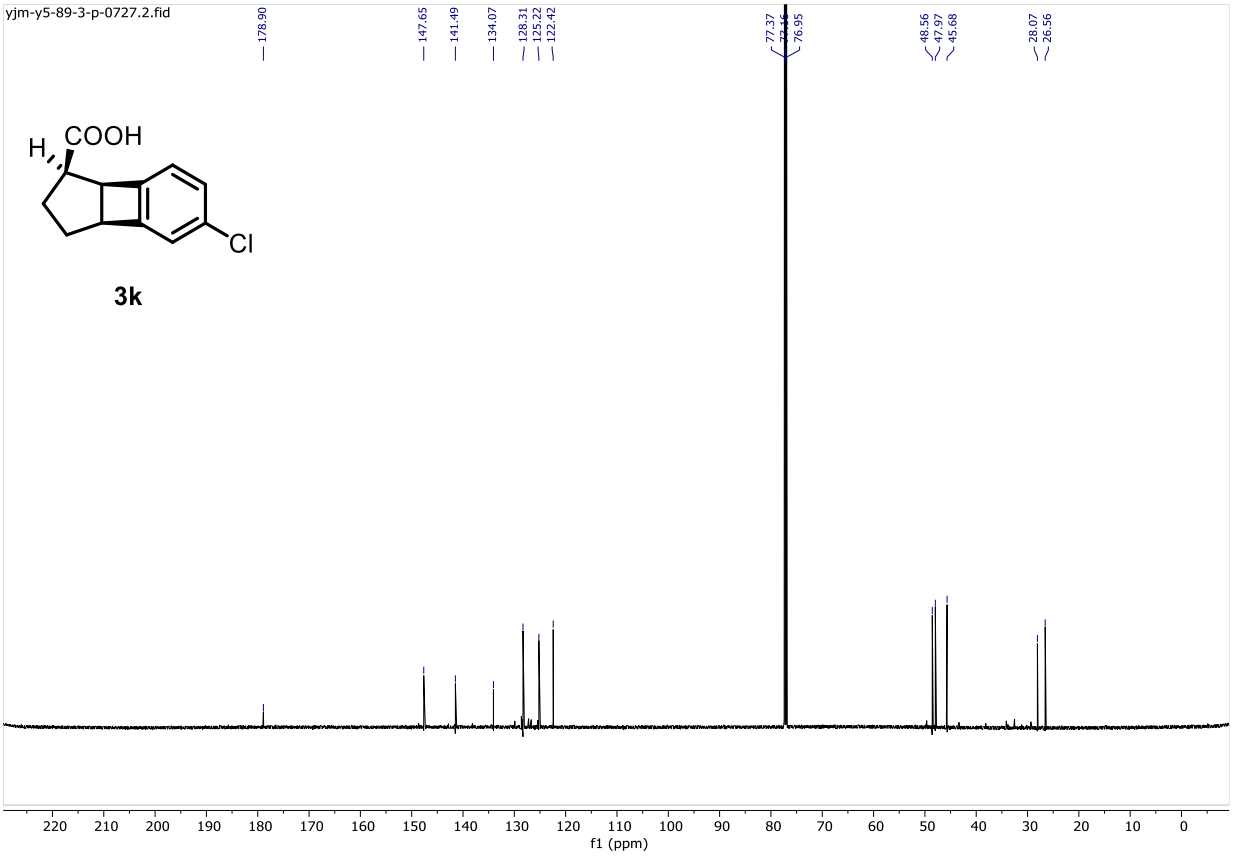
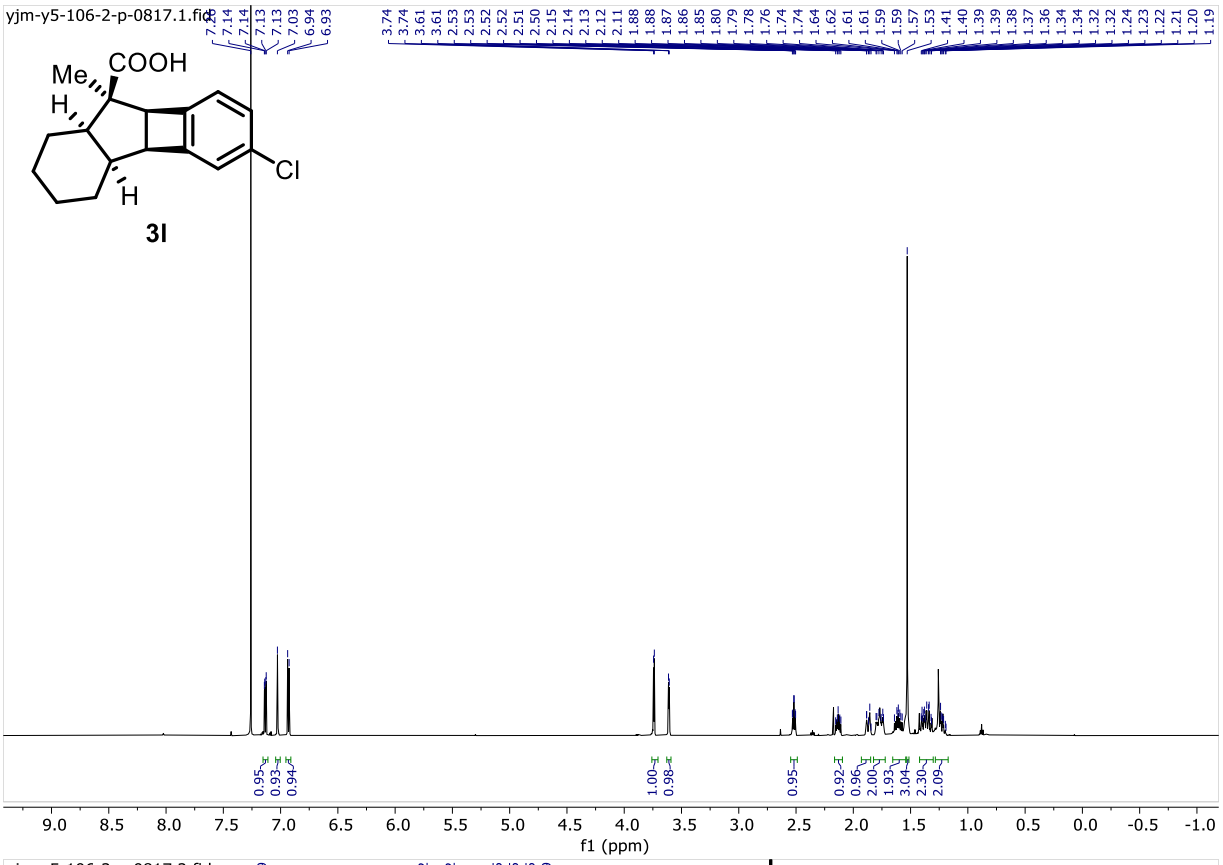
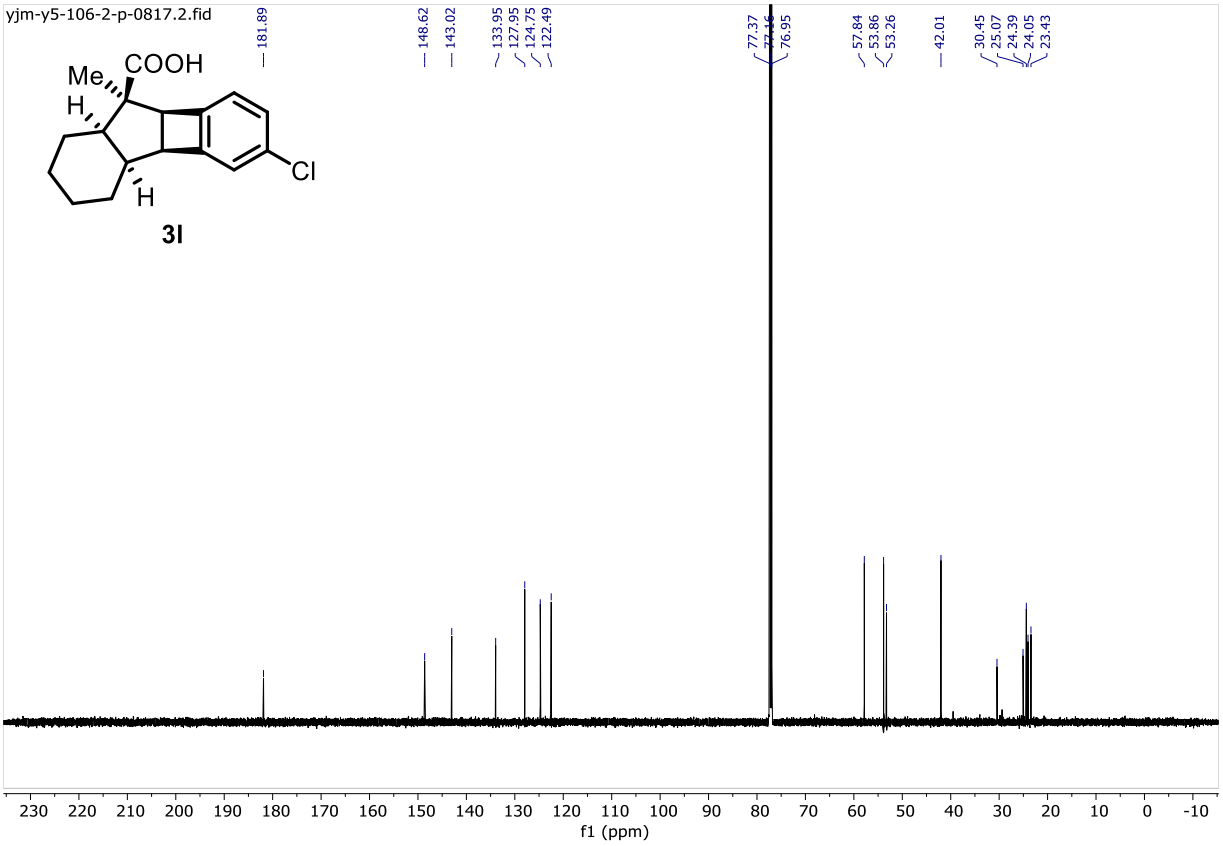
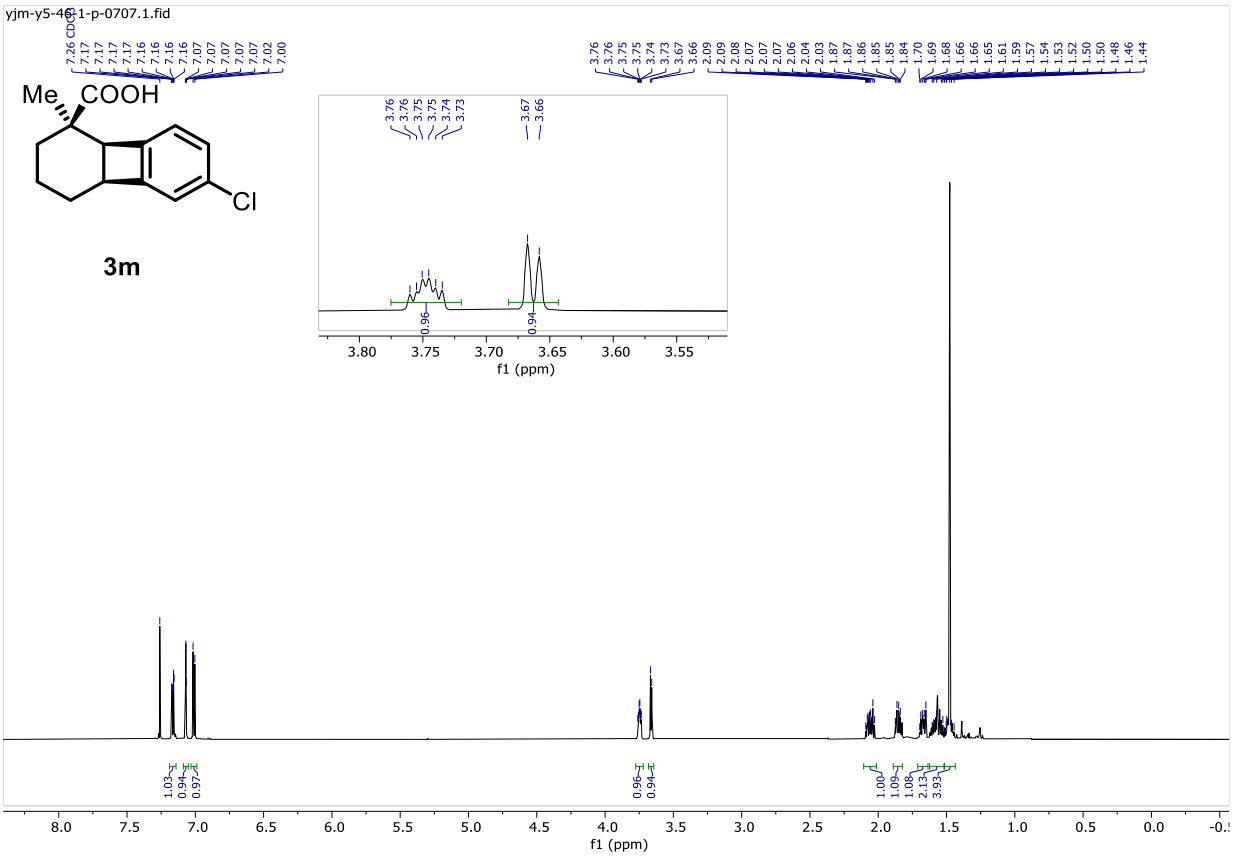
-114.20
COOH
F
Cl
3j
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

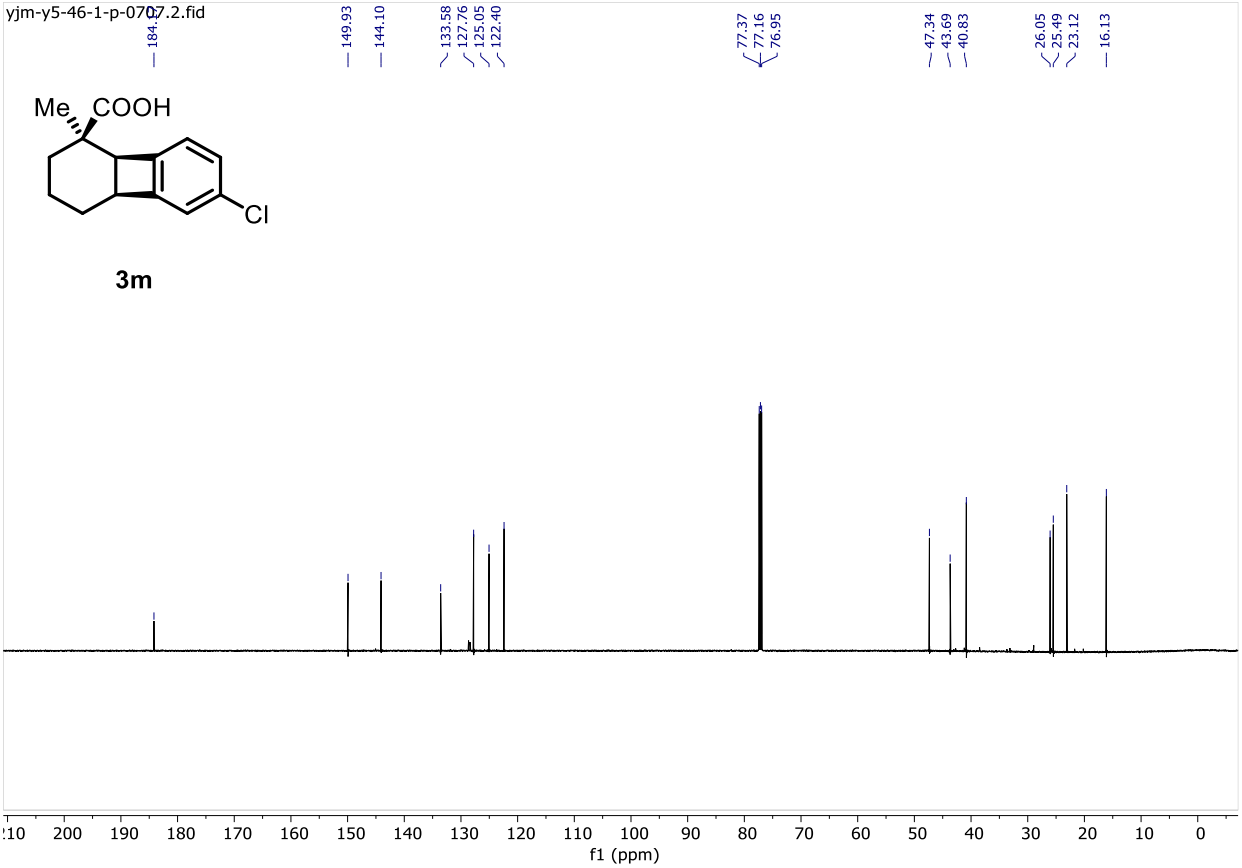

yjm-y5-89-3-H-0728.1.fid
COOH
H
Cl
3k
7.26 CDCl3
7.19
7.19
7.18
7.18
7.02
7.02
7.02
6.99
6.98
4.04
4.04
4.03
4.02
3.91
3.90
3.90
3.89
2.89
2.88
2.86
2.85
2.84
1.98
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.70
1.69
1.69
1.68
1.67
1.67
1.66
1.66
1.65
1.64
1.62
0.94
0.93
4.10
4.05
4.00
3.95
3.90
f1 (ppm)
1.18
0.91
0.93
0.94
0.93
0.95
2.09
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

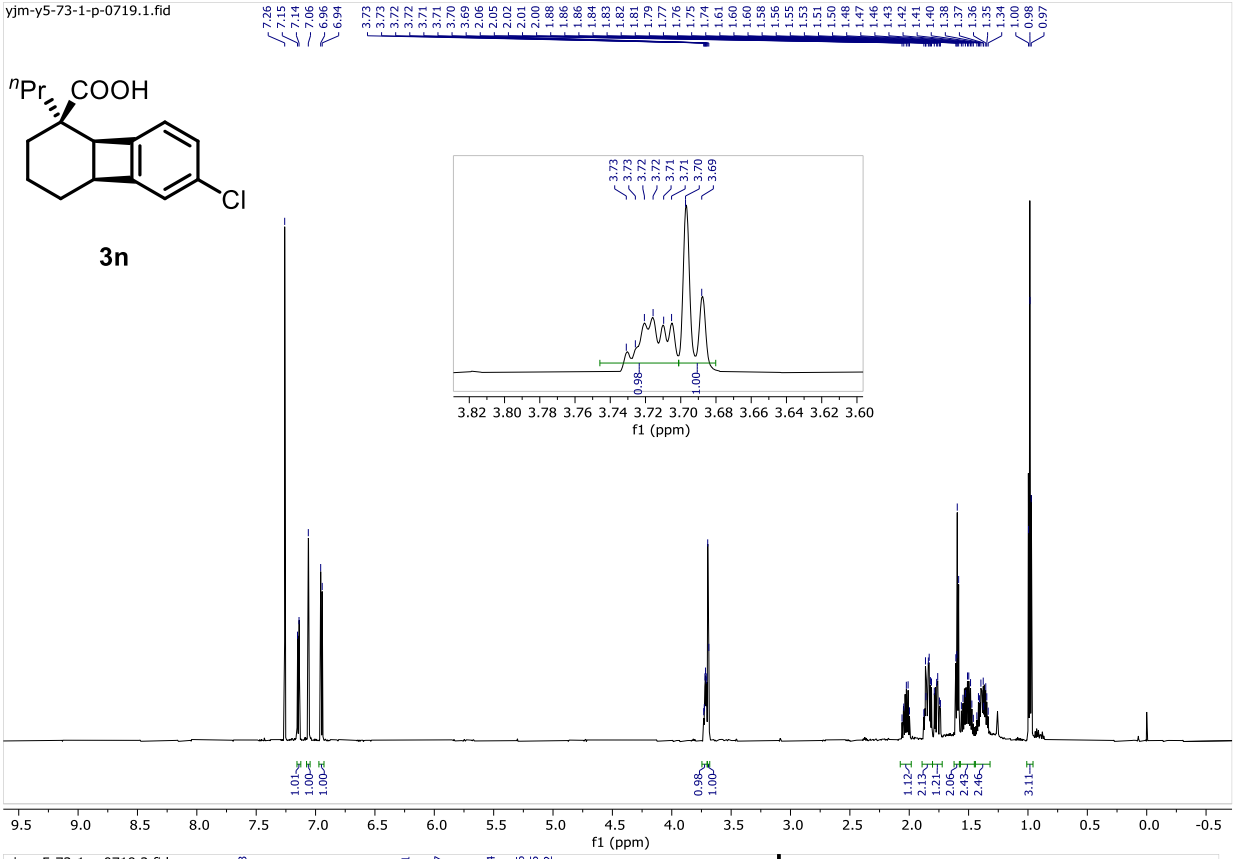

yjm-y5-89-3-p-0727.2.fid
178.90
147.65
141.49
134.07
128.31
125.22
122.42
77.37
77.16
76.95
48.56
47.97
45.68
28.07
26.56
COOH
H
Cl
3k
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

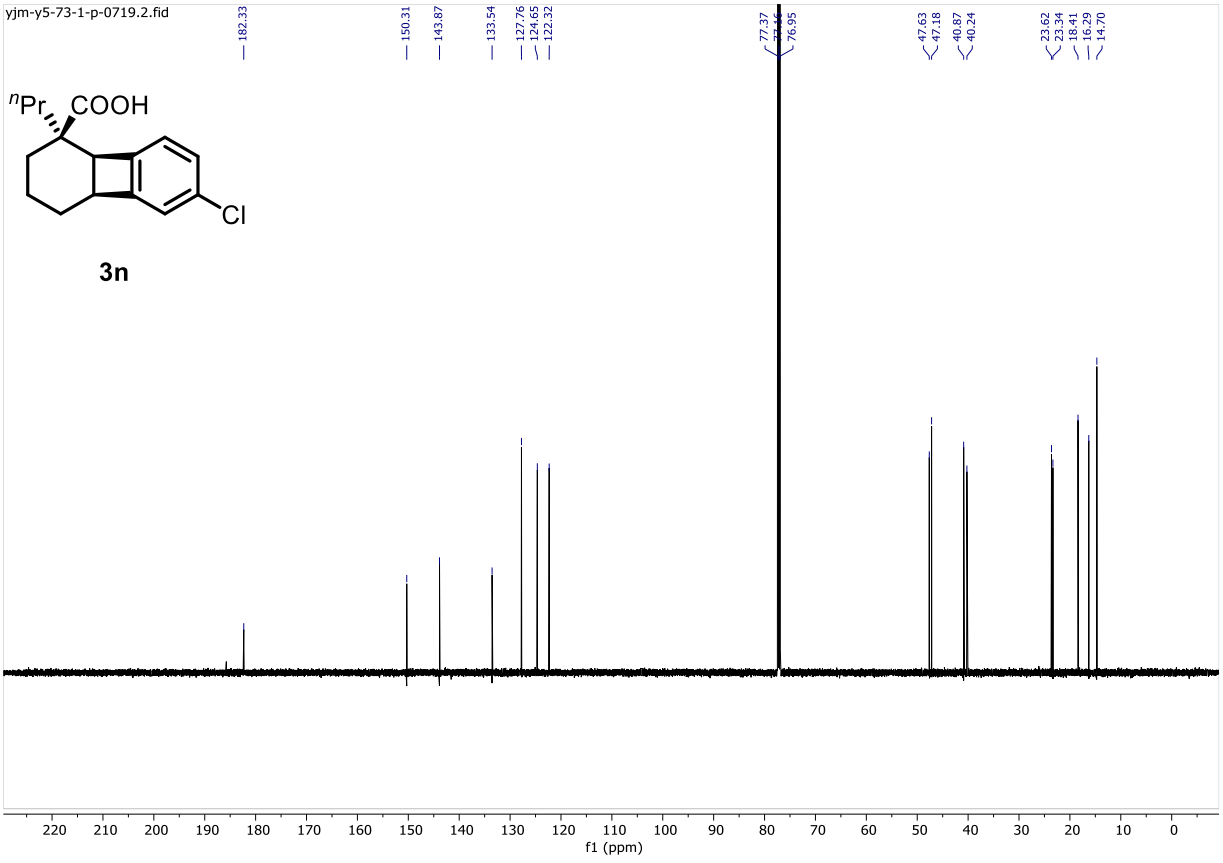

yjm-y5-106-2-p-0817.1.fid
Me
COOH
H
Cl
H
3l
f1 (ppm)


yjm-y5-106-2-p-0817.2.fid
Me
COOH
H
Cl
H
3l
f1 (ppm)


yjm-y5-46-1-p-0707.1.fid
Me
COOH
Cl
3m
f1 (ppm)


yjm-y5-46-1-p-0707.2.fid
Me
COOH
Cl
3m
f1 (ppm)


yjm-y5-73-1-p-0719.1.fid
nPr COOH
Cl
3n
f1 (ppm)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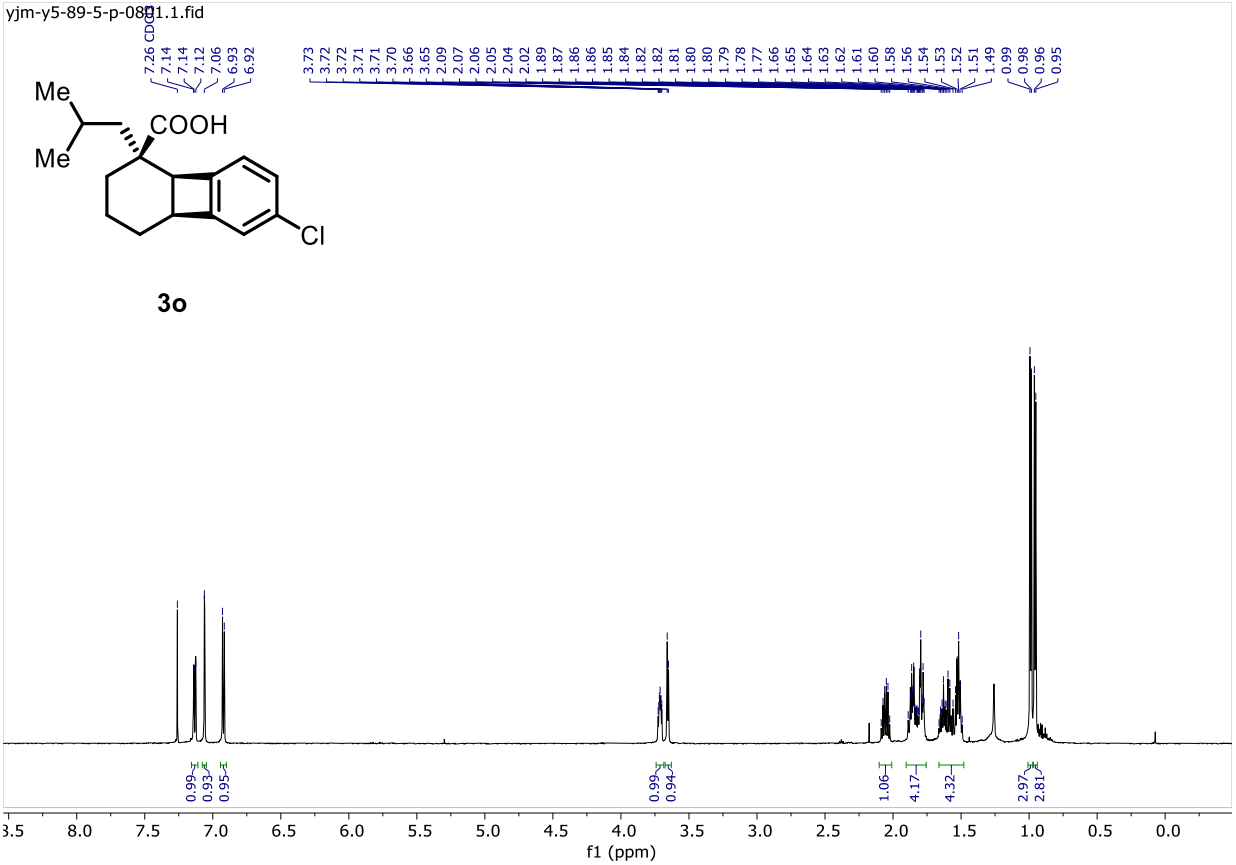
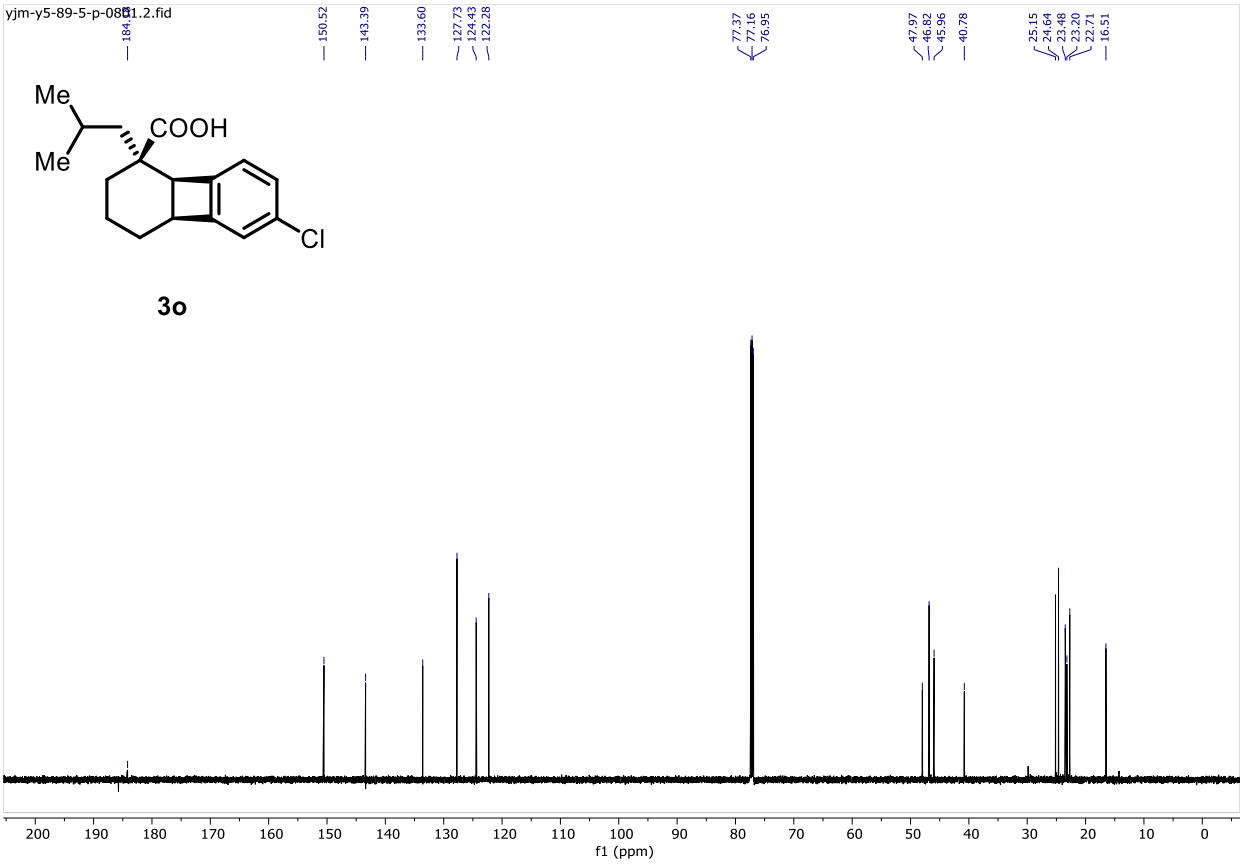
nPr COOH
Cl
3n
f1 (ppm)


yjm-y5-89-5-p-0801.1.fid
Me
Me
COOH
Cl
3o
f1 (ppm)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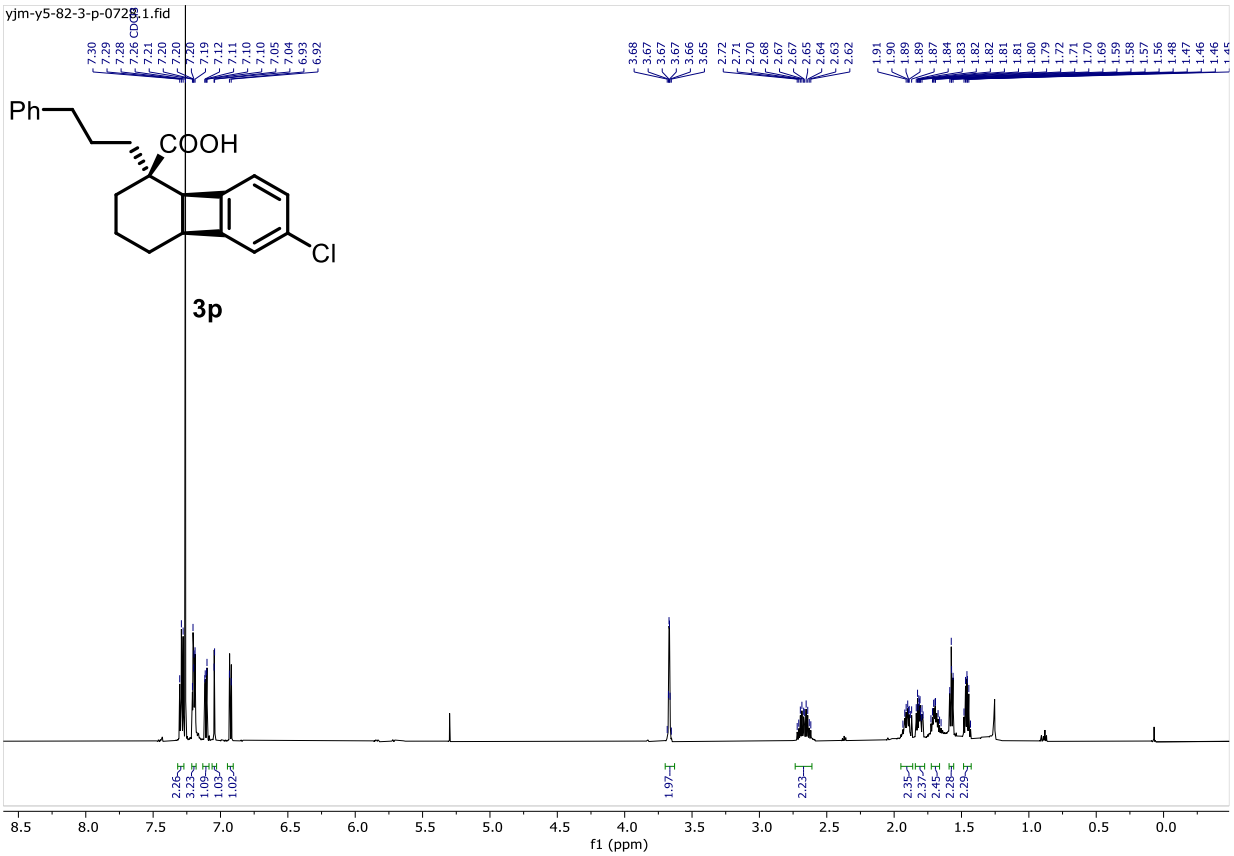
Me
Me
COOH
Cl
3o
f1 (ppm)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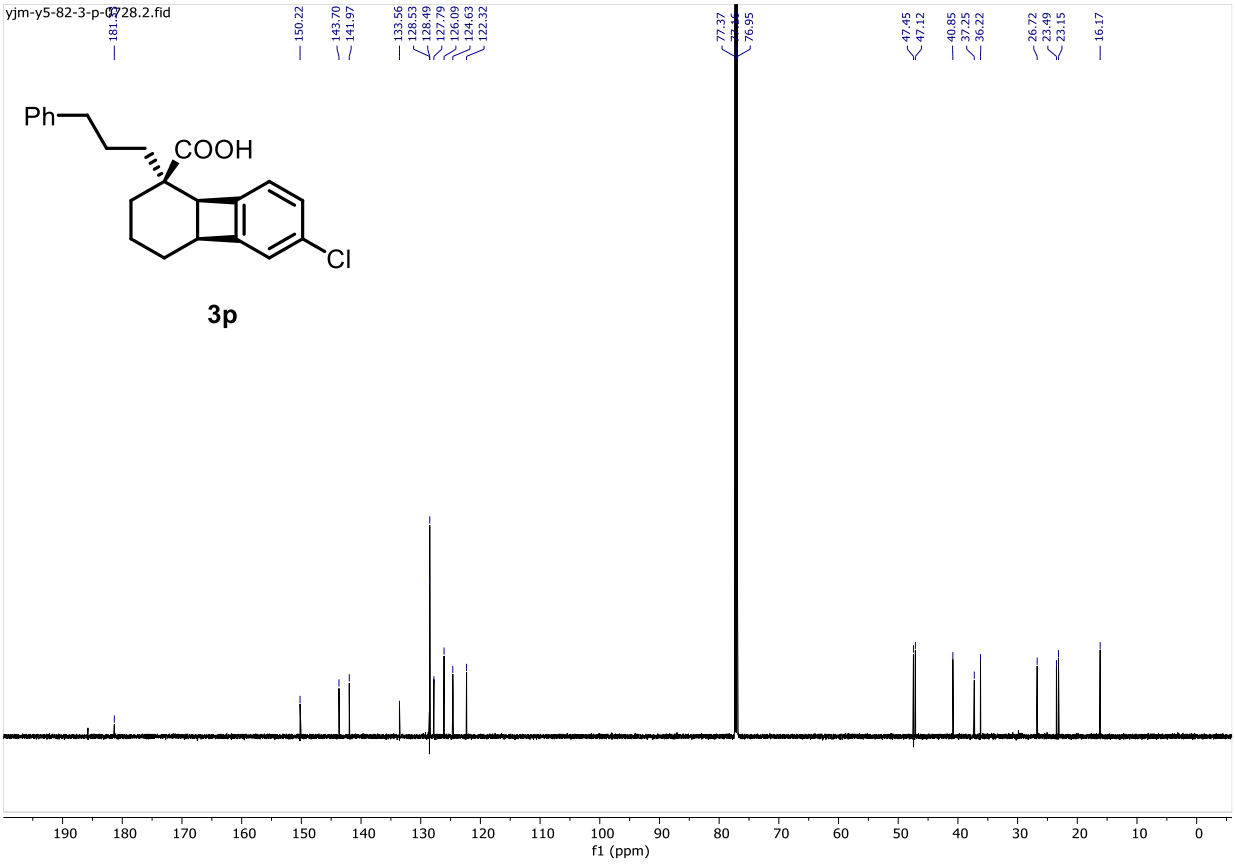
Ph
COOH
Cl
3p
f1 (ppm)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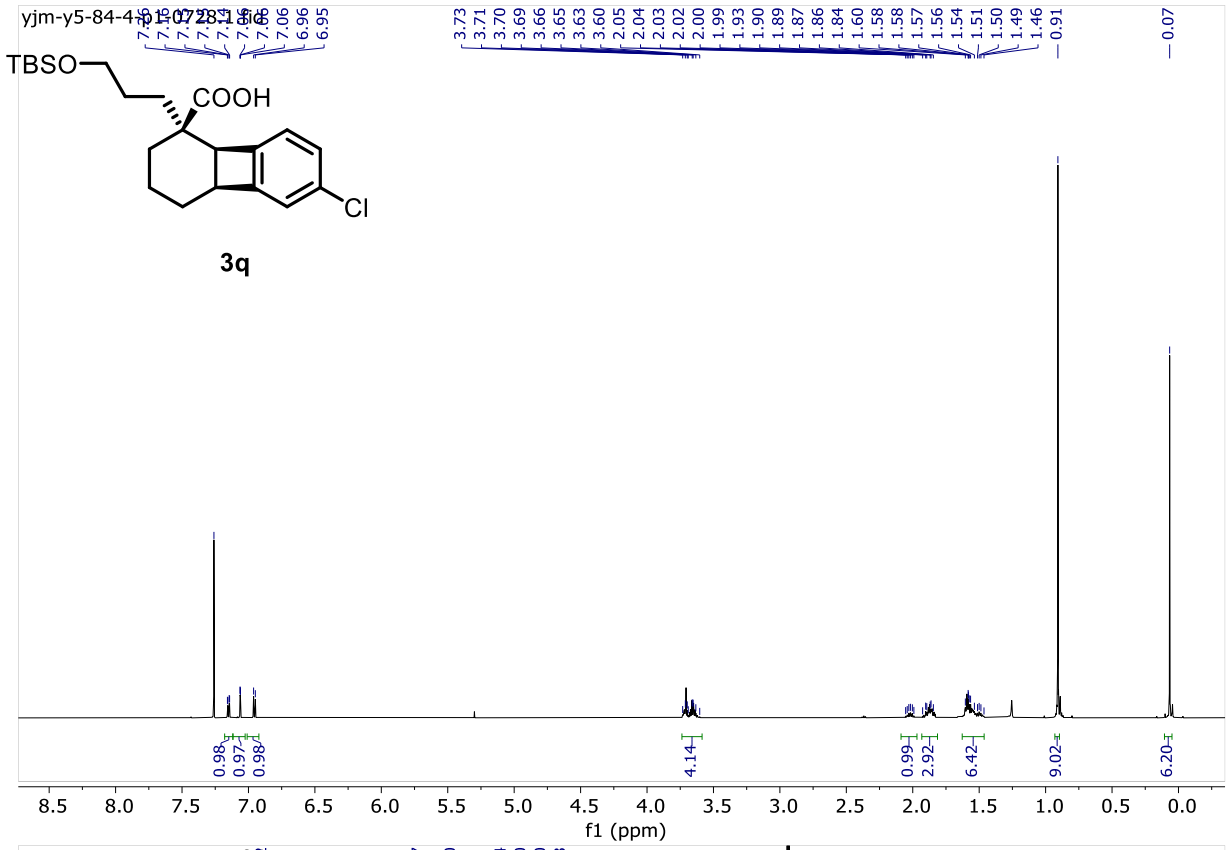
Ph
COOH
Cl
3p
f1 (ppm)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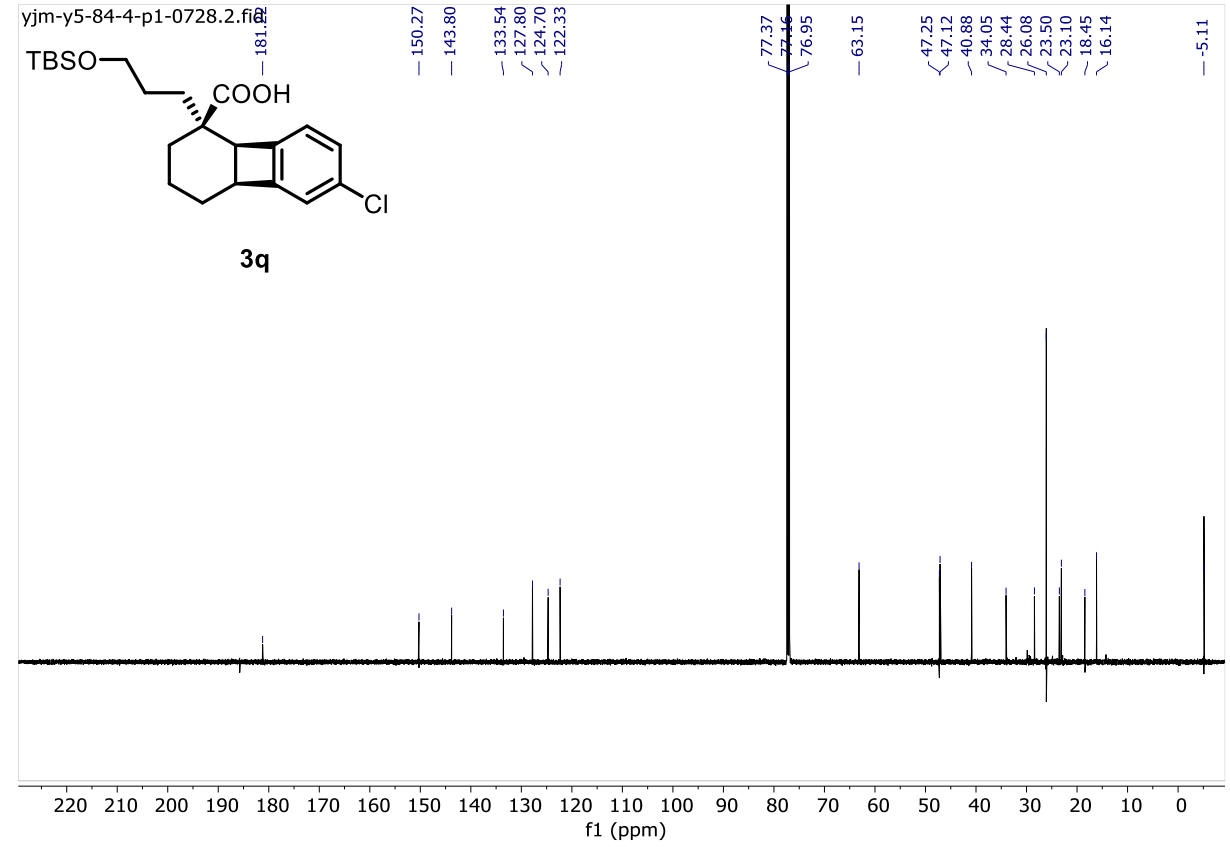
TBSO
COOH
Cl
3q
f1 (ppm)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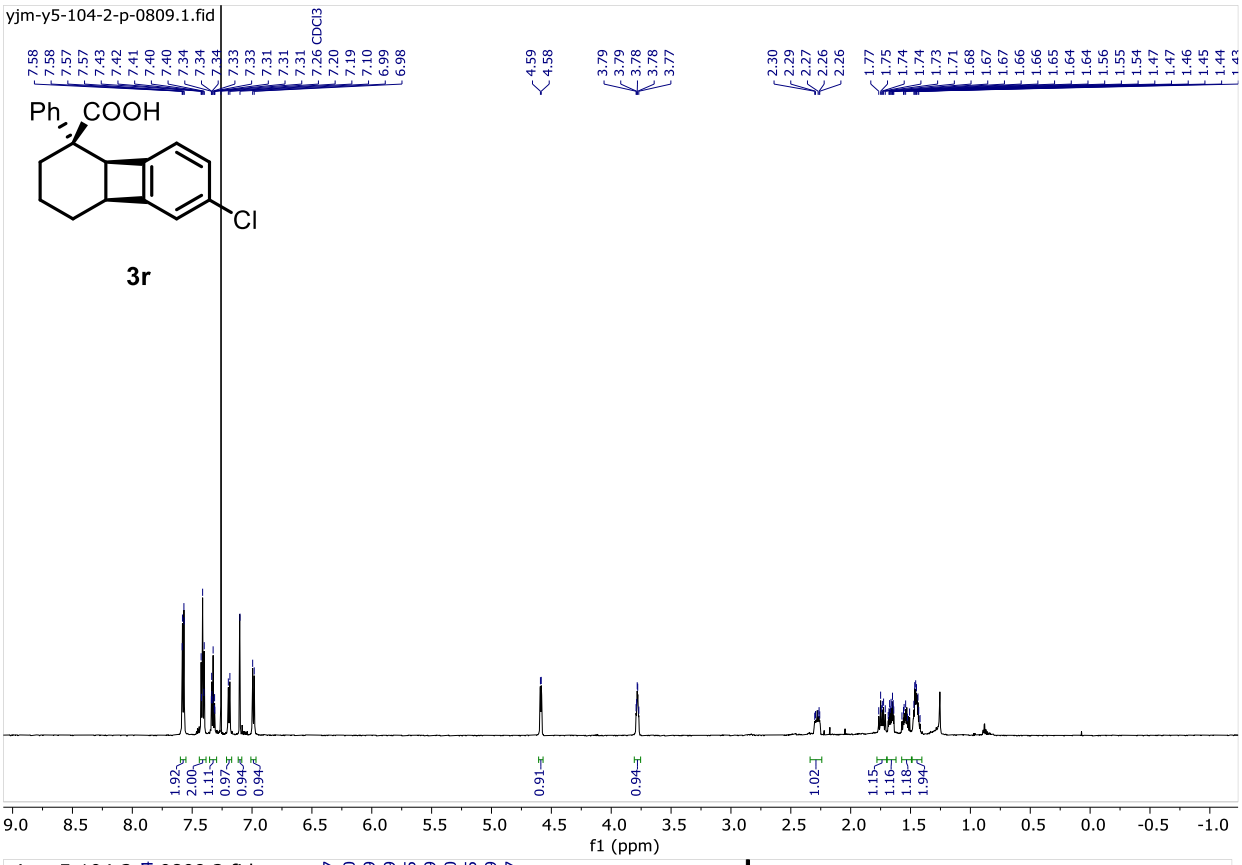
TBSO
COOH
Cl
3q
f1 (ppm)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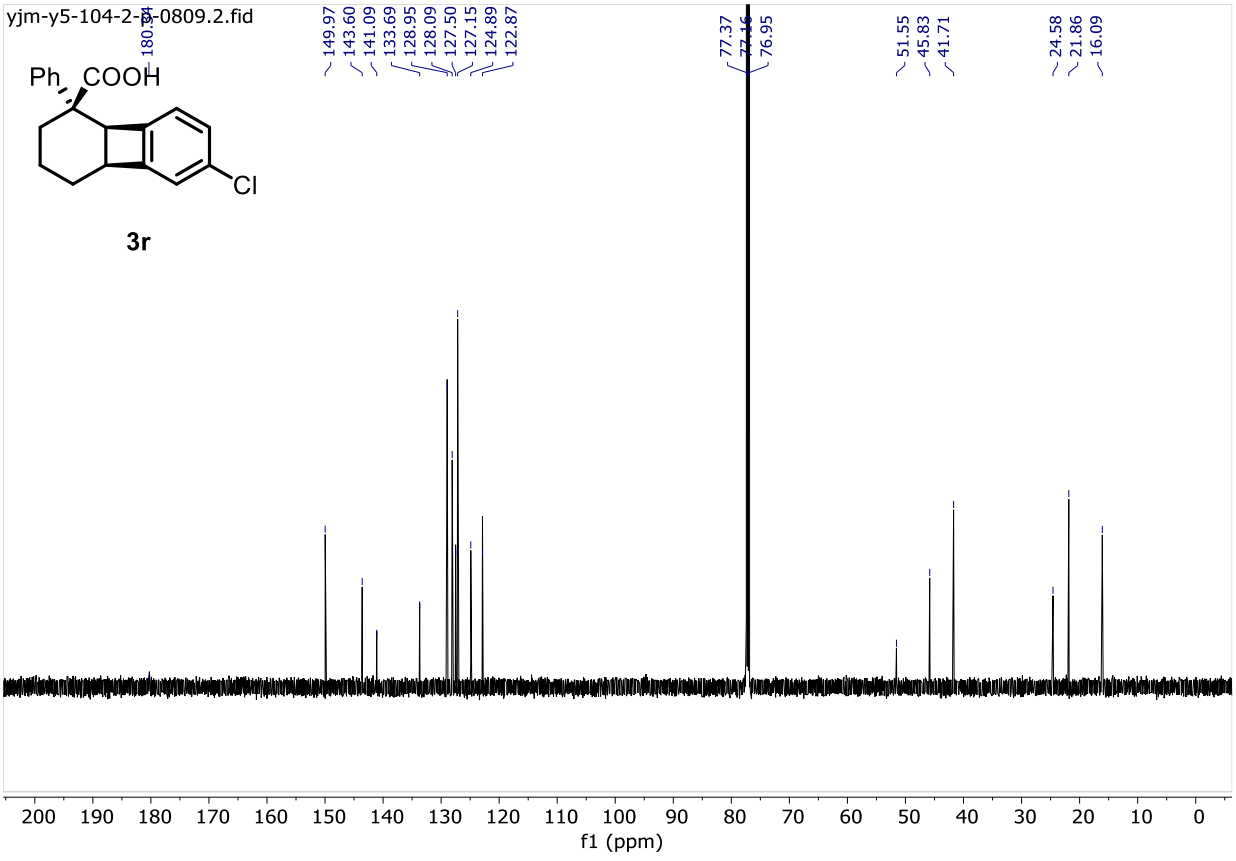
Ph COOH
Cl
3r
f1 (ppm)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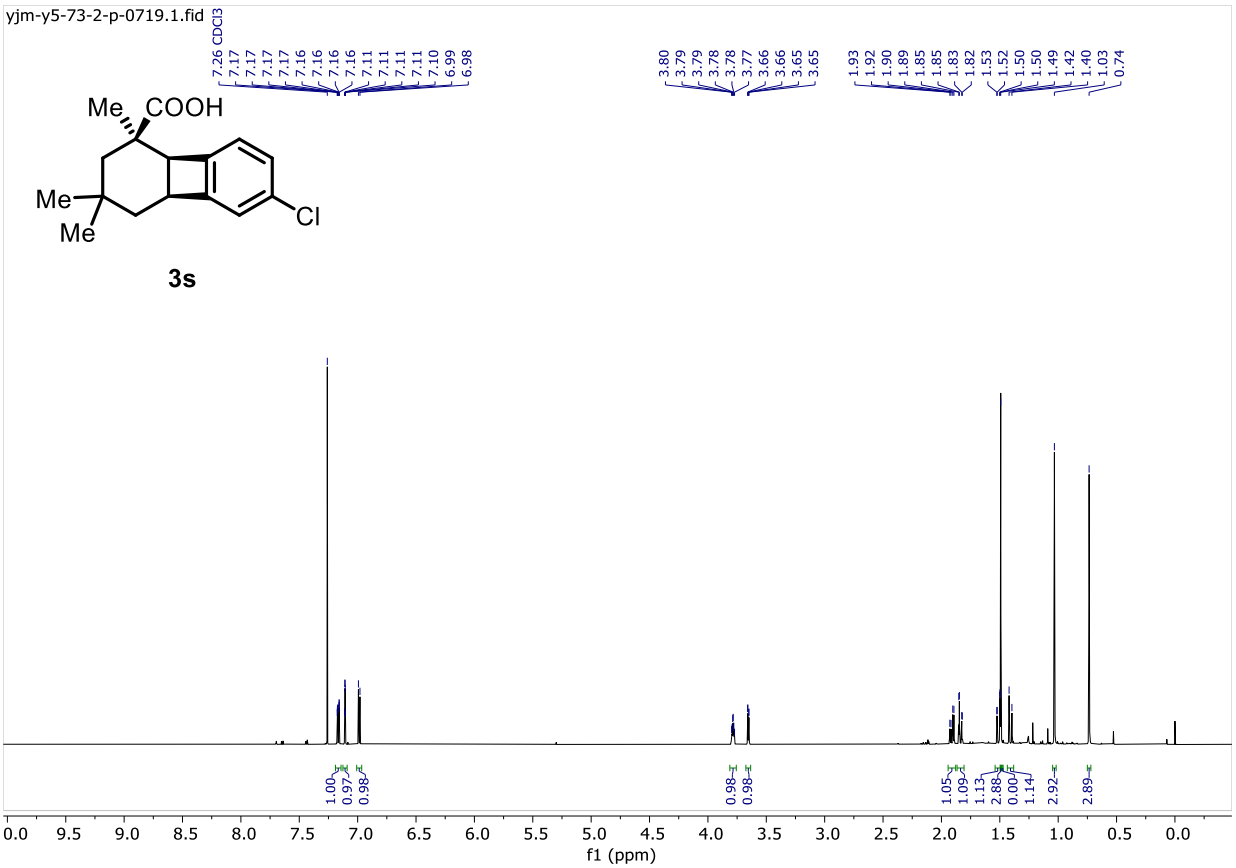
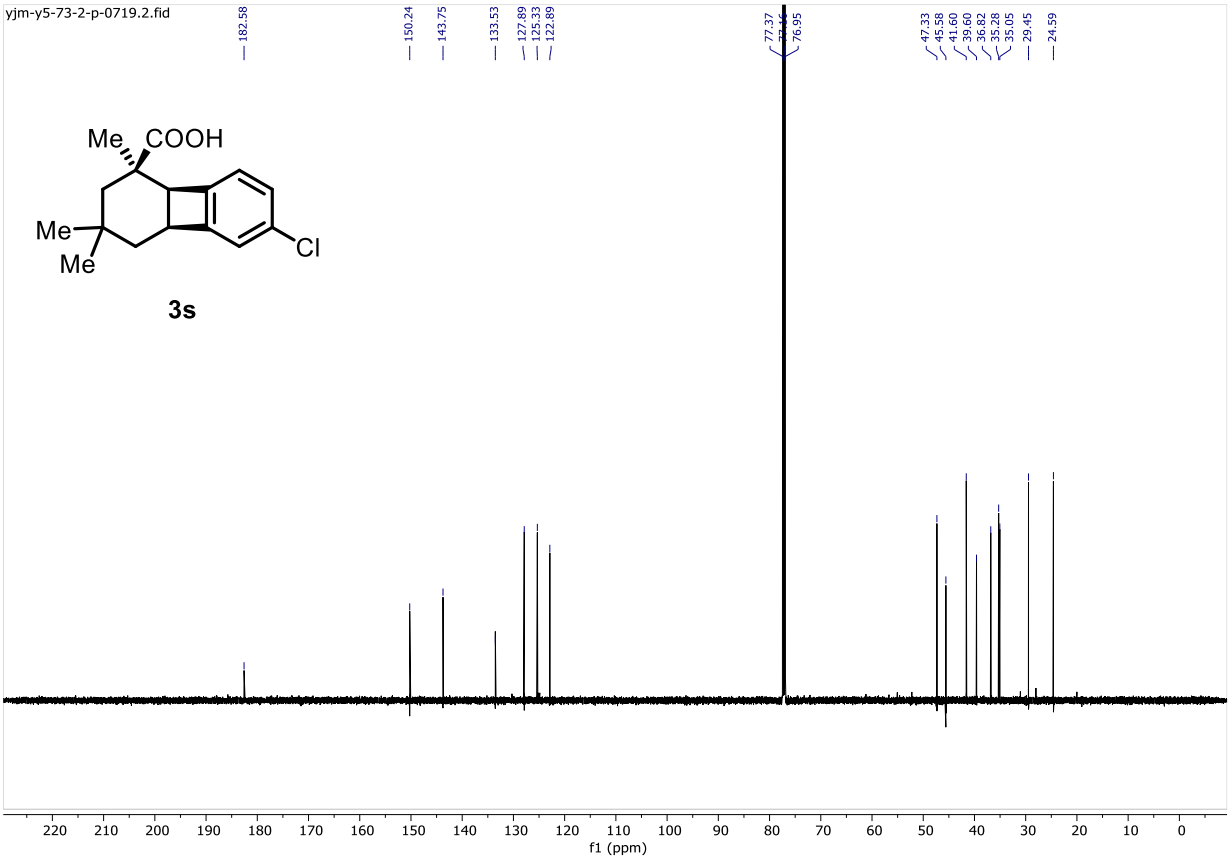
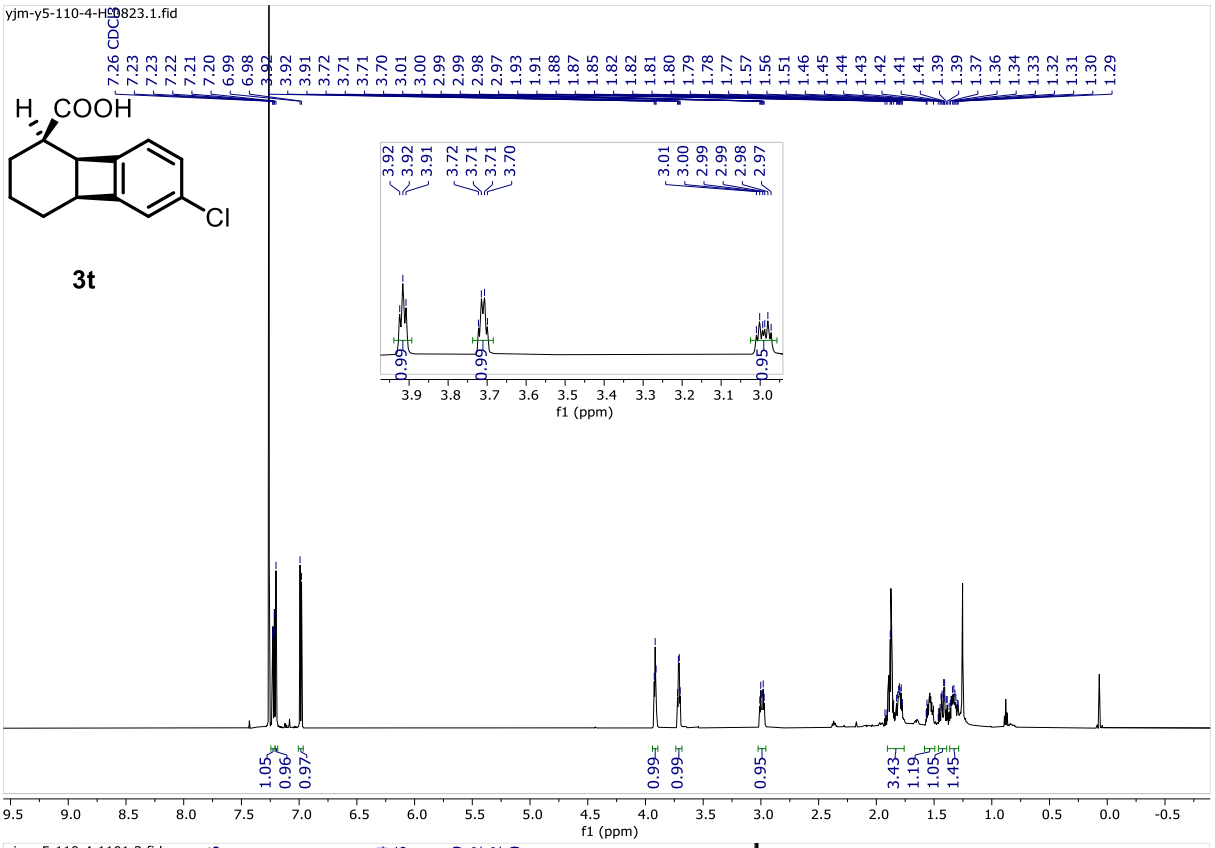
Ph COOH
Cl
3r
f1 (ppm)


yjm-y5-73-2-p-0719.1.fid
Me
COOH
Me
Me
Cl
3s
f1 (ppm)


yjm-y5-73-2-p-0719.2.fid
Me
COOH
Me
Me
Cl
3s
f1 (ppm)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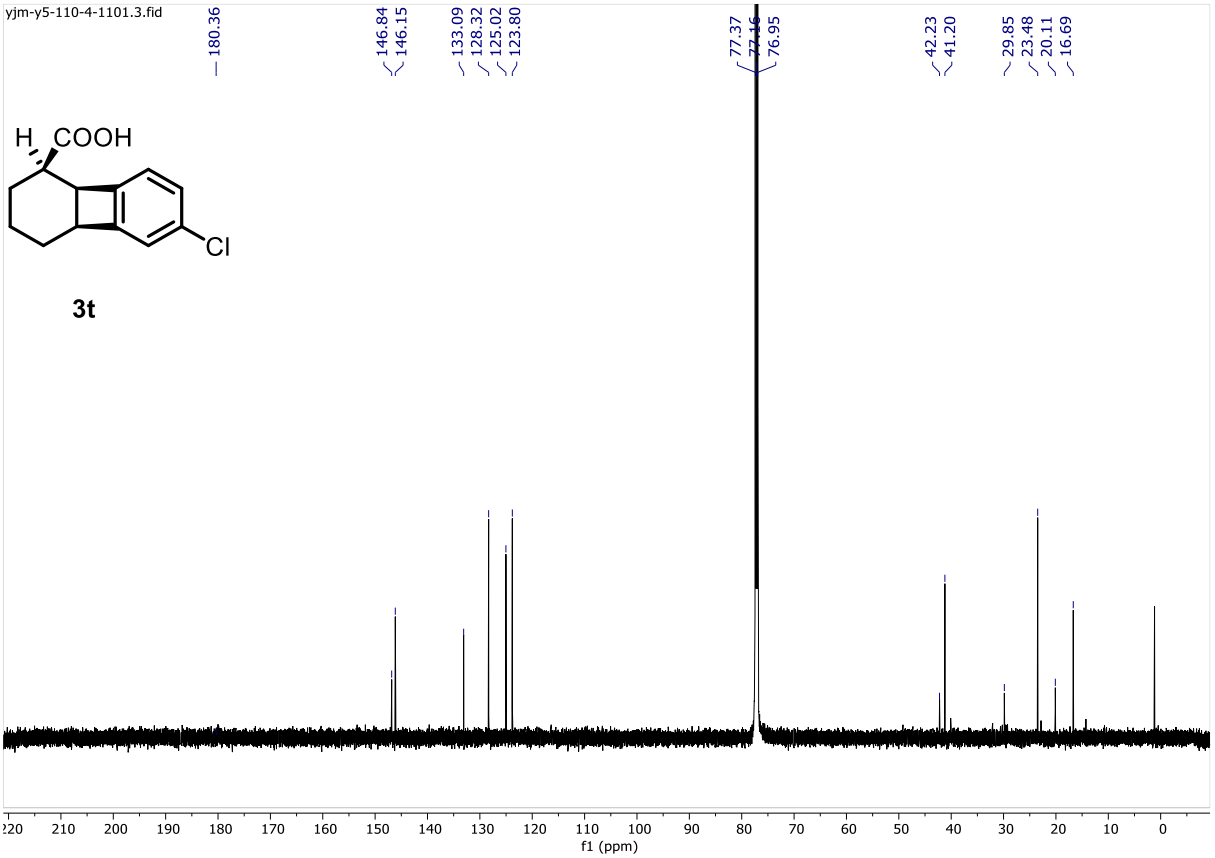
H
COOH
Cl
3t
f1 (ppm)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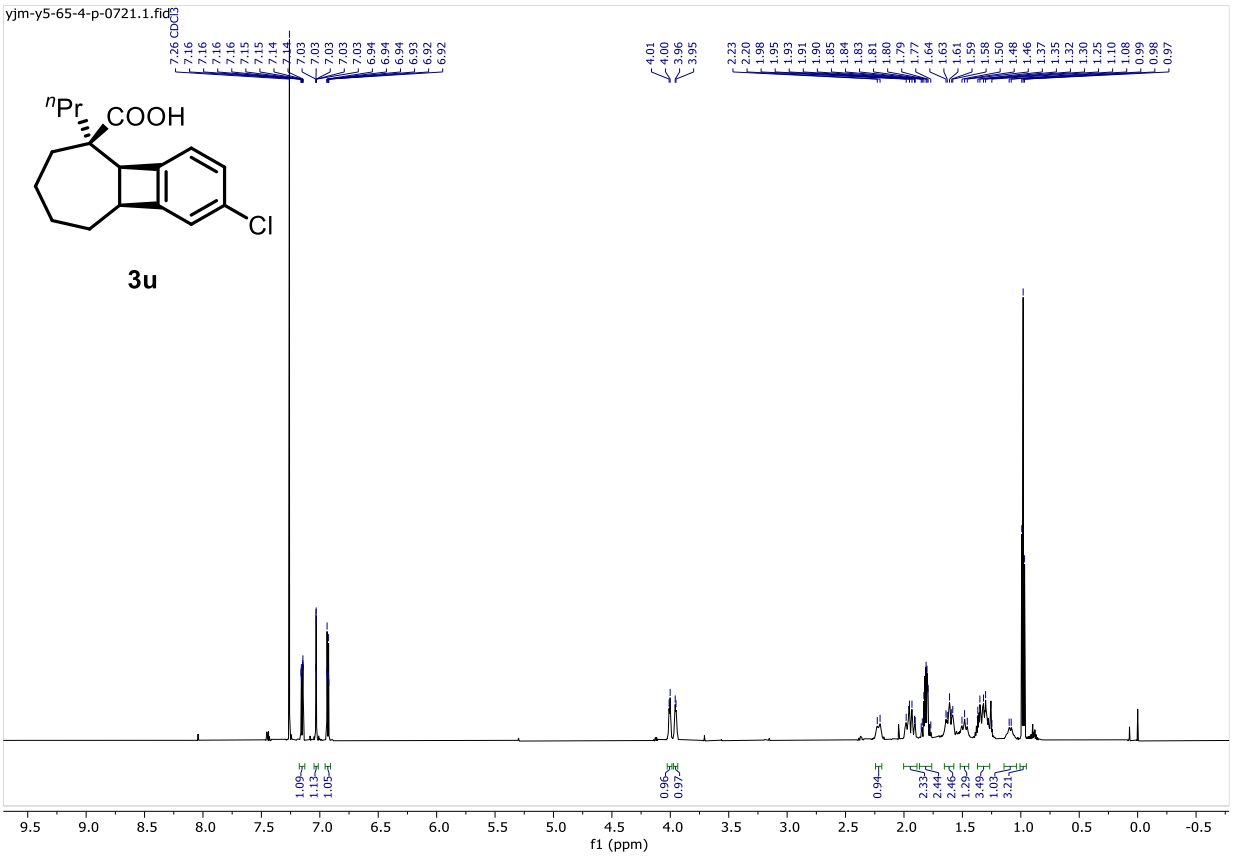
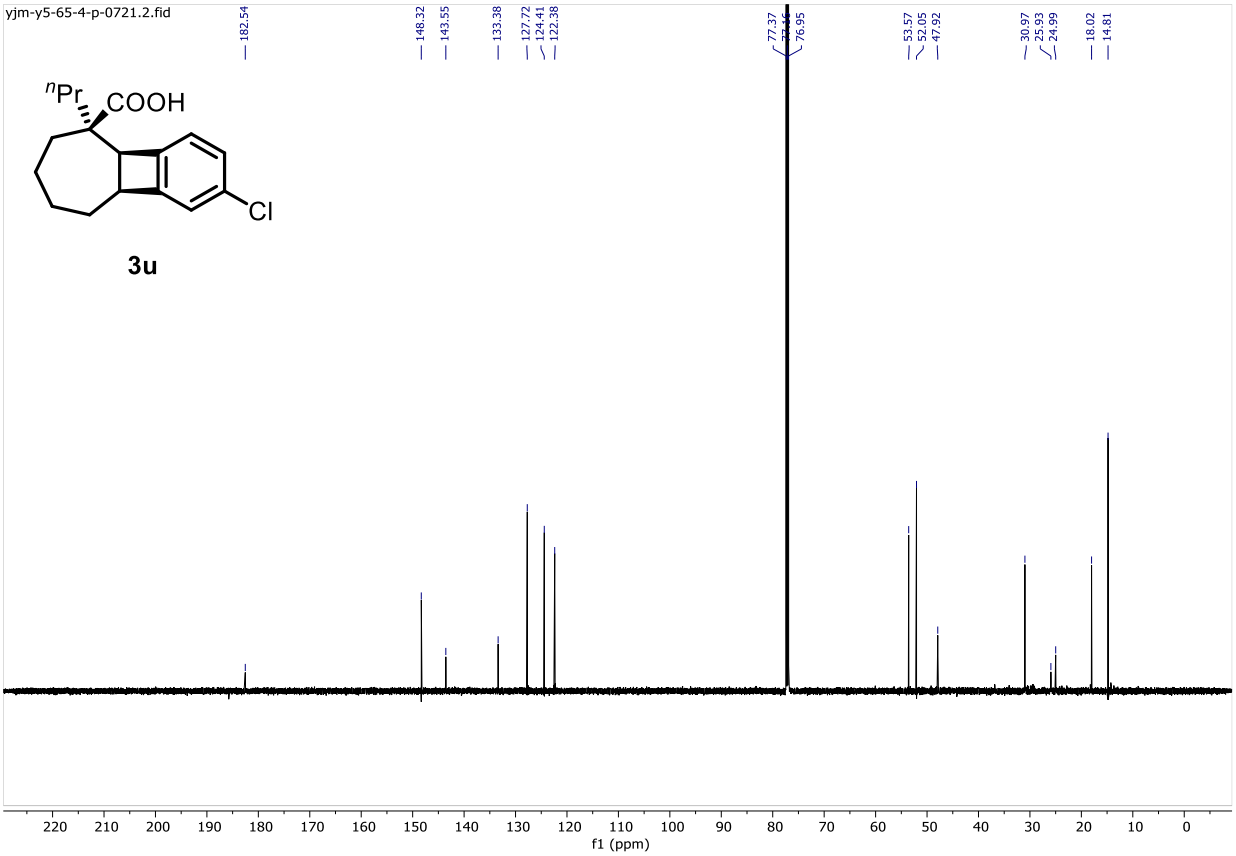
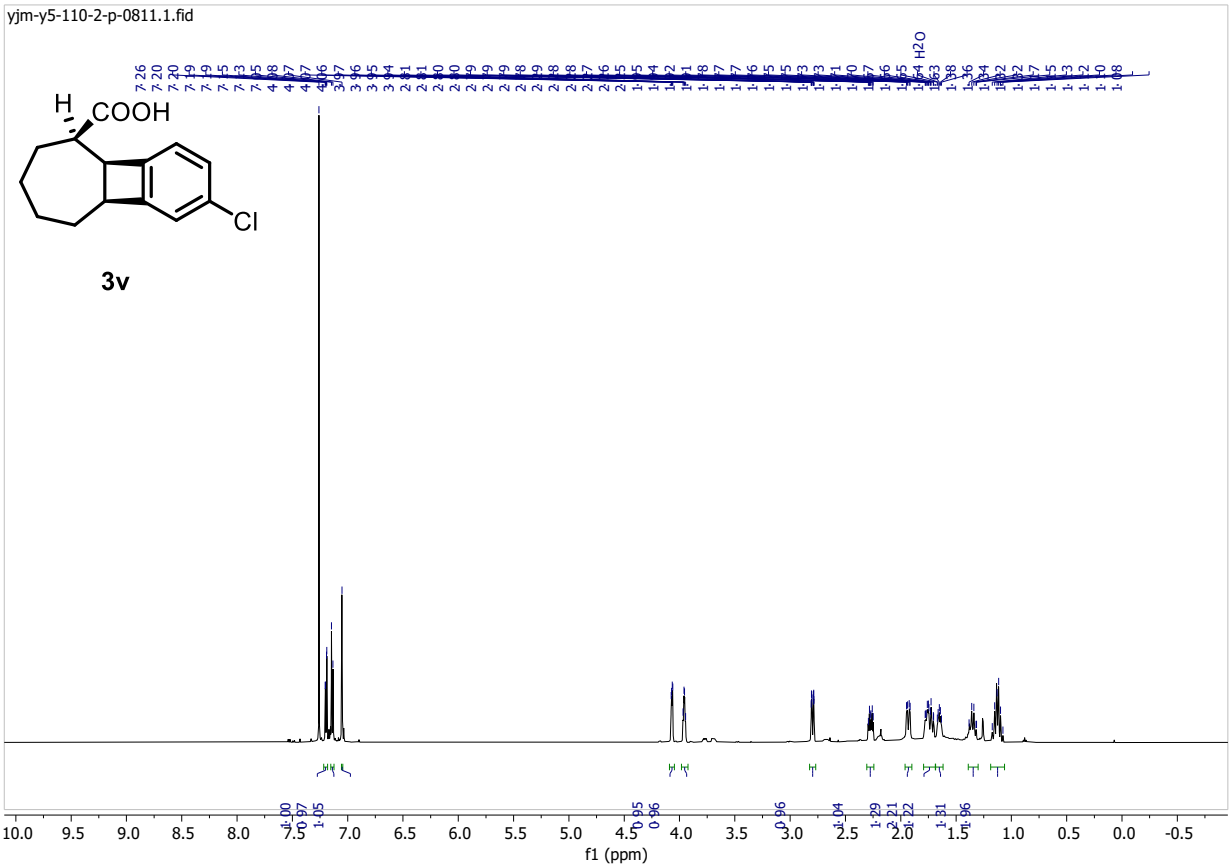
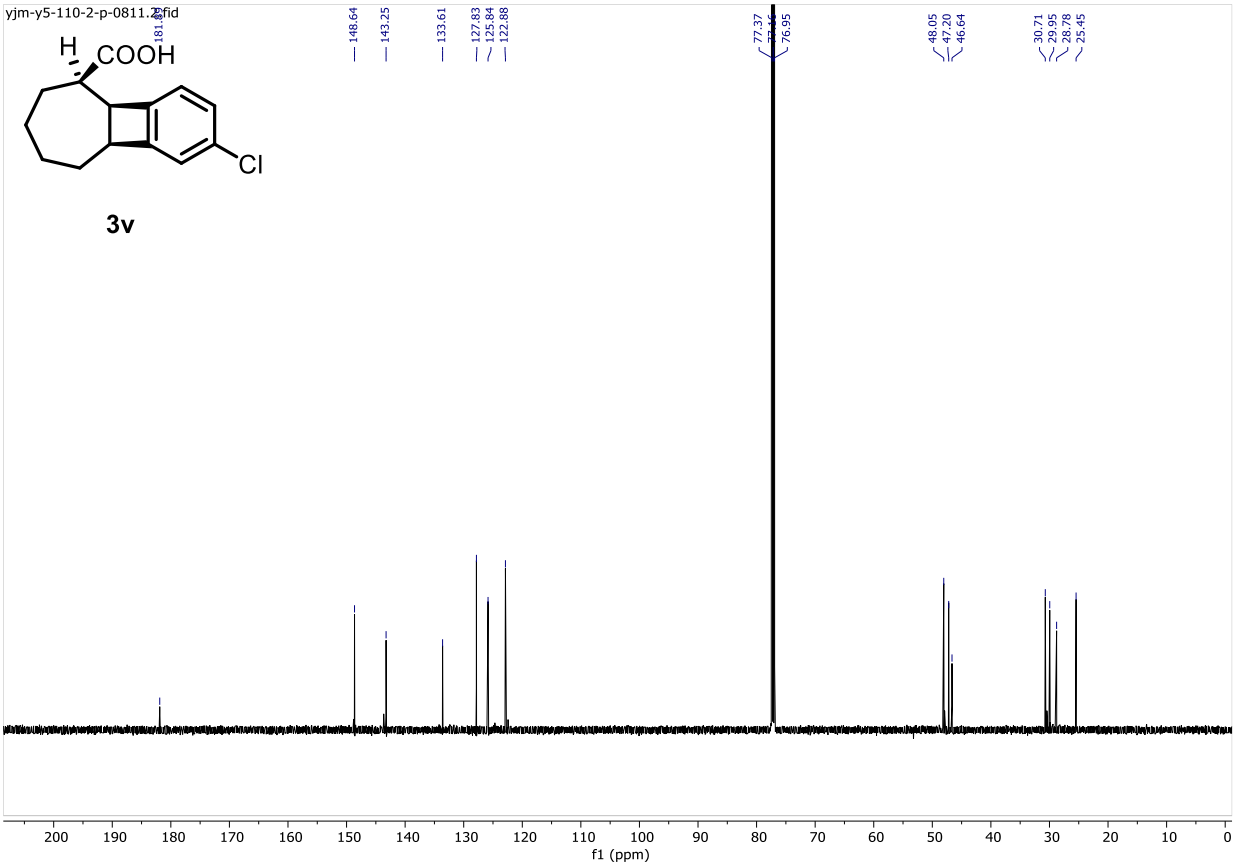
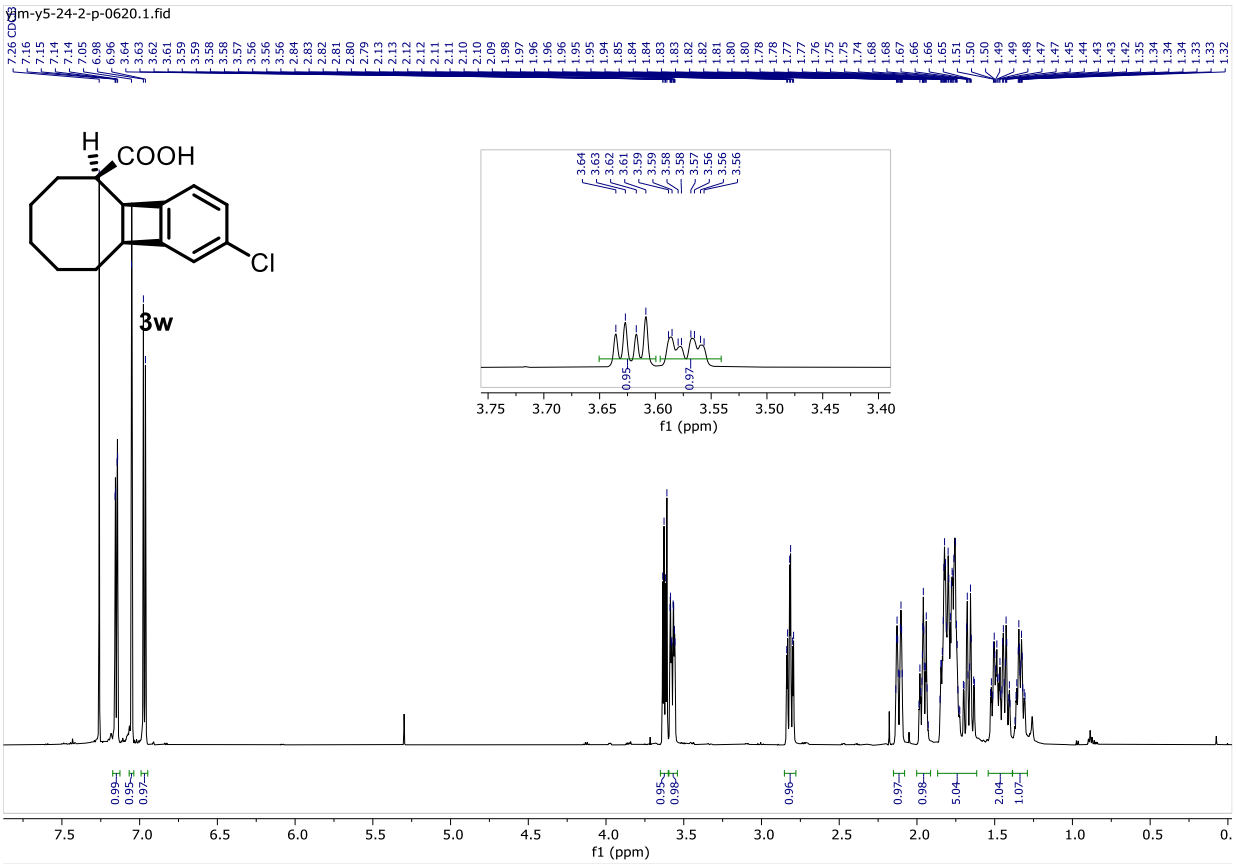
H
COOH
Cl
3t
f1 (ppm)

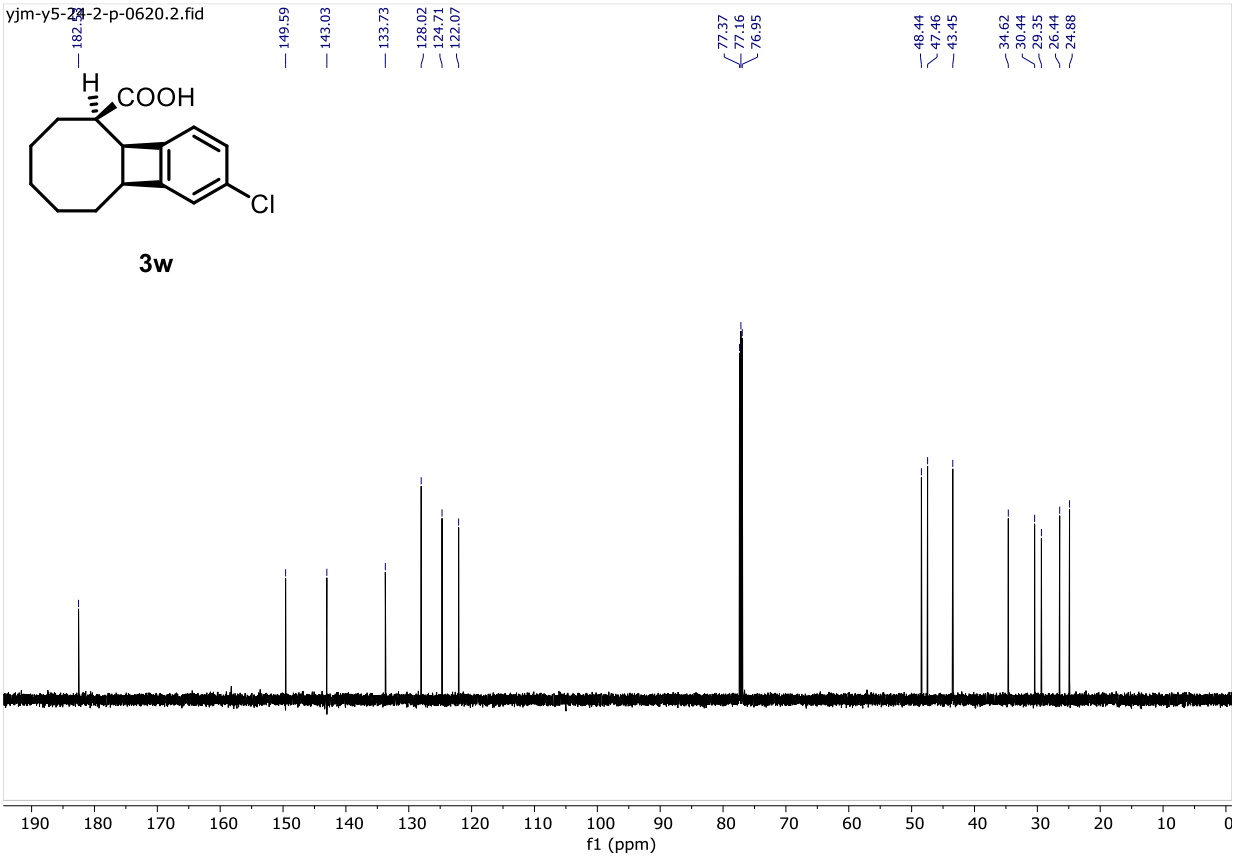

yjm-y5-65-4-p-0721.1.fid
nPr
COOH
Cl
3u
f1 (ppm)

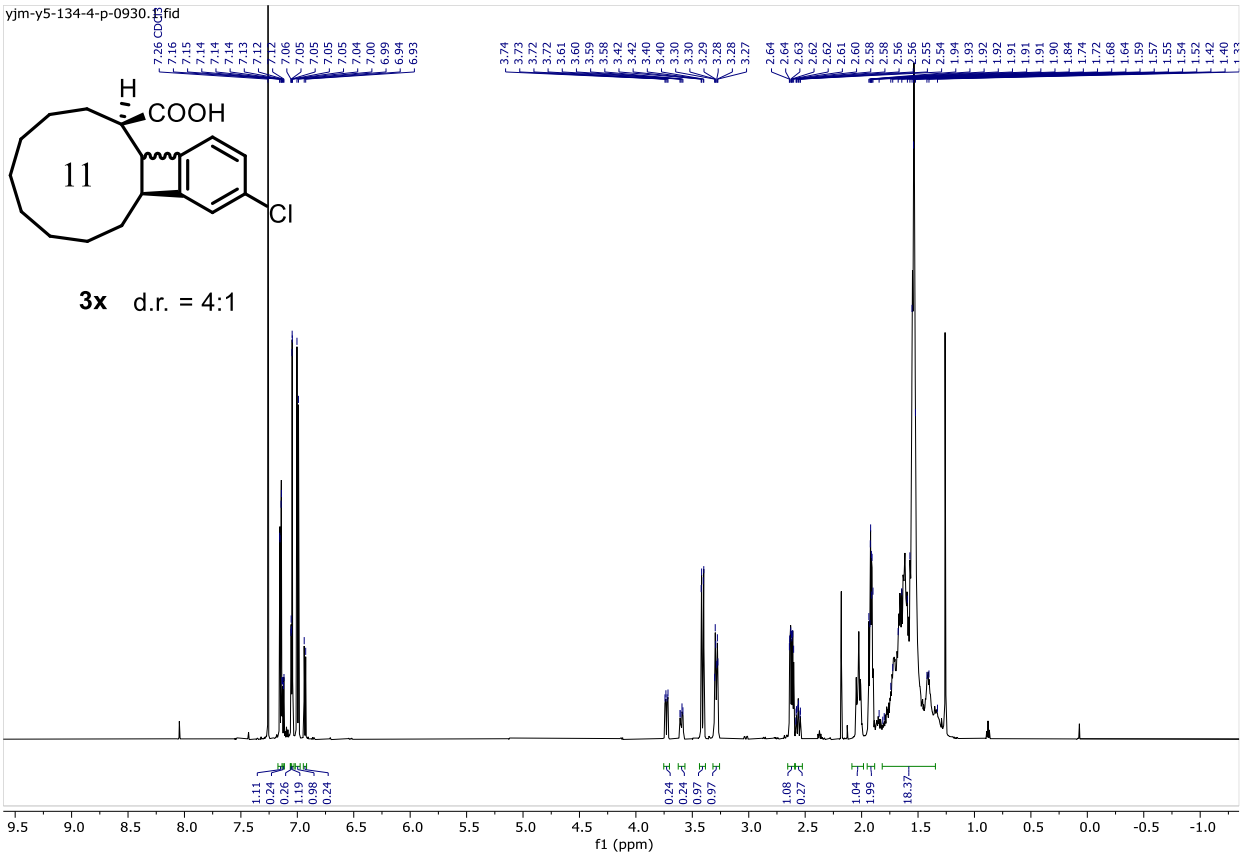

yjm-y5-65-4-p-0721.2.fid
nPr
COOH
Cl
3u
f1 (ppm)

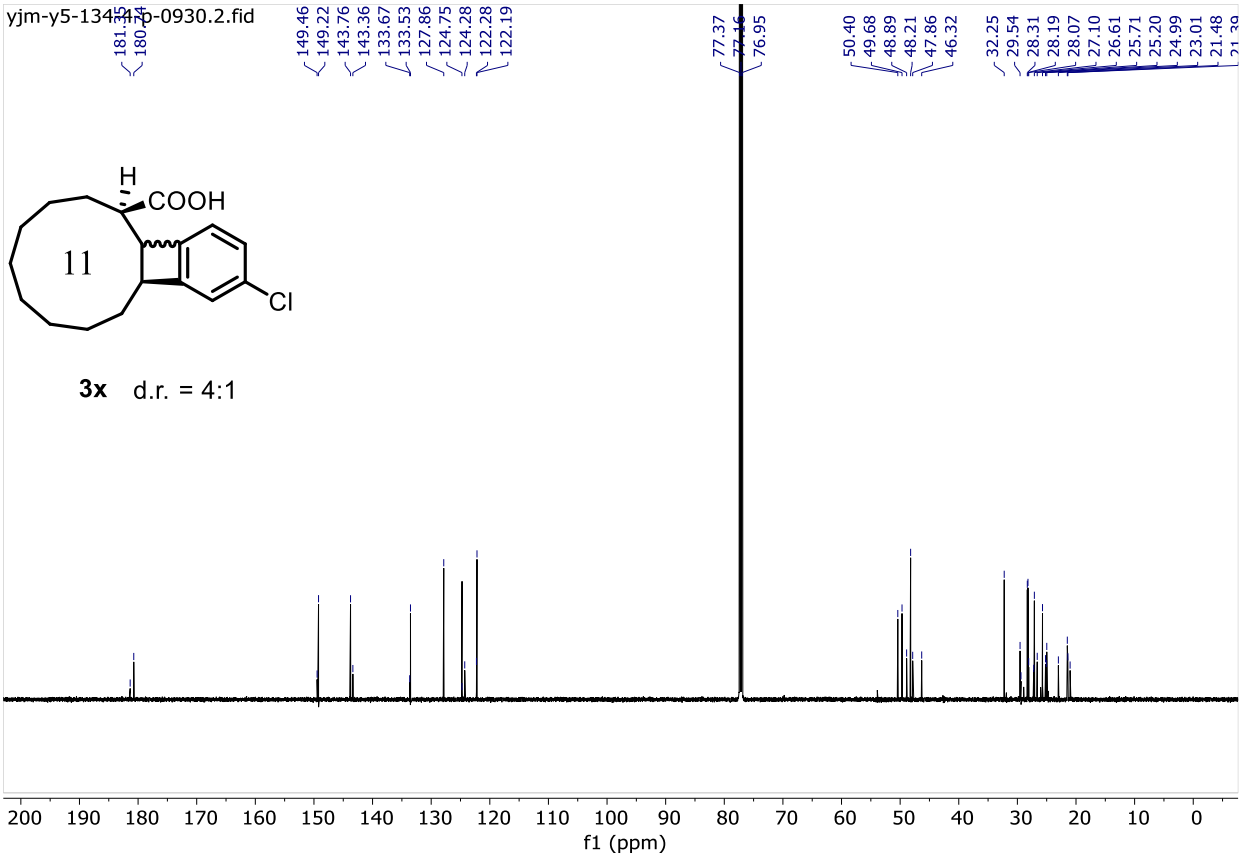

yjm-y5-110-2-p-0811.1.fid
H2O
H
COOH
Cl
3v
f1 (ppm)

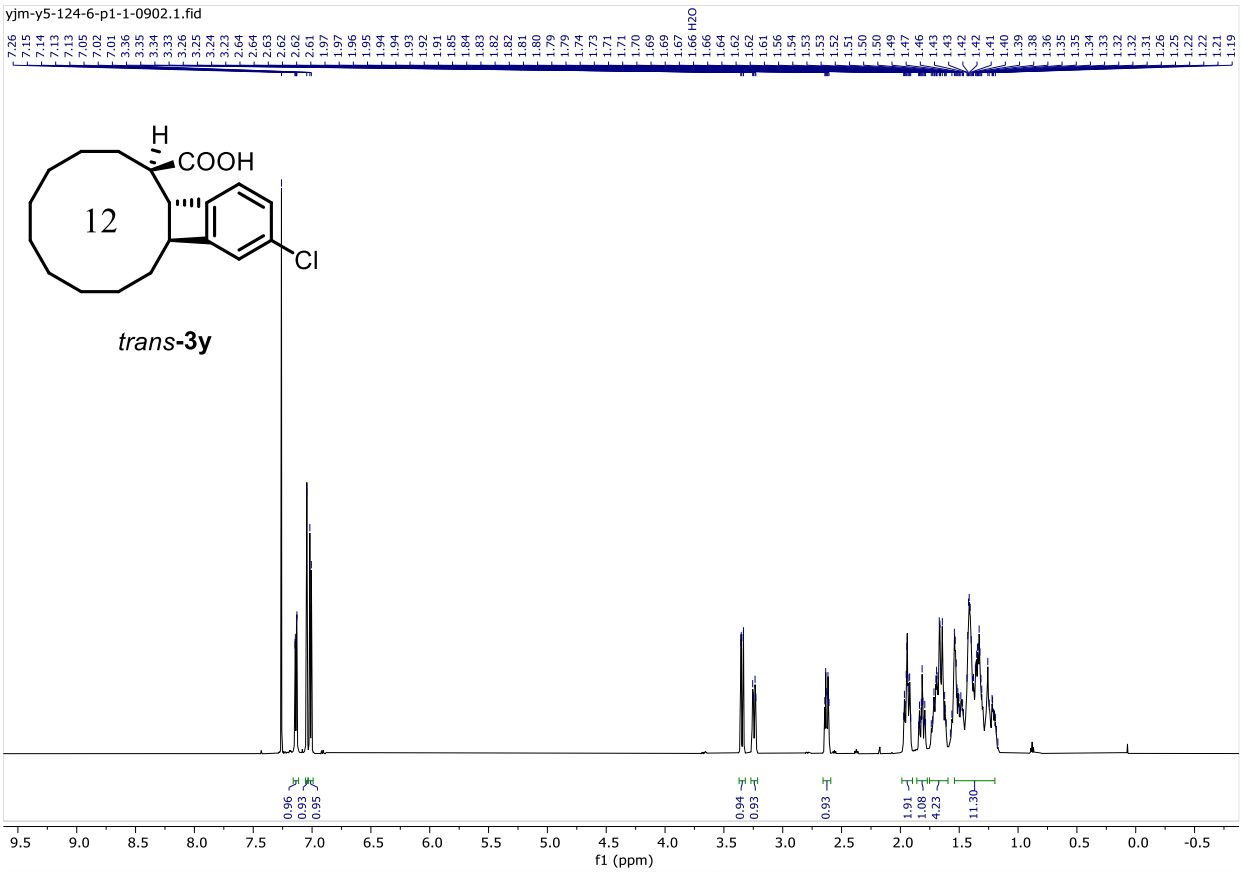

yjm-y5-110-2-p-0811.2.fid
181.42
148.64
143.25
133.61
127.83
125.84
122.88
77.37
77.16
76.95
48.05
47.20
46.64
30.71
29.95
28.78
25.45
H
COOH
Cl
3v
f1 (ppm)

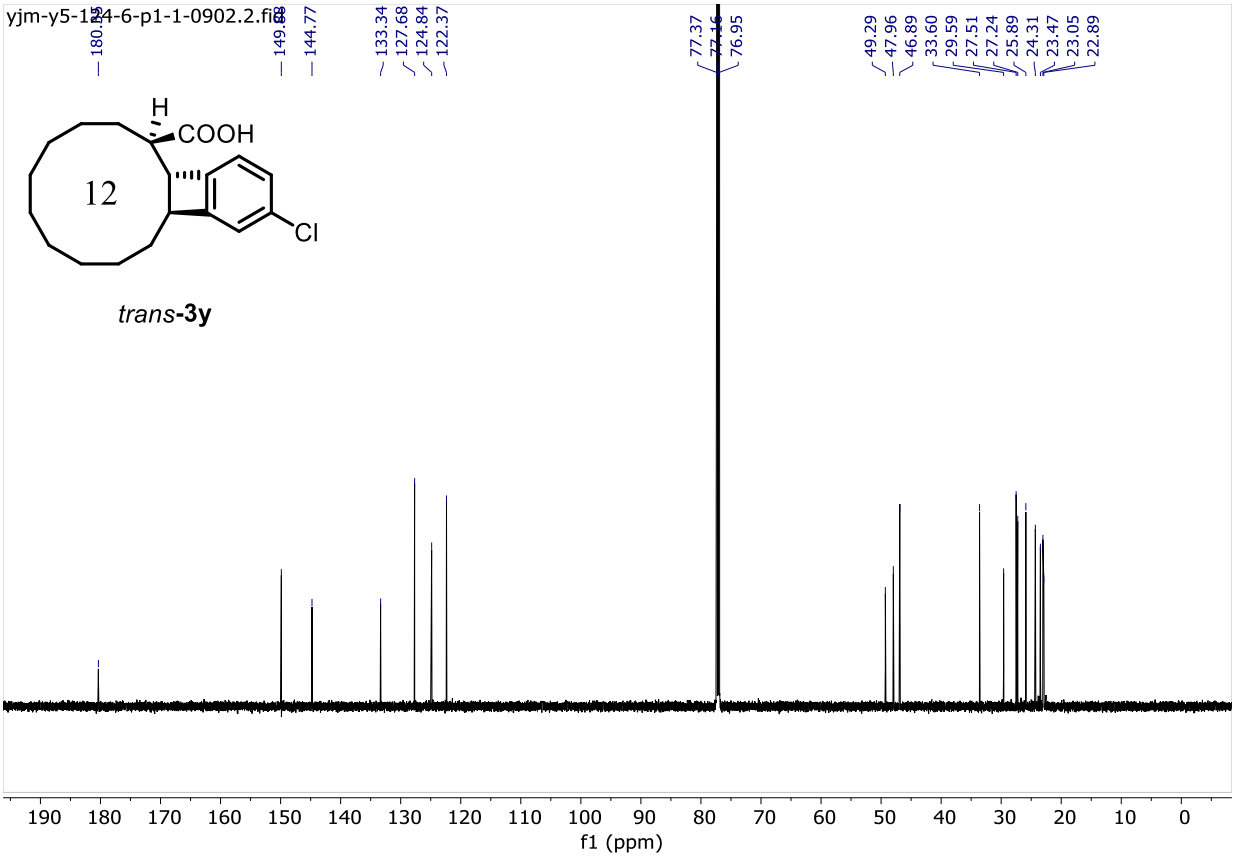

yjm-y5-24-2-p-0620.1.fid
H
COOH
Cl
3w
f1 (ppm)

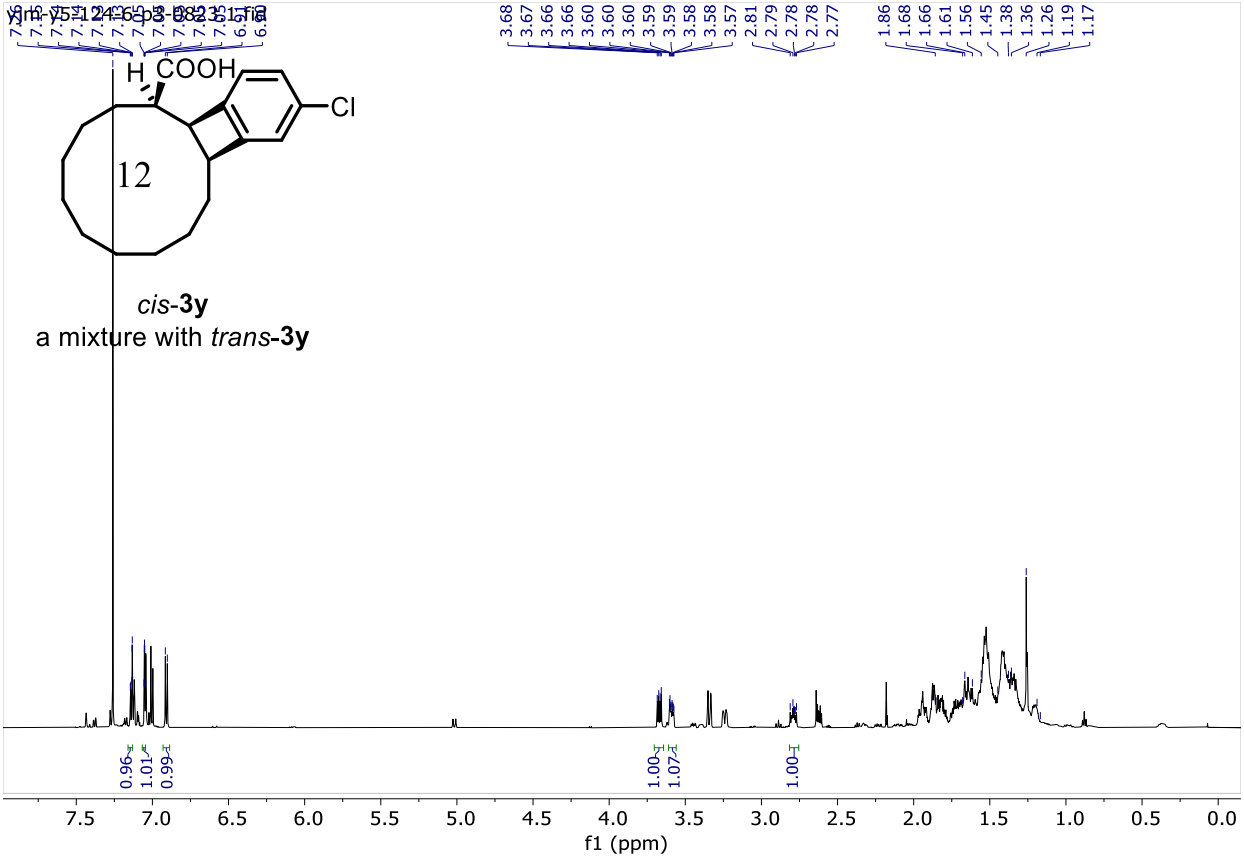

yjm-y5-24-2-p-0620.2.fid
H
COOH
Cl
3w
f1 (ppm)

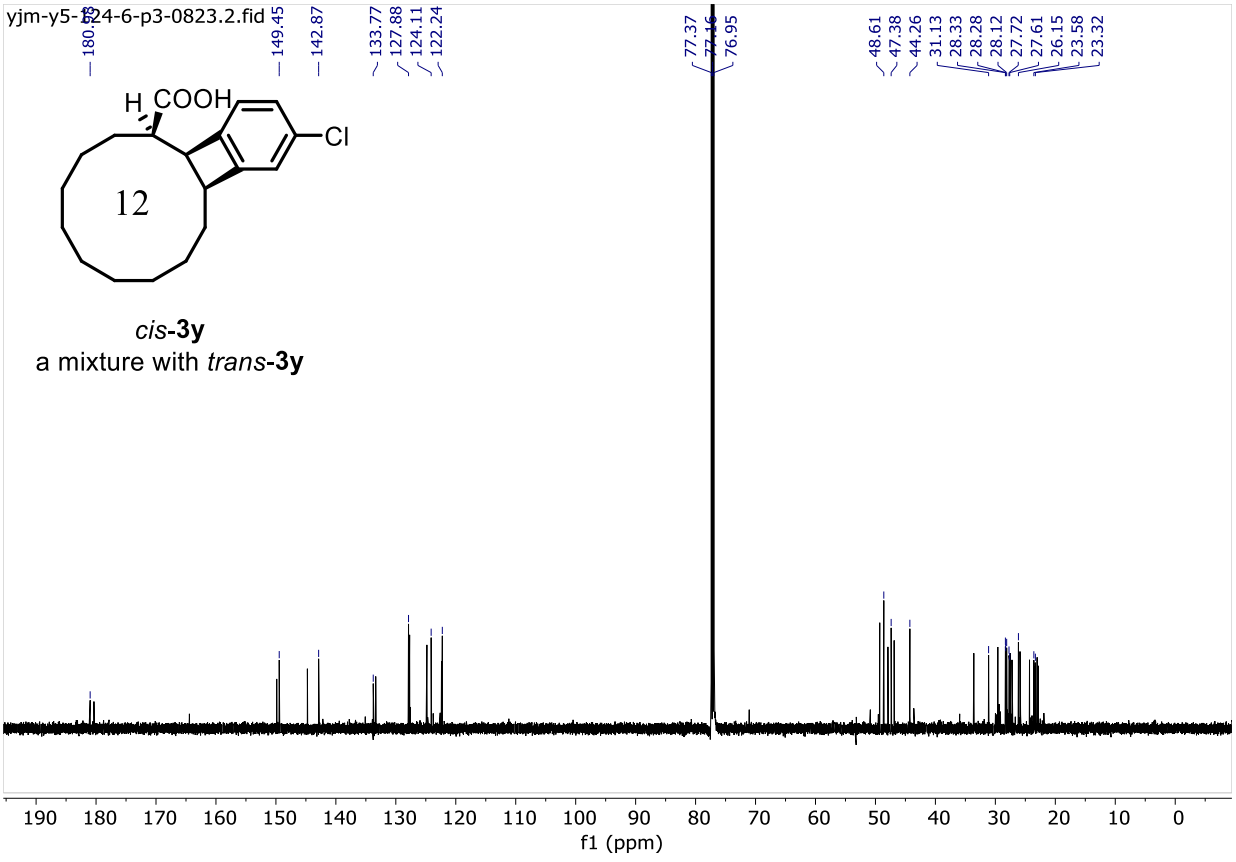

yjm-y5-134-4-p-0930.1.fid
H
COOH
11
Cl
3x d.r. = 4:1
f1 (ppm)

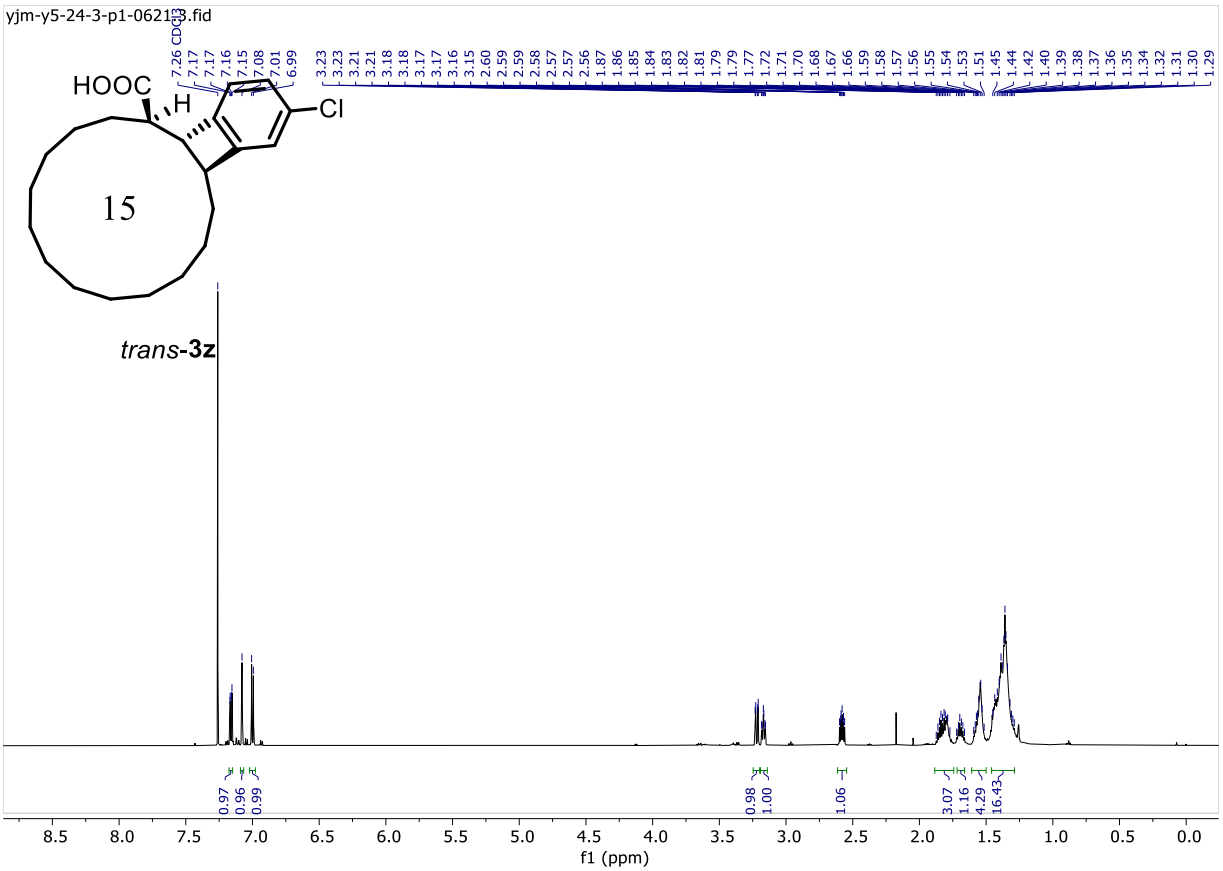

yjm-y5-134-4-p-0930.2.fid
H
COOH
11
Cl
3x d.r. = 4:1
f1 (ppm)

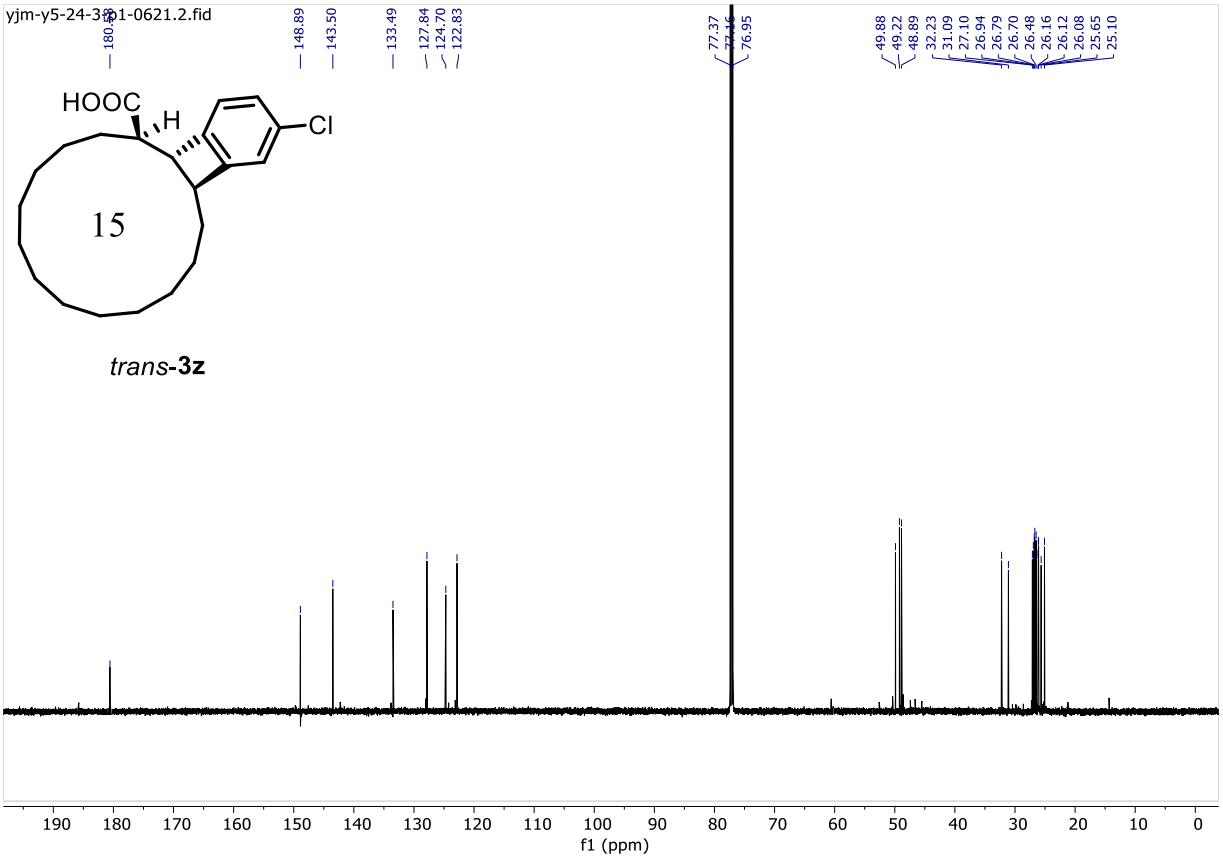

yjm-y5-124-6-p1-1-0902.1.fid
H2O
H
COOH
12
Cl
trans-3y
f1 (ppm)

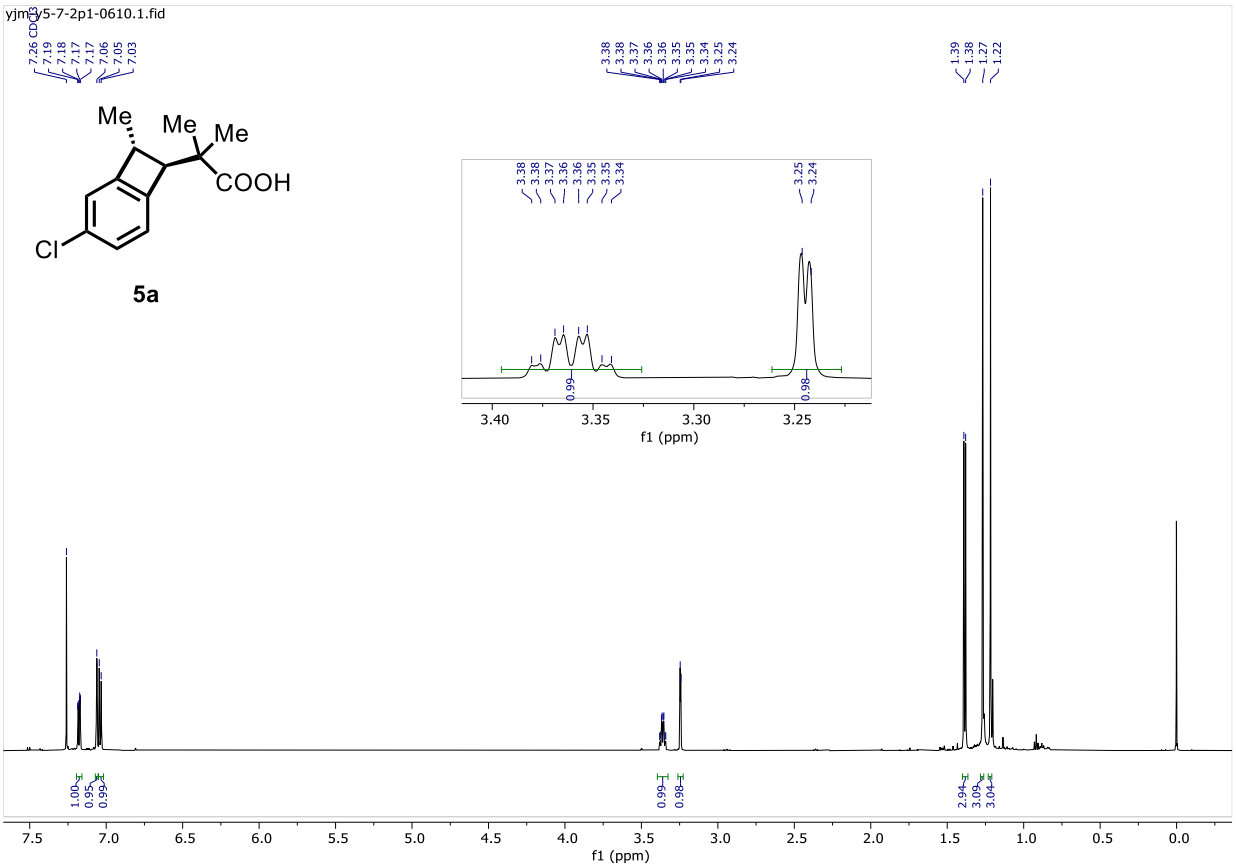

yjm-y5-124-6-p1-1-0902.2.fid
180.45
149.68
144.77
133.34
127.68
124.84
122.37
77.37
77.16
76.95
49.29
47.96
46.89
33.60
29.59
27.51
27.24
25.89
24.31
23.47
23.05
22.89
H
COOH
12
Cl
trans-3y
f1 (ppm)

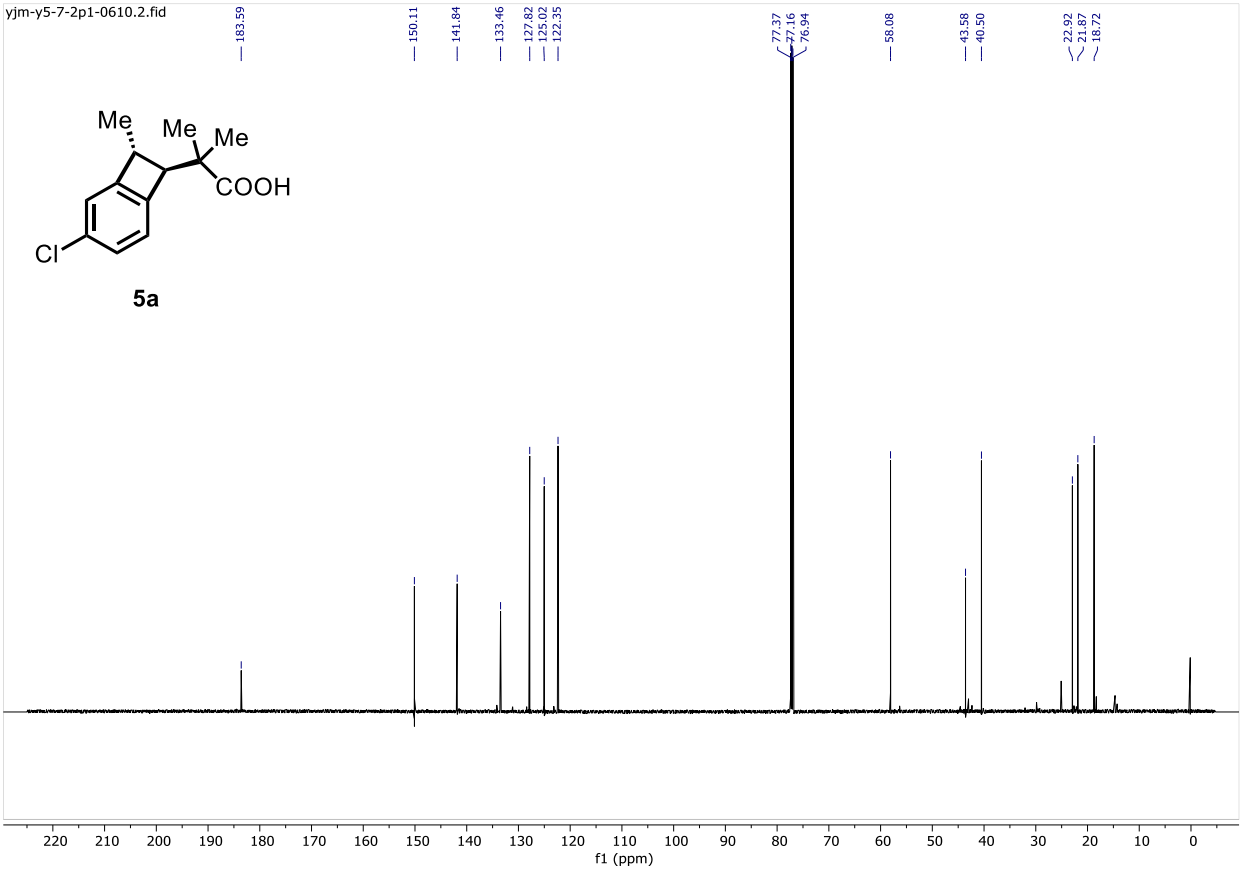

H
COOH
Cl
12
cis-3y
a mixture with trans-3y
f1 (ppm)

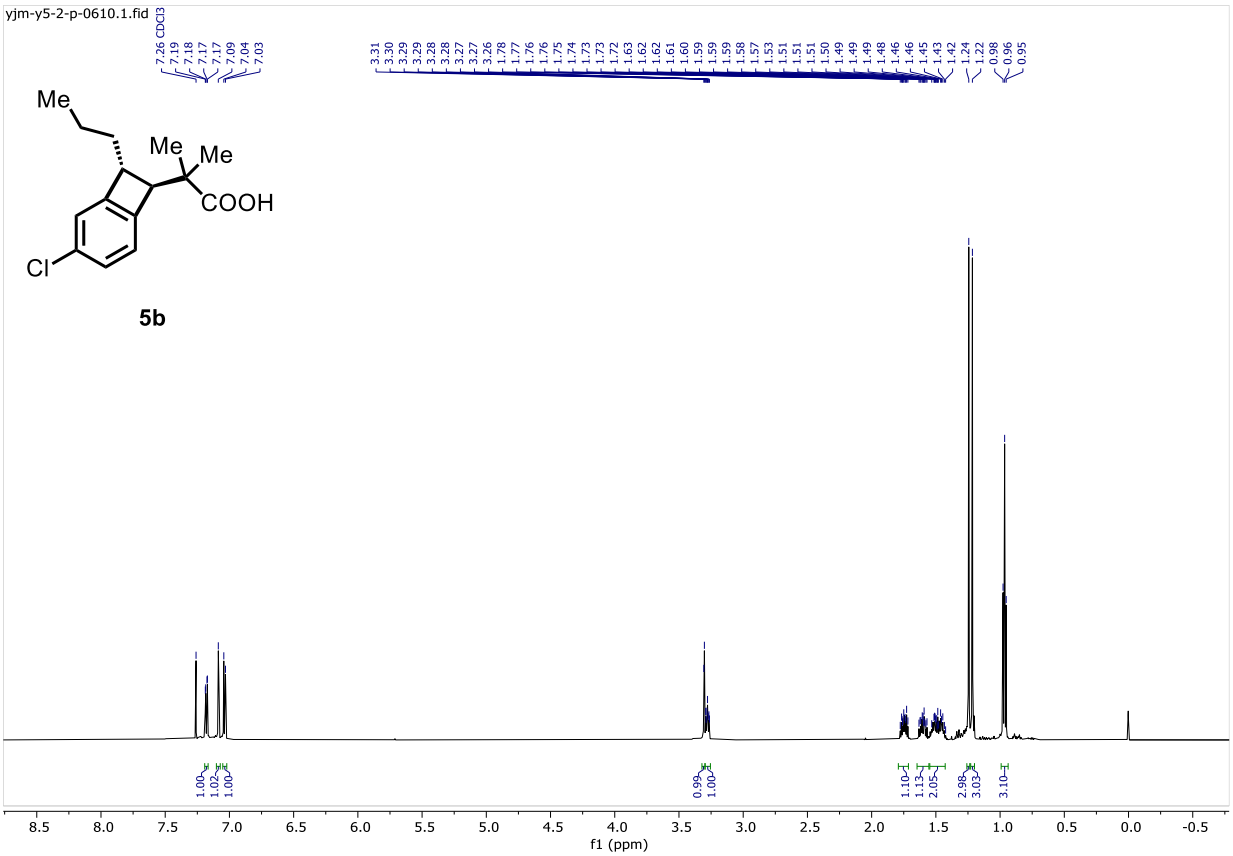

H
COOH
Cl
12
cis-3y
a mixture with trans-3y
f1 (ppm)

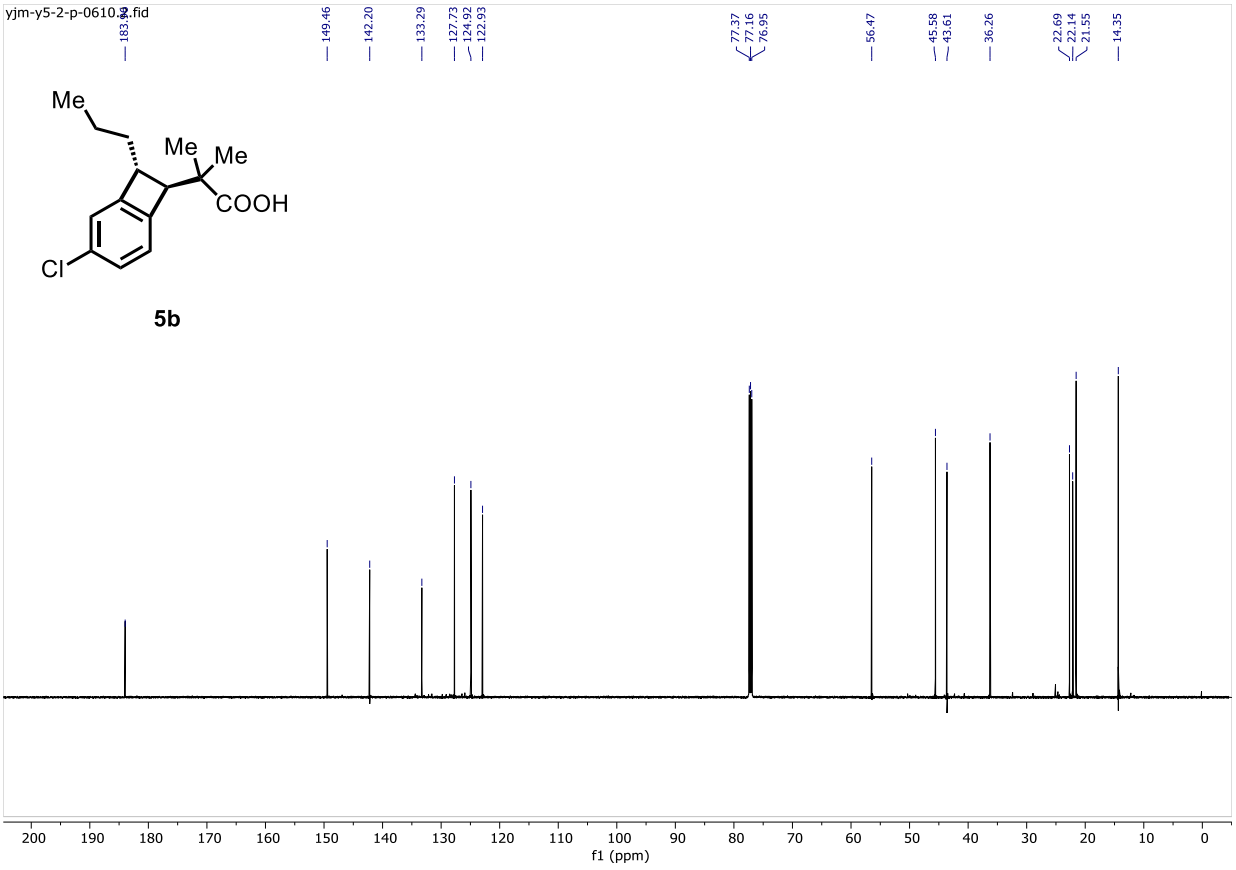

yjm-y5-24-3-p1-062153.fid
HOOC
H
Cl
15
trans-3z
f1 (ppm)


yjm-y5-24-3-p1-0621.2.fid
HOOC
H
Cl
15
trans-3z
f1 (ppm)


yjm-y5-7-2p1-0610.1.fid
Me
Me
Me
COOH
Cl
5a
f1 (ppm)


yjm-y5-7-2p1-0610.2.fid
Me
Me
Me
COOH
Cl
5a
f1 (ppm)


yjm-y5-2-p-0610.1.fid
Me
Me
Me
COOH
Cl
5b
f1 (ppm)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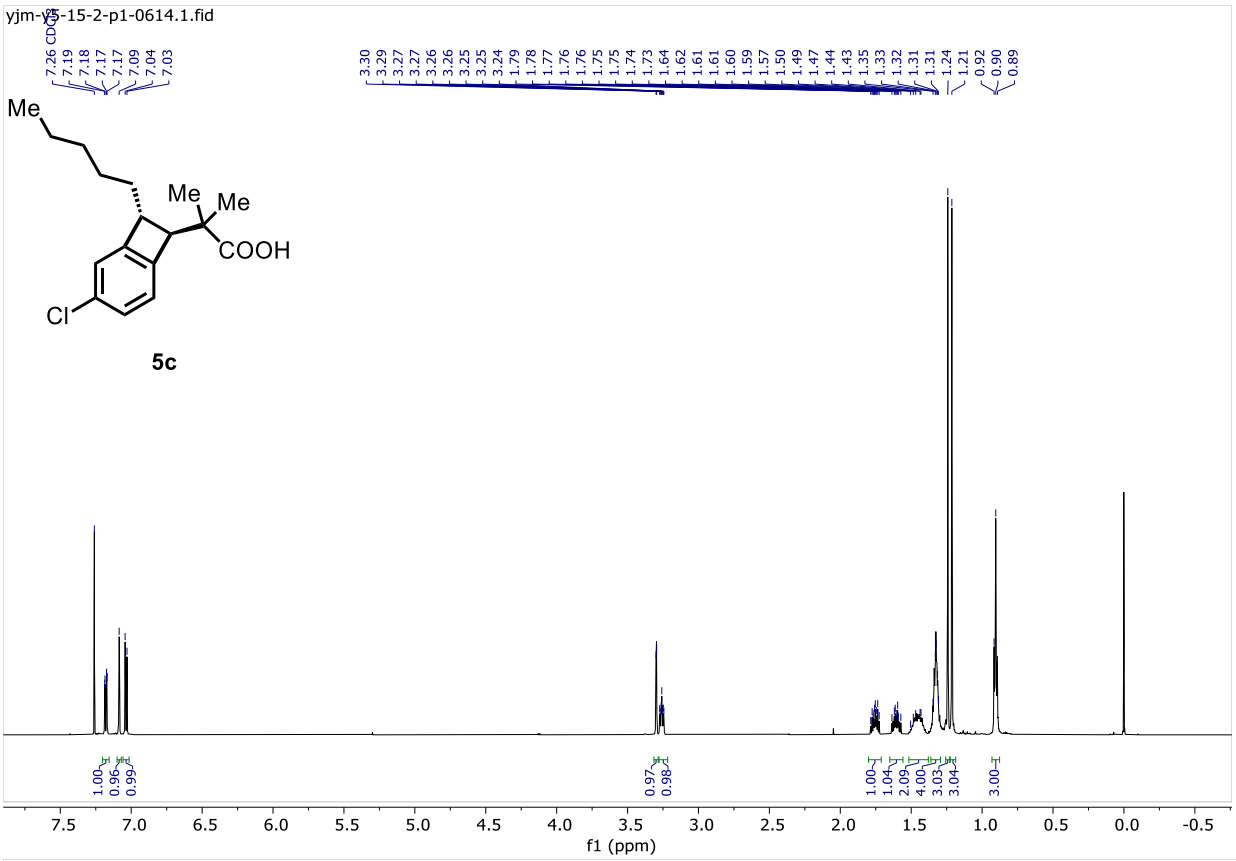
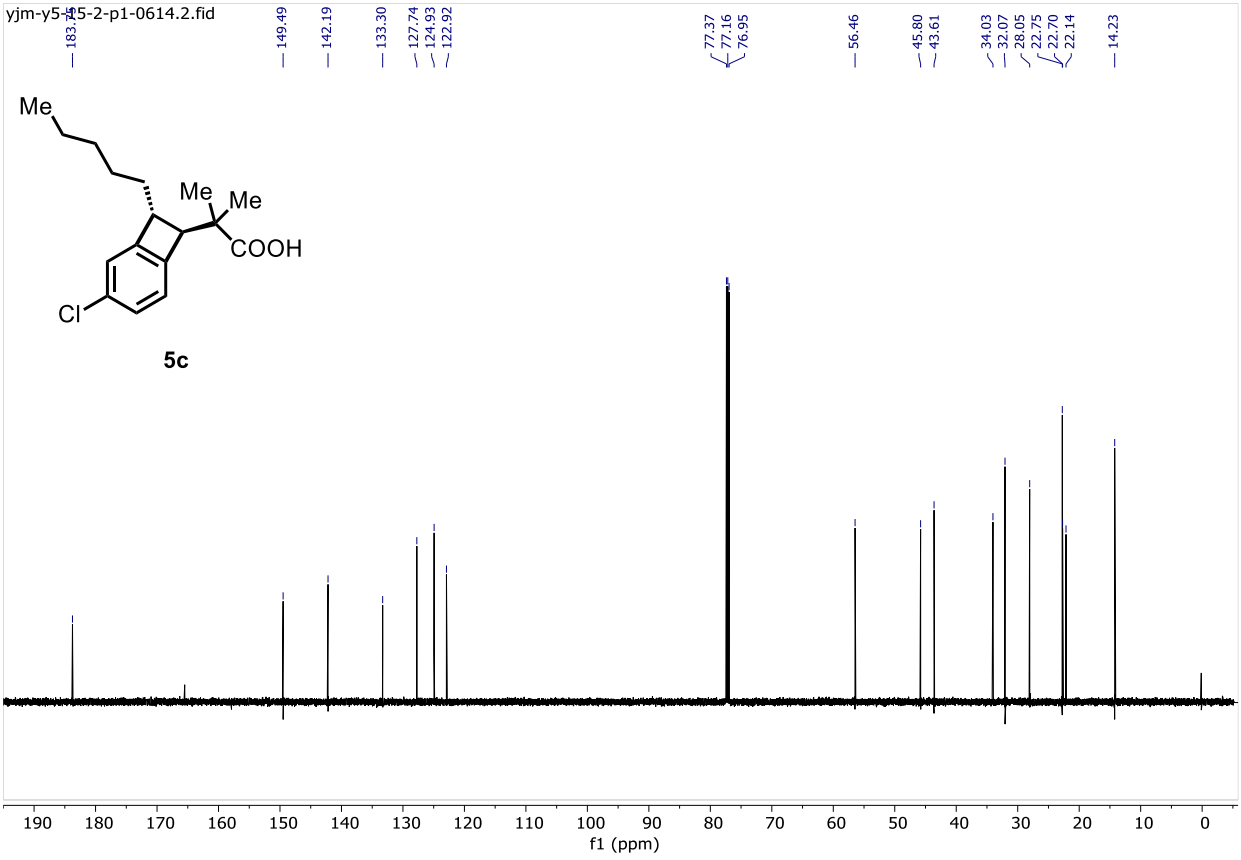
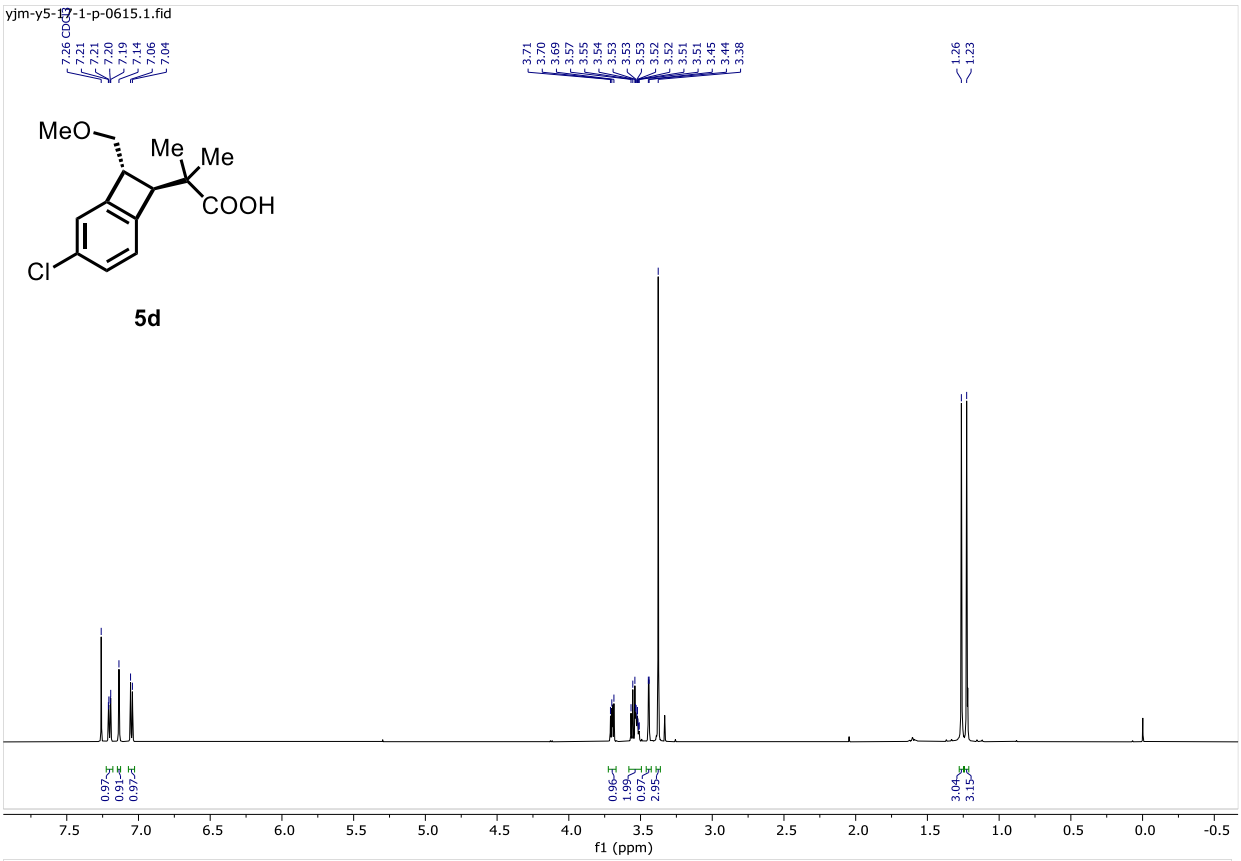
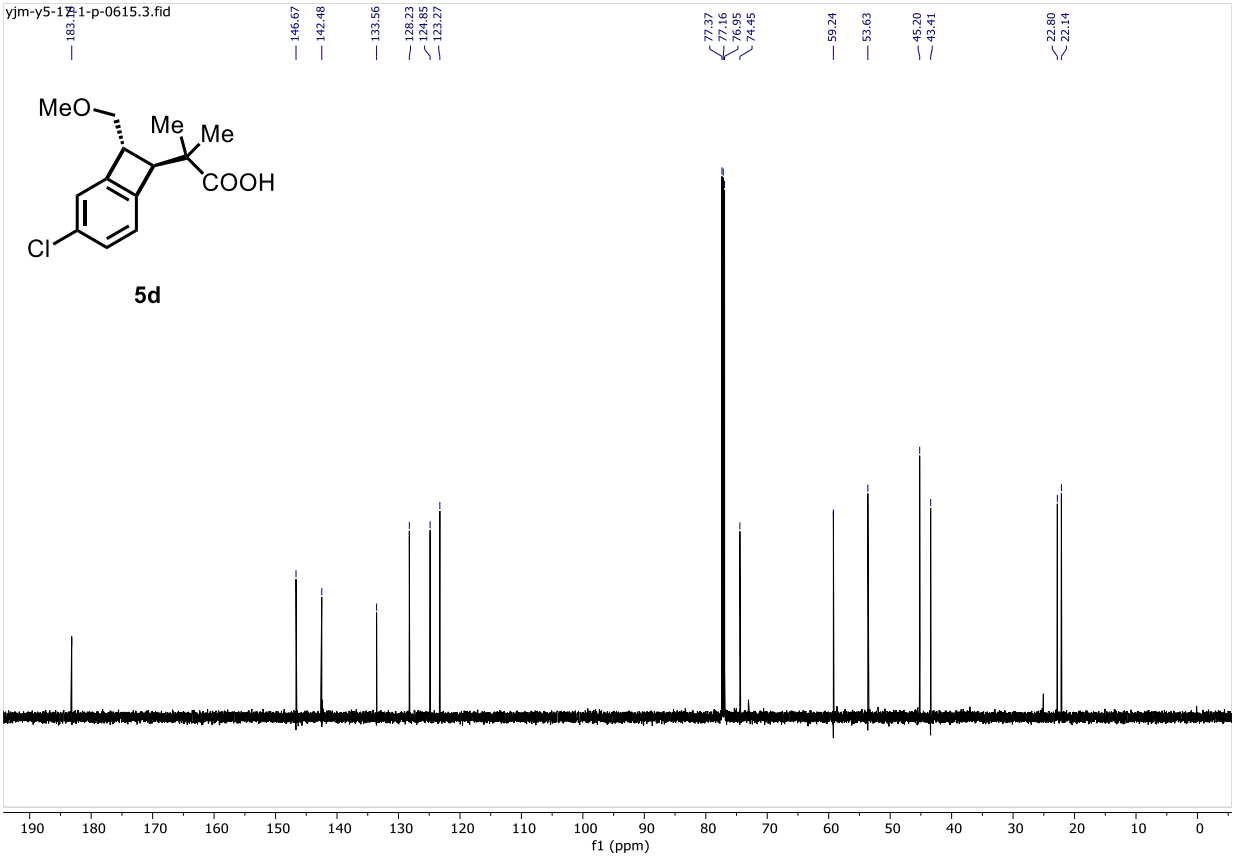
Me
Me
Me
COOH
Cl
5b
f1 (ppm)


yjm-y5-15-2-p1-0614.1.fid
Me
Me
Me
COOH
Cl
5c
f1 (ppm)


yjm-y5-15-2-p1-0614.2.fid
Me
Me
Me
COOH
Cl
5c
f1 (ppm)


yjm-y5-1-1-p-0615.1.fid
MeO
Me
Me
COOH
Cl
5d
f1 (ppm)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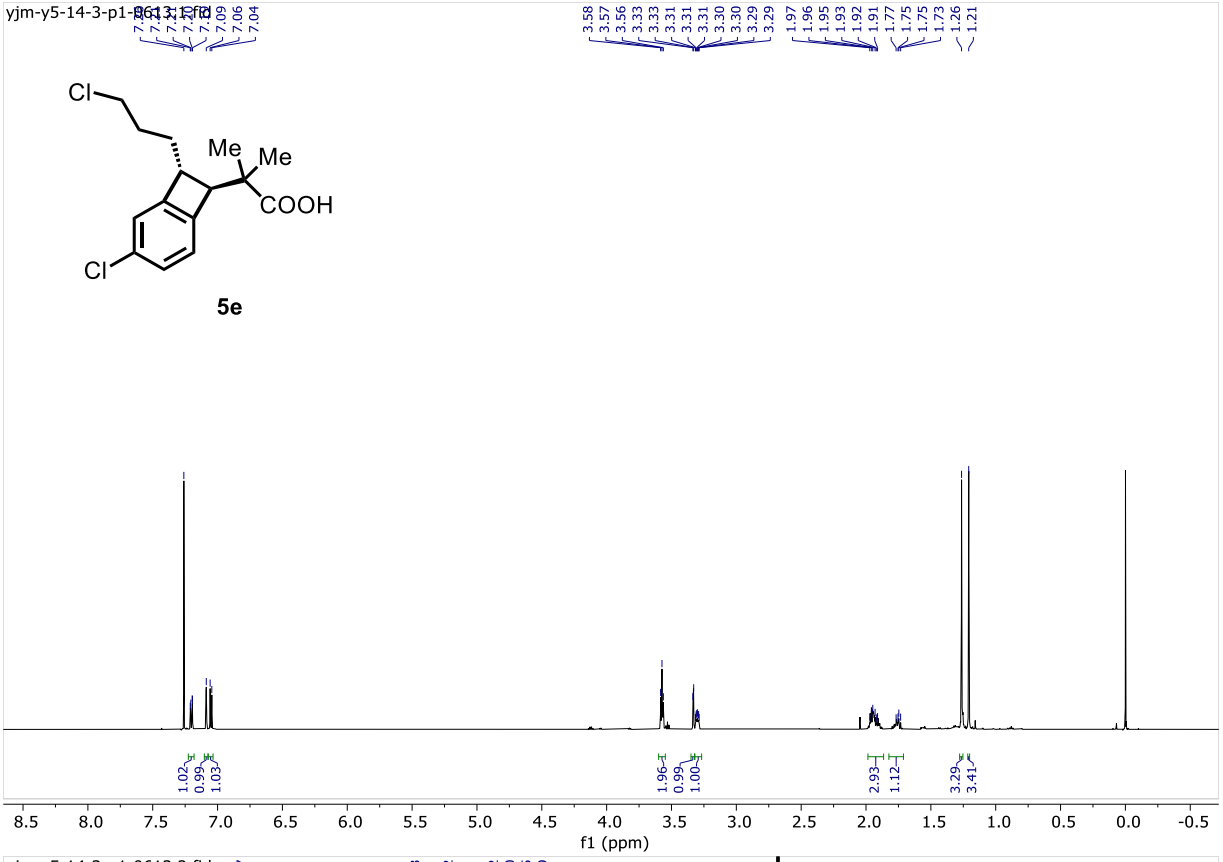
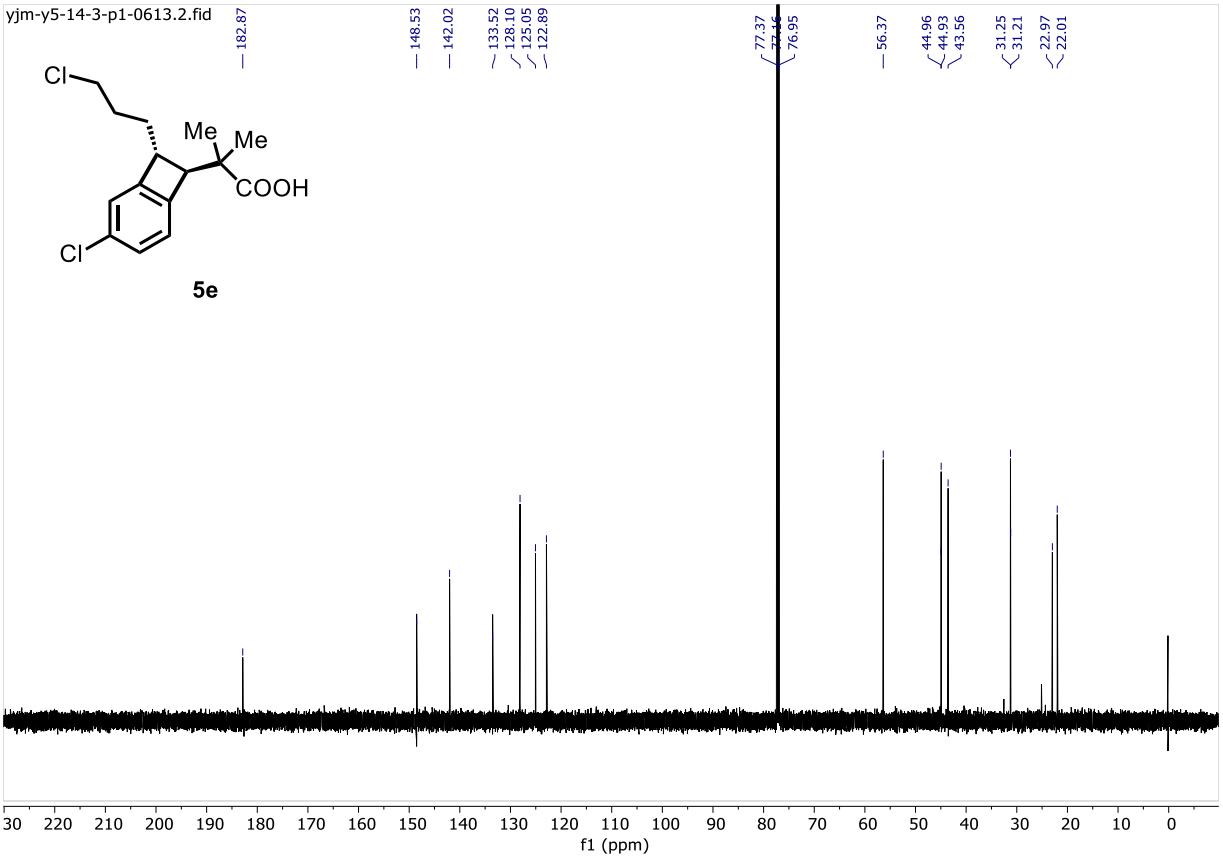
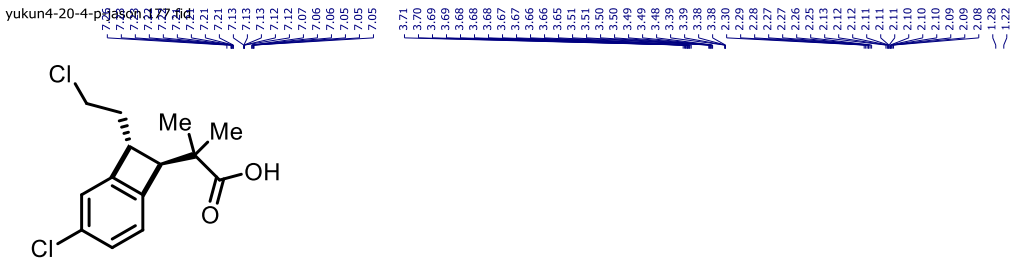
MeO
Me
Me
COOH
Cl
5d
f1 (ppm)

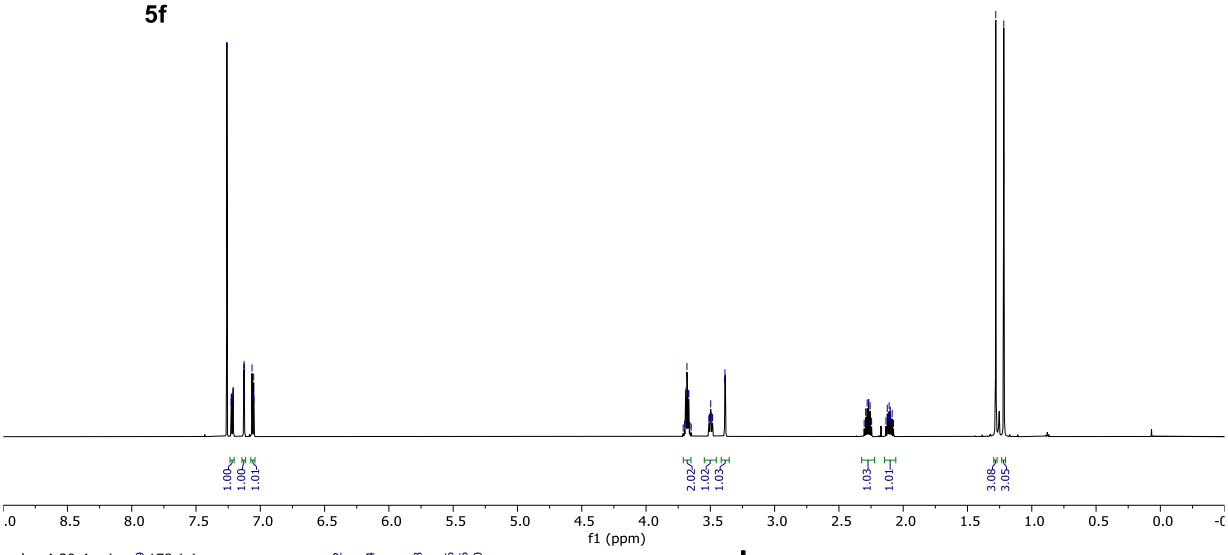

yjm-y5-14-3-p1-0613.1.fid
Cl
Me
Me
COOH
Cl
5e
f1 (ppm)

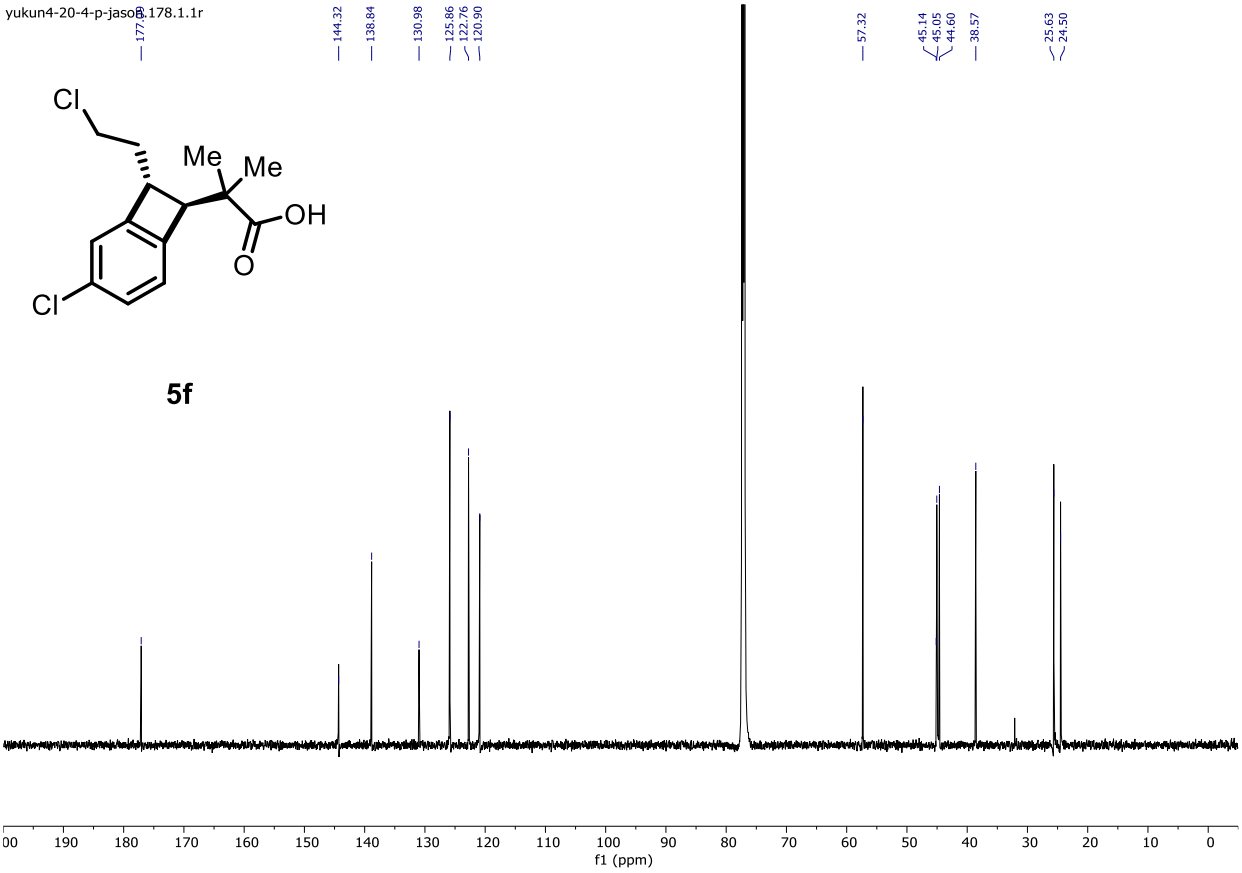

yjm-y5-14-3-p1-0613.2.fid
Cl
Me
Me
COOH
Cl
5e
f1 (ppm)



Cl
Me
Me
OH
O
Cl

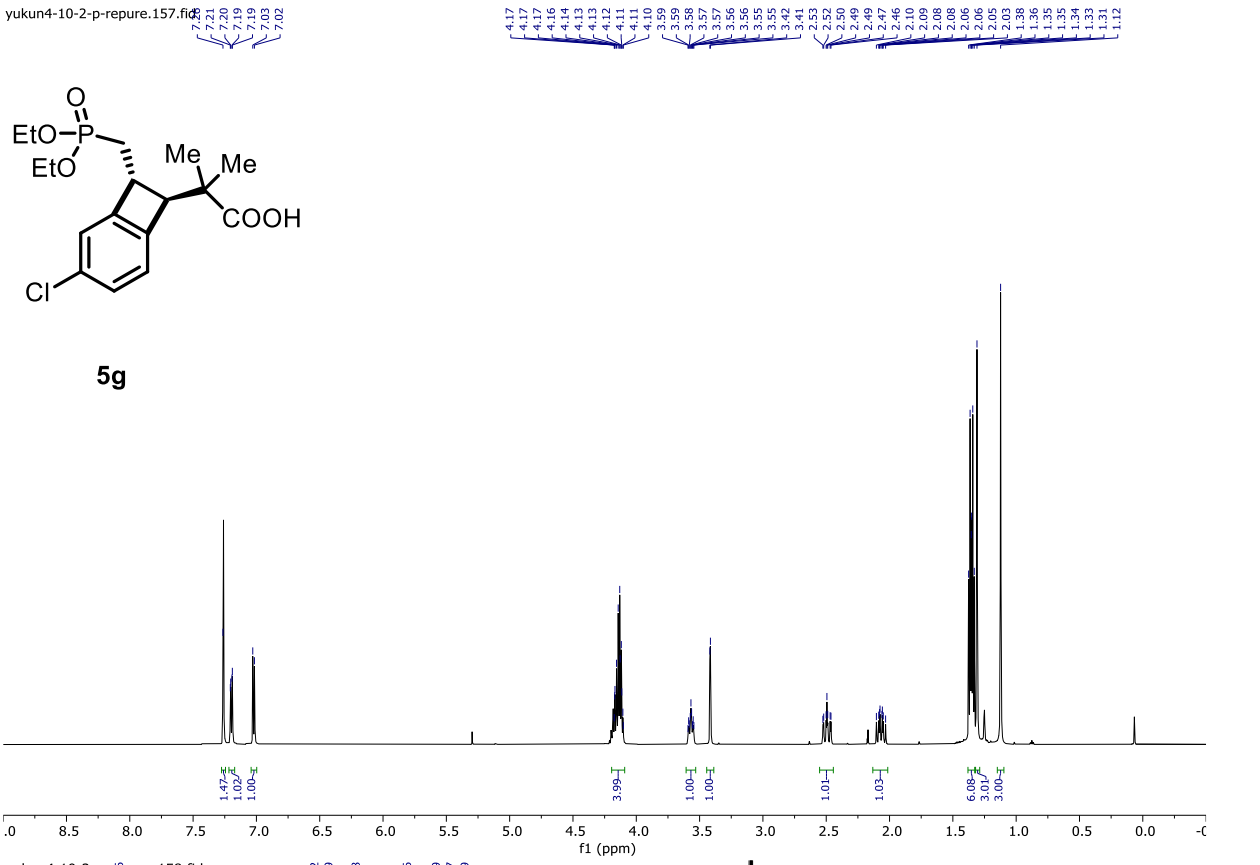
5f

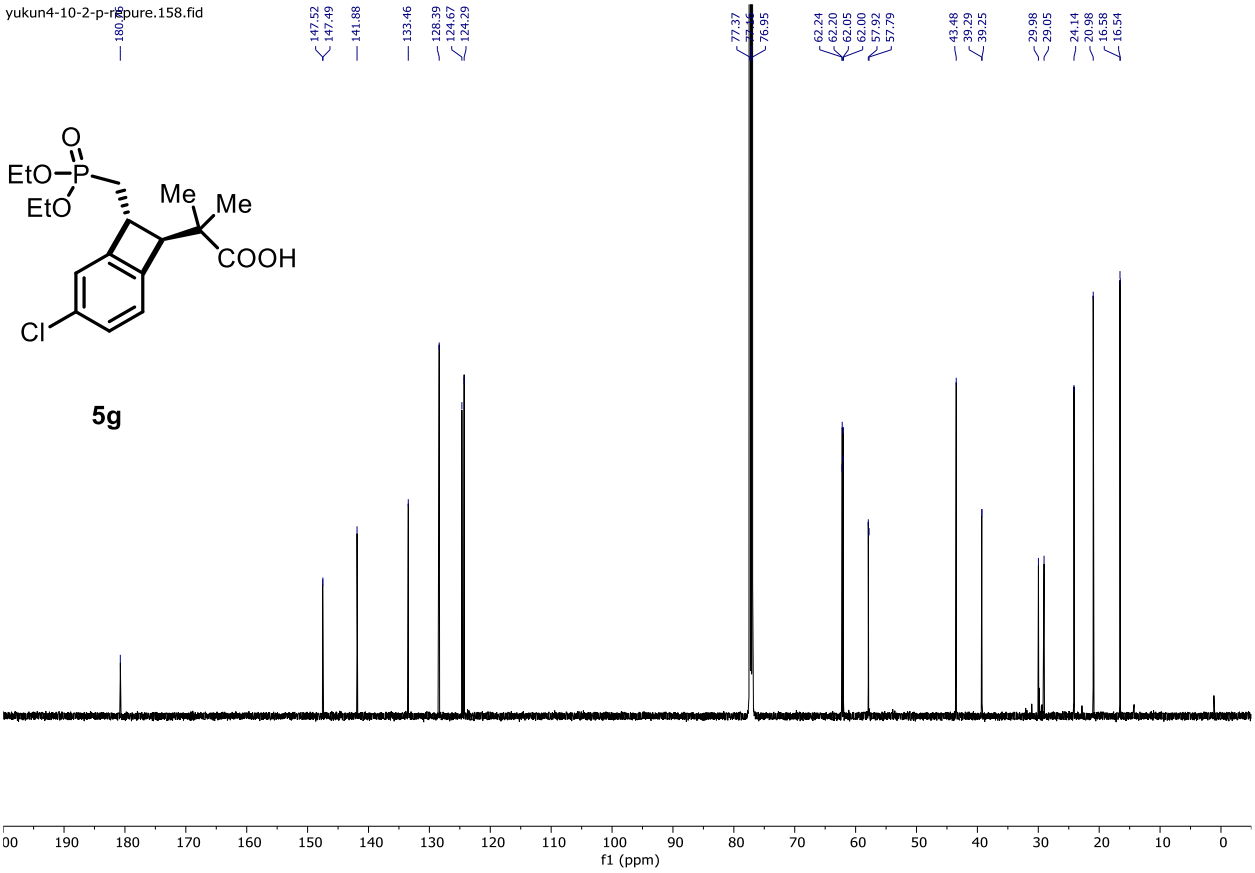

1.00
1.00
1.01
2.02
1.02
1.03
1.03
1.01
3.08
3.05
f1 (ppm)


yukun4-20-4-p-jasob.178.1.1r
177.80
144.32
138.84
130.98
125.86
122.76
120.90
57.32
45.14
45.05
44.60
38.57
25.63
24.50
f1 (ppm)

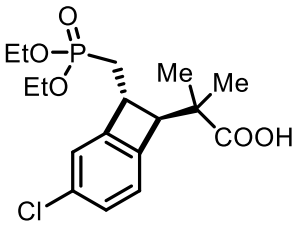
Cl
Me
Me
OH
O
Cl

5f

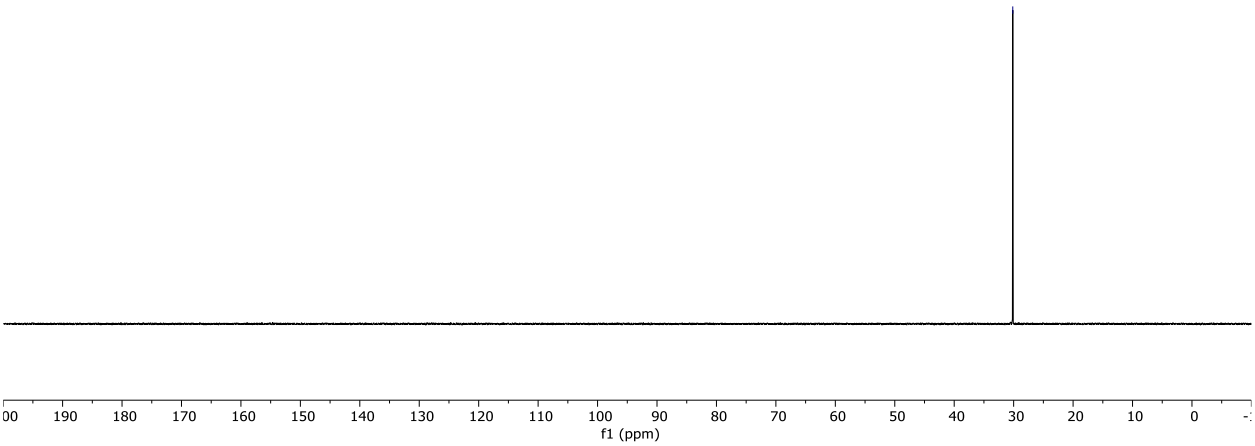

yukun4-10-2-p-repure.157.fid
EtO
P
O
EtO
Me
Me
COOH
Cl
5g
f1 (ppm)

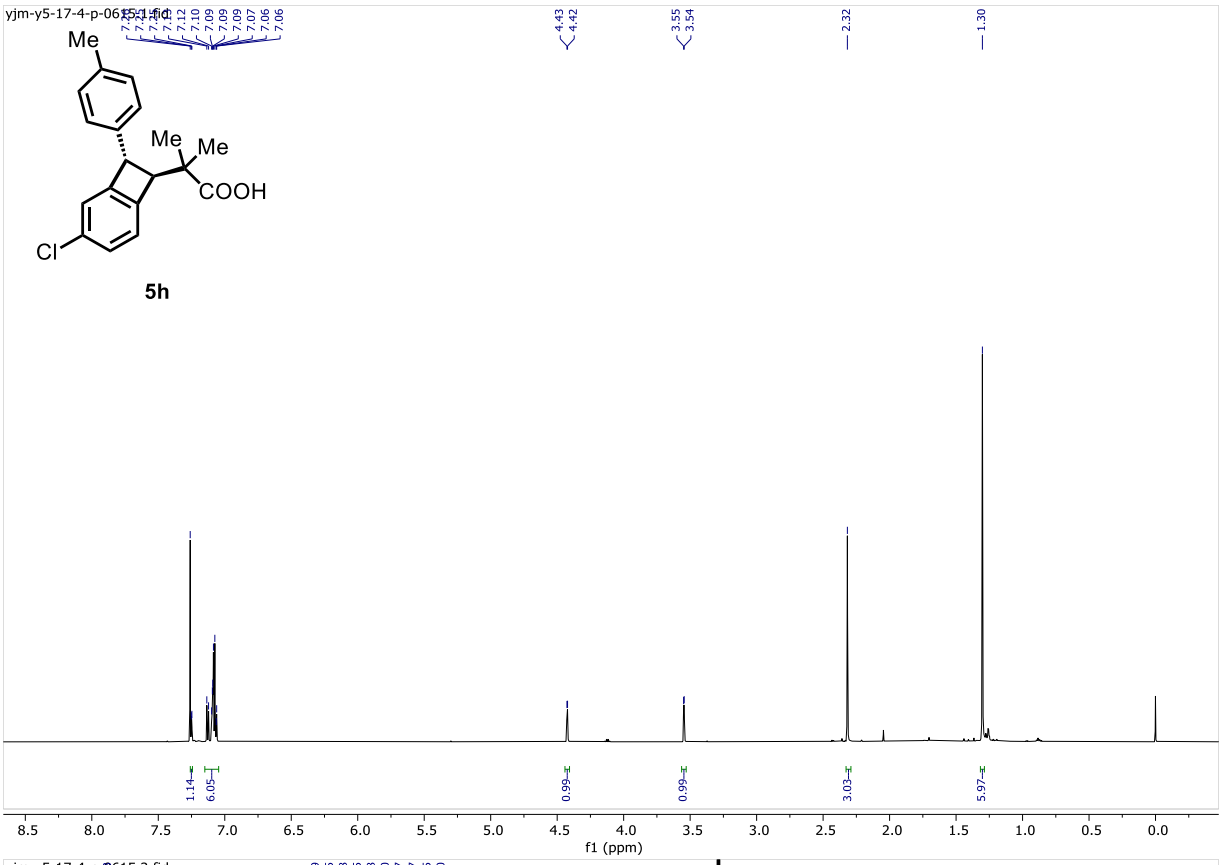

yukun4-10-2-p-repure.158.fid
EtO
P
O
EtO
Me
Me
COOH
Cl
5g
f1 (ppm)

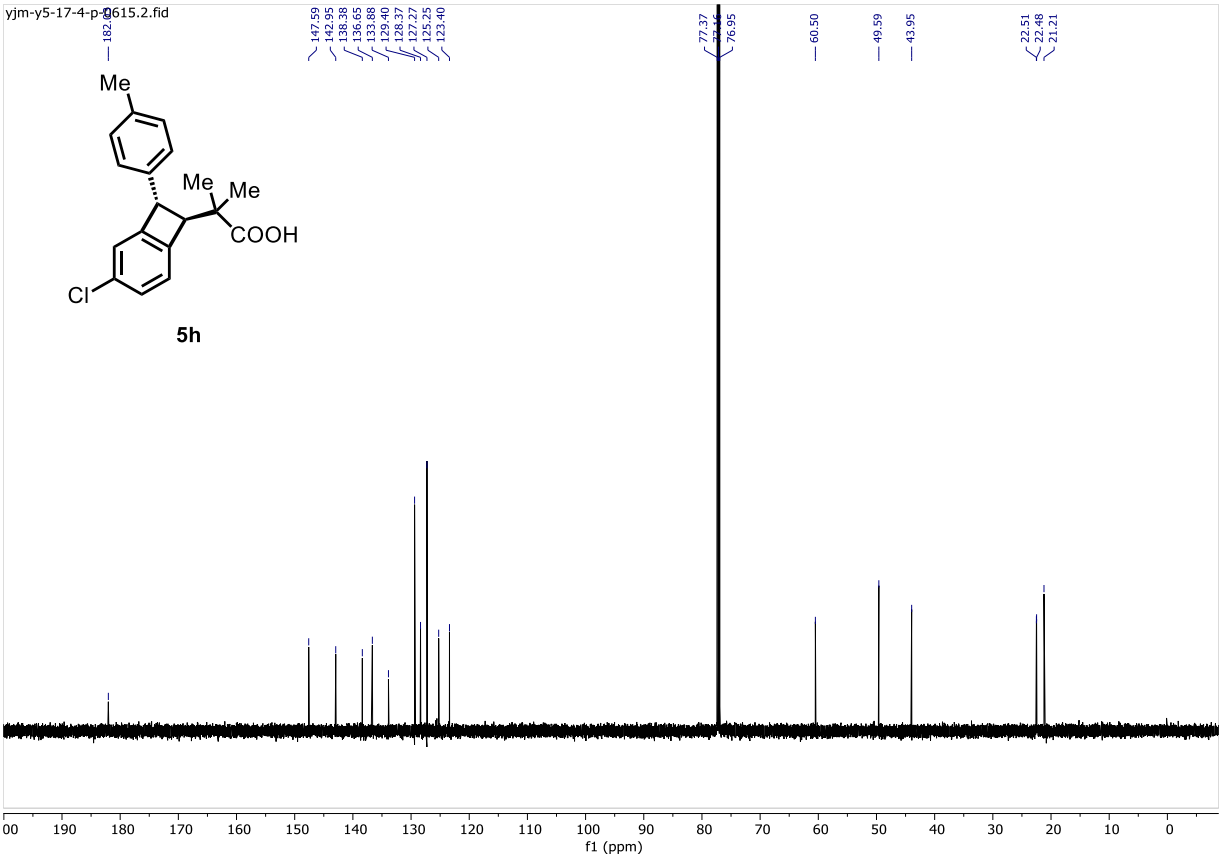
yukun4-10-2-p-repure-1.29.fid

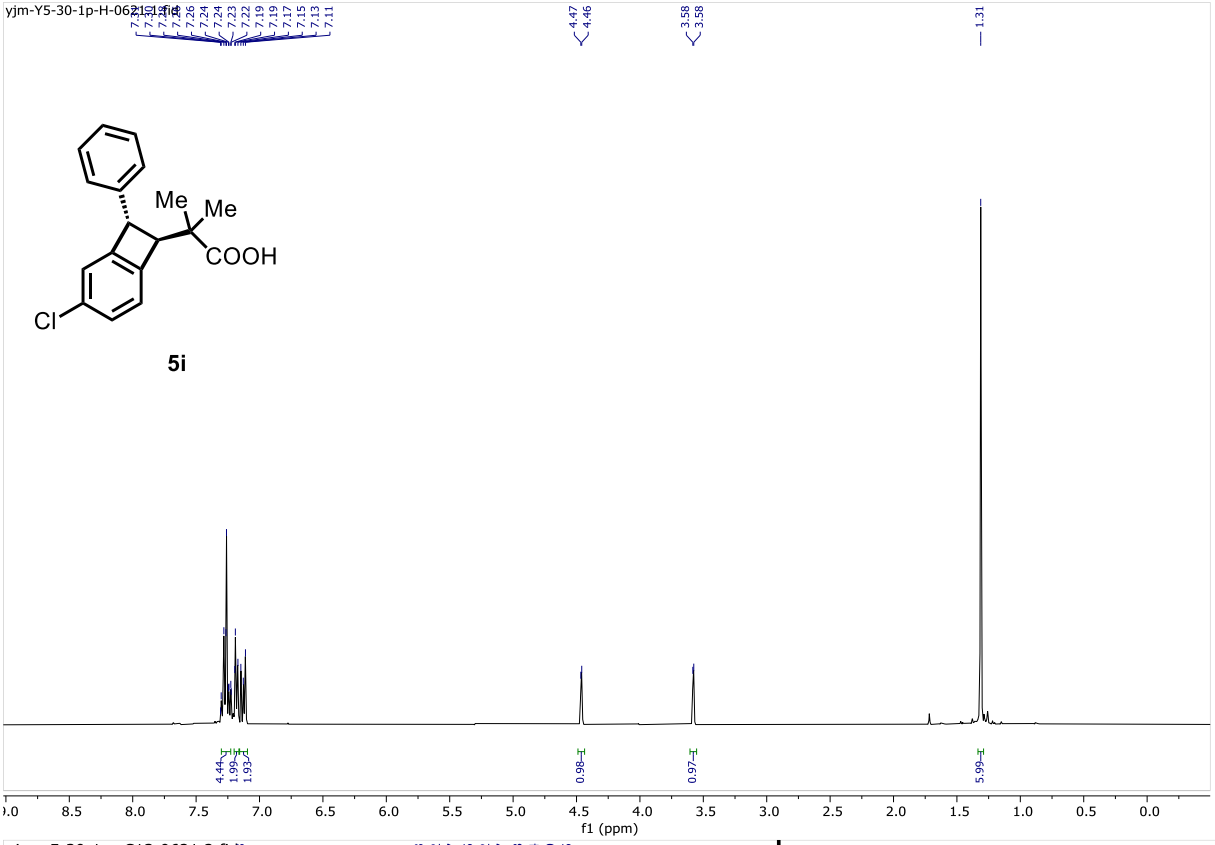


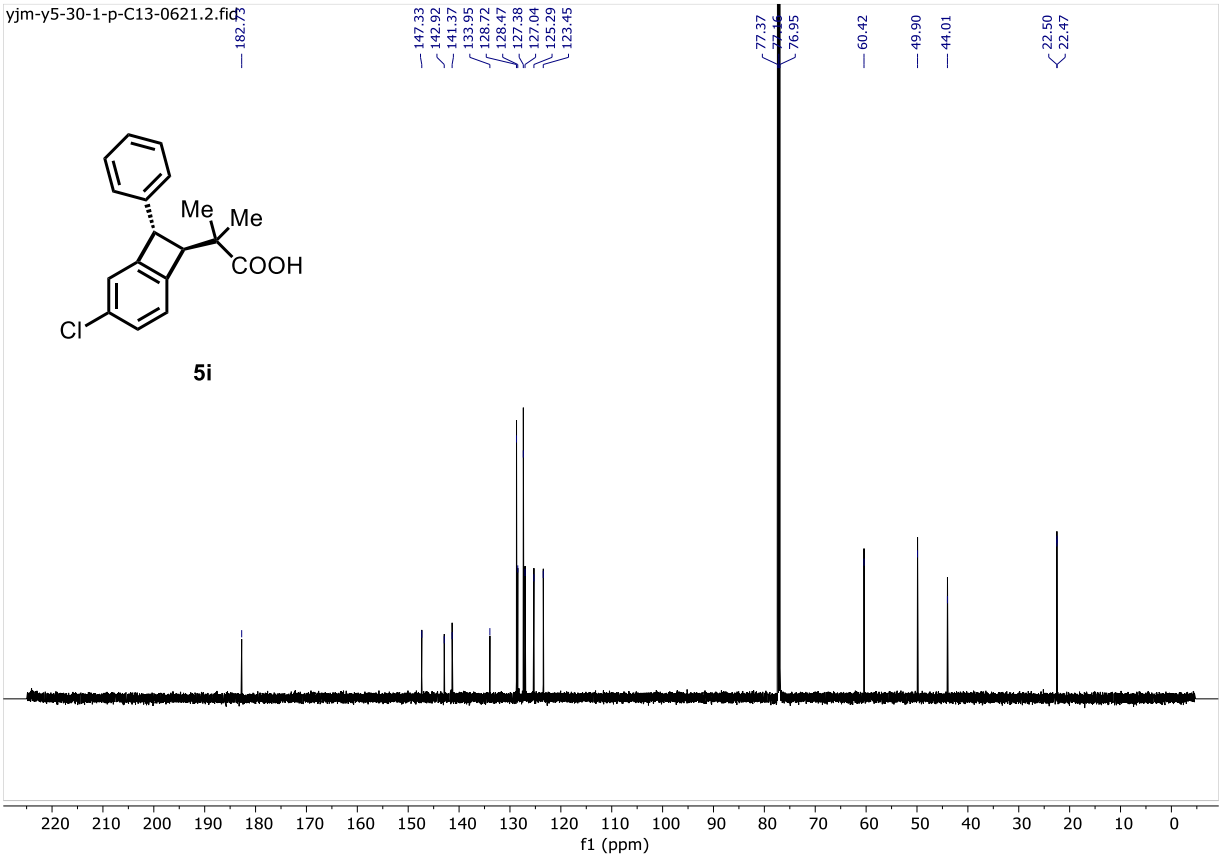
5g

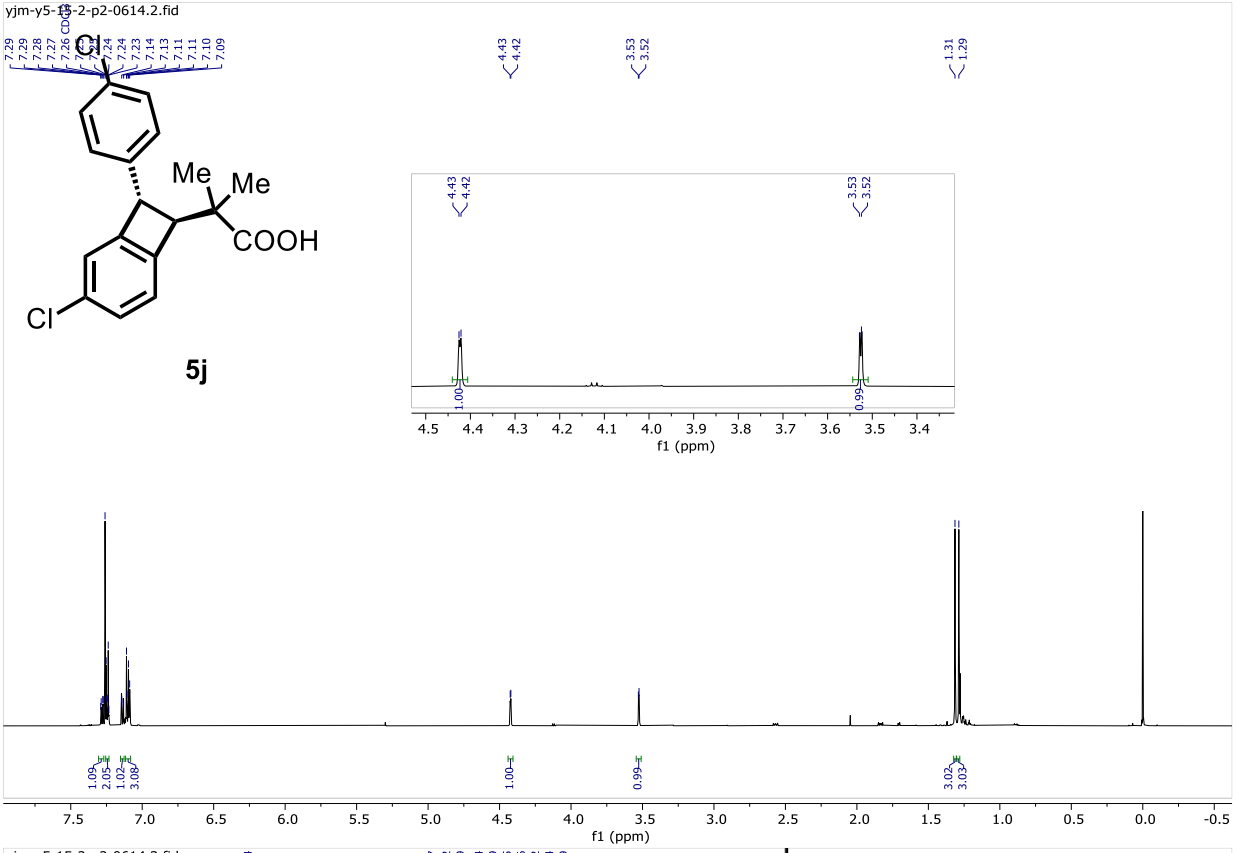


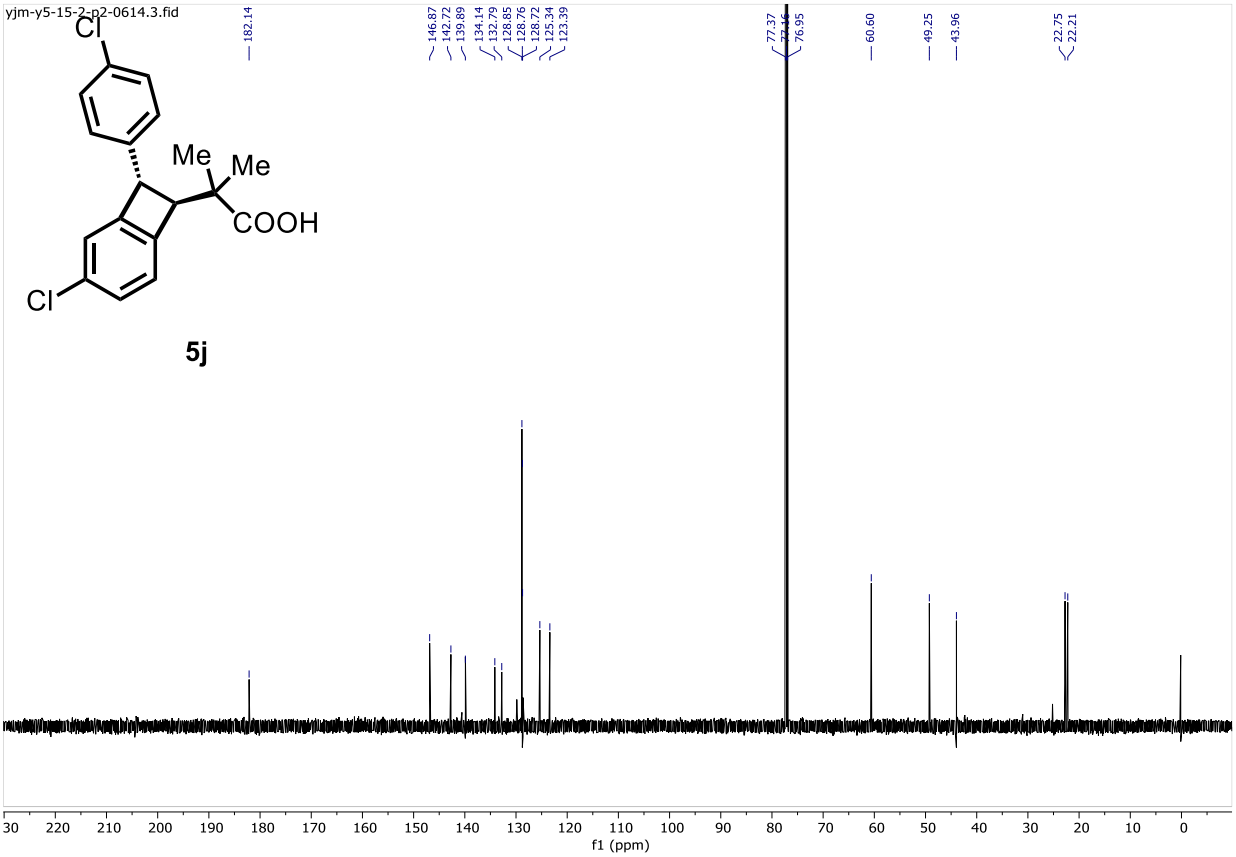

yjm-y5-17-4-p-0615.1.fid
Me
Me
Me
COOH
Cl
5h
4.43
4.42
3.55
3.54
2.32
1.30
1.14
6.05
0.99
0.99
3.03
5.97
f1 (ppm)


yjm-y5-17-4-p-0615.2.fid
Me
Me
Me
COOH
Cl
5h
147.59
142.95
138.38
136.65
133.88
129.40
128.37
127.25
123.40
77.37
77.16
76.95
60.50
49.59
43.95
22.51
22.48
21.21
f1 (ppm)


yjm-Y5-30-1p-H-0621-1.fid
Me
Me
COOH
Cl
5i
f1 (ppm)


yjm-y5-30-1-p-C13-0621.2.fid
Me
Me
COOH
Cl
5i
f1 (ppm)


yjm-y5-15-2-p2-0614.2.fid
Cl
Me
Me
COOH
Cl
5j
f1 (ppm)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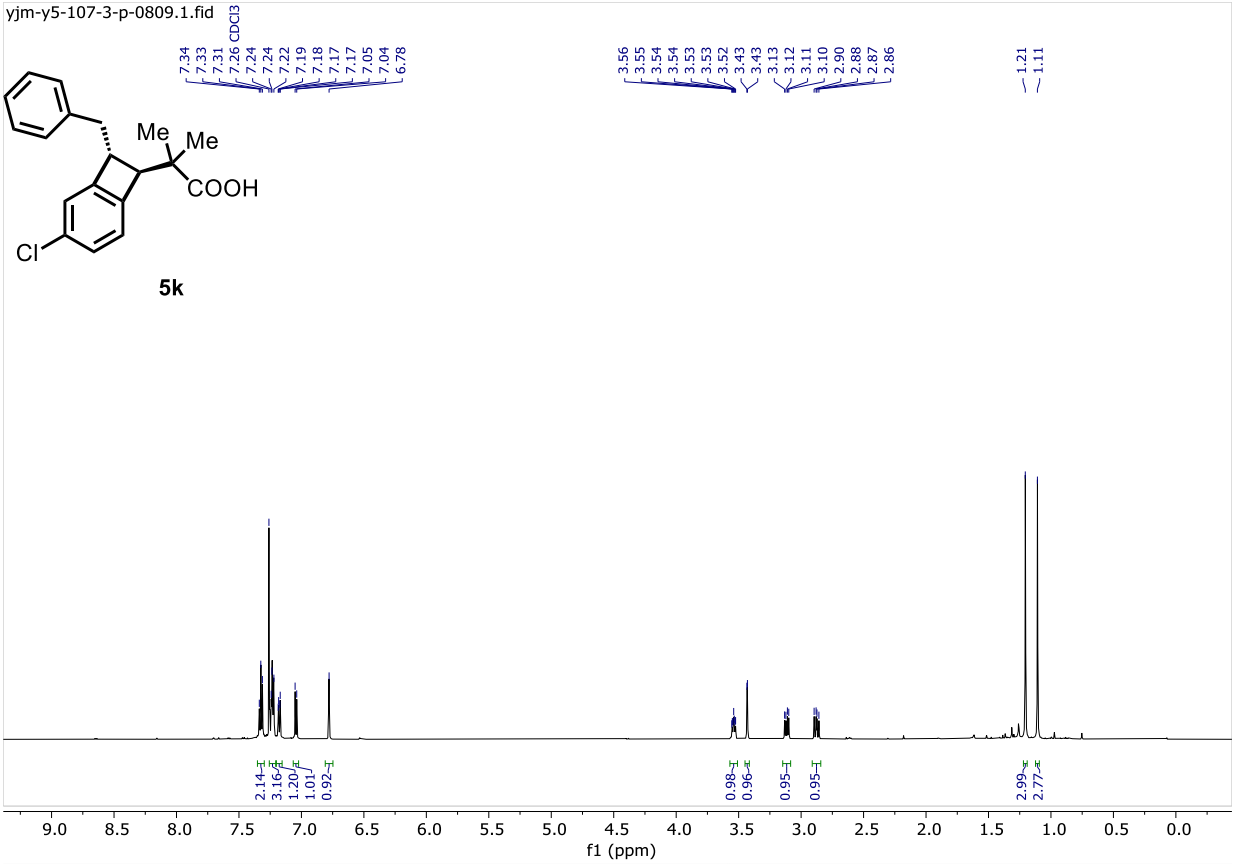
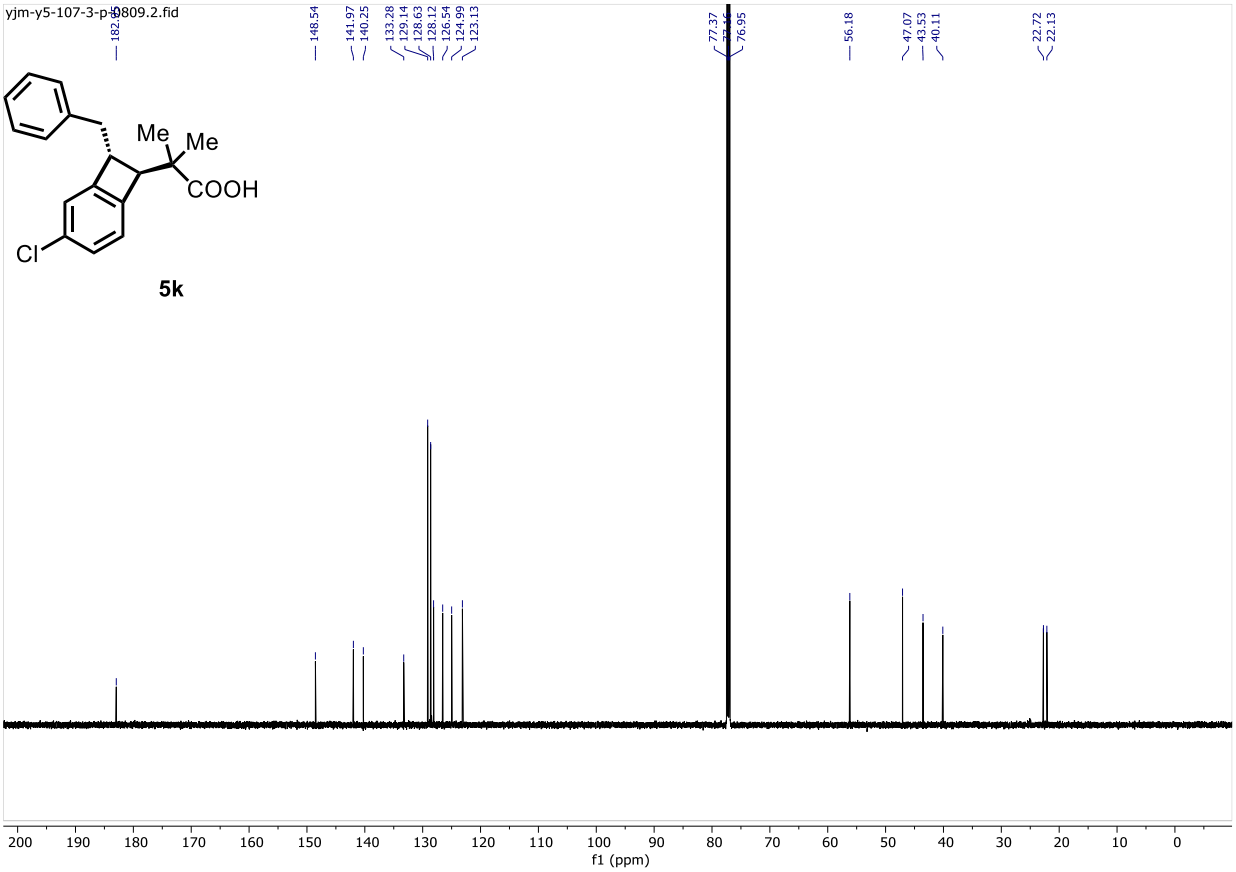
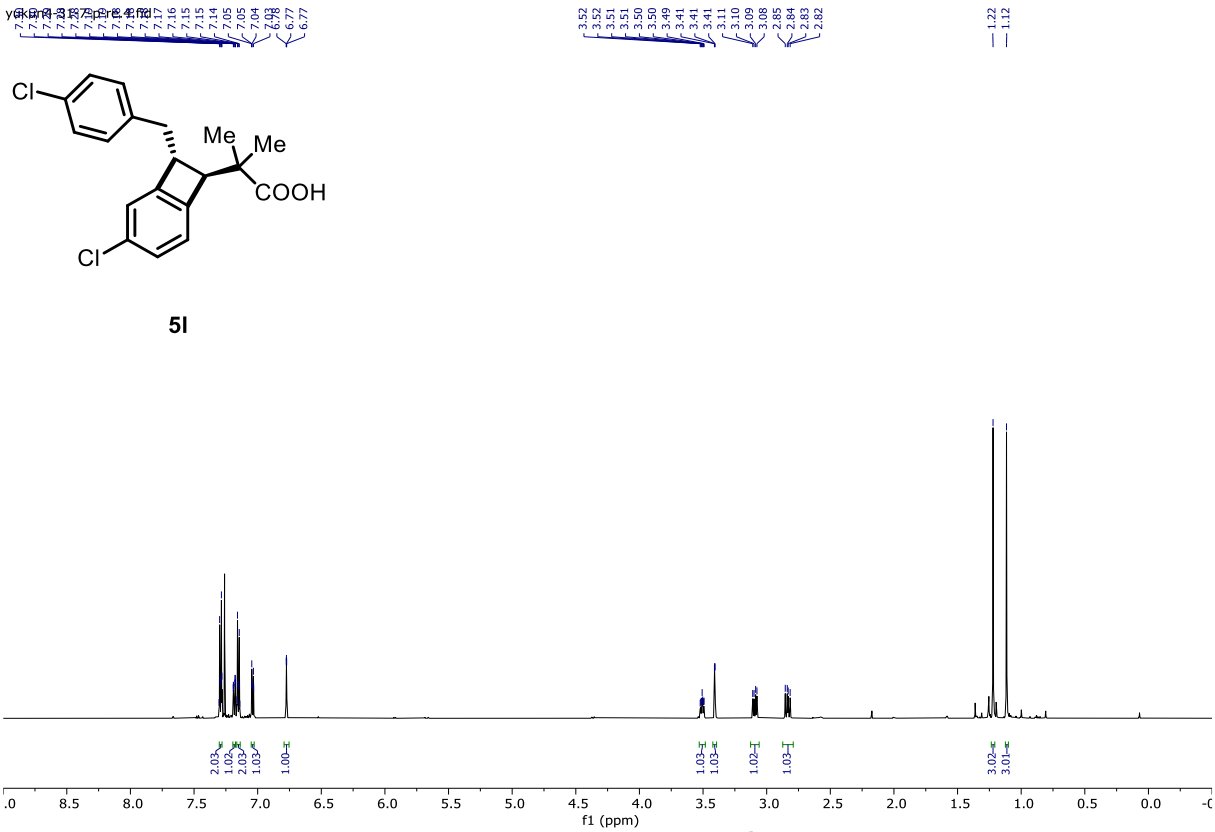
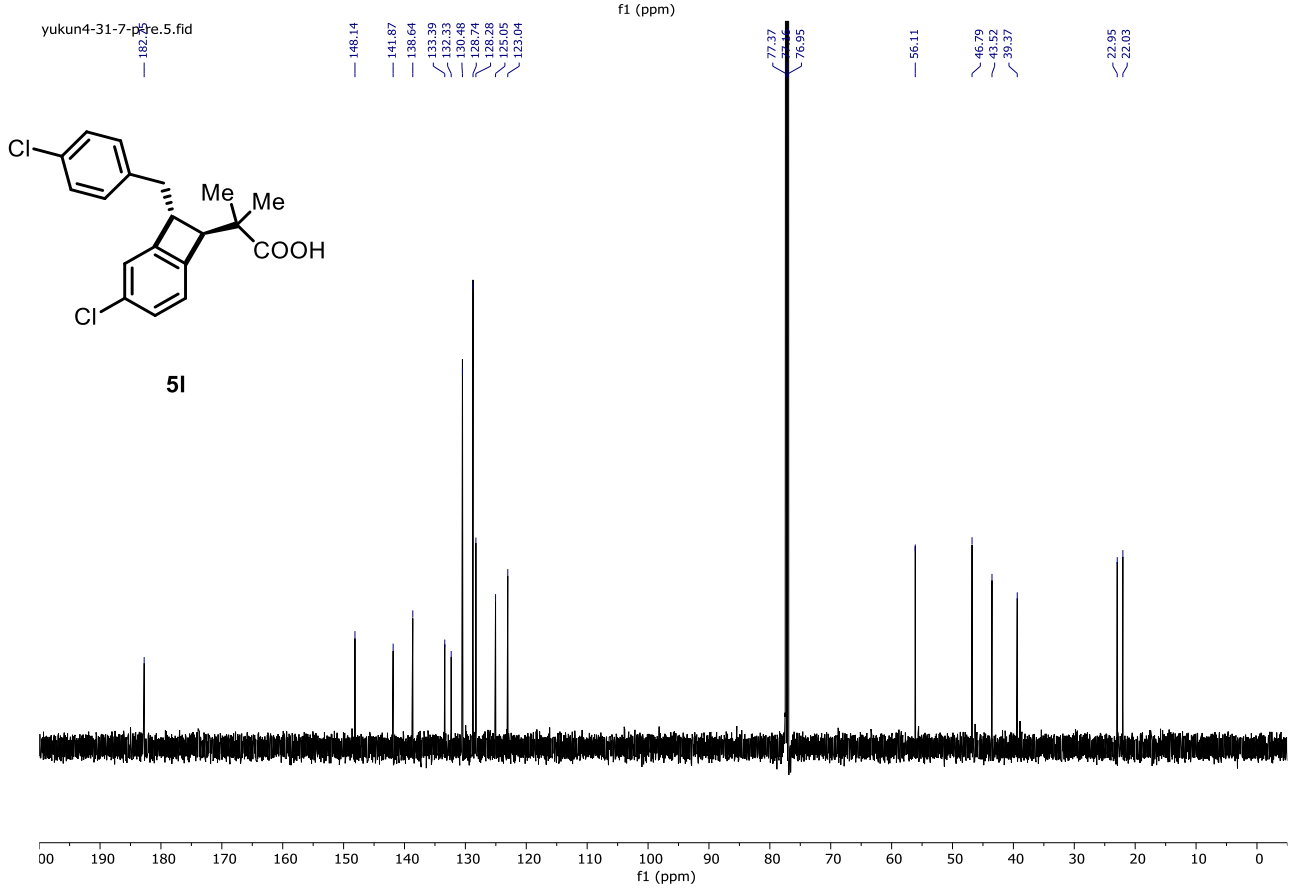
Cl
Me
Me
COOH
Cl
5j
f1 (ppm)


yjm-y5-107-3-p-0809.1.fid
Me
Me
COOH
Cl
5k
f1 (ppm)

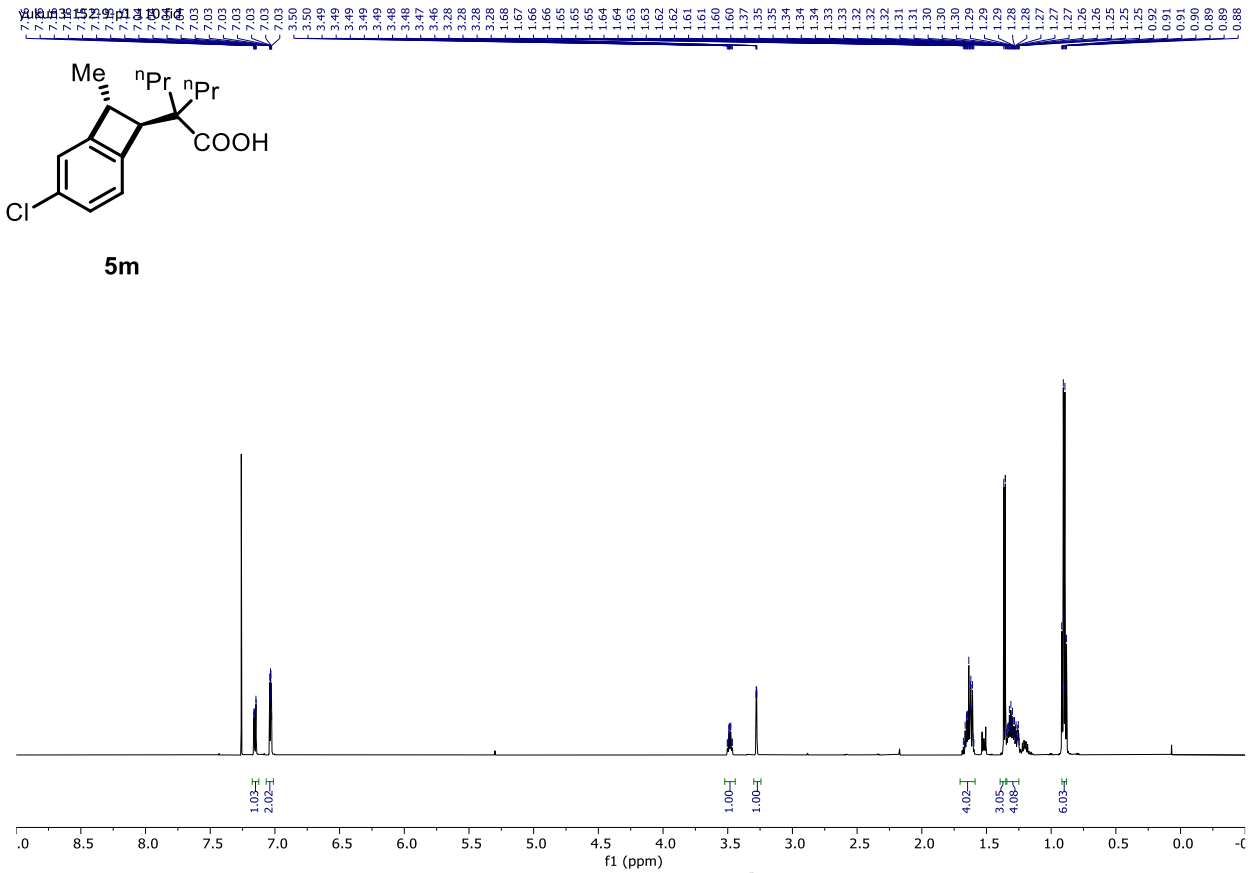

yjm-y5-107-3-p-0809.2.fid
Me
Me
COOH
Cl
5k
f1 (ppm)


Cl
Me
Me
COOH
Cl
f1 (ppm)

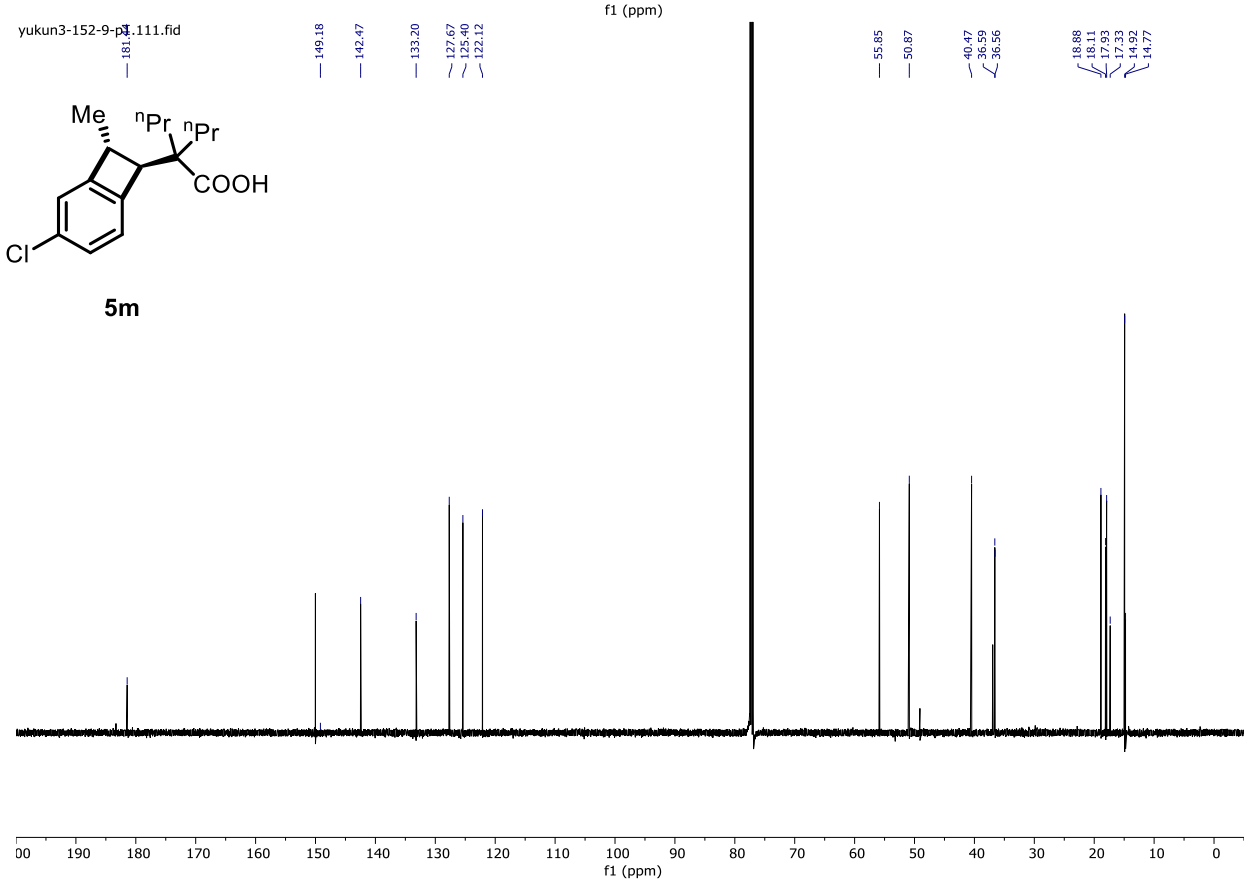
5l


yukun4-31-7-pre.5.fid
Cl
Me
Me
COOH
Cl
f1 (ppm)

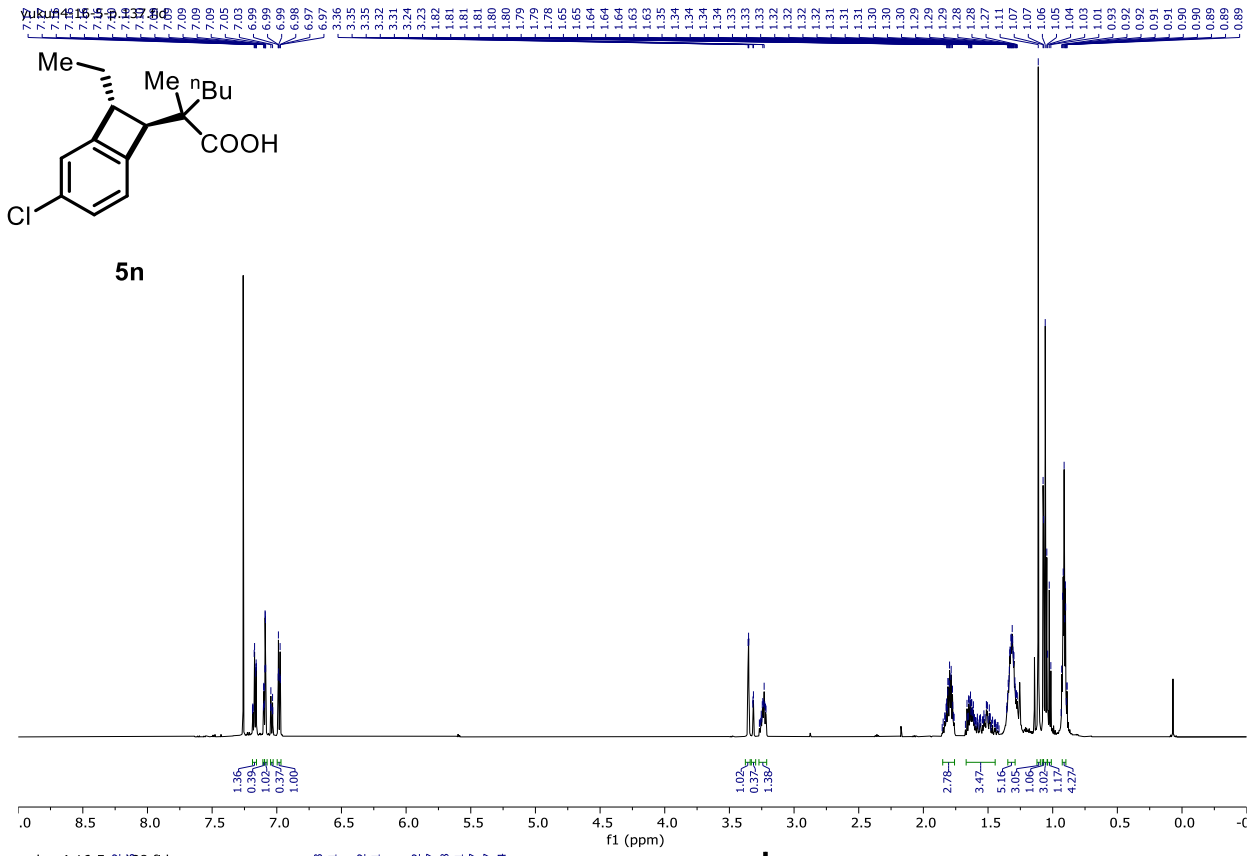
5l

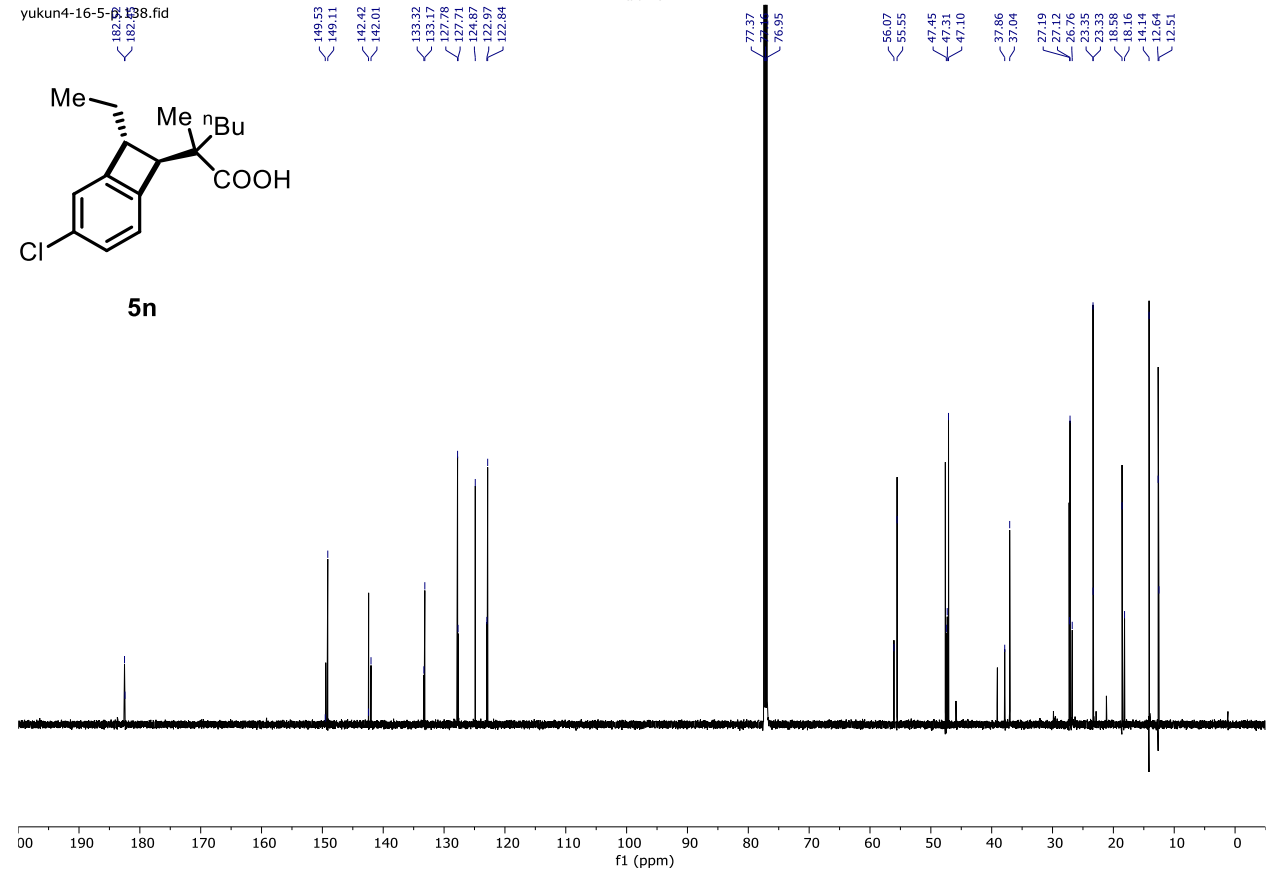

Me
nPr
nPr
COOH
Cl
1.03
2.02
1.00
1.00
4.02
3.05
4.08
6.03
f1 (ppm)

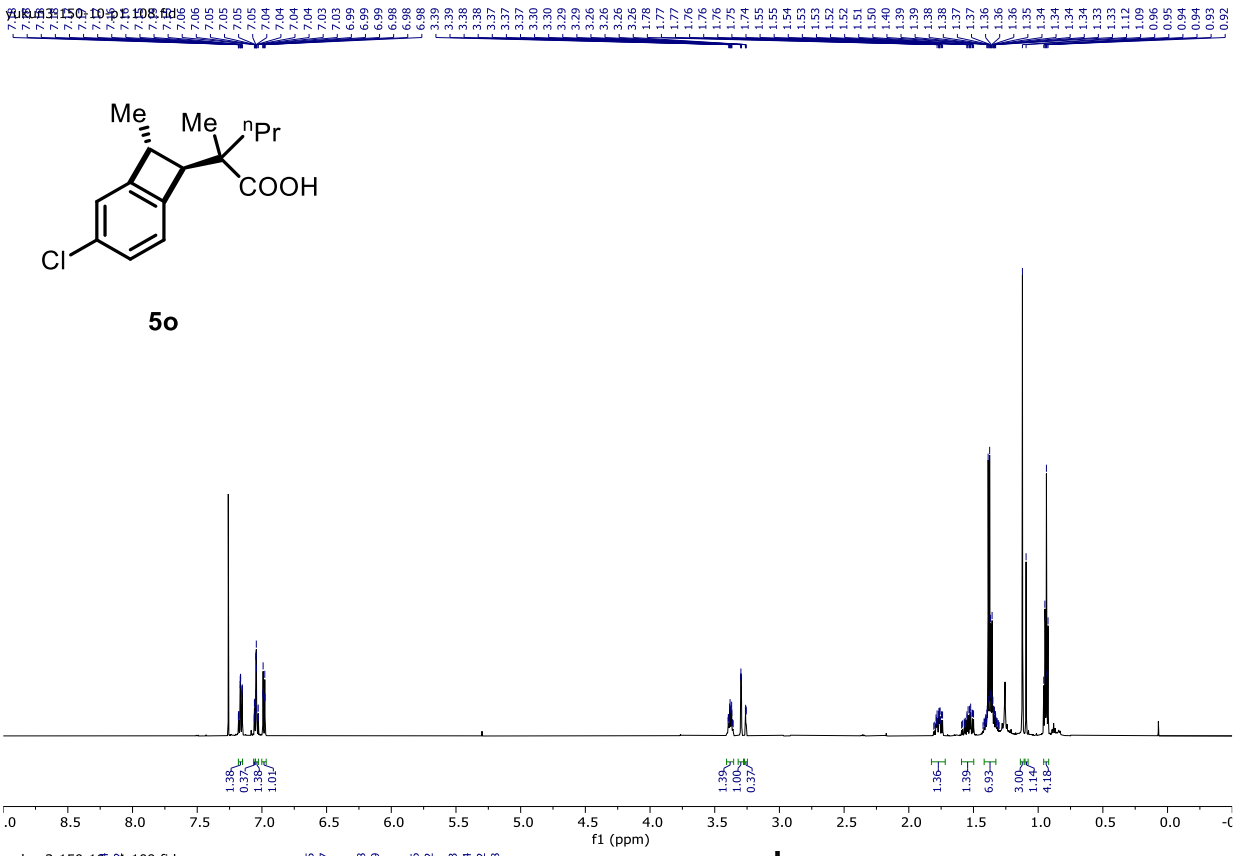
5m

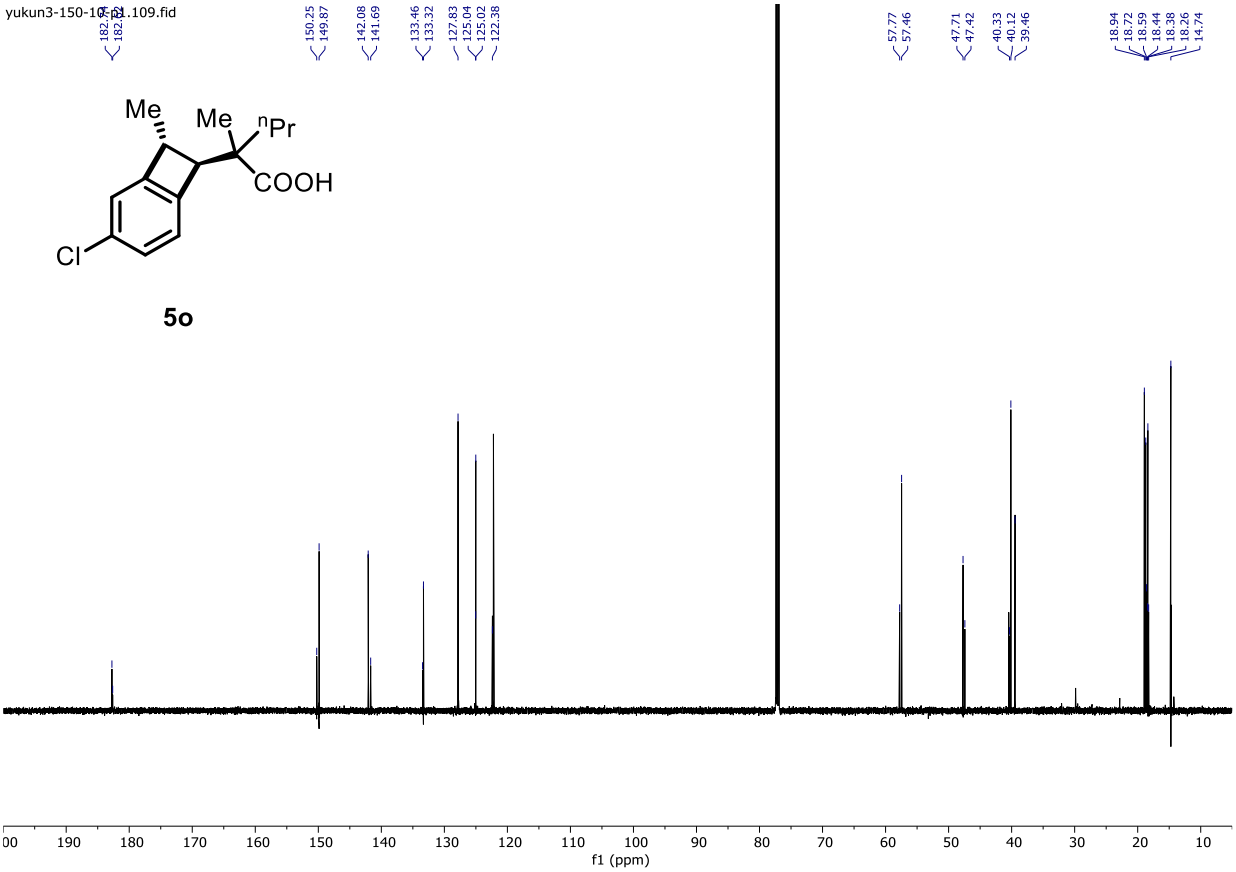

yukun3-152-9-p1.111.fid
181.14
149.18
142.47
133.20
127.67
125.40
122.12
55.85
50.87
40.47
36.59
36.56
18.88
18.11
17.93
17.33
14.92
14.77
Me
nPr
nPr
COOH
Cl
f1 (ppm)

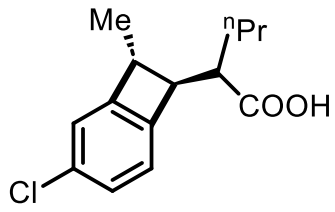
5m


Me
Me
nBu
COOH
Cl
5n
f1 (ppm)

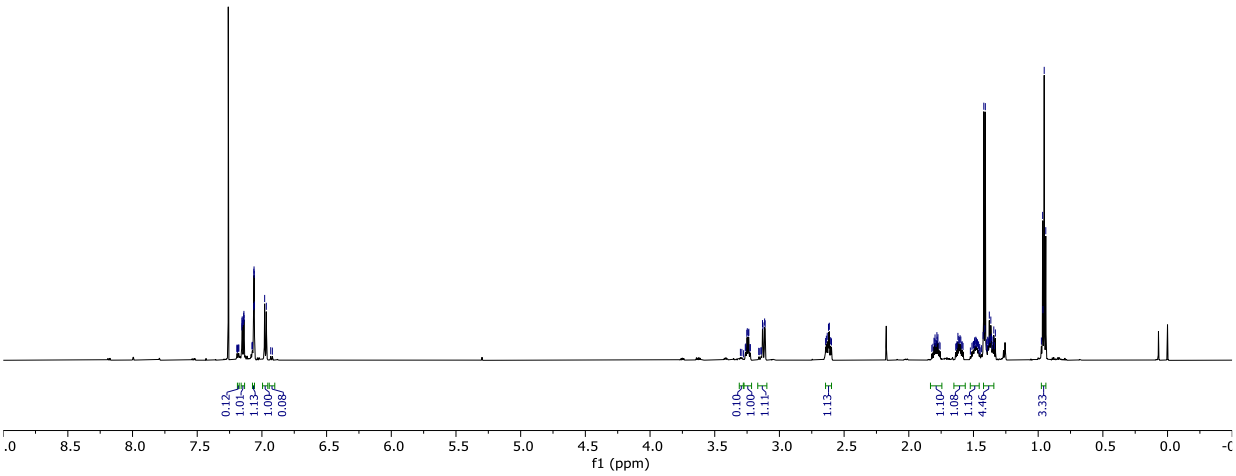

Me
Me
nBu
COOH
Cl
5n
f1 (ppm)

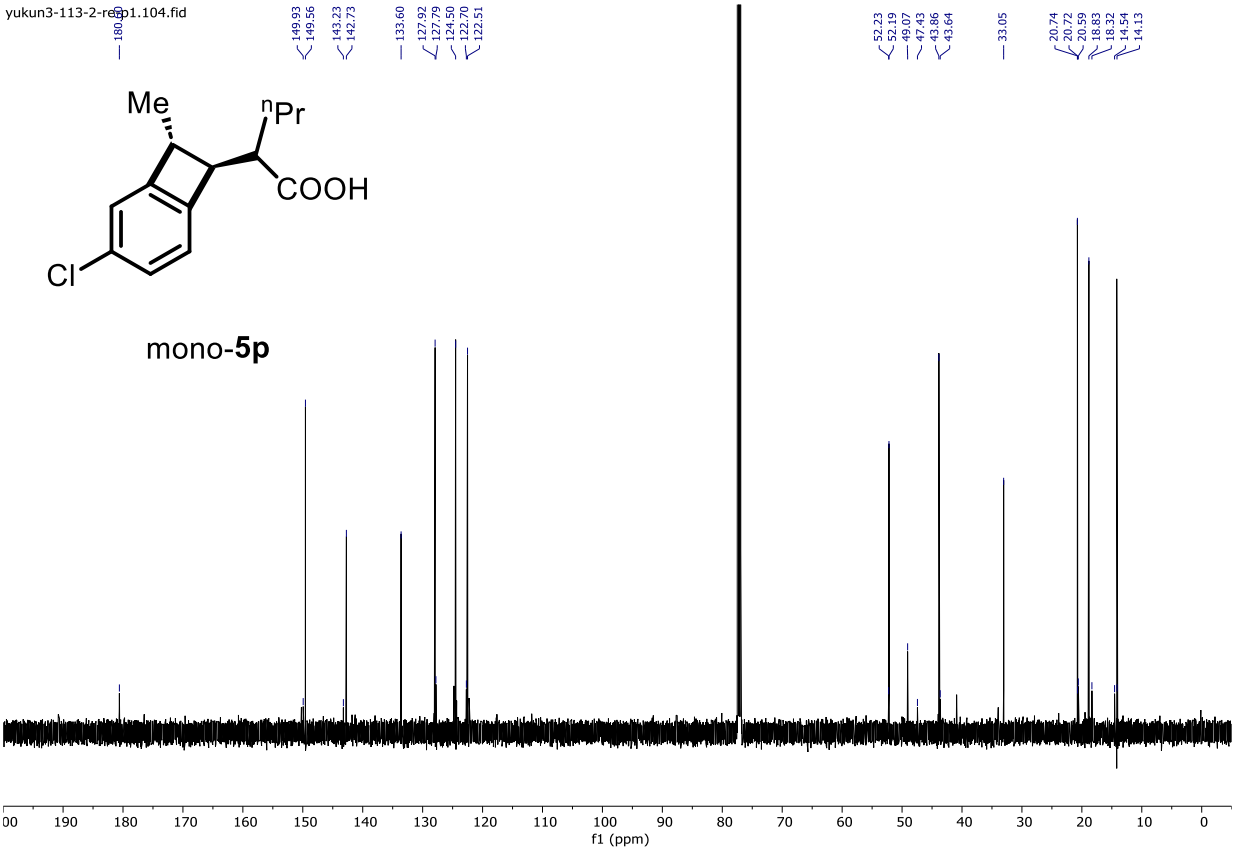

Me
Me
nPr
COOH
Cl
5o
f1 (ppm)


Me
Me
nPr
COOH
Cl
5o
f1 (ppm)

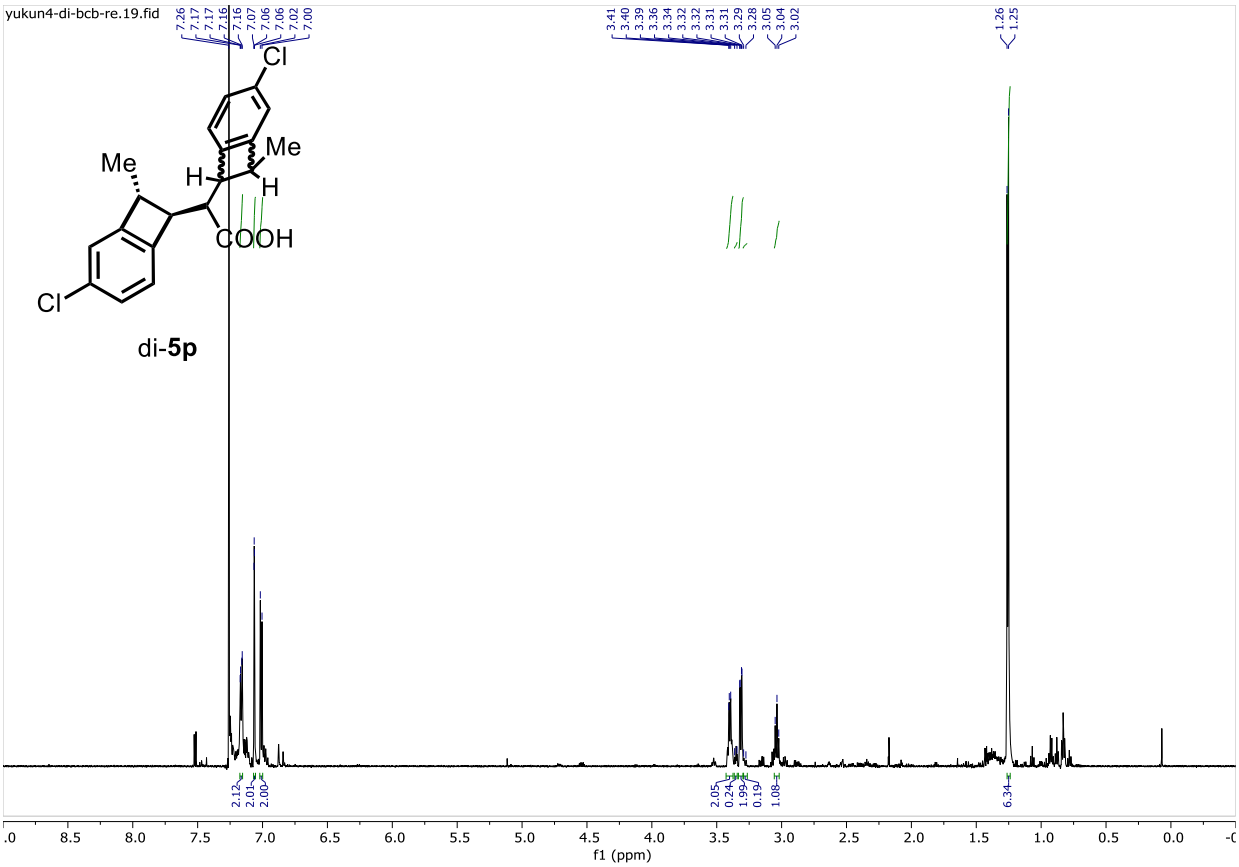


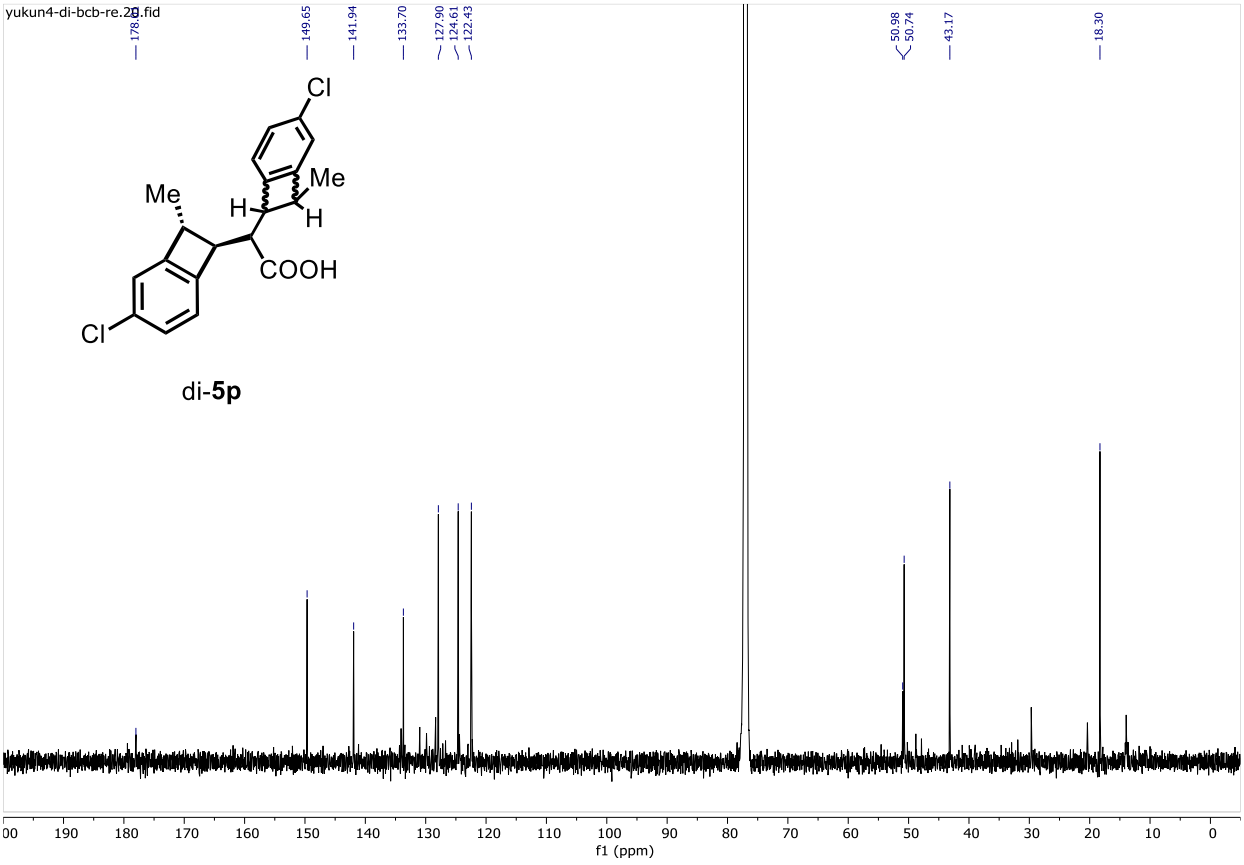
mono-**5p**

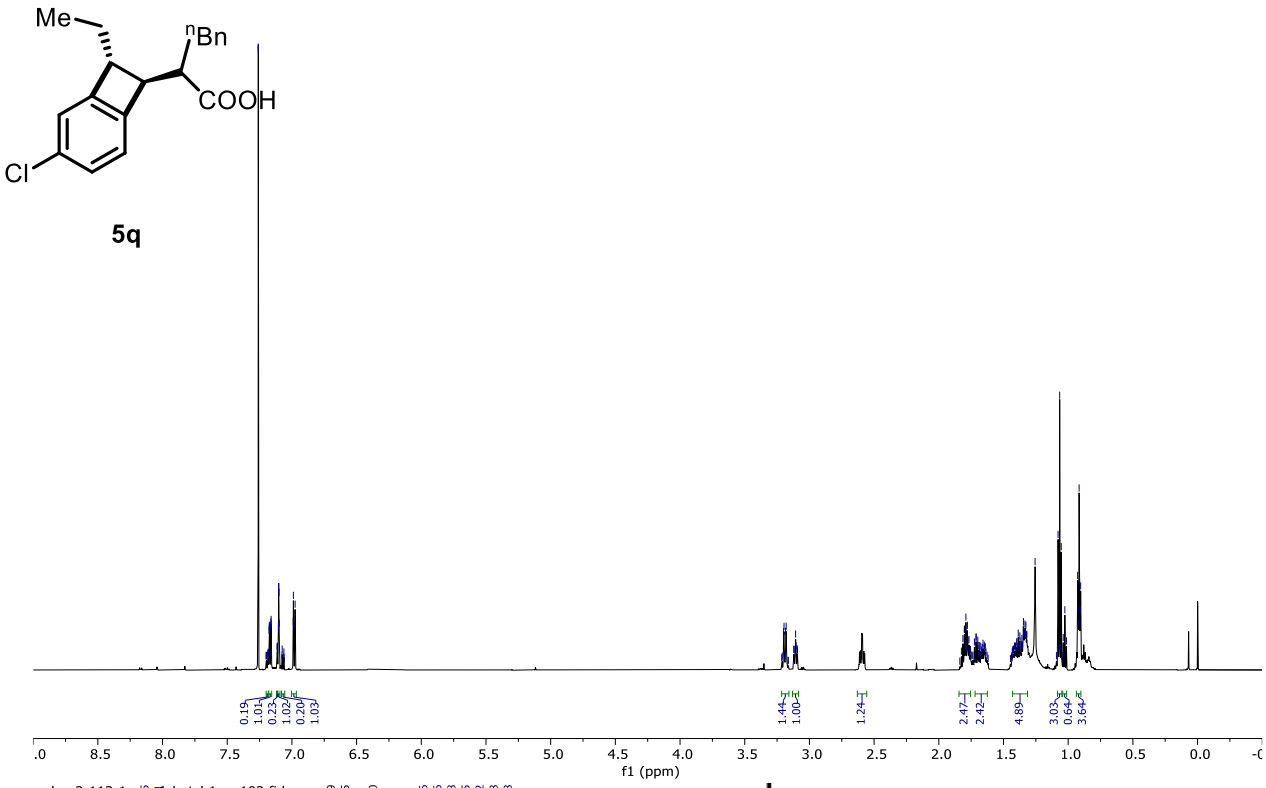




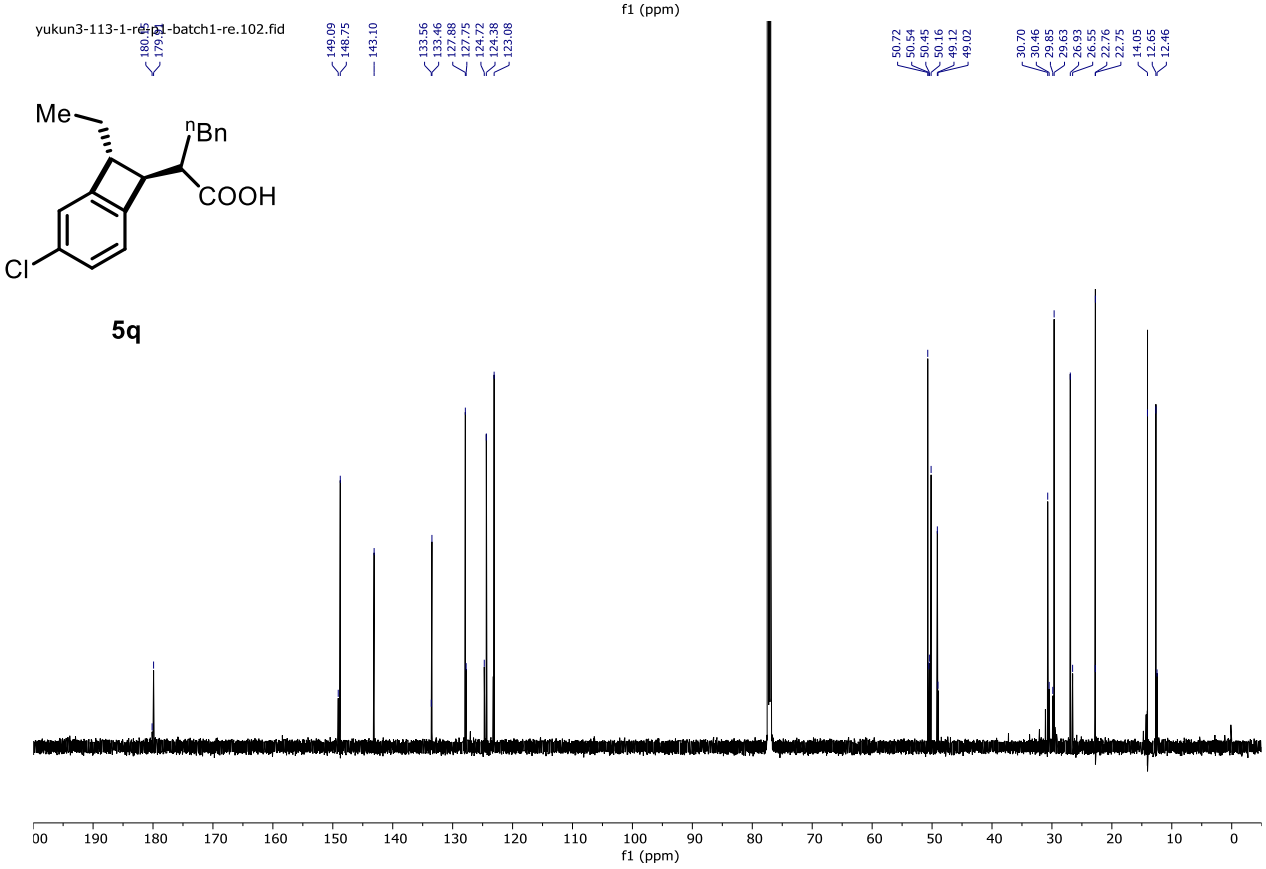
mono-**5p**


yukun4-di-bcb-re.19.fid
Cl
Me
Me
H
H
COOH
Cl
di-5p
f1 (ppm)

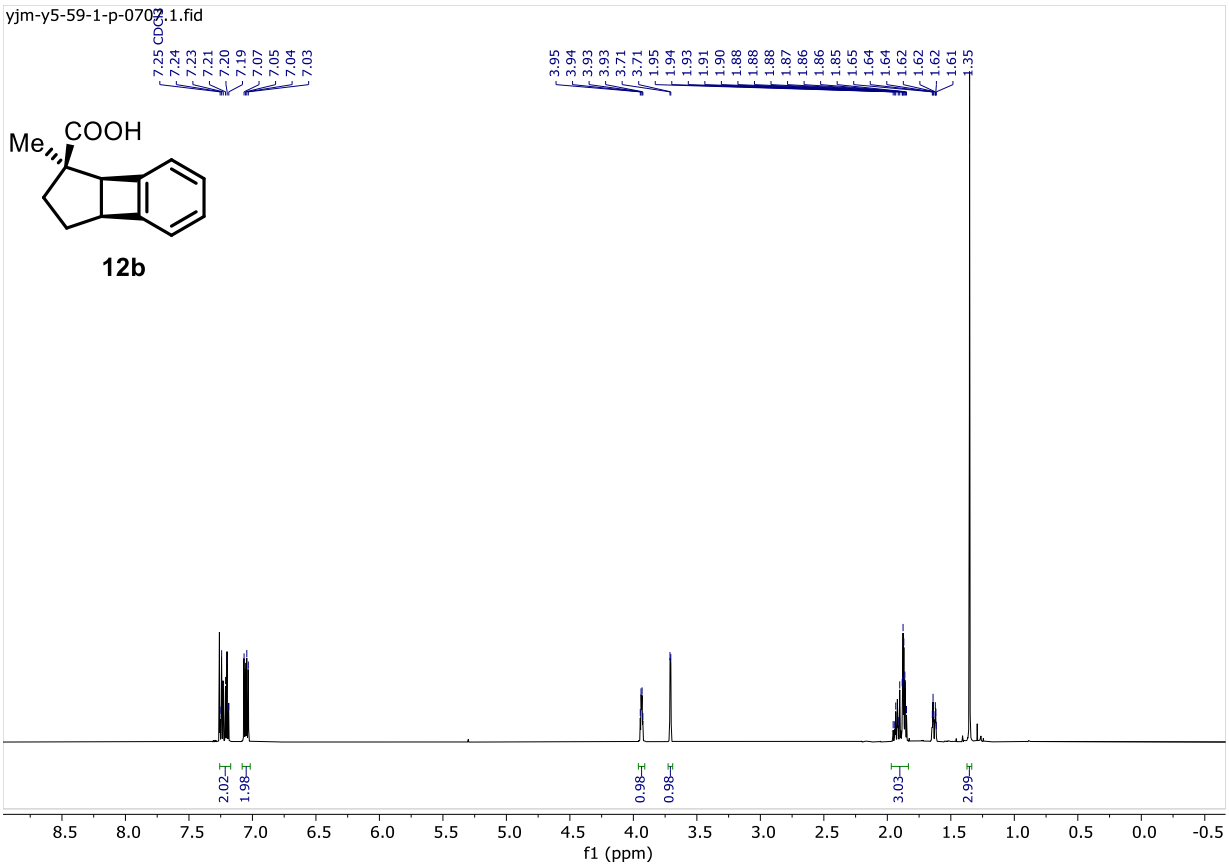

yukun4-di-bcb-re.20.fid
Cl
Me
Me
H
H
COOH
Cl
di-5p
f1 (ppm)

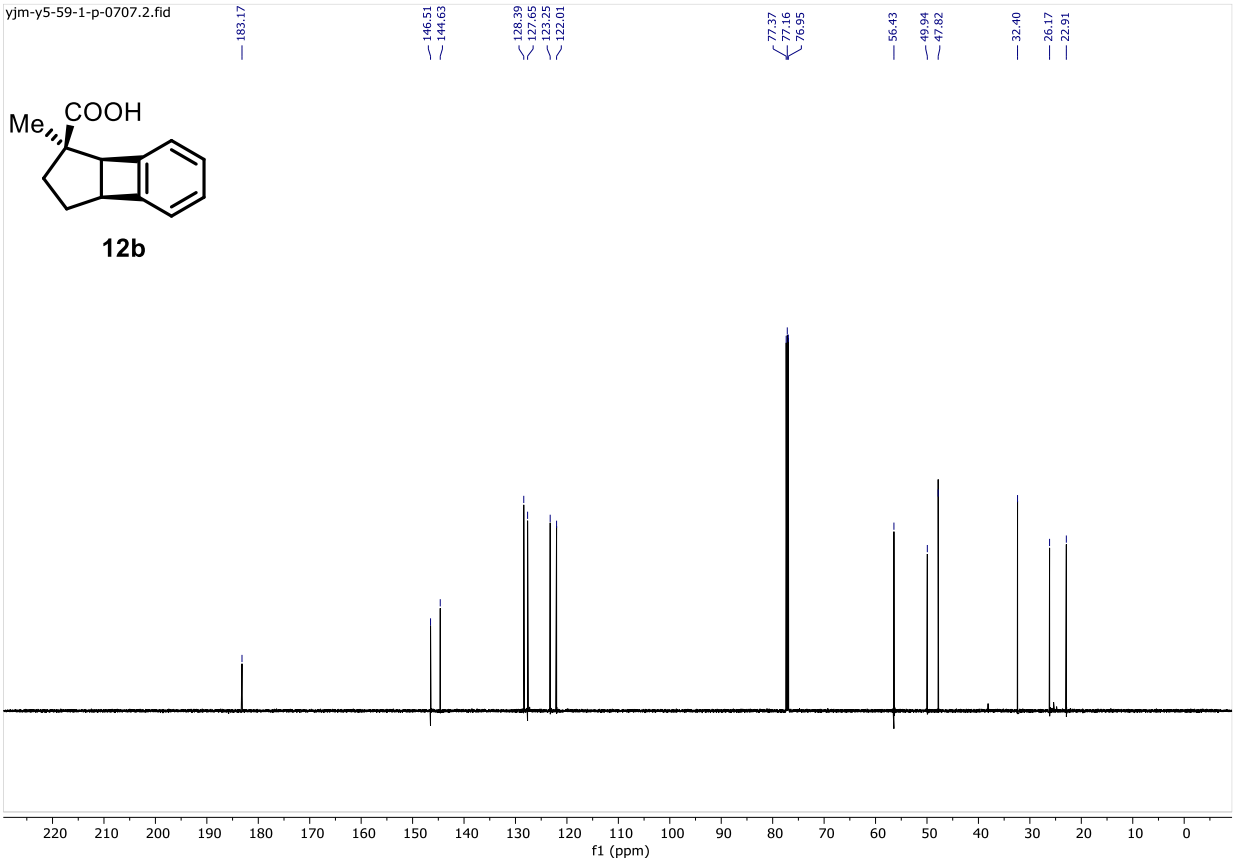


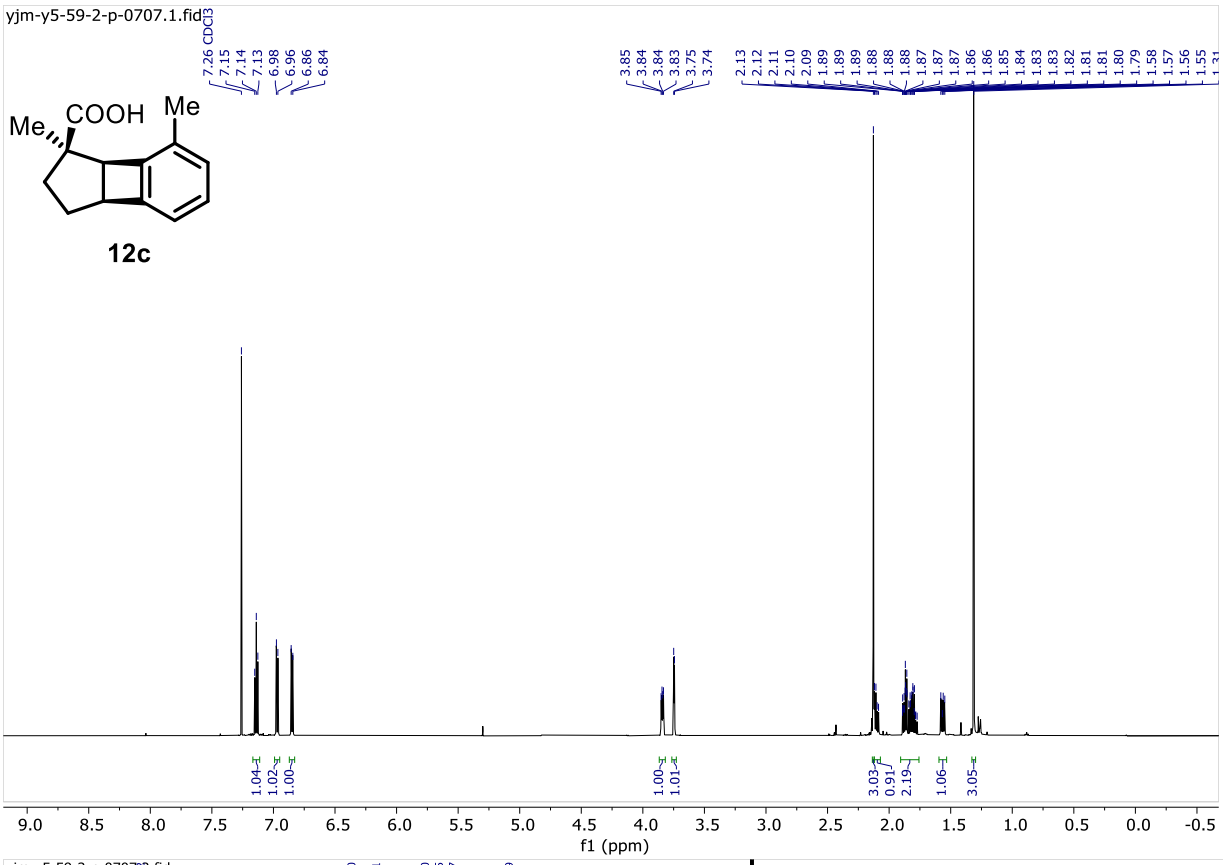
5q

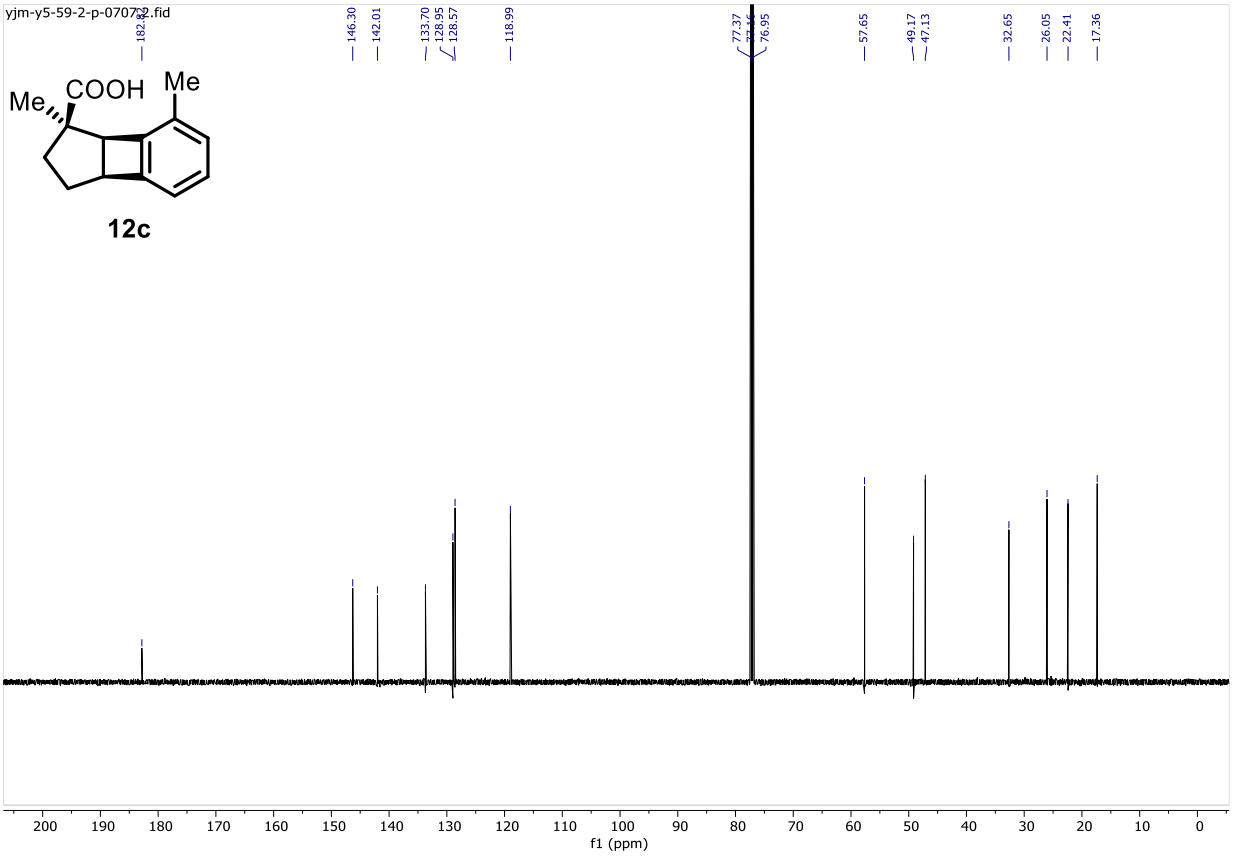


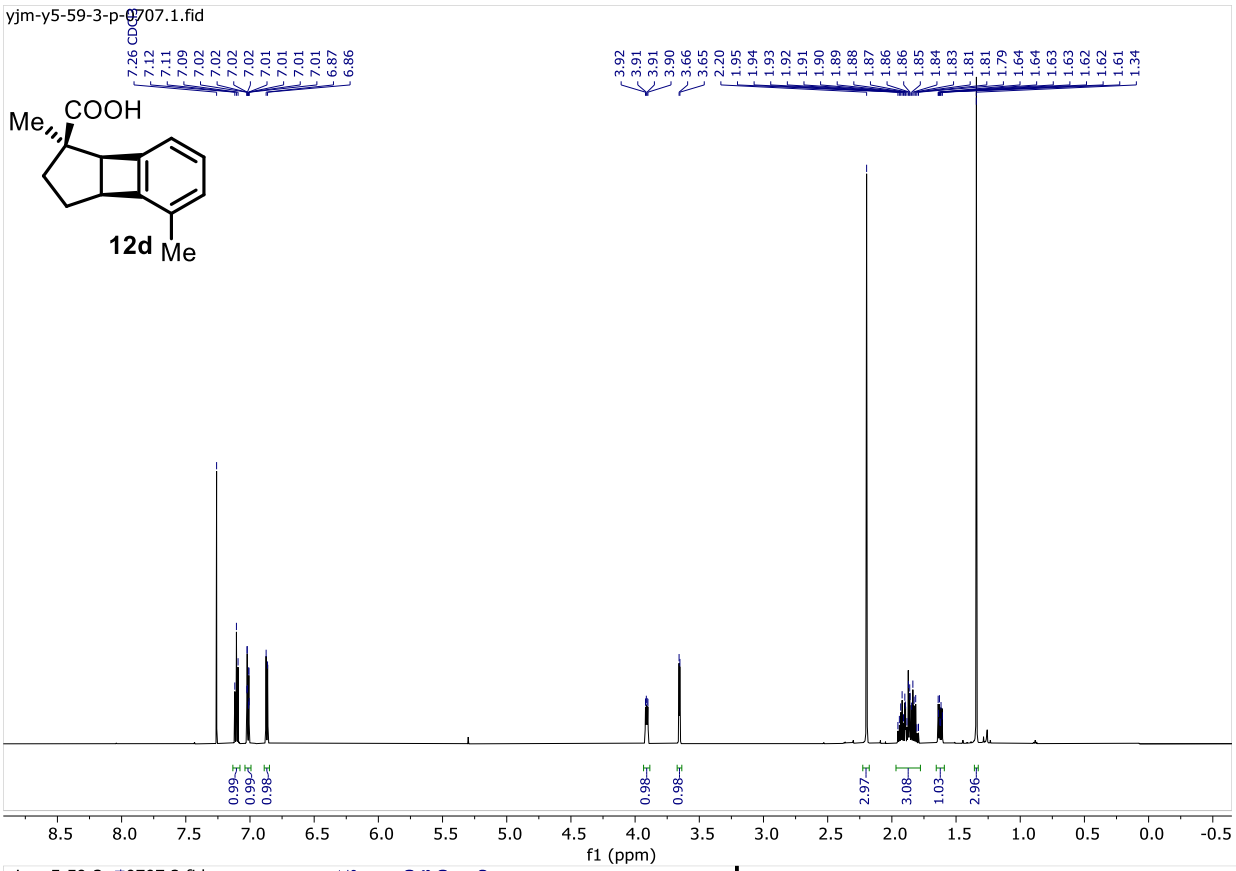
5q

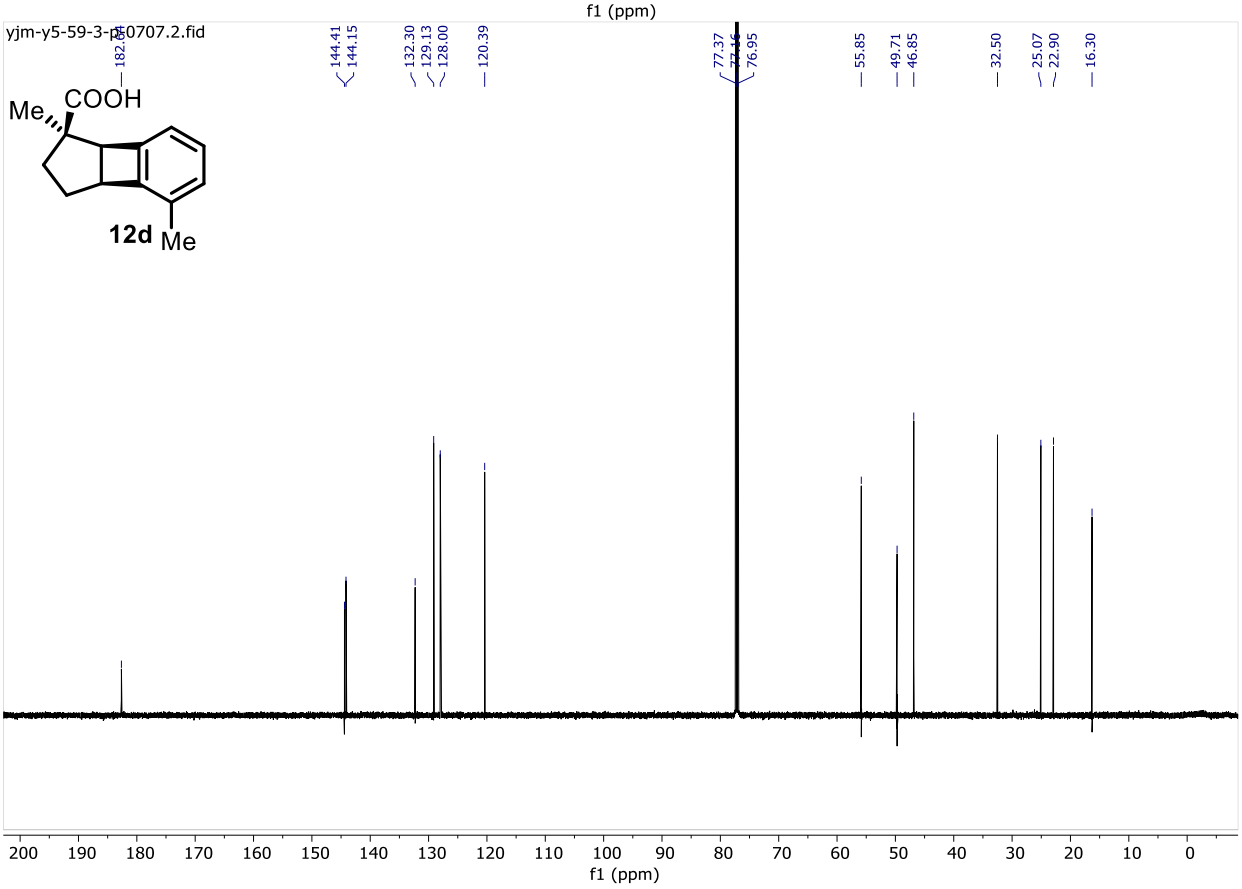

yjm-y5-59-1-p-0707.1.fid
7.25 CDCl3
7.24
7.23
7.21
7.20
7.19
7.07
7.05
7.04
7.03
3.95
3.94
3.93
3.93
3.71
3.71
1.95
1.94
1.93
1.91
1.90
1.88
1.88
1.88
1.87
1.86
1.86
1.85
1.65
1.64
1.64
1.62
1.62
1.62
1.61
1.35
Me
COOH
12b
2.02
1.98
0.98
0.98
3.03
2.99
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

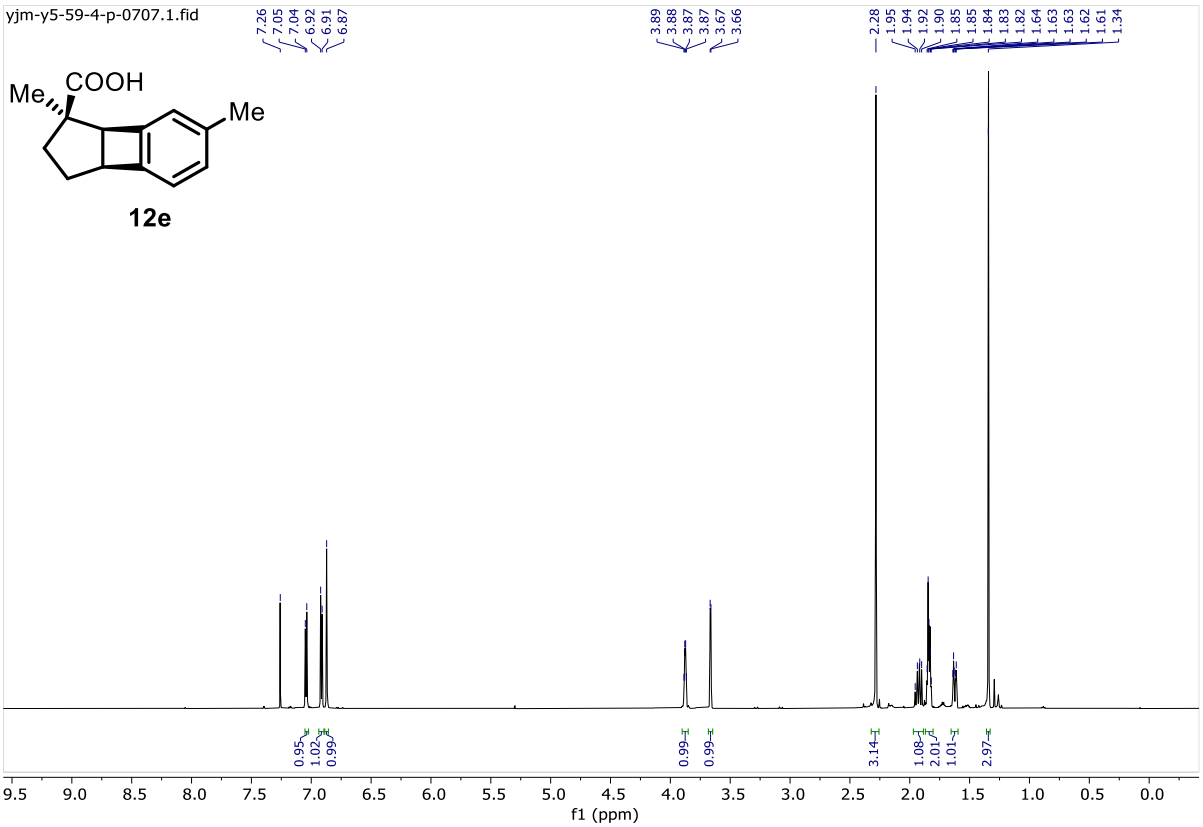

yjm-y5-59-1-p-0707.2.fid
183.17
146.51
144.63
128.39
127.65
123.25
122.01
77.37
77.16
76.95
56.43
49.94
47.82
32.40
26.17
22.91
Me
COOH
12b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

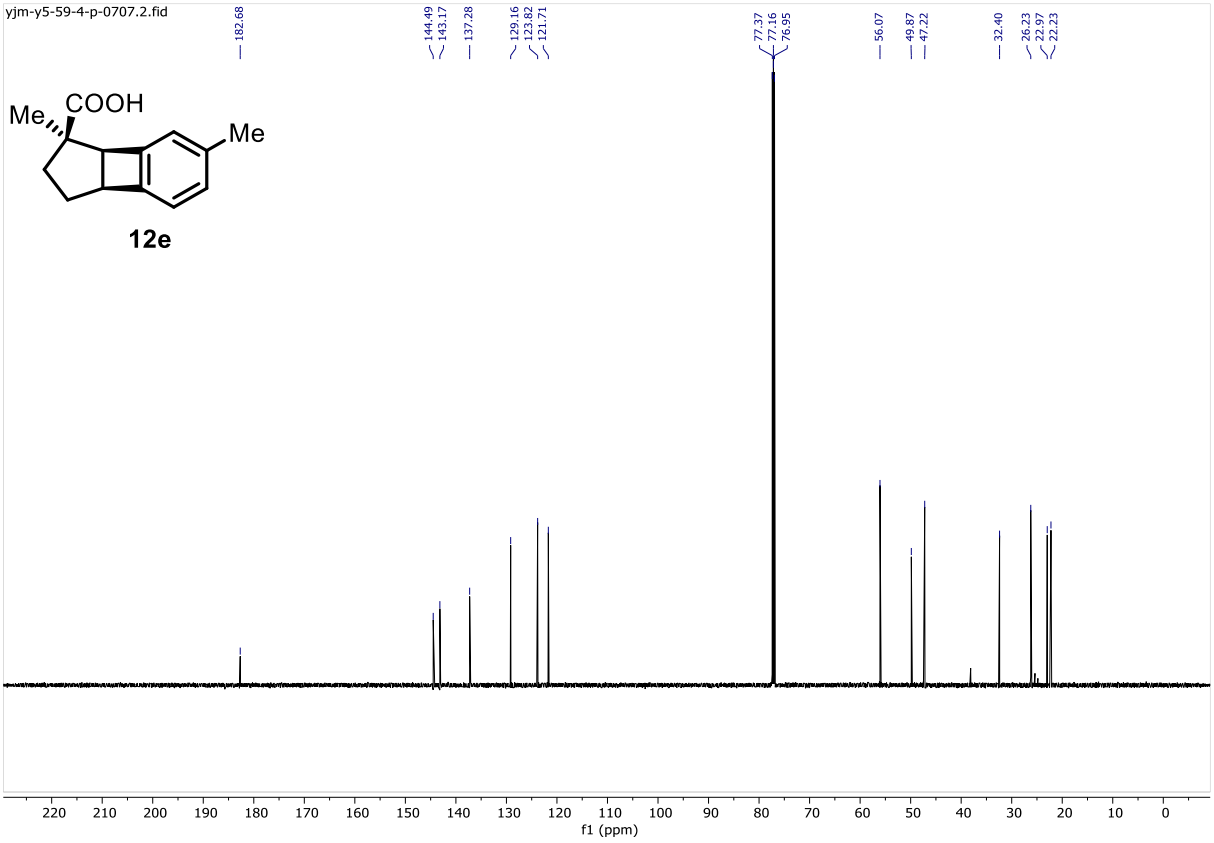

yjm-y5-59-2-p-0707.1.fid
Me
COOH
Me
12c
f1 (ppm)

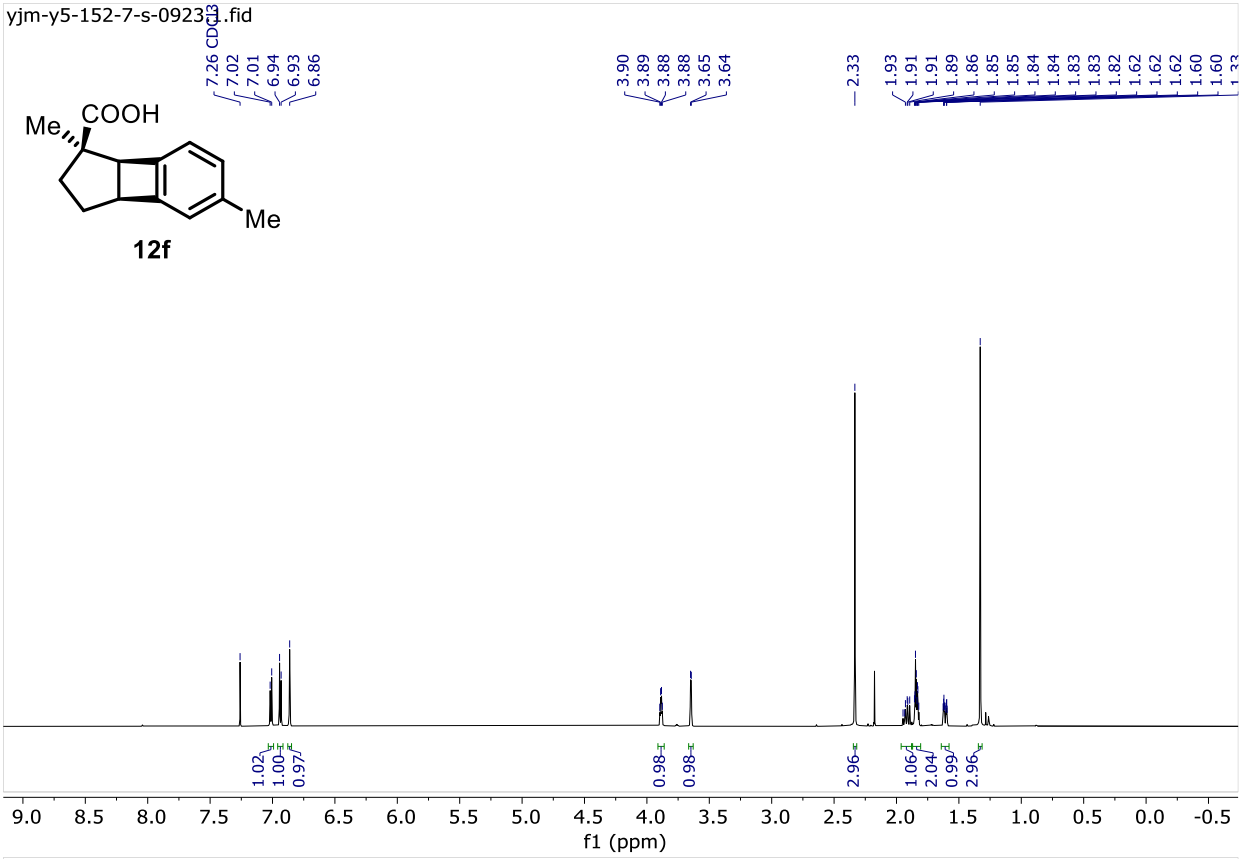

yjm-y5-59-2-p-0707
Me
COOH
Me
12c
f1 (ppm)

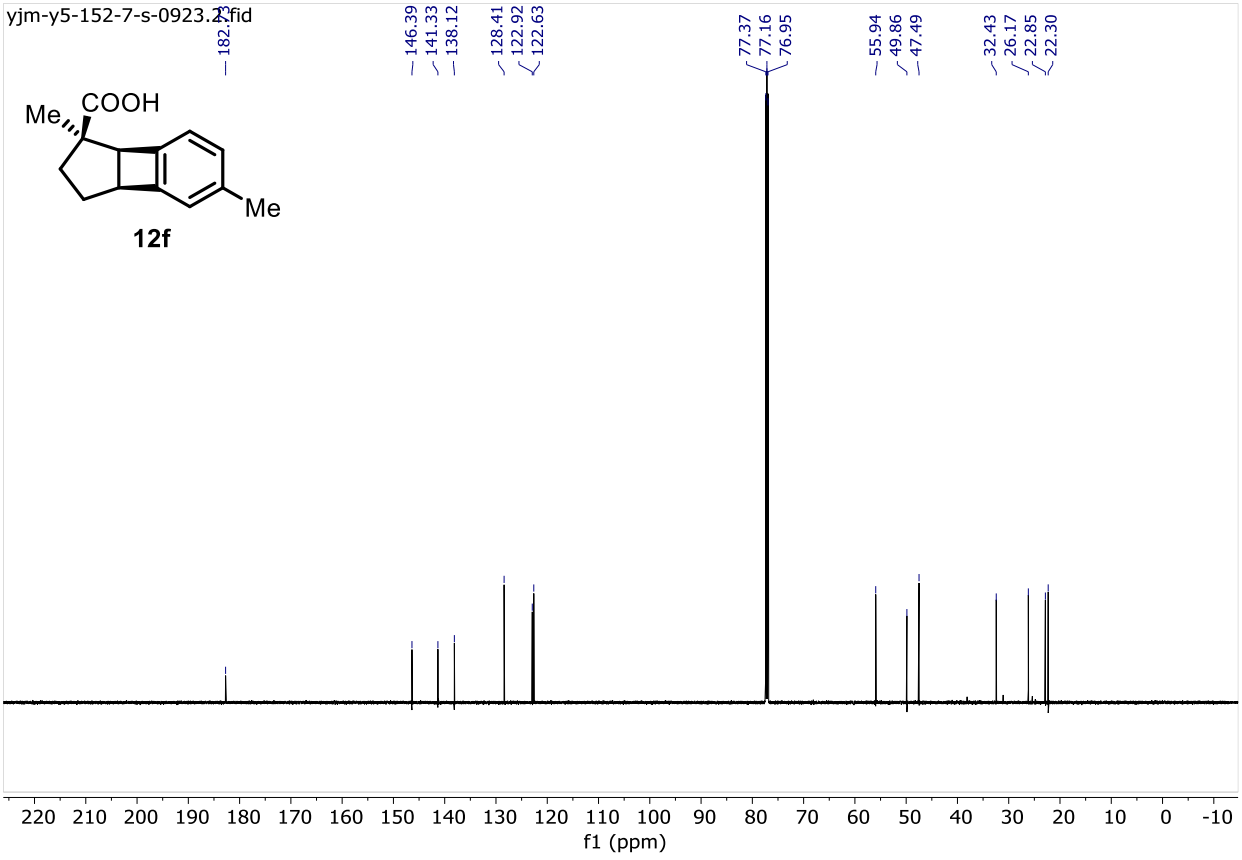

yjm-y5-59-3-p-0707.1.fid
Me
COOH
12d
Me
f1 (ppm)

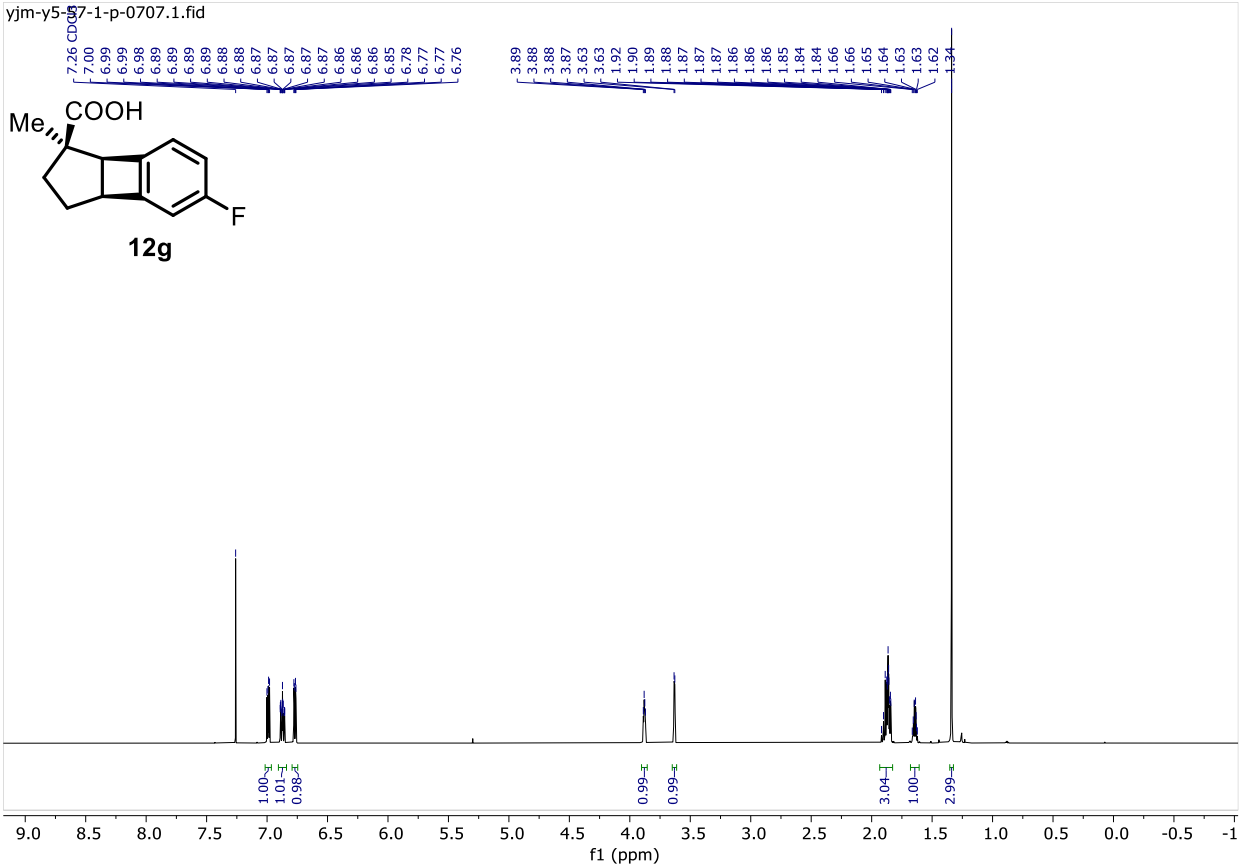

yjm-y5-59-3-p-0707.2.fid
Me
COOH
12d
Me
f1 (ppm)

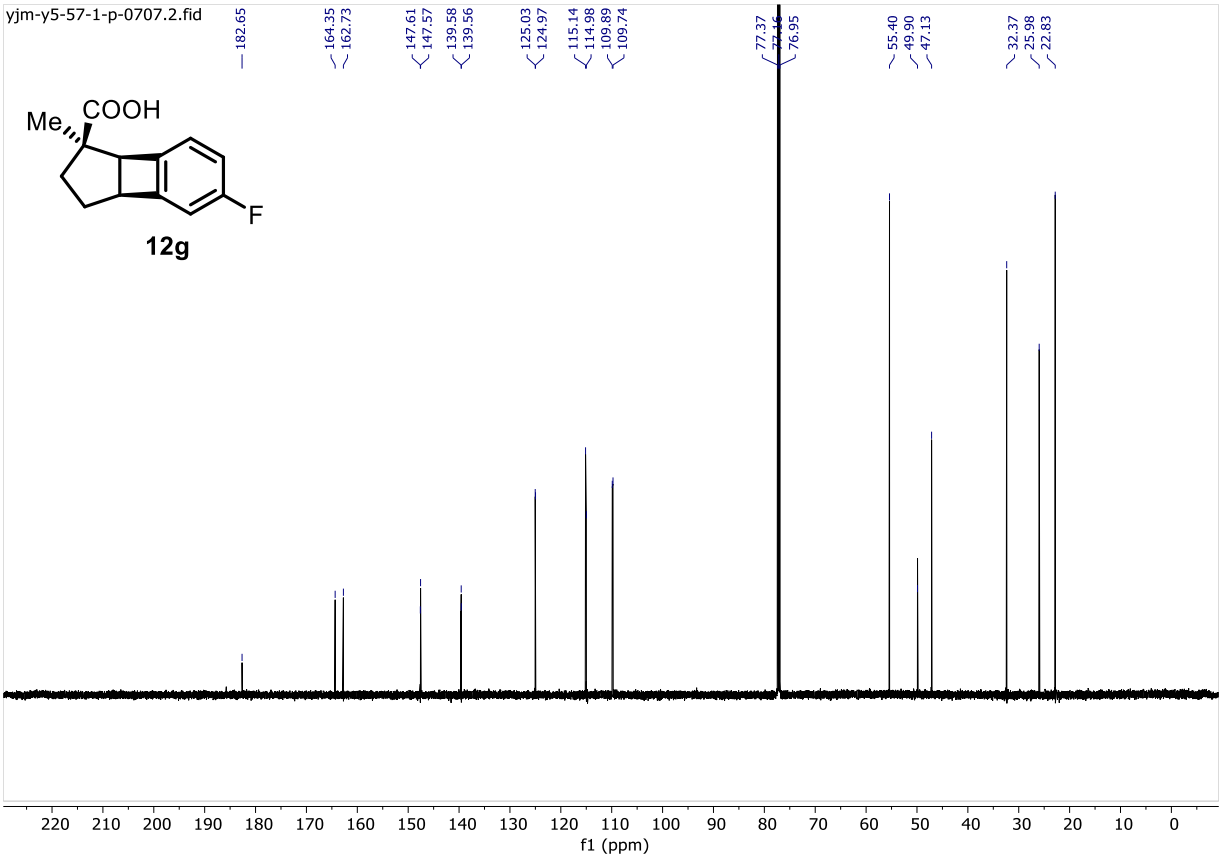

yjm-y5-59-4-p-0707.1.fid
Me
COOH
Me
12e
f1 (ppm)

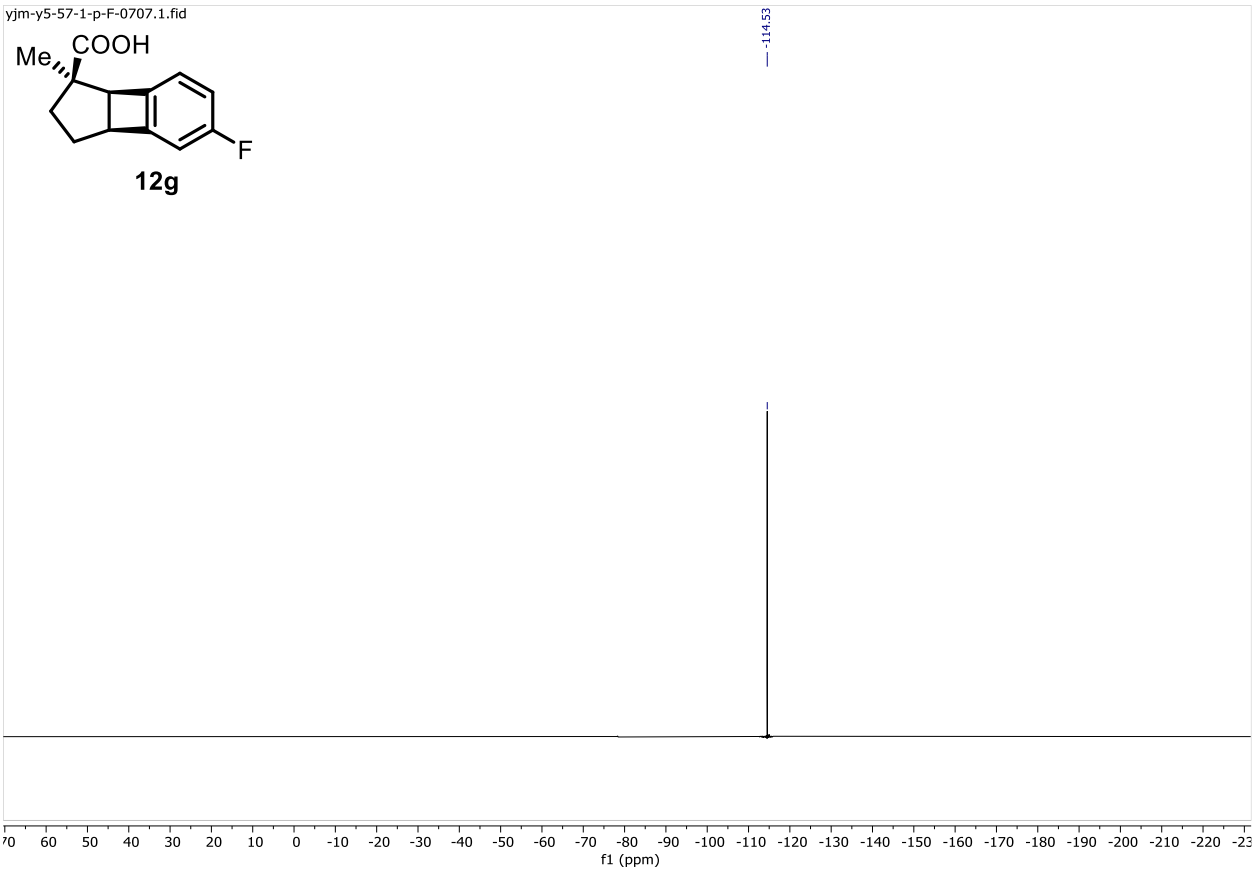

yjm-y5-59-4-p-0707.2.fid
Me
COOH
Me
12e
f1 (ppm)

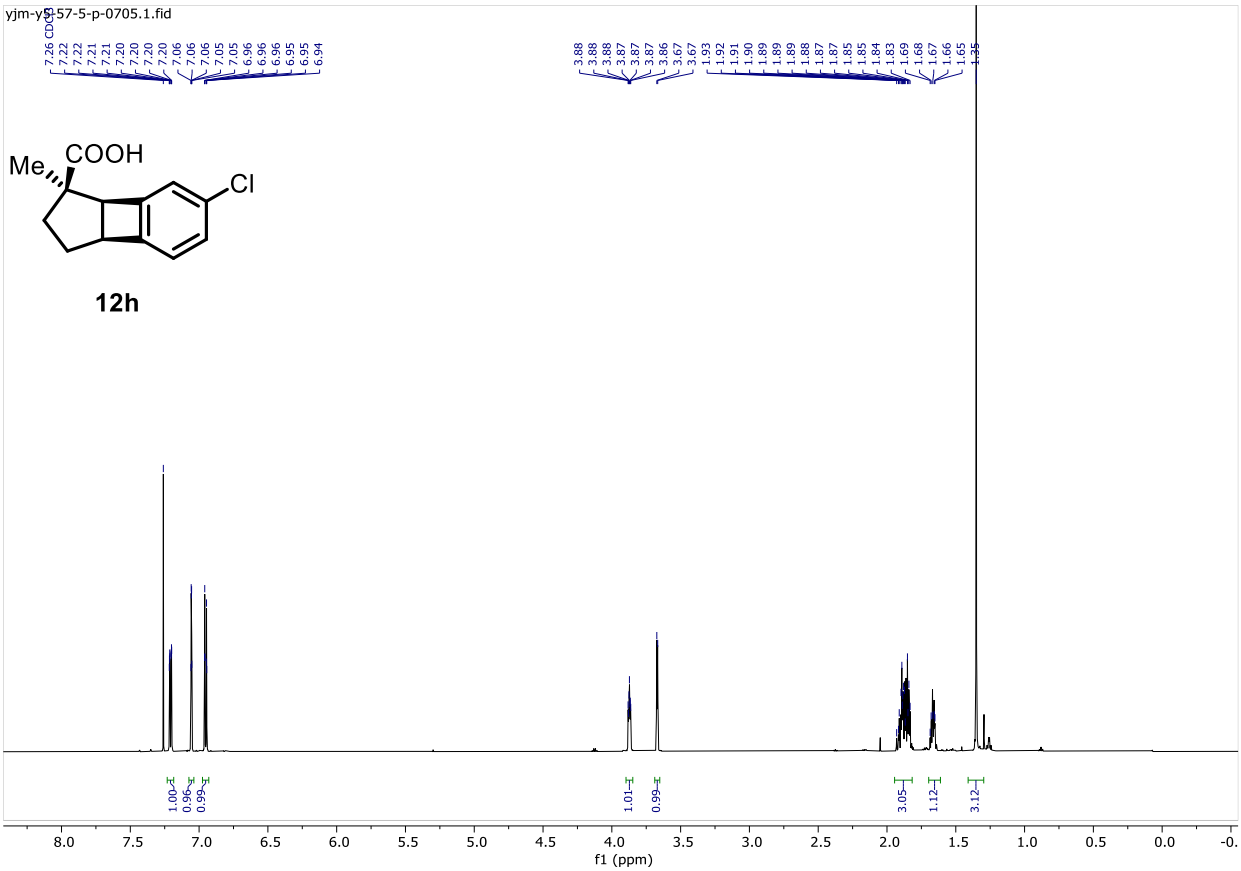

yjm-y5-152-7-s-092321.fid
7.26 CDCl3
7.02
7.01
6.94
6.93
6.86
3.90
3.89
3.88
3.88
3.65
3.64
2.33
1.93
1.91
1.91
1.89
1.86
1.85
1.85
1.84
1.84
1.83
1.82
1.62
1.62
1.62
1.60
1.60
Me
COOH
Me
12f
1.02
1.00
0.97
0.98
0.98
2.96
1.06
2.04
0.99
2.96
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

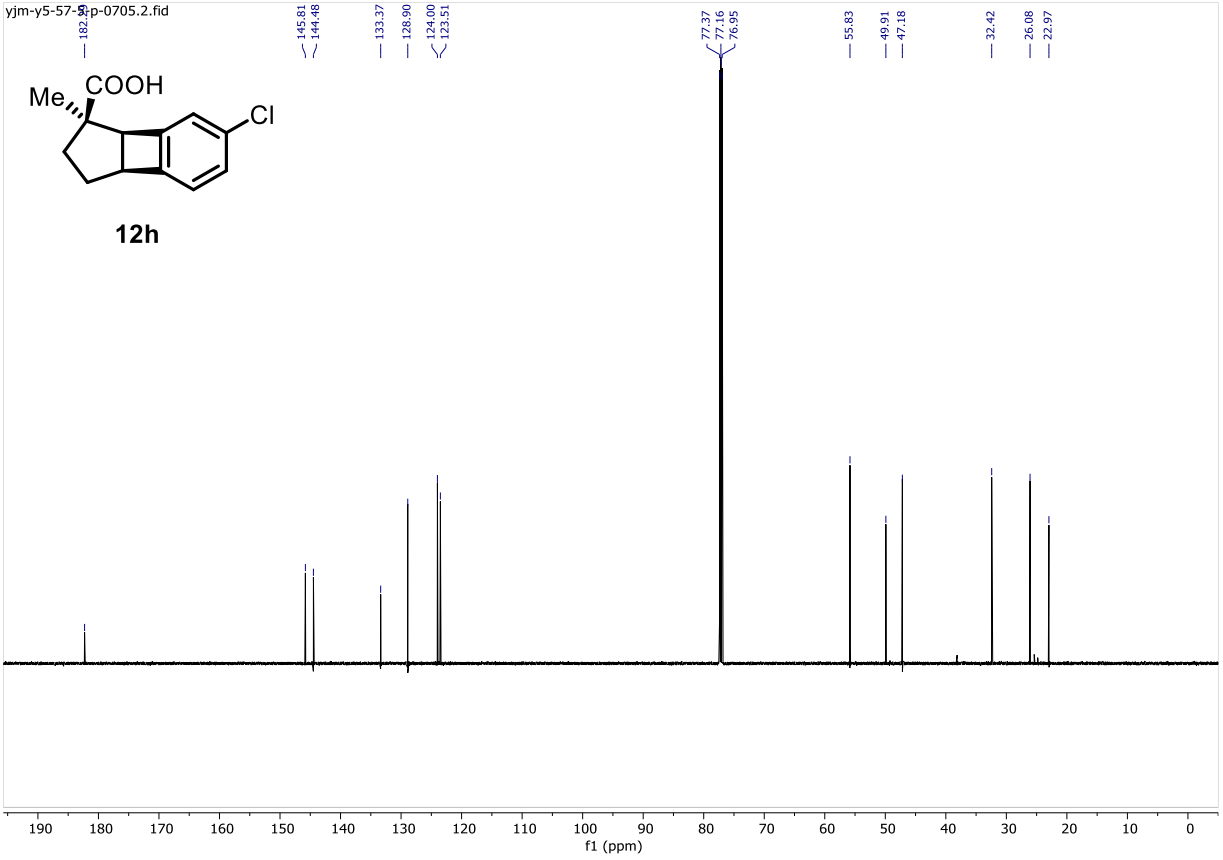

yjm-y5-152-7-s-0923.21.fid
182.23
146.39
141.33
138.12
128.41
122.92
122.63
77.37
77.16
76.95
55.94
49.86
47.49
32.43
26.17
22.85
22.30
Me
COOH
Me
12f
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

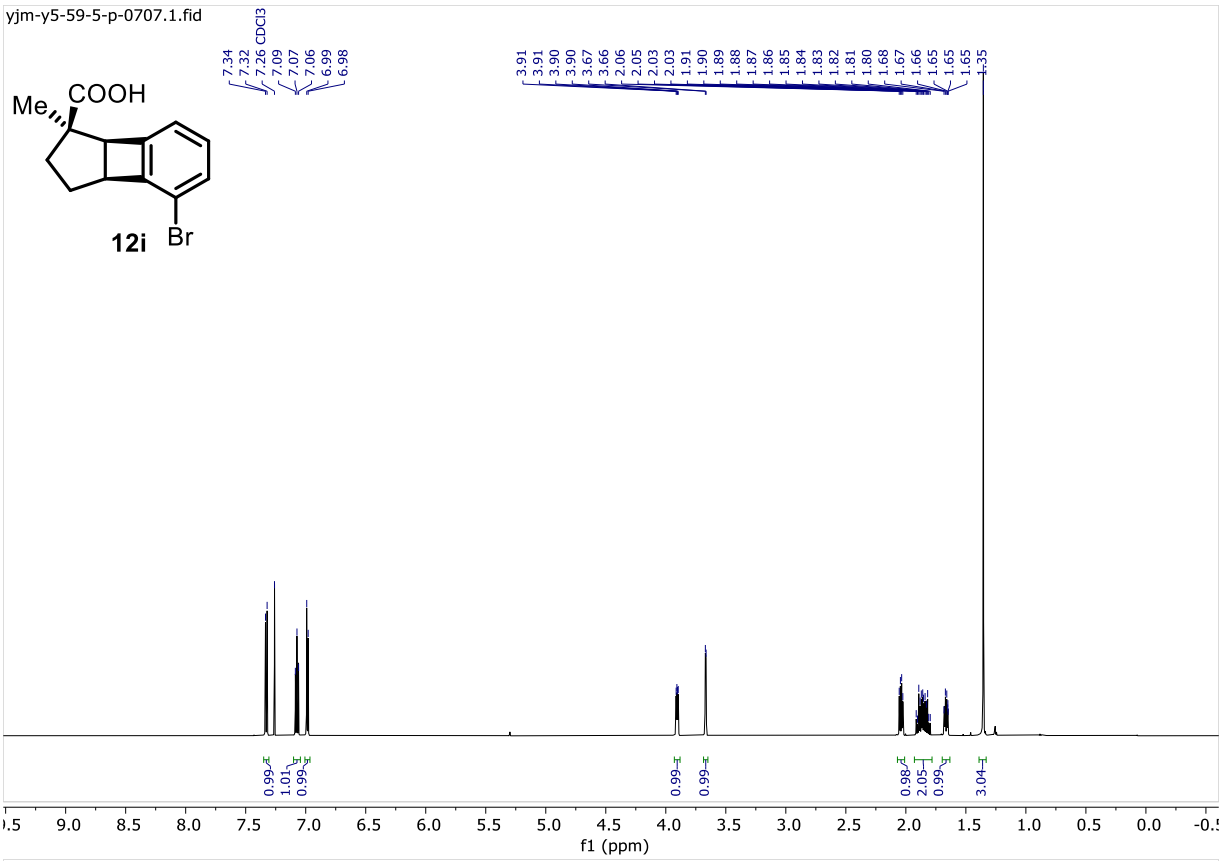

yjm-y5-57-1-p-0707.1.fid
Me
COOH
F
12g
f1 (ppm)

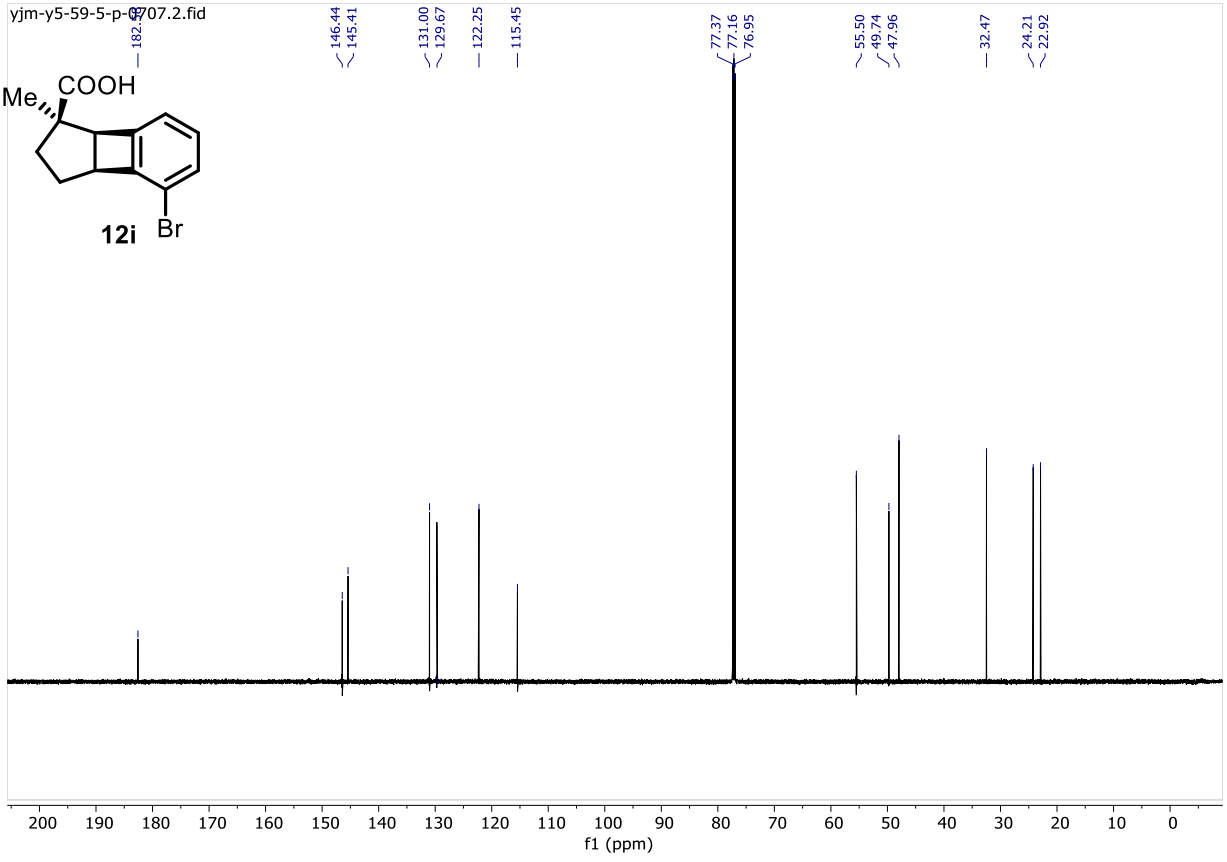

yjm-y5-57-1-p-0707.2.fid
Me
COOH
F
12g
f1 (ppm)

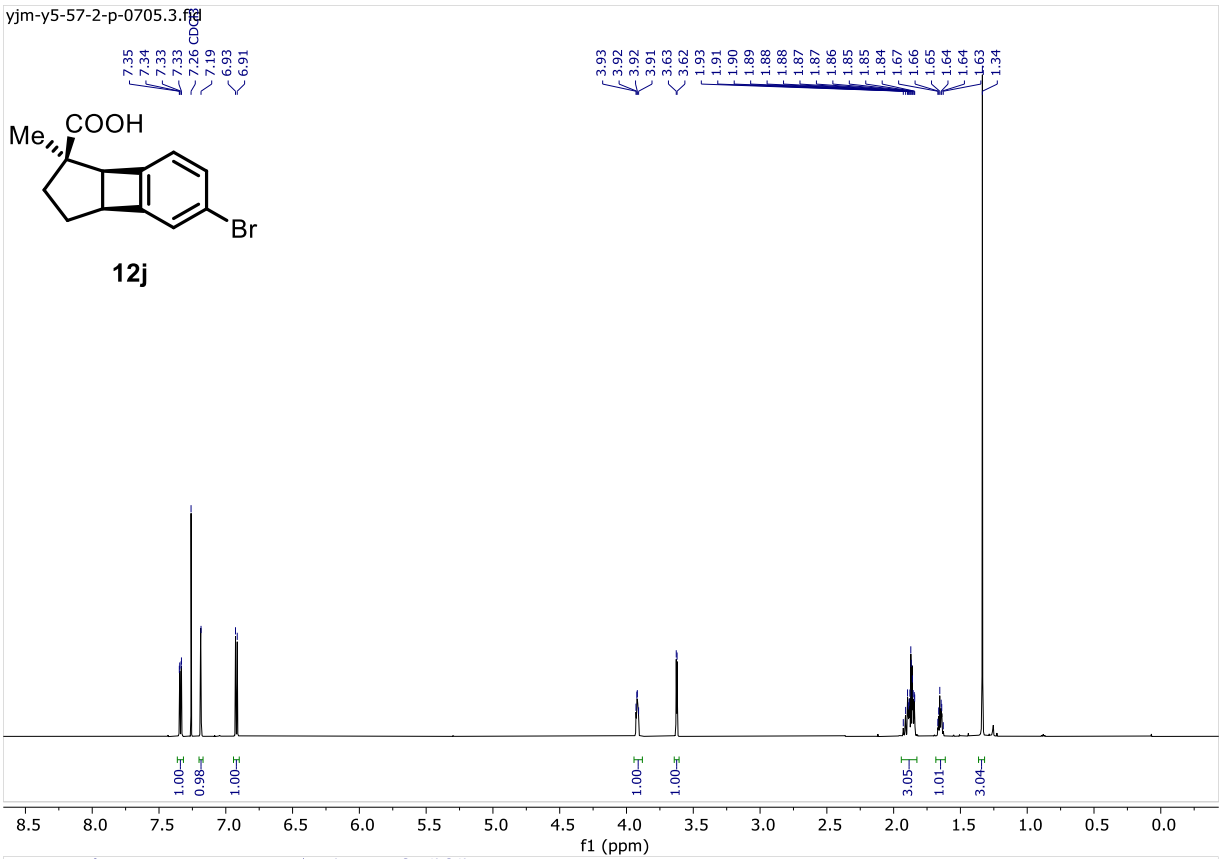

yjm-y5-57-1-p-F-0707.1.fid
Me
COOH
F
12g
-114.53
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -23
f1 (ppm)

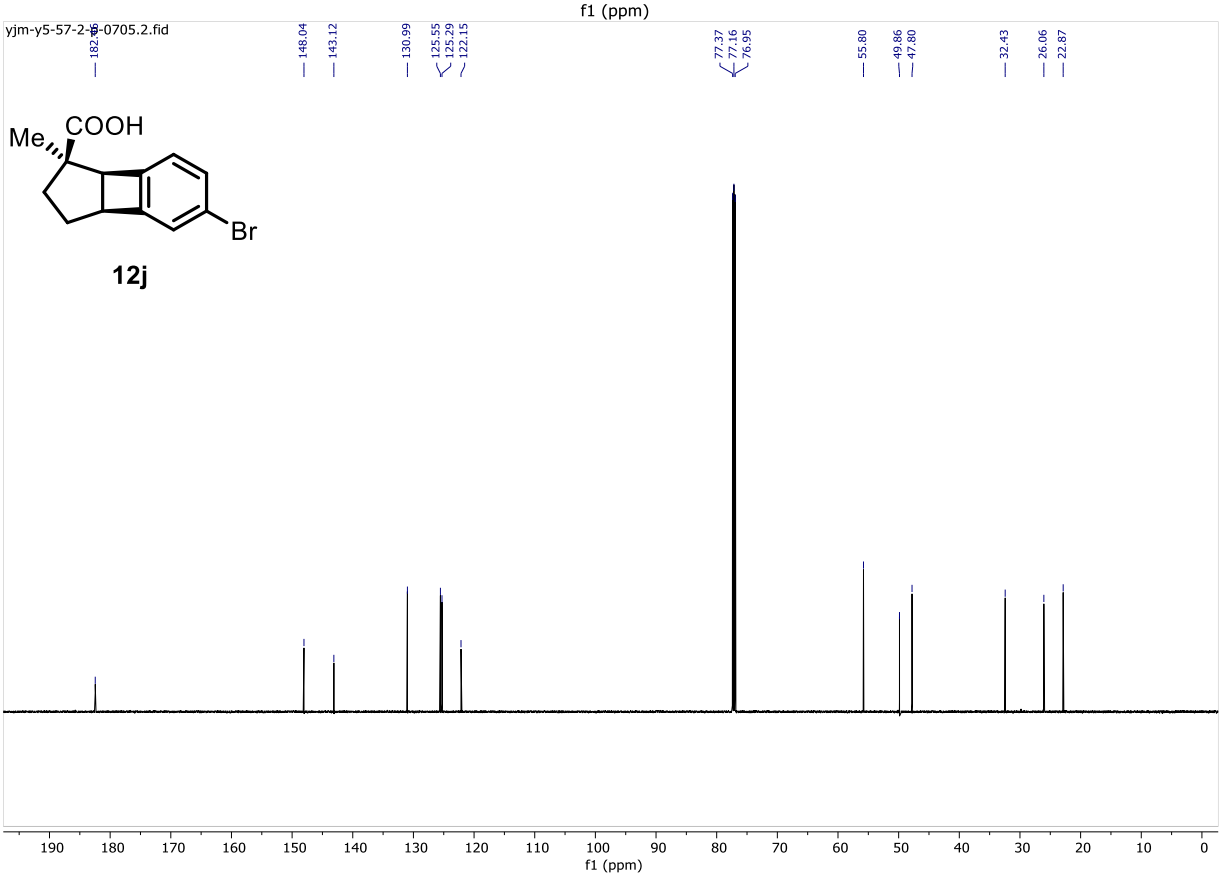

yjm-y5-57-5-p-0705.1.fid
Me
COOH
Cl
12h
f1 (ppm)

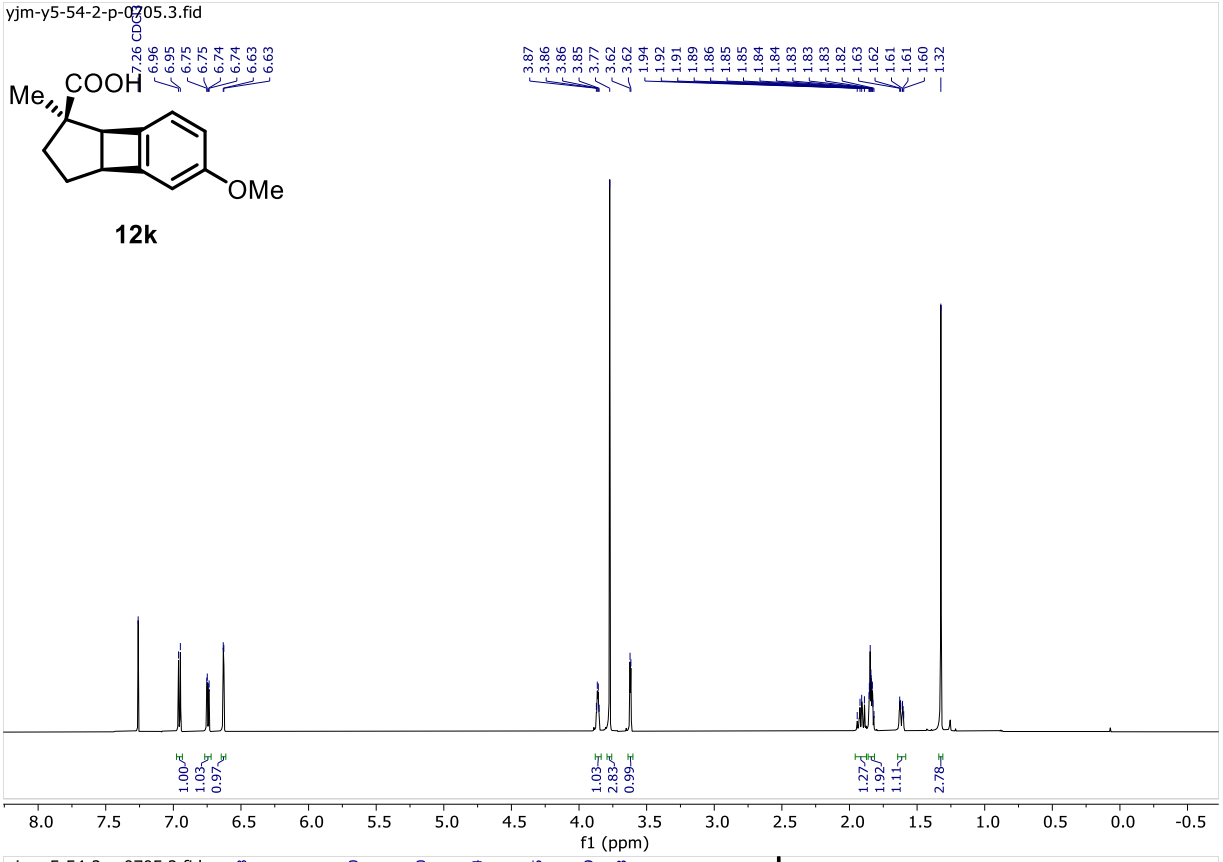

yjm-y5-57-5-p-0705.2.fid
Me
COOH
Cl
12h
f1 (ppm)

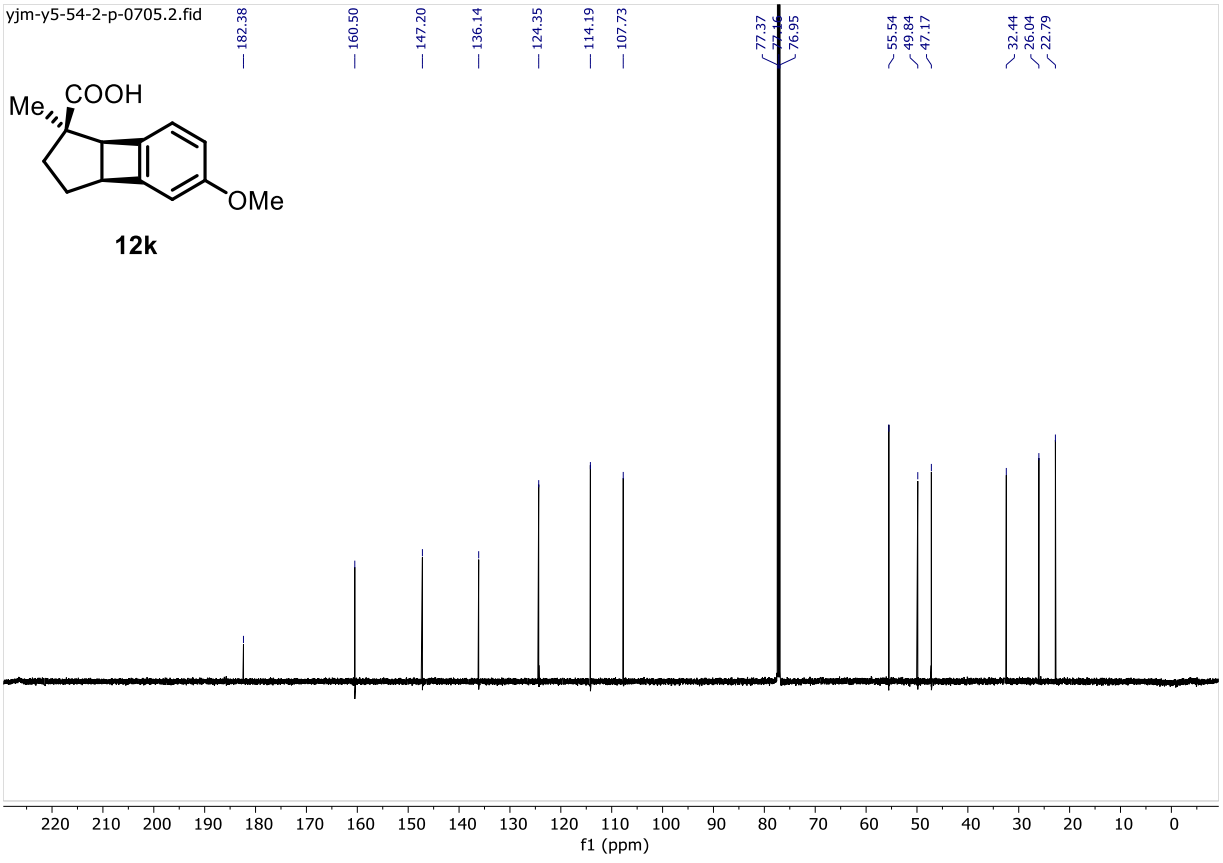

yjm-y5-59-5-p-0707.1.fid
Me
COOH
Br
12i
f1 (ppm)

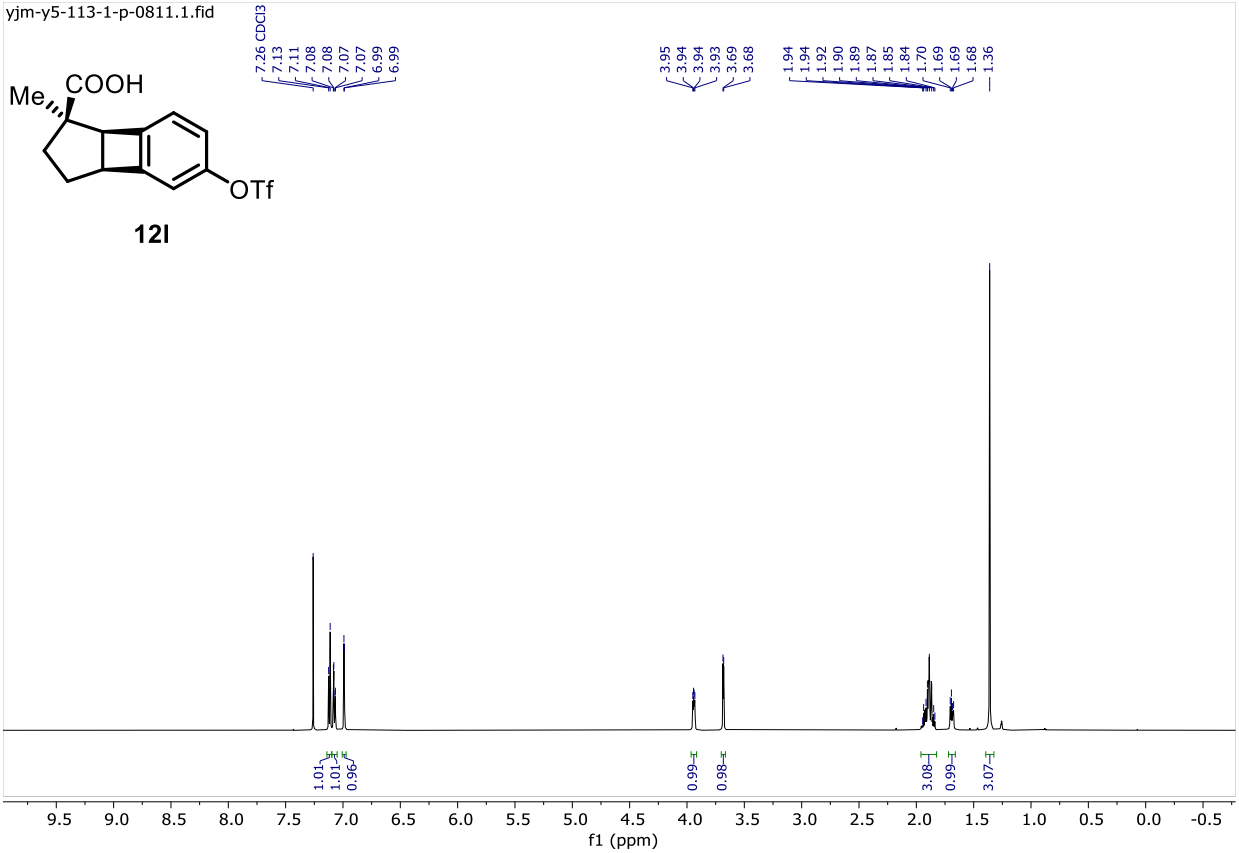

yjm-y5-59-5-p-0707.2.fid
Me
COOH
Br
12i
f1 (ppm)

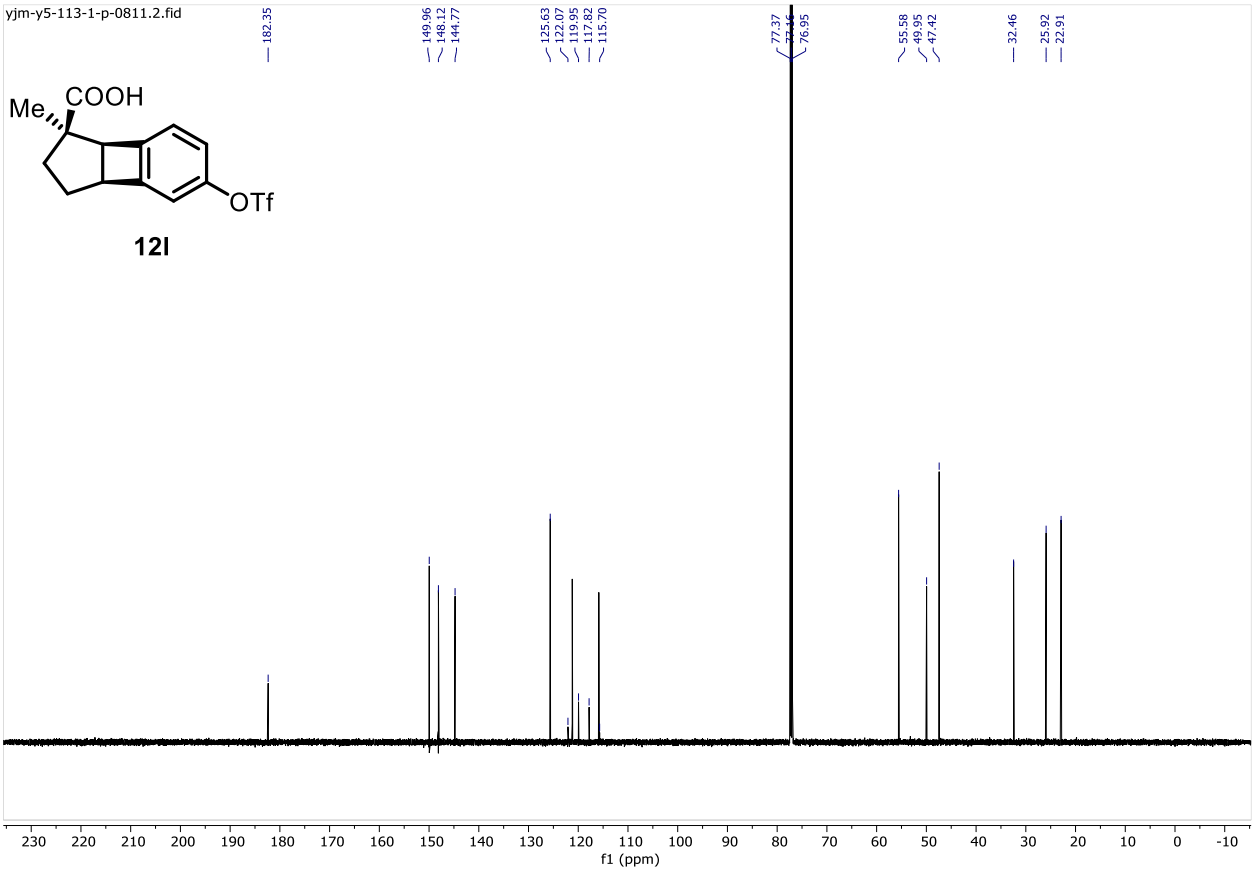

yjm-y5-57-2-p-0705.3.fid
7.35
7.34
7.33
7.26 CDCl3
7.19
6.93
6.91
3.93
3.92
3.92
3.91
3.63
3.62
1.93
1.91
1.90
1.89
1.88
1.88
1.87
1.87
1.86
1.85
1.85
1.84
1.67
1.66
1.65
1.64
1.64
1.63
1.34
Me
COOH
Br
12j
1.00
0.98
1.00
1.00
1.00
3.05
1.01
3.04
f1 (ppm)

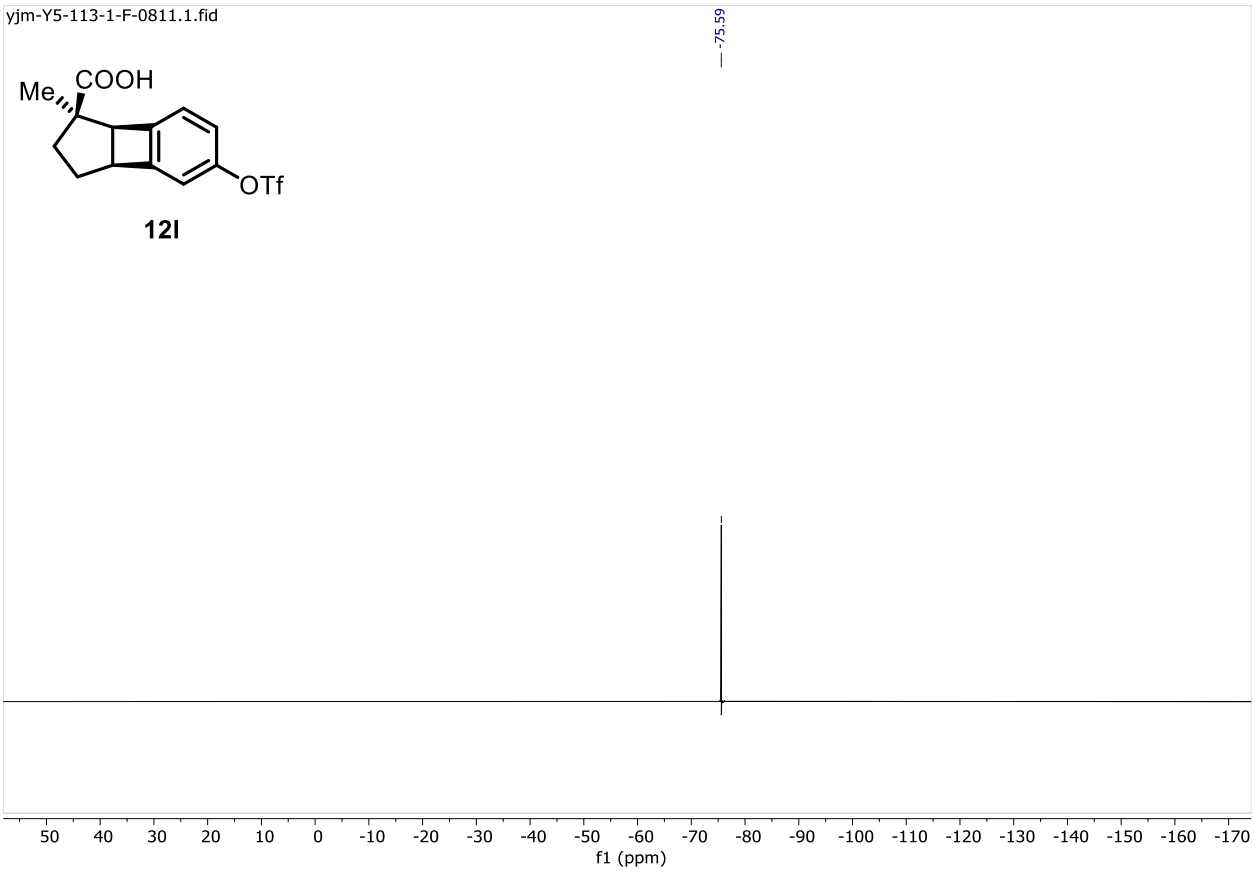

yjm-y5-57-2-p-0705.2.fid
182.46
146.04
143.12
130.99
125.55
125.29
122.15
77.37
77.16
76.95
55.80
49.86
47.80
32.43
26.06
22.87
Me
COOH
Br
12j
f1 (ppm)


yjm-y5-54-2-p-0705.3.fid
Me
COOH
OMe
12k
f1 (ppm)


yjm-y5-54-2-p-0705.2.fid
Me
COOH
OMe
12k
f1 (ppm)


yjm-y5-113-1-p-0811.1.fid
Me
COOH
OTf
12l
f1 (ppm)


yjm-y5-113-1-p-0811.2.fid
Me
COOH
OTf
12l
f1 (ppm)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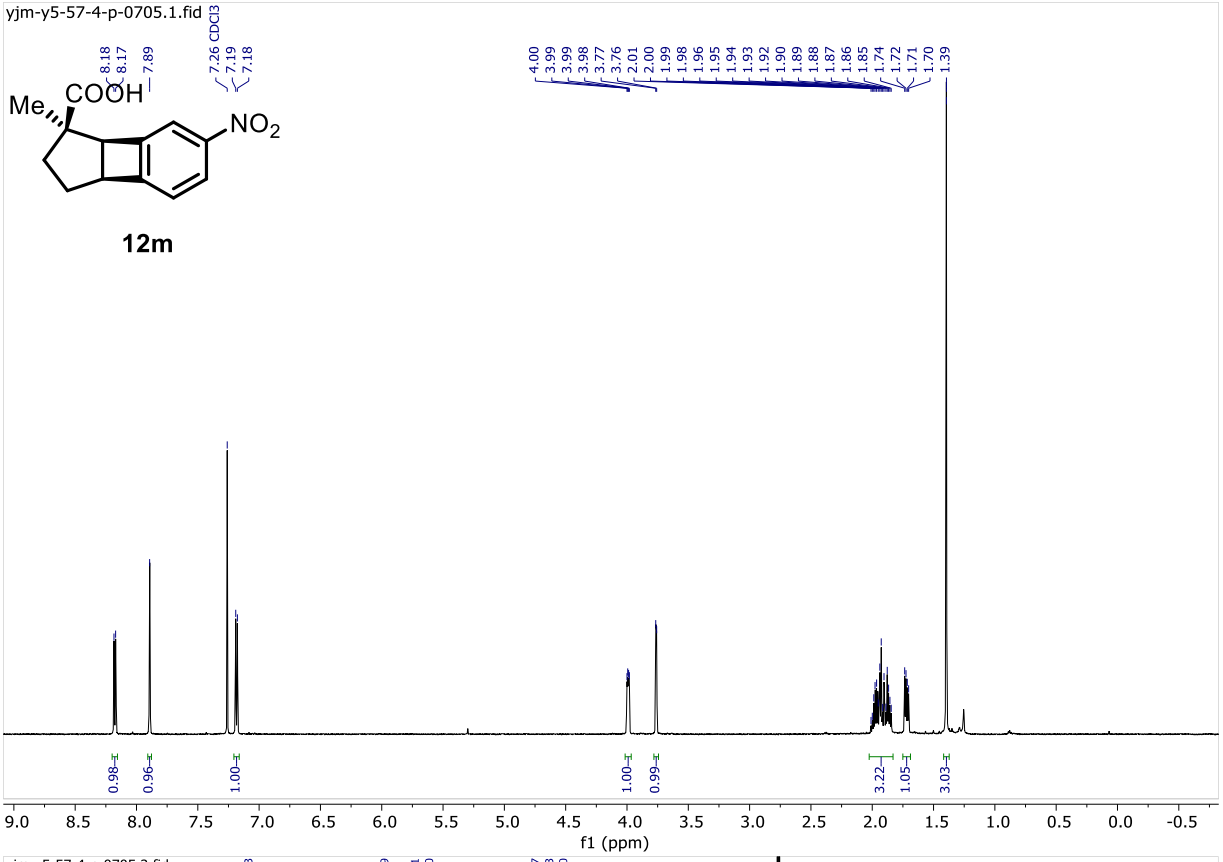
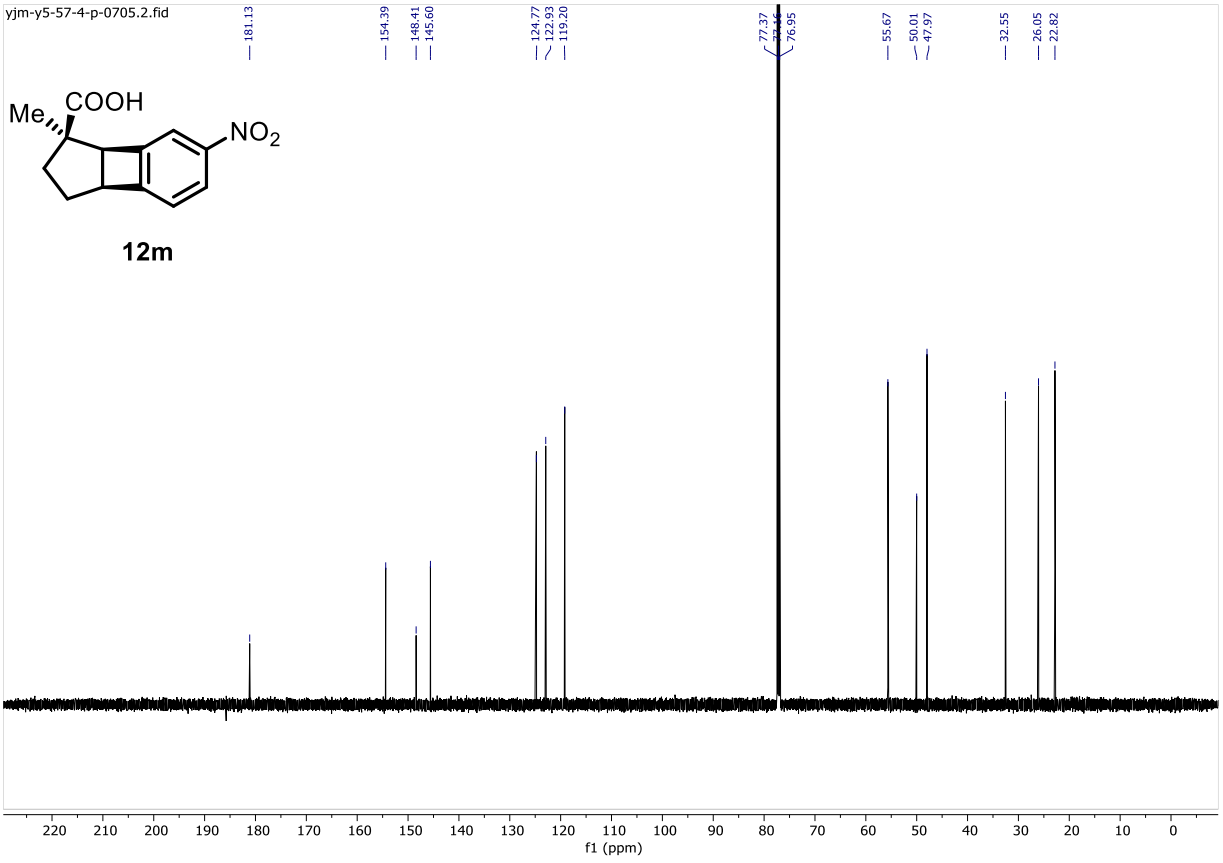
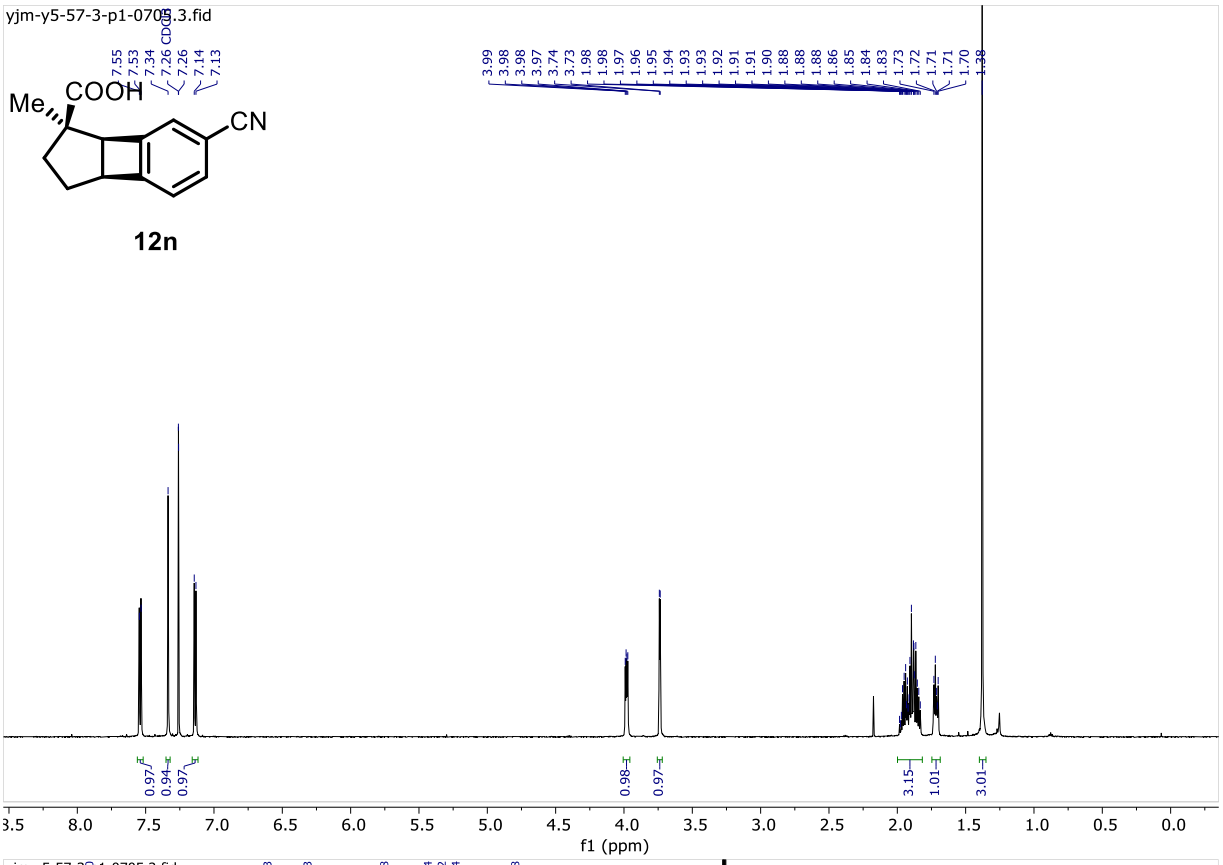
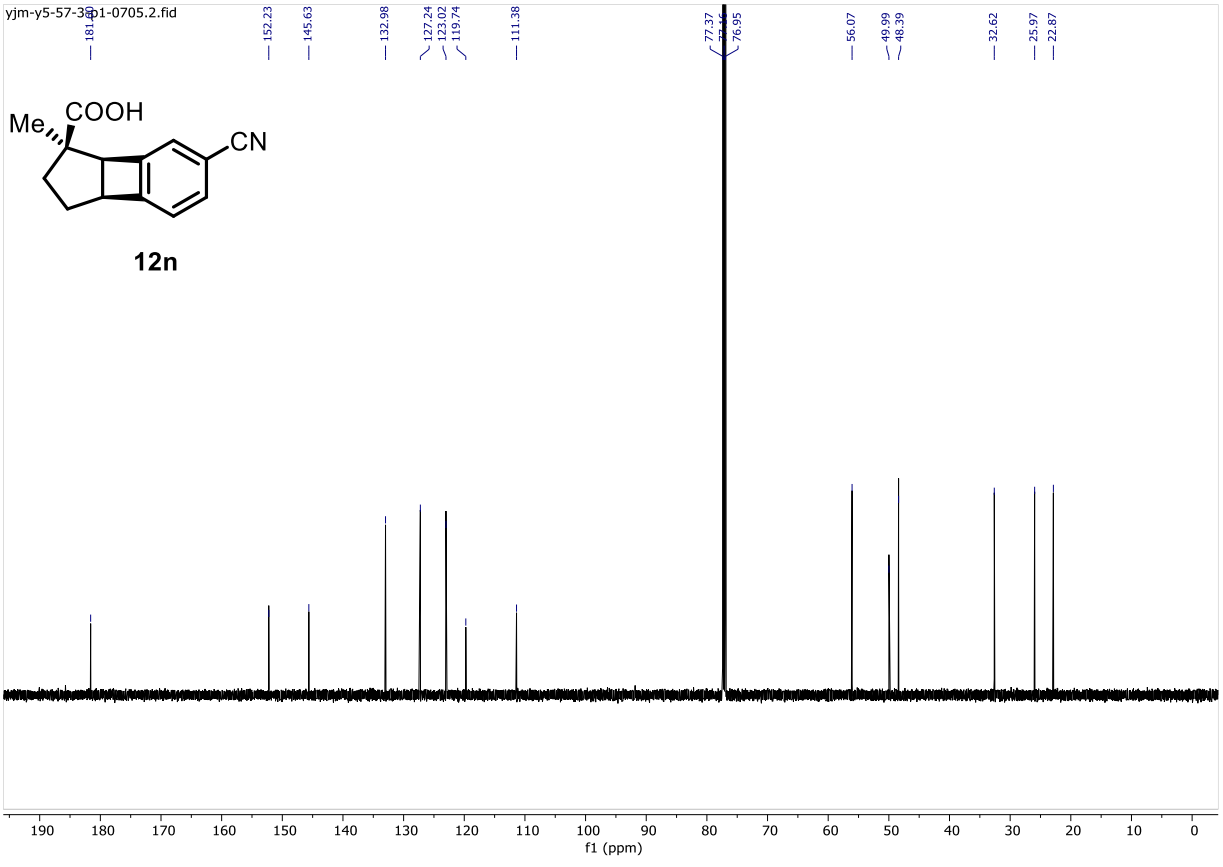
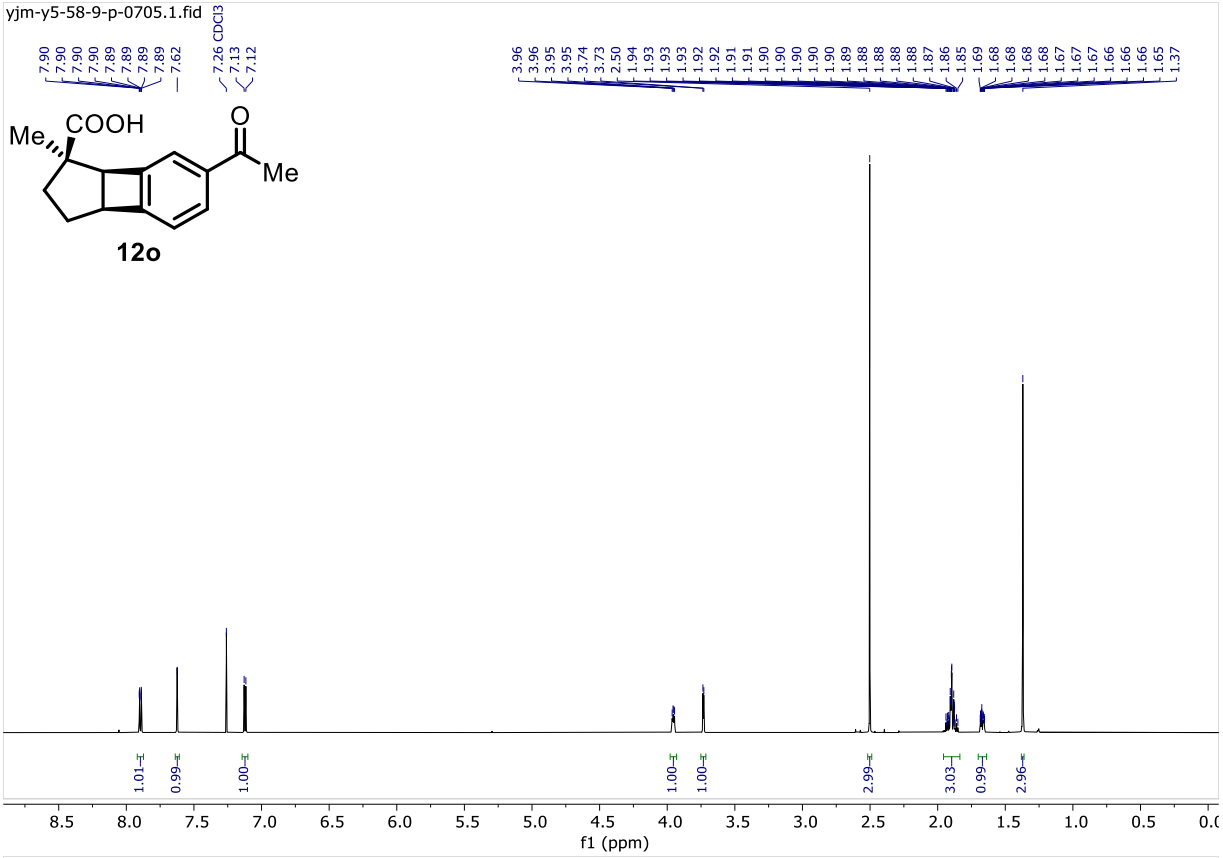
-75.59
Me
COOH
OTf
12l
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

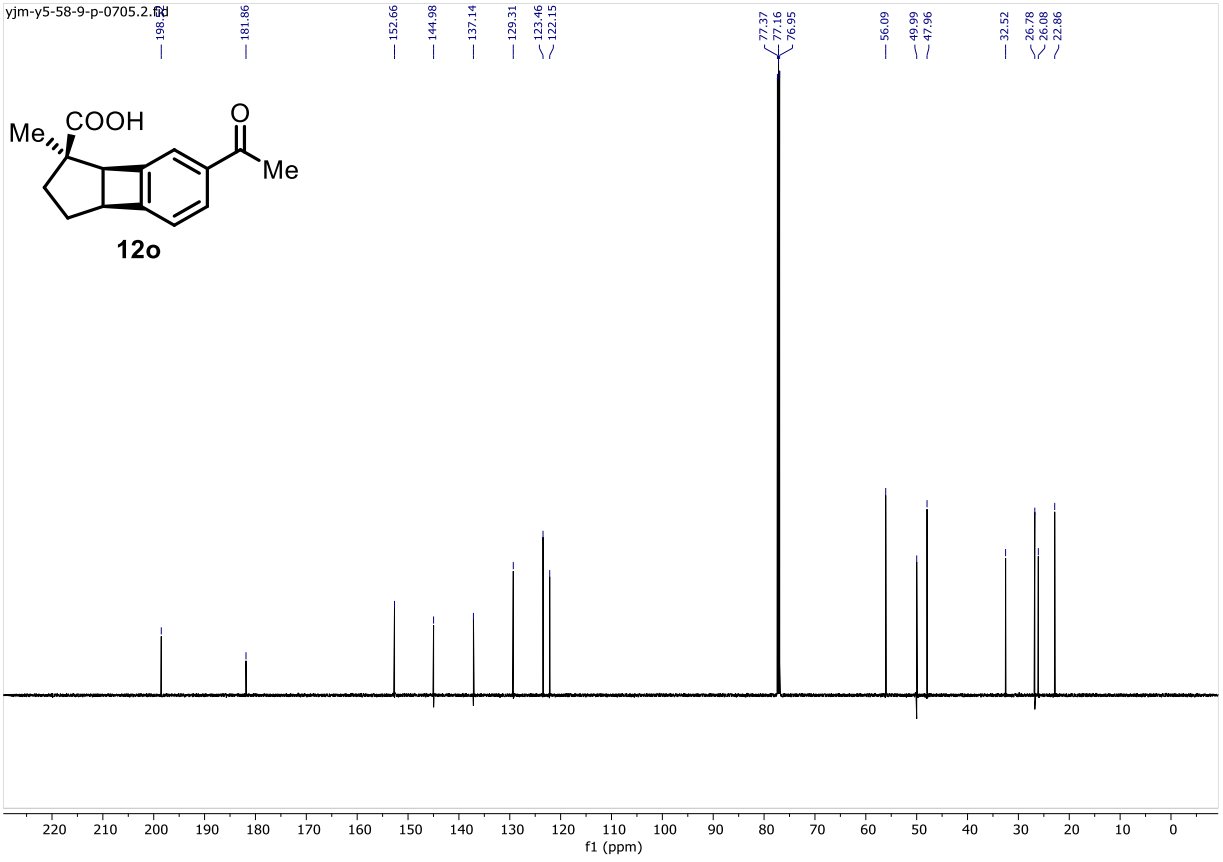

yjm-y5-57-4-p-0705.1.fid
8.18
8.17
7.89
7.26 CDCl3
7.19
7.18
Me
COOH
NO2
12m
4.00
3.99
3.99
3.99
3.98
3.77
3.76
2.01
2.00
1.99
1.98
1.96
1.95
1.94
1.93
1.92
1.90
1.89
1.88
1.87
1.86
1.85
1.74
1.72
1.71
1.70
1.39
0.98
0.96
1.00
1.00
0.99
3.22
1.05
3.03
f1 (ppm)

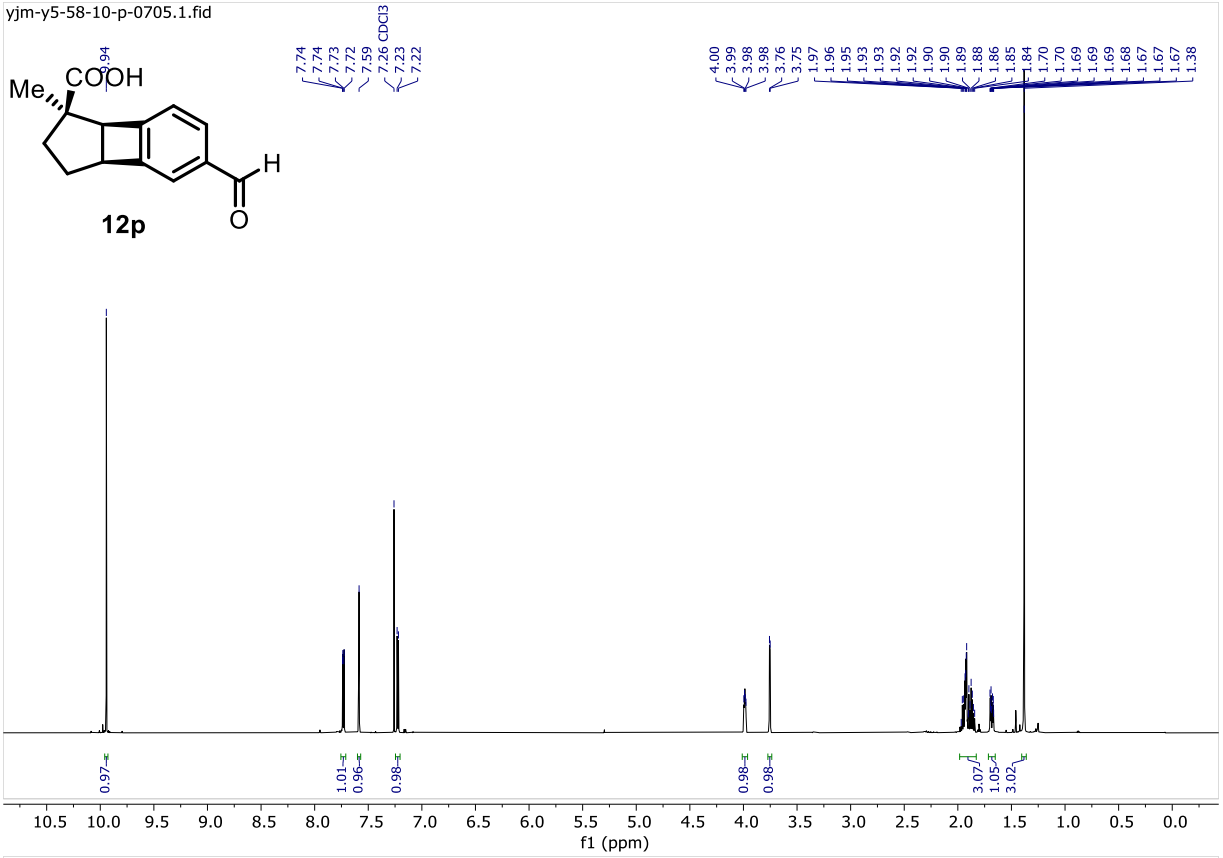

yjm-y5-57-4-p-0705.2.fid
181.13
154.39
148.41
145.60
124.77
122.93
119.20
77.37
77.16
76.95
55.67
50.01
47.97
32.55
26.05
22.82
Me
COOH
NO2
12m
f1 (ppm)

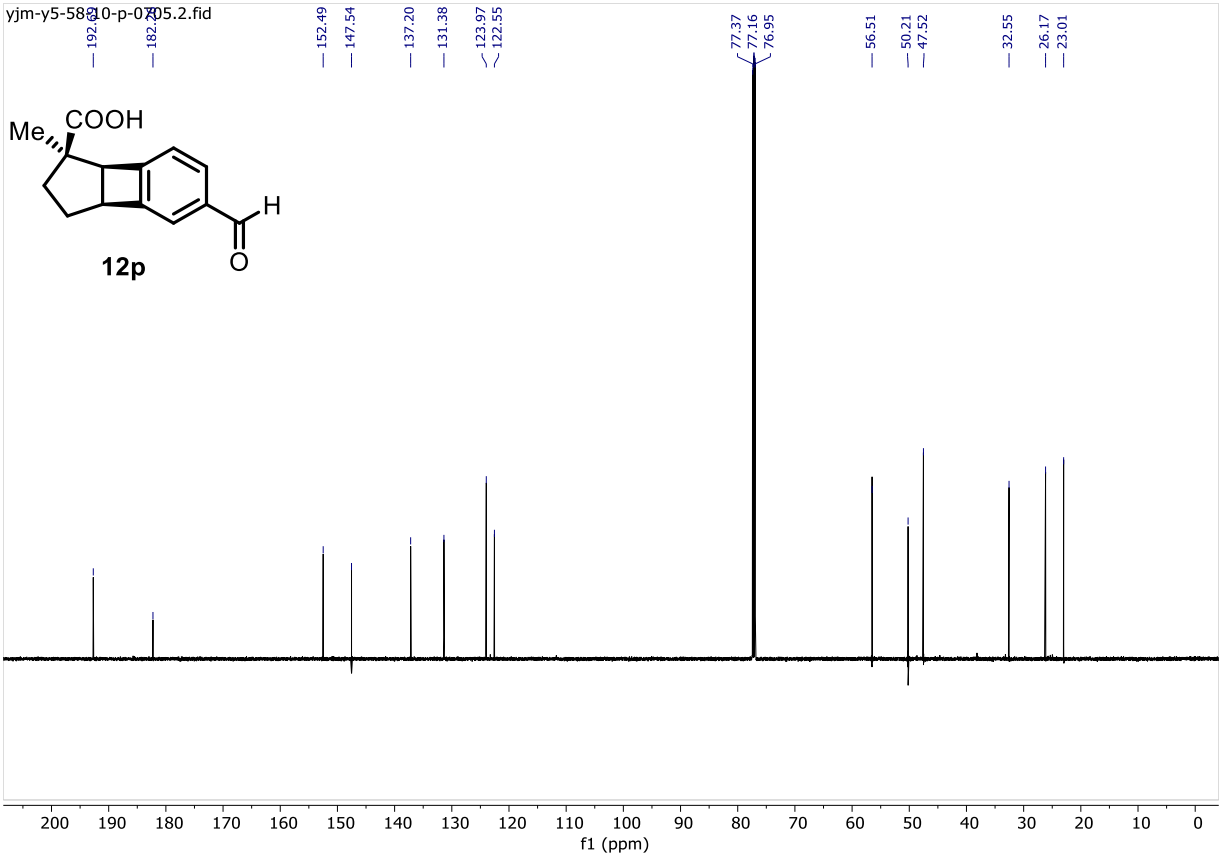

yjm-y5-57-3-p1-0705.3.fid
Me
COOH
CN
12n
f1 (ppm)

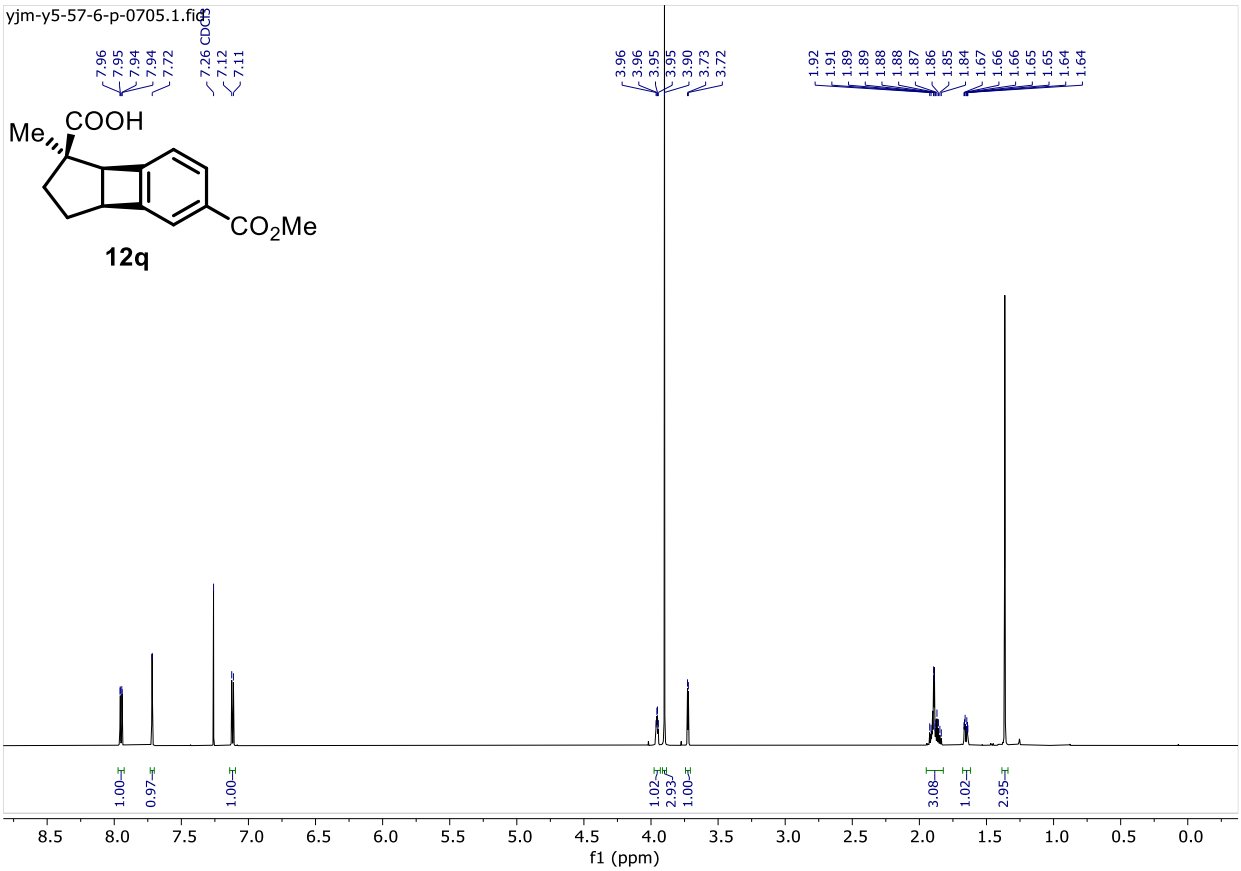

yjm-y5-57-3-p1-0705.2.fid
Me
COOH
CN
12n
f1 (ppm)

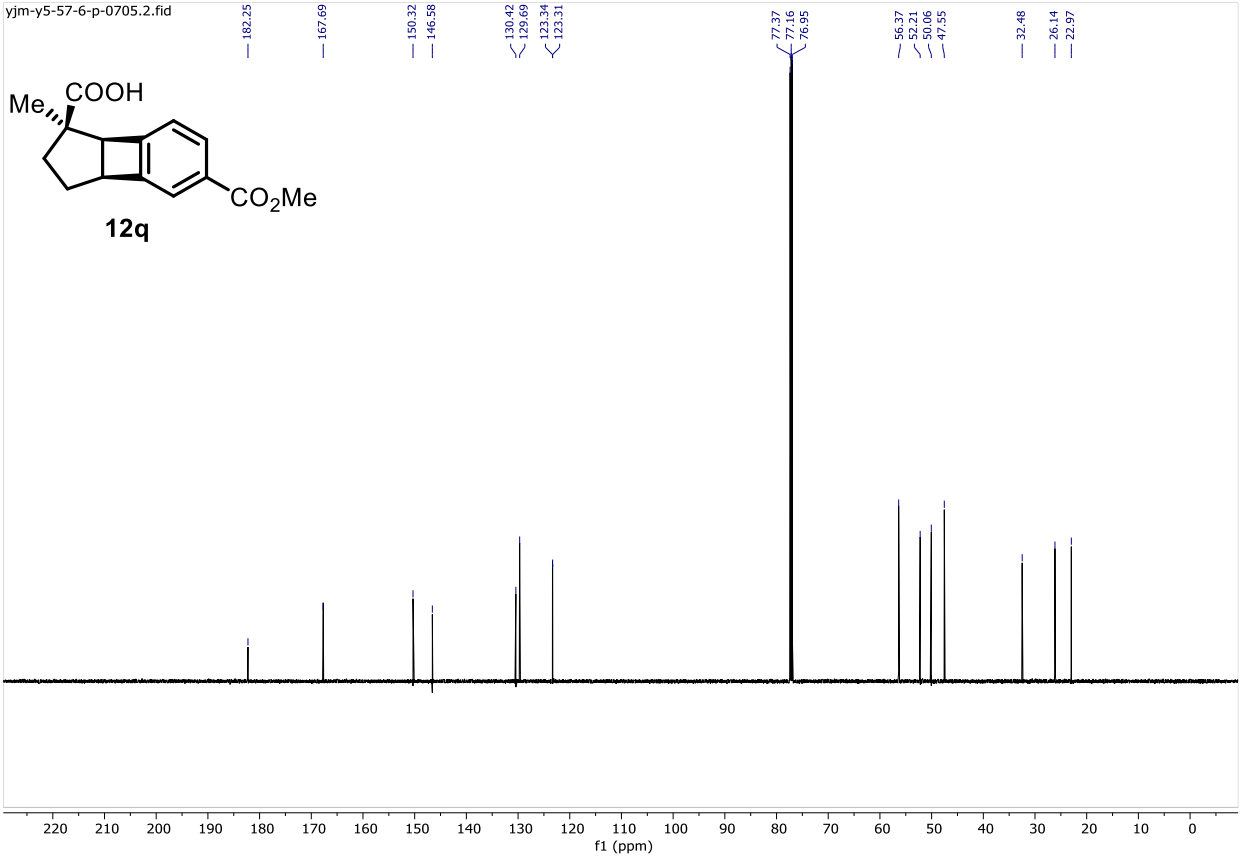

yjm-y5-58-9-p-0705.1.fid
Me
COOH
O
Me
12o
f1 (ppm)


yjm-y5-58-9-p-0705.2.fid
Me
COOH
O
Me
12o
f1 (ppm)


yjm-y5-58-10-p-0705.1.fid
Me
COOH
H
O
12p
7.74
7.74
7.73
7.72
7.59
7.26 CDCl3
7.23
7.22
4.00
3.99
3.98
3.98
3.76
3.75
1.97
1.96
1.95
1.93
1.93
1.92
1.92
1.90
1.90
1.89
1.88
1.86
1.85
1.84
1.70
1.70
1.69
1.69
1.69
1.68
1.67
1.67
1.67
1.38
0.97
1.01
0.96
0.98
0.98
0.98
3.07
1.05
3.02
f1 (ppm)


yjm-y5-58-10-p-0705.2.fid
192.49
182.78
152.49
147.54
137.20
131.38
123.97
122.55
77.37
77.16
76.95
56.51
50.21
47.52
32.55
26.17
23.01
Me
COOH
H
O
12p
f1 (ppm)


yjm-y5-57-6-p-0705.1.fid
7.96
7.95
7.94
7.94
7.72
7.26 CDCl3
7.12
7.11
3.96
3.96
3.95
3.95
3.90
3.73
3.72
1.92
1.91
1.89
1.89
1.88
1.88
1.87
1.86
1.85
1.84
1.67
1.66
1.66
1.65
1.65
1.64
1.64
Me
COOH
CO2Me
12q
1.00
0.97
1.00
1.02
2.93
1.00
3.08
1.02
2.95
f1 (ppm)


yjm-y5-57-6-p-0705.2.fid
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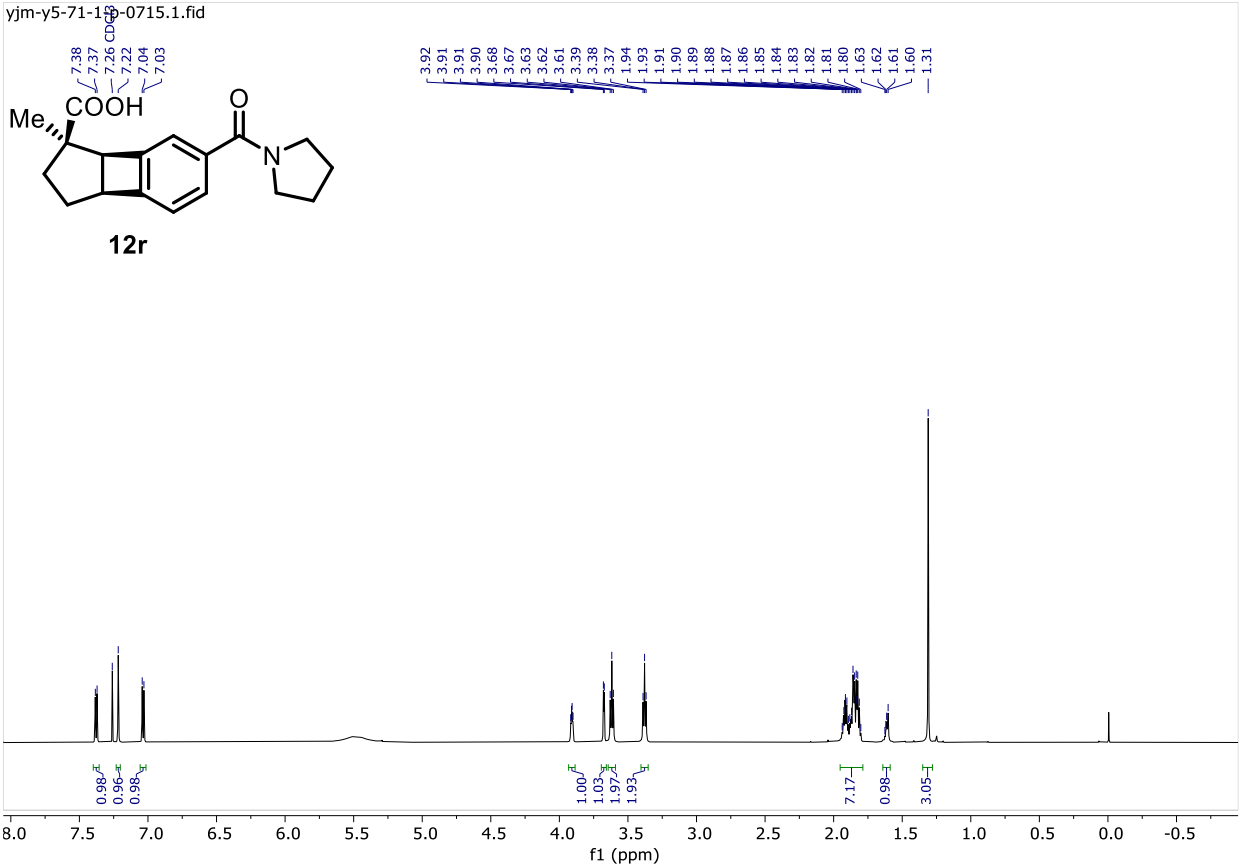
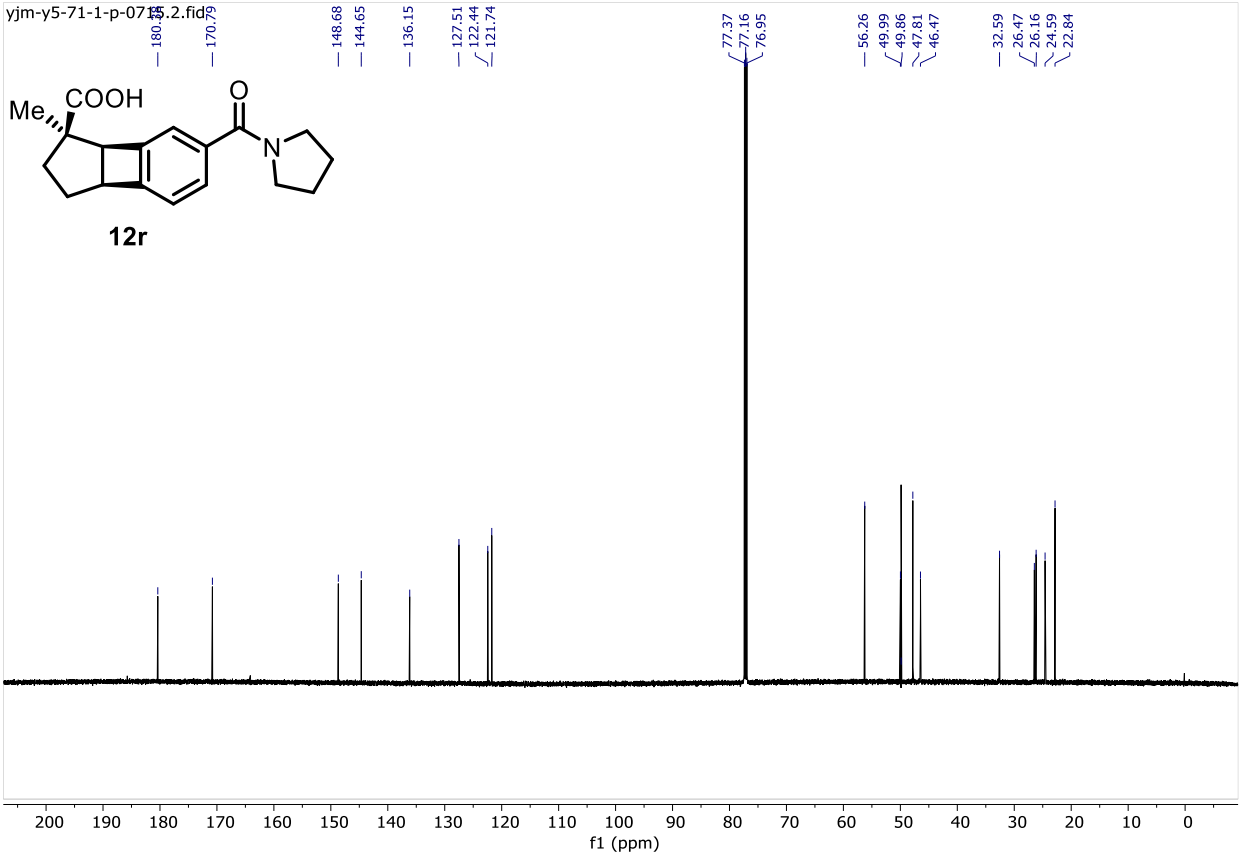
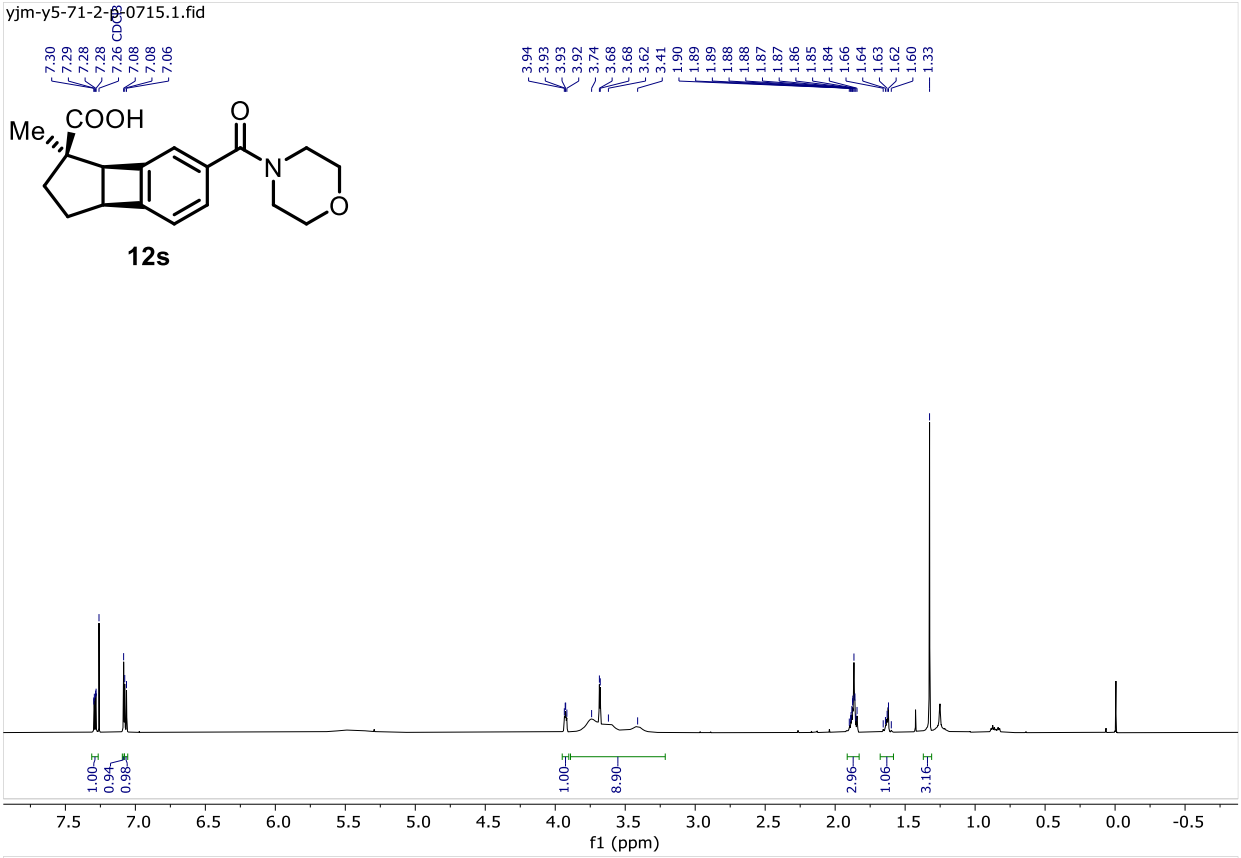
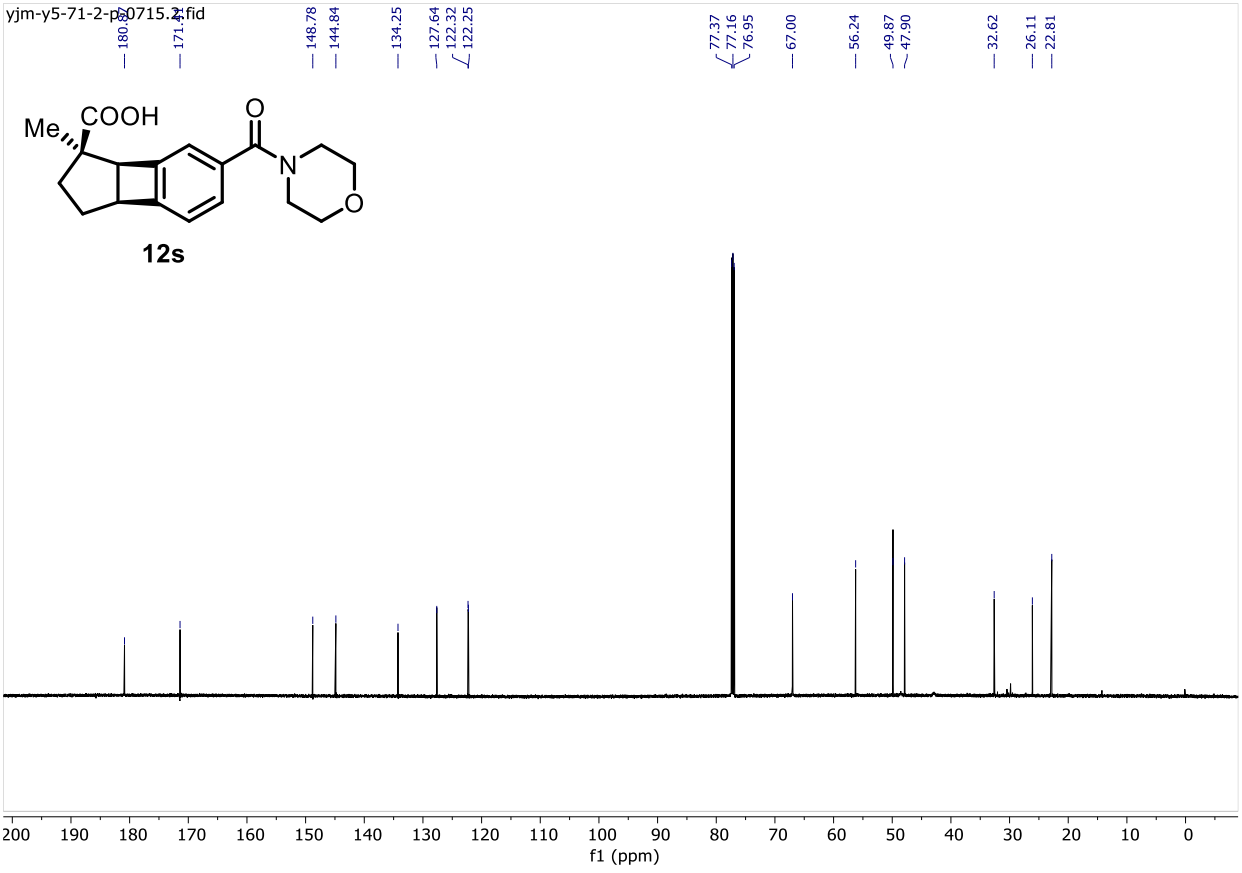
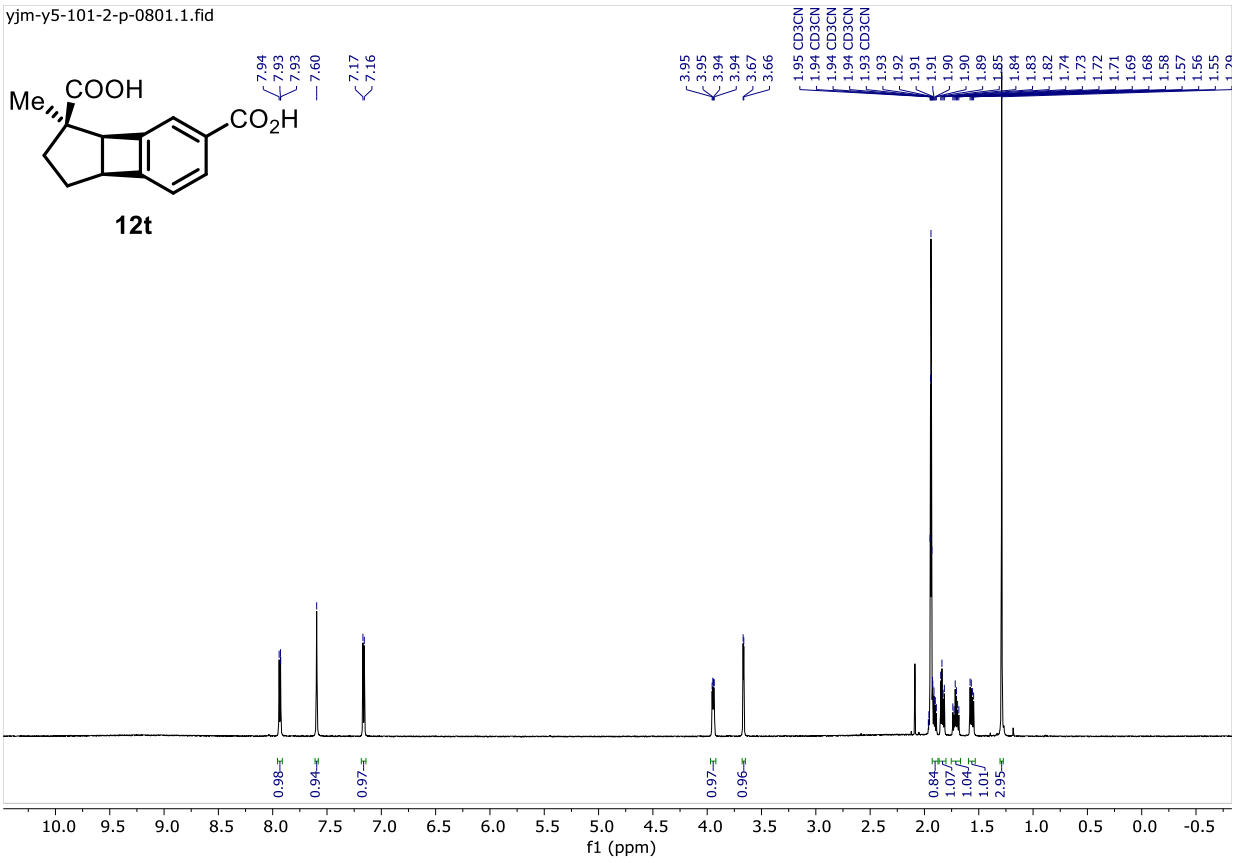
167.69
150.32
146.58
130.42
129.69
123.34
123.31
77.37
77.16
76.95
56.37
52.21
50.06
47.55
32.48
26.14
22.97
Me
COOH
CO2Me
12q
f1 (ppm)

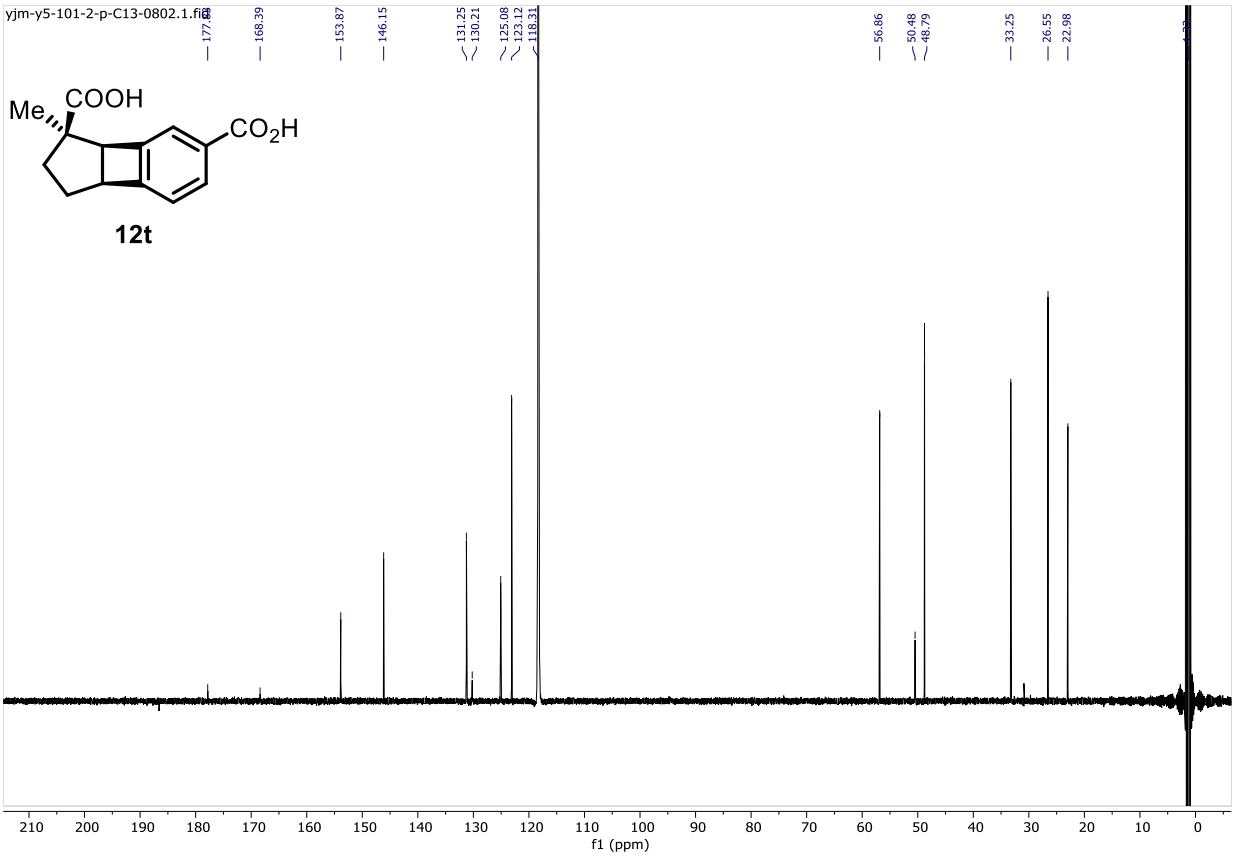

yjm-y5-71-1-p-0715.1.fid
7.38
7.37
7.26 CDCl3
7.22
7.04
7.03
Me
COOH
O
N
12r
3.92
3.91
3.91
3.90
3.68
3.67
3.63
3.62
3.61
3.39
3.38
3.37
1.94
1.93
1.91
1.90
1.89
1.88
1.87
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.63
1.62
1.61
1.60
1.31
0.98
0.96
0.98
1.00
1.03
1.97
1.93
7.17
0.98
3.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

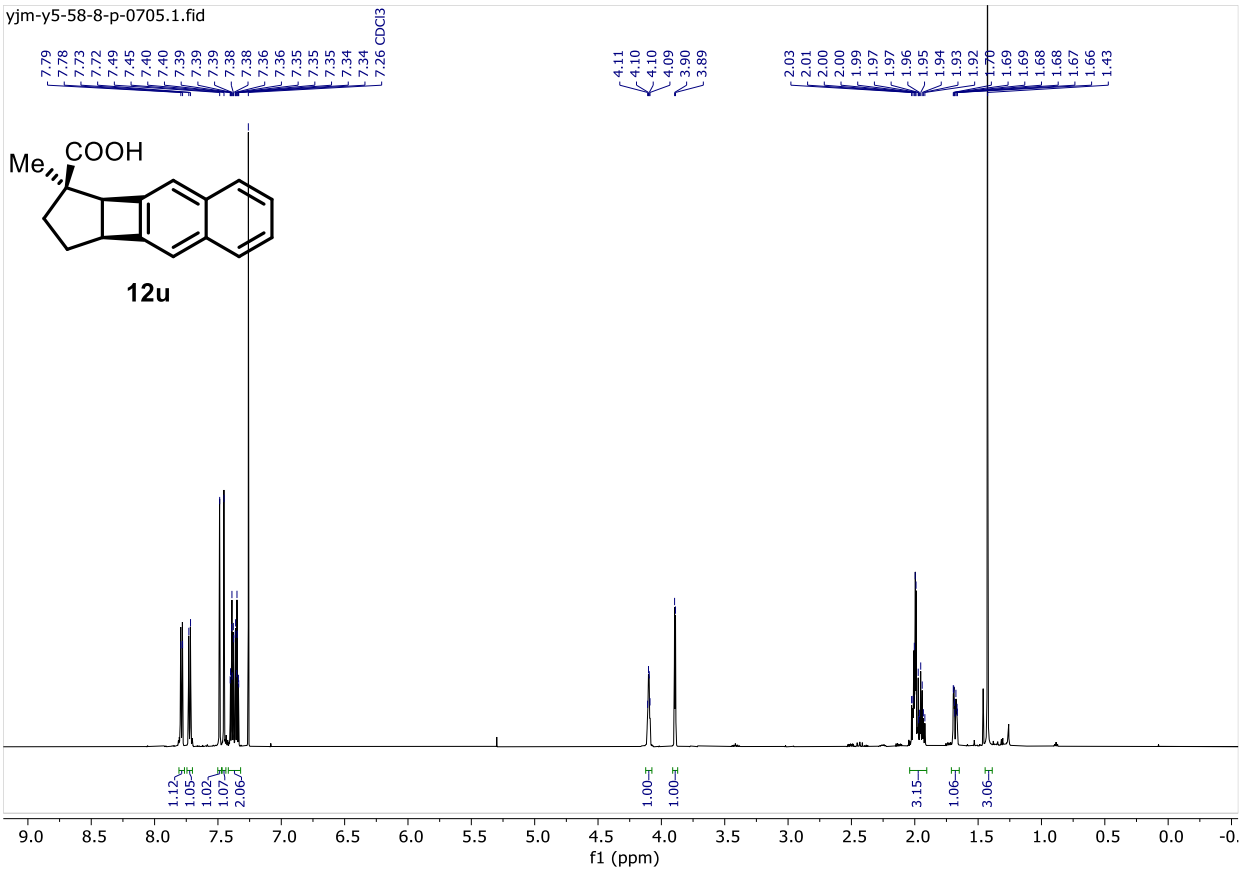

yjm-y5-71-1-p-0715.2.fid
180.45
170.79
148.68
144.65
136.15
127.51
122.44
121.74
77.37
77.16
76.95
56.26
49.99
49.86
47.81
46.47
32.59
26.47
26.16
24.59
22.84
Me
COOH
O
N
12r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

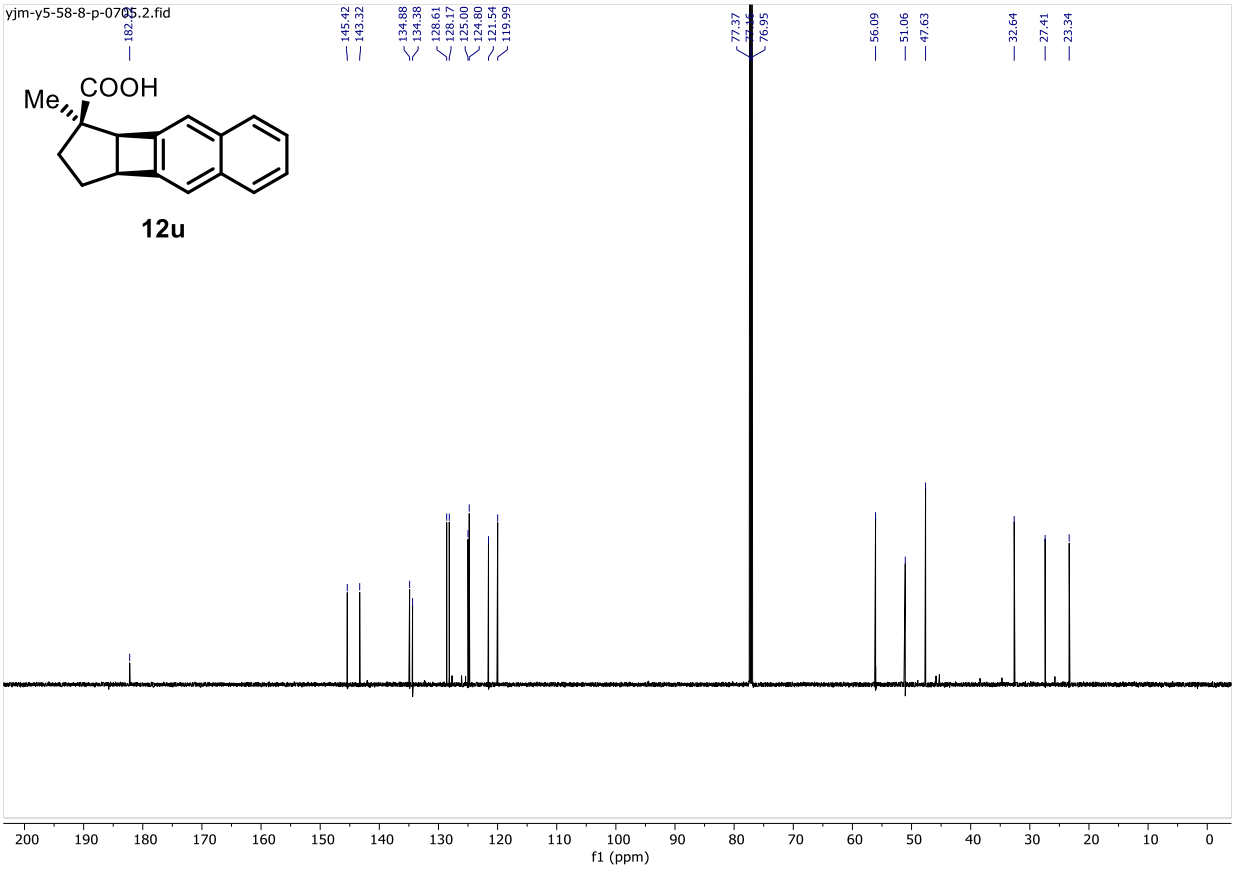

yjm-y5-71-2-p1-0715.1.fid
7.30
7.29
7.28
7.28
7.26 CDCl3
7.08
7.08
7.06
3.94
3.93
3.93
3.92
3.74
3.68
3.68
3.62
3.41
1.90
1.89
1.89
1.88
1.88
1.87
1.87
1.86
1.85
1.84
1.66
1.64
1.63
1.62
1.60
1.33
Me
COOH
O
N
O
12s
1.00
0.94
0.98
1.00
8.90
2.96
1.06
3.16
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

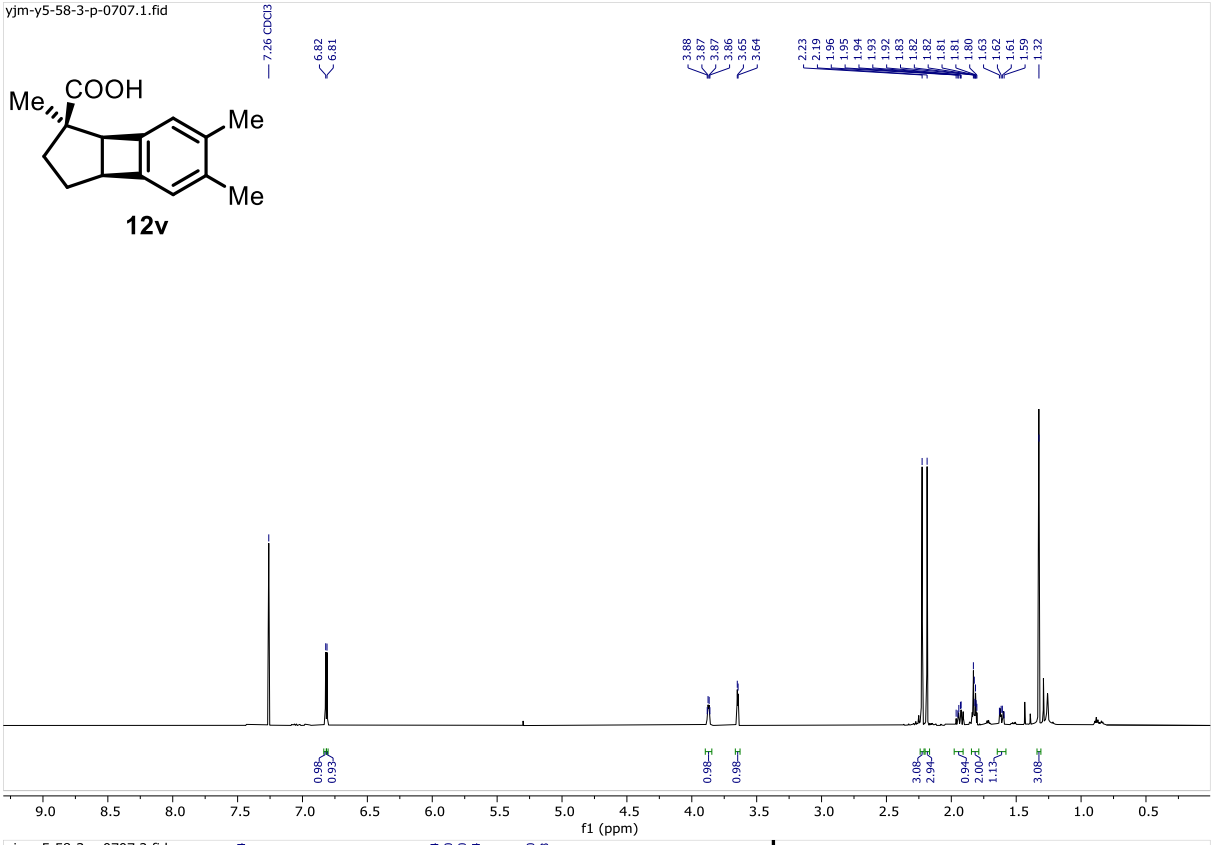

yjm-y5-71-2-p2-0715.2.fid
180.23
171.41
148.78
144.84
134.25
127.64
122.32
122.25
77.37
77.16
76.95
67.00
56.24
49.87
47.90
32.62
26.11
22.81
Me
COOH
O
N
O
12s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

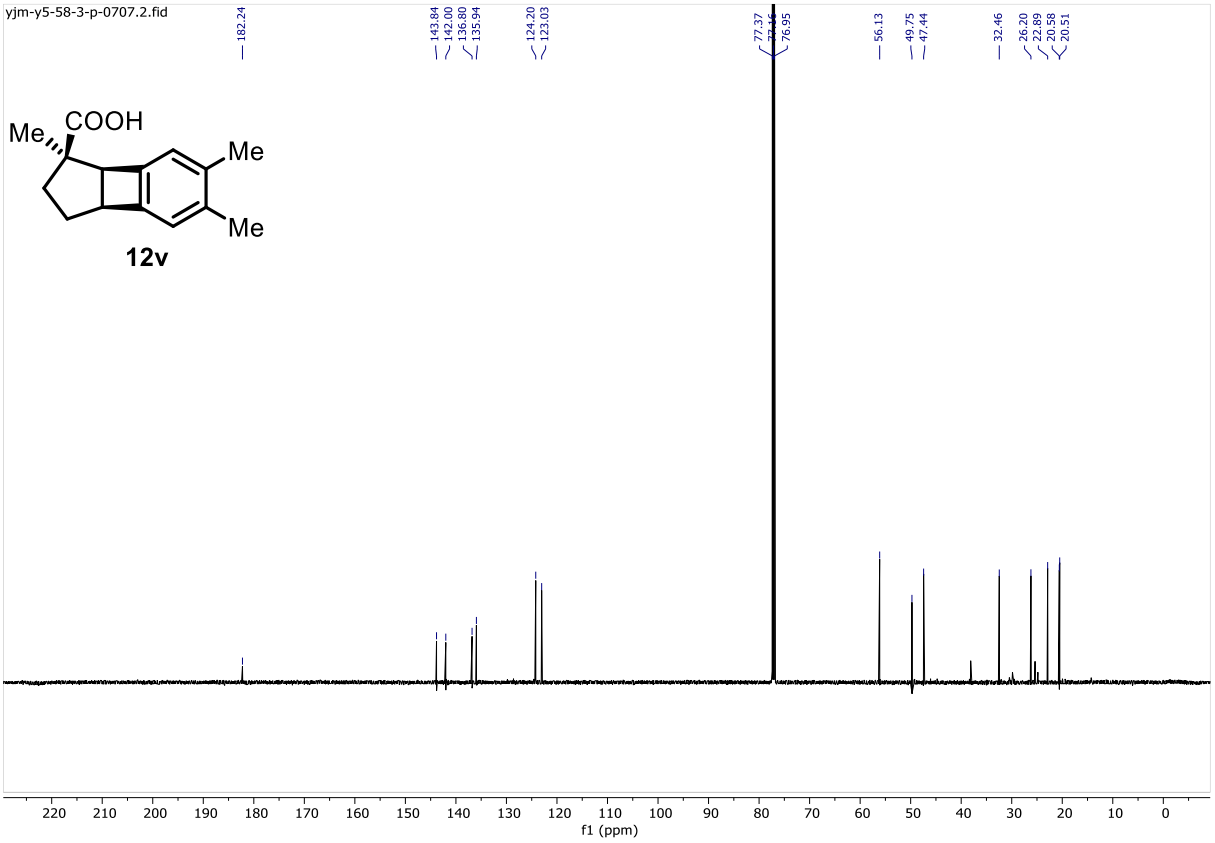

yjm-y5-101-2-p-0801.1.fid
Me
COOH
CO2H
12t
f1 (ppm)

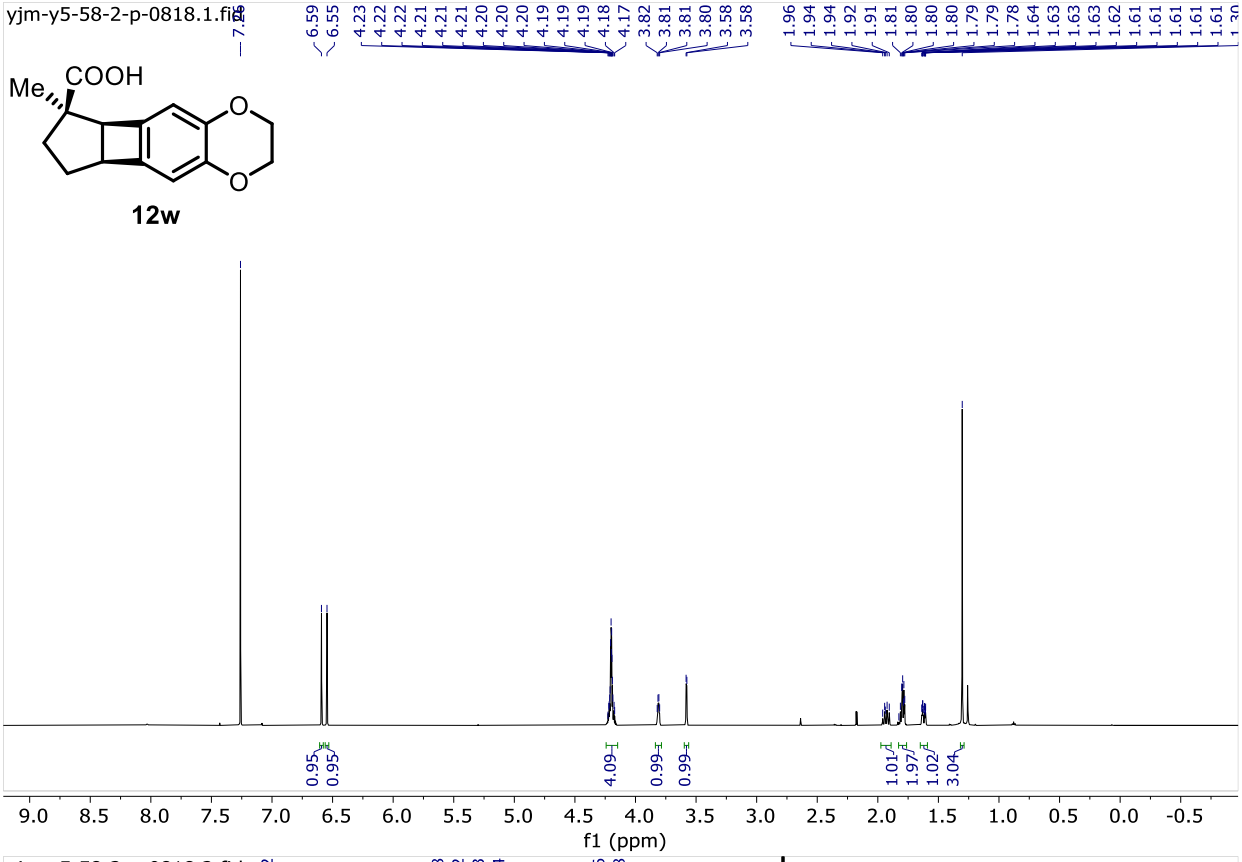

yjm-y5-101-2-p-C13-0802.1.fid
Me
COOH
CO2H
12t
f1 (ppm)

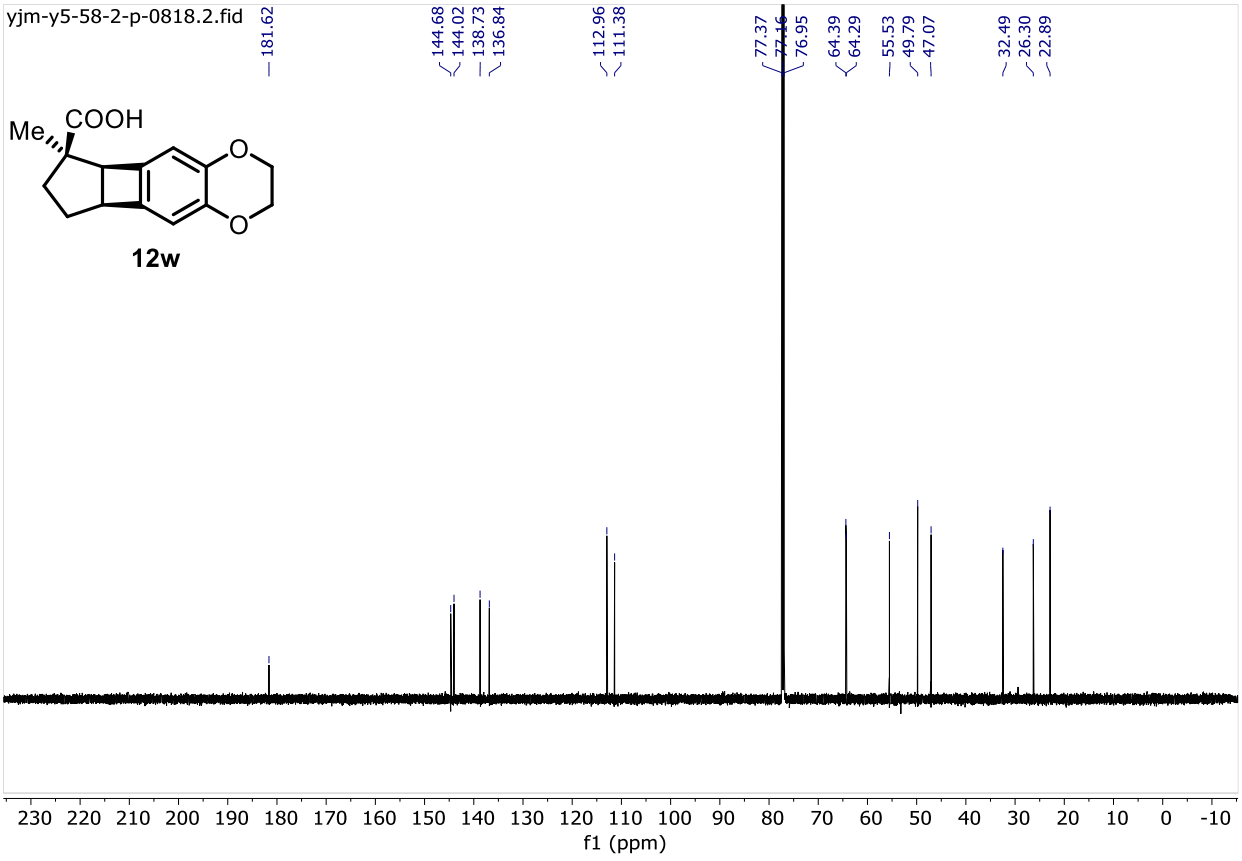

yjm-y5-58-8-p-0705.1.fid
Me
COOH
12u
f1 (ppm)

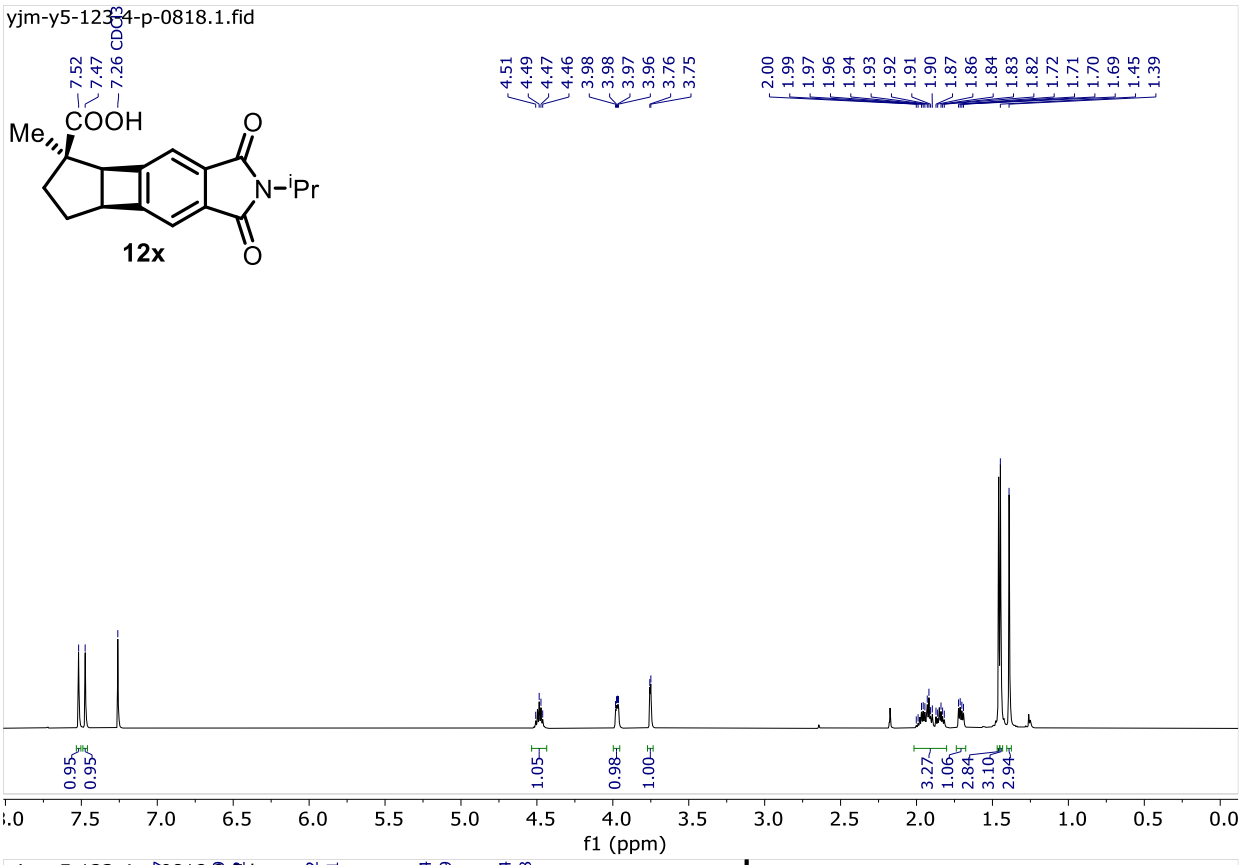

yjm-y5-58-8-p-0705.2.fid
Me
COOH
12u
f1 (ppm)

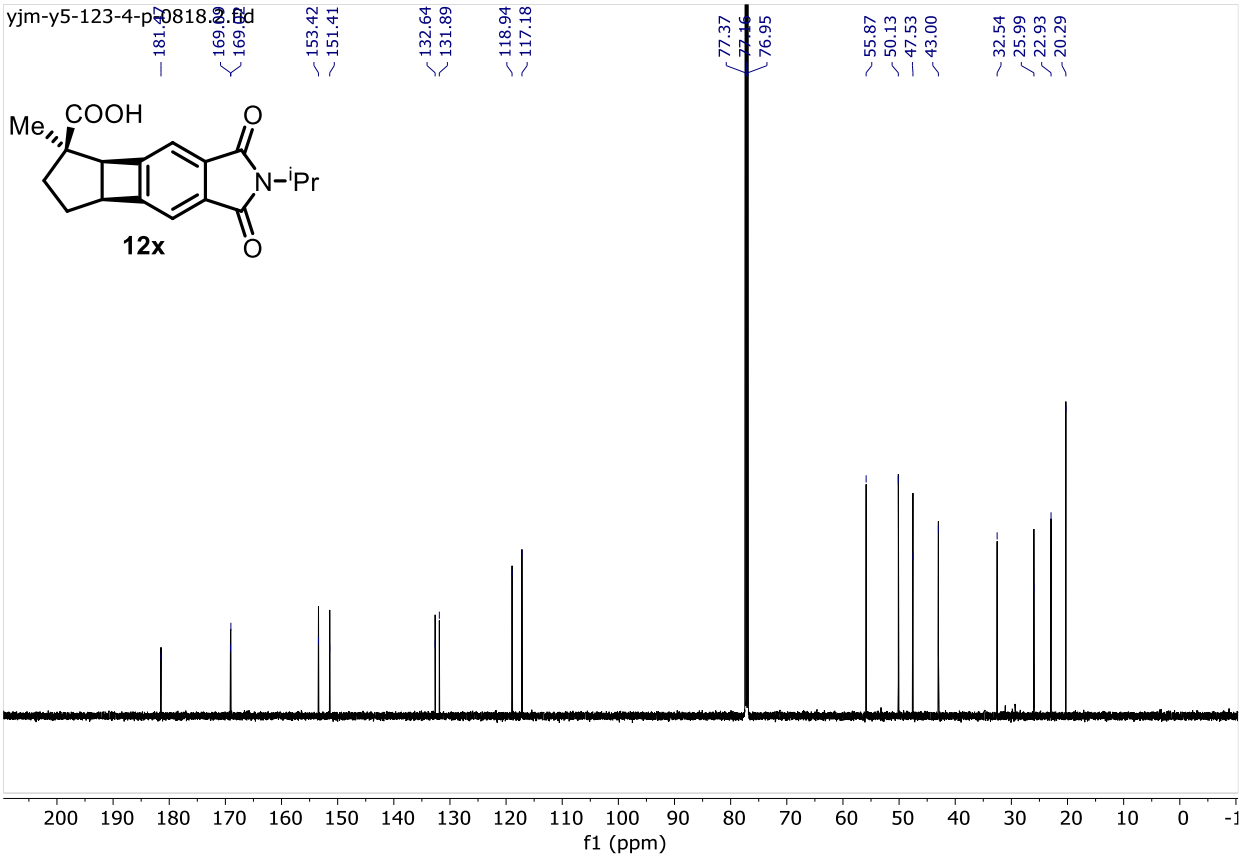

yjm-y5-58-3-p-0707.1.fid
7.26 CDCl3
6.82
6.81
3.88
3.87
3.87
3.86
3.65
3.64
2.23
2.19
1.96
1.95
1.94
1.93
1.92
1.83
1.82
1.82
1.81
1.81
1.80
1.63
1.62
1.61
1.59
1.32
Me
COOH
Me
Me
12v
0.98
0.93
0.98
0.98
3.08
2.94
0.94
2.00
1.13
3.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

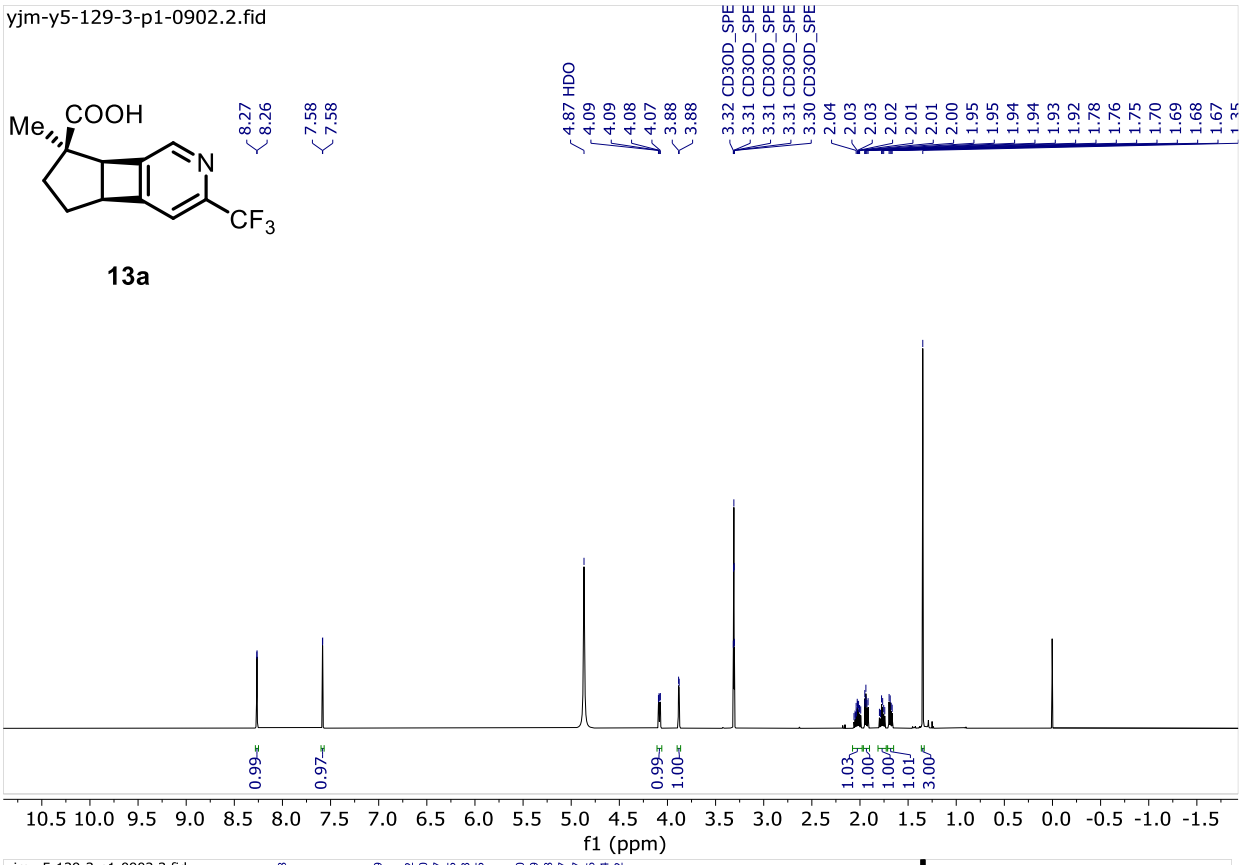

yjm-y5-58-3-p-0707.2.fid
182.24
143.84
142.00
136.80
135.94
124.20
123.03
77.37
77.16
76.95
56.13
49.75
47.44
32.46
26.20
22.89
20.58
20.51
Me
COOH
Me
Me
12v
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

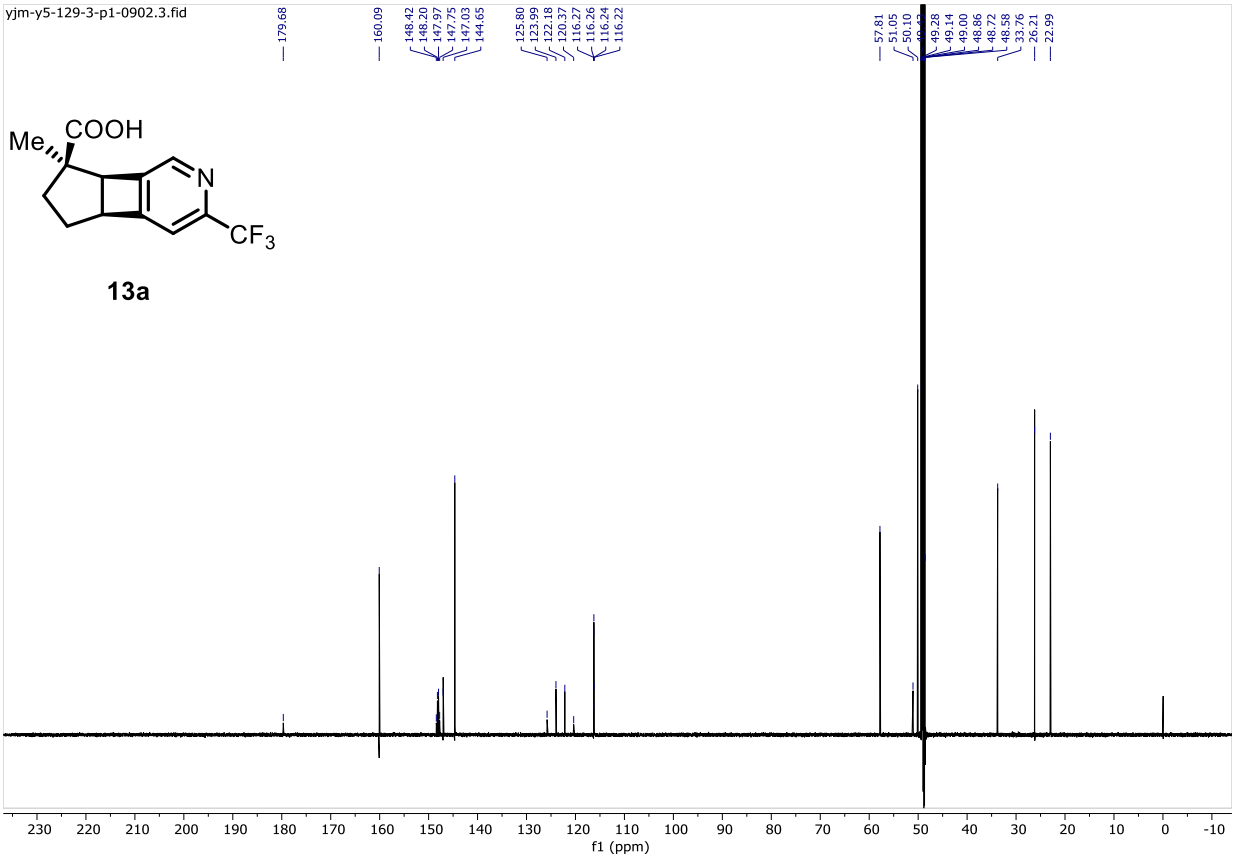

yjm-y5-58-2-p-0818.1.fid
Me
COOH
O
O
12w
f1 (ppm)

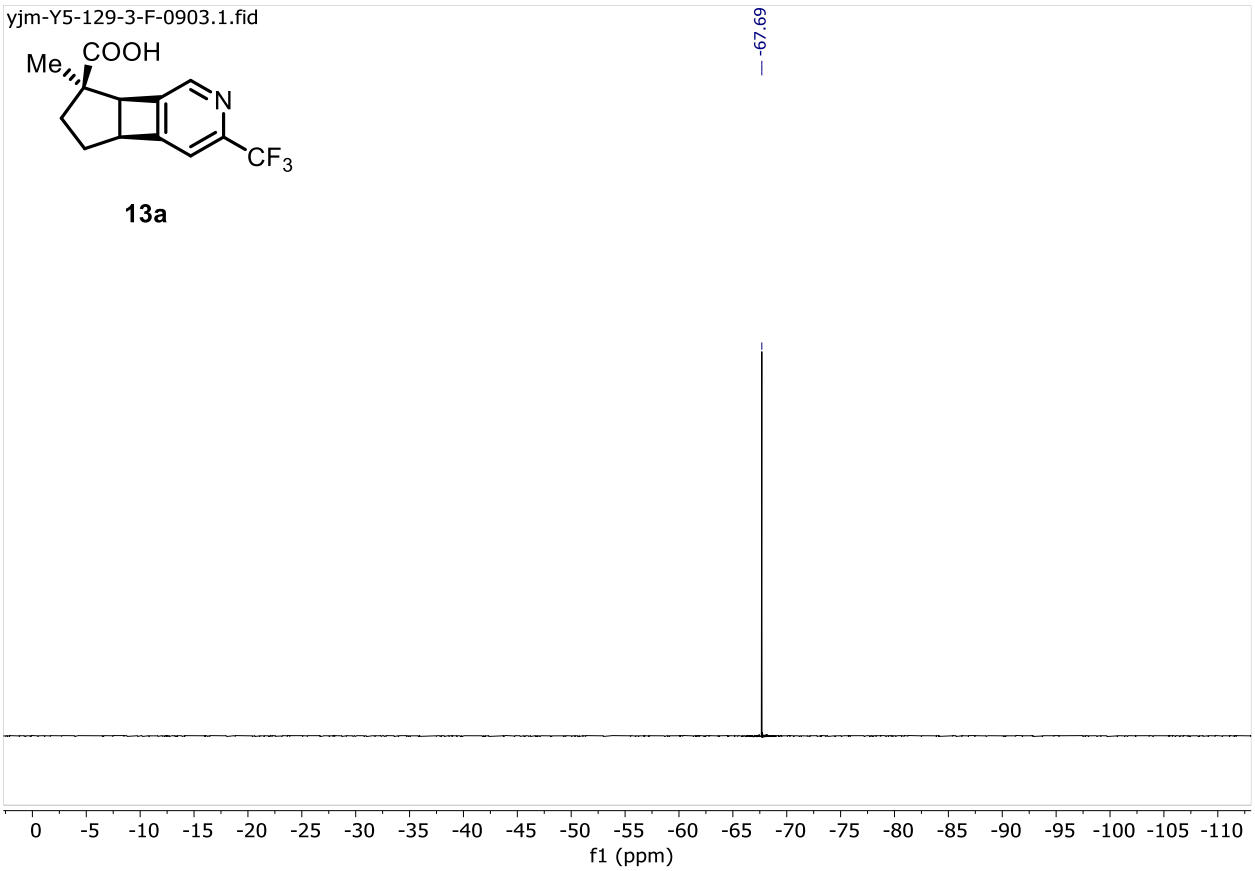

yjm-y5-58-2-p-0818.2.fid
Me
COOH
O
O
12w
f1 (ppm)


yjm-y5-123-4-p-0818.1.fid
7.52
7.47
7.26 CDCl3
4.51
4.49
4.47
4.46
3.98
3.98
3.97
3.96
3.76
3.75
2.00
1.99
1.97
1.96
1.94
1.93
1.92
1.91
1.90
1.87
1.86
1.84
1.83
1.82
1.72
1.71
1.70
1.69
1.45
1.39
COOH
Me
O
N–iPr
O
12x
0.95
0.95
1.05
0.98
1.00
3.27
1.06
2.84
3.10
2.94
f1 (ppm)


yjm-y5-123-4-p-0818.2.fid
181.
169.
169.
153.42
151.41
132.64
131.89
118.94
117.18
77.37
77.16
76.95
55.87
50.13
47.53
43.00
32.54
25.99
22.93
20.29
COOH
Me
O
N–iPr
O
12x
f1 (ppm)


yjm-y5-129-3-p1-0902.2.fid
Me
COOH
N
CF3
13a
8.27
8.26
7.58
7.58
4.87 HDO
4.09
4.09
4.08
4.07
3.88
3.88
3.32 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.30 CD3OD_SPE
2.04
2.03
2.03
2.02
2.01
2.01
2.00
1.95
1.95
1.94
1.94
1.93
1.92
1.78
1.76
1.75
1.70
1.69
1.68
1.67
0.99
0.97
0.99
1.00
1.03
1.00
1.00
1.01
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


yjm-y5-129-3-p1-0902.3.fid
179.68
160.09
148.42
148.20
147.97
147.75
147.03
144.65
125.80
123.99
122.18
120.37
116.27
116.26
116.24
116.22
57.81
51.05
50.10
49.28
49.14
49.00
48.86
48.72
48.58
33.76
26.21
22.99
Me
COOH
N
CF3
13a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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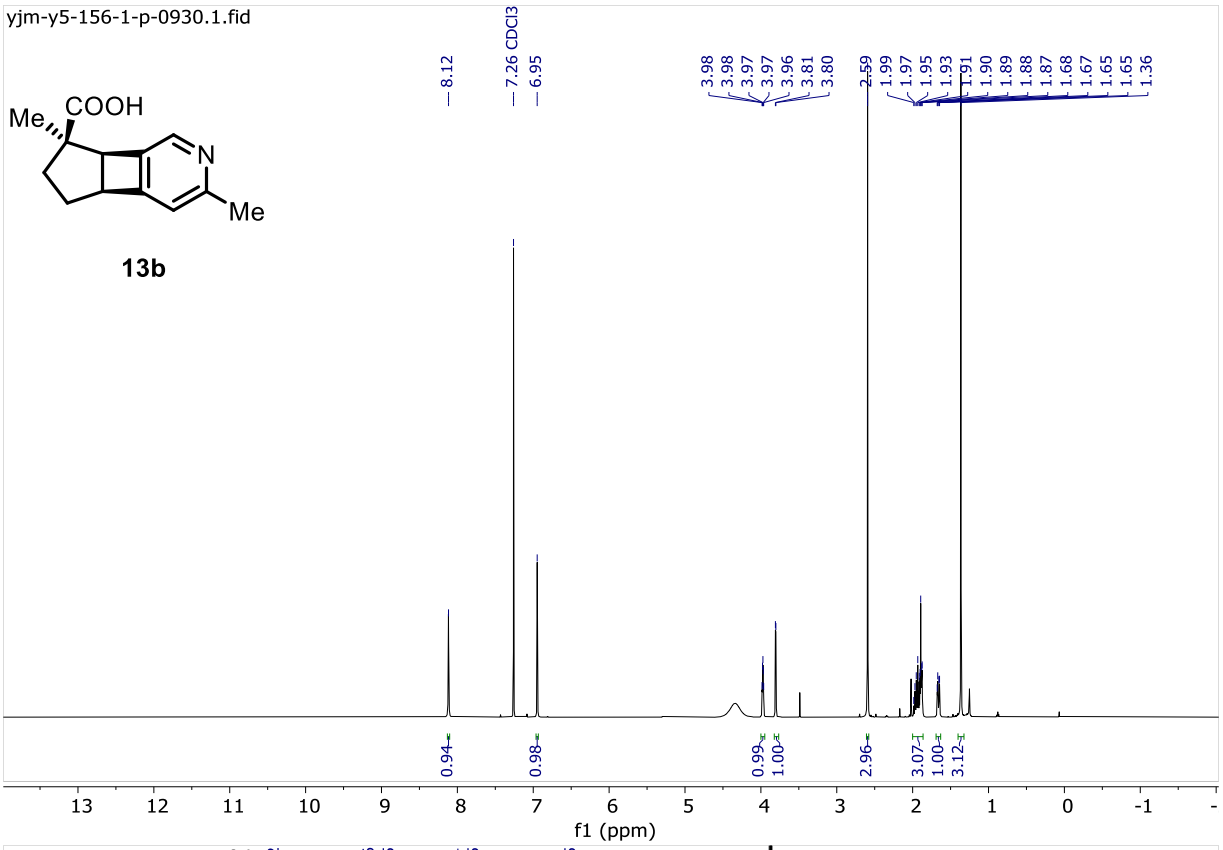
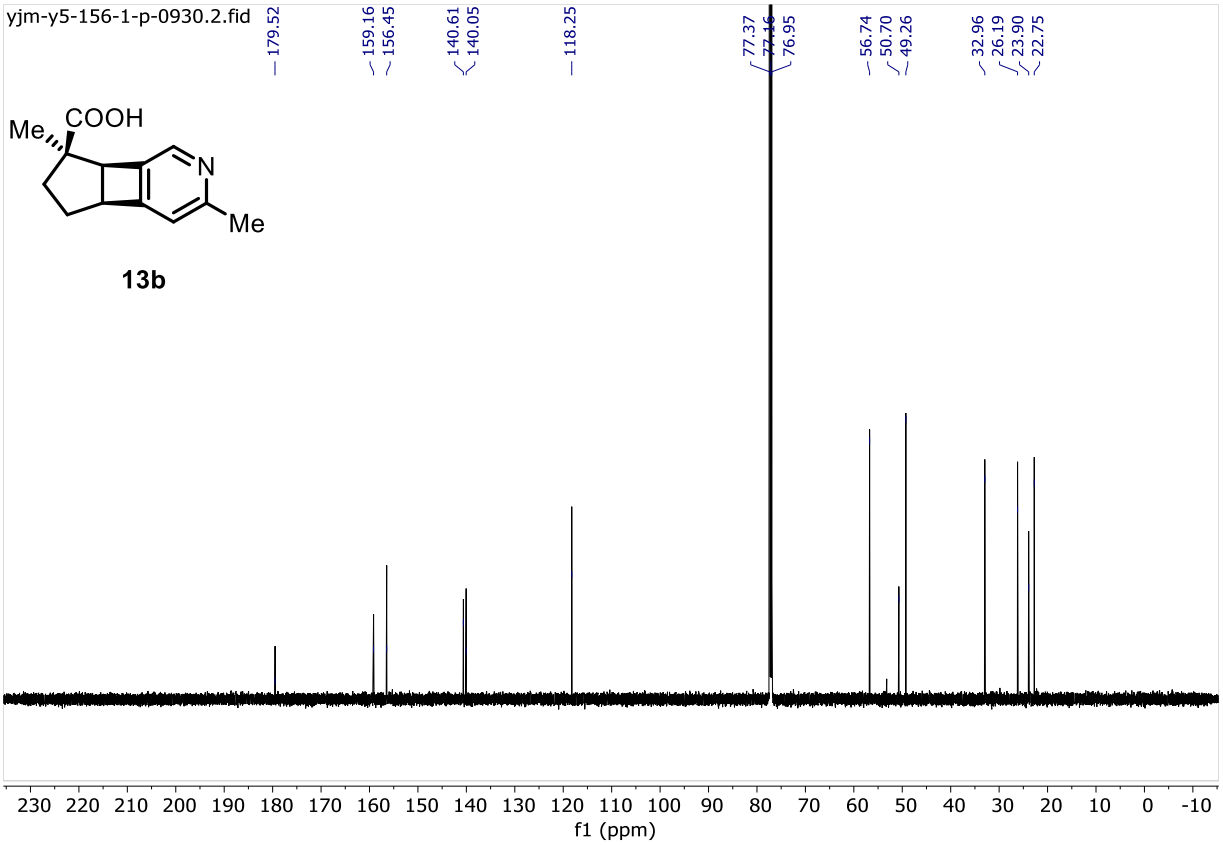
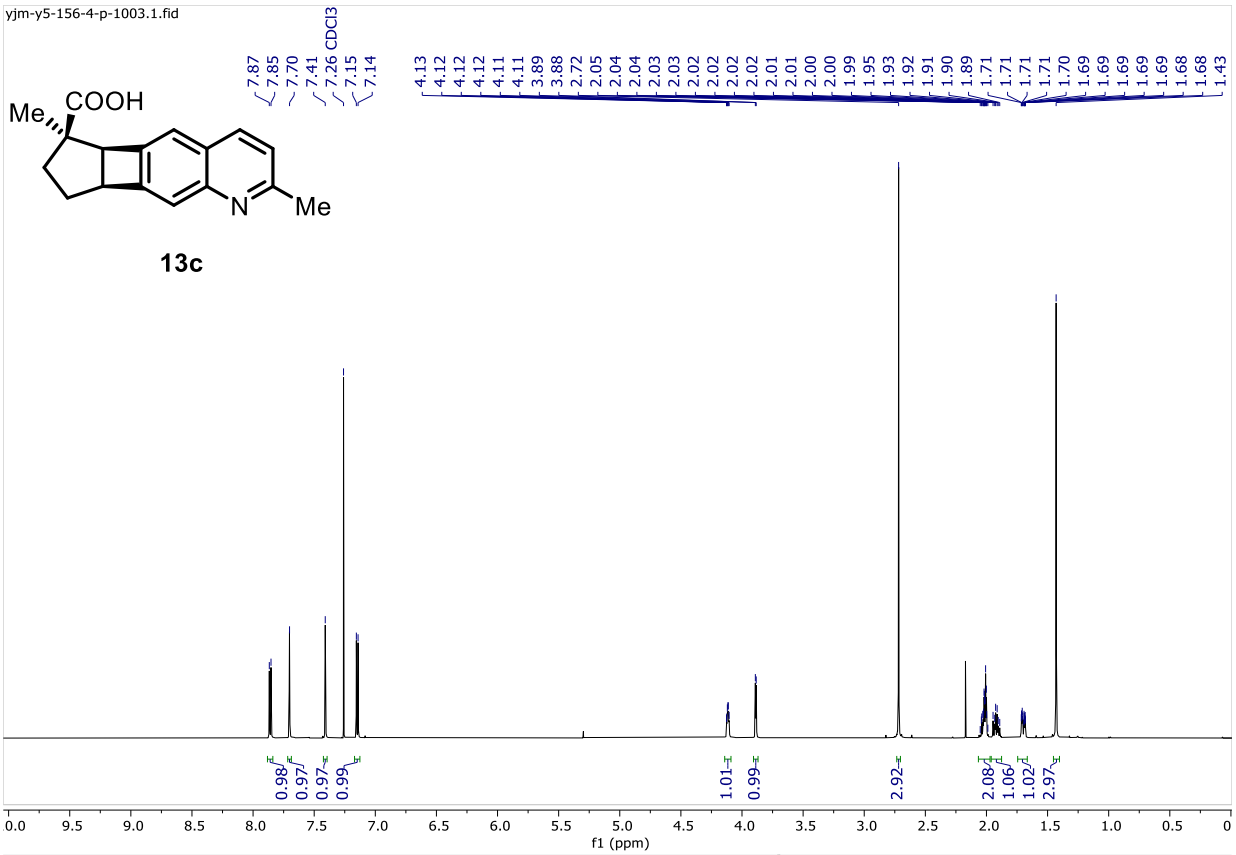
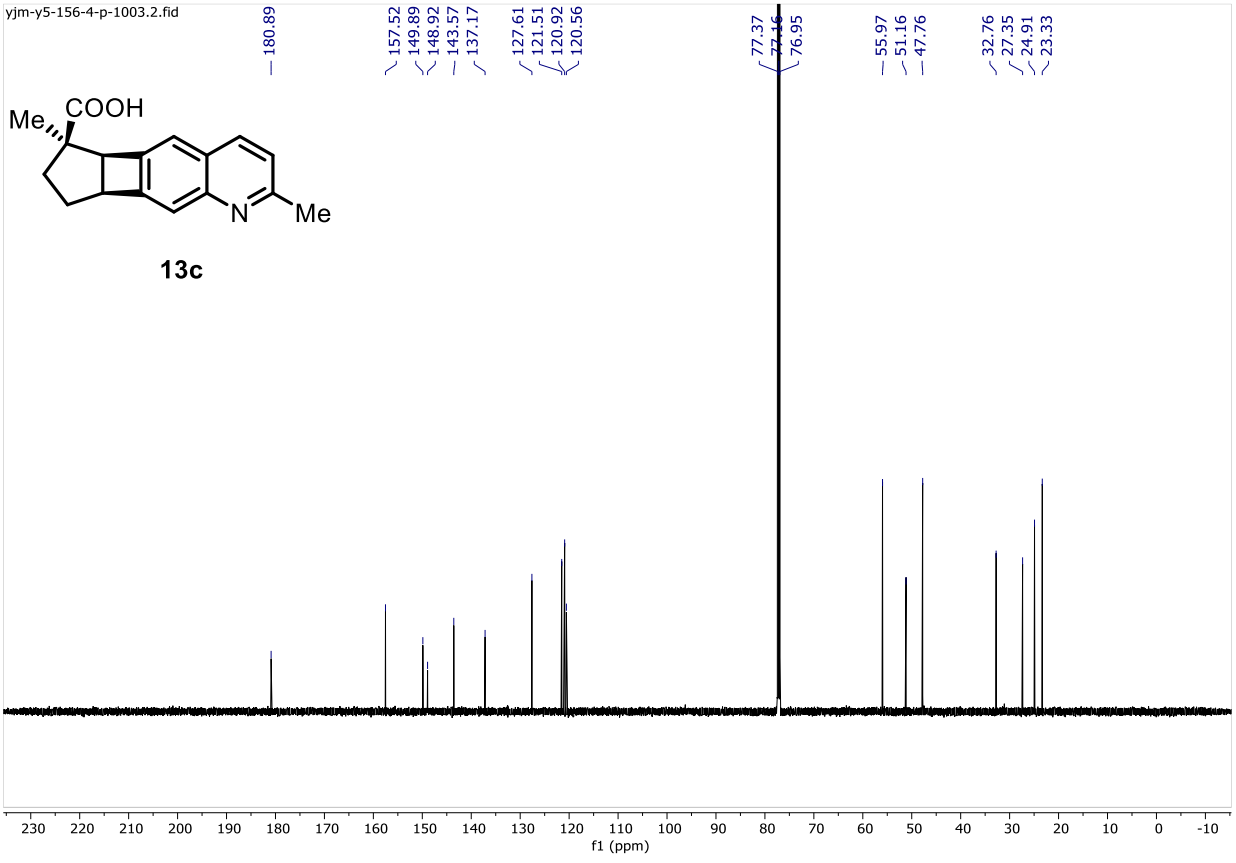
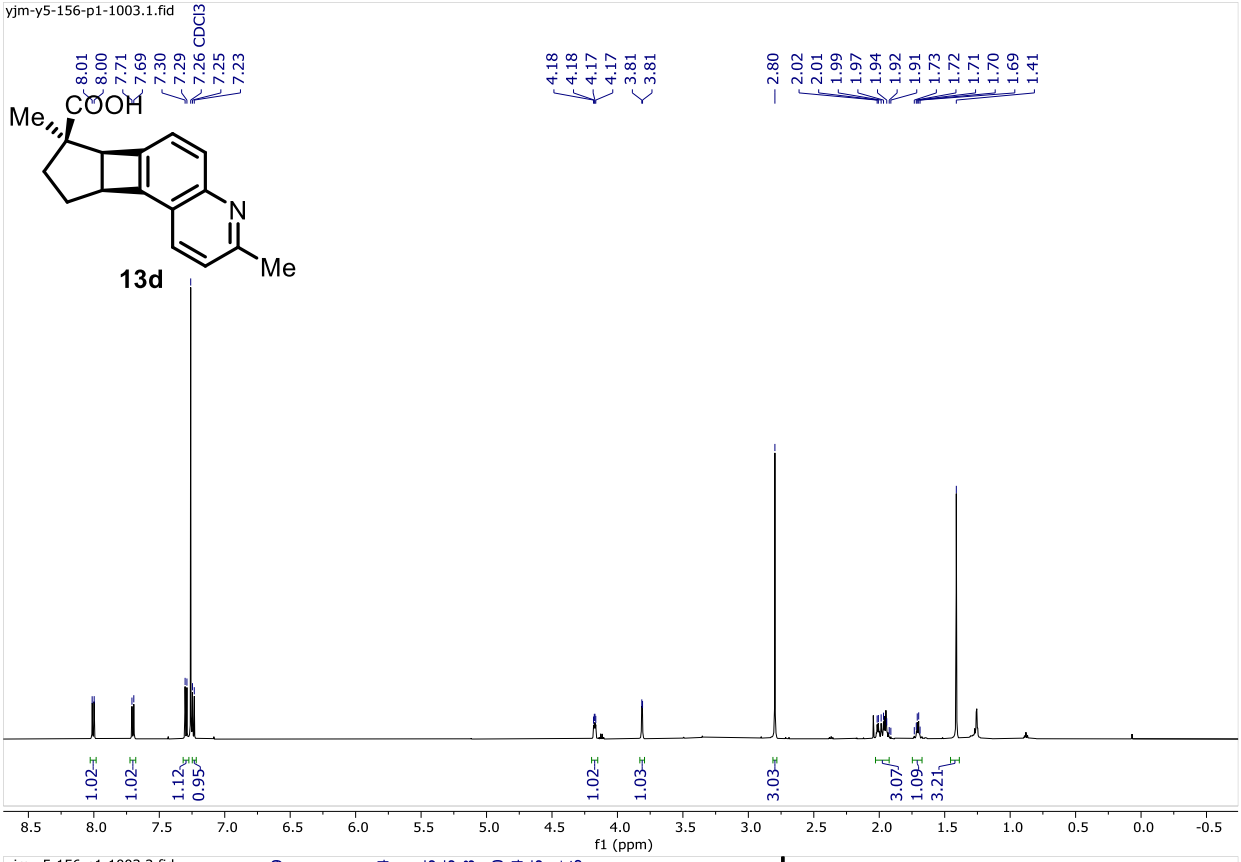
COOH
N
CF3
13a
-67.69
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110
f1 (ppm)

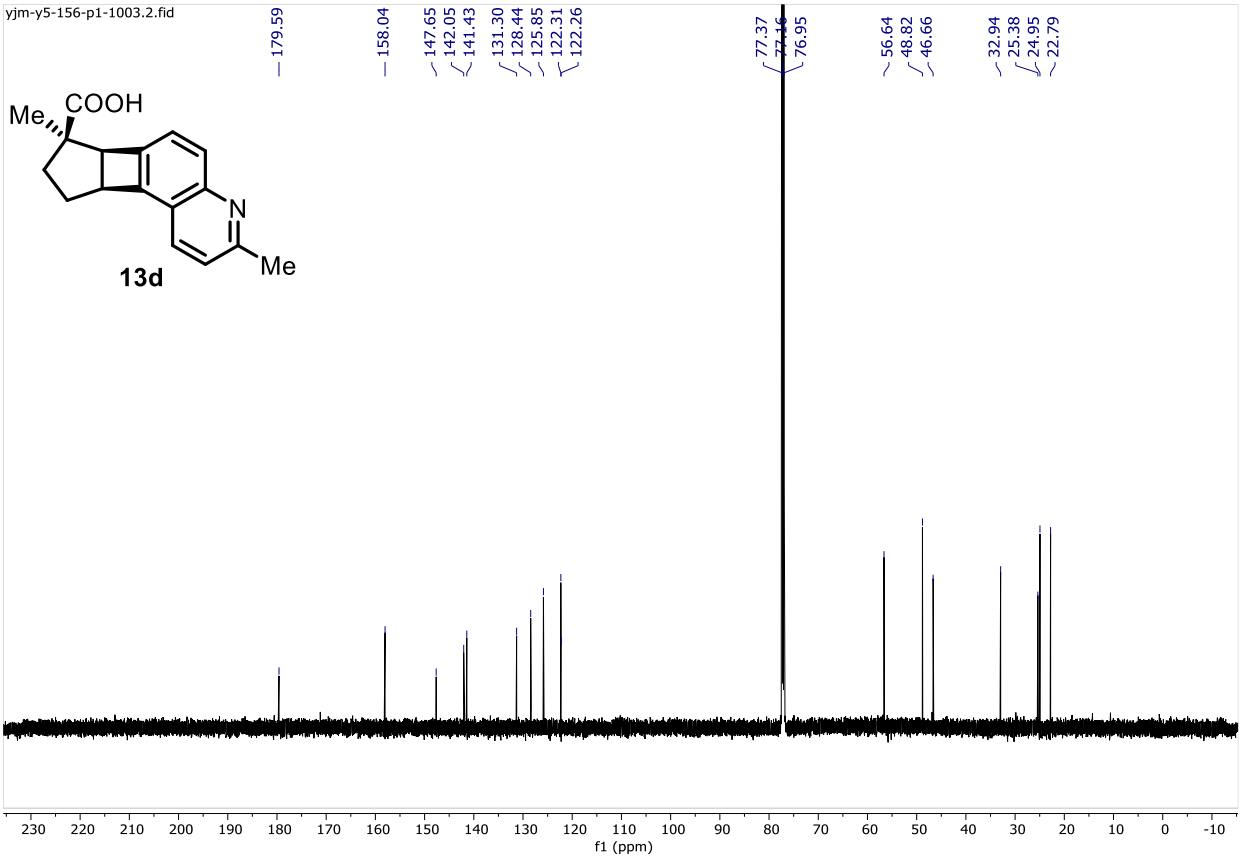

yjm-y5-156-1-p-0930.1.fid
Me
COOH
N
Me
13b
8.12
7.26 CDCl3
6.95
3.98
3.98
3.97
3.97
3.96
3.81
3.80
2.59
1.99
1.97
1.95
1.93
1.91
1.90
1.89
1.88
1.87
1.68
1.67
1.65
1.65
1.36
0.94
0.98
0.99
1.00
2.96
3.07
1.00
3.12
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

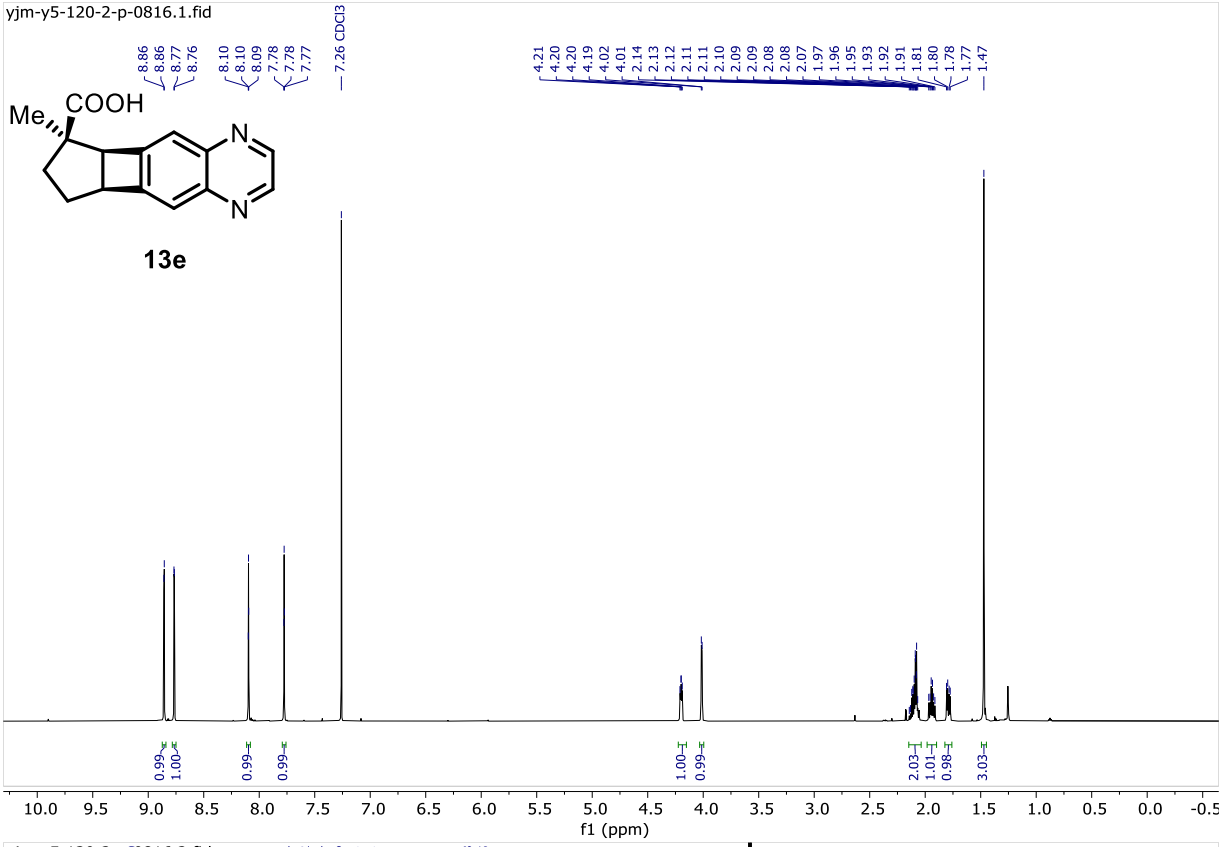

yjm-y5-156-1-p-0930.2.fid
Me
COOH
N
Me
13b
179.52
159.16
156.45
140.61
140.05
118.25
77.37
77.16
76.95
56.74
50.70
49.26
32.96
26.19
23.90
22.75
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

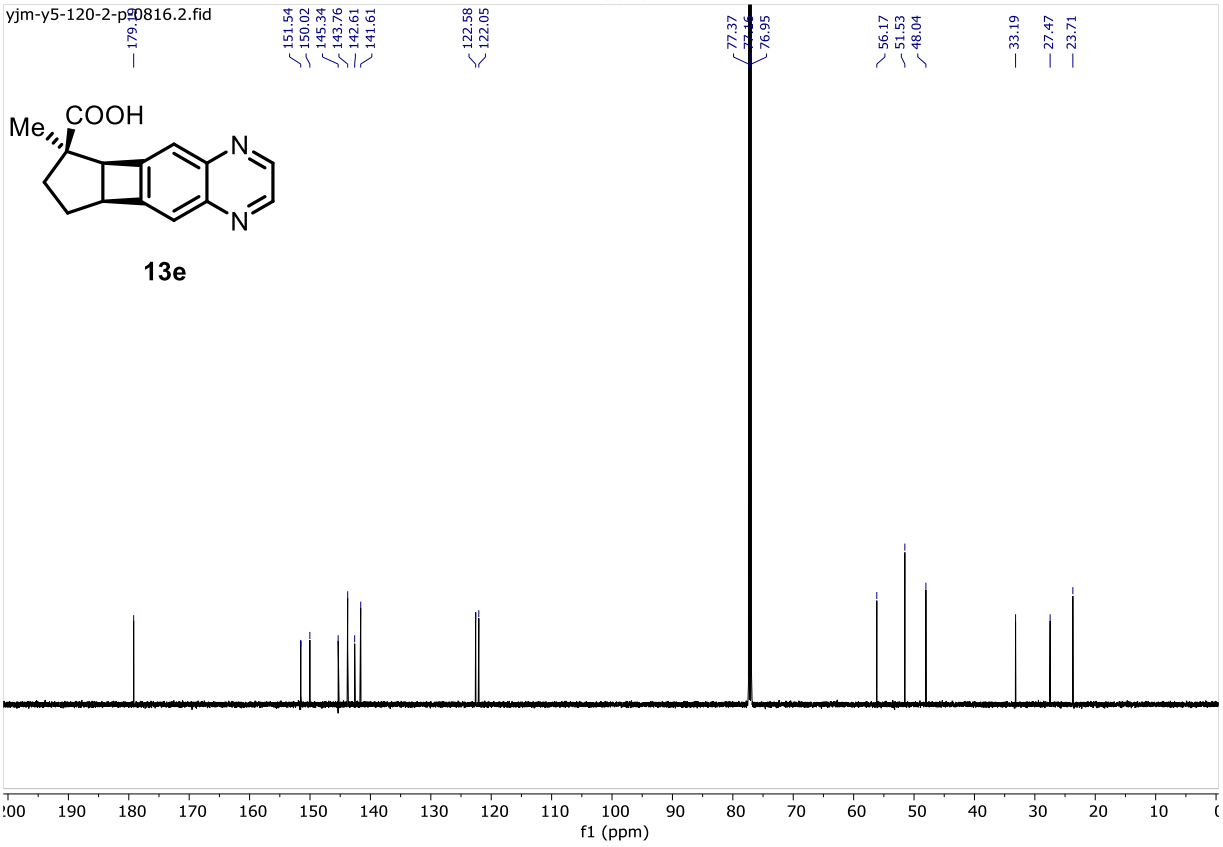

yjm-y5-156-4-p-1003.1.fid
Me
COOH
N
Me
13c
7.87
7.85
7.70
7.41
7.26 CDCl3
7.15
7.14
4.13
4.12
4.12
4.12
4.11
4.11
3.89
3.88
2.72
2.05
2.04
2.04
2.03
2.03
2.02
2.02
2.02
2.02
2.01
2.01
2.00
2.00
1.99
1.95
1.93
1.92
1.91
1.90
1.89
1.71
1.71
1.71
1.71
1.70
1.69
1.69
1.69
1.69
1.68
1.68
1.43
0.98
0.97
0.97
0.99
1.01
0.99
2.92
2.08
1.06
1.02
2.97
f1 (ppm)

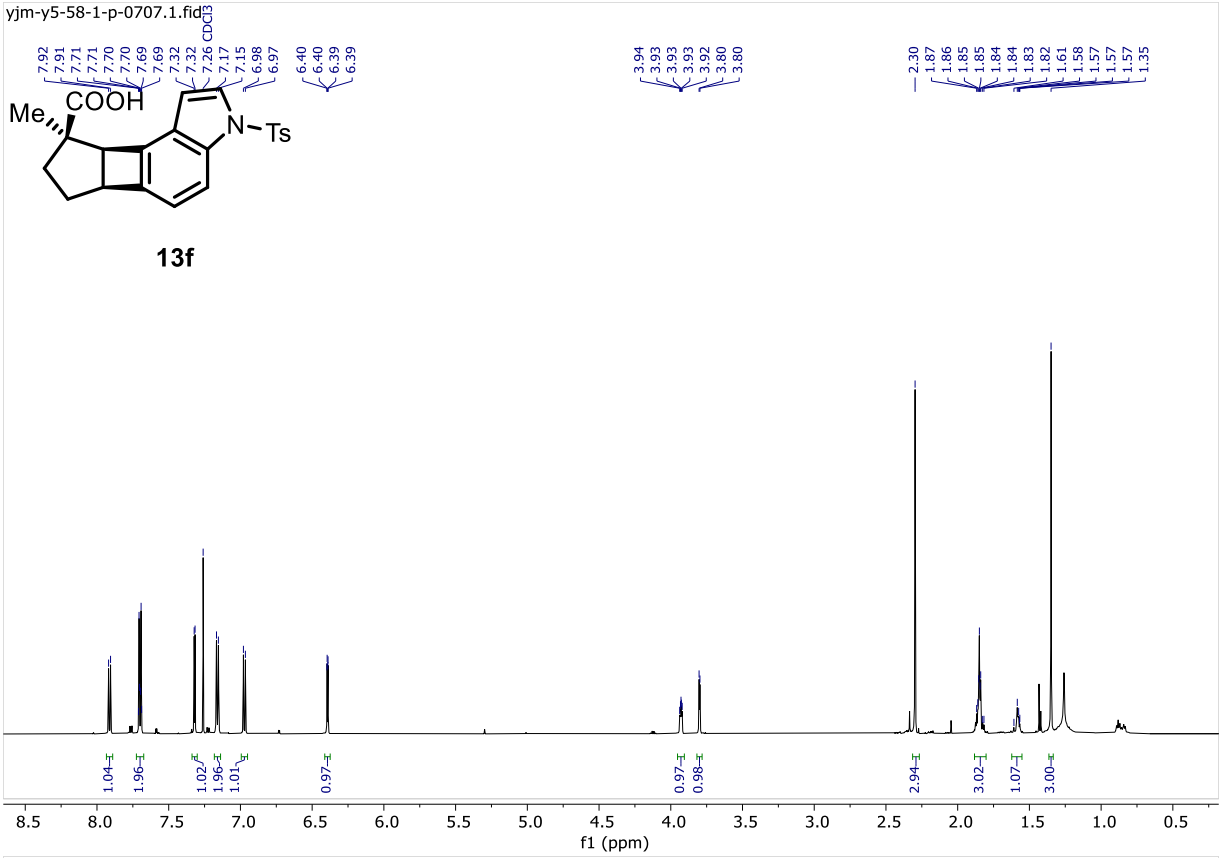

yjm-y5-156-4-p-1003.2.fid
Me
COOH
N
Me
13c
180.89
157.52
149.89
148.92
143.57
137.17
127.61
121.51
120.92
120.56
77.37
77.16
76.95
55.97
51.16
47.76
32.76
27.35
24.91
23.33
f1 (ppm)

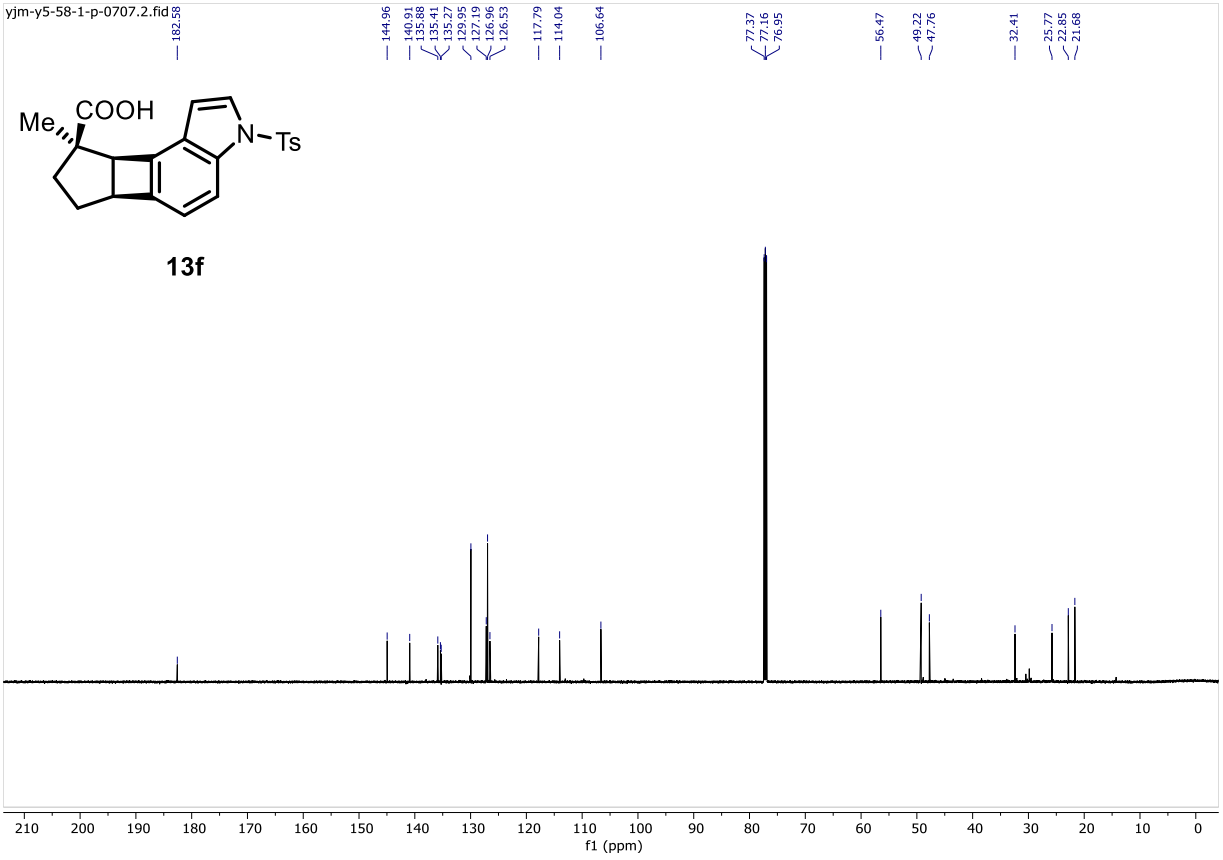

yjm-y5-156-p1-1003.1.fid
8.01
8.00
7.71
7.69
7.30
7.29
7.26 CDCl3
7.25
7.23
4.18
4.18
4.17
4.17
3.81
3.81
2.80
2.02
2.01
1.99
1.97
1.94
1.92
1.91
1.73
1.72
1.71
1.70
1.69
1.41
Me
COOH
N
Me
13d
1.02
1.02
1.12
0.95
1.02
1.03
3.03
3.07
1.09
3.21
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

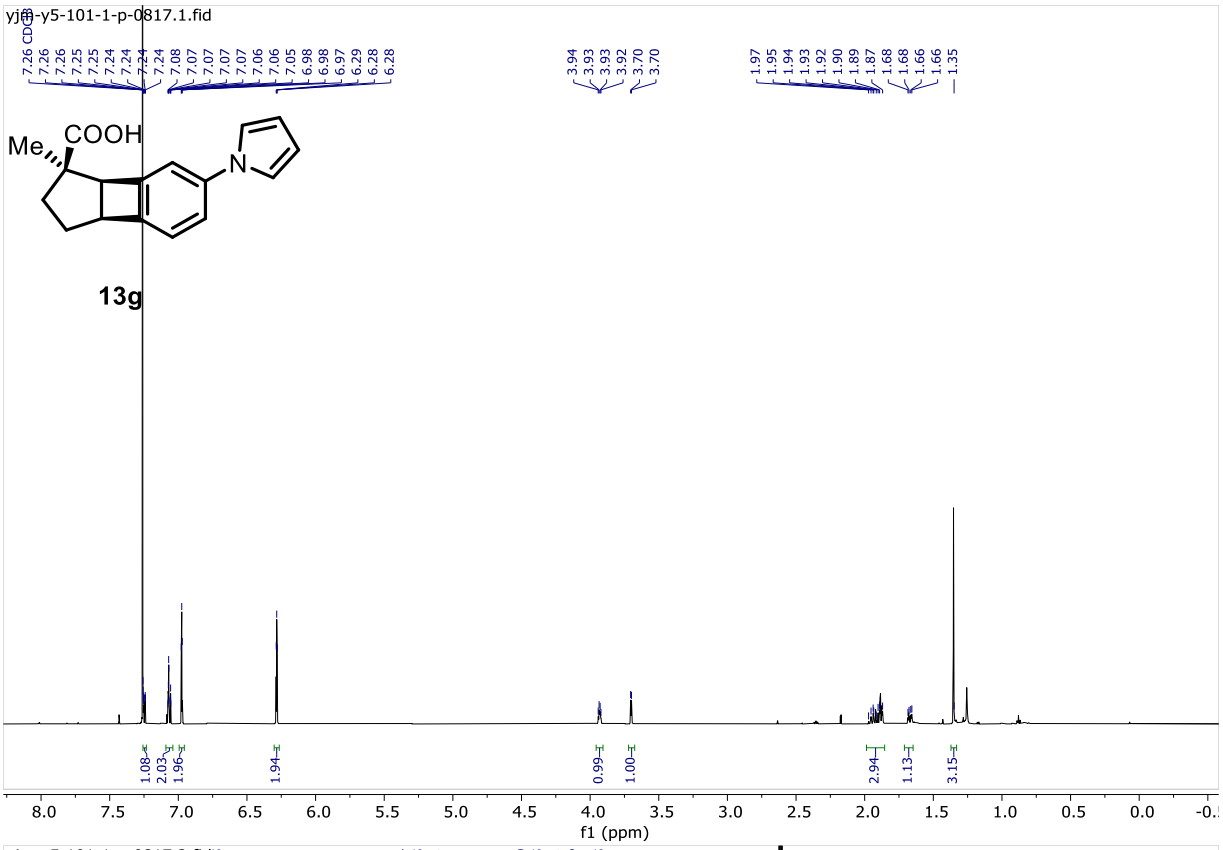

yjm-y5-156-p1-1003.2.fid
179.59
158.04
147.65
142.05
141.43
131.30
128.44
125.85
122.31
122.26
77.37
77.16
76.95
56.64
48.82
46.66
32.94
25.38
24.95
22.79
Me
COOH
N
Me
13d
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

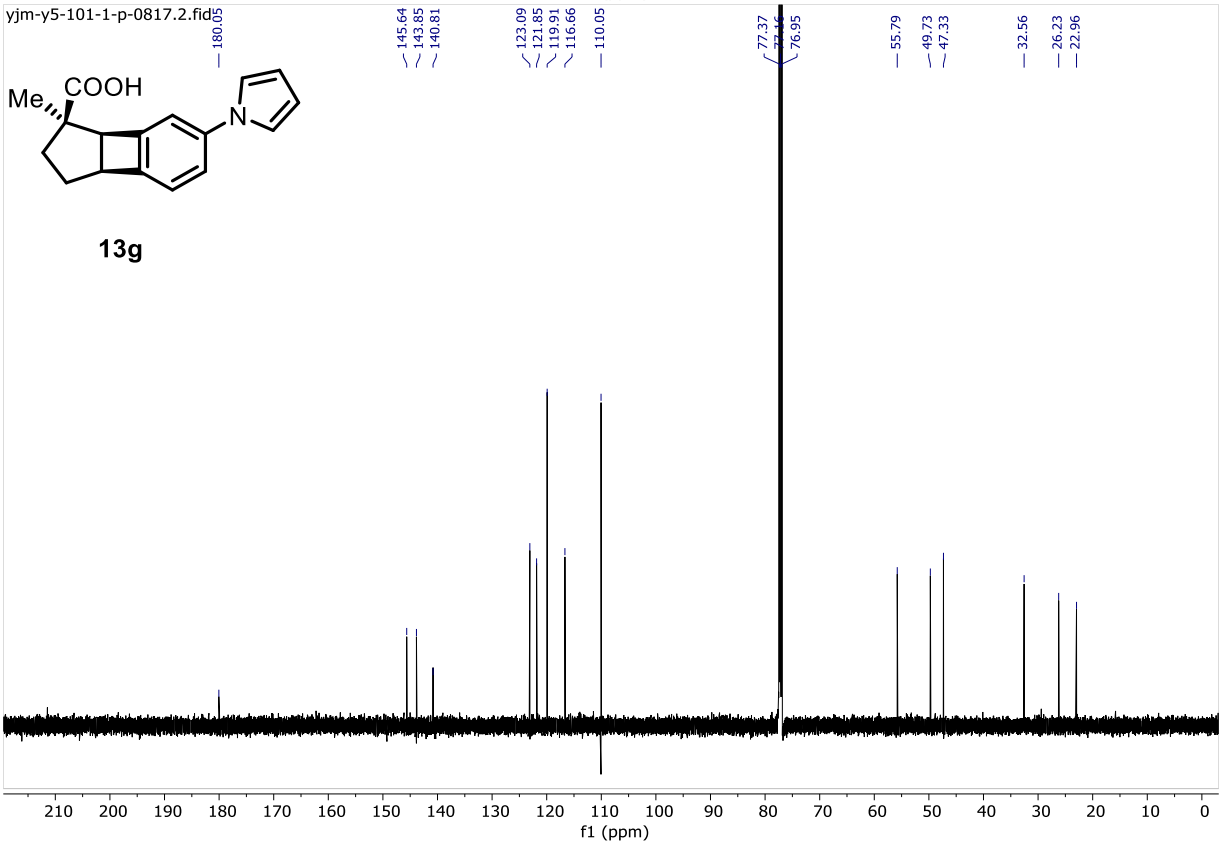

yjm-y5-120-2-p-0816.1.fid
Me
COOH
N
N
13e
f1 (ppm)

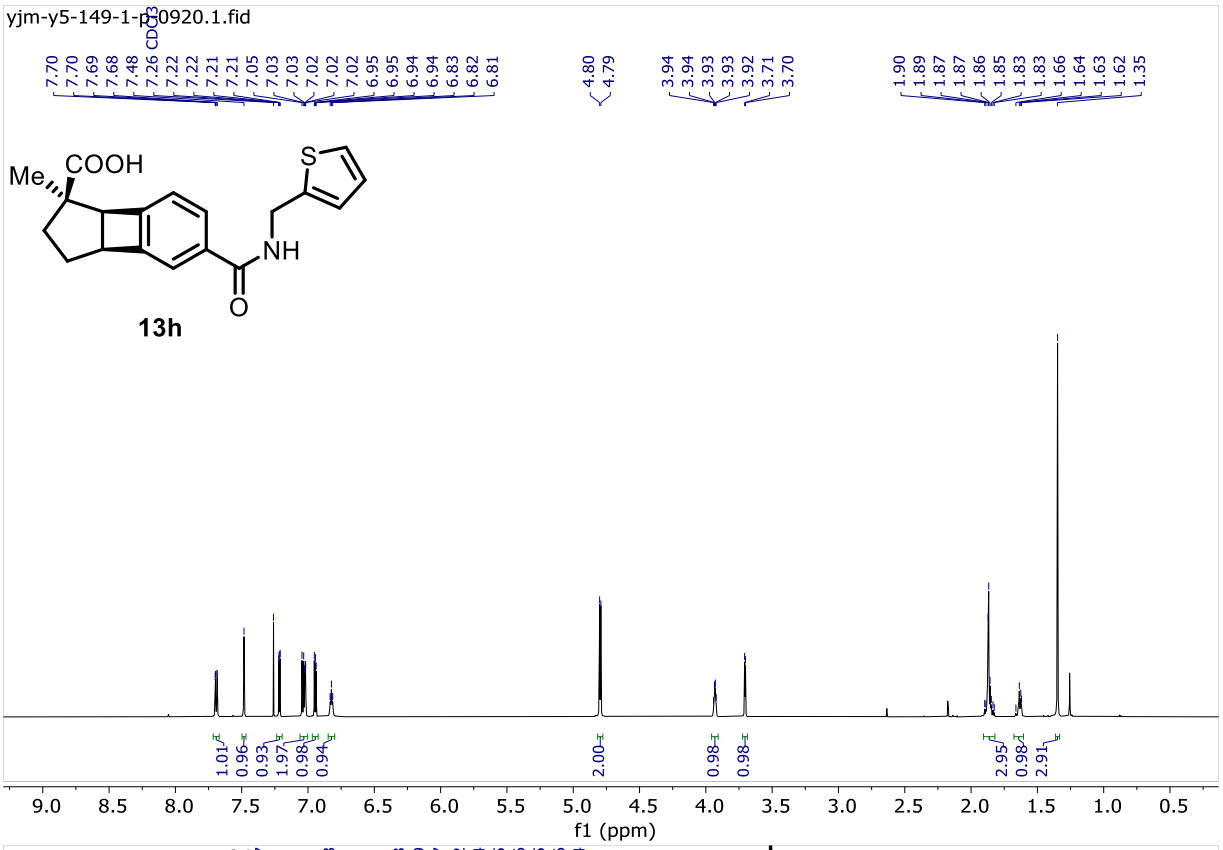

yjm-y5-120-2-p-0816.2.fid
Me
COOH
N
N
13e
f1 (ppm)

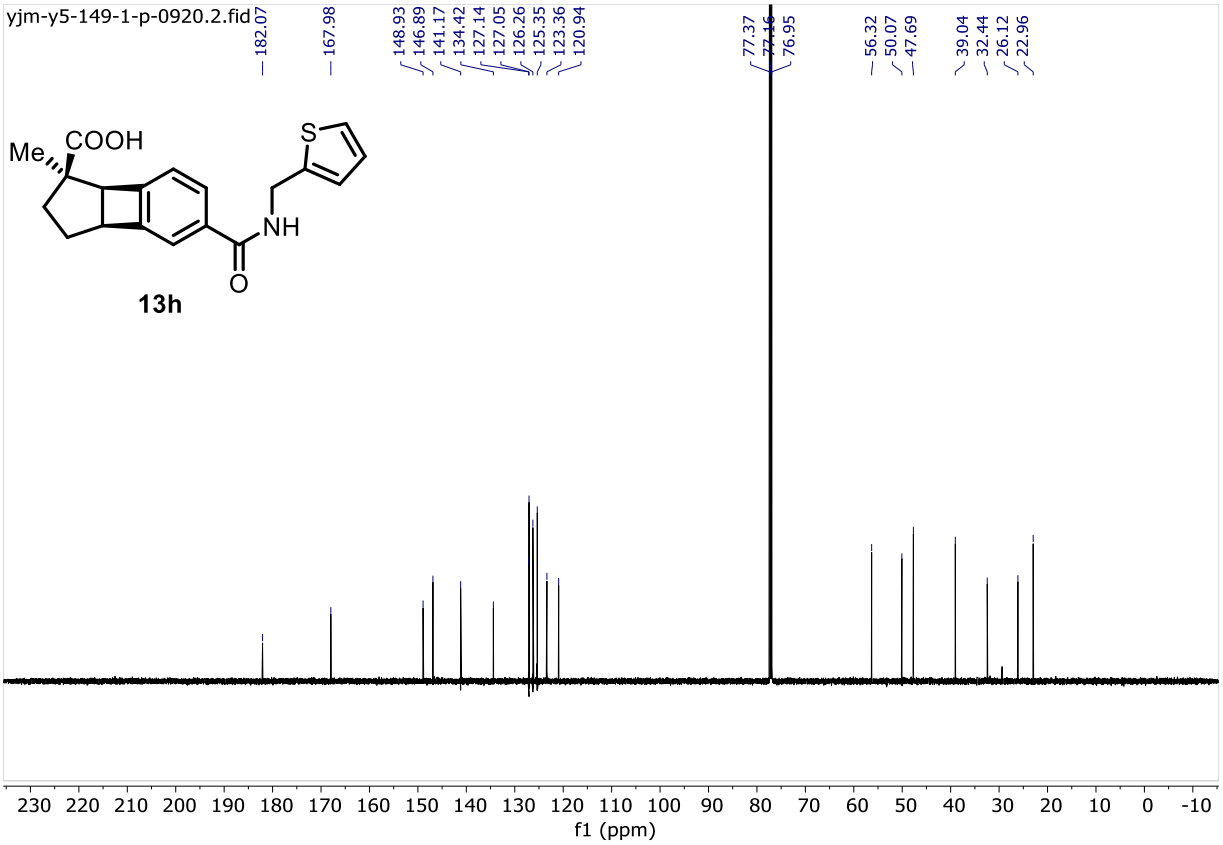

yjm-y5-58-1-p-0707.1.fid
Me
COOH
N
Ts
13f
f1 (ppm)

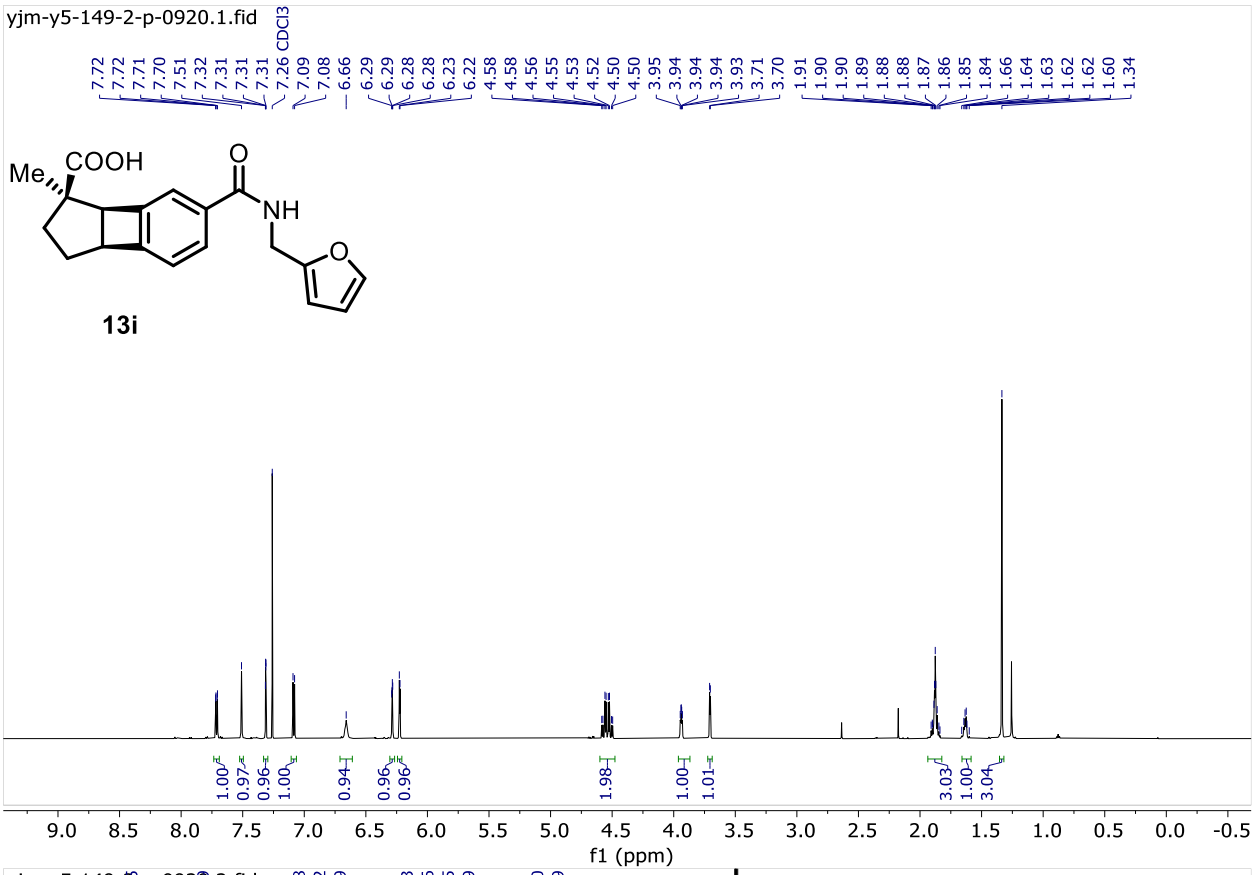

yjm-y5-58-1-p-0707.2.fid
Me
COOH
N
Ts
13f
f1 (ppm)

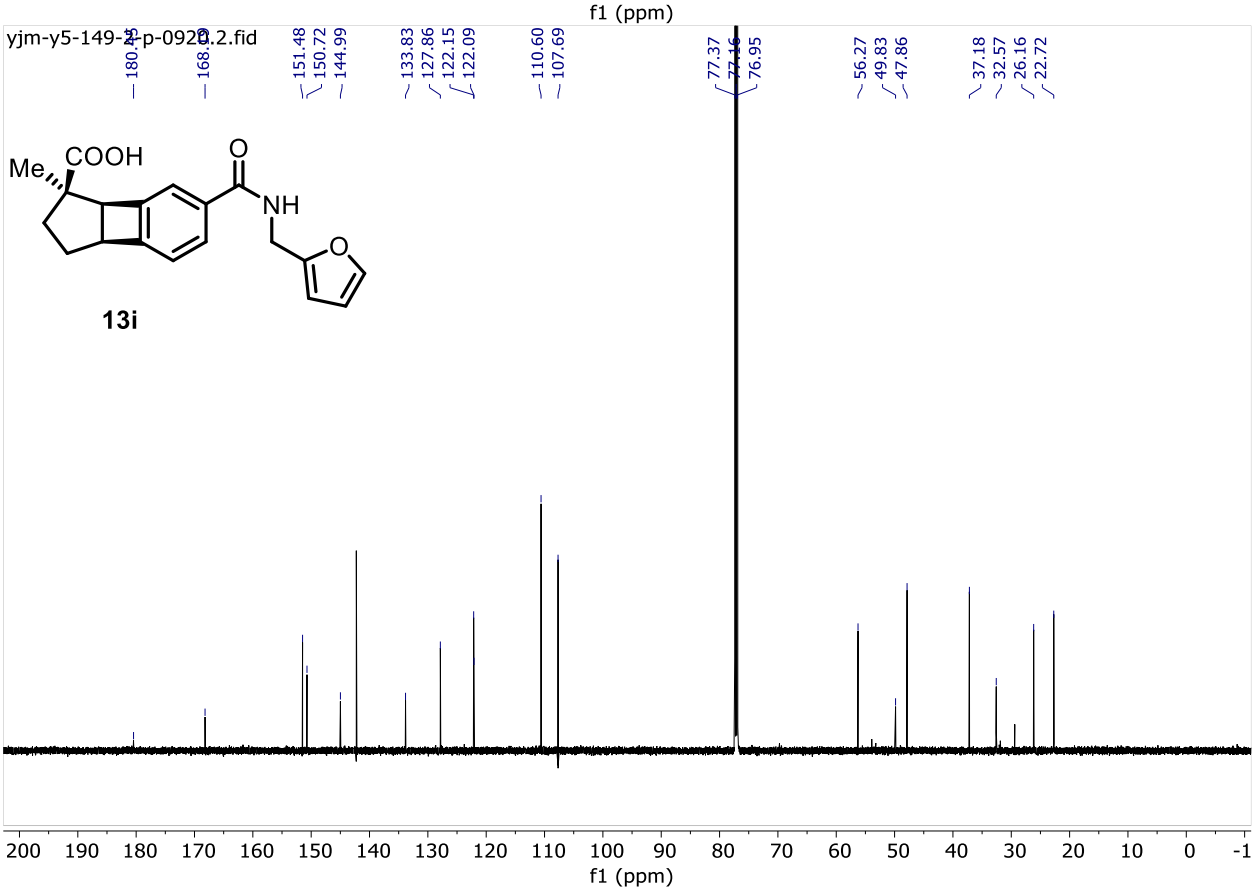

yjm-y5-101-1-p-0817.1.fid
Me
COOH
N
13g
f1 (ppm)

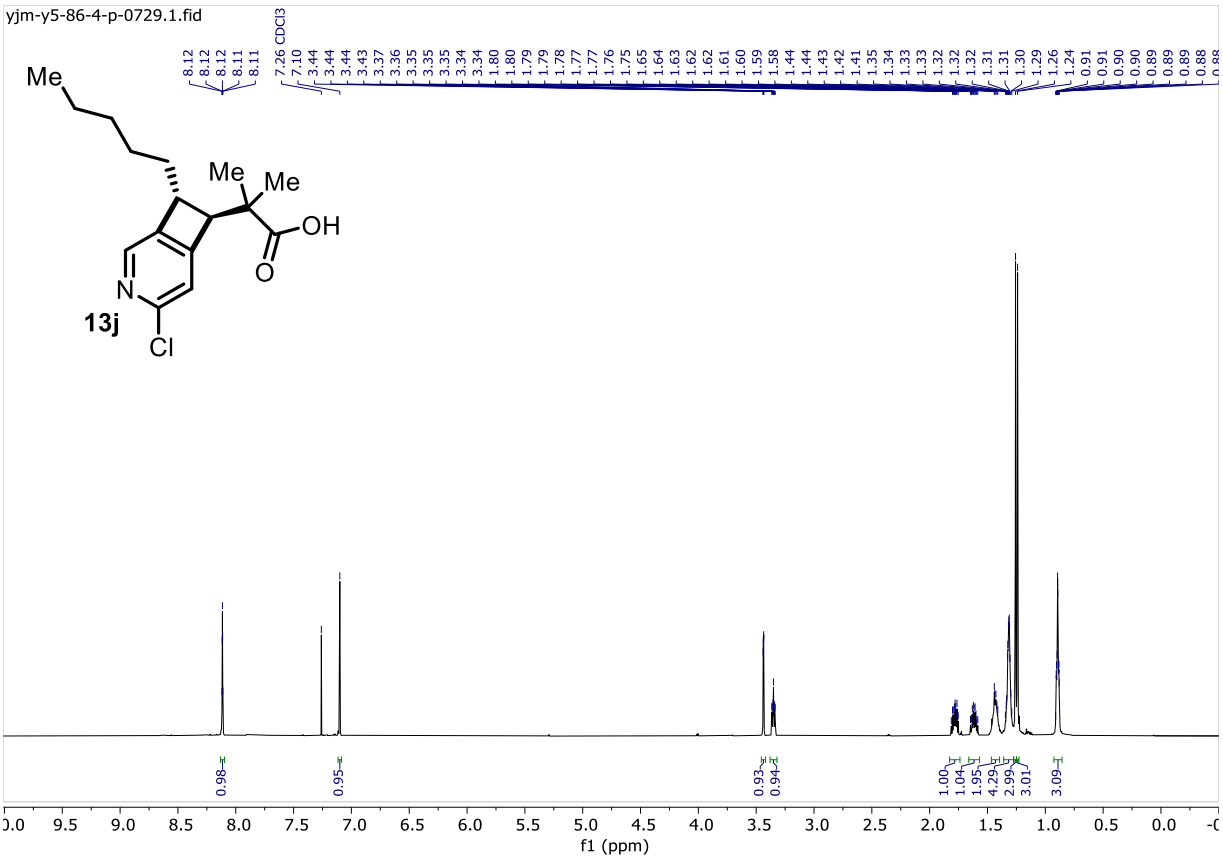

yjm-y5-101-1-p-0817.2.fid
Me
COOH
N
13g
f1 (ppm)

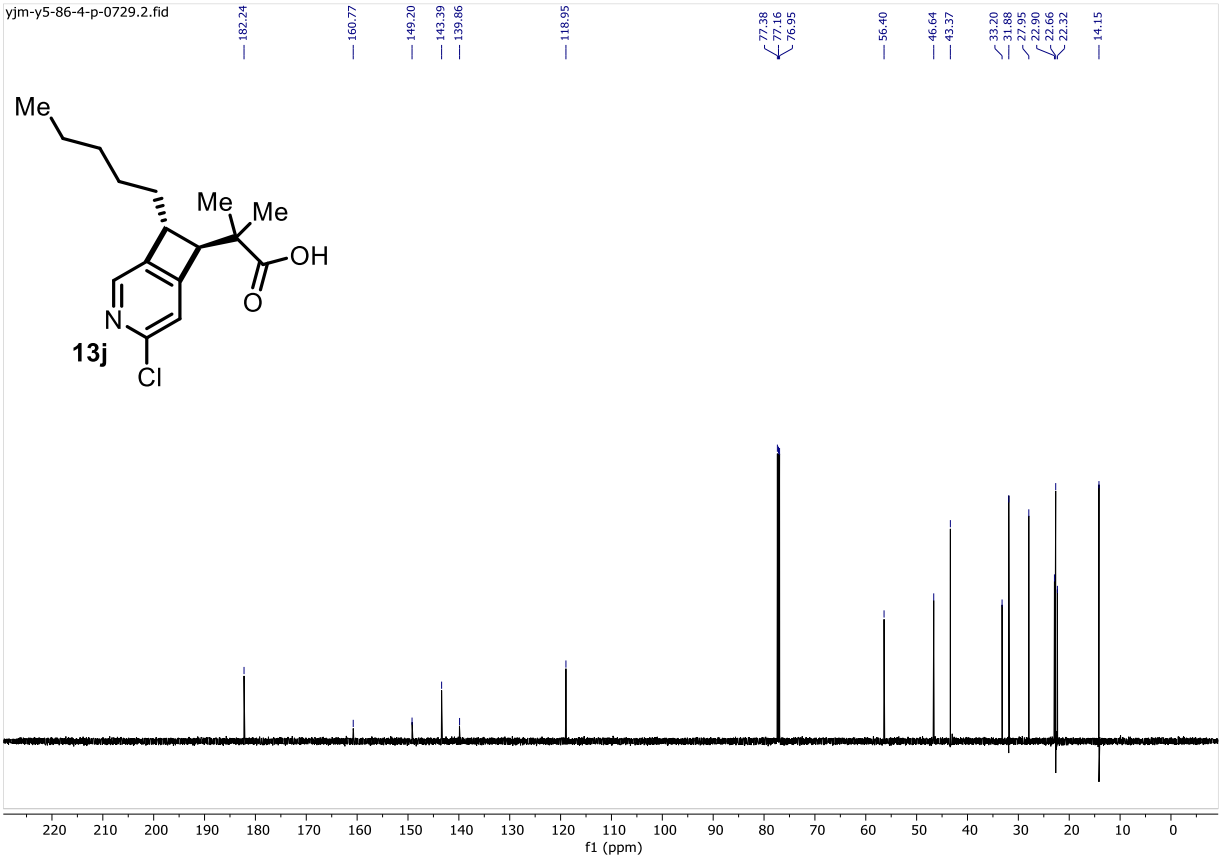

yjm-y5-149-1-p-0920.1.fid
CDCl3
7.70 7.70 7.69 7.68 7.48 7.26 7.22 7.22 7.21 7.21 7.05 7.03 7.03 7.02 7.02 7.02 6.95 6.95 6.94 6.94 6.83 6.82 6.81
4.80 4.79
3.94 3.94 3.93 3.93 3.92 3.71 3.70
1.90 1.89 1.87 1.87 1.86 1.85 1.83 1.83 1.66 1.64 1.63 1.62 1.35
Me
COOH
S
NH
O
13h
1.01 0.96 0.93 1.97 0.98 0.94 2.00 0.98 0.98 2.95 0.98 2.91
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

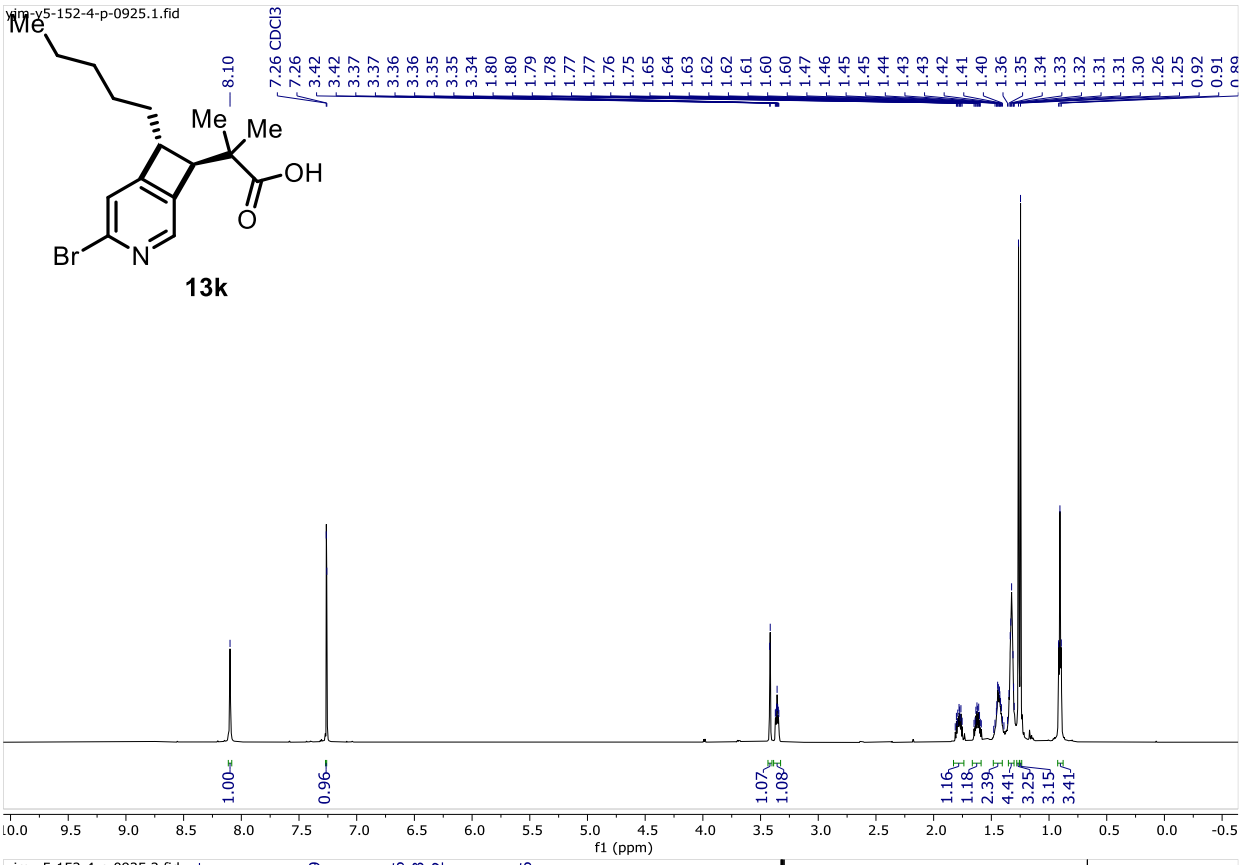

yjm-y5-149-1-p-0920.2.fid
182.07 167.98 148.93 146.89 141.17 134.42 127.14 127.05 126.26 125.35 123.36 120.94
77.37 77.16 76.95
56.32 50.07 47.69 39.04 32.44 26.12 22.96
Me
COOH
S
NH
O
13h
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

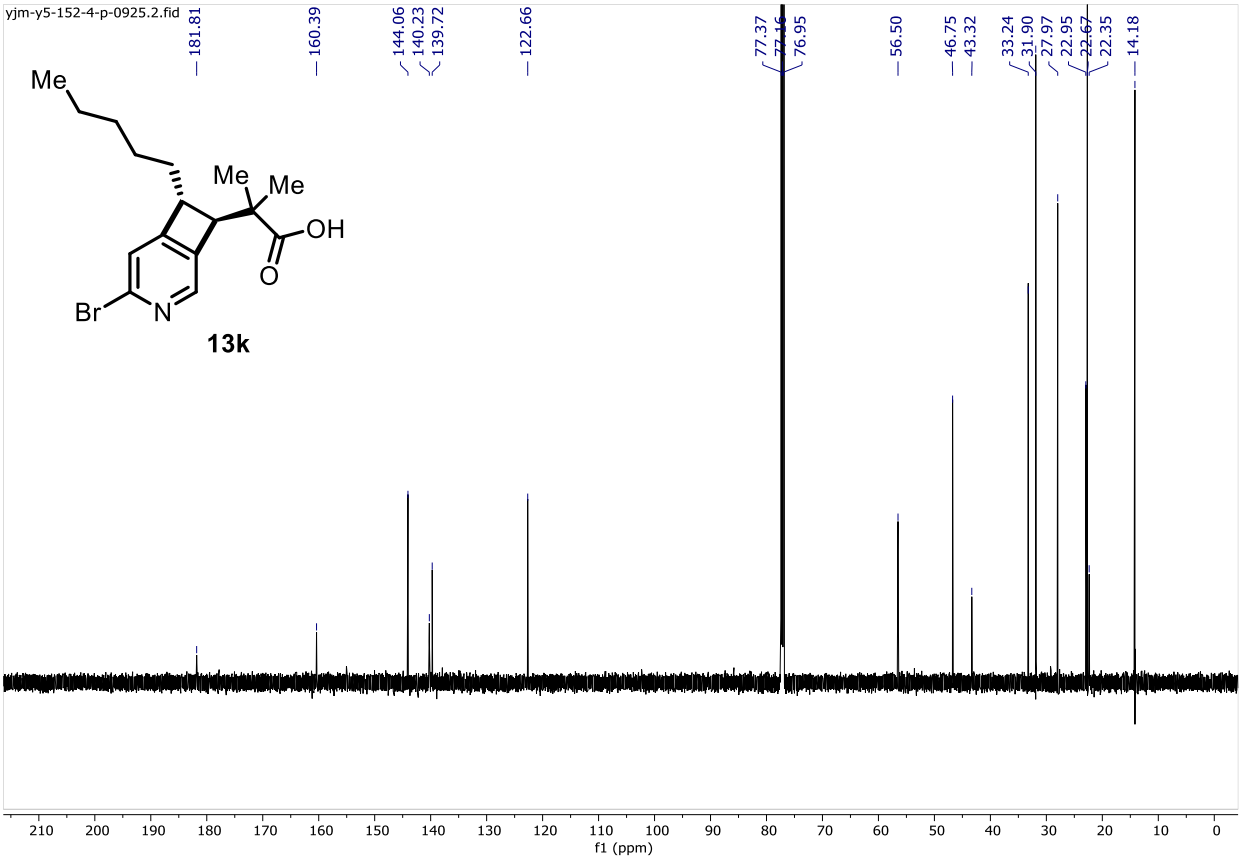

yjm-y5-149-2-p-0920.1.fid
7.72 7.72 7.71 7.70 7.51 7.32 7.31 7.31 7.31 7.26 CDCl3 7.09 7.08 6.66 6.29 6.29 6.28 6.28 6.23 6.22 4.58 4.56 4.55 4.53 4.52 4.50 4.50 3.95 3.94 3.94 3.93 3.71 3.70 1.91 1.90 1.90 1.89 1.88 1.88 1.87 1.86 1.85 1.84 1.66 1.64 1.63 1.62 1.62 1.60 1.34
Me COOH O NH O
13i
1.00 0.97 0.96 1.00 0.94 0.96 0.96 1.98 1.00 1.01 3.03 1.00 3.04
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

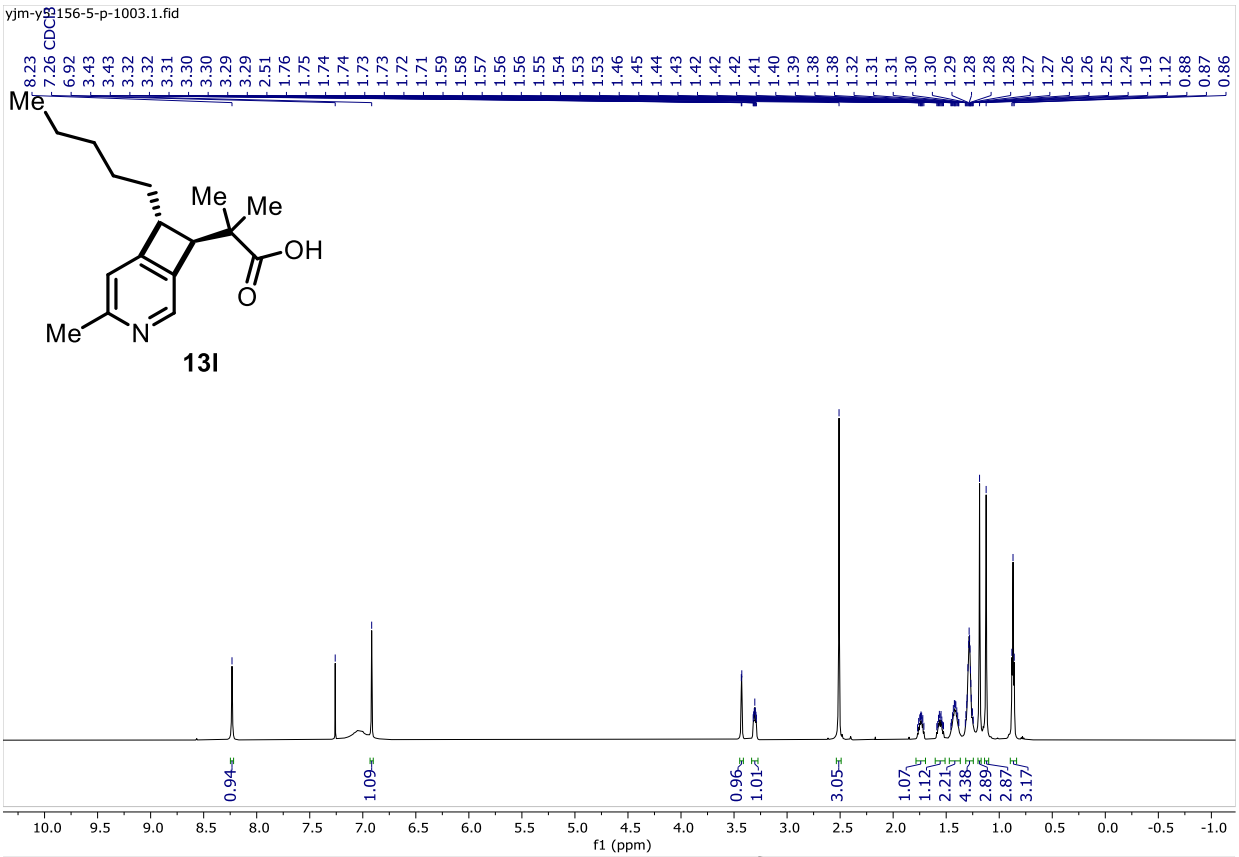

yjm-y5-149-2-p-0920.2.fid
180.45 168.83 151.48 150.72 144.99 133.83 127.86 122.15 122.09 110.60 107.69 77.37 77.16 76.95 56.27 49.83 47.86 37.18 32.57 26.16 22.72
Me COOH O NH O
13i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

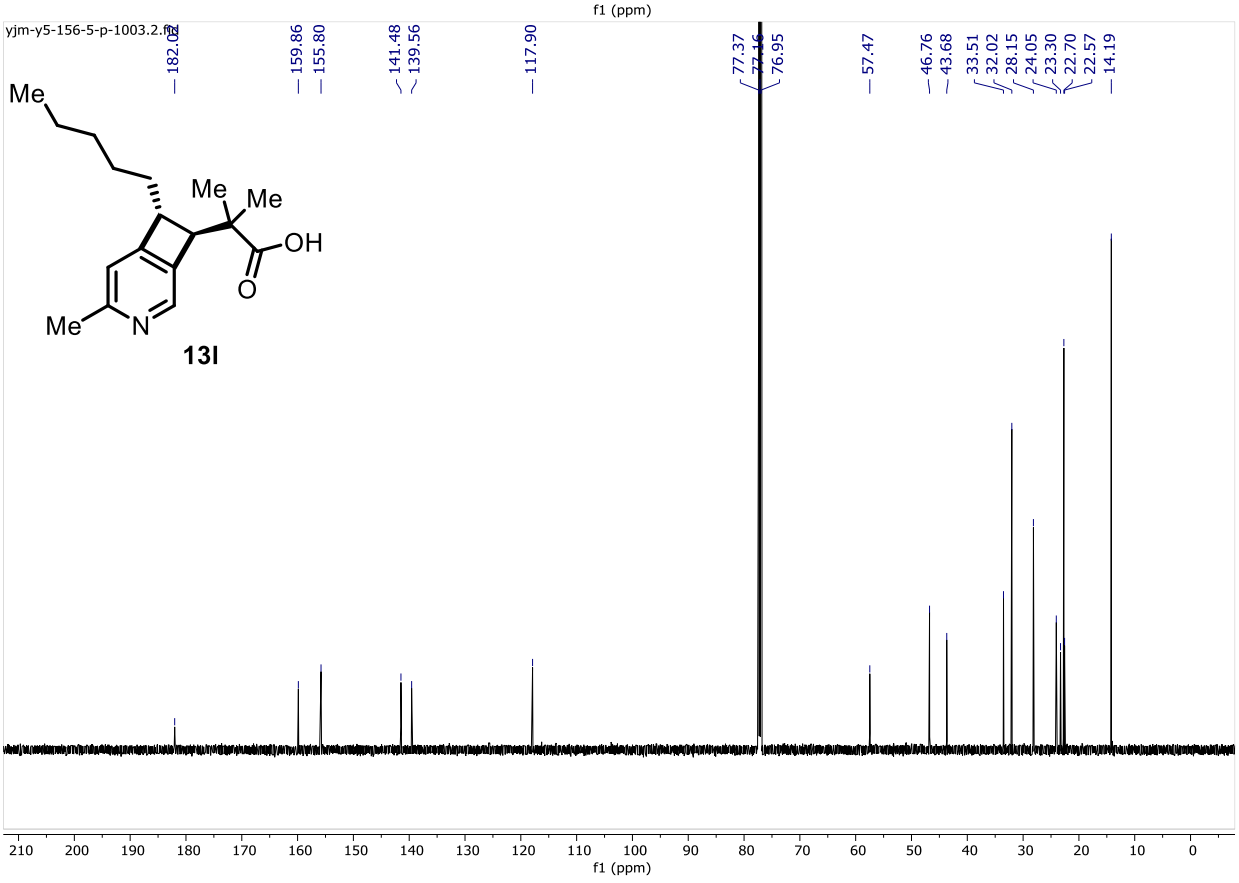

yjm-y5-86-4-p-0729.1.fid
Me
Me
Me
OH
O
N
Cl
13j
f1 (ppm)

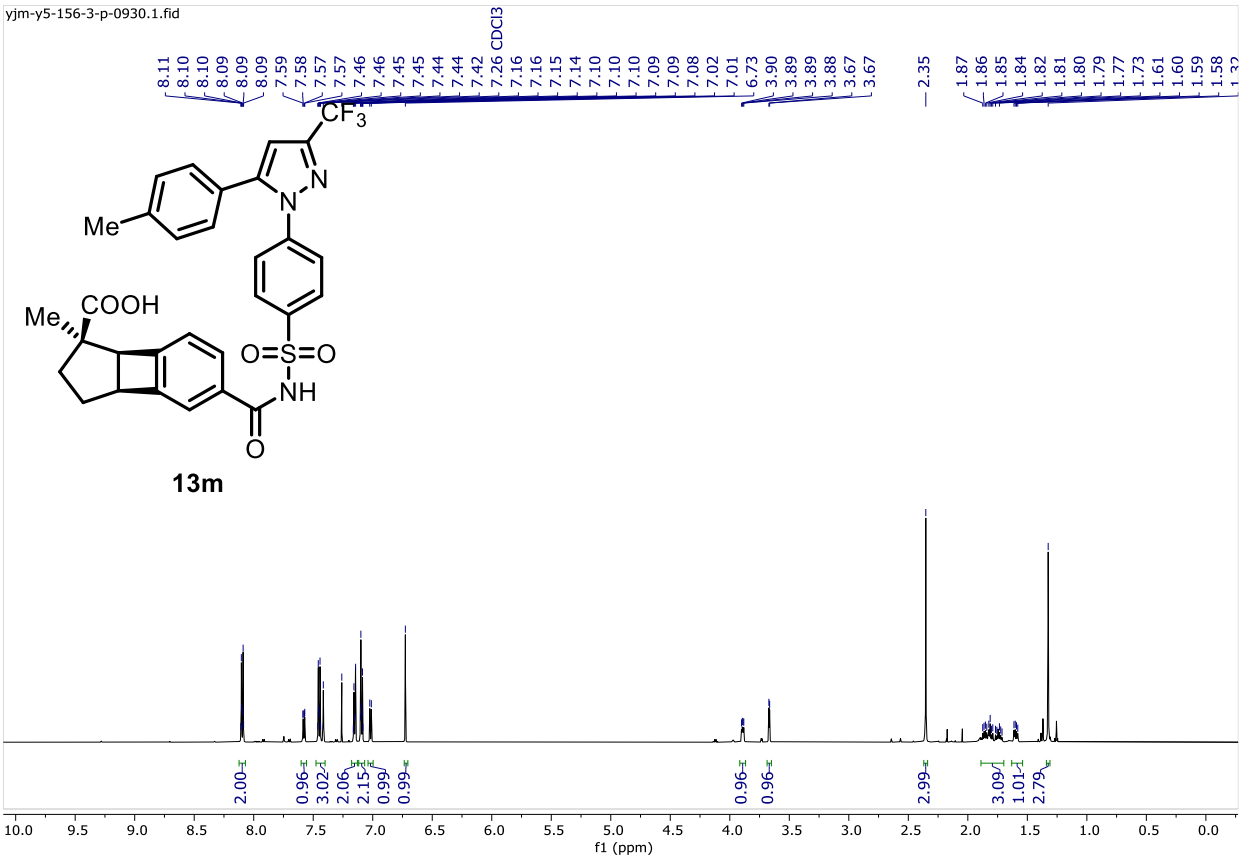

yjm-y5-86-4-p-0729.2.fid
Me
Me
Me
OH
O
N
Cl
13j
f1 (ppm)

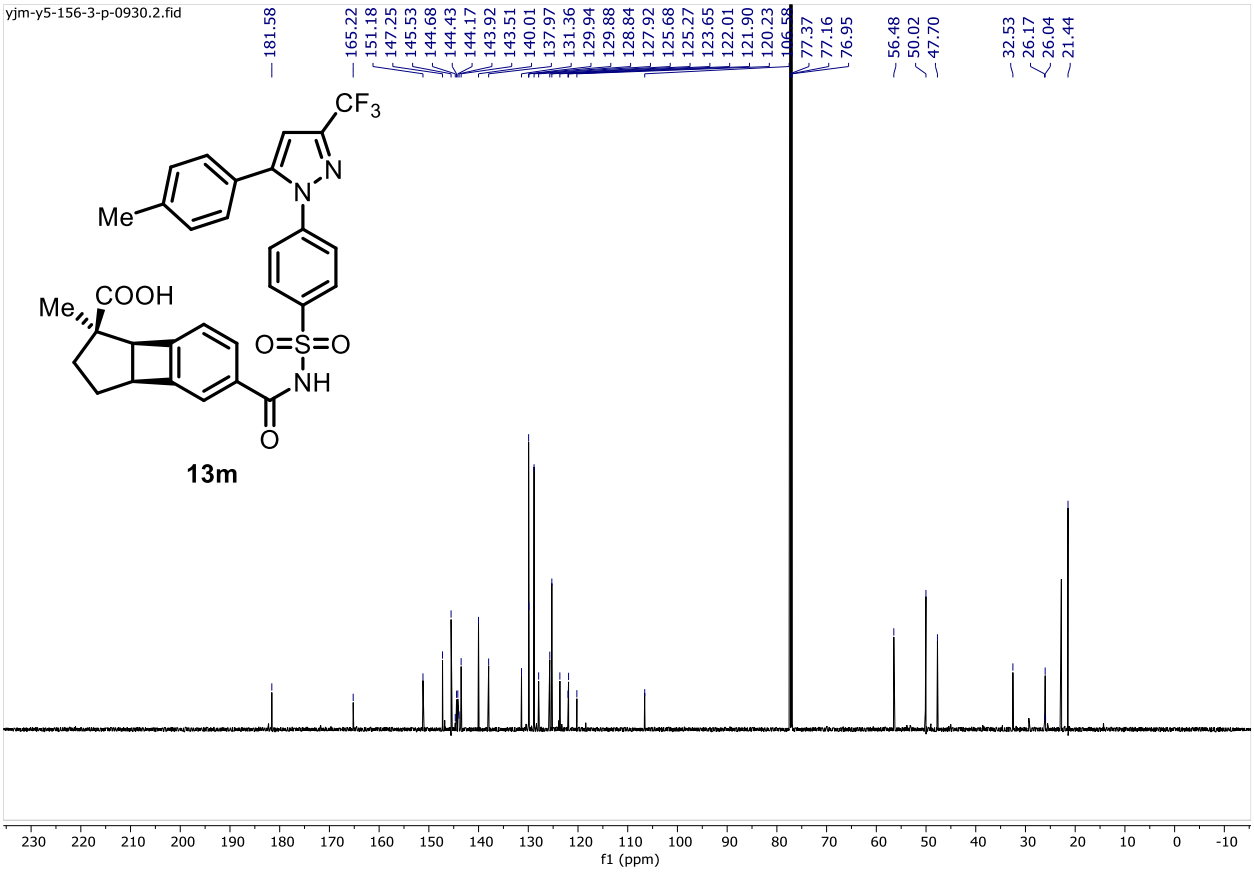

yjm-y5-152-4-p-0925.1.fid
Me
Me
Me
OH
O
Br
N
13k
8.10
7.26 CDCl3
1.00
0.96
1.07
1.08
1.16
1.18
2.39
4.41
3.25
3.15
3.41
f1 (ppm)

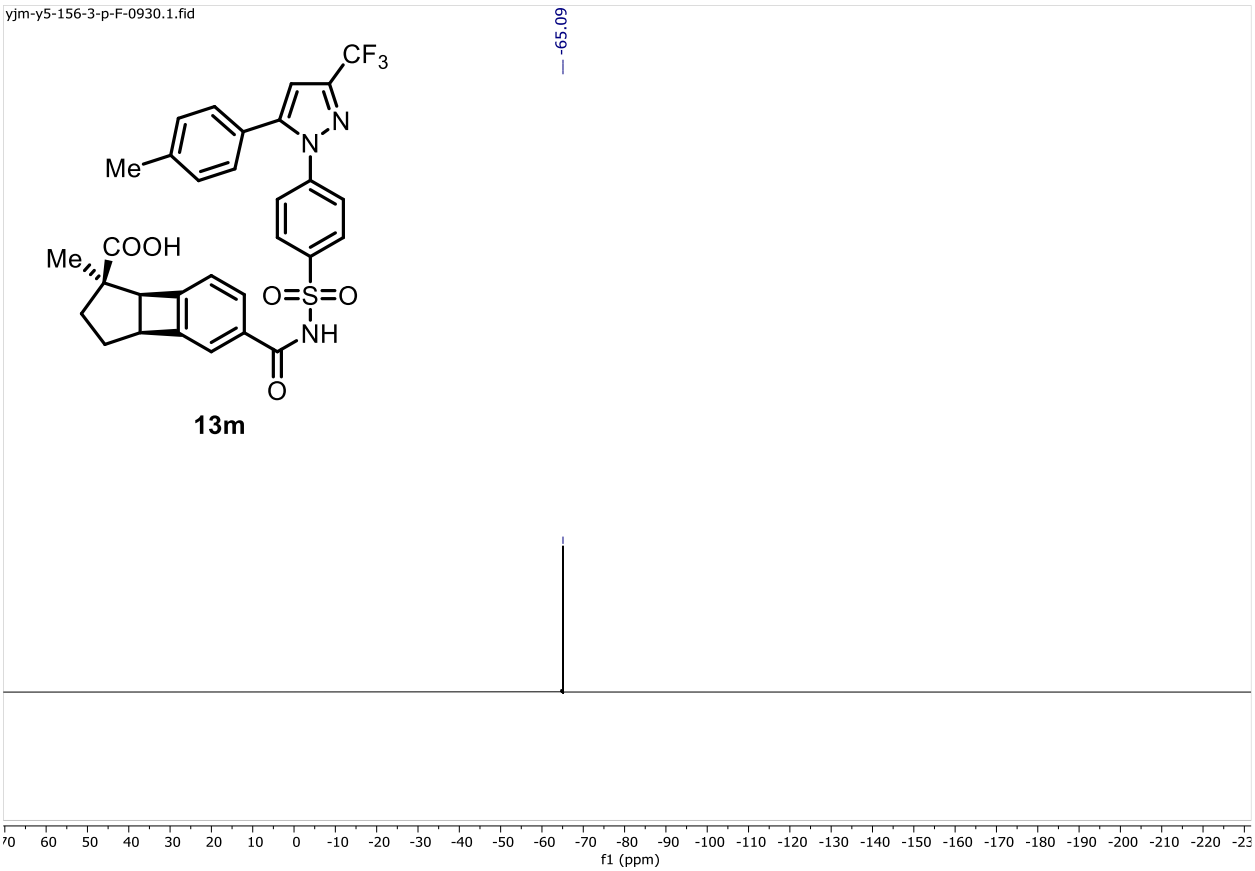

yjm-y5-152-4-p-0925.2.fid
181.81
160.39
144.06
140.23
139.72
122.66
77.37
77.16
76.95
56.50
46.75
43.32
33.24
31.90
27.97
22.95
22.67
22.35
14.18
Me
Me
Me
OH
O
Br
N
13k
f1 (ppm)

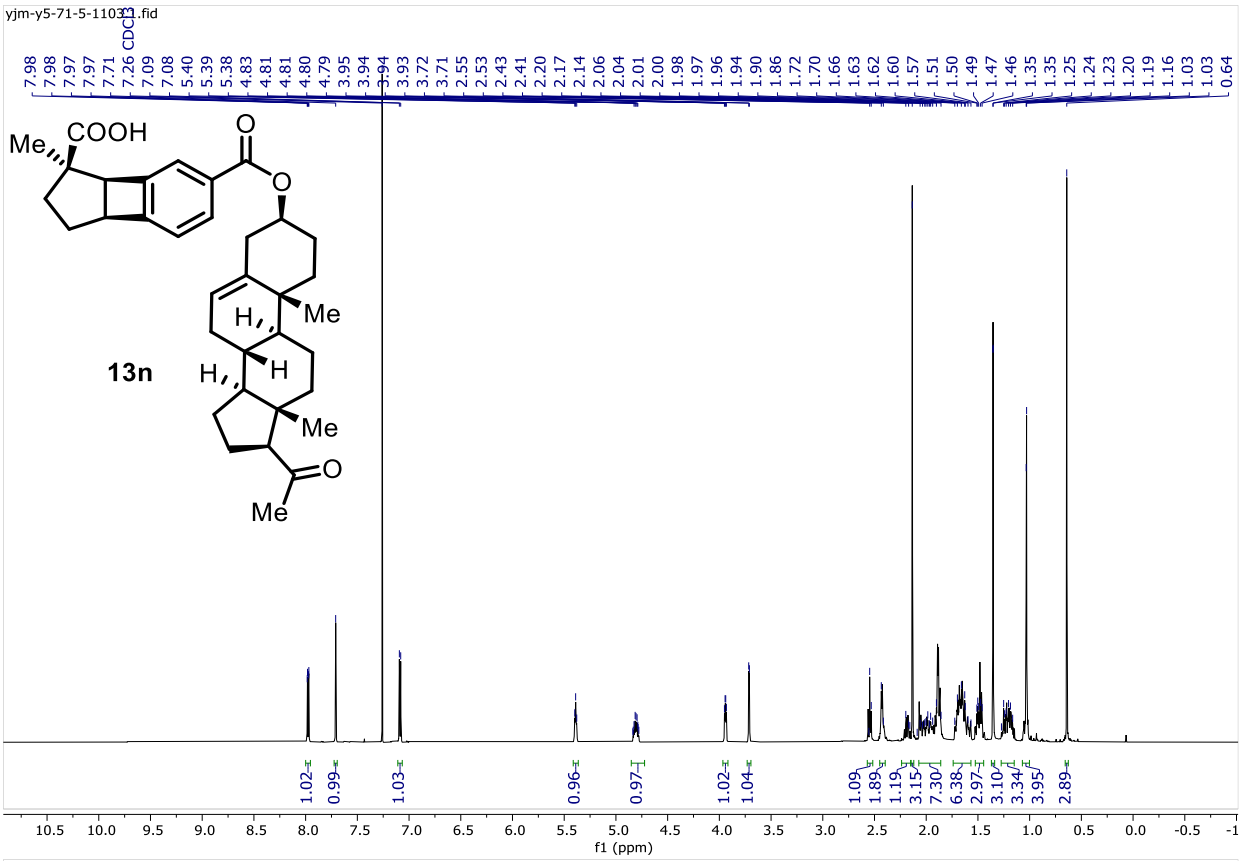

yjm-y5-156-5-p-1003.1.fid
Me
Me
Me
OH
O
Me
N
13l
f1 (ppm)


yjm-y5-156-5-p-1003.2.fid
Me
Me
Me
OH
O
Me
N
13l
f1 (ppm)


yjm-y5-156-3-p-0930.1.fid
CF3
N
N
Me
Me
COOH
O=S=O
NH
O
13m
f1 (ppm)


yjm-y5-156-3-p-0930.2.fid
CF3
N
N
Me
Me
COOH
O=S=O
NH
O
13m
f1 (ppm)


yjm-y5-156-3-p-F-0930.1.fid
-65.09
CF3
N
N
Me
COOH
Me
O=S=O
NH
O
13m
f1 (ppm)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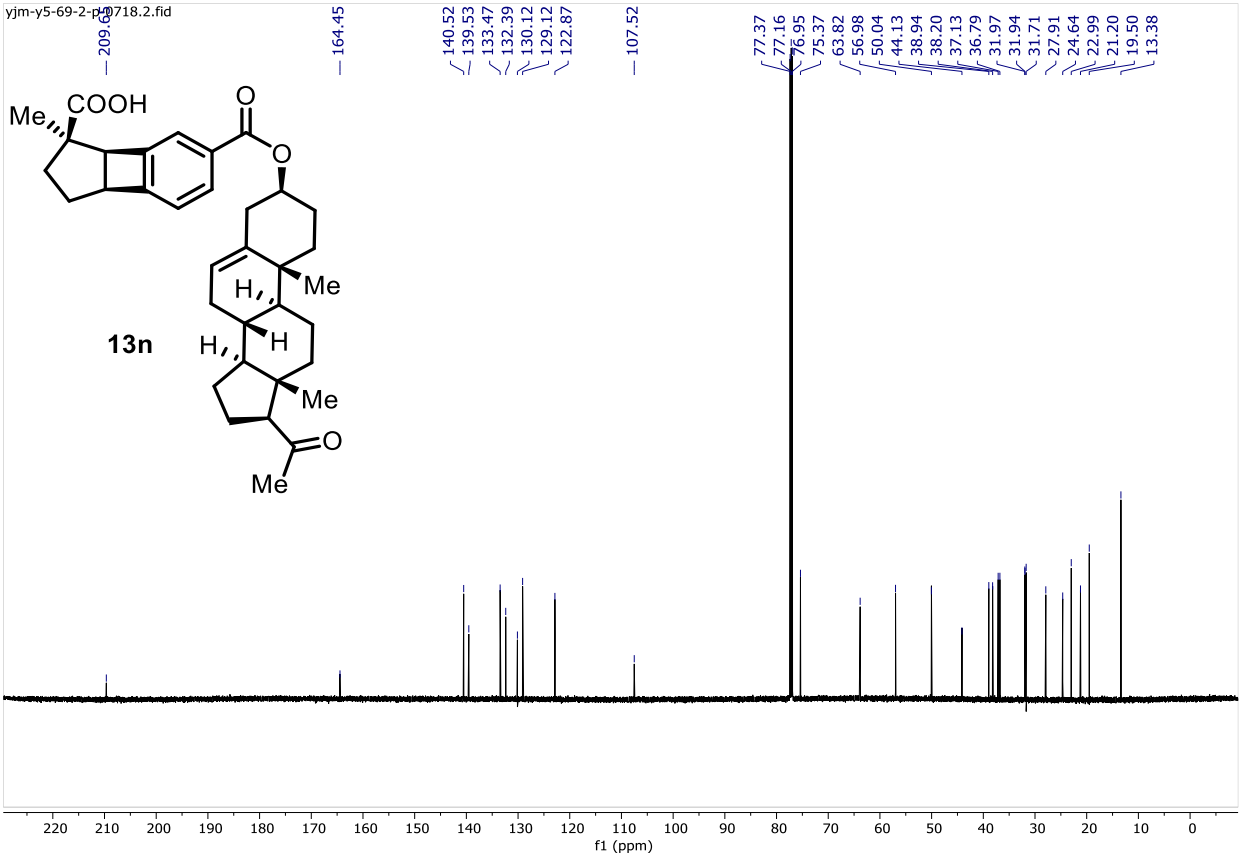
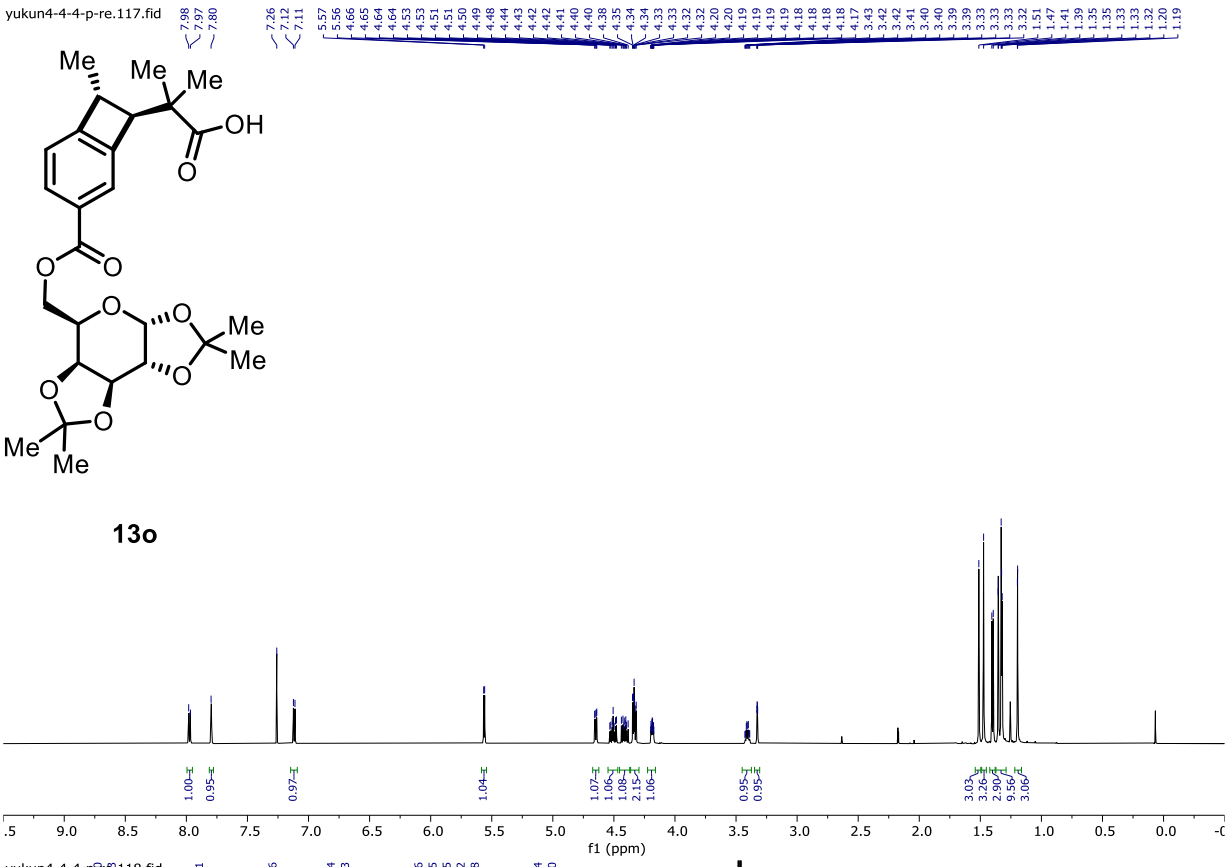
CDCl3
7.98 7.98 7.97 7.97 7.71 7.26 7.09 7.08 5.40 5.39 5.38 4.83 4.81 4.81 4.80 4.79 3.95 3.94 3.94 3.93 3.72 3.71 2.55 2.53 2.43 2.41 2.20 2.17 2.14 2.06 2.04 2.01 2.00 1.98 1.97 1.96 1.94 1.90 1.86 1.72 1.70 1.66 1.63 1.62 1.60 1.57 1.51 1.50 1.49 1.47 1.46 1.35 1.35 1.25 1.24 1.23 1.20 1.19 1.16 1.03 1.03 0.64
Me
COOH
O
O
H
Me
13n
H
H
Me
O
Me
1.02 0.99 1.03 0.96 0.97 1.02 1.04 1.09 1.89 1.19 3.15 7.30 6.38 2.97 3.10 3.34 3.95 2.89
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


yjm-y5-69-2-pd0718.2.fid
209.43
164.45
140.52 139.53 133.47 132.39 130.12 129.12 122.87
107.52
77.37 77.16 76.95 75.37 63.82 56.98 50.04 44.13 38.94 38.20 37.13 36.79 31.97 31.94 31.71 27.91 24.64 22.99 21.20 19.50 13.38
Me
COOH
O
O
H
Me
13n
H
H
Me
O
Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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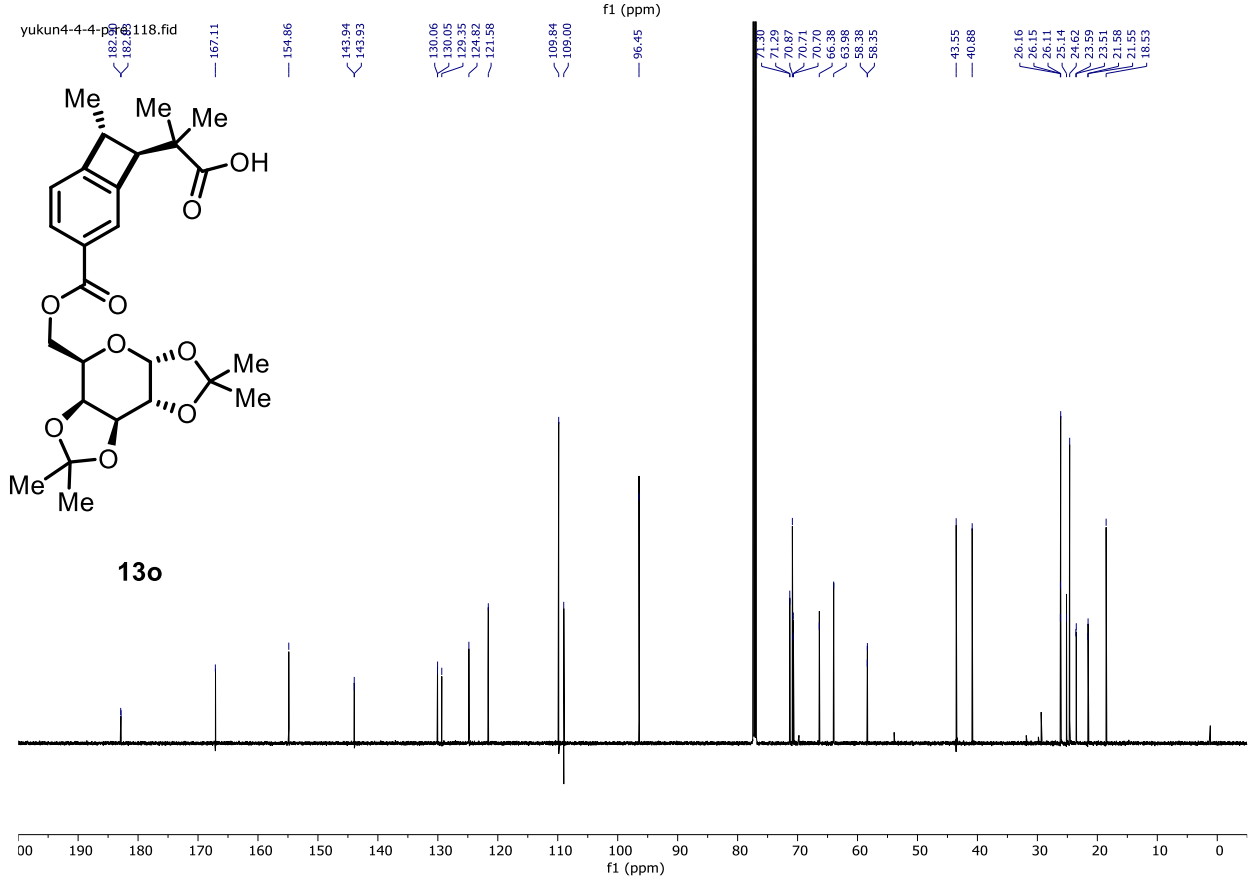
13o
f1 (ppm)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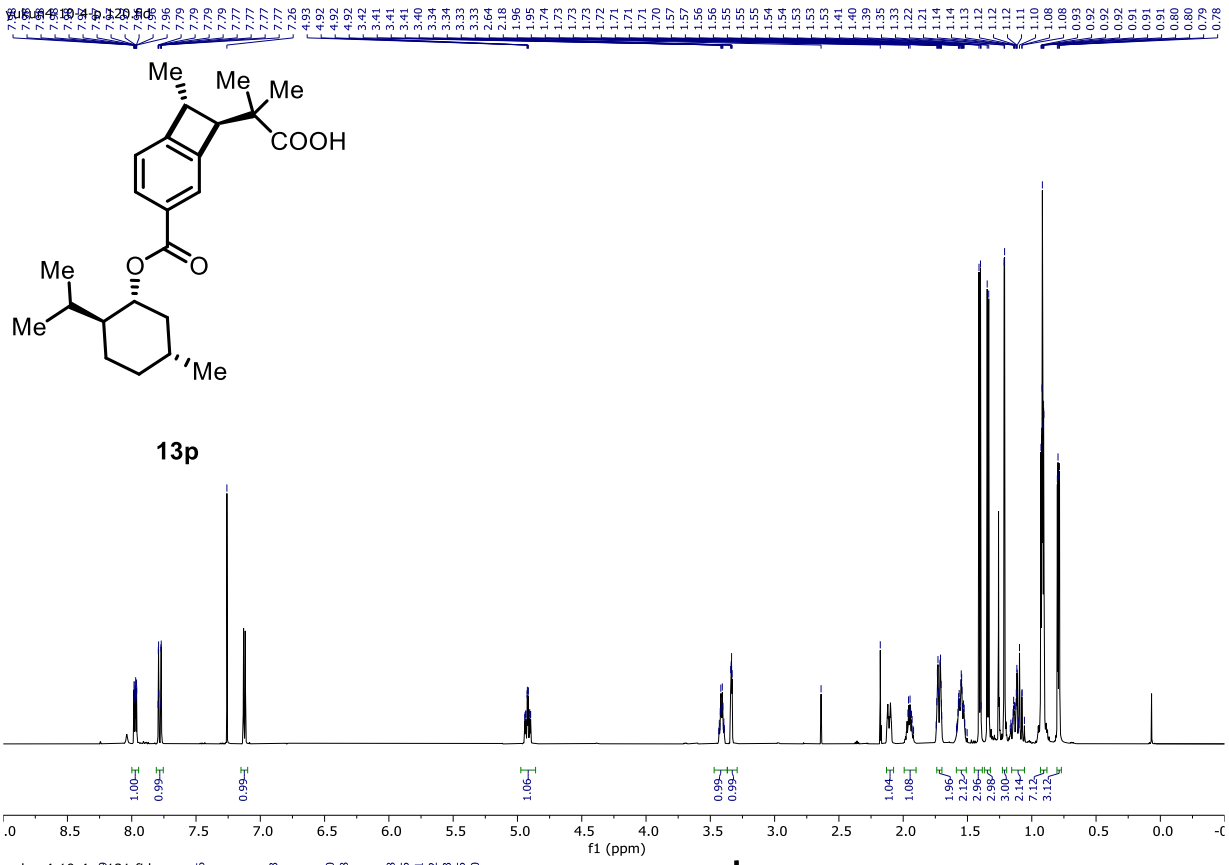
13o
f1 (ppm)

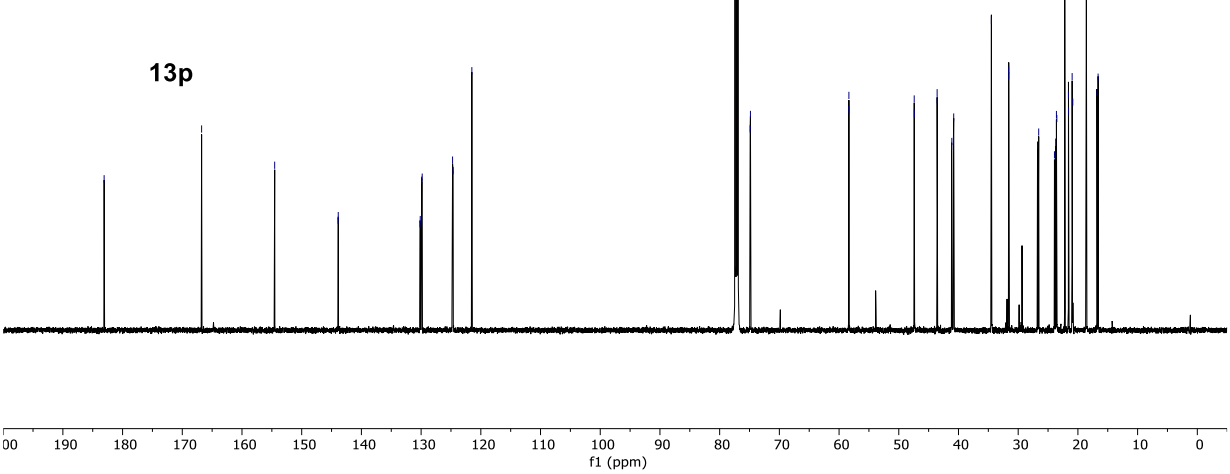

Me
Me
Me
COOH
O
O
Me
Me
Me

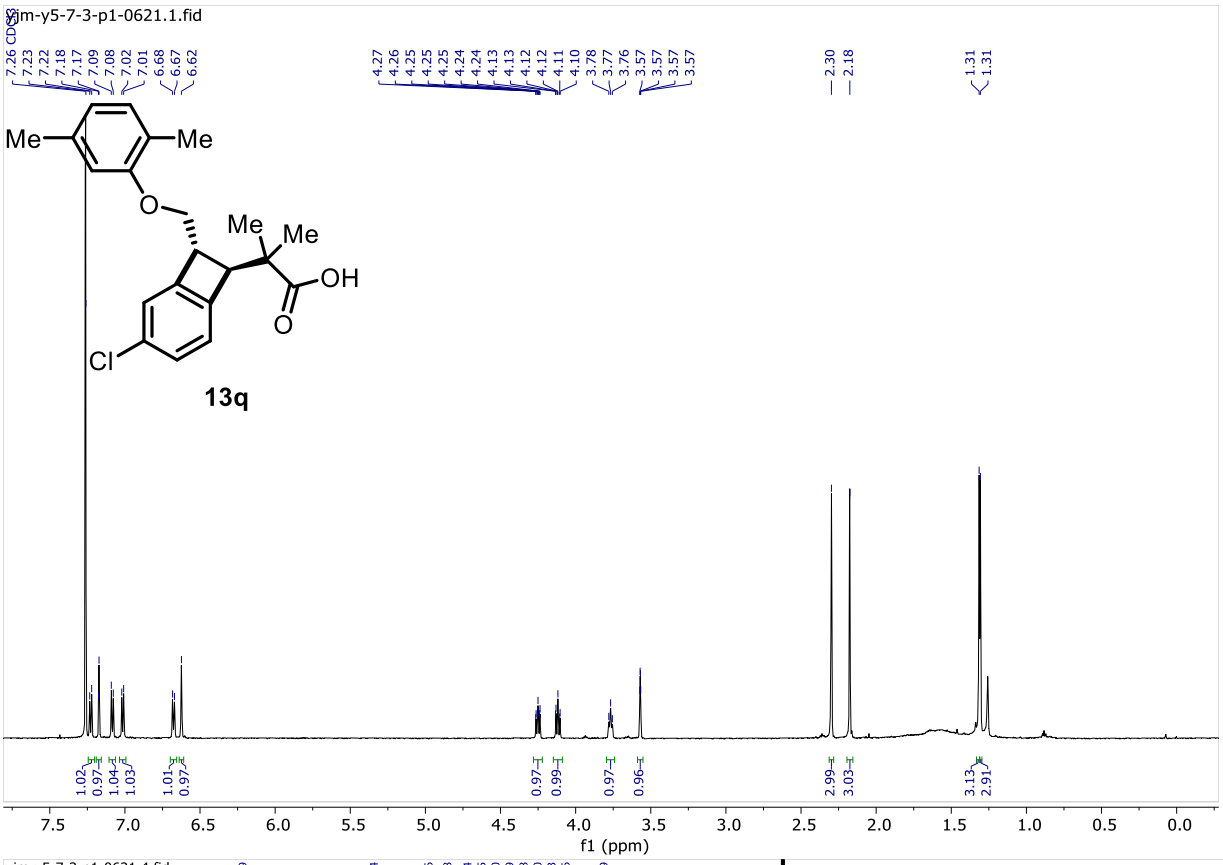
13p

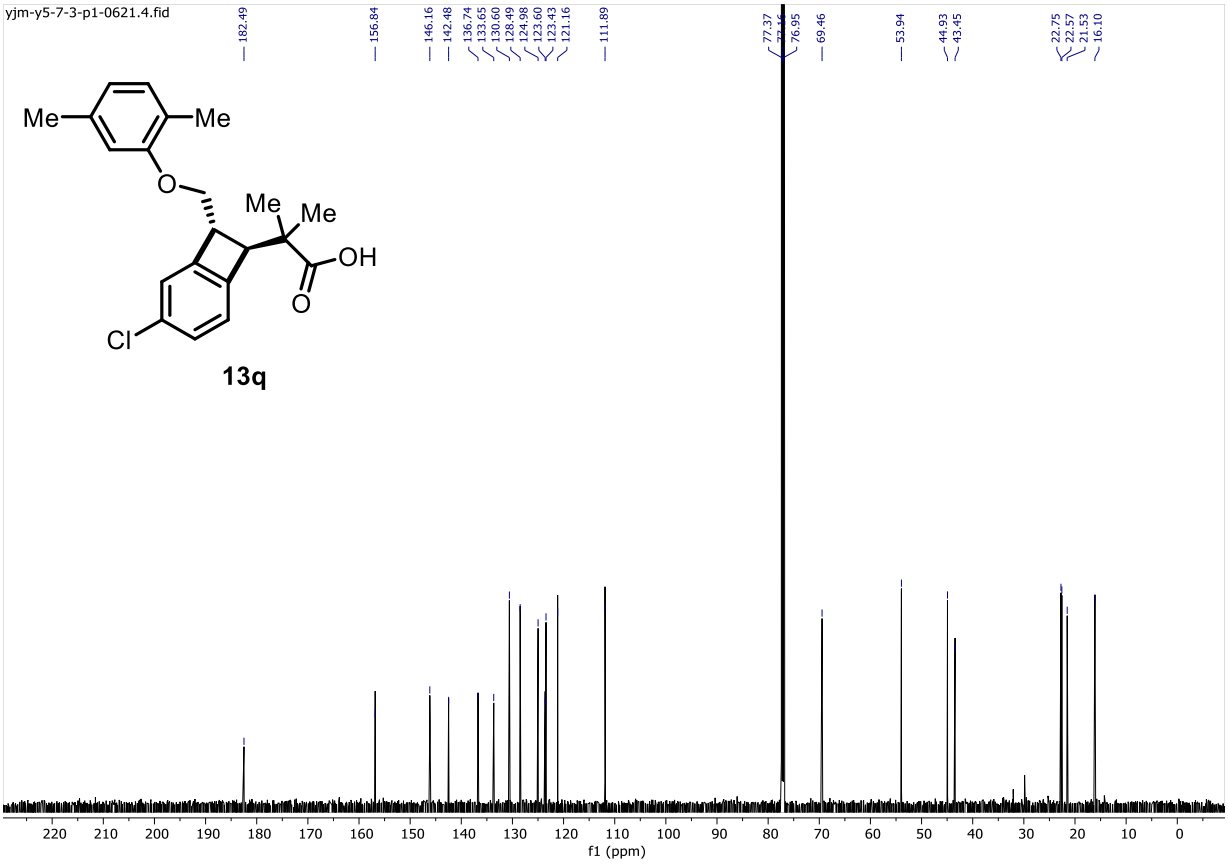
1.00
0.99
0.99
1.06
0.99
0.99
1.04
1.08
1.96
2.12
2.96
2.98
3.00
2.14
7.12
3.12
f1 (ppm)


yukun4-10-4-p2121.fid
Me
Me
Me
COOH
O
O
Me
Me
Me

13p


f1 (ppm)


yjm-y5-7-3-p1-0621.1.fid
7.26 CDCl3
7.23
7.22
7.18
7.17
7.09
7.08
7.02
7.01
6.68
6.67
6.62
4.27
4.26
4.25
4.25
4.25
4.24
4.24
4.13
4.12
4.12
4.11
4.10
3.78
3.77
3.76
3.57
3.57
3.57
3.57
2.30
2.18
1.31
1.31
Me
Me
O
Me
Me
OH
O
Cl
13q
1.02
0.97
1.04
1.03
1.01
0.97
0.97
0.99
0.97
0.96
2.99
3.03
3.13
2.91
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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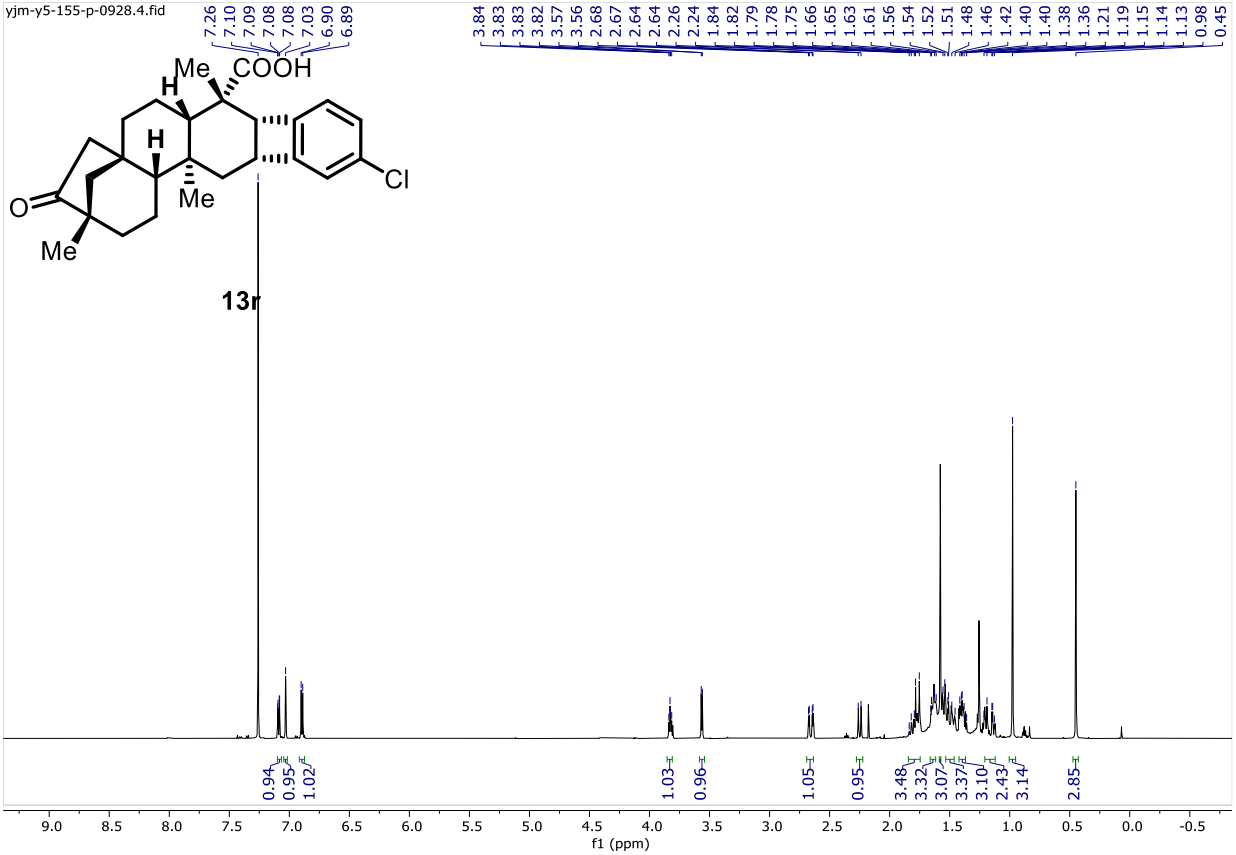
156.84
146.16
142.48
136.74
133.65
130.60
128.49
124.98
123.60
123.43
121.16
111.89
77.37
77.16
76.95
69.46
53.94
44.93
43.45
22.75
22.57
21.53
16.10
Me
Me
O
Me
Me
OH
O
Cl
13q
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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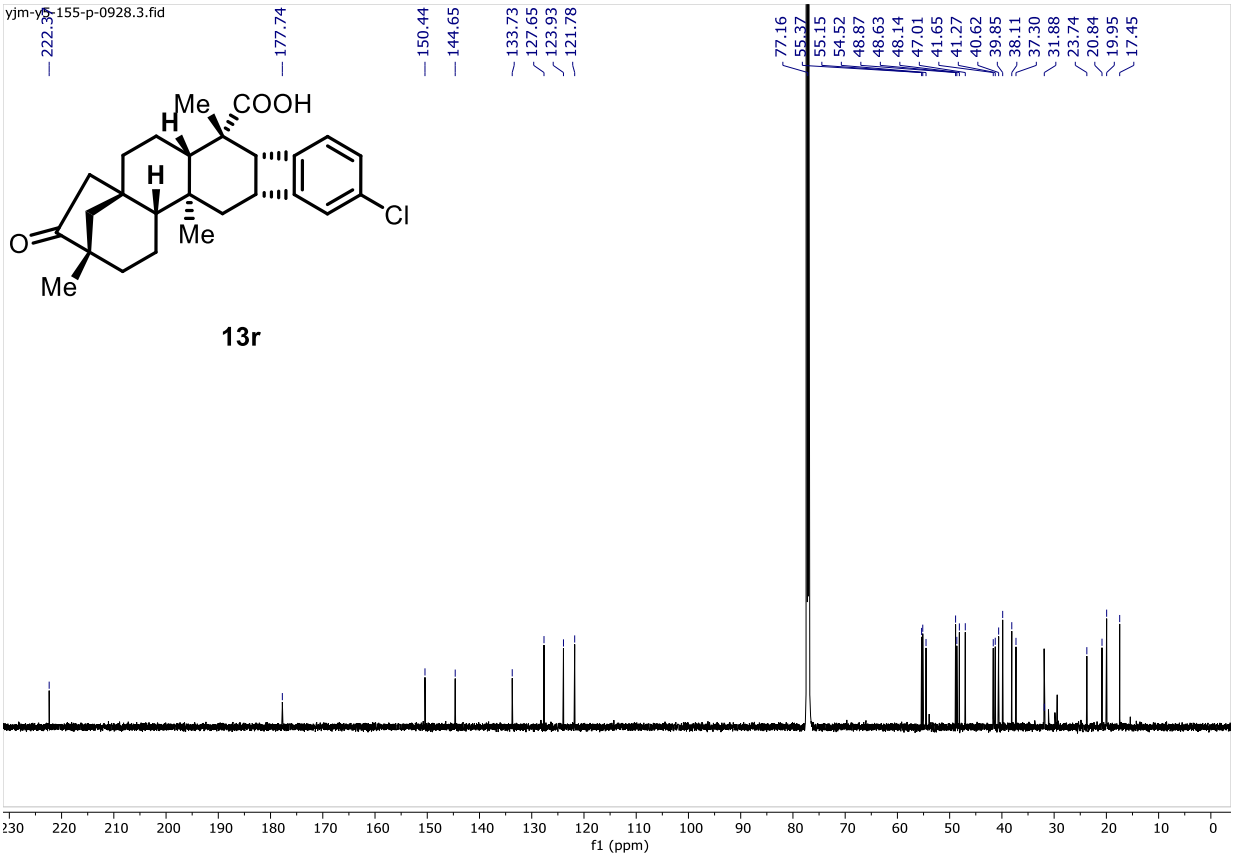
Me
COOH
H
H
Me
Me
O
Cl
13r
f1 (ppm)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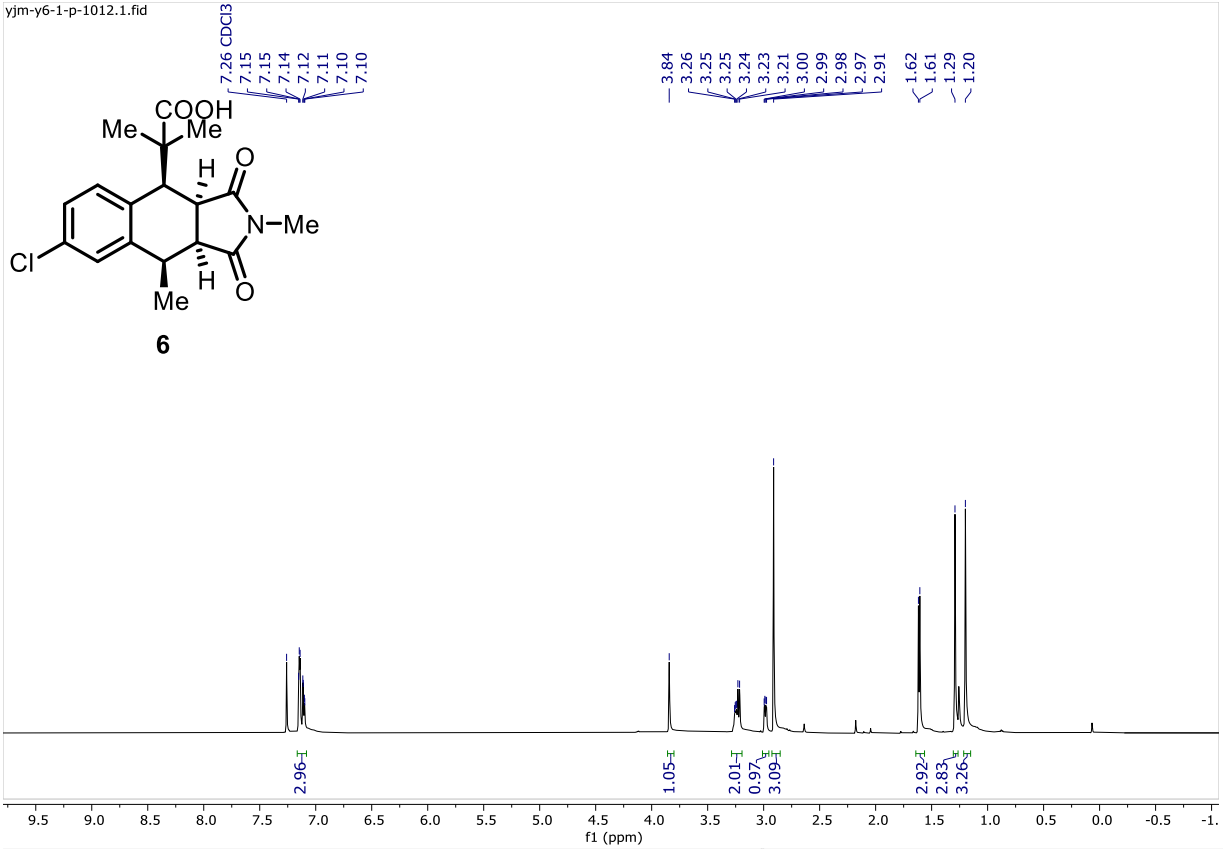
Me
COOH
H
H
Me
Me
O
Cl
13r
f1 (ppm)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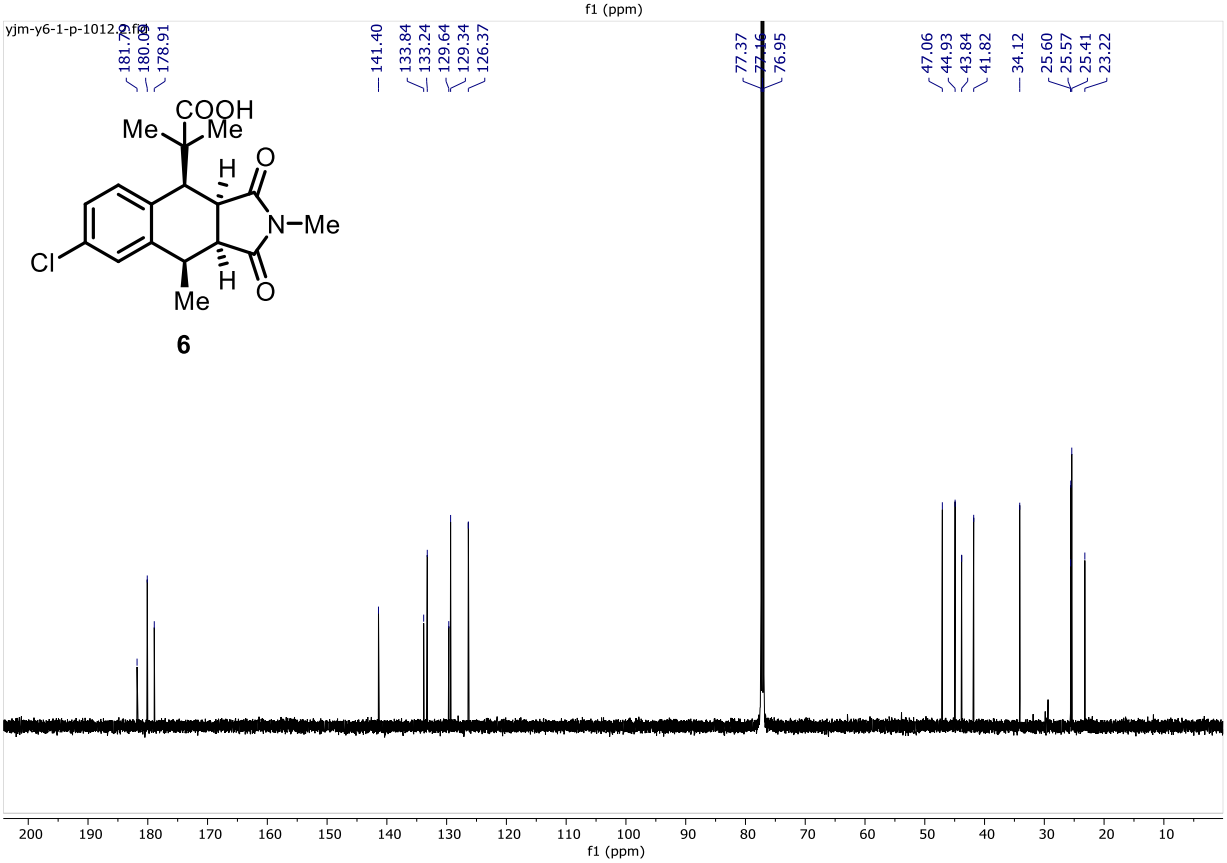
7.15
7.15
7.14
7.12
7.11
7.10
7.10
3.84
3.26
3.25
3.25
3.24
3.23
3.21
3.00
2.99
2.98
2.97
2.91
1.62
1.61
1.29
1.20
COOH
Me
Me
H
O
N−Me
Cl
H
O
Me
6
2.96
1.05
2.01
0.97
3.09
2.92
2.83
3.26
f1 (ppm)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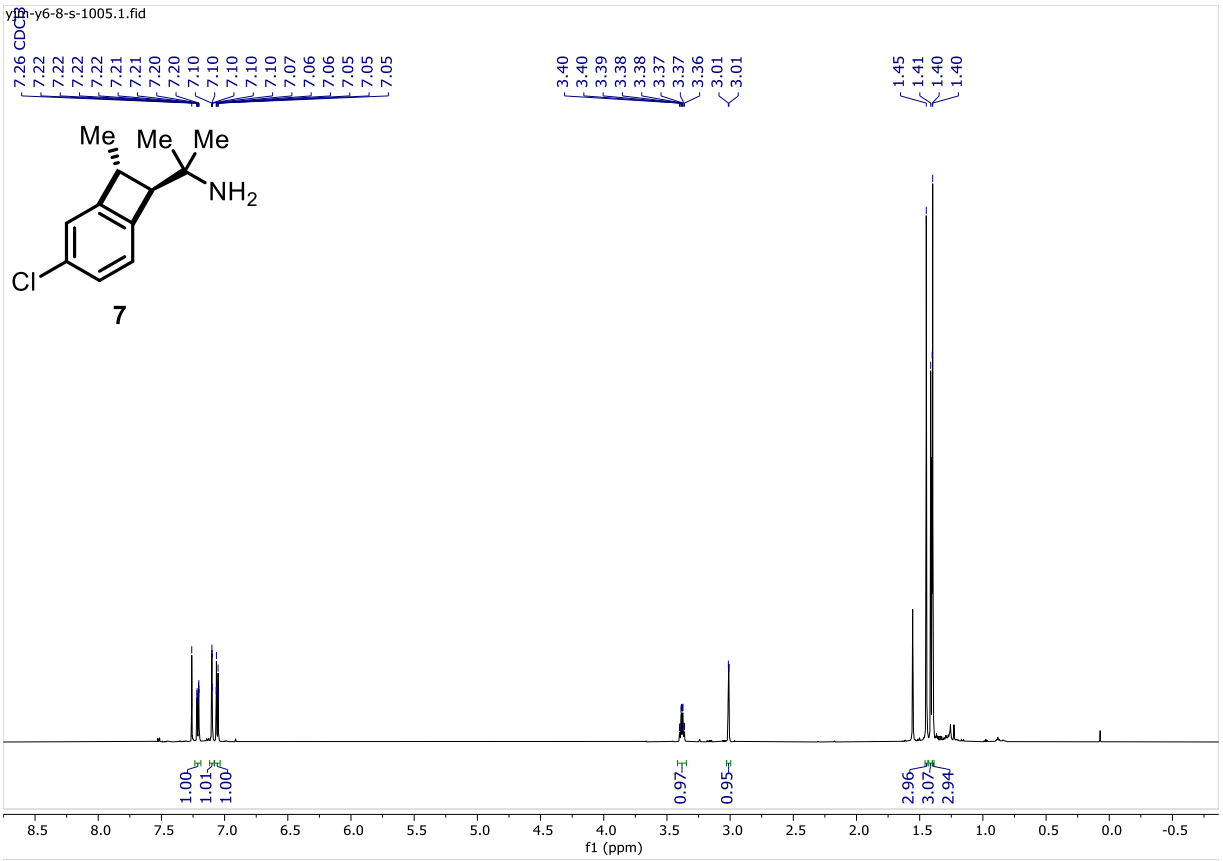
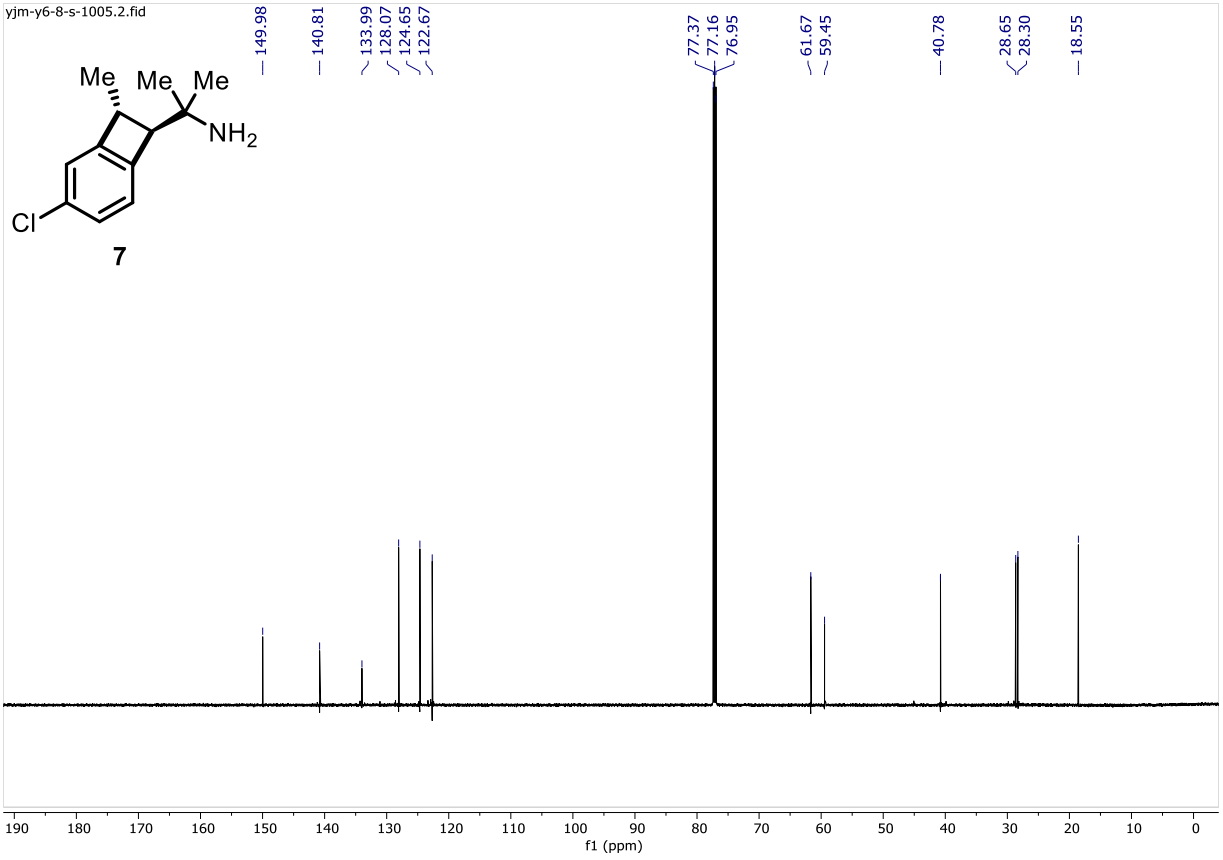
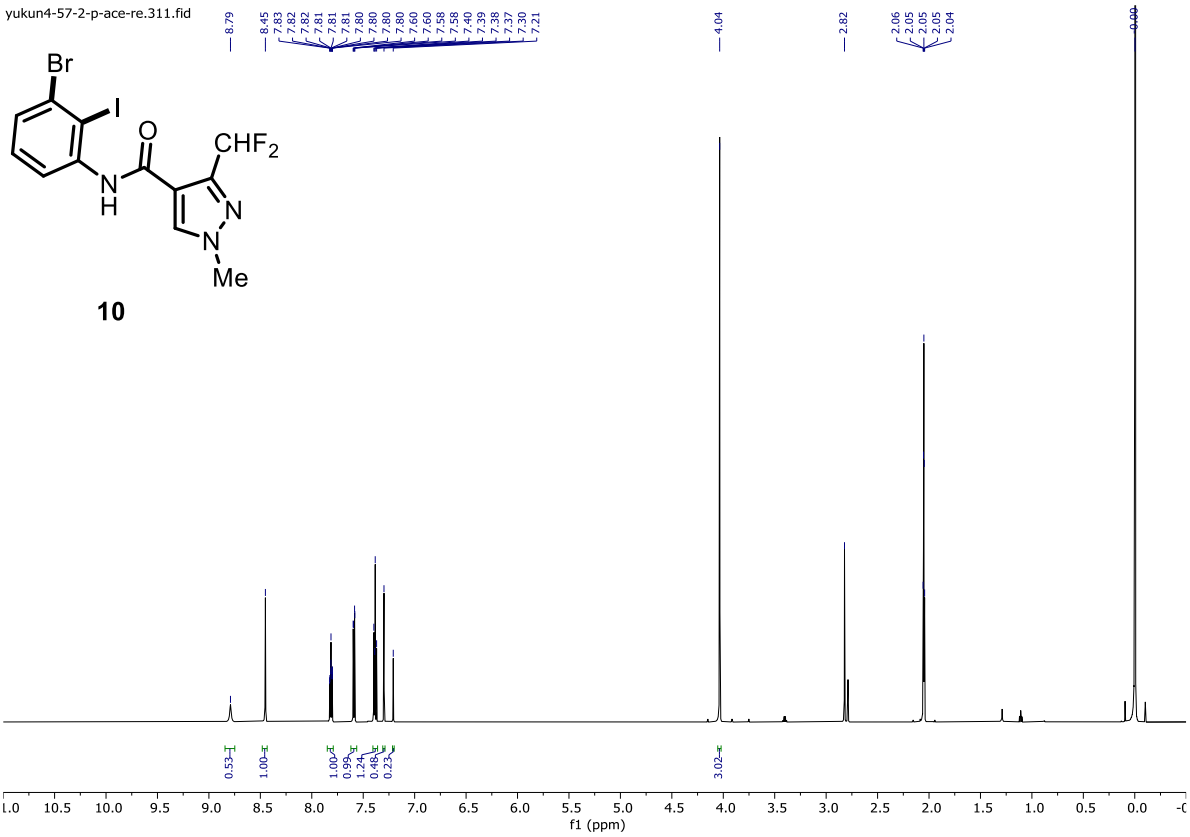
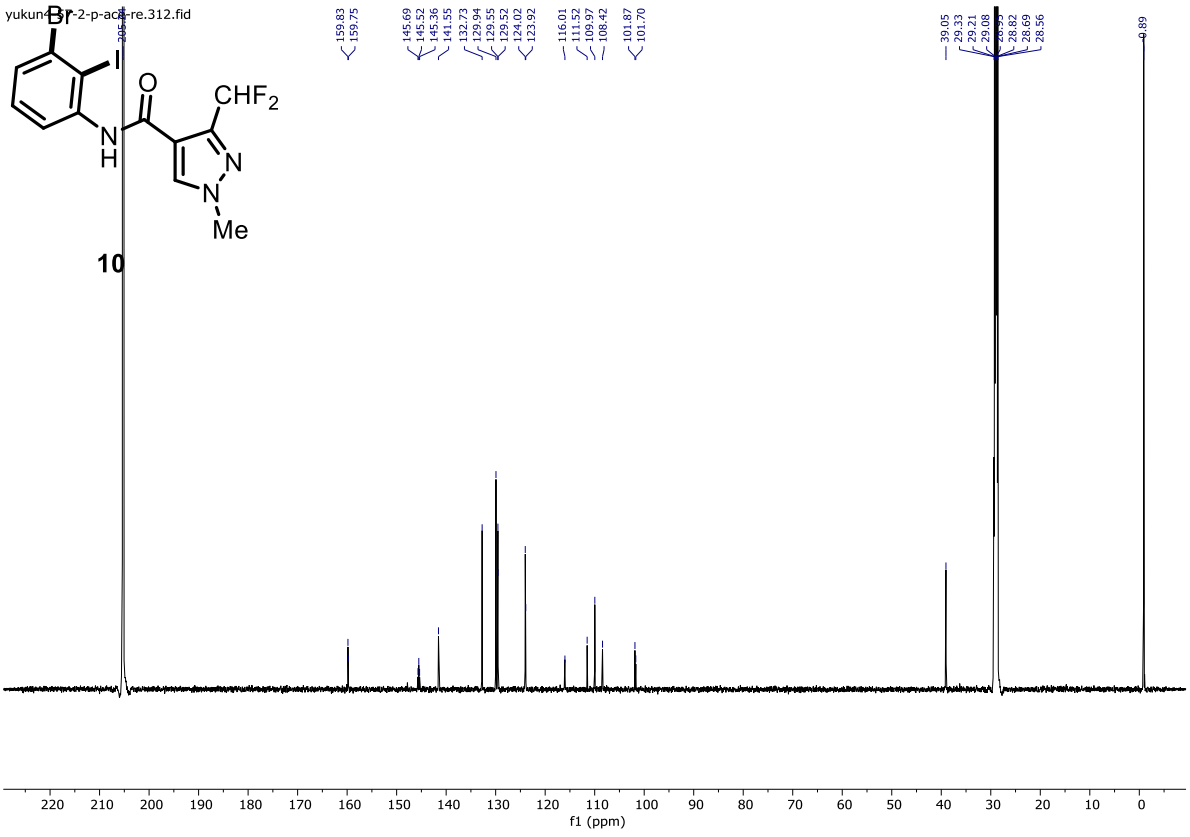
181.72
180.08
178.91
141.40
133.84
133.24
129.64
129.34
126.37
77.37
77.16
76.95
47.06
44.93
43.84
41.82
34.12
25.60
25.57
25.41
23.22
COOH
Me
Me
H
O
N−Me
Cl
H
O
Me
6
f1 (ppm)

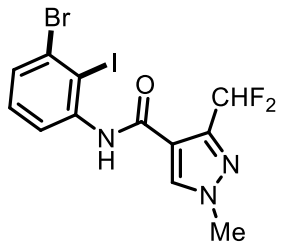

yjm-y6-8-s-1005.1.fid
7.26 CDCl3
7.22 7.22 7.22 7.22 7.21 7.21 7.20 7.20 7.10 7.10 7.10 7.10 7.07 7.06 7.06 7.05 7.05 7.05
3.40 3.40 3.39 3.38 3.38 3.37 3.37 3.36 3.01 3.01
1.45 1.41 1.40 1.40
Me Me Me
NH2
Cl
7
1.00 1.01 1.00 0.97 0.95 2.96 3.07 2.94
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


yjm-y6-8-s-1005.2.fid
149.98 140.81 133.99 128.07 124.65 122.67
77.37 77.16 76.95 61.67 59.45 40.78 28.65 28.30 18.55
Me Me Me
NH2
Cl
7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

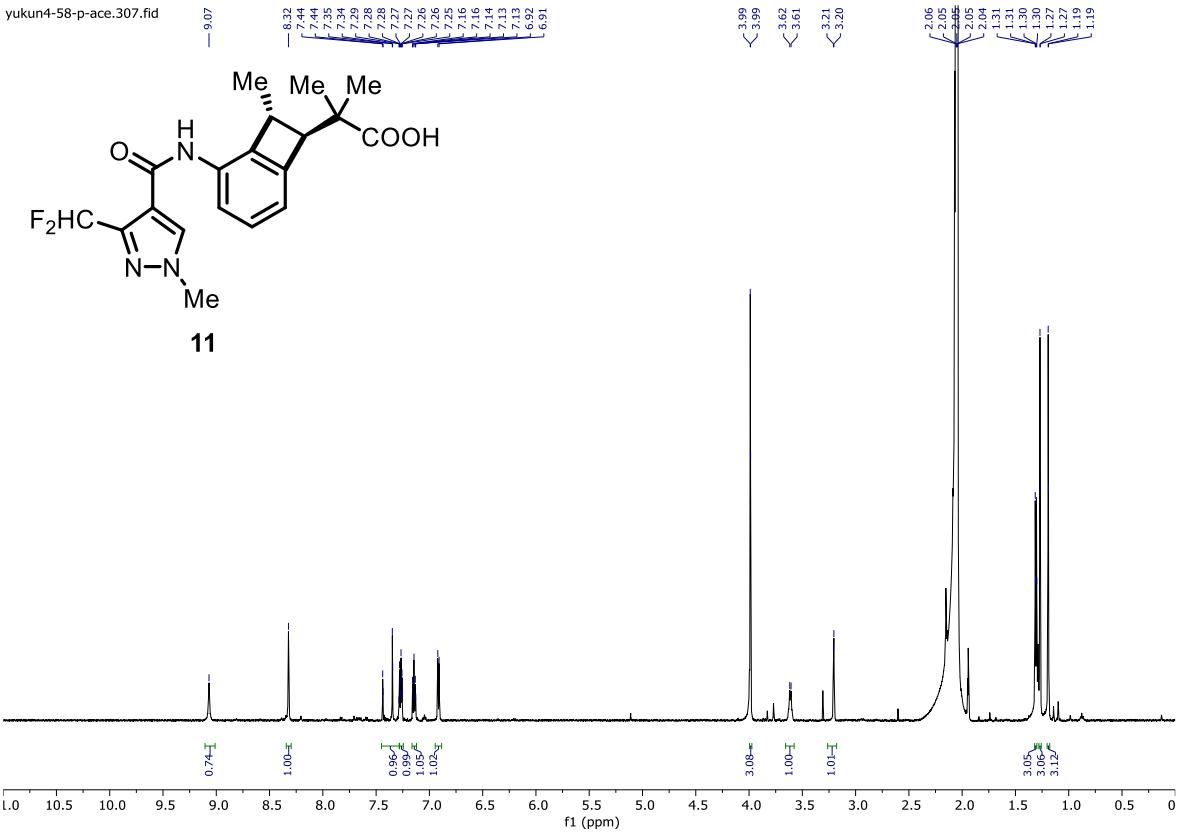

yukun4-57-2-p-ace-re.311.fid
Br
I
O
N
H
CHF2
N
N
Me
10
f1 (ppm)

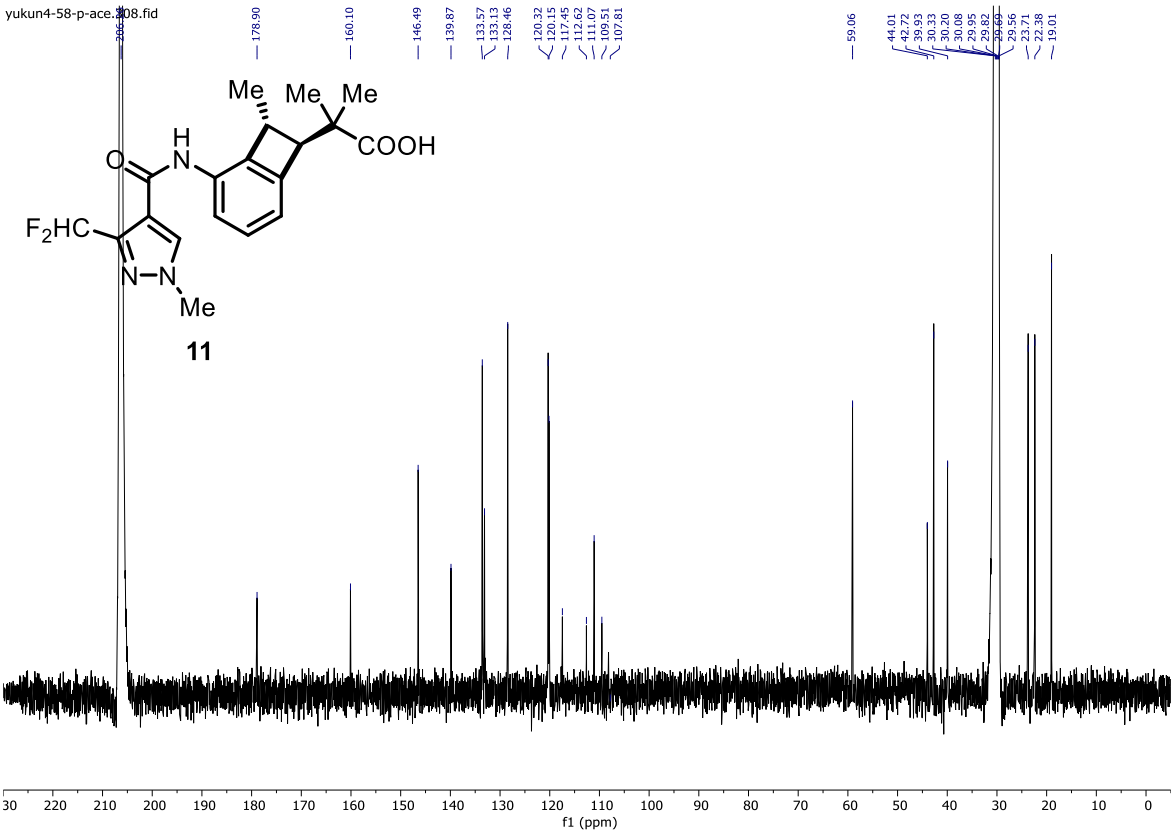

yukun4-57-2-p-ace-re.312.fid
Br
I
O
N
H
CHF2
N
N
Me
10
f1 (ppm)

yukun4-57-2-p.182.fid

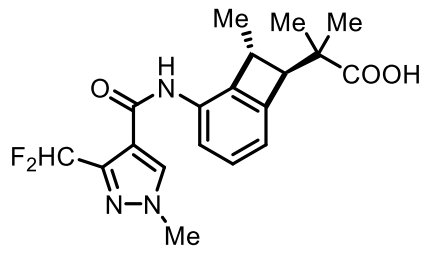


10

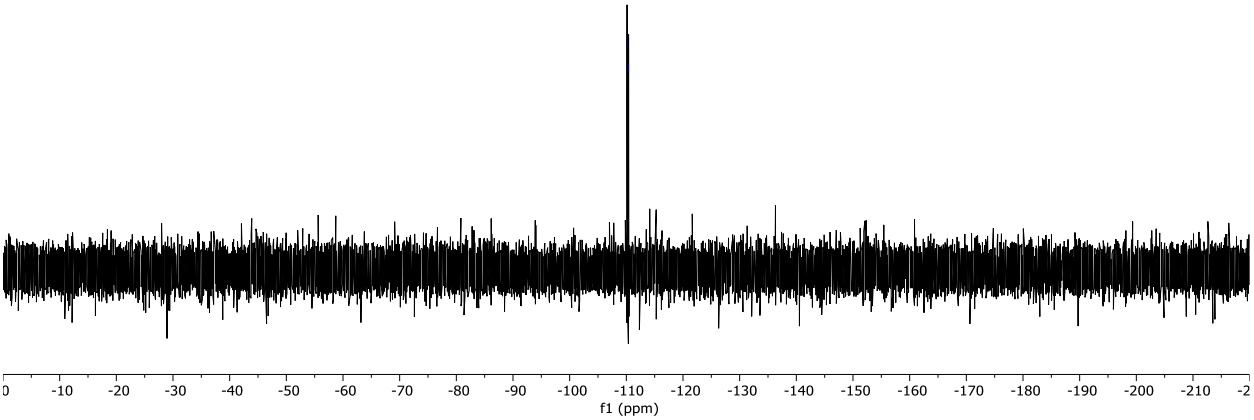

yukun4-58-p-ace.307.fid
Me
Me
Me
COOH
H
N
O
F2HC
N–N
Me
11
f1 (ppm)

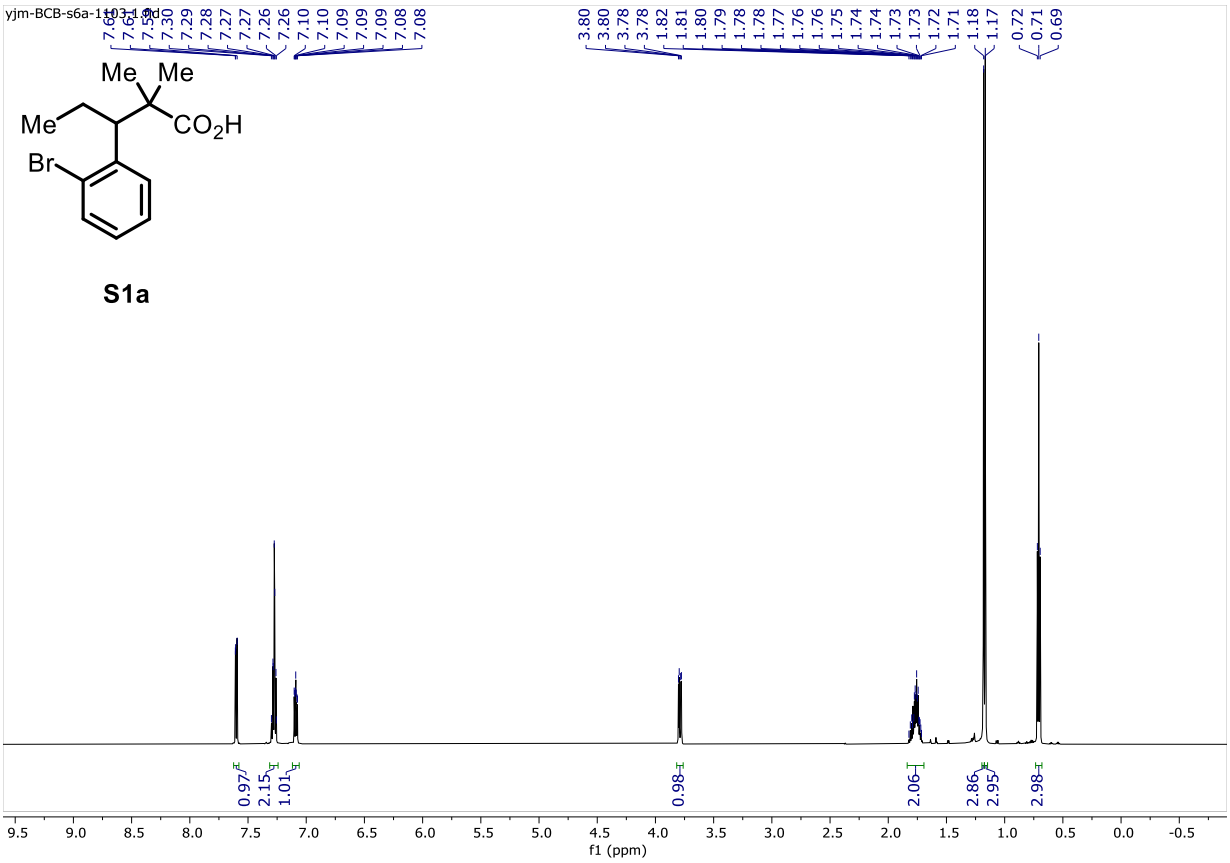

yukun4-58-p-ace.308.fid
Me
Me
Me
COOH
H
N
O
F2HC
N–N
Me
11
f1 (ppm)

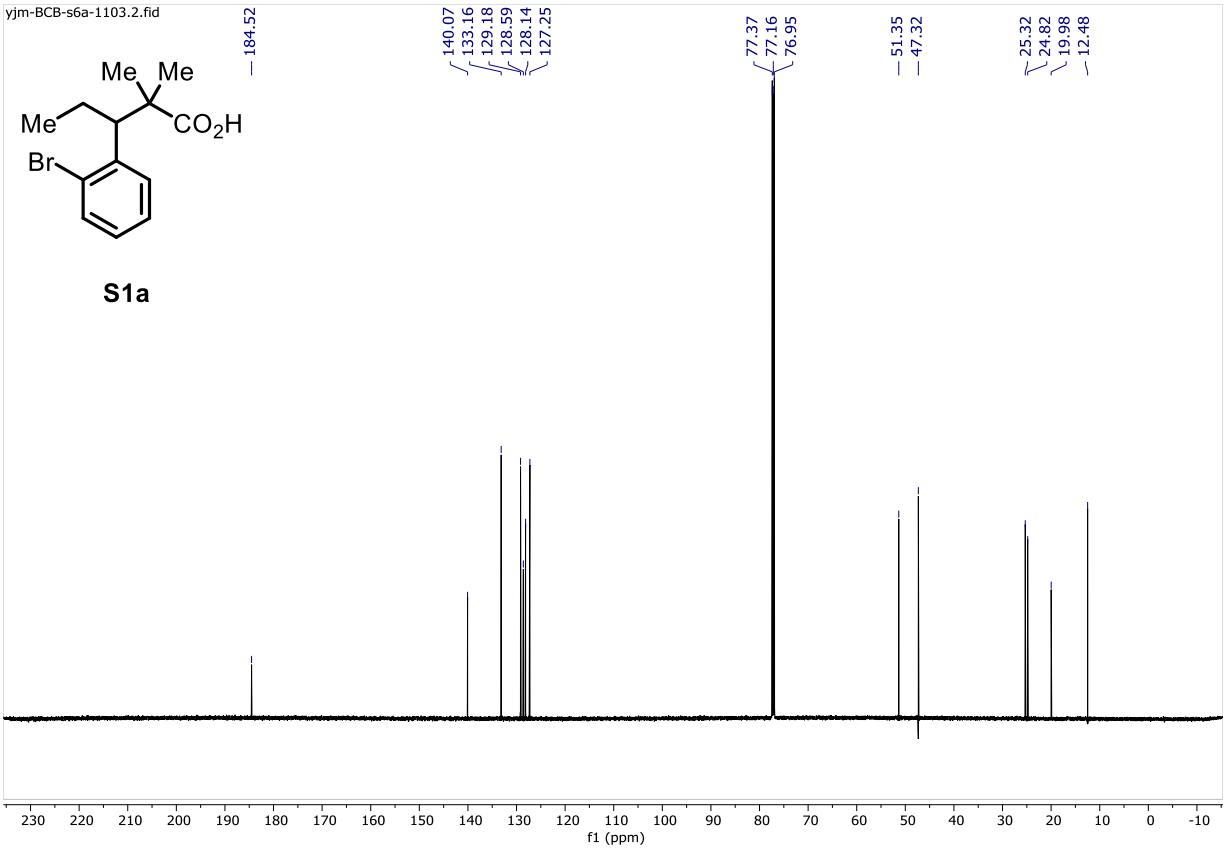
yukun4-58-p-2.190.fid

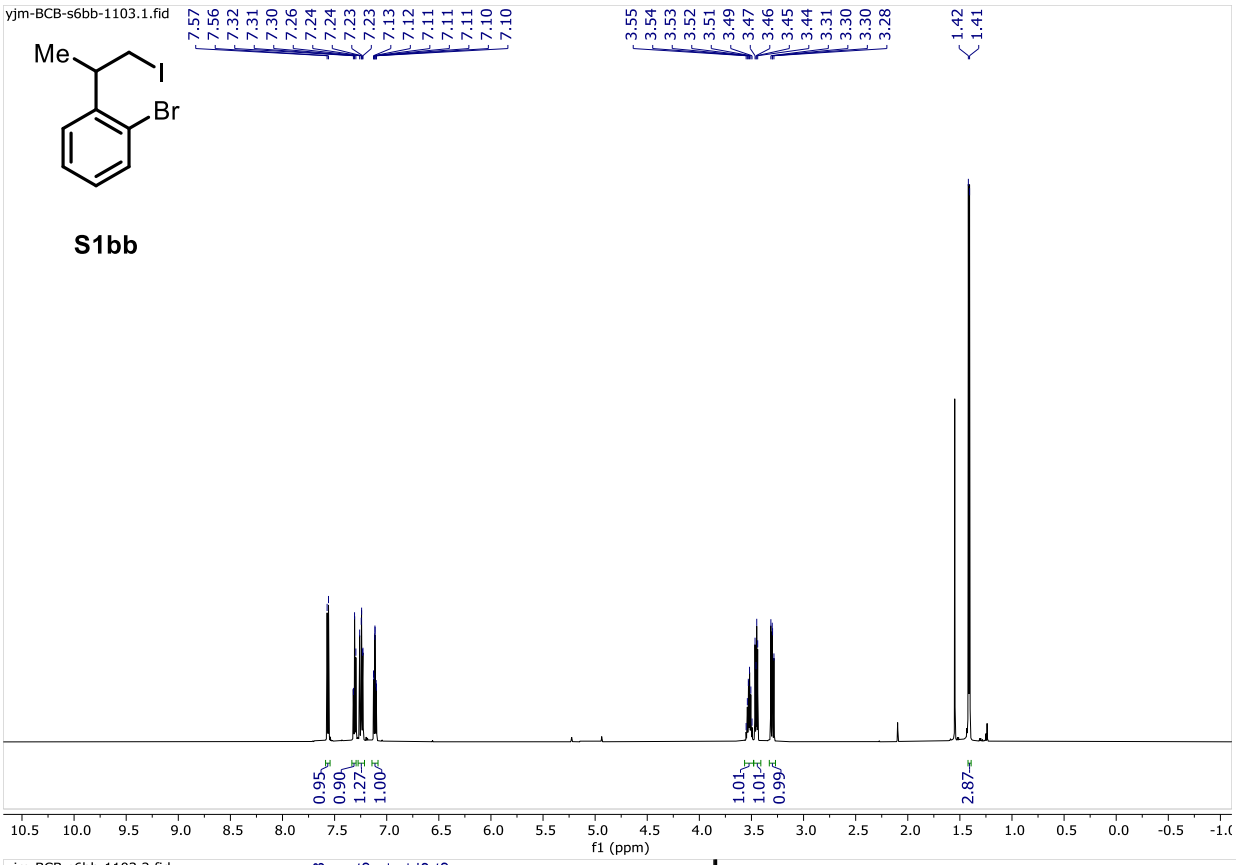


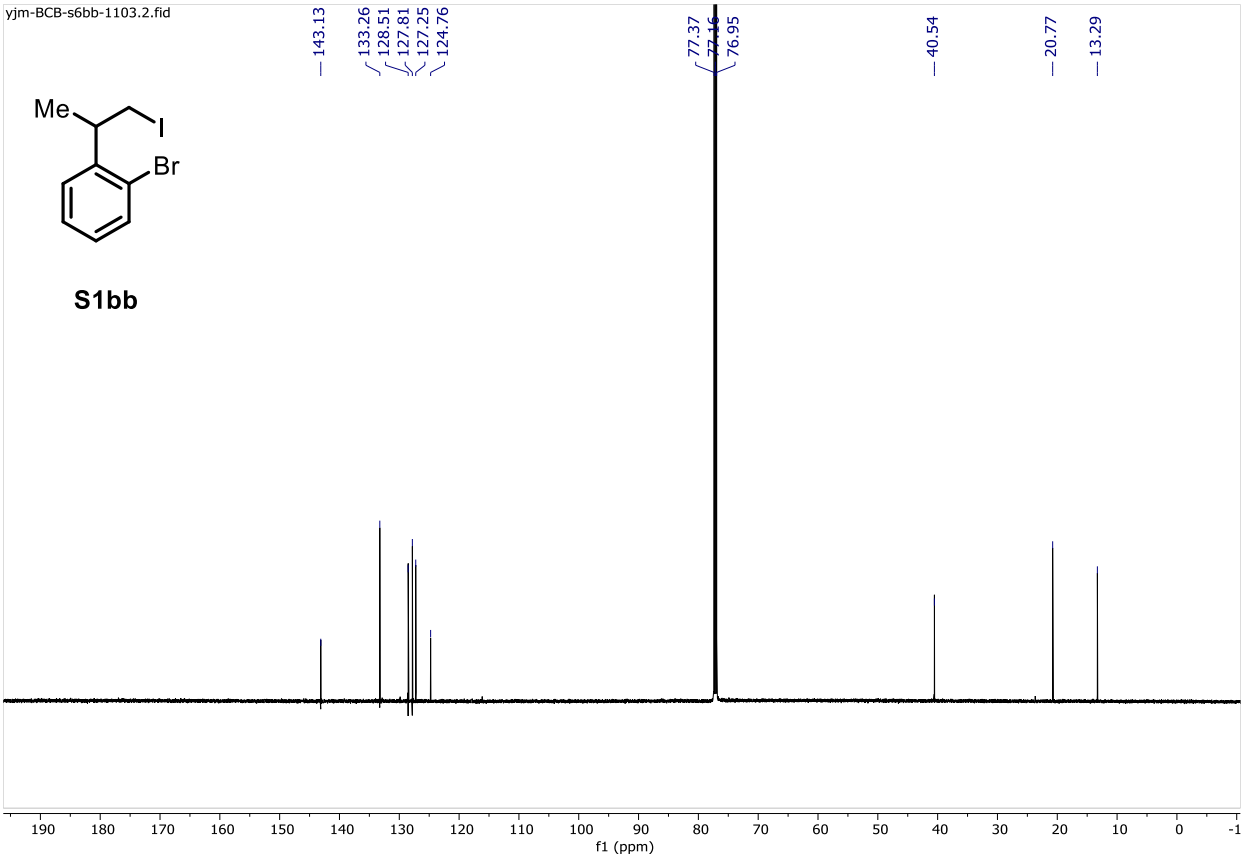
11




yjm-BCB-s6a-1103.1.fid
Me Me
Me
CO2H
Br
S1a
f1 (ppm)


yjm-BCB-s6a-1103.2.fid
Me Me
Me
CO2H
Br
S1a
f1 (ppm)


yjm-BCB-s6bb-1103.1.fid
Me
I
Br
S1bb
7.57
7.56
7.32
7.31
7.30
7.26
7.24
7.24
7.23
7.23
7.13
7.12
7.11
7.11
7.11
7.10
7.10
3.55
3.54
3.53
3.52
3.51
3.49
3.47
3.46
3.45
3.44
3.31
3.30
3.30
3.28
1.42
1.41
0.95
0.90
1.27
1.00
1.01
1.01
0.99
2.87
f1 (ppm)


yjm-BCB-s6bb-1103.2.fid
Me
I
Br
S1bb
143.13
133.26
128.51
127.81
127.25
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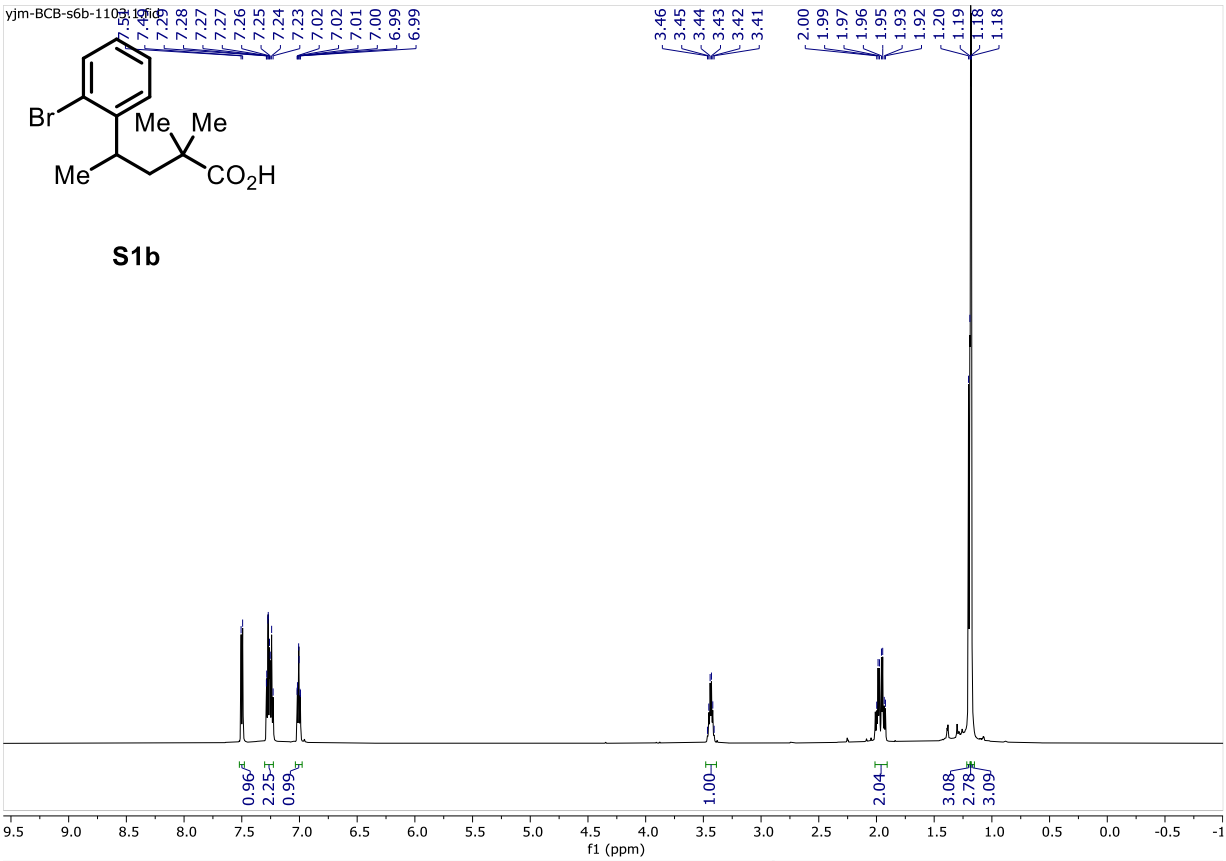
77.16
76.95
40.54
20.77
13.29
f1 (ppm)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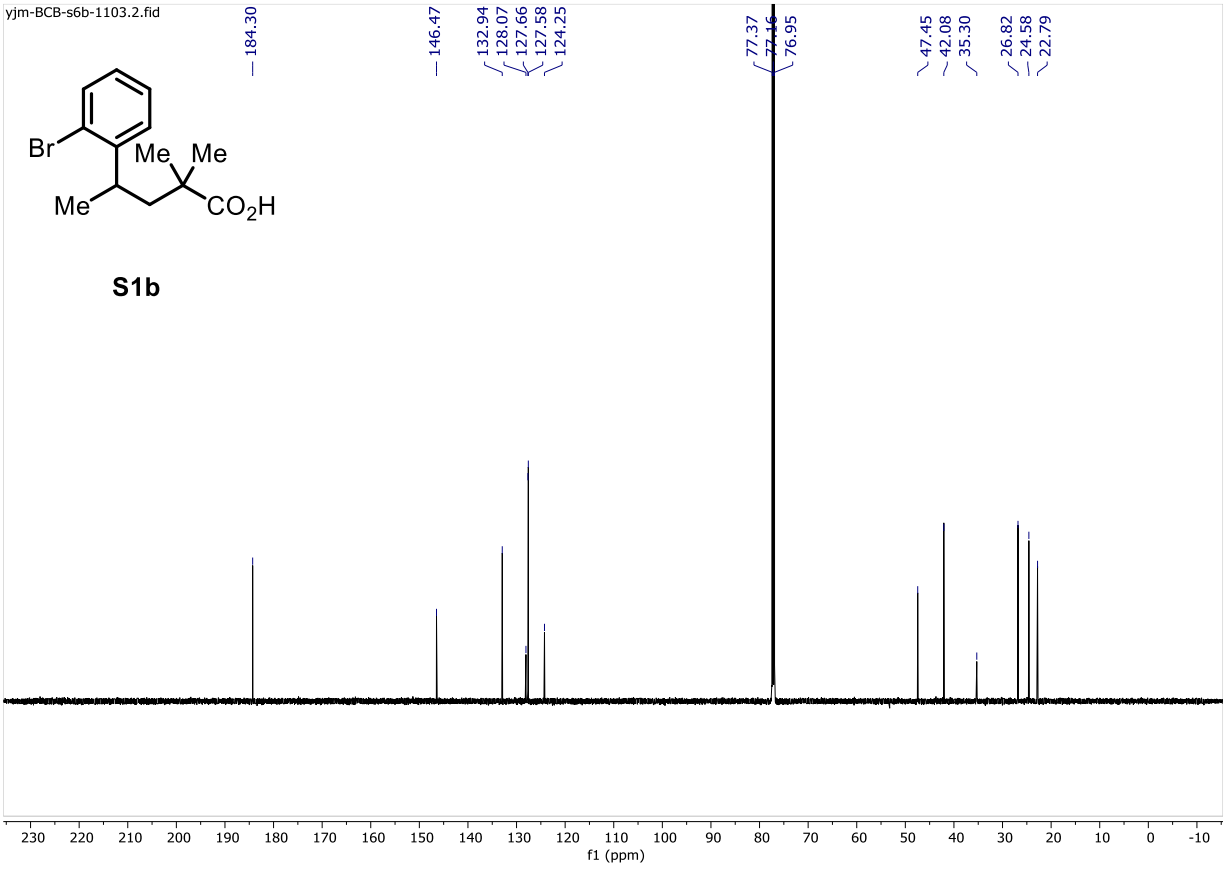
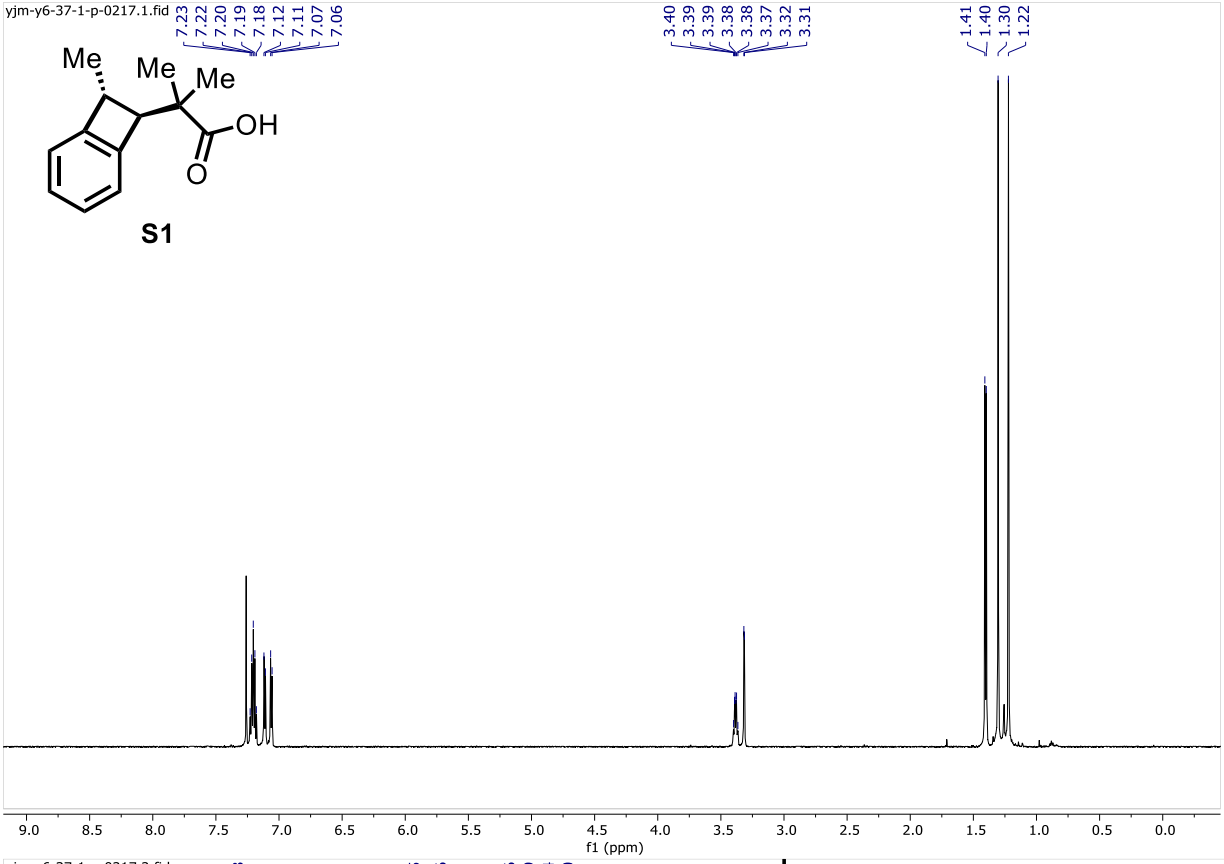
Br
Me
Me
Me
CO2H
S1b
f1 (ppm)


yjm-BCB-s6b-1103.2.fid
Br
Me
Me
Me
CO2H
S1b
f1 (ppm)


yjm-y6-37-1-p-0217.1.fid
7.23
7.22
7.20
7.19
7.18
7.12
7.11
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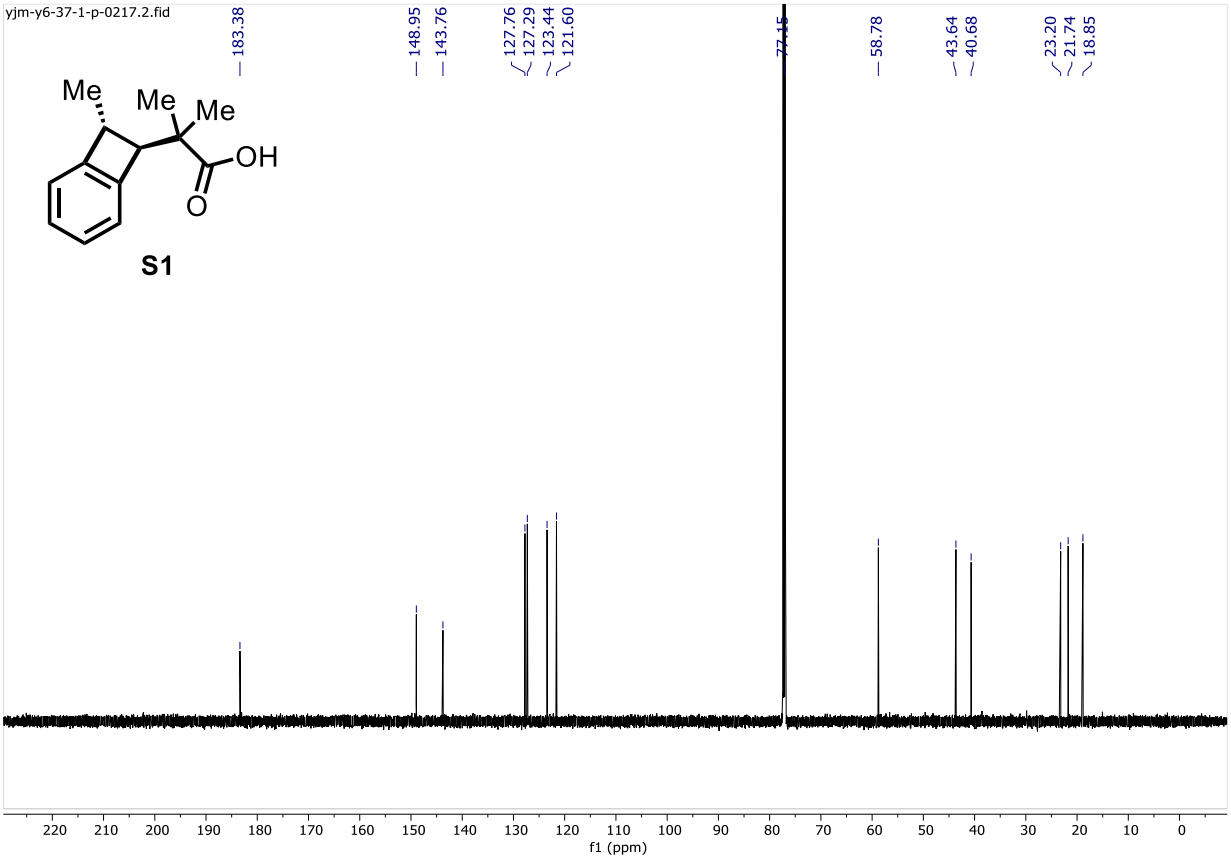
7.06
3.40
3.39
3.39
3.38
3.38
3.37
3.32
3.31
1.41
1.40
1.30
1.22
Me
Me
Me
OH
O
S1
f1 (ppm)


yjm-y6-37-1-p-0217.2.fid
183.38
148.95
143.76
127.76
127.29
123.44
121.60
77.45
58.78
43.64
40.68
23.20
21.74
18.85
Me
Me
Me
OH
O
S1
f1 (ppm)

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