Supporting Information

Catalytic charge transfer complex enabled difluoromethylation of alkenes with difluoromethyltriphenylphosphonium bromide

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contents

1. General information

Chemicals were purchased from HEOWNS or Bidepharm and used without further purification unless otherwise noted. Solvents were predistilled according to standard laboratory methods. N-arylacrylamides,[1] 1,1-disubstituted alkenes,[2] enamides,[3] (difluoromethyl)triphenylphosphonium bromide,[4] and (2-ethoxy-1-fluoro-2-oxoethyl)triphenylphosphonium bromide[5] were prepared according to literature method.

Analytical thin layer chromatography was carried out with silica gel pre-coated glass plates (TLC-Silica gel GF254, coating thickness: 0.25 mm) purchased from Xinnuo Chemical (Yantai, China). Chromatographic purification of the products was performed on silica gel 200-300 mesh. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) or by staining with basic potassium permanganate solution.

High-resolution mass spectra (HRMS) were obtained with the mass analyzer of an orbitrap. The calculated values are based on the most abundant isotope.

IR spectra were taken on a Vertex 70 spectrophotometer and reported as wave numbers (cm^{-1}).

The GC-MS TQ8040 was used in the detection of the reaction mixture.

The SGW X-4 was used to measure the melting point of solids.

UV-vis absorption spectra were acquired on UV-5 spectrophotometer (METTLER TOLEDO).

^{1}H-, ^{13}C- and ^{19}F- NMR spectra were recorded at ambient temperature on a Shimadzu Avance 400/500 Spectrometer. The chemical shifts are reported in ppm downfield of tetramethylsilane (TMS) and referenced to residual solvent peaks resonance as internal standard. The order of citation in parentheses is a) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd= doublet of doublet, ddd= doublet of doublet of doublet, td = triplet of doublet, m = multiplet), b) coupling constants, c) number of protons. Coupling constants (*J*) are reported in Hertz (Hz).

Photochemical experiments were performed magnetically stirred in 10 mL glass Schlenk tubes, sealed with a rubber septum. The tubes were irradiated with blue light using a LED lamp with a power output of 40 W (see below picture). The distance from the light source to

the irradiation vessel is 2 cm to keep the reaction temperature with 45 °C. (The purchase link of LED lamp is https://item.taobao.com/item.htm?spm=a230r.7195193.1997079397.9.212b2e3eGwYjWb&id=520551083325&abbucket=10).

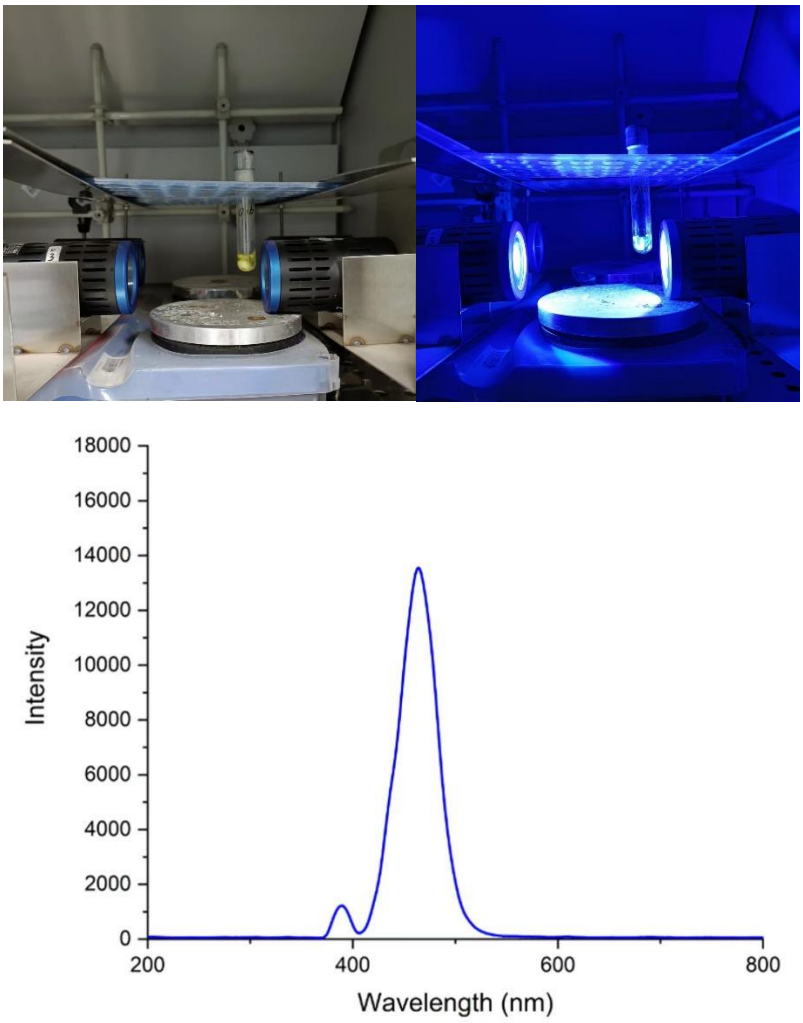
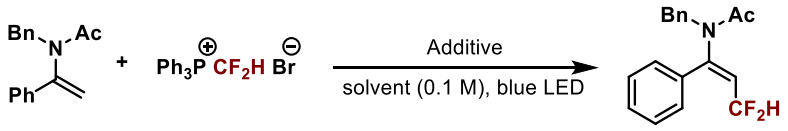


Figure S1. Blue LEDs employed in the reactions

2. Experimental Procedures

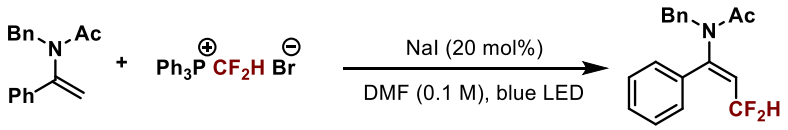
2.1. Preparation of the difluoromethylated enamines

Table 1. Optimization of the reaction conditions



Entry	Solvent	Additive (20 mol%)	Yield (%)[a]	E/Z ratio
1	DMF	NaI	85	>20:1
2	THF	NaI	70	>20:1
3	CH_3CN	NaI	33	>20:1
4	NMP	NaI	81	>20:1
5	DCM	NaI	50	>20:1
6	toluene	NaI	trace	>20:1
7	dioxane	NaI	trace	>20:1
8	DMA	NaI	77	>20:1
9	DMF	KI	80	>20:1
10	DMF	nBu_4NI	78	>20:1
11	DMF	/	NR	--
12[b]	DMF	NaI	NR	--
13[c]	DMF	NaI	44	>20:1
14[b, d]	DMF	NaI	NR	--

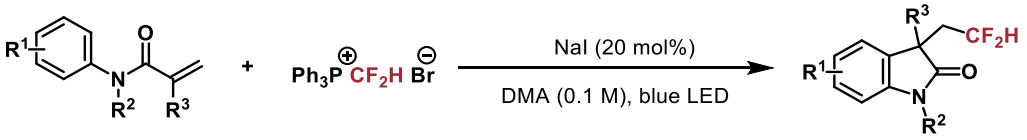
[a]Yield of isolated product; [b]NO Blue LED, [c]reaction temperature is 28[o]C, [d]reaction temperature is 45 [o]C.



General procedures I: In a nitrogen-filled glove box, a 10-mL vial equipped with a magnetic stirring bar was charged sequentially with enamines (0.1 mmol, 1.0 equiv.), difluoromethyltriphenylphosphonium bromide (0.2 mmol, 2.0 equiv.), NaI (0.02 mmol, 20 mol%) and DMF (1.0 mL). The vial was closed and removed from the glove box. The resulting

mixture was allowed to stir at 45±5 ℃ under blue LED (40 W) irradiation for 12 hours. Upon completion, solvent was removed under vacuum and the residue was subjected to silica gel chromatography using petroleum ether and ethyl acetate as eluent to afford the desired product.

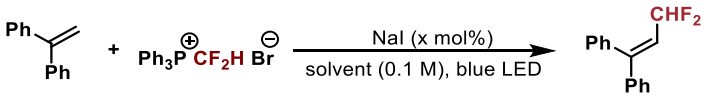
2.2. General procedure for the synthesis of monofluoromethylated oxindoles



General procedures II: In a nitrogen-filled glove box, a 10-mL vial equipped with a magnetic stirring bar was charged sequentially with N-arylacrylamides (0.1 mmol), difluoromethyltriphenylphosphonium bromide (0.2 mmol, 2.0 equiv.), NaI (0.02 mmol, 20 mol%) and DMA (1.0 mL). The vial was closed and removed from the glove box. The resulting mixture was allowed to stir at 45±5 ℃ under blue LED (40 W) irradiation for 12 hours. Upon completion, solvent was removed under vacuum and the residue was subjected to silica gel chromatography using petroleum ether and ethyl acetate as eluent to afford the desired product.

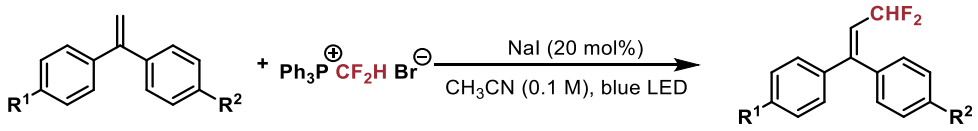
2.3. Preparation of the difluoromethylated olefins

Table 2. Optimization of the reaction conditions



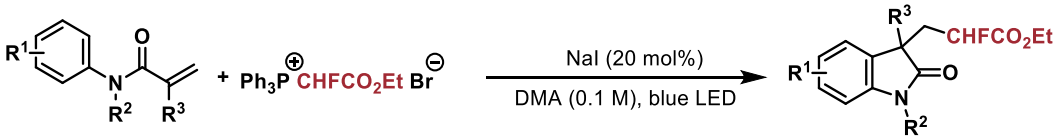
Entry	solvent	X	Yield (%)[a]
1	CH_3CN	20	82
2	Acetone	20	54
3	DMF	20	65
4	THF	20	40
5	DMA	20	62
6	CH_3CN	0	NR
7[b]	CH_3CN	20	NR

[a]Yield of isolated product; [b]NO blue LED.



General procedures III: In a nitrogen-filled glove box, a 10-mL vial equipped with a magnetic stirring bar was charged sequentially with olefins (0.1 mmol), difluoromethyltriphenylphosphonium bromide (0.2 mmol, 2.0 equiv.), NaI (0.02 mmol, 20 mol%) and CH_3CN (1.0 mL). The vial was closed and removed from the glove box. The resulting mixture was allowed to stir at 45±5 °C under blue LED (40 W) irradiation for 12 hours. Upon completion, solvent was removed under vacuum and the residue was subjected to silica gel chromatography using petroleum ether and ethyl acetate as eluent to afford the desired product.

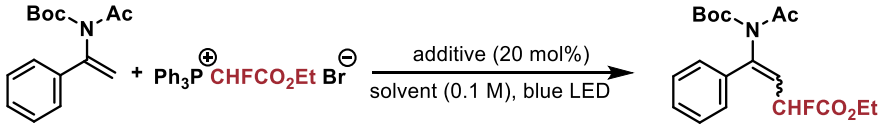
2.4. General procedure for the synthesis of monofluoroacetylated oxindoles



General procedures IV: In a nitrogen-filled glove box, a 10-mL vial equipped with a magnetic stirring bar was charged sequentially with N-arylacrylamides (0.1 mmol), $[Ph_3PCHFCO_2Et]Br$ (0.2 mmol, 2.0 equiv.), NaI (0.02 mmol, 20 mol%) and DMA (1.0 mL). The vial was closed and removed from the glove box. The resulting mixture was allowed to stir at 45±5 °C under blue LED (40 W) irradiation for 12 hours. Upon completion, solvent was removed under vacuum and the residue was subjected to silica gel chromatography using petroleum ether and ethyl acetate as eluent to afford the desired product.

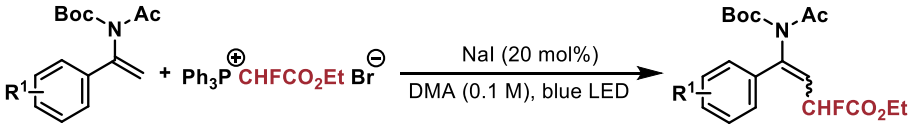
2.5. Preparation of monofluoroacetylated enamines

Table 3. Optimizations of the reaction conditions



Entry	Solvent	Additive	Yield (%)[a]
1	DMA	NaI	58
2	DMF	NaI	44
3	THF	NaI	trace
4	Acetone	NaI	trace
5	DCM	NaI	26
6	CH_3CN	NaI	26
7	DMA	/	/

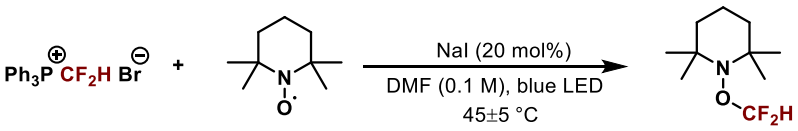
[a]Yield of isolated product.



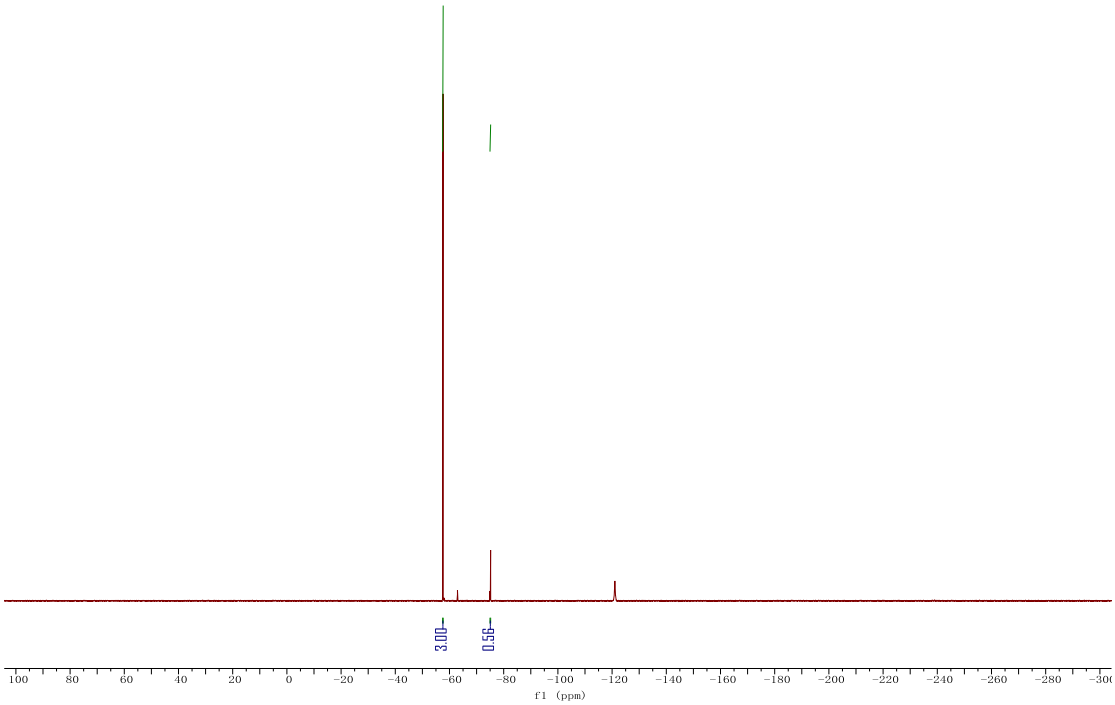
General procedures V: In a nitrogen-filled glove box, a 10-mL vial equipped with a magnetic stirring bar was charged sequentially with enamines (0.1 mmol), $[Ph_3PCHFCO_2Et]Br$ (0.2 mmol, 2.0 equiv.), NaI (0.02 mmol, 20 mol%) and DMA (1.0 mL). The vial was closed and removed from the glove box. The resulting mixture was allowed to stir at 45±5 ℃ under blue LED (40 W) irradiation for 12 hours. Upon completion, solvent was removed under vacuum and the residue was subjected to silica gel chromatography using petroleum ether and ethyl acetate as eluent to afford the desired product.

3. The Mechanism Studies

3.1 Control experiment



In a nitrogen atmosphere, to a dry tube equipped with a stirring bar, difluoromethyltriphenylphosphonium bromide (0.1 mmol, 1.0 equiv.), NaI (0.02 mmol, 20 mol%), TEMPO (46.8 mg, 0.30 mmol, 3.0 equiv.) and DMF (1.0 mL) were added. The mixture was stirred under a 40 W blue LED lamp with an interval of 2 cm from the lamp for 12 hours, and a fan was used to keep the reaction temperature at 45±5 ℃. The trapped radical species was detected with 28% yield by ^{19}F NMR spectra analysis using (trifluoromethyl)benzene as an internal standard.



3.2. UV/vis Absorption Spectrometry

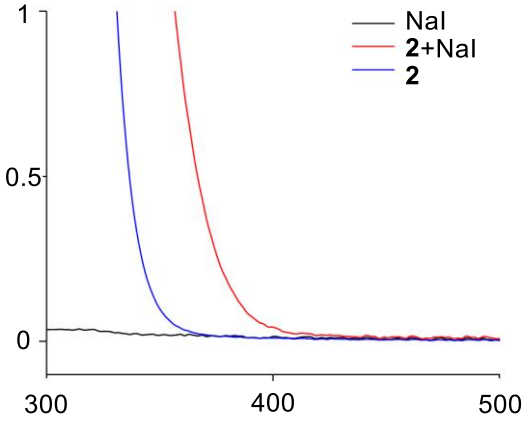
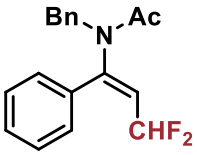


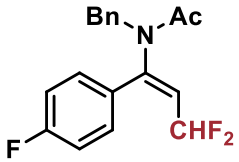
Figure S2. UV/vis spectrum of **2** (recorded 0. 2 M in DMF), NaI (recorded 0.02 M in DMF), and their mixture.

4. Compound Characterization Data



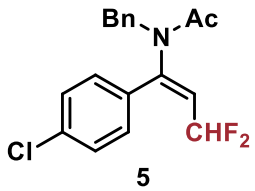
3

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (3): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **3** as a white solid (0.085 mmol, 25.6 mg, 85% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 – 7.41 (m, 3H), 7.31 – 7.22 (m, 5H), 7.17 – 7.13 (m, 2H), 6.05 (td, *J* = 54.8, 7.7 Hz, 1H), 5.59 – 5.53 (m, 1H), 4.57 (s, 2H), 2.18 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 148.3 (t, *J* = 14.1 Hz), 136.8, 133.3, 130.8, 129.3, 129.0 (t, *J* = 1.7 Hz), 128.8, 128.6, 127.7, 121.6 (t, *J* = 27.7 Hz), 113.0 (t, *J* = 229.0 Hz), 49.9, 22.7. Analytical data for compound **3** was consistent with the literature.[6]



4

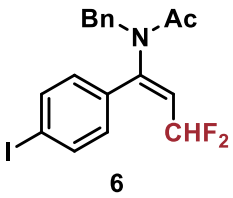
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(4-fluorophenyl)prop-1-en-1-yl)acetamide (4): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **4** as a white solid (0.075 mmol, 23.9 mg, 75% yield, *E*/*Z* = 7:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29 – 7.21 (m, 5H), 7.16 – 7.10 (m, 4H), 6.01 (td, *J* = 54.7, 7.7 Hz, 1H), 5.57 – 5.51 (m, 1H), 4.57 (s, 2H), 2.17 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.3, 164.0 (d, *J* = 250.0 Hz), 147.3 (t, *J* = 14.0 Hz), 136.6, 131.0 (dt, *J* = 8.6, 1.6 Hz), 129.1, 128.7, 128.7, 127.8, 121.6 (t, *J* = 28.0 Hz), 116.5 (d, *J* = 20.0 Hz), 112.9 (d, *J* = 229.0 Hz), 50.0, 22.8. Analytical data for compound **4** was consistent with the literature.[6]



5

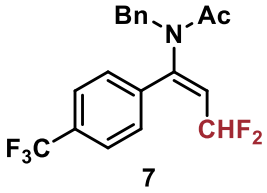
(*E*)-*N*-Benzyl-*N*-(1-(4-chlorophenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (5): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **5** as a white solid (0.070 mmol, 23.4 mg, 70% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.30 – 7.25 (m, 3H), 7.20 – 7.11 (m, 4H), 6.01 (td, *J* = 54.7, 7.7 Hz, 1H), 5.59 – 5.53 (m, 1H), 4.57 (s, 2H), 2.16 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.3, 147.3 (t, *J* = 13.9 Hz), 137.0, 136.5, 131.8, 130.2 (t, *J* = 1.5 Hz), 129.6, 128.7, 128.7, 127.8, 122.0 (t, *J* = 28.1 Hz), 112.7 (t, *J* = 230.8 Hz), 50.0, 22.8. Analytical data

for compound **5** was consistent with the literature.[6]



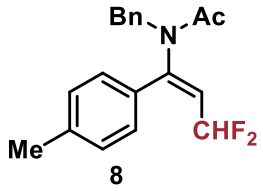
6

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(4-iodophenyl)prop-1-en-1-yl)acetamide (6): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **6** as a white solid (0.074 mmol, 31.6 mg, 74% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 – 7.76 (m, 2H), 7.30 – 7.25 (m, 3H), 7.15 – 7.11 (m, 2H), 6.96 – 6.94 (m, 2H), 6.00 (td, *J* = 54.7, 7.7 Hz, 1H), 5.55 (q, *J* = 7.9 Hz, 1H), 4.57 (s, 2H), 2.16 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 170.3, 147.5 (t, *J* = 13.7 Hz), 138.5, 136.5, 132.9, 130.4, 128.7, 127.8, 125.3, 122.0 (t, *J* = 23.5 Hz), 112.7 (t, *J* = 230.8 Hz), 97.2, 50.0, 22.8. Analytical data for compound **6** was consistent with the literature.[6]



7

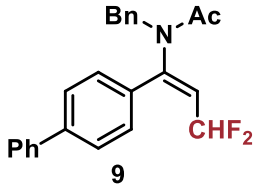
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(4-(trifluoromethyl)phenyl) prop-1-en-1-yl)acetamide (7): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **7** as a white solid (0.080 mmol, 29.5 mg, 80% yield, *E*/*Z* = 6:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.30 – 7.26 (m, 3H), 7.15 – 7.12 (m, 2H), 5.99 (td, *J* = 54.5, 7.6 Hz, 1H), 5.69 – 5.63 (m, 1H), 4.59 (s, 2H), 2.18 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.2, 147.0 (t, *J* = 14.5 Hz), 137.1, 136.4, 132.6 (q, *J* = 32.1 Hz), 129.3, 128.8, 128.7, 127.9, 126.2 (q, *J* = 3.6 Hz), 123.58 (q, *J* = 272.6 Hz), 112.5 (t, *J* = 230.0 Hz), 50.3, 22.7. Analytical data for compound **7** was consistent with the literature.[6]



8

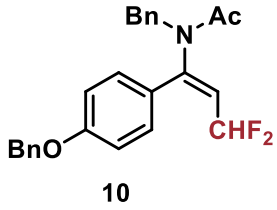
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(p-tolyl)prop-1-en-1-yl)acetamide (8): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **8** as a white solid (0.071 mmol, 22.4 mg, 71% yield, *E*/*Z* = 14:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 – 7.22 (m, 5H), 7.19 – 7.12 (m, 4H), 6.06 (td, *J* = 54.9, 7.7 Hz, 1H), 5.53 – 5.44 (m, 1H), 4.56 (s, 2H), 2.40 (s, 3H), 2.17 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 148.4 (t, *J* = 14.1 Hz), 141.1, 136.9, 130.4 (t, *J* = 1.6 Hz), 129.9, 128.9 (t, *J* = 1.5

Hz), 128.8, 128.6, 127.7, 121.1 (t, J = 25.5 Hz), 113.2 (t, J = 231.2 Hz), 49.9, 22.7, 21.4. Analytical data for compound **8** was consistent with the literature. [6]



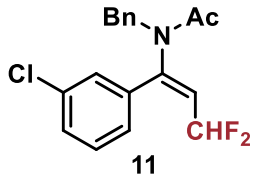
9

(*E*)-*N*-(1-([1,1'-Biphenyl]-4-yl)-3,3-difluoroprop-1-en-1-yl)-*N*-benzylacetamide (9): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10: 1) as the eluent afforded **9** as a colorless oil (0.070 mmol, 26.4 mg, 70% yield, E/Z = 12:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 – 7.60 (m, 4H), 7.51 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 7.35 – 7.27 (m, 5H), 7.22 – 7.18 (m, 2H), 6.14 (td, J = 54.8, 7.7 Hz, 1H), 5.57 (q, J = 7.9 Hz, 1H), 4.63 (s, 2H), 2.21 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 148.1(t, J = 13.8 Hz), 143.6, 139.7, 136.8, 132.1, 129.4, 129.1, 128.8, 128.6, 128.3, 127.9, 127.7, 127.2, 121.6 (t, J = 28.0 Hz), 113.0 (t, J = 231.3 Hz), 50.1, 22.8. Analytical data for compound **9** was consistent with the literature.[6]



10

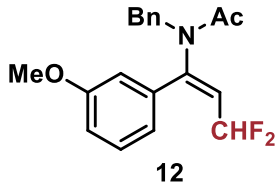
(*E*)-*N*-Benzyl-*N*-(1-(4-(benzyloxy)phenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (10): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **10** as a white solid (0.074 mmol, 30.1 mg, 74% yield, E/Z = 6:1). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.35 (m, 6H), 7.29 – 7.26 (m, 2H), 7.19 – 7.14 (m, 4H), 7.05 – 6.99 (m, 2H), 6.07 (td, J = 54.9, 7.7 Hz, 1H), 5.48 – 5.42 (m, 1H), 5.10 (s, 2H), 4.57 (s, 2H), 2.16 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.5, 160.6, 148.1 (t, J = 14.1 Hz), 136.9, 136.3, 130.5 (t, J = 1.7 Hz), 128.8, 128.6, 128.4, 127.7, 127.6, 125.6, 120.4 (t, J = 2.83 Hz), 115.5, 113.3 (t, J = 229.0 Hz), 70.3, 49.9, 22.8. Analytical data for compound **10** was consistent with the literature. [6]



11

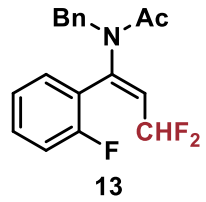
(*E*)-N-Benzyl-*N*-(1-(3-chlorophenyl)-3,3-difluoroprop-1-en-1-yl) acetamide (11): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **11** as a white solid (0.077 mmol, 25.6 mg, 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.43 (m, 1H), 7.37 – 7.35 (m, 1H), 7.30 – 7.26 (m, 3H), 7.20

– 7.18 (m, 1H), 7.16 – 7.11 (m, 3H), 6.18 – 5.87 (m, 1H), 5.60 – 5.54 (m, 1H), 4.57 (s, 2H), 2.18 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.3, 146.9 (t, *J* = 14.1 Hz), 136.5, 135.5, 135.2, 130.9, 130.5, 128.7, 128.7, 127.9, 127.7, 127.3 (t, *J* = 1.7 Hz), 122.5 (t, *J* = 28.5 Hz).112.6 (t, *J* = 232.2 Hz), 55.1, 22.6. Analytical data for compound **11** was consistent with the literature.[6]



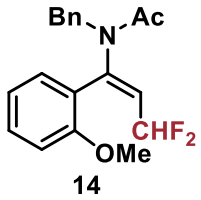
12

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(3-methoxyphenyl)prop-1-en-1-yl)acetamide (12): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **12** as a colorless oil (0.081 mmol, 26.8 mg, 81% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.32 (m, 1H), 7.31 – 7.25 (m, 3H), 7.20 – 7.16 (m, 2H), 7.01 – 6.97 (m, 1H), 6.86 – 6.83 (m, 1H), 6.71 – 6.67 (m, 1H), 6.09 (td, *J* = 54.8, 7.7 Hz, 1H), 5.54 (q, *J* = 7.9 Hz, 1H), 4.59 (s, 2H), 3.76 (s, 3H), 2.16 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 160.1, 148.3 (t, *J* = 14.1 Hz), 136.8, 134.7 (t, *J* = 2.0 Hz), 130.3, 128.8, 128.6, 127.7, 121.4 (t, *J* = 1.9 Hz), 116.3, 115.3, 114.1 (t, *J* = 1.4 Hz), 113.0 (t, *J* = 230.3 Hz), 110.7, 55.5, 50.1, 22.8. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.9 (d, *J* = 55.4 Hz). **IR (ATR)**: 2921, 1659, 1590, 1489, 1379, 1316, 1256, 1203, 1155, 1125, 1081, 1000, 892 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}O_2NF_2^+$:332.1457; found 332.1457.



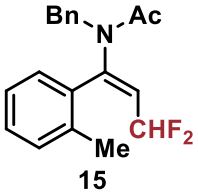
13

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(2-fluorophenyl)prop-1-en-1-yl)acetamide (13): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **13** as a white solid (0.076 mmol, 24.2 mg, 76% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 – 7.42 (m, 1H), 7.29 – 7.25 (m, 2H), 7.24 – 7.18 (m, 2H), 7.16 – 7.09 (m, 4H), 5.95 (td, *J* = 54.6, 7.6 Hz, 1H), 5.64 (q, *J* = 7.7 Hz, 1H), 4.54 (s, 2H), 2.26 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 160.1 (d, *J* = 249.7 Hz), 143.0 (t, *J* = 14.8 Hz), 136.8, 132.6 (d, *J* = 8.6 Hz), 131.7, 128.6, 128.4, 127.6, 124.8 (d, *J* = 3.7 Hz), 123.5 (t, *J* = 30.8 Hz), 120.90 (d, *J* = 14.1 Hz), 116.6 (d, *J* = 11.5 Hz), 112.7 (td, *J* = 232.2, 2.4 Hz), 49.5, 22.6. Analytical data for compound **13** was consistent with the literature.[6]



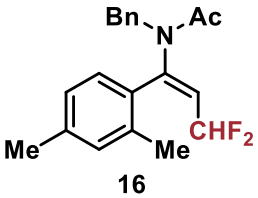
14

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(2-methoxyphenyl)prop-1-en-1-yl)acetamide (14): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **14** as a white solid (0.073 mmol, 24.2 mg, 73% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.38 (m, 1H), 7.25 – 7.19 (m, 3H), 7.11 – 7.07 (m, 2H), 7.03 -6.94 (m, 2H), 6.88 (d, *J* = 8.3 Hz, 1H), 5.90 (td, *J* = 54.9, 7.8 Hz, 1H), 5.60 – 5.55 (m, 1H), 4.48 (s, 2H), 3.75 (s, 3H), 2.30 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.0, 157.6 (t, *J* = 1.7 Hz), 146.4 (t, *J* = 14.0 Hz), 137.3, 132.1, 132.0, 128.4, 128.3, 127.3, 122.2 (t, *J* = 28.0 Hz), 121.4, 120.7, 113.3 (t, *J* = 231.2 Hz), 111.2, 55.5, 49.1, 22.7. Analytical data for compound **14** was consistent with the literature.[6]



15

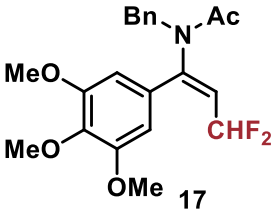
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(o-tolyl)prop-1-en-1-yl)acetamide (15): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **15** as a white solid (0.065 mmol, 20.5 mg, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.32 (m, 1H), 7.30 – 7.19 (m, 5H), 7.08 – 7.03 (m, 3H), 5.96 – 5.60 (m, 2H), 4.50 (s, 2H), 2.34 (s, 3H), 2.18 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.7, 148.3 (t, *J* = 14.1 Hz), 137.1(t, *J* = 1.5 Hz), 137.0, 132.1, 131.4, 131.0 (t, *J* = 1.5 Hz), 130.4, 128.6, 127.8, 127.4, 126.4, 119.8 (t, *J* = 28.3 Hz), 113.5 (t, *J* = 231.3 Hz), 49.2, 23.1, 19.6. Analytical data for compound **15** was consistent with the literature.[6]



16

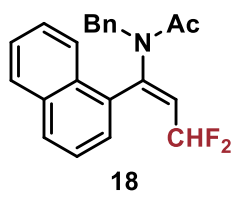
(*E*)-*N*-Benzyl-*N*-(1-(2,4-dimethylphenyl)-3,3-difluoroprop-1-en-1-yl)acetamide (16): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **16** as a colorless oil (0.083 mmol, 27.3 mg, 83% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29 – 7.19 (m, 4H), 7.10 – 7.00 (m, 4H), 6.94 (d, *J* = 7.7 Hz, 1H), 5.84 (dt, *J* = 62.6, 31.3 Hz, 1H), 5.61 (q, *J* = 7.6 Hz, 1H), 4.50 (s, 2H), 2.35 (s, 3H), 2.33 (s, 3H), 2.14 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.7, 148.4 (t, *J* = 13.4 Hz), 137.1, 136.9, 132.1, 131.0, 129.2, 128.5, 127.8, 127.4, 127.1, 119.7 (t, *J* = 27.7 Hz), 113.6 (t, *J* = 231.0 Hz), 49.2, 23.1, 21.3, 19.5. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -110.31 (d, *J* = 572.7 Hz). **IR (ATR)**: 2924,

1655, 1497, 1441, 1372, 1269, 1211, 1143, 1082, 1008, 827 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{20}H_{22}ONF_2^+$:330.1664; found 330.1667.



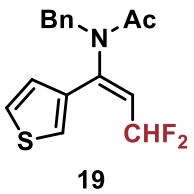
17

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(3,4,5-trimethoxyphenyl)prop-1-en-1-yl)acetamide (17): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **17** as a colorless oil (0.091 mmol, 35.6 mg, 91% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 – 7.25 (m, 3H), 7.22 – 7.19 (m, 2H), 6.33 (s, 2H), 6.12 (td, *J* = 54.9, 7.5 Hz, 1H), 5.59 (q, *J* = 7.9 Hz, 1H), 4.68 (s, 2H), 3.86 (s, 3H), 3.75 (s, 6H), 2.10 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.7, 153.6, 148.9 (t, *J* = 14.1 Hz), 139.8, 137.0, 129.0, 128.7, 127.8, 120.4 (t, *J* = 28.3 Hz), 113.3 (t, *J* = 229.3 Hz), 106.0, 105.9, 105.9, 61.1, 56.3, 50.9, 23.0. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.2 (d, *J* = 55.3 Hz). **IR (ATR)**: 2933, 1652, 1581, 1503, 1457, 1376, 1330, 1248, 1188, 1042, 807 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{21}H_{24}O_4NF_2^+$:392.1668; found 392.1667.



18

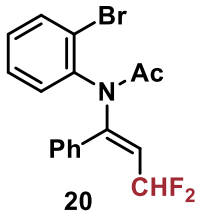
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(naphthalen-1-yl)prop-1-en-1-yl)acetamide (18): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **18** as a colorless oil (0.076 mmol, 26.7 mg, 76% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 (dd, *J* = 15.7, 8.5 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.45 (m, 3H), 7.34 – 7.29 (m, 2H), 7.25 (d, *J* = 6.8 Hz, 3H), 7.08 – 7.01 (m, 2H), 5.93 – 5.54 (m, 2H), 4.46 (s, 2H), 2.45 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.7, 146.4 (t, *J* = 13.9 Hz), 137.1, 133.8, 131.5, 131.1, 130.1, 129.0, 128.9, 128.6, 127.9, 127.7, 127.5, 126.9, 125.2, 124.2, 121.4 (t, *J* = 27.8 Hz), 113.3 (t, *J* = 230.6 Hz), 49.5, 23.1. Analytical data for compound **18** was consistent with the literature.[6]



19

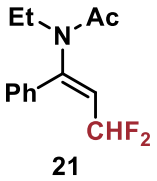
(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-(thiophen-3-yl)prop-1-en-1-yl)acetamide (19): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent

afforded **19** as a white solid (0.083 mmol, 25.5 mg, 83% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.33 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.31 – 7.25 (m, 3H), 7.20 – 7.17 (m, 2H), 6.94 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.19 (td, *J* = 54.9, 7.3 Hz, 1H), 5.53 – 5.47 (m, 1H), 4.63 (s, 2H), 2.10 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.1, 143.4 (t, *J* = 14.1 Hz), 136.8 (t, *J* = 2.2 Hz), 135.2, 128.9, 128.6, 127.9(t, *J* = 2.3 Hz), 127.8, 127.7, 127.1 (t, *J* = 1.5 Hz), 121.5 (t, *J* = 28.2 Hz), 112.8 (t, *J* = 231.8 Hz), 50.5, 22.6. Analytical data for compound **19** was consistent with the literature.[6]



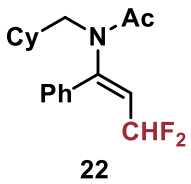
20

(*E*)-*N*-(2-Bromobenzyl)-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (20): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **20** as a white solid (0.071 mmol, 25.9 mg, 71% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 – 7.40 (m, 4H), 7.25 – 7.21 (m, 3H), 7.17 – 7.08 (m, 2H), 6.05 (td, *J* = 54.7, 7.7 Hz, 1H), 5.71 – 5.65 (m, 1H), 4.74 (s, 2H), 2.21 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.6, 148.4 (t, *J* = 14.0 Hz), 135.7, 133.1, 133.0, 130.8, 130.3, 129.2, 129.0 (t, *J* = 2.0 Hz), 127.6, 123.7, 121.5 (t, *J* = 28.2 Hz), 113.0 (t, *J* = 230.5 Hz), 50.2, 22.7. Analytical data for compound **20** was consistent with the literature.[6]



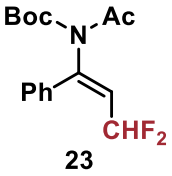
21

(*E*)-*N*-(3,3-Difluoro-1-phenylprop-1-en-1-yl)-*N*-ethylacetamide (21): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **21** as a colorless oil (0.064 mmol, 15.3 mg, 64% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.41 (m, 3H), 7.35 – 7.30 (m, 2H), 6.13 (td, *J* = 54.8, 7.7 Hz, 1H), 5.71 (q, *J* = 7.9 Hz, 1H), 3.40 (q, *J* = 7.1 Hz, 2H), 2.14 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.1, 148.6 (t, *J* = 14.1 Hz), 133.4 (t, *J* = 2.2 Hz), 130.7, 129.2, 128.9 (t, *J* = 3.3 Hz), 120.8 (t, *J* = 28.3 Hz), 113.2 (t, *J* = 316.2 Hz), 41.3, 22.7, 13.0. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.5 (d, *J* = 55.3 Hz). **IR (ATR)**: 2921, 1733, 1644, 1562, 1451, 1386, 1285, 1143, 1079, 1026, 851 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{13}H_{16}ONF_2^+$:240.1195; found 240.1198.



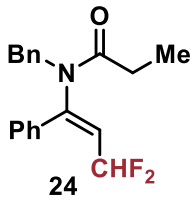
22

(*E*)-*N*-(Cyclohexylmethyl)-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)acetamide (22): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **22** as a colorless oil (0.070 mmol, 21.5 mg, 70% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.42 (m, 3H), 7.31 – 7.27 (m, 2H), 6.11 (td, *J* = 54.8, 7.7 Hz, 1H), 5.76 – 5.70 (m, 1H), 3.11 (d, *J* = 7.1 Hz, 2H), 2.22 (s, 3H), 1.70 – 1.48 (m, 6H), 1.21 – 1.06 (m, 3H), 0.92 – 0.80 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.5, 133.0, 130.7, 129.2, 128.8 (t, *J* = 27.5 Hz), 121.0 (t, *J* = 28.3 Hz), 113.3 (t, *J* = 231.3 Hz), 51.5, 36.9, 30.8, 26.4, 25.8, 22.7. Analytical data for compound **22** was consistent with the literature.[6]



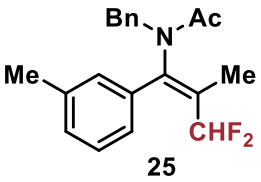
23

Tert-butyl (*E*)-acetyl(3,3-difluoro-1-phenylprop-1-en-1-yl)carbamate (23): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **23** as a colorless oil (0.092 mmol, 28.6 mg, 92% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 – 7.33 (m, 5H), 6.14 (td, *J* = 54.8, 7.6 Hz, 1H), 5.77 (q, *J* = 7.9 Hz, 1H), 2.54 (s, 3H), 1.32 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.7, 151.8, 145.0 (t, *J* = 14.8 Hz), 134.7(d, *J* = 4.2 Hz), 129.8, 128.9, 128.8 (t, *J* = 1.6 Hz), 128.6, 125.7, 123.2 (t, *J* = 27.7 Hz), 113.0 (t, *J* = 230.5 Hz), 84.1, 27.7, 26.3. Analytical data for compound **23** was consistent with the literature.[6]



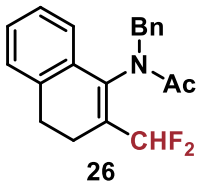
24

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-1-phenylprop-1-en-1-yl)propionamide (24): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **24** as a colorless oil (0.076 mmol, 23.9 mg, 76% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 – 7.40 (m, 3H), 7.31 – 7.22 (m, 5H), 7.20 – 7.15 (m, 2H), 6.21 – 5.91 (m, 1H), 5.54 (q, *J* = 7.9 Hz, 1H), 4.59 (s, 2H), 2.42 (q, *J* = 7.4 Hz, 2H), 1.15 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.1, 148.1 (t, *J* = 14.1 Hz), 137.0, 133.5, 130.7, 129.2, 128.9 (t, *J* = 1.8 Hz), 128.8, 128.6, 127.7, 121.4 (t, *J* =28.3 Hz), 113.1 (t, *J* = 231.4 Hz), 50.4, 27.9, 10.1. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.7 (d, *J* = 55.3 Hz). **IR (ATR)**: 2926, 1649, 1386, 1237, 1196, 1116, 1051, 1004, 768 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}ONF_2^+$:316.1508; found 316.1511.



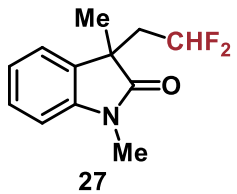
25

(*E*)-*N*-Benzyl-*N*-(3,3-difluoro-2-methyl-1-(m-tolyl)prop-1-en-1-yl)acetamide (25): Prepared according to the general procedure I, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **25** as a colorless oil (0.055 mmol, 18.1 mg, 55% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 – 7.31 (m, 1H), 7.27 – 7.20 (m, 6H), 7.09 – 7.05 (m, 1H), 7.03 – 7.01 (m, 1H), 6.14 (t, *J* = 55.1 Hz, 1H), 5.24 (d, *J* = 14.0 Hz, 1H), 3.53 (d, *J* = 14.0 Hz, 1H), 2.38 (s, 3H), 2.17 (s, 3H), 1.39 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.8, 139.1, 136.5, 133.8, 130.9, 129.7, 128.9, 128.5, 127.8, 126.8, 114.3 (t, *J* = 235.3 Hz), 48.6, 21.6, 21.5, 10.9. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.44 (dd, *J* = 55.5, 31.7 Hz). **IR (ATR)**: 2926, 1655, 1441, 1373, 1304, 1244, 1082, 1006, 793 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{20}H_{21}ONF_2^+$:330.1664; found 330.1667.



26

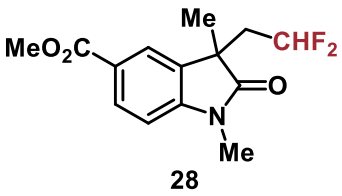
***N*-Benzyl-*N*-(2-(difluoromethyl)-3,4-dihydronaphthalen-1-yl)acetamide (26)**: Prepared according to the general procedure VI, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **26** as a colorless oil (0.066 mmol, 21.6 mg, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 – 7.23 (m, 8H), 7.12 – 7.08 (m, 1H), 5.79 – 5.48 (m, 2H), 3.69 (d, *J* = 13.7 Hz, 1H), 2.91 – 2.79 (m, 2H), 2.57 – 2.50 (m, 1H), 2.46 – 2.34 (m, 1H), 1.96 (s, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.9, 138.0, 136.0, 132.1 (t, *J* = 10.1 Hz), 130.0, 129.9, 128.8, 128.7, 128.5, 128.4, 128.3, 127.4, 123.7, 112.2 (t, *J* = 235.3 Hz), 50.2, 27.0, 21.5, 19.5 ppm. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.44 (dd, *J* = 1037.8, 323.4 Hz). **IR (ATR)**: 2923, 1663, 1438, 1378, 1288, 1238, 1180, 1077, 1005, 755 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}ONF_2^+$:328.1508; found 328.1510.



27

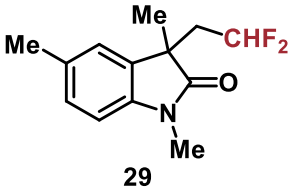
3-(2,2-Difluoroethyl)-1,3-dimethylindolin-2-one (27): Prepared according to the general procedure II, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **27** as a colorless oil (0.077 mmol, 17.3 mg, 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 – 7.27 (m, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.10 – 7.05 (m, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 5.74 – 5.41 (m, 1H), 3.21 (s, 3H), 2.55 – 2.41 (m, 1H), 2.35 – 2.18 (m, 1H), 1.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2, 143.0, 132.1, 128.6, 122.9, 122.8, 115.2 (t, *J* = 239.7 Hz), 108.6, 44.6 (t, *J* = 5.4 Hz), 41.4 (t, *J* = 21.8 Hz), 26.4, 24.4. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.0 – -114.3 (m). **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{12}H_{14}ONF_2^+$:226.1038; found 226.1039. Analytical data for compound **27** was consistent with the literature.[7]



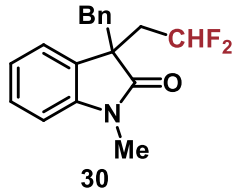
28

Methyl 3-(2,2-difluoroethyl)-1,3-dimethyl-2-oxoindoline -5-carboxylate (28): Prepared according to the general procedure II, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **28** as a white solid (0.061 mmol, 17.3 mg, 61% yield). **Melting Point**: 132-134 ℃. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 8.2 Hz, 1H), 7.88 (s, 1H), 6.92 – 6.85 (m, 1H), 5.72 – 5.37 (m, 1H), 3.89 (s, 3H), 3.23 (s, 3H), 2.59 – 2.23 (m, 2H), 1.41 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 179.5, 166.8, 147.1, 132.1, 131.3, 124.8, 124.2, 114.9 (t, *J* = 240.1 Hz), 108.1, 52.2, 44.4 (t, *J* = 6.1 Hz), 41.3 (t, *J* = 22.1 Hz), 26.6, 24.5. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.3 – -114.6 (m). Analytical data for compound **28** was consistent with the literature.[7]



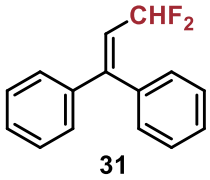
29

3-(2,2-Difluoroethyl)-1,3,5-trimethylindolin-2-one (29): Prepared according to the general procedure II, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **29** as a colorless oil (0.066 mmol, 15.8 mg, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.11 – 7.06 (m, 1H), 7.02 (s, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 5.73 – 5.43 (m, 1H), 3.18 (s, 3H), 2.53 – 2.40 (m, 1H), 2.34 (s, 3H), 2.31 – 2.17 (m, 1H), 1.38 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 179.2, 140.6, 132.4, 132.2, 128.8, 123.7, 115.26 (t, *J* = 239.7 Hz), 108.3, 44.8 – 44.6 (m) (2C), 41.5 (t, *J* = 21.9 Hz), 24.4, 21.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.0 – -114.3 (m). **IR (ATR)**: 2978, 1706, 1611, 1495, 1362, 1245, 1052, 897 cm^{-1}**.** **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{13}H_{16}ONF_2^+$: 240.1195; found 240.1196.



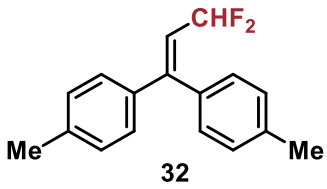
30

3-Benzyl-3-(2,2-difluoroethyl)-1-methylindolin-2-one (30): Prepared according to the general procedure II, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **30** as a white solid (0.080 mmol, 24.1 mg, 80% yield). **Melting Point**: 80-82 ℃. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24 – 7.13 (m, 2H), 7.10 – 7.01 (m, 4H), 6.80 – 6.77 (m, 2H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.71 – 5.40 (m, 1H), 3.12 (d, *J* = 12.9 Hz, 1H), 3.02 (d, *J* = 12.9 Hz, 1H), 2.94 (s, 3H), 2.77 – 2.62 (m, 1H), 2.49 – 2.35 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 177.8, 143.6, 130.1, 129.1, 128.7, 127.6, 126.9, 123.9, 122.3, 115.2 (t, *J* = 240.0 Hz), 108.3, 51.5 – 50.4 (m) (2C), 44.5, 40.16 (t, *J* = 22.0 Hz), 26.1. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -113.7 – -114.0 (m). **IR (ATR)**: 2978, 1712, 1605, 1456, 1390, 1254, 1066, 885 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{18}H_{18}ONF_2^+$: 302.1351; found 302.1354.



31

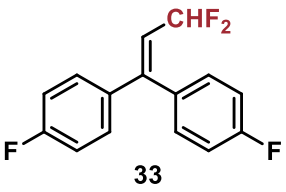
(3,3-Difluoroprop-1-ene-1,1-diyl)dibenzene (31): Prepared according to the general procedure III, the chromatographic purification using PE as the eluent afforded **31** as a colorless oil (0.082 mmol, 18.9 mg, 82% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.20 (m, 10H), 6.24 – 5.87 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 150.7 (t, *J* = 12.8 Hz), 140.1, 137.3, 129.9 (t, *J* = 1.7 Hz), 129.1, 128.8, 128.5, 128.5, 128.1 (t, *J* = 1.4 Hz), 120.1 (t, *J* = 26.7 Hz), 113.8 (t, *J* = 229.3 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.7 (d, *J* = 65.8 Hz). Analytical data for compound **31** was consistent with the literature.[8]



32

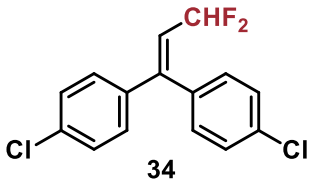
4,4'-(3,3-difluoroprop-1-ene-1,1-diyl)bis(methylbenzene) (32): Prepared according to the general procedure III, the chromatographic purification using PE as the eluent afforded **32** as a colorless oil (0.060 mmol, 15.5 mg, 60% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24 – 7.08 (m, 8H), 6.21 – 5.87 (m, 2H), 2.40 (s, 3H), 2.36 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 150.7 (t, *J* = 12.9 Hz), 139.2, 138.7, 137.6, 134.5, 130.0 - 129.8 (m), 129.1, 128.1 (t, *J* = 1.3 Hz), 127.5, 119.0 (t, *J* = 26.5 Hz), 114.1 (t, *J* = 228.9 Hz), 21.4, 21.3. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.2 (d, *J* = 61.1 Hz). **IR (ATR)**: 2921, 1628, 1507, 1451, 1379, 1253, 1118, 1057, 989, 817 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{17}H_{17}F_2^+$:

259.1293; found 259.1295.



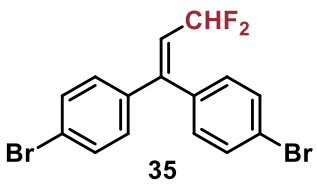
33

4,4'-(3,3-difluoroprop-1-ene-1,1-diyl)bis(fluorobenzene) (33): Prepared according to the general procedure III, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **33** as a colorless oil (0.058 mmol, 15.4 mg, 58% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.25 – 7.16 (m, 4H), 7.14 – 7.08 (m, 2H), 7.05 – 6.98 (m, 2H), 6.15 – 5.81 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.4 (d, *J* = 250.5 Hz), 163.1 (d, *J* = 250.5 Hz), 148.7 (t, *J* = 12.8 Hz), 131.7 (dt, *J* = 8.3, 1.7 Hz), 129.9 (dt, *J* = 8.5, 1.4 Hz), 120.4 (t, *J* = 26.7 Hz), 115.9, 115.7, 115.7, 115.5, 113.5 (t, *J* = 229.7 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.4, -106.6, -1120.0 (d, *J* = 25.7 Hz). **IR (ATR)**: 2920, 1747, 1641, 1598, 1502, 1413, 1330, 1229, 1126, 1065, 1011, 829 cm^{-1}. **HRMS (ESI)**: *m/z* $[M-H]^-$ calcd for $C_{15}H_9F_4^-$: 266.0789; found 266.0792.



34

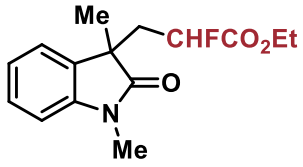
4,4'-(3,3-difluoroprop-1-ene-1,1-diyl)bis(chlorobenzene) (34): Prepared according to the general procedure III, the chromatographic purification using PE as the eluent afforded **34** as a colorless oil (0.083 mmol, 24.8 mg, 83% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 – 7.37 (m, 2H), 7.33 – 7.28 (m, 2H), 7.20 – 7.12 (m, 4H), 6.23 – 5.79 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.4 (t, *J* = 12.6 Hz), 138.2, 135.5, 135.3, 135.2, 131.2 (t, *J* = 1.6 Hz), 129.3 (t, *J* = 1.2 Hz), 129.0, 128.9, 121.0 (t, *J* = 27.0 Hz), 113.3 (t, *J* = 230.3 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.73 (d, *J* = 56.1 Hz). **IR (ATR)**: 2921, 1639, 1591, 1487, 1379, 1124, 1074, 1008, 825 cm^{-1}. **HRMS (ESI)**: *m/z* $[M-H]^-$ calcd for $C_{15}H_9Cl_2F_2^-$: 297.0055; found 297.0059.



35

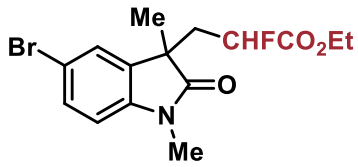
4,4'-(3,3-difluoroprop-1-ene-1,1-diyl)bis(bromobenzene) (35): Prepared according to the general procedure III, the chromatographic purification using PE as the eluent afforded **35** as a colorless oil (0.062 mmol, 23.9 mg, 62% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 – 7.53 (m, 2H), 7.50 – 7.43 (m, 2H), 7.14 – 7.05 (m, 4H), 6.19

– 5.82 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.5 (t, *J* = 12.8 Hz), 138.5 (t, *J* = 1.2 Hz), 135.6 (d, *J* = 4.3 Hz), 132.0, 131.9, 131.5 (t, *J* = 1.6 Hz), 129.6 (t, *J* = 1.2 Hz), 123.8, 123.5, 121.0 (t, *J* = 27.0 Hz), 113.3 (t, *J* = 230.2 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.8 (d, *J* = 55.8 Hz). **HRMS (ESI)**: *m/z* [M-H]$^-$ calcd for $C_{15}H_9Br_2F_2^-$: 384.9049; found 384.9045.



36

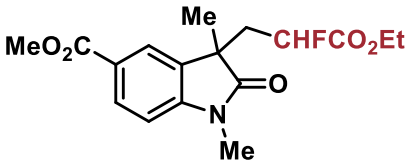
Ethyl 3-(1,3-dimethyl-2-oxoindolin-3-yl)-2-fluoropropanoate (36): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **36** as a colorless oil (0.075 mmol, 20.9 mg, 75% yield, 1.1:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.33 – 7.29 (m, 2H), 7.25 – 7.19 (m, 2H), 7.12 – 7.04 (m, 2H), 6.87 (d, *J* = 7.8 Hz, 2H), 4.87 – 4.55 (m, 2H), 4.21 – 3.97 (m, 4H), 3.24 (s, 3H), 3.21 (s, 3H), 2.62 – 2.24 (m, 4H), 1.43 (s, 3H), 1.42 (s, 3H), 1.27 – 1.20 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.6, 179.5, 169.3 (d, *J* = 22.6 Hz), 169.1 (d, *J* = 22.6 Hz), 143.5, 143.2, 132.1, 131.8, 128.5, 128.2, 123.5, 122.9, 122.6, 122.4, 108.4, 108.3, 86.8 (d, *J* = 187.2 Hz), 86.5 (d, *J* = 187.2 Hz), 61.7, 46.1, 45.8, 39.9 (d, *J* = 20.3 Hz), 39.2 (d, *J* = 20.3 Hz), 26.3, 24.8, 24.2, 14.1, 14.0. **^{19}F NMR (376 MHz, CDCl3) (mixture of diastereomers)** δ -190.29 – -190.56 (m), -190.74 – -191.03 (m). **IR (ATR)**: 3287, 2928, 1708, 1611, 1525, 1484, 1348, 1288, 1208, 1106, 1025, 751 cm^{-1}. **HRMS (ESI)**: *m/z* [M+H]$^+$ calcd for $C_{15}H_{19}O_3NF^+$:280.1344; found 280.1346.



37

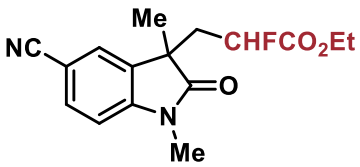
Ethyl 3-(5-bromo-1,3-dimethyl-2-oxoindolin-3-yl) -2-fluoropropanoate (37): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **37** as a colorless oil (0.083 mmol, 29.6 mg, 83% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.43 – 7.35 (m, 2H), 7.32 (d, *J* = 1.9 Hz, 1H), 7.26 (d, *J* = 1.9 Hz, 1H), 6.72 (dd, *J* = 8.2, 4.6 Hz, 2H), 4.85 – 4.54 (m, 2H), 4.19 – 4.01 (m, 4H), 3.19 (s, 3H), 3.16 (s, 3H), 2.64 – 2.14 (m, 4H), 1.39 -1.37 (m, 6H), 1.26 – 1.18 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.1, 179.0, 169.1 (d, *J* = 22.6 Hz), 168.9 (d, *J* = 22.6 Hz), 142.6, 142.4, 134.2, 134.0, 131.4, 131.2, 126.8, 126.3, 115.3, 115.1, 109.9, 109.9, 86.7 (d,

J = 186.0 Hz), 86.5 (d, *J* = 186.0 Hz), 61.9, 46.3, 46.1, 39.8 (d, *J* = 20.2 Hz), 39.2 (d, *J* = 20.2 Hz), 26.6, 26.5, 25.0, 24.2, 14.2, 14.1. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -190.75 – -191.14 (m), -191.33 – -191.58 (m). **IR (ATR)**: 2973, 1712, 1606, 1481, 1345, 1276, 1209, 1116, 1024, 811 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{15}H_{18}O_3NBrF^+$:358.0449; found 358.0449.



38

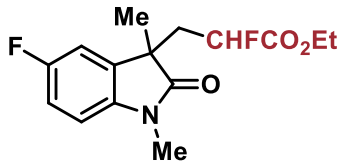
Methyl 3-(3-ethoxy-2-fluoro-3-oxopropyl) -1,3-dimethyl-2-oxoindoline-5-carboxylate (38): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **38** as a colorless oil (0.071 mmol, 23.9 mg, 71% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 8.08 – 8.04 (m, 2H), 7.92 – 7.87 (m, 2H), 6.93 – 6.90 (m, 2H), 4.89 – 4.51 (m, 2H), 4.20 – 4.01 (m, 4H), 3.93 – 3.91 (m, 6H), 3.28 (s, 3H), 3.25 (s, 3H), 2.69 – 2.28 (m, 4H), 1.46 – 1.44 (m, 6H), 1.28 – 1.21 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.9, 179.7, 168.9 (d, *J* = 22.6 Hz), 168.7 (d, *J* = 22.6 Hz), 147.7, 147.4, 132.1, 131.6, 131.3, 131.1, 124.6, 124.4, 124.3, 124.2, 108.0, 107.9, 86.7 (d, *J* = 185.8 Hz), 85.4 (d, *J* = 185.8 Hz), 61.8, 61.7, 52.1, 52.1, 45.8, 45.6, 39.7 (d, *J* = 20.1 Hz), 39.1(d, *J* = 20.1 Hz), 26.6, 26.6, 24.9, 24.2, 14.1, 13.9. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -190.80 – -191.52 (m). **IR (ATR)**: 2946, 1709, 1611, 1948, 1440, 1344, 1266, 1218, 1100, 1027, 732 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{17}H_{21}O_5NF^+$:338.1398; found 338.1398.



39

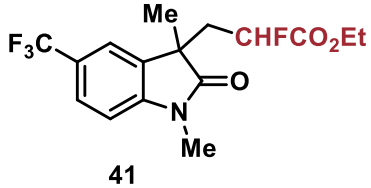
Ethyl 3-(5-cyano-1,3-dimethyl-2-oxoindolin-3-yl) -2-fluoropropanoate (39): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **39** as a colorless oil (0.069 mmol, 21.0 mg, 69% yield, 1:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.65 – 7.59 (m, 2H), 7.48 – 7.41 (m, 2H), 6.94 – 6.90 (m, 2H), 4.83 – 4.51 (m, 2H), 4.20 – 4.02 (m, 4H), 3.25 (s, 3H), 3.22 (s, 3H), 2.69 – 2.23 (m, 4H), 1.43 – 1.41 (m, 6H), 1.27 – 1.20 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ

179.2, 179.1, 168.6 (d, *J* = 23.2), 168. 6 (d, *J* = 23.2), 147.4, 147.1, 133.6, 133.3, 132.9, 132.9, 126.7, 126.4, 119.1, 108.8, 108.8, 105.7, 105.5, 86.5 (d, *J* = 187.2 Hz), 86.2 (d, *J* = 187.2 Hz), 62.0, 61.9, 45.8, 45.6, 39.5 (d, *J* = 19.4 Hz), 39.0 (d, *J* = 19.4 Hz), 26.6, 26.6, 24.9, 24.0, 14.1, 14.0. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -190.75 – -191.04 (m), -191.31 – -191.63 (m). **IR (ATR)**: 2976, 1719, 1610, 1495, 1459, 1342, 1212, 1111, 1025, 825 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{16}H_{17}O_3N_2FNa^+$:327.1115; found 327.1118.



40

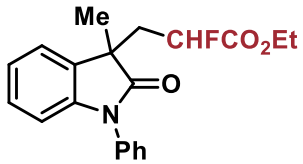
Ethyl 2-fluoro-3-(5-fluoro-1,3-dimethyl-2-oxoindolin-3-yl) propanoate (40): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **40** as a colorless oil (0.081 mmol, 24.1 mg, 81% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.05 – 6.94 (m, 4H), 6.81 – 6.77 (m, 2H), 4.91 – 4.52 (m, 2H), 4.24 – 4.05 (m, 4H), 3.23 (s, 3H), 3.20 (s, 3H), 2.64 – 2.22 (m, 4H), 1.43 – 1.41 (m, 6H), 1.28 – 1.22 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.3, 179.1, 169.0 (d, *J* = 23.2 Hz), 168.9 (d, *J* = 23.2), 159.3 (d, *J* = 241.4 Hz), 159.2 (d, *J* = 241.4 Hz), 139.4 (d, *J* = 2.4 Hz), 139.1 (d, *J* = 2.4 Hz), 133.9 (d, *J* = 8.1 Hz) , 133.5 (d, *J* = 8.1 Hz) , 114. 7 (d, *J* = 23.2 Hz), 114.4 (d, *J* = 23.2 Hz) , 111.6 (d, *J* = 24.2 Hz) , 111.2 (d, *J* = 24.2 Hz) , 108.9 (d, *J* = 8.1 Hz) , 108.8 (d, *J* = 8.1 Hz) , 86.7 (d, *J* = 187.9 Hz) , 86.4 (d, *J* = 187.9 Hz), 61.8, 61.8, 46.6, 46.2, 39.7 (d, *J* = 20.2 Hz), 39.2 (d, *J* = 20.2 Hz) , 26.5, 26.5, 24.9, 24.0, 14.1, 14.0. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -120.34, -120.64, -190.74 – -191.02 (m). **IR (ATR)**: 2975, 1712, 1615, 1489, 1350, 1274, 1211, 1108, 1026, 907, 814 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{15}H_{18}O_3NF_2^+$:298.1249; found 298.1250.



41

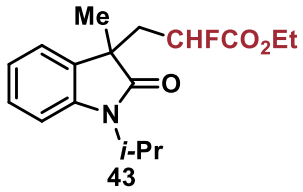
Ethyl 3-(1,3-dimethyl-2-oxo-5-(trifluoromethyl) indolin-3-yl)-2-fluoropropanoate (41): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **41** as a colorless oil (0.079 mmol, 27.4 mg, 79% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.62 – 7.56 (m, 2H), 7.47 – 7.42 (m, 2H),

6.96 – 6.93 (m, 2H), 4.86 – 4.57 (m, 2H), 4.24 – 3.97 (m, 4H), 3.27 (s, 3H), 3.25 (s, 3H), 2.74 – 2.27 (m, 4H), 1.46 – 1.44 (m, 6H), 1.28 – 1.19 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.6, 169.01 (d, *J* = 10.3 Hz), 146.6, 132.7, 125.8 (d, *J* = 3.4 Hz), 126.5 (q, *J* = 4.0 Hz), 124.9 (q, *J* = 32.8 Hz), 120.1 – 120.0 (m), 108.3, 86.4 (d, *J* = 186.0 Hz), 62.0, 45.8, 39.1 (d, *J* = 19.5 Hz), 26.6, 24.2, 14.1 ppm. **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.6, 179.5, 168.9 (d, *J* = 23.2 Hz) , 168.8 (d, *J* = 23.2 Hz), 146.6, 146.3, 132.7, 132.5, 126.5 (q, *J* = 4.0 Hz) , 126.2 (q, *J* = 4.0 Hz) , 124.9 (q, *J* = 32.3 Hz) , 124.7 (q, *J* = 32.3 Hz), 124.5 (q, *J* = 272.7 Hz), 124.4 (d, *J* = 272.7 Hz) , 120.5 (q, *J* = 4.0 Hz), 120.1 (q, *J* = 4.0 Hz), 108.3, 108.2, 86.6 (d, *J* = 187.8 Hz) , 86.4 (d, *J* = 187.8 Hz), 62.0, 61.8, 46.1, 45.8, 39.7 (d, *J* = 20.2 Hz) , 39. 1 (d, *J* = 20.2 Hz), 26.7, 26.6, 25.1, 24.2, 14.1, 14.0. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -61.19, -61.23, -190.69 – -190.97 (m), -191.25 – -191.53 (m). **IR (ATR)**: 2978, 1720, 1618, 1505, 1458, 1325, 1280, 1219, 1111, 1027, 825 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{16}H_{18}O_3NF_4^+$:348.1217; found 348.1218.



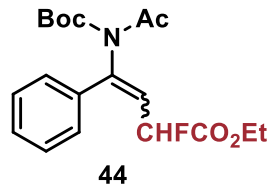
42

Ethyl 2-fluoro-3-(3-methyl-2-oxo-1-phenylindolin-3-yl) propanoate (42): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **42** as a colorless oil (0.075 mmol, 25.6 mg, 75% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.47 – 7.41 (m, 4H), 7.38 – 7.29 (m, 4H), 7.24 – 7.10 (m, 6H), 7.08 – 6.98 (m, 2H), 6.77 – 6.74 (m, 2H), 4.95 – 4.47 (m, 2H), 4.15 – 3.86 (m, 4H), 2.71 – 2.21 (m, 4H), 1.48 (s, 3H), 1.46 (s, 3H), 1.21 – 1.09 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 178.0, 177.9, 168.2 (d, *J* = 22.2 Hz), 168.2 (d, *J* = 22.2 Hz), 142.6, 142.3, 133.5, 130.7, 130.2, 128.6, 128.5, 127.4, 127.1, 127.1, 127.0, 125.7, 125.6, 122.8, 122.1, 122.0, 121.7, 108.6, 108.6, 85.8 (d, *J* = 188.9 Hz), 85.7 (d, *J* = 188.9 Hz), 60.7, 60.7, 45.0, 44.9, 39.3 (d, *J* = 20.2 Hz), 38.5 (d, *J* = 20.2 Hz), 24.2, 23.6, 13.1, 12.9. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -185.66 – -195.56 (m). **IR (ATR)**: 2974, 1720, 1603, 1494, 1457, 1372, 1292, 1206, 1102, 1024, 752 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{20}H_{21}O_3NF^+$:342.1500; found 342.1501.



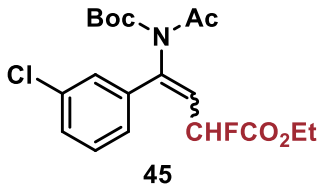
43

Ethyl 2-fluoro-3-(1-isopropyl-3-methyl-2-oxoindolin-3-yl) propanoate (43): Prepared according to the general procedure IV, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **43** as a colorless oil (0.078 mmol, 23.9 mg, 78% yield, 1.2:1 dr). **^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers)** δ 7.27 – 7.15 (m, 4H), 7.06 – 6.97 (m, 4H), 4.88 – 4.41 (m, 4H), 4.20 – 3.90 (m, 4H), 2.63 – 2.13 (m, 4H), 1.48 – 1.42 (m, 12H), 1.39 – 1.36 (m, 6H), 1.24 – 1.16 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$) (mixture of diastereomers)** δ 179.3, 179.2, 169.4 (d, *J* = 23.2 Hz), 169.2 (d, *J* = 23.2 Hz), 142.3, 141.9, 132.7, 132.1, 128.3, 128.0, 123.8, 123.2, 122.0, 121.8, 110.2, 110.1, 86.9 (d, *J* = 188.9 Hz), 86.7 (d, *J* = 188.9 Hz), 61.8, 61.7, 45.8, 45.6, 43.8, 43.7, 40.2 (d, *J* = 20.2 Hz), 39.5 (d, *J* = 20.2 Hz), 25.1, 24.7, 19.4, 19.4, 19.3, 19.1, 14.2, 14.0. **^{19}F NMR (376 MHz, $CDCl_3$) (mixture of diastereomers)** δ -190.71 – -191.07 (m). **IR (ATR)**: 2976, 1706, 1609, 1458, 1360, 1289, 1206, 1163, 1107, 1026, 729 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+H]^+$ calcd for $C_{17}H_{23}O_3NF^+$:308.1657; found 308.1658.



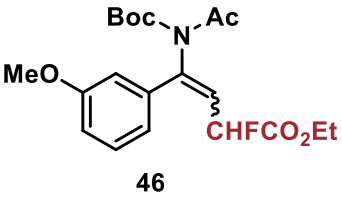
44

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl)acetamido) 2-fluoro-4-phenylbut-3-enoate (44): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **44** as a light yellow oil (0.058 mmol, 21.2 mg, 58% yield, *E*/*Z* = 91:9)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.42 (m, 2H), 7.40 – 7.35 (m, 3H), 5.74 (dd, *J* = 10.1, 8.3 Hz, 1H), 5.40 (dd, *J* = 47.7, 10.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.33 – 1.29 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.6, 168.3 (d, *J* = 26.6 Hz), 152.0, 145.3 (d, *J* = 13.3 Hz), 134.99 (d, *J* = 3.2 Hz), 129.5, 129.03 (d, *J* = 2.6 Hz), 128.5, 122.7, 122.5, 85.1 (d, *J* = 178.6 Hz), 83.9, 62.2, 27.7, 26.2, 14.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -171.62 – -177.97 (m). **IR (ATR)**: 2979, 1736, 1649, 1449, 1370, 1249, 1143, 1028, 851 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{19}H_{24}O_5NFNa^+$:388.1531; found 388.1525.



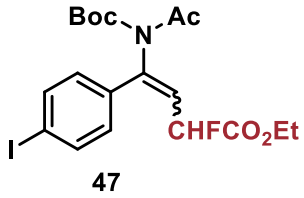
45

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl) acetamido) -4-(3-chlorophenyl)-2-fluorobut-3-enoate (45): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **45** as a light yellow oil (0.052 mmol, 20.7 mg, 52% yield, *E*/*Z* = 67:33). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 – 7.46 (m, 1H), 7.39 – 7.27 (m, 3H), 5.81 – 5.73 (m, 1H), 5.35 (dd, *J* = 47.6, 9.9 Hz, 1H), 4.31 – 4.24 (m, 2H), 2.61 (s, 1H), 2.52 (s, 2H), 1.38 – 1.30 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.6, 168.0 (d, *J* = 26.5 Hz), 151.8, 143.6, 136.8, 134.4, 129.8, 129.6, 129.2 (d, *J* = 2.5 Hz), 127.3 (d, *J* = 2.4 Hz), 123.9, 84.7 (d, *J* = 179.3 Hz), 84.3, 62.3, 27.8, 27.7, 26.3, 14.2 ppm. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -176.3 – -176.4 (m). **IR (ATR)**: 2978, 1739, 1658, 1564, 1469, 1368, 1246, 1142, 1025, 845 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{19}H_{23}O_5NClFNa^+$:422.1141; found 422.1140.



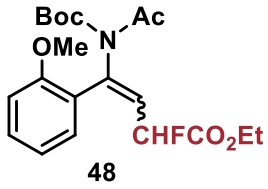
46

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl)acetamido) -2-fluoro -4-(3-methoxyphenyl)but-3-enoate (46): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **46** as a colorless oil. (0.074 mmol, 29.2 mg, 74% yield, *E*/*Z* = 90:10)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 – 7.26 (m, 1H), 7.04 – 7.01 (m, 2H), 6.95 – 6.86 (m, 1H), 5.76 – 5.68 (m, 1H), 5.45 (dd, *J* = 47.7, 10.0 Hz, 1H), 4.27 (q, *J* = 7.3 Hz, 2H), 3.80 (s, 3H), 2.50 (s, 3H), 1.37 – 1.29 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.6, 168.3 (d, *J* = 26.6 Hz), 159.5, 152.0, 145.1 (d, *J* = 13.3 Hz), 136.3, 129.5, 122.7 (d, *J* = 20.4 Hz), 121.3, 115.2, 114.6, 85.0 (d, *J* = 178.8 Hz), 83.9, 62.2, 55.4, 27.8, 26.3, 14.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -168.81 – -178.21 (m). **IR (ATR)**: 2926, 1732, 1588, 1458, 1368, 1245, 1134, 1036, 854 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{26}O_6NFNa^+$:418.1636; found 418.1634.



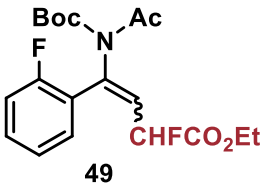
47

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl)acetamido)-2-fluoro -4-(4-iodophenyl) but-3-enoate (47): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **47** as a colorless oil (0.060 mmol, 29.5 mg, 60% yield, *E*/*Z* = 82:18)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 5.78 – 5.71 (m, 1H), 5.32 (dd, *J* = 47.8, 10.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 1H), 2.50 (s, 2H), 1.37 – 1.29 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.6, 168.0 (d, *J* = 26.5 Hz), 151.8, 144.3, 137.7, 130.7, 123.3 (d, *J* = 20.7 Hz), 100.0, 95.7, 84.8 (d, *J* = 179.4 Hz), 83.9, 62.3, 27.8, 27.8, 26.3, 14.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -169.54 – -178.21 (m). **IR (ATR)**: 2977, 1735, 1584, 1484, 1370, 1245, 1137, 1035, 998, 818 cm^{-1}. **HRMS (ESI)**: *m/z* $[M-H]^-$ calcd for $C_{19}H_{22}O_5NFI^-$:490.0532; found 490.0541.



48

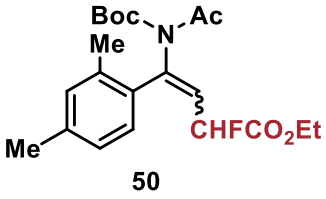
Ethyl (E)-4-(*N*-(tert-butoxycarbonyl)acetamido)-2-fluoro-4-(2-methoxyphenyl)but-3-enoate (48): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **48** as a colorless oil (0.045 mmol, 17.8 mg, 45% yield, *E*/*Z* =96:4). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.30 (m, 2H), 6.98 – 6.88 (m, 2H), 5.80 – 5.75 (m, 1H), 5.34 (dd, *J* = 47.1, 10.2 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.78 (s, 3H), 2.46 (s, 3H), 1.30 – 1.23 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.2, 168.3 (d, *J* = 26.2 Hz), 156.9, 152.2, 140.7 (d, *J* = 13.5 Hz), 132.2, 130.8, 124.3 (d, *J* = 20.8 Hz), 123.4, 120.4, 111.2, 85.8 (d, *J* = 176.4 Hz), 83.3, 62.0, 55.5, 27.7, 26.3, 14.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -178.0 (d, *J* = 47.1 Hz). **IR (ATR)**: 2973, 1727, 1591, 1490, 1455, 1367, 1245, 1152, 1021, 861 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{20}H_{26}O_6NFNa^+$:418.1636; found 418.1635.



49

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl)acetamido)-2-fluoro-4-(2-fluorophenyl)but-3-enoate (49): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **49** as a colorless oil (0.057 mmol, 21.8 mg, 57% yield, *E*/*Z* = 87:13)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45 – 7.31 (m, 2H), 7.19 – 7.03 (m, 2H), 5.90 – 5.80 (m, 1H), 5.32 (dd, *J* = 47.6, 10.5 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.49

(s, 3H), 1.36 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.5, 167.8 (d, *J* = 26.2 Hz), 159.6 (d, *J* = 250.8 Hz), 151.8, 138.0, 132.25 – 131.56 (m), 131.3, 125.81 (d, *J* = 21.4 Hz), 124.2, 122.6, 116.1 (d, *J* = 22.0 Hz), 85.3 (d, *J* = 178.4 Hz), 84.0, 62.2, 27.7, 26.4, 14.1. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -112.8, -176.6 – -182.5 (m). **IR (ATR)**: 2981, 1734, 1619, 1533, 1490, 1451, 1369, 1244, 1148, 1026, 761 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{19}H_{23}O_5NF_2Na^+$:406.1437; found 406.1434.



50

Ethyl (*E*)-4-(*N*-(tert-butoxycarbonyl)acetamido)-4-(2,4-dimethylphenyl)-2-fluorobut-3-enoate (50): Prepared according to the general procedure V, the chromatographic purification using PE and EA (10 : 1) as the eluent afforded **50** as a colorless oil (0.055 mmol, 21.6 mg, 55% yield, *E*/*Z* = 76:24). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.23 (s, 1H), 7.07 – 6.97 (m, 2H), 5.80 – 5.73 (m, 1H), 5.16 (dd, *J* = 47.8, 10.2 Hz, 1H), 4.30 – 4.19 (m, 2H), 2.41 (s, 3H), 2.30 (s, 6H), 1.36 – 1.26 (m, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.1, 168.3 (d, *J* = 27.0 Hz), 152.6, 139.14 , 136.9 (d, *J* = 2.2 Hz), 131.6, 131.6, 130.6 (d, *J* = 2.8 Hz), 126.7, 126.2, 123.1 (d, *J* = 20.7 Hz), 85.8 (d, *J* = 177.4 Hz), 84.1, 62.0, 27.7, 26.3, 21.2, 19.8, 14.1 ppm. **IR (ATR)**: 2977, 1728, 1652, 1533, 1452, 1368, 1239, 1152, 1030, 861 cm^{-1}. **HRMS (ESI)**: *m/z* $[M+Na]^+$ calcd for $C_{21}H_{28}O_5NFNa^+$:416.1844; found 416.1842.

5. References

1. D. C. Fabry, M. Stodulski, D.-C. S. Hoerner and T. Gulder, *Chem. Eur. J.,* 2012, **18**, 10834.
2. H. Yang, E. Wang, P. Yang, H. Lv and X. Zhang, *Org. Lett.,* 2017, **19**, 5062.
3. S. Pankajakshan, Y.-H. Xu, J.-K. Cheng, M.-T. Low and T.-P. Loh, *Angew. Chem. Int. Ed.,* 2012, **51**, 5701.
4. N. B. Heine and A. Studer, *Org. Lett.,* 2017, **19**, 4150.
5. A. Thenappan and D. J. Burton, *J. Org. Chem.,* 1990, **55**, 2311.
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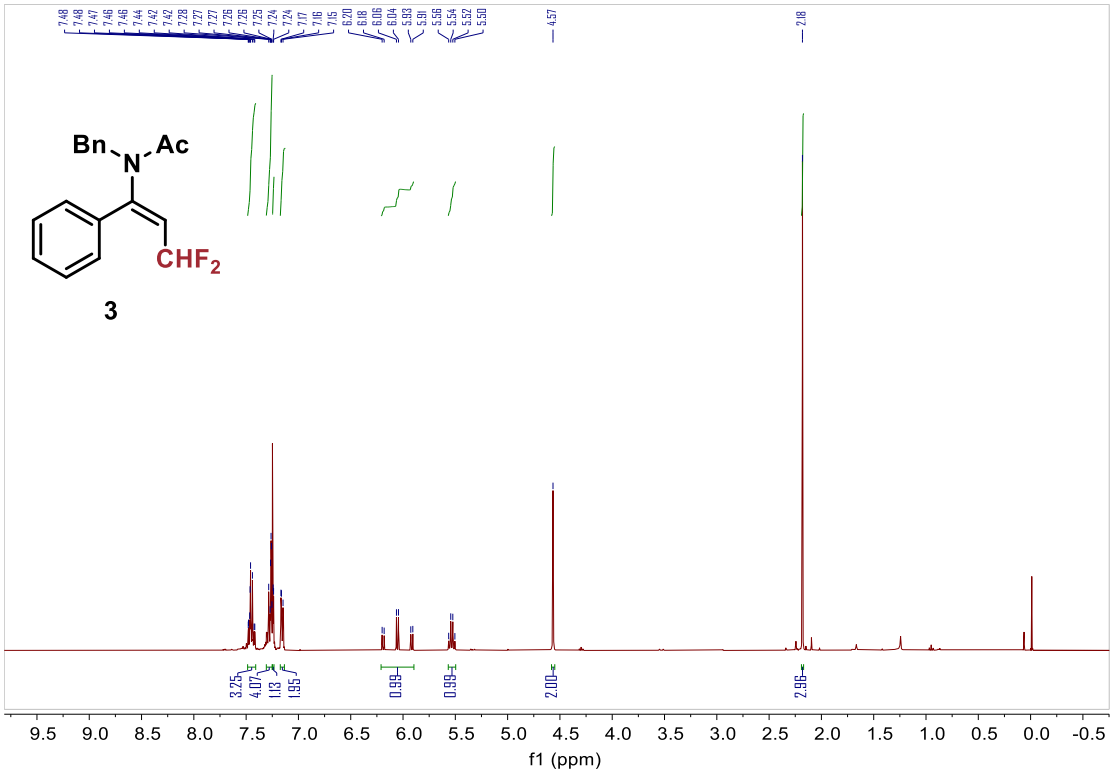
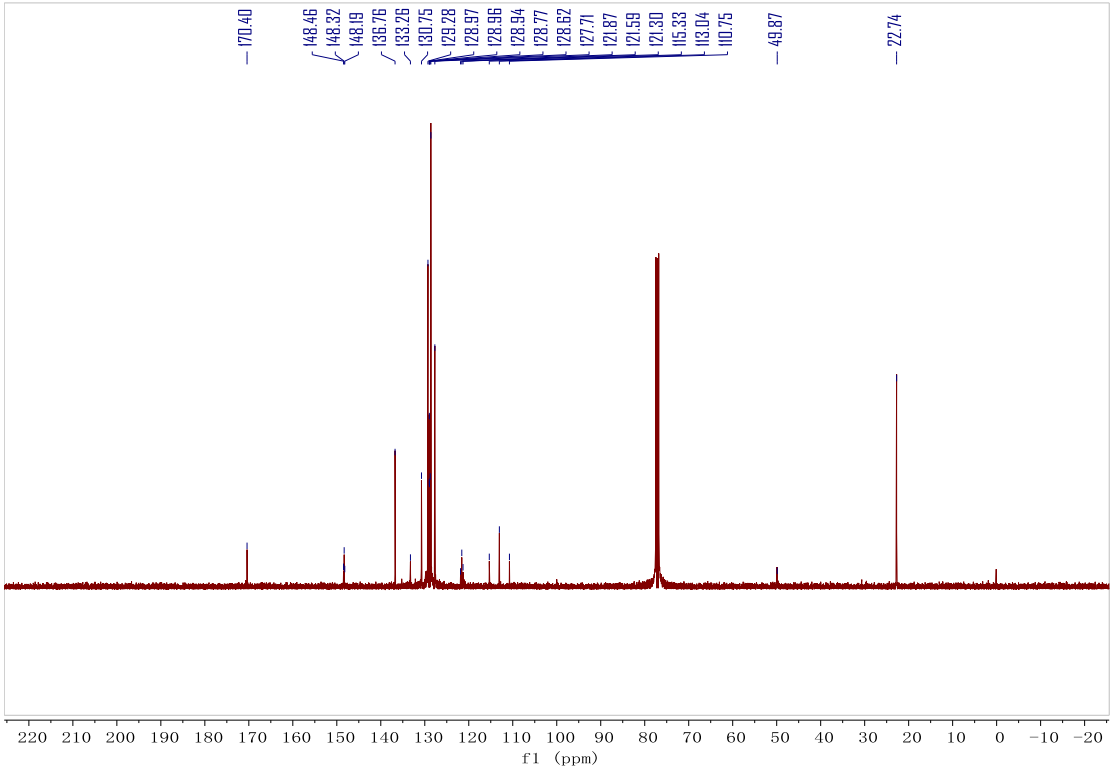
8. D. Chang, Y. Gu and Q.-L. Shen, *Chem. Eur. J.*, 2015, **21**, 6074.

6. NMR Spectra

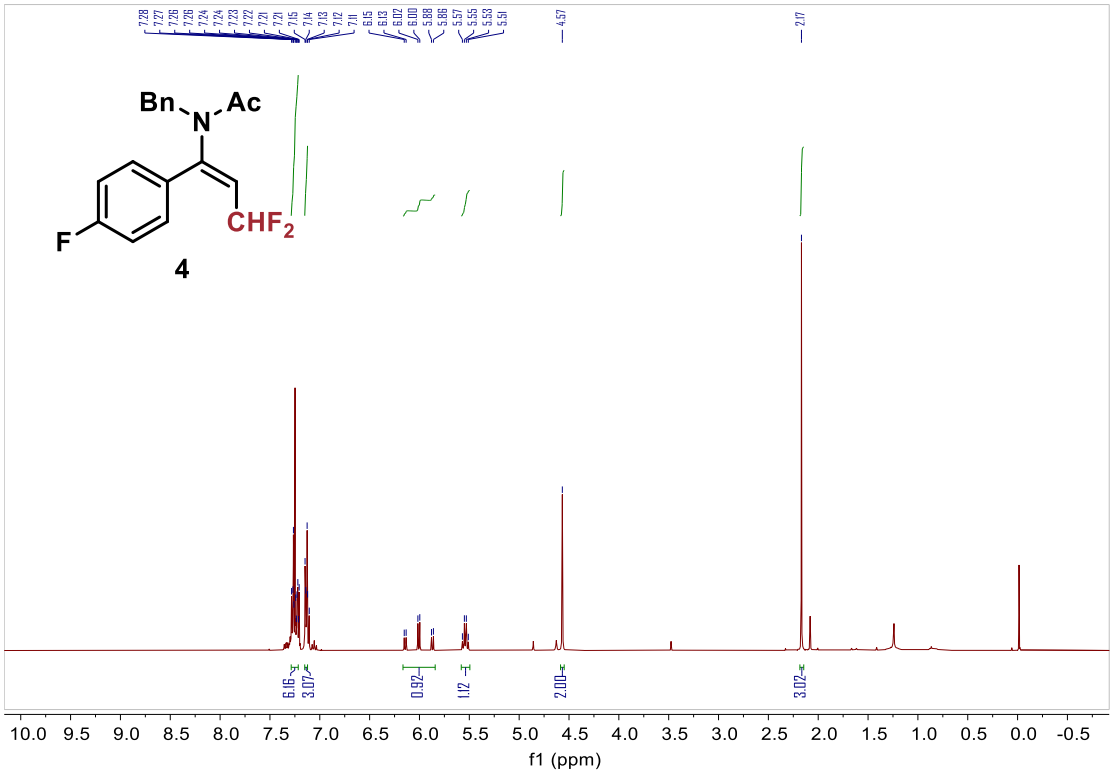
^{1}H NMR of compound 3 (400 MHz in $CDCl_3$)



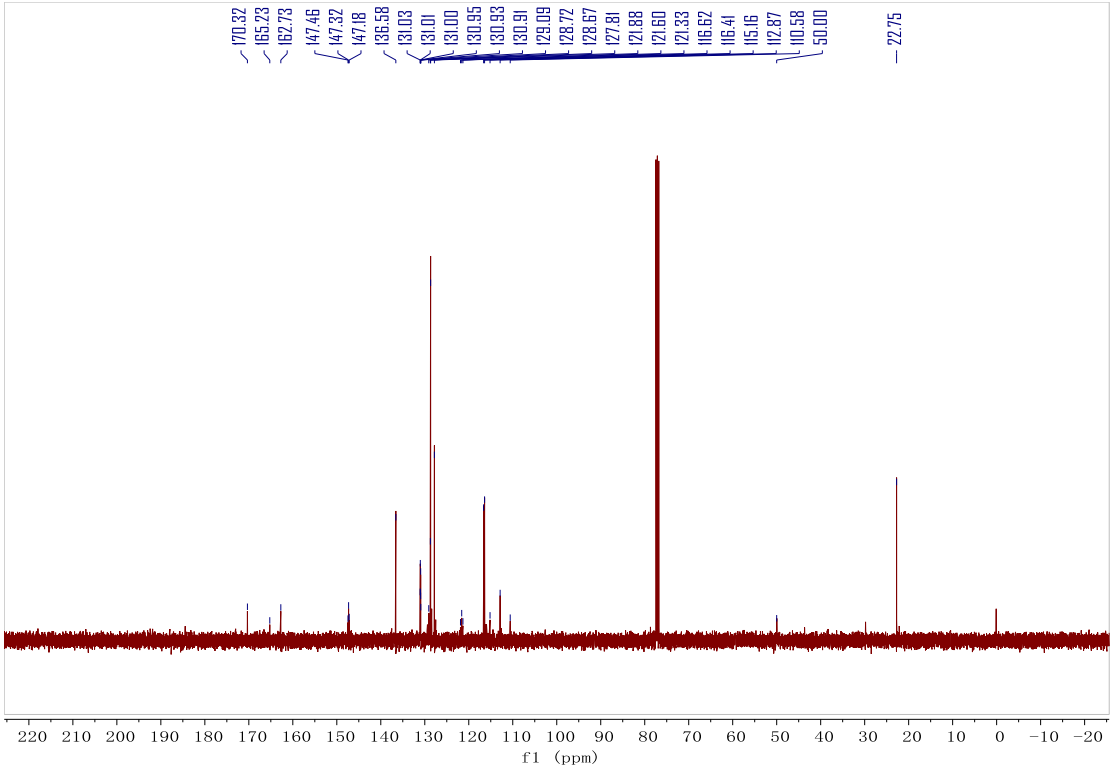
^{13}C NMR of compound 3 (101 MHz in $CDCl_3$)



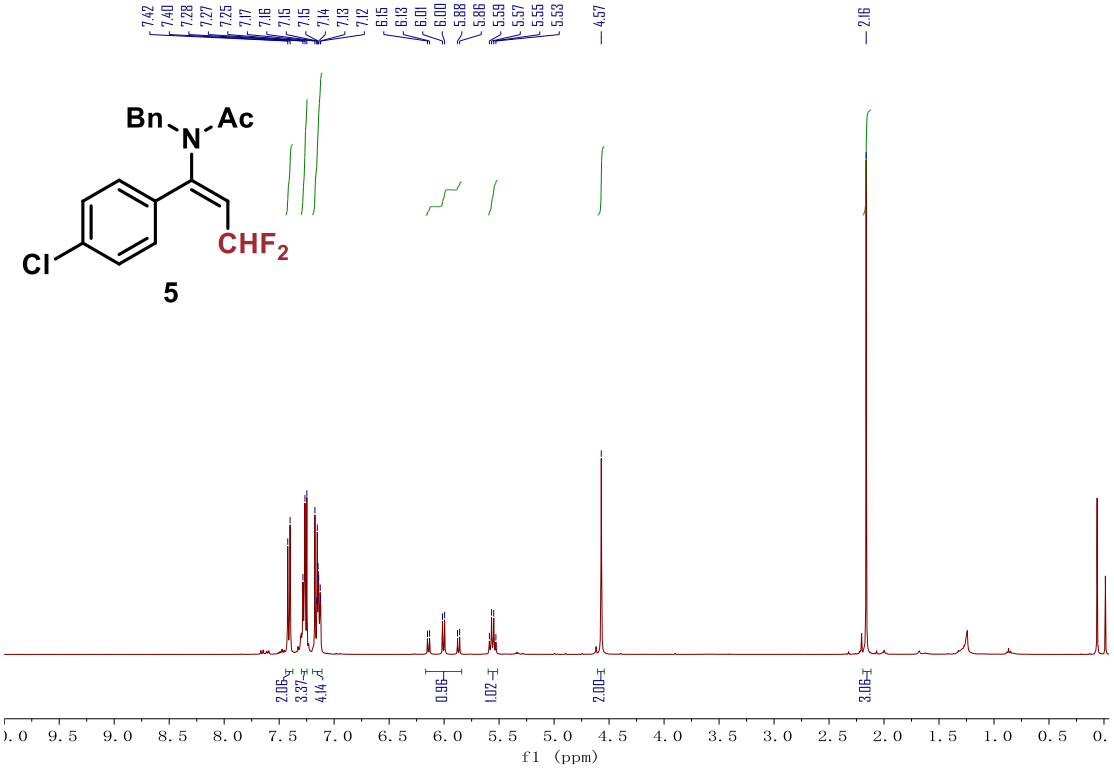
^{1}H NMR of compound 4 (400 MHz in $CDCl_3$)



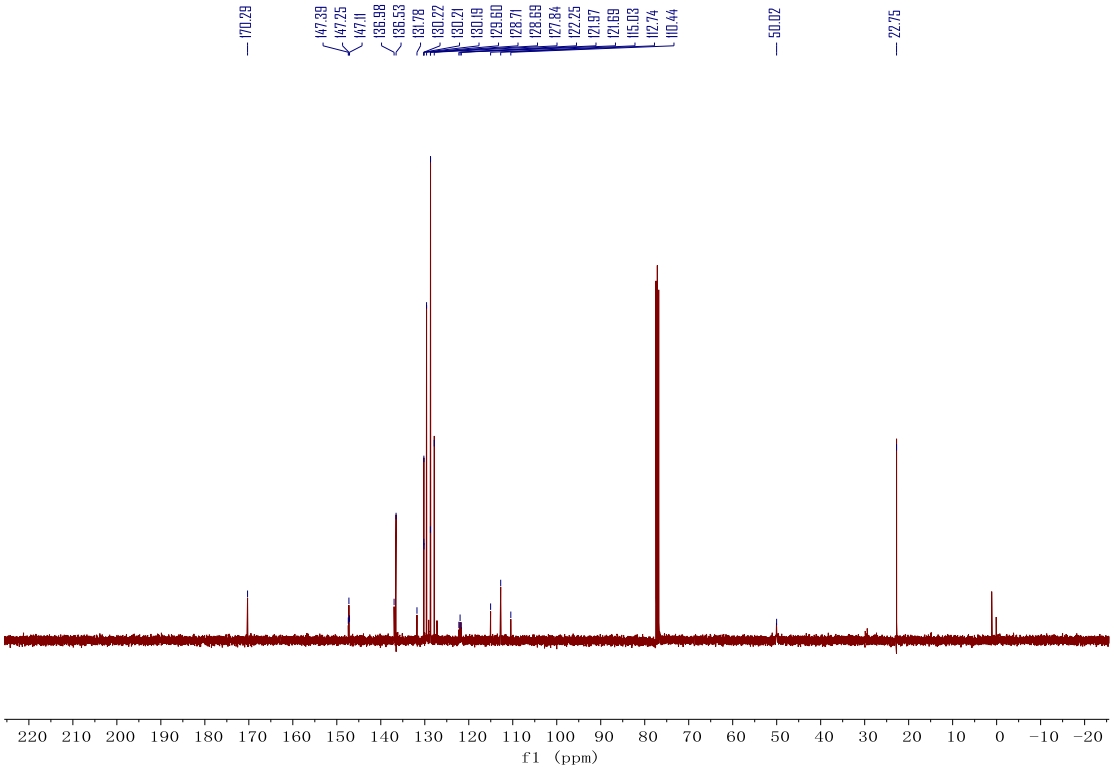
^{13}C NMR of compound 4 (101 MHz in $CDCl_3$)



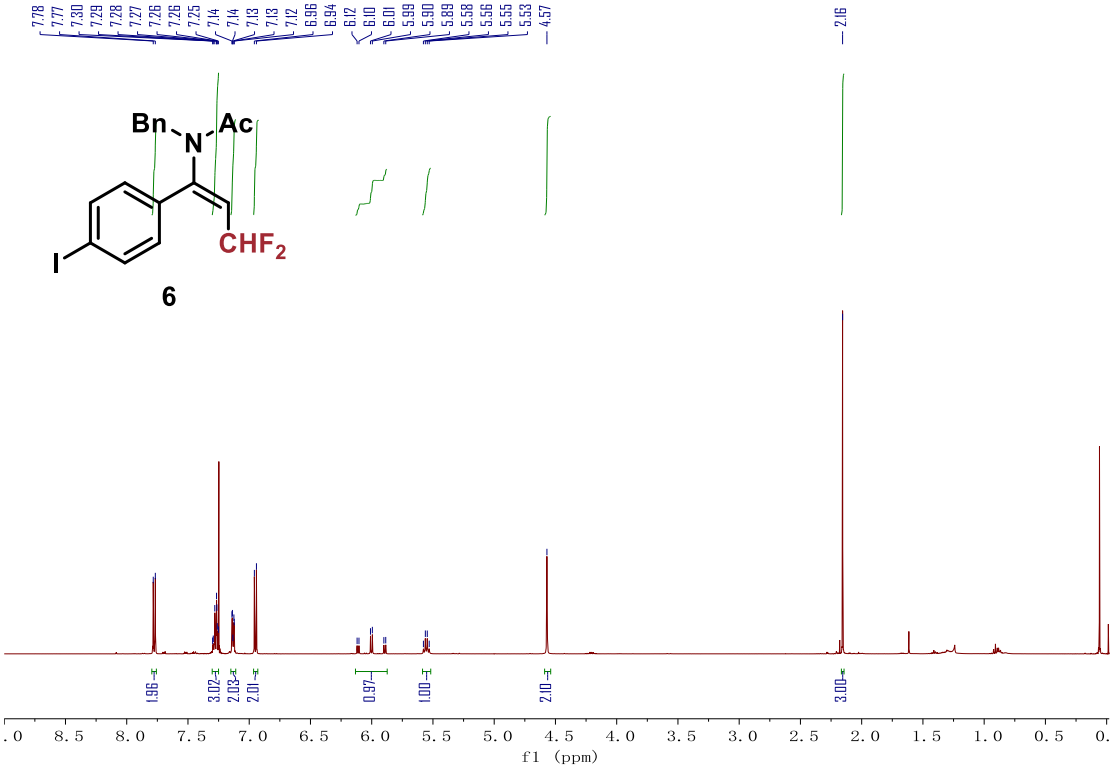
^{1}H NMR of compound 5 (400 MHz in $CDCl_3$)



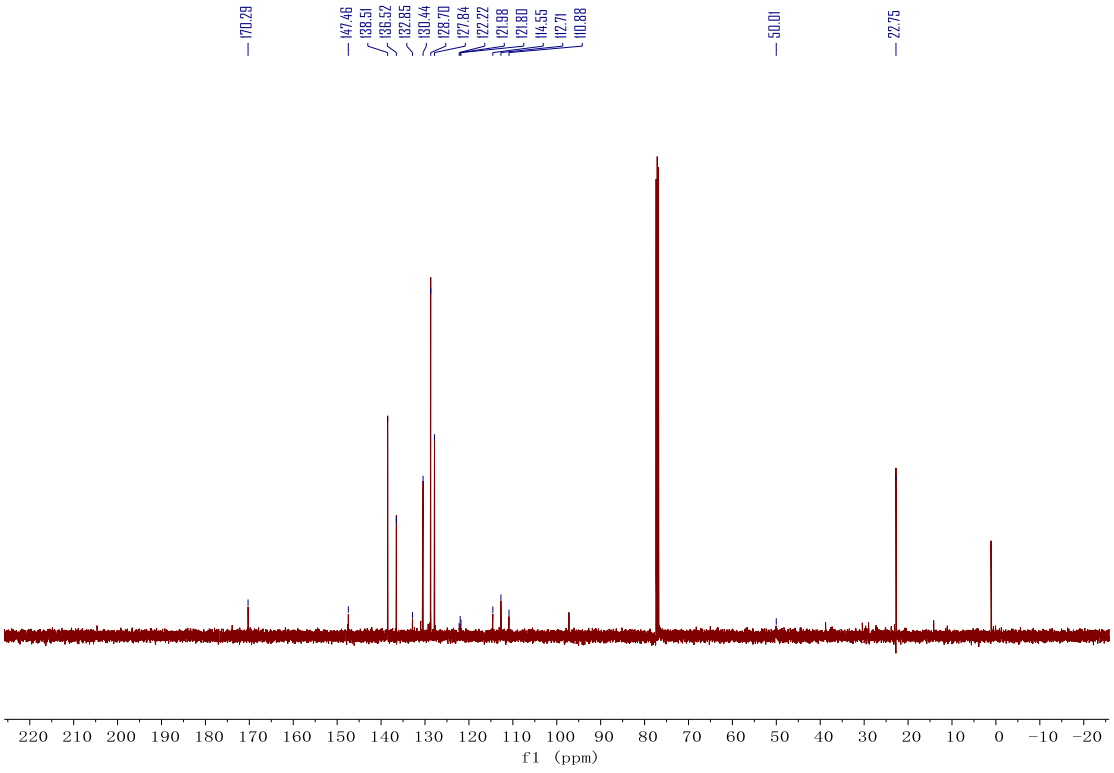
^{13}C NMR of compound 5 (101 MHz in $CDCl_3$)



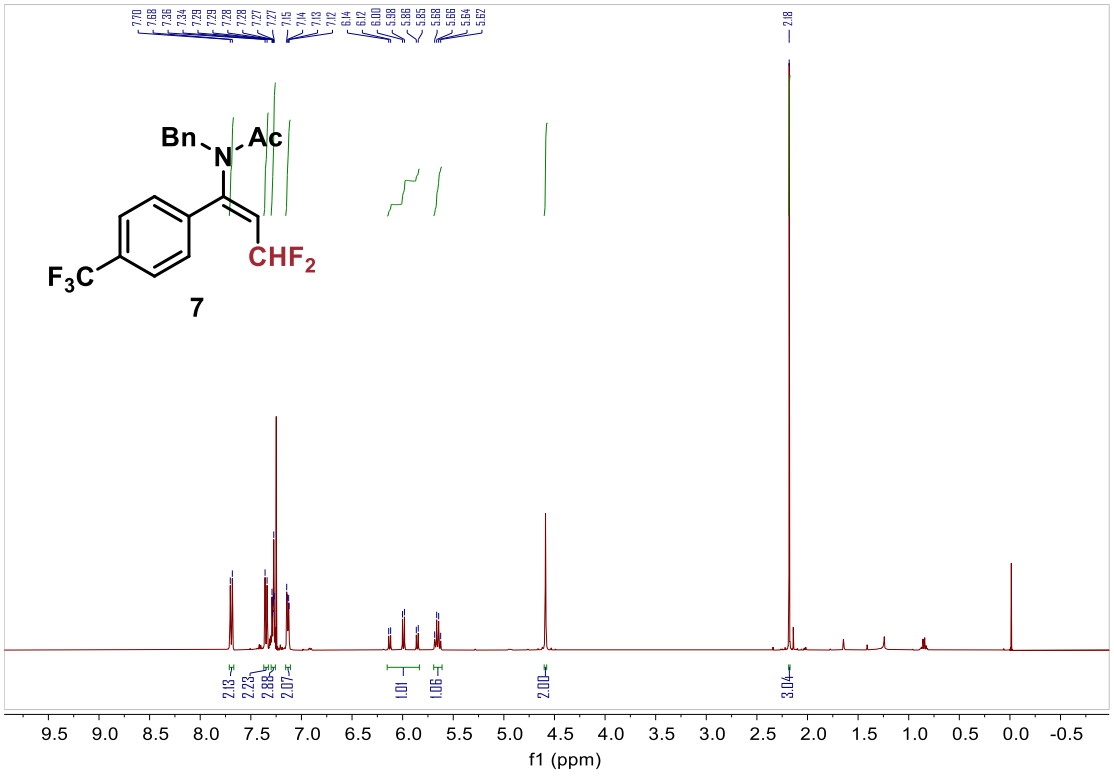
^{1}H NMR of compound 6 (400 MHz in $CDCl_3$)



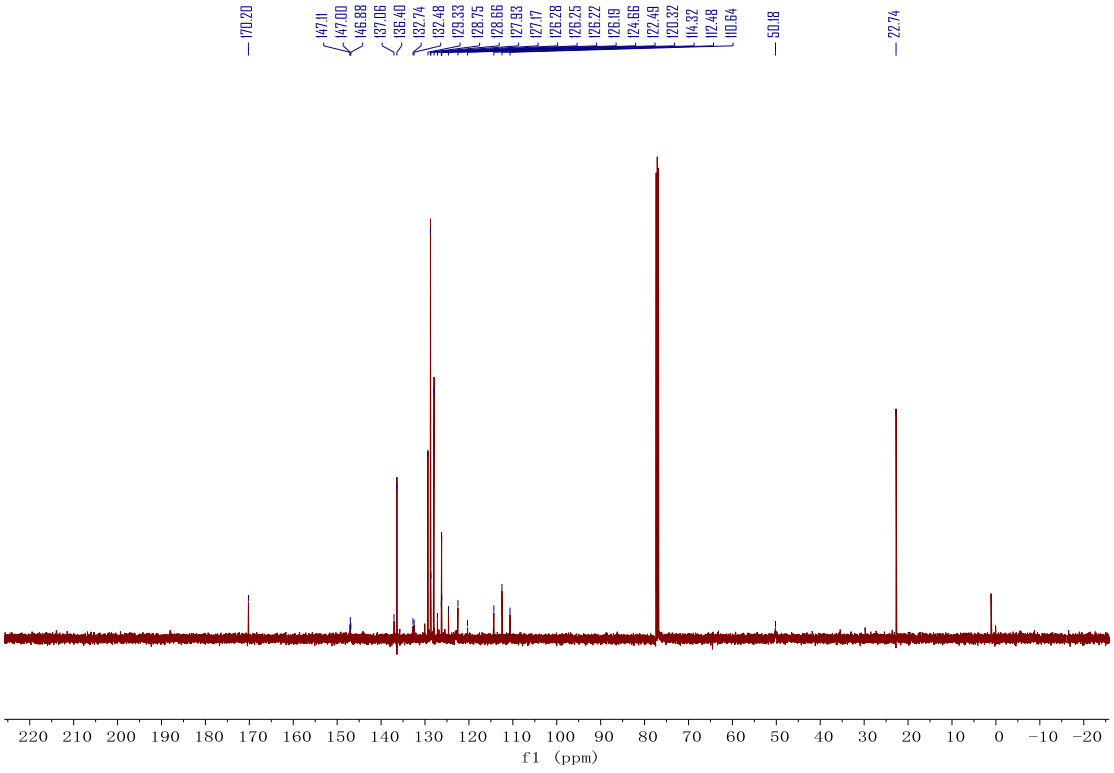
^{13}C NMR of compound 6 (101 MHz in $CDCl_3$)



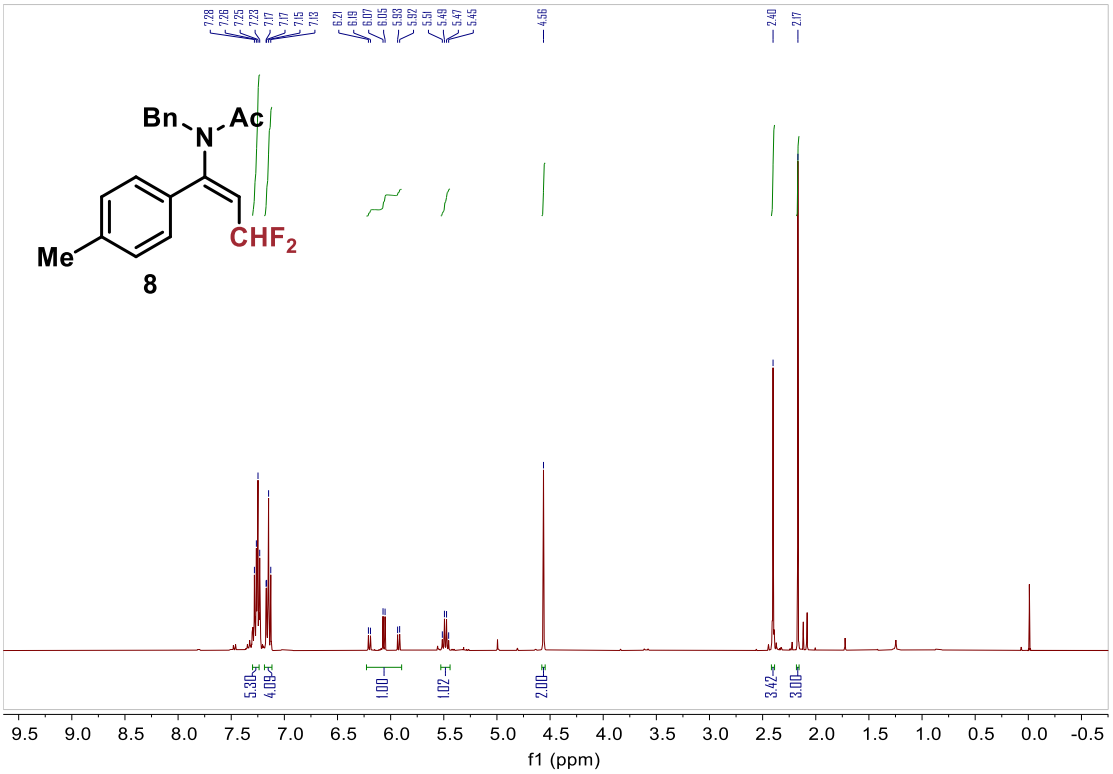
^{1}H NMR of compound 7 (400 MHz in $CDCl_3$)



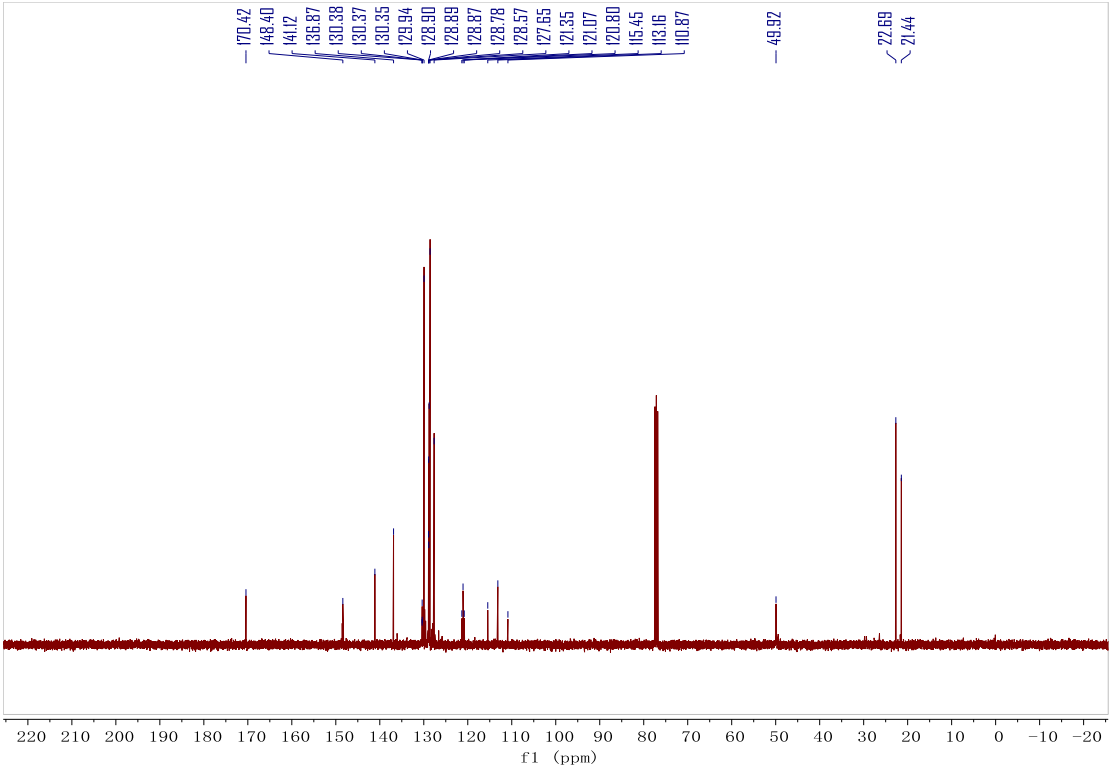
^{13}C NMR of compound 7 (101 MHz in $CDCl_3$)



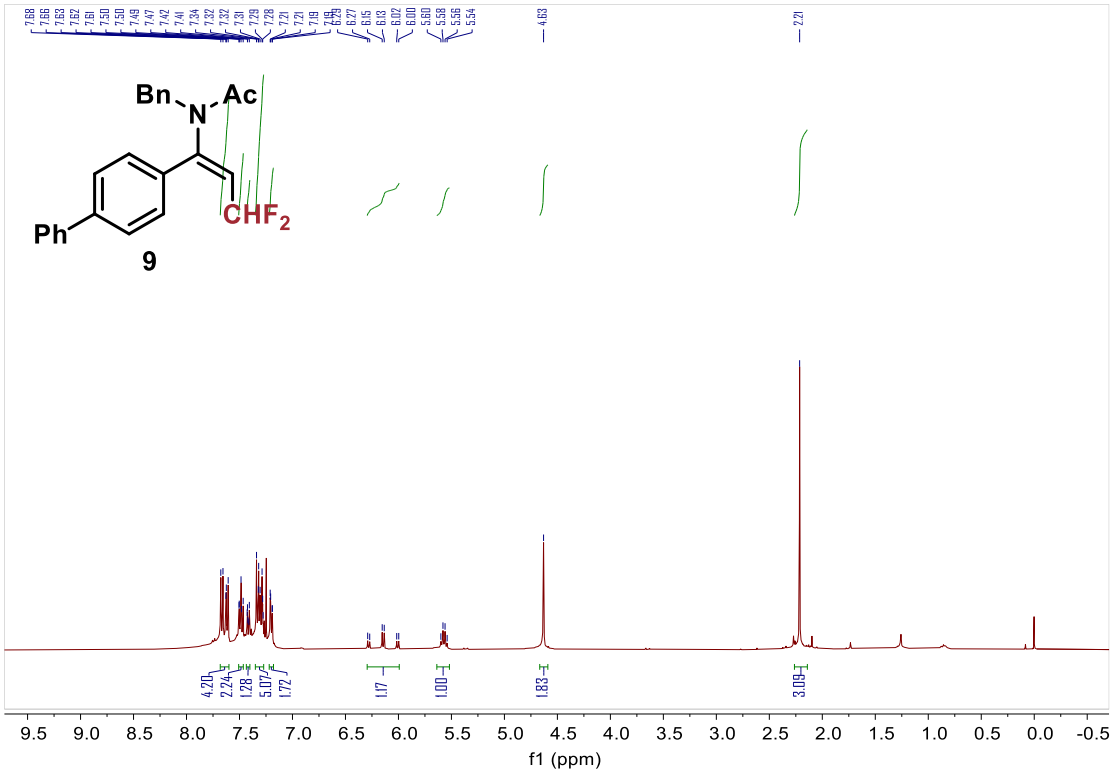
^{1}H NMR of compound 8 (400 MHz in $CDCl_3$)



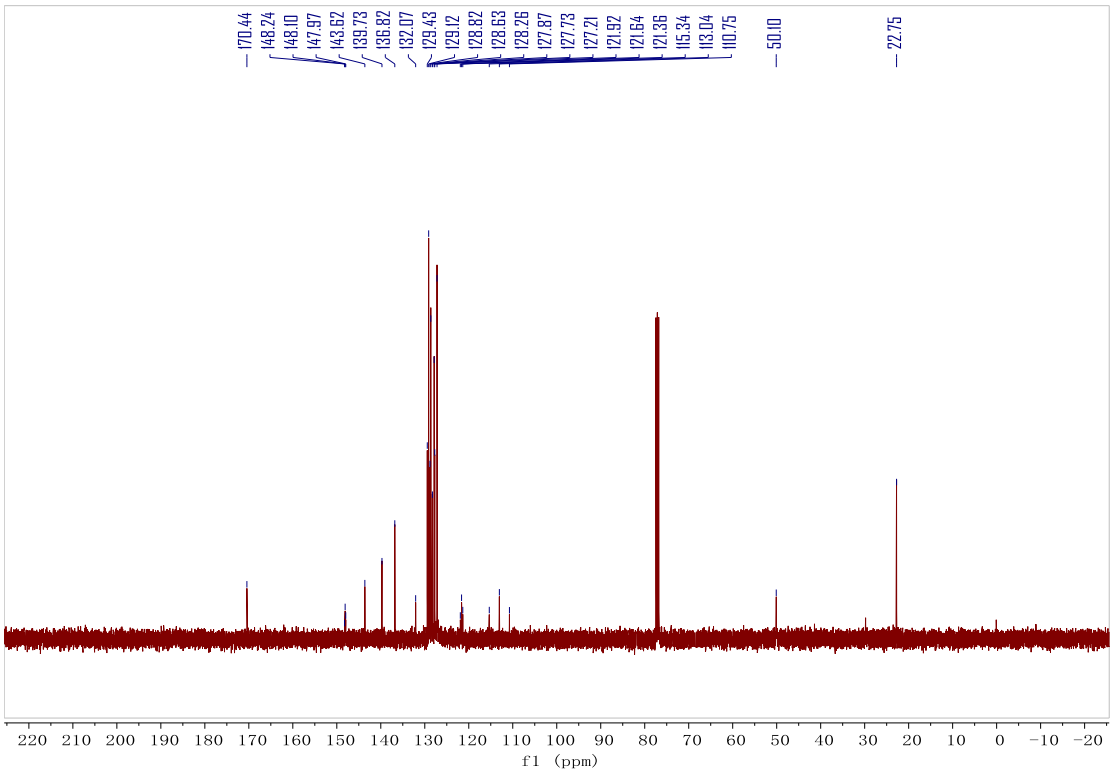
^{13}C NMR of compound 8 (101 MHz in $CDCl_3$)



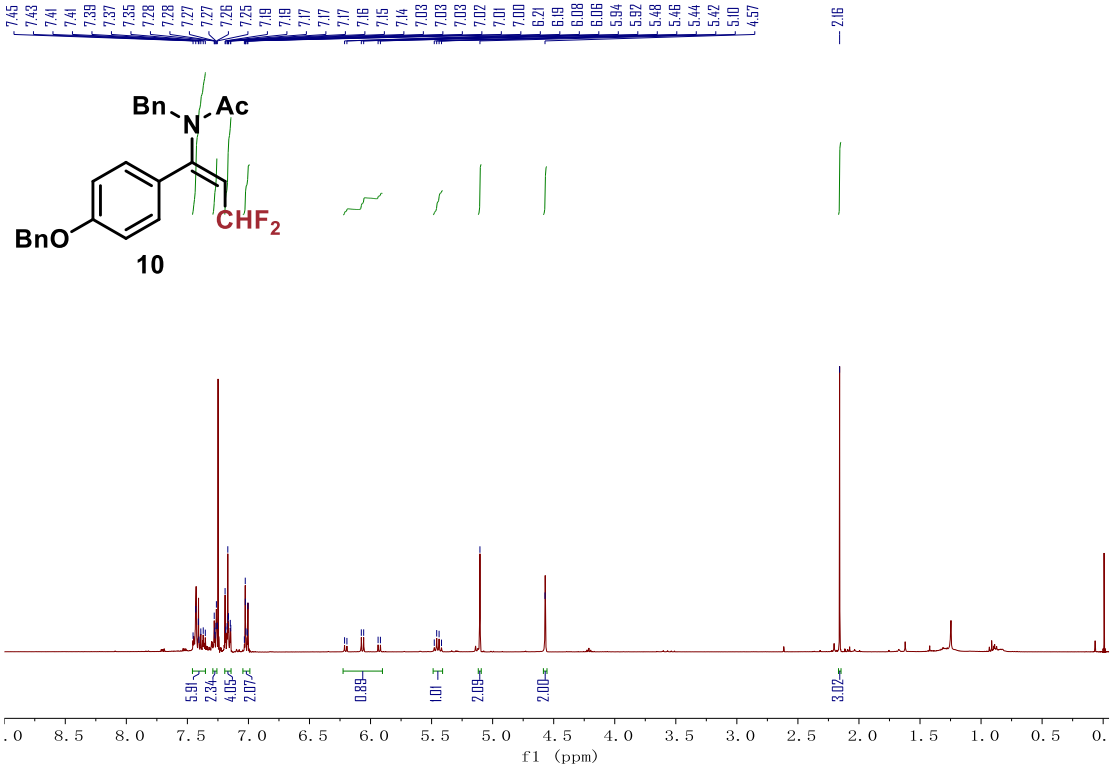
^{1}H NMR of compound 9 (400 MHz in $CDCl_3$)



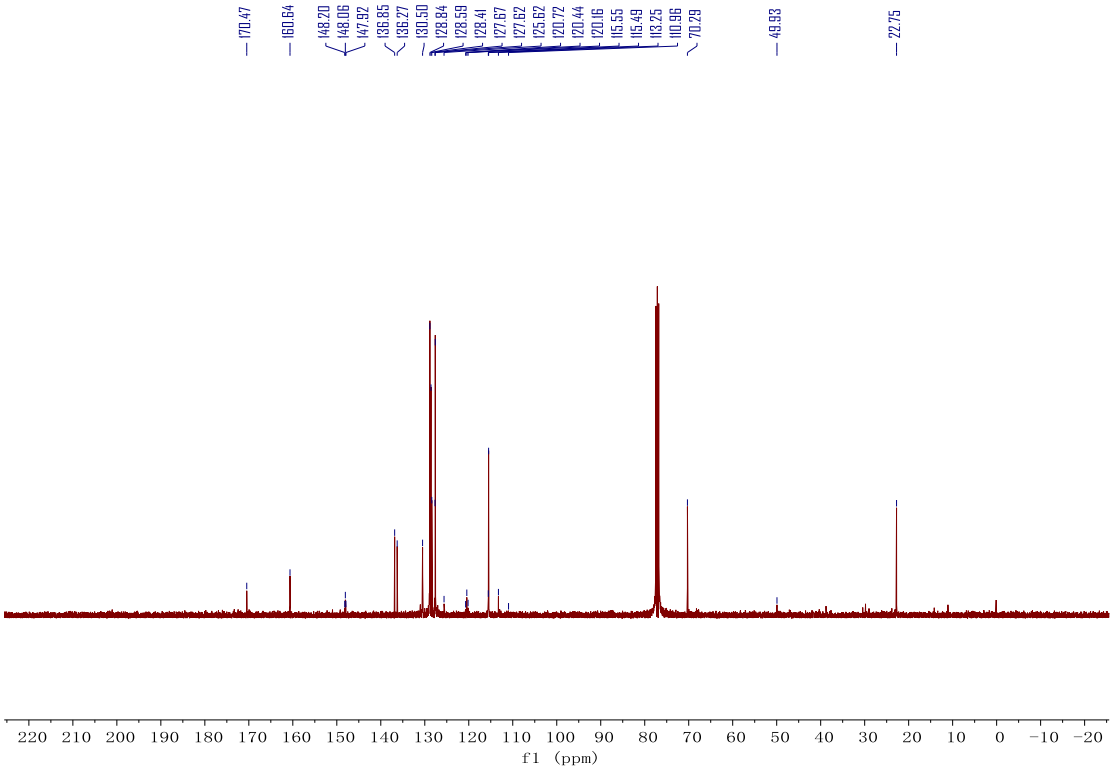
^{13}C NMR of compound 9 (101 MHz in $CDCl_3$)



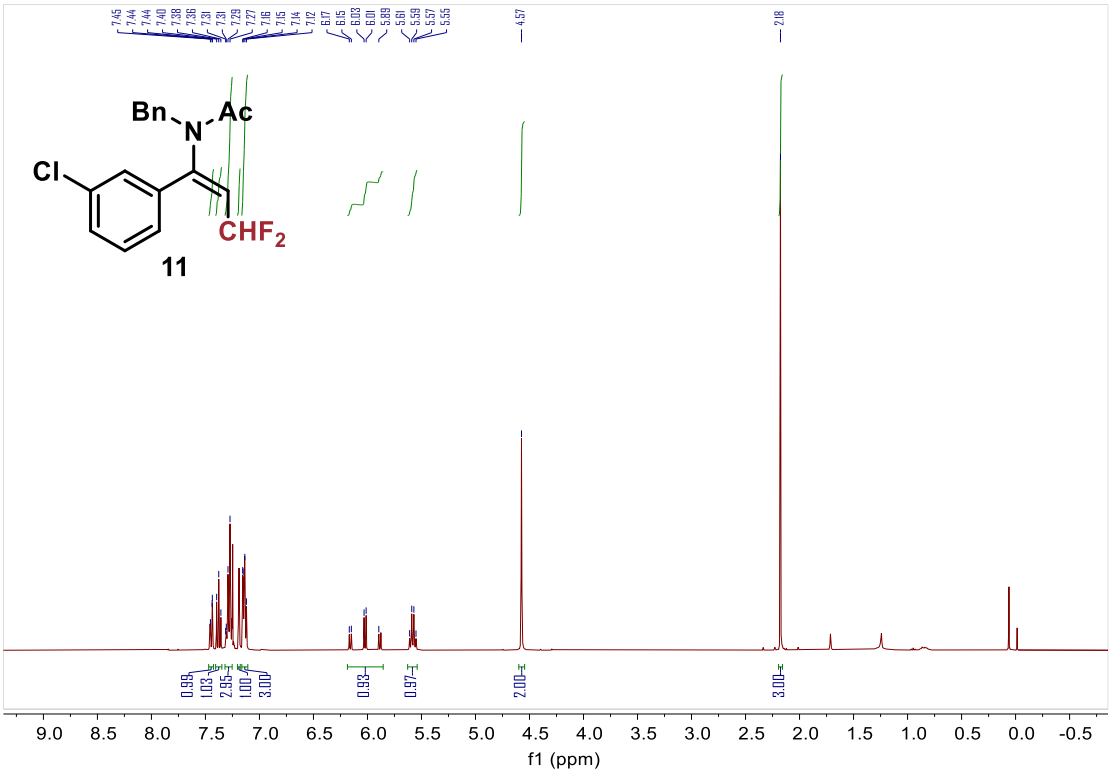
^{1}H NMR of compound 10 (400 MHz in $CDCl_3$)



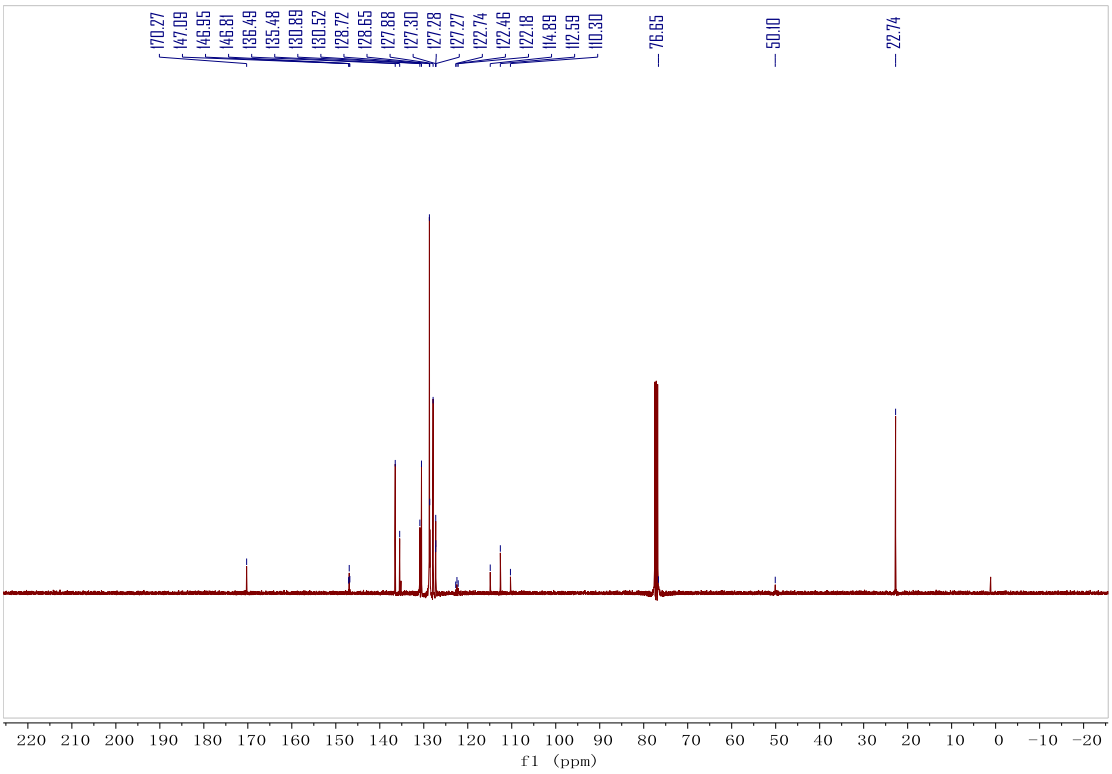
^{13}C NMR of compound 10 (101 MHz in $CDCl_3$)



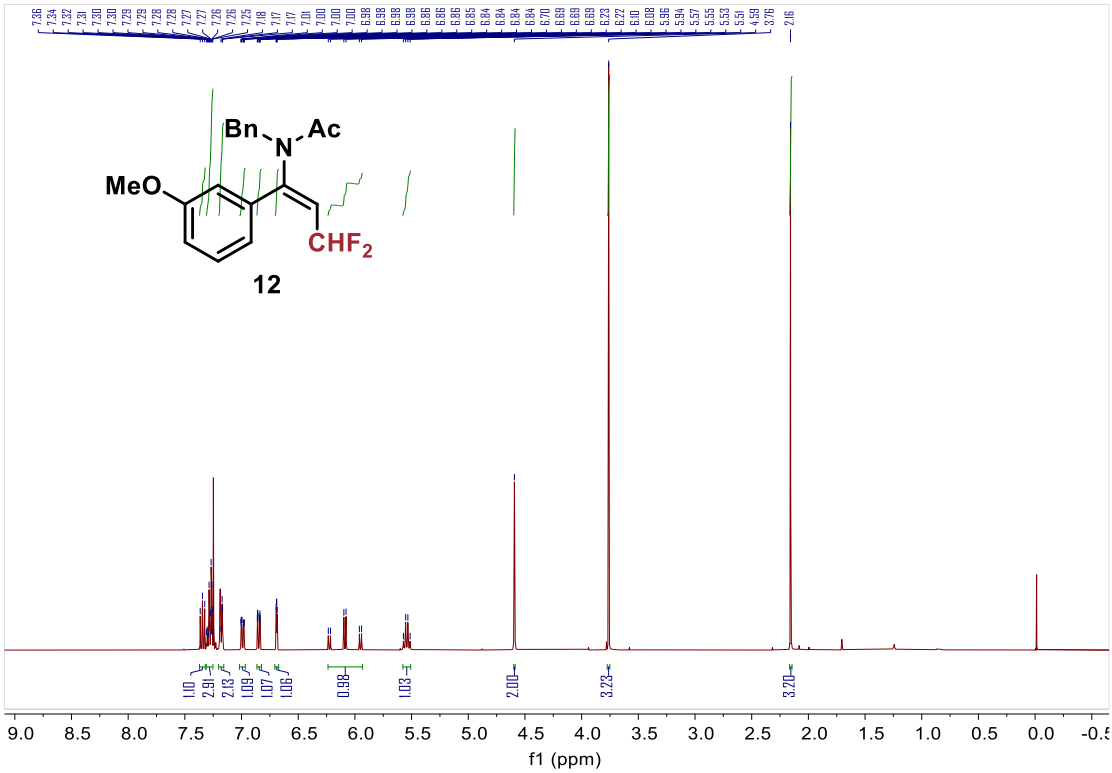
^{1}H NMR of compound 11 (400 MHz in $CDCl_3$)



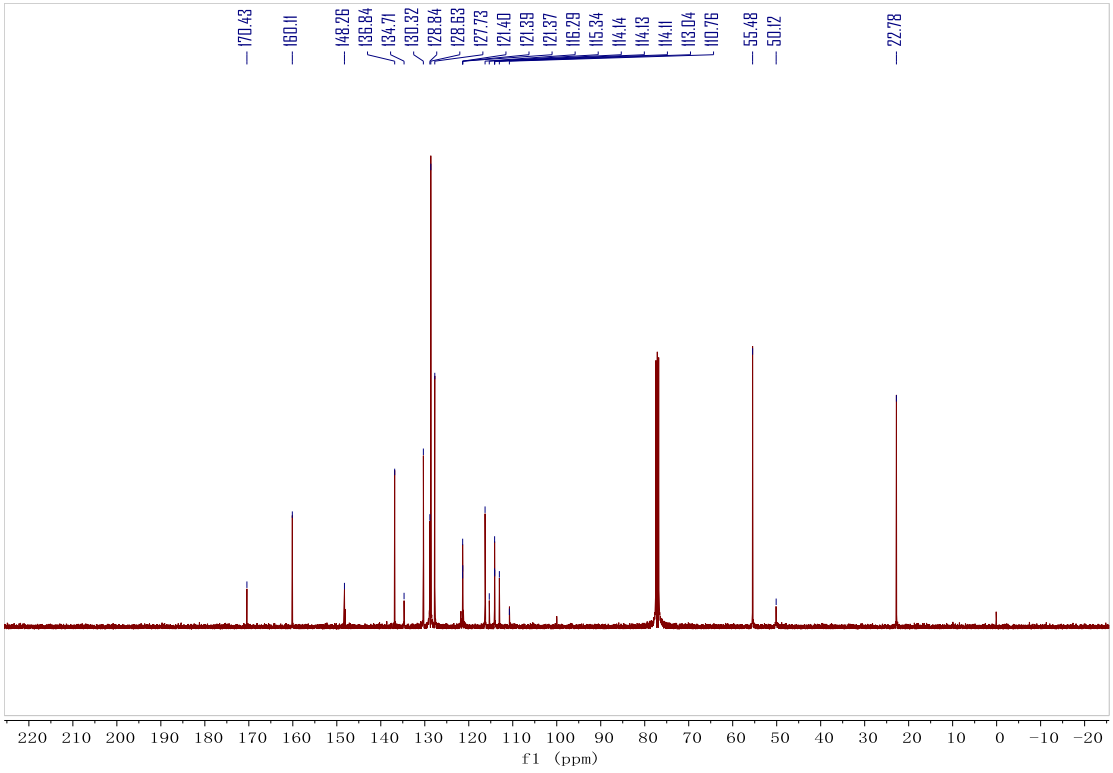
^{13}C NMR of compound 11 (101 MHz in $CDCl_3$)



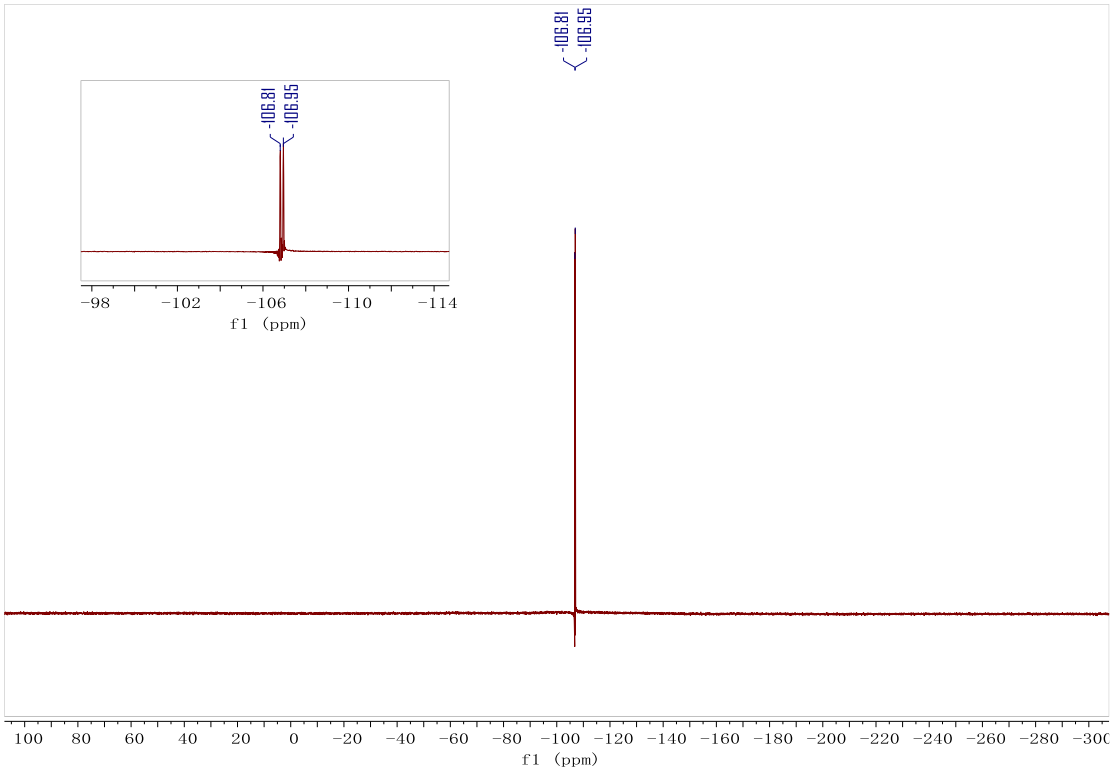
^{1}H NMR of compound 12 (400 MHz in $CDCl_3$)



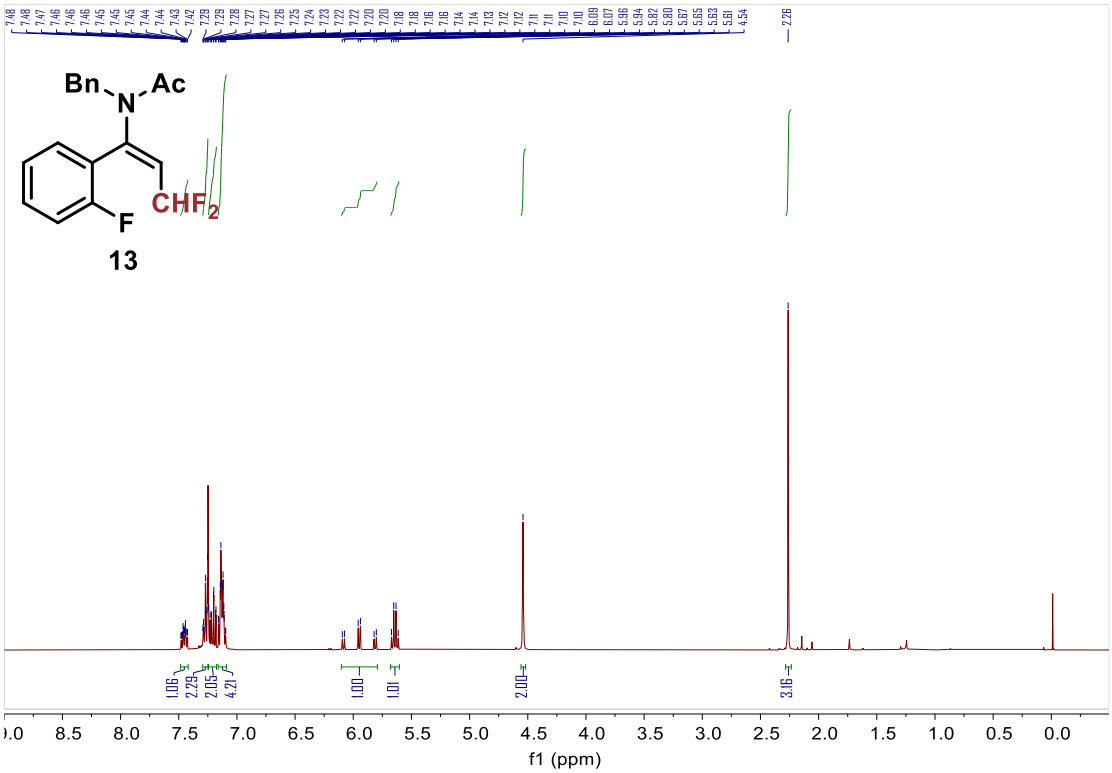
^{13}C NMR of compound 12 (101 MHz in $CDCl_3$)



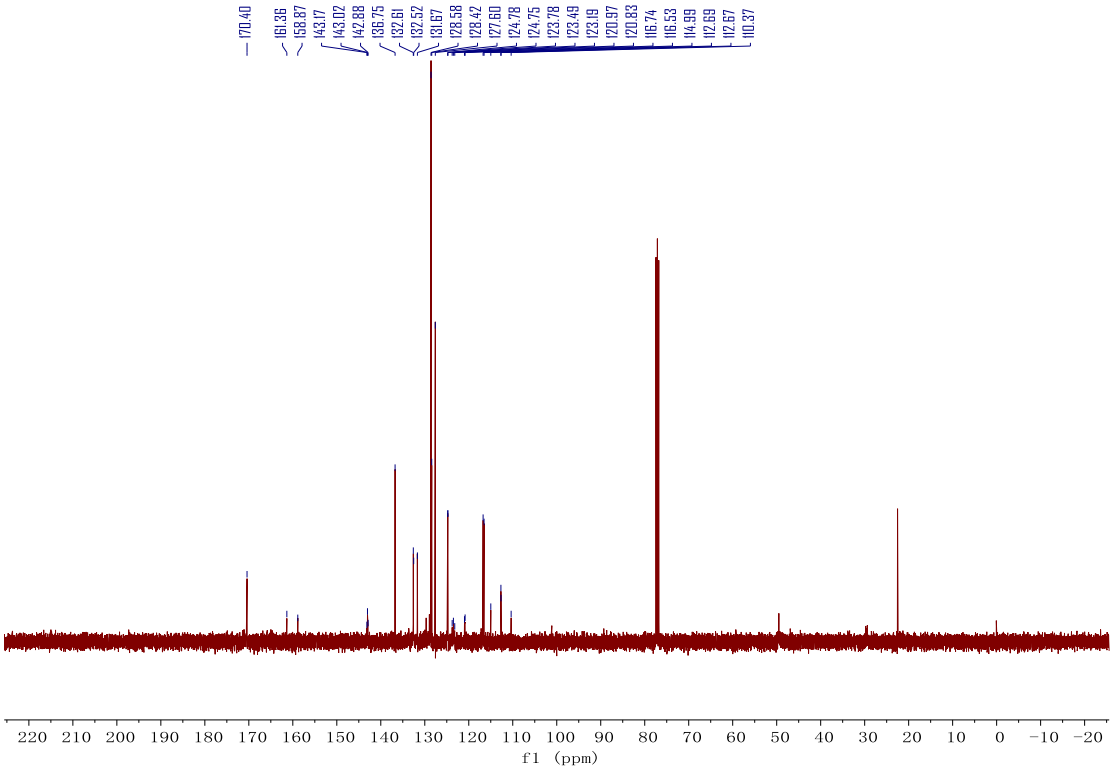
^{19}F NMR of compound 12 (377 MHz in $CDCl_3$)



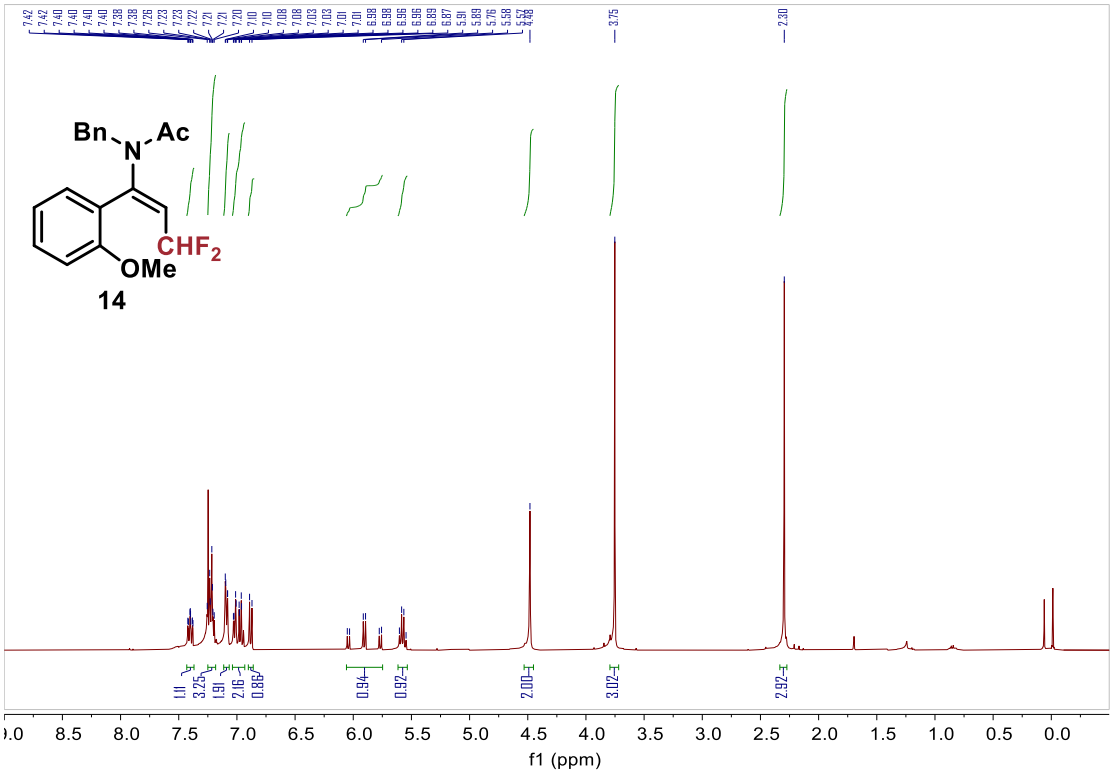
^{1}H NMR of compound 13 (400 MHz in $CDCl_3$)



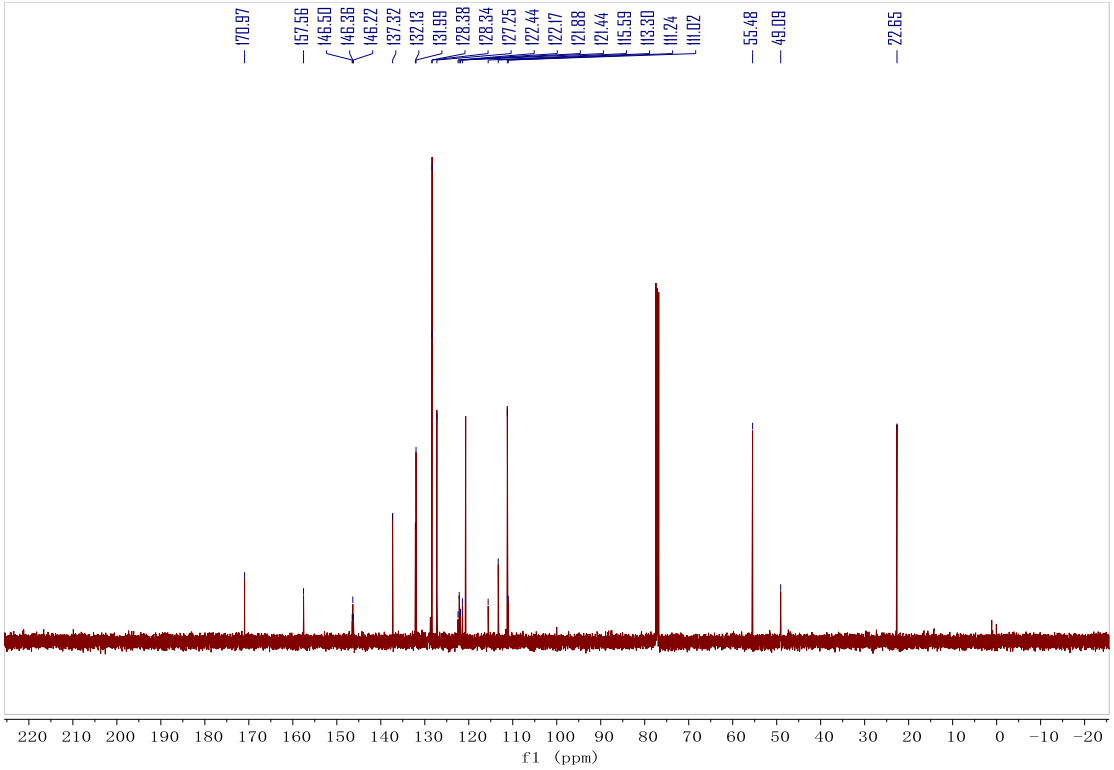
^{13}C NMR of compound 13 (101 MHz in $CDCl_3$)



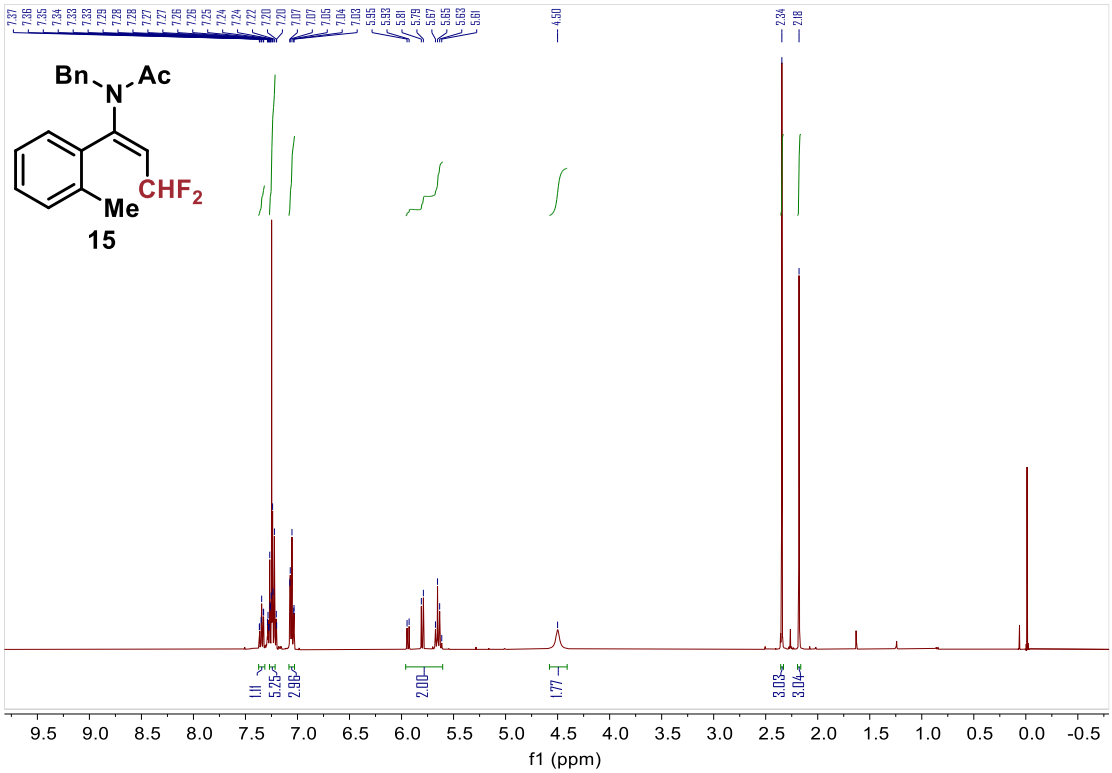
^{1}H NMR of compound 14 (400 MHz in $CDCl_3$)



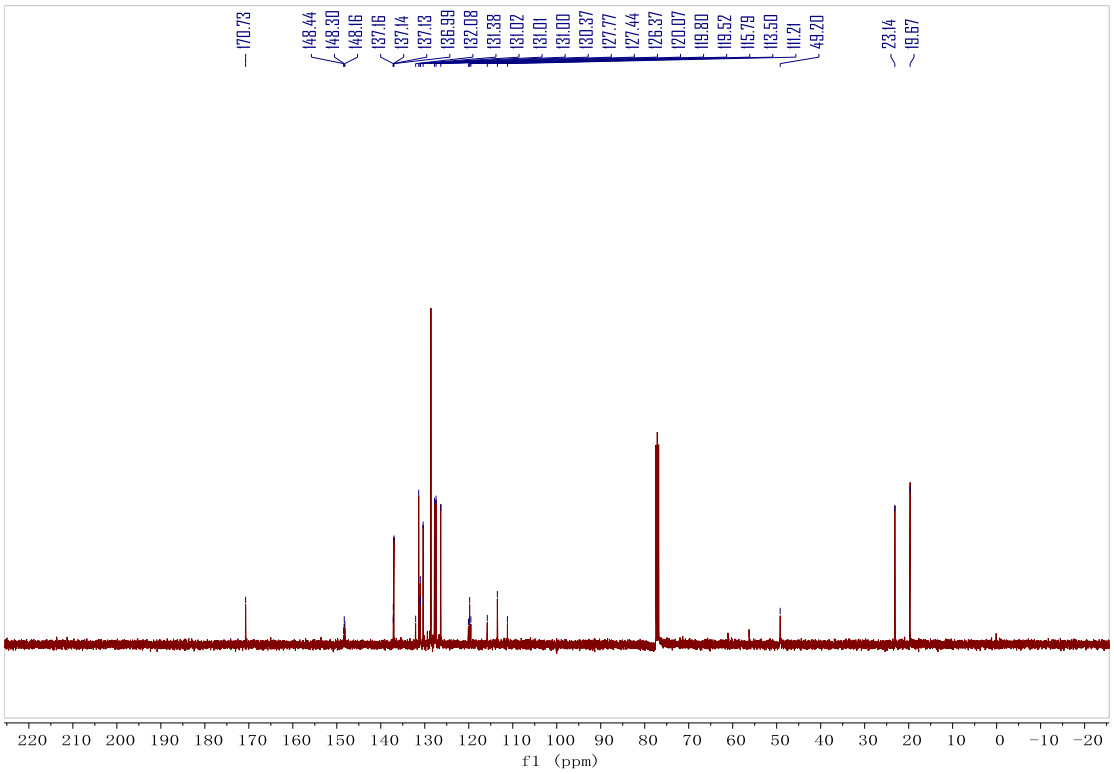
^{13}C NMR of compound 14 (101 MHz in $CDCl_3$)



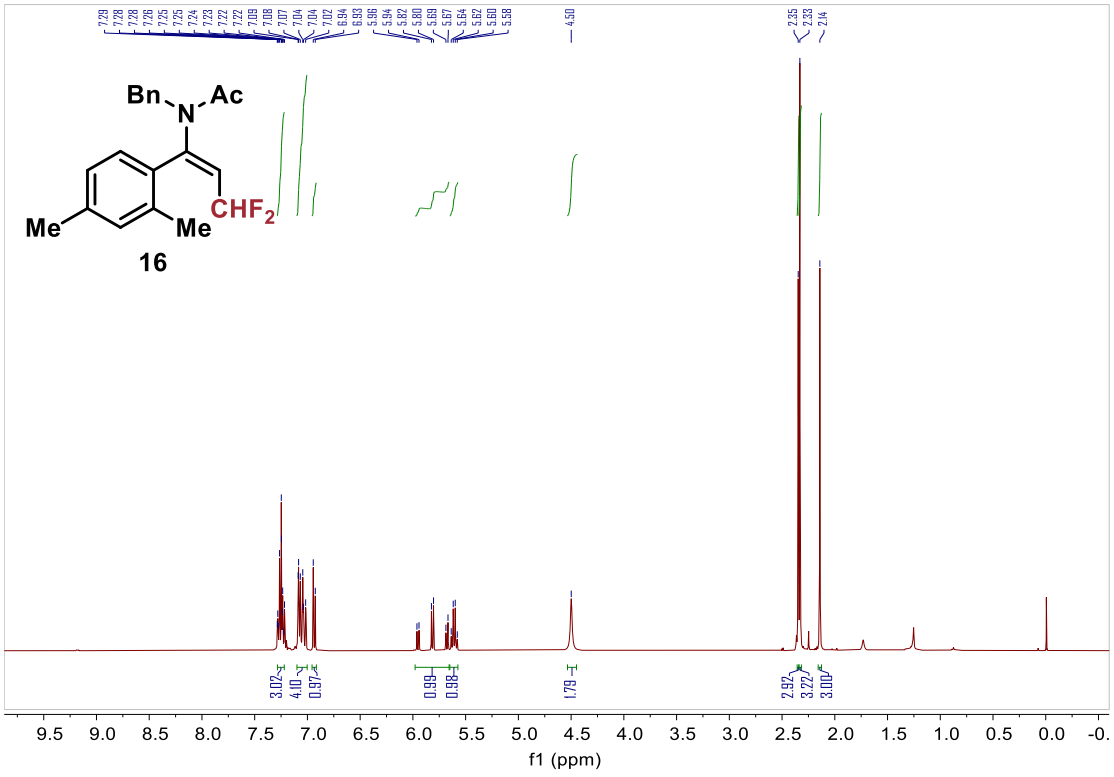
^{1}H NMR of compound 15 (400 MHz in $CDCl_3$)



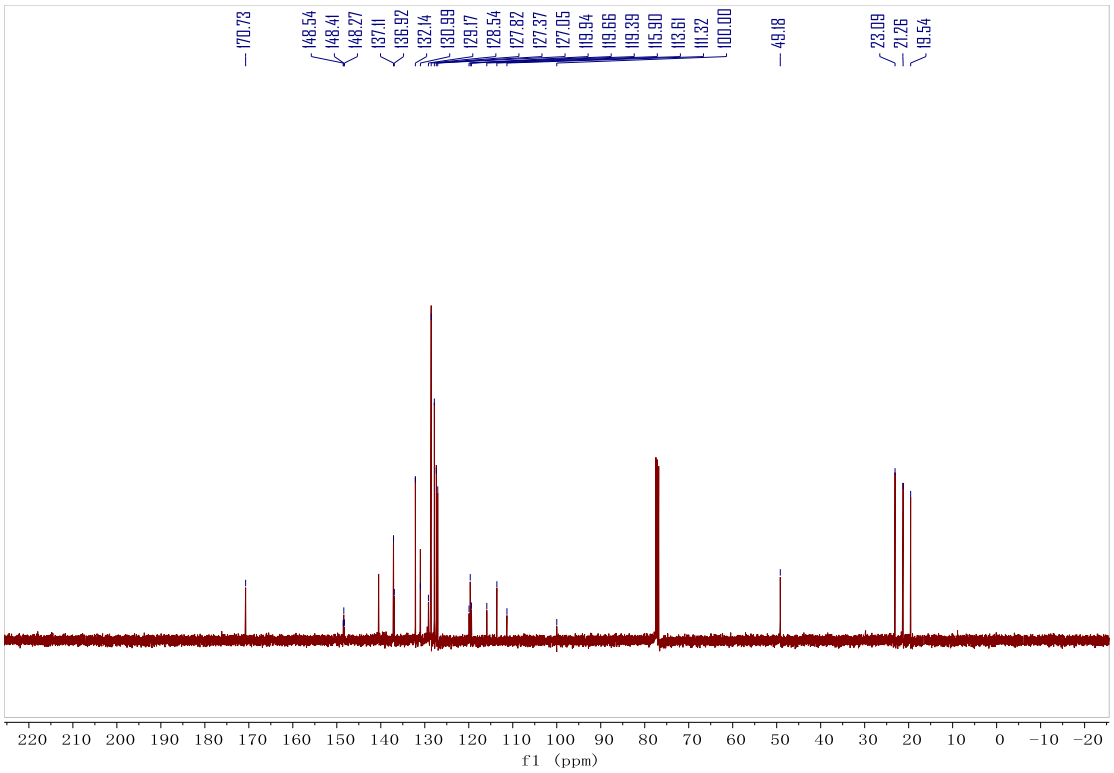
^{13}C NMR of compound 15 (101 MHz in $CDCl_3$)



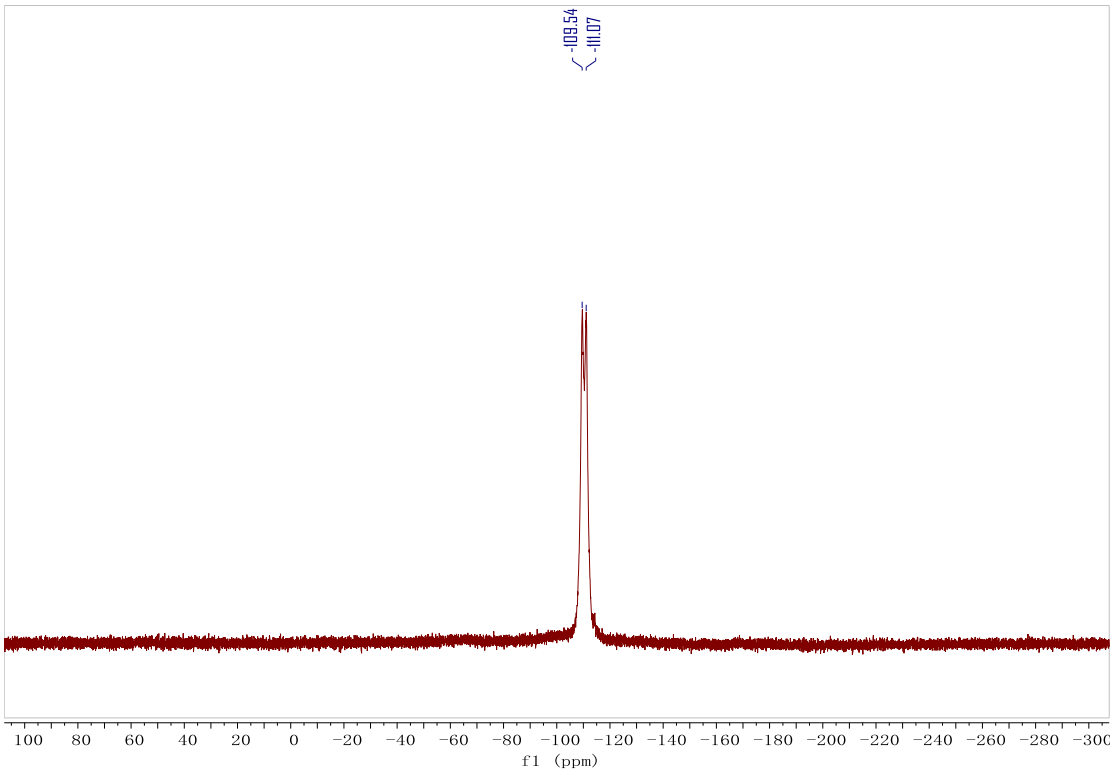
^{1}H NMR of compound 16 (400 MHz in $CDCl_3$)



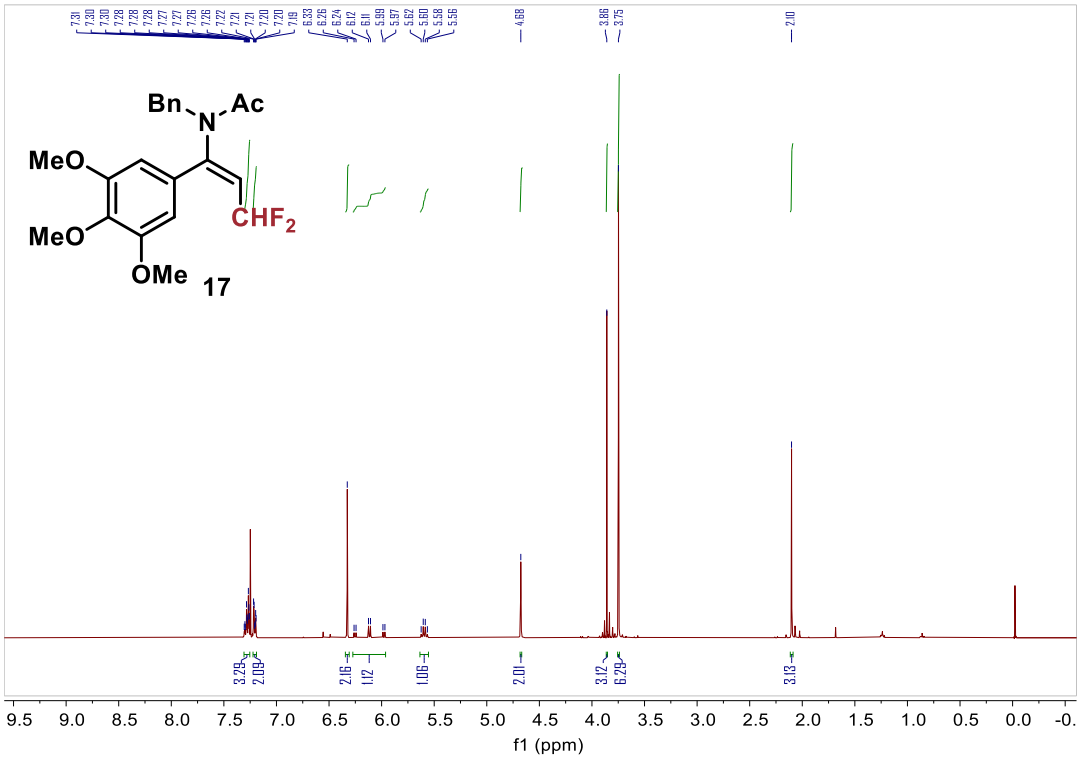
^{13}C NMR of compound 16 (101 MHz in $CDCl_3$)



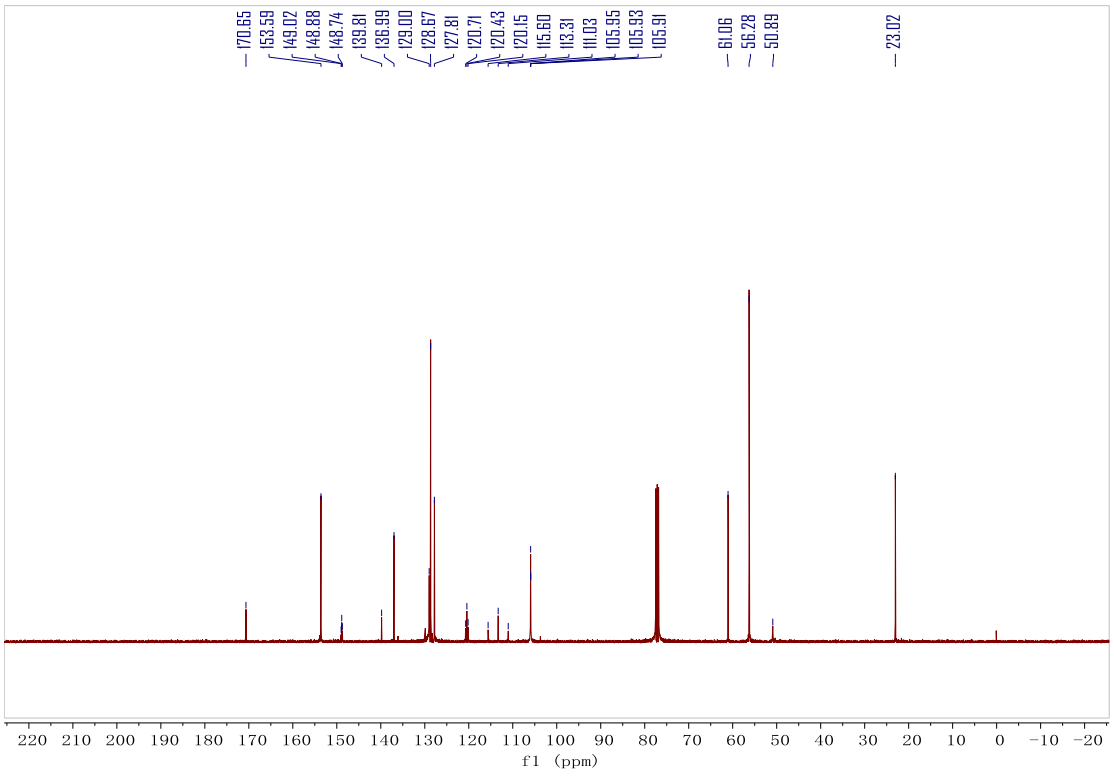
^{19}F NMR of compound 16 (376 MHz, CD_2Cl_2)



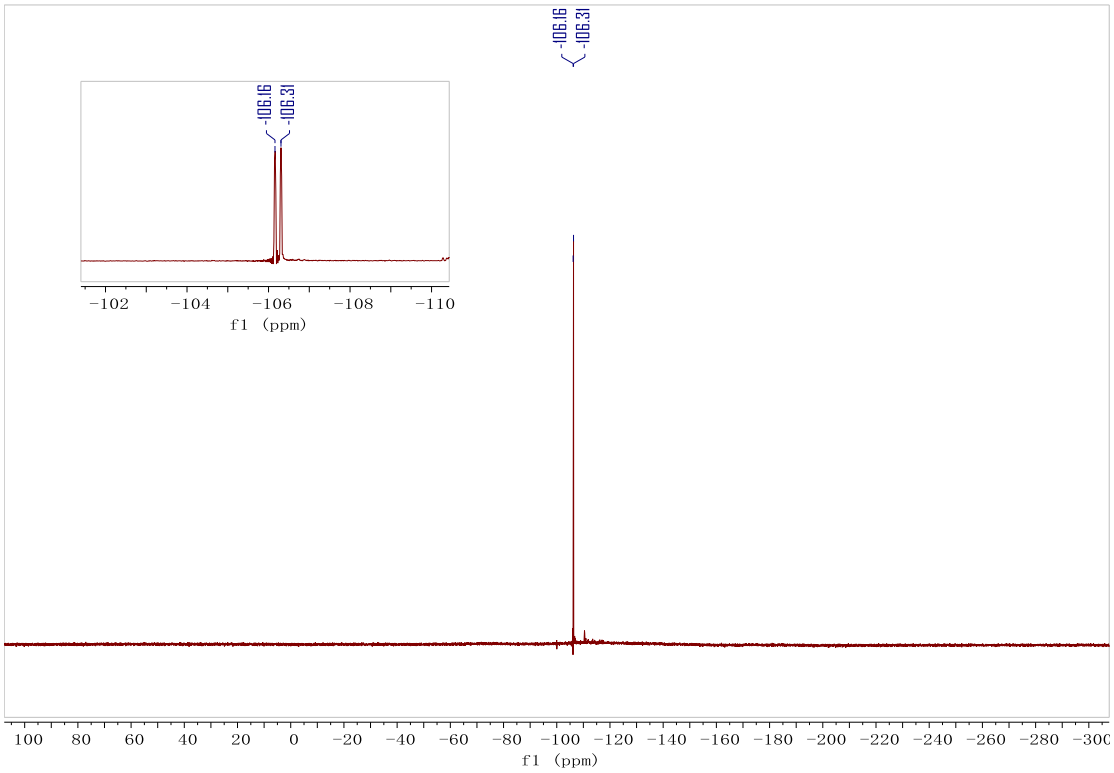
^{1}H NMR of compound 17 (400 MHz in $CDCl_3$)



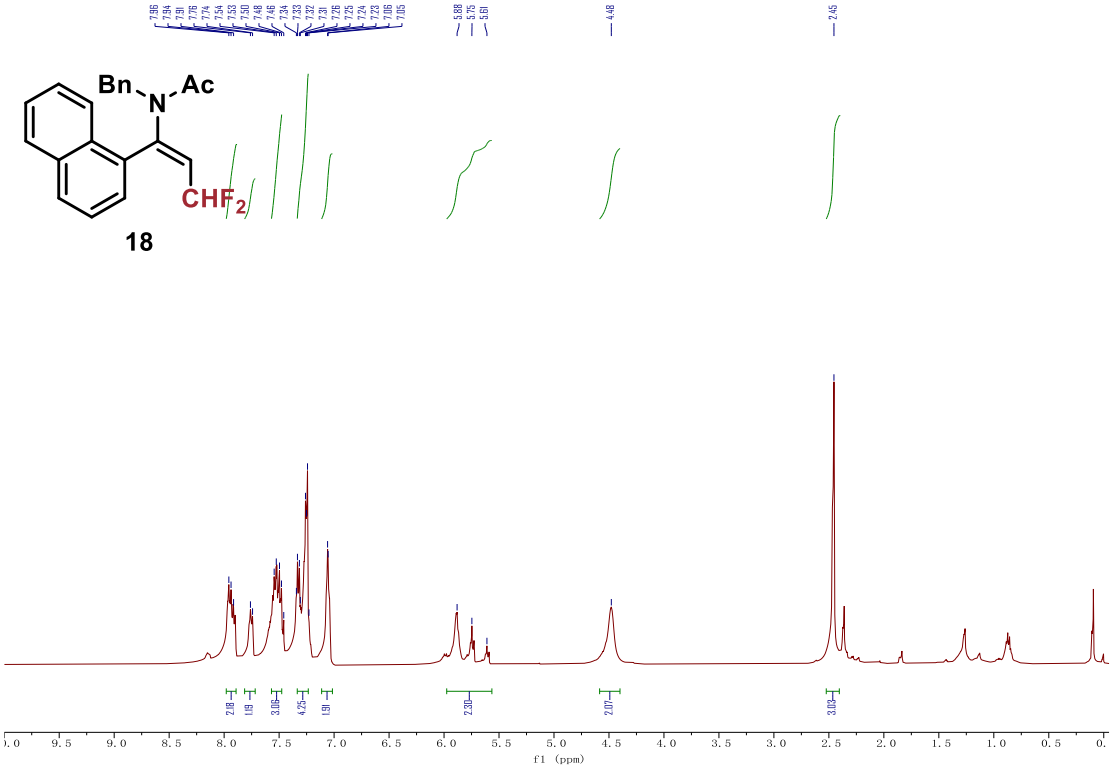
^{13}C NMR of compound 17 (101 MHz in $CDCl_3$)



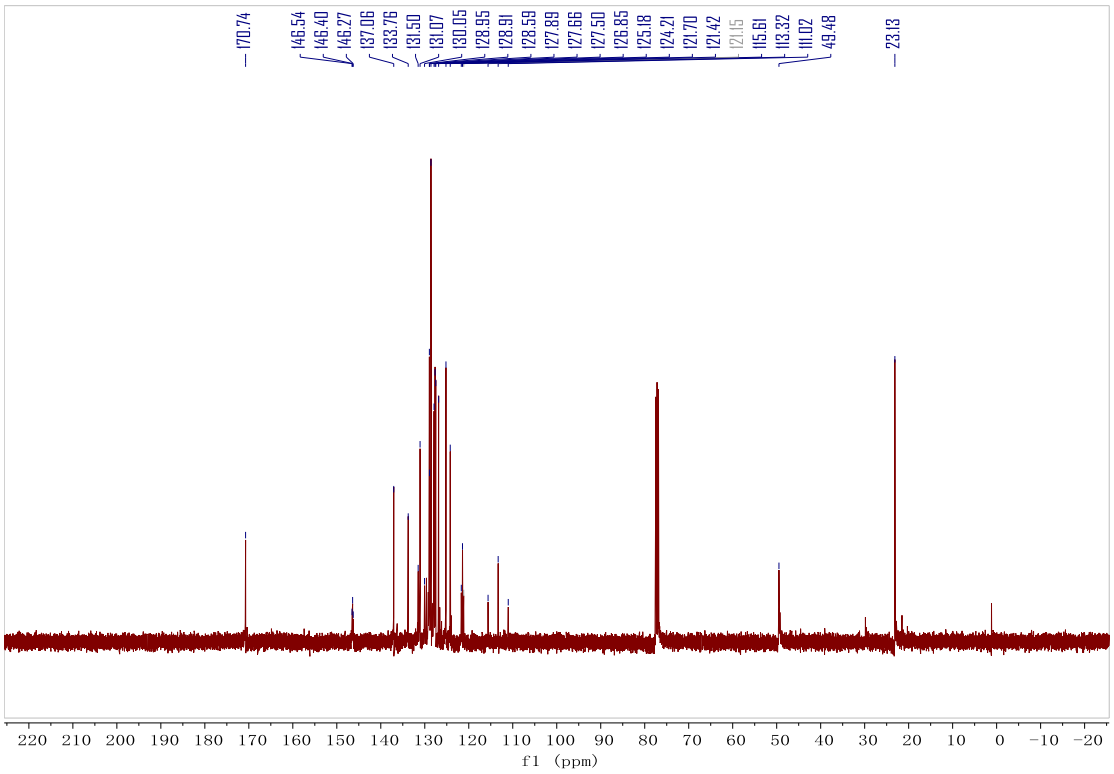
^{19}F NMR of compound 17 (377 MHz in $CDCl_3$)



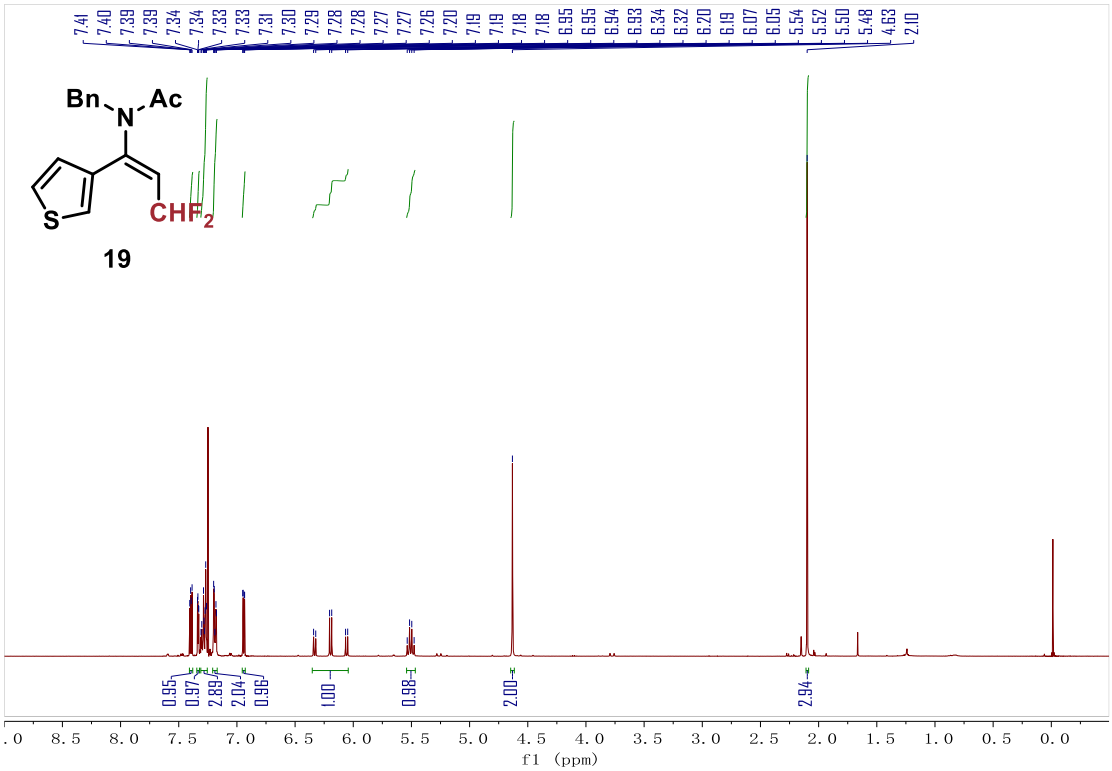
^{1}H NMR of compound 18 (400 MHz in $CDCl_3$)



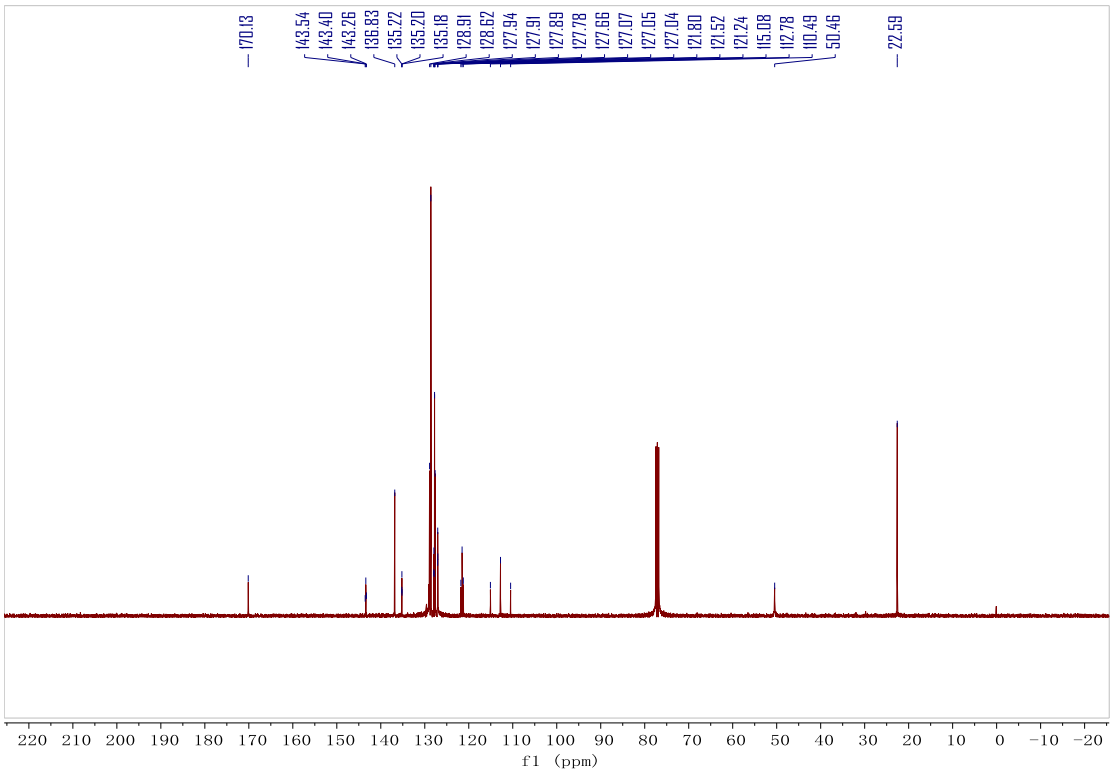
^{13}C NMR of compound 18 (101 MHz in $CDCl_3$)



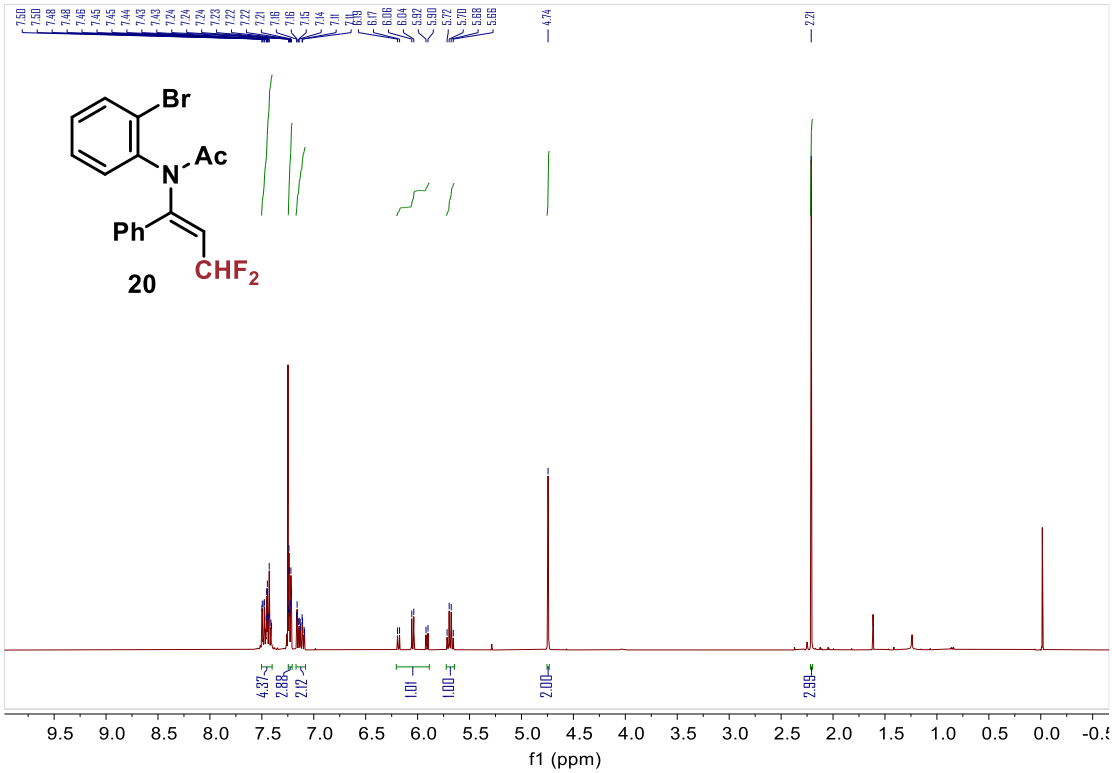
^{1}H NMR of compound 19 (400 MHz in $CDCl_3$)



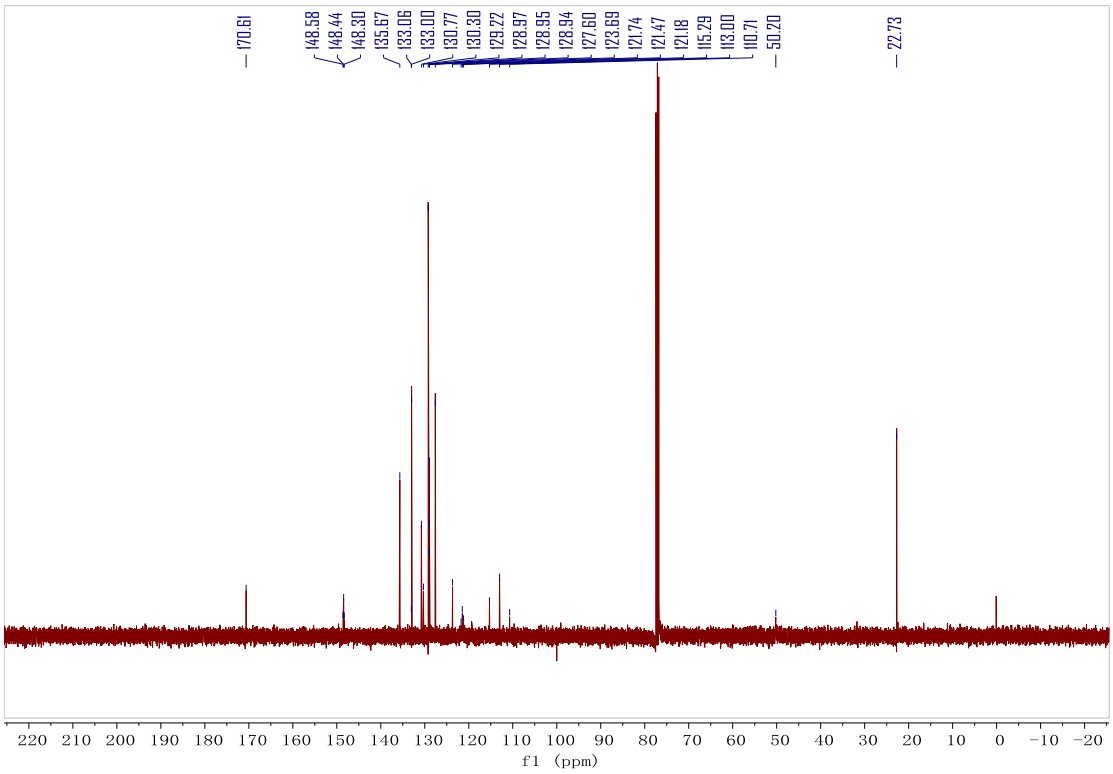
^{13}C NMR of compound 19 (101 MHz in $CDCl_3$)



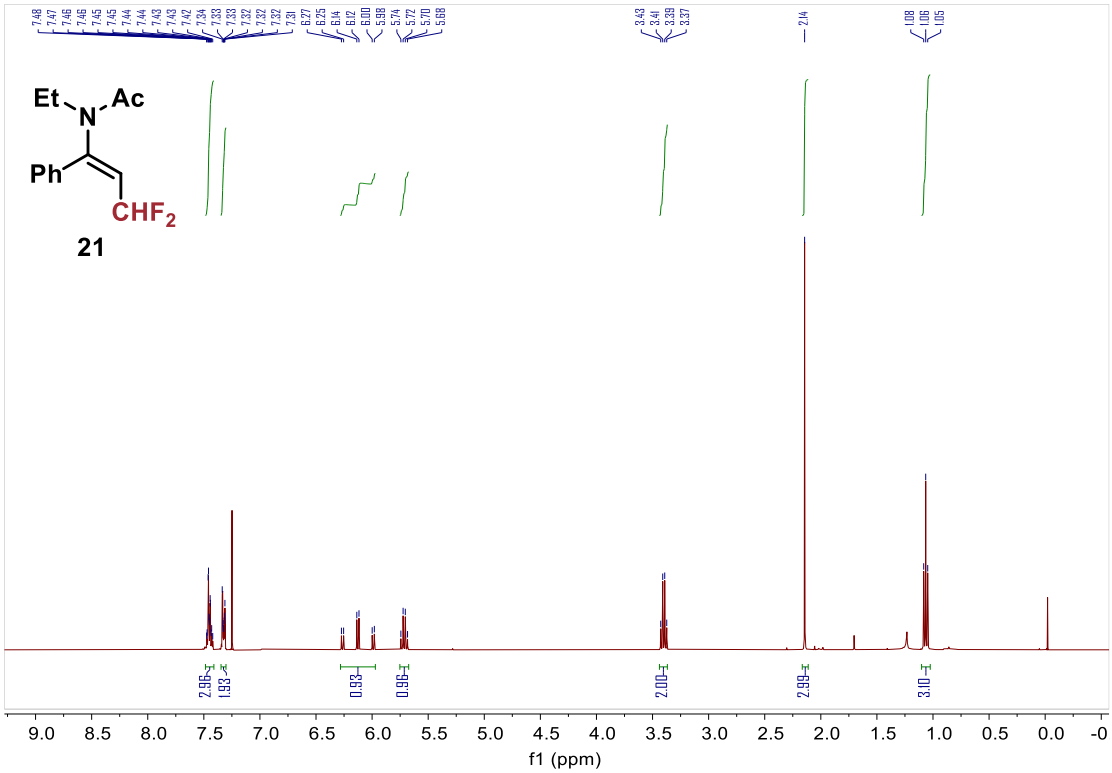
^{1}H NMR of compound 20 (400 MHz in $CDCl_3$)



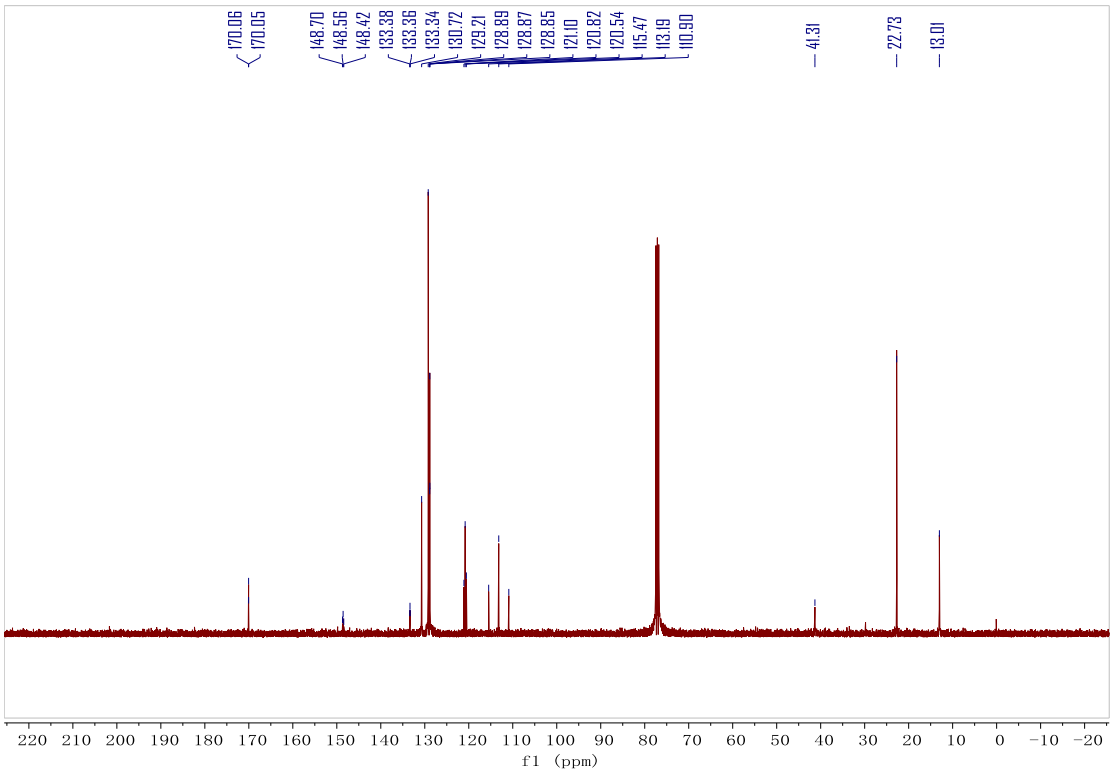
^{13}C NMR of compound 20 (101 MHz in $CDCl_3$)



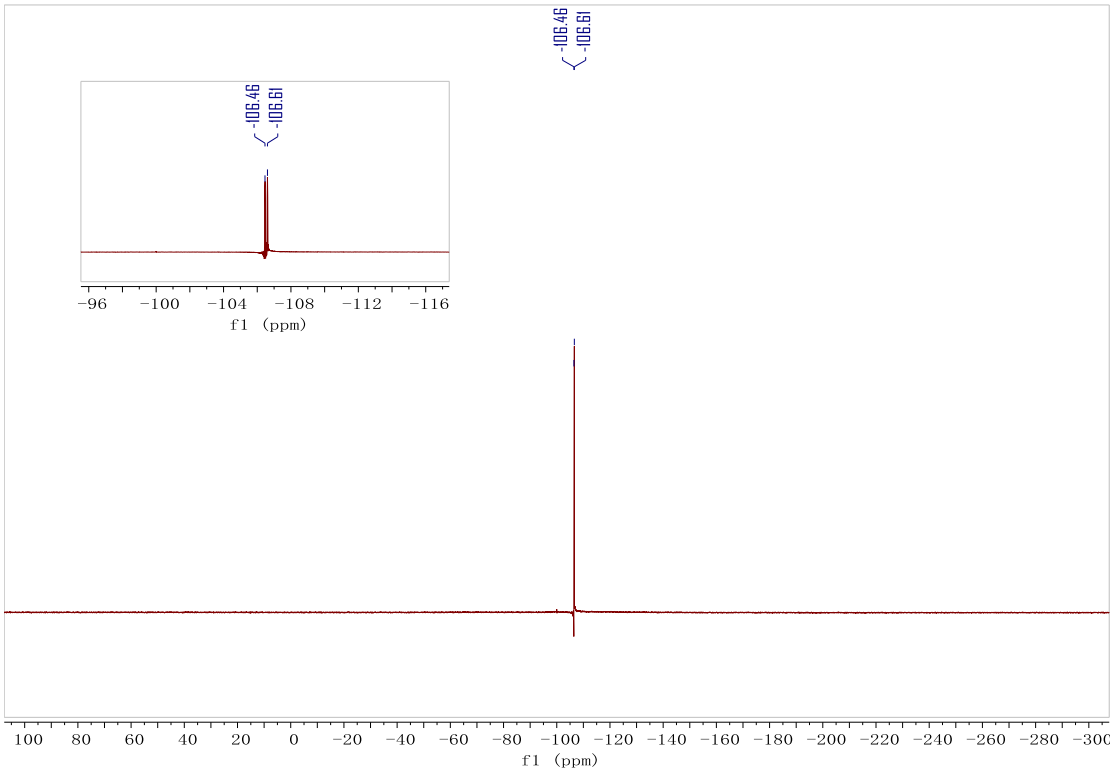
^{1}H NMR of compound 21 (400 MHz in $CDCl_3$)



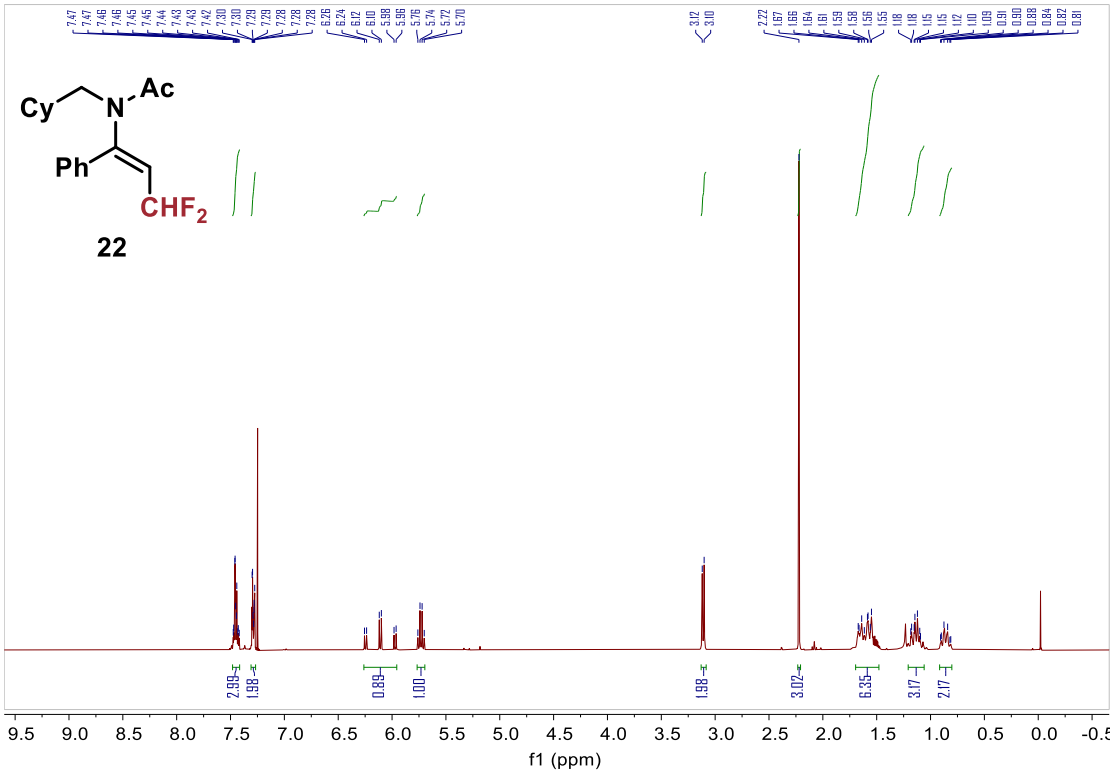
^{13}C NMR of compound 21 (101 MHz in $CDCl_3$)



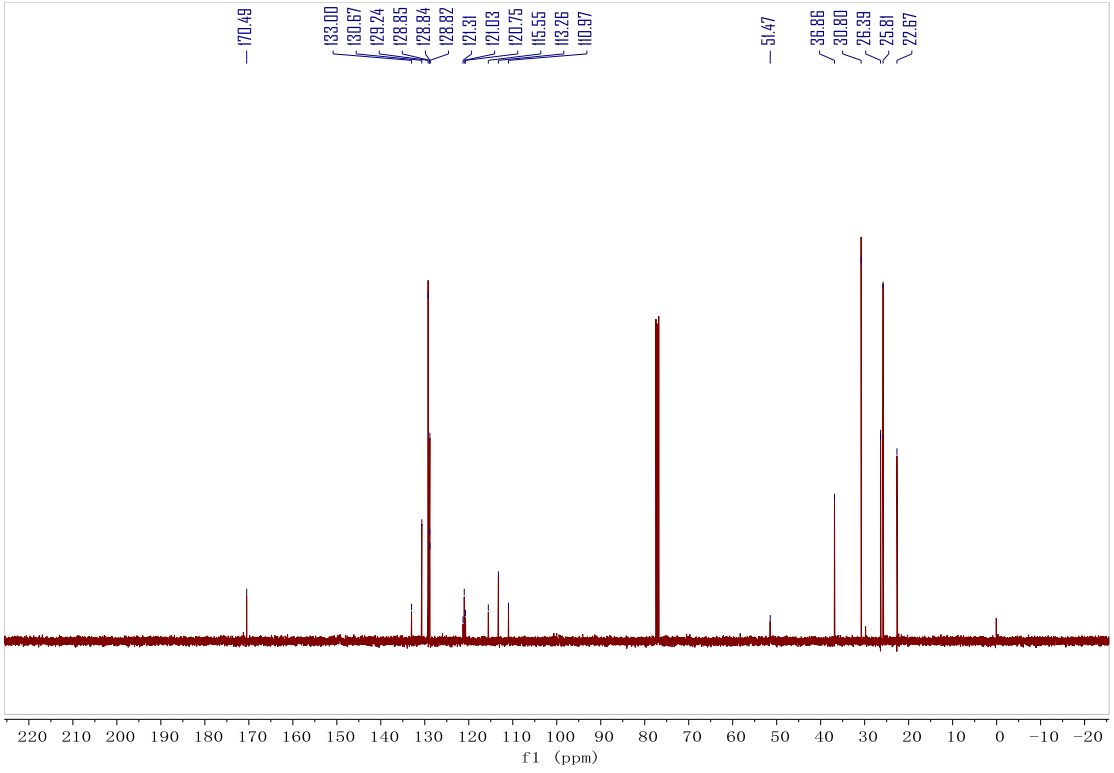
^{19}F NMR of compound 21 (377 MHz in $CDCl_3$)



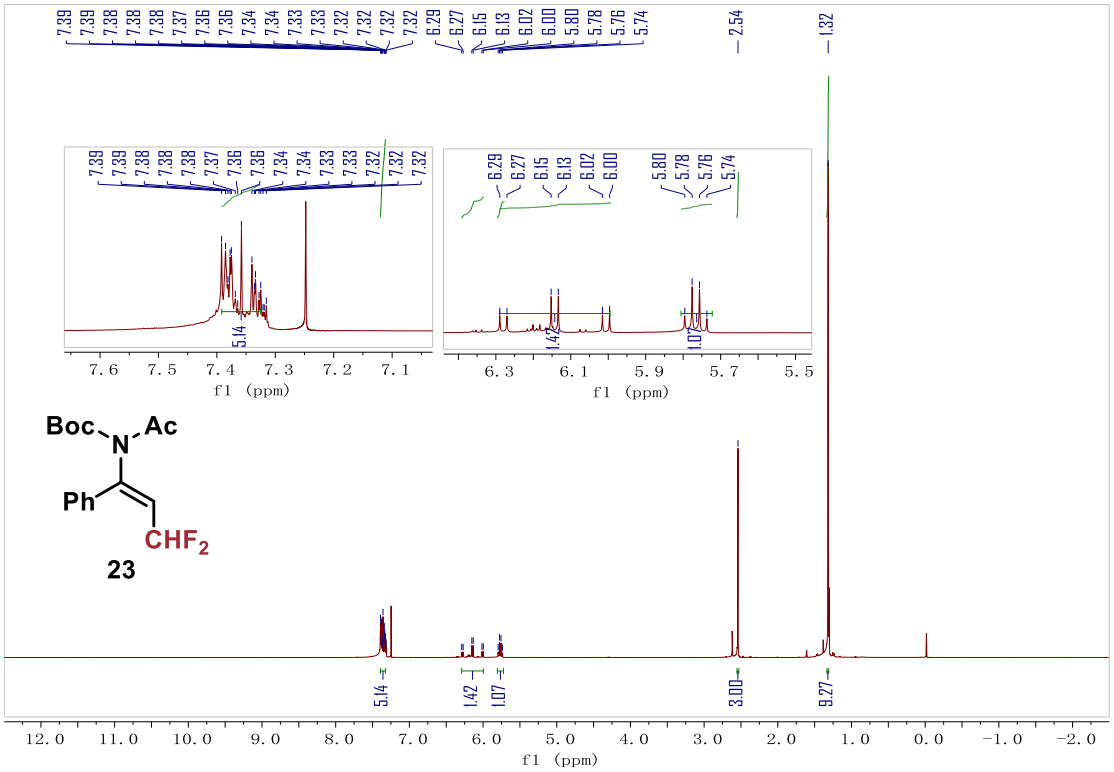
^{1}H NMR of compound 22 (400 MHz in $CDCl_3$)



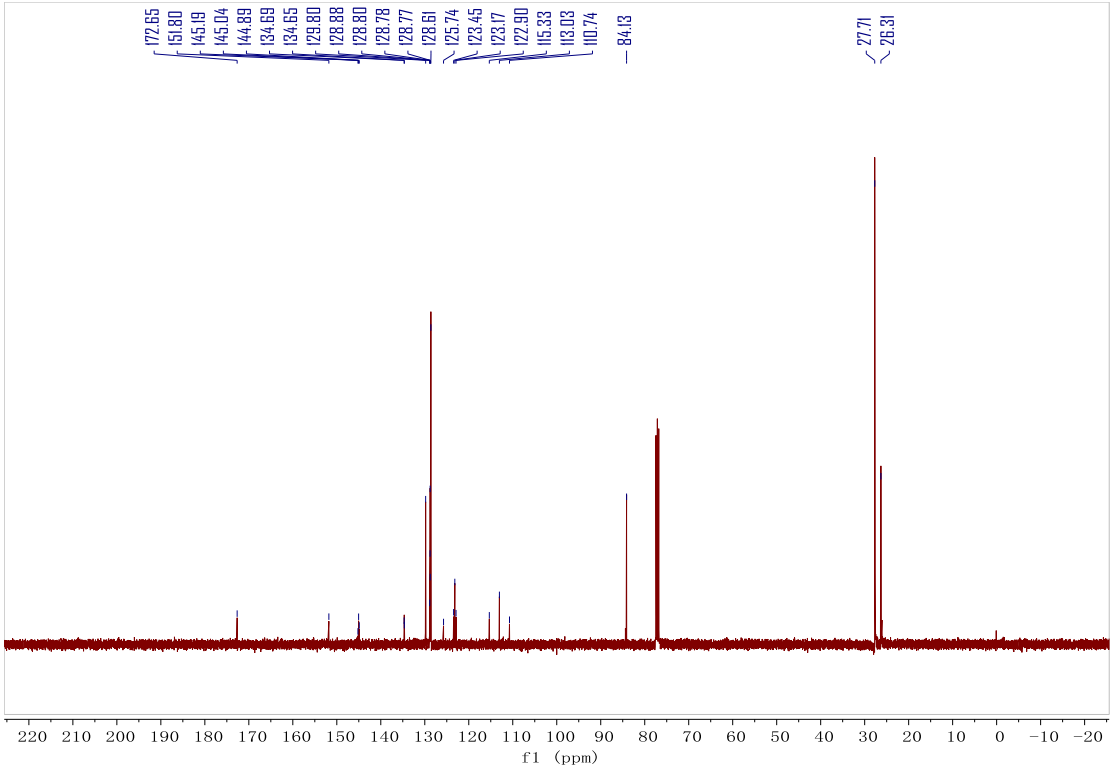
^{13}C NMR of compound 22 (101 MHz in $CDCl_3$)



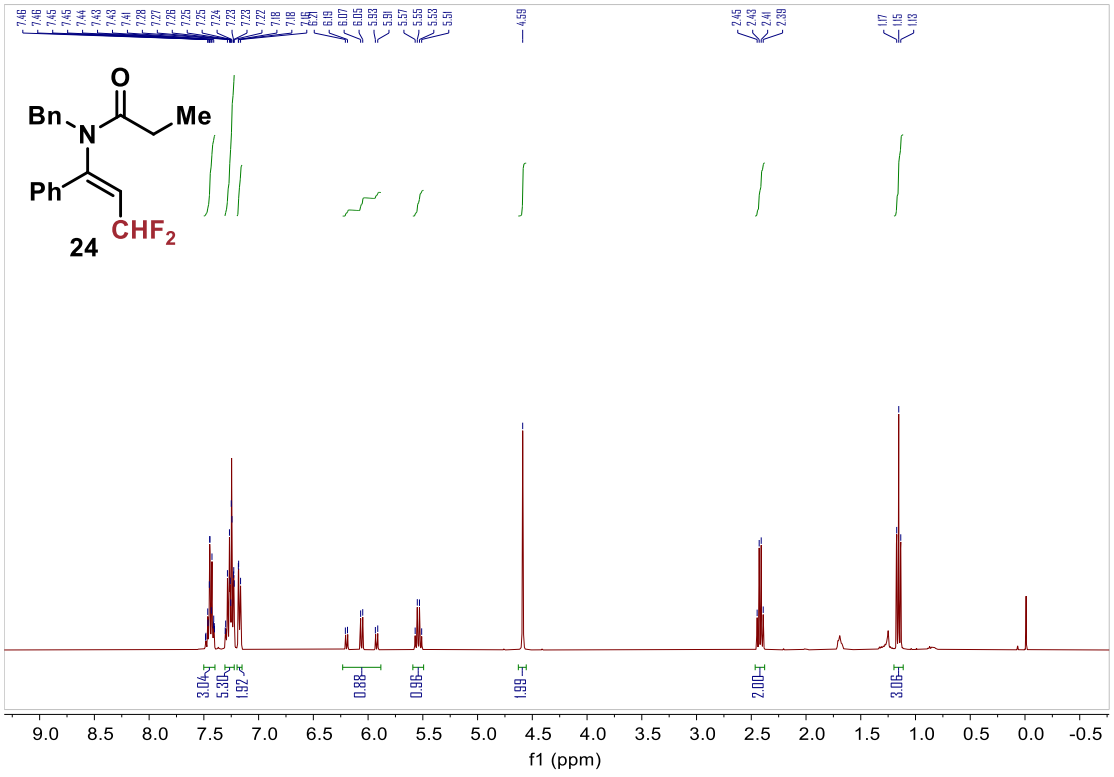
^{1}H NMR of compound 23 (400 MHz in $CDCl_3$)



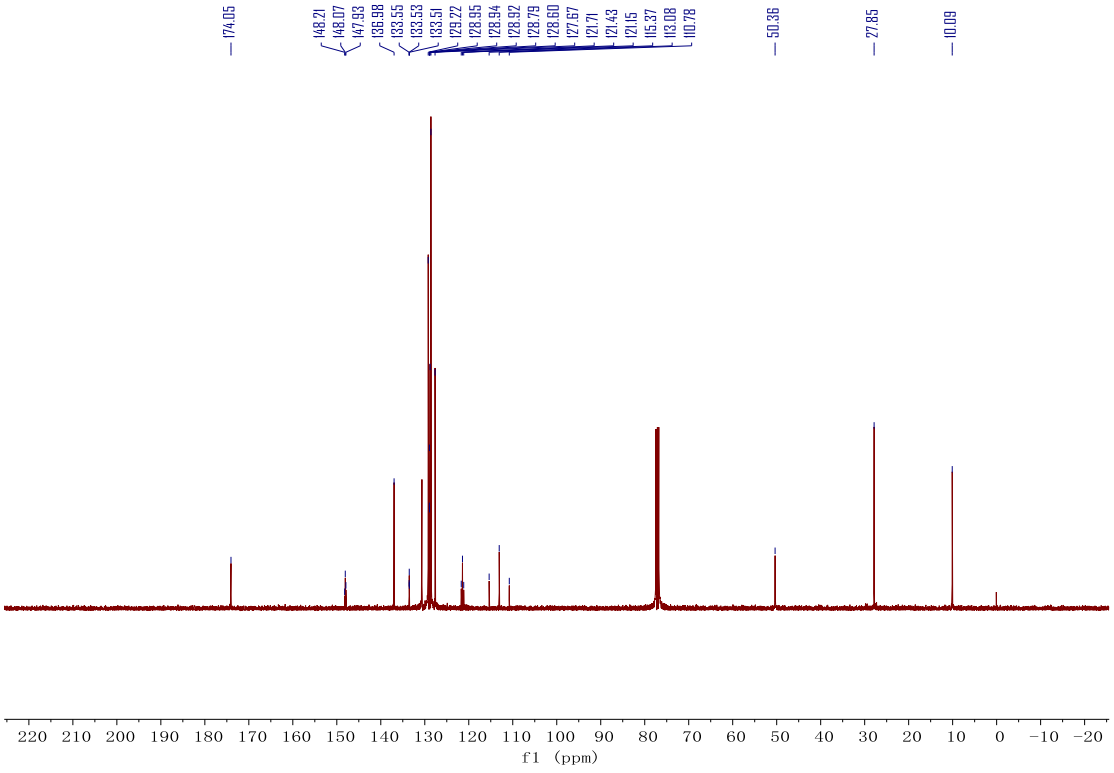
^{13}C NMR of compound 23 (101 MHz in $CDCl_3$)



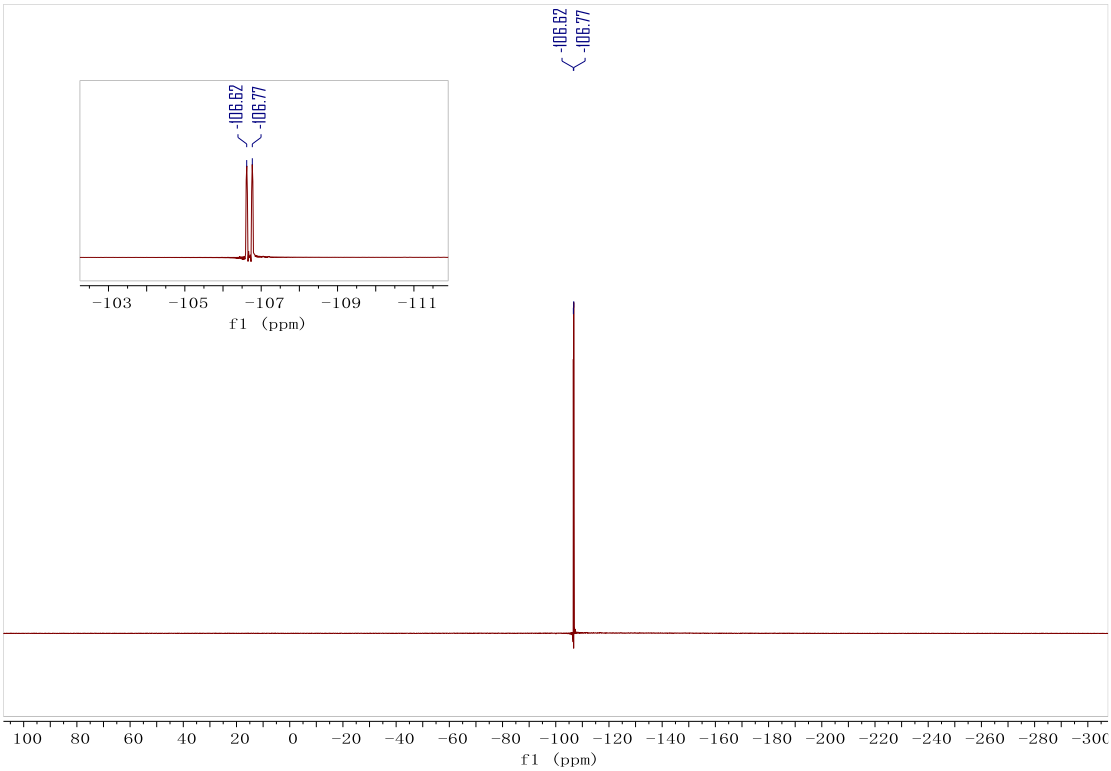
^{1}H NMR of compound 24 (400 MHz in $CDCl_3$)



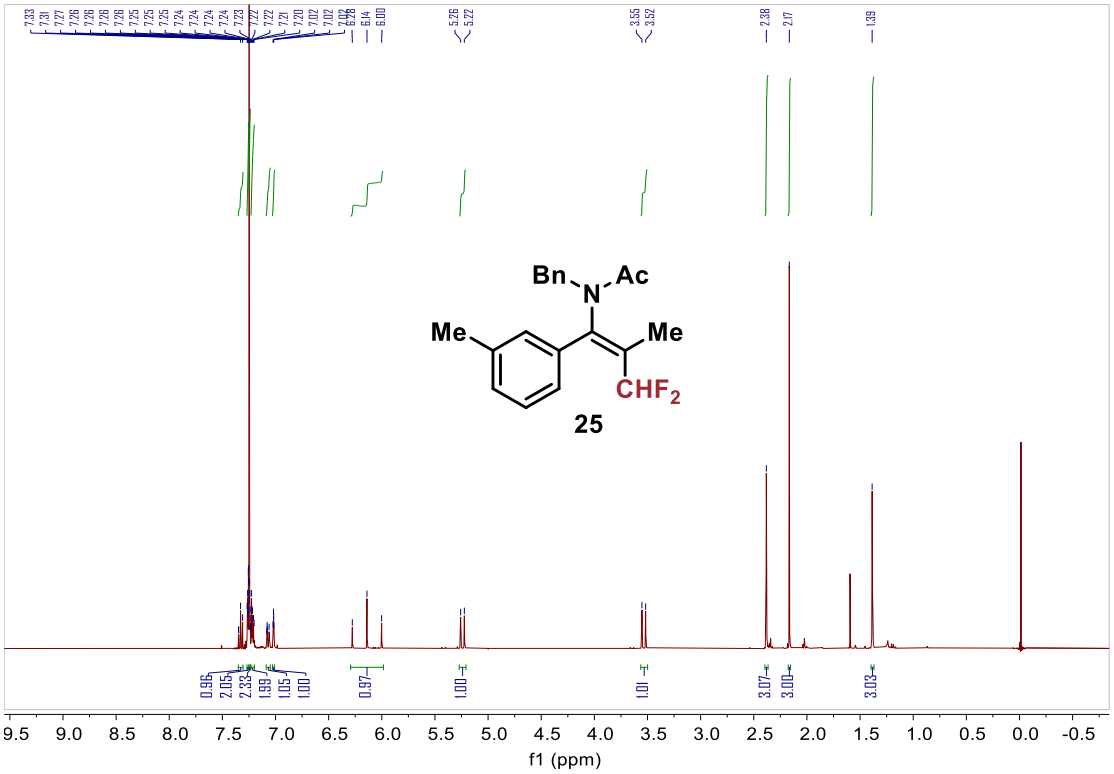
^{13}C NMR of compound 24 (101 MHz in $CDCl_3$)



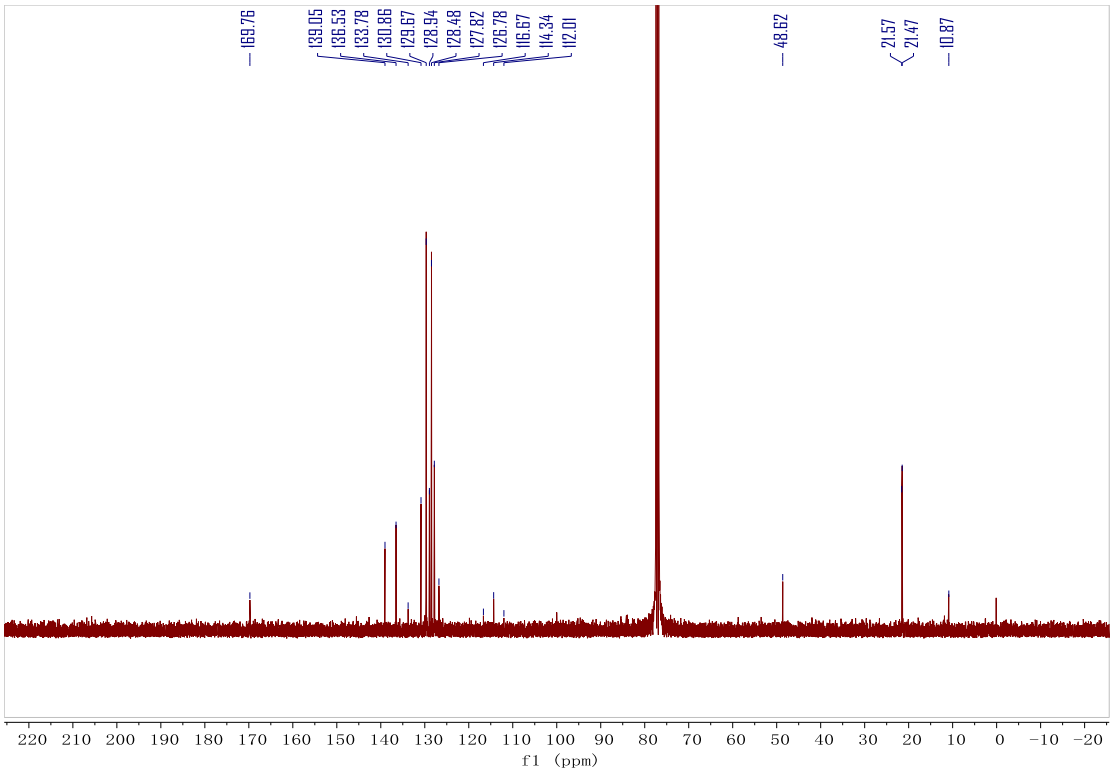
^{19}F NMR of compound 24 (377 MHz in $CDCl_3$)



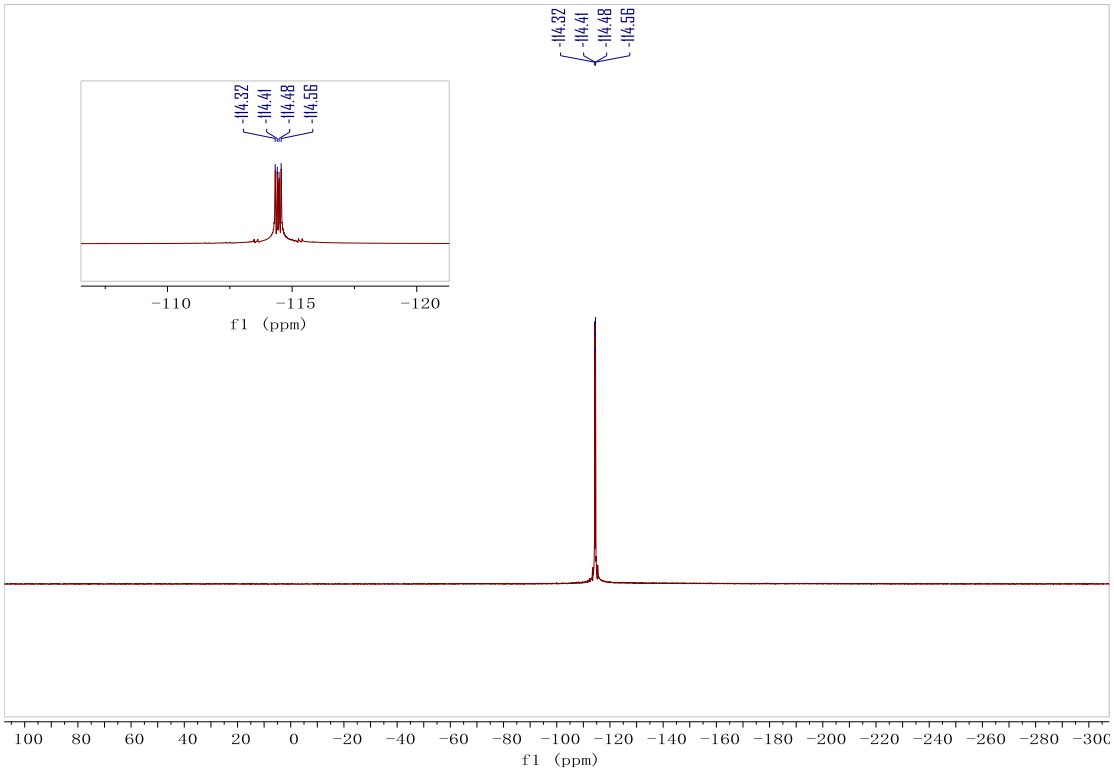
^{1}H NMR of compound 25 (400 MHz in $CDCl_3$)



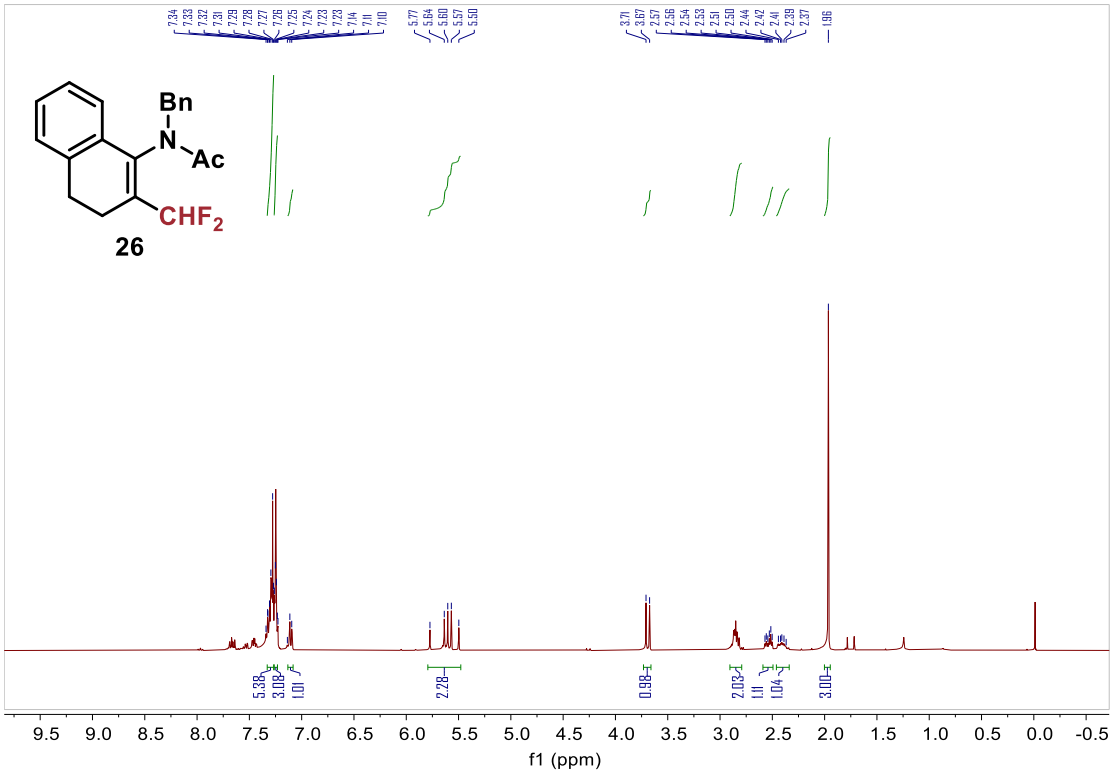
^{13}C NMR of compound 25 (101 MHz in $CDCl_3$)



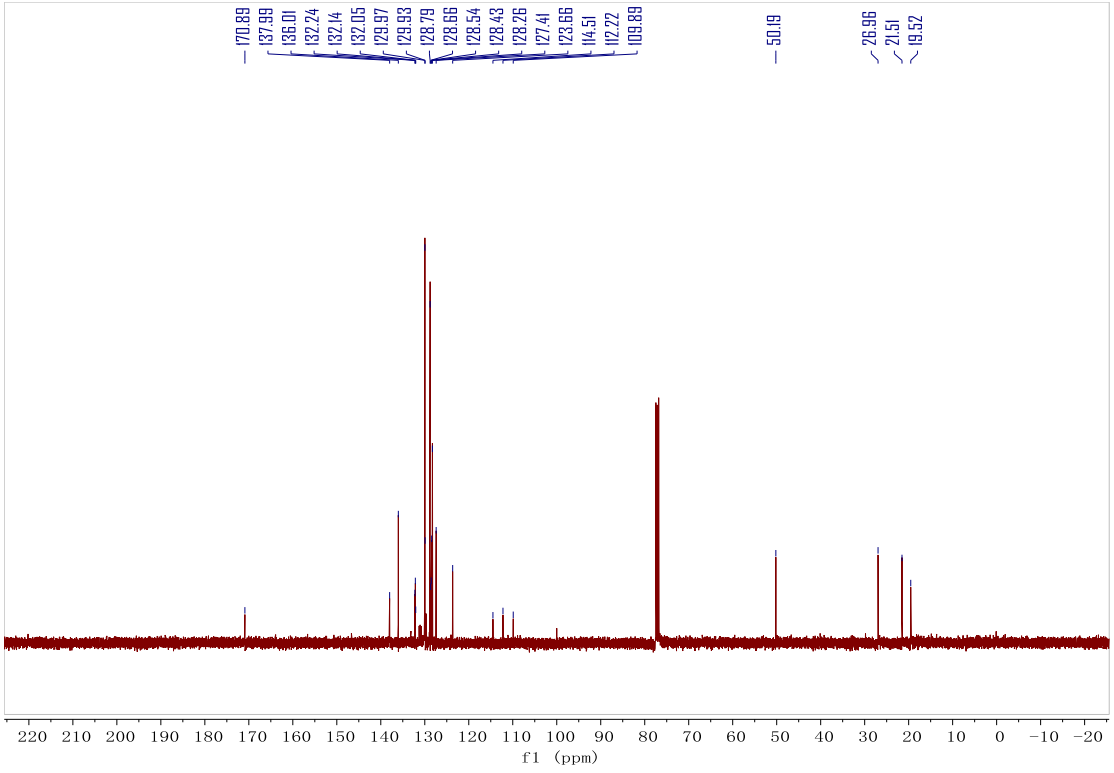
^{19}F NMR of compound 25 (377 MHz in $CDCl_3$)



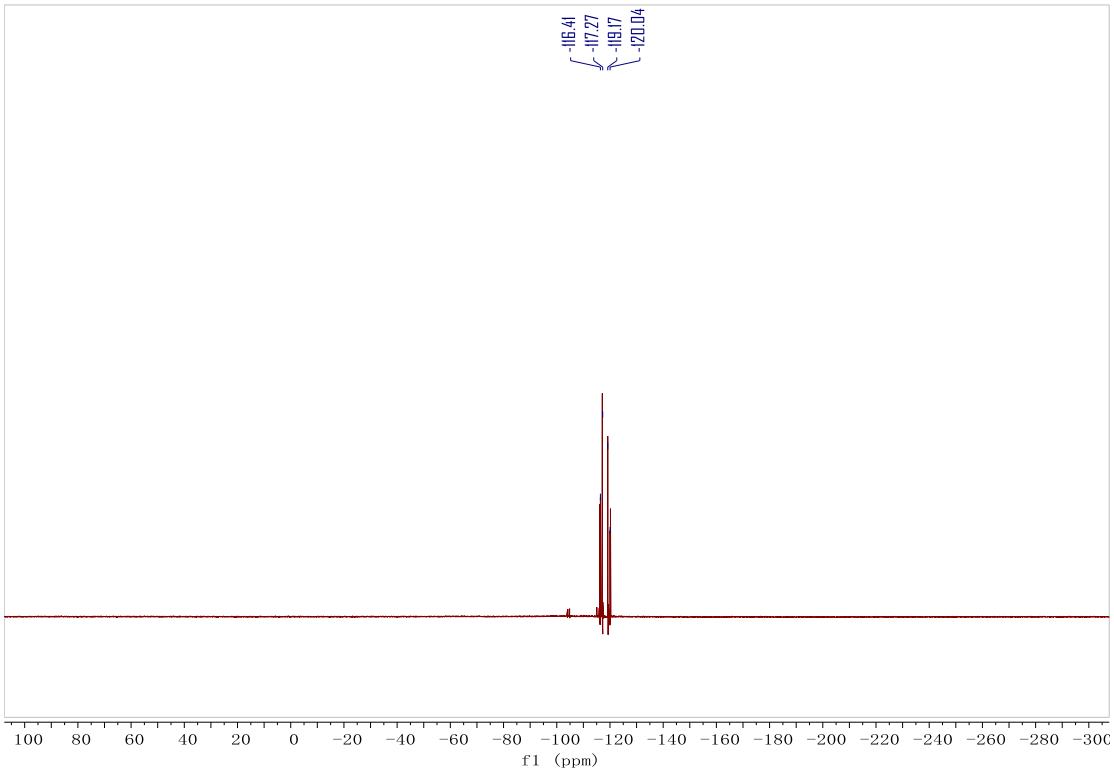
^{1}H NMR of compound 26 (400 MHz in $CDCl_3$)



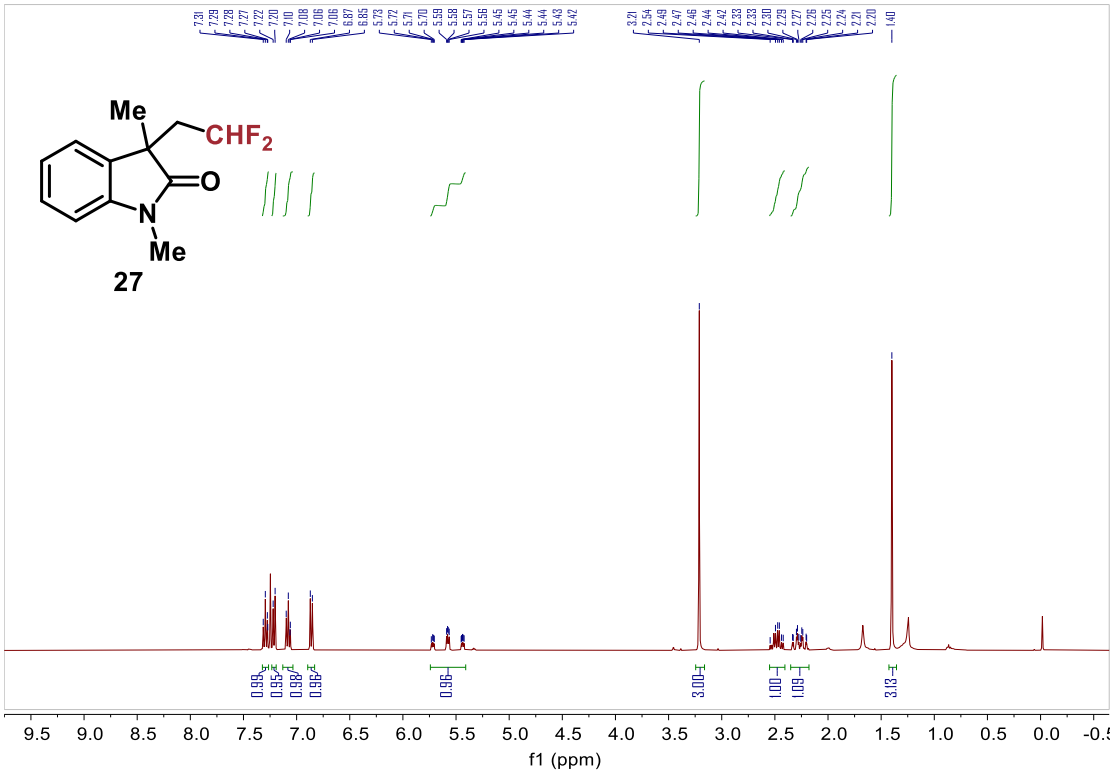
^{13}C NMR of compound 26 (101 MHz in $CDCl_3$)



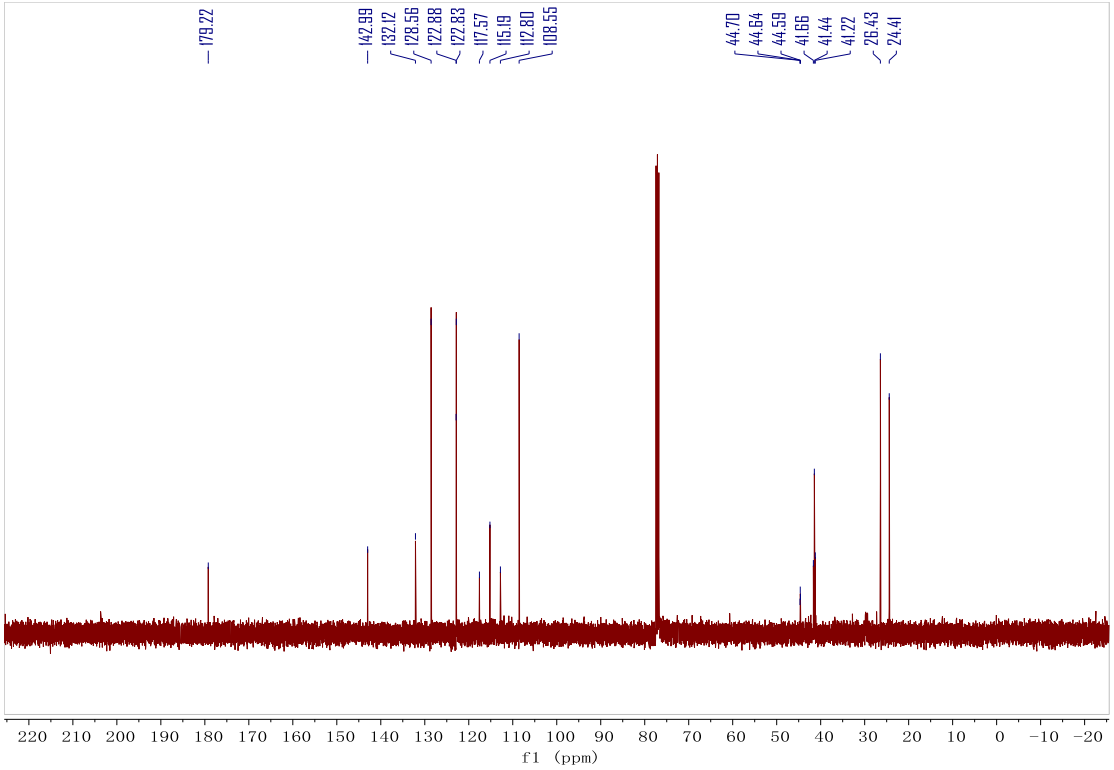
^{19}F NMR of compound 26 (377 MHz in $CDCl_3$)



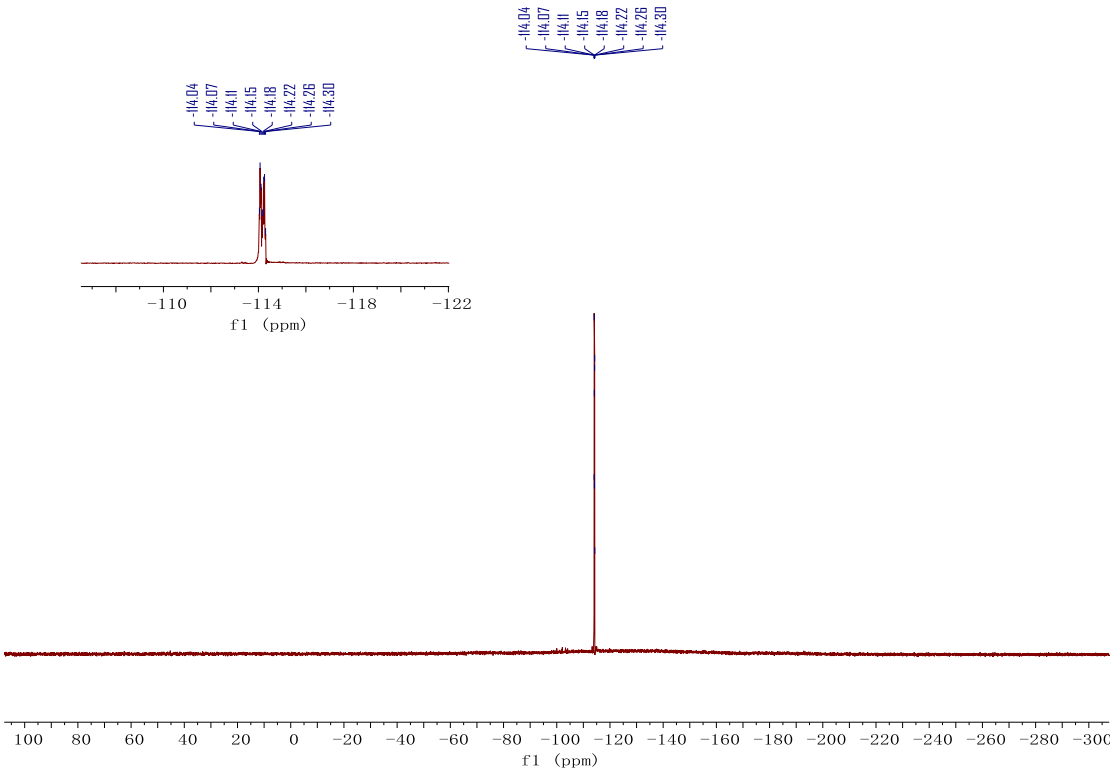
^{1}H NMR of compound 27 (400 MHz in $CDCl_3$)



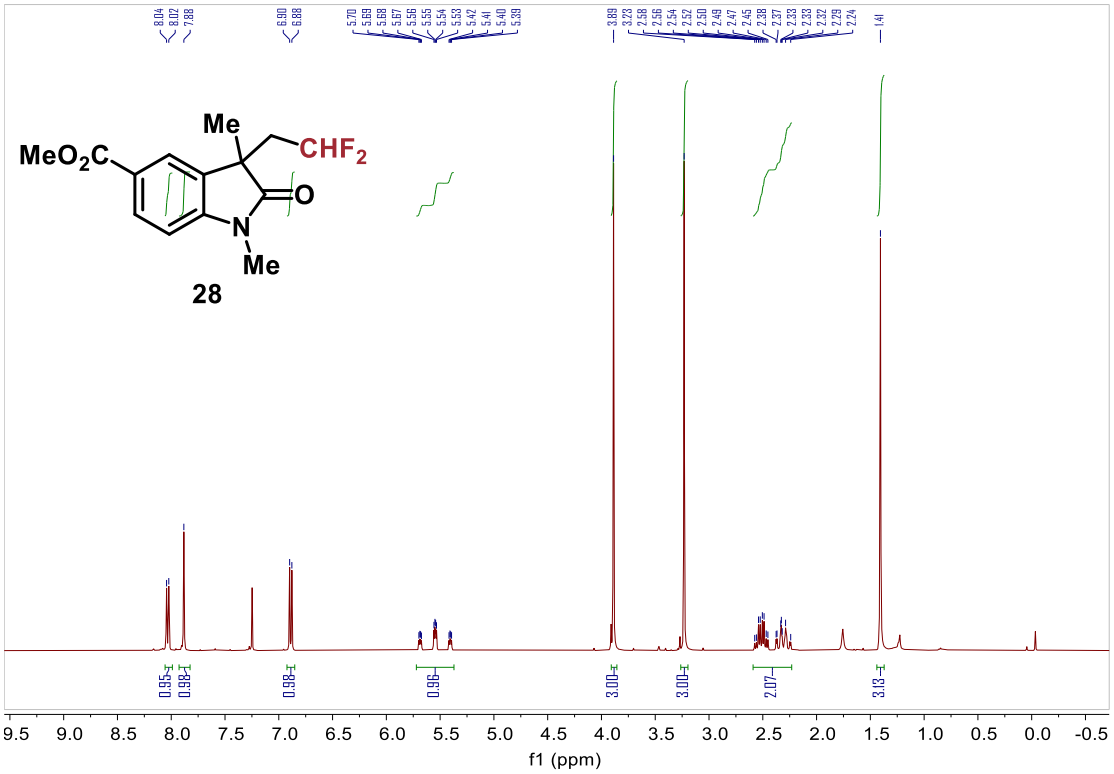
^{13}C NMR of compound 27 (101 MHz in $CDCl_3$)



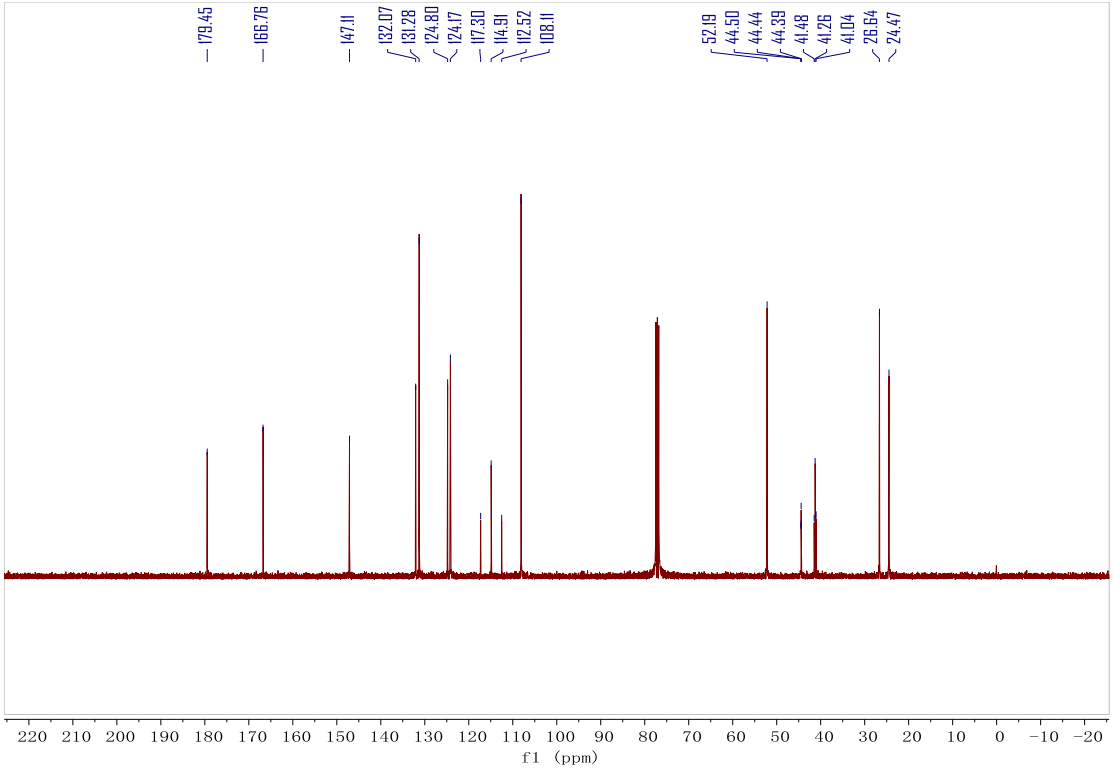
^{19}F NMR of compound 27 (377 MHz in $CDCl_3$)



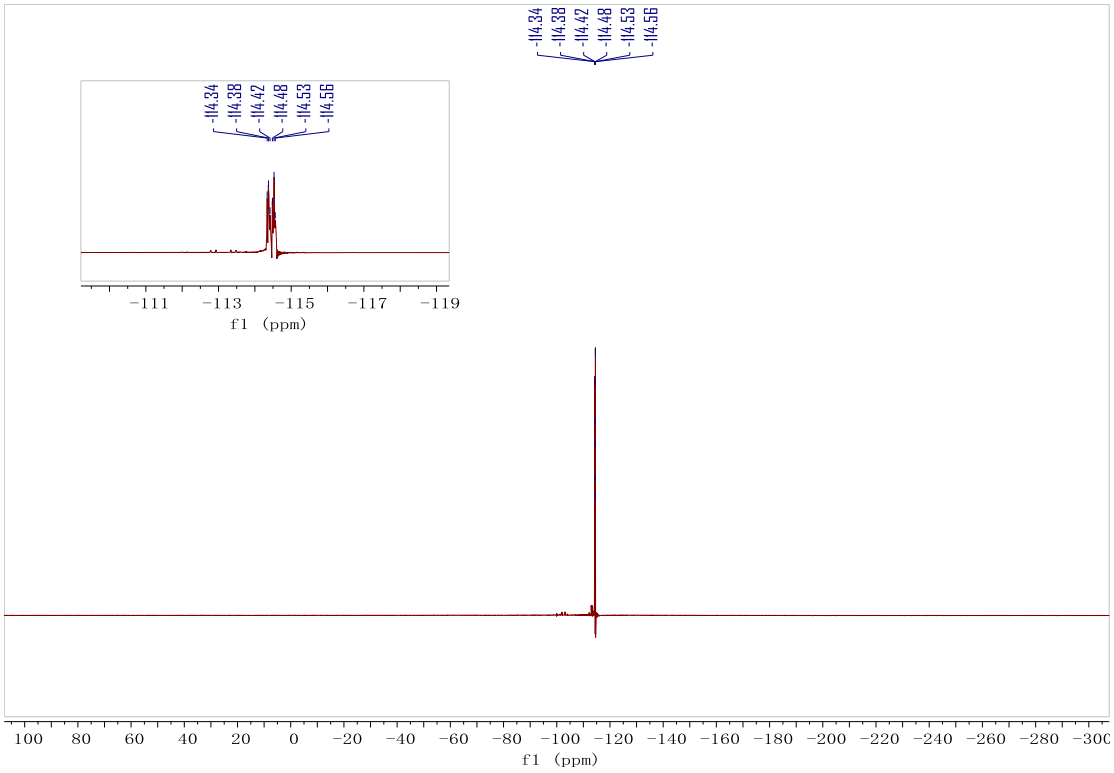
^{1}H NMR of compound 28 (400 MHz in $CDCl_3$)



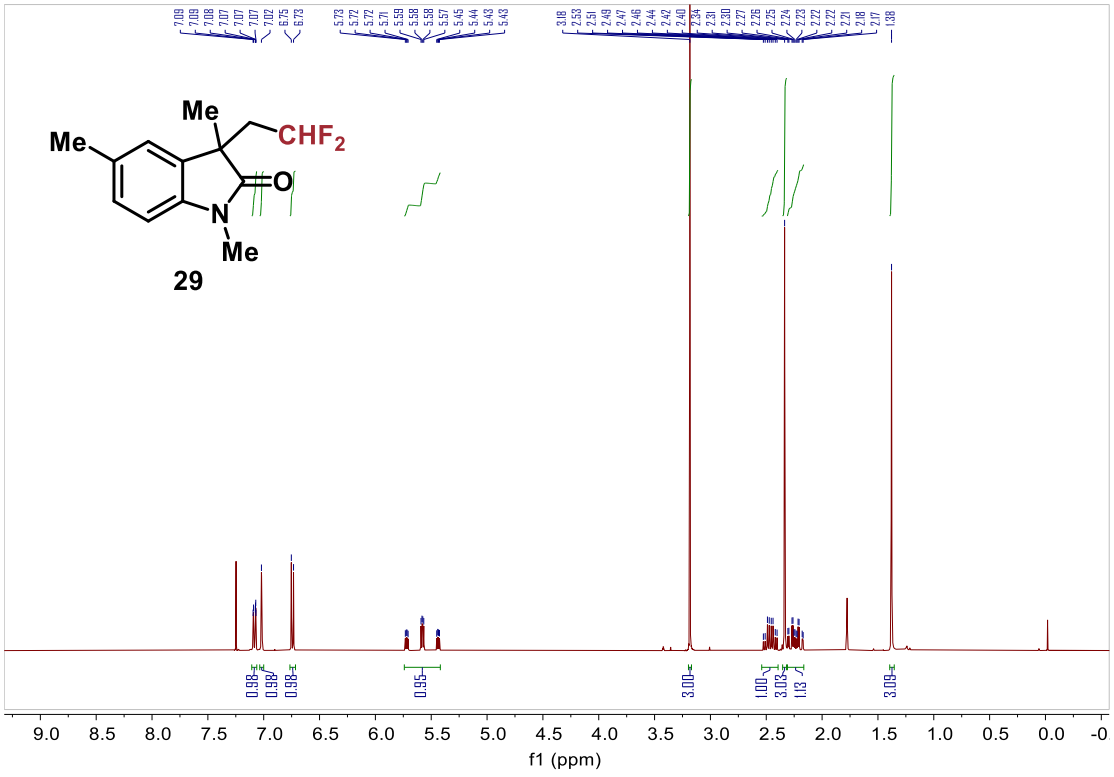
^{13}C NMR of compound 28 (101 MHz in $CDCl_3$)



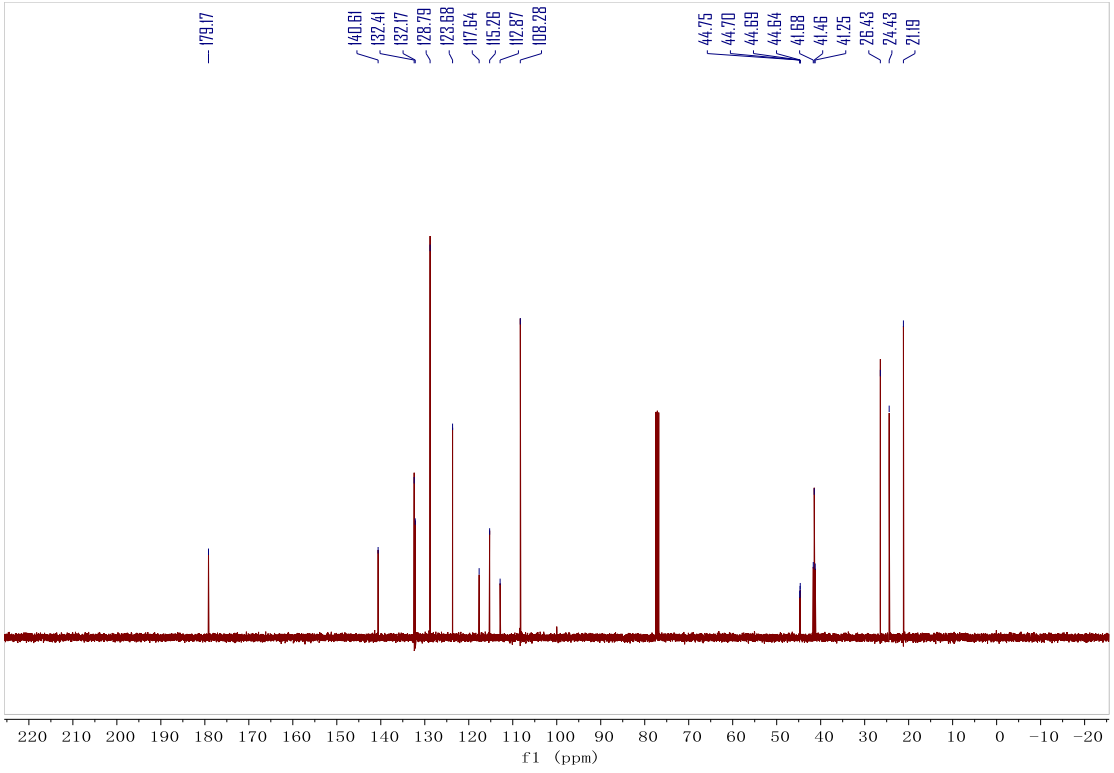
^{19}F NMR of compound 28 (377 MHz in $CDCl_3$)



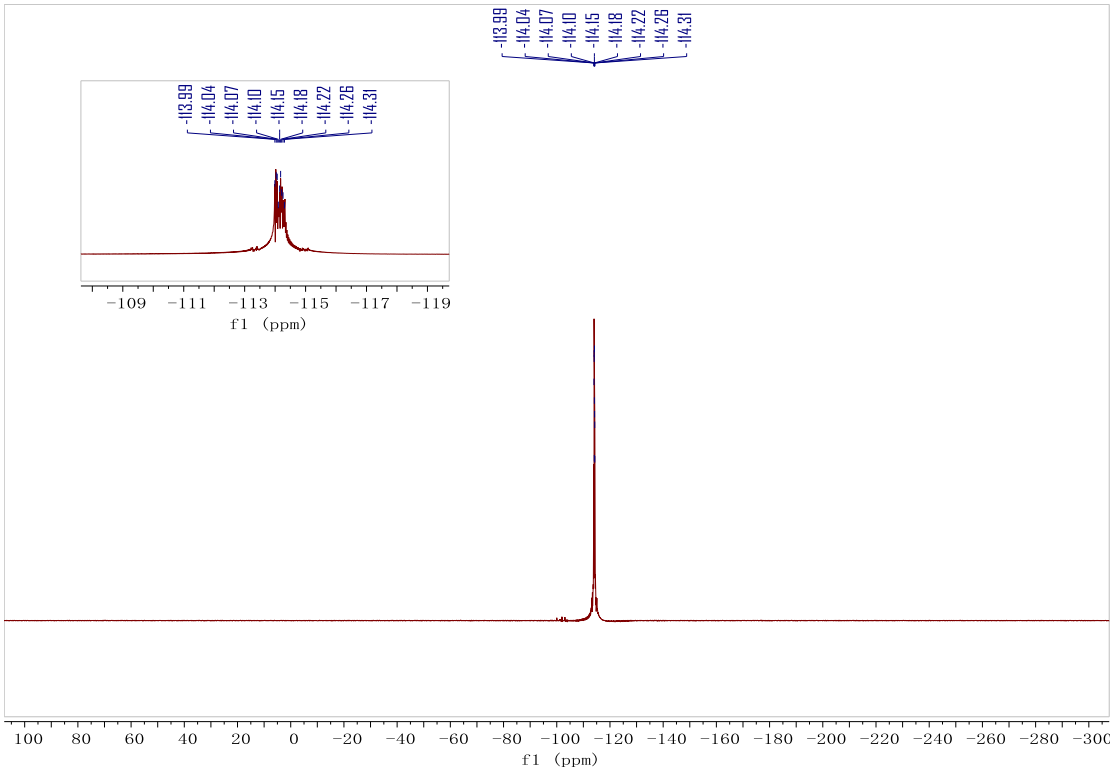
^{1}H NMR of compound 29 (400 MHz in $CDCl_3$)



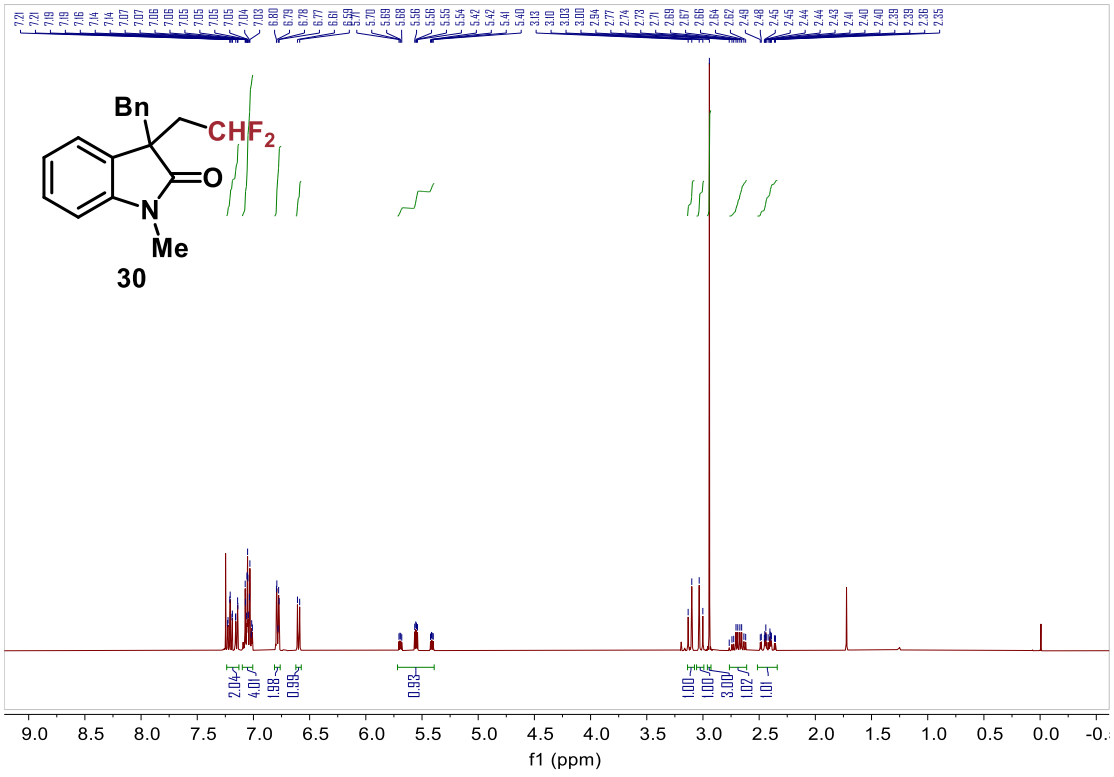
^{13}C NMR of compound 29 (101 MHz in $CDCl_3$)



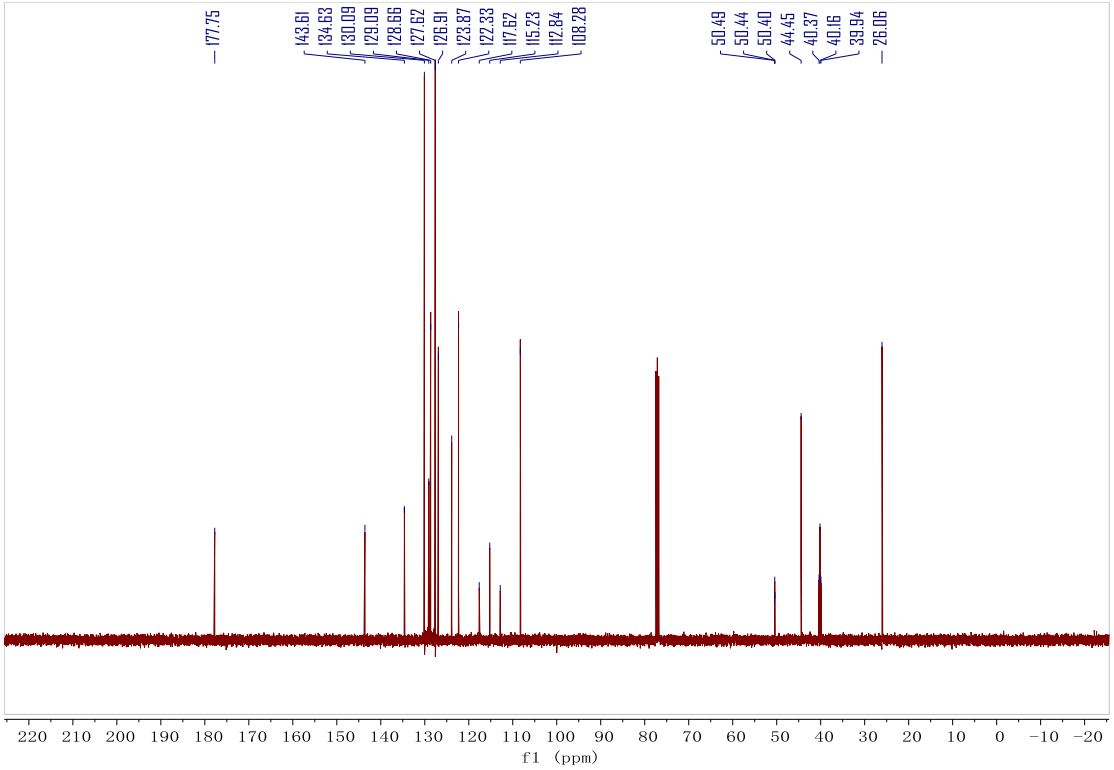
^{19}F NMR of compound 29 (377 MHz in $CDCl_3$)



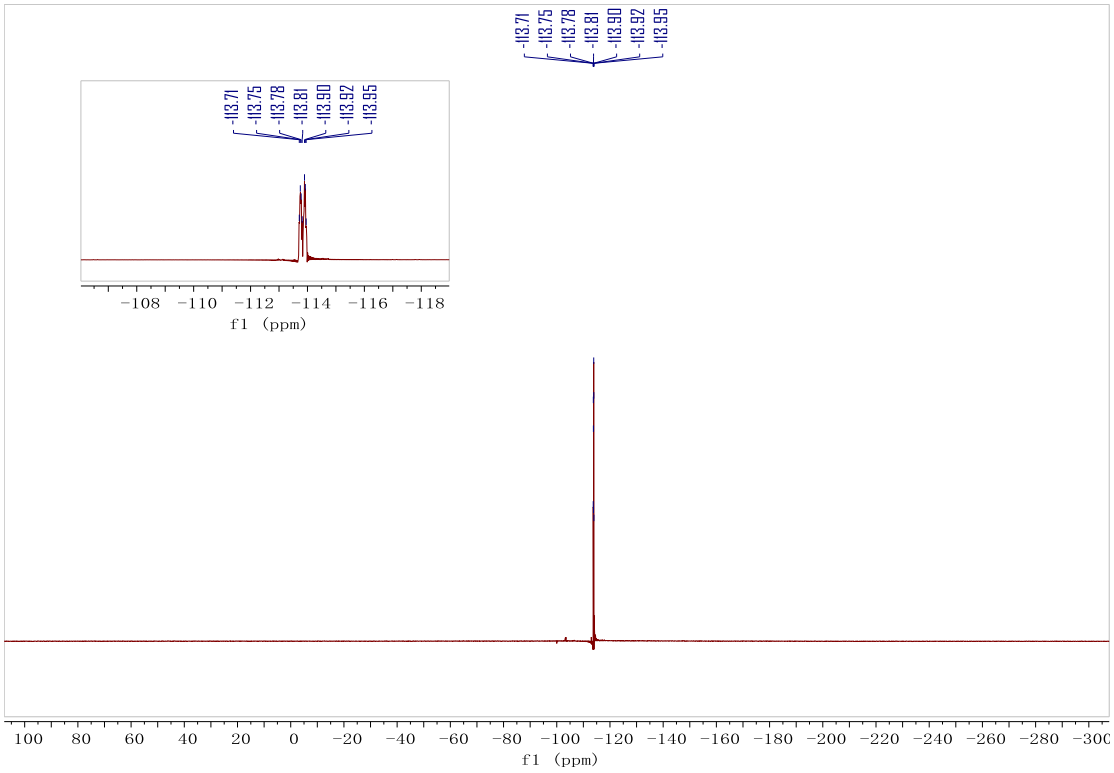
^{1}H NMR of compound 30 (400 MHz in $CDCl_3$)



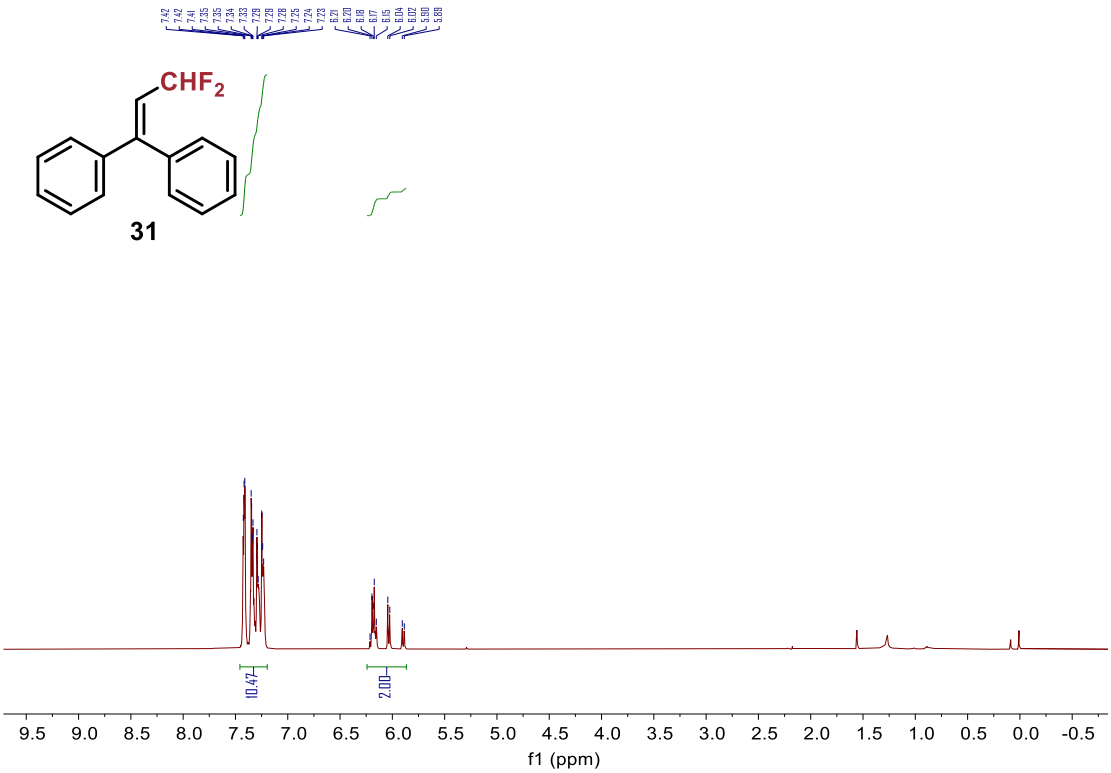
^{13}C NMR of compound 30 (101 MHz in $CDCl_3$)



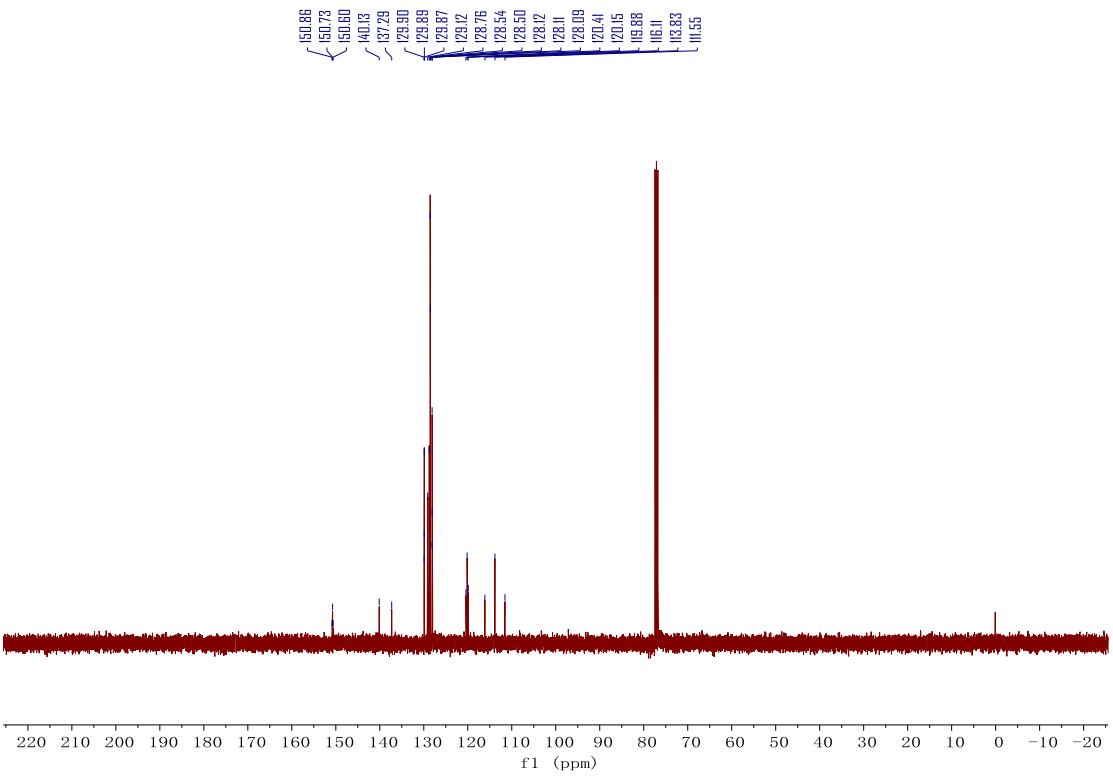
^{19}F NMR of compound 30 (377 MHz in $CDCl_3$)



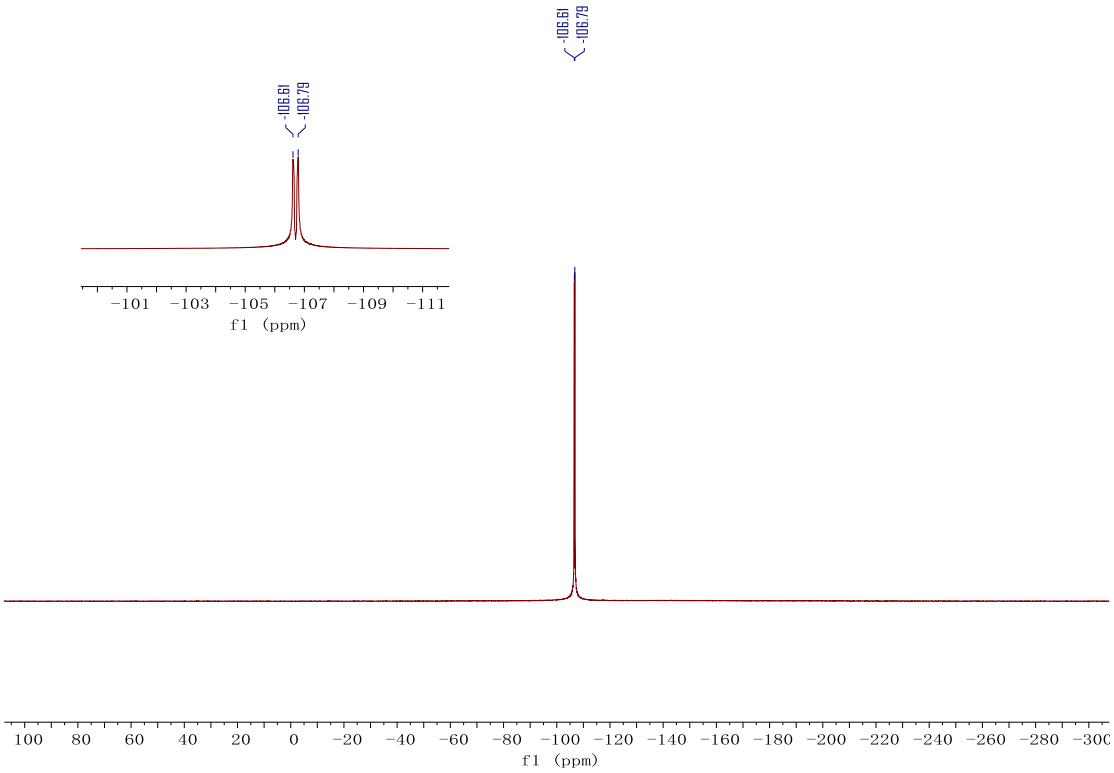
^{1}H NMR of compound 31 (400 MHz in $CDCl_3$)



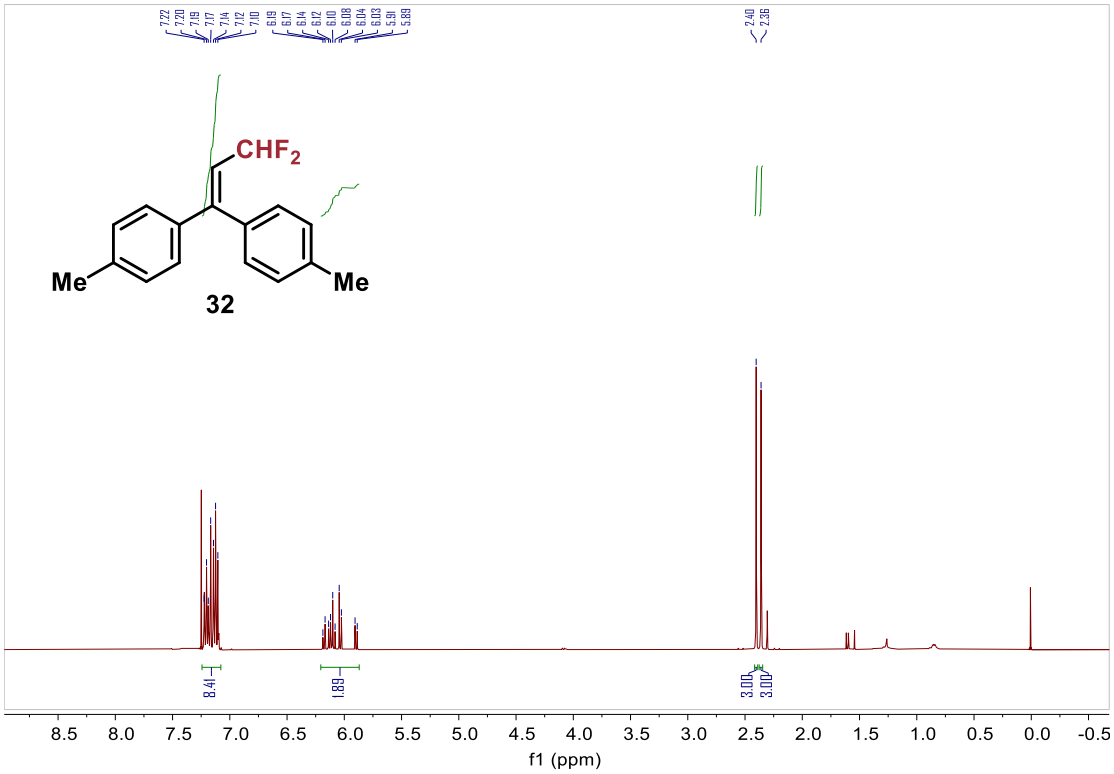
^{13}C NMR of compound 31 (101 MHz in $CDCl_3$)



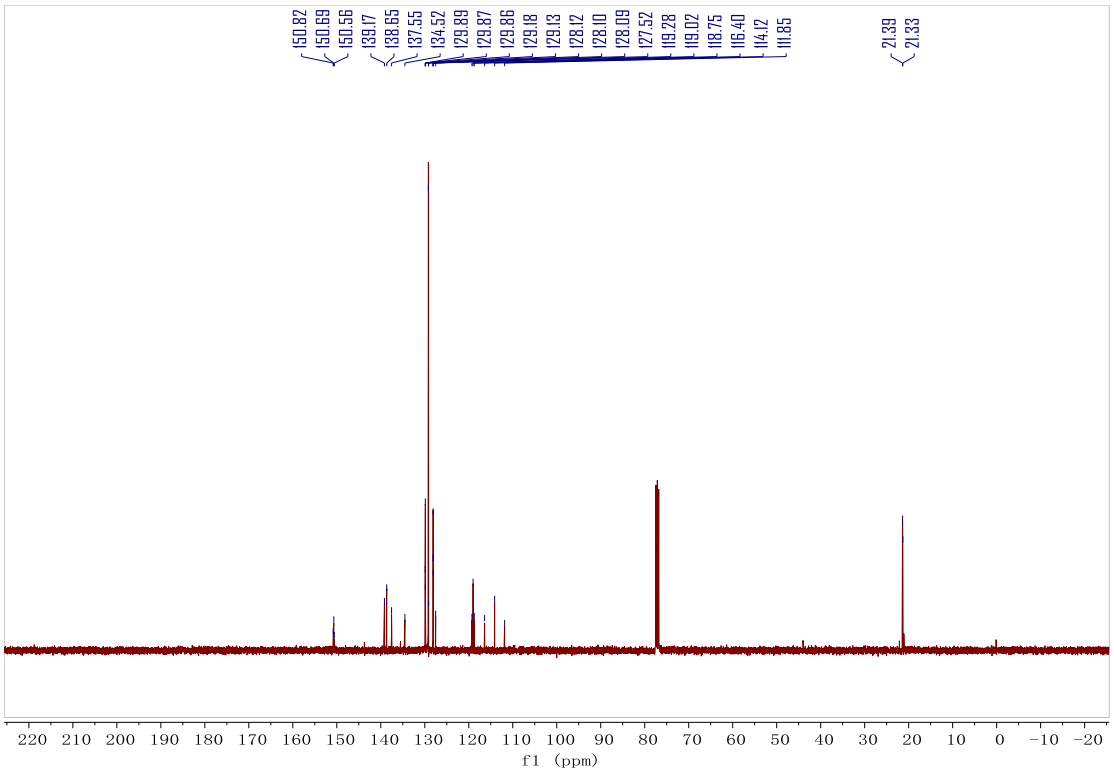
^{19}F NMR of compound 31 (377 MHz in $CDCl_3$)



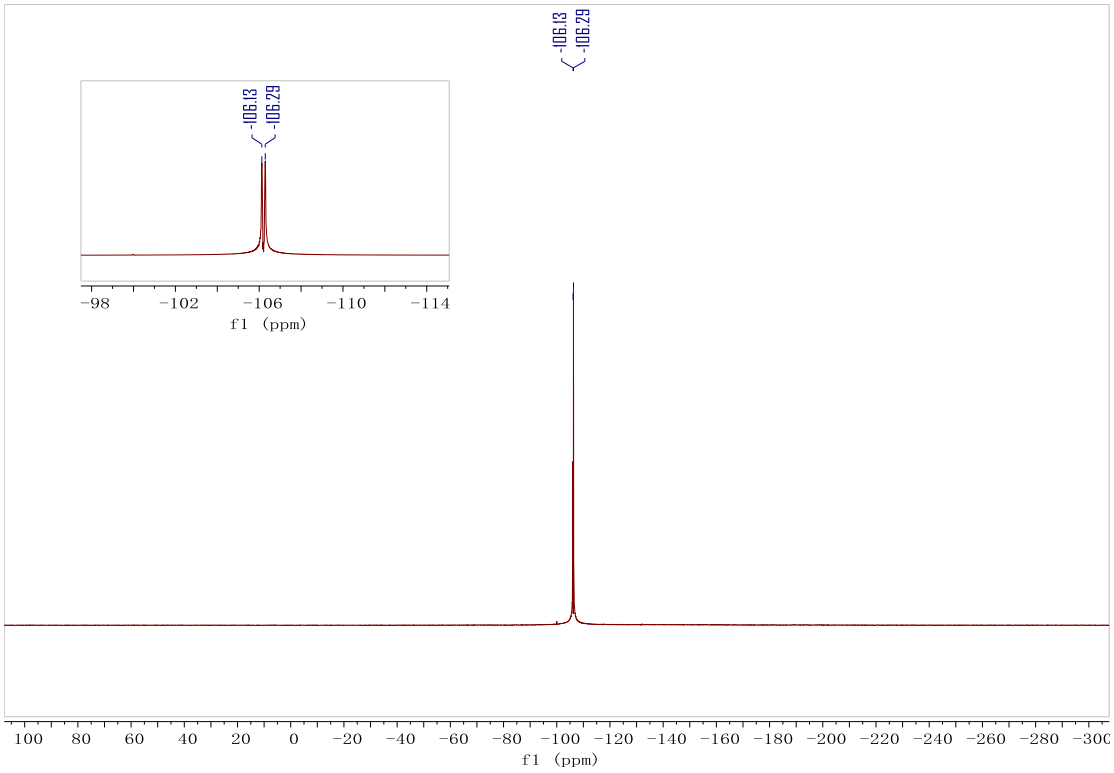
^{1}H NMR of compound 32 (400 MHz in $CDCl_3$)



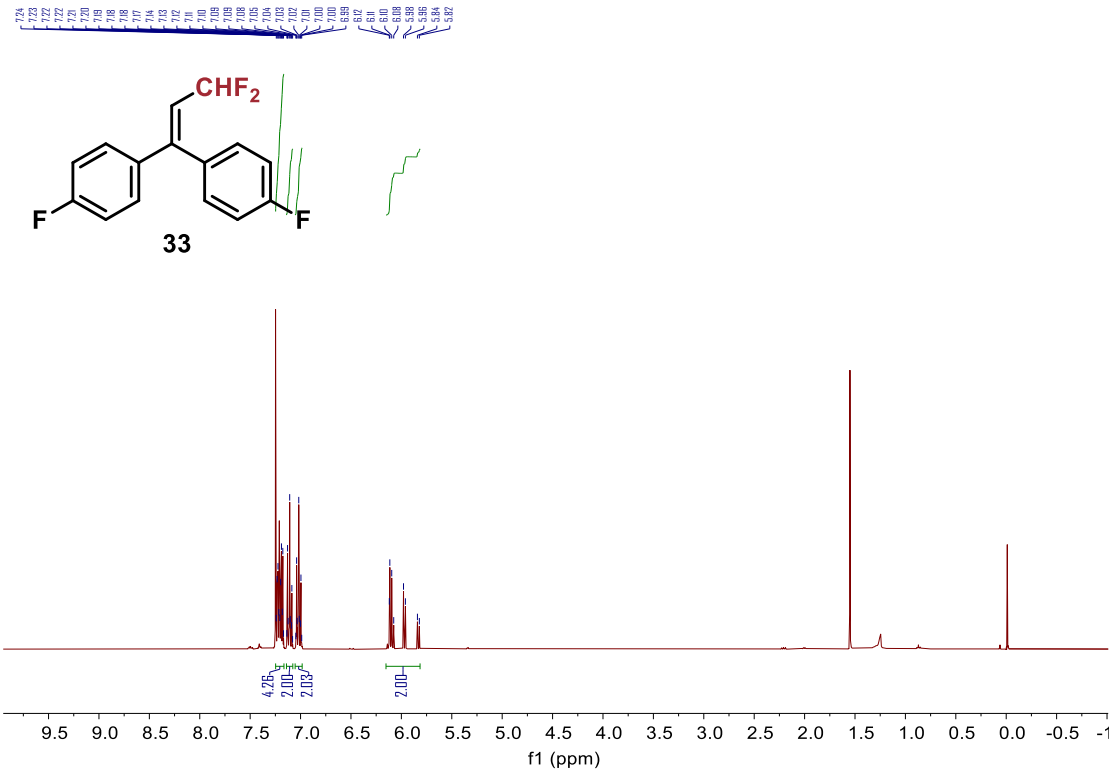
^{13}C NMR of compound 32 (101 MHz in $CDCl_3$)



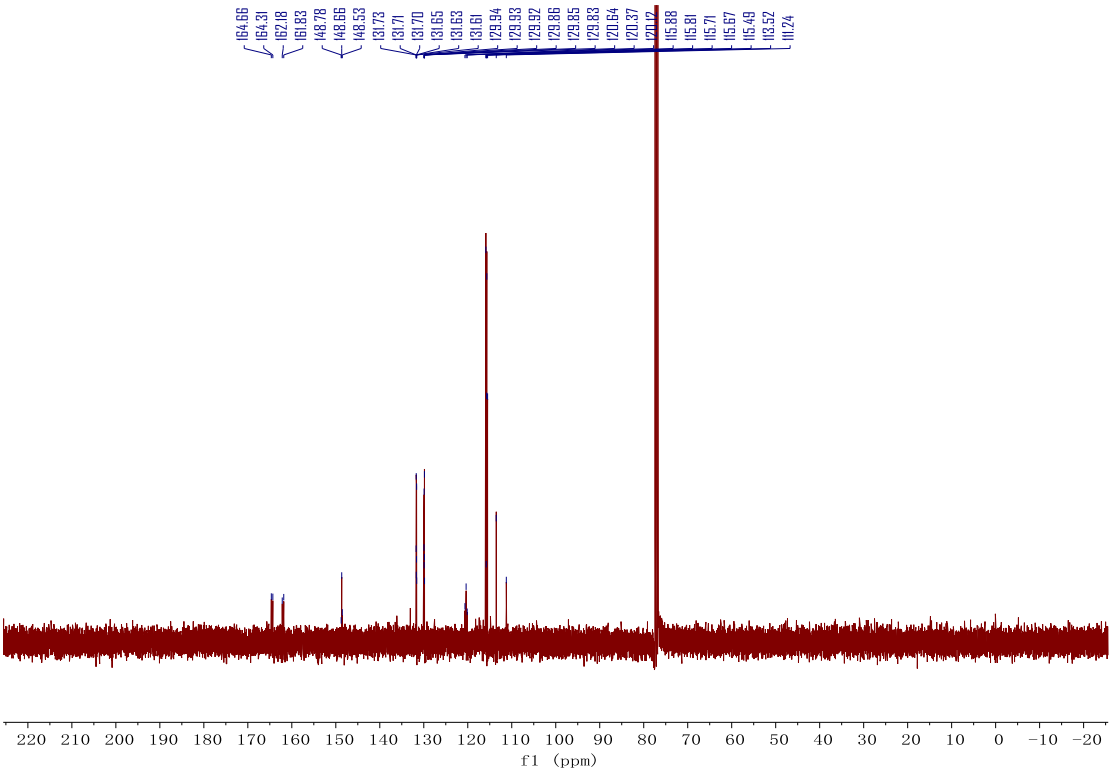
^{19}F NMR of compound 32 (377 MHz in $CDCl_3$)



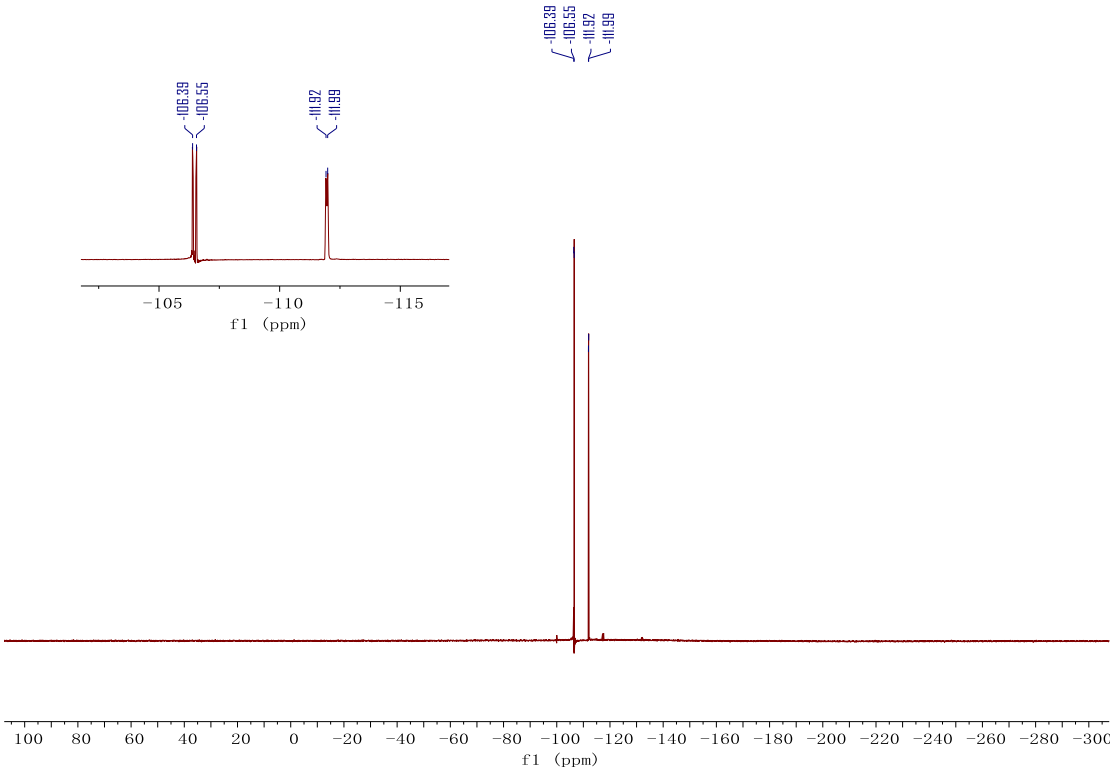
^{1}H NMR of compound 33 (400 MHz in $CDCl_3$)



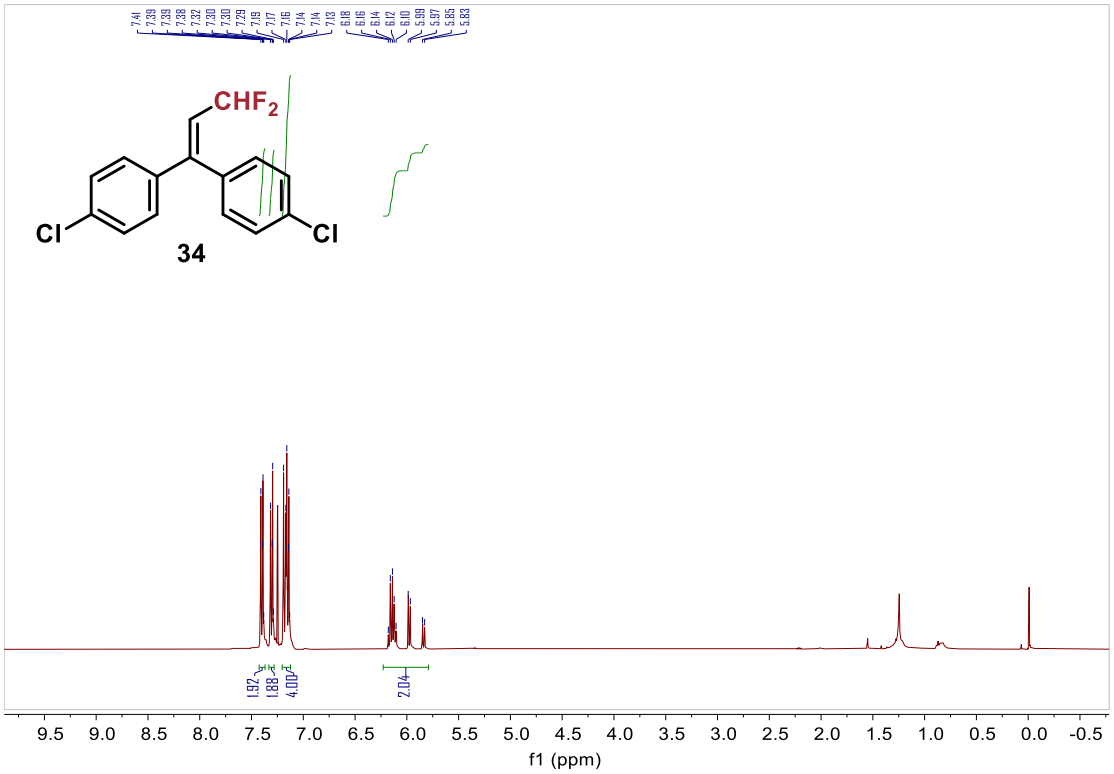
^{13}C NMR of compound 33 (101 MHz in $CDCl_3$)



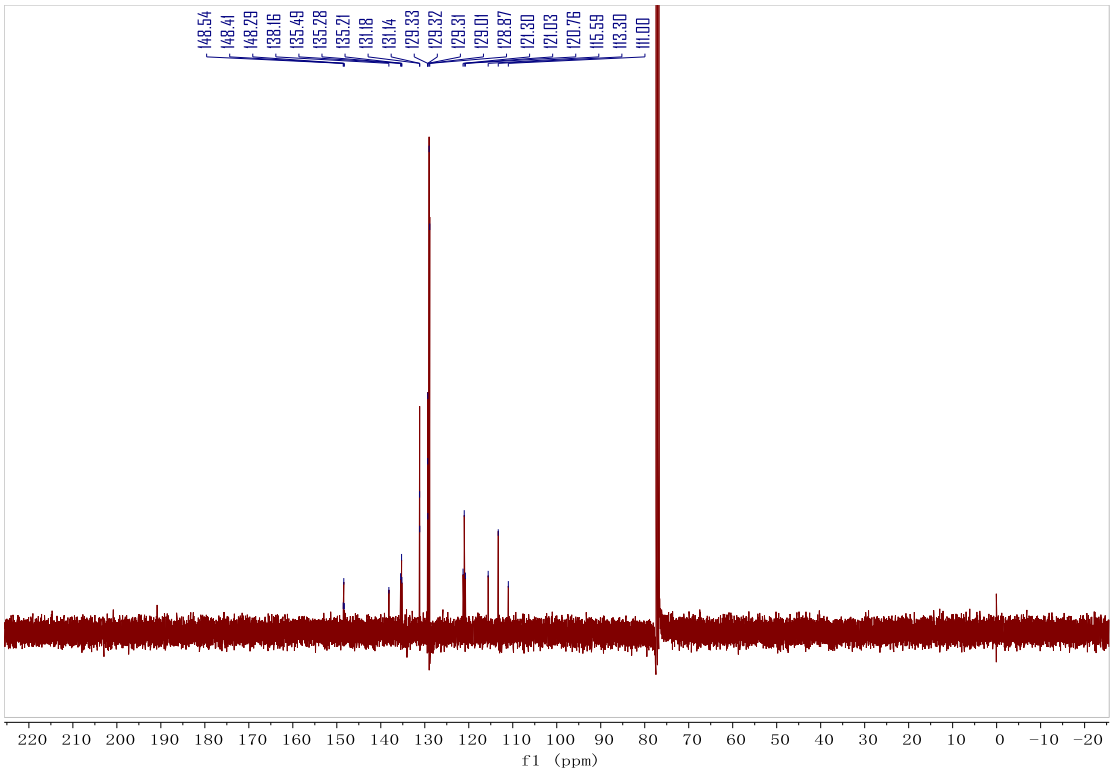
^{19}F NMR of compound 33 (377 MHz in $CDCl_3$)



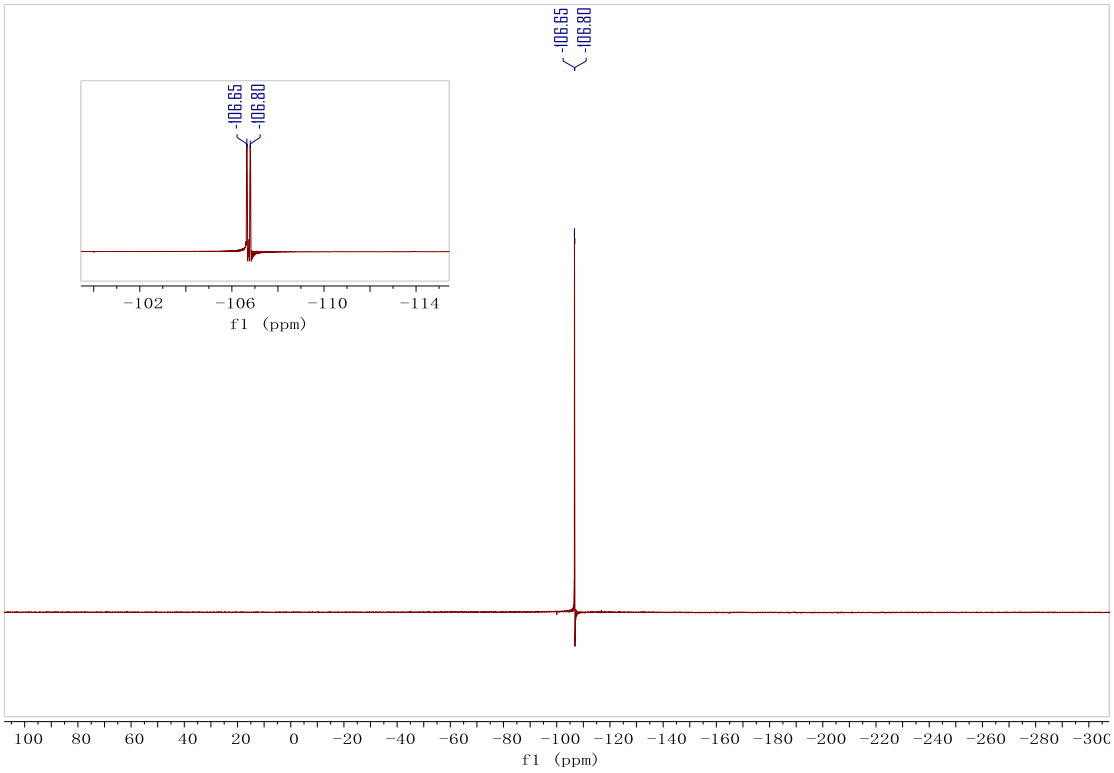
^{1}H NMR of compound 34 (400 MHz in $CDCl_3$)



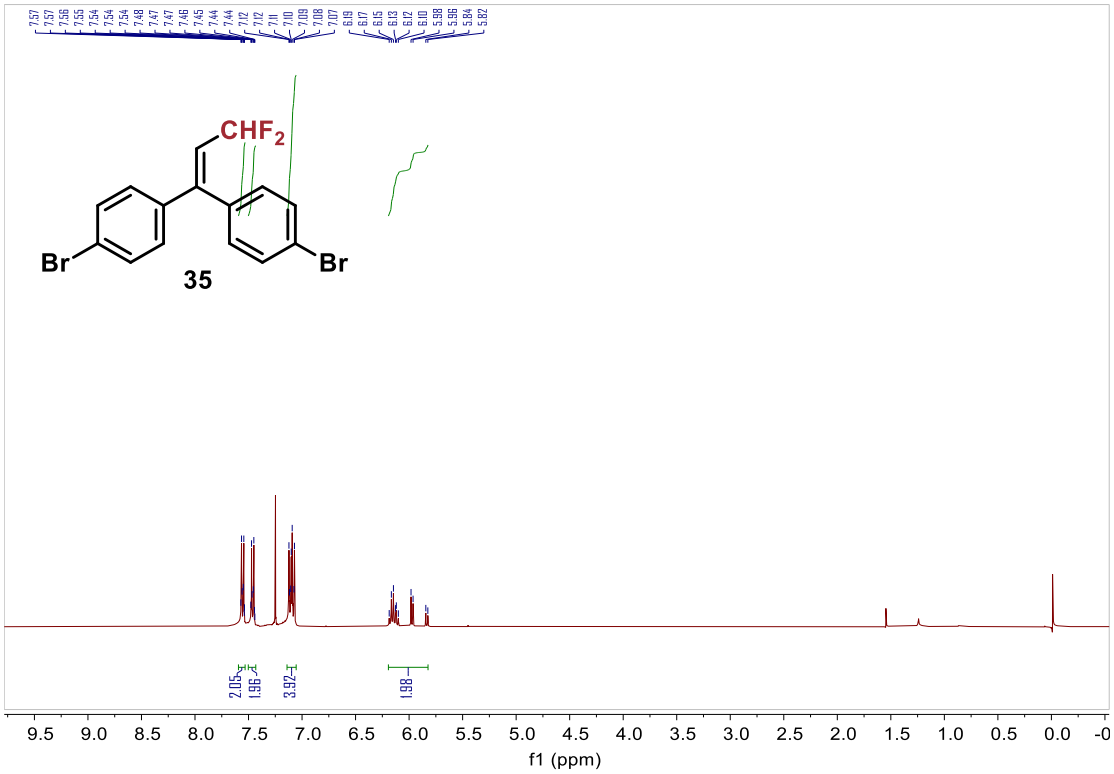
^{13}C NMR of compound 34 (101 MHz in $CDCl_3$)



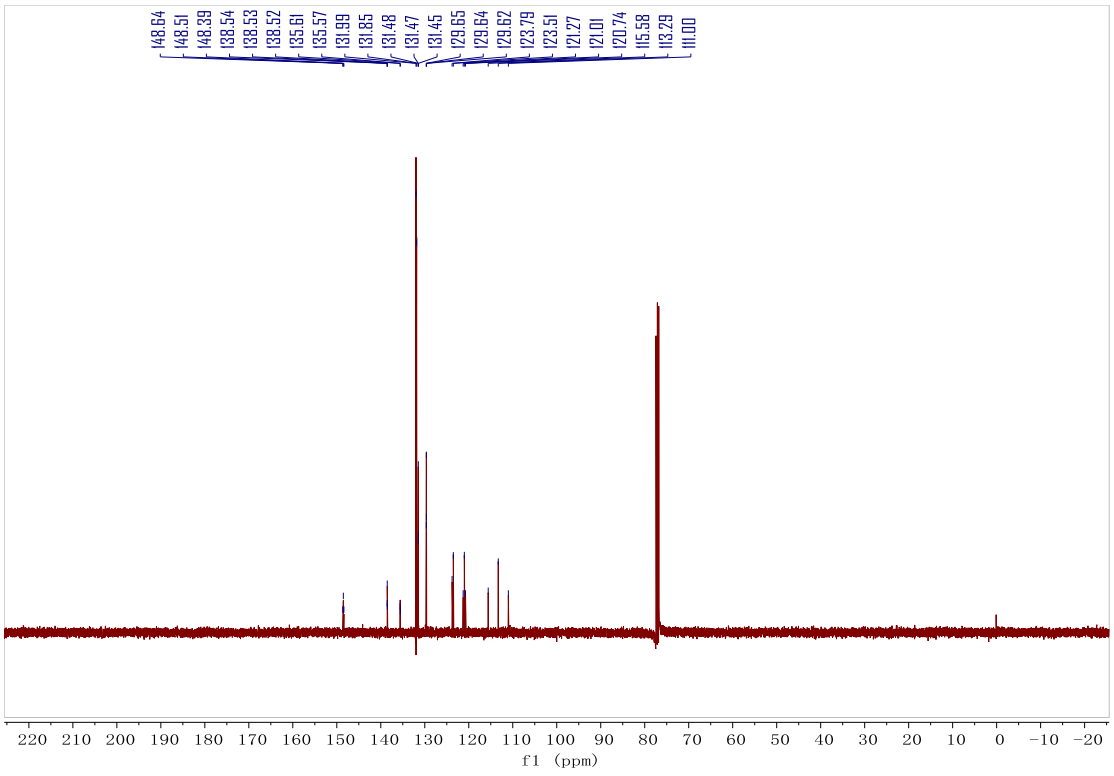
^{19}F NMR of compound 34 (377 MHz in $CDCl_3$)



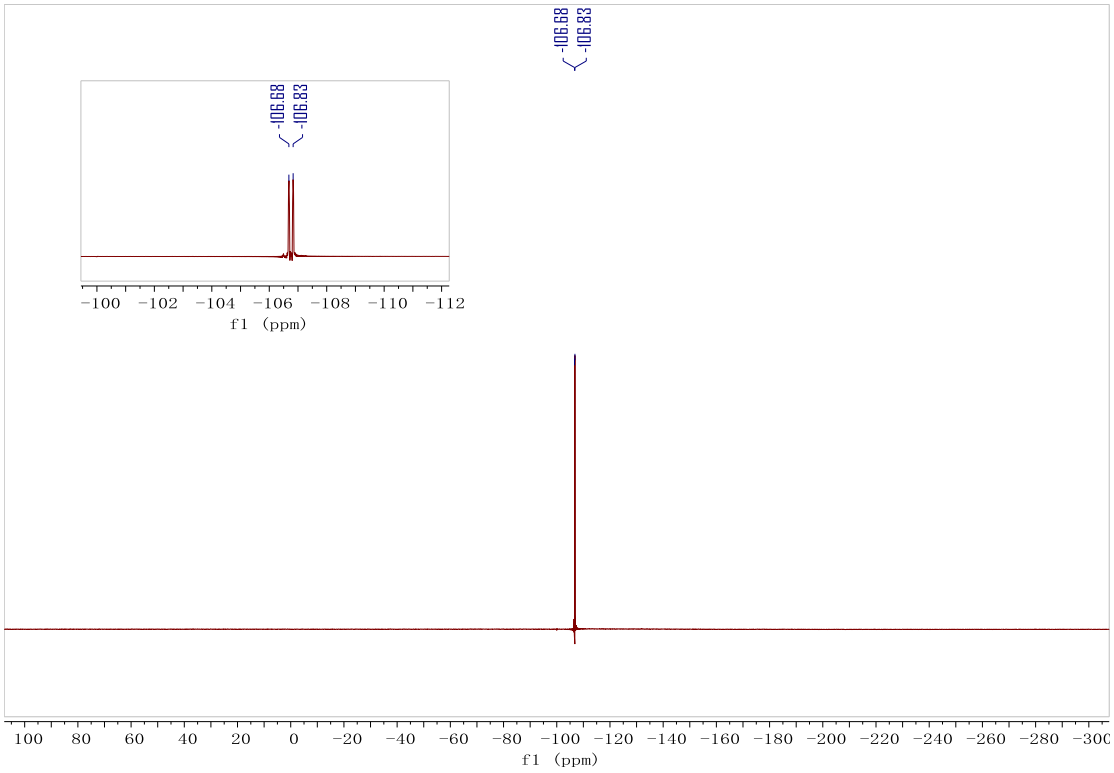
^{1}H NMR of compound 35 (400 MHz in $CDCl_3$)



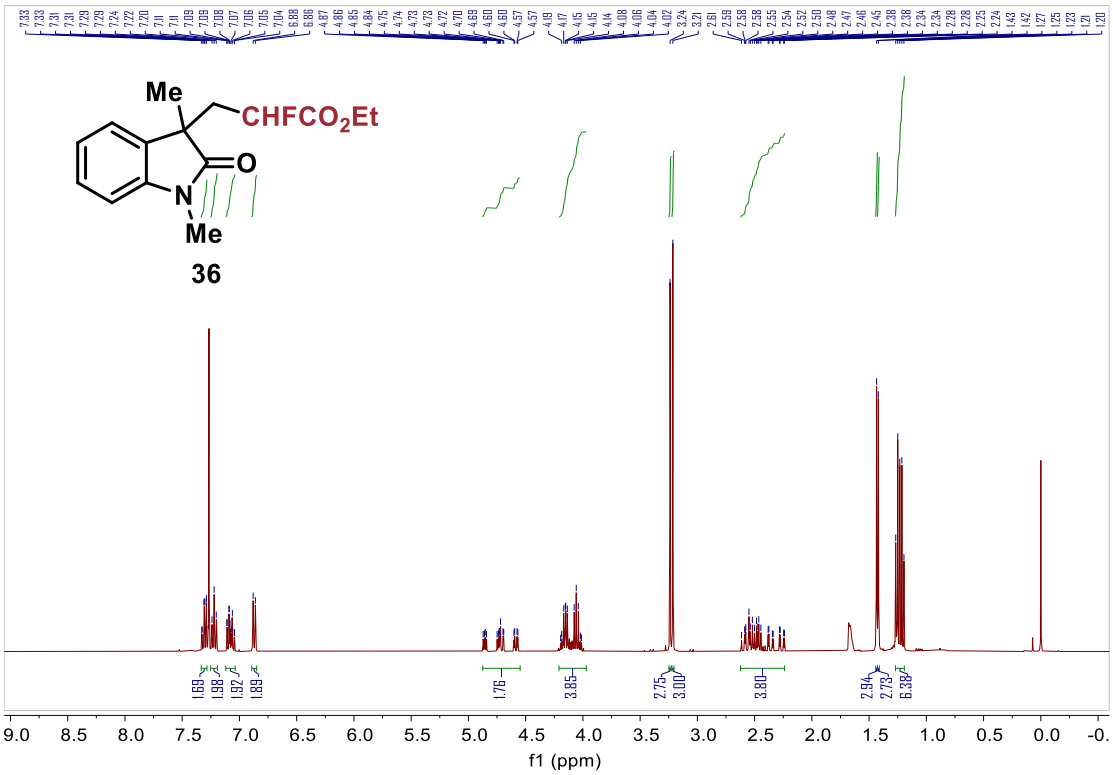
^{13}C NMR of compound 35 (101 MHz in $CDCl_3$)



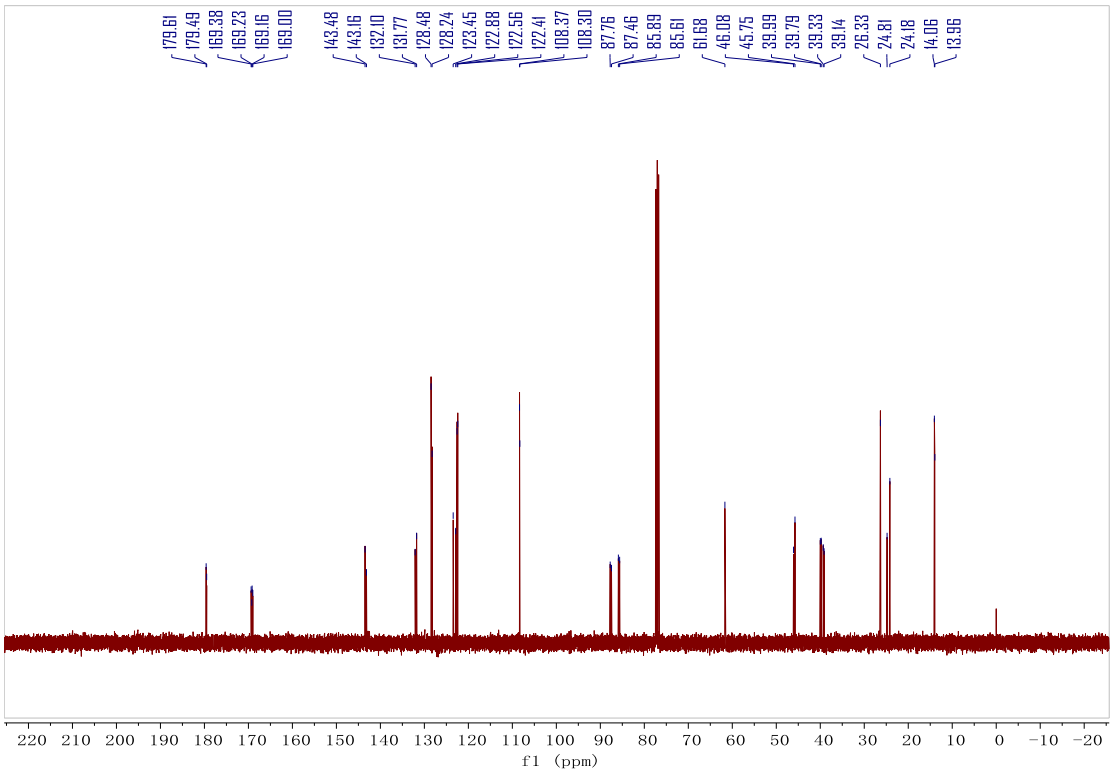
^{19}F NMR of compound 35 (377 MHz in $CDCl_3$)



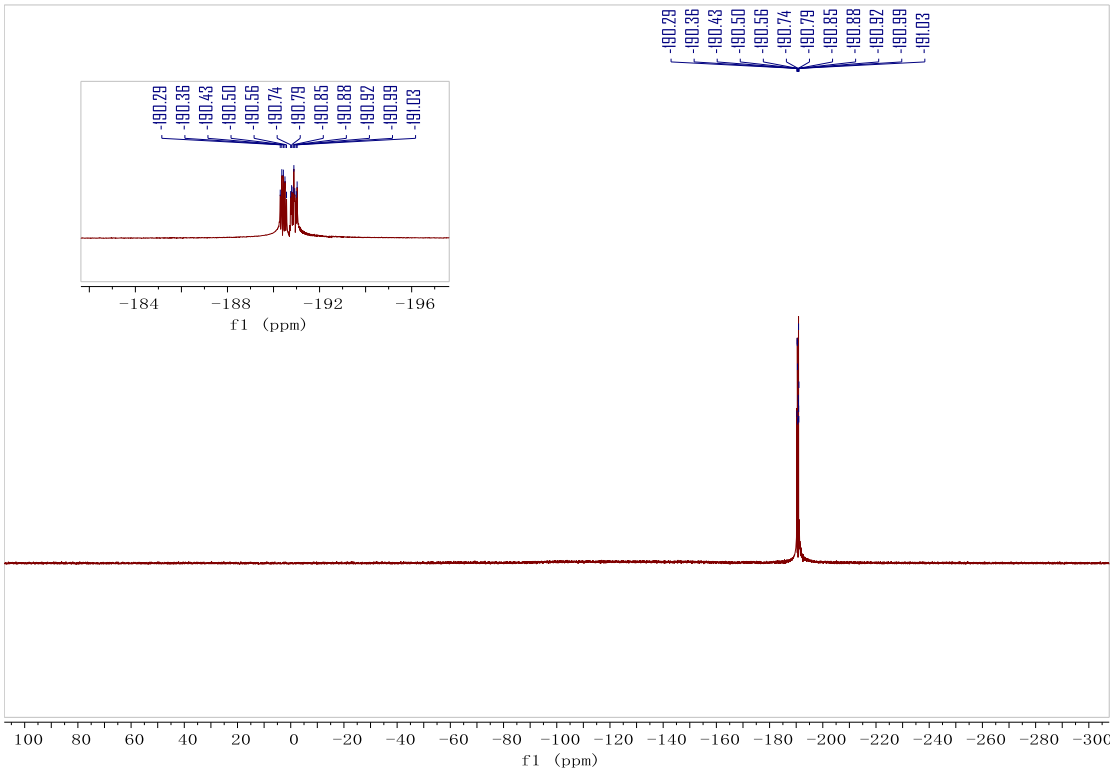
^{1}H NMR of compound 36 (400 MHz in $CDCl_3$)



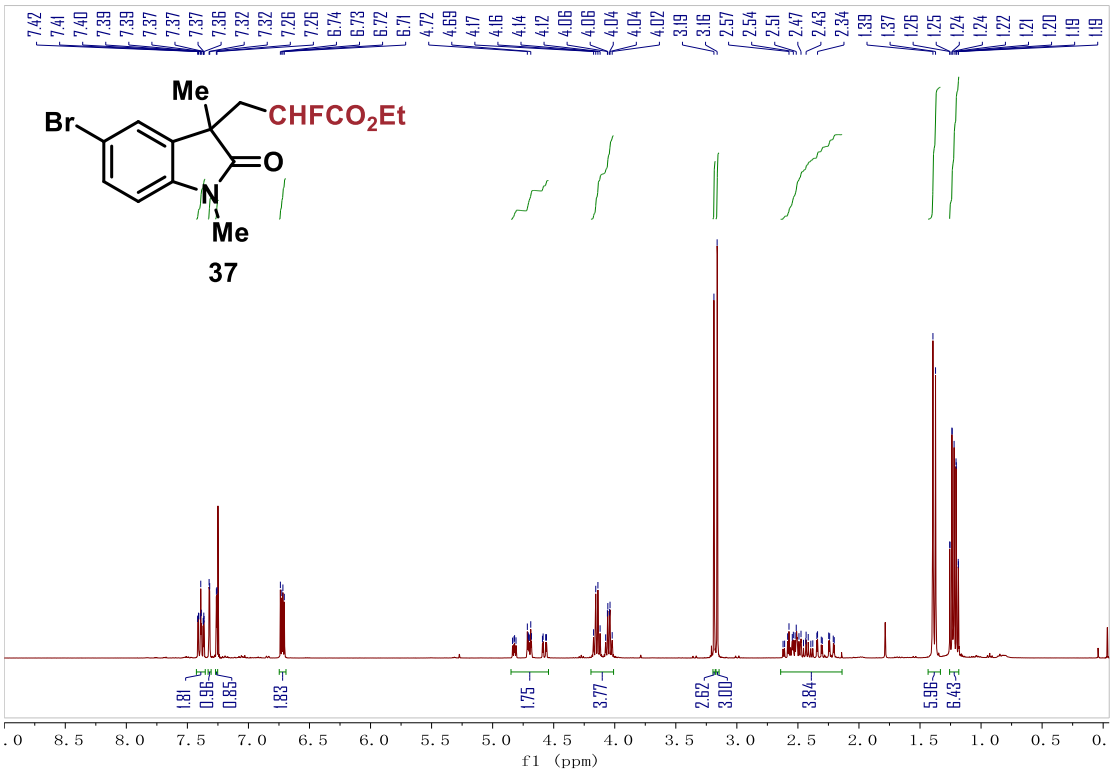
^{13}C NMR of compound 36 (101 MHz in $CDCl_3$)



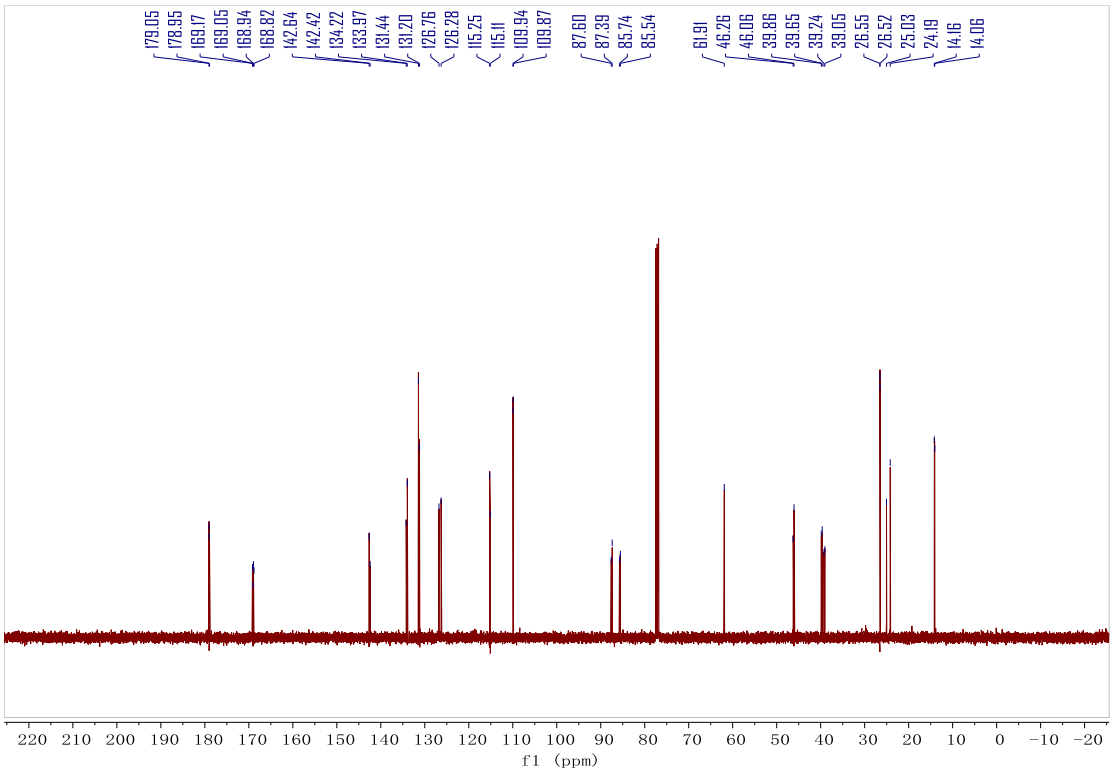
^{19}F NMR of compound 36 (377 MHz in $CDCl_3$)



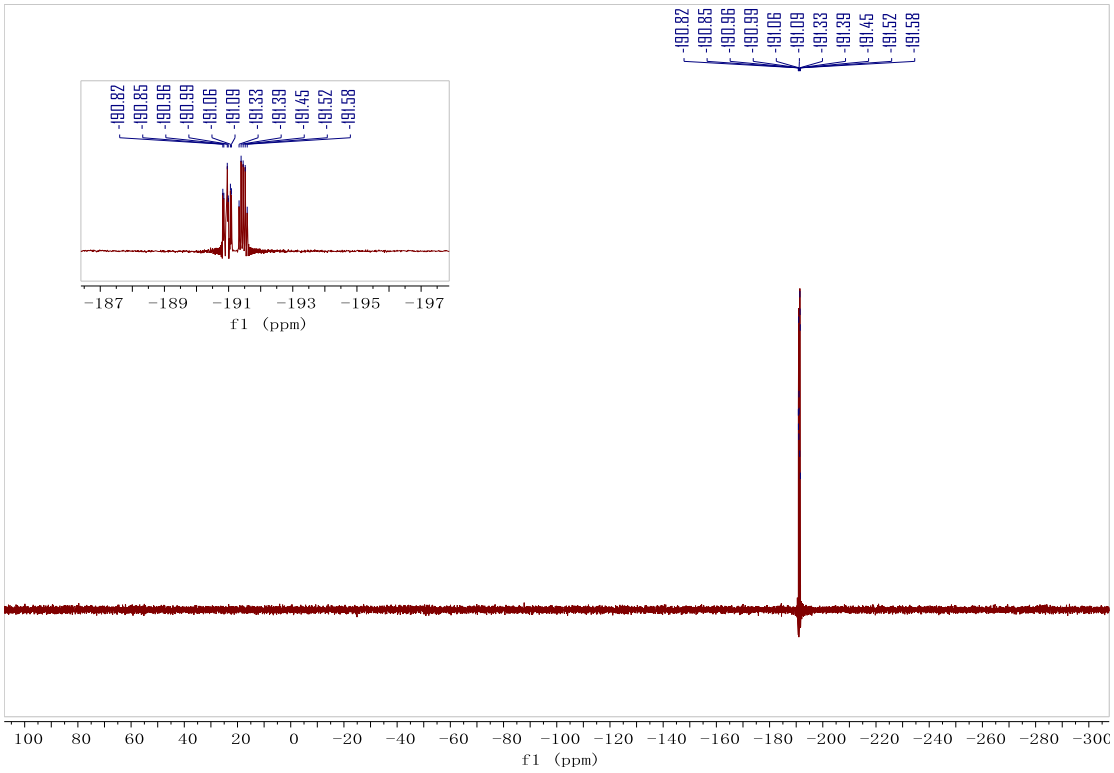
^{1}H NMR of compound 37 (400 MHz in $CDCl_3$)



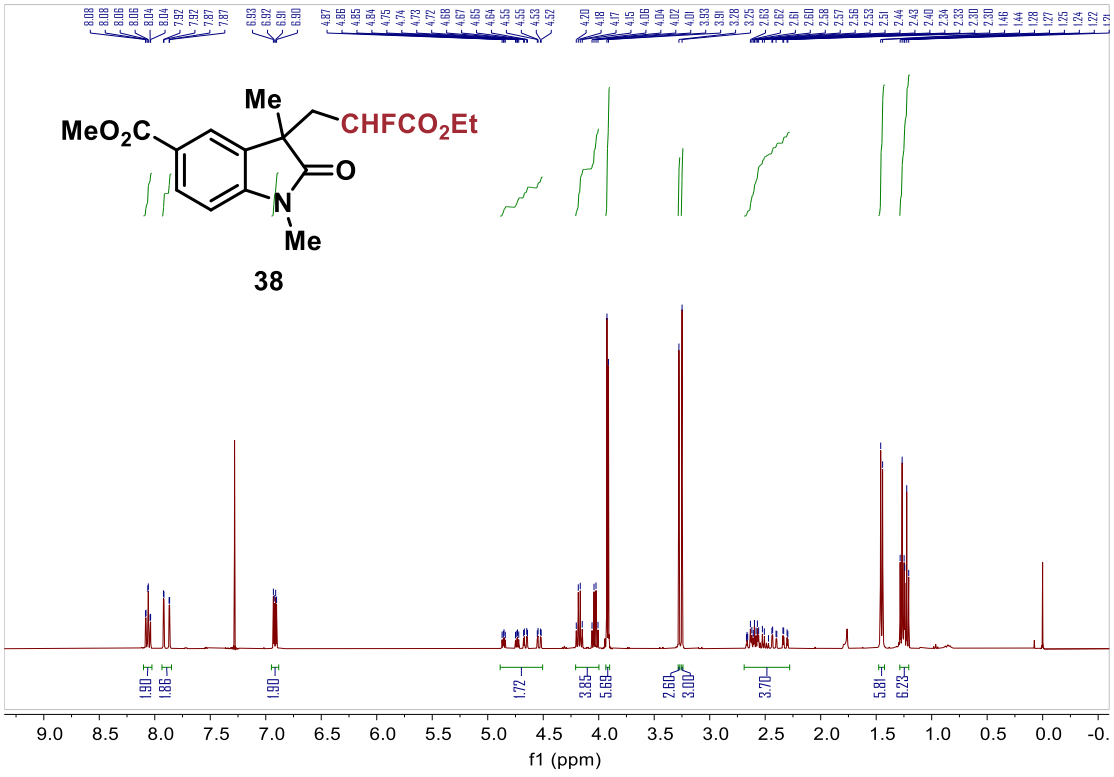
^{13}C NMR of compound 37 (101 MHz in $CDCl_3$)



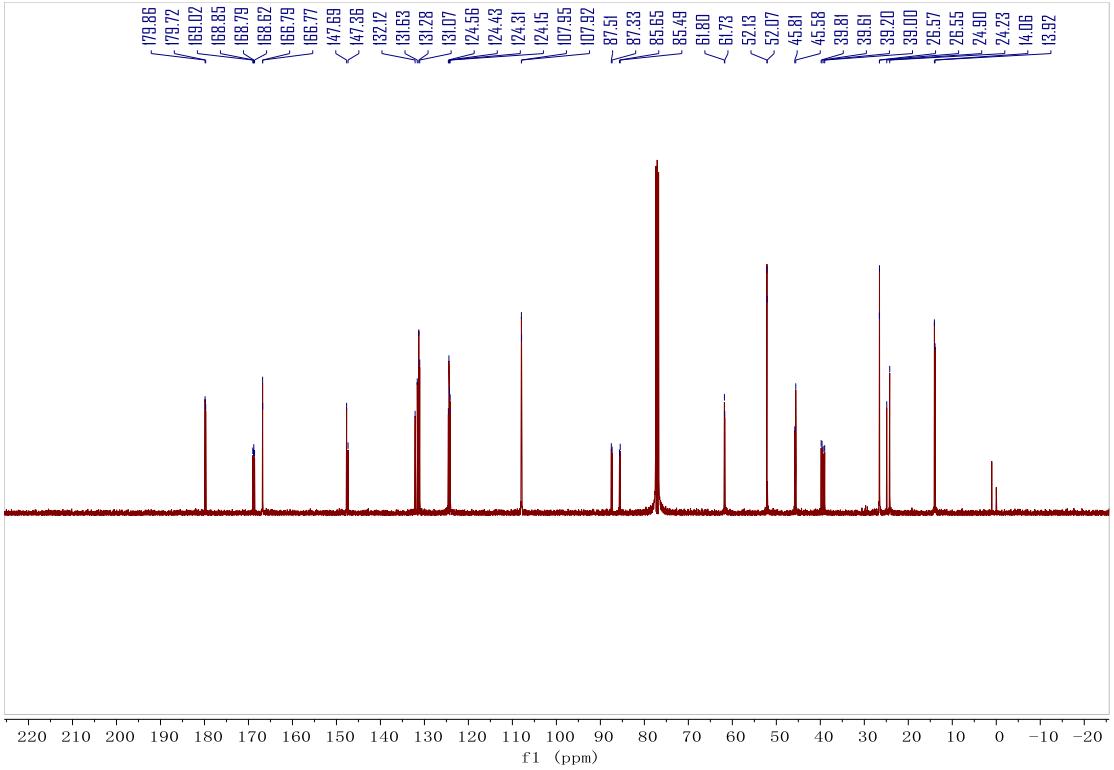
^{19}F NMR of compound 37 (377 MHz in $CDCl_3$)



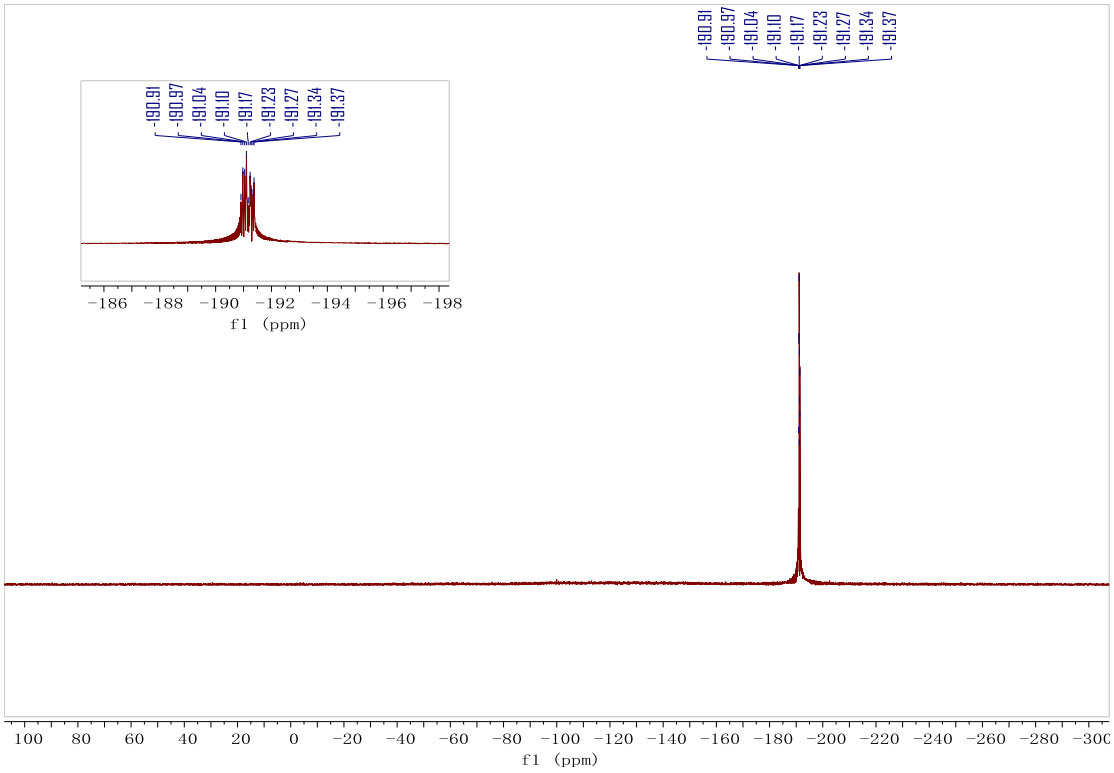
^{1}H NMR of compound 38 (400 MHz in $CDCl_3$)



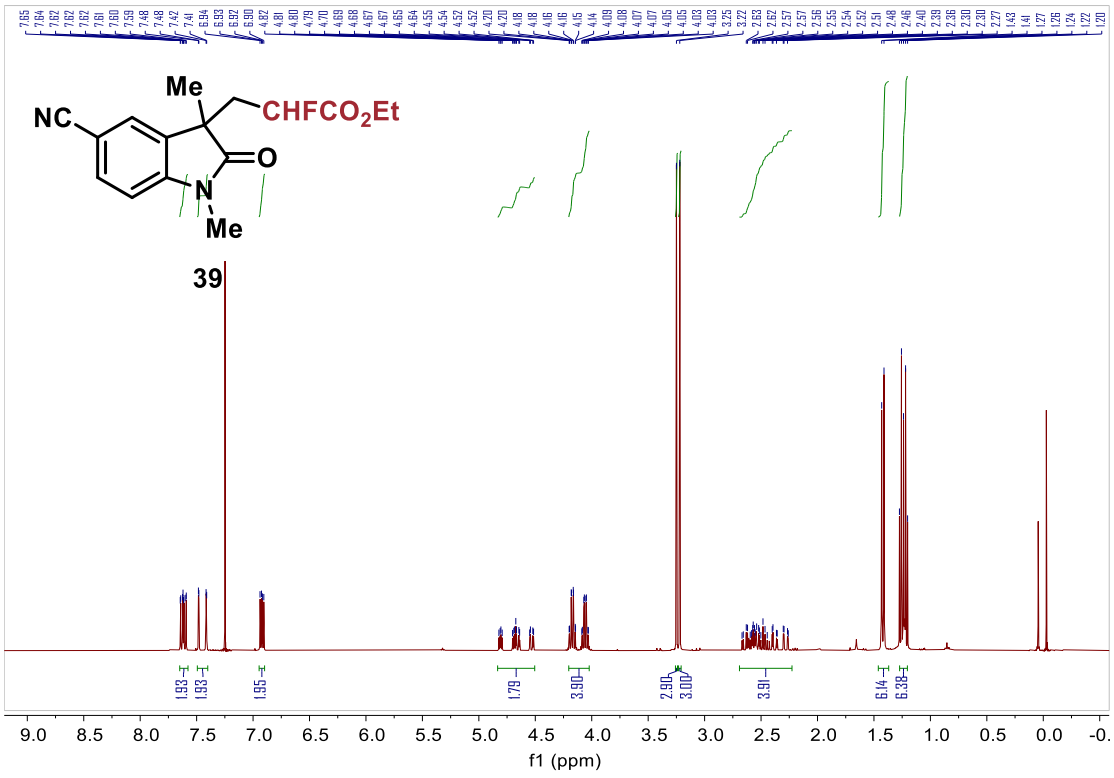
^{13}C NMR of compound 38 (101 MHz in $CDCl_3$)



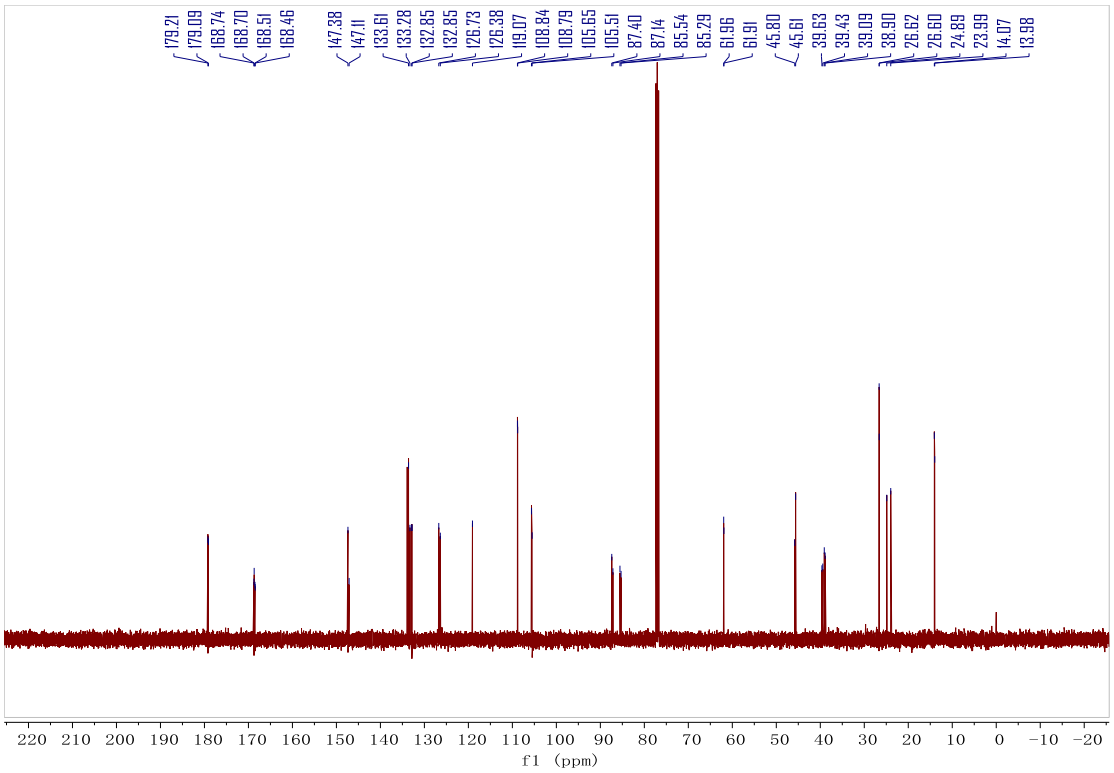
^{19}F NMR of compound 38 (377 MHz in $CDCl_3$)



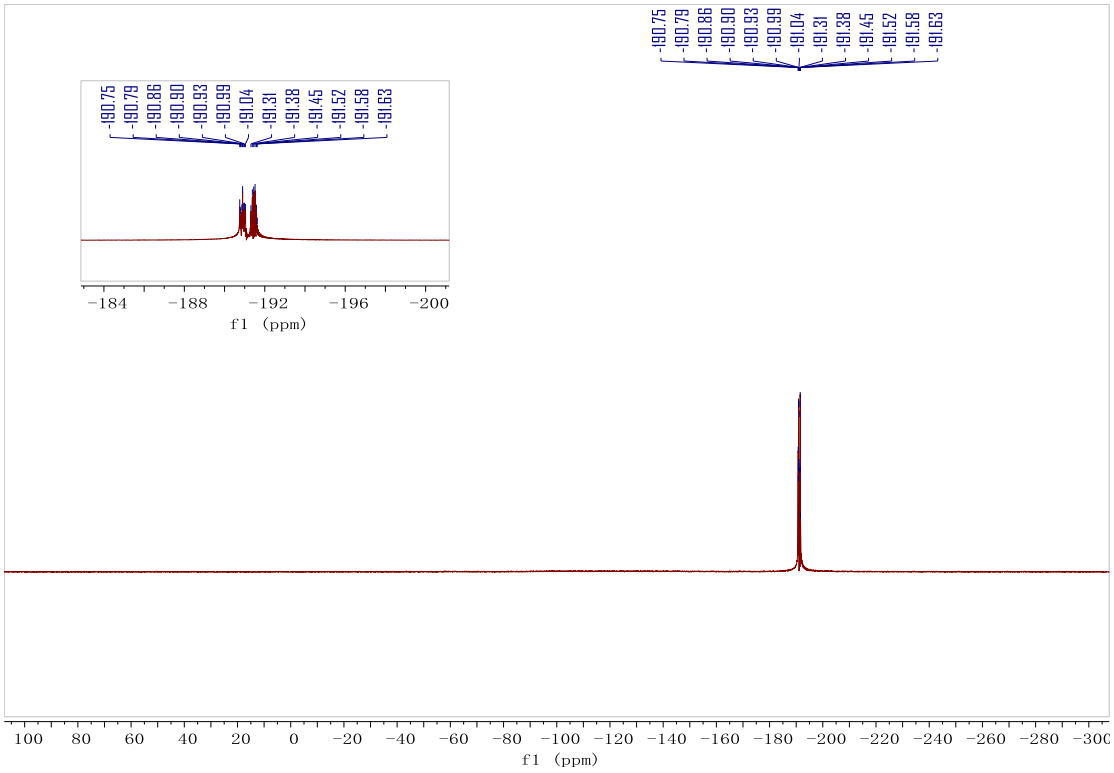
^{1}H NMR of compound 39 (400 MHz in $CDCl_3$)



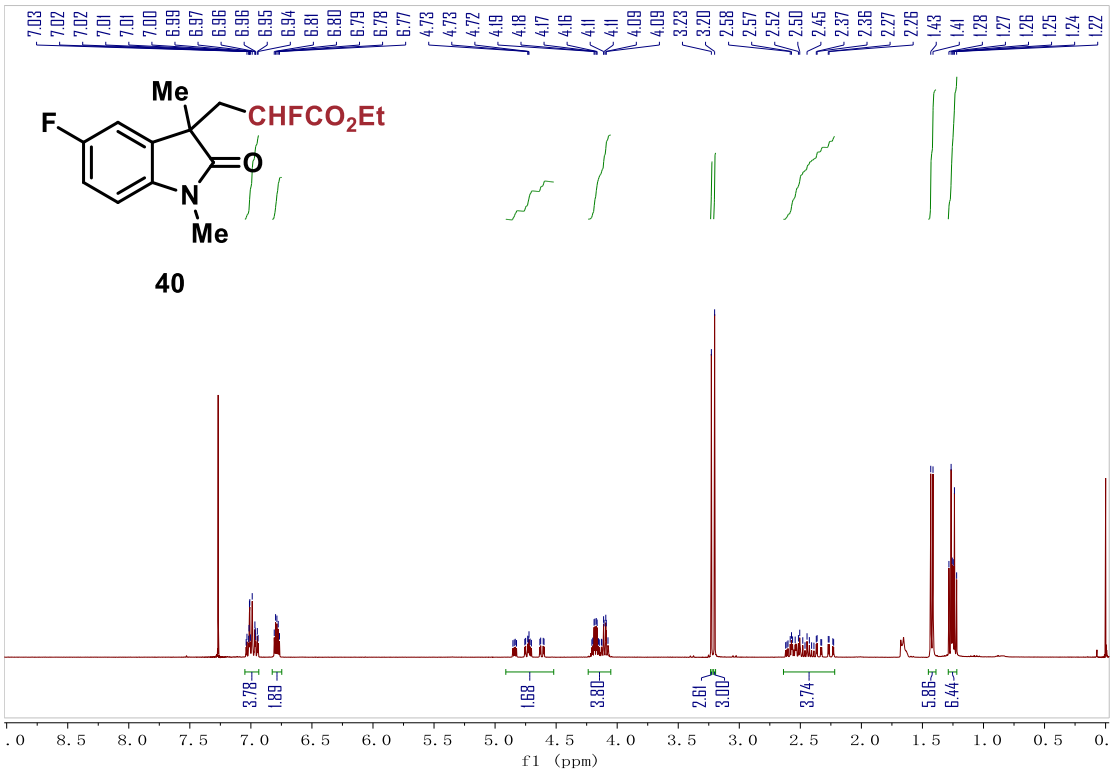
^{13}C NMR of compound 39 (101 MHz in $CDCl_3$)



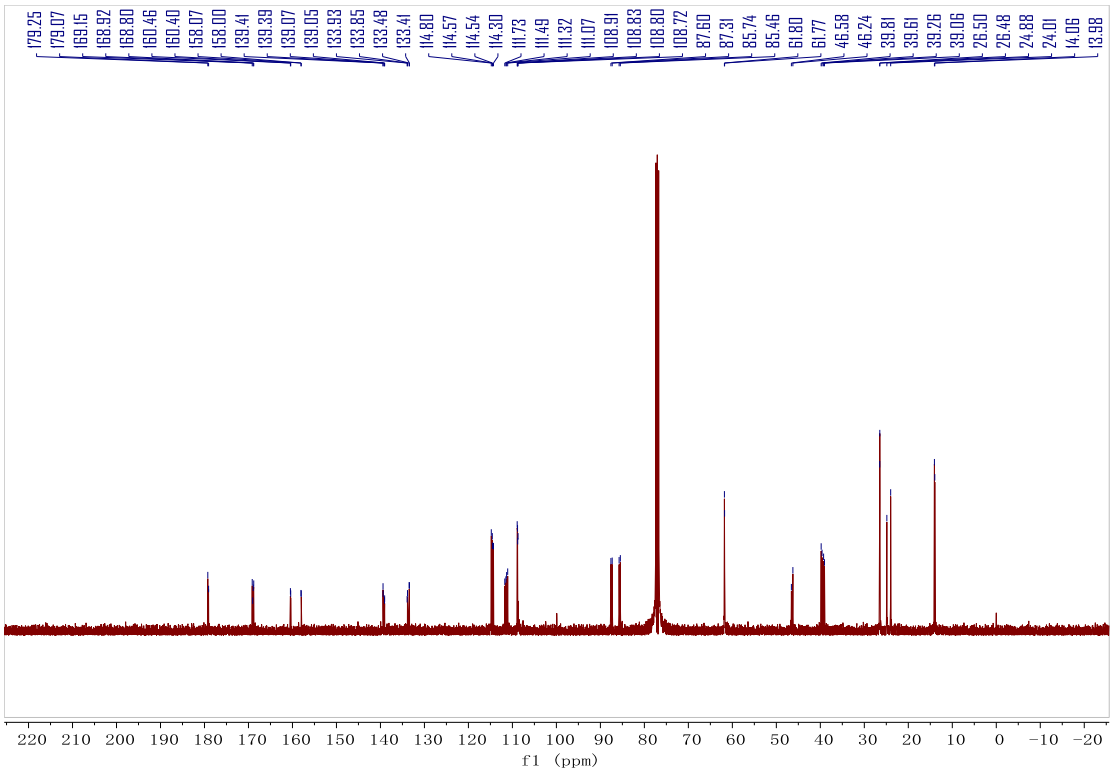
^{19}F NMR of compound 39 (377 MHz in $CDCl_3$)



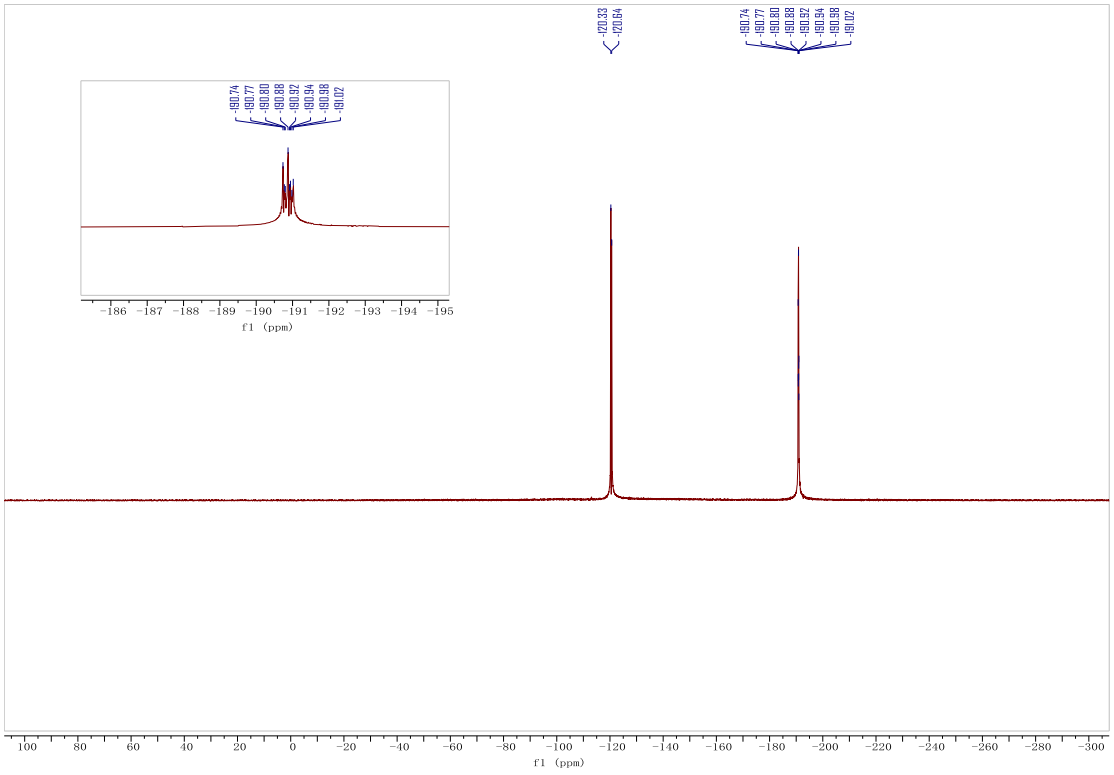
^{1}H NMR of compound 40 (400 MHz in $CDCl_3$)



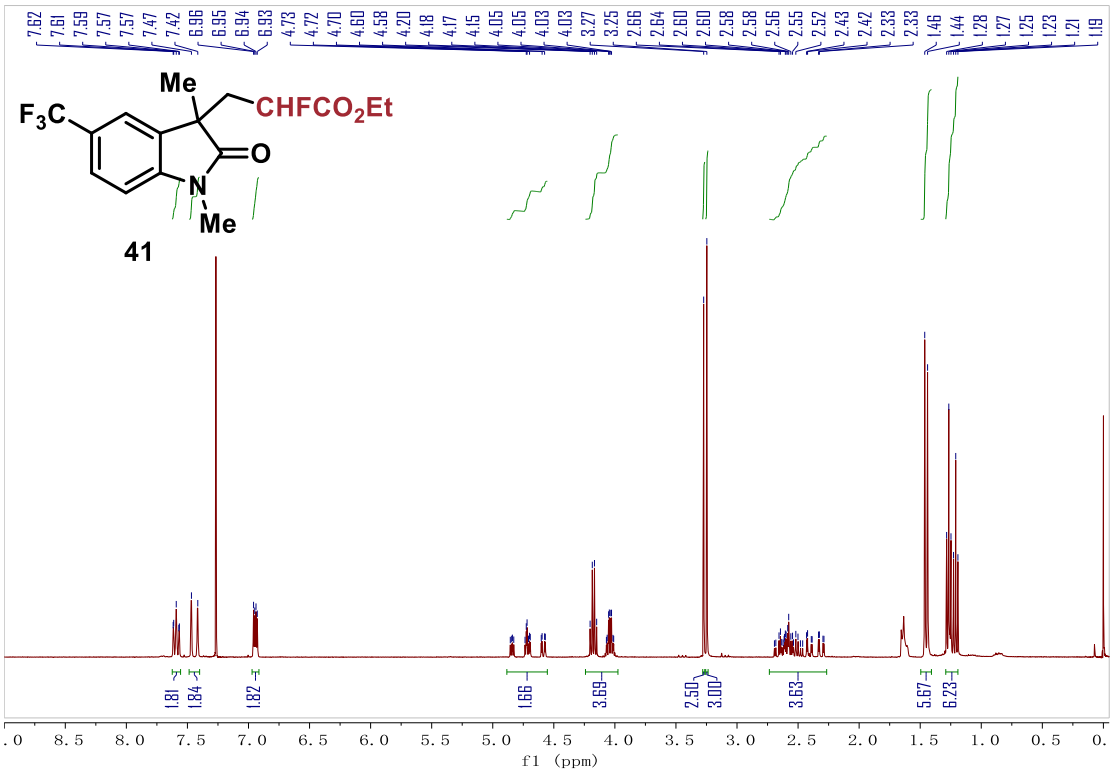
^{13}C NMR of compound 40 (101 MHz in $CDCl_3$)



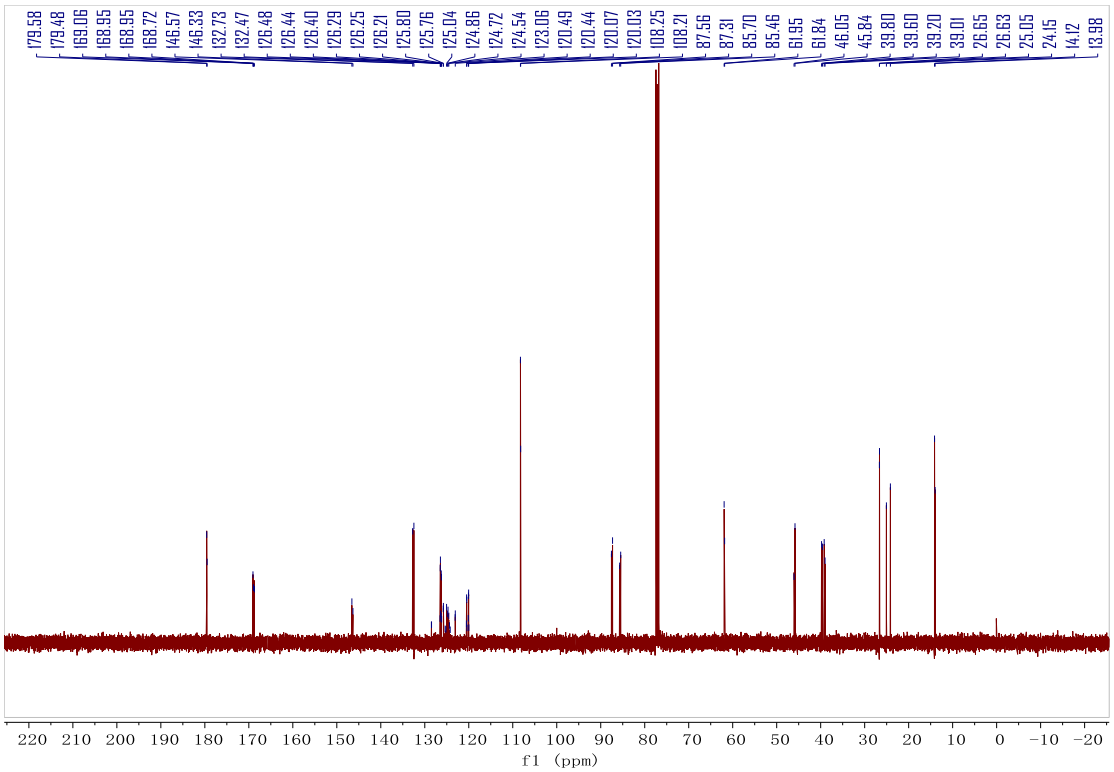
^{19}F NMR of compound 40 (377 MHz in $CDCl_3$)



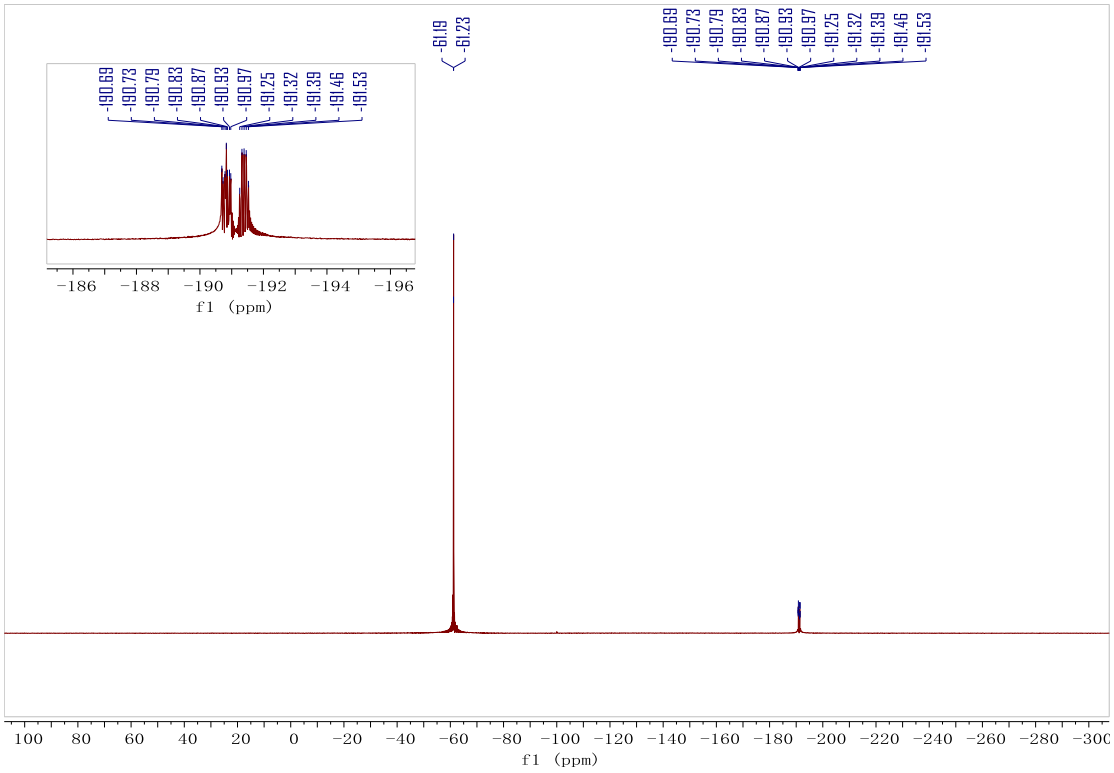
^{1}H NMR of compound 41 (400 MHz in $CDCl_3$)



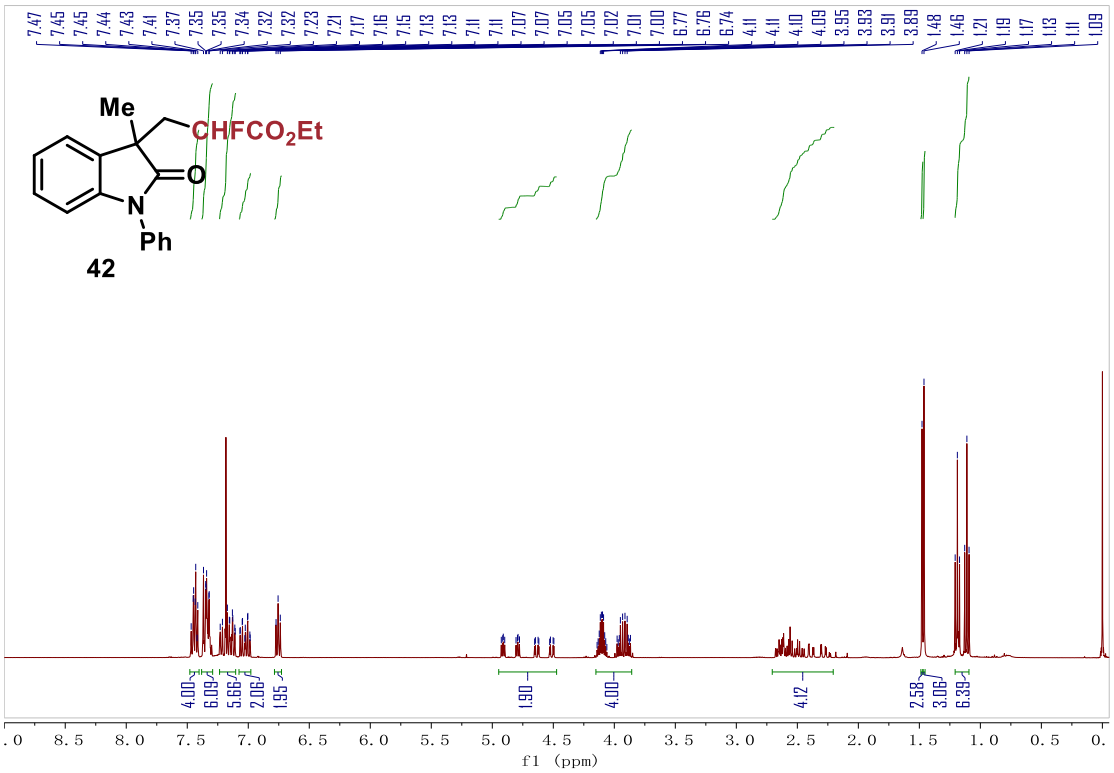
^{13}C NMR of compound 41 (101 MHz in $CDCl_3$)



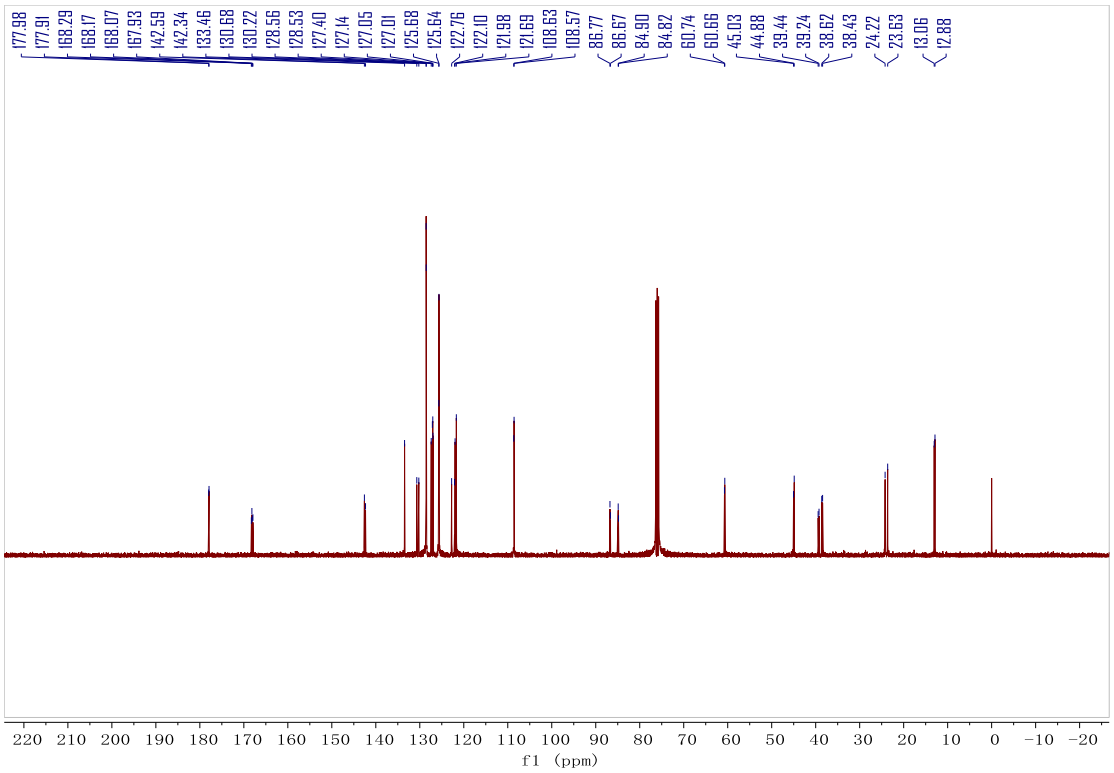
^{19}F NMR of compound 41 (377 MHz in $CDCl_3$)



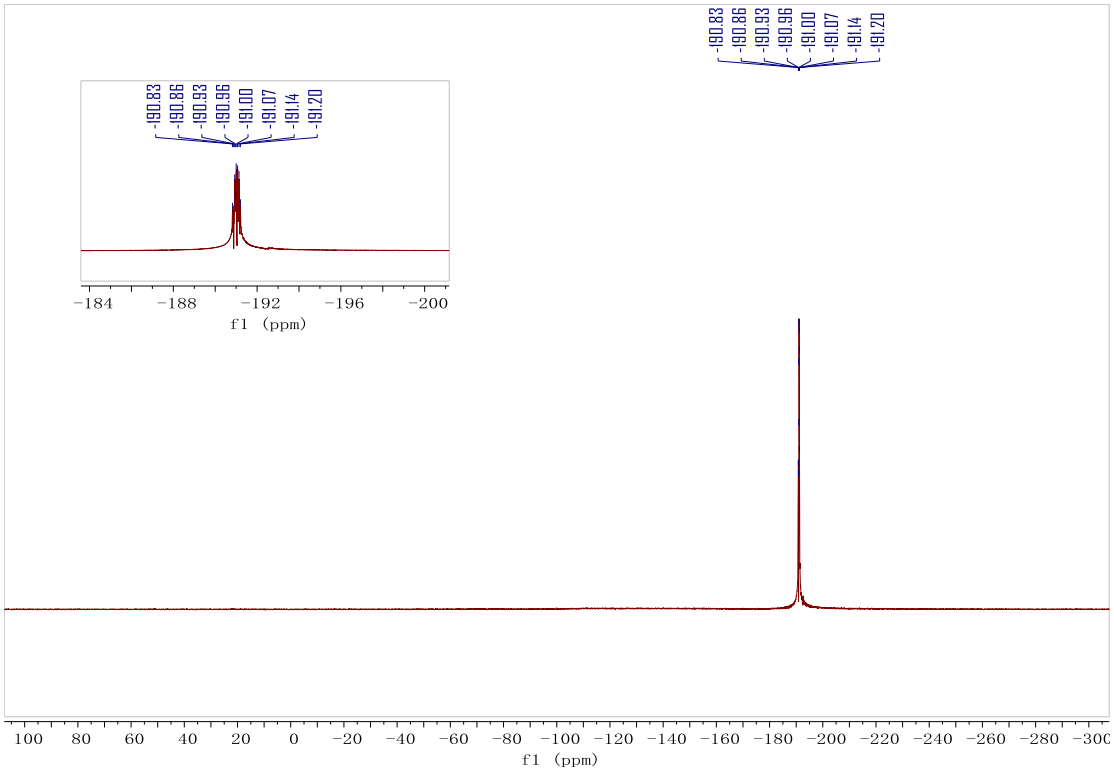
^{1}H NMR of compound 42 (400 MHz in $CDCl_3$)



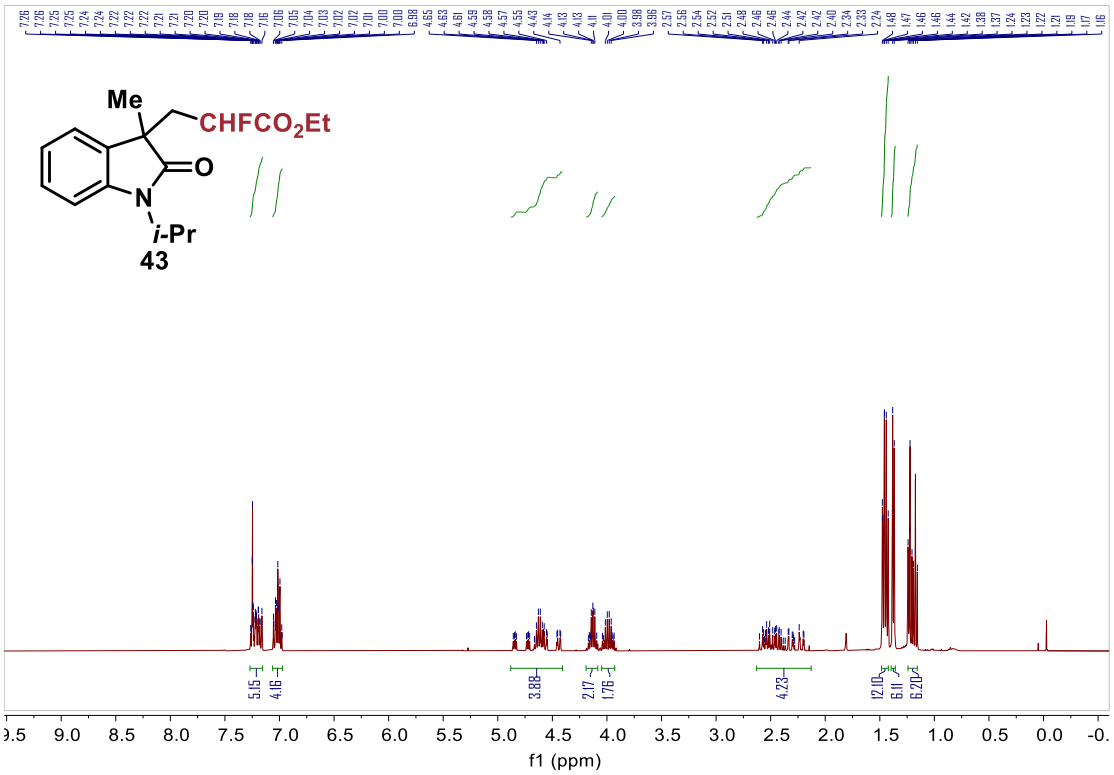
^{13}C NMR of compound 42 (101 MHz in $CDCl_3$)



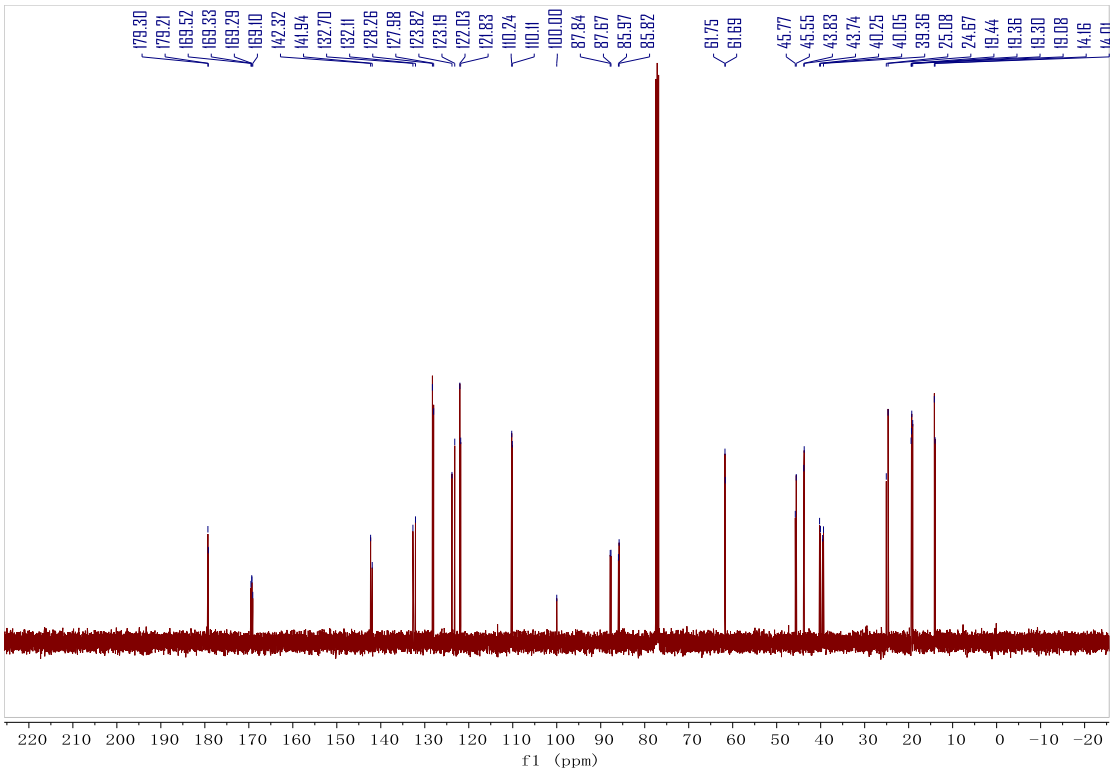
^{19}F NMR of compound 42 (377 MHz in $CDCl_3$)



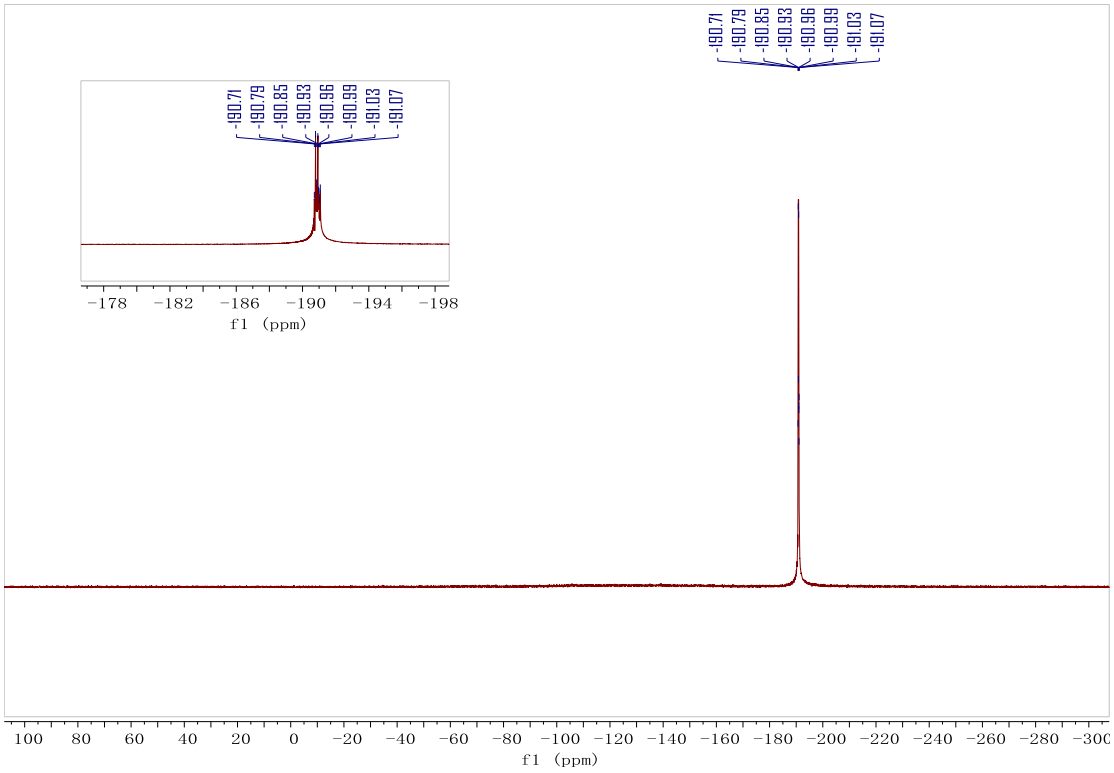
^{1}H NMR of compound 43 (400 MHz in $CDCl_3$)



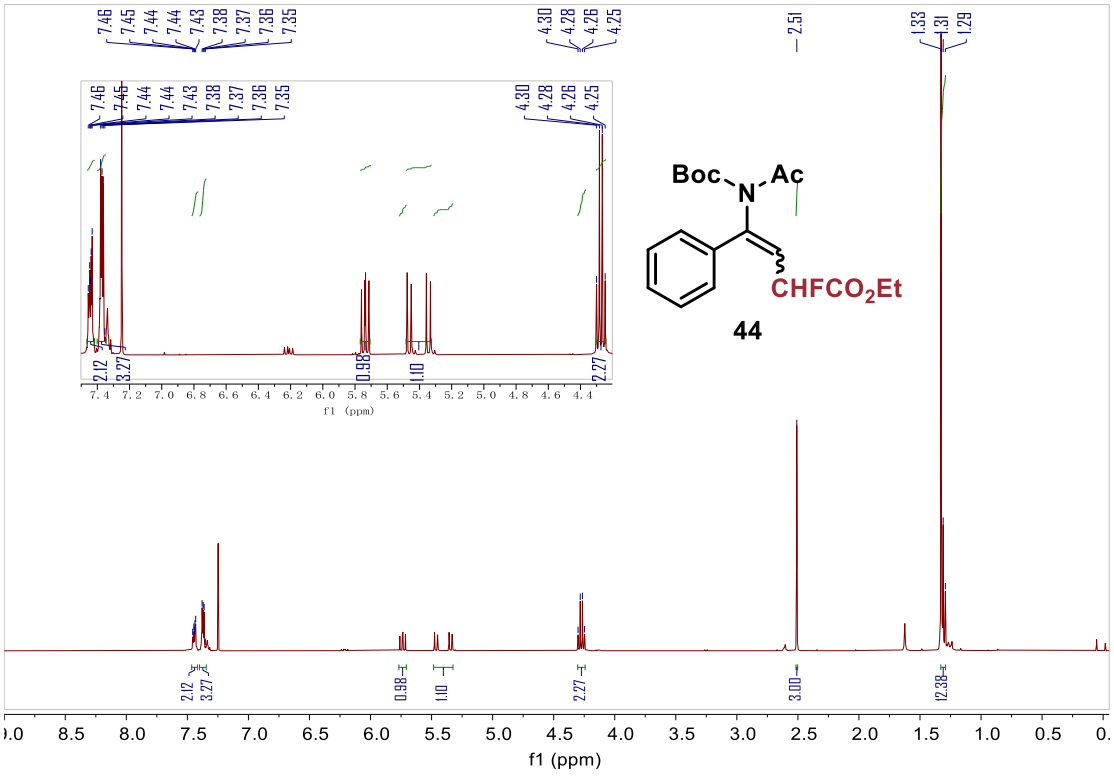
^{13}C NMR of compound 43 (101 MHz in $CDCl_3$)



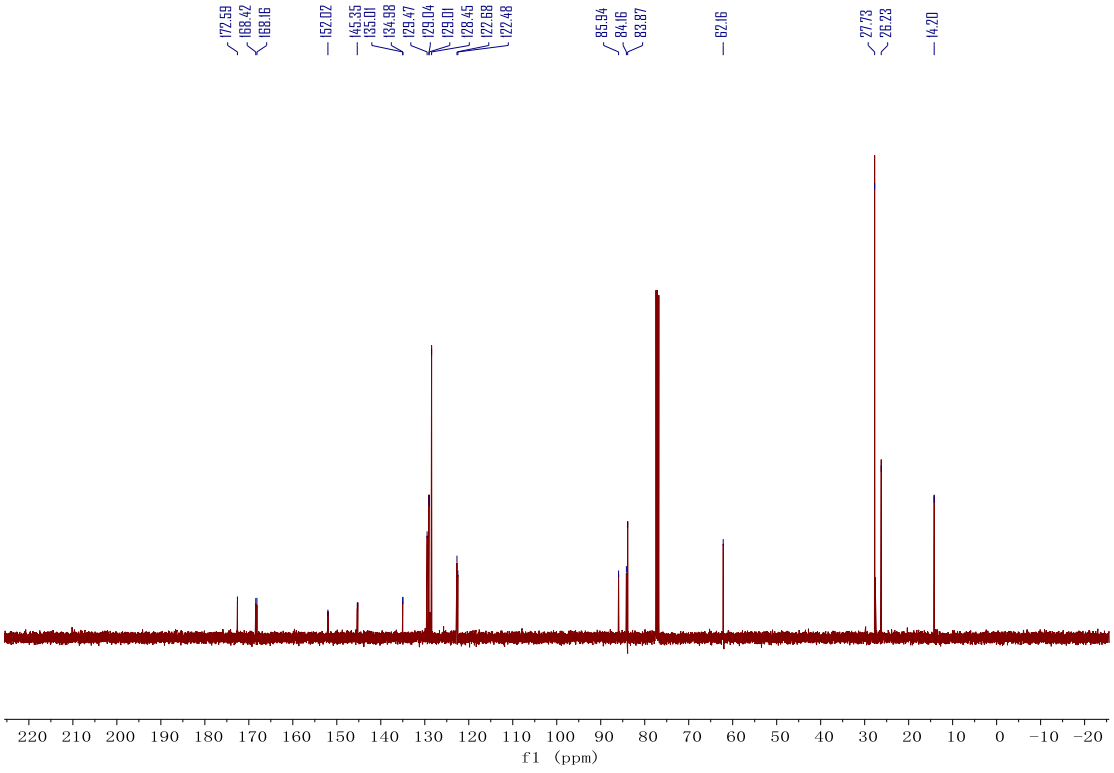
^{19}F NMR of compound 43 (377 MHz in $CDCl_3$)



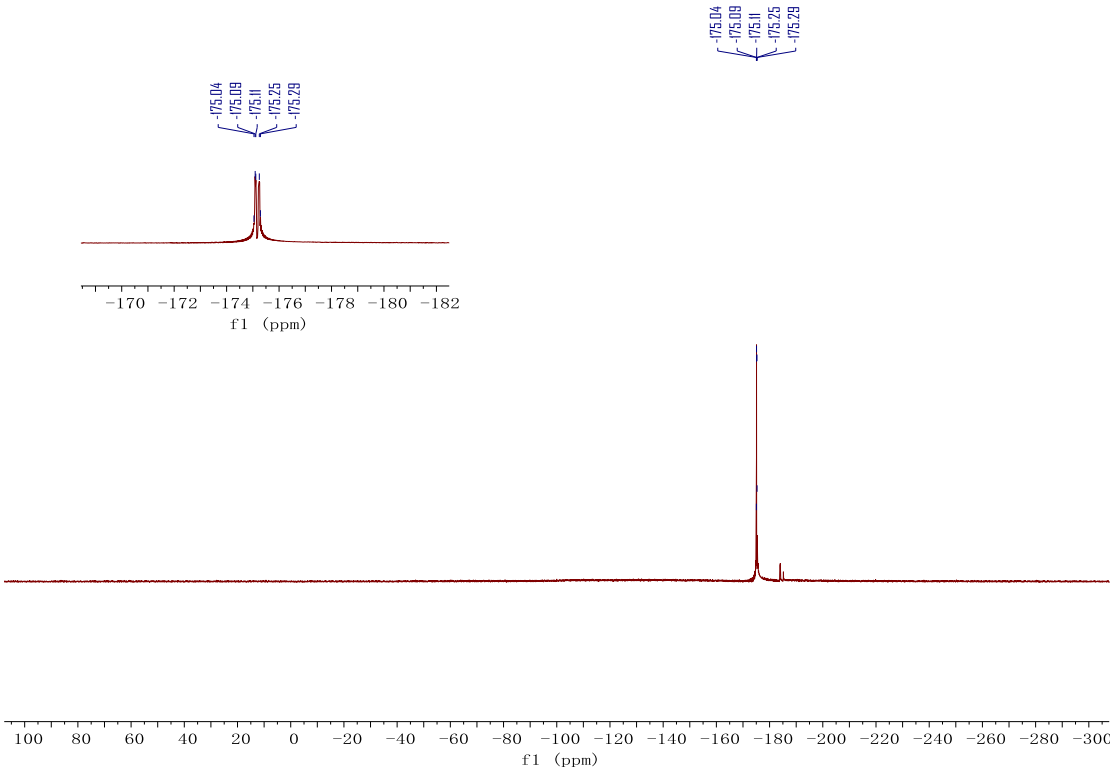
^{1}H NMR of compound 44 (400 MHz in $CDCl_3$)



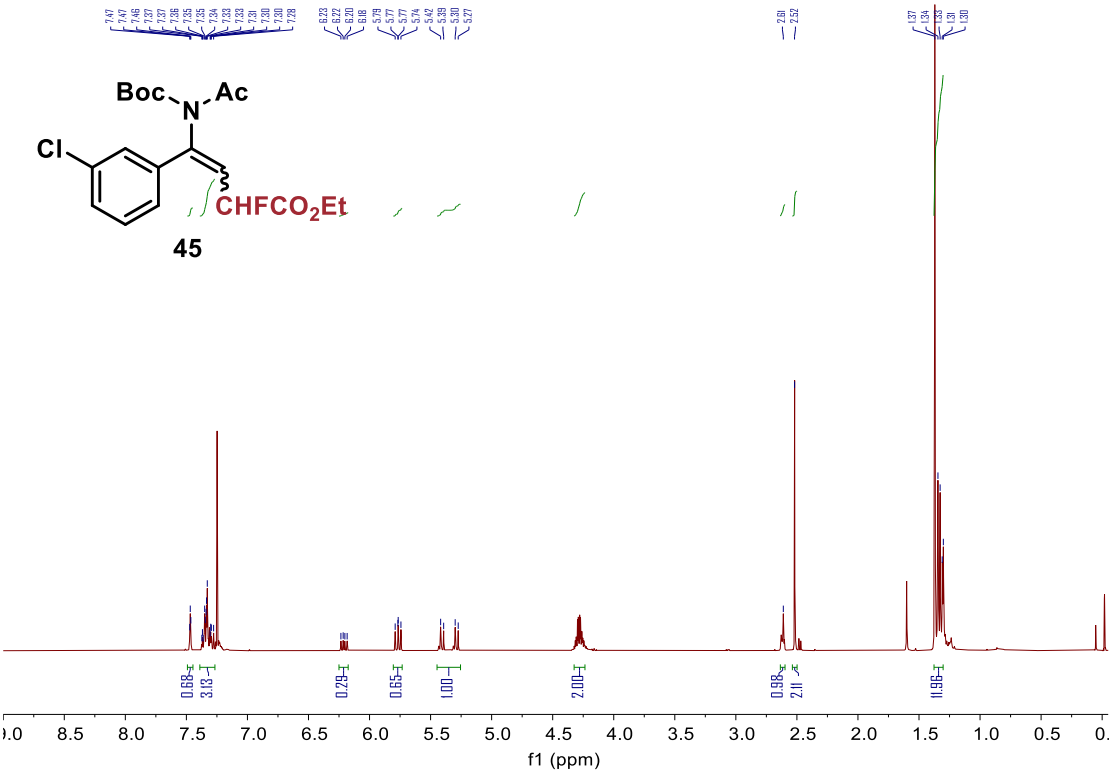
^{13}C NMR of compound 44 (101 MHz in $CDCl_3$)



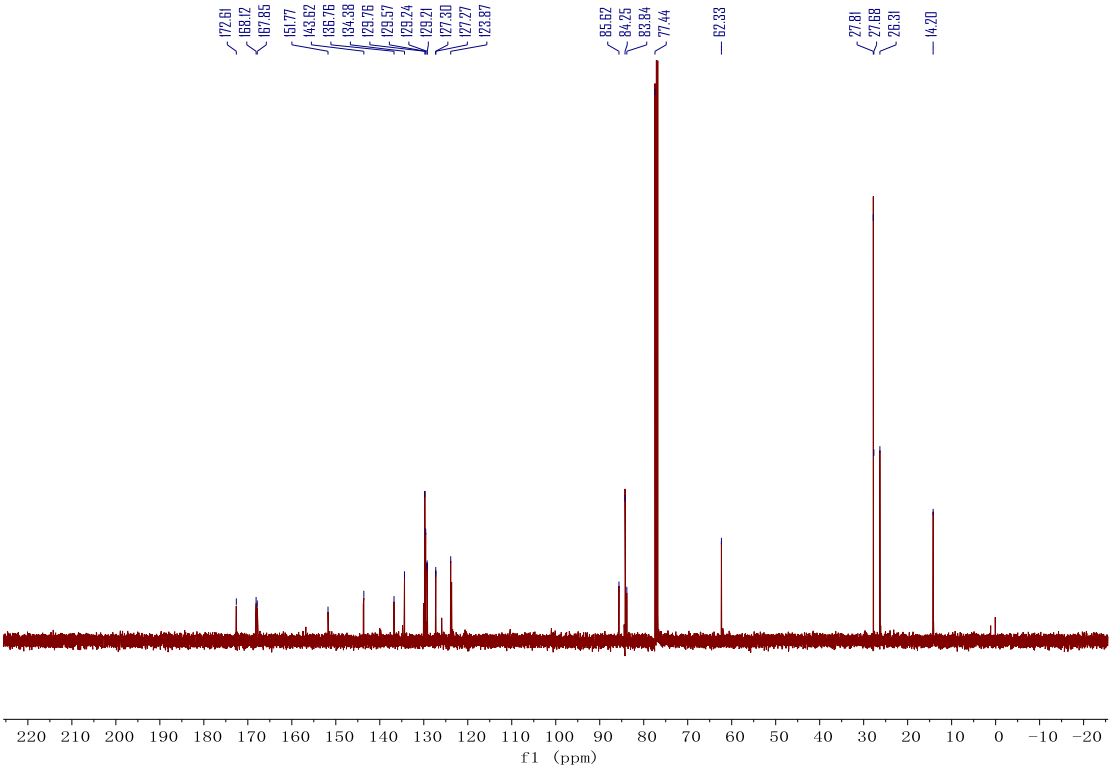
^{19}F NMR of compound 44 (377 MHz in $CDCl_3$)



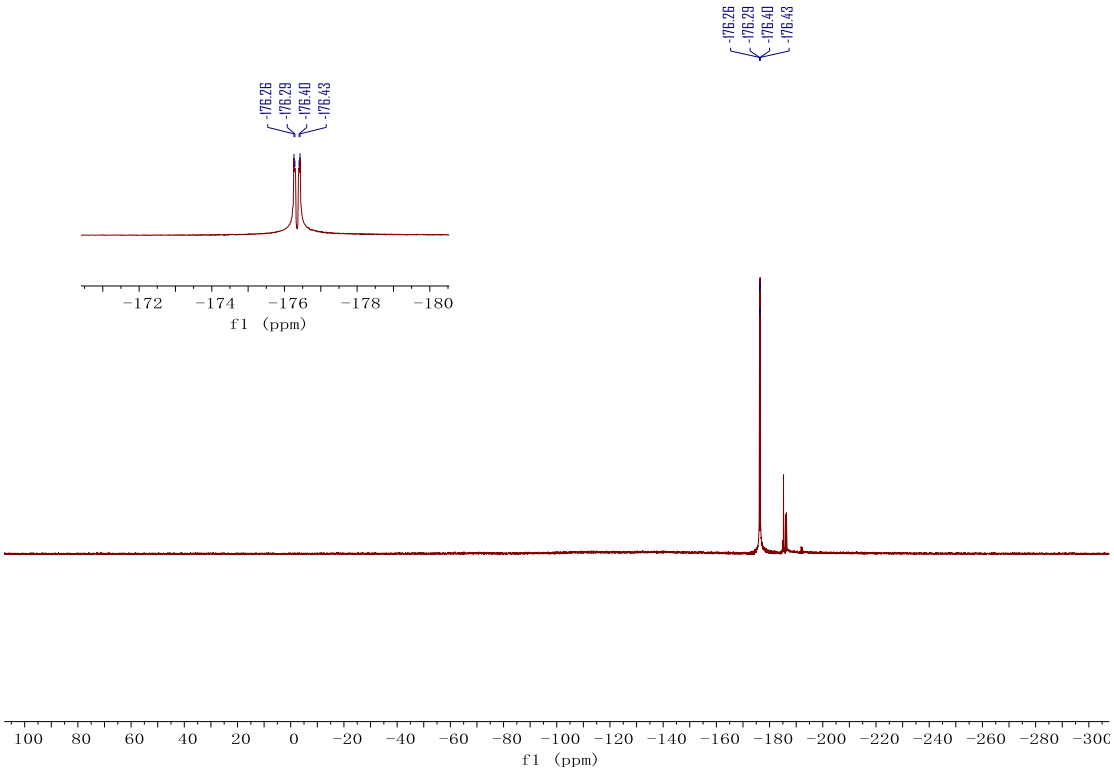
^{1}H NMR of compound 45 (400 MHz in $CDCl_3$)



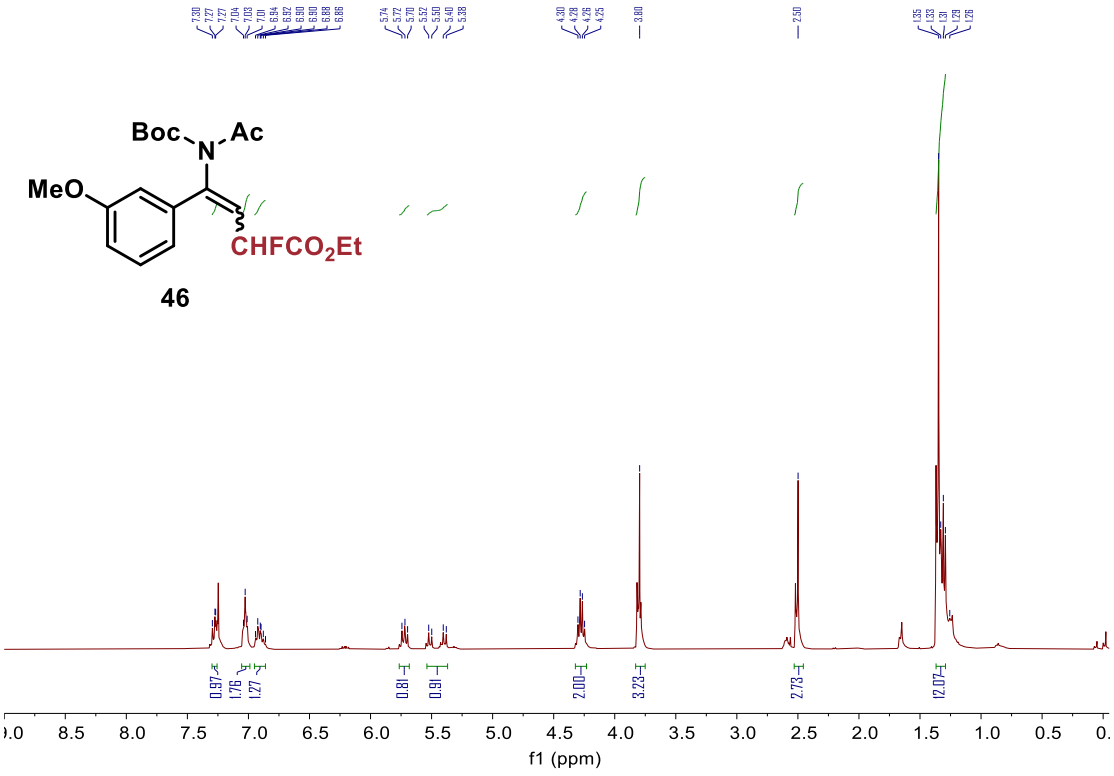
^{13}C NMR of compound 45 (101 MHz in $CDCl_3$)



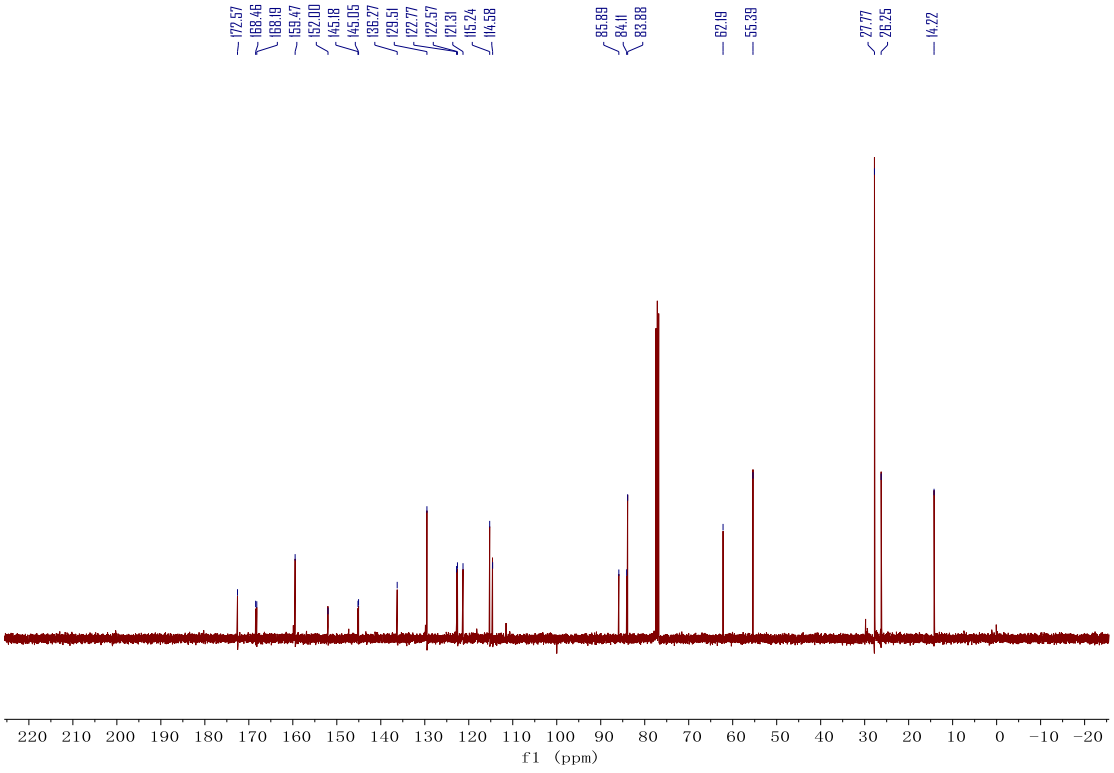
^{19}F NMR of compound 45 (377 MHz in $CDCl_3$)



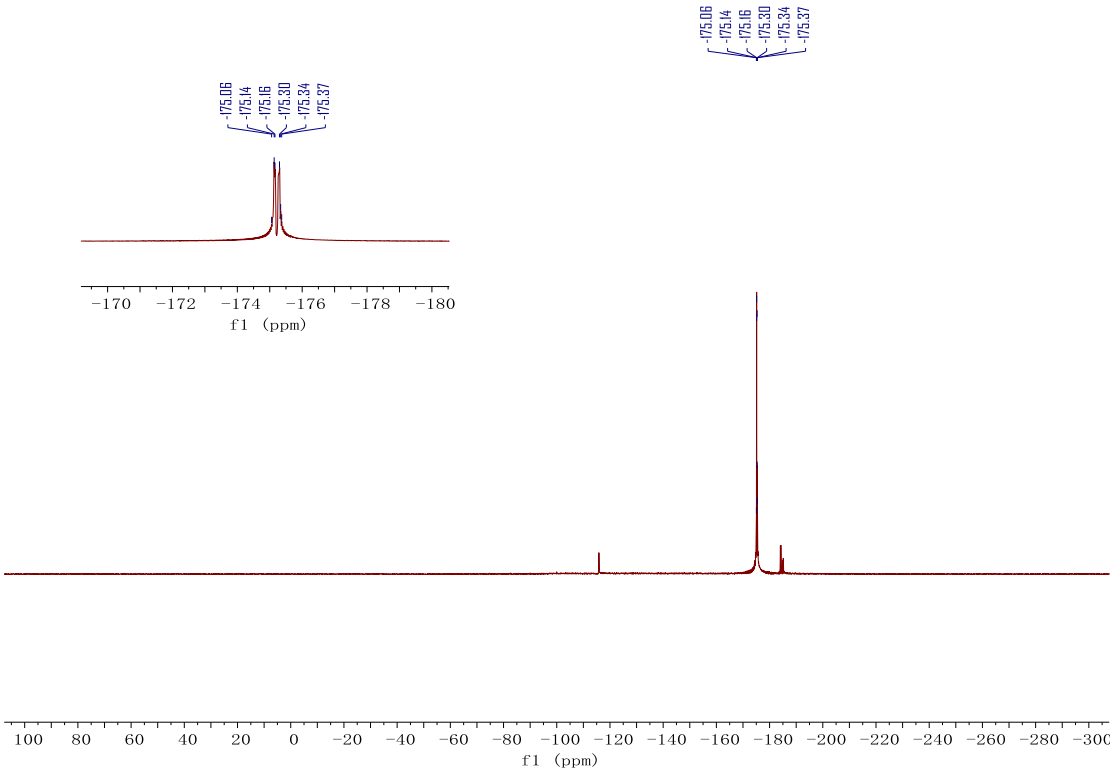
^{1}H NMR of compound 46 (400 MHz in $CDCl_3$)



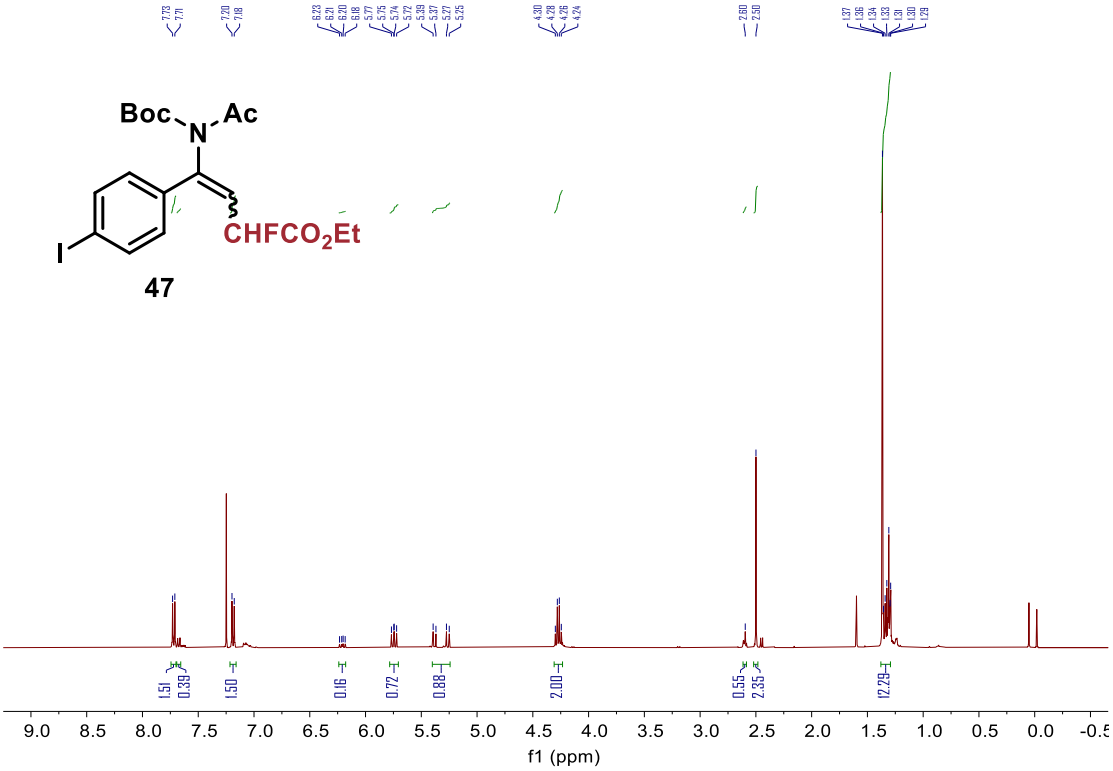
^{13}C NMR of compound 46 (101 MHz in $CDCl_3$)



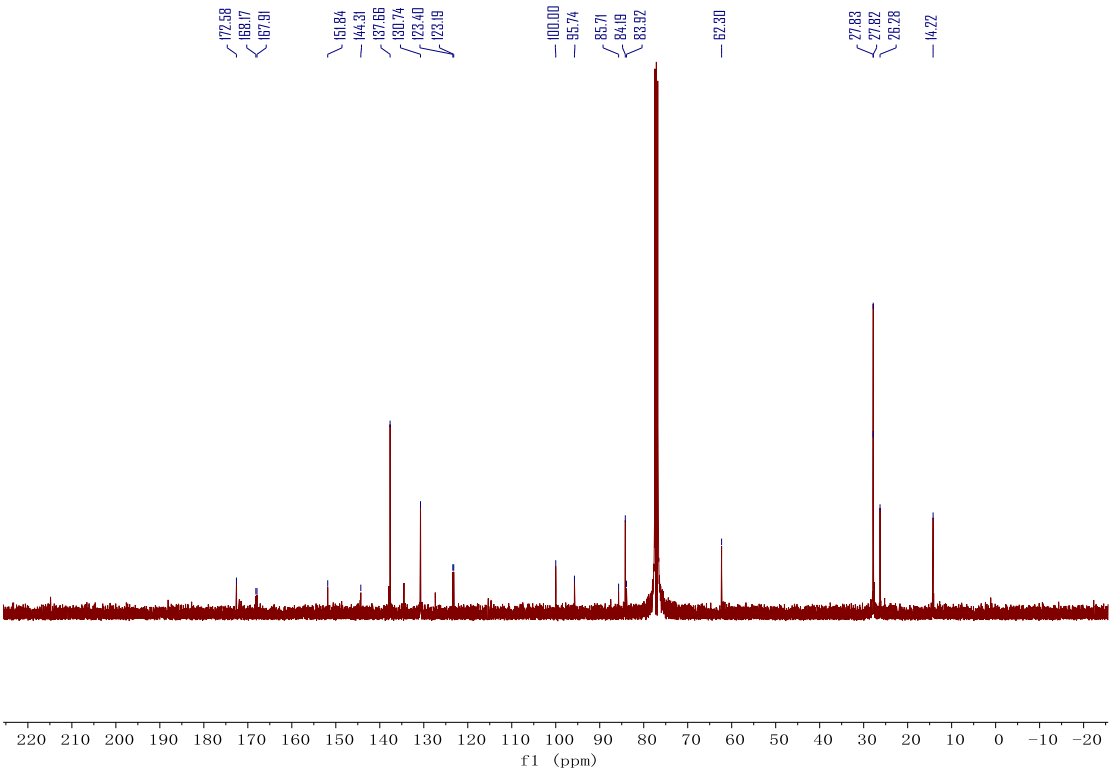
^{19}F NMR of compound 46 (377 MHz in $CDCl_3$)



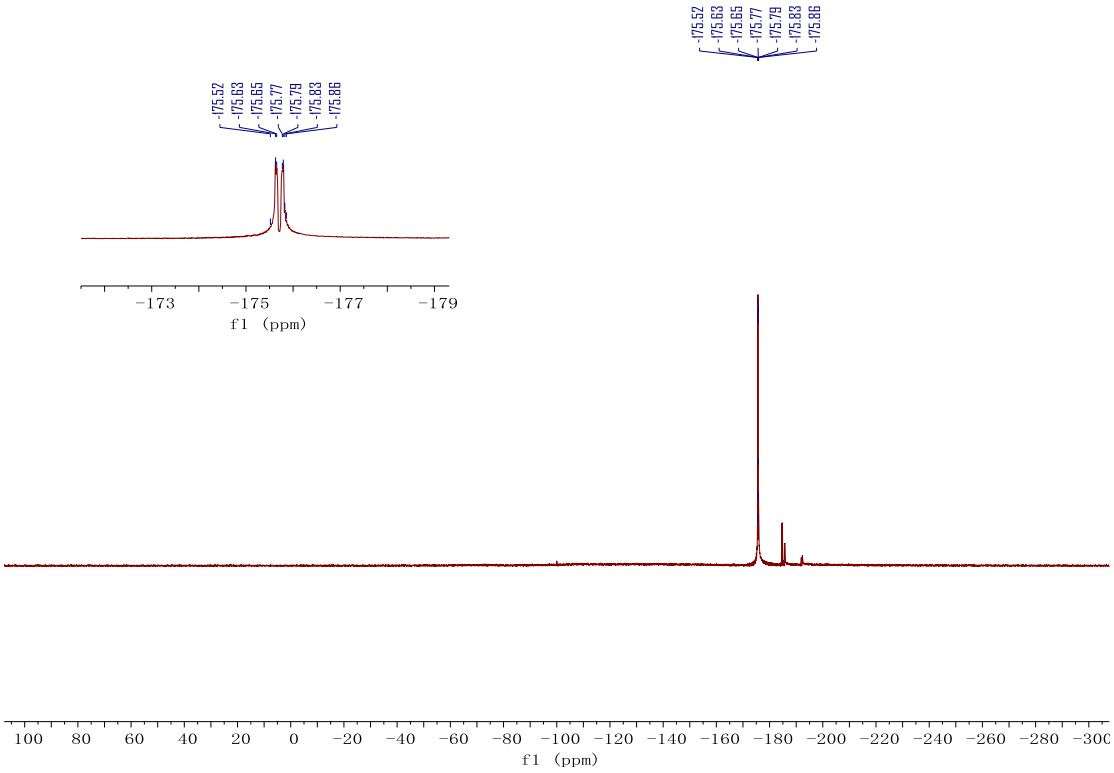
^{1}H NMR of compound 47 (400 MHz in $CDCl_3$)



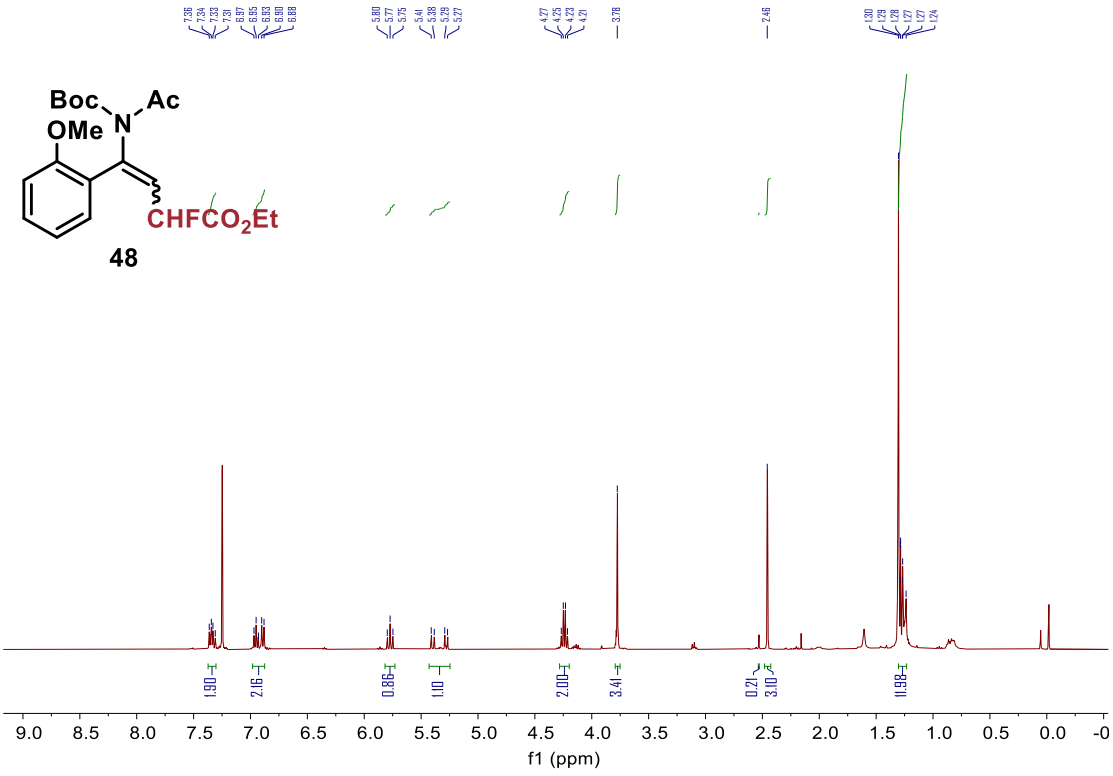
^{13}C NMR of compound 47 (101 MHz in $CDCl_3$)



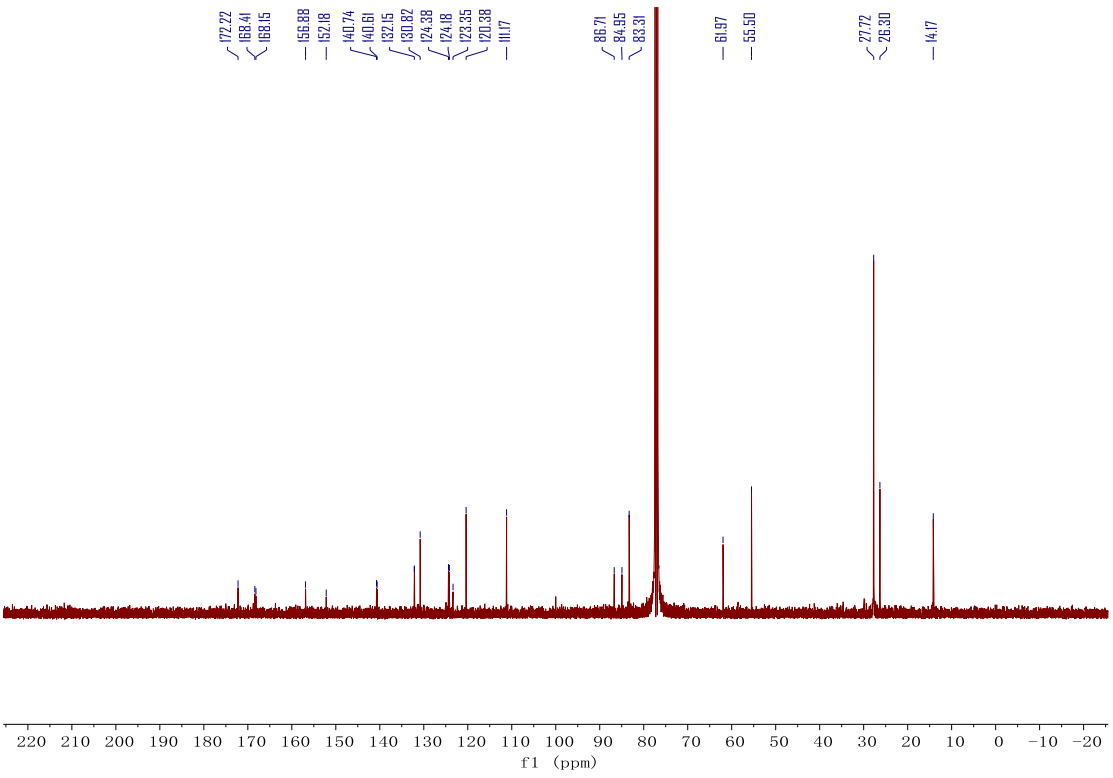
^{19}F NMR of compound 47 (377 MHz in $CDCl_3$)



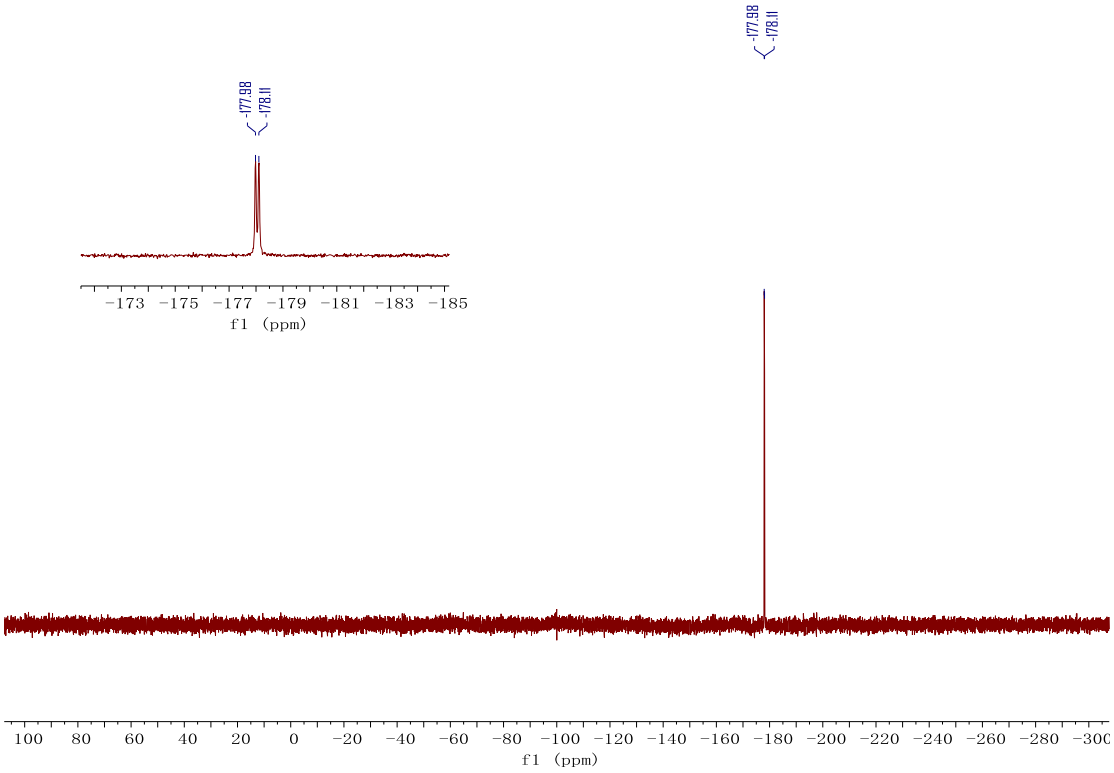
^{1}H NMR of compound 48 (400 MHz in $CDCl_3$)



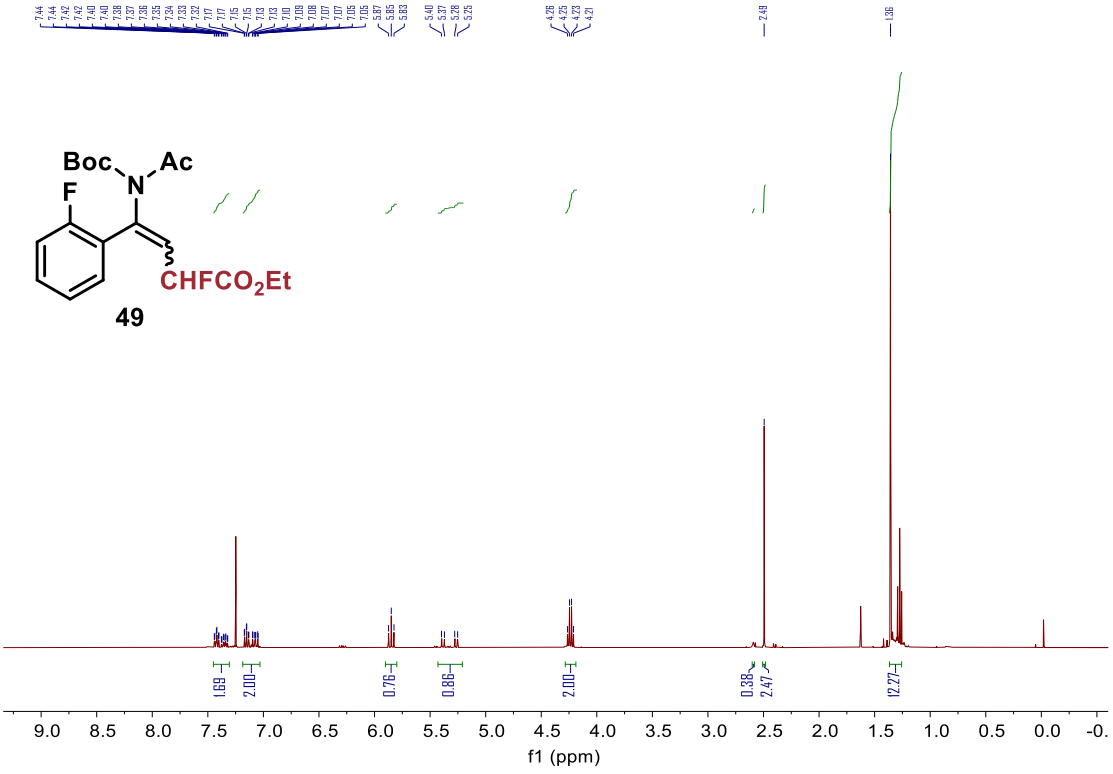
^{13}C NMR of compound 48 (101 MHz in $CDCl_3$)



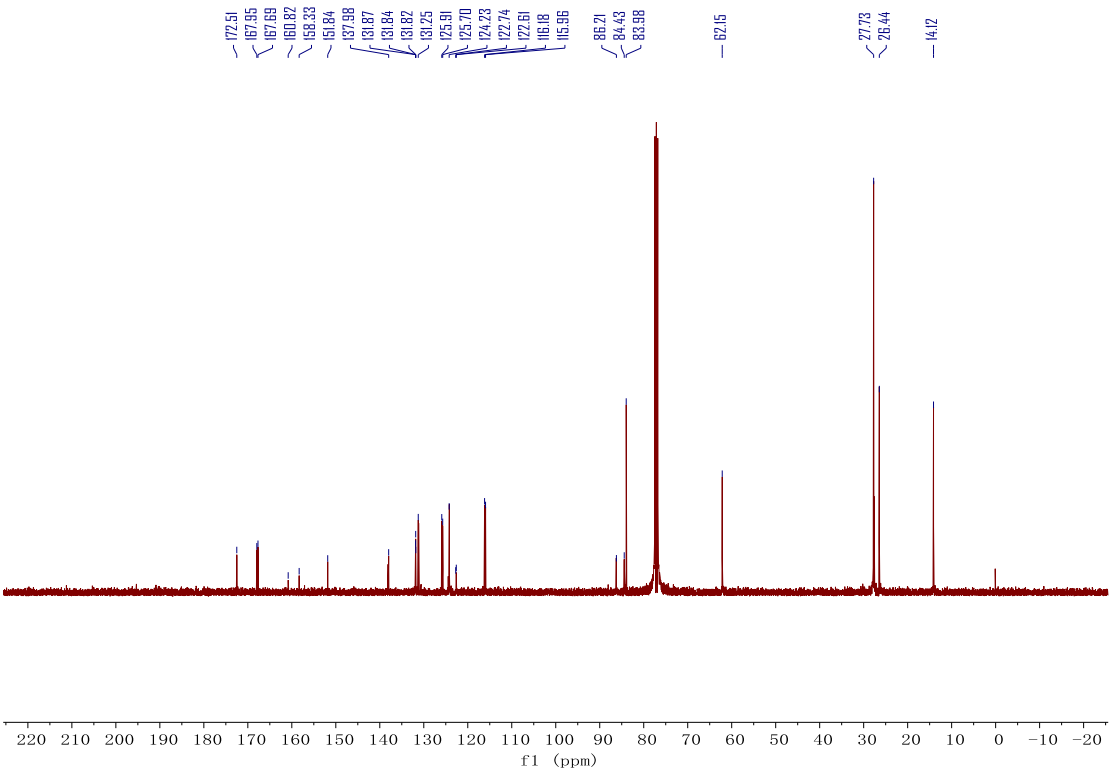
^{19}F NMR of compound 48 (377 MHz in $CDCl_3$)



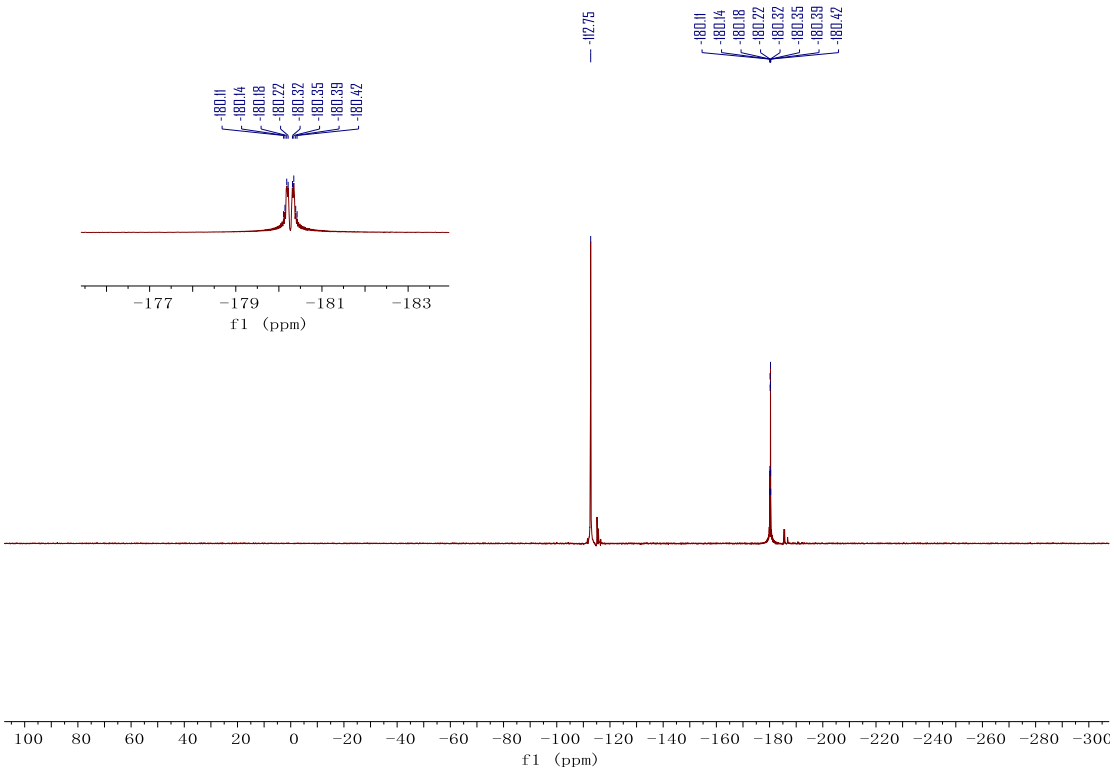
^{1}H NMR of compound 49 (400 MHz in $CDCl_3$)



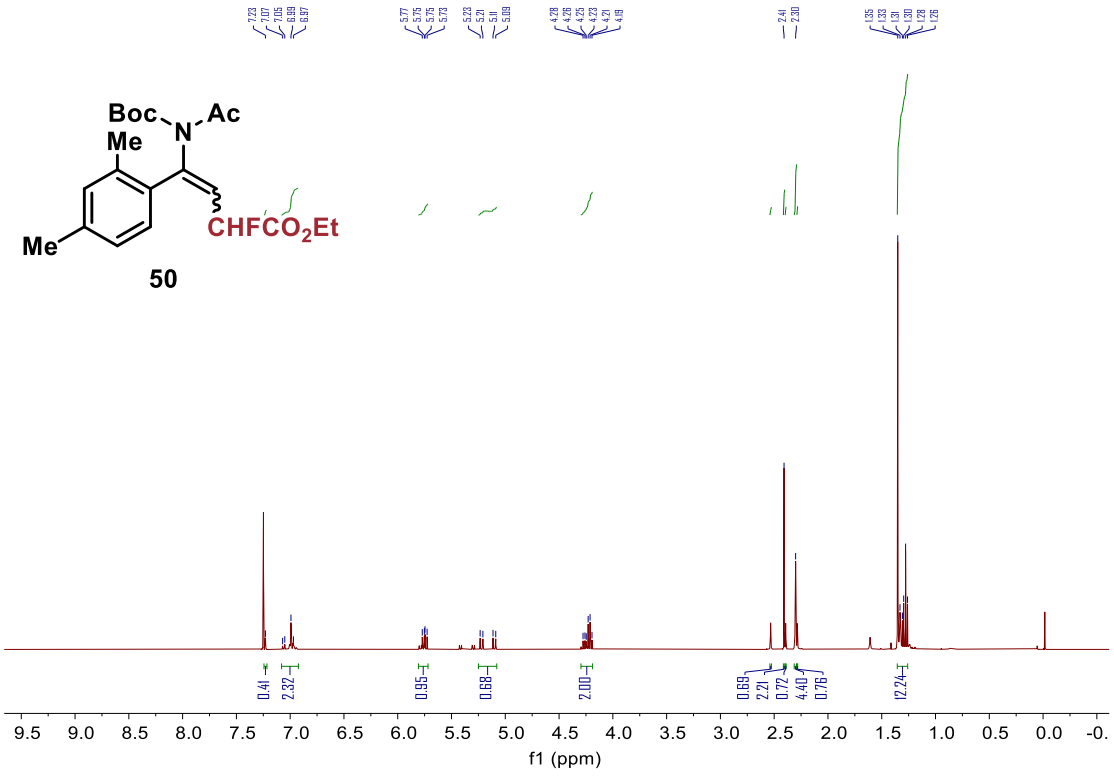
^{13}C NMR of compound 49 (101 MHz in $CDCl_3$)



^{19}F NMR of compound 49 (377 MHz in $CDCl_3$)



^{1}H NMR of compound 50 (400 MHz in $CDCl_3$)



^{13}C NMR of compound 50 (101 MHz in $CDCl_3$)