Supporting Information

Thermo-Induced Decarboxylative *α*-C(sp^3)−H Fluoroalkylation of Glycine Derivatives with Fluorinated Peroxy Esters

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1. General Information

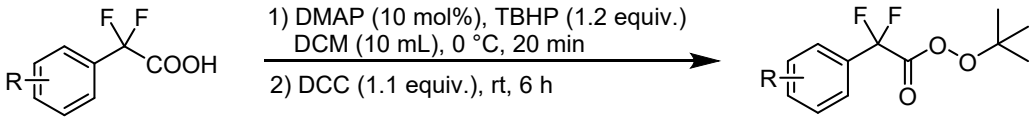
All reactions were conducted in 10 mL oven-dried sealed tube under N_2 atmosphere. Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. ^1H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker 400 MHz (100 MHz for ^{13}C NMR) spectrometer at ambient temperature. Chemical shift are reported in ppm from TMS with the solvent resonance as internal standard ($CDCl_3$: ^1H NMR: $\delta = 7.26$; ^{13}C NMR: $\delta = 77.16$; DMSO: ^1H NMR: $\delta = 2.50$; ^{13}C NMR: $\delta = 39.52$; $CFCl_3$ as an external standard and low field is positive). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), td (triplet of doublets), qd (quartet of doublets) and m (multiplet). FT-IR spectra were recorded on a Bruker V 70 spectrometer and only major peaks are reported in cm-1. HRMS were obtained on a WATERS I-Class VION IMS Q-Tof. Melting points were measured using open glass capillaries in a SGW® X-4A apparatus. Analytical TLC: aluminum backed plates pre-coated (0.25 mm) with Merck Silica Gel 60F-254. Compounds were visualized by exposure to UV-light or by dipping the plates in $KMnO_4$ stain followed by heating.

2. Starting Materials

2.1 Glycine Derivatives

All *N*-arylglycine esters and amides **1** were prepared according to the literature.[1-2]

2.2 General Procedure for the Synthesis of Fluorine-Contained Peroxy Esters 2a-2l:

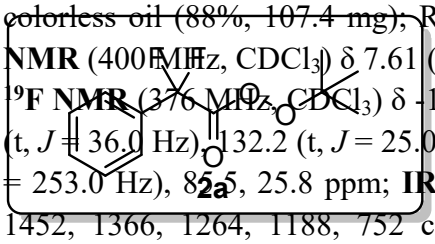


A solution of DMAP (0.5 mmol), TBHP (70% in water, 6.0 mmol, 1.2 equiv.), and 2,2-difluorophenylacetic acid (5.0 mmol, 1.0 equiv.) in DCM (10 mL) was cooled to 0 °C over 20 min, then DCC (5.5 mmol, 1.1 equiv.) was added. The reaction mixture was stirred at room temperature. After completion as detected by TLC, the solution was filtered, the filter liquor was concentrated on a rotary evaporator under vacuum at 10 ~ 15 °C, and the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to give the corresponding fluorine-contained peroxy esters **2a-2l**.

All fluorine-contained peroxy esters heated and concentrated by rotovap at below 30 °C and stored under -20 °C. We have never experienced a safety problem with these materials.

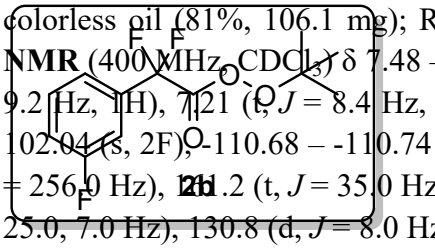
2.3 Characterization of Staring Materials

Tert-butyl-2,2-difluoro-2-phenylethaneperoxoate (2a):



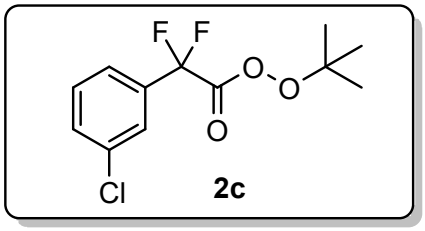
colorless oil (88%, 107.4 mg); R_f = 0.55 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.45 (m, 3H), 1.27 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.00 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.7 (t, *J* = 36.0 Hz), 132.2 (t, *J* = 25.0 Hz), 131.4 , 128.8 , 125.2 (t, *J* = 6.0 Hz), 113.4 (t, *J* = 253.0 Hz), 85.5, 25.8 ppm; **IR (neat)**: υ $_{max}$ 3068, 2362, 2116, 1764, 1695, 1516, 1452, 1366, 1264, 1188, 752 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{15}F_2O_3$ $[M+H]^+$ 245.0984, found 245.0995.

Tert-butyl 2,2-difluoro-2-(3-fluorophenyl)ethaneperoxoate (2b):



colorless oil (81%, 106.1 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 9.2 Hz, 1H), 7.21 (t, *J* = 8.4 Hz, 1H), 1.28 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.04 (s, 2F), -110.68 – -110.74 (m, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.8 (d, *J* = 256.0 Hz), 131.2 (t, *J* = 35.0 Hz), 134.6 – 134.0 (td, *J* = 25.0, 7.0 Hz), 130.8 (d, *J* = 8.0 Hz), 121.1 (td, *J* = 6.0, 3.0 Hz), 118.7 (d, *J* = 21.0 Hz), 112.84 (dt, *J* = 12.0, 6.0 Hz), 112.6 (t, *J* = 253.0 Hz), 85.7, 25.8; **IR (neat)**: υ $_{max}$ 3083, 1799, 1707, 1694, 1679, 1596, 1486, 1393, 1369, 1135, 794 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{14}F_3O_3$ $[M+H]^+$ 263.0889, found 263.0896.

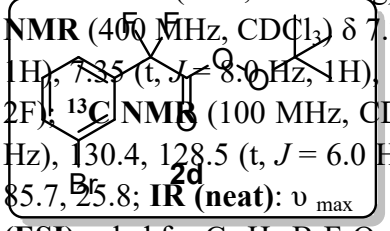
Tert-butyl 2-(3-chlorophenyl)-2,2-difluoroethaneperoxoate (2c):



colorless oil (69%, 95.9 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz,

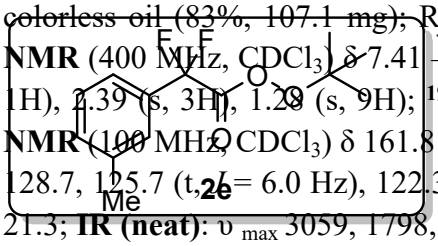
$CDCl_3$) δ 7.60 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.40 (m, 1H), 1.29 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.11 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (t, *J* = 35.0 Hz), 135.0, 134.0 (t, *J* = 26.0 Hz), 131.6, 130.2, 125.7 (t, *J* = 6.0 Hz), 123.6 (t, *J* = 6.0 Hz), 112.7 (t, *J* = 254.0 Hz), 85.7, 25.9; **IR (neat)**: υ_{max} 3074, 1798, 1708, 1679, 1494, 1399, 1369, 982, 830 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}ClF_2O_3$ $[M+H]^+$ 279.0594, found 279.0584.

Tert-butyl 2-(3-bromophenyl)-2,2-difluoroethaneperoxoate (2d):



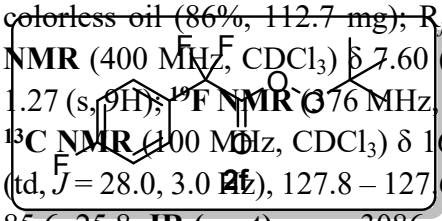
colorless oil (68%, 109.5 mg); R_f = 0.40 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 1.29 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.17 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.1 (t, *J* = 35.0 Hz), 134.6, 134.1 (t, *J* = 25.0 Hz), 130.4, 128.5 (t, *J* = 6.0 Hz), 124.0 (t, *J* = 6.0 Hz), 122.8, 112.5 (t, *J* = 253.0 Hz) 85.7, 25.8; **IR (neat)**: υ_{max} 3037, 1799, 1718, 1570, 1422, 1368, 819 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{14}BrF_2O_3$ $[M+H]^+$ 323.0089, found 323.0087.

Tert-butyl 2,2-difluoro-2-(m-tolyl)ethaneperoxoate (2e):



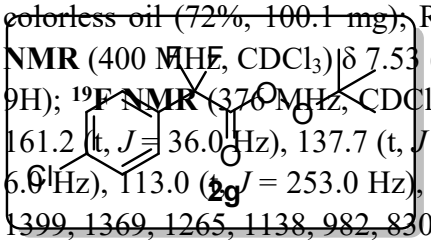
colorless oil (83%, 107.1 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.39 (m, 2H), 7.36 – 7.34 (m, 2H), 7.33 – 7.30 (m, 1H), 2.39 (s, 3H), 1.28 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.79 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8 (t, *J* = 36.0 Hz), 138.7, 132.1 (t, *J* = 25.0 Hz), 132.1, 128.7, 125.7 (t, *J* = 6.0 Hz), 122.3 (t, *J* = 6.0 Hz), 113.5 (t, *J* = 253.0 Hz), 85.5, 25.8, 21.3; **IR (neat)**: υ_{max} 3059, 1798, 1766, 1725, 1694, 1612, 1515, 1370, 1313, 856 cm^{-1}; **HRMS (ESI)** calcd for $C_{13}H_{17}F_2O_3$ $[M+H]^+$ 259.1140, found 259.1132.

Tert-butyl 2,2-difluoro-2-(4-fluorophenyl)ethaneperoxoate (2f):



colorless oil (86%, 112.7 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.4 , 6.8 Hz, 2H), 7.15 (t, *J* = 8.8 Hz, 2H), 1.27 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.12 (s, 2F), -108.17 – -108.20 (m, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4 (d, *J* = 251.0 Hz), 161.5 (t, *J* = 36.0 Hz), 128.3 (td, *J* = 28.0, 3.0 Hz), 127.8 – 127.6 (m), 116.0 (d, *J* = 23.0 Hz), 113.1 (t, *J* = 253.0 Hz), 85.6, 25.8; **IR (neat)**: υ_{max} 3086, 1798, 1768, 1513, 1369, 1266, 1084, 985, 840 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{14}F_3O_3$ $[M+H]^+$ 263.0889, found 263.0891.

Tert-butyl 2-(4-chlorophenyl)-2,2-difluoroethaneperoxoate (2g):



colorless oil (72%, 100.1 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 1.26 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.82 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (t, *J* = 36.0 Hz), 137.7 (t, *J* = 2.0 Hz), 130.7 (t, *J* = 25.0 Hz), 129.1, 126.8 (t, *J* = 6.0 Hz), 113.0 (t, *J* = 253.0 Hz), 85.6, 25.7; **IR (neat)**: υ_{max} 3074, 1798, 1766, 1678, 1399, 1369, 1265, 1138, 982, 830 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{14}ClF_2O_3$ $[M+H]^+$ 279.0594, found 279.0580.

Tert-butyl 2-(4-bromophenyl)-2,2-difluoroethaneperoxoate (2h):

colorless oil (75%, 120.8 mg); R_f = 0.40 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 1.28 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.98 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.3 (t, *J* = 36.0 Hz), 132.1, 131.5, 127.0 (t, *J* = 6.0 Hz), 126.1 (t, *J* = 2.0 Hz), 113.1 (t, *J* = 253.0 Hz), 85.7, 25.9; IR (neat): υ $_{max}$ 3075, 1915, 1766, 1595, 1485, 1449, 1359, 1295, 1185, 1139, 825 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{14}BrF_2O_3$ $[M+H]^+$ 323.0089, found 323.0073.

Tert-butyl 2-(3,5-dimethylphenyl)-2,2-difluoroethaneperoxoate (2i):

colorless oil (78%, 106.1 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 (s, 2H), 7.12 (s, 1H), 2.35 (s, 6H), 1.29 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.63 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9 (t, *J* = 35.0 Hz), 138.6, 132.9, 132.1 (d, *J* = 25.0Hz), 122.9 (t, *J* = 6.0 Hz), 113.6 (t, *J* = 253.0 Hz), 85.4, 25.8, 21.2; **IR (neat)**: υ $_{max}$ 3055, 1799, 1767, 1708, 1612, 1458, 1370, 1231, 1099, 984, 794 cm^{-1}; **HRMS (ESI)** calcd for $C_{14}H_{19}F_2O_3$ $[M+H]^+$ 273.1296, found 273.1297.

Tert-butyl 2,2-difluoro-2-(p-tolyl)ethaneperoxoate (2j):

colorless oil (82%, 105.8 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H), 1.29 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.93 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8 (t, *J* = 36.0 Hz), 141.7, 129.4, 129.3 (t, *J* = 25.0 Hz), 125.1 (t, *J* = 6.0 Hz), 113.6 (t, *J* = 253.0 Hz), 85.3, 25.7, 21.2; **IR (neat)**: υ $_{max}$ 3089, 1766, 1612, 1515, 1370, 1393, 1098, 1050, 981, 750 cm^{-1}; **HRMS (ESI)** calcd for $C_{13}H_{17}F_2O_3$ $[M+H]^+$ 259.1140, found 259.1135.

Tert-butyl 2,2-difluoro-2-(4-methoxyphenyl)ethaneperoxoate (2k):

colorless oil (78%, 106.9 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 3H), 1.26 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -100.52 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9 (t, *J* = 36.0 Hz), 161.8, 126.9 (t, *J* = 6.0 Hz), 124.2 (t, *J* = 26.0 Hz), 114.1, 113.6 (t, *J* = 253.0 Hz), 85.4, 55.3, 25.8; **IR (neat)**: υ $_{max}$ 3061, 1797, 1766, 1616, 1539, 1464, 1423, 1392, 1137, 982, 837 cm^{-1}; **HRMS (ESI)** calcd for $C_{13}H_{17}F_2O_4$ $[M+H]^+$ 275.1089, found 275.1086.

Tert-butyl 2-(4-(tert-butyl)phenyl)-2,2-difluoroethaneperoxoate (2l):

colorless oil (85%, 109.7 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 3H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 3H), 2.29 (s, 3H), 1.23 (s, 9H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -99.25 (s, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.5 (t, *J* = 35.0 Hz), 136.3 (t, *J* = 3.0 Hz), 131.9, 131.1, 130.3 (t, *J* = 23.0 Hz), 125.9, 114.1 (t, *J* = 253.0 Hz), 85.3, 63.0, 25.7, 19.5; **IR (neat)**: υ $_{max}$ 3071, 1799, 1766, 1708, 1609, 1455, 1367, 1187, 1074, 980, 843 cm^{-1}; **HRMS (ESI)** calcd for $C_{13}H_{17}F_2O_3$ $[M+H]^+$ 259.1140, found 259.1131.

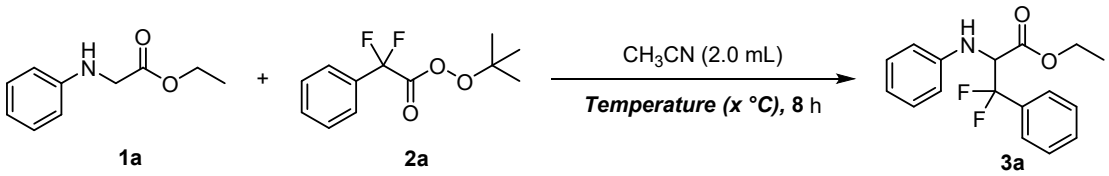
3. General Procedures for the Difluoroalkylation of Ethyl *N*-Phenylglycinate 1a with Peroxy Ester 2a

3.1 Thermolysis Strategy (General Procedure A)

An oven-dried 10 mL sealed tube equipped with a magnetic stir bar was charged with ethyl *N*-phenylglycinate **1a** under N_2 atmosphere (See **Table S1**). Subsequently, a solution of peroxy ester **2a** in solvent (x mL) was added via syringes. The tube was capped with a pressure screw cap and then stirred at specified temperature for specified time. After the reaction completed, the mixture was concentrated in *vacuo.* Purification of the crude product by flash chromatography (silica gel; petroleum ether/ethyl acetate = 20 : 1) yields the desired product **3a** as colorless oil.

Table S1 Optimization of the Reaction of Ethyl *N*-Phenylglycinate 1a and Peroxy Ester 2a

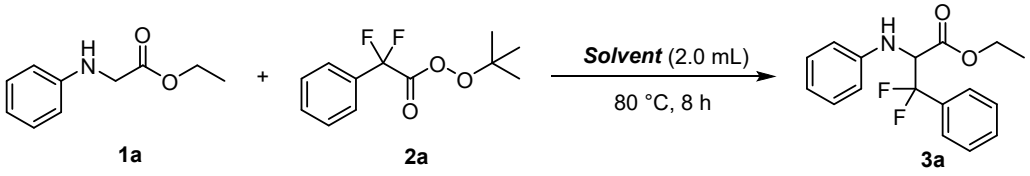
Temperature



Entry	Temperature (°C)	Yields (%) [b]
1	25	trace
2	40	23
3	60	42
4	80	51
5	100	54
6	120	53
7	140	52

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 1.5 equiv.), CH_3CN (2.0 mL), x °C, for 8 h, under N_2. [b] ^{19}F NMR using $PhCF_3$ as an internal standard.

Solvent



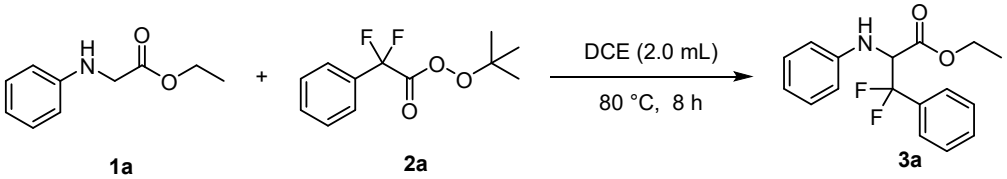
Entry	Solvent	Yield (%) [b]
1	toluene	trace
2	THF	trace
4	EtOAc	43

5	DCE	59
6	CH_3CN	51

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 1.5 equiv.), solvent (2.0 mL), 80 °C, for 8 h, under N_2. [b] ^{19}F NMR yields using $PhCF_3$ as an internal standard.

Ratio of 1a:2a

Entry	Temperature (°C)	Yields (%) [b]
1	80	65
2	100	78
3	120	84
4	140	85



1a **2a** **3a**

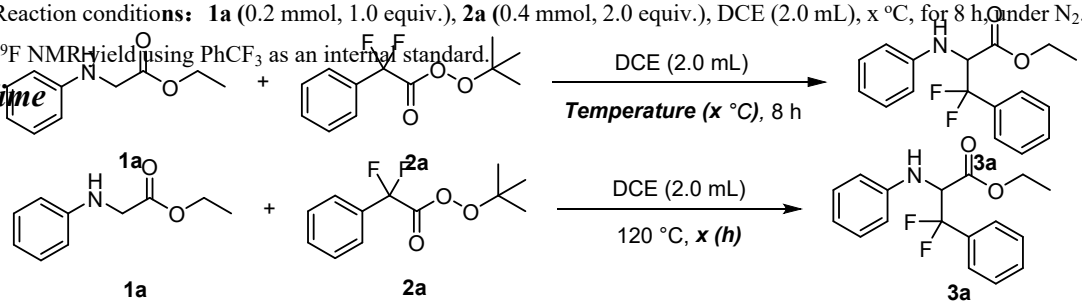
Entry	**1a:2a**	Yield (%) [b]
1	1:1	43
2	1:1.5	59
3	1:2	65
4	1:2.5	66

[a] Reaction conditions: **1a** : **2a** = 1 : x, DCE (2.0 mL), 80 °C, for 8 h, under N_2. [b] ^{19}F NMR yields using $PhCF_3$ as an internal standard.

Temperature

[a] Reaction condition**s**：**1a (**0.2 mmol, 1.0 equiv.), **2a (**0.4 mmol, 2.0 equiv.), DCE (2.0 mL), x °C, for 8 h,under N_2. [b] ^{19}F NMRyield using $PhCF_3$ as an internal standard.

Time

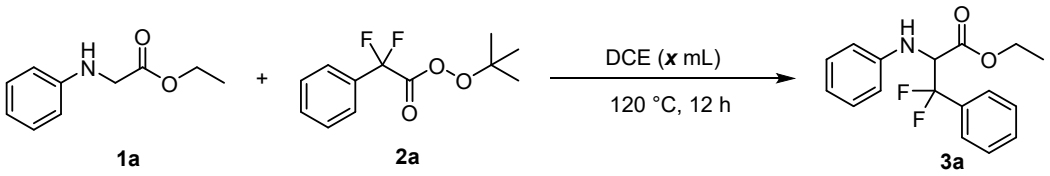


1a **2a** **3a**

Entry	Time (h)	Yield (%) [b]
1	2	43
2	4	49
3	6	63
4	8	67
5	10	84
6	12	99 (93) [c]
7	14	99

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.4 mmol, 2.0 equiv.), DCE (2.0 mL), 120 °C, for x h, under N_2. [b] ^{19}F NMR yield using $PhCF_3$ as an internal standard. [c] Yields of isolated products.

Concentration



1a **2a** **3a**

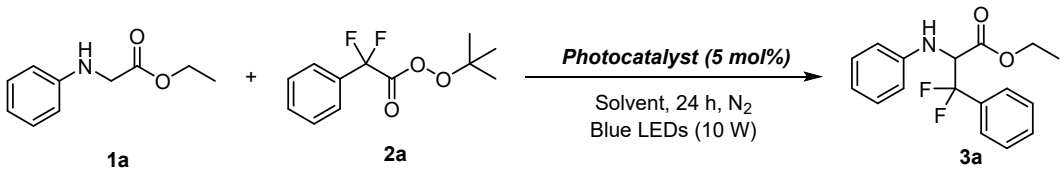
Entry	DCE (mL)	Yield (%)[b]
1	1	88
2	2	93
3	3	92

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.4 mmol, 2.0 equiv.), DCE (x mL), 120 °C, for 12 h, under N_2. [b] Yields of isolated products.

3.2 Photo-induced Strategy (General Procedure B)

An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinate **1a**, photocatalyst, under N_2 atmosphere (See **Table S2**). Subsequently, a solution of peroxy ester **2a** in solvent (2 mL) was added via syringes. The tube was capped with a pressure screw cap and then stirred under the irradiation of a 10 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time at room temperature. After the reaction completed, the mixture was concentrated in *vacuo.* Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20 : 1) yields the desired product **3a** as colorless oil.

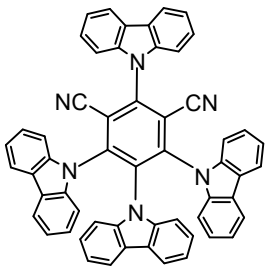
Table S2 Optimization of the Reaction of Ethyl *N*-phenylglycinate 1a and tert-butyl-2,2-difluoro-2-phenylethaneperoxoate 2a



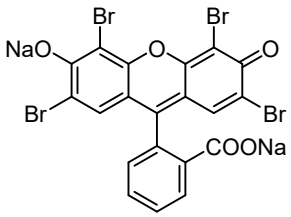
1a **2a** **3a**

PC	Yield (%) [a]
4CzIPN	trace
EsionY	< 10
N-methylphenothiazine	72
Rose bengale	< 10
Methyene blue	trace
N-methylphenothiazine	65 [b]

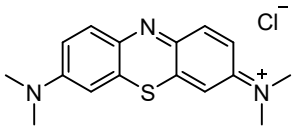
[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.4 mmol, 2.0 equiv.), CH_3CN (2.0 mL), Photocatalyst (5 mol%), for 24 h, rt, under N_2, isolated yields were given. [b] DCE as solvent (2.0 mL), for 24 h, under N_2, isolated yield was given.



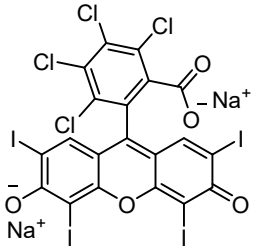
4CzIPN



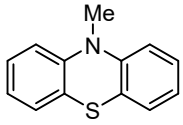
Eosin Y



Methylene Blue

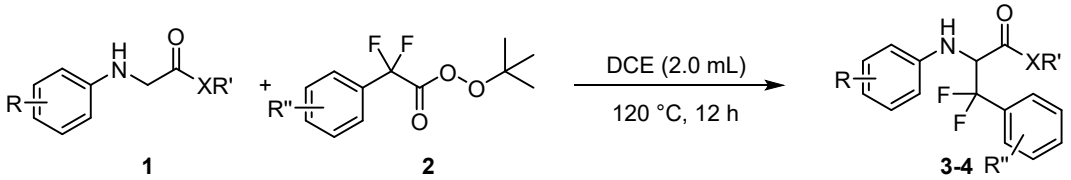


Rose Bengale



***N*-methyphenothiazine**

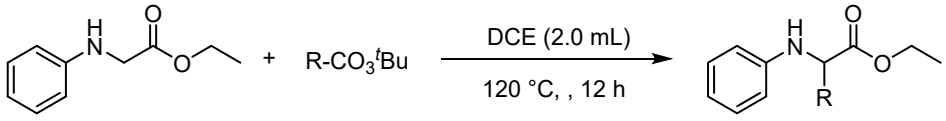
4. Representative Procedure for the Difluoroalkylation of Glycine Derivatives 1 with Peroxy Esters 2



1 **2** **3-4**

An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinate **1** (0.2 mmol, 1.0 equiv.) under N_2 atmosphere. Subsequently, a solution of peroxy ester **2** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) was added *via* syringes. The tube was capped with a pressure screw cap and then stirred at 120 °C for 12 h. After the reaction completed, the mixture was concentrated in *vacuo.* Purification of the crude product by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1 to 30 : 1) yields the desired products **3-4** .

5. Representative Procedure for the Reaction of Ethyl *N*-Phenylglycinate 1a with Peroxy Esters 5



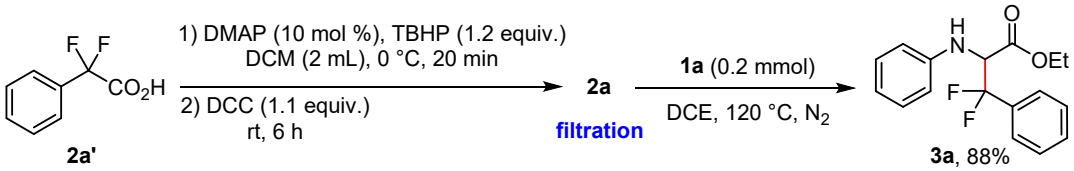
1a **5** **6**

An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinate **1** (0.2 mmol, 1.0 equiv.) under N_2 atmosphere. Subsequently, a solution of peroxy ester **5** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) was added *via* syringes. The tube was capped with a pressure screw cap and then stirred at 120 °C for 12 h. After the reaction completed, the mixture was concentrated in *vacuo.*

Purification of the crude product by flash chromatography on silica gel; (petroleum ether/ethyl acetate = 10 : 1 to 30 : 1) yields the desired products **6** .

6. Telescoped Procedure

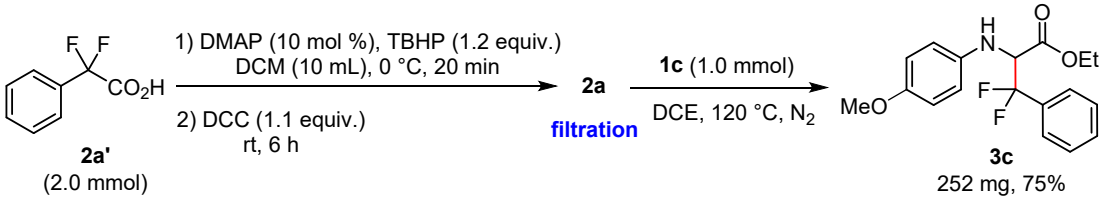
6.1 The Two-Step Difluoroalkylation Reaction of 1a with 2a



A solution of DMAP (0.02 mmol), TBHP (70% in water, 0.24 mmol) and **2a'** (0.4 mmol) was cooled to 0 °C over 20 min, then DCC (0.22 mmol) was added. The mixture was stirred at room temperature for 6 h. After completion as detected by TLC, the solution was diluted by petroleum ether to extract the white solid to give the corresponding peroxy ester **2a**, which was used for the next reaction without further purification.

An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinatl **1a** (0.2 mmol, 1.0 equiv.) under N_2 atmosphere. Subsequently, a solution of peroxy ester **2a** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) was added *via* syringes. The tube was capped with a pressure screw cap and then stirred at specified temperature for specified time. After the reaction completed, the mixture was concentrated in *vacuo*. Purification of the crude product by flash chromatography on silica gel (petrolrum ether/ethyl acetate = 20 : 1) yields the desired product **3a** (53.7 mg, 88%).

6.2 Larger Scale Two-Step Difluoroalkylation Reaction of 1c with 2a

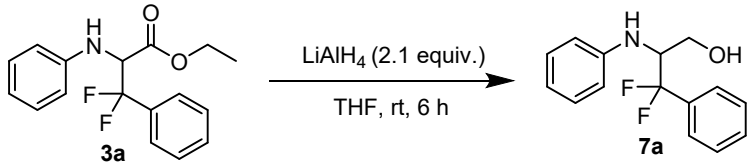


A solution of DMAP (0.2 mmol), TBHP (70% in water, 2.4 mmol), and **2a'** (2.0 mmol) was cooled to 0 °C over 20 min, then DCC (2.2 mmol) was added. The mixture was stirred at room temperature for 6 h. After completion as detected by TLC, the solution was diluted by petroleum ether to extract the white solid to give the corresponding peroxy ester **2a**, which was used for the next reaction without further purification.

An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinate **1c** (0.2 mmol, 1.0 equiv.) under N_2 atmosphere. Subsequently, a solution of peroxy ester **2a** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) was added *via* syringes. The tube was capped with a pressure screw cap and then stirred at specified temperature for specified time. After the reaction completed, the mixture was concentrated in *vacuo*. Purification of the crude product by flash chromatography

on silica gel (petrolrum ether/ethyl acetate = 10 : 1) yields the desired product **3c** (252 mg, 75%).

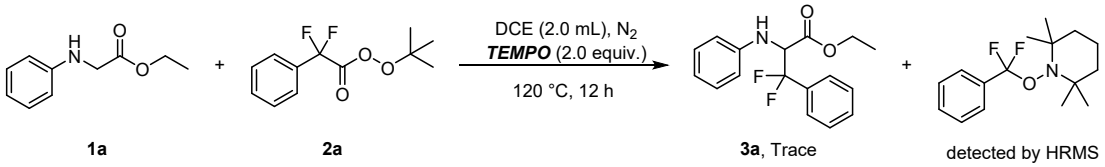
7. Derivatizations of Product



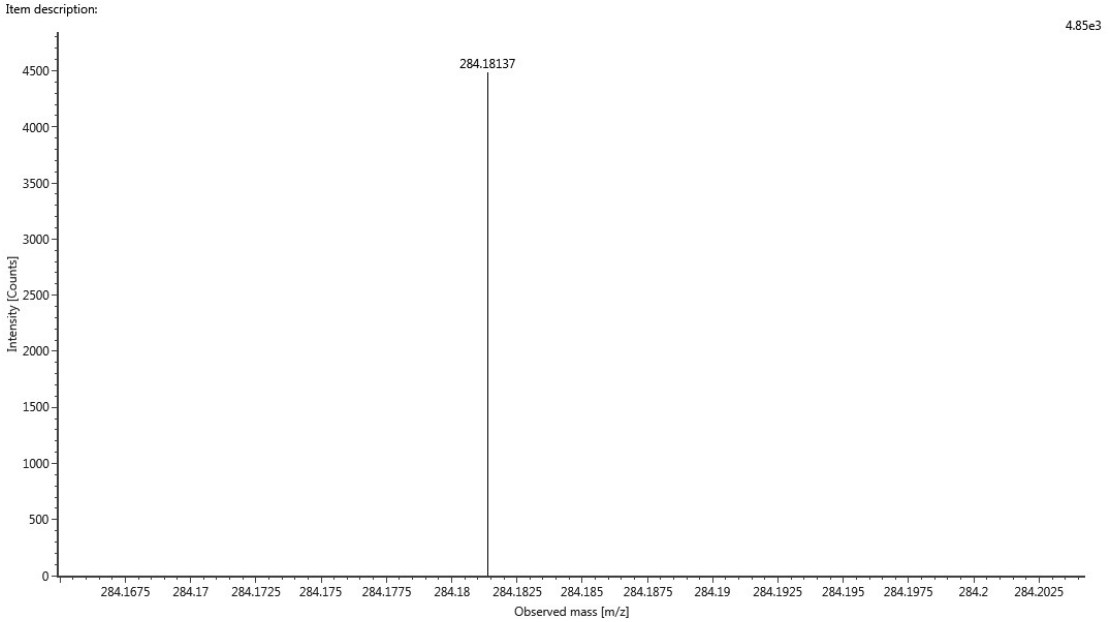
To a solution of reductive product **3a** (0.2 mmol, 1.0 equiv.) in THF (10 mL) was added lithium aluminium tetrahydride (0.42 mmol, 2.1 equiv.) at room temperature. The reaction mixture was stirred for 6 h. After completion as detected by TLC, the reaction was quenched with saturated ammonium chloride aqueous solution. The aqueous layer was extracted with ethyl acetate; the combined organic layer was dried over sodium sulfate, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to afford fluorine-contained amino alcohol **7a** in 97% yield.

8. Mechanism Studies

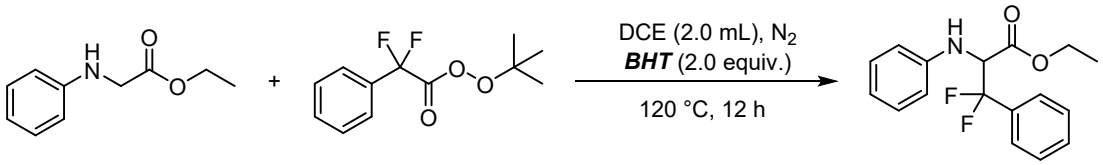
8.1 Radical Trapping Experiments



An oven-dried 10 mL sealed tube equipped with a magnetic stirrer was charged with ethyl *N*-phenylglycinate **1a** (0.2 mmol, 1.0 equiv.), TEMPO (0.4 mmol, 2.0 equiv.) under N_2 atmosphere. Subsequently, a solution of peroxy ester **2a** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) were added *via* syringes. The tube was capped with a pressure screw cap and then stirred at 120 °C for 12 h.



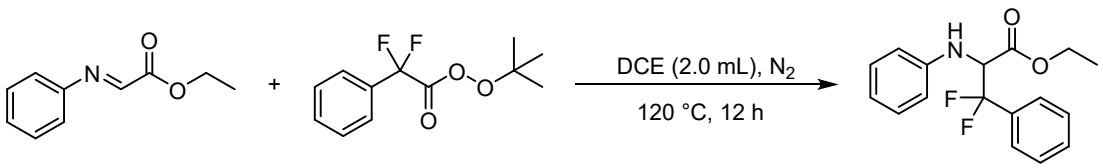
When 2.0 equiv of TEMPO was added to the reaction of ethyl *N*-phenylglycinate **1a** with peroxy ester **2a** under the general procedure A, the reaction was completely suppressed and the TEMPO-adduct product was detected by LC-HRMS. (**HRMS (ESI)** calcd for $C_{16}H_{24}F_2NO$ $[M+H]^+$ 284.1820, found 284.1814). This result indicates that a radical intermediate might be involved in this transformation



1a **2a** **3a**, Trace

When 2.0 equiv of BHT was added of to the reaction of **1a** with peroxy ester **2a** under the general procedure A, no desired product **3a** was observed. This result indicates that a radical intermediate might be involved in this transformation.

8.2 The Reaction of Imine 8 with Peroxy Ester 2

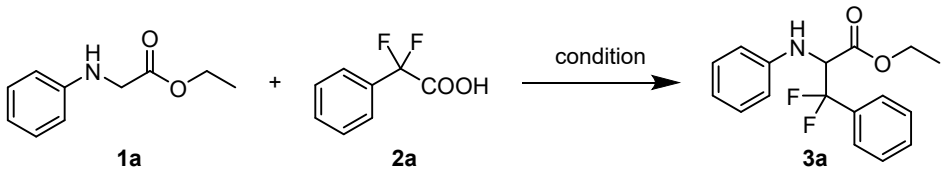


8a **2a** **3a**, 15%

An oven-dried 10 mL sealed tube equipped with a magnetic stir bar was charged with ethyl-2-(phenylimino)acetate **8a** (0.2 mmol, 1.0 equiv.), under N_2 atmosphere. Subsequently, a solution of peroxy ester **2a** (0.4 mmol, 2.0 equiv.) in DCE (2.0 mL) were added via syringes. The tube was capped with a pressure screw cap and then stirred at 120 °C for 12 h. When ethyl-2-(phenylimino)acetate **8a** was used instead of **2a** under

the standard conditions, the product **3a** was isolated in 15% yield. This result indicates that ethyl-2-(phenylimino)acetate **8a** was not the major intermediate in this transformation.

9. Preliminary screening

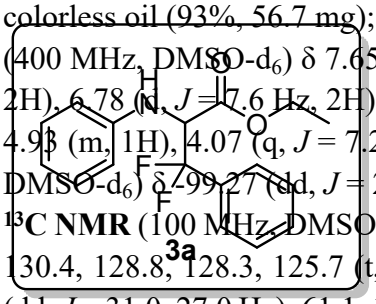


1a + **2a** → **3a**

Conditions	Result
Qing' s condtion[3]**:** Blue LEDs 30 W, $Ir[dF(CF_3)ppy]_2(dtbpy)BF_4$ BIOMe/BIOAC, NMP, rt.	**1a** and **2a** decomposed No desired product
Zhu' s condition[4]**:** Blue LEDs 30 W, $Ir[dF(CF_3)ppy]_2(dtbpy)BF_4$ $PhI(OAc)_2$, DMAc, rt.	**1a** and **2a** decomposed No desired product
Wan and Wu' s condition[5]**:** $AgNO_3$, DMSO, $K_2S_2O_8/(NH_4)_2S_2O_8$, 60 °C	76% recovered starting material **1a** 22% recovered starting material **2a** No desired product

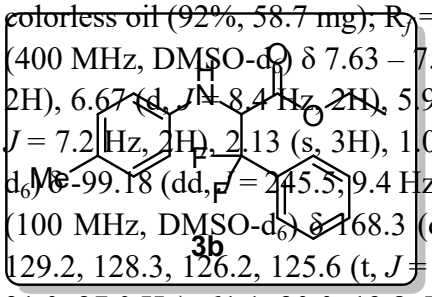
10. Characterization of Products

Ethyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3a):



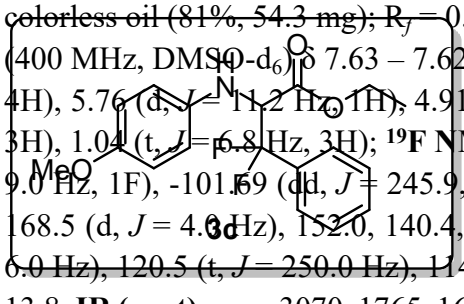
colorless oil (93%, 56.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.62 (m, 2H), 7.49 – 7.47 (m, 3H), 7.06 (t, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 7.6 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.20 (d, *J* = 8.0 Hz, 1H), 5.02 – 4.93 (m, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.27 (dd, *J* = 246.7, 9.8 Hz, 1F), -101.75 (dd, *J* = 245.9, 16.17 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.2 (d, *J* = 3.0 Hz), 146.5, 134.14 (t, *J* = 25.0 Hz), 130.4, 128.8, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 250.0 Hz), 117.6, 113.2, 61.3 (dd, *J* = 31.0, 27.0 Hz), 61.1, 13.9; **IR (neat)**: υ $_{max}$ 3060, 1737, 1646, 1602, 1506, 1017, 883 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{18}F_2NO_2$ $[M+H]^+$ 306.1300, found 306.1310.

Ethyl 3,3-difluoro-3-phenyl-2-(p-tolylamino)propanoate (3b):



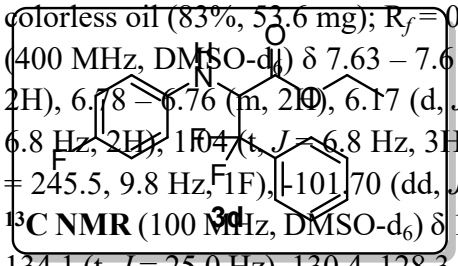
colorless oil (92%, 58.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.63 – 7.62 (m, 2H), 7.49 – 7.57 (m, 3H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 5.94 (d, *J* = 10.8 Hz, 1H), 4.95 – 4.85 (m, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.13 (s, 3H), 1.05 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.18 (dd, *J* = 245.5, 9.4 Hz, 1F), -101.95 (dd, *J* = 245.5, 15.8 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.3 (d, *J* = 3.0 Hz), 144.2, 134.2 (t, *J* = 26.0 Hz), 130.4, 129.2, 128.3, 126.2, 125.6 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 250.0 Hz), 113.4, 61.7 (dd, *J* = 31.0, 27.0 Hz), 61.1, 20.0, 13.8; **IR (neat)**: υ $_{max}$ 3060, 1736, 1516, 1453, 1371, 1234, 1043, 936, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_2$ $[M+H]^+$ 320.1456, found 320.1463.

Ethyl 3,3-difluoro-2-((4-methoxyphenyl)amino)-3-phenylpropanoate (3c):



colorless oil (81%, 54.3 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.63 – 7.62 (m, 2H), 7.49 – 7.48 (m, 3H), 6.70 (q, *J* = 8.8 Hz, 4H), 5.76 (d, *J* = 11.2 Hz, 1H), 4.91 – 4.82 (m, 1H), 4.05 (q, *J* = 6.8 Hz, 2H), 3.62 (s, 3H), 1.04 (t, *J* = 6.8 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -98.24 (dd, *J* = 245.5, 9.0 Hz, 1F), -101.69 (dd, *J* = 245.9, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.5 (d, *J* = 4.0 Hz), 152.0, 140.4, 134.3 (t, *J* = 25.0 Hz), 130.4, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 250.0 Hz), 114.7, 114.3, 62.3 (dd, *J* = 31.0, 27.0 Hz), 61.1, 55.2, 13.8; **IR (neat)**: υ $_{max}$ 3070, 1765, 1674, 1451, 1147, 963, 750 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_3$ $[M+H]^+$ 336.1406, found 336.1418.

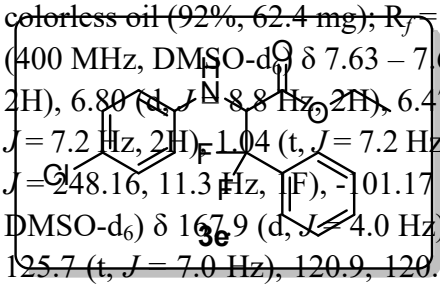
Ethyl 3,3-difluoro-2-((4-fluorophenyl)amino)-3-phenylpropanoate (3d):



colorless oil (83%, 53.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.63 – 7.61 (m, 2H), 7.48 – 7.47 (m, 3H), 6.90 (t, *J* = 8.8 Hz, 2H), 6.78 – 6.76 (m, 2H), 6.17 (d, *J* = 10.8 Hz, 1H), 5.02 – 4.92 (m, 1H), 4.06 (q, *J* = 6.8 Hz, 2H), 1.04 (t, *J* = 6.8 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.35 (dd, *J* = 245.5, 9.8 Hz, 1F), -101.70 (dd, *J* = 245.5, 15.8 Hz, 1F), -127.46 – -127.39 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.2 (d, *J* = 3.8 Hz), 155.2 (d, *J* = 231.0 Hz), 143.2, 134.1 (t, *J* = 25.0 Hz), 130.4, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 247.0 Hz), 115.1

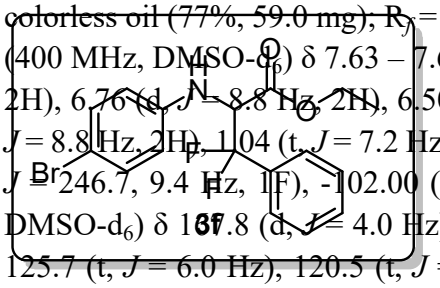
(d, *J* = 22.0 Hz), 114.4 (d, *J* = 7.0Hz), 61.8 (dd, *J* = 30.0, 27.0 Hz), 61.2, 13.8; **IR (neat)**: υ $_{max}$ 3067, 1741, 1694, 1370, 1313, 929, 824 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}F_3NO_2$ $[M+H]^+$ 324.1205, found 324.1215.

Ethyl 2-((4-chlorophenyl)amino)-3,3-difluoro-3-phenylpropanoate (3e):



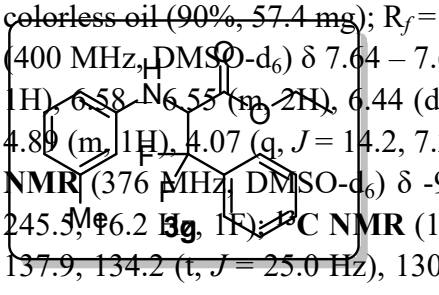
colorless oil (92%, 62.4 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.63 – 7.61 (m, 2H), 7.48 – 4.47 (m, 3H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.47 (d, *J* = 10.4 Hz, 1H), 5.07 – 4.98 (m, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 1.04 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -99.68 (dd, *J* = 248.16, 11.3 Hz, 1F), -101.17 (dd, *J* = 248.16, 15.4 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 167.9 (d, *J* = 4.0 Hz), 145.6, 134.0 (t, *J* = 26.0 Hz), 130.4, 128.5, 128.3 , 125.7 (t, *J* = 7.0 Hz), 120.9, 120.5 (t, *J* = 248.0 Hz), 114.7, 61.2, 61.2 (dd, *J* = 31.0, 27.0 Hz), 14.3; **IR (neat)**: υ $_{max}$ 3062, 1736, 1563, 1448, 1371, 1300, 1234, 1098, 1043, 936, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}ClF_2NO_2$ $[M+H]^+$ 340.0910, found 340.0917.

Ethyl 2-((4-bromophenyl)amino)-3,3-difluoro-3-phenylpropanoate (3f):



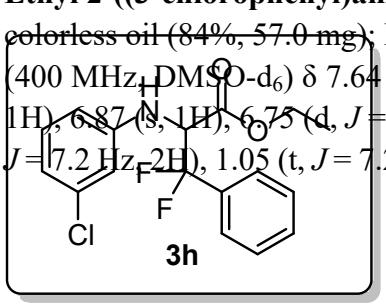
colorless oil (77%, 59.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.63 – 7.61 (m, 2H), 7.48 – 7.47 (m, 3H), 7.19 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.50 (d, *J* = 10.4 Hz, 1H), 5.07 – 4.98 (m, 1H), 4.06 (q, *J* = 8.8 Hz, 2H), 1.04 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -99.02 (dd, *J* = 246.7, 9.4 Hz, 1F), -102.00 (dd, *J* = 246.7, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 167.8 (d, *J* = 4.0 Hz), 146.0, 134.0 (t, *J* = 24.0 Hz), 131.3, 130.5, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 249.0 Hz), 115.2, 108.4, 61.2, 61.1 (dd, *J* = 30.0, 27.0 Hz), 13.8; **IR (neat)**: υ $_{max}$ 3036, 1763, 1647, 1599, 1429, 1283, 1233, 1102, 943, 880 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}BrF_2NO_2$ $[M+H]^+$ 384.0405, found 384.0415.

Ethyl 3,3-difluoro-3-phenyl-2-(m-tolylamino)propanoate (3g):



colorless oil (90%, 57.4 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.64 – 7.62 (m, 2H), 7.49 – 7.47 (m, 3H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.58 – 6.55 (m, 2H), 6.44 (d, *J* = 7.2 Hz, 1H), 6.09 (d, *J* = 10.8 Hz, 1H), 4.98 – 4.89 (m, 1H), 4.07 (q, *J* = 14.2, 7.2 Hz, 2H), 1.05 (s, 3H), 0.81 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -99.22 (dd, *J* = 245.5, 9.8 Hz, 1F), -102.00 (dd, *J* = 245.5, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 168.3 (d, *J* = 4.0 Hz), 146.5, 137.9, 134.2 (t, *J* = 25.0 Hz), 130.4, 128.7, 128.3, 125.8 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 250.0 Hz), 118.0, 113.9, 110.5, 61.4 (dd, *J* = 31.0, 27.0 Hz), 61.1, 21.7, 14.3; **IR (neat)**: υ $_{max}$ 3061, 1736, 1447, 1371, 1301, 1223, 1098, 1043, 936, 785 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_2$ $[M+H]^+$ 320.1456, found 320.1468.

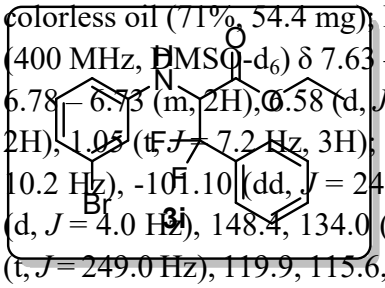
Ethyl 2-((3-chlorophenyl)amino)-3,3-difluoro-3-phenylpropanoate (3h):



colorless oil (84%, 57.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.64 – 7.62 (m, 2H), 7.49 – 7.47 (m, 3H), 7.05 (t, *J* = 8.0 Hz, 1H), 6.87 (s, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.64 – 6.60 (m, 2H), 5.12 (m, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -99.68 (dd,

J = 245.2, 10.2 Hz, 1F), -101.16 (dd, J = 245.2, 15.0 Hz, 1F); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 167.9 (d, J = 4.0 Hz), 148.3, 134.0 (t, J = 25.0 Hz), 133.5, 130.5, 130.3, 128.4, 125.8 (t, J = 6.0 Hz), 120.5 (t, J = 249.0 Hz), 117.0, 112.7, 112.7, 61.3, 60.8 (dd, J = 30.0, 28.0 Hz), 14.3; **IR (neat)**: υ $_{max}$ 3067, 1741, 1598, 1514, 1482, 1451, 1371, 1324, 1246, 1159, 1028, 916, 762 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}ClF_2NO_2$ $[M+H]^+$ 340.0910, found 340.0916.

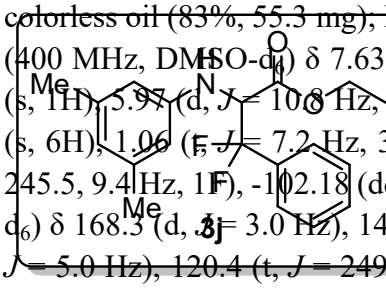
Ethyl 2-((3-bromophenyl)amino)-3,3-difluoro-3-phenylpropanoate (3i):



3i

colorless oil (71%, 54.4 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.63 – 7.62 (m, 2H), 7.49 – 7.47 (m, 3H), 7.01 – 6.97 (m, 2H), 6.78 – 6.73 (m, 2H), 6.58 (d, J = 10.4 Hz, 1H), 5.14 – 5.05 (m, 1H), 4.07 (q, J = 7.2 Hz, 2H), 1.05 (t, J = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.69 (dd, J = 245.5, 10.2 Hz), -101.10 (dd, J = 245.5, 16.9 Hz); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 167.5 (d, J = 4.0 Hz), 148.4, 134.0 (t, J = 25.0 Hz), 130.6, 130.5, 128.3, 125.7, 122.1, 120.5 (t, J = 249.0 Hz), 119.9, 115.6, 112.0, 61.2, 60.5 (dd, J = 31.0, 28.0 Hz), 14.3; **IR (neat)**: υ $_{max}$ 3065, 1736, 1597, 1476, 1453, 1372, 1237, 1044, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}BrF_2NO_2$ $[M+H]^+$ 384.0405, found 384.0415.

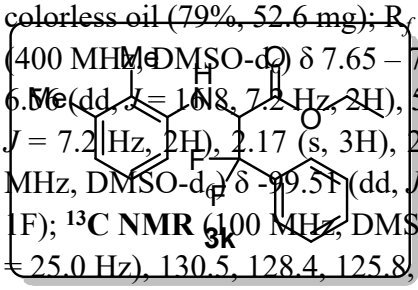
Ethyl 2-((3,5-dimethylphenyl)amino)-3,3-difluoro-3-phenylprop-anoate (3j):



3j

colorless oil (83%, 55.3 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.63 – 7.61 (m, 2H), 7.49 – 7.47 (m, 3H), 6.37 (s, 2H), 6.26 (s, 1H), 5.97 (d, J = 10.8 Hz, 1H), 4.94 – 4.85 (m, 1H), 4.09 (q, J = 7.2 Hz, 2H), 2.11 (s, 6H), 1.06 (t, J = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.21 (dd, J = 245.5, 9.4 Hz, 1F), -102.18 (dd, J = 245.5, 15.0 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.3 (d, J = 3.0 Hz), 146.4, 137.7, 134.2 (t, J = 25.0 Hz), 130.4, 128.3, 125.7 (t, J = 5.0 Hz), 120.4 (t, J = 249.0 Hz), 119.6, 111.2, 61.4 (dd, J = 31.0, 27.0 Hz), 61.1, 21.6, 13.8; **IR (neat)**: υ $_{max}$ 2989, 1917, 1834, 1742, 1605, 1516, 1371, 1193, 821 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{22}F_2NO_2$ $[M+H]^+$ 334.1613, found 334.1619.

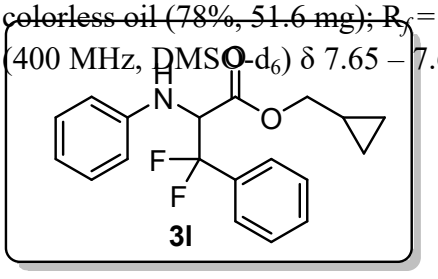
Ethyl 2-((2,3-dimethylphenyl)amino)-3,3-difluoro-3-phenylprop-anoate (3k):



3k

colorless oil (79%, 52.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.63 (m, 2H), 7.50 – 7.49 (m, 3H), 6.88 (t, J = 8.0, 1H), 6.56 (dd, J = 16.8, 7.2 Hz, 2H), 5.01 – 4.92 (m, 1H), 4.60 (d, J = 10.4 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 2.17 (s, 3H), 2.00 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.51 (dd, J = 245.2, 9.4 Hz, 1F), -102.05 (dd, J = 245.2, 14.7 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.4 (d, J = 3.0 Hz), 143.7, 136.4, 133.9 (t, J = 25.0 Hz), 130.5, 128.4, 125.8, 125.7 (t, J = 6.0 Hz), 122.0, 121.0, 120.6 (t, J = 247.0 Hz), 110.2, 62.3 (dd, J = 31.0, 28.0 Hz), 61.6, 20.3, 13.7, 12.4; **IR (neat)**: υ $_{max}$ 3062, 1738, 1647, 1590, 1746, 1372, 1307, 1100, 1046, 760 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{22}F_2NO_2$ $[M+H]^+$ 334.1613, found 334.1618.

Cyclopropylmethyl 3,3-difluoro-3-phenyl-2-(phenylamino) propanoate (3l):

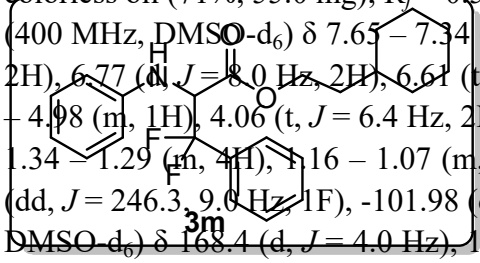


3l

colorless oil (78%, 51.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.63 (m, 2H), 7.49 – 7.47 (m, J = 5.4 Hz, 3H), 7.06 (t,

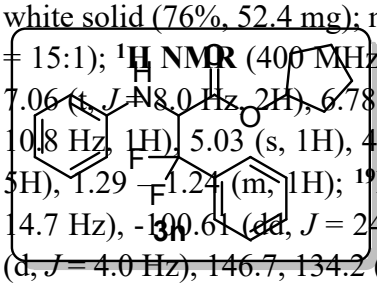
J = 7.6 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.20 (d, *J* = 10.4 Hz, 1H), 5.04 – 4.95 (m, 1H), 3.93 – 3.821 (m, 2H), 1.00 – 0.91 (m, 1H), 0.44 (d, *J* = 7.2 Hz, 2H), 0.17 (s, 2H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.06 (dd, *J* = 245.9, 9.8Hz), -101.68 (dd, *J* = 245.9, 15.8 Hz); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.4 (d, *J* = 4.0 Hz), 146.6, 134.2 (t, *J* = 25.0 Hz), 130.4, 128.8, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.6 (t, *J* = 249.0 Hz), 117.7, 113.3, 69.7, 61.3 (dd, *J* = 31.0, 27.0 Hz), 9.5, 3.1; **IR (neat)**: υ $_{max}$ 3043, 1765, 1627, 1515, 1270, 1246, 1026, 820 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{20}F_2NO_2$ $[M+H]^+$ 332.1456, found 332.1439.

Cyclohexylethyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3m):



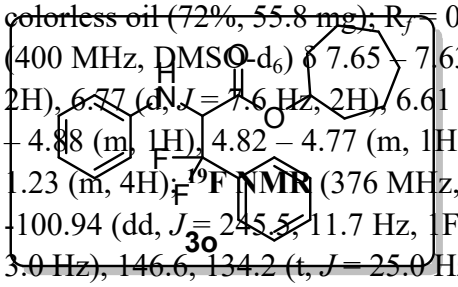
colorless oil (71%, 55.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.34 (m, 2H), 7.45 – 7.47 (m, 3H), 7.05 (t, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 10.8 Hz, 1H), 4.79 – 4.98 (m, 1H), 4.06 (t, *J* = 6.4 Hz, 2H), 1.60 – 1.52 (m, 5H), 1.32 (q, *J* = 6.8 Hz, 2H), 1.34 – 1.29 (m, 4H), 1.16 – 1.07 (m, 2H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -98.97 (dd, *J* = 246.3, 9.0 Hz, 1F), -101.98 (dd, *J* = 246.3, 16.5 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.4 (d, *J* = 4.0 Hz), 146.6, 134.2 (t, *J* = 25.0 Hz), 130.5, 128.8, 128.3, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 247.0 Hz), 117.7, 113.3, 62.93, 61.3 (dd, *J* = 31.0, 27.0 Hz), 35.3, 33.2, 32.4, 26.0, 25.6 25.6 ; **IR (neat)**: υ $_{max}$ 3044, 2124, 1764, 1677, 1515, 1376, 1272, 1244, 1026, 820 cm^{-1}; **HRMS (ESI)** calcd for $C_{23}H_{28}F_2NO_2$ $[M+H]^+$ 388.2082, found 388.2079.

Cyclopentyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3n):



white solid (76%, 52.4 mg); m.p.: 98.6-99.1 °C; R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.63 (m, 2H), 7.49 – 7.48 (m, 3H), 7.06 (t, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 6.8 Hz, 1H), 6.19 (d, *J* = 10.8 Hz, 1H), 5.03 (s, 1H), 4.99 – 6.90 (m, 1H), 1.72 – 1.60 (m, 2H), 1.53 – 1.42 (m, 5H), 1.29 – 1.24 (m, 1H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.29 (dd, *J* = 245.5, 14.7 Hz), -100.61 (dd, *J* = 245.9, 11.3 Hz); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 167.9 (d, *J* = 4.0 Hz), 146.7, 134.2 (t, *J* = 25.0 Hz), 130.5, 128.8, 128.4, 125.7 (t, *J* = 6.0 Hz), 120.6 (t, *J* = 247.0 Hz), 117.7, 113.3, 78.1, 61.3 (dd, *J* = 32.0, 28.0 Hz), 32.0, 31.9, 23.1, 23.0; **IR (neat)**: υ $_{max}$ 3096, 1736, 1603, 1508, 1451, 1368, 1308, 1249, 1104, 956, 835 cm^{-1}; **HRMS (ESI)** calcd for $C_{20}H_{22}F_2NO_2$ $[M+H]^+$ 346.1613, found 346.1606.

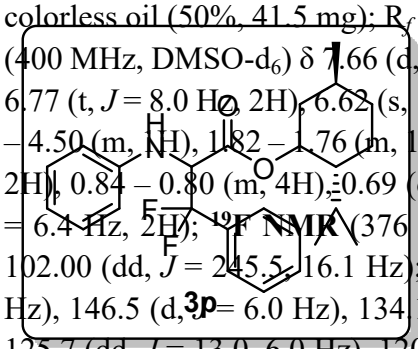
Cycloheptyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3o):



colorless oil (72%, 55.8 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.63 (m, 2H), 7.49 – 7.48 (m, 3H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 6.61 (t, *J* = 6.8 Hz, 1H), 6.18 (d, *J* = 10.4 Hz, 1H), 4.98 – 4.88 (m, 1H), 4.82 – 4.77 (m, 1H), 1.77 – 1.71 (m, 1H), 1.58 – 1.53 (m, 7H), 1.36 – 1.23 (m, 4H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -100.07 (dd, *J* = 245.5, 14.3 Hz, 1F), -100.94 (dd, *J* = 245.5, 11.7 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 167.5 (d, *J* = 3.0 Hz), 146.6, 134.2 (t, *J* = 25.0 Hz), 130.5, 128.8, 128.4, 125.7 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 248.0 Hz), 117.7, 113.3, 75.9, 61.5 (t, *J* = 28.0 Hz), 33.0, 32.8, 28.2, 22.1, 22.1;

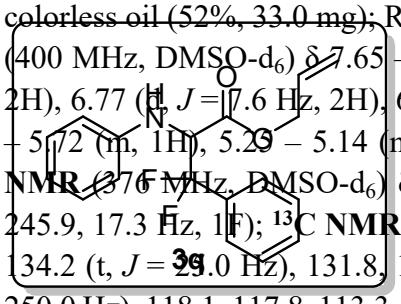
IR (neat): υ $_{max}$ 3045, 1765, 1646, 1547, 1538, 1515, 1273, 1244, 1052, 1027, 820 cm^{-1}; **HRMS (ESI)** calcd for $C_{22}H_{26}F_2NO_2$ $[M+H]^+$ 374.1926, found 374.1917.

(2R,5S)-2-Isopropyl-5-methylcyclohexyl 3,3-difluoro-3-phenyl-2-(phenylamino) propanoate (3p):



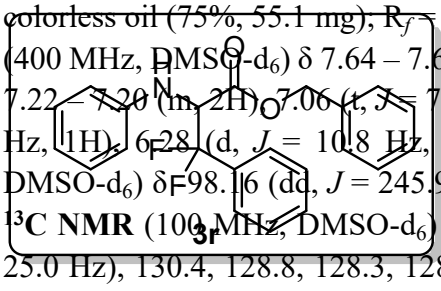
colorless oil (50%, 41.5 mg); R_f = 0.3 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.66 (d, *J* = 6.4 Hz, 2H), 7.49 (s, 3H), 7.05 (t, *J* = 7.2 Hz, 2H), 6.77 (t, *J* = 8.0 Hz, 2H), 6.62 (s, 1H), 6.17 (t, *J* = 9.6 Hz, 1H), 4.99 – 4.90 (m, 1H), 4.59 – 4.50 (m, 1H), 1.82 – 1.76 (m, 1H), 1.58 (s, 2H), 1.39 – 1.25 (m, 3H), 0.94 (q, *J* = 11.6, 2H), 0.84 – 0.80 (m, 4H), 0.69 (d, *J* = 6.4 Hz, 2H), 0.54 (d, *J* = 6.4 Hz, 2H), 0.45 (d, *J* = 6.4 Hz, 2H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -99.22 (dd, *J* = 245.5, 9.8 Hz), -102.00 (dd, *J* = 245.5, 16.1 Hz); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 167.8 (d, *J* = 4.0 Hz), 146.5 (d, *J* = 6.0 Hz), 134.1 (t, *J* = 25.0 Hz), 130.4, 128.6 (d, *J* = 5.0 Hz), 128.3, 125.7 (dd, *J* = 13.0, 6.0 Hz), 120.4 (t, *J* = 247.0 Hz), 117.5 (d, *J* = 9.0 Hz), 113.9 (d, *J* = 23.0 Hz), 74.9 (d, *J* = 20.0 Hz), 62.0 – 61.2 (m), 46.0, 33.5 (d, *J* = 2.0 Hz), 30.6 (d, *J* = 12.0 Hz), 25.2, 24.5, 22.3 (d, *J* = 18.0 Hz), 21.7 (d, *J* = 3.0 Hz), 20.5 (d, *J* = 7.0 Hz), 15.5 (d, *J* = 27.0 Hz); **IR (neat)**: υ $_{max}$ 3054, 1736, 1648, 1618, 1453, 1371, 1301, 1043, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{25}H_{32}F_2NO_2$ $[M+H]^+$ 416.2396, found 416.2402.

Allyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3q):



colorless oil (52%, 33.0 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.65 – 7.3 (m, 2H), 7.48 – 7.47 (m, 3H), 7.05 (t, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 6.60 (t, *J* = 7.2 Hz, 1H), 6.26 (d, *J* = 10.8 Hz, 1H), 5.82 – 5.72 (m, 1H), 5.29 – 5.14 (m, 2H), 5.12 – 5.02 (m, 1H), 4.59 – 4.58 (m, 2H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -97.83 (dd, *J* = 245.9, 8.3 Hz, 1F), -102.77 (dd, *J* = 245.9, 17.3 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 168.09 (d, *J* = 3.0 Hz), 146.5, 134.2 (t, *J* = 25.0 Hz), 131.8, 130.5, 128.9, 128.4, 125.8 (t, *J* = 6.0 Hz), 120.6 (t, *J* = 250.0 Hz), 118.1, 117.8, 113.3, 65.5, 61.2 (dd, *J* = 32.0, 27.0 Hz); **IR (neat)**: υ $_{max}$ 3043, 1765, 1706, 1692, 1676, 1538, 1455, 1375, 1244, 1025, 821 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{18}F_2NO_2$ $[M+H]^+$ 318.1300, found 318.1289.

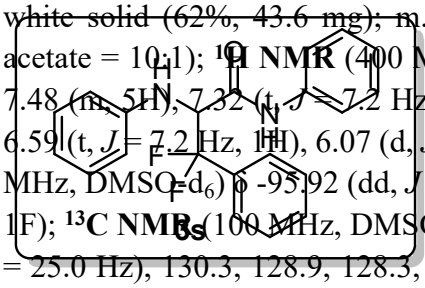
Benzyl 3,3-difluoro-3-phenyl-2-(phenylamino)propanoate (3r):



colorless oil (75%, 55.1 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.64 – 7.62 (m, 2H), 7.49 – 7.43 (m, 3H), 7.33 – 7.31 (m, 3H), 7.22 – 7.20 (m, 2H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.28 (d, *J* = 10.8 Hz, 1H), 5.17 – 5.06 (m, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -98.16 (dd, *J* = 245.9, 8.6 Hz, 1F), -102.09 (dd, *J* = 245.9, 16.5 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 168.3 (d, *J* = 4.0 Hz), 146.5, 135.3, 134.1 (t, *J* = 25.0 Hz), 130.4, 128.8, 128.3, 128.1, 127.9, 125.7 (t, *J* = 6.0 Hz), 120.6 (t, *J* = 247.0 Hz), 117.7, 113.3, 66.6, 61.3 (dd, *J* = 31.0, 27.0 Hz); **IR (neat)**: υ $_{max}$ 3042, 2362, 1765,

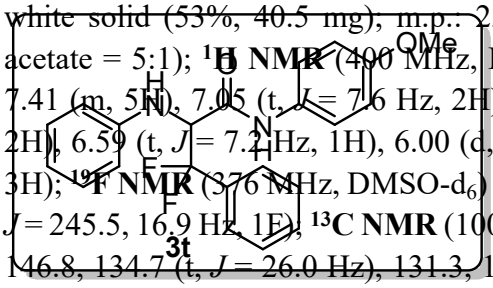
1676, 1646, 1609, 1375, 1244, 1025, 757 cm^{-1}; **HRMS (ESI)** calcd for $C_{22}H_{20}F_2NO_2$ $[M+H]^+$ 368.1456, found 368.1450.

3,3-Difluoro-N,3-diphenyl-2-(phenylamino)propanamide (3s):



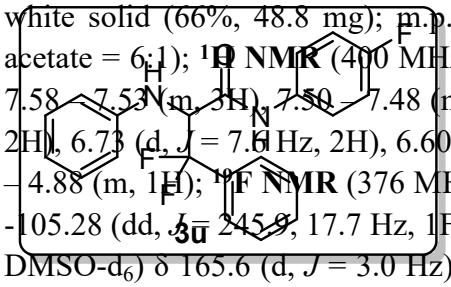
white solid (62%, 43.6 mg); m.p.: 231.4-232.1 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 7.61 (s, 2H), 7.54 – 7.48 (m, 5H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.10 – 7.04 (m, 3H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.59 (t, *J* = 7.2 Hz, 1H), 6.07 (d, *J* = 10.4 Hz, 1H), 5.00 – 4.91 (m, 1H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -95.92 (dd, *J* = 246.3, 6.0 Hz, 1F), -105.41 (dd, *J* = 246.3, 16.5 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 165.6 (d, *J* = 3.0 Hz), 146.7, 138.2, 134.7 (t, *J* = 25.0 Hz), 130.3, 128.9, 128.3, 125.6 (t, *J* = 6.0 Hz), 123.9, 119.7 (t, *J* = 249.0 Hz), 119.3, 117.6, 117.7, 113.3 , 61.8 (dd, *J* = 34.0, 26.0 Hz); **IR (neat)**: υ $_{max}$ 3057, 1767, 1692, 1602, 1552, 1499, 1446, 1315, 1251, 1027, 822, 756 cm^{-1}; **HRMS (ESI)** calcd for $C_{21}H_{19}F_2N_2O$ $[M+H]^+$ 353.1460, found 353.1469.

3,3-Difluoro-N-(4-methoxyphenyl)-3-phenyl-2-(phenylamino)propanamide (3t):



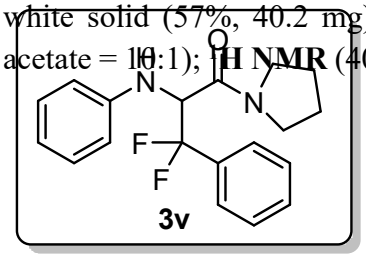
white solid (53%, 40.5 mg); m.p.: 238.5-238.9 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 5:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.14 (s, 1H), 7.59 (s, 2H), 7.48 – 7.41 (m, 5H), 7.05 (t, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 2H), 6.59 (t, *J* = 7.2 Hz, 1H), 6.00 (d, *J* = 10.4 Hz, 1H), 4.94 – 4.86 (m, 1H), 3.71 (s, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -96.36 (dd, *J* = 245.5, 6.4 Hz, 1F), -104.95 (dd, *J* = 245.5, 16.9 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 165.0 (d, *J* = 4.0 Hz), 155.7, 146.8, 134.7 (t, *J* = 26.0 Hz), 131.3, 130.3, 128.9, 128.3, 125.6 (t, *J* = 6.0 Hz), 121.0, 118.5 (t, *J* = 249.0 Hz), 114.0, 113.3, 61.8 (dd, *J* = 32.0, 26.0 Hz), 55.2; **IR (neat)**: υ $_{max}$ 3059, 1765, 1688, 1647, 1605, 1510, 1374, 1243, 1053, 828 cm^{-1}; **HRMS (ESI)** calcd for $C_{22}H_{21}F_2N_2O_2$ $[M+H]^+$ 383.1565, found 383.1573.

3,3-Difluoro-N-(4-fluorophenyl)-3-phenyl-2-(phenylamino)propanamide (3u):



white solid (66%, 48.8 mg); m.p.: 275.2-275.7 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 6:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.62 – 7.60 (m, 2H), 7.58 – 7.53 (m, 3H), 7.50 – 7.48 (m, 2H), 7.17 (t, *J* = 8.8 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 2H), 6.60 (t, *J* = 7.6 Hz, 1H), 6.09 (d, *J* = 10.8 Hz, 1H), 4.97 – 4.88 (m, 1H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -96.13 (dd, *J* = 245.9, 6.3 Hz, 1F), -105.28 (dd, *J* = 245.9, 17.7 Hz, 1F), -118.32 – -118.39 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 165.6 (d, *J* = 3.0 Hz), 158.3 (d, *J* = 241.0 Hz), 146.7, 134.6 (t, *J* = 25.0 Hz), 134.6 (d, *J* = 2.0 Hz), 130.3, 128.6 (d, *J* = 57.0 Hz), 127.6, 125.6 (t, *J* = 6.0 Hz), 121.1 (d, *J* = 8.0 Hz), 120.4 (t, *J* = 249.0 Hz) 117.6, 115.5 (d, *J* = 22.0 Hz), 113.2, 61.8 (dd, *J* = 33.0, 26.0 Hz); **IR (neat)**: υ $_{max}$ 3061, 1766, 1692, 1605,1508, 1315, 1249, 1054, 837 cm^{-1}; **HRMS (ESI)** calcd for $C_{21}H_{18}F_3N_2O$ $[M+H]^+$ 371.1365, found 371.1371.

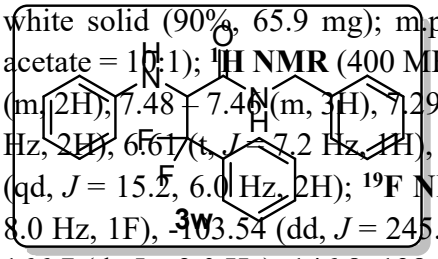
3,3-Difluoro-3-phenyl-2-(phenylamino)-1-(pyrrolidin-1-yl)propan-1-one (3v):



white solid (57%, 40.2 mg); m.p.: 211.2-211.9 °C; R_f = 0.4 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.59 – 7.57 (m, 2H), 7.48 – 7.46 (m,

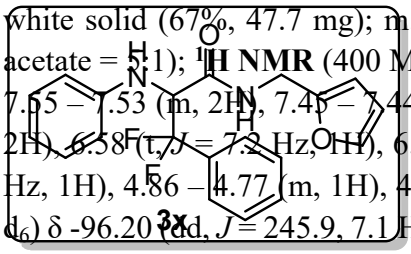
3H), 7.04 (t, *J* = 7.2 Hz 2H), 6.75 (d, *J* = 7.2 Hz, 2H), 6.59 (t, *J* = 5.6 Hz 1H), 5.84 (d, *J* = 10.8 Hz, 1H), 5.00 – 4.92 (m, 1H), 3.26 – 3.20 (m, 4H), 1.75 – 1.65 (m, 4H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.24 (dd, *J* = 244.4, 7.5 Hz, 1F), -101.74 (dd, *J* = 244.4, 12.0 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 164.9 (d, *J* = 3.0 Hz), 146.8, 134.6 (t, *J* = 26.0 Hz), 130.2, 128.8, 128.1, 125.9 (t, *J* = 6.0 Hz), 121.3 (t, *J* = 249.0 Hz), 117.4, 113.3, 59.0 (dd, *J* = 20.0, 28.0 Hz), 46.3, 45.8, 25.5, 23.5; **IR (neat)**: υ $_{max}$ 3056, 1646, 1601, 1504, 1312, 1281, 1257, 1160, 1031, 889 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{21}F_2N_2O$ $[M+H]^+$ 353.1435, found 353.1447.

***N*-benzyl-3,3-difluoro-3-phenyl-2-(phenylamino)propanamide (3w):**



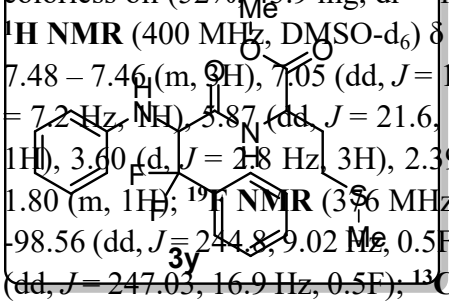
white solid (90%, 65.9 mg); m.p.: 246.5-247.3 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.75 (t, *J* = 5.2 Hz, 1H), 7.59 – 7.57 (m, 2H), 7.48 – 7.46 (m, 3H), 7.29 – 7.23 (m, 3H), 7.11 – 7.04 (m, 4H), 6.74 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 5.93 (d, *J* = 10.4 Hz, 1H), 4.91 – 4.82 (m, 1H), 4.31 (qd, *J* = 15.2, 6.0 Hz, 2H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -97.35 (dd, *J* = 245.5, 8.0 Hz, 1F), -103.54 (dd, *J* = 245.5, 17.6 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.7 (d, *J* = 3.0 Hz), 146.8, 138.5, 134.8 (t, *J* = 25.0 Hz), 130.2, 128.8, 128.3, 127.1, 126.9, 125.7 (t, *J* = 6.0 Hz), 121.0 (t, *J* = 249.0 Hz), 120.4, 117.4, 113.4, 61.3 (dd, *J* = 32.0, 26.0 Hz), 42.3; **IR (neat)**: υ $_{max}$ 3061, 2362, 1767, 1676, 1602, 1504, 1449, 1316, 1256, 1028, 755 cm^{-1}; **HRMS (ESI)** calcd for $C_{22}H_{21}F_2N_2O$ $[M+H]^+$ 367.1616, found 367.1621.

3,3-Difluoro-N-(furan-2-ylmethyl)-3-phenyl-2-(phenylamino)propanamide (3x):



white solid (67%, 47.7 mg); m.p.: 261.7-262.5 °C; R_f = 0.5 (petroleum ether/ethyl acetate = 5:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.72 (t, *J* = 5.2 Hz, 1H), 7.58 (s, 1H), 7.55 – 7.53 (m, 2H), 7.45 – 7.44 (m, 3H), 7.03 (t, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.58 (t, *J* = 7.2 Hz, 1H), 6.38 (s, 1H), 6.14 (d, *J* = 3.2 Hz, 1H), 5.90 (d, *J* = 10.4 Hz, 1H), 4.86 – 4.77 (m, 1H), 4.30 (d, *J* = 5.2 Hz, 2H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -96.20 (dd, *J* = 245.9, 7.1 Hz, 1F), -104.84 (dd, *J* = 245.9, 17.3 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.6 (d, *J* = 3.0 Hz), 151.4, 146.8, 142.3, 134.7 (t, *J* = 25.0 Hz), 130.1, 128.8, 128.2, 125.6 (t, *J* = 6.0 Hz), 120.9 (t, *J* = 249.0 Hz), 117.4, 113.2, 110.4, 107.0, 61.0 (dd, *J* = 32.0, 27.0 Hz), 35.7; **IR (neat)**: υ $_{max}$ 3060, 2361, 1765, 1665, 1602, 1448, 1250, 1151, 1054, 1025, 882 cm^{-1}; **HRMS (ESI)** calcd for $C_{20}H_{19}F_2N_2O_2$ $[M+H]^+$ 357.1409, found 357.1418.

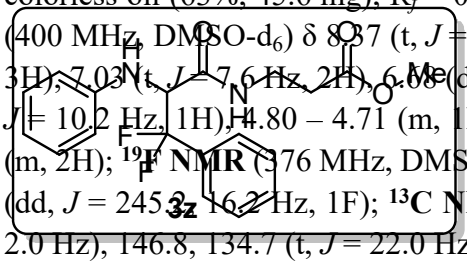
Methyl (3,3-difluoro-3-phenyl-2-(phenylamino)propanoyl)-methioninate (3y):



colorless oil (52%, 43.9 mg, dr = 1:1); R_f = 0.4 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.70 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.57 – 7.57 (m, 2H), 7.48 – 7.46 (m, 3H), 7.05 (dd, *J* = 14.0, 7.6 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 2H), 6.59 (t, *J* = 7.2 Hz, 1H), 5.87 (dd, *J* = 21.6, 10.4 Hz, 1H), 4.90 – 4.80 (m, 1H), 4.47 – 4.38 (m, 1H), 3.60 (d, *J* = 2.8 Hz, 3H), 2.39 – 2.18 (m, 3H), 1.98 (s, 2H), 1.94 (s, 1H), 1.89 – 1.80 (m, 1H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -96.05 (dd, *J* = 247.0, 7.1 Hz, 0.5F), -98.56 (dd, *J* = 244.8, 9.02 Hz, 0.5F), -102.69 (dd, *J* = 244, 78, 15.79 Hz, 0.5F), -104.33 (dd, *J* = 247.03, 16.9 Hz, 0.5F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.7, 171.4, 166.8

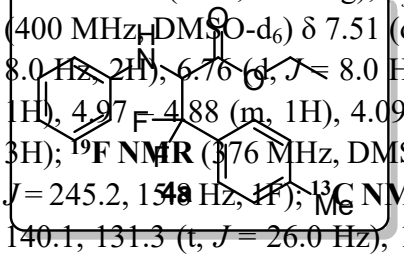
(d, J = 7.0 Hz), 146.7, 146.7, 134.6 (td, J = 32.3, 7.0 Hz), 134.6 (td, J = 32.3, 7.0 Hz) 130.2, 130.1, 128.7, 128.2, 128.2, 125.6 (t, J = 7.0 Hz), 120.8 (t, J = 252.0 Hz), 117.5, 117.4, 113.4, 113.3, 61.0 (dd, J = 53.0, 27.0 Hz), 52.0, 52.0, 50.9, 50.7, 30.8, 30.6, 29.2, 29.0, 14.5, 14.4; **IR (neat)**: υ $_{max}$ 3061, 1736, 1647, 1562, 1549, 1453, 1372, 1300, 1234, 1098, 1043, 936 cm^{-1}; **HRMS (ESI)** calcd for $C_{21}H_{25}F_2N_2O_3S$ $[M+H]^+$ 423.1548, found 423.1556.

Methyl 3-(3,3-difluoro-3-phenyl-2-(phenylamino)propanamido)propanoate (3z):



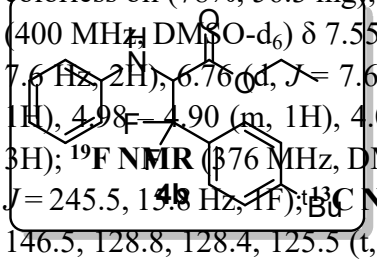
colorless oil (63%, 45.6 mg); R_f = 0.3 (petroleum ether/ethyl acetate = 5:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 8.37 (t, J = 4.8 Hz, 1H), 7.54 – 7.53 (m, 2H), 7.46 – 7.45 (m, 3H), 7.03 (t, J = 7.6 Hz, 2H), 6.68 (d, J = 8.0 Hz, 2H), 6.58 (t, J = 7.2 Hz, 1H), 5.83 (d, J = 10.2 Hz, 1H), 4.80 – 4.71 (m, 1H), 3.57 (s, 3H), 3.32 – 3.21 (m, 2H), 2.42 – 2.29 (m, 2H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -97.75 (dd, J = 245.2, 7.9 Hz, 1F), -103.60 (dd, J = 245.2, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 171.6, 166.8 (d, J = 2.0 Hz), 146.8, 134.7 (t, J = 22.0 Hz), 130.2, 128.8, 128.2, 125.6 (t, J = 6.0 Hz), 120.9 (t, J = 249.0 Hz), 117.4, 113.2, 61.0 (dd, J = 31.0, 26.0 Hz), 51.4, 34.7, 33.3; **IR (neat)**: υ $_{max}$ 3061, 1738, 1678, 1604, 1453, 1372, 1244, 1052, 755 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{21}F_2N_2O_3$ $[M+H]^+$ 363.1514, found 363.1526.

Ethyl 3,3-difluoro-2-(phenylamino)-3-(p-tolyl)propanoate (4a):



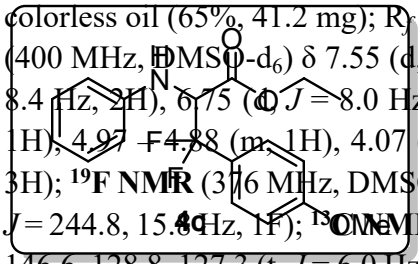
colorless oil (91%, 58.1 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.51 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 7.6 Hz, 2H), 7.06 (t, J = 8.0 Hz, 2H), 6.76 (d, J = 8.0 Hz, 2H), 6.61 (t, J = 7.2 Hz, 1H), 6.16 (d, J = 10.8 Hz, 1H), 4.97 – 4.88 (m, 1H), 4.09 (q, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.06 (t, J = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -98.48 (dd, J = 245.2, 9.0 Hz, 1F), -101.55 (dd, J = 245.2, 15.8 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 168.3 (d, J = 4.0 Hz), 146.6, 140.1, 131.3 (t, J = 26.0 Hz), 128.8, 128.8, 125.6 (t, J = 6.0 Hz), 120.6 (t, J = 249.0 Hz), 118.2, 113.2, 61.3 (dd, J = 31.0, 27.0 Hz), 61.1, 20.8, 13.8; **IR (neat)**: υ $_{max}$ 3060, 1736, 1647, 1561, 1453, 1371, 1165, 1008, 936 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_2$ $[M+H]^+$ 320.1456, found 320.1462.

Ethyl 3-(4-(tert-butyl)phenyl)-3,3-difluoro-2-(phenylamino) propanoate (4b):



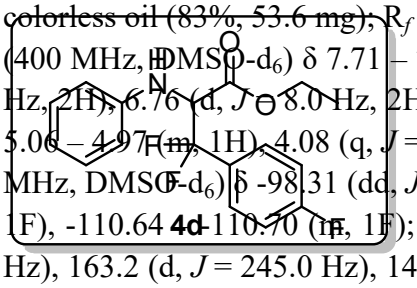
colorless oil (78%, 56.3 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d$_6$) δ 7.55 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.06 (t, J = 7.6 Hz, 2H), 6.76 (d, J = 7.6 Hz, 2H), 6.01 (t, J = 7.2 Hz, 1H), 6.18 (d, J = 10.8 Hz, 1H), 4.98 – 4.90 (m, 1H), 4.06 (q, J = 7.2 Hz, 2H), 1.28 (s, 9H), 1.03 (t, J = 7.1 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d$_6$) δ -98.45 (dd, J = 245.5, 9.4 Hz, 1F), -101.57 (dd, J = 245.5, 15.8 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d$_6$) δ 168.3 (d, J = 4.0 Hz), 153.0, 146.5, 128.8, 128.4, 125.5 (t, J = 6.0 Hz), 125.1, 120.6 (t, J = 248.0 Hz), 117.6, 113.3, 61.3 (dd, J = 31.0, 26.0 Hz), 61.1, 34.5, 30.9, 13.8; **IR (neat)**: υ $_{max}$ 3058, 1736, 1647, 1453, 1371, 1301, 1043, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{21}H_{26}F_2NO_2$ $[M+H]^+$ 362.1926, found 362.1936.

Ethyl 3,3-difluoro-3-(4-methoxyphenyl)-2-(phenylamino)propanoate (4c):



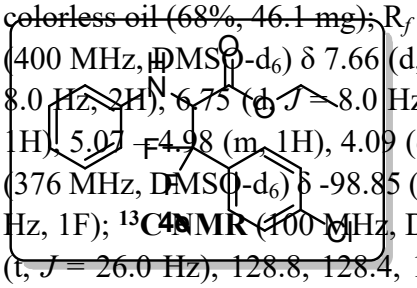
colorless oil (65%, 41.2 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 10:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.60 (t, *J* = 7.2 Hz, 1H), 6.17 (d, *J* = 10.4 Hz, 1H), 4.97 – 4.88 (m, 1H), 4.07 (q, *J* = 6.8 Hz, 2H), 3.77 (s, 3H), 1.07 (t, *J* = 6.8 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -97.55 (dd, *J* = 244.8, 9.0 Hz, 1F), -100.49 (dd, *J* = 244.8, 15.8 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.4 (d, *J* = 3.0 Hz), 160.7, 146.6, 128.8, 127.3 (t, *J* = 6.0 Hz), 126.2 (t, *J* = 26.0 Hz), 120.7 (t, *J* = 249.0 Hz), 117.6, 113.6, 113.2, 61.4 (dd, *J* = 32.0, 28.0 Hz), 61.1, 55.3, 13.9; **IR (neat)**: υ $_{max}$ 3045, 1765, 1678, 1646, 1539, 1245, 1053, 1027, 820 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_3$ $[M+H]^+$ 336.1405, found 336.1403.

Ethyl 3,3-difluoro-3-(4-fluorophenyl)-2-(phenylamino)propanoate (4d):



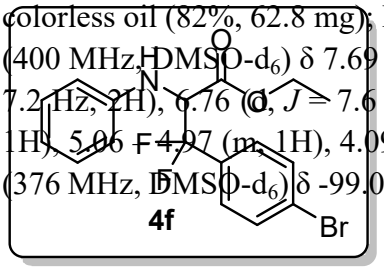
colorless oil (83%, 53.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.71 – 7.68 (m, 2H), 7.31 (t, *J* = 8.8 Hz, 2H), 7.05 (t, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.22 (d, *J* = 10.4 Hz, 1H), 5.06 – 4.97 (m, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -98.31 (dd, *J* = 246.3, 9.0 Hz, 1F), -100.93 (dd, *J* = 246.5, 16.2 Hz, 1F), -110.64 – 110.70 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.2 (d, *J* = 3.0 Hz), 163.2 (d, *J* = 245.0 Hz), 146.5, 13.06 (t, *J* = 25.0 Hz), 128.8, 128.4 (dd, *J* = 15.0, 6.0 Hz), 120.3 (t, *J* = 249.0 Hz), 117.8, 115.3 (d, *J* = 22.0 Hz), 113.3, 61.2, 61.1 (dd, *J* = 31.0, 27.0 Hz), 14.3; **IR (neat)**: υ $_{max}$ 3045, 1765, 1547, 1515, 1375, 1243, 1053, 1028, 820 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}F_3NO_2$ $[M+H]^+$ 324.1205, found 324.1197.

Ethyl 3-(4-chlorophenyl)-3,3-difluoro-2-(phenylamino)propanoate (4e):



colorless oil (68%, 46.1 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.66 (d, *J* = 8.8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.05 (t, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.21 (d, *J* = 10.8 Hz, 1H), 5.07 – 4.98 (m, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -98.85 (dd, *J* = 246.3, 9.4 Hz, 1F), -101.87 (dd, *J* = 246.3, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.1 (d, *J* = 3.0 Hz), 146.5, 135.3, 133.1 (t, *J* = 26.0 Hz), 128.8, 128.4, 127.8 (t, *J* = 6.0 Hz), 120.3 (t, *J* = 249.0 Hz), 117.7, 113.3, 61.3, 61.0 (dd, *J* = 31.0, 27.0 Hz), 13.8; **IR (neat)**: υ $_{max}$ 3058, 1743, 1676, 1603, 1531, 1499, 1456, 1310, 1052, 824 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}ClF_2NO_2$ $[M+H]^+$ 340.0910, found 340.0914.

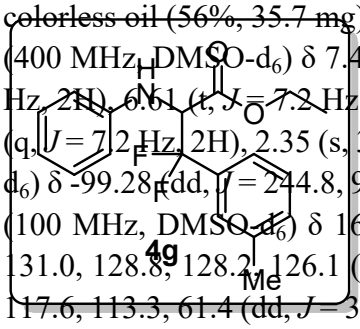
Ethyl 3-(4-bromophenyl)-3,3-difluoro-2-(phenylamino)propanoate (4f):



colorless oil (82%, 62.8 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 2H), 6.76 (d, *J* = 7.6 Hz, 2H), 6.61 (t, *J* = 6.8 Hz, 1H), 6.18 (d, *J* = 10.8 Hz, 1H), 5.06 – 4.97 (m, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.01 (dd, *J* = 246.7, 9.0 Hz, 1F), -102.00 (dd, *J* = 246.7, 16.2

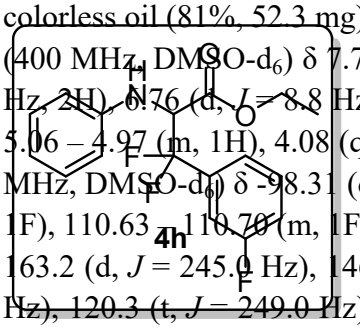
Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.0 (d, *J* = 3.0 Hz), 146.4, 133.4 (t, *J* = 25.0 Hz), 131.3, 128.8, 128.0 (t, *J* = 6.0 Hz), 124.1, 120.3 (t, *J* = 249.0 Hz), 117.7, 113.3, 61.3, 61.0 (dd, *J* = 27.0, 23.0 Hz), 13.8; **IR (neat)**: υ $_{max}$ 3061, 1736, 1647, 1453, 1371, 1098, 1043, 936 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}BrF_2NO_2$ $[M+H]^+$ 384.0405, found 384.0414.

Ethyl 3,3-difluoro-2-(phenylamino)-3-(m-tolyl)propanoate (4g):



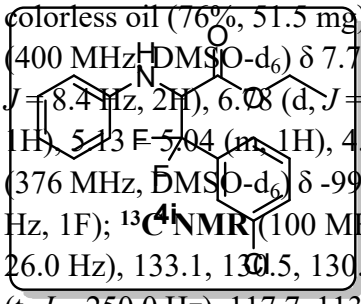
colorless oil (56%, 35.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.44 – 7.29 (m, 5H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.16 (d, *J* = 10.4 Hz, 1H), 4.98 – 4.89 (m, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.04 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.28 (dd, *J* = 244.8, 9.4 Hz, 1F), -101.70 (dd, *J* = 245.2, 15.4 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.2 (d, *J* = 4.0 Hz), 146.6, 137.7, 134.1 (t, *J* = 26.0 Hz), 131.0, 128.8, 128.2, 126.1 (t, *J* = 6.0 Hz), 122.8 (t, *J* = 6.0 Hz), 120.5 (t, *J* = 249 Hz), 117.6, 113.3, 61.4 (dd, *J* = 30.0, 27.0 Hz), 61.1, 20.9, 13.8; **IR (neat)**: υ $_{max}$ 3061, 1737, 1606, 1549, 1449, 1235, 1044, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{18}H_{20}F_2NO_2$ $[M+H]^+$ 320.1456, found 320.1463.

Ethyl 3,3-difluoro-3-(3-fluorophenyl)-2-(phenylamino)propanoate (4h):



colorless oil (81%, 52.3 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.71 – 7.68 (m, 2H), 7.31 (t, *J* = 8.8 Hz, 2H), 7.05 (t, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.22 (d, *J* = 10.4 Hz, 1H), 5.06 – 4.97 (m, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -98.31 (dd, *J* = 246.3, 9.0 Hz, 1F), -100.93 (dd, *J* = 246.3, 16.2 Hz, 1F), 110.63 – 110.70 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.2 (d, *J* = 4.0 Hz), 163.2 (d, *J* = 245.0 Hz), 146.5, 130.6 (t, *J* = 26.0 Hz), 129.3, 128.4 (dd, *J* = 15.0, 6.0 Hz), 120.3 (t, *J* = 249.0 Hz), 117.7, 115.3 (d, *J* = 22.0 Hz), 113.3, 61.2, 61.1 (dd, *J* = 31.0, 26.0 Hz), 13.9; **IR (neat)**: υ $_{max}$ 3043, 1835, 1765, 1676, 1375, 1244, 1025, 757 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}F_3NO_2$ $[M+H]^+$ 324.1205, found 324.1198.

Ethyl 3-(3-chlorophenyl)-3,3-difluoro-2-(phenylamino)propanoate (4i):



colorless oil (76%, 51.5 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.72 (s, 1H), 7.62 – 7.57 (m, 2H), 7.53 – 7.49 (m, 1H), 7.06 (t, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.23 (d, *J* = 10.8 Hz, 1H), 5.13 – 5.04 (m, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.14 (dd, *J* = 246.7, 9.8 Hz, 1F), -101.92 (dd, *J* = 246.3, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.0 (d, *J* = 4.0 Hz), 146.5, 136.3 (t, *J* = 26.0 Hz), 133.1, 130.5, 130.4, 128.8, 125.9 (t, *J* = 6.0 Hz), 124.5 (t, *J* = 6.0 Hz), 119.9 (t, *J* = 250.0 Hz), 117.7, 113.3, 61.3, 60.9 (dd, *J* = 31.0, 27.0 Hz), 13.8; **IR (neat)**: υ $_{max}$ 3062, 1736, 1649, 1562, 1549, 1371, 1098, 1043, 936 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}ClF_2NO_2$ $[M+H]^+$ 340.0910, found 340.0919.

Ethyl 3-(3-bromophenyl)-3,3-difluoro-2-(phenylamino)propanoate (4j):

colorless oil (76%, 58.2 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.86 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.06 (t, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.26 (d, *J* = 10.8 Hz, 1H), 5.15 – 5.05 (m, 1H), 4.09 (q, *J* = 6.8 Hz, 2H), 1.07 (t, *J* = 6.8 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.14 (dd, *J* = 246.3, 9.4 Hz, 1F), -101.96 (dd, *J* = 246.7, 17.3 Hz, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.1 (d, *J* = 4.0 Hz), 146.5, 136.5 (t, *J* = 26.0 Hz), 133.4, 130.6, 128.8, 128.7 (t, *J* = 7.0 Hz), 124.9 (t, *J* = 6.0 Hz), 121.6, 119.9 (t, *J* = 250.0 Hz), 117.8, 113.3, 61.3, 60.9 (dd, *J* = 30.0, 27.0 Hz), 13.9; **IR (neat)**: υ $_{max}$ 3043, 1766, 1677, 1455, 1425, 1374, 1248, 1025, 757 cm^{-1}; **HRMS (ESI)** calcd for $C_{17}H_{17}BrF_2NO_2$ $[M+H]^+$ 384.0405, found 384.0415.

Ethyl 3-(3,5-dimethylphenyl)-3,3-difluoro-2-(phenylamino)-propanoate (4k):

colorless oil (85%, 56.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.23 (s, 2H), 7.11 (s, 1H), 7.07 (t, *J* = 7.2, 2H), 6.79 (d, *J* = 7.6 Hz, 2H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.15 (d, *J* = 10.4 Hz, 1H), 4.96 – 4.87 (m, 1H), 4.06 (q, *J* = 6.8 Hz, 2H), 2.30 (s, 6H), 1.04 (t, *J* = 6.8 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.39 (dd, *J* = 244.4, 10.2 Hz, 1F), -101.64 (dd, *J* = 244.4, 14.7 Hz, 1F); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.3 (d, *J* = 4.0 Hz), 146.6, 137.6, 134.1 (t, *J* = 24.0 Hz), 131.7, 128.8, 123.3 (t, *J* = 5.0 Hz), 120.5 (t, *J* = 249.0 Hz), 117.7, 113.3, 61.5 (dd, *J* = 30.0, 27.0 Hz), 61.1, 20.8, 13.8; **IR (neat)**: υ $_{max}$ 3061, 1647, 1453, 1371, 1301, 1043, 847 cm^{-1}; **HRMS (ESI)** calcd for $C_{19}H_{22}F_2NO_2$ $[M+H]^+$ 334.1613, found 334.1619.

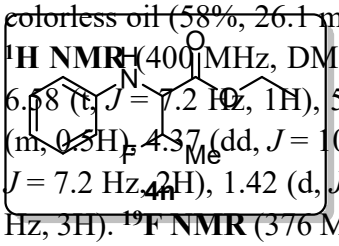
Ethyl 3,3-difluoro-2-(phenylamino)butanoate (4l):

colorless oil (53%, 25.8 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.10 (t, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.64 (t, *J* = 7.2 Hz, 1H), 6.15 (d, *J* = 10.4 Hz, 1H), 4.72 – 4.63 (m, 1H), 4.16 (qd, *J* = 6.8, 2.0 Hz, 2H), 1.76 (t, *J* = 19.6 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -93.37 – -94.20 (m, 1F), -95.55 – -96.39 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7 (dd, *J* = 3.0, 2.0 Hz), 146.8, 128.9, 122.7 (t, J = 244.0Hz), 117.6, 113.2, 61.2, 60.4 (dd, *J* = 27.0, 29.0 Hz), 21.0 (t, *J* = 25.0 Hz), 14.0; **IR (neat)**: υ $_{max}$ 3076, 1733, 1648, 1613, 1454, 1372, 1238, 1098, 937 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{16}F_2NO_2$ $[M+H]^+$ 244.1143, found 244.1148.

Ethyl 3-fluoro-3-methyl-2-(phenylamino)butanoate (4m):

colorless oil (72%, 34.4 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.09 (t, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.61 (t, *J* = 7.2 Hz, 1H), 5.83 (d, *J* = 10.4 Hz, 1H), 4.22 (dd, *J* = 16.0, 10.0 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 1.51 (d, *J* = 5.2 Hz, 3H), 1.45 (d, *J* = 4.8 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -141.66 – -146.41 (m, 1F); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.1 (d, *J* = 2.0 Hz), 147.5, 128.9, 117.1, 113.0, 95.6 (d, *J* = 174.0 Hz), 62.8 (d, *J* = 24.0 Hz), 60.5, 24.8 (d, *J* = 23.0 Hz), 23.9 (d, *J* = 23.0 Hz) 14.1; **IR (neat)**: υ $_{max}$ 3043, 1765, 1646, 1538, 1455, 1374, 1273, 1244, 1027, 756 cm^{-1}; **HRMS (ESI)** calcd for $C_{13}H_{19}FNO_2$ $[M+H]^+$ 240.1394, found 240.1385.

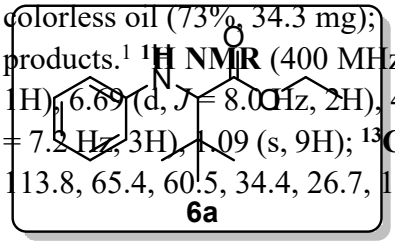
Ethyl 3-fluoro-2-(phenylamino)butanoate (4n):



4n

colorless oil (58%, 26.1 mg, dr = 1:1); R_f = 0.6 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.07 (t, *J* = 7.6 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.58 (t, *J* = 7.2 Hz, 1H), 5.88 (d, *J* = 9.6 Hz, 1H), 5.23 – 5.17 (m, 0.5H), 5.11 – 5.05 (m, 0.5H), 4.37 (dd, *J* = 10.0, 3.2 Hz, 0.5H), 4.30 (dd, *J* = 10.0, 3.2 Hz, 0.5H), 4.13 (q, *J* = 7.2 Hz, 2H), 1.42 (d, *J* = 6.0 Hz, 1.5H), 1.35 (d, *J* = 6.0 Hz, 1.5H), 1.18 (t, *J* = 7.2 Hz, 3H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -180.85 – -183.78 (m, 1F). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.0 (d, *J* = 4.0 Hz), 147.9, 128.8, 116.8, 112.7, 90.5 (d, *J* = 171.0 Hz), 60.8, 59.6 (d, *J* = 20.0 Hz), 17.4 (d, *J* = 22.0 Hz), 14.1. **IR (neat)**: υ_{max} 3074, 1591, 1460, 1379, 1330, 1024, 908 cm^{-1}; **HRMS (ESI)** calcd for $C_{12}H_{17}FNO_2$ $[M+H]^+$ 226.1238, found 226.1228.

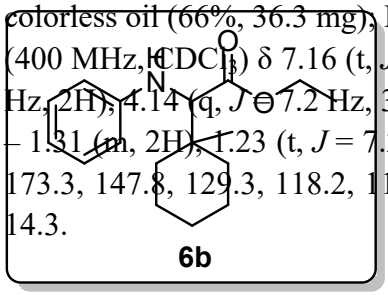
Ethyl 3,3-dimethyl-2-(phenylamino)butanoate (6a):



6a

colorless oil (73%, 34.3 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); Known products.[1] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.2 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 4.21 – 4.14 (m, 3H), 3.81 (d, *J* = 10.0 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.09 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.3, 147.7, 129.2, 118.2, 113.8, 65.4, 60.5, 34.4, 26.7, 14.2.

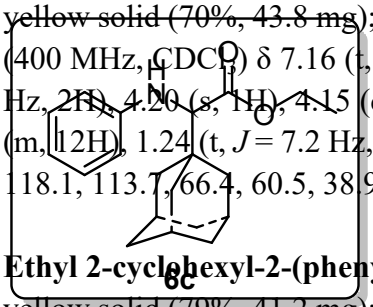
Ethyl 2-(1-methylcyclohexyl)-2-(phenylamino)acetate (6b):



6b

colorless oil (66%, 36.3 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 8.0 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 3H), 3.94 (d, *J* = 10.8 Hz, 1H), 1.64 – 1.48 (m, 8H), 1.34 – 1.31 (m, 2H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.3, 147.8, 129.3, 118.2, 113.8, 64.4, 60.5, 37.1, 34.9, 34.9, 26.1, 21.7, 21.6, 20.3, 14.3.

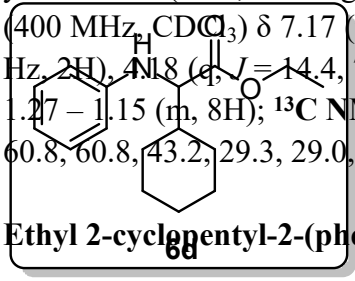
Ethyl 2-(adamantan-1-yl)-2-(phenylamino)acetate (6c):



6c

yellow solid (70%, 43.8 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 7.6 Hz, 2H), 4.20 (s, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.66 (s, 1H), 2.03 (s, 3H), 1.82 – 1.58 (m, 12H), 1.24 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 147.8, 129.2, 118.1, 113.7, 66.4, 60.5, 38.9, 36.8, 36.3, 28.3, 14.3.

Ethyl 2-cyclohexyl-2-(phenylamino)acetate (6d):

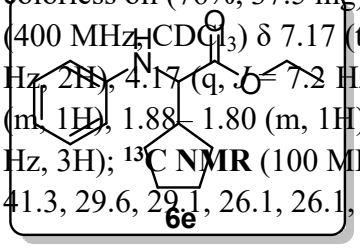


6d

yellow solid (79%, 41.2 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 2H), 4.18 (q, *J* = 14.4, 7.2 Hz, 2H), 3.88 (d, *J* = 6.0 Hz, 1H), 1.88 – 1.70 (m, 7H), 1.27 – 1.15 (m, 8H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.2, 147.3, 129.2, 118.2, 113.5, 60.8, 60.8, 43.2, 29.3, 29.0, 25.3, 25.1, 14.3.

Ethyl 2-cyclopentyl-2-(phenylamino)acetate (6e):

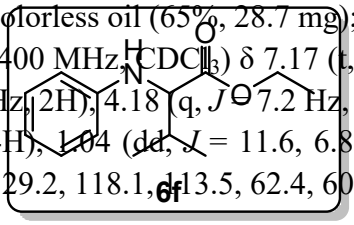
colorless oil (76%, 37.5 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.6 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 4.11 (s, 1H), 3.87 (d, *J* = 7.6 Hz, 1H), 2.30 – 2.20 (m, 1H), 1.88 – 1.80 (m, 1H), 1.75 – 1.56 (m, 5H), 1.52 – 1.43 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.6, 147.4, 129.2, 118.0, 113.4, 62.0, 60.8, 41.3, 29.6, 29.1, 26.1, 26.1, 14.3.



6e

Ethyl phenylvalinate (6f):

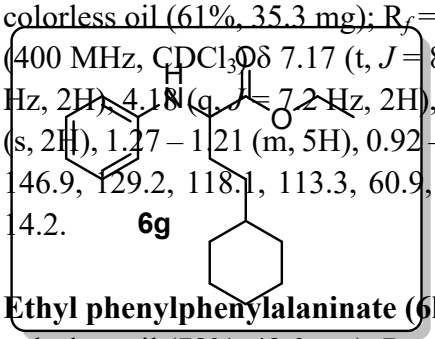
colorless oil (65%, 28.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 30:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.86 (s, 1H), 2.17 – 2.09 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 4H), 1.04 (dd, *J* = 11.6, 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.6, 147.3, 129.2, 118.1, 113.5, 62.4, 60.8, 31.5, 19.0, 18.7 14.3.



6f

Ethyl 4-cyclohexyl-2-(phenylamino)butanoate (6g):

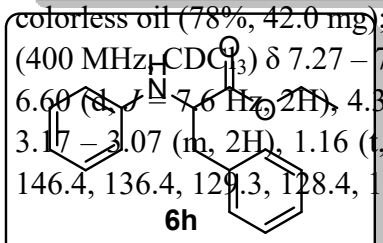
colorless oil (61%, 35.3 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.12 (s, 1H), 4.02 (s, 1H), 1.86 – 1.64 (m, 8H), 1.33 (s, 2H), 1.27 – 1.21 (m, 5H), 0.92 – 0.87 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 146.9, 129.2, 118.1, 113.3, 60.9, 56.8, 37.4, 33.2, 33.1, 33.0, 30.4, 26.5, 26.2, 26.1, 14.2.



6g

Ethyl phenylphenylalaninate (6h):

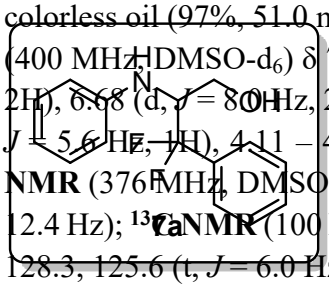
colorless oil (78%, 42.0 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 25:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.23 (m, 4H), 7.18 – 7.14 (m, 3H), 6.73 (t, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 2H), 4.34 (s, 1H), 4.16 (s, 1H), 4.11 (qd, *J* = 12.8, 10.8 Hz, 2H), 3.17 – 3.07 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.1, 146.4, 136.4, 129.3, 128.4, 126.9, 118.3, 113.6, 61.1, 57.7, 38.6, 14.1.



6h

3,3-Difluoro-3-phenyl-2-(phenylamino)propan-1-ol (7a):

colorless oil (97%, 51.0 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 15:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.57 – 7.55 (m, 2H), 7.47 – 7.45 (m, 3H), 7.03 (t, *J* = 7.6 Hz, 2H), 6.68 (d, *J* = 8.0 Hz, 2H), 6.52 (t, *J* = 7.2 Hz, 1H), 5.61 (d, *J* = 8.8 Hz, 1H), 4.80 (t, *J* = 5.6 Hz, 1H), 4.11 – 4.06 (m, 1H), 3.69 – 3.65 (m, 1H), 3.48 – 3.42 (m, 1H); **^{19}F NMR** (376 MHz, DMSO-d_6) δ -99.65 (dd, *J* = 245.9, 11.7 Hz), -102.02 (dd, *J* = 245.2, 12.4 Hz); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 148.5, 135.3 (t, *J* = 25.0 Hz), 130.0, 128.7, 128.3, 125.6 (t, *J* = 6.0 Hz), 122.7 (t, *J* = 246.0 Hz), 116.2, 112.2, 60.1 (t, *J* = 26.0 Hz), 59.7; **IR (neat)**: υ_{max} 2982, 1766, 1627, 1604, 1538, 1509, 1426, 1272 cm^{-1}; **HRMS (ESI)** calcd for $C_{15}H_{16}F_2NO$ $[M+H]^+$ 264.1194, found 264.1187.



7a

11. Refenrences

1. C. Wang, M. Guo, R. Qi, Q. Shang, Q. Liu, S. Wang, L. Zhao, R. Wang and Z. Xu, *Angew. Chem. Int. Ed*., 2018, **57**, 15841–15846.
2. H. Xin, Z.-H. Yuan, M. Yang, M. Wang, X.-H. Duan and L.-N. Guo, *Green. Chem.* 2021, **23**, 9549−9553.
3. B. Yang, X.-H. Xu and F.-L. Qing, *Org. Lett*., 2016, **18**, 5956–5959.
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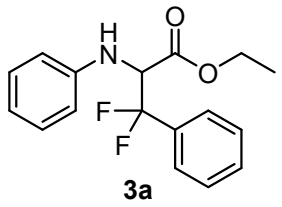
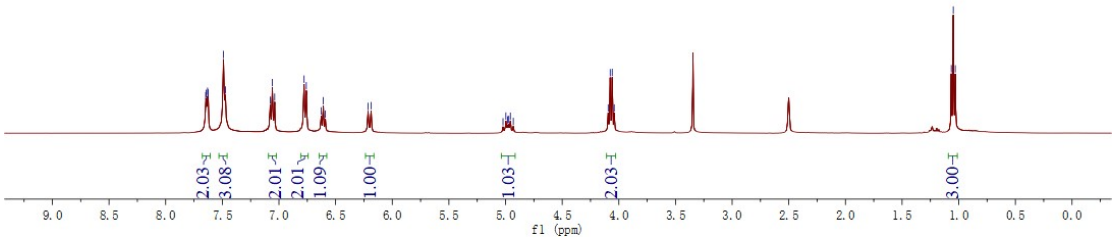
5. H. Zhao, G. Ma, X. Xie, Y. Wang, J. Hao and W. Wan, *Chem. Commun*., 2019, **55**, 3927–3930.

12. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR Spectra of Starting Materials 2 and Products 3, 4, and 6,7a

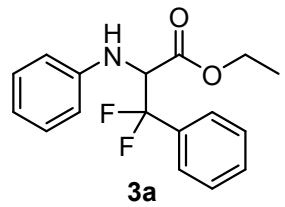
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3a:



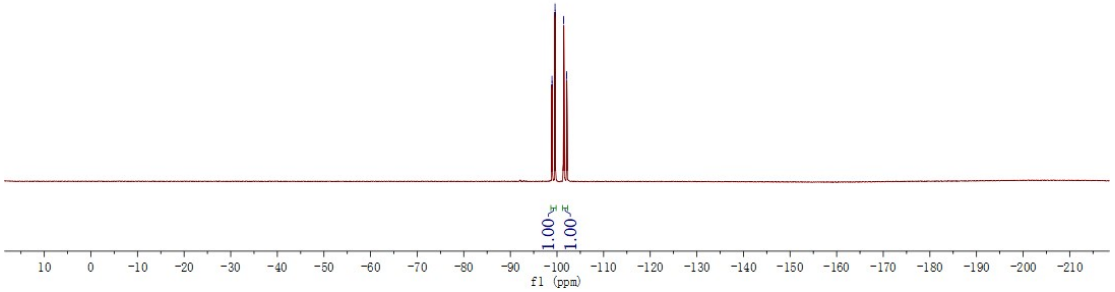
3a



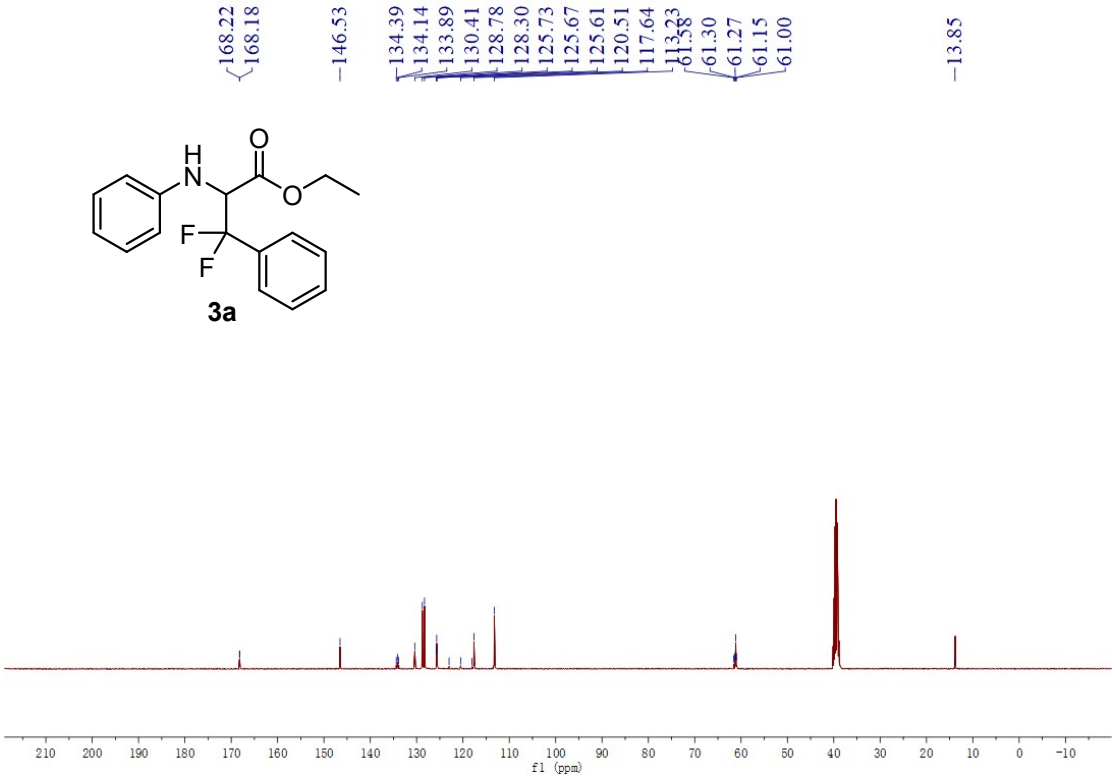
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 3a:



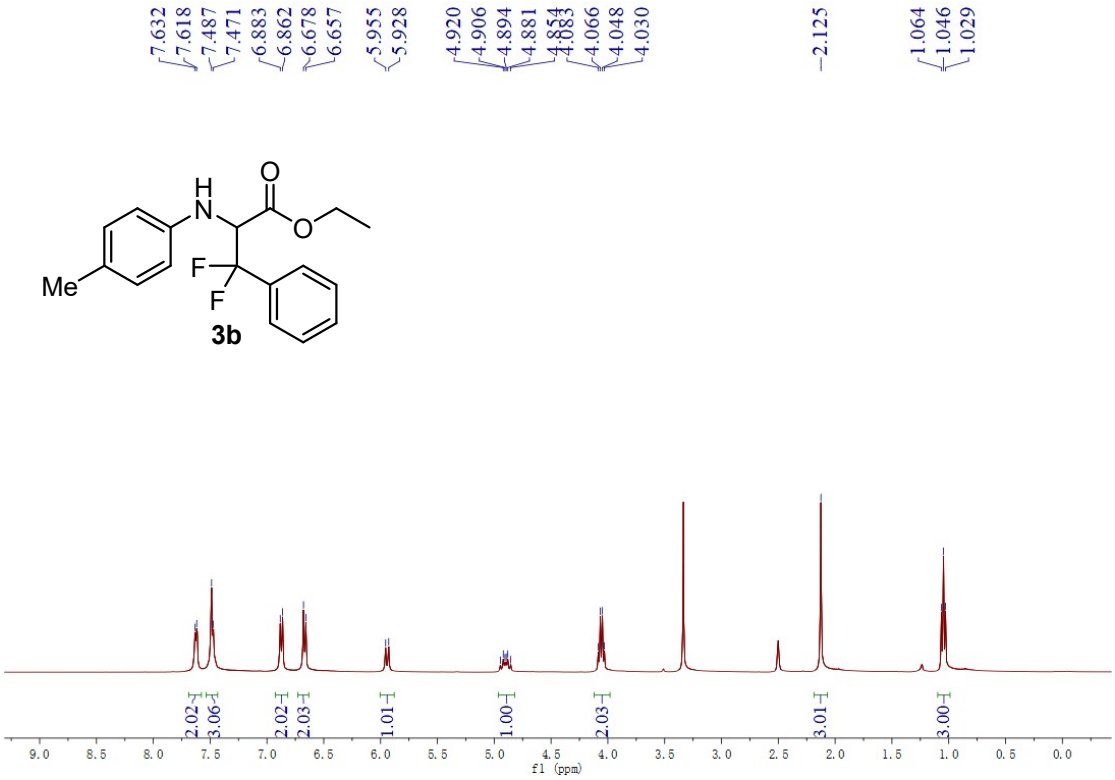
3a



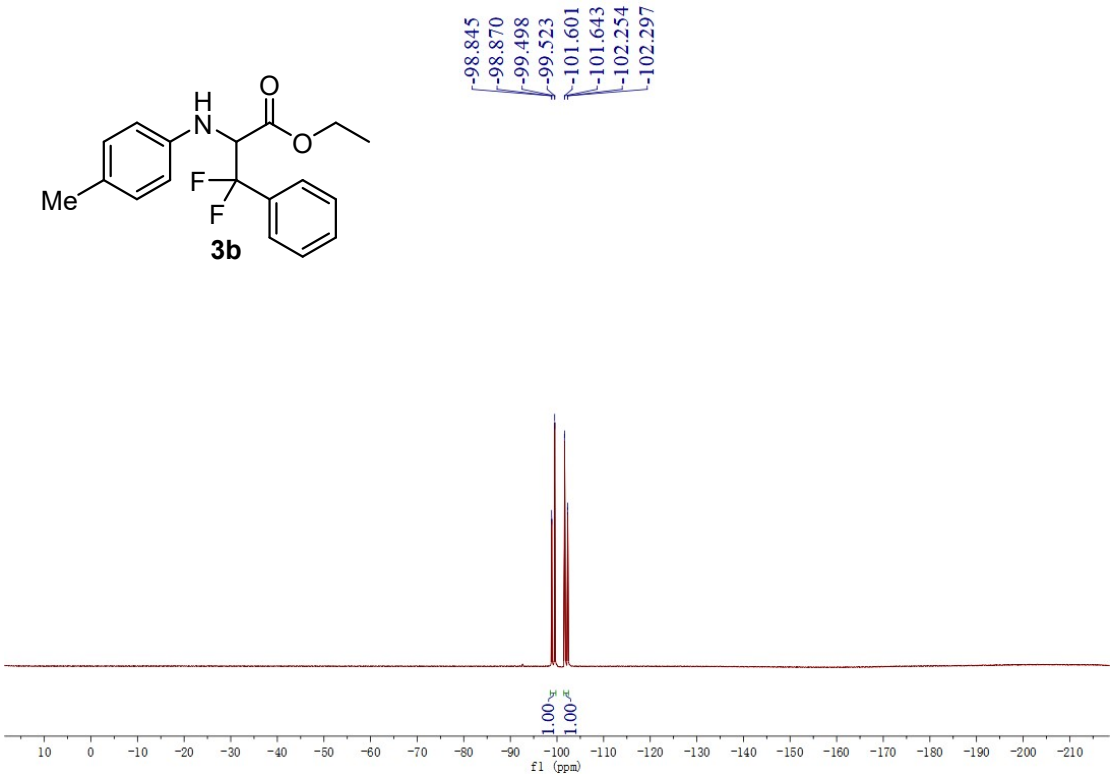
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3a:



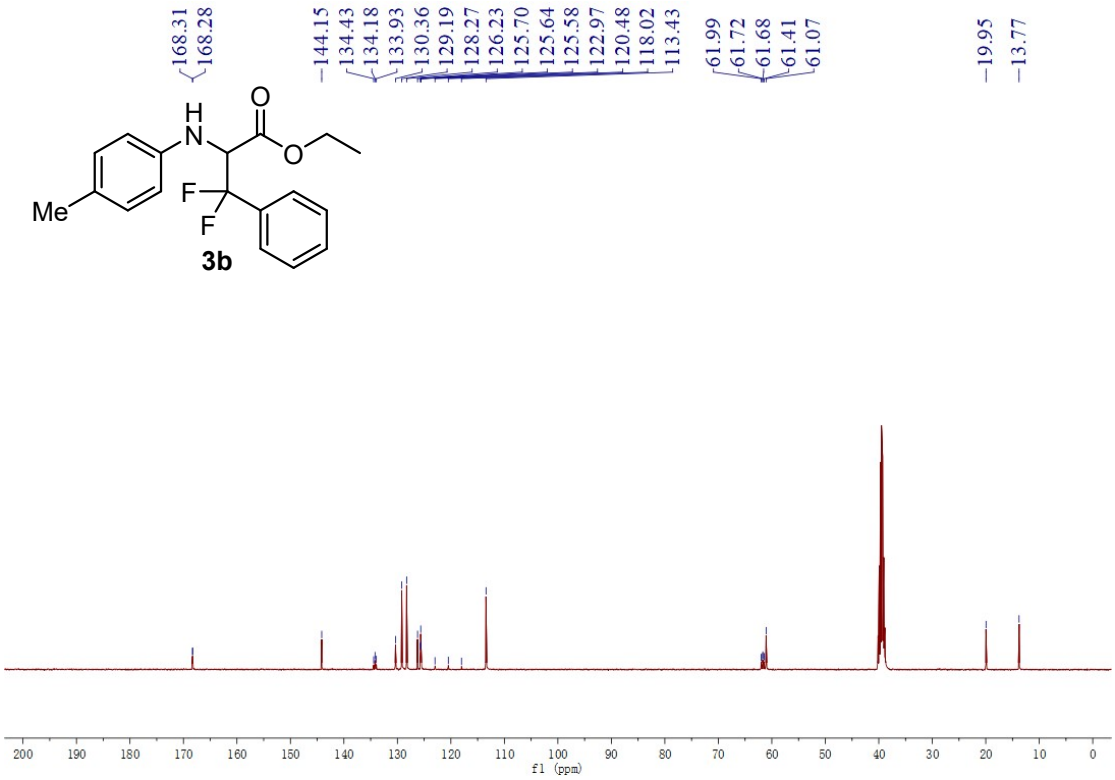
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3b:



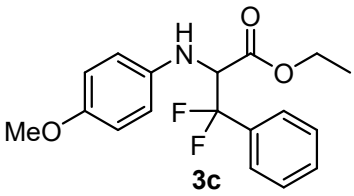
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3b:



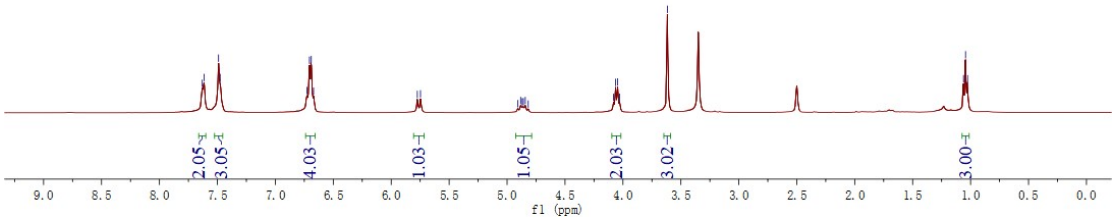
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3b:



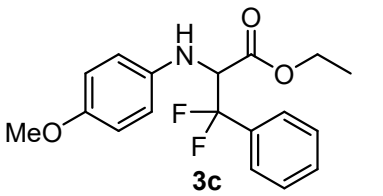
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3c:



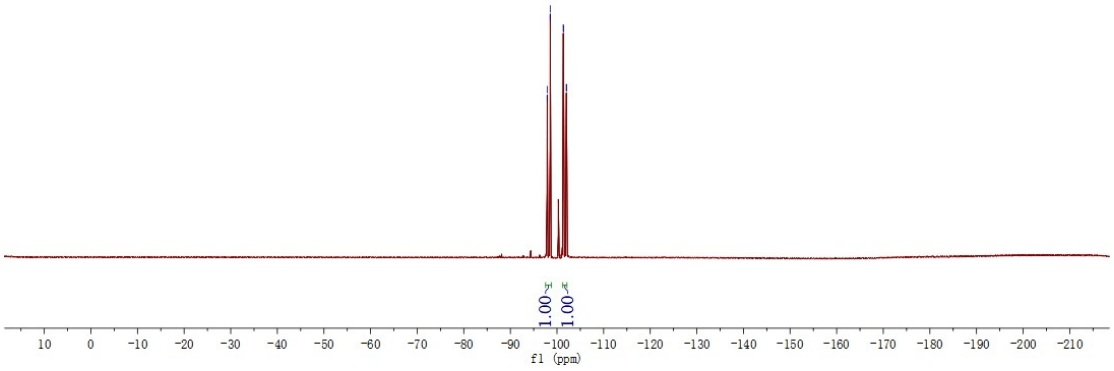
3c



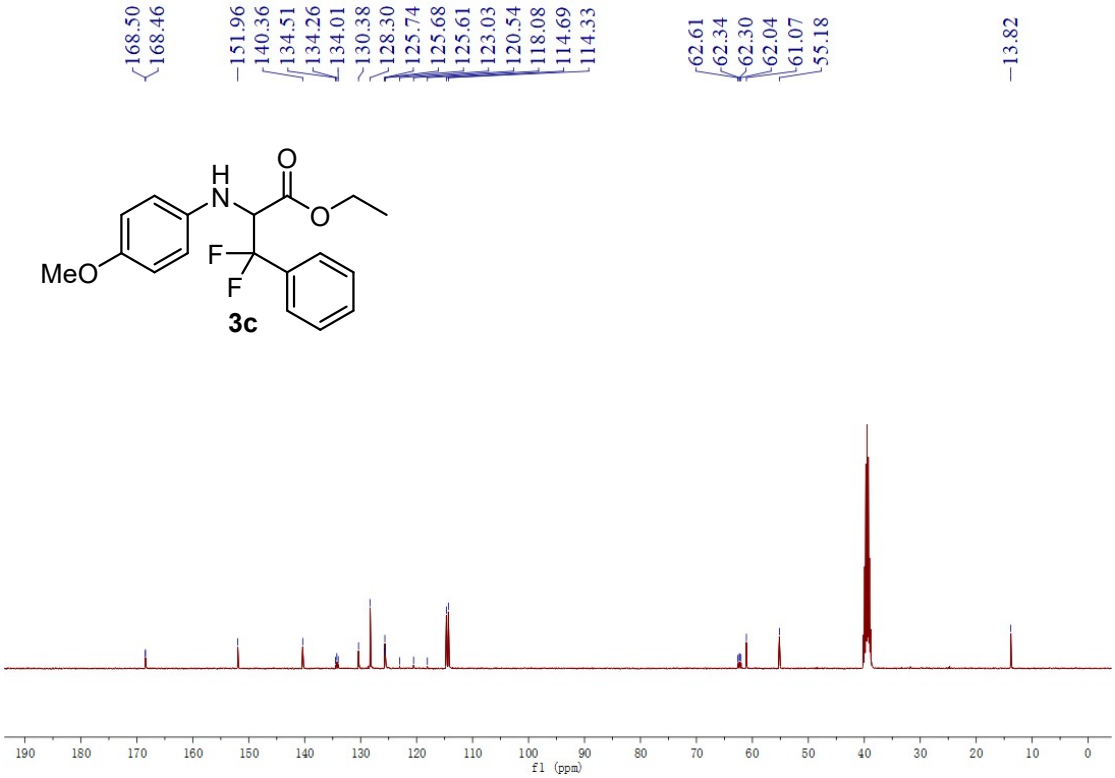
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3c:



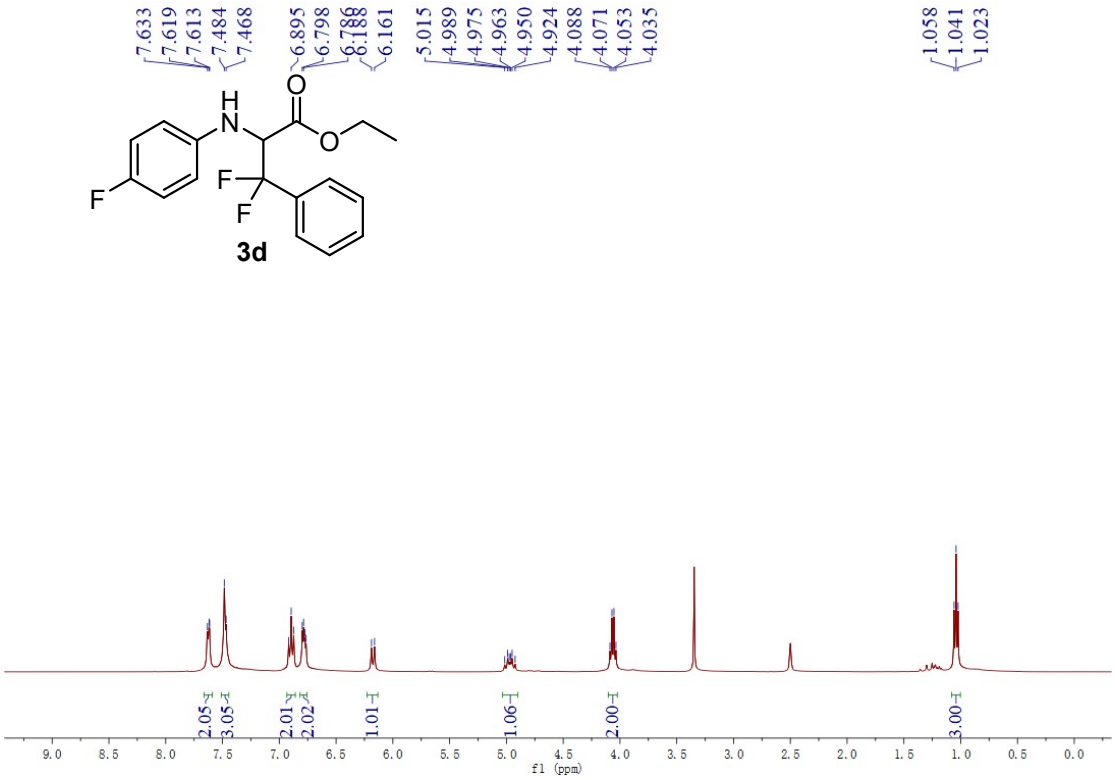
3c



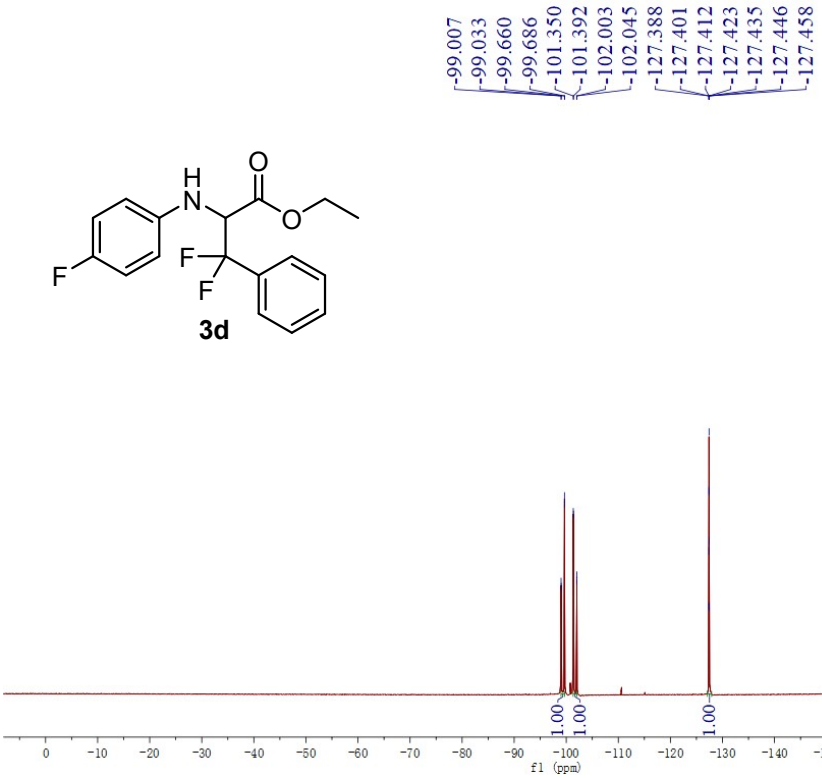
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3c:



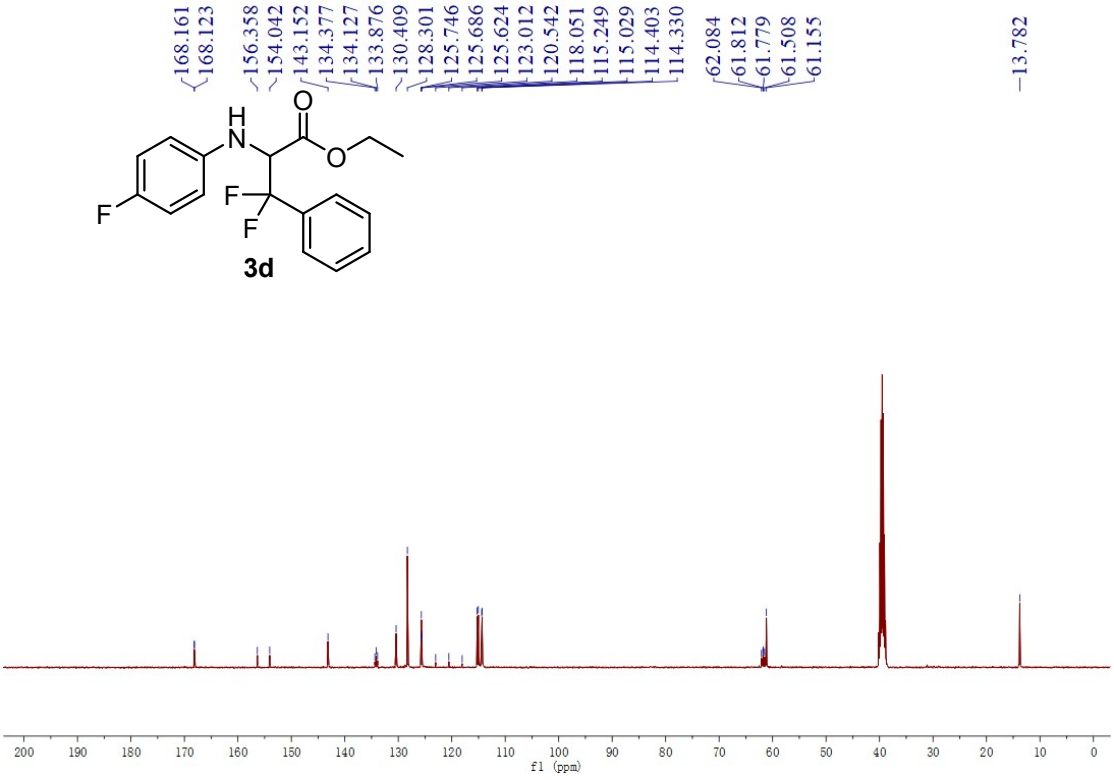
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3d:



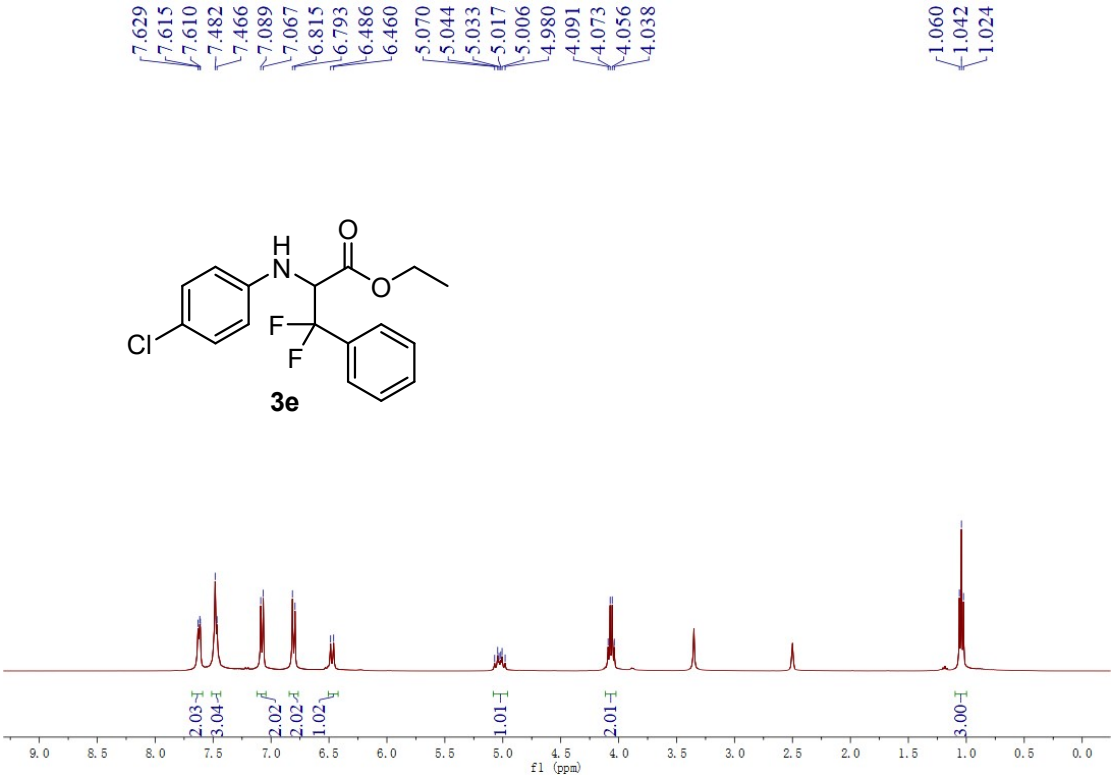
^{1}H NMR (DMSO-d_6, 376 MHz) spectrum of compound 3d:



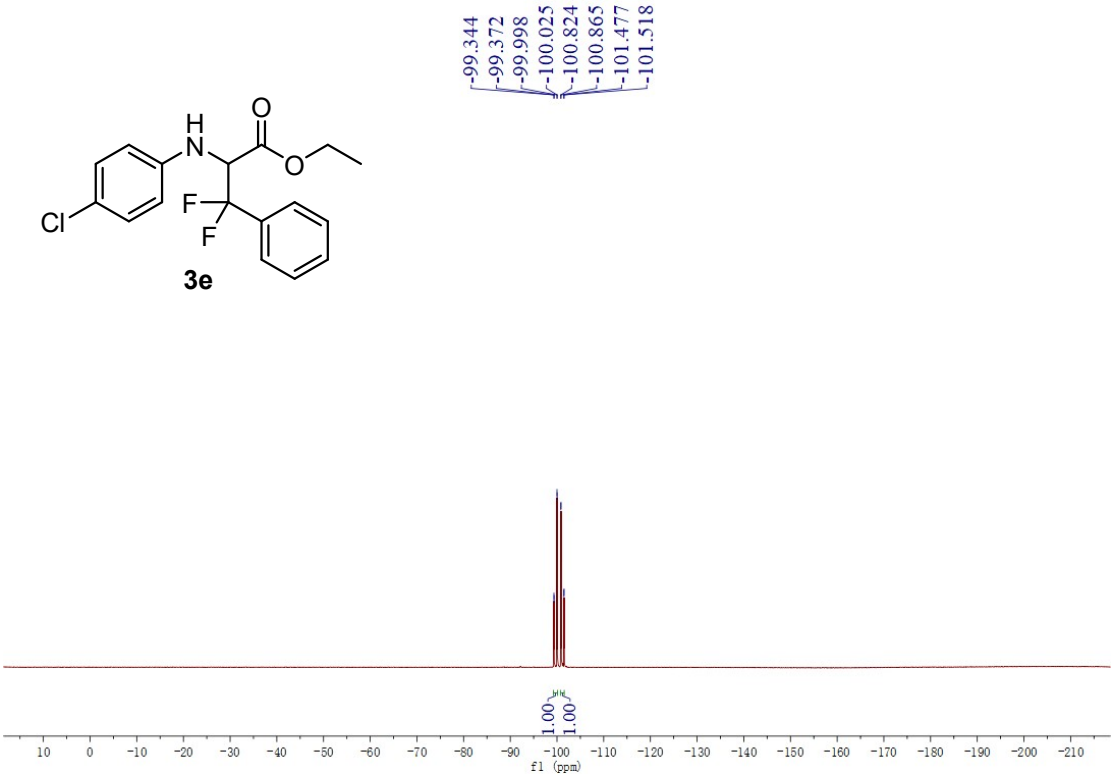
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3d:



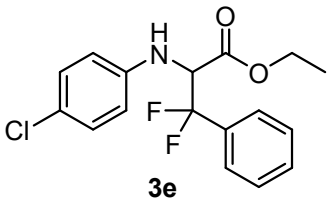
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3e:



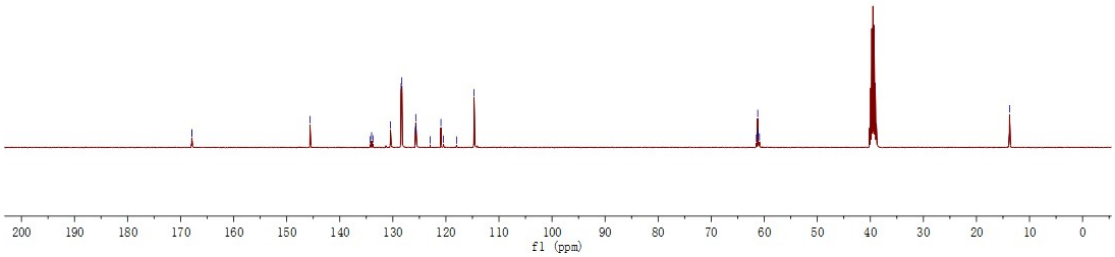
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3e:



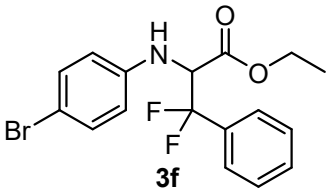
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3e:



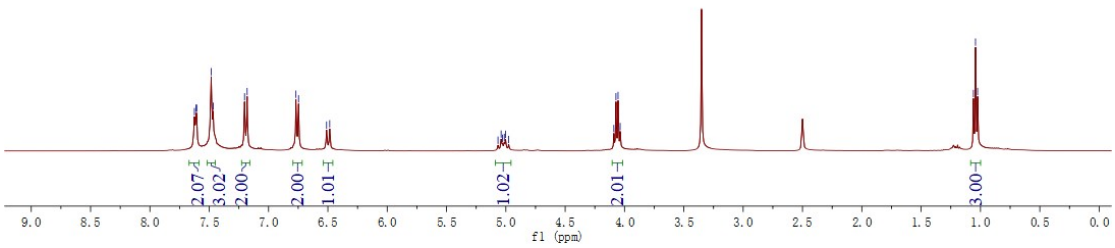
3e



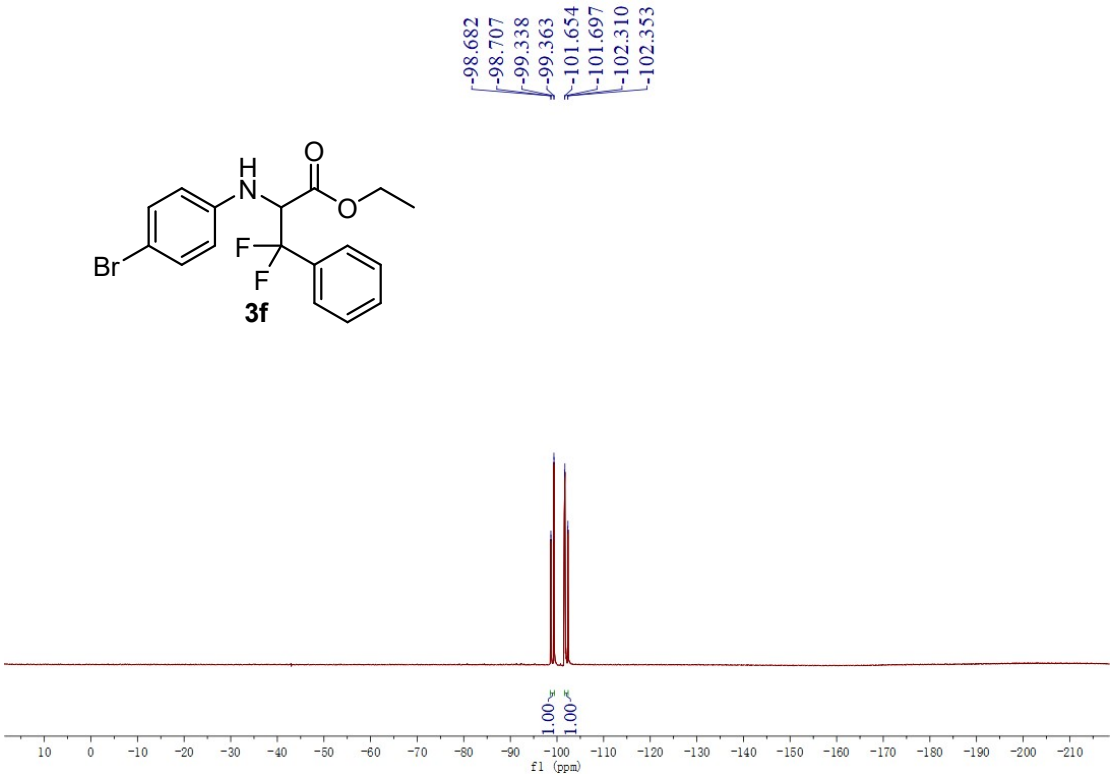
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3f:



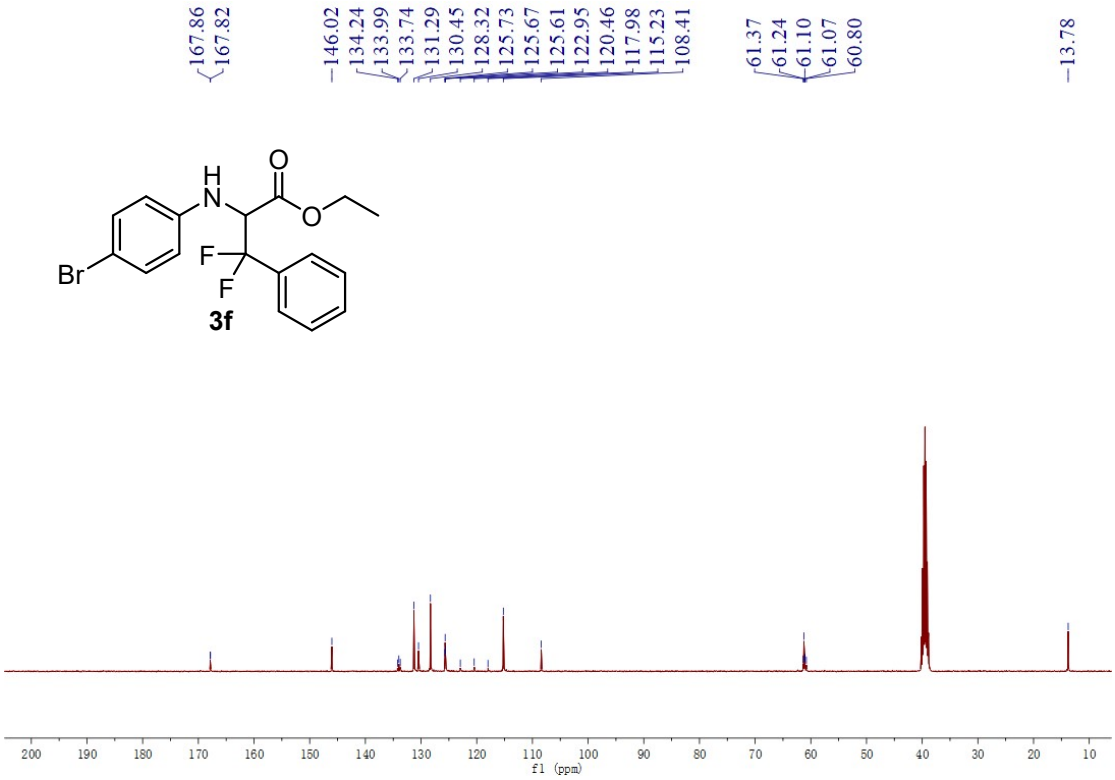
3f



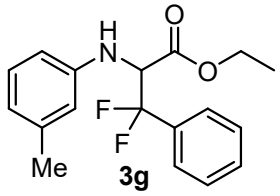
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3f:

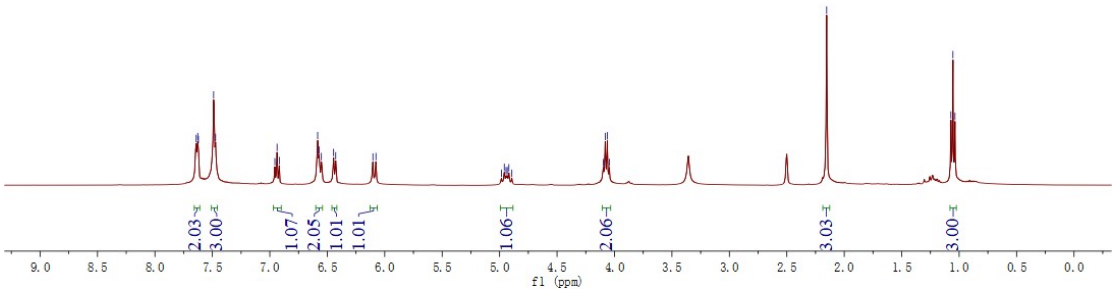


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3f:

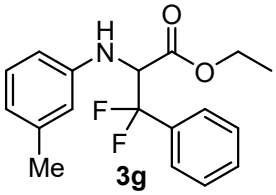


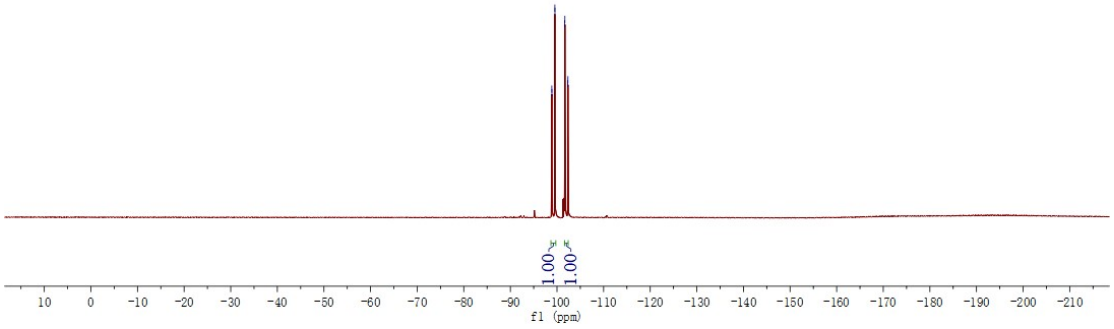
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3g:



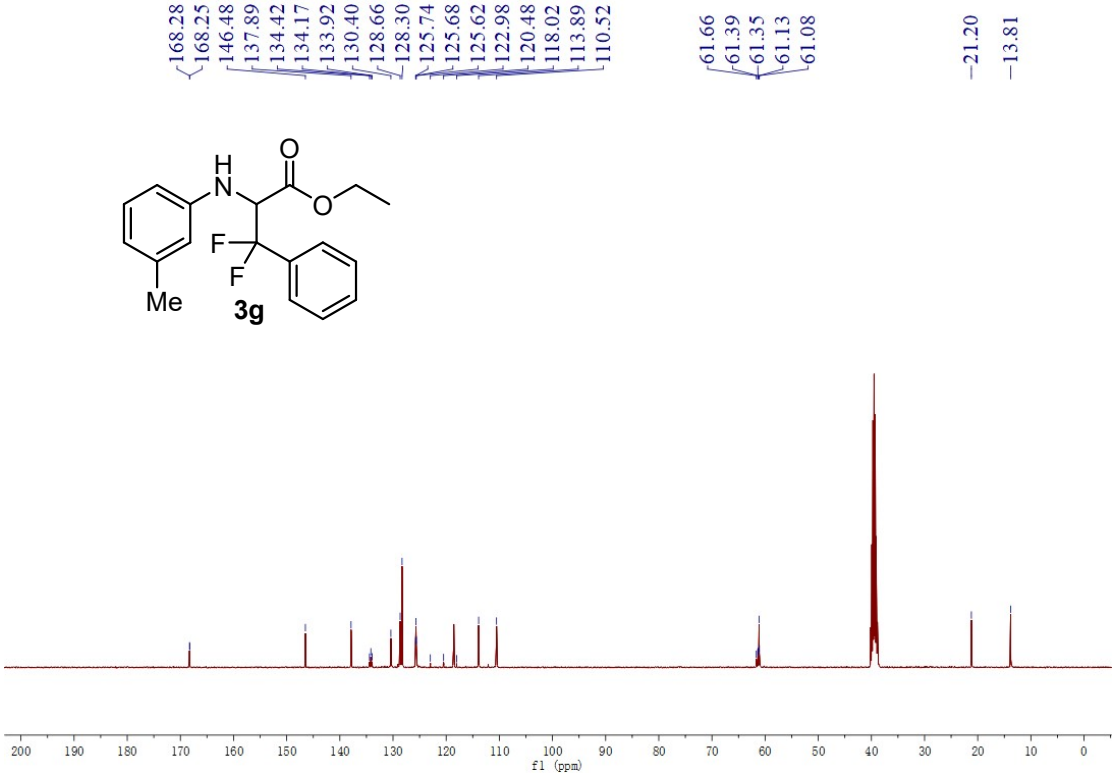


^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3g:

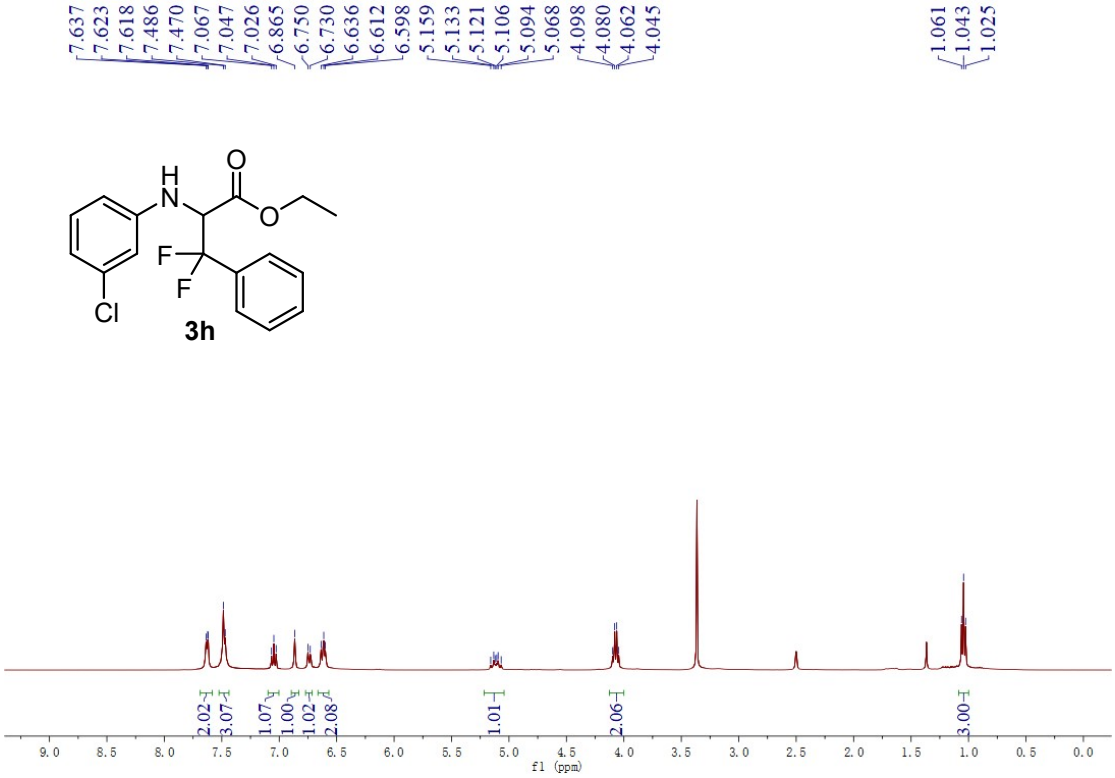




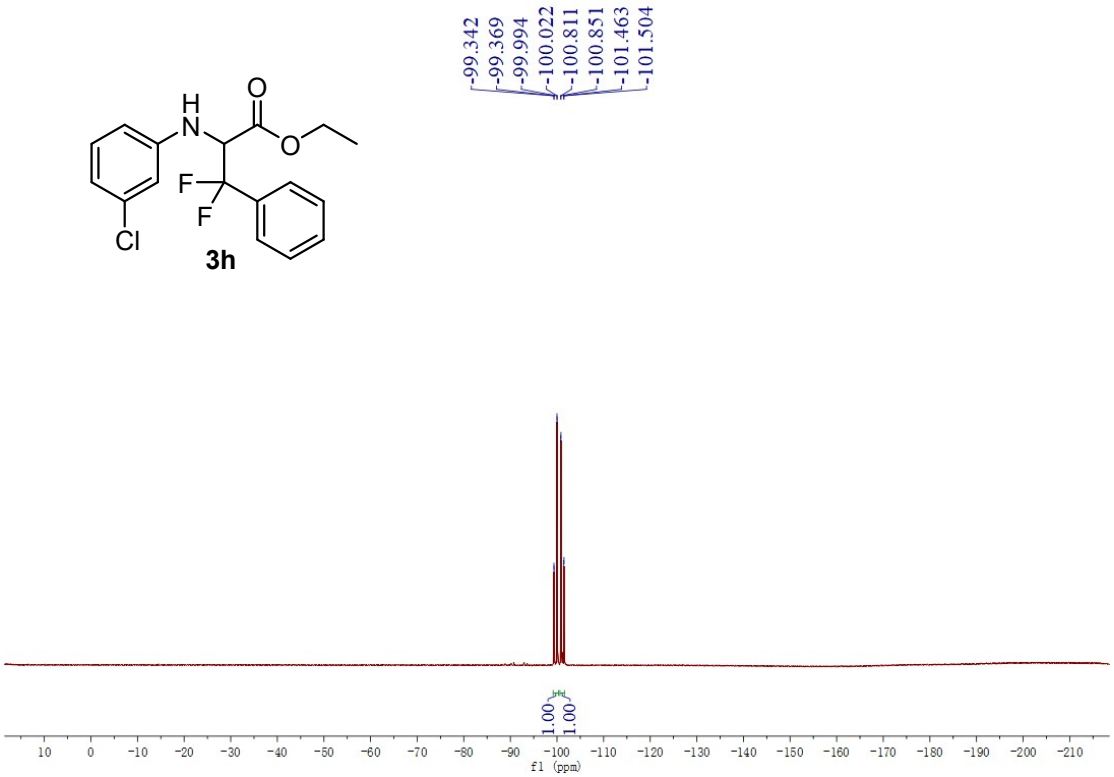
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3g:



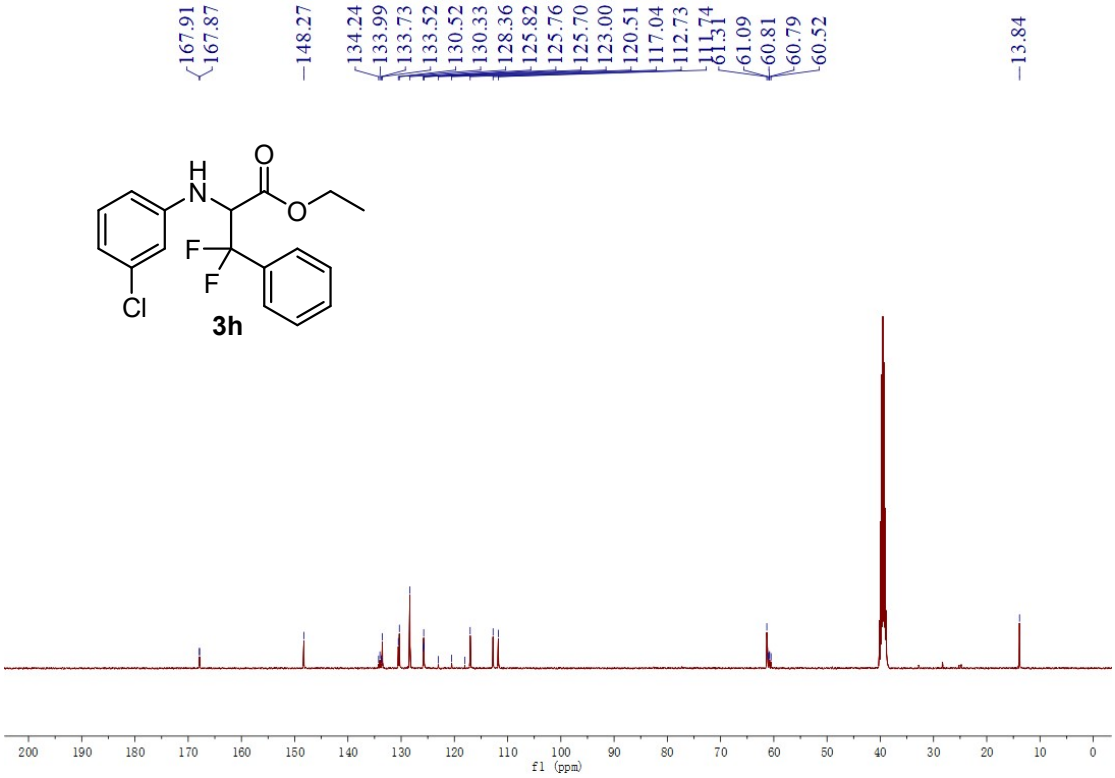
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3h:



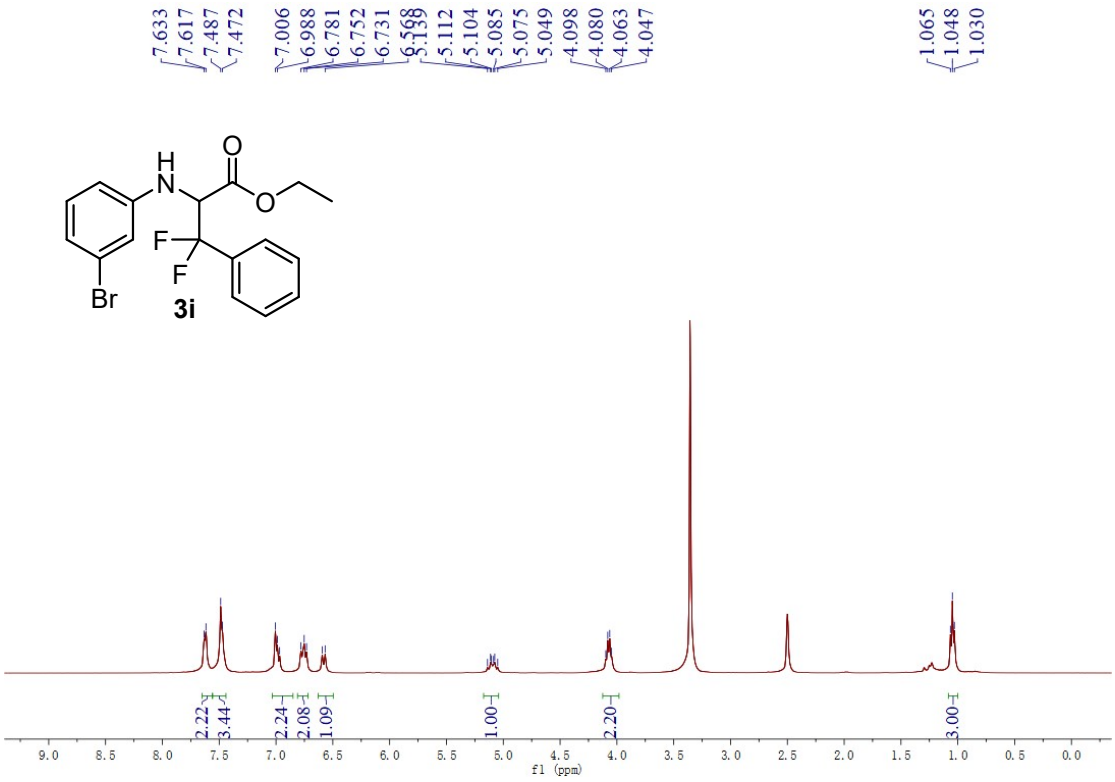
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3h:



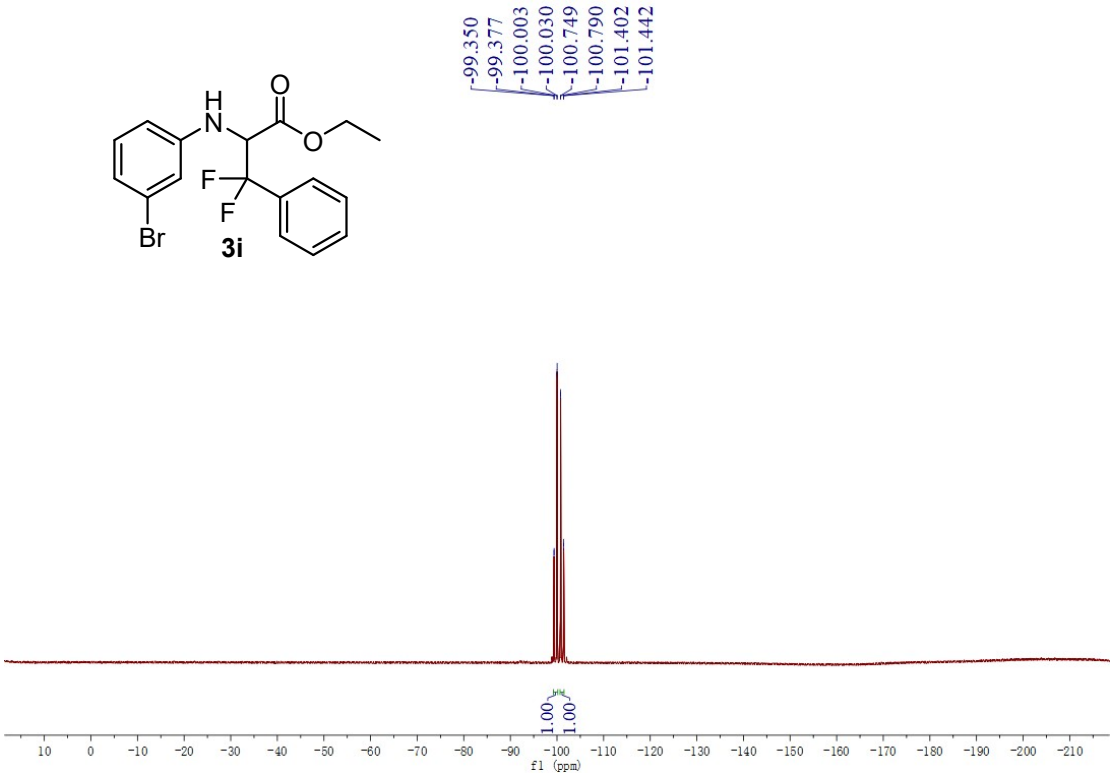
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3h:



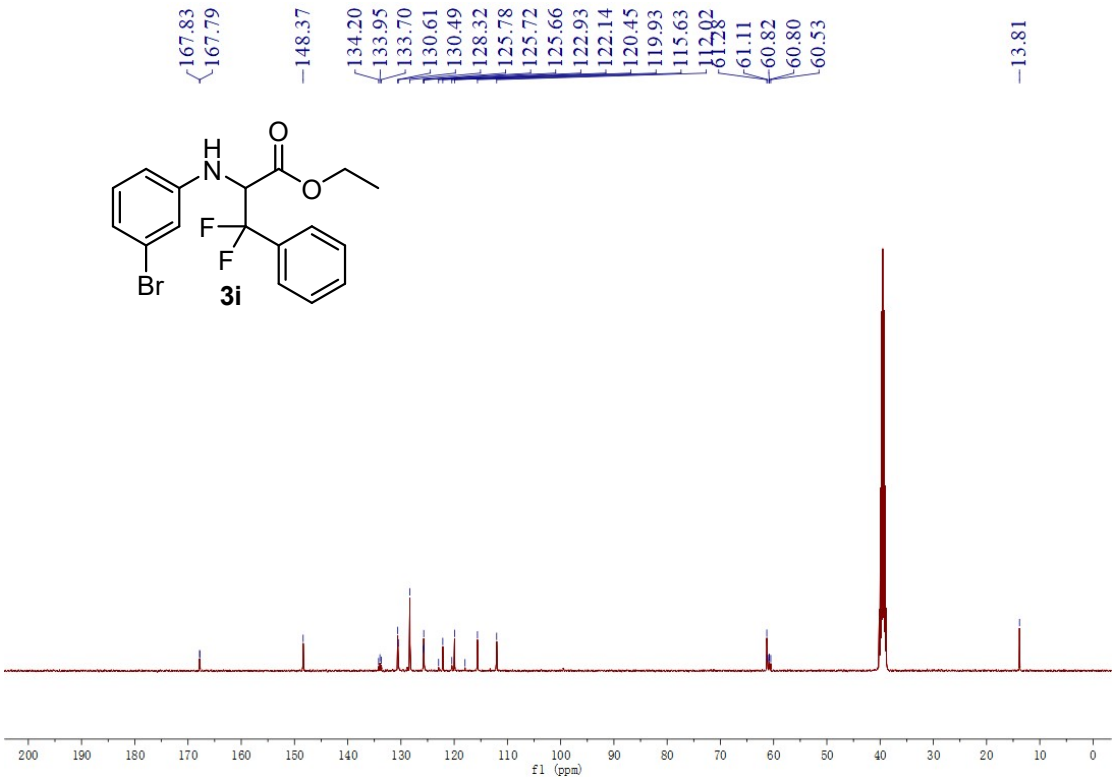
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3i:



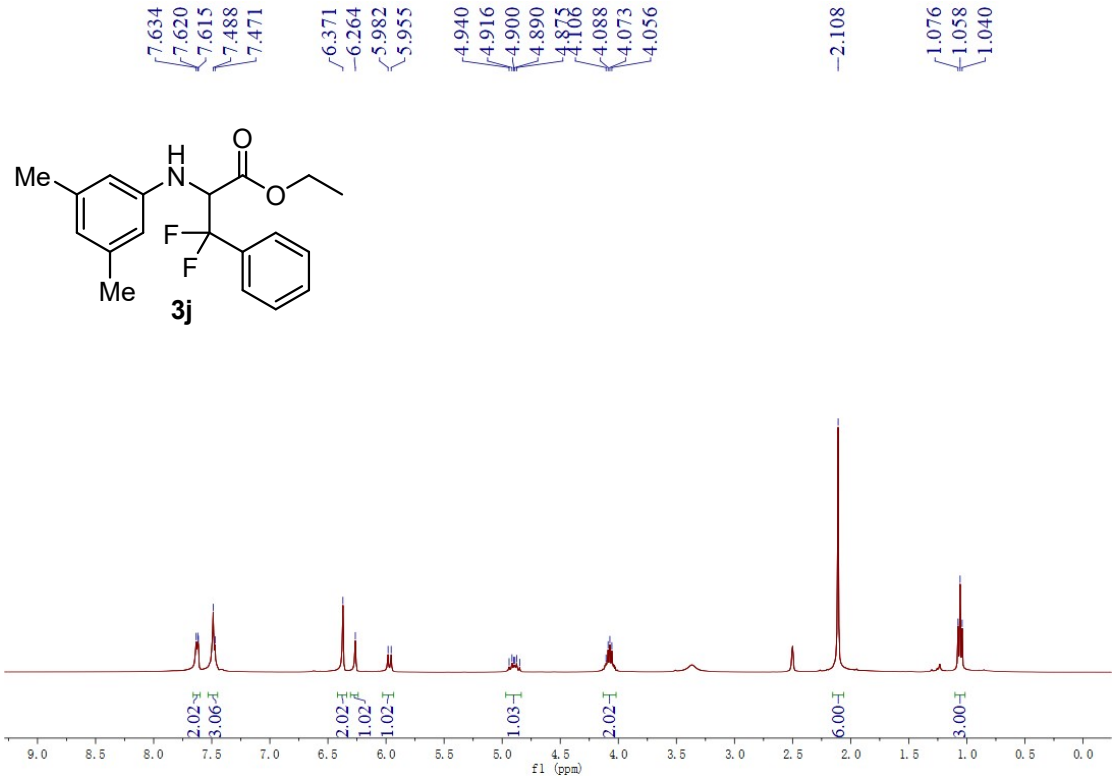
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3i:



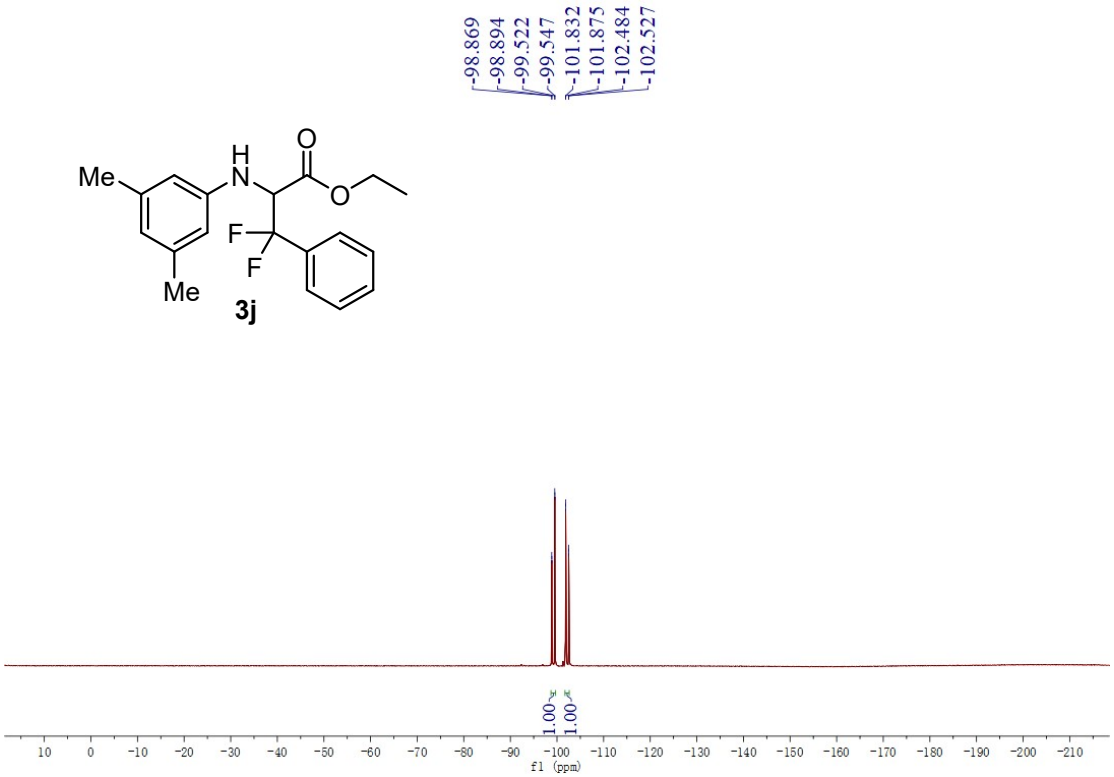
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3i:



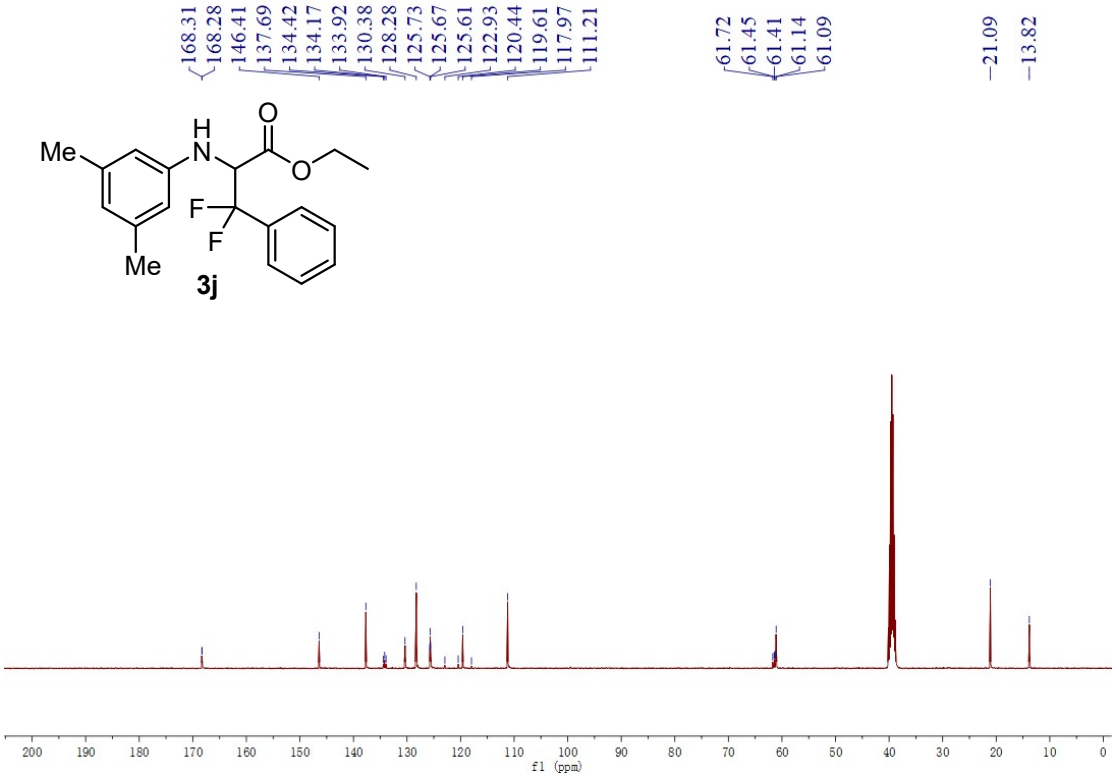
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3j:



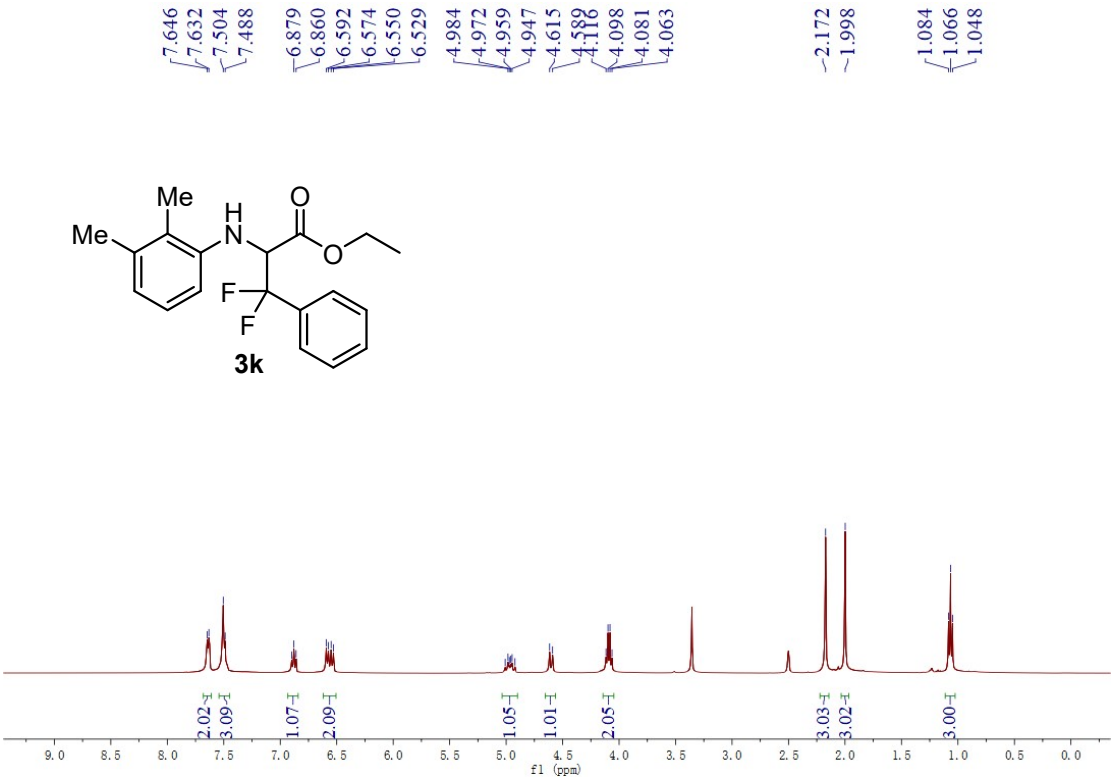
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3j:



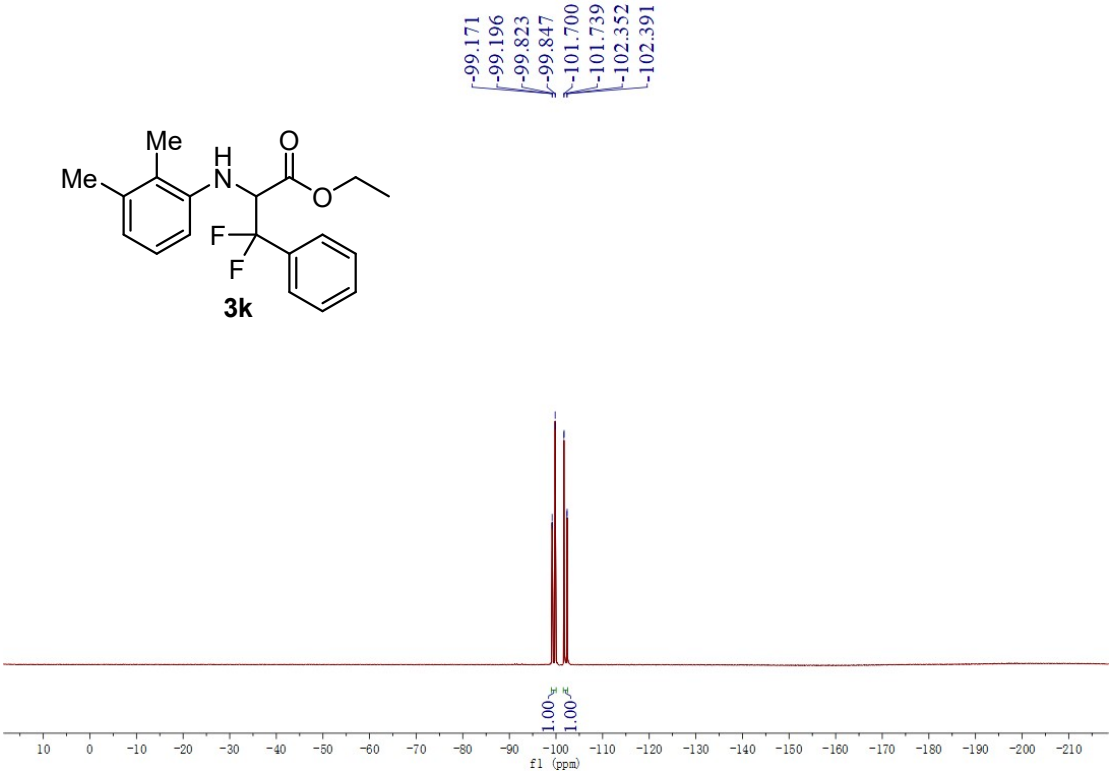
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3j:



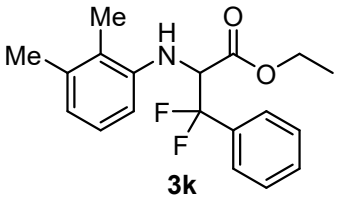
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3k:



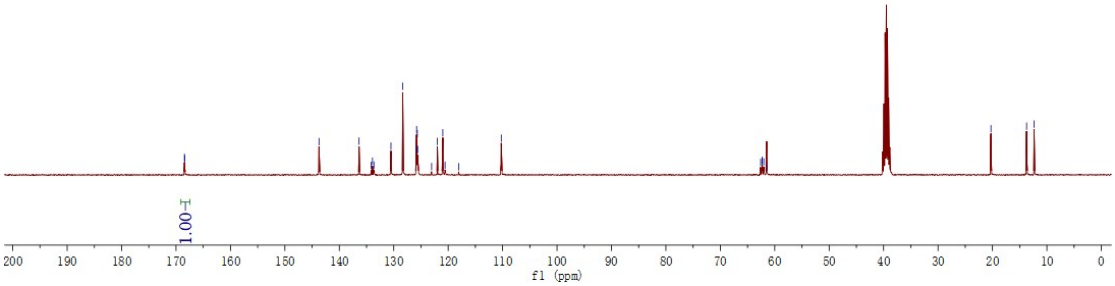
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3e:



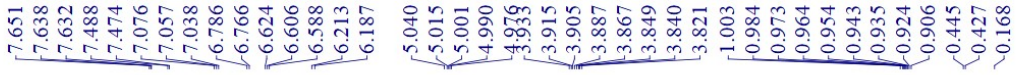
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3k:

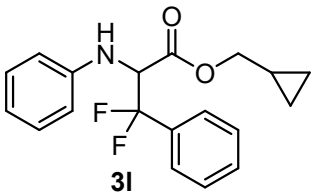


3k

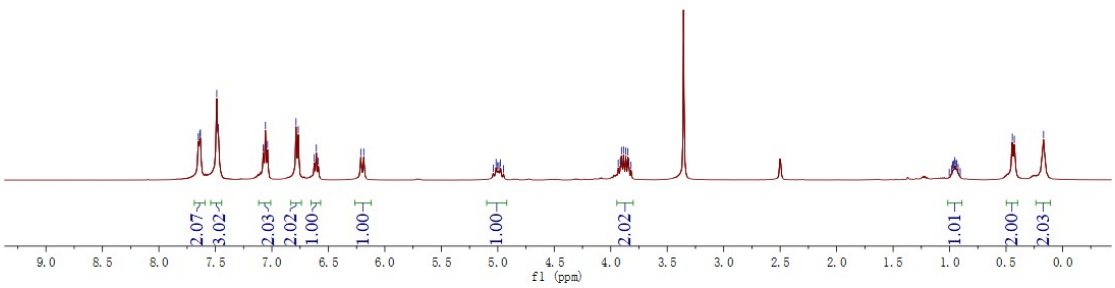


^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3l:

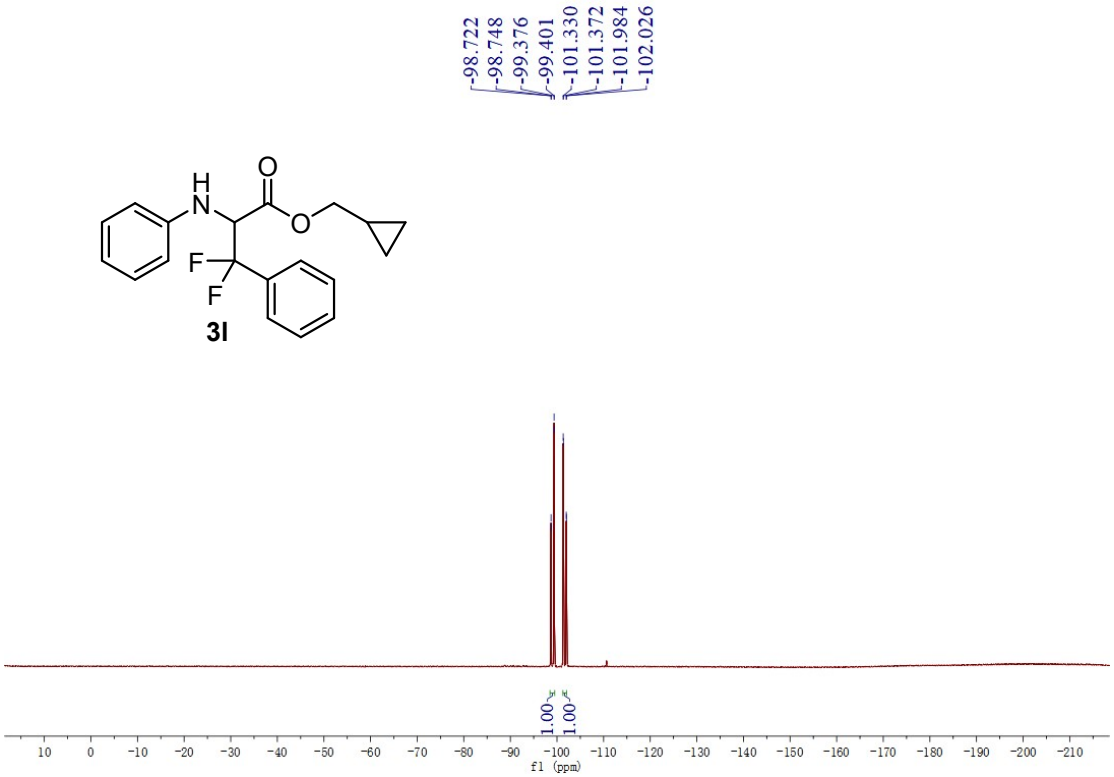




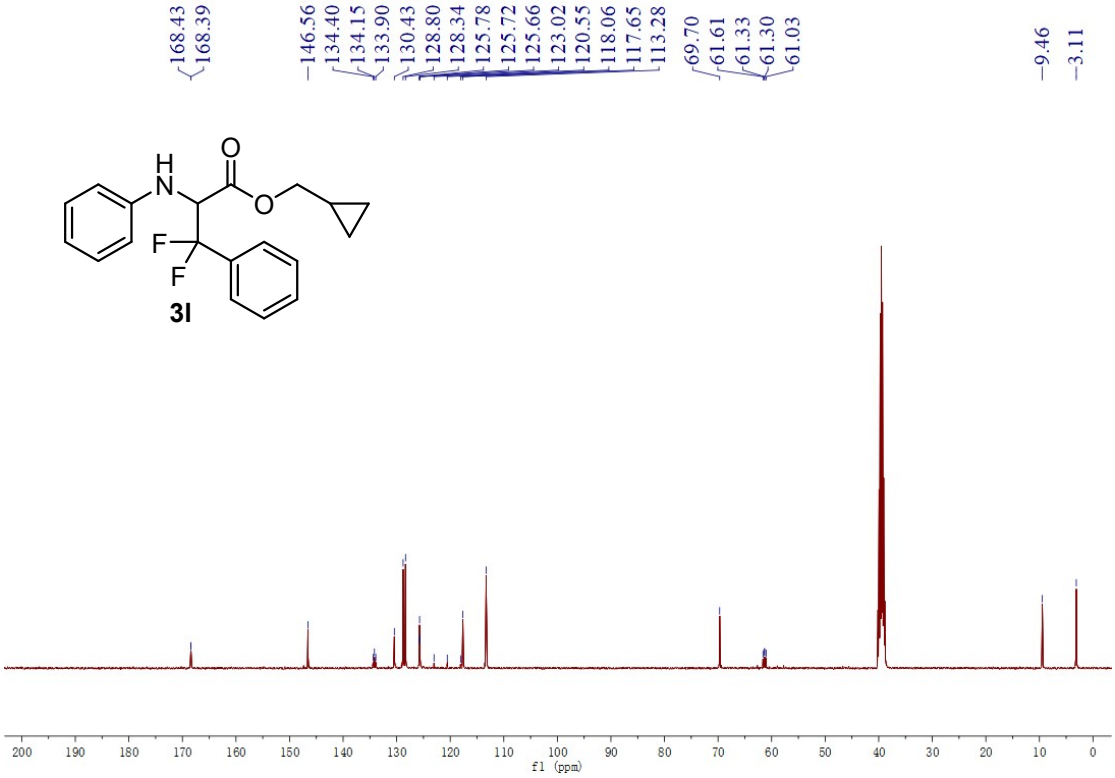
3l



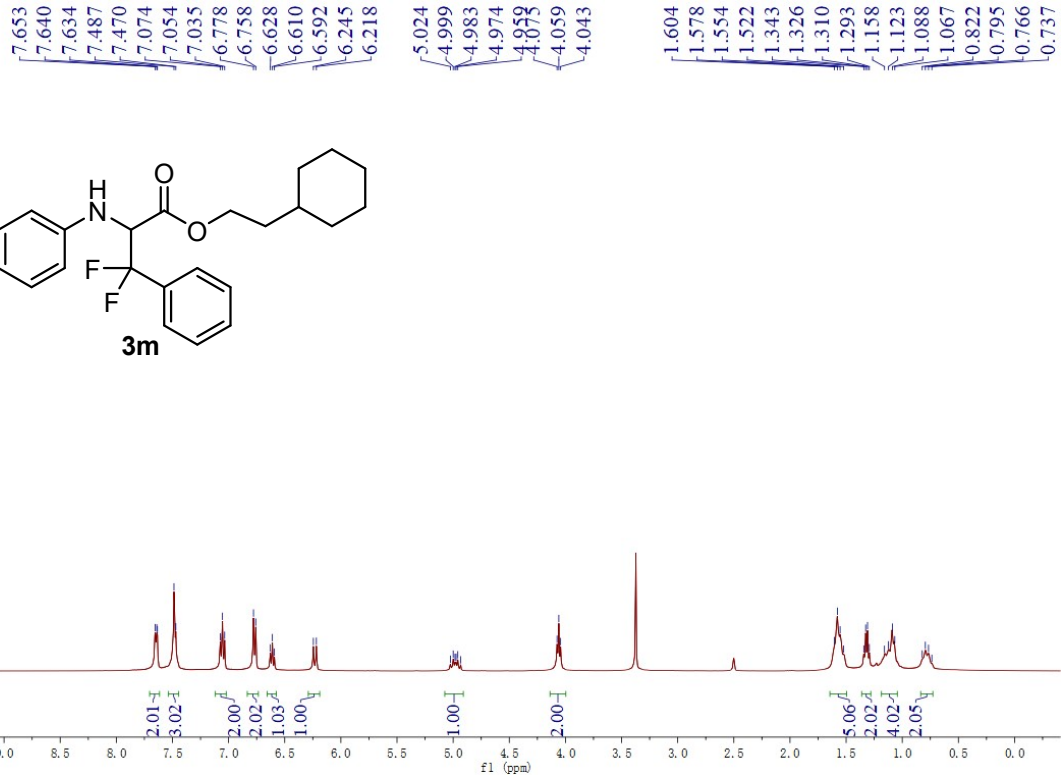
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3l:



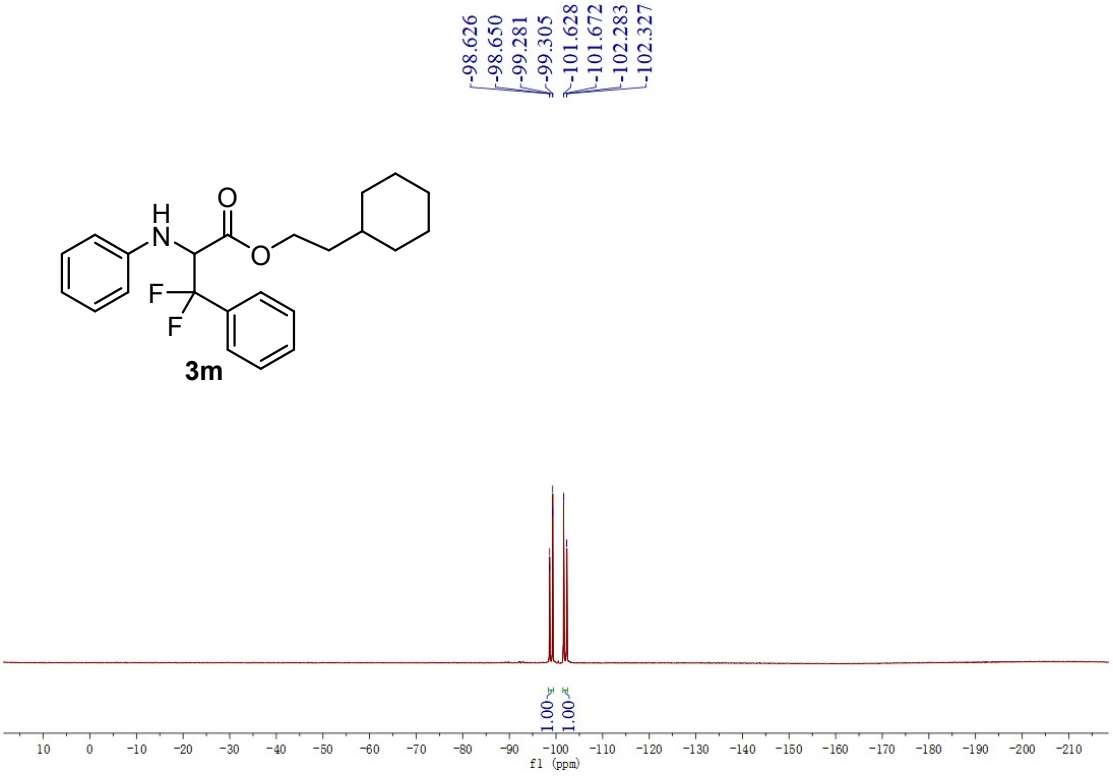
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3l:



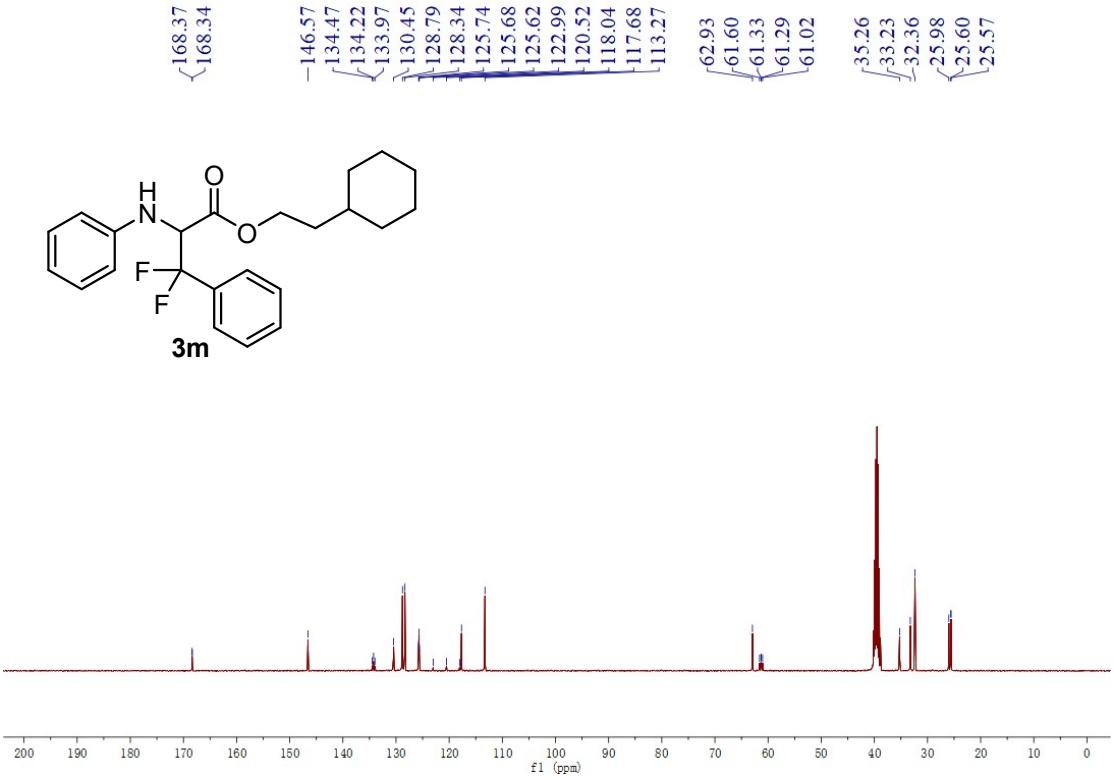
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3m:



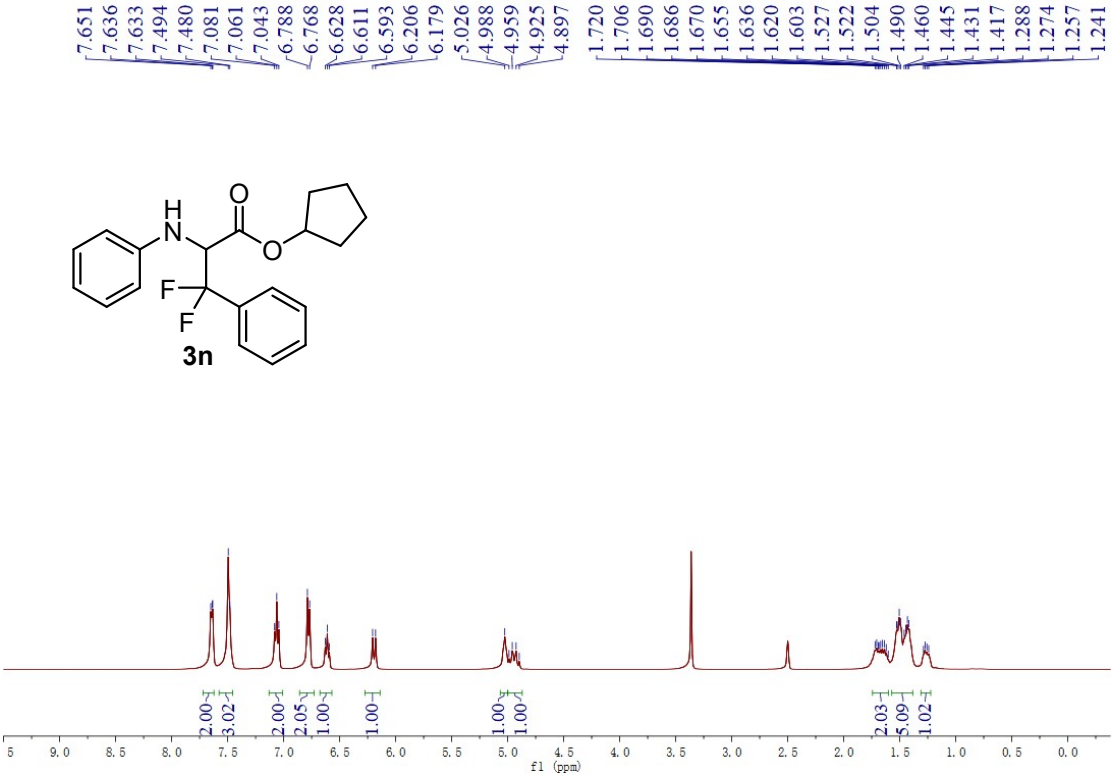
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3m:



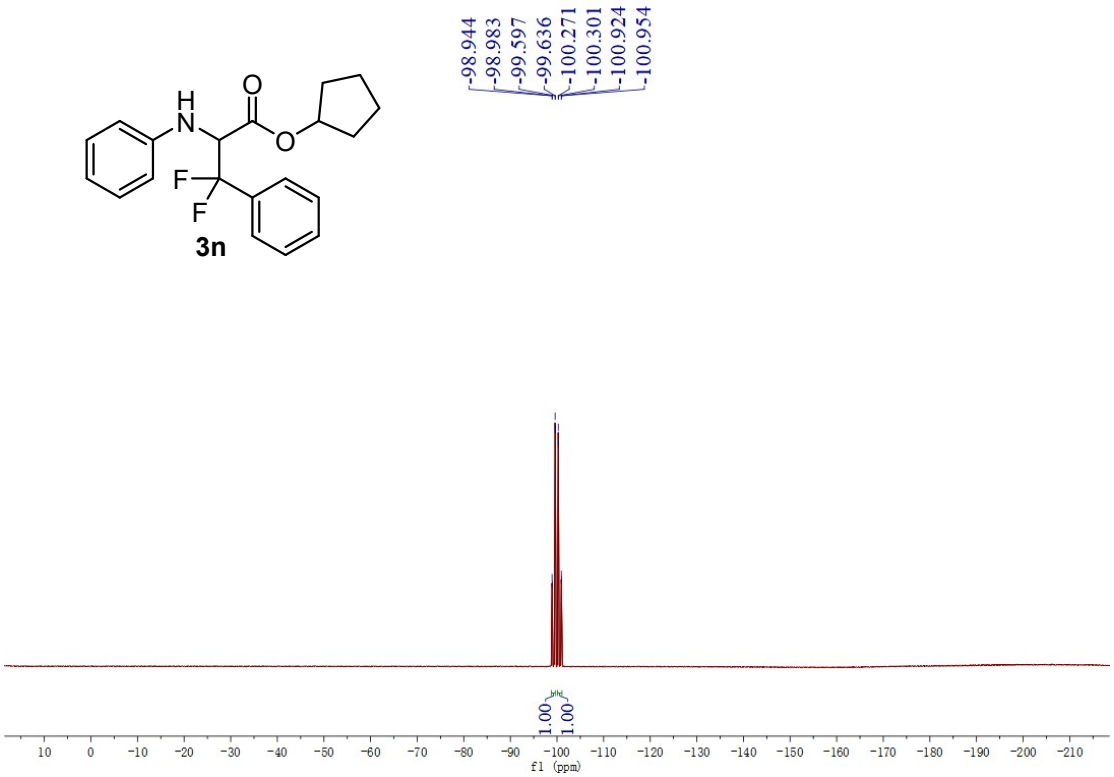
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3m:



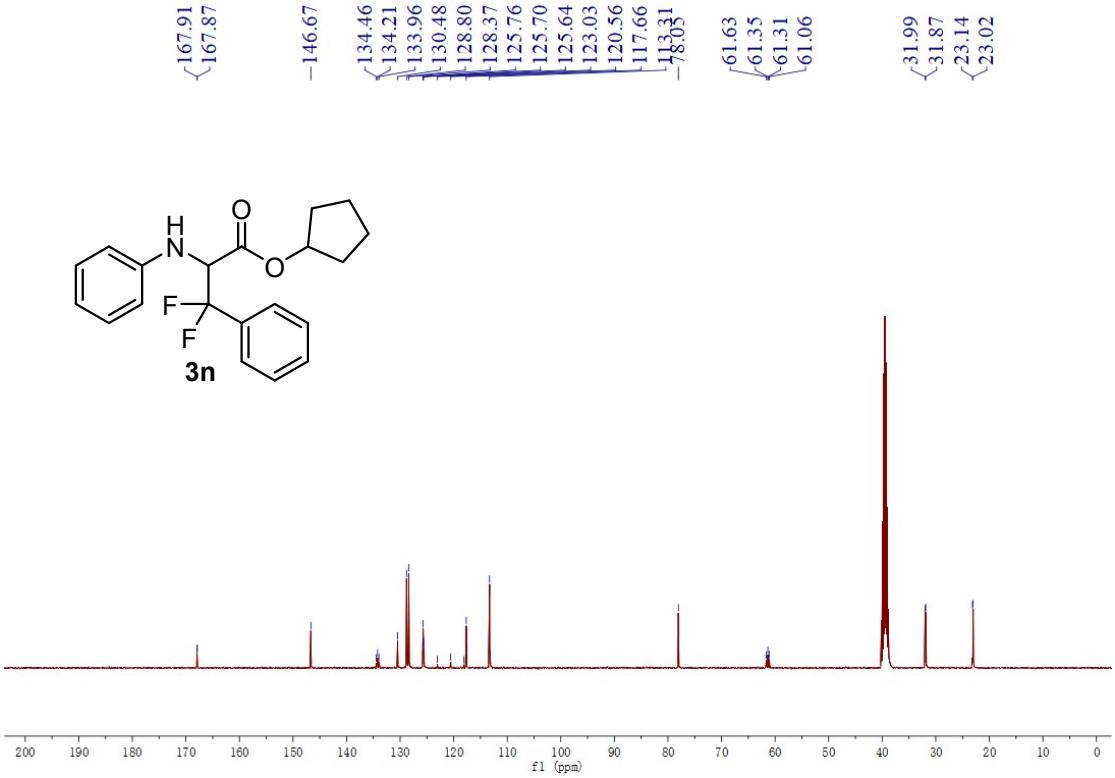
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3n:



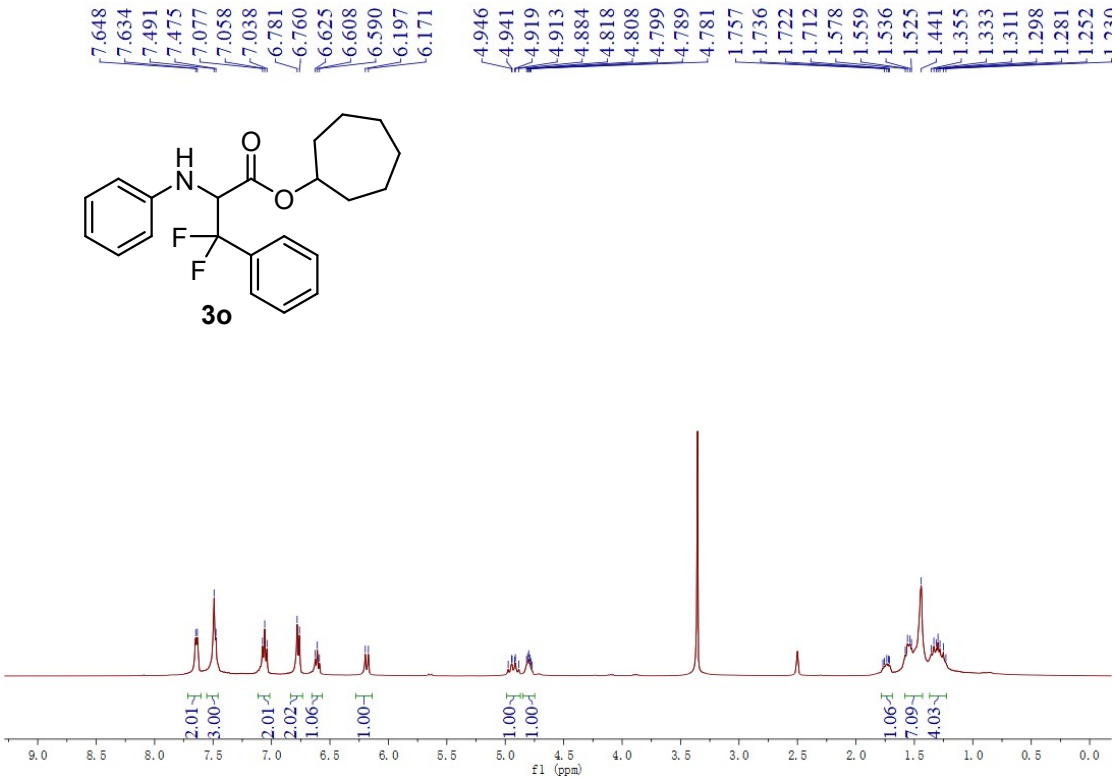
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3n:



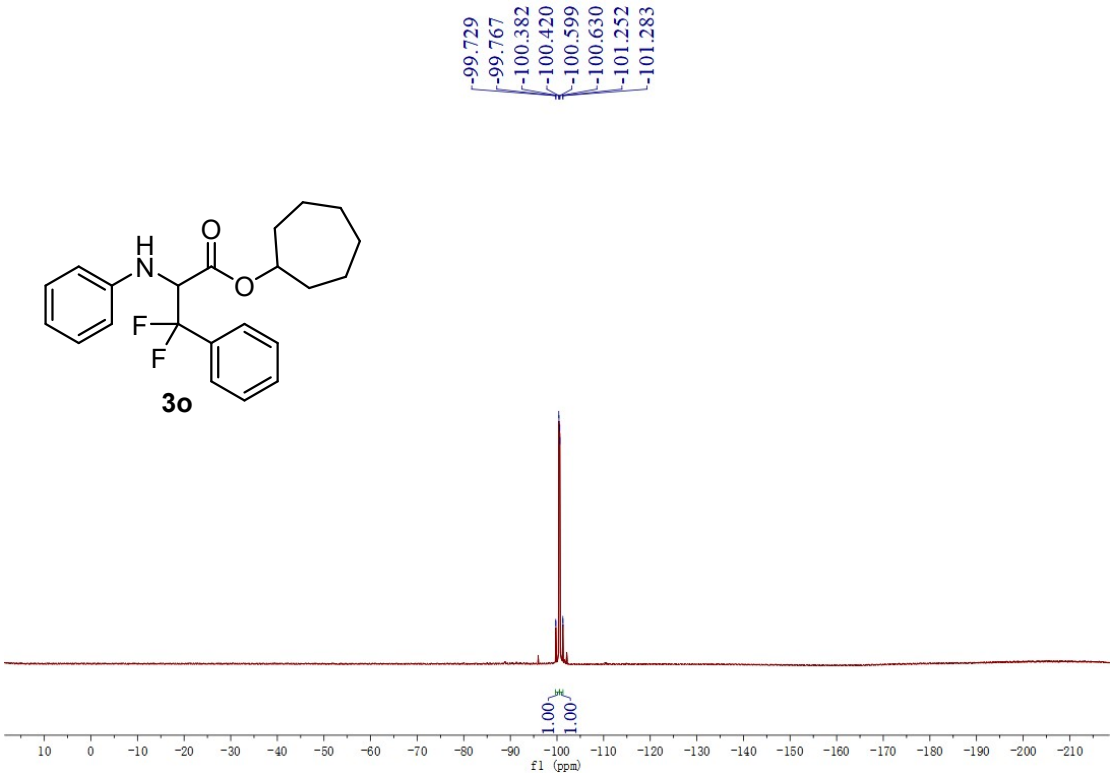
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3n:



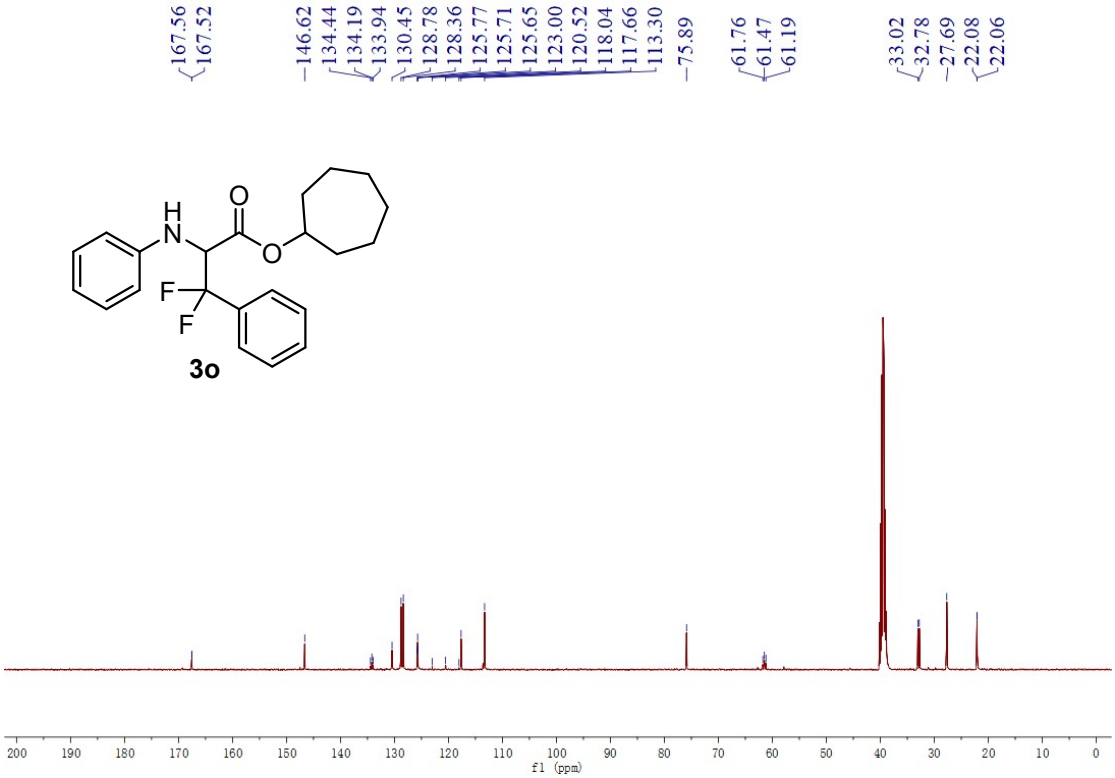
^{1}H NMR (DMSO-d$_6$, 400 MHz) spectrum of compound 3o:



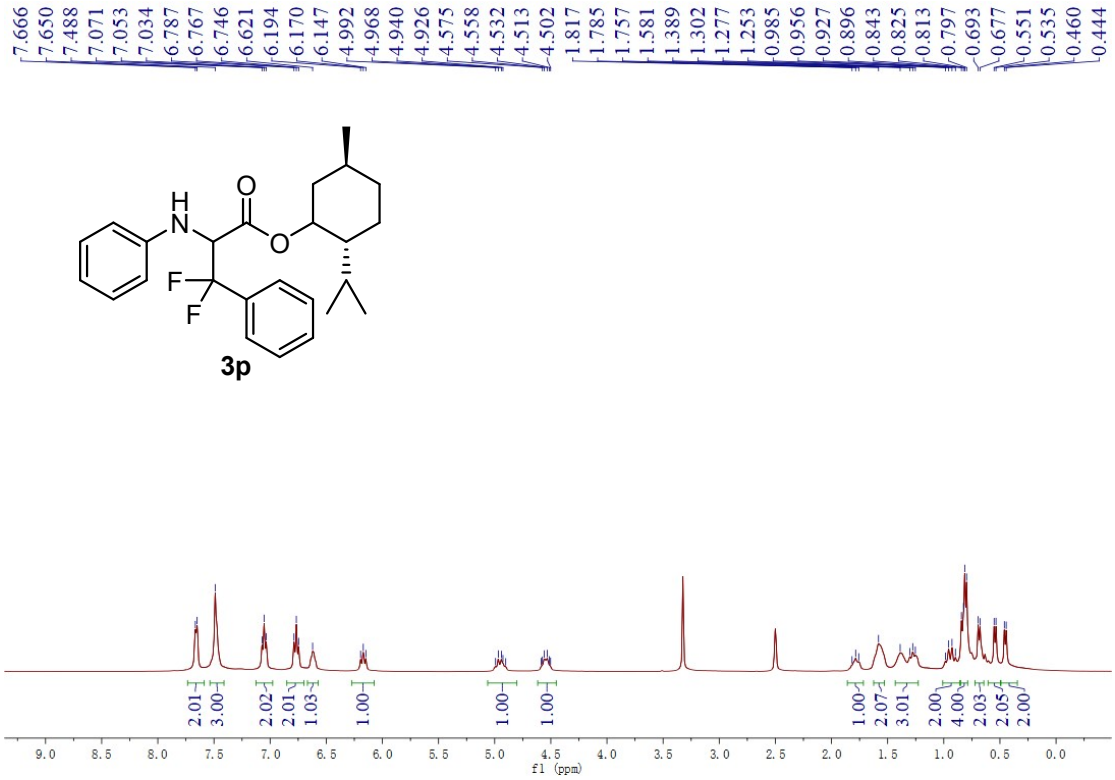
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 3o:



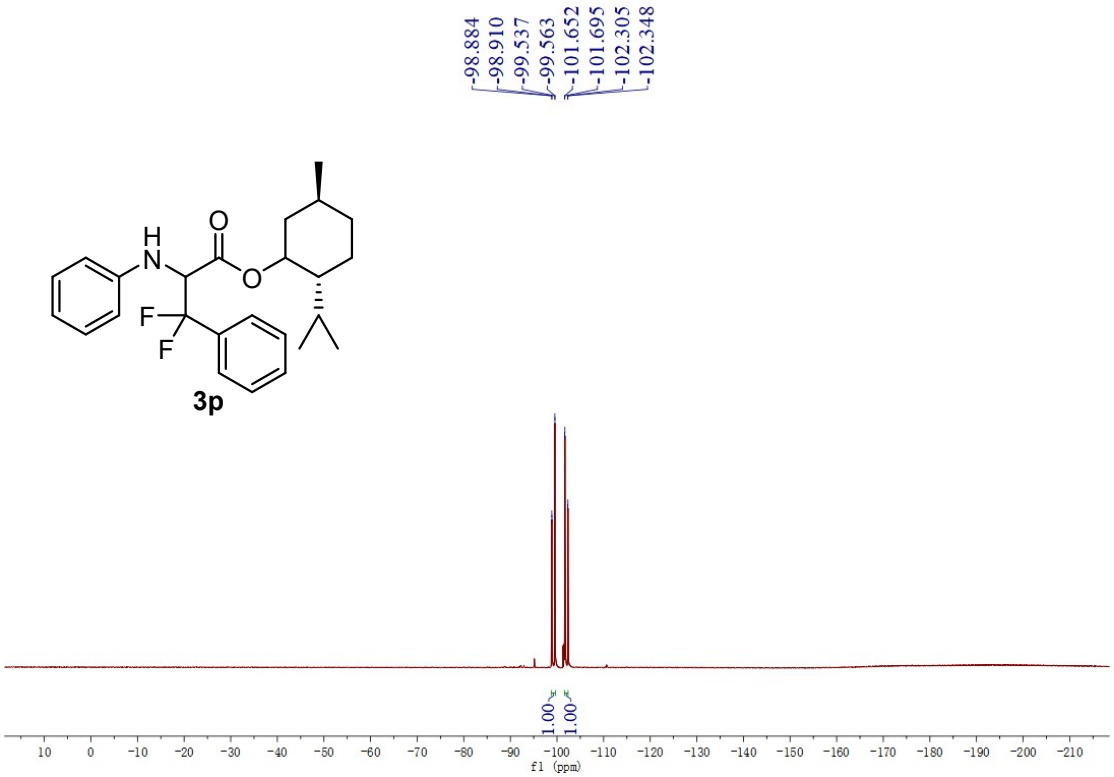
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3o:



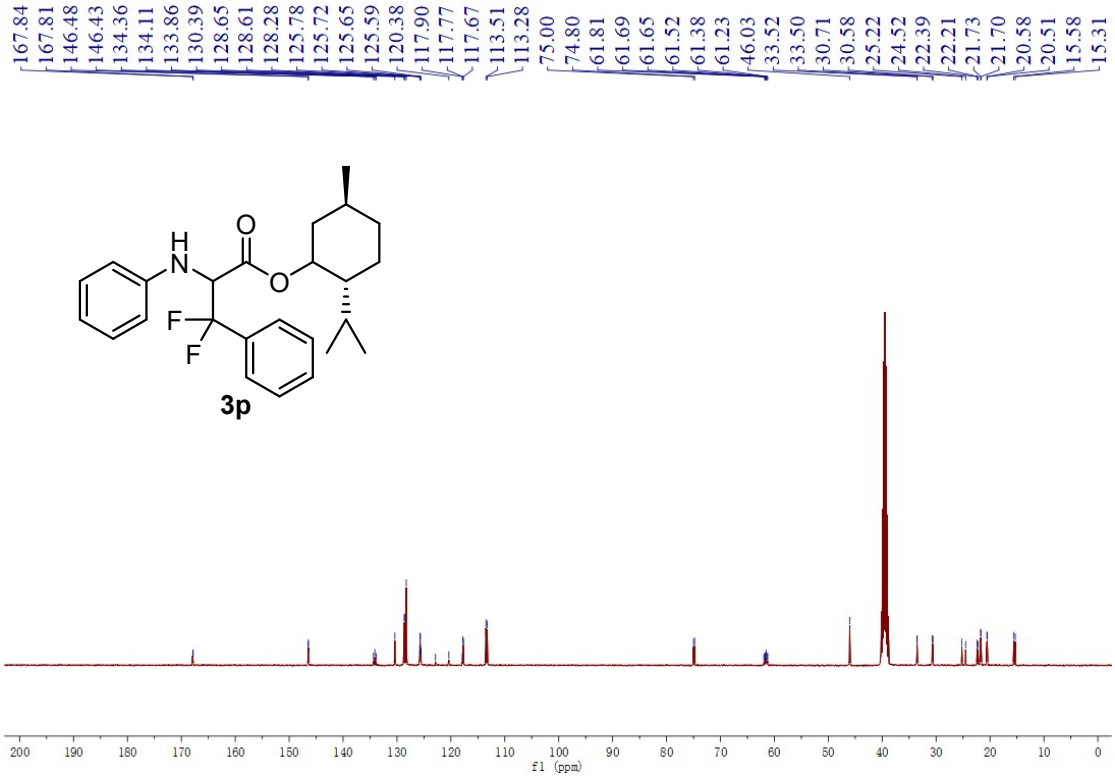
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3p:



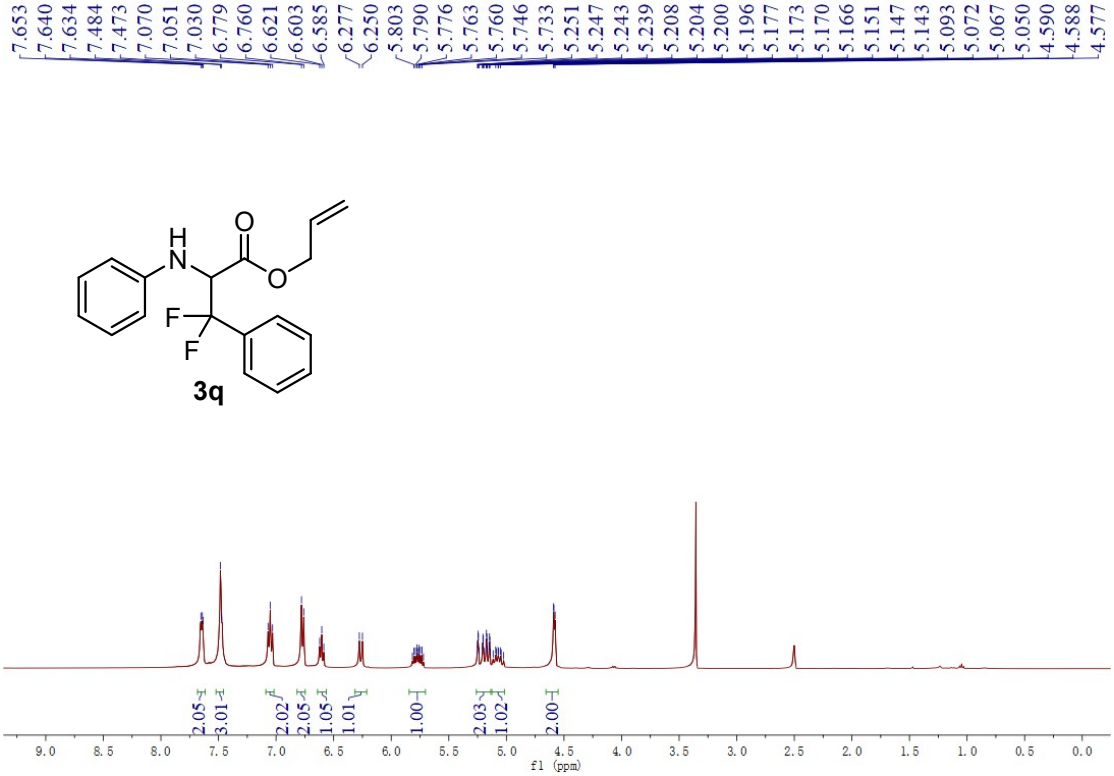
^{1}H NMR (DMSO-d_6, 376 MHz) spectrum of compound 3p:



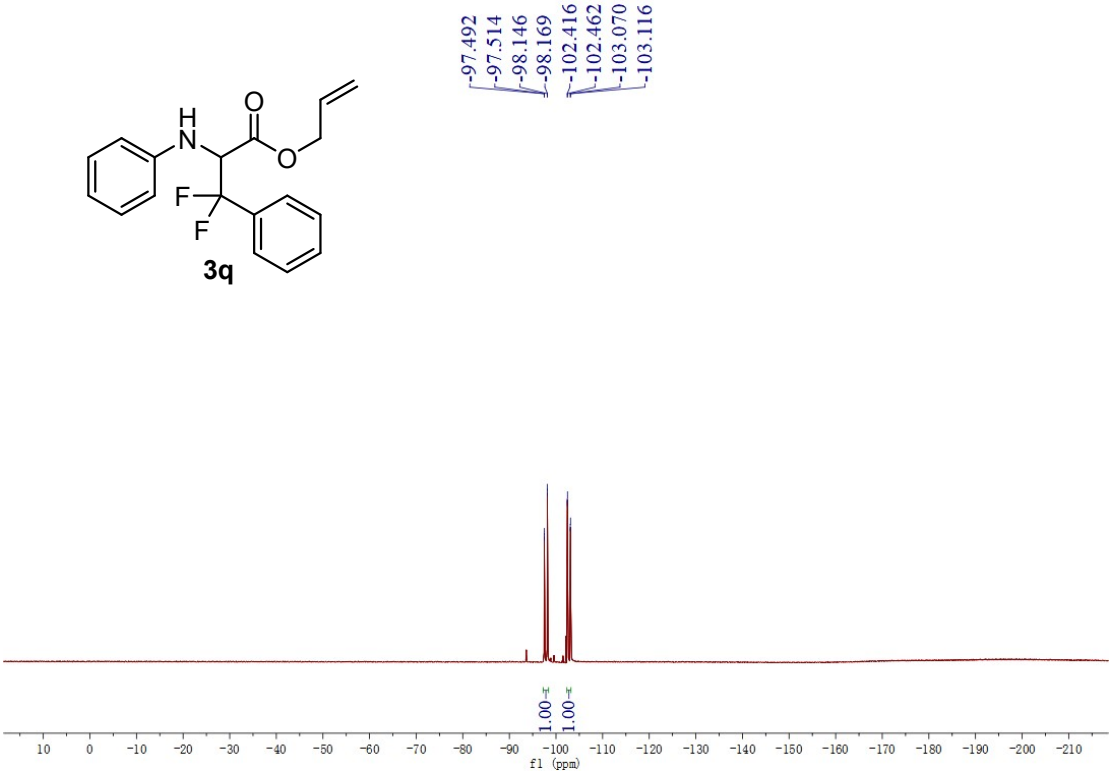
^{1}H NMR (DMSO-d_6, 100 MHz) spectrum of compound 3p:



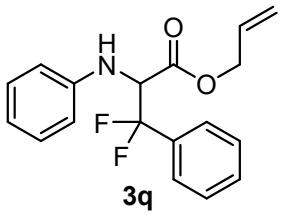
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3q:



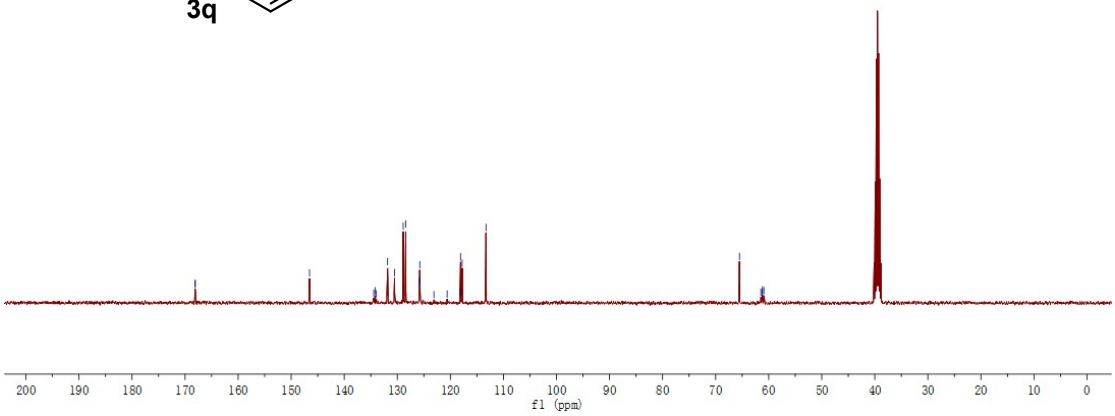
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3q:



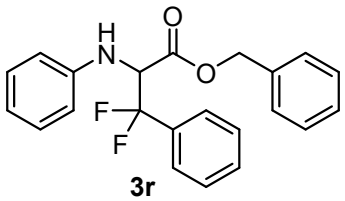
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3q:



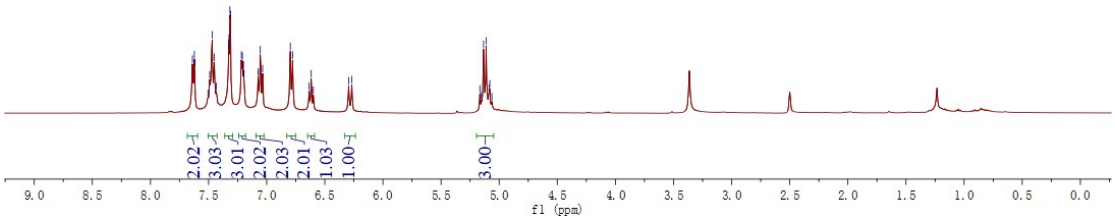
3q



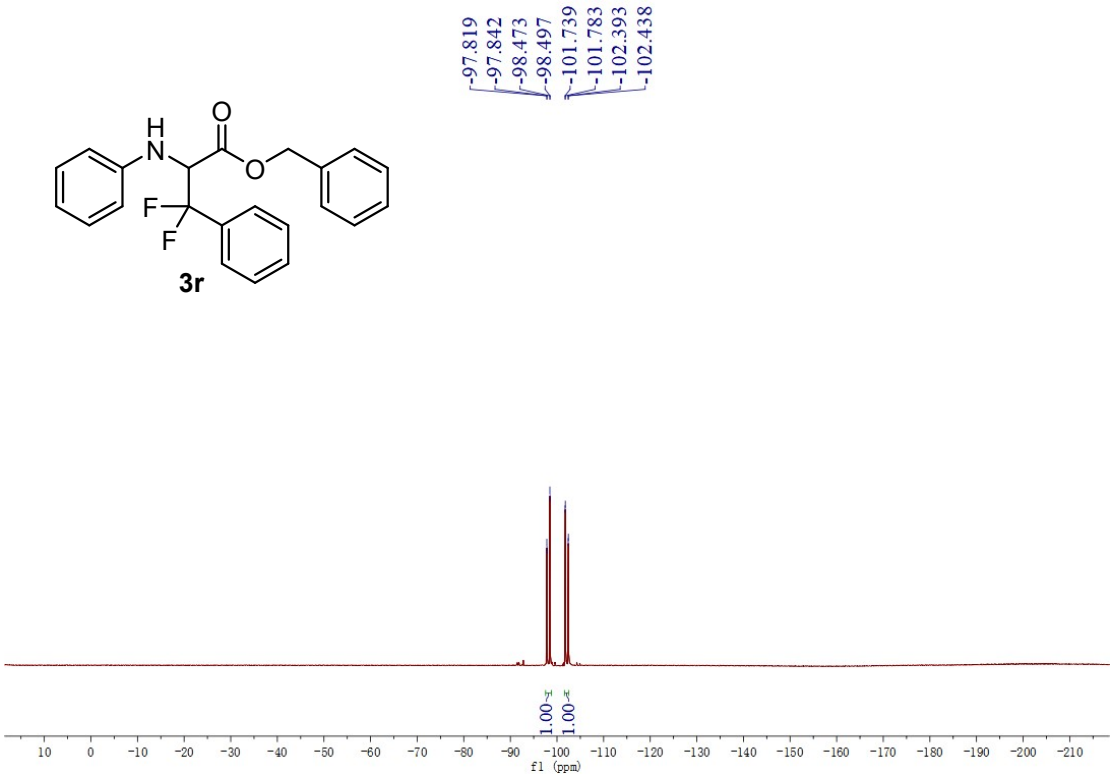
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3r:



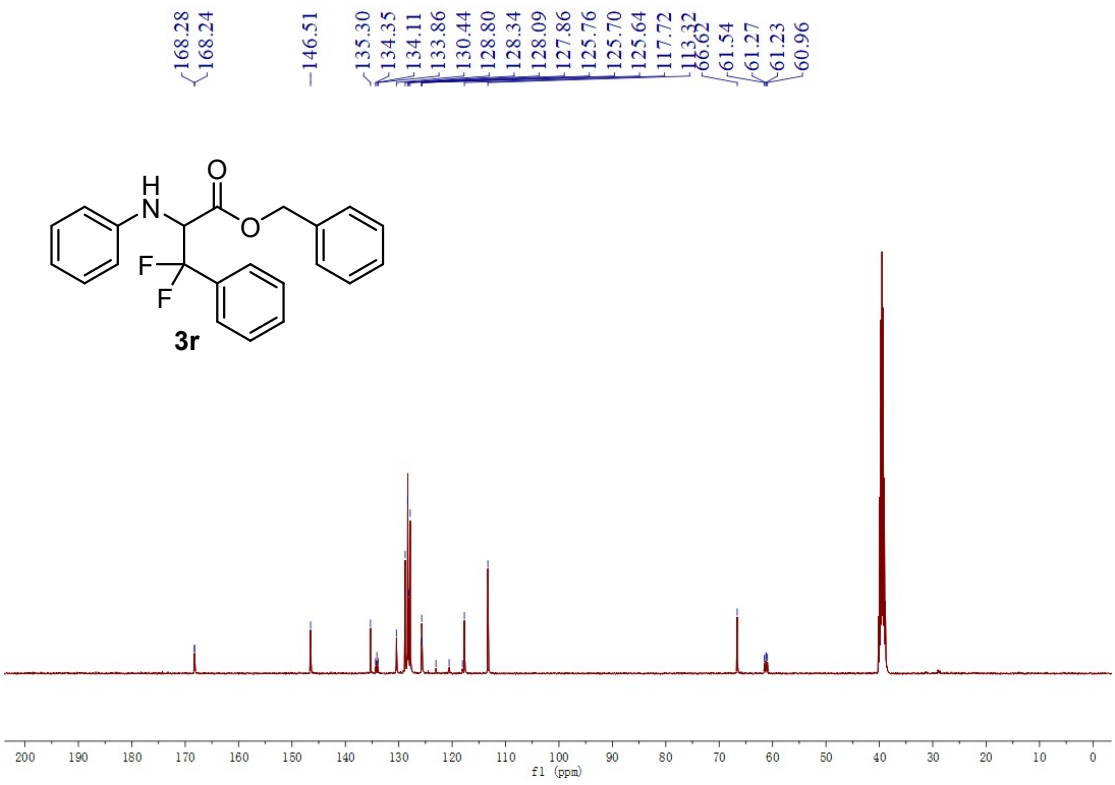
3r



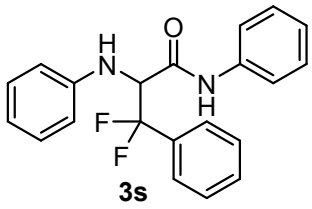
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3r:

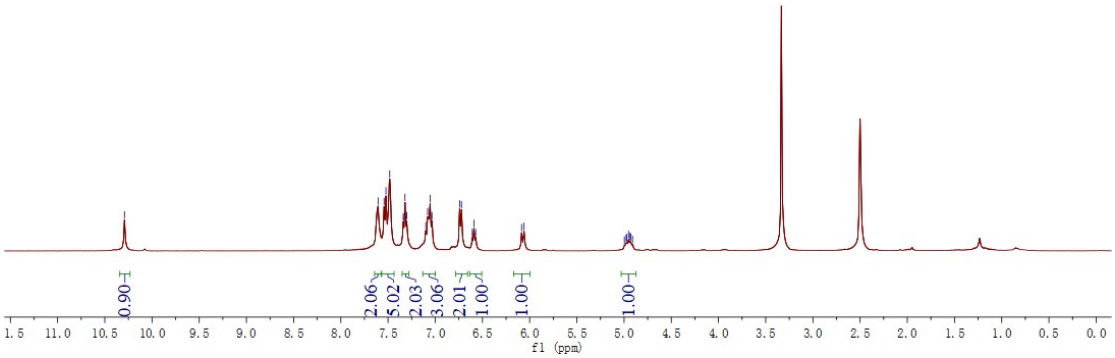


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3r:

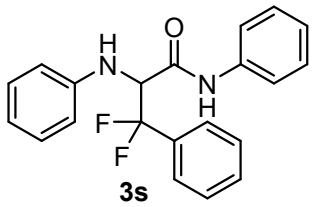


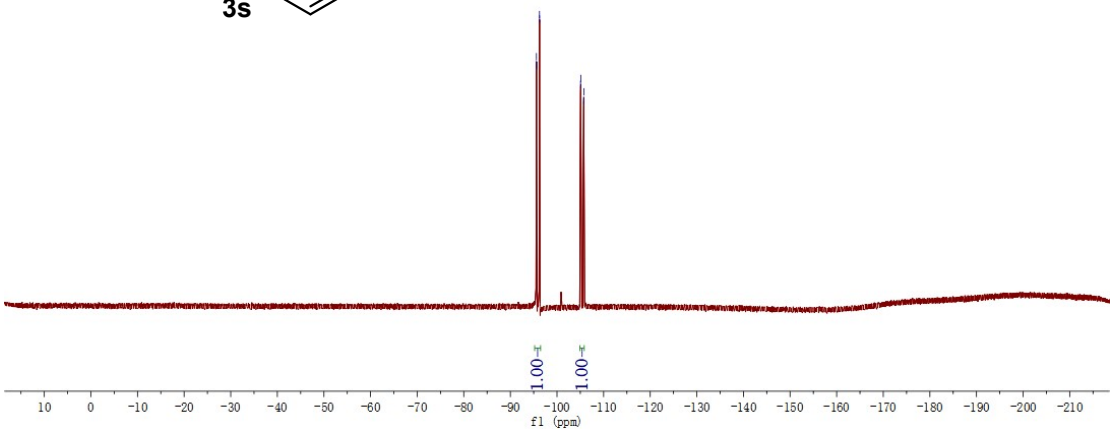
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3s:



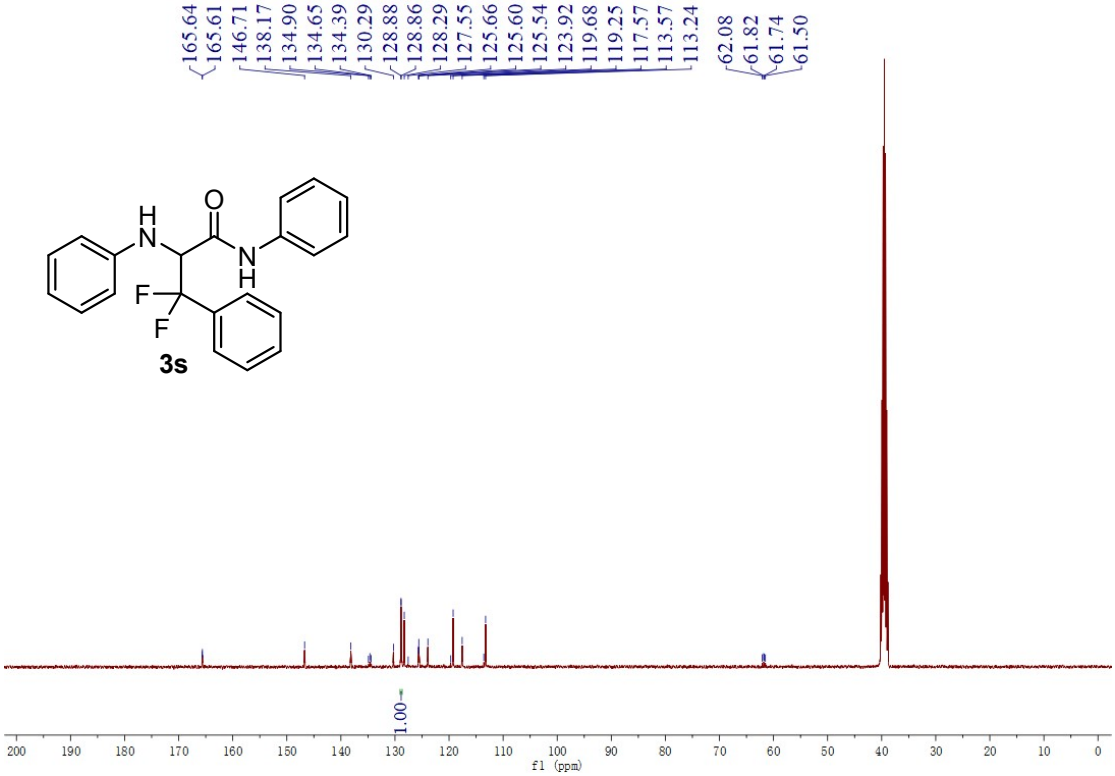


^{19}H NMR (DMSO-d_6, 376 MHz) spectrum of compound 3s:

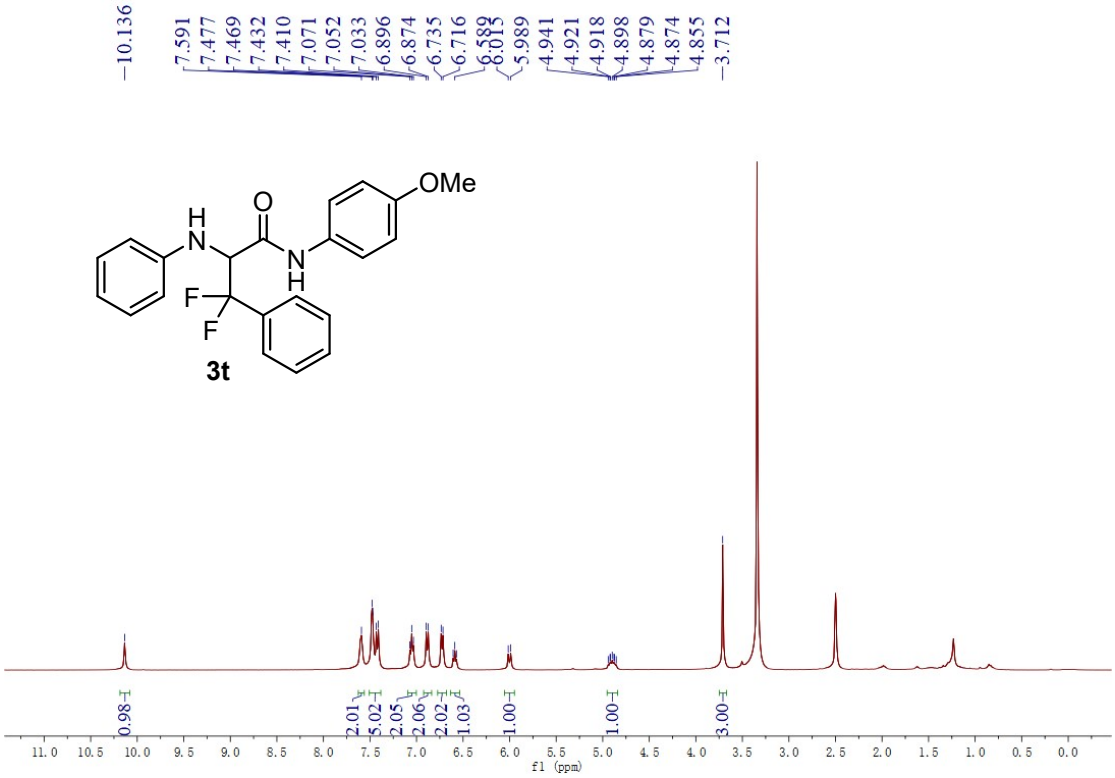




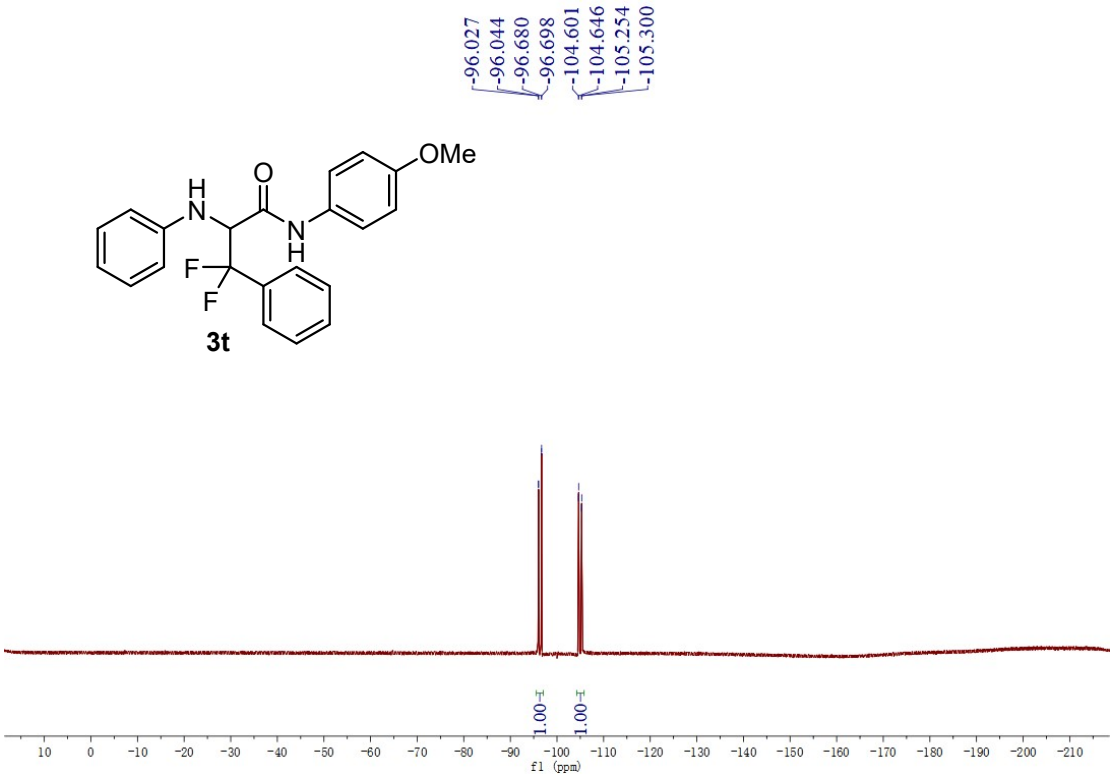
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3s:



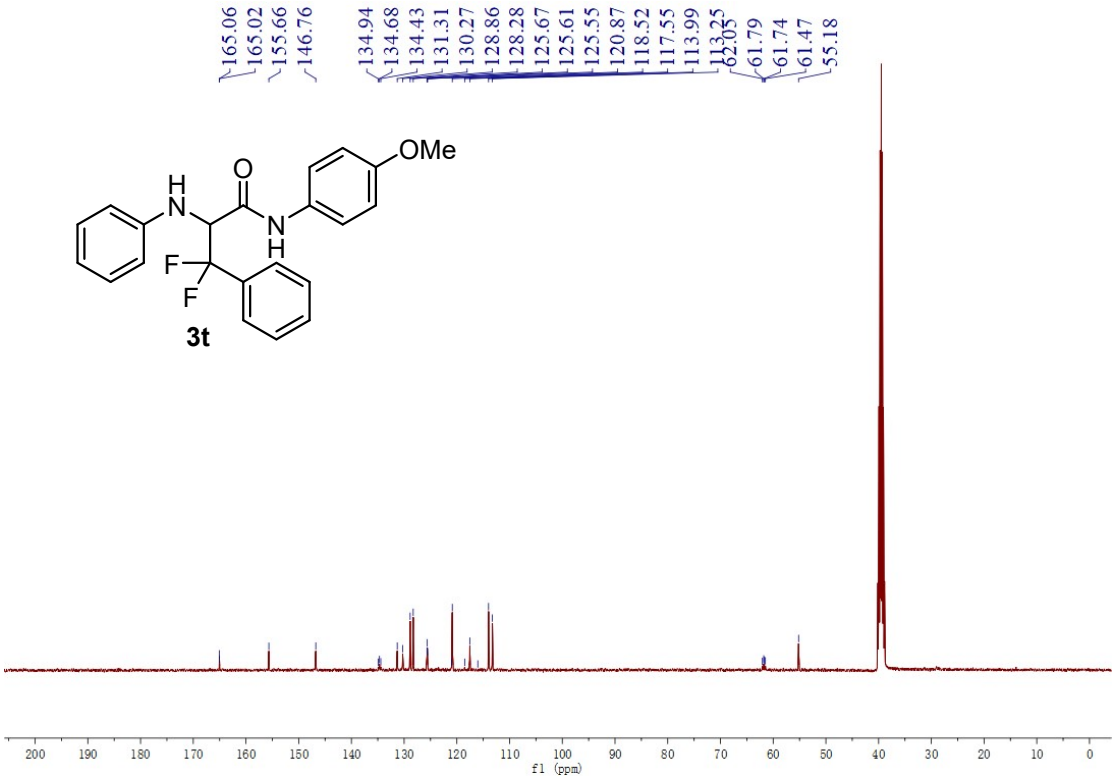
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3t:



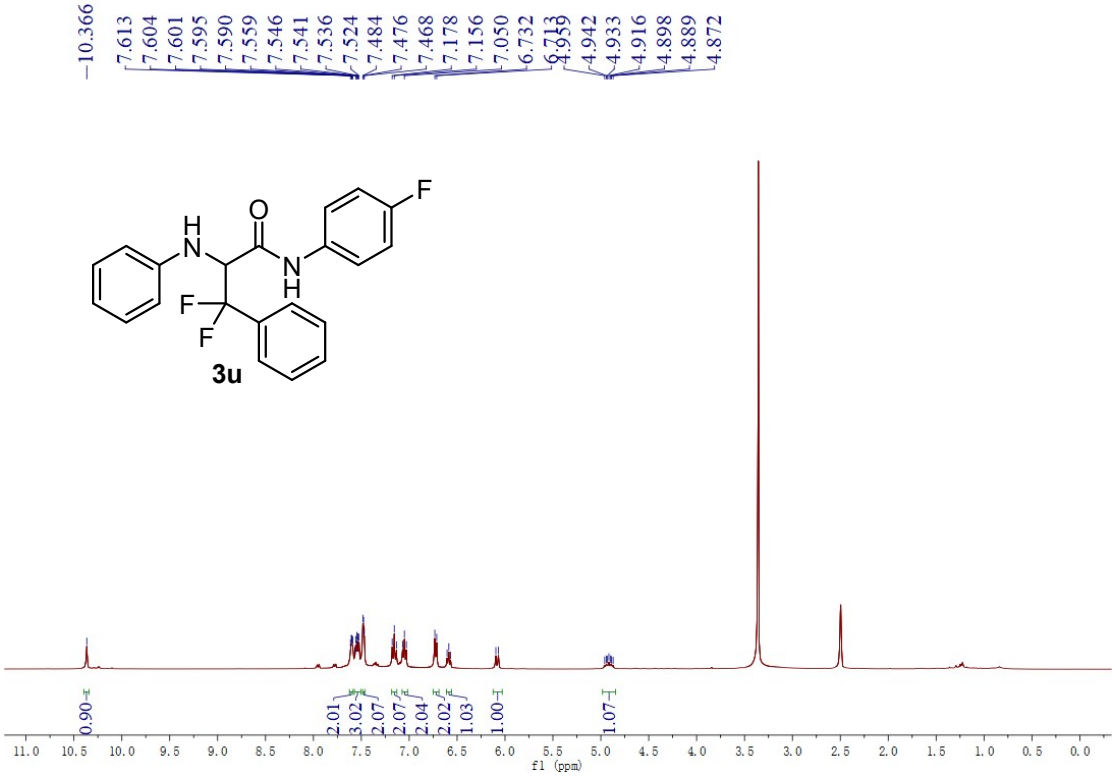
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3t:



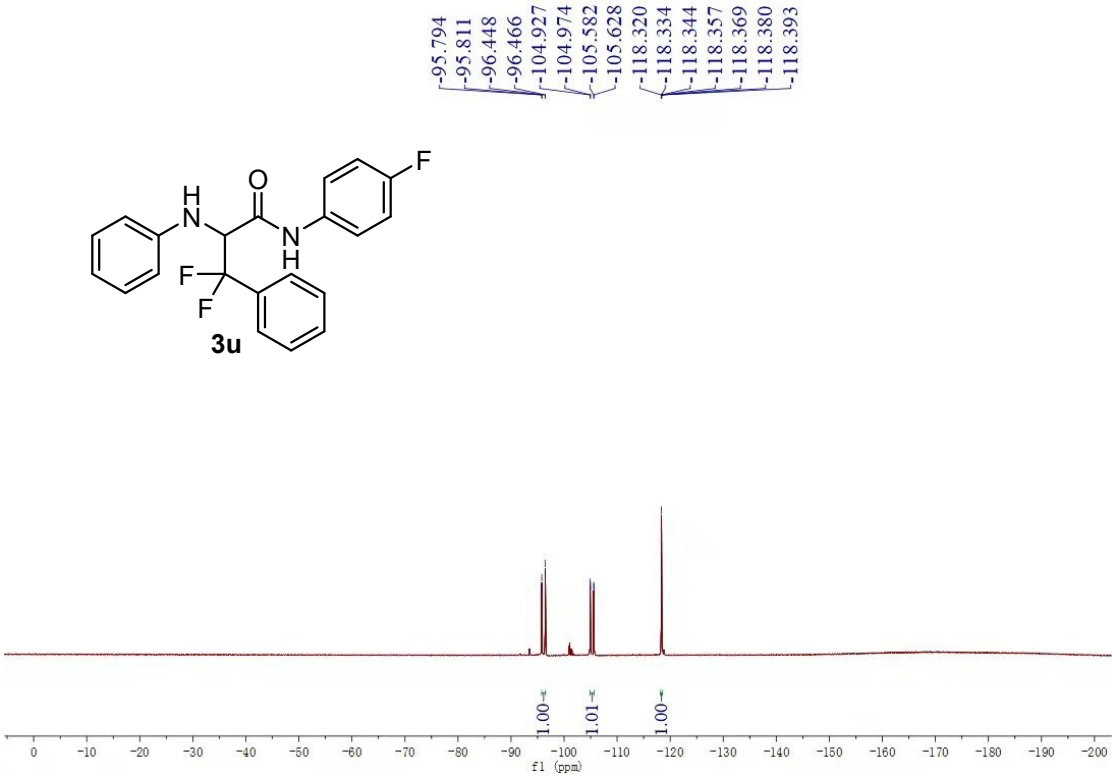
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3t:



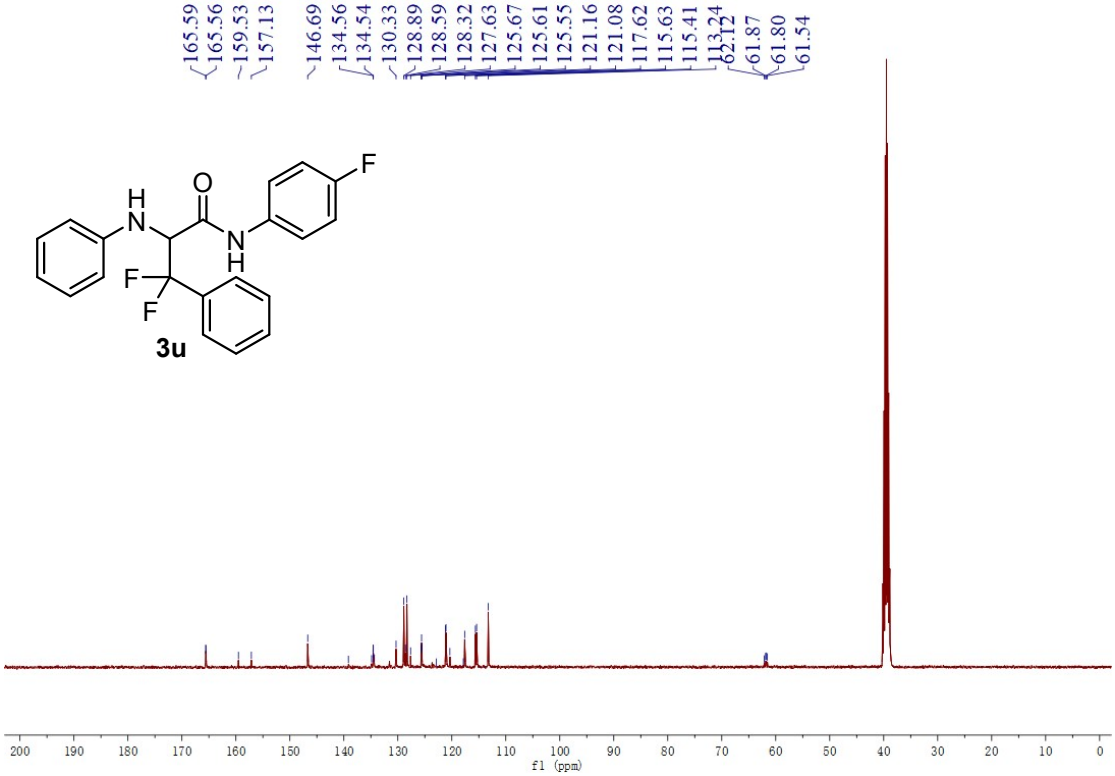
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3u:



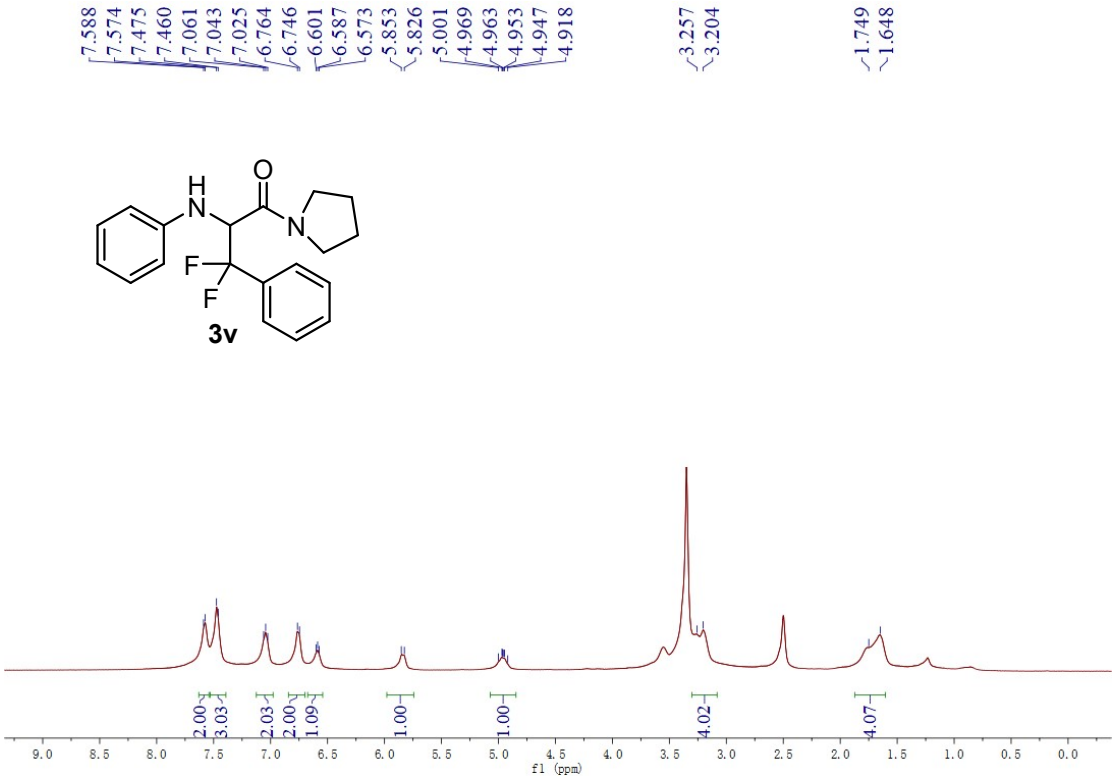
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3u:



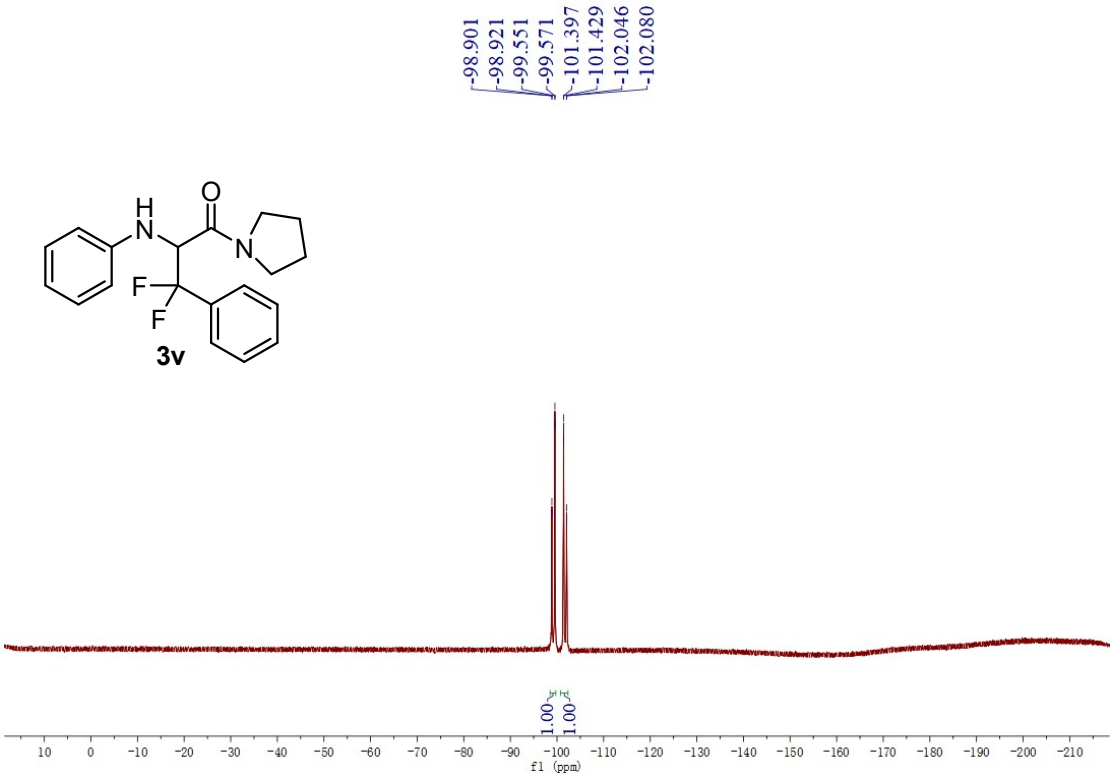
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3u:



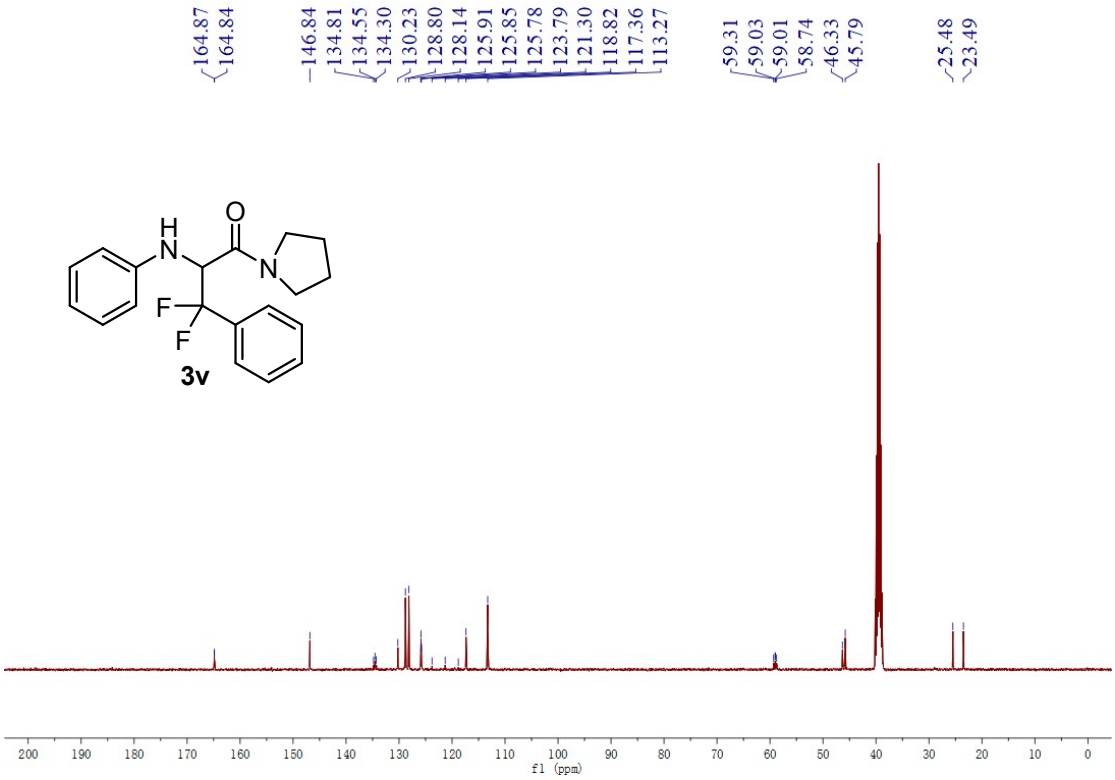
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3v:



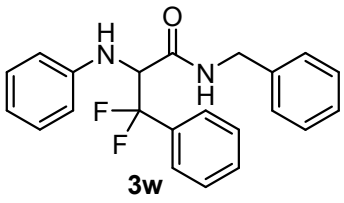
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3v:

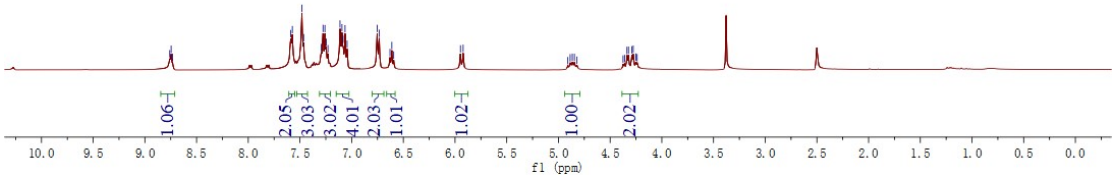


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3v:

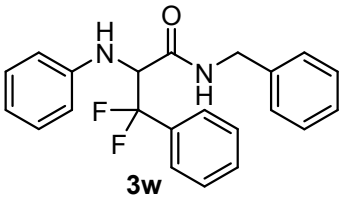


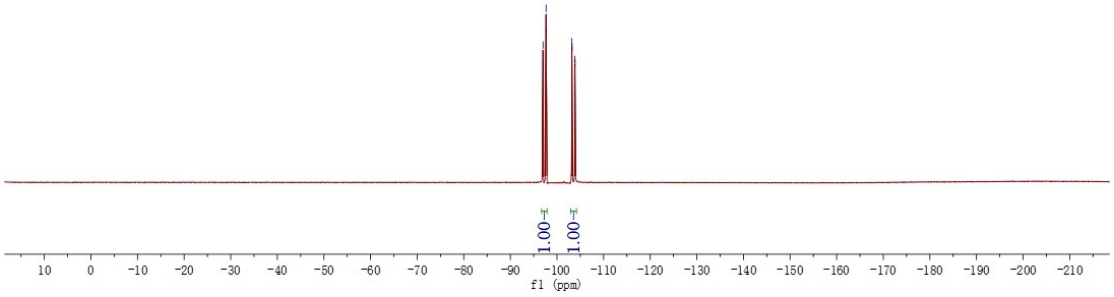
^{1}H NMR (DMSO-d$_6$, 400 MHz) spectrum of compound 3w:



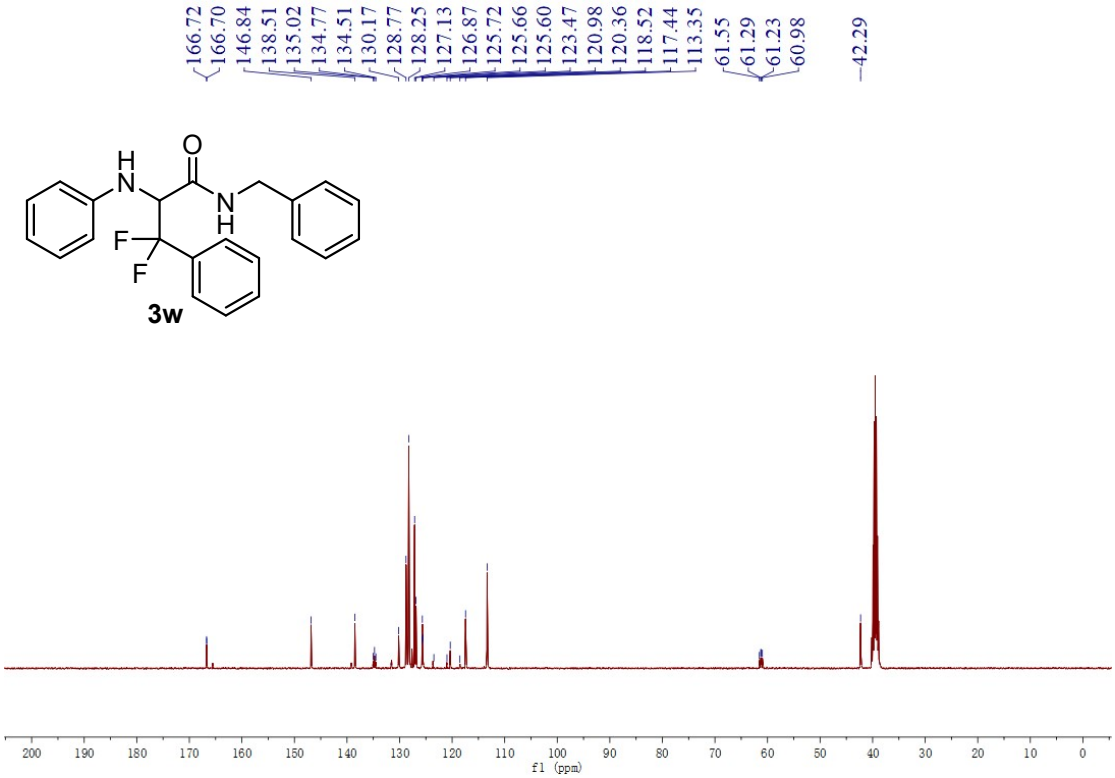


^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 3w:

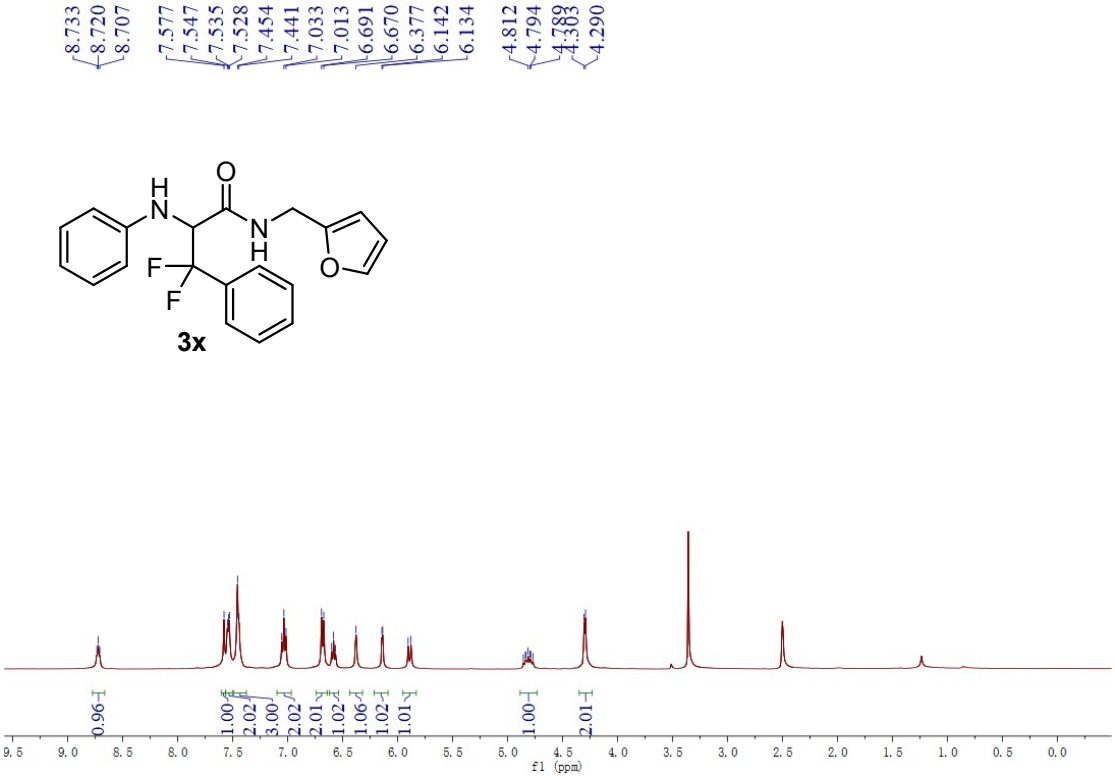




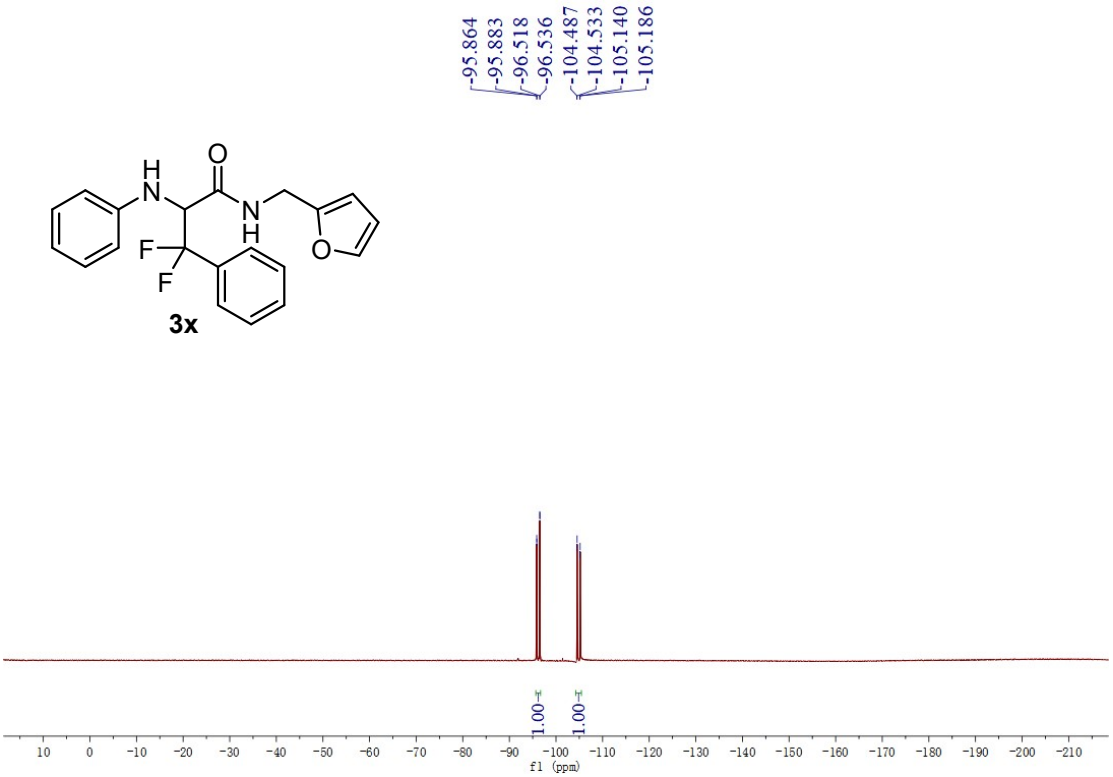
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3w:



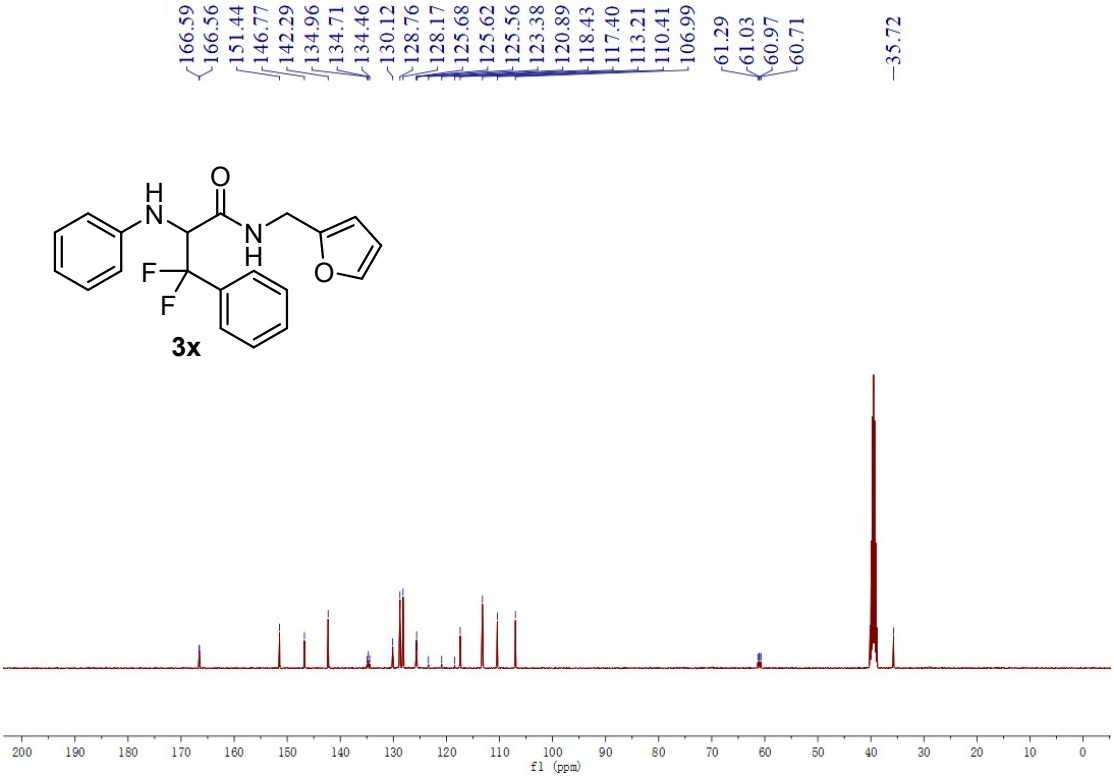
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3x:



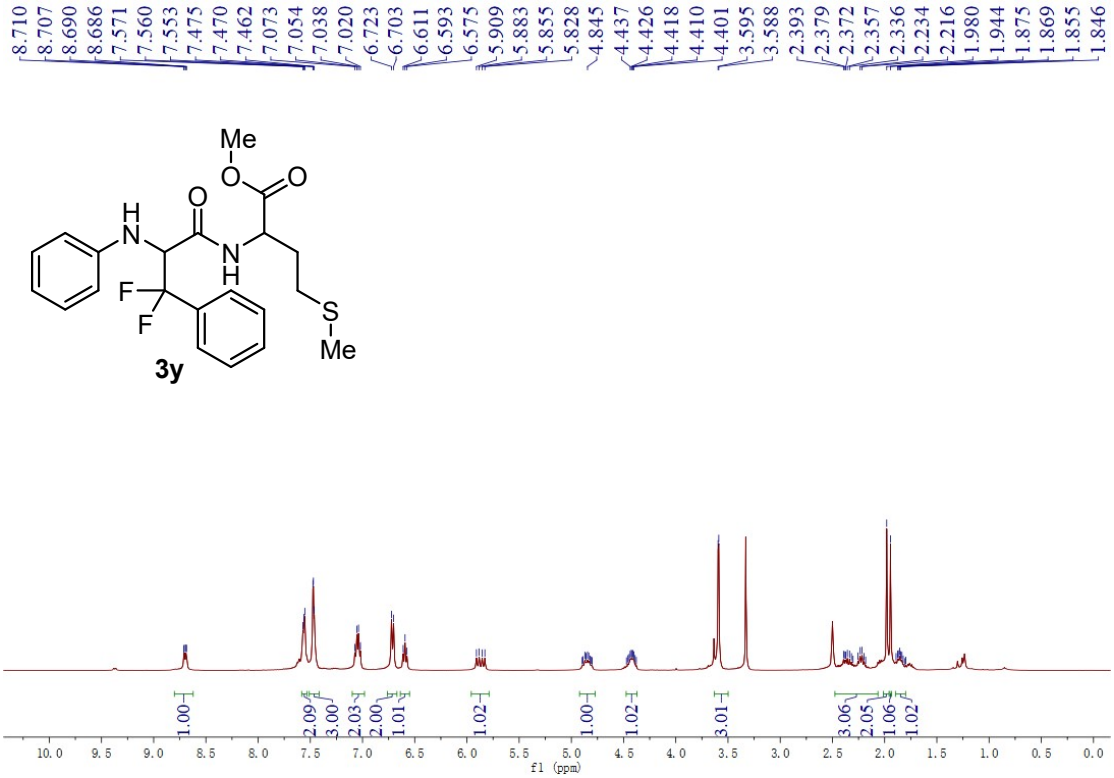
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 3x:



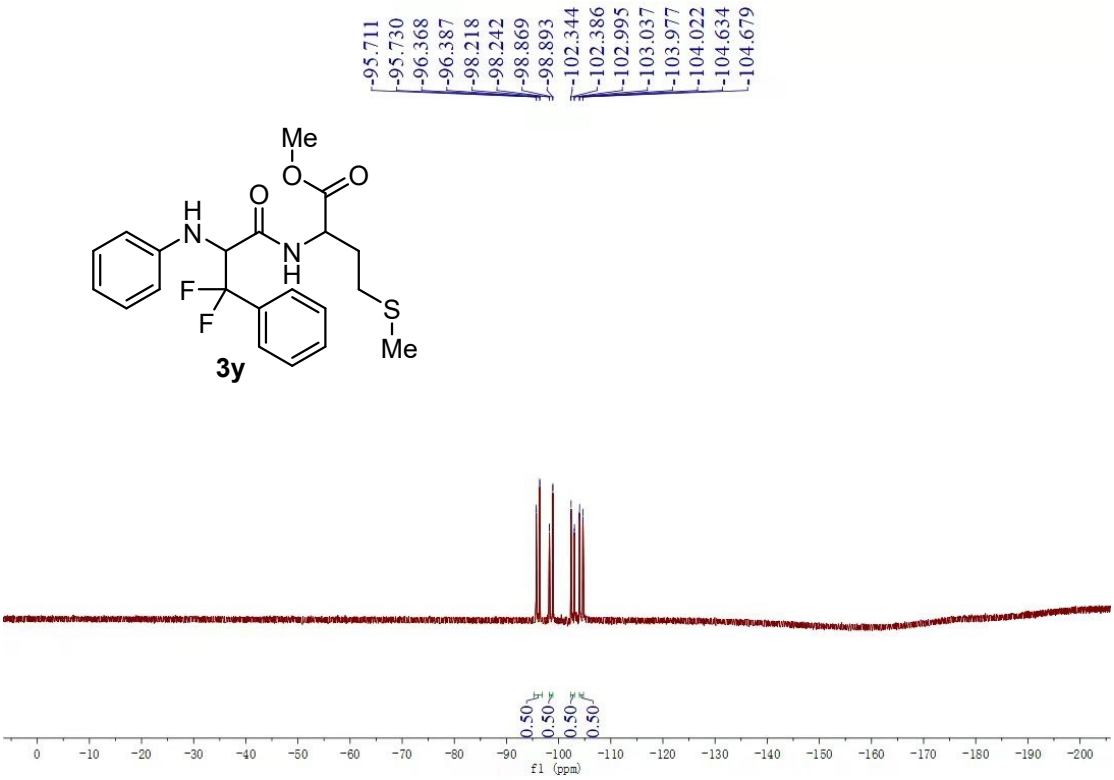
^{13}C NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 3x:



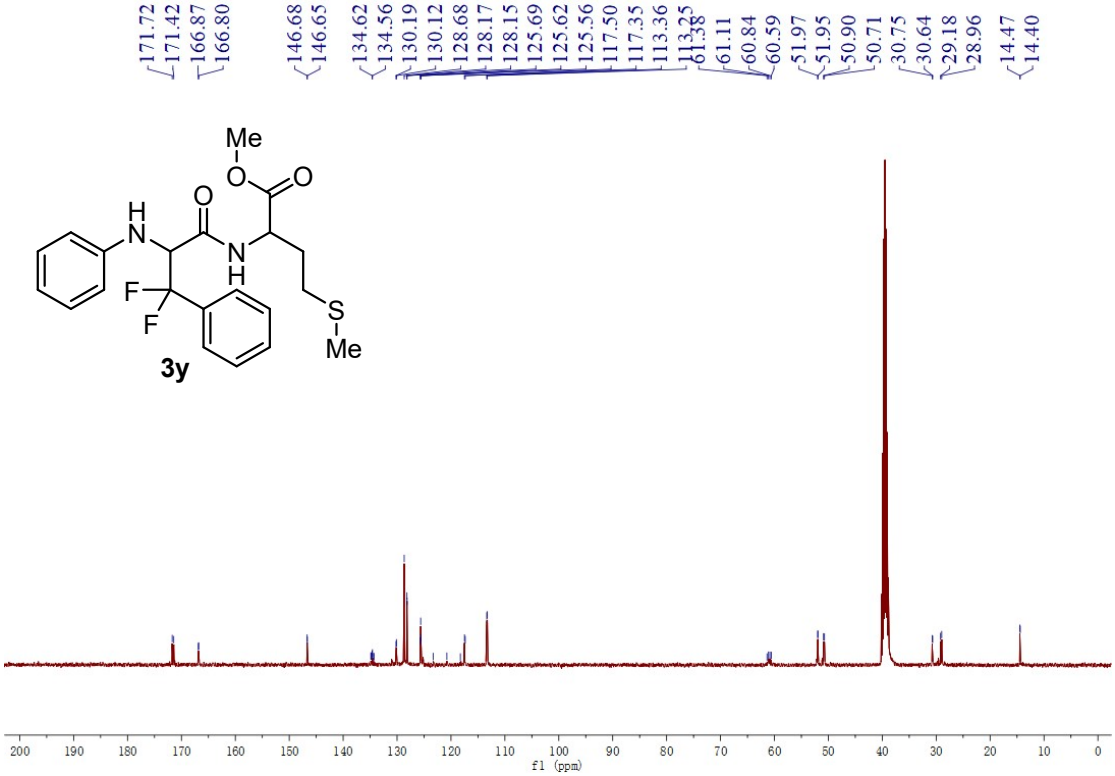
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3y:



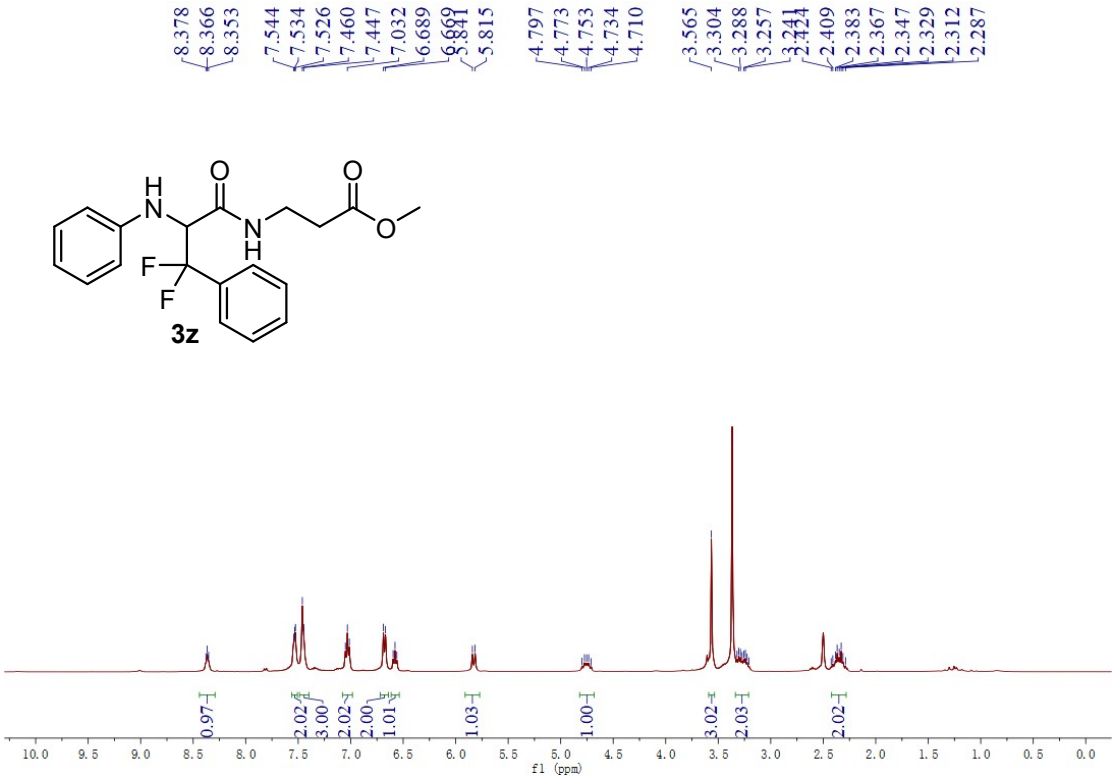
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3e:



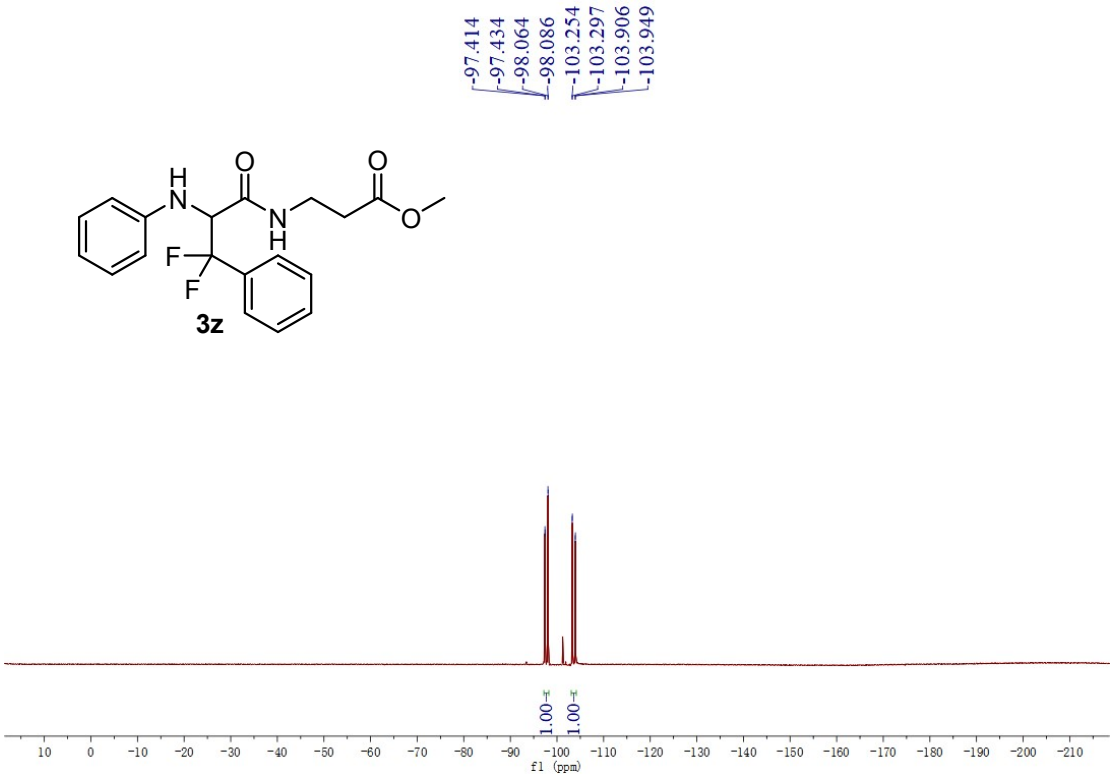
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3y:



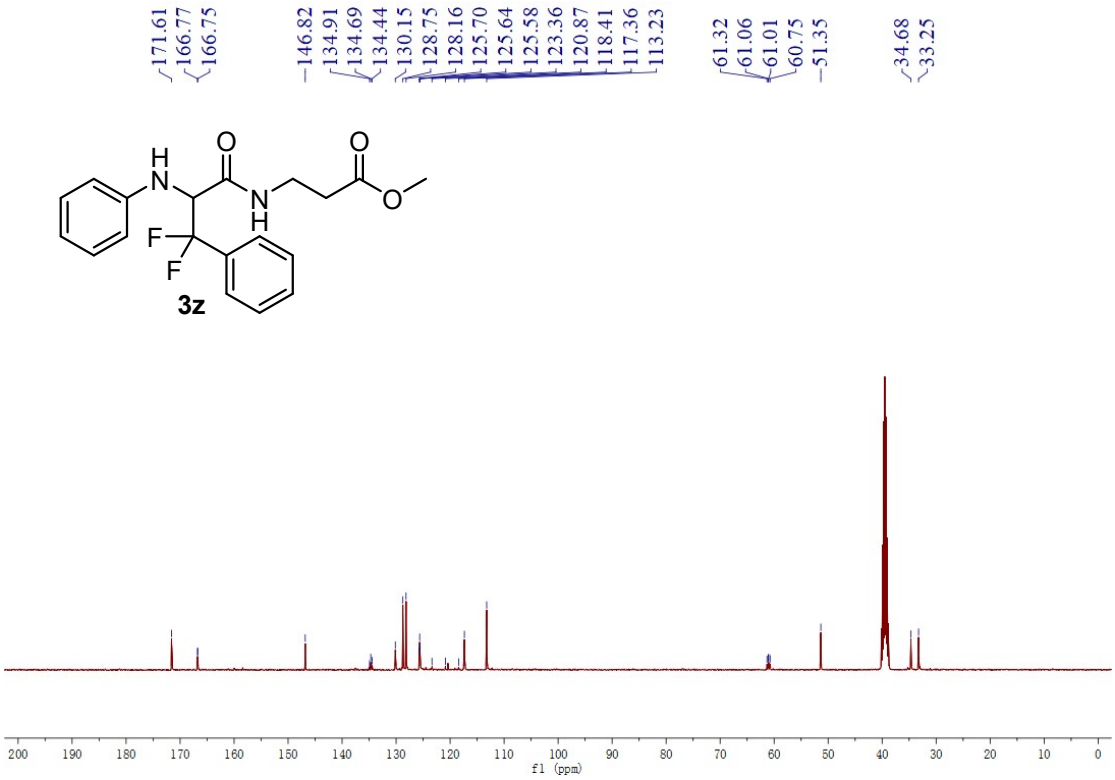
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 3z:



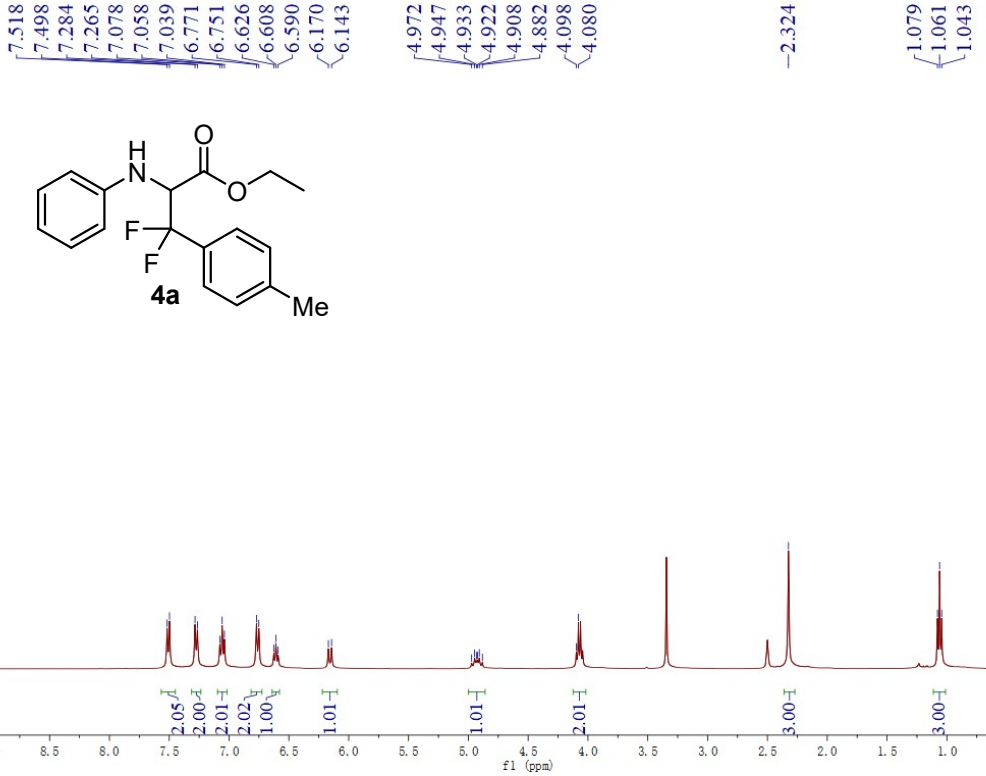
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 3z:



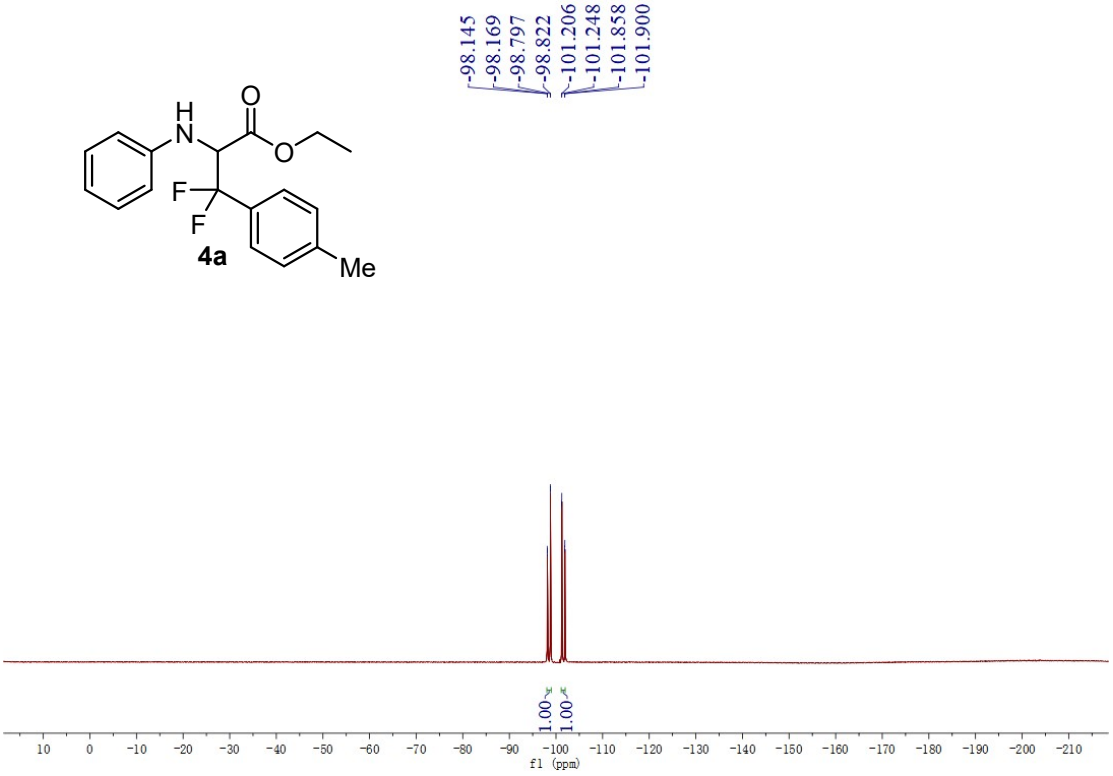
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 3z:



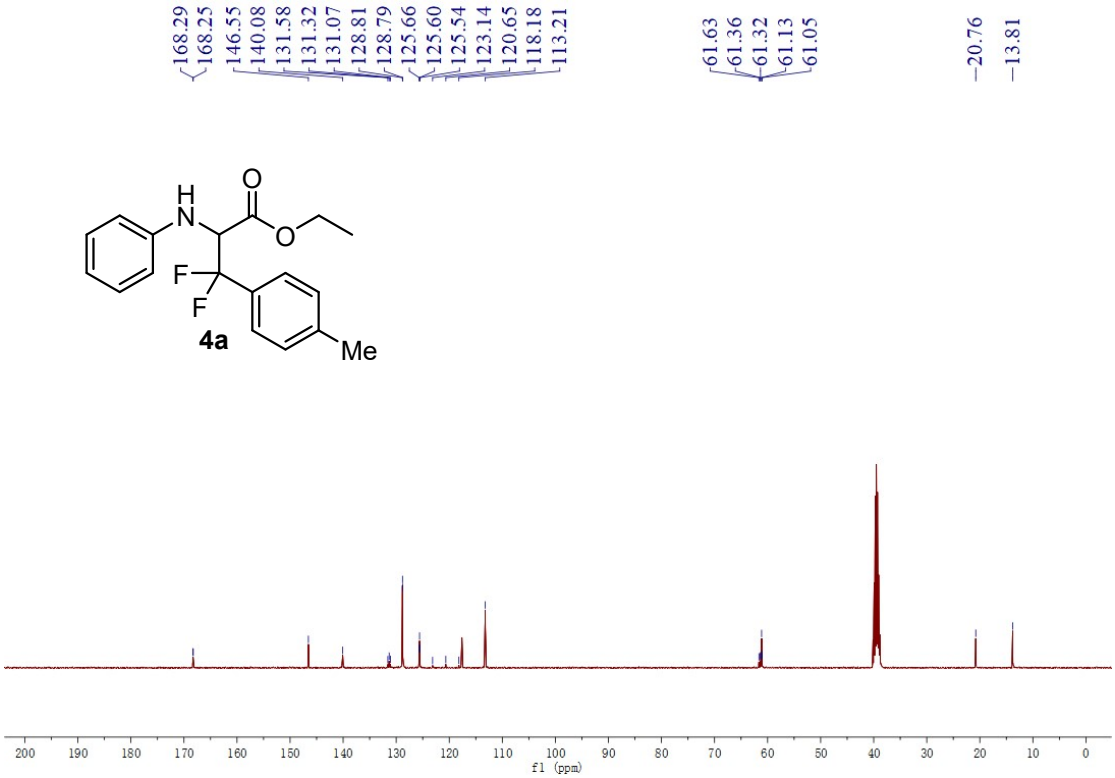
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4a:



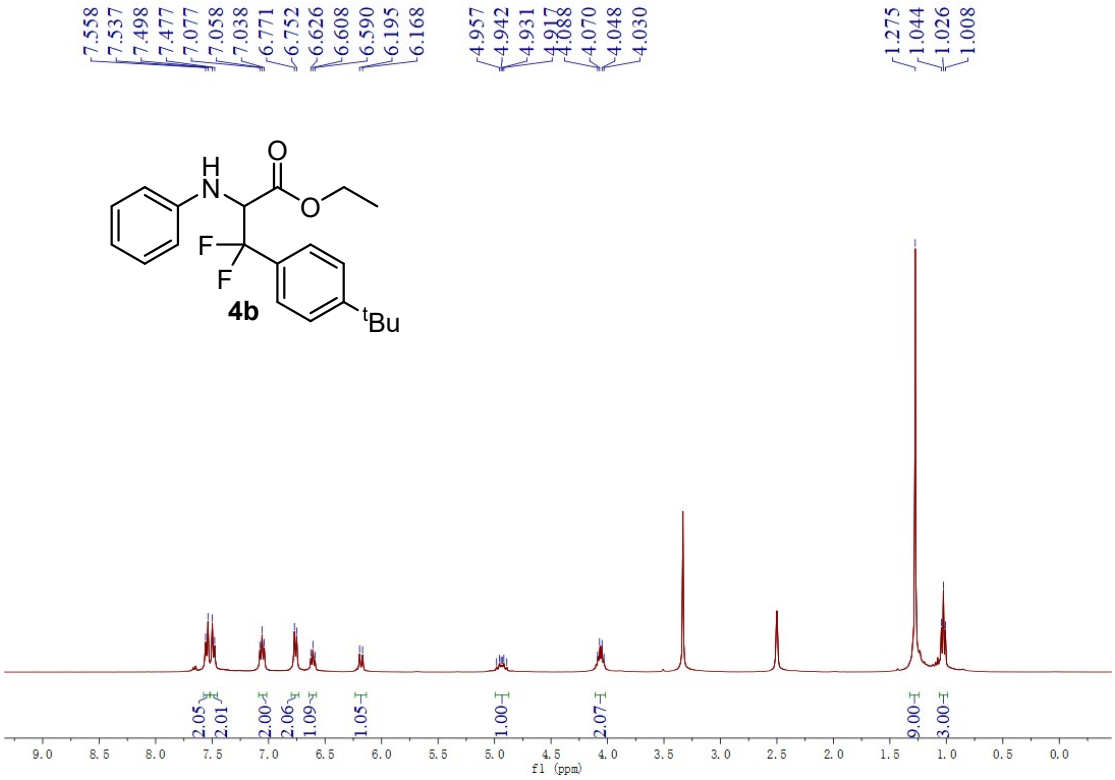
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4a:



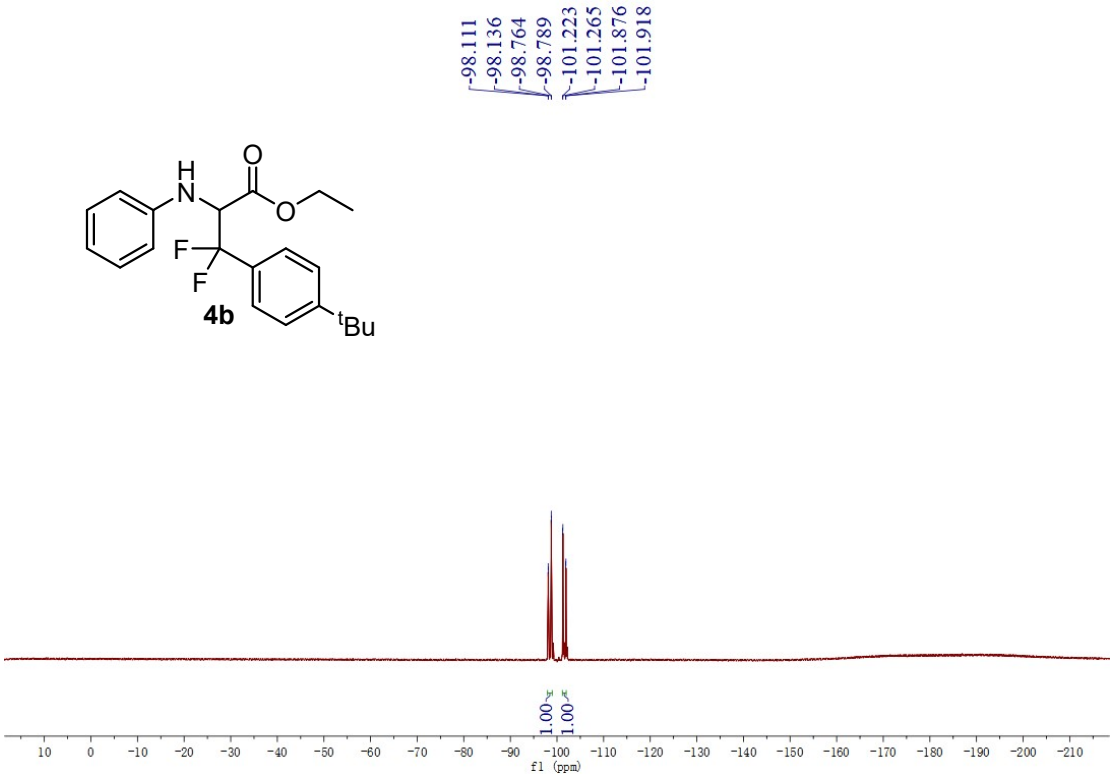
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4a:



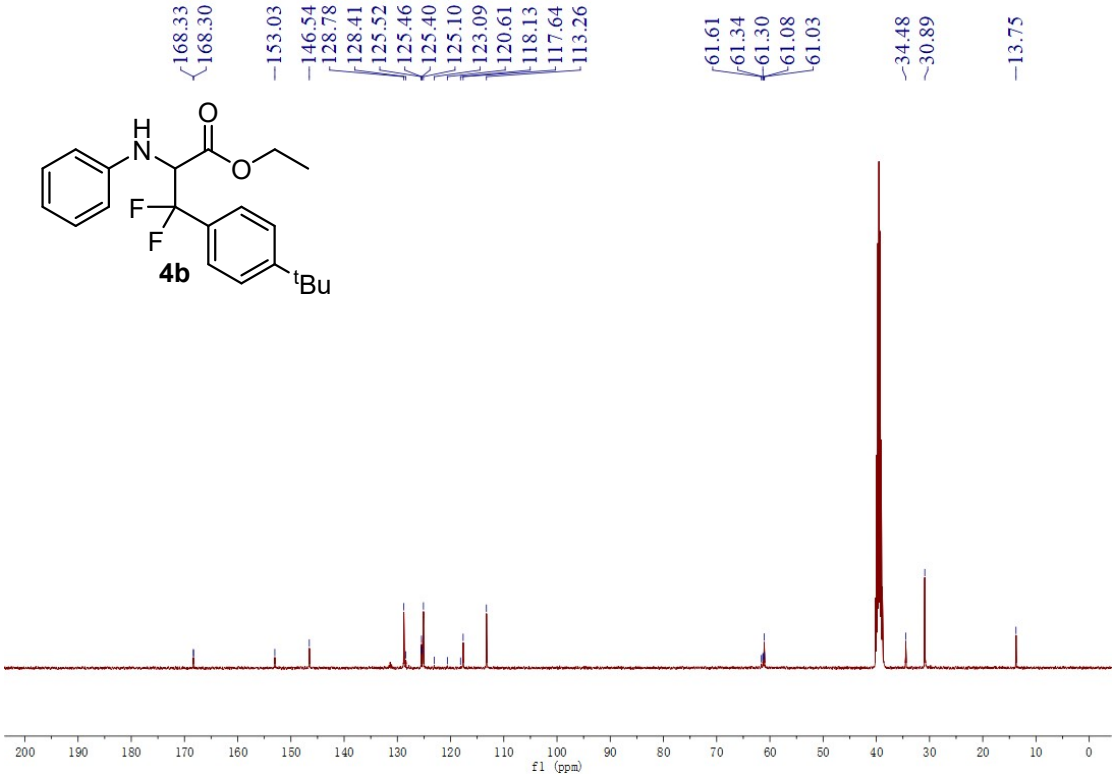
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4b:



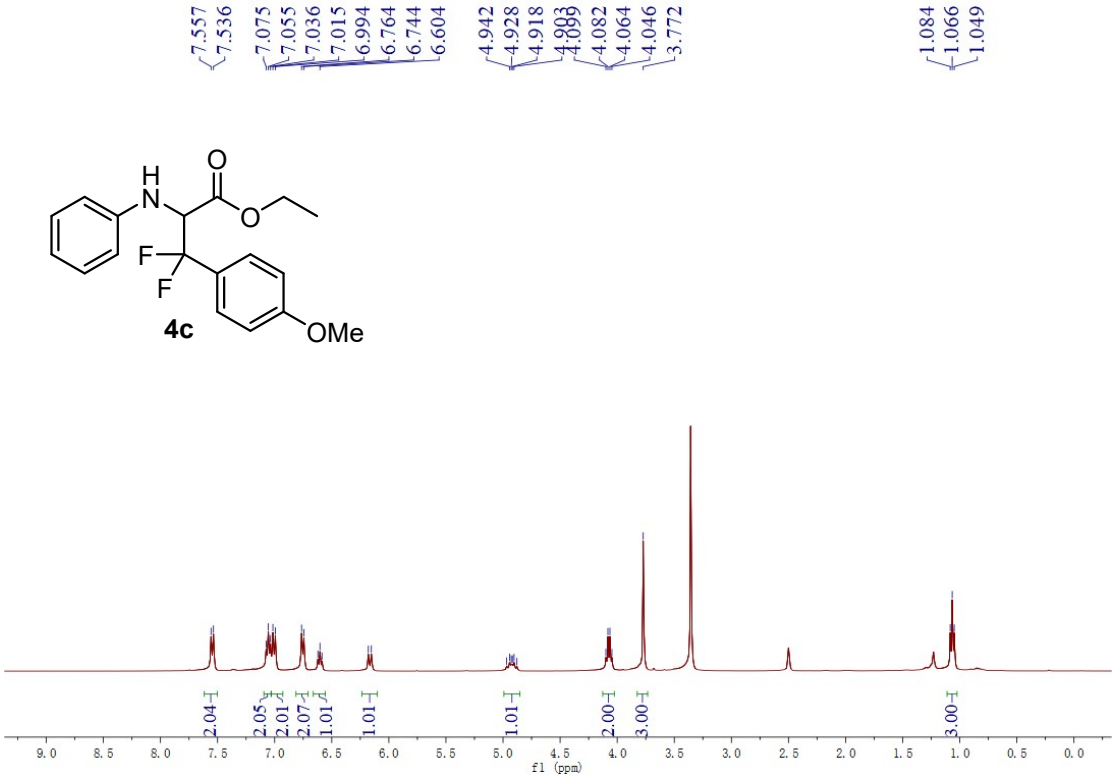
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 4b:



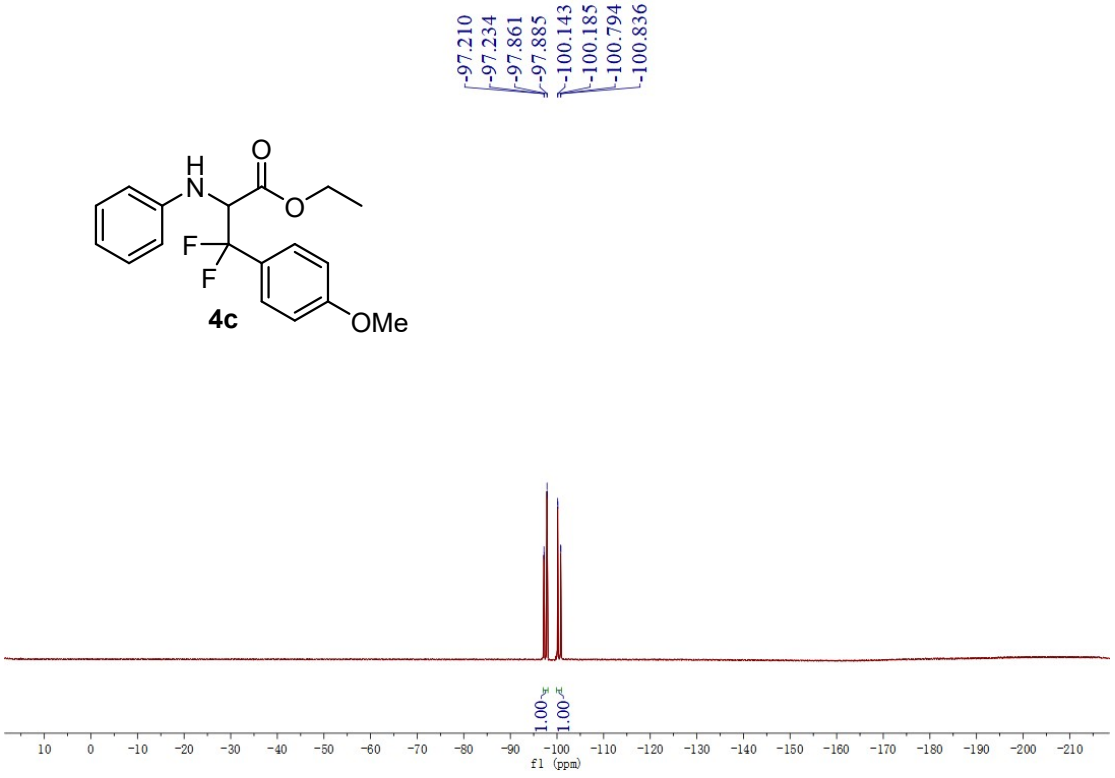
^{13}C NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 4b:



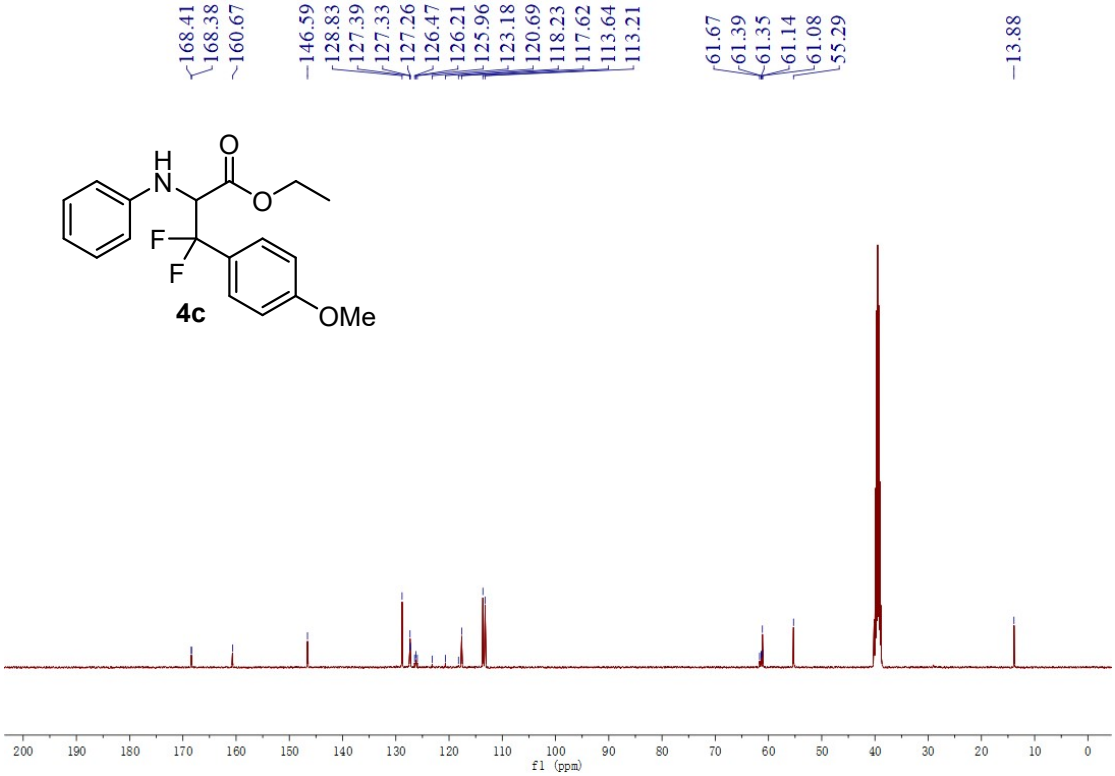
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4c:



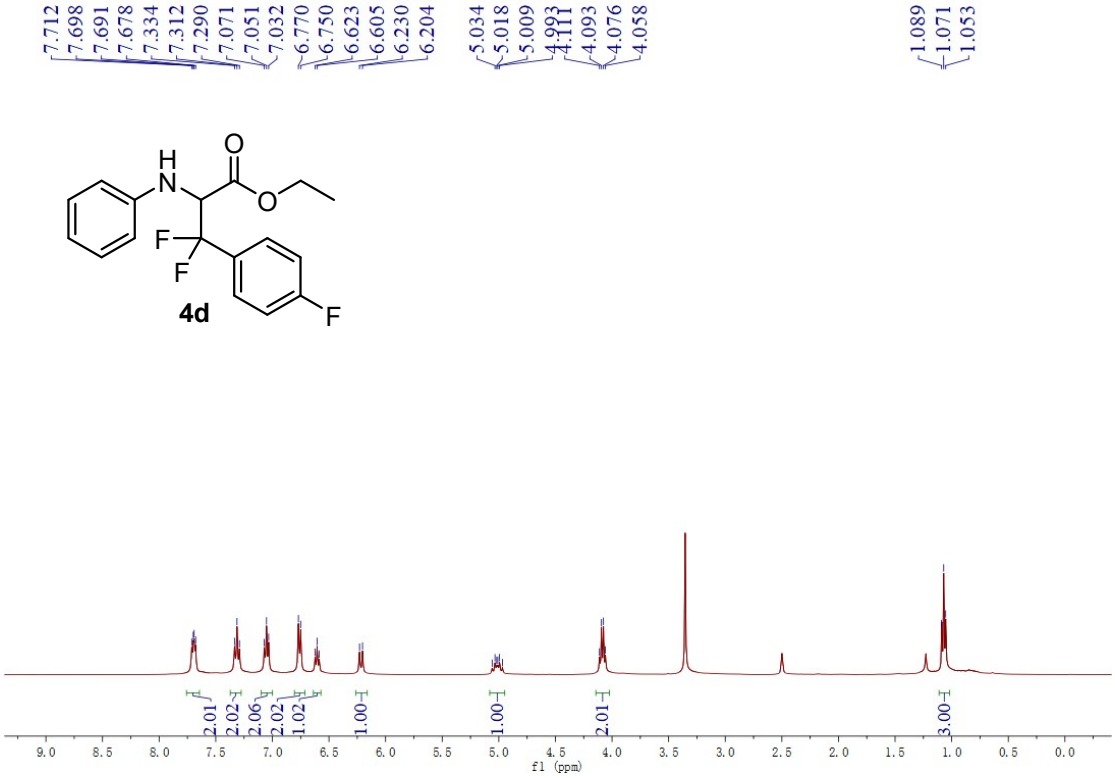
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4c:



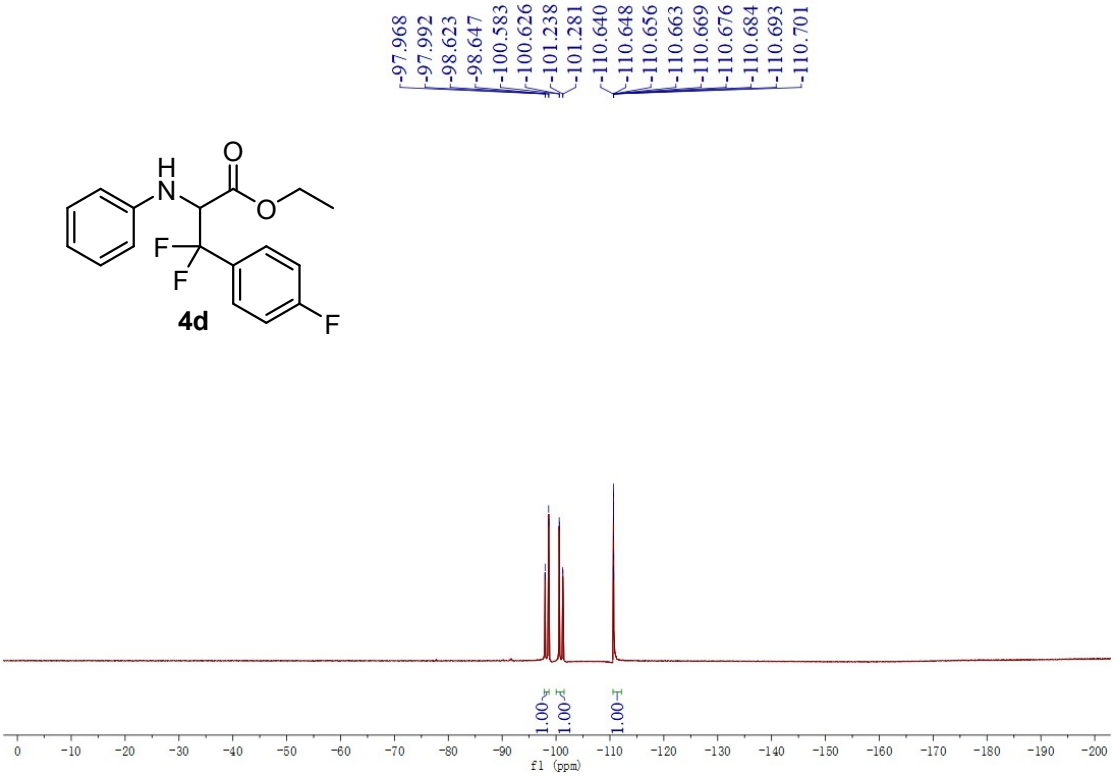
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4c:



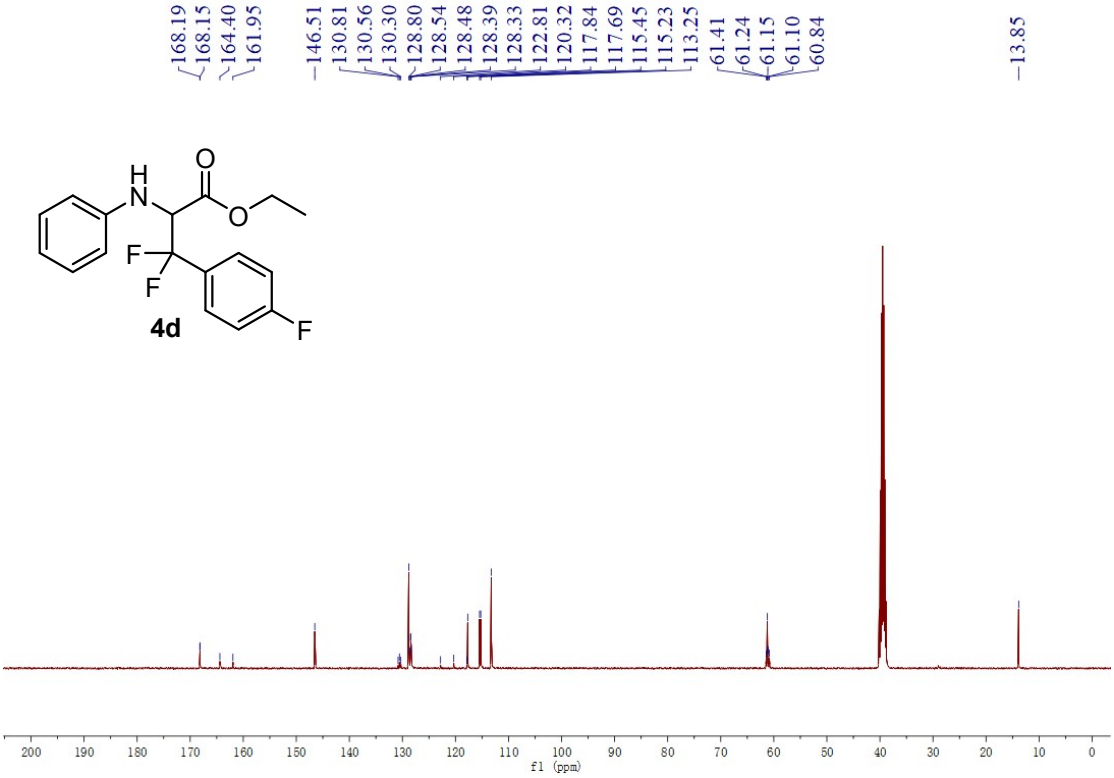
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4d:



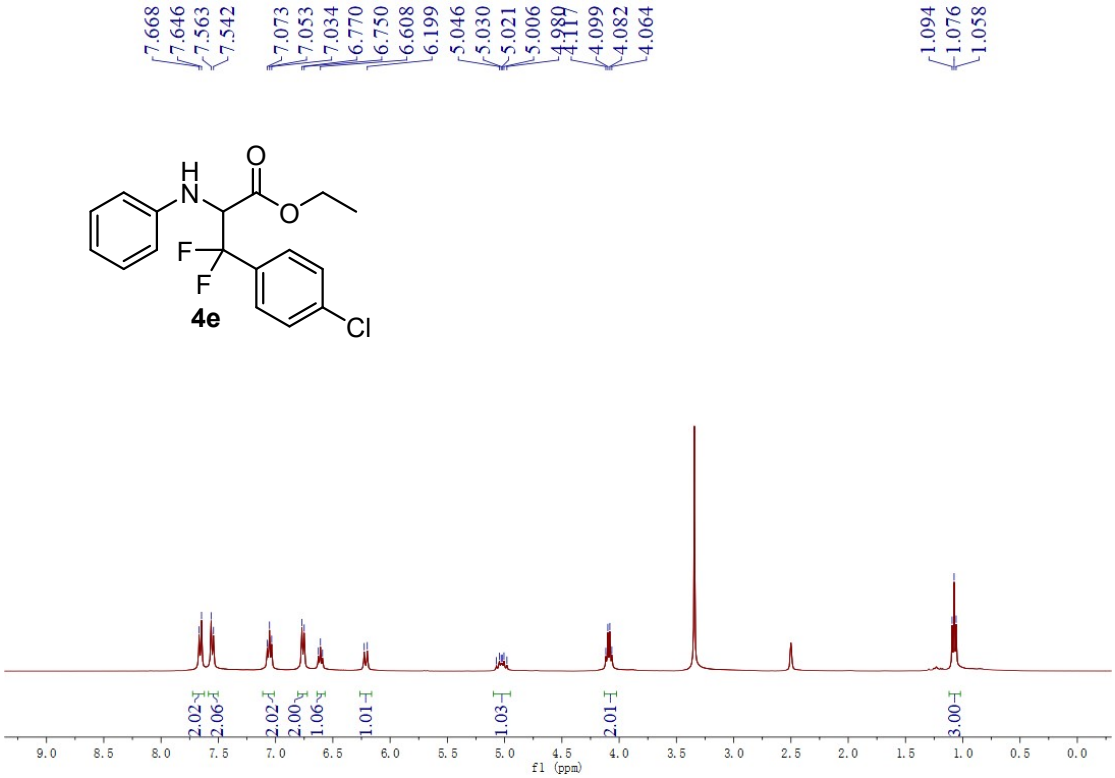
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 4d:



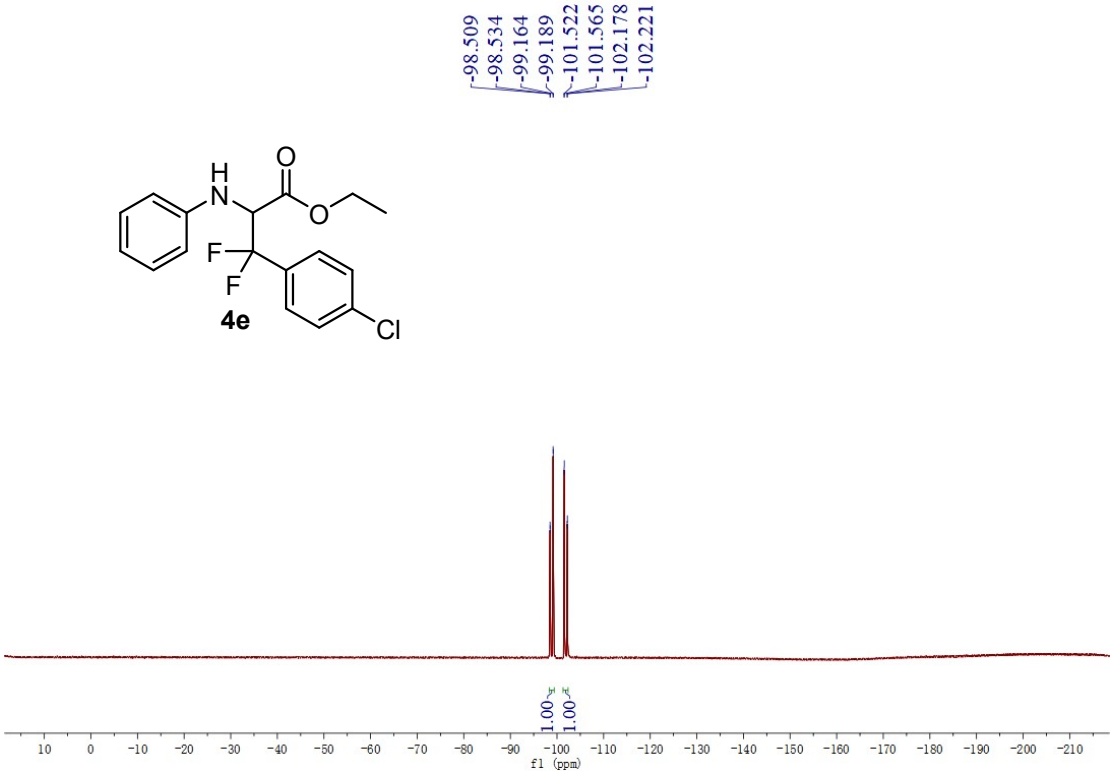
^{13}C NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 4d:



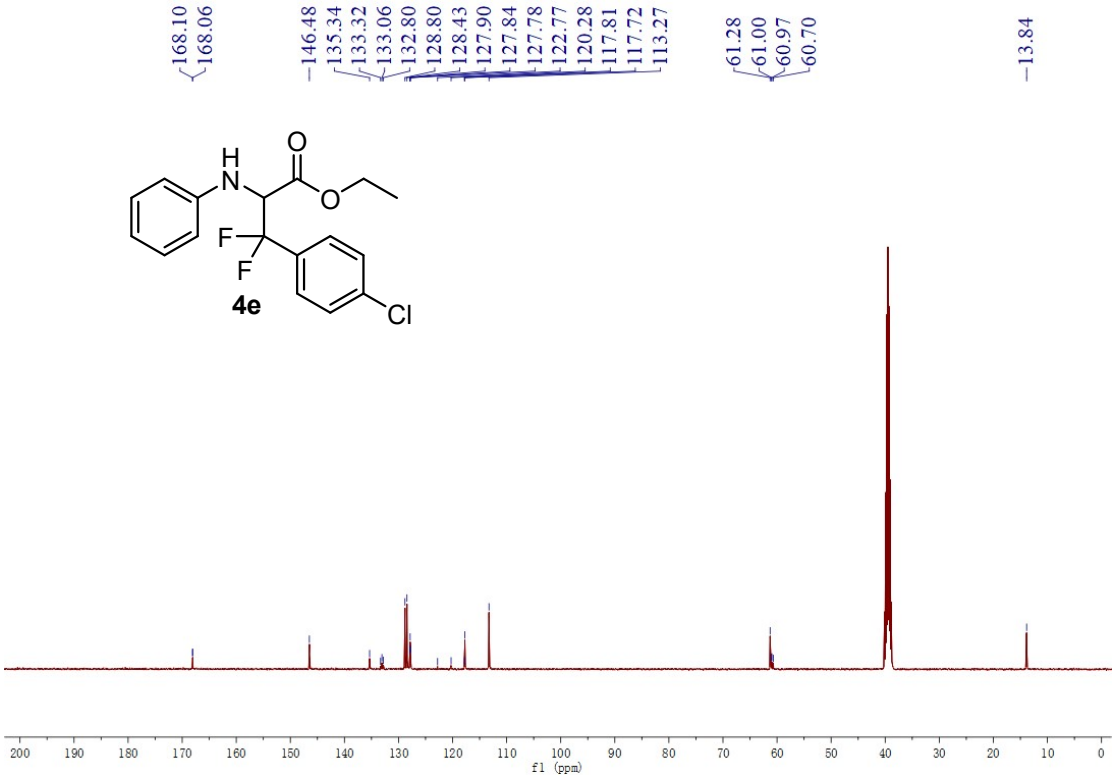
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4e:



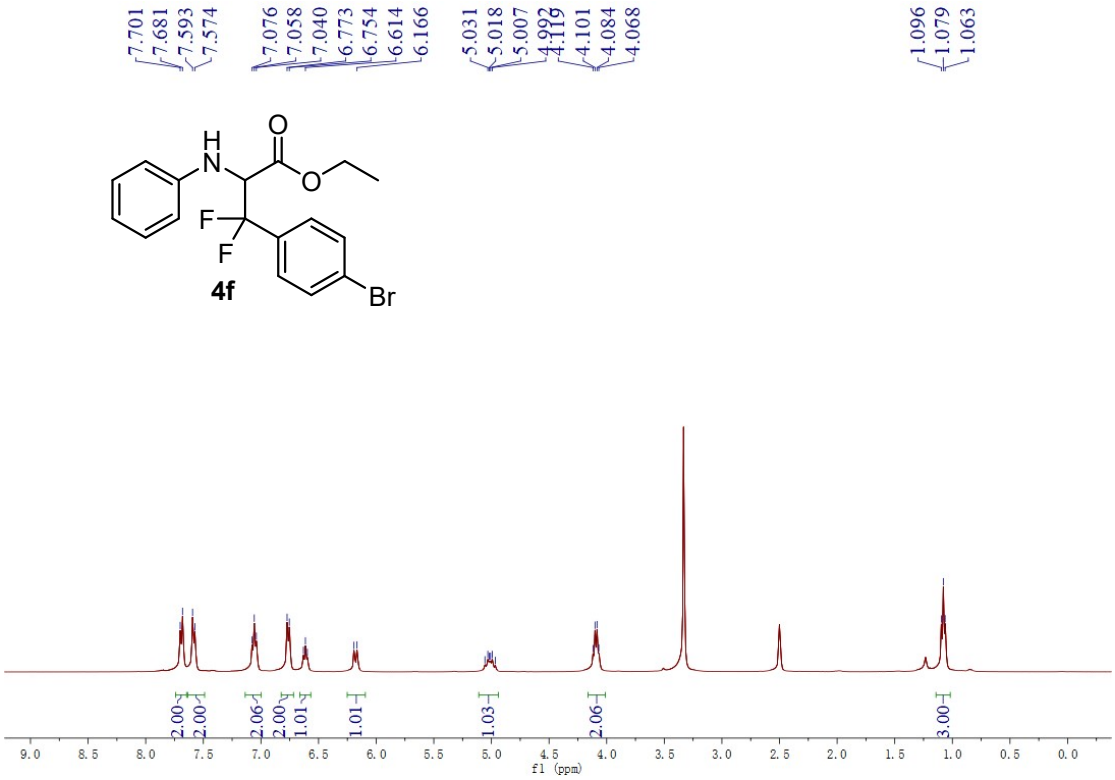
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4e:



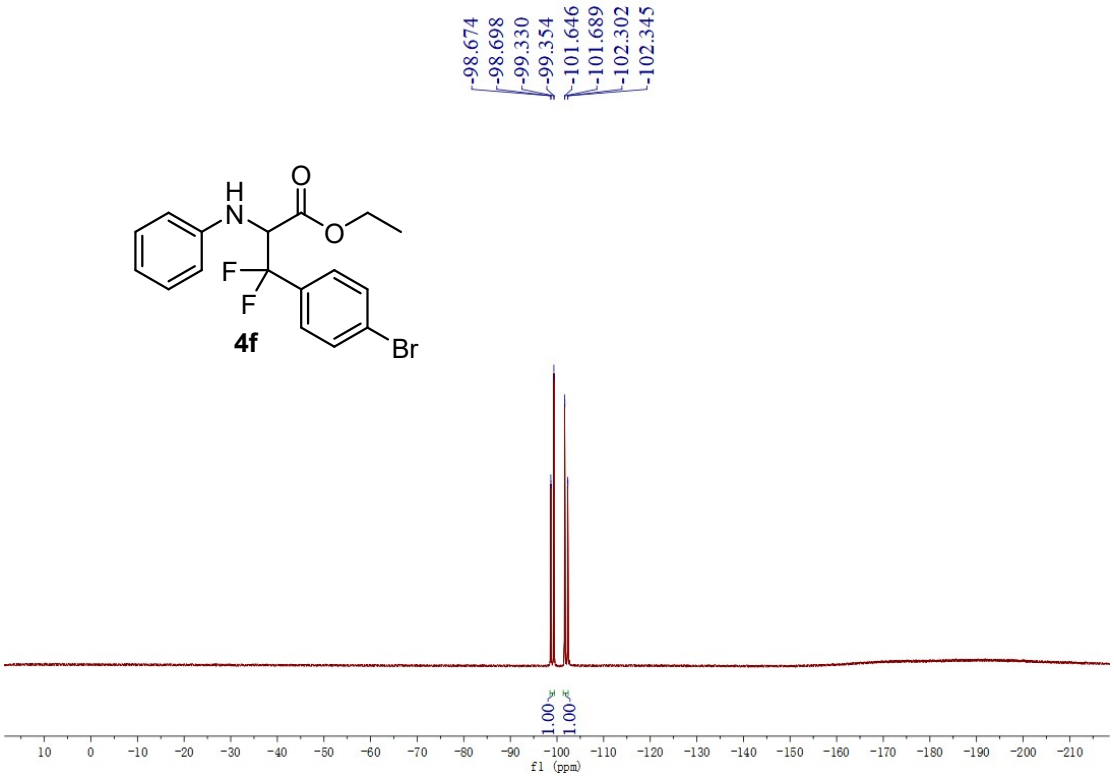
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4e:



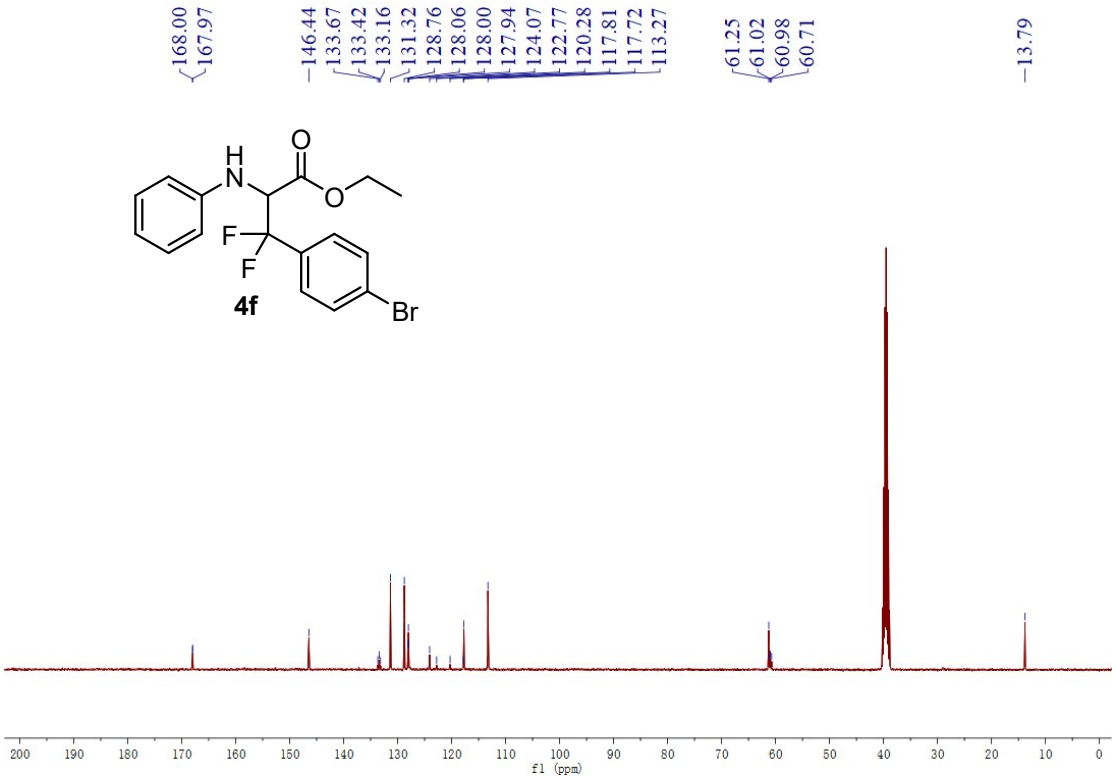
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4f:



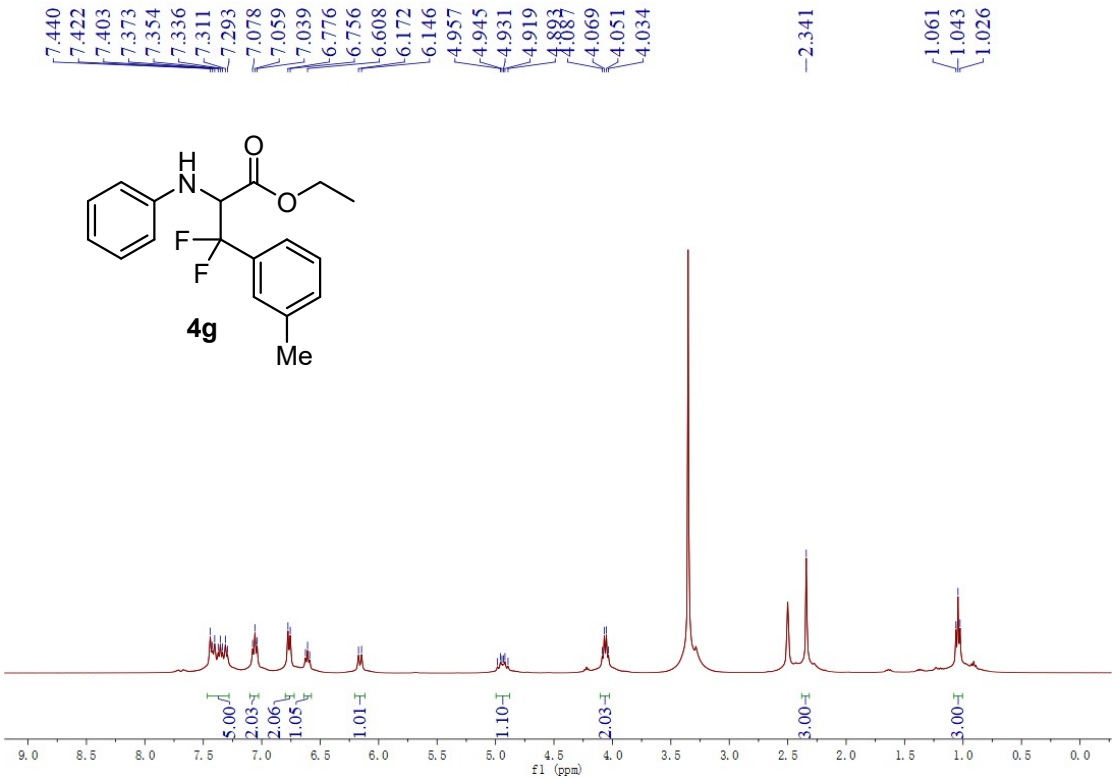
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4f:



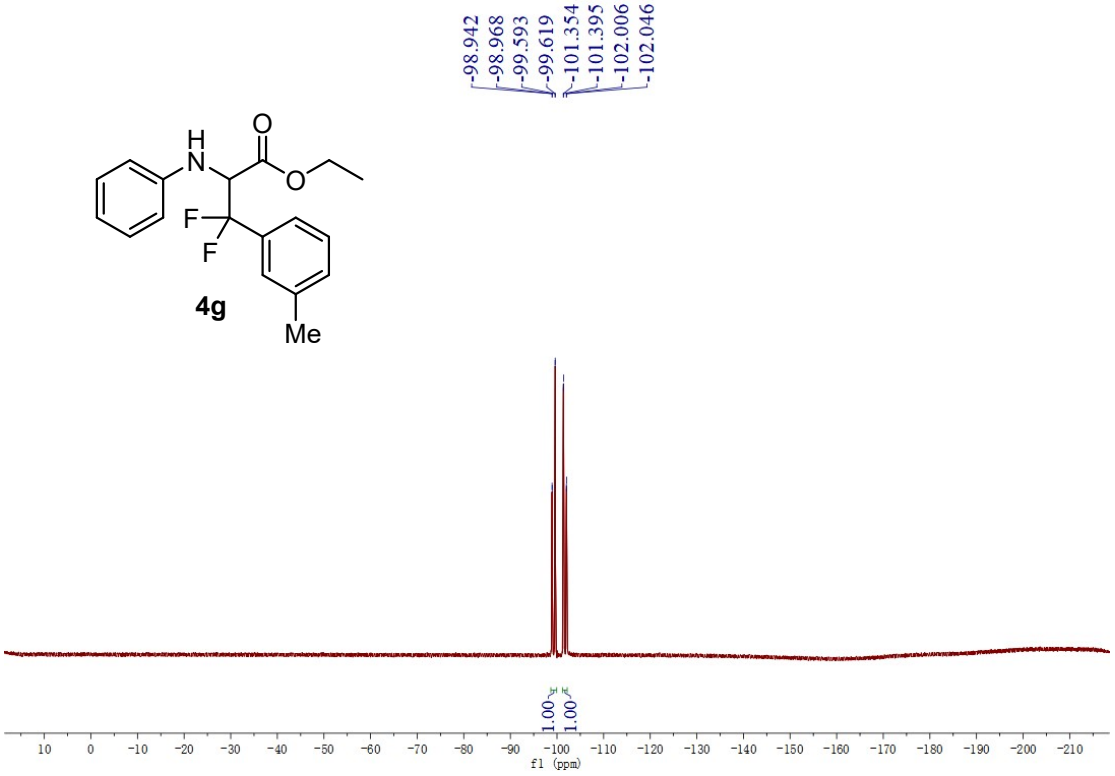
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4f:



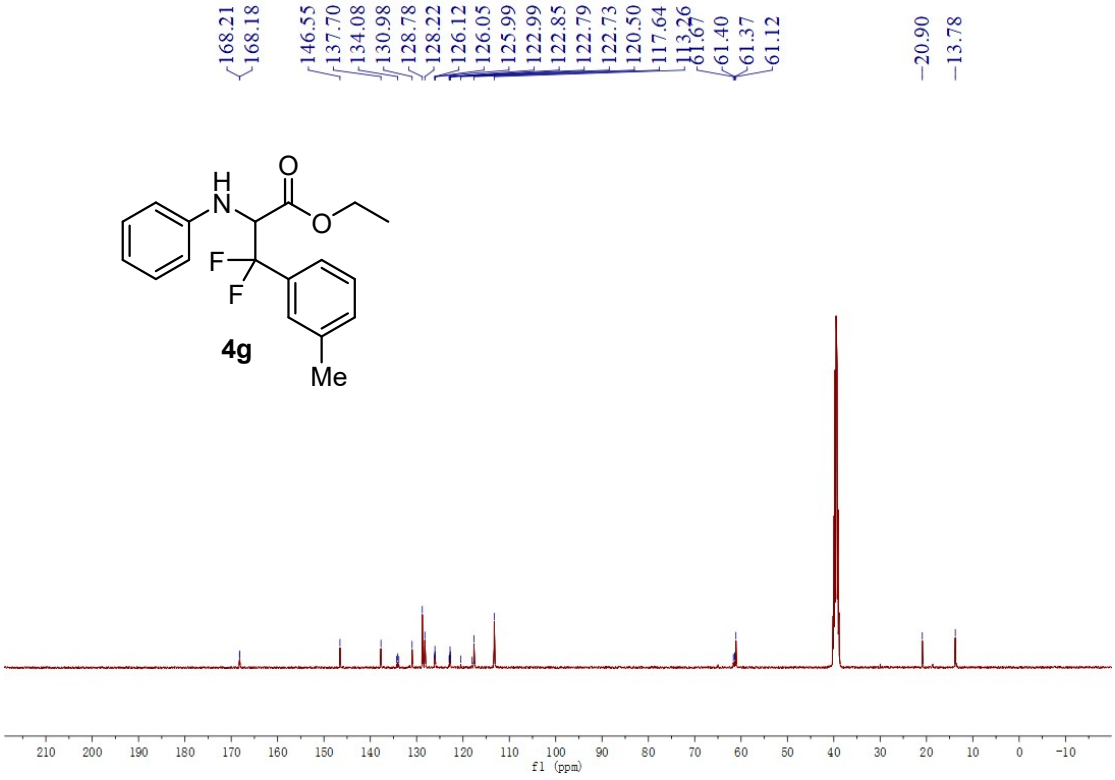
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4g:



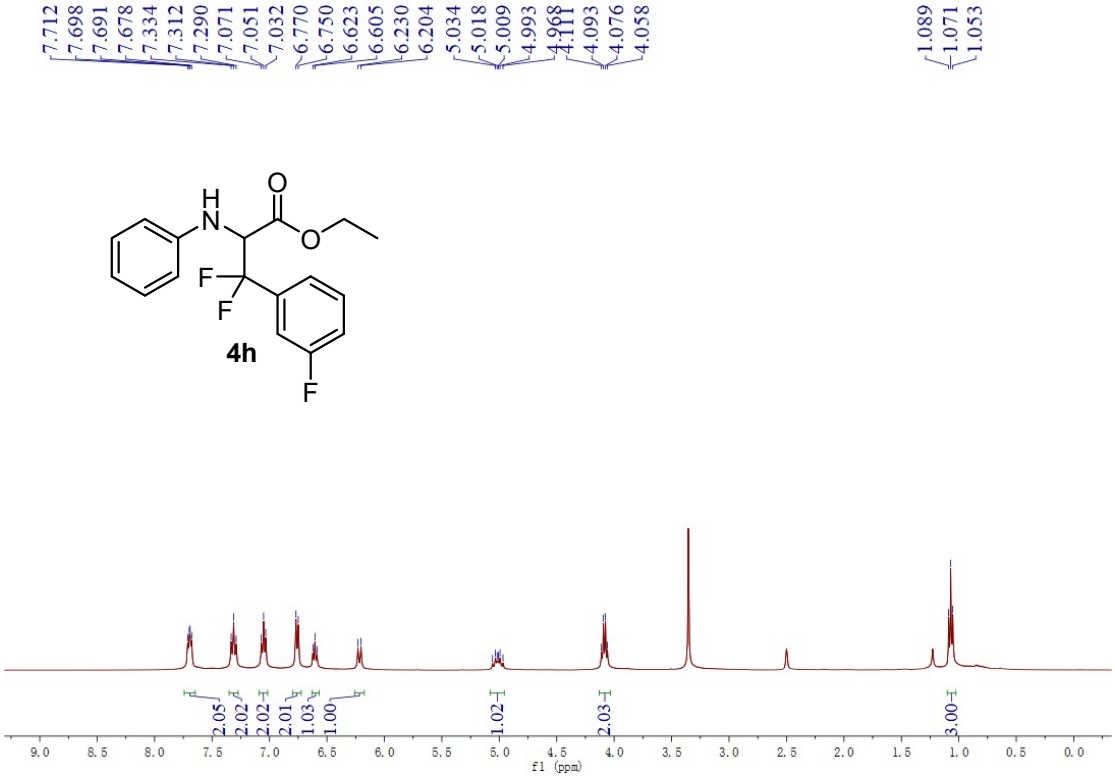
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4g:



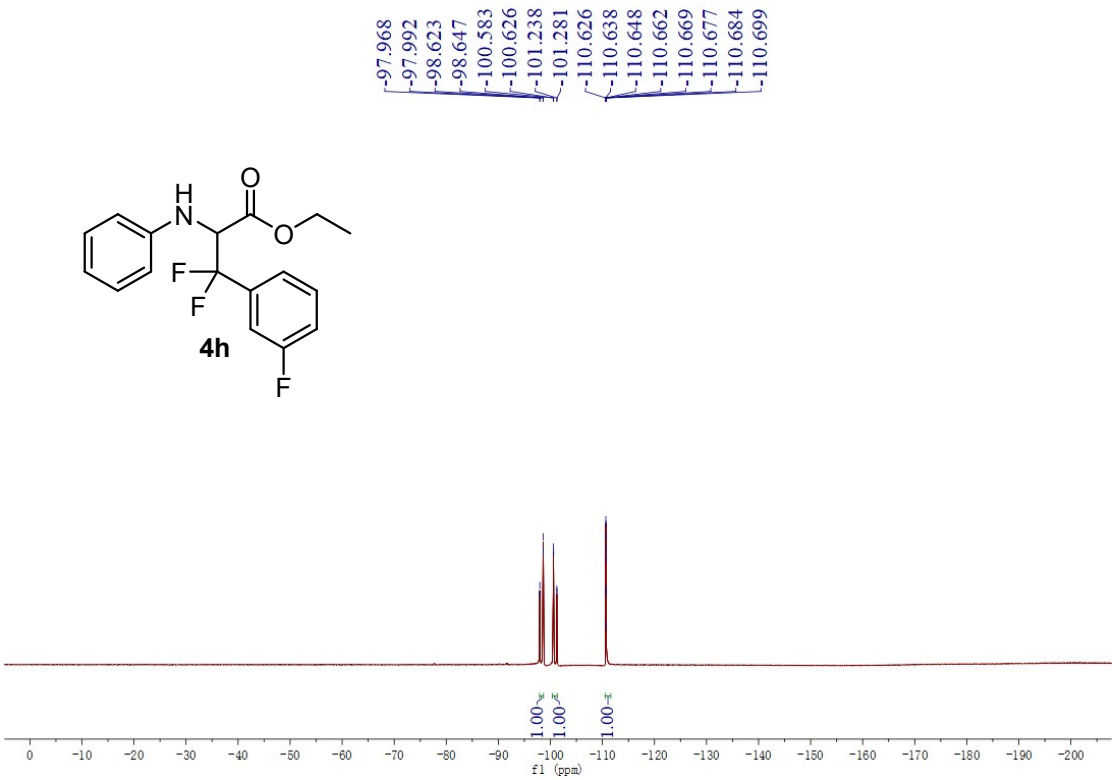
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4g:



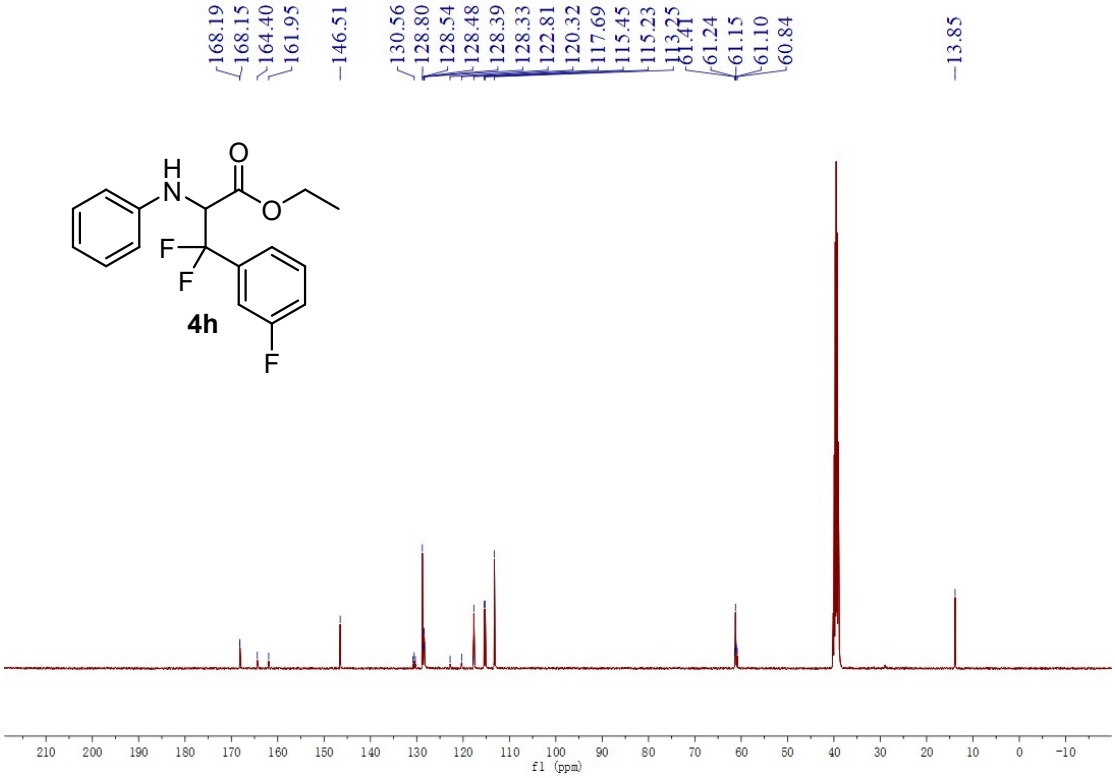
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4h:



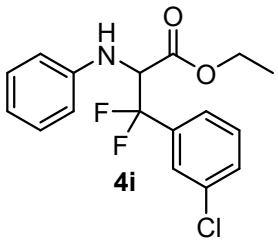
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 4h:



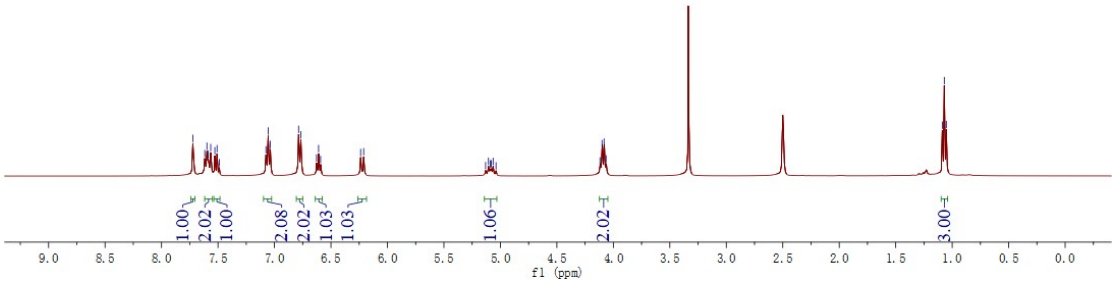
^{13}H NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 4h:



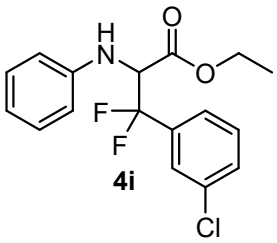
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4i:



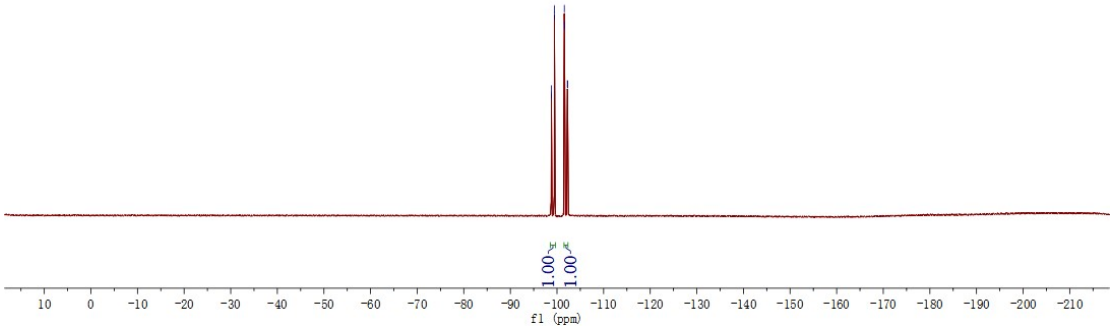
4i



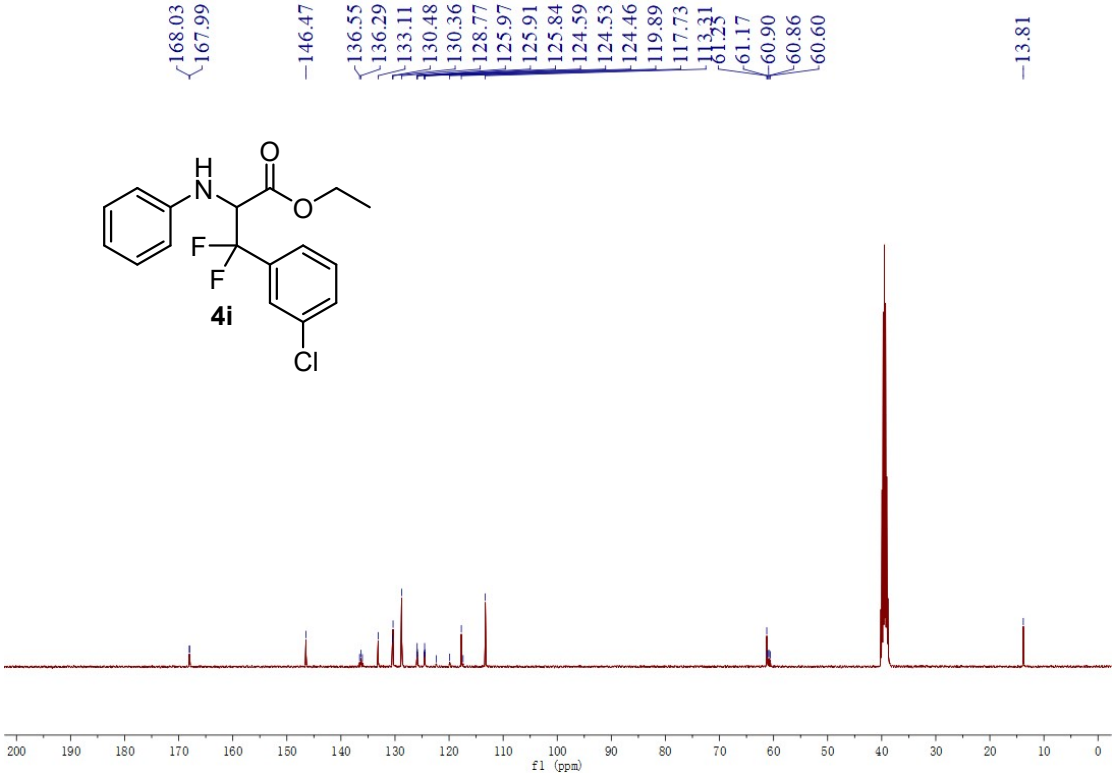
^{19}H NMR (DMSO-d_6, 376 MHz) spectrum of compound 4i:



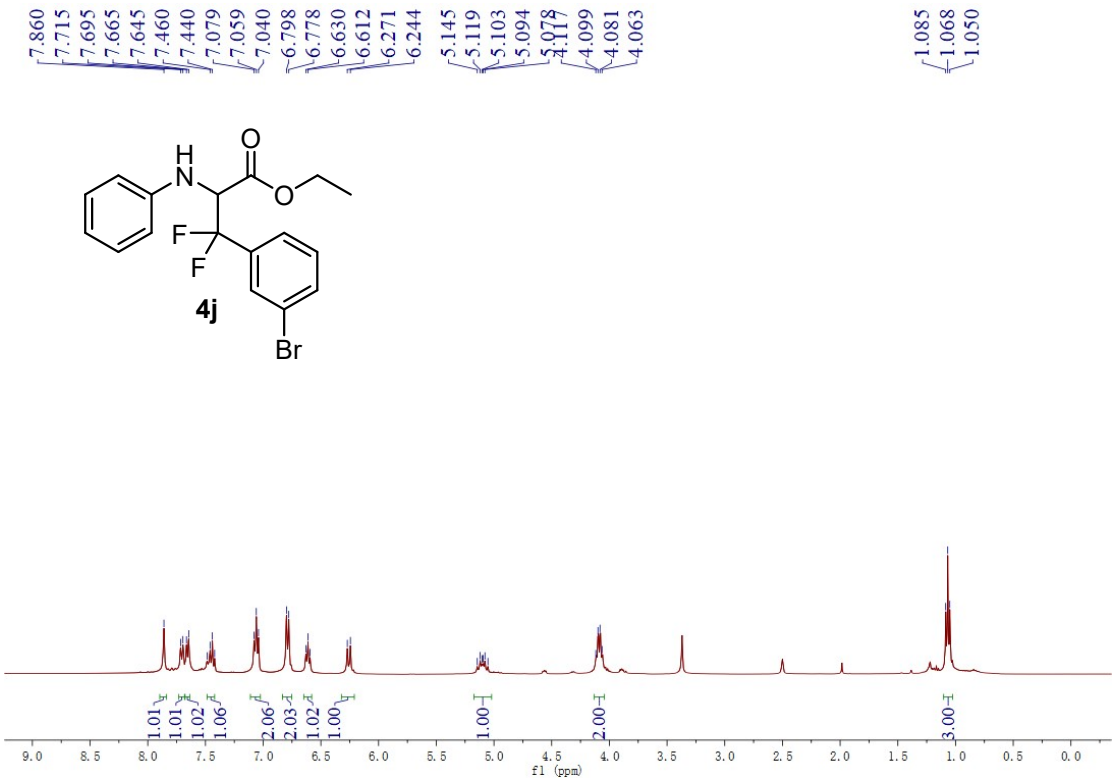
4i



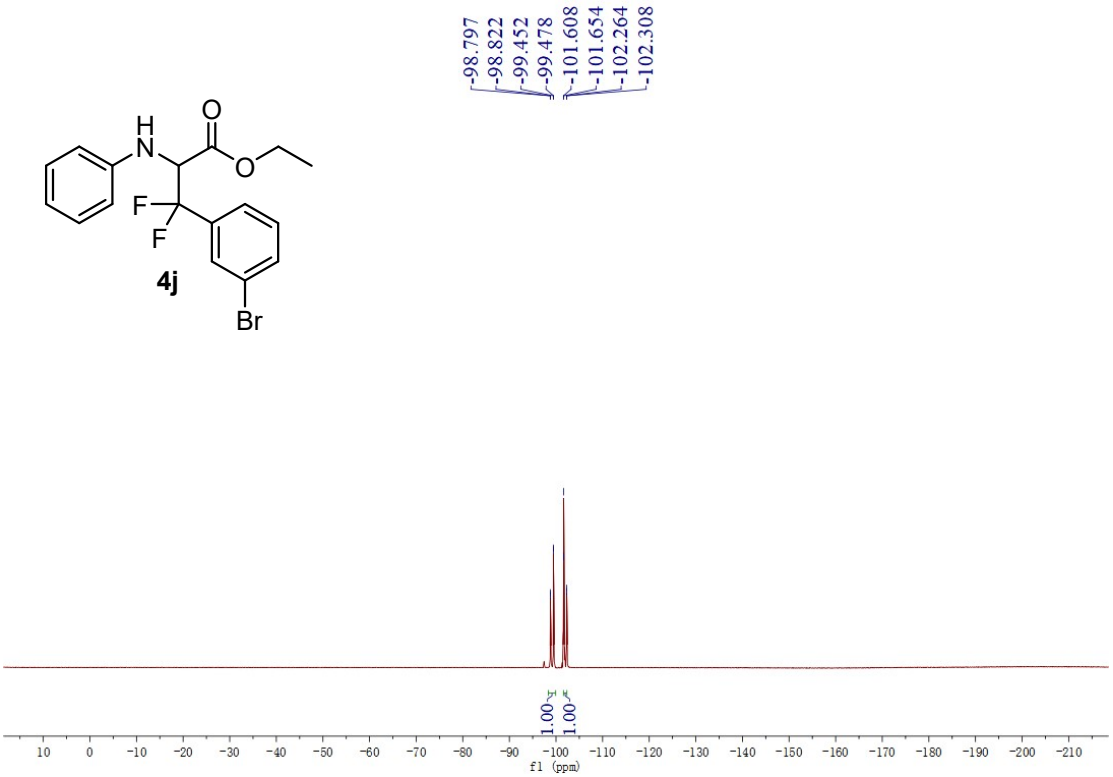
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4i:



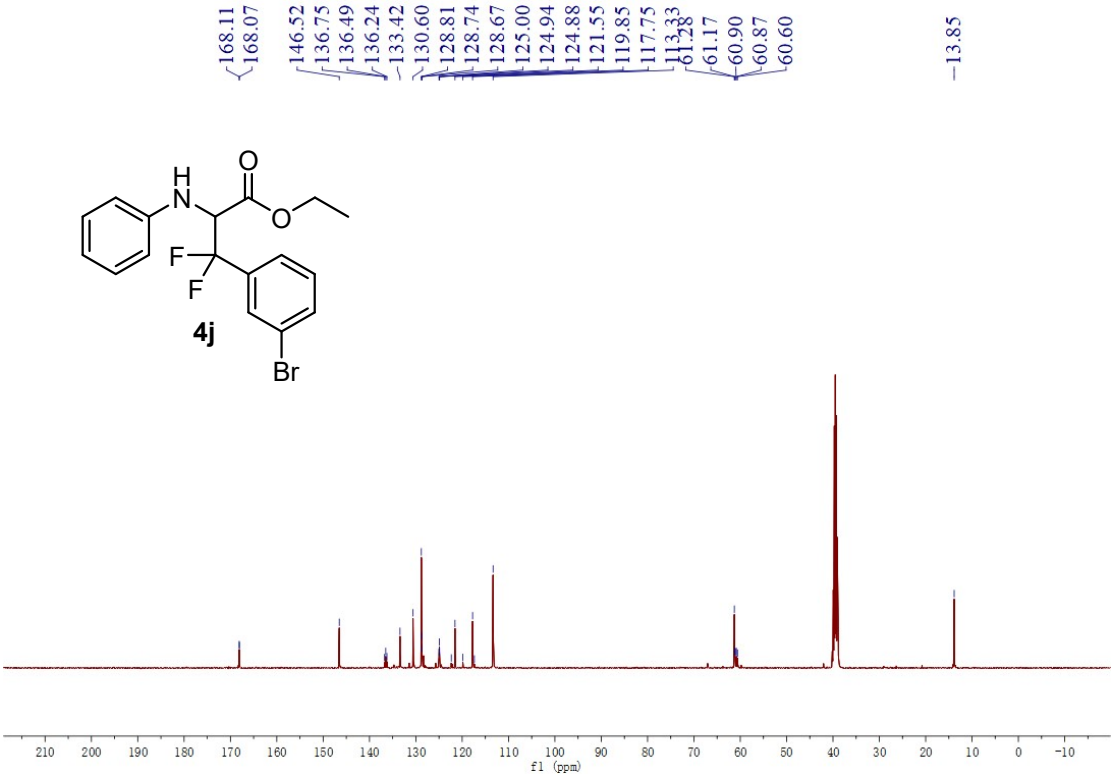
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4j:



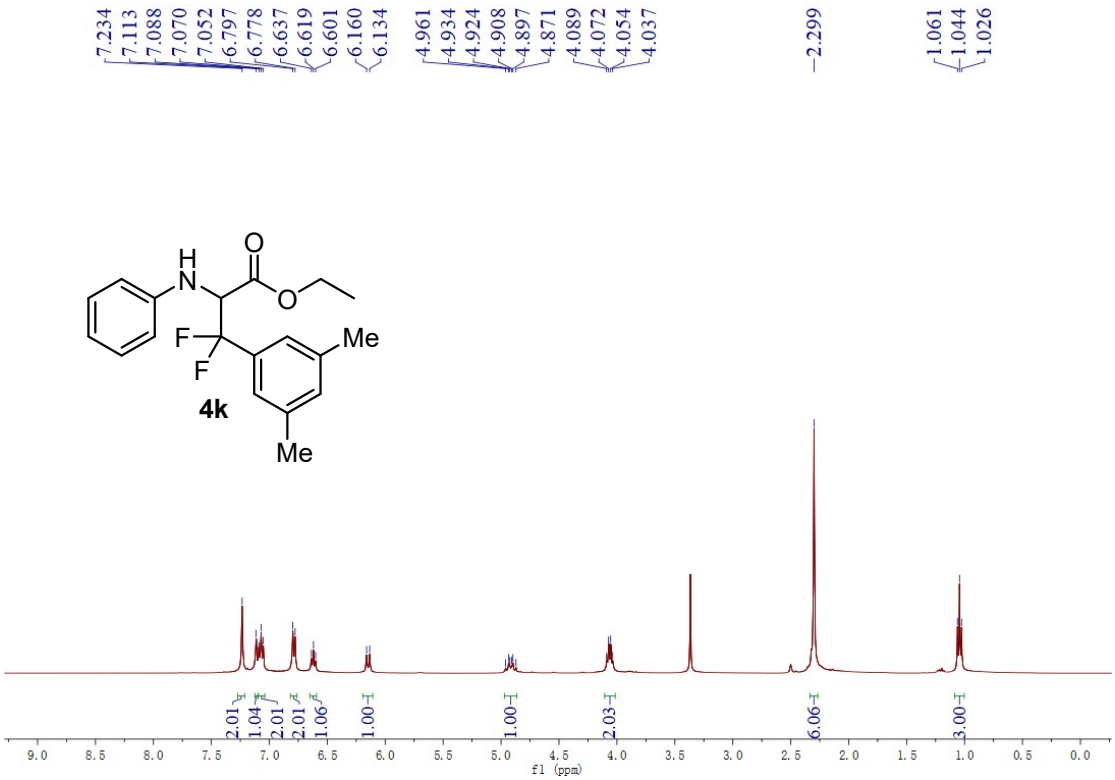
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 4j:



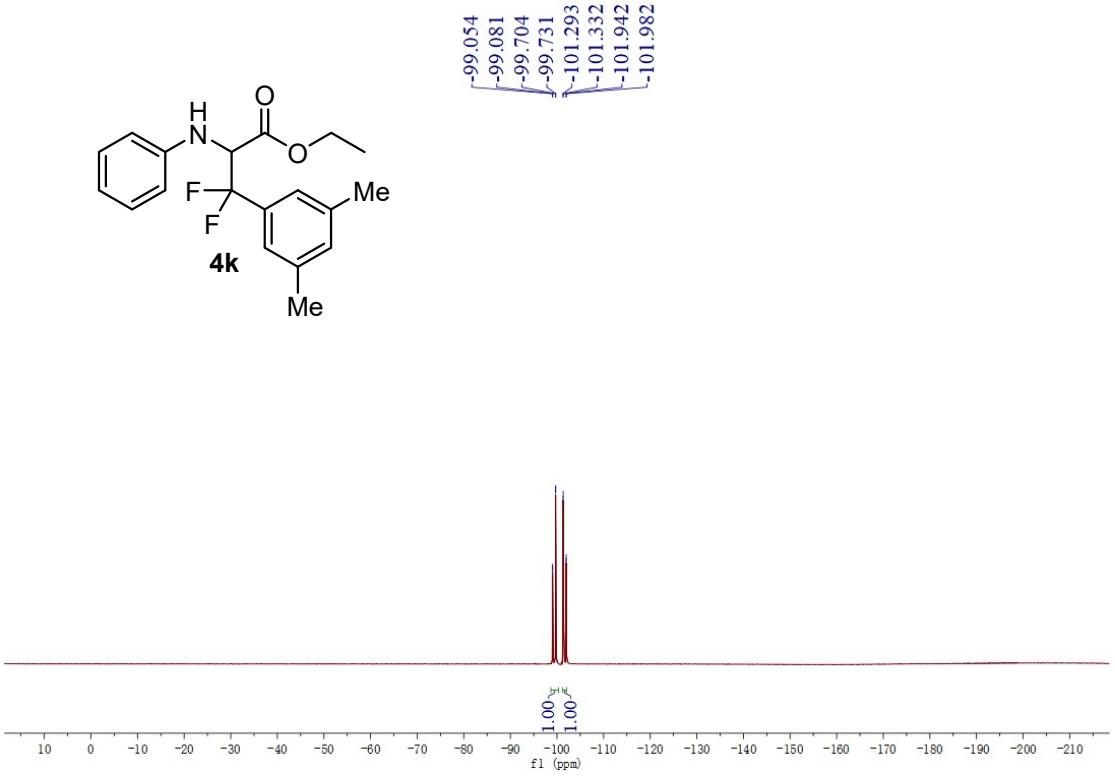
^{13}C NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 4j:



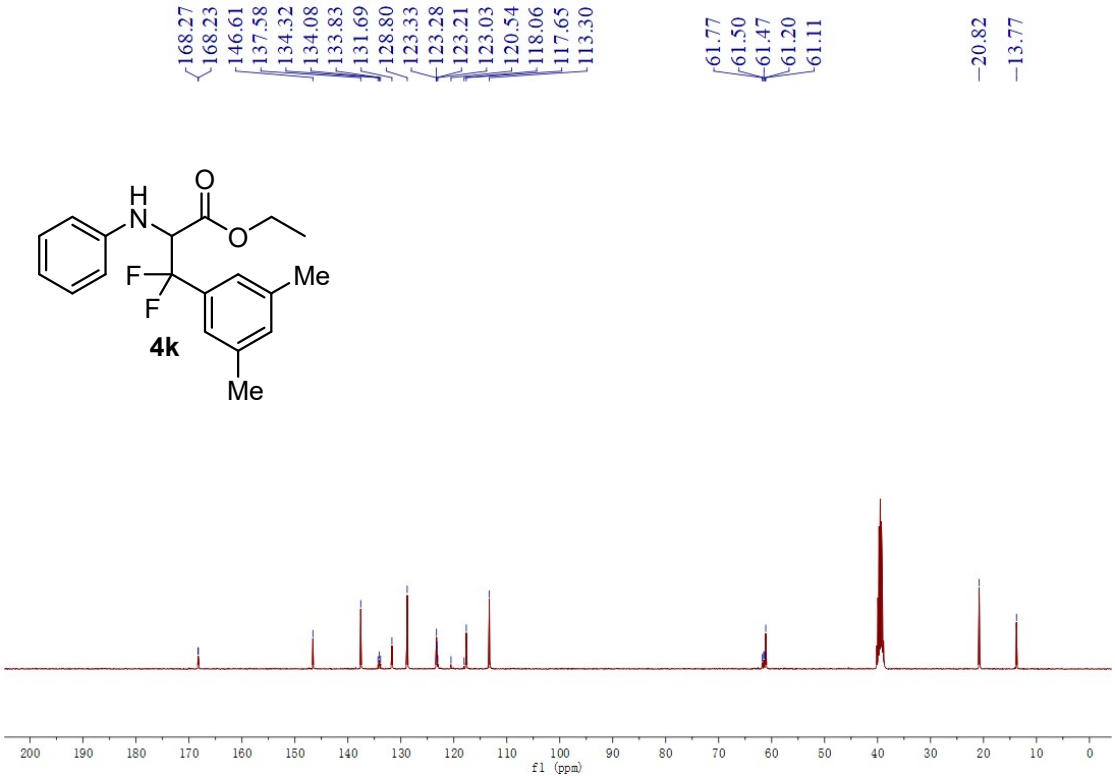
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4k:



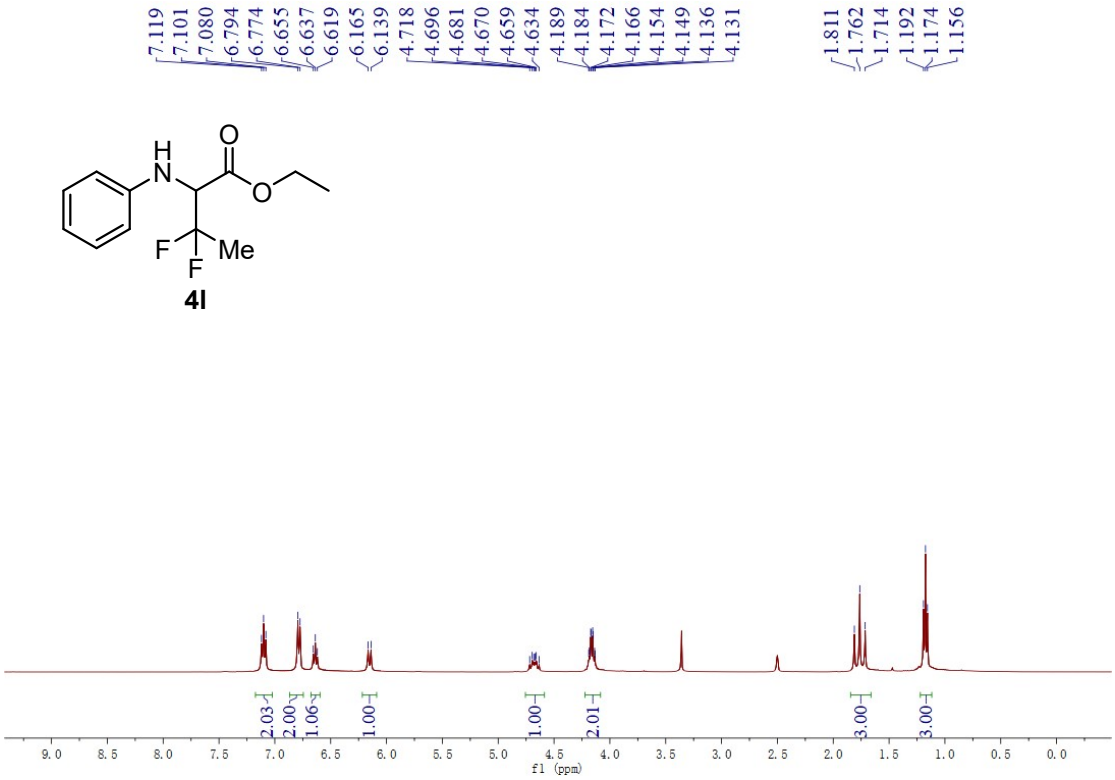
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4k:



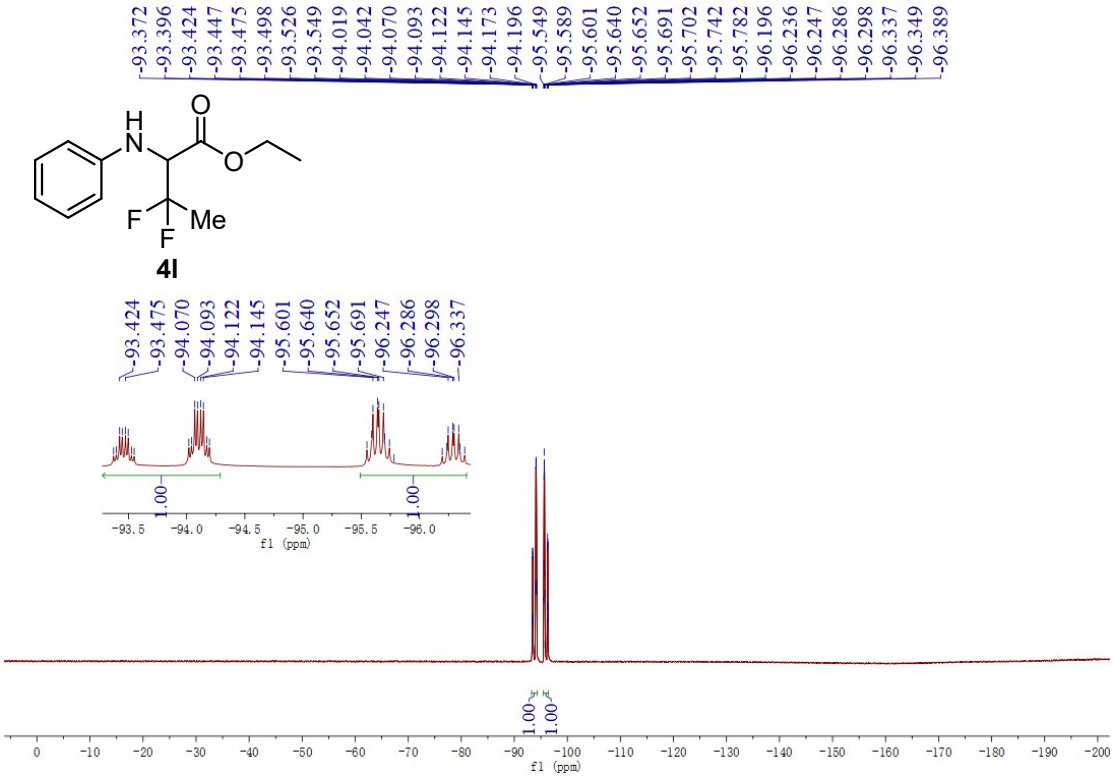
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4k:



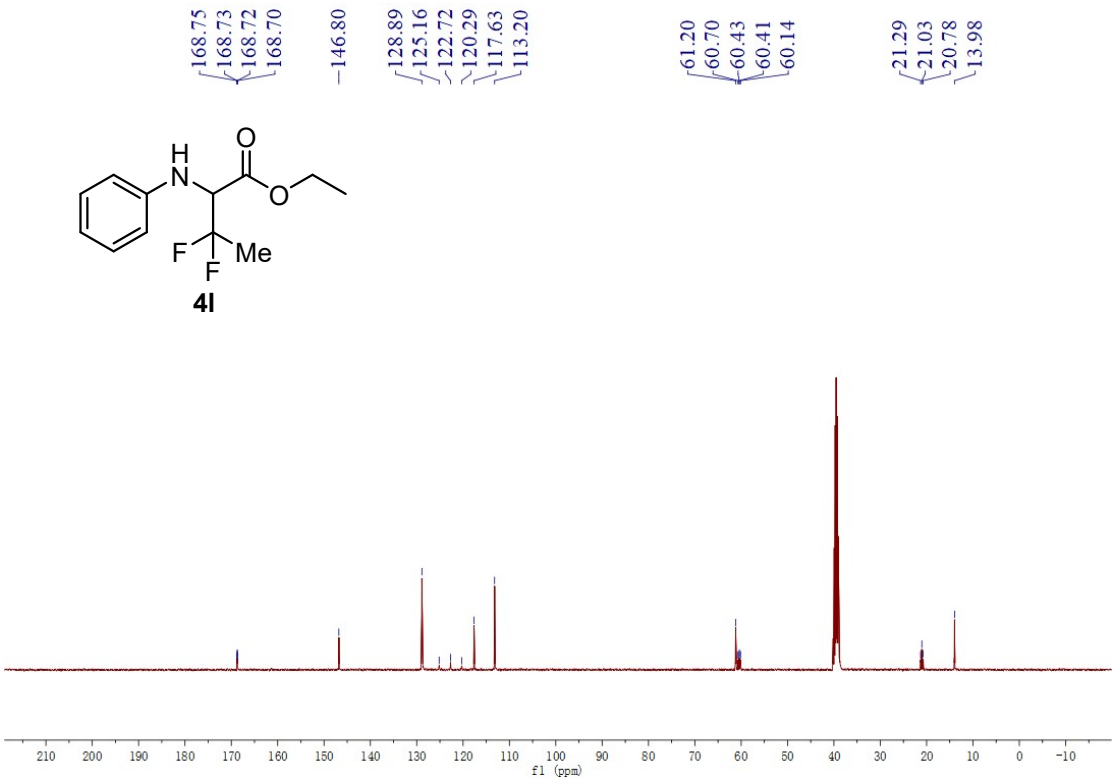
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4l:



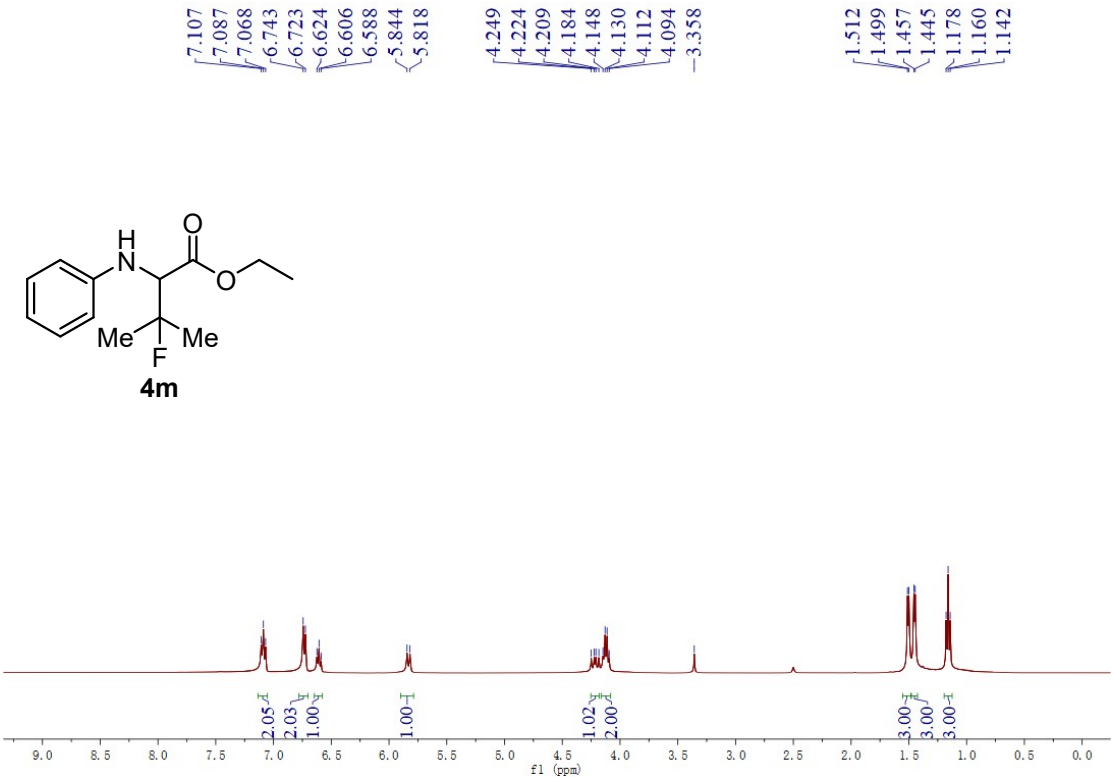
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4l:



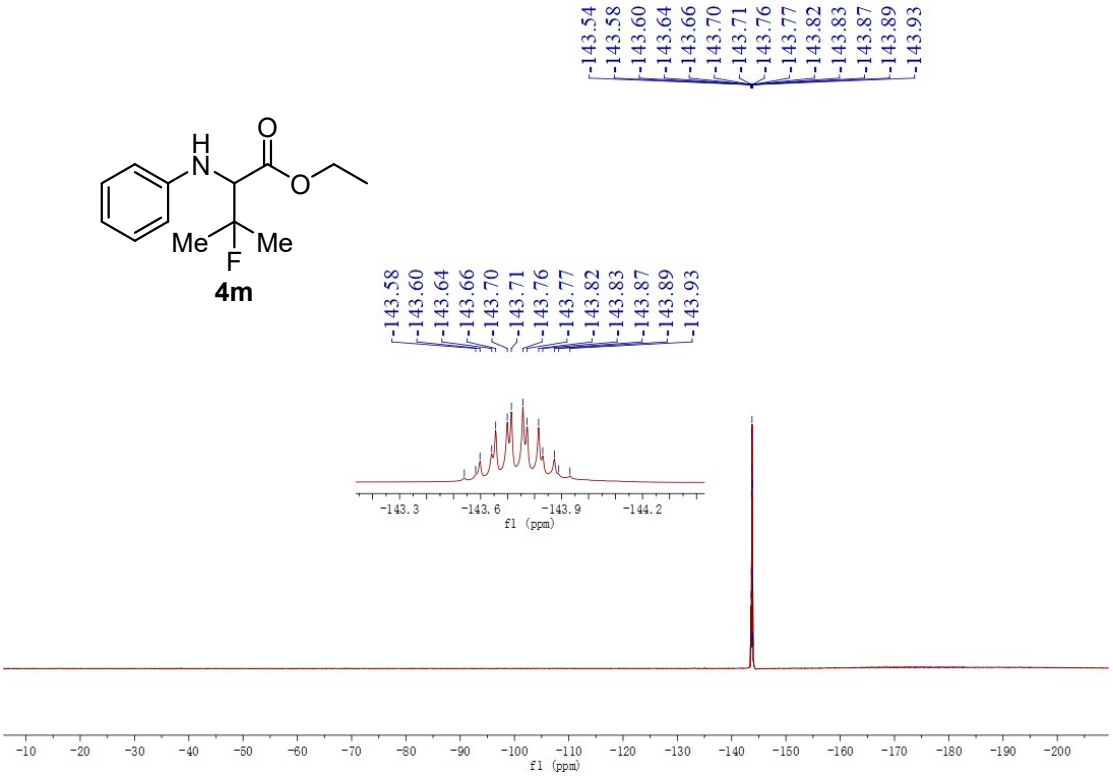
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4l:



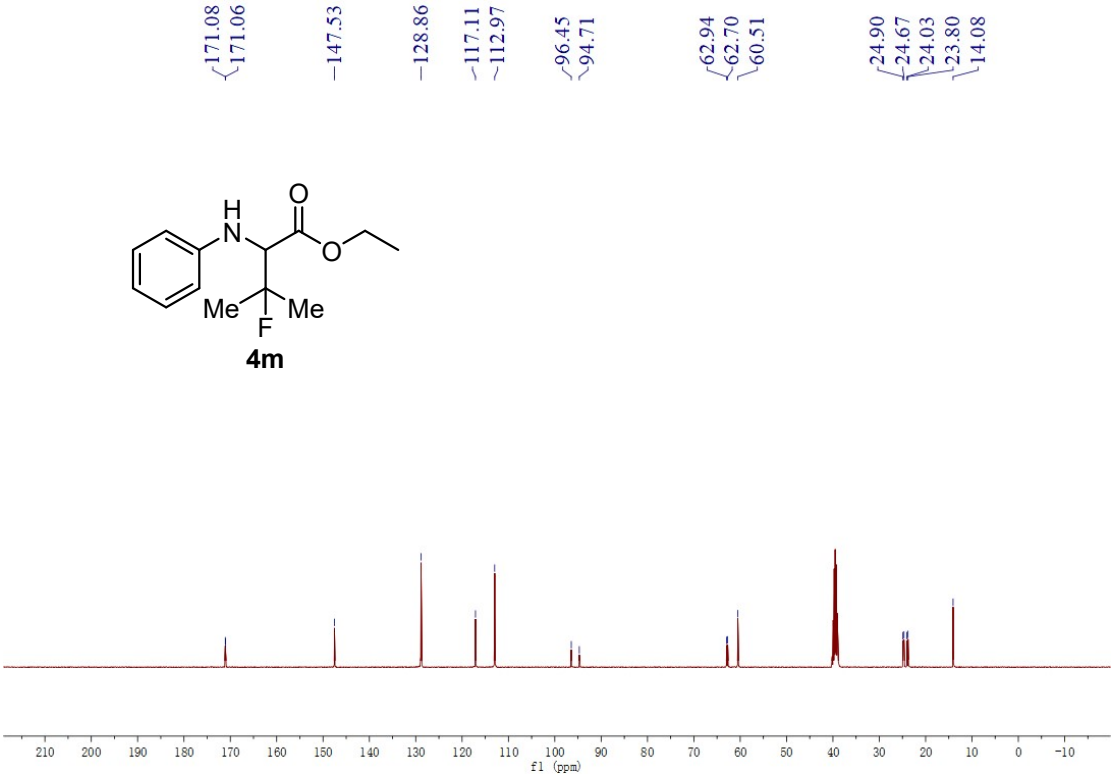
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4m:



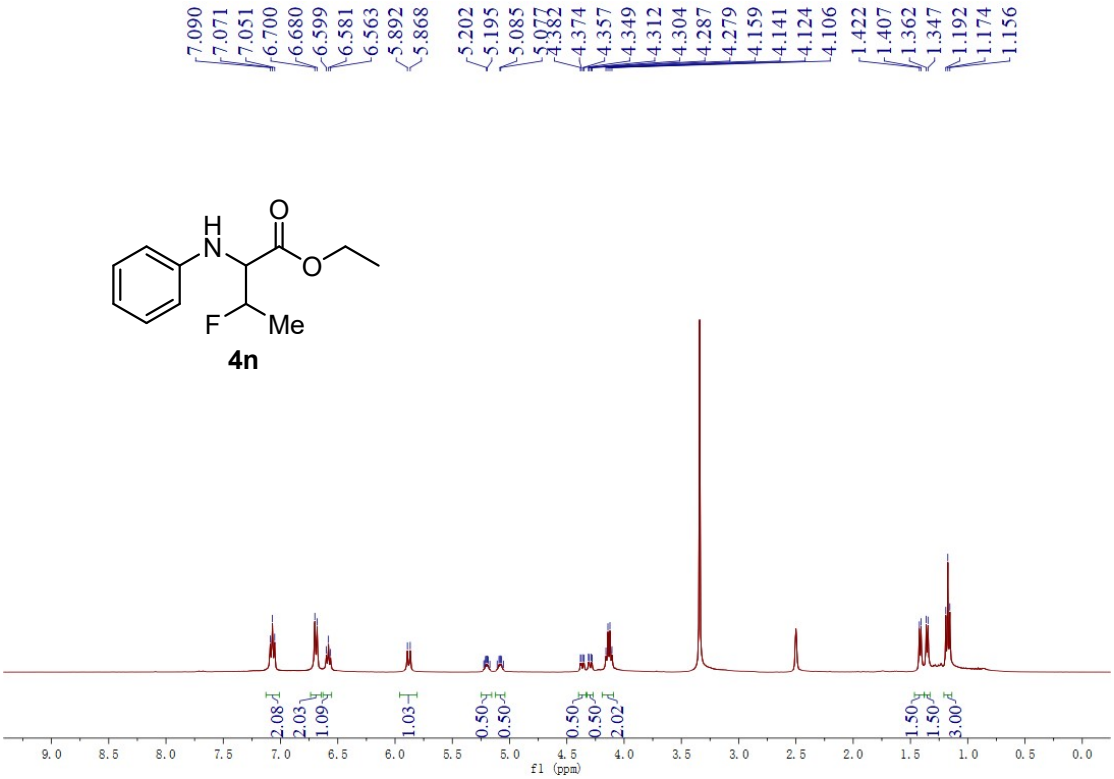
^{19}F NMR (DMSO-d_6, 376 MHz) spectrum of compound 4m:



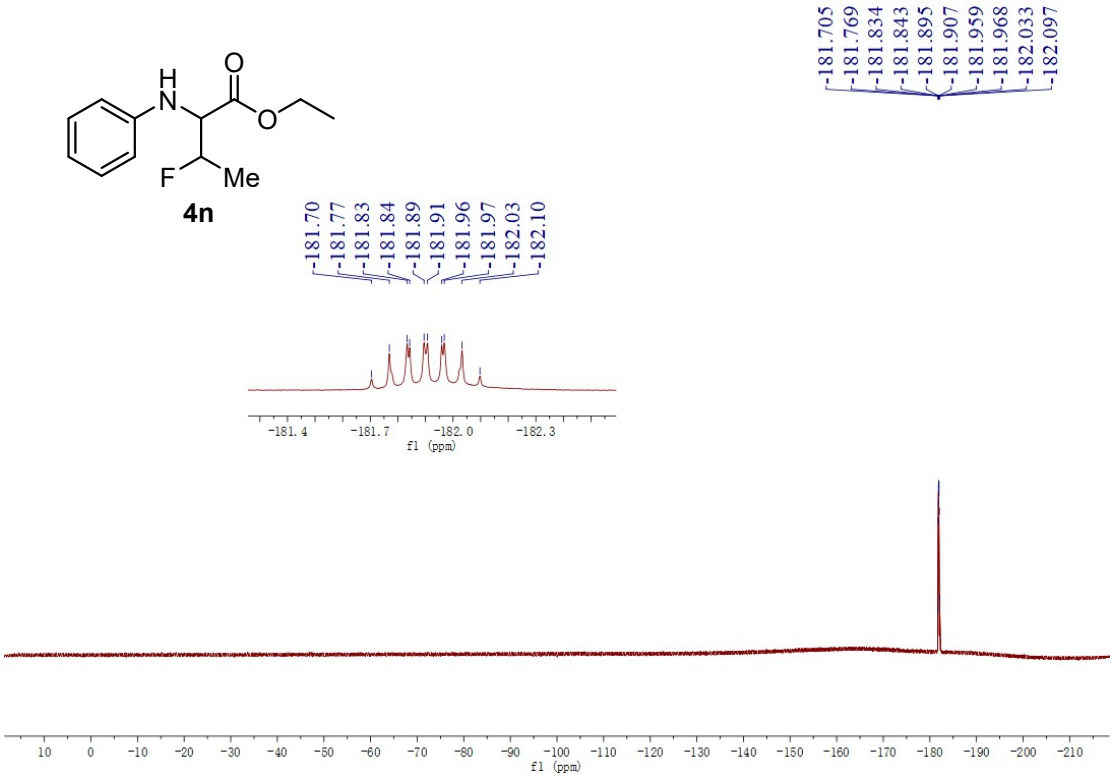
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 4m:



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound 4n:

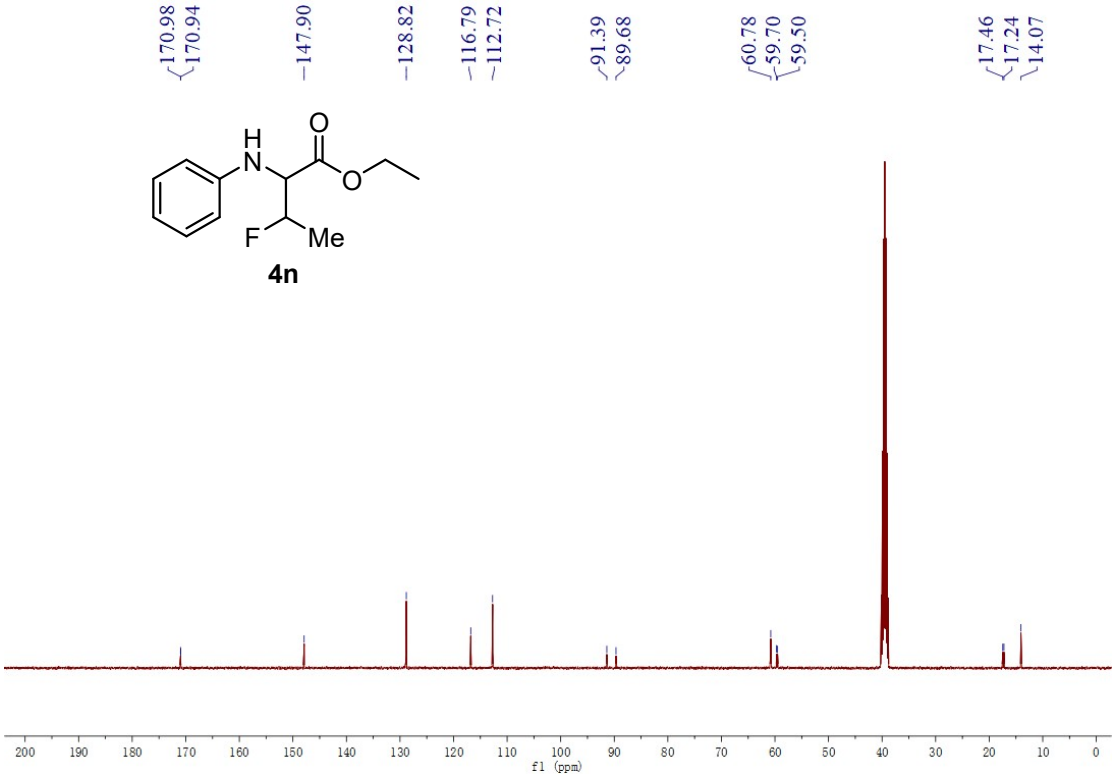


^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 4n:



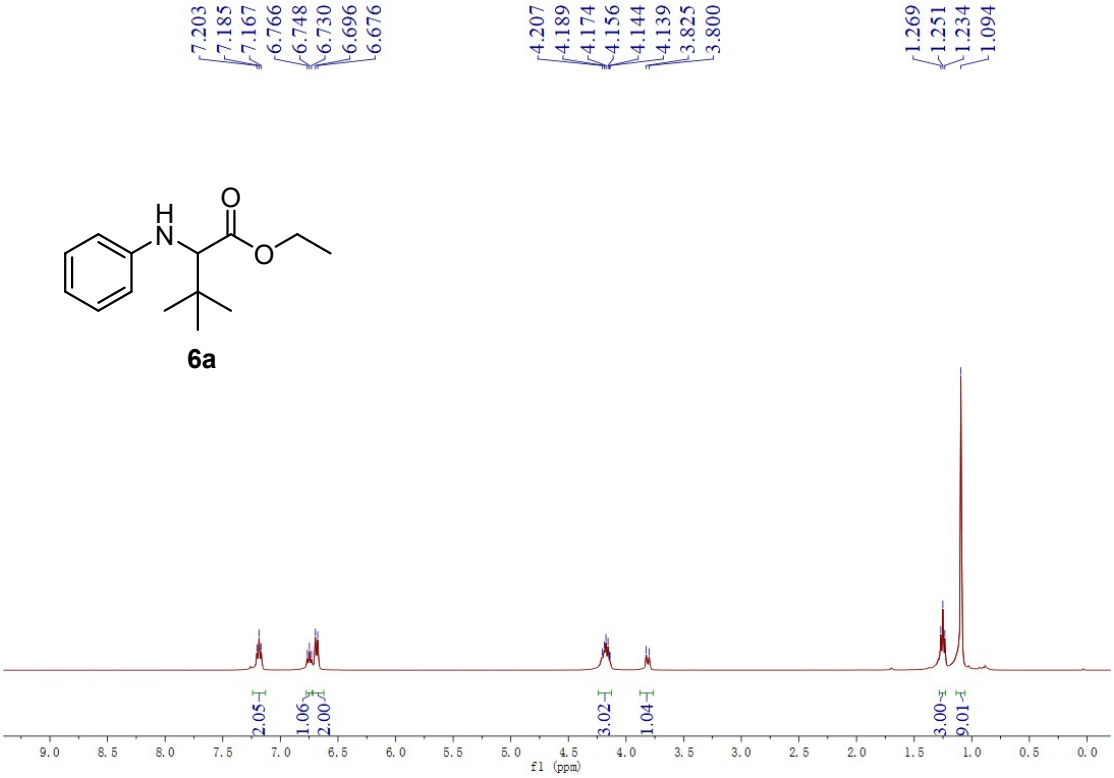
4n

^{13}C NMR (DMSO-d$_6$, 100 MHz) spectrum of compound 4n:

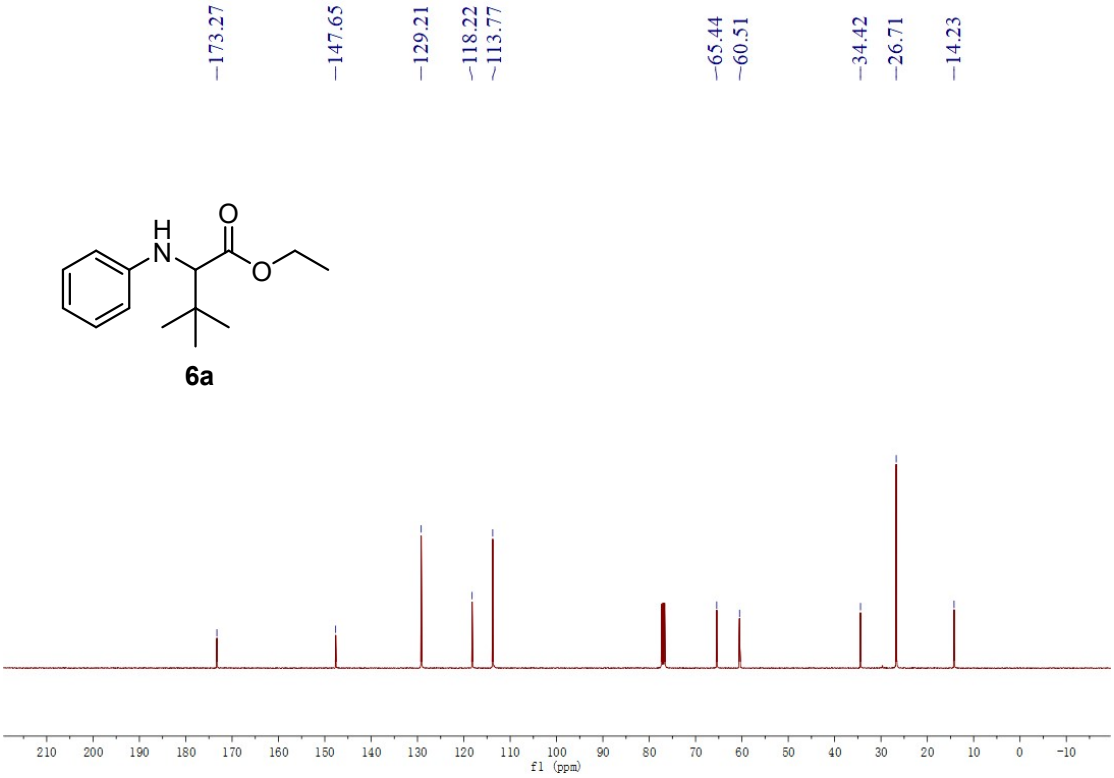


4n

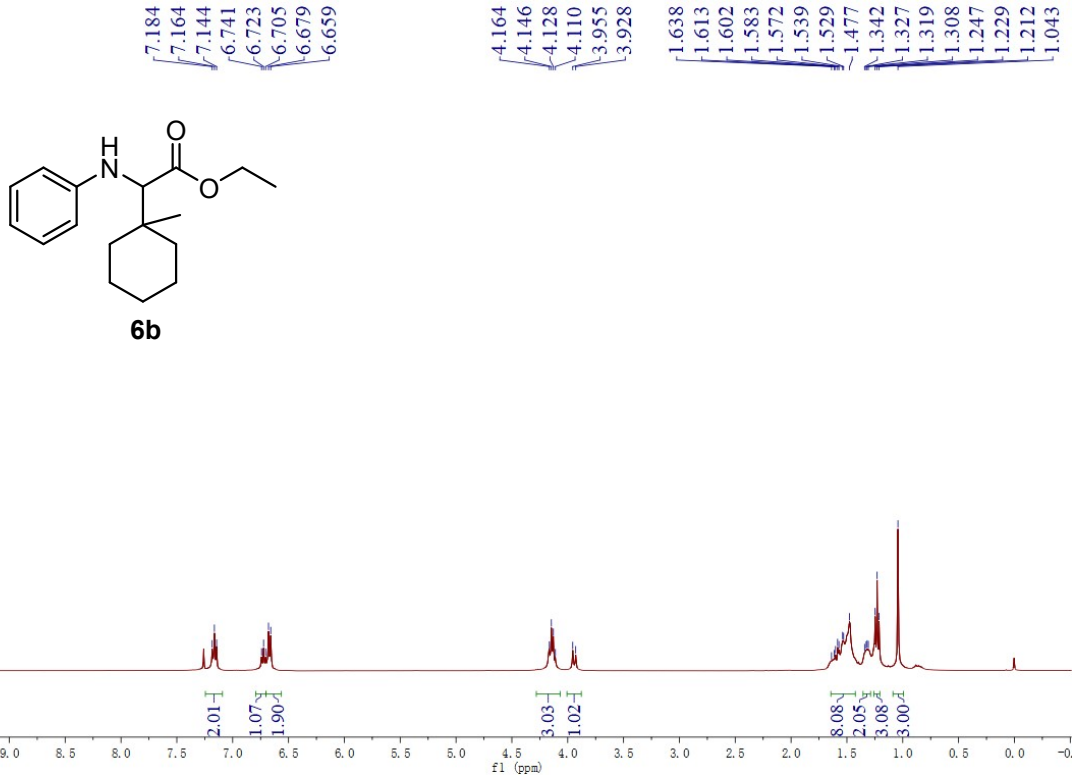
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6a:



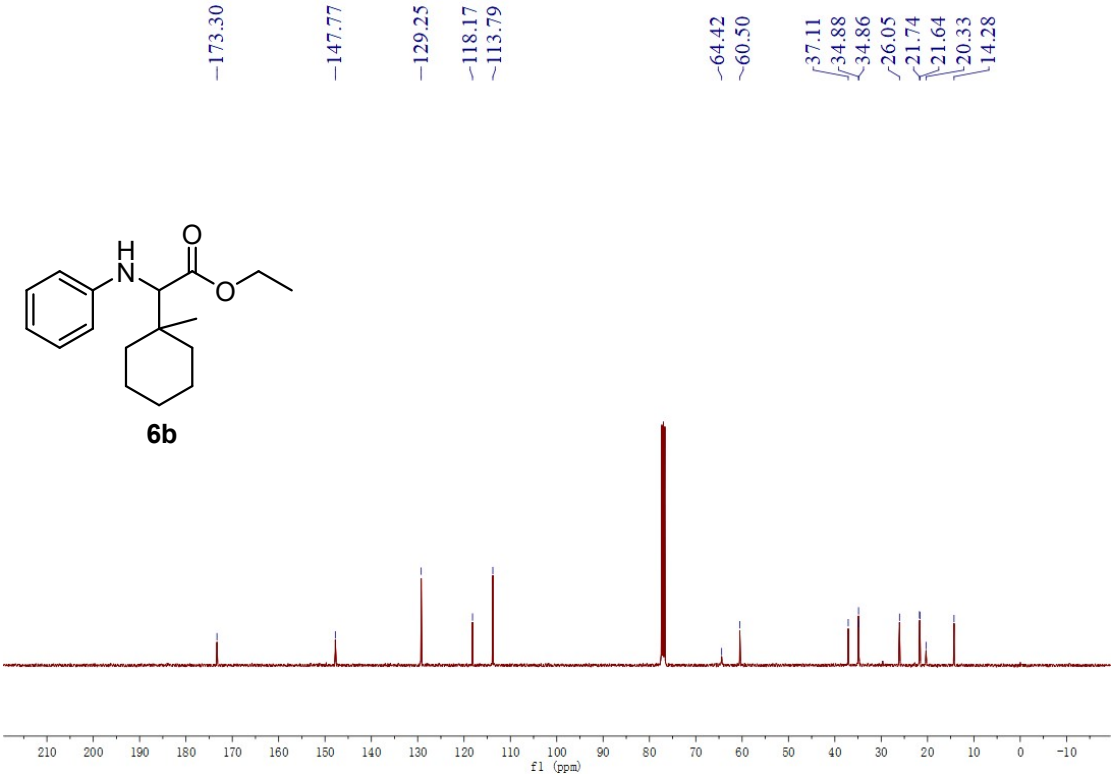
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6a:



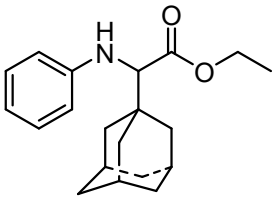
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6b:



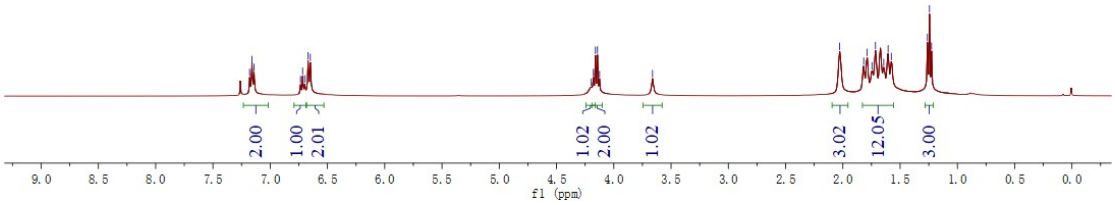
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6b:



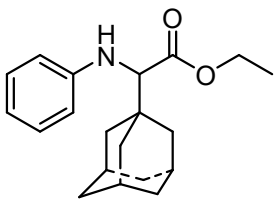
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6c:



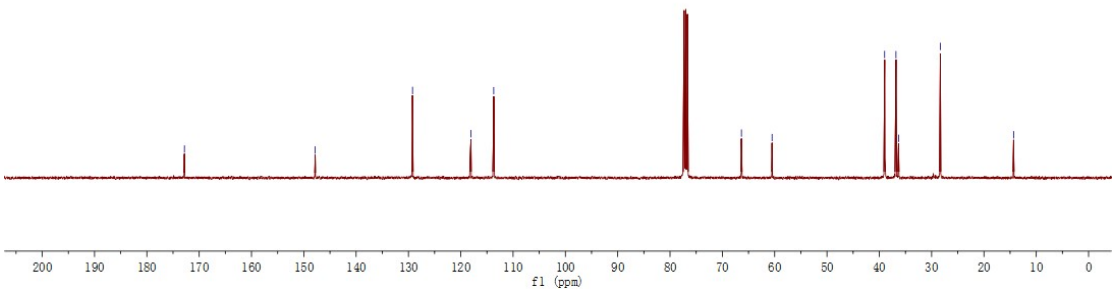
6c



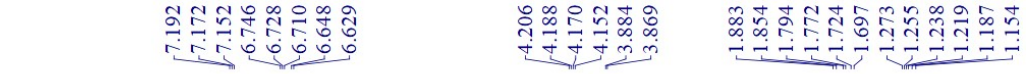
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6c:

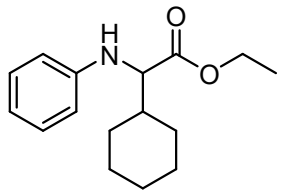


6c

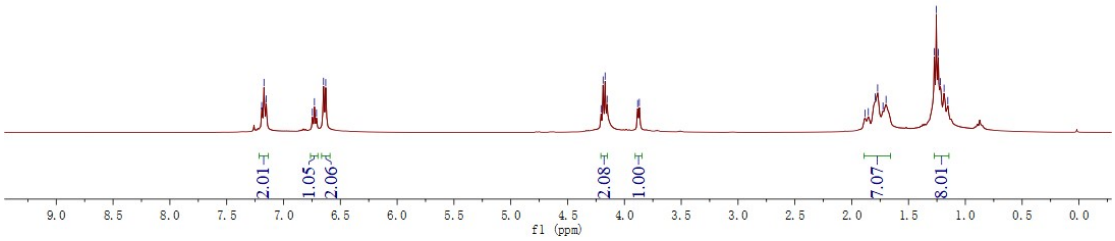


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6d:

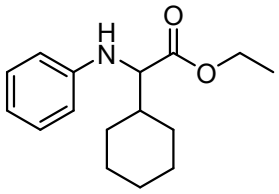




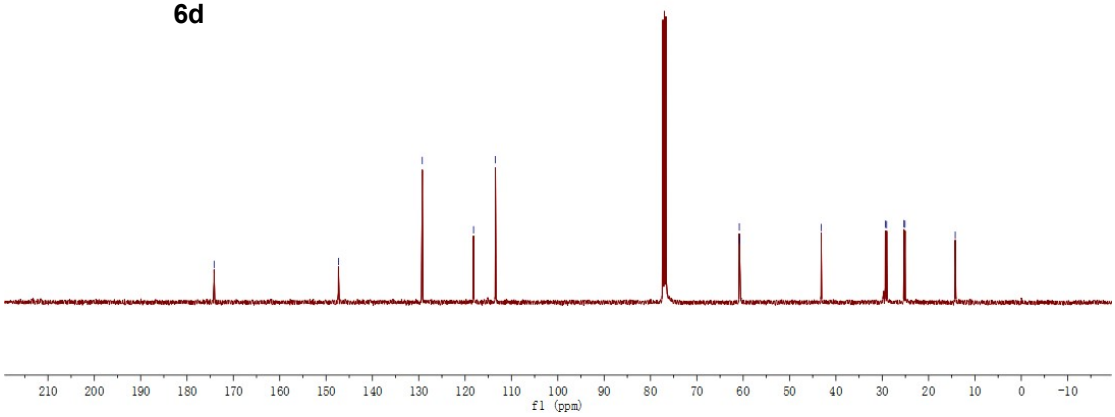
6d



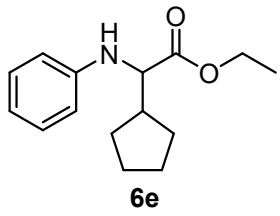
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6d:



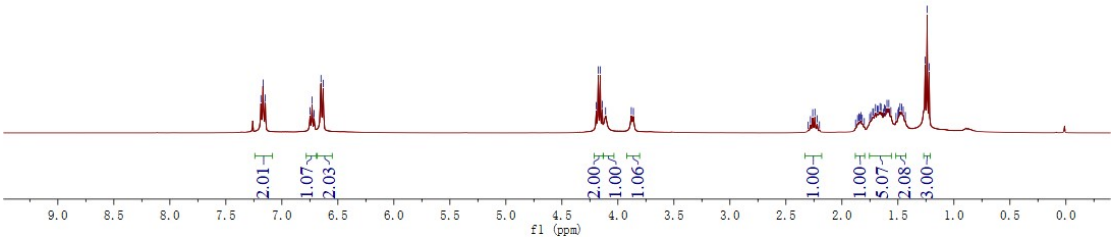
6d



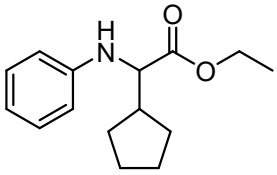
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6e:



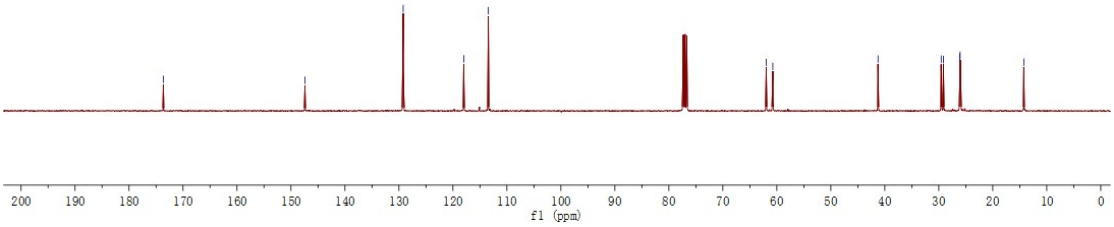
6e



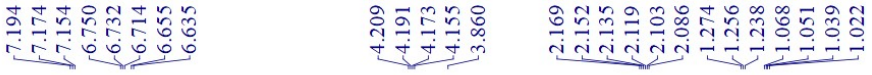
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6e:

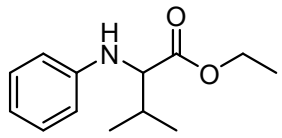


6e

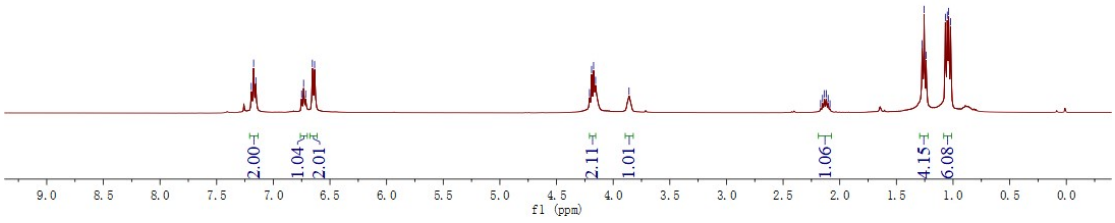


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6f:

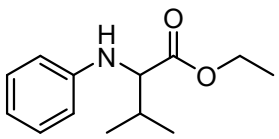




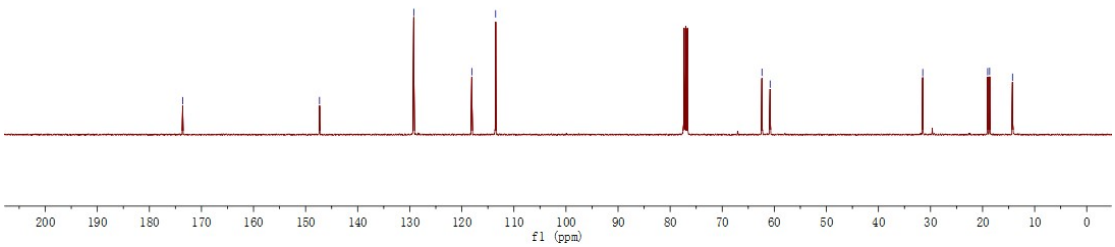
6f



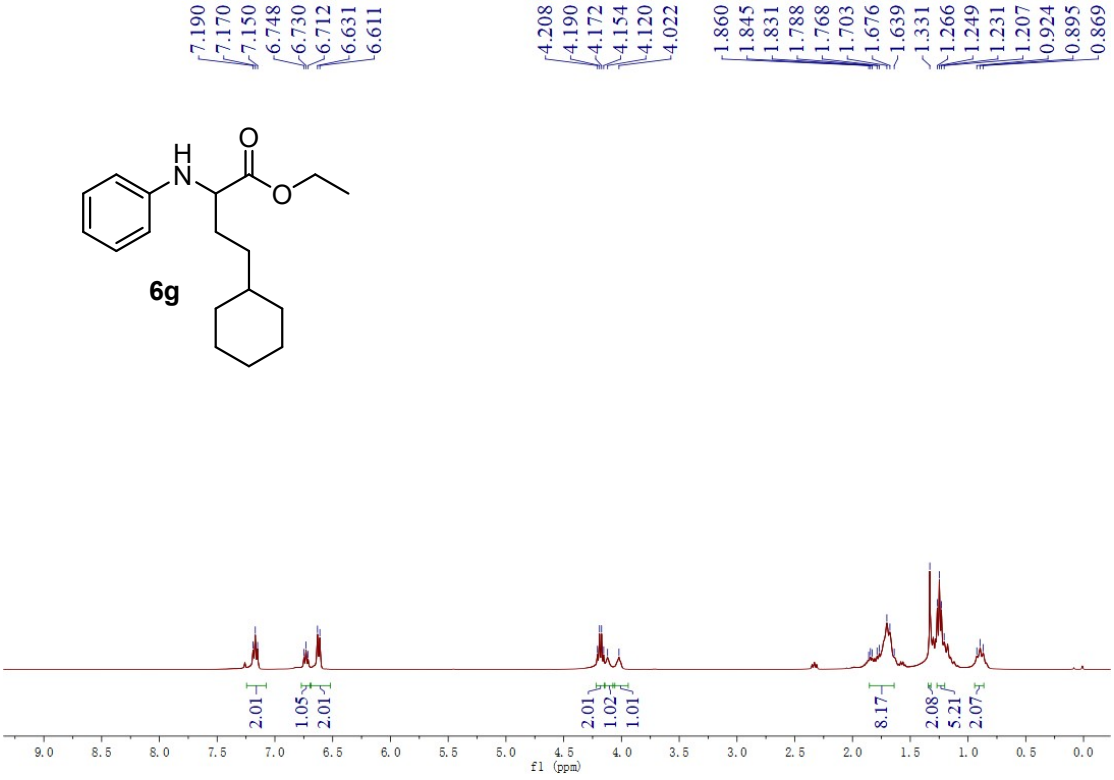
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6f:



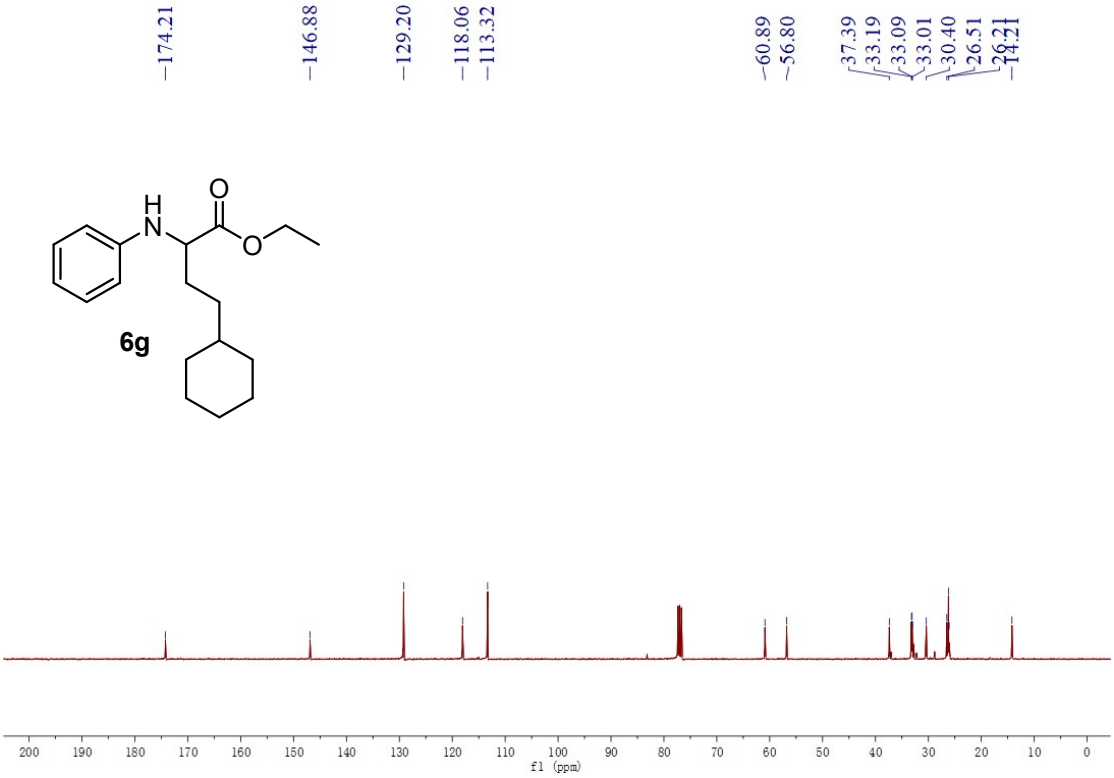
6f



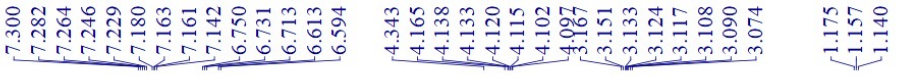
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6g:

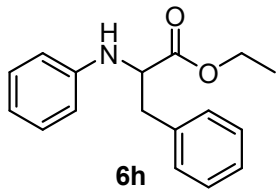


^{1}H NMR ($CDCl_3$, 100 MHz) spectrum of compound 6g:

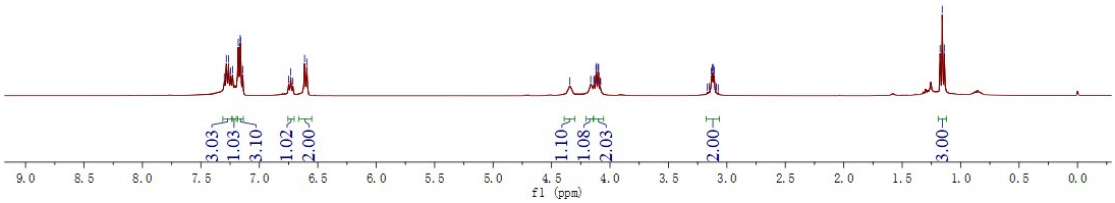


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 6h:

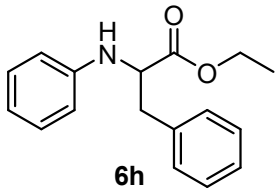




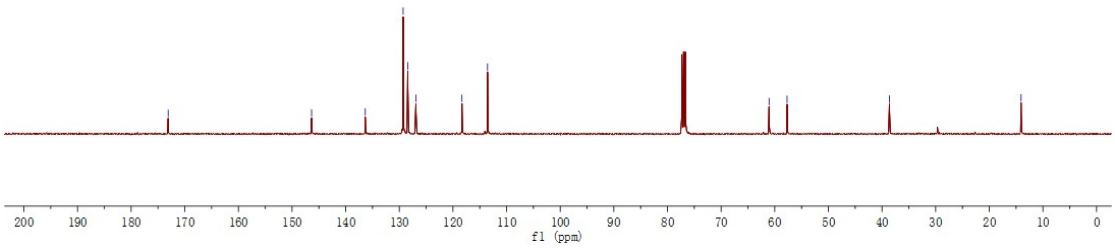
6h



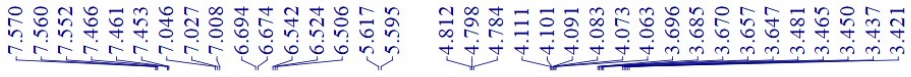
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 6h:

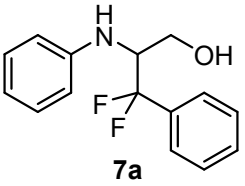


6h

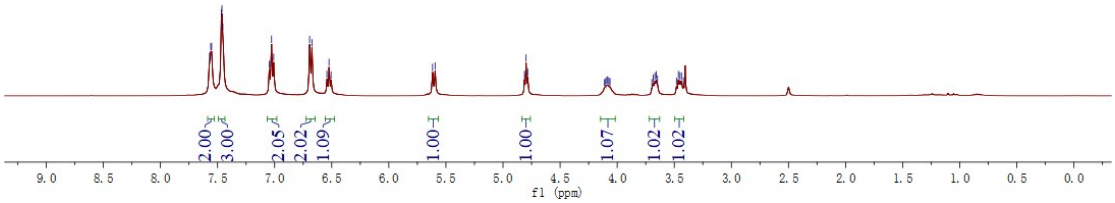


^{1}H NMR (DMSO-d$_6$, 400 MHz) spectrum of compound 7a:

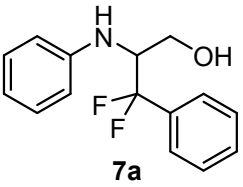




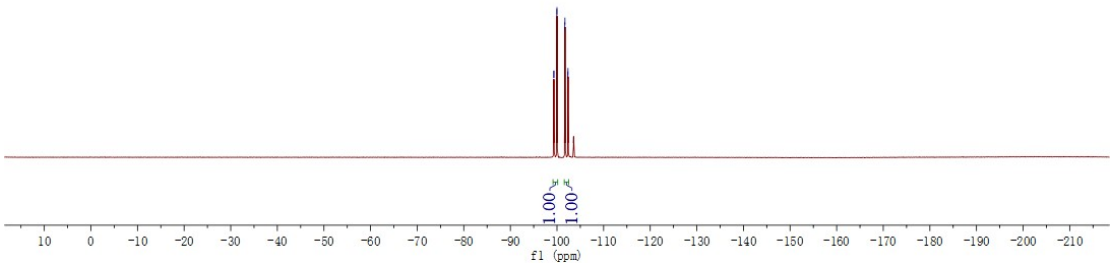
7a



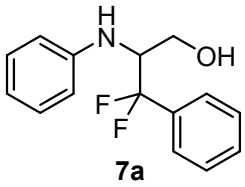
^{19}F NMR (DMSO-d$_6$, 376 MHz) spectrum of compound 7a:



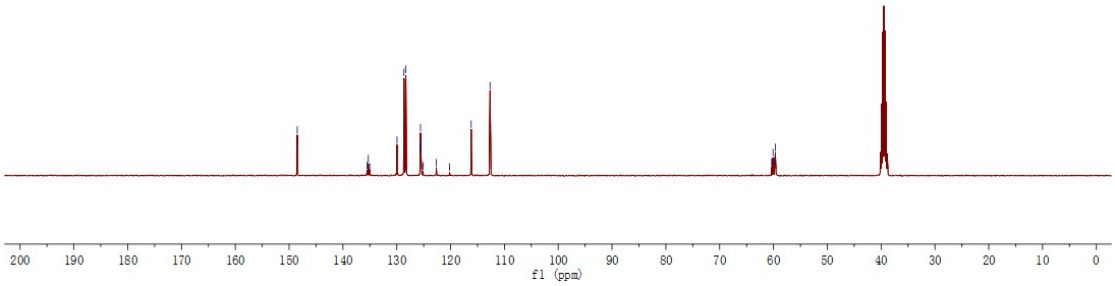
7a



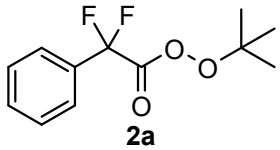
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound 7a:



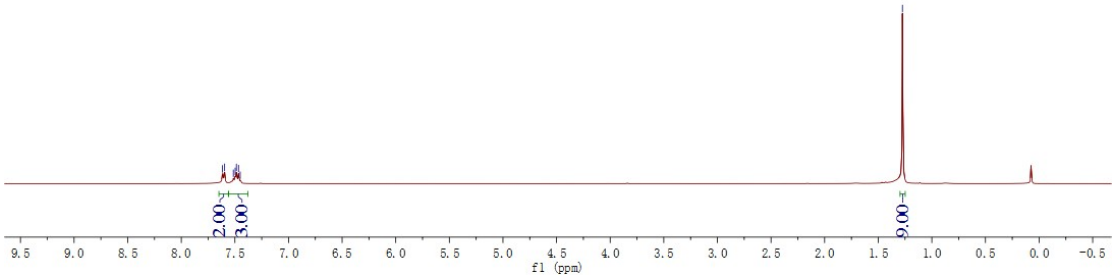
7a



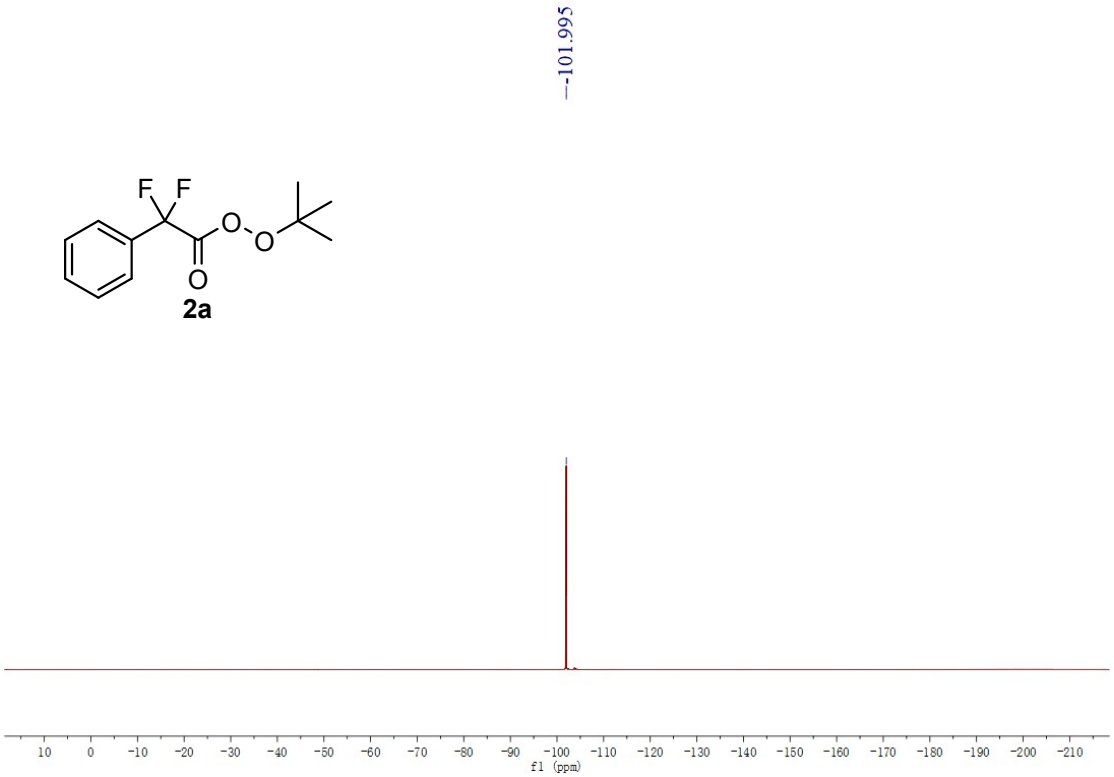
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2a:



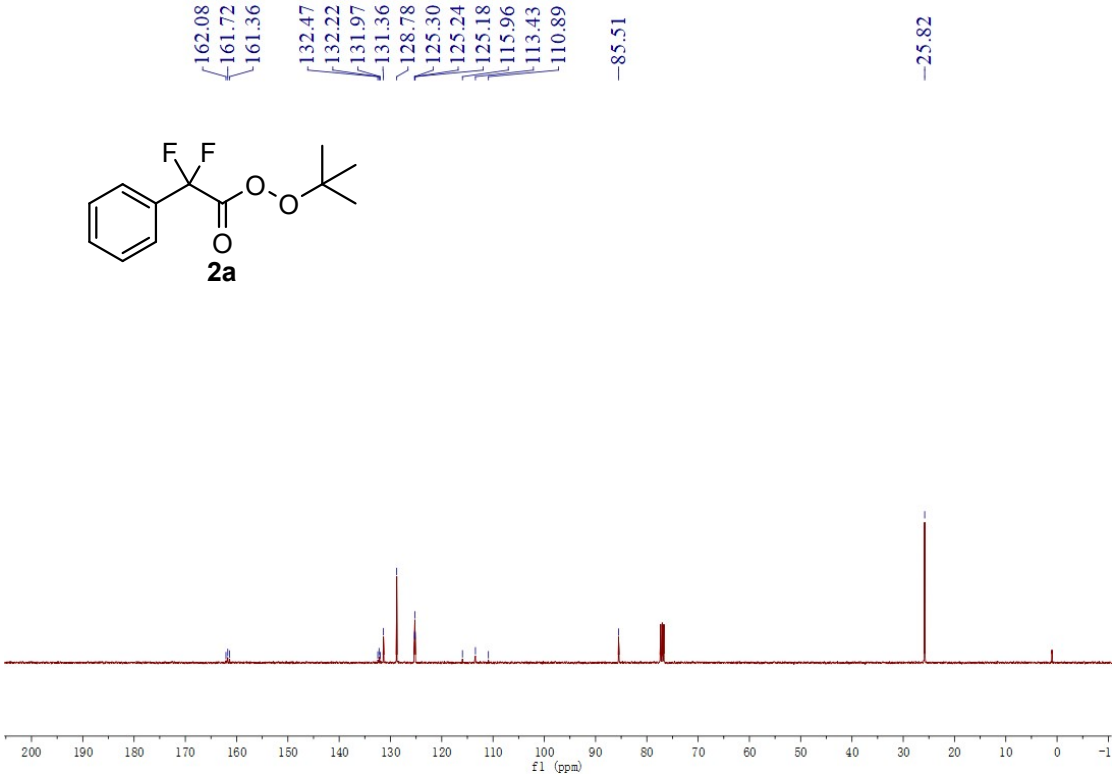
2a



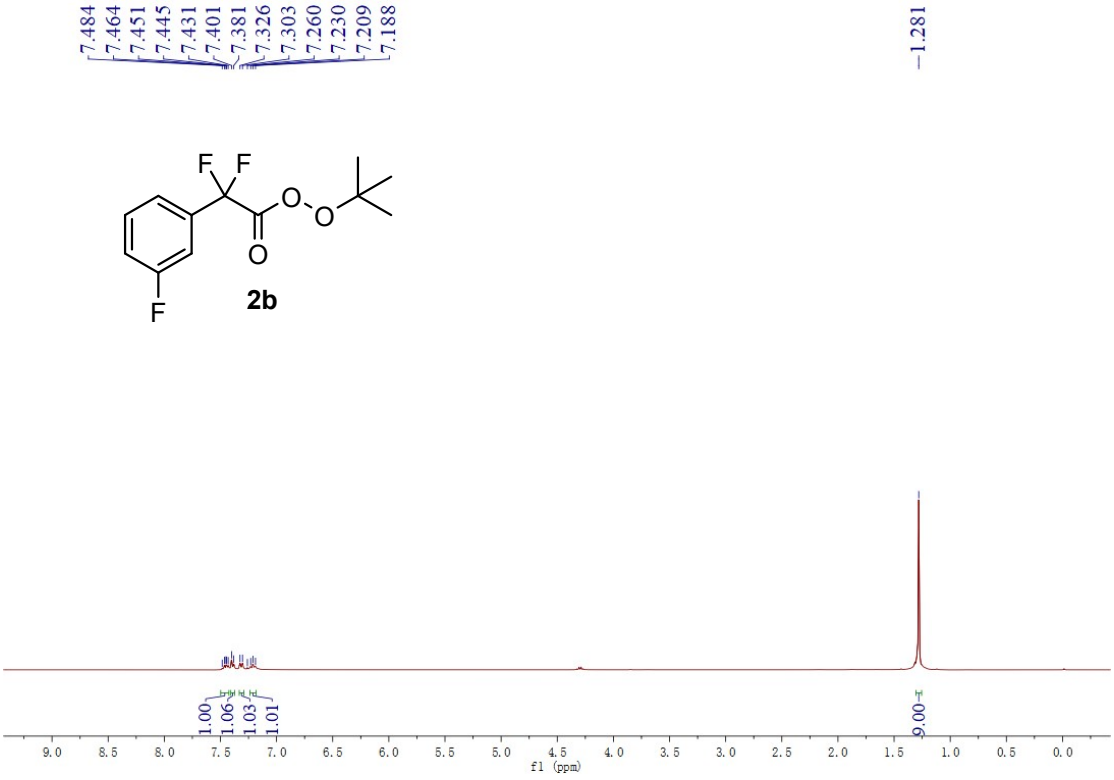
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2a:



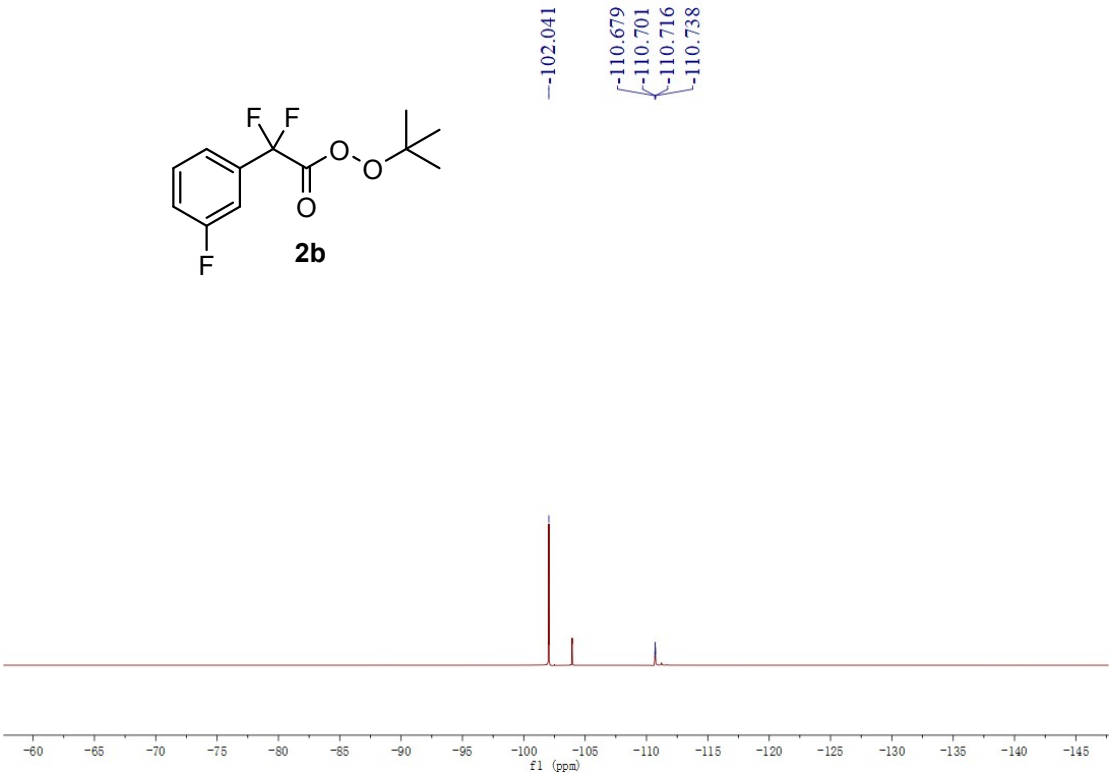
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2a:



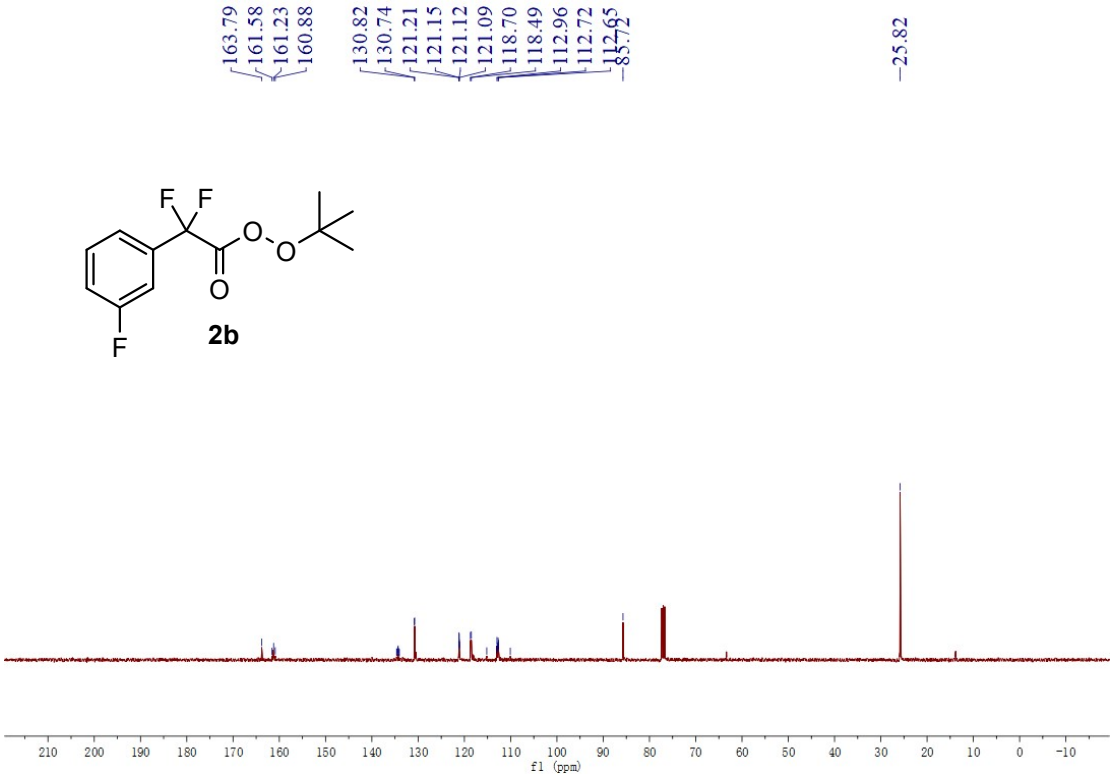
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2b:



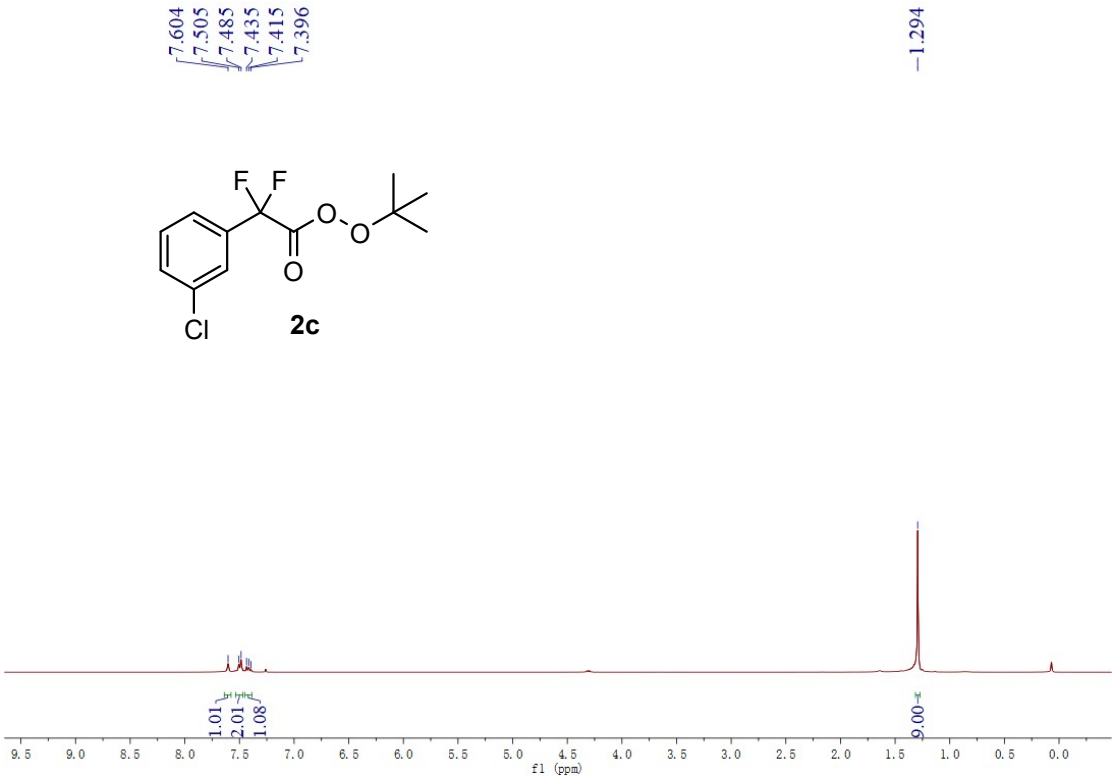
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2b:



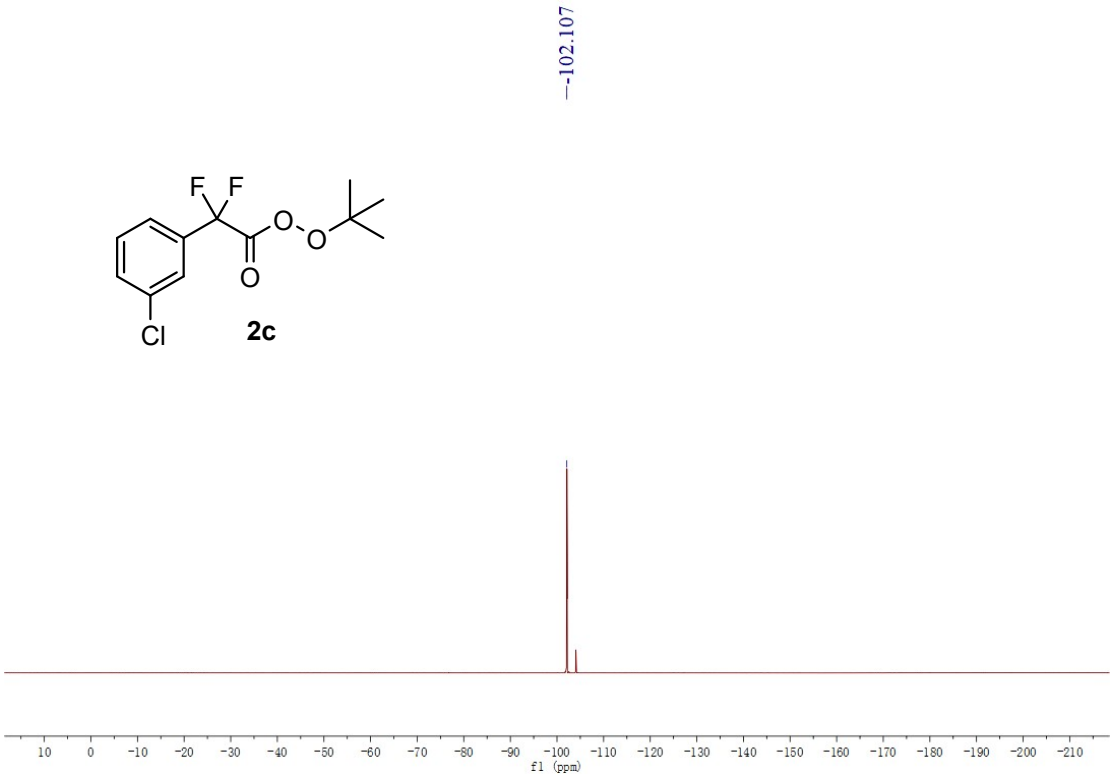
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2b:



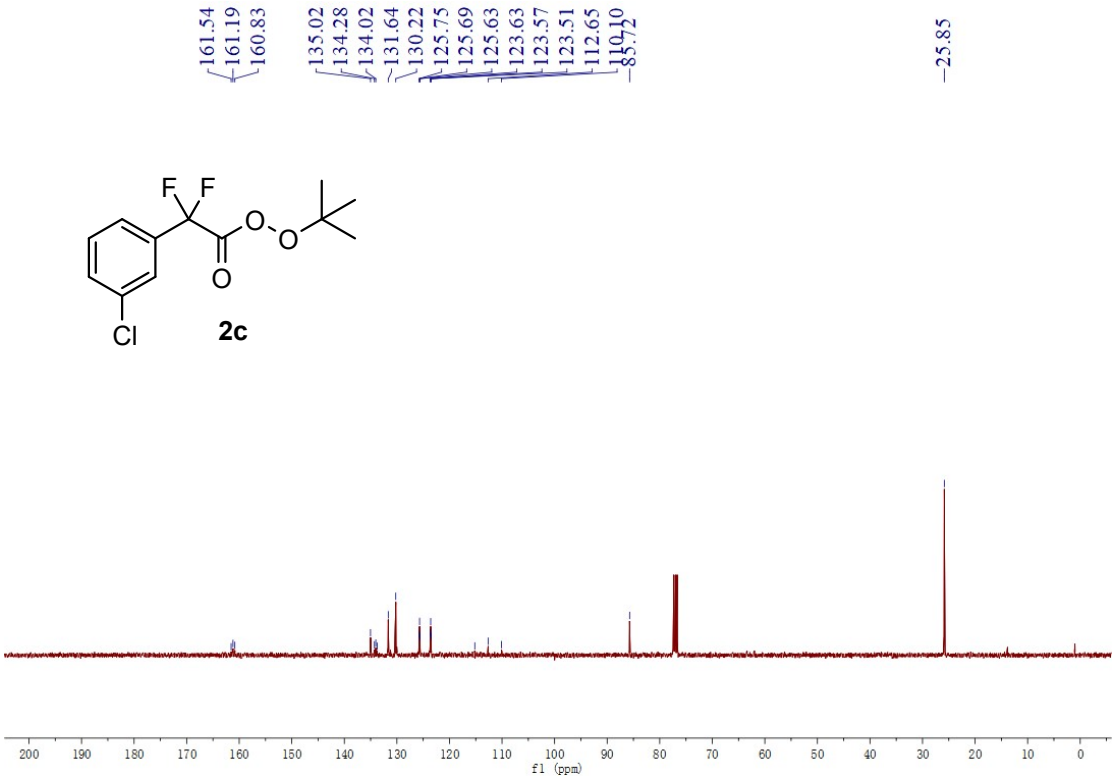
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2c:



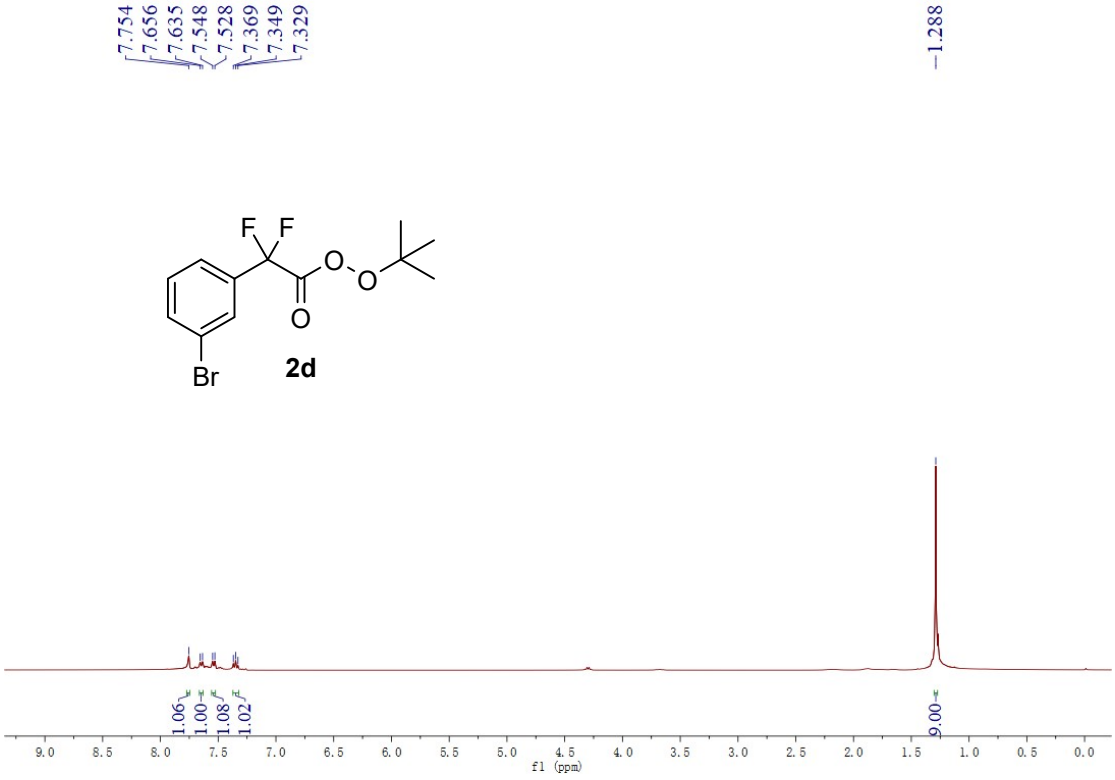
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2c:



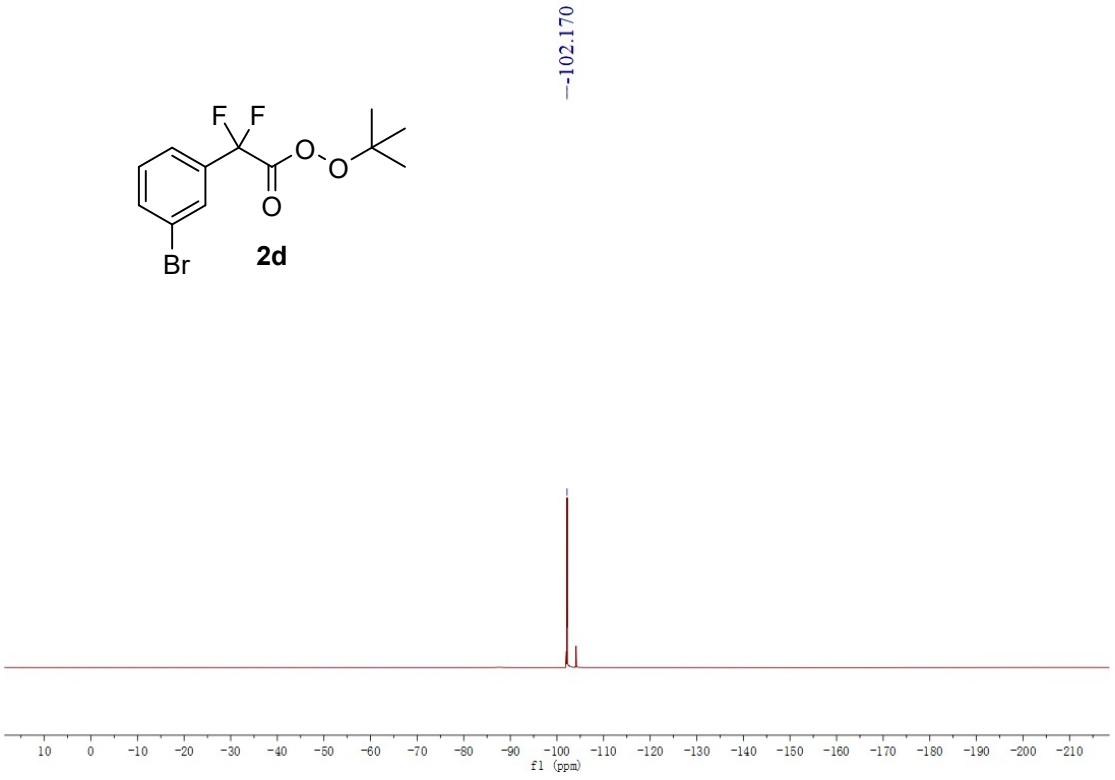
^{1}H NMR ($CDCl_3$, 100 MHz) spectrum of compound 2c:



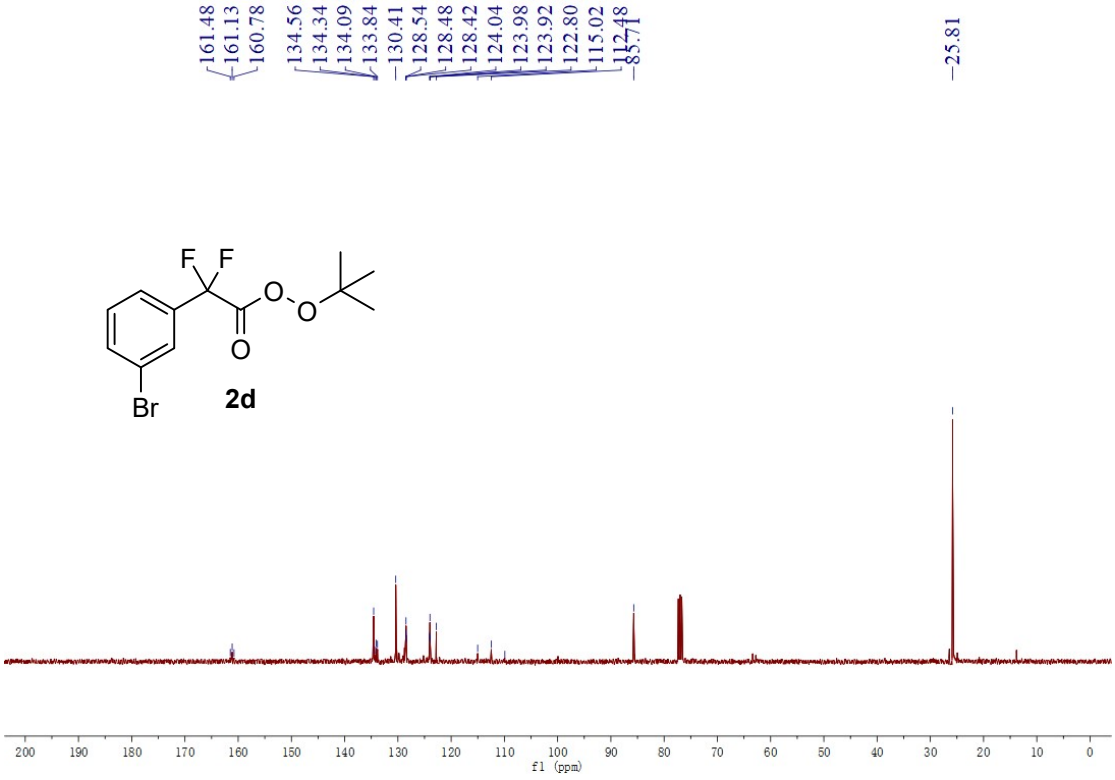
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2d:



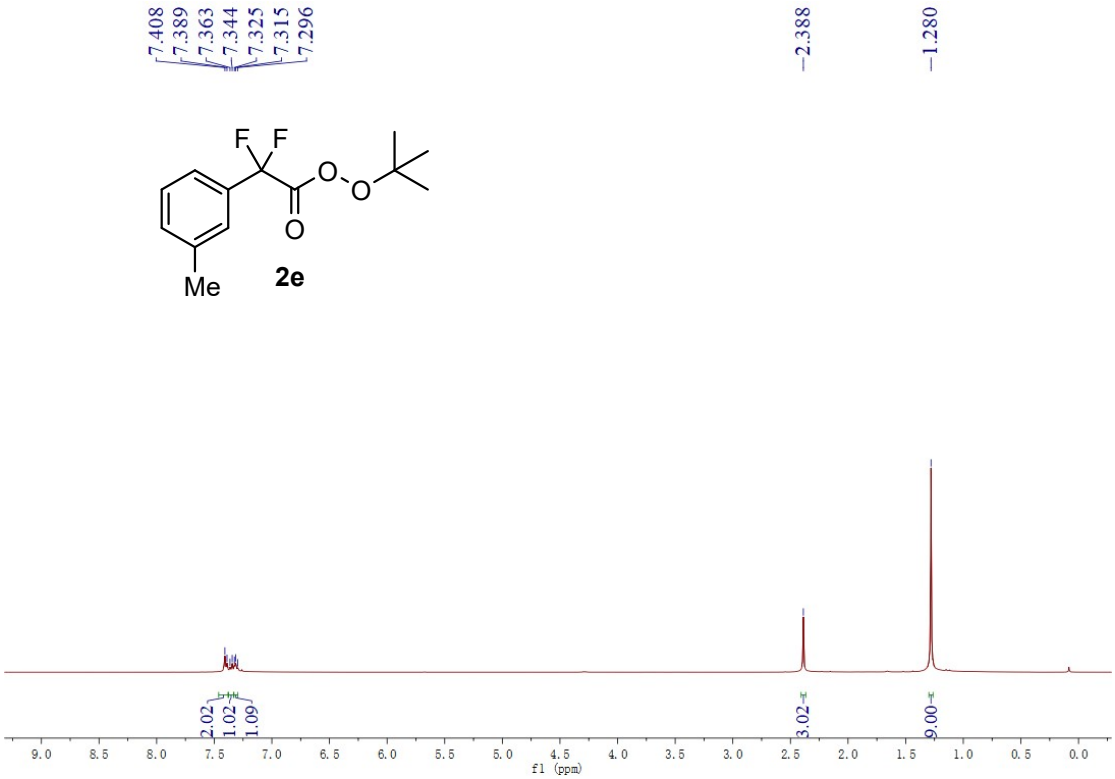
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2d:



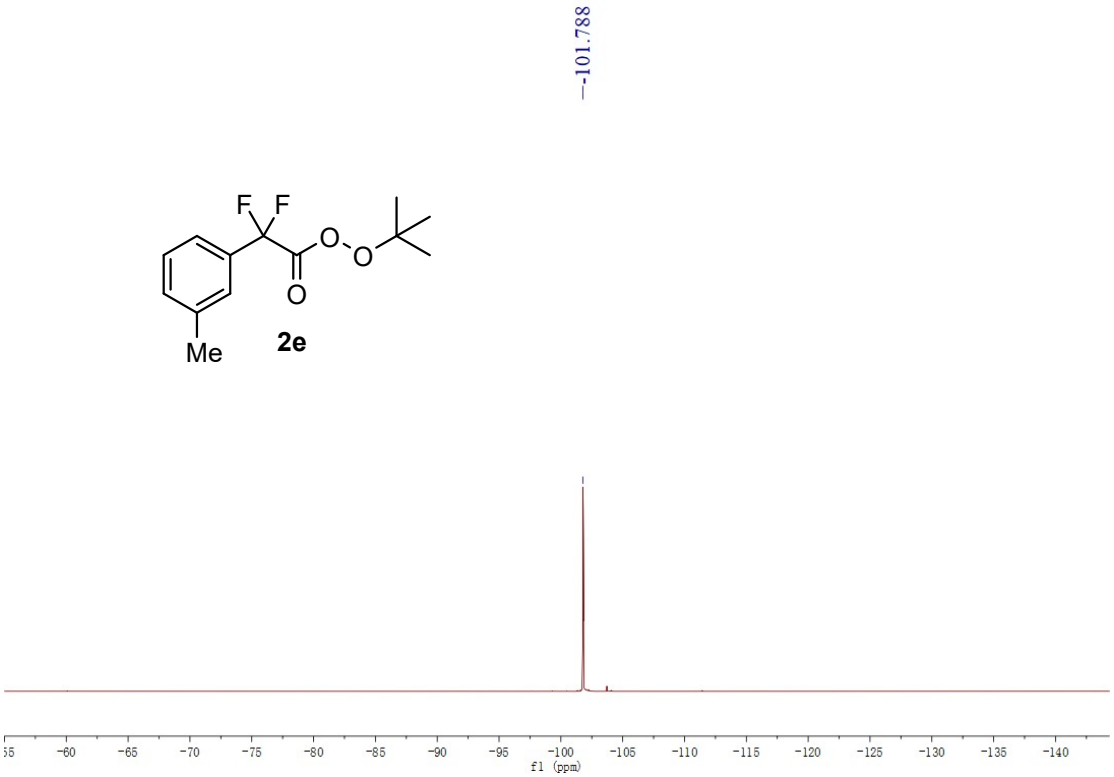
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2d:



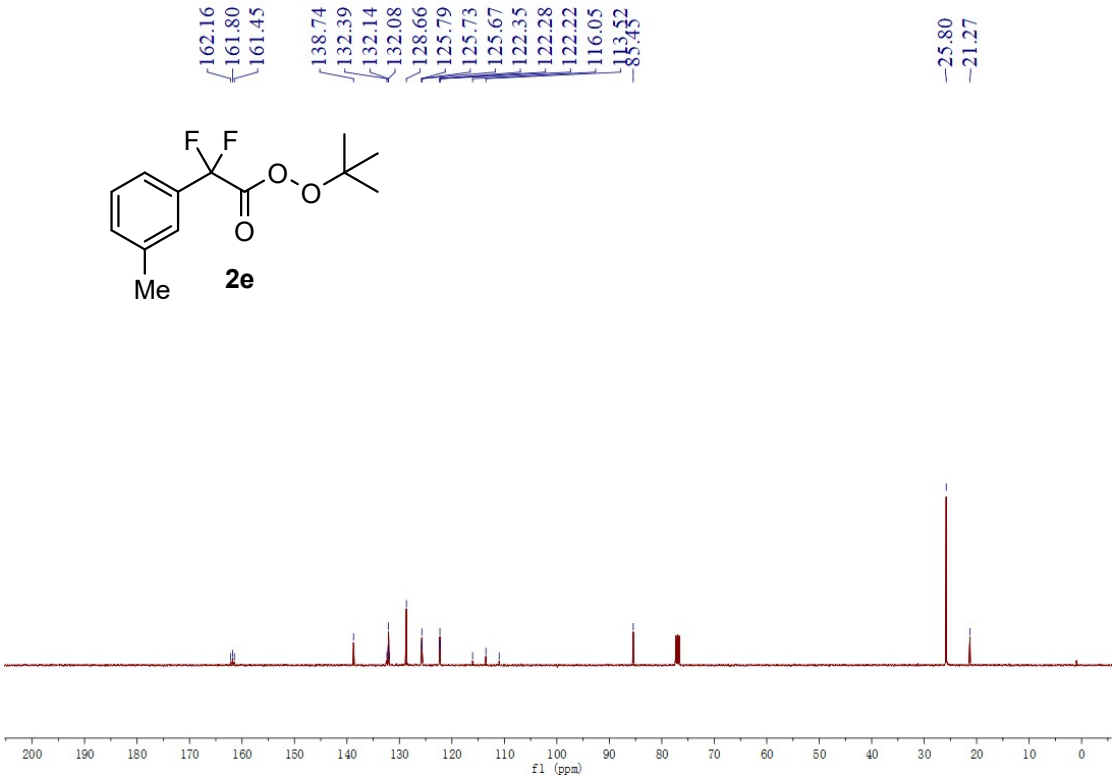
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2e:



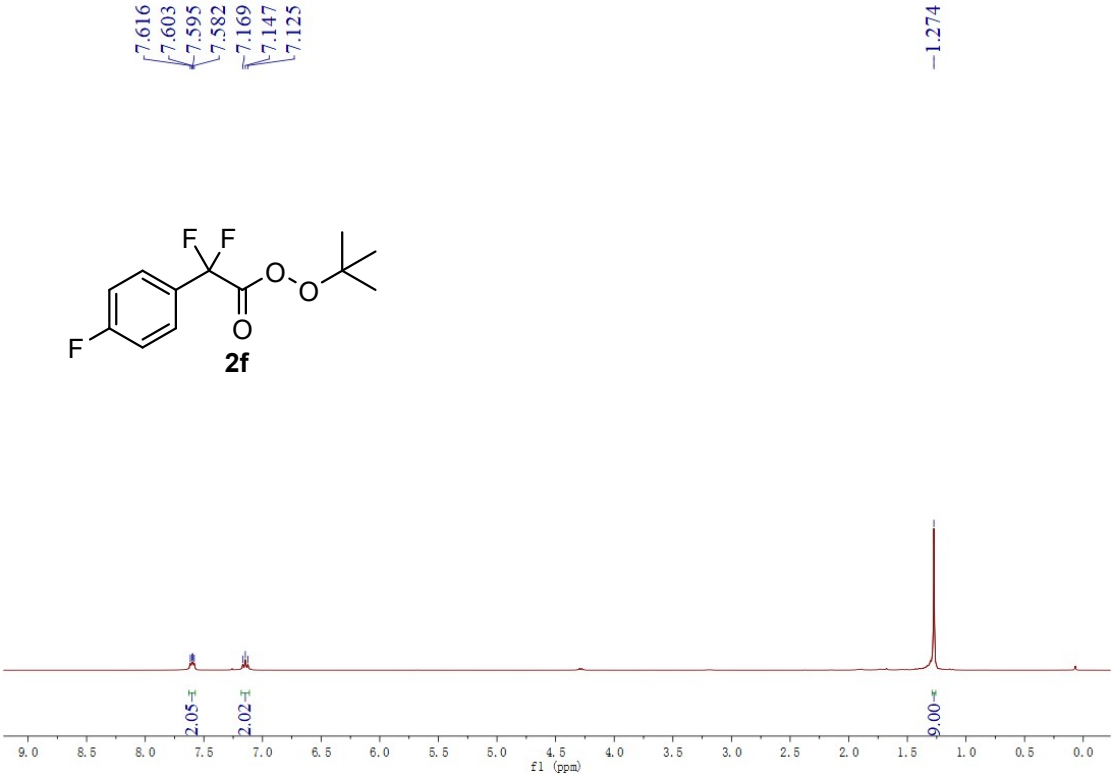
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2e:



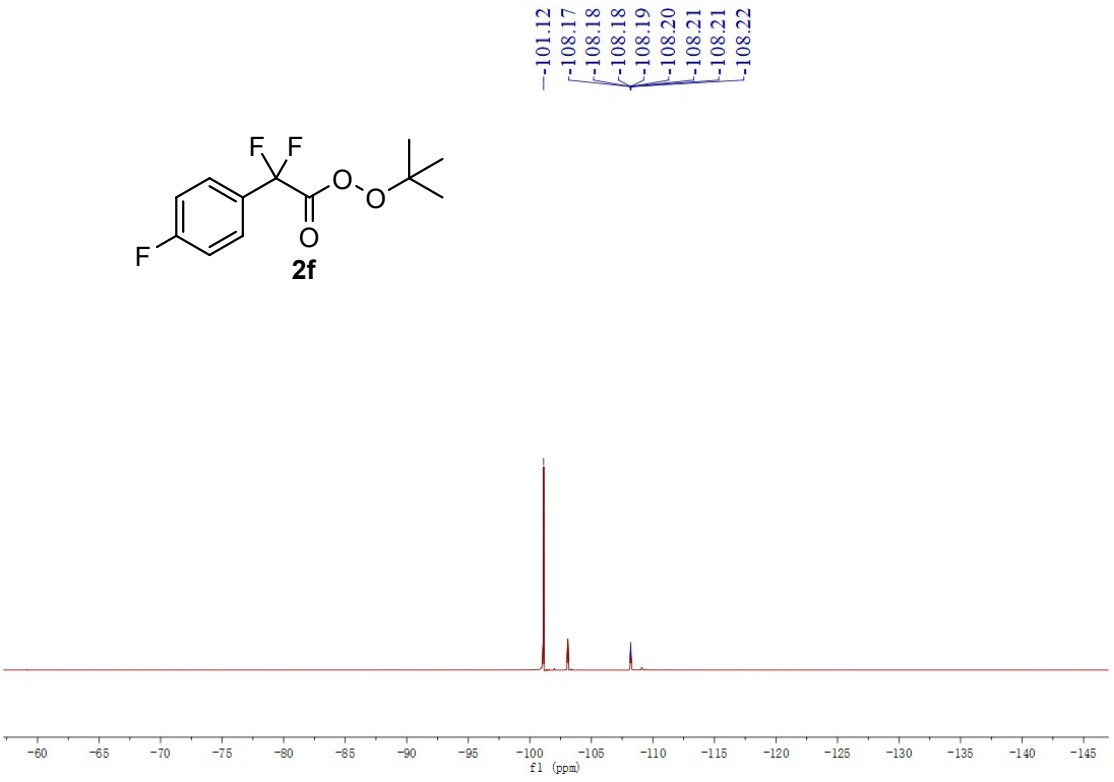
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2e:



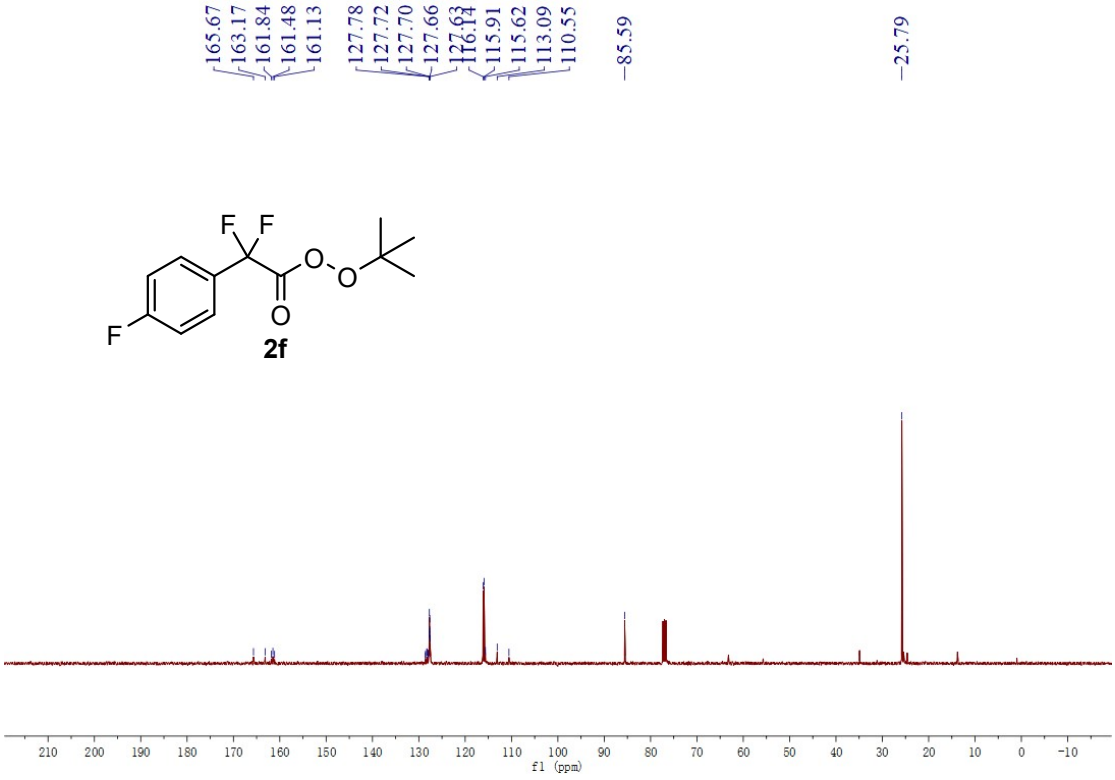
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2f:



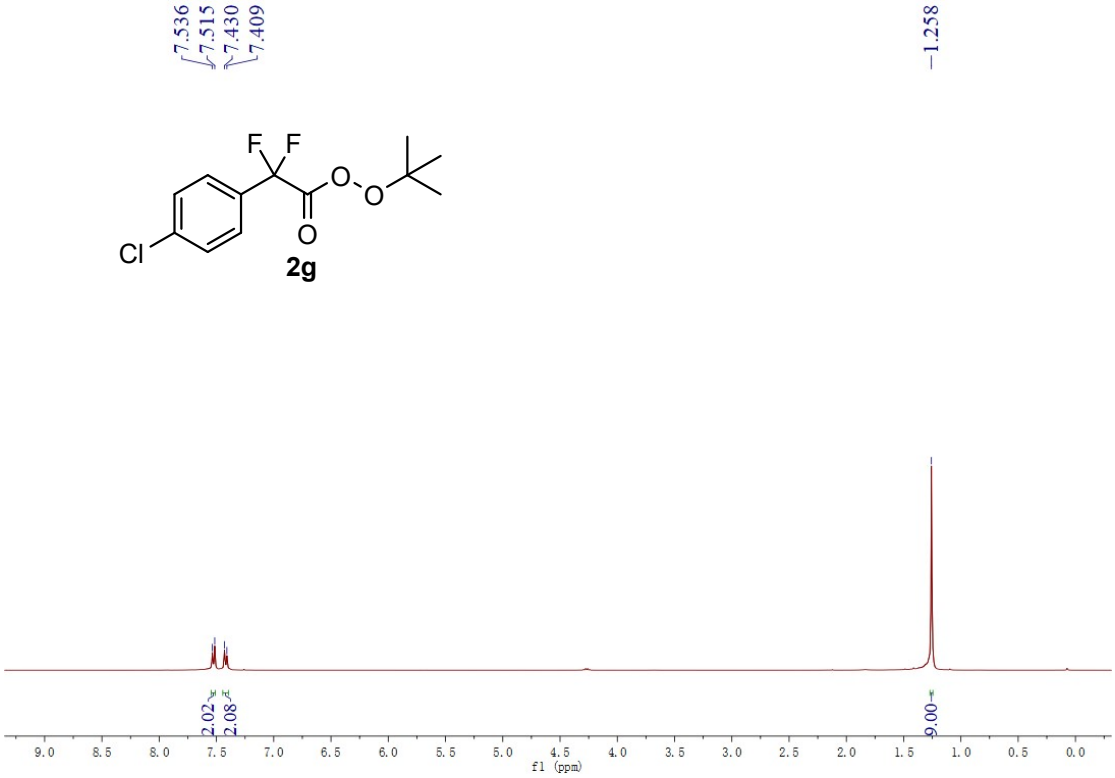
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2f:



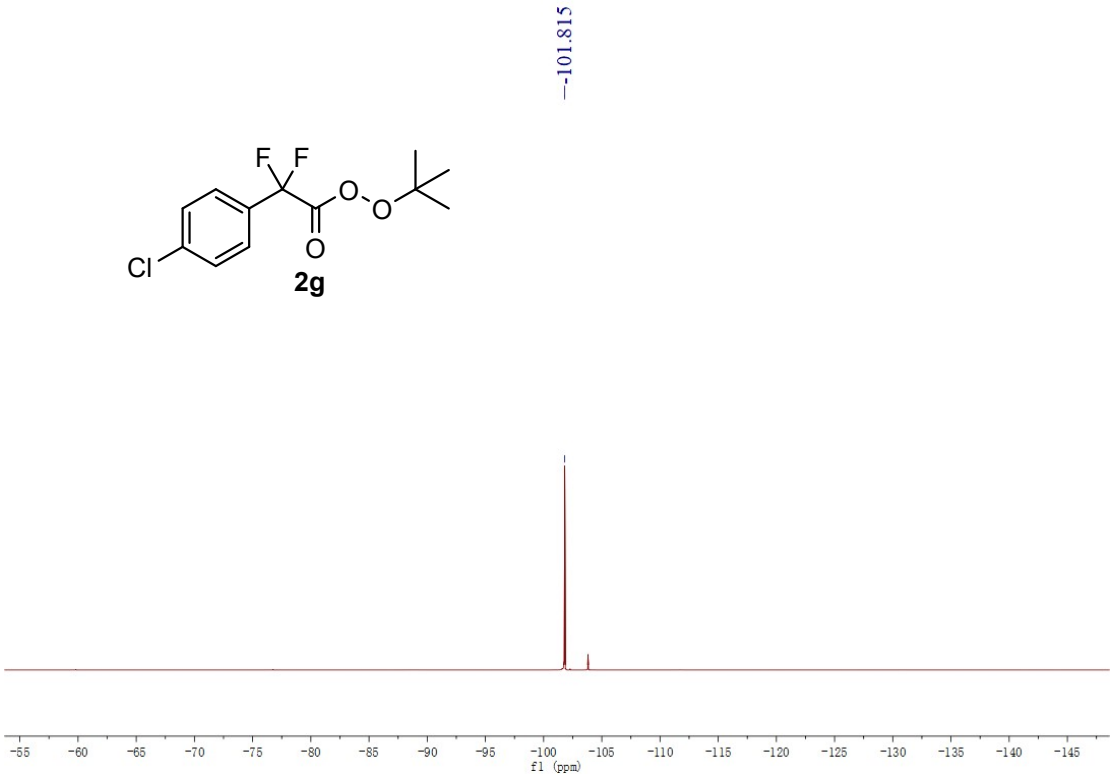
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2f:



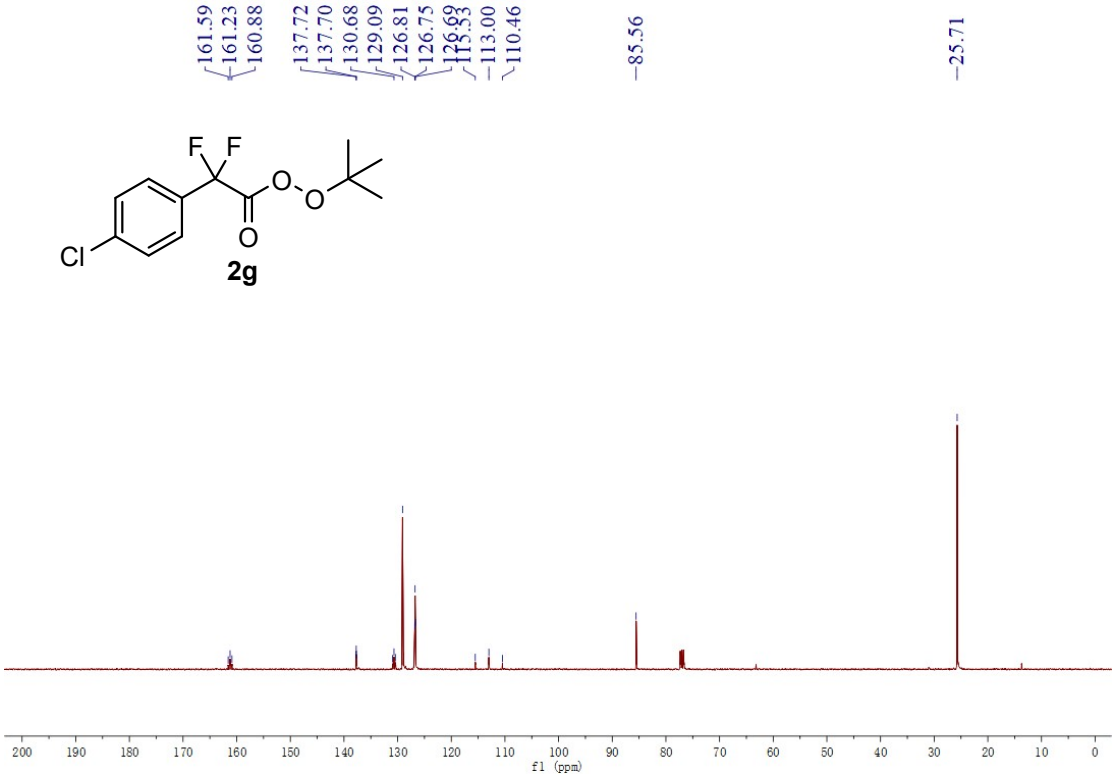
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2g:



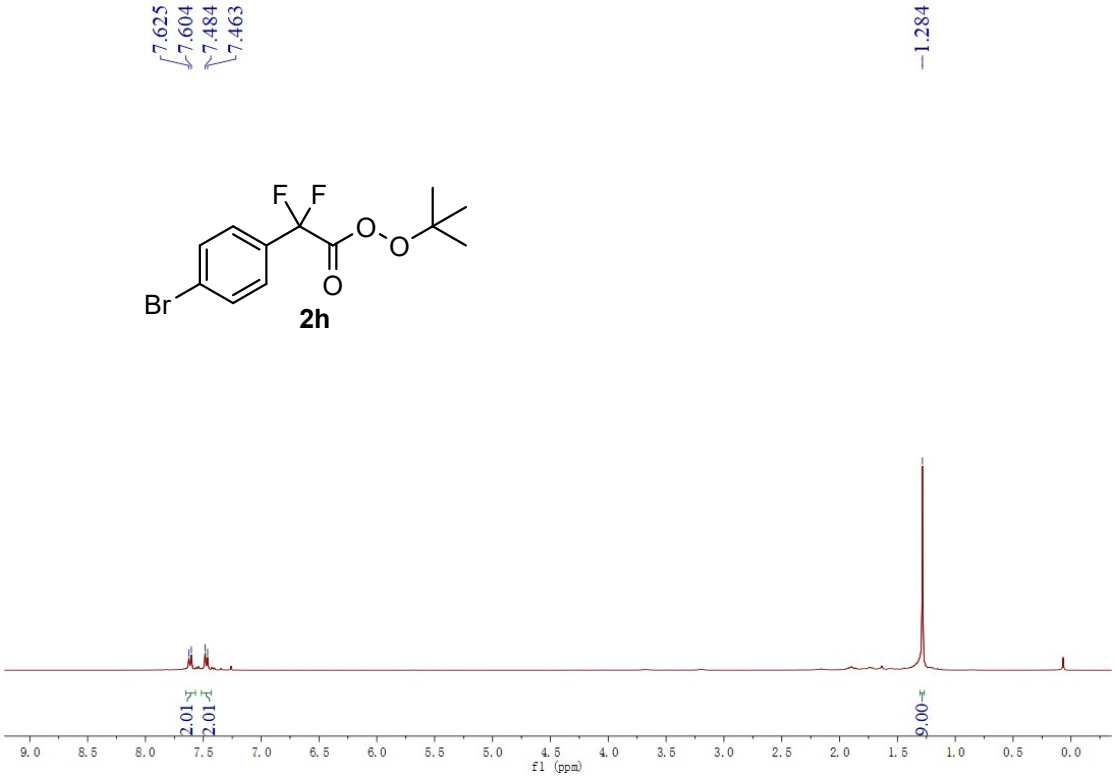
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2g:



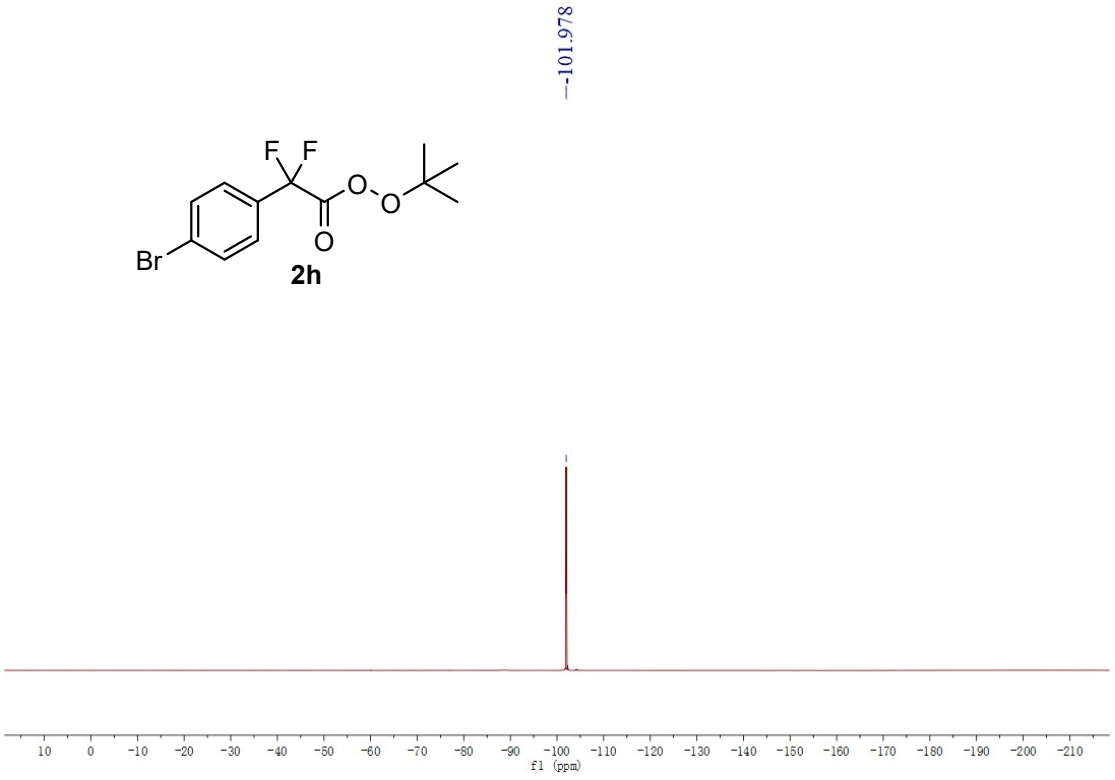
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2g:



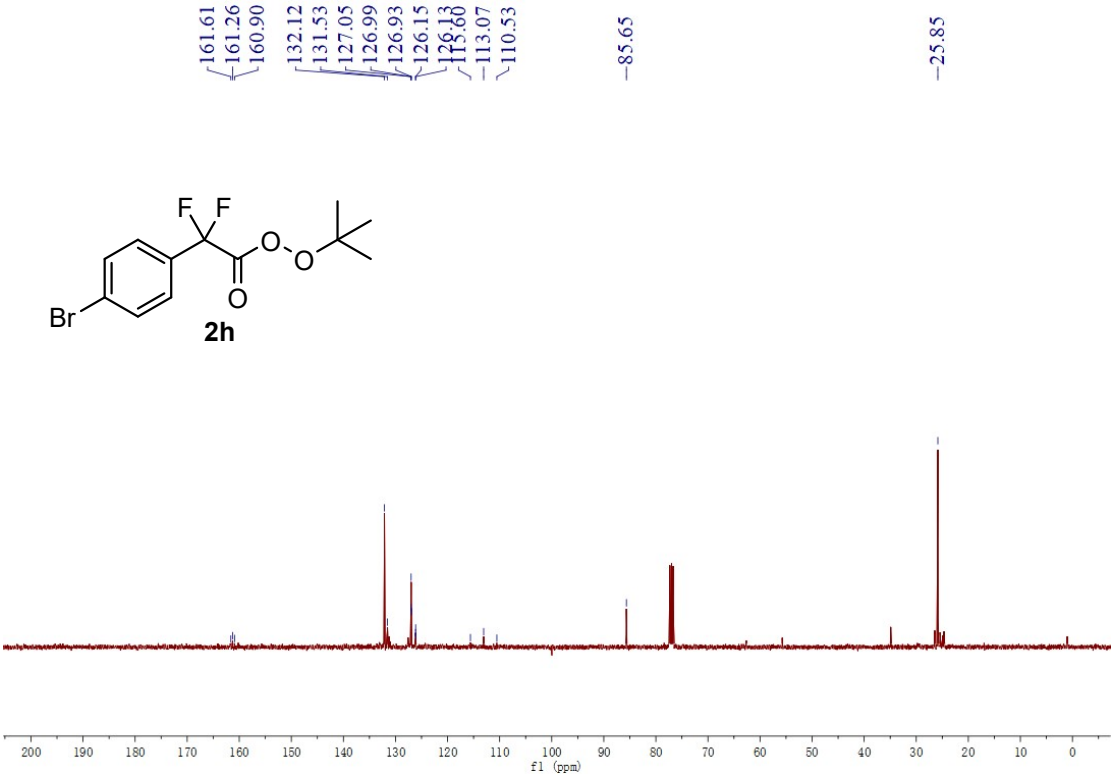
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2h:



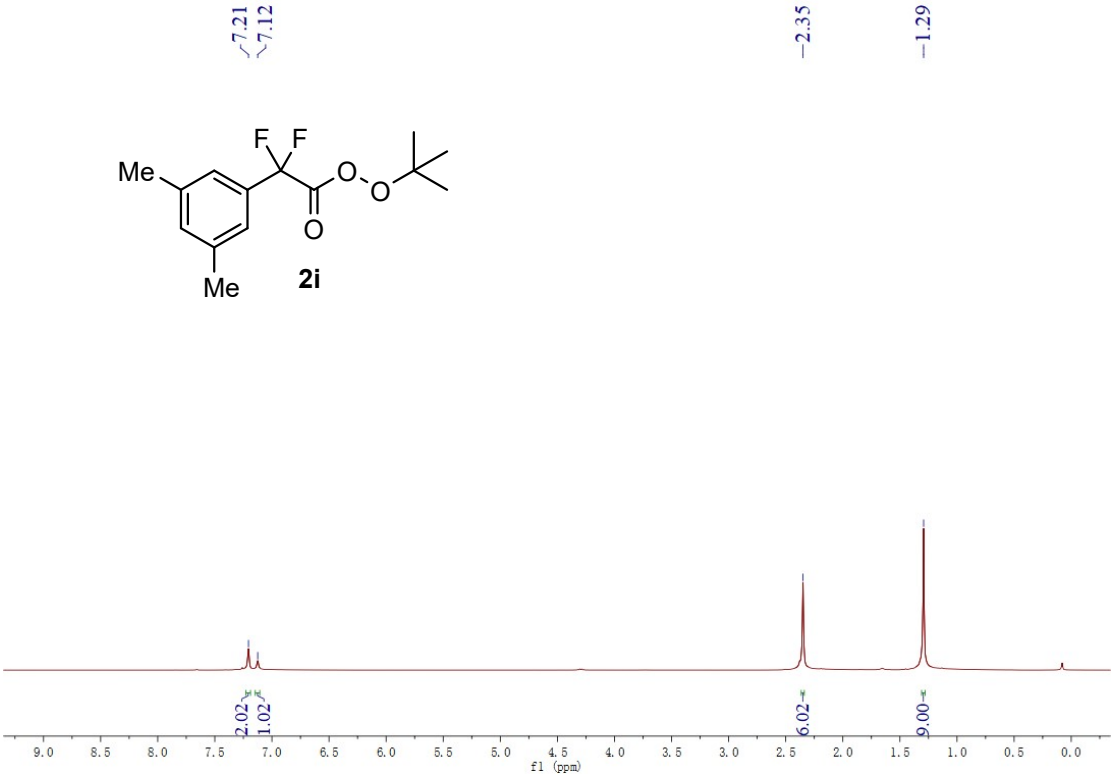
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2h:



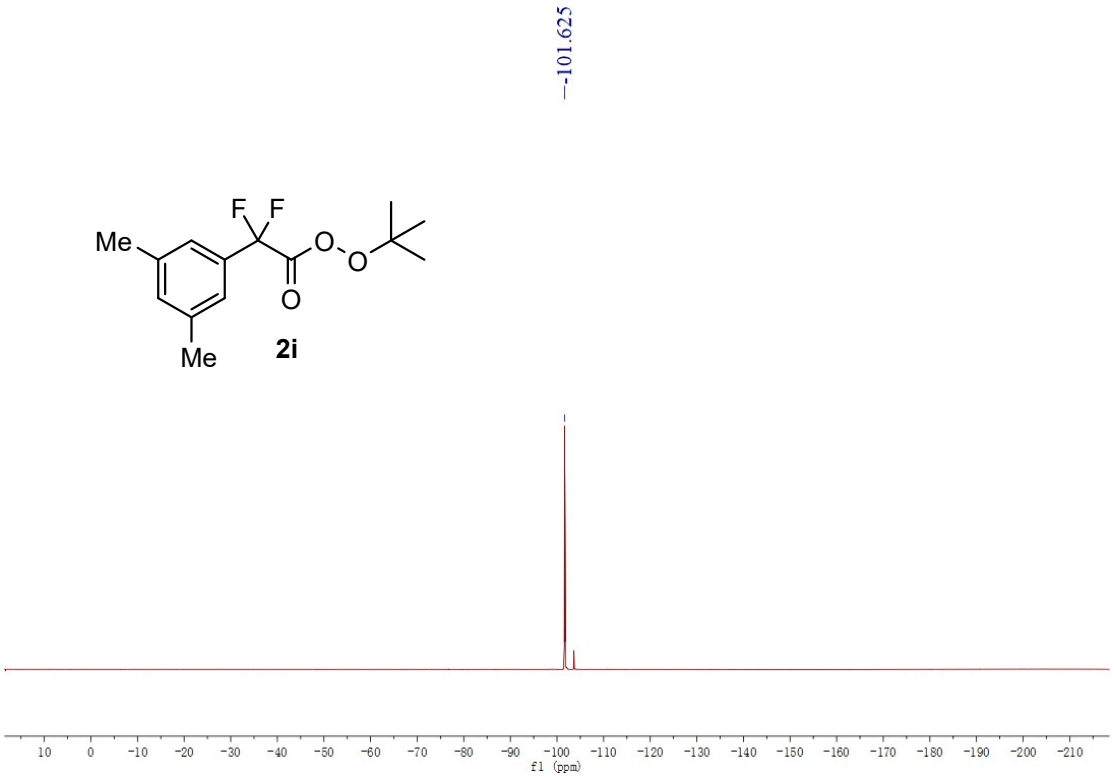
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2h:



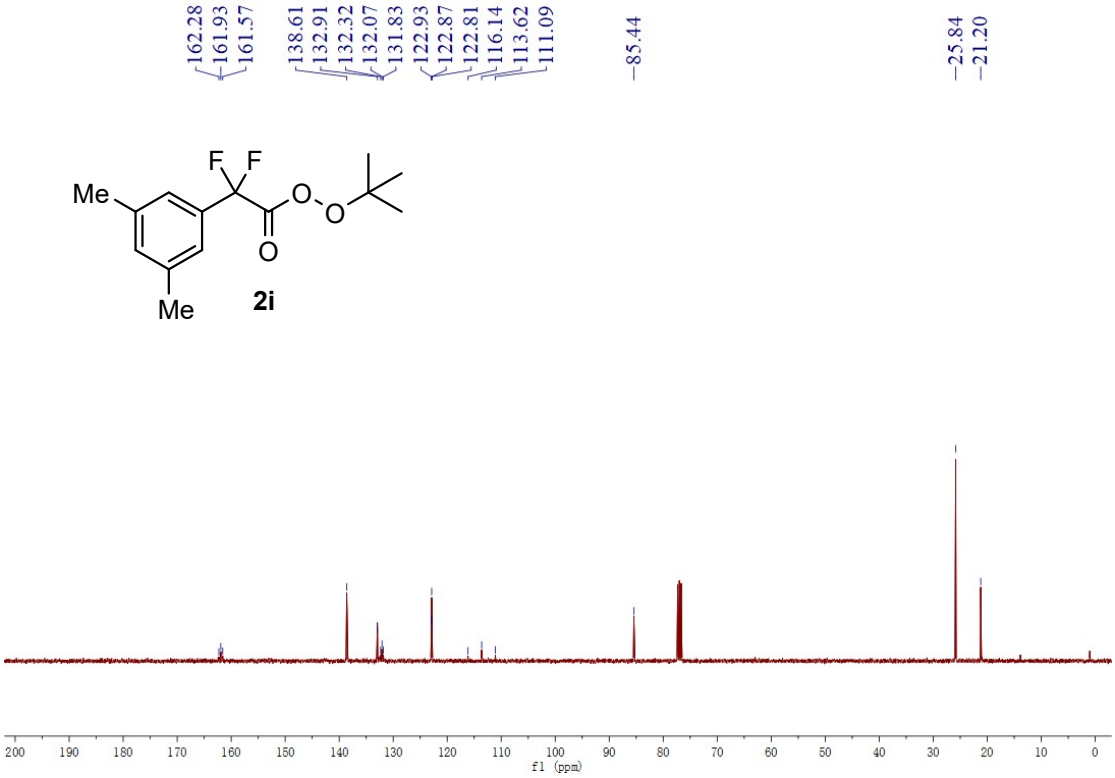
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2i:



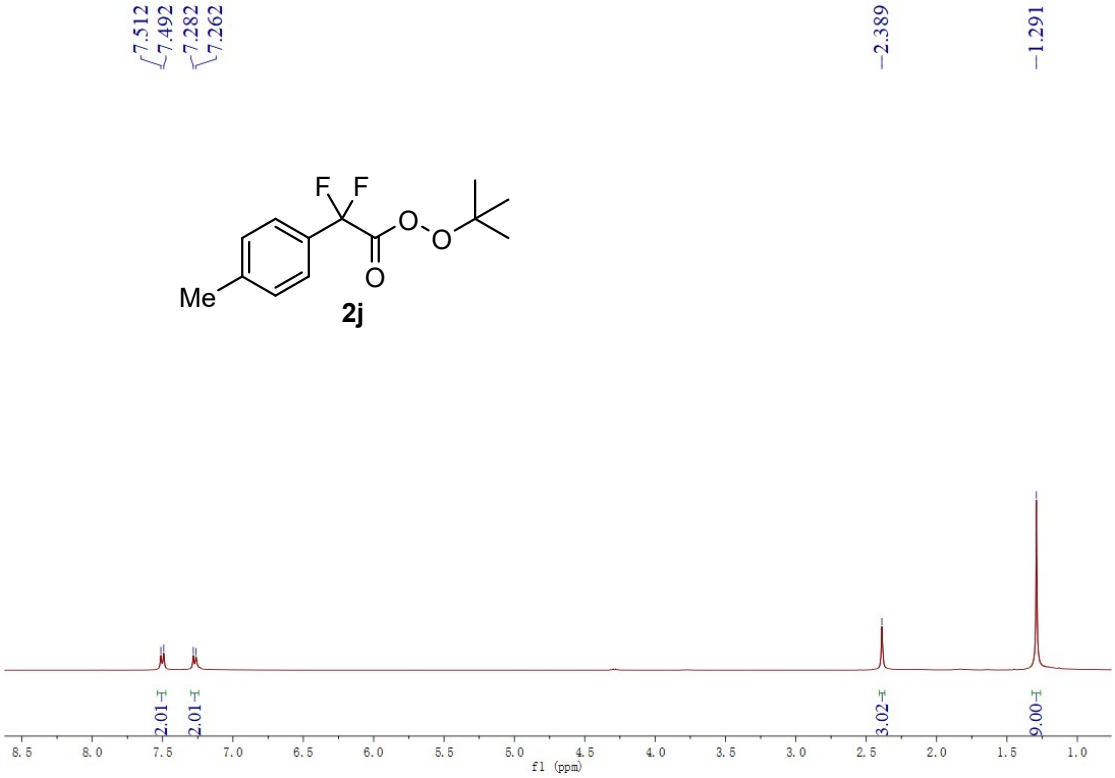
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2i:



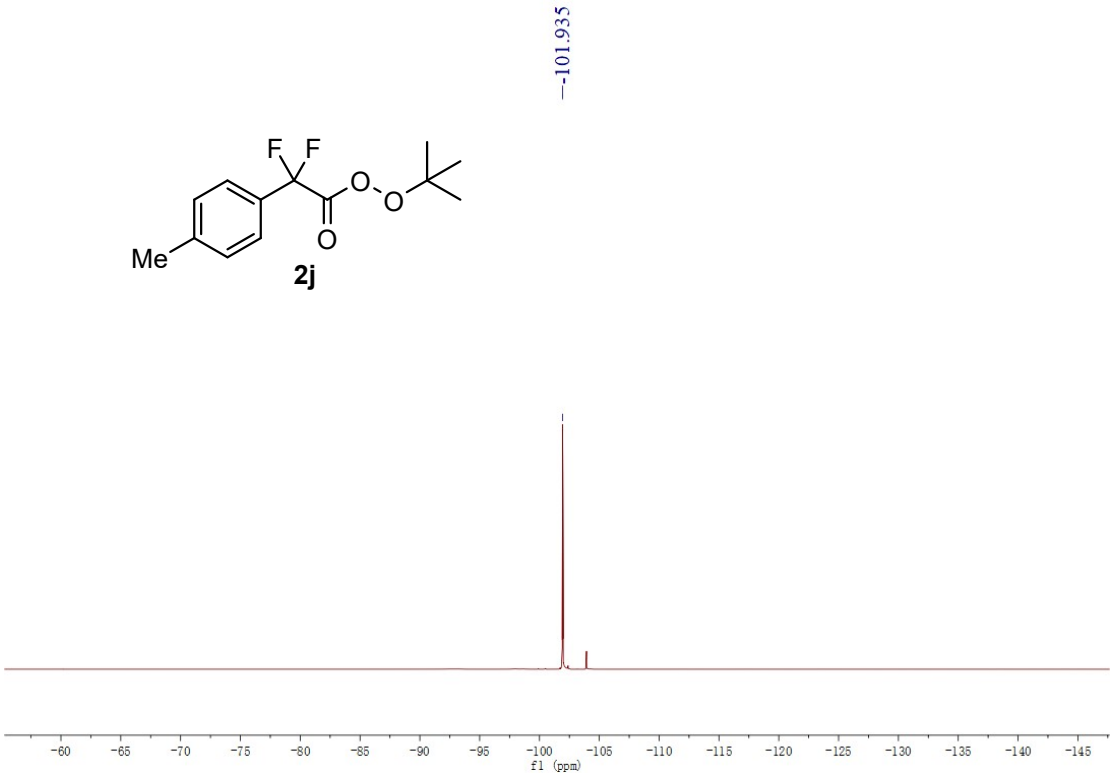
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2i:



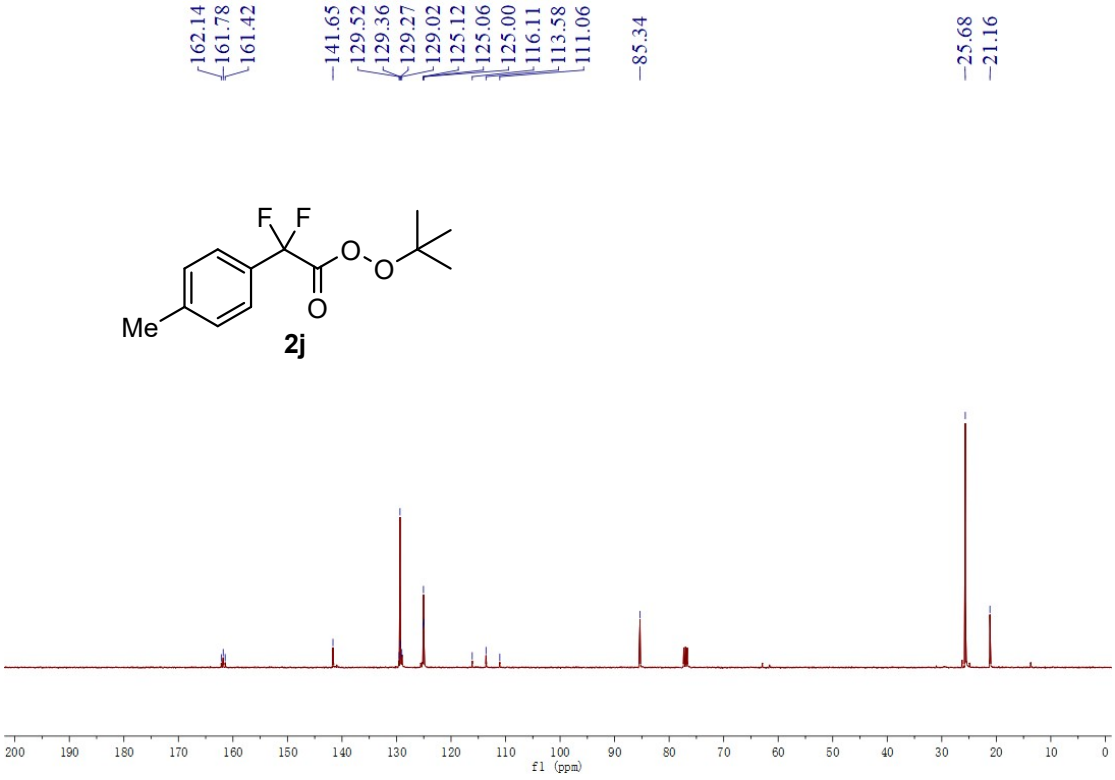
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2j:



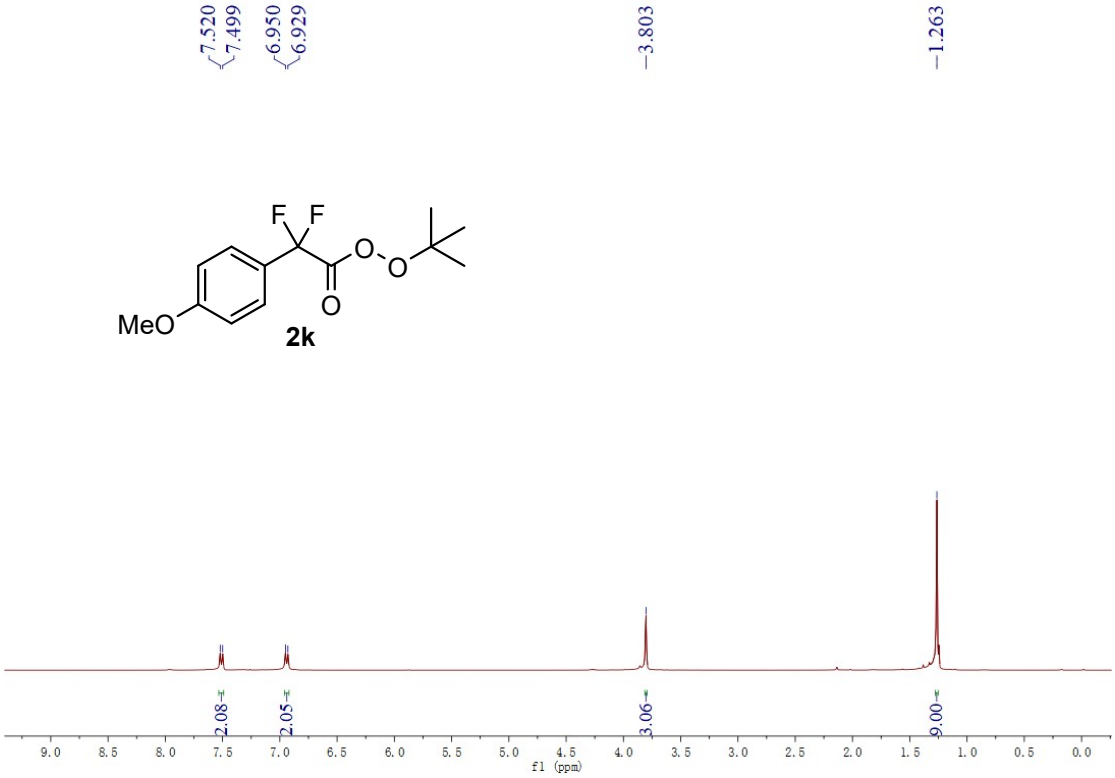
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2j:



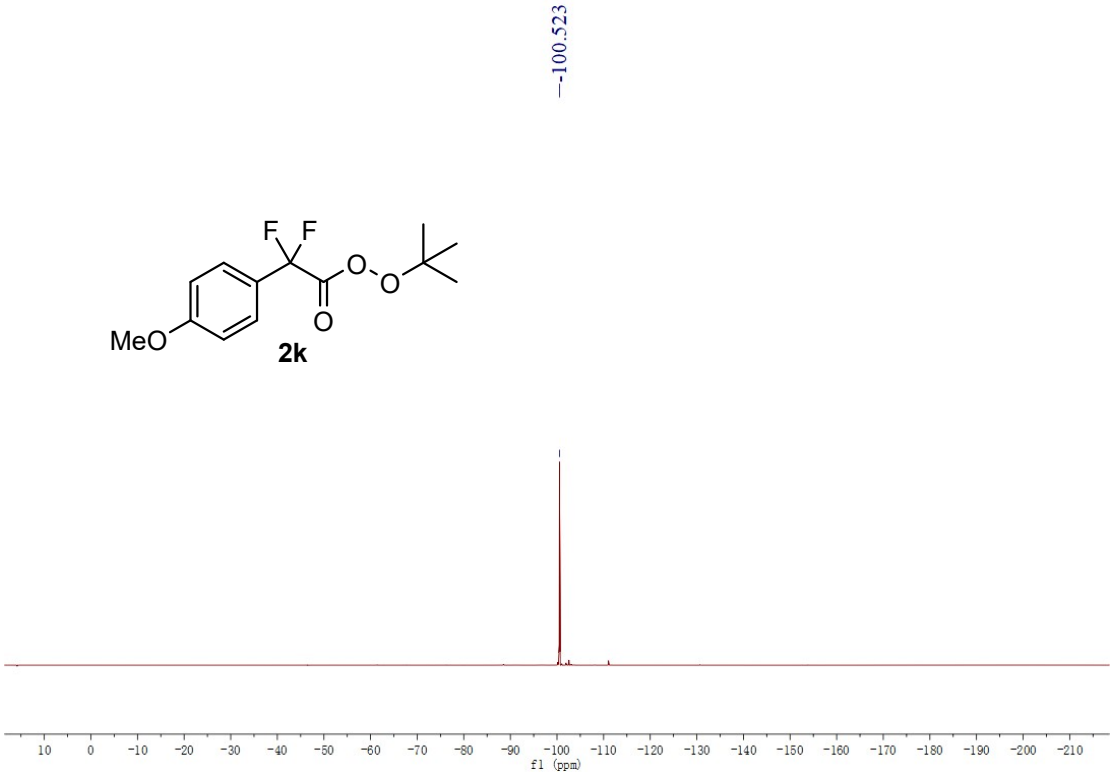
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2j:



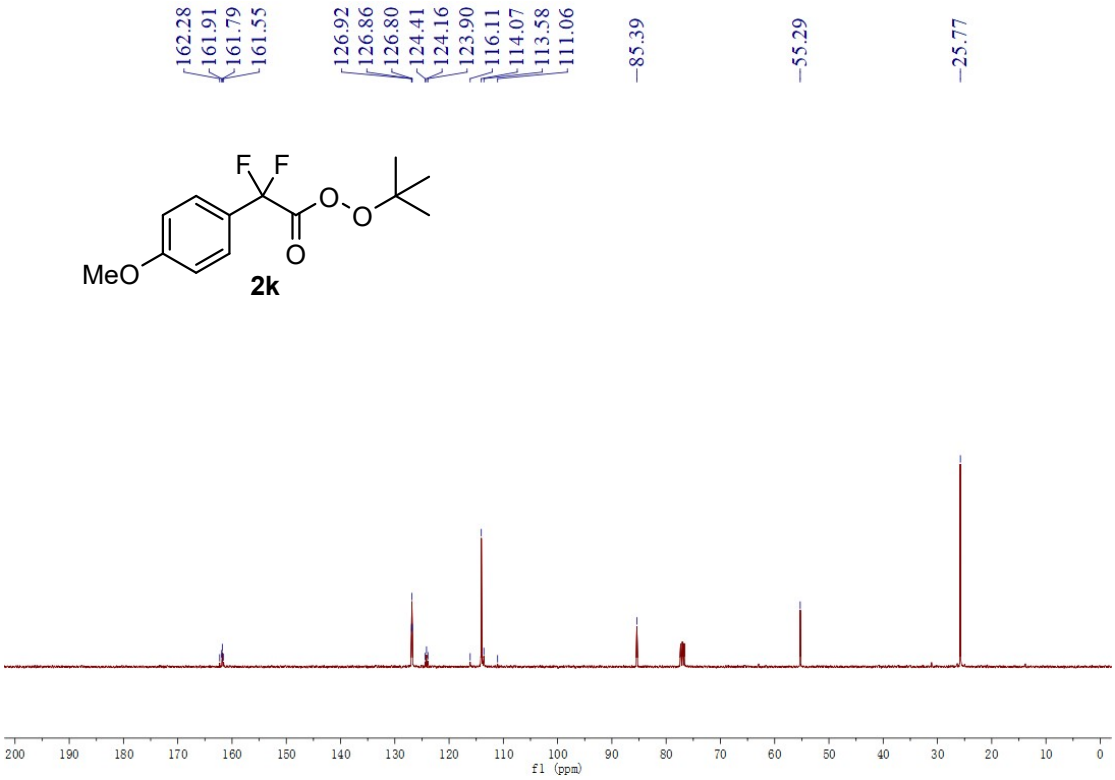
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2k:



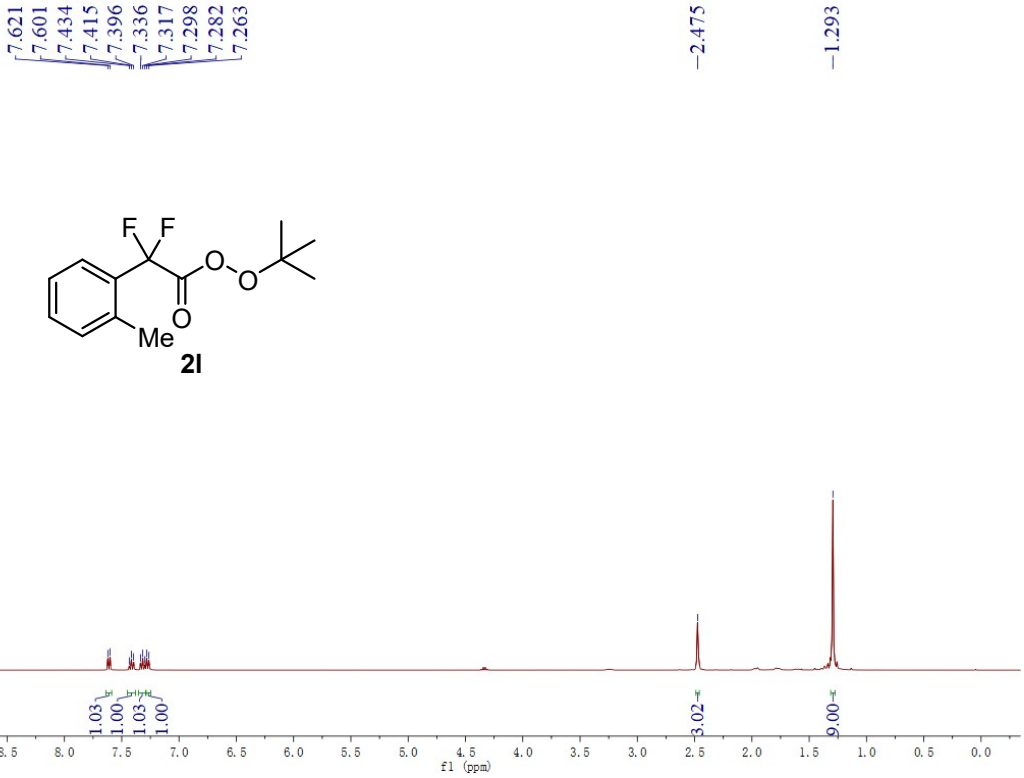
^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2k:



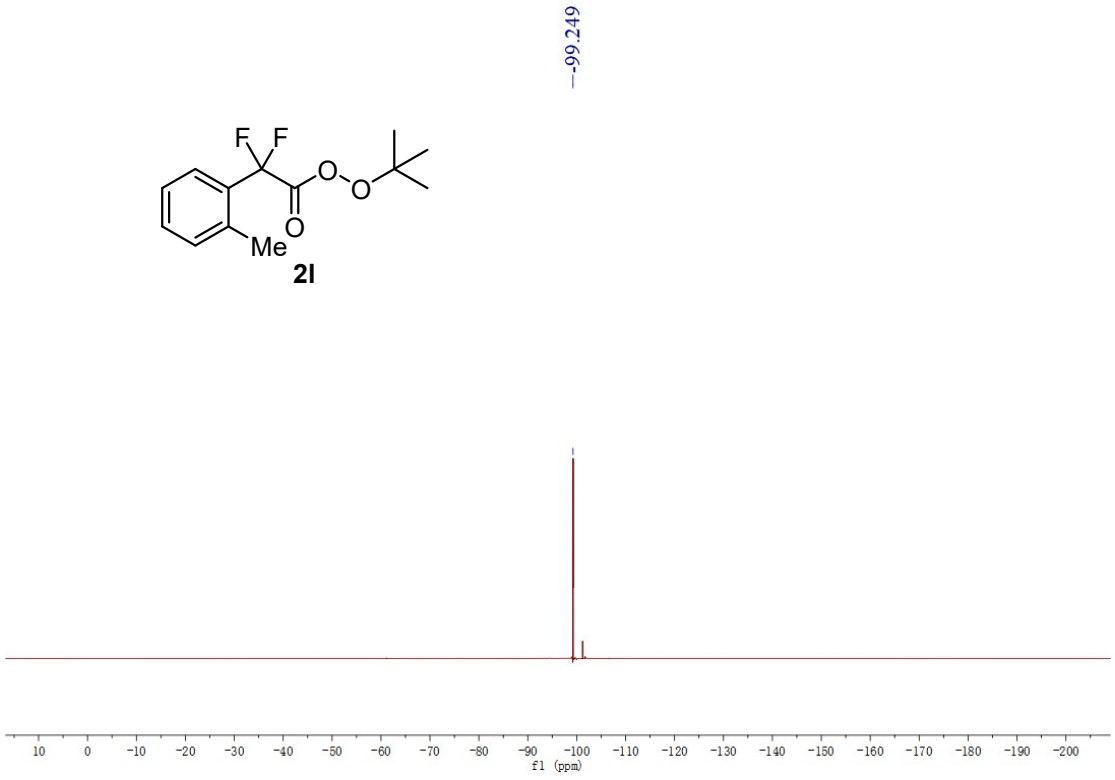
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2k:



^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound 2l:



^{19}F NMR ($CDCl_3$, 376 MHz) spectrum of compound 2l:



^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound 2l: