Supporting Information

Visible-Light-Promoted Defluorinative Ring-Opening *gem*-Difluoroallylation of Cycloalkanols Using 1-Trifluoromethyl Alkenes

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General

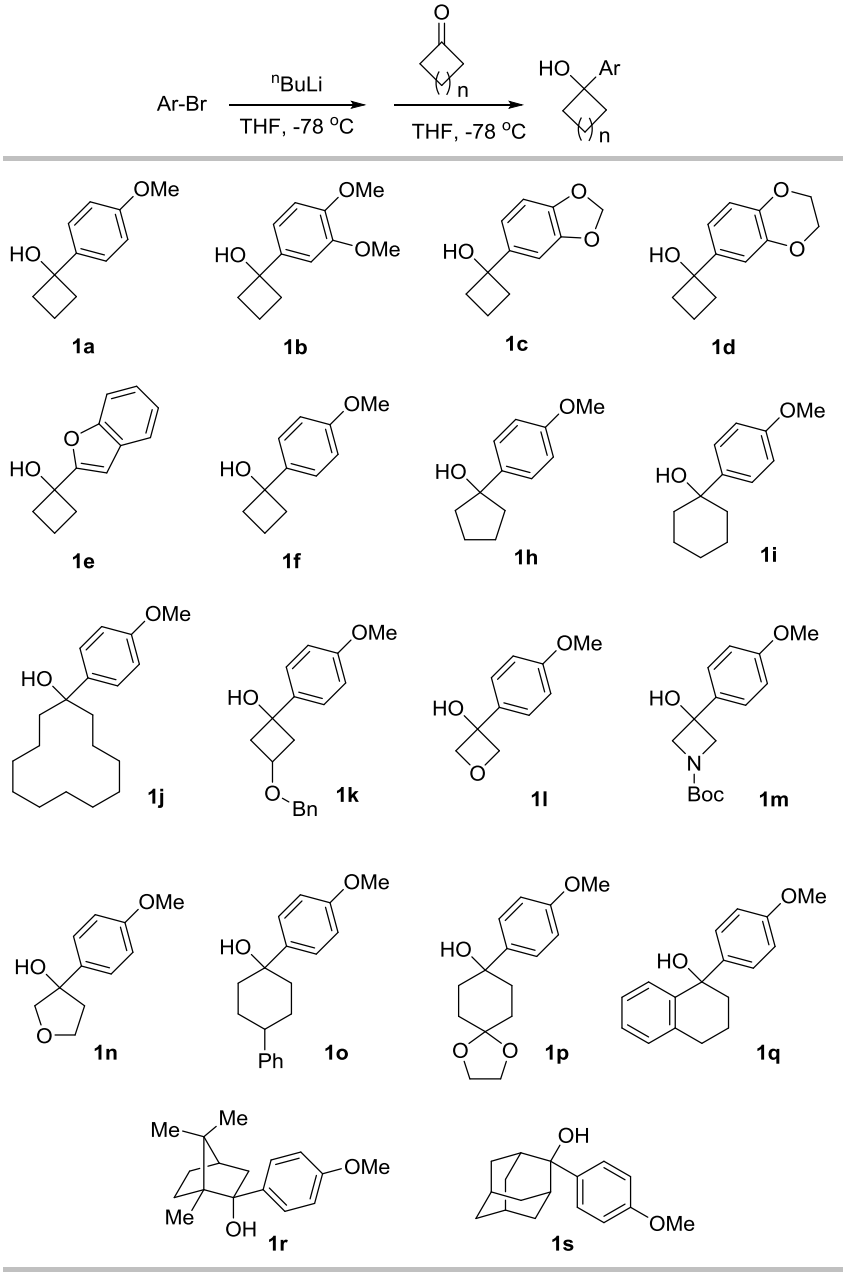
Unless otherwise noted, all reactions were performed in a 1.0 mL test tube at room temperature. Photo-irradiation was carried out with a 5 W blue LED. For chromatography, 200-300 mesh silica gel (Qingdao, China) was employed. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were measured in $CDCl_3$ and recorded on Brucker ARX 400 MHz or 600 MHz spectrometer. Chemical shifts (δ) were given in ppm, referenced to the residual proton resonance of $CDCl_3$ (7.26), to the carbon resonance of $CDCl_3$ (77.16). Coupling constants (J) were given in Hertz (Hz). The term m, q, t, d, s referred to multiplet, quartet, triplet, doublet, singlet. High resolution mass spectra (HRMS) were obtained on a Thermo MAT95XP high resolution mass spectrometer or Thermofisher LTQ Orbitrap LCMS mass spectrometer. α-CF_3 alkenes were prepared via the palladium catalyzed Suzuki coupling of commercially available 2-bromo-3,3,3-trifluoropropene with various boric acids or α-(trifluoromethyl)ethenyl boronic acid with a series of aryl halides according to the previous reports.[1] Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

Synthesis of cyclic alcohols

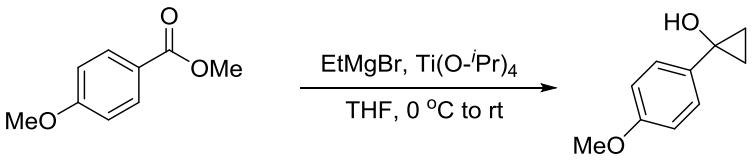
Except for cyclopropanol **1g**, cyclic alcohols **1a**-**1f** and **1h**-**1s** were prepared by the method described below:[2]

Aryl bromide (1.0 equiv) was added into a 100 mL over-dried round bottom flask containing a stir bar, and dissolved in anhydrous THF. The solution was purged with argon and cooled to –78 ℃. Then ^{n}BuLi (1.1 equiv, 2.5 mol/L in THF) was added slowly into the solution. The reaction mixture was stirred at -78 ℃. When the aryl bromide was fully consumed, the ketone (1.0 equiv) was added dropwise via syringe. The reaction was allowed to warm up to room temperature and the consumption of ketone was monitored by TLC. Upon completion, the reaction mixture was quenched by slow addition of 30 mL saturated ammonium chloride. The aqueous solution was

extracted with EtOAc three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, concentrated, and purified by silica column chromatography (petroleum ether /EtOAc) to give the pure cycloalkanols.



Cyclopropanol **1g** was prepared from methyl 4-methoxybenzoate according to the reported method:[3]



An over-dried 100 mL round-bottomed flask equipped with a stir bar was charged with methyl 4-methoxybenzoate (5 mmol, 0.83 g), titanium tetraisopropoxide (7 mmol, 1.99 g), and 30 mL of freshly distilled THF. The resulting solution cooled to 0 ℃ with an ice bathm, and ethylmagnesium bromide (14 mmol, 2.5 mol/L in THF) was added dropwise via a syringe over a period of 30 minutes. Then the reaction was then allowed to warm to room temperature and stirring overnight. Upon the completion, the reaction mixture was quenched with ice-cold distilled water and the precipitated solid was removed by filtration. The filtrate was extracted with EtOAc, washed with brine and dried over Na_2SO_4. Concentration in vacuo followed by silica gel column purification with petroleum ether/ethyl acetate eluent to afford the cyclopropanol **1g**.

Cyclic Voltammetry Data

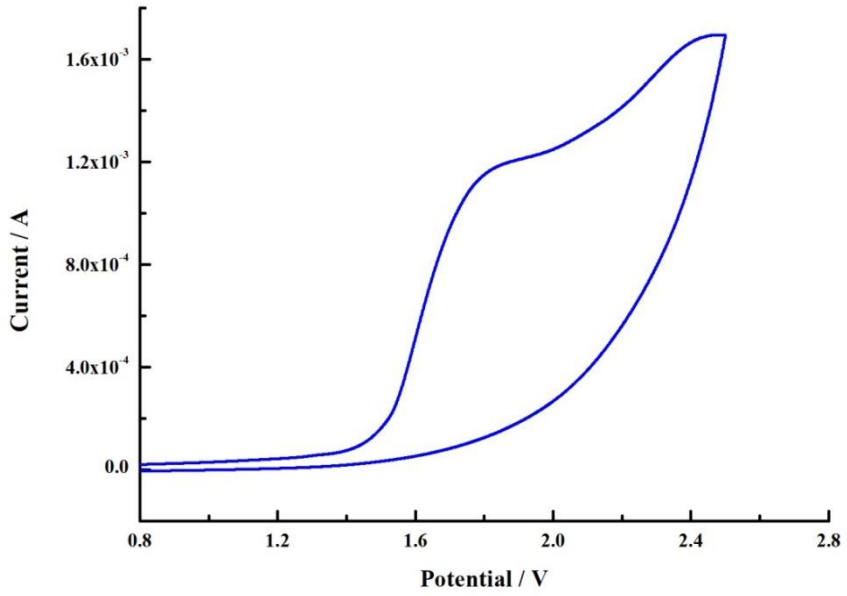
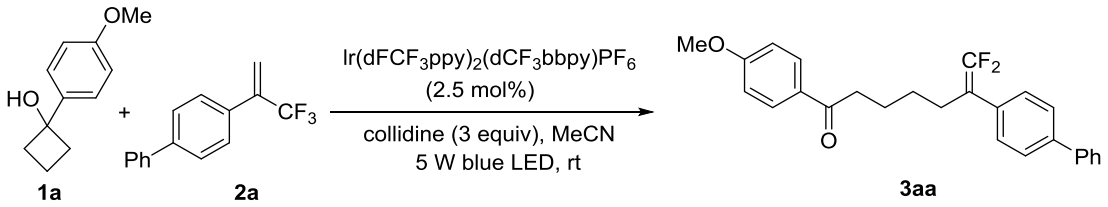


Fig. S1 Cyclic voltammogram of **1a** in MeCN shows an irreversible oxidation event at 1.80V (vs Ag^+/Ag).

Cyclic voltammograms were recorded on a CHI750E Electrochemical Analyzer using a three-electrode cell at room temperature. The reference electrode was a saturated $AgNO_3/Ag$. A glassy carbon electrode was used as the working electrode

and a platinum wire as the auxiliary electrode. Tetrabutylammonium hexafluorophosphate (0.1 M in MeCN) was used as the supporting electrolyte. Voltammograms were taken in N_2-sparged MeCN where the tertiary alcohol **1a** concentration was 1 mM. The sweep rate was 10 mV/s and no reversible electrochemical event was observed. The values for $E_{p/2}$ are referenced to Ferrocene reference electrode (Fc^+/FC) by reducing 0.55 V to the measured potential.

Typical procedure for photocatalytic synthesis of 3aa

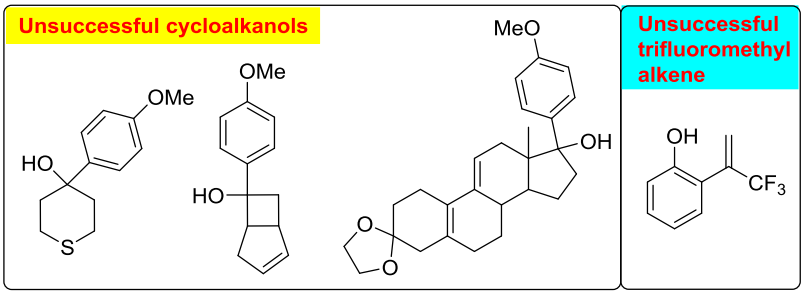


1a **2a** **3aa**

In a dry test tube, trifluoromethyl alkene **2a** (99.2 mg, 0.4 mmol), cyclobutanol **1a** (35.6 mg, 0.2 mmol), $Ir(dFCF_3ppy)_2(dCF_3bbpy)PF_6$ (5.7mg, 2.5 mol %), and collidine (72.6 mg, 0.6 mmol, 3.0 equiv) were added. The test tube was sealed with a septum and charged with argon then add 1mL of MeCN. The reaction was irradiated with a 5 W blue LED at room temperature for 48 hours. After consumption of the starting material, 10 mL of water was added and the mixture was extracted with ethyl acetate (3 × 10 mL), washed with brine and dried with anhydrous Na_2SO_4. The crude product was purified by column chromatography using petroleum ether/ethyl acetate (20: 1) as the eluent.

Unless other notes, all the carbonyl containing *gem*-difluoroalkenes were prepared using the same procedure described above.

Except the examples given in the manuscript, below are four unsuccessful cases:



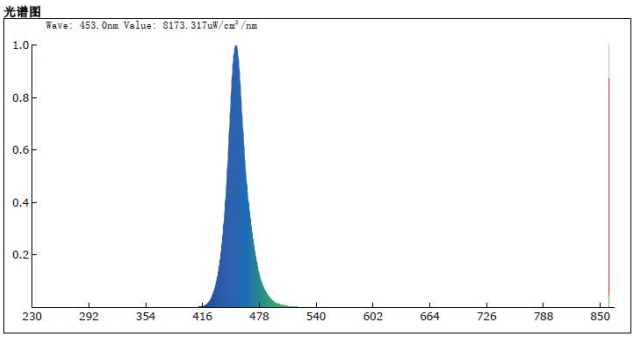
Light source and apparatus

The reactions were performed using RLH-18 8-position Photo Reaction System, which manufactured by Beijing Rogertech Co. ltd based in Beijing, China (http://www.rogertech.cn/). This Photo reactor are equipped with eight 10 W blue light LEDs, and their power can be tuned by connecting a controller.

The emission spectrum of blue LEDs is about 416 to 510 nm, and its λ_{max} is 453.6 nm. The strength of irradiation @5 W is about 246 mW/cm^2.

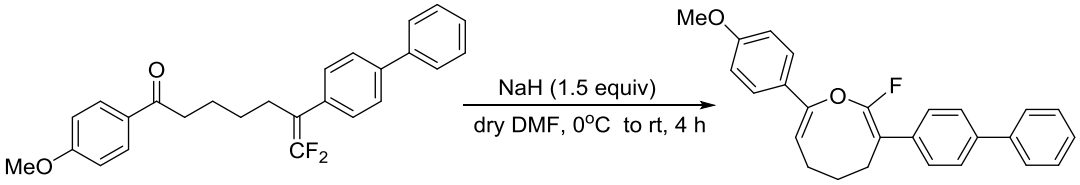
Irradiation vessel is borosilicate glass test tube. The reaction was irradiated through a high-reflection channel from blue LED to the test tube, which length is 2 cm without any filters.

The emission spectrum of the light source and the picture of the apparatus are shown below:



Experimental procedures for the synthetic manipulations of the products.

a) Intramoleular S_NV reaction for the synthesis of 2-fluoro-5,6-dihydro-4H-oxocine 4.[4]

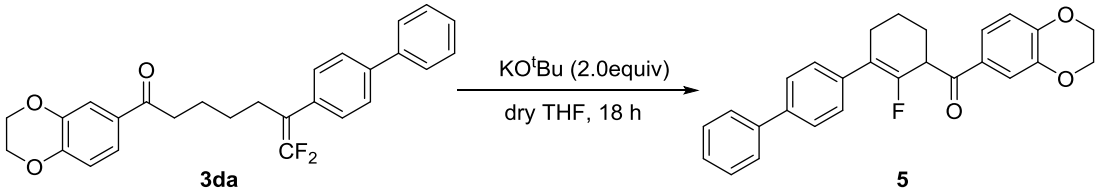


3aa **4**

To a solution of **3aa** (81 mg, 0.2 mmol.) in dry DMF (2 mL), NaH (12 mg, 0.3 mmol, 60% dispersion in mineral oil) was added at 0 ℃. Then the reaction mixture was stirred for 4 h at room temperature. The reaction was quenched by water and extracted with EtOAc (10 mL x 3), dried with anhydrous Na_2SO_4 and concentrated in vacuo. Purification by silica column chromatography using petroleum ether as the only eluent afforded the desired product **4**.

b) Synthesis of mono-fluorinated cyclohexene 5.

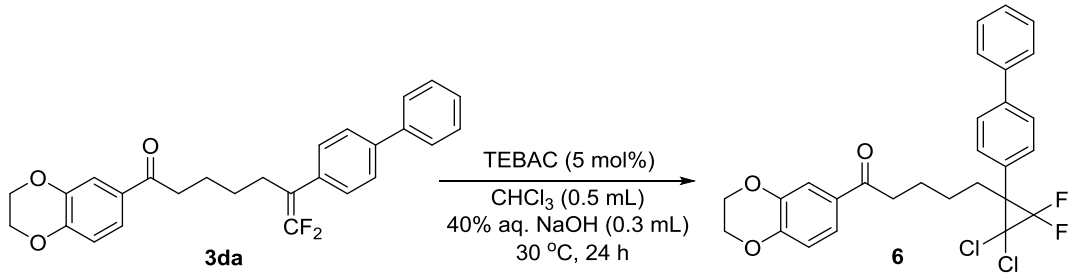
The intramoleular S_NV reaction of *gem*-difluoroalkenes *via* the C-cyclization of enolate intermediate has never reported previously.



3da **5**

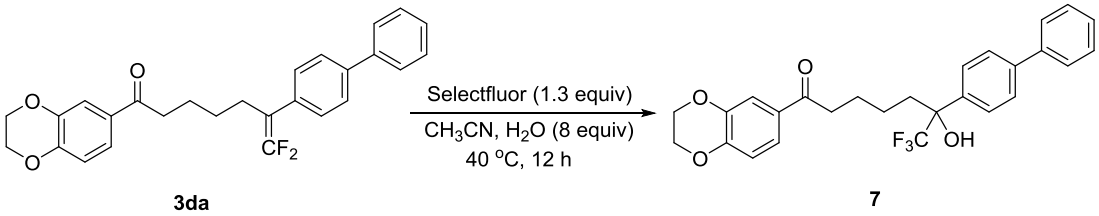
An oven-dried test tube was charged with ^{t}BuOK (44.8 mg, 0.4 mmol) and dry THF (1 mL) under argon atmosphere. Then a solution of *gem*-difluoroalkene **3da** (86.8 mg, 0.2 mmol) in 1 mL of THF was added though syringe at room temperature. After consumption of **3da** (by TLC monitoring), saturated NH_4Cl solution was added and the reaction mixture was extracted with EtOAc, dried with Na_2SO_4. The crude product was purified by column chromatography using petroleum ether/ethyl acetate (30: 1) as the eluent.

c) Cyclopropanation of 3da using $CHCl_3$/NaOH.[5]



A mixture of 2',2'-difluorostyrene **3da** (86.8mg, 0.2mmol), $CHCl_3$ (0.5 mL), NaOH (40%, 0.3mL) and benzyl triethylammonium chloride (4.5 mg) was stirred at room temperature for 24 h. The mixture was poured into H_2O (50 mL) and then extracted with $CHCl_3$ (3 × 20 mL). The $CHCl_3$ layer was washed with H_2O (3 × 20 mL), dried ($MgSO_4$) and filtered. The resultant $CHCl_3$ solution was concentrated and purified by chromatography on a silica gel column with hexane as an eluent to give product **6.**

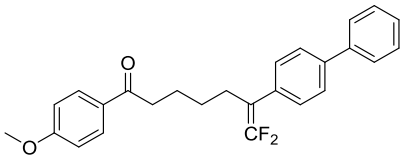
d) Synthesis of α-CF_3 alcohol 7 via fluoro-hydroxylation of 3da.[6]



Selectfluor (92.0 mg, 0.26 mmol, 1.3 equiv) and **3da** (0.20 mmol, 1.0 equiv) were dissolved in 2 mL of CH_3CN, followed by the addition of H_2O (32.0 mg, 1.6 mmol, 8.0 equiv). The reaction mixture was stirred at 40 °C for 12 h. After the completion of the reaction the reaction mixture was diluted with ethyl acetate (20.0 mL) and dried with Na_2SO_4. The solvent was evaporated under vacuum, and the residue was purified by column chromatography using petroleum ether/ethyl acetate (5:1) as the eluent to give product **7**.

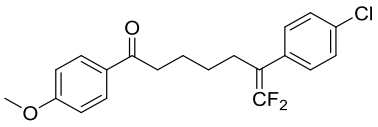
Compound characterization data

6-([1,1'-biphenyl]-4-yl)-7,7-difluoro-1-(4-methoxyphenyl)hept-6-en-1-one (3aa)



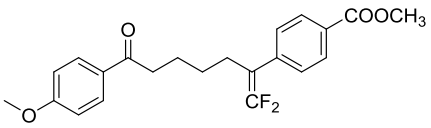
Colorless oil (64.9 mg, 80% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.9 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 2H), 3.8 (s, 3H), 2.9 – 2.8 (m, 2H), 2.5 – 2.4 (m, 2H), 1.9 – 1.7 (m, 2H), 1.6 – 1.4 (m, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.5 Hz), -91.1 (d, *J* = 43.1 Hz)., -91.09 (d, *J* = 43.1 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 163.5, 153.8 (dd, *J* = 290.3, 287.4 Hz), 140.6, 140.1, 132.6 (t, *J* = 3.2 Hz), 130.4, 130.1, 128.9, 128.7 (t, *J* = 3.3 Hz), 127.5, 127.2 (d, *J* = 11.5 Hz), 113.8, 92.0 (dd, *J* = 21.0, 13.6 Hz), 55.5, 37.9, 27.5 (d, *J* = 10.8 Hz), 23.9. **HRMS (ESI)** calcd for $C_{26}H_{25}F_2O_2$ $[M+H]^+$: 407.1817; found 407.1803.

6-(4-chlorophenyl)-7,7-difluoro-1-(4-methoxyphenyl)hept-6-en-1-one (3ab)



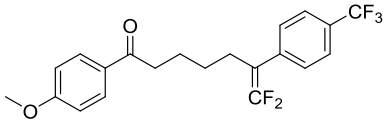
Colorless oil (56.1 mg, 77% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.1 – 7.7 (m, 2H), 7.3 – 7.3 (m, 2H), 7.3 – 7.2 (m, 2H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.6 – 2.2 (m, 2H), 1.8 – 1.7 (m, 2H), 1.5 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.7 (d, *J* = 42.4 Hz), -90.9 (d, *J* = 42.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.7, 163.5, 153.7 (dd, *J* = 298.0, 295.0 Hz), 133.2, 132.2, 130.4, 130.1, 129.7 (t, *J* = 3.2 Hz), 128.8, 113.8, 91.5 (dd, *J* = 21.5, 13.9 Hz), 55.6, 37.9, 27.5 (dd, *J* = 5.1, 2.6 Hz), 23.9; **HRMS (ESI)** calcd for $C_{20}H_{20}ClF_2O_2$ $[M+H]^+$: 345.1114; found 345.1113.

methyl 4-(1,1-difluoro-7-(4-methoxyphenyl)-7-oxohept-1-en-2-yl)benzoate (3ac)



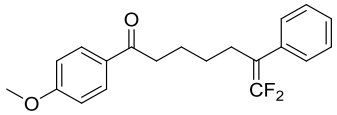
Colorless oil (48.1 mg, 62% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.1 – 8.0 (m, 2H), 7.9 – 7.8 (m, 2H), 7.4 – 7.3 (m, 2H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 3.9 (s, 3H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.6 – 2.4 (m, 2H), 1.8 – 1.7 (m, 2H), 1.5 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.2 (d, *J* = 39.7 Hz), -89.4. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.6, 166.8, 163.5, 154.0 (dd, *J* = 292.4, 288.1 Hz), 141.3 – 136.7 (m), 130.4, 130.1, 129.8, 129.0, 128.3 (t, *J* = 3.4 Hz), 113.8, 92.0 (dd, *J* = 22.2, 12.5 Hz), 55.6, 52.2, 37.8, 31.9 – 26.0 (m), 23.8; **HRMS (ESI)** calcd for $C_{25}H_{23}F_2O_2$ $[M+H]^+$: 389.1559; found 389.1547.

7,7-difluoro-1-(4-methoxyphenyl)-6-(4-(trifluoromethyl)phenyl)hept-6-en-1-one (3ad)



Colorless oil (32.6 mg, 41% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 2H), 7.6 – 7.5 (m, 2H), 7.5 – 7.3 (m, 2H), 7.0 – 6.7 (m, 2H), 3.9 (s, 3H), 2.9 (t, *J* = 7.2 Hz, 2H), 2.6 – 2.4 (m, 2H), 1.8 – 1.7 (m, 2H), 1.5 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.6, -89.4 (d, *J* = 40.0 Hz), -89.9 (d, *J* = 39.7 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.6, 163.6, 154.0 154.0 (dd, *J* = 293.0, 287.0 Hz), 137.6, 130.4, 130.2, 128.7 (t, *J* = 3.4 Hz), 125.6 (d, *J* = 3.8 Hz), 113.9, 91.7 (dd, *J* = 22.9, 12.3 Hz), 55.6, 37.8, 27.5 (d, *J* = 7.2 Hz), 23.9; **HRMS (ESI)** calcd for $C_{21}H_{20}F_5O_2$[M+H] $^+$: 399.1378; found 399.1374.

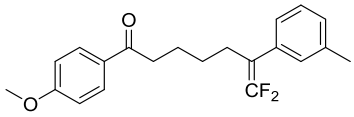
7,7-difluoro-1-(4-methoxyphenyl)-6-phenylhept-6-en-1-one (3ae)



Colorless oil (40.3mg, 61% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.7 (m, 2H),

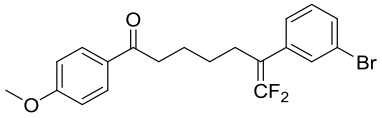
7.5 – 7.1 (m, 5H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 3.1 – 2.7 (m, 2H), 2.4 (tt, *J* = 7.6, 2.4 Hz, 2H), 1.8 – 1.7 (m, 2H), 1.5 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.6 (dd, *J* = 13.0, 11.0 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 163.5, 156.7 – 150.7 (m), 133.7 (d, *J* = 2.3 Hz), 130.4, 130.2, 128.6, 128.4 (t, *J* = 3.1 Hz), 127.4, 113.8, 92.2 (dd, *J* = 19.0, 15.8 Hz), 55.6, 38.0, 30.2 – 25.3 (m), 23.9; **HRMS (ESI)** calcd for $C_{20}H_{21}F_2O_2[M+H]^+$: 331.1504; found 331.1500.

7,7-difluoro-1-(4-methoxyphenyl)-6-(m-tolyl)hept-6-en-1-one (3af)



Colorless oil (48.8 mg, 71% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.3 – 7.2 (m, 1H), 7.1 – 7.0 (m, 3H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 2.9 (t, *J* = 7.4 Hz, 2H), 2.4 (tt, *J* = 7.6, 2.4 Hz, 2H), 2.3 (s,3H), 1.8 – 1.6 (m, 2H), 1.5 – 1.3 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.8 (d, *J* = 44.5 Hz), -92.0 (d, *J* = 45.1 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.9, 163.5, 153.7 (dd, *J* = 289.6, 286.6 Hz), 138.2, 135.7 – 132.1 (m), 130.4, 130.2, 129.1 (t, *J* = 3.1Hz), 128.4, 128.2, 125.5 (t, *J* = 3.0 Hz), 113.8, 92.3 (dd, *J* = 21.0, 13.8 Hz), 55.6, 38.0,27.9 – 27.4 (m), 24.0, 21.6; **HRMS (ESI)** calcd for $C_{21}H_{23}F_2O_2$ $[M+H]^+$: 345.1660; found 345.1657.

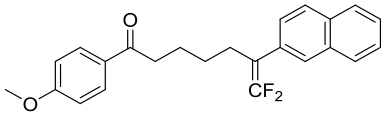
6-(3-bromophenyl)-7,7-difluoro-1-(4-methoxyphenyl)hept-6-en-1-one (3ag)



Colorless oil (66.1 mg, 81% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.9 (m, 2H), 7.5 – 7.4 (m, 1H), 7.4 – 7.4 (m, 1H), 7.2 – 7.2 (m, 2H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.5 – 2.4 (m, 2H), 1.8 – 1.7 (m, 2H), 1.5 – 1.3 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.2; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.7, 163.5, 153.8 (t, *J* = 289.5 Hz), 135.9, 131.3 (t, *J* = 3.3 Hz), 130.4 (d, *J* = 10.0 Hz), 130.1 (d, *J* = 2.0 Hz), 127.0 (t, *J* = 3.2 Hz), 122.6, 113.8, 91.5 (t, *J* = 17.6 Hz), 55.6, 37.9, 27.5 (d, *J* = 4.1 Hz), 23.8; HRMS (ESI) calcd. For $C_{20}H_{20}BrF_2O_2$ $[M+H]^+$: 409.0609; found

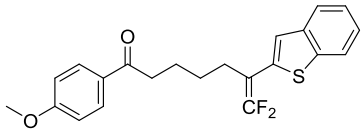
409.0603.

7,7-difluoro-1-(4-methoxyphenyl)-6-(naphthalen-2-yl)hept-6-en-1-one (3ah)



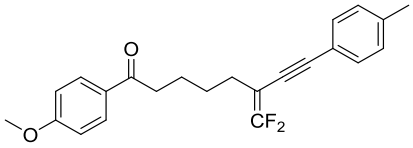
Colorless oil 54.0 mg, 71% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.9 (m, 2H), 7.9 – 7.8 (m, 3H), 7.8 (s, 1H), 7.6 – 7.4 (m, 3H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 2.9 – 2.8 (m, 2H), 2.7 – 2.5 (m, 2H), 1.9 – 1.7 (m, 2H), 1.6 – 1.5 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.0 (d, *J* = 43.2 Hz), -91.3 (d, *J* = 43.4 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 163.5, 153.9 (dd, *J* = 290.5, 286.9 Hz), 133.4, 132.6, 131.1 (d, *J* = 3.6 Hz), 130.4, 130.1, 128.1 (d, *J* = 14.0 Hz), 127.7, 127.4 (t, *J* = 3.3 Hz), 92.4 (dd, *J* = 21.7,13.0 Hz), 55.5, 37.9, 30.9 – 26.2 (m), 23.9; **HRMS (ESI)** calcd for $C_{24}H_{23}F_2O_2$ $[M+H]^+$: 381.1660; found 381.1658.

6-(benzo[b]thiophen-2-yl)-7,7-difluoro-1-(4-methoxyphenyl)hept-6-en-1-one (3ai)



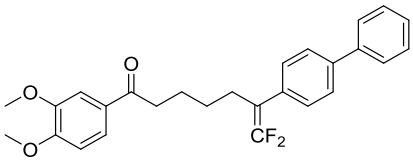
Colorless oil (36.3 mg, 47% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 2H), 7.7 – 7.7 (m, 1H), 7.7 – 7.5 (m, 1H), 7.3 – 7.2 (m, 2H), 7.2 (d, *J* = 3.5 Hz, 1H), 6.9 – 6.8 (m, 2H), 3.8 (s, 3H), 2.8 (t, *J* = 7.3 Hz, 2H), 2.6 – 2.4 (m, 2H), 1.8 – 1.7 (m, 2H), 1.6 – 1.5 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -83.5 (d, *J* = 30.7 Hz), -88.4 (d, *J* = 30.7 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.7, 163.5, 154.2 (dd, *J* = 297.1, 289.3 Hz), 139.7, 139.4 (d, *J* = 4.8 Hz), 136.2 (dd, *J* = 7.2, 4.2 Hz), 130.4, 124.6, 124.4, 123.4, 122.3 – 121.9 (m), 113.8, 88.9 (dd, *J* = 26.5, 11.6 Hz), 55.6, 37.9, 31.9 – 26.3 (m), 24.0; **HRMS (ESI)** calcd for $C_{22}H_{21}F_2O_2S$ $[M+H]^+$: 387.1225; found 387.1220.

6-(difluoromethylene)-1-(4-methoxyphenyl)-8-(p-tolyl)oct-7-yn-1-one (3aj)



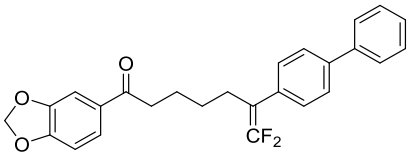
Colorless oil (30.9 mg, 42% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.9 (m, 2H), 7.4 – 7.3 (m, 2H), 7.1 – 7.1 (m, 2H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 3.0 (t, *J* = 7.3 Hz, 2H), 2.3 (s, 3H), 2.2 – 2.1 (m, 2H), 1.9 – 1.7 (m, 2H), 1.7 – 1.6 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.3 (d, *J* = 18.0 Hz), -85.5 (d, *J* = 18.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 163.5, 158.7 (dd, *J* = 293.0, 291.0 Hz), 138.6, 131.5, 130.4, 130.2, 129.2, 120.0, 113.8, 93.8, 78.6 (dd, *J* = 38.0, 18.0 Hz), 55.6, 38.0, 27.6 (t, *J* = 2.4 Hz), 27.1, 23.8, 21.6; **HRMS (ESI)** calcd for $C_{23}H_{23}F_2O_2$ $[M+H]^+$: 369.1661; found 369.1657.

6-([1,1'-biphenyl]-4-yl)-1-(3,4-dimethoxyphenyl)-7,7-difluorohept-6-en-1-one(3ba)



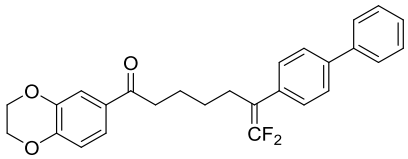
Colorless oil (68.9 mg, 79% yield); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.7 – 7.6 (m, 4H), 7.6 – 7.5 (m, 2H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 1H), 4.2 – 3.6 (m, 6H), 2.9 (q, *J* = 7.8, 7.4 Hz, 2H), 2.7 – 2.4 (m, 2H), 1.8 (q, *J* = 7.4 Hz, 2H), 1.5 (q, *J* = 7.8 Hz, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.4 Hz), -91.1 (d, *J* = 43.5 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.8, 153.8 (dd, *J* = 291.0, 287.0 Hz),, 153.3, 149.1 (d, *J* = 2.7 Hz), 140.6 (d, *J* = 2.7 Hz), 140.1, 132.6, 130.3, 128.9 (d, *J* = 2.9 Hz), 128.6 (t, *J* = 3.2 Hz), 127.5 (d, *J* = 2.6 Hz), 127.1 (dd, *J* = 18.7, 2.7 Hz), 122.7 (d, *J* = 2.3 Hz), 110.1 (d, *J* = 27.2 Hz), 91.9 (dd, *J* = 21.4, 13.4 Hz), 56.1 (d, *J* = 11.7 Hz), 37.7, 27.5 (d, *J* = 17.2 Hz), 24.1; **HRMS (ESI)** calcd for $C_{27}H_{27}F_2O_3$ $[M+H]^+$: 437.1923; found 439.1917.

6-([1,1'-biphenyl]-4-yl)-1-(benzo[d][1,3]dioxol-5-yl)-7,7-difluorohept-6-en-1-one (3ca)



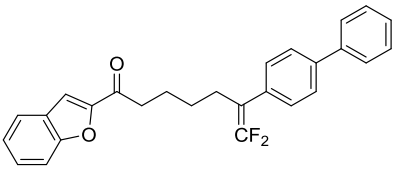
Colorless oil (75.6 mg, 90% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.6 – 7.5 (m, 4H), 7.5 – 7.5 (m, 1H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 2H), 6.8 (d, *J* = 8.1 Hz, 1H), 6.0 (d, *J* = 0.9 Hz, 2H), 2.9 (t, *J* = 7.4 Hz, 2H), 2.7 – 2.4 (m, 2H), 2.0 – 1.7 (m, 2H), 1.6 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.5 Hz), -91.1 (d, *J* = 43.1 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.3, 153.8 (dd, *J* = 289.0, 285.0 Hz), 151.8, 148.3, 140.7, 140.2, 132.6 (d, *J* = 2.9 Hz), 132.0, 128.9, 128.7 (t, *J* = 3.3 Hz), 127.5, 127.3, 127.1, 124.3, 108.0 (d, *J* = 4.9 Hz), 101.9, 91.9 (dd, *J* = 20.7, 14.0 Hz), 38.1, 27.6 (t, *J* = 2.6 Hz), 27.5, 24.0; **HRMS (ESI)** calcd for $C_{26}H_{23}F_2O_3$ $[M+H]^+$:421.1610; found 421.1601.

6-([1,1'-biphenyl]-4-yl)-1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-7,7-difluorohept-6-en-1-one (3da)



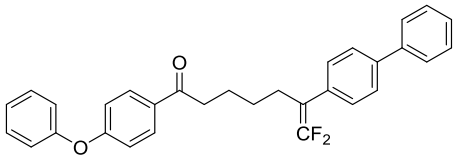
White solid (79.8 mg, 92% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 1H), 4.3 – 4.2 (m, 4H), 2.9 – 2.8 (m, 2H), 2.6 – 2.3 (m, 2H), 1.9 – 1.7 (m, 2H), 1.5 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.2 Hz), -91.1 (d, *J* = 43.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.7, 153.8 (dd, *J* = 290.0, 287.0 Hz), 148.0, 143.4, 140.7, 140.2, 132.7, 131.0, 128.9, 128.7, 127.5, 127.3 – 127.0 (m), 122.3, 117.7, 117.3, 92.0 (dd, *J* = 7.1 Hz), 64.8, 64.2, 38.0, 30.9 – 25.3 (m), 24.0; **HRMS (ESI)** calcd for $C_{27}H_{25}F_2O_2$ $[M+H]^+$: 435.1766; found 435.1763.

6-([1,1'-biphenyl]-4-yl)-1-(benzofuran-2-yl)-7,7-difluorohept-6-en-1-one (3ea)



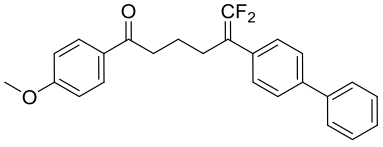
Colorless oil (60.7 mg, 73% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 – 7.6 (m, 1H), 7.6 – 7.5 (m, 5H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 4H), 2.9 (t, *J* = 7.4 Hz, 2H), 2.6 – 2.2 (m, 2H), 2.0 – 1.7 (m, 2H), 1.5 (t, *J* = 7.7 Hz, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.7 – -91.1 (m); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.3, 155.7, 153.8 (dd, *J* = 290.2, 287.5 Hz), 152.7, 140.6, 140.2, 132.5 (t, *J* = 2.4 Hz), 128.9, 128.7 (t, *J* = 3.3 Hz), 128.3, 127.5, 127.2, 127.1 (d, *J* = 4.0 Hz), 112.7, 112.5, 91.9 (dd, *J* = 20.1, 14.6 Hz), 38.6, 30.2 – 26.3 (m), 23.6; **HRMS (ESI)** calcd for $C_{27}H_{23}F_2O_2$ $[M+H]^+$: 417.1661; found 417.1653.

6-([1,1'-biphenyl]-4-yl)-7,7-difluoro-1-(4-phenoxyphenyl)hept-6-en-1-one (3fa)



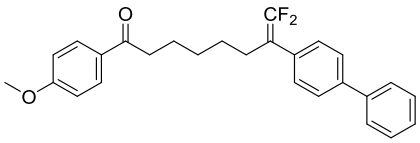
Colorless oil (42.1 mg, 45% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 3H), 7.4 – 7.3 (m, 4H), 7.2 – 7.2 (m, 1H), 7.1 – 7.0 (m, 2H), 7.0 – 6.9 (m, 2H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.6 – 2.4 (m, 2H), 2.0 – 1.7 (m, 2H), 1.6 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.1 Hz), -91.1 (d, *J* = 43.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.8, 162.0, 153.8 (dd, *J* = 277.0, 270.0 Hz), 140.7, 140.2, 132.6, 131.8, 130.4 (d, *J* = 4.4 Hz), 130.2 (d, *J* = 4.6 Hz), 128.9 (d, *J* = 4.3 Hz), 128.7 (d, *J* = 3.7 Hz), 127.5, 127.2 (d, *J* = 18.4 Hz), 124.7, 120.3, 117.5, 91.9 (dd, *J* = 14.5 Hz), 38.1, 27.6 (d, *J* = 10.3 Hz), 23.9; **HRMS (ESI)** calcd for $C_{31}H_{27}F_2O_2$ $[M+H]^+$: 469.1970; found 469.1974.

5-([1,1'-biphenyl]-4-yl)-6,6-difluoro-1-(4-methoxyphenyl)hex-5-en-1-one (3ga)



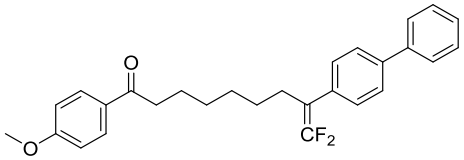
Colorless oil (69.8 mg, 89% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 1H), 7.0 – 6.8 (m, 2H), 3.8 (s, 3H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.7 – 2.5 (m, 2H), 2.0 – 1.8 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.4 (d, *J* = 42.2 Hz), -90.6 (d, *J* = 41.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.4, 163.5, 154.0 (dd, *J* = 290.0, 287.0 Hz), 140.7, 140.2, 132.4 (t, *J* = 3.2 Hz), 130.4, 130.1, 128.9, 128.7 (t, *J* = 3.4 Hz), 127.5, 127.3, 127.1, 113.8, 91.8 (dd, *J* = 21.0, 13.2 Hz), 55.6, 37.3, 27.0, 22.7 (t, *J* = 2.6 Hz); **HRMS (ESI)** calcd for $C_{22}H_{23}F_2O_4$ $[M+H]^+$: 393.1648; found 393.1661.

7-([1,1'-biphenyl]-4-yl)-8,8-difluoro-1-(4-methoxyphenyl)oct-7-en-1-one (3ha)



Colorless oil (53.8 mg, 64% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.9 (m, 2H), 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 7.0 – 6.8 (m, 2H), 3.8 (s, 3H), 2.9 (t, *J* = 7.3 Hz, 2H), 2.6 – 2.4 (m, 2H), 1.8 – 1.6 (m, 2H), 1.5 – 1.4 (m, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.1 (d, *J* = 43.7 Hz), -91.3 (d, *J* = 43.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 163.4, 140.7, 140.1, 132.8, 130.4, 130.2, 128.9, 128.7 (t, *J* = 3.3 Hz), 127.5, 127.1 (d, *J* = 8.4 Hz), 113.8, 92.1, 55.5, 38.1, 28.8, 27.7, 27.4, 24.2; **HRMS (ESI)** calcd for $C_{27}H_{27}F_2O_2$ $[M+H]^+$: 421.1974; found 421.1967.

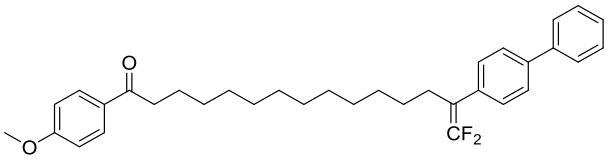
8-([1,1'-biphenyl]-4-yl)-9,9-difluoro-1-(4-methoxyphenyl)non-8-en-1-one (3ia)



Colorless oil (52.1 mg, 60% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 7.0 – 6.8 (m, 2H), 3.8 (s, 3H), 2.9 (t, *J* = 7.4 Hz, 2H), 2.5 – 2.3 (m, 2H), 1.7 (t, *J* = 7.2 Hz, 2H), 1.5 – 1.0 (m, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.2 (d, *J* = 43.7 Hz), -91.4 (d, *J* = 44.0 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.2, 163.5, 153.8 (dd, *J* = 290.4, 286.7 Hz), 140.7,

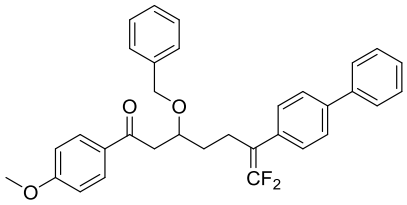
140.1, 132.9 (d, *J* = 3.6 Hz), 130.4, 130.3, 128.9, 128.7 (t, *J* = 3.4 Hz), 127.5, 127.2 (d, *J* = 10.9 Hz), 113.8, 92.2 (dd, *J* = 21.3, 13.0 Hz), 55.6, 38.3, 29.1 (d, *J* = 27.7 Hz), 27.6, 24.6; **HRMS (ESI)** calcd for $C_{28}H_{29}F_2O_2$ $[M+H]^+$: 435.2130; found 435.2128.

14-([1,1'-biphenyl]-4-yl)-15,15-difluoro-1-(4-methoxyphenyl)pentadec-14-en-1-one (3ja)



White solid (52.8 mg, 51% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.9 (m, 2H), 7.6 (t, *J* = 7.0 Hz, 4H), 7.5 – 7.4 (m, 12H), 7.4 – 7.3 (m, 3H), 7.0 – 6.8 (m, 2H), 3.8 (s, 3H), 2.9 (t, *J* = 7.4 Hz, 2H), 2.6 – 2.3 (m, 2H), 1.7 (q, *J* = 7.4 Hz, 2H), 1.5 – 1.3 (m, 18H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.3 (d, *J* = 43.8 Hz), -91.5 (d, *J* = 43.9 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.4, 163.4, 153.8 (dd, *J* = 290.3, 286.8 Hz), 140.7, 140.0, 133.0 (t, *J* = 3.5 Hz), 130.4 (d, *J* = 13.0 Hz), 128.9, 128.7 (t, *J* = 3.3 Hz), 127.5, 127.1 (d, *J* = 8.3 Hz), 113.8, 92.3 (dd, *J* = 21.3, 13.0 Hz), 55.5, 38.4, 29.8 – 29.5 (m), 29.4, 29.2, 27.9, 27.6, 24.8; **HRMS (ESI)** calcd for $C_{34}H_{41}F_2O_2[M+H]^+$:519.3069; found 519.3065.

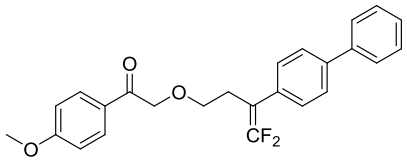
6-([1,1'-biphenyl]-4-yl)-3-(benzyloxy)-7,7-difluoro-1-(4-methoxyphenyl)hept-6-en-1-one (3ka)



Colorless oil (42.0mg, 41% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 4H), 7.0 – 6.8 (m, 2H), 4.6 – 4.4 (m, 2H), 4.1 (p, *J* = 5.9 Hz, 1H), 3.8 (s, 3H), 3.3 (dd, *J* = 15.9, 6.5 Hz, 1H), 2.9 (dd, *J* = 15.9, 5.9 Hz, 1H), 2.7 – 2.5 (m, 2H), 1.9 – 1.7 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.5 (d, *J* = 42.4 Hz), -90.7 (d, *J* = 42.4 Hz); **^{13}C NMR** (150

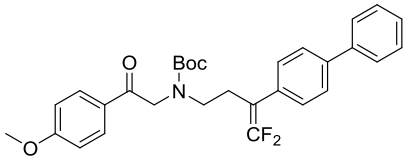
MHz, $CDCl_3$) δ 197.3, 163.7, 153.7 (dd, *J* = 290.0, 282.0 Hz), 140.7, 140.2, 138.5, 132.5 (t, *J* = 3.6 Hz), 130.7, 130.5, 128.9, 128.7, 128.5, 127.9, 127.7, 127.5, 127.3, 127.2, 113.9, 92.0 (dd, *J* = 21.4, 13.2 Hz), 75.5, 72.0, 55.6, 43.3, 33.3 (d, *J* = 2.9 Hz), 23.6. **HRMS (ESI)** calcd for $C_{33}H_{31}F_2O_3$ $[M+H]^+$: 513.2236; found 513.2231.

2-((3-([1,1'-biphenyl]-4-yl)-4,4-difluorobut-3-en-1-yl)oxy)-1-(4-methoxyphenyl) ethan-1-one (3la)



Colorless oil (49.8 mg, 61% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 6.9 – 6.9 (m, 2H), 4.6 (s, 2H), 3.8 (s, 3H), 3.6 (t, *J* = 7.0 Hz, 2H), 2.9 – 2.7 (m, 2H); **^{19}F NMR** (564 MHz, $CDCl_3$) δ -89.3 (d, *J* = 40.4 Hz), -89.6 (d, *J* = 39.3 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.1, 163.9, 154.3 (dd, *J* = 291.0, 289.0 Hz), 140.4 (d, *J* = 34.6 Hz), 132.3 (t, *J* = 3.6 Hz), 130.5, 128.9, 128.7 (t, *J* = 3.4 Hz), 128.0, 127.6, 127.2 (d, *J* = 14.3 Hz), 113.9, 89.2 (dd, *J* = 21.5, 14.7 Hz), 73.9, 69.4 (t, *J* = 3.2 Hz), 55.6, 28.4; **HRMS (ESI)** calcd for $C_{25}H_{23}F_2O_3$ $[M+H]^+$: 409.1610; found 409.1605.

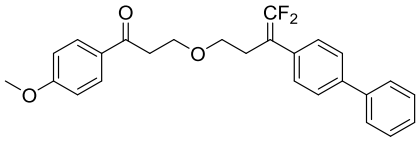
tert-butyl (3-([1,1'-biphenyl]-4-yl)-4,4-difluorobut-3-en-1-yl)(2-(4-methoxyphenyl) -2-oxoethyl)carbamate (3ma)



Colorless oil (71.0 mg, 70% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.0 – 8.8 (m, 2H), 8.6 – 8.5 (m, 4H), 8.5 – 8.4 (m, 4H), 8.4 – 8.3 (m, 1H), 8.0 – 7.9 (m, 2H), 5.5 (d, *J* = 52.3 Hz, 2H), 4.9 (d, *J* = 6.3 Hz, 3H), 4.5 – 4.3 (m, 2H), 3.9 – 3.6 (m, 2H), 2.5 (s, 6H), 2.3 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.1 (d, *J* = 39.5 Hz), -89.3 (d, *J* = 39.5 Hz), -89.5; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.5, 163.8, 155.8, 155.3, 154.3, 140.6,

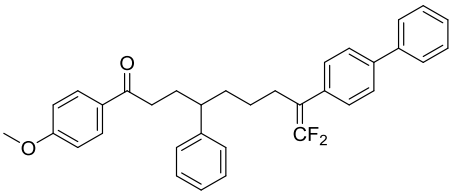
140.5, 140.3, 140.1, 132.3, 132.1, 130.3, 130.0, 128.9 (d, *J* = 2.8 Hz), 128.6 – 128.1 (m), 127.5 (d, *J* = 9.1 Hz), 127.3, 127.1, 113.9, 89.7, 80.4, 55.5 (d, *J* = 3.1 Hz), 54.3, 53.6, 47.6, 47.1 (d, *J* = 3.8 Hz), 28.3 (d, *J* = 15.2 Hz), 26.9, 26.7; **HRMS (ESI)** calcd for $C_{30}H_{31}F_2O_4Na$ $[M + Na]^+$: 530.2109; found 530.2113.

3-((3-([1,1'-biphenyl]-4-yl)-4,4-difluorobut-3-en-1-yl)oxy)-1-(4-methoxyphenyl) propan-1-one (3na)



Colorless oil (56.5 mg, 67% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 7.0 – 6.8 (m, 2H), 3.8 (s, 3H), 3.8 (d, *J* = 6.6 Hz, 2H), 3.5 (t, *J* = 6.9 Hz, 2H), 3.1 (t, *J* = 6.5 Hz, 2H), 2.8 – 2.6 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.8 (d, *J* = 40.8 Hz), -90.1 (d, *J* = 40.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.1, 163.7, 154.2 (dd, *J* = 291.0, 287.0 Hz), 140.4 (d, *J* = 70.8 Hz), 130.6, 130.3, 128.9, 128.8, 127.5, 127.2 (d, *J* = 11.1 Hz), 113.8, 89.6 (dd, *J* = 21.7, 14.4 Hz), 68.8 (d, *J* = 3.7 Hz), 66.5, 55.6, 38.5, 28.4; **HRMS (ESI)** calcd for $C_{25}H_{23}F_2O_3[M+H]^+$: 409.1610; found 409.1603.

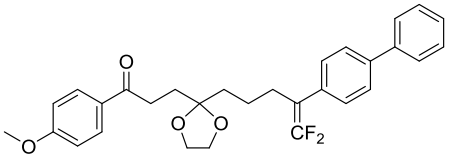
8-([1,1'-biphenyl]-4-yl)-9,9-difluoro-1-(4-methoxyphenyl)-4-phenylnon-8-en-1-one (3oa)



Colorless oil (52.0 mg, 51% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.7 (m, 2H), 7.6 – 7.6 (m, 2H), 7.6 – 7.5 (m, 2H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 1H), 7.3 – 7.2 (m, 4H), 7.2 – 7.1 (m, 1H), 7.1 – 7.0 (m, 2H), 6.9 – 6.6 (m, 2H), 3.8 (s, 3H), 2.8 – 2.6 (m, 2H), 2.6 – 2.5 (m, 1H), 2.4 – 2.3 (m, 2H), 2.2 – 2.0 (m, 1H), 2.0 – 1.8 (m, 1H), 1.8 –

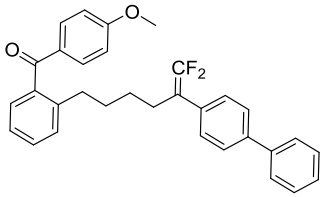
1.6 (m, 2H), 1.4 – 1.2 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.0 (d, *J* = 43.5 Hz), -91.2 (d, *J* = 43.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.0, 163.4, 153.8 (dd, *J* = 290.5, 286.8 Hz), 144.8, 140.7, 140.0, 132.7 (t, *J* = 3.6 Hz), 130.4, 130.2, 128.9, 128.7 – 128.3 (m), 127.8, 127.5, 127.2 (d, *J* = 5.4 Hz), 126.4, 113.7, 92.0 (dd, *J* = 21.4, 12.8 Hz), 55.5, 45.2, 36.3, 31.4, 27.4, 25.6 (d, *J* = 2.8 Hz); **HRMS (ESI)** calcd for $C_{34}H_{33}F_2O_2$ $[M+H]^+$: 511.2443; found 511.2438.

3-(2-(4-([1,1'-biphenyl]-4-yl)-5,5-difluoropent-4-en-1-yl)-1,3-dioxolan-2-yl)-1-(4-methoxyphenyl)propan-1-one(3pa)



Colorless oil (65.9 mg, 67% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.8 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 2H), 3.9 (s, 4H), 3.8 (s, 3H), 3.0 – 2.8 (m, 2H), 2.6 – 2.4 (m, 2H), 2.1 – 2.0 (m, 2H), 1.7 – 1.6 (m, 2H), 1.6 – 1.4 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.9 (d, *J* = 43.0 Hz), -91.1 (d, *J* = 43.0 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.5, 163.5, 153.9 (dd, *J* = 298.5, 295.5 Hz), 140.4 (d, *J* = 76.2 Hz), 132.6, 130.4, 130.2, 128.9, 128.7, 127.5, 127.3, 127.2, 113.8, 111.1, 92.0 (dd, *J* = 21.4, 12.9 Hz), 65.1, 55.6, 36.6, 31.4, 27.7, 22.2; **HRMS (ESI)** calcd for $C_{30}H_{31}F_2O_4$ $[M+H]^+$: 493.2185; found 493.2181.

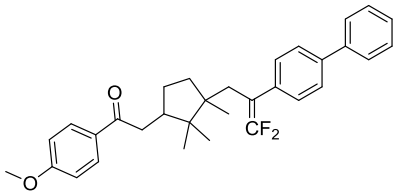
(2-(5-([1,1'-biphenyl]-4-yl)-6,6-difluorohex-5-en-1-yl)phenyl)(4-methoxyphenyl)-methanone (3qa)



Colorless oil (38.6 mg, 40% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.8 – 7.7 (m, 2H), 7.6 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 12H), 7.3 – 7.2 (m, 5H), 6.9 – 6.8 (m, 1H), 3.8 (s, 3H), 2.6 (t, *J* = 7.9 Hz, 2H), 2.4 – 2.3 (m, 2H), 1.6 – 1.5 (m, 2H), 1.4 – 1.3 (m, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -91.2 (d, *J* = 43.6 Hz), -91.3 (d, *J* =

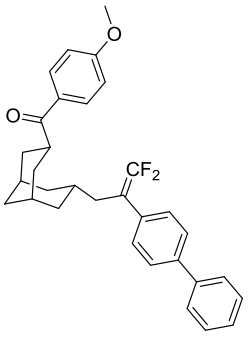
43.6 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.5, 163.9, 153.7 (dd, *J* = 288.0, 285.0 Hz), 141.0, 140.8, 140.1, 139.2, 132.7, 130.8, 130.0 (d, *J* = 24.0 Hz), 129.0 – 128.6 (m), 128.1, 127.5, 127.2 (d, *J* = 5.6 Hz), 125.3, 113.8, 92.0 (dd, *J* = 21.2, 13.4 Hz), 55.6, 33.0, 31.0, 27.6 (d, *J* = 2.9 Hz), 27.3; **HRMS (ESI)** calcd for $C_{32}H_{29}F_2O_2$ $[M+H]^+$: 483.2130; found 483.2128.

2-(3-(2-([1,1'-biphenyl]-4-yl)-3,3-difluoroallyl)-2,2,3-trimethylcyclopentyl)-1-(4-methoxyphenyl)ethan-1-one (3ra)



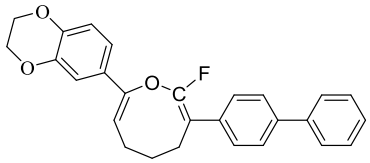
White solid (81.0 mg, 83% yield), dr >20:1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.0 – 7.9 (m, 2H), 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 7.0 – 6.9 (m, 2H), 3.8 (s, 3H), 3.1 – 2.9 (m, 1H), 2.8 – 2.7 (m, 1H), 2.6 – 2.5 (m, 2H), 2.4 – 2.3 (m, 1H), 1.8 – 1.7 (m, 1H), 1.5 – 1.4 (m, 1H), 1.3 – 1.0 (m, 2H), 1.0 (s, 3H), 0.8 (d, *J* = 5.0 Hz, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -89.2 (d, *J* = 40.2 Hz), -91.0 (d, *J* = 40.2 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.3, 163.4, 154.6 (dd, *J* = 290.5, 287.6 Hz), 140.6, 139.8, 134.9 (dd, *J* = 4.8, 2.8 Hz), 130.6, 130.4, 128.9, 128.7, 127.4, 127.1 (d, *J* = 1.7 Hz), 113.8, 91.2 (dd, *J* = 21.1, 12.7 Hz), 55.5, 48.7, 46.1, 43.4, 40.8, 33.2 (d, *J* = 6.1 Hz), 28.1, 21.9, 20.7, 19.9; **HRMS (ESI)** calcd for $C_{32}H_{35}F_2O_2$ $[M+H]^+$: 489.2599; found 489.2597.

(7-(2-([1,1'-biphenyl]-4-yl)-3,3-difluoroallyl)bicyclo[3.3.1]nonan-3-yl)(4-methoxyphenyl)-methanone (3sa)



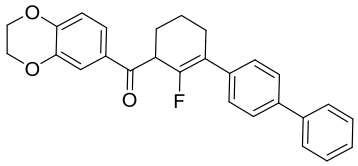
Colorless oil (34.0 mg, 35% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 2H), 7.7 – 7.6 (m, 4H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 2H), 3.8 (s, 3H), 3.5 – 3.3 (m, 1H), 2.3 (dt, *J* = 7.3, 2.6 Hz, 2H), 2.2 – 2.1 (m, 2H), 2.1 – 1.9 (m, 3H), 1.8 – 1.7 (m, 1H), 1.6 (s, 1H), 1.4 – 1.2 (m, 3H), 1.2 – 1.0 (m, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.4 (d, *J* = 42.8 Hz), -91.1 (d, *J* = 42.9 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 202.8, 163.3, 154.2 (dd, *J* = 290.5, 287.3 Hz), 140.9, 140.1, 133.3, 130.5, 129.9, 129.1 – 128.3 (m), 127.6 – 126.9 (m), 113.8, 90.9 (dd, *J* = 21.9, 12.6 Hz), 55.5, 40.1, 37.6, 35.5, 29.9, 29.3, 26.1, 25.5; **HRMS (ESI)** calcd for $C_{32}H_{33}F_2O_2$ $[M+H]^+$: 487.2443; found 487.2440.

6-((2Z,7Z)-7-([1,1'-biphenyl]-4-yl)-8-fluoro-5,6-dihydro-4H-oxocin-2-yl)-2,3-dihydrobenzo[b][1,4]dioxine (4)



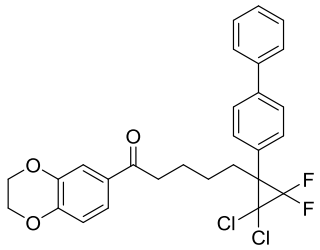
White solid (68.7 mg, 83% yield) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 – 7.6 (m, 1H), 7.5 – 7.4 (m, 1H), 7.4 – 7.3 (m, 0H), 7.2 – 7.2 (m, 0H), 7.2 (dt, *J* = 8.6, 2.0 Hz, 0H), 6.9 (dd, *J* = 8.5, 1.7 Hz, 0H), 5.6 (t, *J* = 6.8 Hz, 0H), 4.3 (s, 1H), 2.8 – 2.7 (m, 0H), 2.5 (q, *J* = 6.4 Hz, 1H), 2.1 – 2.0 (m, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -82.4. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 154.8, 152.9, 152.3 (d, *J* = 2.9 Hz), 143.8, 143.3, 140.8, 139.4, 136.4 (d, *J* = 4.0 Hz), 129.2, 128.8, 128.5 (d, *J* = 4.4 Hz), 127.2, 127.0 (d, *J* = 18.3 Hz), 118.6, 117.1, 114.4, 109.2, 97.7 (d, *J* = 23.1 Hz), 64.5, 64.4, 29.5 (d, *J* = 2.0 Hz), 25.0, 23.6. **HRMS (ESI)** calcd for $C_{28}H_{23}FO_3[M+H]^+$: 415.1688; found 415.1704.

(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)(2-fluoro-3,4,5,6-tetrahydro-[1,1':4',1''-terphenyl]-3-yl)methanone (5)



White solid (75.3 mg, 91% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 – 7.5 (m, 8H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 1H), 7.0 – 6.9 (m, 1H), 4.5 – 4.4 (m, 4H), 4.4 – 4.3 (m, 1H), 2.6 (q, *J* = 6.2 Hz, 2H), 2.3 – 2.0 (m, 2H), 2.0 – 1.8 (m, 1H), 1.8 – 1.7 (m, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.9 (d, *J* = 2.6 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.1, 153.8, 152.0, 148.3, 143.5, 140.9, 139.7, 135.9, 129.8, 128.8, 128.3 (d, *J* = 4.4 Hz), 127.2, 127.0, 126.8, 64.7, 64.1, 45.2, 45.0, 28.2 (d, *J* = 3.6 Hz), 27.8 (d, *J* = 6.8 Hz), 20.2; **HRMS (ESI)** calcd for $C_{27}H_{24}FO_3$ $[M+H]^+$: 415.1704; found 415.1691.

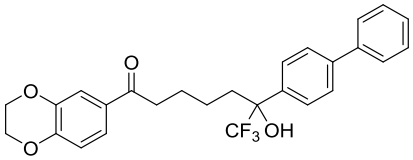
5-(1-([1,1'-biphenyl]-4-yl)-2,2-dichloro-3,3-difluorocyclopropyl)-1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)pentan-1-one (6)



Colorless oil (91.8 mg, 89% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 – 7.5 (m, 4H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 3H), 6.9 – 6.8 (m, 1H), 4.3 – 4.2 (m, 4H), 2.8 (t, *J* = 7.3 Hz, 2H), 2.1 – 2.0 (m, 2H), 1.9 – 1.6 (m, 2H), 1.5 – 1.3 (m, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.9 (d, *J* = 147.1 Hz), -138.1 (d, *J* = 147.0 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.2, 147.9, 143.3, 141.0, 140.3, 131.8, 130.8, 130.2, 128.9, 127.6, 127.2 (d, *J* = 7.1 Hz), 122.1, 117.5, 117.2, 109.2 (dd, *J* = 306.8, 302.5 Hz), 64.7, 64.1, 46.1 (dd, *J* = 8.0, 6.0 Hz), 37.8, 33.5 (d, *J* = 4.3 Hz), 25.9, 23.9; **HRMS (ESI)** calcd for $C_{28}H_{24}Cl_2FO_3[M+H]^+$:517.1443; found 517.1435.

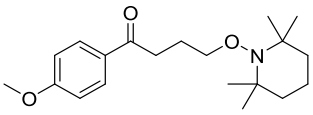
6-([1,1'-biphenyl]-4-yl)-1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-7,7,7-trifluoro-6-

hydroxyheptan-1-one (7)



Colorless oil (86.5 mg, 92% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.6 – 7.6 (m, 6H), 7.5 – 7.4 (m, 4H), 7.4 – 7.3 (m, 1H), 6.9 – 6.8 (m, 1H), 4.3 – 4.2 (m, 4H), 2.9 (d, *J* = 4.2 Hz, 1H), 2.9 – 2.8 (m, 2H), 2.3 – 2.2 (m, 1H), 2.1 – 2.0 (m, 1H), 1.8 – 1.7 (m, 2H), 1.5 – 1.4 (m, 1H), 1.2 – 1.1 (m, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.1; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.8, 148.1, 143.4, 141.3, 140.5, 135.6, 130.8, 128.9, 127.7, 127.2 (d, *J* = 19.3 Hz), 126.9, 122.3, 117.7, 117.3, 64.8, 64.2, 37.9, 34.9, 24.3, 22.2; **HRMS (ESI)** calcd for $C_{27}H_{26}F_3O_4$ $[M+H]^+$: 477.1778; found 477.1765.

1-(4-methoxyphenyl)-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butan-1-one (8)



Colorless oil (11.4 mg, 17% yield); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.1 – 7.8 (m, 2H), 7.0 – 6.8 (m, 2H), 3.9 (s, 3H), 3.8 (t, *J* =6.2 Hz, 2H), 3.0 (t, *J* = 7.5 Hz, 2H), 2.0 – 1.9 (m, 2H), 1.4 (dd, *J* = 8.4, 4.9 Hz, 4H), 1.3 (d, *J* = 11.5 Hz, 2H), 1.1 (s, 6H), 1.1 (s, 6H). **^{13}C NMR** (100 MHz, $CHCl_3$) δ 199.0, 163.4, 130.5, 130.3, 113.8, 75.7, 59.8, 55.6, 39.7, 35.3, 33.2, 24.0, 20.3, 17.3; **HRMS (ESI)** calcd for $C_{20}H_{32}NO_3$ $[M+H]^+$: 334.2377; found 334.2369.

Reference

1. (a) T. Ichitsuka, T. Fujita, T. Arita and J. Ichikawa, *Angew. Chem. Int. Ed.*, 2014, **53**, 7564. (b) B. M. Trost and L. Debien, *J. Am. Chem. Soc.*, **2015**, *137*, 11606.
2. L. Huang, T. Ji and M. Rueping, *J. Am. Chem. Soc.*, 2020, **142**, 3532.
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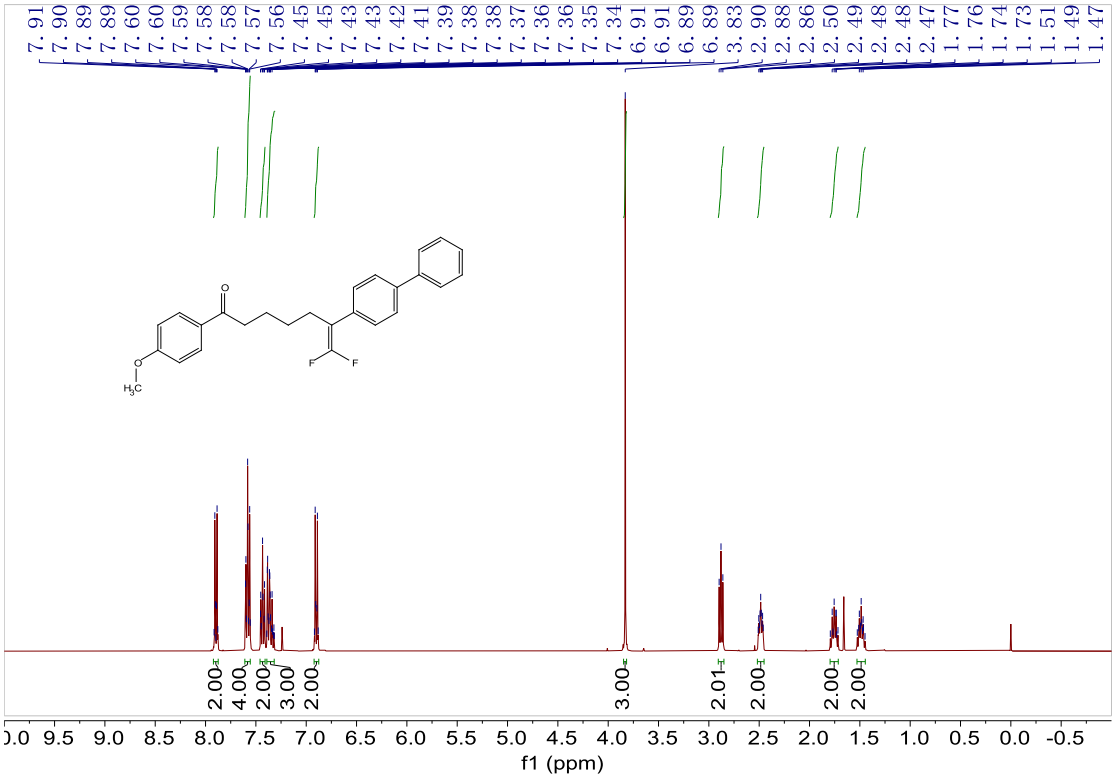
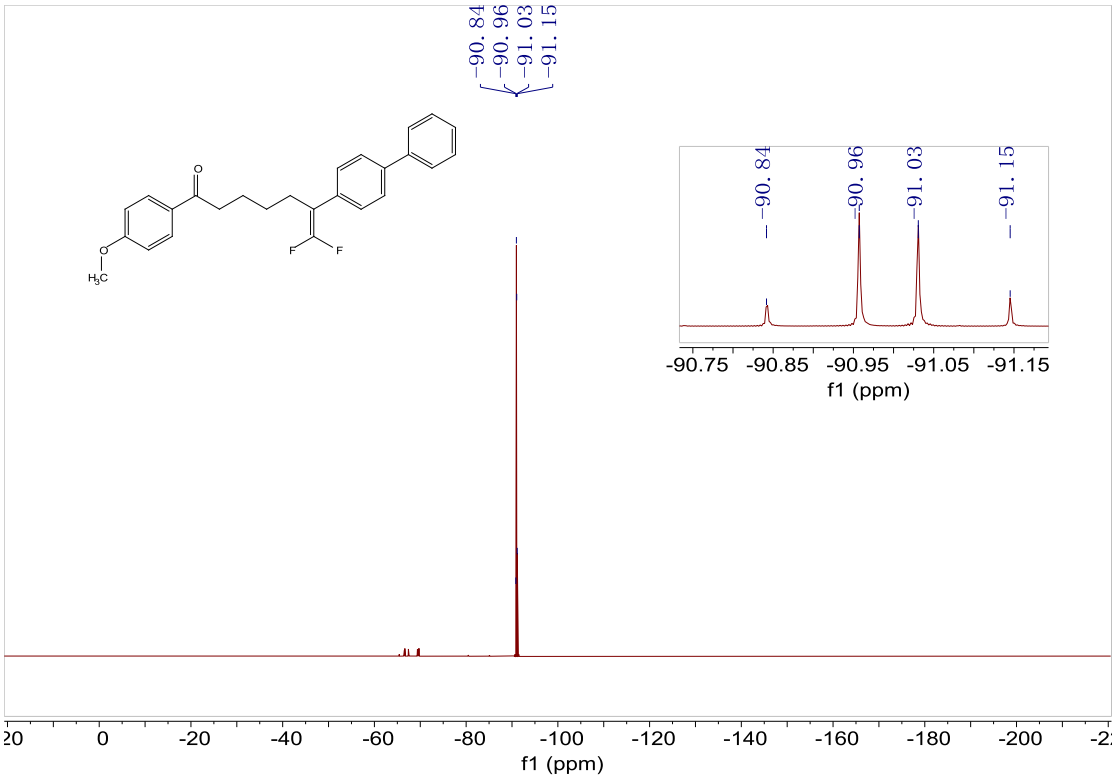
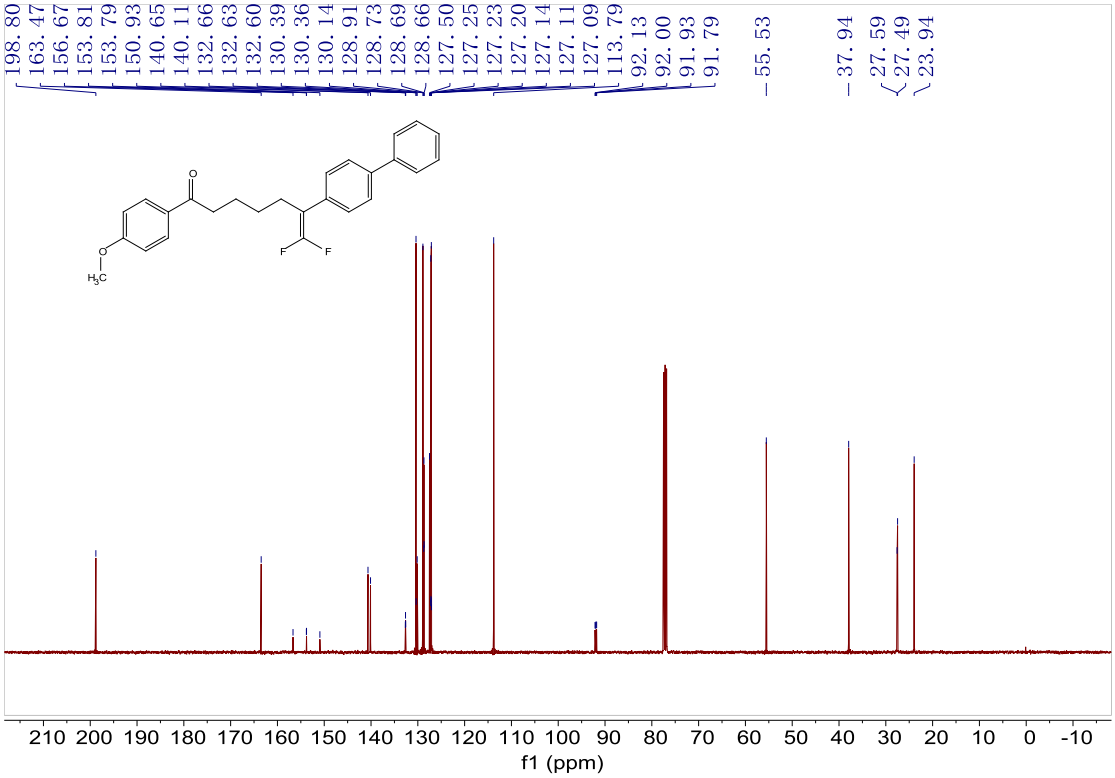
^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra



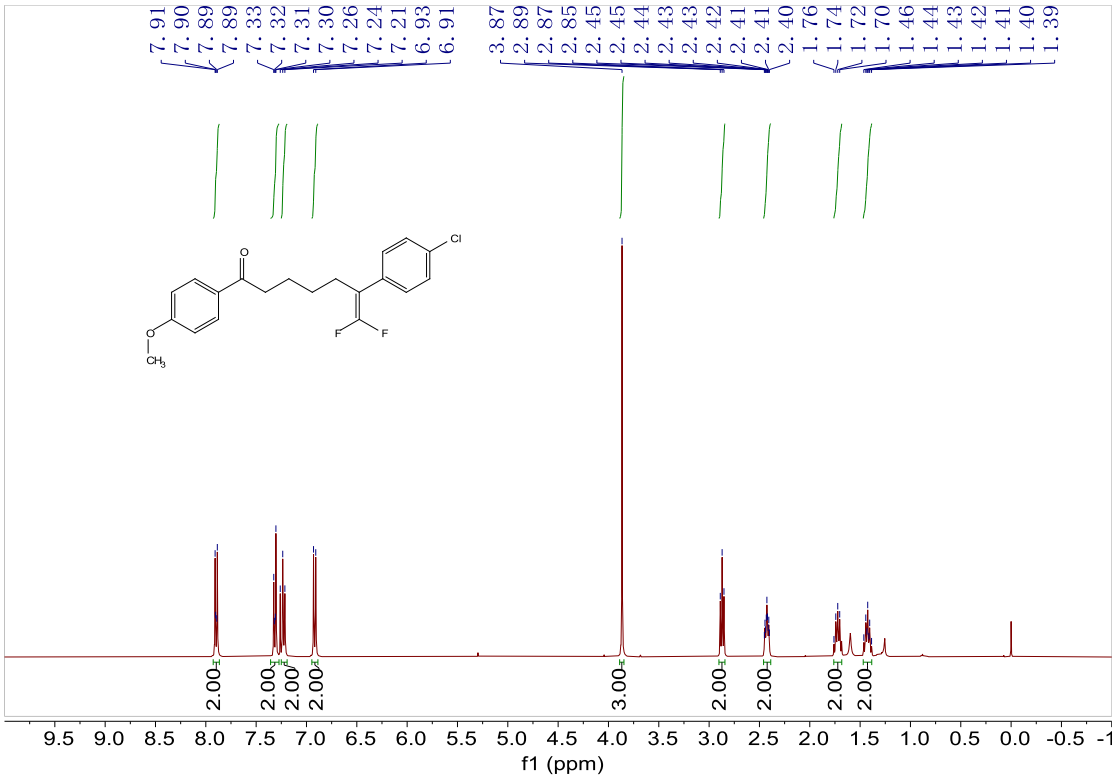
^{1}H NMR of 3aa (400 MHz, $CDCl_3$)



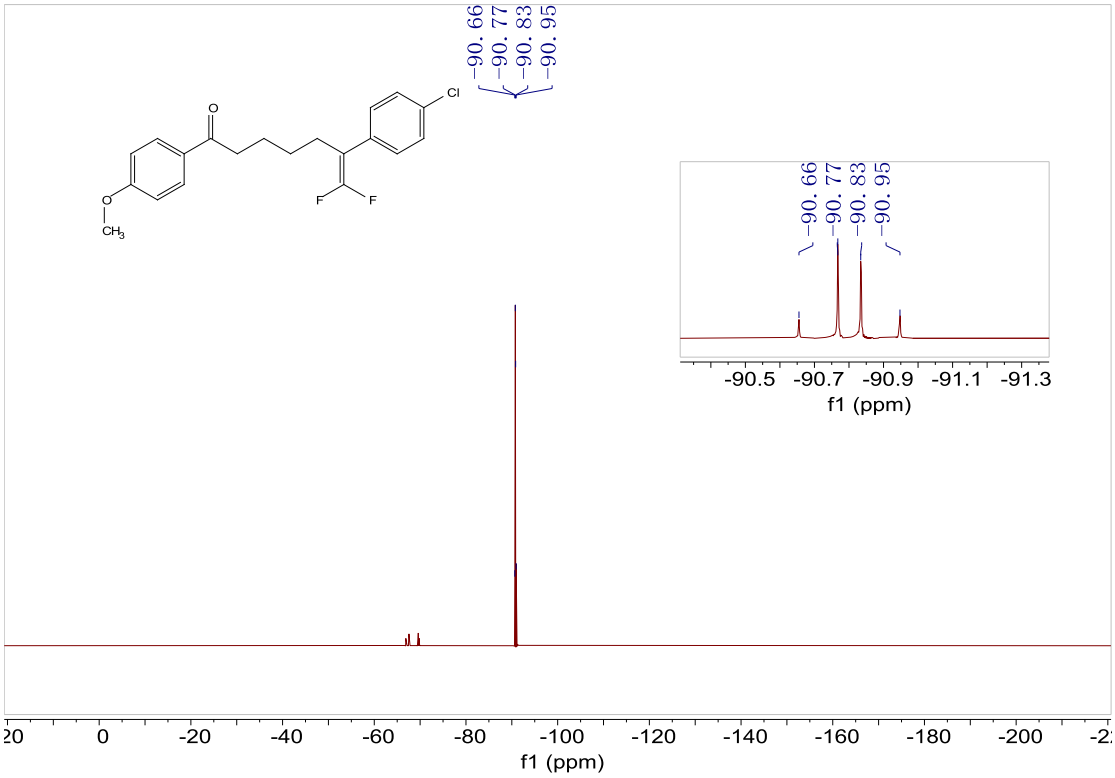
^{19}F NMR of 3aa (376 MHz, $CDCl_3$)



^{13}C NMR of 3aa (100 MHz, $CDCl_3$)



^{1}H NMR of 3ab (400 MHz, $CDCl_3$)



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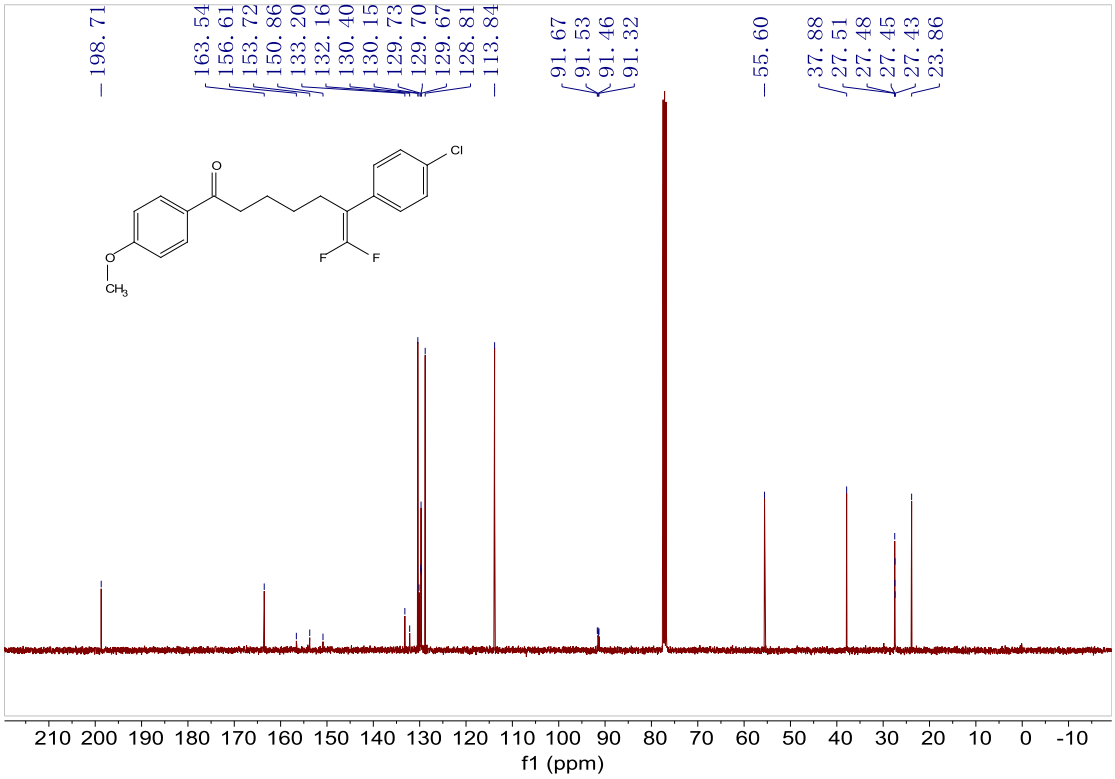

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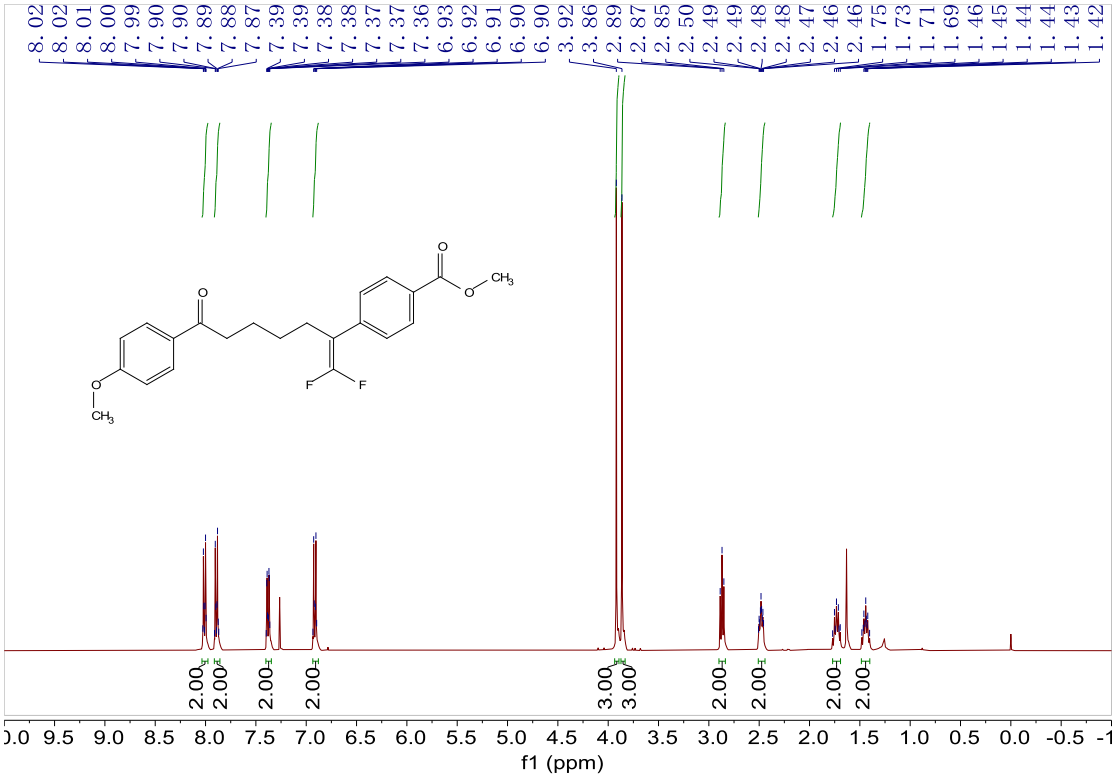

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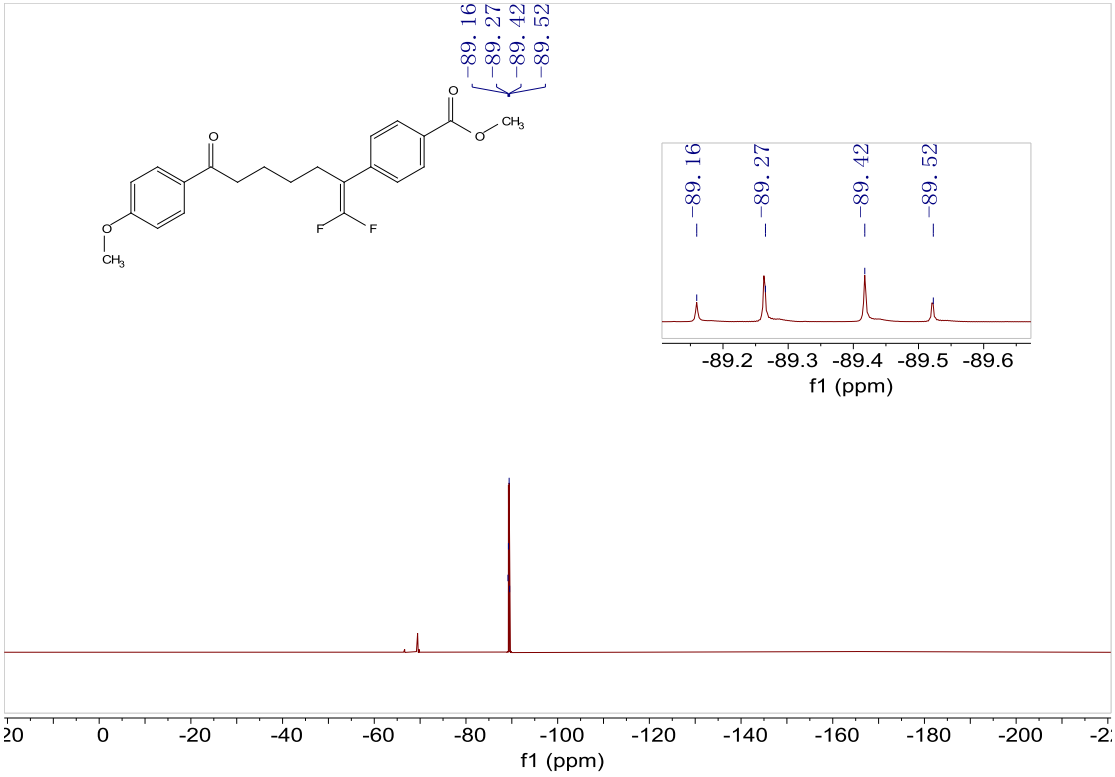
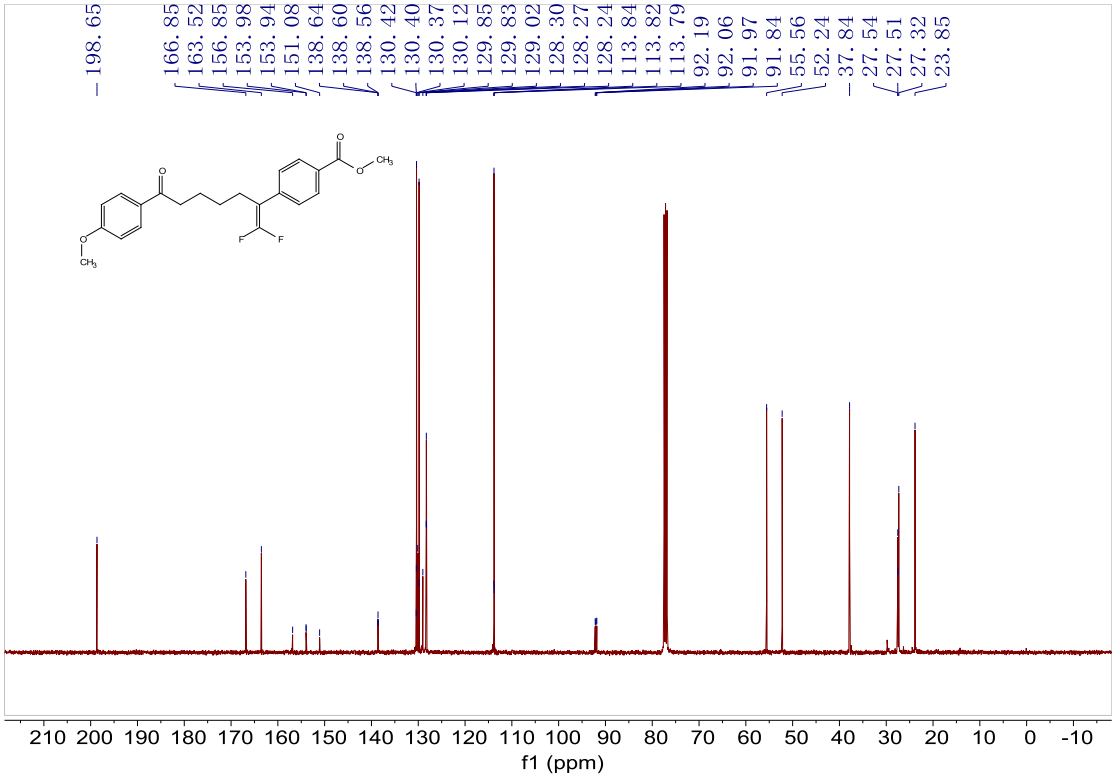
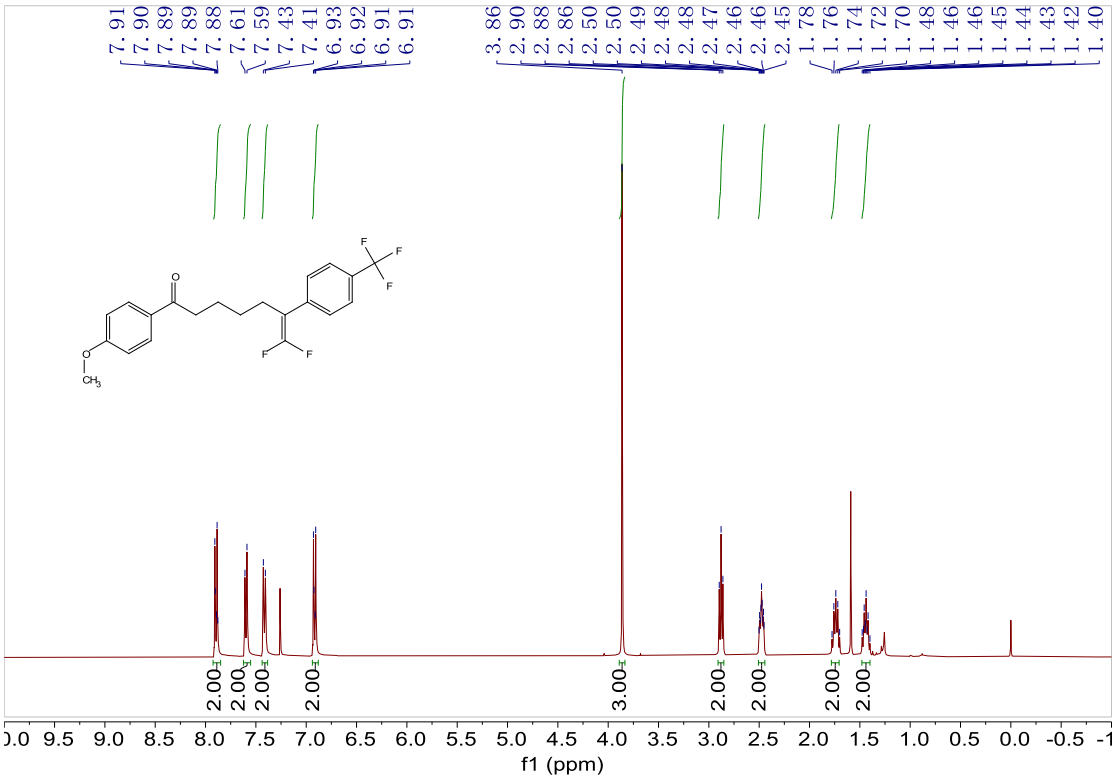


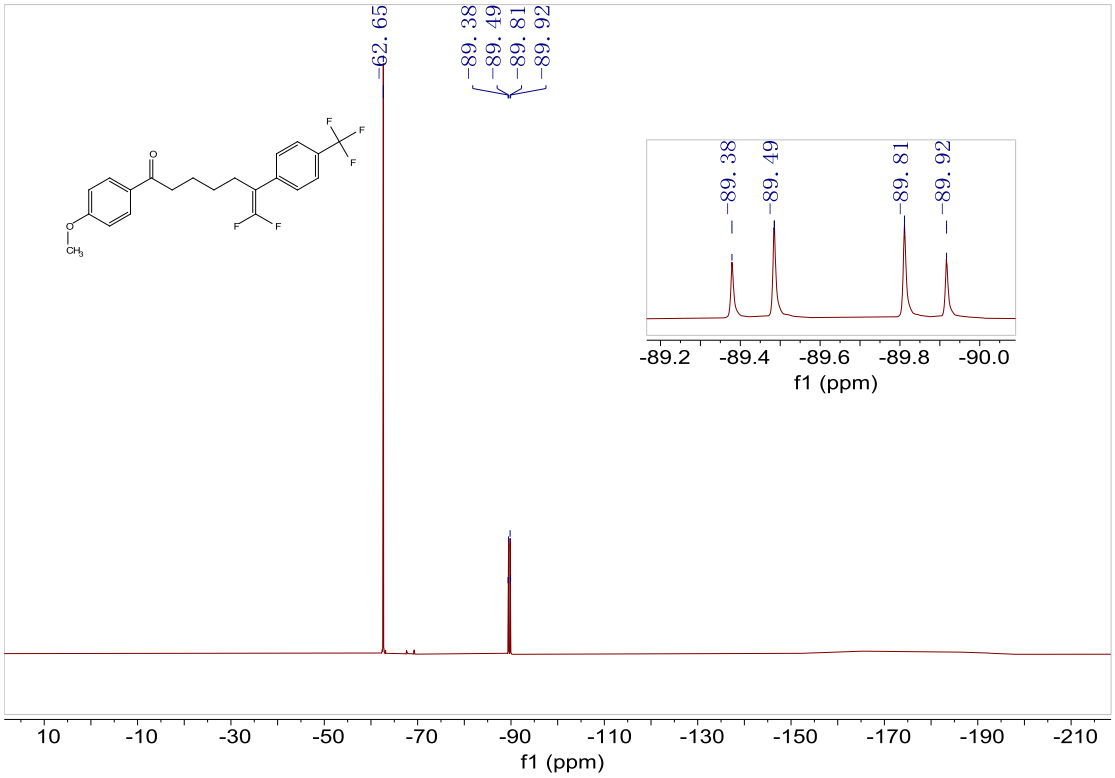
^{19}F NMR of 3ac (376 MHz, $CDCl_3$)



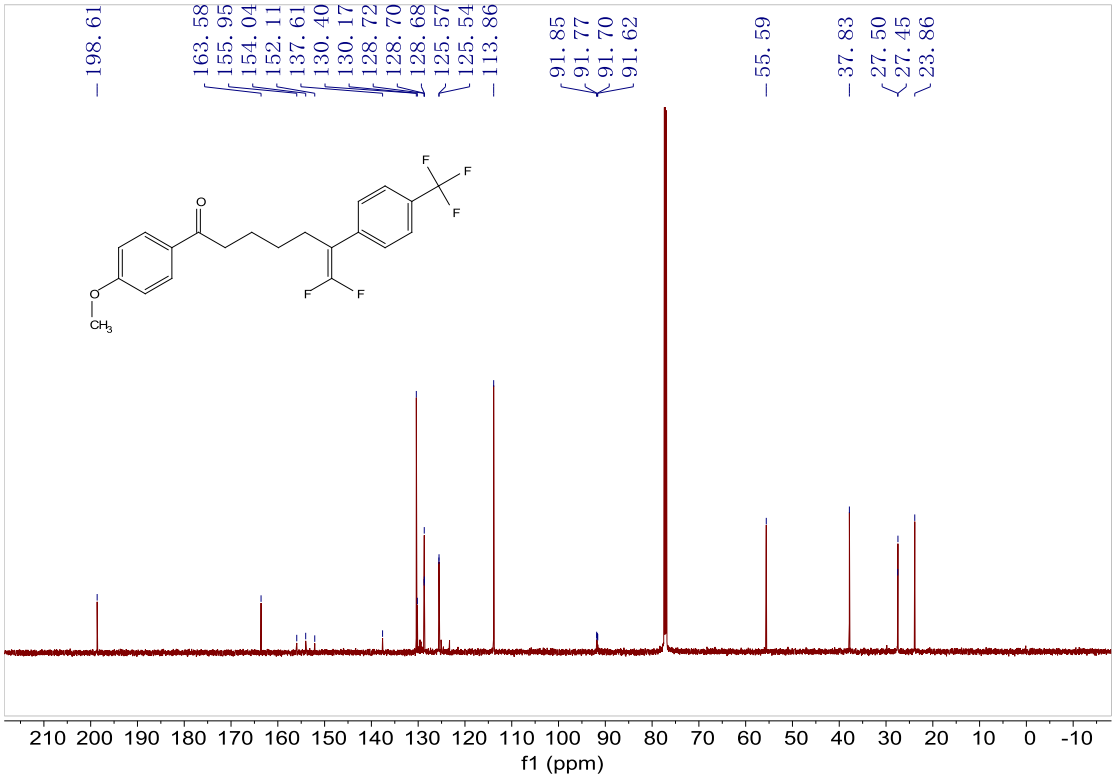
^{13}C NMR of 3ac (100 MHz, $CDCl_3$)



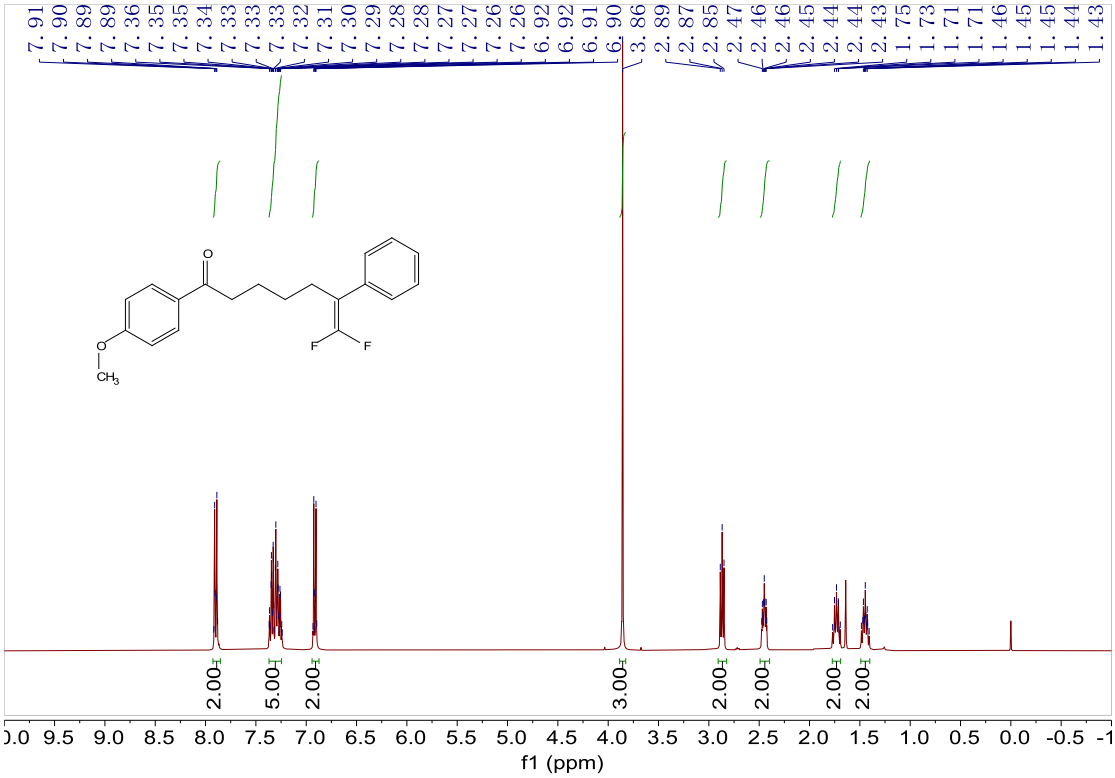
^{1}H NMR of 3ad (400 MHz, $CDCl_3$)



^{19}F NMR of 3ad (376 MHz, $CDCl_3$)



^{13}C NMR of 3ad (150 MHz, $CDCl_3$)



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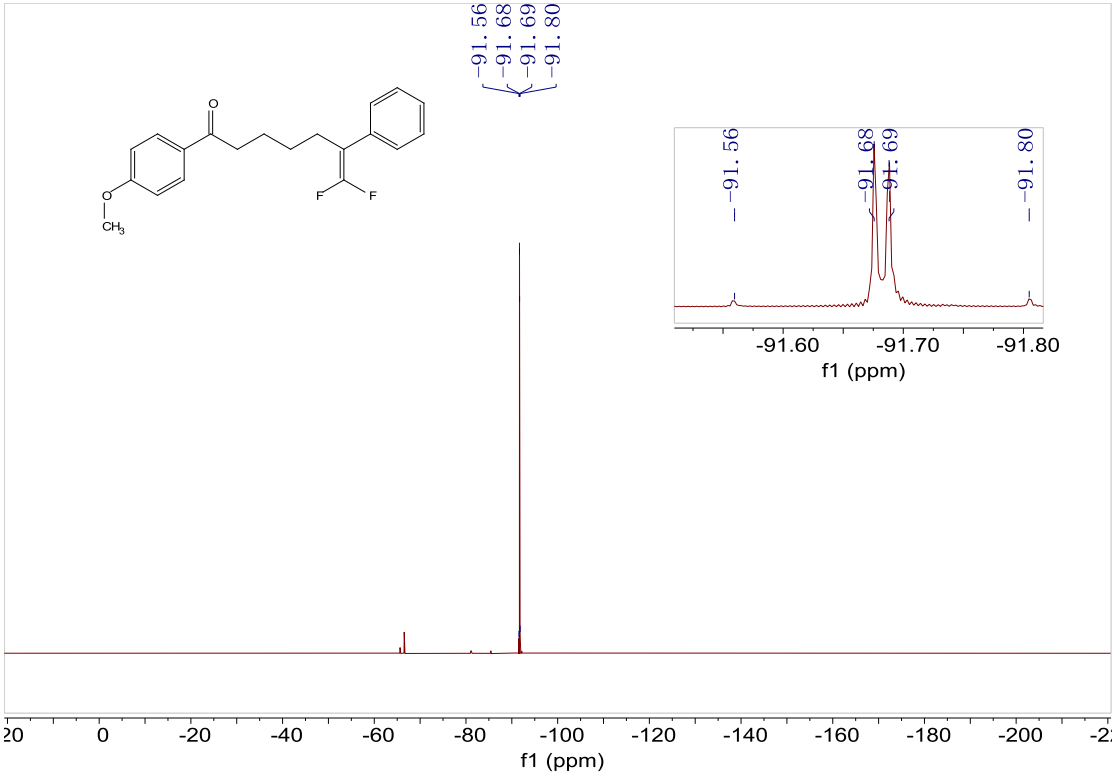
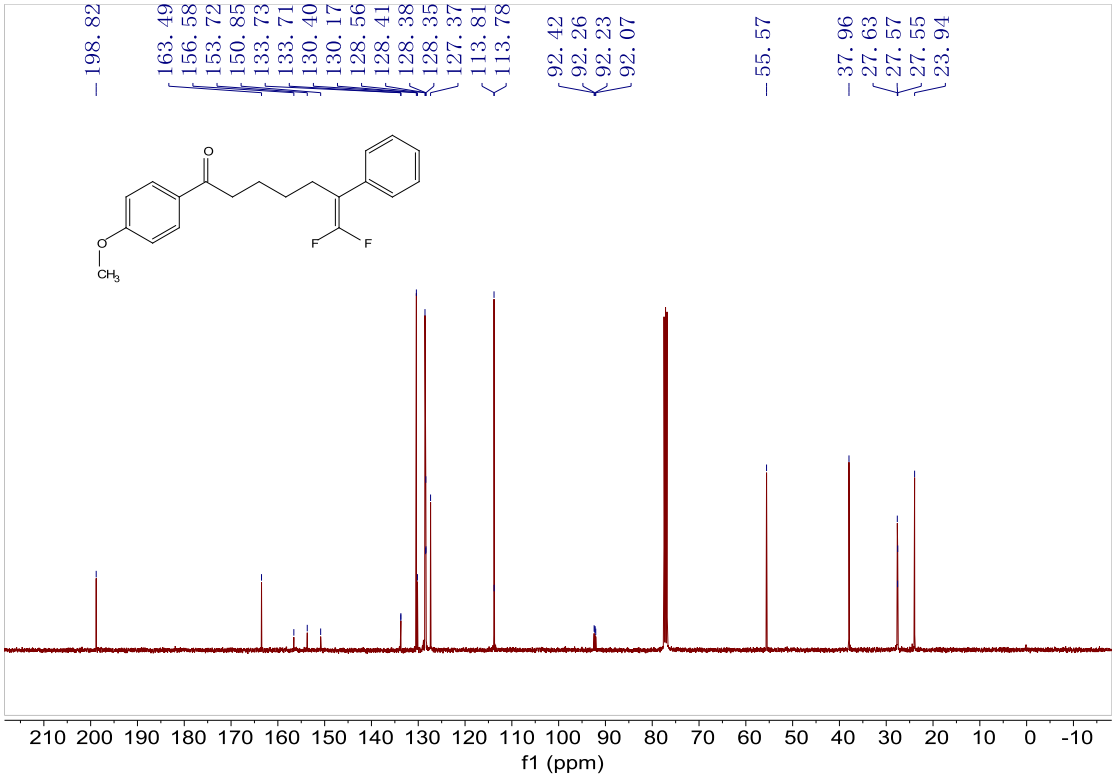


^{19}F NMR of 3ae (376 MHz, $CDCl_3$)



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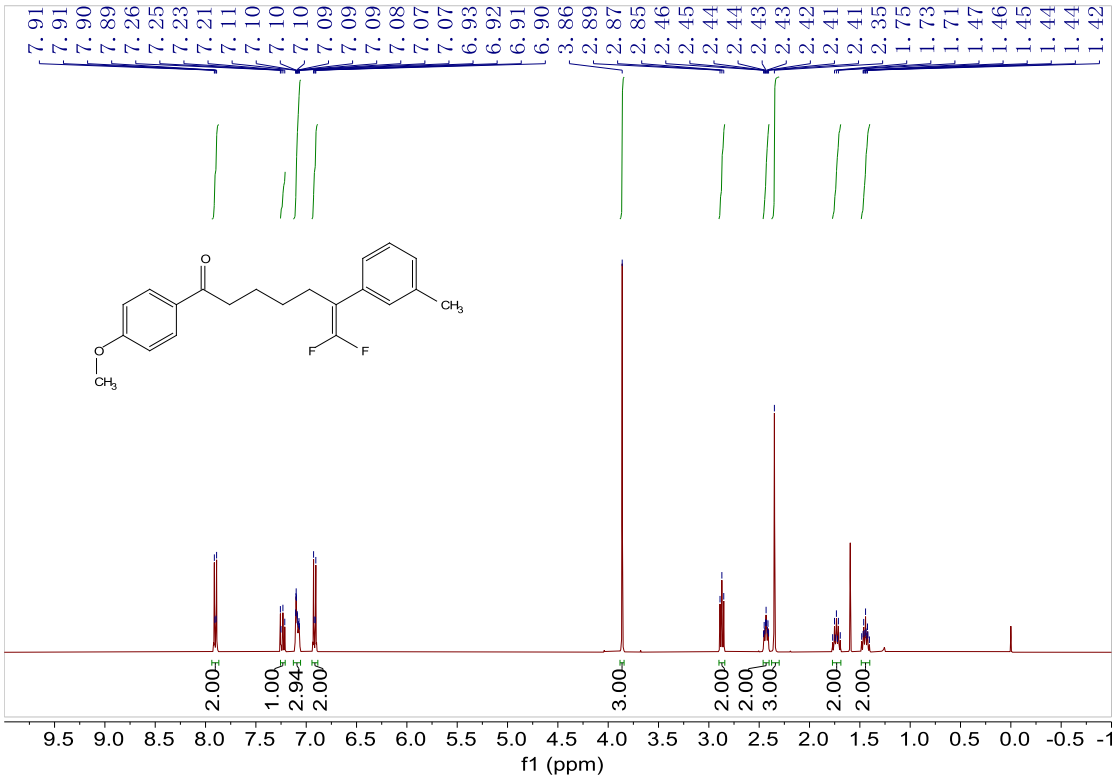

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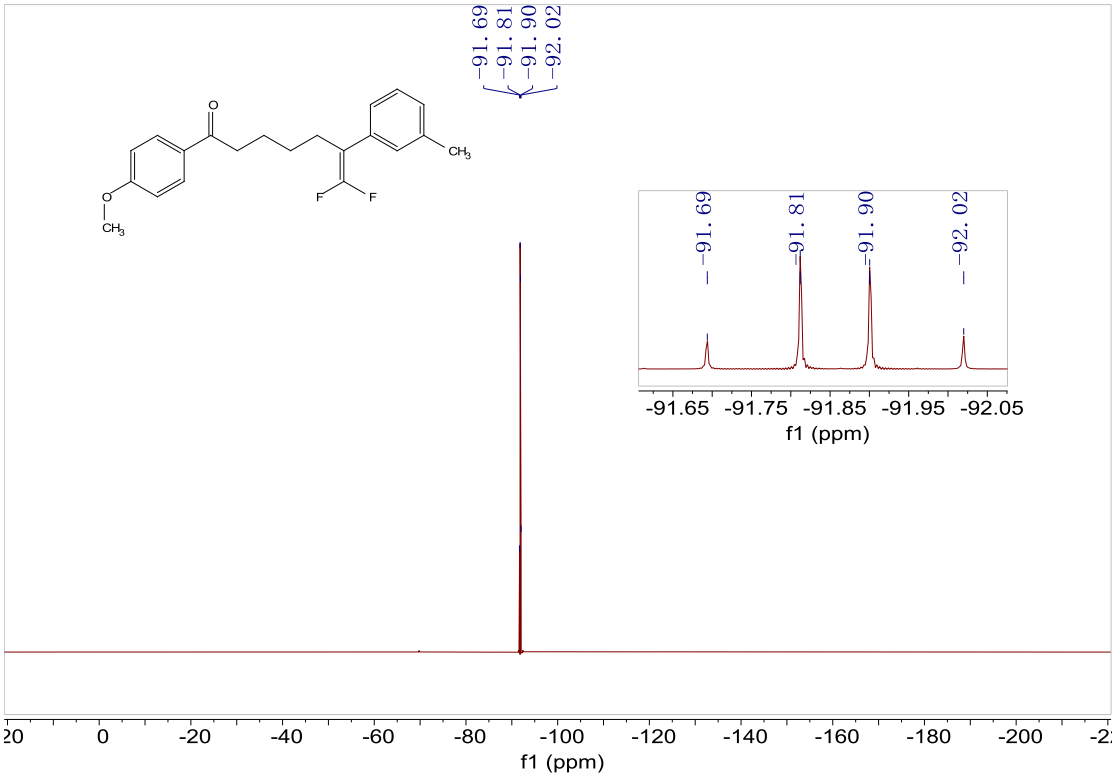
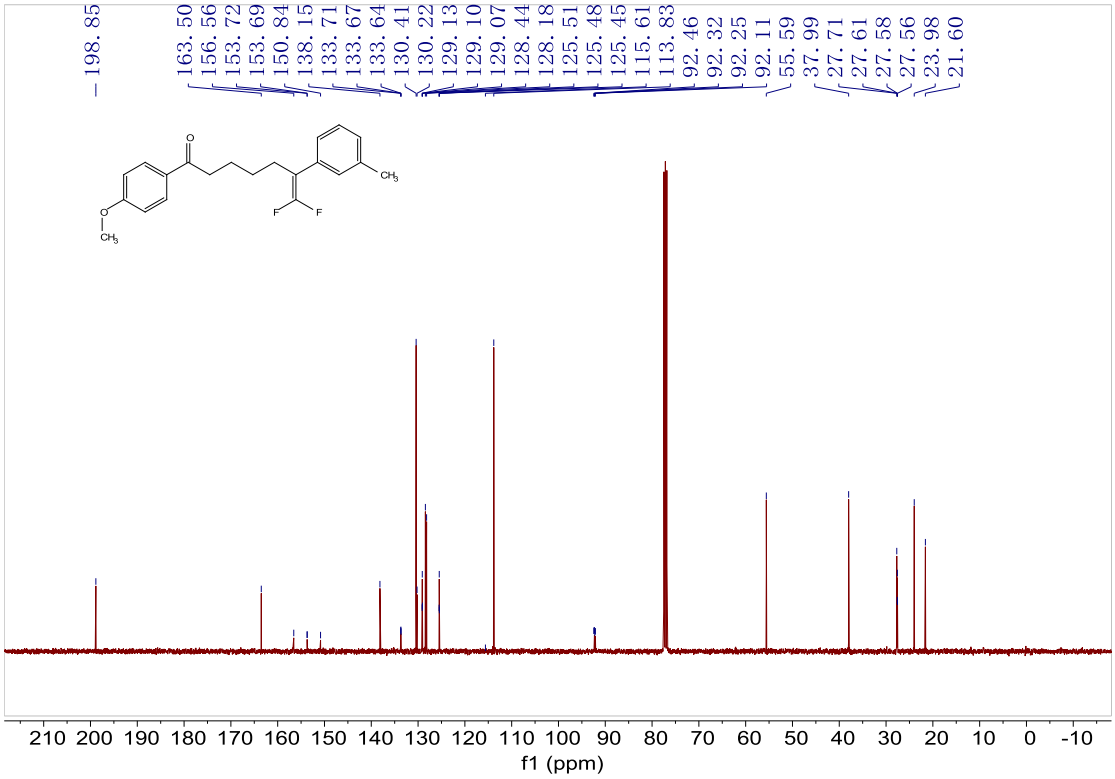


^{19}F NMR of 3af (376 MHz, $CDCl_3$)



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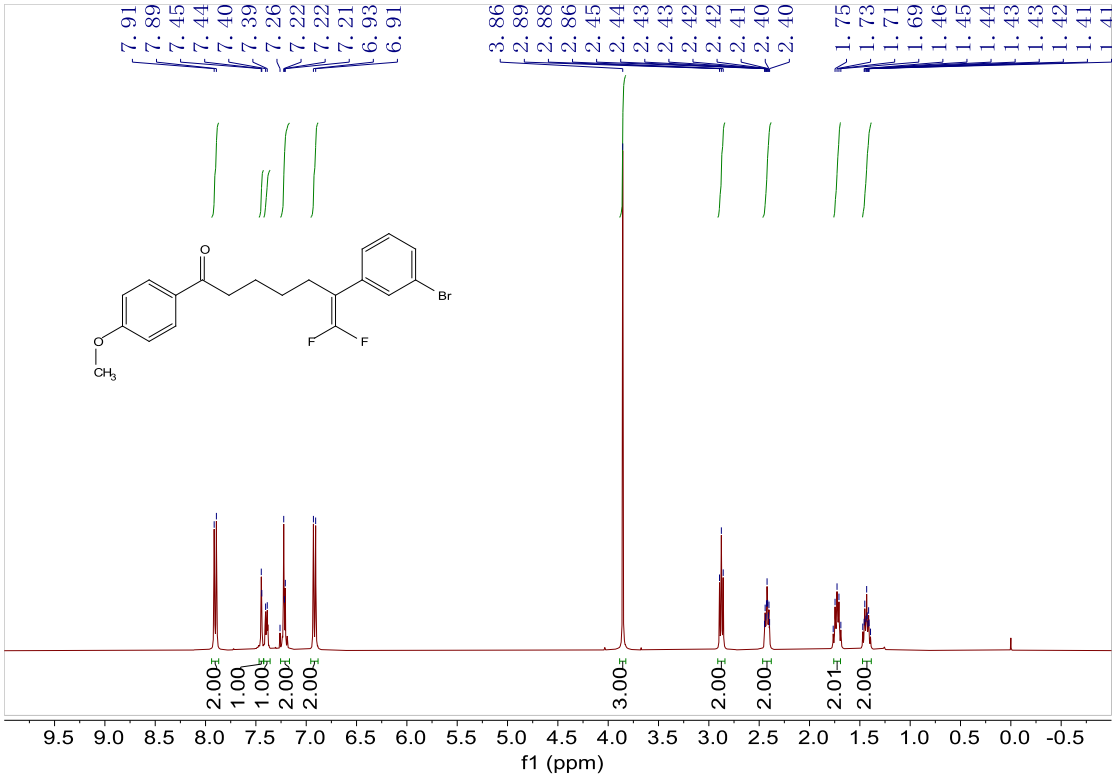

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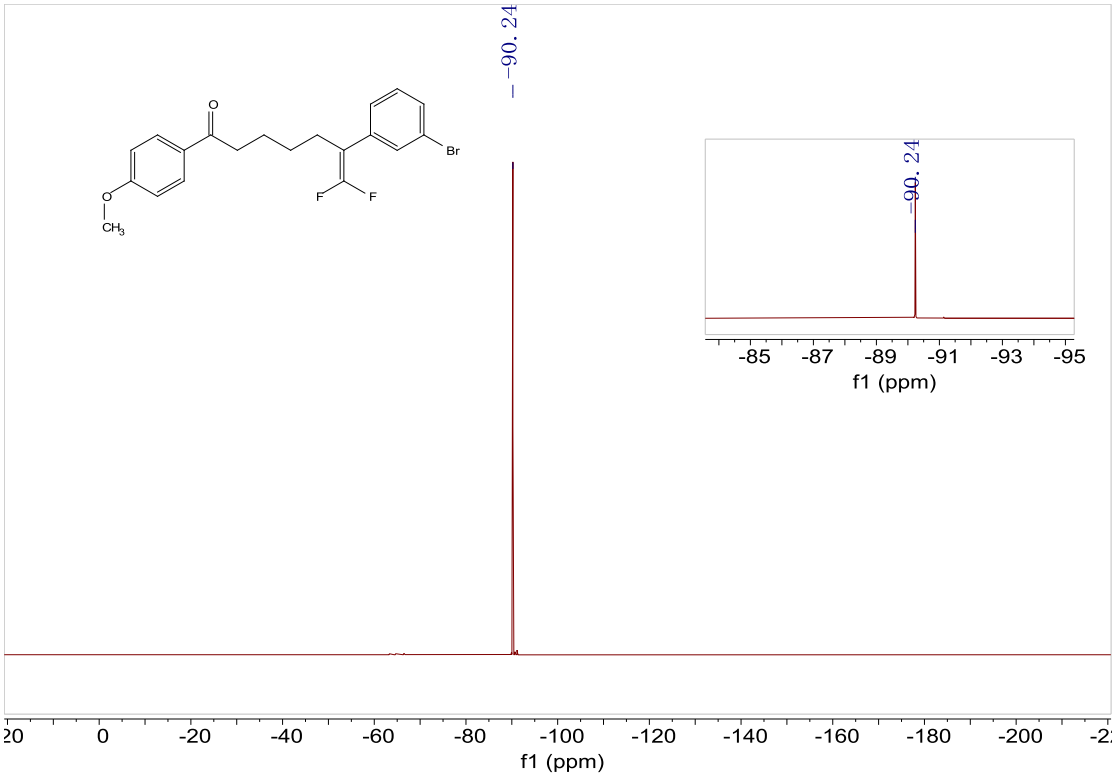

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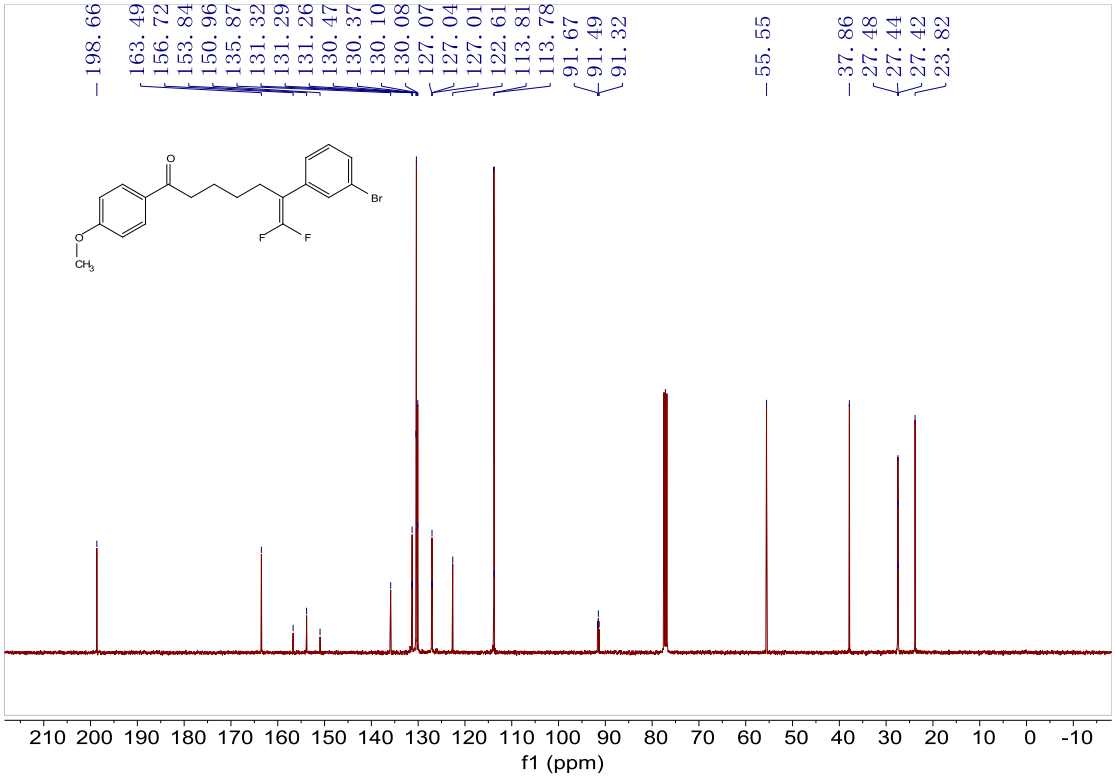

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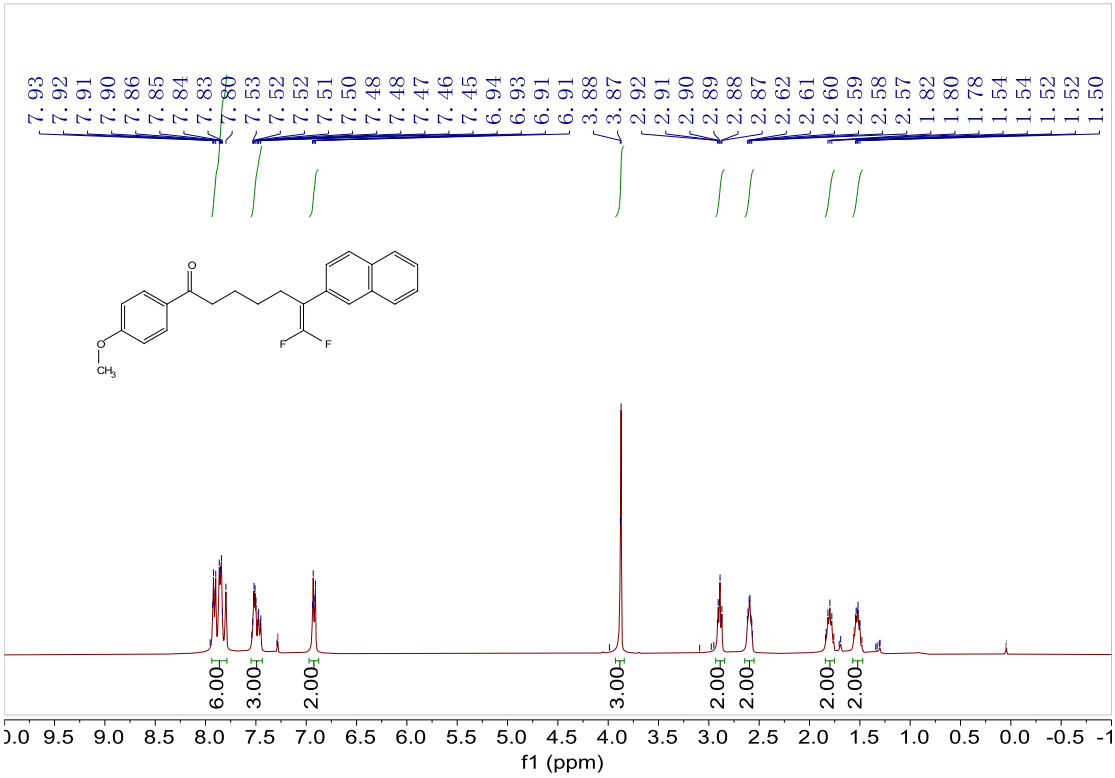

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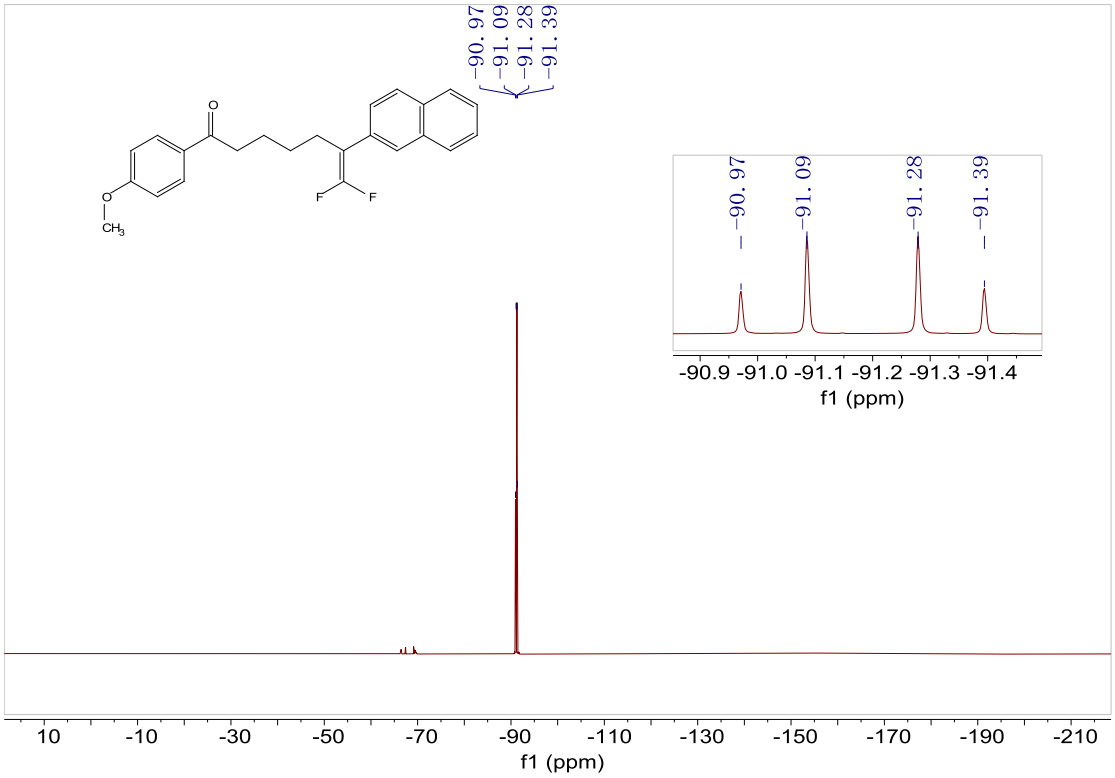
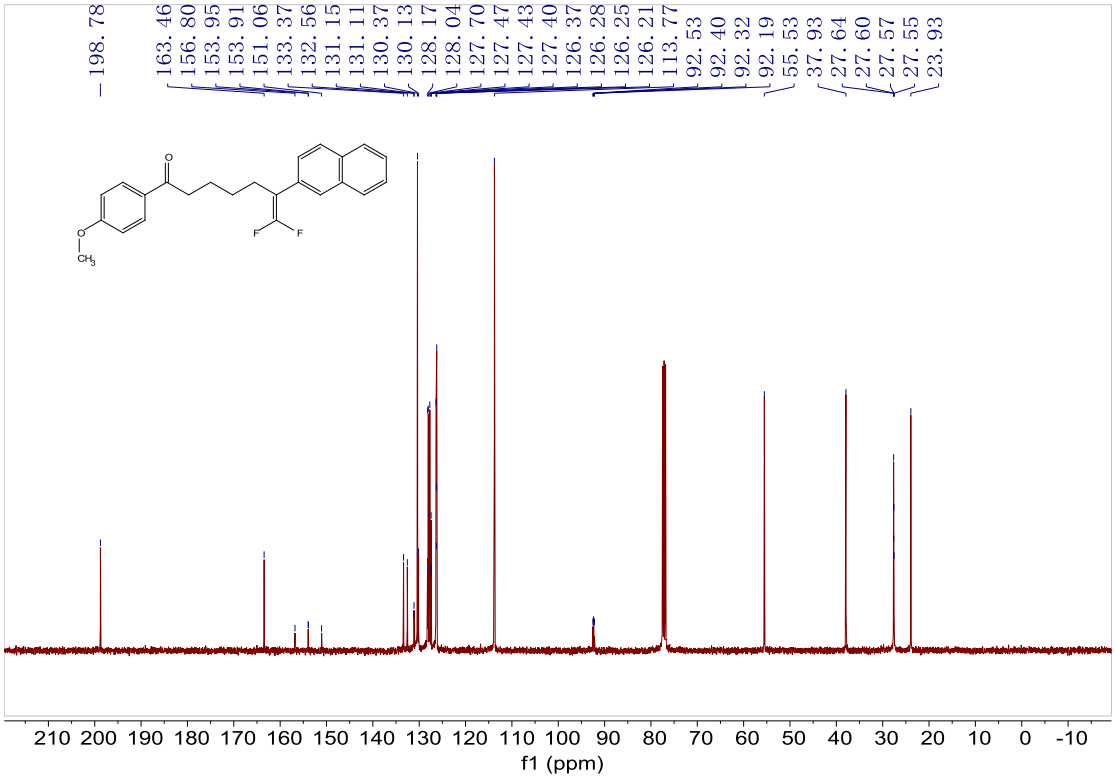


^{19}F NMR of 3ah (376 MHz, $CDCl_3$)



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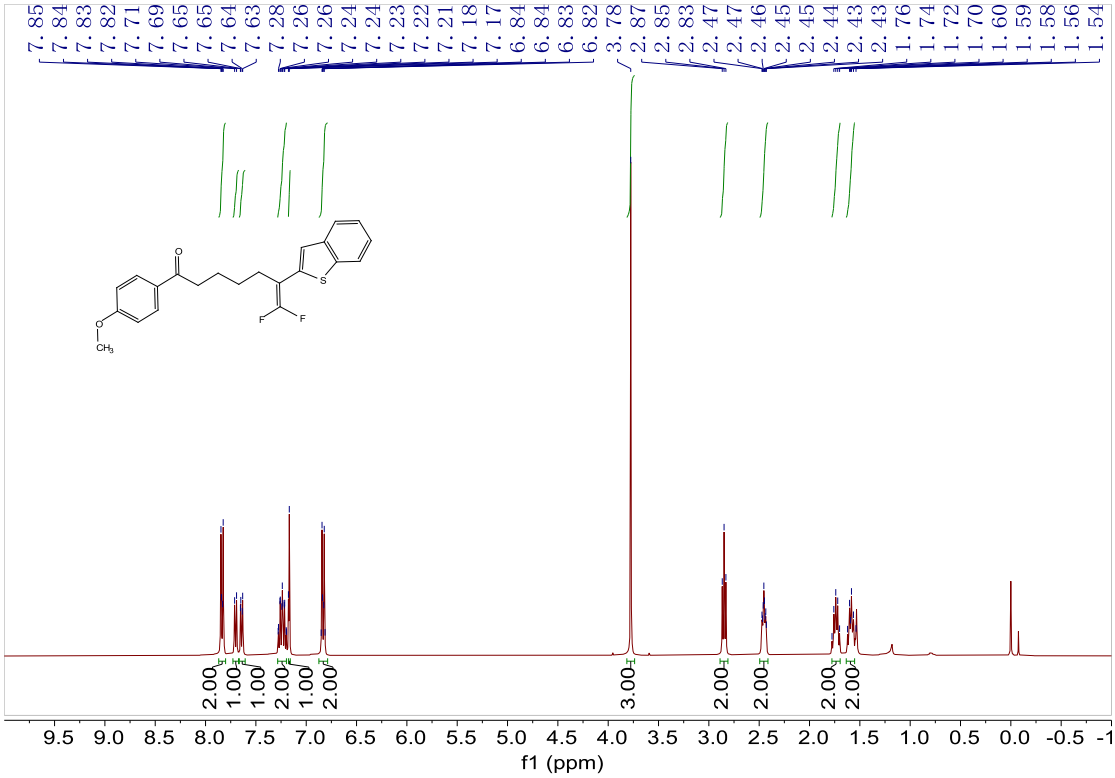

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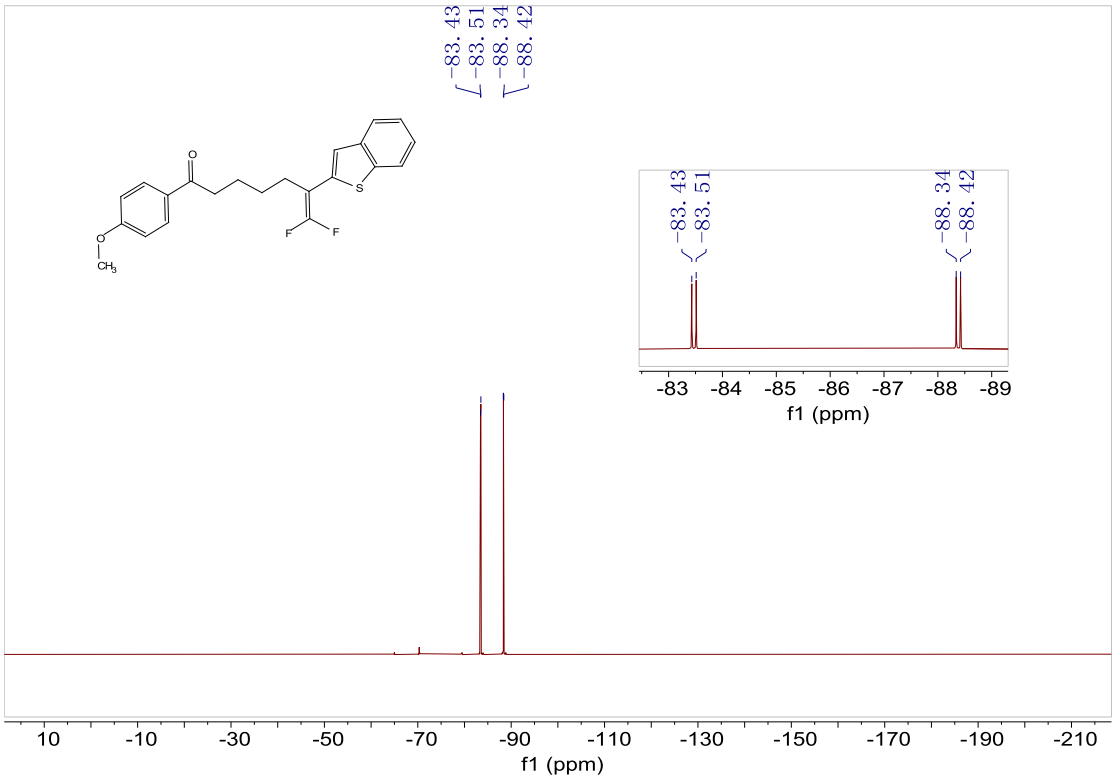
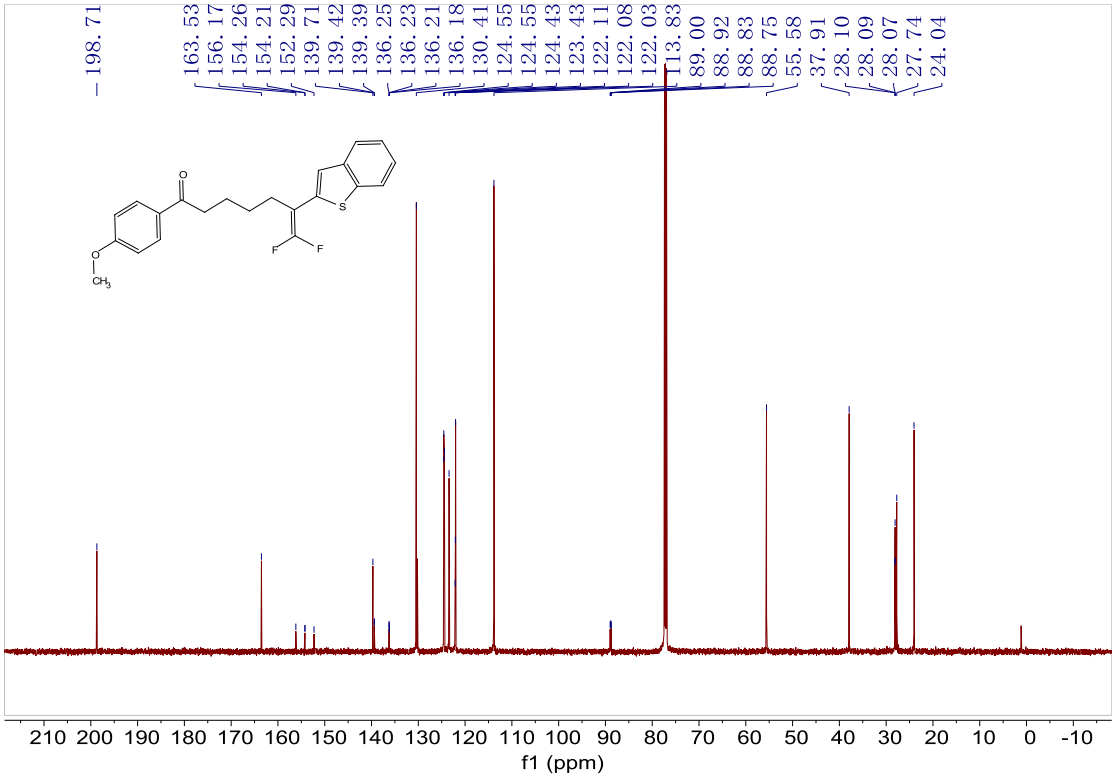


^{19}F NMR of 3ai (376 MHz, $CDCl_3$)



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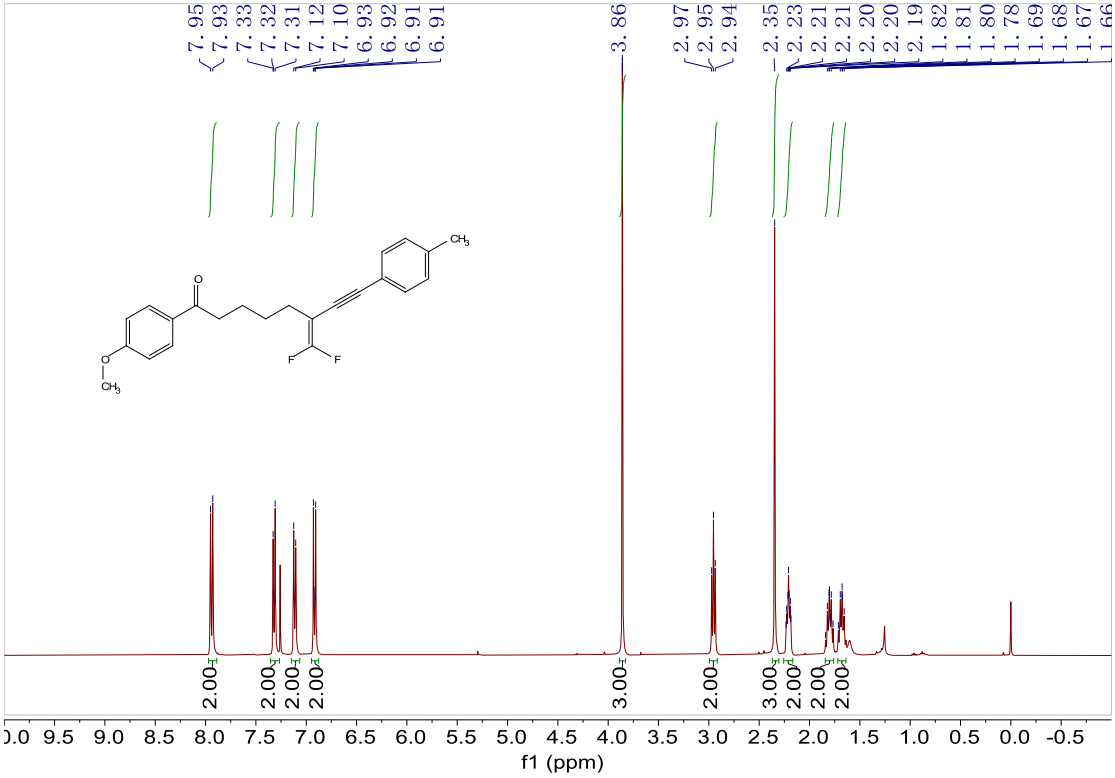

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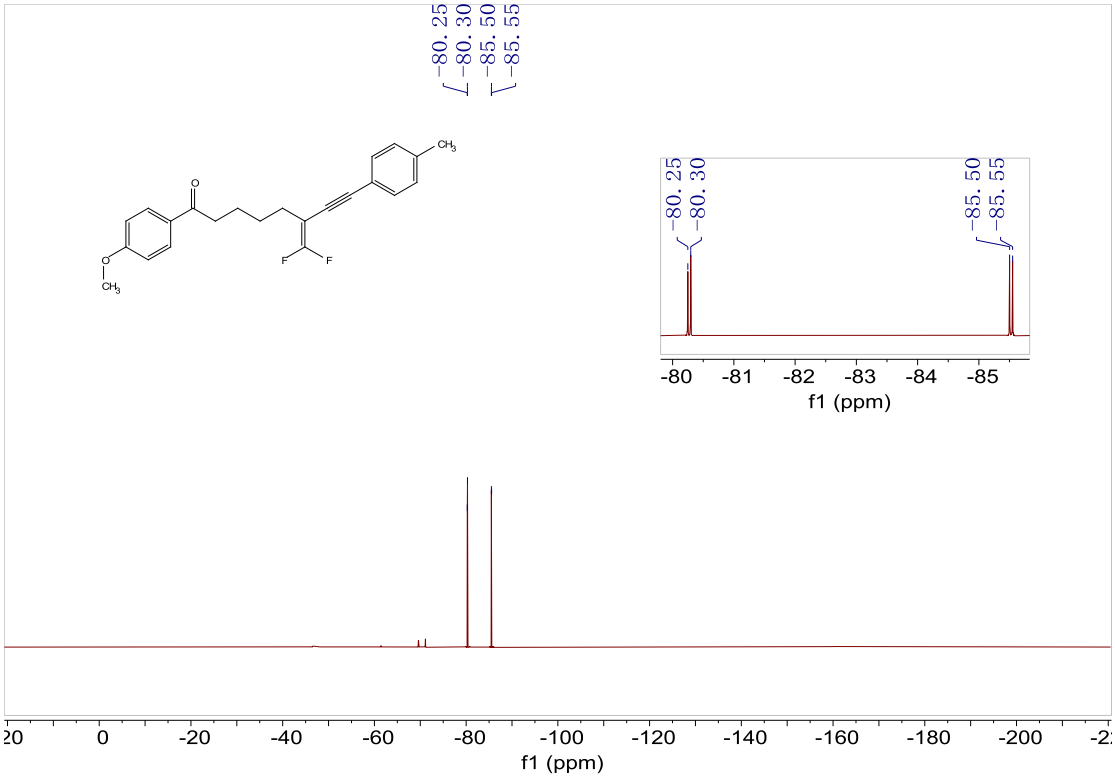

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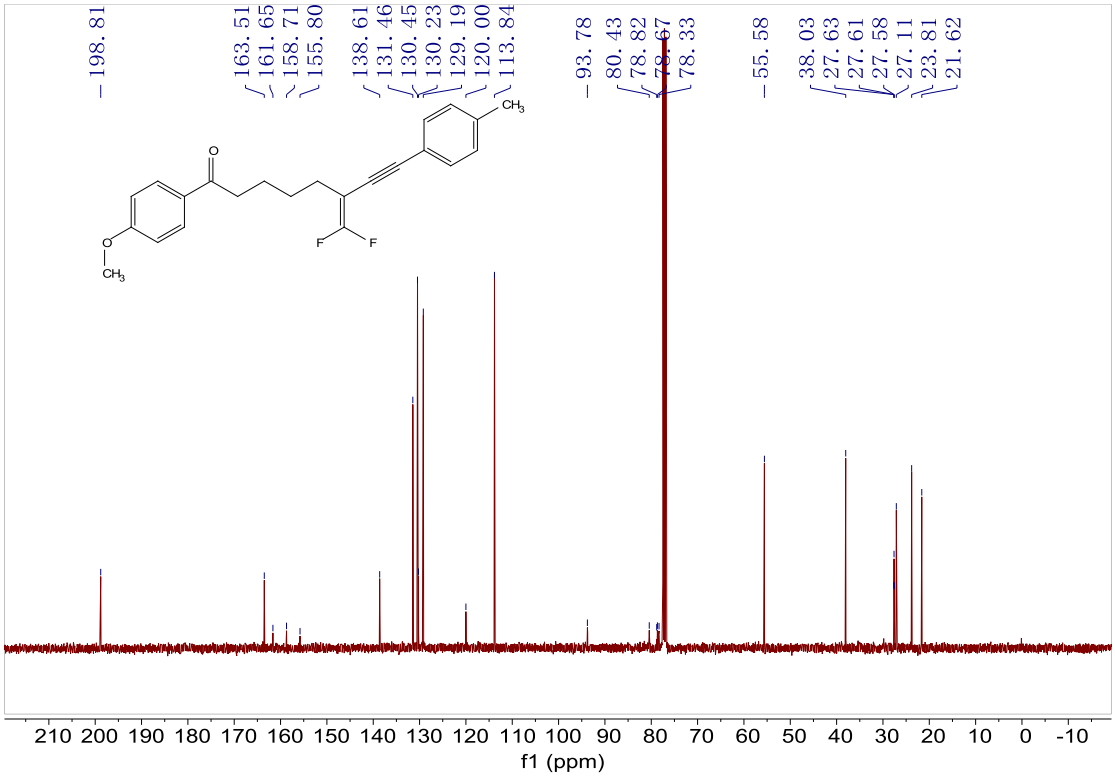

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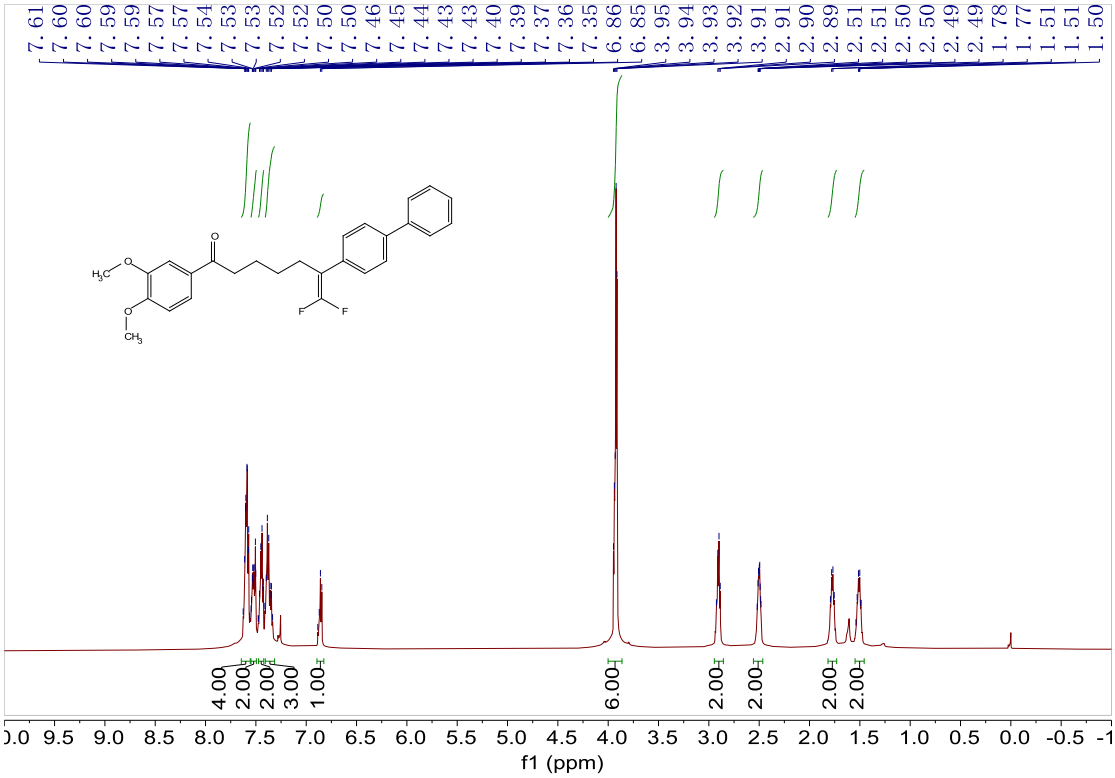

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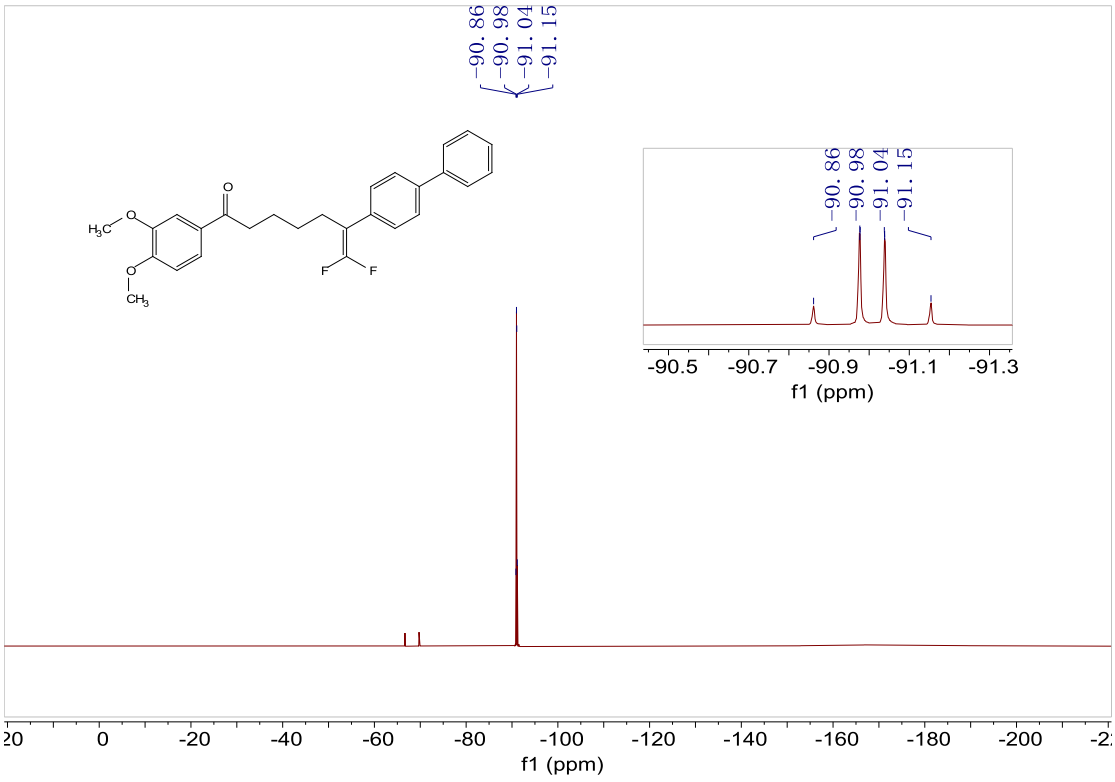
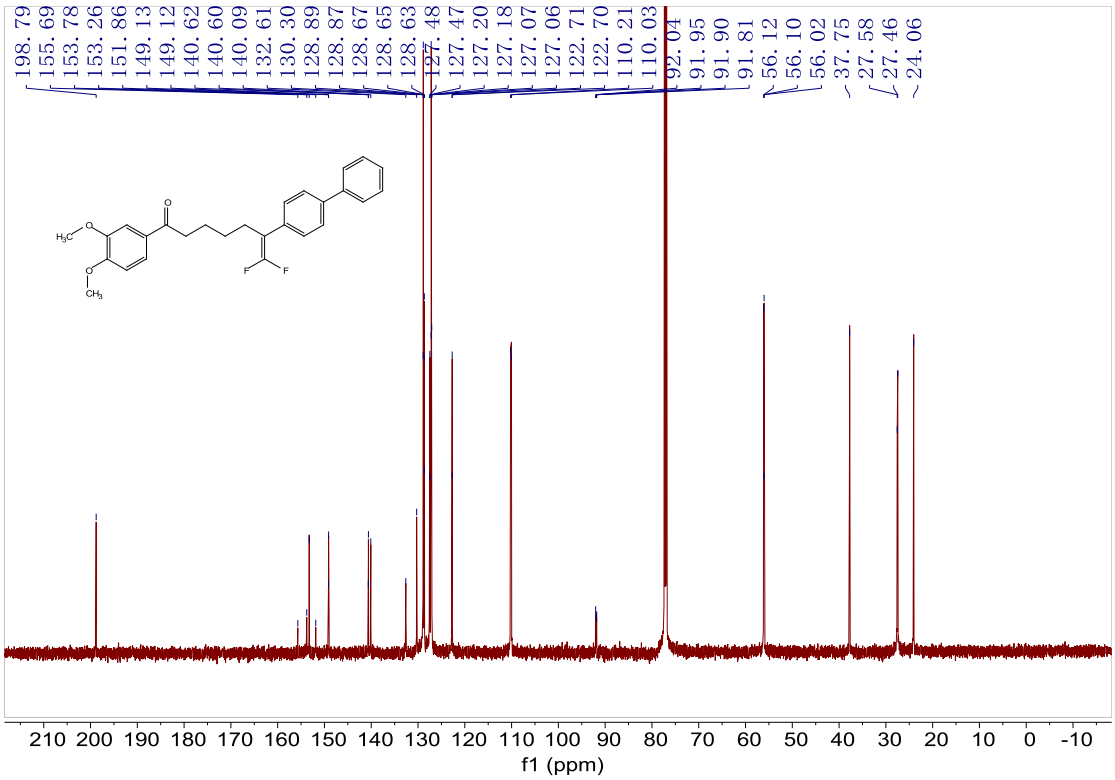
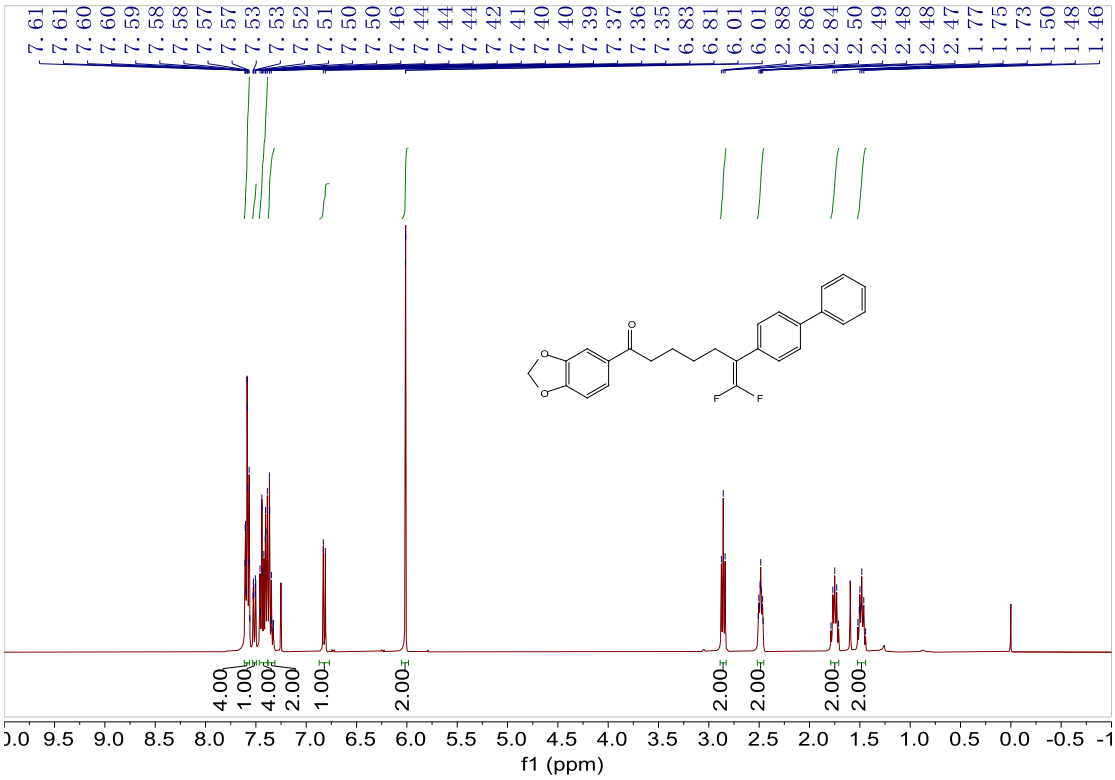


^{19}F NMR of 3ba (376 MHz, $CDCl_3$)



^{13}C NMR of 3ba (150 MHz, $CDCl_3$)



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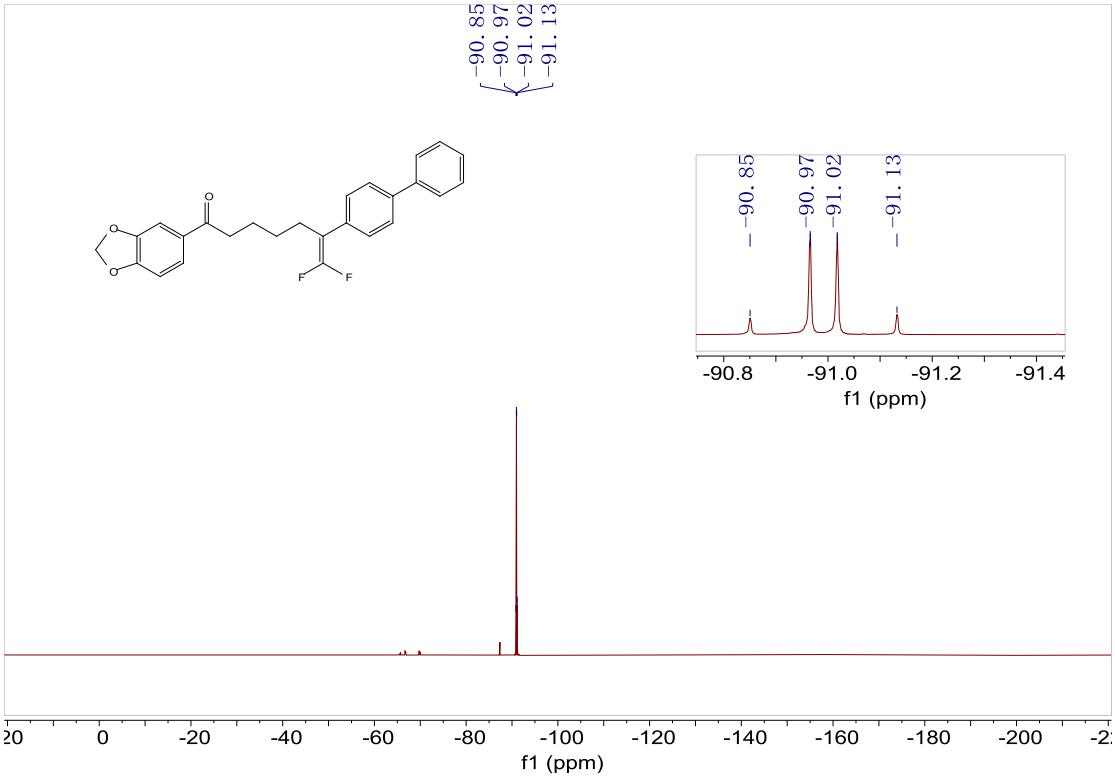
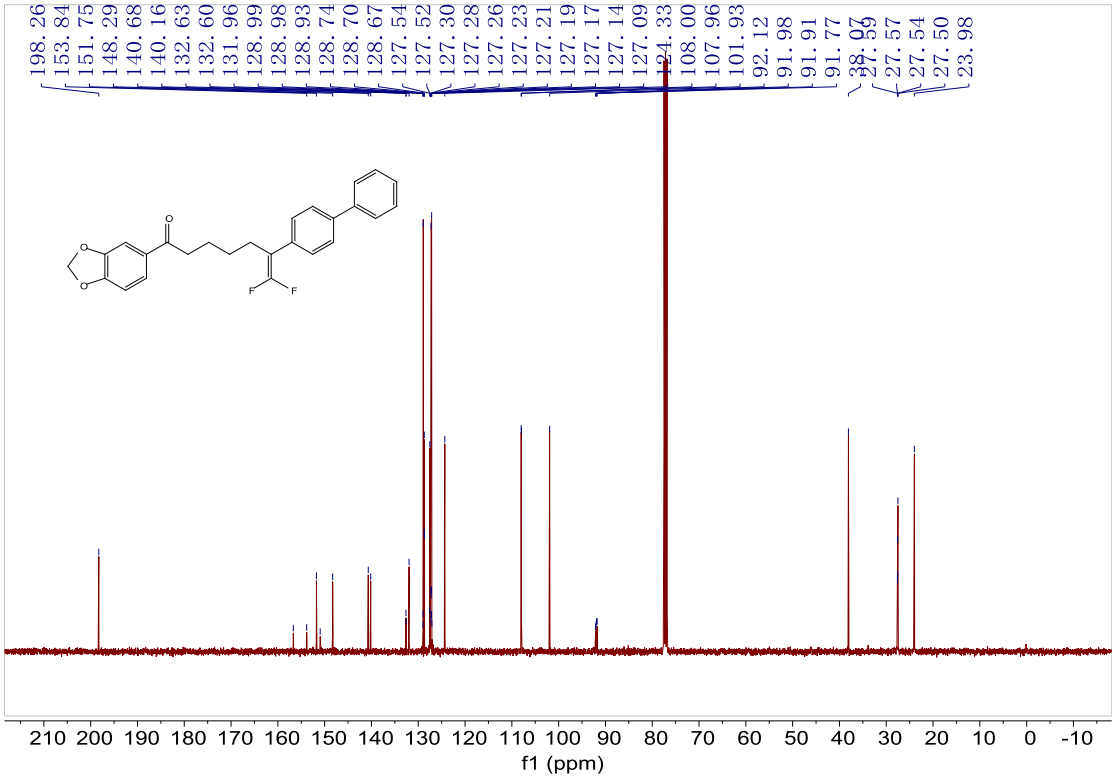


^{19}F NMR of 3ca (376 MHz, $CDCl_3$)



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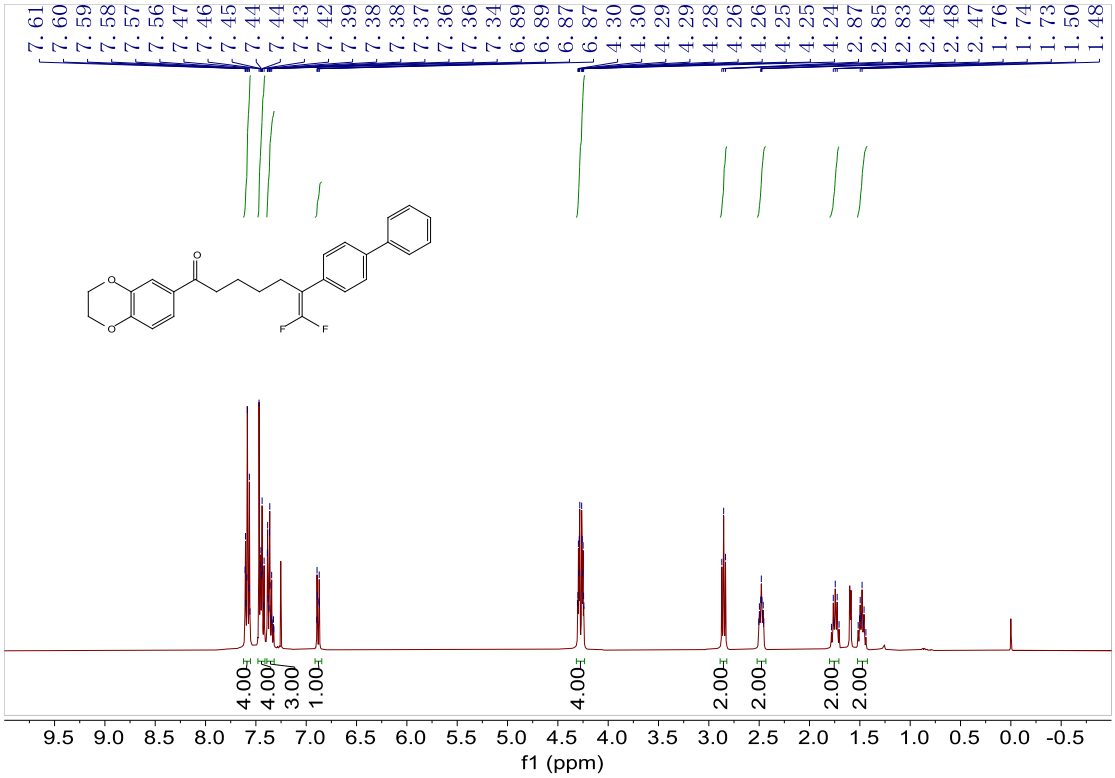

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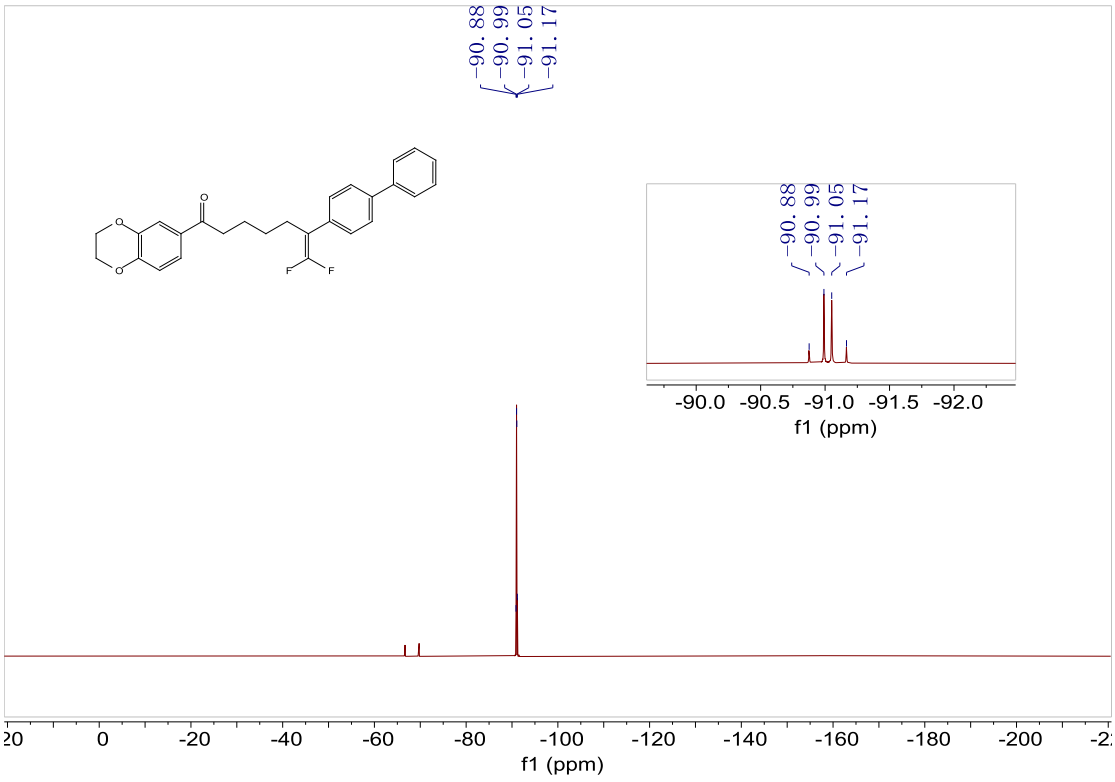

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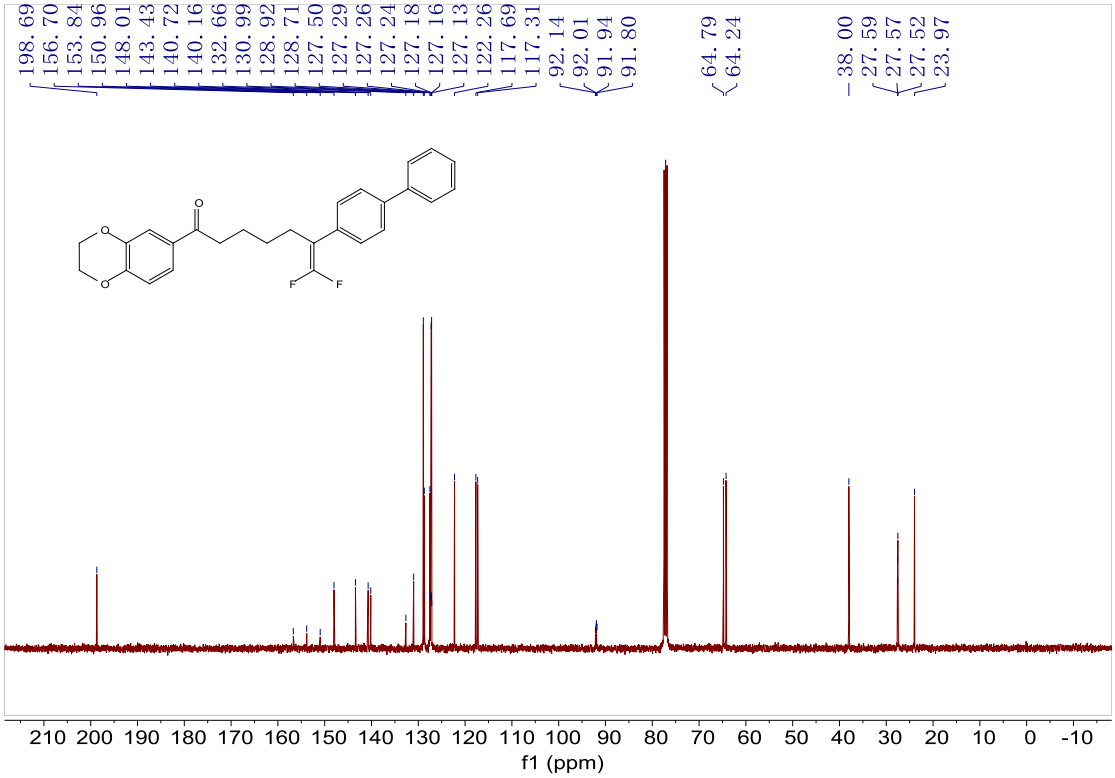

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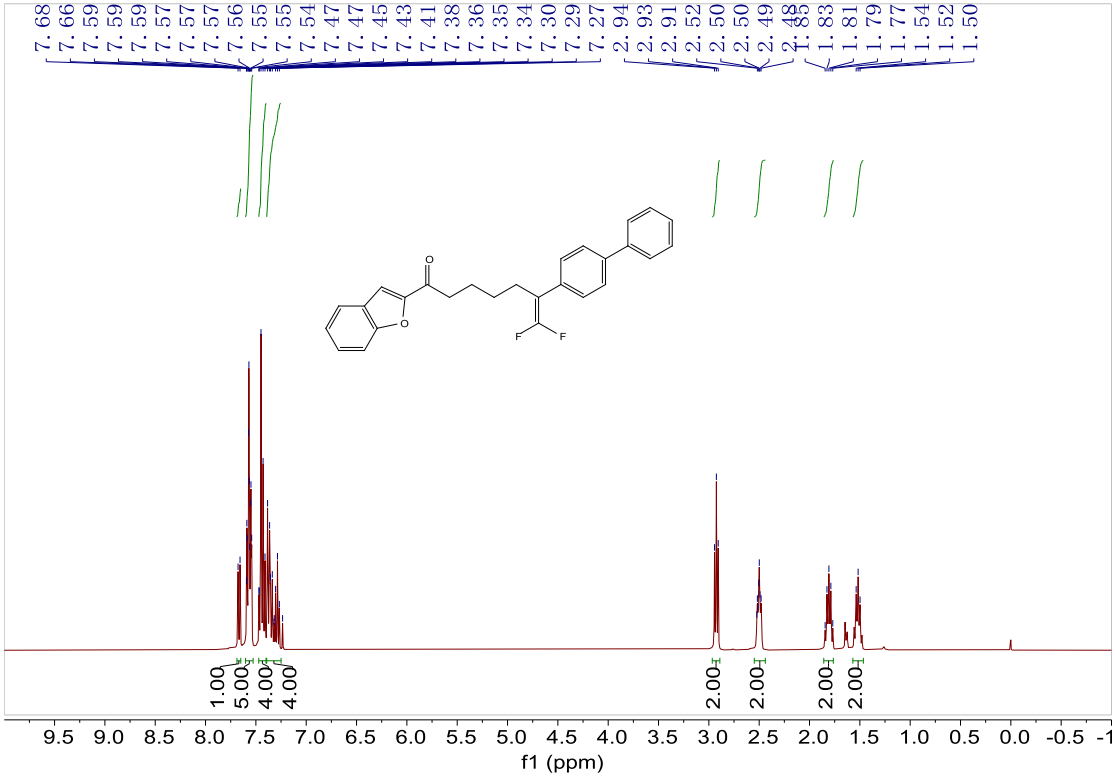

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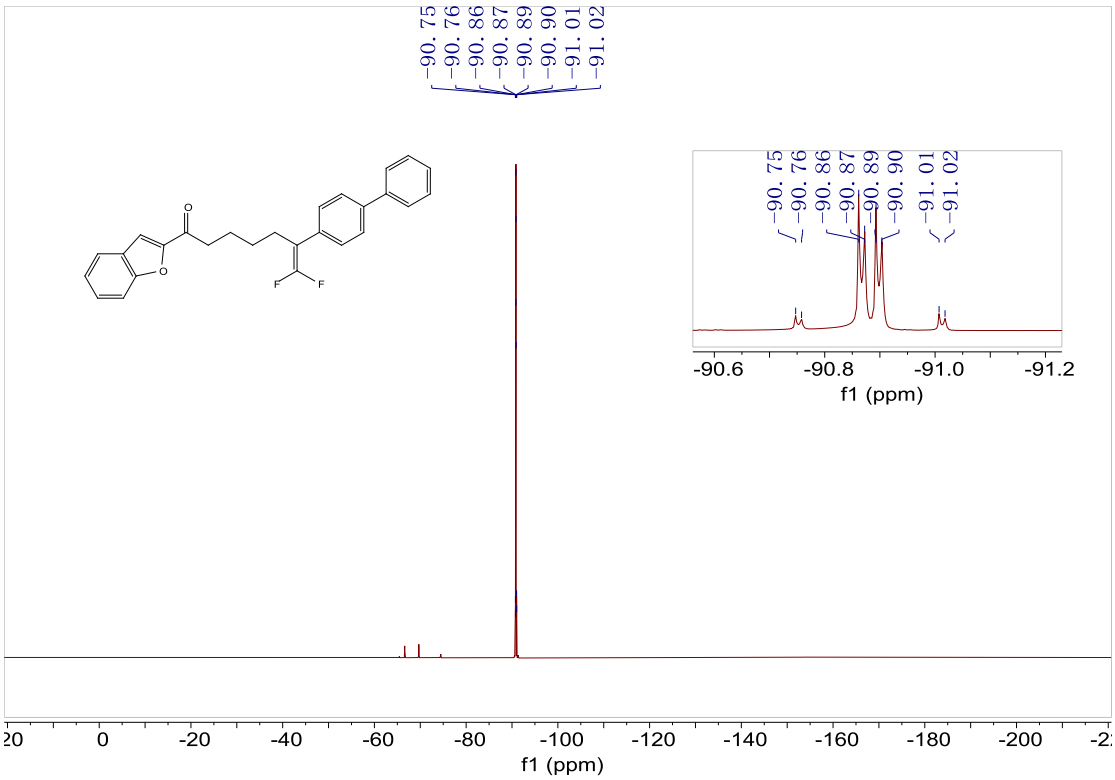

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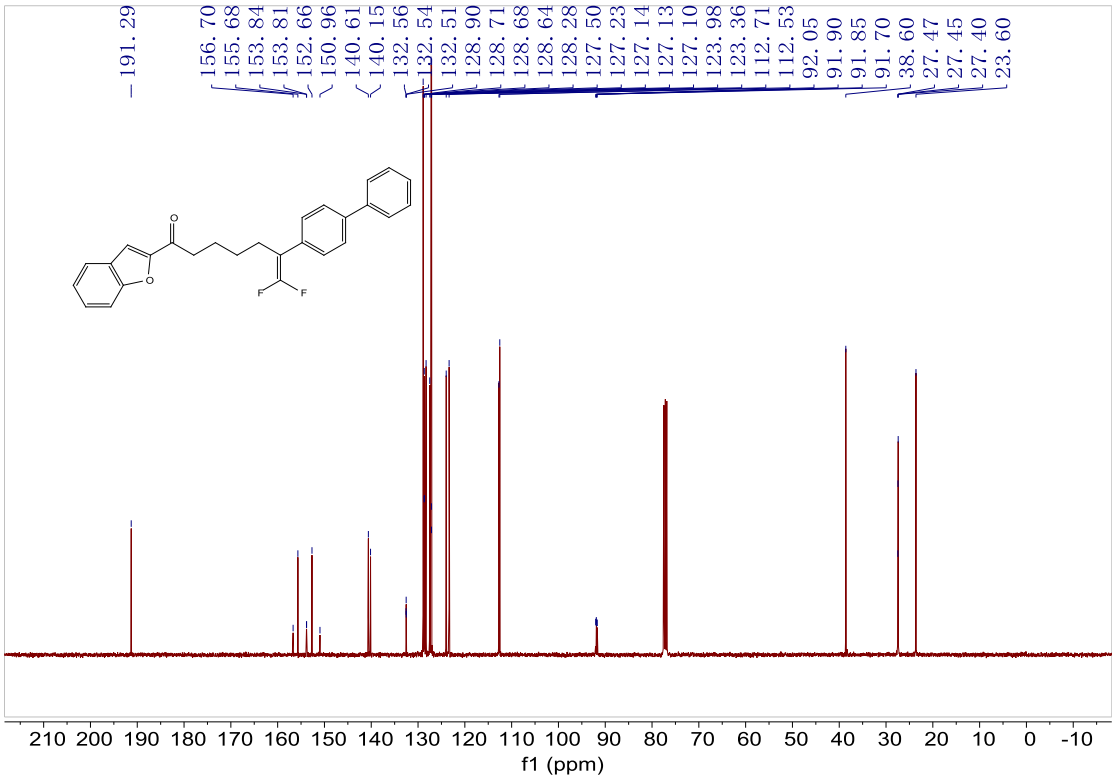

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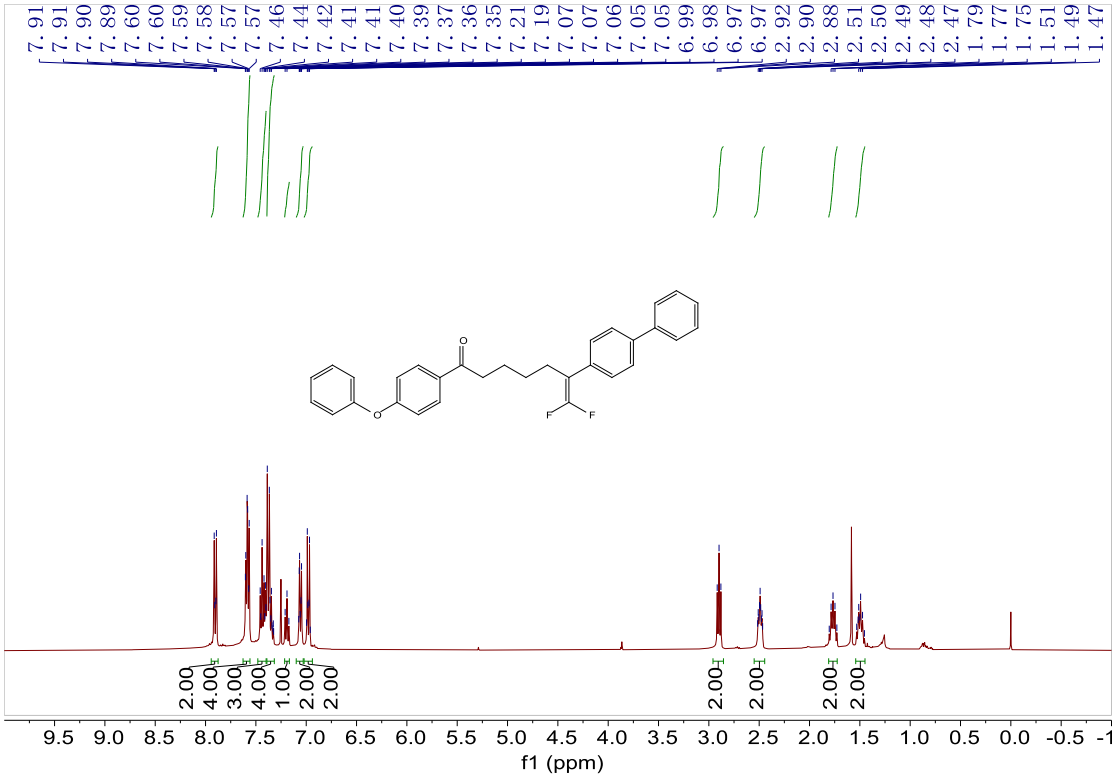

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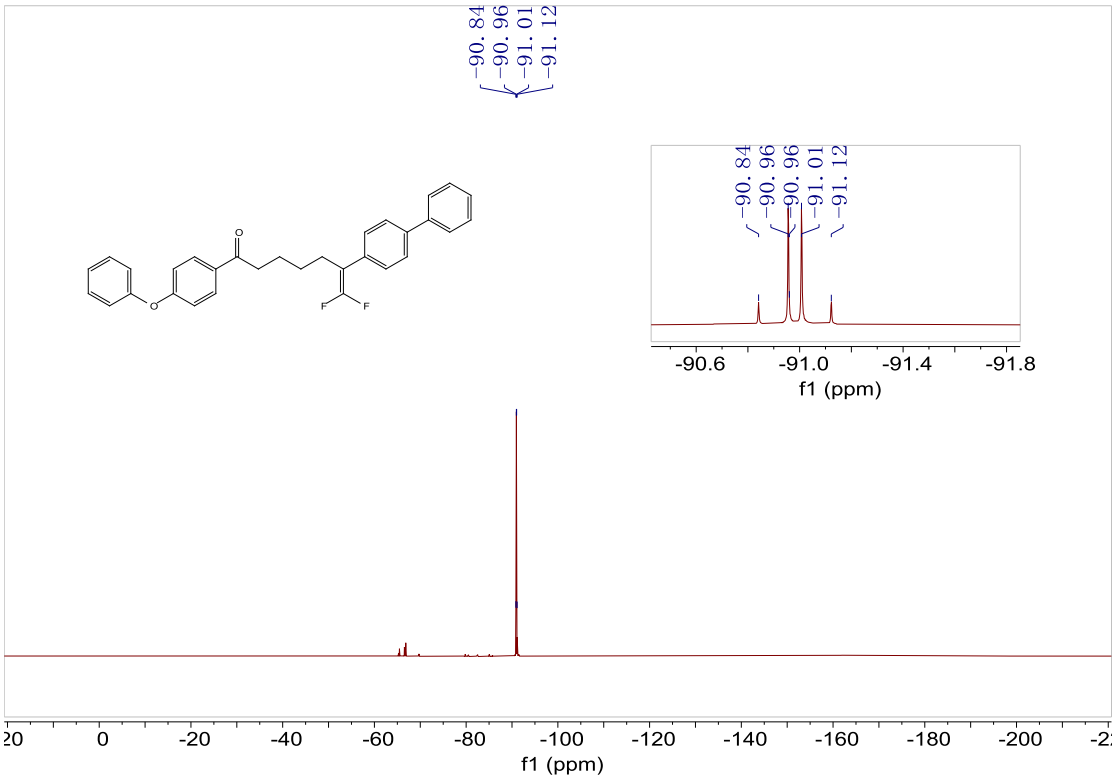

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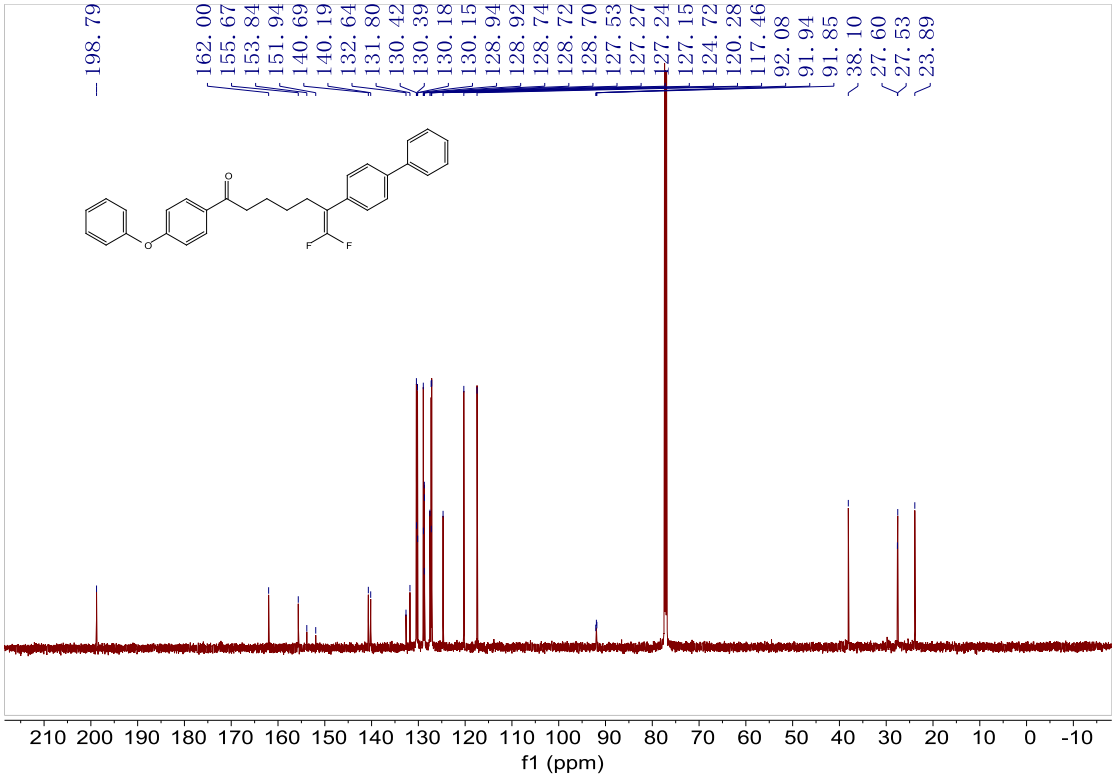

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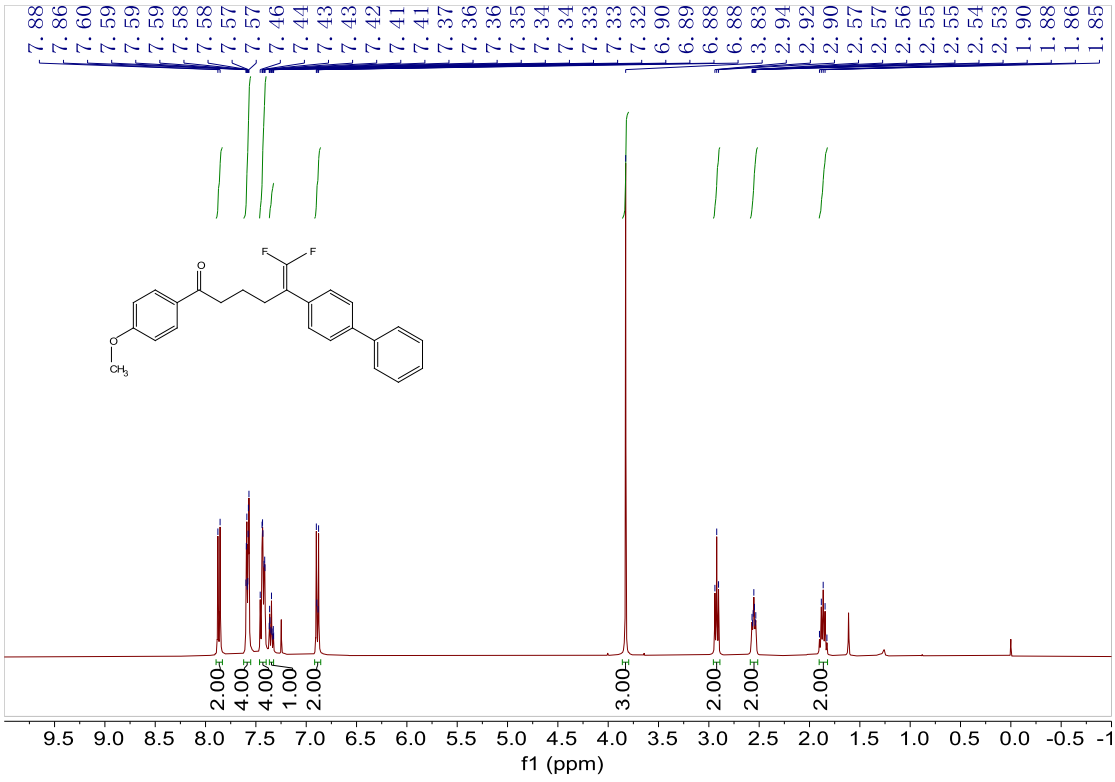

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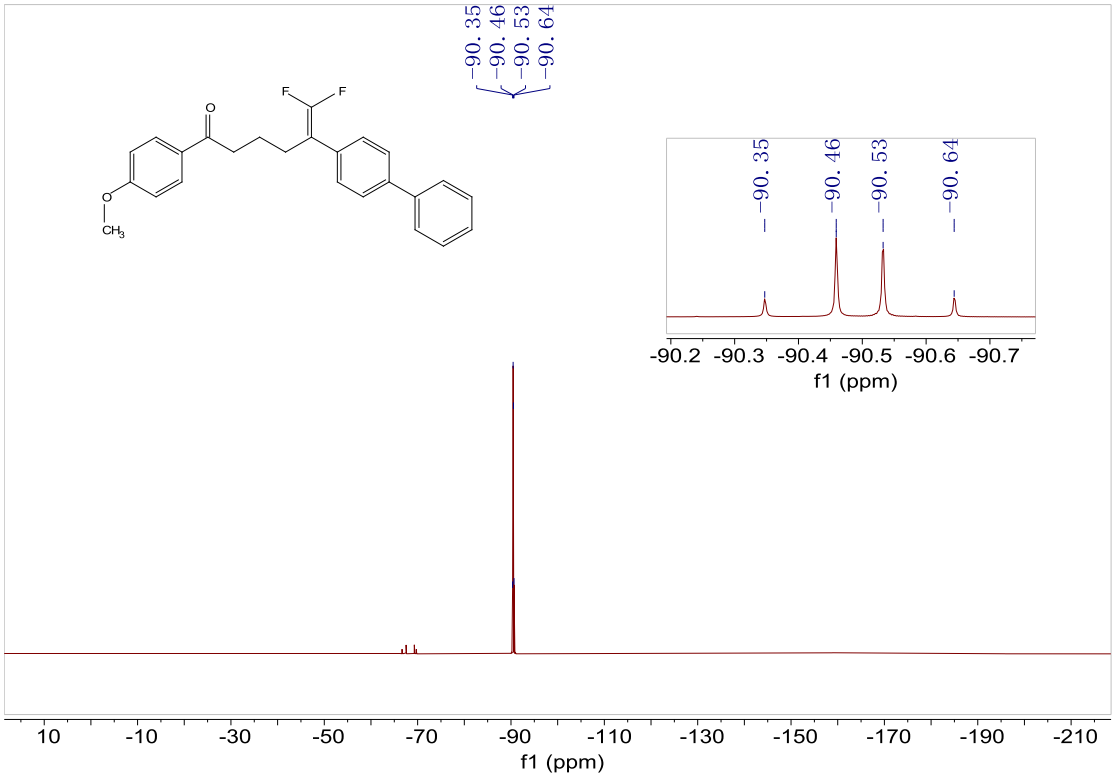

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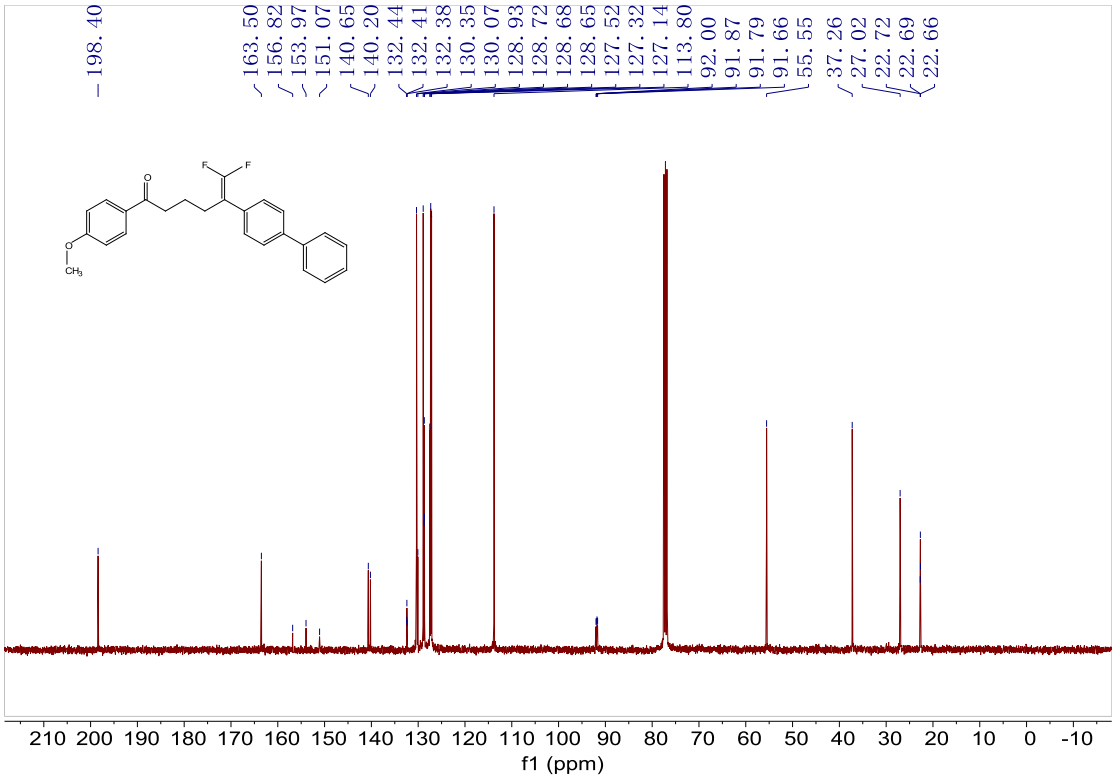
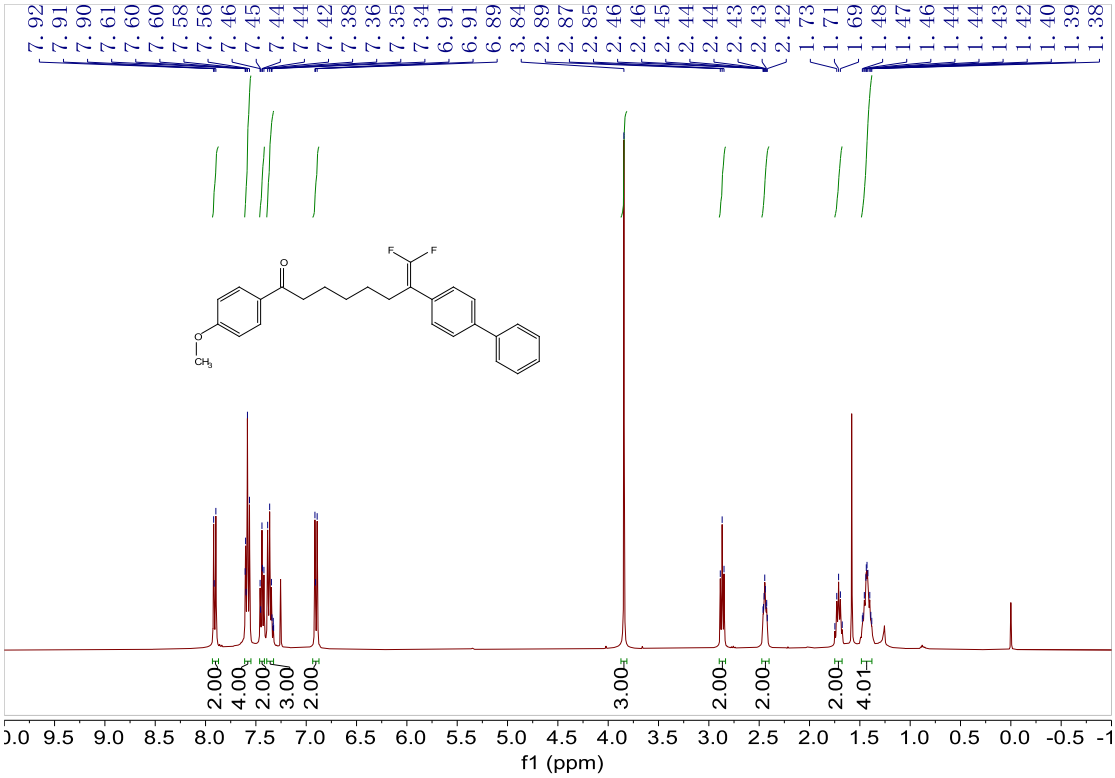
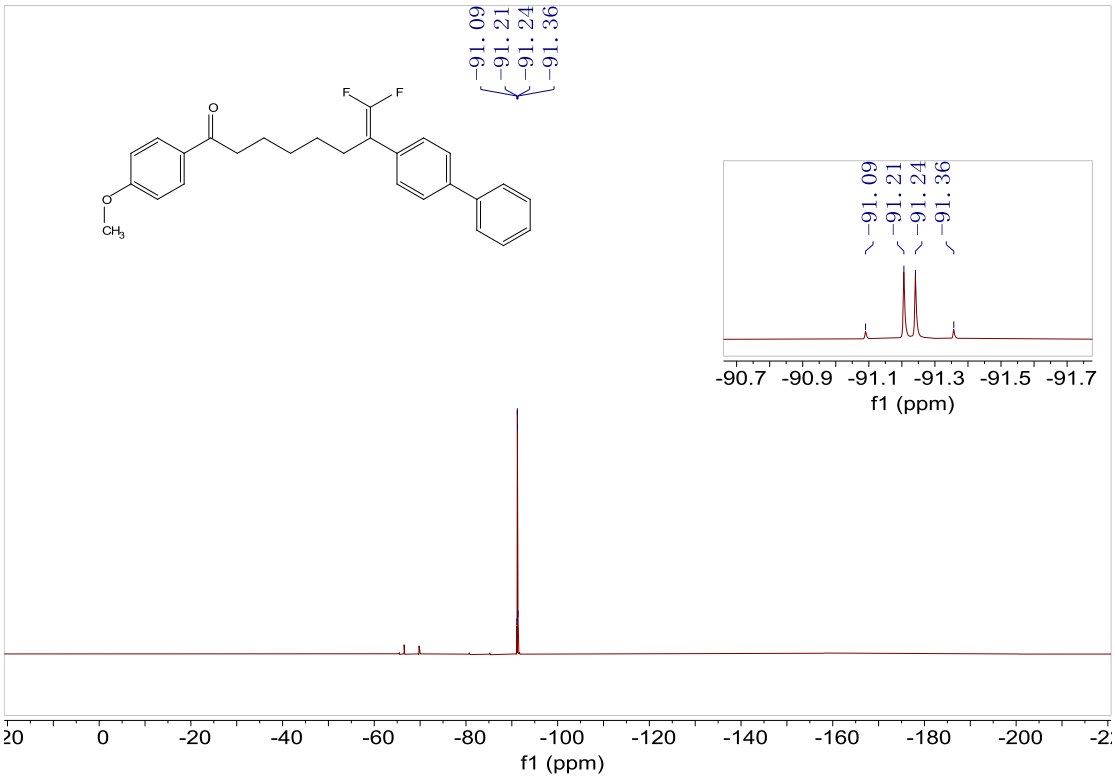


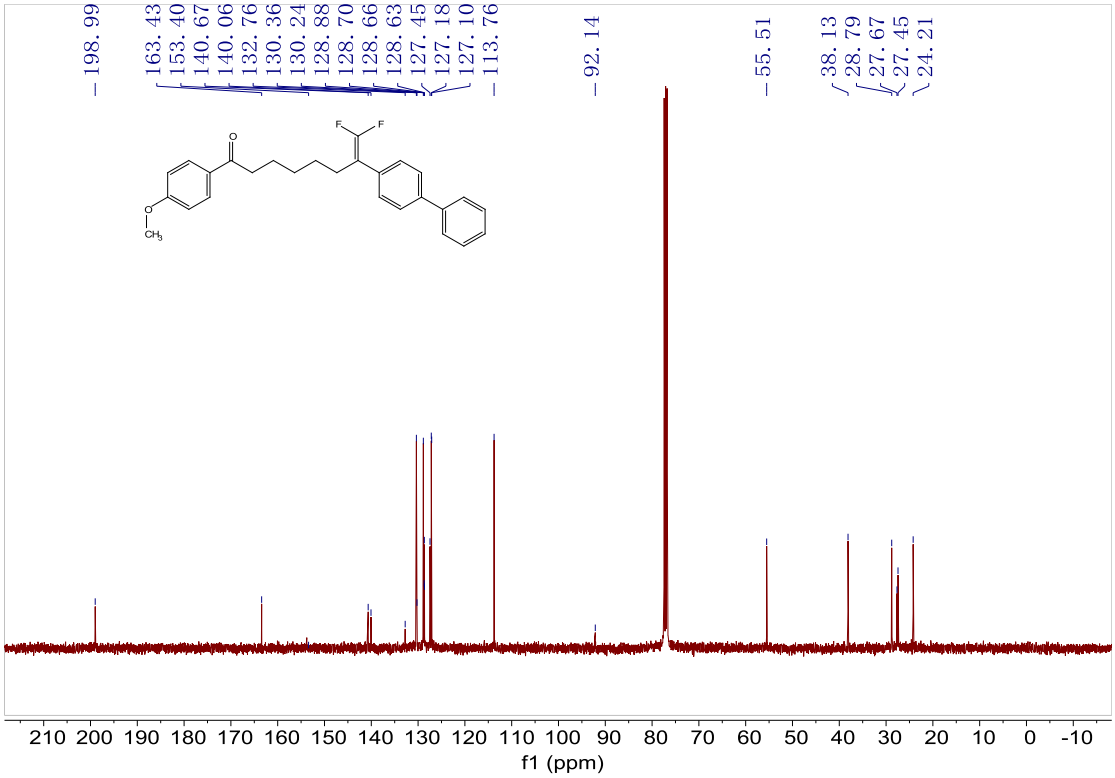
^{13}C NMR of 3ga (100 MHz, $CDCl_3$)



^{1}H NMR of 3ha (400 MHz, $CDCl_3$)



^{19}F NMR of 3ha (376 MHz, $CDCl_3$)



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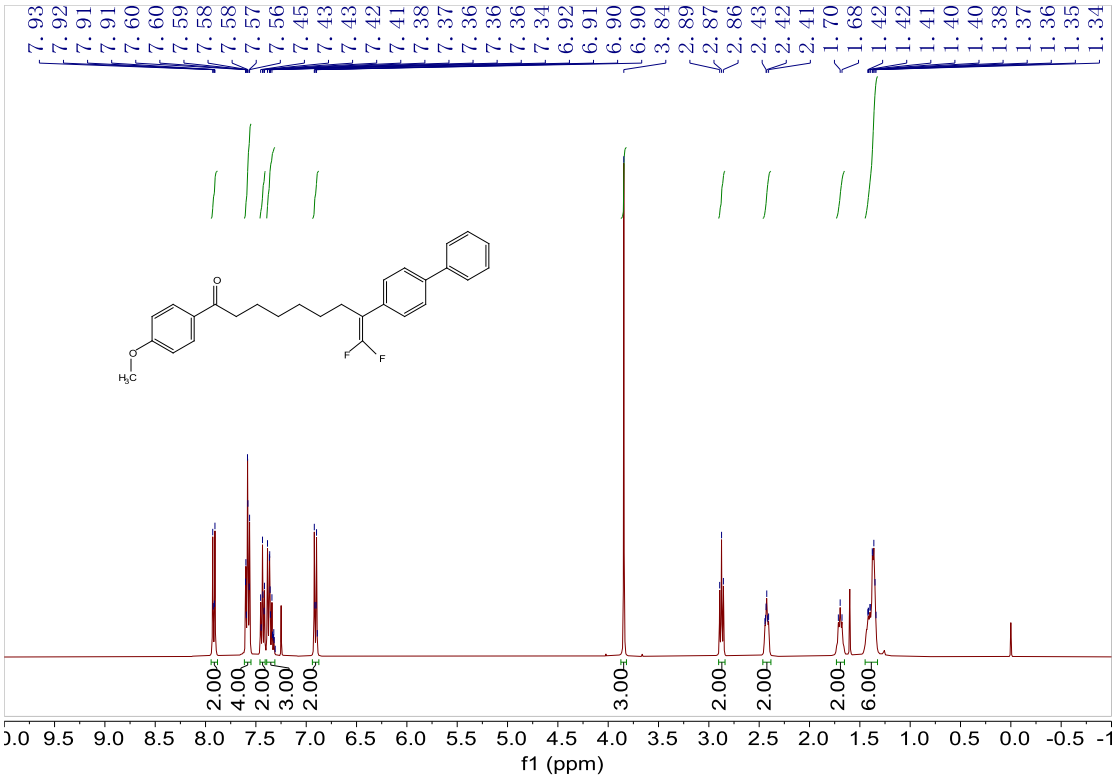
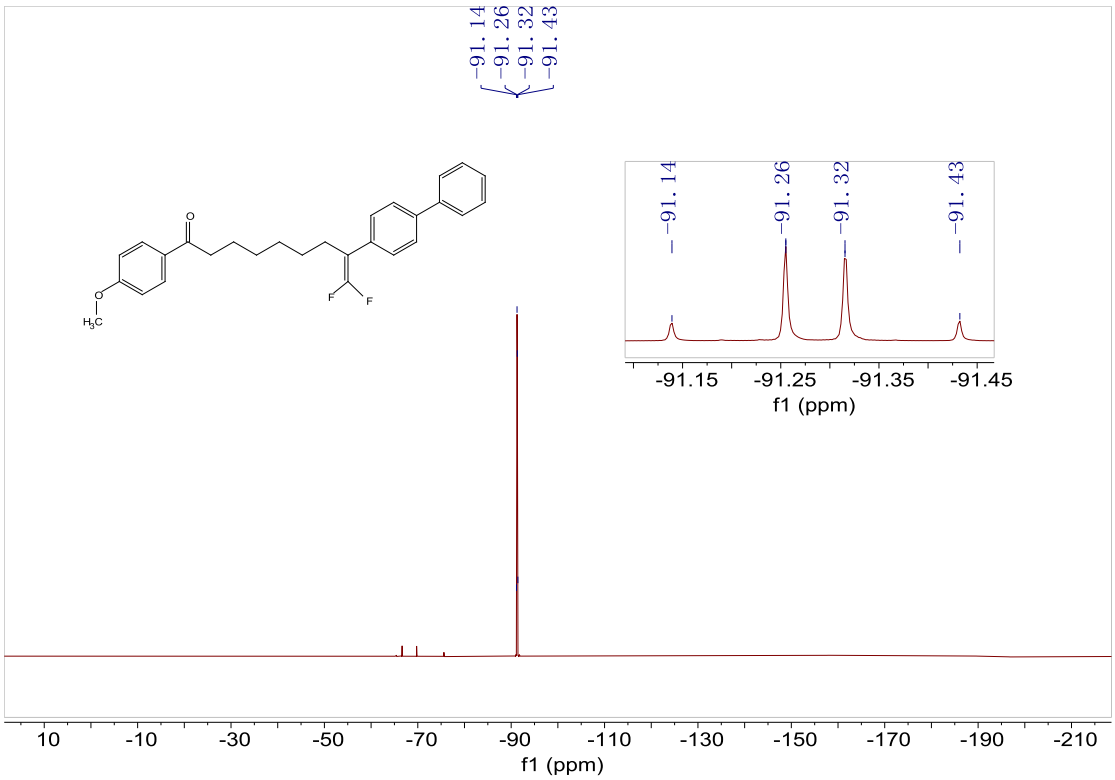
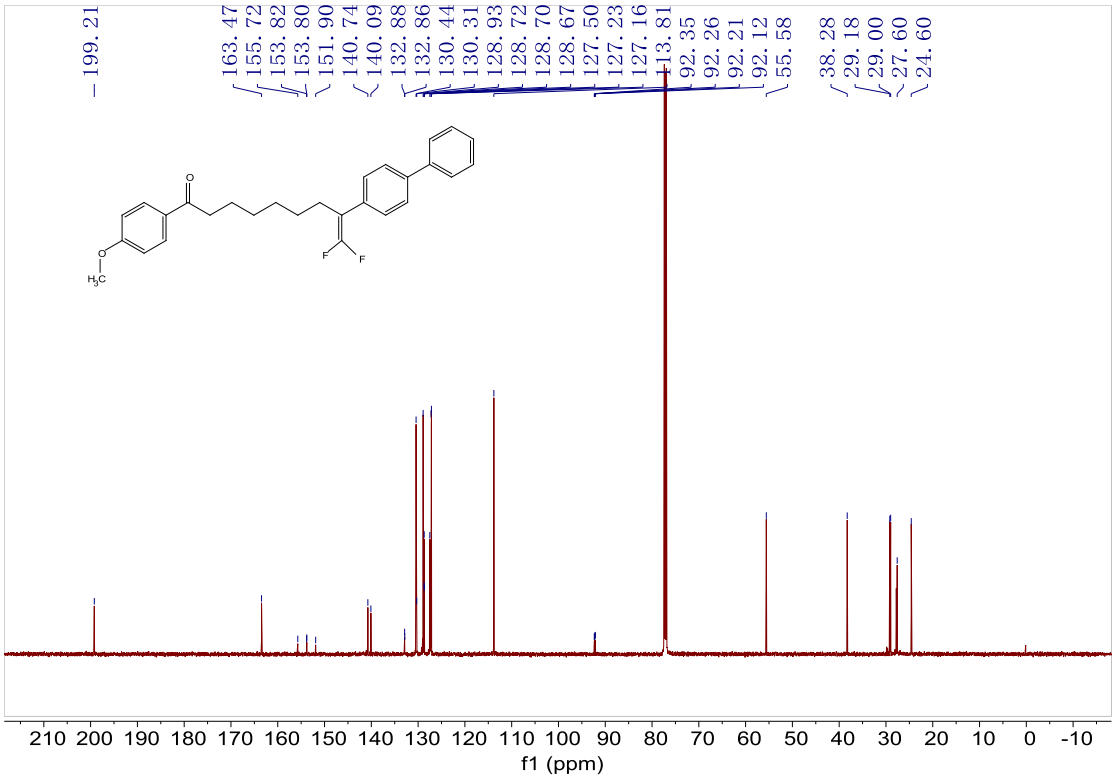


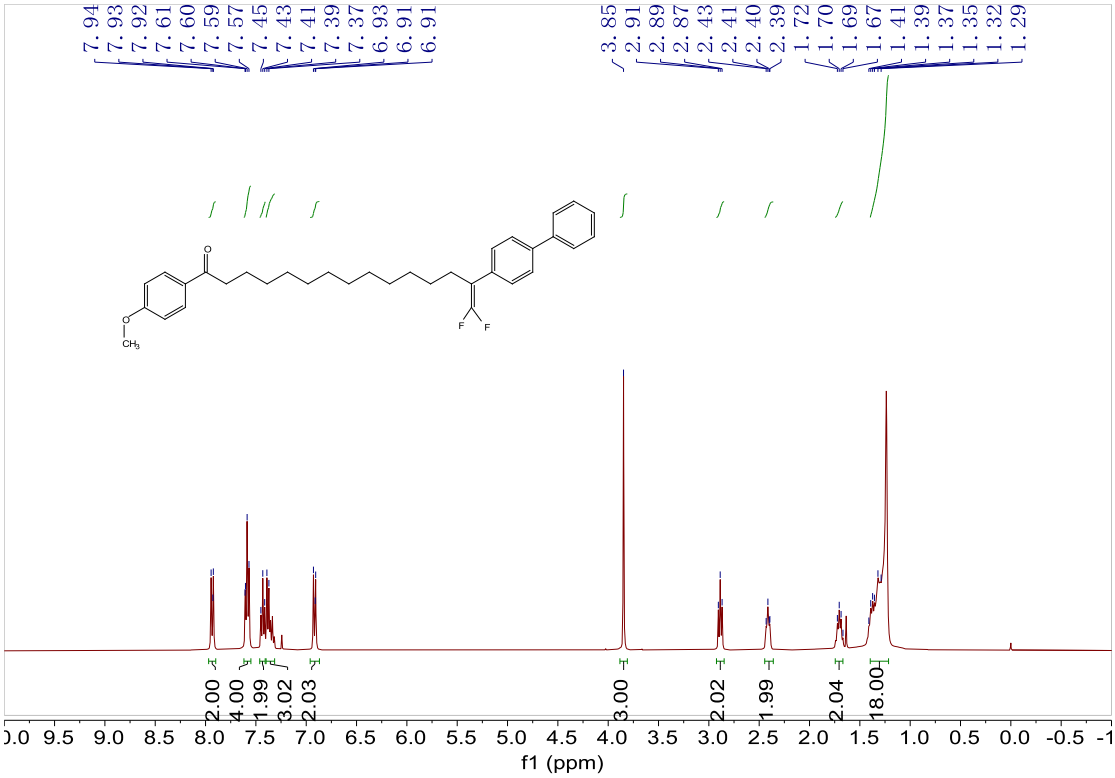
^{1}H NMR of 3ia (400 MHz, $CDCl_3$)



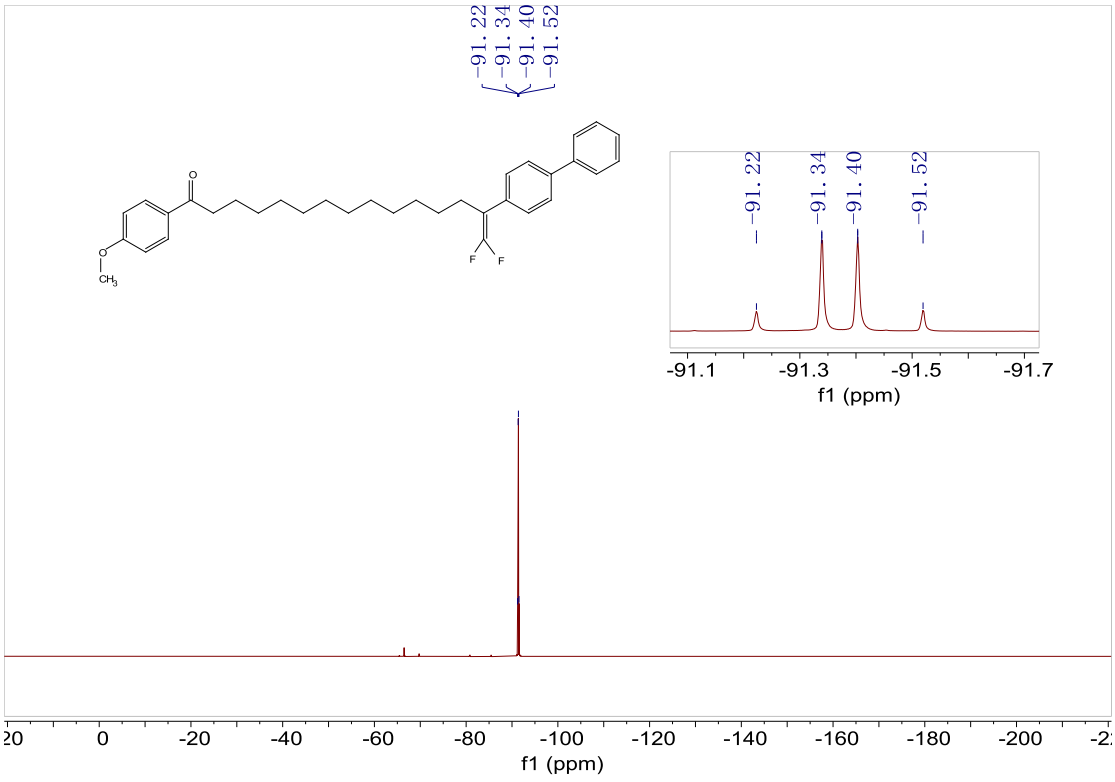
^{19}F NMR of 3ia (376 MHz, $CDCl_3$)



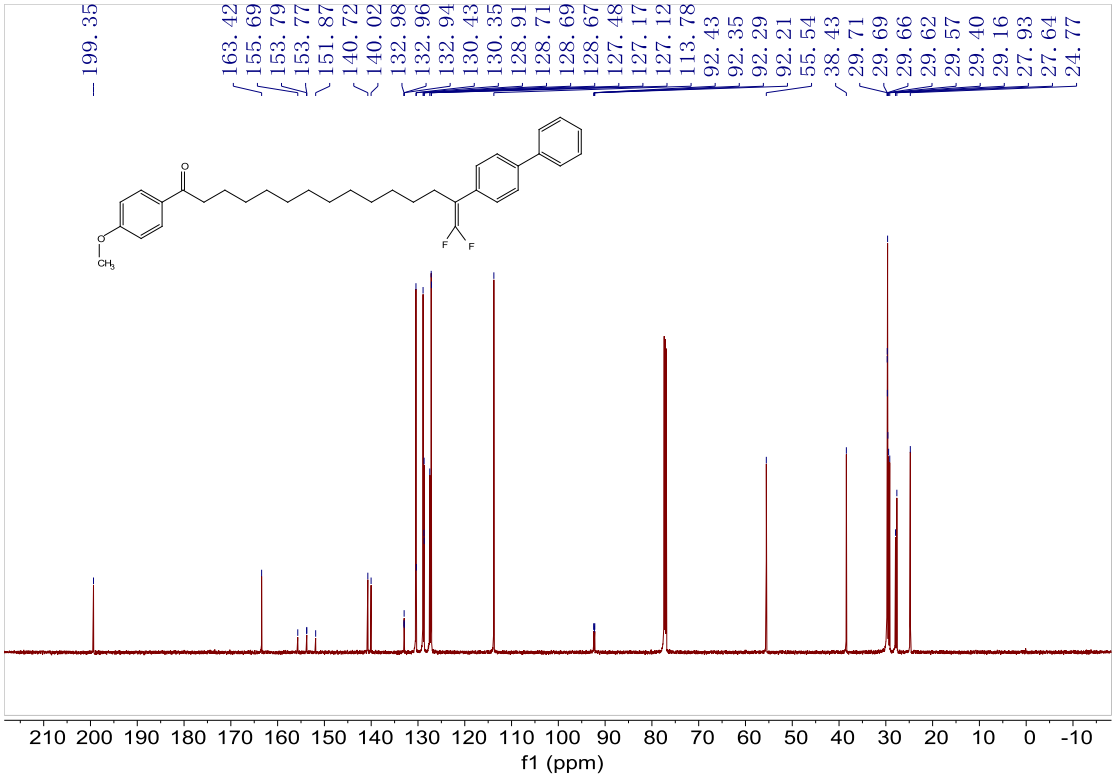
^{13}C NMR of 3ia (150 MHz, $CDCl_3$)



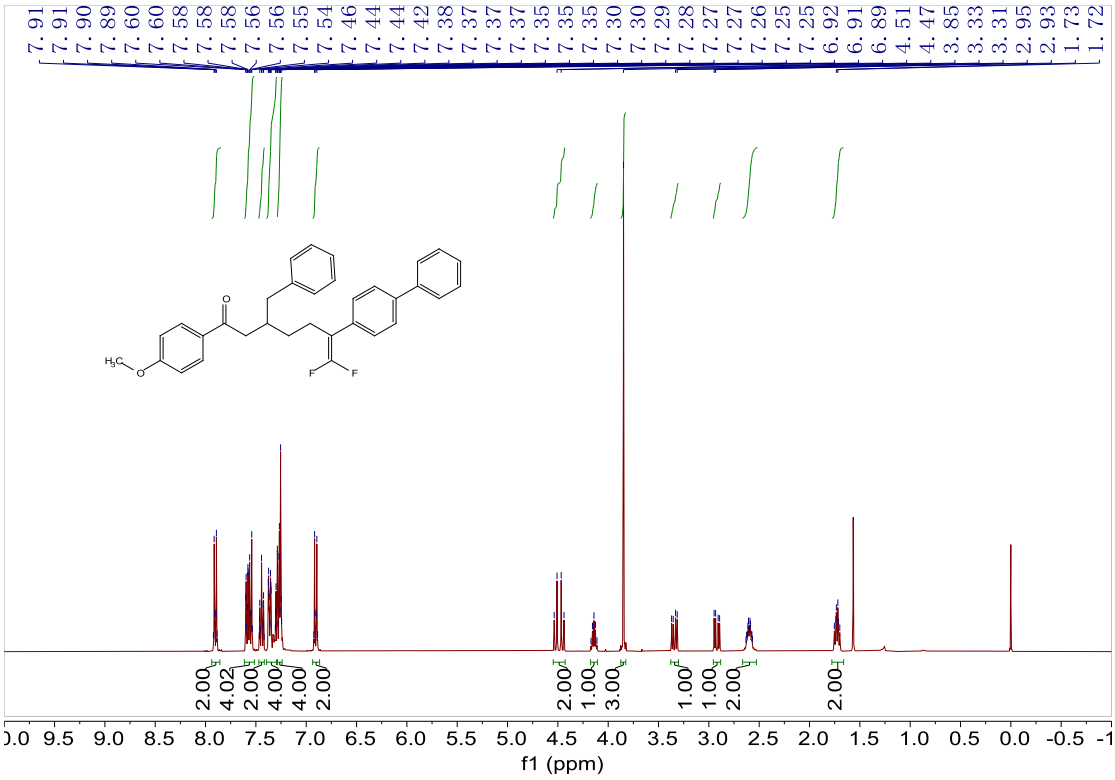
^{1}H NMR of 3ja (400 MHz, $CDCl_3$)



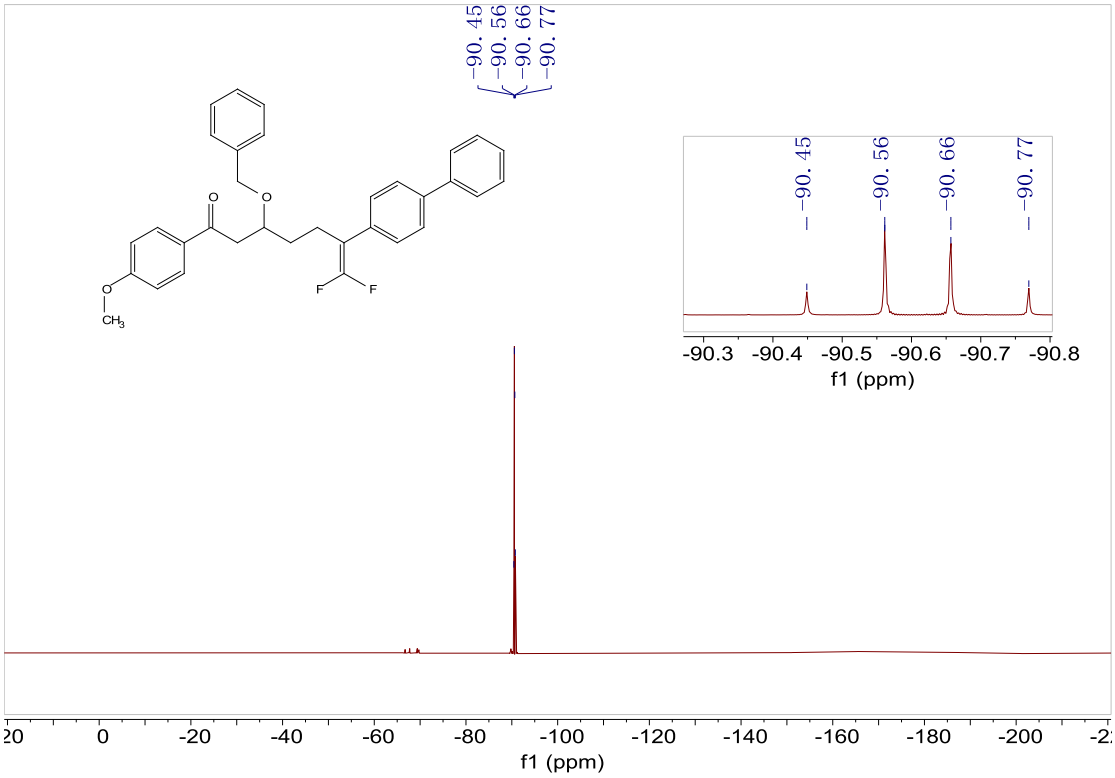
^{19}F NMR of 3ja (376 MHz, $CDCl_3$)



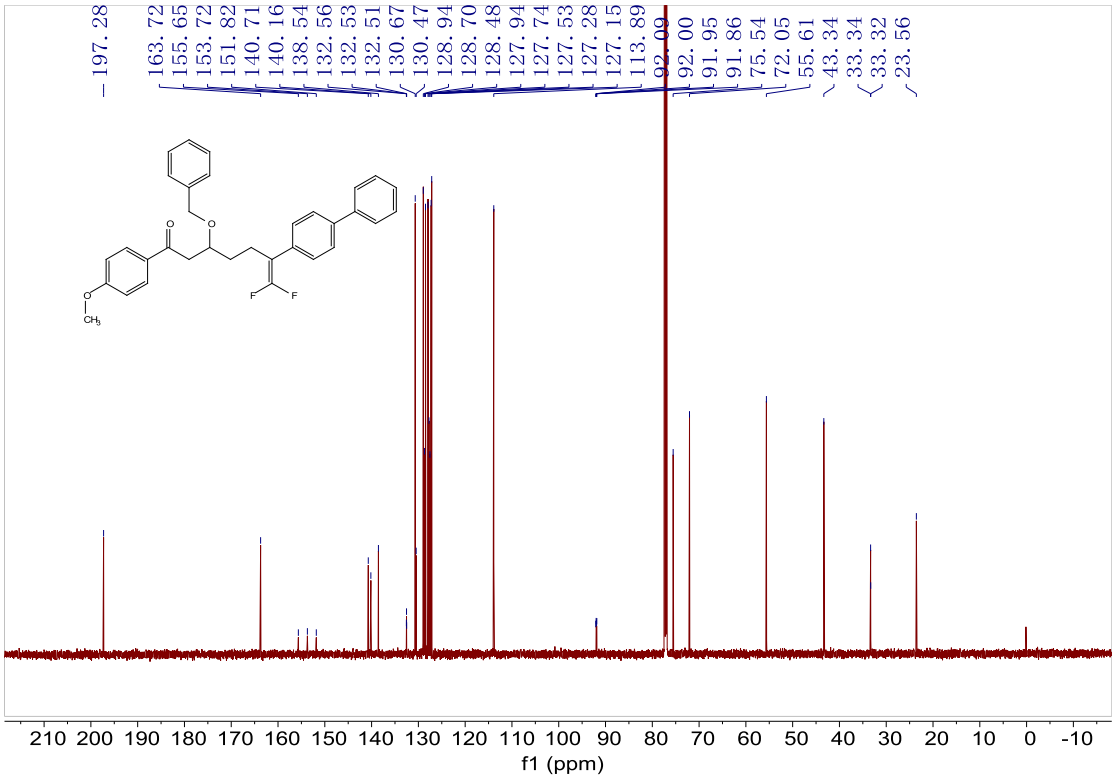
^{13}C NMR of 3ja (150 MHz, $CDCl_3$)



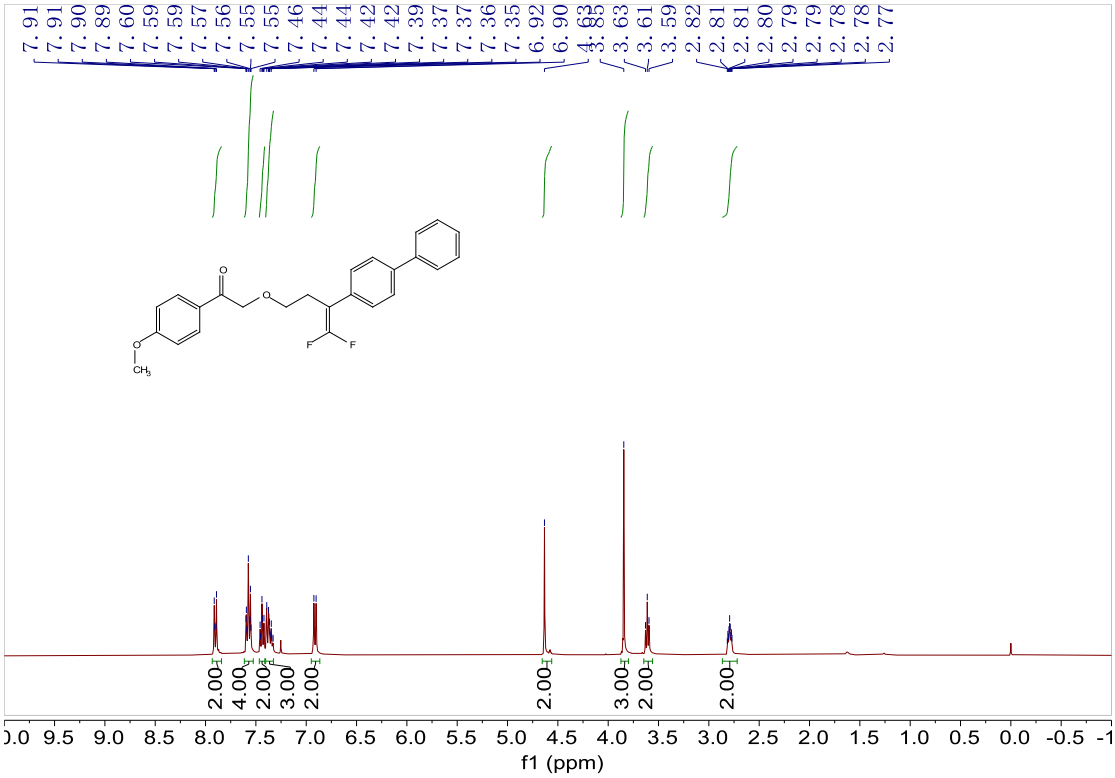
^{1}H NMR of 3ka (400 MHz, $CDCl_3$)



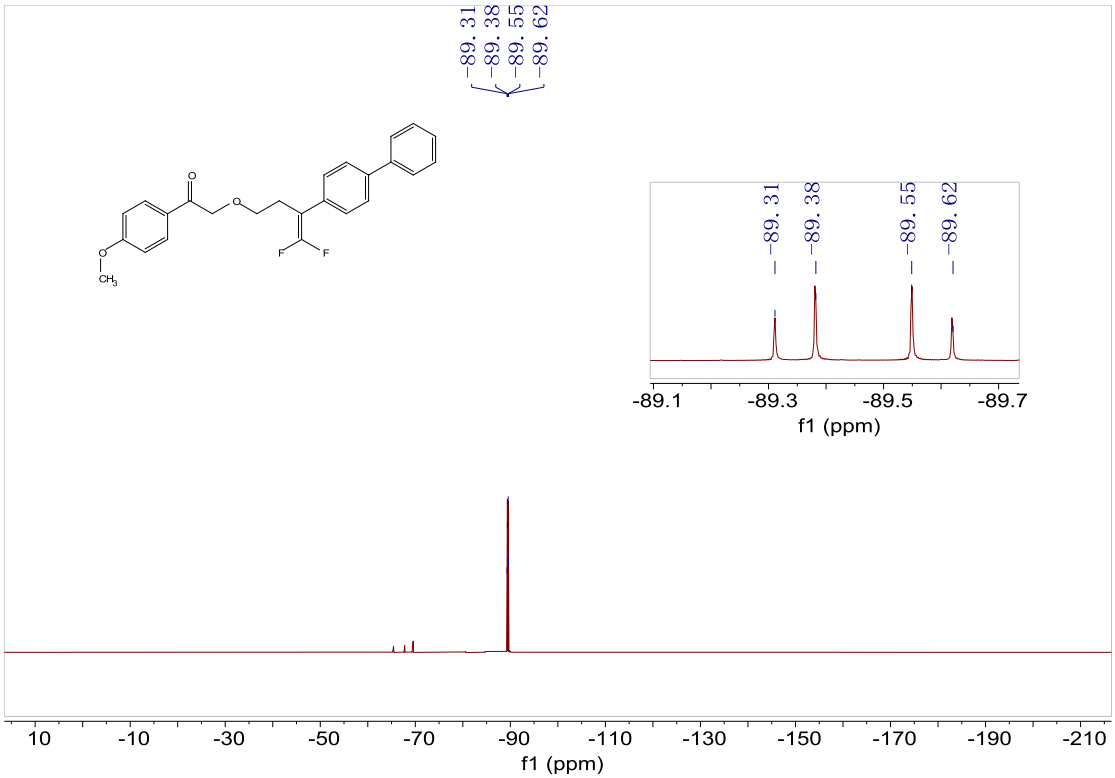
^{19}F NMR of 3ka (376 MHz, $CDCl_3$)



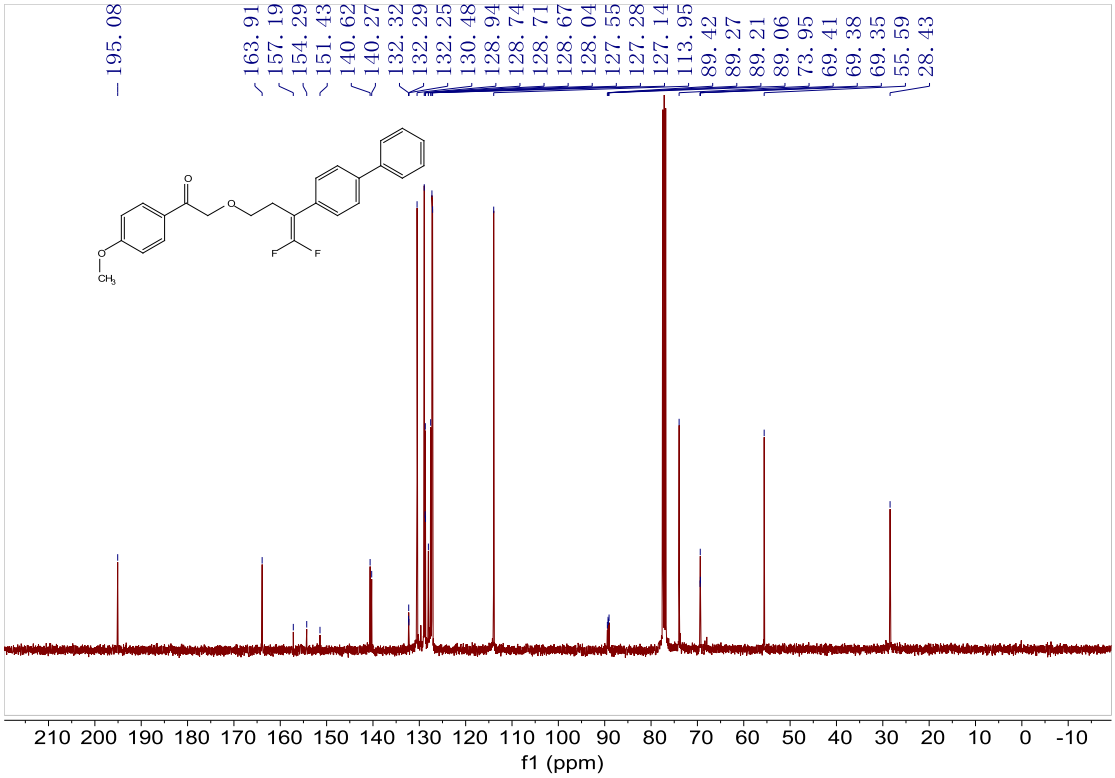
^{13}C NMR of 3ka (150 MHz, $CDCl_3$)



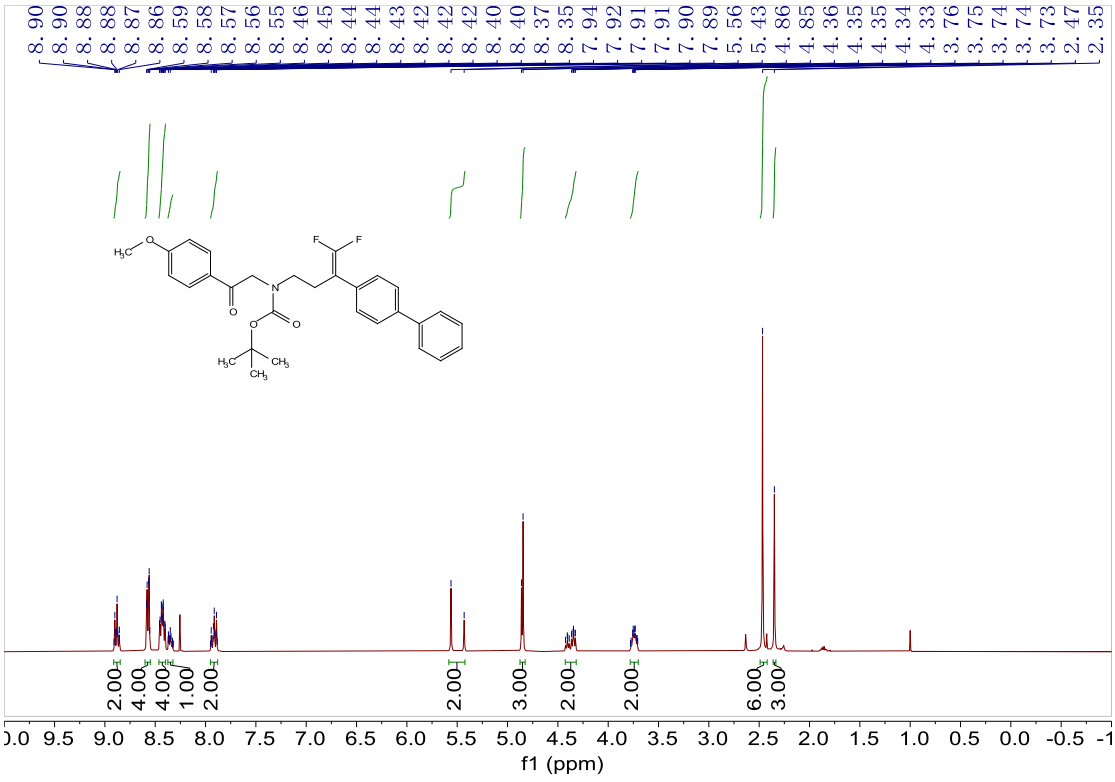
^{1}H NMR of 3la (400 MHz, $CDCl_3$)



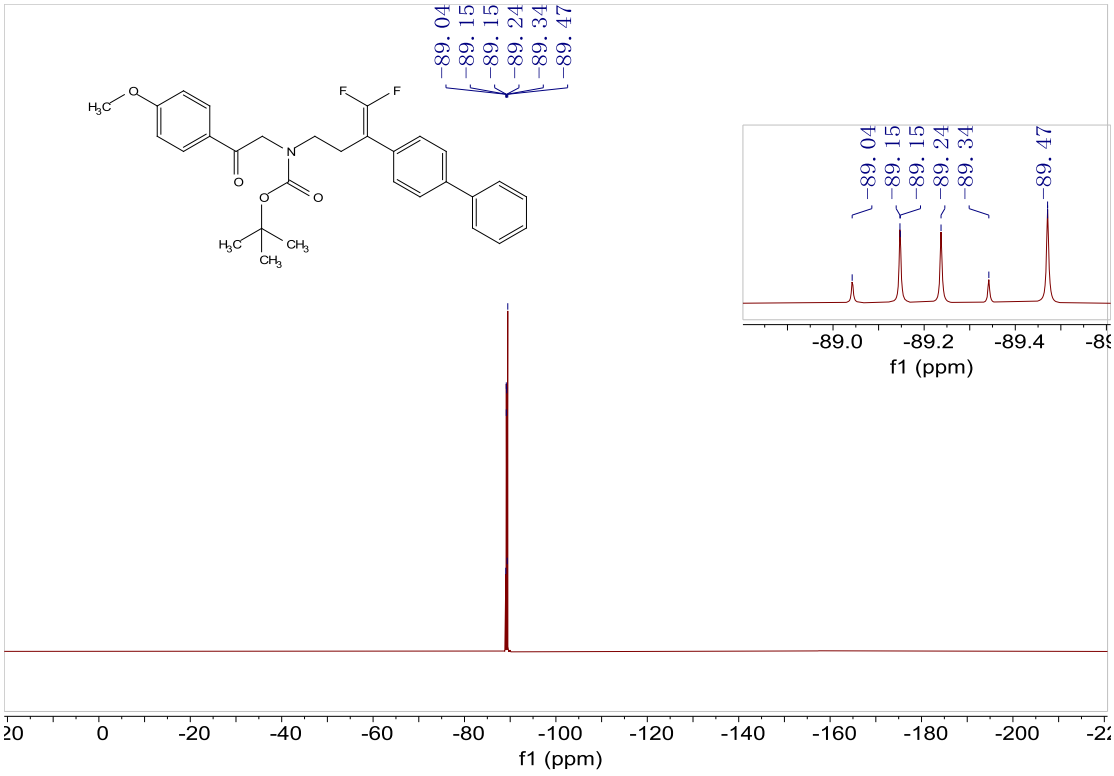
^{19}F NMR of 3la (564 MHz, $CDCl_3$)



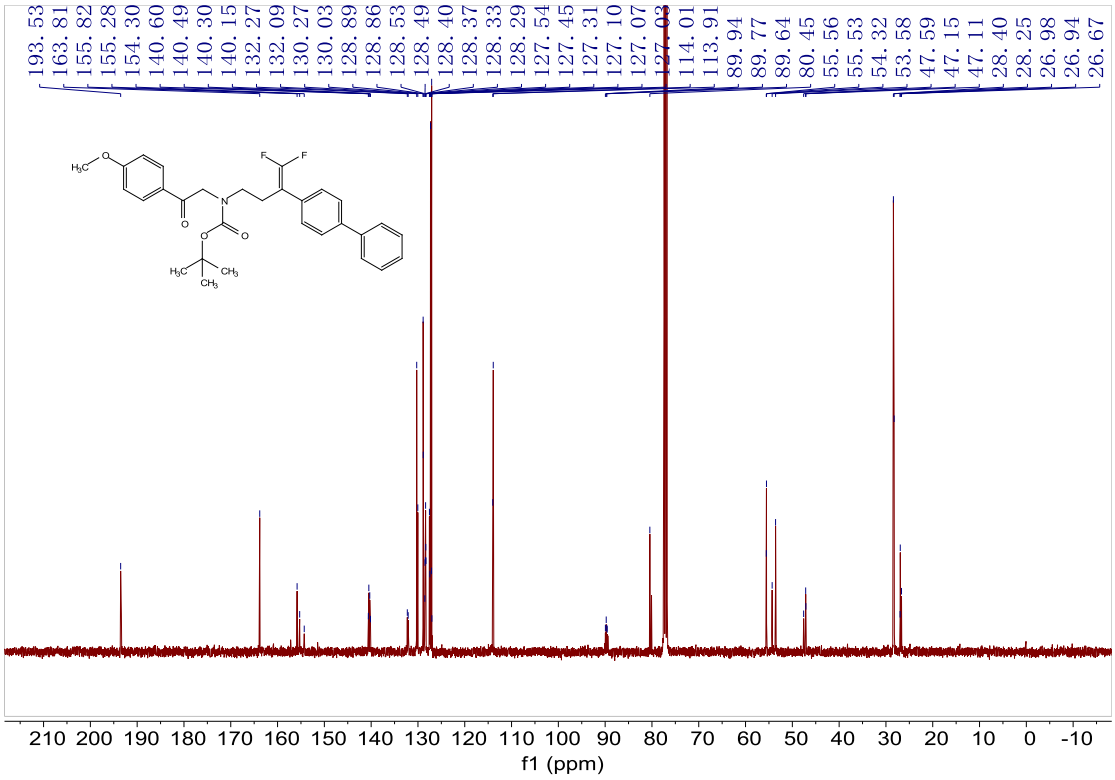
^{13}C NMR of 3la (100 MHz, $CDCl_3$)



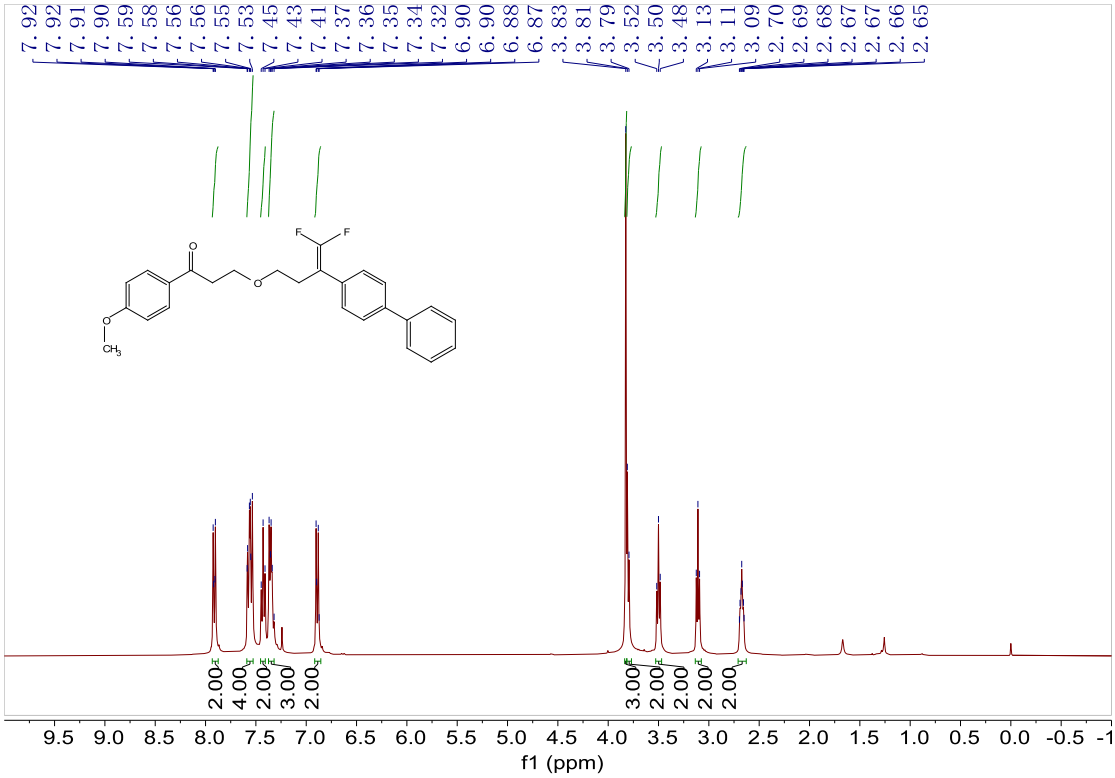
^{1}H NMR of 3ma (400 MHz, $CDCl_3$)



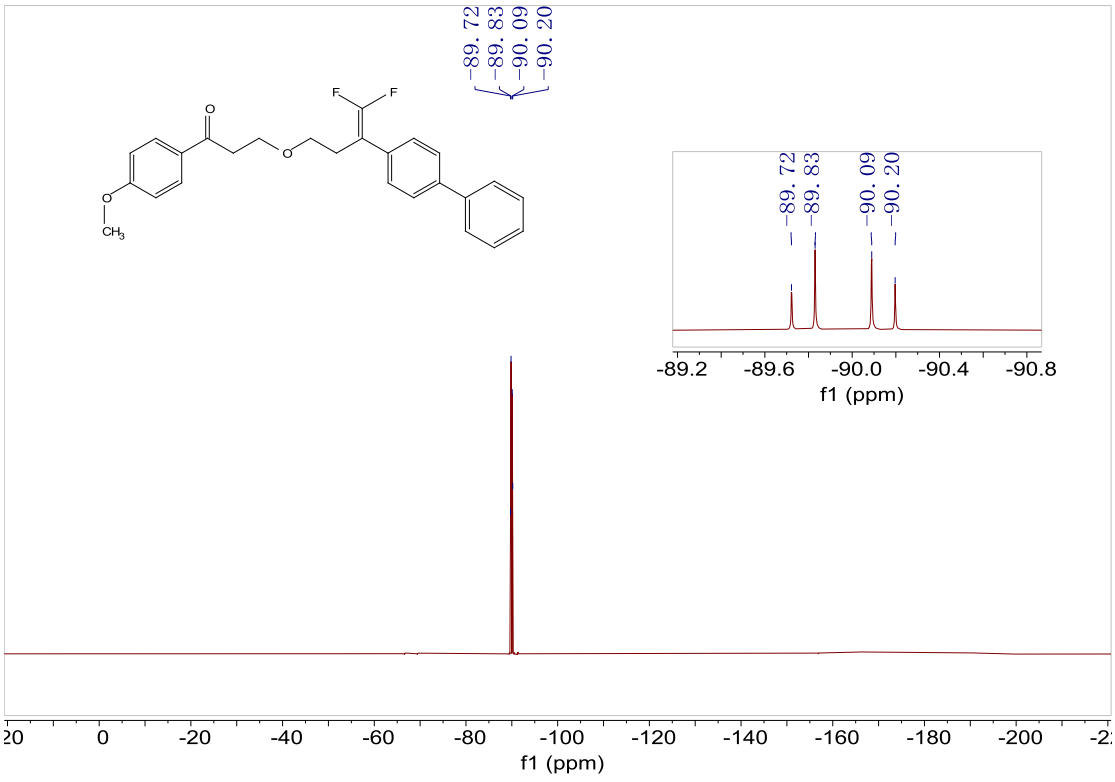
^{19}F NMR of 3ma (376 MHz, $CDCl_3$)



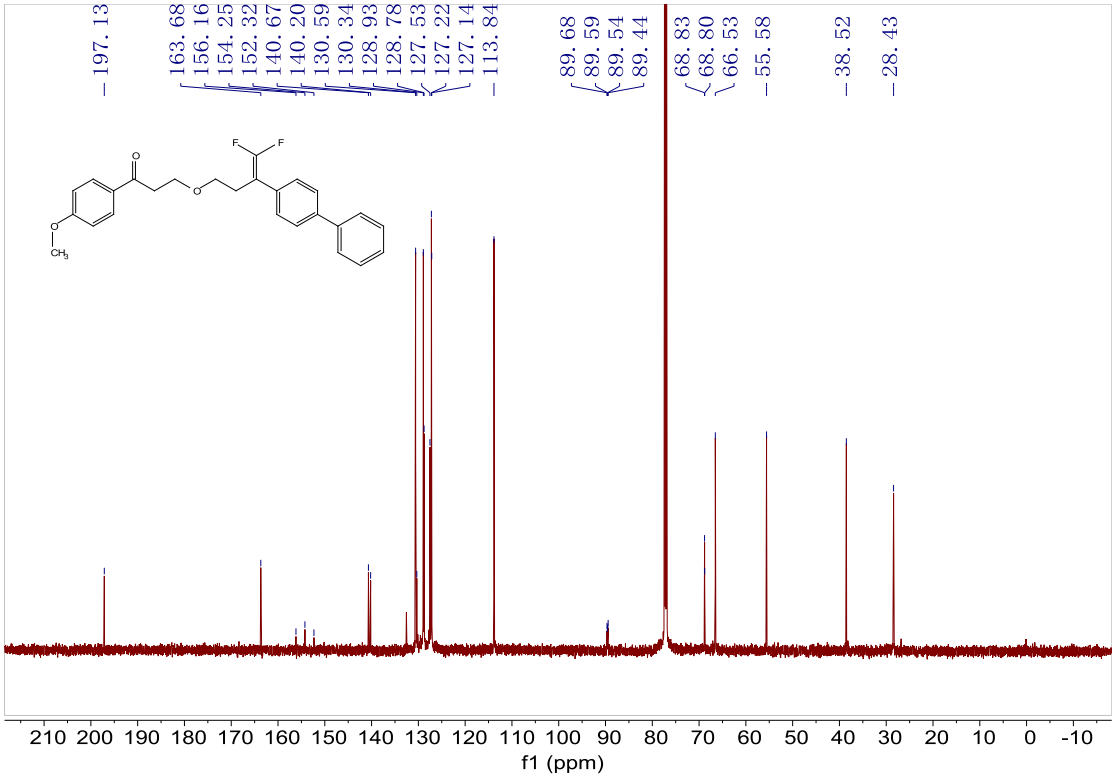
^{13}C NMR of 3ma (100 MHz, $CDCl_3$)



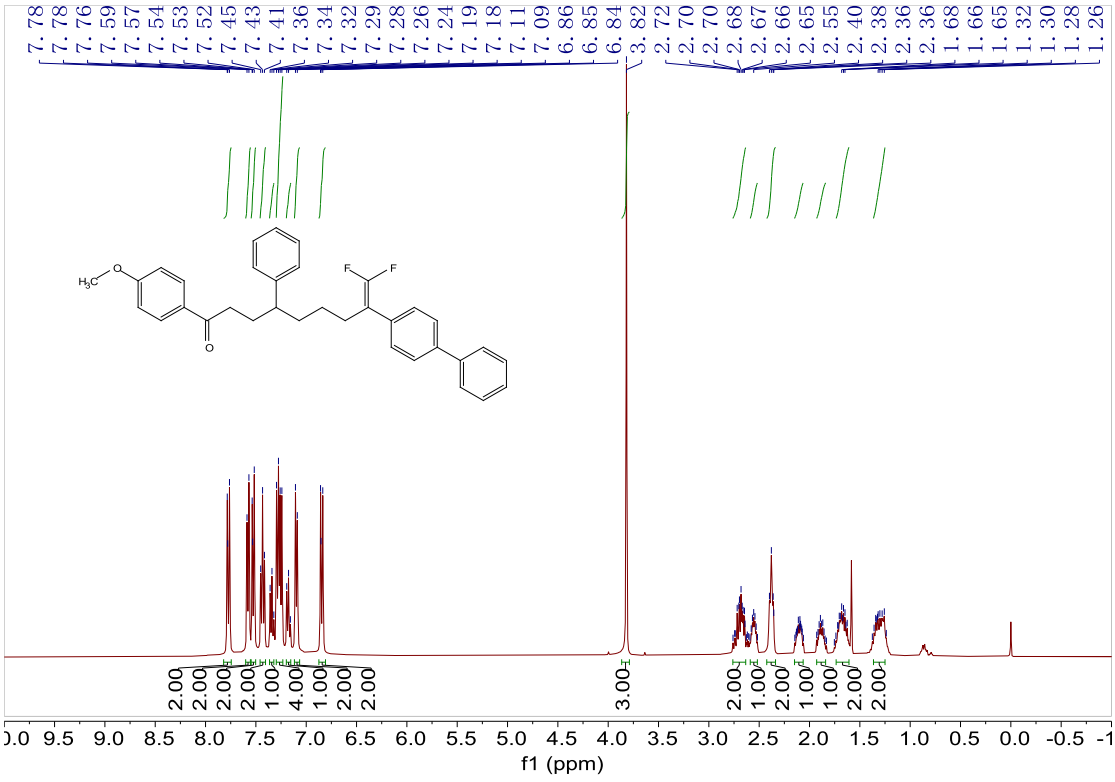
^{1}H NMR of 3na (400 MHz, $CDCl_3$)



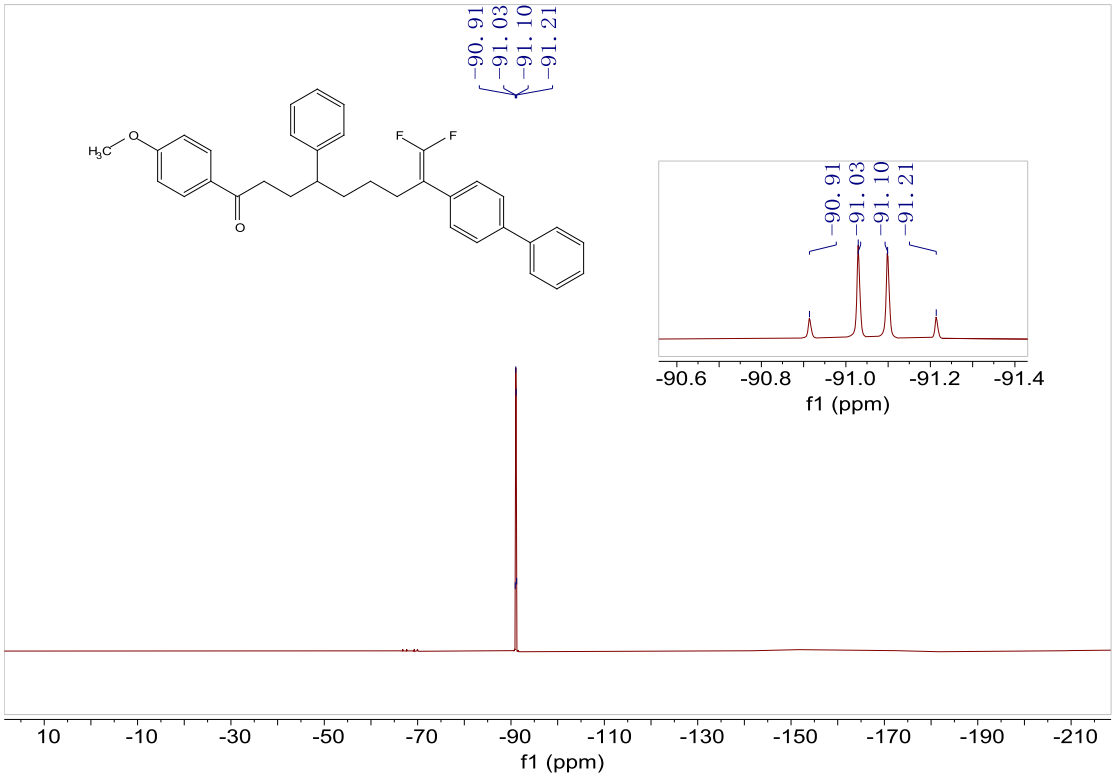
^{19}F NMR of 3na (376 MHz, $CDCl_3$)



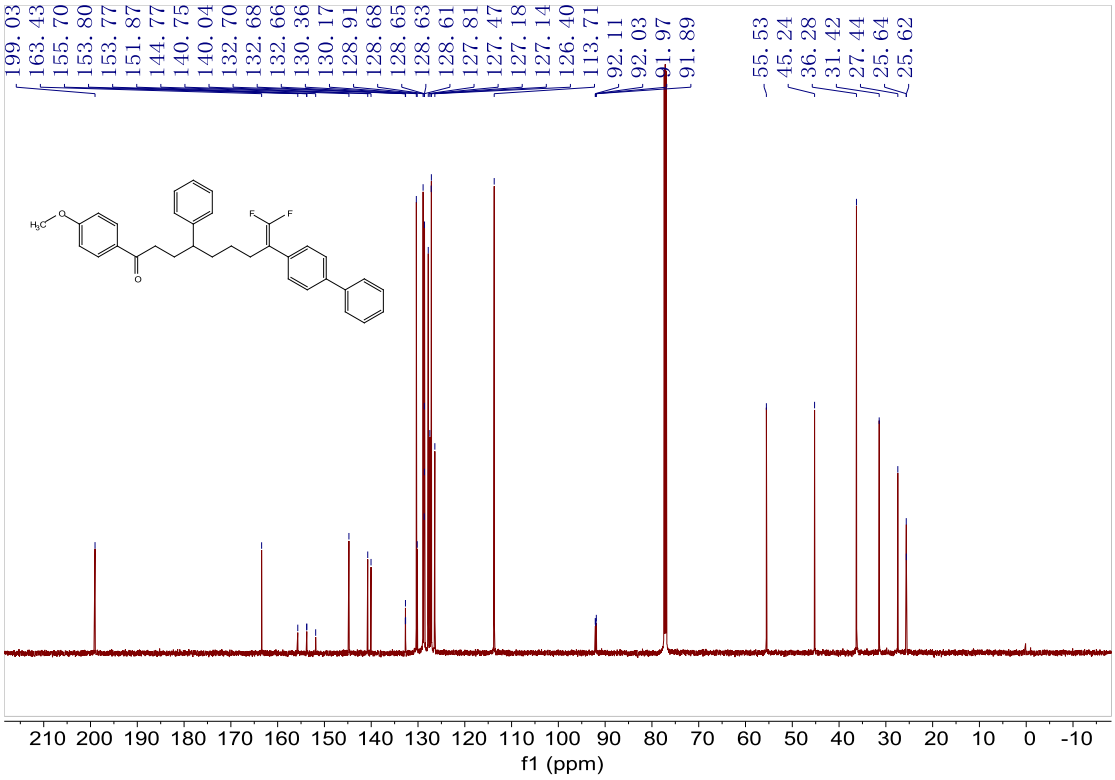
^{13}C NMR of 3na (150 MHz, $CDCl_3$)



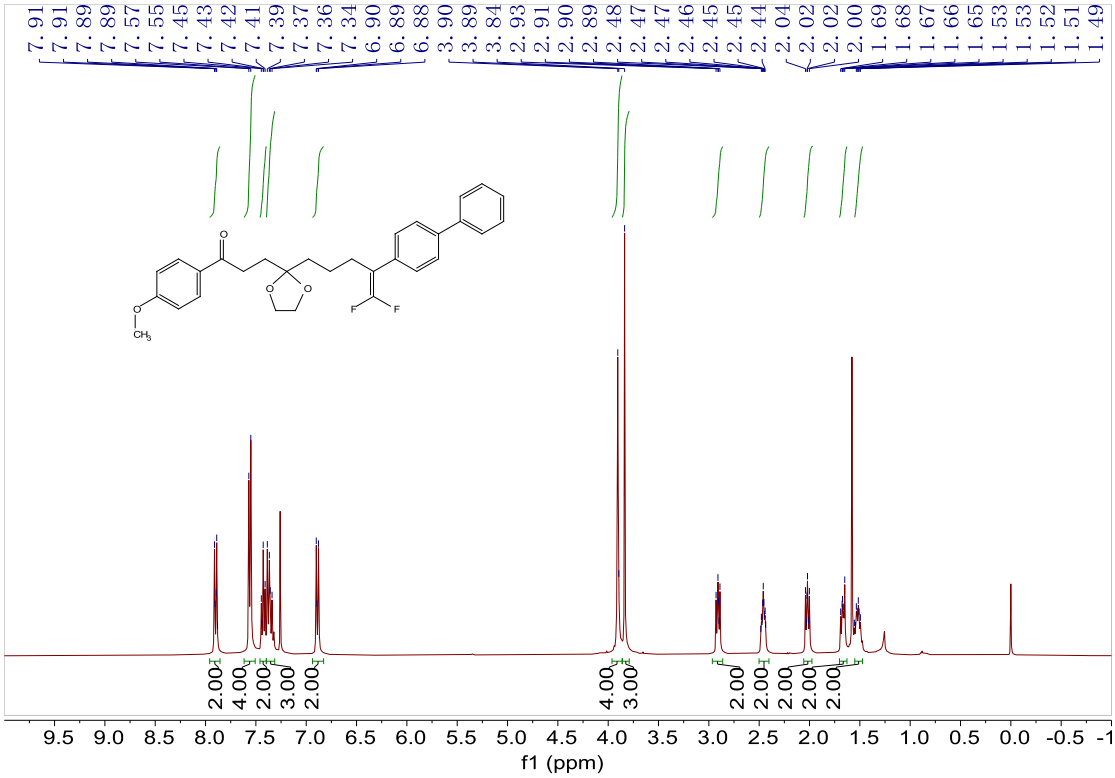
^{1}H NMR of 3oa (400 MHz, $CDCl_3$)



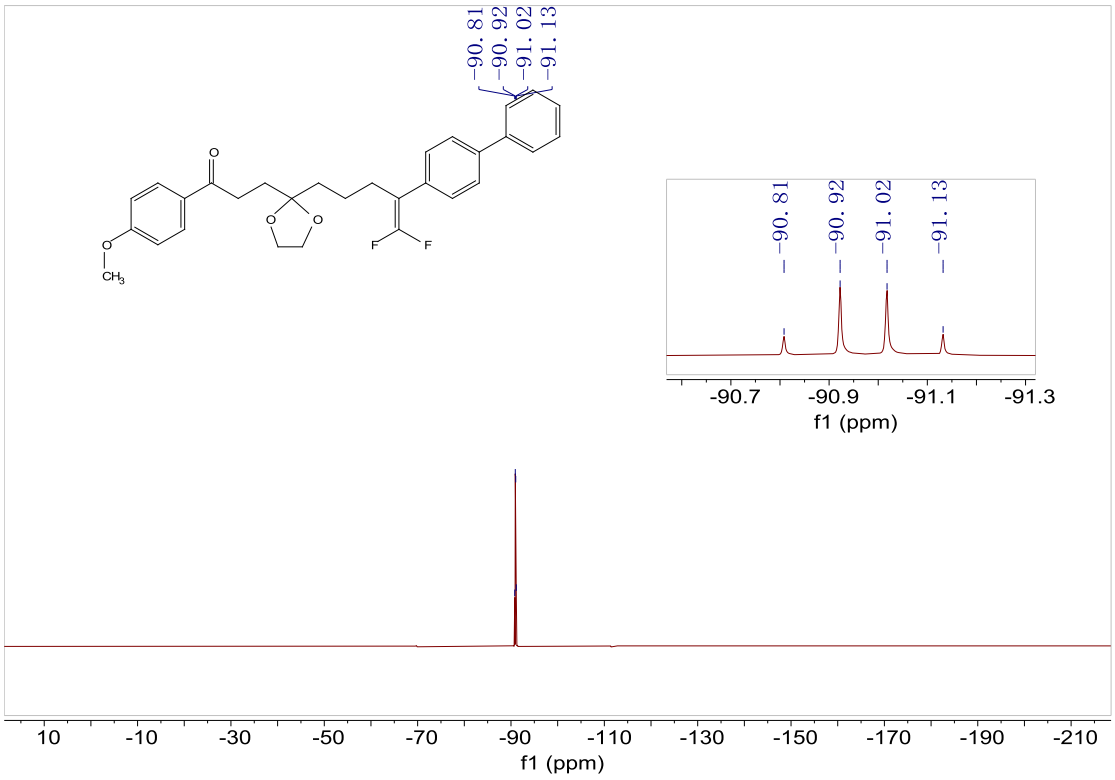
^{19}F NMR of 3na (376 MHz, $CDCl_3$)



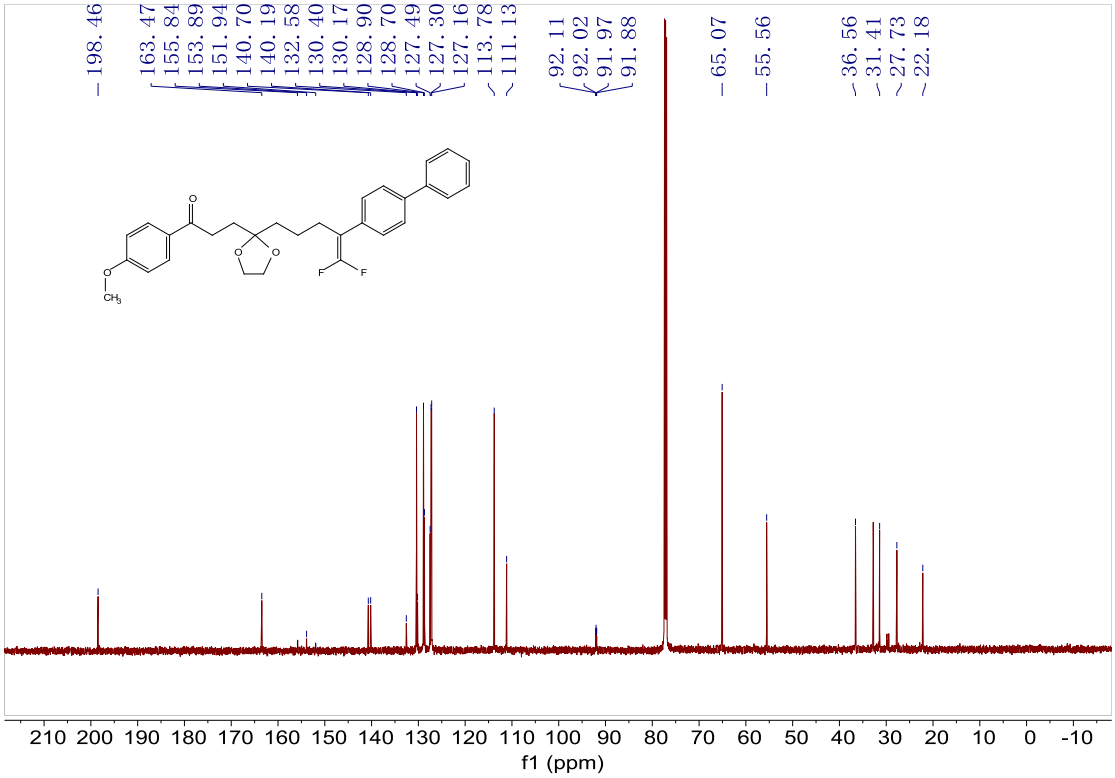
^{13}C NMR of 3na (150 MHz, $CDCl_3$)



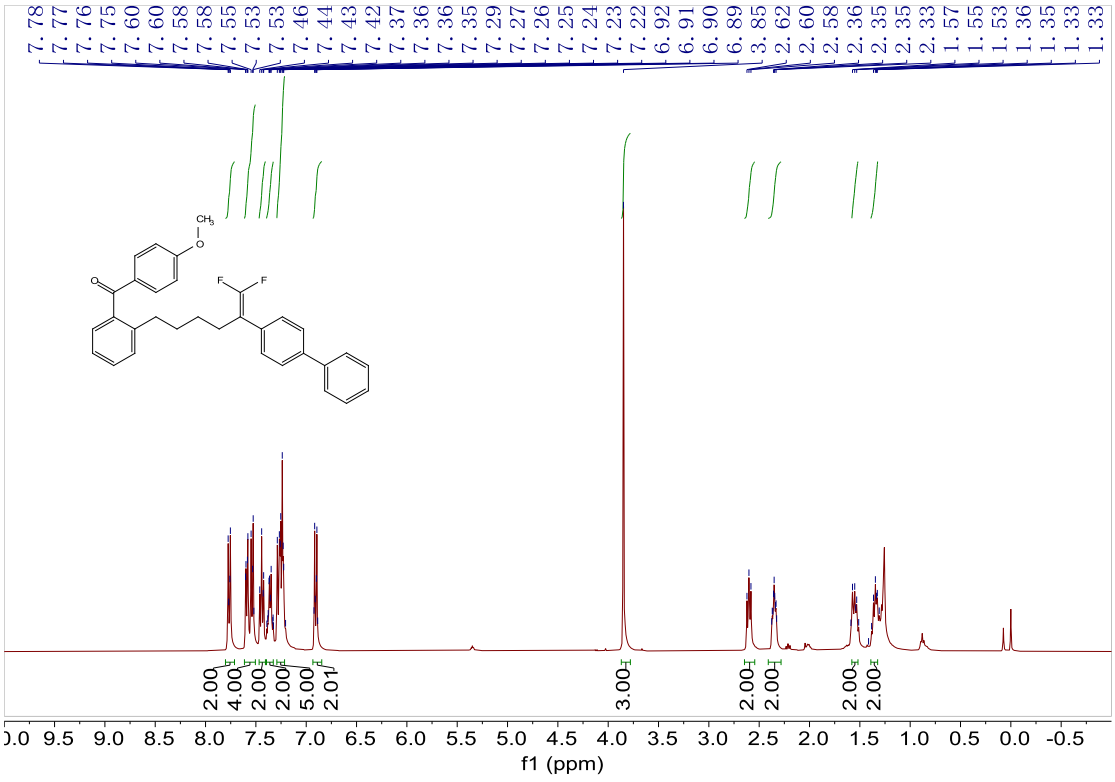
^{1}H NMR of 3pa (400 MHz, $CDCl_3$)



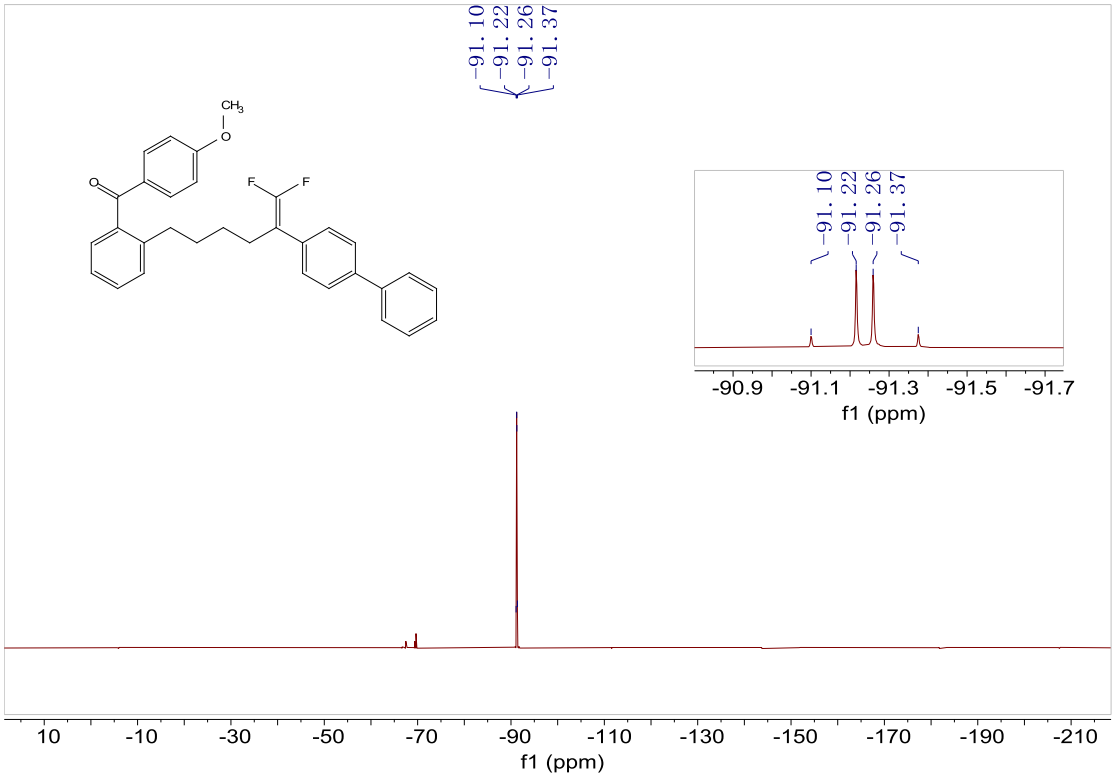
^{19}F NMR of 3pa (376 MHz, $CDCl_3$)



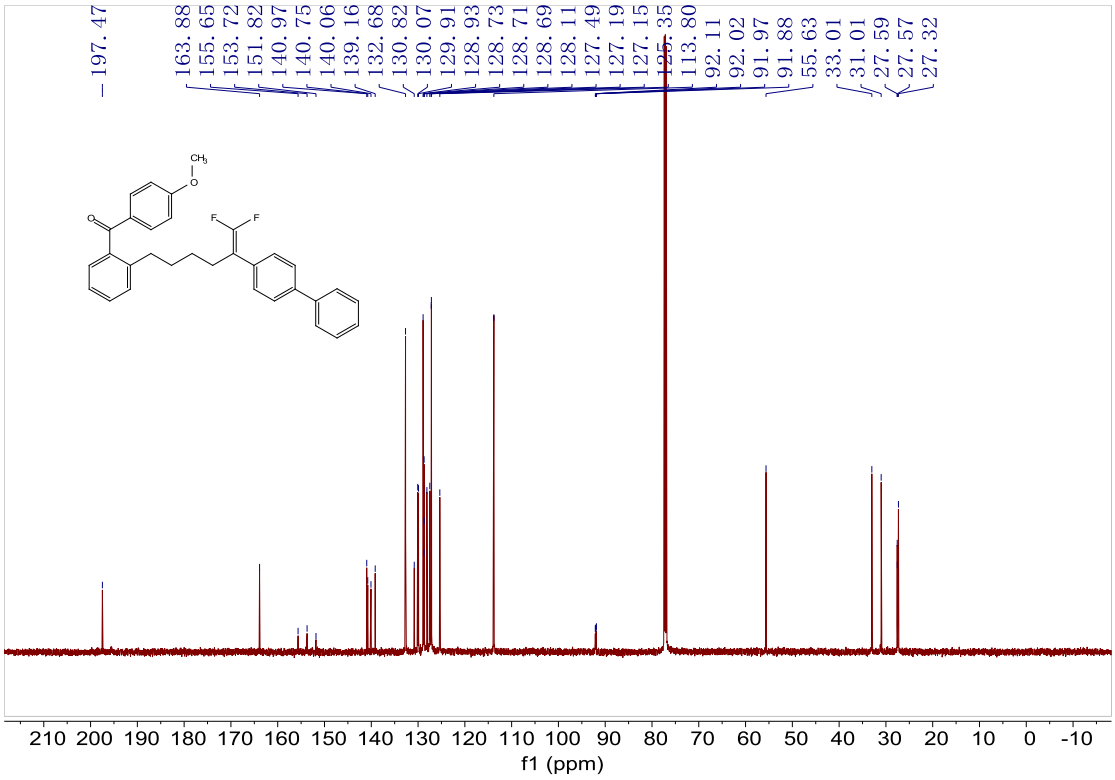
^{13}C NMR of 3pa (150 MHz, $CDCl_3$)



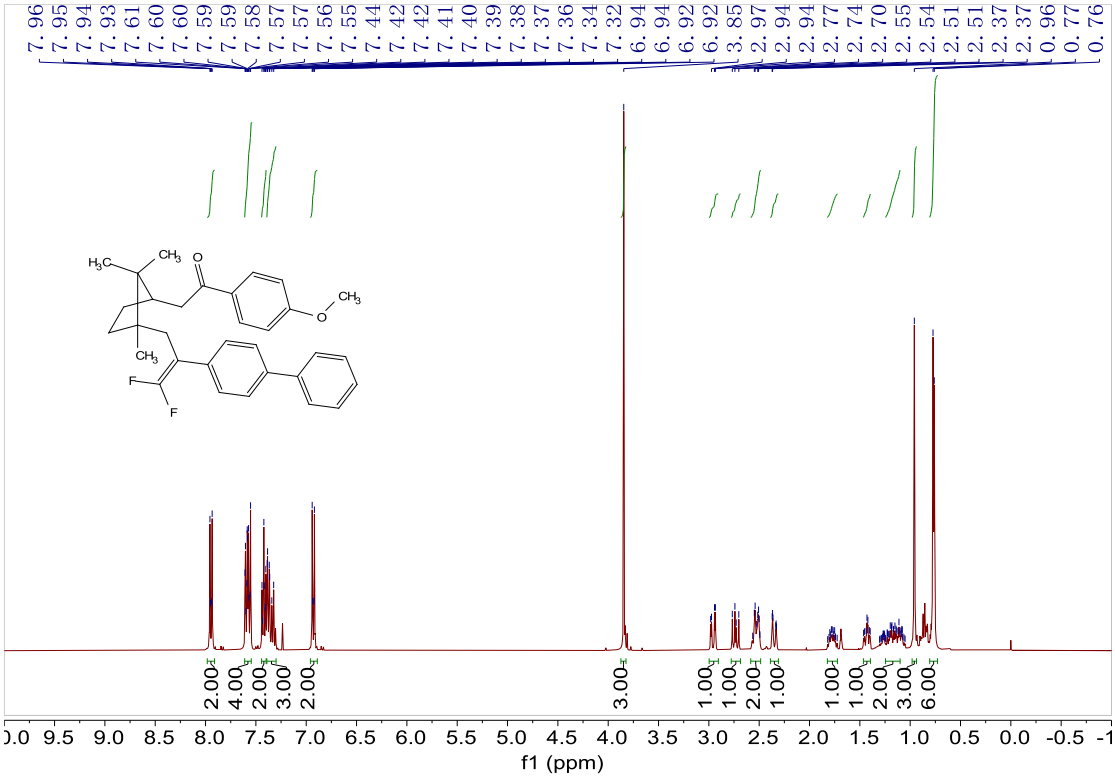
^{1}H NMR of 3qa (400 MHz, $CDCl_3$)



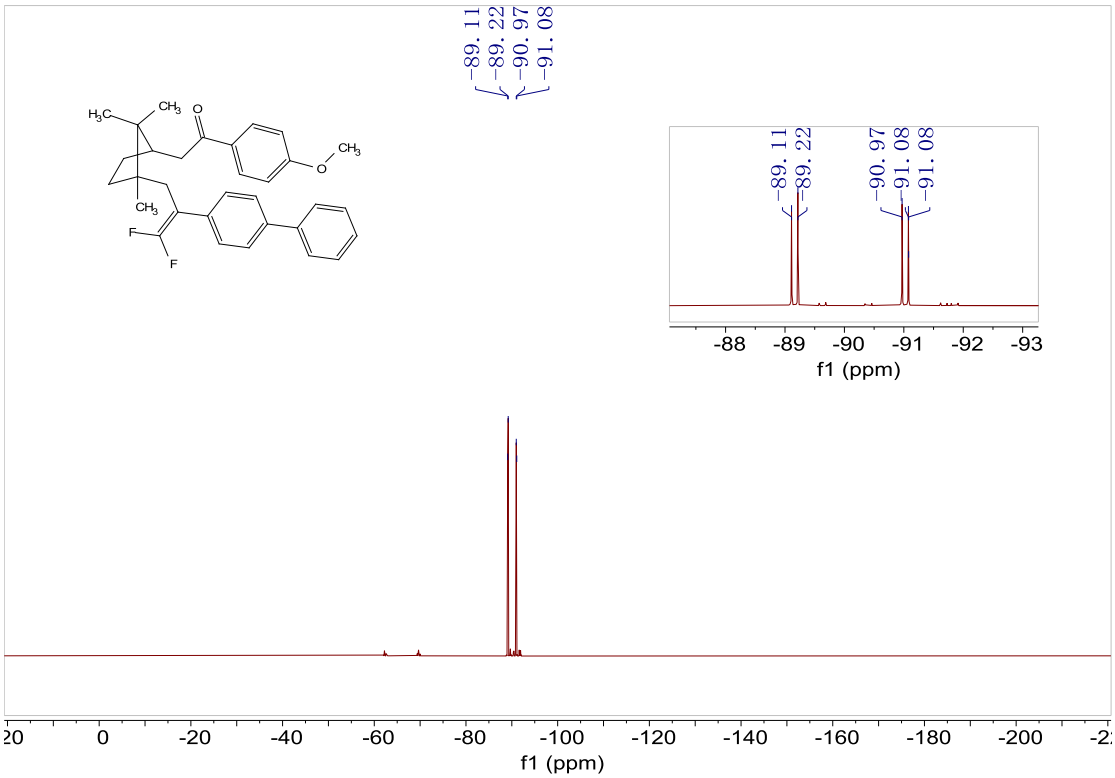
^{19}F NMR of 3qa (376 MHz, $CDCl_3$)



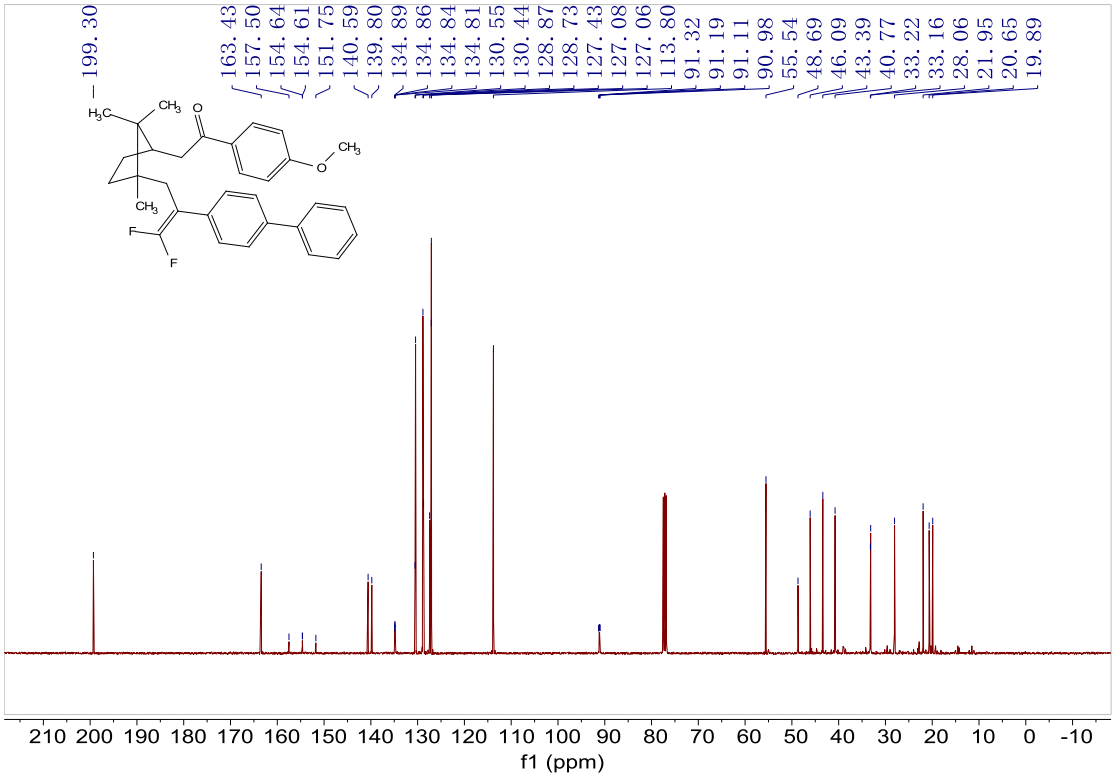
^{13}C NMR of 3qa (150 MHz, $CDCl_3$)



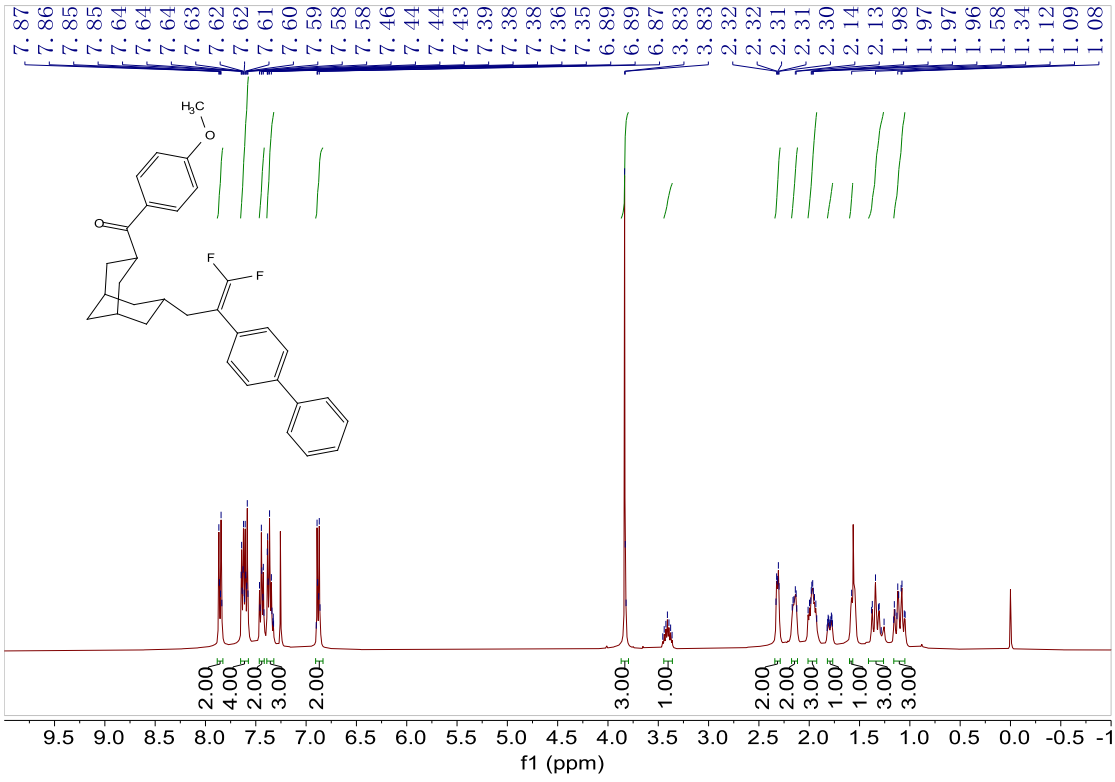
^{1}H NMR of 3ra (400 MHz, $CDCl_3$)



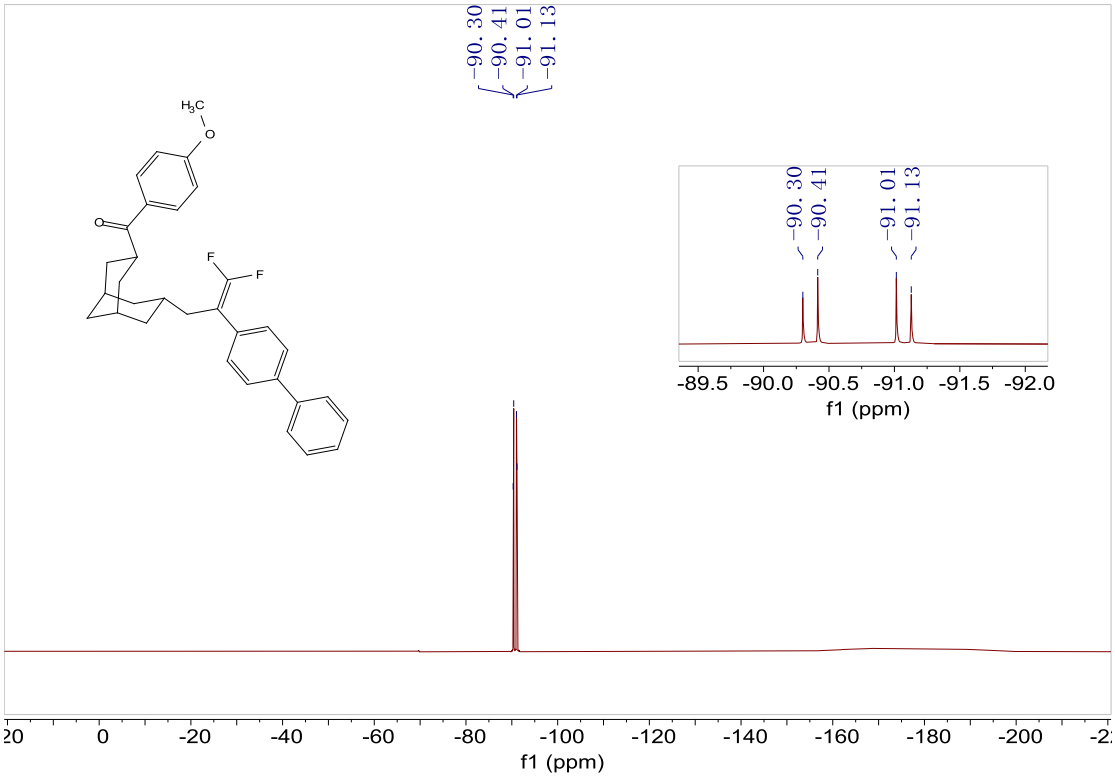
^{19}F NMR of 3ra (376 MHz, $CDCl_3$)



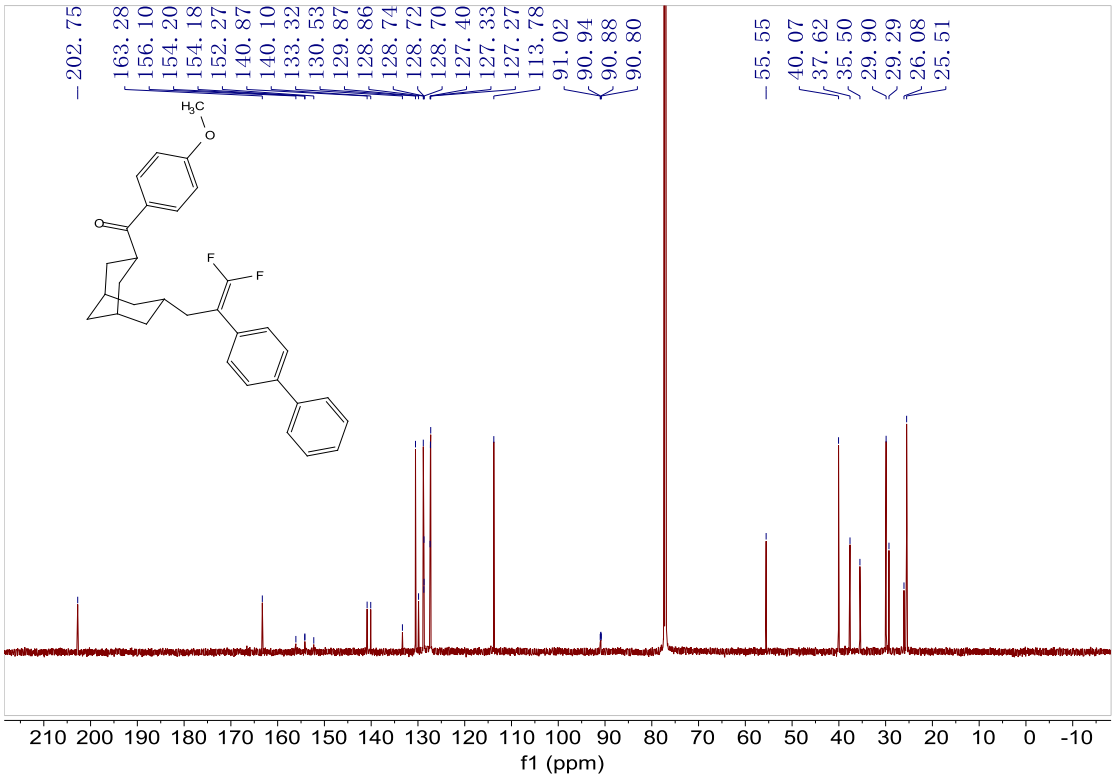
^{13}C NMR of 3ra (100 MHz, $CDCl_3$)



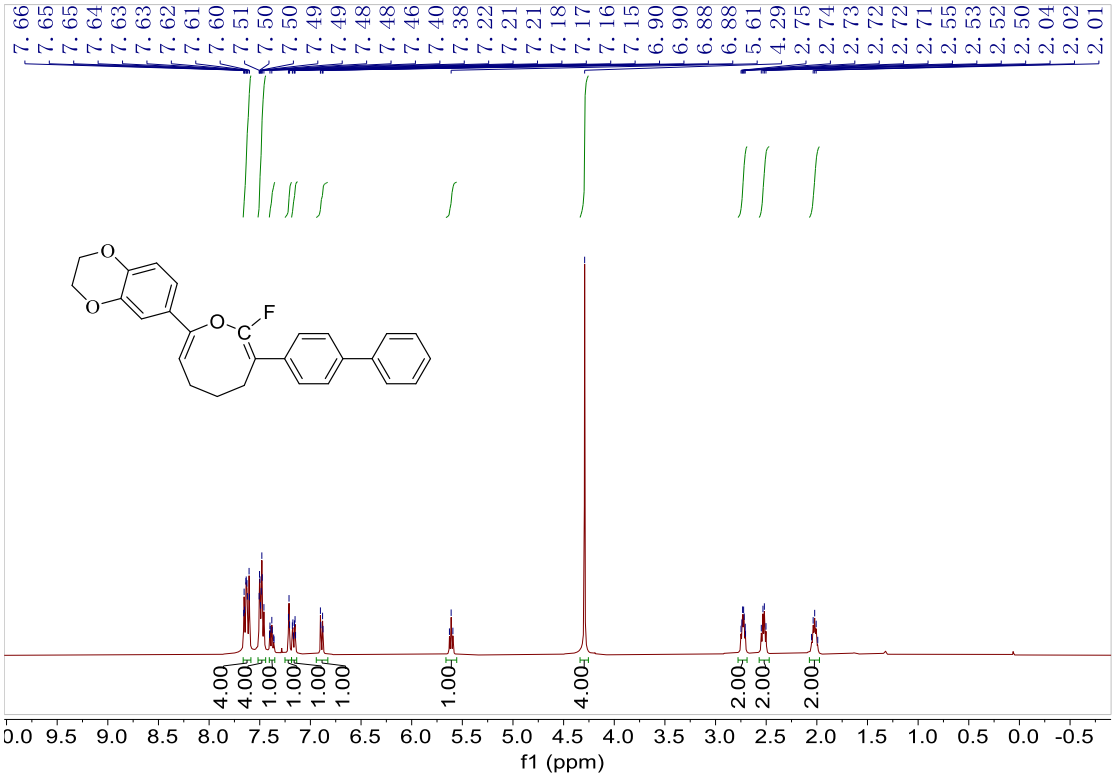
^{1}H NMR of 3sa (400 MHz, $CDCl_3$)



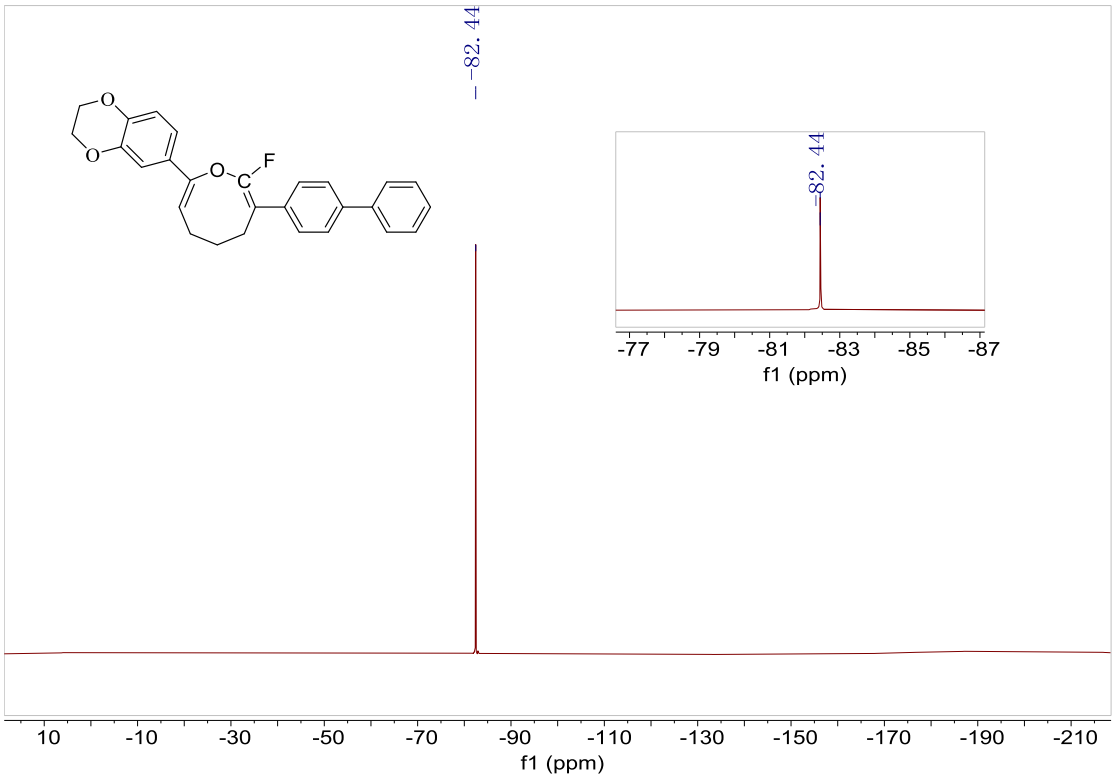
^{19}F NMR of 3sa (376 MHz, $CDCl_3$)



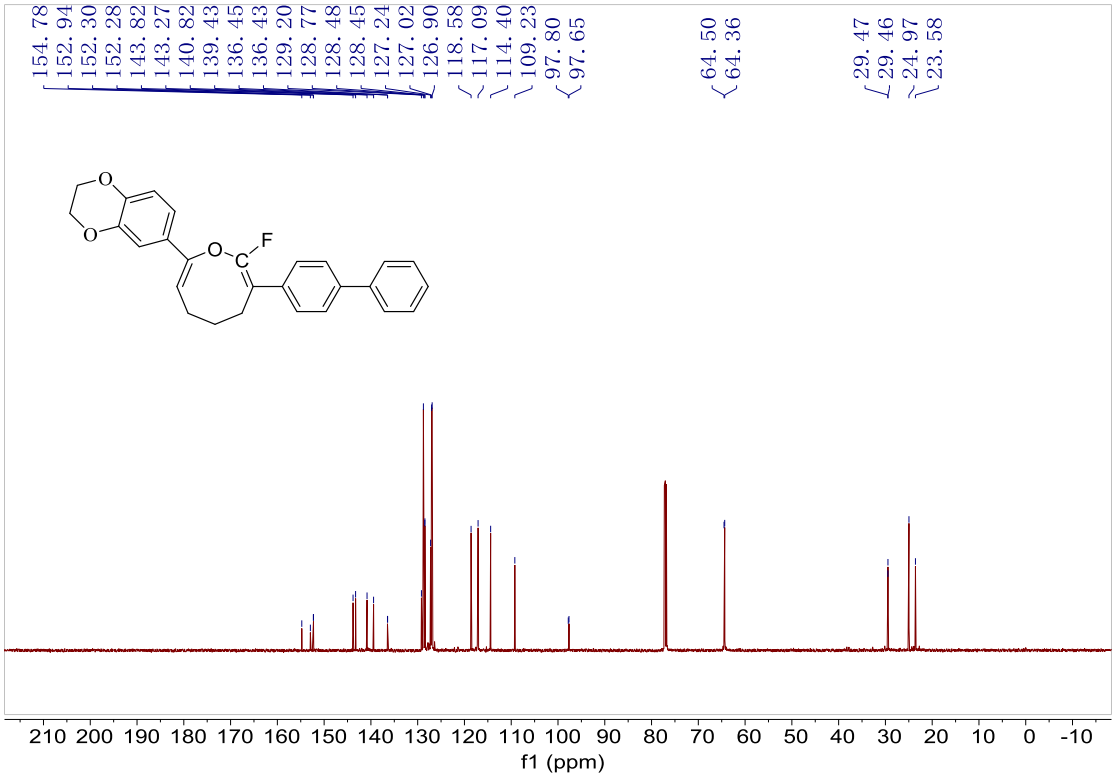
^{13}C NMR of 3sa (150 MHz, $CDCl_3$)



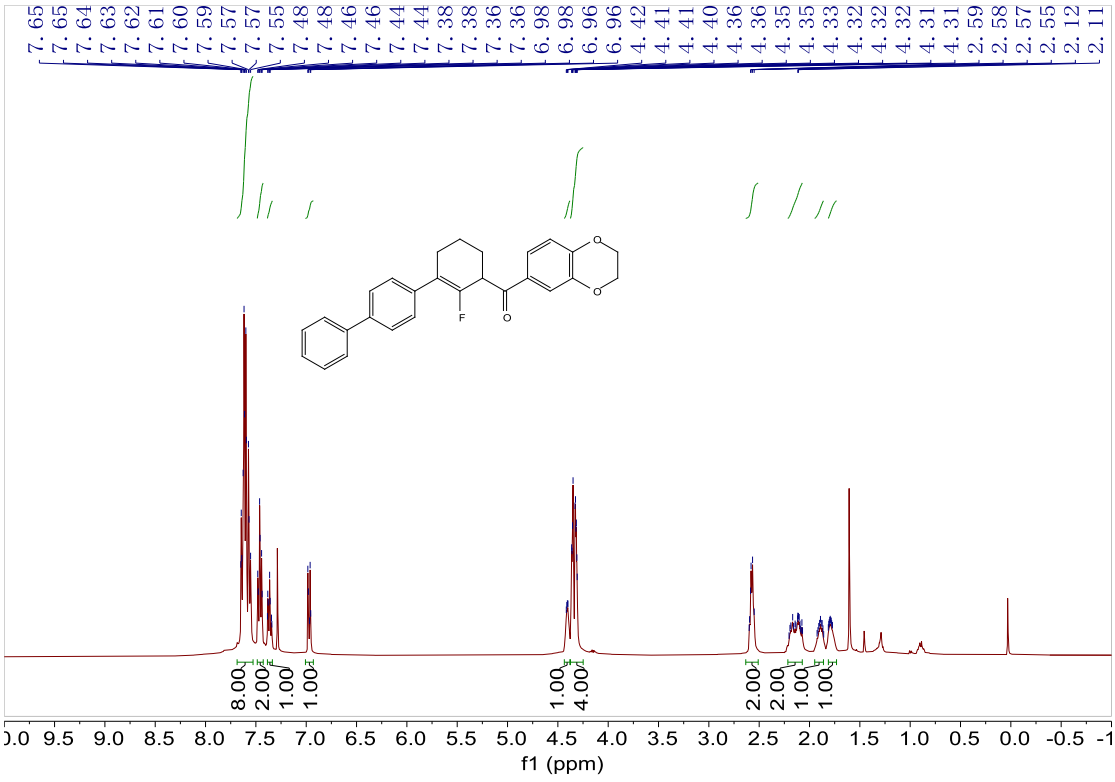
^{1}H NMR of 4 (400 MHz, $CDCl_3$)



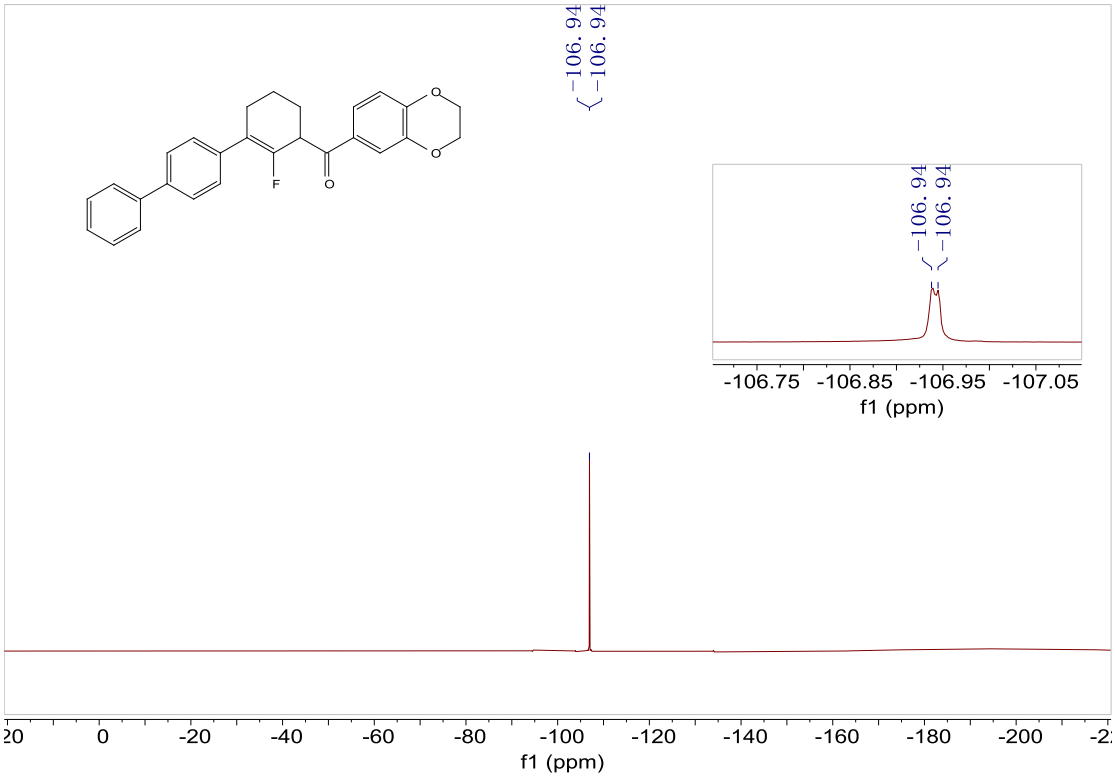
^{19}F NMR of 4 (376 MHz, $CDCl_3$)



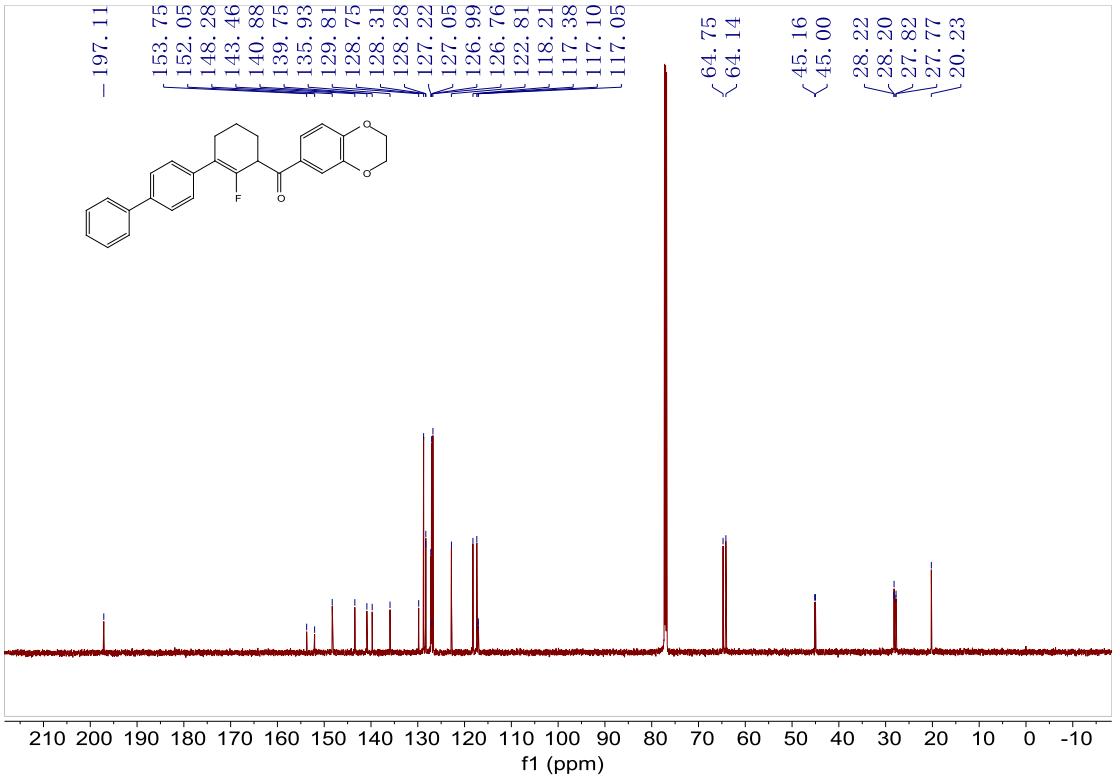
^{13}C NMR of 4 (100 MHz, $CDCl_3$)



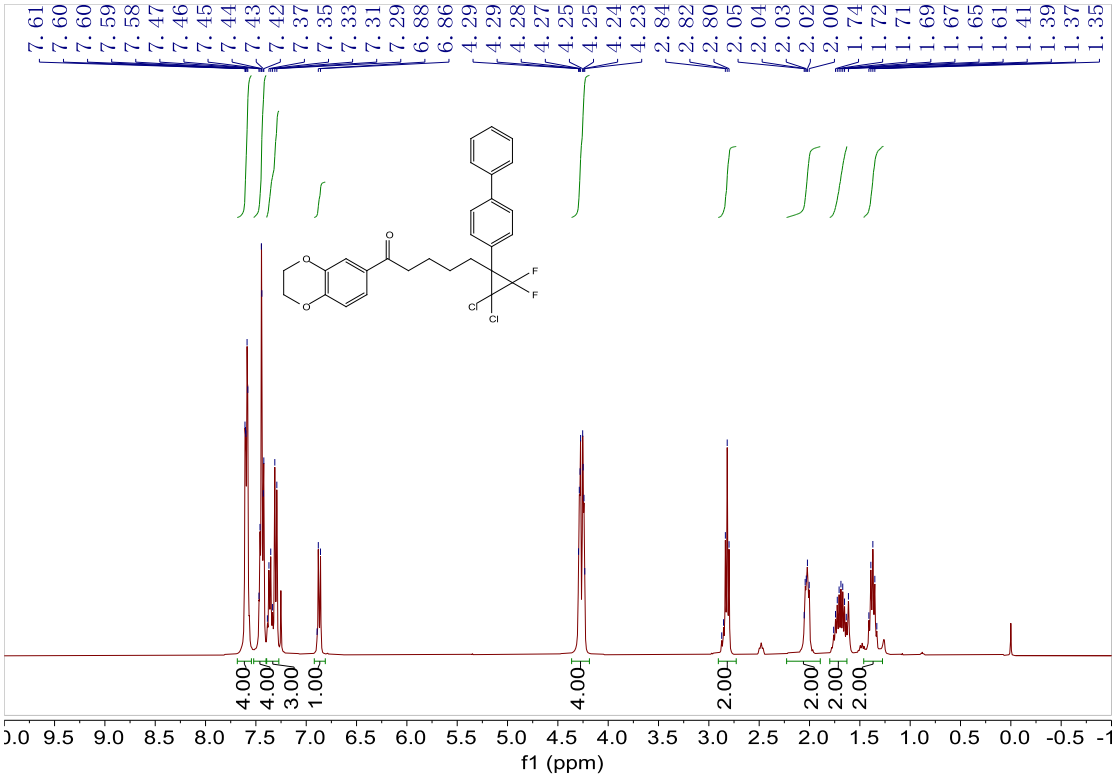
^{1}H NMR of 5 (400 MHz, $CDCl_3$)



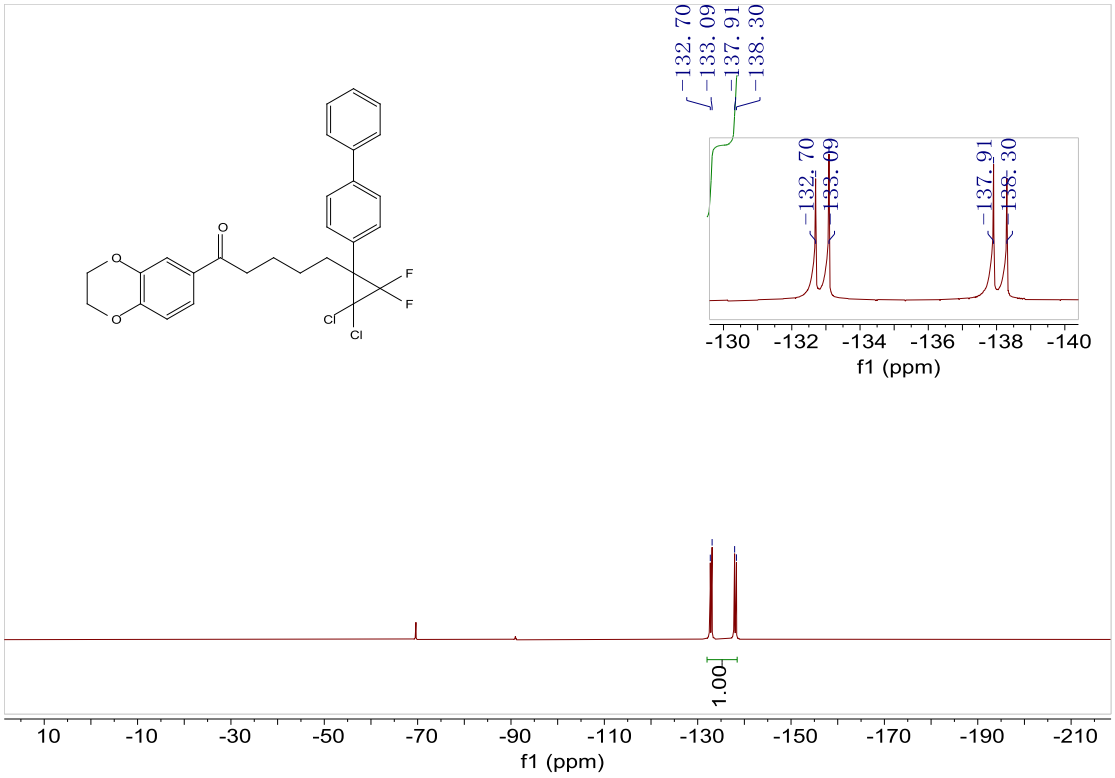
^{19}F NMR of 5 (376 MHz, $CDCl_3$)



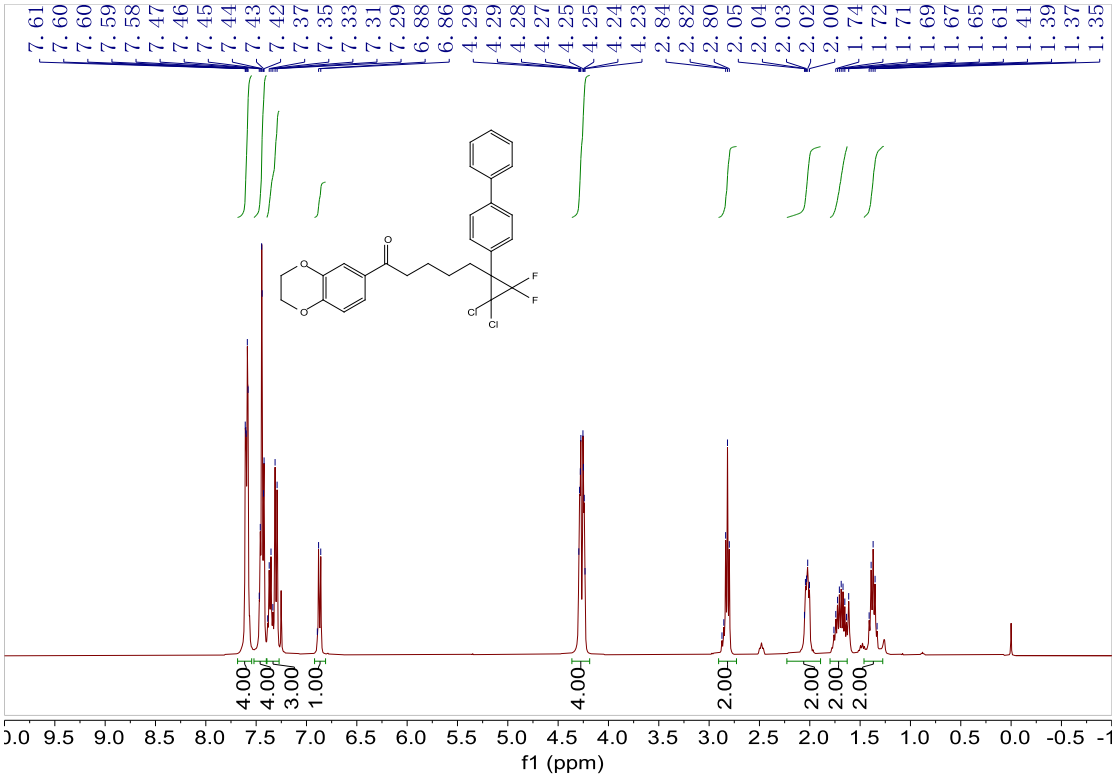
^{13}C NMR of 5 (150 MHz, $CDCl_3$)



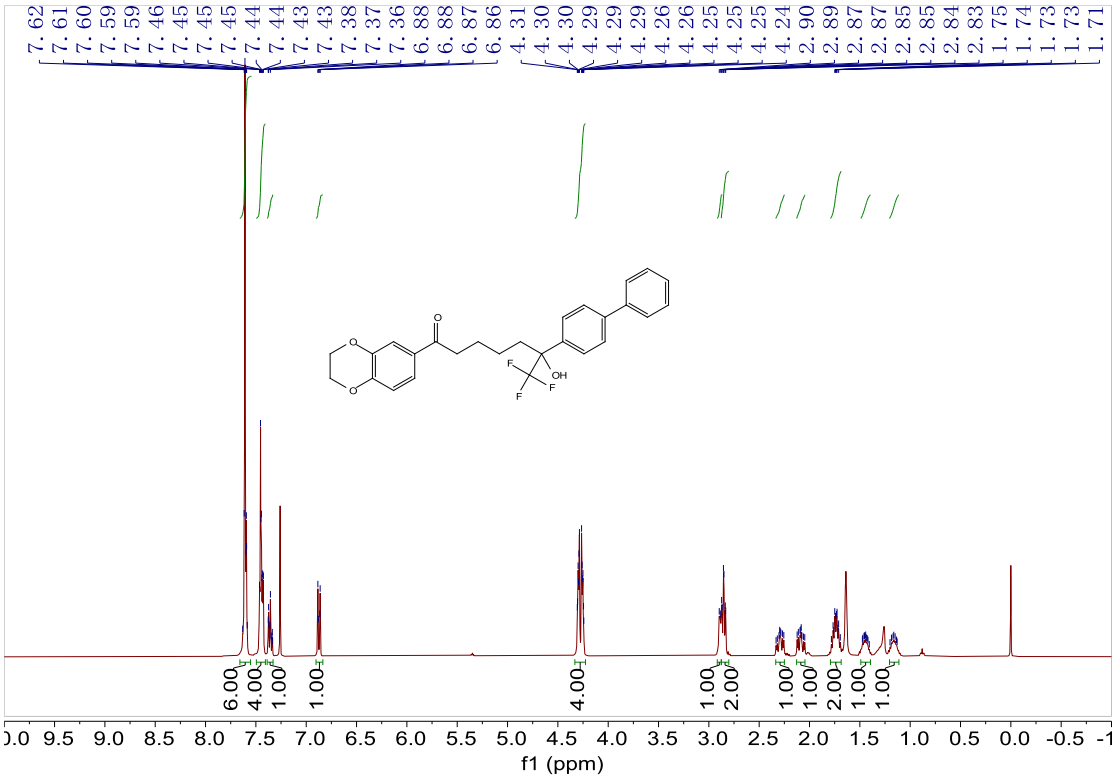
^{1}H NMR of 6 (400 MHz, $CDCl_3$)



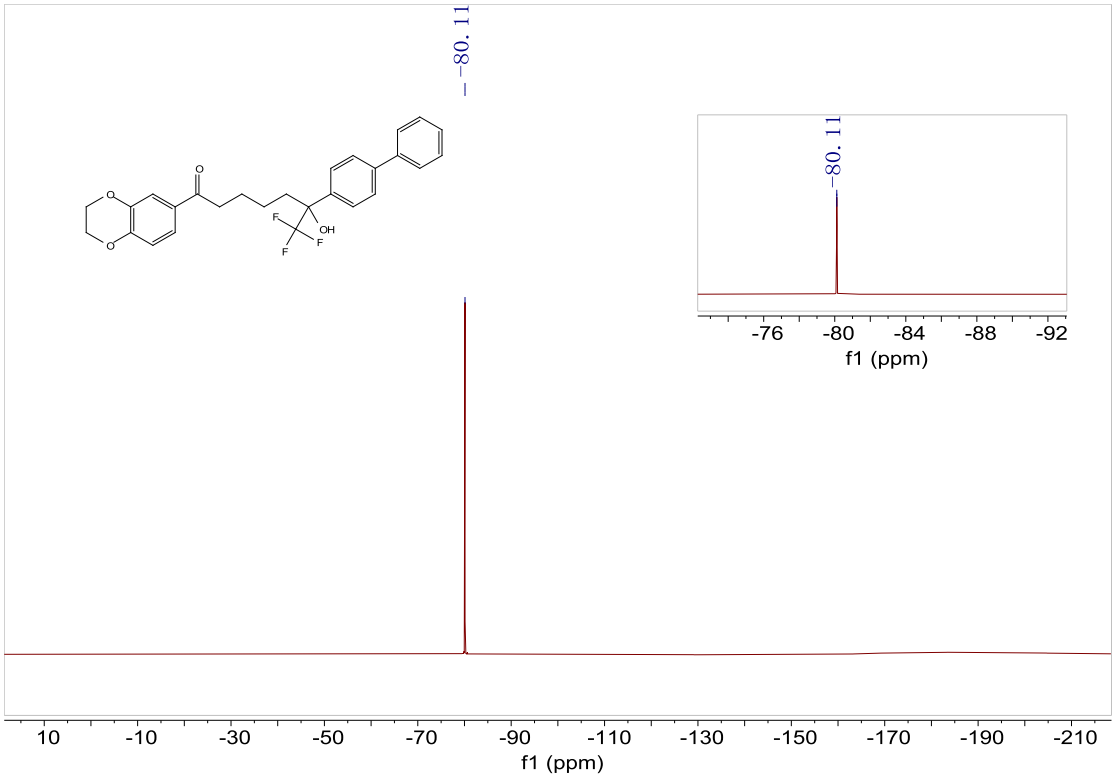
^{19}F NMR of 6 (376 MHz, $CDCl_3$)



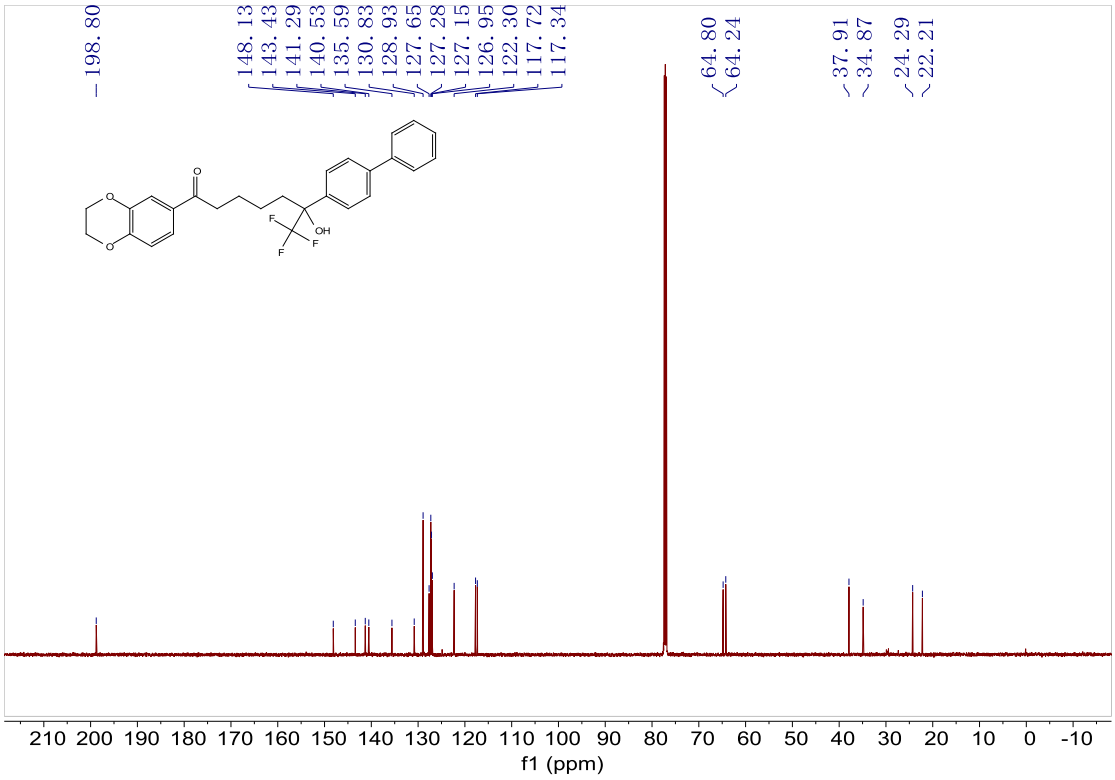
^{13}C NMR of 6 (150 MHz, $CDCl_3$)



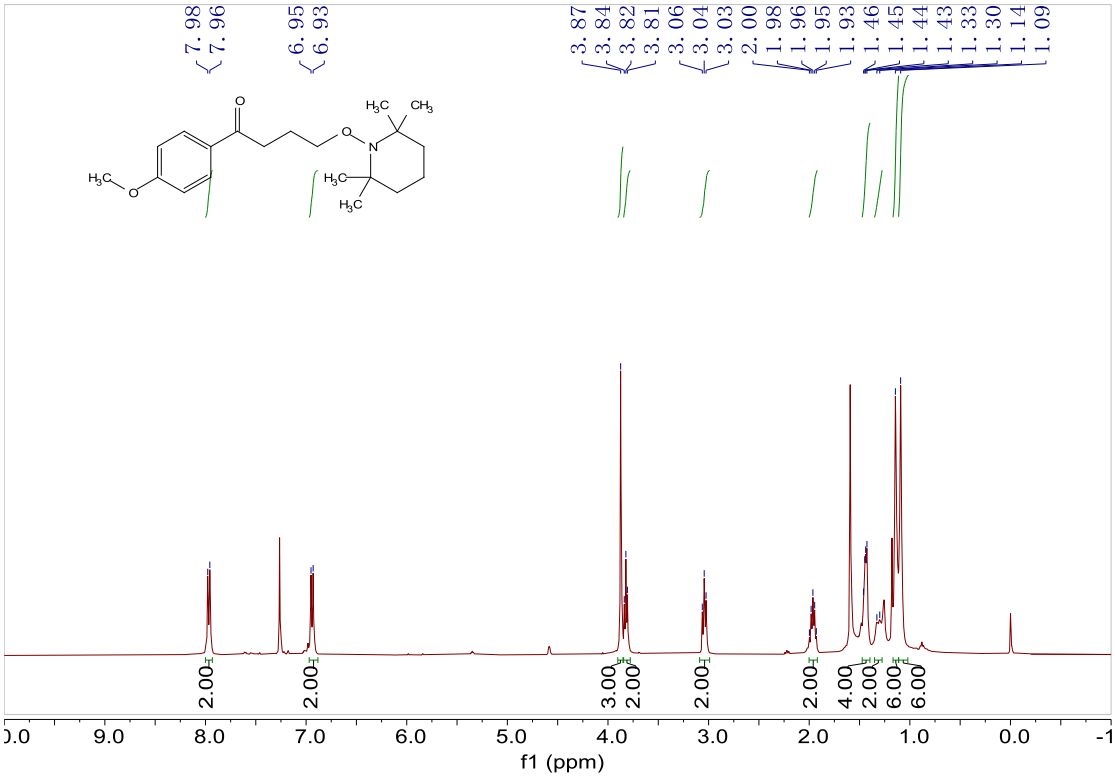
^{1}H NMR of 7 (400 MHz, $CDCl_3$)



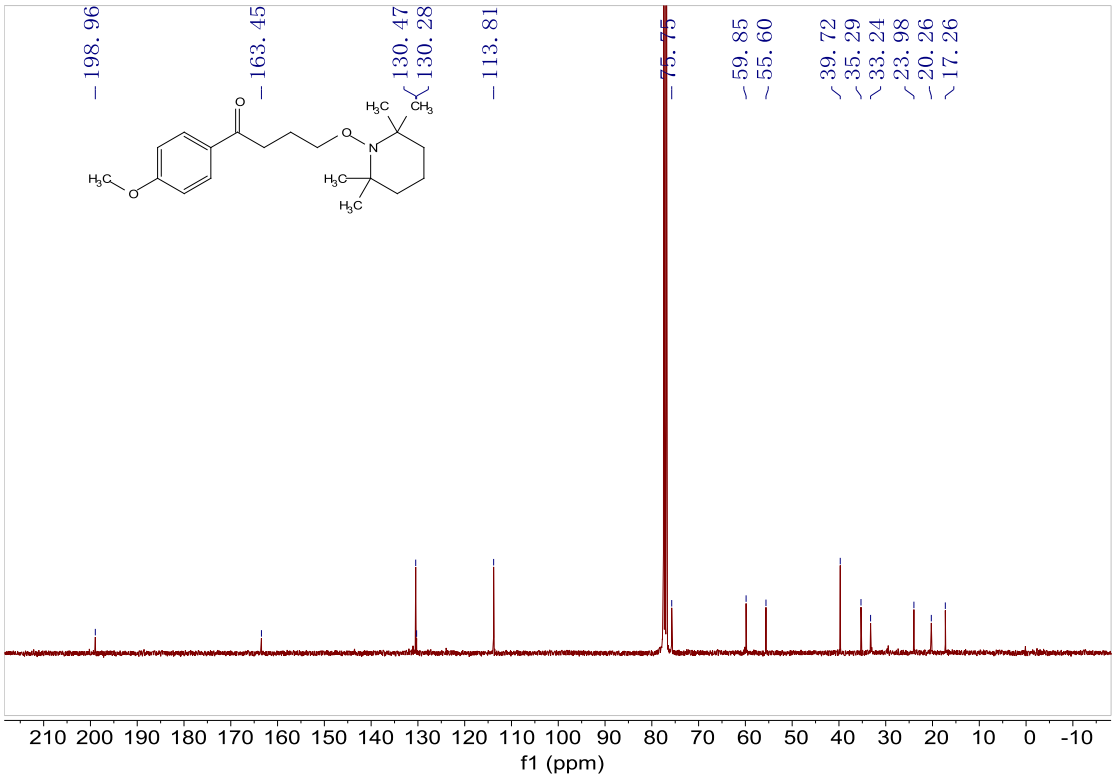
^{19}F NMR of 7 (376 MHz, $CDCl_3$)



^{13}C NMR of 7 (150 MHz, $CDCl_3$)



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



^{13}C NMR of 8 (100 MHz, $CDCl_3$)