

## Photo-Induced C(sp<sup>2</sup>)-H Difluoroalkylation of Anilines

Xing-Li Zhu,<sup>#</sup> Hua Wang,<sup>#</sup> Chen-Kai Zhai, Wei He\*

Department of Chemistry, School of Pharmacy, Air Force Medical University, Xi'an  
710032, P.R.China.

<sup>#</sup>These authors contributed equally to this work

\* Corresponding author, [weihechem@fmmu.edu.cn](mailto:weihechem@fmmu.edu.cn)

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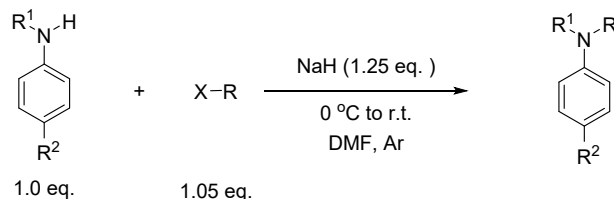
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## 1. General information

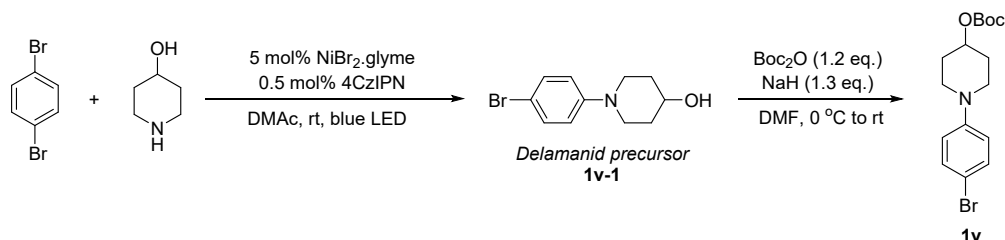
Unless stated otherwise, all reactions were carried out under argon atmosphere. All solvents and chemicals for starting materials were purchased from Adamas-beta and FuYu Chemical and Energy chemical, and were used without further purification unless otherwise specified. The rest of the compounds were prepared according to the literature reports in the reference section.  $^1\text{H}$  NMR spectra were recorded using a Bruker 400 MHz instrument with tetramethylsilane (TMS) as an internal standard.  $^{13}\text{C}$  NMR spectra were obtained at 101 MHz and referenced to the internal solvent signals.  $^{19}\text{F}$  NMR spectra were obtained at 376 MHz. High-resolution mass spectra (HRMS) were performed on an AB Sciex X500<sub>R</sub> QTOF spectrometer. UV-Vis was performed with a HITACHI U-2910 UV/Vis spectro-photometer. Column chromatography was performed with silica gel (200-300 mesh) using petroleum ether and ethyl acetate as eluents. Commercially available reagents were used without further purification unless indicated otherwise, Photocatalytic reactions were performed with 385 nm LEDs (OSRAM Oslon SSL 80 royal - blue LEDs ( $\lambda = 385 \text{ nm} (\pm 15 \text{ nm})$ , 21 V, 700 mA).

## 2. Synthesis of the starting materials

### 2.1 Preparation of *N,N*-disubstituted aromatic amines



**General procedure A:** Under an argon atmosphere, to a 50 mL Schlenk tube equipped with a magnetic stirring bar was added NaH (1.25 eq. 6.25 mmol) and DMF (10 mL) at 0 °C, followed by the addition of the aromatic amine (5.0 mmol, 1.0 equiv). After 0.5 h, alkyl halide (5.25 mmol, 1.05 eq.) was added, then the reaction was stirred at rt. After 8h, the reaction was carefully quenched with water (10 mL) [Caution! Dropwise, Gas evolution], before EtOAc (30 mL) was added. The organic phase was washed with brine (30 mL), and then dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. Purification by flash column chromatography (2% to 10%, EtOAc in petroleum ether) on silica gel afforded *N,N*-disubstituted aromatic amine.

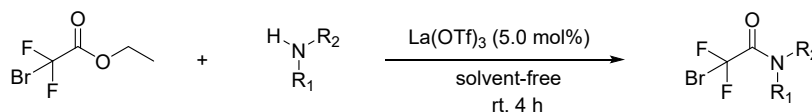


**General procedure B:** To six parallel dry vials (8 mL) with stir bars were charged with 1,4-bromobenzene (0.2 mmol, 46.8 mg), piperidin-4-ol (0.3 mmol, 30.3 mg), NiBr<sub>2</sub>•glyme (3.2 mg, 0.01 mmol, 0.05 equiv.) and 4CzIPN (0.5 mol%, 0.001 mmol, 0.005 equiv.). These vials were evacuated and backfilled with Ar three times. Then, dry DMAc (0.4 mL) was added by a syringe, irradiated with a 455 nm LED and stirred at rt for 3.5 h. After 24 h, this reaction mixture was diluted with EtOAc and washed with H<sub>2</sub>O. The combined organic phase was concentrated in vacuum and the residue was purified by chromatography on silica gel (10:1, EtOAc in petroleum ether) to give the desired **1v-1** in a yield of 83%.<sup>1</sup>

NaH (1.3 mmol, 1.3 eq) and **1v-1** (1.0 mmol, 1.0 eq) were added in a dry flask with Ar. The flask was closed with a septum, evacuated, and backfilled with Ar. Then, dry

DMF (5 mL) was added at 0 °C (ice water). [Caution! Gas evolution.]. After 20 min, Boc<sub>2</sub>O (1.2 mmol) was added at 0 °C and the solution was stirred at ambient temperature. After 2 h, the reaction mixture was carefully quenched with water (5 mL), before EtOAc (10 mL) was added. The organic phase was washed with water (3 × 10 mL) and brine (10 mL), and then dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. Purification by flash column chromatography (10%, EtOAc in hexanes) on silica gel provided the isolated **1v** as a white solid. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 9.2 Hz, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 4.74-4.68 (m, 1H), 3.50 – 3.45 (m, 2H), 3.01-2.94 (m, 2H), 2.09 – 2.02 (m, 2H), 1.87-1.80 (m, 2H), 1.50 (s, 9H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 152.9, 150.1, 131.8, 118.1, 111.7, 82.1, 72.7, 47.0, 30.4, 27.8. HRMS (ESI) *m/z*: C<sub>16</sub>H<sub>23</sub>BrNO<sub>3</sub> [M + H]<sup>+</sup> Calcd 356.0856; Found 356.0858.

## 2.2 Preparation of bromodifluoroamides



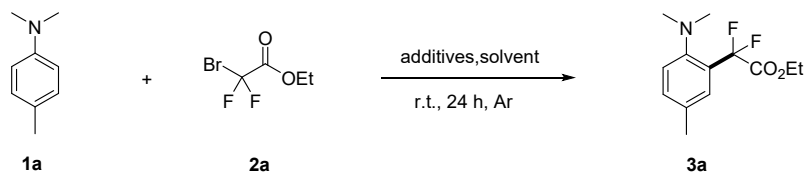
**General procedure C:** To a round-bottom flask equipped with a stir bar was added La(OTf)<sub>3</sub>, ethyl bromodifluoroacetate under air, then equimolar of amine was added. The mixture was stirred at room temperature and monitored by TLC. After the amine was consumed, the mixture was quenched by 10% aqueous HCl. The whole mixture was extracted with AcOEt, and then the extract was washed with brine and dried over MgSO<sub>4</sub>. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give the corresponding amide.<sup>2</sup>

### 3. Experimental procedures



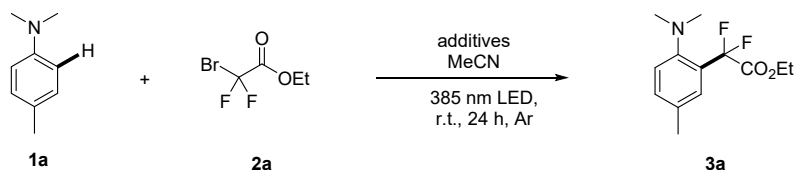
**General procedure D:** To a 8 mL dry vial with a stir bar was charged with anhydrous sodium carbonate (0.1 mmol, 0.5 eq.). The vial was evacuated and backfilled with Ar three times. Then, the aromatic amine (**1**, 0.2 mmol) and bromodifluoroalkyl compounds (**2**, 0.4 mmol, 2.0 eq.) in dry acetonitrile (1.5 mL) was added by a syringe, the mixture was irradiated by a 385 nm LED (1.5 W) and stirred at rt. After 24 h, The reaction mixture was concentrated in vacuum and the residue was purified by chromatography on silica gel (1:80 to 1:60, EtOAc in petroleum ether) to give the desired product.

#### 4. Optimization of reaction conditions



**General Procedure E:** To a dry vial with a stir bar was charged with anhydrous  $\text{Na}_2\text{CO}_3$  (0.5 eq. 10.6 mg). The vial was evacuated and backfilled with Ar three times. Then, **1a** (0.2 mmol, 1.0 eq., 27 mg) and  $\text{BrCF}_2\text{COOEt}$  (2.0 eq. 80.8 mg) in dry acetonitrile (1.5 mL) was added by a syringe, the mixture was irradiated by a 385 nm LED (1.5 W) and stirred at rt. After 24 h, The reaction mixture was concentrated in vacuum and the yield was determined by  $^{19}\text{F}$  NMR by using trifluorotoluene as an internal standard.

**Table S1.** Evaluation of additives for the C-H difluoroalkylation of aromatic amines<sup>a</sup>

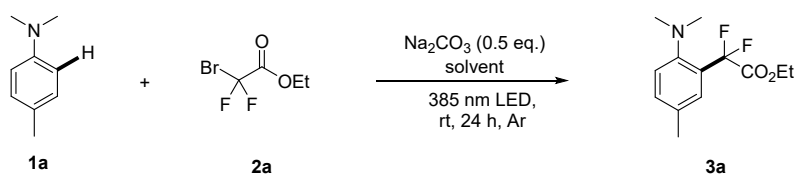


Entry	Additives	Yield (%)
1	$\text{Na}_2\text{CO}_3$ (2.0 eq.)	74
2	TMEDA (2.0 eq.)	59
3	$\text{Cs}_2\text{CO}_3$ (2.0 eq.)	56
4	$\text{K}_2\text{CO}_3$ (2.0 eq.)	39
5	$\text{K}_3\text{PO}_4$ (2.0 eq.)	46
6	$\text{Et}_3\text{N}$ (2.0 eq.)	33
7	$\text{Na}_2\text{CO}_3$ (1.5 eq.)	88
8	$\text{Na}_2\text{CO}_3$ (1.0 eq.)	96
9	$\text{Na}_2\text{CO}_3$ (0.5 eq.)	98
10	$\text{Na}_2\text{CO}_3$ (0.3 eq.)	82
11	$\text{Na}_2\text{CO}_3$ (0.1 eq.)	49
12	—	35

<sup>a</sup>Reaction conditions: unless otherwise noted, all reactions were performed with **1a** (0.2 mmol, 1.0 eq.), **2a** (0.4 mmol, 2.0 eq.), additives, MeCN (2 mL), 385 nm LED

(1.5 W), rt, 24 h. yields were determined by  $^{19}\text{F}$  NMR by using trifluorotoluene as an internal standard.

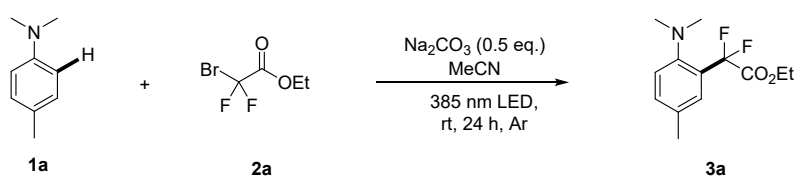
**Table S2.** Evaluation of solvents<sup>a</sup>



Entry	Solvent	Yield (%)
1	DCM (2 mL)	48
2	Acetone (2 mL)	63
3	THF (2 mL)	14
4	1,4-dioxane (2 mL)	24
5	MTBE (2 mL)	15
<b>6</b>	<b>CH<sub>3</sub>CN (1.5 mL)</b>	<b>99 (94)<sup>b</sup></b>
7	CH <sub>3</sub> CN (1.0 mL)	68
8	CH <sub>3</sub> CN (0.5 mL)	43

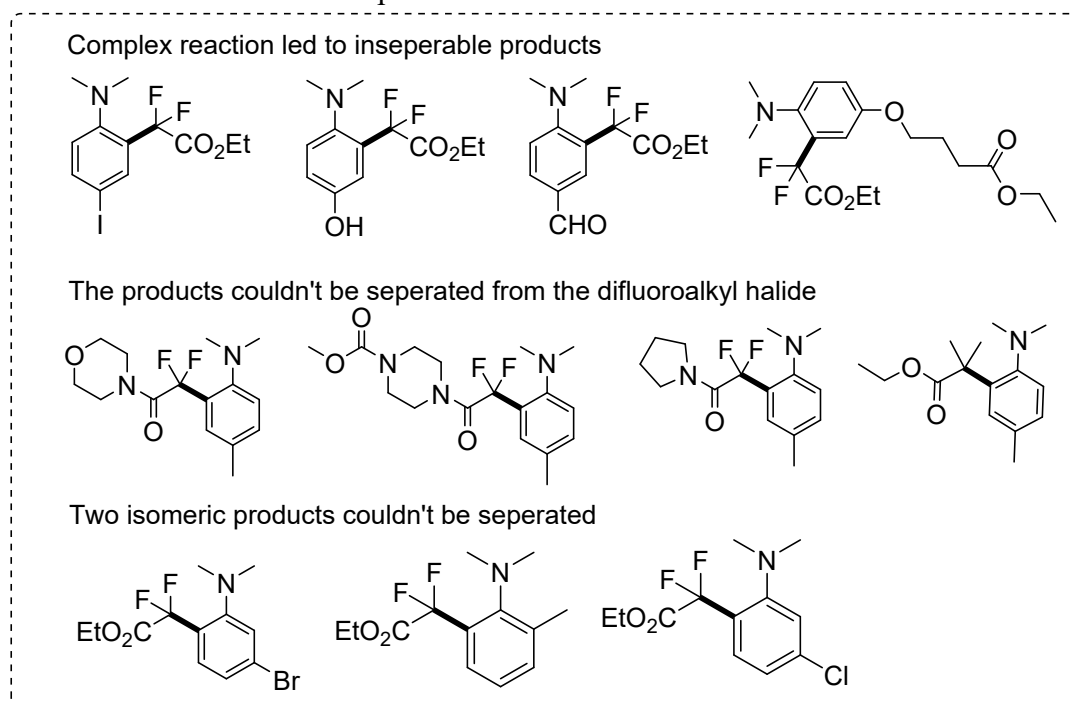
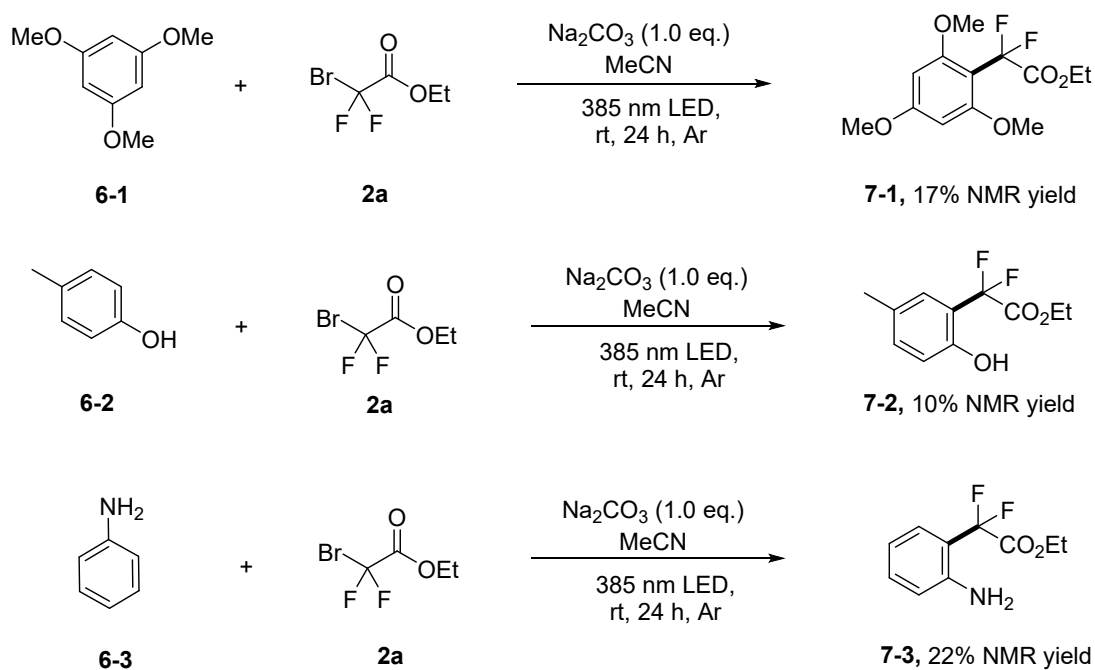
<sup>a</sup>Reaction conditions: unless otherwise noted, all reactions were performed with **1a** (0.2 mmol, 1.0 eq.), **2a** (0.4 mmol, 2.0 eq.), Na<sub>2</sub>CO<sub>3</sub> (0.5 eq.), solvent, 385 nm LED (1.5 W), rt, 24 h. Yields were determined by  $^{19}\text{F}$  NMR by using trifluorotoluene as an internal standard. <sup>b</sup>Isolated yield.

**Table S3.** Control experiments and amounts of **2a**<sup>a</sup>



Entry	Variations	Yield (%)
1	<b>2a</b> (1.5 eq.)	36
2	<b>2a</b> (1.2 eq.)	33
3	Without light irradiation	n.d.

<sup>a</sup>Reaction conditions: unless otherwise noted, all reactions were performed with **1a** (0.2 mmol, 1.0 eq.), **2a**, Na<sub>2</sub>CO<sub>3</sub> (0.5 eq.), MeCN (1.5 mL), 385 nm LED (1.5 W), rt, 24 h. Yields were determined by  $^{19}\text{F}$  NMR by using trifluorotoluene as an internal standard.

**Table S4.** Unsuccessful examples**Table S5.** Difluoroalkylation of other electron-rich arenes



## 5. Mechanistic studies

### 5.1 UV-Vis spectroscopic investigation

Optical absorption spectra of the reaction components and their combinations were measured in MeCN (0.1 M). As shown in Figure S1, the absorption spectrum of **1a** was observed to have an absorption peak on 385 nm region and the addition of **2a** into the solution of **1a** led to a slight redshift. This result suggested the formation of an electron donor-acceptor (EDA) complex between **1a** and **2a**.

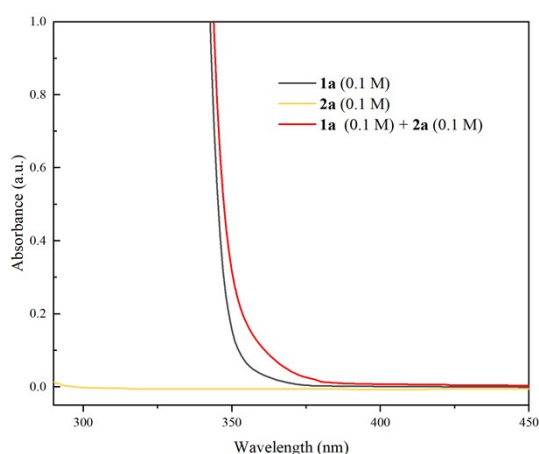
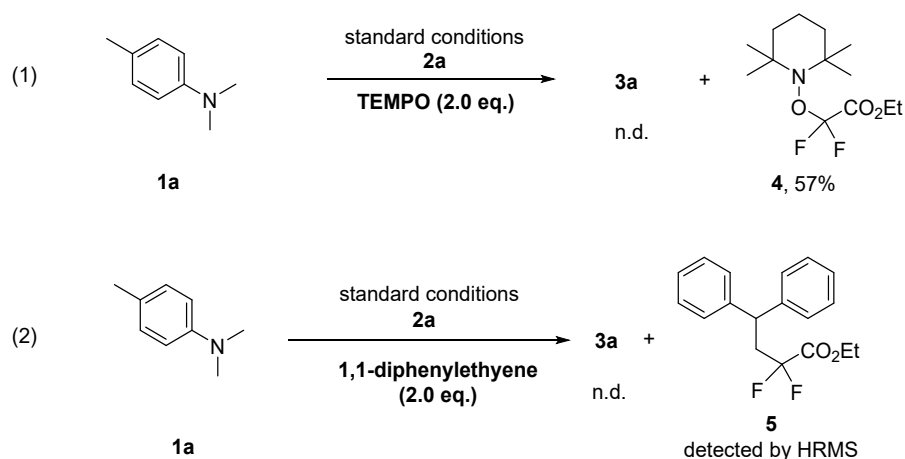


Figure S1. UV-vis spectra

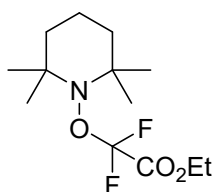
### 5.2 Radical trapping experiments

Under standard reaction conditions, 2 equivalents of radical scavenger TEMPO and 1,1-diphenylethylene were added to the reaction mixture respectively (Scheme S1, eq. 1 and 2). Both reactions were completely inhibited and no desired product was detected, the TEMPO trapped adduct **4** was obtained in a 57% yield. And the trapped product **5** was detected in HRMS. **HRMS (ESI) m/z:** C<sub>18</sub>H<sub>17</sub>F<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> Calcd 303.1191; Found 303.1199.



**Scheme S 1.** Radical trapping experiments

***Ethyl 2,2-difluoro-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate (4)*<sup>3</sup>**



**<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  4.32 (q,  $J = 7.2$  Hz, 2H), 1.62 – 1.51 (m, 6H), 1.34 (t,  $J = 7.2$  Hz, 3H), 1.17 – 1.14 (m, 12H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)**  $\delta$  161.13 (t,  $J = 42.7$  Hz), 115.98 (t,  $J = 272.2$  Hz), 63.4, 61.79, 40.62, 33.80 (t,  $J = 4.3$  Hz), 21.14, 17.31, 14.29. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -73.47. **HRMS(ESI)**  $m/z$ : C<sub>13</sub>H<sub>23</sub>F<sub>2</sub>NO<sub>3</sub> [M + H]<sup>+</sup> Calcd 280.1680; Found 280.1683.

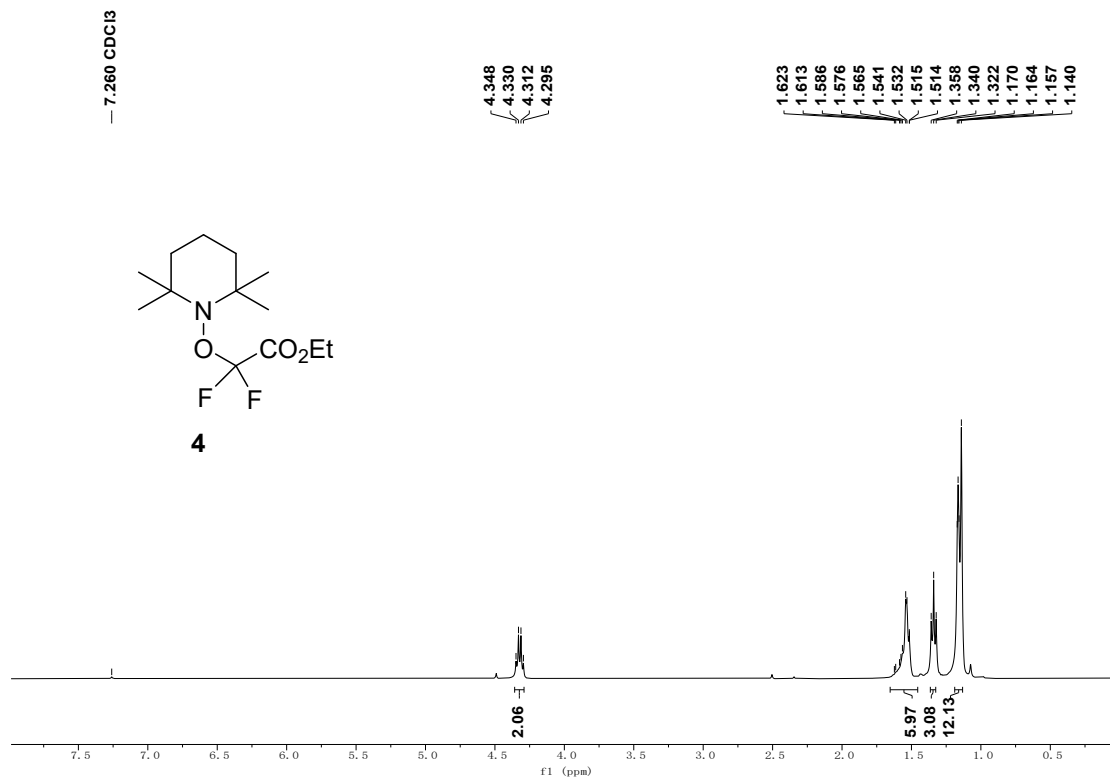


Figure S2. <sup>1</sup>H-NMR spectrum of **4**

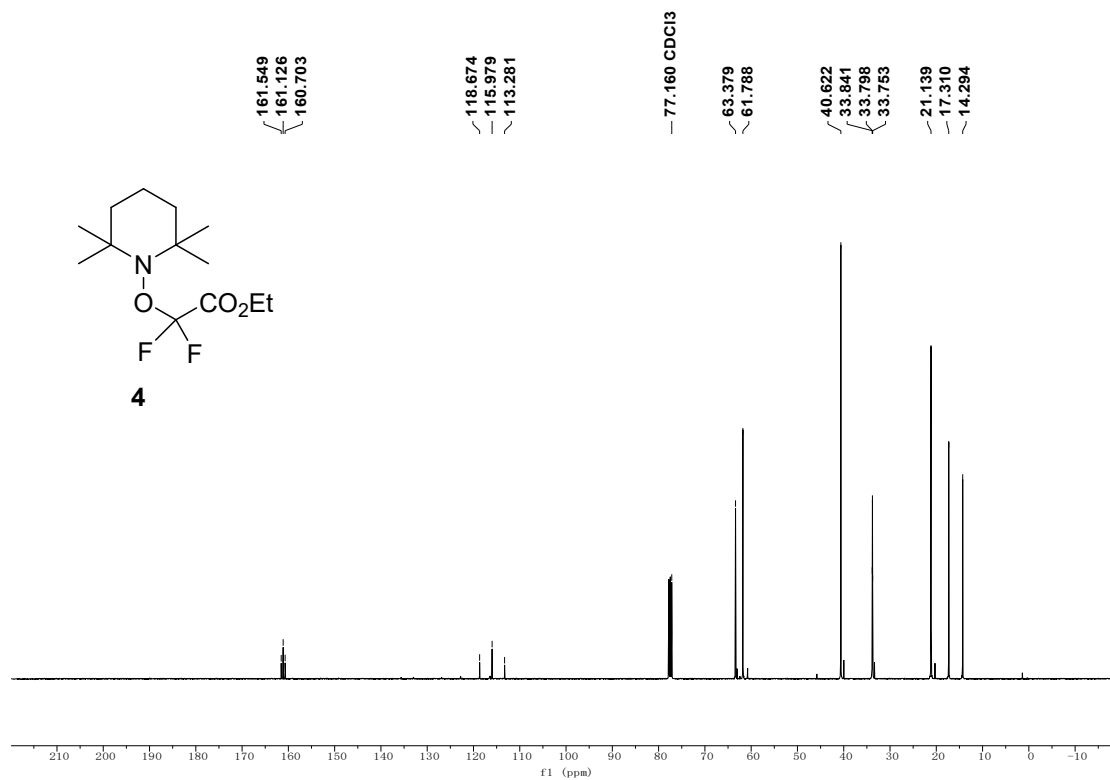
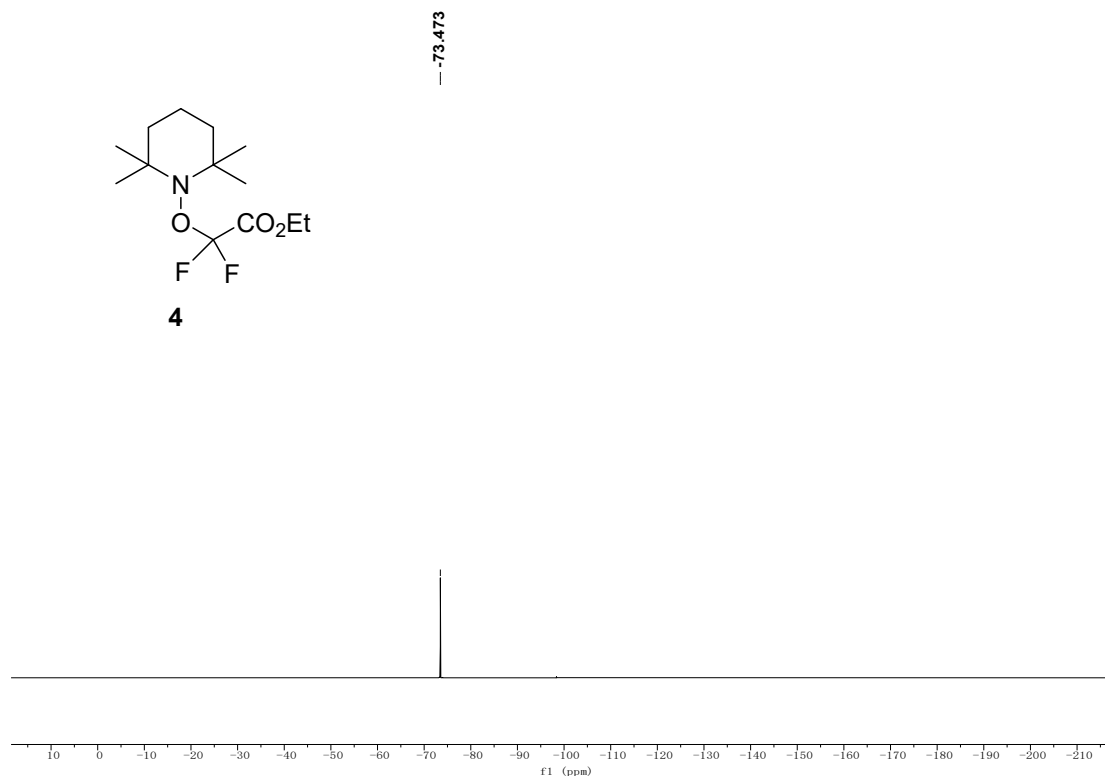
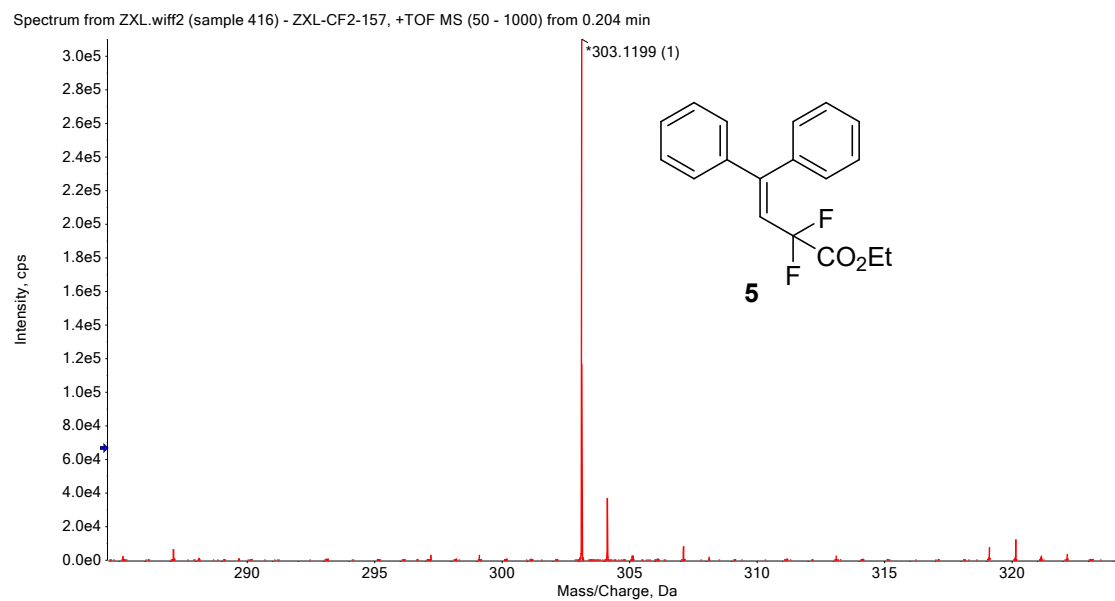


Figure S3. <sup>13</sup>C-NMR spectrum of **4**

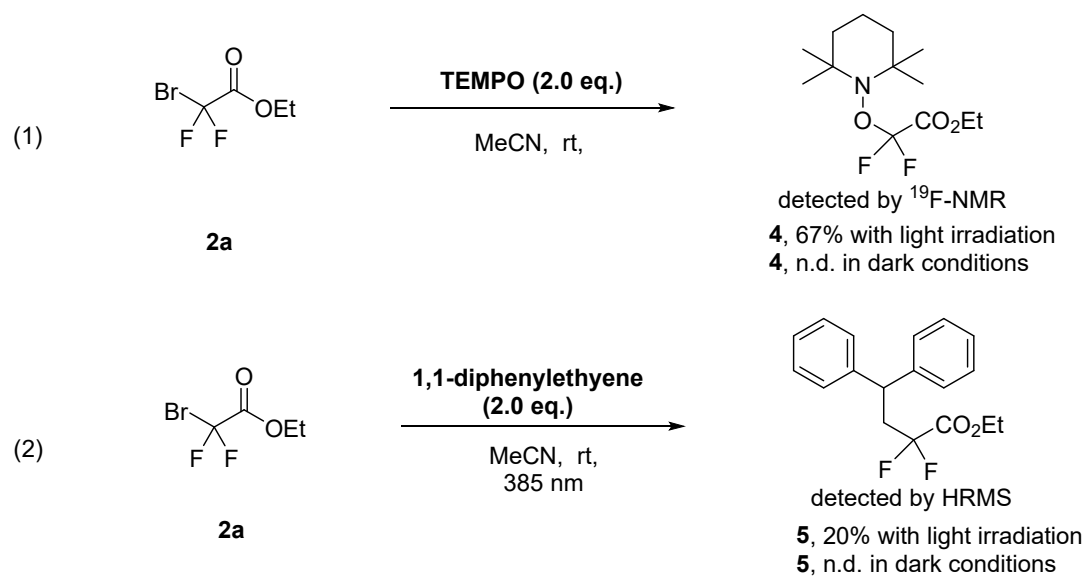


**Figure S4.**  $^{19}\text{F}$ -NMR spectrum of **4**

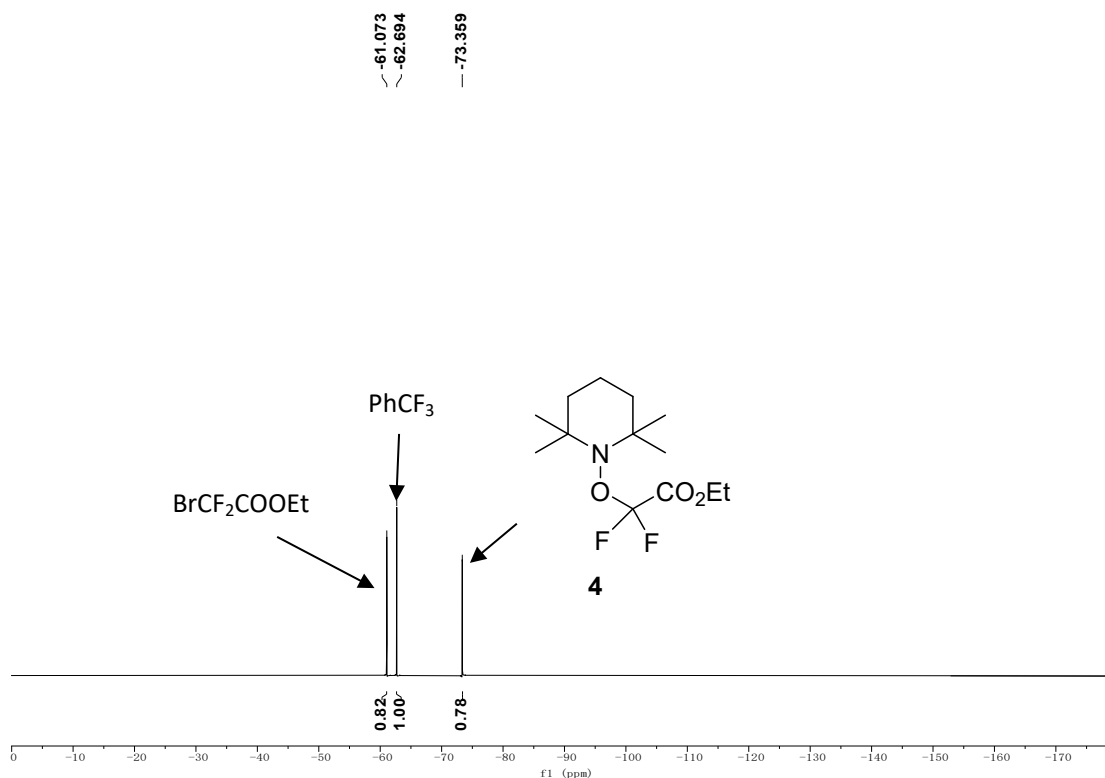


**Figure S 5.** HRMS spectrum of compound **5**

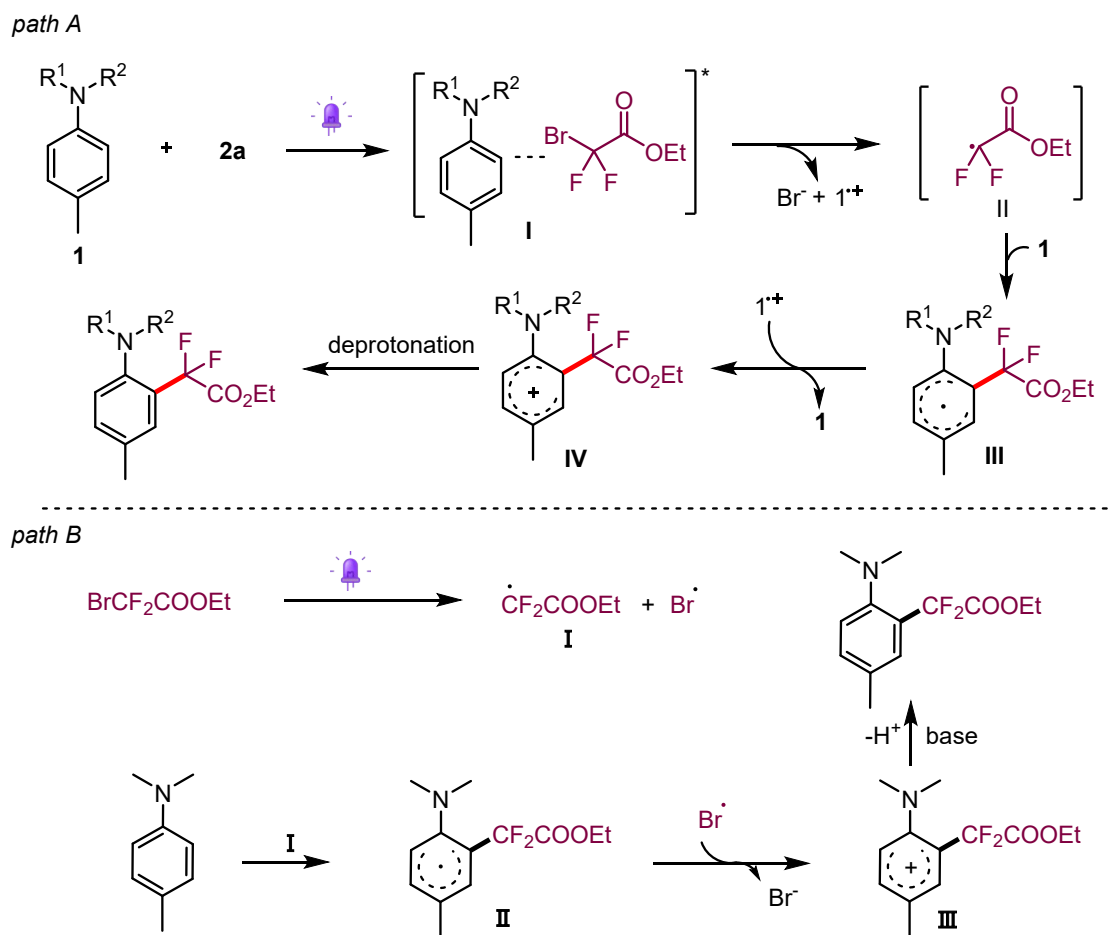
Treated **2a** with 2 equivalents of radical scavengers both TEMPO and 1,1-diphenylethylene respectively under light irradiation and dark conditions independently (Scheme S1, eq. 1 and 2). As shown in Scheme S1, **2a** could undergoes a photolysis to give the difluoroalkyl radical under light irradiation, and the generated radical could be trapped by TEMPO and 1,1-diphenylethylene to give **4** and **5**.



**Scheme S2.** Radical trapping experiments between **2a** with TEMPO and 1,1-diphenylethylene



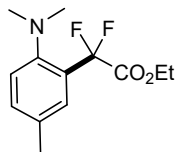
**Figure S7.**  $^{19}\text{F}$ -NMR spectrum of the reaction mixture of Eq.1 in Scheme S2.  $\text{PhCF}_3$  (24.2 mg) was used as an internal standard.



**Figure S8.** Proposed reaction mechanism

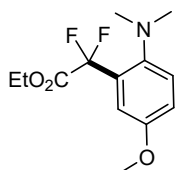
## 6. Characterization of products

### *Ethyl 2-(2-(dimethylamino)-5-methylphenyl)-2,2-difluoroacetate (3a)*



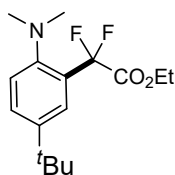
Following the general procedure D, **3a** was obtained as a pale yellow oil, 48.4 mg, in 94% yield. **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.51 (s, 1H), 7.29 (d,  $J = 8.4$  Hz, 1H), 7.22 (d,  $J = 8.0$  Hz, 1H), 4.30 (q,  $J = 7.2$  Hz, 2H), 2.54 (s, 6H), 2.37 (s, 3H), 1.31 (t,  $J = 7.0$ , 3H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)**  $\delta$  164.1 (t,  $J = 33.1$  Hz), 149.8 (t,  $J = 5.2$  Hz), 135.2, 132.5 (t,  $J = 1.9$  Hz), 130.7 (t,  $J = 23.6$  Hz), 126.5 (t,  $J = 6.4$  Hz), 122.3, 112.6 (t,  $J = 246.0$  Hz), 62.1, 45.4, 21.0, 14.1. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -98.3. All spectroscopic data are consistent with literature reports.<sup>4</sup>

### *Ethyl 2-(2-(dimethylamino)-5-methoxyphenyl)-2,2-difluoroacetate (3b)*



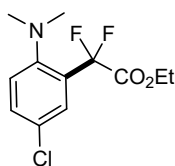
Following the general procedure D, **3b** was obtained as a pale yellow oil, 40.4 mg, in 74% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 30:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.25 (s, 1H), 7.20 (d,  $J = 3.2$  Hz, 1H), 7.01 (dd,  $J = 8.8, 2.8$  Hz, 1H), 4.31 (q,  $J = 7.2$  Hz, 2H), 3.82 (s, 3H), 2.52 (s, 6H), 1.32 (t,  $J = 7.2$  Hz, 3H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)**  $\delta$  163.8 (t,  $J = 33.1$  Hz), 157.1, 145.0 (t,  $J = 5.3$  Hz), 132.1 (t,  $J = 23.6$  Hz), 123.7, 117.96, 112.4 (t,  $J = 248.0$  Hz), 110.5 (t,  $J = 7.0$  Hz), 62.0, 55.5, 45.5, 14.09. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -98.6. **HRMS (ESI) m/z:** C<sub>13</sub>H<sub>18</sub>F<sub>2</sub>NO<sub>3</sub> [M + H]<sup>+</sup> Calcd 274.1249, Found 274.1247. All spectroscopic data are consistent with literature reports.<sup>5</sup>

### *Ethyl 2-(5-(tert-butyl)-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3c)*



Following the general procedure D, **3c** was obtained as a pale yellow oil, 36.5 mg, in 61% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 100:1).  **$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.61 (d,  $J = 2.8$  Hz, 1H), 7.41 (dd,  $J = 8.4, 2.4$  Hz, 1H), 7.16 (d,  $J = 8.4$  Hz, 1H), 4.21 (q,  $J = 7.2$  Hz, 2H), 2.45 (s, 6H), 1.24-1.20 (m, 12H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  164.2 (t,  $J = 33.1$  Hz), 149.6 (t,  $J = 5.2$  Hz), 148.4, 130.3 (t,  $J = 23.5$  Hz), 128.9, 122.7 (t,  $J = 6.5$  Hz), 122.0, 112.8 (t,  $J = 247.4$  Hz), 62.0, 45.3, 34.6, 31.2, 14.1.  **$^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)**  $\delta$  -97.7. **HRMS (ESI)  $m/z$ :**  $\text{C}_{16}\text{H}_{24}\text{F}_2\text{NO}_2$  [ $\text{M} + \text{H}$ ] $^+$  Calcd 300.1770, Found 300.1769. All spectroscopic data are consistent with literature reports.<sup>5</sup>

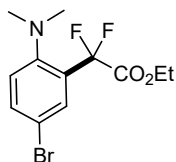
***Ethyl 2-(5-chloro-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3d)***



Following the general procedure D, **3d** was obtained as pale yellow oil, 48.0 mg, in 82% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 100:1).  **$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.61 (s, 1H), 7.38 (d,  $J = 8.4$  Hz, 1H), 7.20 (d,  $J = 6.8$  Hz, 1H), 4.23 (qd,  $J = 7.2, 2.0$  Hz, 2H), 2.48 (s, 6H), 1.24 (td,  $J = 7.2, 2.0$  Hz, 3H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  163.5 (t,  $J = 32.8$  Hz), 151.0 (t,  $J = 4.9$  Hz), 132.7 (t,  $J = 24.1$  Hz), 132.0, 130.9, 126.6 (t,  $J = 7.2$  Hz), 124.1, 111.8 (t,  $J = 248.6$  Hz), 62.3, 45.4, 14.1.  **$^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)**  $\delta$  -98.8. **HRMS (ESI)  $m/z$ :**  $\text{C}_{12}\text{H}_{15}\text{ClF}_2\text{NO}_2$  [ $\text{M} + \text{H}$ ] $^+$  Calcd for 278.0754, Found 278.0750. All spectroscopic data are consistent with literature reports.<sup>5</sup>

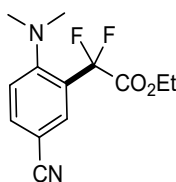
***Ethyl 2-(5-bromo-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3e)***





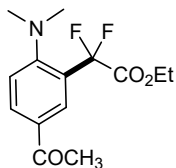
Following the general procedure D, **3e** was obtained as a pale yellow oil, 47.0 mg, in 73% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 100:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  7.82 – 7.78 (m, 1H), 7.60 – 7.57 (m, 1H), 7.21-7.17 (m, 1H), 4.29 (p,  $J = 7.2$  Hz, 2H), 2.53 (d,  $J = 6.4$  Hz, 6H), 1.32-1.27 (m, 4H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  163.5 (t,  $J = 32.6$  Hz), 151.5 (t,  $J = 5.1$  Hz), 135.0, 132.9 (t,  $J = 24.2$  Hz), 129.7 (t,  $J = 7.3$  Hz), 124.5, 118.5, 111.7 (t,  $J = 248.3$  Hz), 62.3, 45.3, 14.1.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -98.6. All spectroscopic data are consistent with literature reports.<sup>6</sup>

***Ethyl 2-(5-cyano-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3f)***



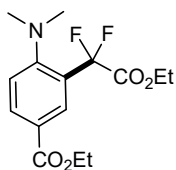
Following the general procedure D, **3f** was obtained as a pale yellow oil, 31.5 mg, in 59% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 20:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  8.01 (d,  $J = 2.0$  Hz, 1H), 7.77 (dd,  $J = 8.4, 2.0$  Hz, 1H), 7.38 (dt,  $J = 8.4, 1.2$  Hz, 1H), 4.30 (q,  $J = 7.2$  Hz, 2H), 2.63 (s, 6H), 1.30 (t,  $J = 7.2$  Hz, 3H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  163.2 (t,  $J = 32.7$  Hz), 156.7 (t,  $J = 4.4$  Hz), 135.6, 131.7 (t,  $J = 24.2$  Hz), 131.0 (t,  $J = 7.3$  Hz), 123.4, 118.0, 111.4 (t,  $J = 249.2$  Hz), 108.7, 62.6, 45.1, 29.7, 14.1.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -98.3. All spectroscopic data are consistent with literature reports. All spectroscopic data are consistent with literature reports.<sup>5</sup>

***Ethyl 2-(5-acetyl-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3g)***



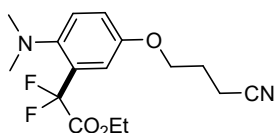
Following the general procedure D, **3g** was obtained as a pale yellow oil, 36.0 mg, in 63% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 30:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  8.3 (s, 1H), 8.10 (d,  $J = 8.4$  Hz, 1H), 7.37 (d,  $J = 8.4$  Hz, 1H), 4.29 (q,  $J = 7.2$  Hz, 2H), 2.61 (m, 9H), 1.29 (t,  $J = 7.2$  Hz, 3H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  196.47, 163.71 (t,  $J = 33.0$  Hz), 156.87 (t,  $J = 4.6$  Hz), 133.80, 131.78, 130.64 (t,  $J = 23.8$  Hz), 127.19 (t,  $J = 6.8$  Hz), 122.45, 112.06 (t,  $J = 247.8$  Hz), 62.39, 45.17, 26.49, 14.07.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -97.85. **HRMS** (ESI)  $m/z$ :  $\text{C}_{14}\text{H}_{18}\text{F}_2\text{NO}_3$   $[\text{M} + \text{H}]^+$  Calcd 286.1249, Found 286.1239.

***Ethyl 4-(dimethylamino)-3-(2-ethoxy-1,1-difluoro-2-oxoethyl)benzoate (3h)***



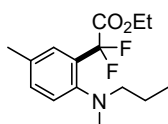
Following the general procedure D, **3h** was obtained as a pale yellow oil, 39.0 mg, in 62% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 20:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  8.39 (d,  $J = 2.0$  Hz, 1H), 8.16 (dd,  $J = 8.4, 2.0$  Hz, 1H), 7.34 (d,  $J = 8.4$  Hz, 1H), 4.38 (q,  $J = 7.2$  Hz, 2H), 4.29 (q,  $J = 7.2$  Hz, 2H), 2.61 (m, 6H), 1.39 (t,  $J = 7.0$  Hz, 3H), 1.29 (t,  $J = 7.2$  Hz, 3H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  165.5, 163.8 (t,  $J = 33.0$  Hz), 156.7 (t,  $J = 4.5$  Hz), 133.2, 130.7 (t,  $J = 24.2$  Hz), 128.2 (t,  $J = 6.8$  Hz), 127.3, 122.3, 112.1 (t,  $J = 248.1$  Hz), 62.3, 61.2, 45.2, 14.3, 14.1.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -98.2. **HRMS** (ESI)  $m/z$ :  $\text{C}_{15}\text{H}_{20}\text{F}_2\text{NO}_4$   $[\text{M} + \text{H}]^+$  Calcd 316.1355, Found 316.1351.

***Ethyl 2-(5-(3-cyanopropoxy)-2-(dimethylamino)phenyl)-2,2-difluoroacetate (3i)***



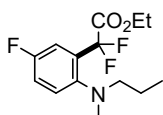
Following the general procedure D, **3i** was obtained as yellow oil, 39.8 mg, in 61% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 30:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.28-7.26 (m, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.01 (dd, *J* = 8.8, 3.0 Hz, 1H), 4.34-4.28 (m, 2H), 4.10 (t, *J* = 5.6 Hz, 2H), 2.61-2.52 (m, 9H), 2.18-2.12 (m, 2H), 1.32 (t, *J* = 7.6 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)** δ 163.5 (t, *J* = 32.8 Hz), 155.7, 145.4 (t, *J* = 5.2 Hz), 132.0 (t, *J* = 23.7 Hz), 123.8, 119.0, 118.0, 112.1 (t, *J* = 248.0 Hz), 111.2 (t, *J* = 6.9 Hz), 65.6, 61.9, 45.3, 25.1, 13.9, 13.8. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -98.6. **HRMS (ESI) m/z:** C<sub>16</sub>H<sub>21</sub>F<sub>2</sub>N<sub>2</sub>O<sub>3</sub> [M+H]<sup>+</sup> Calcd 327.1515, Found 327.1512.

***Ethyl 2,2-difluoro-2-(5-methyl-2-(methyl(propyl)amino)phenyl)acetate (3j)***



Following the general procedure D, **3j** was obtained as yellow oil, 48.0 mg, in 85% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.48 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 2.64 (t, *J* = 8.0 Hz, 2H), 2.48 (s, 3H), 2.35 (s, 3H), 1.51-1.43 (m, 2H), 1.29 (t, *J* = 7.0 Hz, 3H), 0.82 (t, *J* = 7.0 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)** δ 164.2 (t, *J* = 33.2 Hz), 149.9 (t, *J* = 5.1 Hz), 135.0, 132.3, 130.8 (t, *J* = 23.3 Hz), 126.6 (t, *J* = 6.8 Hz), 123.3, 112.7 (t, *J* = 247.3 Hz), 62.1, 60.5, 42.0, 21.0, 19.9, 14.0, 11.6. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -96.5. **HRMS (ESI) m/z:** C<sub>15</sub>H<sub>22</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 286.1613 ; Found 286.1612.

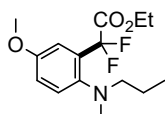
***Ethyl 2,2-difluoro-2-(5-fluoro-2-(methyl(propyl)amino)phenyl)acetate (3k)***



Following the general procedure D, **3k** was obtained as yellow oil, 49.0 mg, in 84% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.40-7.37 (m, 1H), 7.29-7.26 (m, 1H), 7.19-7.14 (m, 1H), 4.30 (q, *J*

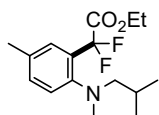
= 7.2 Hz, 2H), 2.66-2.62 (m, 2H), 2.50 (s, 3H), 1.55-1.46 (m, 2H), 1.33-1.30 (m, 3H), 0.85 (t,  $J = 7.4$  Hz, 3H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  163.6 (t,  $J = 33.4$  Hz), 159.8 (d,  $J = 246.5$  Hz), 148.5 (t,  $J = 4.9$  Hz), 133.09 (t,  $J = 3.8$  Hz), 125.3 (d,  $J = 8.2$  Hz), 118.6 (t,  $J = 22.2$  Hz), 113.4 (dt,  $J = 24.7, 7.4$  Hz), 111.9 (t,  $J = 248.7$  Hz), 62.3, 60.7, 42.0, 20.0, 14.0, 11.6.  **$^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)**  $\delta$  -99.0, -115.5. **HRMS (ESI) m/z:**  $\text{C}_{14}\text{H}_{19}\text{F}_3\text{NO}_2$   $[\text{M}+\text{H}]^+$  Calcd 290.1362, Found 290.1360.

***Ethyl 2,2-difluoro-2-(5-methoxy-2-(methyl(propyl)amino)phenyl)acetate (3l)***



Following the general procedure D, **3l** was obtained as yellow oil, 43.6 mg, in 72% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 20:1).  **$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.32-7.05 (m, 2H), 7.06 (d,  $J = 8.8$  Hz, 1H), 4.36 (q,  $J = 7.2$  Hz, 2H), 3.88 (s, 3H), 2.71-2.66 (m, 2H), 2.54 (s, 3H), 1.58-1.52 (m, 2H), 1.39-1.35 (m, 3H), 0.91-0.86 (m, 3H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  165.9 (t,  $J = 30.1$  Hz), 159.5, 134.9 (t,  $J = 4.2$  Hz), 131.0 (t,  $J = 25.8$  Hz), 123.2, 117.8, 112.7 (t,  $J = 255.2$  Hz), 112.5 (t,  $J = 10.0$  Hz), 61.7, 55.8, 43.9, 18.8, 11.0.  **$^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)**  $\delta$  -97.5. **HRMS (ESI) m/z:**  $\text{C}_{15}\text{H}_{22}\text{F}_2\text{NO}_3$   $[\text{M}+\text{H}]^+$  Calcd 302.1562, Found 302.1565.

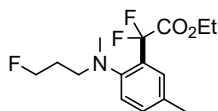
***Ethyl 2,2-difluoro-2-(2-(isobutyl(methyl)amino)-5-methylphenyl)acetate (3m)***



Following the general procedure D, **3m** was obtained as yellow oil, 45.0 mg, in 76% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 100:1).  **$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.48 (s, 1H), 7.28-7.22 (m, 2H), 4.29 (q,  $J = 7.2$  Hz, 2H), 2.52-2.46 (m, 5H), 2.37 (s, 3H), 1.90-1.81 (m, 1H), 1.32-1.28 (m, 3H), 0.89 (d,  $J = 6.8$  Hz, 6H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  164.0 (t,  $J = 33.3$  Hz), 151.1 (t,  $J = 4.6$  Hz), 135.0, 132.4, 130.3 (t,  $J = 22.7$  Hz), 126.5 (t,  $J = 7.7$  Hz), 123.7, 112.8 (t,  $J = 248.36$

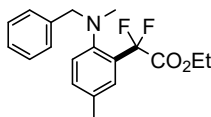
Hz), 67.2, 62.3, 42.3, 29.7, 26.6, 21.1, 13.9. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -97.9. HRMS (ESI) m/z: C<sub>16</sub>H<sub>24</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 300.1770, Found 300.1772.

**Ethyl 2,2-difluoro-2-(2-((3-fluoropropyl)(methyl)amino)-5-methylphenyl)acetate (3n)**



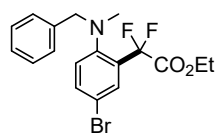
Following the general procedure D, **3n** was obtained as yellow oil, 52.0 mg, in 86% yield, R<sub>f</sub> = 0.3 (silica gel, petroleum ether/ethyl acetate = 50:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.50 (s, 1H), 7.28-7.18 (m, 2H), 4.49 (t, *J* = 6.0 Hz, 1H), 4.37 (t, *J* = 6.0 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 8.0 Hz, 2H), 2.50 (s, 3H), 2.37 (s, 3H), 1.93-1.79 (m, 2H), 1.29 (t, *J* = 6.8 Hz, 3H). NMR (101 MHz, Chloroform-*d*) δ 164.1 (t, *J* = 33.7 Hz), 149.3 (t, *J* = 5.2 Hz), 135.5, 132.5, 130.7 (t, *J* = 23.2 Hz), 126.6 (t, *J* = 6.9 Hz), 123.2, 112.6 (t, *J* = 247.6 Hz), 82.4 (d, *J* = 164.8 Hz), 62.2, 54.7 (d, *J* = 5.2 Hz), 42.2, 28.1 (d, *J* = 19.8 Hz), 21.0, 14.0. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -98.7, -101.3. HRMS (ESI) m/z: C<sub>15</sub>H<sub>21</sub>F<sub>3</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 304.1519, Found 304.1518.

**Ethyl 2-(2-(benzyl(methyl)amino)-5-methylphenyl)-2,2-difluoroacetate (3o)**



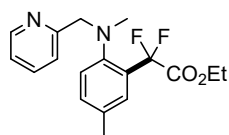
Following the general procedure D, **3o** was obtained as yellow oil, 46.0 mg, in 69% yield, R<sub>f</sub> = 0.3 (silica gel, petroleum ether/ethyl acetate = 50:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.54 (s, 1H), 7.34-7.26 (m, 6H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.8 (s, 2H), 2.39 (s, 3H), 2.35 (s, 3H), 1.23 (t, *J* = 6.8 Hz, 3H). NMR (101 MHz, Chloroform-*d*) δ 164.2 (t, *J* = 33.4 Hz), 149.5 (t, *J* = 4.8 Hz), 137.2, 135.5, 132.3, 130.6 (t, *J* = 22.8 Hz), 129.8, 128.1, 127.3, 126.6 (d, *J* = 7.3 Hz), 124.1, 112.9 (t, *J* = 248.2 Hz), 63.2, 62.3, 40.7, 21.1, 14.0. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -96.5. HRMS (ESI) m/z: C<sub>19</sub>H<sub>22</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 334.1613, Found 334.1610.

**Ethyl 2-(2-(benzyl(methyl)amino)-5-bromophenyl)-2,2-difluoroacetate (3p)**



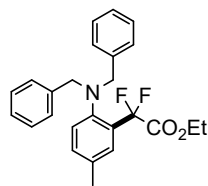
Following the general procedure D, **3p** was obtained as yellow oil, 57.0 mg, in 72% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.9 (d,  $J$  = 2.4 Hz, 1H), 7.34-7.26 (d,  $J$  = 8.8 Hz, 1H), 7.34-7.26 (m, 5H), 7.12 (d,  $J$  = 8.8 Hz, 1H), 4.24 (q,  $J$  = 7.2 Hz, 2H), 3.9 (s, 2H), 2.38 (s, 3H), 1.26 (t,  $J$  = 7.2 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  163.6 (t,  $J$  = 33.0 Hz), 151.1 (t,  $J$  = 4.6 Hz), 136.5, 134.7, 132.9 (t,  $J$  = 23.6 Hz), 129.8, 129.6 (t,  $J$  = 8.0 Hz), 128.2, 127.5, 126.4, 118.9, 112.9 (t,  $J$  = 249.8 Hz), 63.0, 62.6, 40.6, 13.9. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -97.4. **HRMS (ESI) m/z:** C<sub>18</sub>H<sub>19</sub>BrF<sub>2</sub>NO<sub>2</sub> [M + H]<sup>+</sup> Calcd 398.0562, Found 398.0564.

**Ethyl 2,2-difluoro-2-(5-methyl-2-(methyl(pyridin-2-ylmethyl)amino)phenyl)acetate (3q)**



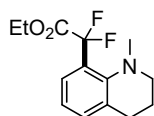
Following the general procedure D, **3q** was obtained as yellow oil, 44.0 mg, in 66% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 10:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  8.49 (s, 1H), 7.70-7.66 (t,  $J$  = 8.0 Hz, 1H), 7.55-7.50 (m, 2H), 7.28-7.15 (m, 3H), 4.17 (q,  $J$  = 7.2 Hz, 2H), 4.0 (s, 2H), 2.41 (s, 3H), 2.36 (s, 3H), 1.19 (t,  $J$  = 7.2 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)**  $\delta$  164.2 (t,  $J$  = 34.0 Hz), 157.6, 149.3 (t,  $J$  = 4.7 Hz), 148.0, 137.1, 135.8, 132.5, 130.2 (t,  $J$  = 22.8 Hz), 126.5 (t,  $J$  = 7.4 Hz), 124.2, 124.1, 122.4, 112.8 (t,  $J$  = 247.6 Hz), 64.2, 62.3, 41.6, 21.0, 13.9. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -97.8. **HRMS (ESI) m/z:** C<sub>18</sub>H<sub>21</sub>F<sub>2</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> Calcd 335.1566, Found 335.1565.

**Ethyl 2-(2-(dibenzylamino)-5-methylphenyl)-2,2-difluoroacetate (3r)**



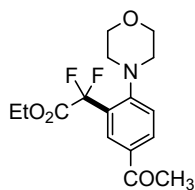
Following the general procedure D, **3r** was obtained as yellow oil, 49.8 mg, in 61% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.55 (d, *J* = 1.6 Hz, 1H), 7.30-7.23 (m, 6H), 7.12-7.10 (m, 5H), 6.68 (d, *J* = 8.0 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.0 (s, 4H), 2.36 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)** δ 164.3 (t, *J* = 34.0 Hz), 147.1 (t, *J* = 4.4 Hz), 136.4, 135.0, 131.4 (t, *J* = 2.2 Hz), 129.8, 129.7, 128.5, 128.0, 127.5, 127.1, 127.1 (t, *J* = 8.5 Hz), 126.5, 113.0 (t, *J* = 237.2 Hz), 62.6, 56.7, 21.0, 13.8. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -97.8. **HRMS (ESI) m/z:** C<sub>25</sub>H<sub>26</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 410.1926, Found 410.1923.

***Ethyl 2,2-difluoro-2-(1-methyl-1,2,3,4-tetrahydroquinolin-8-yl)acetate (3s)***



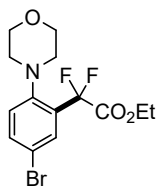
Following the general procedure D, **3s** was obtained as yellow oil, 28.5 mg, in 53% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 50:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 4.27 (q, *J* = 7.6 Hz, 2H), 2.91-2.82 (m, 4H), 2.65 (s, 3H), 1.93-1.90 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). **NMR (101 MHz, Chloroform-*d*)** δ 164.5 (t, *J* = 32.9 Hz), 147.8 (t, *J* = 4.5 Hz), 132.2, 131.4, 128.7 (t, *J* = 23.7 Hz), 124.1 (t, *J* = 6.9 Hz), 123.3, 112.6 (t, *J* = 246.4 Hz), 62.2, 50.0, 44.8, 25.9, 15.8, 14.0. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -98.7. **HRMS (ESI) m/z:** C<sub>14</sub>H<sub>18</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 270.1300, Found 270.1301.

***Ethyl 2-(5-acetyl-2-morpholinophenyl)-2,2-difluoroacetate (3t)***



Following the general procedure D, **3t** was obtained as yellow oil, 44.5 mg, in 68% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 20:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  8.31 (s, 1H), 8.13 (d,  $J = 6.0$  Hz, 1H), 7.42 (d,  $J = 8.8$  Hz, 1H), 4.32 (q,  $J = 7.2$  Hz, 2H), 3.76 (t,  $J = 4.4$  Hz, 4H), 2.88 (t,  $J = 4.6$  Hz, 4H), 2.63 (s, 3H), 1.31 (t,  $J = 7.2$  Hz, 3H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  196.4, 163.8 (t,  $J = 33.3$  Hz), 155.3 (t,  $J = 4.6$  Hz), 134.6, 132.0, 131.1 (t,  $J = 23.7$  Hz), 127.0 (t,  $J = 7.3$  Hz), 123.2, 113.2 (t,  $J = 128.9$  Hz), 66.4, 62.6, 53.4, 26.5, 14.0.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -98.3. **HRMS** (ESI)  $m/z$ :  $\text{C}_{16}\text{H}_{21}\text{F}_2\text{NO}_4$   $[\text{M}+\text{H}]^+$  Calcd 328.1355, Found 328.1355.

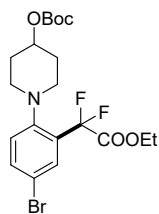
***Ethyl 2-(5-bromo-2-morpholinophenyl)-2,2-difluoroacetate (3u)***



Following the general procedure D, **3u** was obtained as yellow oil, 51.0 mg, in 70% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 100:1).  **$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)**  $\delta$  7.84 (s, 1H), 7.64 (d,  $J = 8.0$  Hz, 1H), 7.23 (d,  $J = 8.8$  Hz, 1H), 4.32 (t,  $J = 7.2$  Hz, 2H), 3.74-3.72 (m, 4H), 2.81 (m, 4H), 1.32 (t,  $J = 7.2$  Hz, 3H).  **$\text{NMR}$  (101 MHz, Chloroform-*d*)**  $\delta$  163.7 (t,  $J = 33.2$  Hz), 149.9 (t,  $J = 4.8$  Hz), 135.1, 132.9 (t,  $J = 23.5$  Hz), 129.6 (t,  $J = 7.9$  Hz), 125.0, 119.3, 111.7 (t,  $J = 249.0$  Hz), 66.5, 62.5, 53.4, 14.0.  **$^{19}\text{F NMR}$  (376 MHz, Chloroform-*d*)**  $\delta$  -99.5. **HRMS** (ESI)  $m/z$ :  $\text{C}_{14}\text{H}_{17}\text{BrF}_2\text{NO}_3$   $[\text{M}+\text{H}]^+$  Calcd 364.0354, Found 364.0355.

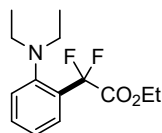
***Ethyl 2-(5-bromo-2-(4-((tert-butoxycarbonyl)oxy)piperidin-1-yl)phenyl)-2,2-difluoroacetate (3v)***





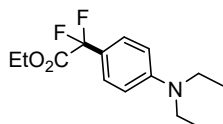
Following the general procedure D, **3v** was obtained as yellow oil, 30 mg, in 31% yield, Rf = 0.2 (silica gel, petroleum ether/ethyl acetate = 30:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.82 (d, *J* = 2.4 Hz, 1H), 7.60 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 4.68 (m, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 2.98-2.93 (m, 2H), 2.74-2.68 (m, 2H), 1.99-1.95 (m, 2H), 1.81 (m, 2H), 1.49 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)** δ 163.6 (t, *J* = 33.4), 153.0, 150.6, 134.9 (t, *J* = 1.8), 132.7 (t, *J* = 23.7), 129.5 (t, *J* = 7.8), 124.9, 119.0, 111.6 (t, *J* = 248.6), 82.1, 62.4, 30.4, 27.8, 14.0. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -99.9. **HRMS (ESI) m/z:** C<sub>20</sub>H<sub>27</sub>BrF<sub>2</sub>NO<sub>5</sub> [M+H]<sup>+</sup> Calcd 478.1035, Found 478.1032.

***Ethyl 2-(2-(diethylamino)phenyl)-2,2-difluoroacetate (3w<sup>o</sup>)***



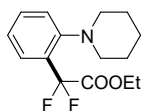
Following the general procedure D, **3w<sup>o</sup>** was obtained as yellow oil, 37.9 mg, in 70% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (600 MHz, Chloroform-*d*)** δ 7.73 (d, *J* = 8.4, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 4.31-4.28 (m, 2H), 2.91 (q, *J* = 7.2 Hz, 4H), 1.30 (t, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 6H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)** δ 164.3 (t, *J* = 32.9 Hz), 150.3 (t, *J* = 4.9 Hz), 131.2, 129.3, 126.6 (t, *J* = 7.8 Hz), 124.9, 124.6, 112.6 (t, *J* = 247.6 Hz), 62.1, 47.5, 13.9, 11.1. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)** δ -99.5. **HRMS (ESI) m/z:** C<sub>14</sub>H<sub>20</sub>F<sub>2</sub>NO<sub>2</sub> [M + H]<sup>+</sup> Calcd 272.1457; Found 272.1455. All spectroscopic data are consistent with literature reports.<sup>5</sup>

***Ethyl 2-(4-(diethylamino)phenyl)-2,2-difluoroacetate (3w<sup>p</sup>)***



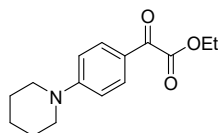
Following the general procedure D, **3w<sup>p</sup>** was obtained as yellow oil, 4.1 mg, in 8% yield,  $R_f = 0.25$  (silica gel, petroleum ether/ethyl acetate = 100:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.88 (d,  $J = 9.2$  Hz, 2H), 6.65 (d,  $J = 9.2$  Hz, 2H), 4.43-4.38 (m, 2H), 3.45 – 3.41 (m, 4H), 1.40 (t,  $J = 7.0$  Hz, 3H), 1.20 (t,  $J = 7.0$  Hz, 6H). **HRMS (ESI) m/z:** C<sub>14</sub>H<sub>20</sub>F<sub>2</sub>NO<sub>2</sub> [M + H]<sup>+</sup> Calcd 272.1457; Found 272.1457. All spectroscopic data are consistent with literature reports.<sup>5</sup>

***Ethyl 2,2-difluoro-2-(2-(piperidin-1-yl)phenyl)acetate (3x<sup>o</sup>)***



Following the general procedure D, **3x<sup>o</sup>** was obtained as yellow oil, 12.4 mg, in 22% yield,  $R_f = 0.2$  (silica gel, petroleum ether/ethyl acetate = 30:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.70 (dd,  $J = 7.8, 1.6$  Hz, 1H), 7.51 – 7.46 (m, 1H), 7.34 – 7.25 (m, 2H), 4.32 (q,  $J = 7.2$  Hz, 2H), 2.76 (s, 4H), 1.64 – 1.56 (m, 6H), 1.29 (t,  $J = 7.2$  Hz, 3H). **<sup>13</sup>C NMR (101 MHz, Chloroform-*d*)**  $\delta$  164.2 (t,  $J = 33.8$ ), 152.7 (t,  $J = 5.3$ ), 131.7 (t,  $J = 2.1$ ), 130.9 (t,  $J = 23.4$ ), 126.1 (t,  $J = 7.4$ ), 125.3, 123.0, 112.5 (t,  $J = 244.5$ ), 62.1, 54.7, 25.6, 24.1, 14.0. **<sup>19</sup>F NMR (376 MHz, Chloroform-*d*)**  $\delta$  -99.3. **HRMS (ESI) m/z:** C<sub>15</sub>H<sub>20</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 284.1457, Found 284.1461.

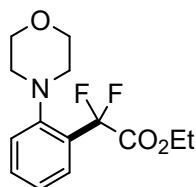
***Ethyl 2-oxo-2-(4-(piperidin-1-yl)phenyl)acetate (3x<sup>p</sup>)***



Following the general procedure D, **3x<sup>p</sup>** was obtained as yellow oil, 12.5 mg, in 24% yield,  $R_f = 0.3$  (silica gel, petroleum ether/ethyl acetate = 10:1). **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  7.88 (d,  $J = 8.8$  Hz, 2H), 6.83 (d,  $J = 8.8$  Hz, 2H), 4.41 (q,  $J = 7.2$  Hz, 2H), 3.43 – 3.42 (m, 4H), 1.68 – 1.67 (m, 6H), 1.40 (t,  $J = 7.0$  Hz, 3H). **<sup>13</sup>C NMR**

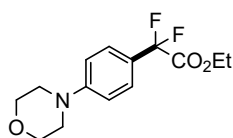
(101 MHz, Chloroform-*d*)  $\delta$  183.99, 164.86, 155.07, 132.58, 121.01, 112.74, 61.78, 48.2, 25.3, 24.3, 14.1. HRMS (ESI)  $m/z$ : C<sub>15</sub>H<sub>20</sub>F<sub>2</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 284.1457, Found 284.1460.

***Ethyl 2,2-difluoro-2-(2-morpholinophenyl)acetate (3y<sup>o</sup>)***



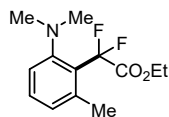
Following the general procedure D, 3y<sup>o</sup> was obtained as yellow oil, 12.8 mg, in 22% yield, R<sub>f</sub> = 0.2 (silica gel, petroleum ether/ethyl acetate = 30:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.72 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.52 (td, *J* = 8.0, 1.6 Hz, 1H), 7.37-7.30 (m, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 3.75 (t, *J* = 4.6 Hz, 4H), 2.86-2.84 (m, 4H), 1.31 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  164.3 (t, *J* = 33.6), 150.9, 132.0 (t, *J* = 1.8), 131.0 (t, *J* = 23.4), 126.3 (t, *J* = 7.3), 126.0, 123.1, 113.7 (t, *J* = 251.3), 66.6, 62.3, 53.5, 14.0. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*)  $\delta$  -99.1. HRMS (ESI)  $m/z$ : C<sub>14</sub>H<sub>18</sub>F<sub>2</sub>NO<sub>3</sub> [M+H]<sup>+</sup> Calcd 286.1249, Found 286.1245.

***Ethyl 2,2-difluoro-2-(4-morpholinophenyl)acetate (3y<sup>p</sup>)***



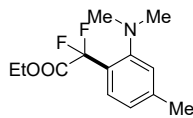
Following the general procedure D, 3y<sup>p</sup> was obtained as yellow oil, 14.1 mg, in 25% yield, R<sub>f</sub> = 0.2 (silica gel, petroleum ether/ethyl acetate = 20:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.49 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.87 – 3.84 (m, 4H), 3.23 – 3.21 (m, 4H), 1.30 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  164.5 (t, *J* = 36.5), 152.9, 126.6 (t, *J* = 6.1), 123.1 (t, *J* = 26.4), 114.5, 113.7 (t, *J* = 252.3), 66.7, 62.9, 48.2, 13.9. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*)  $\delta$  -102.5. HRMS (ESI)  $m/z$ : C<sub>14</sub>H<sub>18</sub>F<sub>2</sub>NO<sub>3</sub> [M+H]<sup>+</sup> Calcd 286.1249, Found 286.1247.

***Ethyl 2-(2-(dimethylamino)-6-methylphenyl)-2,2-difluoroacetate (3z<sup>02</sup>)***



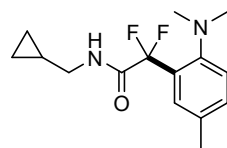
Following the general procedure D, **3z<sup>02</sup>** was obtained as yellow oil, 21.2 mg, in 41% yield, R<sub>f</sub> = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). <sup>1</sup>H NMR (600 MHz, Chloroform-*d*) δ 7.33 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 2.55-2.53 (m, 3H), 2.51 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (151 MHz, Chloroform-*d*) δ 163.6 (t, *J* = 32.8), 152.7 (t, *J* = 6.2), 139.3, 131.2, 129.5, 128.9 (t, *J* = 23.6), 119.7, 114.8 (t, *J* = 47.8), 61.7, 45.3, 20.8 (t, *J* = 5.7), 14.2. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -93.5. HRMS (ESI) *m/z*: C<sub>13</sub>H<sub>18</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 258.1300, Found 258.1303.

***Ethyl 2-(4-(dimethylamino)-2-methylphenyl)-2,2-difluoroacetate (3z<sup>06</sup>)***



Following the general procedure D, **3z<sup>06</sup>** was obtained as yellow oil, 7.1 mg, in 14% yield, R<sub>f</sub> = 0.3 (silica gel, petroleum ether/ethyl acetate = 100:1). <sup>1</sup>H NMR (600 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.11 (s, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 2.55 (s, 6H), 2.38 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (151 MHz, Chloroform-*d*) δ 164.2 (t, *J* = 33.2), 152.2 (t, *J* = 5.1), 142.2, 128.1 (t, *J* = 23.9), 126.2, 126.0 (t, *J* = 19.2), 123.0, 112.7 (t, *J* = 245.5), 62.1, 45.4, 21.4, 14.1. <sup>19</sup>F NMR (376 MHz, Chloroform-*d*) δ -97.8. HRMS (ESI) *m/z*: C<sub>13</sub>H<sub>18</sub>NO<sub>2</sub> [M+H]<sup>+</sup> Calcd 258.1300, Found 258.1301.

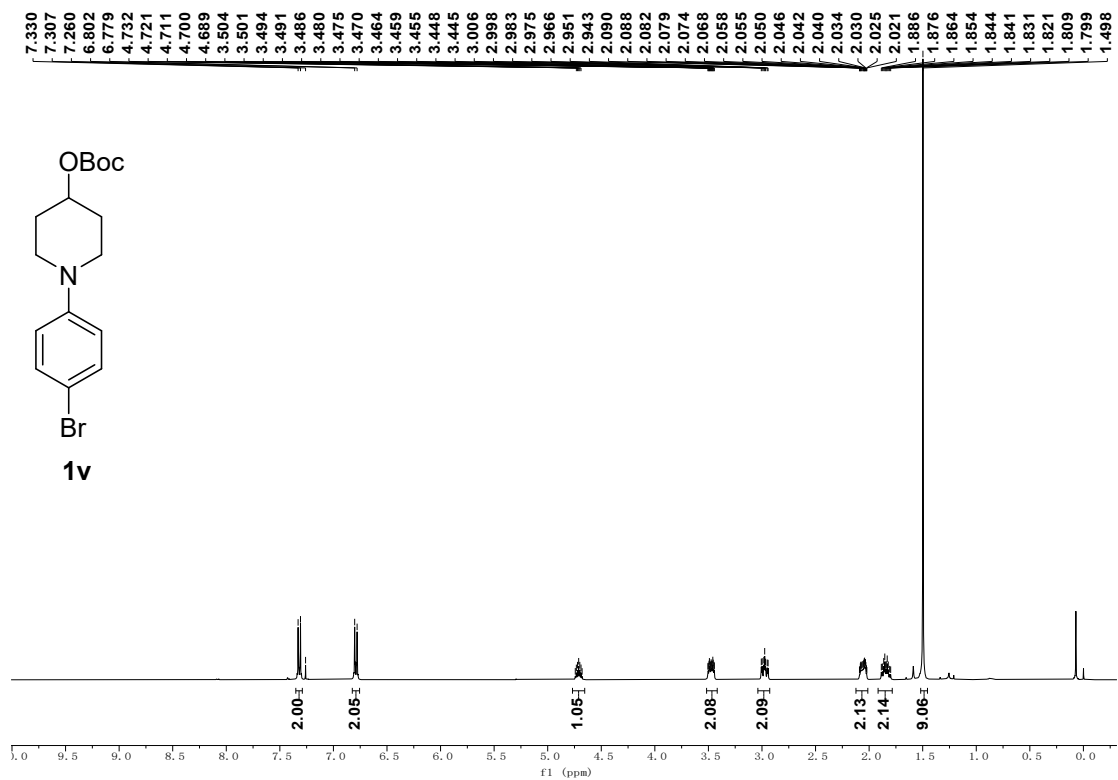
***N-(cyclopropylmethyl)-2-(2-(dimethylamino)-5-methylphenyl)-2,2-difluoroacetamide (3aa)***



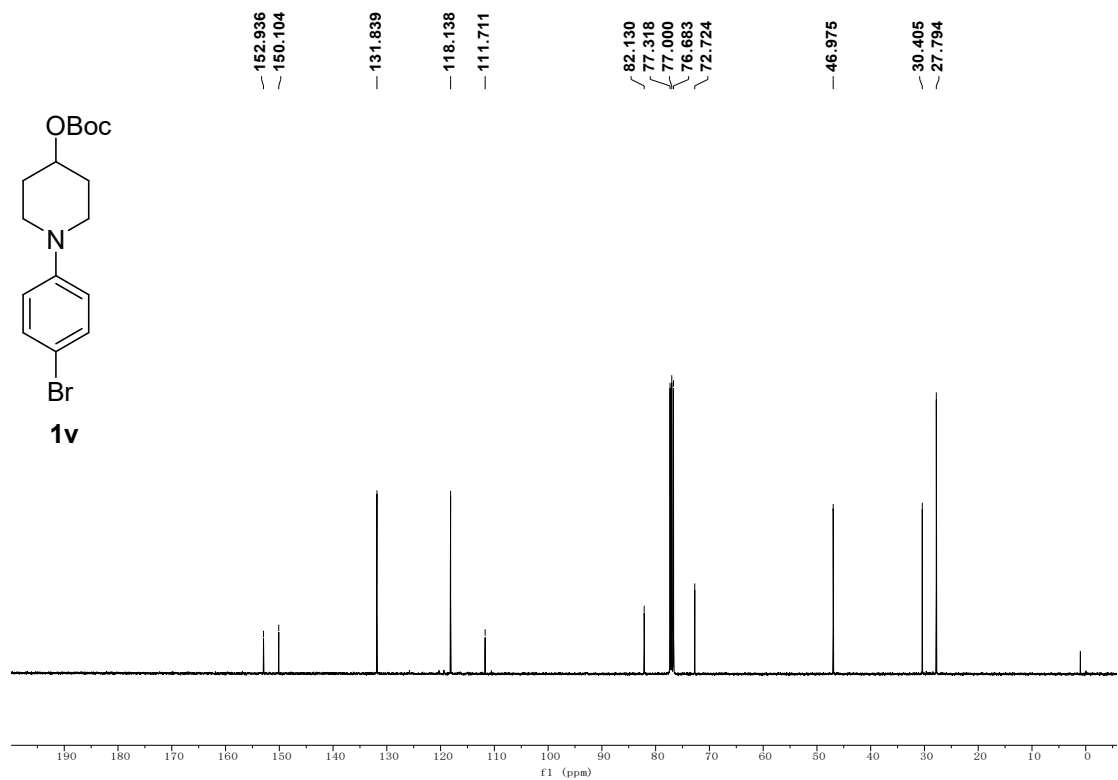
Following the general procedure D, **3aa** was obtained as yellow oil, 48.5 mg, in 86% yield, Rf = 0.3 (silica gel, petroleum ether/ethyl acetate = 10:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.51 (s, 1H), 7.28-7.26 (m, 2H), 6.94 (s, 1H), 3.22-3.19 (m, 2H), 2.56 (s, 6H), 2.36 (s, 3H), 1.07-0.98 (m, 1H), 0.58-0.54 (m, 2H), 0.28-0.24 (m, 2H). **NMR (101 MHz, Chloroform-*d*)** δ 164.7 (t, *J* = 29.5 Hz), 150.2 (t, *J* = 4.2 Hz), 135.4, 132.5, 130.6 (t, *J* = 23.1 Hz), 127.3 (t, *J* = 7.6 Hz), 123.2, 114.7 (t, *J* = 251.8 Hz), 45.9, 44.5, 21.0, 10.5, 3.5. **<sup>19</sup>F NMR** (376 MHz, Chloroform-*d*) δ -99.7. **HRMS** (ESI) *m/z*: C<sub>15</sub>H<sub>22</sub>F<sub>2</sub>N<sub>2</sub>O [M+H]<sup>+</sup> Calcd 283.1616, Found 283.1617.

## 7. Copies of NMR spectra

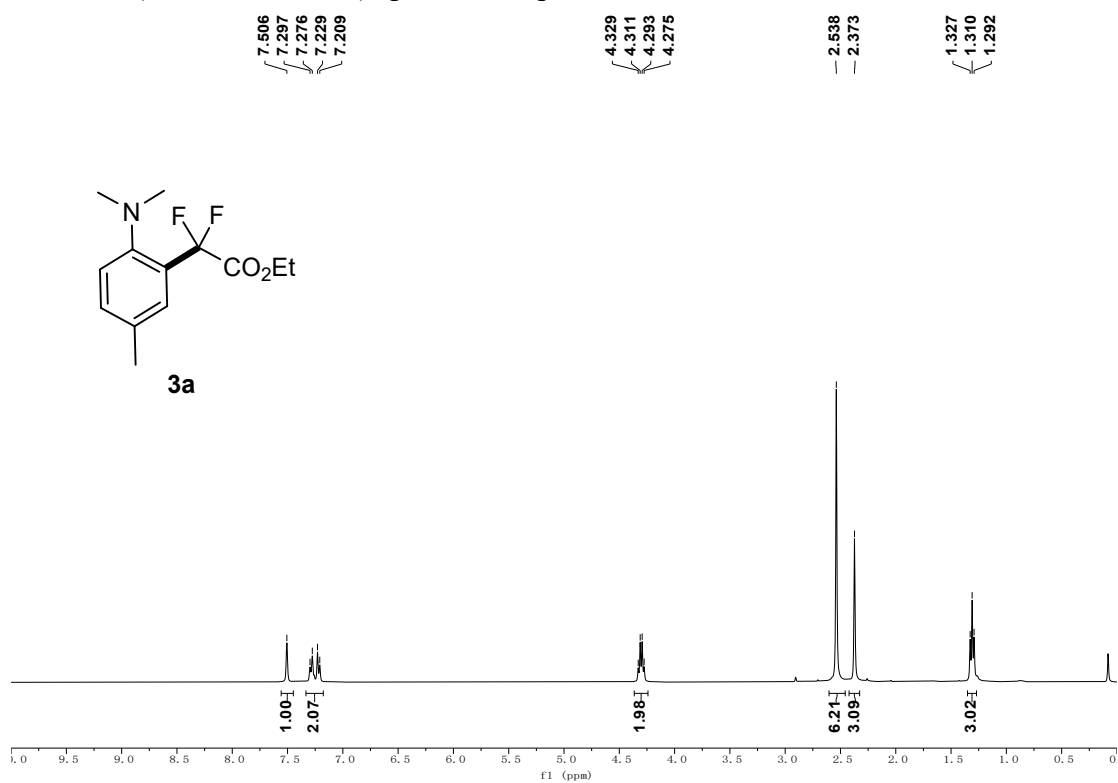
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of starting material **1v**



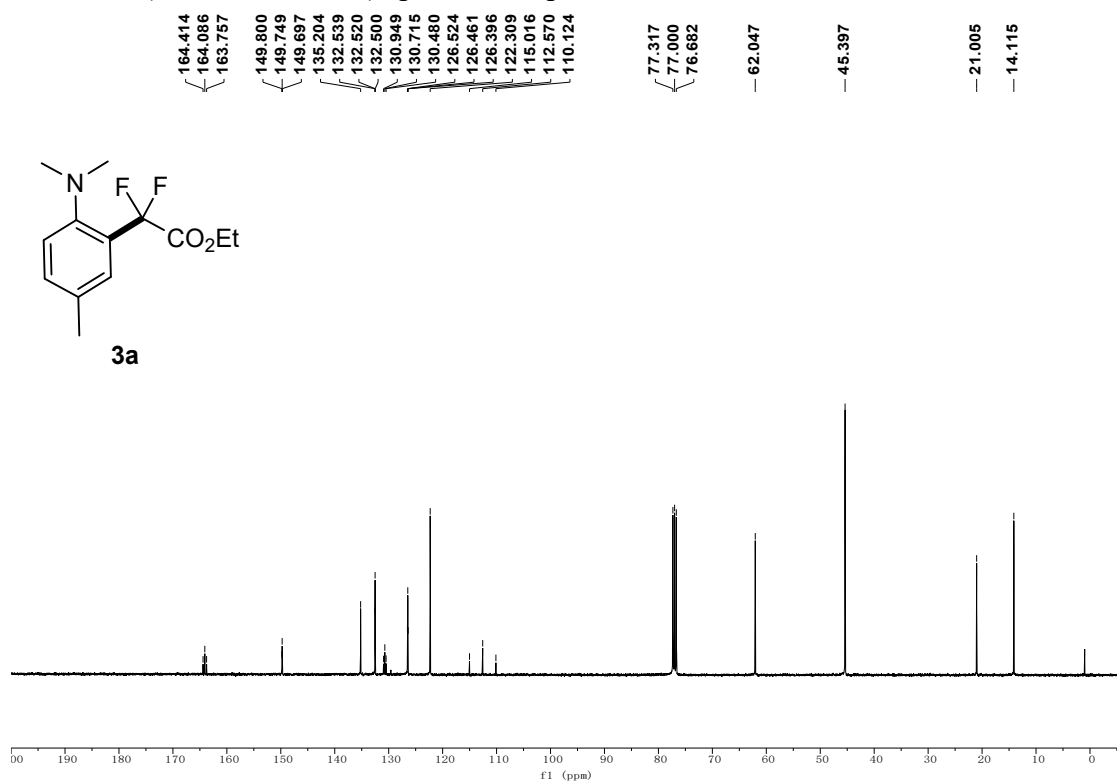
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of starting material **1v**



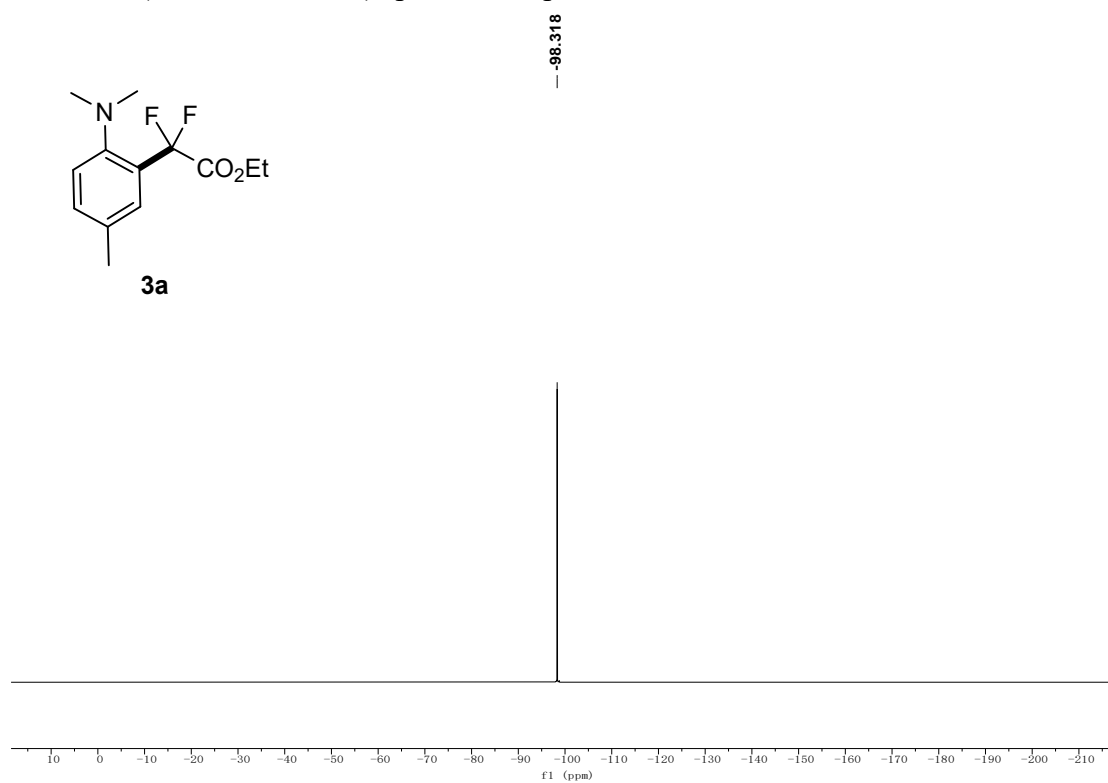
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3a**



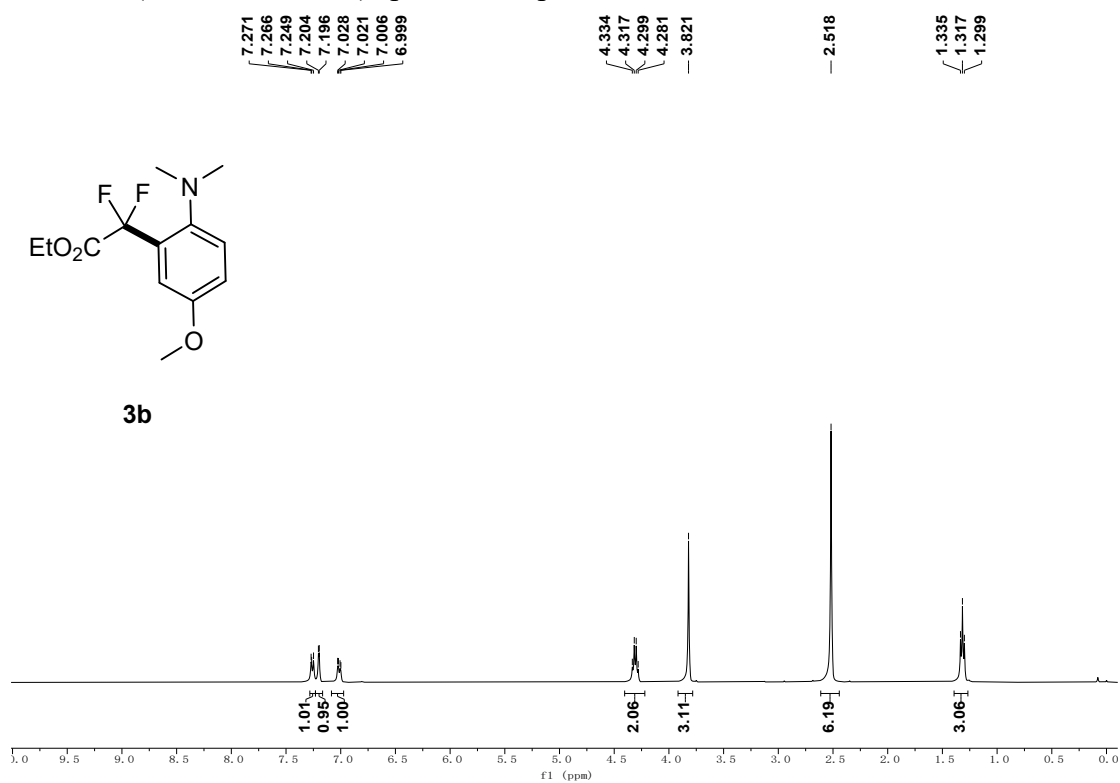
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3a**



$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3a**

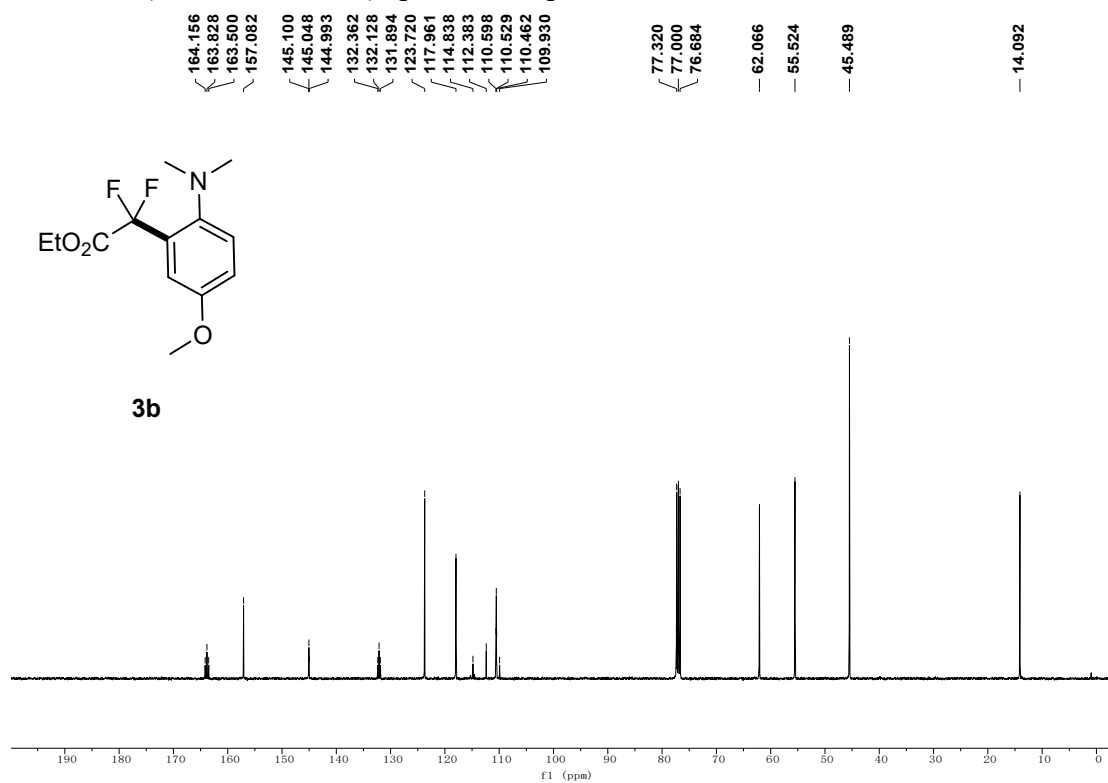


$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3b**

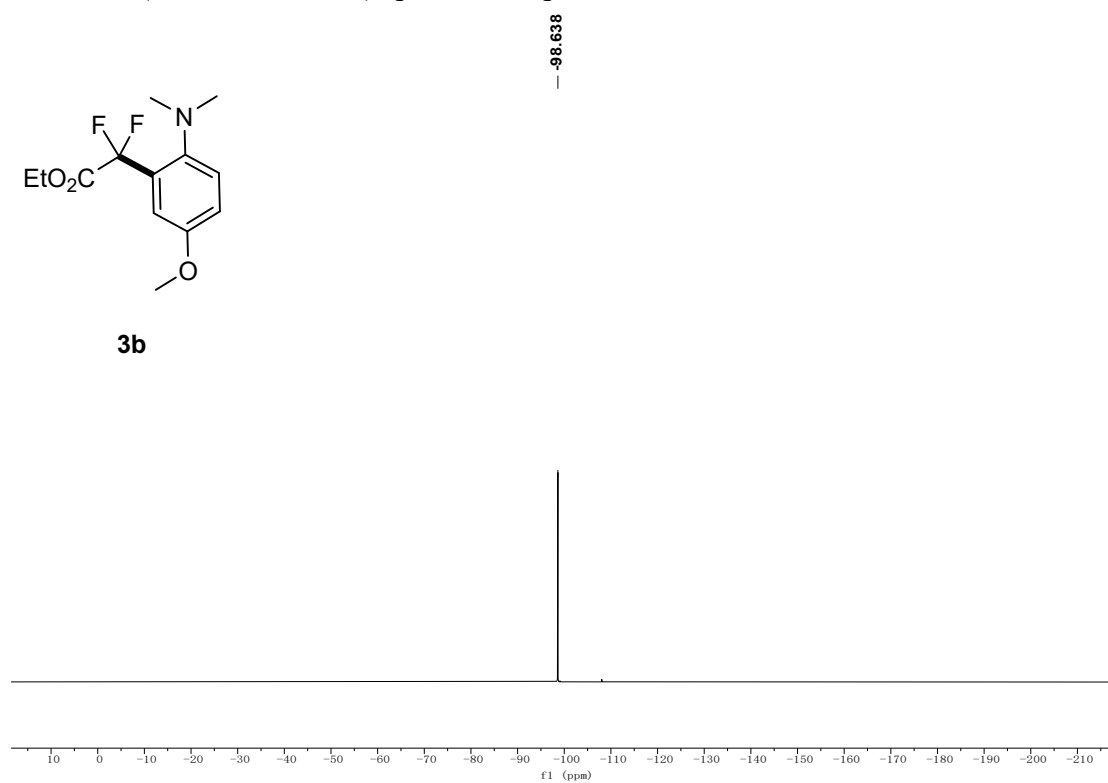




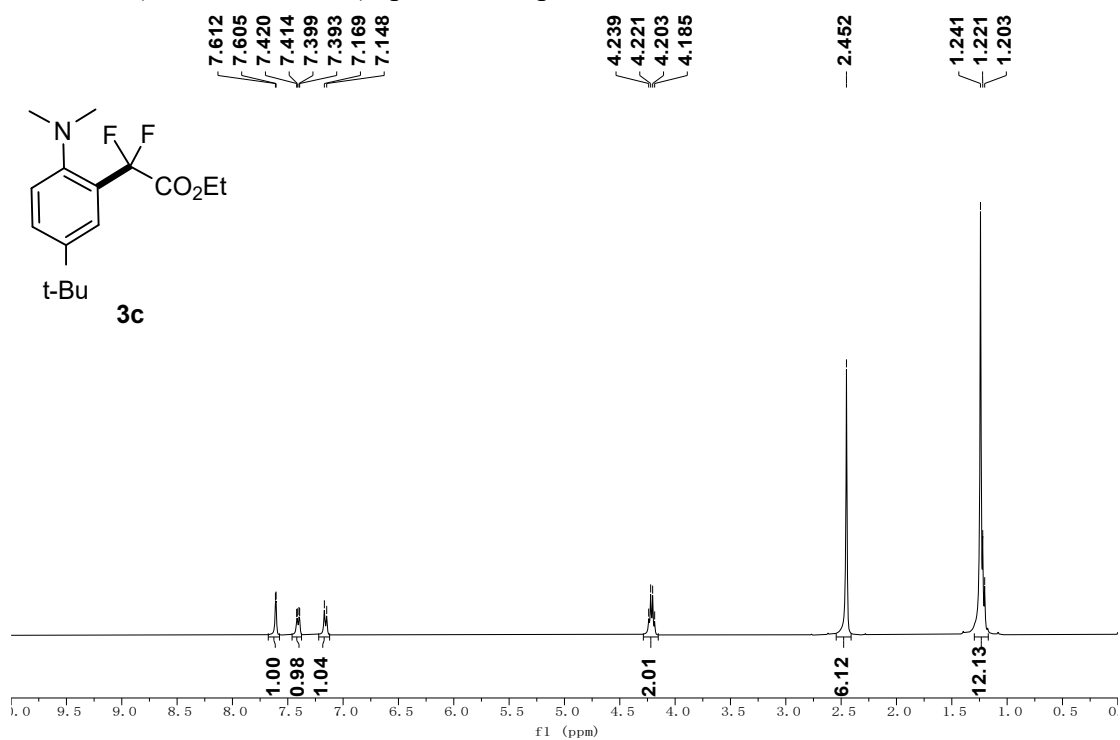
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3b**



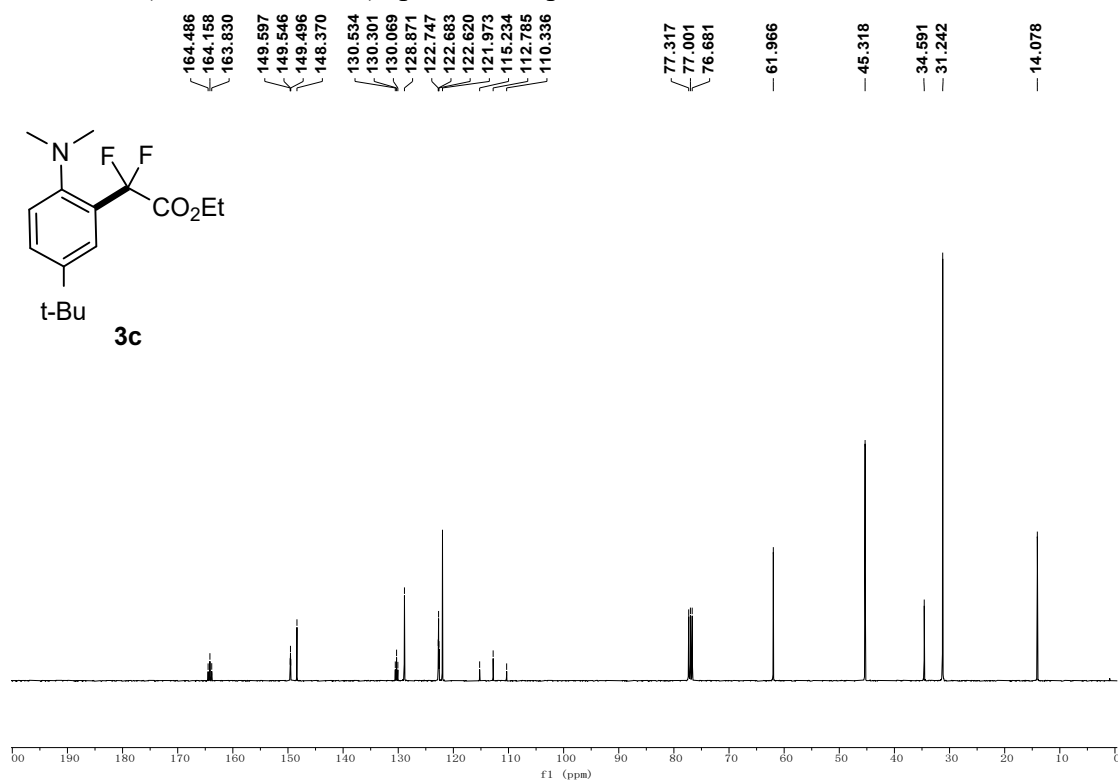
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3b**



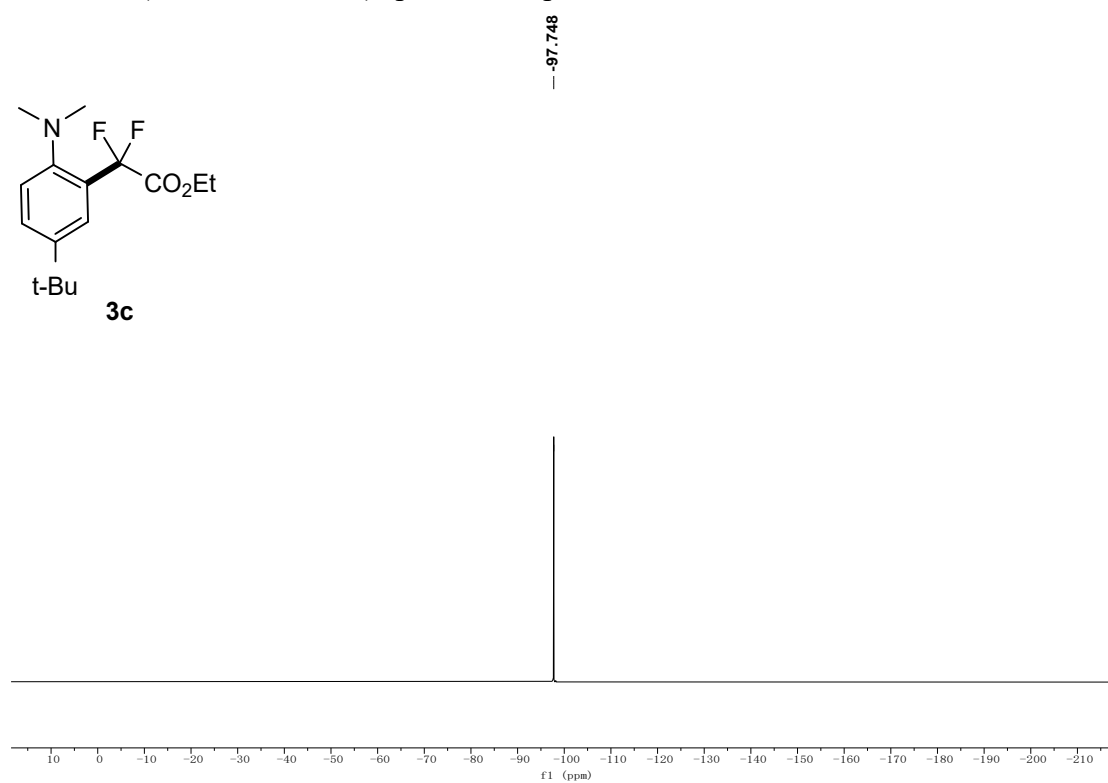
<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3c**



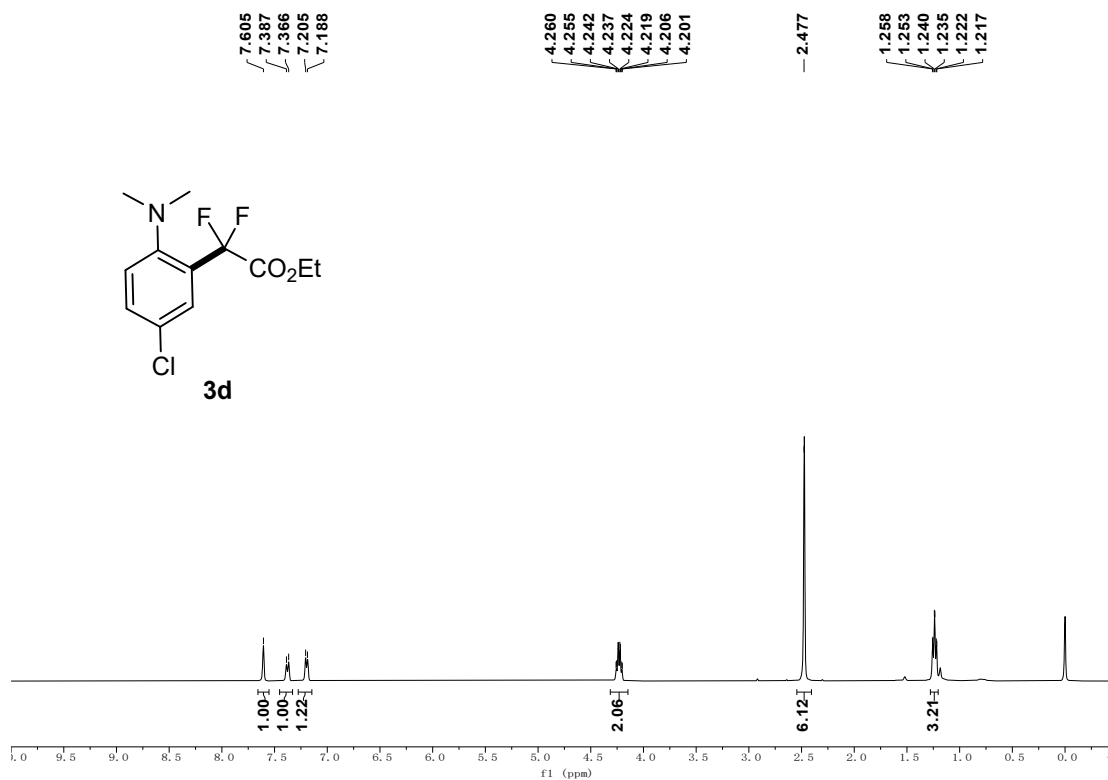
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3c**



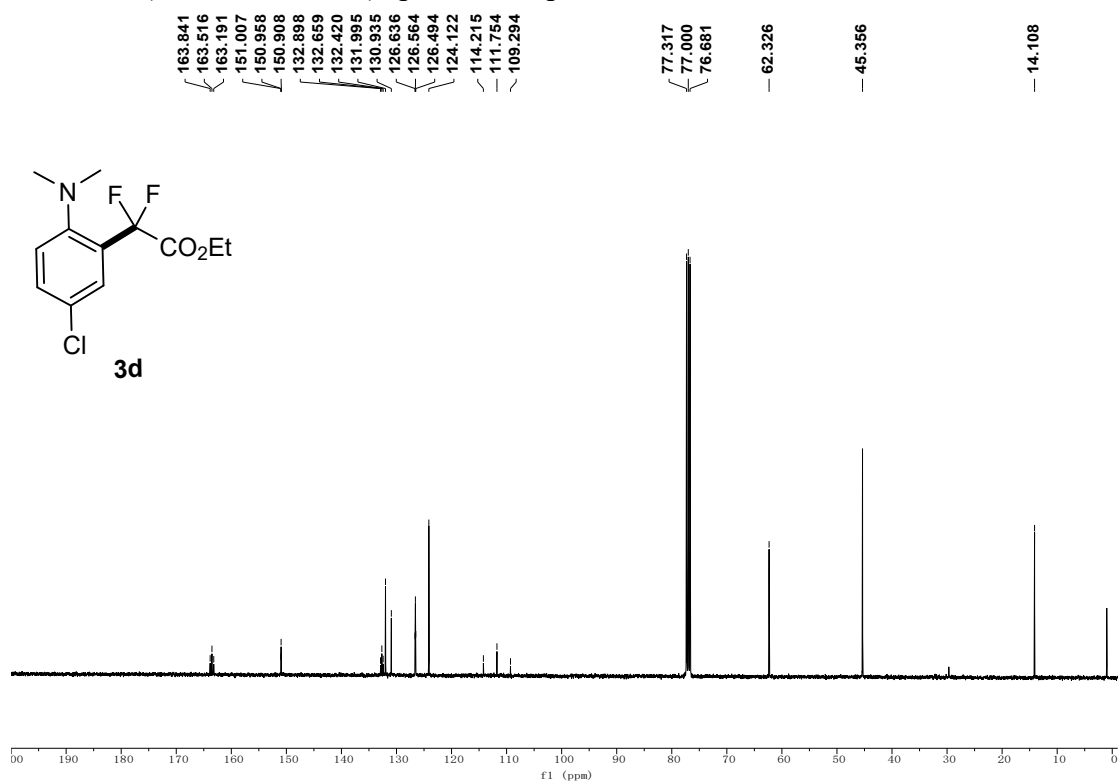
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3c**



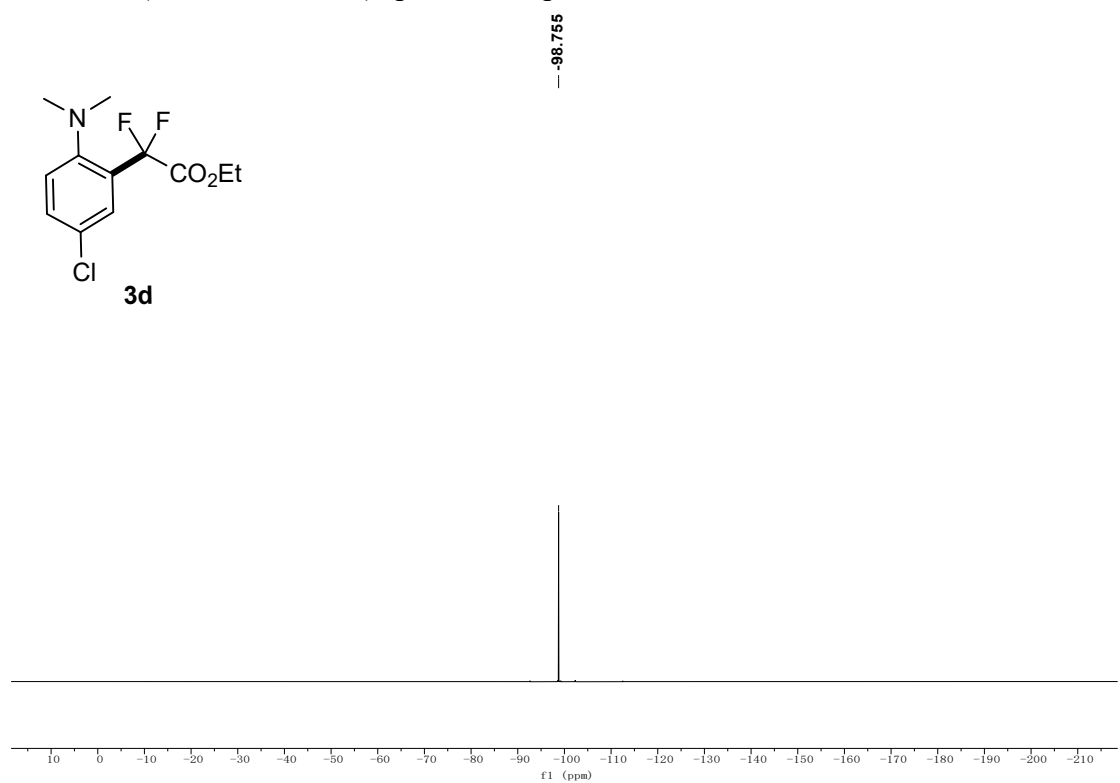
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3d**



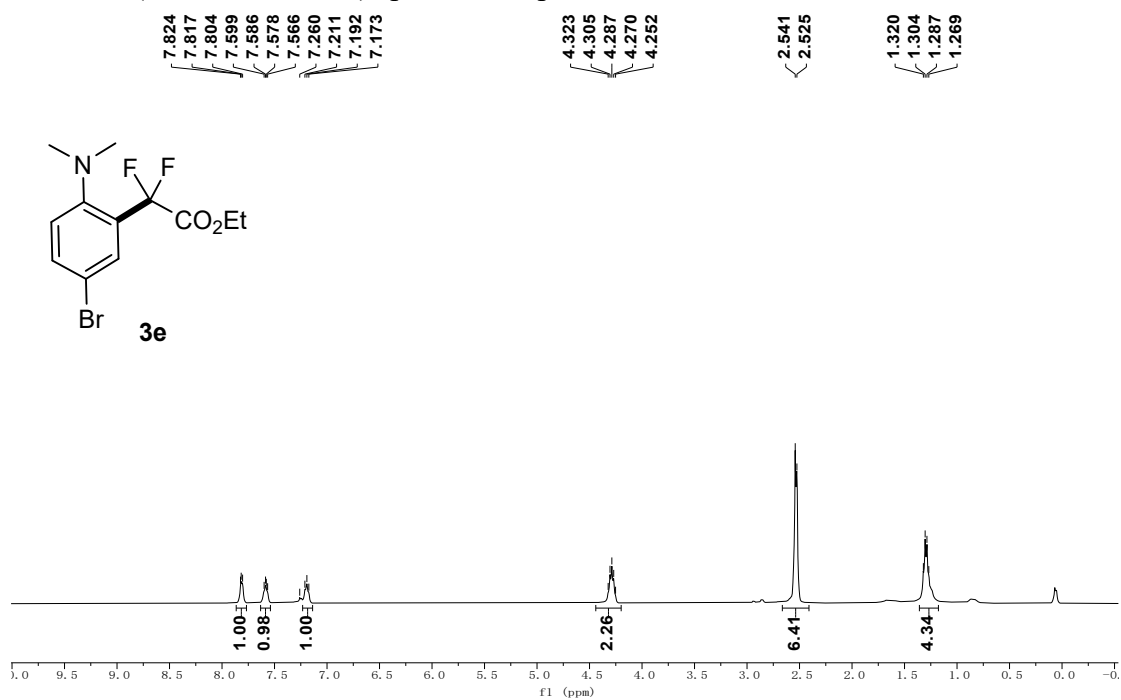
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3d**



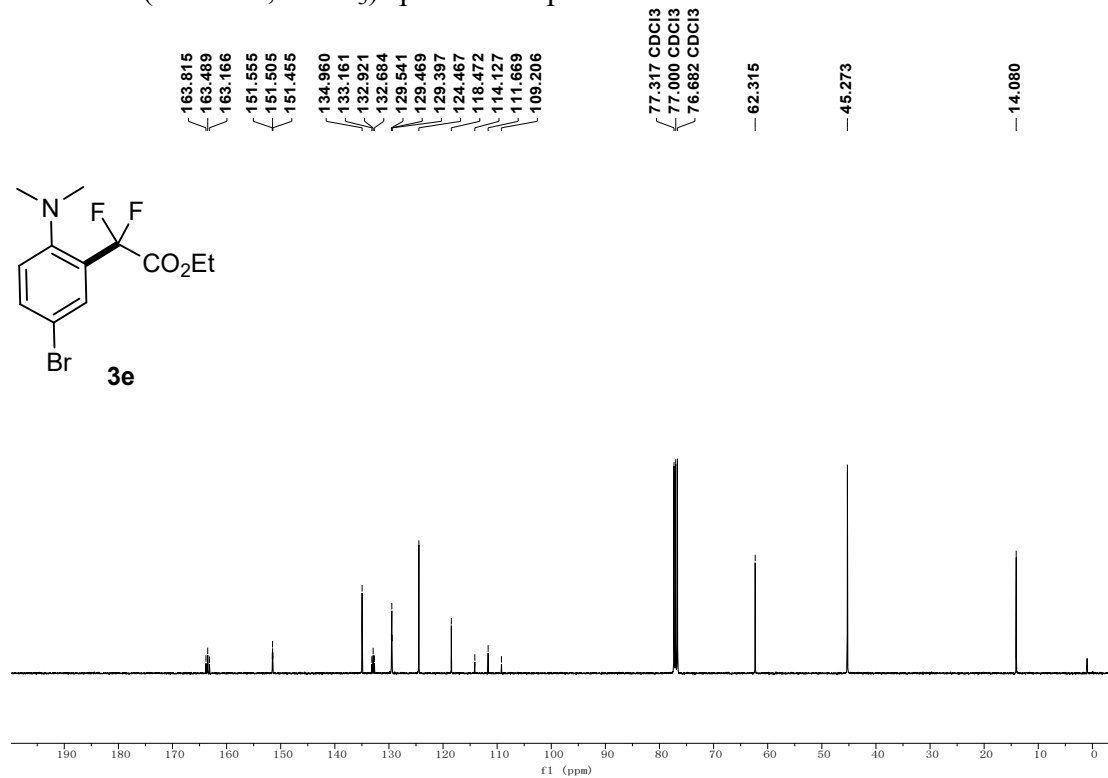
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3d**



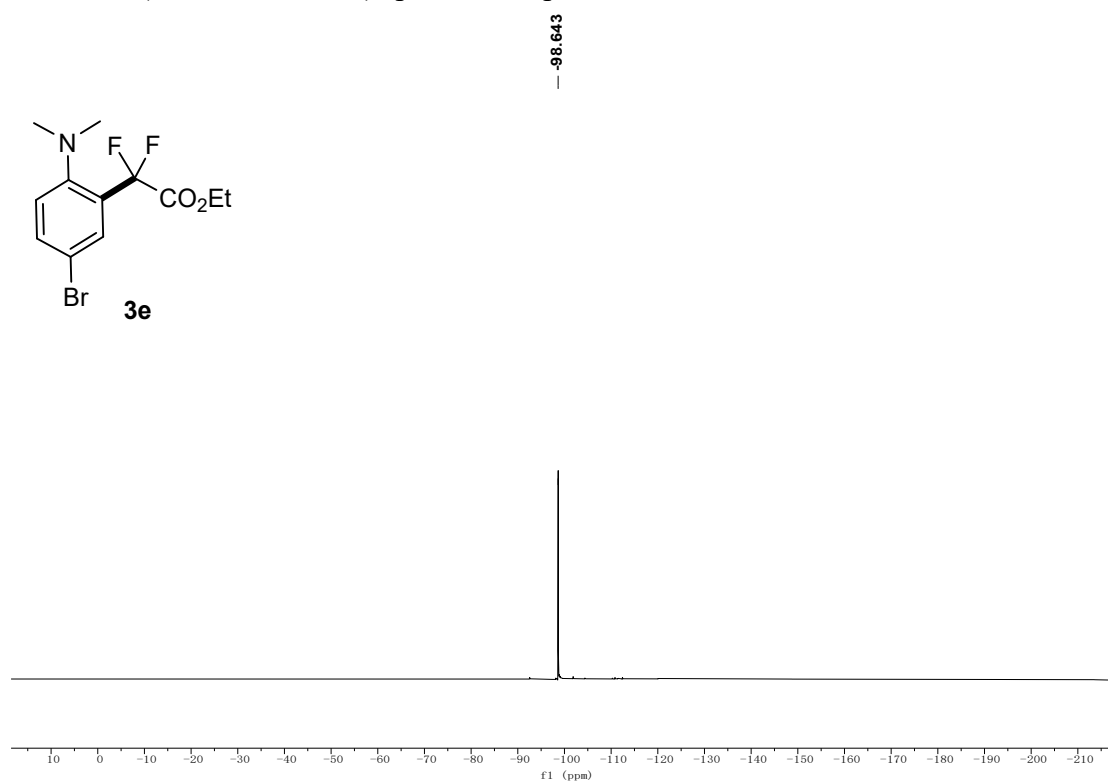
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3e**



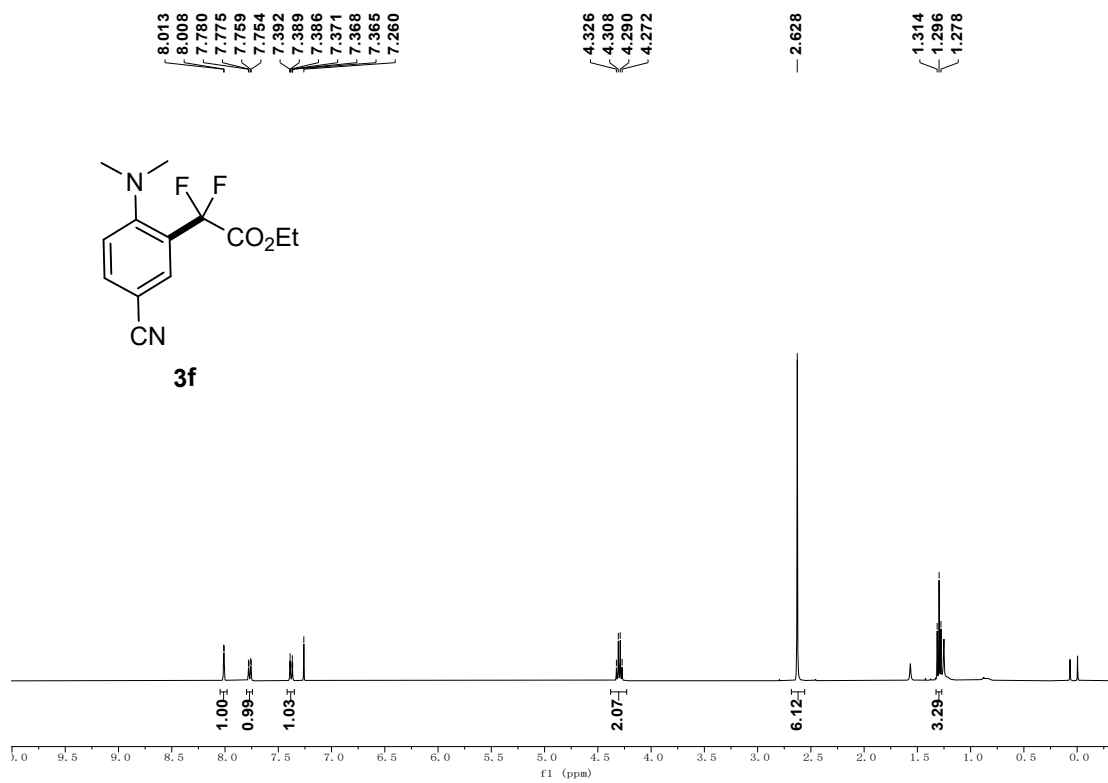
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3e**



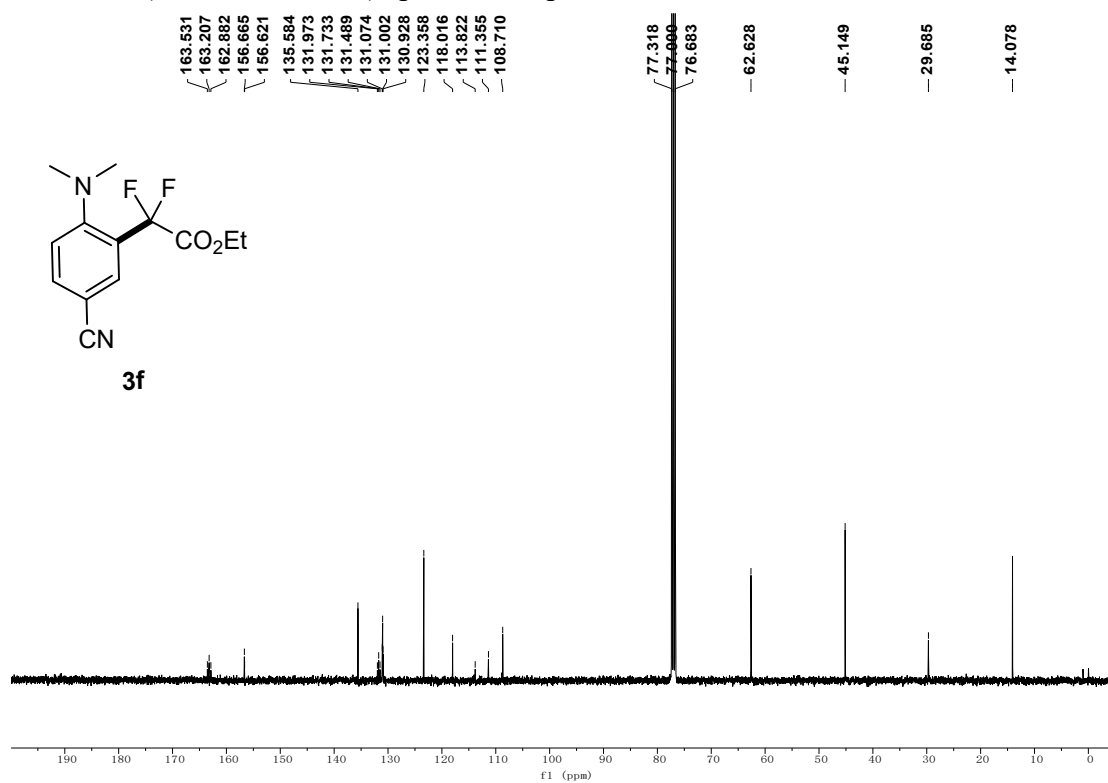
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3e**



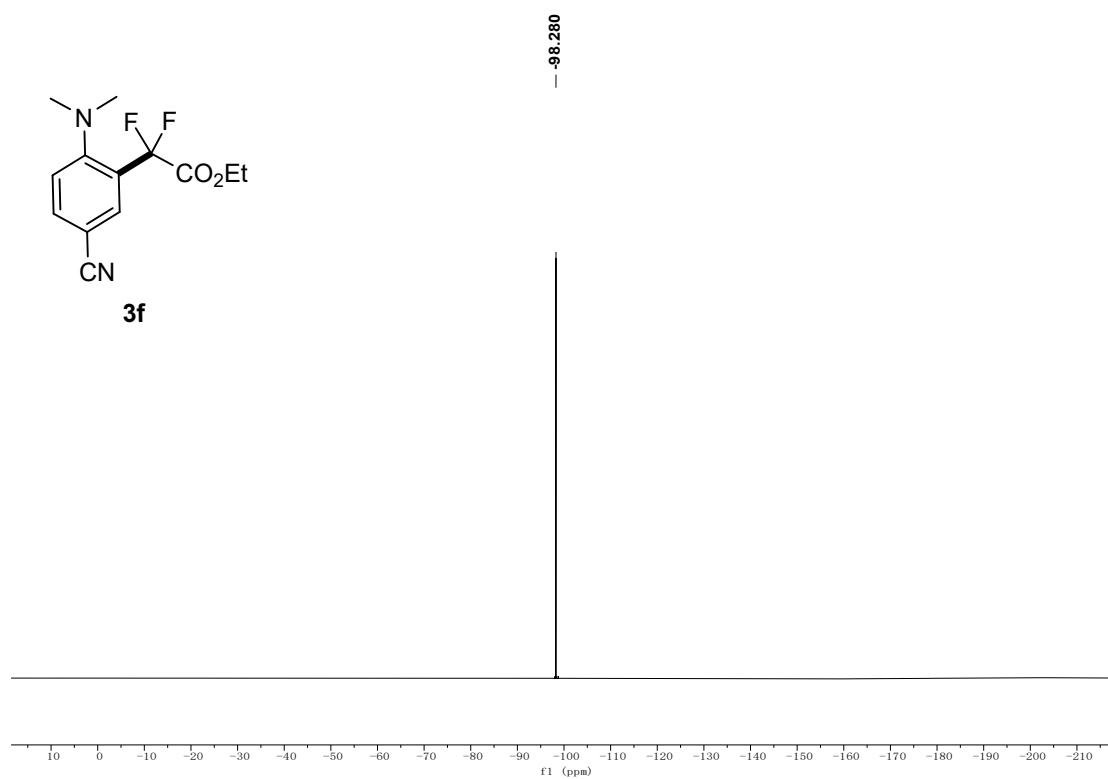
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3f**



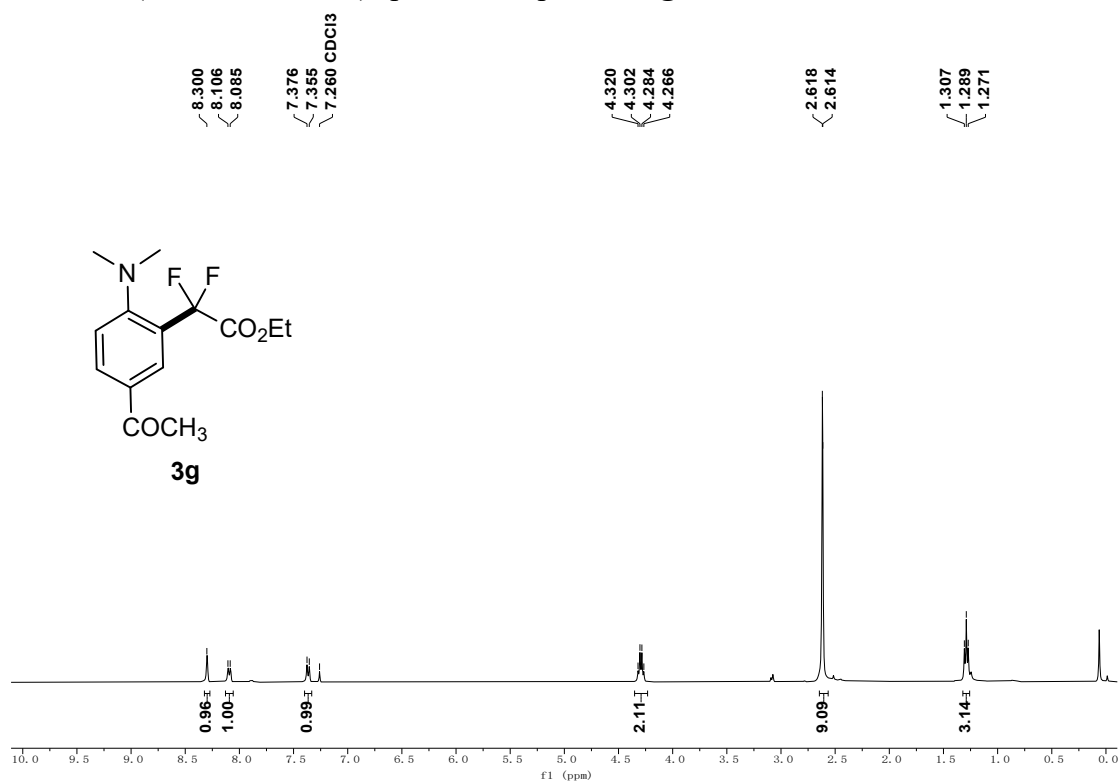
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3f**



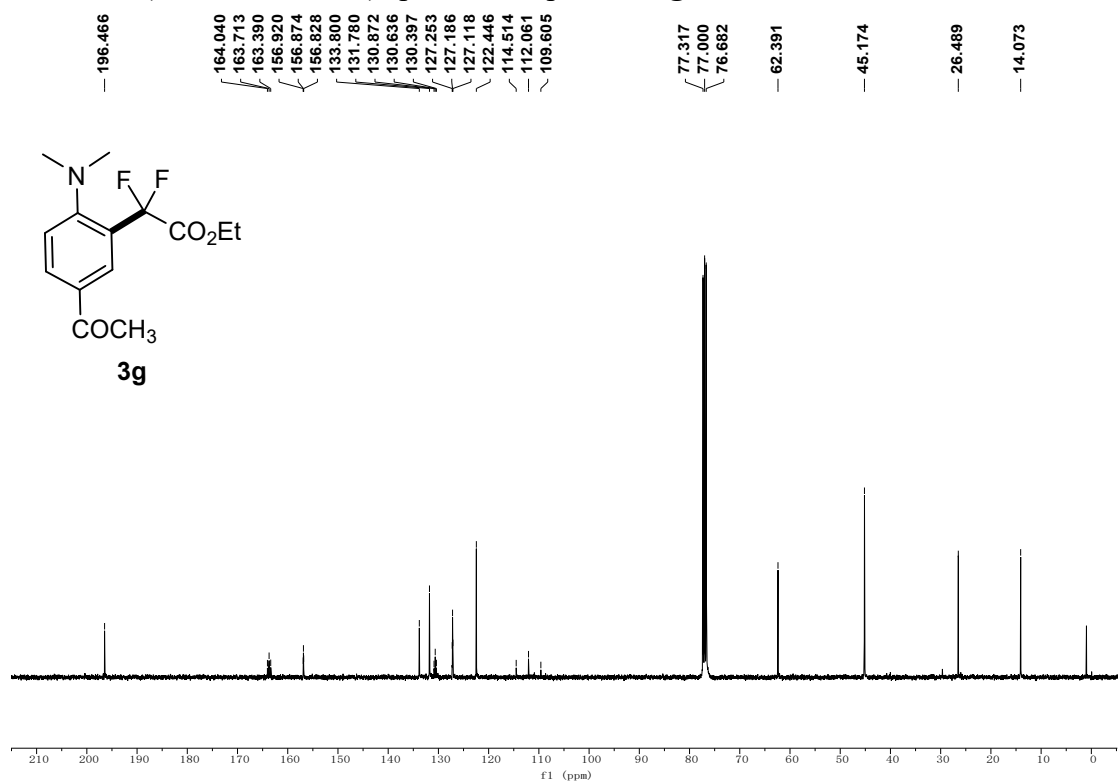
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3i**



<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3g**

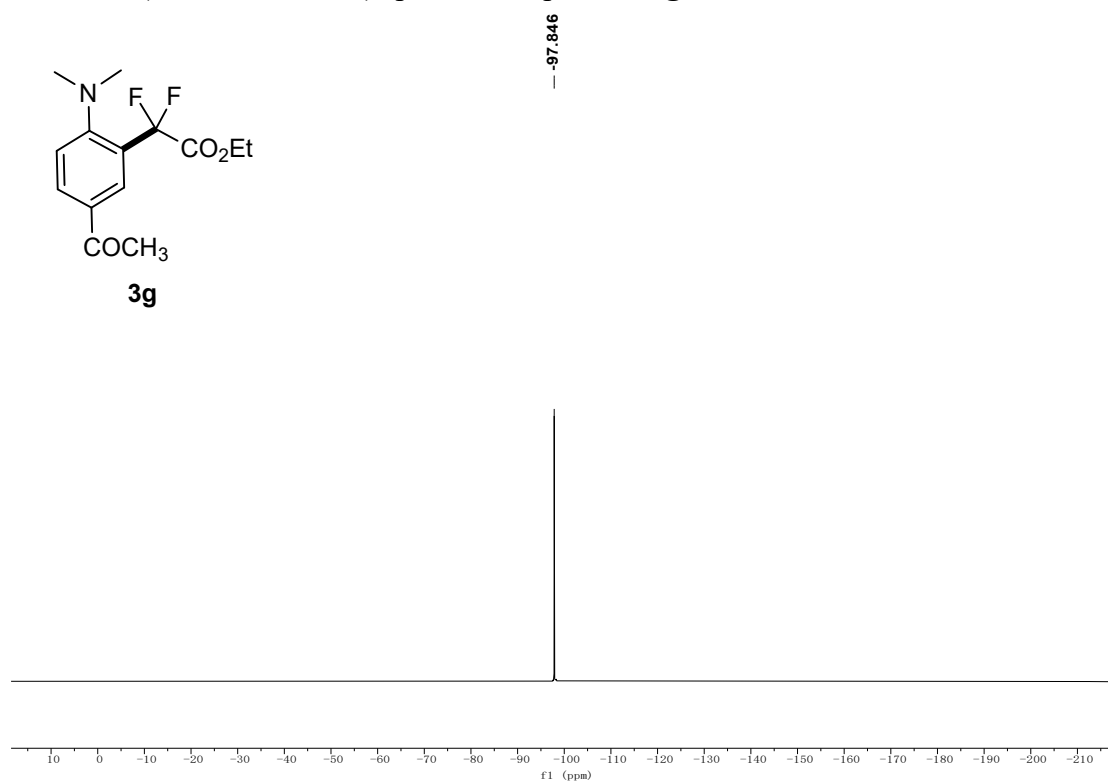


<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3g**

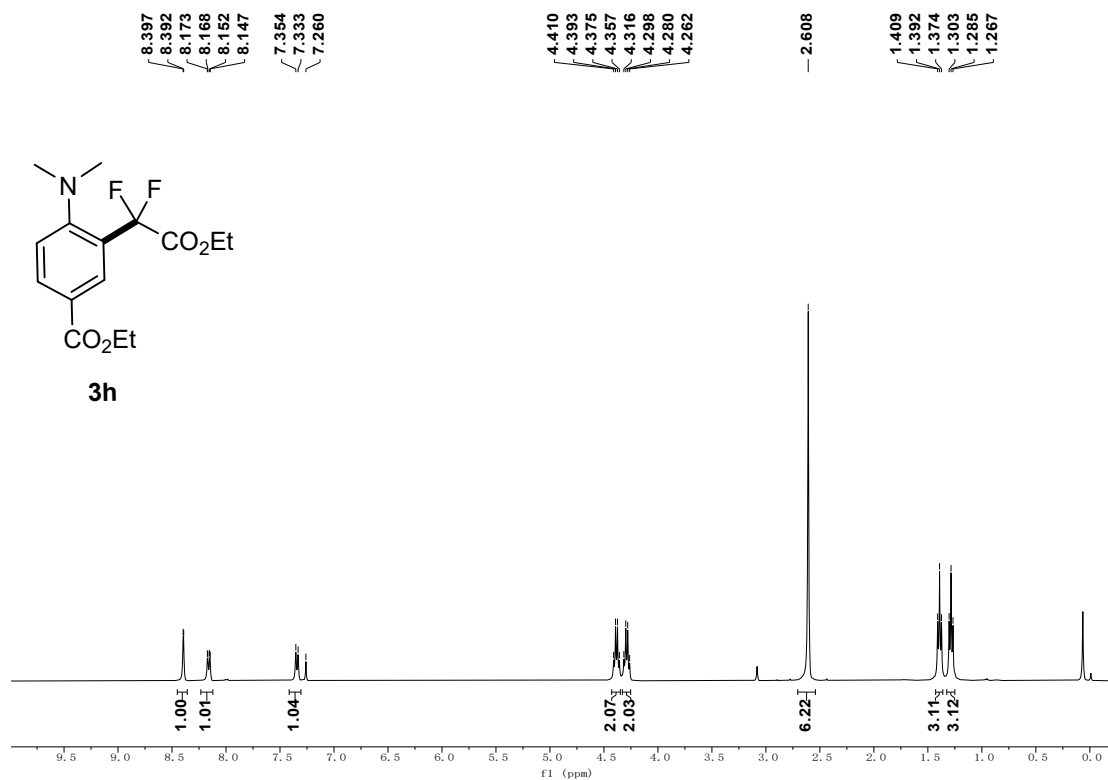




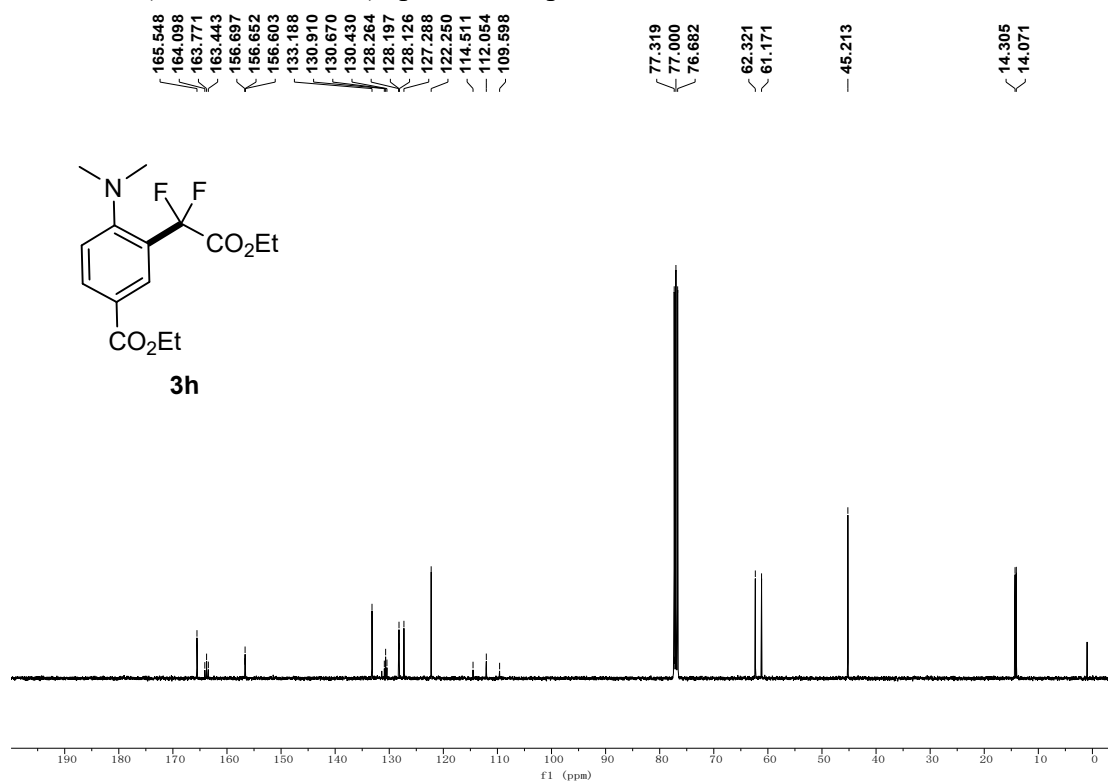
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3g**



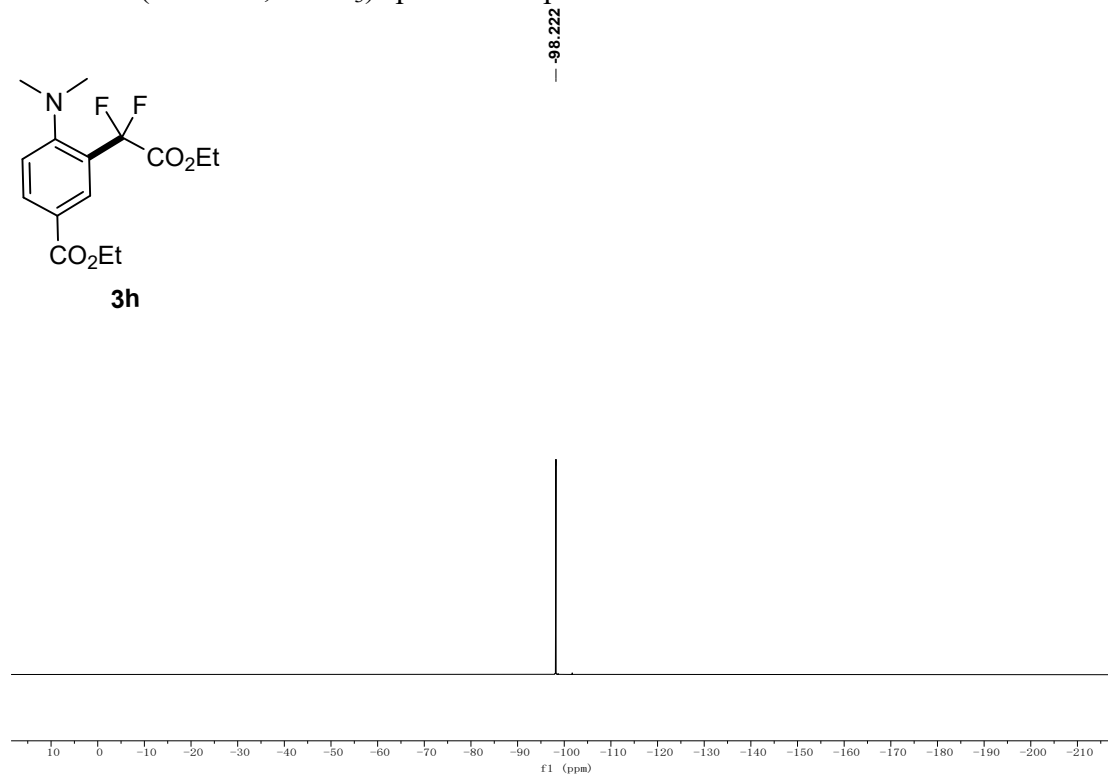
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3h**



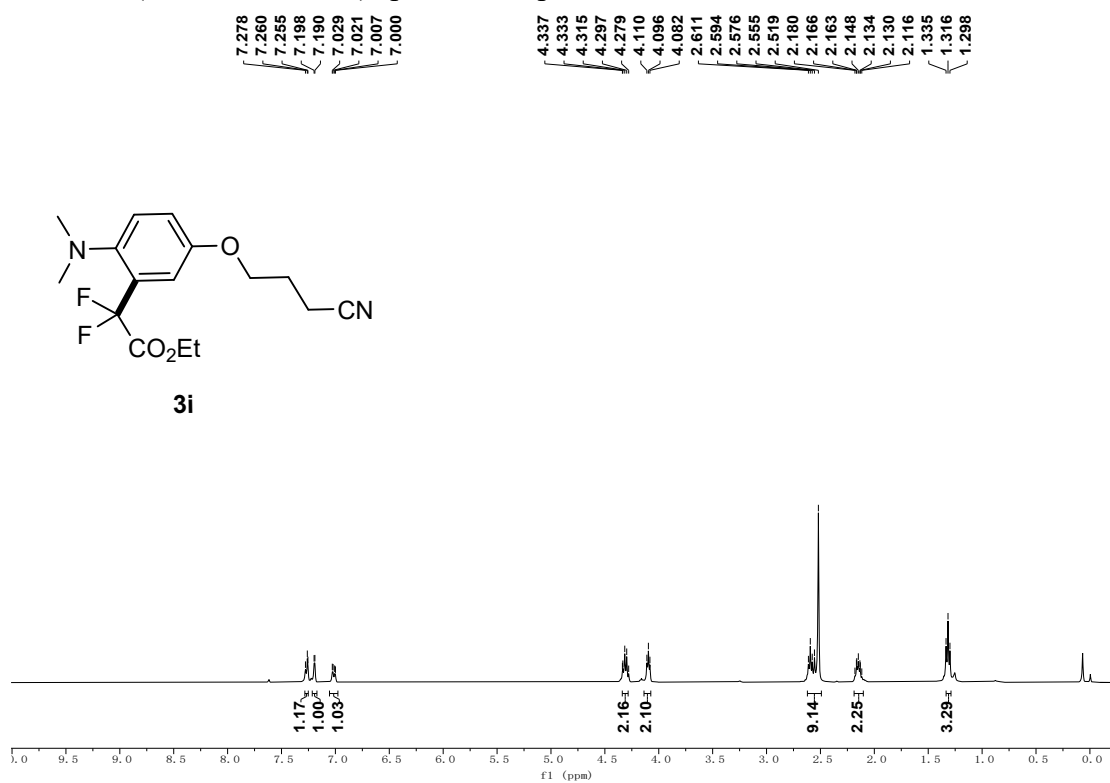
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3h**



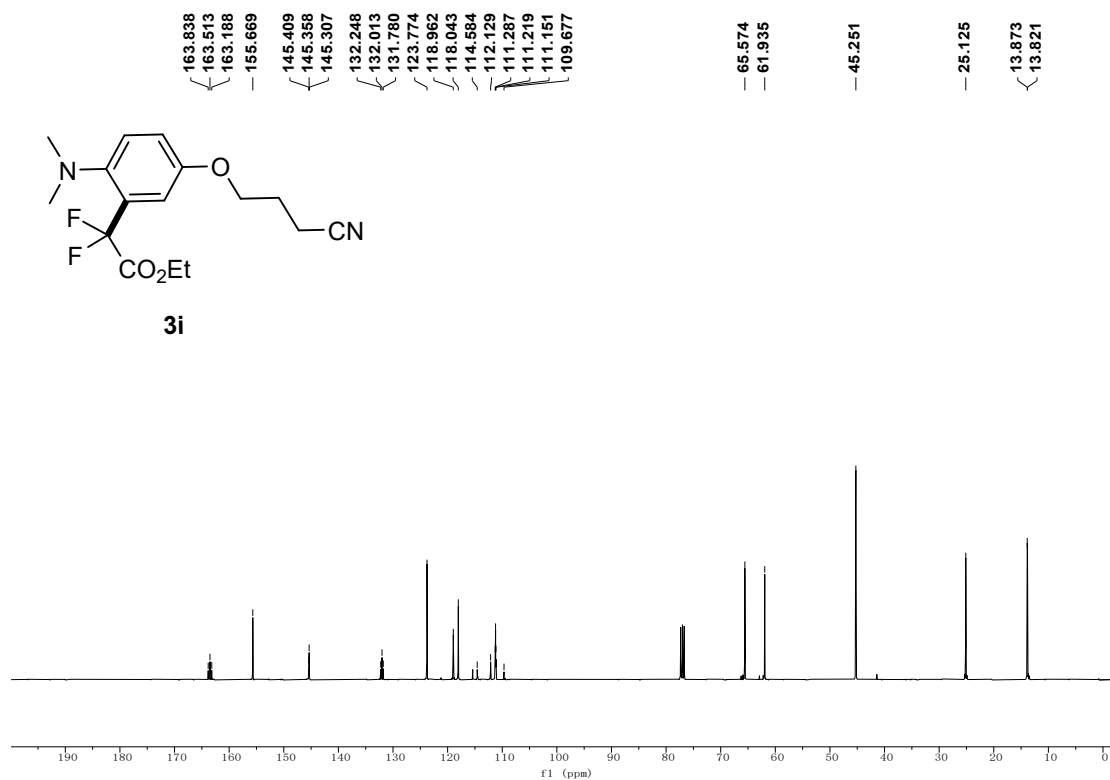
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3h**



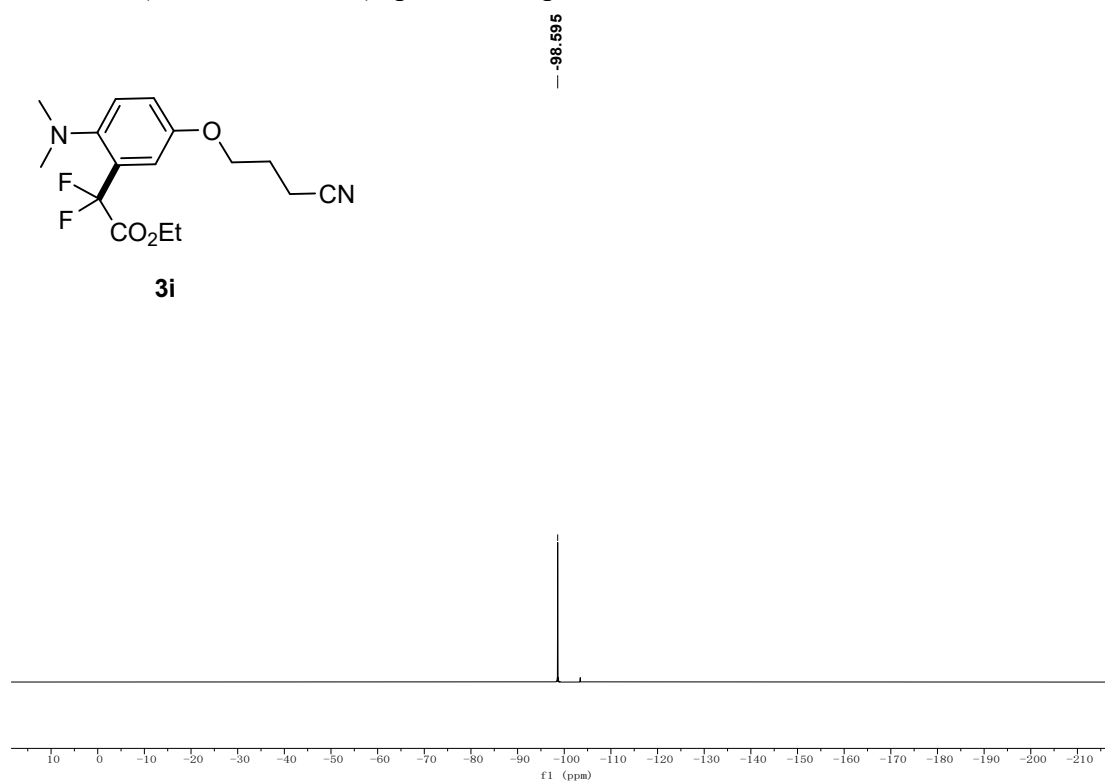
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3i**



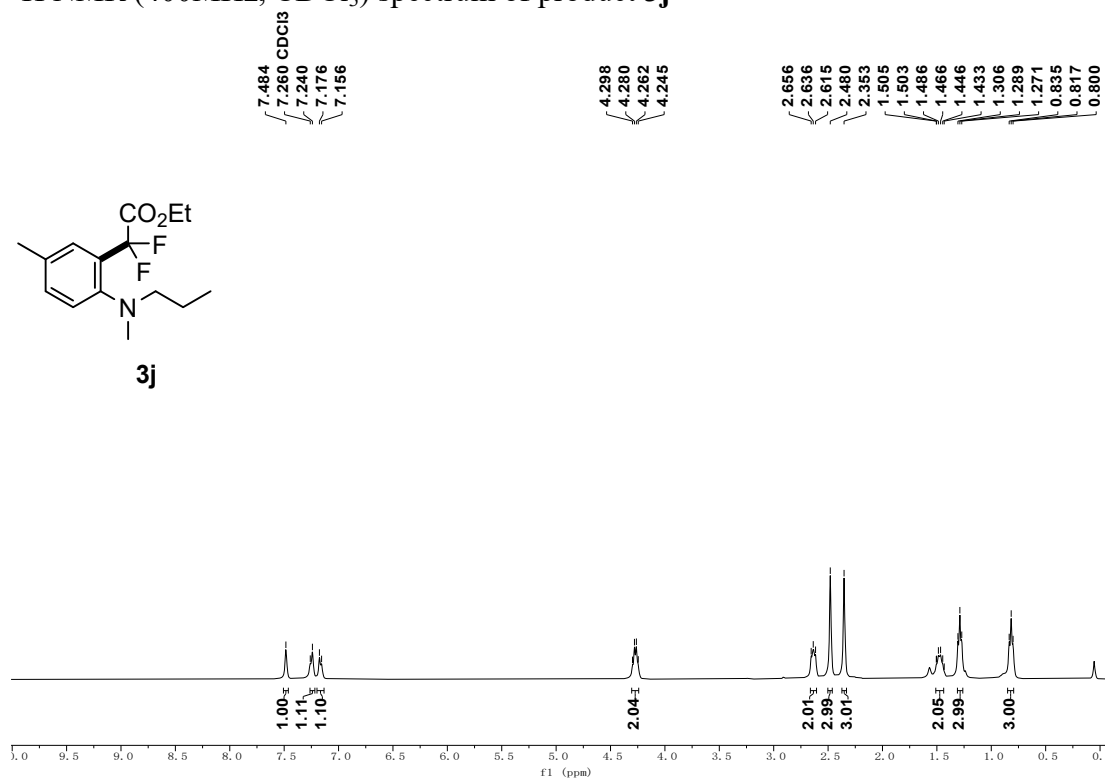
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3i**



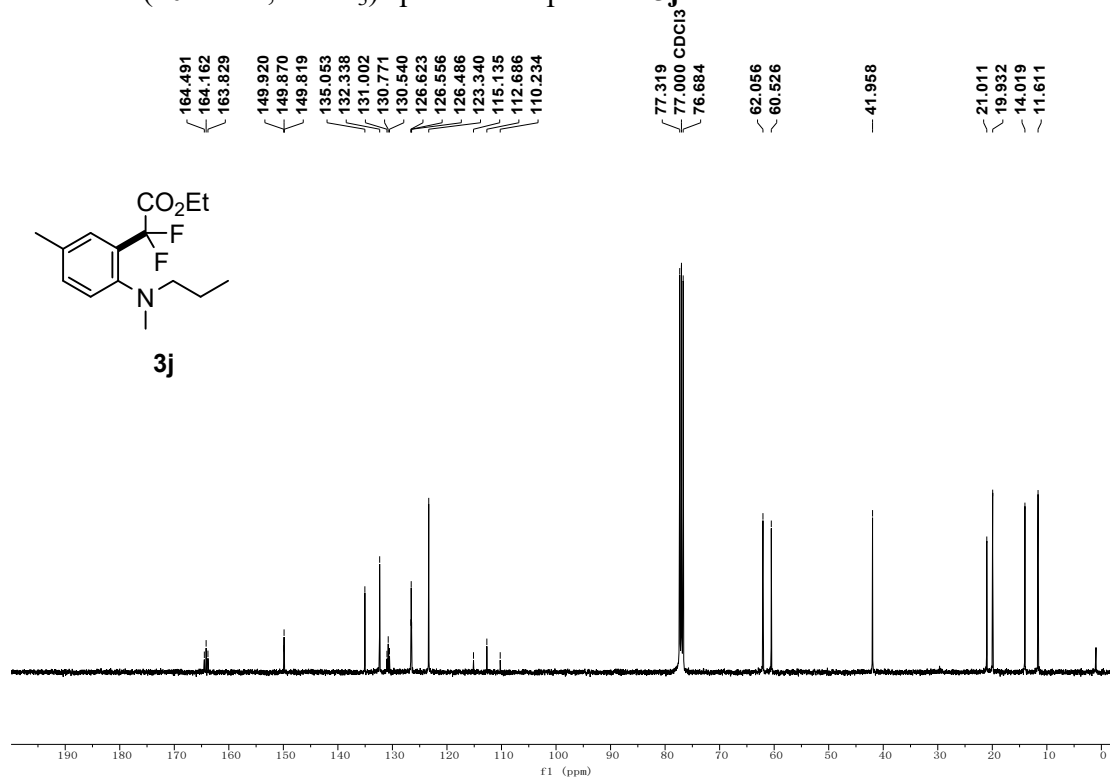
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3i**



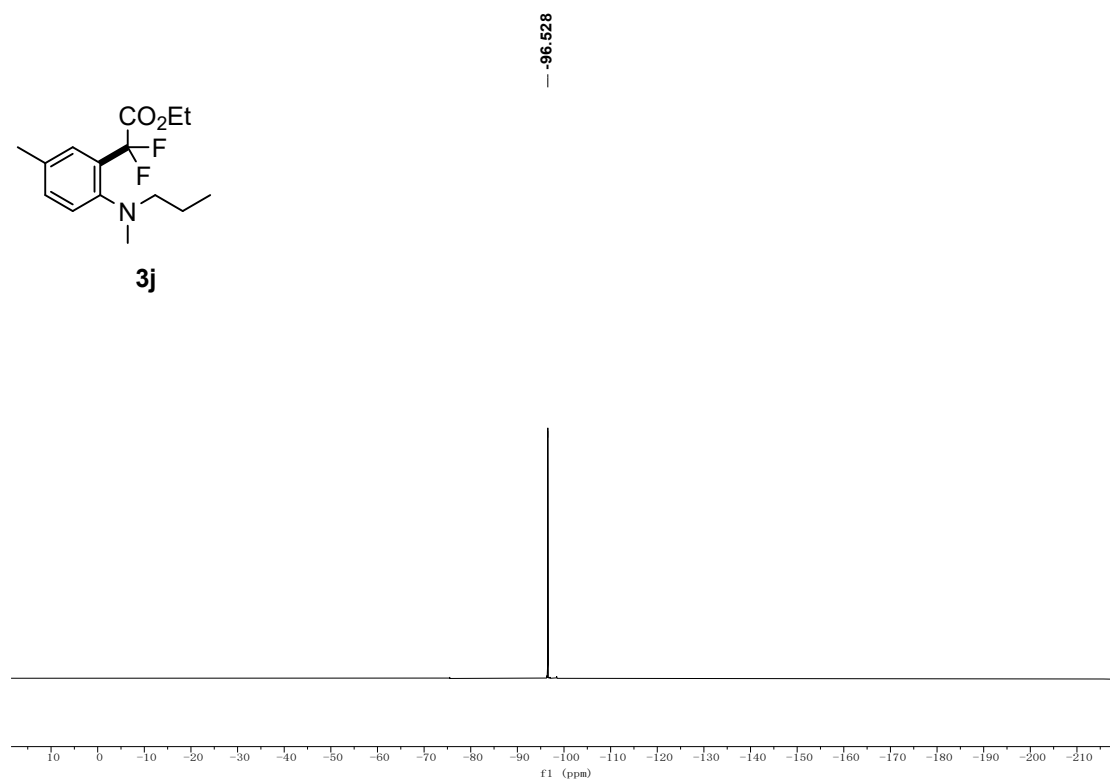
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3j**



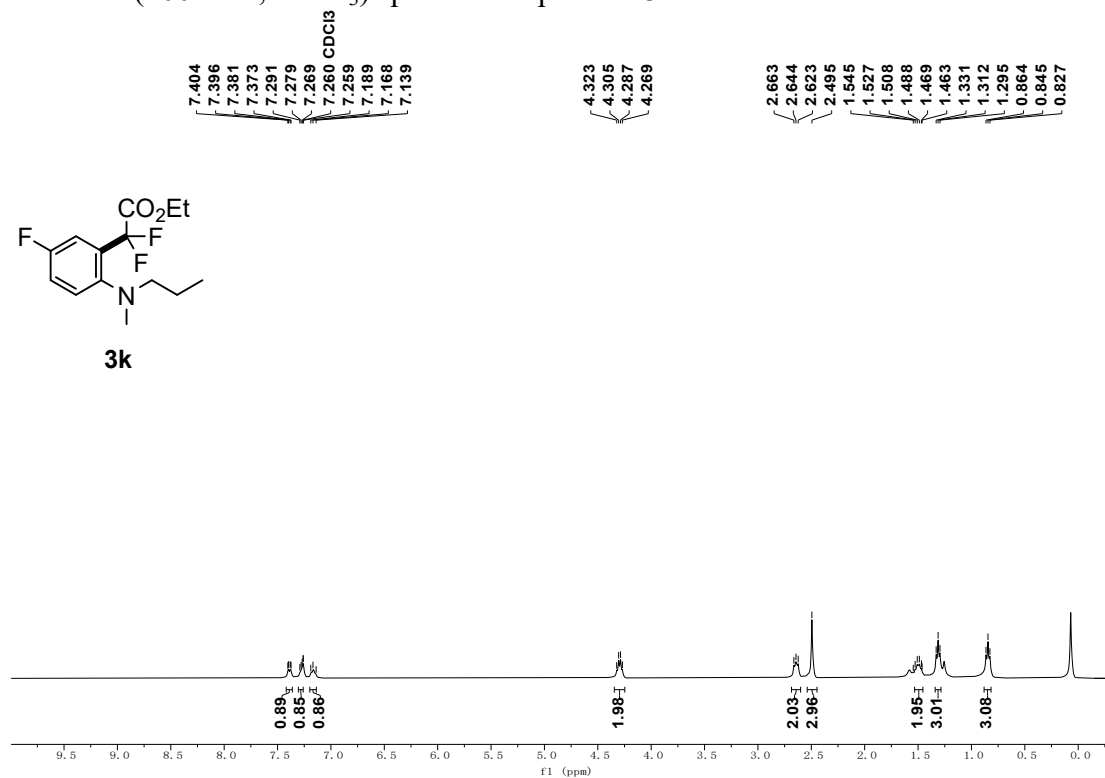
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3j**



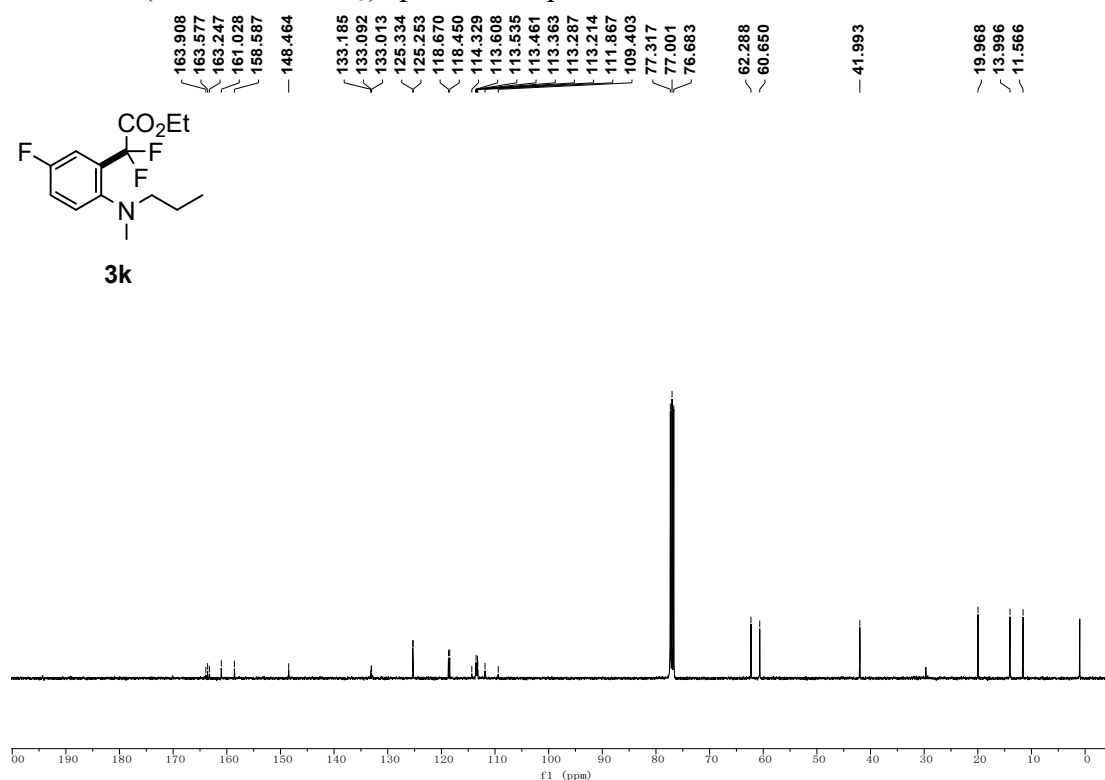
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3j**



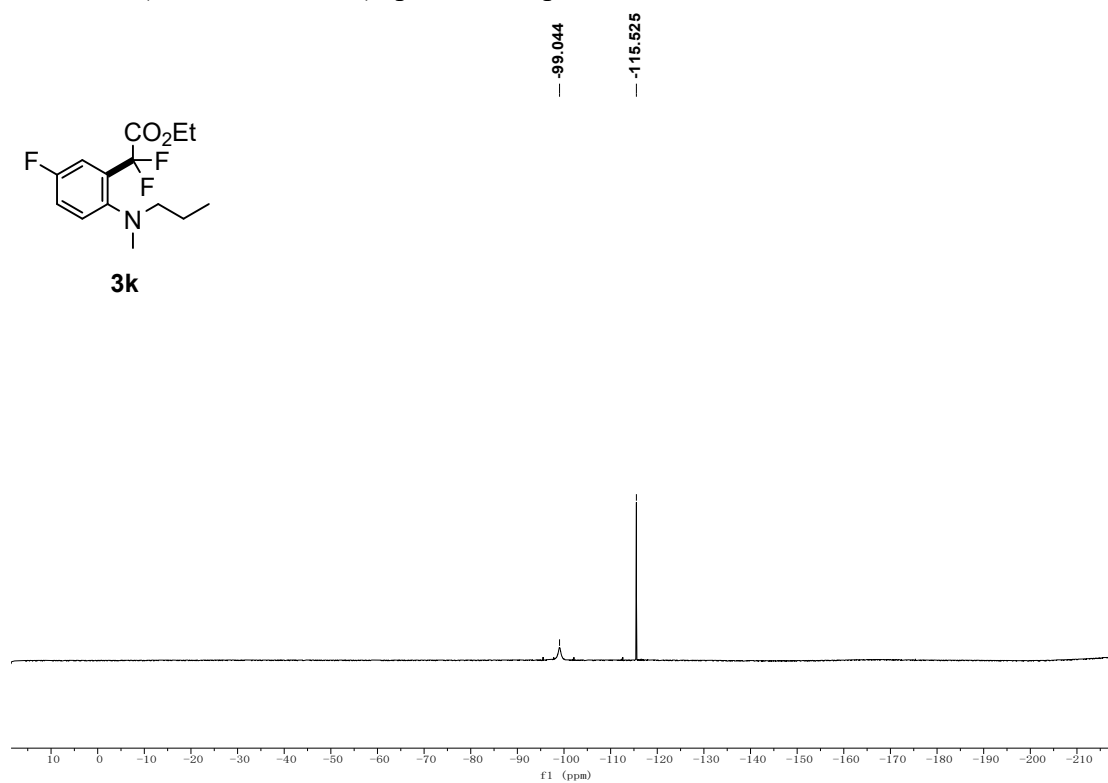
<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3k**



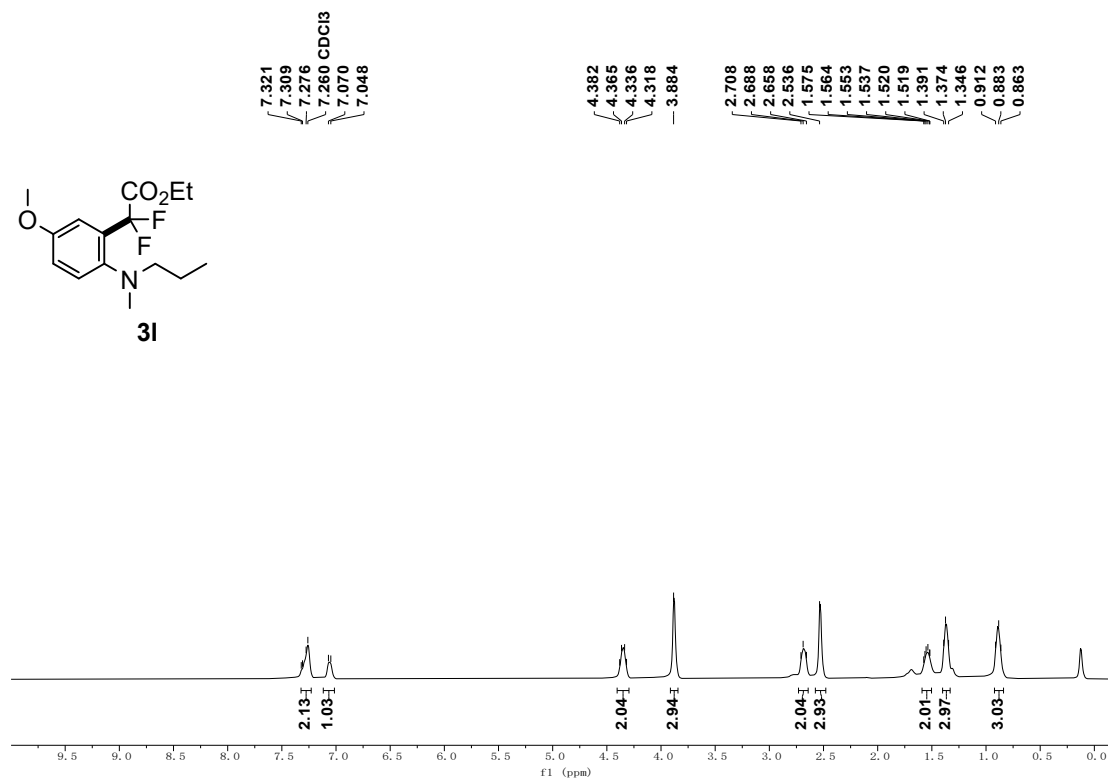
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3k**



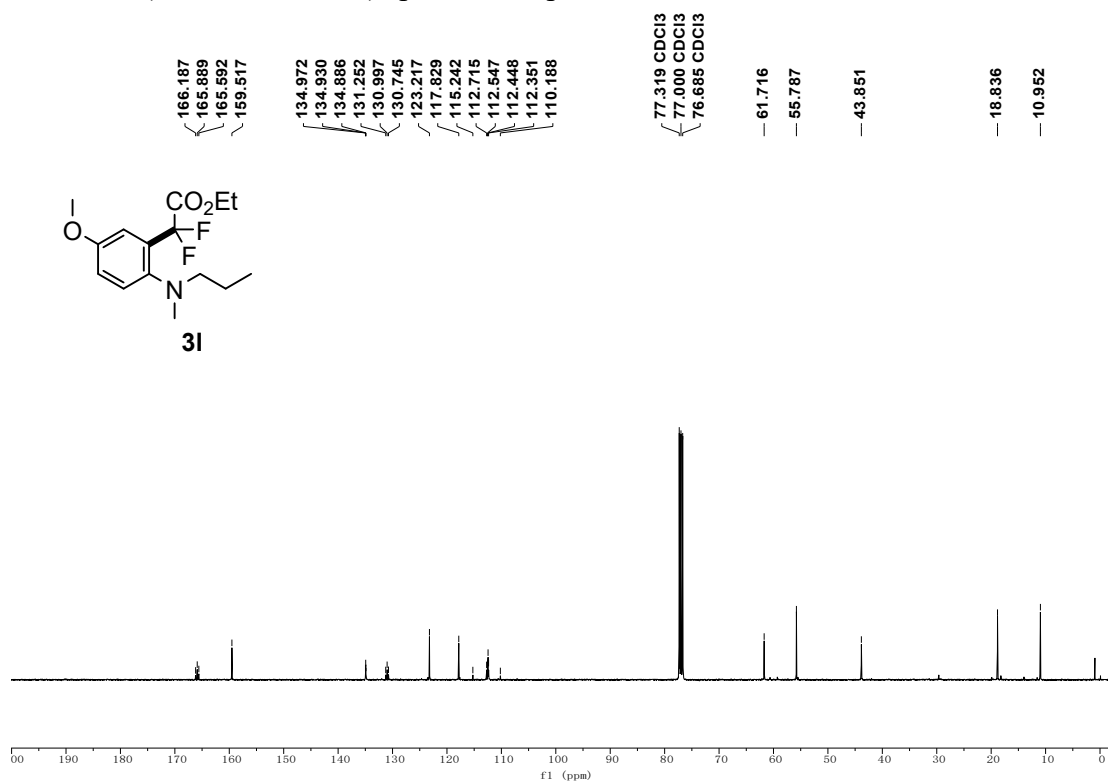
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3k**



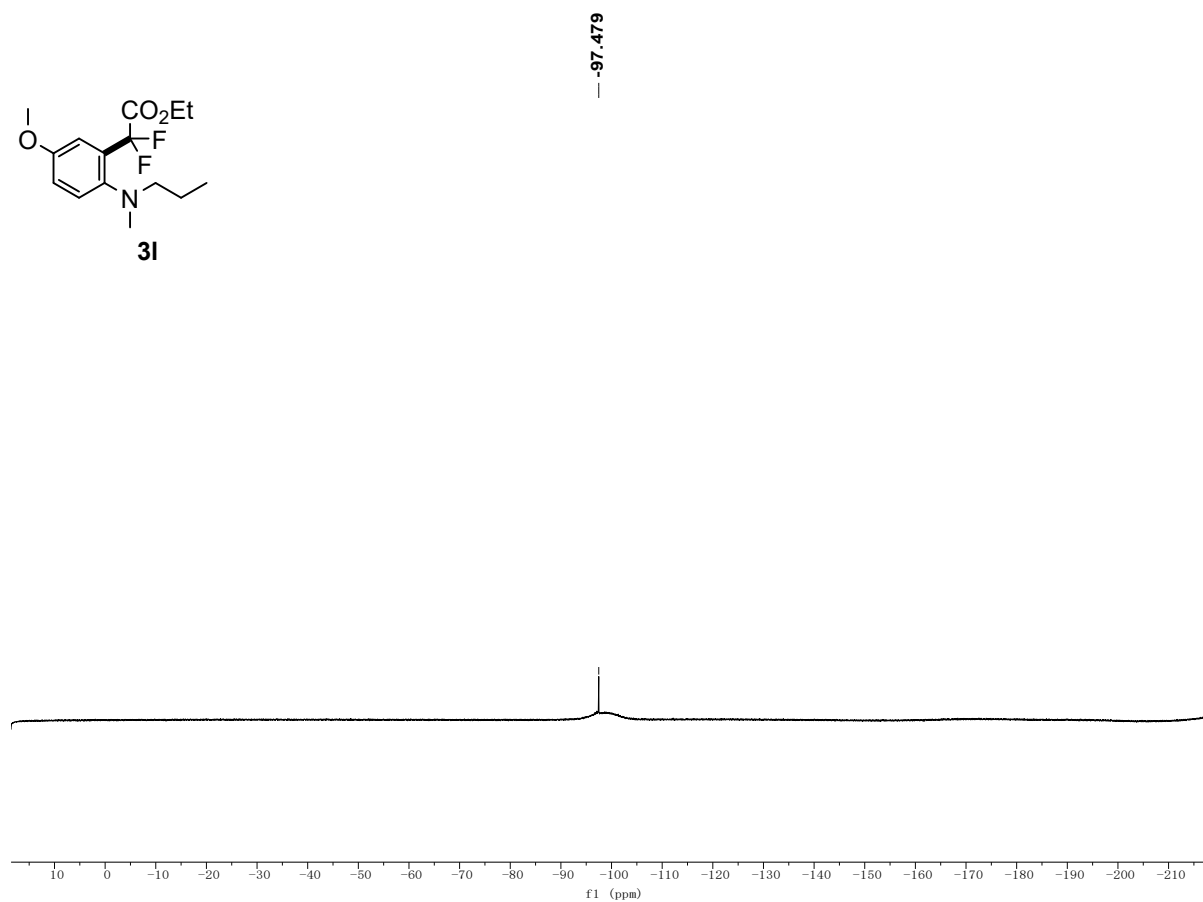
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3l**



$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **31**

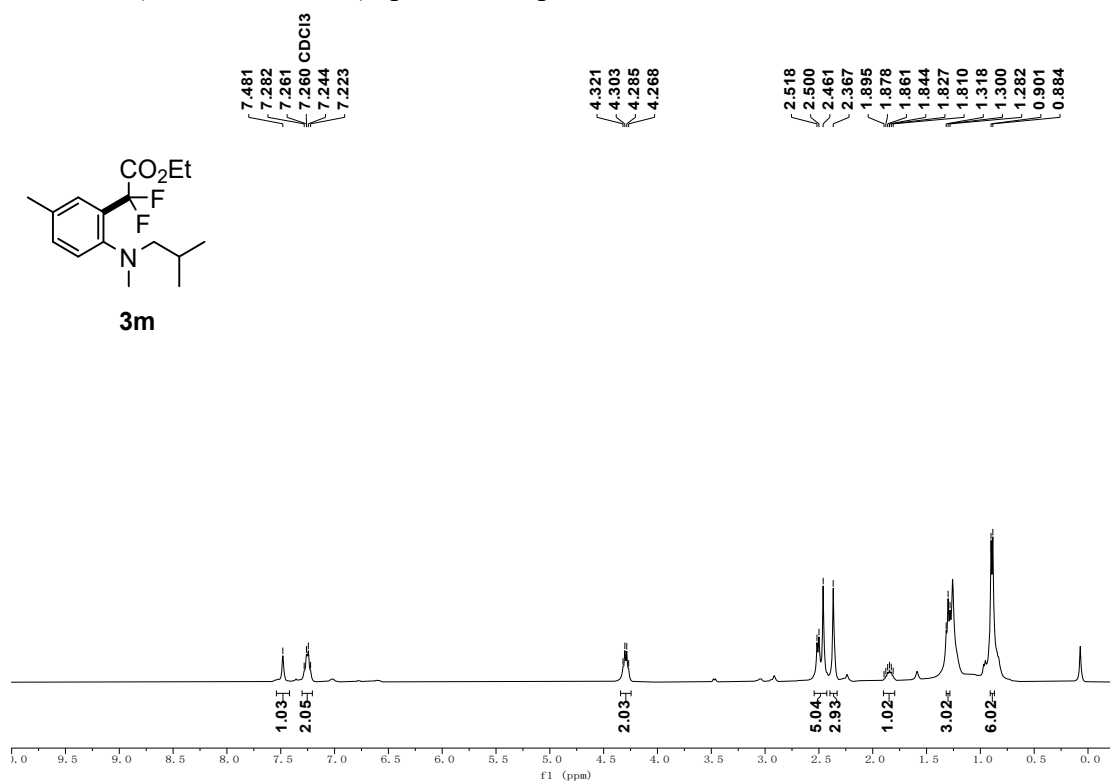


$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **31**

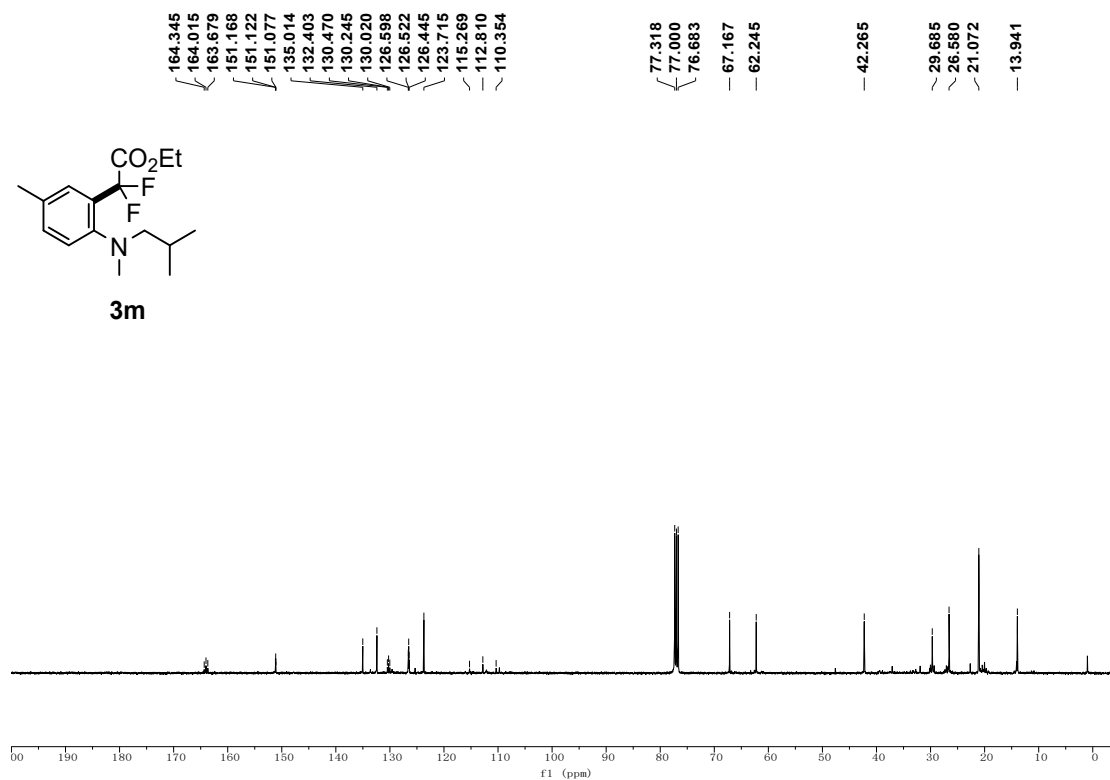




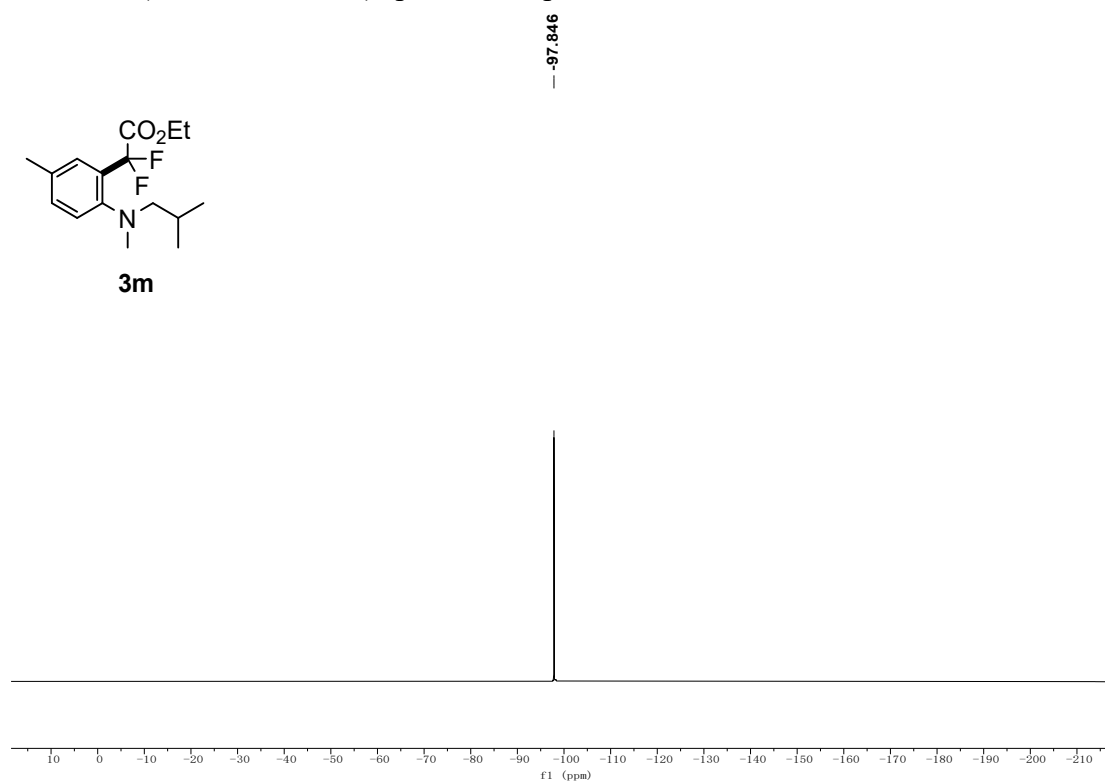
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3m**



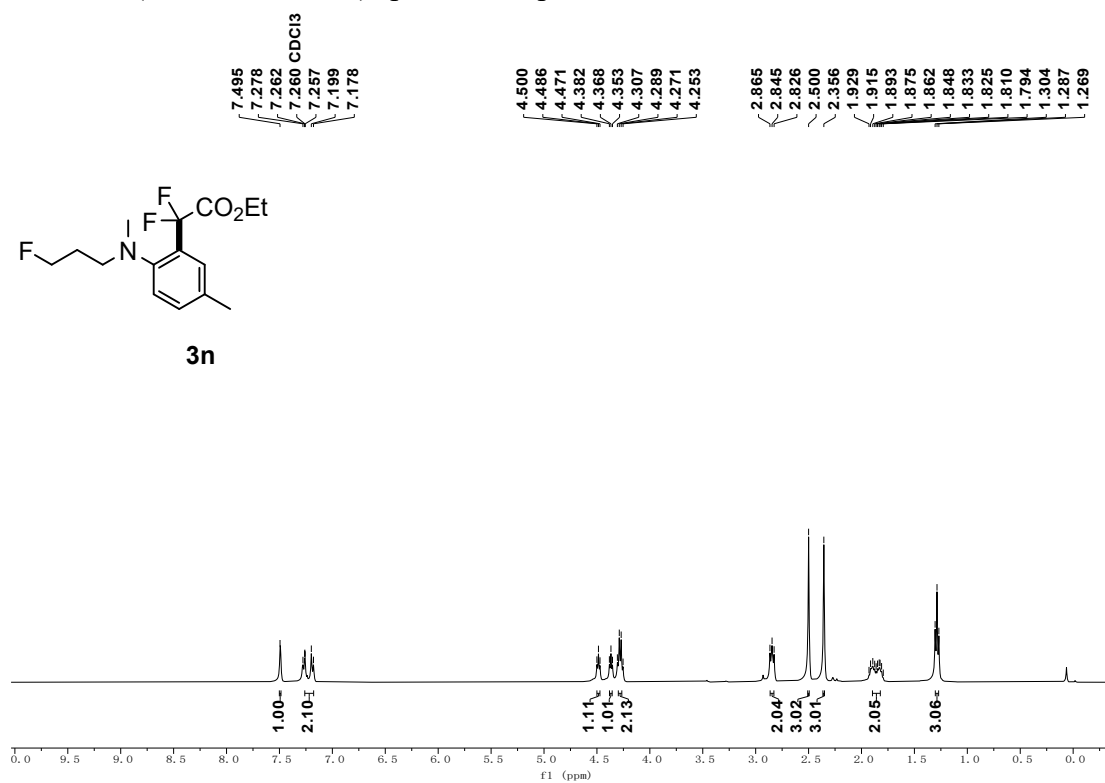
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3m**



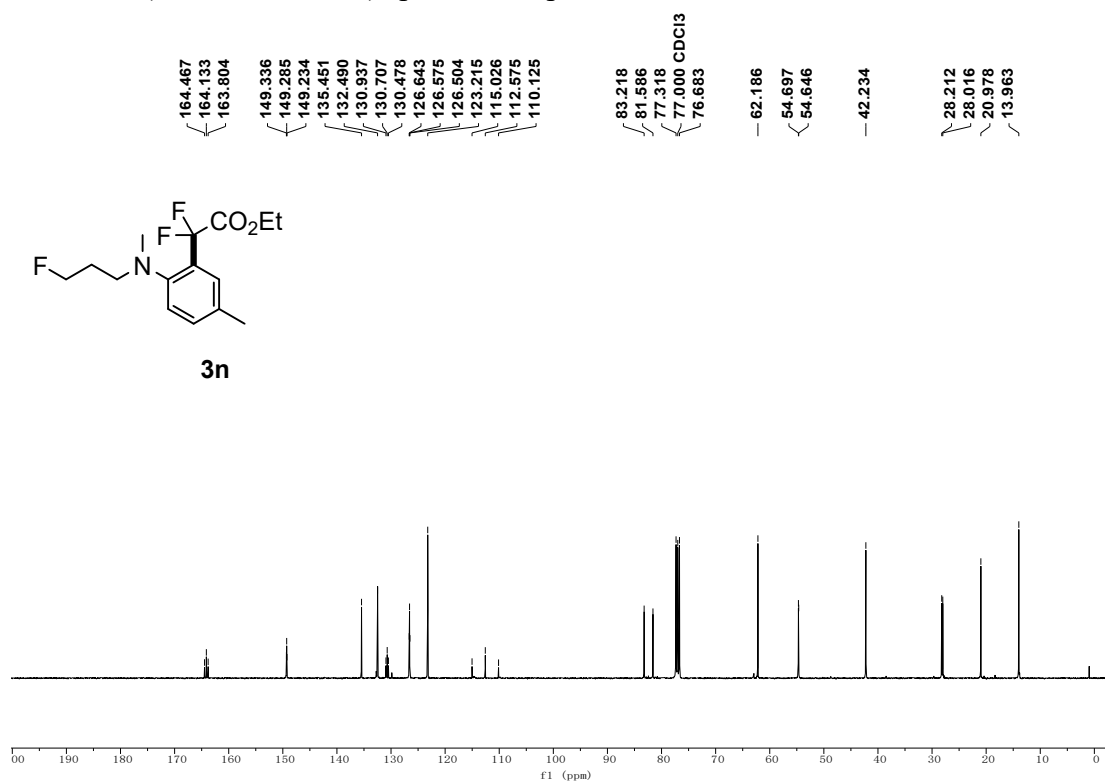
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3m**



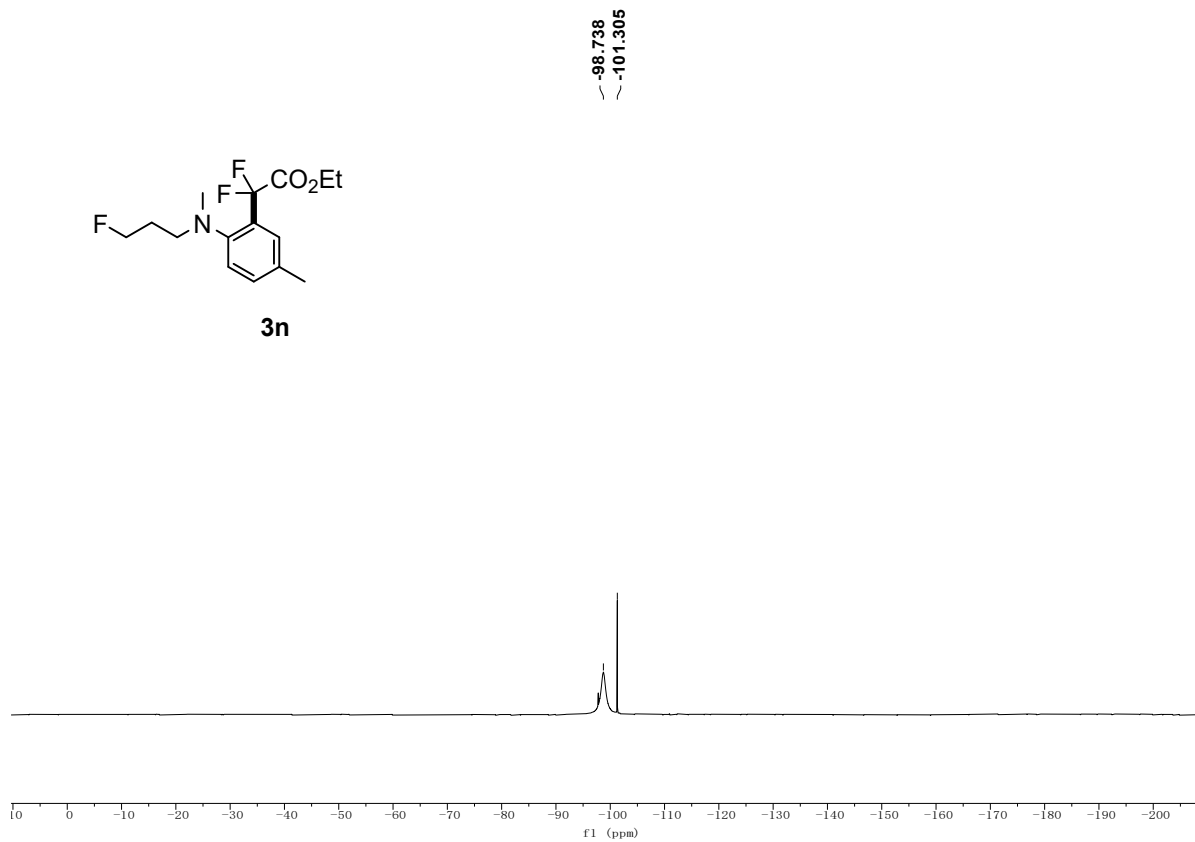
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3n**



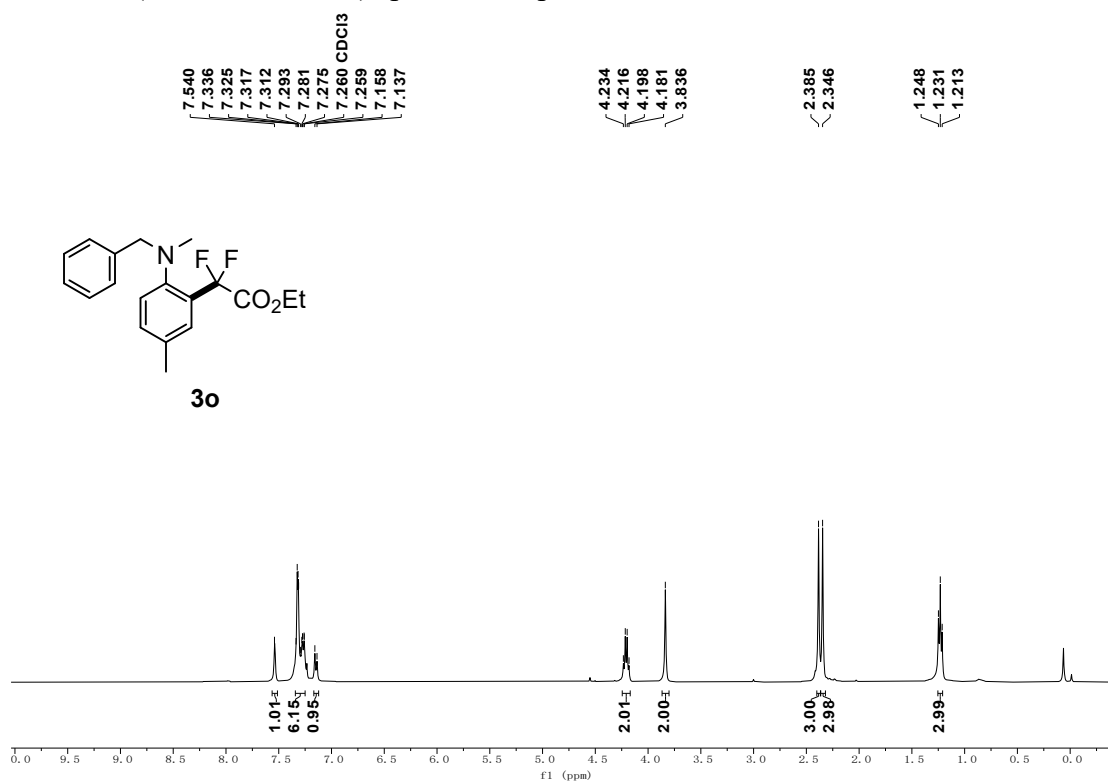
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3n**



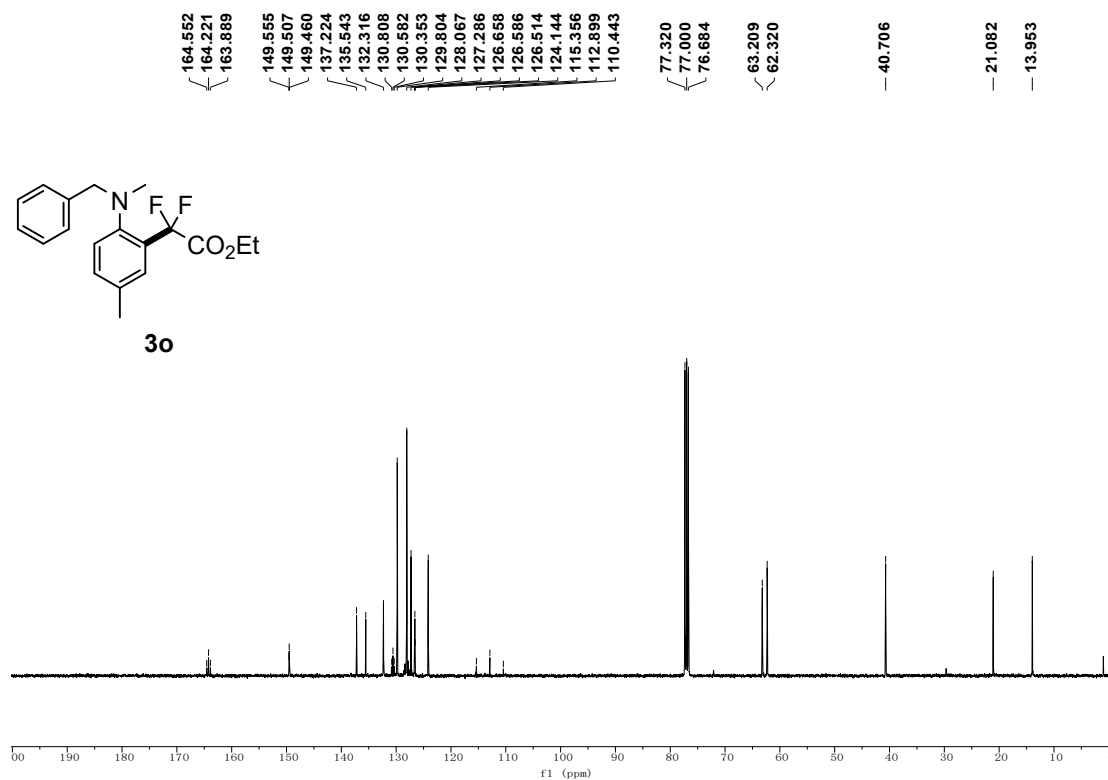
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3n**



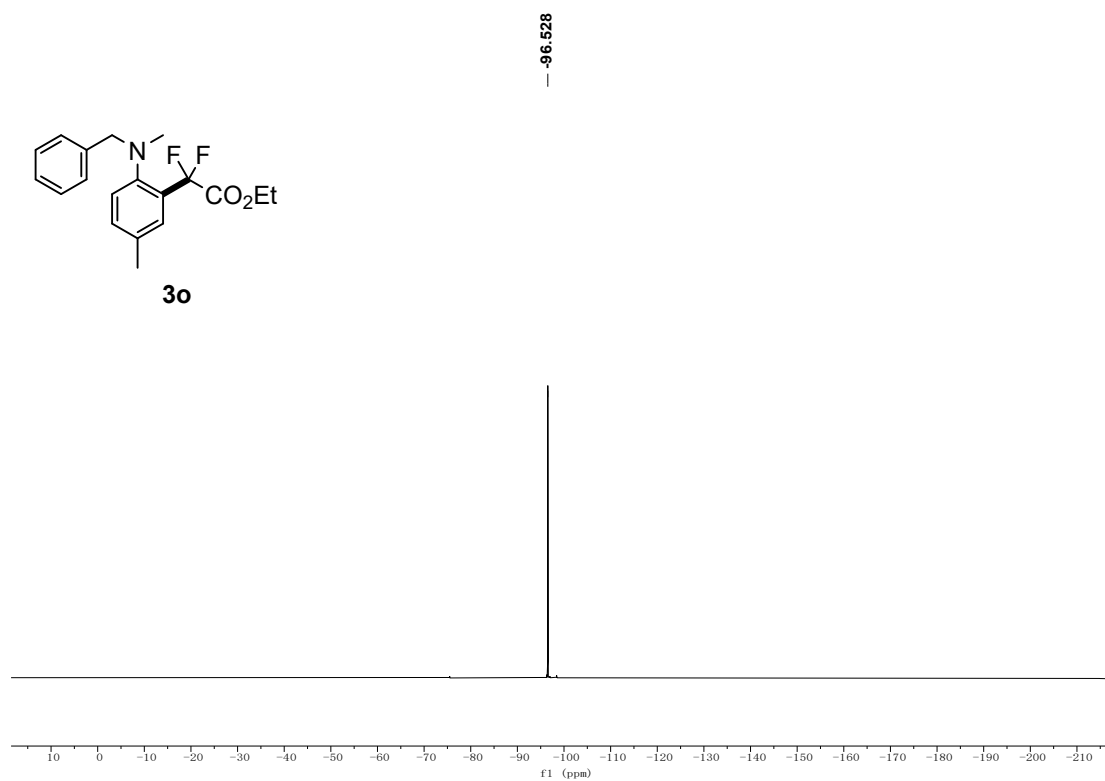
<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3o**



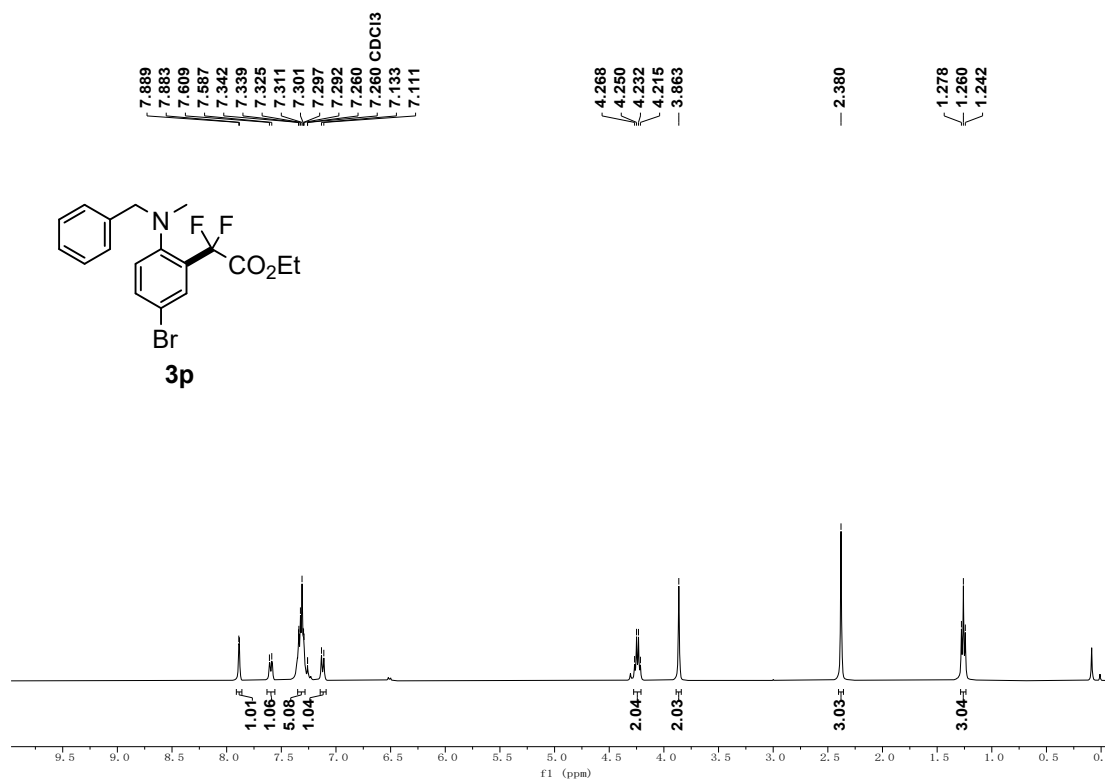
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3o**



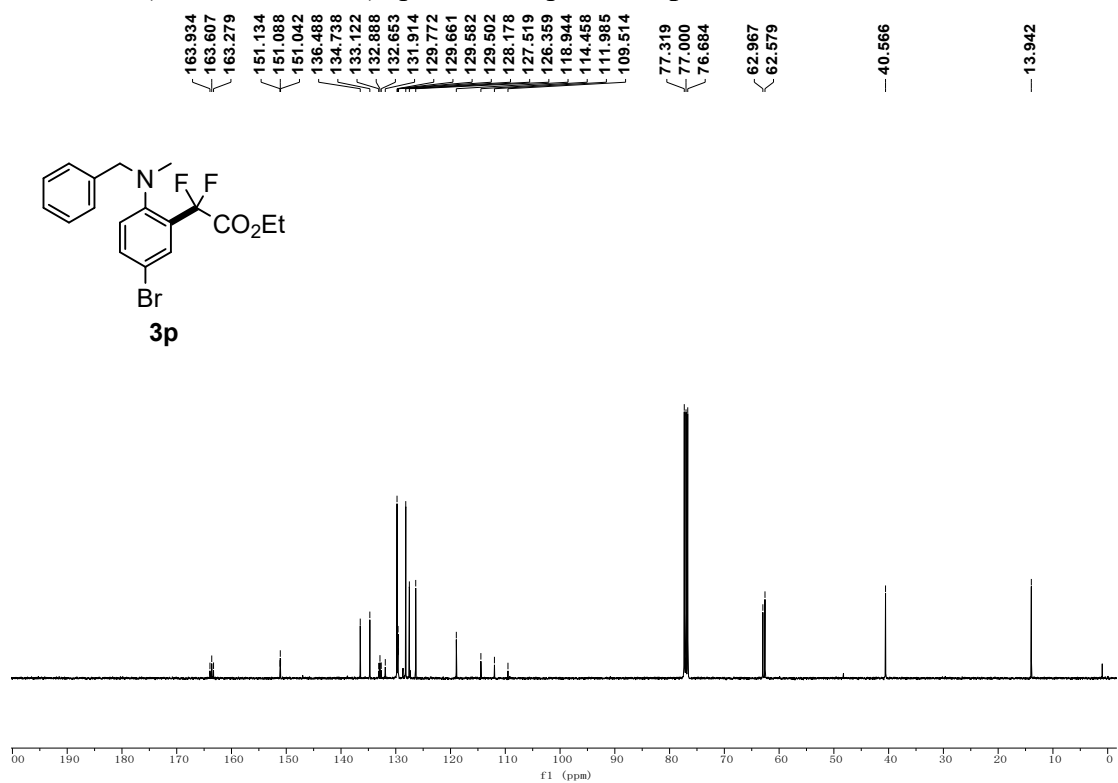
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3o**



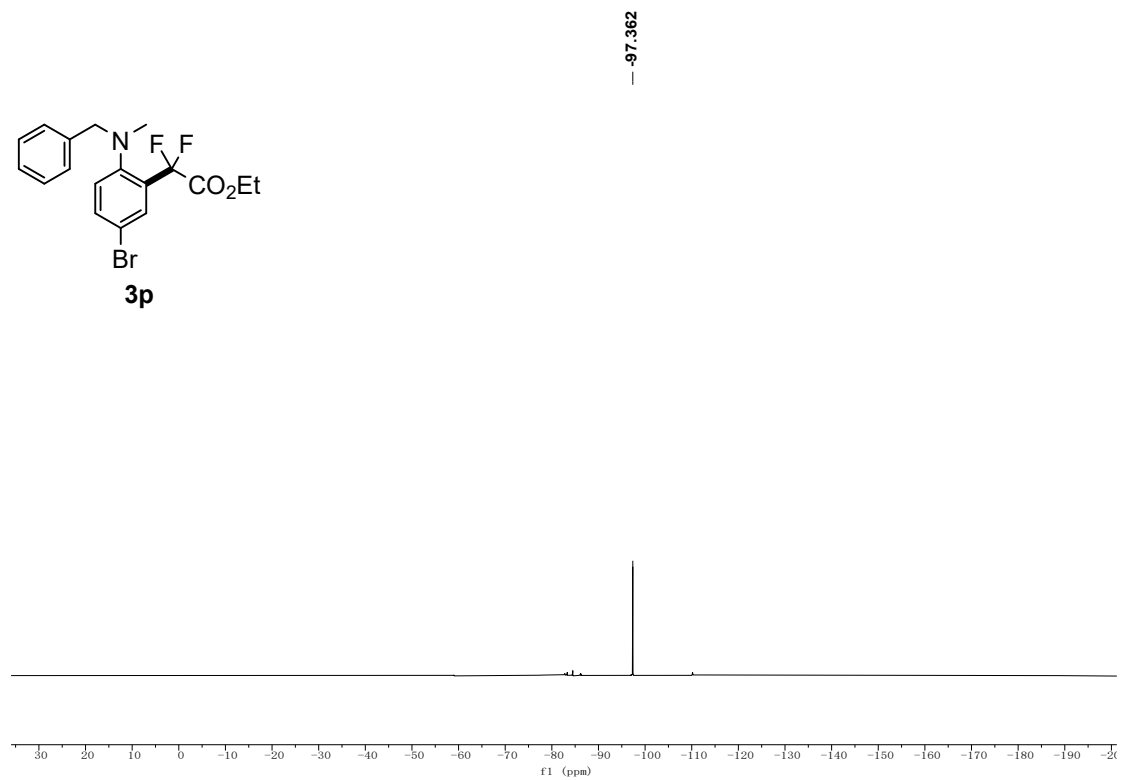
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3p**



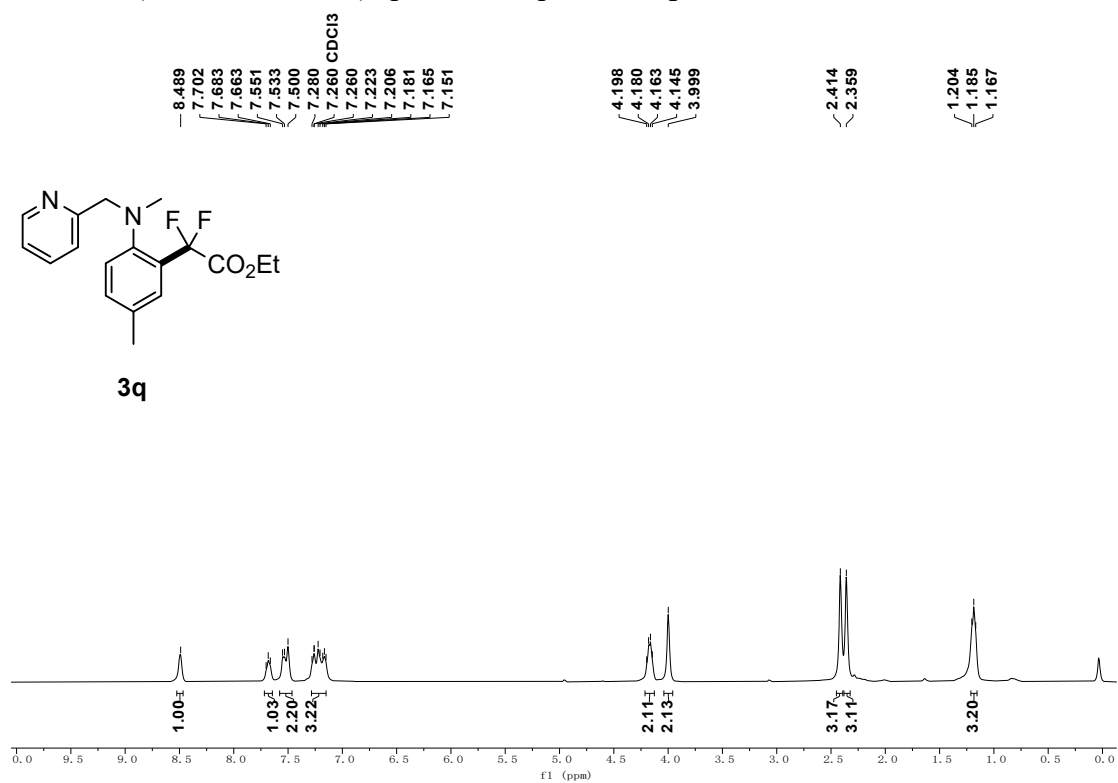
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **3p**



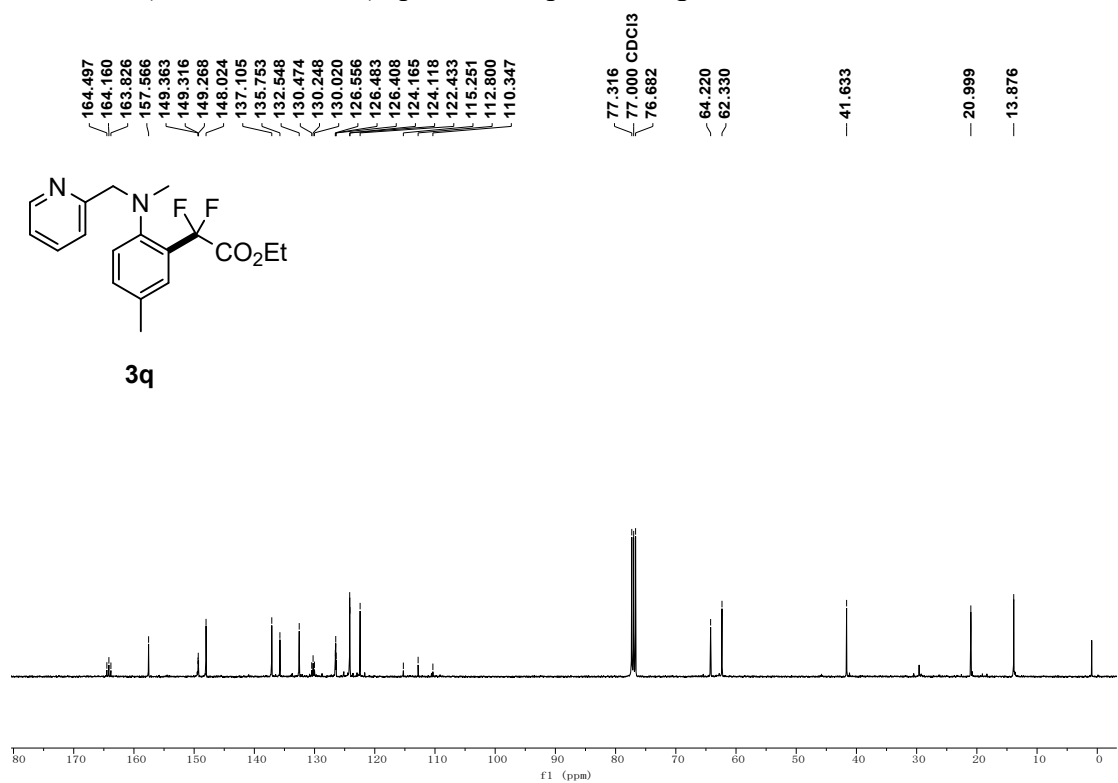
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3p**



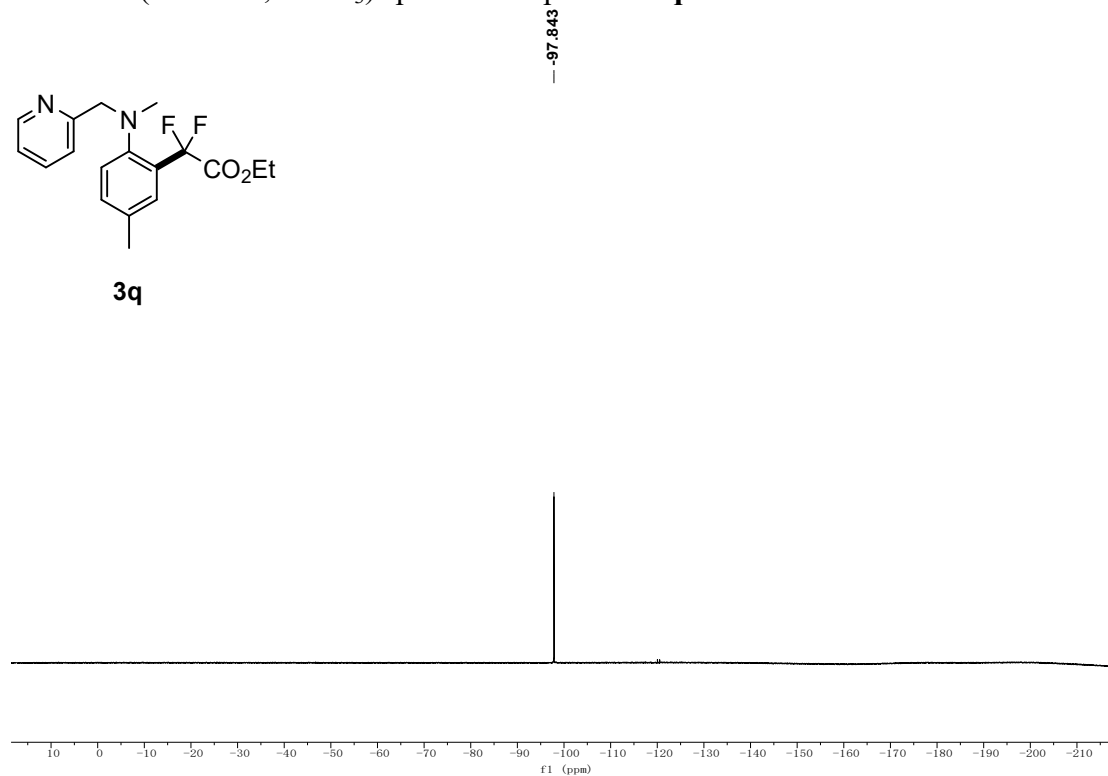
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3q**



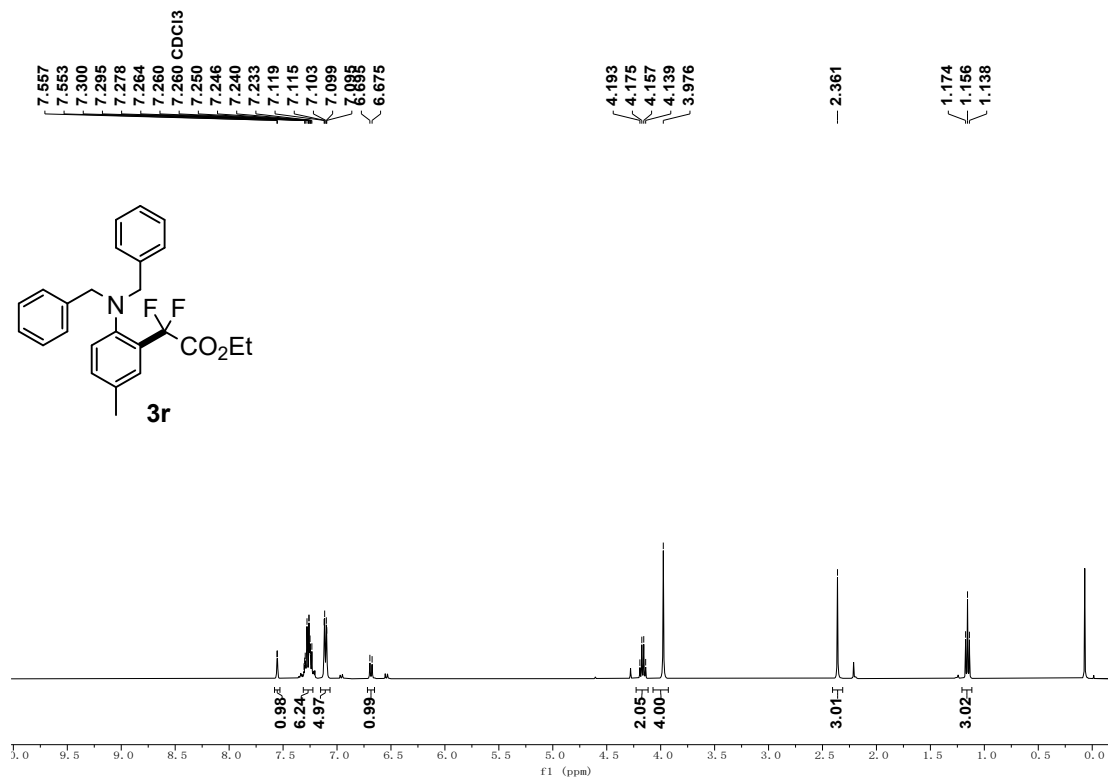
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3q**



$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3q**

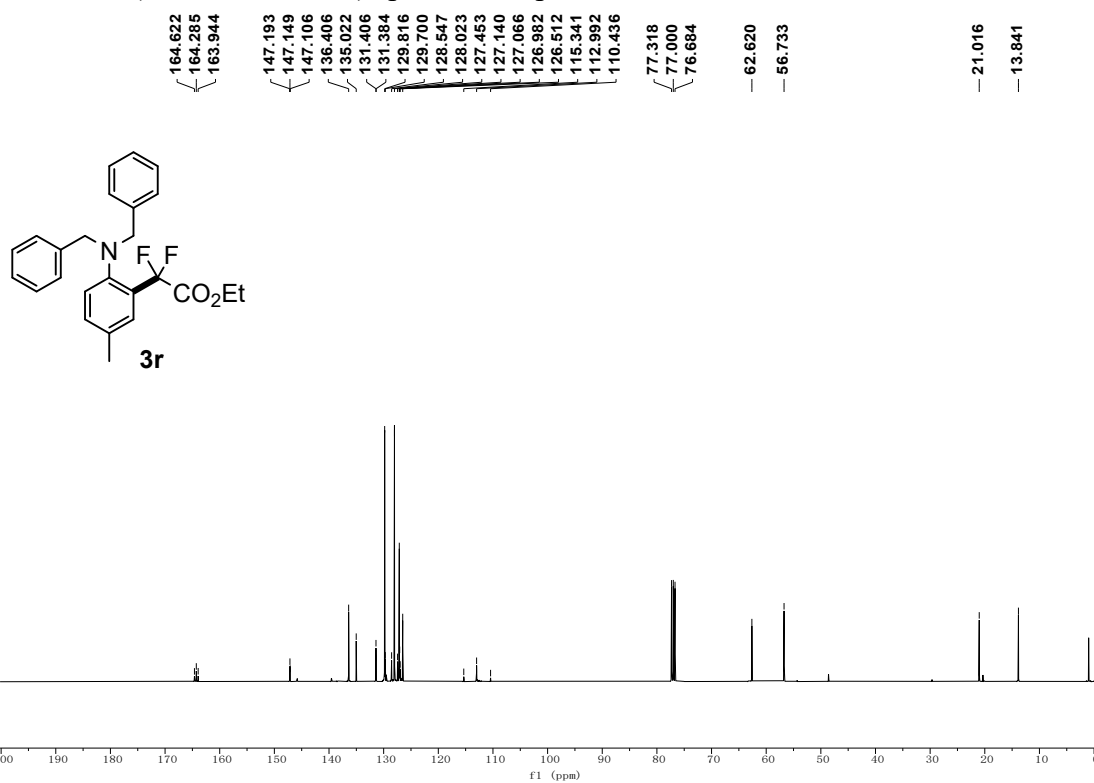


$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3r**

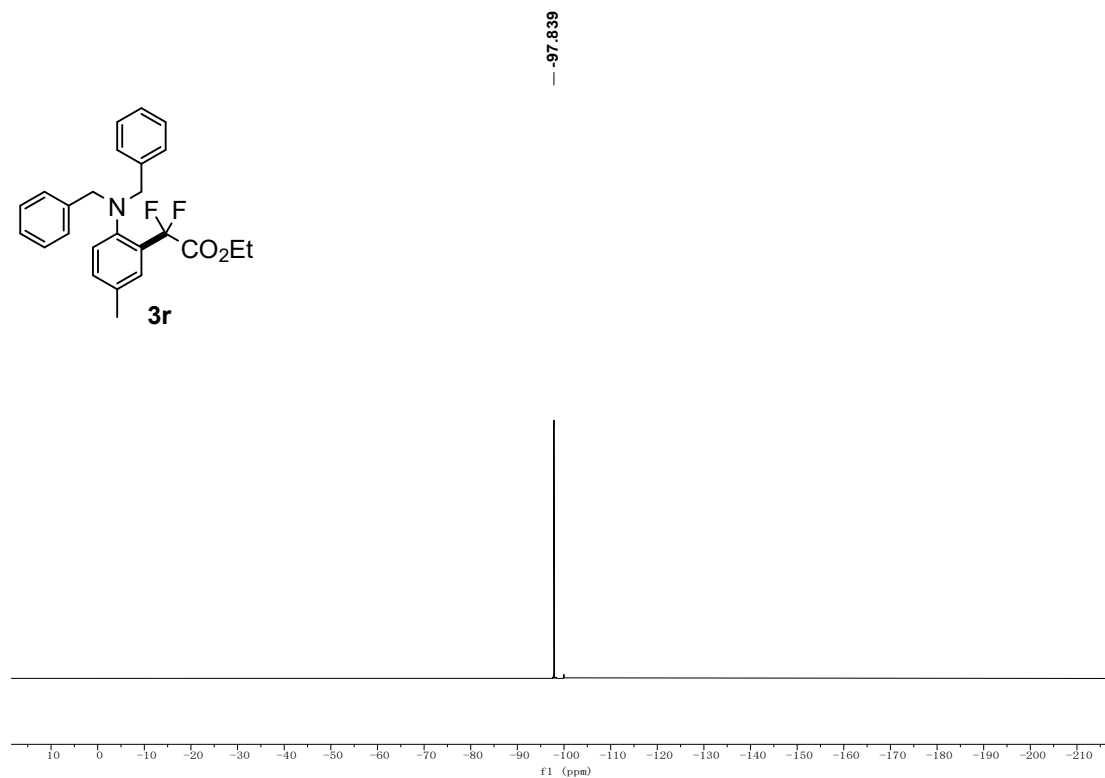




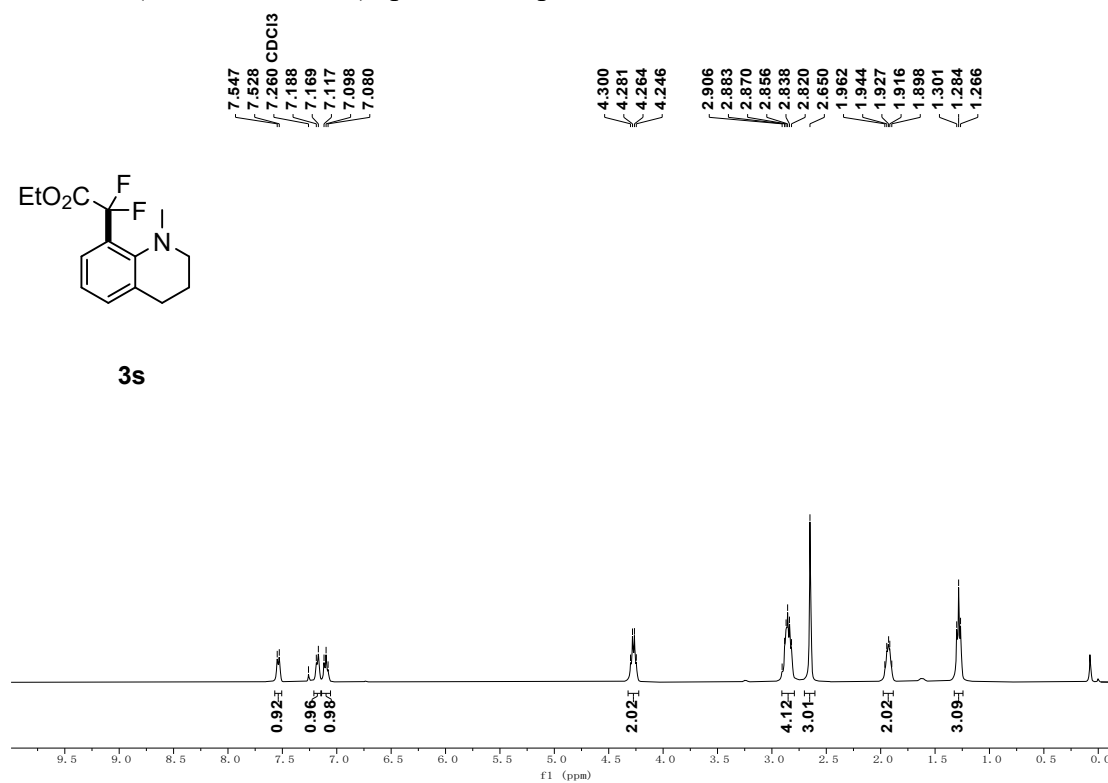
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3r**



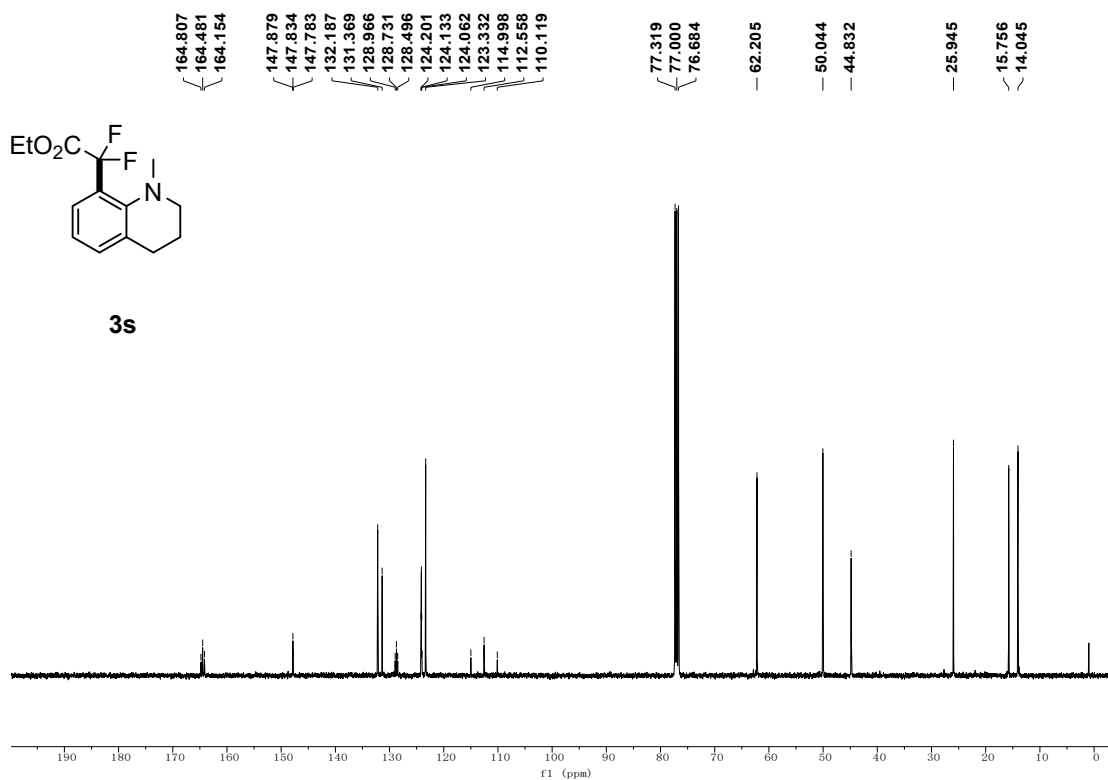
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3r**



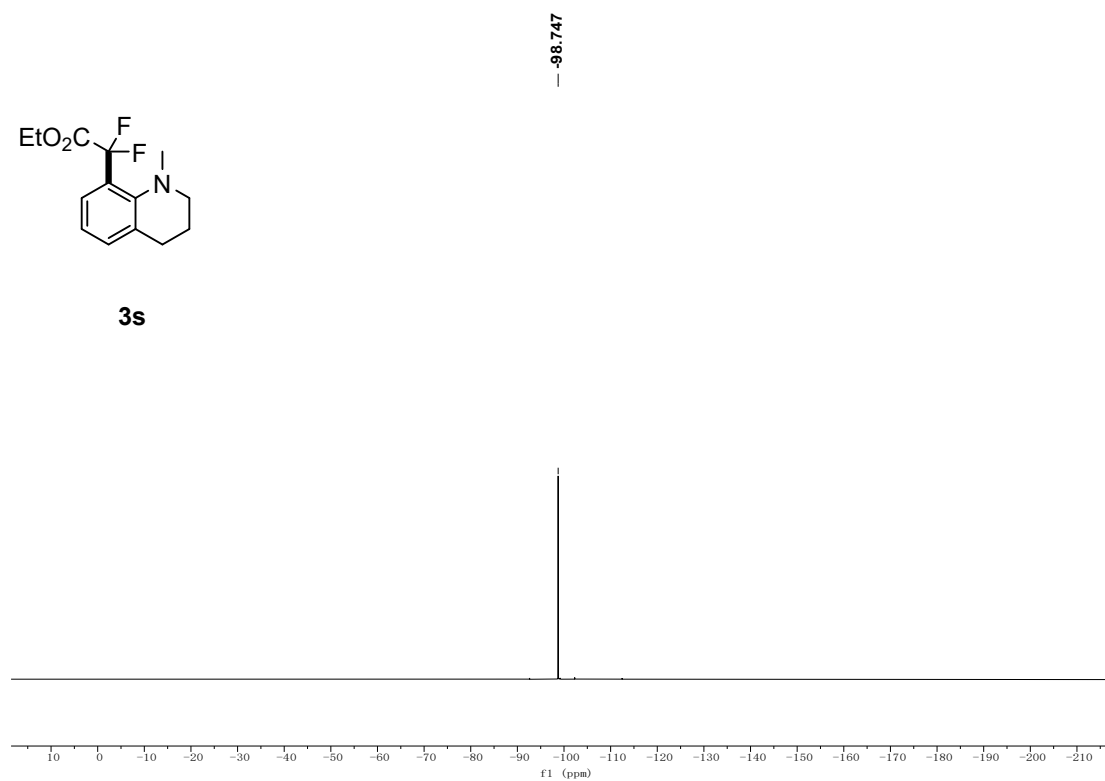
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3s**



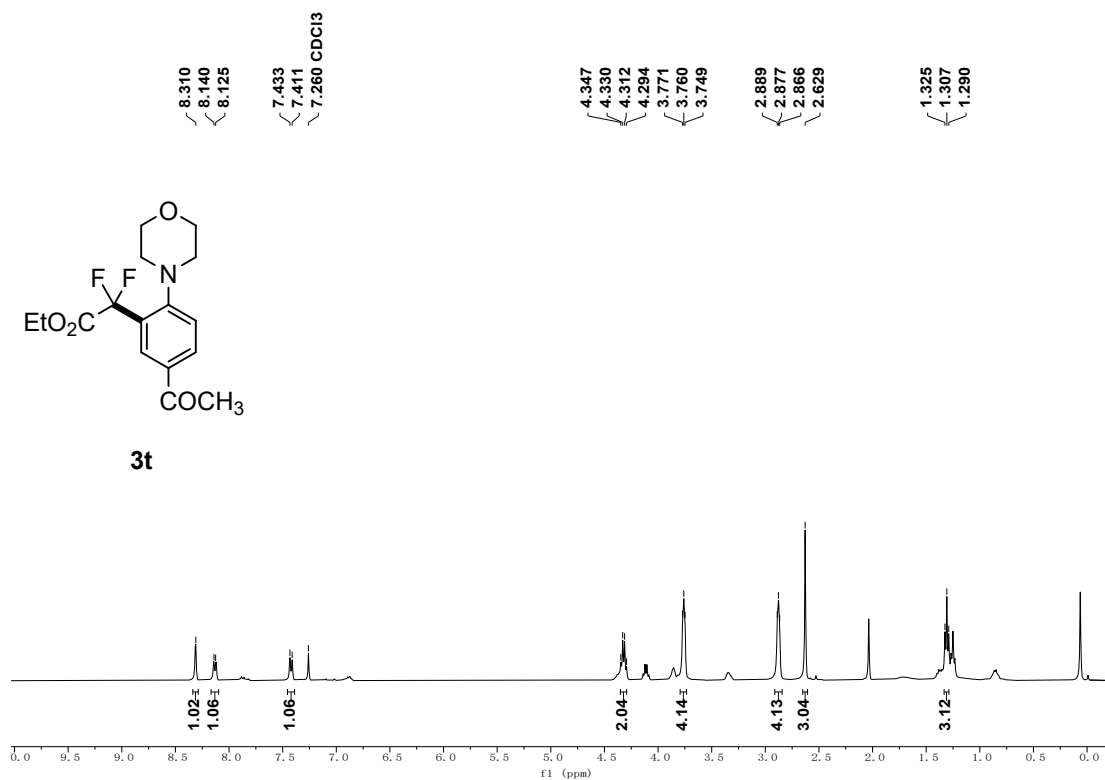
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3s**



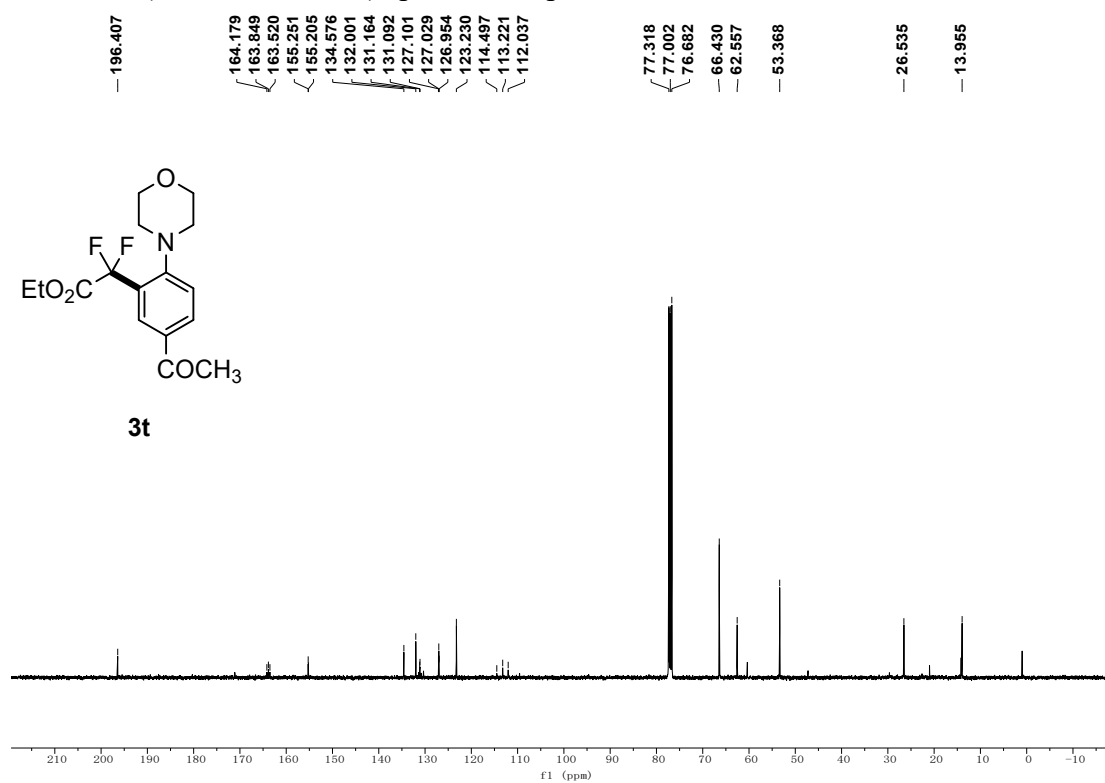
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3s**



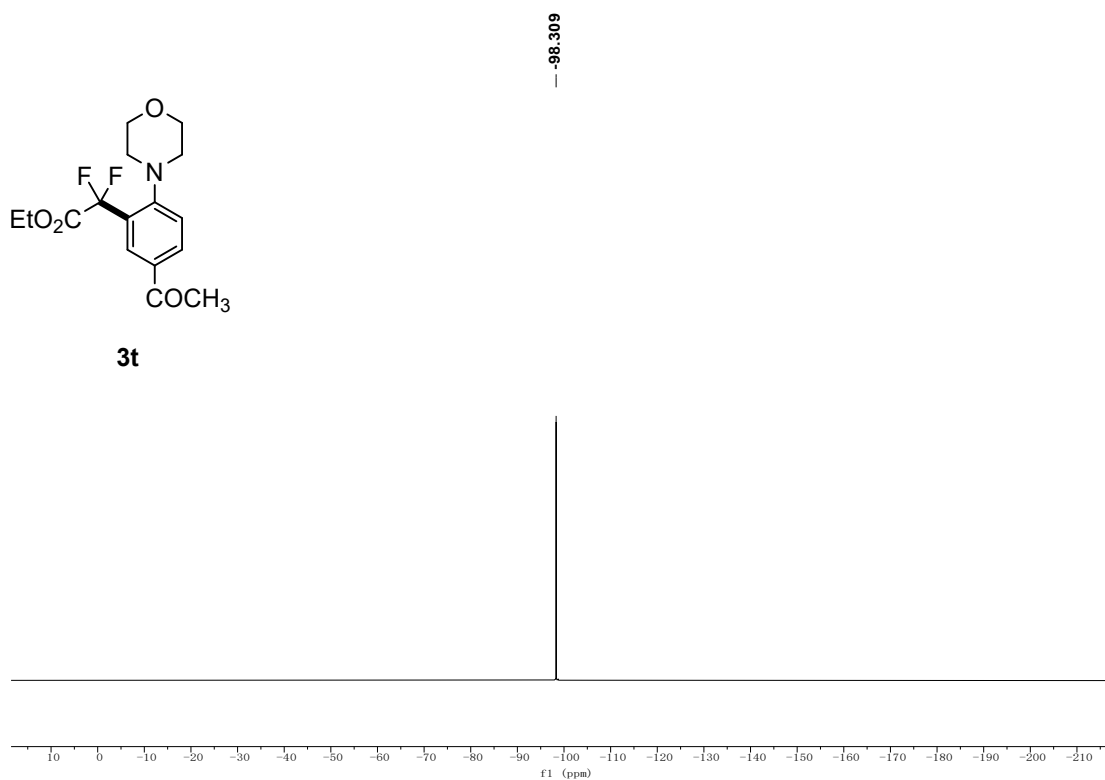
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3t**



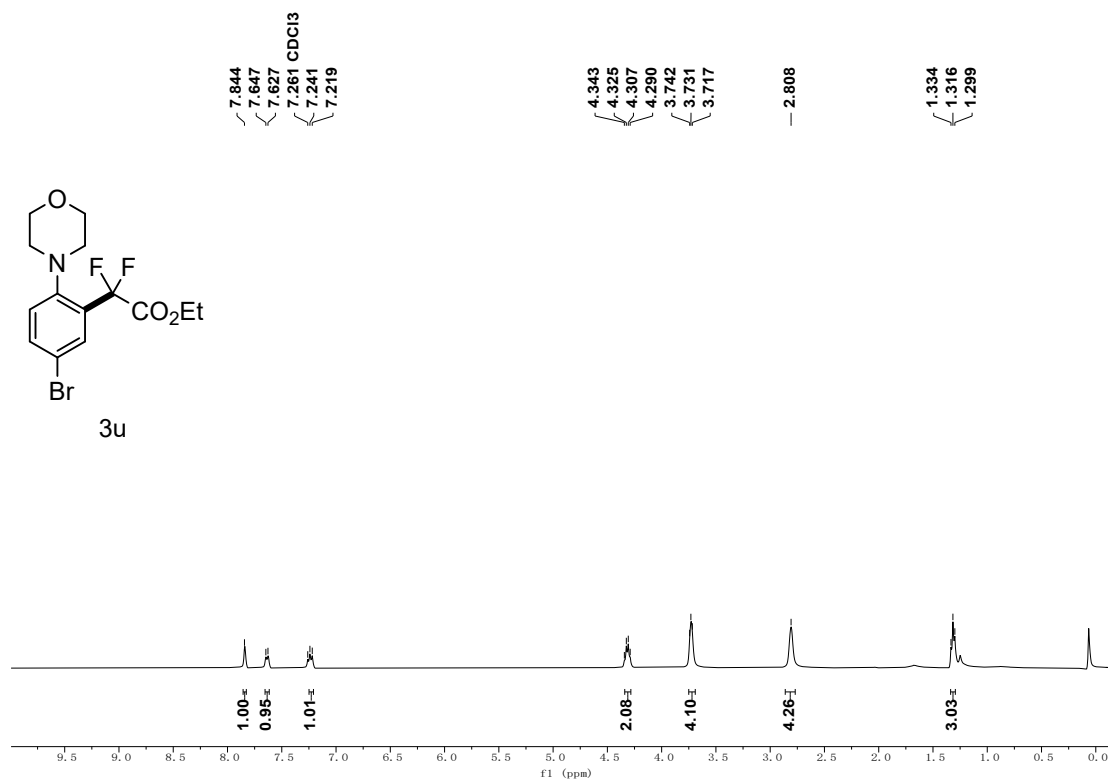
<sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) spectrum of product **5r**



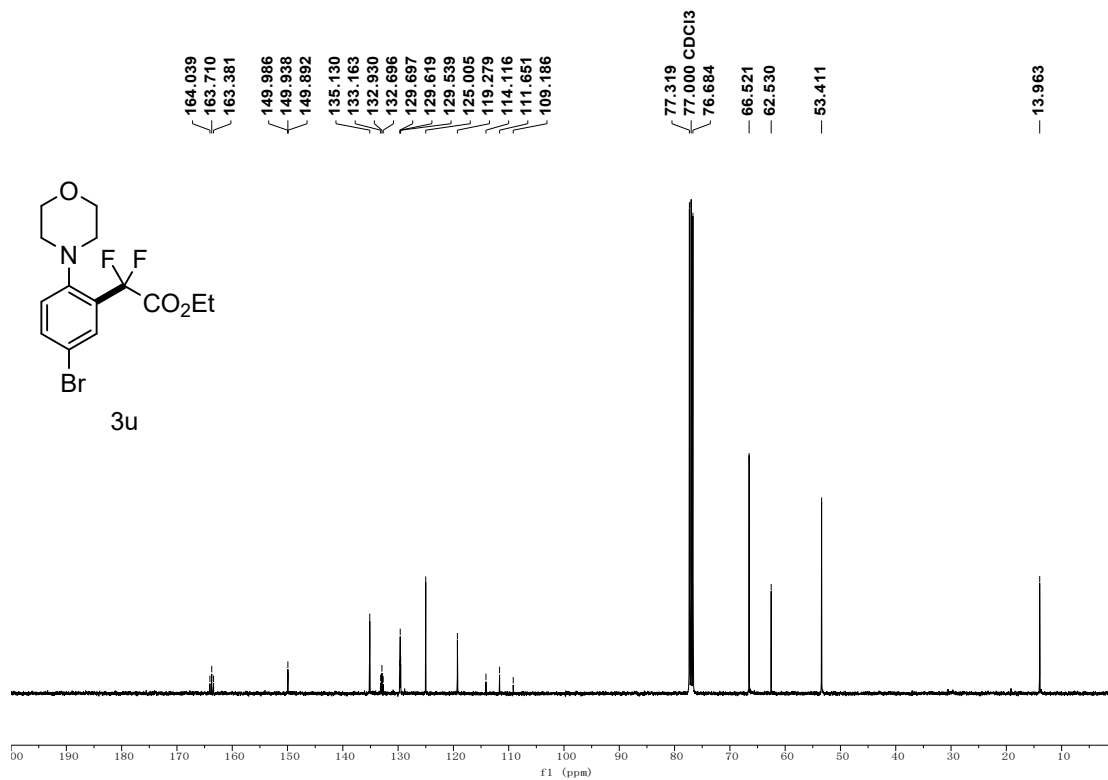
<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **5r**



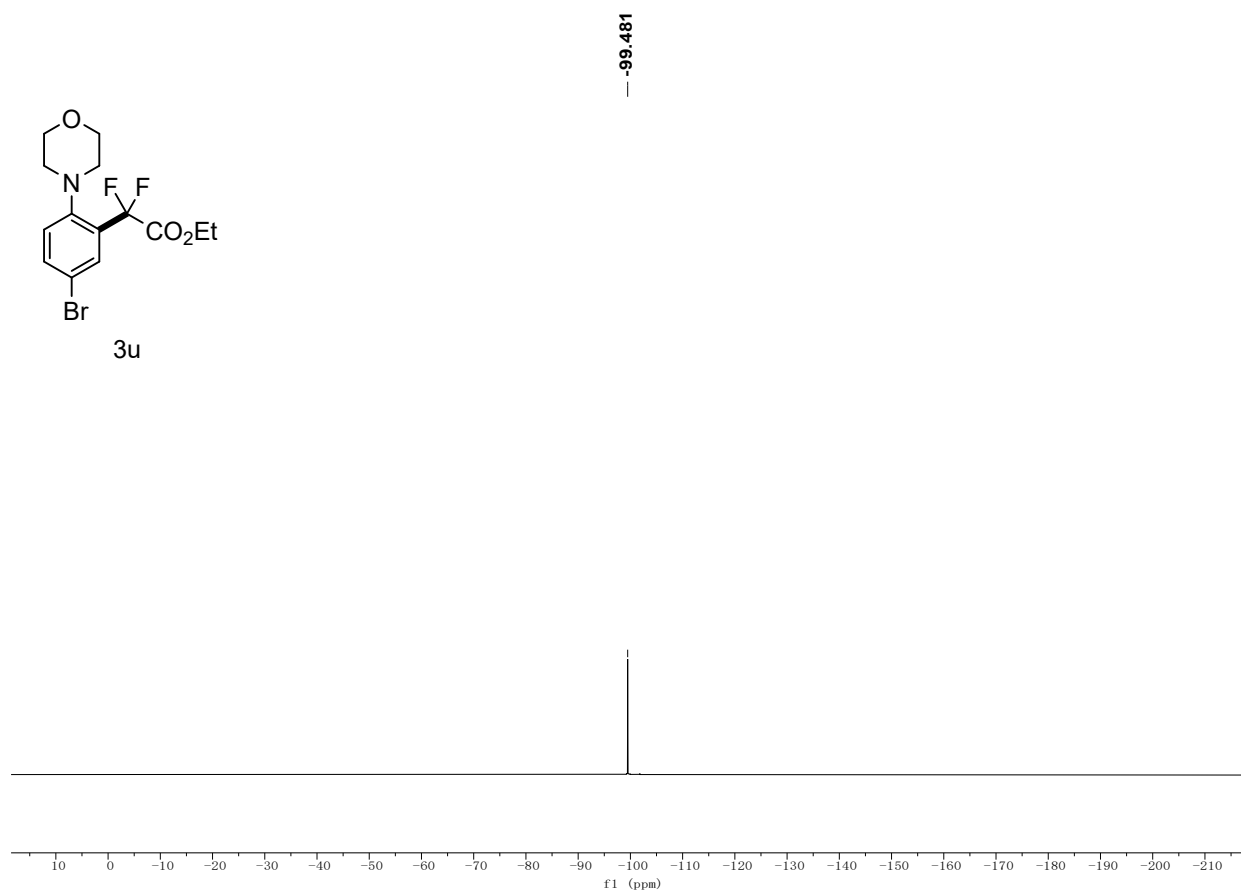
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3u**



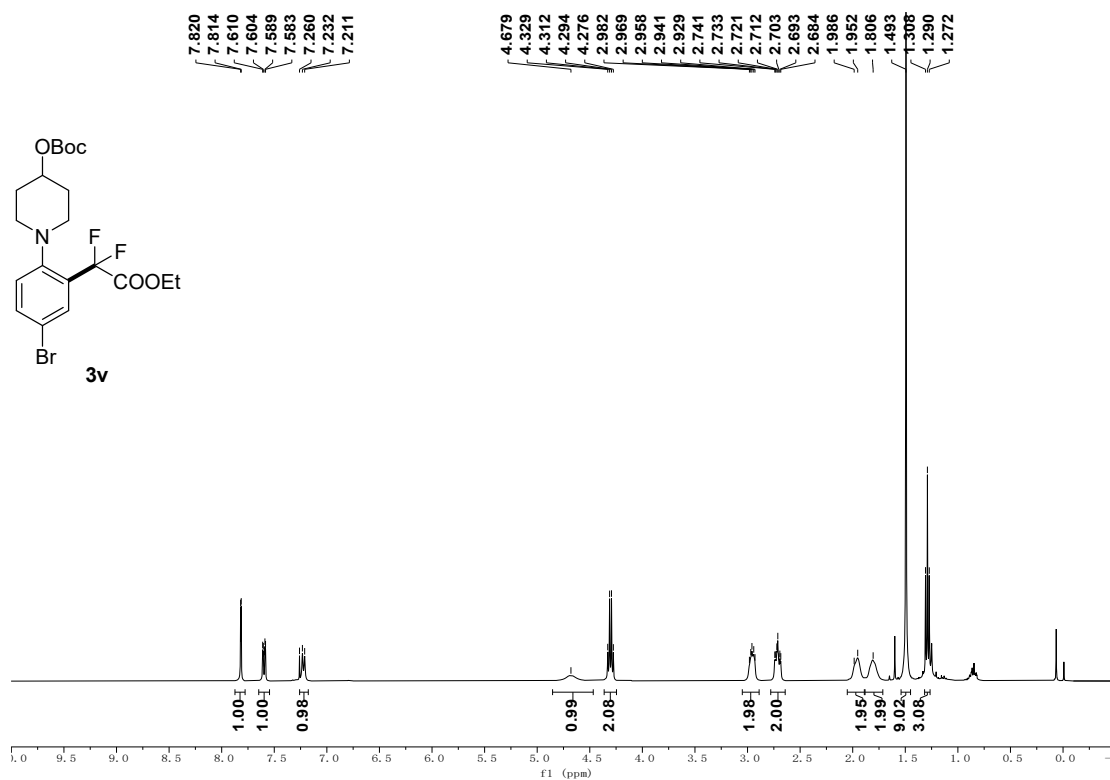
$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3u**



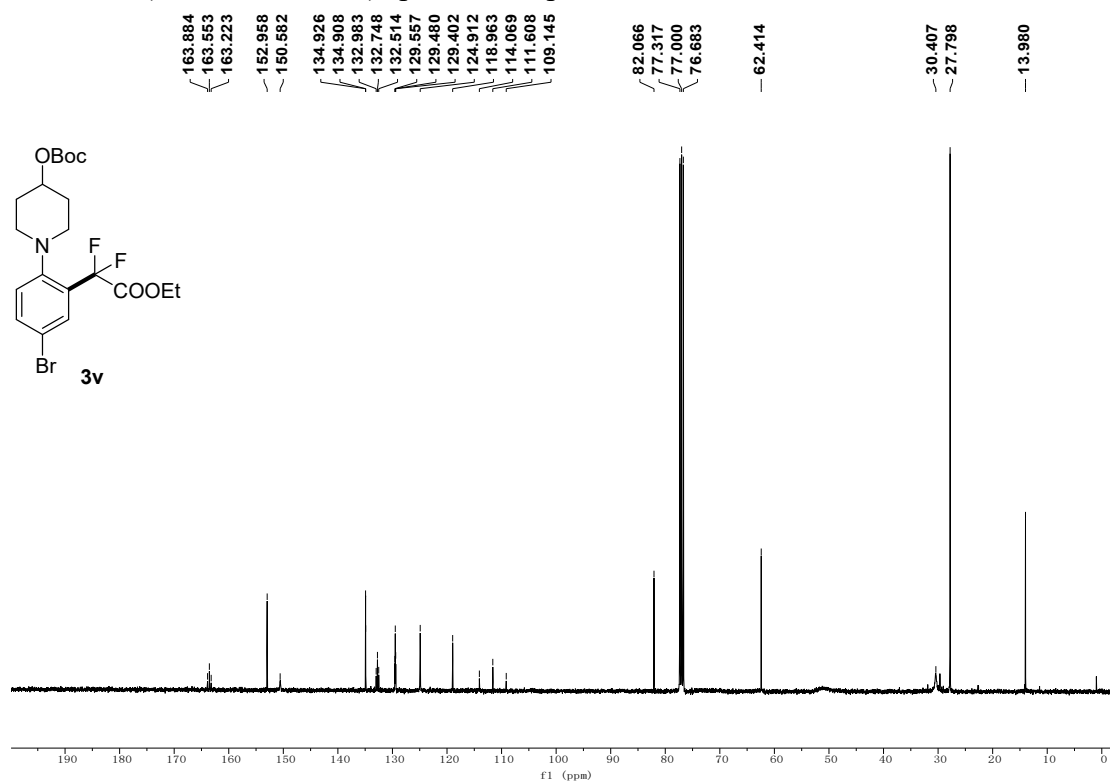
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3u**



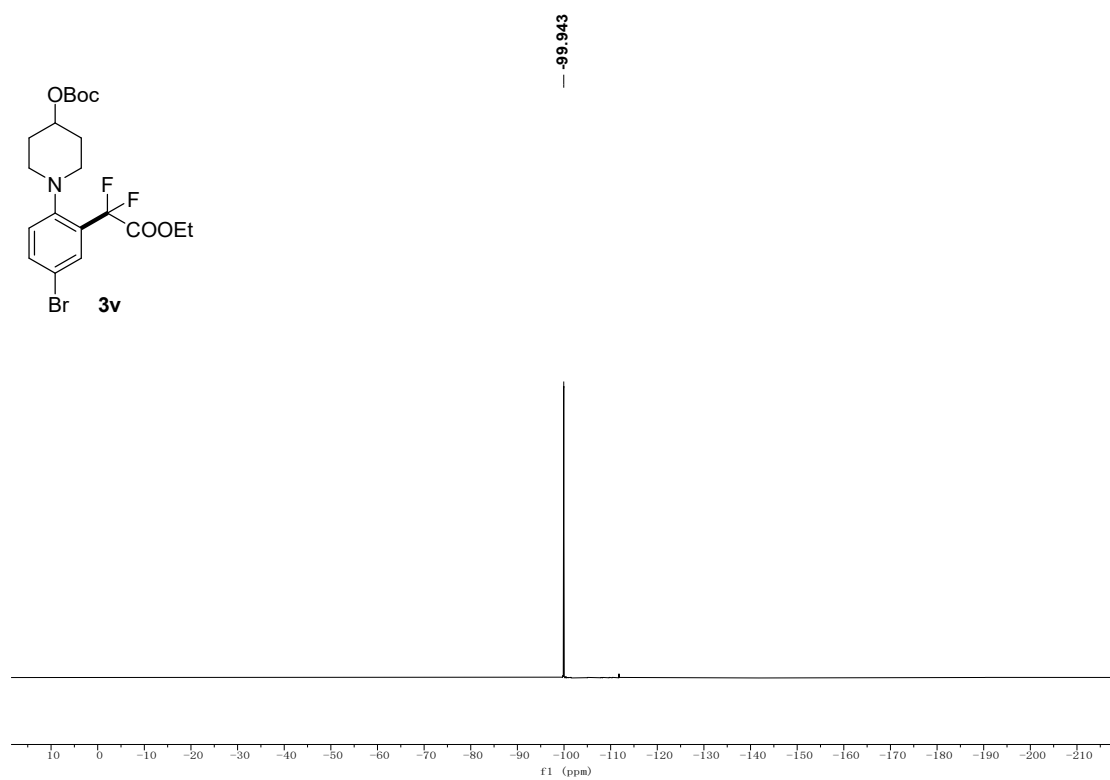
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3v**



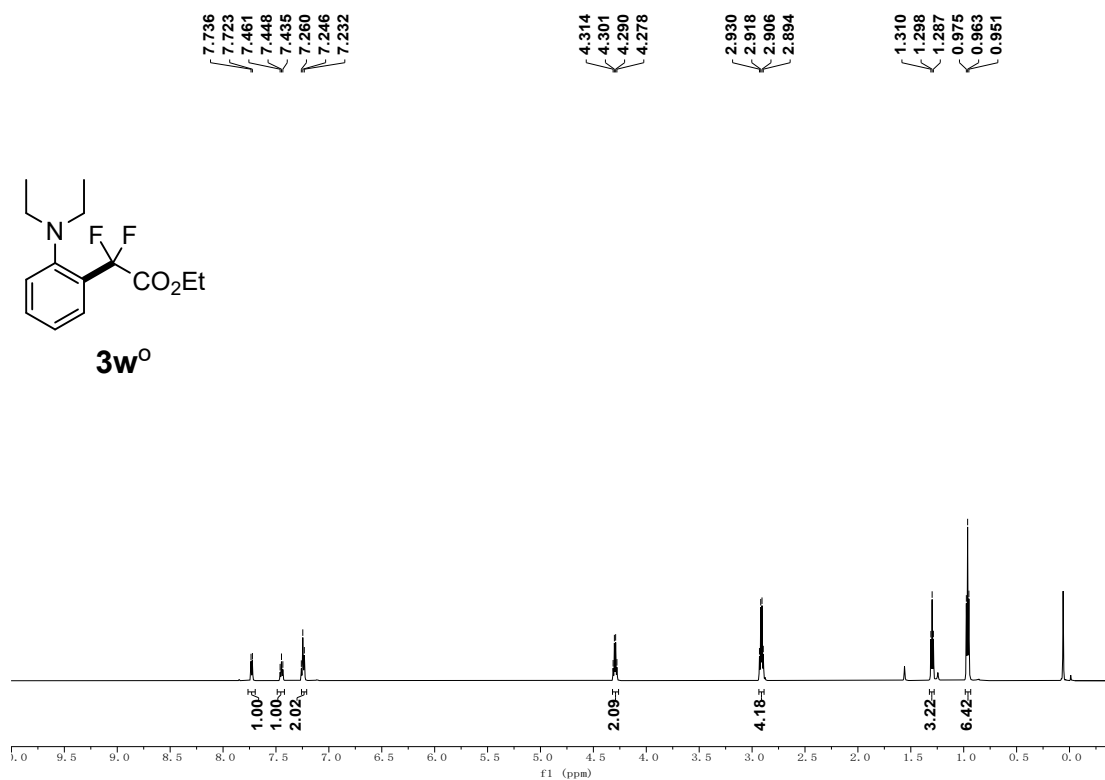
$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ ) spectrum of product **3v**



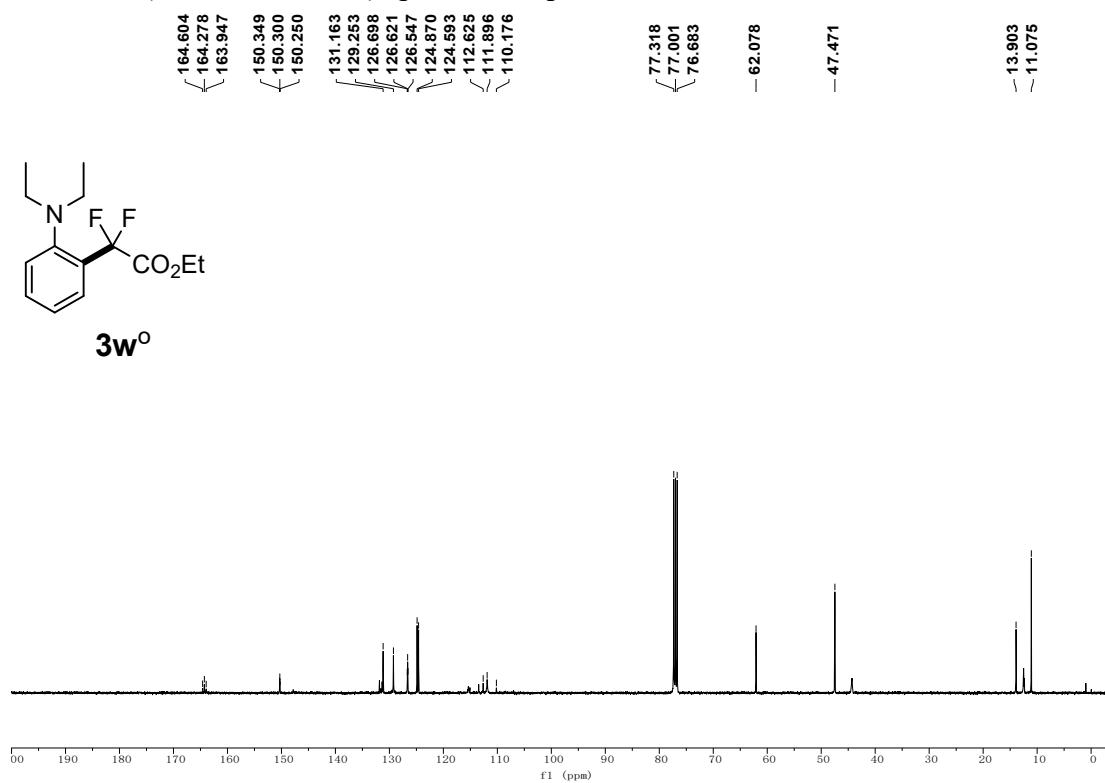
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3v**



$^1\text{H}$  NMR (600MHz,  $\text{CDCl}_3$ ) spectrum of product **3w**<sup>o</sup>

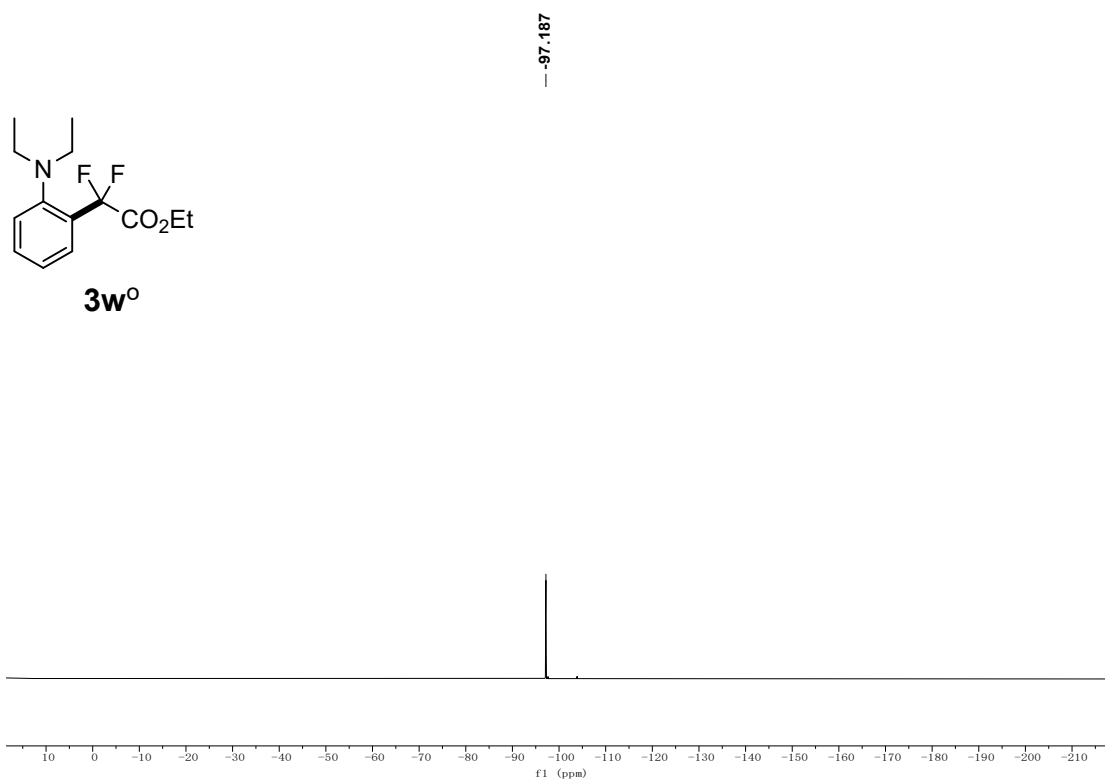


$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ ) spectrum of product **3w**<sup>o</sup>

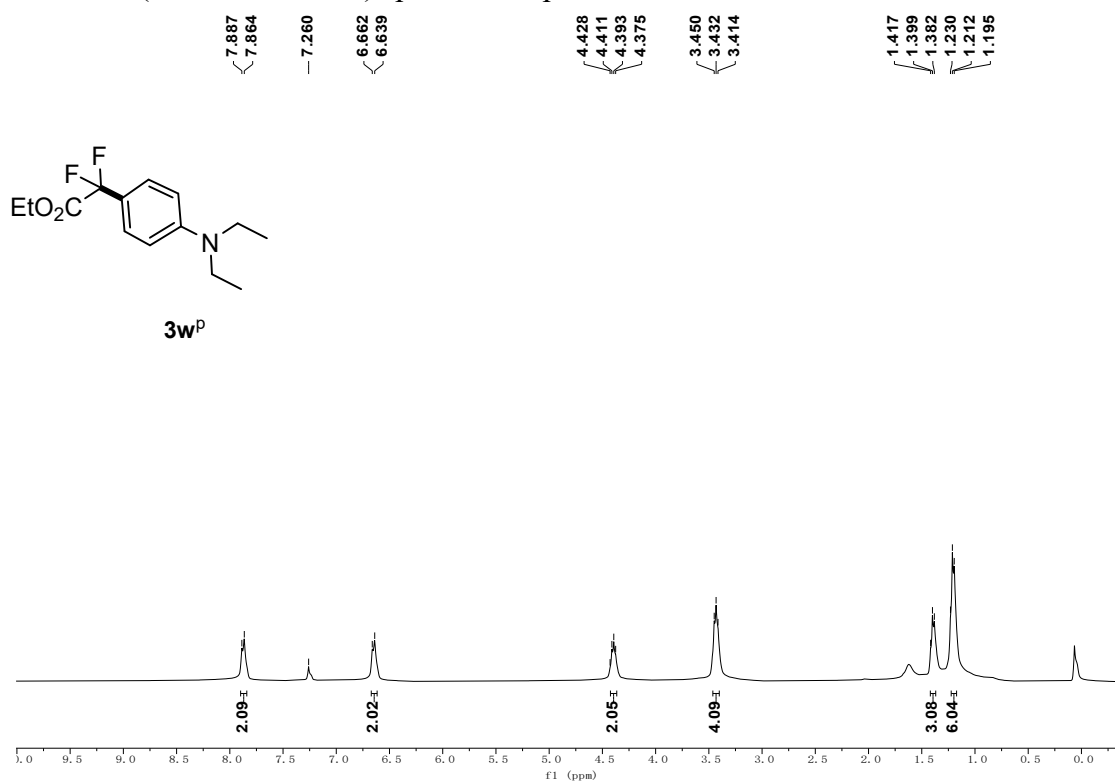


$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3w**<sup>o</sup>

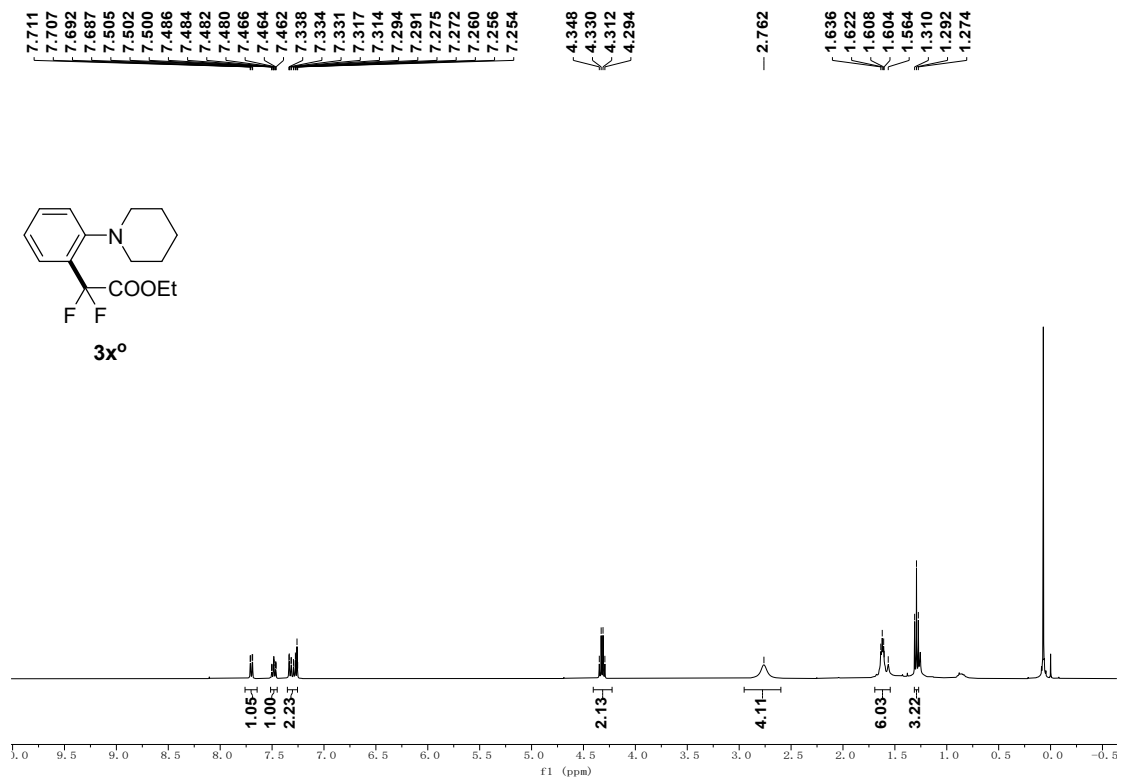




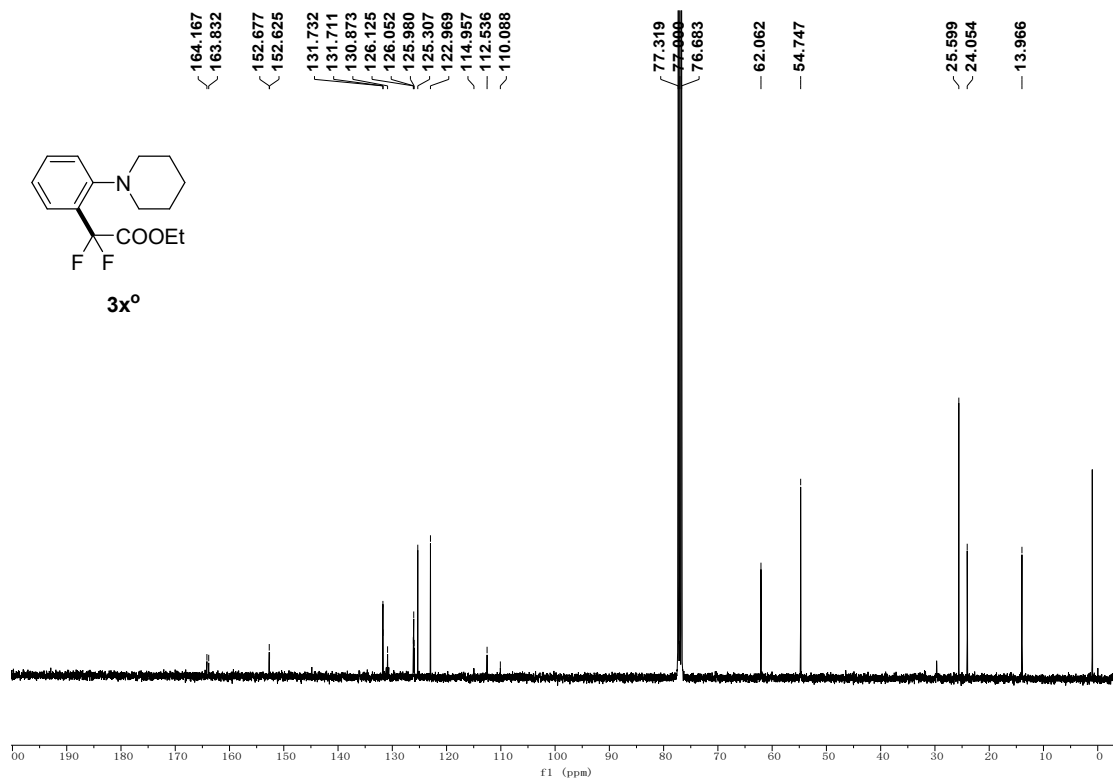
<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3w<sup>p</sup>**



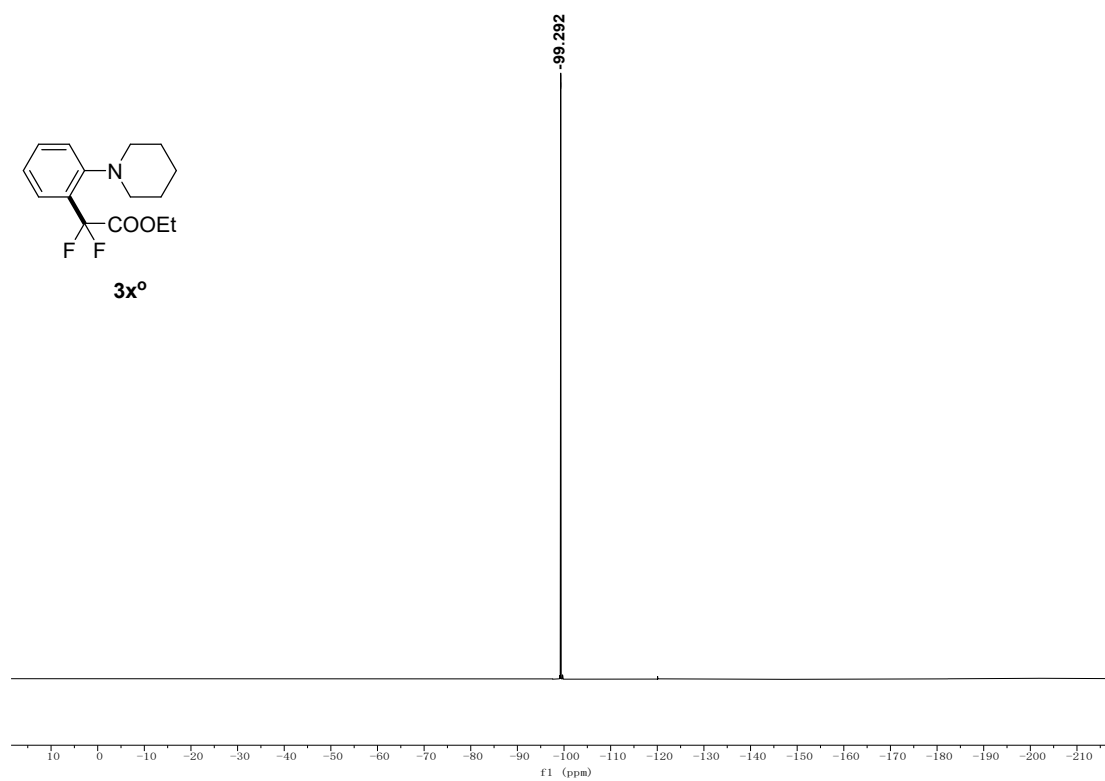
<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) spectrum of product **3x<sup>o</sup>**



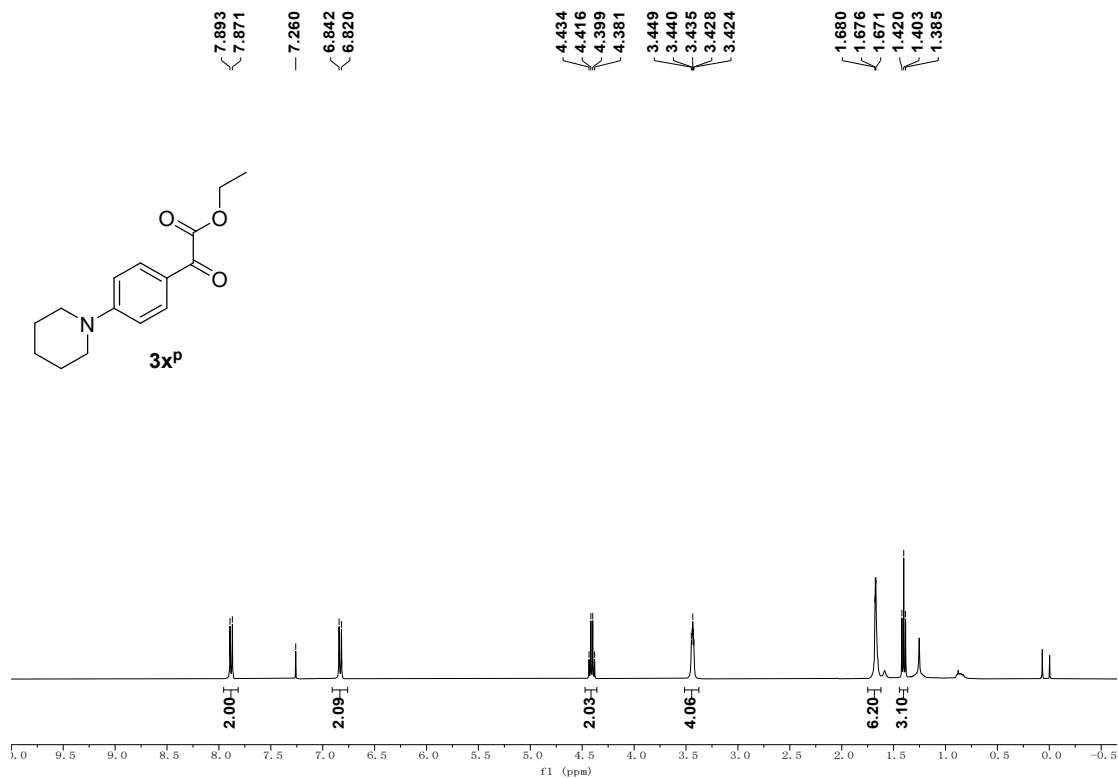
<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) spectrum of product **3x<sup>o</sup>**



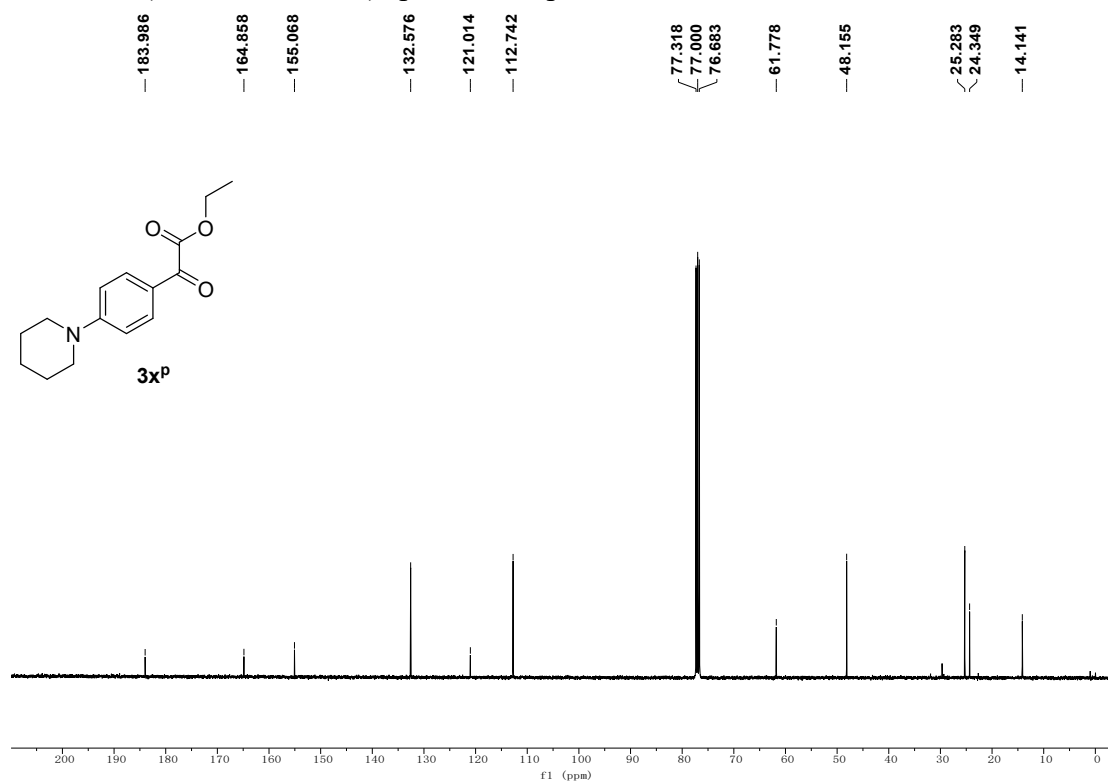
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3x<sup>o</sup>**



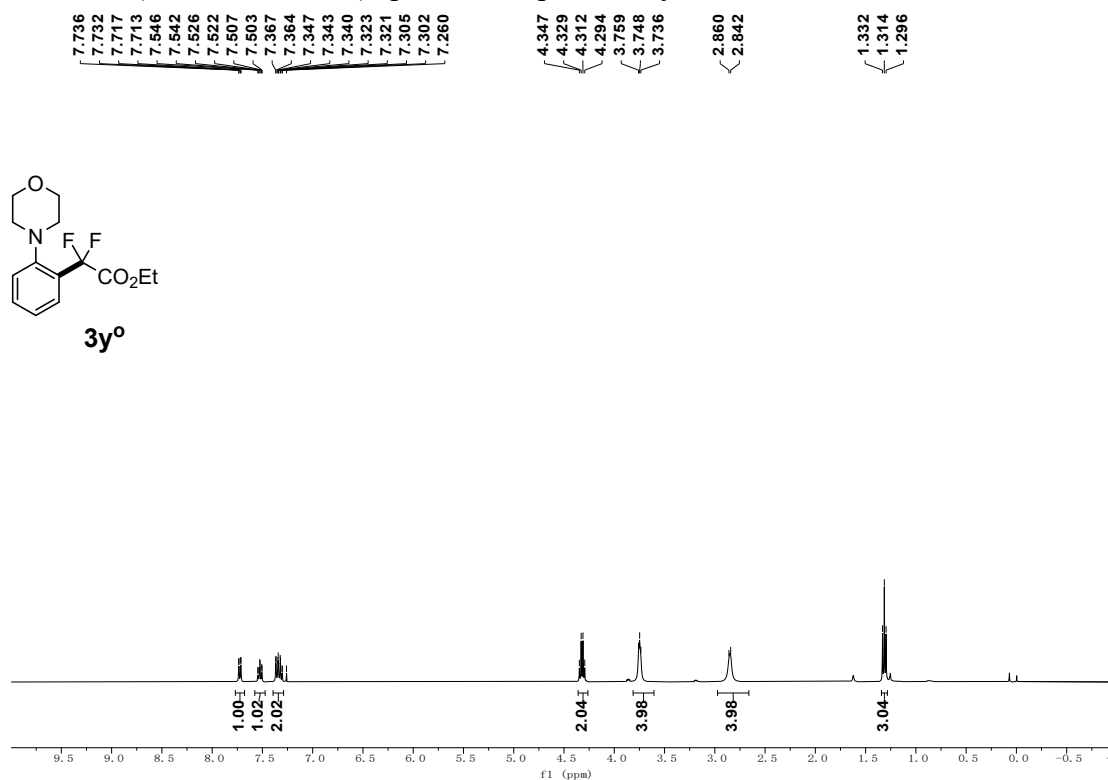
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3x<sup>p</sup>**



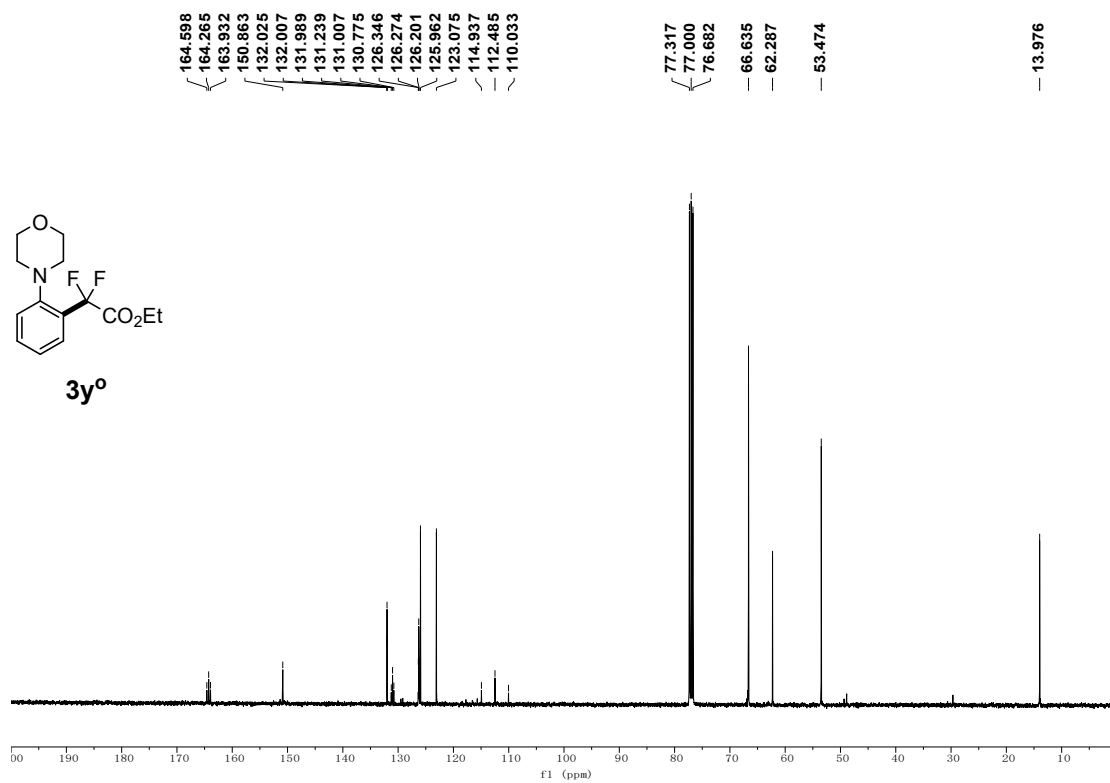
$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ ) spectrum of product **3x<sup>p</sup>**



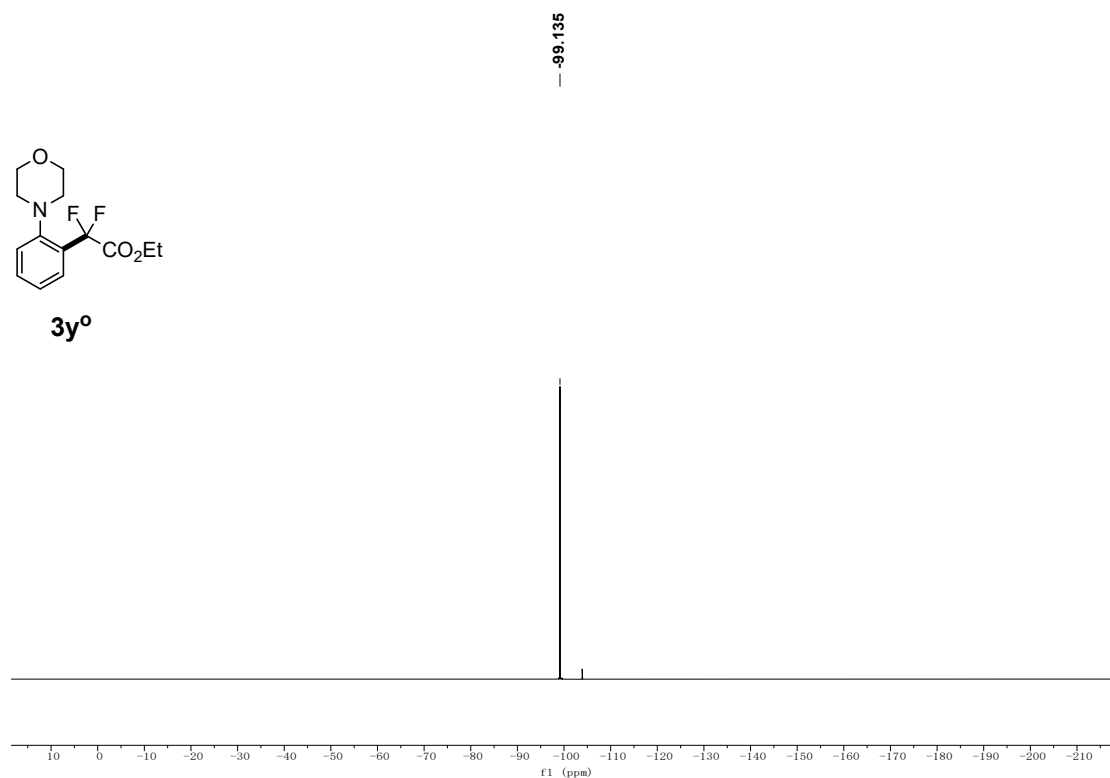
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3y<sup>o</sup>**



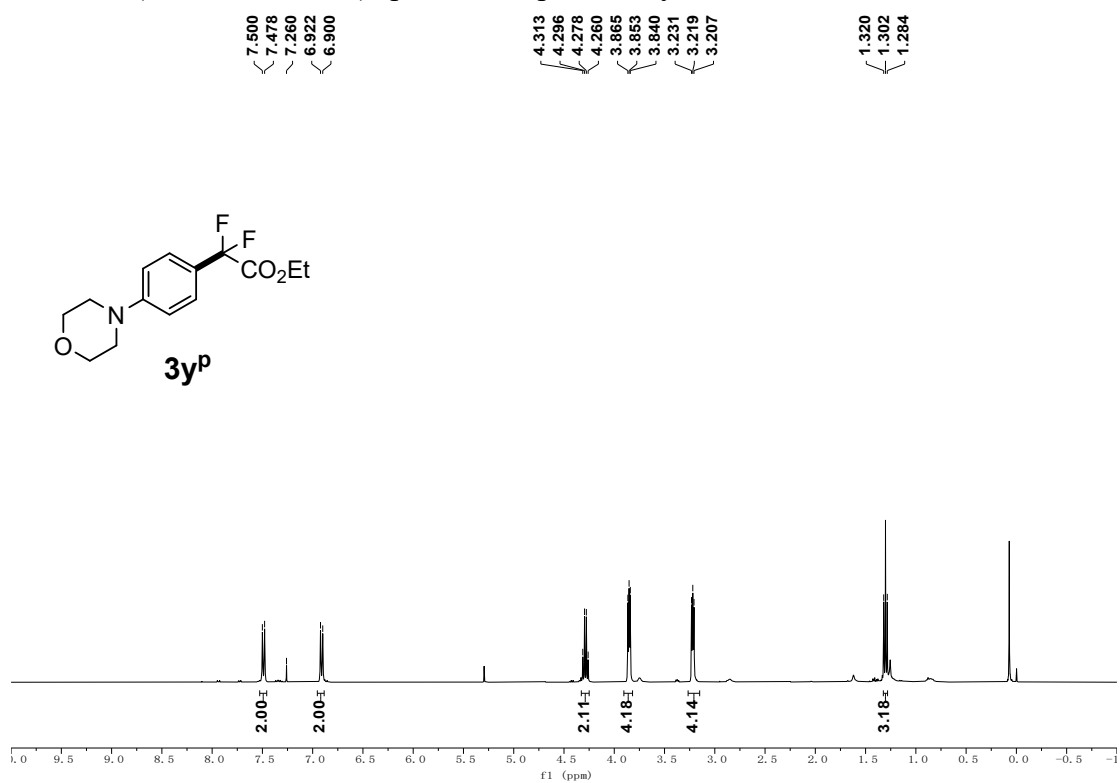
$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ ) spectrum of product **3y<sup>o</sup>**



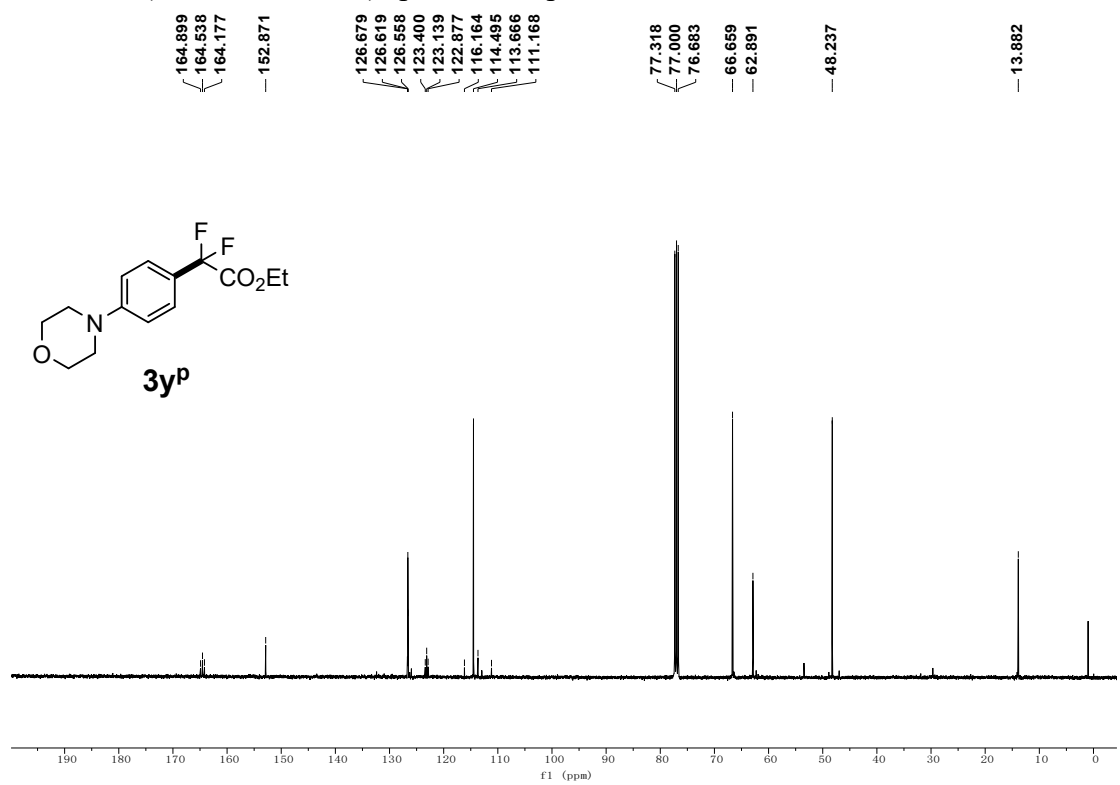
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3y<sup>o</sup>**



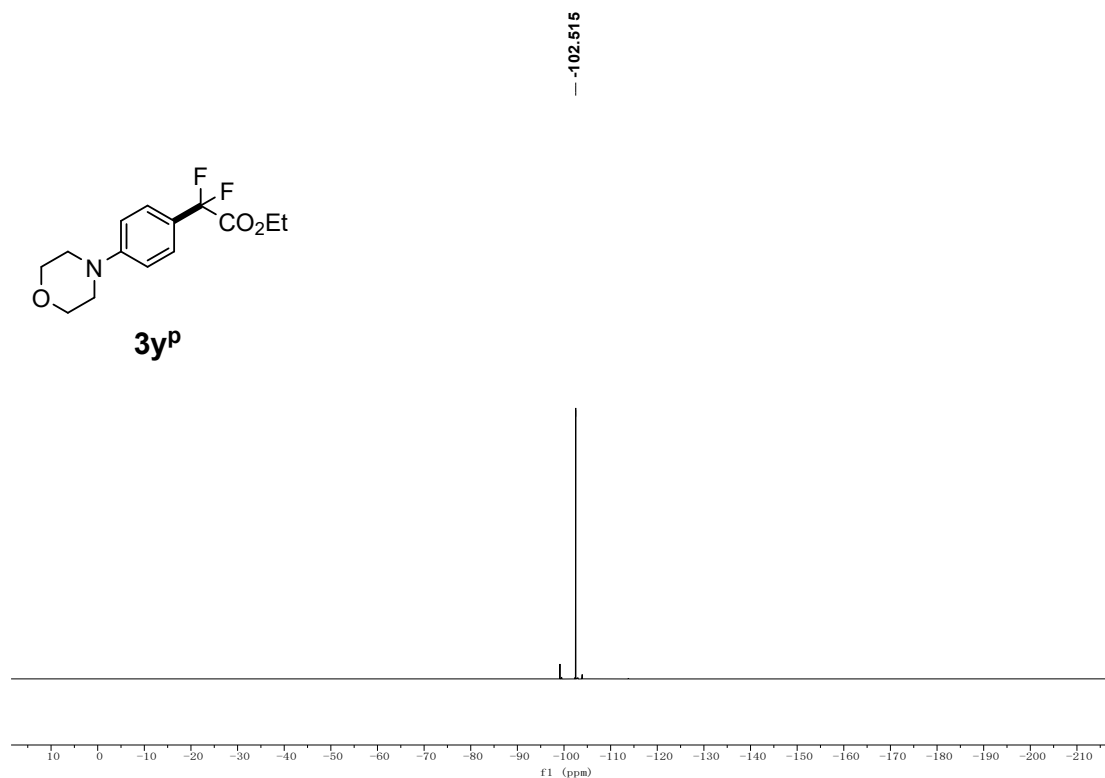
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3y<sup>p</sup>**



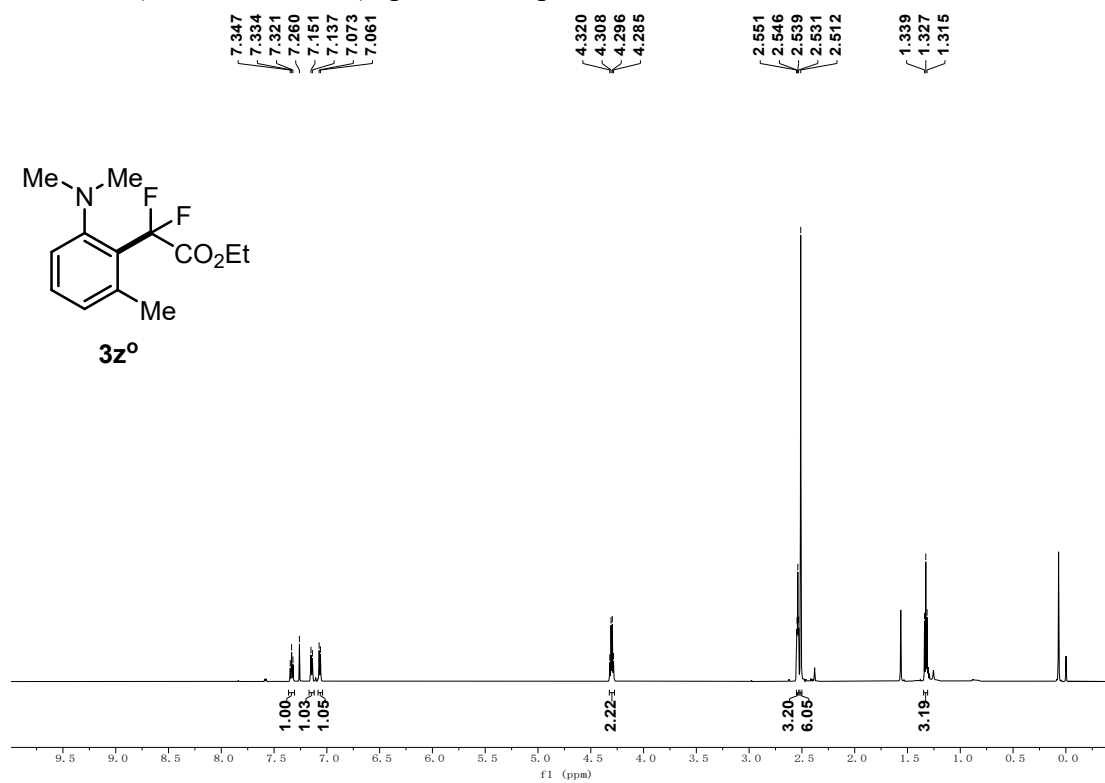
$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ ) spectrum of product **3w<sup>p</sup>**



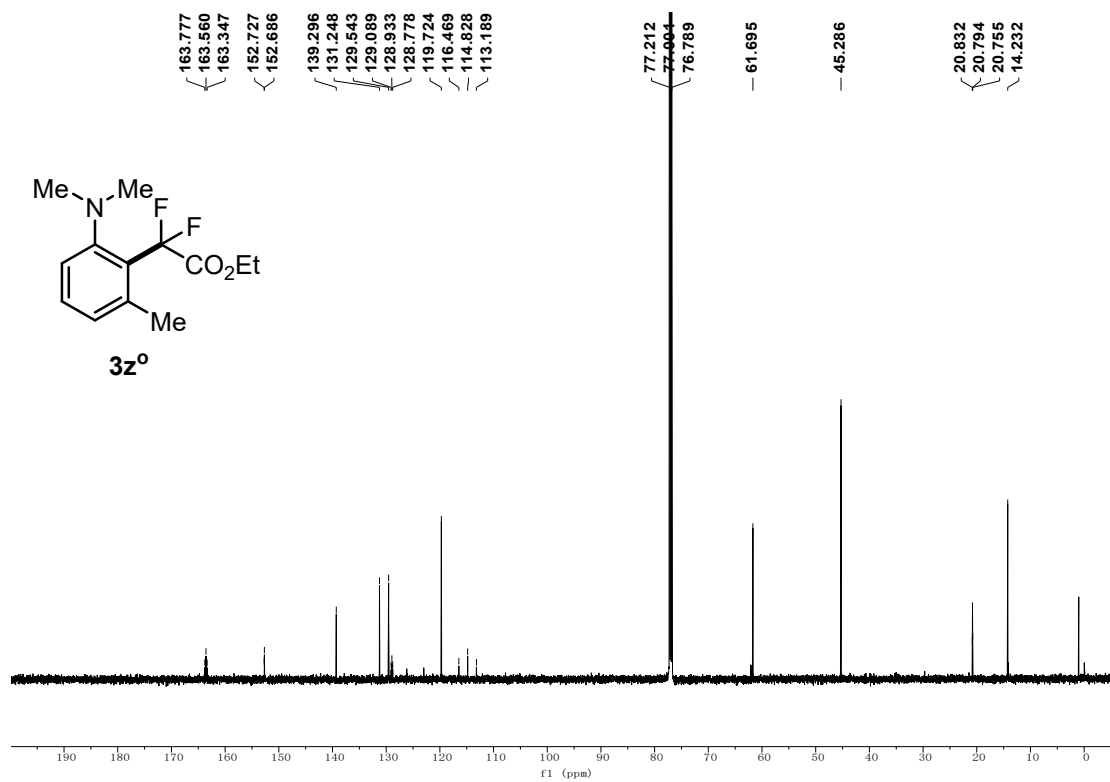
$^{19}\text{F}$  NMR (376MHz,  $\text{CDCl}_3$ ) spectrum of product **3y<sup>p</sup>**



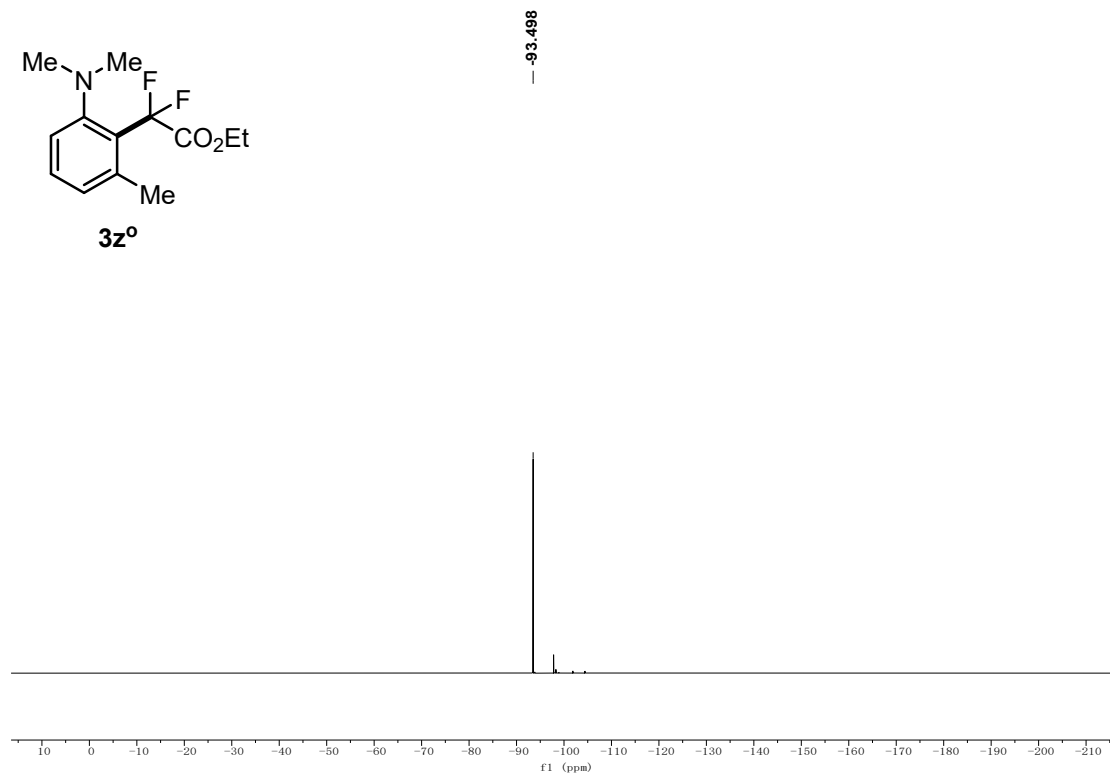
$^1\text{H}$  NMR (600MHz,  $\text{CDCl}_3$ ) spectrum of product **3z<sup>o</sup>**



$^{13}\text{C}$  NMR (151MHz,  $\text{CDCl}_3$ ) spectrum of product **3z<sup>0</sup>**

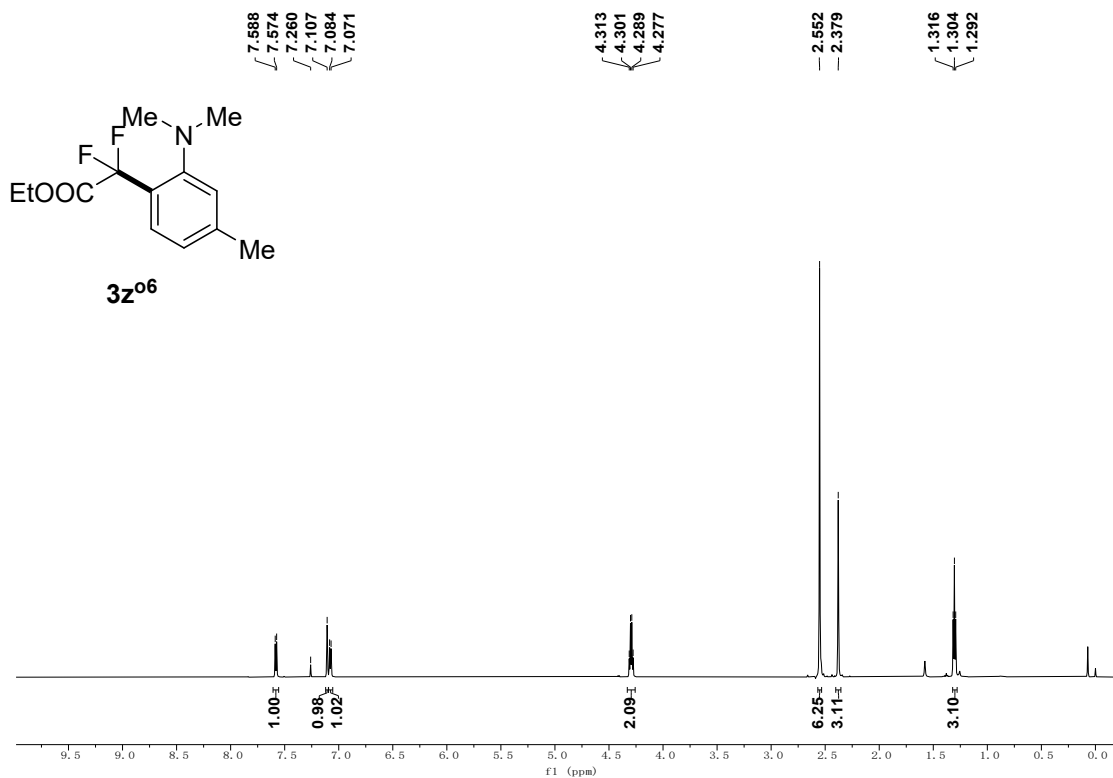


$^{19}\text{F}$  NMR (565 MHz, Chloroform-*d*) spectrum of product **3z<sup>0</sup>**

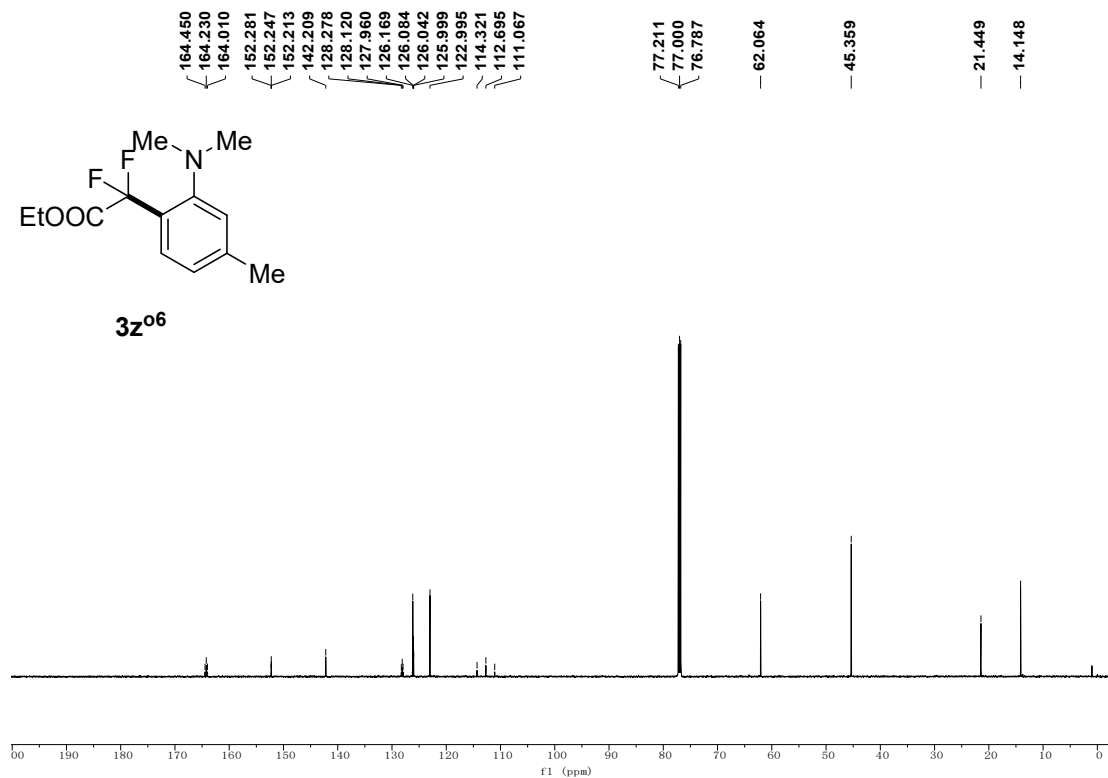




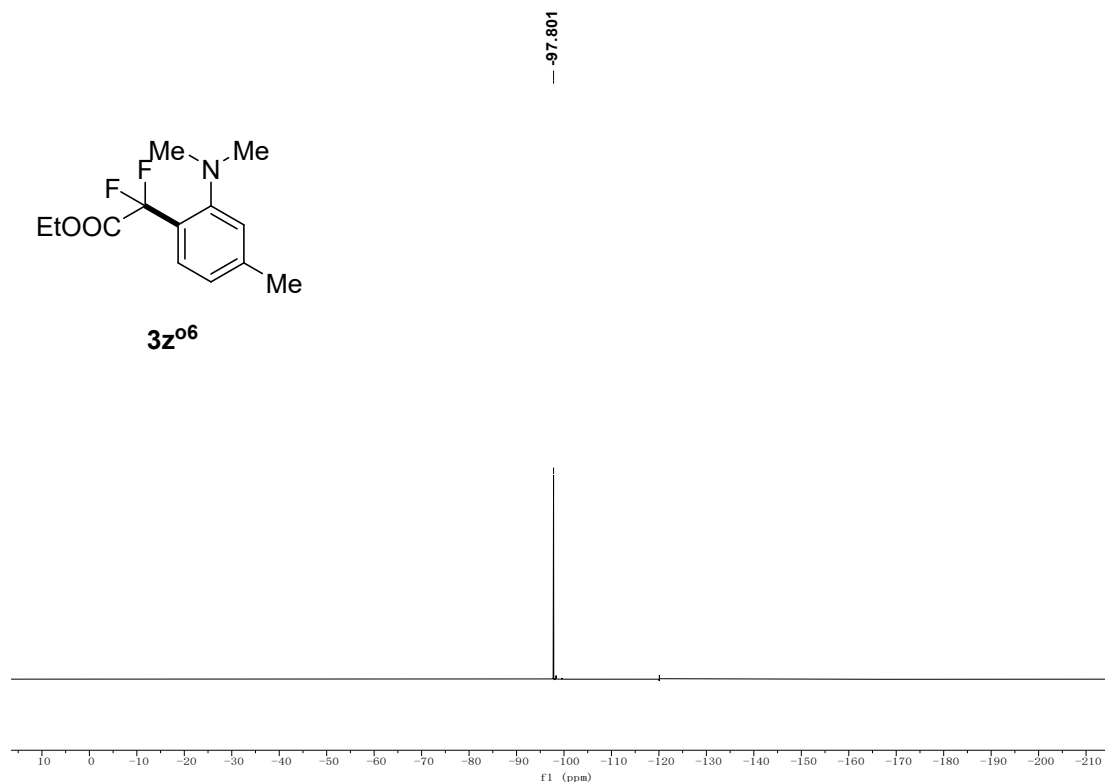
$^1\text{H}$  NMR (600MHz,  $\text{CDCl}_3$ ) spectrum of product **3z<sup>06</sup>**



$^{13}\text{C}$  NMR (151MHz,  $\text{CDCl}_3$ ) spectrum of product **3z<sup>06</sup>**

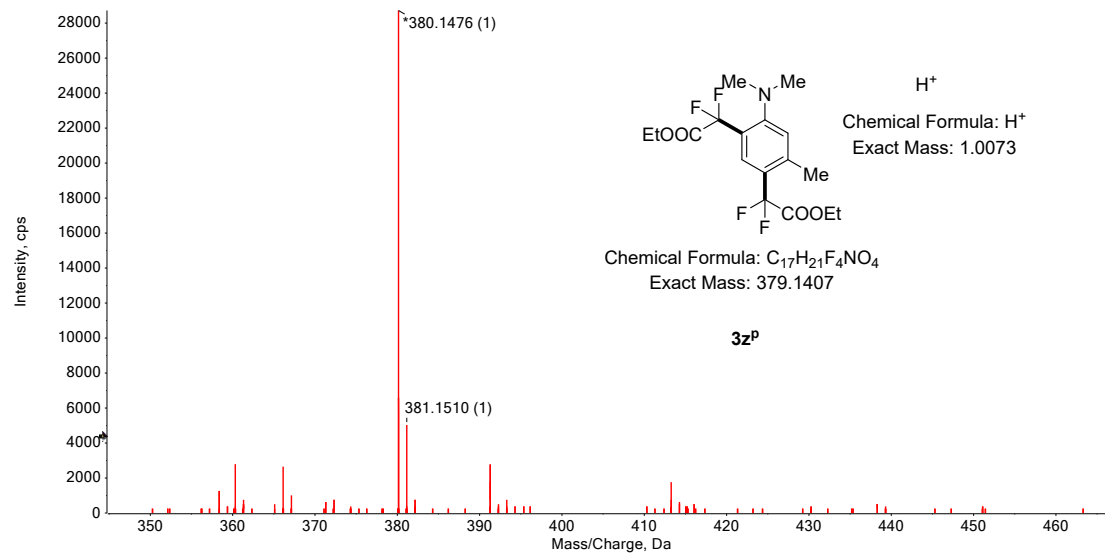


<sup>19</sup>F NMR (565 MHz, Chloroform-*d*) spectrum of product **3z**<sup>06</sup>

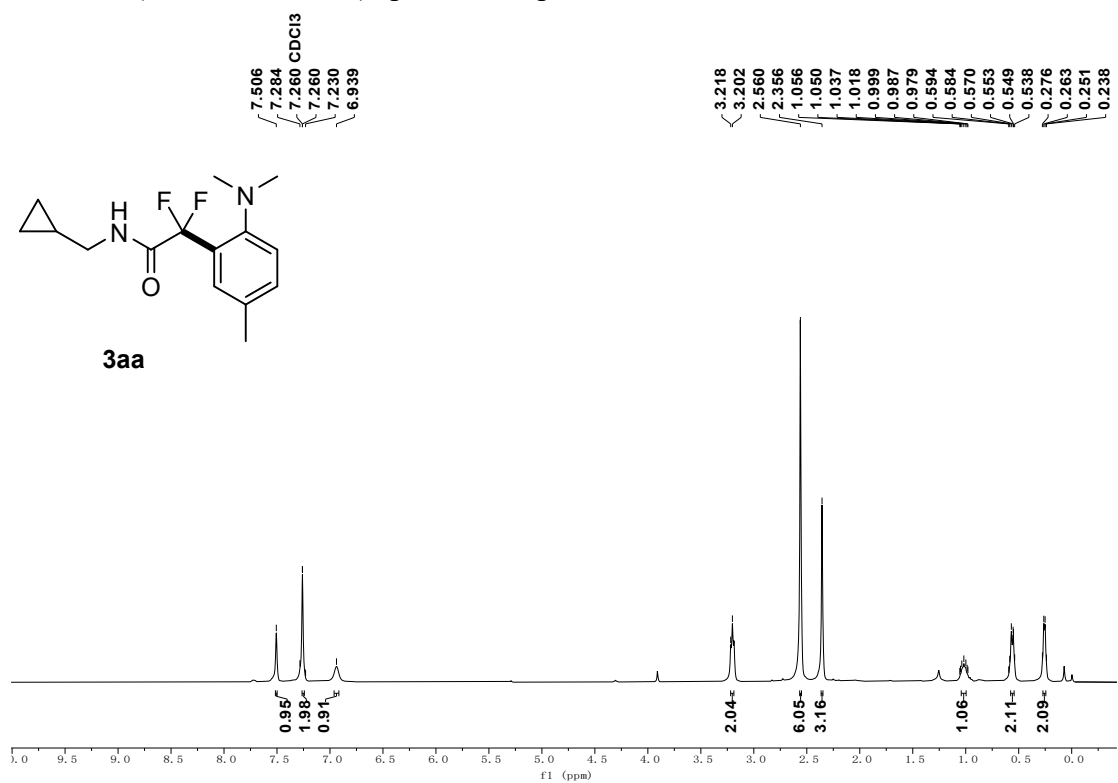


HRMS spectrum of product **3z**<sup>P</sup>

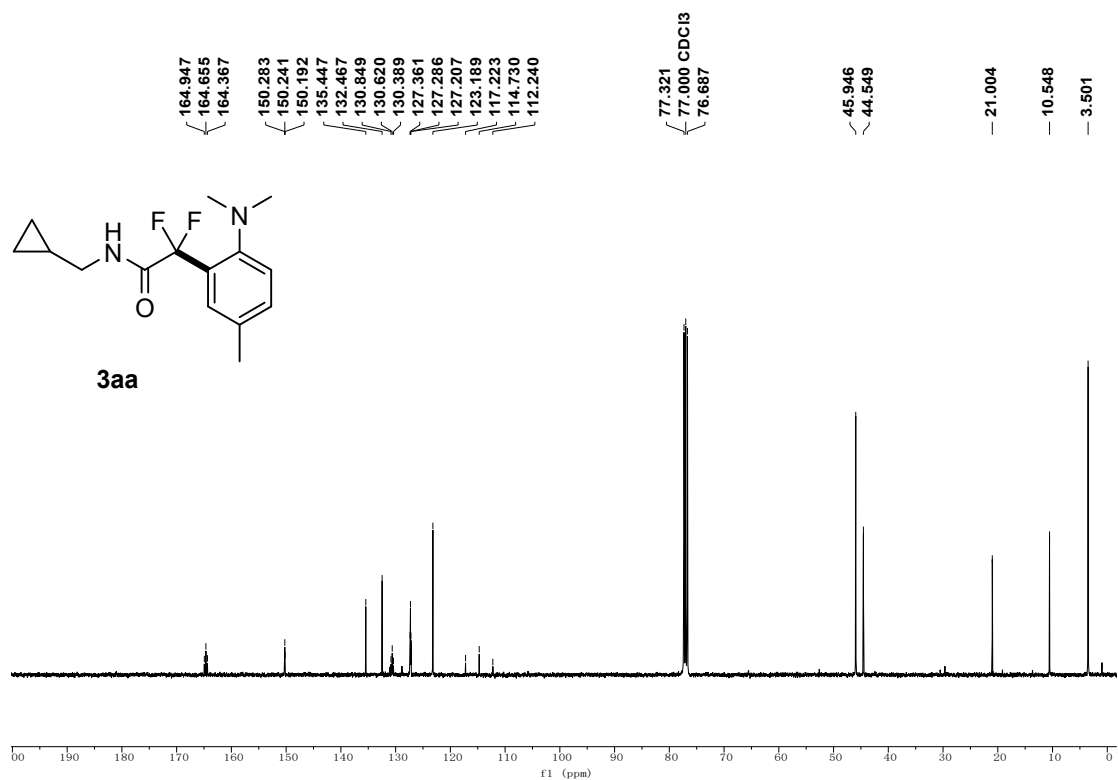
Spectrum from WH.wiff2 (sample 381) - CF2-REV-68-P3, +TOF MS (50 - 3000) from 0.566 min



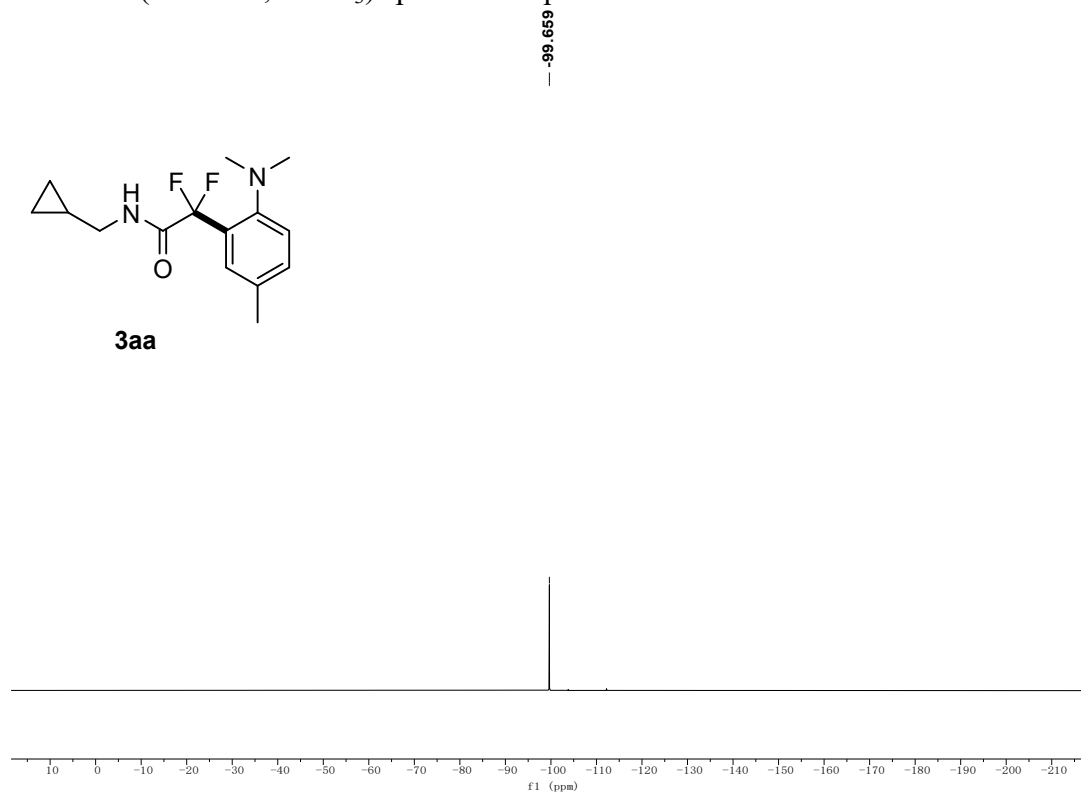
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ) spectrum of product **3aa**



$^{13}\text{C}$  NMR (101MHz,  $\text{CDCl}_3$ ) spectrum of product **3aa**

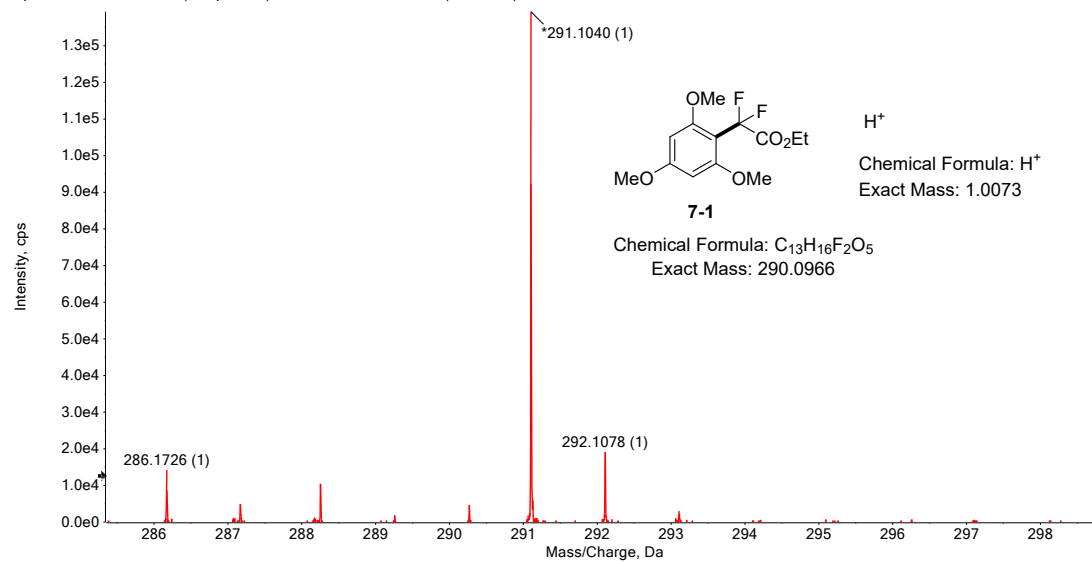


<sup>19</sup>F NMR (376MHz, CDCl<sub>3</sub>) spectrum of product **3aa**



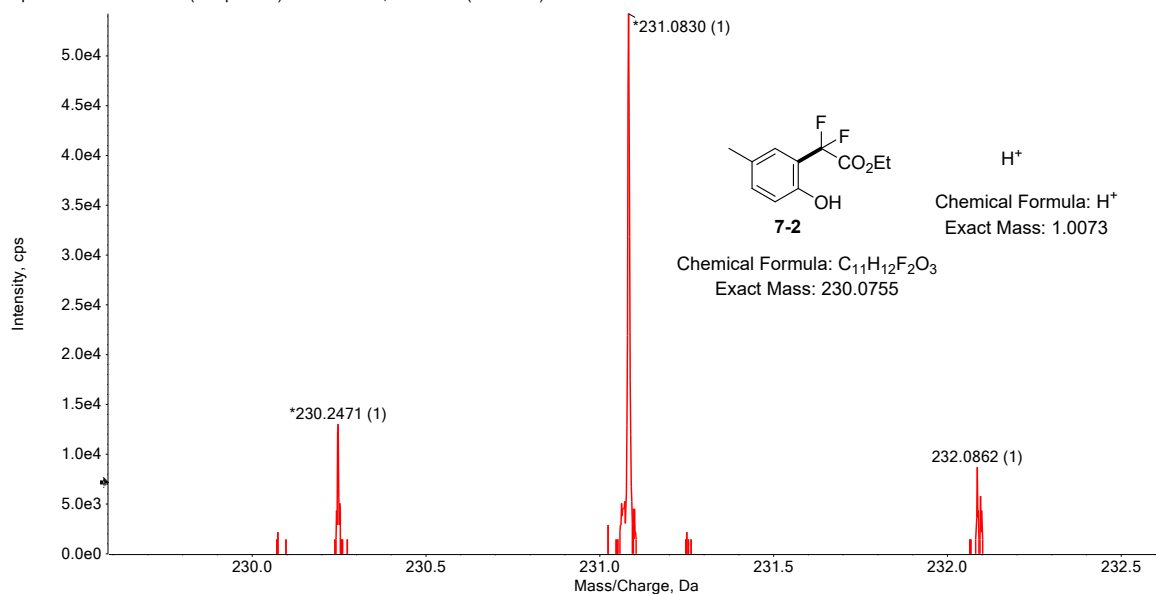
HRMS spectrum of **7-1**

Spectrum from WH.wiff2 (sample 345) - WH-CF2-67, +TOF MS (50 - 2000) from 0.236 min



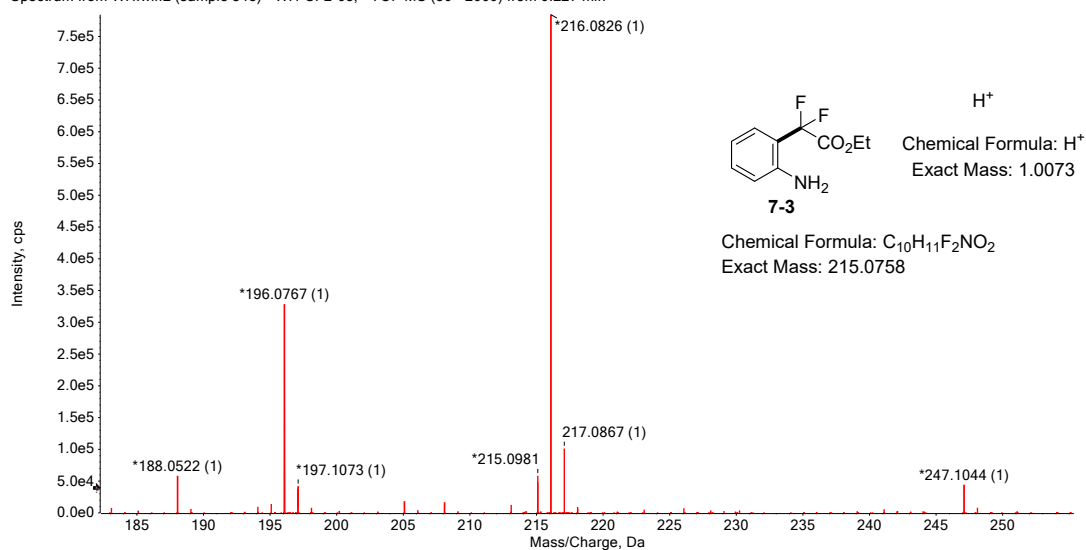
## HRMS spectrum of 7-2

Spectrum from WH.wiff2 (sample 342) - WH-CF2-64, +TOF MS (50 - 2000) from 0.194 min



## HRMS spectrum of 7-3

Spectrum from WH.wiff2 (sample 343) - WH-CF2-65, +TOF MS (50 - 2000) from 0.227 min



## 8. Reference

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