

Boron-Catalyzed α -C-H Fluorination of Aryl Acetic Acids

Haipeng Hu,^{*a} Cuilin Wang,^b Xin Wu,^b Yangu Liu,^a Guizhou Yue,^a Gehong Su,^a Juhua Feng^a

^aCollege of Science Sichuan Agricultural University, Ya'an, Sichuan, 625014 (P. R. China)

^bSichuan Normal University, Chengdu 610068, (P. R. China).

E-mail: chemhhp@yeah.net.

Content

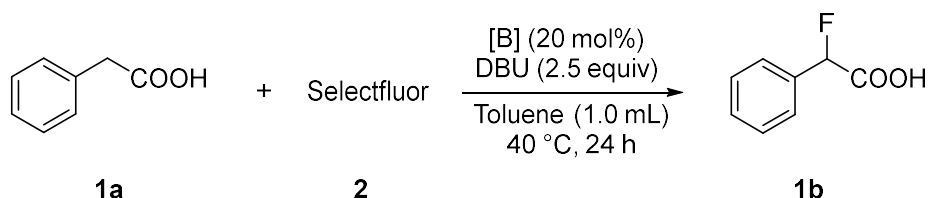
| | |
|---|----|
| 1. General Information..... | 3 |
| 2. Optimization of Reaction Conditions. | 4 |
| 3. General Procedure for the Catalytic α -Fluorination Reaction of Free Carboxylic acids. | 8 |
| 4. Gram-Scale Synthesis. | 8 |
| 5. Failed Examples..... | 9 |
| 6. The X-ray Structure of Product 4b..... | 9 |
| 7. Characterization of the Products..... | 11 |
| 8. Reference | 23 |
| 9. Copy of ^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F NMR Spectra..... | 25 |

1. General Information

Unless otherwise noted, all the reactions were performed under nitrogen atmosphere in the glove box. The solvents (THF, toluene and CH₂Cl₂) were dried according to the standard procedures. ¹H NMR spectra were recorded on a Bruker DRX400 (400 MHz), Bruker DRX600 (600 MHz) by using CDCl₃ as solvent. Chemical shifts (δ) values were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. ¹³C{¹H} NMR spectra were collected on commercial instruments (150 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (CDCl₃, δ = 77.0). ¹⁹F NMR spectra were collected at 565 MHz. HRMS was recorded on a commercial apparatus (ESI Source). The aryl acetic acids **2a-9a**, **11a-24a**, **30a-34a**, **39a-42a** and boron catalysts (PhB(OH)₂, B(OH)₃, C₆F₅B(OH)₂, B₂pin₂) were commercially available. Carboxylic acids **1a**,¹ **10a**,¹ **25a-29a**,²⁻⁶ (AcO)₄B₂O⁷ were prepared according to reported procedures.

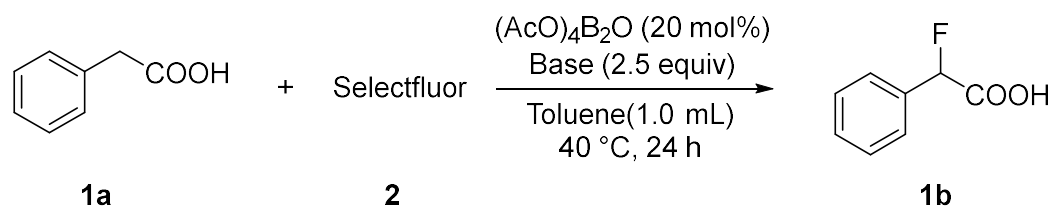
2. Optimization of Reaction Conditions.

Table S1. The screening of catalyst and [F] sources.



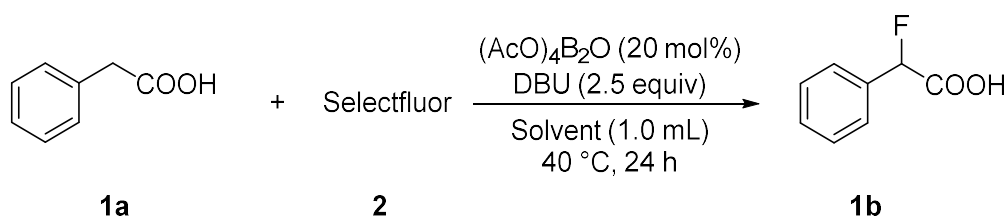
| Entry ^[a] | Catalyst | Base | Yield ^[b] (%) |
|----------------------|--|------|--------------------------|
| 1 | (AcO) ₄ B ₂ O | DBU | 88 |
| 2 | PhB(OH) ₂ | DBU | 64 |
| 3 | B(OH) ₃ | DBU | 74 |
| 4 | C ₆ F ₅ B(OH) ₂ | DBU | 66 |
| 5 | B ₂ pin ₂ | DBU | 60 |
| 6 ^[c] | (AcO) ₄ B ₂ O | DBU | 22 |

[a] All the reactions were performed with **1a** (0.10 mmol), **2** (0.10 mmol), [B] (20 mol%), DBU (2.5 equiv) in toluene (1.0 mL) at 40 °C under N₂ atmosphere for 24 h. [b] The yield was determined by ¹H NMR by using dimethyl terephthalate as internal standard. [c] The reaction was performed with **1a** (0.10 mmol), NFSI (0.10 mmol), [B] (20 mol%), DBU (2.5 equiv) in toluene (1.0 mL) at 40 °C under N₂ atmosphere for 24 h.

Table S2. The screening of base.

| Entry ^[a] | Base | Cat. | Yield ^[b] (%) |
|----------------------|---------------------------------|-------------------------------------|--------------------------|
| 1 | Pyrrolidine | (AcO) ₄ B ₂ O | NR |
| 2 | Pyridine | (AcO) ₄ B ₂ O | 24 |
| 3 | Et ₃ N | (AcO) ₄ B ₂ O | NR |
| 4 | DABCO | (AcO) ₄ B ₂ O | NR |
| 5 | DMAP | (AcO) ₄ B ₂ O | 60 |
| 6 | DBU | (AcO) ₄ B ₂ O | 88 |
| 7 | TMG | (AcO) ₄ B ₂ O | 54 |
| 8 | Na ₂ CO ₃ | (AcO) ₄ B ₂ O | NR |

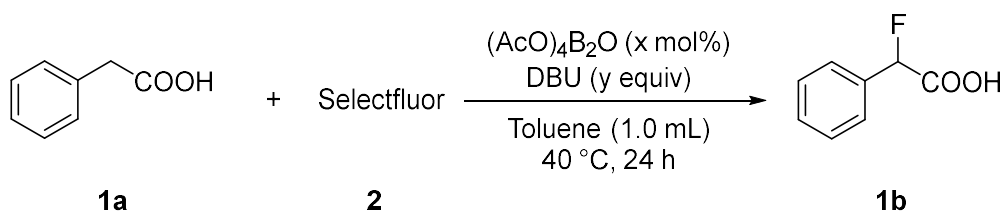
[a] All the reactions were performed with **1a** (0.10 mmol), **2** (0.10 mmol), (AcO)₄B₂O (20 mol%), base (2.5 equiv) in toluene (1.0 mL) at 40 °C under N₂ atmosphere for 24 h. [b] The yield was determined by ¹H NMR by using dimethyl terephthalate as internal standard; NR = No Reaction.

Table S3. The screening of solvents and reaction temperature.

| Entry ^[a] | Solvent | Base | Yield ^[b] % |
|----------------------|-------------------|------|------------------------|
| 1 | MTBE | DBU | NR |
| 2 | MeCN | DBU | NR |
| 3 | Et ₂ O | DBU | NR |
| 4 | THF | DBU | 70 |
| 5 | DME | DBU | 84 |
| 6 | Toluene | DBU | 96 |
| 7 ^[c] | Toluene | DBU | 67 |
| 8 ^[d] | Toluene | DBU | 91 |
| 9 ^[e] | Toluene | DBU | 60 |

[a] All the reactions were performed with **1a** (0.10 mmol), **2** (0.10 mmol), (AcO)₄B₂O (20 mol%), DBU (2.5 equiv) in toluene (1.0 mL) at 40 °C under N₂ atmosphere for 24 h. [b] The yield was determined by ¹H NMR by using dimethyl terephthalate as internal standard. [c] The reaction temperature was 0 °C. [d] The reaction temperature was 35 °C. [e] The reaction temperature was 60 °C. NR = No Reaction.

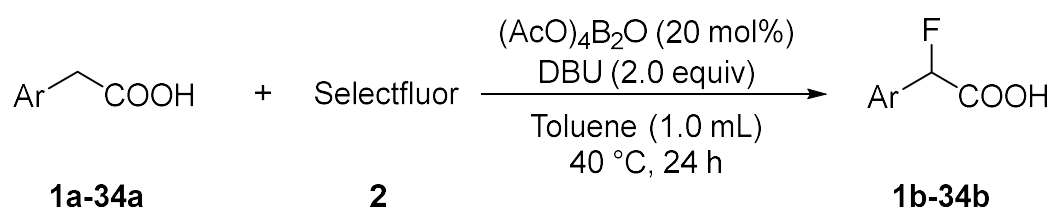
Table S4. Screening on the base and catalyst loading, and the ratio of carboxylic acid to selectfluor.



| Entry ^[a] | 1a:2 (x:y) | DBU (x equiv) | Yield ^[b] (%) |
|----------------------|----------------------|---------------|--------------------------|
| 1 | 1:1 | 2.5 | 88 |
| 2 | 1:1.05 | 2.5 | 88 |
| 3 | 1:1.2 | 2.5 | 95 |
| 4 | 1:1.5 | 2.5 | 96 |
| 5 | 1:2 | 2.5 | 32 |
| 6 | 1:3 | 2.5 | 20 |
| 7 | 1:1.5 | 1.0 | 69 |
| 8 | 1:1.5 | 1.5 | 84 |
| 9 | 1:1.5 | 2.0 | 96 |
| 10 ^[c] | 1:1.5 | 2.0 | trace |
| 11 ^[d] | 1:1.5 | 2.0 | 26 |
| 12 ^[e] | 1:1.5 | 2.0 | 90 |

[a] All the reactions were performed with **1a** (0.10 mmol), **2** (0.10 mmol), $(\text{AcO})_4\text{B}_2\text{O}$ (20 mol%), DBU (2.5 equiv) in toluene (1.0 mL) at 40 °C under N_2 atmosphere for 24 h. [b] The yield was determined by ^1H NMR by using dimethyl terephthalate as internal standard. [c]. The catalyst loading was 5 mol%. [d] The catalyst loading was 10 mol%. [e] The catalyst loading was 15 mol%.

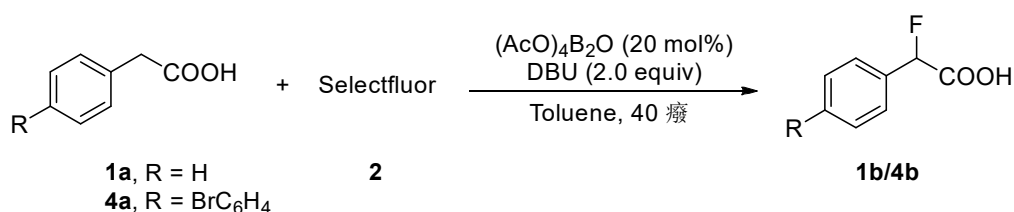
3. General Procedure for the Catalytic α -Fluorination Reaction of Free Carboxylic acids.



Procedure: In the glove-box, a dry reaction tube was charged with free carboxylic acids **1a-34a** (0.1 mmol), $(\text{AcO})_4\text{B}_2\text{O}$ (20 mol%, 5.5 mg), DBU (2.0 equiv, 38.1 mg) and toluene (1.0 mL). After stirring for 0.5 h, the selectfluor **2** (1.5 equiv) was added to the mixture and kept stirring at 40 °C for the indicated time.

Work up: The solvent was removed under reduced pressure, and 1M HCl was added to the obtained residue. Next, the mixture was extracted with MTBE (2 mL \times 3), and the combined organic phase was extracted with 1.0 M NaOH(aq.) (2 mL \times 3). The collected aqueous phase was acidified with 1M HCl to PH =1, and subsequently extracted with MTBE (2 mL \times 3). The combined organic phase was removed under reduced pressure and the residue was subjected to column chromatography on silica gel, eluting with petroleum ether–ethyl acetate (20% EA to 100% EA) to afford the corresponding product **1b-34b**.

4. Gram-Scale Synthesis.



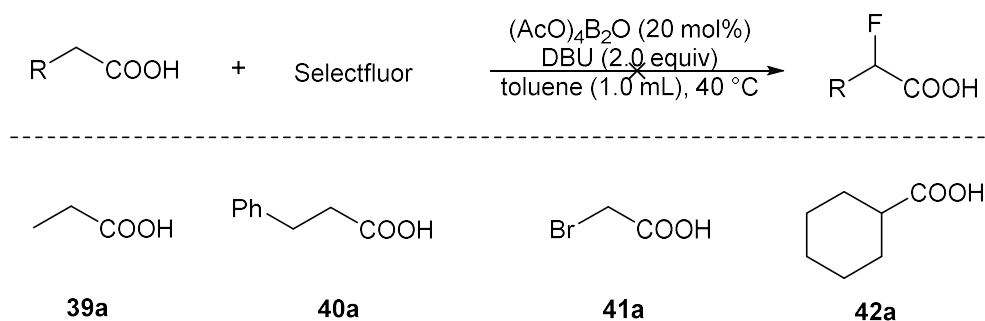
Procedure for the gram-scale synthesis of 1b: In the glove-box, a dry reaction tube was charged with free carboxylic acids **1a** (8.0 mmol, 1.09 g), $(\text{AcO})_4\text{B}_2\text{O}$ (20 mol%, 0.44 g), DBU (16.0 mmol, 2.43 g) and toluene (40.0 mL). After stirring for 0.5 h, the selectfluor **2** (12.0 mmol, 4.20 g) was added to the mixture. And the reaction mixture was stirred at 40 °C for 24 h.

Procedure for the gram-scale synthesis of 4b: In the glove-box, a dry reaction tube was charged with free carboxylic acids **4a** (7.0 mmol, 1.50 g), (AcO)₄B₂O (20 mol%, 0.38 g), DBU (14.0 mmol, 2.10 g) and toluene (70.0 mL). After stirring for 0.5 h, the selectfluor **2** (10.5 mmol, 3.70 g) was added to the mixture. Then, the reaction mixture was stirred at 40 °C for 24 h.

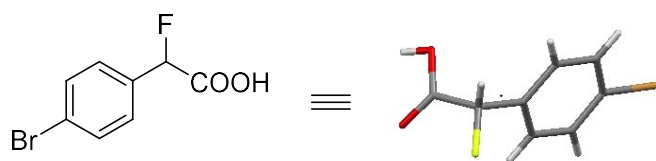
Work up: The solvent was removed under reduced pressure, and 1M HCl was added to the obtained residue. Next, the mixture was extracted with MTBE (20 mL × 3), and the combined organic phase was extracted with 1.0 M NaOH(aq.) (20 mL × 3). The collected aqueous phase was acidified with 1M HCl to PH =1, and subsequently extracted with MTBE (20 mL × 3). The combined organic phase was removed under reduced pressure and the residue was subjected to column chromatography on silica gel, eluting with petroleum ether–ethyl acetate (v/v, 4:1 to 1:1) to afford the corresponding product.

5. Failed Examples.

The following alkyl carboxylic acids **39a-42a** were not applicable under the standard reaction conditions, possibly due to the lack of conjugation effect of the phenyl ring leading to poorer nucleophilicity of α-position of alkyl carboxylic acids.



6. The X-ray Structure of Product 4b.



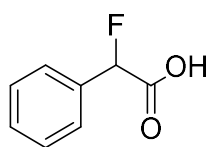
Single crystal of compound **4b** [C₈H₆BrFO₂] was obtained in PE and CH₂Cl₂. CCDC 2120636 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via <https://www.ccdc.cam.ac.uk/structures/>.

Table 1 Crystal data and structure refinement for compound 4b

| | |
|---|---|
| Identification code | compound 4b |
| Empirical formula | C ₁₆ H ₁₂ O ₄ F ₂ Br ₂ |
| Formula weight | 466.08 |
| Temperature/K | 300(2) |
| Crystal system | monoclinic |
| Space group | Pc |
| a/Å | 18.9959(7) |
| b/Å | 6.0086(3) |
| c/Å | 7.7051(3) |
| α/° | 90 |
| β/° | 91.911(4) |
| γ/° | 90 |
| Volume/Å ³ | 878.96(6) |
| Z | 2 |
| ρ _{calc} /cm ³ | 1.761 |
| μ/mm ⁻¹ | 6.202 |
| F(000) | 456.0 |
| Radiation | CuKα (λ = 1.54178) |
| 2θ range for data collection/° | 4.654 to 151.758 |
| Index ranges | -23 ≤ h ≤ 23, -7 ≤ k ≤ 7, -9 ≤ l ≤ 7 |
| Reflections collected | 2780 |
| Independent reflections | 2780 [R _{int} = ?, R _{sigma} = 0.0450] |
| Data/restraints/parameters | 2780/5/226 |
| Goodness-of-fit on F ² | 1.107 |
| Final R indexes [I ≥ 2σ (I)] | R ₁ = 0.0635, wR ₂ = 0.1894 |
| Final R indexes [all data] | R ₁ = 0.0730, wR ₂ = 0.2036 |
| Largest diff. peak/hole / e Å ⁻³ | 0.76/-0.49 |
| Flack parameter | 0.00(3) |

7. Characterization of the Products.

2-fluoro-2-phenylacetic acid (1b)



Following the general procedure, the optimized time is 24 h. Yield: 96% (14.8 mg); white solid; m.p. 80 – 85 °C.

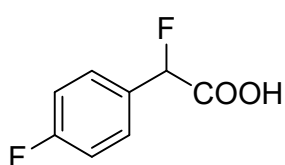
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.46 (s, 1H), 7.48 (dd, $J = 6.9, 2.9$ Hz, 2H), 7.42 (q, $J = 3.8$ Hz, 3H), 5.81 (d, $J = 47.4$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 174.00 (d, $J = 28.5$ Hz), 133.47 (d, $J = 21.0$ Hz), 129.95, 128.92, 126.71, 126.68, 88.83 (d, $J = 186.0$ Hz);

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -180.78 (d, $J = 45.2$ Hz).

HRMS (ESI⁻): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_8\text{FO}_2]^-$: 153.0346, found: 153.0346.

2-fluoro-2-(4-fluorophenyl)acetic acid (2b)



Following the general procedure, the optimized time is 24 h. Yield: 92% (15.8 mg); white solid; m.p. 92 – 103 °C.

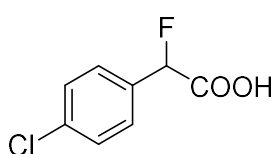
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.46 (s, 1H), 7.47 (dd, $J = 8.5, 5.2$ Hz, 2H), 7.11 (t, $J = 8.6$ Hz, 2H), 5.80 (d, $J = 47.2$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.69 (d, $J = 25.5$ Hz), 163.62 (d, $J = 247.5$ Hz), 129.46, 129.44, 129.32, 129.30, 128.82, 128.78, 128.76, 128.72, 116.12, 115.97, 88.20 (d, $J = 187.5$ Hz);

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -110.69 – -110.75 (m, 1F), -179.30 (d, 45.2 Hz).

HRMS (ESI⁻): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_5\text{F}_2\text{O}_2]^-$: 153.0346, found: 153.0346.

2-(4-chlorophenyl)-2-fluoroacetic acid (3b)



Following the general procedure, the optimized time is 24 h. Yield: 92% (17.3 mg); white solid; m.p. 71 – 80 °C.

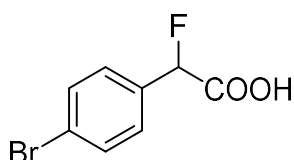
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.40 (s, 1H), 7.49 – 7.34 (m, 4H), 5.80 (d, $J = 47.1$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.55 (d, $J = 27.0$ Hz), 136.09 (d, $J = 1.5$ Hz), 131.87 (d, $J = 21.0$ Hz), 129.20, 127.99, 127.95, 88.09 (d, $J = 186.0$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -181.75 (d, J = 45.2 Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_5\text{Cl}^{35}\text{FO}_2]^-$: 186.9957, found: 186.9960;
 $[\text{C}_8\text{H}_5\text{Cl}^{37}\text{FO}_2]^-$: 188.9927, found: 188.9930.

2-(4-bromophenyl)-2-fluoroacetic acid (4b)



Following the general procedure, the optimized time is 24 h. Yield: 94%
(21.9 mg); white solid; m.p. 96 –103 °C.

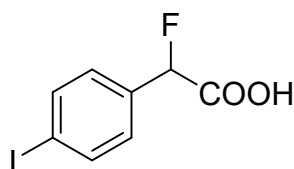
^1H NMR (600 MHz, CDCl_3) δ 7.56 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 5.78 (d, J = 47.2 Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.28 (d, J = 25.5 Hz), 132.4 (d, J = 21.0 Hz), 132.16, 128.20 (d, J = 7.5 Hz), 124.29, 88.14 (d, J = 187.5 Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -182.21 (d, J = 50.1 Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_5\text{Br}^{79}\text{FO}_2]^-$: 230.9451, found: 230.9458;
 $[\text{C}_8\text{H}_5\text{Br}^{81}\text{FO}_2]^-$: 232.9431, found: 232.9437.

2-fluoro-2-(4-iodophenyl)acetic acid (5b)



Following the general procedure, the optimized time is 24 h. Yield: 92%
(25.8 mg); white solid; m.p. 129 –135 °C.

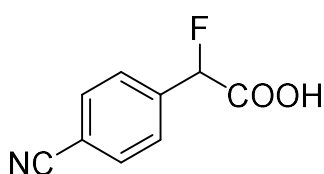
^1H NMR (600 MHz, CDCl_3) δ 7.77 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 6.09 (s, 1H), 5.77 (d, J = 47.2 Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 172.82 (d, J = 27.0 Hz), 138.09, 133.10 (d, J = 19.5 Hz), 128.27 (d, J = 6.0 Hz), 96.11, 88.24 (d, J = 187.5 Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -182.61 (d, J = 45.2 Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_5\text{IFO}_2]^-$: 278.9313, found: 278.9322.

2-(4-cyanophenyl)-2-fluoroacetic acid (6b)



Following the general procedure, the optimized time is 24 h. Yield: 60%
(10.8 mg); white solid; m.p. 90 – 111 °C.

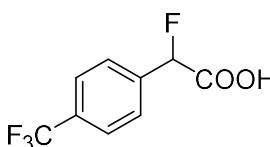
^1H NMR (600 MHz, CDCl_3) δ 7.73 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 7.32 (s, 1H), 5.90 (d, J = 47.1 Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 171.77 (d, $J = 27.0$ Hz), 138.43 (d, $J = 19.5$ Hz), 132.66, 126.96, 126.92, 117.98, 113.62, 87.82 (d, $J = 189.0$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -186.37 (d, $J = 45.2$ Hz).

HRMS (ESI⁻): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_9\text{H}_5\text{FNO}_2]^-$: 178.0299, found: 178.0300.

2-fluoro-2-(4-(trifluoromethyl)phenyl)acetic acid (7b)

 Following the general procedure, the optimized time is 24 h. Yield: 87% (19.3 mg); white solid; m.p. 82 – 92 °C.

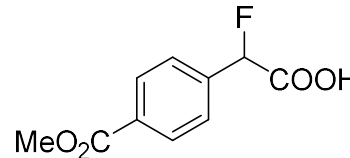
^1H NMR (600 MHz, CDCl_3) δ 8.01 (s, 1H), 7.69 (d, $J = 8.1$ Hz, 2H), 7.62 (d, $J = 8.1$ Hz, 2H), 5.90 (d, $J = 47.1$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.01 (d, $J = 30.0$ Hz), 137.15 (d, $J = 21.0$ Hz), 132.02 (d, $J = 31.5$ Hz), 126.76, 126.72, 126.27, 125.94, 125.91, 125.89, 125.86, 125.82, 123.68 (d, $J = 270.0$ Hz), 88.01 (d, $J = 187.5$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -62.92 (s, 3F), -185.09 (d, $J = 45.2$ Hz).

HRMS (ESI⁻): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_9\text{H}_5\text{F}_4\text{O}_2]^-$: 221.0220, found: 221.0226.

2-fluoro-2-(4-(methoxycarbonyl)phenyl)acetic acid (8b)

 Following the general procedure, the optimized time is 24 h. Yield: 92% (19.5 mg); white solid; m.p. 77 – 84 °C.

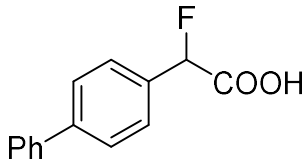
^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 8.0$ Hz, 2H), 7.57 (d, $J = 8.0$ Hz, 2H), 5.89 (d, $J = 47.3$ Hz, 1H), 3.93 (s, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 177.86, 167.47, 132.37, 131.07, 127.37, 127.32, 89.23 (d, $J = 199.5$ Hz), 53.40;

^{19}F NMR (565 MHz, CDCl_3) δ -184.35 (d, $J = 50.9$ Hz).

HRMS (ESI⁻): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_{10}\text{H}_8\text{FO}_4]^-$: 211.0401, found: 211.0405.

2-([1,1'-biphenyl]-4-yl)-2-fluoroacetic acid (9b)

 Following the general procedure, the optimized time is 24 h. Yield: 95% (21.9 mg); white solid; m.p. 162 – 168 °C.

^1H NMR (600 MHz, $\text{DMSO}-d$) δ 7.73 (d, $J = 8.0$ Hz, 2H), 7.70 – 7.65 (m,

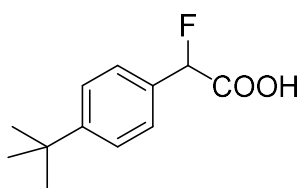
2H), 7.56 – 7.44 (m, 4H), 7.39 (t, $J = 7.4$ Hz, 1H), 6.03 (d, $J = 47.6$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, DMSO- d) δ 170.08 (d, $J = 27.0$ Hz), 141.50, 139.75, 134.59, 134.46, 129.33, 128.14, 127.89, 127.86, 127.37, 127.12, 88.83 (d, $J = 178.5$ Hz);

^{19}F NMR (565 MHz, DMSO- d) δ -170.75 (d, $J = 50.9$ Hz).

HRMS (ESI-): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_{10}\text{H}_8\text{FO}_4]^-$: 229.0659, found: 229.0665.

2-(4-(tert-butyl)phenyl)-2-fluoroacetic acid (10b)



Following the general procedure, the optimized time is 24 h. Yield: 95% (19.9 mg); white solid; m.p. 98 – 108 °C

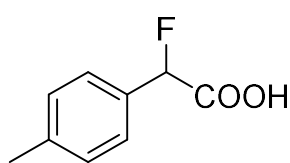
^1H NMR (600 MHz, CDCl_3) δ 8.70 (s, 1H), 7.47 – 7.25 (m, 4H), 5.71 (d, $J = 47.5$ Hz, 1H), 1.24 (s, 9H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 174.36 ($J = 28.5$ Hz), 153.23, 130.49 ($J = 4.5$ Hz), 126.60 ($J = 4.5$ Hz), 125.92, 88.78 ($J = 186.0$ Hz), 34.79, 31.24;

^{19}F NMR (565 MHz, CDCl_3) δ -179.19 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_{14}\text{H}_{10}\text{FO}_2]^-$: 209.0972, found: 209.0977.

2-fluoro-2-(p-tolyl)acetic acid (11b)



Following the general procedure, the optimized time is 24 h. Yield: 80% (13.4 mg); oil.

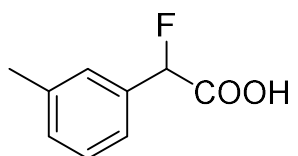
^1H NMR (600 MHz, CDCl_3) δ 7.29 (d, $J = 7.7$ Hz, 2H), 7.15 (d, $J = 7.8$ Hz, 2H), 5.71 (d, $J = 47.5$ Hz, 1H), 2.30 (s, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.86, 140.13, 130.55 (d, $J = 21.0$ Hz), 129.61, 126.82, 126.79, 88.83 (d, $J = 184.5$ Hz), 21.32;

^{19}F NMR (565 MHz, CDCl_3) δ -178.61 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M}-\text{H}]^-$ for $[\text{C}_9\text{H}_8\text{FO}_2]^-$: 167.0503, found: 167.0503.

2-fluoro-2-(m-tolyl)acetic acid (12b)



Following the general procedure, the optimized time is 24 h. Yield: 89% (15.1 mg); light yellow oil.

^1H NMR (600 MHz, CDCl_3) δ 9.09 (s, 1H), 7.33 – 7.19 (m, 4H), 5.77 (d, J

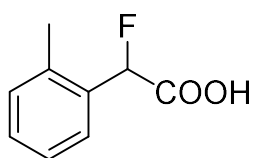
= 47.5 Hz, 1H), 2.37 (s, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 174.33 (d, $J = 28.5$ Hz), 138.85, 133.41, 133.27, 130.76, 128.83, 127.3 (d, $J = 6.0$ Hz) 127.32, 127.28, 123.88 (d, $J = 7.5$ Hz), 88.89 (d, $J = 186.0$ Hz), 21.36;

^{19}F NMR (565 MHz, CDCl_3) δ -180.18 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_9\text{H}_8\text{FO}_2]^-$: 167.0503, found: 167.0503.

2-fluoro-2-(*o*-tolyl)acetic acid (13b)



Following the general procedure, the optimized time is 24 h. Yield: 90% (15.1 mg); white solid; m.p. 47 – 54 °C.

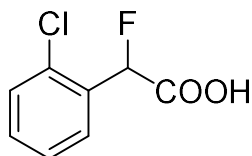
^1H NMR (600 MHz, CDCl_3) δ 7.42 (d, $J = 7.6$ Hz, 1H), 7.33 – 7.20 (m, 3H), 6.02 (d, $J = 47.0$ Hz, 1H), 5.67 (s, 1H), 2.45 (s, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.87, 136.66 (d, $J = 4.5$ Hz), 132.12, 131.99, 131.03, 129.96, 127.32 (d, $J = 7.5$ Hz), 126.46 (d, $J = 4.5$ Hz), 86.76 (d, $J = 184.5$ Hz), 19.19;

^{19}F NMR (565 MHz, CDCl_3) δ -180.08 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_9\text{H}_8\text{FO}_2]^-$: 167.0503, found: 167.0504.

2-(2-chlorophenyl)-2-fluoroacetic acid (14b)



Following the general procedure, the optimized time is 24 h. Yield: 92% (17.3 mg); colorless oil.

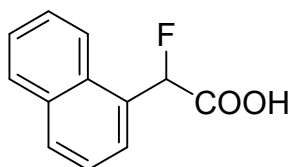
^1H NMR (600 MHz, CDCl_3) δ 7.52 (dd, $J = 7.5, 1.9$ Hz, 1H), 7.44 (d, $J = 7.7$ Hz, 1H), 7.40 – 7.31 (m, 2H), 7.11 (s, 1H), 6.27 (d, $J = 46.4$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 172.87 (d, $J = 28.5$ Hz), 133.67 (d, $J = 4.5$ Hz), 131.68 (d, $J = 21.0$ Hz), 131.28, 130.06, 128.71 (d, $J = 6.0$ Hz), 127.41, 85.80 (d, $J = 184.5$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -181.06 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_5\text{Cl}^{35}\text{FO}_2]^-$: 186.9957, found: 186.9959; $[\text{C}_8\text{H}_5\text{Cl}^{37}\text{FO}_2]^-$: 188.9927, found: 188.9929.

2-fluoro-2-(naphthalen-1-yl)acetic acid (15b)



Following the general procedure, the optimized time is 24 h. Yield: 93% (19.0 mg); white solid; m.p. 145 – 151 °C.

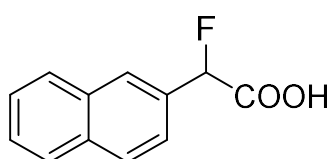
¹H NMR (600 MHz, CDCl₃) δ 8.14 (d, *J* = 8.3 Hz, 1H), 7.97 – 7.83 (m, 2H), 7.61 (d, *J* = 7.1 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 6.39 (d, *J* = 46.8 Hz, 1H);

¹³C{¹H} NMR (150 MHz, CDCl₃) δ 174.11 (d, *J* = 27.0 Hz), 133.89, 130.90, 130.51, (d, *J* = 19.5 Hz), 128.92, 127.24, 127.00 (d, *J* = 9.0 Hz), 126.35, 125.11, 123.58, 88.08 (d, *J* = 186.0 Hz);

¹⁹F NMR (565 MHz, CDCl₃) δ -178.63 (d, *J* = 45.2 Hz).

HRMS (ESI-): calculated *m/z* [M-H]⁻ for [C₁₂H₈FO₂]⁻: 203.0503, found: 203.0506.

2-fluoro-2-(naphthalen-2-yl)acetic acid (16b)



Following the general procedure, the optimized time is 24 h. Yield: 87% (17.8 mg); white solid; m.p. 161 – 171 °C.

¹H NMR (600 MHz, DMSO-*d*) δ 8.04 (s, 1H), 7.99 (dd, *J* = 8.8, 3.9 Hz, 2H), 7.97 – 7.92 (m, 1H), 7.62 – 7.52 (m, 3H), 6.18 (d, *J* = 47.4 Hz, 1H),

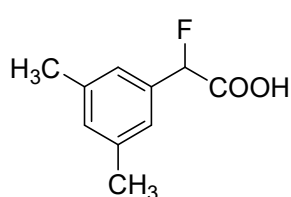
3.44 (s, 1H);

¹³C{¹H} NMR (150 MHz, DMSO-*d*) δ 170.09 (d, *J* = 27.0 Hz), 133.43, 132.91, 132.81, 132.77, 128.88, 128.50, 128.01, 127.31, 127.08, 126.98, 126.94, 126.91, 124.28 (d, *J* = 4.5 Hz), 89.2 (d, *J* = 150 Hz);

¹⁹F NMR (565 MHz, DMSO-*d*) δ -171.01 (d, *J* = 50.9 Hz).

HRMS (ESI-): calculated *m/z* [M-H]⁻ for [C₁₂H₈FO₂]⁻: 203.0503, found: 203.0507.

2-(3,5-dimethylphenyl)-2-fluoroacetic acid (17b)



Following the general procedure, the optimized time is 24 h. Yield: 92% (16.8 mg); white solid; m.p. 70 – 81 °C.

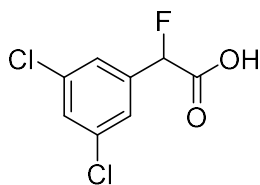
¹H NMR (600 MHz, CDCl₃) δ 8.23 (s, 1H), 7.07 (d, *J* = 20.0 Hz, 3H), 5.73 (d, *J* = 47.6 Hz, 1H), 2.33 (s, 6H);

¹³C{¹H} NMR (150 MHz, CDCl₃) δ 174.25 (d, *J* = 37.5 Hz), 138.72, 133.29 (d, *J* = 19.5 Hz), 131.66, 124.55, 124.51, 88.98 (d, *J* = 184.5 Hz), 21.24;

¹⁹F NMR (565 MHz, CDCl₃) δ -179.42 (d, *J* = 45.2 Hz).

HRMS (ESI-): calculated *m/z* [M-H]⁻ for [C₁₀H₁₀FO₂]⁻: 181.0659, found: 181.0667.

2-(3,5-dichlorophenyl)-2-fluoroacetic acid (18b)



Following the general procedure, the optimized time is 24 h. Yield: 94% (21.0 mg); white solid; m.p. 82 – 85 °C.

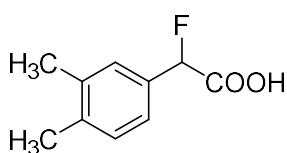
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 9.12 (s, 1H), 7.31 (dd, $J = 14.3, 1.9$ Hz, 3H), 5.69 (d, $J = 47.0$ Hz, 1H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 172.84 (d, $J = 27.0$ Hz), 136.36 (d, $J = 22.5$ Hz), 135.68, 130.03, 124.89, 124.84, 87.27 (d, $J = 189.0$ Hz).

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -184.86 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_8\text{H}_4\text{Cl}^{35}_2\text{FO}_2]^-$: 220.9567, found: 220.9572; $[\text{C}_8\text{H}_4\text{Cl}^{37}_2\text{FO}_2]^-$: 222.9537, found: 222.9542.

2-(3,4-dimethylphenyl)-2-fluoroacetic acid (19b)



Following the general procedure, the optimized time is 24 h. Yield: 90% (16.4 mg); white solid; m.p. 47 – 55 °C.

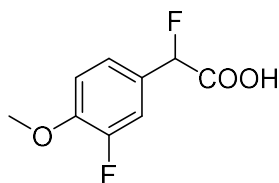
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.32 (s, 1H), 7.18 – 7.08 (m, 3H), 5.66 (d, $J = 47.6$ Hz, 1H), 2.20 (s, 6H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 174.32 (d, $J = 28.5$ Hz), 138.82, 137.42, 130.94 (d, $J = 21.0$ Hz), 130.12, 127.98 (d, $J = 6.0$ Hz), 124.44 (d, $J = 4.5$ Hz), 88.91 (d, $J = 184.5$ Hz), 19.77, 19.67;

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -178.73 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{10}\text{H}_{10}\text{FO}_2]^-$: 181.0659, found: 181.0660.

2-fluoro-2-(3-fluoro-4-methoxyphenyl)acetic acid (20b)



Following the general procedure, the optimized time is 24 h. Yield: 90% (18.2 mg); white solid; m.p. 103 – 111 °C

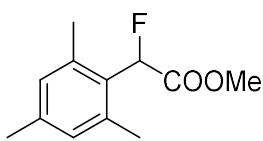
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.18 – 7.11 (m, 2H), 6.92 (t, $J = 8.7$ Hz, 1H), 5.68 (d, $J = 47.2$ Hz, 1H), 4.37 (s, 1H), 3.84 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 172.47 (d, $J = 28.5$ Hz), 153.10, 151.46, 149.05 (d, $J = 186.0$ Hz), 126.20, 126.15, 126.01, 123.25, 114.70 (dd, $J = 19.5, 6.0$ Hz), 113.38, 88.01 (d, $J = 186.0$ Hz), 56.29.

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -177.74 (d, $J = 11.3$ Hz), -133.52 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_9\text{H}_7\text{F}_2\text{O}_3]^-$: 201.0358, found: 201.0361.

methyl 2-fluoro-2-mesitylacetate (21b)



Following the general procedure, the optimized time is 24 h. Yield: 20% (4.3 mg); colorless oil.

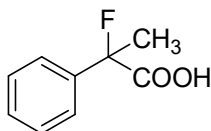
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.80 (s, 2H), 6.10 (d, $J = 46.1$ Hz, 1H), 3.70 (s, 3H), 2.29 (d, $J = 2.3$ Hz, 6H), 2.20 (d, $J = 2.1$ Hz, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 170.00, (d, $J = 28.5$ Hz), 139.38 (d, $J = 1.5$ Hz), 137.62 (d, $J = 3.0$ Hz), 129.85, 128.22 (d, $J = 16.5$ Hz), 85.93 (d, $J = 181.5$ Hz), 52.63, 21.00, 19.83.

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -182.71 (d, $J = 45.2$ Hz).

HRMS (ESI-TOF): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{12}\text{H}_{15}\text{FO}_2 + \text{H}^+]$: 211.1134, found: 211.1133.

2-fluoro-2-phenylpropanoic acid (22b)



Following the general procedure, the optimized time is 24 h. Yield: 65% (10.9 mg); colorless oil.

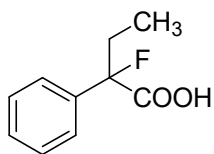
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.57 – 7.50 (m, 2H), 7.43 – 7.32 (m, 3H), 6.83 (s, 1H), 1.95 (d, $J = 22.3$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.69 (d, $J = 22.5$ Hz), 138.52 (d, $J = 22.5$ Hz), 128.89, 128.58, 124.75, 124.69, 94.42 (d, $J = 220.5$ Hz), 24.49 (d, $J = 24.0$ Hz);

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -151.26 (q, $J = 22.6$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_9\text{H}_8\text{FO}_2]^-$: 167.0503, found: 167.0503.

2-fluoro-2-phenylbutanoic acid (23b)



Following the general procedure, the optimized time is 24 h. Yield: 46% (8.4 mg); light yellow oil.

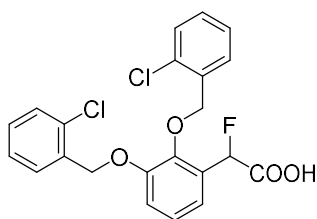
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.51 (q, $J = 8.6$ Hz, 2H), 7.41 – 7.27 (m, 3H), 6.74 (s, 1H), 2.47 – 2.11 (m, 2H), 0.97 (p, $J = 7.6$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.38 (d, $J = 31.5$ Hz), 137.32 (d, $J = 24.0$ Hz), 128.71, 128.54, 124.86, 124.80, 97.18, 97.18 (d, $J = 187.5$ Hz), 31.27 (d, $J = 22.5$ Hz), 7.45;

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -166.72 (s, 1F).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{10}\text{H}_{10}\text{FO}_2]^-$: 181.0659, found: 181.0661.

2-(2,3-bis((2-chlorobenzyl)oxy)phenyl)-2-fluoroacetic acid (25b)



Following the general procedure, the optimized time is 24 h. Yield: 82% (35.7 mg); colorless oil.

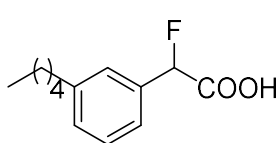
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.50 (s, 1H), 7.48 (dd, $J = 6.5, 2.8$ Hz, 1H), 7.38 (dd, $J = 7.6, 1.6$ Hz, 1H), 7.29 (d, $J = 7.9$ Hz, 1H), 7.27 – 7.22 (m, 1H), 7.19 – 7.10 (m, 4H), 7.06 – 6.95 (m, 3H), 6.09 (d, $J = 47.1$ Hz, 1H), 5.19 (d, $J = 2.5$ Hz, 2H), 5.12 (s, 2H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.59 (d, $J = 21.0$ Hz), 151.66, 146.33, 146.31, 135.02, 134.03, 132.86 (d, $J = 12.0$ Hz), 129.73, 129.44, 129.31, 129.25, 129.17, 129.15, 128.49 (d, $J = 19.5$ Hz), 127.04, 126.88, 124.91, 120.82, 120.79, 115.88, 84.4 (d, $J = 183.0$ Hz), 72.48, 68.18;

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -177.57 (d, $J = 50.9$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{22}\text{H}_{16}\text{Cl}^{35}_2\text{FO}_4]^-$: 433.0404, found: 433.0414; $[\text{C}_{22}\text{H}_{16}\text{Cl}^{37}_2\text{FO}_4]^-$: 435.0375, found: 435.0384.

2-fluoro-2-(3-pentylphenyl)acetic acid (26b)



Following the general procedure, the optimized time is 24 h. Yield: 74% (16.5 mg); colorless oil.

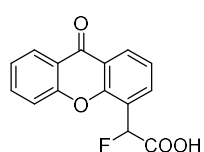
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.29 (q, $J = 7.2$ Hz, 3H), 7.23 (d, $J = 7.4$ Hz, 1H), 5.78 (d, $J = 47.6$ Hz, 1H), 2.61 (t, $J = 7.9$ Hz, 2H), 1.61 (t, $J = 7.5$ Hz, 2H), 1.32 (ddt, $J = 11.3, 7.4, 4.8$ Hz, 4H), 0.88 (td, $J = 7.0, 2.9$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 173.70, 143.87, 133.41 (d, $J = 21.0$ Hz), 130.03, 128.79, 126.70 (d, $J = 21.0$ Hz), 126.70 (d, $J = 4.5$ Hz), 124.03 (d, $J = 4.5$ Hz), 89.03 (d, $J = 184.5$ Hz), 35.80, 31.49, 31.02, 22.50, 14.01;

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -179.90 (d, $J = 45.2$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{13}\text{H}_{16}\text{FO}_2]^-$: 223.1129, found: 223.1134.

2-fluoro-2-(9-oxo-9,10-dihydroanthracen-2-yl)acetic acid (27b)



Following the general procedure, the optimized time is 24 h. Yield: 30% (8.1 mg); white solid; m.p. 165 – 174 °C.

$^1\text{H NMR}$ (600 MHz, $\text{DMSO}-d_6$) δ 8.27 (dt, $J = 8.0, 1.5$ Hz, 1H), 8.18 (dd, $J = 7.9,$

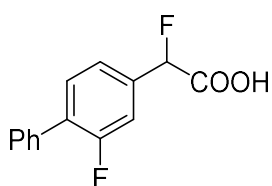
1.5 Hz, 1H), 7.99 (d, $J = 7.4$ Hz, 1H), 7.89 (ddd, $J = 8.7, 7.1, 1.6$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.55 (t, $J = 7.7$ Hz, 1H), 7.49 (t, $J = 7.5$ Hz, 1H), 6.55 (d, $J = 46.2$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, DMSO- d_6) δ 176.07, 169.86 (d, $J = 27.0$ Hz), 155.50, 153.66 (d, $J = 1.5$ Hz), 136.30, 135.91 (d, $J = 4.5$ Hz), 128.26, 126.50, 125.29, 124.98 (d, $J = 21.0$ Hz), 124.68, 121.93, 121.36, 118.52, 84.72 (d, $J = 21.0$ Hz);

^{19}F NMR (565 MHz, DMSO- d_6) δ -176.66 (d, $J = 50.9$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{15}\text{H}_8\text{FO}_4]^-$: 271.0401, found: 271.0410.

2-fluoro-2-(2-fluoro-[1,1'-biphenyl]-4-yl)acetic acid (28b)



Following the general procedure, the optimized time is 24 h. Yield: 90% (22.3 mg); white solid; m.p. 165 – 170 °C.

^1H NMR (600 MHz, DMSO- d_6) δ 7.66 (t, $J = 8.0$ Hz, 1H), 7.62 (d, $J = 7.7$ Hz, 2H), 7.55 (t, $J = 7.6$ Hz, 2H), 7.48 (t, $J = 7.4$ Hz, 1H), 7.46 – 7.41 (m, 2H),

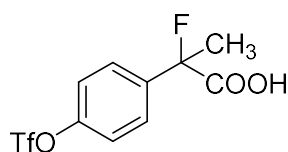
6.12 (d, $J = 47.4$ Hz, 1H), 3.72 (s, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, DMSO- d_6) δ 169.79 (d, $J = 27.0$ Hz), 160.06, 158.43, 137.37, 137.32, 137.23, 137.19, 134.91, 131.72, 131.70, 129.54 (d, $J = 13.5$ Hz), 129.28, 129.15, 128.64, 123.62, 123.59, 123.56, 114.99 (d, $J = 6.0$ Hz), 88.36 (d, $J = 180.0$ Hz);

^{19}F NMR (565 MHz, DMSO- d_6) δ -117.64 (t, $J = 11.3$ Hz), -177.36 (d, $J = 50.9$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{14}\text{H}_9\text{F}_2\text{O}_2]^-$: 247.0565, found: 247.0571.

2-fluoro-2-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoic acid (29b)



Following the general procedure, the optimized time is 24 h. Yield: 93% (29.4 mg); white solid; m.p. 132 – 138 °C.

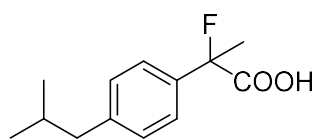
^1H NMR (600 MHz, Chloroform- d) δ 7.64 (d, $J = 8.9$ Hz, 2H), 7.49 (s, 1H), 7.31 (d, $J = 8.9$ Hz, 2H), 1.97 (d, $J = 22.2$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.22 (d, $J = 24.0$ Hz), 149.74, 138.88 (d, $J = 22.5$ Hz), 127.00, 126.94, 121.90, 121.59, 119.77, 117.65, 115.52, 93.69 (d, $J = 187.5$ Hz), 24.76 (d, $J = 24.0$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -72.82 (s, 1F), -152.48 (q, $J = 22.6$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{10}\text{H}_7\text{F}_4\text{O}_5\text{S}]^-$: 314.9945, found: 314.9953.

2-fluoro-2-(4-isobutylphenyl)propanoic acid (30b)



Following the general procedure, the optimized time is 24 h. Yield: 54% (12.2 mg); white solid; m.p. 70 – 76 °C

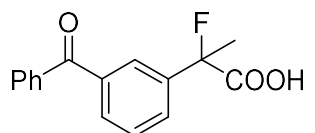
$^1\text{H NMR}$ (600 MHz, Chloroform-*d*) δ 8.30 (s, 1H), 7.42 (d, $J = 8.2$ Hz, 2H), 7.17 (d, $J = 8.1$ Hz, 2H), 2.48 (d, $J = 7.2$ Hz, 2H), 1.95 (d, $J = 22.2$ Hz, 3H), 1.86 (dq, $J = 13.5$, 6.7, 6.1 Hz, 1H), 0.90 (d, $J = 6.6$ Hz, 6H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 176.57 (d, $J = 27.0$ Hz), 142.73, 135.58 (d, $J = 22.5$ Hz), 129.33, 129.22, 124.56 (d, $J = 7.5$ Hz), 94.84, 93.61, 45.03, 30.16, 24.40, 24.25, 22.38;

$^{19}\text{F NMR}$ (565 MHz, CDCl_3) δ -150.42 (q, $J = 22.6$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{13}\text{H}_{16}\text{FO}_2]^-$: 223.1129, found: 223.1134.

2-(3-benzoylphenyl)-2-fluoropropanoic acid (31b)



Following the general procedure, the optimized time is 24 h. Yield: 80% (21.8 mg); colorless oil.

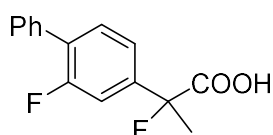
$^1\text{H NMR}$ (600 MHz, DMSO-*d*) δ 7.92 (t, $J = 1.9$ Hz, 1H), 7.71 (ddd, $J = 9.5$, 6.7, 3.0 Hz, 4H), 7.55 – 7.51 (m, 1H), 7.43 (dt, $J = 22.3$, 7.8 Hz, 3H), 6.05 (s, 1H), 1.92 (d, $J = 22.3$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, DMSO-*d*) δ 196.37, 174.85 (d, $J = 28.5$ Hz), 138.97 (d, $J = 28.5$ Hz), 137.90, 137.08, 132.85, 130.64, 130.16, 128.72 (d, $J = 7.5$ Hz), 128.66, 128.45, 126.35 (d, $J = 7.5$ Hz), 94.05 (d, $J = 186.0$ Hz), 24.69, 24.54;

$^{19}\text{F NMR}$ (565 MHz, DMSO-*d*) δ -151.98 (q, $J = 22.6$ Hz).

HRMS (ESI-): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{16}\text{H}_{12}\text{FO}_3]^-$: 271.0765, found: 271.0773.

2-fluoro-2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoic acid (32b)



Following the general procedure, the optimized time is 24 h. Yield: 95% (24.9 mg); white solid; m.p. 98 – 107 °C.

$^1\text{H NMR}$ (600 MHz, Chloroform-*d*) δ 7.55 – 7.50 (m, 2H), 7.45 (dt, $J = 11.7$, 7.9 Hz, 3H), 7.41 – 7.33 (m, 3H), 1.98 (d, $J = 22.1$ Hz, 3H);

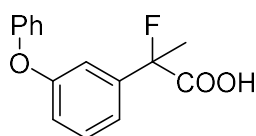
$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.94, 159.59 (d, $J = 247.5$ Hz), 139.78, 139.73, 139.62, 139.57, 134.98, 130.99 (d, $J = 3.0$ Hz), 129.67 (d, $J = 13.5$ Hz), 128.99, 128.97, 128.55, 128.04,

120.76, 120.74, 120.71, 120.68, 113.17, 113.12, 113.01, 112.94, 94.38, 93.13, 24.59 (d, $J = 22.5$ Hz);

^{19}F NMR (565 MHz, CDCl_3) δ -116.50 (m, 1F), -151.59.

HRMS (ESI⁻): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{15}\text{H}_{11}\text{F}_2\text{O}_2]^-$: 261.0722, found: 261.0729.

2-fluoro-2-(3-phenoxyphenyl)propanoic acid (33b)



Following the general procedure, the optimized time is 24 h. Yield: 65% (16.9 mg); colorless oil.

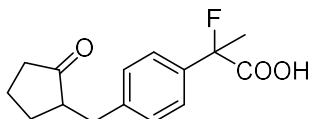
^1H NMR (600 MHz, Chloroform- d) δ 7.29 – 7.24 (m, 3H), 7.19 – 7.17 (m, 1H), 7.15 (t, $J = 2.1$ Hz, 1H), 7.05 (tt, $J = 7.5, 1.2$ Hz, 1H), 6.98 – 6.92 (m, 2H), 6.89 (ddd, $J = 8.2, 2.5, 1.0$ Hz, 1H), 1.86 (d, $J = 22.3$ Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.83 (d, $J = 28.5$ Hz), 157.60, 156.64, 140.34 (d, $J = 22.5$ Hz), 129.98, 129.90, 123.70, 119.41 (d, $J = 9.0$ Hz), 119.12, 118.86, 115.40 (d, $J = 9.0$ Hz), 94.47 (d, $J = 186.0$ Hz), 24.60, 24.45;

^{19}F NMR (565 MHz, CDCl_3) δ -151.45 (q, $J = 22.6$ Hz).

HRMS (ESI⁻): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{15}\text{H}_{13}\text{FO}_3]^-$: 259.0765, found: 259.0773.

2-fluoro-2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoic acid (34b)



Following the general procedure, the optimized time is 24 h. Yield: 60% (15.8 mg); light yellow oil.

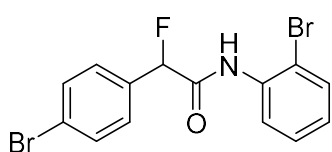
^1H NMR (600 MHz, Chloroform- d) δ 7.41 – 7.32 (m, 2H), 7.11 (d, $J = 8.1$ Hz, 2H), 7.06 – 6.82 (m, 1H), 3.06 (dd, $J = 14.0, 4.2$ Hz, 1H), 2.50 – 2.43 (m, 1H), 2.34 – 2.24 (m, 2H), 2.09 – 1.97 (m, 2H), 1.93 – 1.83 (m, 4H), 1.71 – 1.60 (m, 1H), 1.46 (dtd, $J = 12.7, 11.0, 6.7$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 175.54 (d, $J = 28.5$ Hz), 140.89, 136.40 (d, $J = 22.5$ Hz), 129.11, 124.92, 124.87, 94.22 (d, $J = 184.5$ Hz), 50.94, 38.19, 35.15, 29.17, 24.48, 24.46, 24.32, 24.30, 20.52;

^{19}F NMR (565 MHz, CDCl_3) δ -150.62 (m, 1F).

HRMS (ESI⁻): calculated m/z $[\text{M-H}]^-$ for $[\text{C}_{15}\text{H}_{16}\text{FO}_3]^-$: 263.1078, found: 263.1086.

N-(2-bromophenyl)-2-(4-bromophenyl)-2-fluoroacetamide (35)

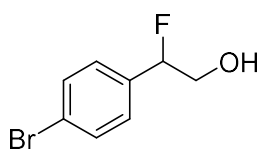


Following the reported procedure,⁸ the reaction time is 24 h. Yield: 72% (14.8 mg); white solid; m.p. 121 – 129 °C.

¹H NMR (600 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 8.33 (ddd, *J* = 8.2, 4.1, 1.6 Hz, 1H), 7.58 (dddd, *J* = 7.0, 5.2, 4.0, 1.2 Hz, 3H), 7.47 – 7.38 (m, 2H), 7.33 (tdd, *J* = 8.3, 4.1, 1.5 Hz, 1H), 7.04 (dddd, *J* = 7.8, 6.2, 4.1, 2.1 Hz, 1H), 5.89 (dd, *J* = 48.0, 3.8 Hz, 1H);
¹³C{¹H} NMR (150 MHz, CDCl₃) δ 166.06 (d, *J* = 21.0 Hz), 134.44, 133.27 (d, *J* = 21.0 Hz), 132.47, 132.04, 128.51, 128.15 (d, *J* = 7.5 Hz), 126.12, 124.00, 121.87, 113.97, 91.25 (d, *J* = 190.5 Hz);
¹⁹F NMR (565 MHz, CDCl₃) δ -178.19 (m, 1F).

HRMS (ESI⁻): calculated *m/z* [M-H]⁻ for [C₁₄H₉Br₂⁷⁹FNO]⁻: 383.9029, found: 383.9039; [C₈H₅Br⁸¹FO₂]⁻: 385.9009, found: 385.9019.

2-(4-bromophenyl)-2-fluoroethan-1-ol (36)



Following the reported procedure,⁹ the reaction time is 24 h. Yield: 79% (14.8 mg); colorless oil.

¹H NMR (600 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 5.44 (ddd, *J* = 48.3, 7.5, 3.1 Hz, 1H), 3.84 – 3.65 (m, 2H), 2.24 (s, 1H).
¹³C{¹H} NMR (150 MHz, CDCl₃) δ 135.48, 135.35, 131.80, 127.45, 127.41, 122.85, 94.74, 93.59, 66.37, 66.21.
¹⁹F NMR (565 MHz, CDCl₃) δ -187.48 (m, 1F).

HRMS (ESI⁻): calculated *m/z* [M-H]⁻ for [C₈H₇Br⁷⁹FO]⁻: 216.9659, found: 216.9660; [C₈H₅Br⁸¹FO₂]⁻: 218.9638, found: 218.9643.

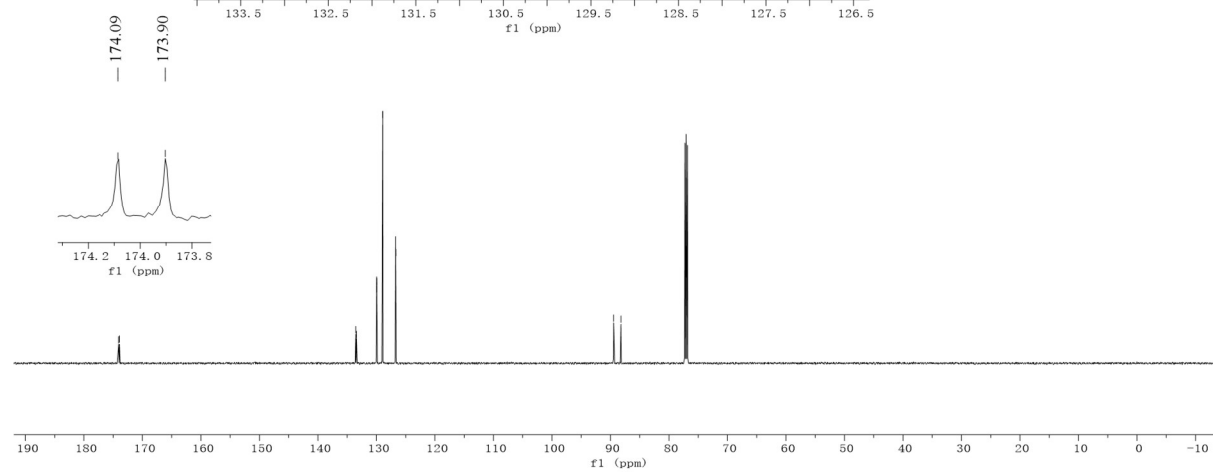
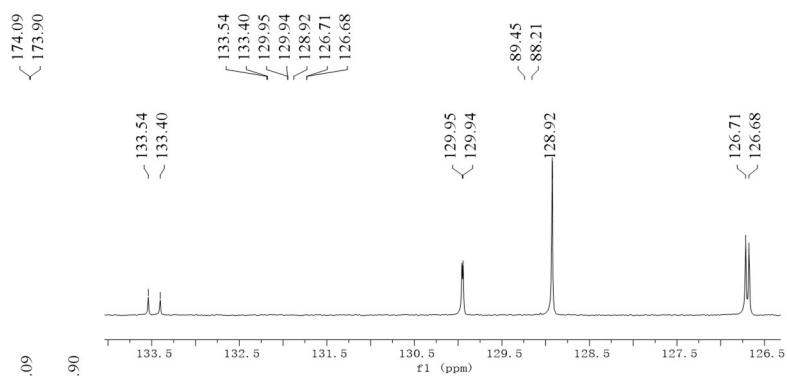
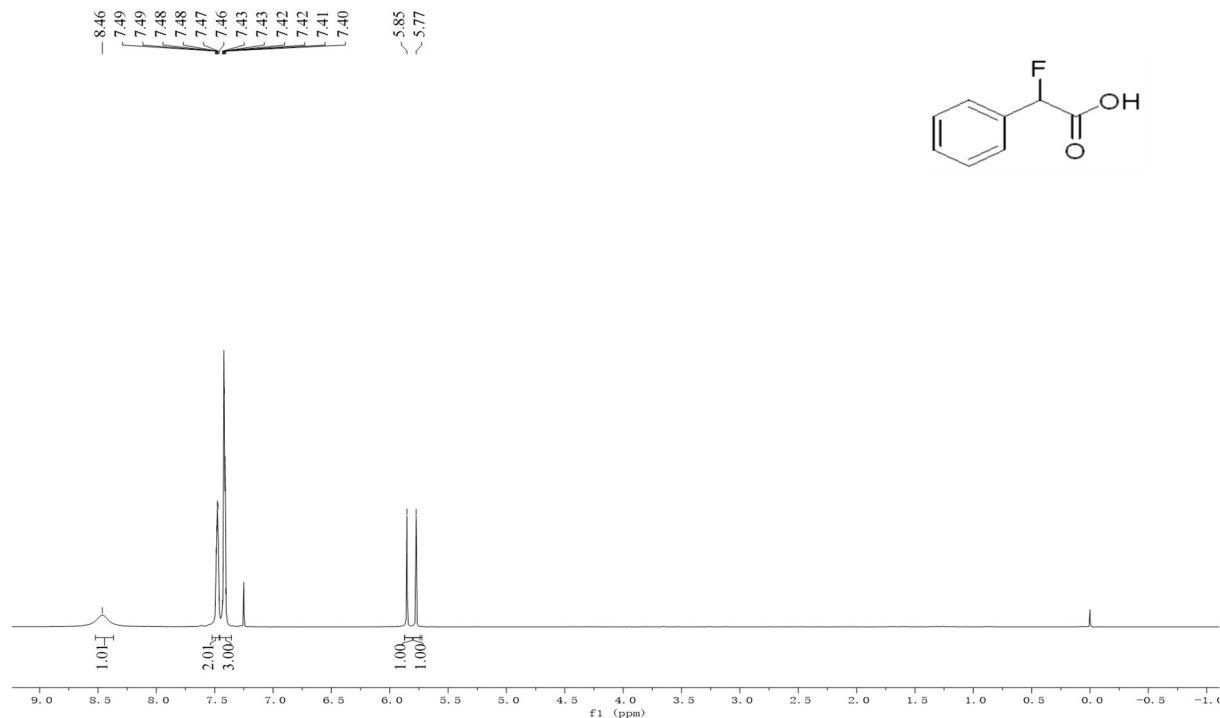
8. Reference

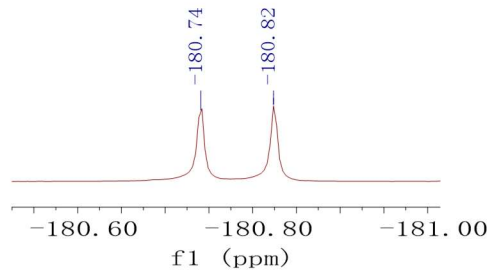
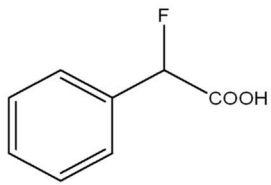
1. X. P. Yin, Z. Li, M. Aliakbar, R. C. Brian, W. D. Wulff, *J. Org. Chem.*, **2020**, *85*, 10432.
2. D. R. Magnin, R. B. Sulsky, J. A. Rob; T. J. Caulfield, R. A. Parker. US 20030225091A1.
3. G. Lyne; G. Brigitte, WO2016054728A1.
4. J. A. Blake, E. Gagnon, M. Lukeman, J. C. Scaiano, *Org. Lett.*, **2006**, *8*, 1057.

5. L. Aureli, G. Cruciani, M. C. Cesta, R. Anacardio, L. De Simone, A. Moriconi, *J. Med. Chem.*, **2005**, *48*, 2469.
6. C. C. Li, P. Zhao, R. L. Li, B. Zhang, W. X. Zhao, *Angew. Chem., Int. Ed.*, **2020**, *59*, 10913.
7. T. Knauber, F. Arikian, G. Röschenthaler, L. J. Gooßen, *Chem. Eur. J.*, **2011**, *17*, 2689.
8. L. L. Wu, L. Falivene, E. Drinkel, S. Grant, A. Linden, L. Cavallo, R. Dorta, *Angew. Chem., Int. Ed.*, **2012**, *51*, 2870.
9. M. J. Maclean, S. Walker, T. F. Wang, P. C. H. Eichinger, P. J. Shermana, J. H. Bowie, *Org. Biomol. Chem.*, **2010**, *8*, 371.

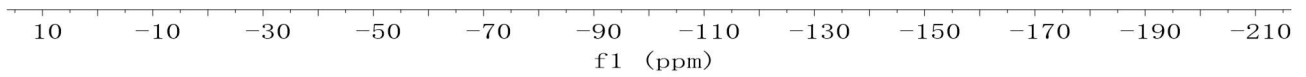
9. Copy of ^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F NMR Spectra.

Compound 1b

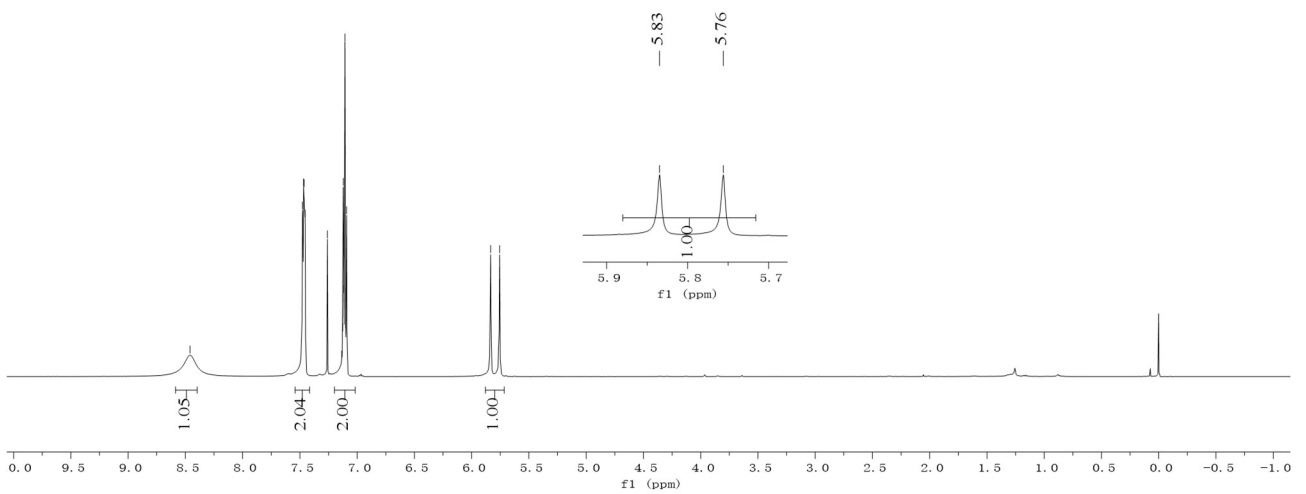
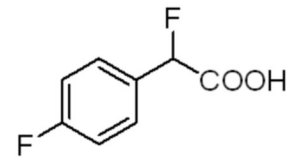
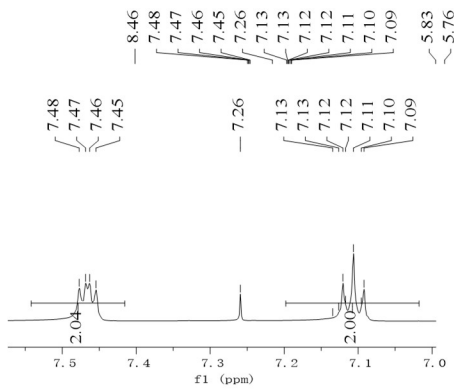


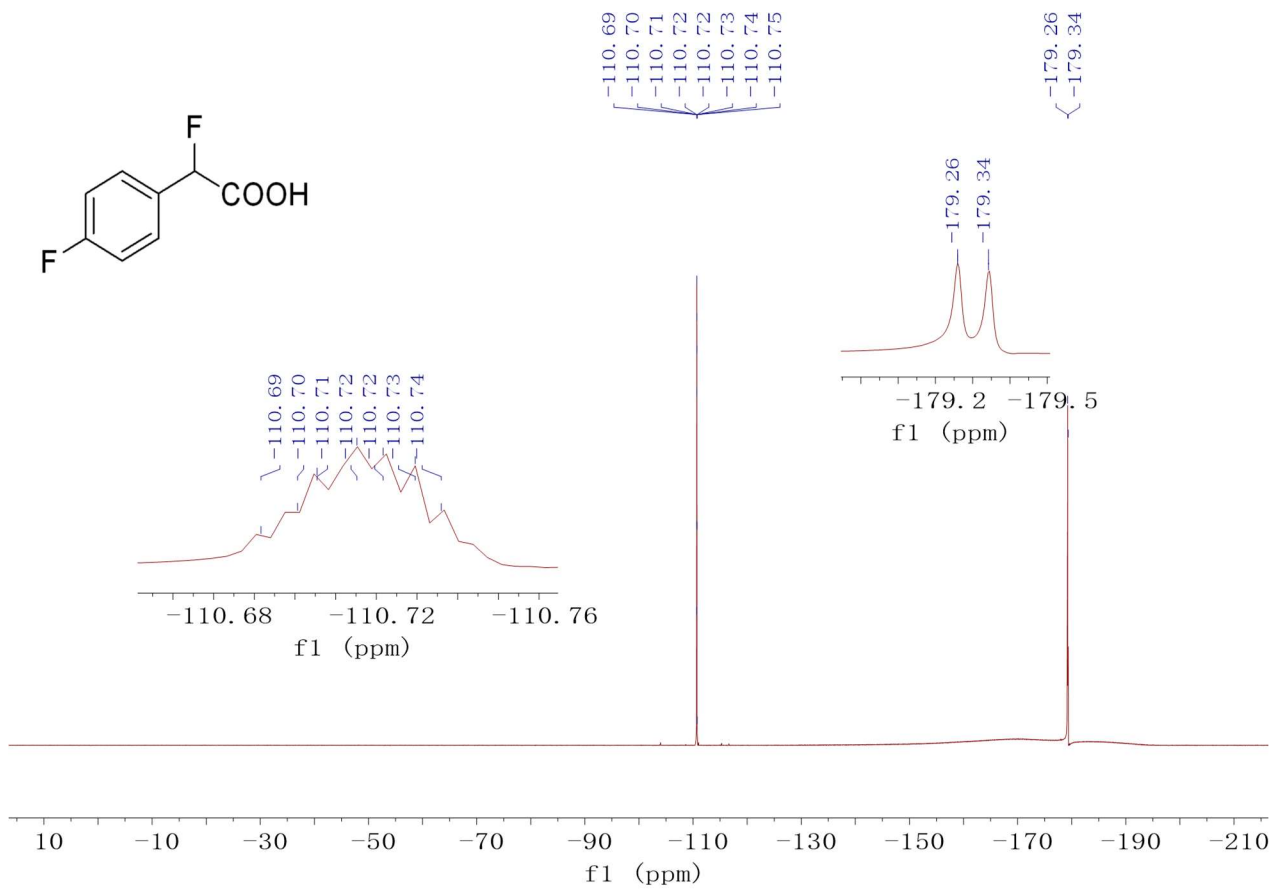
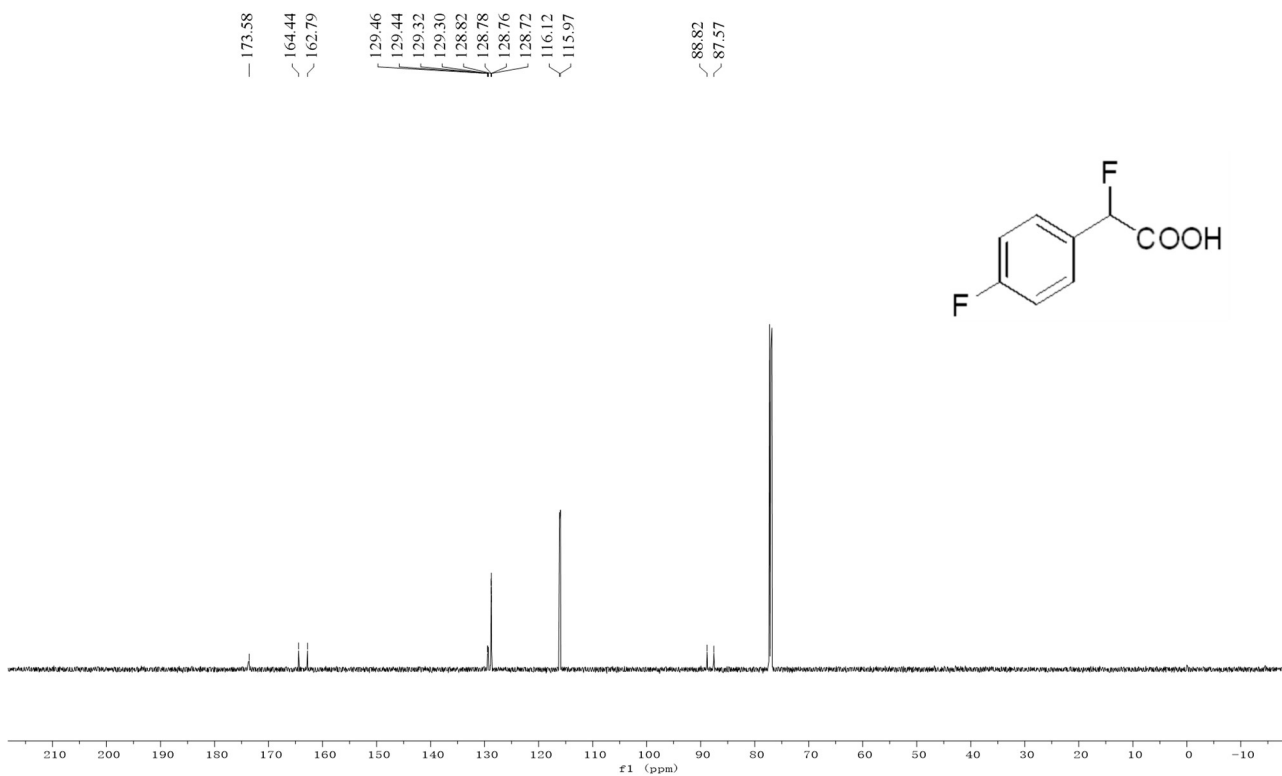


-180.74
-180.82

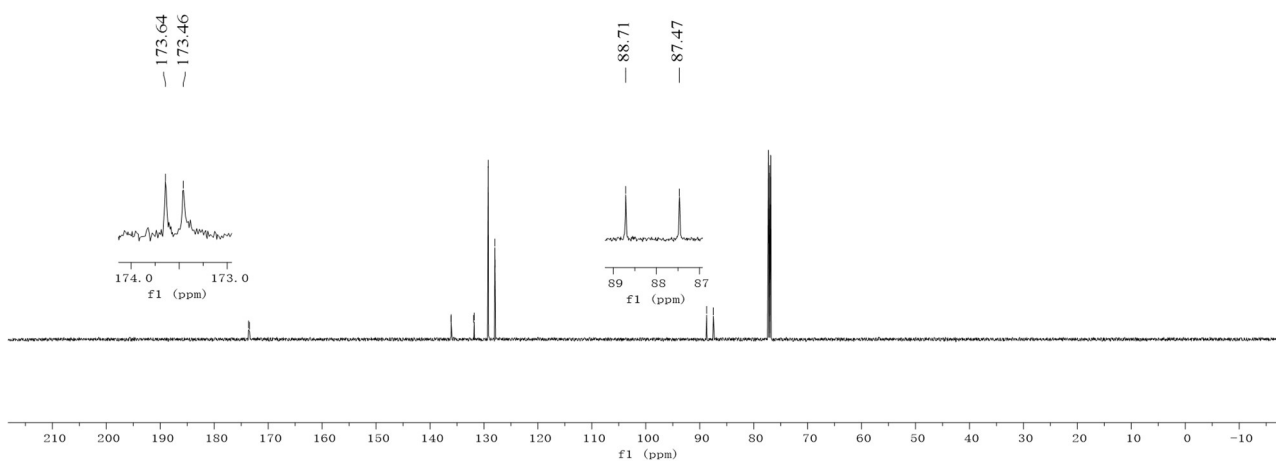
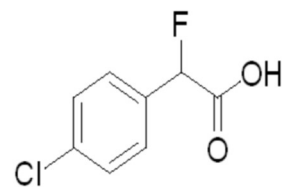
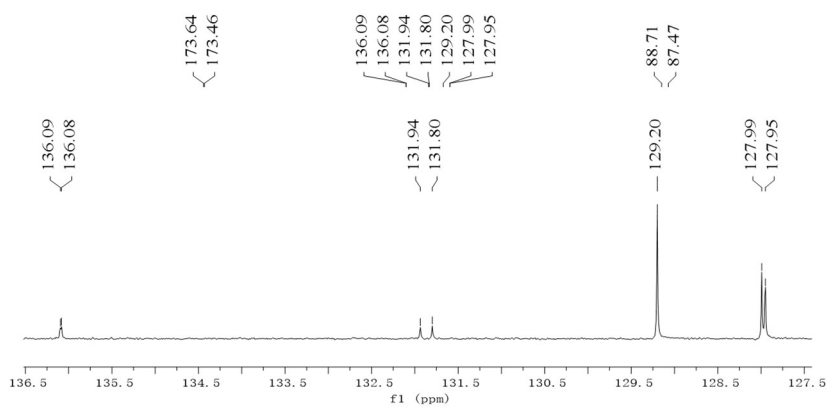
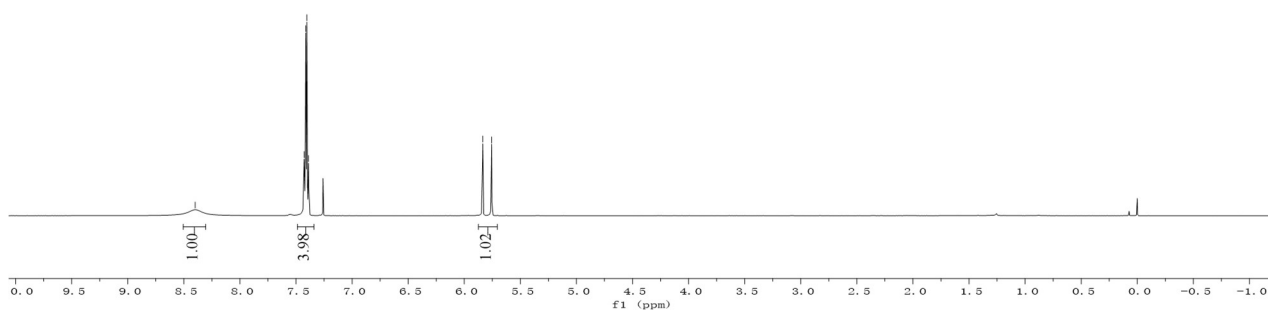
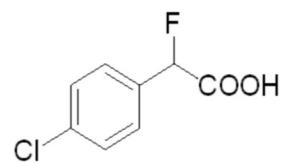
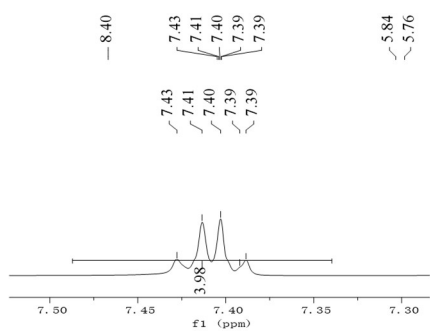


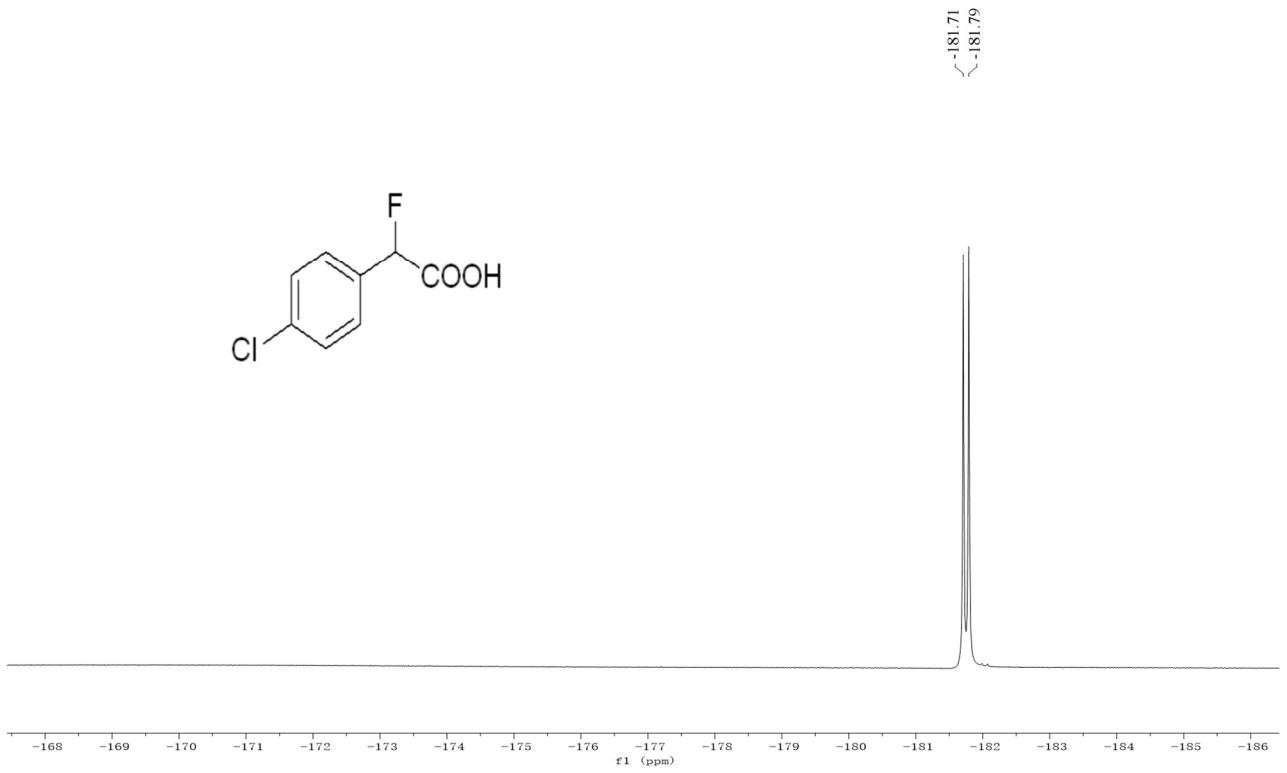
Compound 2b



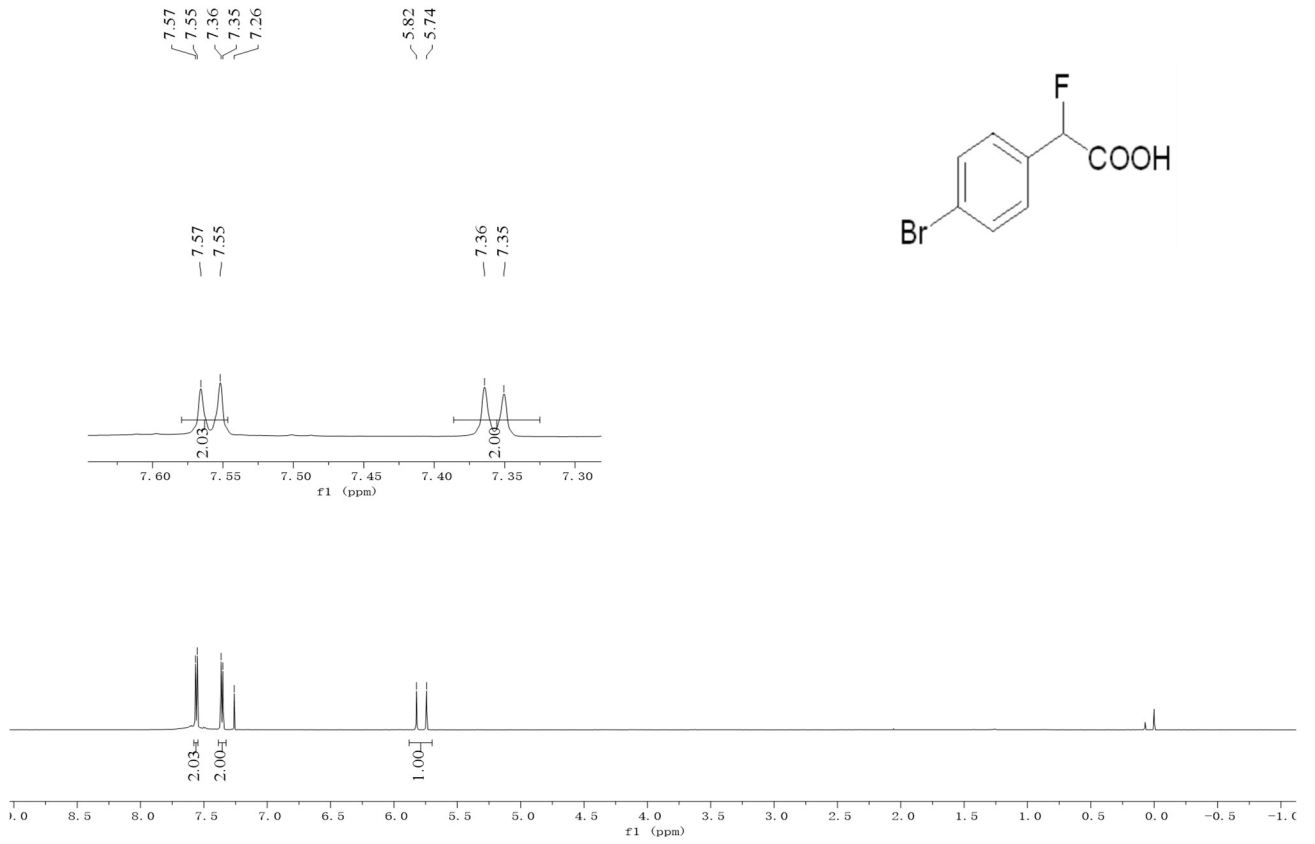


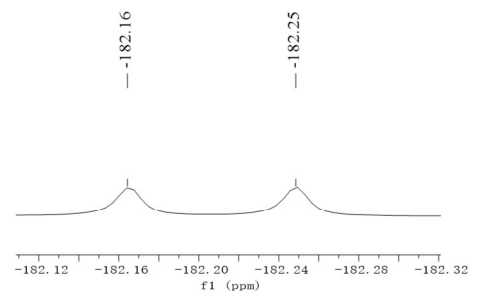
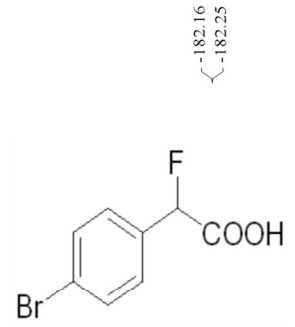
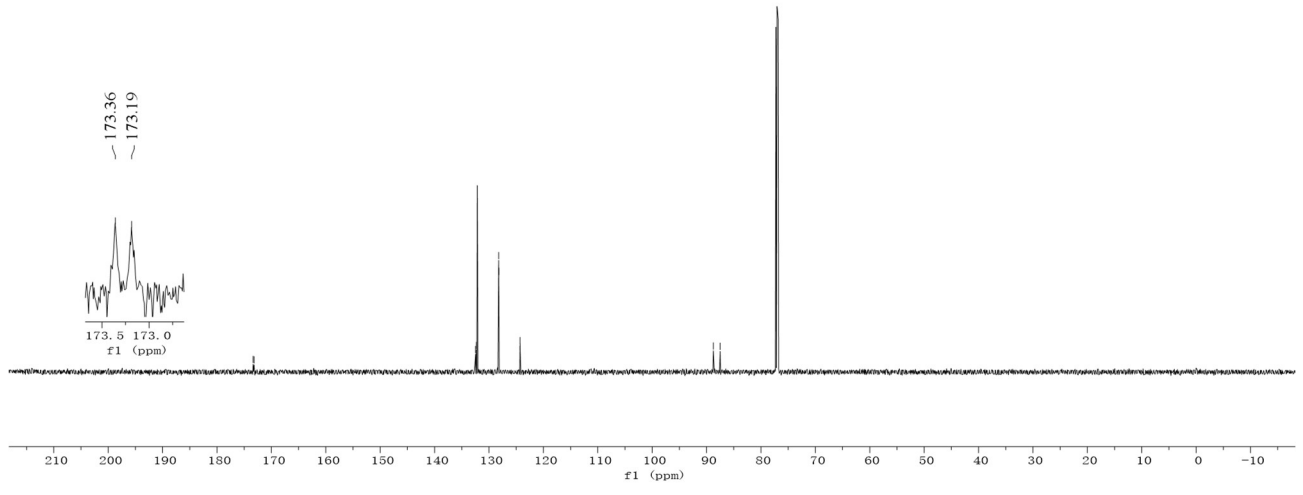
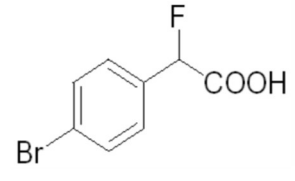
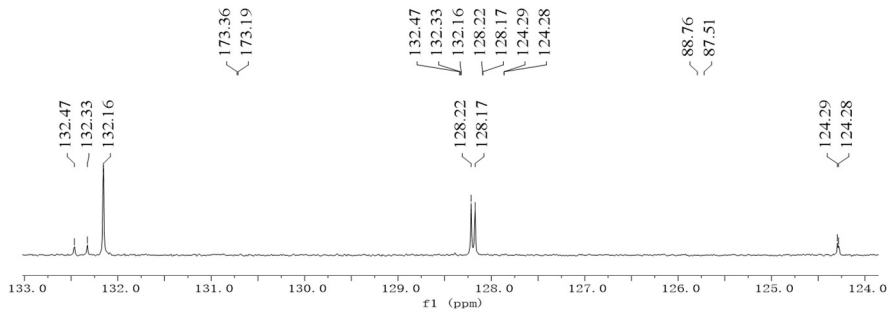
Compound 3b



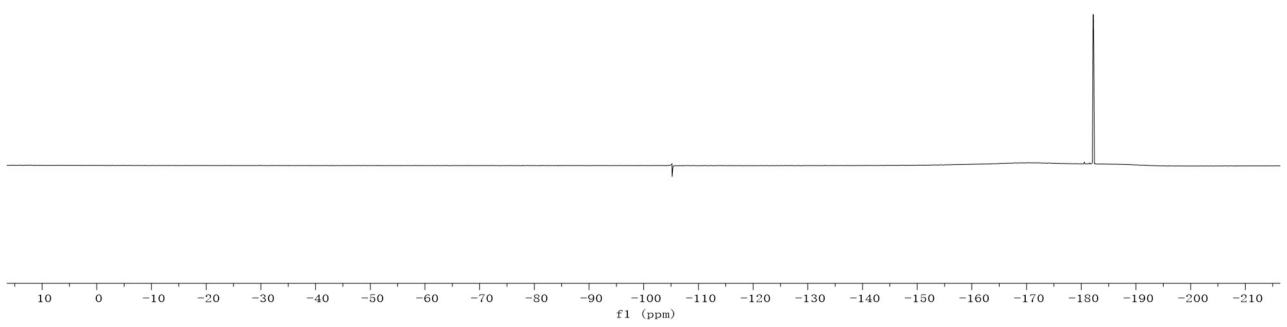


Compound 4b





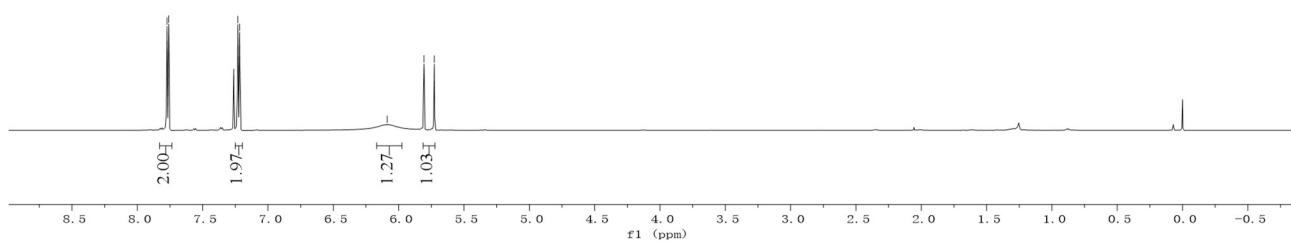
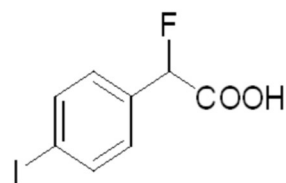
-182.16
-182.25



Compound 5b

7.77
7.76
7.23
7.22

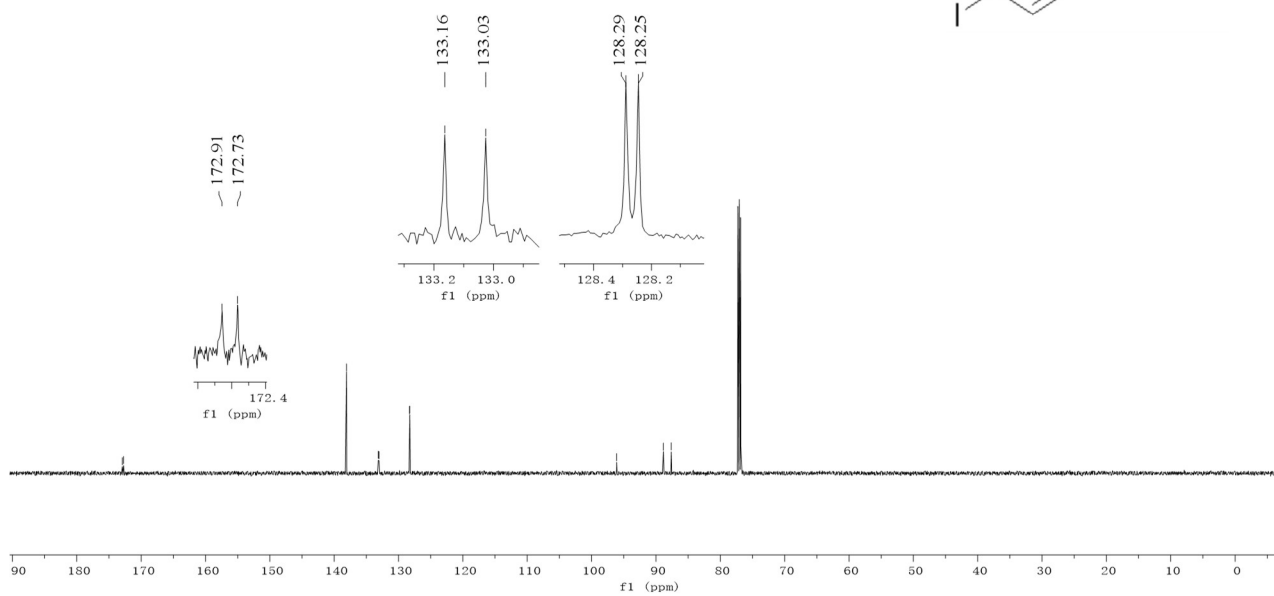
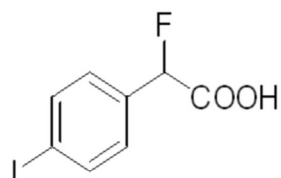
6.09
5.81
5.73

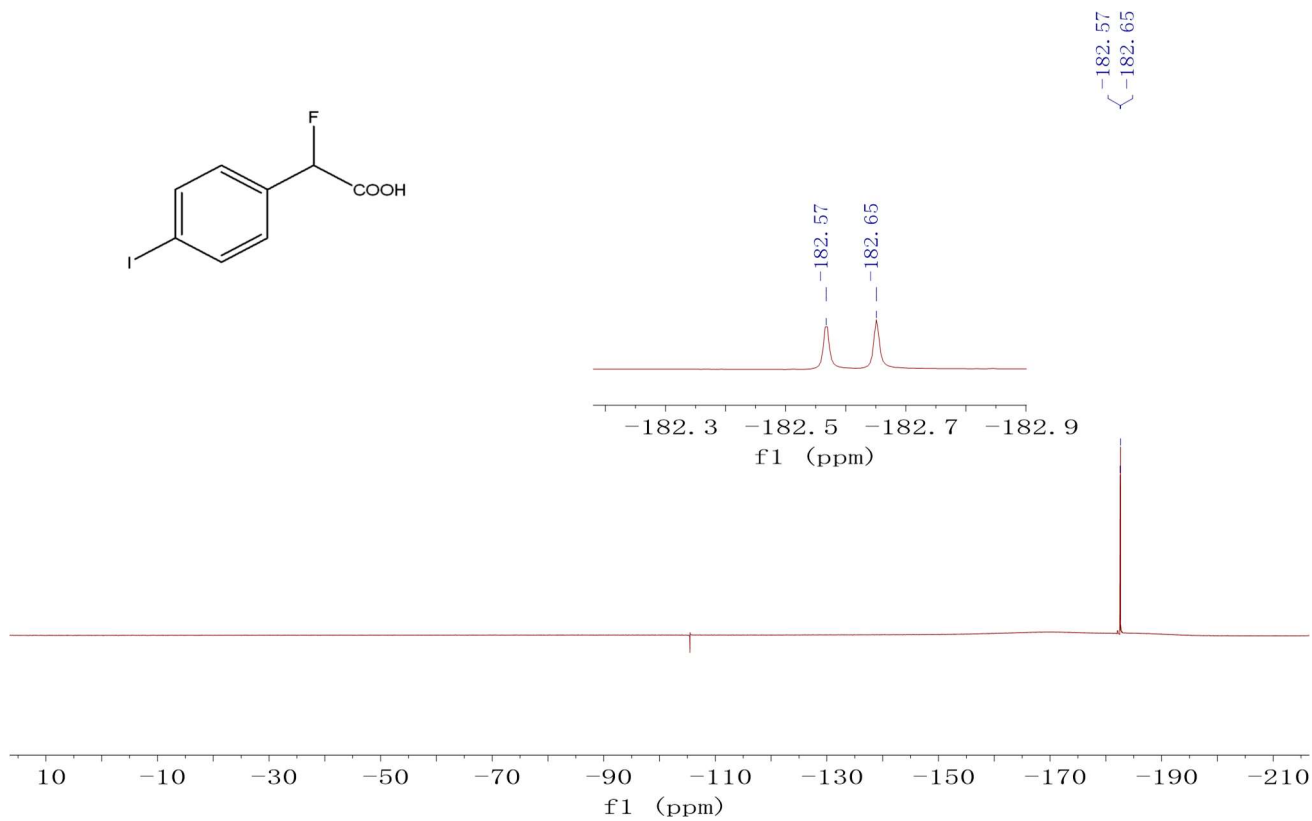


172.91
172.73

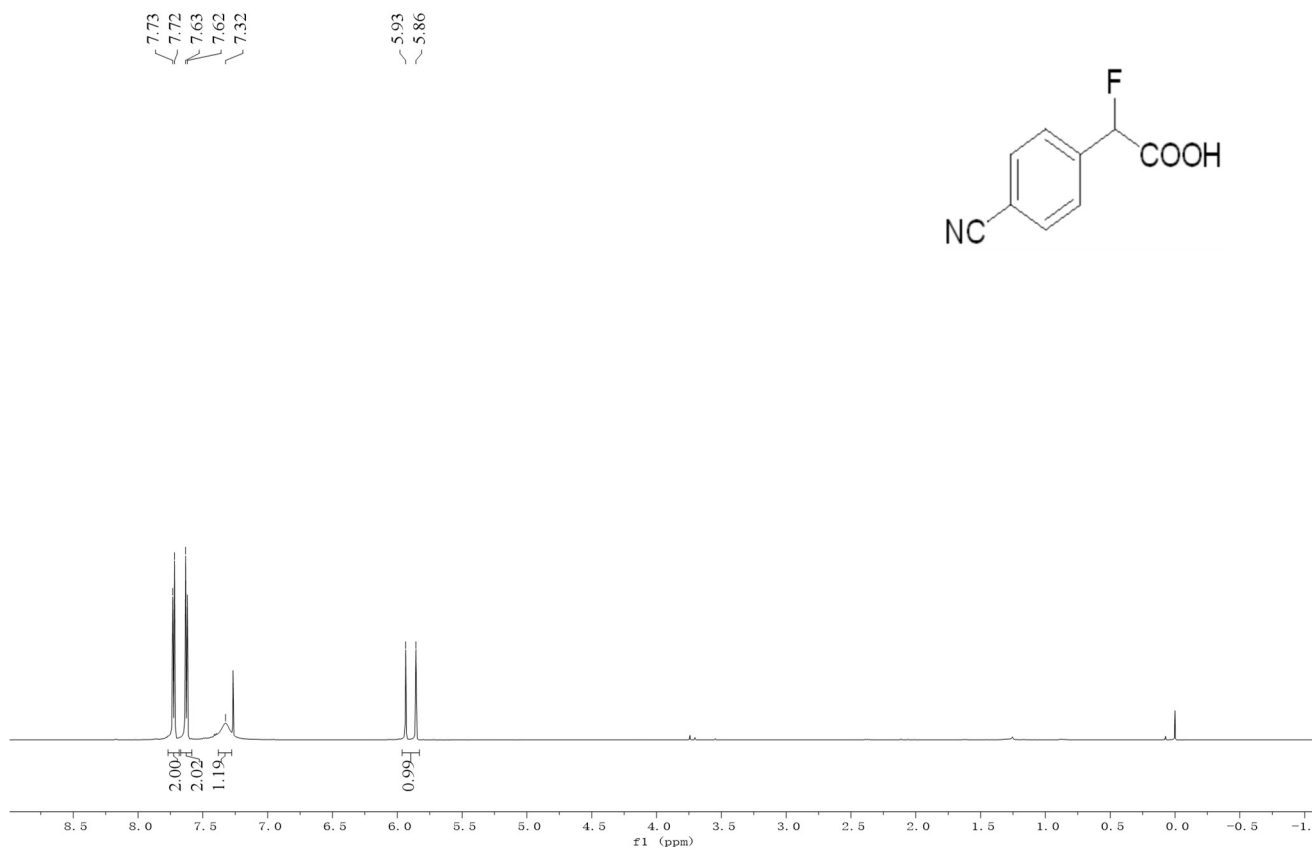
138.09
133.16
133.03
128.29
128.25

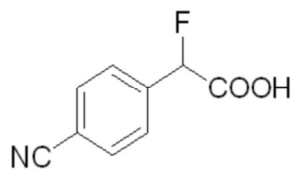
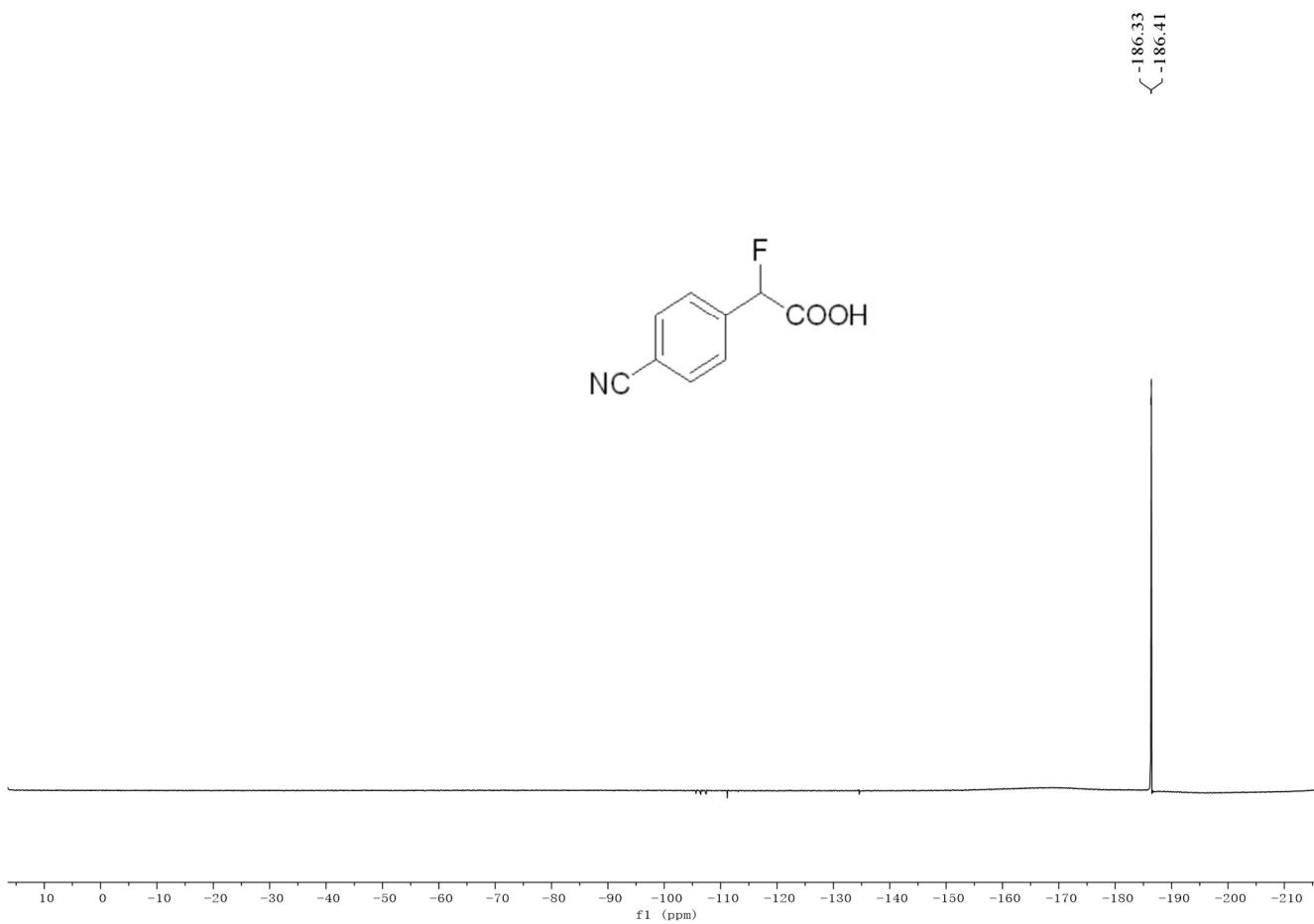
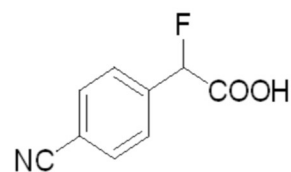
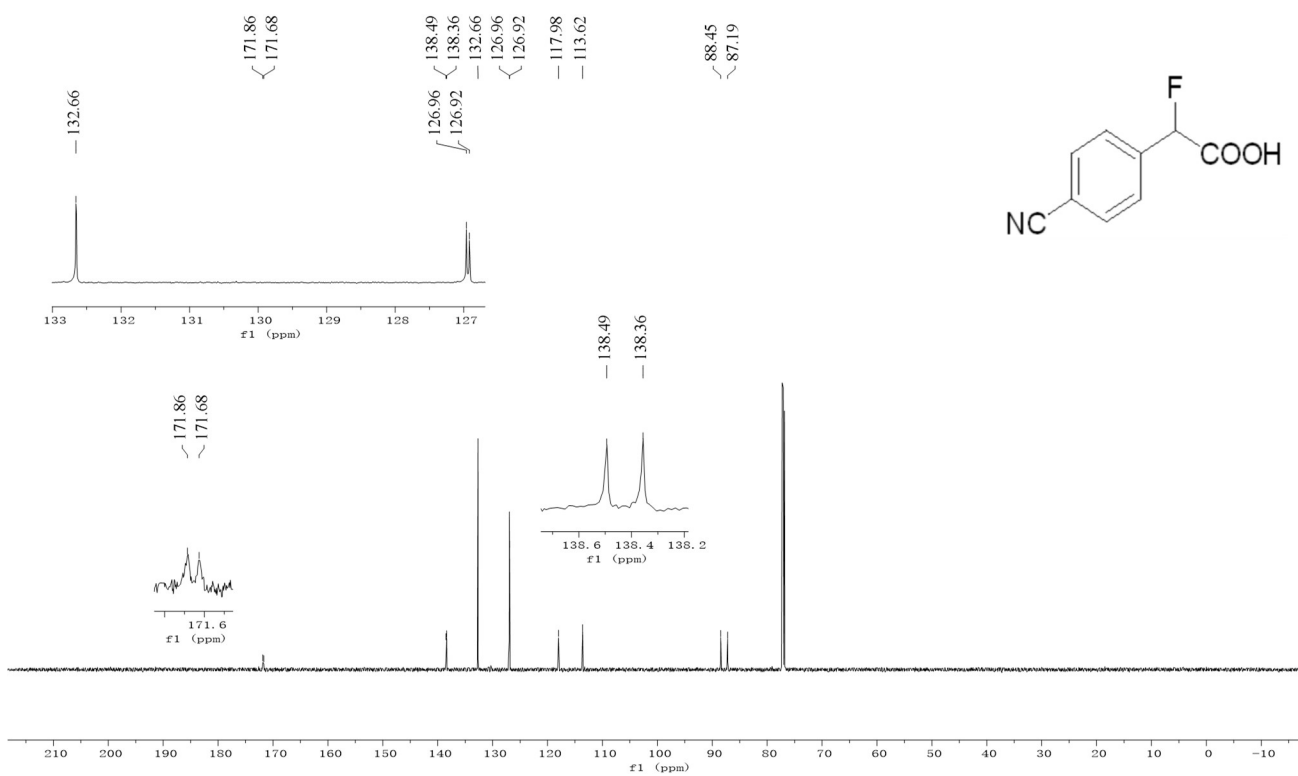
96.11
88.86
87.61





Compound 6b

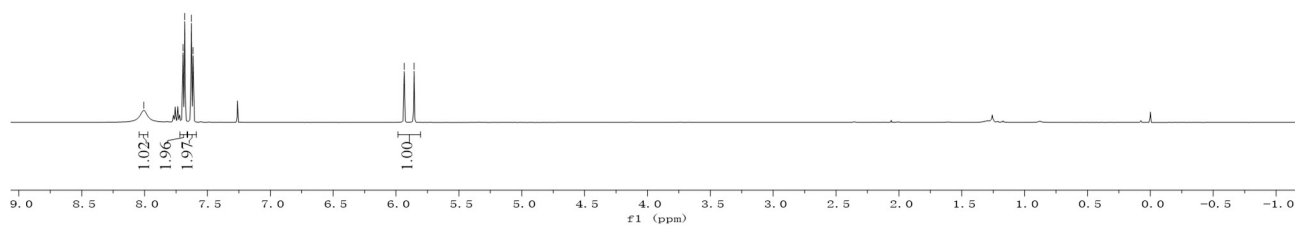
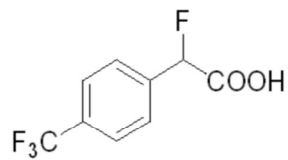




Compound 7b

8.01
7.69
7.68
7.63
7.61

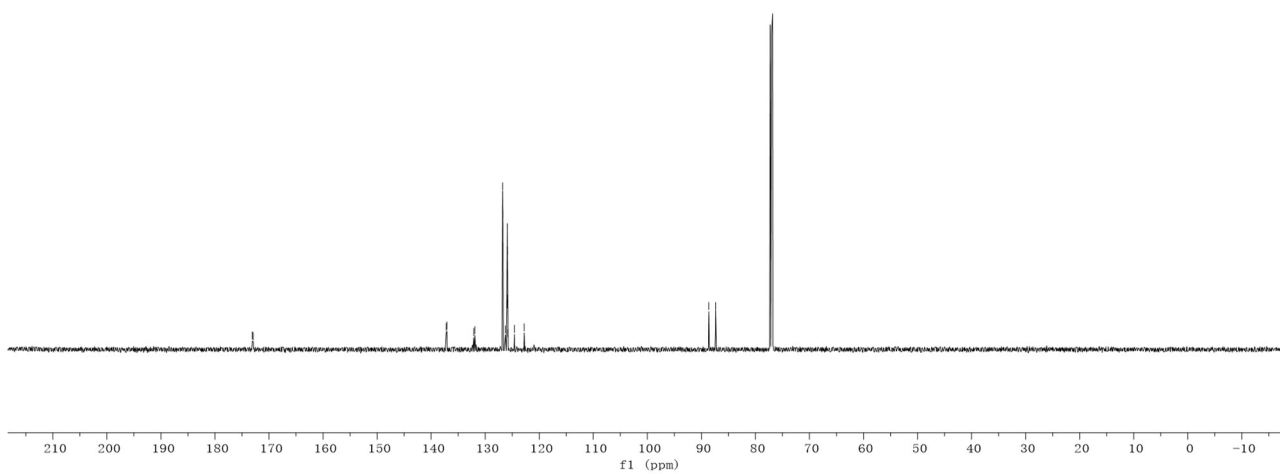
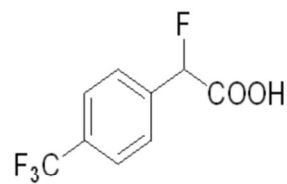
5.93
5.86

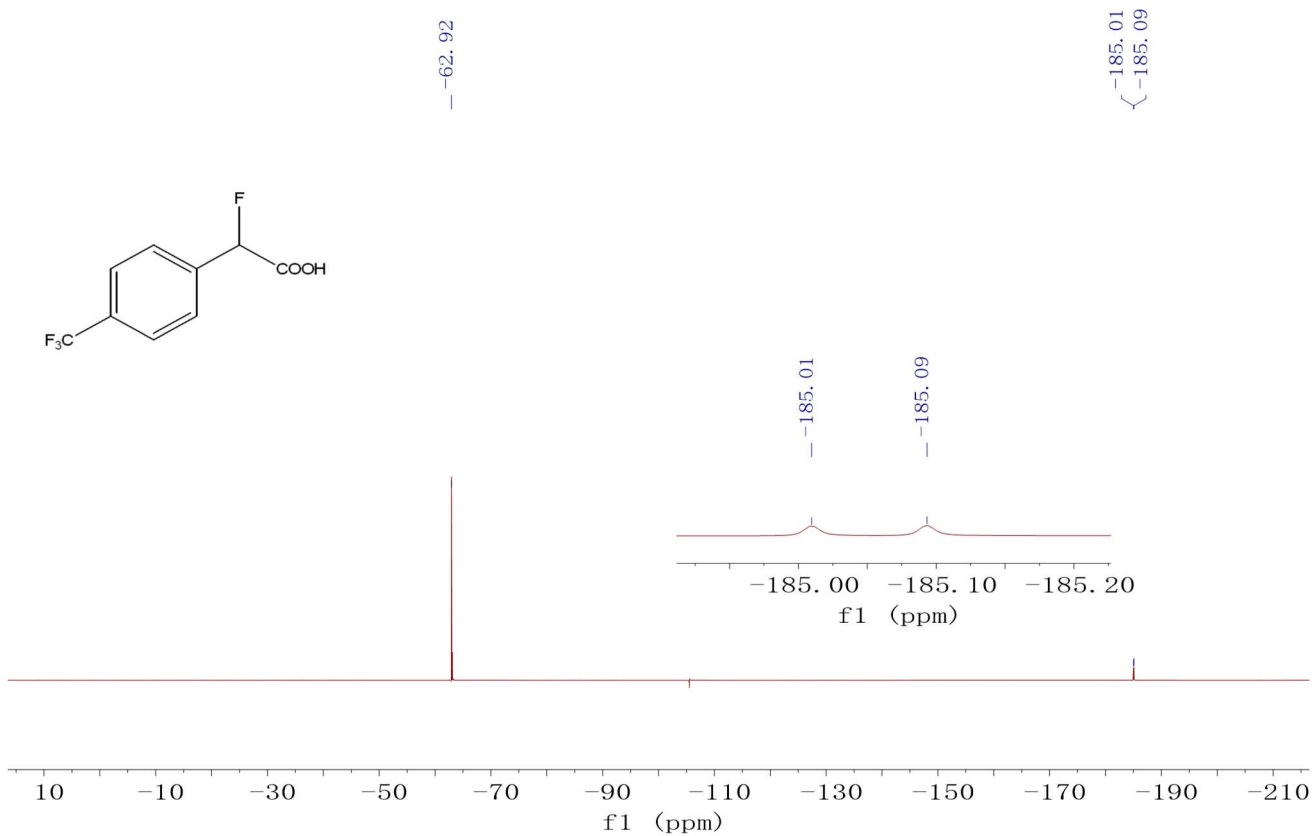


173.10
172.92

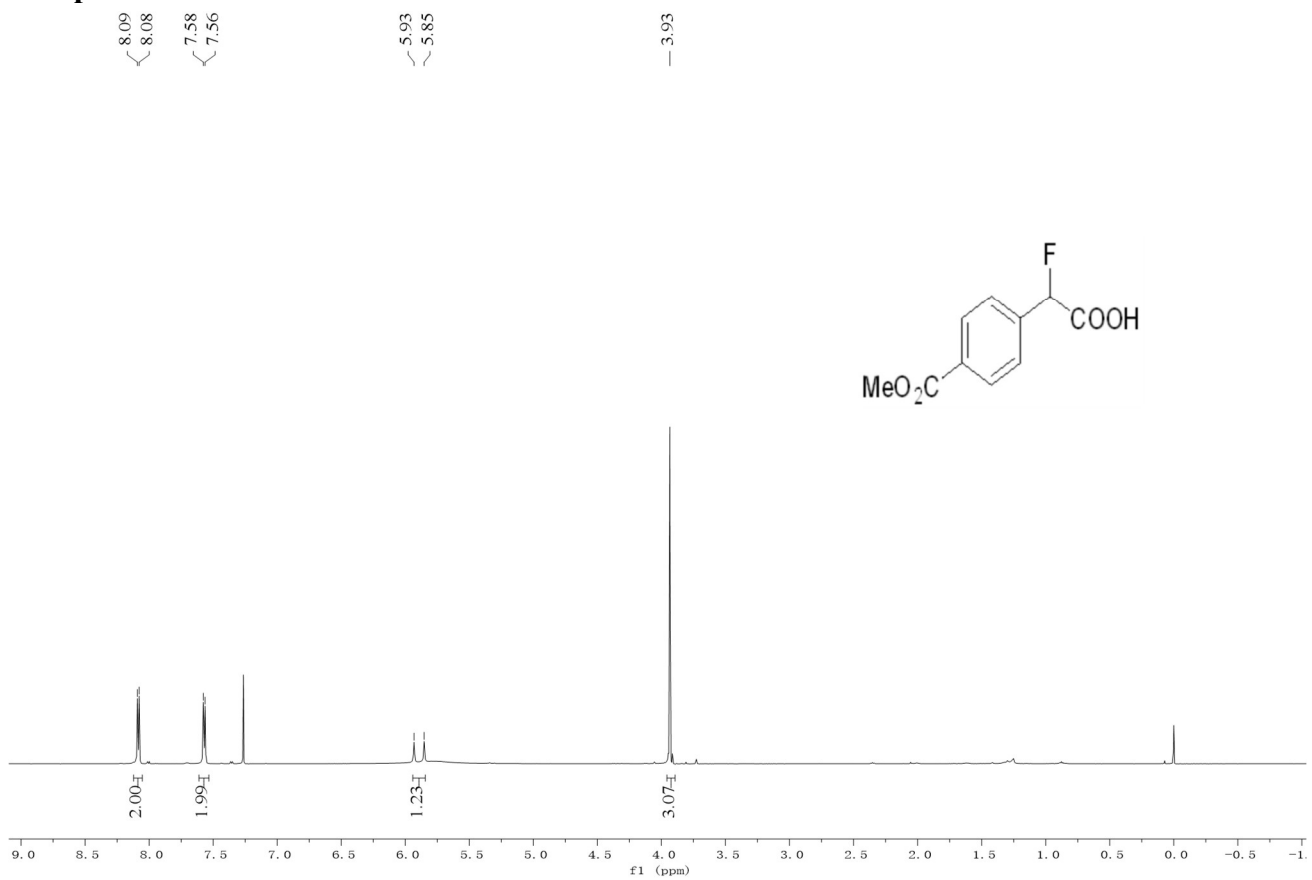
137.22
137.08
132.12
131.91
126.76
126.72
126.27
125.94
125.91
125.89
125.86
125.82
124.58
122.78

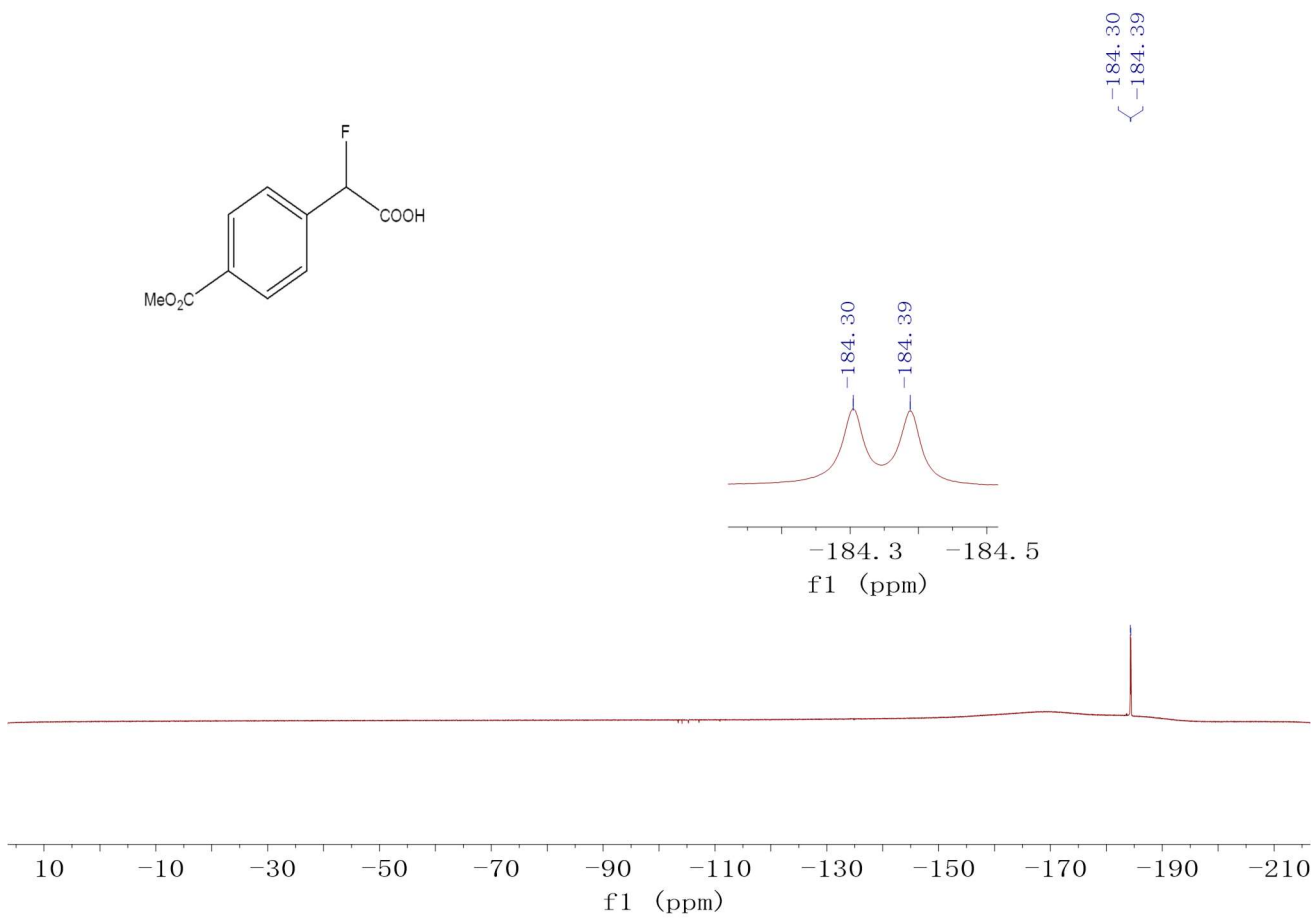
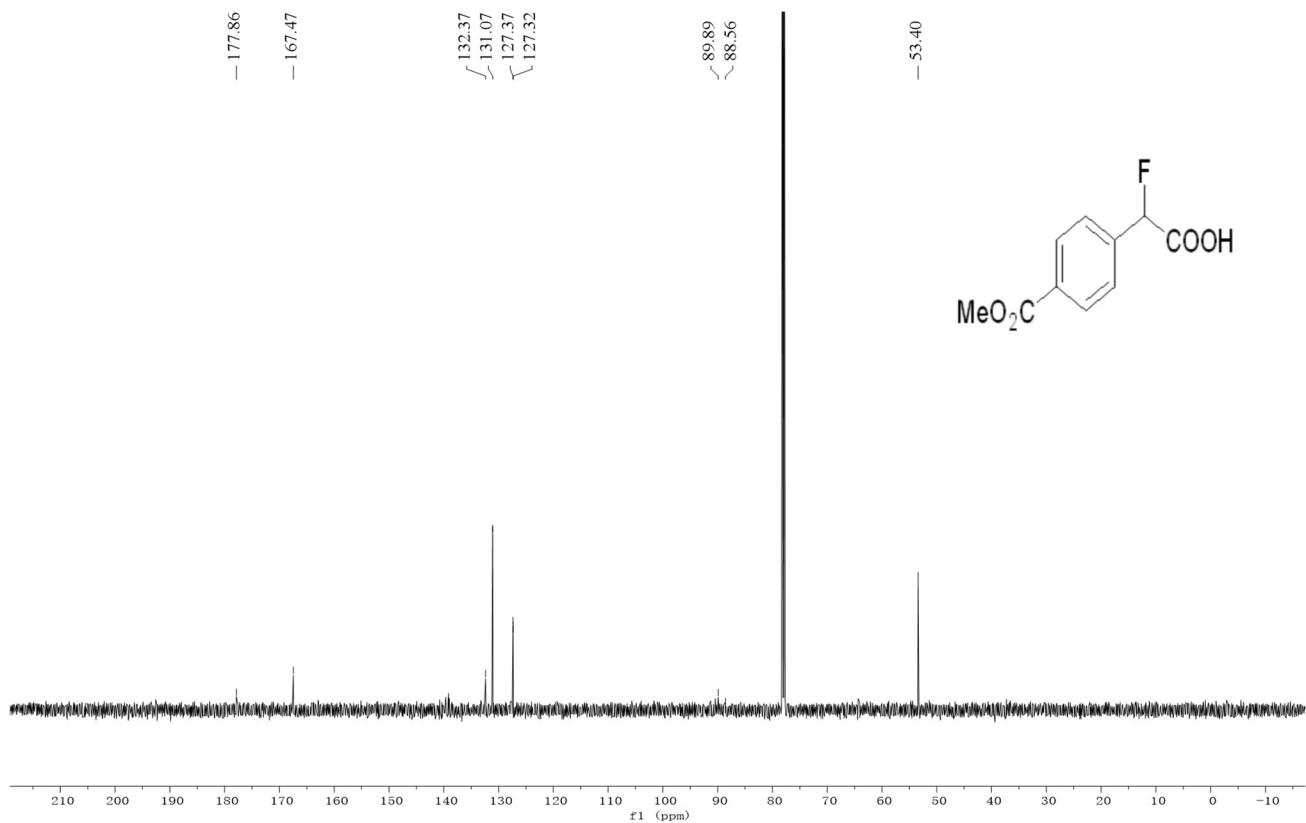
88.63
87.38



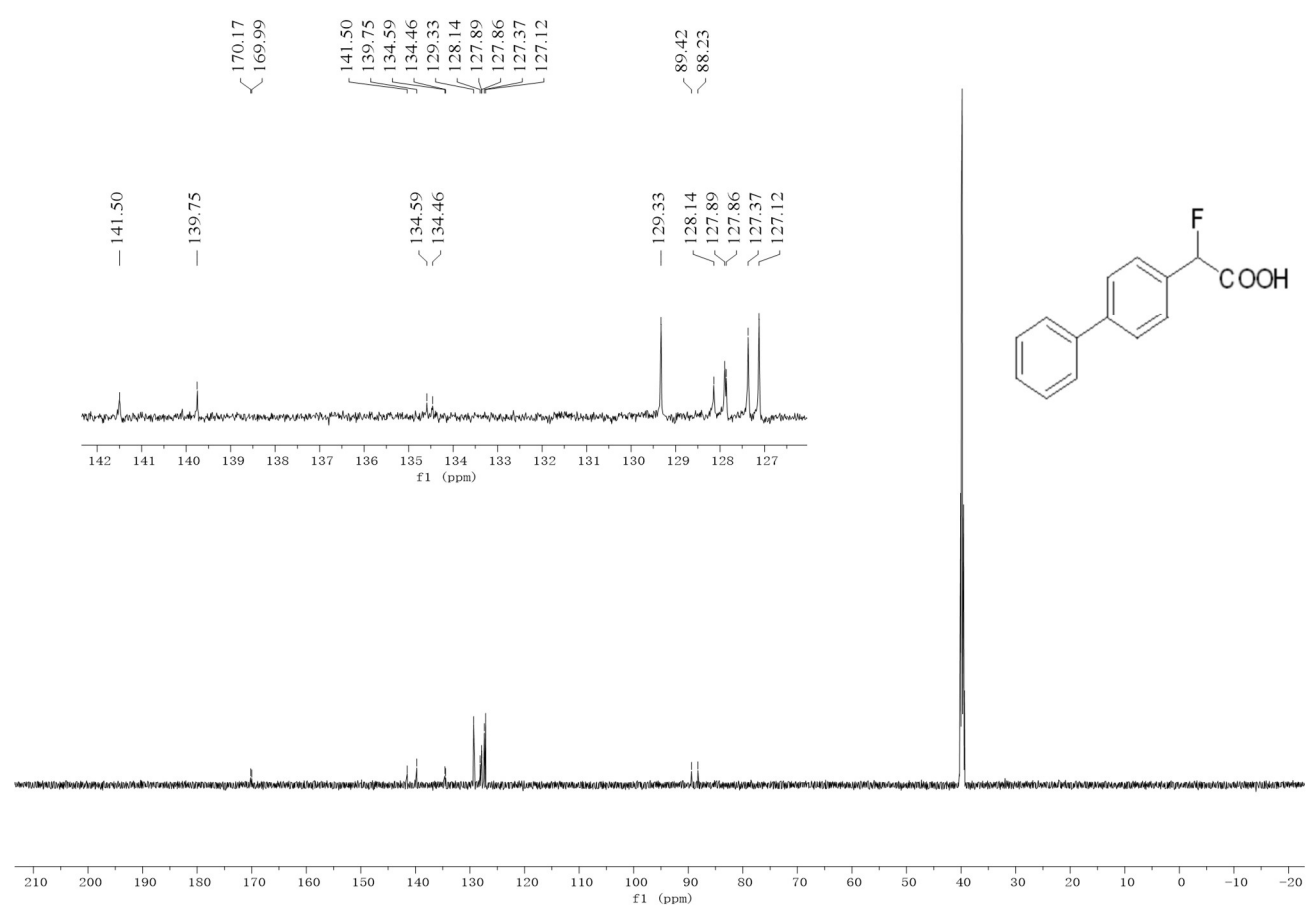
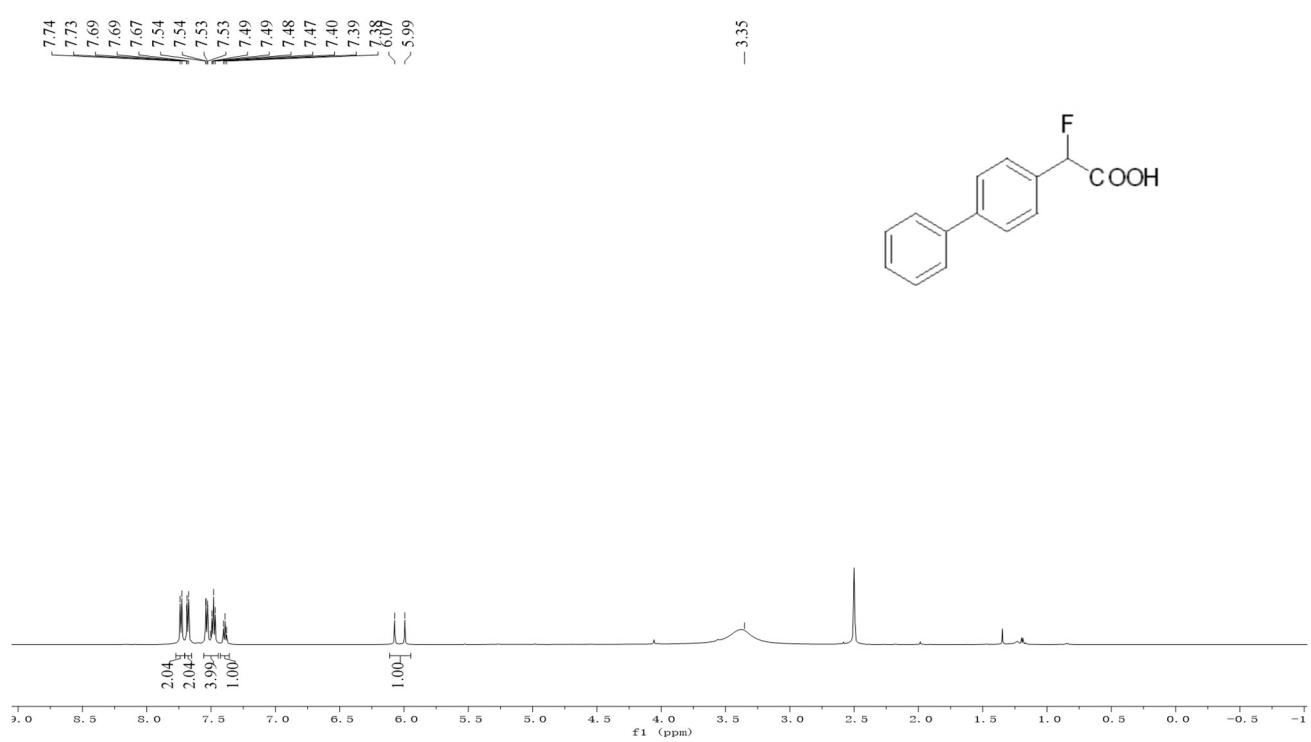


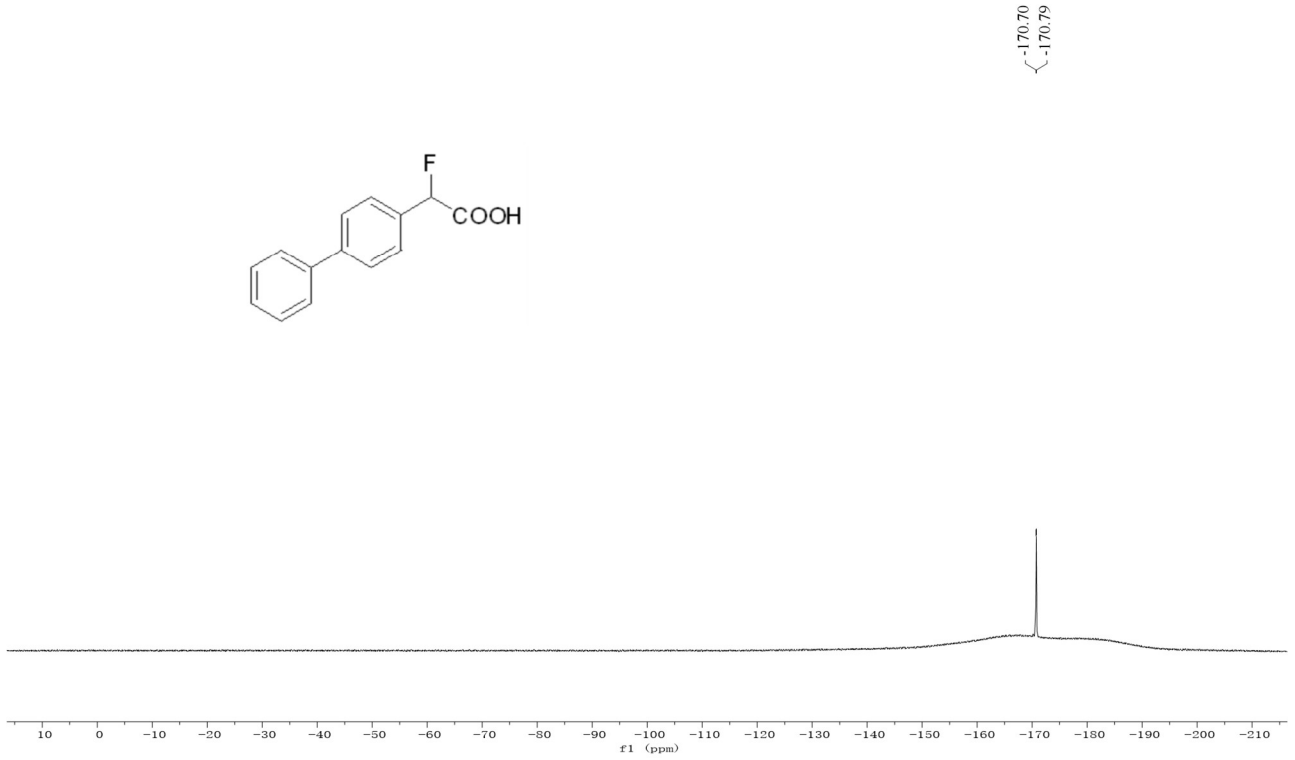
Compound 8b





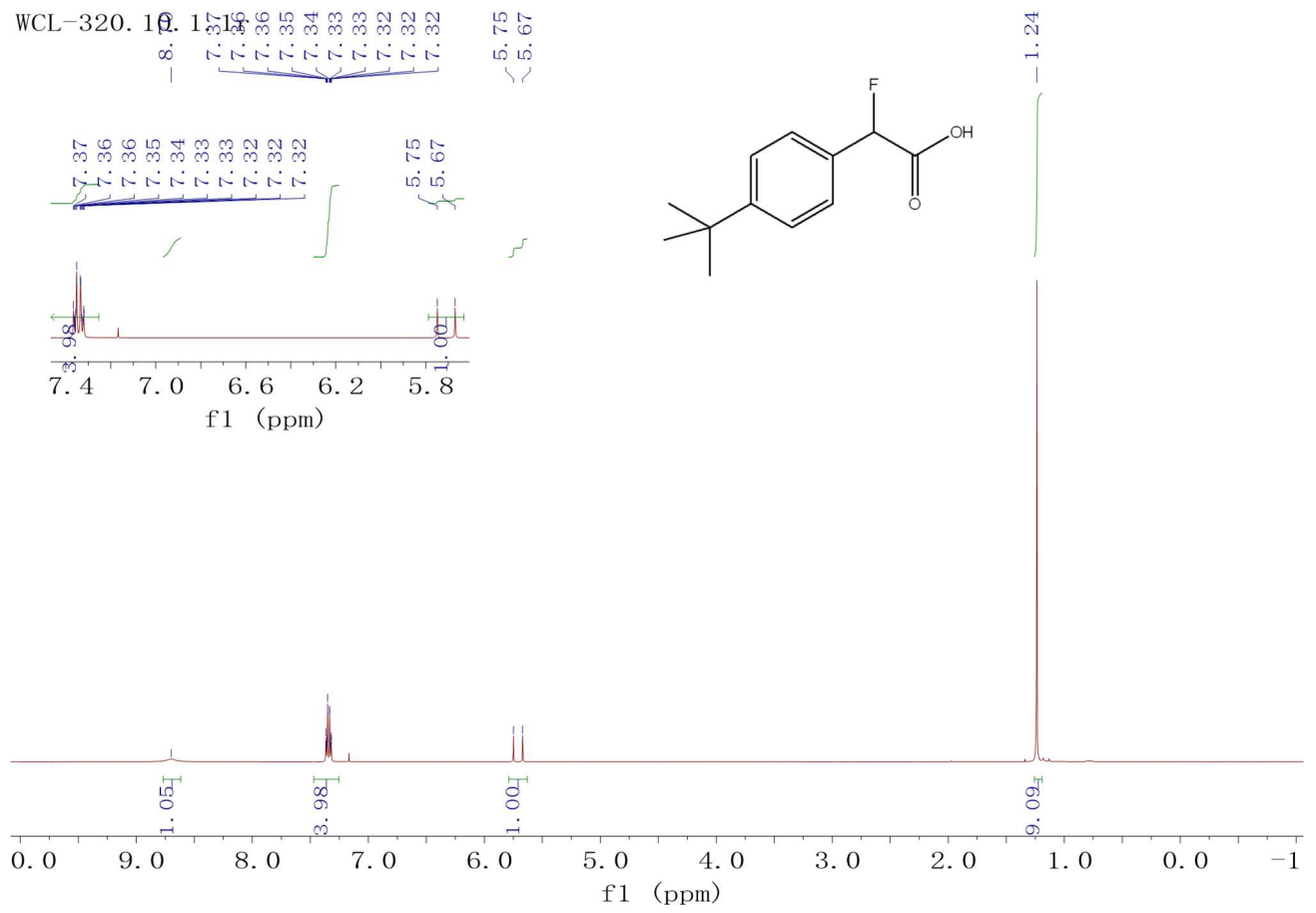
Compound 9b



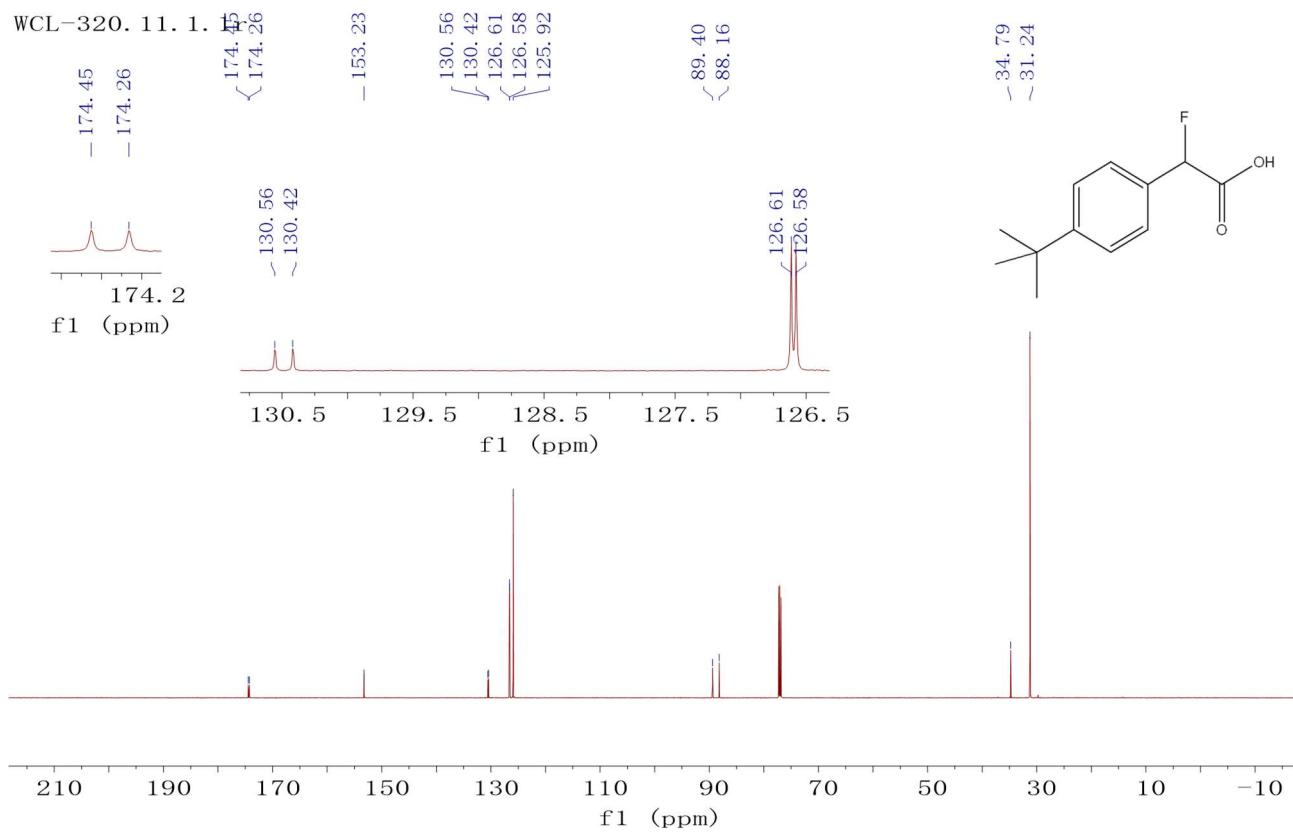


Compound 10b

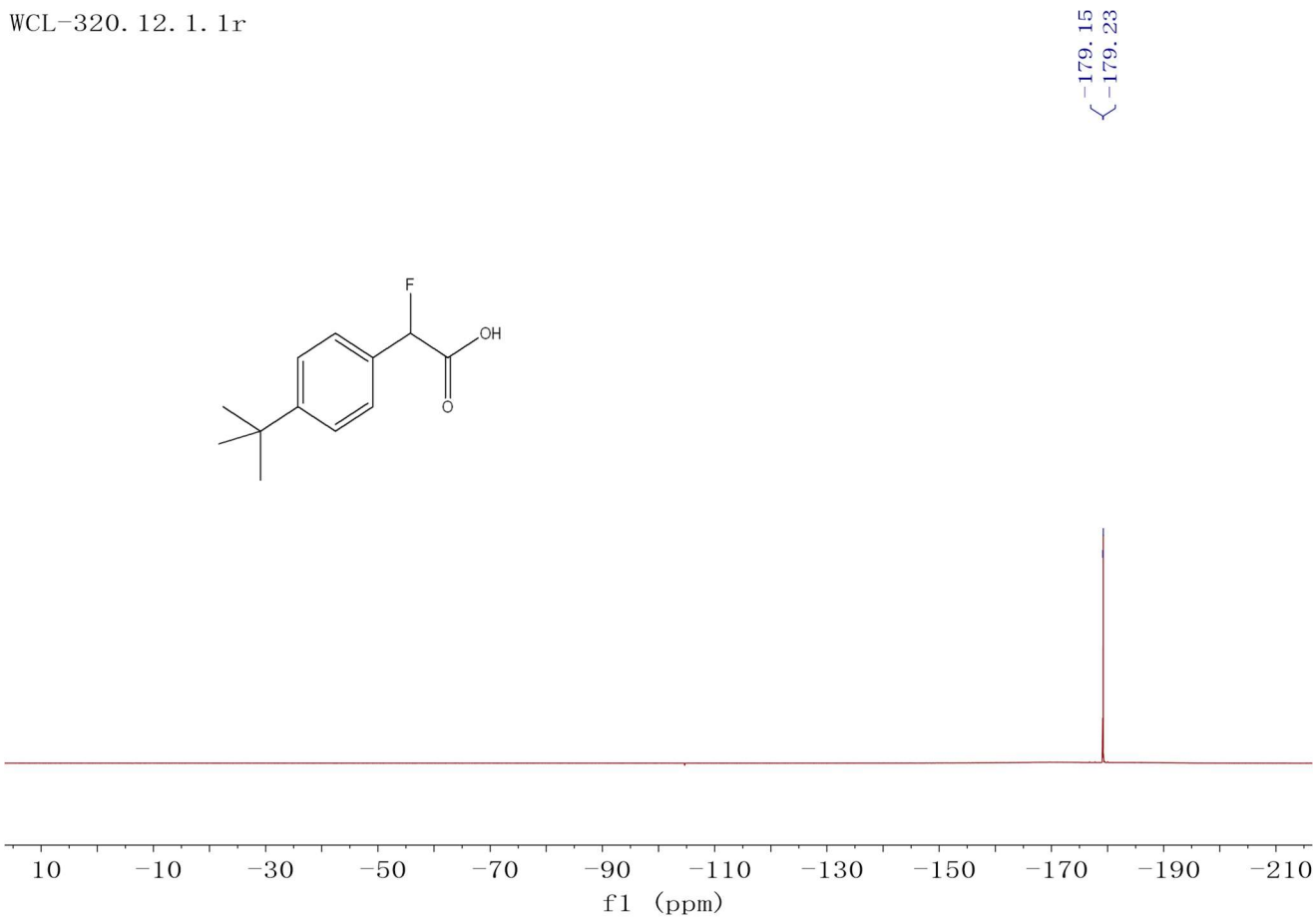
WCL-320.10



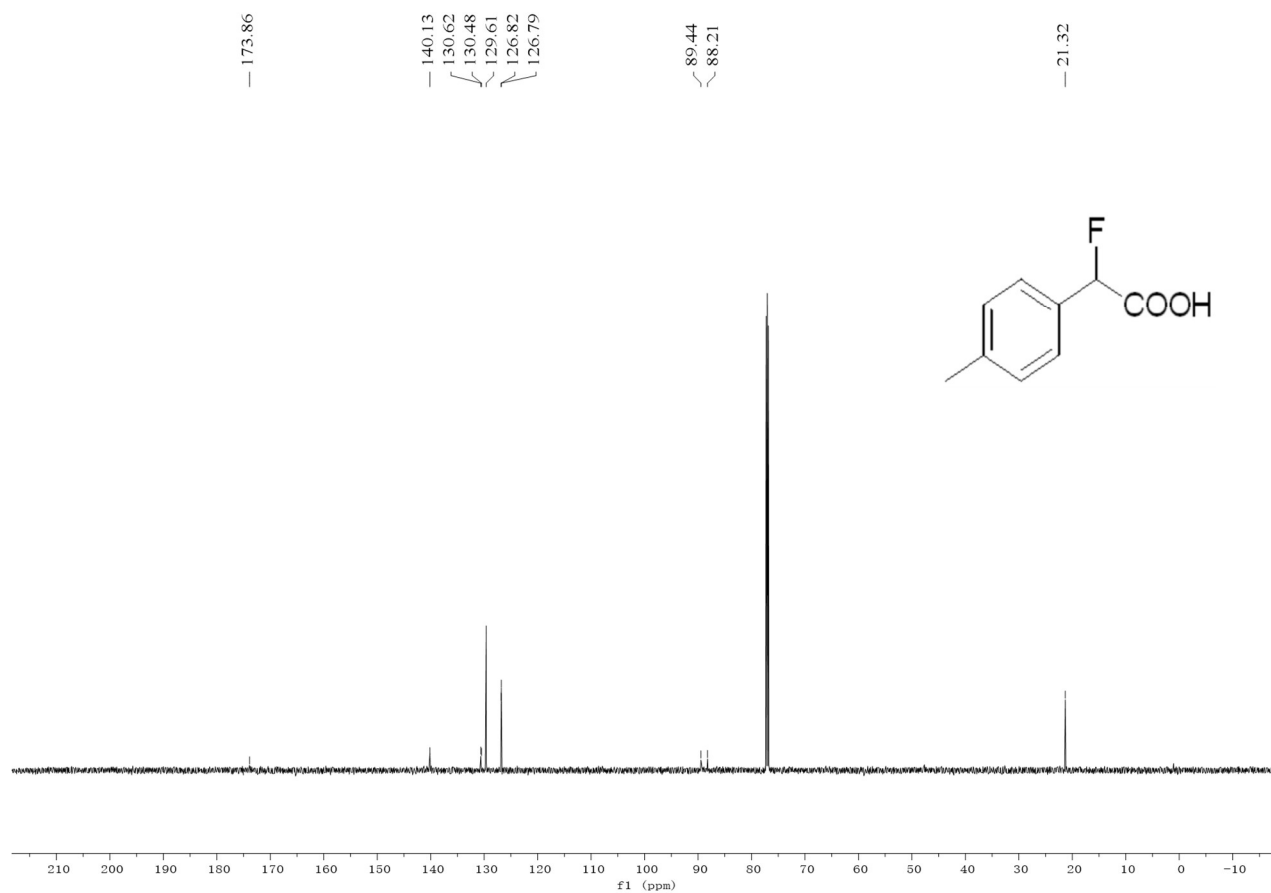
WCL-320. 11. 1.

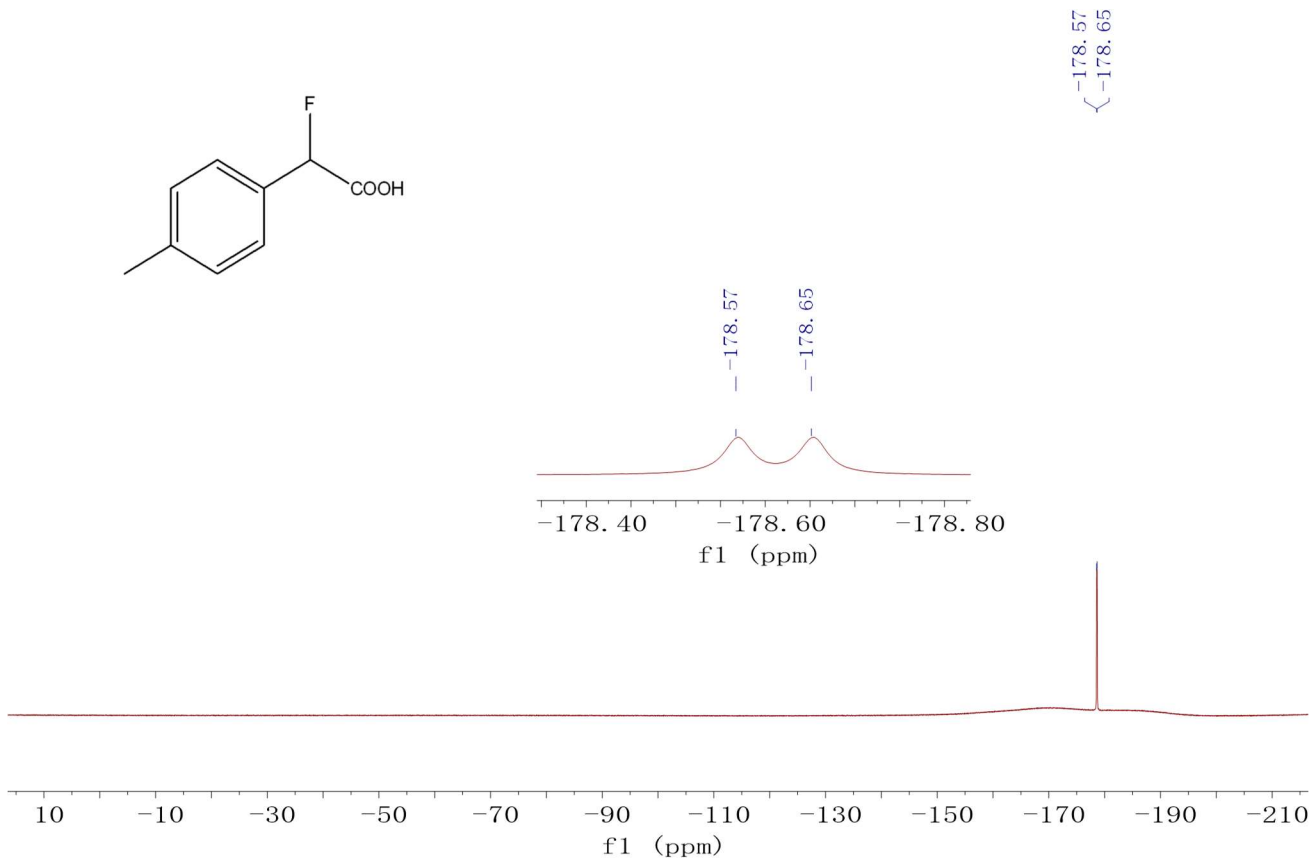
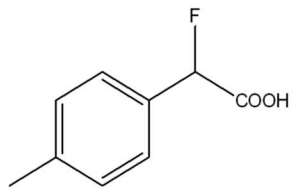


WCL-320. 12. 1. 1r

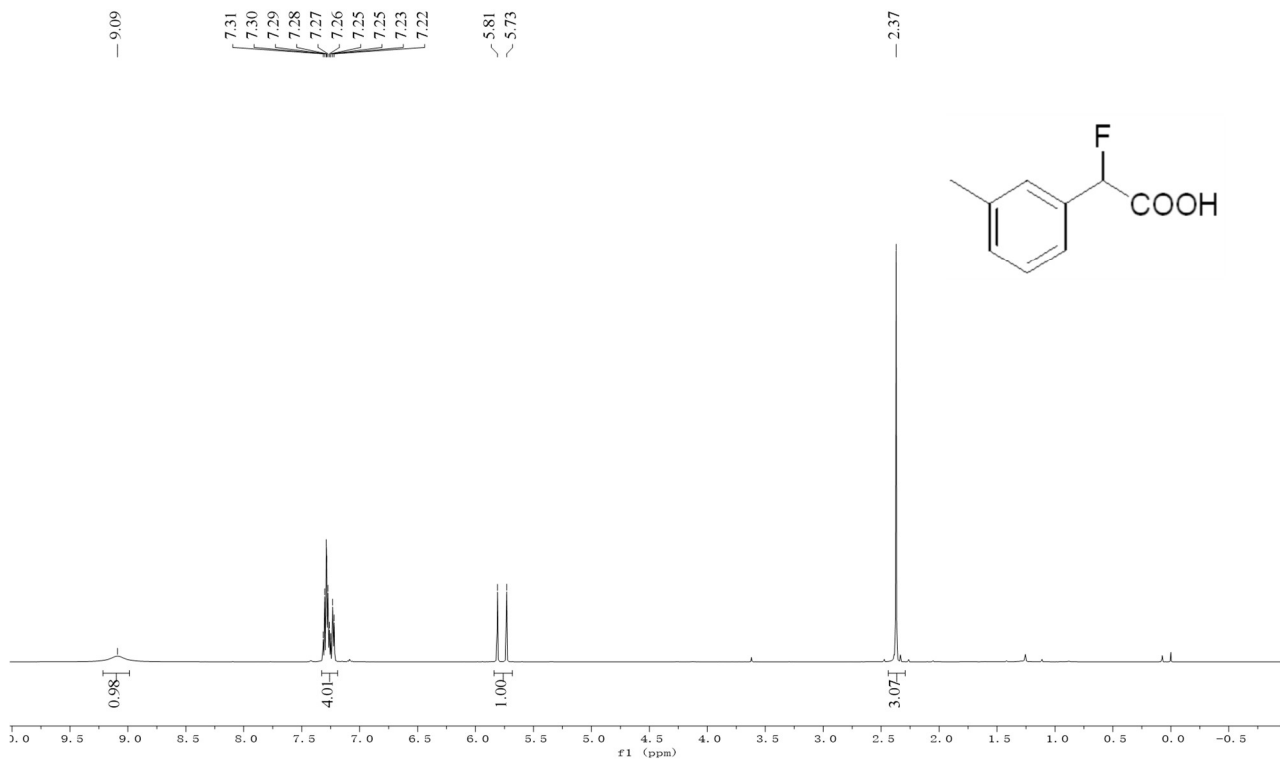


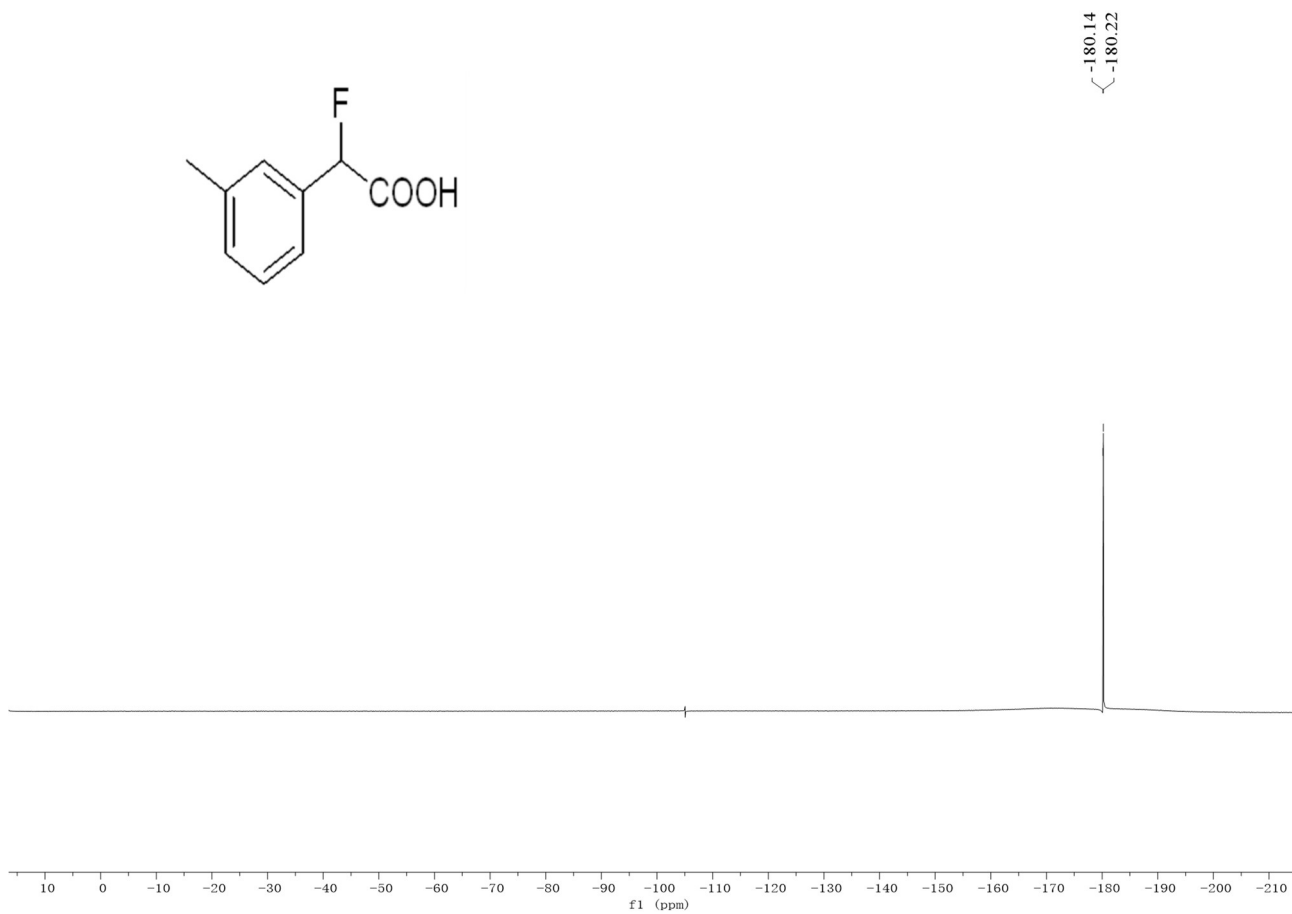
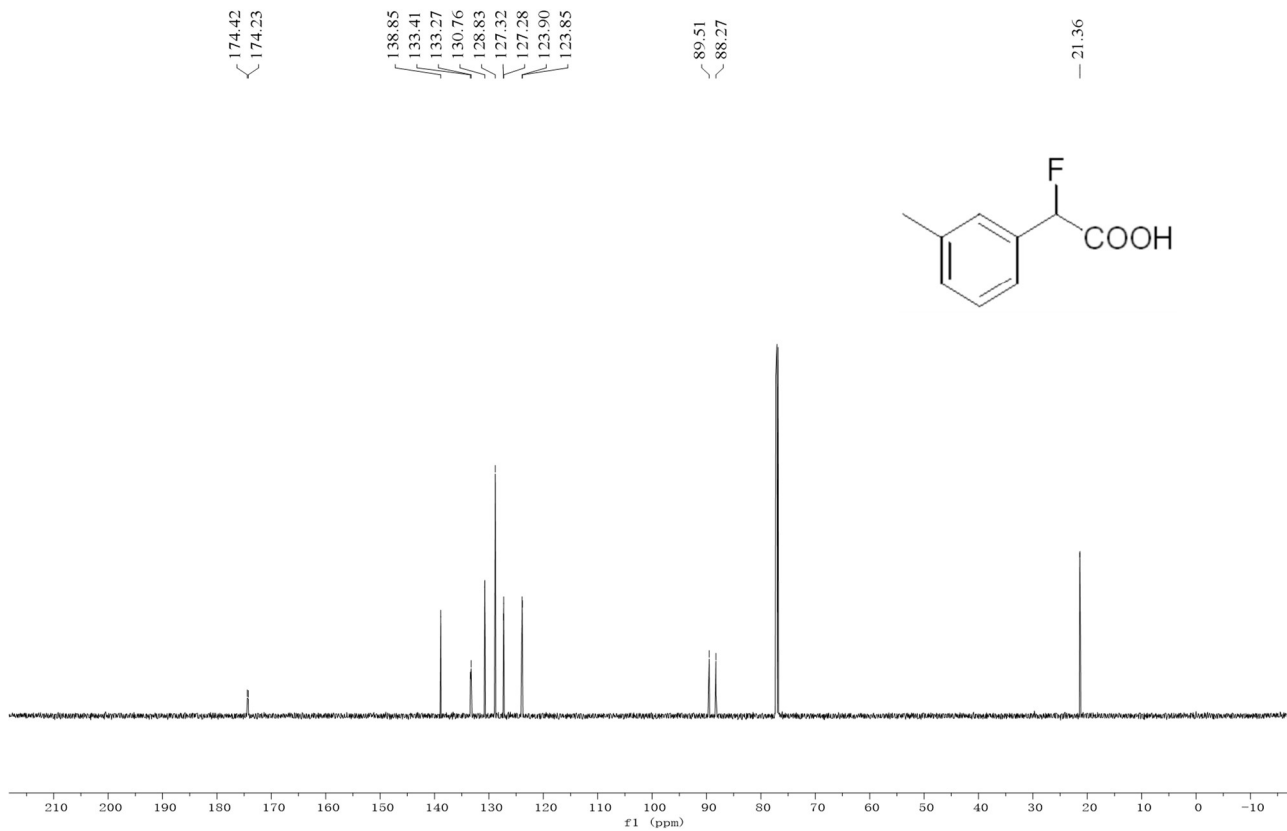
Compound 11b





Compound 12b



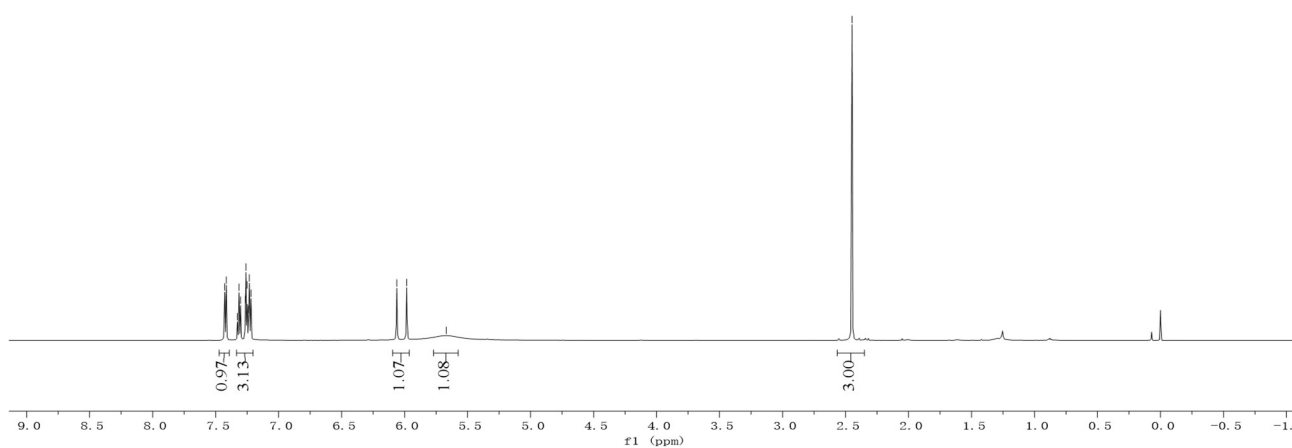
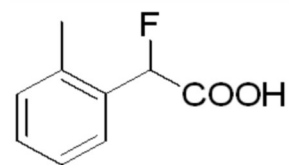


Compound 13b

7.43
7.42
7.33
7.31
7.30
7.26
7.26
7.25
7.24
7.23
7.22

6.06
5.98
5.67

2.45



136.67
136.64

173.87

136.67
136.64
132.12
131.99
131.03
129.96
127.34
127.29
126.46

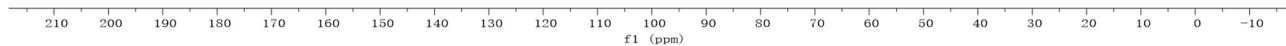
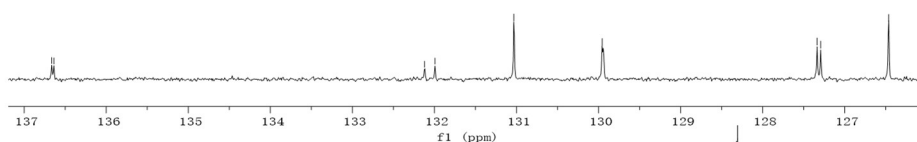
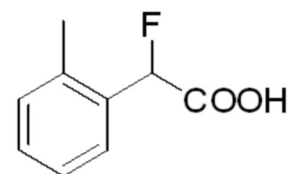
129.96

87.37
86.14

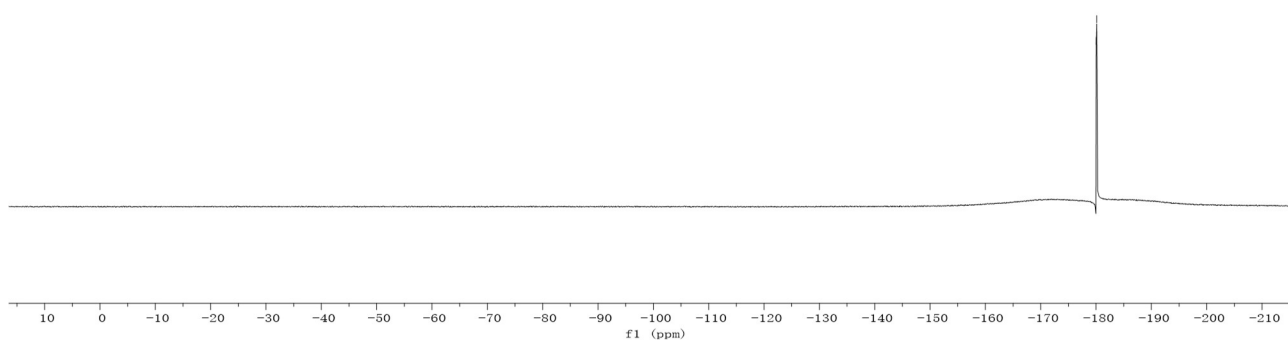
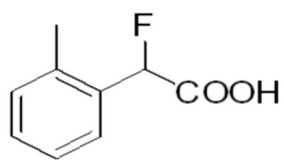
19.19

127.34
127.29

126.46

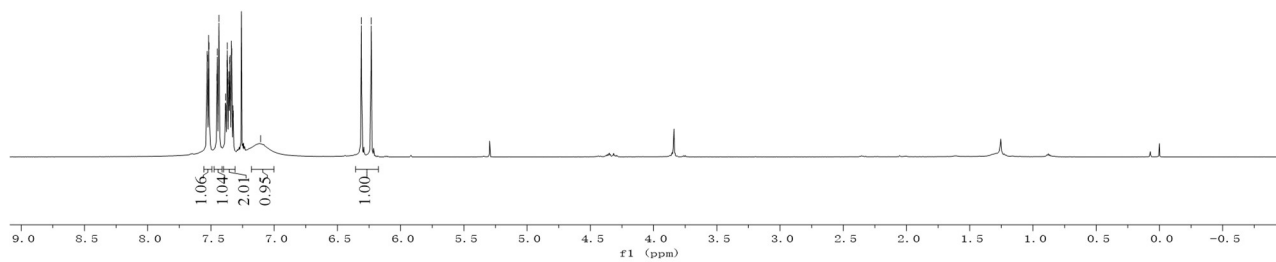
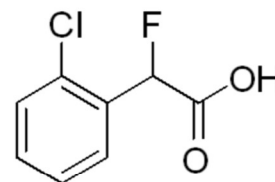


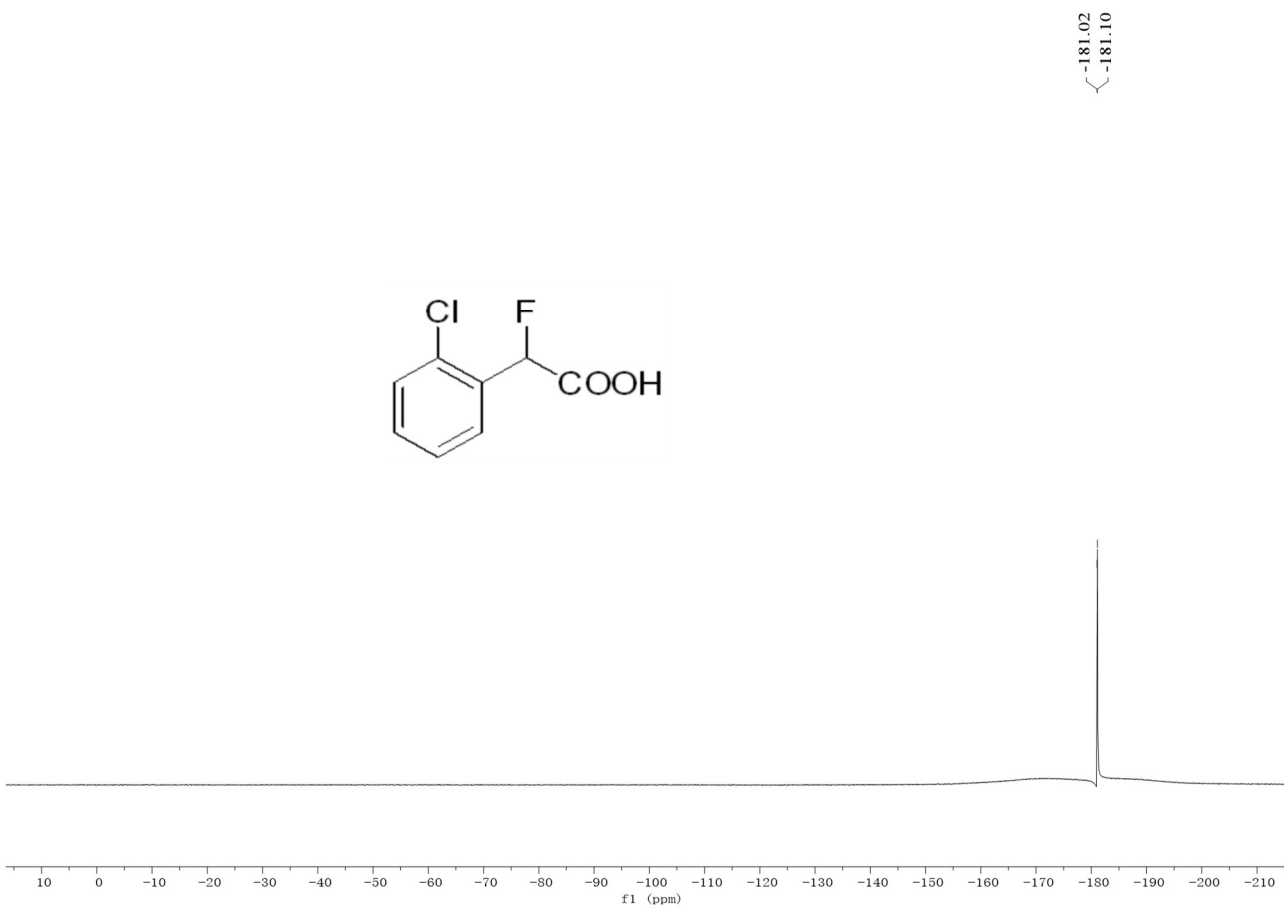
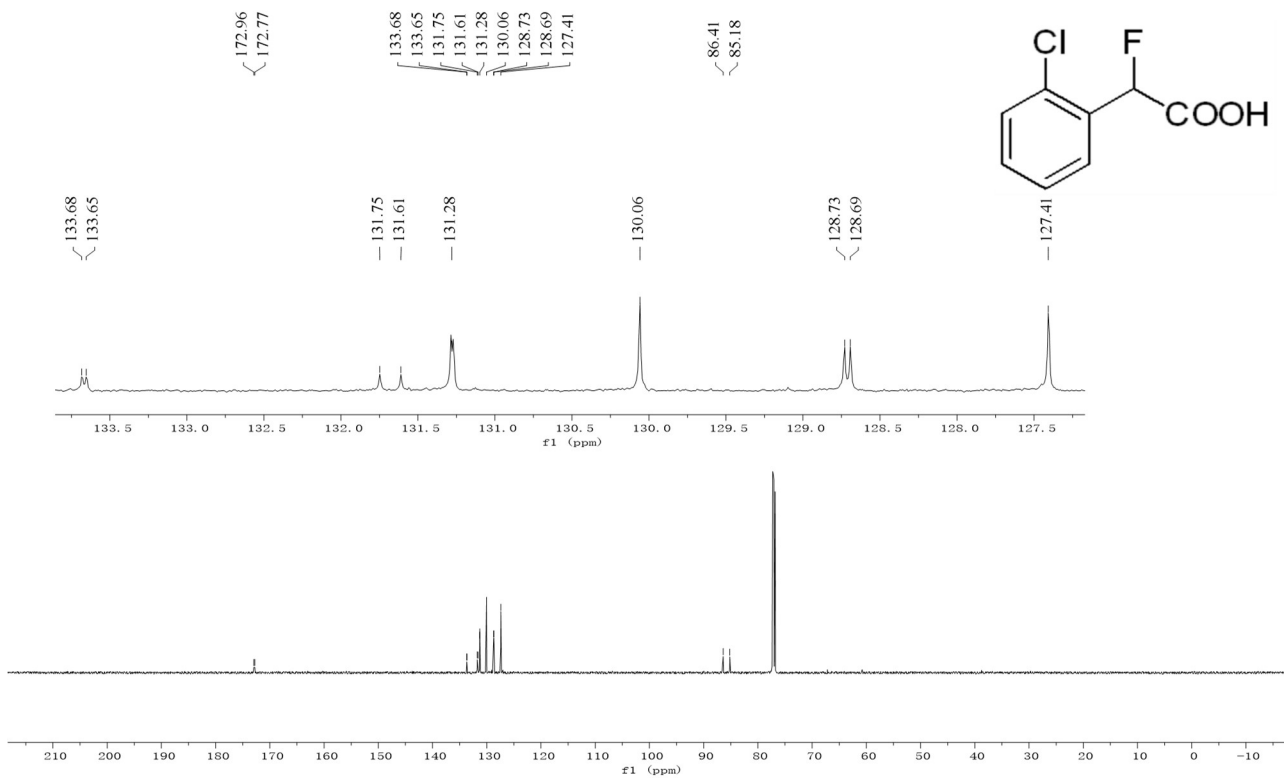
-180.04
-180.12



Compound 14b

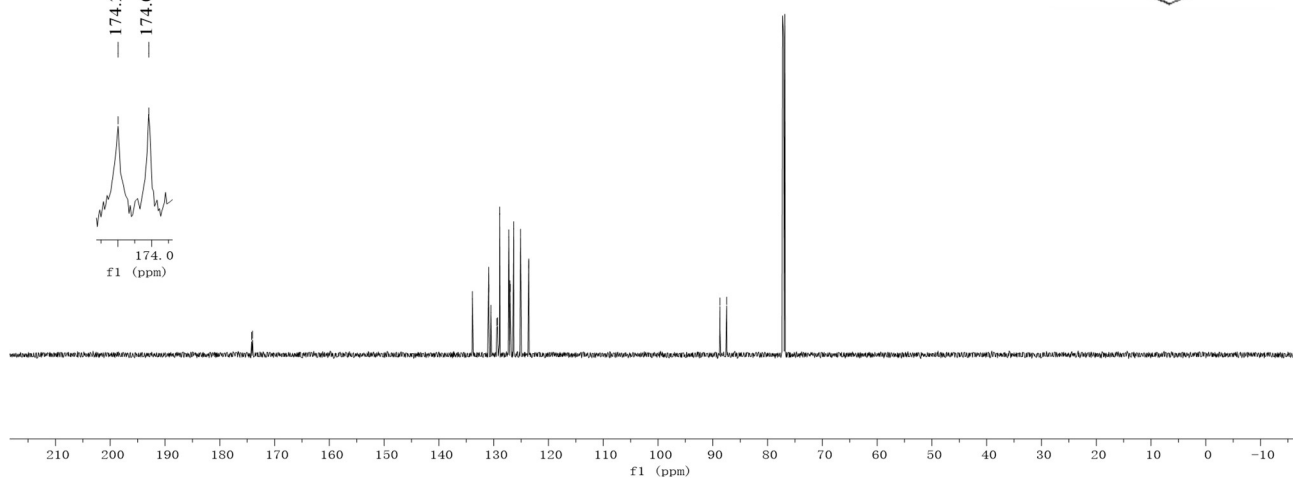
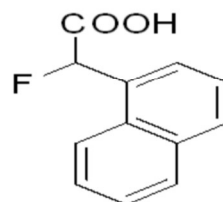
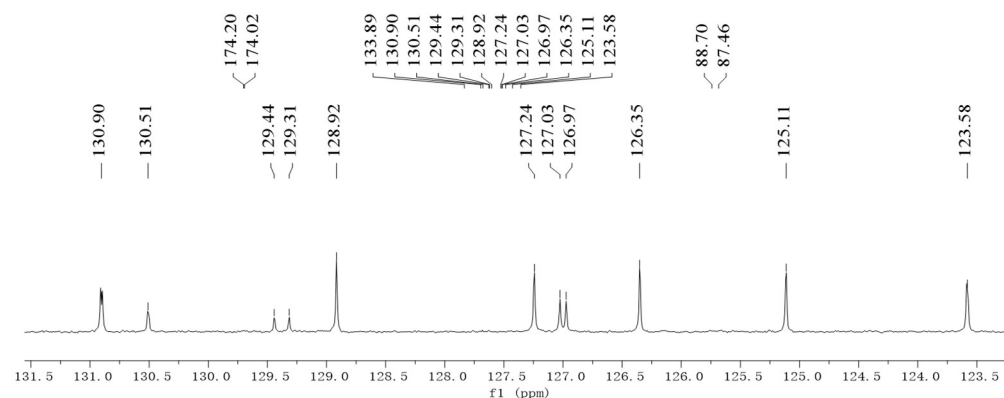
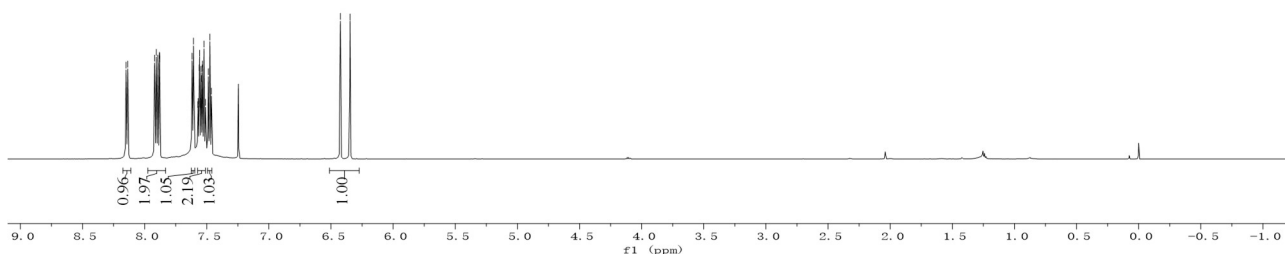
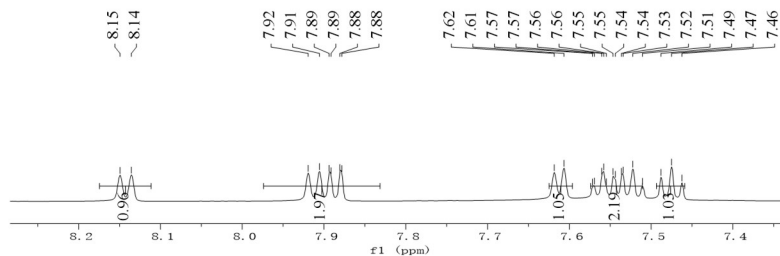
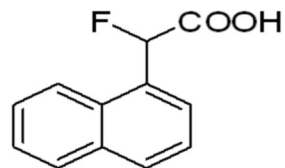
7.53
7.53
7.52
7.52
7.45
7.45
7.44
7.39
7.38
7.38
7.37
7.37
7.37
7.36
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.11
6.23

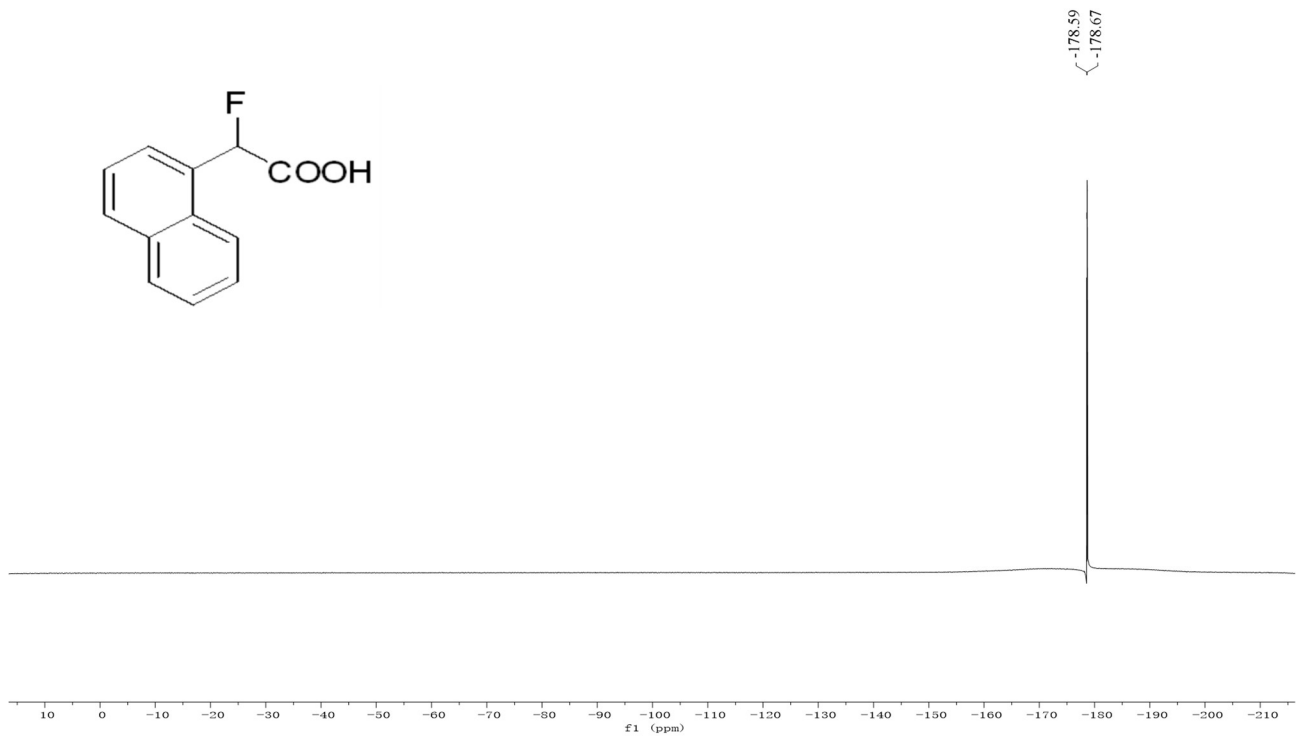




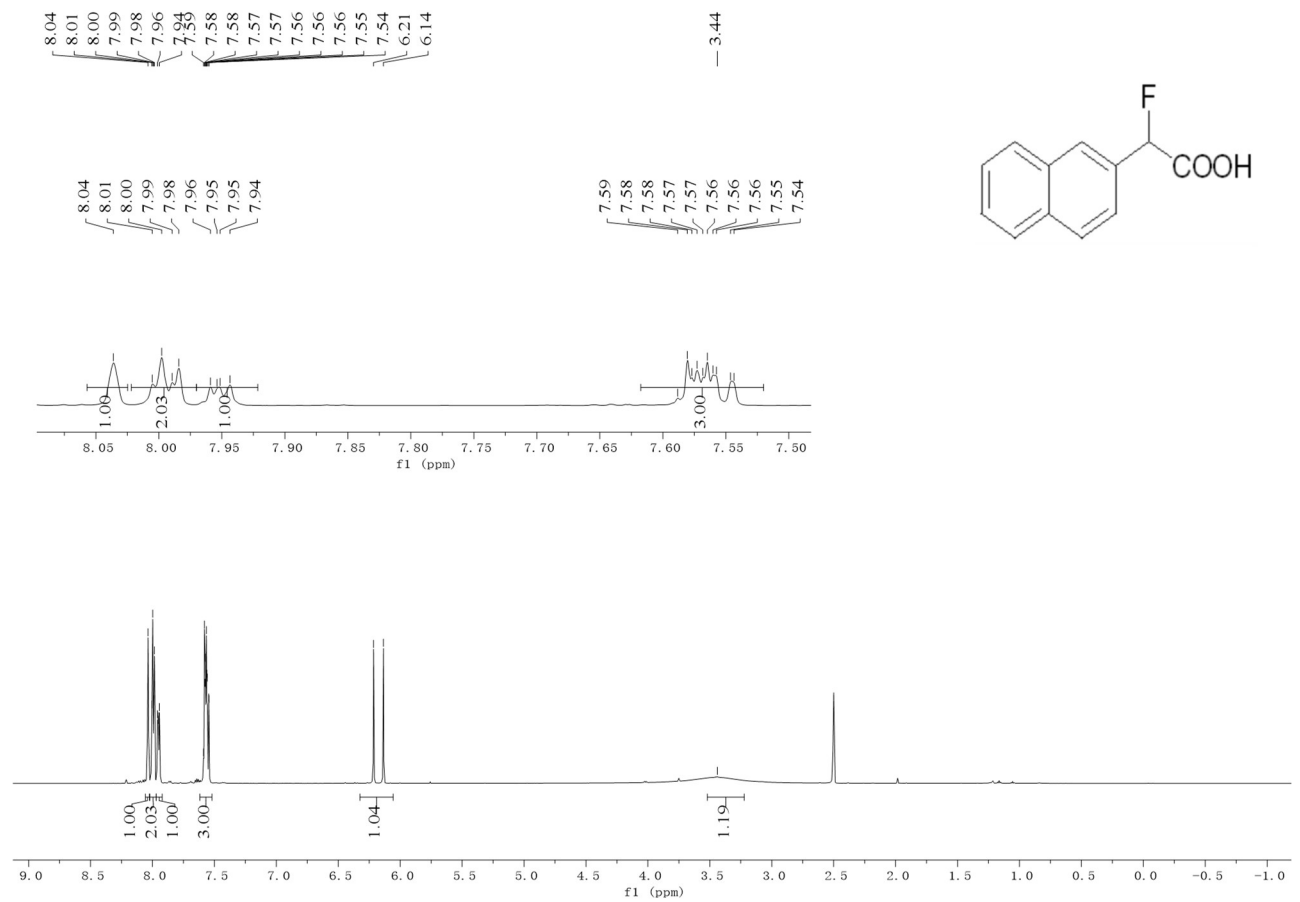
Compound 15b

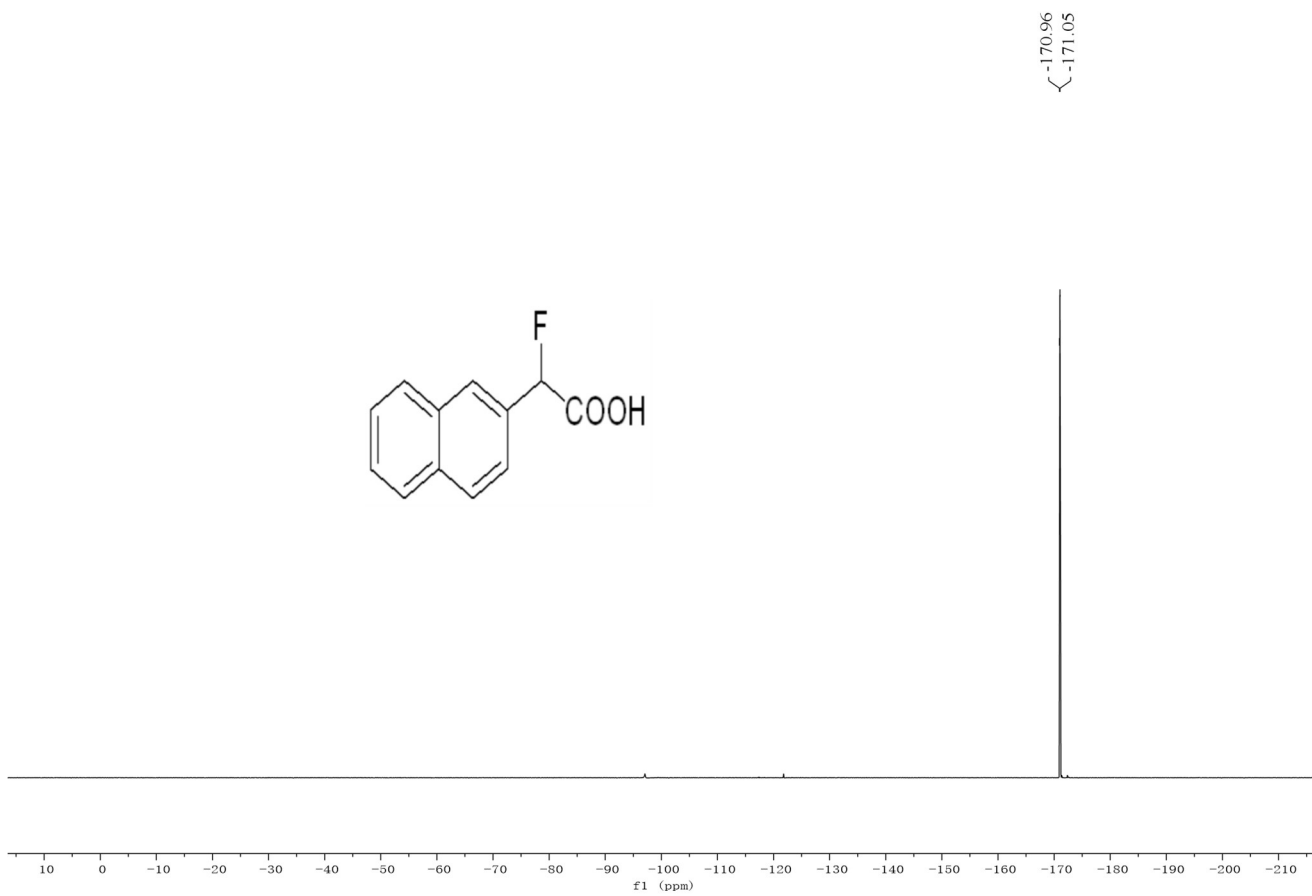
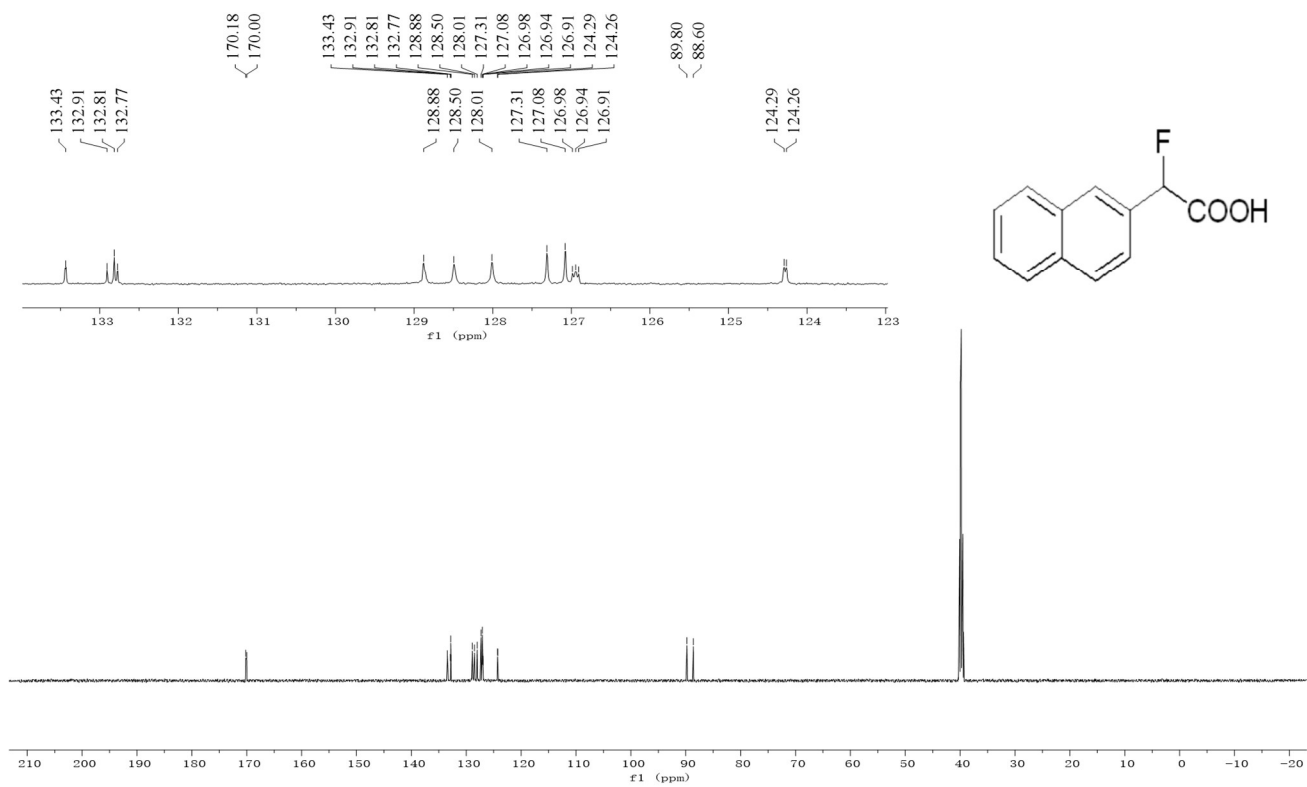
8.15
8.14
7.92
7.91
7.89
7.88
7.62
7.61
7.57
7.57
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.52
7.51
7.49
7.47
7.46
6.42
6.35



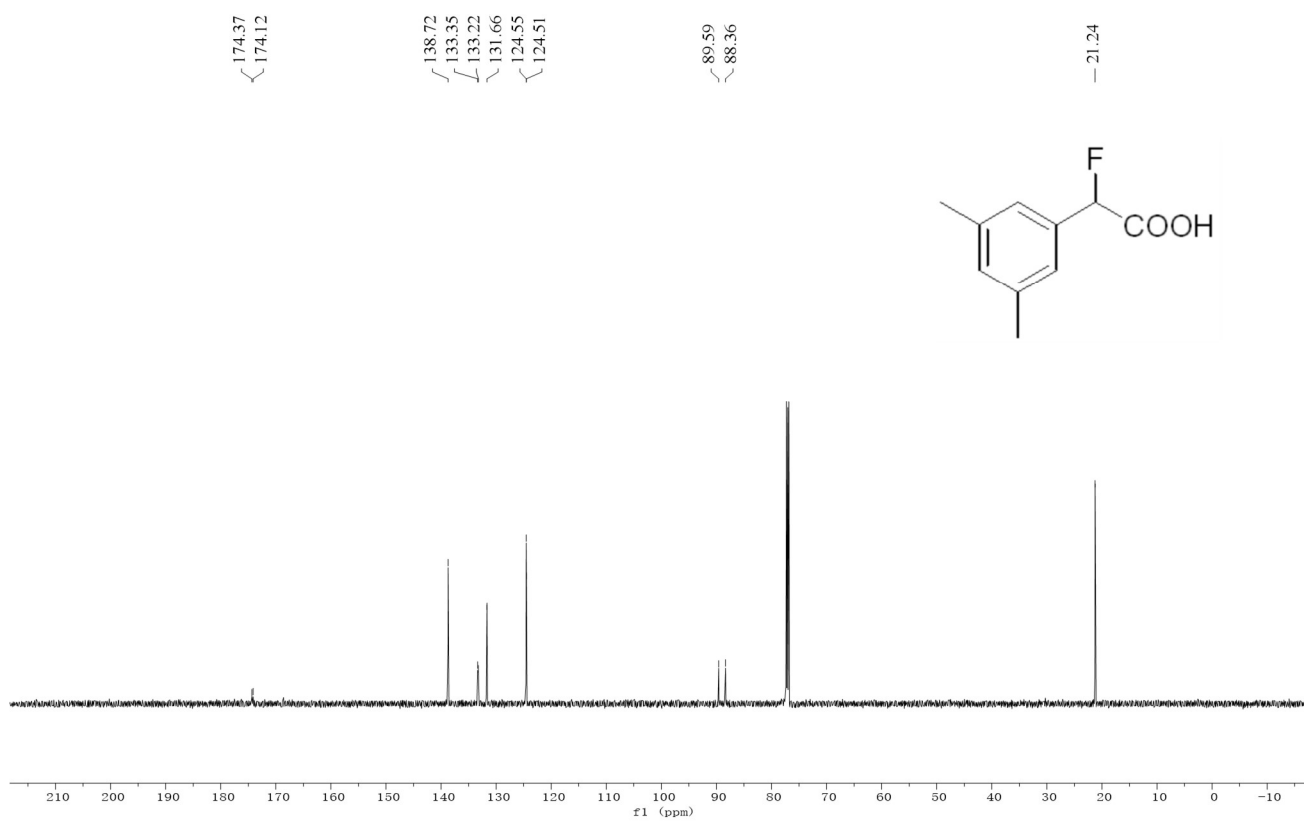
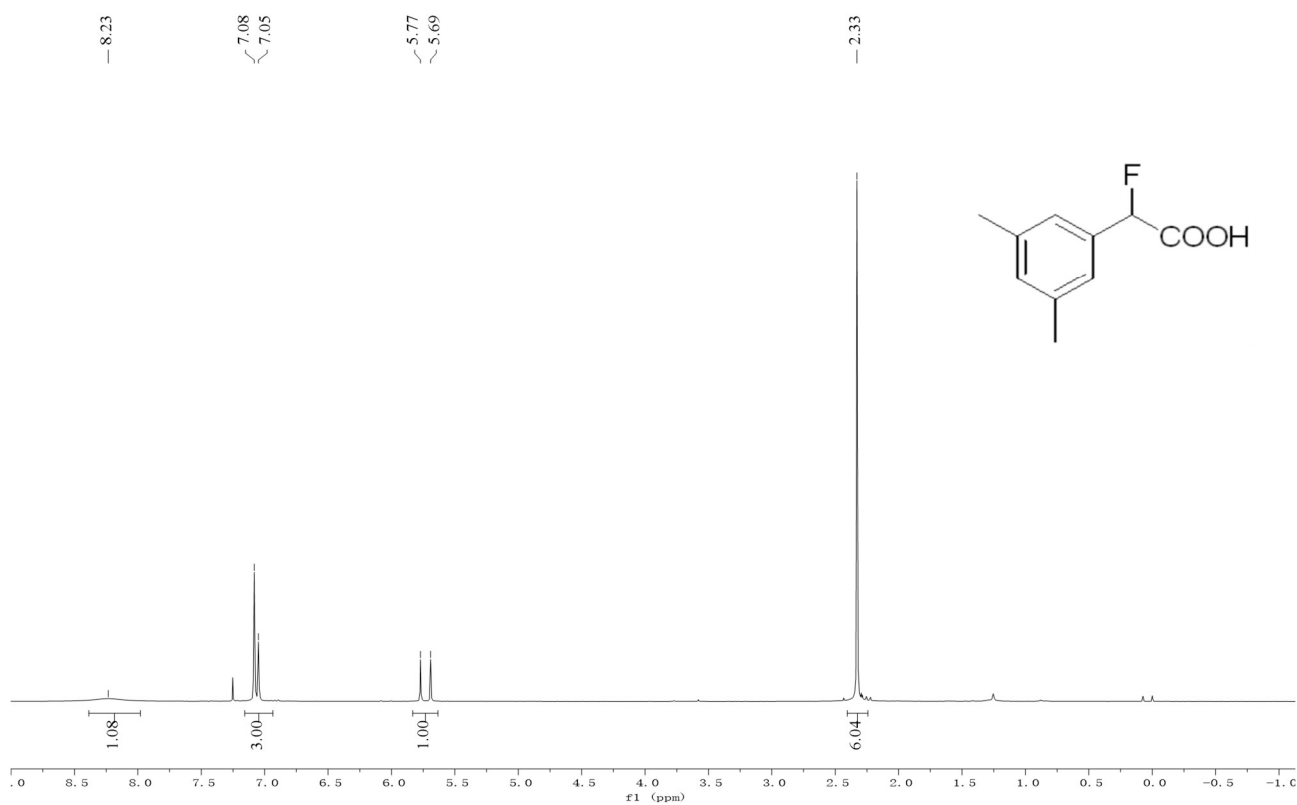


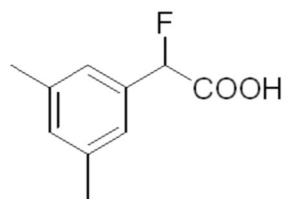
Compound 16b



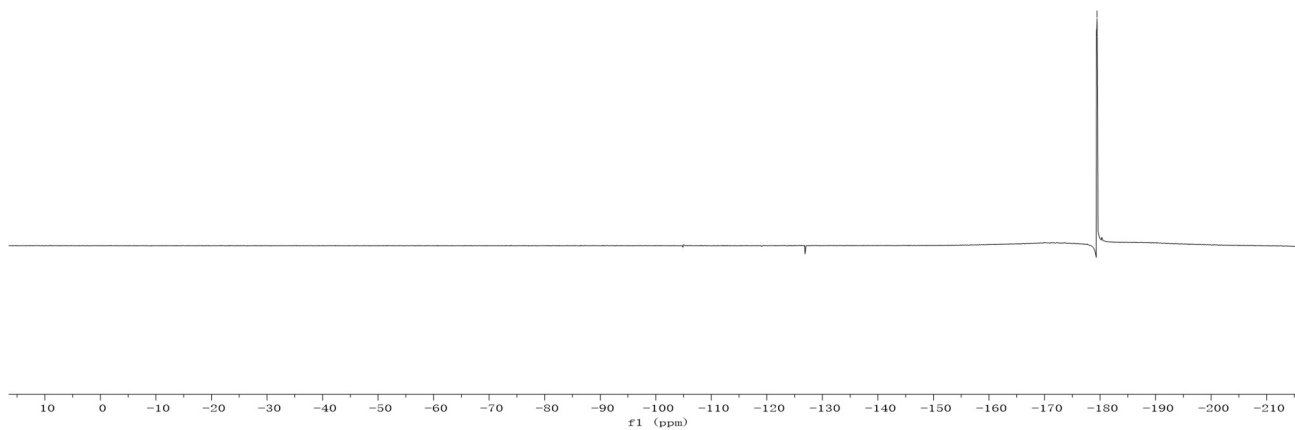


Compound 17b



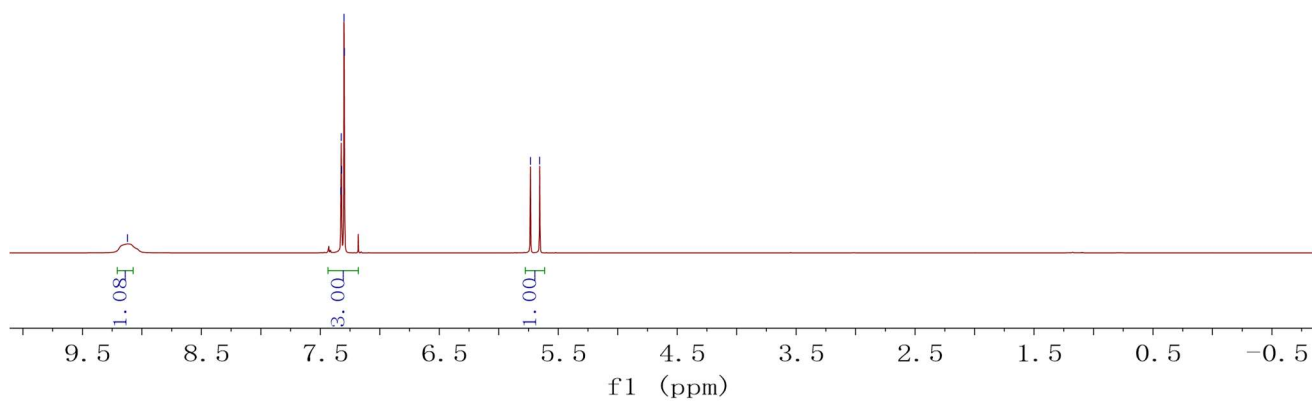
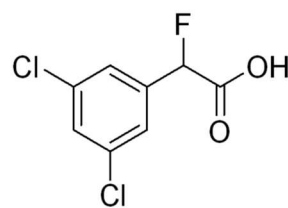
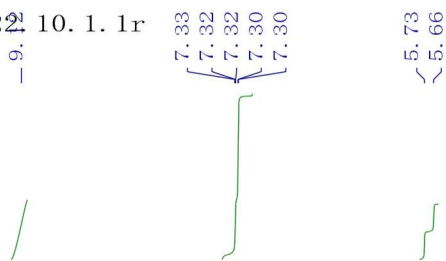


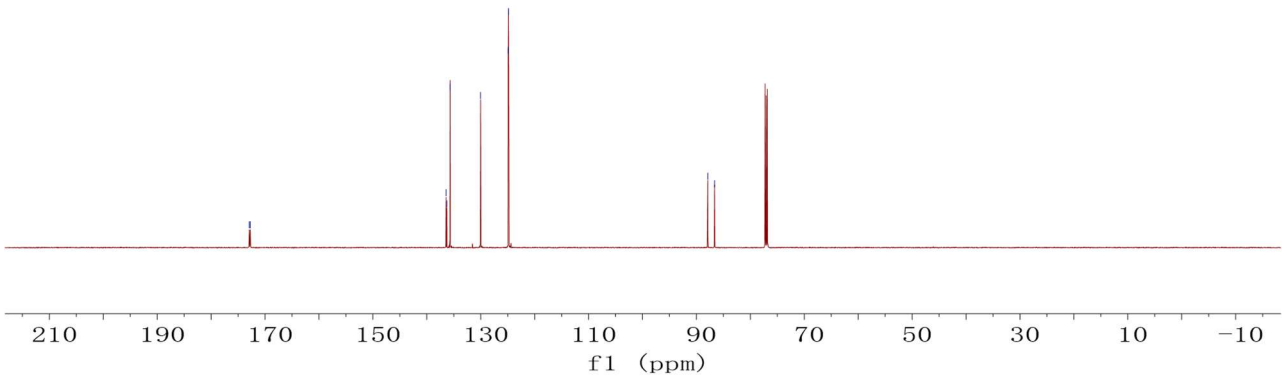
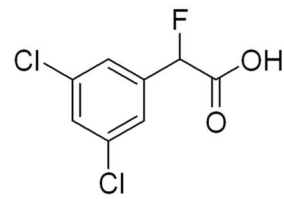
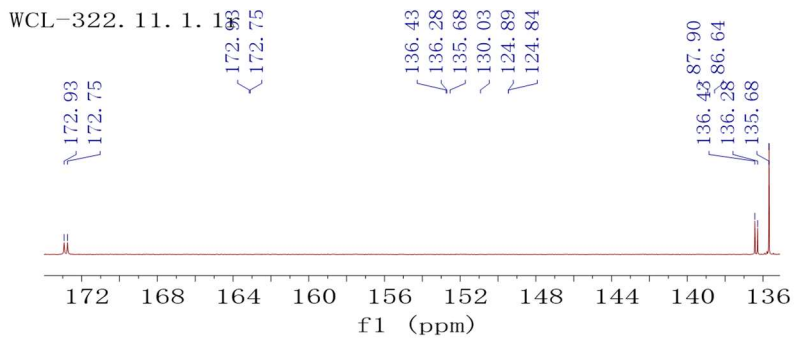
-179.38
-179.46



Compound 18b

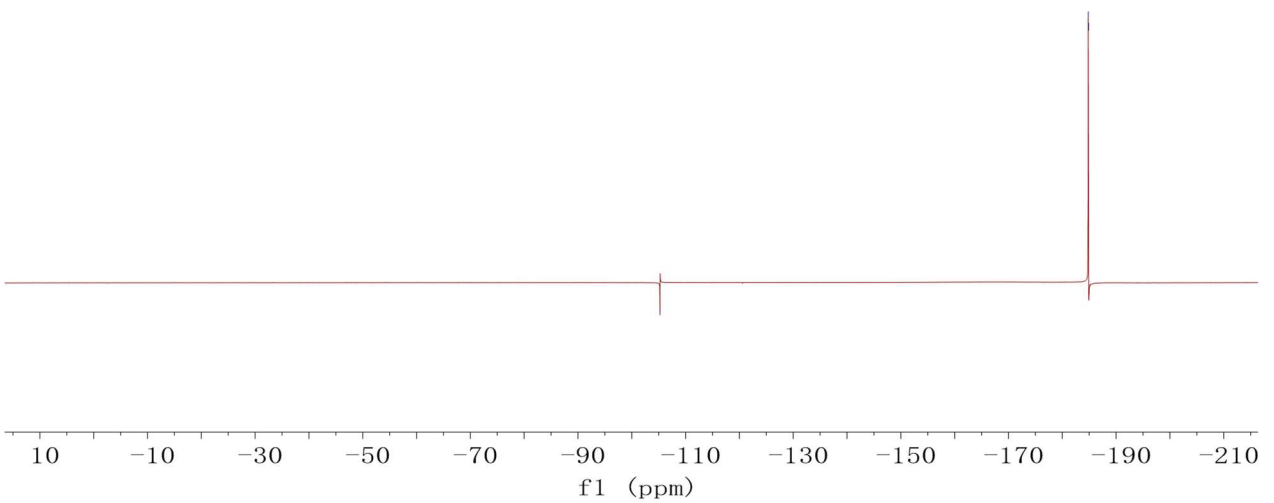
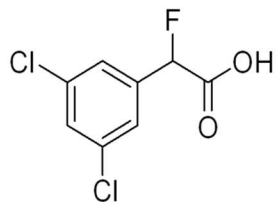
WCL-3222 10. 1. 1r



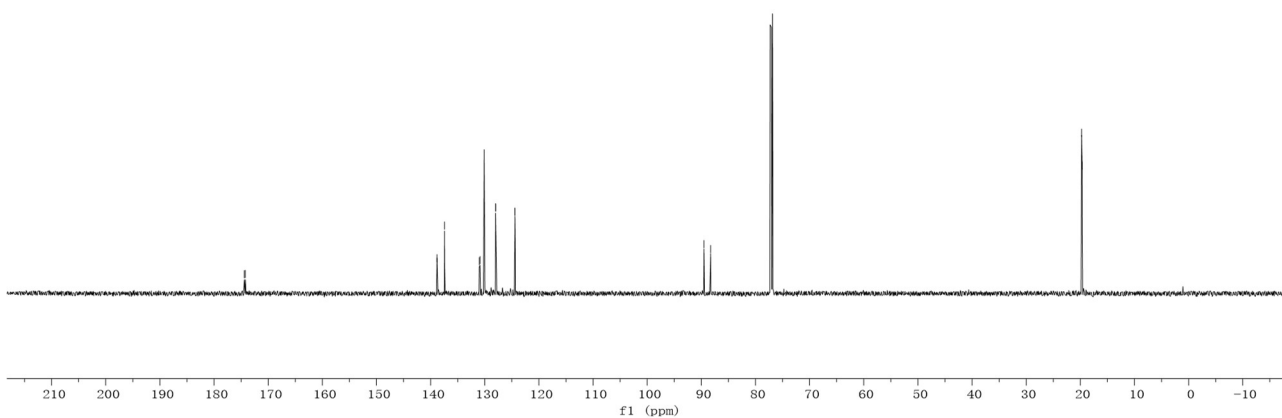
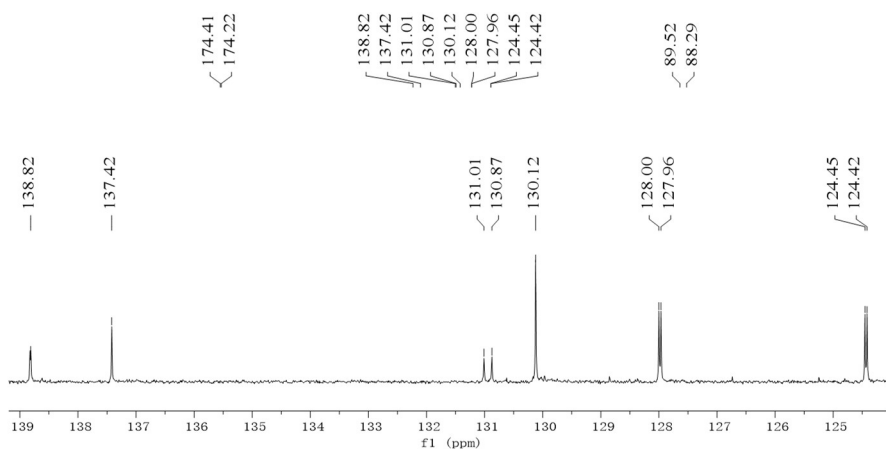
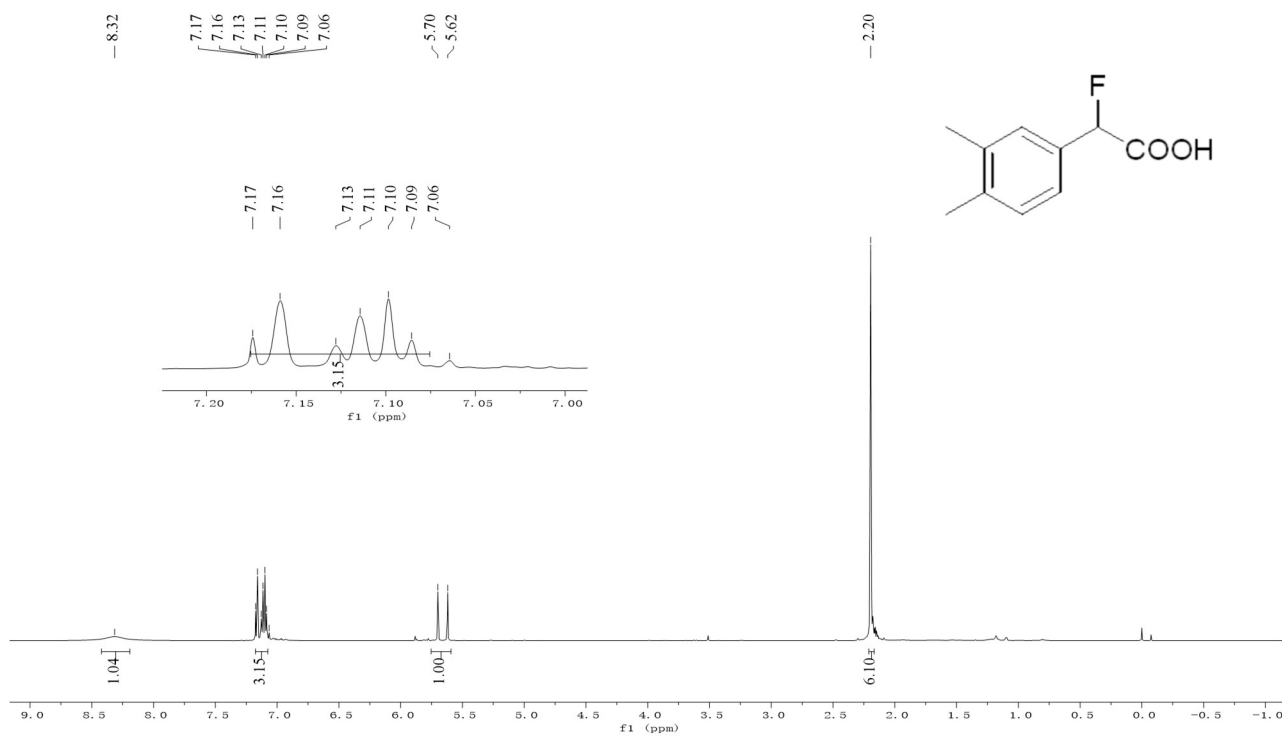


WCL-322. 12. 1. 1r

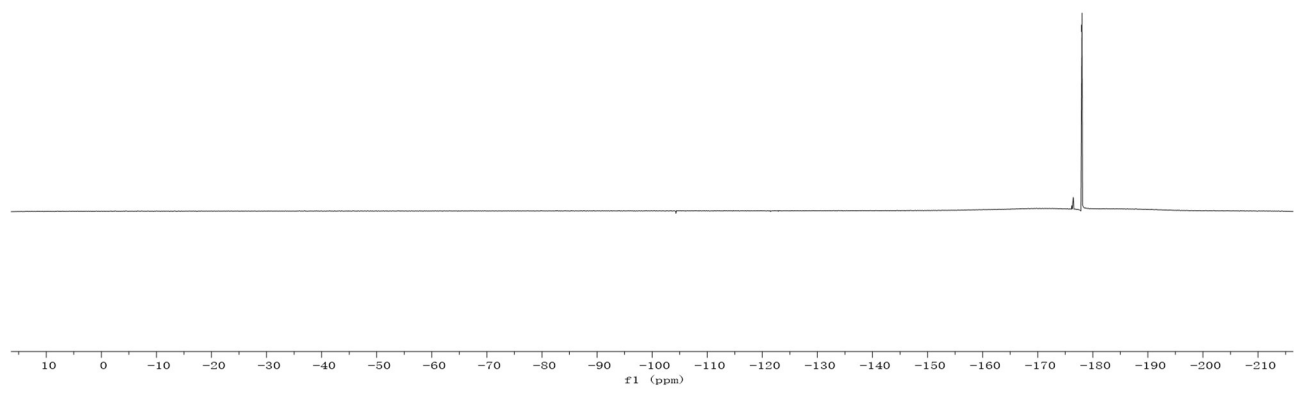
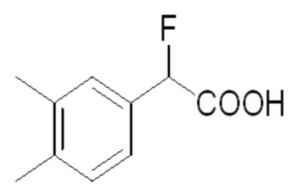
-184.82
-184.90



Compound 19b

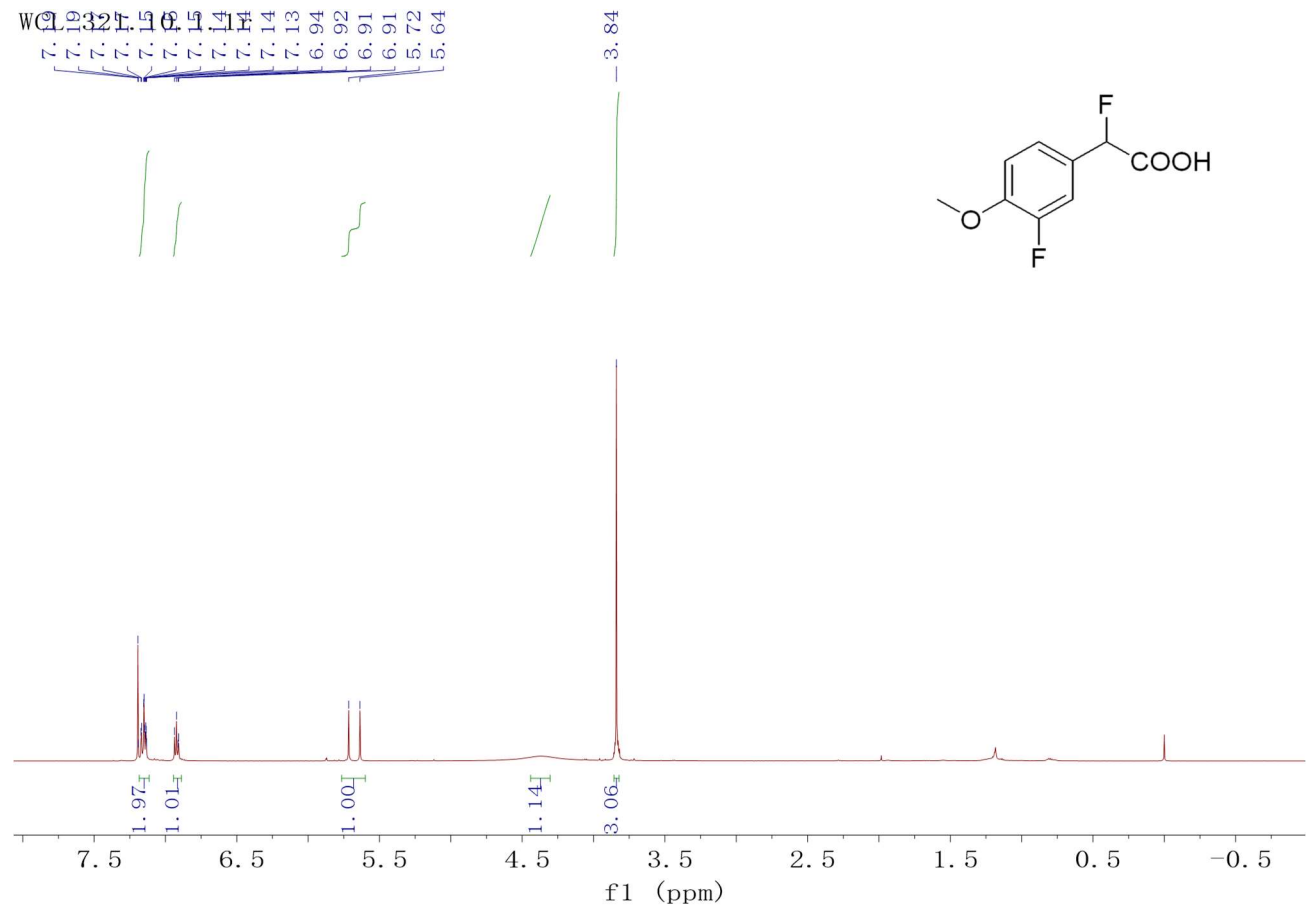
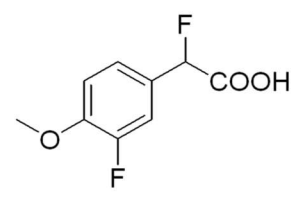


-177.95
-178.04

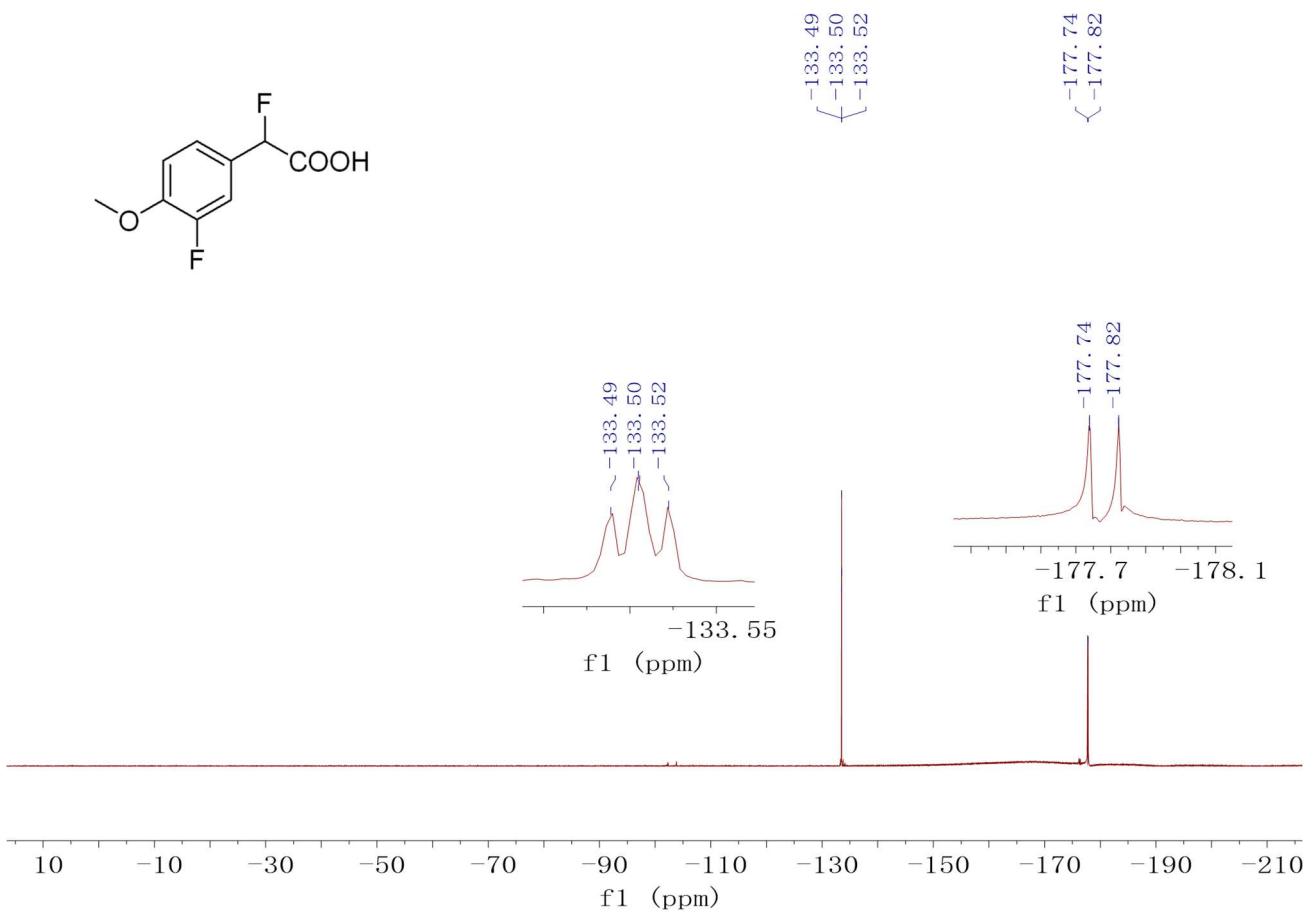
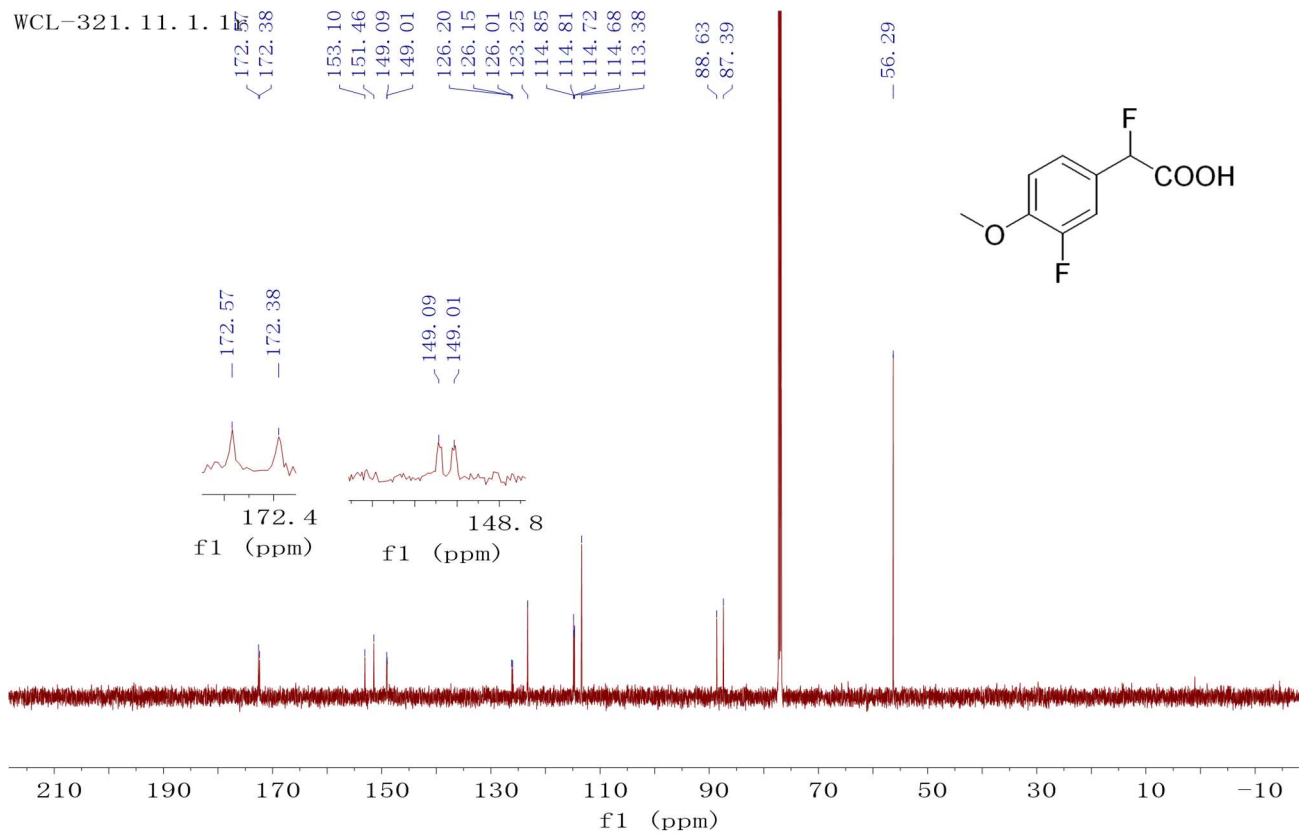


Compound 20b

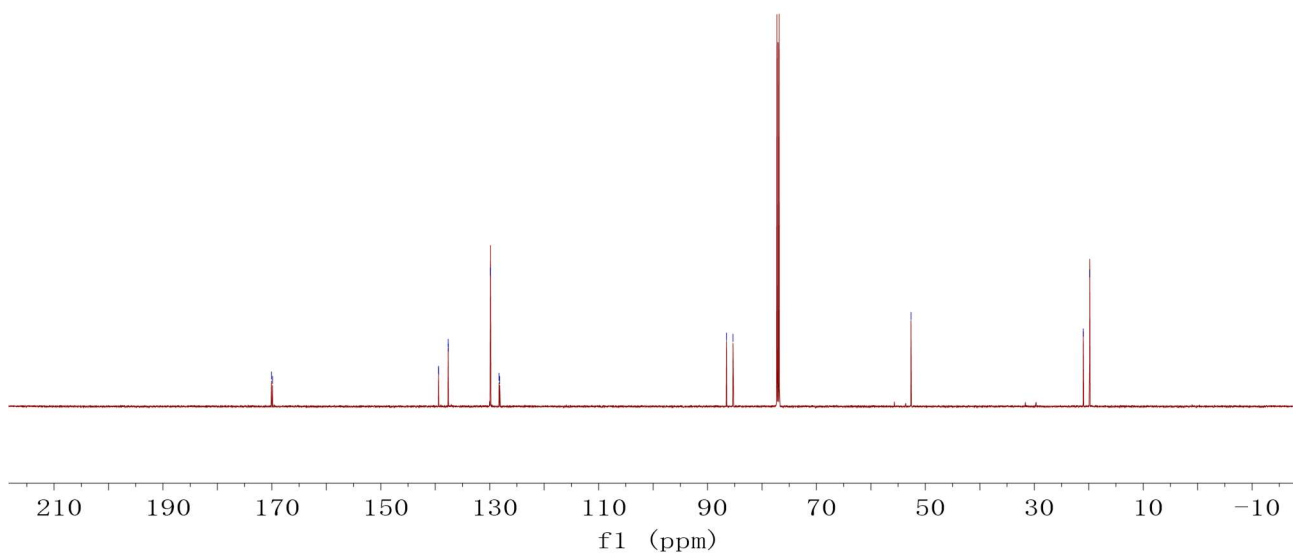
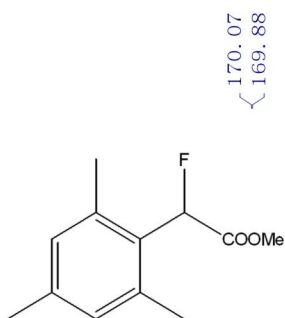
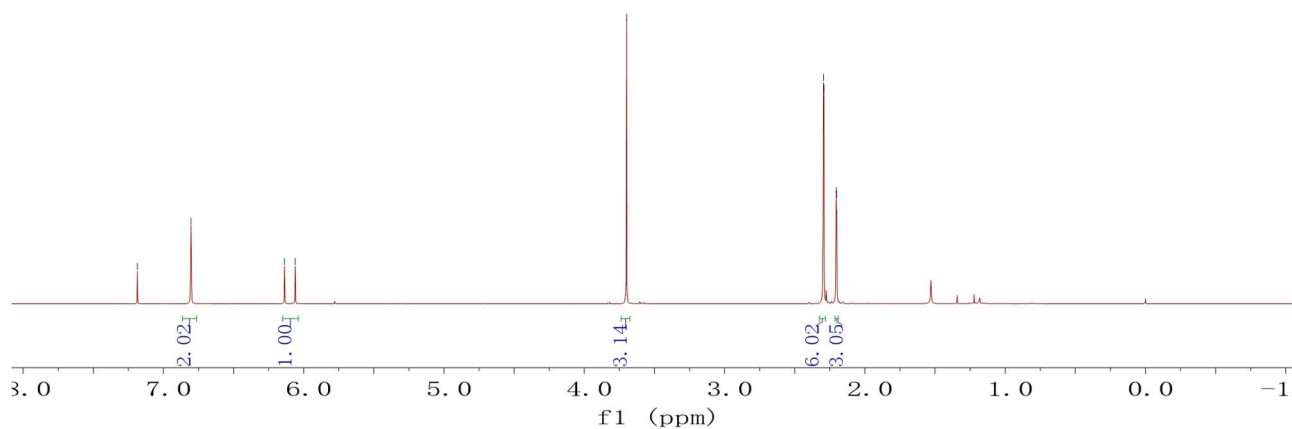
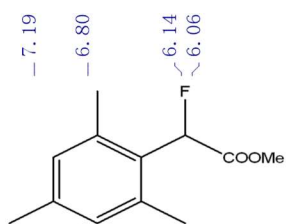
7.19
7.15
7.15
7.14
7.14
7.13
6.94
6.91
6.91
5.64
3.84

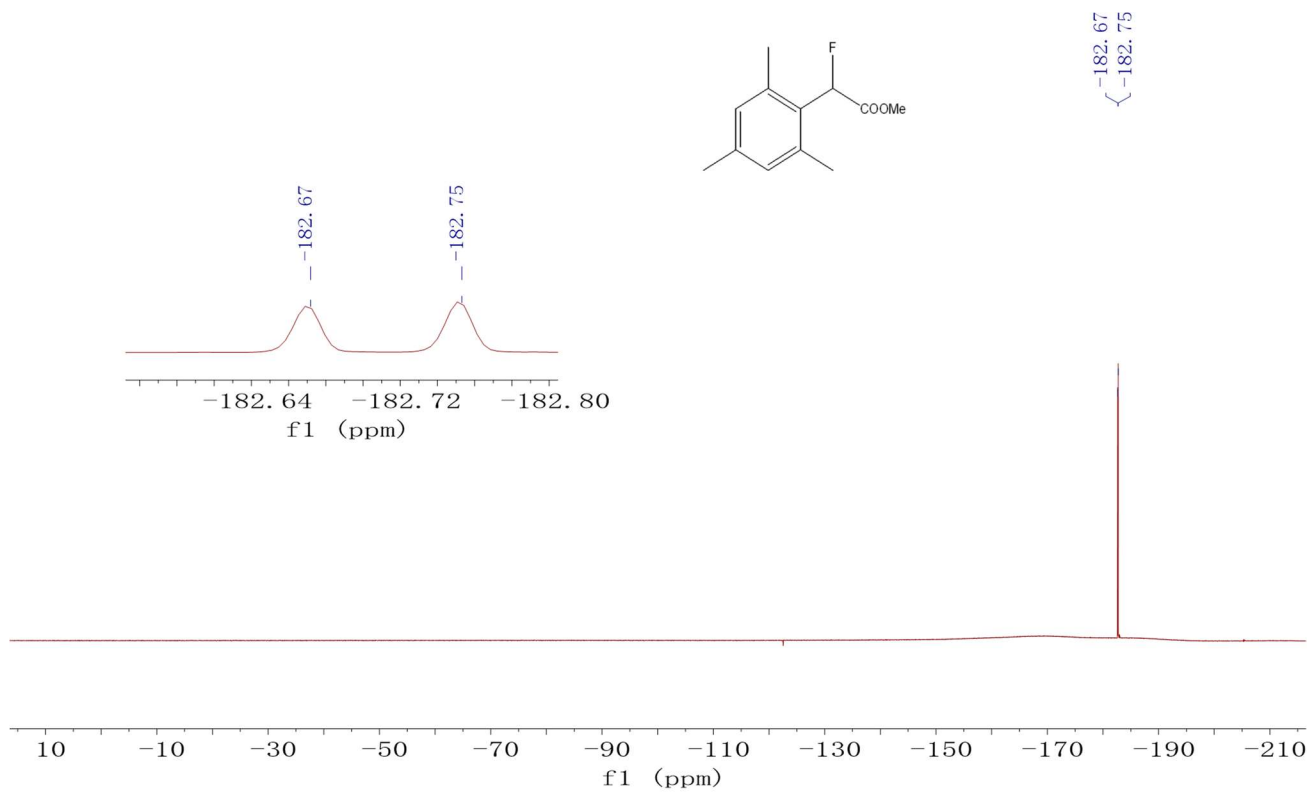


WCL-321. 11. 1. 157

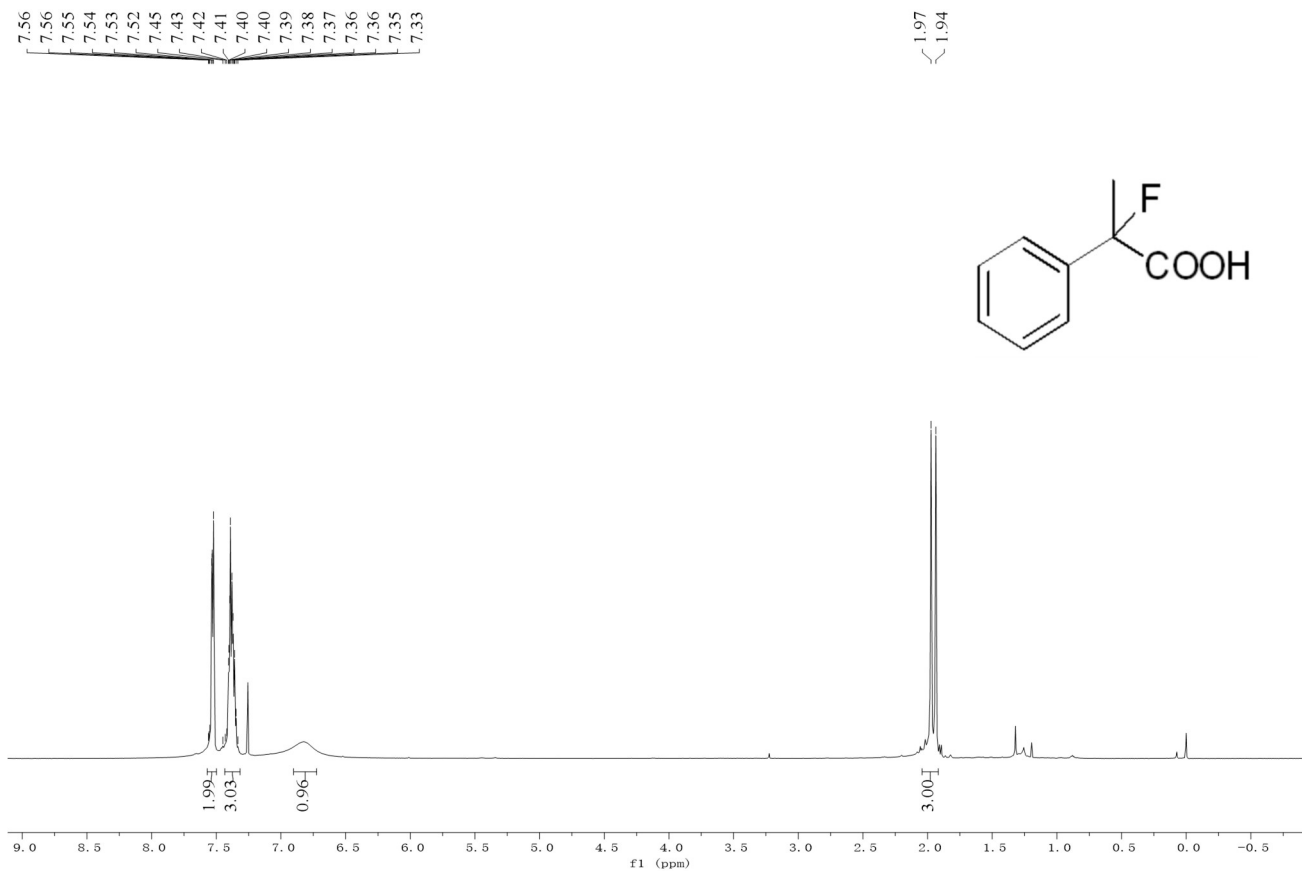


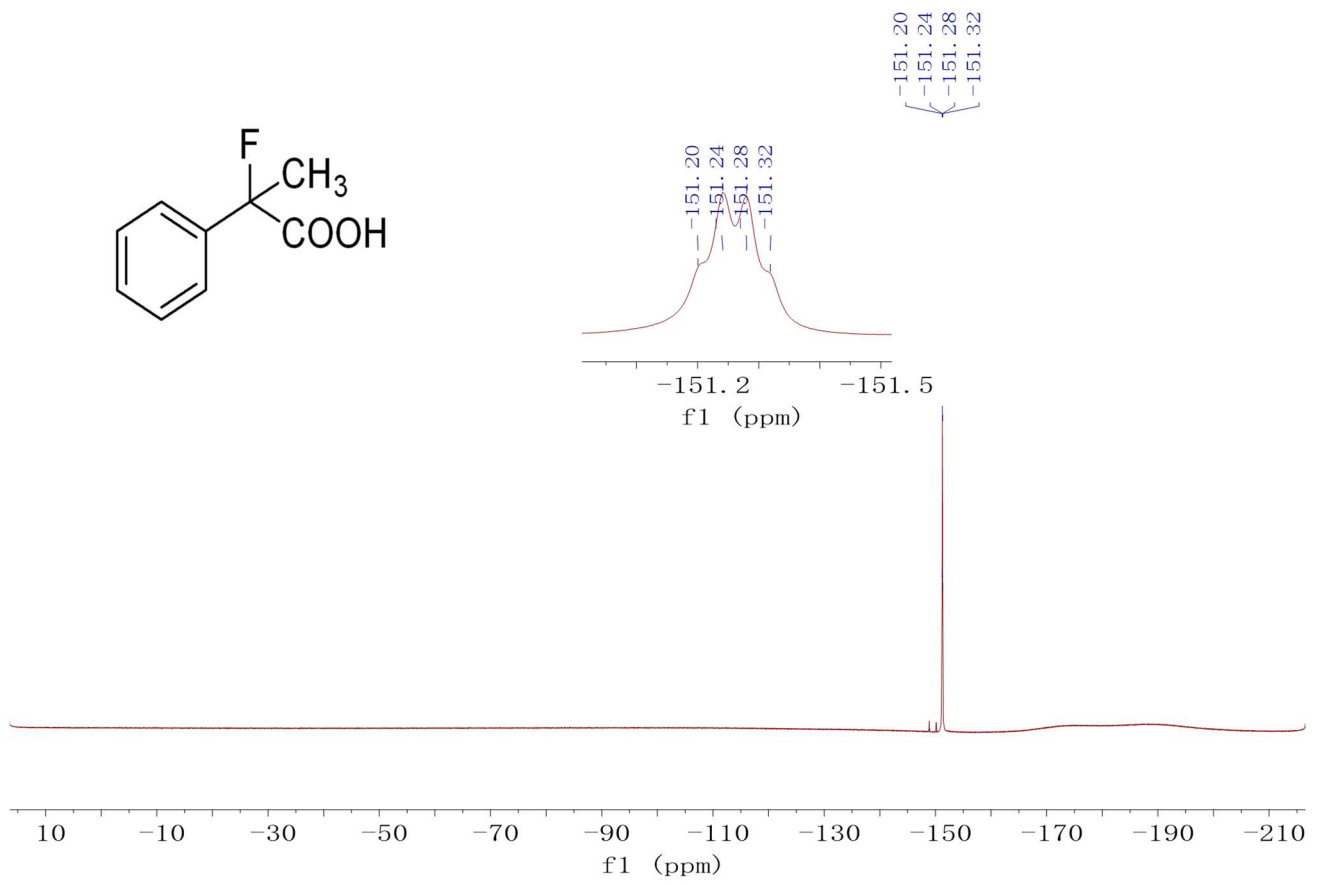
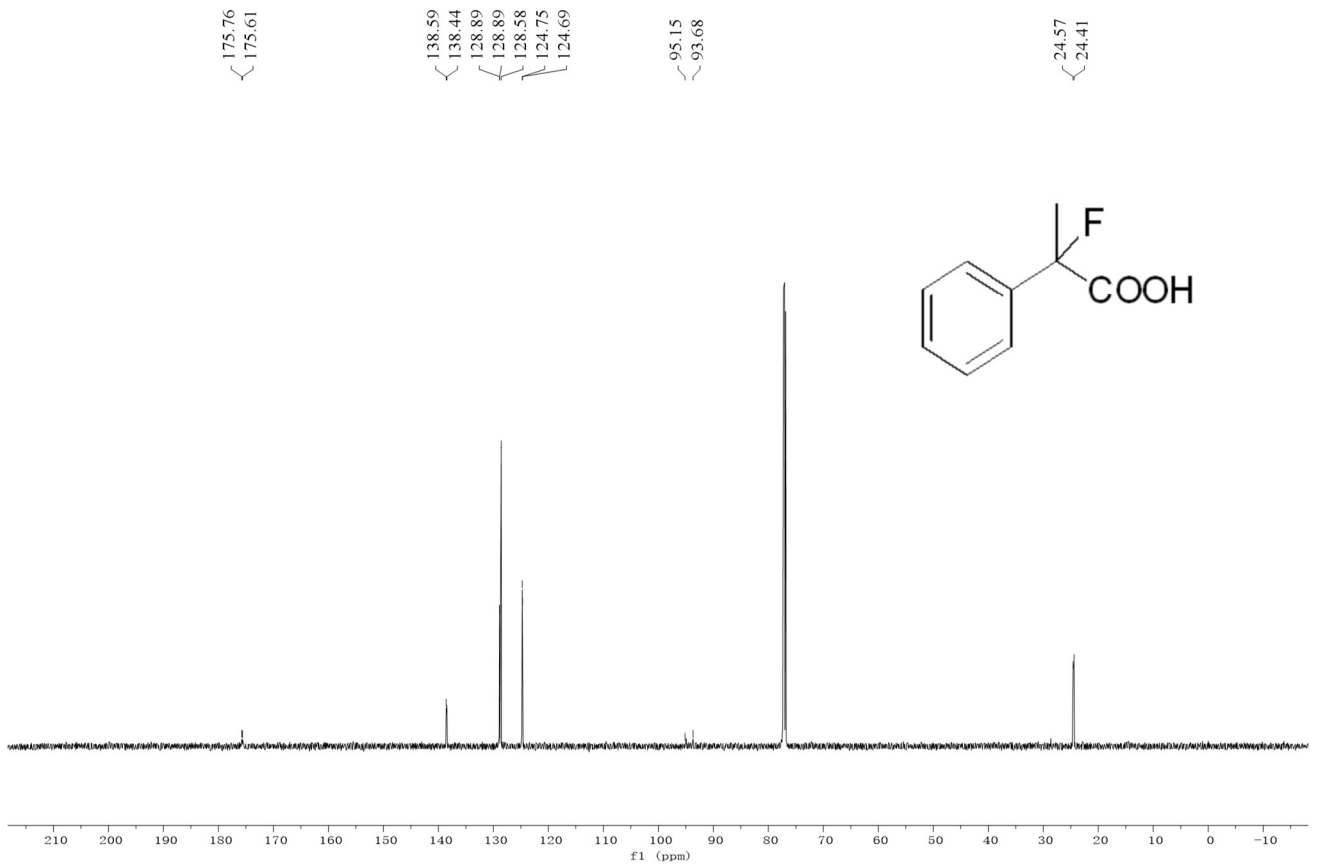
Compound 21b



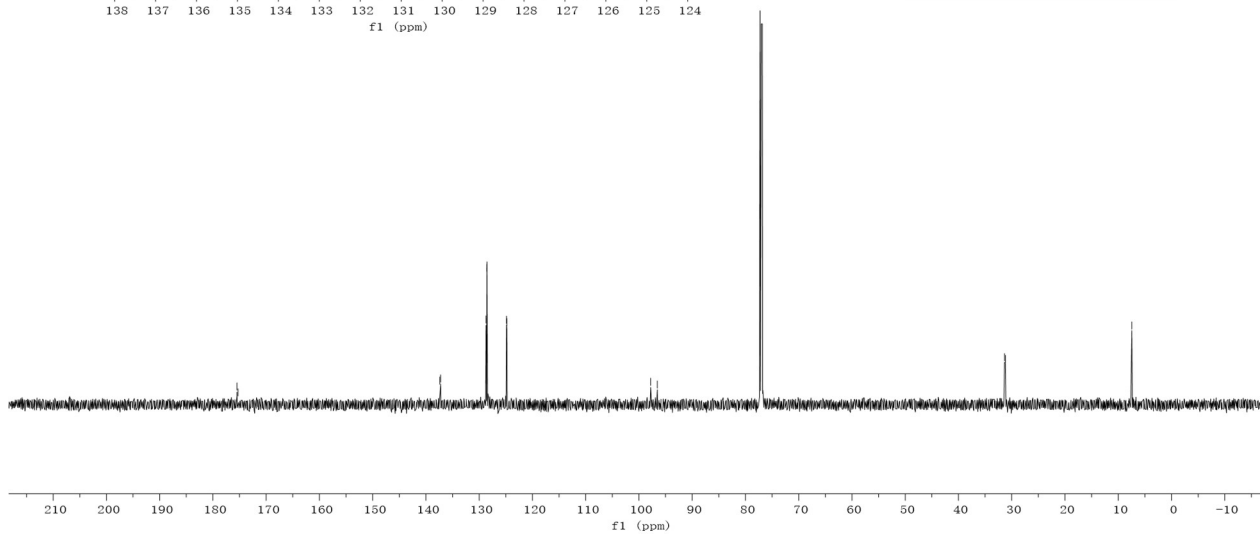
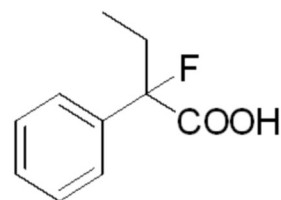
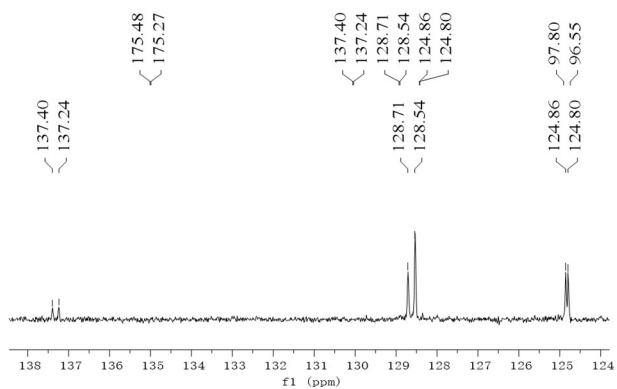
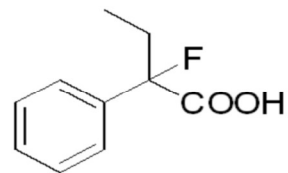
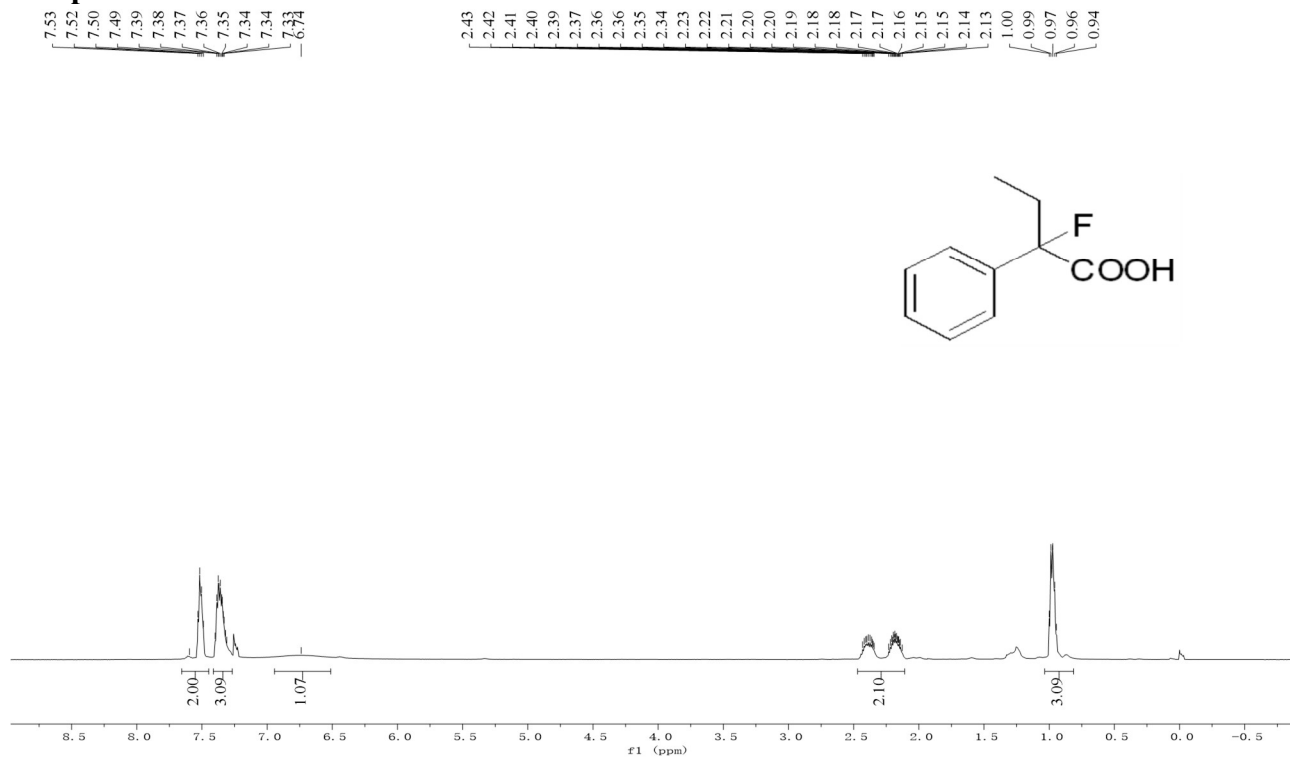


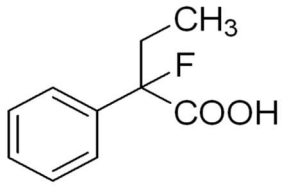
Compound 22b



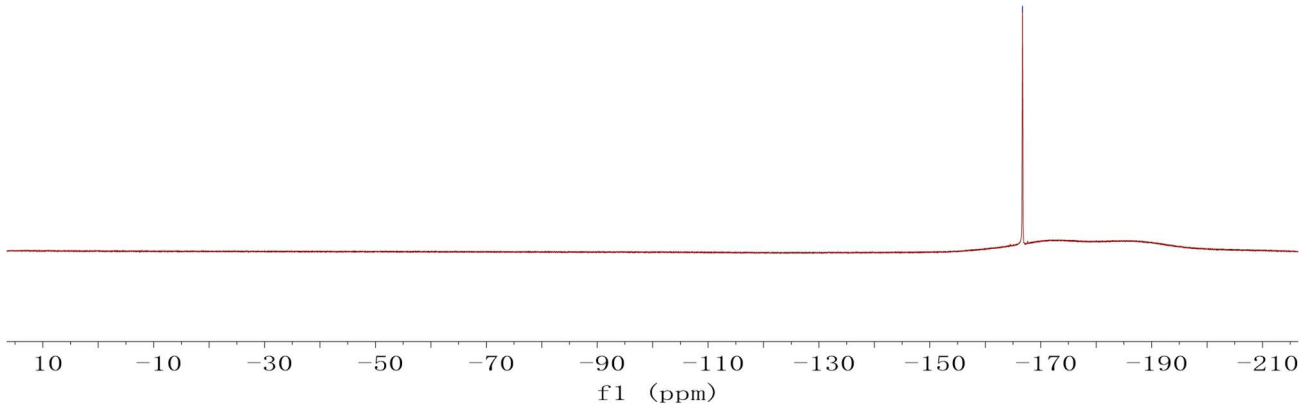


Compound 23b



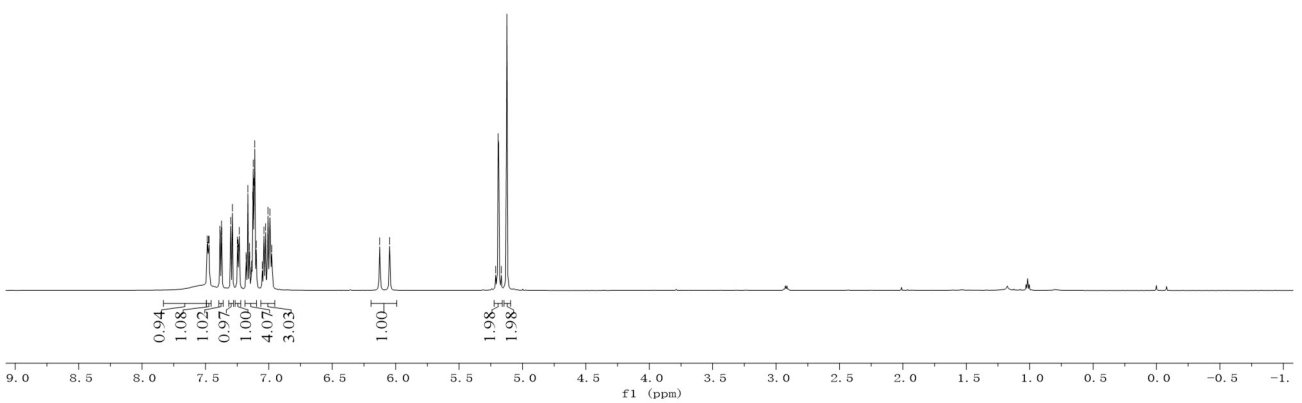
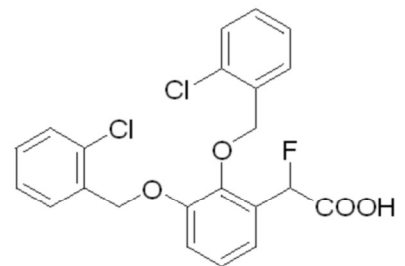
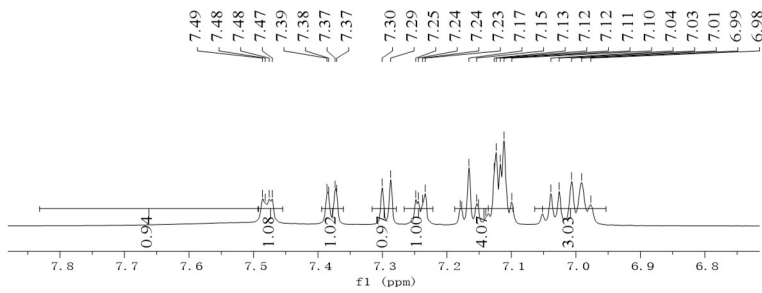


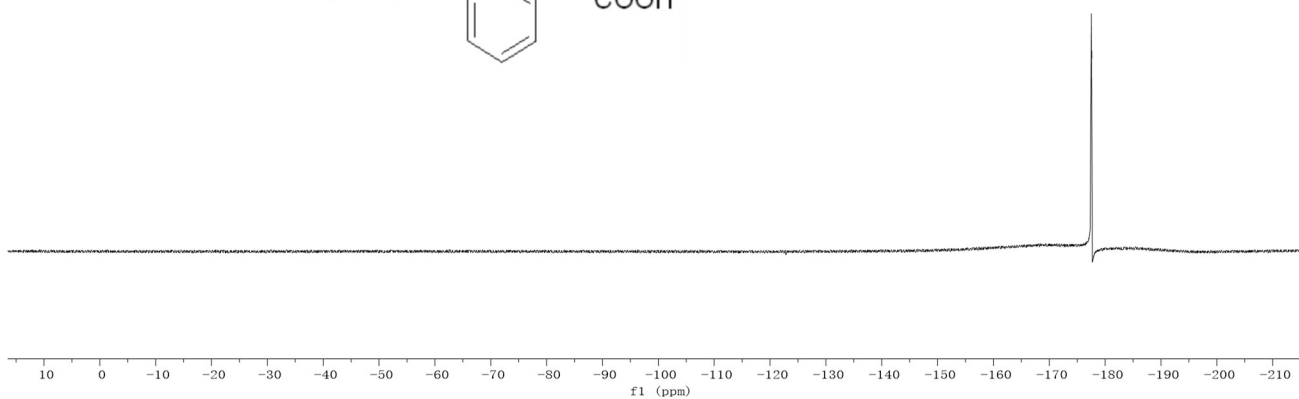
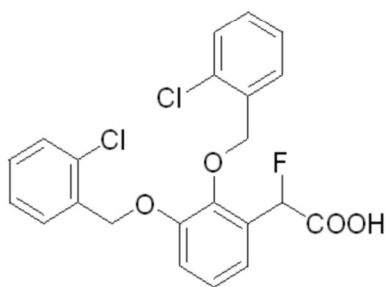
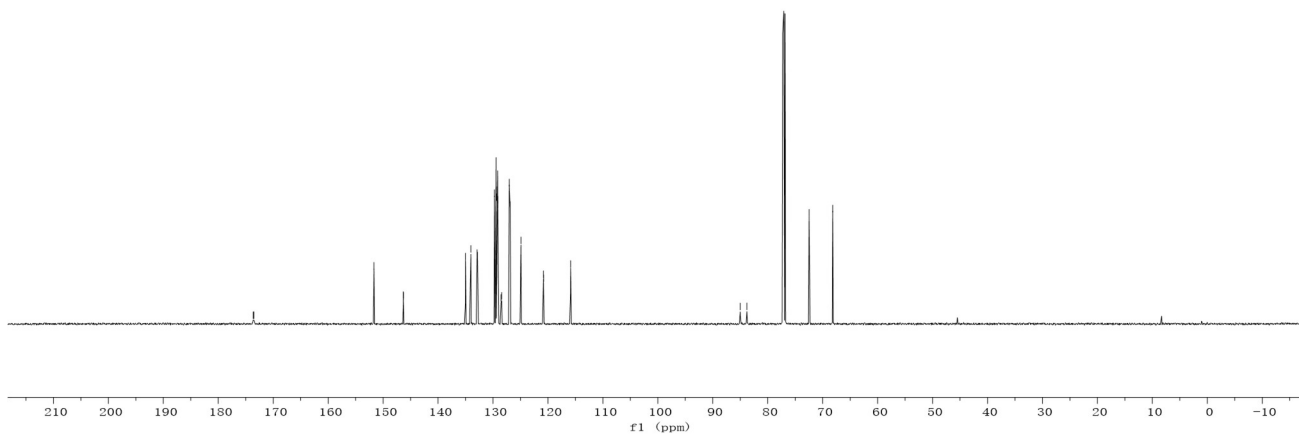
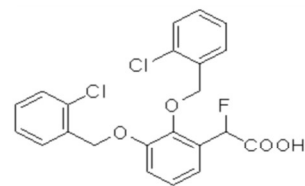
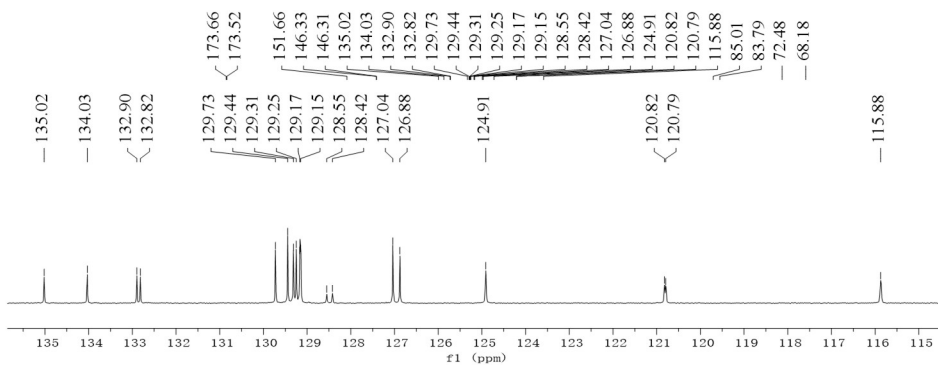
-166.72



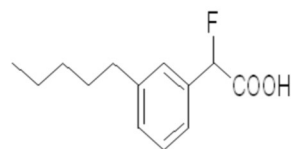
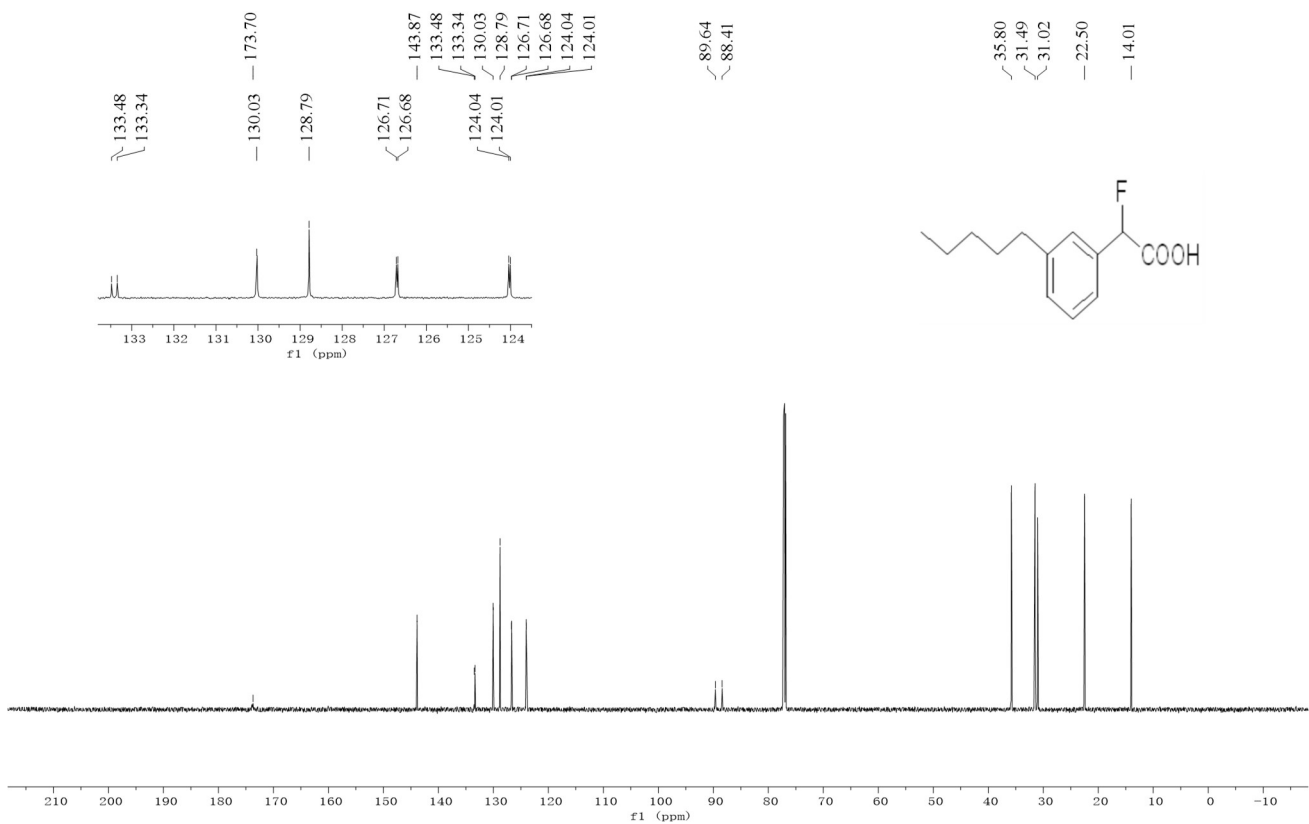
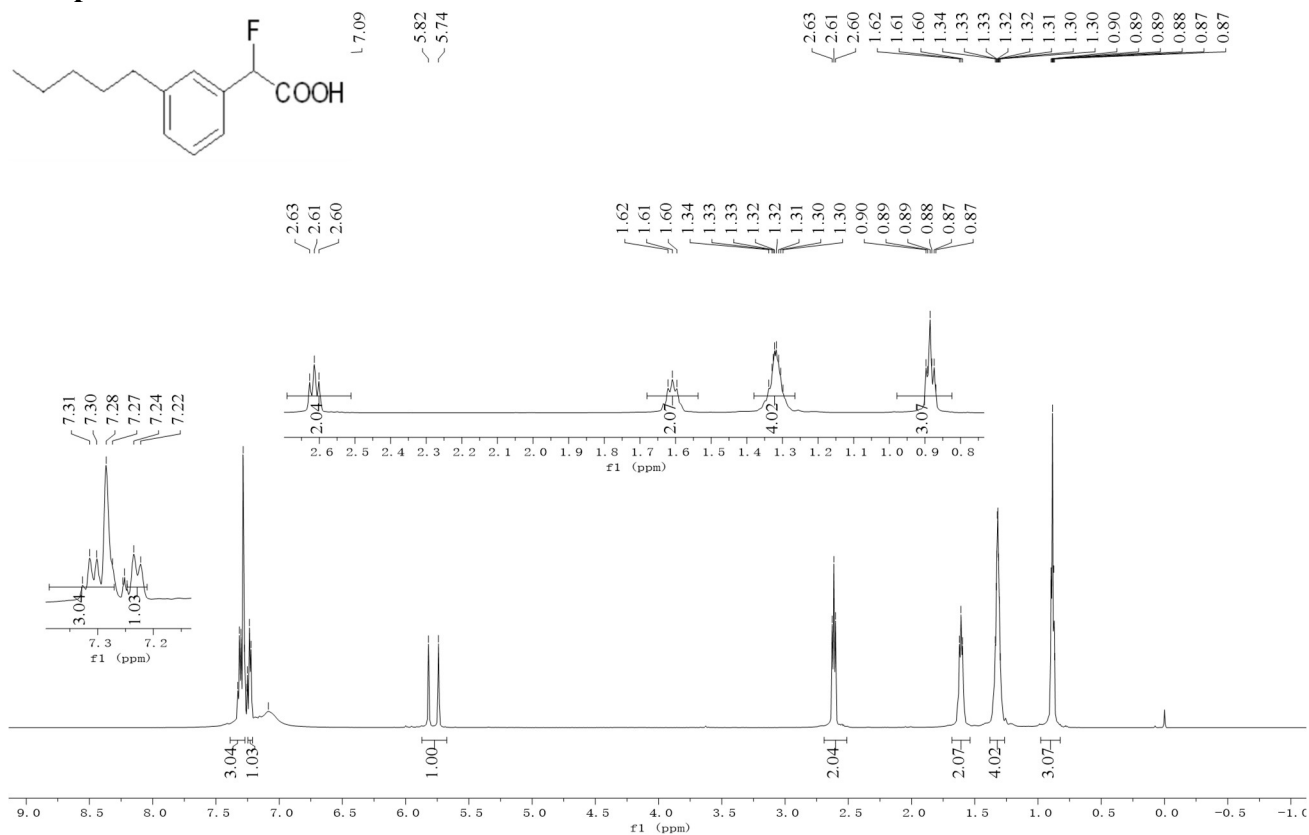
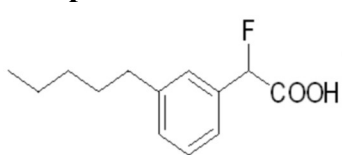
Compound 25b

7.49
7.48
7.48
7.47
7.47
7.39
7.38
7.37
7.37
7.30
7.29
7.25
7.24
7.24
7.23
7.23
7.18
7.18
7.18
7.17
7.15
7.15
7.14
7.14
7.13
7.12
7.12
7.11
7.11
7.10
7.10
7.05
7.04
7.03
7.01
7.01
6.99
6.98
6.13
6.05
5.21
5.19
5.19
5.17
5.17
5.12

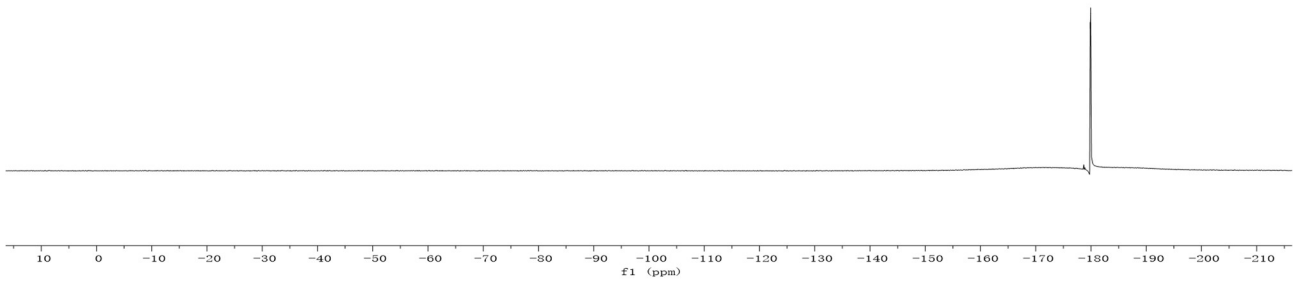
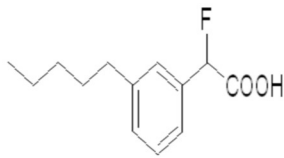




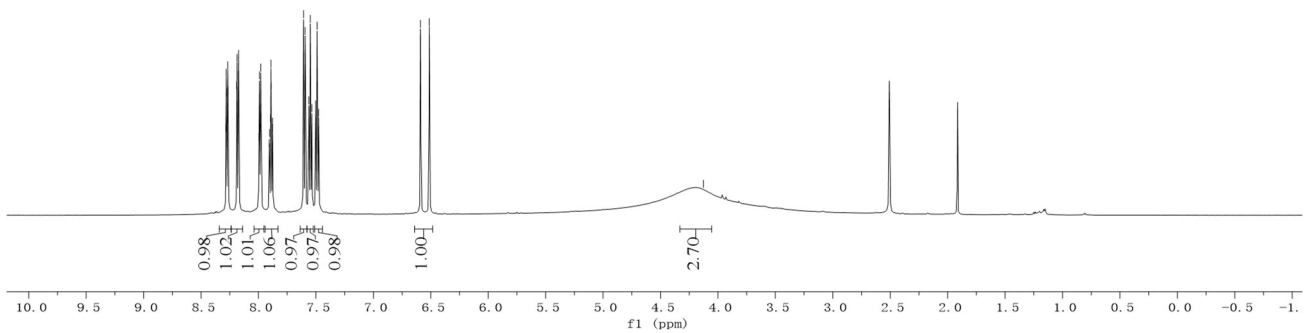
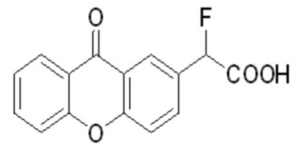
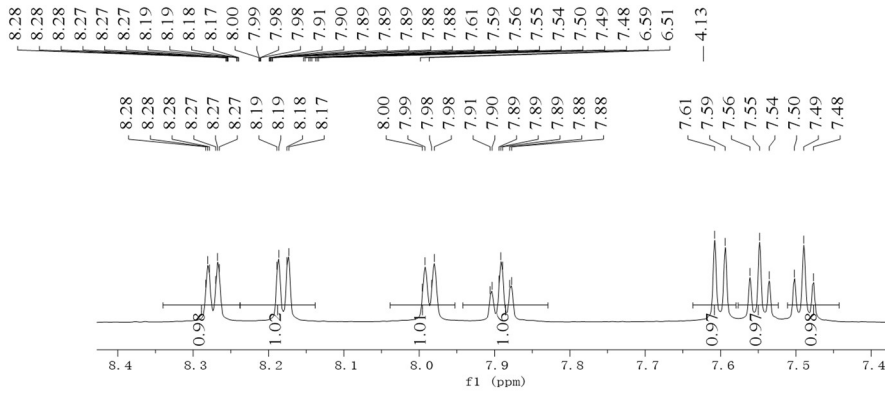
Compound 26b

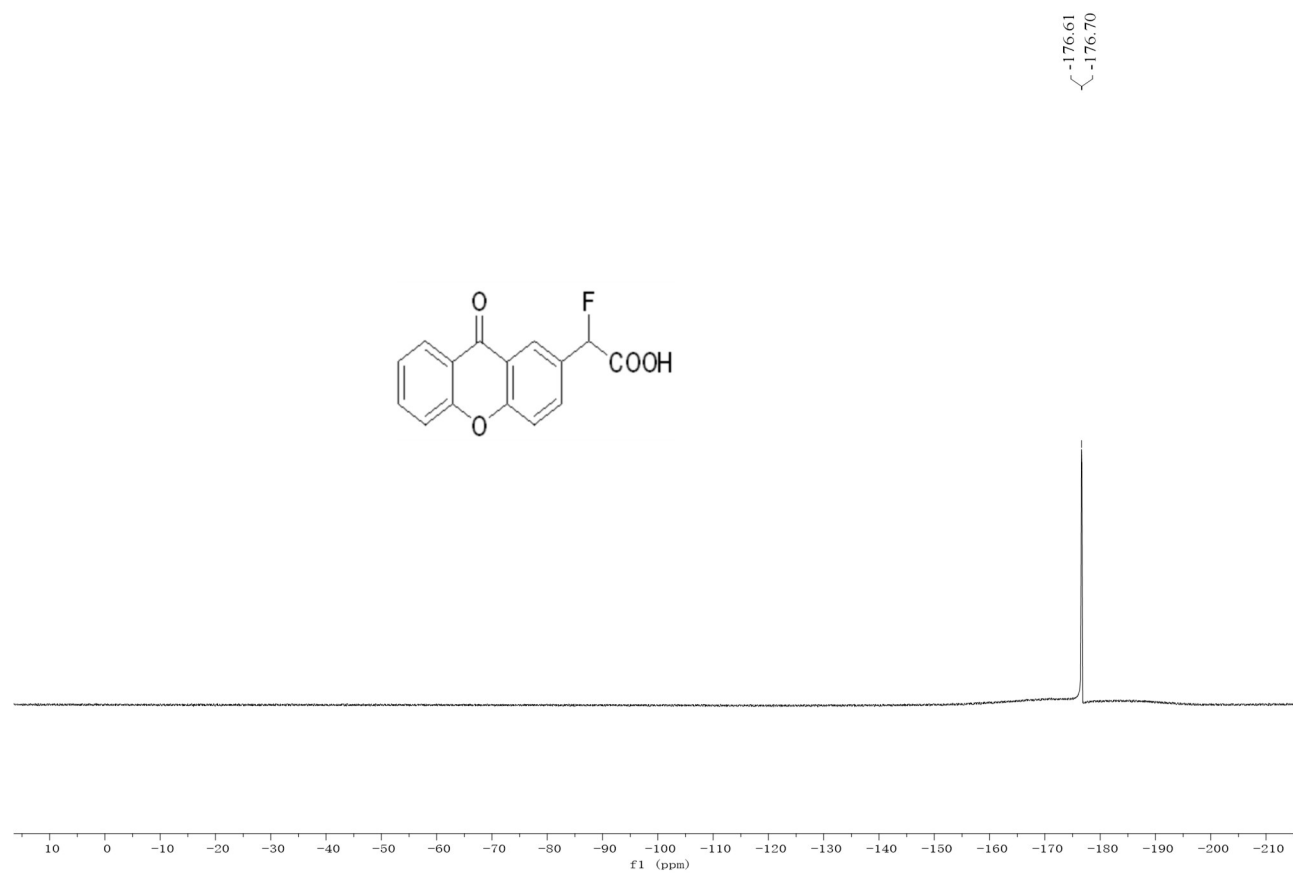
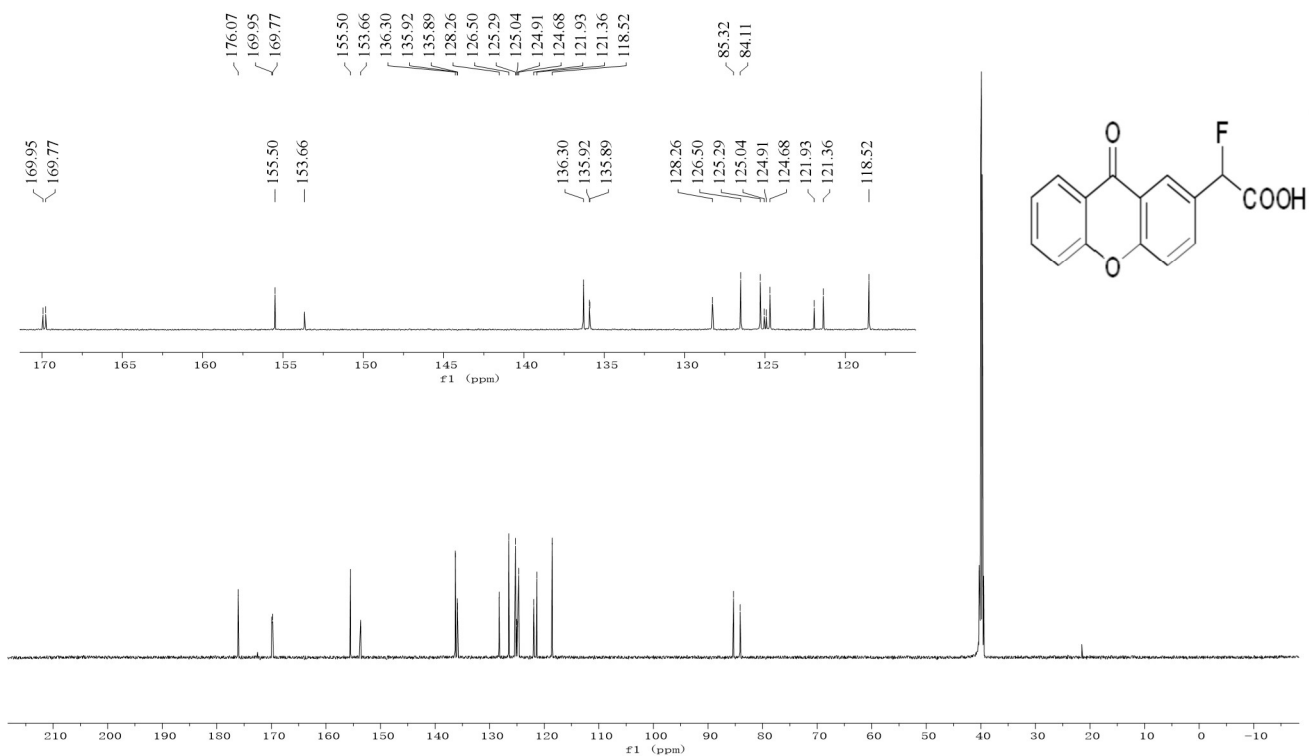


-179.86
-179.94



Compound 27b



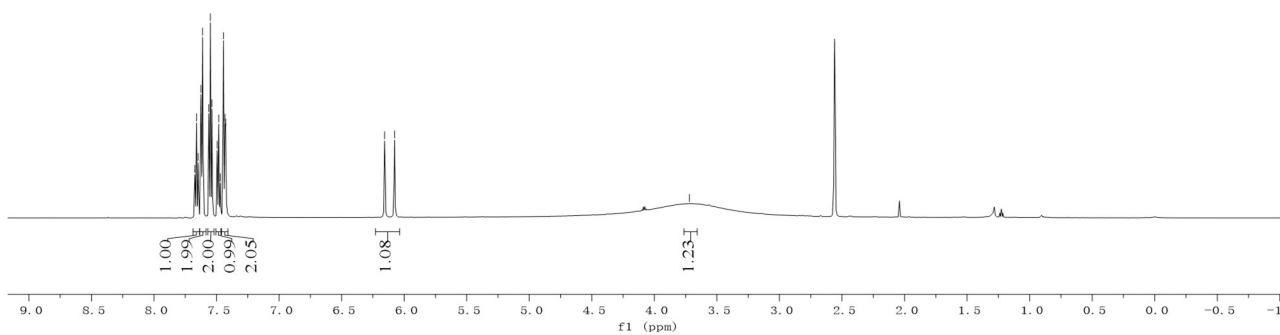
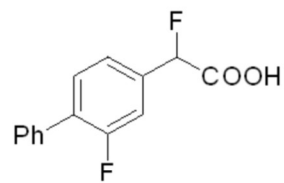
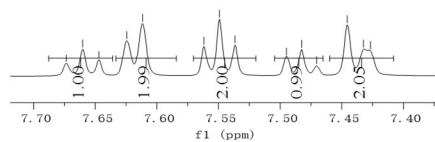


Compound 28b

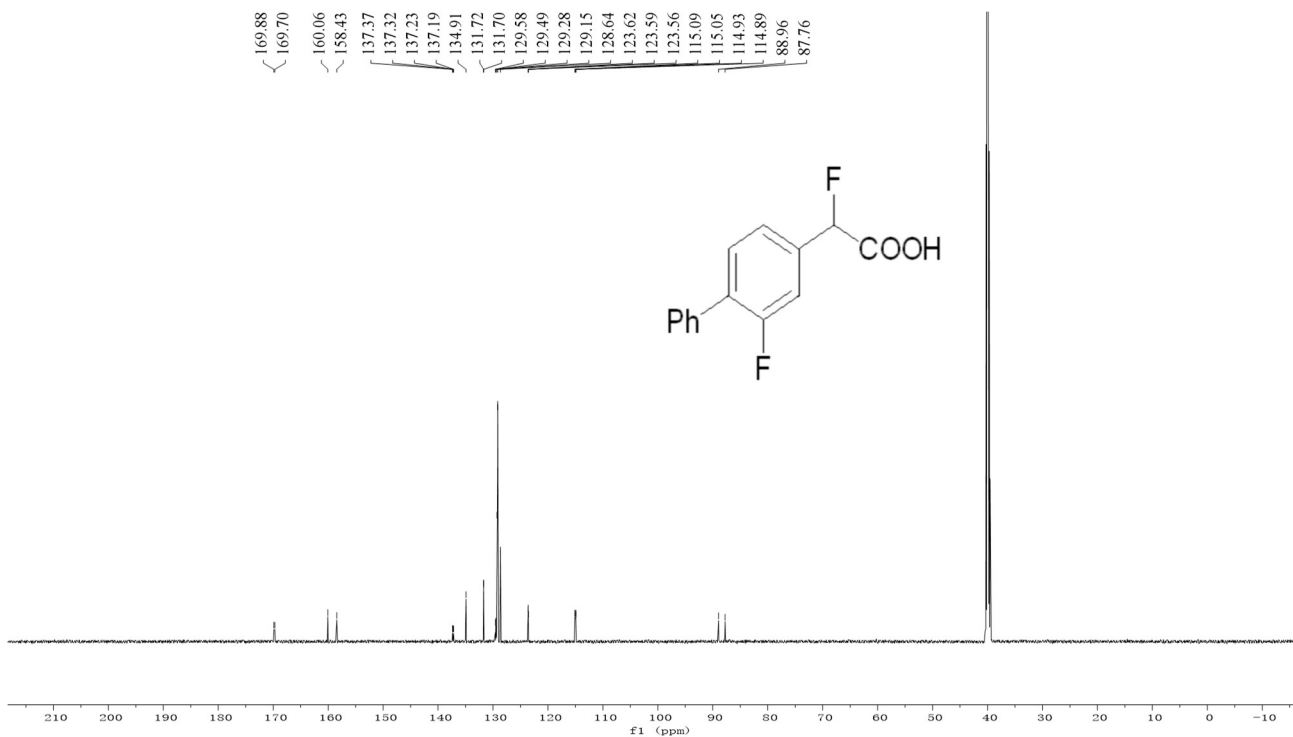
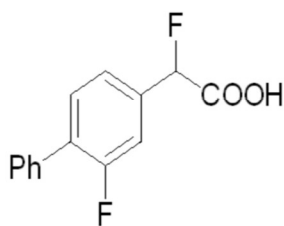
7.67
7.66
7.65
7.62
7.61
7.56
7.55
7.54
7.49
7.48
7.47
7.45
7.43
7.43
6.16
6.08

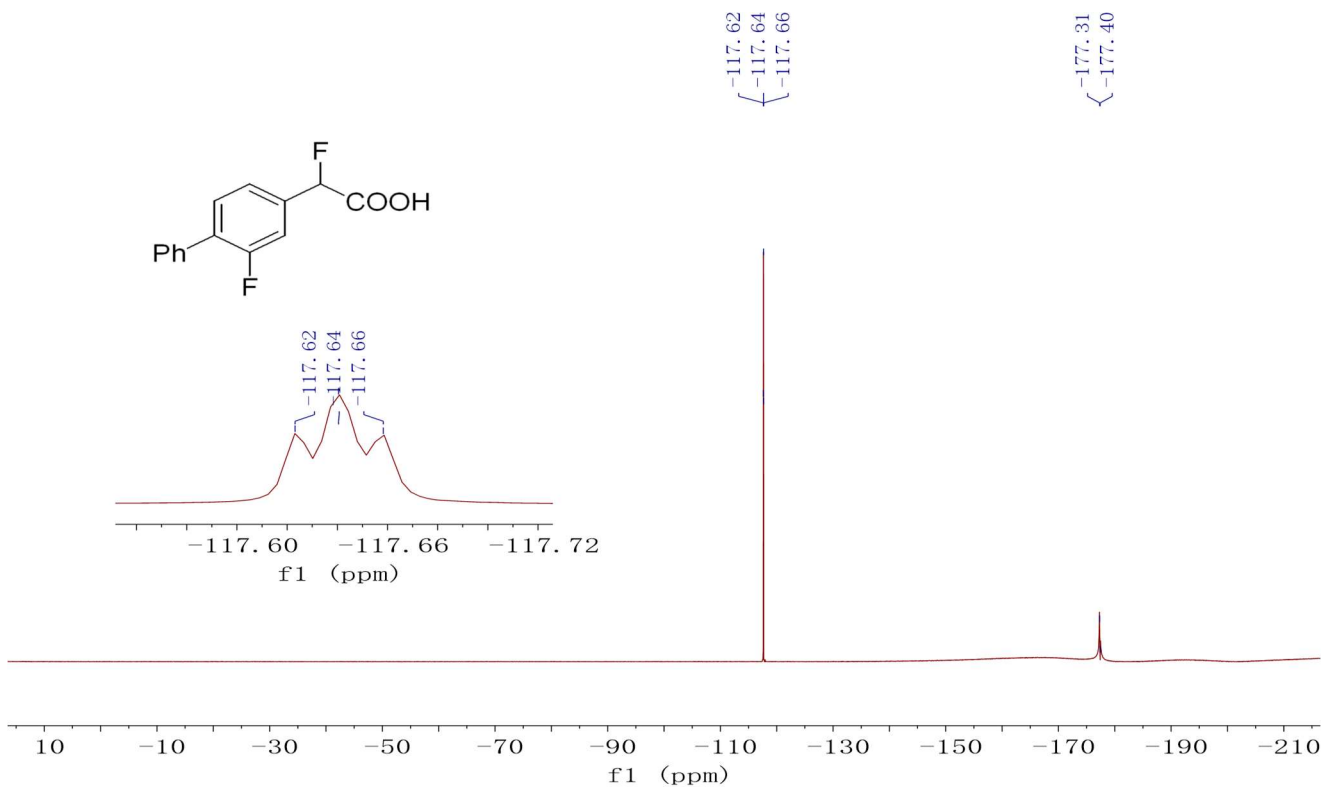
7.67
7.66
7.65
7.62
7.61
7.56
7.55
7.54
7.49
7.48
7.47
7.45
7.43
7.43

3.72



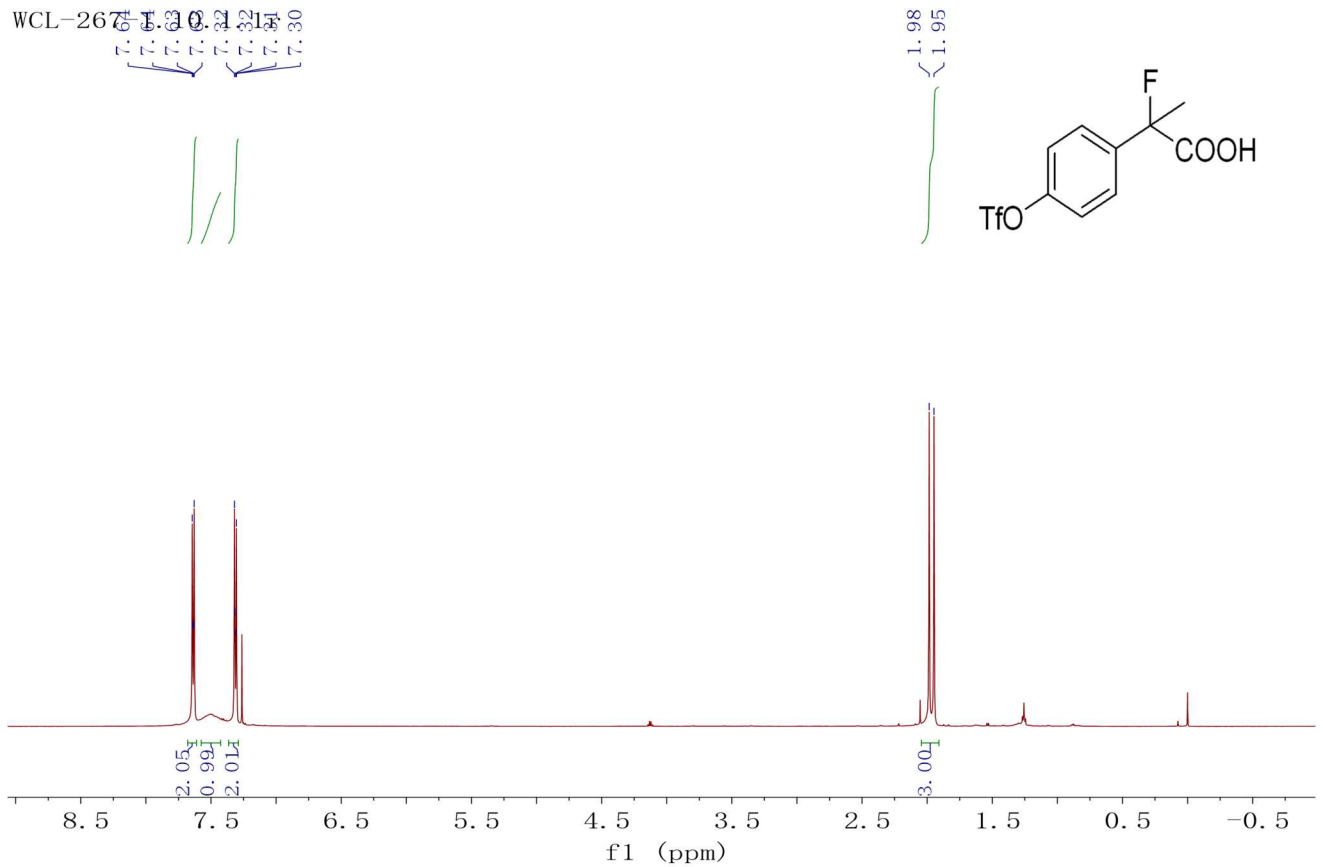
169.88
169.70
160.06
158.43
137.37
137.32
137.23
137.19
134.91
131.72
131.70
129.58
129.49
129.28
129.15
128.64
123.62
123.59
123.56
115.09
115.05
114.93
114.89
88.96
87.76

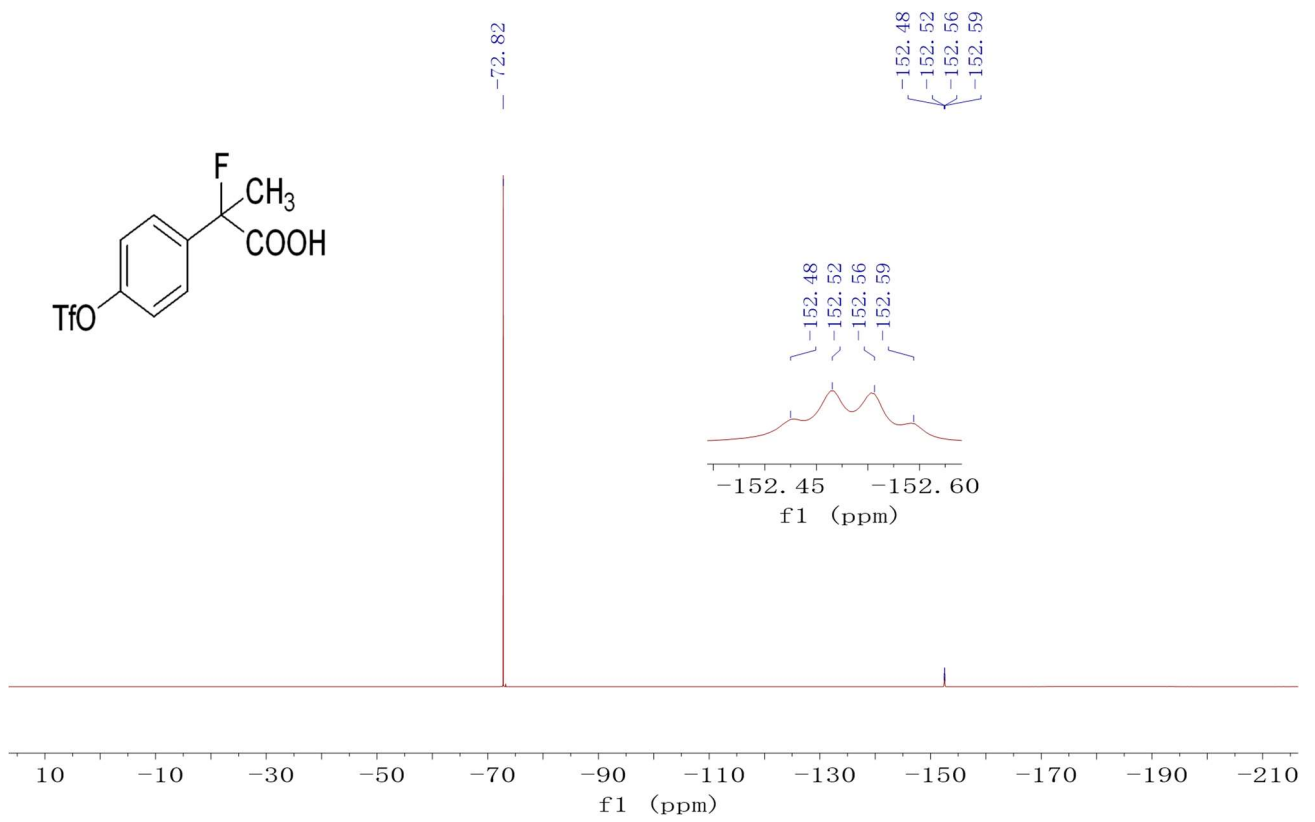
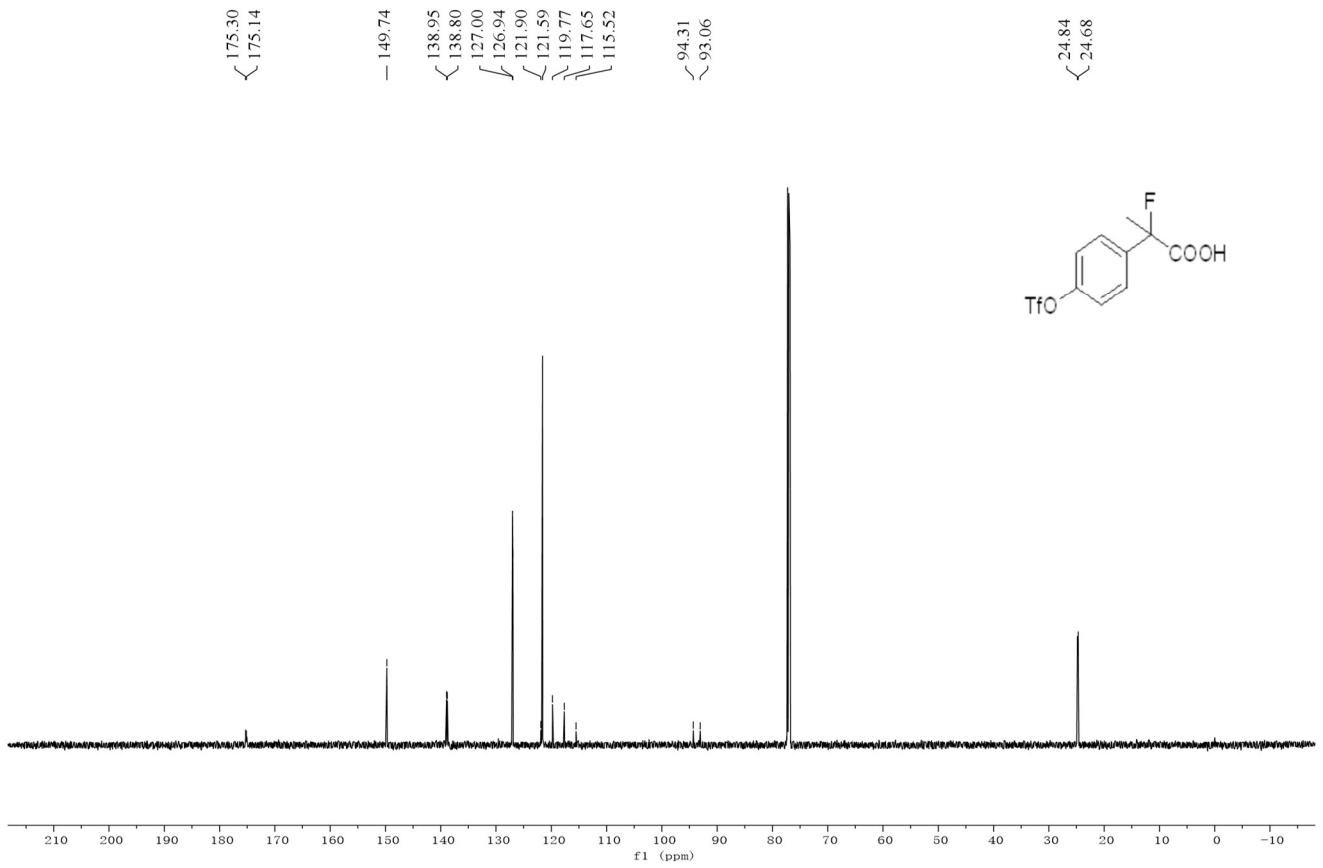




Compound 29b

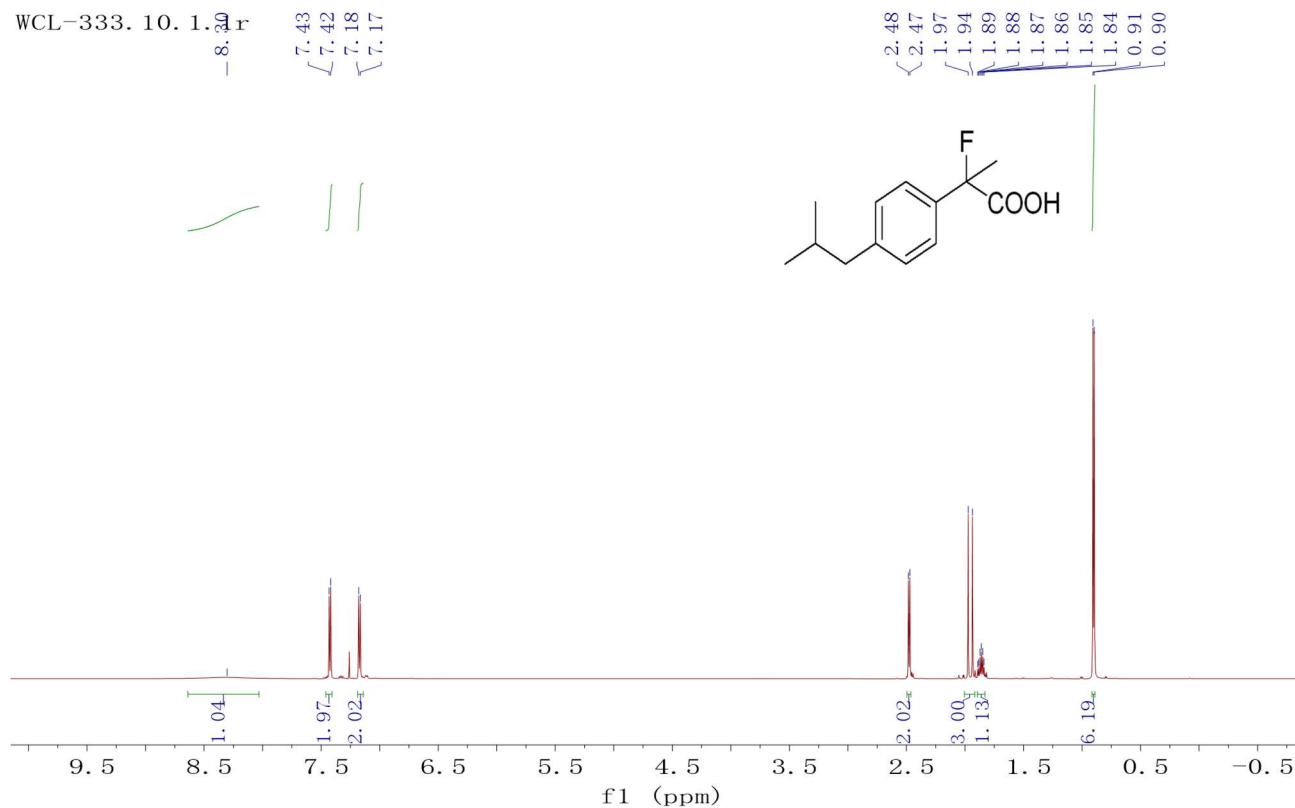
WCL-2674



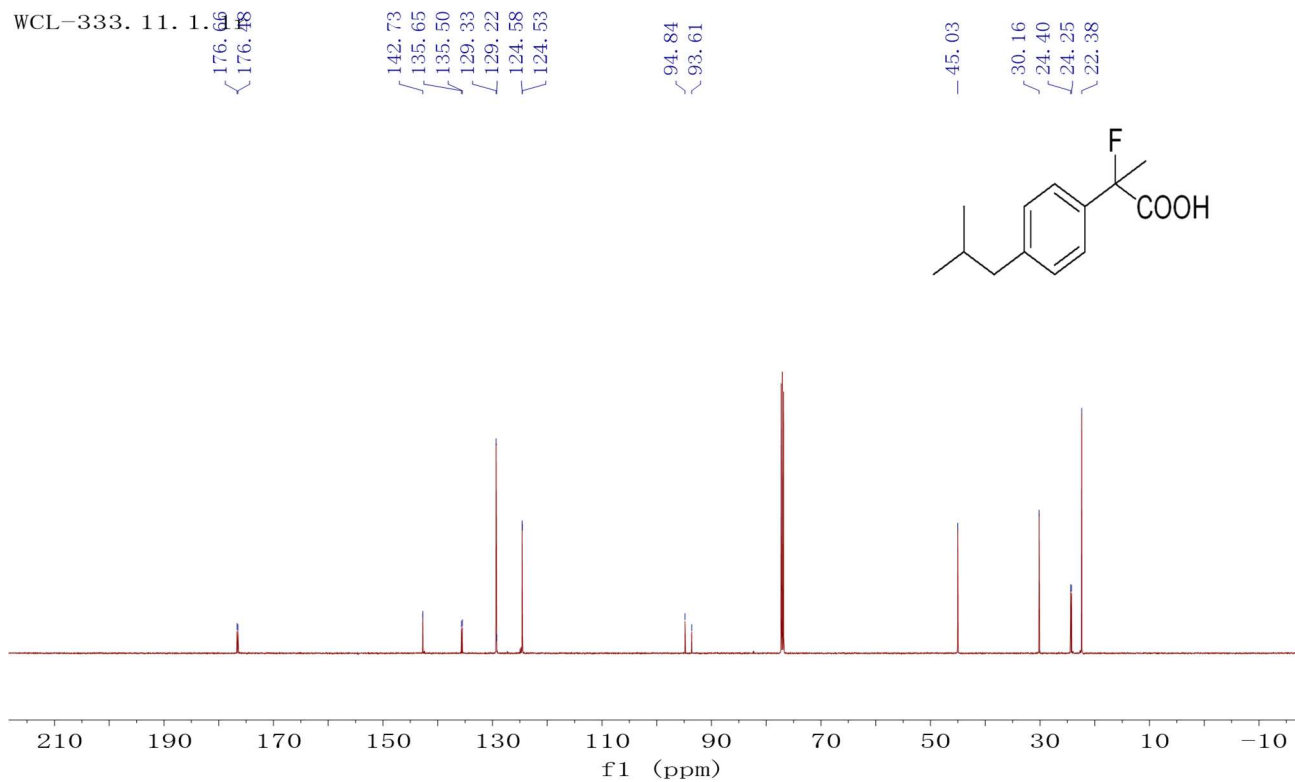


Compound 30b

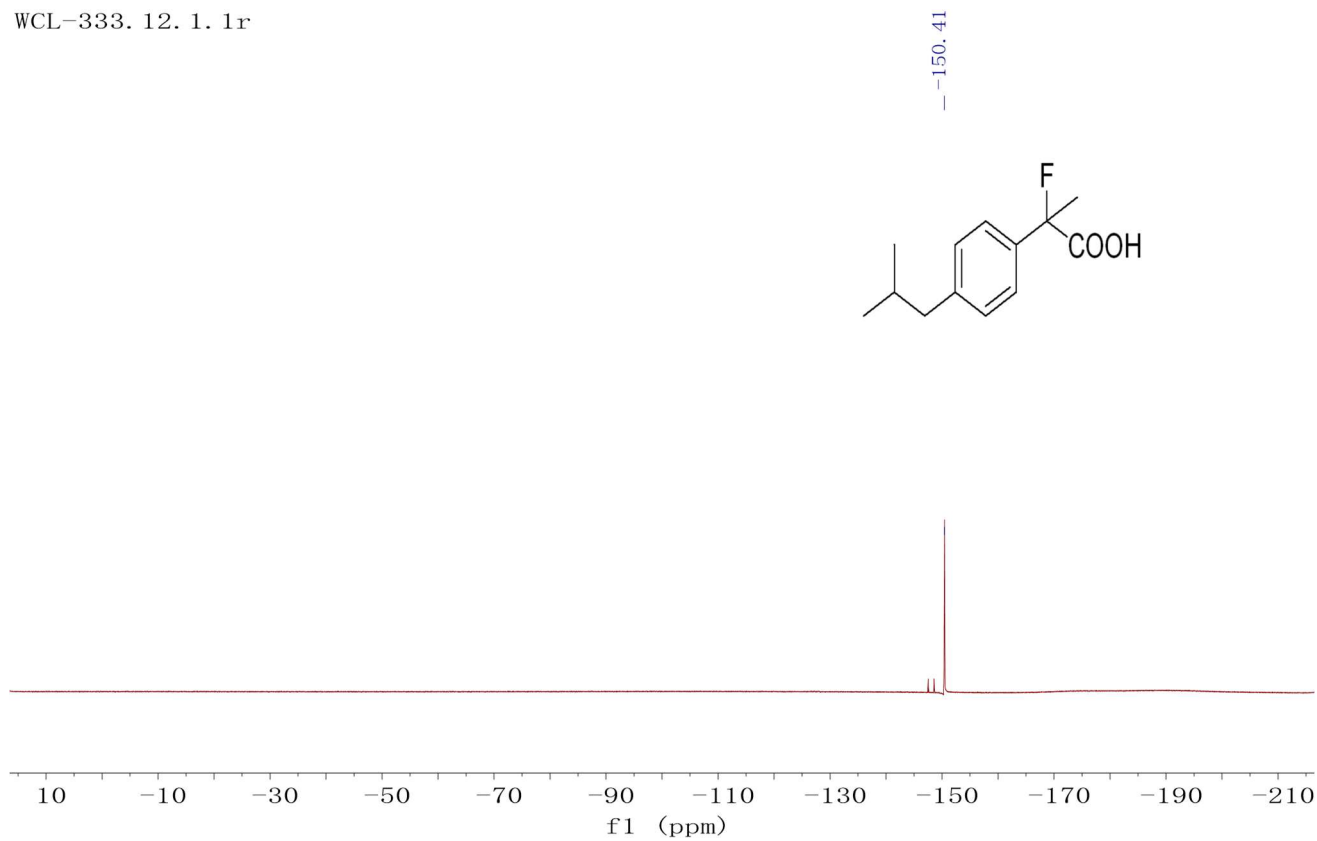
WCL-333. 10. 1. 30



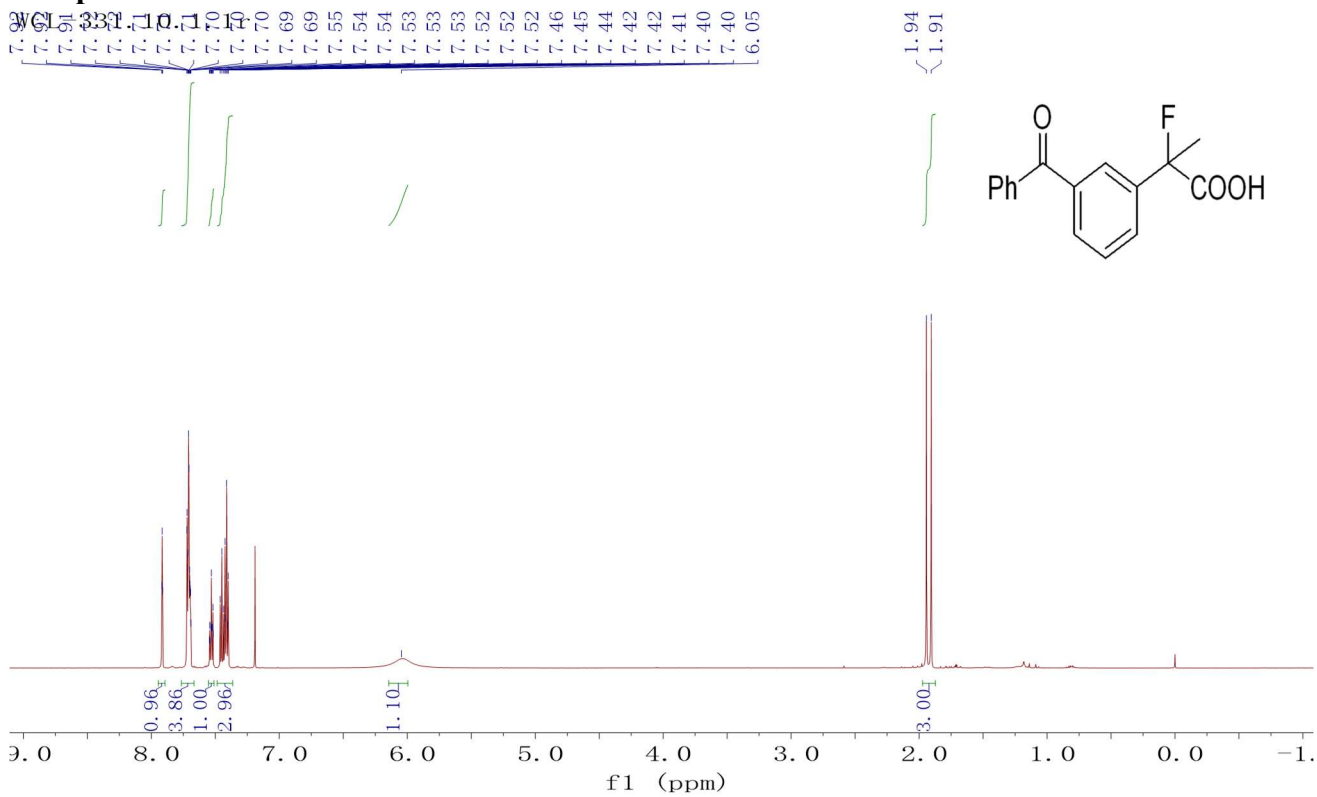
WCL-333. 11. 1. 48

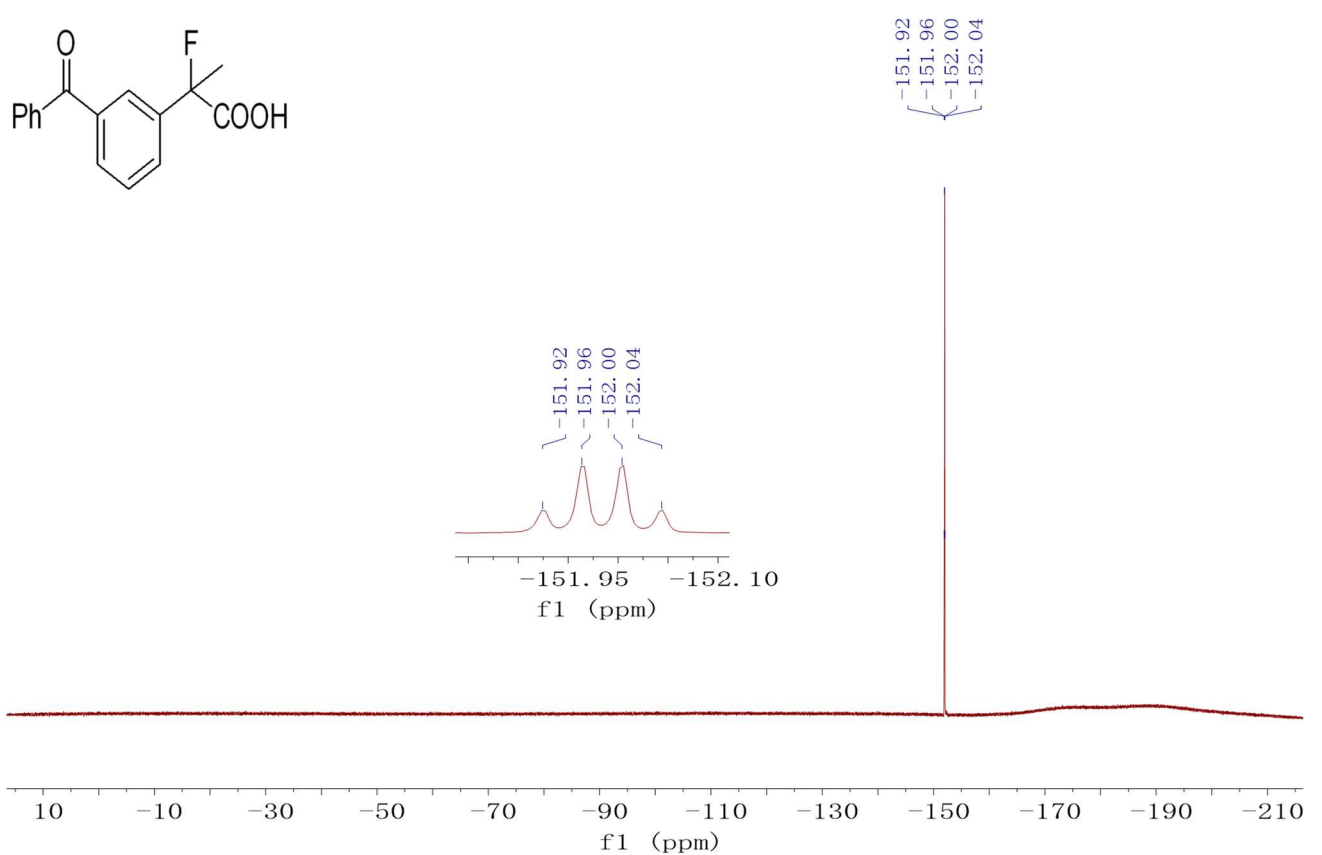
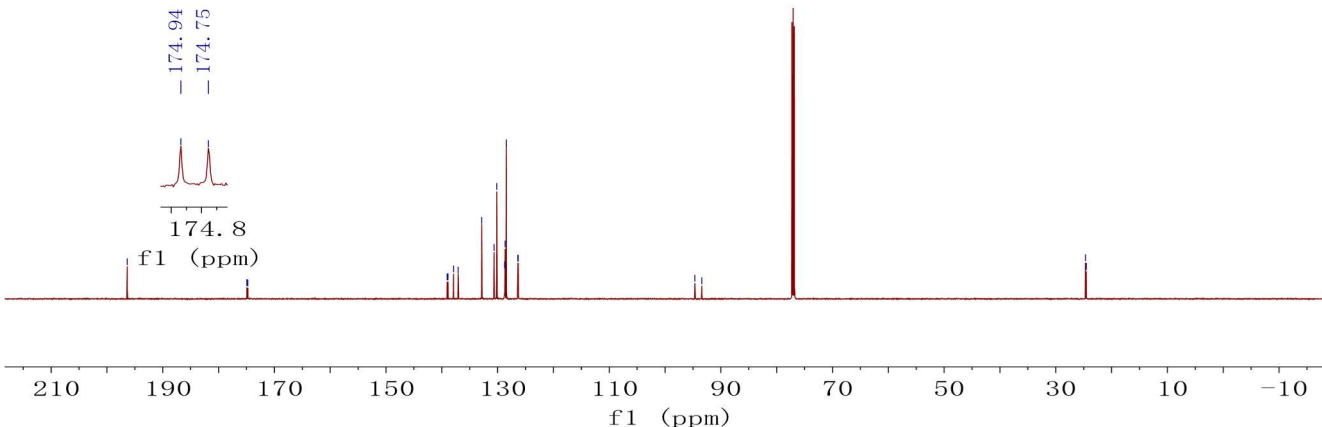
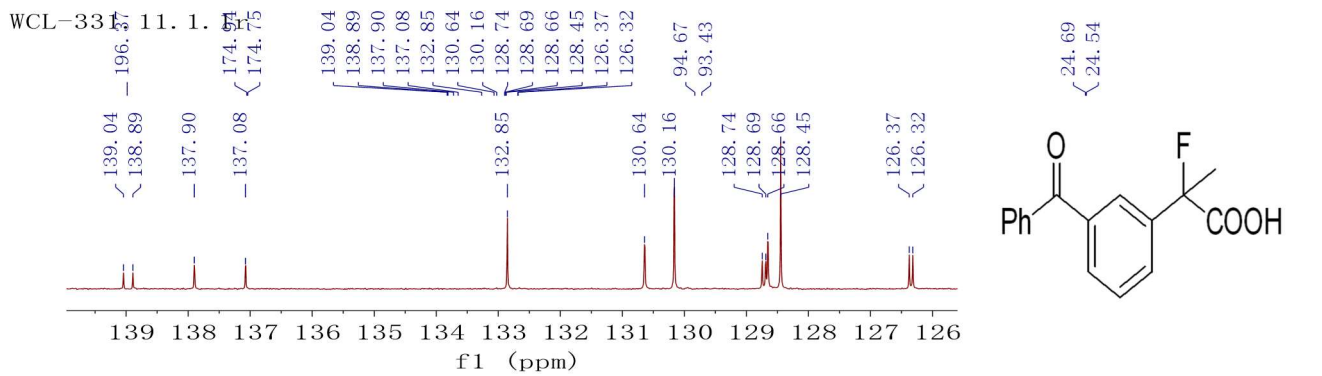


WCL-333. 12. 1. 1r

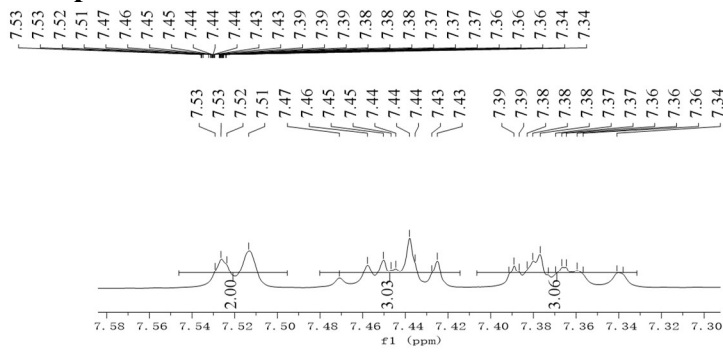


Compound 31b

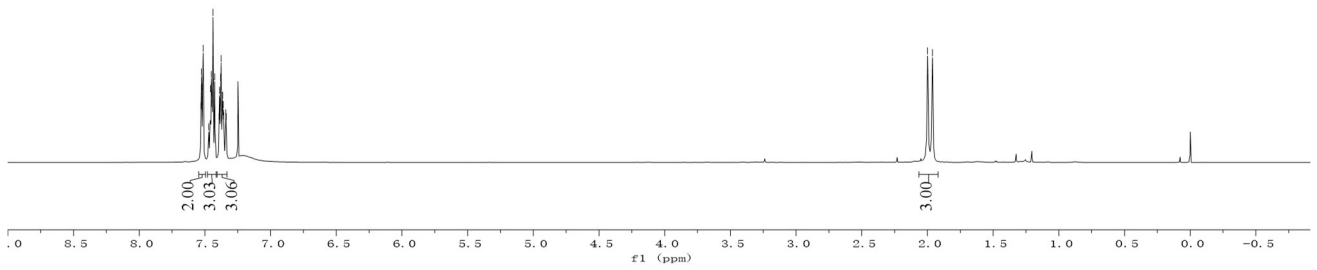
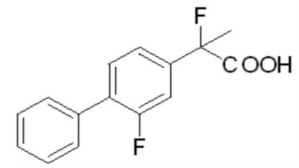




Compound 32b

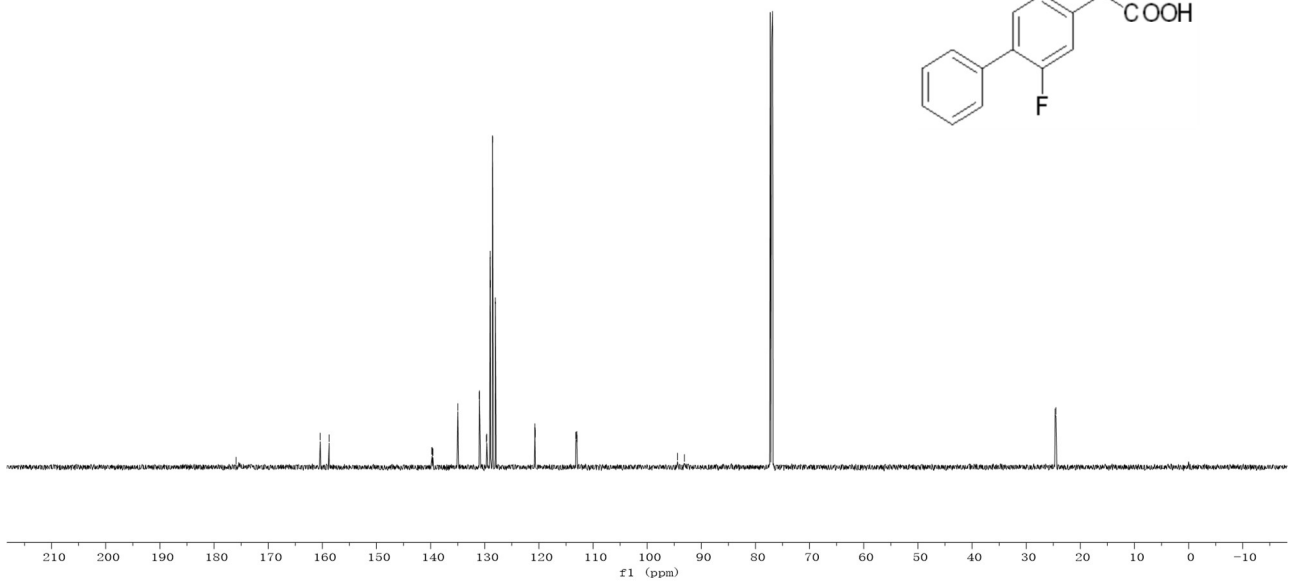
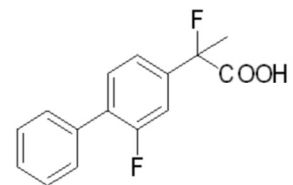


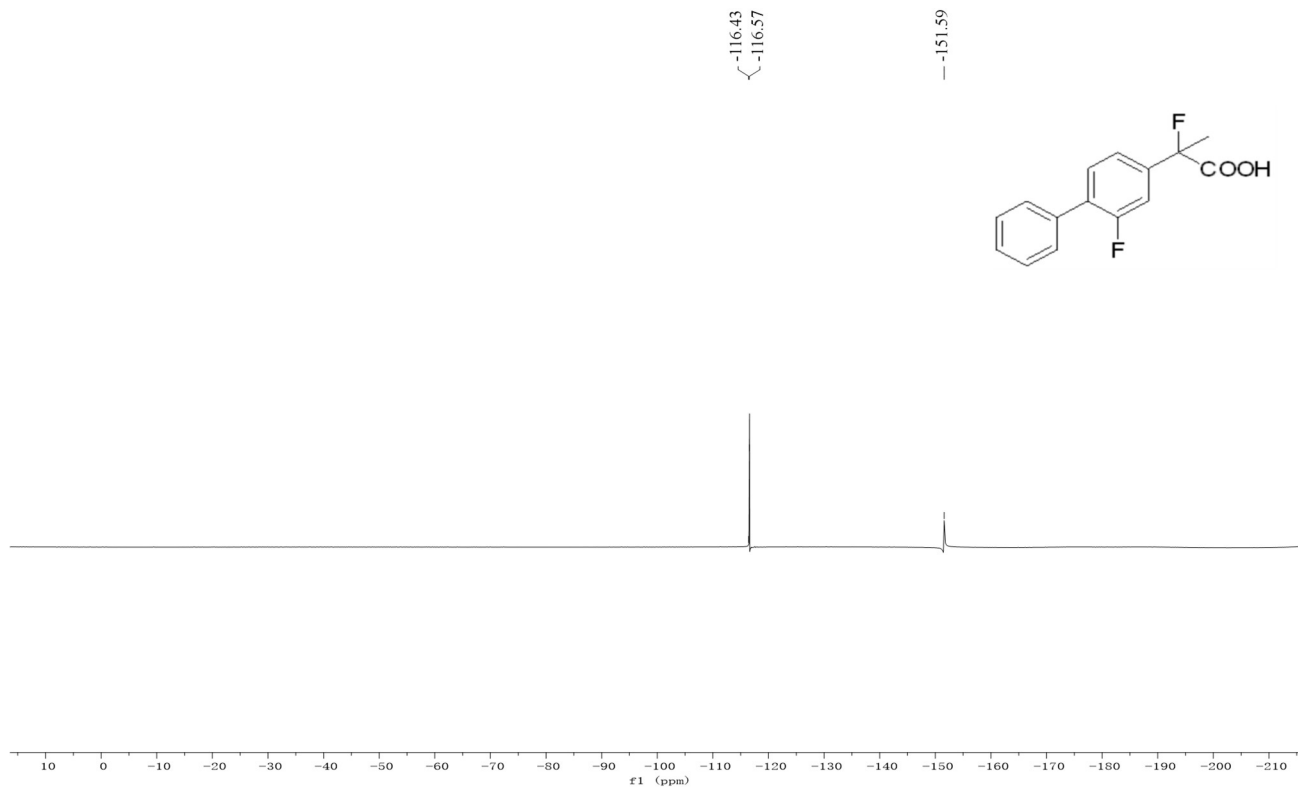
2.00
1.96



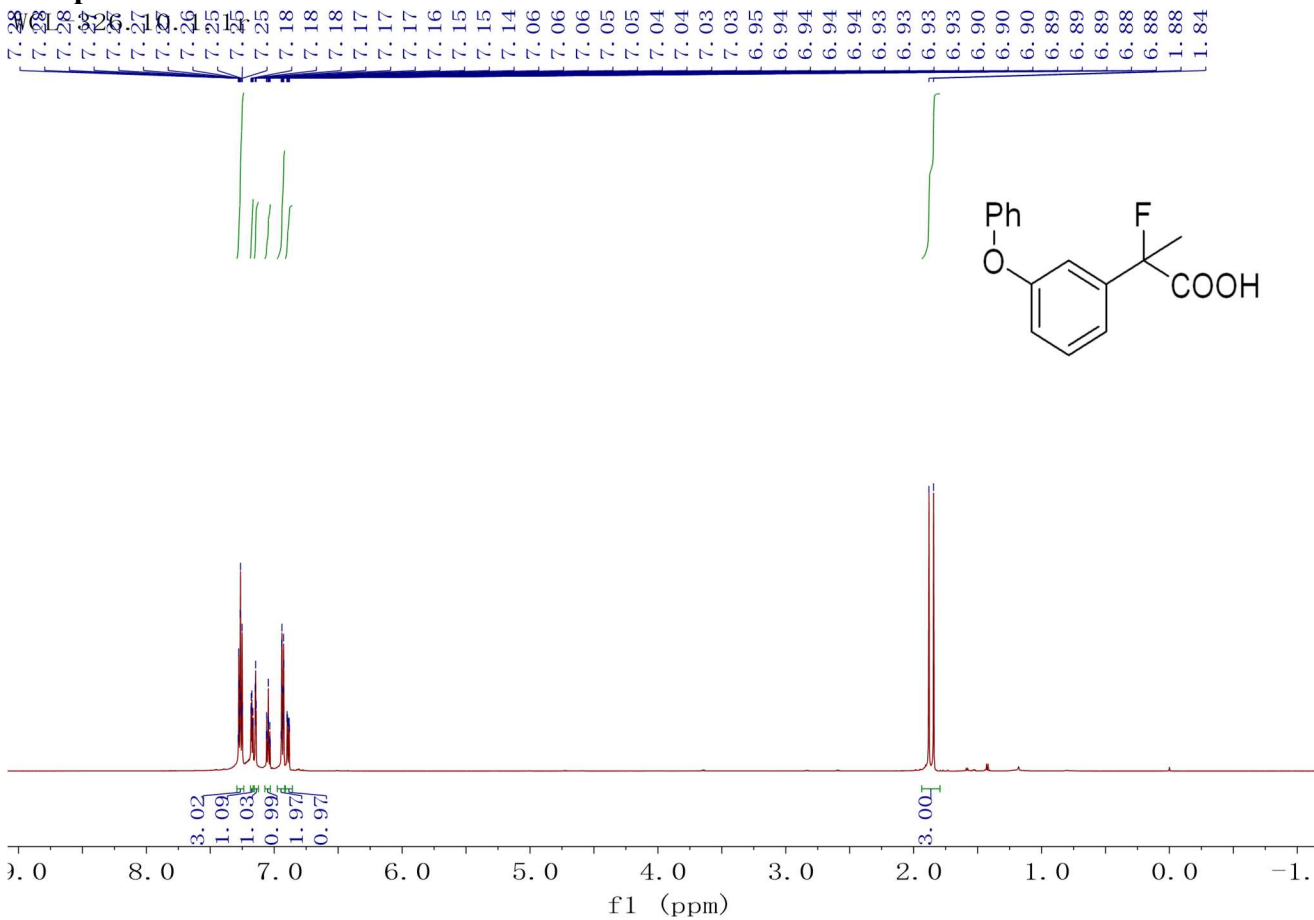
175.94, 160.40, 158.75, 139.78, 139.73, 139.62, 139.57, 134.98, 131.00, 130.98, 129.71, 129.62, 129.99, 128.97, 128.55, 128.04, 120.76, 120.74, 120.71, 120.68, 113.17, 113.12, 113.01, 112.94, 94.38, 93.13.

24.66
24.51

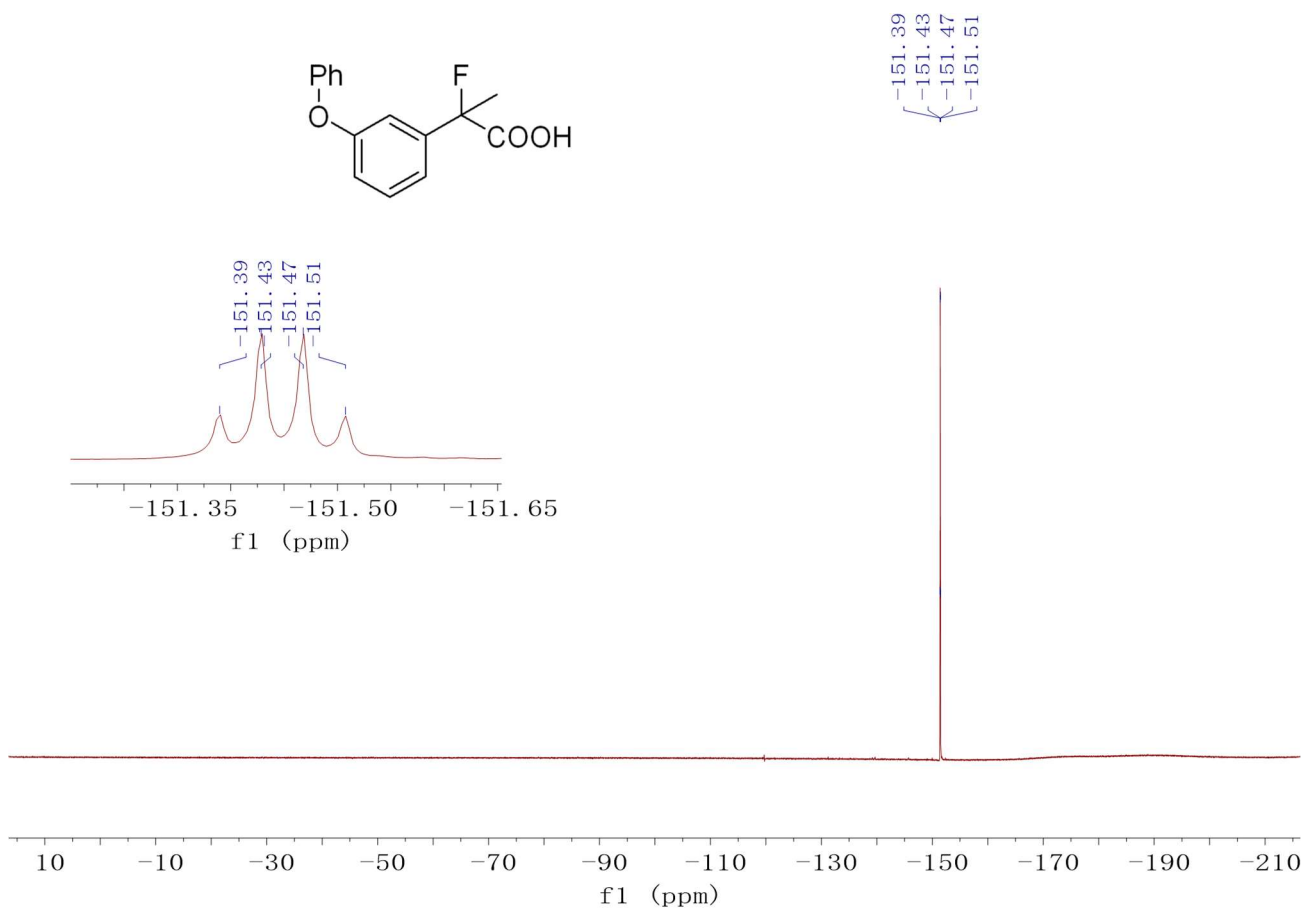
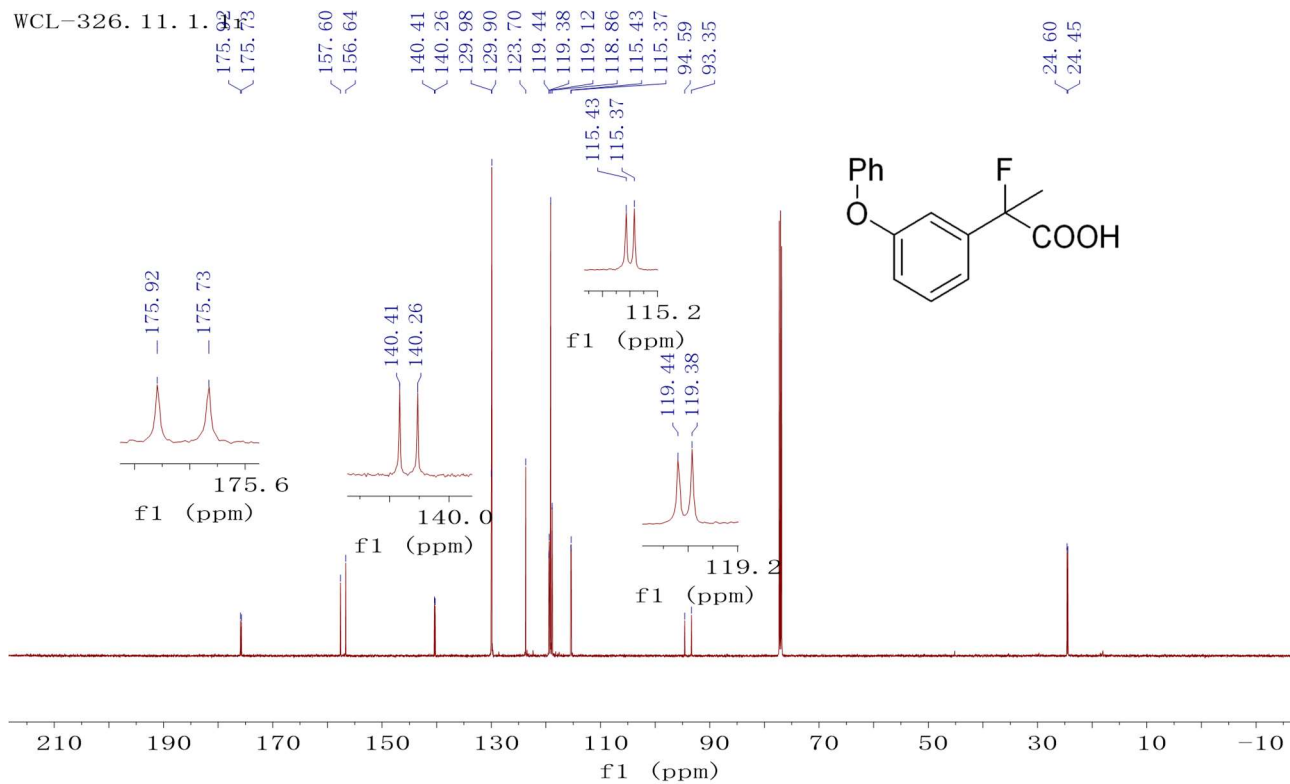




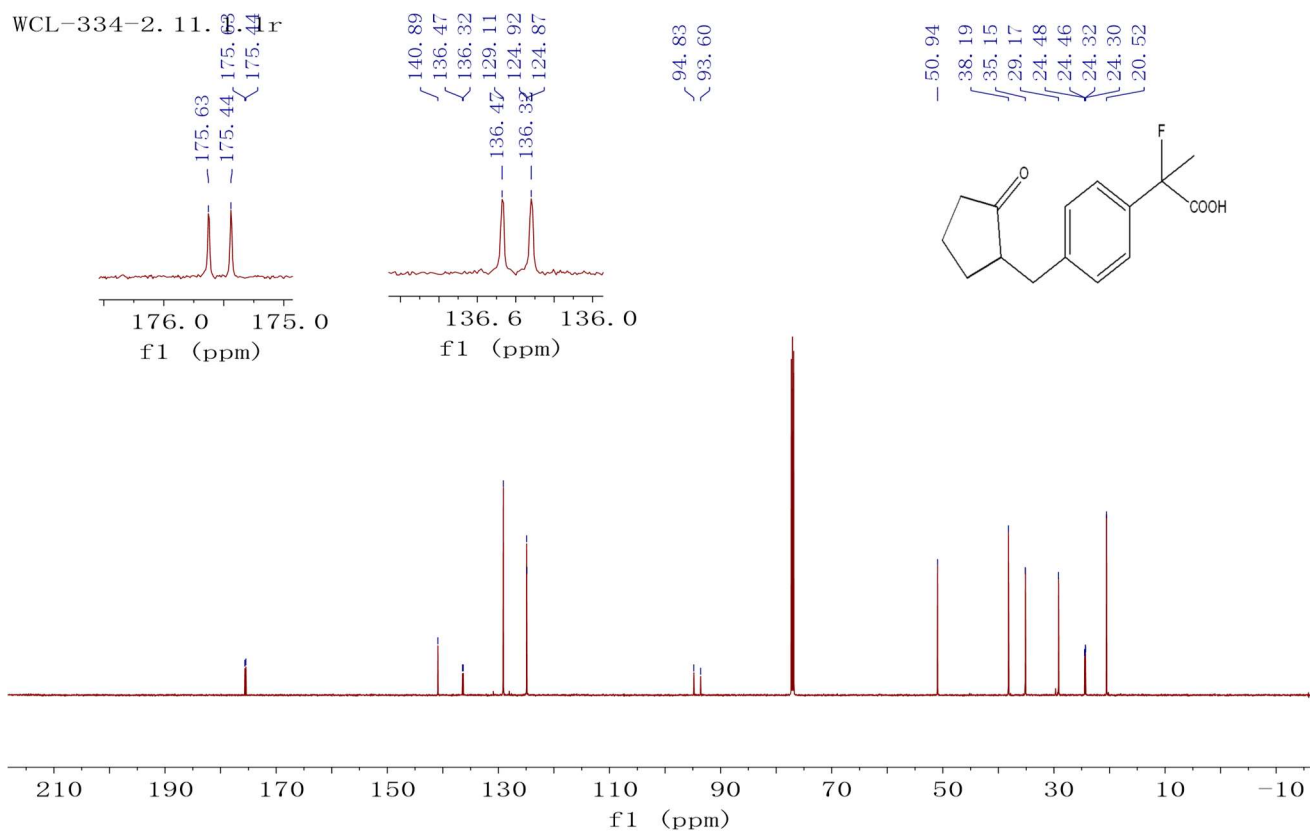
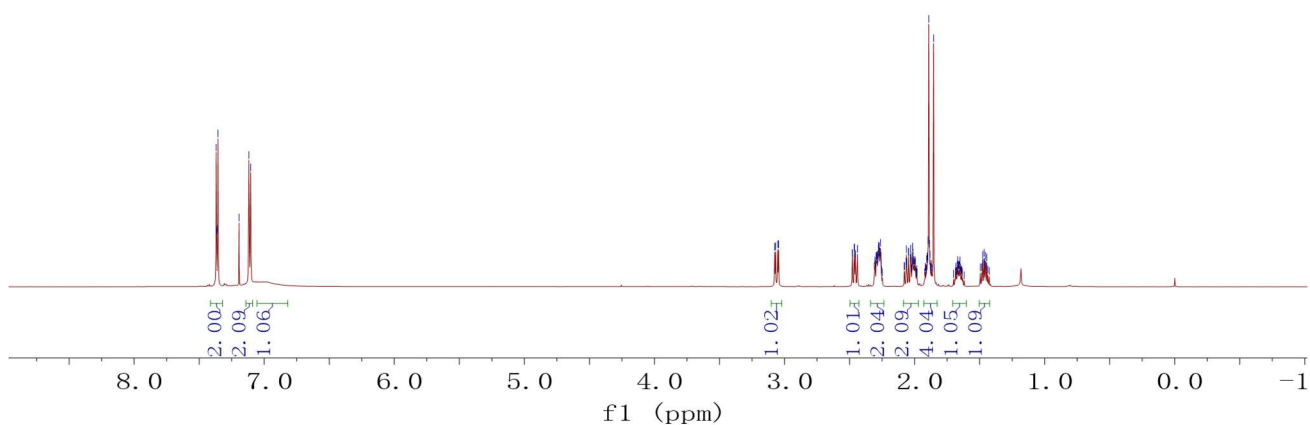
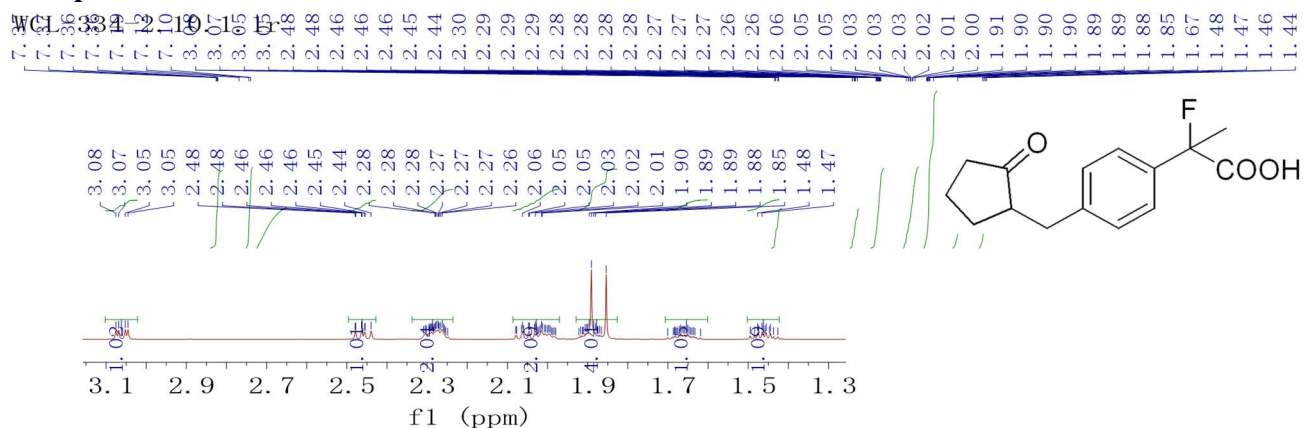
Compound 33b

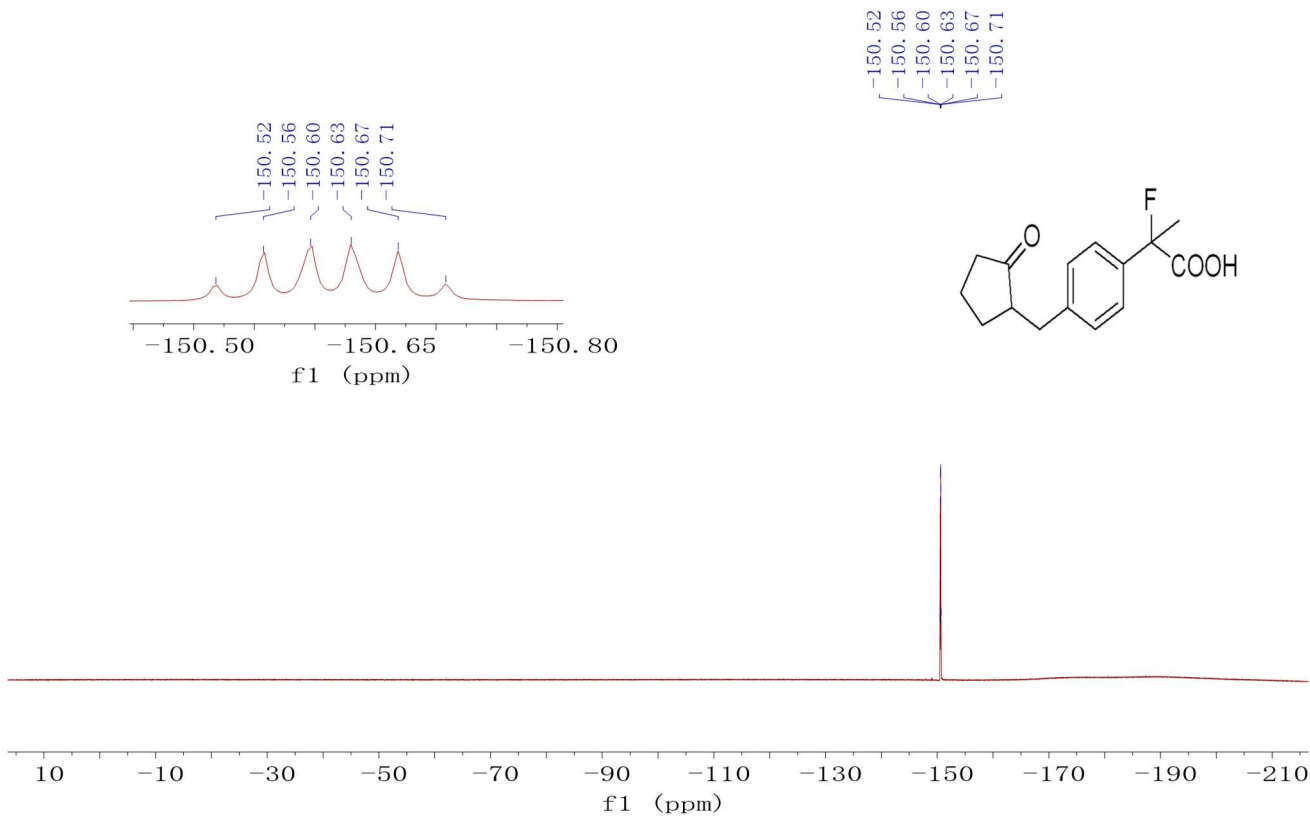


WCL-326. 11. 1. 1.

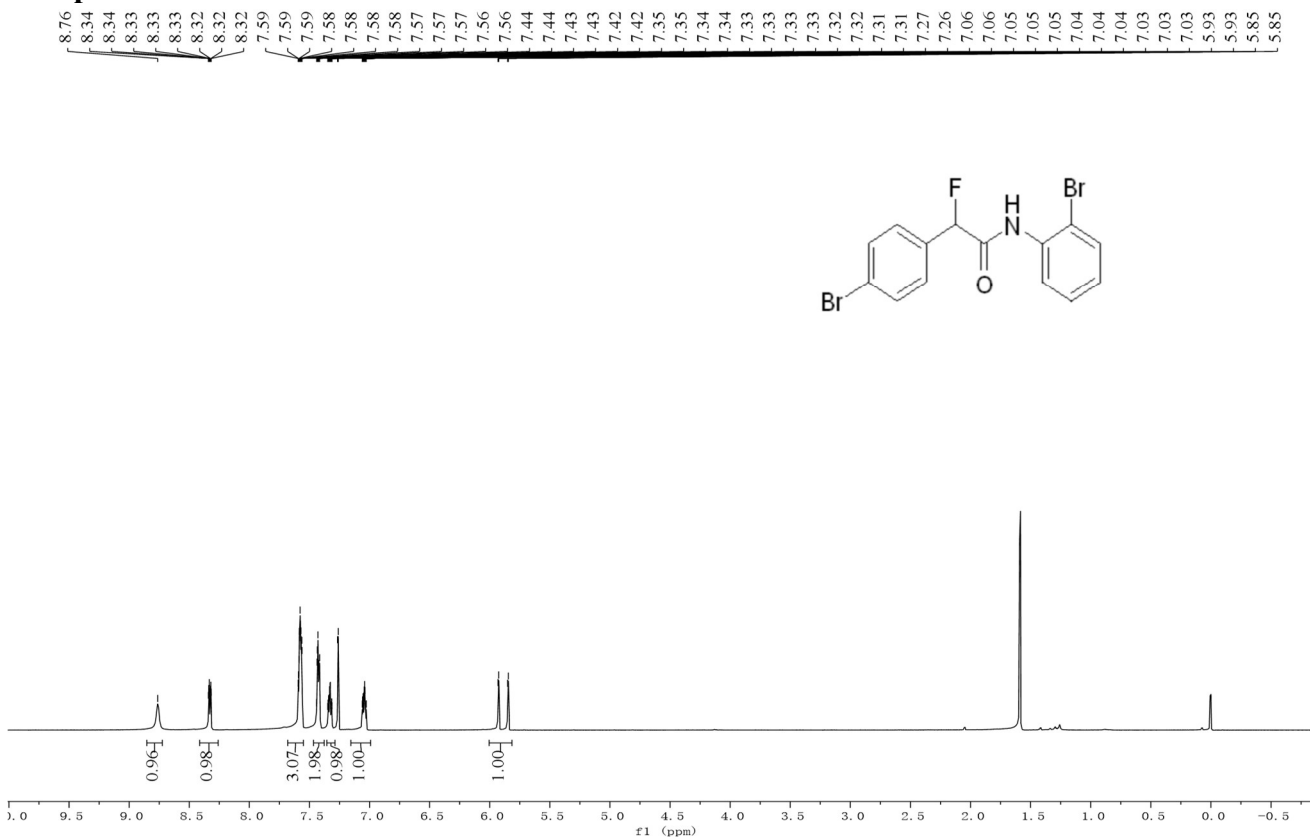


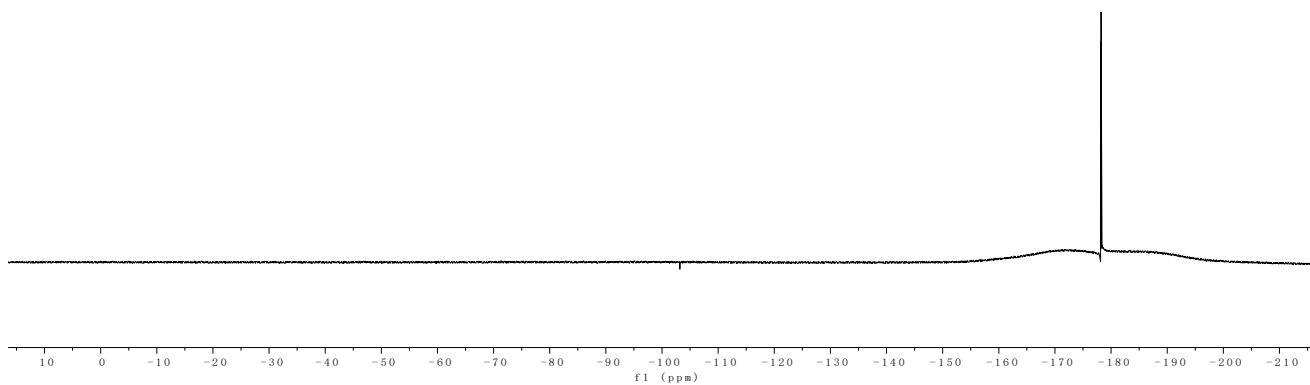
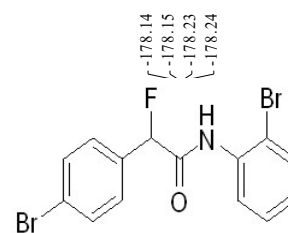
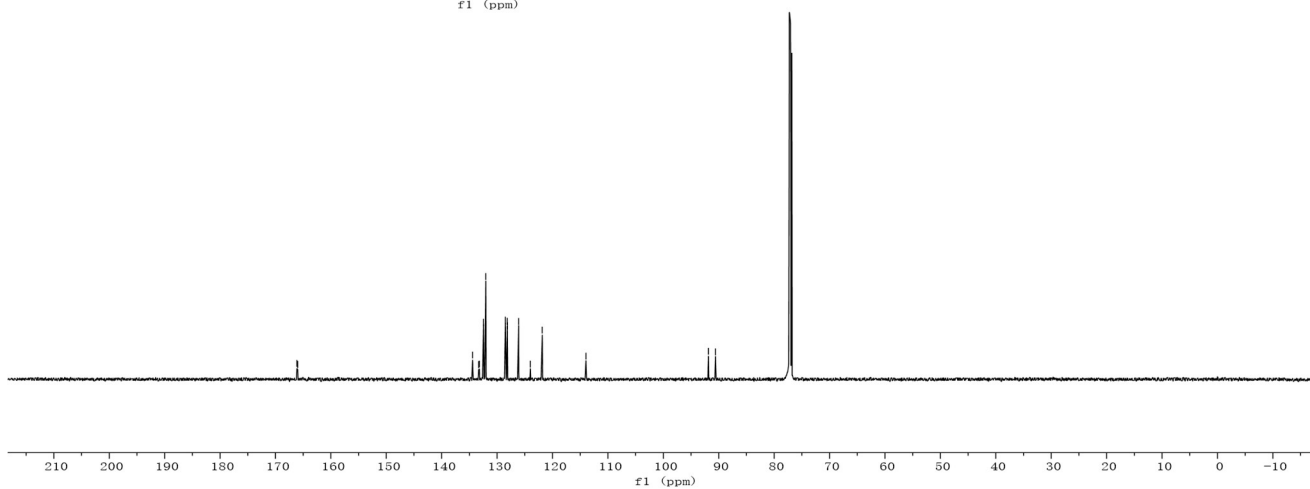
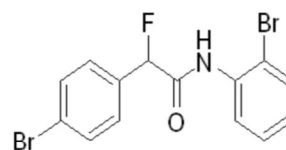
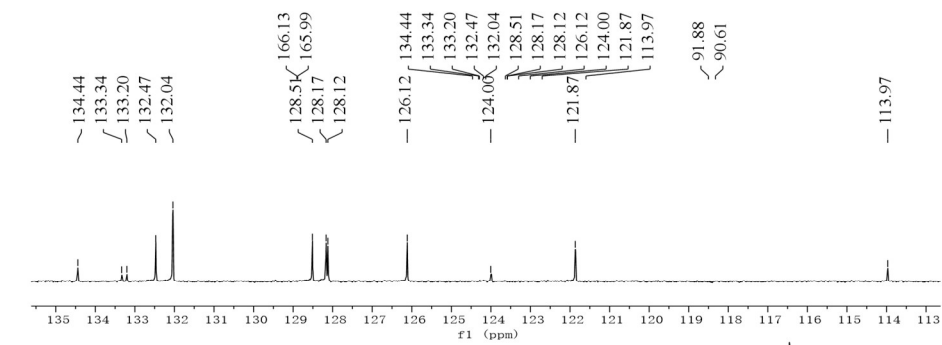
Compound 34b





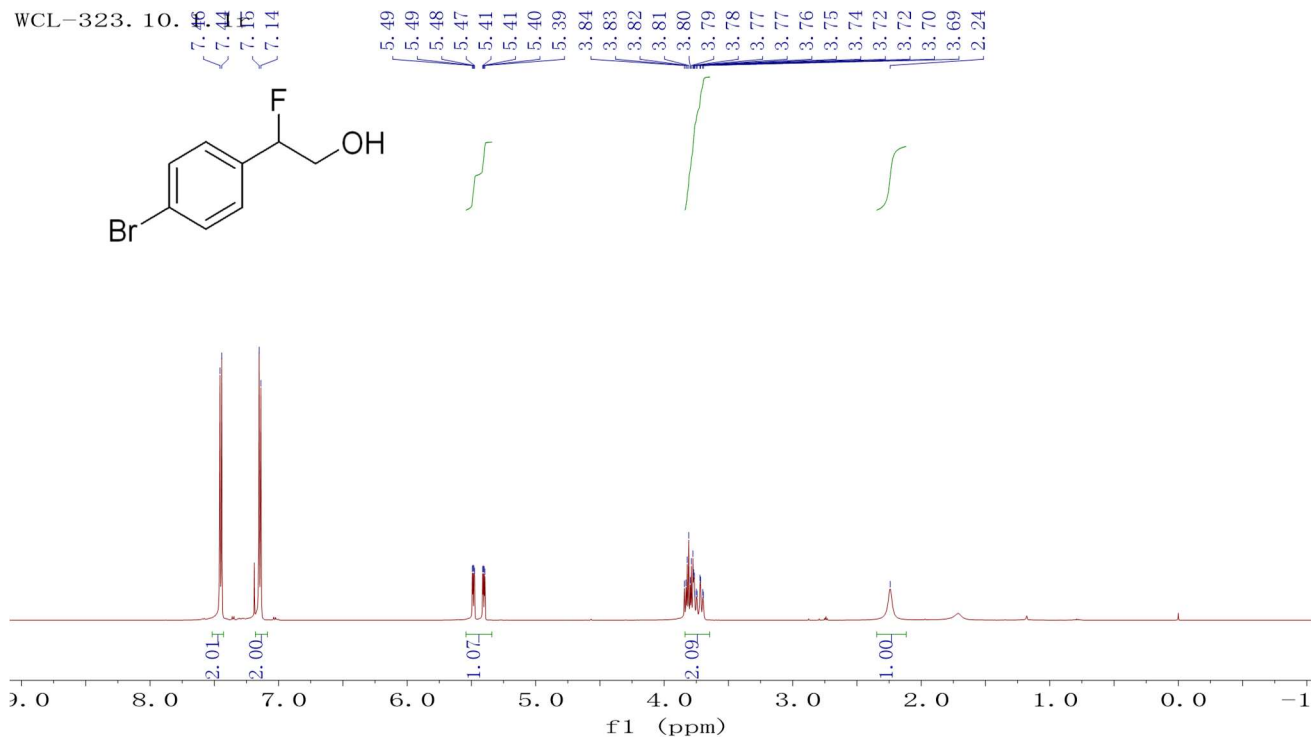
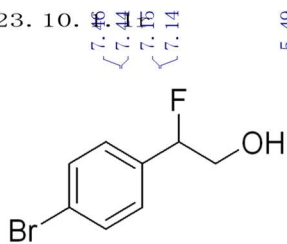
Compound 35



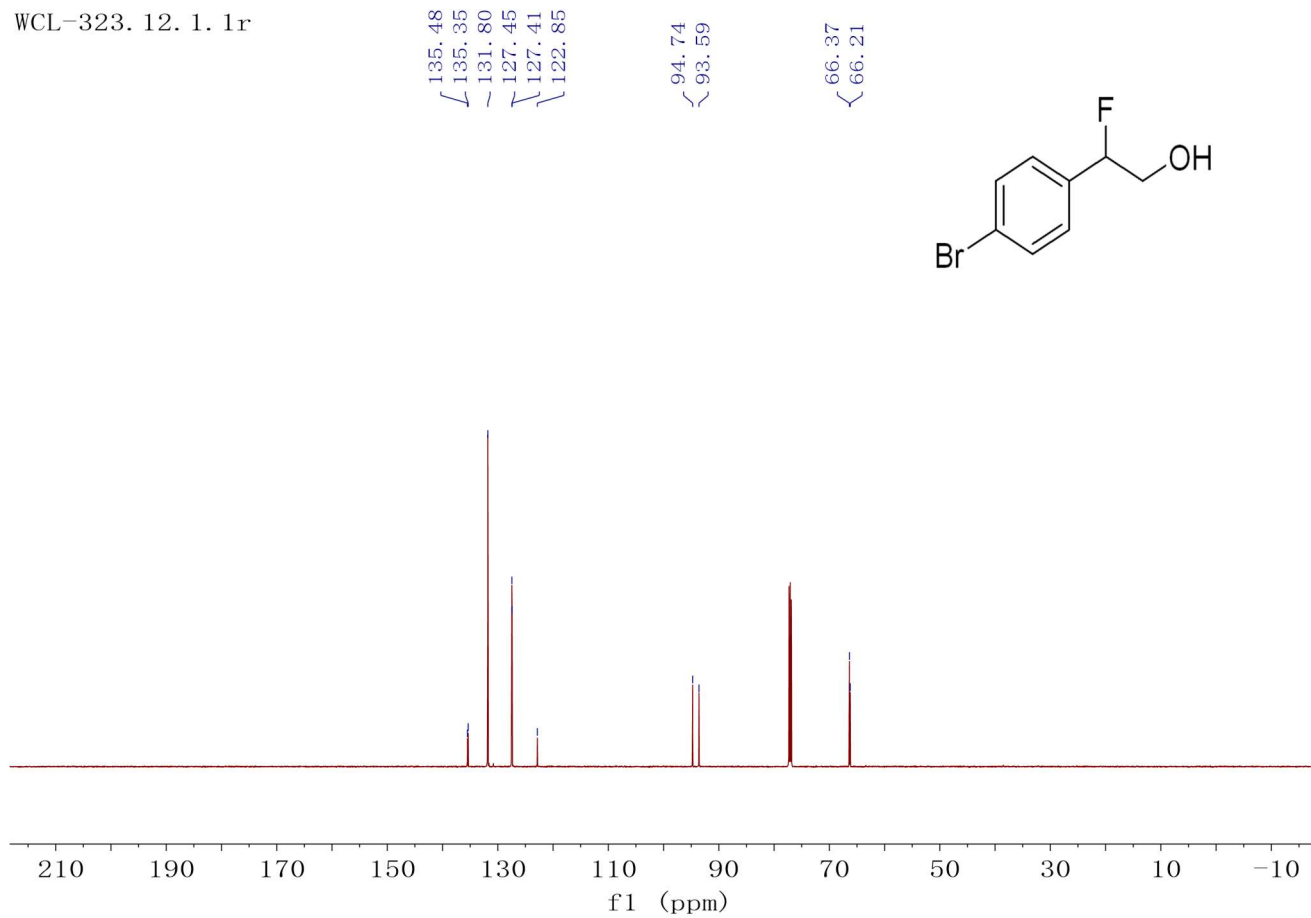
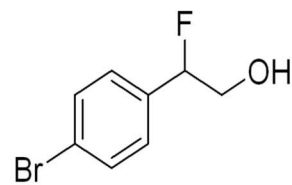


Compound 36

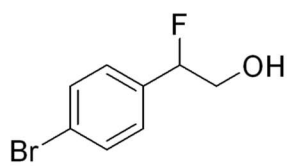
WCL-323. 10.



WCL-323. 12. 1. 1r



WCL-323. 11. 1. 1r



-187.39
-187.43
-187.44
-187.48
-187.51
-187.53
-187.56

