Supporting information

Nickel-Catalysed Radical Tandem Cyclization/Arylation: Practical Synthesis of 4-Benzyl-3,3-Difluoro-γ-Lactams

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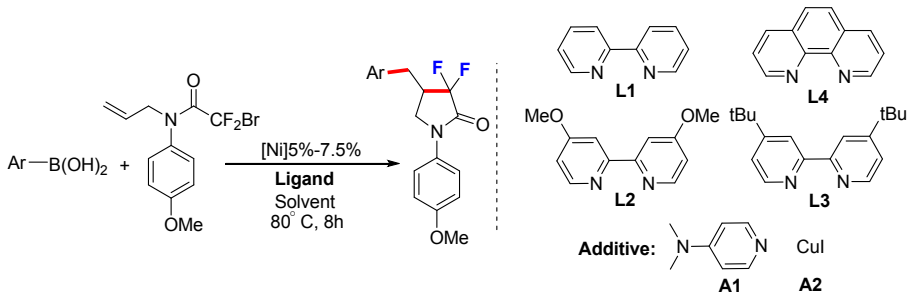
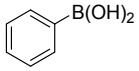
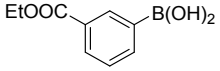
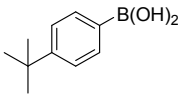
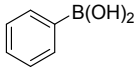
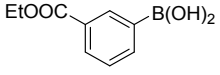
1. General Information:

All experiments were carried out using common flaskin N_2. All substrates were purchased from commercial suppliers and used asreceived directly unless otherwise noted. All solvents and othercommercially availablereagents were purchased from J&Kor TCI companies and used directly. Reactions were monitored by thin layer chromatography(TLC) (*Qingdao Haiyang Chemical Co. Ltd. Silica gel 60 F254)*. Products were detected using a UV/Vis lamp (254nm). Column chromatography was performed on *Qingdao Haiyang Chemical Co. Ltd. Gel 60* (200–300 mesh). The ^{1}H and ^{13}C NMR spectras were obtained on a Bruker 400 MHz NMR Fourier transform spectrometer. ^{1}H NMR data were reported as: chemical shift (δppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR data were reported in termsof chemical shift (δ ppm), multiplicity, and coupling constant (Hz).^{19}F NMR data were reported in terms of chemical shift (δ ppm) and multiplicity.The spectra are referenced against the internal solvent ($CDCl_3$, δ ^{1}H= 7.26 ppm,^{13}C= 77.0 ppm). ^{1}H, ^{13}C and ^{19}F spectra were recorded on a Varian Mercury-400 MHz (400 MHz for ^{1}H, 376 MHz for ^{19}F, 100 MHz for ^{13}C). ESI-MS spectra were recorded on a Bruker Esquire 3000. High resolution mass spectra (HR MS) were obtained on a Waters Micromass Q-TofMicroTM instrument using the ESI technique.

2. Table S1. The Optimization of Radical Cascade Reaction Conditions[a]



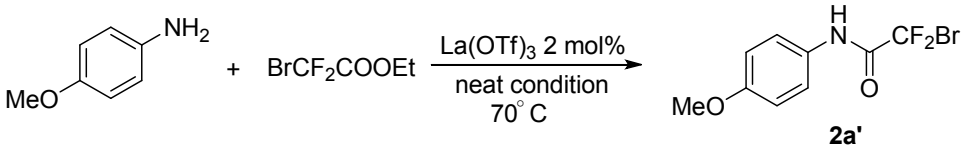
Substrate	Ni catalyst (mol %)	Ligand (mol %)	Solvent	Isolatedyield
	$Ni(NO_3)_2·6H_2O$ (5)	**L1**(5)	1,4-dioxane	33
	$Ni(NO_3)_2·6H_2O$ (5)	**L2**(5)	1,4-dioxane	51
	$Ni(NO_3)_2·6H_2O$ (5)	**L3**(5)	1,4-dioxane	55
	$Ni(NO_3)_2·6H_2O$ (5)	**L4**(5)	1,4-dioxane	trace
	$NiCl_2$·DME (5)	**L3**(5)	1,4-dioxane	36
	$NiCl_2$·DME (5)	**L3**(5)/**A1**(10)	1,4-dioxane	30
	$Ni(OTf)_2$ (5)	**L3**(5)	1,4-dioxane	64
	$Ni(NO_3)_2·6H_2O$ (5)	**L3**(5)	1,4-dioxane	0
	$NiCl_2$·DME (5)	**L3**(5)	1,4-dioxane	trace
	$NiCl_2$·DME (5)	**L3**(5)/**A1**(10)	1,4-dioxane	16
	$NiCl_2$·DME (5)	**L3**(5)/**A2**(5)	1,4-dioxane	trace
	$Ni(OTf)_2$ (5)	**L3**(5)	1,4-dioxane	37
	$Ni(NO_3)_2·6H_2O$ (5)	**L3**(5)	1,4-dioxane	57
	$NiCl_2$·DME (5)	**L3**(5)	1,4-dioxane	48
	$Ni(OTf)_2$ (5)	**L3**(5)	1,4-dioxane	70
	$Ni(acac)_2$ (5)	**L3**(5)	1,4-dioxane	0
	$Ni(OAc)_2·4H_2O$ (5)	**L3**(5)	1,4-dioxane	0
	$Ni(OTf)_2$ (5)	**L3**(5)/PPh_3(5)	1,4-dioxane	79
	$Ni(OTf)_2$ (5)	**L3**(5)/PPh_3(10)	1,4-dioxane	83
	$Ni(OTf)_2$ (7.5)[b]	**L3**(7.5)/PPh_3(15)	1,4-dioxane	88
	$Ni(OTf)_2$ (7.5)[b]	**L3**(7.5)/PPh_3(15)	1,4-dioxane	92
	$Ni(OTf)_2$ (7.5)[b]	PPh_3(15)	1,4-dioxane	0
	$Ni(OTf)_2$ (7.5)[b]	**L3**(7.5)/PPh_3(15)	1,4-dioxane	77
	$Ni(OTf)_2$ (7.5)[b]	**L3**(7.5)/PCy_3(15)	1,4-dioxane	74

[a]1: 2a = 1.5 :1[b]1:2a =2.0:1, K_2CO_3 (3.0 equiv) as base.

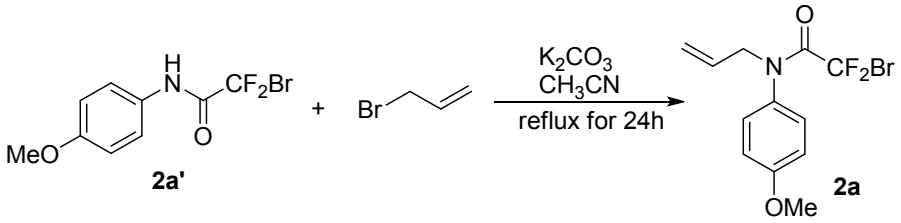
After the screening of solvents such as DCE, CH_3CN, DMF, THF, DMSO and 1,4-dioxane**, 1,4-dioxane** is the best choice.

3. Typical Procedures for the Synthesis of Substrates 2

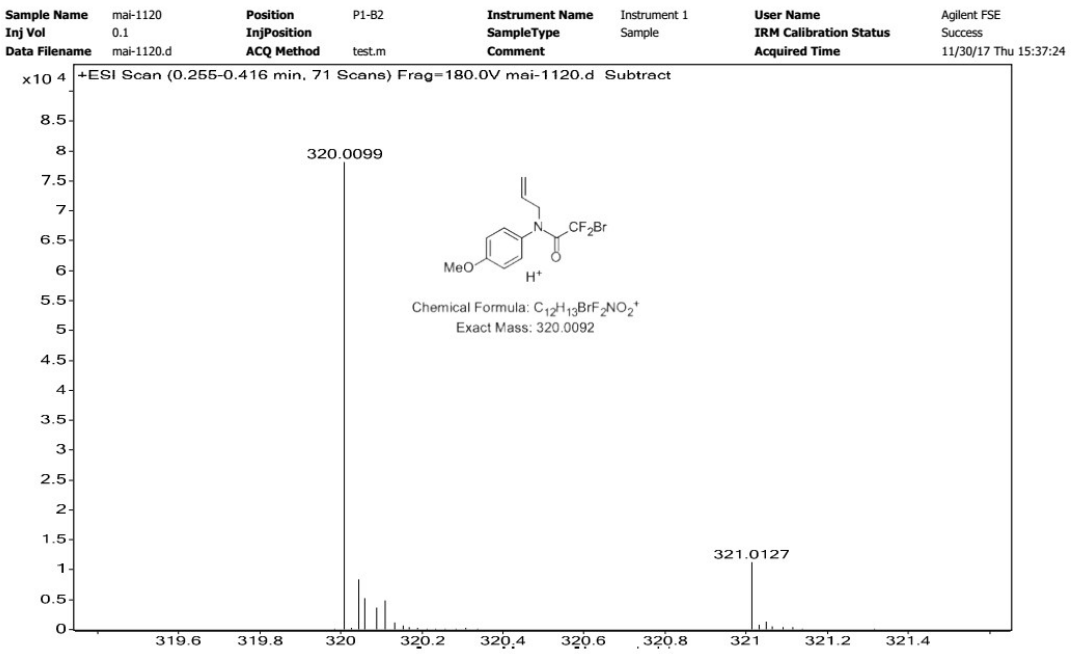
2a as an example**:**



To a 50mLround bottom flask, 4-methoxyaniline (1.23g, 10.0 mmol), ethyl bromodifluoroacetate(1.56 mL, 12.0 mmol) and $La(OTf)_3$ (117 mg, 0.2mmol) were added.The reaction mixture was stirred at 70 ^oC and monitored by TLC. After the amine was exhausted, the mixture was washed by aqueous HCl solution and then purified by silica gel column chromatography to give the pale yellow solid**2a'** (2.66g, 95%).

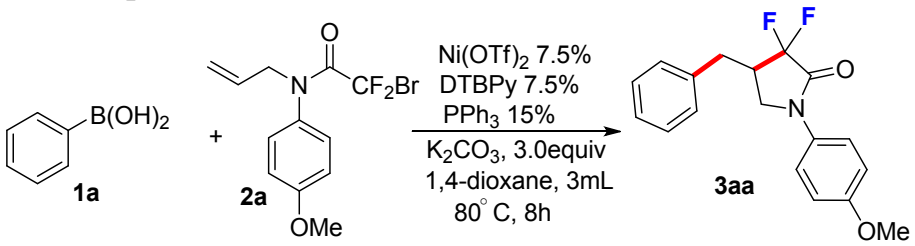


To a solution of **2a'** (5.0 mmol) in acetonitrile (50 mL) was added K_2CO_3 (3.0 equiv) and3-bromoprop-1-ene (15 mmol). The reaction mixture was heated to reflux and stirred for 24 hours. Then the solvent was evaporated under reduced pressure followed by quenched with H_2O and extracted with EtOAc (3x10 mL). The organic layers were combined and dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography using petroleum ether :EtOAc (50 : 1 to 10 :1) as eluent. The yield of product **2a** is 1.28g (80%).

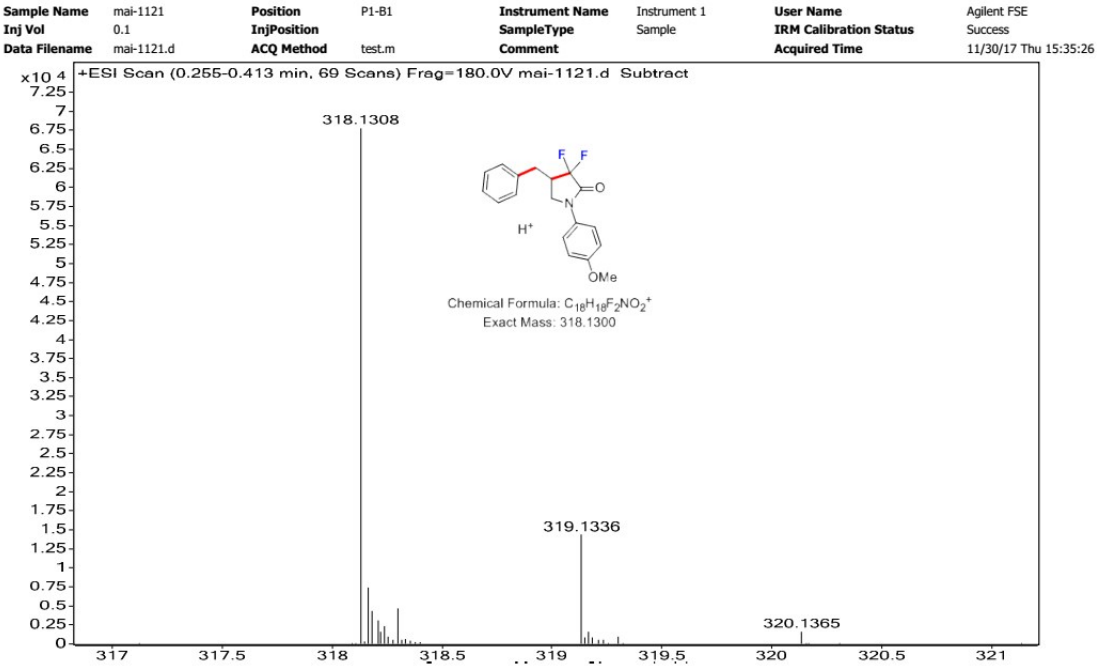


4. General Procedure for the Radical Tandem Cyclization-Arylation

3aaas an example**:**

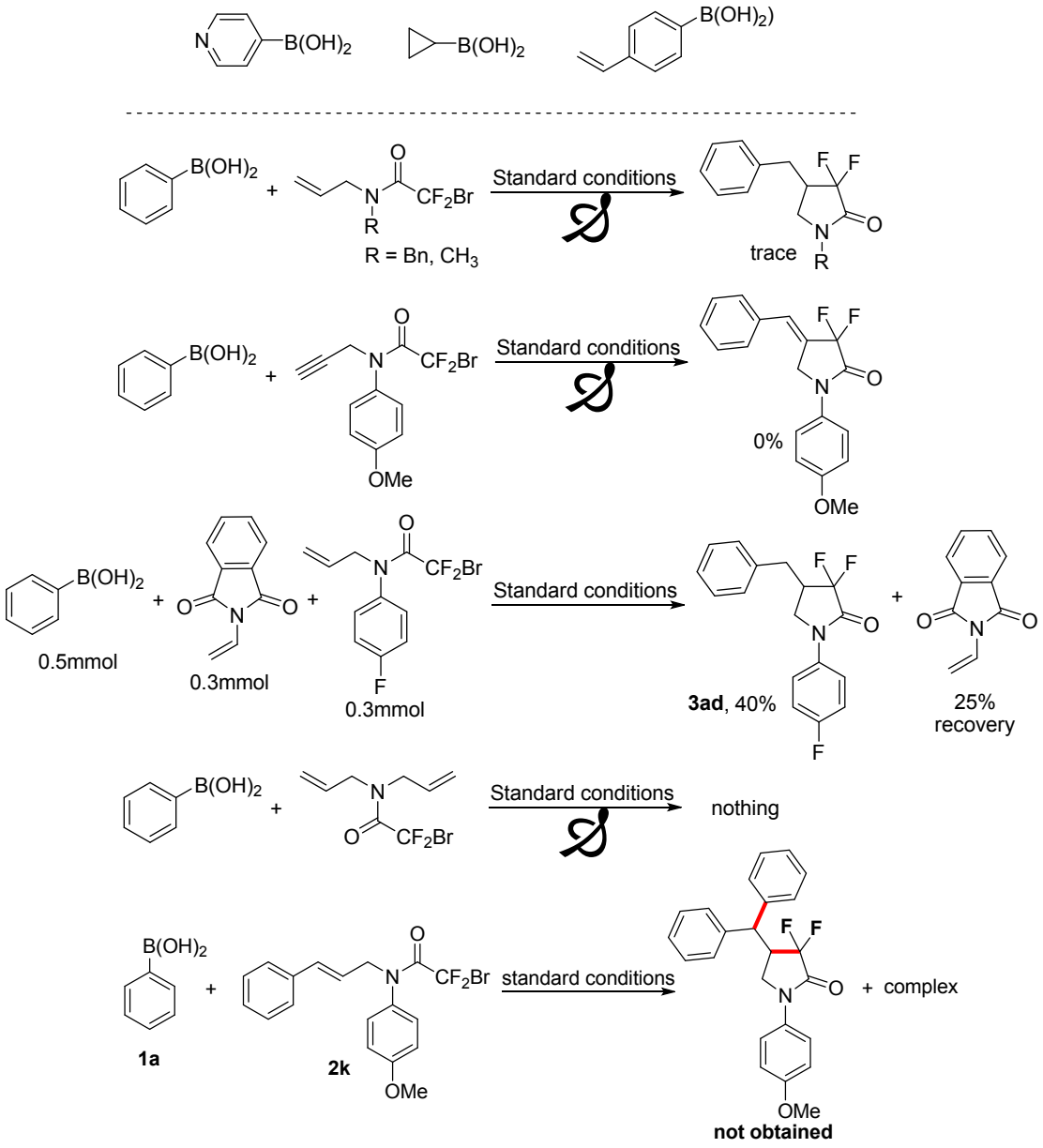


To a 25 mL of Schlenck tube were added phenylboronic acid **1a** (1.0mmol, 0.122g, 2.0equiv),**2a** (0.5 mmol, 0.16g), $Ni(OTf)_2$ (7.5 mmol %, 13 mg), DTBPy (7.5 mmol %, 10 mg), PPh_3 (15 mmol %, 19.6 mg) under air, followed by K_2CO_3 (1.5 mmol, 3.0 equiv). The mixture wasthen evacuated and backfilled with N_2 (3 times), dioxane (3 mL) were added subsequently. The tube was put into a preheated oil bath (80 ^oC). After stirring for 8 h,the reaction mixture was cooled to roomtemperature and was evaporated under reduced pressure. The residue was extracted with EtOAc (15 mlx 2) and then dried by Na_2SO_4.After removing EtOAc, the residue was purified with silica gel chromatography to give product **3aa** in 92% yield.

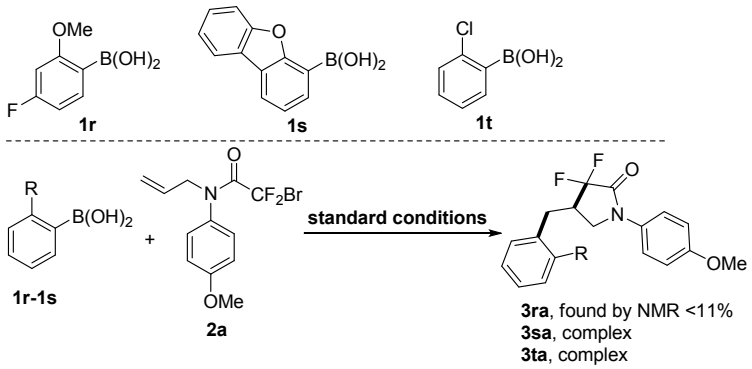


5. Screening of other substrates

unsuccessful boronic acids :

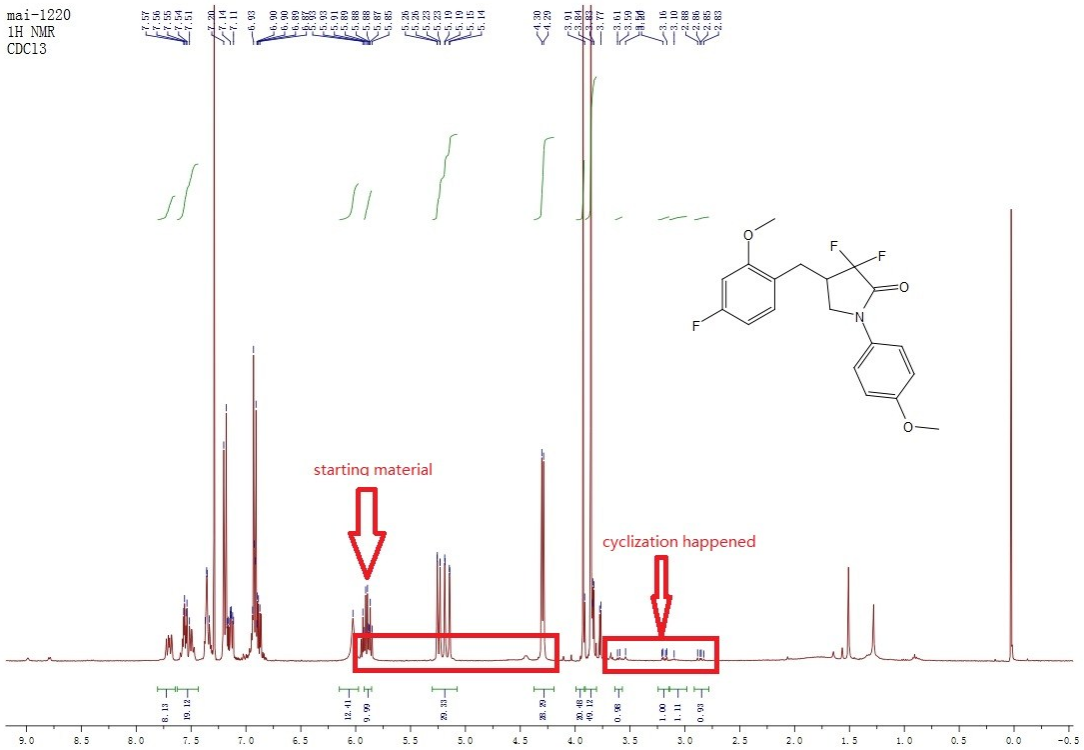


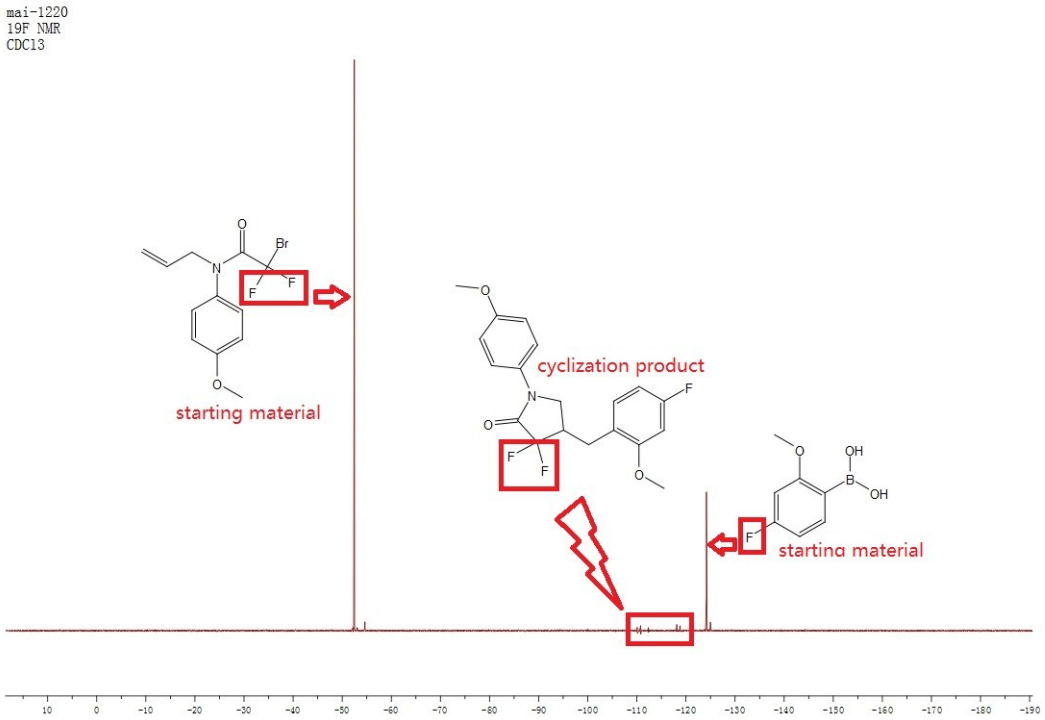
Scheme S1

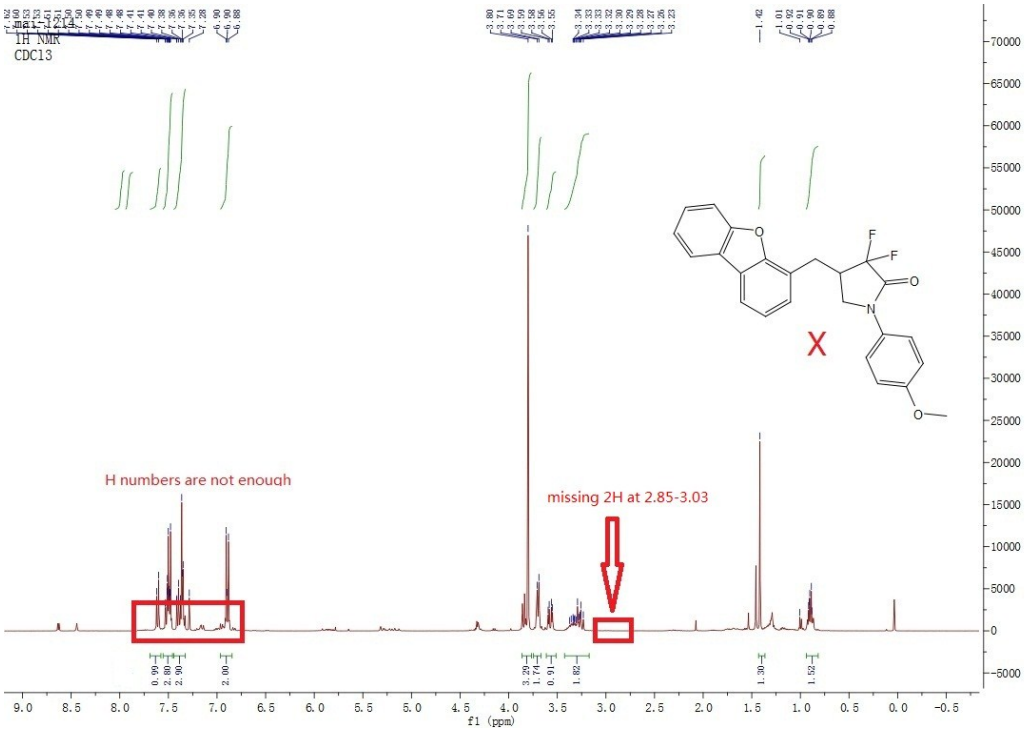


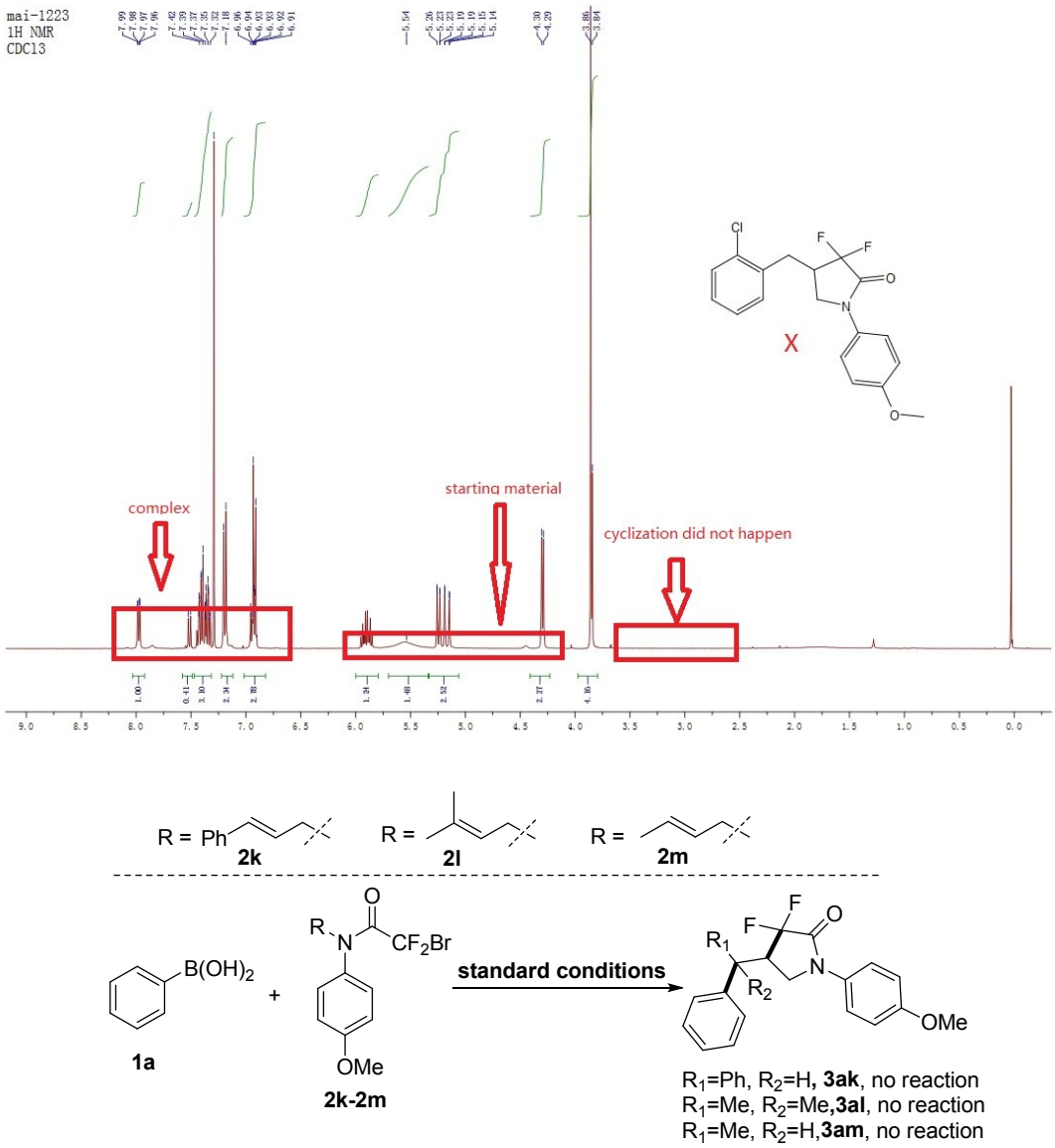
Scheme S2. Information of failed ortho-substituted aryl boronic acids

Some *ortho*-substituted aryl boronic acids (shown in Scheme S2) do not perform well in this reaction under current conditions. The reason is mainly due to their hindrance plus the steric effect of the other substrate. The other reason is the ligand's efficiency. In addition, we found alkyl radical coupling with aryl boronic acid catalyzed by copper has similar results. (See: *ACS catal*, 2016, 6, 1329-1333.)



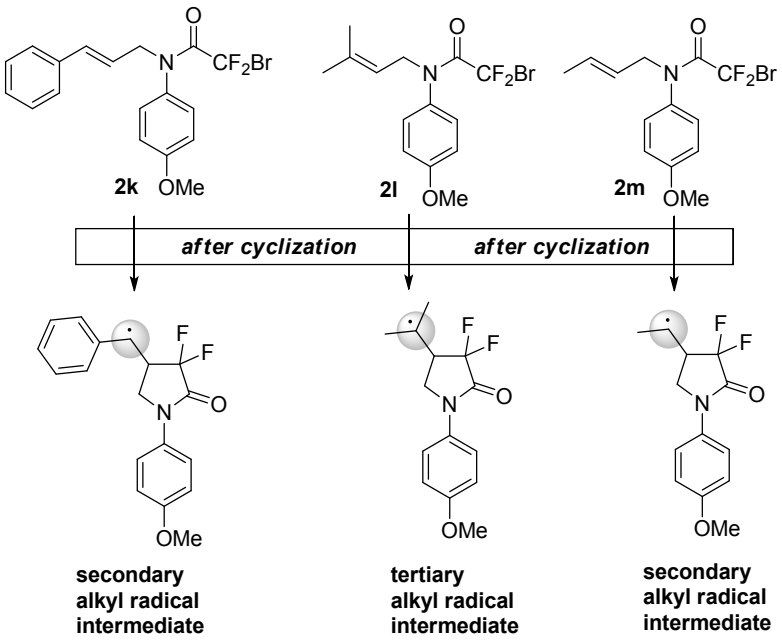

mai-1220
19F NMR
CDCl3
starting material
cyclization product
starting material


mai-1214
1H NMR
CDCl3
X
H numbers are not enough
missing 2H at 2.85-3.03
f1 (ppm)

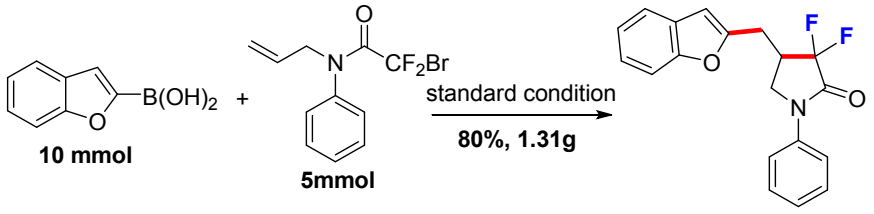


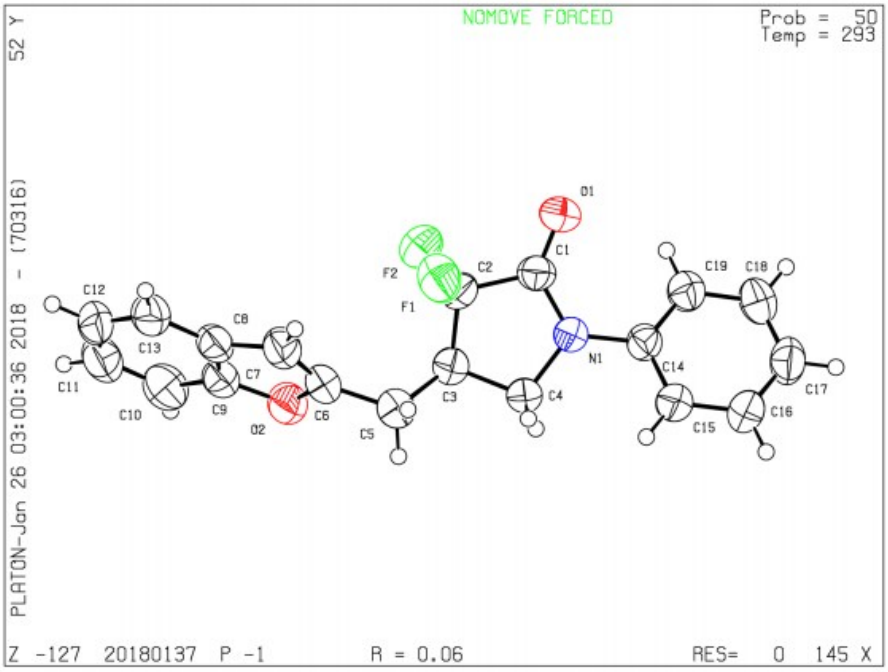
Scheme S3. Limitation of the substrate **2**

As shown in Scheme S3, when different isomeric methylallyl analogues such as **2k-2m** reacted with phenyl boronic acid under the standard conditions, the results are disappointing. After referring to many literatures, we found secondary or tertiary alkyl radical have rarely been employed in alkyl–aryl cross-coupling using a Ni-Suzuki protocol (*Angew. Chem. Int .Ed*. 2017, 56, 3319-3323). For **2k-2m**, the intermediates are secondary or tertiary alkyl radicals after cyclization, thus the cross-couplings catalyzed by Ni-Suzuki protocol do not proceed.


2k
2l
2m
OMe
after cyclization
after cyclization
secondary alkyl radical intermediate
tertiary alkyl radical intermediate
secondary alkyl radical intermediate

6. X-ray structures and data





Crystal data and structure refinement for 20180137.	
Identification code	20180137
Empirical formula	$C_{19}H_{15}F_2NO_2$
Formula weight	327.32
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	9.5617(18)
b/Å	9.7384(18)
c/Å	10.228(2)
α /°	75.270(17)
β /°	68.659(18)
γ /°	61.422(19)
Volume/Å^3	775.2(3)
Z	2
ρ_{calc}g/cm^3	1.402
μ /mm^{-1}	0.902

Continued:

F(000)	340.0
Crystal size/mm^3	0.2 × 0.16 × 0.14
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.328 to 134.13
Index ranges	-7 ≤ h ≤ 11, -11 ≤ k ≤ 11, -10 ≤ l ≤ 12
Reflections collected	5510
Independent reflections	2767 [R_{int} = 0.0232, R_{sigma} = 0.0342]
Data/restraints/parameters	2767/0/217
Goodness-of-fit on F^2	1.093
Final R indexes [I>=2σ(I)]	R_1 = 0.0582, wR_2 = 0.1635
Final R indexes [all data]	R_1 = 0.0719, wR_2 = 0.1824
Largest diff. peak/hole / e $Å^{-3}$	0.33/-0.30

7. References

1. An, L.; Xu, C.; Zhang, X. *Nat. Commun*. **2017**, *8*, 1460.

2. Wu, Y.; Zhang, H.-R.; Cao, Y.-X.; Lan, Q.; Wang, X.-S. *Org. Lett*. **2016**, *18*, 5564

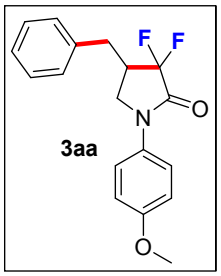
3. Sheng, J.; Ni, H.-Q.; Liu, G.; Li, Y.; Wang, X.-S. *Org. Lett*. **2017**, *19*, 4480.

4. Gu, J.-W.; Min, Q.-Q.; Yu, L.-C.; Zhang, X. *Angew. Chem., Int. Ed*. **2016**, *55*, 12270.

5. Li, G.; Wang, T.; Fei, F.; Su, Y.-M.; Li, Y.; Lan, Q.; Wang, X.-S.*Angew.Chem., Int. Ed*. **2016**, *55*, 3491.

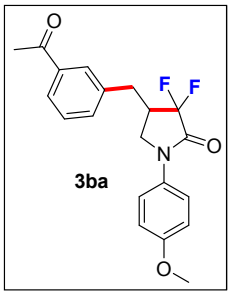
6. Morimoto,H.; Fujiwara, Risa.; Shimizu, Y.; Morisaki, K.; Ohshima, T. *Org. Lett*. **2014**, *16*, 2018.

8. Characterization Data



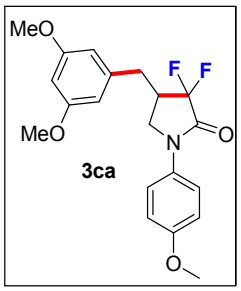
4-benzyl-3,3-difluoro-1-(4-methoxyphenyl)pyrrolidin-2-one

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 12.0 Hz, 2H), 7.30-7.36 (m, 2H), 7.26-7.30 (m, 3H), 6.93 (dd, *J* = 8.0, 4.0 Hz, 2H), 3.82 (s, 3H), 3.69 (t, *J* = 8.0 Hz, 1H), 3.60 (t, *J* = 8.0 Hz, 1H), 3.30 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.95-2.99 (m, 1H), 2.79-2.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.13 (t), 157.67, 136.96, 129.92, 128.97, 128.73, 127.10, 121.73, 114.95 (t, *J* = 257 Hz), 114.18, 55.48, 48.54, 41.67 (t, *J* = 21 Hz), 31.53; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.44(d, *J* = 266.96 Hz), -117.03 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{18}F_2NO_2$ $[M+H]^+$: 318.1300; found: 318.1308.



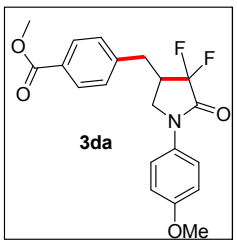
4-(3-acetylbenzyl)-3,3-difluoro-1-(4-methoxyphenyl)pyrrolidin-2-one

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 4H), 6.92 (d, *J* = 8.0 Hz, 2H), 3.81 (s, 3H), 3.72 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.33 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.97-3.02 (m, 1H), 2.88-2.94 (m, 1H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.90, 161.93 (t), 157.72, 137.72, 133.48, 129.27, 128.22, 127.37, 121.75, 117.35 (t, *J* = 247 Hz), 114.32, 55.49, 48.49, 41.30 (t, *J* = 21 Hz), 31.45, 26.71; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.13 (d, *J* = 266.96 Hz), -116.60 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{20}H_{20}F_2NO_3$ $[M+H]^+$: 360.1406; found: 360.1411.



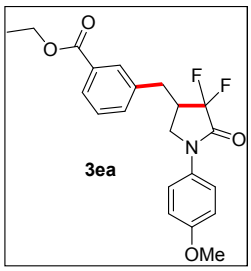
4-(3,5-dimethoxybenzyl)-3,3-difluoro-1-(4-methoxyphenyl)pyrrolidin-2-one

Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.40 (s, 3H), 3.82 (s, 9H), 3.71 (t, *J* = 8.0 Hz, 1H), 3.57 (t, *J* = 8.0 Hz, 1H), 3.24 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.91-2.96 (m, 1H), 2.70-2.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.79, 161.20, 157.67, 139.24, 130.97, 121.75, 117.37 (t, *J* = 244 Hz), 114.29, 106.81, 98.63, 55.50, 48.53, 41.51 (t, *J* = 21 Hz), 31.77; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.44 (d, *J* = 366.96 Hz), -116.97 (d, *J* = 366.96 Hz); HRMS (ESI) calcd for $C_{20}H_{22}F_2NO_4$ $[M+H]^+$: 378.1511; found: 378.1514.



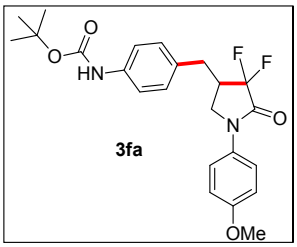
methyl4-((4,4-difluoro-1-(4-methoxyphenyl)-5-oxopyrrolidin-3-yl)methyl)benzoate

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.0 Hz, 2.0Hz), 7.50 (d, *J* = 8.0 Hz, 2.0Hz), 7.36 (d, *J* = 8.0 Hz, 2.0Hz), 6.92 (d, *J* = 8.0 Hz, 2.0Hz), 3.94 (s, 3H), 3.81 (s, 3H), 3.72 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.34 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.94-2.98 (m, 1H), 2.86-2.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.72, 161.89 (t), 157.72, 142.28, 130.85, 130.25, 129.18, 128.81, 121.69, 117.14 (t, *J* = 255 Hz), 114.32, 55.49, 52.18, 48.43 (d), 41.40 (t, *J* = 21 Hz), 31.57; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.24 (d, *J* = 266.96 Hz), -116.68 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{20}H_{20}F_2NO_4$ $[M+H]^+$: 376.1355, found: 376.1355.



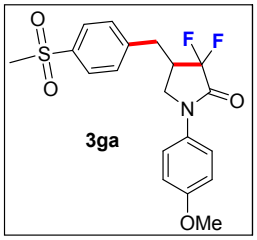
ethyl3-((4,4-difluoro-1-(4-methoxyphenyl)-5-oxopyrrolidin-3-yl)methyl)benzoate

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95-7.99 (m, 2H), 7.44-7.50 (m, 4H), 6.91 (d, *J* = 8.0 Hz), 4.43 (q, *J* = 8.0 Hz, 2H), 3.80 (s, 3H), 3.69 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.33 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.94-3.00 (m, 1H), 2.86-2.92 (m, 1H), 1.42 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.31, 162.29 (t), 157.70, 137.32, 133.22, 130.88, 129.65, 129.04, 128.34, 121.75, 117.45 (t, *J* = 233 Hz), 114.30, 61.18, 55.48, 48.47 (d), 41.51 (t, *J* = 21 Hz), 31.33, 14.34; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.28 (d, *J* = 266.96 Hz), -116.67 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{21}H_{22}F_2NO_4$ $[M+H]^+$: 390.1511, found: 390.1515.



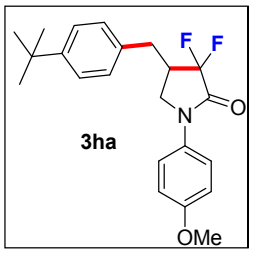
tert-butyl(4-((4,4-difluoro-1-(4-methoxyphenyl)-5-oxopyrrolidin-3-yl)methyl)phenyl)carbamate

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.58 (s, 1H), 3.81 (s, 3H), 3.69 (t, *J* = 8.0 Hz, 1H), 3.56 (t, *J* = 8.0 Hz, 1H), 3.24 (dd, *J* = 12.0, 8.0 Hz, 1H), 2.85-2.93 (m, 1H), 2.72-2.78 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.16 (t), 157.64, 152.83, 137.42, 131.33, 130.98, 129.24, 121.69, 119.86, 117.55 (t, *J* = 231 Hz), 114.29, 80.64, 55.49, 48.49, 41.70 (t, *J* = 21 Hz), 30.82, 28.34; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.26 (d, *J* = 266.96 Hz), -116.99 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{23}H_{27}F_2N_2O_4$ $[M+H]^+$: 433.1933, found: 433.1930.



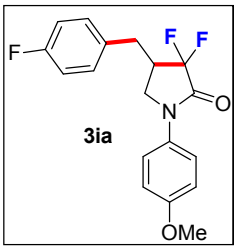
3,3-difluoro-1-(4-methoxyphenyl)-4-(4-(methylsulfonyl)benzyl)pyrrolidin-2-one

Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 4H), 6.93 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 3.75 (t, *J* = 8.0 Hz, 1H), 3.58 (t, *J* = 8.0 Hz, 1H), 3.36 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.08 (s, 3H), 2.93-3.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.69 (t), 157.79, 143.51, 139.53, 130.71, 129.81, 128.07, 121.71, 117.24 (t, *J* = 248 Hz), 114.36, 55.51, 48.38, 44.48, 41.26 (t, *J* = 21 Hz), 31.59; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.85 (d, *J* = 266.96 Hz), -116.31 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{20}F_2NO_4S$ $[M+H]^+$: 396.1076, found: 396.1080.



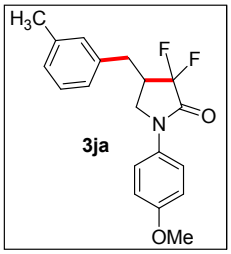
4-(4-(tert-butyl)benzyl)-3,3-difluoro-1-(4-methoxyphenyl)pyrrolidin-2-one

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 3.72 (t, *J* = 8.0 Hz, 1H), 3.56 (t, *J* = 8.0 Hz, 1H), 3.28 (dd, *J* = 16.0, 12.0 Hz, 1H), 2.91-2.99 (m, 1H), 2.76-2.82 (m, 1H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.20 (t), 157.67, 150.03, 133.80, 131.04, 128.39, 125.86, 121.80, 117.60 (t, *J* = 235 Hz), 114.29, 55.49, 48.65, 41.46 (t, *J* = 21 Hz), 34.49, 31.35; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.31 (d, *J* = 266.96 Hz), -117.16 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{22}H_{26}F_2NO_2$ $[M+H]^+$: 374.1926; found: 374.1923.



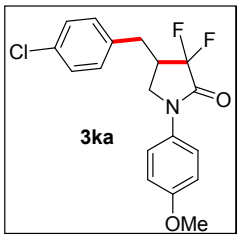
3,3-difluoro-4-(4-fluorobenzyl)-1-(4-methoxyphenyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 8.0 Hz, 2H), 7.22-7.23 (m, 2H), 7.05 (t, *J* = 8.0 Hz, 2H), 6.91-6.94 (m, 2H), 3.82 (s, 3H), 3.71 (t, *J* = 8.0 Hz, 1H), 3.56 (t, *J* = 8.0 Hz, 1H), 3.25 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.87-2.95 (m, 1H), 2.78-2.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.14 (d, *J* = 244 Hz), 162.02 (t), 157.71, 132.64, 130.92, 130.19, 121.71, 117.40 (t, *J* = 243 Hz), 115.72, 114.32, 55.49, 48.47, 41.53 (t, *J* = 21 Hz), 30.80; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.14 (d, *J* = 266.96 Hz), -115.54, -116.90 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{17}F_3NO_2$ $[M+H]^+$: 336.1206, found: 336.1211.



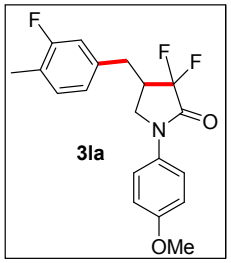
3,3-difluoro-1-(4-methoxyphenyl)-4-(3-methylbenzyl)pyrrolidin-2-one

Pale white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 8.0 Hz, 2H), 7.24-7.28 (m, 1H), 7.05-7.10 (m, 3H), 6.94 (d, *J* = 12.0 Hz, 2H), 3.82 (s, 3H), 3.69 (t, *J* = 8.0 Hz, 1H), 3.57 (t, *J* = 8.0 Hz, 1H), 3.28 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.91-2.98 (m, 1H), 2.74-2.80 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.19, 157.65, 138.68, 136.87, 131.01, 129.48, 128.84, 127.84, 125.70, 121.75, 117.48 (t, *J* = 242 Hz), 55.50, 48.59, 41.69 (t, *J* = 21 Hz), 31.42, 21.42; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.48 (d, *J* = 266.96 Hz), -117.07 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{20}F_2NO_2$ $[M+H]^+$: 332.1457, found: 332.1460.



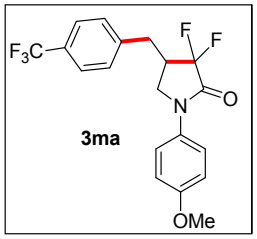
4-(4-chlorobenzyl)-3,3-difluoro-1-(4-methoxyphenyl)pyrrolidin-2-one

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0, 4.0 Hz, 2H), 3.82 (s, 3H), 3.73 (t, *J* = 8.0 Hz, 1H), 3.57 (t, *J* = 8.0 Hz, 1H), 3.27 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.88-2.95 (m, 1H), 2.78-2.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.95 (t), 157.71, 135.39, 133.03, 130.87, 130.08, 129.13, 121.70, 119.87 (t, *J* = 269 Hz), 114.33, 55.51, 48.43, 41.58 (t, *J* = 21 Hz), 30.97; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.07 (d, *J* = 266.96 Hz), -116.78 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{17}ClF_2NO_2$ $[M+H]^+$: 352.0910, found: 352.0915.



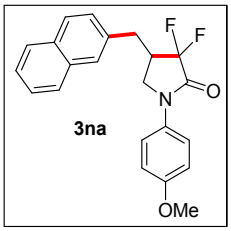
3,3-difluoro-4-(3-fluoro-4-methylbenzyl)-1-(4-methoxyphenyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 12 Hz, 2.0Hz), 7.17 (t, *J* = 8.0 Hz, 1H), 6.91-6.95 (m, 4H), 3.82 (s, 3H), 3.71 (t, *J* = 12 Hz, 1H), 3.58 (t, *J* = 12 Hz, 1H), 3.25 (dd, *J* = 12.0, 8.0 Hz, 1H), 2.87-2.93 (m, 1H), 2.75-2.81 (m, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.63, 162.03 (t, *J* = 32 Hz), 160.19, 157.69, 136.5(d), 131.96, 130.93, 124.11, 123.51, 121.72, 117.26 (t, *J* = 252 Hz), 115.35(d), 114.31, 55.49, 48.47, 41.54 (t, *J* = 21 Hz), 30.97(d), 14.22(d); ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.26 (d, *J* = 266.96 Hz), -116.74, -116.86 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{19}F_3NO_2$ $[M+H]^+$: 350.1362, found: 350.1366.



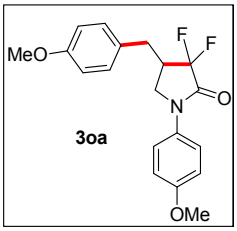
3,3-difluoro-1-(4-methoxyphenyl)-4-(4-(trifluoromethyl)benzyl)pyrrolidin-2-one

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 3.73 (t, *J* = 8.0 Hz, 1H), 3.62 (t, *J* = 8.0 Hz, 1H), 3.34 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.88-2.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.79 (t), 157.76, 141.07, 130.79, 129.13, 125.88 (d, *J* = 4.0 Hz), 121.72, 117.18 (t, *J* = 274 Hz), 114.35, 55.50, 48.41, 41.24 (t, *J* = 20 Hz), 31.47; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.53, -109.15 (d, *J* = 266.96 Hz), -116.66 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{17}F_5NO_2$ $[M+H]^+$: 386.1174; found: 386.1172.



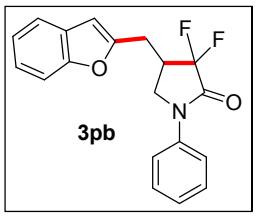
3,3-difluoro-1-(4-methoxyphenyl)-4-(naphthalen-2-ylmethyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83-7.88 (m, 3H), 7.72 (s, 1H), 7.50-7.52 (m, 4H), 7.41 (d, *J* = 12 Hz, 1H), 6.92 (d, *J* = 12 Hz, 2H), 3.81 (s, 3H), 3.59-3.70 (m, 2H), 3.48 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.06-3.11 (m, 1H), 2.98-3.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.13 (t), 157.65, 134.38, 133.55, 132.45, 130.98, 128.82, 127.75, 127.53, 127.37, 126.49, 125.97, 121.68, 117.31 (t, J = 214 Hz), 114.29, 55.49, 48.55, 41.59 (t, *J* = 21 Hz), 31.70; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.29 (d, *J* = 266.96 Hz), -116.82 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{22}H_{20}F_2NO_2$ $[M+H]^+$: 368.1457, found: 368.1455.



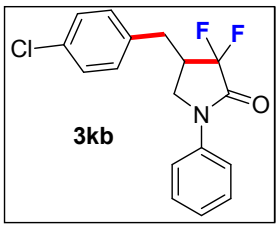
3,3-difluoro-4-(4-methoxybenzyl)-1-(4-methoxyphenyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.93 (t, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 3.69 (t, *J* = 8.0 Hz, 1H), 3.58 (t, *J* = 8.0 Hz, 1H), 3.25 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.85-2.94 (m, 1H), 2.73-2.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.19 (t), 158.65, 157.64, 131.02, 129.71, 128.82, 121.70, 121.61, 117.58 (t, *J* = 244 Hz), 114.34, 114.29, 55.50 (d, *J* = 20 Hz), 48.53, 41.85 (t, *J* = 20 Hz), 30.65; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.25 (d, *J* = 266.96 Hz), -117.07 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{20}F_2NO_3$ $[M+H]^+$: 348.1406, found: 348.1406.



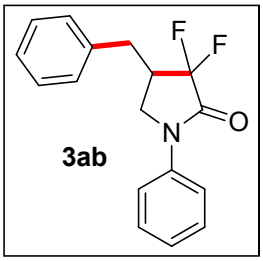
4-(benzofuran-2-ylmethyl)-3,3-difluoro-1-phenylpyrrolidin-2-one

Pure crystal; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.40-7.47 (m, 3H), 7.24-7.32 (m, 3H), 6.60 (s, 1H), 3.96 (t, *J* = 8.0 Hz, 1H), 3.76 (t, *J* = 8.0 Hz, 1H), 3.43 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.15-3.22 (m, 1H), 3.05-3.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.02 (t), 154.96, 153.69, 137.80, 129.22, 128.33, 126.29, 124.14, 123.01, 120.76, 120.01, 117.17 (t, *J* = 241 Hz), 111.01, 104.54, 48.28 (d), 38.94 (t, *J* = 21 Hz), 24.89; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.64 (d, *J* = 266.96 Hz), -118.80 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{16}F_2NO_2$ $[M+H]^+$: 328.1144, found: 328.1141.



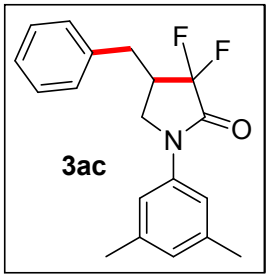
4-(4-chlorobenzyl)-3,3-difluoro-1-phenylpyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.21-7.28 (m, 3H), 3.76 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.28 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.89-2.97 (m, 1H), 2.79-2.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.25 (t), 137.81, 135.32, 133.07, 130.08, 129.21, 129.15, 126.26, 119.96, 117.18 (t, *J* = 249 Hz), 48.04, 41.32 (t, *J* = 21 Hz), 30.92; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.17 (d, *J* = 266.96 Hz), -117.49 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{17}H_{15}ClF_2NO$ $[M+H]^+$: 322.0805, found: 322.0801.



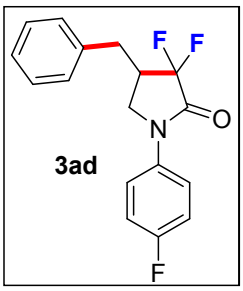
4-benzyl-3,3-difluoro-1-phenylpyrrolidin-2-one

Pure crystal; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 8.0 Hz, 2H), 7.33-7.41 (m, 4H), 7.23-7.29 (m, 4H), 3.74 (t, *J* = 8.0 Hz, 1H), 3.62 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.92-3.01 (m, 1H), 2.80-2.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.87 (t), 137.91, 136.89, 129.17, 129.01, 128.72, 127.15, 126.18, 119.99, 117.33 (t, *J* = 21 Hz), 48.16 (d), 41.65 (t, *J* = 21 Hz), 31.48 (d); ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.57 (d, *J* = 266.96 Hz), -117.24 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{17}H_{16}F_2NO$ $[M+H]^+$: 288.1194, found: 288.1192.



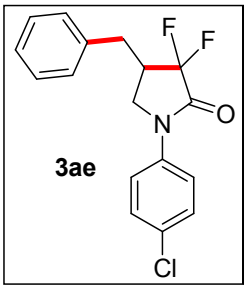
4-benzyl-1-(3,5-dimethylphenyl)-3,3-difluoropyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (t, *J* = 8.0 Hz, 2H), 7.27-7.33 (m, 3H), 7.21 (s, 2H), 6.90 (s, 1H), 3.74 (t, *J* = 8.0 Hz, 1H), 3.61 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.90-3.00 (m, 1H), 2.79-2.85 (m, 1H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.68 (t), 138.93, 137.76, 136.98, 128.99, 128.74, 128.01, 127.10, 118.00, 117.42 (t, *J* = 245 Hz), 48.44, 41.68 (t, *J* = 21 Hz), 31.55, 21.43; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.50 (d, *J* = 266.96 Hz), -117.29 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{20}F_2NO$ $[M+H]^+$: 316.1507, found: 316.1504.



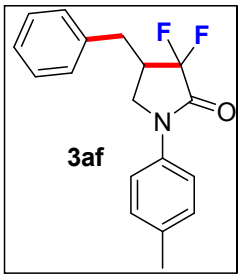
4-benzyl-3,3-difluoro-1-(4-fluorophenyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (q, *J* = 4.0 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.27-7.31 (m, 3H), 7.12 (t, *J* = 8.0 Hz, 2H), 3.71 (t, *J* = 8.0 Hz, 1H), 3.60 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.91-3.04 (m, 1H), 2.80-2.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.36 (t), 161.6 (d, *J* = 245 Hz), 136.78, 133.97, 129.03, 128.72, 127.19, 121.90, 117.30 (t, *J* = 249 Hz), 116.09, 115.87, 48.40, 41.42 (t, *J* = 21 Hz), 31.44; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.63 (d, *J* = 266.96 Hz), -115.10, -117.14 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{17}H_{15}F_3NO$ $[M+H]^+$: 306.1100, found: 306.1108.



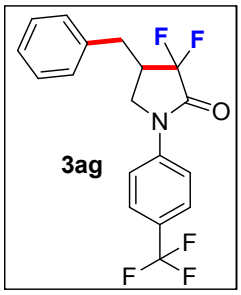
4-benzyl-1-(4-chlorophenyl)-3,3-difluoropyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.0 Hz, 2H), 7.31-7.40 (m, 5H), 7.28 (d, *J* = 8.0 Hz, 2H), 3.71 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.92-2.98 (m, 1H), 2.80-2.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.44 (t), 136.70, 136.45, 131.44, 129.23, 129.05, 128.71, 127.22, 117.13 (t, *J* = 241 Hz), 48.05 (d), 41.55 (t, *J* = 21 Hz), 31.42 (d); ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.20 (d, *J* = 266.96 Hz), -118.70 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{17}H_{15}ClF_2NO$ $[M+H]^+$: 322.0805, found: 322.0800.



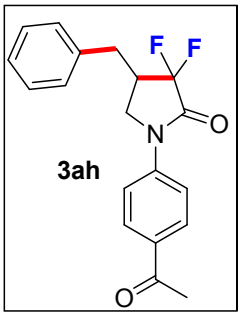
4-benzyl-3,3-difluoro-1-(p-tolyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.27-7.33 (m, 3H), 7.20 (d, *J* = 8.0 Hz, 2H), 3.74 (t, *J* = 8.0 Hz, 1H), 3.61 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.89-3.02 (m, 1H), 2.79-2.85 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.49 (t), 136.95, 136.07, 135.40, 129.68, 128.99, 128.73, 127.12, 119.98, 114.92 (t, *J* = 252 Hz), 48.26, 41.66 (t, *J* = 21 Hz), 31.52, 20.96; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.00 (d, *J* = 266.96 Hz), -118.73 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{18}F_2NO$ $[M+H]^+$: 302.1351, found: 302.1357.



4-benzyl-3,3-difluoro-1-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one

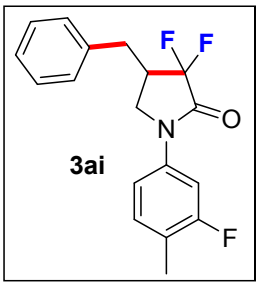
white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.28-7.34 (m, 3H), 3.78 (t, *J* = 8.0 Hz, 1H), 3.64 (t, *J* = 8.0 Hz, 1H), 3.33 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.94-3.09 (m, 1H), 2.82-2.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.79 (t), 140.79, 136.59, 129.07, 128.70, 127.27, 126.37 (q), 116.96 (t, J = 244 Hz), 47.88, 41.30 (t, *J* = 21 Hz), 31.36; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.46, -109.87 (d, *J* = 266.96 Hz), -117.29 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{15}F_5NO$ $[M+H]^+$: 356.1068, found: 356.1065.



1-(4-acetylphenyl)-4-benzyl-3,3-difluoropyrrolidin-2-one

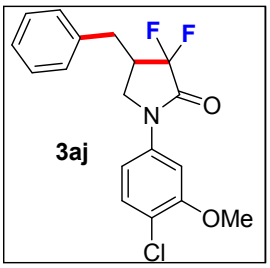
white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.27-7.33 (m, 3H), 3.79 (t, *J* = 8.0 Hz, 1H), 3.65 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.92-3.03 (m, 1H), 2.81-2.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.80, 163.11 (t), 141.75, 141.76, 136.61, 134.26, 129.52, 129.07, 128.71, 127.25, 119.12, 117.04 (t, *J* = 249 Hz), 47.86, 41.26 (t, *J* = 21 Hz), 31.37, 26.55; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.82 (d, *J* = 266.96 Hz), -117.17 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{19}H_{18}F_2NO_2$ $[M+H]^+$: 330.1300,

found: 330.1308.



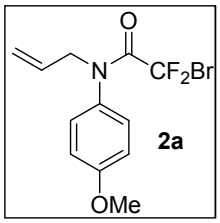
4-benzyl-3,3-difluoro-1-(3-fluoro-4-methylphenyl)pyrrolidin-2-one

white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.17-7.46 (m, 8H), 3.71 (t, *J* = 8.0 Hz, 1H), 3.57 (t, *J* = 8.0 Hz, 1H), 3.30 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.91-2.99 (m, 1H), 2.79-2.85 (m, 1H), 2.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.79 (t), 162.24 (d, *J* = 243 Hz), 136.93, 131.62, 129.03, 128.71, 127.19, 122.81, 117.25 (t, *J* = 248 Hz), 114.82, 107.36, 107.07, 48.08, 41.31 (t, *J* = 21 Hz), 31.45, 14.19; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.15 (d, *J* = 266.96 Hz), -115.99, -118.66 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{17}F_3NO$ $[M+H]^+$: 320.1257, found: 320.1253.



4-benzyl-1-(4-chloro-3-methoxyphenyl)-3,3-difluoropyrrolidin-2-one

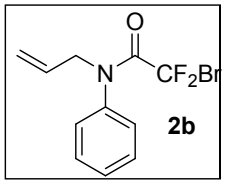
white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74 (s, 1H), 7.27-7.33 (m, 6H), 6.78 (d, *J* = 8.0 Hz, 1H), 3.93 (s, 3H), 3.74 (t, *J* = 8.0 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.32 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.91-2.98 (m, 1H), 2.80-2.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.55 (t), 155.30, 137.63, 136.69, 130.06, 129.05, 128.71, 127.22, 119.82, 117.29 (t, *J* = 236 Hz), 111.36, 104.81, 56.30, 48.19, 41.27 (t, *J* = 21 Hz), 31.44; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.48 (d, *J* = 266.96 Hz), -117.48 (d, *J* = 266.96 Hz); HRMS (ESI) calcd for $C_{18}H_{17}ClF_2NO_2$ $[M+H]^+$: 352.0910, found: 352.0913.



S25

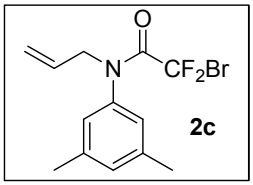
***N*-allyl-2-bromo-2,2-difluoro-*N*-(4-methoxyphenyl)acetamide**

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.19 (d, J = 8.0 Hz, 2H); 6.92 (d, J = 8.0 Hz, 2H); 5.84-5.92 (m, 1H), 5.13-5.22 (m, 2H), 4.29 (d, J = 8.0 Hz, 2H); 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.64, 159.02 (t), 132.12, 130.92, 129.91, 119.77, 114.16, 111.50 (t, J = 310 Hz), 55.63, 55.44; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -51.97; HRMS (ESI) calcd for $C_{12}H_{13}BrF_2NO_2$ $[M+H]^+$: 320.0092, found: 320.0099.



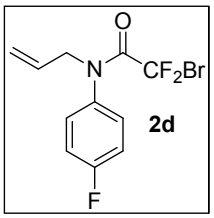
***N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide**

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 (d, J = 8.0 Hz, 3H), 7.27 (d, J = 8.0 Hz, 2H), 5.85-5.95 (m, 1H), 5.26 (d, J = 12 Hz, 1H), 5.19 (d, J = 20 Hz, 1H), 4.34 (d, J = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.82 (t), 139.61, 130.79, 129.18, 128.96, 128.71, 119.86, 111.58 (t, J = 320 Hz), 55.54; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -51.94; HRMS (ESI) calcd for $C_{11}H_{11}BrF_2NO$ $[M+H]^+$: 289.9987, found: 289.9980.



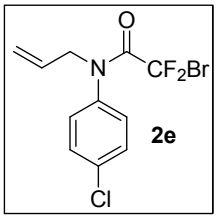
***N*-allyl-2-bromo-*N*-(3,5-dimethylphenyl)-2,2-difluoroacetamide**

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.03 (s, 1H), 6.88 (s, 2H), 5.85-5.94 (m, 1H), 5.17-5.26 (m, 2H), 4.30 (d, J = 4.0 Hz, 2H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.83, 139.52, 138.89, 130.96, 130.49, 126.03, 119.51, 111.67 (t, J = 316 Hz), 55.52, 21.16; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -51.79; HRMS (ESI) calcd for $C_{13}H_{15}BrF_2NO$ $[M+H]^+$: 318.0300, found: 318.0303.



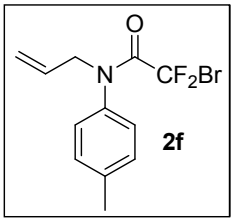
***N*-allyl-2-bromo-2,2-difluoro-*N*-(4-fluorophenyl)acetamide**

Pale yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24-7.28 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 5.84-5.92 (m, 1H), 5.27 (d, *J* = 12 Hz, 1H), 5.18 (d, *J* = 16 Hz, 1H), 4.31 (d, *J* = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.68 (d, *J* = 248 Hz), 158.81 (t), 135.43, 130.73, 120.15, 116.27, 116.04, 111.48 (t, *J* = 318 Hz), 55.54; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -53.56, -113.14; HRMS (ESI) calcd for $C_{11}H_{10}BrF_3NO$ $[M+H]^+$: 307.9892, found: 307.9895.



***N*-allyl-2-bromo-*N*-(4-chlorophenyl)-2,2-difluoroacetamide**

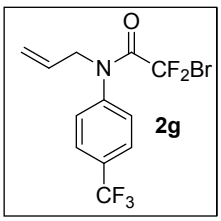
Pale yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.83-5.93 (m, 1H), 5.27 (d, *J* = 8.0 Hz, 1H), 5.18 (d, *J* = 16 Hz, 1H), 4.31 (d, *J* = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.05 (t), 137.99, 135.02, 130.51, 130.17, 129.48, 120.31, 111.37 (t, *J* = 330 Hz), 55.49; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -53.65; HRMS (ESI) calcd for $C_{11}H_{10}BrClF_2NO$ $[M+H]^+$: 323.9597, found: 323.9591.



***N*-allyl-2-bromo-2,2-difluoro-*N*-(p-tolyl)acetamide**

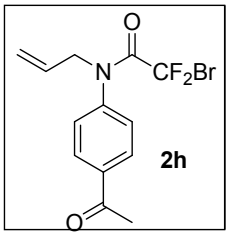
Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.85-5.93 (m, 1H), 5.25 (d, *J* = 12.0 Hz, 1H), 5.19 (d, *J* = 20.0 Hz, 1H),

4.31 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.18 (t), 138.98, 136.98, 130.91, 129.75, 128.43, 119.72, 111.56 (t, *J* = 316 Hz), 55.57, 21.17; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -53.38; HRMS (ESI) calcd for $C_{12}H_{13}BrF_2NO$ $[M+H]^+$: 304.0143, found: 304.0145.



***N*-allyl-2-bromo-2,2-difluoro-*N*-(4-(trifluoromethyl)phenyl)acetamide**

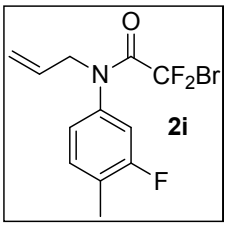
Pale yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 5.85-5.95 (m, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 5.19 (d, *J* = 16.0 Hz, 1H), 4.35 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.61, 142.75, 130.34, 129.32, 126.45, 120.48, 111.24 (t, *J* = 317 Hz), 55.39; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -52.23, -62.74; HRMS (ESI) calcd for $C_{12}H_{10}BrF_5NO$ $[M+H]^+$: 357.9860, found: 357.9865.



***N*-(4-acetylphenyl)-*N*-allyl-2-bromo-2,2-difluoroacetamide**

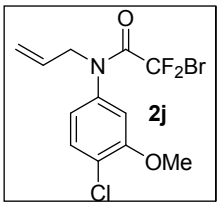
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 5.83-5.93 (m, 1H), 5.26 (d, *J* = 12 Hz, 1H), 5.13 (d, *J* = 12 Hz, 1H), 4.35 (d, *J* = 4.0 Hz, 2H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.89, 158.58

(t), 143.59, 137.18, 130.46, 129.34, 129.00, 120.37, 116.16 (t, J = 324 Hz), 55.35, 26.74; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -52.18; HRMS (ESI) calcd for $C_{13}H_{13}BrF_2NO_2$ $[M+H]^+$: 332.0092, found: 332.0086.



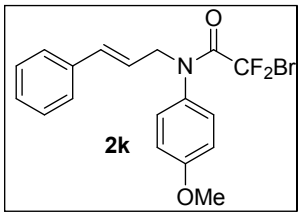
***N*-allyl-2-bromo-2,2-difluoro-*N*-(3-fluoro-4-methylphenyl)acetamide**

Pale yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, J = 8.0 Hz, 1H), 6.95-6.98 (m, 2H), 5.84-5.94 (m, 1H), 5.27 (d, J = 12.0 Hz, 1H), 5.19 (d, J = 16.0 Hz, 1H), 4.31 (d, J = 8.0 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.93 (d, J = 246 Hz), 158.57 (t), 131.63, 131.57, 130.63, 126.26, 126.10, 124.28, 120.07, 115.79, 115.55, 111.37 (t, J = 324 Hz), 55.48, 14.42; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -53.63, -116.09; HRMS (ESI) calcd for $C_{12}H_{12}BrF_3NO$ $[M+H]^+$: 322.0049, found: 322.0048.



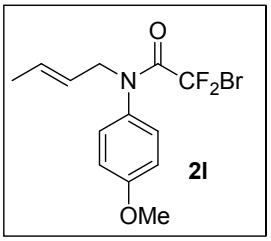
***N*-allyl-2-bromo-*N*-(4-chloro-3-methoxyphenyl)-2,2-difluoroacetamide**

Pale yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, J = 8.0 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 5.86-5.95 (m, 1H), 5.28 (d, J = 8.0 Hz, 1H), 5.21 (d, J = 20.0 Hz, 1H), 4.32 (d, J = 8.0 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.68 (t), 155.27, 139.01, 130.70, 130.43, 121.34, 120.25, 112.65, 111.38 (t, J = 324 Hz), 56.35, 55.53; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -52.05; HRMS (ESI) calcd for $C_{12}H_{12}BrClF_2NO_2$ $[M+H]^+$: 353.9703, found: 353.9705.



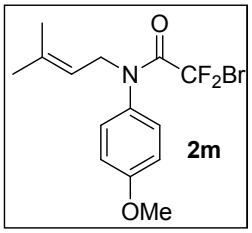
2-bromo-*N*-cinnamyl-2,2-difluoro-*N*-(4-methoxyphenyl)acetamide

Thick yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.39 (m, 5H), 7.22 (d, *J* = 12.0 Hz, 2H), 6.93 (d, *J* = 12.0 Hz, 2H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.24-6.32 (m, 1H), 4.46 (d, *J* = 8.0 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.68, 159.12 (t), 136.29, 135.20, 132.06, 130.00, 128.63, 128.08, 126.5, 121.87, 114.24, 117.57 (t, *J* = 323 Hz), 55.45, 55.24; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -51.86; HRMS (ESI) calcd for $C_{18}H_{17}BrF_2NO_2$ $[M+H]^+$: 396.0405, found: 396.0401.



2-bromo-*N*-(but-2-en-1-yl)-2,2-difluoro-*N*-(4-methoxyphenyl)acetamide

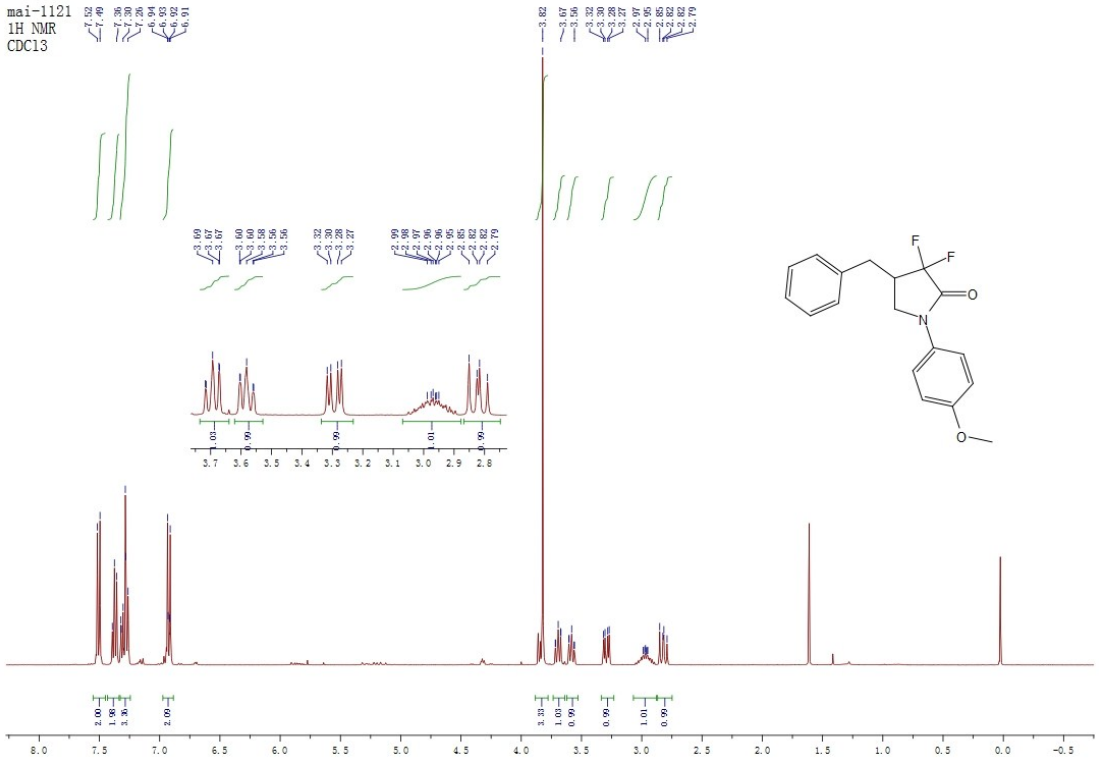
Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.15 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 5.55 (m, 2H), 4.21 (m, 2H), 3.85 (s, 3H), 1.70 (d, *J* = 4.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.55, 158.90, 132.13, 131.65, 129.99, 123.58, 122.80, 114.12, 111.64 (t, *J* = 323 Hz), 55.43, 55.01, 17.79; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -51.94; HRMS (ESI) calcd for $C_{13}H_{15}BrF_2NO_2$ $[M+H]^+$: 334.0249, found: 334.0241.

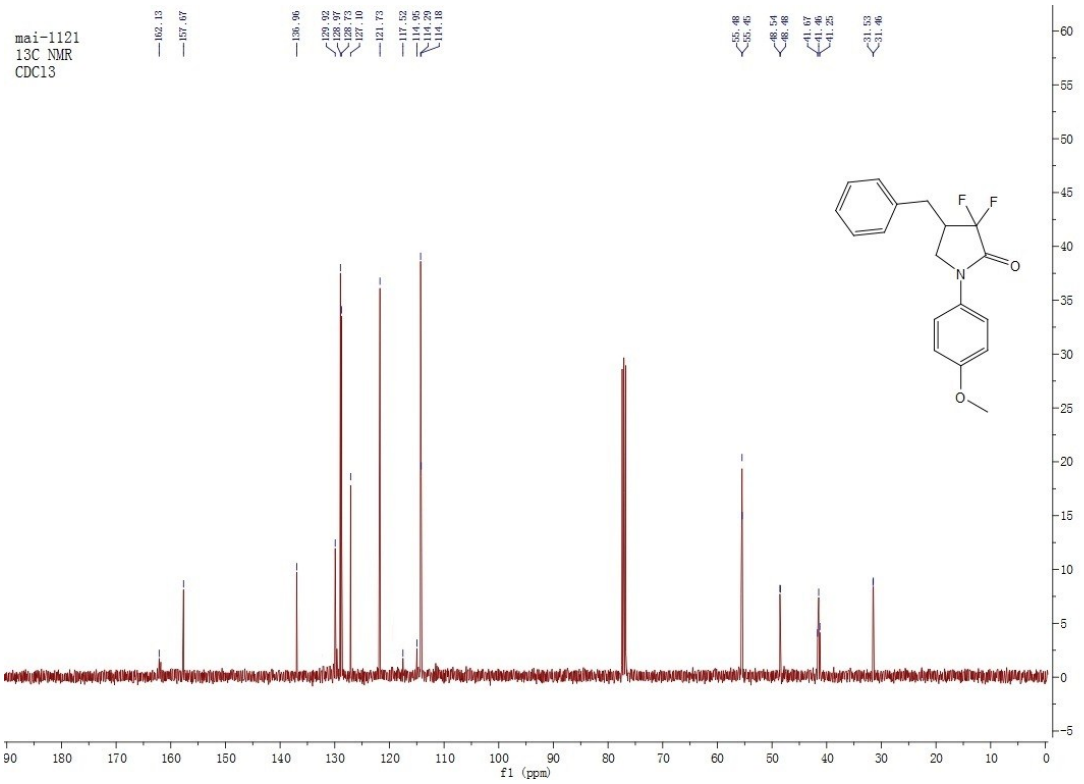


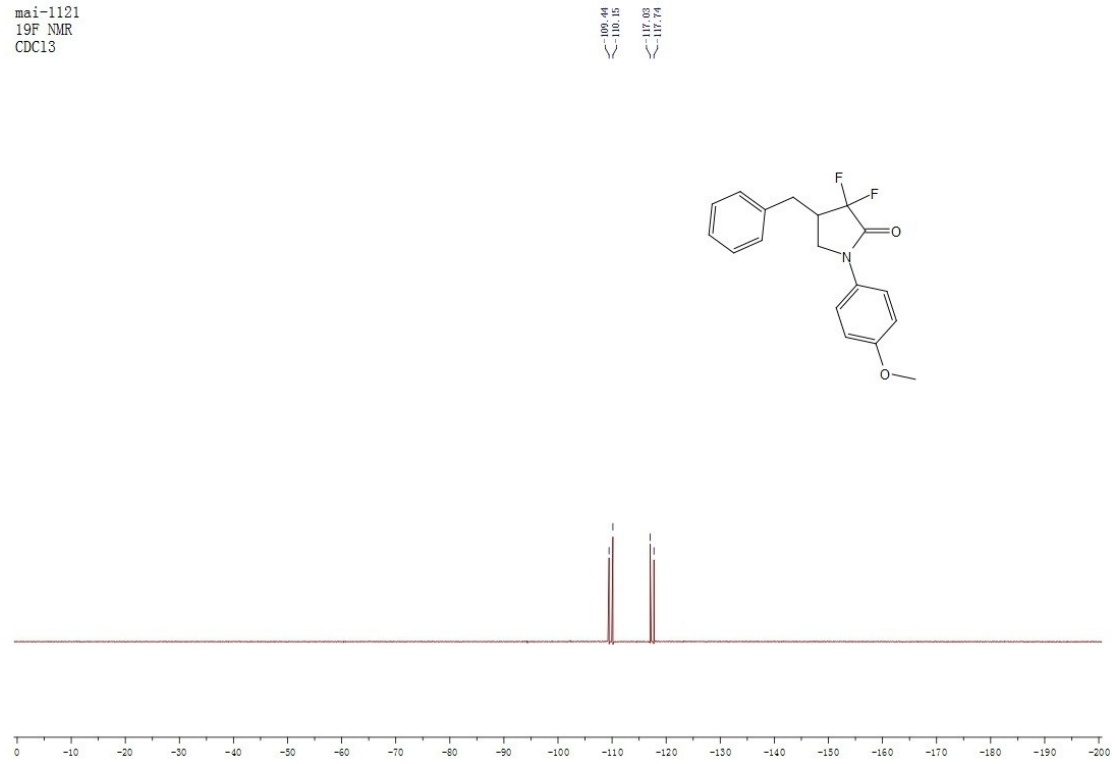
2-bromo-2,2-difluoro-*N*-(4-methoxyphenyl)-*N*-(3-methylbut-2-en-1-yl)acetamide

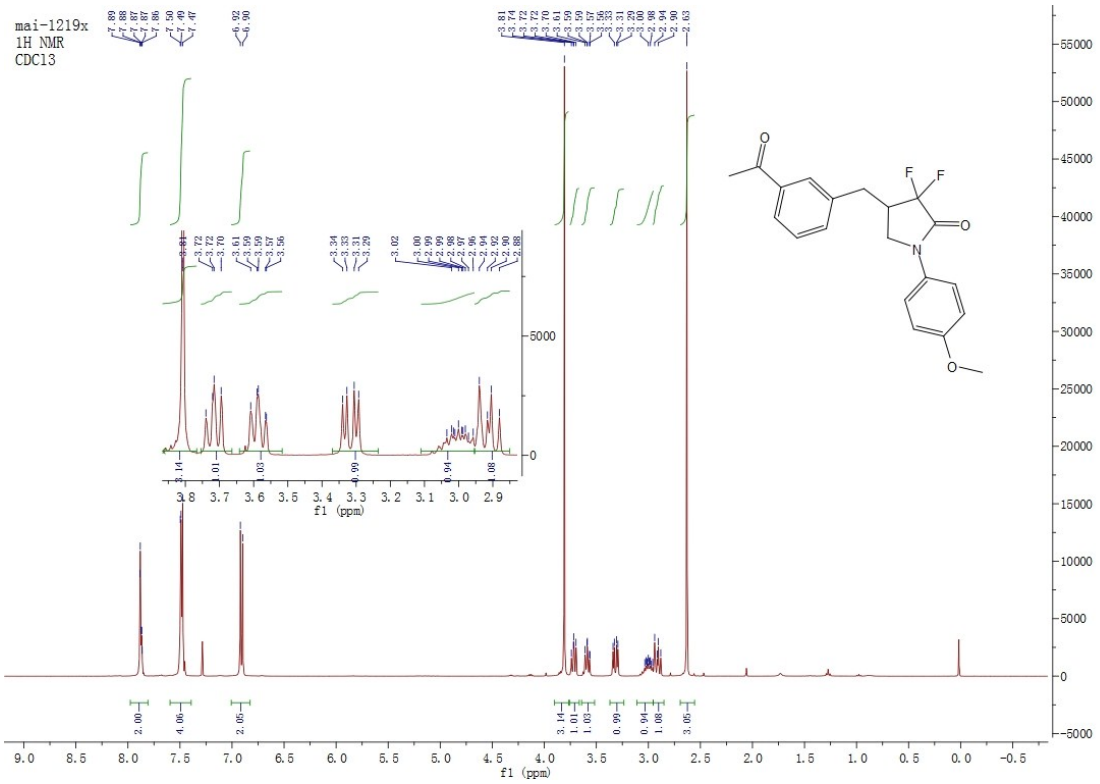
Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.15 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 5.25-5.29 (m, 1H), 4.30 (d, *J* = 8.0 Hz, 2H), 3.85 (s, 3H), 1.73 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.92, 158.89, 138.52, 132.13, 129.97, 117.09, 114.04, 111.74 (t, *J* = 323 Hz), 55.43, 50.48, 25.76, 17.72; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -52.15; HRMS (ESI) calcd for $C_{14}H_{17}BrF_2NO_2$ $[M+H]^+$: 348.0405, found: 348.0402.

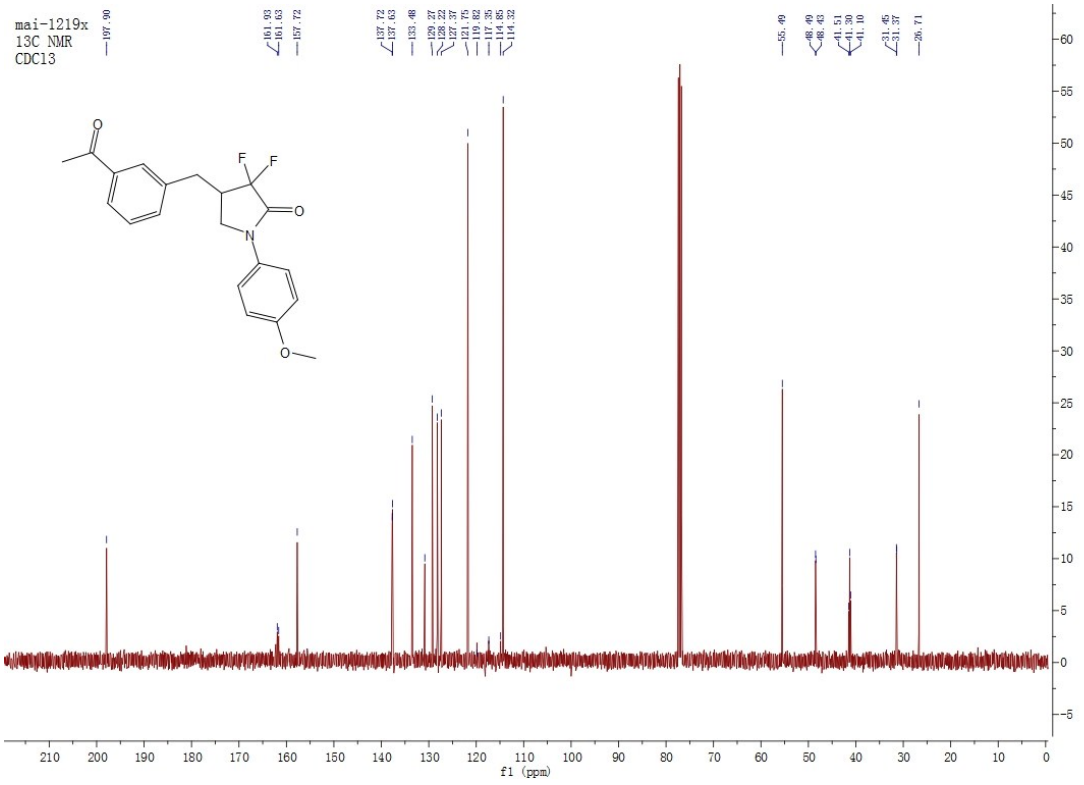
^{1}H, ^{19}F, and ^{13}C NMR Spectra

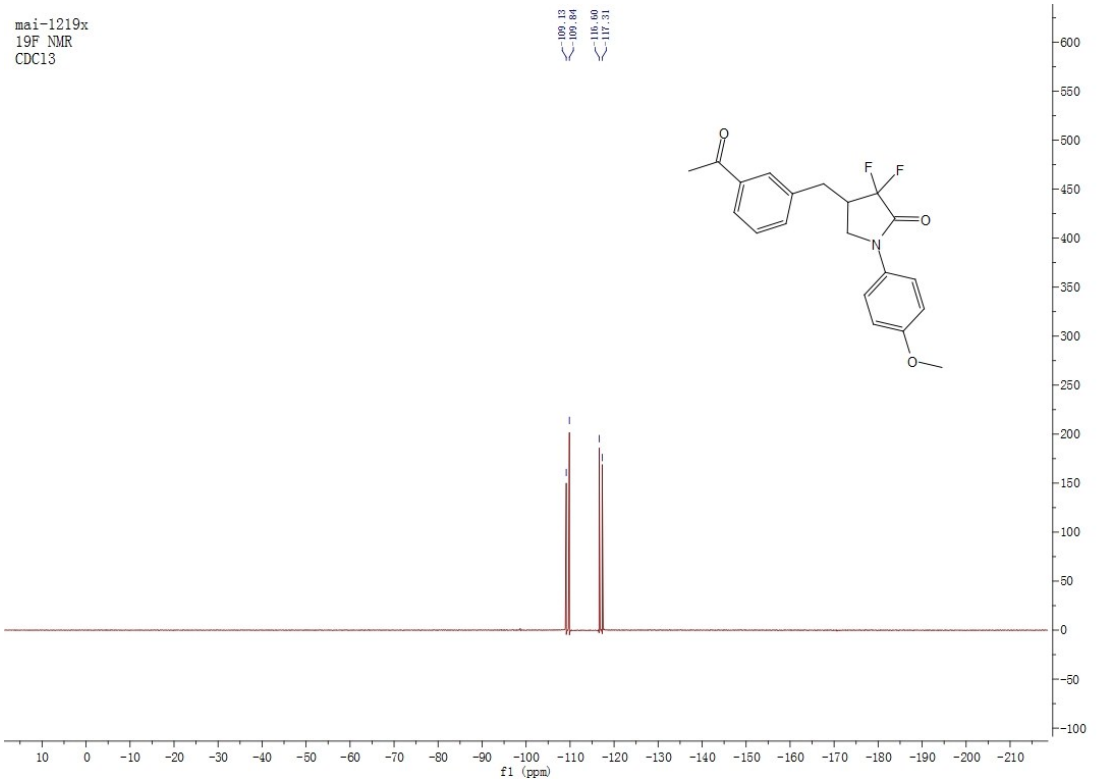


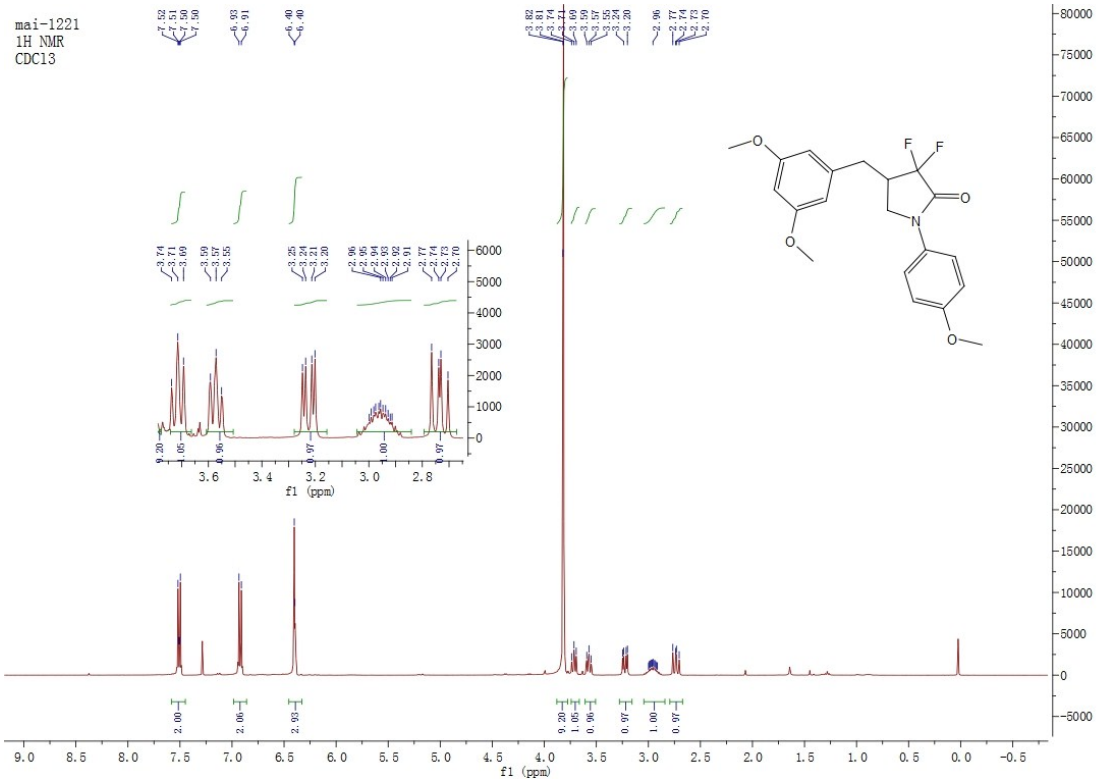

mai-1121
13C NMR
CDCl3
162.13
157.67
136.96
129.92
128.97
128.73
127.10
121.73
117.52
114.95
114.29
114.18
55.48
55.45
48.54
48.48
41.67
41.46
41.25
31.53
31.46
F
F
O
N
O
f1 (ppm)

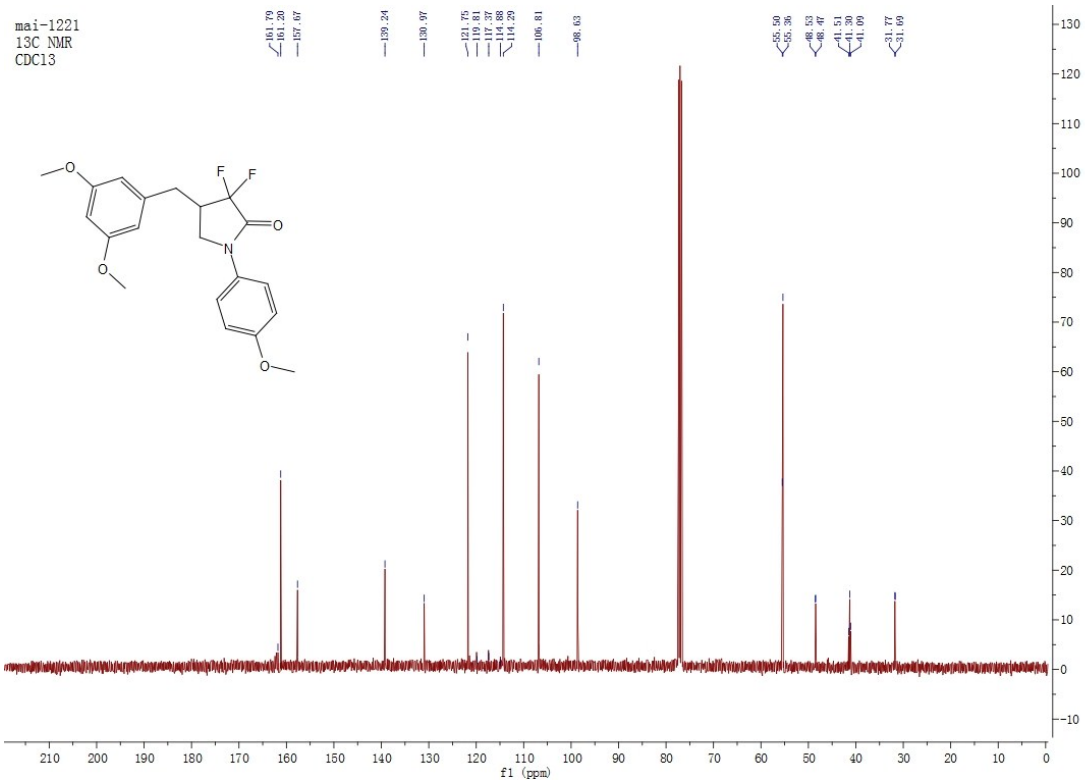

mai-1121
19F NMR
CDCl3
-109.44
-110.15
-117.03
-117.74
F
F
O
N
O

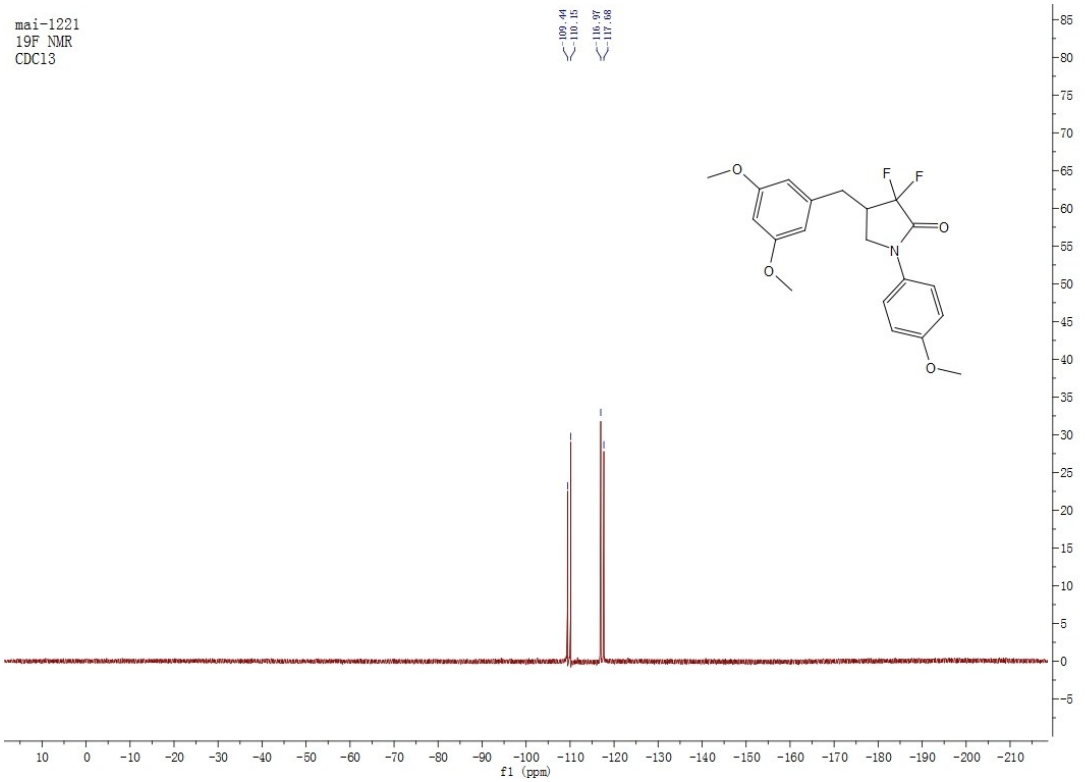

mai-1219x
1H NMR
CDCl3
f1 (ppm)

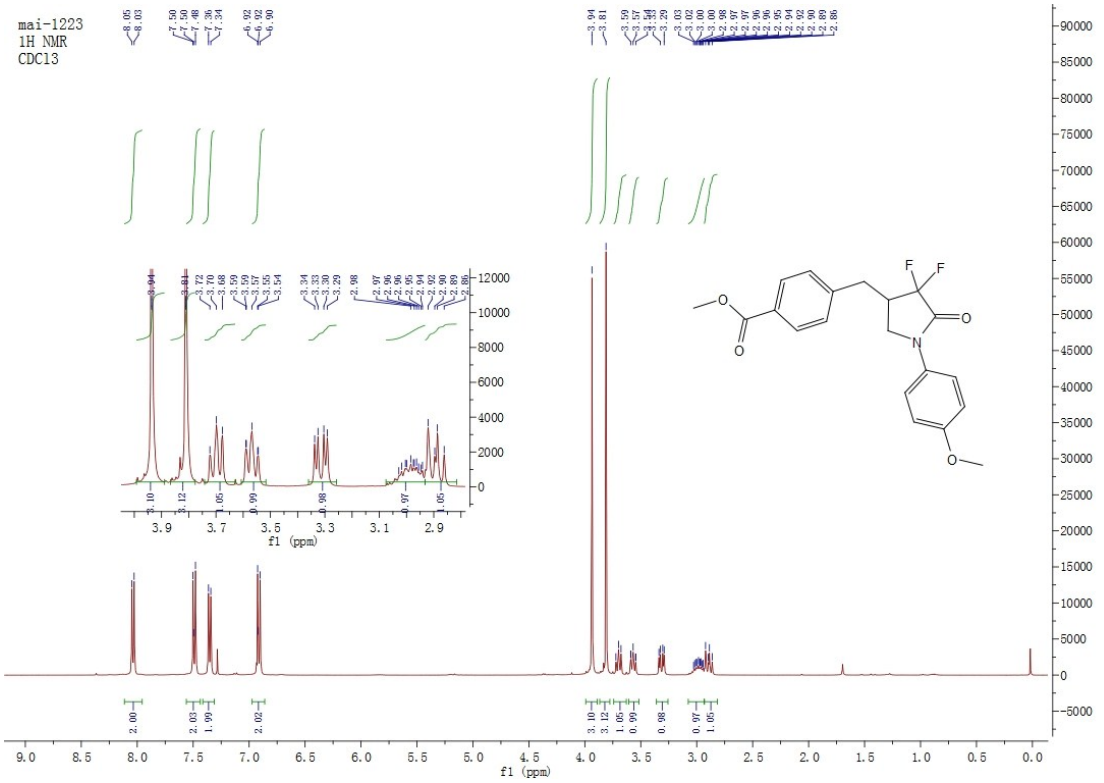

mai-1219x
13C NMR
CDCl3
f1 (ppm)

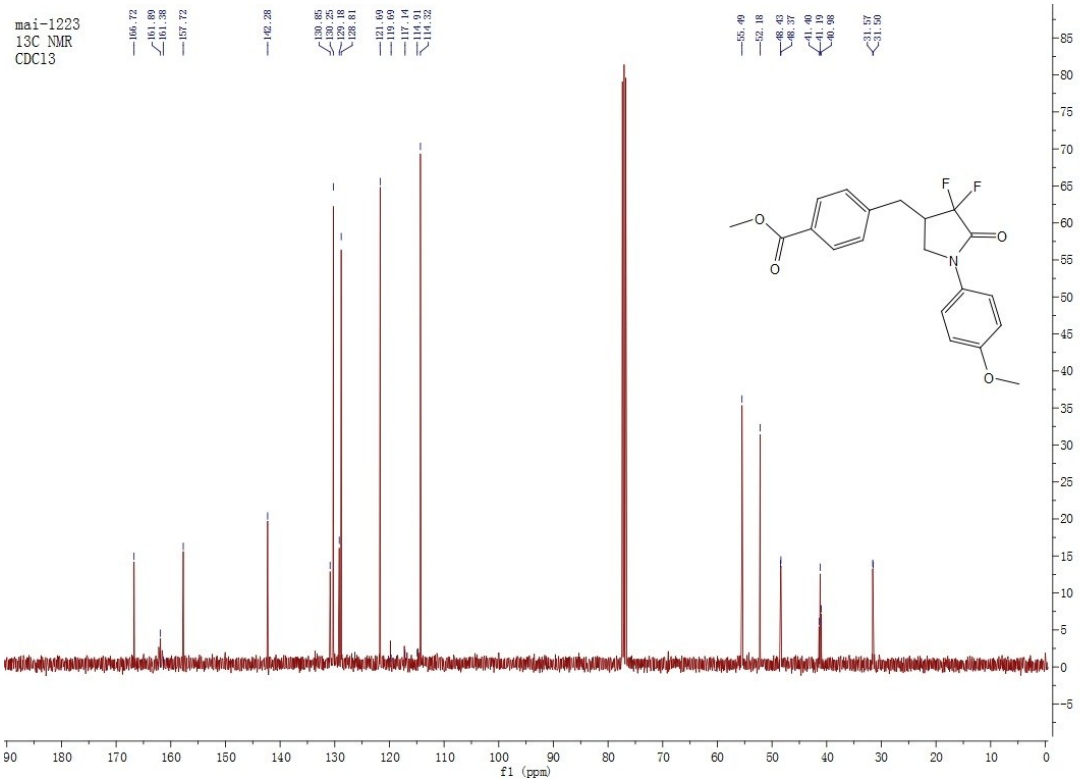

mai-1219x
19F NMR
CDCl3
109.13
109.84
116.60
117.31
O
F
F
O
N
O
f1 (ppm)

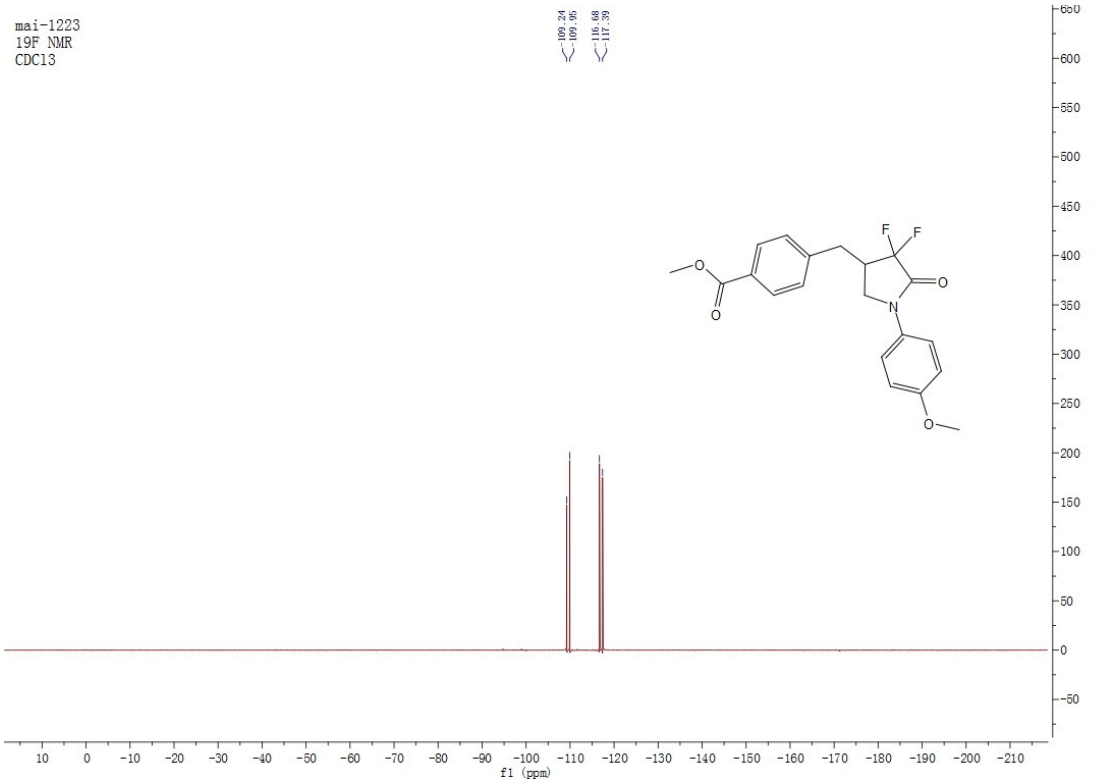

mai-1221
1H NMR
CDCl3
7.52
7.51
7.50
7.50
6.93
6.91
6.40
6.40
3.82
3.81
3.74
3.71
3.69
3.60
3.59
3.57
3.55
3.25
3.24
3.21
3.20
2.96
2.95
2.94
2.93
2.92
2.91
2.77
2.74
2.73
2.70
O
F
F
O
N
O
O
f1 (ppm)

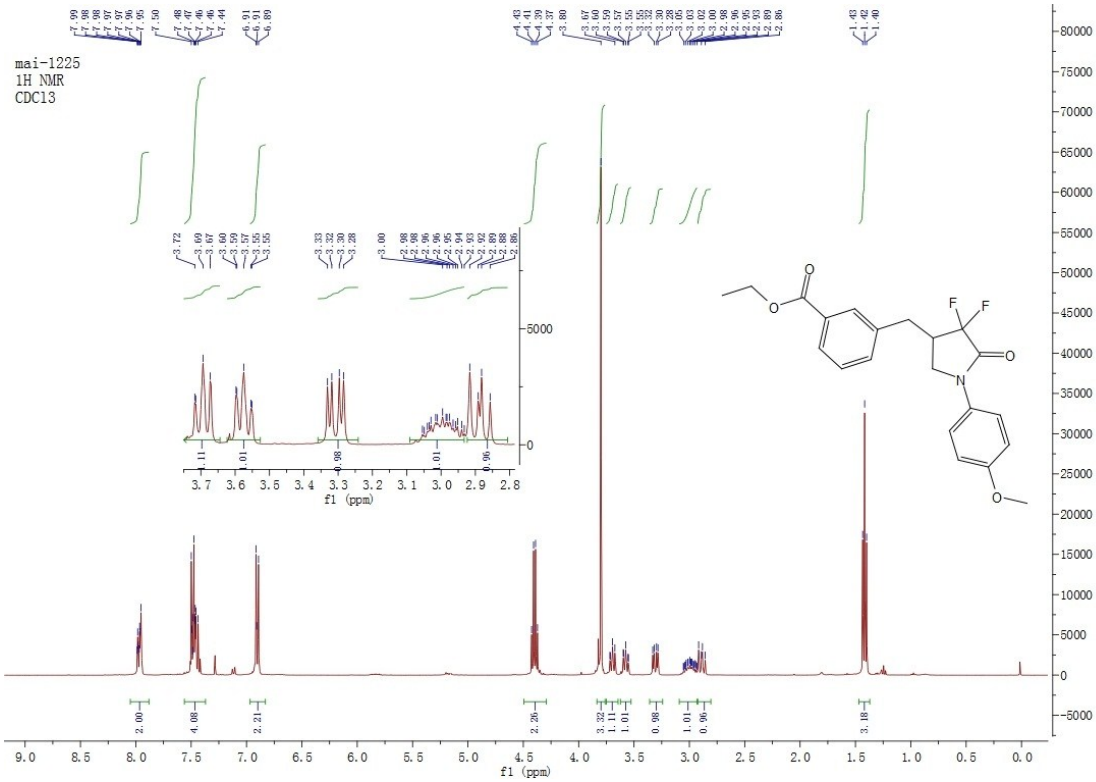

mai-1221
13C NMR
CDC13
161.79
161.20
157.67
139.24
130.97
121.75
119.81
117.37
114.88
114.29
106.81
98.63
55.50
55.36
48.53
48.47
41.51
41.30
41.09
31.77
31.69
F
F
O
N
O
O
f1 (ppm)

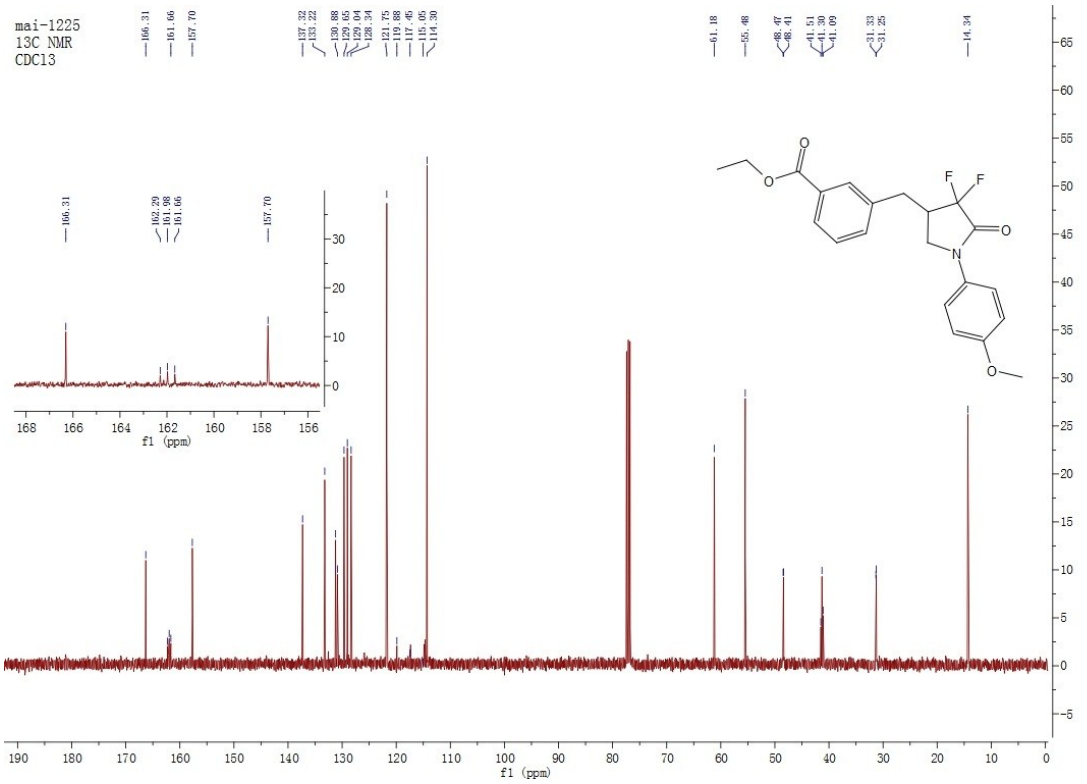

mai-1221
19F NMR
CDC13
-109.44
-110.15
-116.97
-117.68
F
F
O
N
O
O
f1 (ppm)

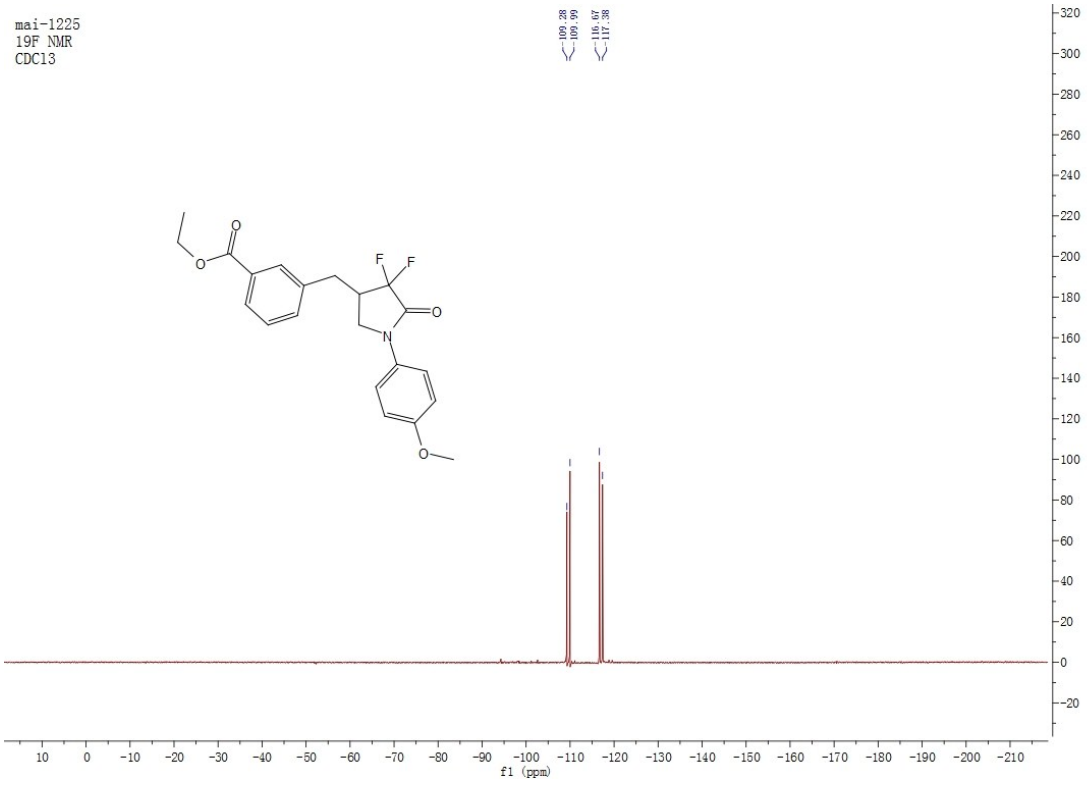

mai-1223
1H NMR
CDC13
f1 (ppm)

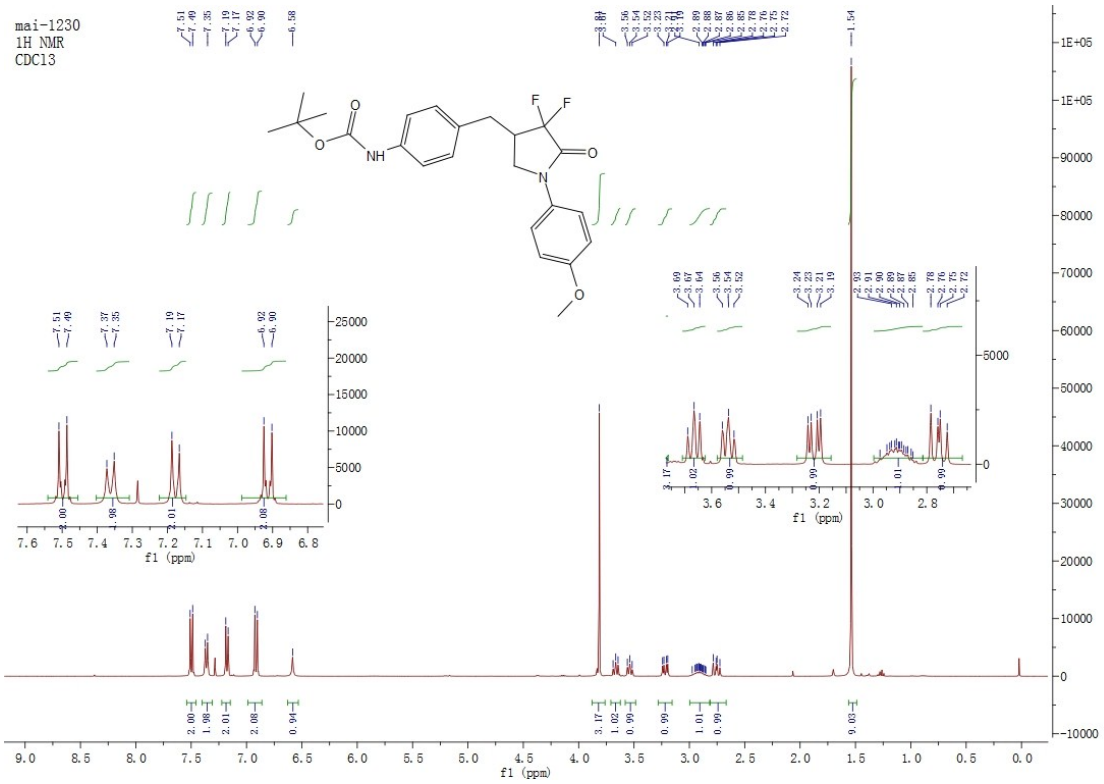

mai-1223
13C NMR
CDC13
f1 (ppm)

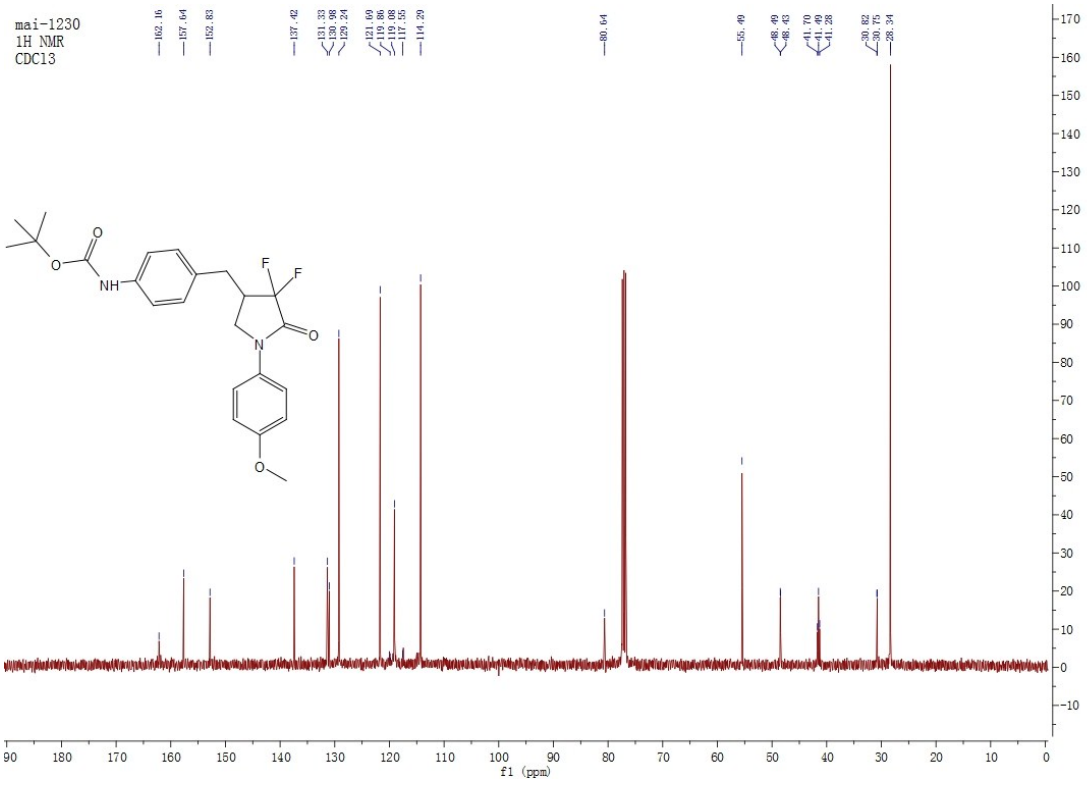

mai-1223
19F NMR
CDCl3
109.24
109.95
116.68
117.39
f1 (ppm)


mai-1225
1H NMR
CDCl3
f1 (ppm)

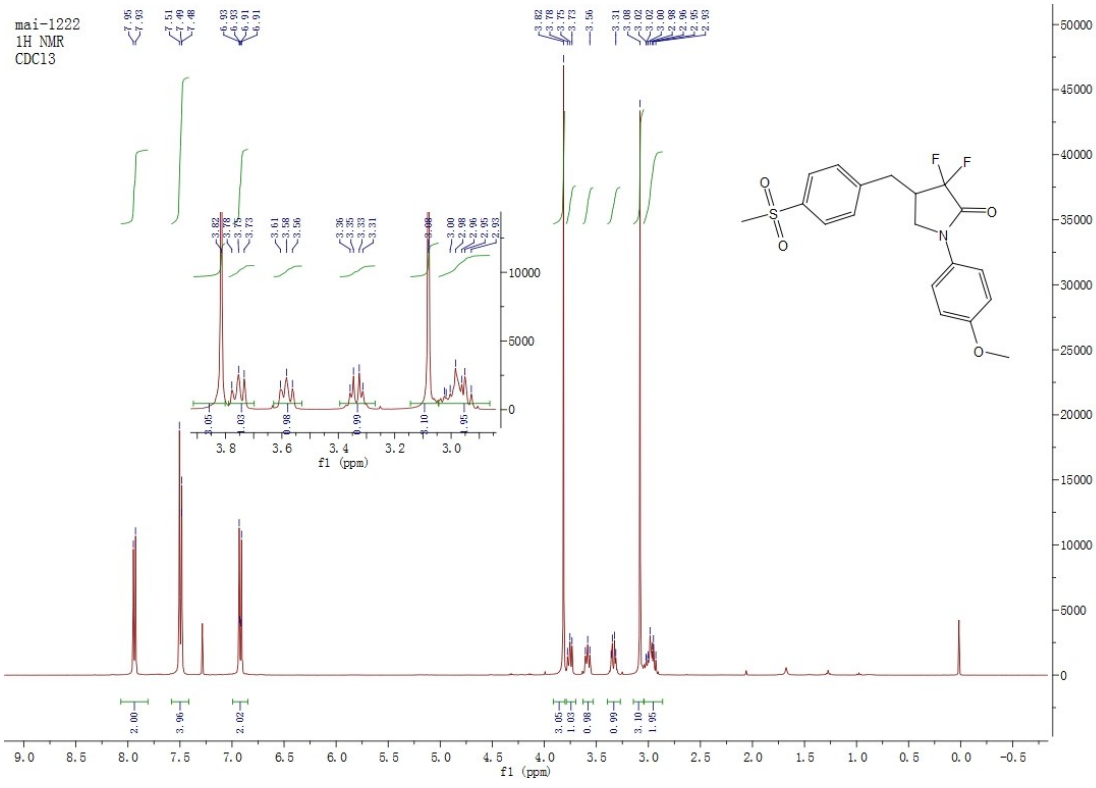

mai-1225
13C NMR
CDC13
166.31
161.66
157.70
137.32
133.22
130.88
129.65
129.04
128.34
121.75
119.88
117.45
115.05
114.30
61.18
55.48
48.47
48.41
41.51
41.30
41.09
31.33
31.25
14.34
f1 (ppm)

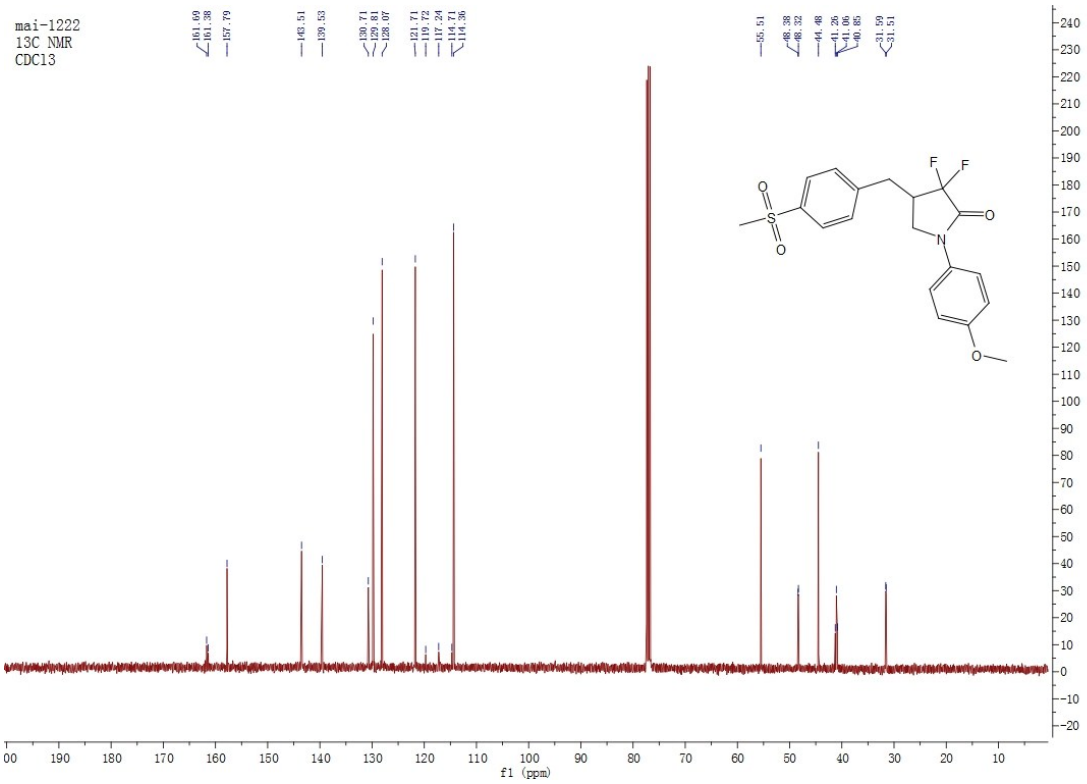

mai-1225
19F NMR
CDC13
-109.28
-109.99
-116.67
-117.38
f1 (ppm)


mai-1230
1H NMR
CDCl3
f1 (ppm)


mai-1230
1H NMR
CDCl3
f1 (ppm)


mai-1230
19F NMR
CDCl3
109.26
109.97
116.99
117.70
f1 (ppm)


mai-1222
1H NMR
CDCl3
f1 (ppm)


mai-1222
13C NMR
CDC13
161.69
161.38
157.79
145.51
139.53
130.71
129.81
128.07
121.71
119.72
117.24
114.71
114.36
55.51
48.38
48.32
44.48
41.26
41.06
40.85
31.59
31.51
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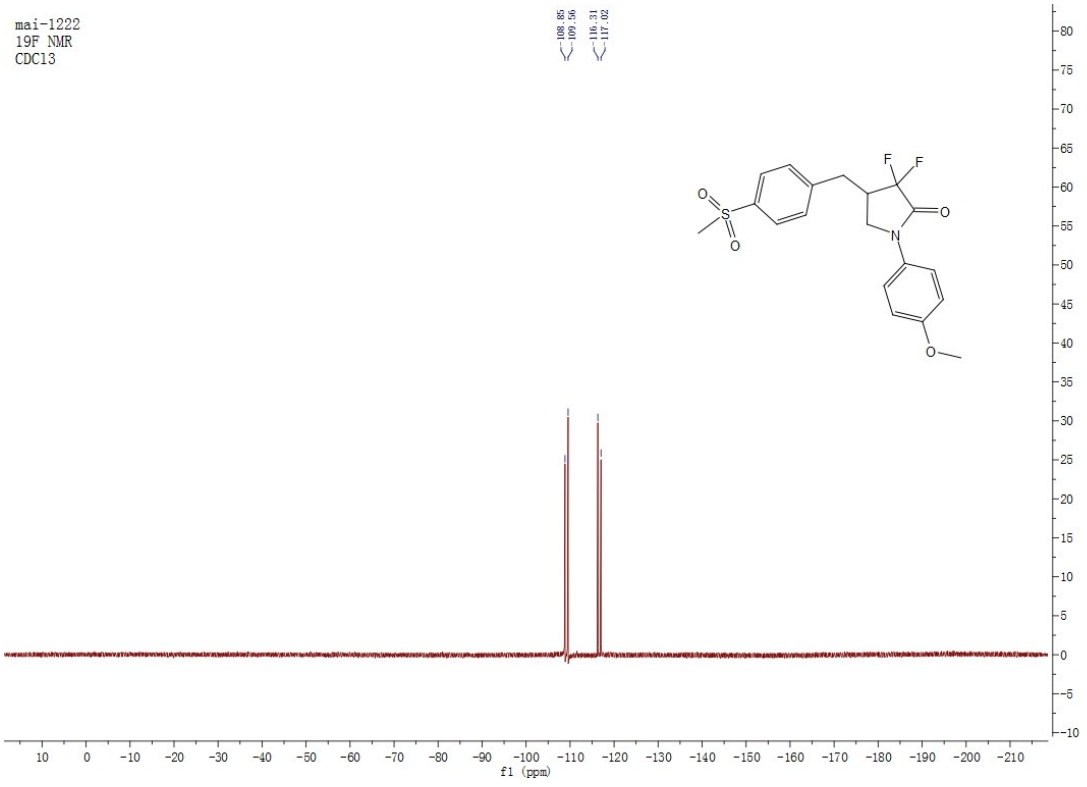
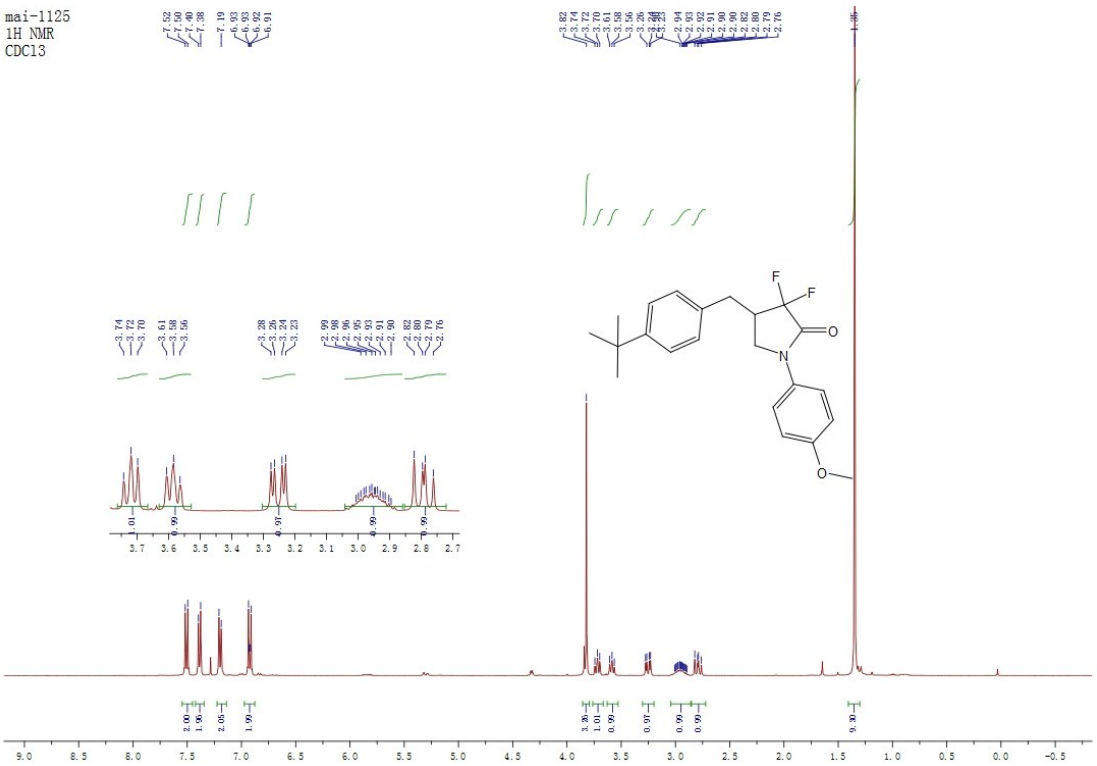
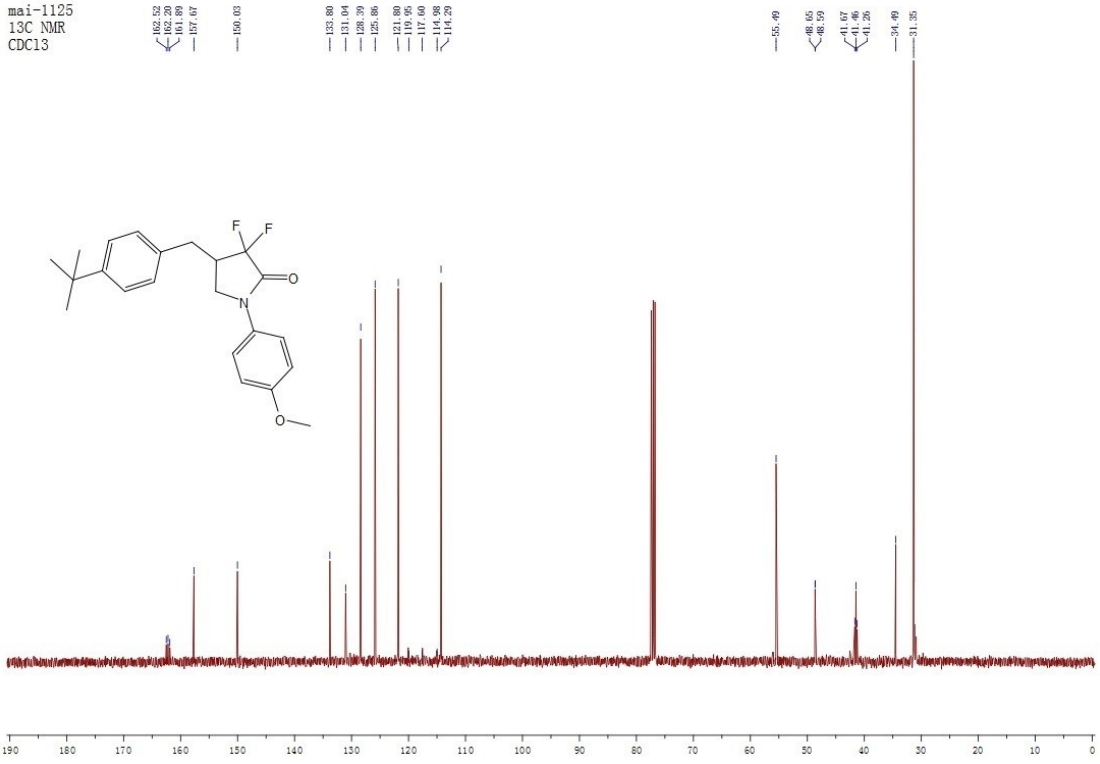
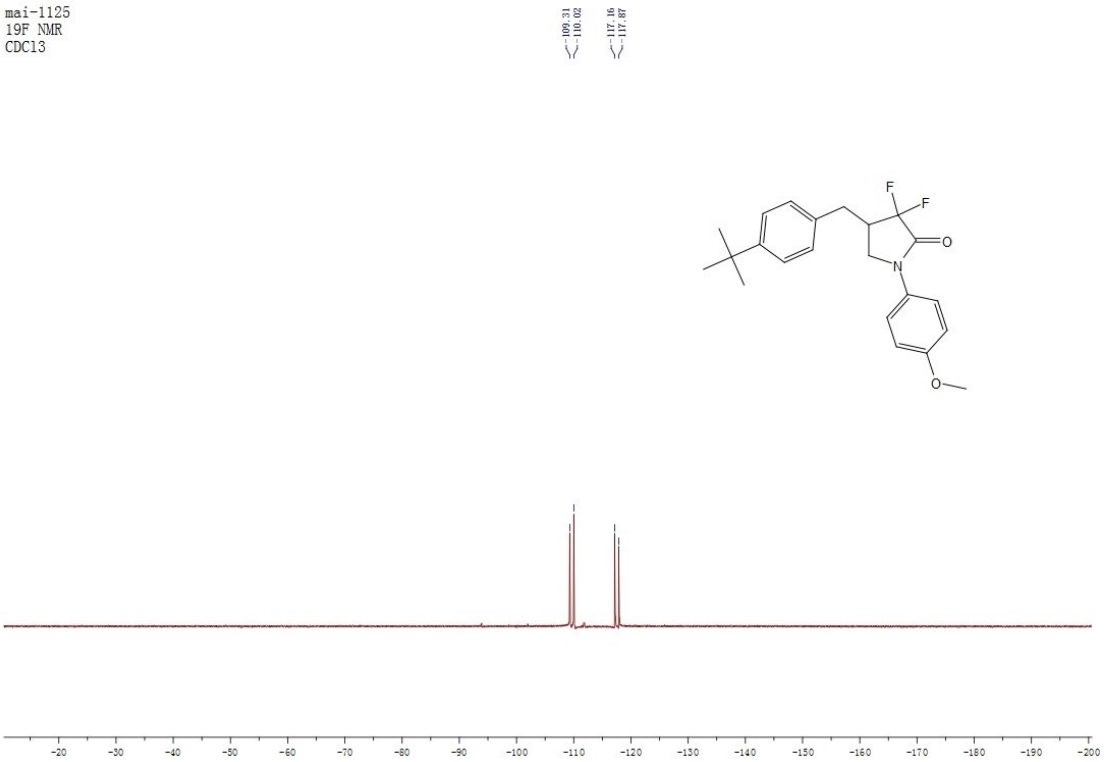
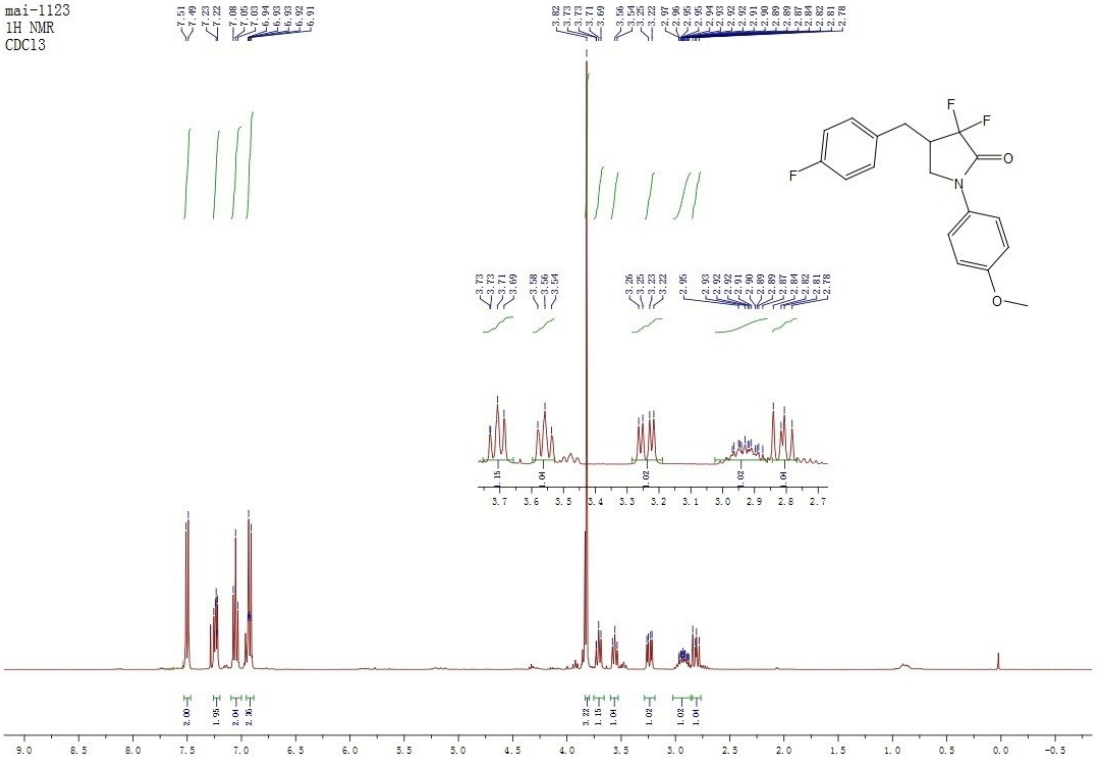
F
O
S
O
O
N
O
f1 (ppm)

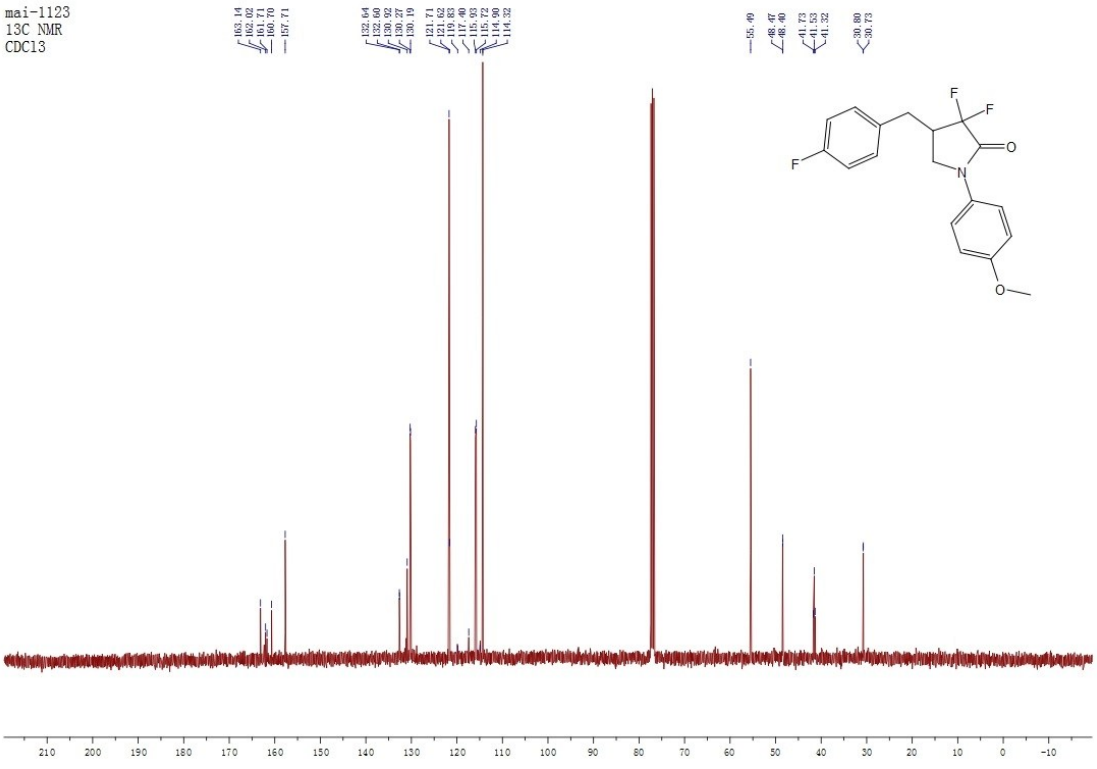

mai-1222
19F NMR
CDC13
108.85
109.56
116.31
117.02
F
F
O
S
O
O
N
O
f1 (ppm)


mai-1125
1H NMR
CDC13


mai-1125
13C NMR
CDC13


mai-1125
19F NMR
CDCl3
-109.31
-110.02
-117.16
-117.87
F
F
O
N
O


mai-1123
1H NMR
CDCl3
F
F
O
N
F
O


mai-1123
13C NMR
CDC13
163.14
162.02
161.71
160.70
157.71
132.64
132.60
130.92
130.27
130.19
121.71
121.62
121.53
117.40
115.93
115.72
115.49
114.32
55.49
48.47
48.40
41.73
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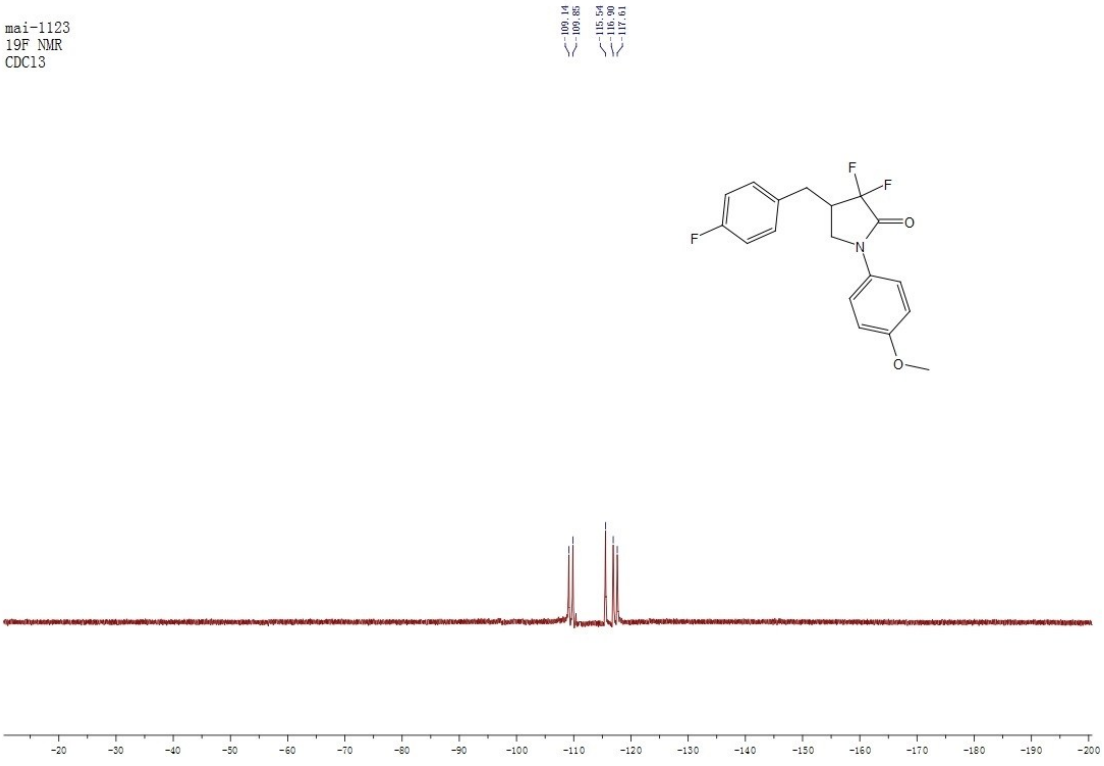
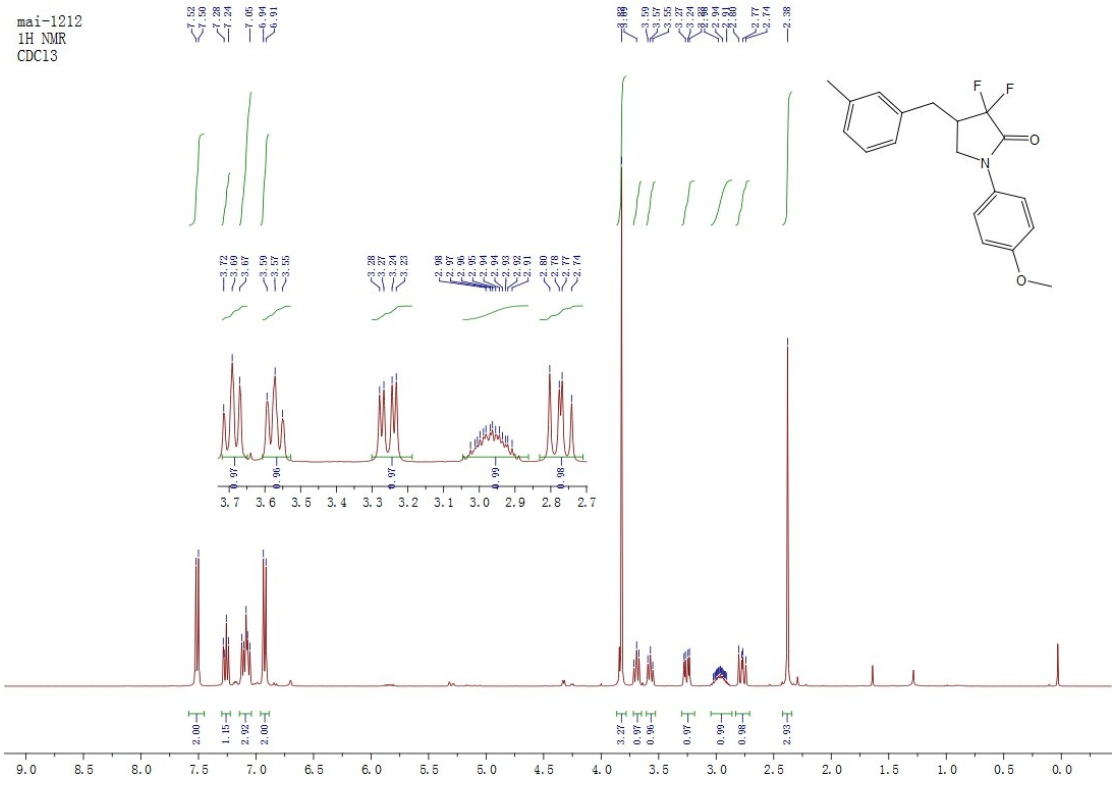
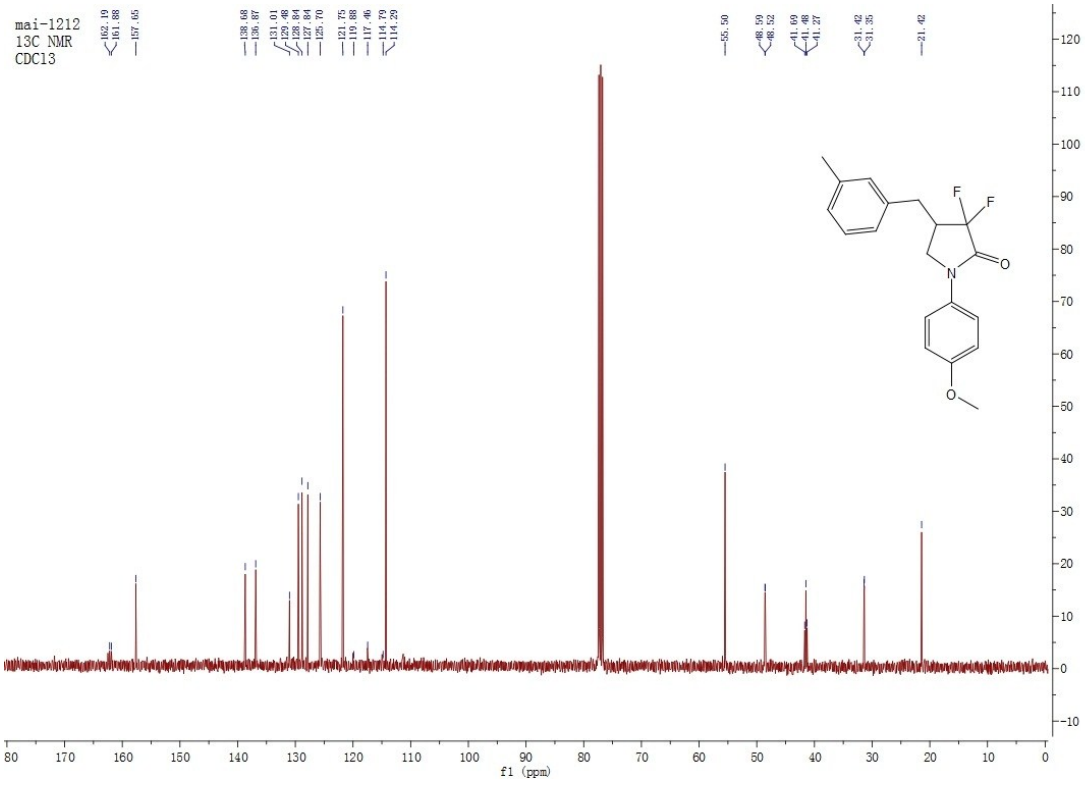
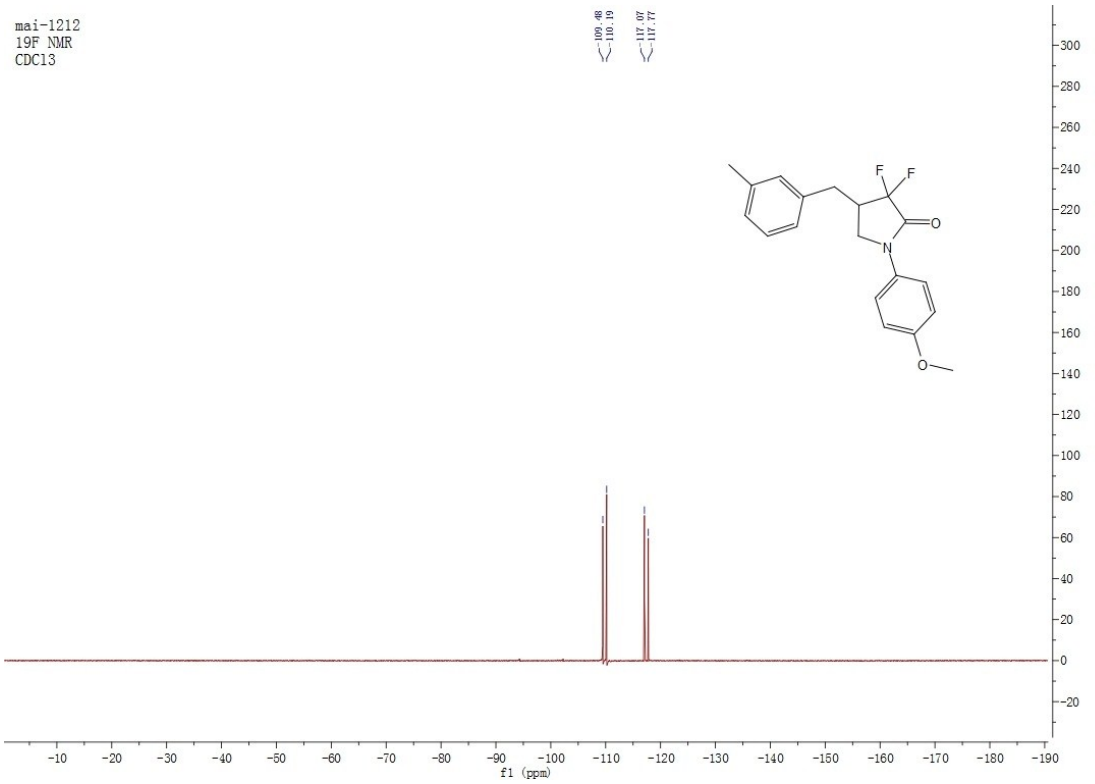
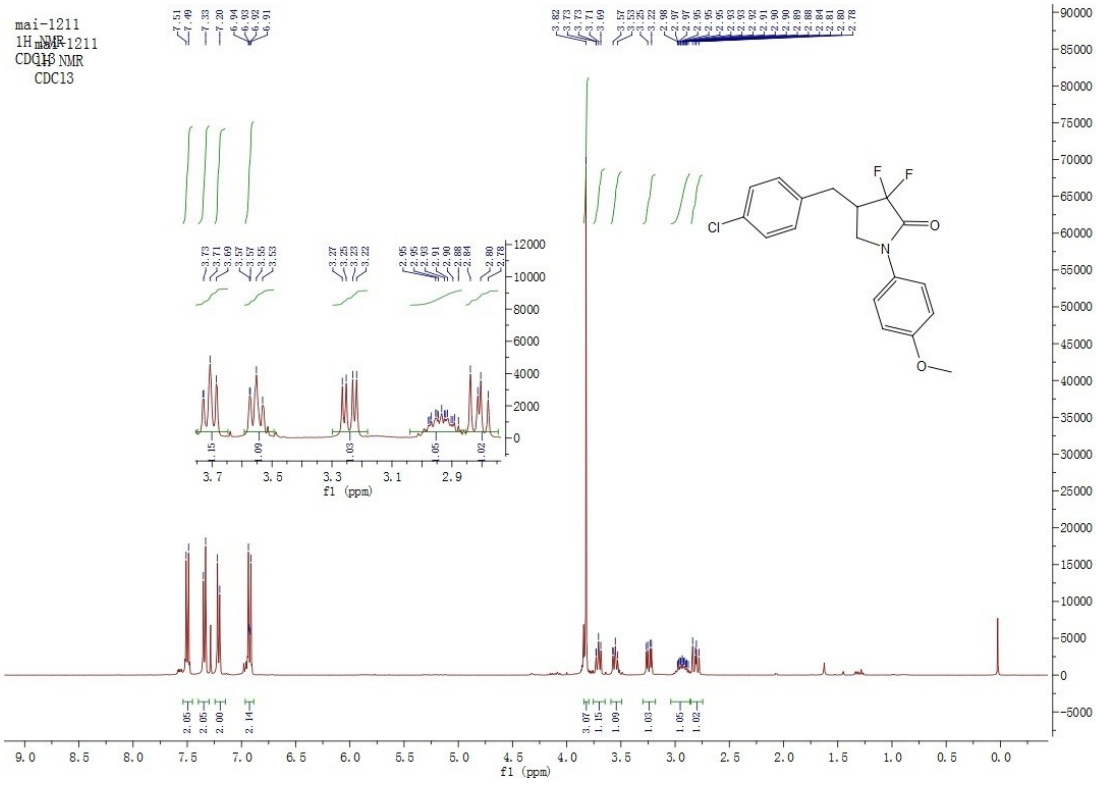
30.80
30.73
F
F
F
O
N
O

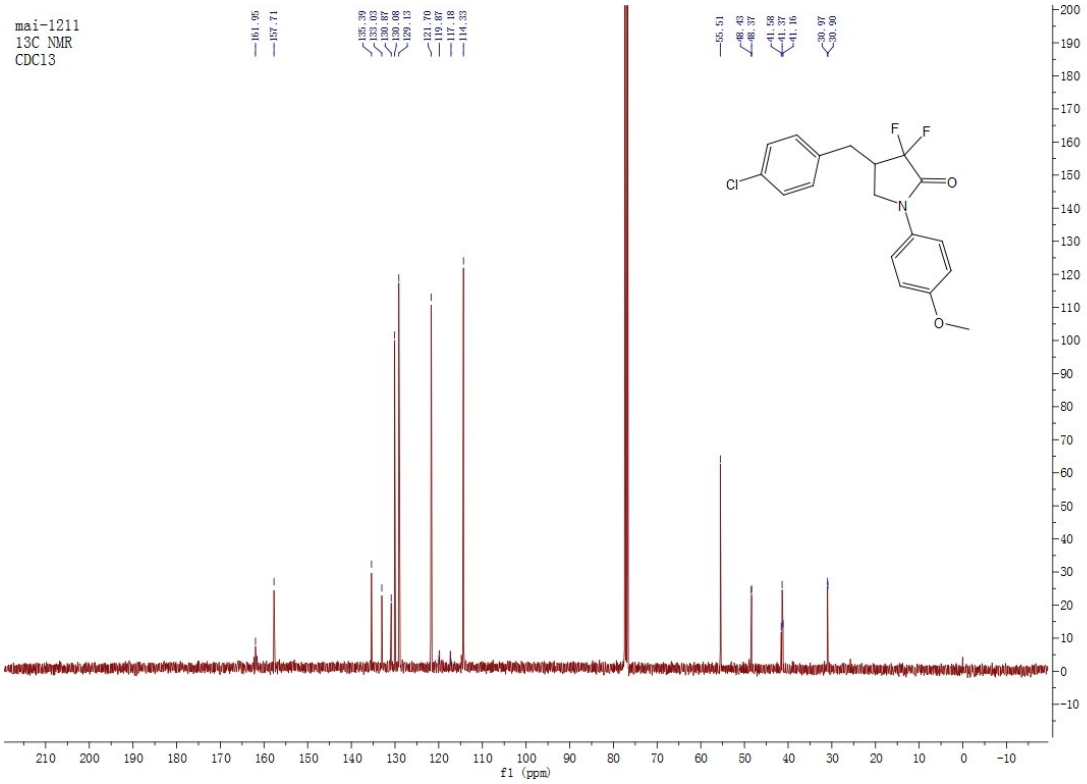

mai-1123
19F NMR
CDC13
-109.14
-109.85
-115.54
-116.90
-117.61
F
F
F
O
N
O


mai-1212
1H NMR
CDC13


mai-1212
13C NMR
CDC13
f1 (ppm)


mai-1212
19F NMR
CDCl3
-109.48
-110.19
-117.07
-117.77
F
F
O
N
O
f1 (ppm)


mai-1211
1H NMR
CDCl3
Cl
F
F
O
N
O
f1 (ppm)


mai-1211
13C NMR
CDC13
161.95
157.71
135.39
133.03
130.87
130.08
129.13
121.70
119.87
117.18
114.33
55.51
48.43
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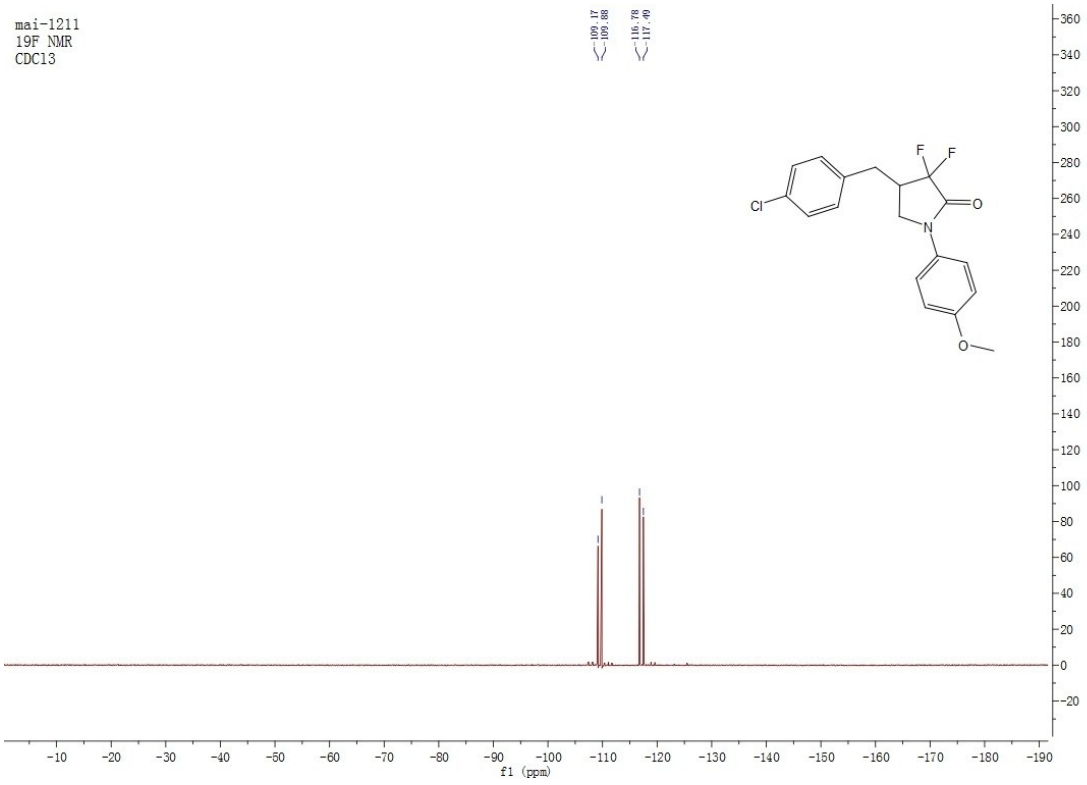
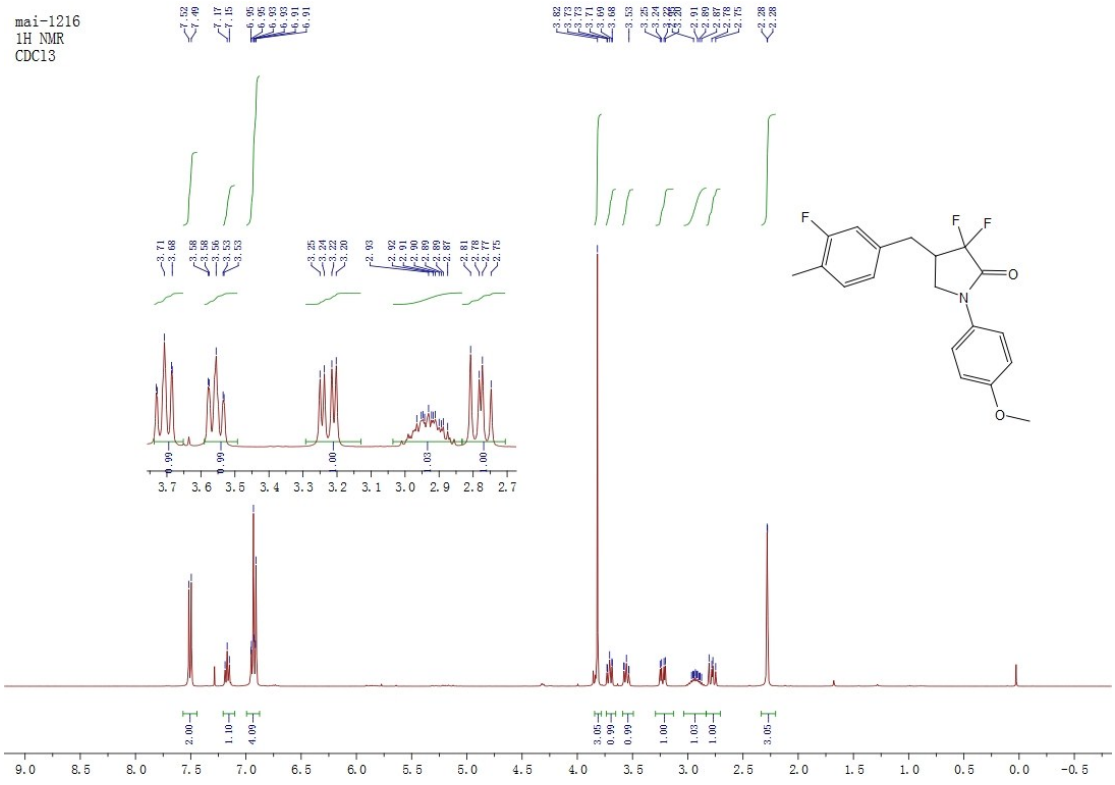
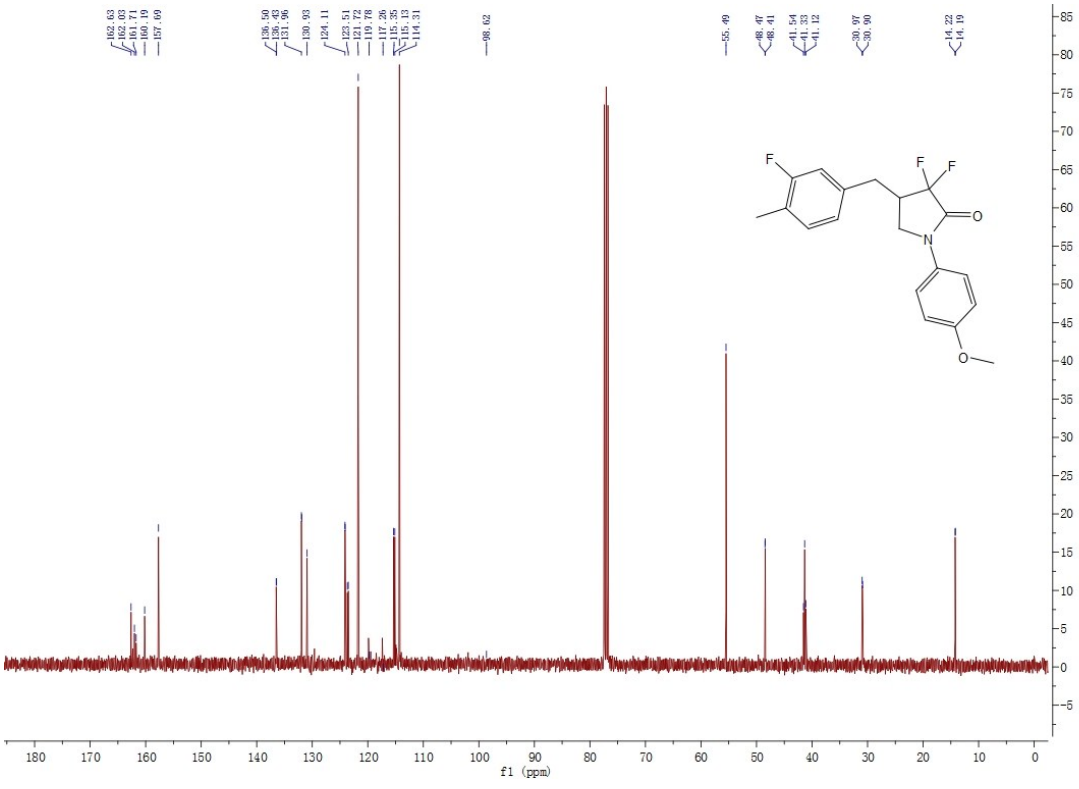
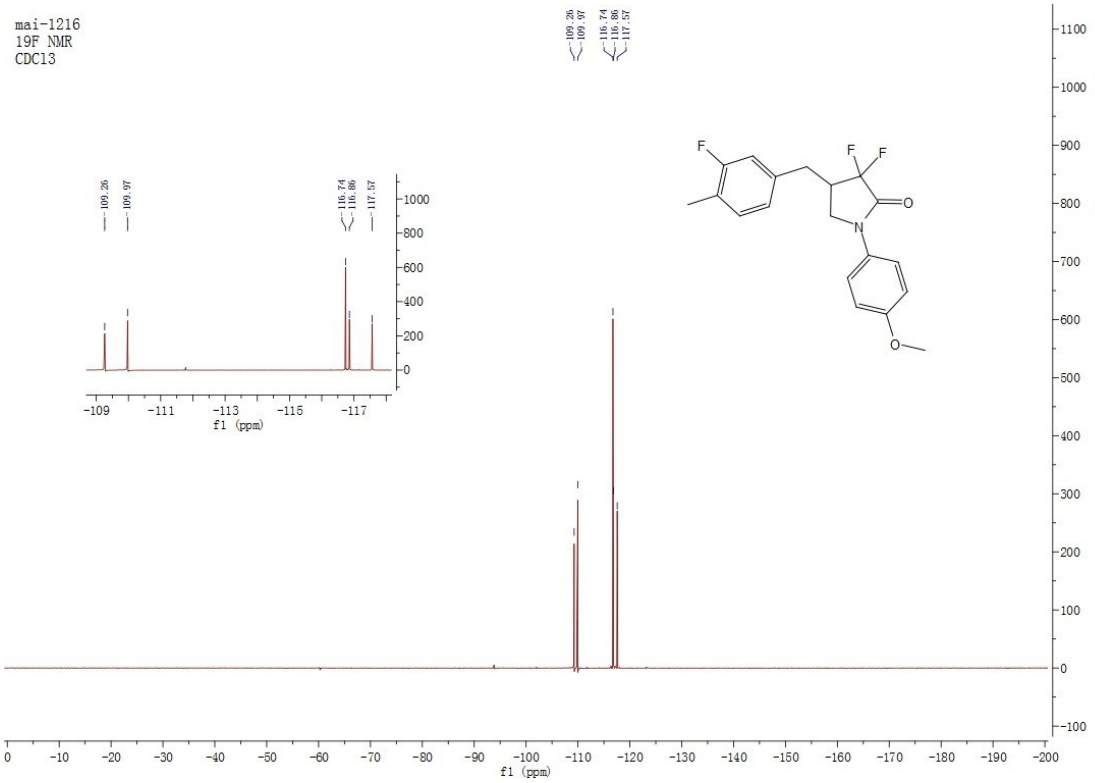
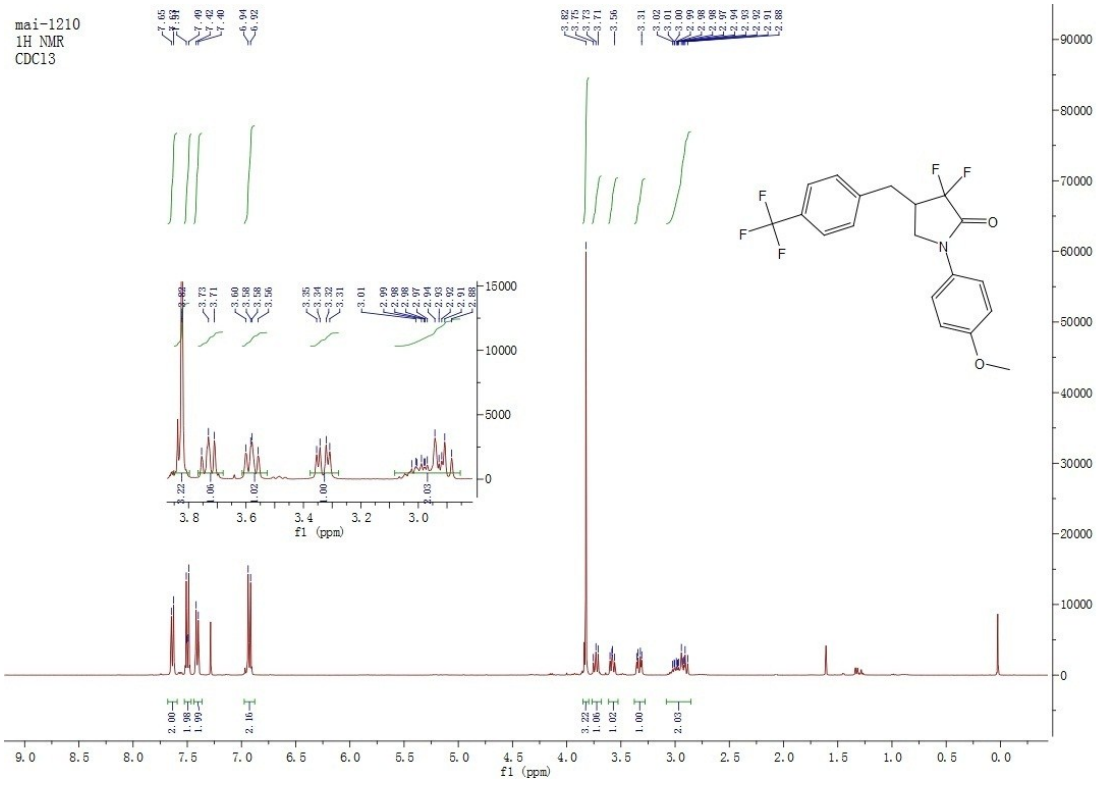
41.37
41.16
30.97
30.90
F
F
Cl
O
N
O
f1 (ppm)

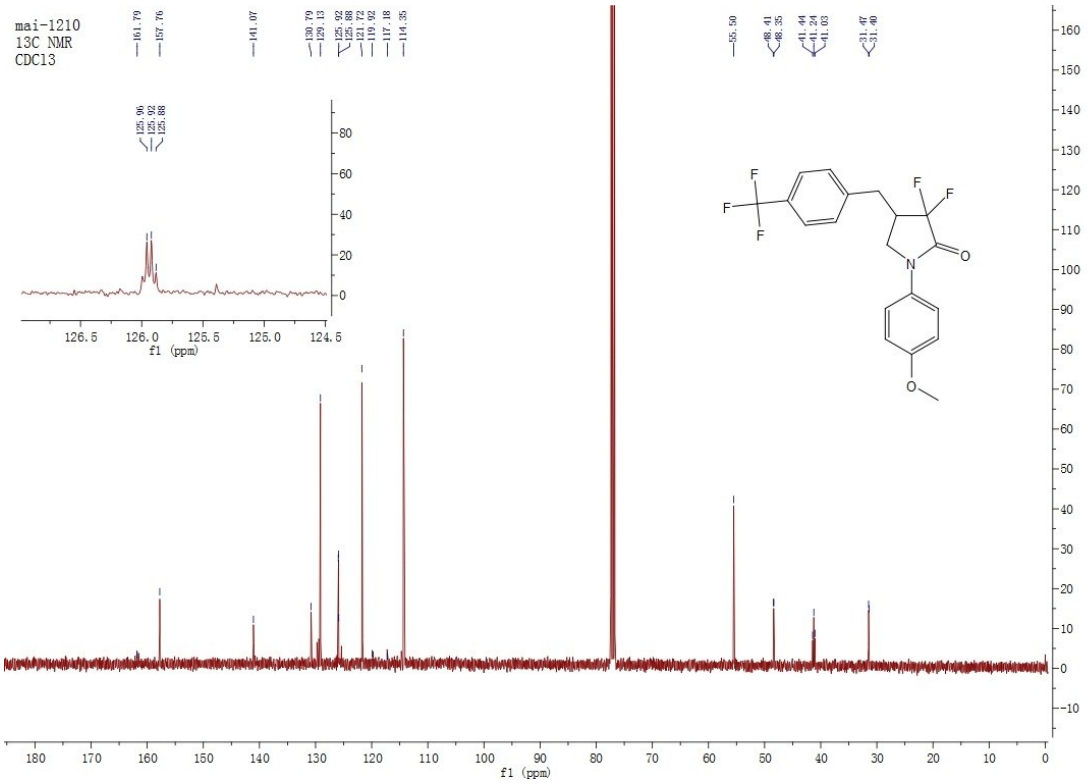

mai-1211
19F NMR
CDC13
-109.17
-109.88
-116.78
-117.49
F
F
Cl
O
N
O
f1 (ppm)

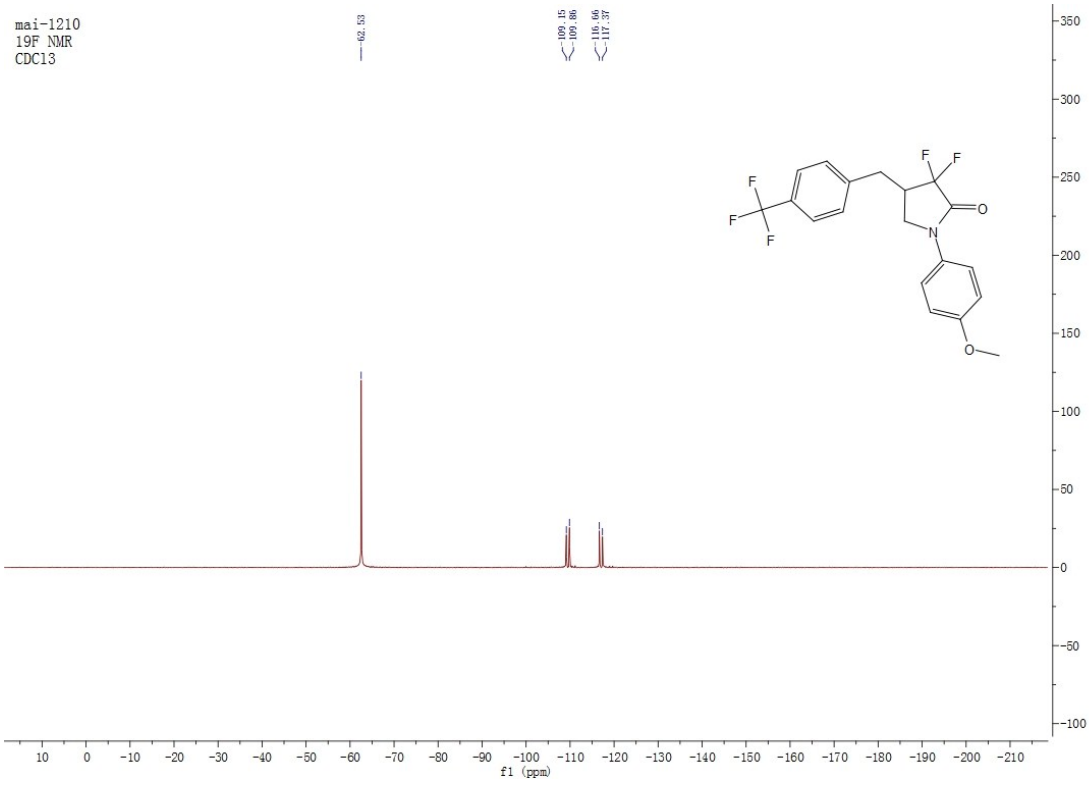

mai-1216
1H NMR
CDCl3

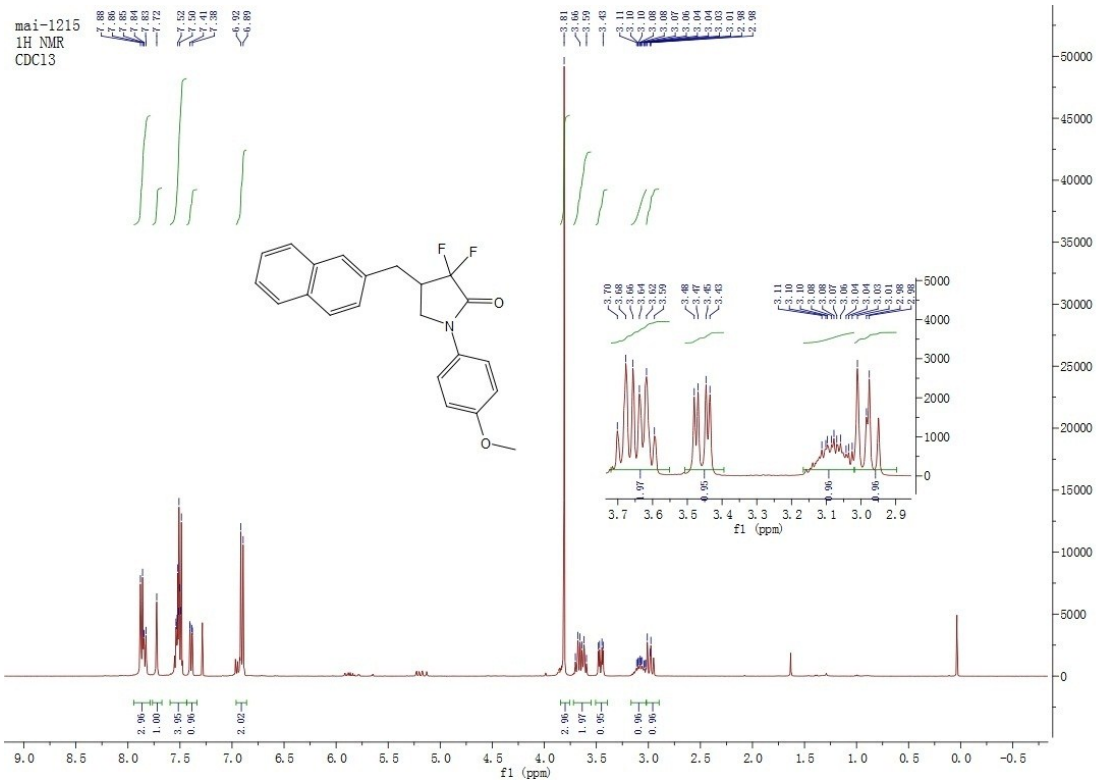

f1 (ppm)


mai-1216
19F NMR
CDCl3
f1 (ppm)


mai-1210
1H NMR
CDCl3
f1 (ppm)


mai-1210
13C NMR
CDC13
161.79
157.76
141.07
130.79
129.13
125.92
125.88
121.72
119.92
117.18
114.35
55.50
48.41
48.35
41.44
41.24
41.03
31.47
31.40
125.96
125.92
125.88
f1 (ppm)
f1 (ppm)


mai-1210
19F NMR
CDC13
-62.53
-109.15
-109.86
-116.66
-117.37
f1 (ppm)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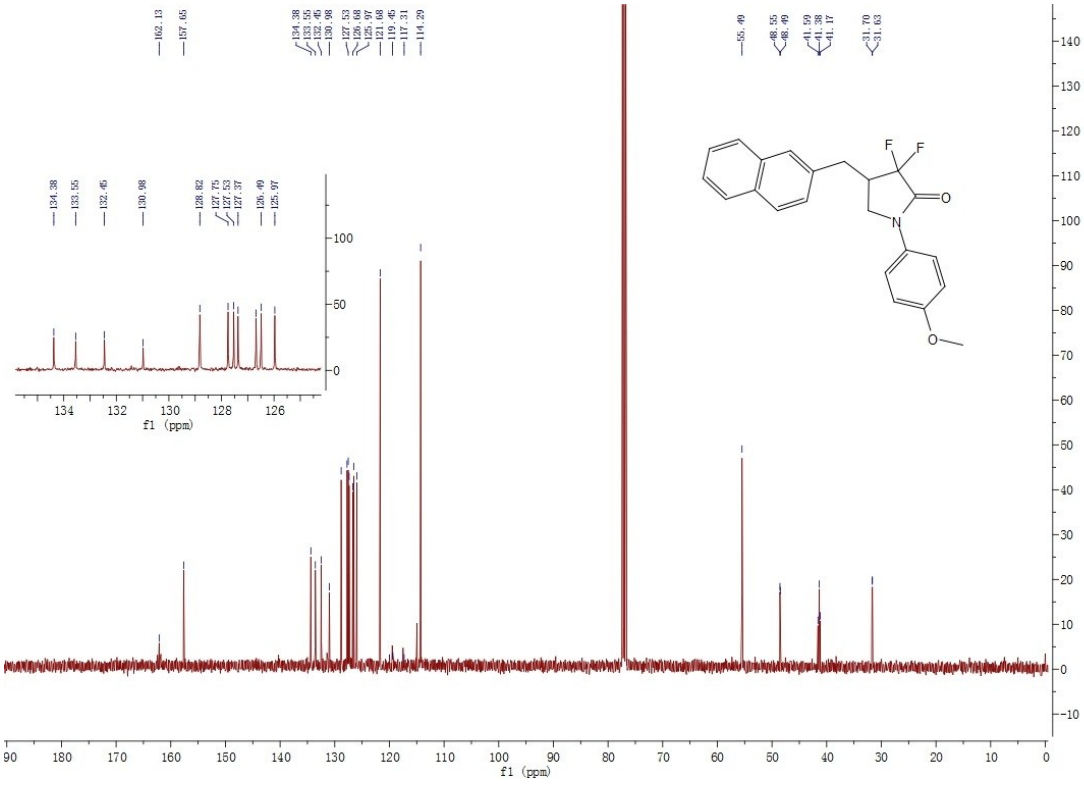
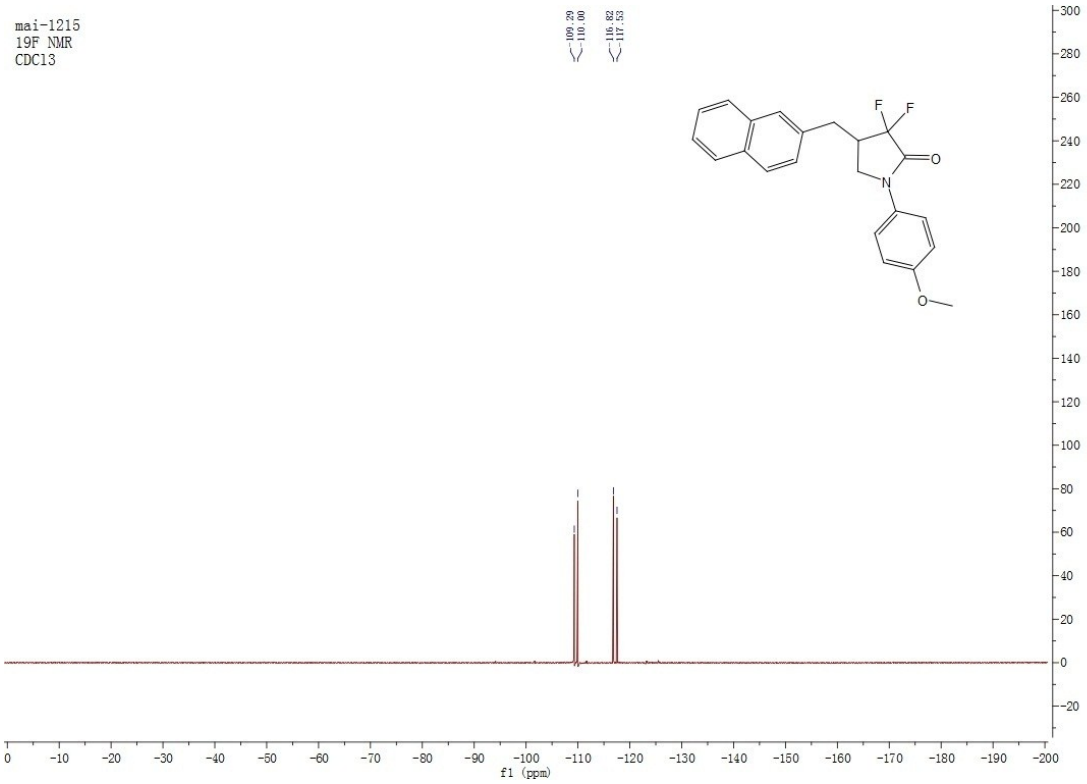
1H NMR
CDCl3
f1 (ppm)


f1 (ppm)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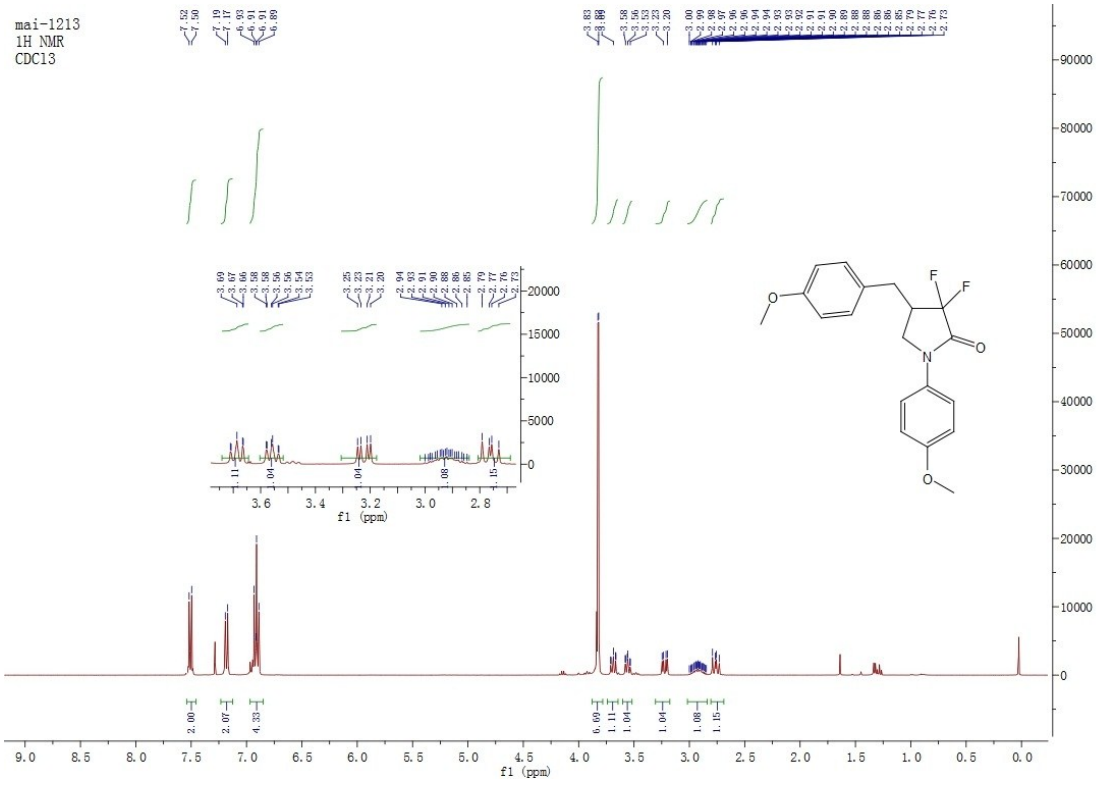
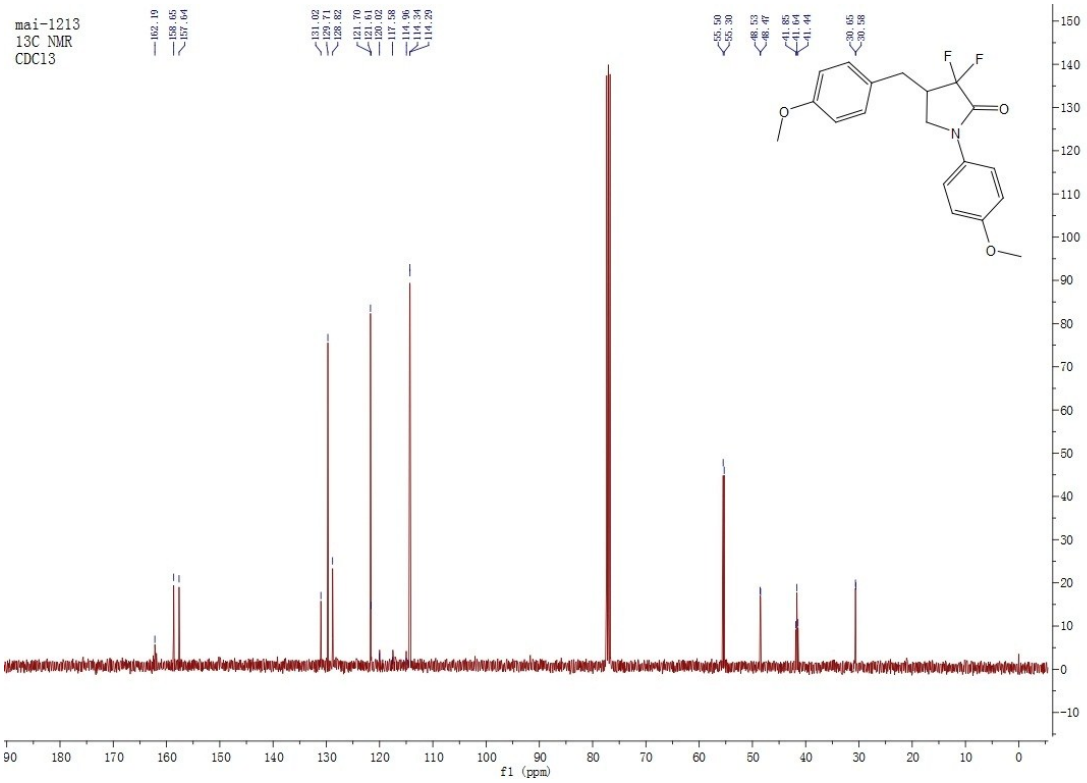
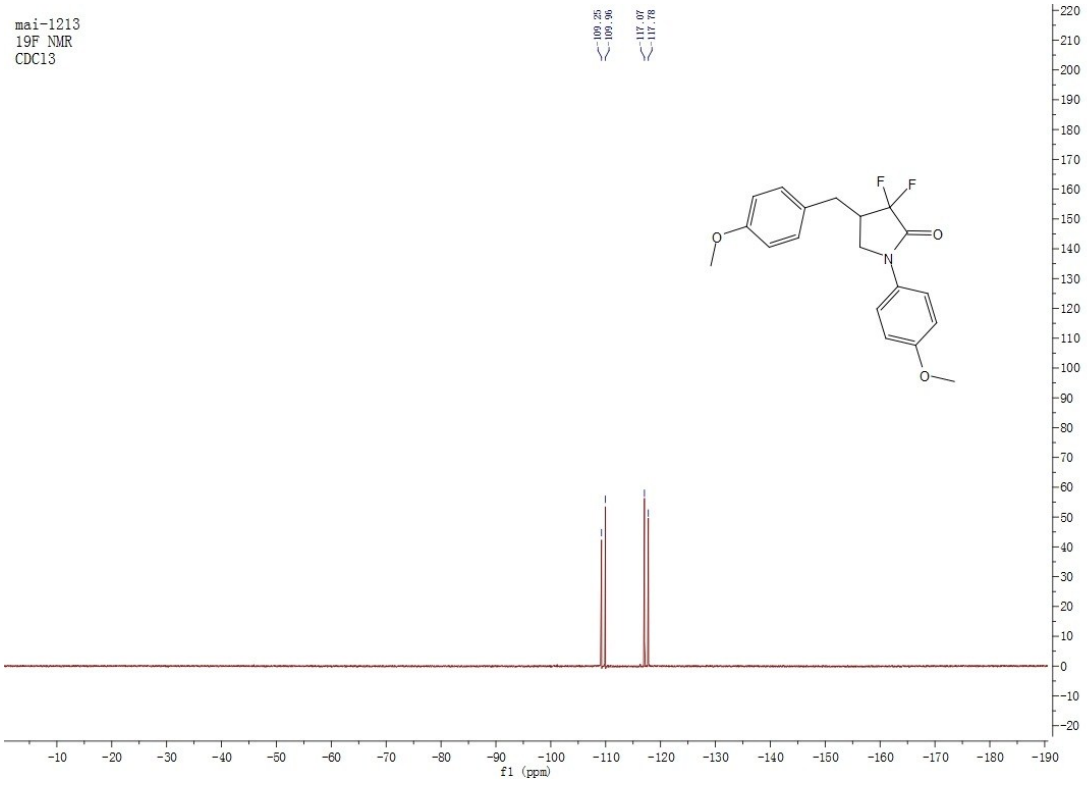
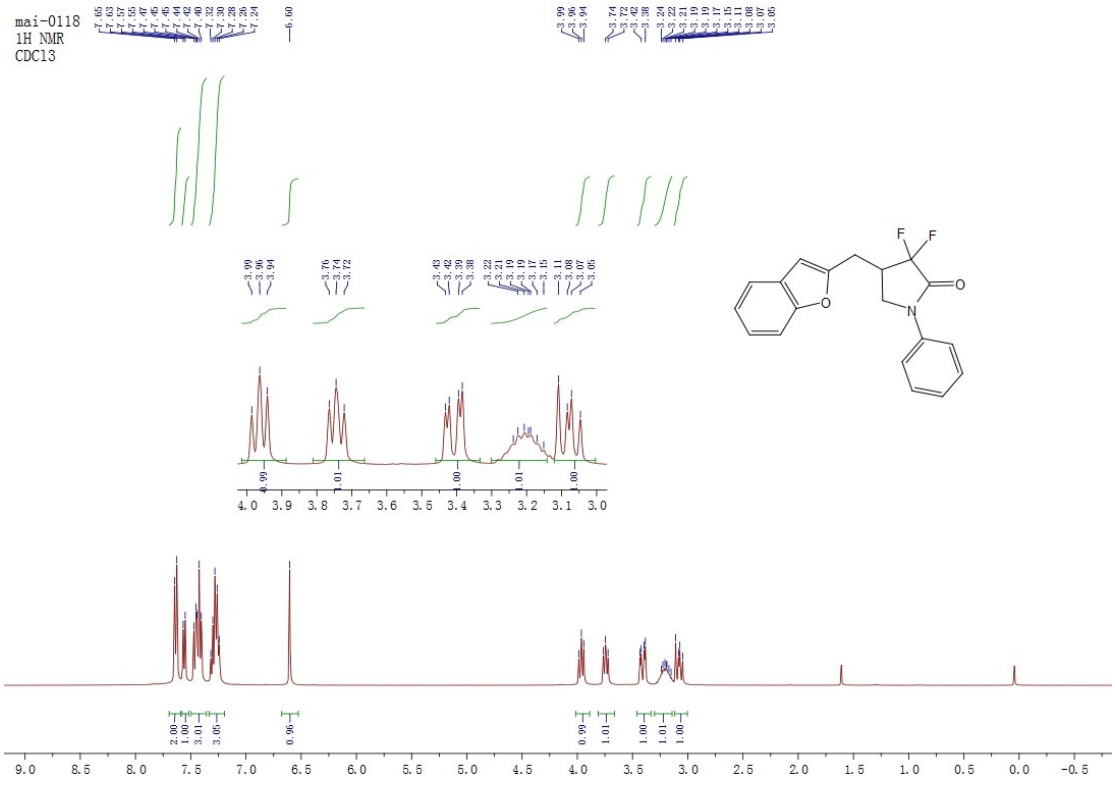
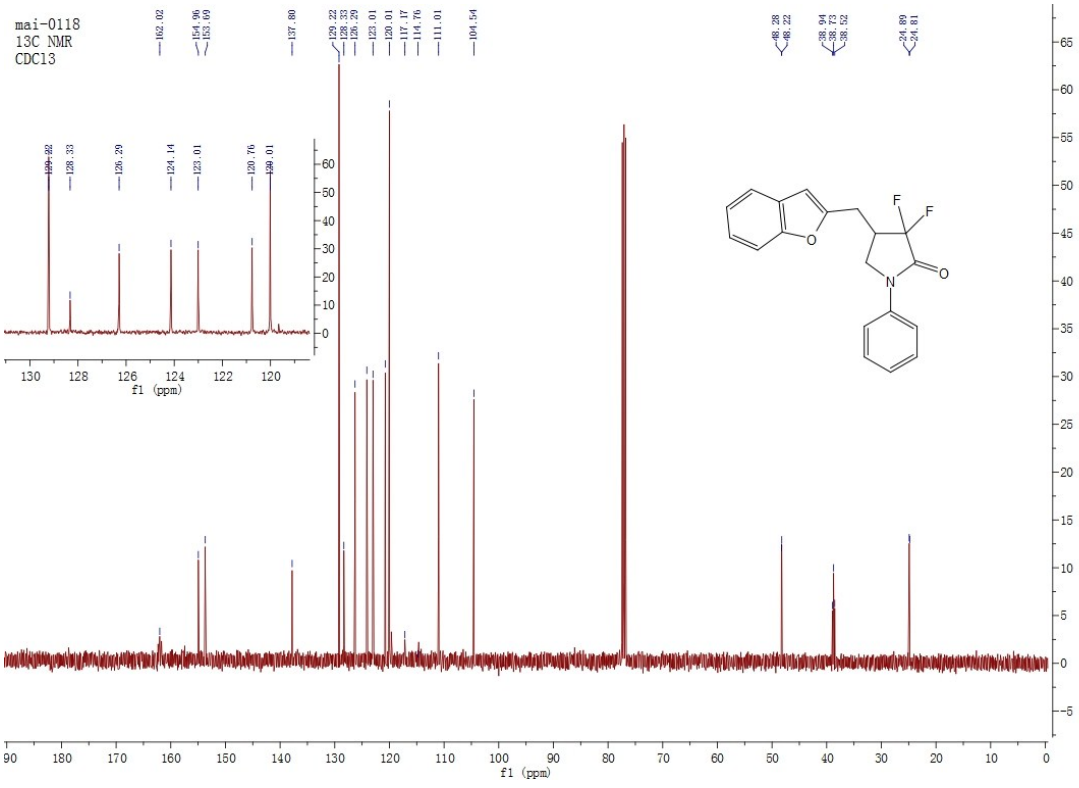
CDCl3
109.29
110.00
116.82
117.53
F
F
O
N
O
f1 (ppm)

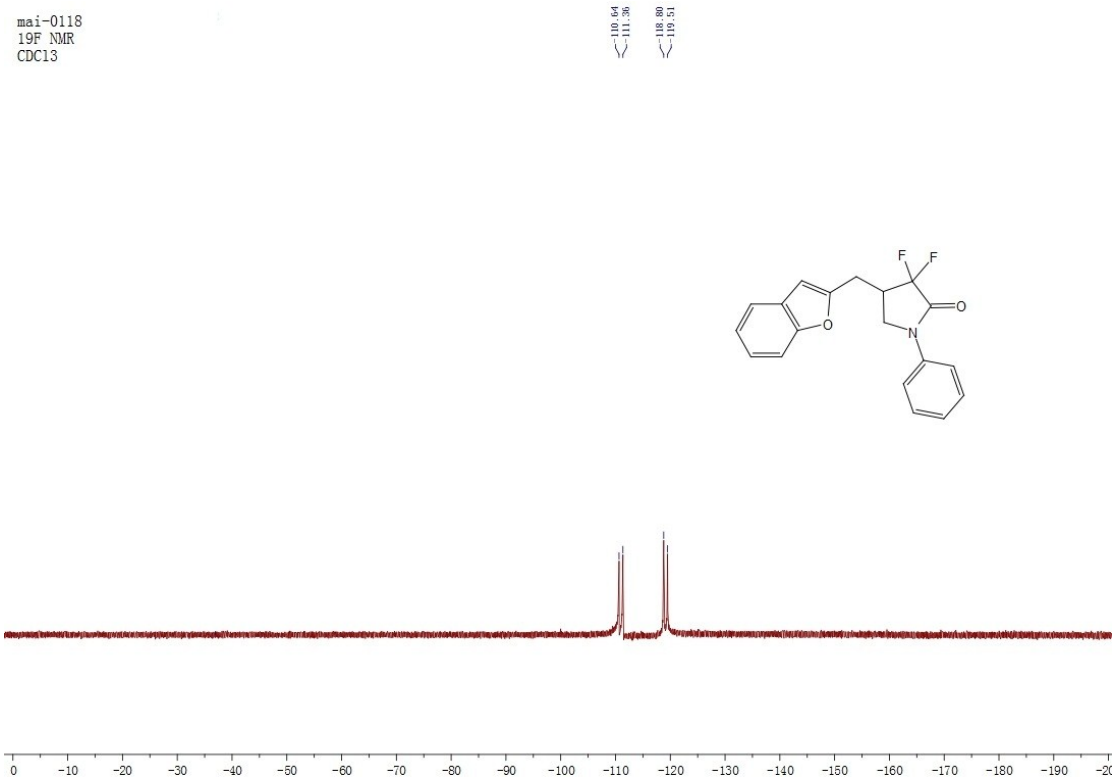

mai-1213
1H NMR
CDCl3
F
F
O
N
O
f1 (ppm)

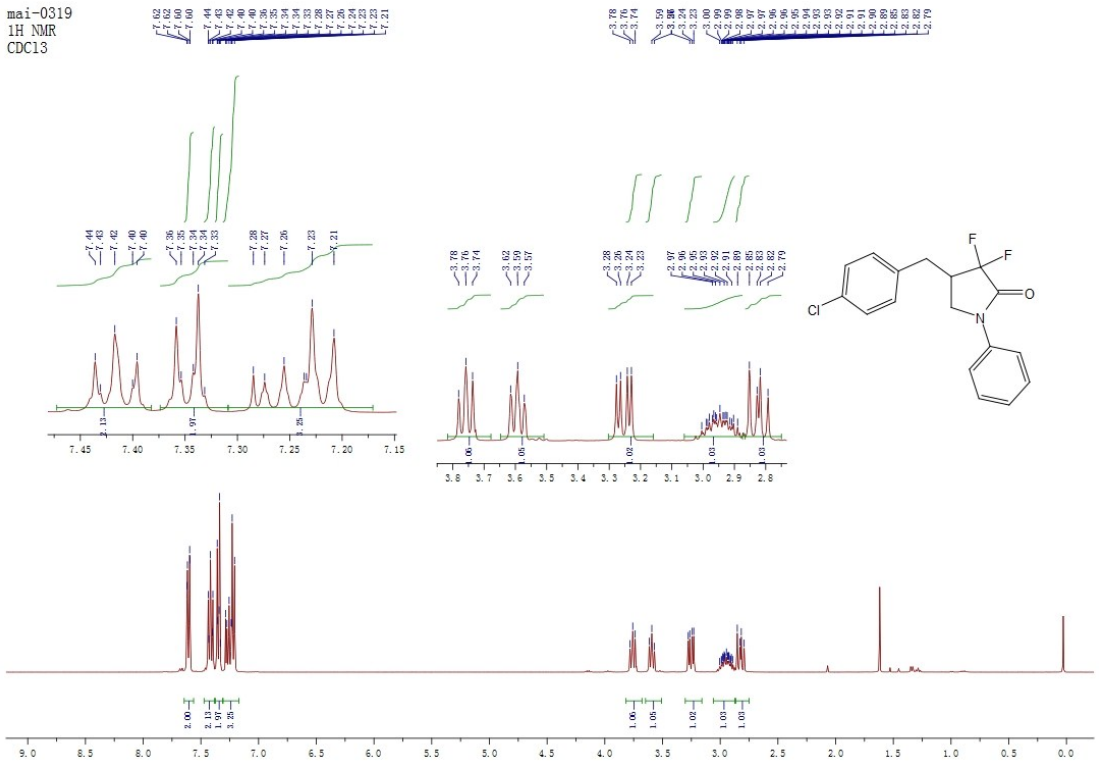

mai-1213
13C NMR
CDC13
162.19
158.65
157.64
131.02
129.71
128.82
121.70
121.61
120.02
117.58
114.96
114.34
114.29
55.50
55.30
48.53
48.47
41.85
41.64
41.44
30.65
30.58
F
F
O
N
O
O
f1 (ppm)

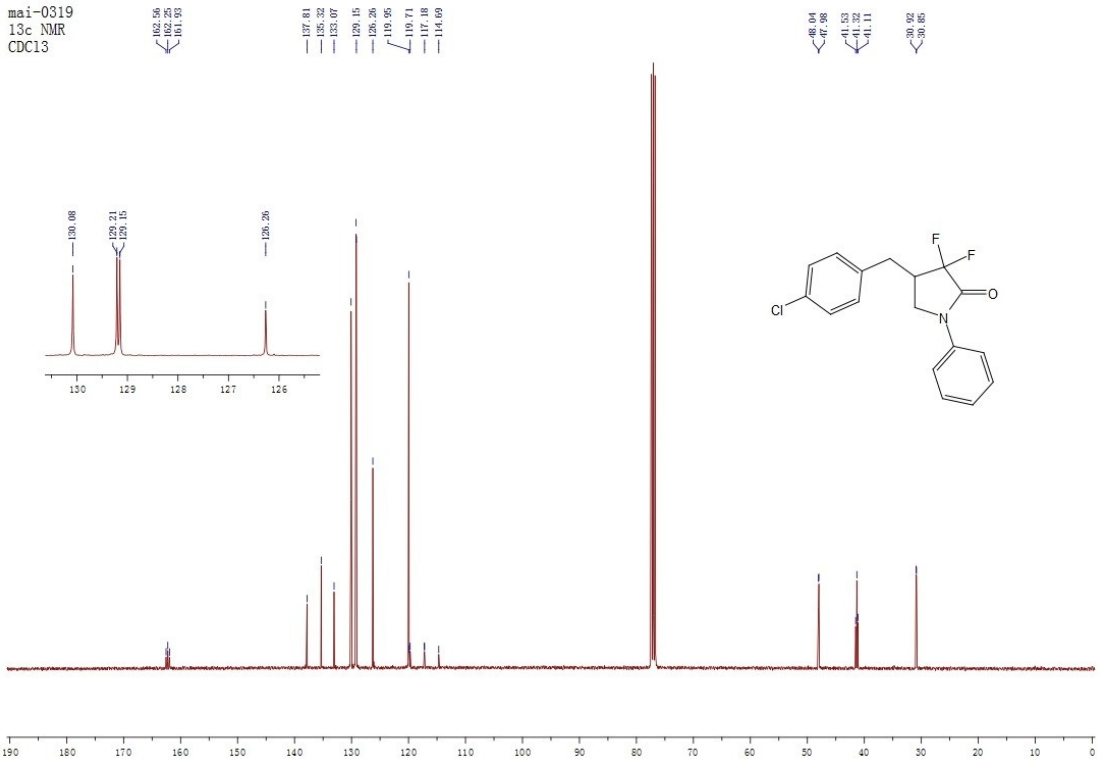

mai-1213
19F NMR
CDC13
109.25
109.96
117.07
117.78
F
F
O
N
O
O
f1 (ppm)

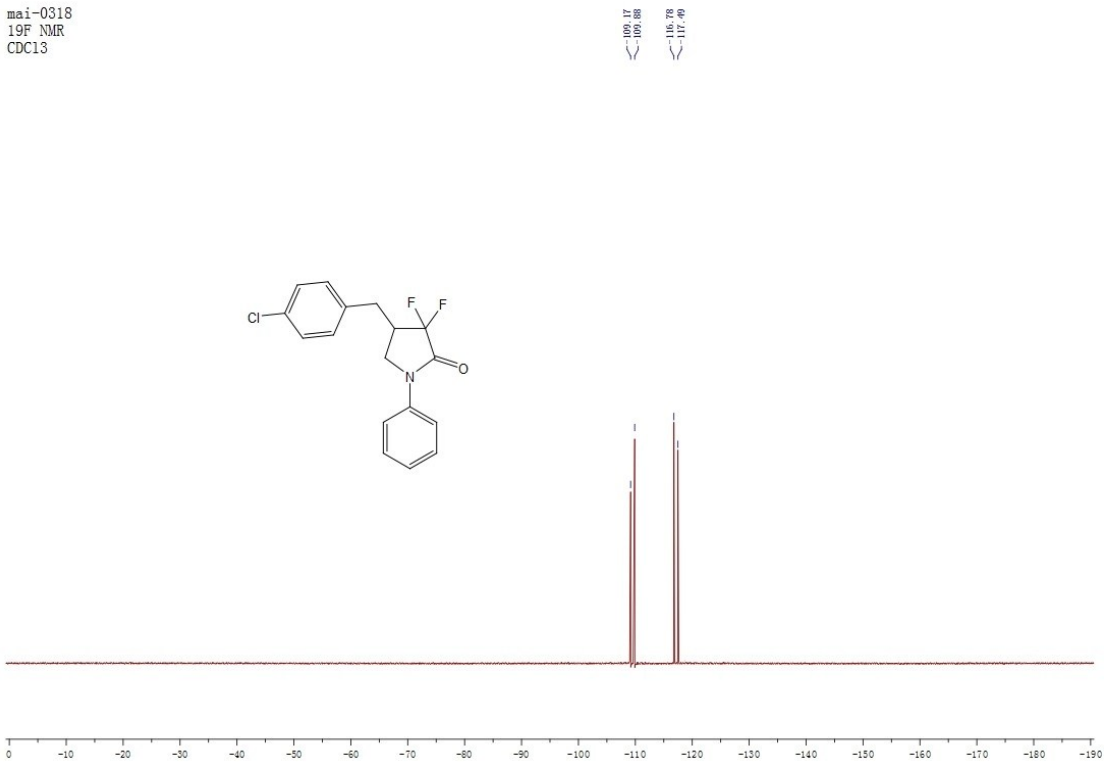

mai-0118
1H NMR
CDCl3

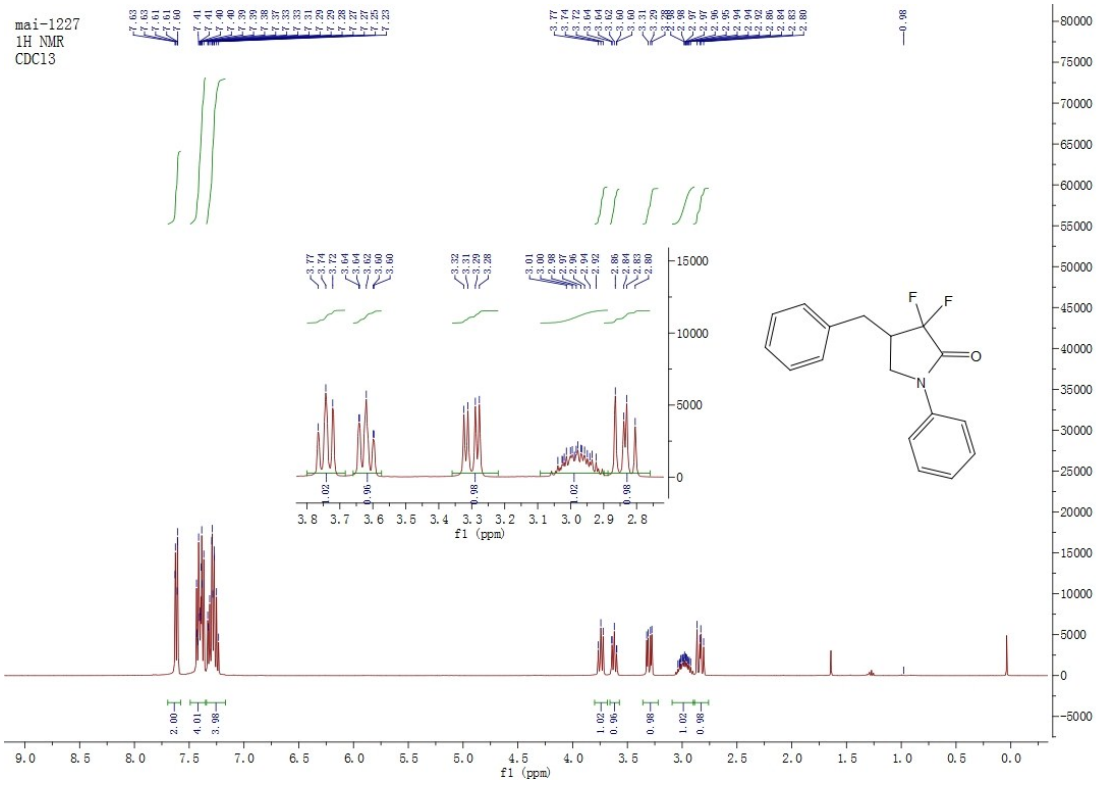

mai-0118
13C NMR
CDCl3
f1 (ppm)

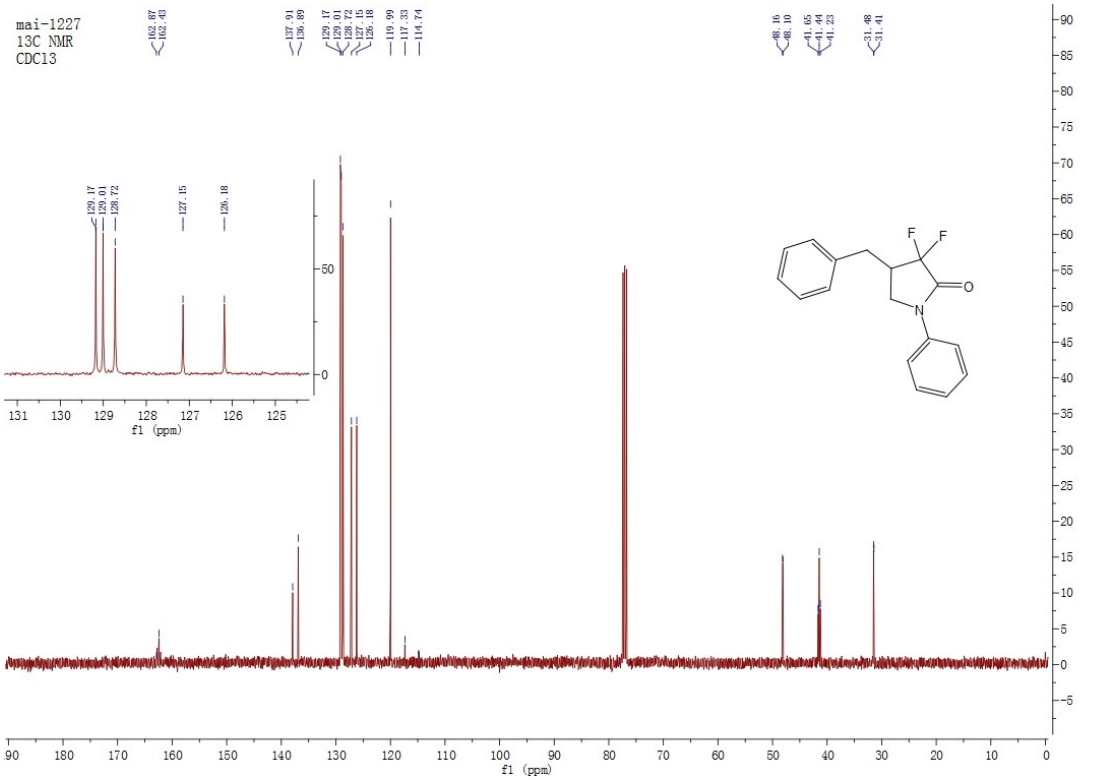

mai-0118
19F NMR
CDCl3
110.64
111.36
118.80
119.51
F
F
O
N
O

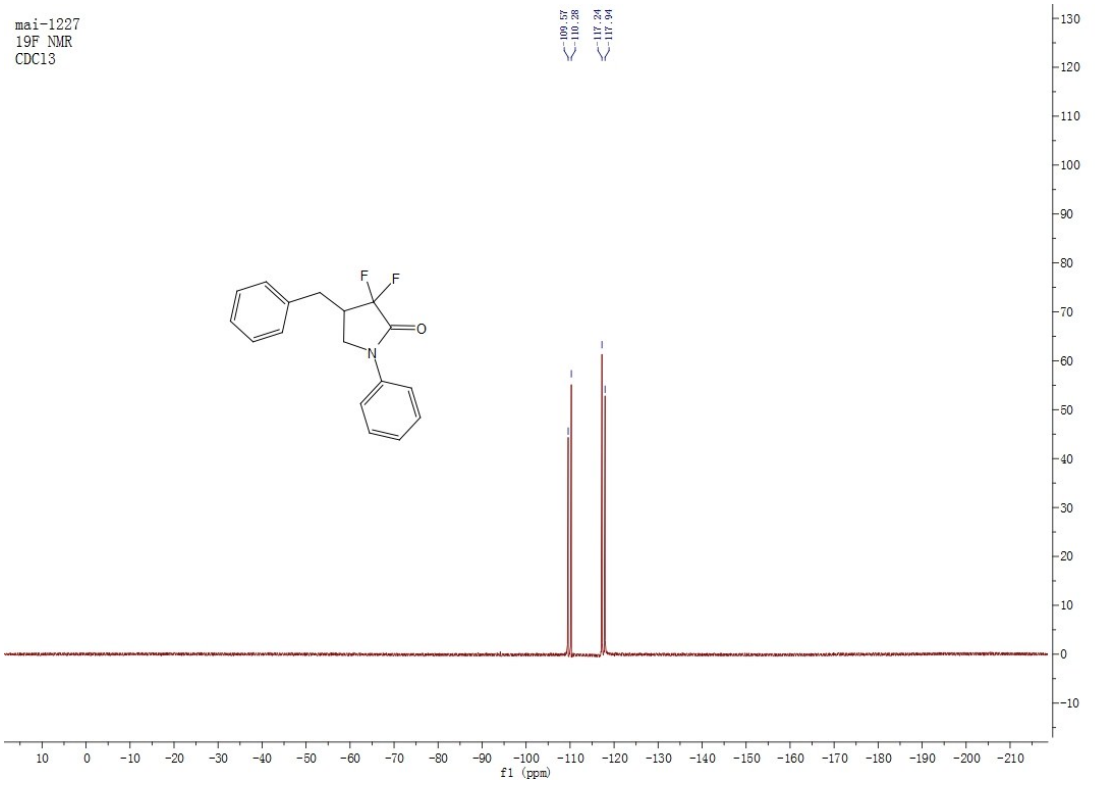

mai-0319
1H NMR
CDCl3
F
F
O
N
Cl

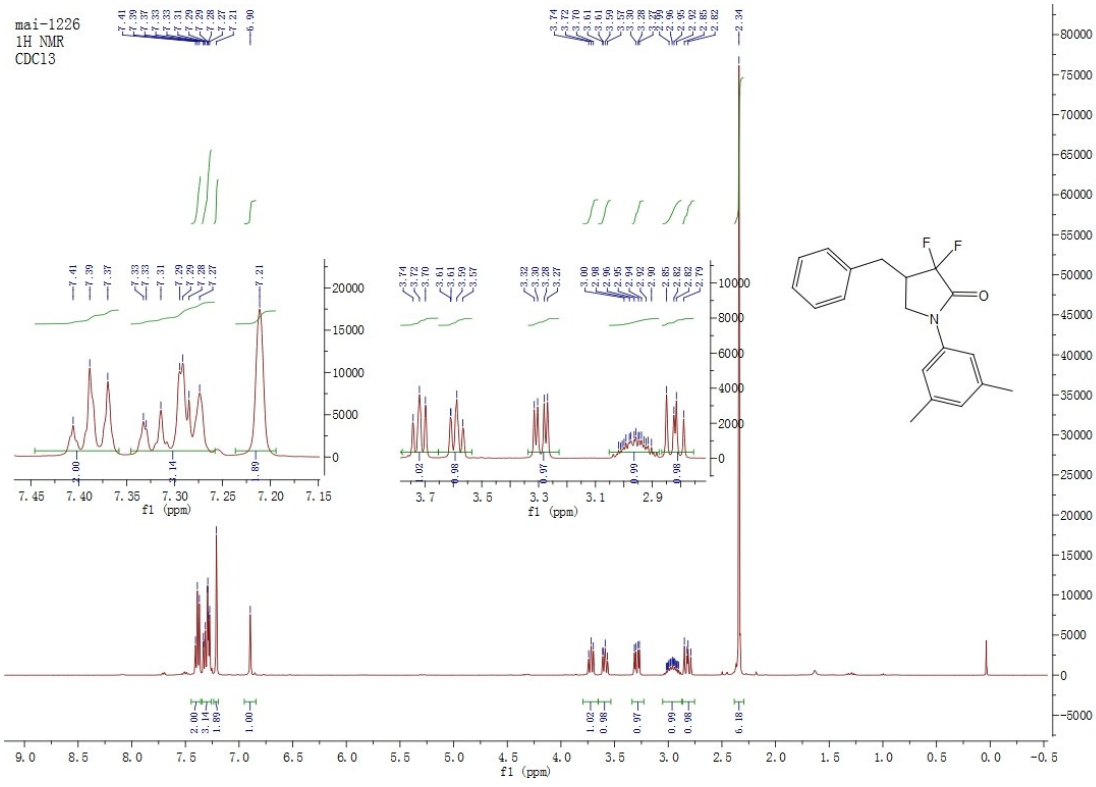

mai-0319
13c NMR
CDCl3
162.56
162.25
161.93
137.81
135.32
133.07
129.15
126.26
119.95
119.71
117.18
114.69
48.04
47.98
41.53
41.32
41.11
30.92
30.85
130.08
129.21
129.15
126.26
F
F
O
N
Cl

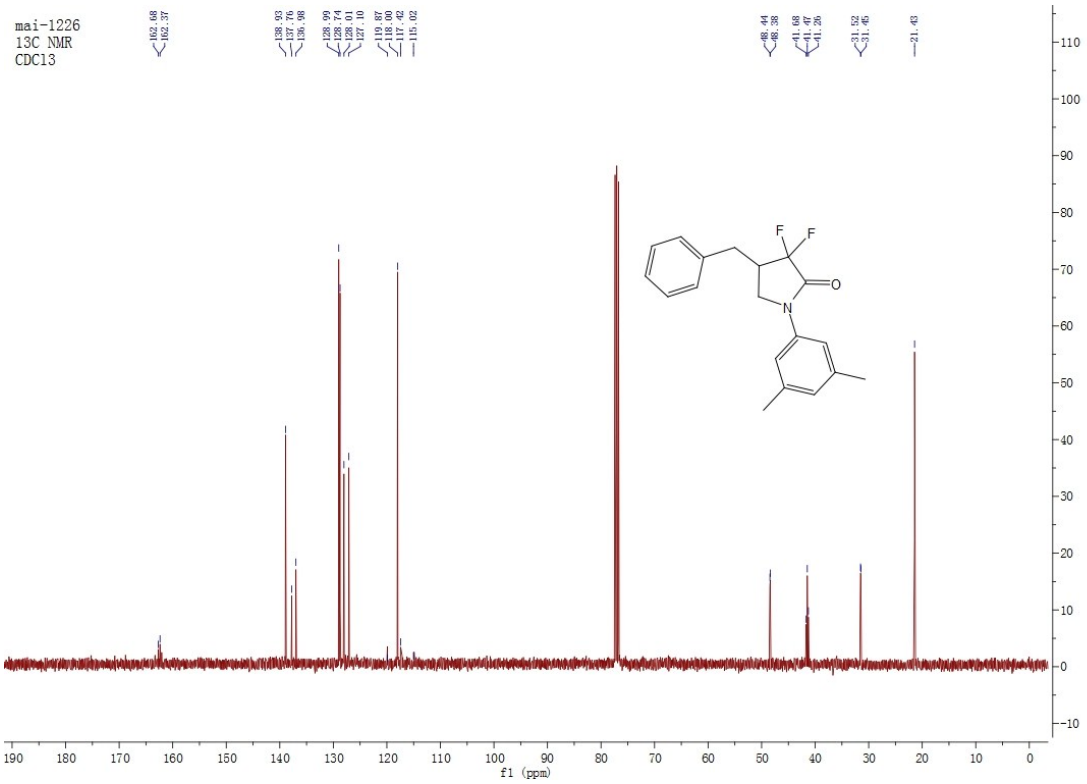

mai-0318
19F NMR
CDCl3
-109.17
-109.68
-116.78
-117.49
F
F
O
N
Cl

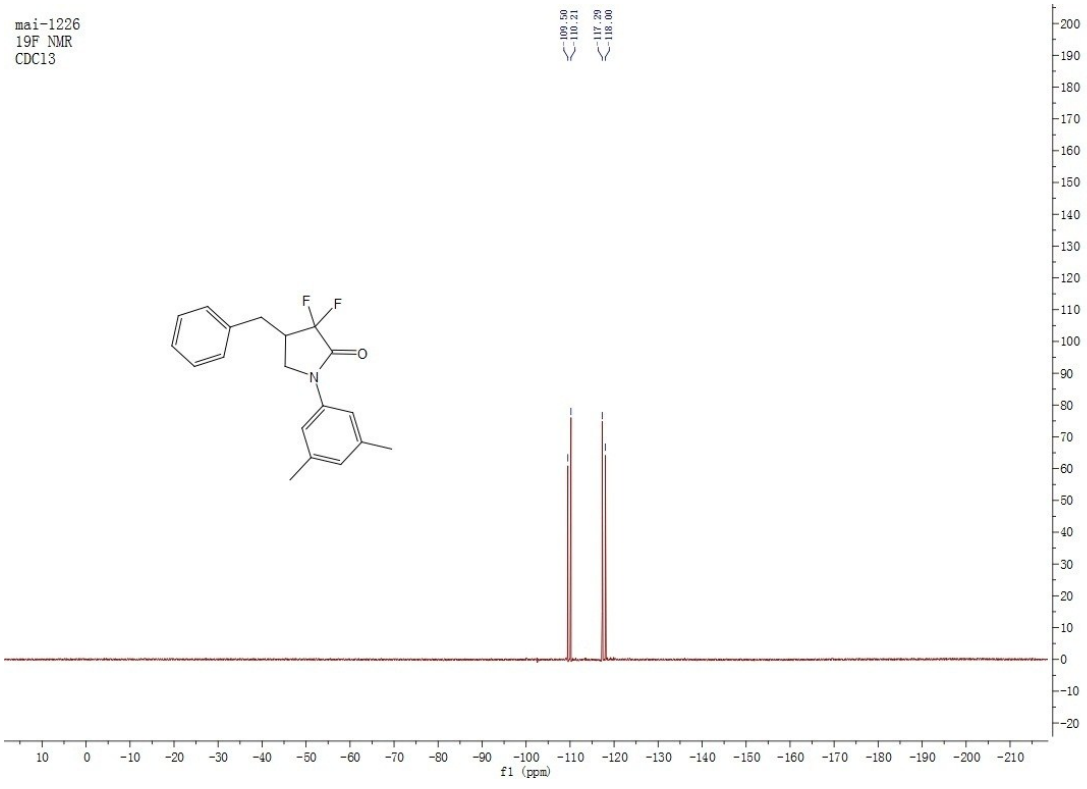

mai-1227
1H NMR
CDCl3
f1 (ppm)

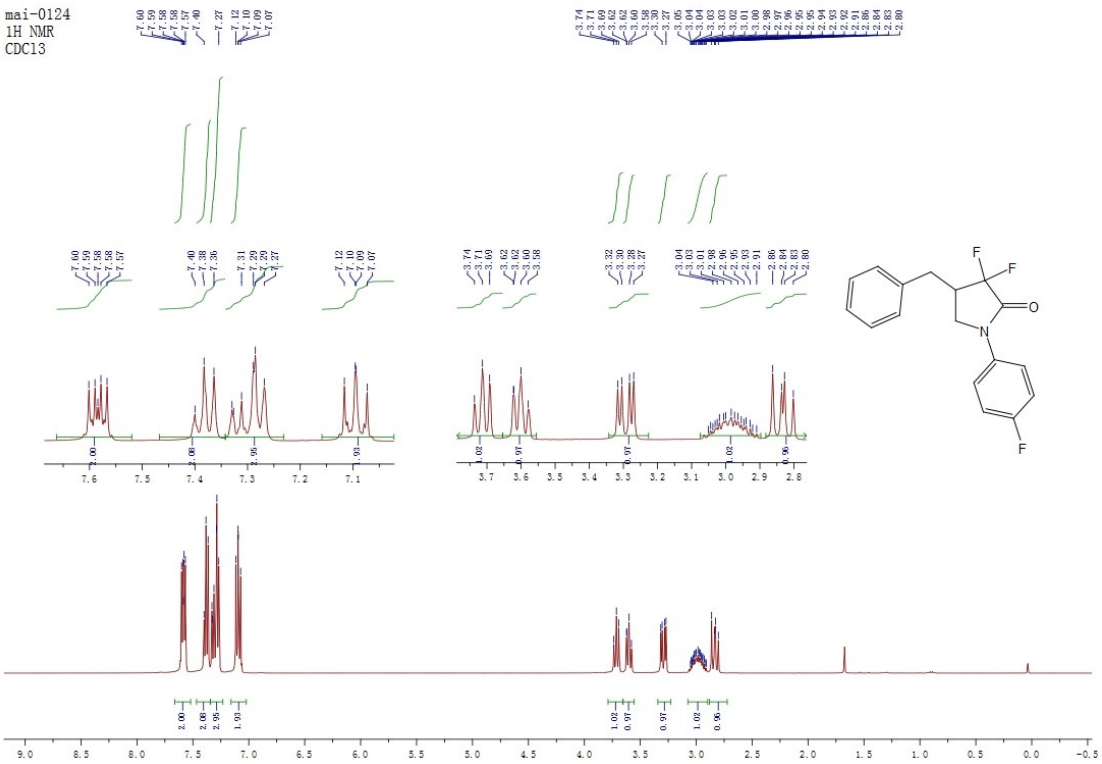

mai-1227
13C NMR
CDCl3
f1 (ppm)

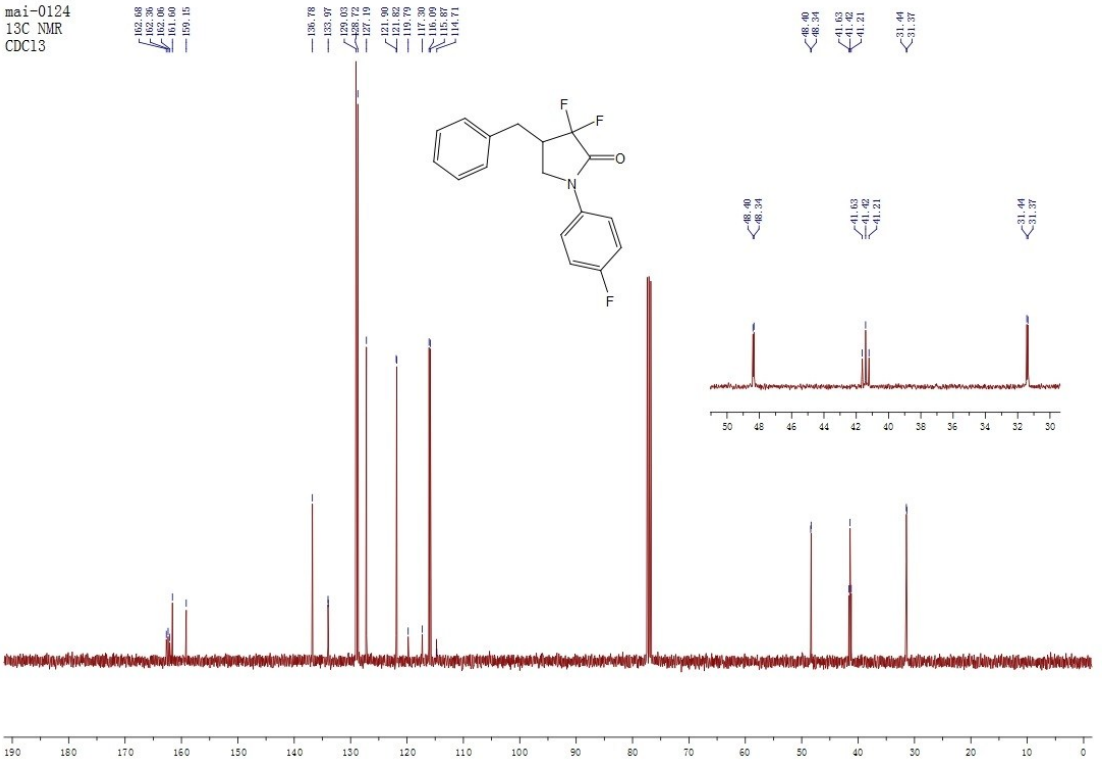

mai-1227
19F NMR
CDCl3
109.57
110.28
117.24
117.94
F
F
O
N
f1 (ppm)

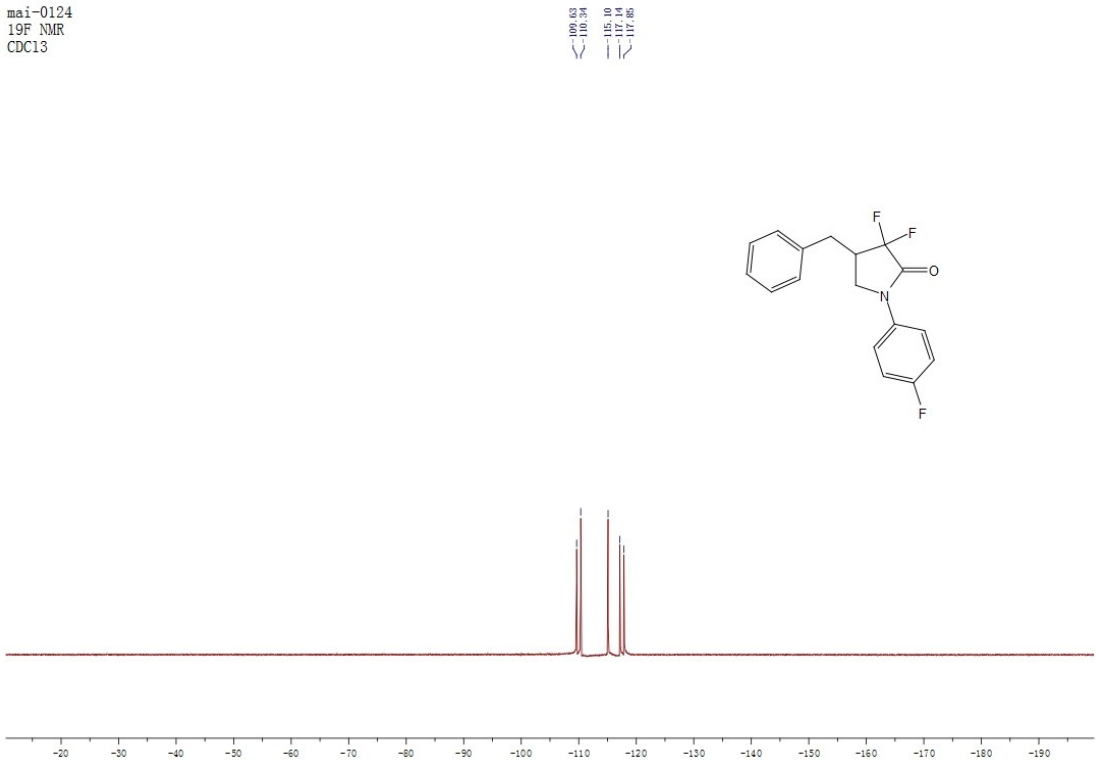

mai-1226
1H NMR
CDCl3
F
F
O
N
f1 (ppm)

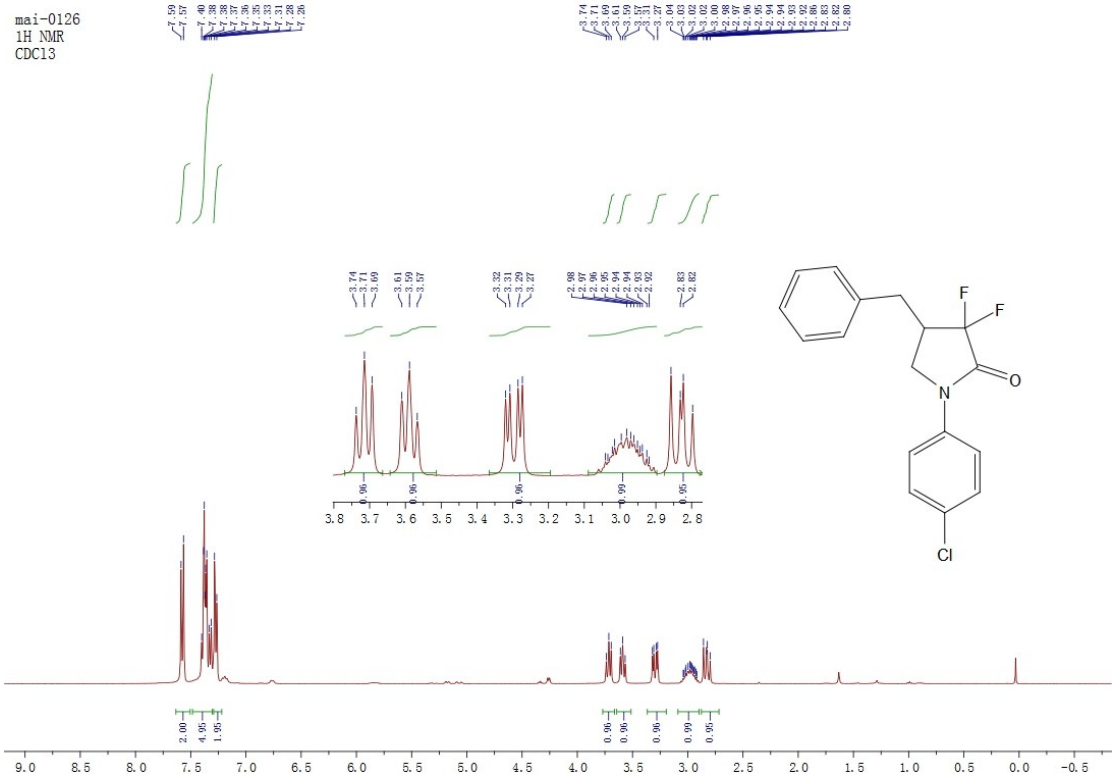

mai-1226
13C NMR
CDC13
162.68
162.37
138.93
137.76
136.98
128.99
128.74
128.01
127.10
119.87
118.00
117.42
115.02
48.44
48.38
41.68
41.47
41.26
31.52
31.45
21.43
F
F
O
N
f1 (ppm)


mai-1226
19F NMR
CDC13
109.50
110.21
117.29
118.00
F
F
O
N
f1 (ppm)


mai-0124
1H NMR
CDCl3


mai-0124
13C NMR
CDCl3


mai-0124
19F NMR
CDCl3
-109.63
-110.34
-115.10
-117.14
-117.85
F
F
O
N
F
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190


mai-0126
1H NMR
CDCl3
7.59
7.57
7.40
7.38
7.37
7.36
7.35
7.33
7.31
7.28
7.26
3.74
3.71
3.69
3.61
3.59
3.57
3.32
3.31
3.29
3.27
3.04
3.03
3.02
3.00
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.86
2.83
2.82
2.80
F
F
O
N
Cl
2.00
4.95
1.95
0.96
0.96
0.96
0.99
0.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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1.5
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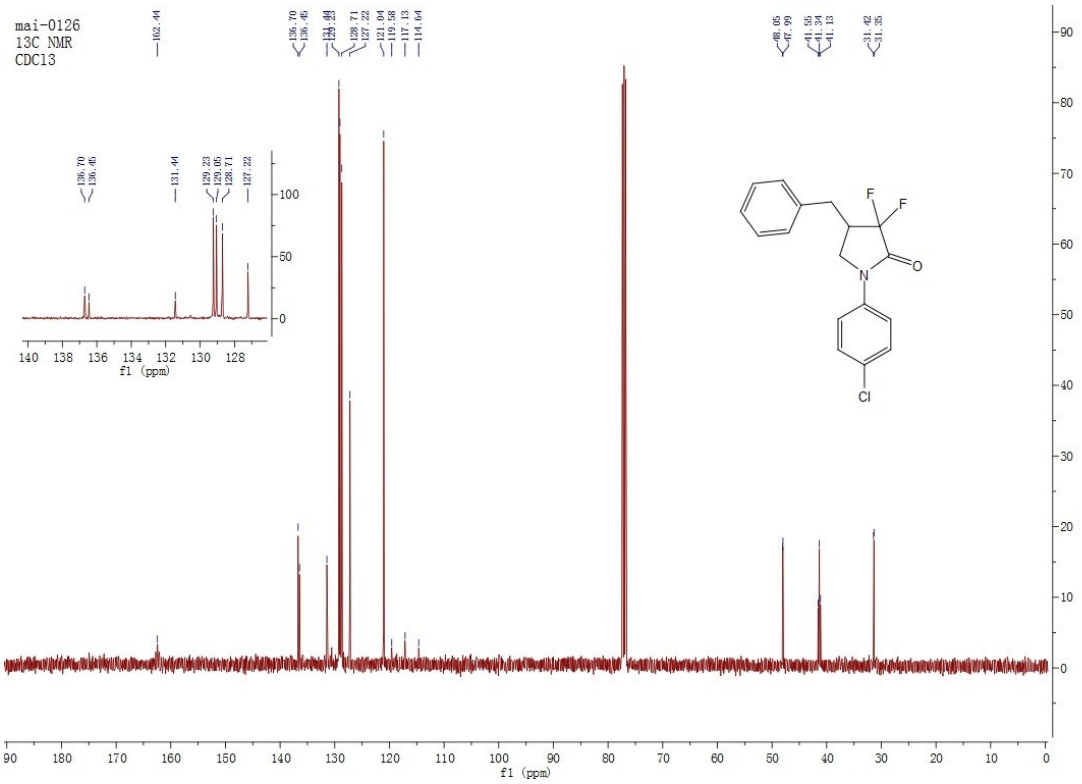
0.0
-0.5


mai-0126
13C NMR
CDC13
162.44
136.70
136.45
131.44
129.23
129.05
128.71
127.22
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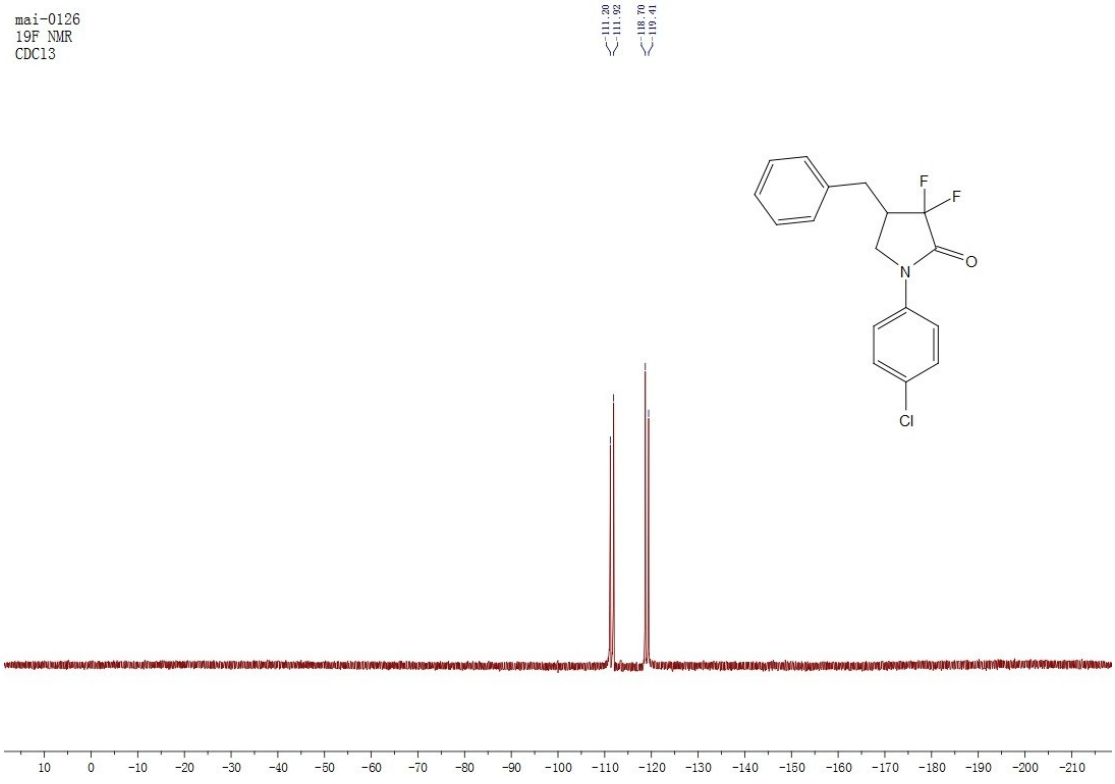
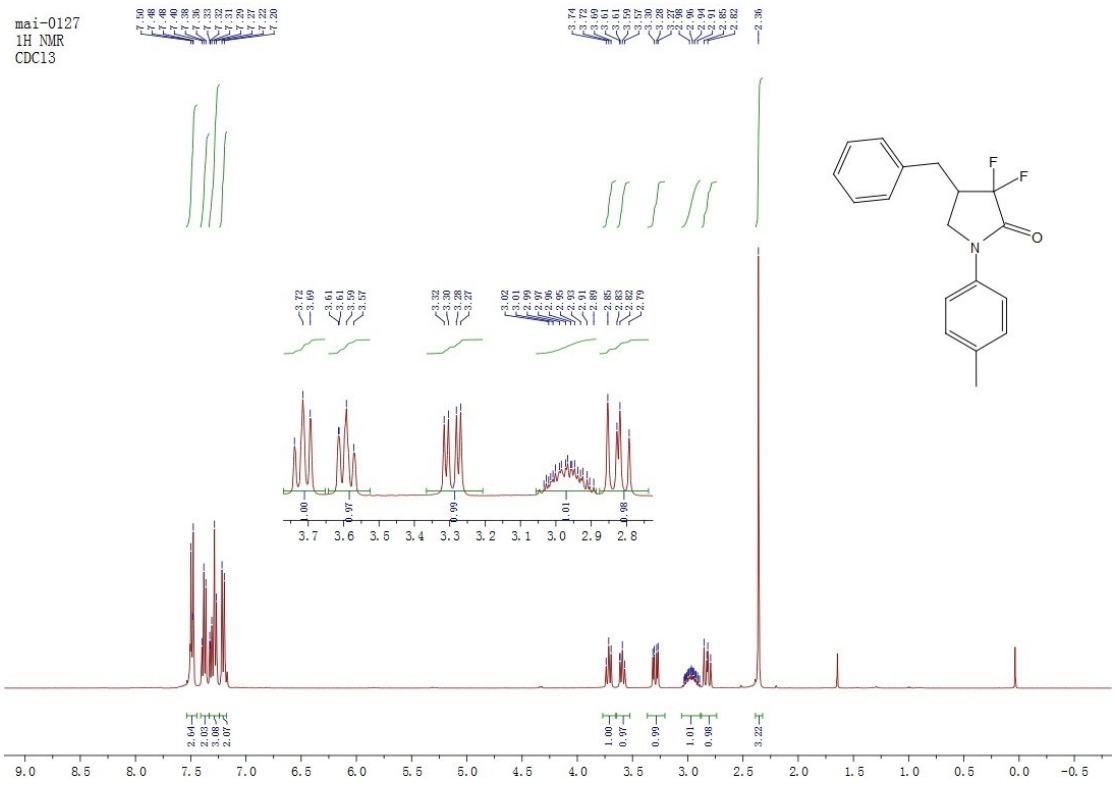
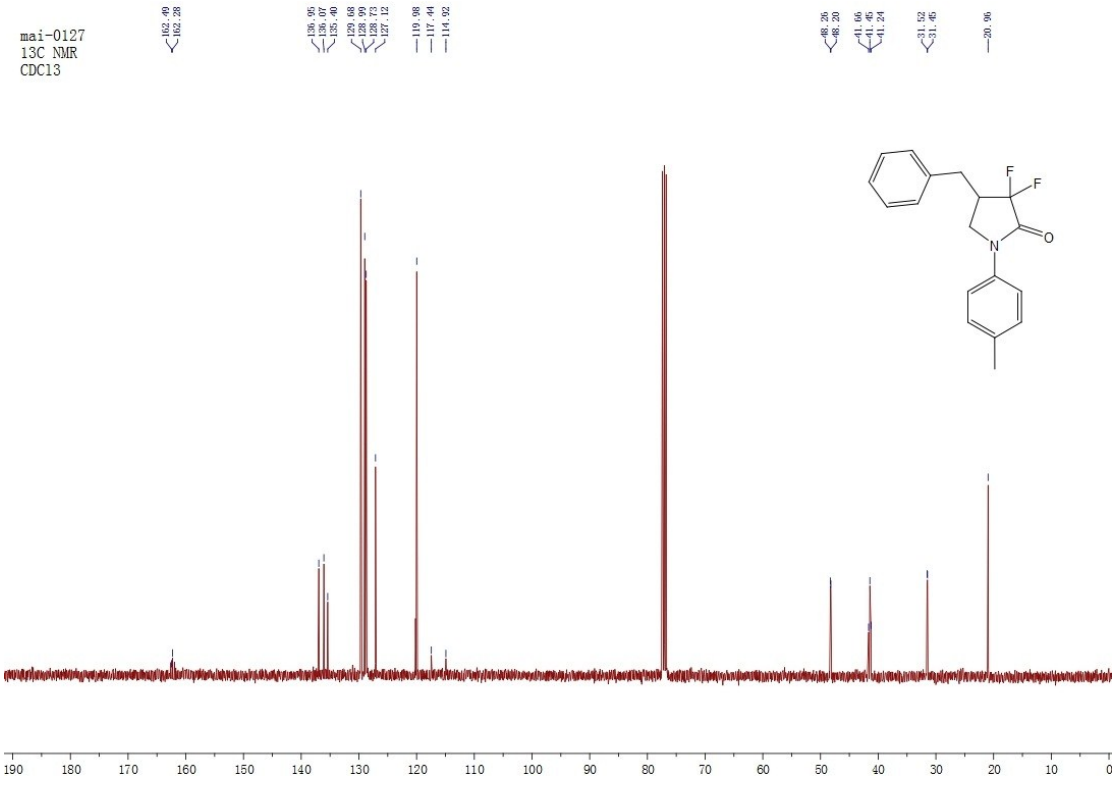
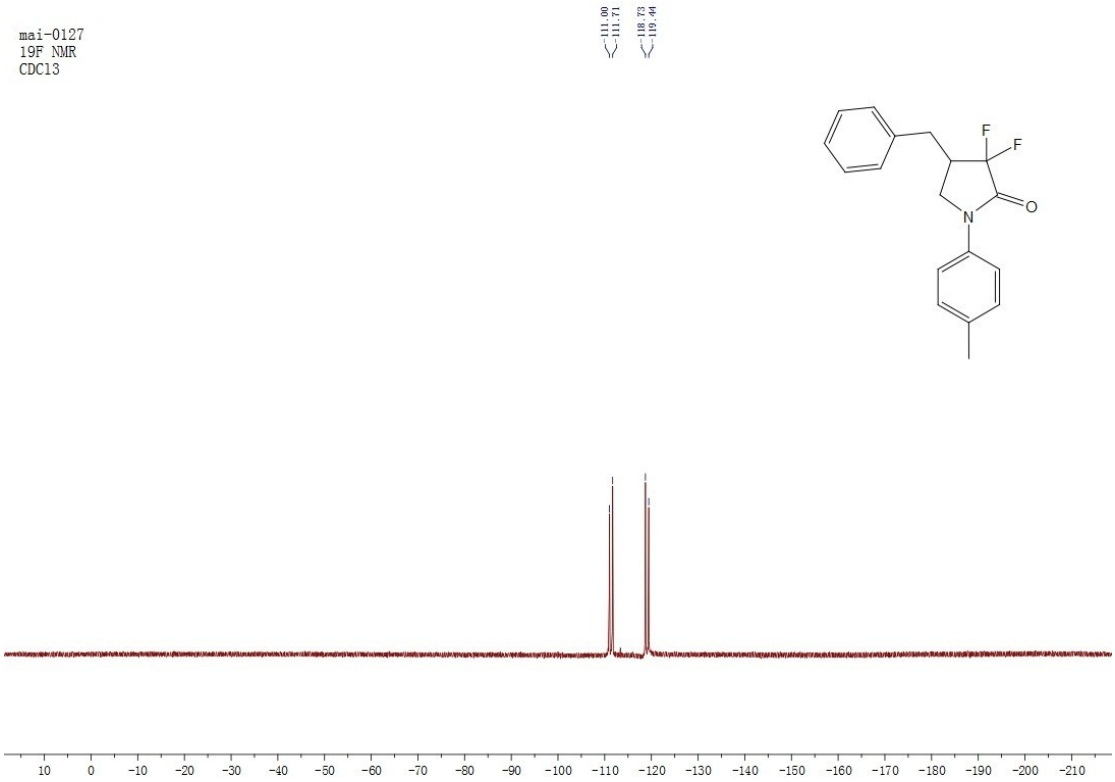
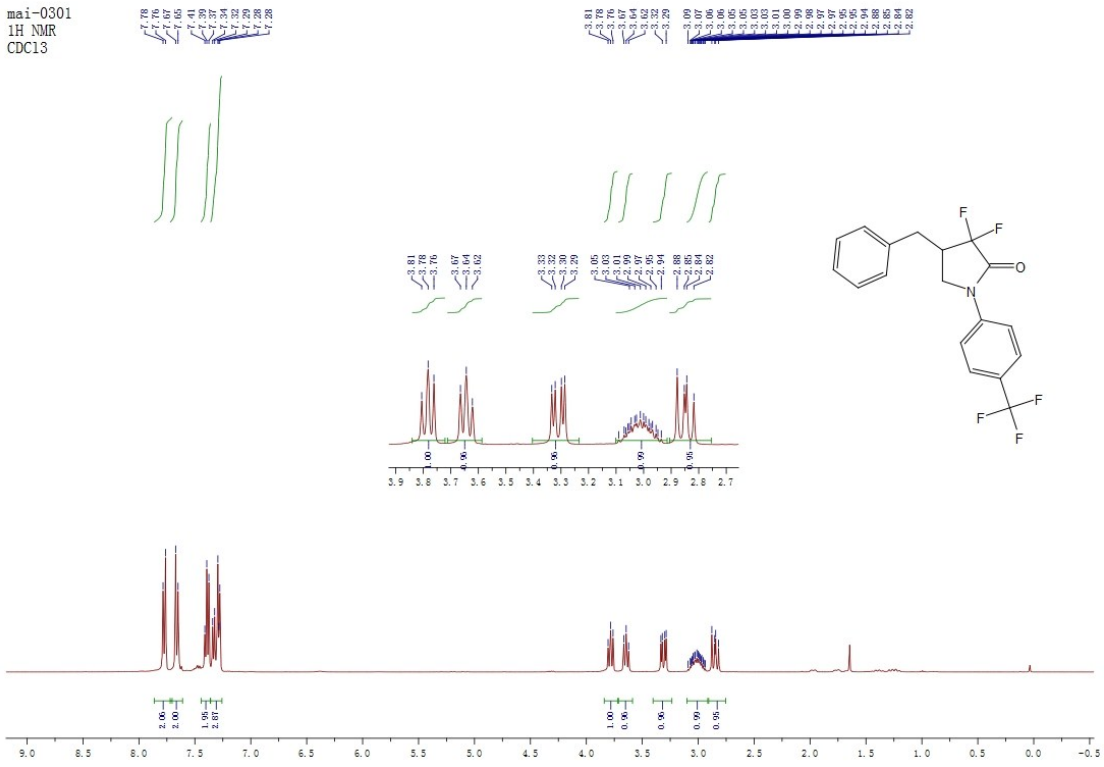
41.55
41.34
41.13
31.42
31.35
F
F
O
N
Cl
f1 (ppm)


mai-0126
19F NMR
CDC13
111.20
111.92
118.70
119.41
F
F
O
N
Cl
f1 (ppm)


mai-0127
1H NMR
CDC13
F
F
O
N


mai-0127
13C NMR
CDC13
F
F
O
N


mai-0127
19F NMR
CDC13
111.00
111.71
118.73
119.44
F
F
O
N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210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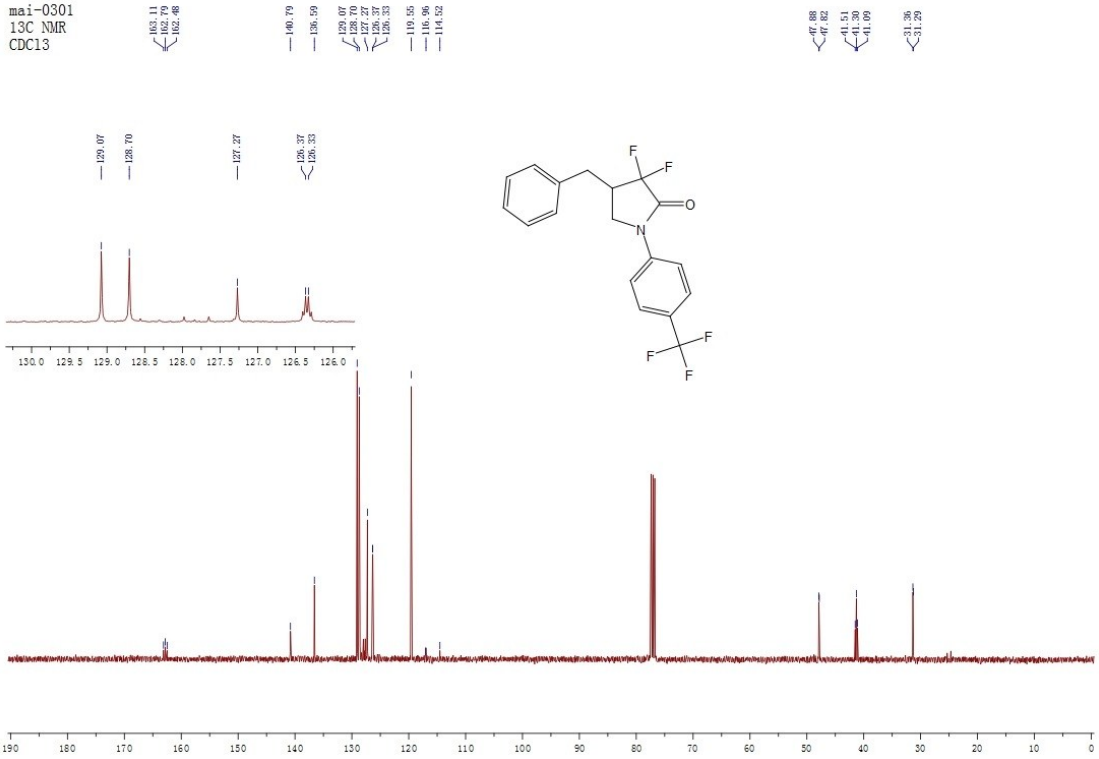
1H NMR
CDC13
7.78
7.76
7.67
7.65
7.41
7.39
7.37
7.34
7.32
7.29
7.28
7.28
3.81
3.78
3.76
3.67
3.64
3.62
3.52
3.29
3.09
3.07
3.06
3.05
3.05
3.03
3.03
3.01
3.00
2.99
2.98
2.97
2.97
2.95
2.94
2.88
2.85
2.84
2.82
F
F
O
N
F
F
F
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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13C NMR
CDC13
163.11
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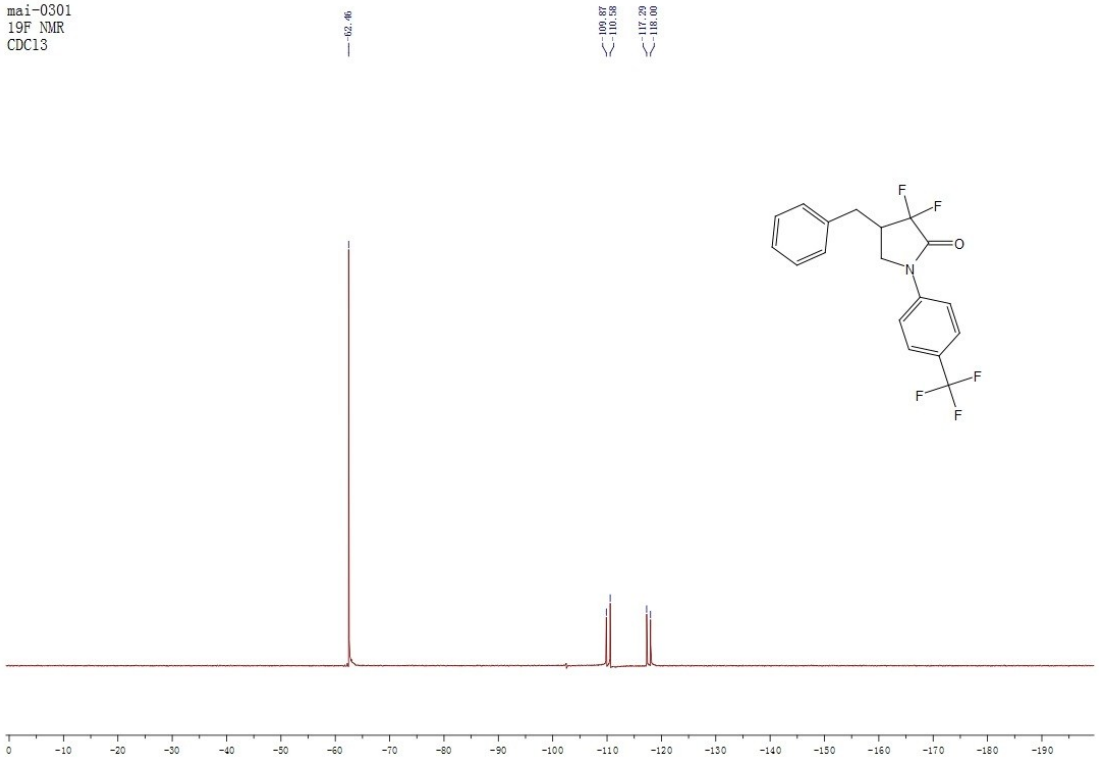
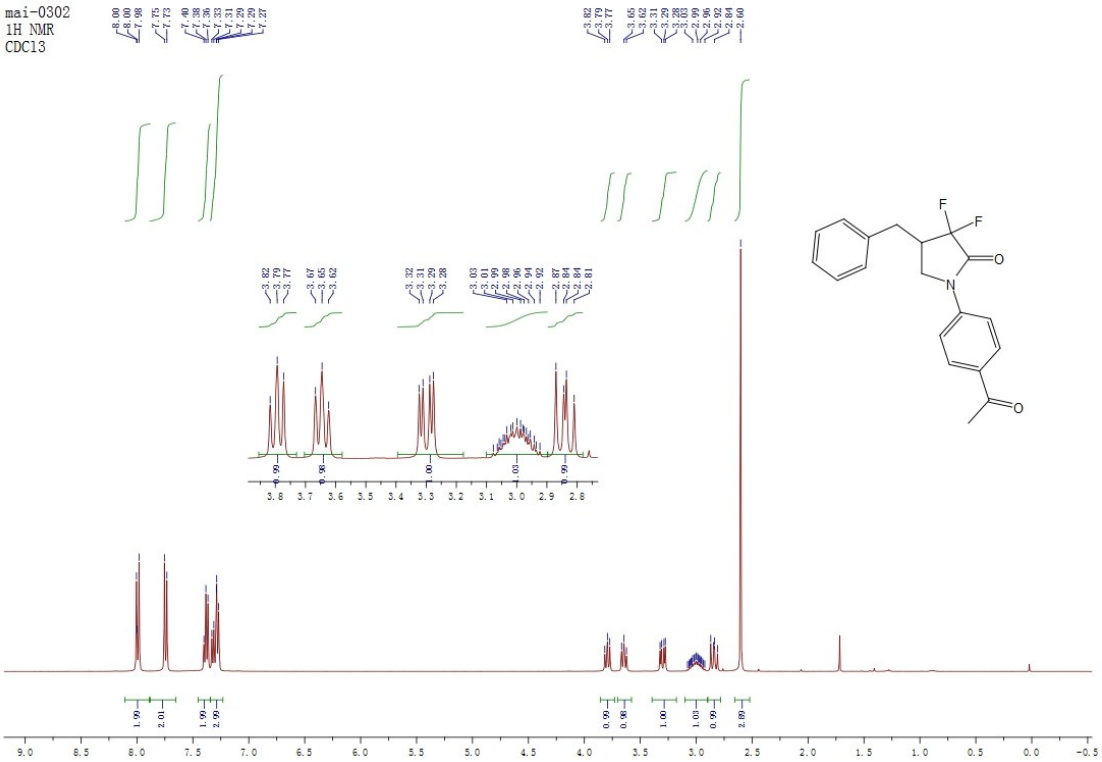
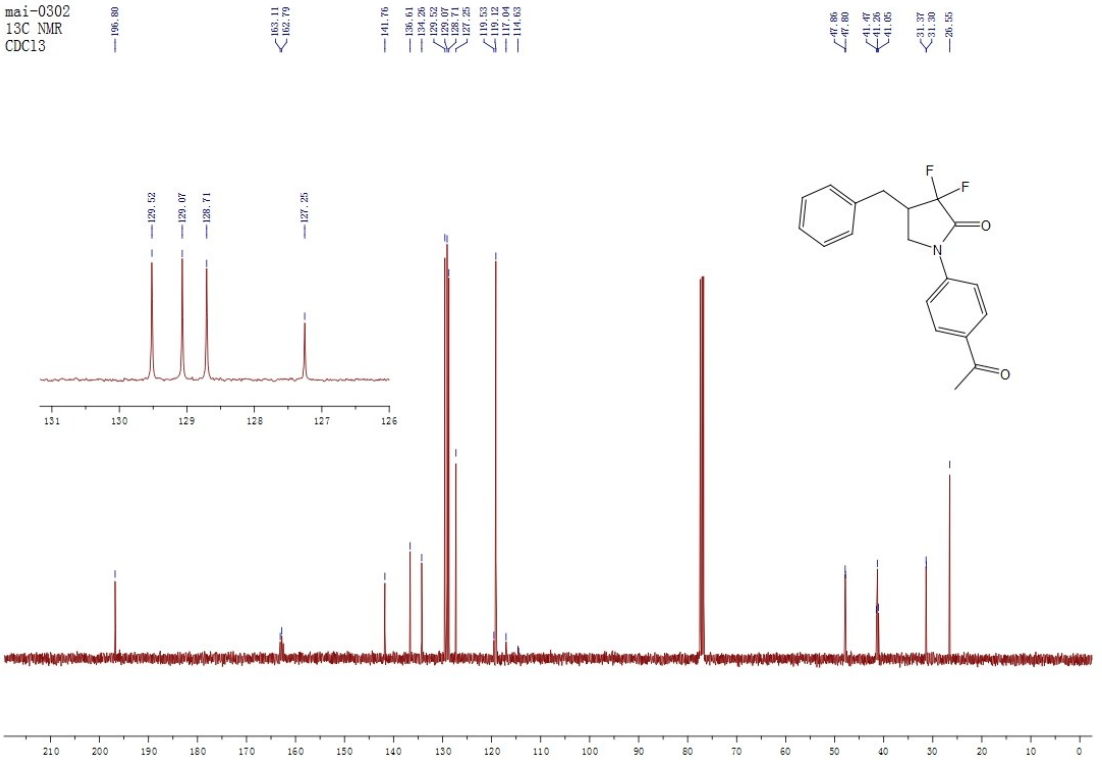
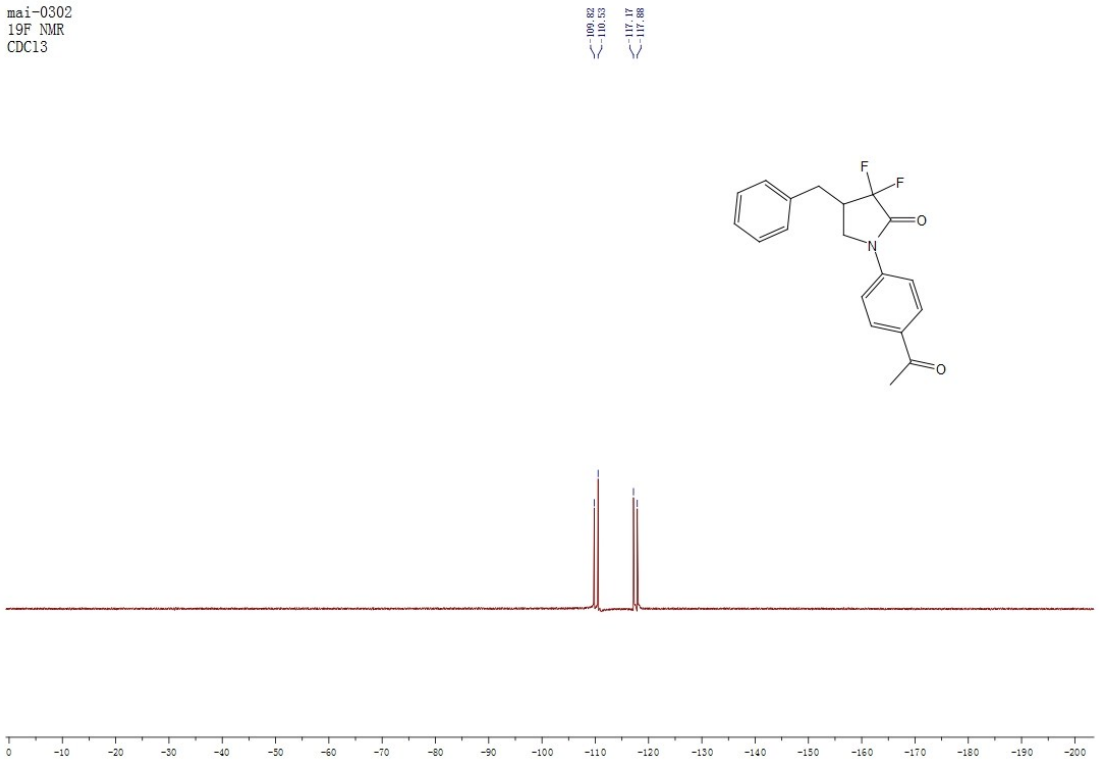
162.46
140.79
136.59
129.07
128.70
127.27
126.37
126.33
119.55
116.96
114.52
47.88
47.82
41.51
41.30
41.09
31.36
31.29
F
F
O
N
F
F
F

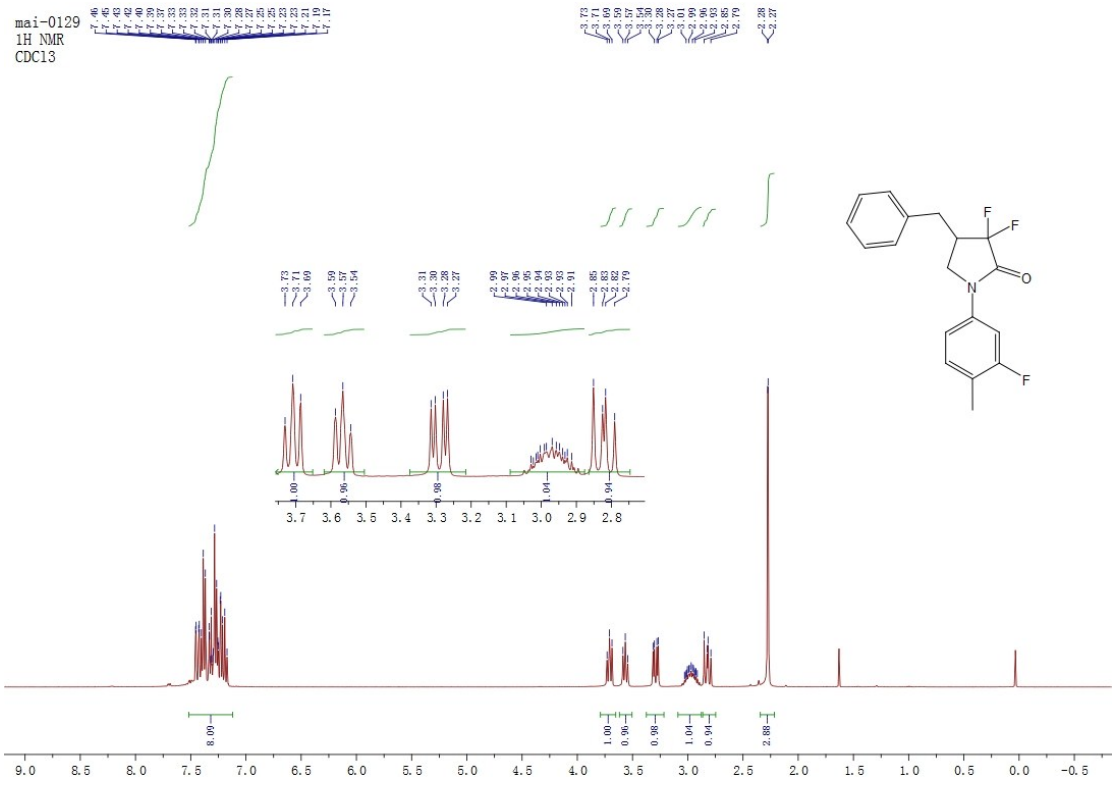

mai-0301
19F NMR
CDC13
-62.46
-109.87
-110.58
-117.29
-118.00
F
F
O
N
F
F
F

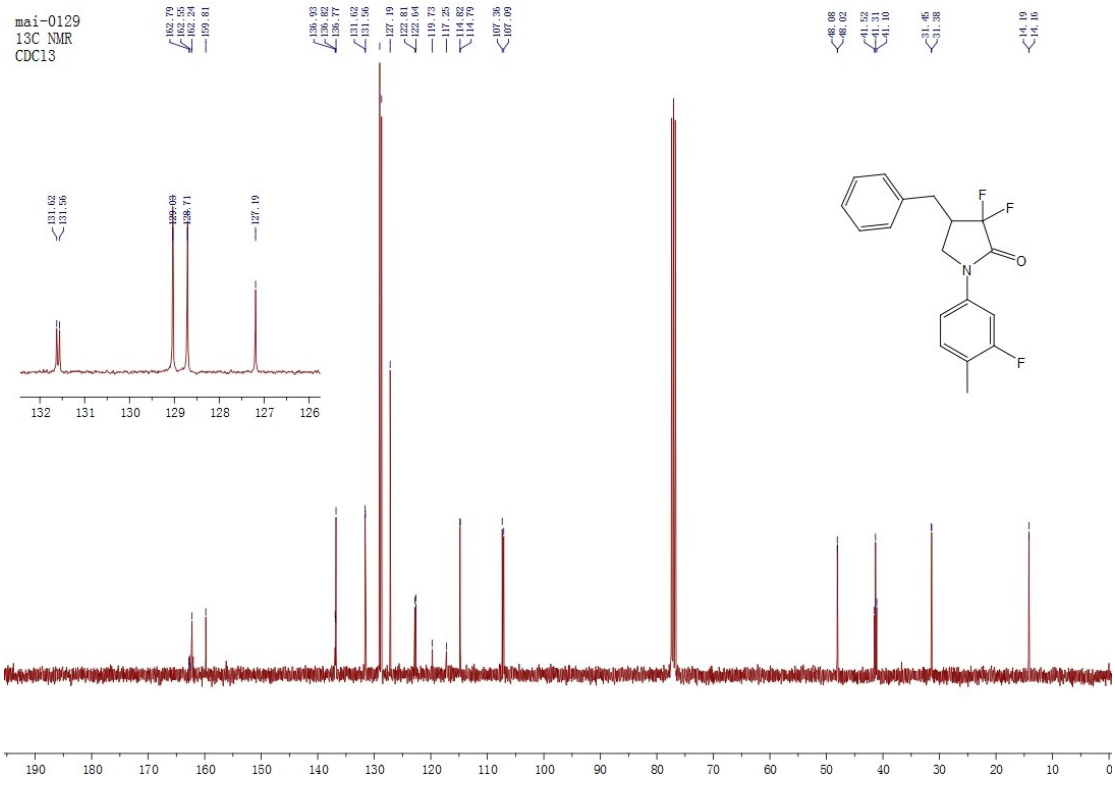

mai-0302
1H NMR
CDCl3

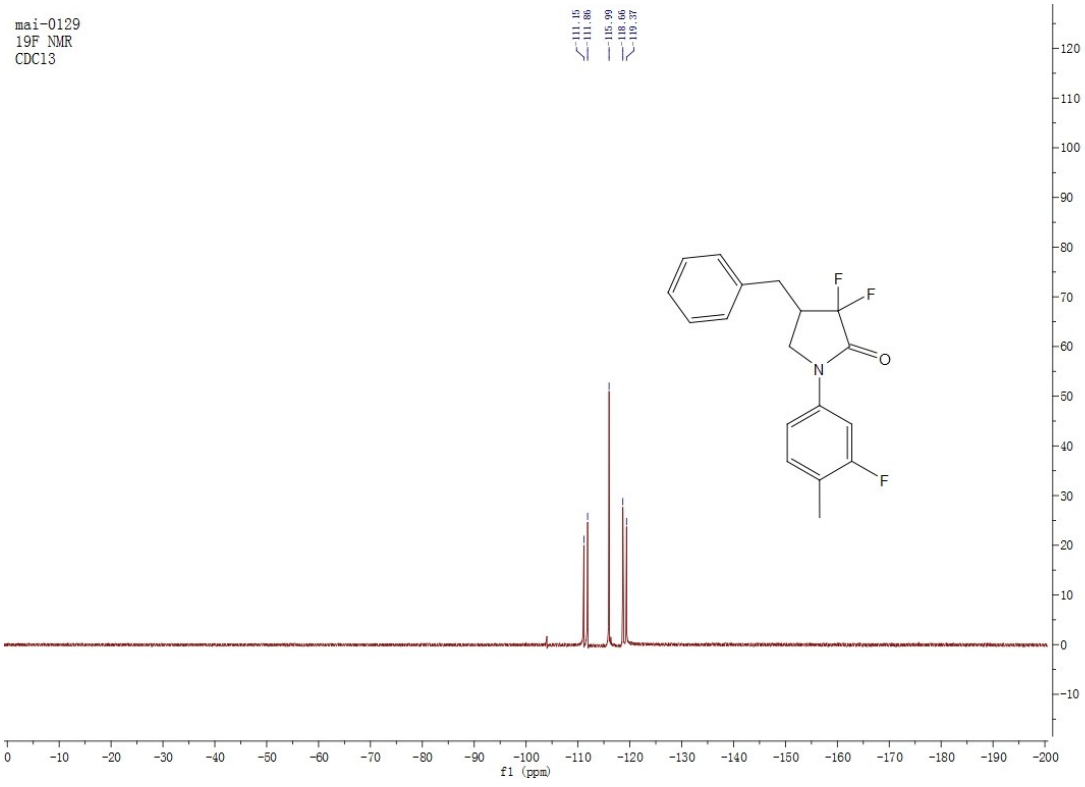

mai-0302
13C NMR
CDCl3

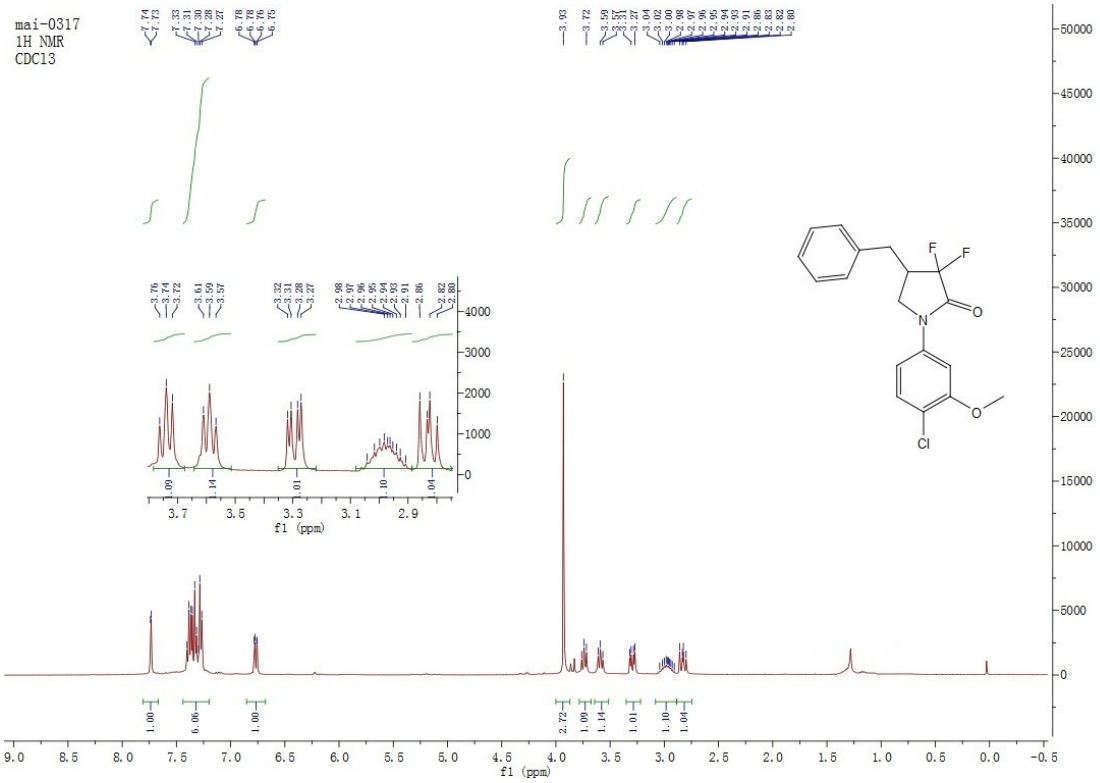

mai-0302
19F NMR
CDCl3
-109.82
-110.53
-117.17
-117.88
F
F
O
N
O

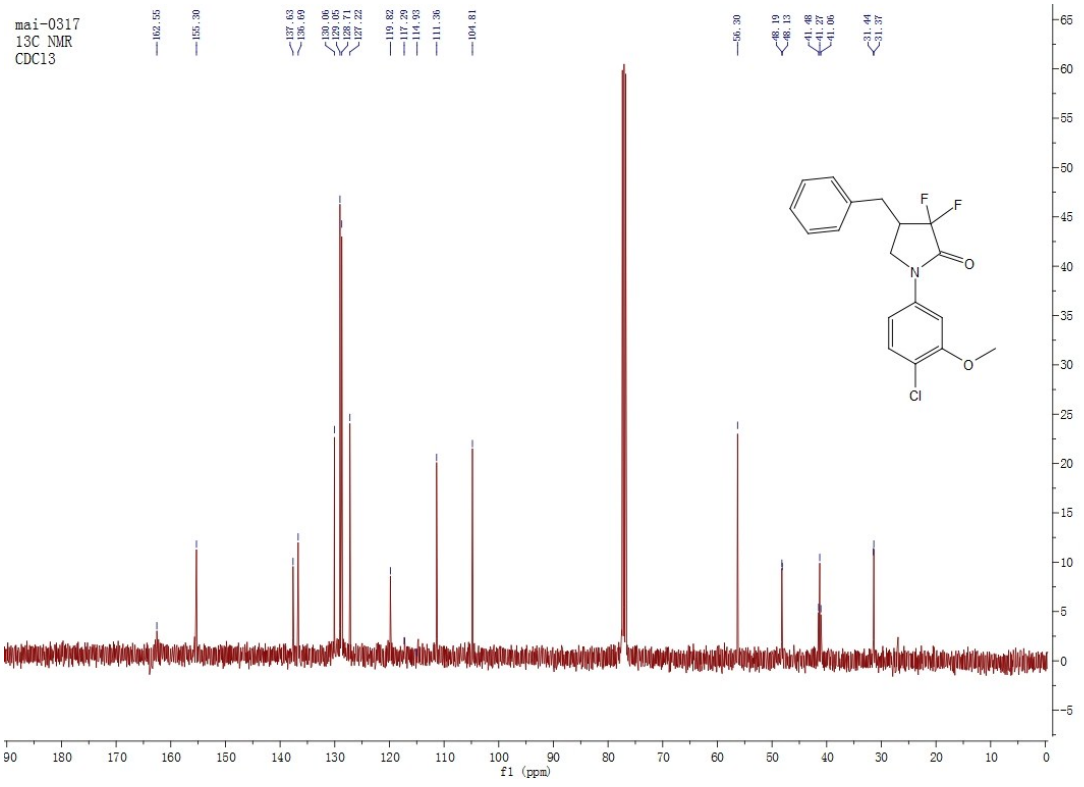
S66

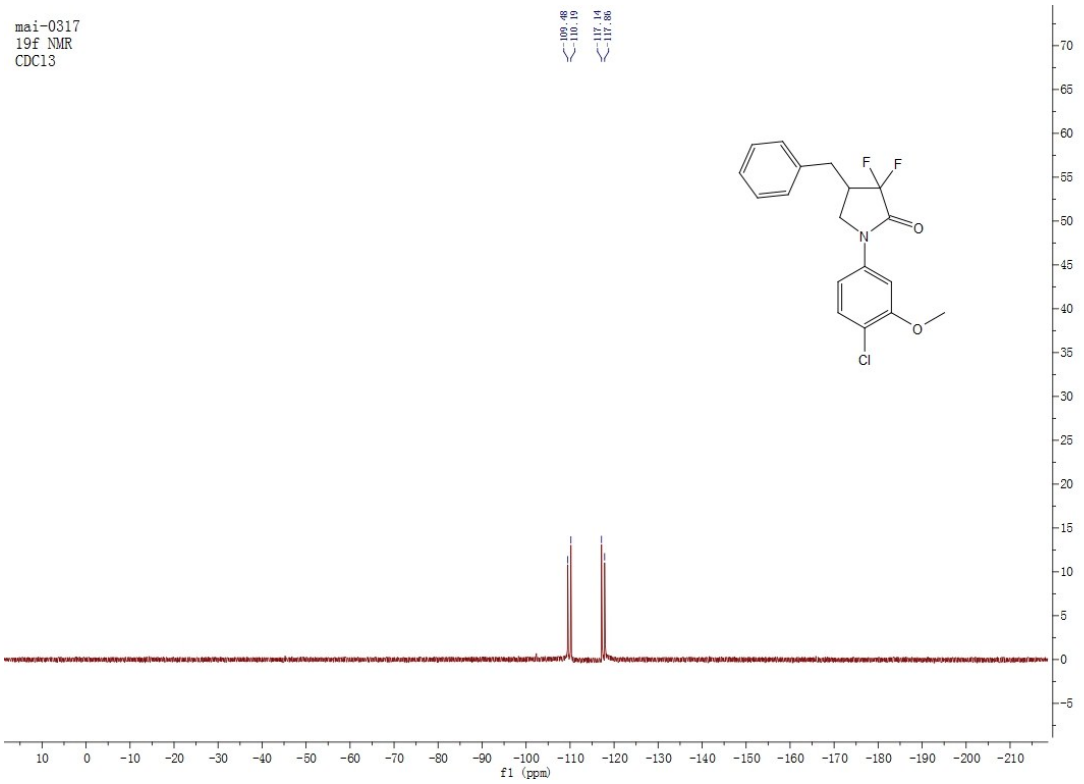

mai-0129
1H NMR
CDCl3
F
F
O
N
F
8.09
1.00
0.96
0.98
1.04
0.94
2.88

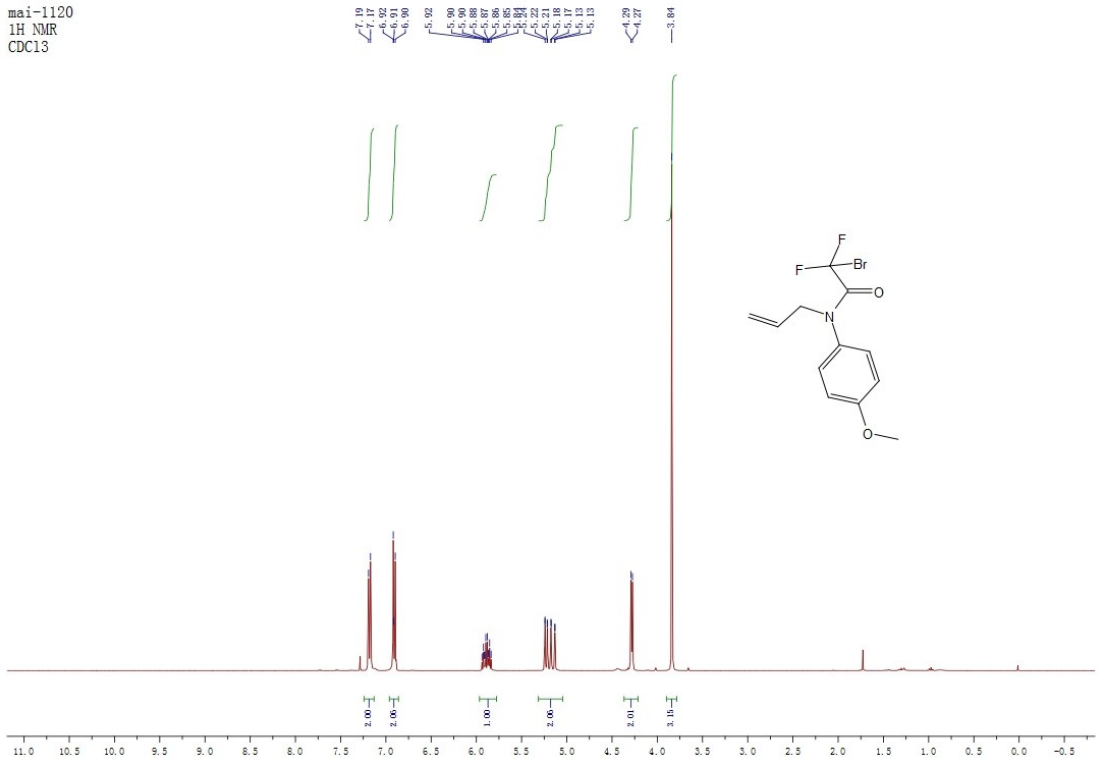

mai-0129
13C NMR
CDC13
F
F
O
N
F

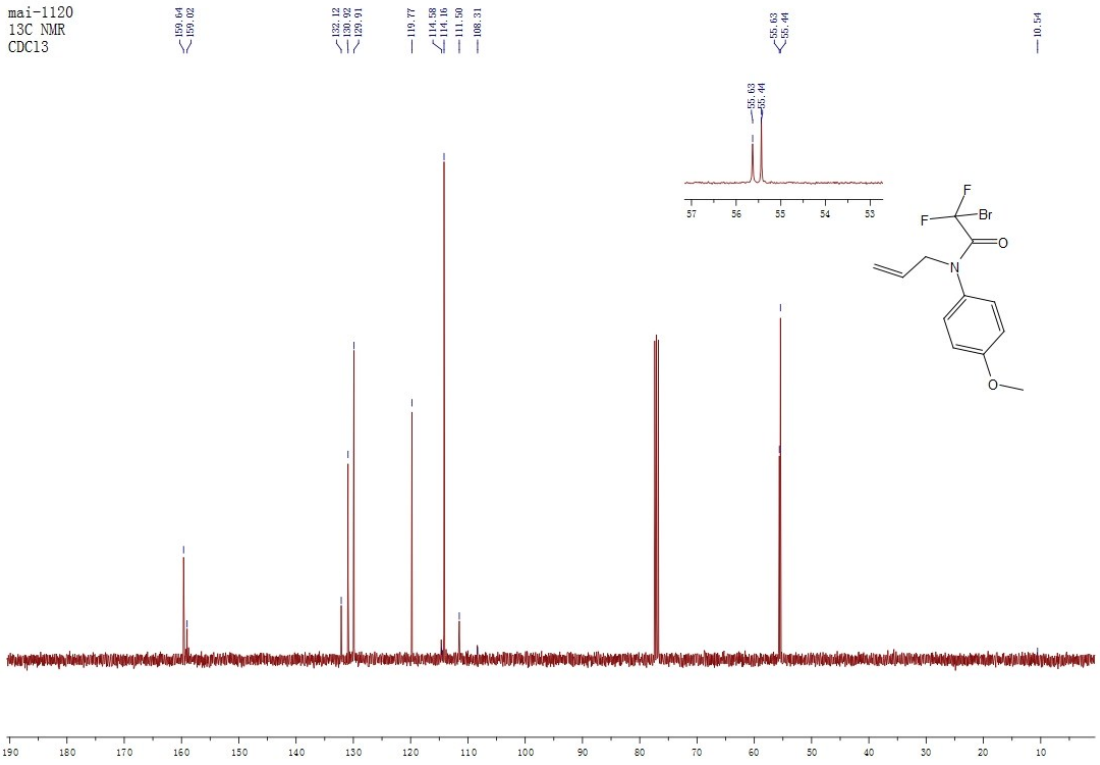

mai-0129
19F NMR
CDC13
F
F
O
N
F
f1 (ppm)

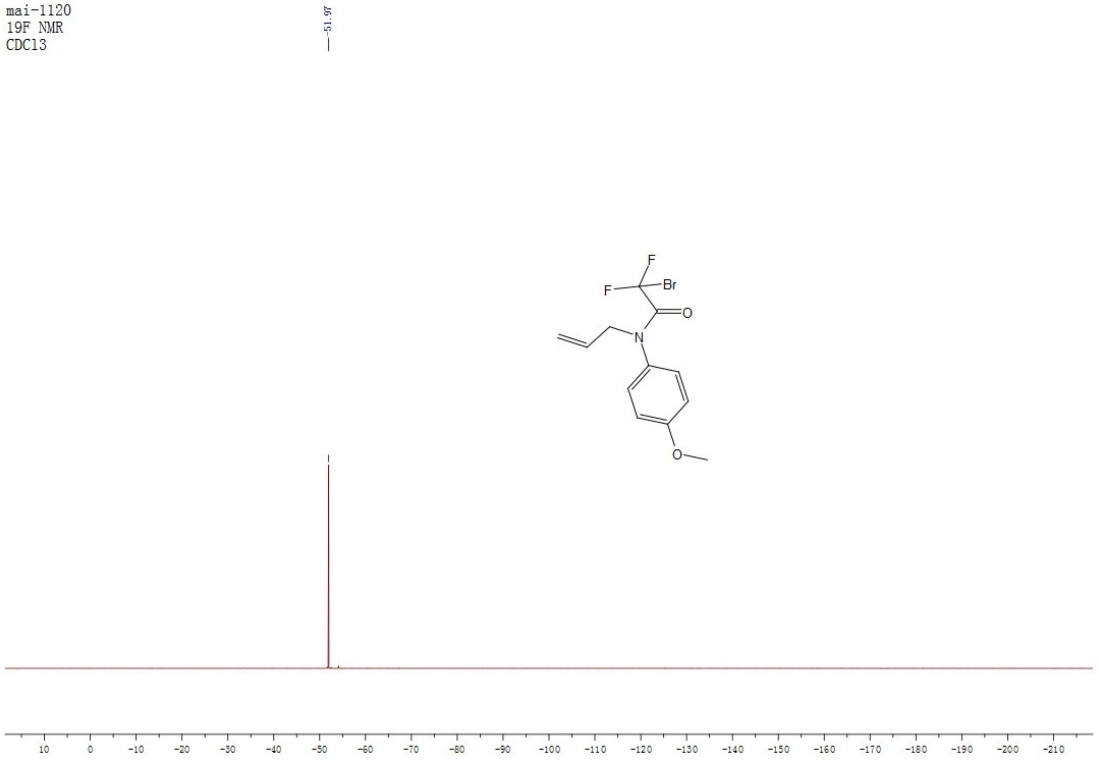

mai-0317
1H NMR
CDCl3
f1 (ppm)

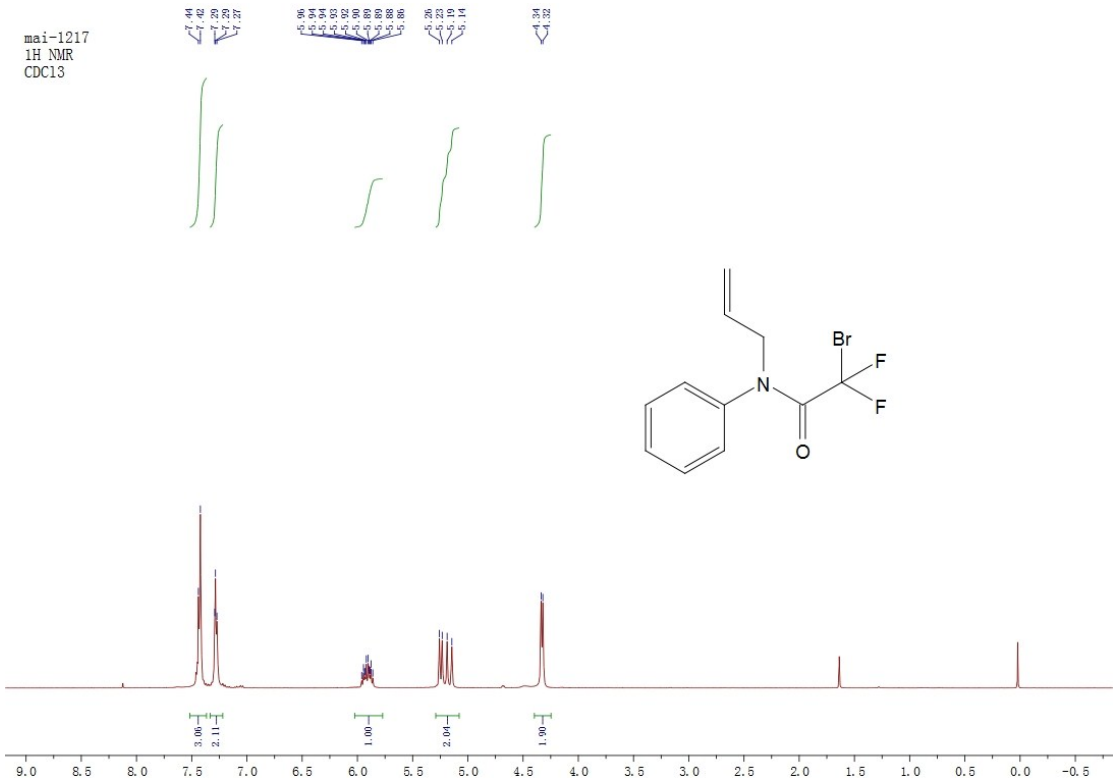

mai-0317
13C NMR
CDCl3
f1 (ppm)

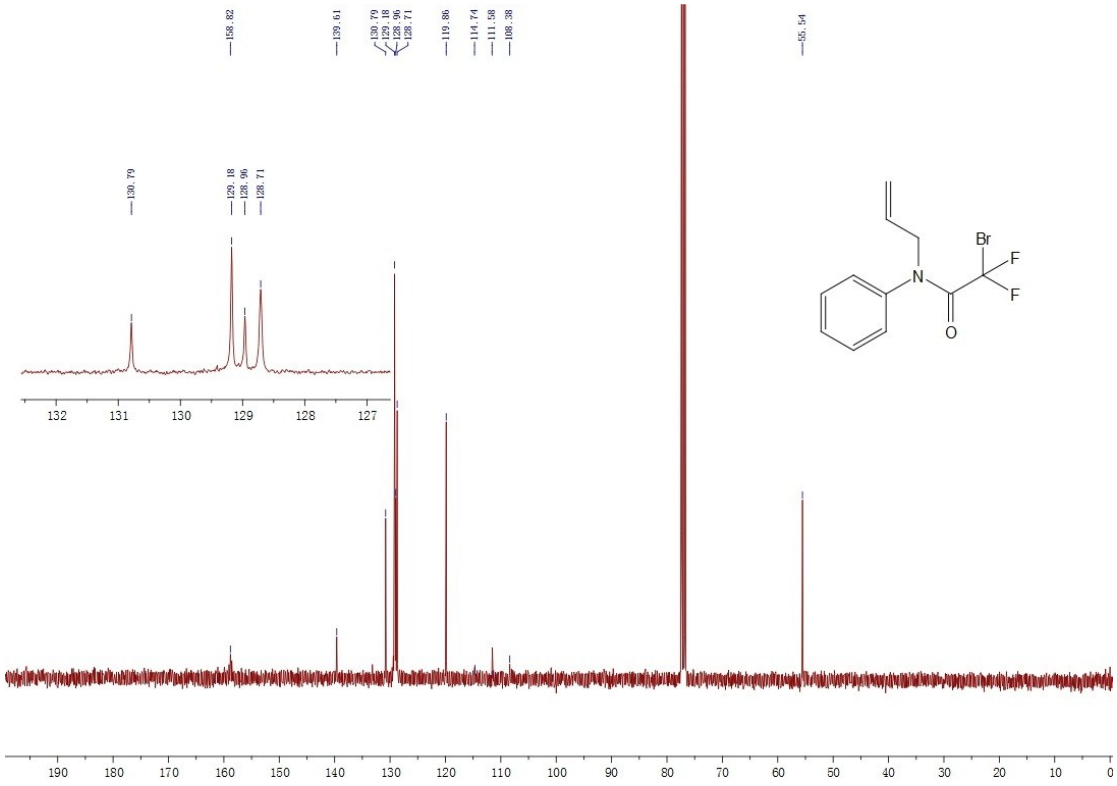

mai-0317
19f NMR
CDC13
-109.48
-110.19
-117.14
-117.86
F
F
O
N
O
Cl
f1 (ppm)

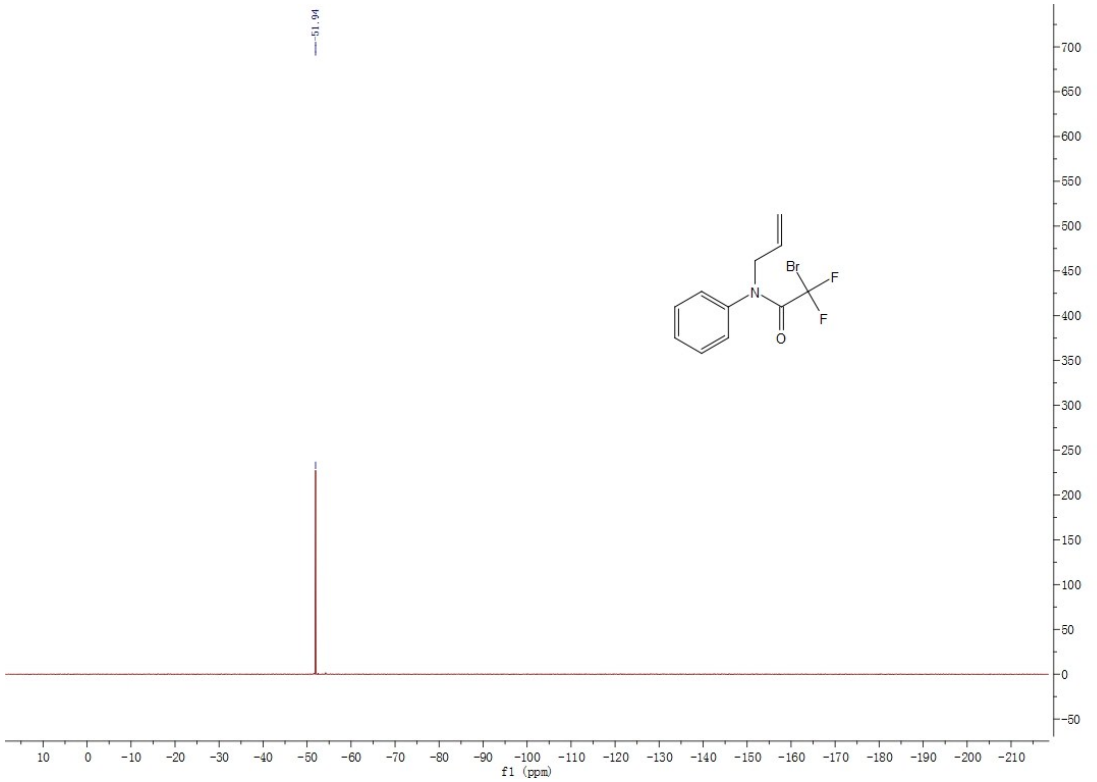

mai-1120
1H NMR
CDC13
7.19
7.17
6.92
6.91
6.90
5.92
5.90
5.90
5.88
5.87
5.86
5.85
5.84
5.22
5.21
5.18
5.17
5.13
5.13
4.29
4.27
3.84
F
F
Br
O
N
O
2.00
2.06
1.00
2.00
2.01
3.16

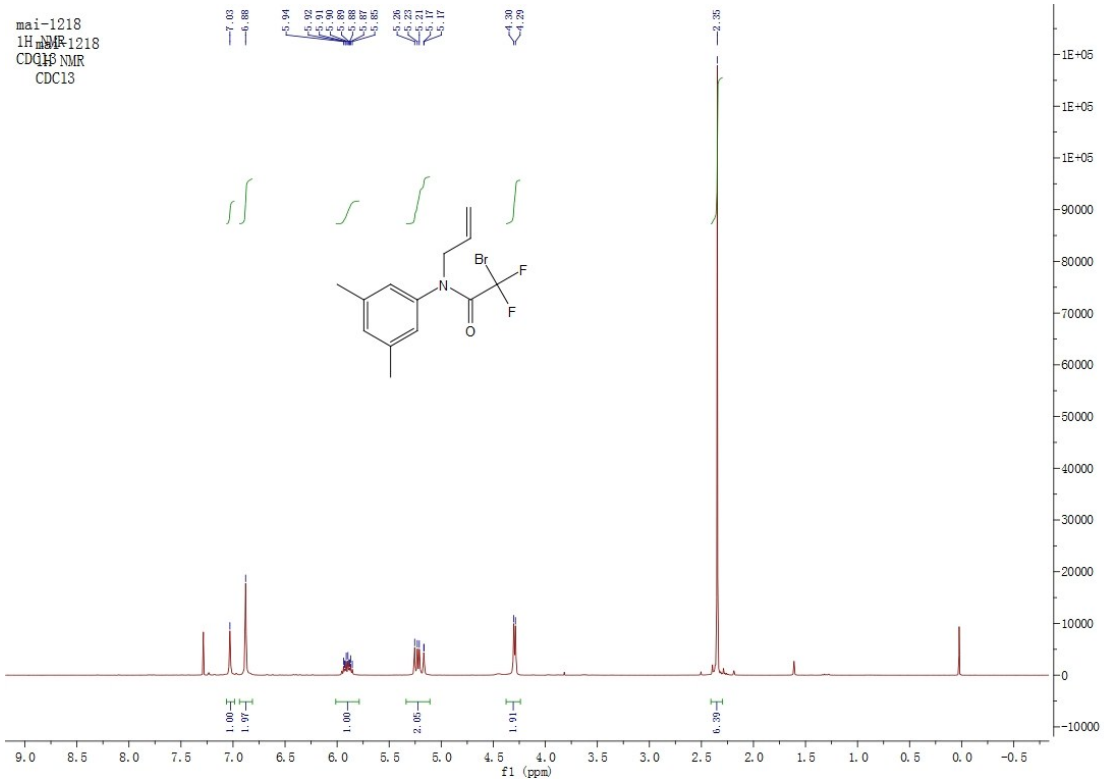

mai-1120
13C NMR
CDC13
159.64
159.02
132.12
130.92
129.91
119.77
114.58
114.16
111.50
108.31
55.63
55.44
10.54
F
F
Br
O
N
O

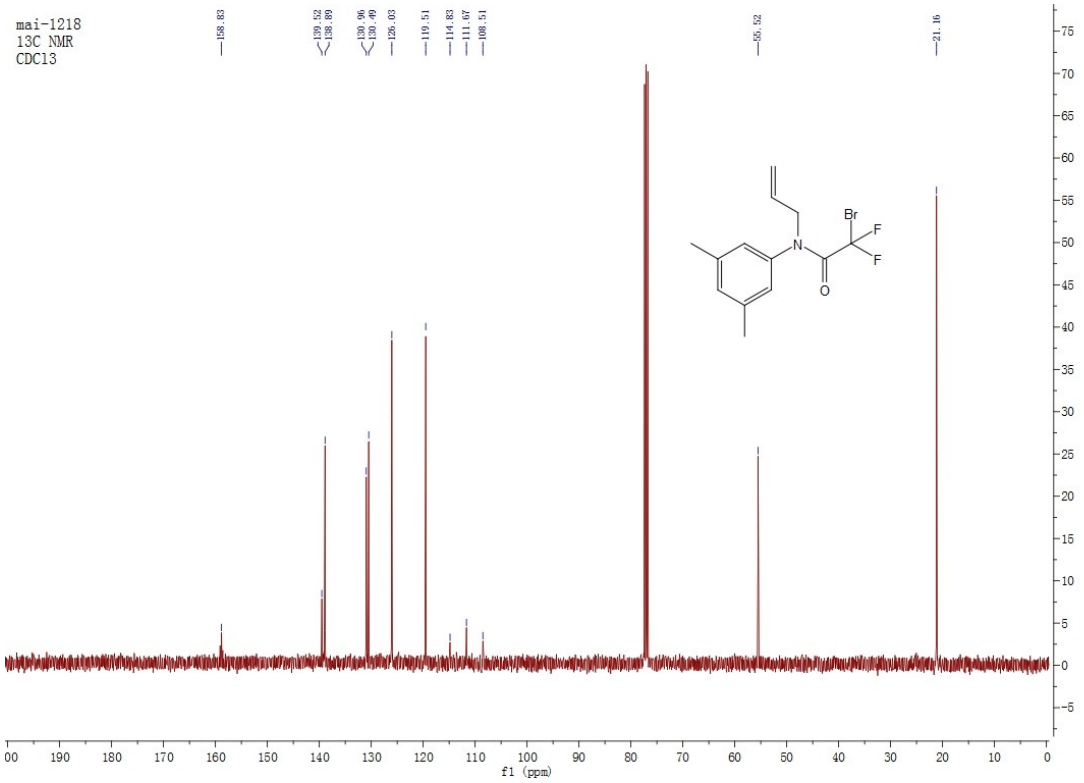

mai-1120
19F NMR
CDC13
-51.97
F
F
Br
O
N
O

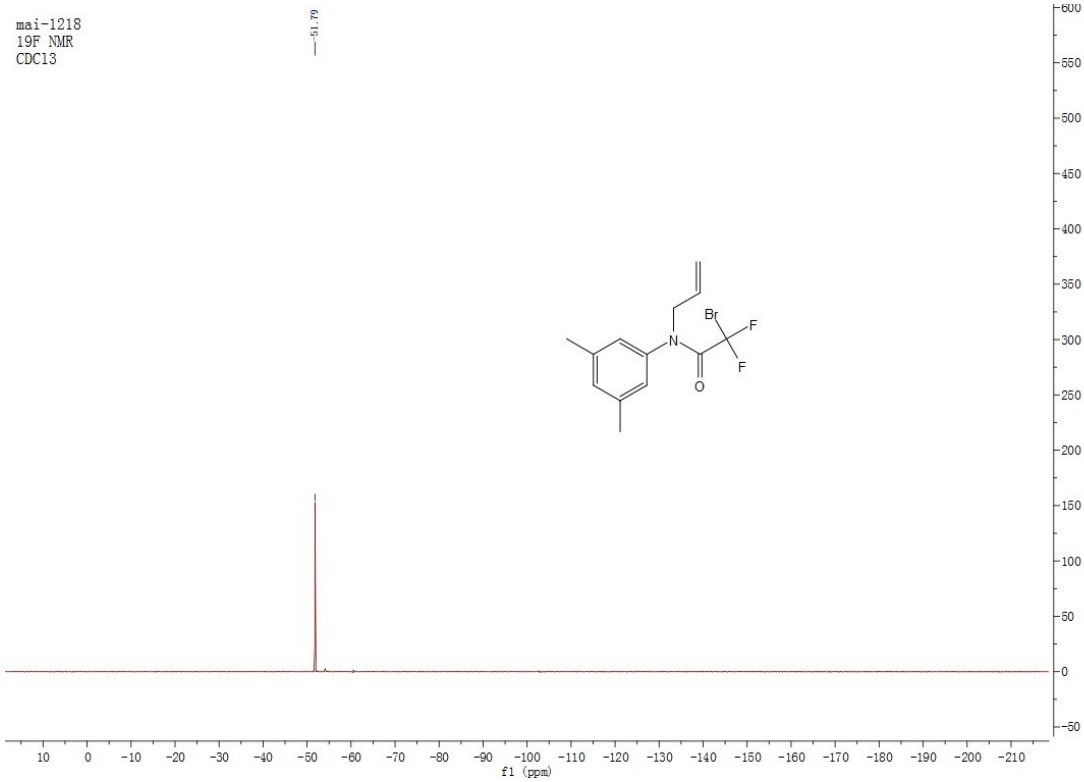

mai-1217
1H NMR
CDCl3
Br
F
F
N
O

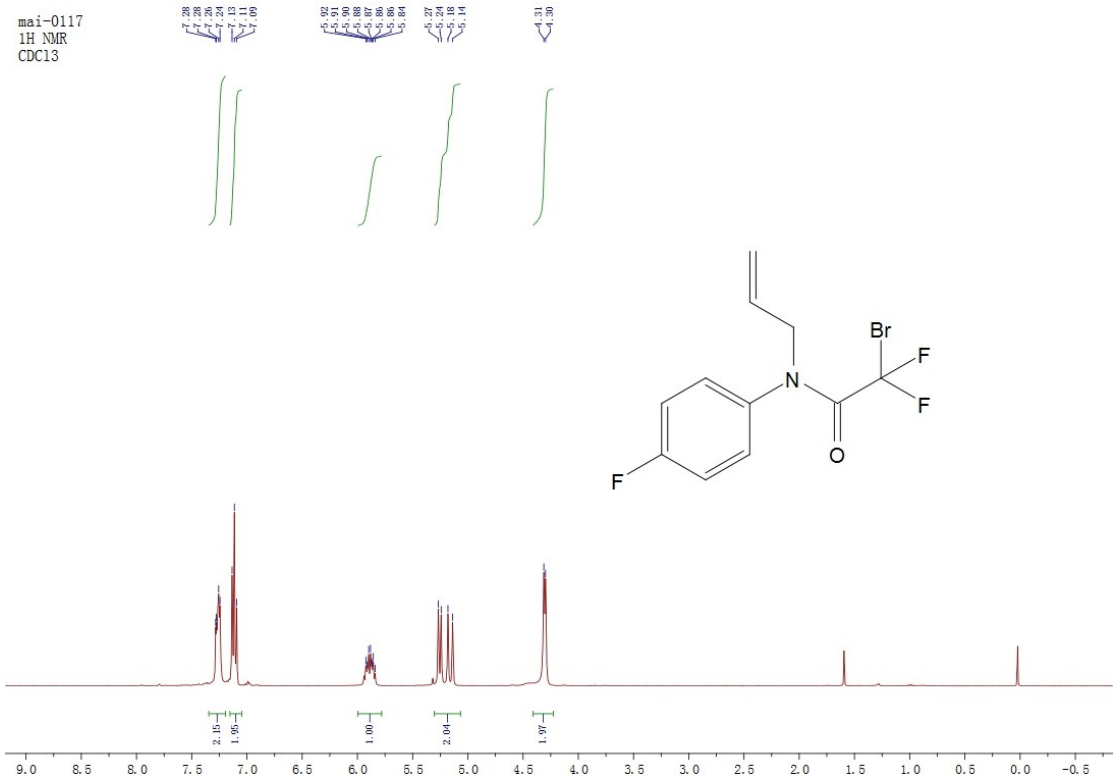

Br
F
F
N
O

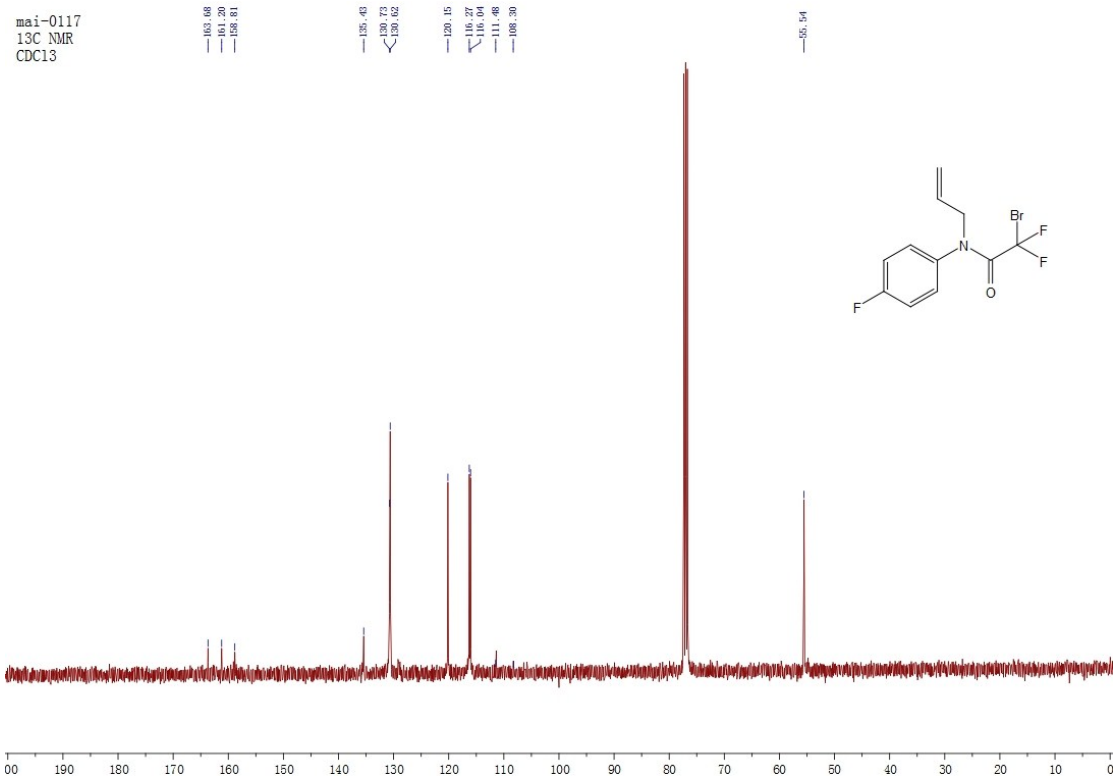

-51.94
Br
F
F
N
O
f1 (ppm)


mai-1218
1H NMR
CDCl3
7.03
6.88
5.94
5.92
5.91
5.90
5.89
5.88
5.87
5.86
5.26
5.23
5.21
5.17
4.30
4.29
2.35
Br
F
F
N
O
1.00
1.97
1.00
2.05
1.91
6.39
f1 (ppm)

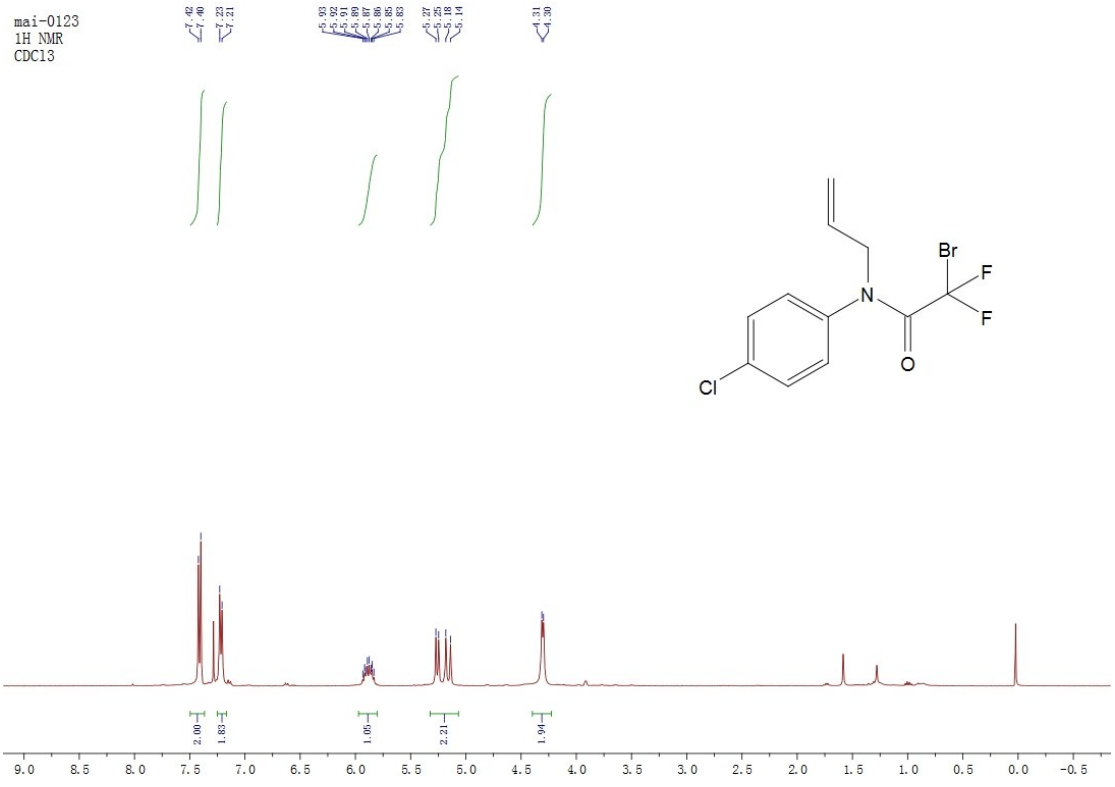

mai-1218
13C NMR
CDC13
158.83
139.52
138.89
130.96
130.49
126.03
119.51
114.83
111.67
108.51
55.52
21.16
Br
F
F
N
O
f1 (ppm)

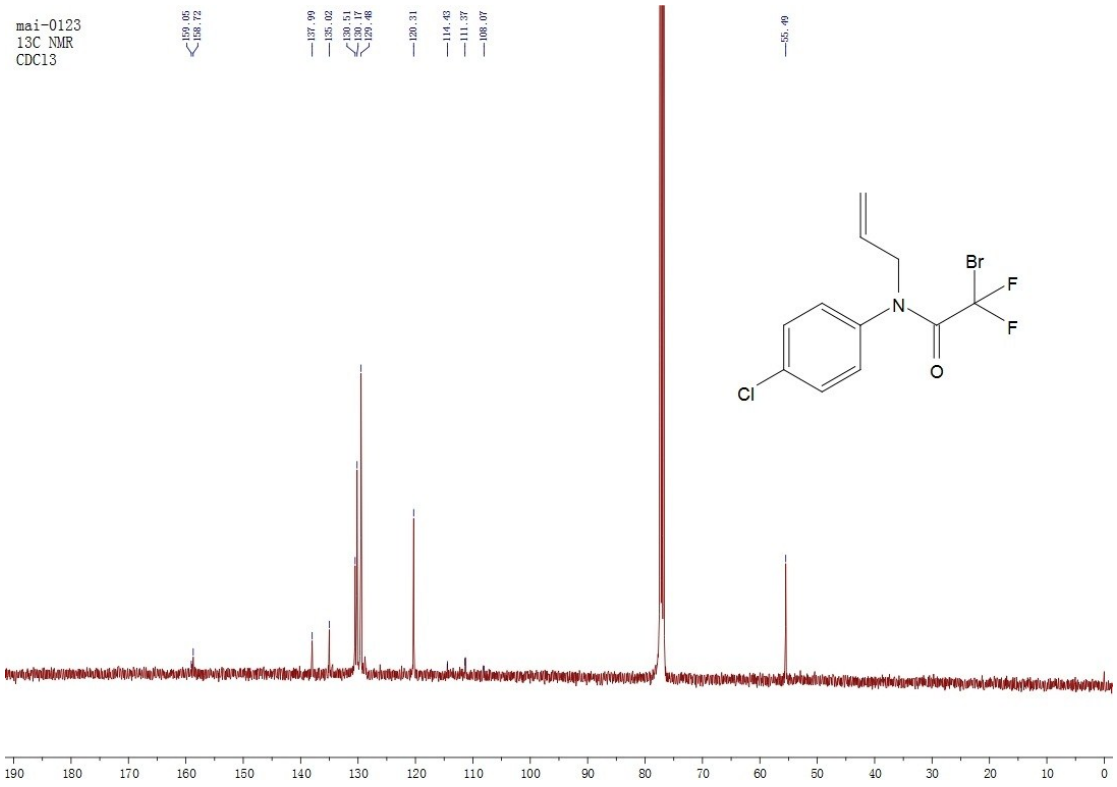

mai-1218
19F NMR
CDC13
51.79
Br
F
F
N
O
f1 (ppm)

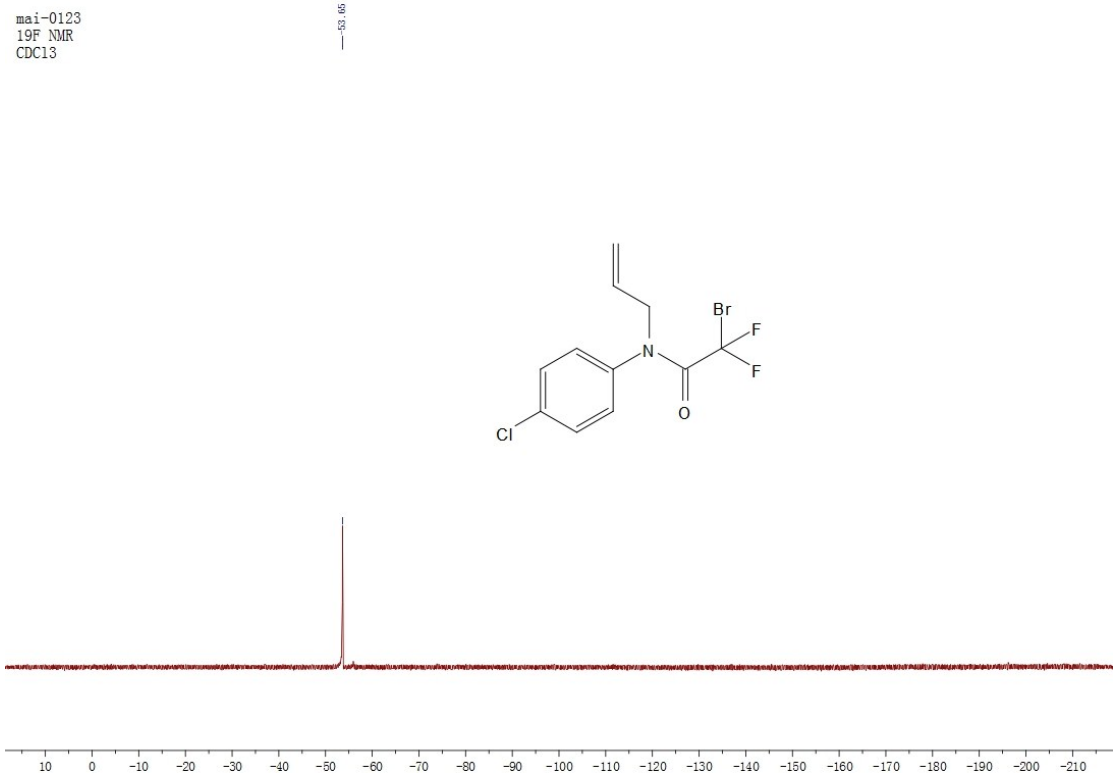

mai-0117
1H NMR
CDC13
Br
F
F
N
O
F

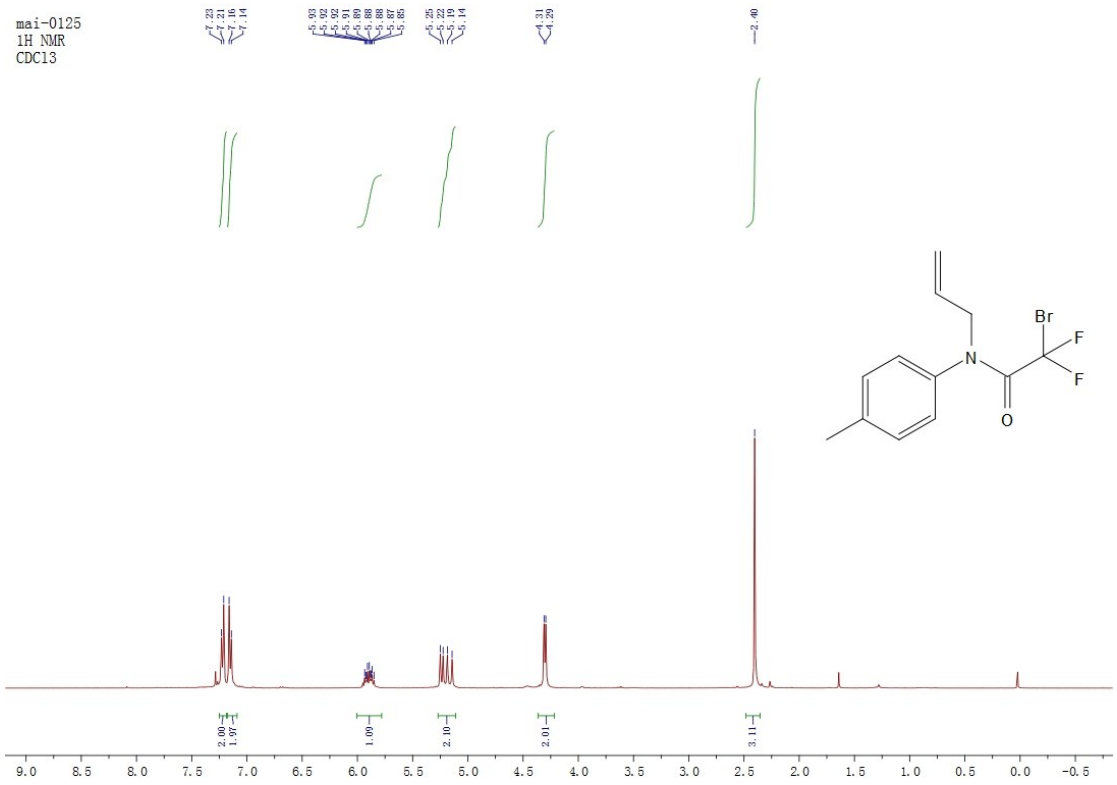

mai-0117
13C NMR
CDC13
Br
F
F
N
O
F

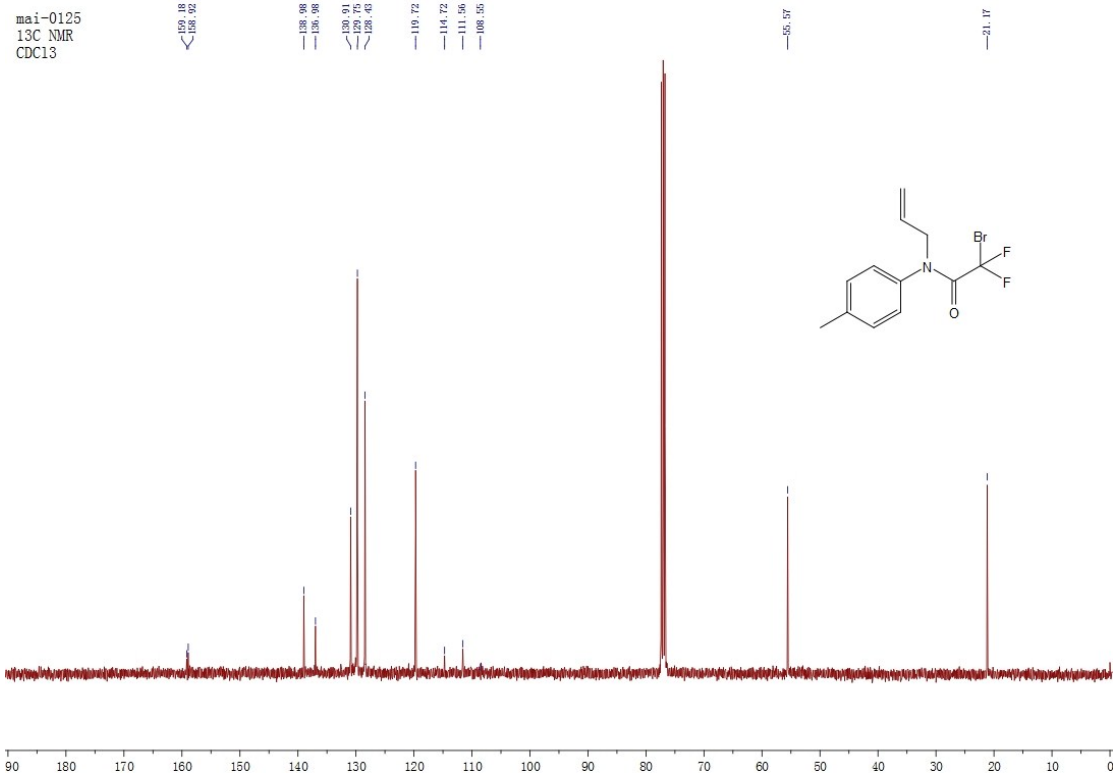

mai-0117
19F NMR
CDC13
-53.56
-113.14
Br
F
F
N
O
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

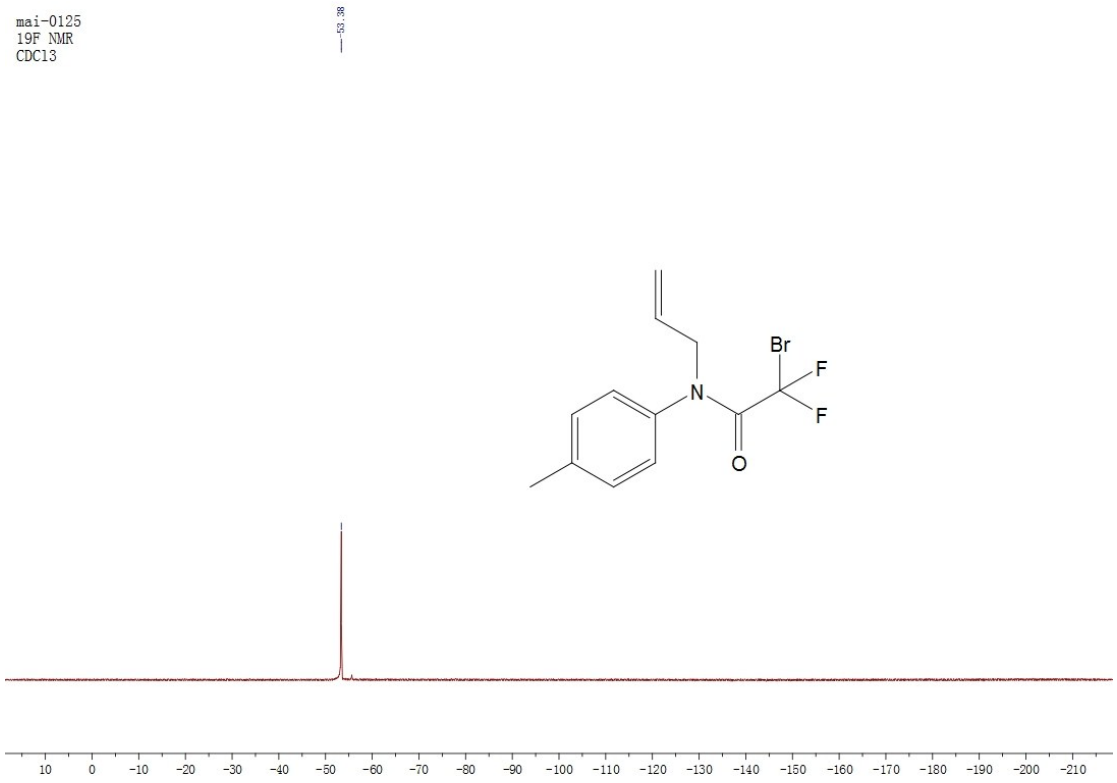

mai-0123
1H NMR
CDC13
7.42
7.40
7.23
7.21
5.93
5.92
5.91
5.89
5.87
5.86
5.85
5.83
5.27
5.25
5.18
5.14
4.31
4.30
Br
F
F
N
O
Cl
2.00
1.83
1.05
2.21
1.94
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

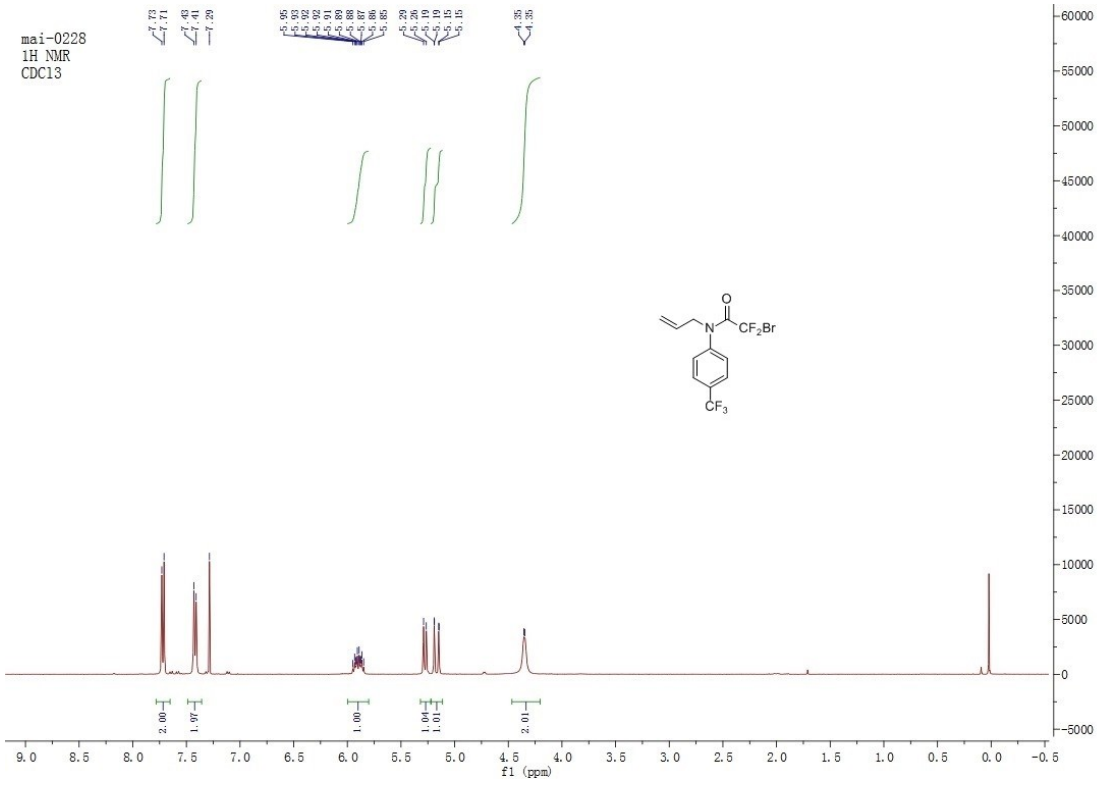

mai-0123
13C NMR
CDC13
159.05
158.72
137.99
135.02
130.51
130.17
129.48
120.31
114.43
111.37
108.07
55.49
Br
F
F
N
O
Cl
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

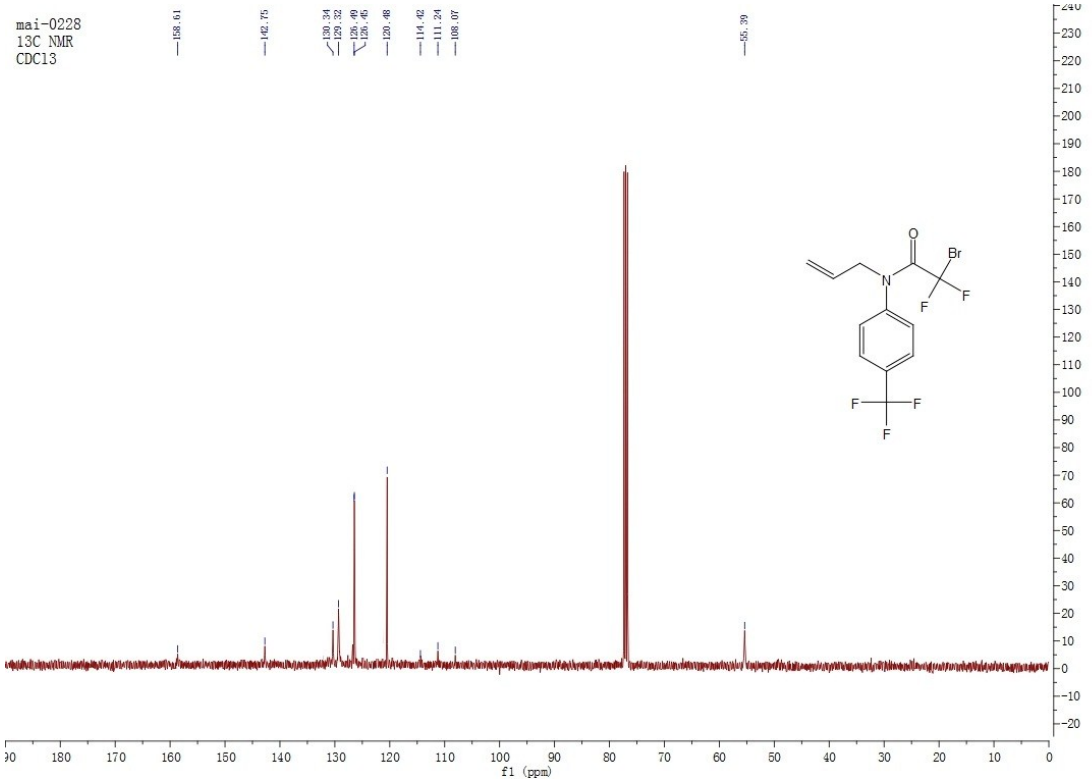

mai-0123
19F NMR
CDC13
-53.65
Br
F
F
N
O
Cl
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

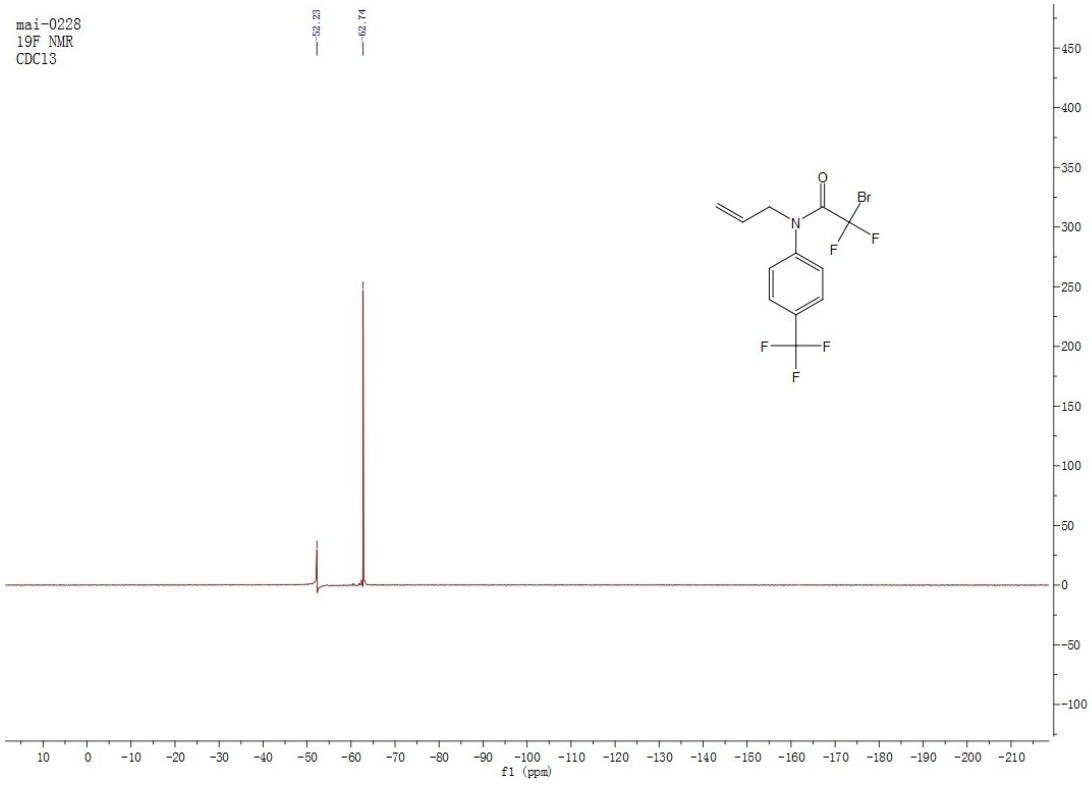

mai-0125
1H NMR
CDC13
Br
F
F
N
O

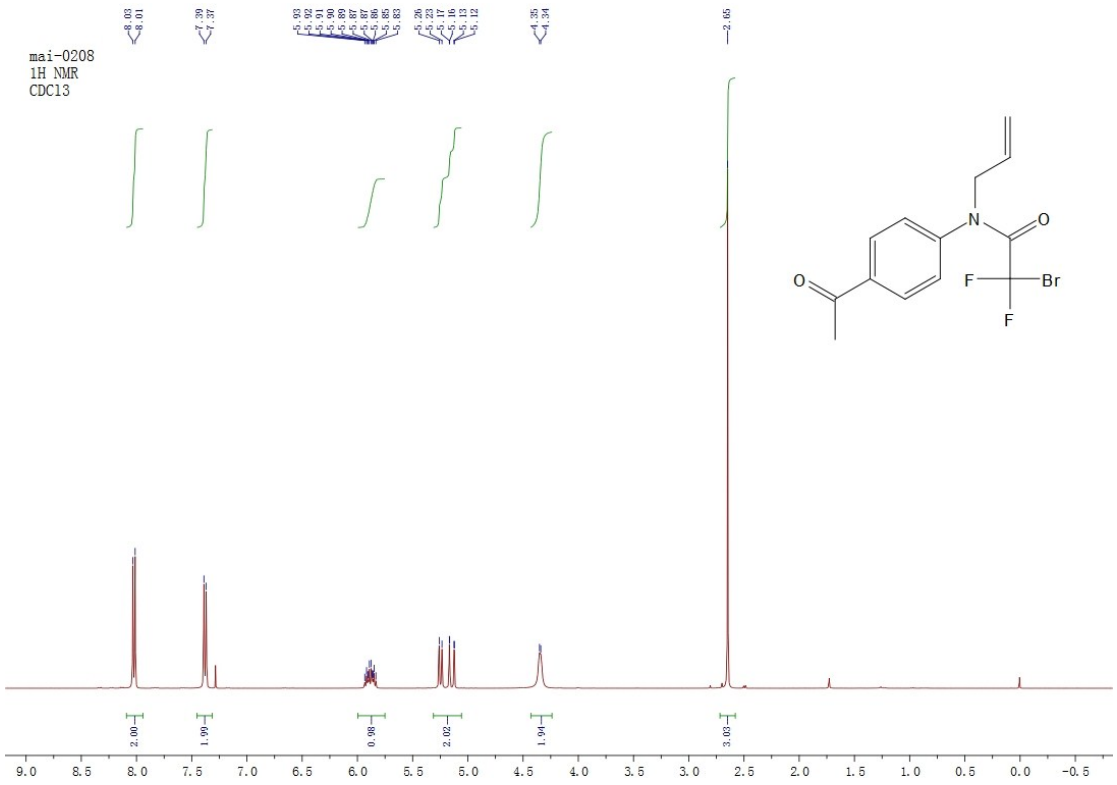

mai-0125
13C NMR
CDC13
Br
F
F
N
O

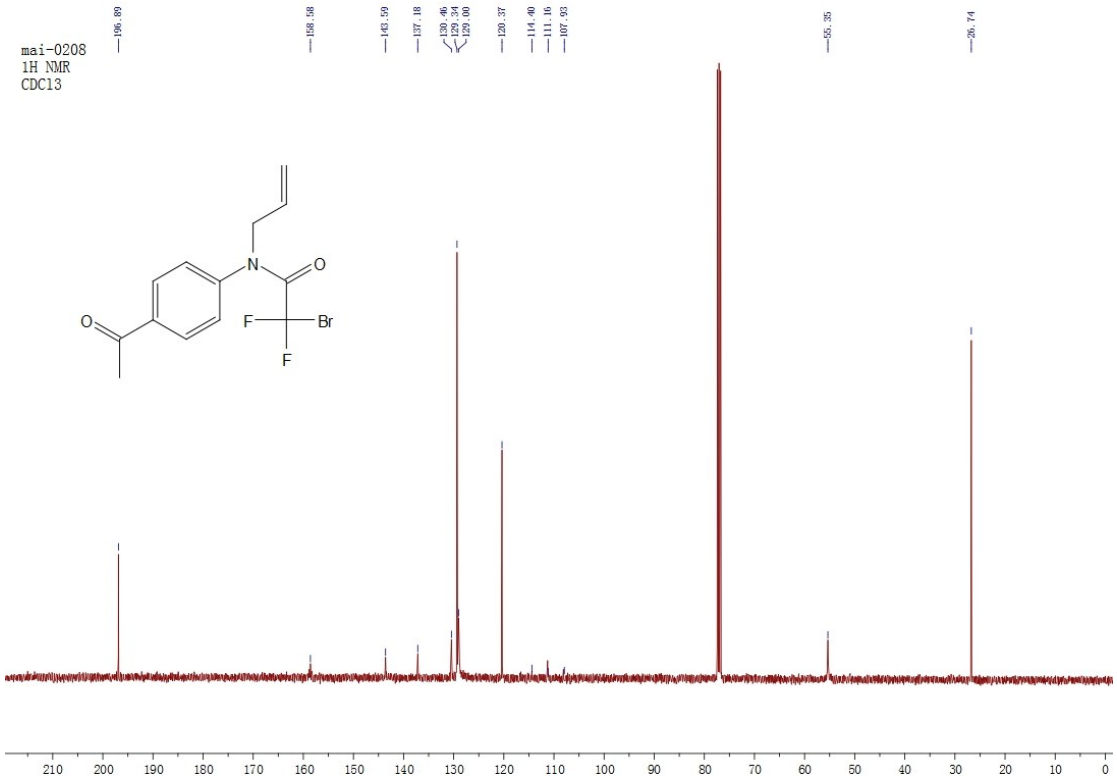

mai-0125
19F NMR
CDC13
-53.38
Br
F
F
N
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

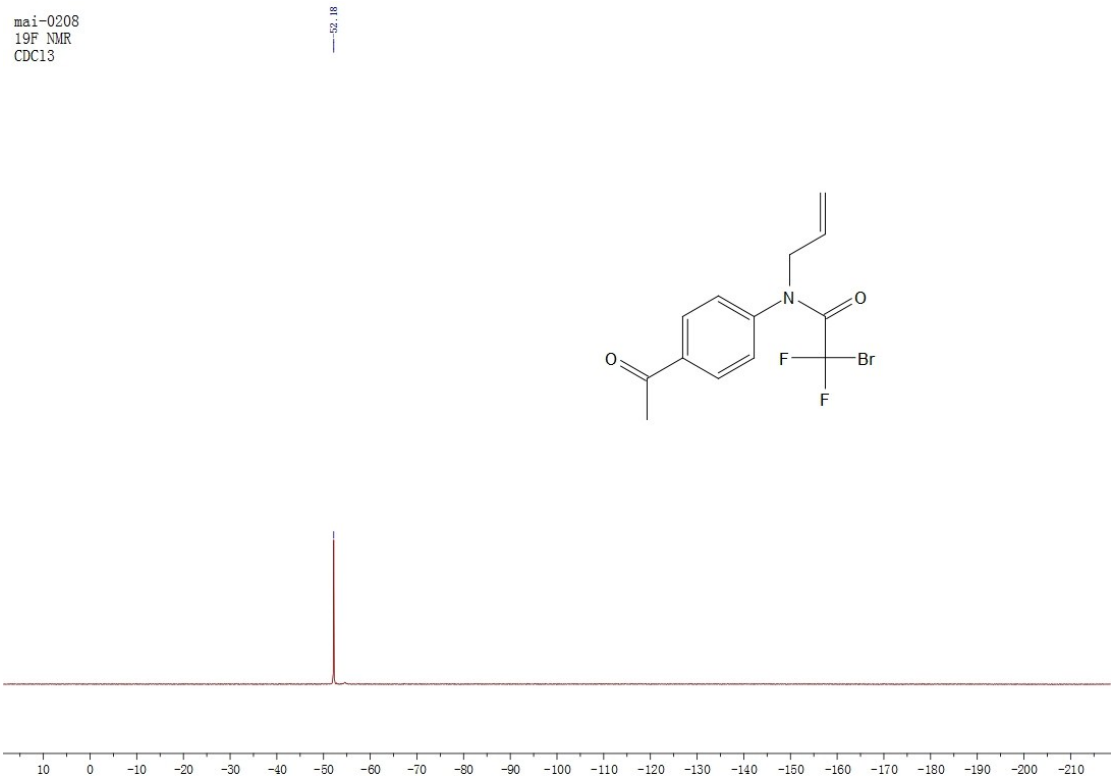

mai-0228
1H NMR
CDC13
7.73
7.71
7.45
7.44
7.29
5.95
5.93
5.92
5.91
5.89
5.88
5.87
5.86
5.85
5.29
5.26
5.19
5.15
5.15
4.35
4.34
O
N
CF2Br
CF3
2.00
1.97
1.00
1.04
1.01
2.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
60000 55000 50000 45000 40000 35000 30000 25000 20000 15000 10000 5000 0 -5000

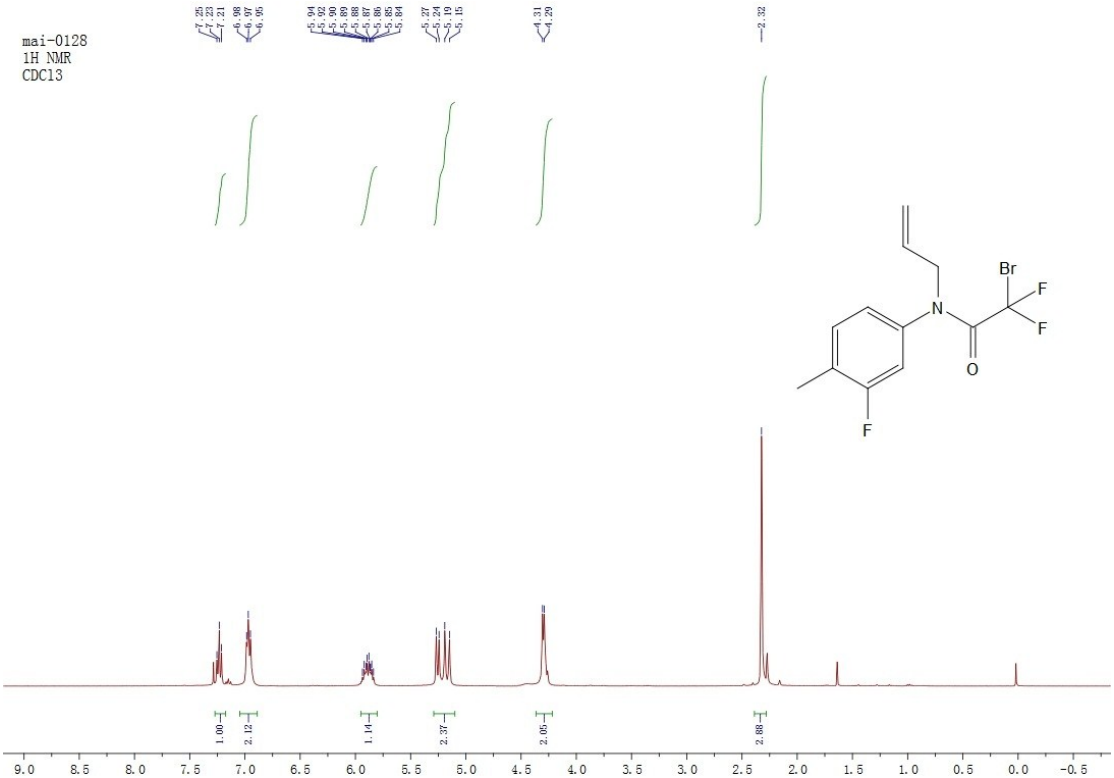

mai-0228
13C NMR
CDC13
158.61
142.75
130.34
129.32
126.49
126.45
120.48
114.42
111.24
108.07
55.39
O
Br
N
F
F
F
F
F
f1 (ppm)


mai-0228
19F NMR
CDC13
-52.23
-62.74
O
Br
N
F
F
F
F
F
f1 (ppm)


mai-0208
1H NMR
CDC13
8.03
8.01
7.39
7.37
5.93
5.92
5.91
5.90
5.89
5.87
5.87
5.86
5.85
5.83
5.26
5.23
5.17
5.16
5.13
5.12
4.35
4.34
2.65
N
O
O
F
Br
F
2.00
1.99
0.98
2.02
1.94
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


mai-0208
1H NMR
CDC13
196.89
158.58
143.59
137.18
130.46
129.34
129.00
120.37
114.40
111.16
107.93
55.35
26.74
N
O
O
F
Br
F
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


mai-0208
19F NMR
CDC13
-52.18
O
N
O
F
Br
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210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1H NMR
CDC13
7.25
7.23
7.21
6.98
6.97
6.95
5.94
5.92
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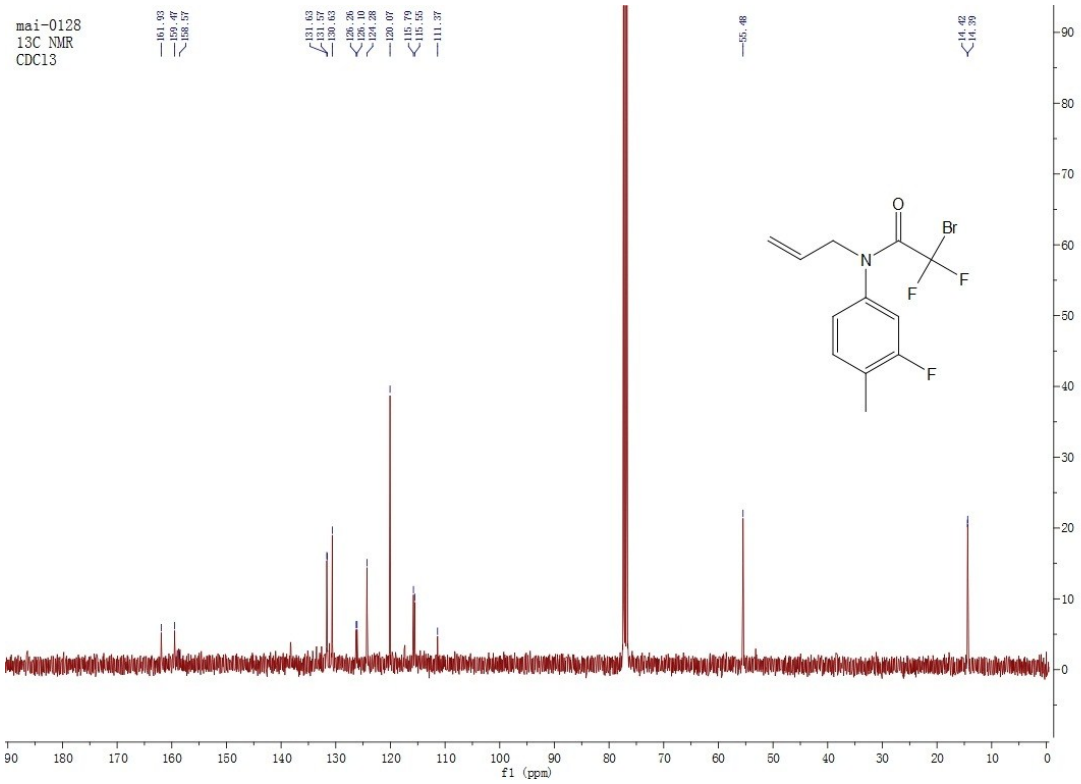
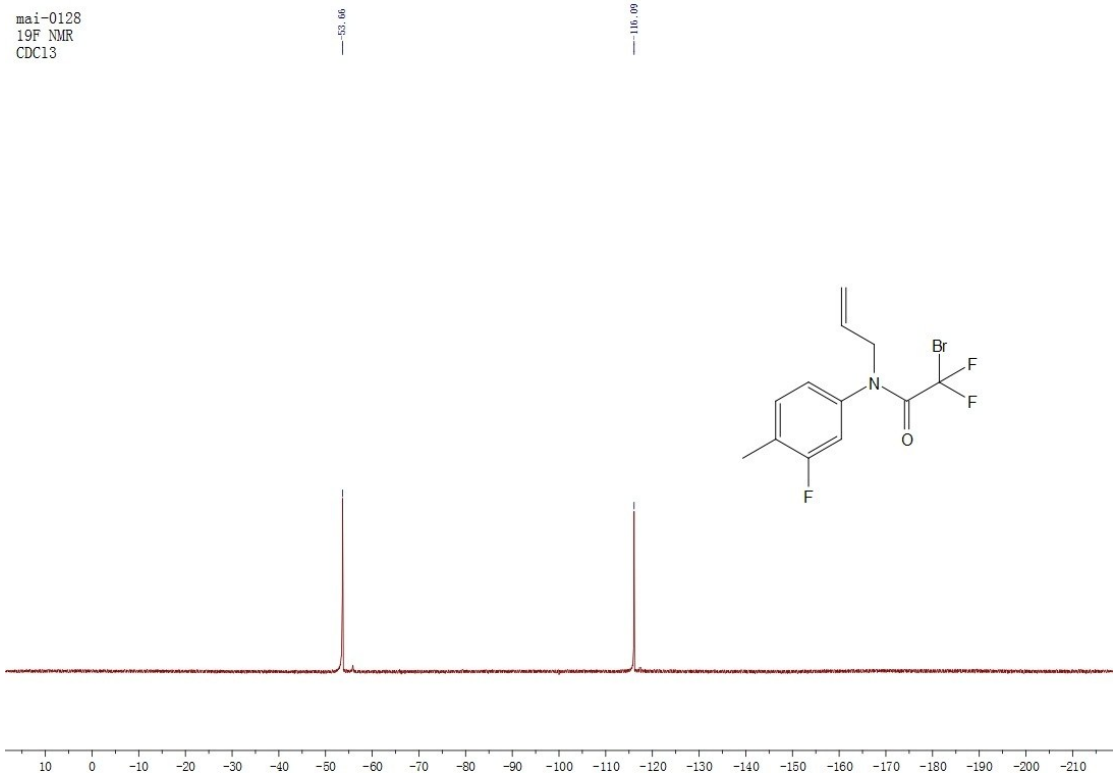
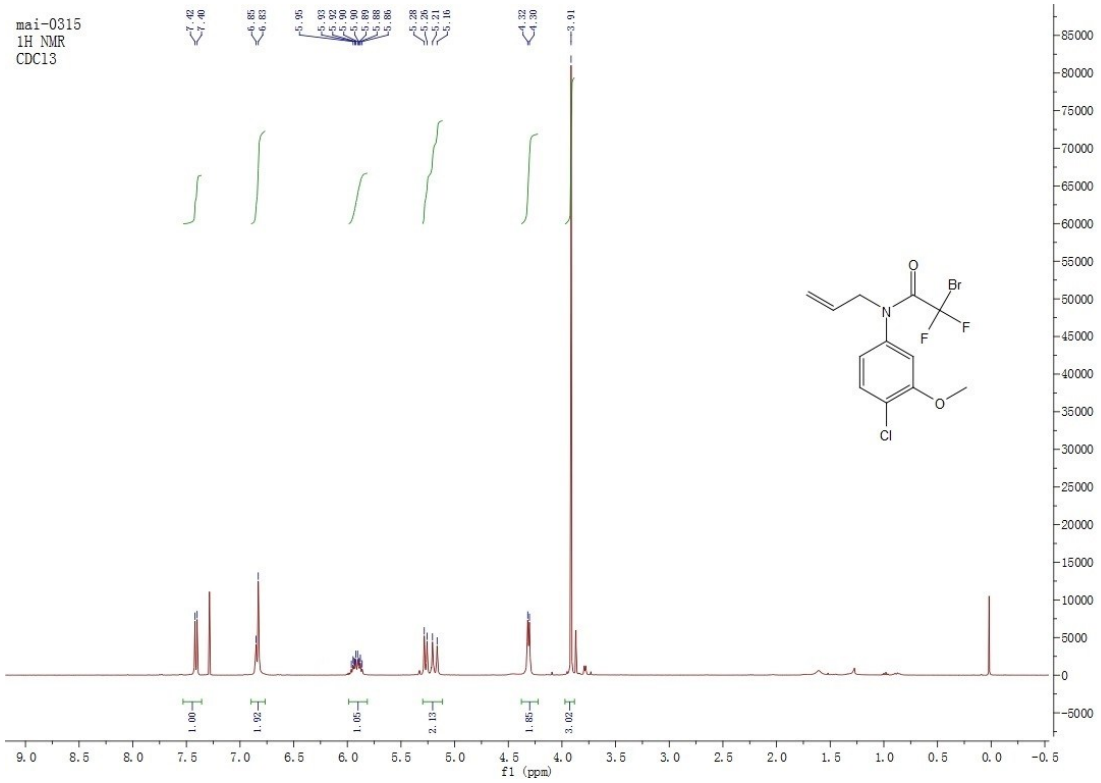
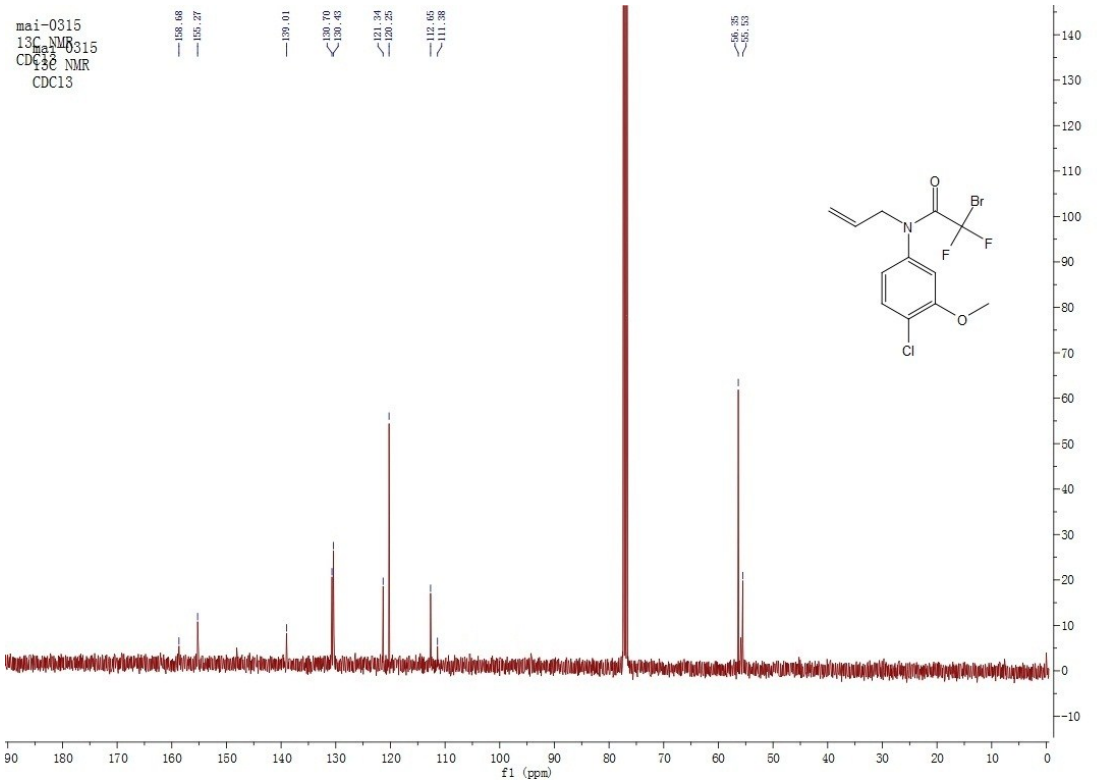
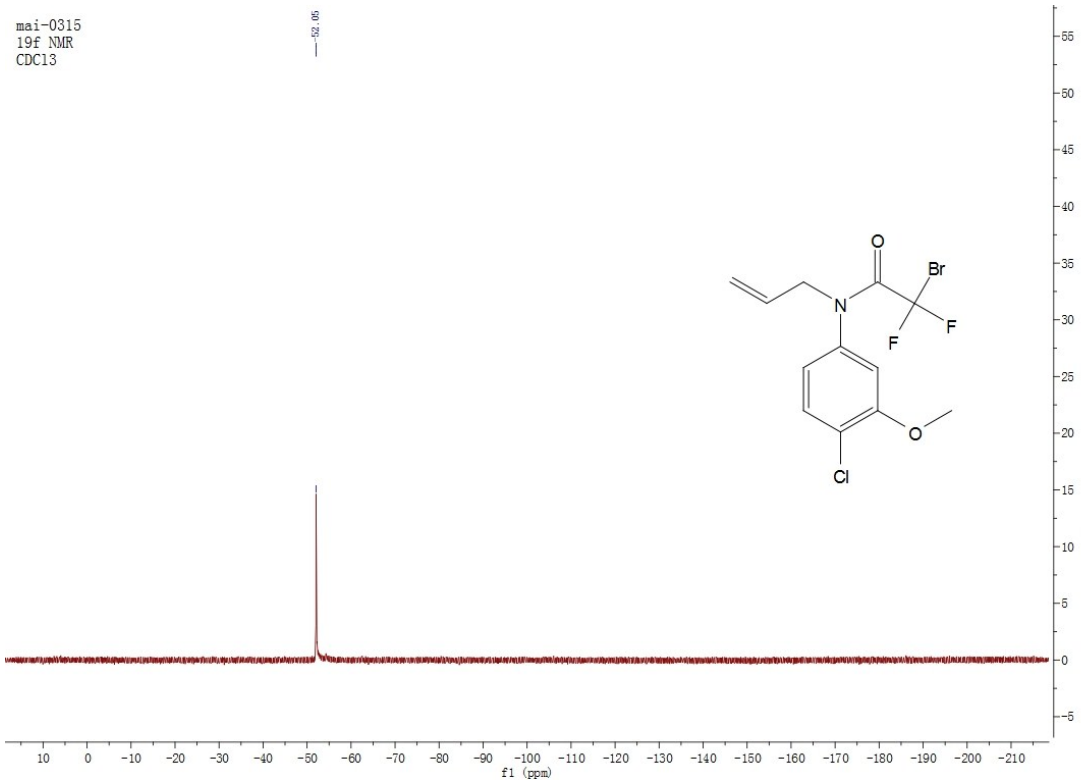
5.89
5.88
5.87
5.86
5.85
5.84
5.27
5.24
5.19
5.15
4.31
4.29
2.32
Br
F
F
N
O
F
1.00
2.12
1.14
2.37
2.05
2.88
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

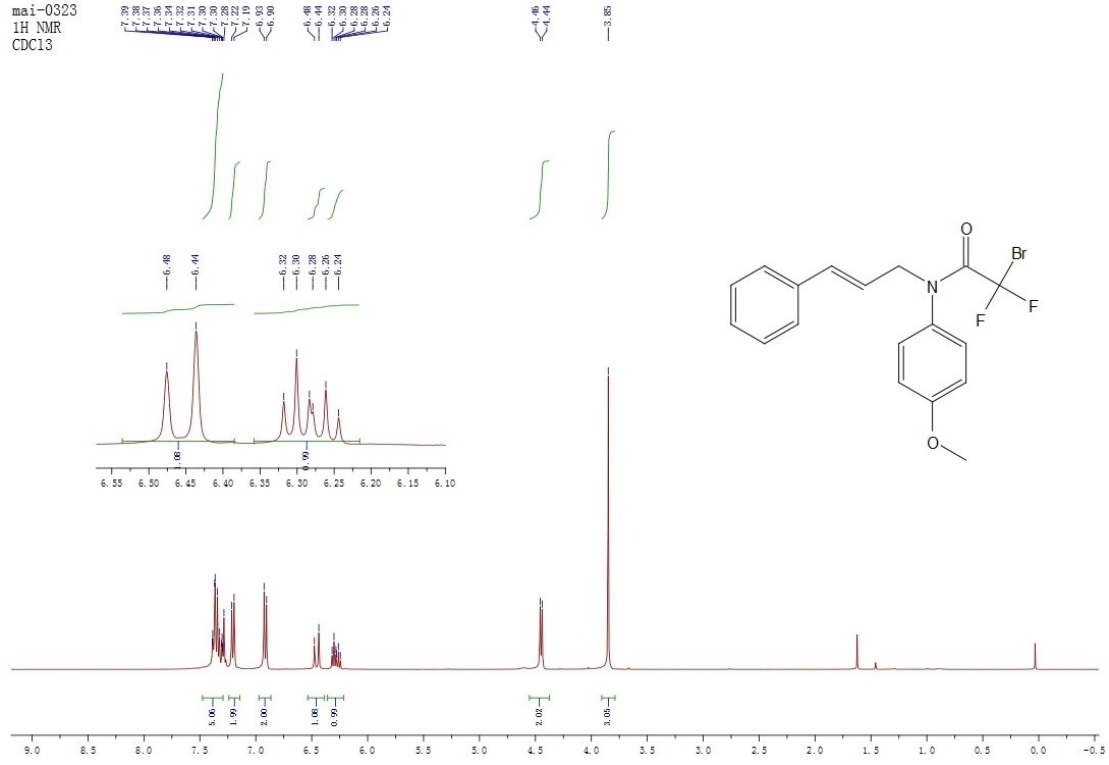

mai-0128
13C NMR
CDC13
161.93
159.47
158.57
131.63
131.57
130.63
126.26
126.10
124.28
120.07
115.79
115.55
111.37
55.48
14.42
14.39
O
Br
N
F
F
F
f1 (ppm)

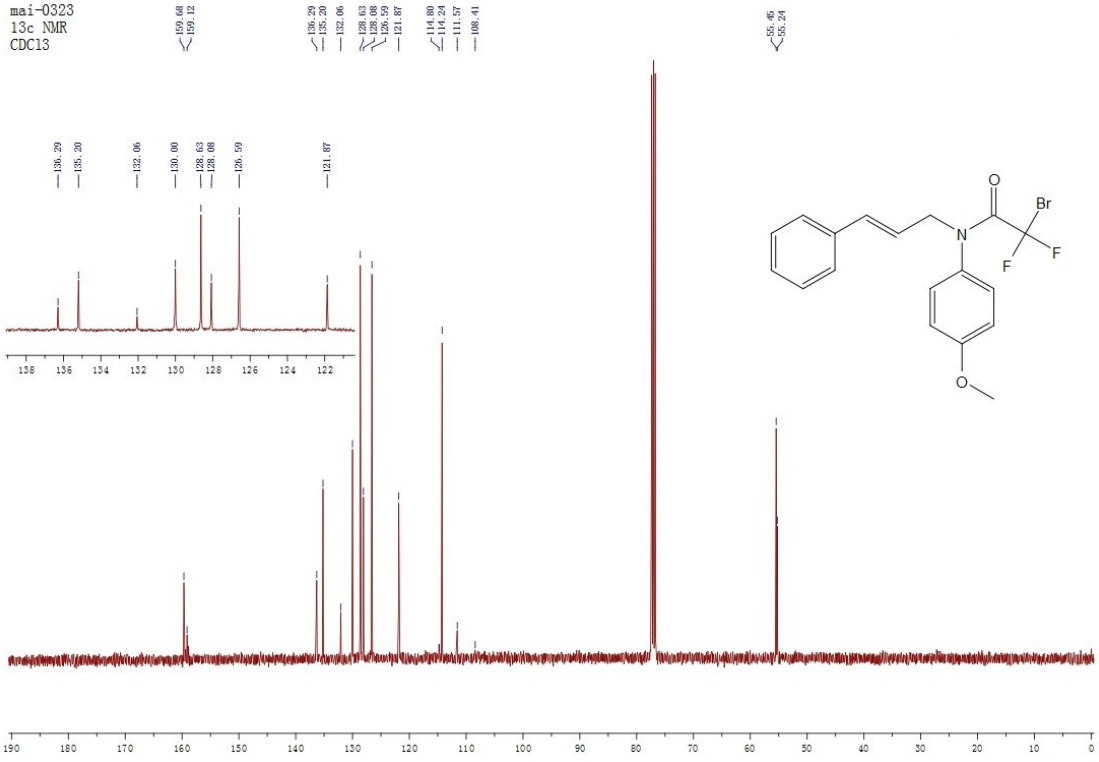

mai-0128
19F NMR
CDC13
-53.66
-116.09
Br
F
F
N
O
F

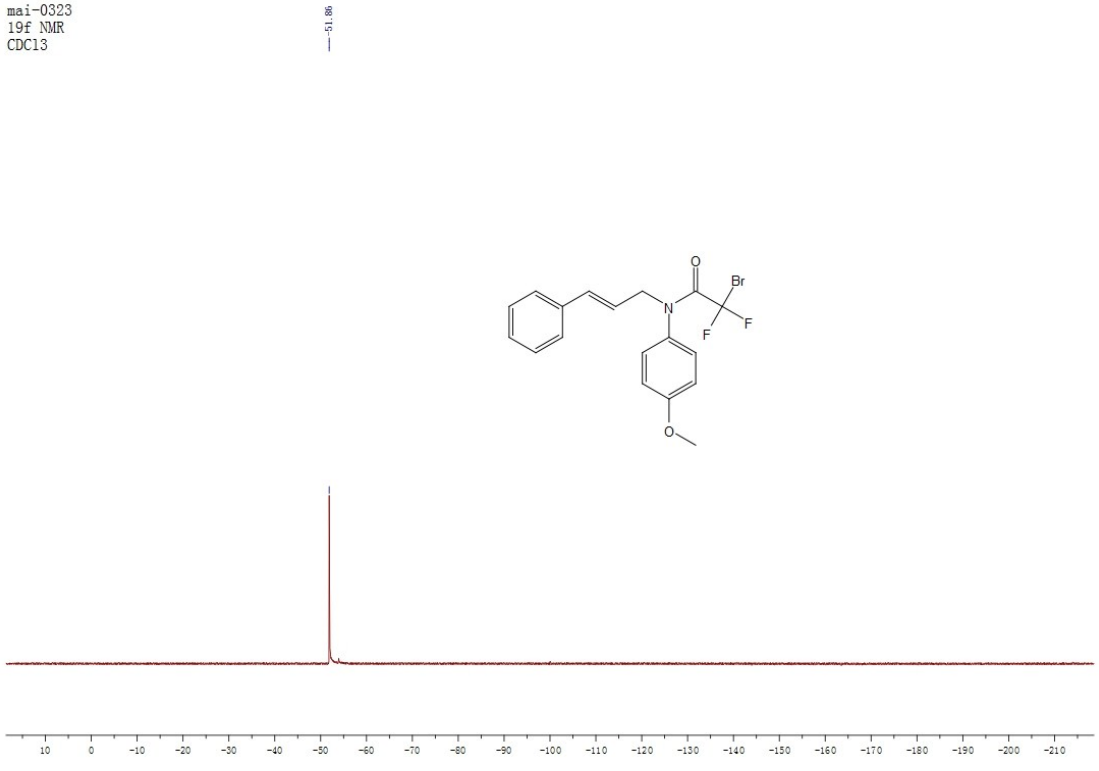

mai-0315
1H NMR
CDC13
f1 (ppm)

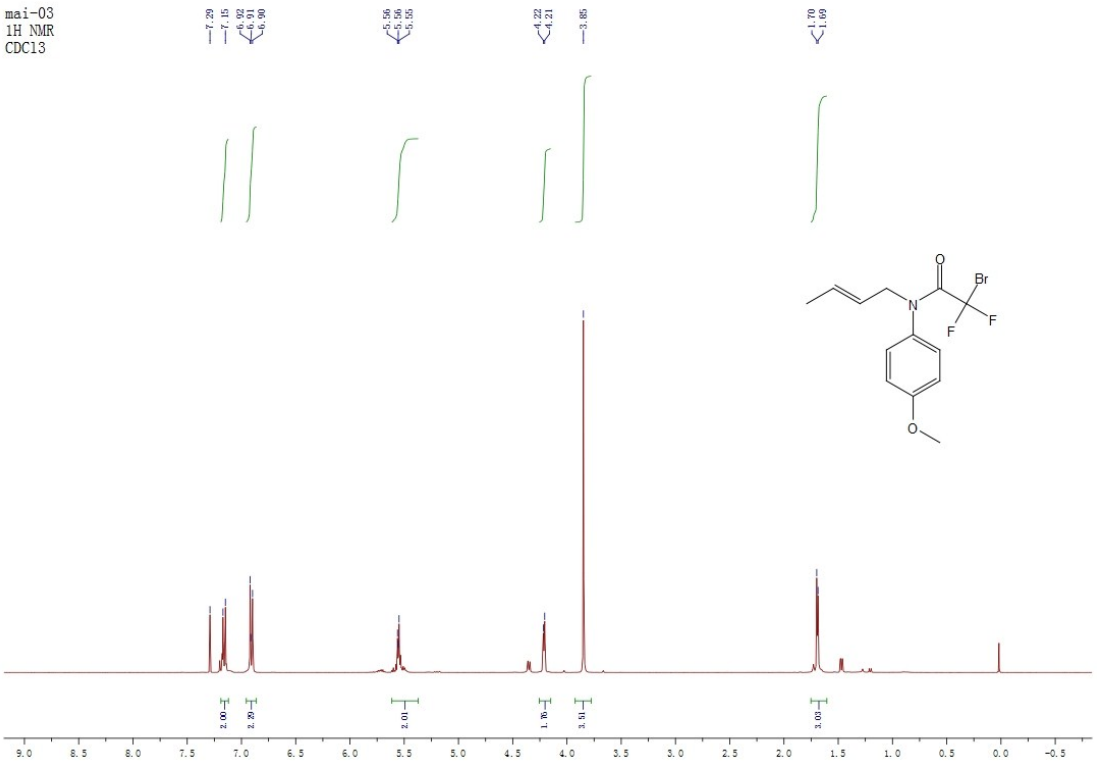

mai-0315
13C NMR
CDC13
f1 (ppm)

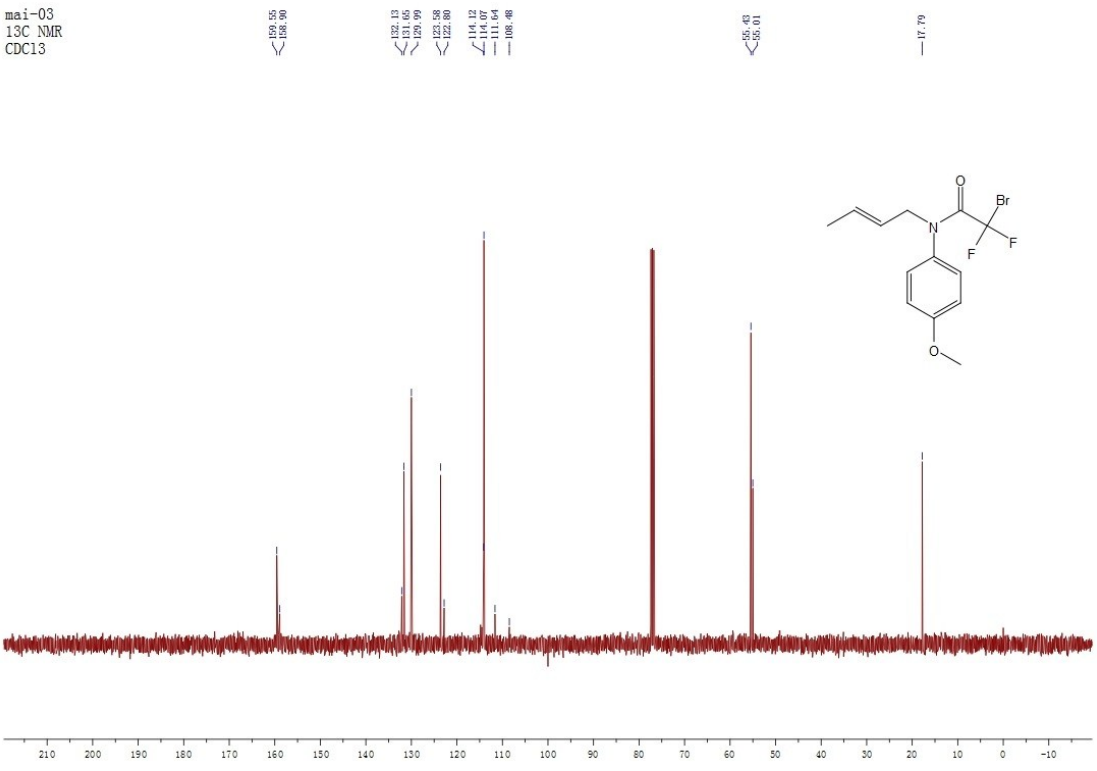

mai-0315
19f NMR
CDC13
-52.05
O
Br
N
F
F
O
Cl
f1 (ppm)

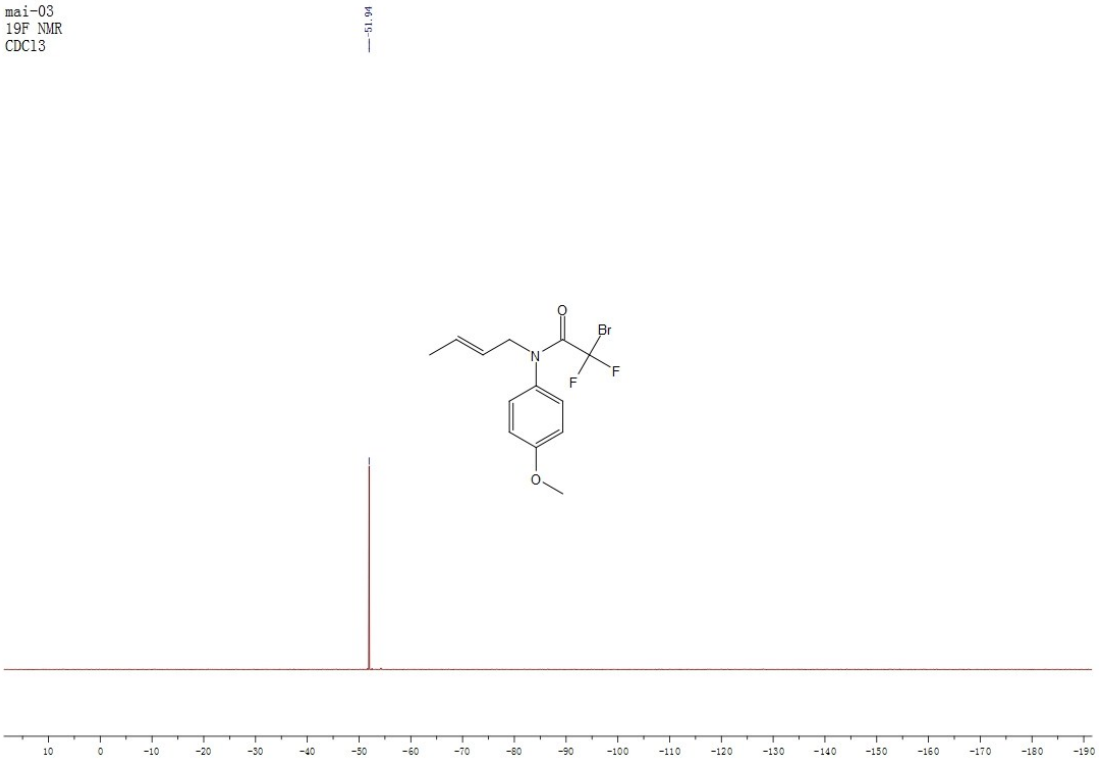

mai-0323
1H NMR
CDC13
6.48
6.44
6.32
6.30
6.28
6.26
6.24
4.46
4.44
3.85
O
Br
N
F
F
O

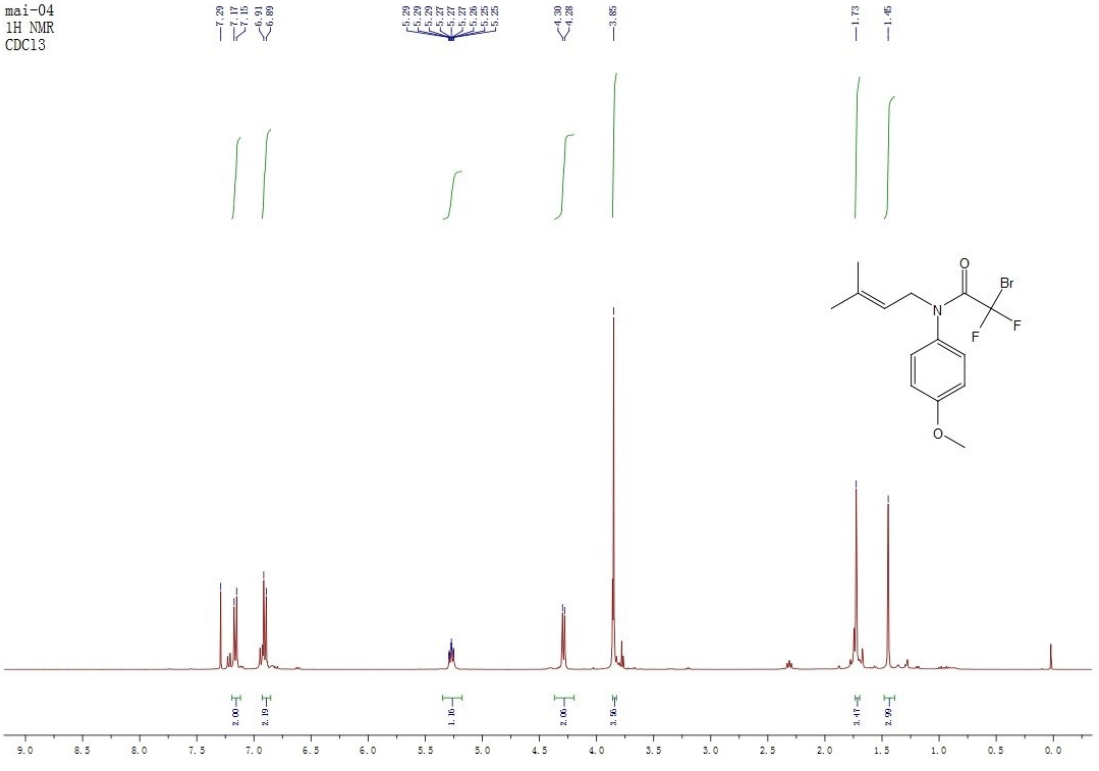

mai-0323
13c NMR
CDC13
199.68
159.12
136.29
135.20
132.06
128.63
128.08
126.59
121.87
114.80
114.24
111.57
108.41
55.45
55.24
Br
F
F
N
O
O

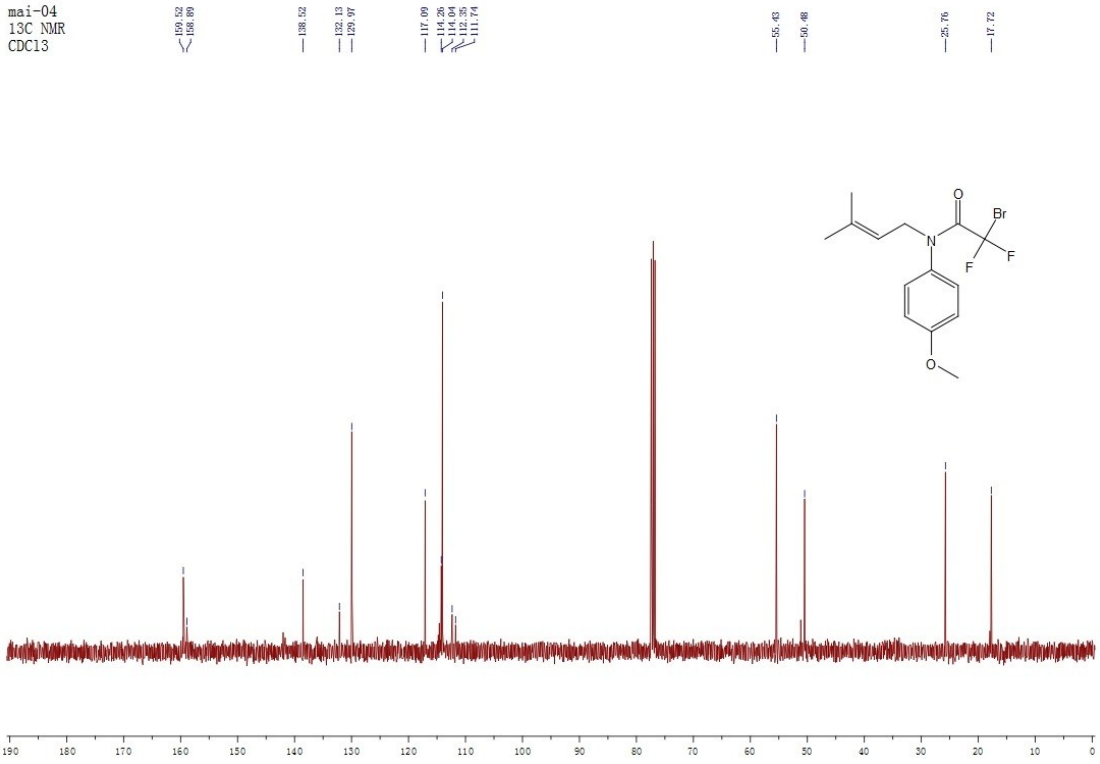

mai-0323
19f NMR
CDC13
-51.86
Br
F
F
N
O
O

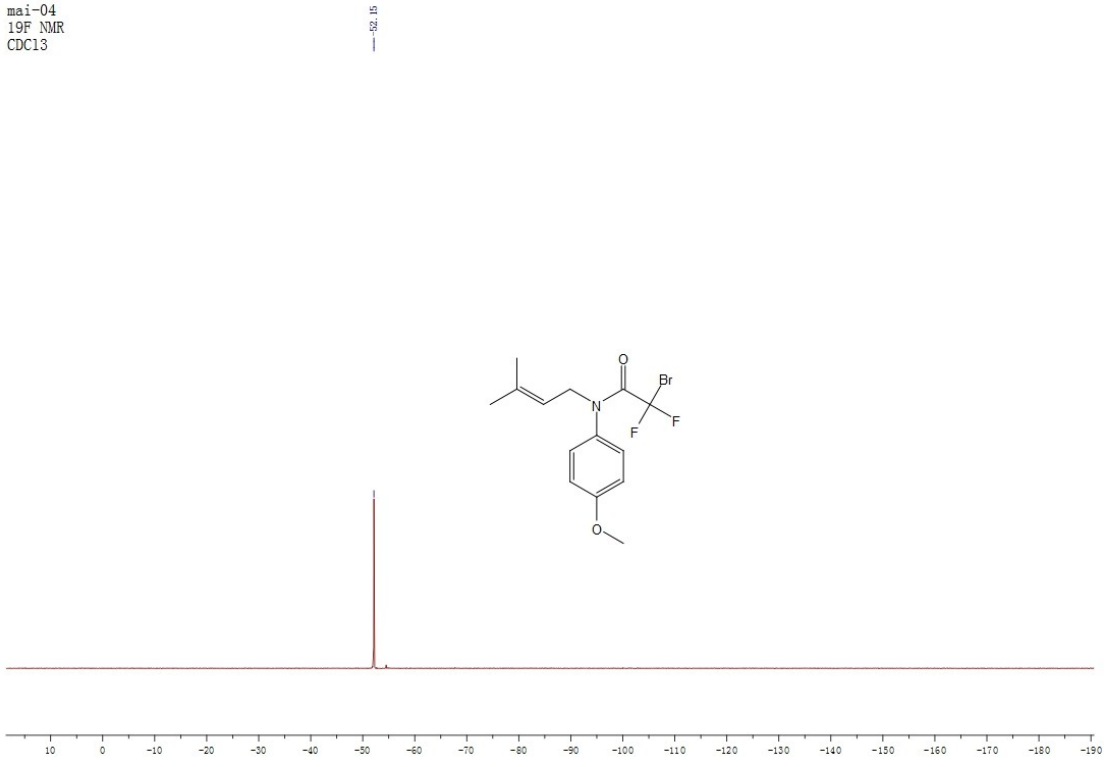

mai-03
1H NMR
CDCl3
7.29
7.15
6.92
6.91
6.90
5.56
5.56
5.55
4.22
4.21
3.85
1.70
1.69
O
Br
N
F
F
O
2.00
2.99
2.01
1.76
3.01
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


mai-03
13C NMR
CDCl3
159.55
158.99
132.13
131.65
129.99
123.58
122.80
114.12
114.07
113.64
108.48
55.43
55.01
17.79
O
Br
N
F
F
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


mai-03
19F NMR
CDCl3
-51.94
O
Br
N
F
F
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190


mai-04
1H NMR
CDCl3
7.29
7.17
7.15
6.91
6.89
5.29
5.29
5.29
5.27
5.27
5.27
5.26
5.25
5.25
4.30
4.28
3.85
1.73
1.45
O
Br
N
F
F
O
2.00
2.19
1.16
2.06
3.96
3.47
2.93
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


mai-04
13C NMR
CDCl3
159.52
158.89
138.52
132.13
129.97
117.09
114.26
114.04
112.35
111.74
55.43
50.48
25.76
17.72
O
Br
N
F
F
O


mai-04
19F NMR
CDCl3
-52.15
O
Br
N
F
F
O