Supporting Information

Bromine-radical-induced C_{sp^2}-H difluoroalkylation of quinoxalinones and hydrazones through visible-light-promoted C_{sp^3}-Br bond homolysis

Chuan-Hua Qu, Run Huang, Yuan Liu, Tong Liu and Gui-Ting Song*

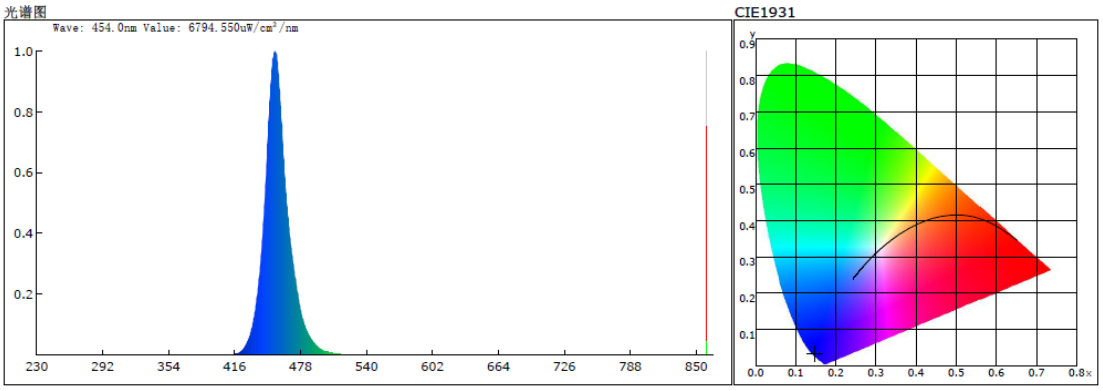
College of Pharmacy, National & Local Joint Engineering Research Center of Targeted and Innovative Therapeutics, Chongqing Key Laboratory of Kinase Modulators as Innovative Medicine, Chongqing University of Arts and Sciences, Chongqing 402160, China.

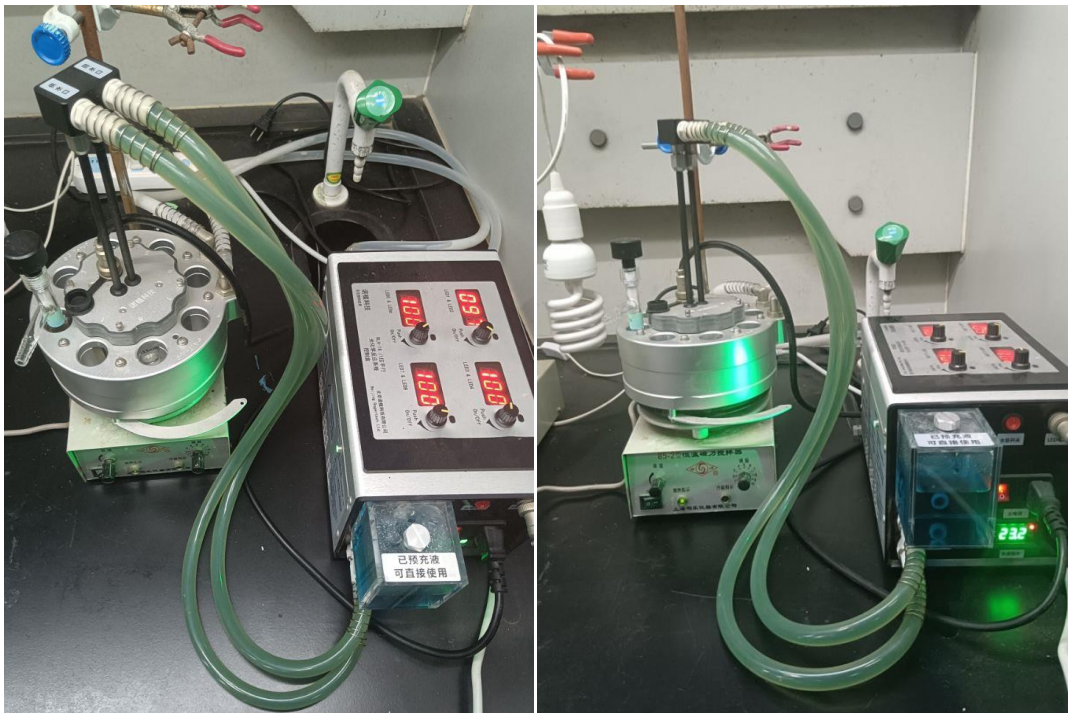
Table of Contents

1. General information

^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were measured on 400 MHz spectrometer, using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts (δ) are given in ppm relative to TMS, the coupling constants *J* are given in Hz. HRMS were obtained in the ESI mode. All reactions were carried out under N_2 atmosphere unless otherwise noted. All solvents were obtained from commercial suppliers. Reactions were monitored by TLC on silica gel plates (GF254), and the analytical thin-layer chromatography (TLC) was performed on percolated, glass-backed silica gel plates. The 33W CFL were directly got from the supermarket (daylight, energy saving, 220 V). Monochromatic light source device is a customized product. α-Bromo difluoroacyl arenes[1], quinoxalin-2(1*H*)ones[2], hydrazones[3], α-bromo monofluoroacetophenone[4-5], and bromodifluoromethyl-4-methoxyphenyl-keton-4-methoxyphenylimine[6] were prepared according to the literature.

454nm monochromatic light source is shown in the figure below





photoreaction device with refrigeration circulating fluid

Fluorescent light (CFL) spectrum

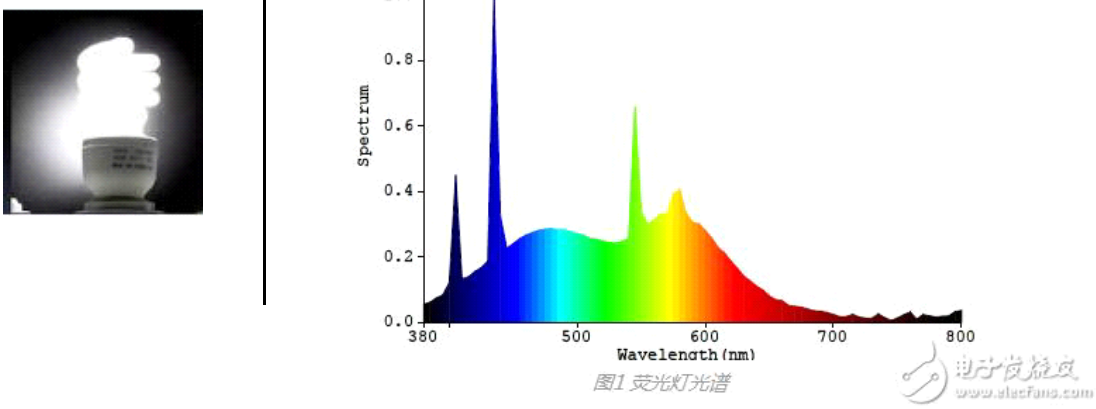
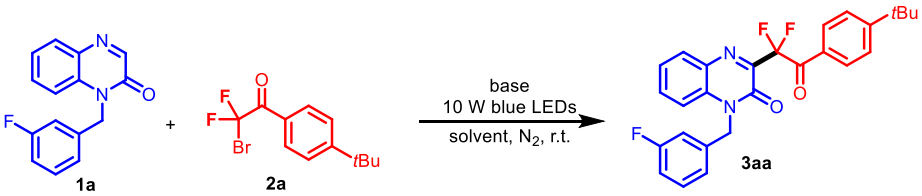


图1 荧光灯光谱

2. Optimization of the reaction conditions of radical difluoroalkylation of 1a.[a]

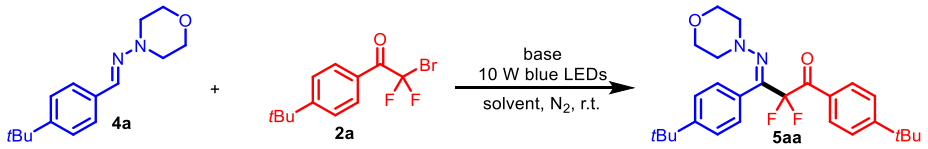


entry	Base (2.0 equiv.)	Solvent	yield (%) of **3aa**[b]
1	TMEDA	MeCN	20
2	DIPEA	MeCN	25
3	Et_3N	MeCN	35
4	DBU	MeCN	NR
5	Cs_2CO_3	MeCN	10
6	Na_2CO_3	MeCN	NR
7	DABCO	MeCN	NR
8	DMAP	MeCN	NR
9	2,6-lutidine	MeCN	NR
10	2,4,6-trimethylpyridine	MeCN	23
11	Et_3N	DMF	32
12	Et_3N	DMSO	29
13	Et_3N	DCM	40
14	**Et_3N**	**THF**	**87**
15[c]	Et_3N	THF	74
16[d]	Et_3N	THF	trace

17[e]	Et_3N	THF	trace
18		THF	trace

[a]Reaction were performed on a 0.2 mmol scale using 1.5 equiv. of **2a** and 2.0 equiv. of base, and 10 W blue LEDs to illuminate the reaction vessel at N_2 atmosphere and room temperature reaction for 48 h. [b]Yield are those of products isolated by column chormatography. [c]33 W CFL was used in the reaction. [d]Reaction in the dark. [e]Reaction carried out at 80 °C in a sealed tube without irradiation. DMA = *N*, *N*-dimethylacetamide, MTBE = methyl *tert*-butyl ether, Et_3N = triethylamine, DIPEA = *N*, *N*-diisopropylethylamine, TMEDA = tetramethylethylenediamine.

3. Optimization of the reaction conditions of radical difluoroalkylation of 4a.[a]

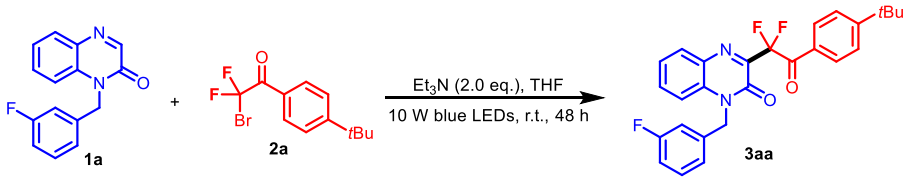


entry	Base (2.0 equiv.)	Solvent	yield (%) of **5aa**[b]
1	Et_3N	THF	54
2	DIPEA	THF	46
3	TMEDA	THF	37
4	PMDETA	THF	41
5	DBU	THF	69
6	DBU	MeCN	72
7	DBU	DCE	57
8	DBU	DMA	86
9[c]	**DBU**	**DMA**	**92**
10[d]	DBU	DMA	35
11[e]	DBU	DMA	trace
12[f]	DBU	DMA	trace
13		DMA	trace

[a]Reaction were performed on a 0.2 mmol scale of **4a** using 1.5 equiv. of **2a** (0.3 mmol) and 2.0 equiv. of base (0.4 mmol), and a 10 W blue LEDs bulb to illuminate the reaction vessel at N_2 atmosphere and room temperature reaction for 48 h. [b]Yield are those of products isolated by column chormatography. [c]0.15 mmol scale of **4a** was used. [d]33 W CFL was used in the reaction. [e]Reaction in the dark. [f]Reaction carried out at 80 °C in a sealed tube without irradiation. DMA = *N*, *N*-dimethylacetamide, Et_3N = triethylamine, DIPEA = *N*, *N*-diisopropylethylamine, TMEDA = tetramethylethylenediamine, PMDETA = pentamethyldiethylenetriamine.

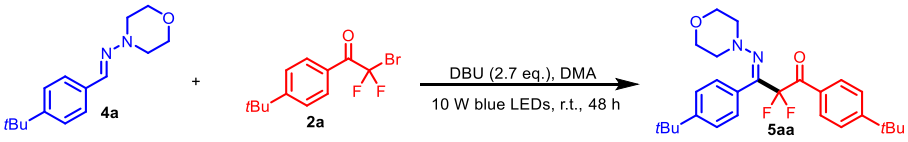
4. General experimental procedures for C_{sp}^3-Br bond homolytic reaction

4.1 Experimental procedures for the difluoroalkylation of quinoxalinones



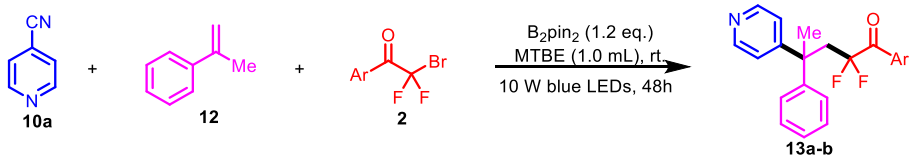
Method A: Triethylamine (56 μL, 0.4 mmol, 2.0 eq.), quinoxalinones **1a** (51 mg, 0.2 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 1.5 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 48 h, the crude products were purified by column chromatography over silica gel using petroleum / EtOAc = 4/1 as eluent to yield **3aa** (81 mg, 87%).

4.2 Experimental procedures for the difluoroalkylation of aldehyde hydrazones



Method B: DBU (60 μL, 0.4 mmol, 2.7 eq.), aldehyde hydrazone **4a** (51 mg, 0.15 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous DMA (1 ml) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 48 h, the crude products were extracted with ethyl acetate and water for three times. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (silica gel, petroleum / EtOAc = 10/1) afforded compound **5aa** (63 mg, 92%).

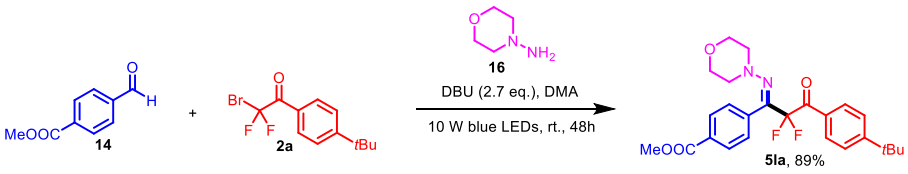
4.3 Experimental procedures for the difluoroalkylation and pyridation of alkenes



B_2pin_2 (62 mg, 0.24 mmol, 1.2 eq.), 4-cyanopyridine **10a** (32 mg, 0.3 mmol, 1.5 eq.), alkene **12** (52 μL, 0.4 mmol, 2.0 eq.) and α-bromo difluoroacylarenes **2** (0.2 mmol, 1.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous methyl *tert*-butyl ether (MTBE, 1 ml) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs at room temperature. After 48 h, the reaction was quenched with saturated sodium bicarbonate for 15 minutes and then extracted with ethyl acetate. The extract was dried over anhydrous Na_2SO_4, and the

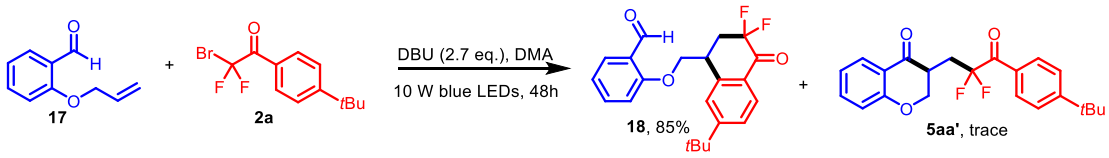
solvent was removed. Flash chromatography (silica gel, petroleum / EtOAc = 5/1) afforded compound **13a-b**.

4.4 Experimental procedures for the difluoroalkylation of aldehydes using morpholin-4-amine



DBU (60 μL, 0.4 mmol, 2.7 eq.), aldehyde **14** (25 mg, 0.15 mmol, 1.0 eq.), morpholin-4-amine **16** (15μL, 0.15 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous DMA (1 ml) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 48 h, the crude products were extracted with ethyl acetate and water for three times. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (silica gel, petroleum / EtOAc = 10/1) afforded compound **5la** (61 mg, 89%).

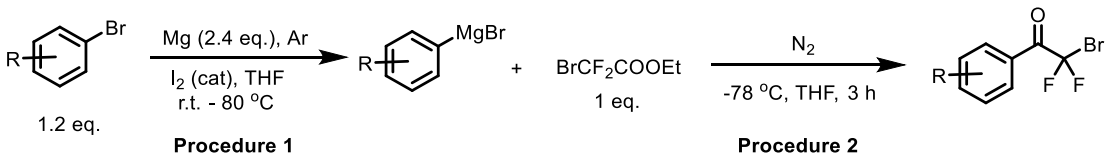
4.5 Experimental procedures for the difluoroalkylation and radical cyclization of alkenes



DBU (60 μL, 0.4 mmol, 2.7 eq.), aldehyde **17** (24 mg, 0.15 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous DMA (1 ml) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 48 h, the crude products were extracted with ethyl acetate and water for three times. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (silica gel, petroleum / EtOAc = 20/1) afforded compound **18** (46 mg, 85%).

5. Preparation of the substrates

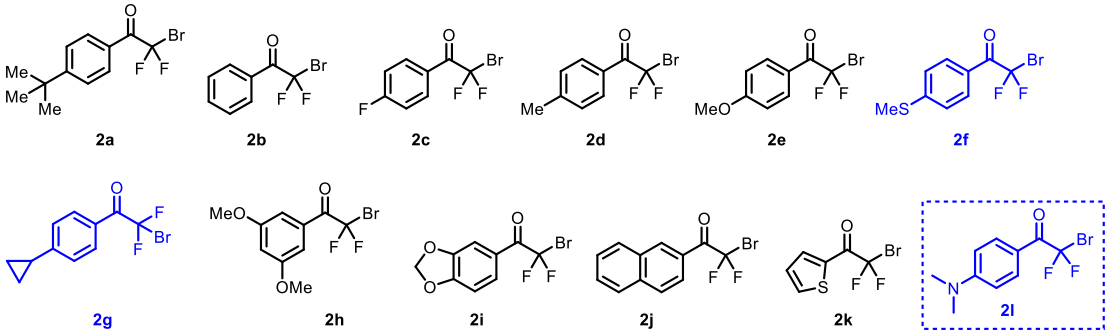
5.1 General procedure for the preparation of α-bromo difluoroacyl arenes:[1]



Procedure 1: To a flame dried 100 mL round bottom flask equipped with a magnetic stir bar was added 1.44 g of magnesium (60 mmol) and catalytic amount of iodine. To the mixture was added aryl bromide (30 mmol) in THF (30 mL) dropwise *via* constant pressure dropping funnel under an N_2

atmosphere. (*Note: in order to promote the initiation of Grignard reagent, we need to heat by hair dryer*). Afterward, this was set to reflux for 3-5 hours.

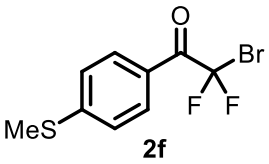
Procedure 2: To a mixture of ethyl bromodifluoroacetate (3.2 mL, 25 mmol) and THF (30 mL) was added a newly prepared solution of arylmagnesium bromide in THF at -78 ℃ under an N_2 atmosphere. After the solution was stirred at that temperature for 3 h, the mixture was quenched with 3N HCl and then extracted with ethyl acetate. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (silica gel, hexanes) afforded compound **2a-2k.**



The ^{1}H-NMR, ^{19}F NMR and ^{13}C NMR of **2b** were reported by the reference *J. Org. Chem*., **2005**, *70*, 5912.

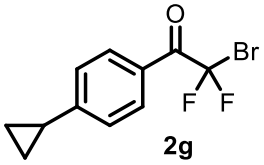
The ^{1}H-NMR, ^{19}F NMR and ^{13}C NMR of **2a, 2c-2e,** and **2h-2k** were reported by the reference *Org. Lett.* **2019**, *21*, 8169.

2-bromo-2,2-difluoro-1-(4-(methylthio)phenyl)ethan-1-one (2f)

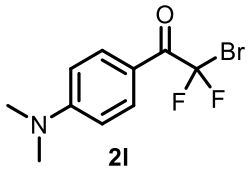


colorless oil, purified by flash column chromatography over *n*-hexane, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 2.55 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5 (t, *J* = 25.7 Hz), 149.6, 130.9, 128.8, 126.6, 124.8, 113.7 (t, *J* = 318.4 Hz), 14.5 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.4 (s) ppm.

2-bromo-1-(4-cyclopropylphenyl)-2,2-difluoroethan-1-one (2g)



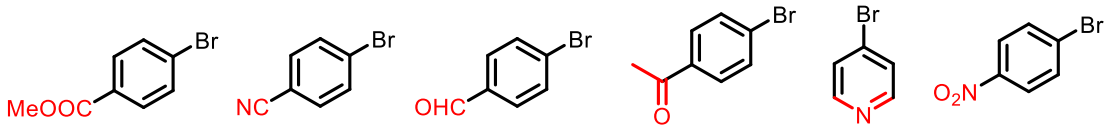
colorless oil, purified by flash column chromatography over *n*-hexane, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 1.90 (ddd, *J* = 13.4, 8.4, 5.0 Hz, 1H), 1.12–0.99 (m, 2H), 0.86–0.61 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9 (t, *J* = 25.7 Hz), 153.4, 130.9 (t, *J* = 2.8 Hz), 125.7, 113.9 (t, *J* = 318.7 Hz), 16.1, 11.1 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -57.4 (s) ppm.



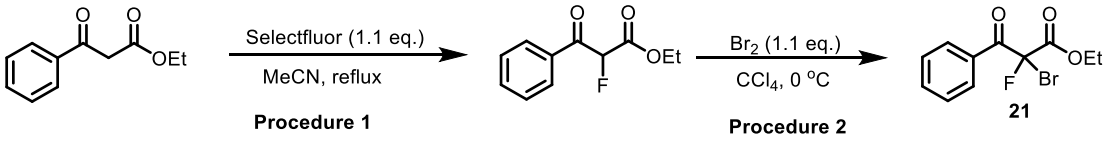
2l

green solid, purified by flash column chromatography over *n*-hexane ~ 5% petroleum ether/EtOAc ,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 3.12 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4 (t, *J* = 24.5 Hz), 154.4, 133.2 (t, *J* = 2.9 Hz), 116.0, 114.5 (t, *J* = 316.7 Hz), 110.8, 40.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -55.7 (s) ppm.

Unsuccessful use of aryl bromides in Grignard reagents



5.2 Synthesis of α-bromo monofluoroacyl arene **21**:



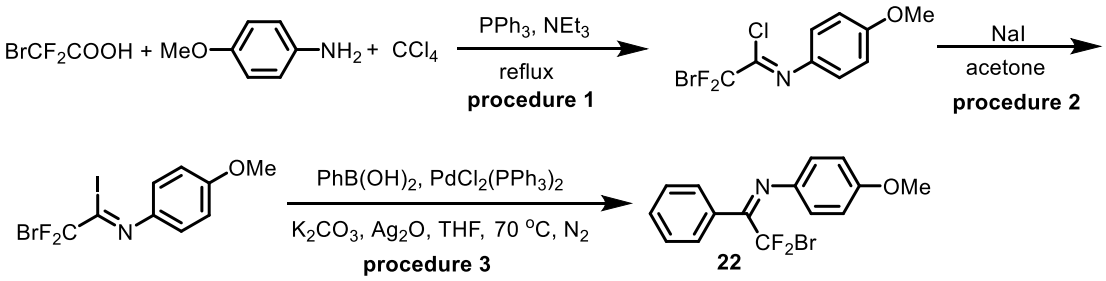
Procedure 1: The requisite methyl 2-fluoro-3-oxo-3-phenylpropanoates were prepared according to the previous report.[4]

To a flame dried 100 mL round bottom flask equipped with a magnetic stir bar was added 1.92 grams of ethyl 3-oxo-3-phenylpropanoate (10 mmol) and 3.90 grams of Selectfluor (11 mmol). Afterward, this was set to reflux for 2 hours. After the reaction was detected by TLC, the solvent was removed under reduced pressure. The residual liquid was washed with water and extracted with ethyl acetate. The organic phases were combined, dried over anhydrous sodium sulfate, filtered, removed under reduced pressure. Flash chromatography (petroleum ether/EtOAc = 20:1) afforded ethyl 2-fluoro-3-oxo-3-phenylpropanoate 1.47 g (70%).

Procedure 2: The α-bromo monofluoroacyl arene **6** was prepared according to the previous report.[5]

To a mixture of 2-fluoro-3-oxo-3-phenylpropanoate (1.47 g, 7 mmol) and CCl_4 (30 mL) was added 8 mL bromine (8 mmol, 1.1 equiv., 1 M Br_2 in DCM) at 0 ℃ *via* constant pressure dropping funnel. After the solution was stirred at that temperature overnight, the mixture was extracted with ethyl acetate and water. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (petroleum ether/EtOAc = 20:1) afforded compound **21**, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.65 (dd, *J* = 10.5, 4.3 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 4.38 (dd, *J* = 9.1, 3.9 Hz, 2H), 1.28 (t, *J* = 10.0, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8 (d, *J* = 24.9 Hz), 163.4 (d, *J* = 26.4 Hz), 134.7, 131.0 (d, *J* = 2.9 Hz), 130.2 (d, *J* = 4.4 Hz), 128.8, 97.6 (d, *J* = 274.4 Hz), 64.2, 13.7 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.3 (s). This compound is known.[5]

5.3 Synthesis of bromodifluoromethyl-4-methoxyphenyl-keton-4-methoxyphenylimine **22**:



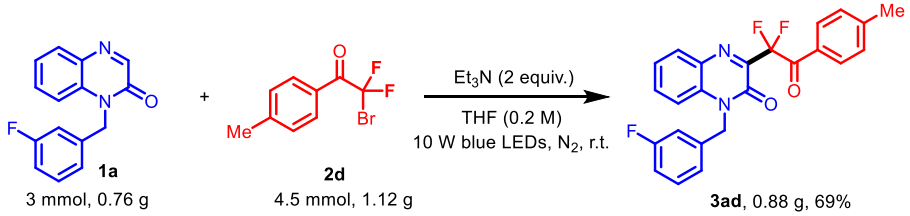
The requisite bromodifluoromethyl-4-methoxyphenyl-keton-4-methoxyphenylimine **22** was prepared according to the previous report.[6]

Procedure 1: PPh_3 (11.8 g, 45 mmol), Et_3N (2.1 ml, 15 mmol), CCl_4 (30 ml), $BrCF_2COOH$ (2.625 g, 15 mmol) and *p*-anisidine (2.22 g, 18 mmol) was added to a 100 ml flask. After stirring for 5 h under refluxing, the solvent was removed under reduced pressure, and the residue was extracted with hexane (3×50 ml). The filtrate was concentrated under reduced pressure and subsequent column chromatography with 5% ethyl acetate in hexane as eluent to afford bromodifluoroacetimidoyl chlorides (3.6 g, 81%) as a yellow oil.

Procedure 2: A mixture of bromodifluoroacetimidoyl chlorides (1.5 g, 5 mmol) and NaI (0.9 g, 6 mmol) in 10 ml acetone was stirred under N_2 atmosphere at room temperature for 10 h. The mixture was washed with saturated $Na_2S_2O_3$ and extracted with Et_2O (2×15 ml). The extracts were dried with Na_2SO_4 and concentrated under reduced pressure. Flash column chromatography with hexane as elucent gave *N*-(p-Anisyl)-2-bromo-2,2-difluoroace-timidoyl idide (1.7 g, 87%), yellow oil.

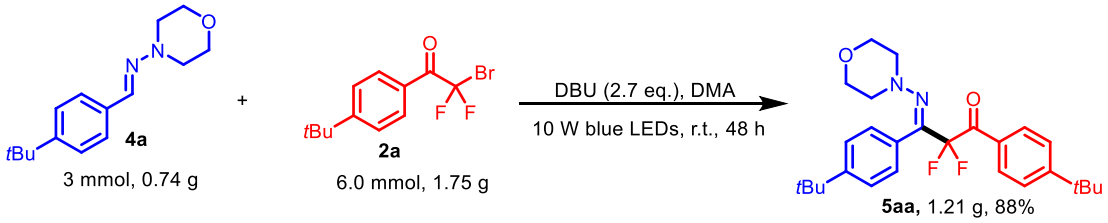
Procedure 3: A mixture of *N*-(*p*-Anisyl)-2-bromo-2,2-difluoroace-timidoyl idide (1.56 g, 4 mmol), phenylboronic acid (586 mg, 4.8 mmol), $PdCl_2(PPh_3)_2$ (140 mmg, 0.2 mmol), K_2CO_3 (1.1 mg, 8 mmol) and Ag_2O (463 mg, 2 mmol) was stirred in THF at 70 °C under N_2 atmosphere for 8 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography with 2% ethyl acetate in hexanes as elucent affording to **22** (1.02 g, 75%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.08 (m, 4H), 6.71 (q, *J* = 9.1 Hz, 4H), 3.73 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (t, *J* = 24.2 Hz), 157.8, 139.5 (, 130.9, 129.9, 129.3, 128.6, 123.6, 117.3 (t, *J* = 308.8 Hz), 113.9, 55.31 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -52.8 (s). This compound is known.[6]

6. Scale-up experiment



An oven-dried Schlenk tube (50 mL) was equipped with a magnetic stir bar, **1a** (3 mmol, 0.76 g), **2d** (1.5 equiv., 4.5 mmol, 1.12 g), Et_3N (2.0 equiv., 6 mmol, 0.8 mL). The flask was evacuated and

backfilled with N_2 for 3 times. 15 ml THF was added with syringe under N_2. The resulting solution was stirred at ambient temperature under 10 W blue LEDs irradiation and monitored by TLC. After the reaction was finished, the mixture was concentrated under vacuum to remove THF, and the residue was purified by chromatography on silica gel (EA/PE = 1/4) to afford the **3ad** 0.88 g, yellow oil.



5aa, 1.21 g, 88%

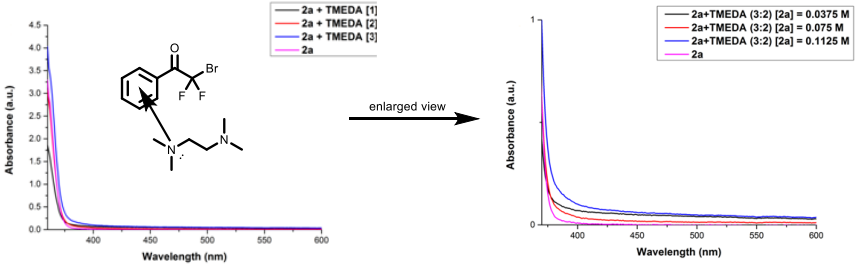
An oven-dried Schlenk tube (50 mL) was equipped with a magnetic stir bar, **4a** (3 mmol, 0.74 g), **2a** (2.0 equiv., 6.0 mmol, 1.75 g), DBU (2.7 equiv., 8.1 mmol, 1.2 mL). The flask was evacuated and backfilled with N_2 for 3 times. 15 ml DMA was added with syringe under N_2. The resulting solution was stirred at ambient temperature under 10 W blue LEDs irradiation and monitored by TLC. After 48 h, the crude products were extracted with ethyl acetate and water for three times. The extract was dried over anhydrous Na_2SO_4, and the solvent was removed. Flash chromatography (silica gel, petroleum / EtOAc = 10/1) afforded compound **5aa** (1.21 g, 88%).

7. Mechanistic consideration

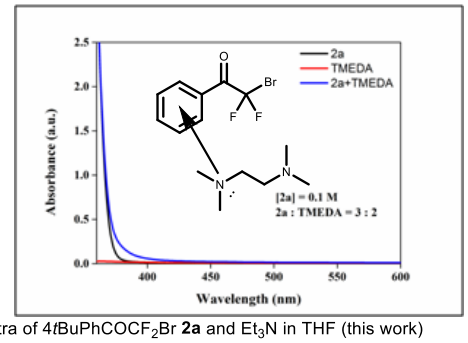
7.1 A brief mechanistic overview on C_{sp}^3-Br homolysis of $ArCOCF_2Br$ discovered by us

In the previous work[7] and this work, we proposed that photo-induced C_{sp}^3-Br bond homolysis from bromodifluoroacylarenes ($ArCOCF_2Br$) is the key step for the success of the radical difluoroalkylation reaction. The main reason that led us to propose this assumption is because the UV/Vis absorption spectrum does not show an obvious bathochromic shift in the visible range (Figure S1).

a) UV/Vis absorption spectra of $PhCOCF_2Br$ and TMEDA in MTBE



b) UV/Vis absorption spectra of $PhCOCF_2Br$ and TMEDA in MeCN



c) UV/Vis absorption spectra of 4*t*BuPhCOCF$_2$Br **2a** and Et_3N in THF (this work)

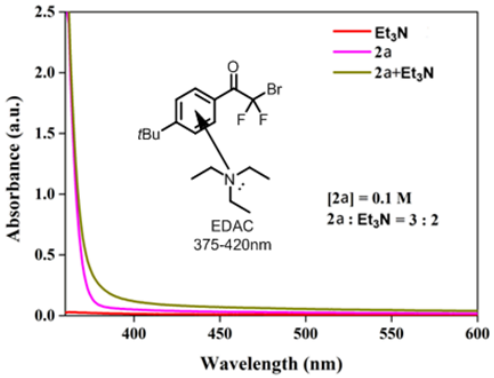


Figure S1. Optical absorption spectra of **PhCOCF$_2$Br** with **TMEDA**: a) reference from ***Adv. Synth. Catal.* 2017, *359*, 1672-1677**, b) reference from *Org. Lett.* 2019, *21*, 8169-8173, c) this work, optical absorption spectra of **2a** with Et_3N (recorded in THF in 1 mm path length quartz cuvettes using a Beijing Persee T9 series double beam UV-visible spectrophotometer).

On the contrary, the new curve of the solution between $PhCOCF_2Br$ and TMEDA (no visual appearance of the mixture) can be superimposed to the one of $PhCOCF_2Br$ in visible range (from 400nm) and ultraviolet zone (below 375 nm). In fact, most of the light absorption area of the reported EDACs is mainly concentrated in the visible light region (> 400 nm), thus the solution of the formed EDACs tends to have a color change, and the light source used can be blue LED strips. However, the residual near-ultraviolet zone (380-400 nm) of the compact fluorescent light (CFL) (Figure S2) maybe responsible for the observed reactivity.[8]

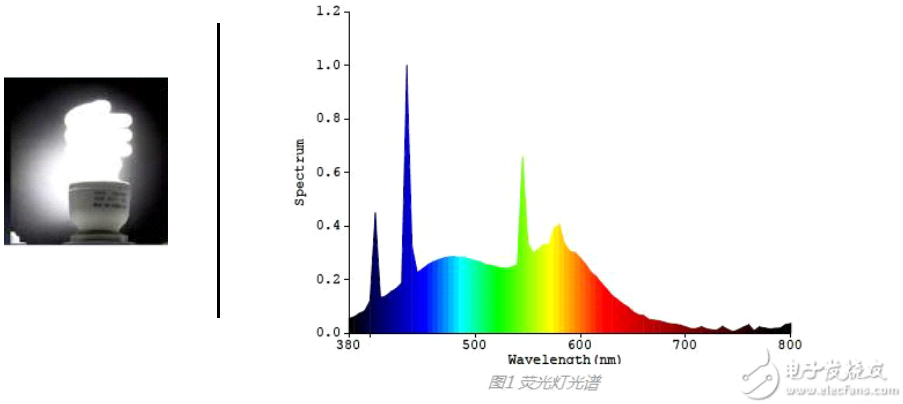


Figure S2. Fluorescent light spectrum.

To determine whether the residual near-ultraviolet zone (380-400 nm) of the CFL is responsible for the observed reactivity. Therefore, four monochromatic light sources were screened in the reaction of quinoxalin-2(1*H*)-one **1a** difluoroalkylation with bromodifluoroacylarene **2a** to explore the possibility of the reaction (Figure S3,). However, contrary to our hypothesis, after 16 hours of reaction, TLC detected that the near-ultraviolet light source (365nm and 394nm light source) could not make the reaction proceed, but the blue light (454nm) and green light (518nm) could make the reaction proceed smoothly. These results indicated that the near-ultraviolet light region of the fluorescent light had nothing to do with the reaction reactivity. The specific reaction operation is as follows:

Experimental procedure for monochromatic light experiments

There are four kinds of light source were screened in the reaction to explore the reaction possibility. The wavelengths of these monochromatic light sources are 365nm, 394nm, 454nm and 518nm respectively. To explore the reaction possibility under the irradiation of monochromatic light source, four reactions were conducted under the irradiation of above four monochromatic light source.

Procedures and results: triethylamine (56 μL, 0.4 mmol, 2.0 eq.), quinoxalinones **1a** (51 mg, 0.2 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 1.5 eq.) were added to four flame-dried Schlenk flasks, and each Schlenk flask was put into a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 mL, 0.2 M) was added and the flasks were sealed. The four reactions were then stirred under irradiation from 365nm, 394nm, 454nm, and 518nm monochromatic light source. After 16 hours, they were detected by TLC that the near-ultraviolet light source (365nm and 394nm light source) could not make the reaction proceed, but the blue light (454nm) and green light (518nm) could make the reaction proceed smoothly. The crude products of **DW-80c** and **DW-80d** were purified by column chromatography over silica gel using petroleum / EtOAc = 4/1 as eluent to yield **3aa** with yields of 54% (50 mg) and 63% (58 mg), respectively.

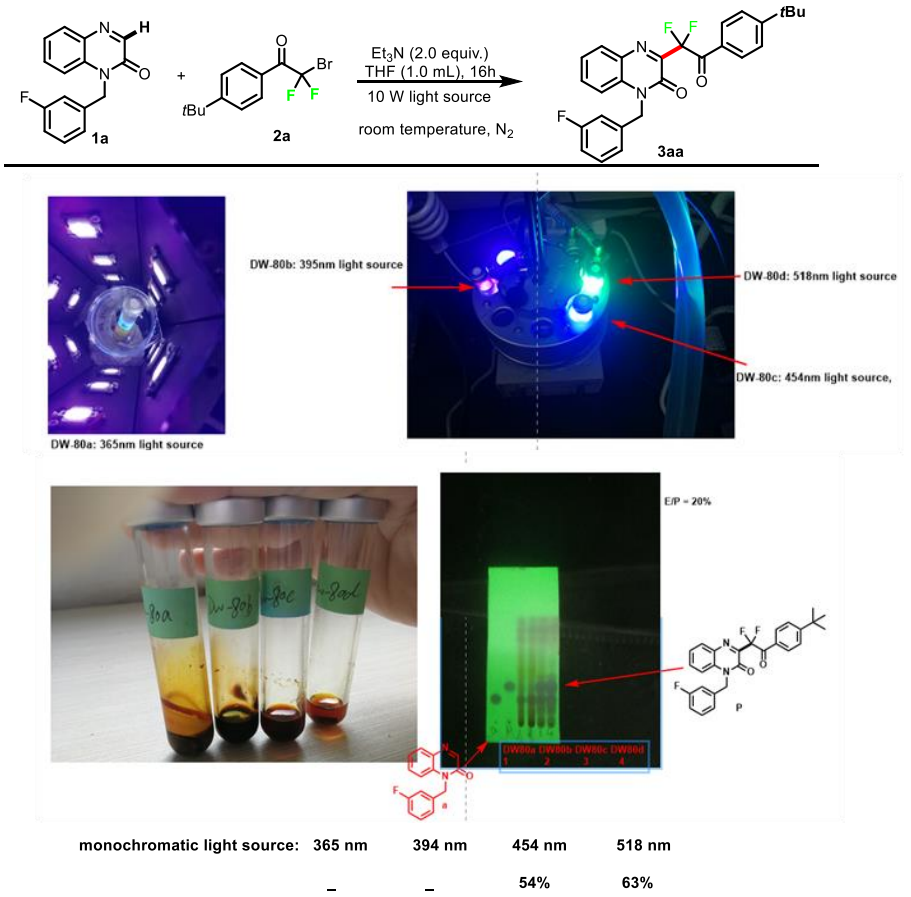


Figure S3. Monochromatic light experiments.

Stern-Volmer fluoresence quenching analysis showed that the excited state of $PhCOCF_2Br$ **2b*** could not be quenched by Et_3N, with the emission of **2b***, upon excitation at 362 nm, being abnormally enhanced by Et_3N (Figure S4).This result may indicate that there is no electron transfer event between **2b** and Et_3N.[9] The enhanced fluorescence may indicate that triethylamine promotes the generation of difluoroalkyl radicals (see Figure 8).

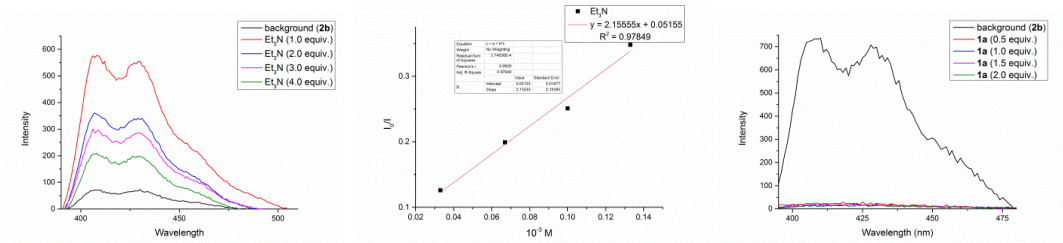


Figure S4. Fluorescence quenching studies of **2b** with Et_3N or **1a**.

Luminescence quenching experiments

Stern–Volmer studies were carried out on an Agilent Cary Eclipse fluorescence spectrophotometer.

Experimental procedures: All the bromodifluoroacylarene $PhCOCF_2Br$ **2b** (*in this manuscript*) solutions were excited at 362 nm and the emission intensity was collected at 380-500 nm. A screw-top

quartz cuvette was charged with a solution of **2b** (0.1 mmol, 16 uL) in dry THF (3.0 mL) and the initial emission was collected. Another two series of samples, 33 mM (M = mol/L) **2b** in THF with $Et_3N$and compound **1a** as quencher in gradient concentrations, were tested and the emissions were collected.

Figure S5. Agilent Cary Eclipse fluorescence spectrophotometer

The intensity of the emission peak at 407 nm (λ_{ex} = 362 nm) expressed as the ratio I_0/I, where I_0 is the emission intensity of **2b** at 407 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured. Quenching of **2b** was not observed for Et_3N, but fluorescence enhancement was observed.

Also, we performed a series of radical capture experiments to search for the ways to generate difluoroalkyl radical (33 W CFL). Indeed, after irradiation of **2b** and Et_3N in the presence of radical inhibitors, 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO), the oxyamination adduct of the bromodifluoroacylarene **2b-tempo** was formed in 23% yield by ^{19}F NMR. Next, we investigated the feasibility of the photolysis of the bromodifluoroacylarene in the presence of inorganic base or absence of base (Figure S6). Under CFL irradiation, upon addition of Cs_2CO_3 to the reaction mixture instead of Et_3N, we detected the formation of radical trapping product **2b-tempo**. On the other hand, when the trapping experiment was carried out under base-free conditions, the photolysis of **2b** still occurred albeit with low efficience at room temperature for 24h. These results indicated that the photo-induced C-Br bond homolysis of **2b** occurred to generate the difluoroacyl radical. In fact, a series of papers about light-induced C-I bond homolysis lately appeared and the light sources they used were usually blue LED strips.[10] Compared with the well-documented visible light-induced C-I bond homolysis, literatures about visible light induced C-Br bond homolysis are rare. This lack of development stems from the difficulty in the homolysis of the C-Br bond compared to the C-I bond when using low-energy visible light as the energy source.

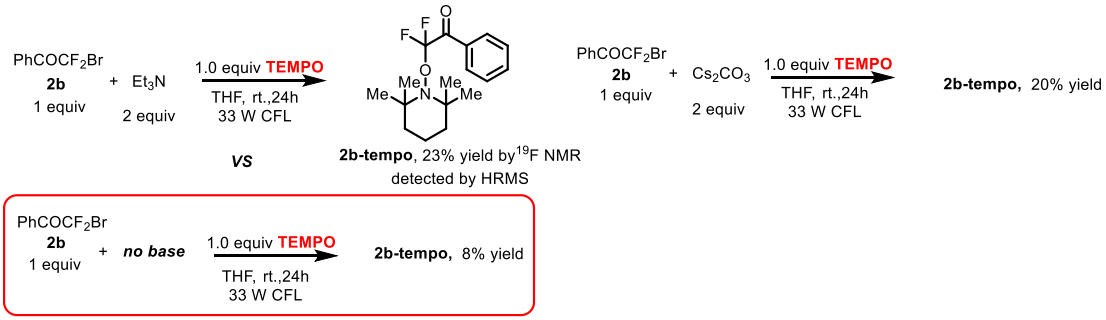
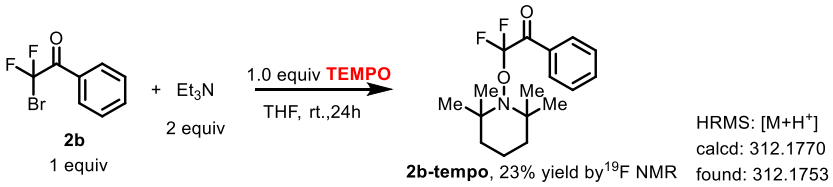
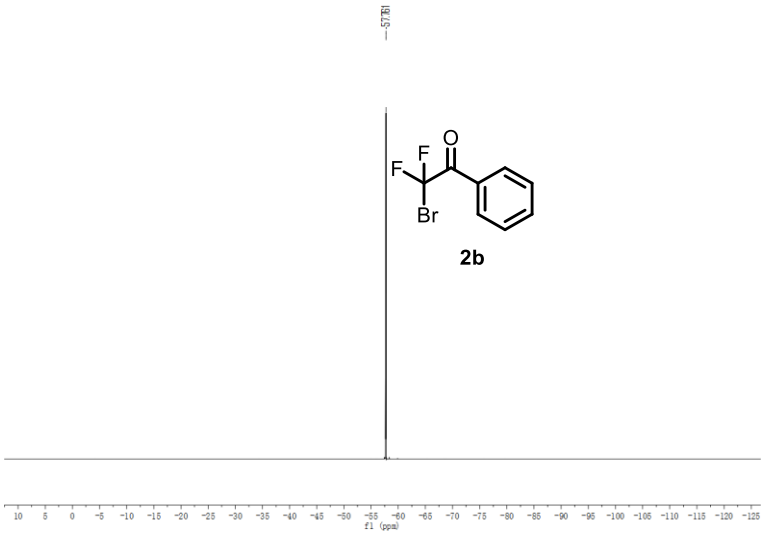


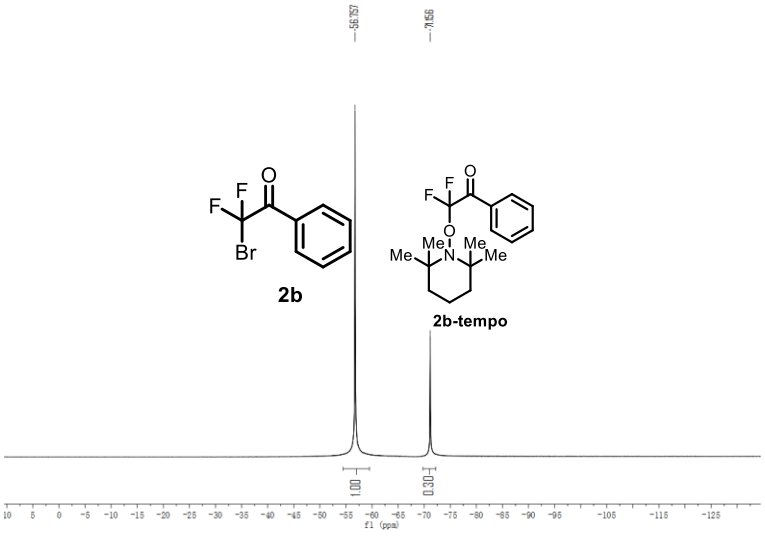
Figure S6. Radical capture experiments (33 W CFL).

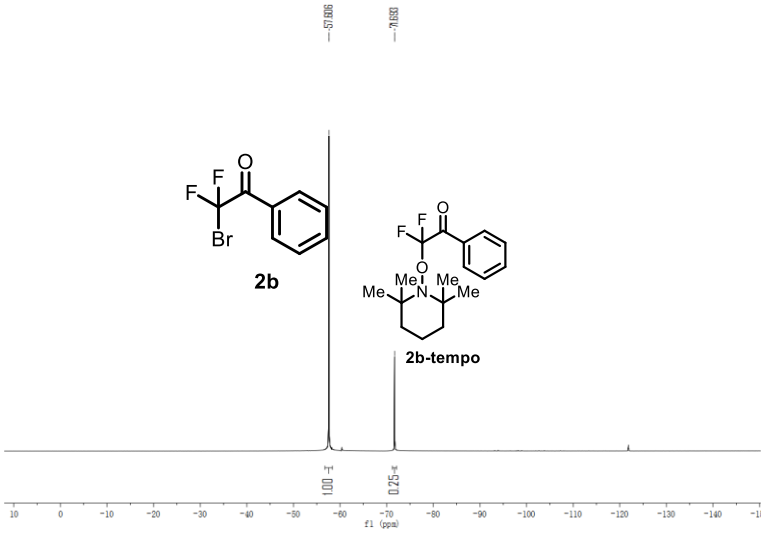
Trapping experiment with TEMPO radical (33 W CFL)

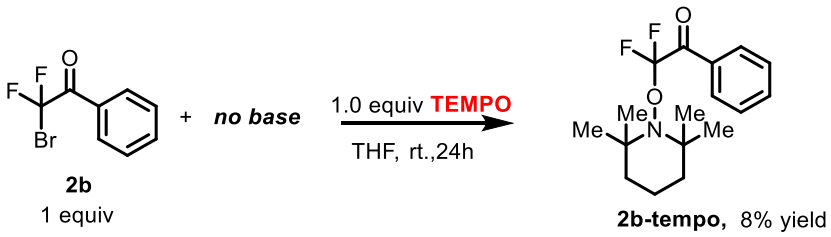
In four separate experiments, namely under standard conditions with organic bases in the absence of substrate **1a**, with inorganic base and no base, when 1.0 equivalent of TEMPO (with respect to the bromo derivatives) was added to the reactions, after long exposure to irradiation (24h), the corresponding alkylfragment of the halides (oxyamination at the *alpha*-phenacyl positions) were formed. The results may suggest the formation of the radical species involved in our reaction conditions.

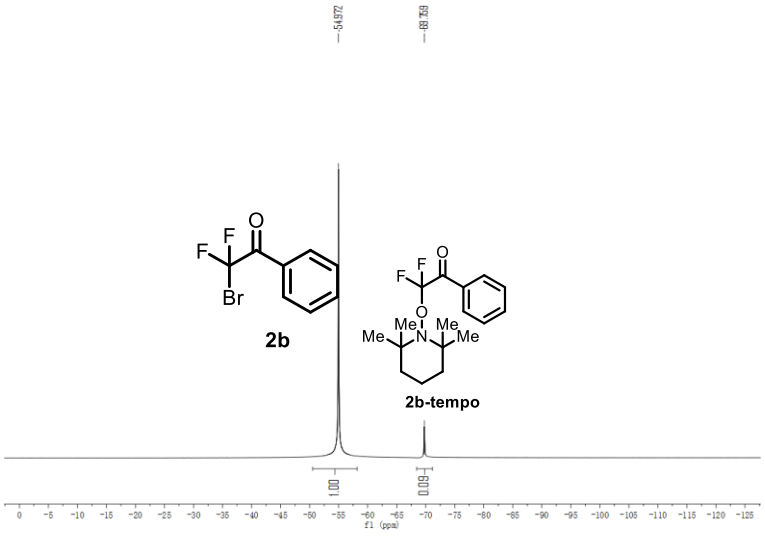












To determine whether the blue light zone (around 450 nm) of the CFL plays an important role in the reactivity of this transformation, and to further find evidence that C-Br bond homolysis is indeed present in the transformation. We synthesized the difluorobromoaryl ketone containing a nitrogen atom (**2l**), which will help to better detect the reaction intermediates in high-resolution mass spectrometry (HRMS) analysis. With **2l** in hand, three experiments were operated under irradiation of 10 W blue LEDs (454 nm) at room temperature (Figure S7). First, subjecting **2l** alone to blue LEDs irradiation observed the formation of a dimer **2l-dimer** and H-atom-transfer product **2l-H** by HRMS analysis. This result indicated that C-Br bond homolytic pathway indeed occurs in

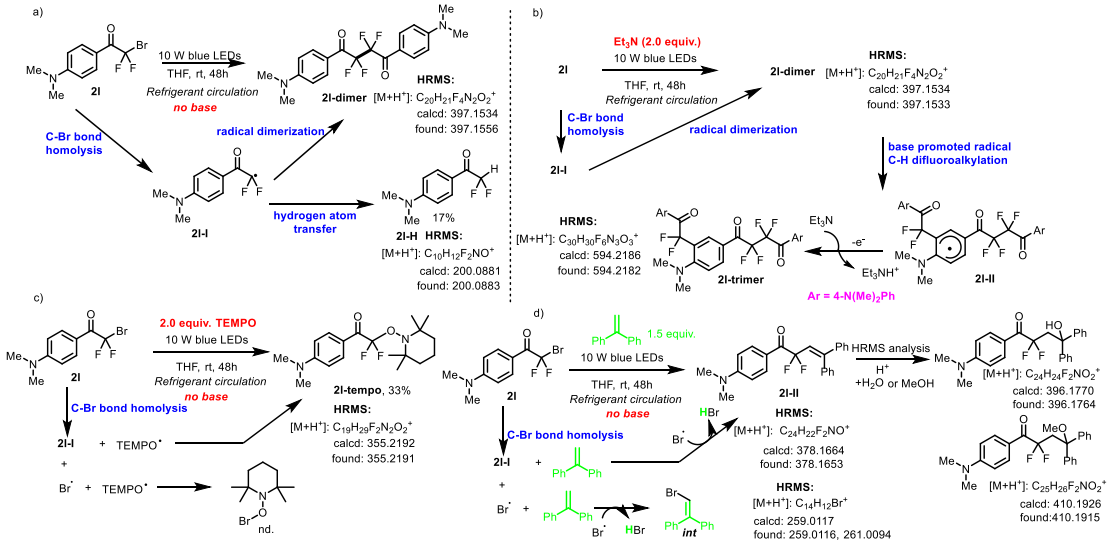
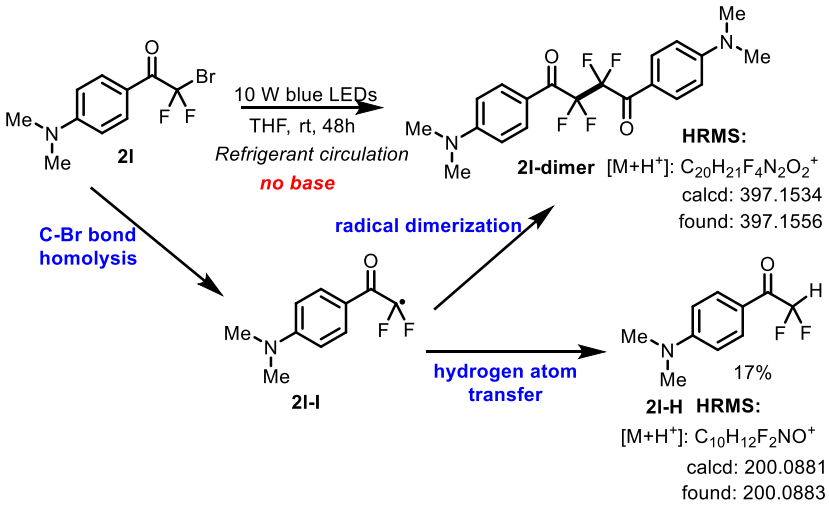


Figure S7. Evidence of C-Br bond homolysis under irradiation of blue LEDs.

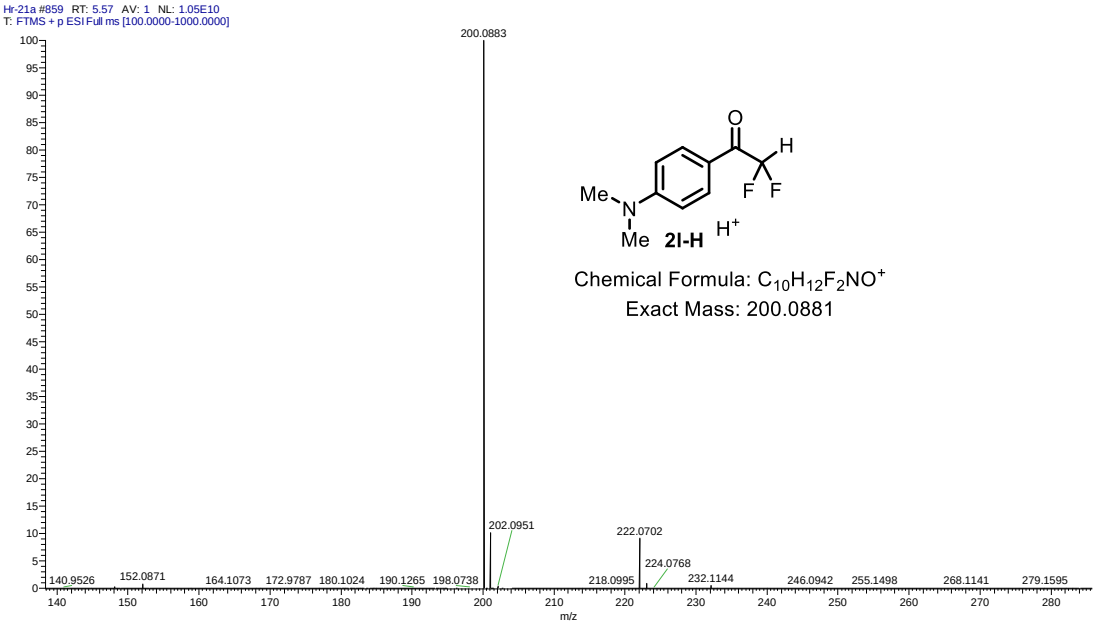
our method. Subsequently, irradiating **2l** in the presence of Et_3N could not only form **2l-dimer**, but also produce radical C-H difluoroalkylation product **2l-trimer** via base-promoted homolytic aromatic substitution (BHAS).[11] This result further confirmed that C-Br bond homolysis can also proceed in the presence of tertiary amines, and also emphasized the role of tertiary amines in C-H difluoroalkylation[7b] or tandem radical cyclization.[7a] In addition, the role of tertiary amines is far more than that, it may also be a quencher of bromine radicals produced during the transformation (*vide infra*). Finally, irradiating

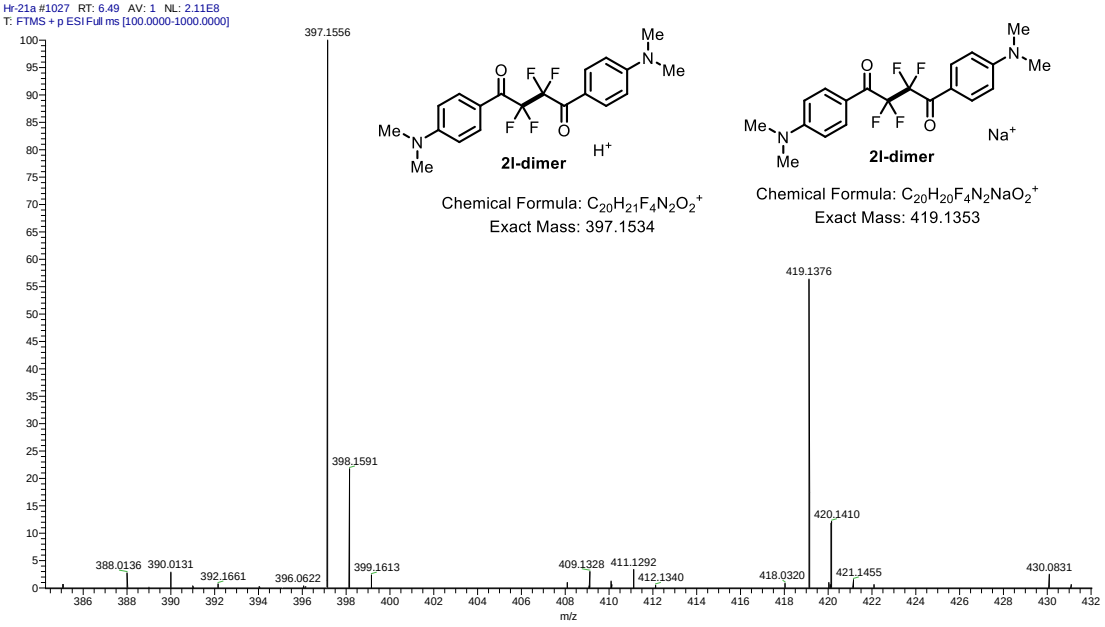
2l alone in the presence of TEMPO confirmed that the reaction proceeds *via* radical pathway, with difluoroalkyl radical trapping product **2l-tempo** detected by HRMS analysis (Figure S7).

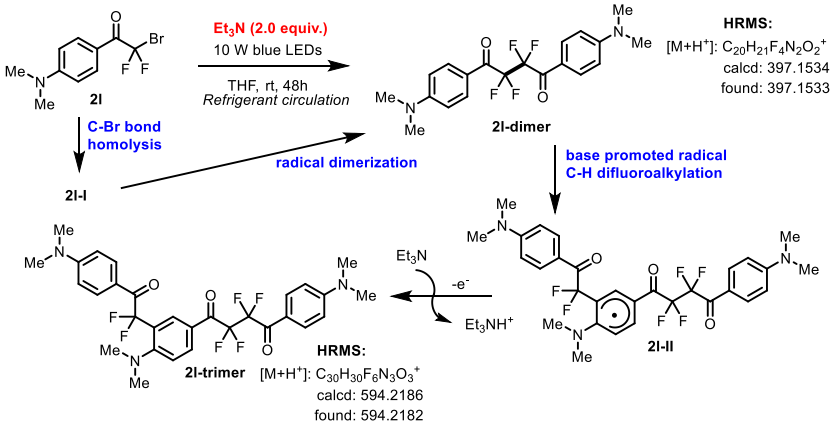
Experiments for evidence of C-Br bond homolysis under irradiation of blue LEDs



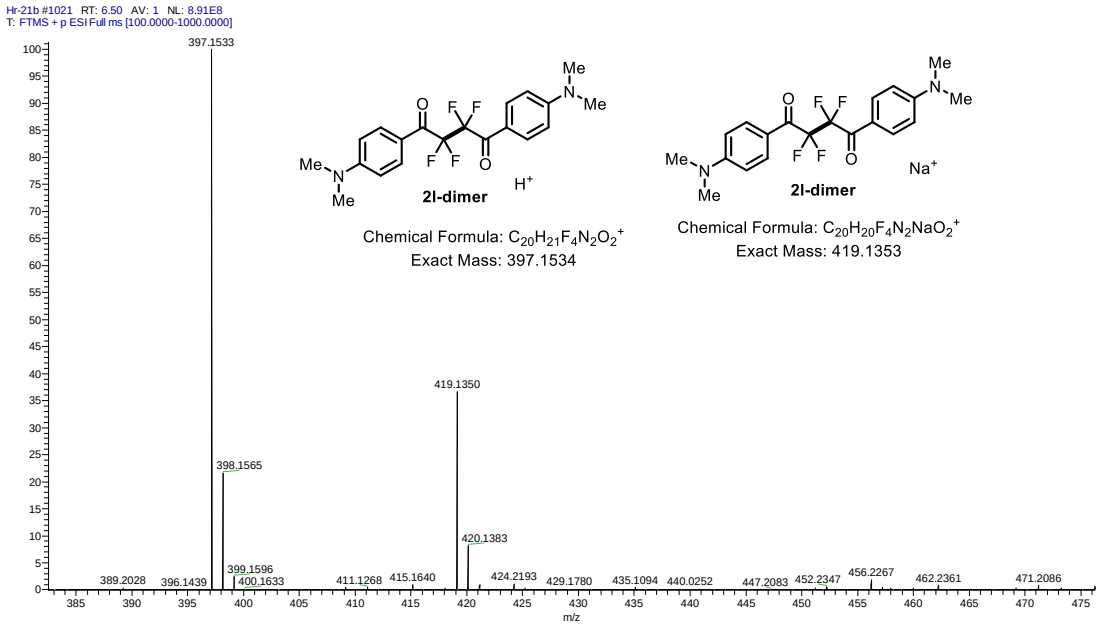
α-Bromo difluoroacylarene **2l** (56 mg, 0.2 mmol) was added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs (λ_{max} = 454 nm). After 48 h, the reaction solution was directly used for high-resolution mass spectrometry (HRMS) analysis. The reaction mixture was purified by column chromatography over silica gel using petroleum/EtOAc = 20/1 as eluent to yield **2l-H** (9 mg, 17%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 9.0 Hz, 2H), 6.26 (t, *J* = 54.0 Hz, 1H), 3.11 (s, 6H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 185.1 (*t*, *J* = 24.2 Hz), 154.4, 132.0, 132.0, 119.3, 111.8 (t, *J* = 253.3 Hz), 110.9, 40.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.02 (d, *J* = 53.8 Hz) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{10}H_{12}F_2NO^+$ 200.0881; found 200.0883.

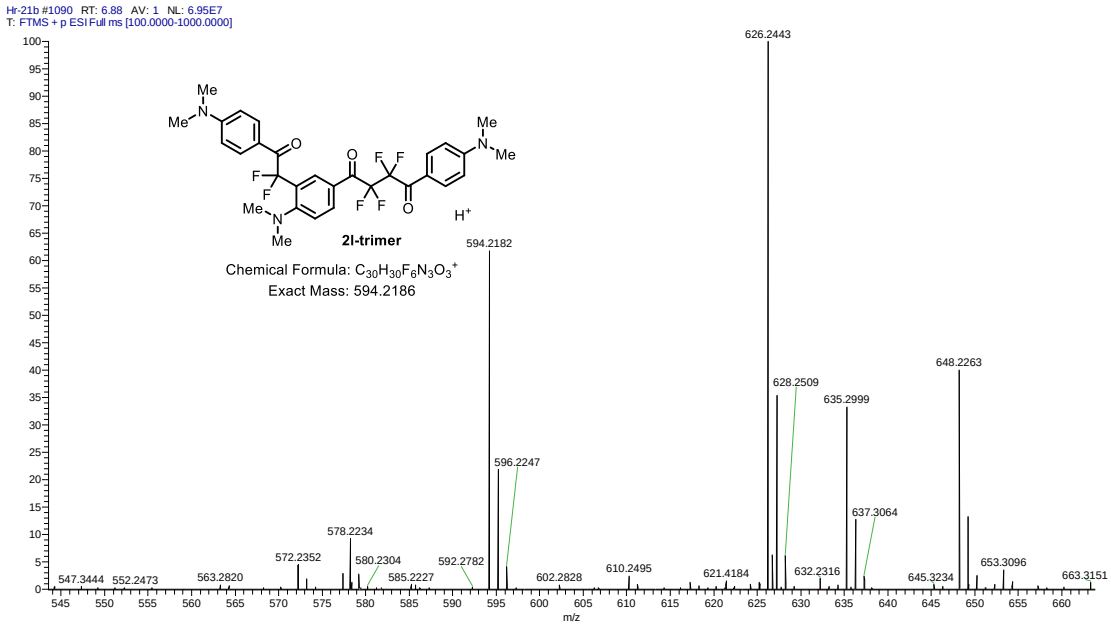


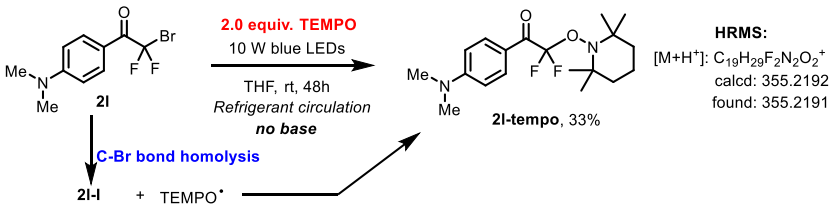




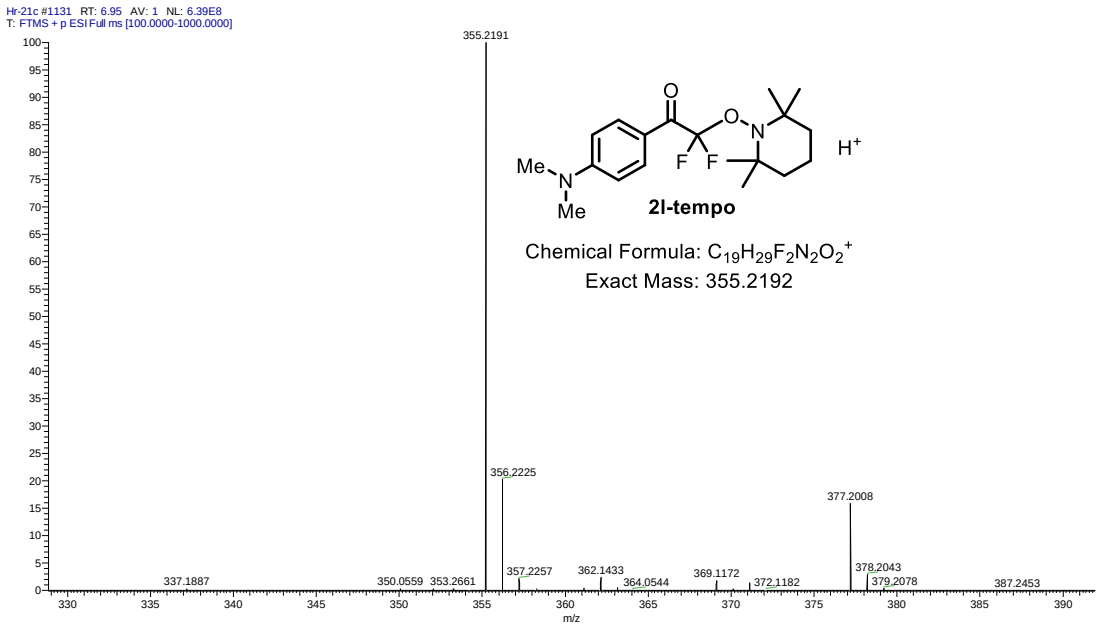
α-Bromo difluoroacylarene **2l** (56 mg, 0.2 mmol) and triethylamine (56 μL, 0.4 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three time**s**. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs (λ_{max} = 454 nm). After 48 h, the reaction solution is directly used for HRMS analysis.

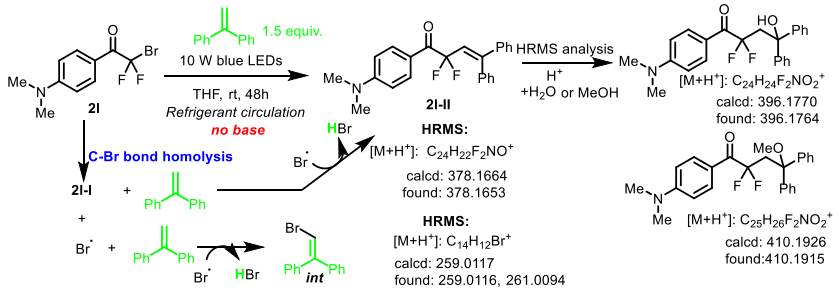




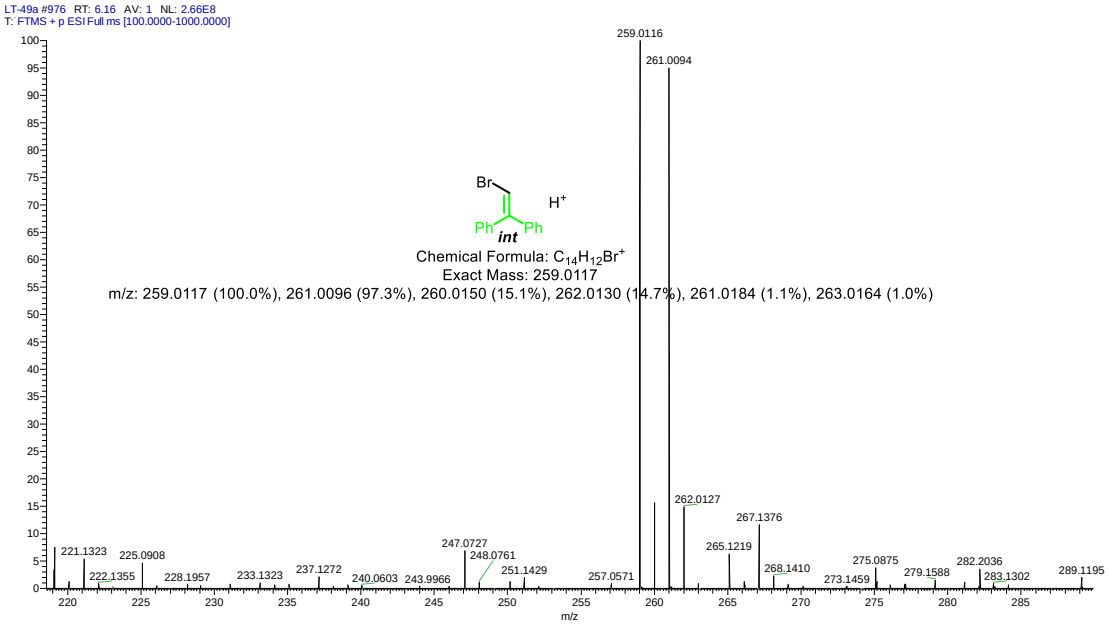


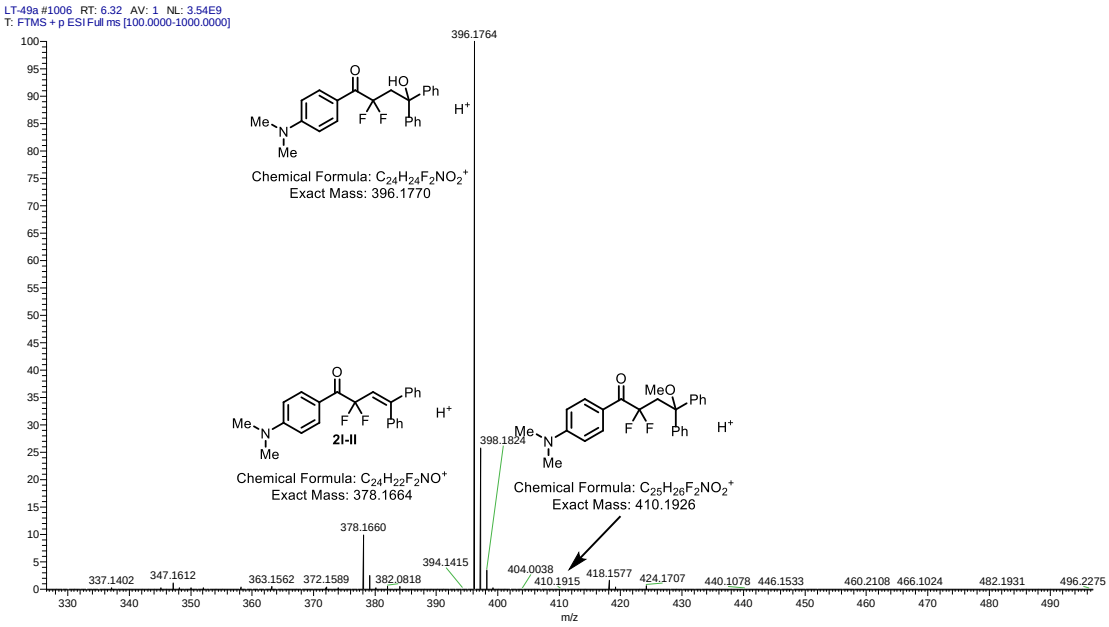
α-Bromo difluoroacylarene **2l** (56 mg, 0.2 mmol) and TEMPO (62 mg, 0.4 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs (λ_{max} = 454 nm). After 48 h, the reaction solution is directly used for HRMS analysis. The reaction mixture was purified by column chromatography over silica gel using petroleum/EtOAc = 20/1 as eluent to yield **2l-tempo** (23 mg, 33%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 9.0 Hz, 2H), 3.10 (s, 6H), 1.71–1.52 (m, 5H), 1.26 (s, 7H), 1.14 (s, 6H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 182.0 (t, *J* = 35.9 Hz), 154.1, 132.9, 119.0, 117.6 (t, *J* = 277.5 Hz) 110.7, 61.1, 40.2, 40.1, 33.9, 21.0, 17.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.29 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{19}H_{29}F_2N_2O2^+$ 355.2192; found 355.2191.





α-Bromo difluoroacylarene **2l** (56 mg, 0.2 mmol) and ethene-1,1-diyldibenzene (53 μL, 0.3 mmol, 1.5 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs (λ_{max} = 454 nm). After 48 h, the reaction solution is directly used for HRMS analysis.





Combining the results of UV/Vis absorption, monochromatic light experiments, Stern-Volmer fluoresence quenching analysis, radical trapping experiments as well as other control and comparative experiments, our investigations support a mechanism that the photo-induced C_{sp}^3-Br bond homolysis of bromodifluoroacylarenes instead of photochemical EDACs of tertiary amines and bromodifluoroacylarenes occurs to generate the difluoroacyl radicals and bromine radicals

simutaneously. Regardless of the mechanism proceeded, the role of the tertiary amines in this strategy is very important, which could be confirmed in our previous and current work.

7.2 Experimental demonstration of the HAT of N=C_{sp}^2-H of aldehyde hydrazones or quinoxalinones by bromine radical

Although we have made the above latest progress on the visible light-induced C_{sp}^3-Br bond homolysis mechanism of difluorobromoaryl ketones, the exact role of tertiary amines in the reaction system cannot be fully explained, mainly manifested in reactivity (the reaction cannot proceed smoothly without the tertiary amines) and TEMPO-mediated radical quenching experiments, compared with no tertiary amines, the addition of tertiary amines will promote the formation of more difluoroalkyl radical quenchers, which indicates that tertiary amines can promote difluoroalkyl radicals formation. If it is not the EDACs mechanism, how does it promote it? It may be inspired by a report recently published by Leonori in *Science* **2020**, *367*, 1021 that α-amine alkyl radicals can induce a series of alkyl halides to generate alkyl radicals through XAT (halogen atom transfer),[12] but this assumption is yet to be tested.

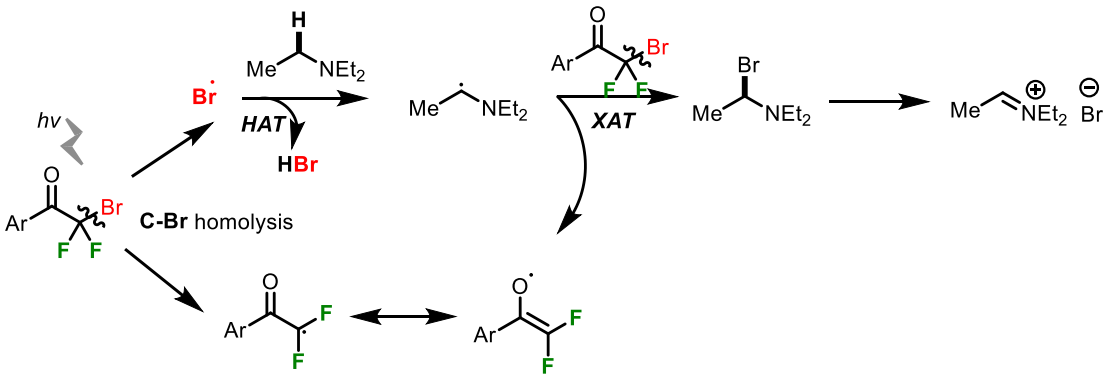


Figure S8. Hypothesis for tertiary amines to promote the generation of difluoroalkyl radicals.

As shown in Figure S8, the electrophilic bromine radicals generated by visible light-induced homolysis of the C-Br bonds of difluorobromoaryl ketones can mediate tertiary amines to generate nucleophilic α-amine alkyl radicals through hydrogen atom transfer (HAT)[13]. According to Leonori's report, the nucleophilic amine alkyl radicals are electrically matched with the electrophilic active alkyl halide $ArCOCF_2Br$, and the nucleophilic difluoroalkyl radical will be obtained by the XAT process. In fact, the last five years have seen a boom in chemical transformations mediated by bromine radicals,[14-16] in which bromine radicals often act as HAT reagents (Figure S9).[14-15]

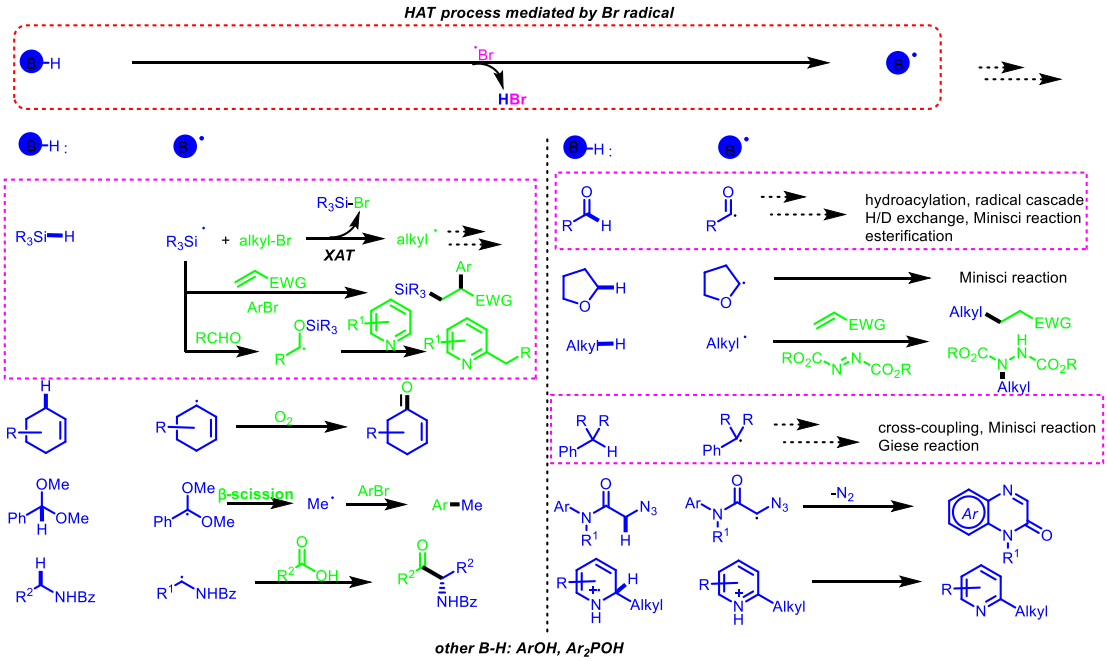


Figure S9. Known bromine radical-mediated HAT types.

For example, MacMillan reported in 2016 that visible light/nickel synergistic catalysis of bromine radical-mediated HAT of silicon-hydrogen could generate nucleophilic silane radicals, and silane radicals could activate alkyl bromides through the XAT process to obtain nucleophilic alkyl radicals, and then realized the coupling reaction of alkyl bromide and aryl bromide.[14a] After that, reports using this strategy to induce silanes to generate silane radicals sprang up, and a series of interesting chemical transformations were developed.[14] In addition, bromine radicals can also cleave many types of C-H bonds to obtain nucleophilic carbon radicals, such as allyl C_{sp}^{3}-H[15a], acetal C_{sp}^{3}-H[15b], amine α-C_{sp}^{3}-H[15c], ether α-C_{sp}^{3}-H[15d-e], alkyl C_{sp}^{3}-H[15f], carbonyl α-C_{sp}^{3}-H[15g], benzyl C_{sp}^{3}-H[15h-l] aldehyde C_{sp}^{2}-H[15m-o], and some reaction intermediates C-H[14j]. In particular, the aldehyde C_{sp}^{2}-H and benzyl C_{sp}^{3}-H are the most widely studied.

Based on the background of the above-mentioned bromine radicals and the activity of N=C_{sp}^{2}-H, an analog of aldehyde C_{sp}^{2}-H derived from hydrazones or quinoxalinones, we believe that the reaction mechanism of this work may be different from the radical chain mode we reported previously (Figure S10).

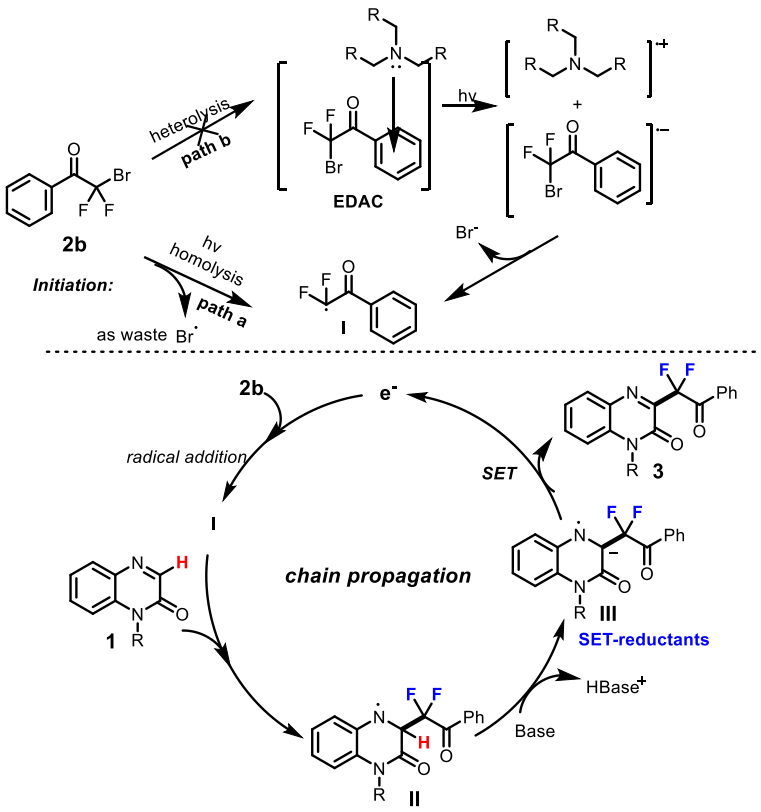


Figure S10. Radical chain mechanism (electron as a catalyst).

In order to prove whether the reaction is a radical chain mechanism, we performed a photon quantum yield and light on/off experiments. However, both the quantum yield (**Φ** < 0.055), estimated by chemical actinometry, and the light on/off experiment of this C-H difluoroalkylation reaction indicate that closed radical chain pathway is not possible in this reaction[16] and indirectly proves the important role of continuous irradiation in keeping the difluoroalkyl radical induced as the persistent $ArCOCF_2^{\cdot}$ species. The following is the specific experimental operation for measuring quantum yield and "On/off" experiment.

Reaction quantum yield (Φ)measurment

According to the above experimental results, we plan to use a monochromatic light source with a wavelength of 454nm as the light source of the reaction quantum yield experiment.

Determination of the light intensity at 454 nm

The quantum yield of the reaction was measured by chemical actinometry using 454 nm blue LEDs using potassium ferrioxalate following the procedure of E. E. Wegner (*J. Am. Chem. Soc.* **1966**, *88*, 394), J. N. Demas (*J. Phys. Chem.* **1981**, *85*, 2766), F. Glorius (*Org. Lett.* **2018**, *20*, 1546), R. Shang (*Science*, **2019**, *363*, 1429), J. Zhong (*Chem. Commun.* **2019**, *55*, 10848) and T. P. Yoon (*Chem. Sci.* **2015**, *6*, 5426).

0.737 g of potassium ferrioxalate trihydrate was dissolved in 10 mL H2SO4 (0.05 M) and stored in the dark. Then, a buffer solution was prepared by dissolving 2.5 g of sodium acetate and 0.5 mL of H2SO4 (95-98%) in 50 mL of distilled water.

General Protocol to assess the photon flux of the 454 nm blue LEDs:

To a 10 mL Schlenk flask containing a stirring bar, 1 mL of the actinometer solution was added. Then, the solution was irradiated for 60 s. Immediately, a 100 µL aliquot was taken and added to a 10 mL volumetric flask containing 15 mg of 1, 10-phenanthroline in 3 mL of the buffer solution. The flask was filled with distilled water. The absorbance of this solution was then measured at 510 nm by UV/Vis spectrophotometry. In a similar manner, this procedure is repeated with the actinometer solution stored in the dark. Using then the Beer's Law, the number of moles of Fe2+ produced by light irradiation is obtained by:

$$Fe^{2+} = \frac{v_1 v_3 \Delta A(510\,nm)}{10^3 v_2 l \varepsilon(510\,nm)}$$

Where:

v1 = Irradiated volume (1 mL).

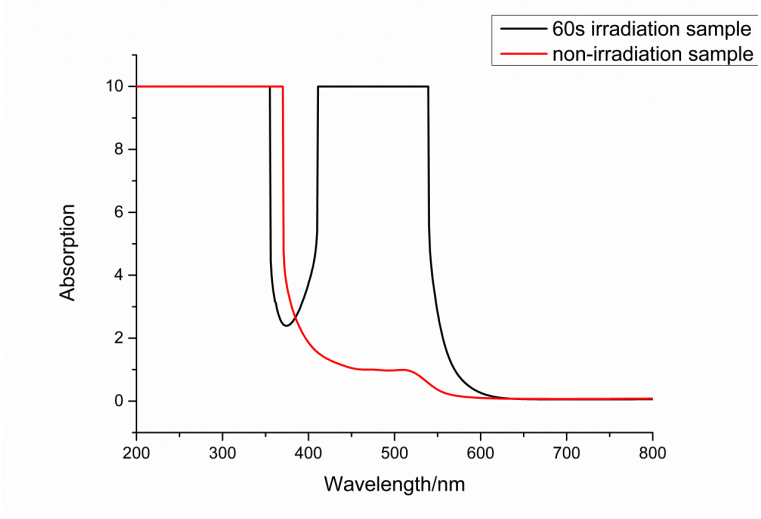
v2 = The aliquot of the irradiated solution taken for the estimation of Fe^{+} ions (0.100 mL).

v3 = Final volume of the solution after complexation with 1, 10-phenanthroline (10 mL).

ε(510 nm) = Molar extinction coefficient of $[Fe(Phen)3]^{2+}$ complex (11100 L $mol^{-1}cm^{-1}$).

l = Optical path-length of the cuvette (1 cm).

ΔA(510 nm) = absorbance difference between the irradiated solution and the solution stored in dark.



Sample calculation:

The photon flux (**F**) is obtained by using the following equation:

$$\text{photon flux} = \frac{\text{mol } Fe^{2+}}{\Phi \bullet t \bullet f}$$

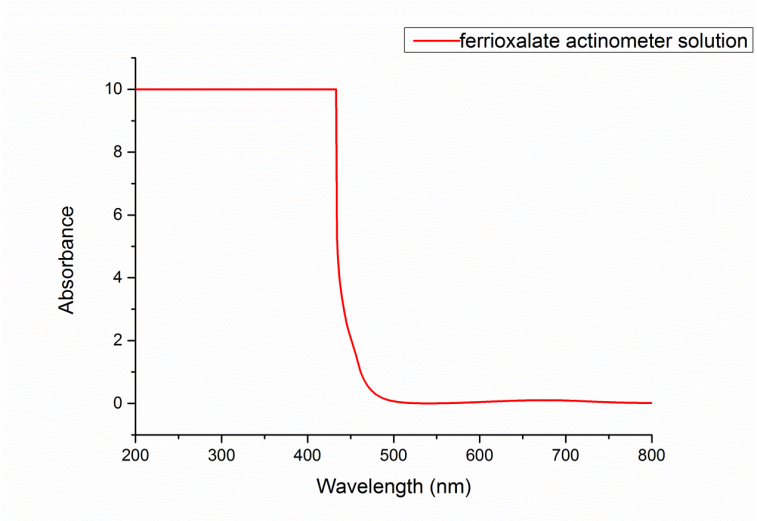
Where:

Φ (λ) = The quantum yield for Fe^{2+} formation at 454 nm is 0.95 (Hatchard, C. G.; Parker, C. A. *Proc. Roy. Soc. (London)* **1956**, *A235*, 518–536). t is the time (60 s), and f is the fraction of light absorbed at λ = 454 nm by the ferrioxalate actinometer. This value is calculated using the following equation where

A is the absorbance of the ferrioxalate solution at 454 nm.

$$f = 1 - 10^{-A}$$

A(λ) = ferrioxalate actinometer absorbance at 454 nm, which was measured placing 1 mL of the solution in a cuvette of path length 1 cm by UV/Vis spectrophotometry. The absorbance of the above ferrioxalate solution at 454 nm was measured to be 1.735, so the value of f is 0.9816.



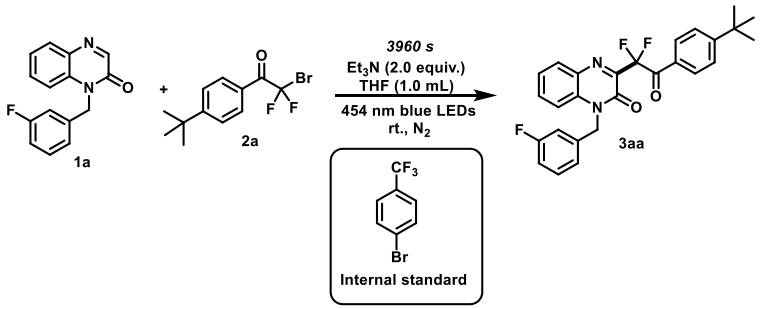
The photon flux was calculated to be 1.45 x 10^{-6} einstein s^{-1}

Sample calculation:

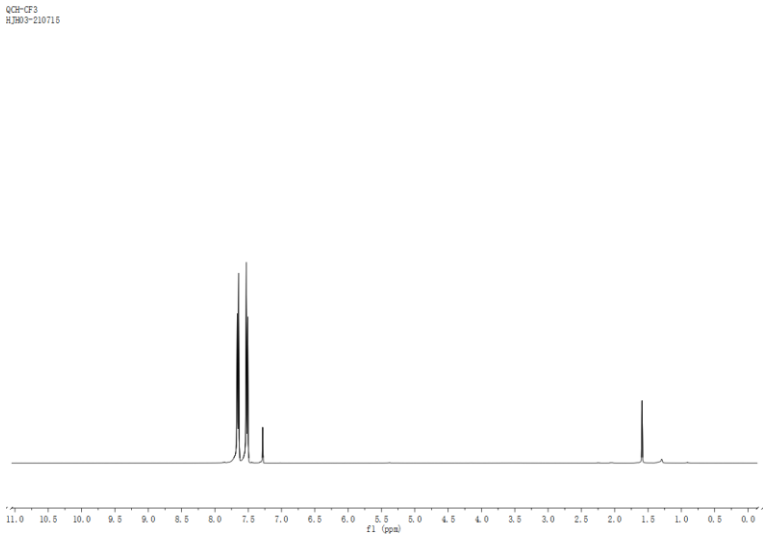
$$\text{photon flux} > \frac{8.1 \times 10^{-5}\ \text{mol}}{0.95 \times 60\ \text{s} \times 0.9816} = 1.45 \times 10^{-6}\ \text{einstein}\ \text{s}^{-1}$$

Determination of the reaction quantum yield

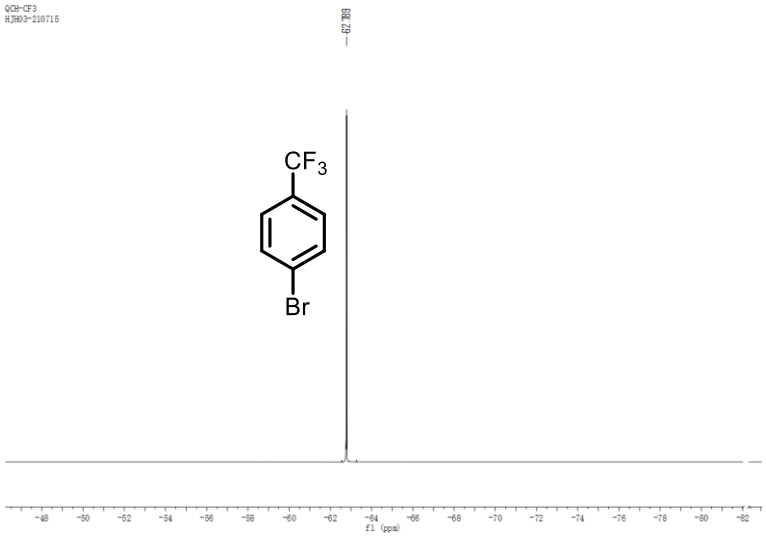
To obtain the quantum yield (Φ) of the difluoroalkylation of quinoxalinones. The number of moles of the product **3aa** were determined by ***^{19}F NMR*** analysis using 1-bromo-4-(trifluoromethyl)benzene (0.1 mmol, 14 uL) as internal standard. As such, this reaction was performed under the set of optimized reaction conditions (Table 1, entry 1) under visible light irradiation of 454 nm blue LEDs. After 3960 s of light irradiation, 6.4 x 10^{-5} moles of **3aa** were obtained.



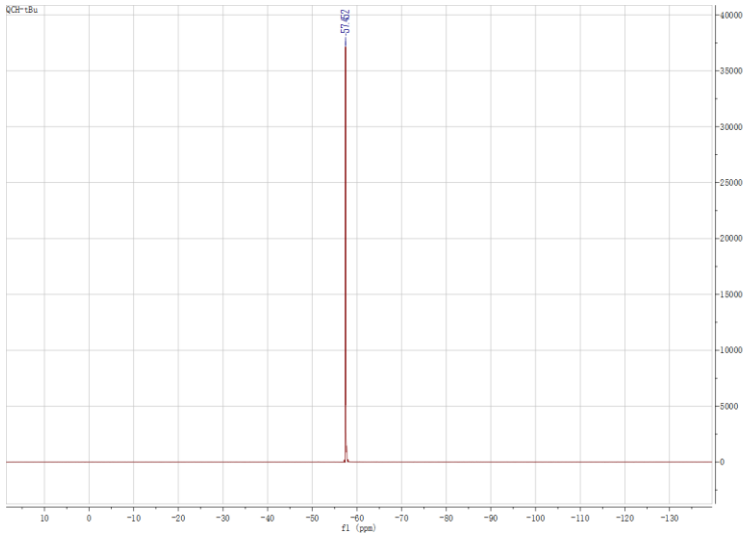
^{1}H-NMR of internal standard



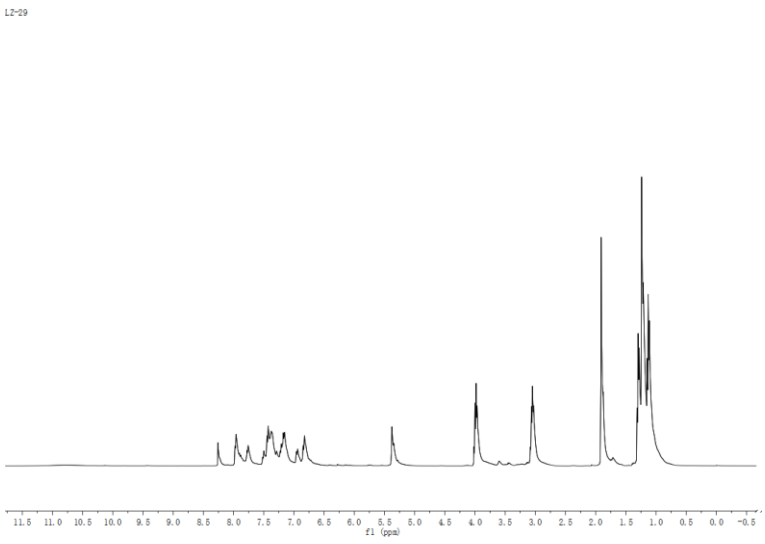
^{19}F-NMR of internal standard



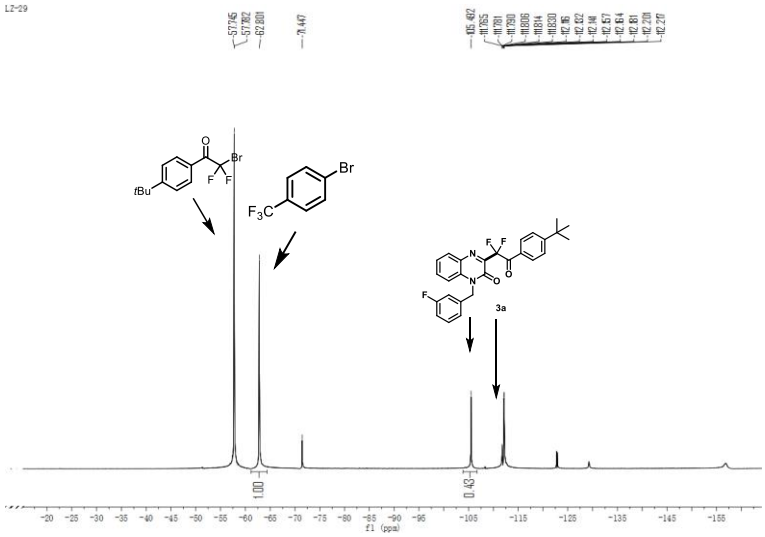
^{19}F-NMR of **2a**



^{1}H-NMR of reaction mixture



^{19}F-NMR of reaction mixture



The quantum yield of this reaction was calculated using the following equation:

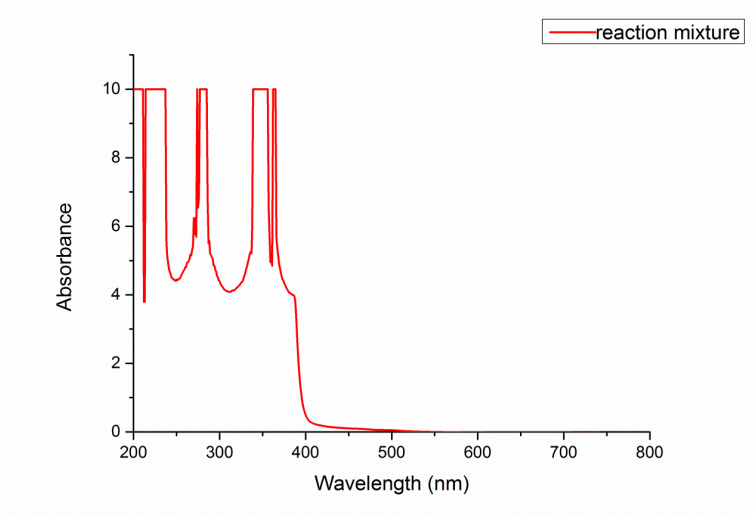
$$\Phi = = \frac{mol\ of\ product\ formed}{photon\ flux \bullet t \bullet f}$$

$$f = 1 - 10^{-A}$$

Where:

A(454 nm) = is the absorbance at 454 nm of the reaction which was measured placing 1 mL of the solution in a cuvette of path length 1 cm by UV/Vis spectrophotometry. The absorbance of the reaction mixture at 454 nm was measured to be 0.098, so the value of f is 0.202.

t = is the reaction time 3960 s

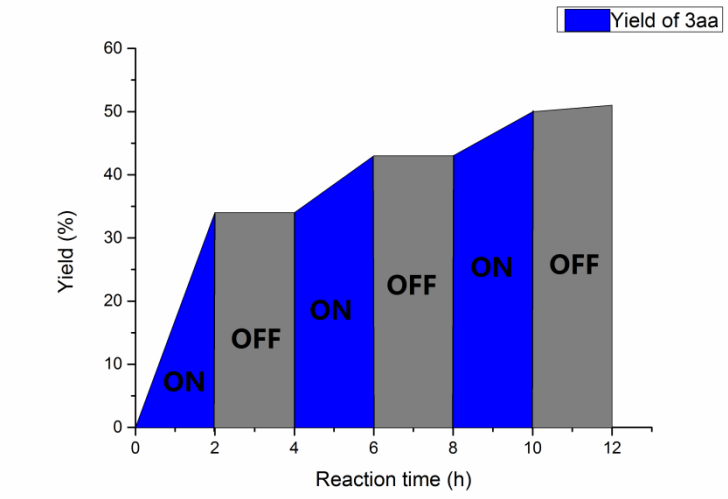


The quantum yield (Φ) of the reaction is less than 0.055 (see calculation below)

$$\Phi = \frac{mol\ of\ product\ formed}{photon\ flux \bullet t \bullet f} < \frac{6.4 \times 10^{-5}\ mol}{1.45 \times 10^{-6}\ einstein\ s^{-1} \times 3960 \times 0.202} = 0.055$$

"On/off" experiment

According to the **Method A**. The reaction mixture was irradiated for 2 hours. An aliquot of 0.10 mL was taken from the reaction mixture and injected into a vial containing 0.50 mL of $CDCl_3$ containing 1-bromo-4-(trifluoromethyl)benzene (0.1 mmol, 14 uL) as the internal standard. The yield of product was determined by crude ***^{19}F NMR*** analysis. The reaction mixture was then sealed under N_2 atmosphere and re-subjected to 10 W blue LEDs. The yields later on were determined in the same way after some time light on or off.



From the quantum yield and light on/off experiments, we knew that the reaction is not a radical chain mechanism and considering the HAT properties of the aforementioned bromine radicals, we speculated that the reaction mechanism may involve the imine or aldehyde hydrazone radicals through

the HAT of N=C_{sp}^2-H of aldehyde hydrazones or quinoxalinones mediated by bromine radicals, which then were coupled with the difluoroalkyl radical to obtain the target products (Figure S11).

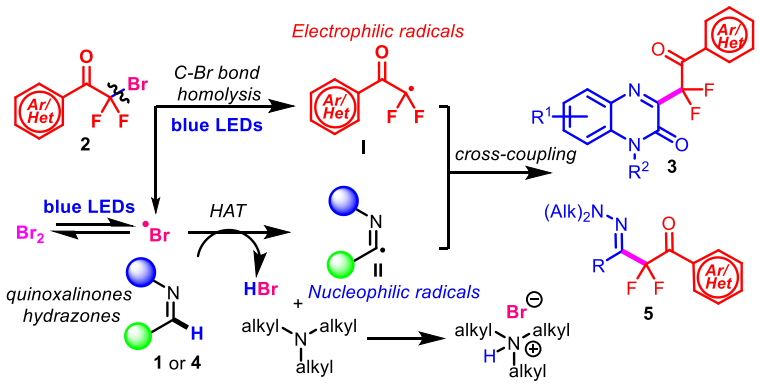
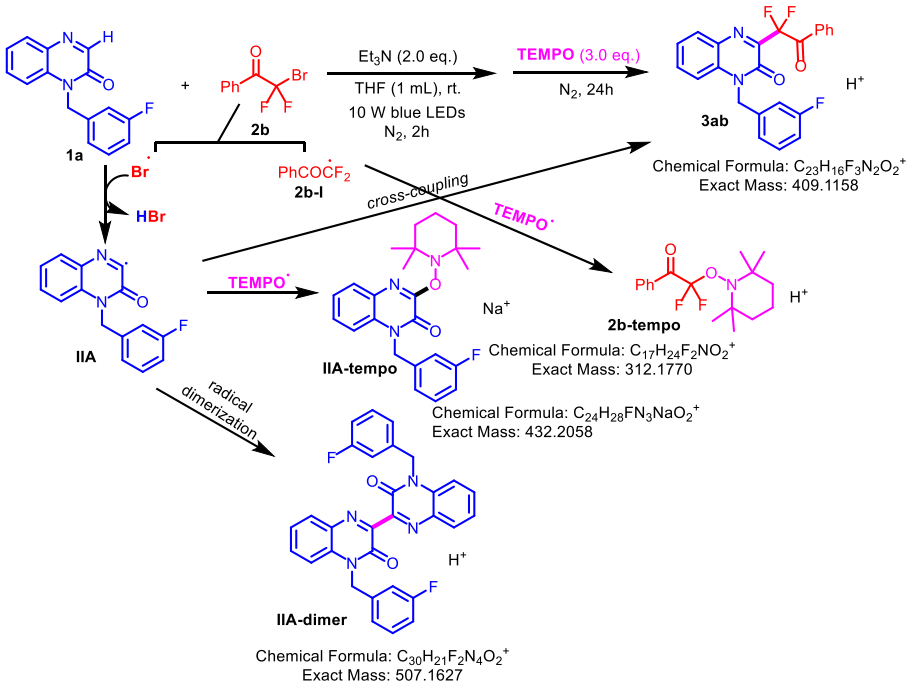


Figure S11. Non-radical chain mechanism (Br radicals mediated the C_{sp}^2-H coupling)

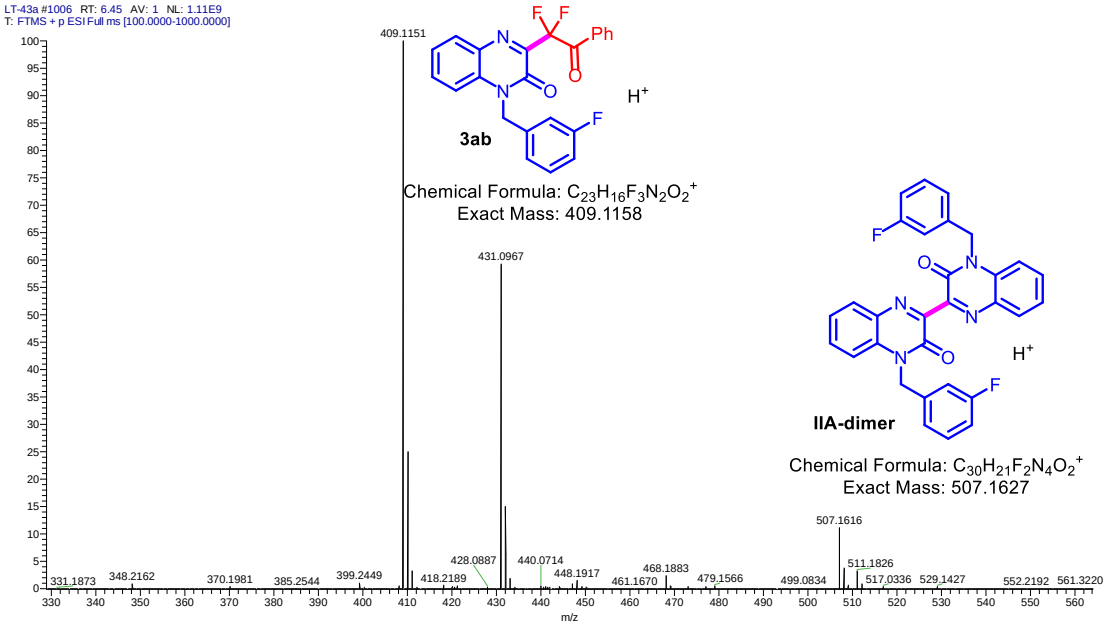
This inference was confirmed in subsequent radical trapping experiments and HRMS analysis, as shown in Figure S12 and S13, we detected TEMPO radical-trapping products of quinoxalinone or hydrazone radicals and their dimers.

The following are the specific experimental operations:

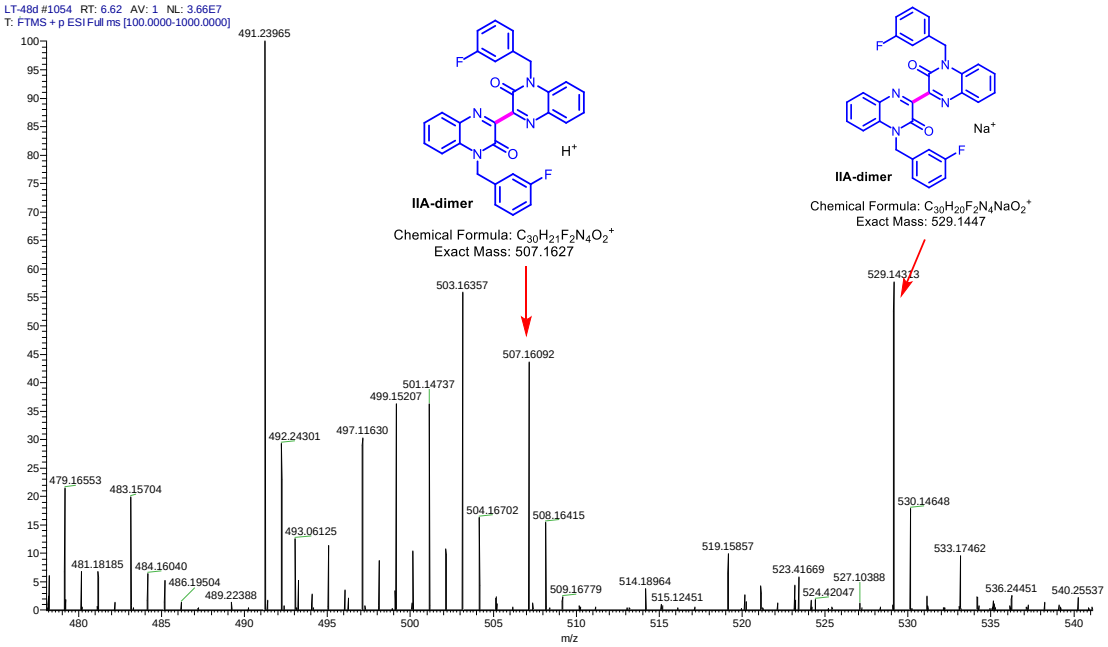


Experimental procedure: Triethylamine (56 μL, 0.4 mmol, 2.0 eq.), quinoxalinones **1a** (51 mg, 0.2 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2b** (71 mg, 0.3 mmol, 1.5 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with nitrogen three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After two hours, 3 equivalents of TEMPO were added to the reaction under nitrogen protection, followed by stirring under irradiation from 10 W blue LEDs for 24 hours. After which, the ESI-HRMS analysis of the crude reaction mixture was carried out. The mass for intermediate ***IIA-tempo*** is $C_{24}H_{29}FN_3O_2^+$

$[M+Na]^+$ calcd. 432.2058, found 432.1978 (Figure S12). The radical dimer ***IIA-dimer*** was also detected by HRMS. The mass for ***IIA-dimer*** is $C_{30}H_{21}F_2N_4O_2^+$ $[M+H]^+$ calcd. 507.1627, found 507.1616 (Figure S12).



Repeat the test a second time



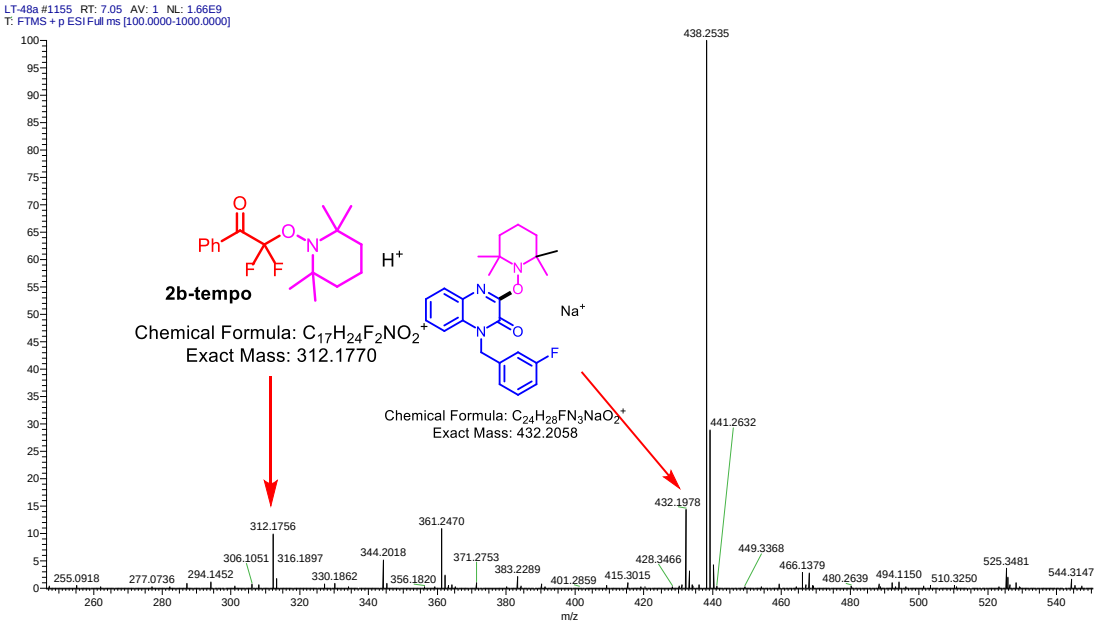
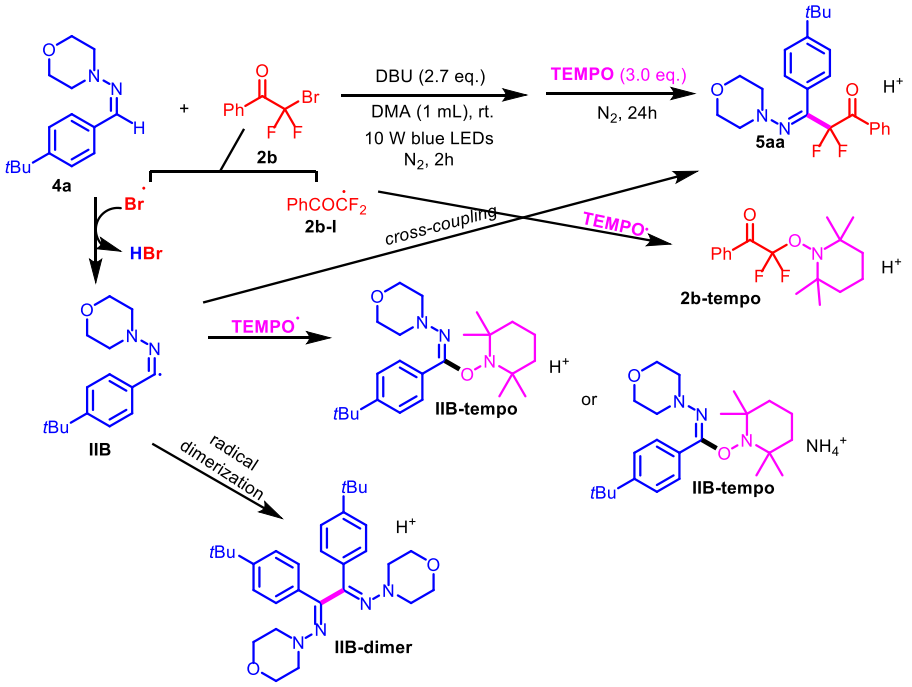
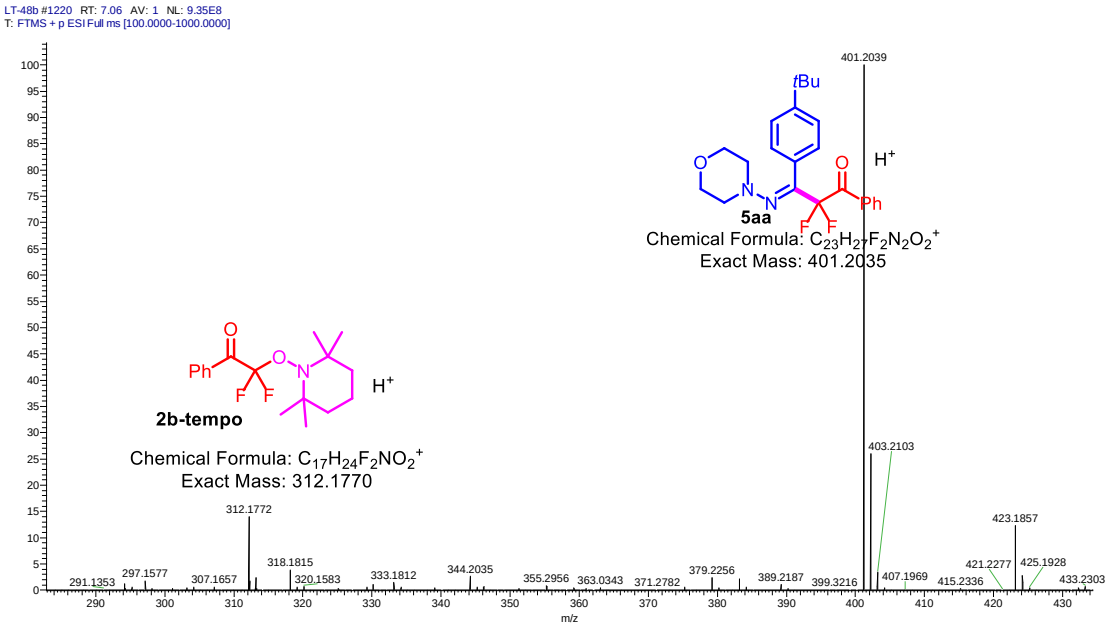


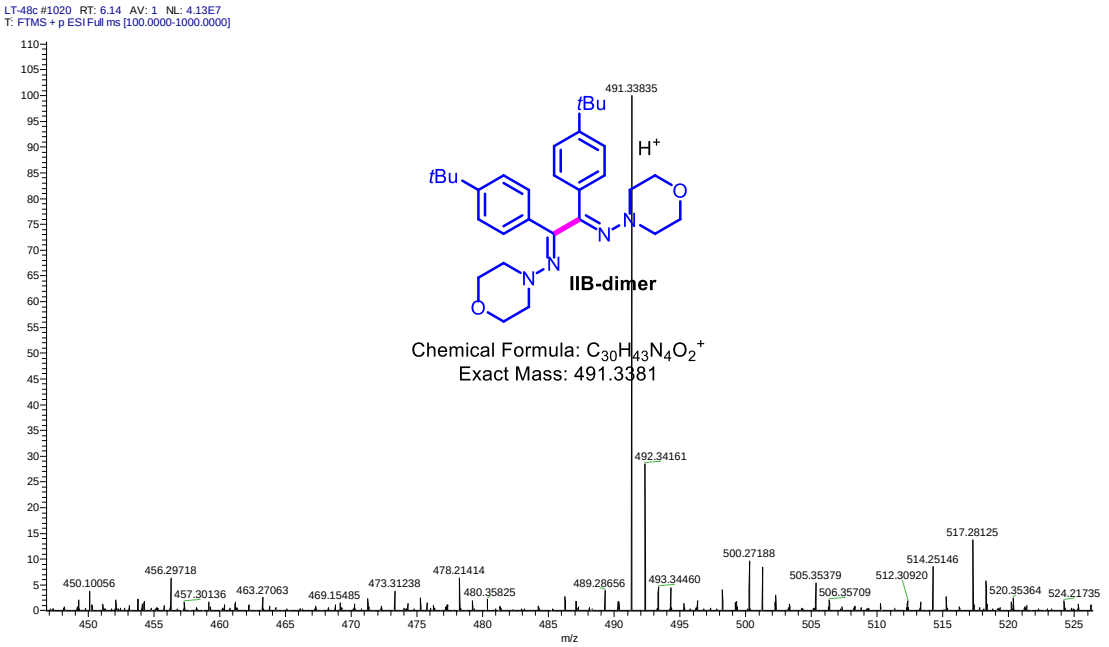
Figure S12. Bromine radical-mediated cross-coupling mechanism for quinoxalinones.



Experimental procedure: DBU (60 μL, 0.4 mmol, 2.7 eq.), aldehyde hydrazone **4a** (51 mg, 0.15 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2b** (71 mg, 0.3 mmol, 2.0 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with nitrogen three times. In the absence of light, anhydrous DMA (1 ml) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After two hours, 3 equivalents of TEMPO were added to the reaction under nitrogen protection, followed by stirring under irradiation from 10 W blue LEDs for 24 hours. After which, the ESI-HRMS analysis of the crude reaction mixture was carried out. The mass for intermediate ***IIB-tempo*** is $C_{24}H_{40}N_3O_2^+$ $[M+H]^+$ calcd. 402.3115 or $C_{24}H_{43}N_4O_2^+$ $[M+NH_4]^+$ calcd. 419.3381, found 402.3082 or 419.3359 (Figure S13). The

radical dimer ***IIB-dimer*** was also detected by HRMS. The mass for ***IIB-dimer*** is $C_{30}H_{43}N_4O_2^+$ $[M+H]^+$ calcd. 491.3381, found 491.33835 (Figure S13).





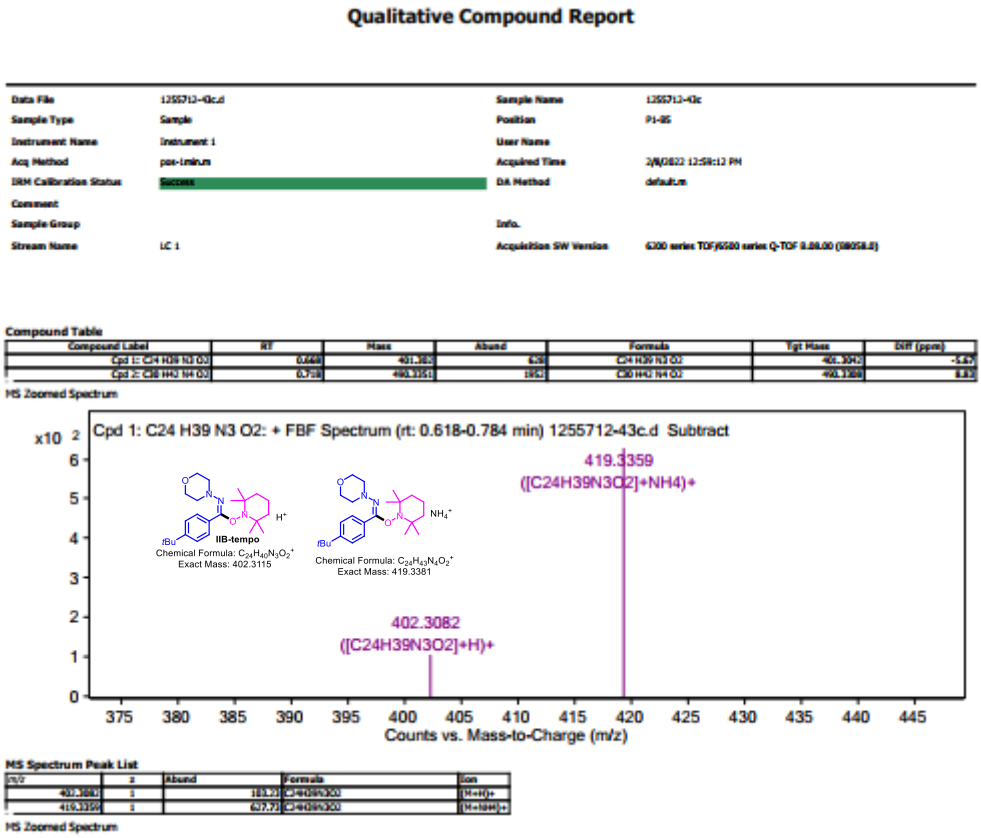
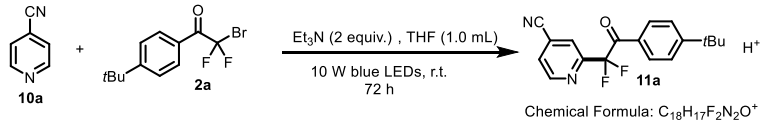


Figure S13. Bromine radical-mediated cross-coupling mechanism for aldehyde hydrazones.

8. Other H-C=X bond study

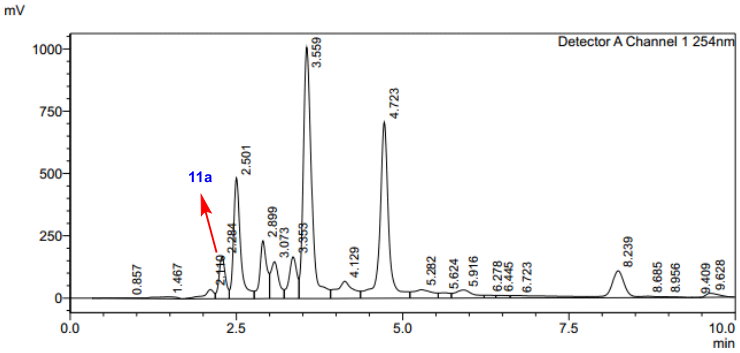


Chemical Formula: $C_{18}H_{17}F_2N_2O^+$
Exact Mass: 315.1303
HRMS found: 315.1304
LCMS found: 315

Triethylamine (56 μL, 0.4 mmol, 2.0 eq.), isonicotinonitrile **10a** (21 mg, 0.2 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 1.5 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 72 h, the product **11a** was detected by LCMS m/z calcd for $C_{18}H_{17}F_2N_2O^+$ $(M+H)^+$ 315, found *m/z* 315 and HRMS (ESI) m/z calcd for $C_{18}H_{17}F_2N_2O^+$ $(M+H)^+$ 315.1303, found *m/z* 315.1304.

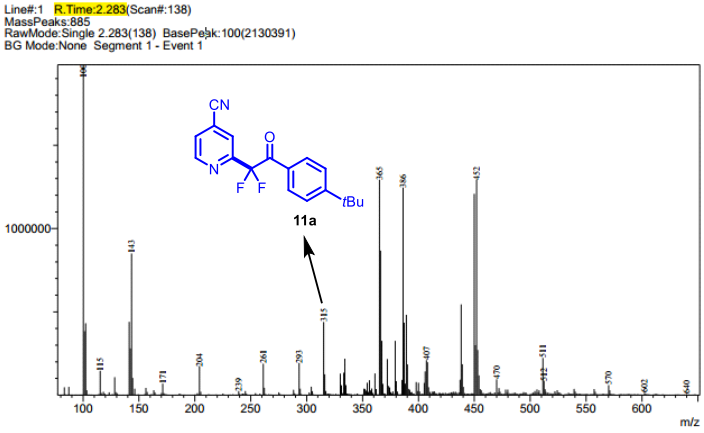
LCMS:

<Chromatogram>

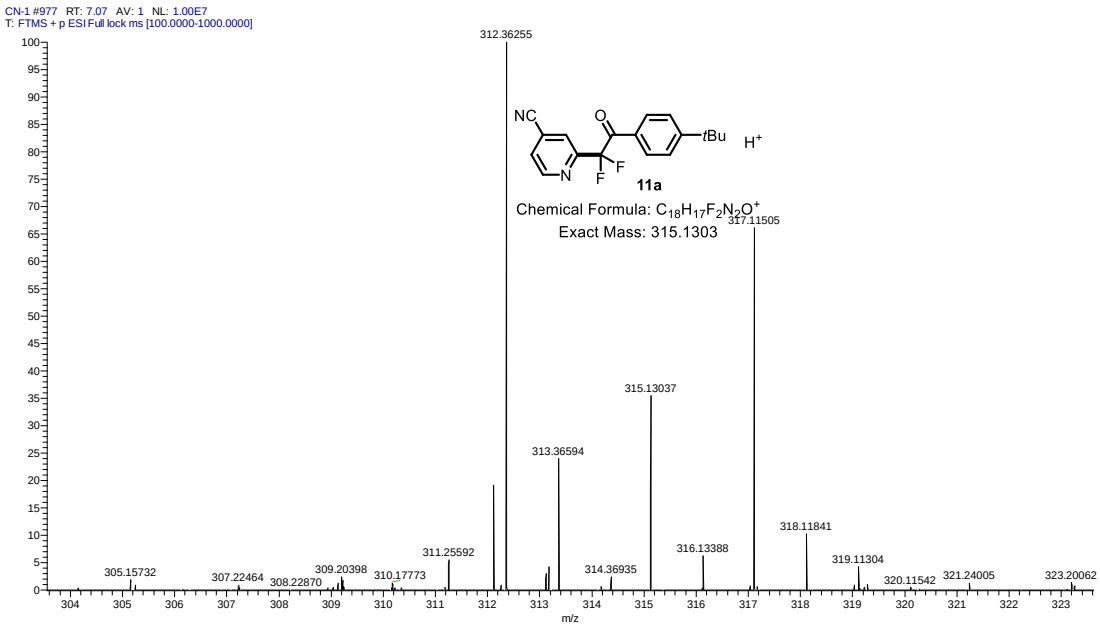


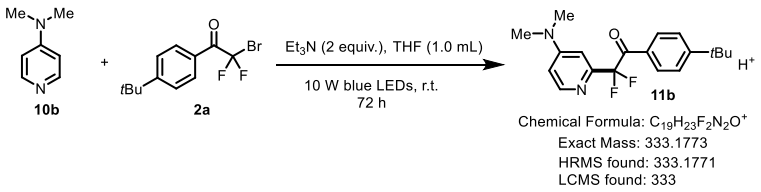
Retention time of 11a is 2.284

<Spectrum>



HRMS:

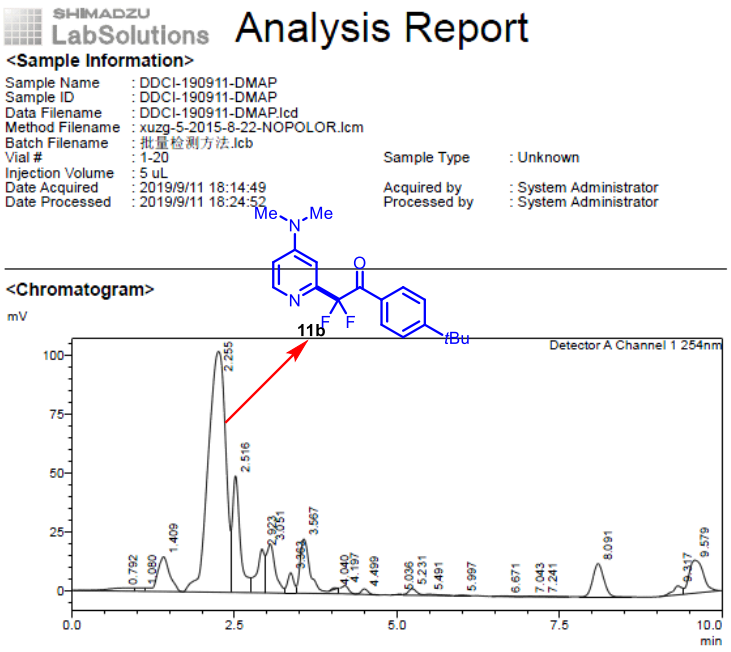




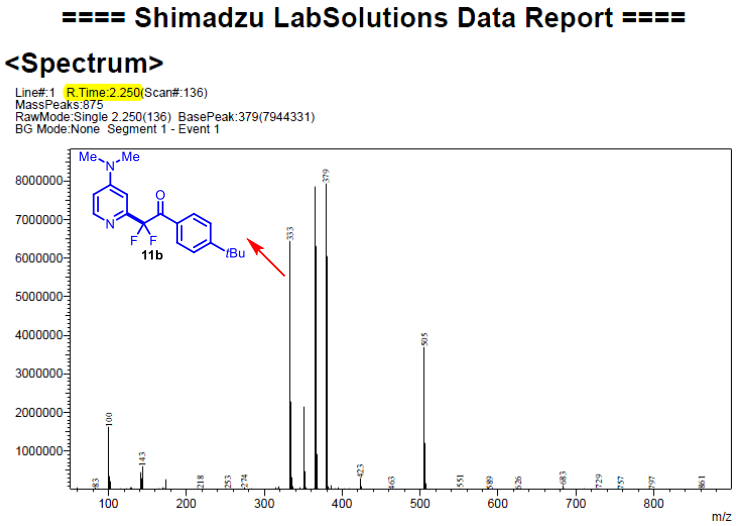
Chemical Formula: $C_{19}H_{23}F_2N_2O^+$
Exact Mass: 333.1773
HRMS found: 333.1771
LCMS found: 333

Triethylamine (56 μL, 0.4 mmol, 2.0 eq.), DMAP **10b** (24 mg, 0.2 mmol, 1.0 eq.) and α-bromo difluoroacylarenes **2a** (87 mg, 0.3 mmol, 1.5 eq.) were added to a flame-dried Schlenk flask containing a stirring bar and purged by evacuating the flask and backfilling with N_2 three times. In the absence of light, anhydrous tetrahydrofuran (1 ml, 0.2 M) was added and the flask was sealed. The mixture was then stirred under irradiation from 10 W blue LEDs. After 72 h, the product **11b** was detected by LCMS m/z calcd for $C_{19}H_{23}F_2N_2O^+$ $(M+H)^+$ 333, found *m/z* 333 and HRMS (ESI) m/z calcd for $C_{19}H_{23}F_2N_2O^+$ $(M+H)^+$ 333.1773, found *m/z* 333.1771.

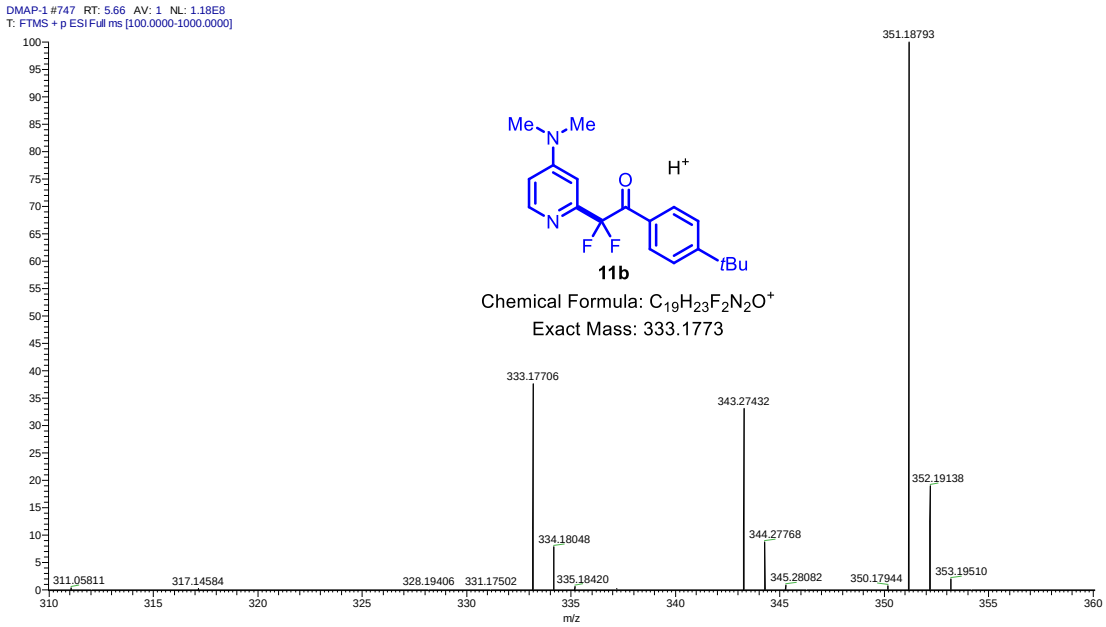
LCMS:



Retention time of 11b is 2.255



HRMS:



*We tried to separate these two products **11a** and **11b**, but found it difficult to separate them to get the target products.*

9. Influencing factors of fluorobromide structure in homocleavage of C_{sp}^3-Br bonds

Currently, there are few other types of bromoalkanes other than difluorobromoaryl ketones in the examples of direct light irradiation to generate free radicals. Most of them require iodination or direct use of iodoalkanes (Figure S14),[10] which may be related to the physical and chemical properties of iodine: the larger the radius of the iodine atom is less attractive to the outermost electrons and the weaker the electronegativity of the iodine is easier to give electrons.

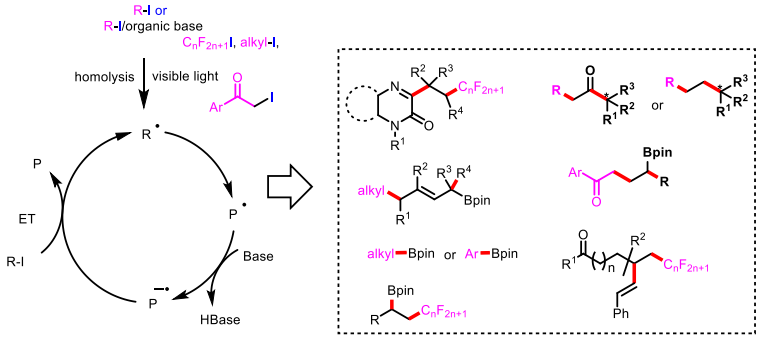


Figure S14. Visible light-induced homo-cleavage of C_{sp}^{3}-I bonds

Recently, the visible light-induced homolysis of C_{sp}^{3}-Br bonds has achieved a breakthrough in the synthesis application (Figure S15).[17,7] For example, Fan's group reported that visible light-induced C_{sp}^{3}-X homocleavage of ethyl difluorobromo/iodoacetate could achieve difluoroalkylation of aryl ketones.[17a] Wu's group found that diethyl bromomalonate could also induce C_{sp}^{3}-Br bond homocleavage by visible light and used this property to achieve indole C-3 functionalization.[17b] However, these three bromides (ethyl bromodifluoroacetate, diethyl bromomalonate and difluorobromoaryl ketones) are currently only used as C_{sp}^{3} radical precursors in the reaction, and the utilization of bromine radicals activity to achieve related transformations has not been reported yet.

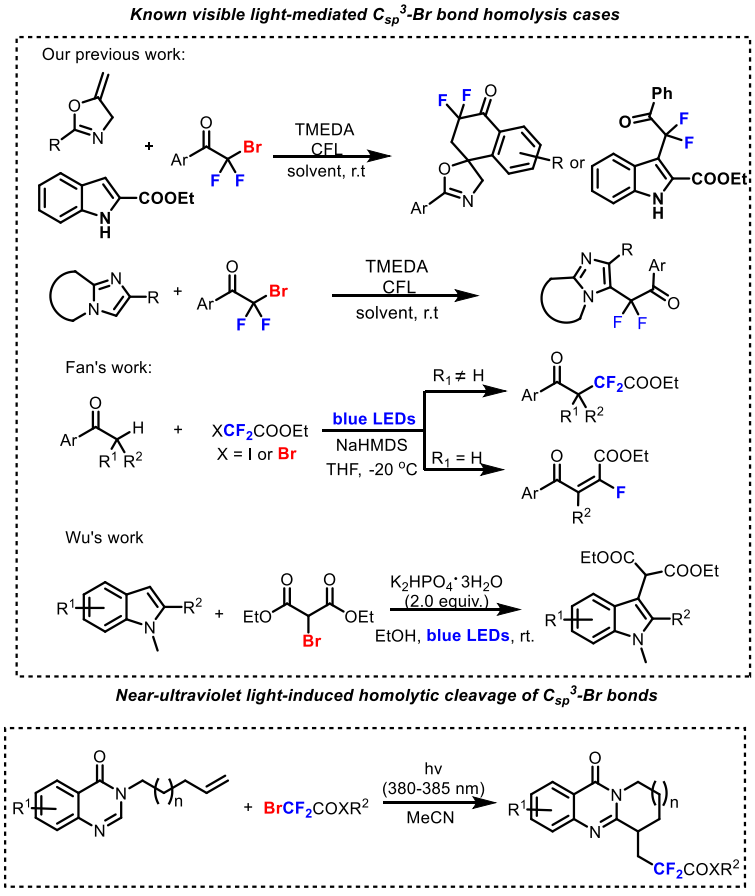


Figure S15. Visible light-induced homo-cleavage of C_{sp}^{3}-Br bonds

The most economical and greenest way to obtain bromine radicals should be to directly homogenize bromide through visible light (Figure S16). Compared with NBS and Br_2 homolysis, C_{sp}^3-Br bond homolysis has more potential application value.

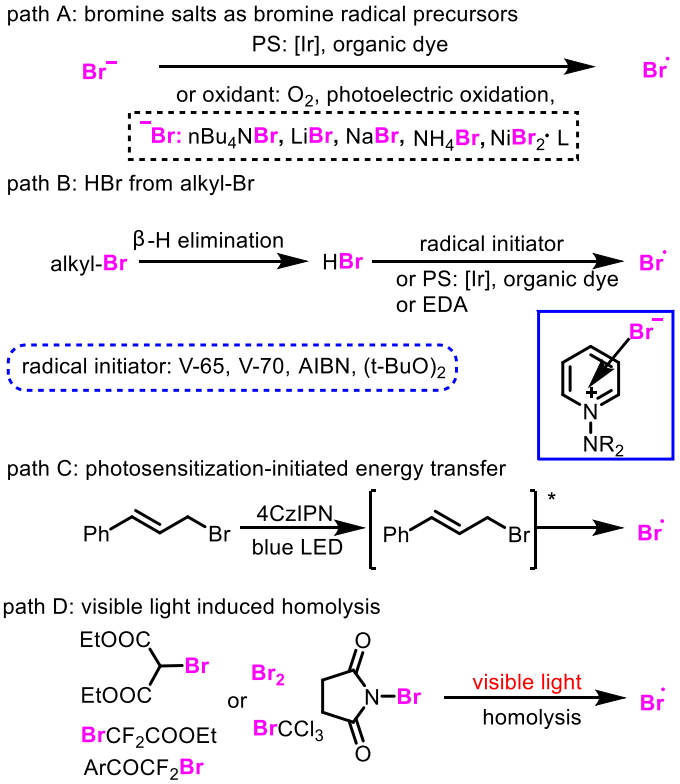


Figure S16. The generation of Br radicals reported in the literature

Therefore, in order to better understand the photochemical properties of difluorobromoaryl ketones, we have designed similar bromoalkane substrates to complete our understanding of it (Figure S17).

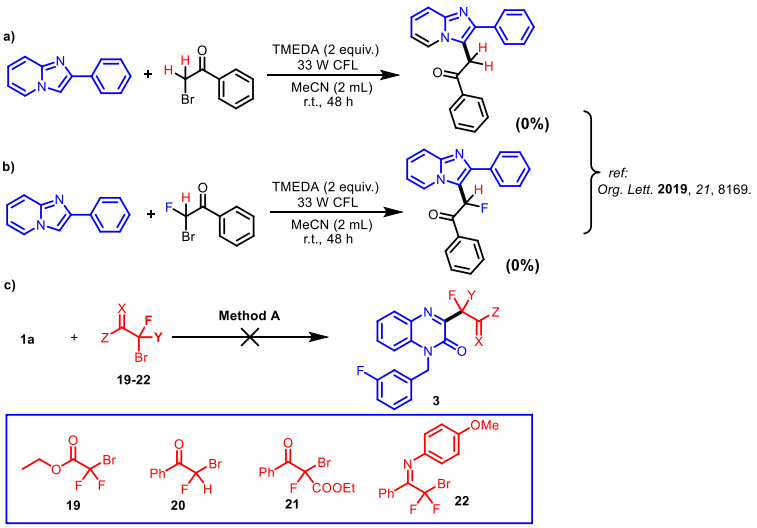


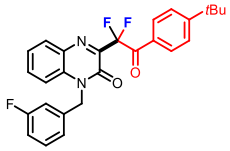
Figure S17. Influencing factors of fluorobromide structure in homocleavage of C_{sp}^3-Br bonds

Conclusion: According to our previous work (*Adv. Synth. Catal.* **2017**, *359*, 1672; *Org. Lett.* **2019**, *21*, 8169) and present work, we already know that *aromatic rings*, *CF_2*, and *electrical requirements for*

the structure of the electron-deficient macroconjugation system composed of carbonyl and aryl groups are important for the bromine radical direct generation.

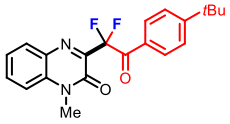
10. Characterization data of compounds

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one **(3aa)**



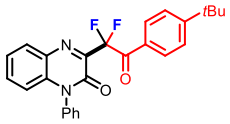
yellow oil, 48 h, 81 mg, 87% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 13.7, 8.9 Hz, 3H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 6.4 Hz, 2H), 6.95 (d, *J* = 7.4 Hz, 2H), 6.85 (d, *J* = 9.4 Hz, 1H), 5.44 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.1 Hz), 164.3, 161.9, 158.2, 152.8, 149.8 (t, *J* = 24.0 Hz), 137.0 (d, *J* = 7.3 Hz), 133.3, 132.6, 132.1, 131.8, 130.7 (d, *J* = 8.4 Hz), 129.9 (t, *J* = 2.6 Hz), 125.7, 124.6, 122.5 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.9, 113.2 (t, *J* = 258.3 Hz), 45.3, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.31 (s), -111.48 – -111.64 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{24}F_3N_2O_2^+$ 465.1784; found 465.1780.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-methylquinoxalin-2(1H)-one **(3ba)**



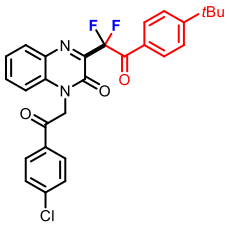
colorless oil, 48 h, 45 mg, 62% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 3.68 (s, 3H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.36 (t, *J* = 28.2 Hz), 158.1, 152.8, 149.7 (t, *J* = 23.9 Hz), 134.2, 132.6, 131.9, 131.5, 130.0, 125.7, 124.4, 114.0, 113.3 (t, *J* = 259.1 Hz), 35.3, 31.0, 29.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) -105.48 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{21}F_2N_2O_2^+$ 371.1566; found 371.1564.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-phenylquinoxalin-2(1H)-one **(3ca)**



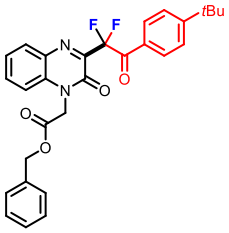
colorless oil, 48 h, 61 mg, 71% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02-7.99 (m, 3H), 7.52-7.45 (m, 3H), 7.41-7.38 (m, 3H), 7.35-7.31 (m, 1H), 7.21-7.18 (m, 2H), 6.70 (dd, *J* = 8.4, 0.9 Hz, 1H), 1.25 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ187.6 (t, *J* = 27.7 Hz), 158.0, 152.5, 150.4 (t, *J* = 24.0 Hz), 135.0, 134.6, 132.2, 131.7, 131.1, 130.4, 130.1, 130.1, 130.1, 130.0, 129.8, 129.6, 128.2, 126.0, 125.6, 124.5, 115.8, 113.4 (t, *J* = 256.9 Hz), 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.09 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{23}F_2N_2O_2^+$ 433.1722; found 433.1719.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(2-(4-chlorophenyl)-2-oxoethyl)quinoxalin-2(1H)-one (**3da**)



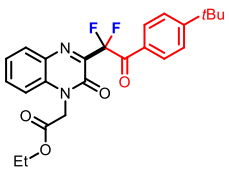
slight yellow oil, 48 h, 76 mg, 75% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (t, *J* = 6.9 Hz, 3H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.51 – 7.49 (m, 4H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.66 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 189.5, 187.3 (t, *J* = 28.1 Hz), 158.2, 152.5, 149.3 (t, *J* = 23.2 Hz), 141.1, 133.6, 132.7, 132.6, 132.0, 131.8, 130.0, 129.8, 129.6, 129.5, 125.7, 124.6, 113.9, 113.3 (t, *J* = 258.4 Hz), 48.2, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.98 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{28}H_{24}ClF_2N_2O_3^+$ 509.1438; found 509.1436.

benzyl 2-(3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2H)-yl)acetate (**3ea**)



slight yellow oil, 48 h, 77 mg, 76% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.35 – 7.31 (m, 3H), 7.26 (t, *J* = 3.5 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 1H), 5.17 (s, 2H), 5.03 (s, 2H), 1.33 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.3 (t, *J* = 28.3 Hz), 166.3, 158.2, 152.3, 149.5 (t, *J* = 24.4 Hz), 134.7, 133.3, 132.7, 131.8 (d, *J* = 3.2 Hz), 130.0 (t, *J* = 2.5 Hz), 129.8 (t, *J* = 1.8 Hz), 128.6 (d, *J* = 1.9 Hz), 128.3, 125.7, 124.6, 113.5, 113.3 (t, *J* = 258.6 Hz), 67.8, 43.3, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.03 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{29}H_{27}F_2N_2O_4^+$ 505.1933; found 505.1934.

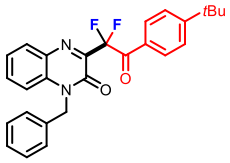
ethyl 2-(3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2H)-yl)acetate (**3fa**)



slight yellow oil, 48 h, 62 mg, 70% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 3H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.99 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.34 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.2 Hz), 166.3, 158.1, 152.3, 149.5 (t, *J* =

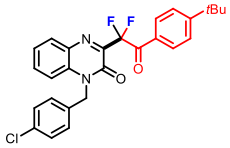
24.3 Hz), 133.4, 132.7, 131.8, 130.0, 125.7, 124.6, 113.5, 113.3 (t, *J* = 258.5 Hz), 62.2, 43.3, 35.3, 31.0, 14.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.10 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{25}F_2N_2O_4^+$ 443.1777; found 443.1778.

1-benzyl-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin-2(1H)-one (**3ga**)



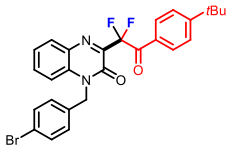
slight yellow oil, 48 h, 66 mg, 74% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 8.05 (d, *J* = 7.9 Hz, 1H), 7.58 – 7.49 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.29 (dd, *J* = 18.2, 8.3 Hz, 4H), 7.16 (d, *J* = 6.8 Hz, 2H), 5.45 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.3 (t, *J* = 28.1 Hz), 158.1, 152.9, 149.8 (t, *J* = 23.9 Hz), 134.5, 133.5, 132.4, 132.1, 131.6, 129.9 (t, *J* = 2.6 Hz), 129.0, 127.9, 126.9, 125.7, 124.4, 114.8, 113.3 (t, *J* = 258.1 Hz), 45.8, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.36 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{25}F_2N_2O_2^+$ 447.1879; found 447.1878.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-chlorobenzyl)-quinoxalin-2(1H)-one (**3ha**)



slight yellow oil, 48 h, 77 mg, 81% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 3H), 7.11 (d, *J* = 8.4 Hz, 2H), 5.41 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.3 (t, *J* = 28.1 Hz), 158.2, 152.8, 149.8 (t, *J* = 23.9 Hz), 133.9, 133.2, 133.0, 132.6, 132.1, 131.8, 129.9 (d, *J* = 2.6 Hz), 129.2, 128.3, 125.7, 124.6, 114.5, 113.3 (t, *J* = 258.3 Hz), 45.1, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.31 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{24}ClF_2N_2O_2^+$ 481.1489; found 481.1491.

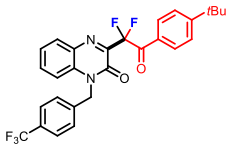
1-(4-bromobenzyl)-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin -2(1H)-one (**3ia**)



slight yellow oil, 48 h, 81 mg, 78% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 3H), 7.26 (d, *J* = 4.8 Hz, 1H), 7.05 (d, *J* = 8.2 Hz, 2H), 5.39 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.3 Hz), 158.2, 152.8, 149.8 (t, *J* = 23.8 Hz), 133.6, 133.2, 132.6, 132.2, 131.7, 129.9 (d, *J* = 2.7 Hz), 128.7, 125.7, 124.6, 121.9, 114.5, 113.3 (t, *J* = 258.4 Hz), 45.2, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.30 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{24}BrF_2N_2O_2^+$ 525.0984; found 525.0987.

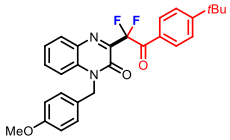
3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1H)-o

ne **(3ja)**



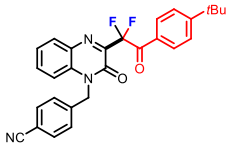
slight yellow oil, 48 h, 68 mg, 66% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.06 (m, 3H), 7.59 – 7.51 (m, 5H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 5.50 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.2 Hz), 158.3, 152.8, 149.8 (t, *J* = 24.0 Hz), 138.5, 133.2, 132.7, 132.1, 131.8, 130.5, 130.2, 129.9 (t, *J* = 2.6 Hz), 129.8, 127.2, 126.0 (q, *J* = 3.7 Hz), 125.8, 124.7, 114.3, 113.2 (t, *J* = 258.5 Hz), 45.3, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.72 (s), -105.31 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$calcd for $C_{28}H_{24}F_5N_2O_2^+$ 515.1752; found 515.1753.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-methoxybenzyl)quinoxalin-2(1H)-one **(3ka)**



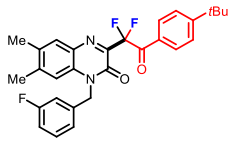
slight yellow oil, 48 h, 69 mg, 73% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 5.38 (s, 2H), 3.74 (s, 3H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.3 (t, *J* = 28.1 Hz), 159.3, 158.1, 152.9, 149.8 (t, *J* = 23.9 Hz), 133.4, 132.5, 132.1, 131.6, 129.9, 128.4, 126.6, 125.7, 124.3, 114.8, 114.4, 113.3 (t, *J* = 258.0 Hz), 55.2, 45.3, 35.3, 31.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.36 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{28}H_{27}F_2N_2O_3^+$ 477.1984; found 477.1981.

4-((3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2H)-yl)methyl)benzonitril e **(3la)**



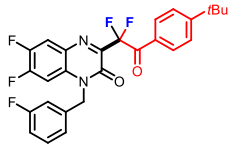
slight yellow oil, 48 h, 63 mg, 67% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 8.07 (m, 3H), 7.62 – 7.50 (m, 5H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 1H), 5.50 (s, 2H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.3 (t, *J* = 28.5 Hz), 158.4, 152.8, 149.8 (t, *J* = 24.1 Hz), 139.8, 133.1, 132.9, 132.7, 132.1, 132.0, 130.0, 129.8, 127.6, 125.8, 124.8, 118.2, 114.1, 113.3 (t, *J* = 259.0 Hz), 112.1, 110.7, 45.4, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.18 (s) ppm; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{28}H_{24}F_2N_3O_2^+$ 472.1831; found 472.1837.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)-6,7-dimethylquinoxalin-2(1H)-one **(3ma)**



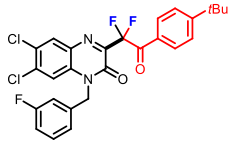
slight yellow oil, 72 h, 76 mg, 77% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.3 Hz, 2H), 7.81 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.01 (s, 1H), 6.94 (dd, *J* = 10.9, 5.1 Hz, 2H), 6.81 (d, *J* = 9.5 Hz, 1H), 5.40 (s, 2H), 2.34 (s, 6H), 1.33 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 29.0 Hz), 164.3, 161.9, 158.0, 152.9, 148.4 (t, *J* = 23.5 Hz), 143.2, 137.2 (d, *J* = 7.2 Hz), 133.8, 131.6, 131.4, 130.6 (d, *J* = 7.8 Hz), 130.1, 129.8, 125.7, 122.4 (d, *J* = 2.8 Hz), 115.0, 114.8, 114.0, 113.8, 113.3 (t, *J* = 257.5 Hz), 45.1, 35.2, 31.0, 20.9, 19.2 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.24 (s), -111.70 – -111.75 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{29}H_{28}F_3N_2O_2^+$ 493.2097; found 493.2099.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-difluoro-1-(3-fluoro-benzyl)quinoxalin-2(1H)-one (**3na**)



colorless oil, 72 h, 83 mg, 83% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 2H), 7.87 (t, *J* = 8.7 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.35 – 7.27 (m, 1H), 7.09 – 6.93 (m, 3H), 6.84 (d, *J* = 8.9 Hz, 1H), 5.37 (s, 2H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.1 (t, *J* = 28.2 Hz), 164.4, 161.9, 158.5, 154.3 (d, *J* = 14.8 Hz), 152.4, 151.7 (d, *J* = 14.4 Hz), 150.3 (t, *J* = 22.3 Hz), 148.5 (d, *J* = 14.1 Hz), 146.0 (d, *J* = 13.9 Hz), 136.1 (d, *J* = 7.2 Hz), 131.0 (d, *J* = 8.3 Hz), 130.8 (d, *J* = 8.8 Hz), 130.0, 129.6, 128.3 (d, *J* = 9.3 Hz), 125.8, 125.5, 122.4 (d, *J* = 3.0 Hz), 119.2 (d, *J* = 18.3 Hz), 115.5 (d, *J* = 21.1 Hz), 113.9 (d, *J* = 22.5 Hz), 113.2 (t, *J* = 259.2 Hz), 103.3 (d, *J* = 23.5 Hz), 45.8, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.26 (s), -111.01 (s), -125.55 (d, *J* = 22.3 Hz), -139.49 (d, *J* = 22.3 Hz) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{22}F_5N_2O_2^+$ 501.1596; found 501.1597.

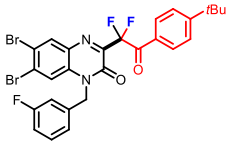
3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dichloro-1-(3-fluoro-benzyl)quinoxalin-2(1H)-one (**3oa**)



colorless oil, 72 h, 84 mg, 79% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.09 (d, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.38 – 7.28 (m, 2H), 7.04 – 6.91 (m, 2H), 6.84 (d, *J* = 8.5 Hz, 1H), 5.37 (s, 2H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.0 (t, *J* = 28.2 Hz), 164.4, 161.9, 158.6, 152.2, 151.1 (t, *J* = 24.2 Hz), 137.2, 136.1 (d, *J* = 7.2 Hz), 132.5, 132.3, 131.0 (t, *J* = 4.0 Hz), 130.0 (t, *J* = 2.5 Hz), 129.5, 128.8, 125.9, 122.4 (d, *J* = 3.0 Hz), 116.0, 115.6, 115.4, 114.1, 113.8, 113.1 (t, *J* = 259.6 Hz), 45.5, 35.3, 31.0 ppm; **^{19}F NMR** (376

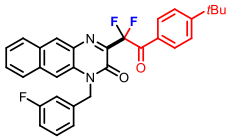
MHz, $CDCl_3$) δ -105.27 (s), -110.98 – -111.05 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{22}Cl_2F_3N_2O_2^+$ 533.1005; found 533.1005.

6,7-dibromo-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluoro-benzyl)quinoxalin-2(1H)-one (**3pa**)



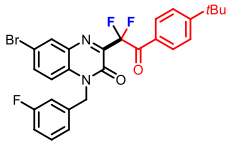
colorless oil, 72 h, 91 mg, 74% yield, R_f = 0.4 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 2H), 7.55 – 7.51 (m, 3H), 7.33 – 7.26 (m, 1H), 7.01 – 6.93 (m, 2H), 6.84 (d, *J* = 9.3 Hz, 1H), 5.36 (s, 2H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 186.9 (t, *J* = 28.2 Hz), 164.4, 161.9, 158.6, 152.2, 151.2 (t, *J* = 24.3 Hz), 136.1 (d, *J* = 7.3 Hz), 135.4, 132.9, 131.6, 131.0 (d, *J* = 8.3 Hz), 130.0 (t, *J* = 2.5 Hz), 129.6, 129.5, 125.9, 122.4 (d, *J* = 3.0 Hz), 120.1, 119.1, 115.6, 115.4, 114.1, 113.9, 113.1 (t, *J* = 259.6 Hz), 45.5, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.29 (s), -111.01 – 111.05 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{22}Br_2F_3N_2O_2^+$ 620.9995; found 620.9994.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)benzo[g]quinoxalin-2(1H)-one (**3qa**)



yellow oil, 72 h, 70 mg, 68% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.51 (m, 5H), 7.39 – 7.24 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.96 – 6.90 (m, 2H), 5.50 (s, 2H), 1.34 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.1 Hz), 164.4, 161.9, 158.3, 152.7, 150.2 (t, *J* = 23.9 Hz), 137.1 (d, *J* = 7.2 Hz), 134.7, 131.9, 131.1, 130.8, 130.6 (d, *J* = 5.8 Hz), 130.0 (t, *J* = 2.4 Hz), 129.9, 129.8, 129.2, 128.9, 127.4, 126.1, 125.8, 122.4, 115.1, 114.9, 114.0, 113.8, 113.2 (t, *J* = 258.6 Hz), 111.3, 45.3, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.12 (s), -111.64 – -111.68 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{31}H_{26}F_3N_2O_2^+$ 515.1941; found 515.1943.

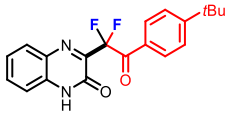
6-bromo-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (3ra)



colorless oil, 48 h, 79 mg, 73% yield, R_f = 0.4 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.57 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.46–7.44 (m, 2H), 7.20–7.16 (m, 1H), 7.06 (d, *J* = 9.0 Hz, 1H), 6.90–6.84 (m, 2H), 6.76 (d, *J* = 9.3 Hz, 1H), 5.33 (s, 2H), 1.27 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.0 (t, *J* = 28.1 Hz), 164.3, 161.9,

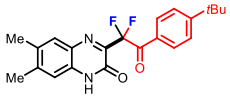
158.4, 152.5, 151.0 (t, *J* = 24.0 Hz), 136.5 (d, *J* = 7.3 Hz), 135.4, 134.0, 132.8, 132.3, 130.8 (d, *J* = 8.4 Hz), 130.0, 129.6, 125.8, 122.4 (d, *J* = 2.9 Hz), 117.3, 116.0, 115.3, 115.1, 114.1, 113.8, 113.1 (t, *J* = 257.7 Hz), 45.4, 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.36 (s), -111.27 – 111.31 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{23}BrF_3N_2O_2^+$ 543.0890; found 543.0892.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin-2(1H)-one (**3sa**)



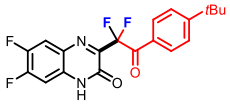
slight yellow solid, 72 h, 31 mg, 44% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.25 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 2H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.0 (t, *J* = 28.3 Hz), 158.3, 154.4, 149.8 (t, *J* = 24.4 Hz), 132.7, 132.0, 131.8, 130.4, 130.0 (t, *J* = 2.5 Hz), 129.9, 125.8, 125.1, 116.2, 113.2 (t, *J* = 257.9 Hz), 35.3, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) -105.13 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{20}H_{19}F_2N_2O_2^+$ 357.1409; found 357.1409.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dimethylquinoxalin-2(1H)-one (**3ta**)



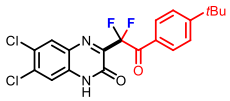
light yellow solid, 72h, 23mg, 30% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.49 (s, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.74 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.00 (s, 1H), 2.36 (s, 6H), 1.33 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.1 Hz), 158.0, 154.6, 148.2 (t, *J* = 24.4 Hz), 143.6, 134.5, 130.5, 130.2, 130.0, 125.7, 116.3, 113.3 (t, *J* = 256.8 Hz), 35.3, 31.0, 20.4, 19.5 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.91 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{22}H_{23}F_2N_2O_2^+$ 385.1722; found 385.1721.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-difluoroquinoxalin-2(1H)-one (**3ua**)



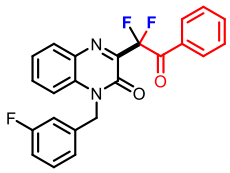
light yellow solid, 72 h, 30 mg, 38% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.09 (d, *J* = 6.6 Hz, 2H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 6.7 Hz, 2H), 7.05 (d, *J* = 6.6 Hz, 1H), 1.36 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.2 (t, *J* = 28.4 Hz), 158.8, 157.6, 154.7 (d, *J* = 15.0 Hz), 154.4, 152.1 (d, *J* = 15.0 Hz), 150.1 (t, *J* = 23.3 Hz), 149.2 (d, *J* = 14.2 Hz), 146.8 (d, *J* = 14.2 Hz), 130.0, 129.5, 129.4 (d, *J* = 10.2 Hz), 128.1 (d, *J* = 9.8 Hz), 125.9, 125.5, 117.9, 113.2 (t, *J* = 259.2 Hz), 104.3, 104.1, 35.4, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.01 (s), -125.37 – -125.61 (m), -137.86 – -137.96 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{20}H_{17}F_4N_2O_2^+$ 393.1221; found 393.1220.

3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dichloroquinoxalin-2(1H)-one (**3va**)



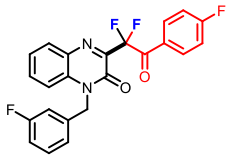
light yellow solid, 72 h, 28 mg, 33% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.35 (s, 1H), 8.11 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.35 (s, 1H), 1.35 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.0 (t, *J* = 28.5 Hz), 158.7, 154.1, 151.0 (t, *J* = 24.3 Hz), 137.3, 131.2, 131.0, 130.6, 130.0, 129.4, 129.2, 126.0, 117.3, 113.1 (t, *J* = 259.4 Hz), 35.4, 31.0 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.93 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{20}H_{17}Cl_2F_2N_2O_2^+$ 425.0630; found 425.0627.

3-(1,1-difluoro-2-oxo-2-phenylethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3ab**)



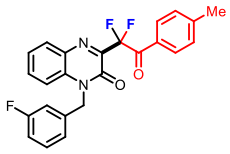
slight yellow oil, 48 h, 62 mg, 76% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.8 Hz, 2H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.27 – 7.22 (m, 2H), 6.98 – 6.89 (m, 2H), 6.81 (d, *J* = 9.4 Hz, 1H), 5.43 (s, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.6 (t, *J* = 28.3 Hz), 164.3, 161.9, 152.8, 149.6 (t, *J* = 24.1 Hz), 136.9 (d, *J* = 7.3 Hz), 134.1, 133.2, 132.7, 132.1, 131.8, 130.7 (d, *J* = 8.3 Hz), 129.8 (t, *J* = 2.6 Hz), 128.7, 124.6, 122.4 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.0, 113.8, 113.0 (t, *J* = 258.2 Hz), 45.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.54 (s), -111.58 – -111.62 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{16}F_3N_2O_2^+$ 409.1158; found 409.1161.

3-(1,1-difluoro-2-(4-fluorophenyl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3ac**)



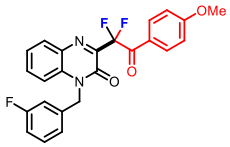
slight yellow oil, 48 h, 61 mg, 72% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 8.3, 5.6 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.27 (dd, *J* = 7.1, 4.3 Hz, 2H), 7.18 (t, *J* = 8.6 Hz, 2H), 6.99 – 6.92 (m, 2H), 6.83 (d, *J* = 9.4 Hz, 1H), 5.44 (s, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 186.3 (t, *J* = 28.6 Hz), 167.7, 165.1, 164.4, 161.9, 152.8, 149.4 (t, *J* = 23.9 Hz), 136.9 (d, *J* = 7.3 Hz), 133.3, 132.8 (dd, *J* = 9.0, 3.6 Hz), 132.1, 131.8, 131.2, 130.7 (d, *J* = 8.4 Hz), 129.0, 124.7, 123.9, 122.4 (d, *J* = 3.0 Hz), 116.2, 115.9, 115.2, 115.0, 114.5, 114.1, 113.8, 113.1 (t, *J* = 258.3 Hz), 45.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.19 – -102.46 (m), -105.39 (s), -111.55– -111.61 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{15}F_4N_2O_2^+$ 427.1064; found 427.1069.

3-(1,1-difluoro-2-oxo-2-(p-tolyl)ethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3ad**)



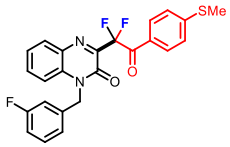
slight yellow oil, 48 h, 65 mg, 77% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (t, *J* = 7.8 Hz, 3H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.31 – 7.24 (m, 4H), 6.94 (t, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 9.4 Hz, 1H), 5.43 (s, 2H), 2.42 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.0 (t, *J* = 28.0 Hz), 164.3, 161.9, 152.8, 149.8 (t, *J* = 24.0 Hz), 145.4, 137.0 (d, *J* = 7.3 Hz), 133.2, 132.7, 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 130.0 (t, *J* = 2.5 Hz), 129.5, 124.6, 122.5 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.8, 113.1 (t, *J* = 258.3 Hz), 45.2, 21.8 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.46 (s), -111.65 – -111.69 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{18}F_3N_2O_2^+$423.1315; found 423.1312.

3-(1,1-difluoro-2-(4-methoxyphenyl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3ae**)



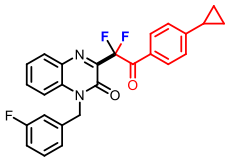
slight yellow oil, 48 h, 65 mg, 74% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 5.3 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.95 (t, *J* = 9.2 Hz, 4H), 6.83 (d, *J* = 9.4 Hz, 1H), 5.44 (s, 2H), 3.88 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 185.9 (t, *J* = 28.0 Hz), 164.4, 161.9, 152.8, 149.9 (t, *J* = 23.9 Hz), 137.0 (d, *J* = 7.3 Hz), 133.3, 132.6, 132.5 (t, *J* = 2.8 Hz), 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 125.3, 124.6, 122.5 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.9, 113.4 (t, *J* = 258.6 Hz), 55.6, 45.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.03 (s), -111.64 – -111.78 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{18}F_3N_2O_3^+$ 439.1264; found 439.1263.

3-(1,1-difluoro-2-(4-(methylthio)phenyl)-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1H)-one (**3af**)



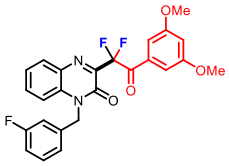
slight yellow oil, 48 h, 62 mg, 68% yield, R_f = 0.2 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.4 Hz, 3H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.22 (m, 4H), 6.97 – 6.88 (m, 2H), 6.85 (d, *J* = 9.4 Hz, 1H), 5.43 (s, 2H), 2.51 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 186.4 (t, *J* = 28.1 Hz), 164.3, 161.8, 152.8, 149.6 (t, *J* = 24.2 Hz), 147.9, 137.0 (d, *J* = 7.1 Hz), 133.2, 132.7, 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 130.2, 128.6, 124.9, 124.6, 123.8, 122.4 (d, *J* = 2.7 Hz), 115.1, 114.9, 114.5, 114.1, 113.9, 113.2 (t, *J* = 258.1 Hz), 45.2, 14.6 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.28 (s), -111.58 – -111.68 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{18}F_3N_2O_2S^+$ 455.1036; found 455.1031.

3-(2-(4-cyclopropylphenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1H)-one (**3ag**)



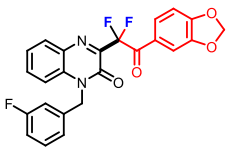
slight yellow oil, 48 h, 72 mg, 80% yield, R_f = 0.5 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (t, *J* = 8.4 Hz, 3H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.97 – 6.82 (m, 3H), 5.43 (s, 2H), 1.98 – 1.92 (m, 1H), 1.11 – 1.06 (m, 2H), 0.82 – 0.78 (m, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 186.8 (t, *J* = 28.0 Hz), 164.3, 161.9, 152.8, 151.9, 149.8 (t, *J* = 24.0 Hz), 137.0 (d, *J* = 7.3 Hz), 133.2, 132.6, 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 130.1 (t, *J* = 2.6 Hz), 129.7, 125.6, 124.6, 122.4 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.9, 113.2 (t, *J* = 258.2 Hz), 45.2, 15.9, 10.6 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.36 (s), -111.64 – -111.66 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{20}F_3N_2O_2^+$ 449.1471; found 449.1469.

3-(2-(3,5-dimethoxyphenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1H)-one (**3ah**)



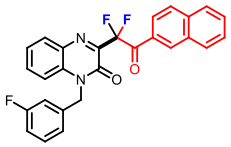
slight yellow oil, 48 h, 69 mg, 74% yield, R_f = 0.3 (ethyl acetate/hexane = 25%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.27 – 7.22 (m, 4H), 6.95 (td, *J* = 8.5, 2.2 Hz, 1H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.81 (d, *J* = 9.4 Hz, 1H), 6.70 (t, *J* = 2.2 Hz, 1H), 5.43 (s, 2H), 3.80 (s, 6H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 186.8 (t, *J* = 27.9 Hz), 164.3, 161.9, 160.8, 152.8, 149.7 (t, *J* = 24.0 Hz), 136.9 (d, *J* = 7.2 Hz), 134.1, 133.2, 132.7, 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 124.7, 122.4 (d, *J* = 3.0 Hz), 115.2, 114.9, 114.5, 114.0, 113.8, 112.8 (t, *J* = 257.9 Hz), 107.4, 107.1, 55.6, 45.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.46 (s), -111.64 – -111.66 (m) ppm; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{20}F_3N_2O_4^+$ 469.1370; found 469.1369.

3-(2-(benzo[d][1,3]dioxol-5-yl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1H)-one (**3ai**)



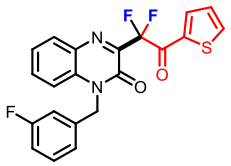
slight yellow oil, 48 h, 70 mg, 78% yield, R_f = 0.2 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 9.4 Hz, 1H), 6.06 (s, 2H), 5.44 (s, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 185.5 (t, *J* = 28.1 Hz), 164.3, 161.9, 152.9, 152.8, 149.75 (t, *J* = 24.0 Hz), 148.2, 137.0 (d, *J* = 7.3 Hz), 133.2, 132.7, 132.1, 131.7, 130.7 (d, *J* = 8.3 Hz), 126.9 (t, *J* = 3.6 Hz), 124.6, 122.5 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.8, 113.2 (t, *J* = 258.6 Hz), 109.6, 108.3, 102.1, 45.2 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.77 (s), -111.66 – -111.81 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{16}F_3N_2O_4^+$ 453.1057; found 453.10450.

3-(1,1-difluoro-2-(naphthalen-2-yl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3aj**)



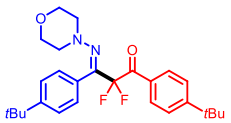
slight yellow oil, 48 h, 71 mg, 77% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.14 – 8.07 (m, 2H), 7.98 – 7.85 (m, 3H), 7.64 – 7.53 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 5.1 Hz, 1H), 7.17 – 7.11 (m, 1H), 6.91 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 2H), 5.42 (s, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.4 (t, *J* = 28.0 Hz), 164.3, 161.8, 152.9, 149.7 (t, *J* = 24.1 Hz), 136.9 (d, *J* = 7.3 Hz), 136.0, 133.3, 132.7, 132.3, 132.2 (t, *J* = 3.6 Hz), 132.1, 131.8, 130.7, 130.0, 129.2, 128.6, 127.8, 126.9, 124.8, 124.6, 122.3 (d, *J* = 3.0 Hz), 115.1, 114.9, 114.5, 114.1, 113.9, 113.2 (t, *J* = 258.3 Hz), 45.3, 29.7, 29.4, 14.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.01 (s), -111.68 – -111.70 (m), ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{18}F_3N_2O_2^+$ 459.1315; found 459.1307.

3-(1,1-difluoro-2-oxo-2-(thiophen-2-yl)ethyl)-1-(3-fluorobenzyl)quinoxalin-2(1H)-one (**3ak**)



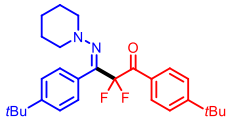
colorless oil, 48 h, 70 mg, 84% yield, R_f = 0.4 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.9 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 4.9 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 5.0 Hz, 1H), 7.22 (t, *J* = 4.4 Hz, 1H), 6.98 – 6.93 (m, 2H), 6.88 (d, *J* = 9.4 Hz, 1H), 5.45 (s, 2H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 180.7 (t, *J* = 29.5 Hz), 164.3, 161.9, 152.8, 149.2 (t, *J* = 24.0 Hz), 138.0 (t, *J* = 2.2 Hz), 136.9 (d, *J* = 7.3 Hz), 136.3, 135.8 (t, *J* = 4.8 Hz), 133.3, 132.8, 132.1, 131.8, 130.7 (d, *J* = 8.3 Hz), 128.7, 124.6, 122.4 (d, *J* = 2.6 Hz), 115.2, 114.9, 114.5, 114.1, 113.9, 112.9 (t, *J* = 258.2 Hz), 45.3 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.29 (s), -111.61 – -111.67 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{14}F_3N_2O_2S^+$ 415.0723; found 415.0720.

1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5aa)



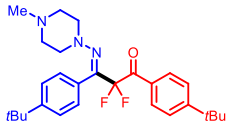
colorless oil, 48 h, E/Z = 6.7/1, 63 mg, 92% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.46 (t, *J* = 6.4 Hz, 2H), 7.41-7.36 (m, 4H), 3.49–3.39 (m, 4H), 2.84–2.61 (m, 4H), 1.37–1.16 (m, 18H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.6 (t, *J* = 27.3 Hz), 157.1, 153.1, 143.2 (t, *J* = 31.0 Hz), 130.8, 130.0, 128.3, 128.3, 128.1, 125.7, 125.7, 125.4, 125.3, 116.0 (t, *J* = 248.5 Hz), 65.9, 64.4, 54.5 54.1, 35.2, 34.9, 31.1, 31.2, 31.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.29 (s), -96.9 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{35}F_2N_2O_2^+$ 457.2661; found 457.2668.

1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-(piperidin-1-ylimino)propan-1-one (5ba)



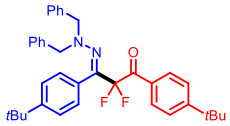
colorless oil, 48 h, E/Z > 20/1, 56 mg, 81% yield, R_f = 0.3 (ethyl acetate/hexane = 4%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.7 Hz, 4H), 2.73 (s, 4H), 1.28-1.26 (m, 24H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 189.0 (t, *J* = 28 Hz), 156.8, 152.5, 139.7 (t, *J* = 31.0 Hz), 131.1, 130.0, 129.0, 128.1, 126.0, 125.5, 125.2, 116.5 (t, *J* = 248.0 Hz), 54.6, 35.2, 34.8, 31.3, 31.1, 30.9, 24.5, 23.9 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.26 (s), -102.76 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{28}H_{37}F_2N_2O^+$ 455.2868; found 455.2869.

1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-((4-methylpiperazin-1-yl)imino)propan-1-one (5ca)



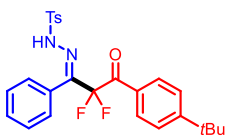
colorless oil, 48 h, E/Z > 20/1, 52 mg, 74% yield, R_f = 0.3 (ethyl acetate/hexane = 40%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (t, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.40 (dd, *J* = 8.4, 4.5 Hz, 4H), 3.01–2.77 (m, 4H), 2.37–2.16 (m, 4H), 2.13 (s, 3H), 1.28 (d, *J* = 3.5 Hz, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.6 (t, *J* = 27.5 Hz), 170.4, 166.9, 157.0, 155.6, 153.0, 130.9, 130.0, 129.5, 128.3, 128.1, 125.7, 125.3, 125.1, 116.1 (d, *J* = 249.7 Hz), 53.1, 52.9, 45.4, 35.2, 34.9, 31.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.93 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{28}H_{38}F_2N_3O^+$ 470.2977; found 470.2982.

1,3-bis(4-(tert-butyl)phenyl)-3-(2,2-dibenzylhydrazono)-2,2-difluoropropan-1-one (5ea)



colorless oil, 48 h, E/Z > 20/1, 79 mg, 94% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.18 (q, *J* = 8.5 Hz, 4H), 7.09 – 7.02 (m, 6H), 6.81 – 6.59 (m, 4H), 3.99 (s, 4H), 1.30 (s, 4H), 1.21 (s, 4H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.9 (t, *J* = 27.7 Hz), 156.9, 152.2, 137.3, 136.9, 130.9, 130.1, 129.1, 128.3, 128.2, 127.8, 127.1, 125.3, 124.9, 116.5 (t, *J* = 248.1 Hz), 59.2, 35.2, 34.7, 31.2, 31.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -95.93 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{37}H_{41}F_2N_2O^+$ 567.3181; found 567.3185.

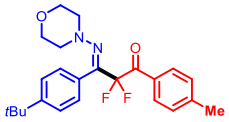
N'-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-oxo-1-phenylpropylidene)-4-methylbenzenesulfonohydrazide (5fa)



colorless oil, 48 h, E/Z > 20/1, 51 mg, 70% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.05 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 7.2 Hz,

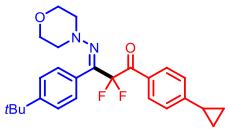
2H), 7.43 (t, *J* = 7.0 Hz, 3H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H), 1.27 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 182.1 (t, *J* = 29.4 H), 166.6, 158.1, 145.8, 133.6, 132.5, 132.4, 130.2, 129.7, 129.5, 129.0, 128.9, 125.7, 114.4 (t, *J* = 267.7 Hz), 35.3, 31.0, 21.8 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -84.96 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{27}F_2N_2O_3S^+$ 485.1705; found 485.1706.

3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-1-(p-tolyl)propan-1-one (5ab)



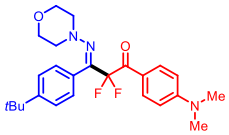
colorless oil, 48 h, E/Z = 7.8/1, 50 mg, 81% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 1.66H), 7.71 (dd, *J* = 16.0, 8.3 Hz, 0.61H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.17 (dd, *J* = 10.8, 6.5 Hz, 2H), 3.43 (dd, *J* = 12.6, 7.7 Hz, 4H), 2.82–2.59 (m, 3.45H), 2.41 (s, 0.44H), 2.34 (s, 2.38H), 2.32 (s, 0.5H), 1.29-1.27 (m, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.5 (t, *J* = 27.5 Hz), 154.7, 153.2, 144.2, 143.9, 143.1 (t, *J* = 31.2 Hz), 131.0, 130.2, 129.2, 129.0, 128.4, 128.3, 128.2, 128.1, 125.7, 116.0 (t, *J* = 250.0 Hz), 65.9, 64.4, 54.5, 54.0, 35.0, 34.9, 31.3, 31.2, 31.2, 21.8, 21.7; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.9 (s), -98.8 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{29}F_2N_2O_2^+$ 415.2192; found 415.2197.

3-(4-(tert-butyl)phenyl)-1-(4-cyclopropylphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ac)



colorless oil, 48 h, E/Z = 6.2/1, 51 mg, 77% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 1.65H), 7.71 (dd, *J* = 18.6, 8.1 Hz, 0.61H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 1.67H), 7.05-7.01 (m, 2H), 3.48–3.38 (m, 4H), 2.80–2.68 (m, 3.36H), 2.42 (s, 0.54H), 1.93–1.81 (m, 1H), 1.30-1.28 (m, 9H), 1.01 (dt, *J* = 6.6, 4.6 Hz, 2H), 0.72 (ddt, *J* = 6.7, 4.9, 3.2 Hz, 2H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.3 (t, *J* = 27.5 Hz), 154.7, 153.1, 150.8, 150.5, 143.2 (t, *J* = 31.4 Hz), 130.7, 130.2, 128.5, 128.3, 128.2, 128.1, 125.7, 125.3, 125.1, 116.0 (t, *J* = 250.2 Hz), 65.9, 64.4, 54.5, 54.0, 35.0, 34.9, 31.3, 31.23, 31.2, 15.9, 10.7, 10.6; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.92 (s), -98.77 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{31}F_2N_2O_2^+$ 441.2348; found 441.2341.

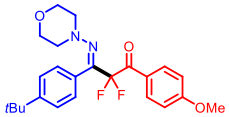
3-(4-(tert-butyl)phenyl)-1-(4-(dimethylamino)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ad)



reddish brown oil, 48 h, E/Z = 10.8/1, 53 mg, 80% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H**

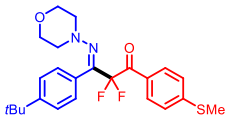
NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.9 Hz, 1.9H), 7.70 (dd, *J* = 8.4, 3.7 Hz, 0.37H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 6.58-6.55 (m, 2H), 3.47–3.44 (m, 4H), 3.00-2.97 (m, 6H), 2.77–2.74 (m, 3.58H), 2.44 (s, 0.33H), 1.29-1.27 (m, 9H); **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 186.7 (t, *J* = 27.0 Hz), 153.4, 152.9, 143.9 (t, *J* = 30.8 Hz), 132.5, 128.6, 128.1, 125.6, 125.6, 121.0, 116.1 (t, *J* = 250.0 Hz), 110.4, 65.9, 64.7, 54.6, 54.1, 40.0, 34.9, 31.2, 31.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.36 (s), -98.06 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{32}F_2N_3O_2^+$ 444.2457; found 444.2459.

3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ae)



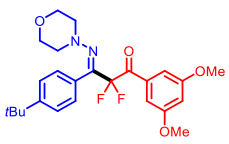
colorless oil, 48 h, E/Z = 6.4/1, 50 mg, 78% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^1H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1.65H), 7.85 (dd, *J* = 21.7, 8.5 Hz, 0.58H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 1.65H), 6.97-6.93 (m, *2*H), 3.90-3.88 (m, 3H), 3.63–3.41 (m, 4H), 2.96–2.73 (m, 3.38H), 2.52 (s, 0.53H), 1.39-1.37 (m, 9H); **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 187.5 (t, *J* = 27.5 Hz), 163.6, 163.3, 154.6, 153.1, 143.2 (t, *J* = 31.2 Hz), 132.5, 130.6, 128.3, 128.1, 126.4, 125.7, 125.4, 116.0 (t, *J* = 248.2 Hz), 113.7, 113.5, 65.9, 64.5, 55.5, 54.6, 54.1, 35.0, 34.9, 31.2, 31.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.73 (s), -98.53 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{29}F_2N_2O_3^+$ 431.2141; found 431.2150.

3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-(methylthio)phenyl)-3-(morpholinoimino)propan-1-one (5af)



colorless oil, 48 h, E/Z = 6.8/1, 57 mg, 85% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 1.66H), 7.72 (dd, *J* = 11.1, 8.5 Hz, 0.56H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.3 Hz,1.70H), 7.18 (dd, *J* = 11.4, 6.4 Hz, 2H), 3.51–3.35 (m, 4H), 2.85–2.67 (m, 3.41H), 2.45-2.43 (m, 3.5H), 1.29-1.28 (m, 9H); **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 187.9 (t, *J* = 27.7 Hz), 154.7, 153.2, 146.5, 146.1, 143.0 (t, *J* = 31.4 Hz), 130.4, 129.7, 128.6, 128.3, 128.2, 128.1, 125.7, 124.7, 124.5, 116.0 (t, *J* = 250.0 Hz), 65.9, 64.4, 54.6, 54.0, 34.9, 31.2, 31.2, 14.6; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.87 (s), -98.76 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{29}F_2N_2O_2S^+$ 447.1912; found 447.1917.

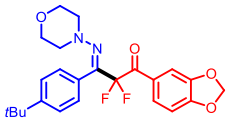
3-(4-(tert-butyl)phenyl)-1-(3,5-dimethoxyphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ag)



colorless oil, 48 h, E/Z = 6.4/1, 46 mg, 67% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 0.38H), 7.44 (dd, *J* = 8.6, 2.1 Hz, 2H), 7.39 (d, *J* = 8.6 Hz,

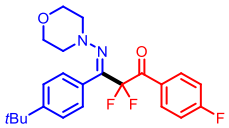
1.62H), 7.08 (d, *J* = 2.2 Hz, 1.54H), 6.93 (d, *J* = 2.2 Hz, 0.37H), 6.60 (t, *J* = 2.3 Hz, 0.76H), 6.55 (t, *J* = 2.2 Hz, 0.20H), 3.76-3.72 (m,6H), 3.47–3.45 (m, 4H), 2.77–2.75 (m, 3.23H), 2.46 (s, 0.68H), 1.29-1.28 (m, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.49 (t, *J* = 27.8 Hz) 160.60, 160.42, 154.79, 153.22, 142.91 (t, *J* = 31.2 Hz), 135.19, 134.35, 128.24, 128.09, 125.74, 115.84 (t, *J* = 250.2 Hz), 107.83, 106.07, 105.86, 105.35, 65.89, 64.37, 55.61, 54.49, 54.05, 34.91, 31.21, 31.16; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.65 (s), -98.50 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{31}F_2N_2O_4^+$ 461.2246; found 461.2255.

1-(benzo[d][1,3]dioxol-5-yl)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ah)



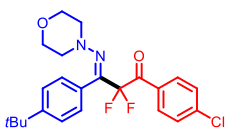
colorless oil, 48 h, E/Z = 8.9/1, 63 mg, 95% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 0.22H), 7.56 (d, *J* = 8.3 Hz, 0.87H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2.62H), 7.33 (d, *J* = 10.6 Hz, 0.33H), 6.80-6.74 (m, 1H), 5.99-5.98 (m, 2H), 3.52–3.35 (m, 4H), 2.83–2.66 (m, 3.54H), 2.47 (s, 0.4H), 1.29-1.28 (m, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ187.1 (t, *J* = 27.5 Hz), 154.7, 153.2, 151.9, 151.6, 148.0, 147.7, 143.0 (t, *J* = 31.0 Hz), 128.3, 128.2, 128.1, 128.0, 126.8, 125.7, 116.0 (t, *J* = 250.2 Hz), 109.7, 107.9, 101.9, 65.9, 64.5, 54.6, 54.1, 34.9, 31.2, 31.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.36 (s), -98.12 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{27}F_2N_2O_4^+$ 445.1933; found 445.1944.

3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-fluorophenyl)-3-(morpholinoimino)propan-1-one (5ai)



colorless oil, 48 h, E/Z = 10.4/1, 61 mg, 98% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.6, 5.5 Hz, 1.77H), 7.83 (dd, *J* = 8.6, 5.3 Hz, 0.19H), 7.74 (d, *J* = 8.2 Hz, 0.19H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 1.75H), 7.06 (t, *J* = 8.6 Hz, 2H), 3.52–3.34 (m, 4H), 2.79–2.61 (m, 3.64H), 2.44 (s, 0.35H), 1.29-1.27 (m, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.5 (t, *J* = 27.9 Hz), 167.0, 164.4, 153.3, 142.7 (t, *J* = 31.2 Hz), 132.7 (d, *J* = 9.2 Hz), 130.0 (d, *J* = 2.9 Hz), 128.1, 128.0, 125.8, 115.9 (t, *J* = 248.5 Hz), 115.7, 115.4, 113.4, 65.9, 64.3, 54.5, 54.0, 34.9, 31.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.9 (s), -98.78 (s), -104.12--104.19 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{26}F_3N_2O_2^+$ 419.1941; found 419.1942.

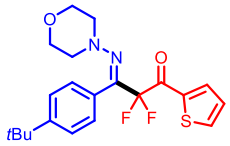
3-(4-(tert-butyl)phenyl)-1-(4-chlorophenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5aj)



colorless oil, 48 h, E/Z = 7.6/1, 64 mg, 99% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 1.67H), 7.74 (d, *J* = 8.4 Hz, 0.49H), 7.47–7.42 (m, 2H), 7.40-7.29 (m, 2H), 3.46-3.39 (m, 4H), 2.74–2.66 (m, 3.49H), 2.44 (s, 0.46H), 1.29-1.28 (m, 9H);

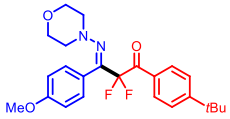
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 187.8 (t, *J* = 28.1 Hz), 153.3, 142.6 (t, *J* = 31.4 Hz), 139.8, 132.0, 131.4, 128.9, 128.7, 128.1, 128.0, 125.8, 115.9 (t, *J* = 250.2 Hz), 65.9, 64.2, 54.5, 54.0, 34.9, 31.2, 31.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.02 (s), -98.94 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{26}ClF_2N_2O_2^+$ 435.1645; found 435.1647.

3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-1-(thiophen-2-yl)propan-1-one (5ak)



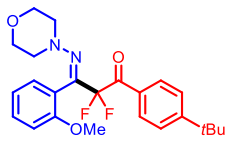
colorless oil, 48 h, E/Z = 5.2/1, 57 mg, 93% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77–7.73 (m, 0.81H), 7.69–7.59 (m, 1.50H), 7.48–7.35 (m, 3.71H), 7.10–7.04 (m, 1H), 3.56–3.36 (m, 4H), 2.85–2.68 (m, 3.35H), 2.55 (s, 0.64H), 1.28-1.27 (m, 9H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 182.2 (t, *J* = 29.5 Hz), 154.6, 153.1, 142.1 (t, *J* = 31.4 Hz), 139.9, 134.7, 134.7, 134.6, 134.5, 128.3, 128.3, 128.2, 125.7, 125.6, 115.8 (t, *J* = 250.5 Hz), 65.9, 64.7, 54.2, 54.1, 34.9, 31.2, 31.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.73 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{25}F_2N_2O_2S^+$ 407.1599; found 407.1603.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(4-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ga)



colorless oil, 48 h, E/Z > 20/1, 54 mg, 84% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.63–3.34 (m, 4H), 3.00–2.67 (m, 4H), 1.27 (s, 9H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 188.5 (t, *J* = 27.7 Hz), 160.6, 157.1, 143.6 (t, *J* = 31.0 Hz), 130.8, 130.0, 129.9, 125.3, 123.2, 115.9 (t, *J* = 248.6 Hz), 113.4, 65.9, 55.3, 54.0, 35.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.02 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{29}F_2N_2O_3^+$ 431.2141; found 431.2153.

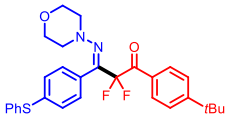
1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(2-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ha)



colorless oil, 48 h, E/Z > 20/1, 52 mg, 81% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.47–7.41 (m, 1H), 7.39 (d, *J* = 7.0 Hz, 1H), 7.05 (td, *J* = 7.5, 0.6 Hz, 1H), 7.00 (d, *J* = 8.3 Hz, 1H), 3.95 (s, 3H), 3.64–3.37 (m, 4H), 2.91 (s, 4H), 1.38 (s, 9H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 189.0 (t, *J* = 27.9 Hz), 157.6, 156.9, 136.0 (t, *J* = 32.5 Hz), 131.3, 131.0, 130.5, 130.4, 125.1, 121.3, 120.9, 116.2 (t, *J* = 249.4 Hz), 111.0, 66.1, 55.8, 53.3, 35.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.49--99.36 (m), -101.5 (s) ppm; **HRMS**

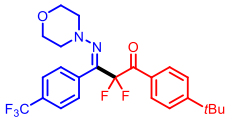
(ESI) m/z: $[M+H]^+$ calcd for $C_{24}H_{29}F_2N_2O_3^+$ 431.2141; found 431.2144.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(4-(phenylthio)phenyl)propan-1-one (5ia)



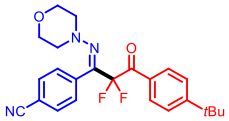
colorless oil, 48 h, E/Z = 20/1, 62 mg, 82% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 1.78H), 7.73–7.67 (m, 0.29H), 7.45–7.37 (m, 5.70H), 7.34-7.29 (m, 3.18H), 7.20–7.16 (m, 2H), 3.52–3.35 (m, 4H), 2.80–2.68 (m, 3.79H), 2.39 (s, 0.19H), 1.26-1.24 (m, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.4 (t, *J* = 27.7 Hz), 157.2, 142.3 (t, *J* = 31.2 Hz), 140.3, 133.5, 132.6, 130.7, 130.0, 129.6, 129.0, 128.7, 128.6, 128.4, 125.3, 115.8 (t, *J* = 250.2 Hz), 65.9, 64.3, 54.6, 54.1, 35.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.82 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{29}H_{31}F_2N_2O_2S^+$ 509.2069; found 509.2072.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(4-(trifluoromethyl)phenyl)propan-1-one (5ja)



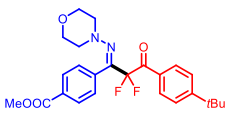
colorless oil, 48 h, E/Z = 17/1, 64 mg, 91% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.66 (s, 4H), 7.42 (d, *J* = 8.6 Hz, 2H), 3.52–3.37 (m, 4H), 2.83–2.69 (m, 3.74H), 2.45 (s, 0.22H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.2 (t, *J* = 27.5 Hz), 157.4, 140.3 (t, *J* = 31.7 Hz), 135.3, 131.8 (q, *J* = 32.6 Hz), 130.7, 130.0, 129.1, 125.8 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 270.8 Hz) 119.6, 115.7 (t, *J* = 250.5 Hz), 65.8, 54.2, 35.2, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.93 (s), -96.67 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{26}F_5N_2O_2^+$ 469.1909; found 469.1905.

4-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)benzonitrile (5ka)



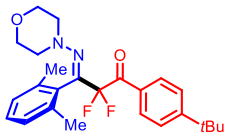
colorless oil, 48 h, E/Z > 20/1, 58 mg, 90% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 3.56–3.31 (m, 4H), 2.82–2.63 (m, 4H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.0 (t, *J* = 27.5 Hz), 157.6, 139.5 (t, *J* = 31.5 Hz), 136.2, 132.6, 130.6, 130.0, 129.4, 125.4, 118.03, 115.6 (t, *J* = 249.0 Hz), 113.7, 113.1, 65.7, 54.3, 35.3, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.44 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{26}F_2N_3O_2^+$ 426.1988; found 426.1997.

methyl-4-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)benzoate (5la)



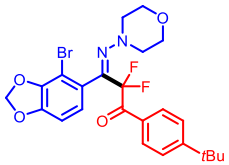
colorless oil, 48 h, E/Z = 15/1, 66 mg, 96% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H), 3.52–3.39 (m, 4H), 2.87–2.66 (m, 3.68H), 2.44 (s, 0.25H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.2 (t, *J* = 27.5 Hz), 166.3, 157.4, 140.9 (t, *J* = 31.5 Hz), 136.1, 131.3, 130.7, 130.0, 128.7, 125.4, 115.7 (t, *J* = 250.3 Hz), 65.8, 54.2, 52.4, 35.2, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.71 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{29}F_2N_2O_4^+$ 459.2090; found 459.2087.

1-(4-(tert-butyl)phenyl)-3-(2,6-dimethylphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ma)



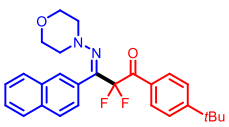
colorless oil, 48 h, E/Z > 20/1, 52 mg, 82% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.17–7.11 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 3.48–3.34 (m,4H), 2.86–2.65 (m, 4H), 2.32 (s, 6H), 1.29 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 190.9 (t, *J* = 28.6 Hz), 156.9, 139.4 (t, *J* = 33.6 Hz), 137.8, 132.0, 131.8, 130.3, 130.3, 129.4, 127.7, 125.1, 117.1 (t, *J* = 250.9 Hz), 66.4, 53.0, 35.2, 31.1, 20.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.31 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{31}F_2N_2O_2^+$ 429.2348; found 429.2344.

3-(4-bromobenzo[d][1,3]dioxol-5-yl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5na)



colorless oil, 48 h, Z/E > 20/1, 70 mg, 89% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.01 (s, 1H), 6.89 (d, *J* = 1.5 Hz, 1H), 5.99 (dd, *J* = 5.7, 1.2 Hz, 2H), 3.49 (t, *J* = 4.8 Hz, 4H), 3.01–2.88 (m, 2H), 2.87–2.73 (m, 2H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ189.7–188.8 (m), 157.1, 149.7, 147.4, 133.9 (dd, *J* = 35.0, 30.6 Hz), 131.1, 130.3, 126.1, 125.1, 115.7 (dd, *J* = 455.0, 207.3 Hz), 115.6, 114.2, 112.8, 110.9, 102.4, 66.3, 53.2, 35.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ-96.45 (q, *J* = 270.8 Hz), -104.07 (dd, *J* = 293.9, 234.7 Hz) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{24}H_{26}BrF_2N_2O_4^+$ 523.1039; found523.1041.

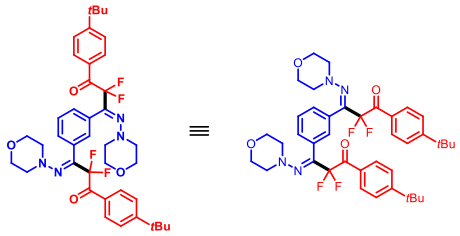
1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(naphthalen-2-yl)propan-1-one (5oa)



colorless oil, 48 h, E/Z > 20/1, 57 mg, 84% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.91 (d, *J* = 8.3 Hz, 2H), 7.87–7.78 (m, 3H), 7.63 (dd, *J* = 8.5, 1.2

Hz, 1H), 7.53–7.46 (m, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 3.60–3.33 (m, 4H), 2.87 – 2.69 (m, 4H), 1.28 (s, 9H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 188.5 (t, *J* = 27.5 Hz), 157.2, 142.7 (t, *J* = 31.2 Hz), 133.6, 132.9, 130.8, 130.0, 128.7, 128.6, 128.6, 128.3, 127.9, 127.5, 126.9, 125.3, 125.3, 116.0 (t, *J* = 250.2 Hz), 65.9, 54.2, 35.2, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.62 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{27}H_{29}F_2N_2O_2^+$ 451.2192; found 451.2197.

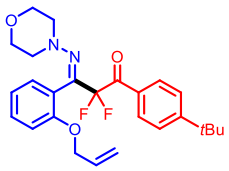
3,3'-(1,3-phenylene)bis(1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one) (5pa)



colorless oil, 48 h, E/Z = 11.7/1, 69 mg (**0.1 mmol amount was used**), 96% yield, R_f = 0.3 (ethyl acetate/hexane = 25%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 3.86H), 7.74 (t, *J* = 7.1 Hz, 0.57H), 7.69 (s, 0.8H), 7.54 (dt, *J* = 8.7, 7.1 Hz, 2.84H), 7.42 (dd, *J* = 10.3, 8.1 Hz, 4H), 3.58–3.31 (m, 8H), 2.95–2.68 (m, 7.39H), 12.9 (s, 18H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 188.5 (t, *J* = 27.7 Hz), 157.5, 140.2 (t, *J* = 31.4 Hz), 132.4, 130.8, 130.0, 129.7, 129.5, 129.0, 125.4, 115.9 (t, *J* = 250.0 Hz), 65.8, 54.2, 35.3, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.86 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{40}H_{47}F_4N_4O_4^+$ 723.3528; found 723.3530.

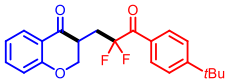
3-(2-(allyloxy)phenyl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one（5qa）

The structure is not completely determined



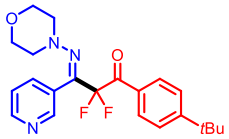
colorless oil, 48 h, E/Z = 2/1, 37 mg, 55% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 1.26H), 7.83 (d, *J* = 8.3 Hz, 0.61H), 7.45–7.27 (m, 3.84H), 7.20 (dd, *J* = 7.4, 1.5 Hz, 0.29H), 7.00–6.93 (m, 1H), 6.92–6.84 (m, 1H), 6.12–5.88 (m, 1H), 5.49–5.16 (m, 2H), 4.66–4.50 (m, 2H), 3.50–3.45 (m, 1.30H), 3.41 (t, *J* = 4.8 Hz, 2.61H), 3.22–3.14 (m, 1.31H), 2.94–2.72 (m, 2.75H), 1.33–1.24 (m, 9H) ppm; **$^{13}C\{^{1}H\}$ NMR** (100 MHz, $CDCl_3$) δ 197.6, 194.1, 189.1 (t, *J* = 27.9 Hz), 156.7 (dd, *J* = 75.7, 40.9 Hz), 136.3–135.1 (m), 134.9, 132.8, 131.9, 131.1, 131.0, 130.9, 130.8, 130.5, 130.4, 129.3, 125.5, 125.1, 122.0, 121.4, 121.0, 121.0, 117.8, 117.4, 116.3 (t, *J* = 248.7 Hz), 111.8, 69.0, 68.7, 66.3, 66.1, 53.8, 53.2, 35.2, 31.1, 31.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.80 (s), -97.96 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{31}F_2N_2O_3^+$ 457.2297; found 457.2314.

3-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-oxopropyl)chroman-4-one (5qa')



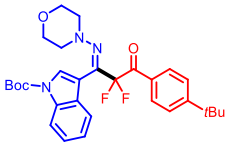
colorless oil, 48 h, 18 mg, 32% yield, R_f = 0.4 (ethyl acetate/hexane = 5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.84 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.50–7.44 (m, 2H), 7.44–7.39 (m, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 4.71 (dd, *J* = 11.4, 5.2 Hz, 1H), 4.23 (t, *J* = 11.7 Hz, 1H), 3.19 (ddt, *J* = 10.3, 5.0, 3.4 Hz, 1H), 3.13–2.98 (m, 1H), 2.10 (dddd, *J* = 24.2, 15.8, 11.0, 8.7 Hz, 1H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 191.9, 188.2 (t, *J* = 30.6 Hz), 161.6, 158.6, 136.1, 130.3, 128.9, 127.6, 125.8, 125.2, 122.0, 120.3, 119.4 (t, *J* = 254.4 Hz), 117.8, 72.5, 40.4, 35.3, 31.0, 29.5 (t, *J* = 23.1 Hz) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{22}H_{23}F_2O_3^+$ 373.1610; found 373.1611.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(pyridin-3-yl)propan-1-one （5ra）



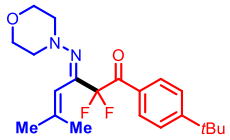
colorless oil, 48 h, E/Z = 9.7/1, 40 mg, 67% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.68–8.61 (m, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.44–7.41 (m, 2H), 7.38 (dd, *J* = 7.9, 5.0 Hz, 1H), 3.51–3.34 (m, 4H), 2.86–2.69 (m, 3.59H), 1.29 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.1 (t, *J* = 27.5 Hz), 170.4, 157.5, 157.1, 150.6, 149.2, 139.0 (t, *J* = 31.9 Hz), 136.2, 130.6, 130.0, 130.0, 128.1, 127.0, 125.5, 125.4, 123.8, 115.7 (t, *J* = 250.4 Hz), 65.8, 54.2, 35.3, 31.1, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.81 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{22}H_{26}F_2N_3O_2^+$ 402.1988; found 402.1987.

tert-butyl-3-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)-1H-indole-1-carboxylate (5sa)



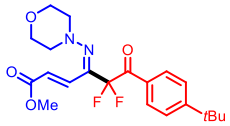
colorless oil, 48 h, E/Z = 14.1/1, 58 mg, 72% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 7.9 Hz, 1H), 8.07 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 3.89–3.78 (m, 4H), 3.20–3.10 (m, 4H), 1.49 (s, 9H), 1.28 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ186.5 (t, *J* = 30.7 Hz), 157.2, 149.8, 136.1, 131.2 (t, *J* = 7.2 Hz), 130.3, 129.7, 127.3 (t, *J* = 29.7 Hz), 126.8, 126.5, 125.6, 124.5, 123.7, 121.8, 116.6 (t, *J* = 252.8 Hz), 115.1, 85.7, 66.5, 51.6, 35.2, 31.1, 28.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -88.91 (s), -97.89 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{30}H_{36}F_2N_3O_4^+$ 540.2668; found 540.2679.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-5-methyl-3-(morpholinoimino)hex-4-en-1-one (5ta)



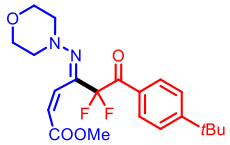
colorless oil, 48 h, E/Z > 20/1, 59 mg, 85% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.6 Hz, 2H), 5.83 (s, 1H), 3.64–3.44 (m, 4H), 3.07–2.73 (m, 4H), 1.85 (s, 3H), 1.63 (s, 3H), 1.27 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ188.7 (t, *J* = 27.8 Hz), 157.1, 146.0, 143.0 (t, *J* = 31.1 Hz), 130.8, 130.0, 129.0, 125.2, 115.9 (t, *J* = 250.6 Hz) , 113.4, 66.4, 53.4, 35.2, 31.0, 25.8, 21.7; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -99.09 ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{29}F_2N_2O_2^+$ 379.2192; found 379.2200.

methyl (2E,4E)-6-(4-(tert-butyl)phenyl)-5,5-difluoro-4-(morpholinoimino)-6-oxohex-2-enoate (5ua)



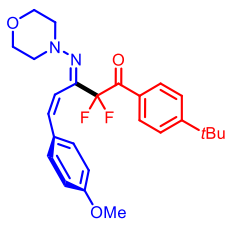
colorless oil, 48 h, 24 mg, 39% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.70 (dd, *J* = 10.2 Hz,, *J* = 17.1 Hz, 2H), 7.45–7.37 (m, 2H), 3.92–3.74 (m, 4H), 3.58 (s, 3H), 3.41–3.20 (m, 4H), 1.27 (s, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.1 (t, *J* = 29.8 Hz), 165.2 (t, *J* = 6.6 Hz), 157.6, 144.6, 130.0, 129.6, 128.4 (t, *J* = 5.8 Hz), 125.6, 120.7–120.3 (m), 116.5 (t, *J* = 252.5 Hz), 66.0, 52.2, 50.8, 35.2, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -93.69 ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{27}F_2N_2O_4^+$ 409.1933; found 409.1933.

methyl (2Z,4E)-6-(4-(tert-butyl)phenyl)-5,5-difluoro-4-(morpholinoimino)-6-oxohex-2-enoate (5ua')



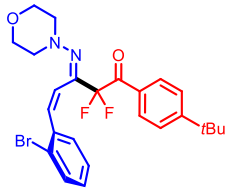
colorless oil, 48 h, 34 mg, 57% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9.3 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 9.3 Hz, 1H), 3.89–3.73 (m, 4H), 3.58 (s, 3H), 3.42–3.23 (m, 4H), 1.27 (s, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.0 (t, *J* = 31.2 Hz), 164.2, 157.8, 143.2 (t, *J* = 8.9 Hz), 130.8, 129.9, 129.8, 125.6, 120.4 (t, *J* = 22.1 Hz), 115.4 (t, *J* = 254.8 Hz), 66.1, 51.7, 50.8, 35.2, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.08 ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{21}H_{27}F_2N_2O_4^+$ 409.1933; found 409.1931.

(3E,4Z)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-5-(4-methoxyphenyl)-3-(morpholinoimino)pent-4-en-1-one (5va)



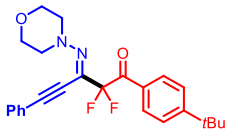
colorless oil, 48 h, 58 mg, 86% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 2H), 7.03 (d, *J* = 9.1 Hz, 1H), 6.84 (d, *J* = 9.1 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.74 (s, 3H), 3.72–3.67 (m, 4H), 2.98–2.90 (m, 4H), 1.25 (s, 9H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.0 (t, *J* = 30.1 Hz), 159.7, 158.1, 135.0 (t, *J* = 22.3 Hz), 132.9, 131.4, 131.1 (t, *J* = 8.7 Hz), 130.1, 129.8, 125.6, 124.7, 116.7 (t, *J* = 242.9 Hz), 113.9, 66.2, 55.2, 51.1, 35.3, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.25 ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{26}H_{31}F_2N_2O_3^+$ 457.2297; found 457.2304.

(3E,4Z)-5-(2-bromophenyl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)pent-4-en-1-one (5wa)



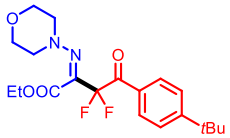
colorless oil, 48 h, 56 mg, 70% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.32–7.25 (m, 2H), 7.18–7.06 (m, 1H), 6.82 (d, *J* = 9.2 Hz, 1H), 6.69 (d, *J* = 9.2 Hz, 1H), 3.73–3.64 (m, 4H), 2.94 (dd, *J* = 7.5, 4.2 Hz, 4H), 1.26 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.4 (t, *J* = 30.0 Hz), 158.2, 133.6–133.5 (m), 133.1, 132.3, 131.7, 130.5 (t, *J* = 2.8 Hz), 130.2, 130.0, 127.4, 125.6, 124.9, 116.8 (t, *J* = 252.6 Hz)., 66.1, 50.9, 35.3, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -96.63 (dd, *J* = 596.6 Hz, 263.7 Hz) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{28}BrF_2N_2O_2^+$ 505.1297; found 505.1299.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-5-phenylpent-4-yn-1-one (5xa)



colorless oil, 48 h, E/Z = 10/1, 50 mg, 79% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.5 Hz, 1.62H), 7.76–7.66 (m, 0.29H), 7.45–7.37 (m, 3.75H), 7.35–7.22 (m, 3.32H), 3.86–3.74 (m, 0.39H), 3.62 (dd, *J* = 5.7, 3.4 Hz, 3.27H), 3.58–3.51 (m, 3.58H), 3.15–3.07 (m, 0.35H), 1.27-1.20 (m, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 187.8 (t, *J* = 27.8 Hz), 157.4, 131.5, 130.4 (t, *J* = 13.5 Hz), 130.1, 129.7, 128.6, 125.4, 121.5, 119.7 (t, *J* = 33.3 Hz), 117.9, 114.9 (t, *J* = 251.3 Hz), 101.3, 79.2, 66.1, 53.4, 35.2, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -98.28 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{27}F_2N_2O_2^+$ 425.2035; found 425.2033.

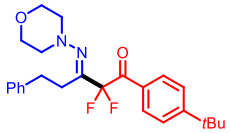
ethyl-4-(4-(tert-butyl)phenyl)-3,3-difluoro-2-(morpholinoimino)-4-oxobutanoate (5ya)



colorless oil, 48 h, E/Z > 20/1, 58 mg, 97% yield, R_f = 0.3 (ethyl acetate/hexane = 15%); **^{1}H NMR**

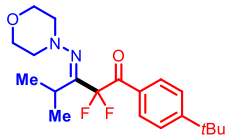
(400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.66–3.53 (m, 4H), 3.26–3.10 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.26 (d, *J* = 6.0 Hz, 9H) ppm; **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 187.5 (t, *J* = 27.9 Hz), 161.7, 157.5, 130.2, 130.0, 130.0, 125.4, 124.7 (t, *J* = 33.1 Hz), 115.3 (t, *J* = 250.7 Hz)., 66.0, 62.2, 53.7, 35.2, 31.0, 14.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -97.01 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{20}H_{27}F_2N_2O_4^+$ 397.1933; found 397.1939.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-5-phenylpentan-1-one (5za)



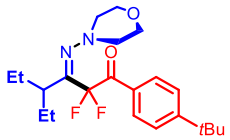
colorless oil, 48 h, E/Z = 6.4/1, 47 mg, 74% yield, R_f = 0.3 (ethyl acetate/hexane = 25%); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.25-7.24 (m, 5H), 3.29 (s, 4H), 2.98 (qd, *J* = 6.6, 3.7 Hz, 4H), 2.29 (s, 4H), 1.32–1.10 (m, 9H) ppm; **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 180.3 (t, *J* = 26.1 Hz), 169.0 (t, *J* = 26.5 Hz), 157.1, 140.5, 130.1, 128.7, 128.6, 128.5, 128.3, 126.3, 125.4, 125.2, 111.3 (t, *J* = 254.4 Hz), 64.4, 54.1, 35.2, 32.1, 31.8, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -101.63 (s), -102.95 ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{25}H_{31}F_2N_2O_2^+$ 429.2348; found 429.2355.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-4-methyl-3-(morpholinoimino)pentan-1-one (5bb)



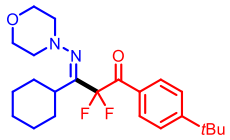
colorless oil, 48 h, E/Z > 20/1, 48 mg, 87% yield, R_f = 0.3 (ethyl acetate/hexane = 25%); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 3.31 (s, 4H), 3.08 (dt, *J* = 13.6, 6.8 Hz, 1H), 2.32 (s, 4H), 1.26 (s, 9H) ppm; **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 176.6–171.9 (m), 156.9, 130.3, 128.4 (t, *J* = 2.3 Hz), 125.4, 112.1 (t, *J* = 254.7 Hz), 64.5, 54.0, 35.2, 31.1, 29.8, 20.5; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.38 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{20}H_{29}F_2N_2O_2^+$ 367.2192; found 367.2199.

1-(4-(tert-butyl)phenyl)-4-ethyl-2,2-difluoro-3-(morpholinoimino)hexan-1-one (5cc)



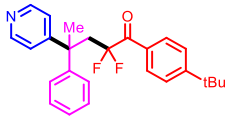
colorless oil, 48 h, Z/E = 9.9/1, 52 mg, 89% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^1H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7 .39 (d, *J* = 8.5 Hz, 2H), 3.28 (s, 3.55H), 2.76–2.66 (m, 1H), 2.37 (s, 3.57H), 1.78 (td, *J* = 14.3, 7.2 Hz, 2H), 1.69–1.55 (m, 2H), 1.27 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 6H) ppm; **$^{13}C\{^1H\}$ NMR** (100 MHz, $CDCl_3$) δ 180.4 (t, *J* = 26.9 Hz), 171.9 (t, *J* = 25.6 Hz), 156.9, 130.6, 128.6, 128.6, 125.3, 112.2 (t, *J* = 255.7 Hz), 64.4, 54.0, 42.8, 35.2, 31.1, 24.6, 11.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -100.45 (s), -102.58 (s), -112.91 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{22}H_{33}F_2N_2O_2^+$ 395.2505; found 395.2510.

1-(4-(tert-butyl)phenyl)-3-cyclohexyl-2,2-difluoro-3-(morpholinoimino)propan-1-one (5dd)



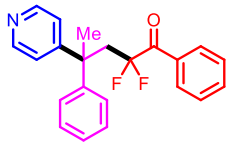
colorless oil, 48 h, E/Z > 20/1, 46 mg, 76% yield, R_f = 0.3 (ethyl acetate/hexane = 10%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 3.30 (s, 4H), 2.81–2.66 (m, 1H), 2.30 (s, 4H), 2.00 (d, *J* = 12.2 Hz, 2H), 1.85–1.75 (m, 2H), 1.68 (d, *J* = 12.5 Hz, 1H), 1.51–1.37 (m, 3H), 1.37–1.31 (m, 2H), 1.26 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 180.0 (t, *J* = 26.6 Hz), 173.7, 173.4, 173.2, 156.9, 130.3, 128.3, 125.3, 114.4, 111.8, 109.3, 64.4, 54.1, 39.2, 35.2, 31.1, 31.0, 26.1, 25.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.35 (s) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{33}F_2N_2O_2^+$ 407.2505; found 407.2508.

1-(4-(tert-butyl)phenyl)-2,2-difluoro-4-phenyl-4-(pyridin-4-yl)pentan-1-one (13a)



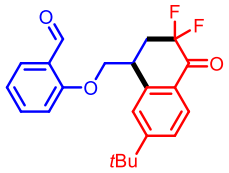
colorless oil, 48 h, 63 mg, 77% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 5.7 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 7.20–7.14 (m, 2H), 7.12–7.03 (m, 5H), 3.13 (t, *J* = 18.1 Hz, 2H), 1.81 (s, 3H), 1.24 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.4 (t, *J* = 30.5 Hz), 158.3, 157.6, 150.8, 149.6, 146.7, 130.2, 130.1, 130.1, 128.9, 128.3, 127.0, 126.7, 125.6, 125.3, 122.4, 119.6 (t, *J* = 255.8 Hz), 43.1 (t, *J* = 21.0 Hz), 42.8, 35.2, 31.0, 27.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -93.03 – -95.53 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{33}F_2N_2O_2^+$ 407.2505; found 407.2508.

2,2-difluoro-1,4-diphenyl-4-(pyridin-4-yl)pentan-1-one (13b)



colorless oil, 48 h, 44 mg, 63% yield, R_f = 0.3 (ethyl acetate/hexane = 20%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.6 Hz, 2H), 7.81 (d, *J* = 7.7 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 2H), 7.12 (t, *J* = 5.0 Hz, 1H), 7.10–7.03 (m, 4H), 3.23–3.02 (m, 2H), 1.82 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 188.8 (t, *J* = 30.8 Hz), 157.6, 149.5, 146.6, 134.2, 130.1, 130.1, 130.1, 128.6, 128.3, 127.1, 126.7, 122.4, 122.1, 119.6 (t, *J* = 256.0 Hz), 44.3, 43.0 (t, *J* = 20.9 Hz), 27.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -92.61 – -95.72 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{33}F_2N_2O_2^+$ 407.2505; found 407.2508.

2-((7-(tert-butyl)-3,3-difluoro-4-oxo-1,2,3,4-tetrahydronaphthalen-1-yl)methoxy)benzaldehyde (18)

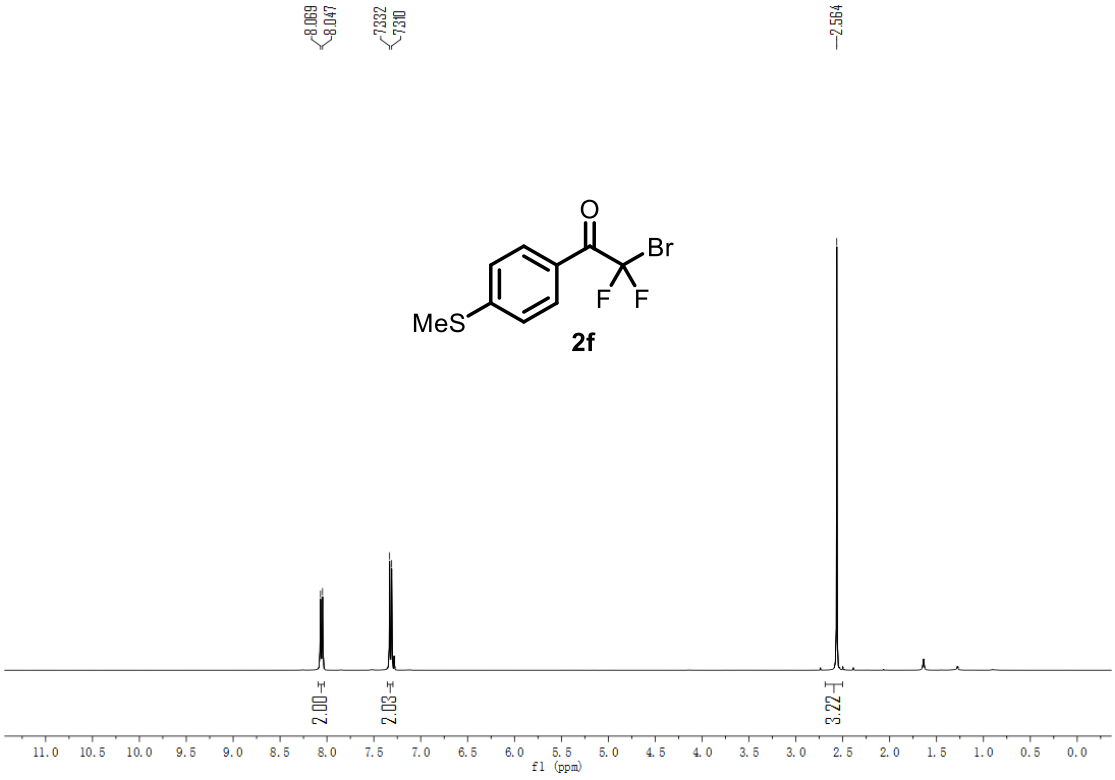


colorless oil, 48 h, 46 mg, 85% yield, R_f = 0.3 (ethyl acetate/hexane = 5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.40 (s, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.52–7.43 (m, 2H), 7.41 (s, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 4.37 (t, *J* = 8.3 Hz, 1H), 4.33–4.23 (m, 1H), 3.81–3.64 (m, 1H), 2.95–2.47 (m, 2H), 1.25 (s, 9H) ppm; **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 184.3 (t, *J* = 25.6 Hz), 184.0, 160.5, 159.8, 141.9, 136.1, 129.2, 129.0, 127.6, 126.1, 125.5, 124.9, 121.5, 113.2 (dd, *J* = 249.7, 246.4 Hz), 112.6, 71.3, 71.3, 36.9 (d, *J* = 5.6 Hz), 35.5, 34.6 (t, *J* = 22.7 Hz), 30.9; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -102.04 (ddd, *J* = 280.3, 28.7, 10.9 Hz), -104.87–-110.02 (m) ppm; **HRMS (ESI)** m/z: $[M+H]^+$ calcd for $C_{23}H_{33}F_2N_2O_2^+$ 407.2505; found 407.2508.

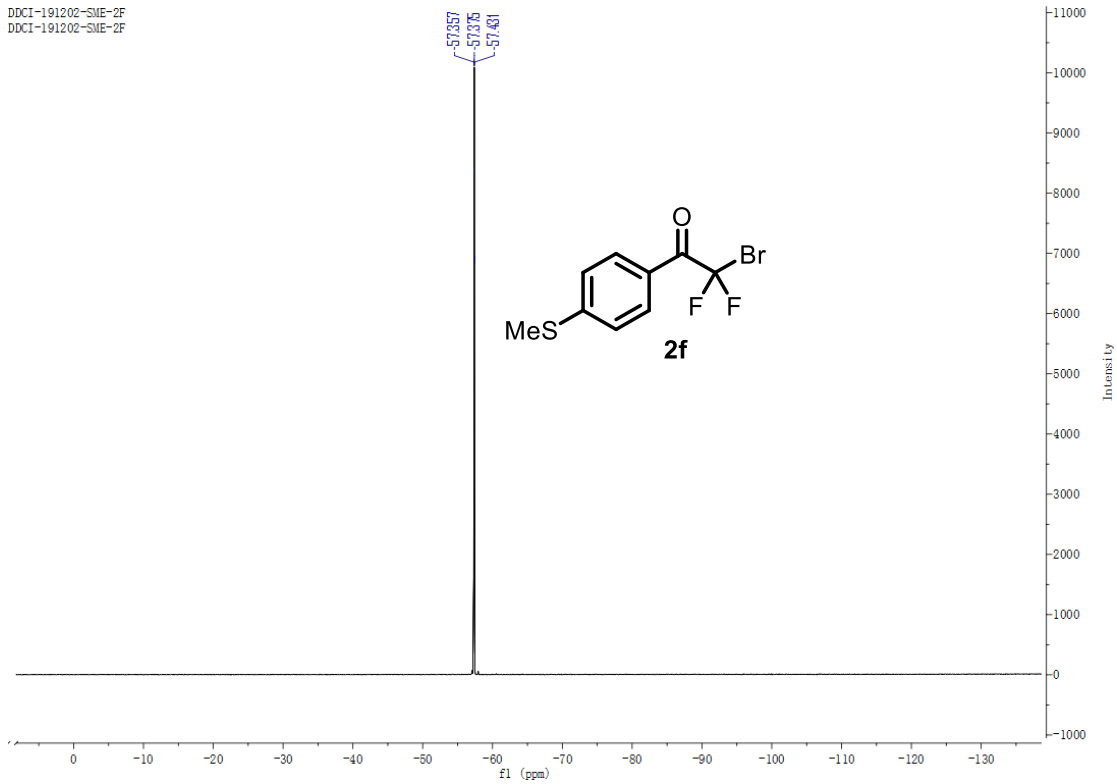
11. Copies ^{1}H NMR, ^{13}C NMR, ^{19}F NMR

2-bromo-2,2-difluoro-1-(4-(methylthio)phenyl)ethan-1-one (2f)

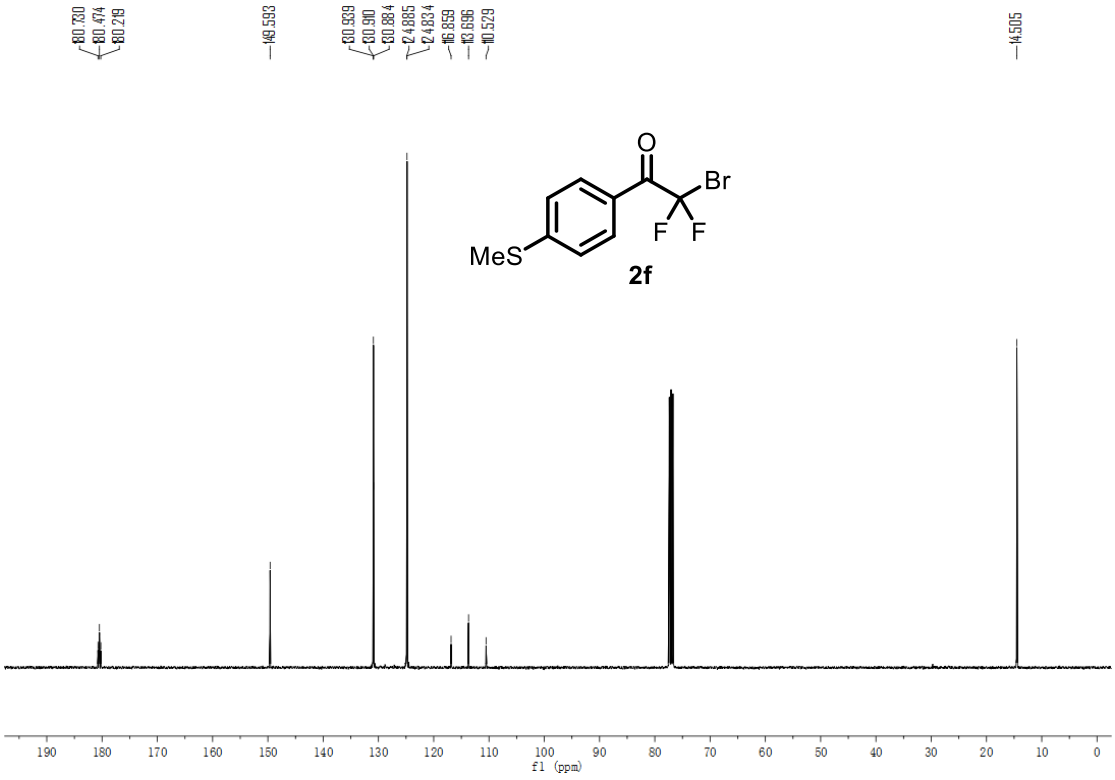
^{1}H NMR (400 MHz, $CDCl_3$):



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

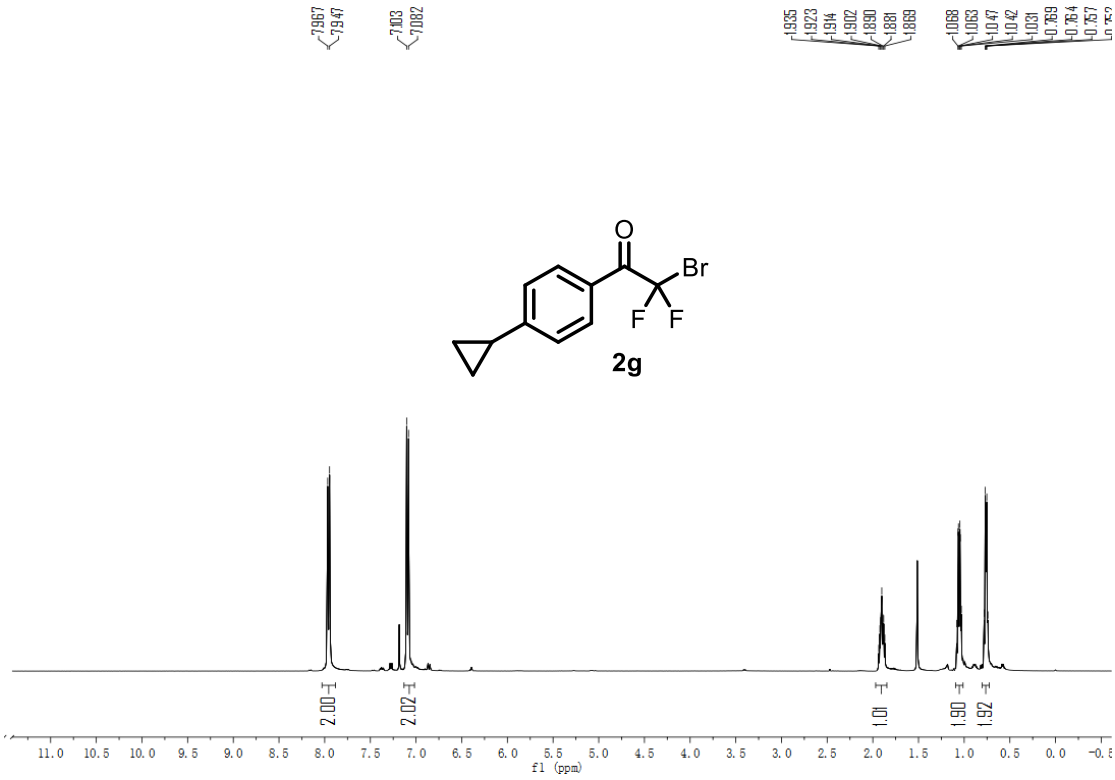


^{13}C NMR (100 MHz, $CDCl_3$):

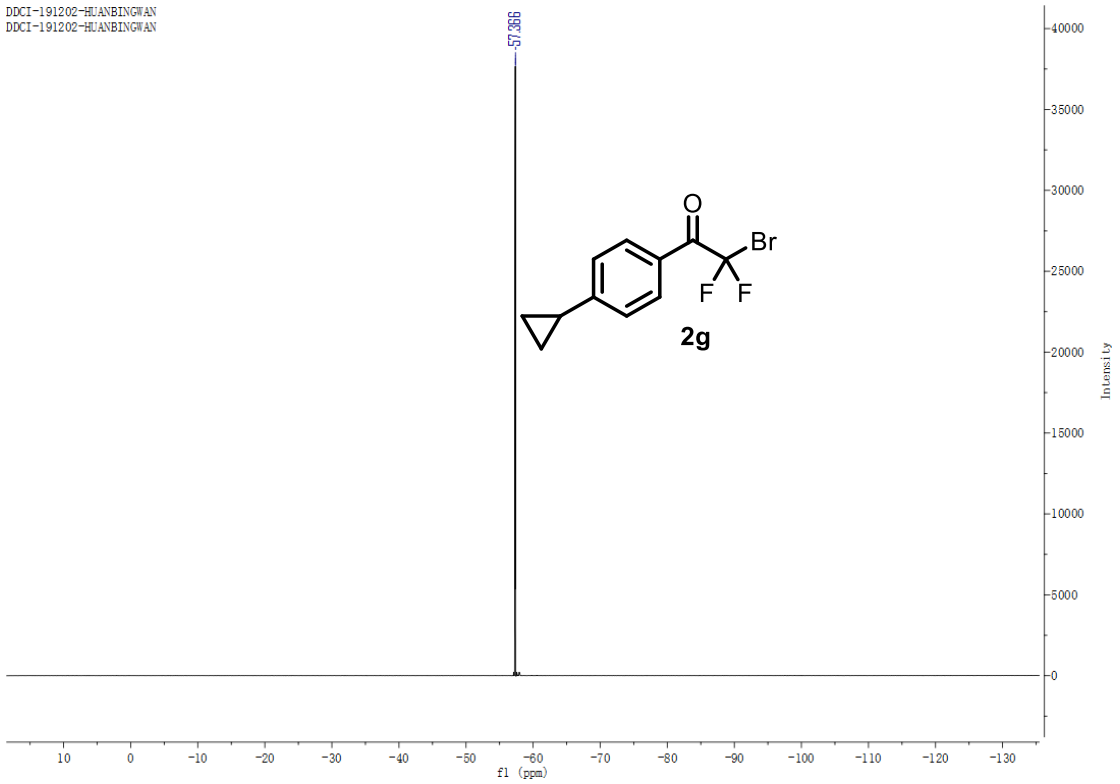


2-bromo-1-(4-cyclopropylphenyl)-2,2-difluoroethan-1-one (2g)

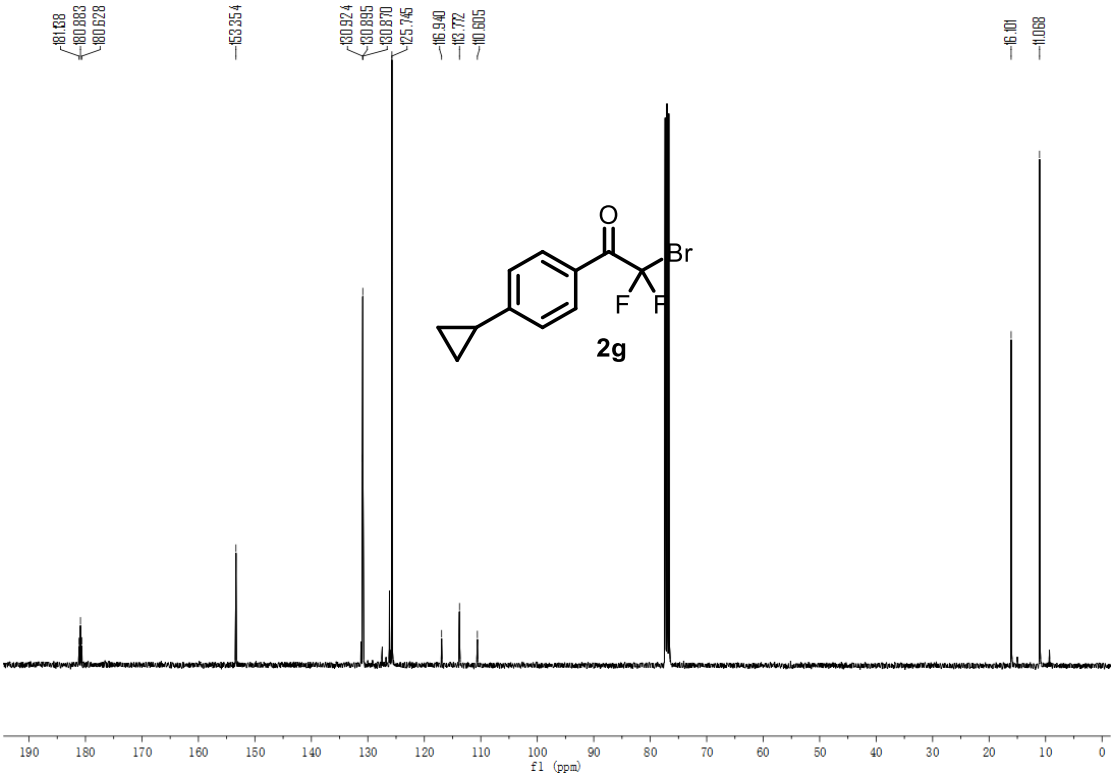
^{1}H NMR (400 MHz, $CDCl_3$):



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

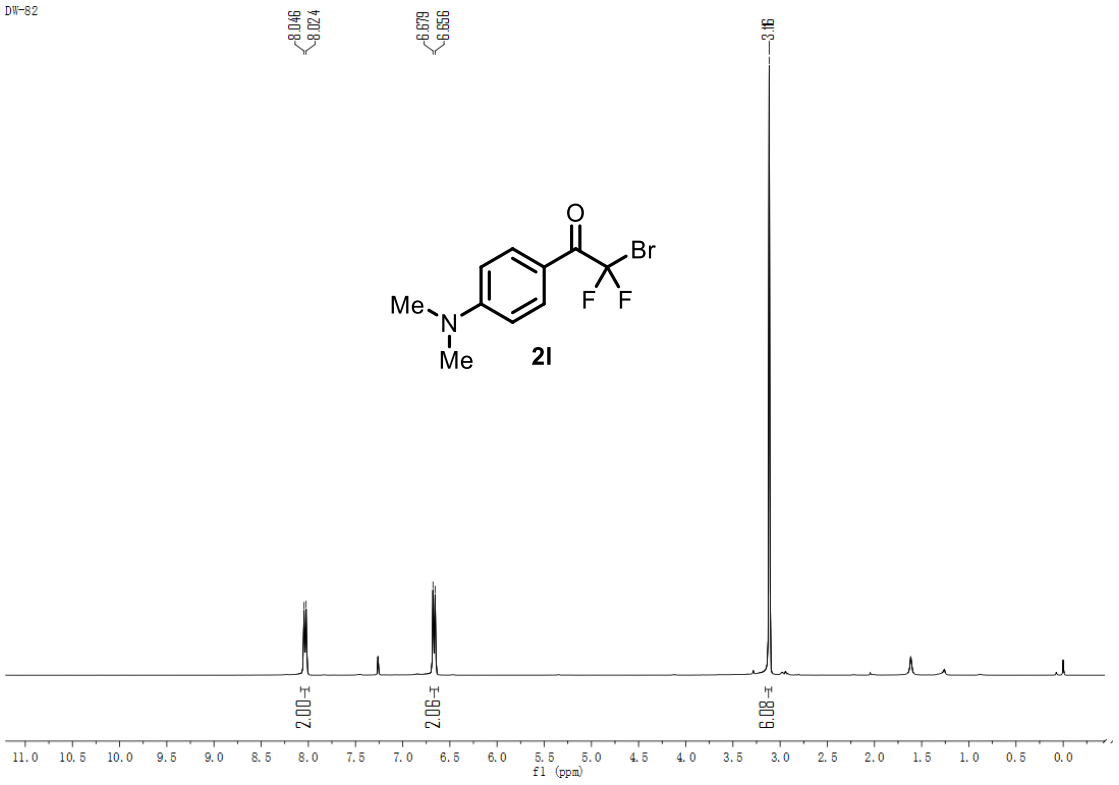


^{13}C NMR (100 MHz, $CDCl_3$):

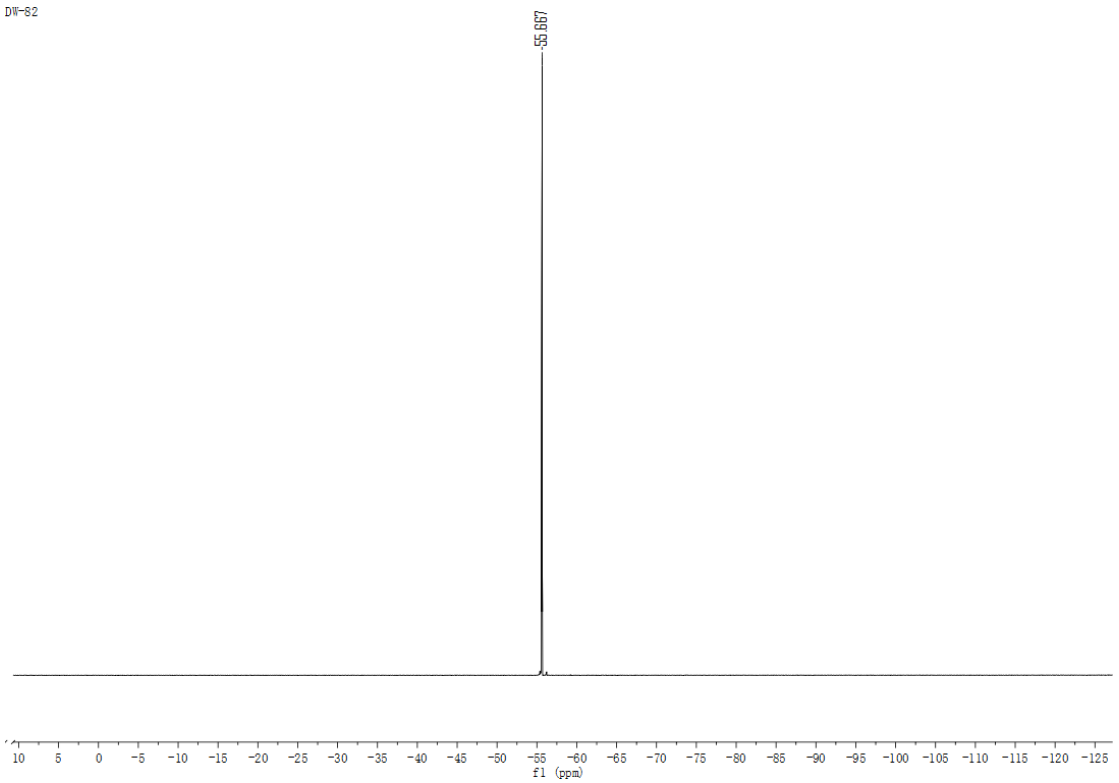


2-bromo-1-(4-(dimethylamino)phenyl)-2,2-difluoroethan-1-one (2l)

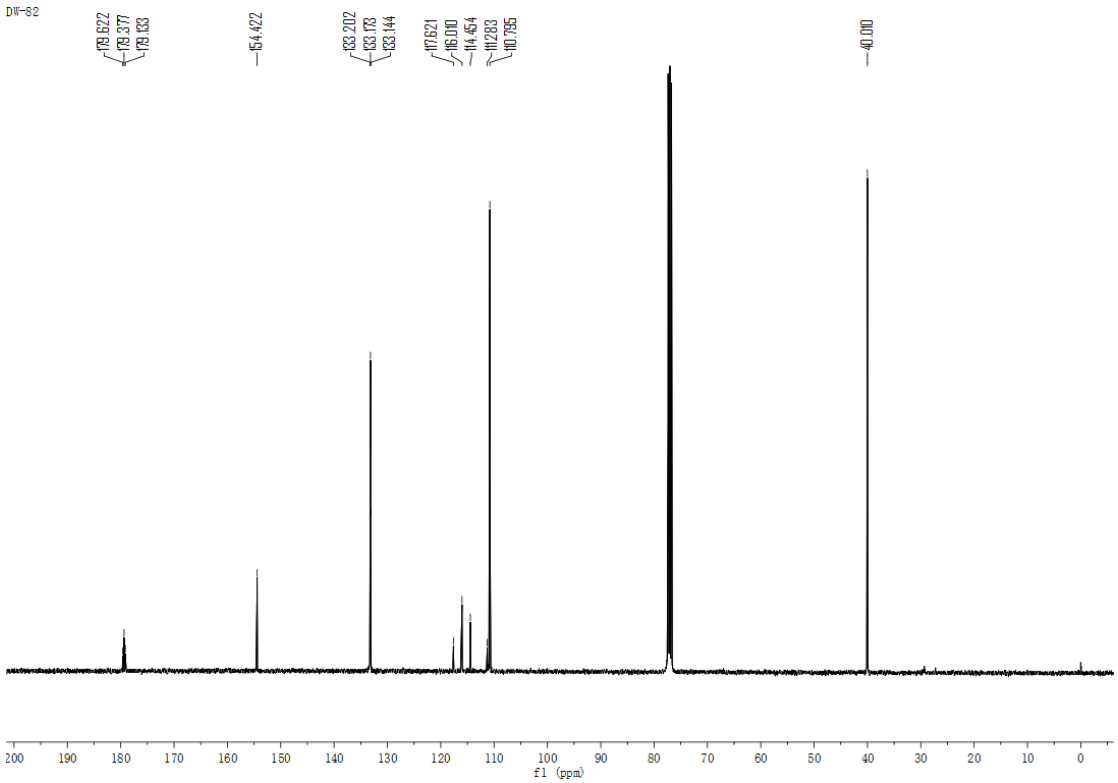
^{1}H NMR (400 MHz, $CDCl_3$):



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

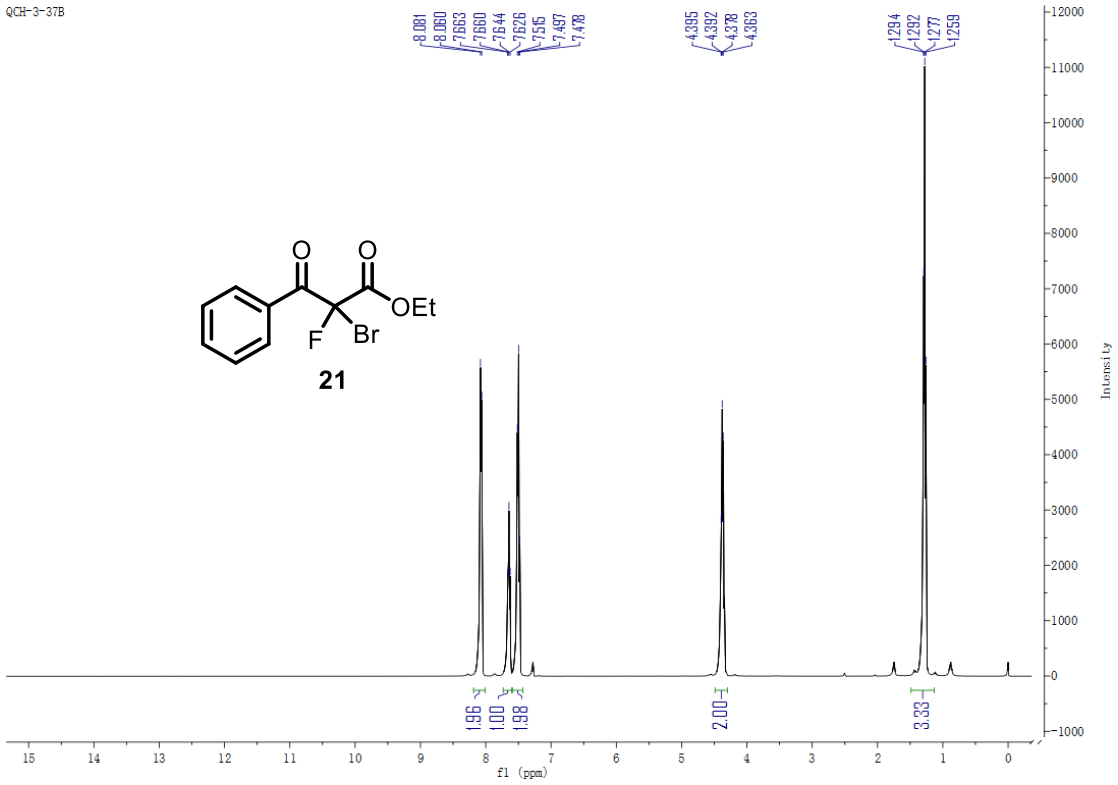


^{13}C NMR (100 MHz, $CDCl_3$):

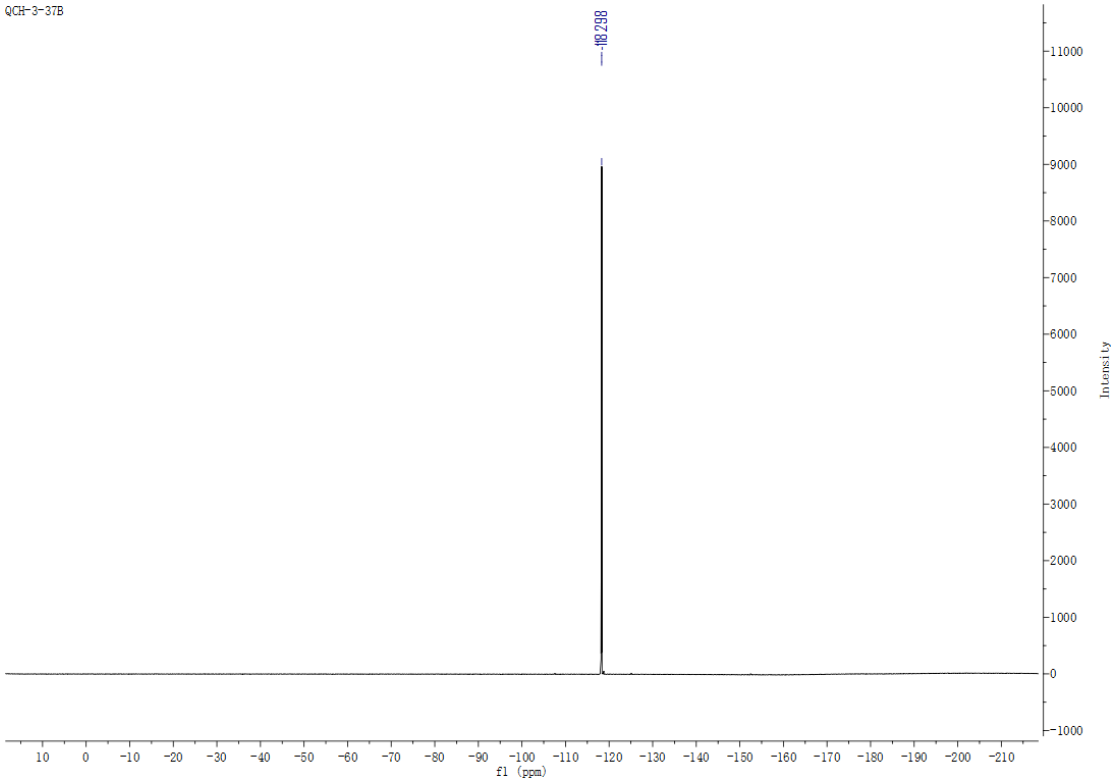


ethyl 2-bromo-2-fluoro-3-oxo-3-phenylpropanoate (21)

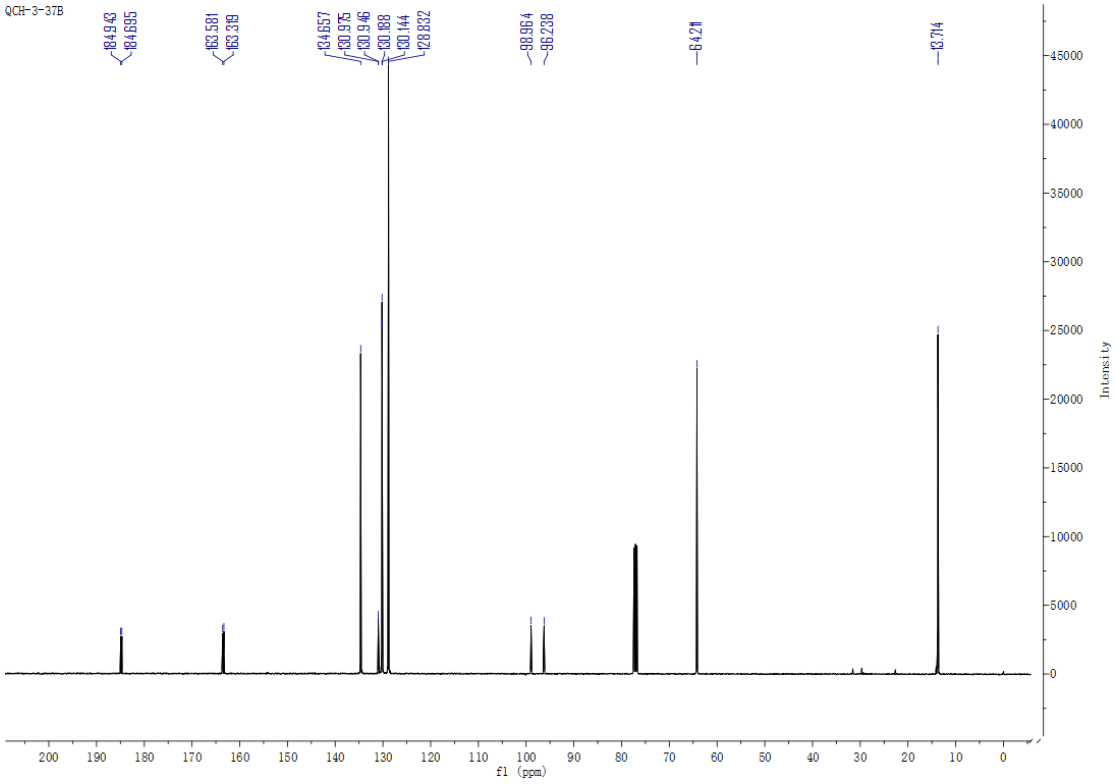
^{1}H NMR (400 MHz, $CDCl_3$):



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

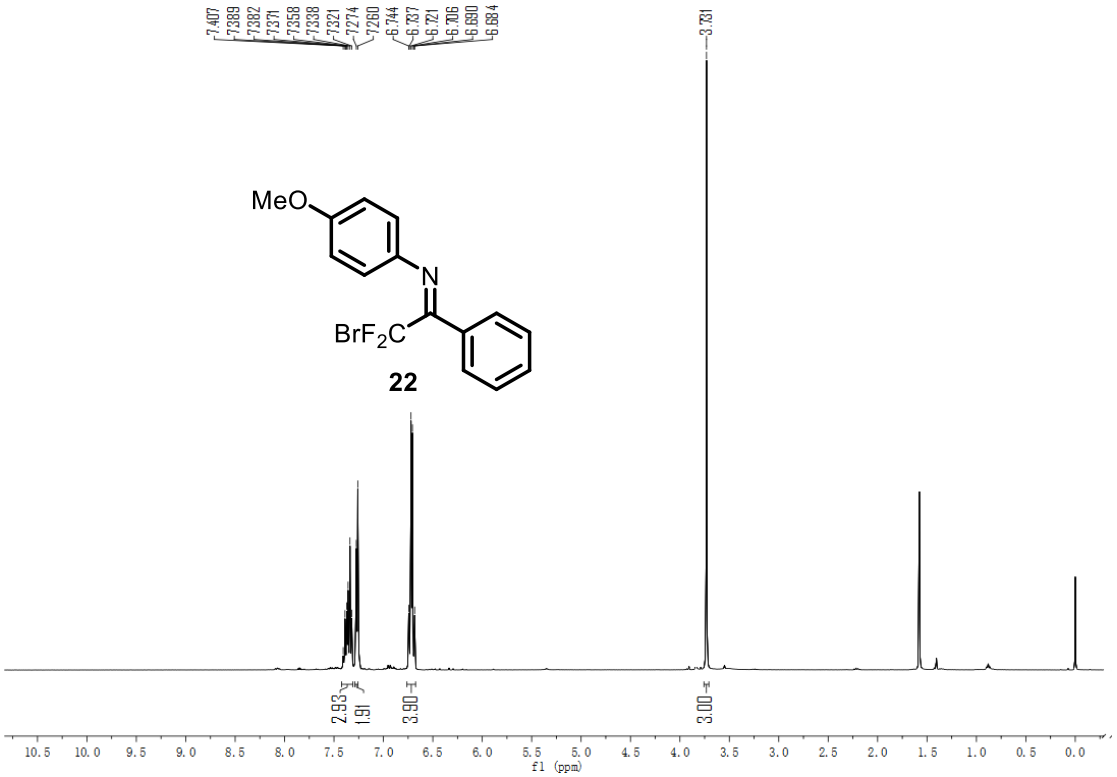


^{13}C NMR (100 MHz, $CDCl_3$):

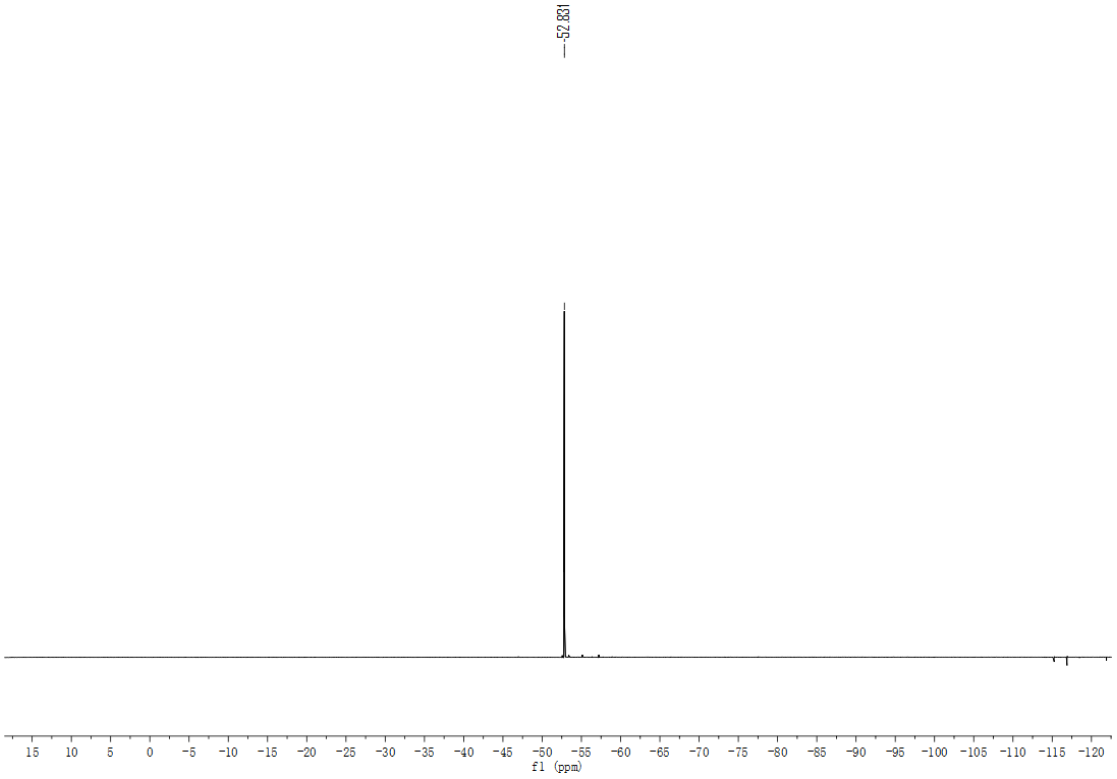


(*Z*)-2-bromo-2,2-difluoro-*N*-(4-methoxyphenyl)-1-phenylethan-1-imine (22)

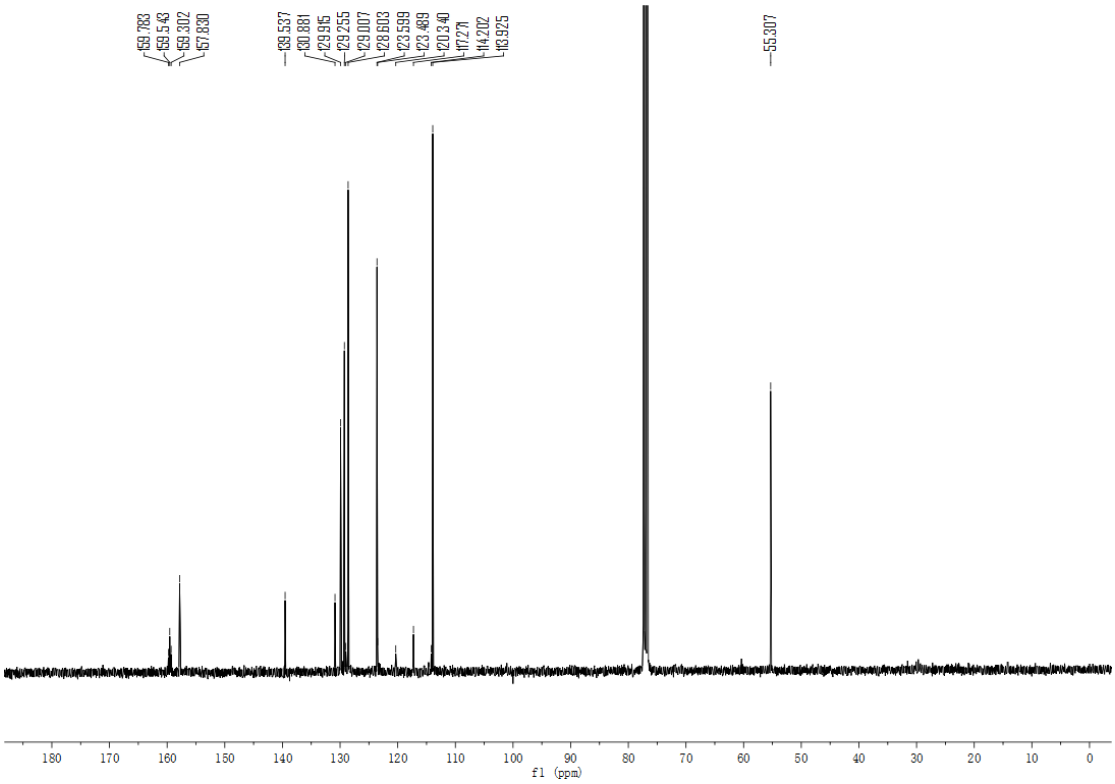
^{1}H NMR (400 MHz, $CDCl_3$):



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

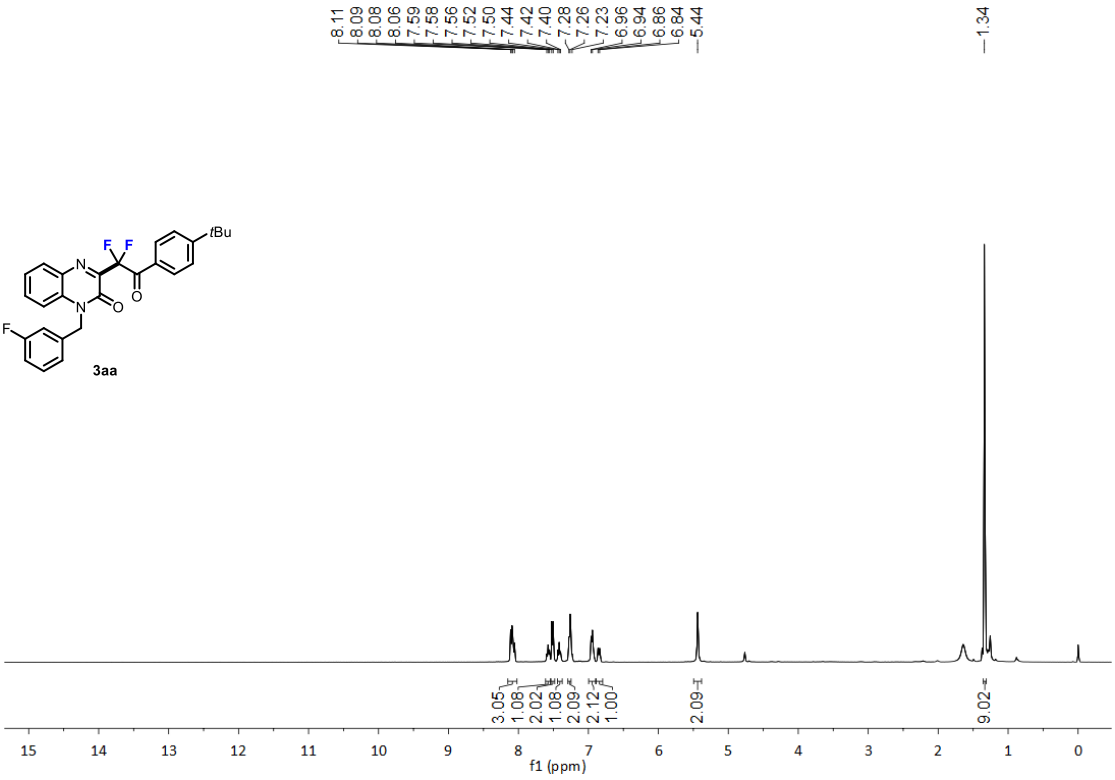


^{13}C NMR (100 MHz, $CDCl_3$):

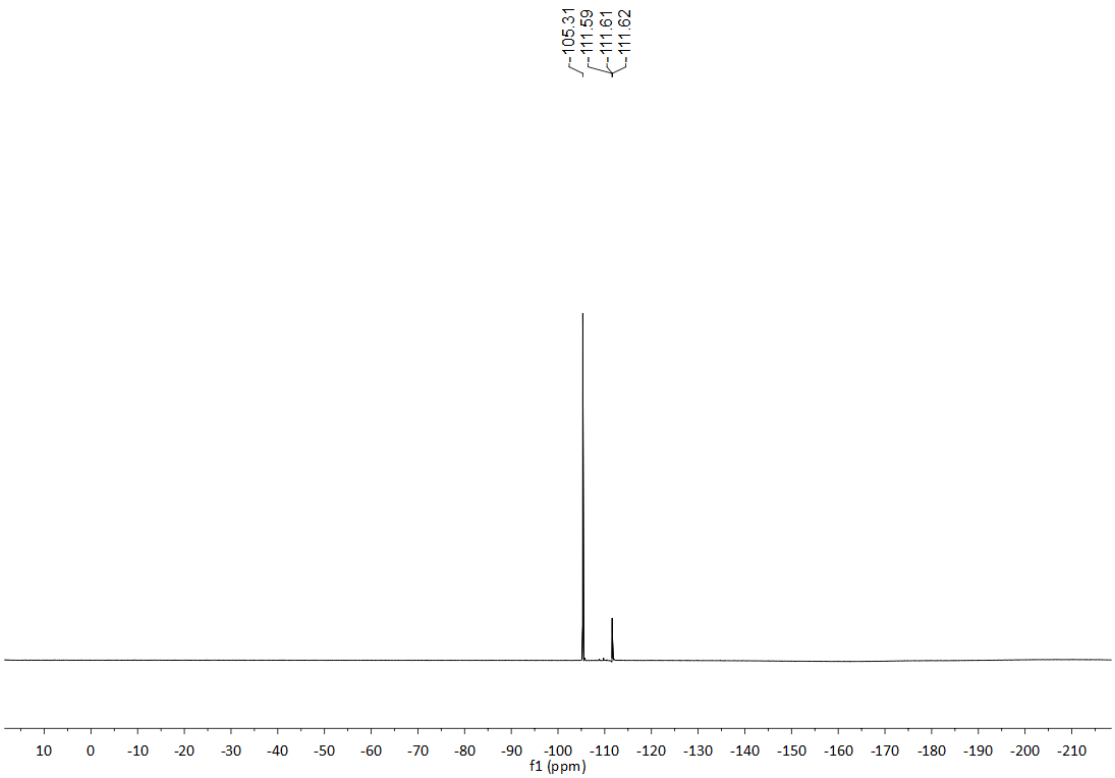


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3aa)

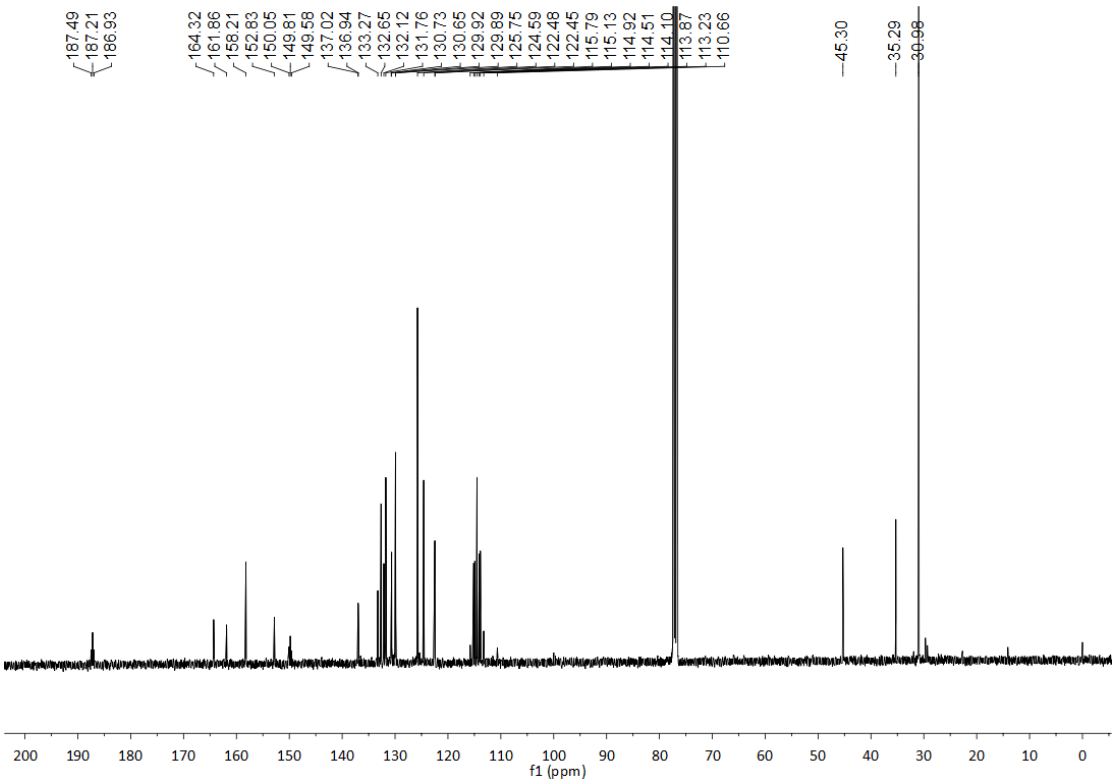
^{1}H NMR (400 MHz, $CDCl_3$):



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



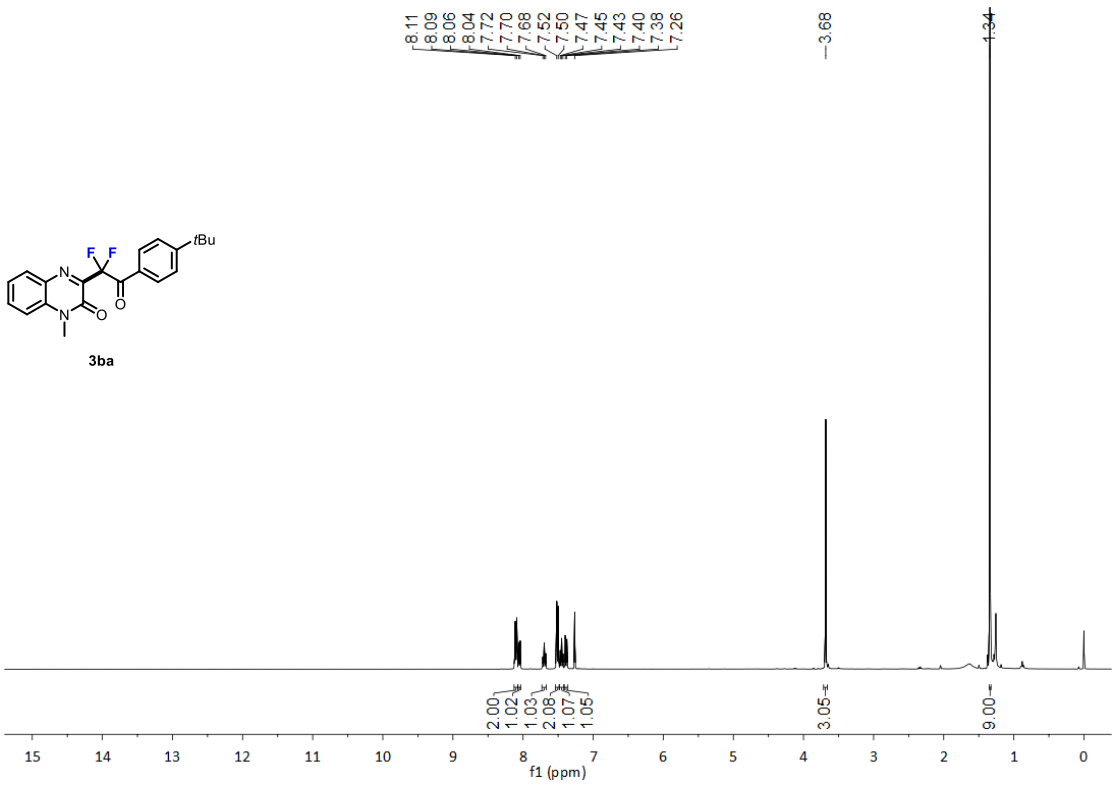
^{13}C NMR (100 MHz, $CDCl_3$):



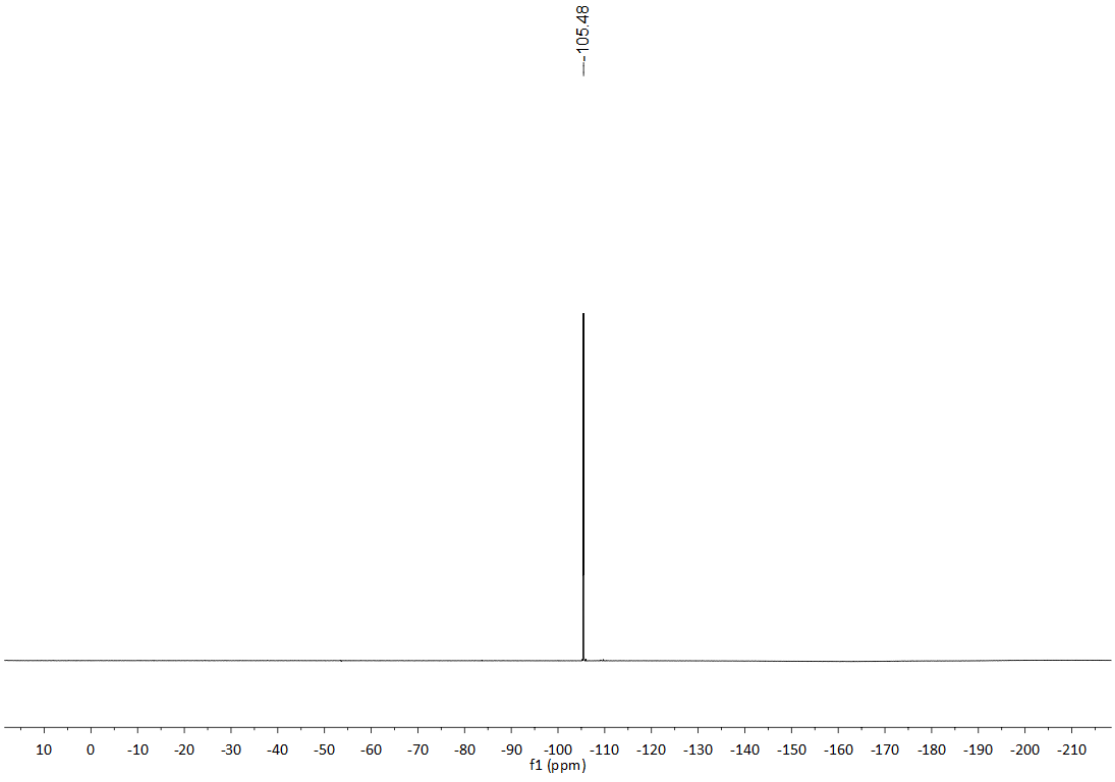
3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-methylquinoxalin-2(1*H*)-on

e (3ba)

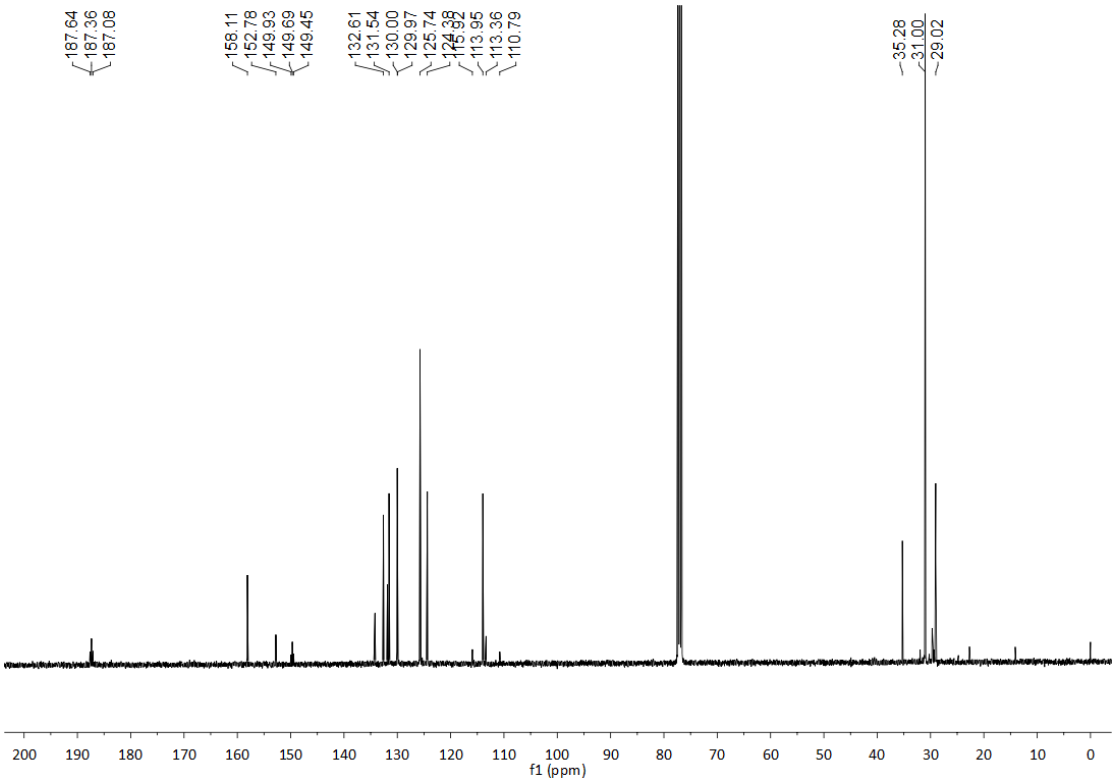
^{1}H NMR (400 MHz, $CDCl_3$):



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

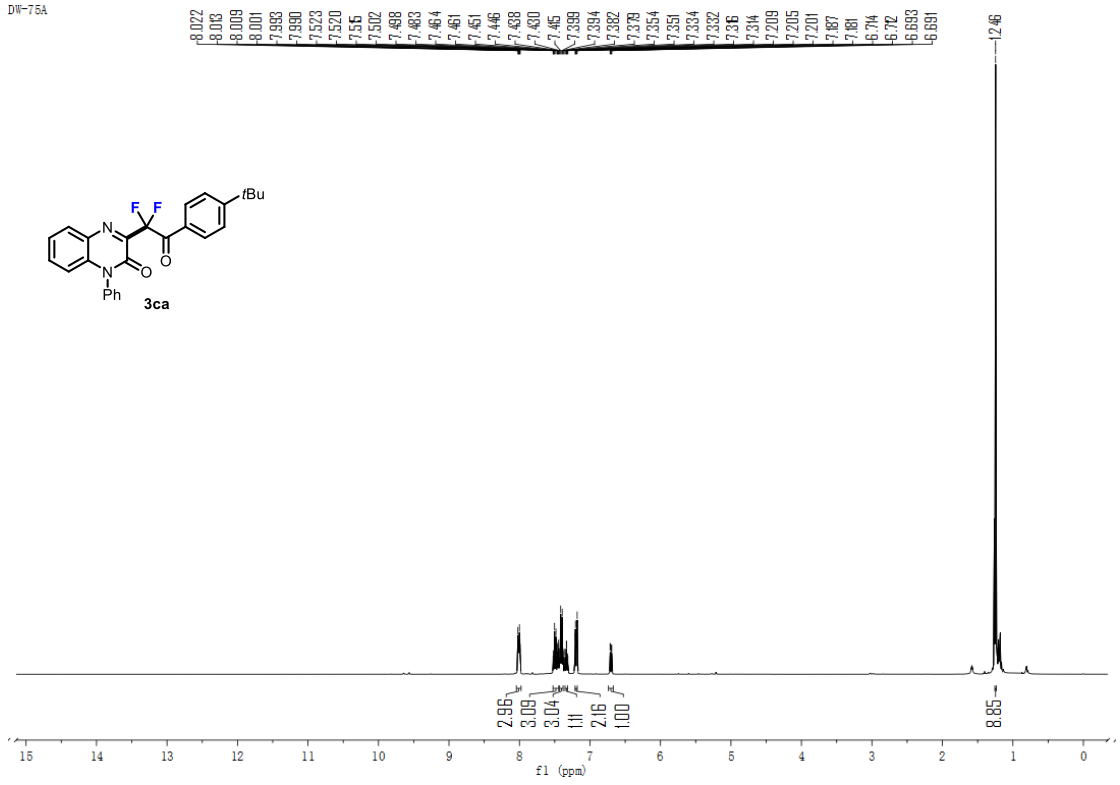


^{13}C NMR (100 MHz, $CDCl_3$):

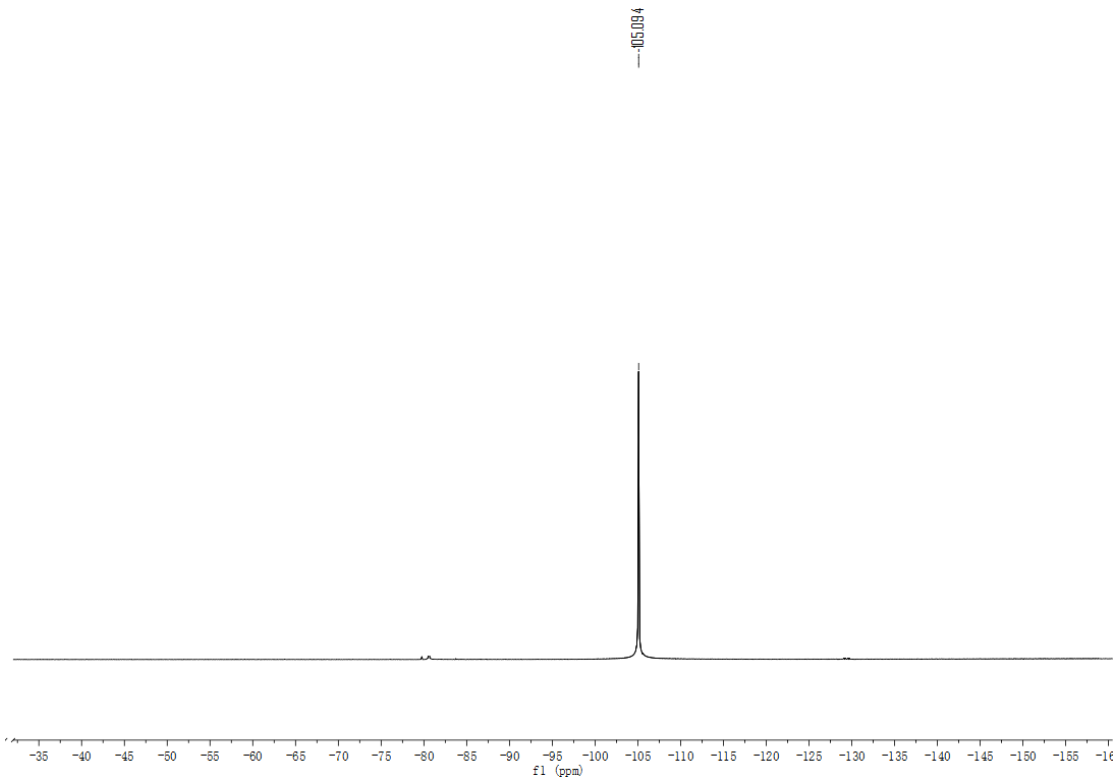


3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-phenylquinoxalin-2(1H)-one (3ca)

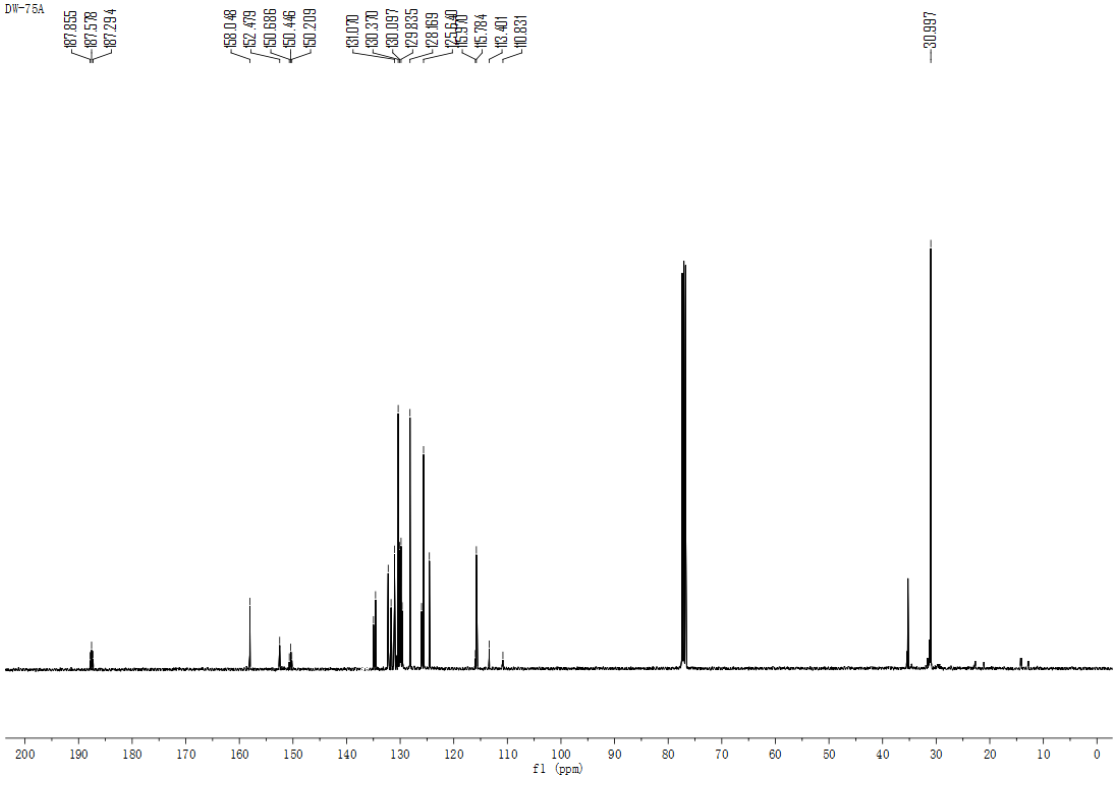
^{1}H NMR (400 MHz, $CDCl_3$):



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

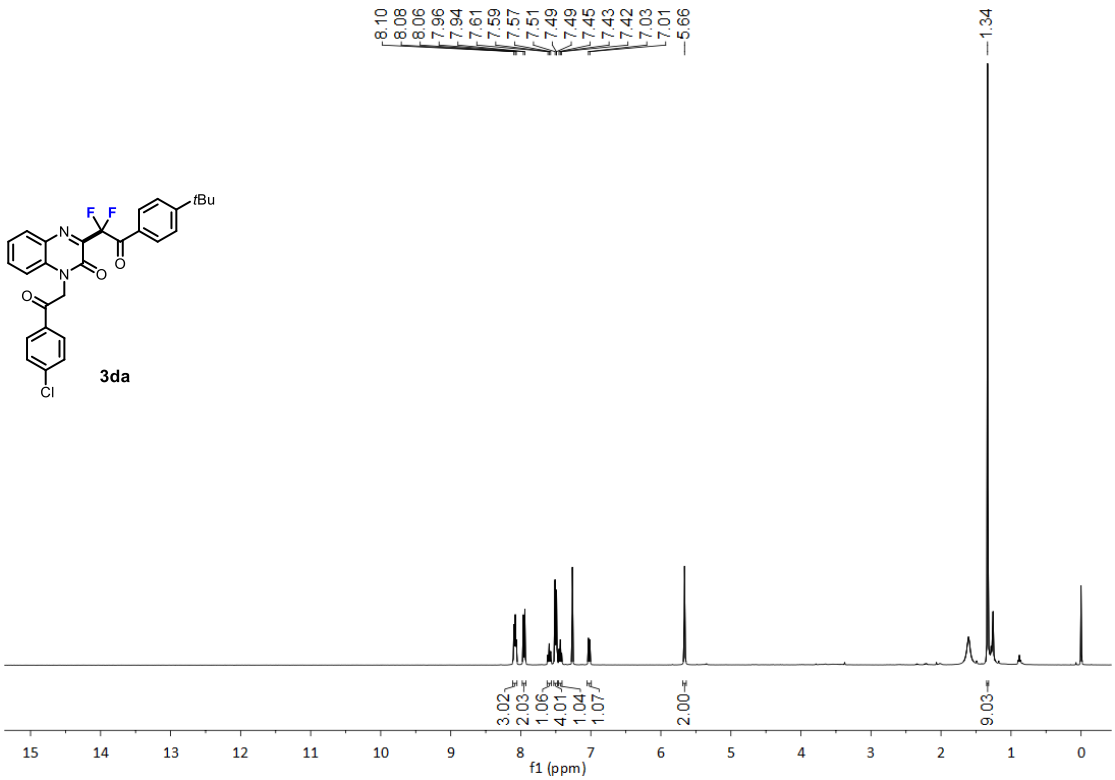


^{13}C NMR (100 MHz, $CDCl_3$):

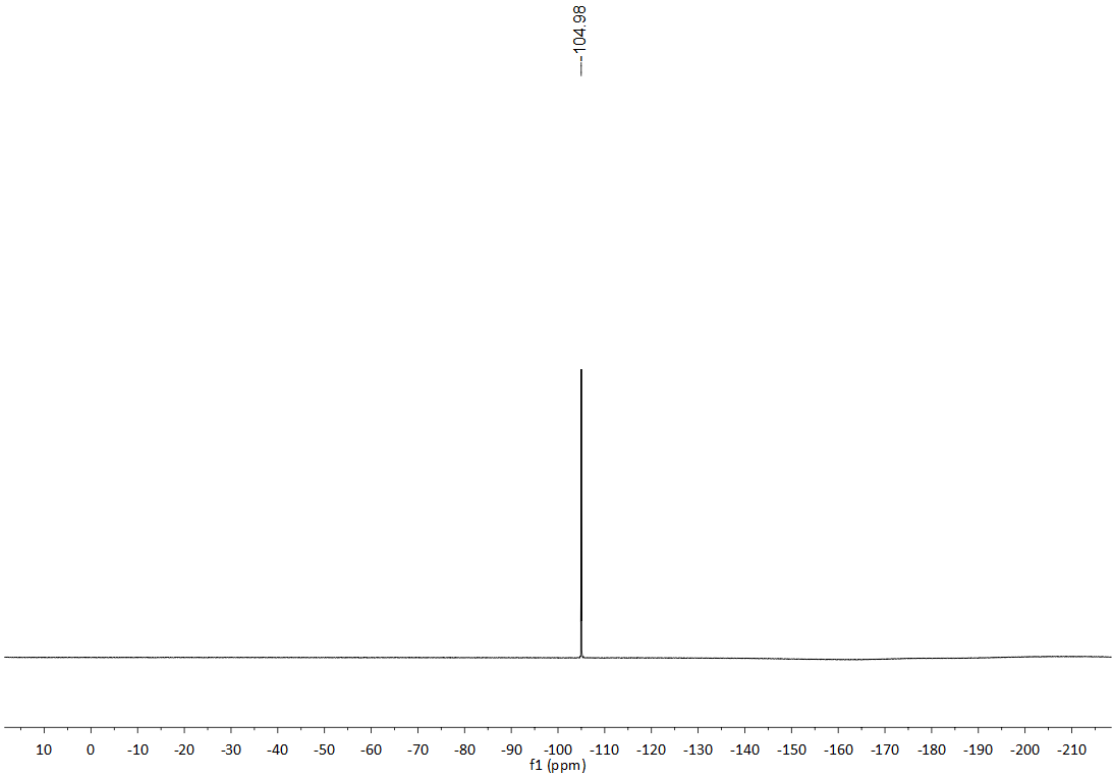


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(2-(4-chlorophenyl)-2-oxoethyl)quinoxalin-2(1*H*)-one (3da)

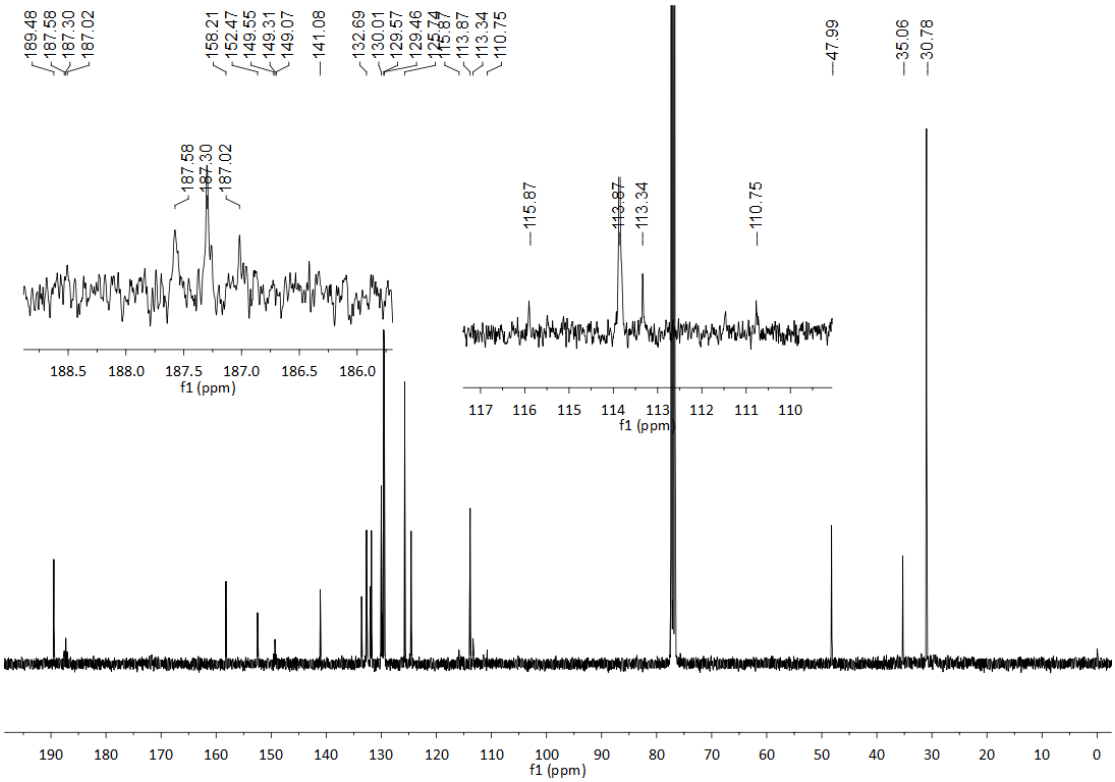
^{1}H NMR (400 MHz, $CDCl_3$):



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

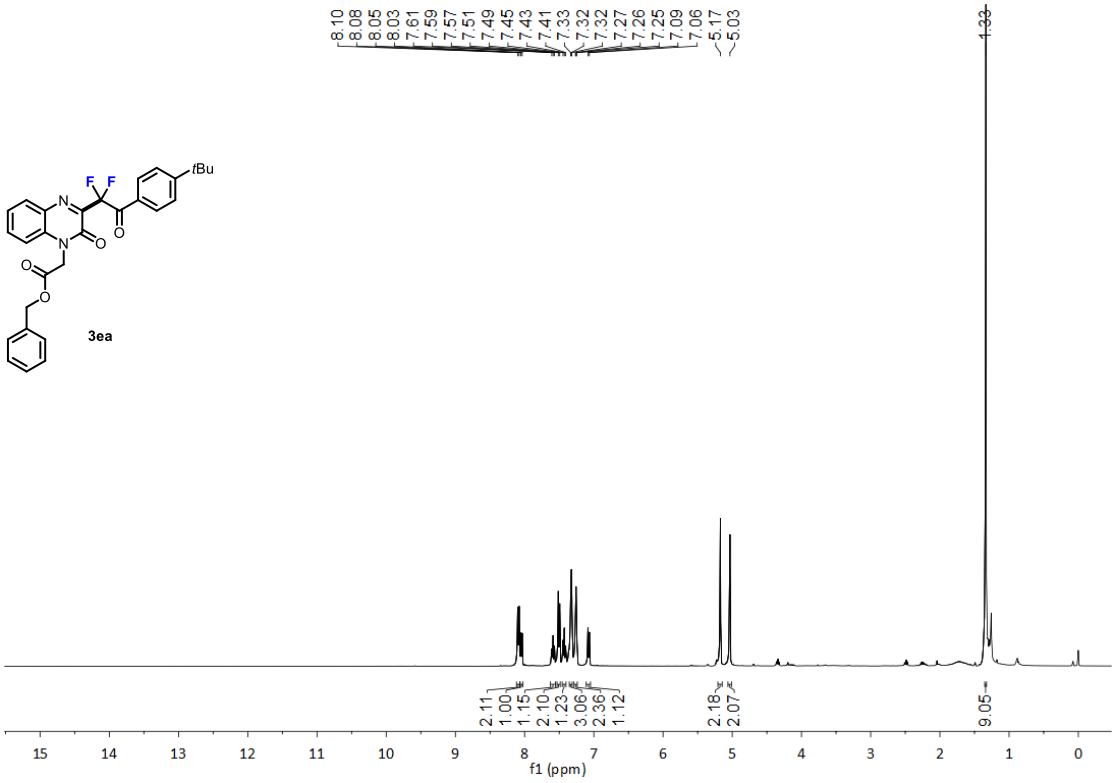


^{13}C NMR (100 MHz, $CDCl_3$):

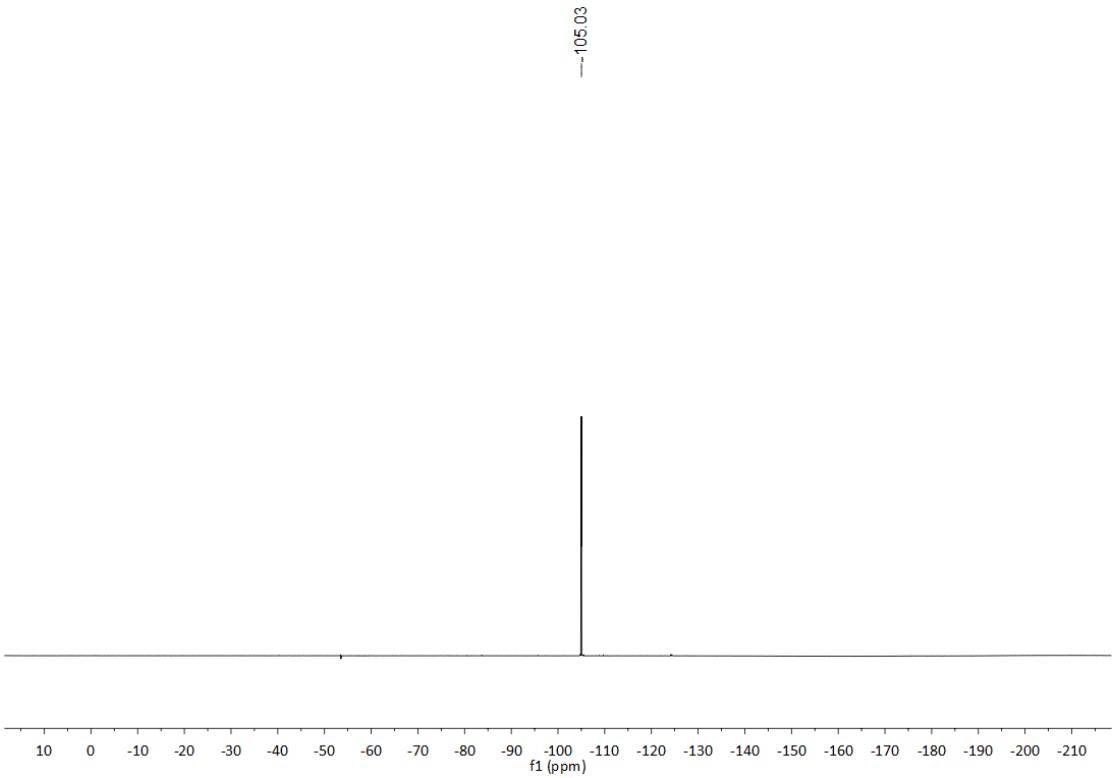


benzyl 2-(3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (3ea)

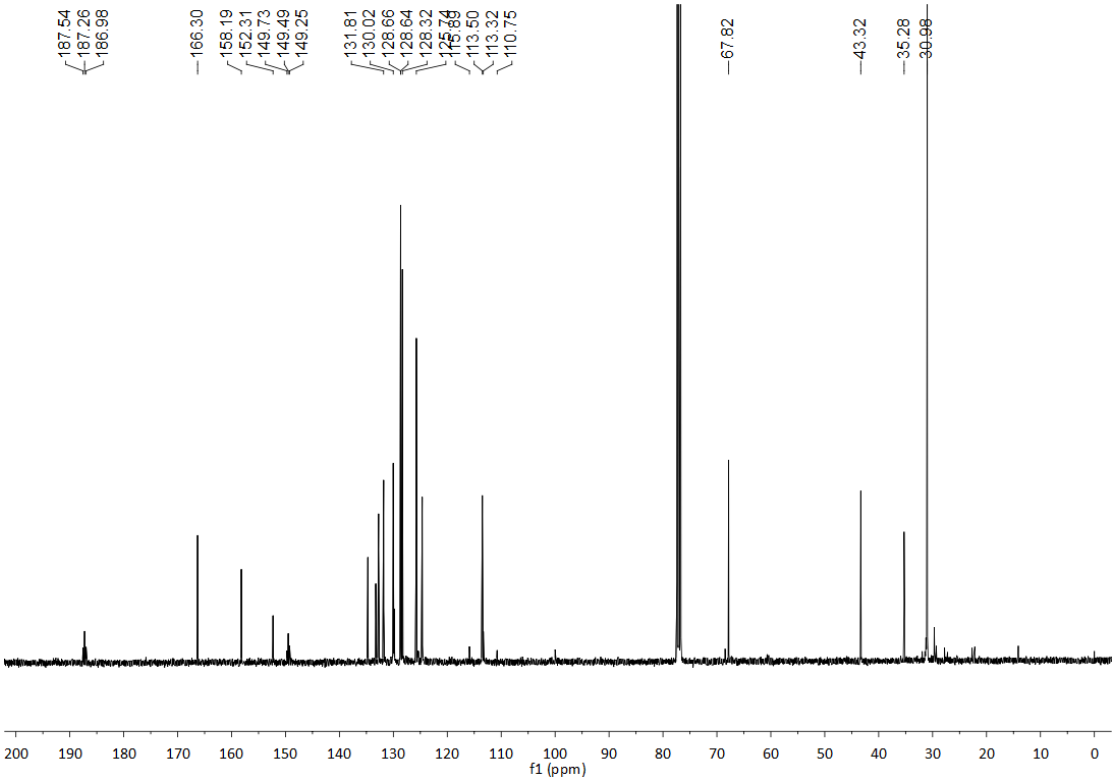
^{1}H NMR (400 MHz, $CDCl_3$):



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

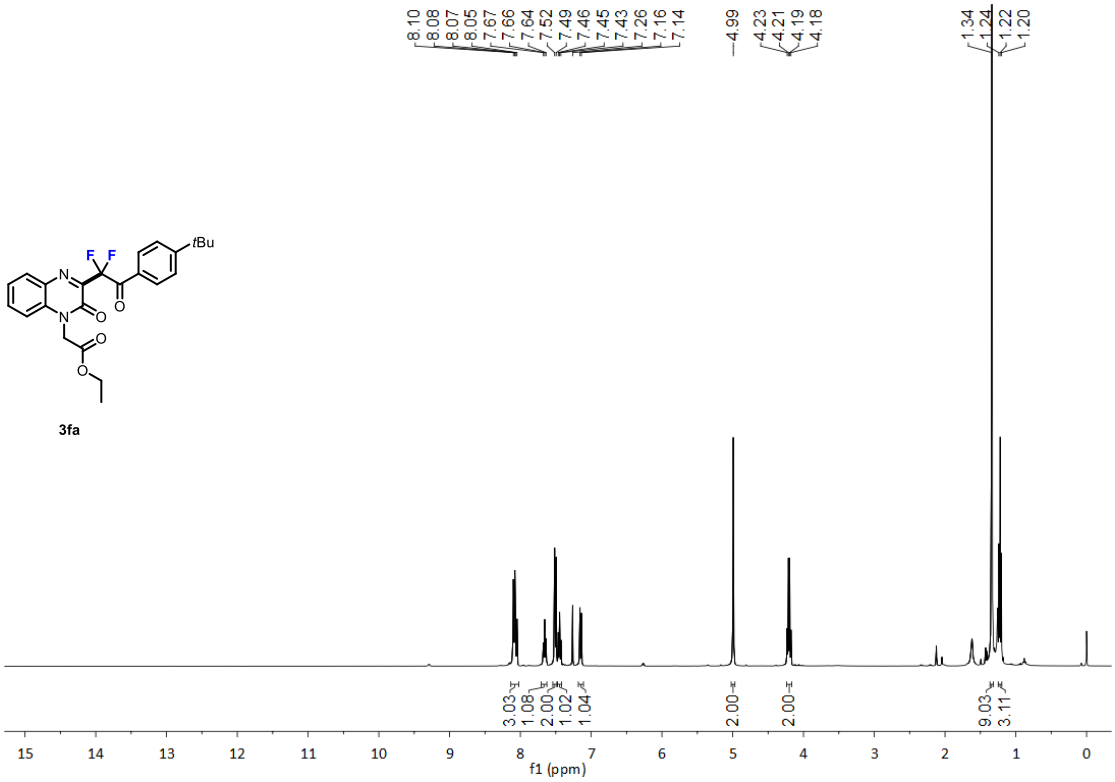


^{13}C NMR (100 MHz, $CDCl_3$):



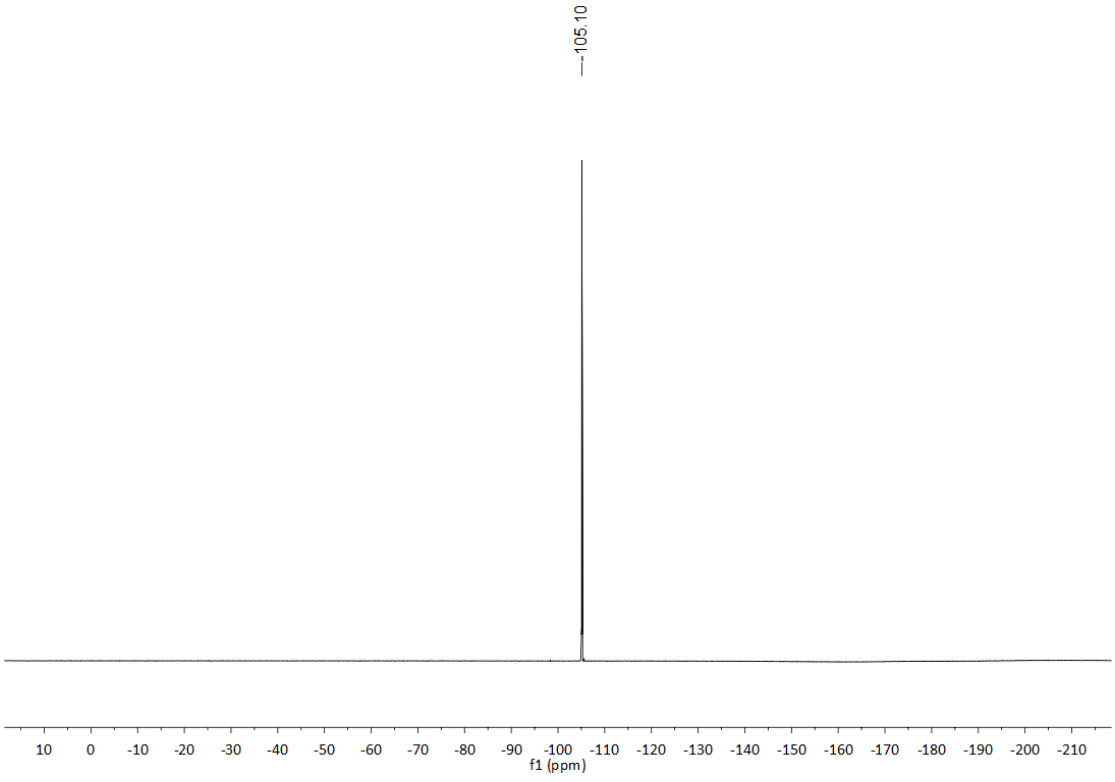
ethyl 2-(3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (3fa)

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

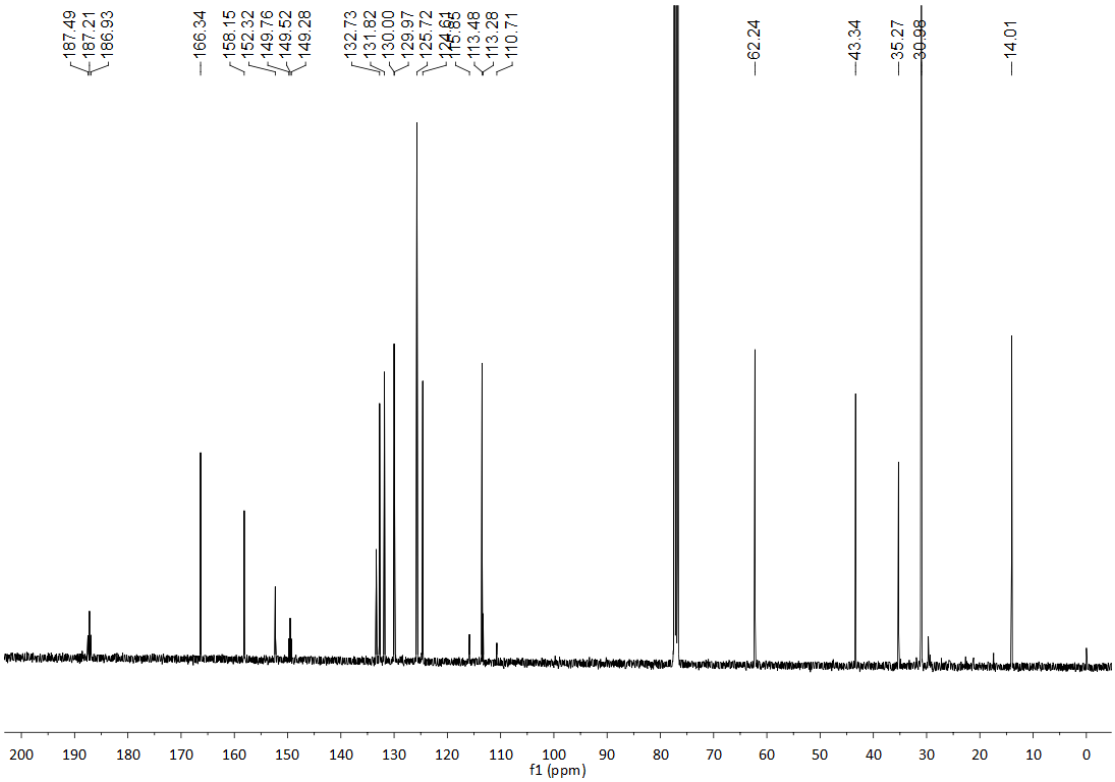


3fa

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

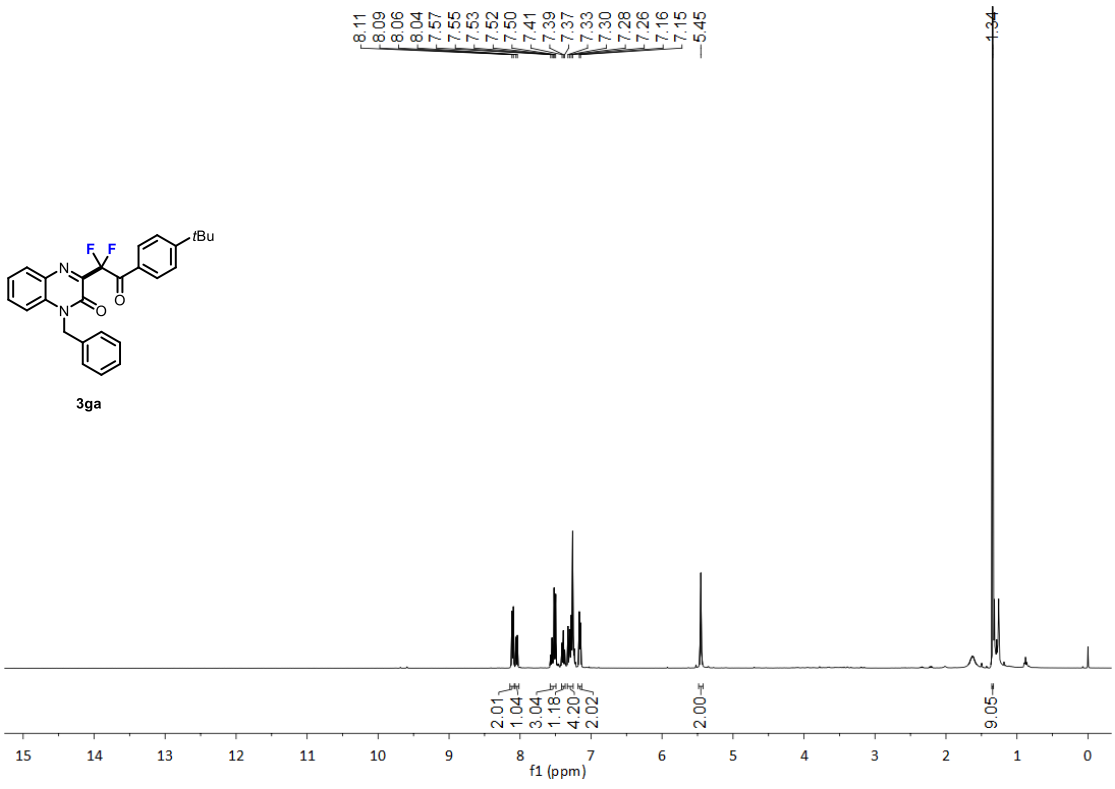


^{13}C NMR (100 MHz, $CDCl_3$):

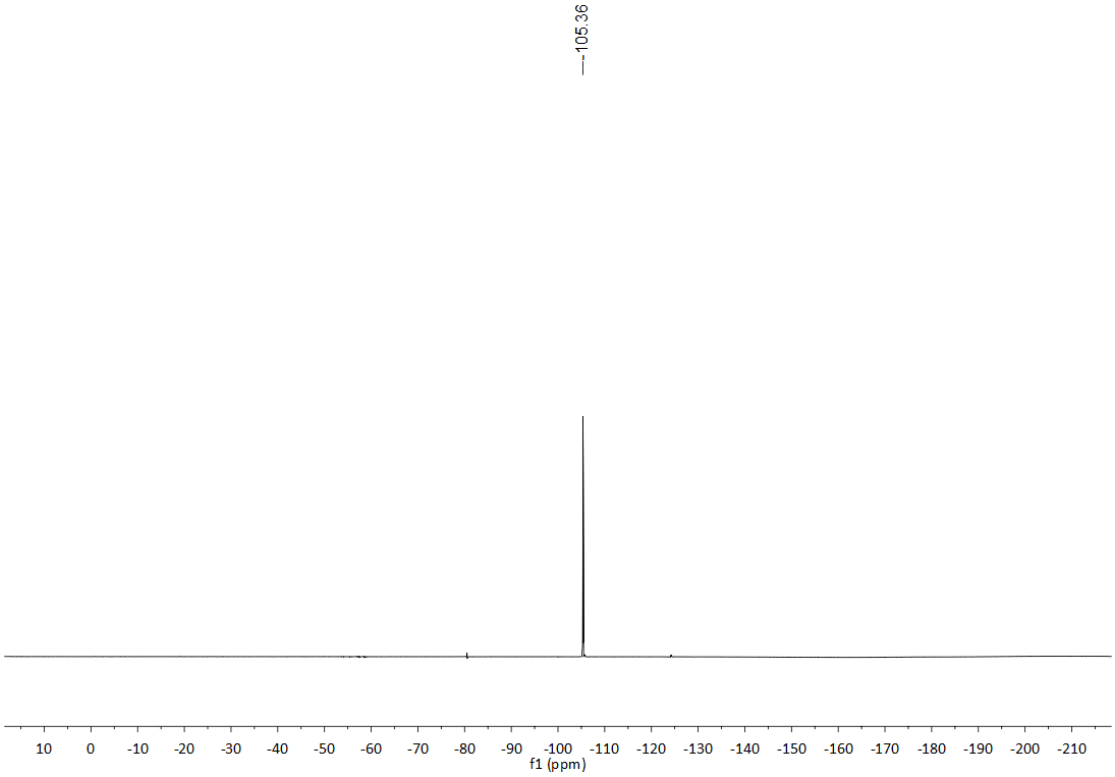


1-benzyl-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin-2(1*H*)-one (3ga)

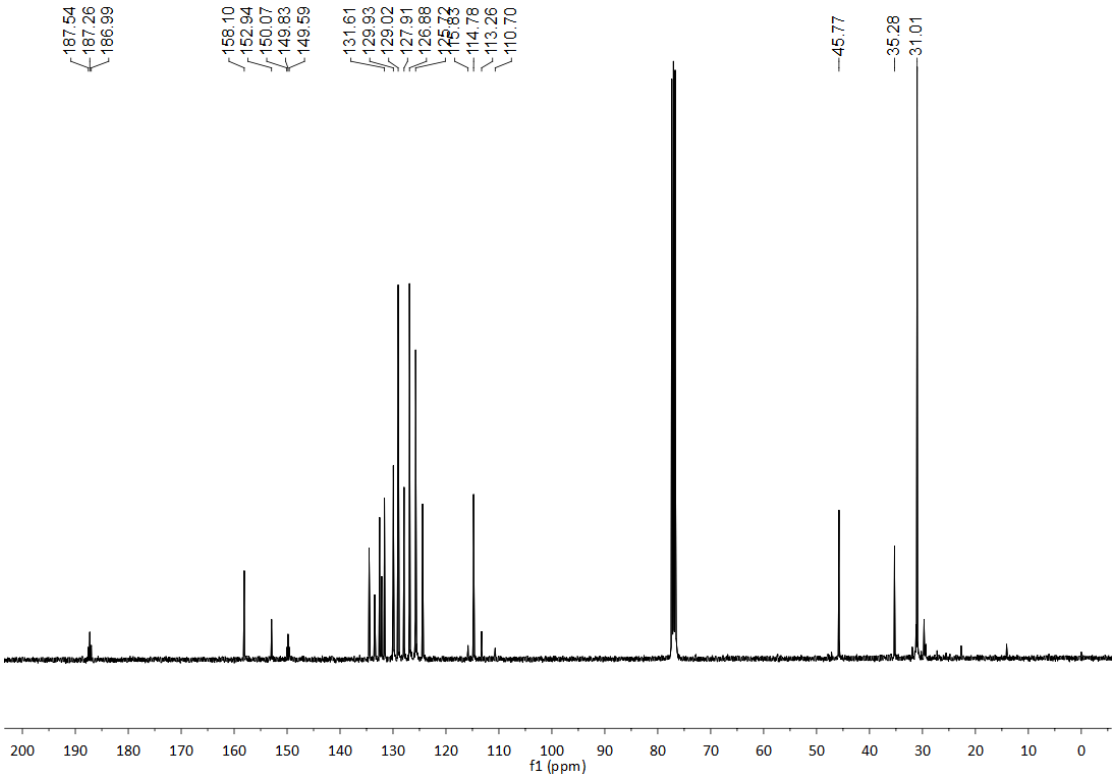
^{1}H NMR (400 MHz, $CDCl_3$):



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

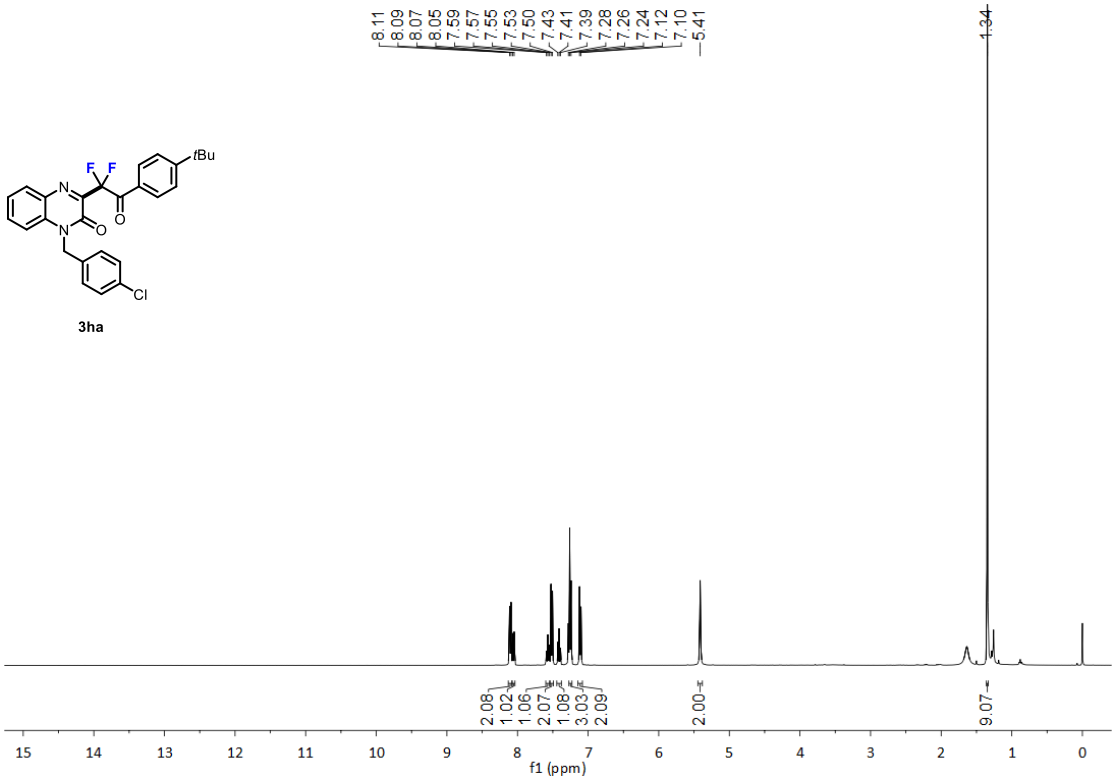


^{13}C NMR (100 MHz, $CDCl_3$):

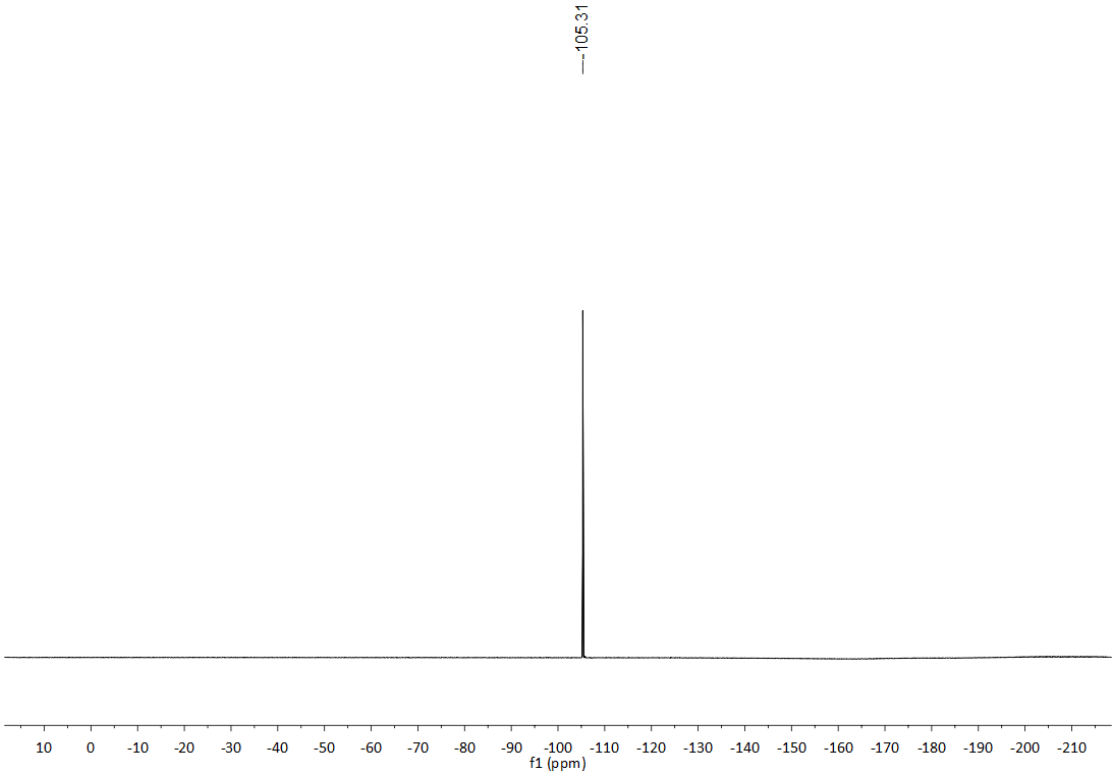


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-chlorobenzyl)-quinoxalin-2(1*H*)-one (3ha)

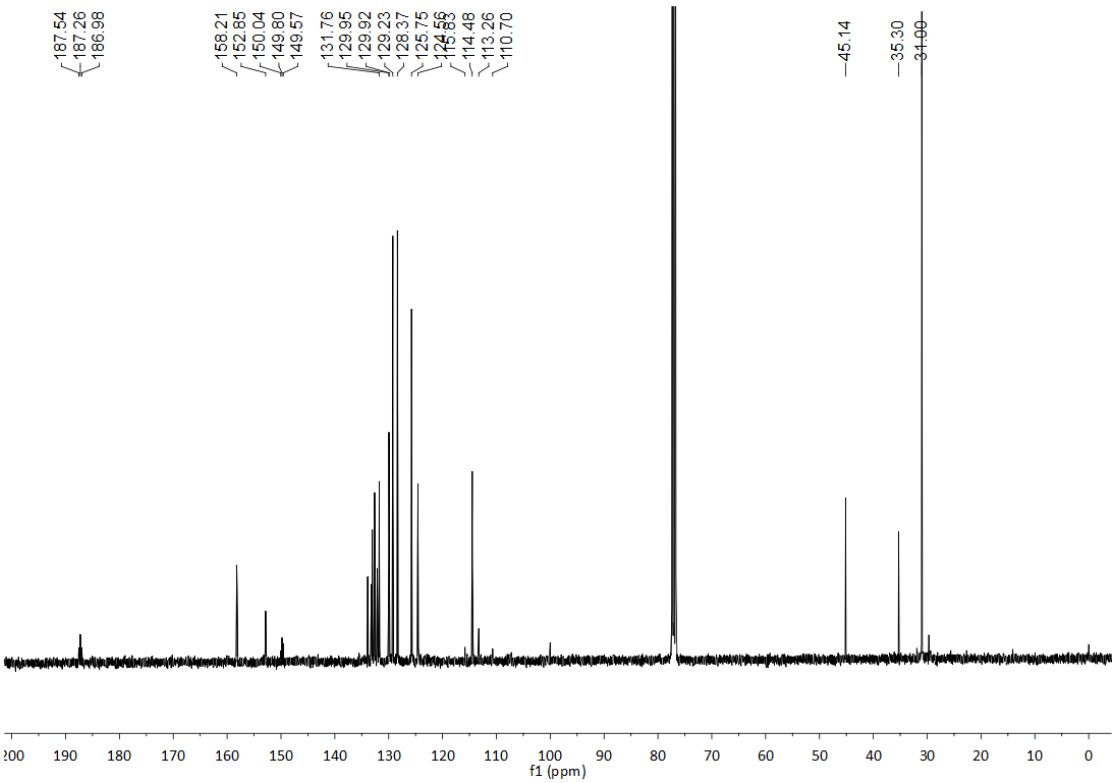
^{1}H NMR (400 MHz, $CDCl_3$):



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

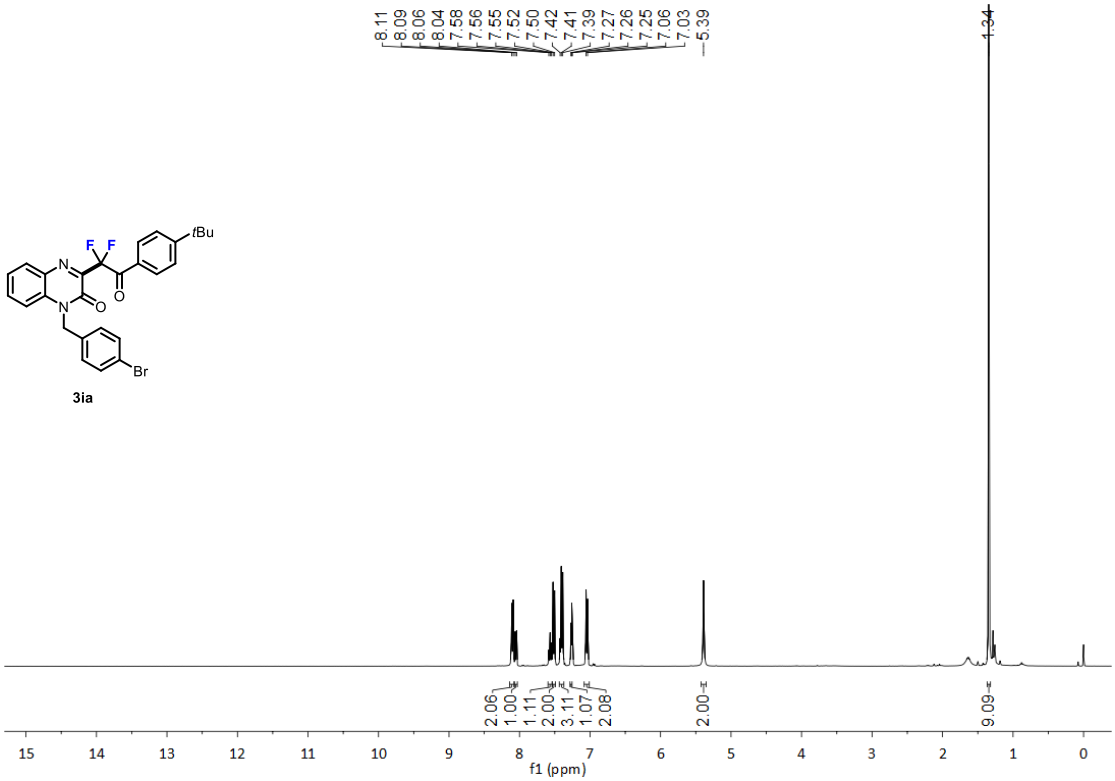


^{13}C NMR (100 MHz, $CDCl_3$):

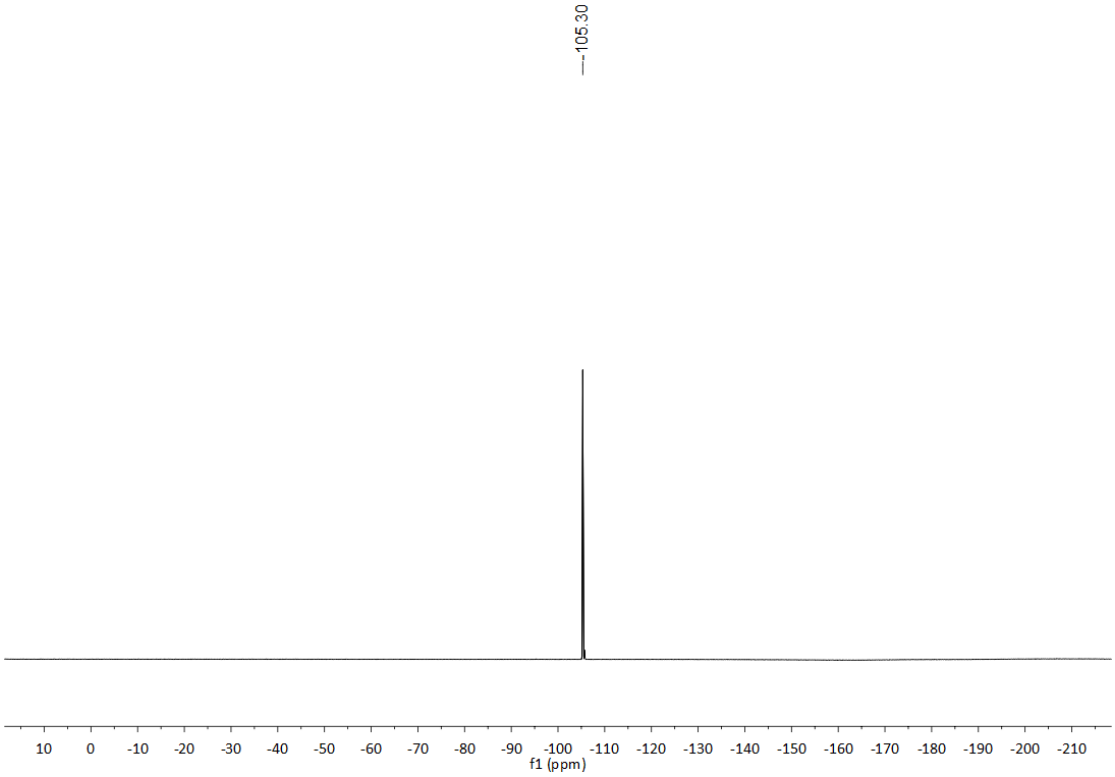


1-(4-bromobenzyl)-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin-2(1*H*)-one (3ia)

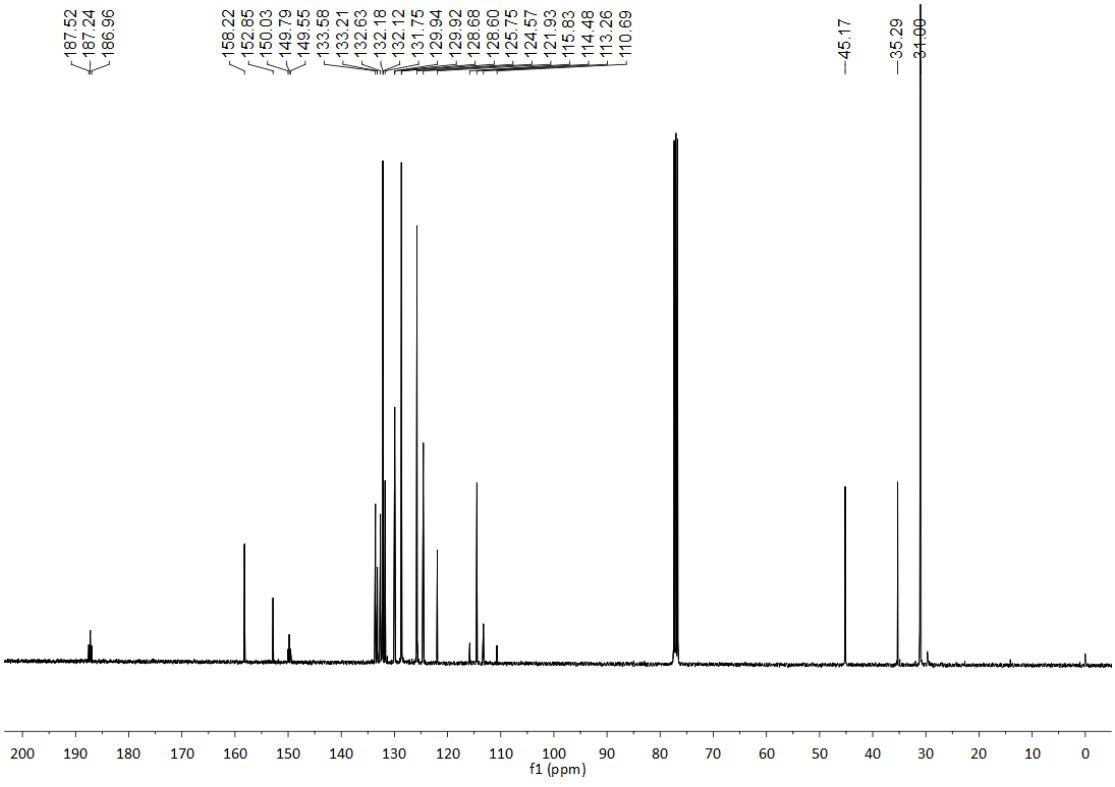
^{1}H NMR (400 MHz, $CDCl_3$):



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

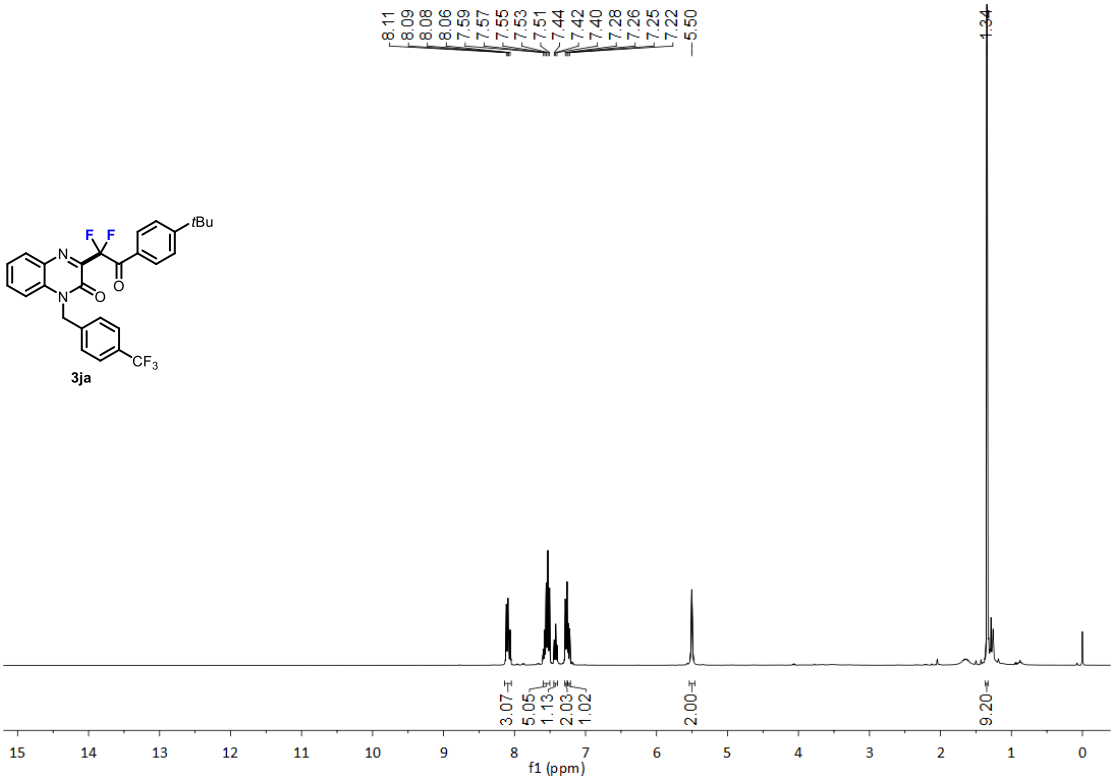


^{13}C NMR (100 MHz, $CDCl_3$):

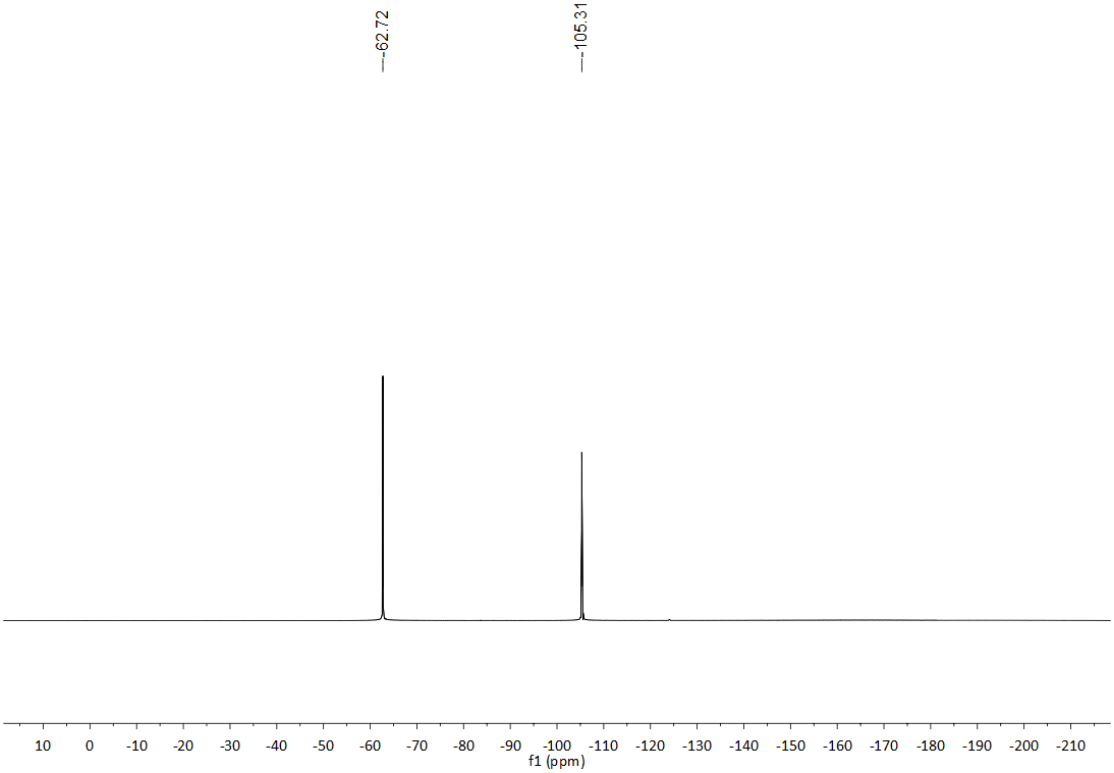


3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-(trifluoromethyl)benzyl) quinoxalin-2(1*H*)-one (3ja)

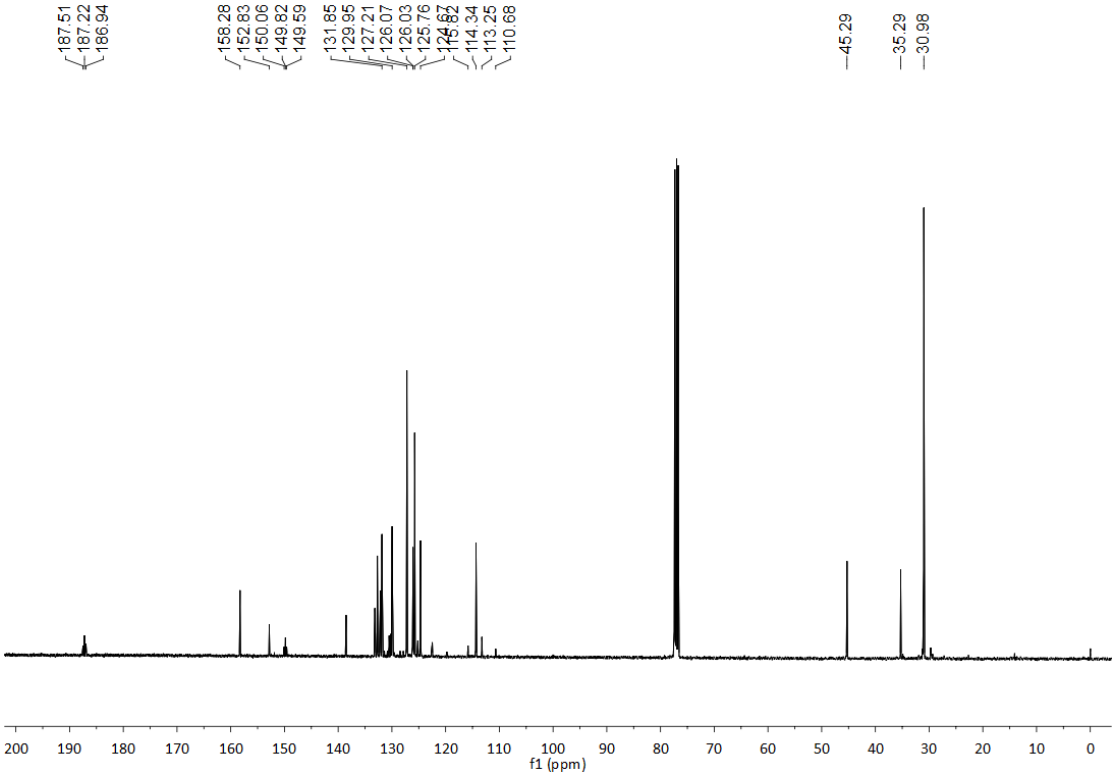
^{1}H NMR (400 MHz, $CDCl_3$):



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

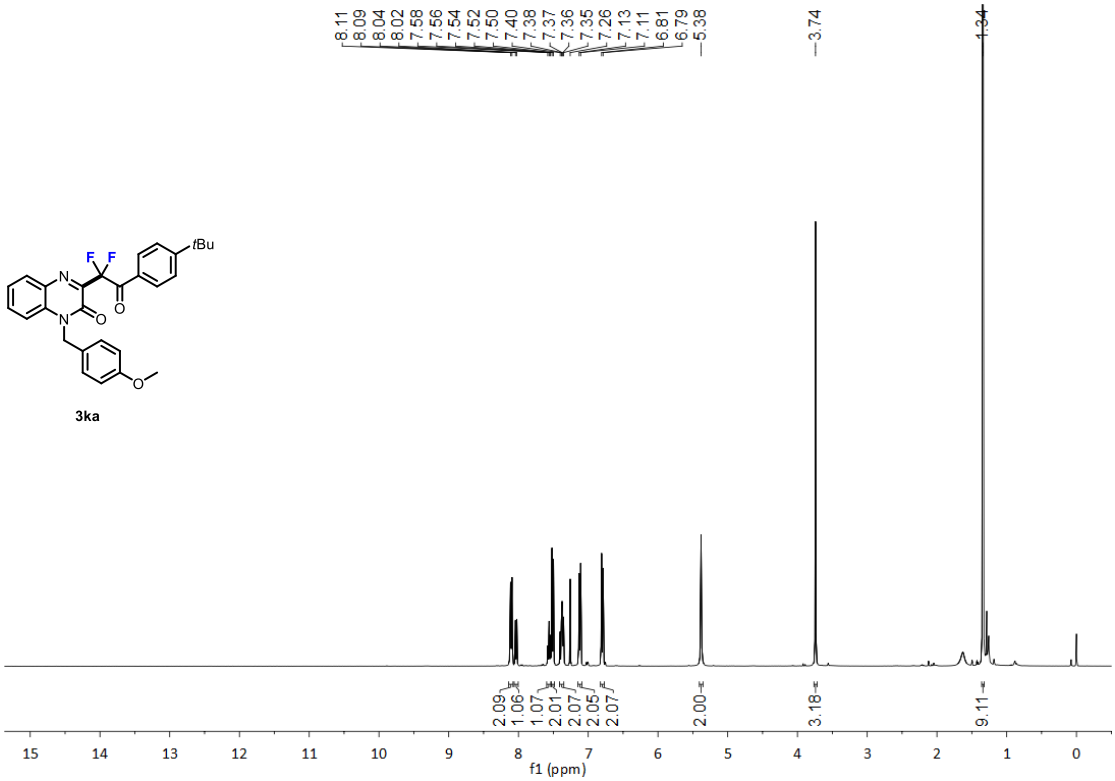


^{13}C NMR (100 MHz, $CDCl_3$):



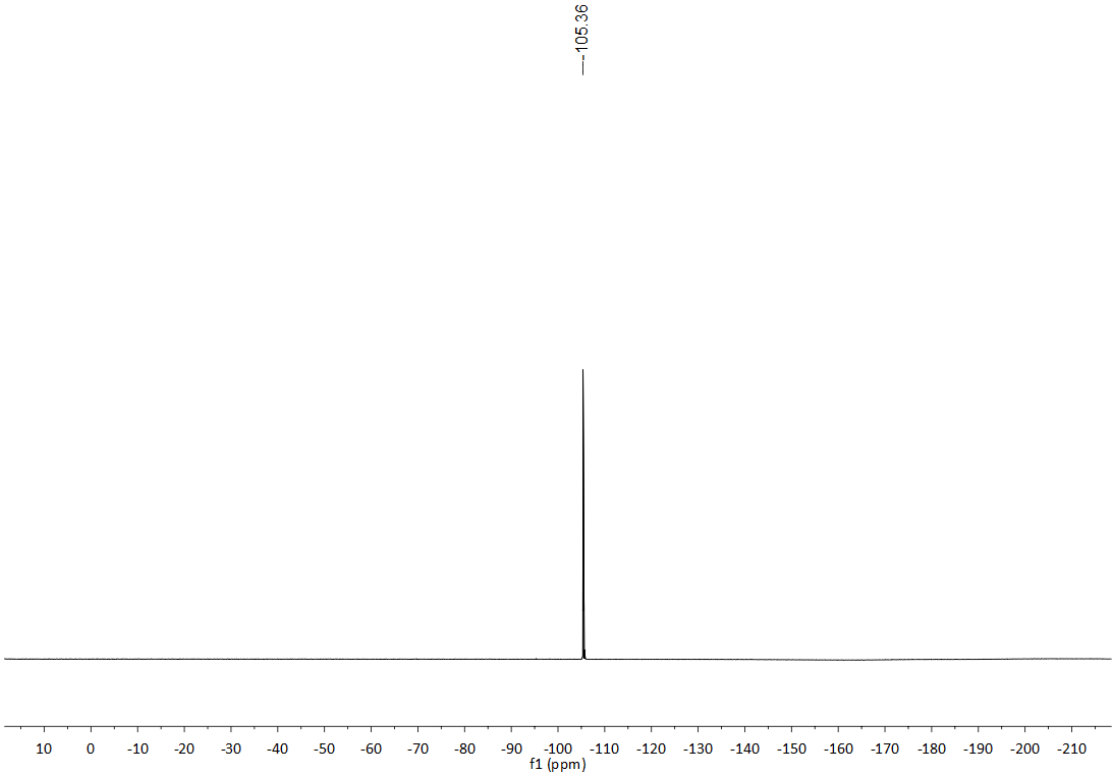
3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(4-methoxybenzyl) quinoxalin-2(1*H*)-one (3ka)

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

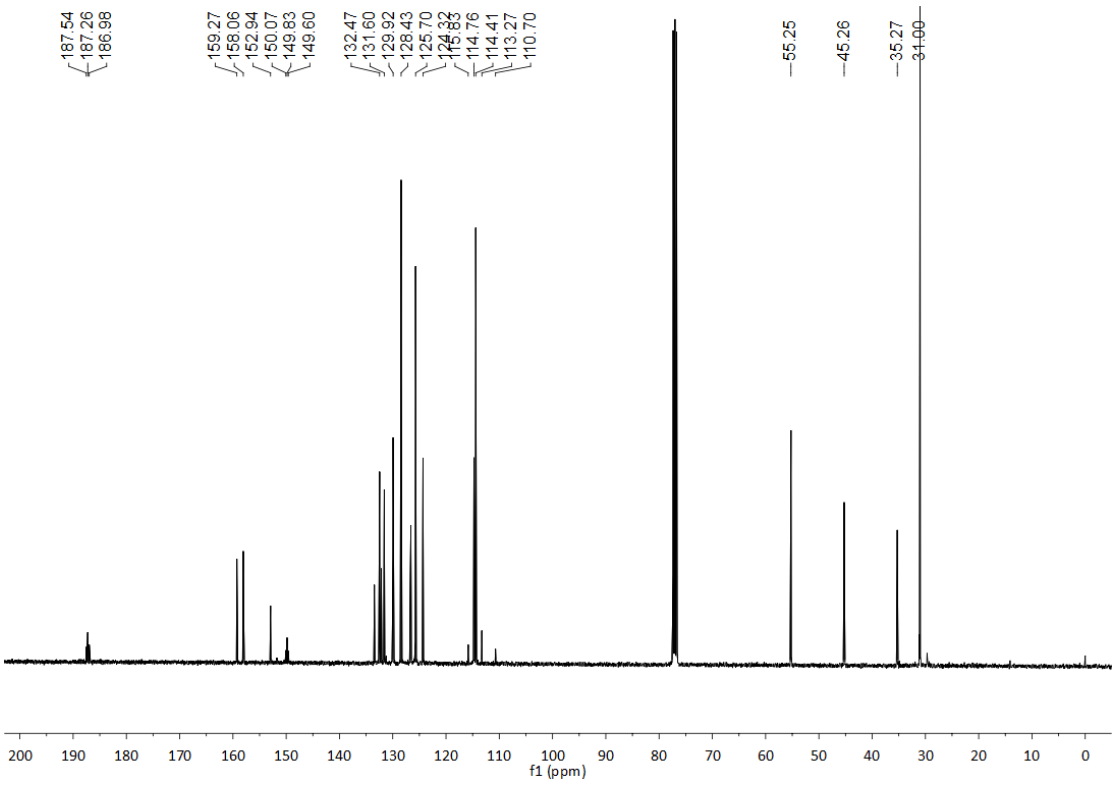


3ka

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

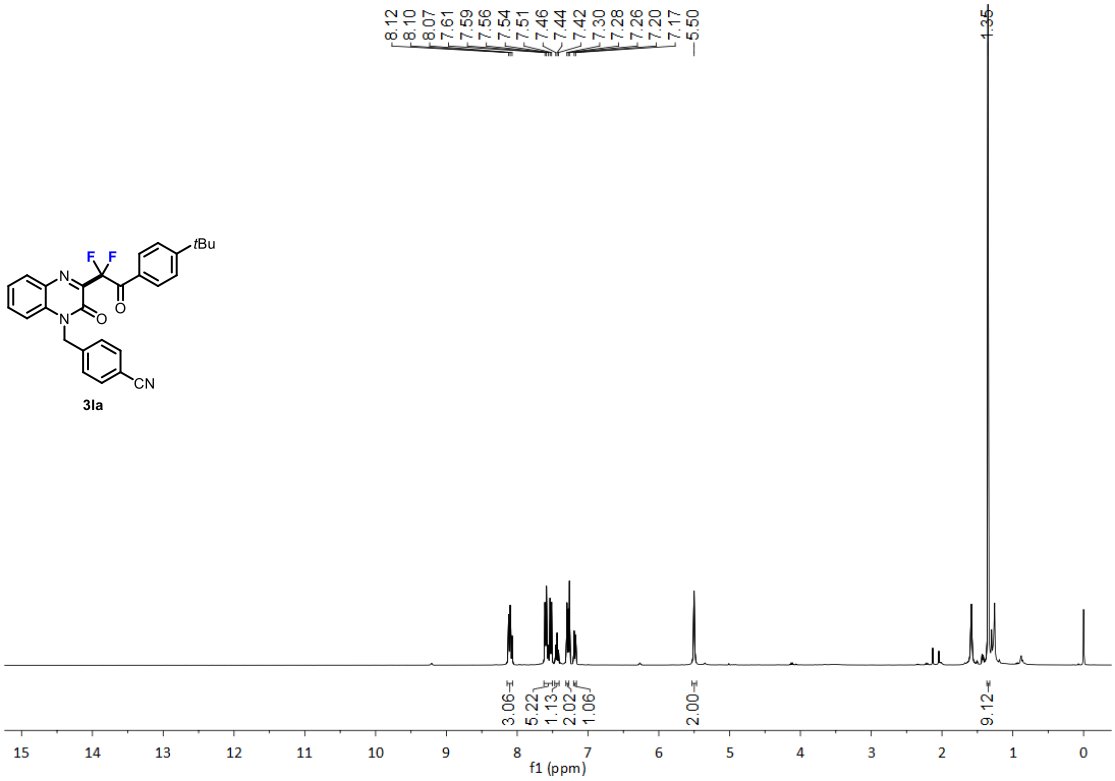


^{13}C NMR (100 MHz, $CDCl_3$):

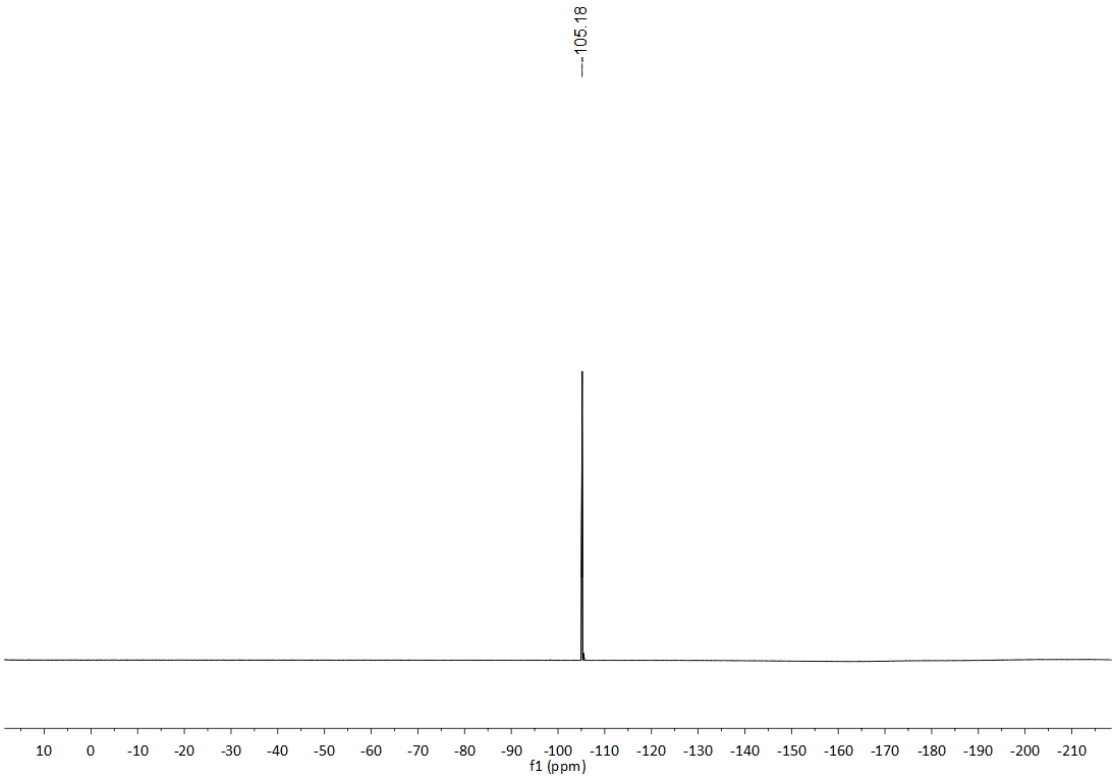


4-((3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-2-oxoquinoxalin-1(2*H*)-yl) methyl)benzonitrile (3la)

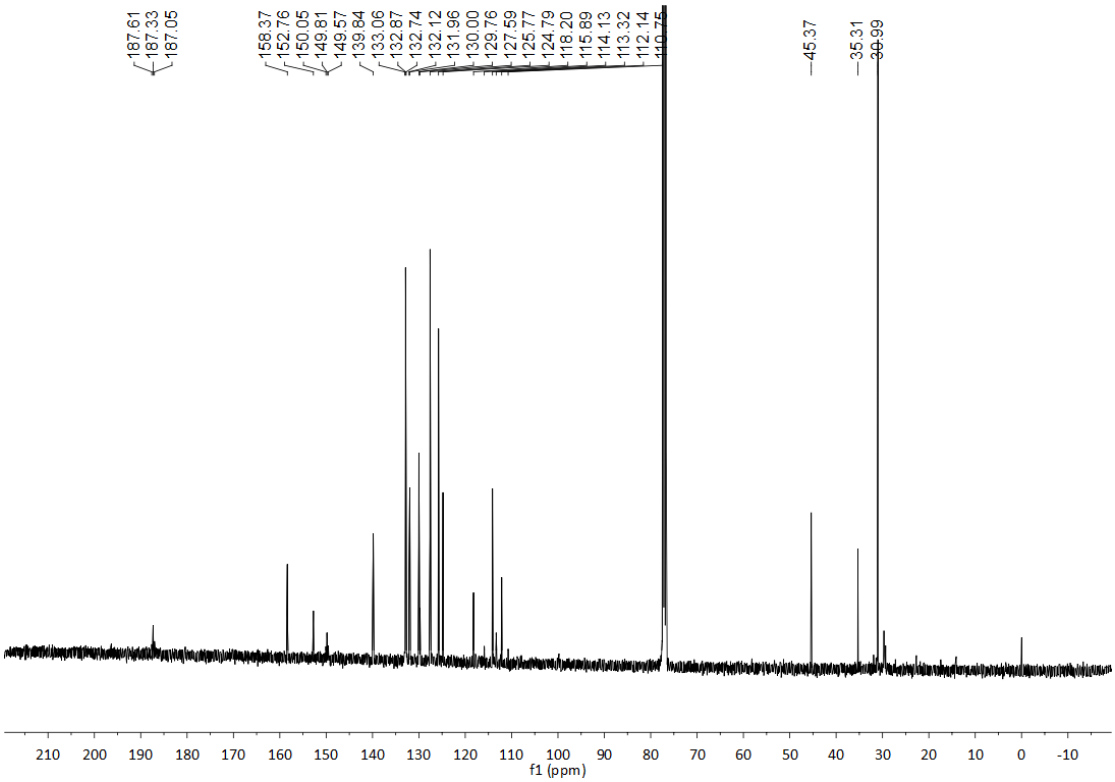
^{1}H NMR (400 MHz, $CDCl_3$):



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

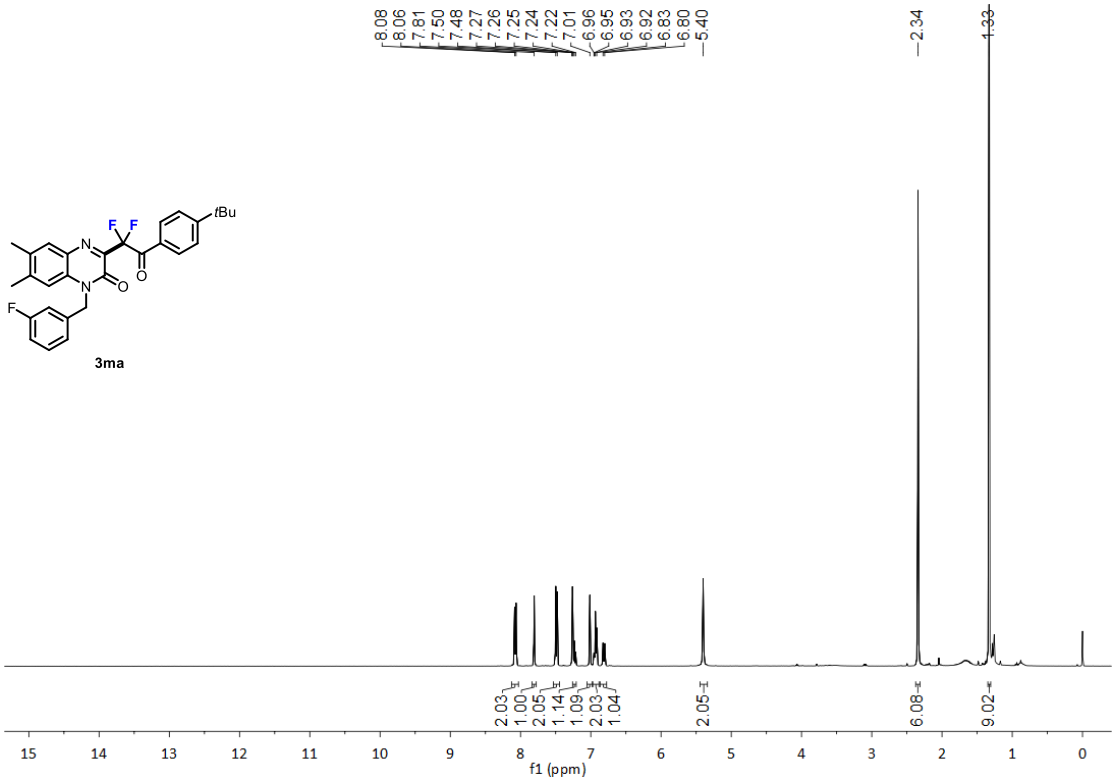


^{13}C NMR (100 MHz, $CDCl_3$):

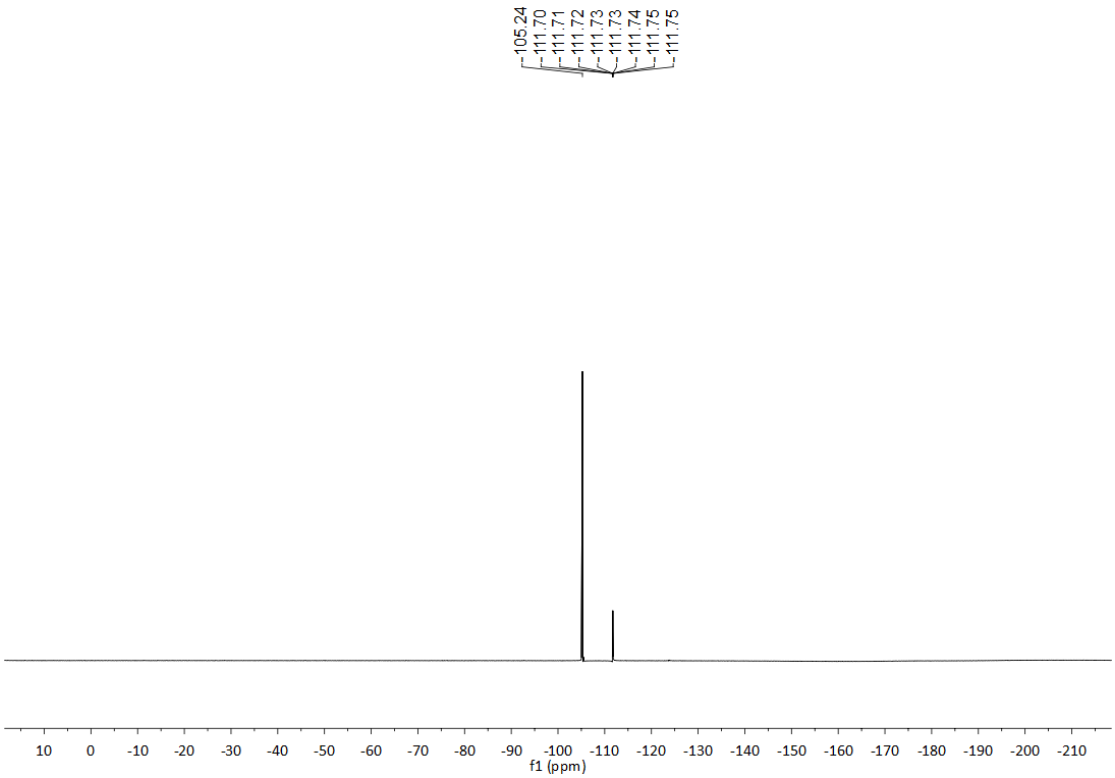


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)-6,7-dimethylquinoxalin-2(1*H*)-one (3ma)

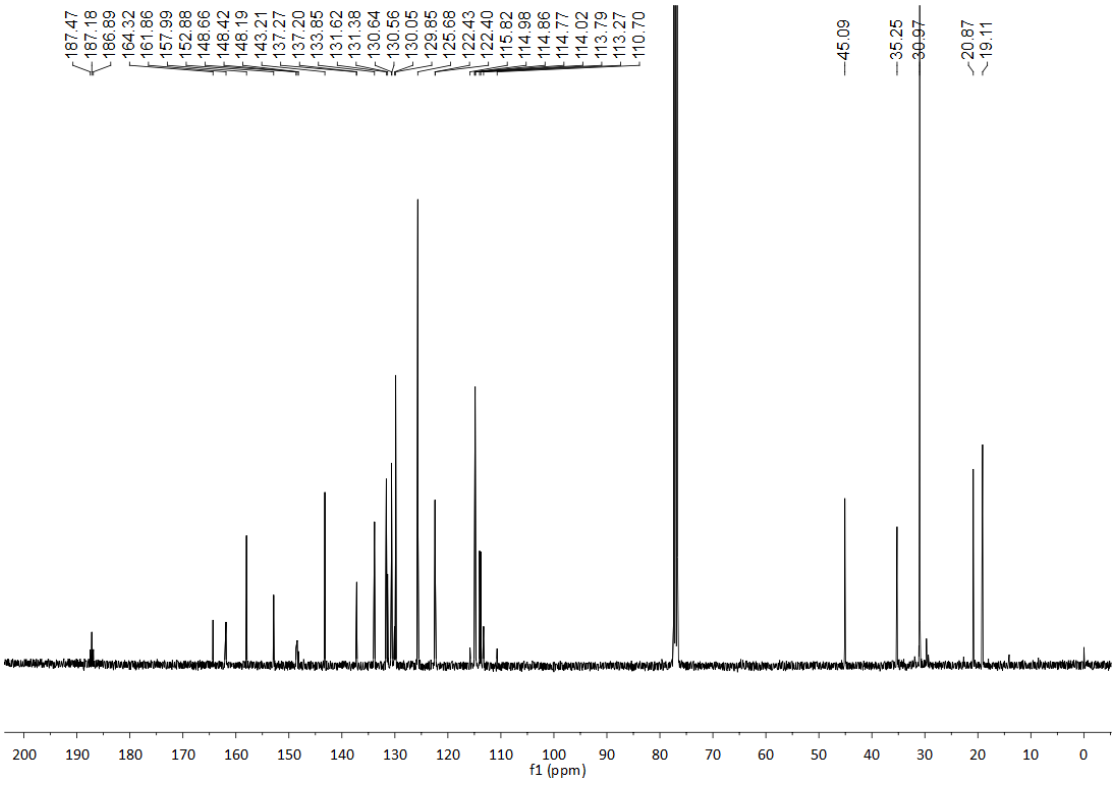
^{1}H NMR (400 MHz, $CDCl_3$):



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

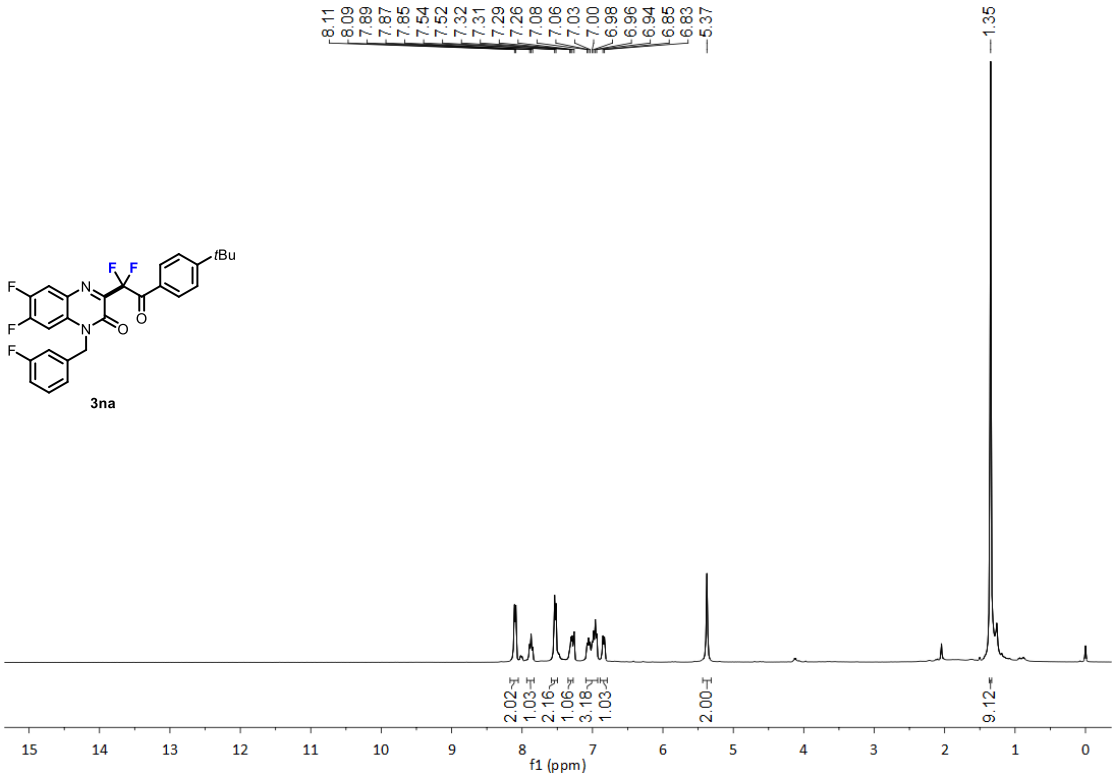


^{13}C NMR (100 MHz, $CDCl_3$):

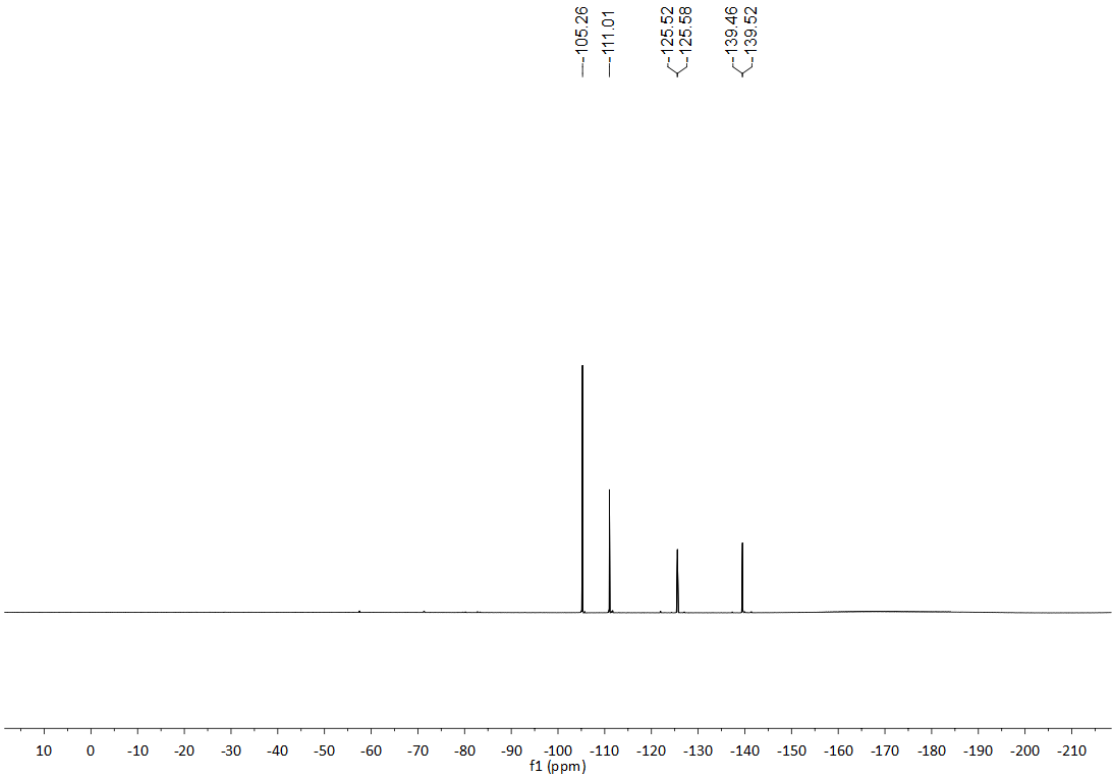


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-difluoro-1-(3-fluoro-benzyl)quinoxalin-2(1*H*)-one (3na)

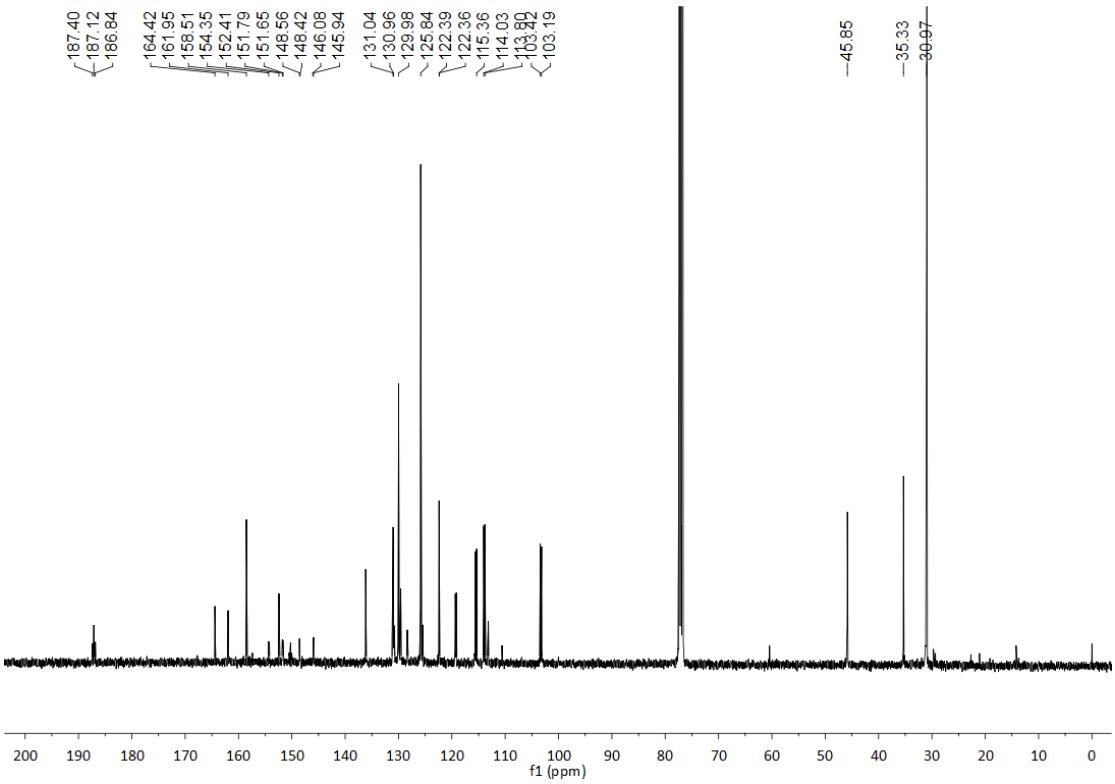
^{1}H NMR (400 MHz, $CDCl_3$):



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

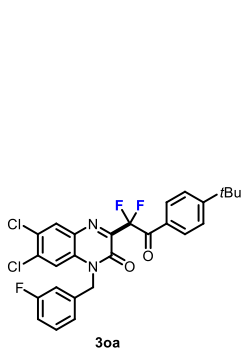


^{13}C NMR (100 MHz, $CDCl_3$):



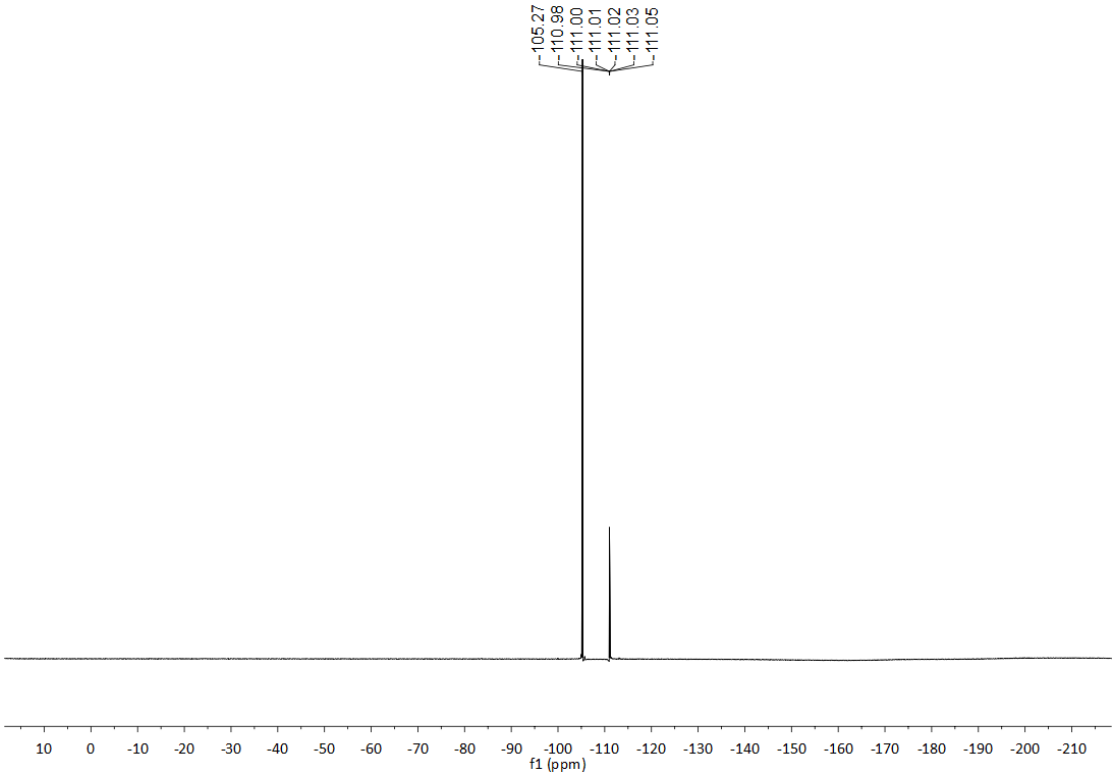
3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dichloro-1-(3-fluoro-benzyl)quinoxalin-2(1*H*)-one (3oa)

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

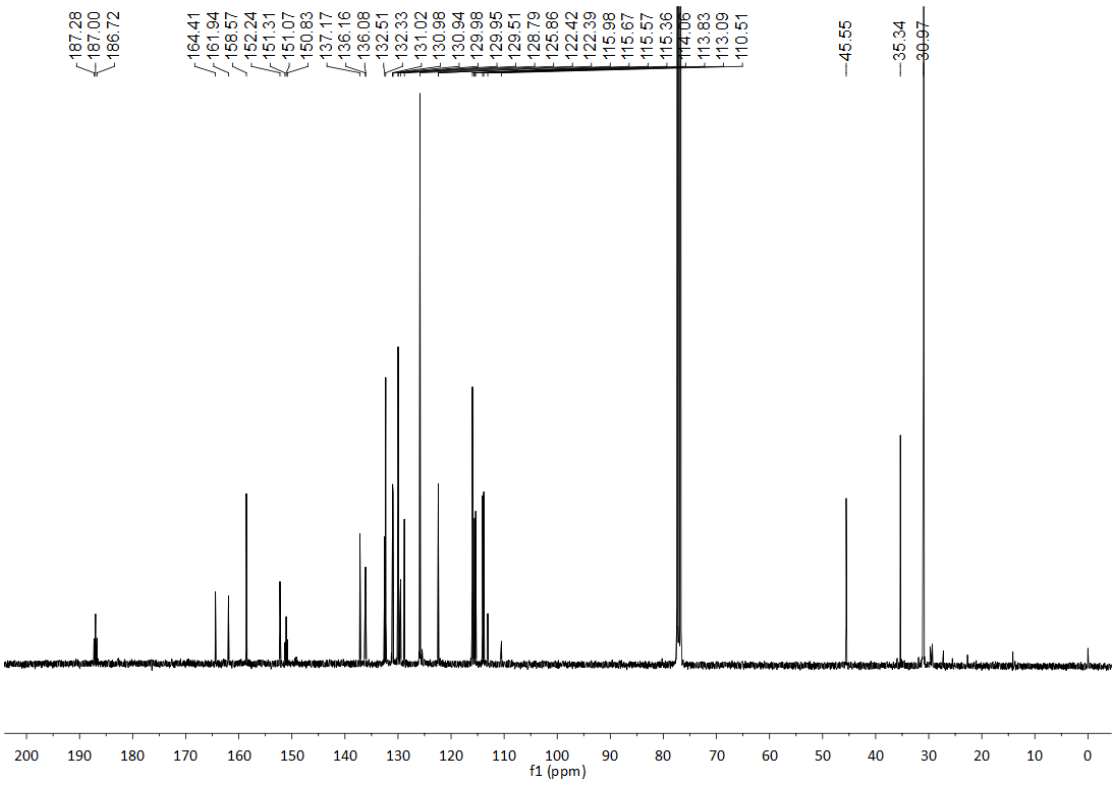


3oa

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

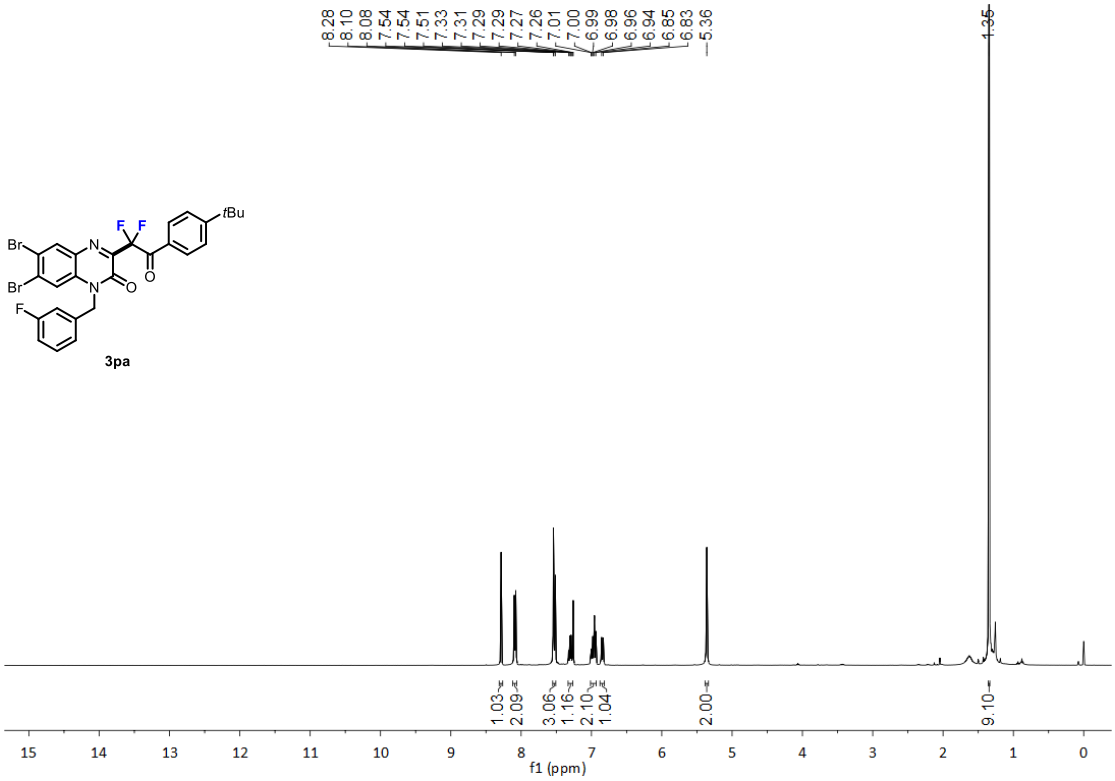


^{13}C NMR (100 MHz, $CDCl_3$):



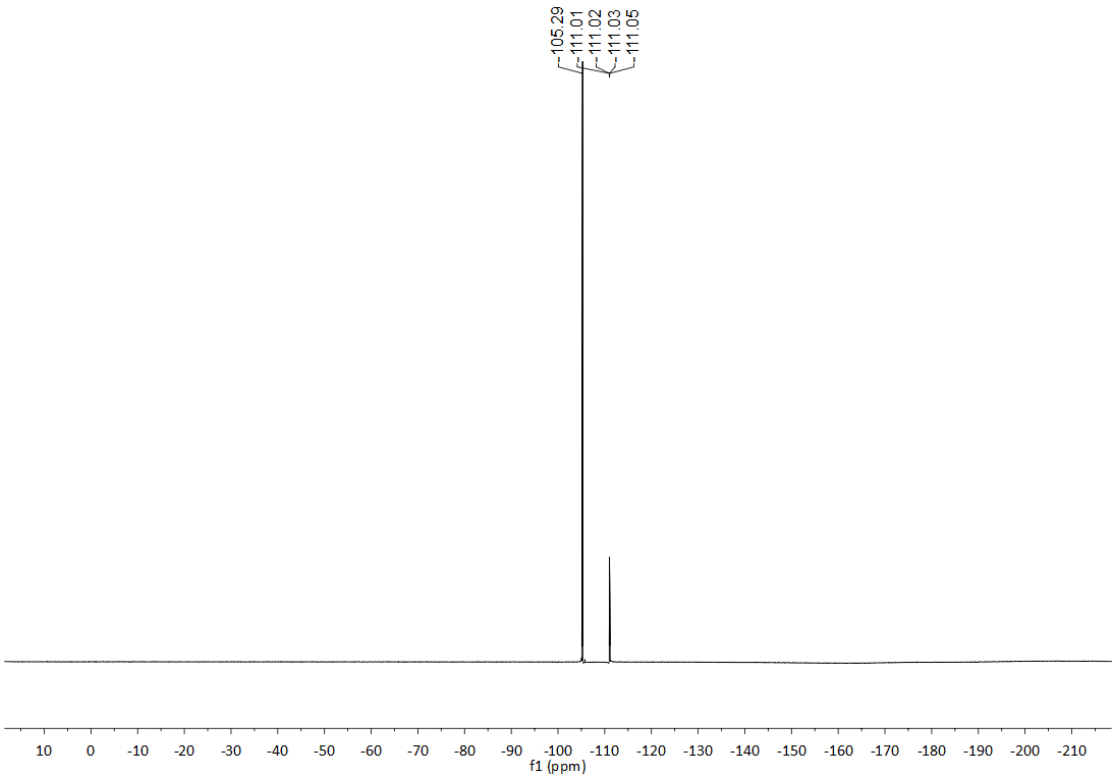
6,7-dibromo-3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluoro-benzyl)quinoxalin-2(1*H*)-one (3pa)

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

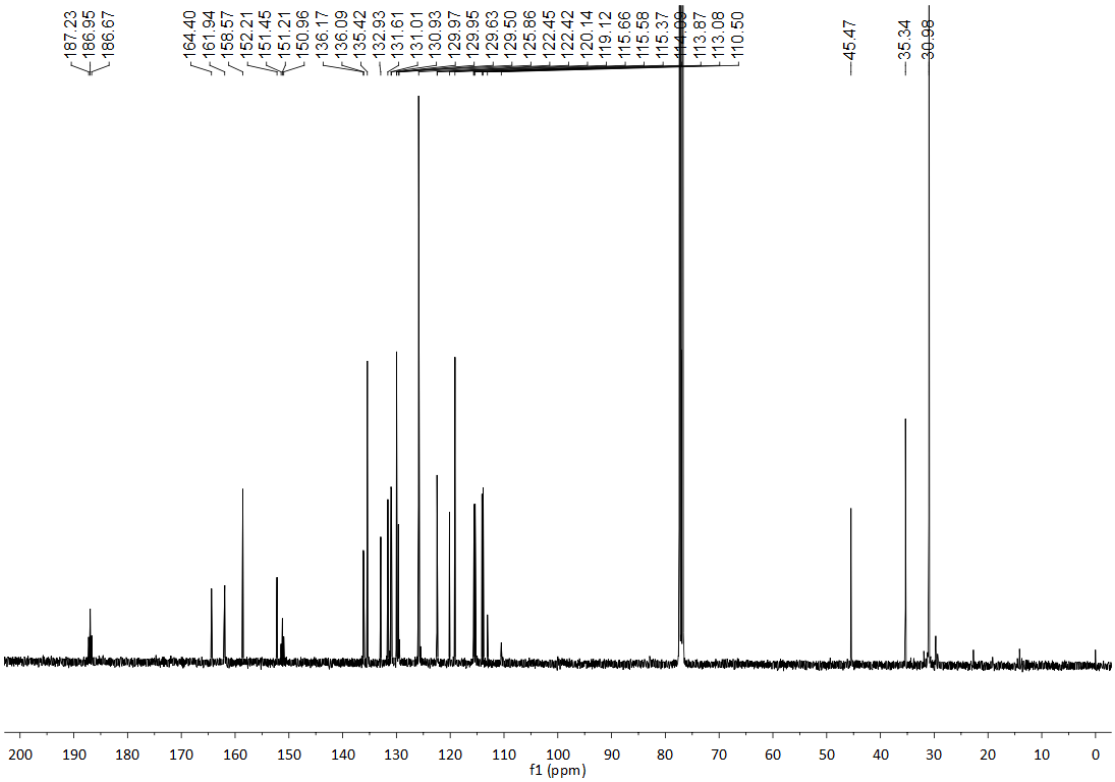


3pa

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

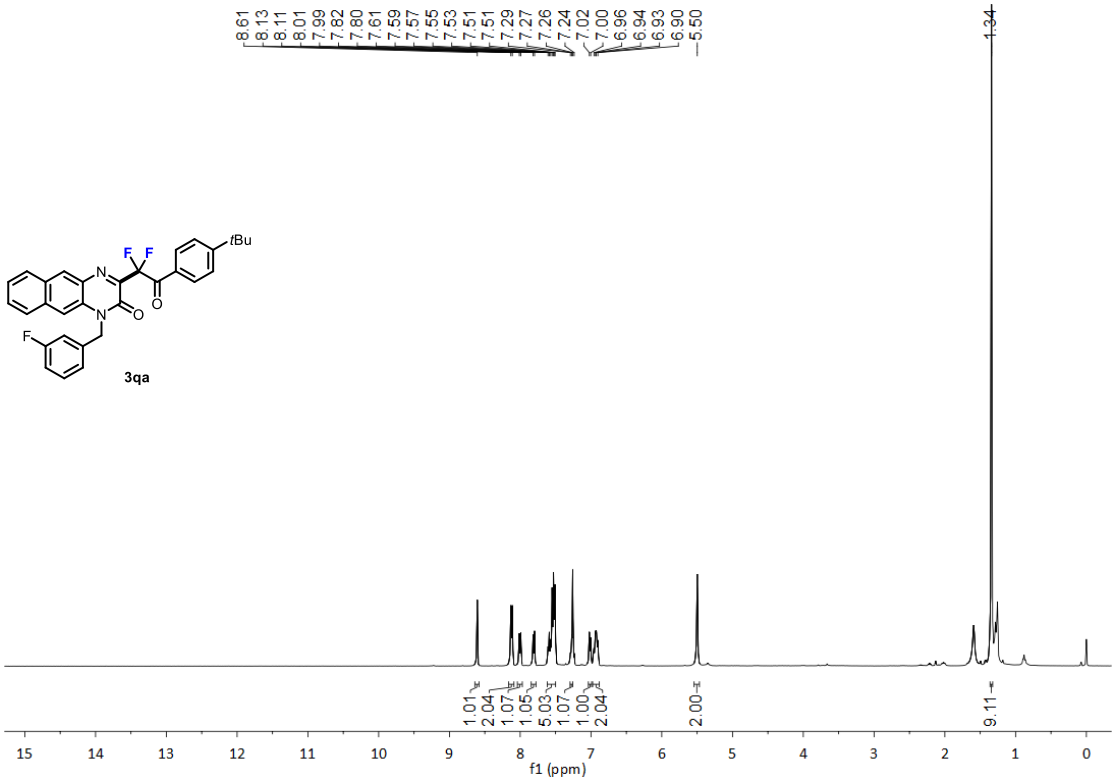


^{13}C NMR (100 MHz, $CDCl_3$):

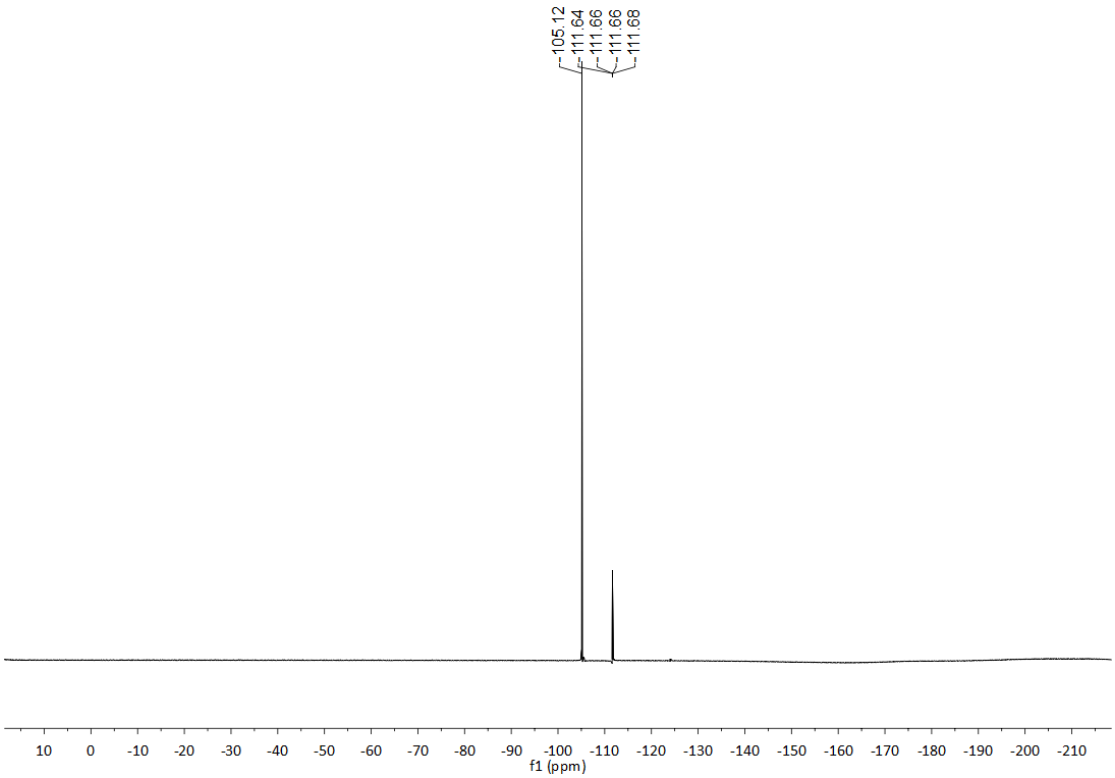


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) benzo[g]quinoxalin-2(1*H*)-one (3qa)

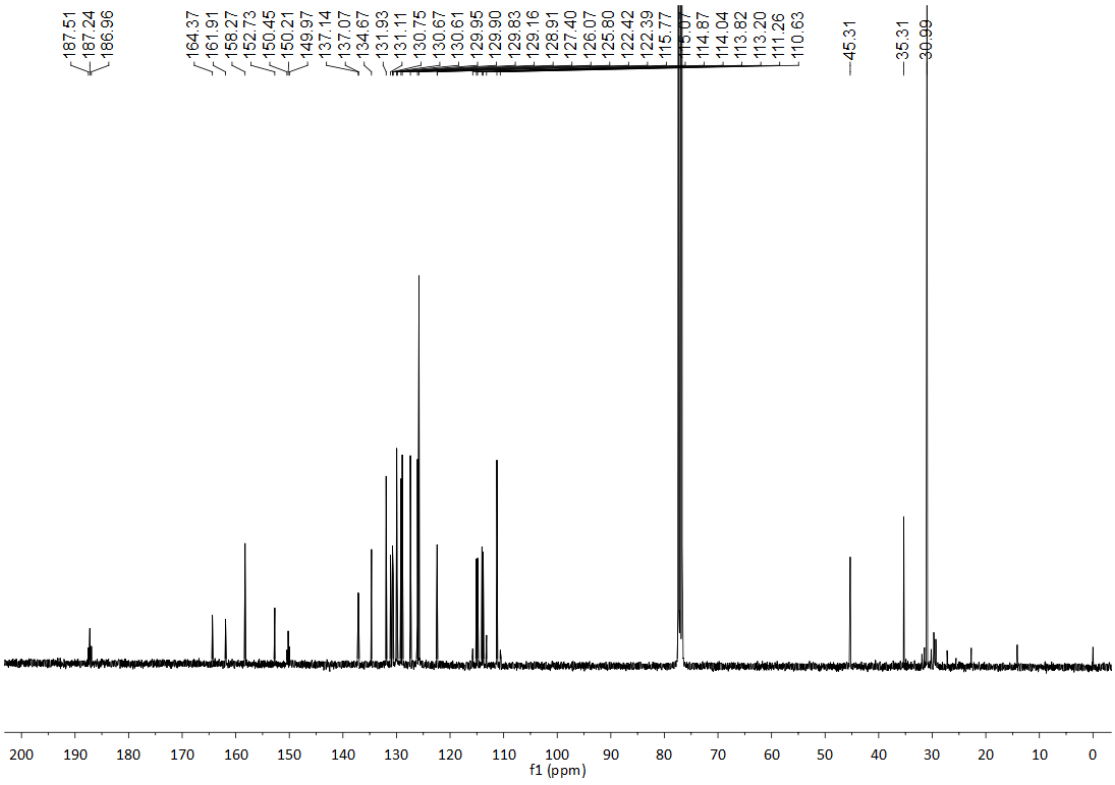
^{1}H NMR (400 MHz, $CDCl_3$):



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



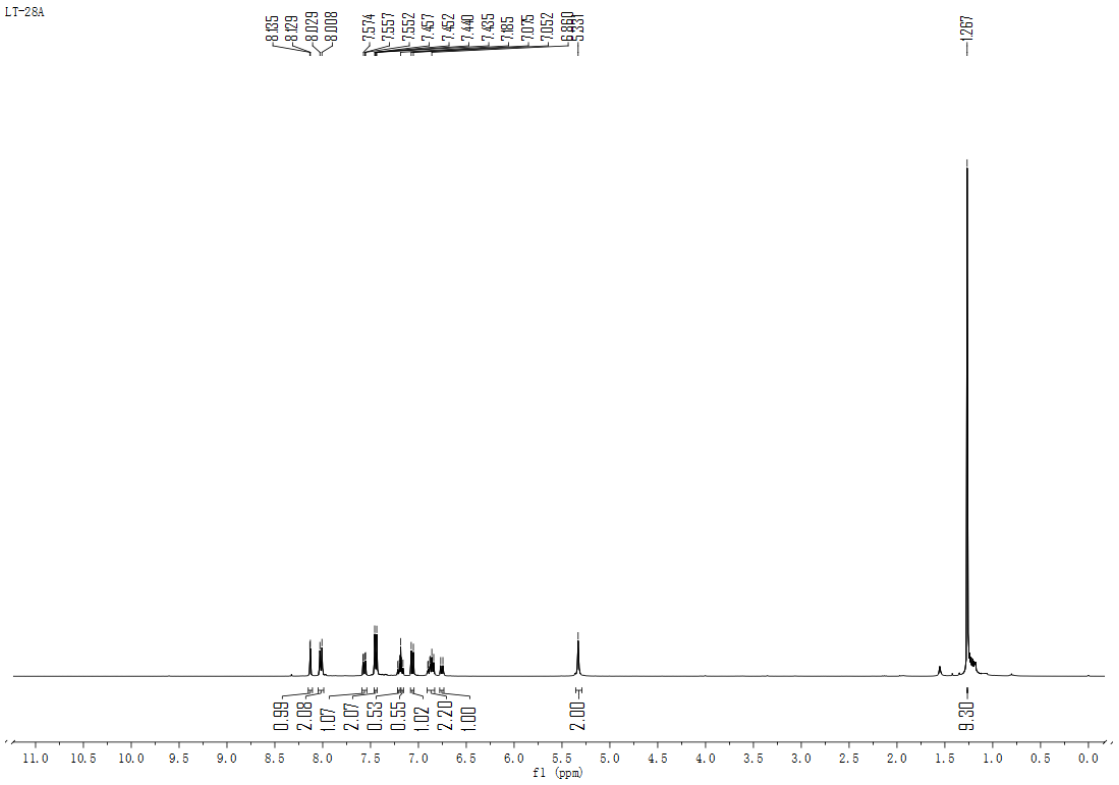
^{13}C NMR (100 MHz, $CDCl_3$):



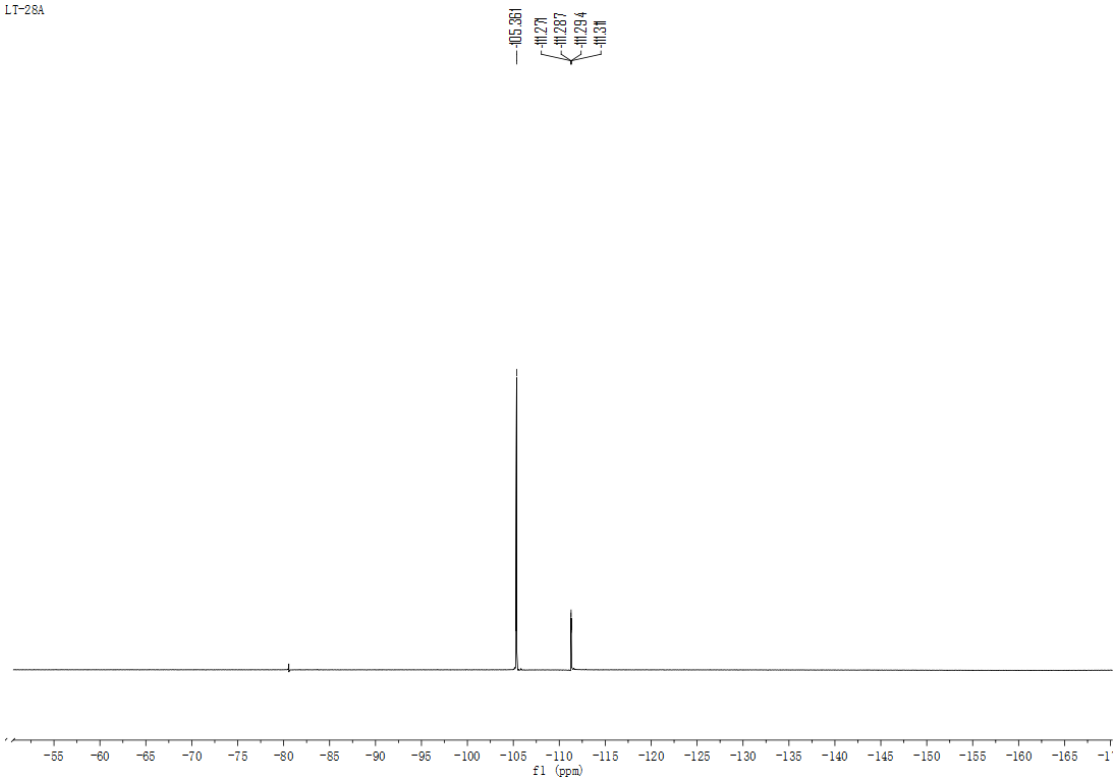
6-bromo-3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl)q

uinoxalin-2(1H)-one (3ra)

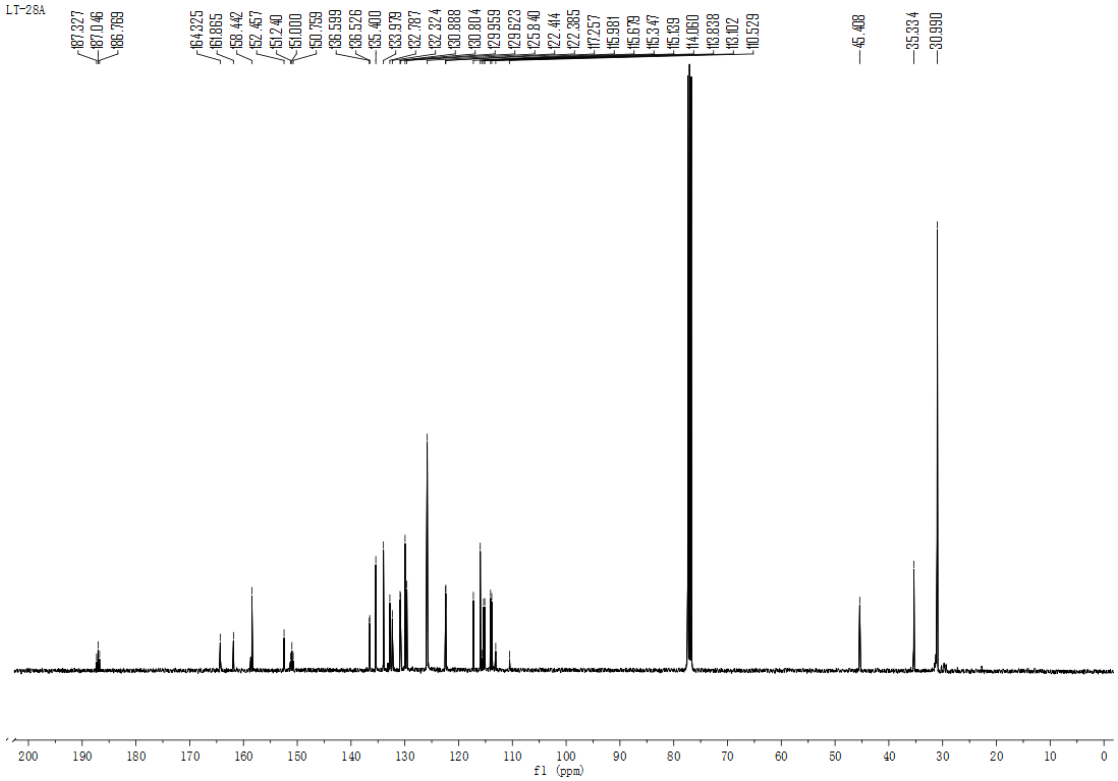
^{1}H NMR (400 MHz, $CDCl_3$):



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

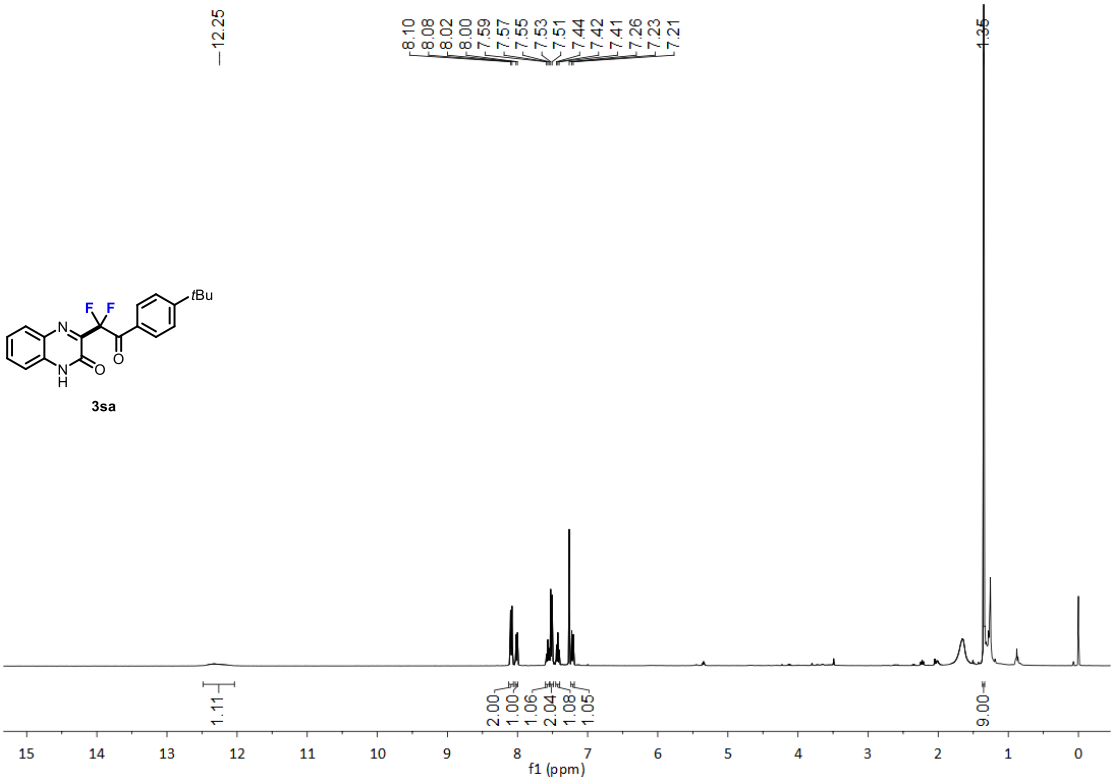


^{13}C NMR (100 MHz, $CDCl_3$):

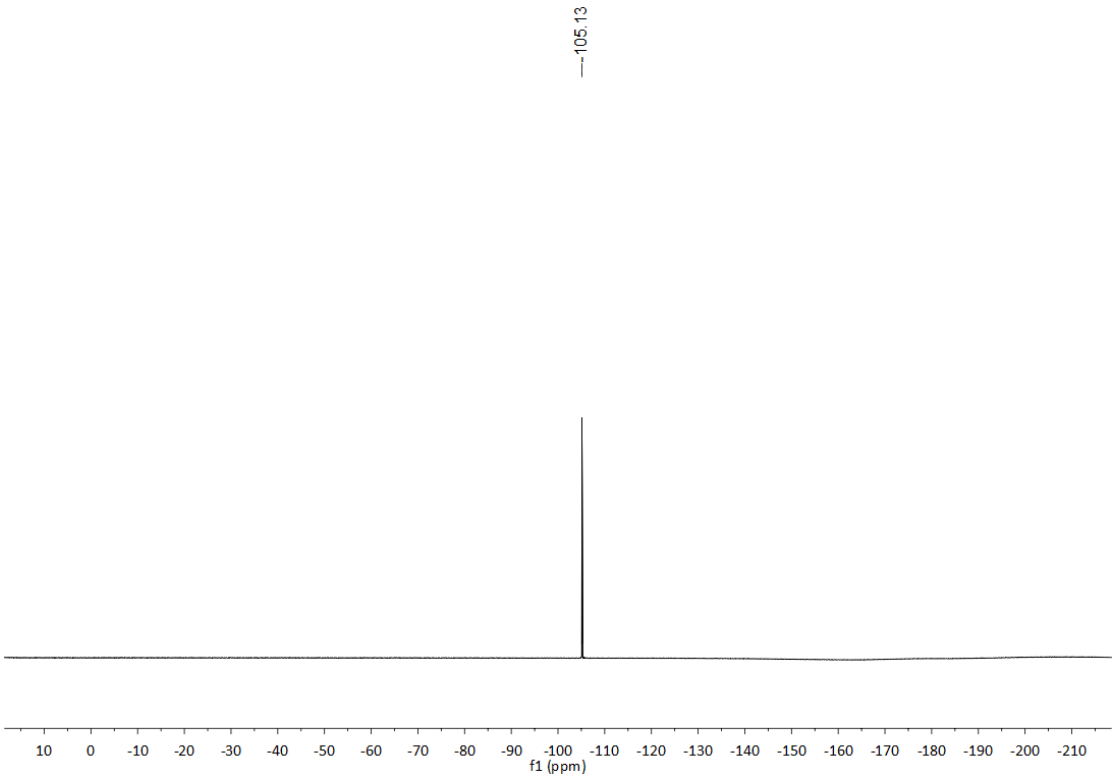


3-(2-(4-(tert-butyl)phenyl)-1,1-difluoro-2-oxoethyl)quinoxalin-2(1*H*)-one (3sa)

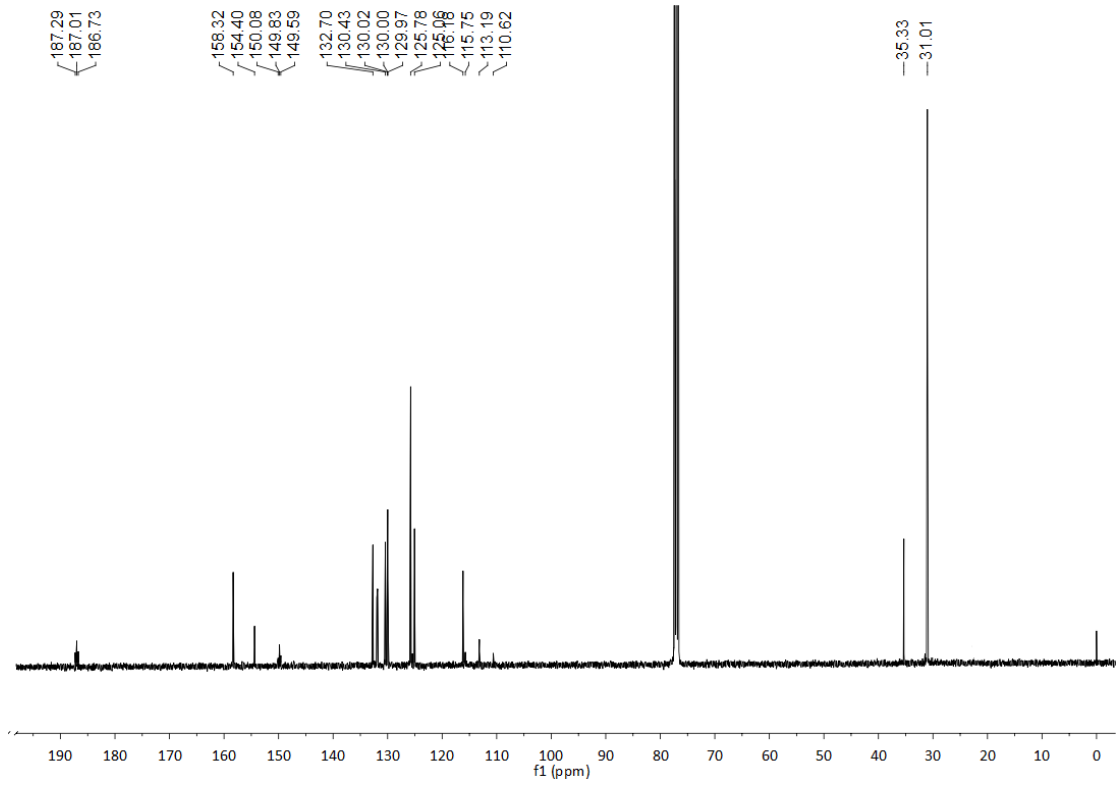
^{1}H NMR (400 MHz, $CDCl_3$):



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

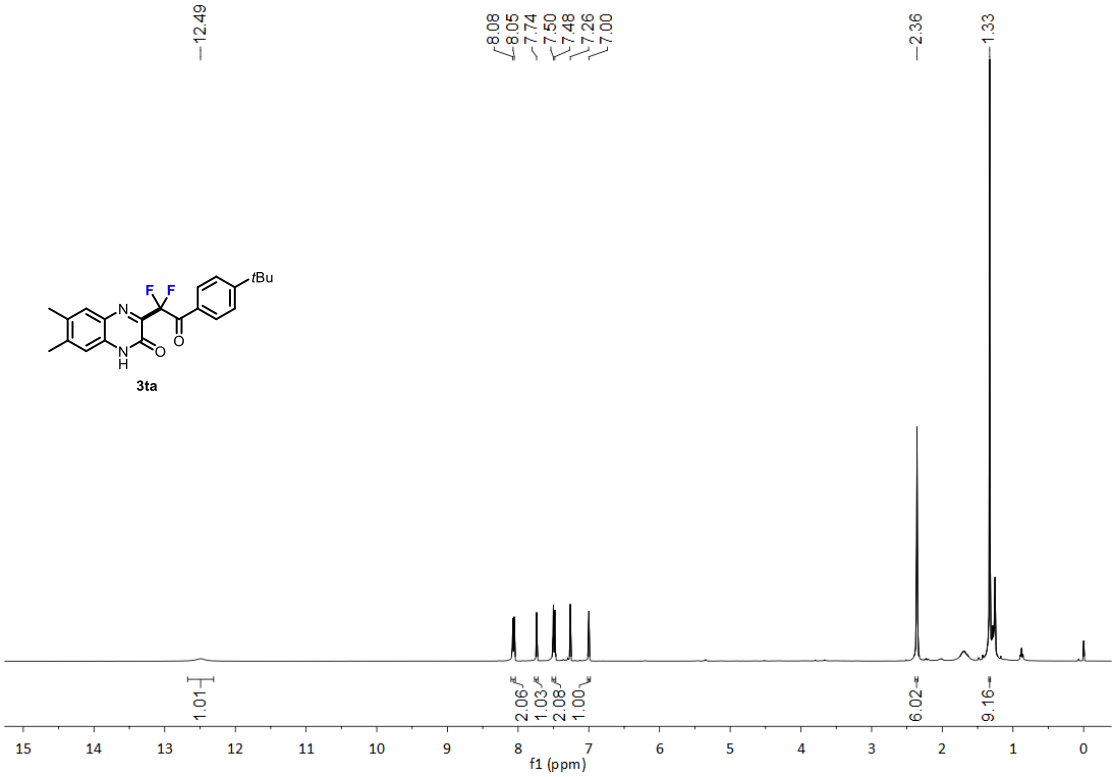


^{13}C NMR (100 MHz, $CDCl_3$):

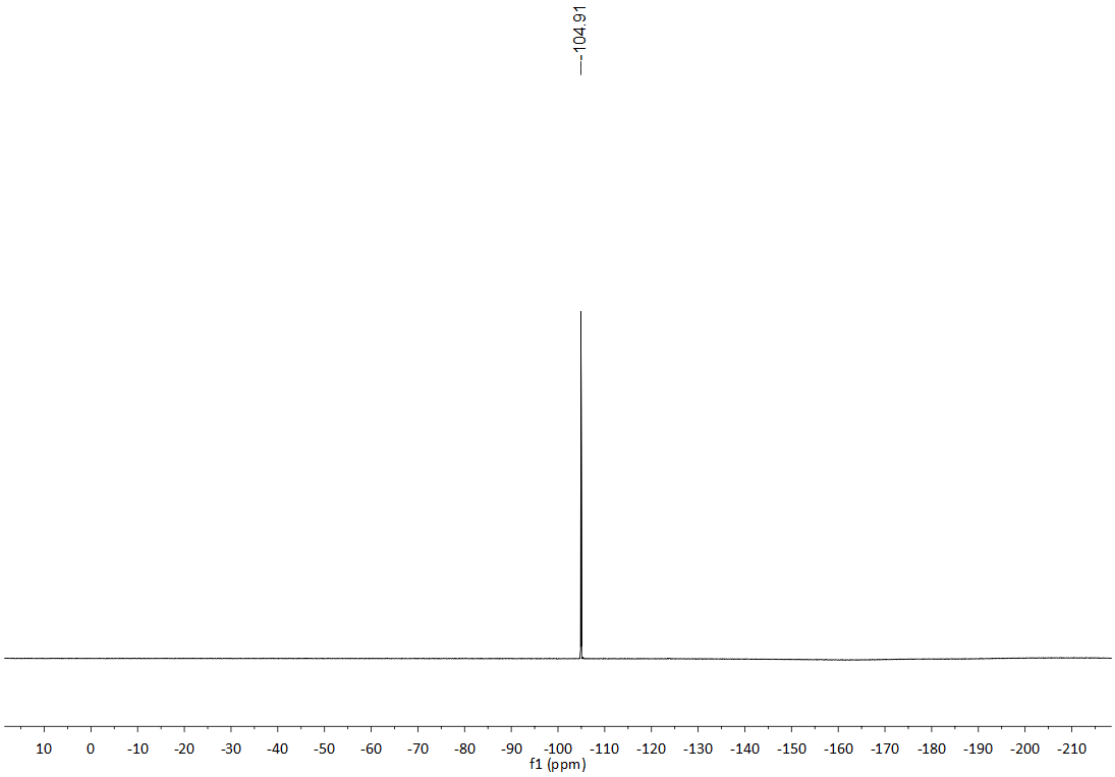


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dimethylquinoxalin-2(1*H*)-one (3ta)

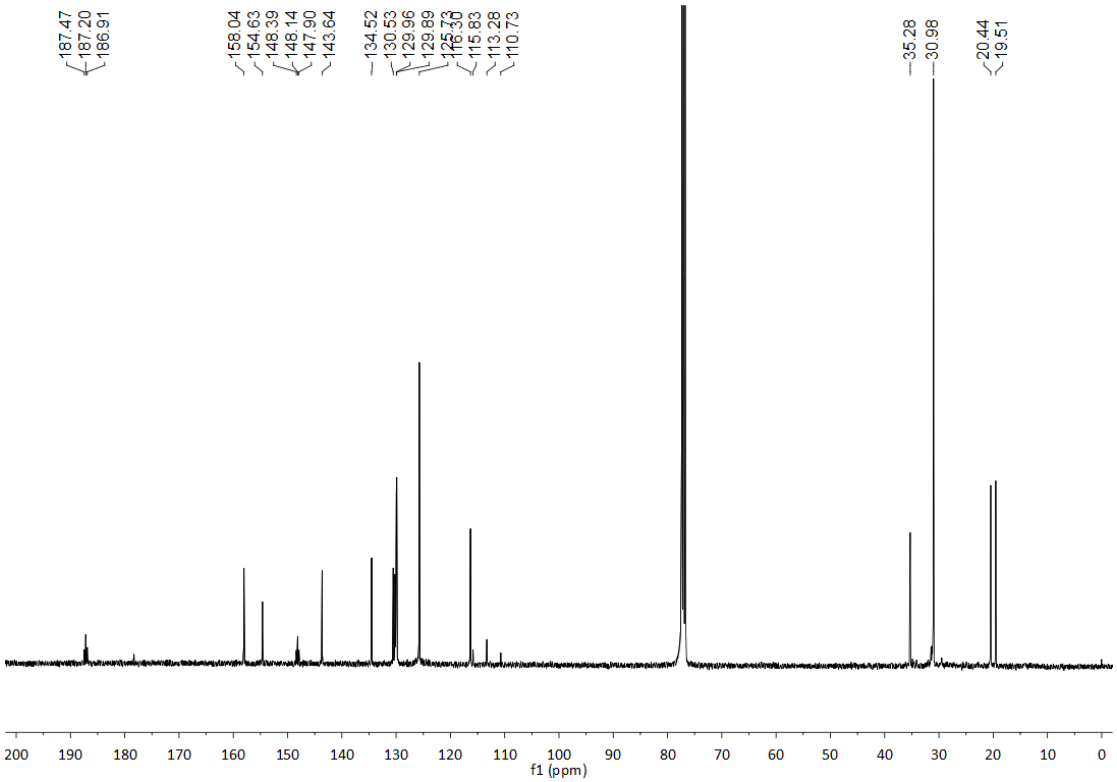
^{1}H NMR (400 MHz, $CDCl_3$):



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

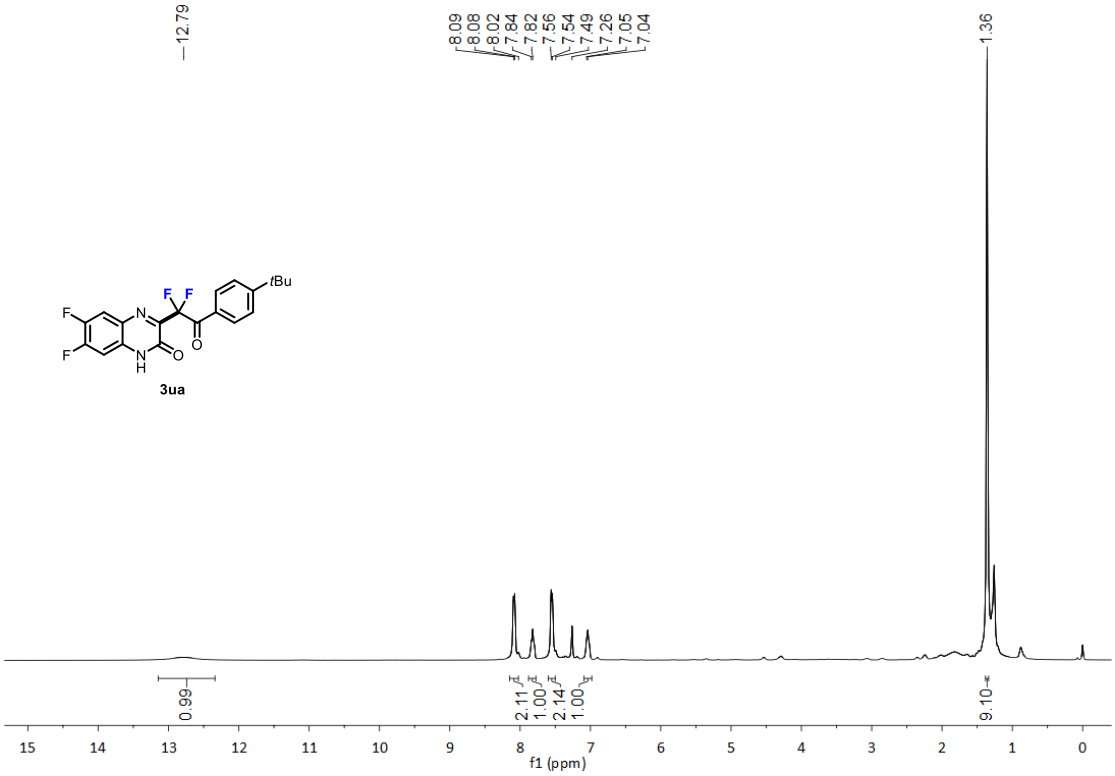


^{13}C NMR (100 MHz, $CDCl_3$):

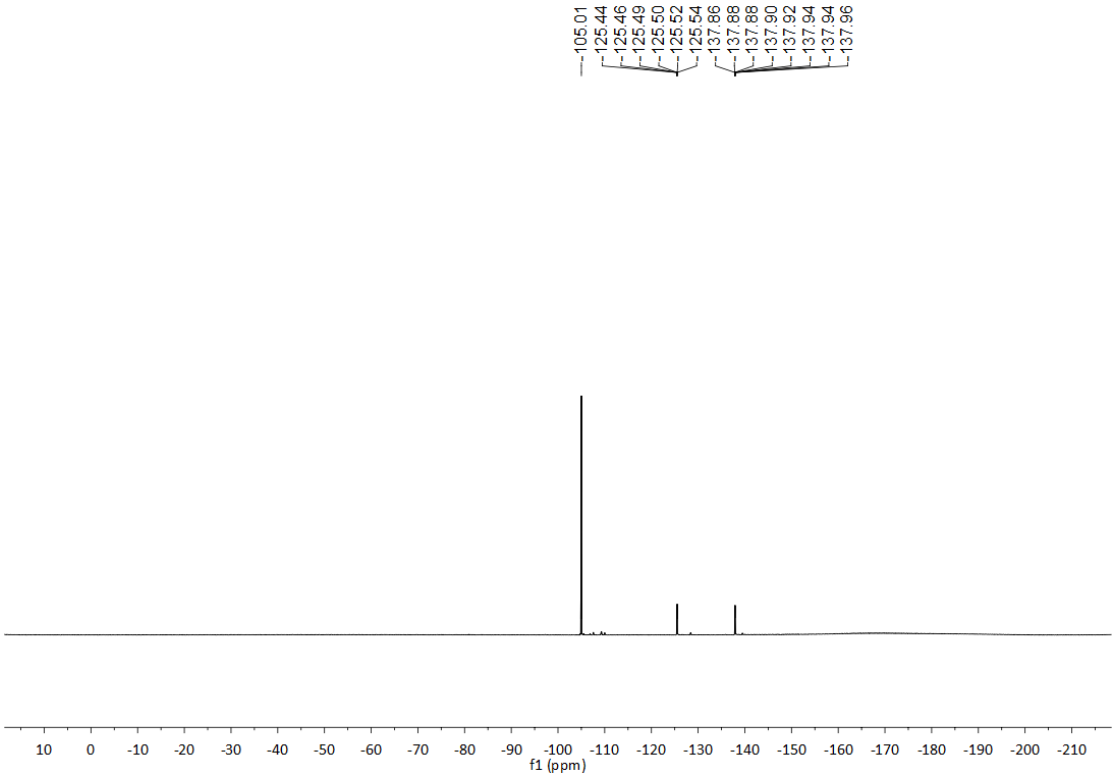


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-difluoroquinoxalin-2(1*H*)-one (3ua)

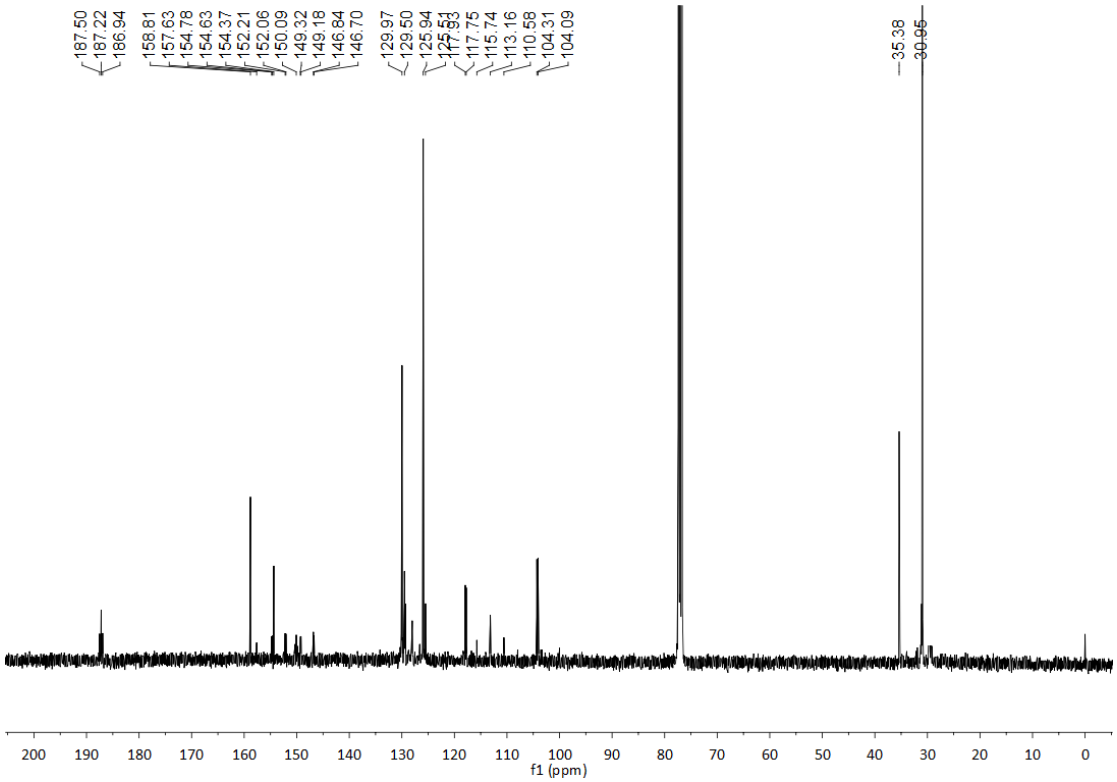
^{1}H NMR (400 MHz, $CDCl_3$):



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

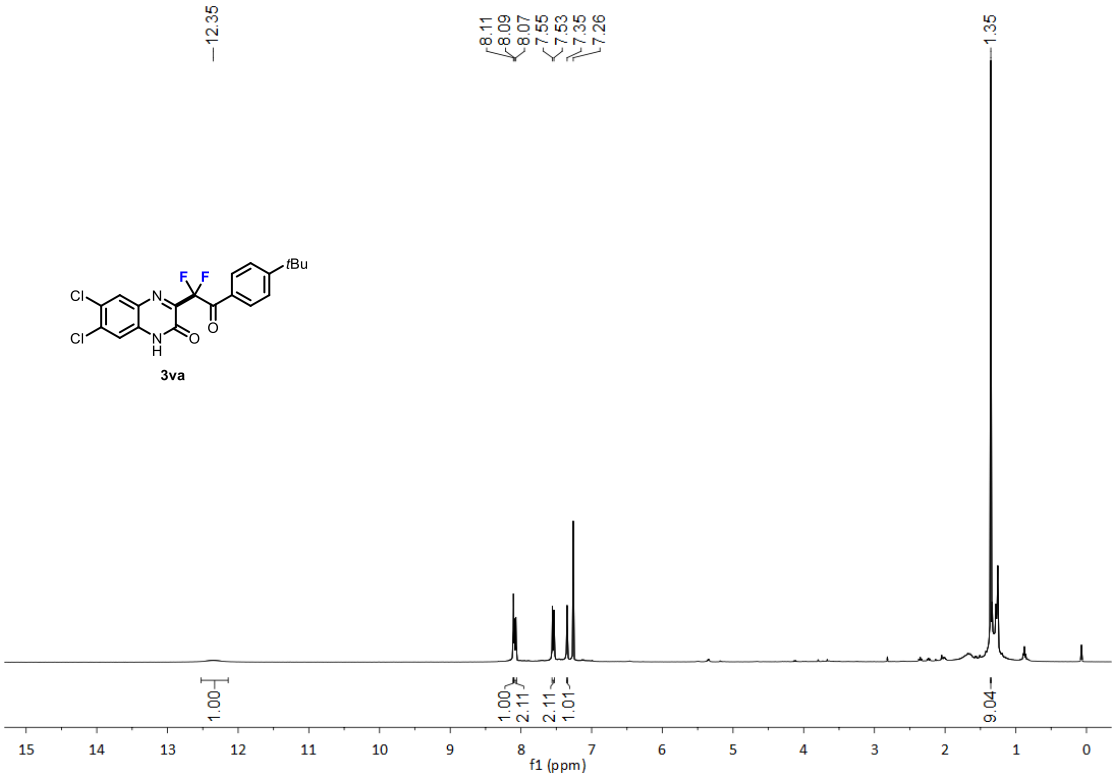


^{13}C NMR (100 MHz, $CDCl_3$):

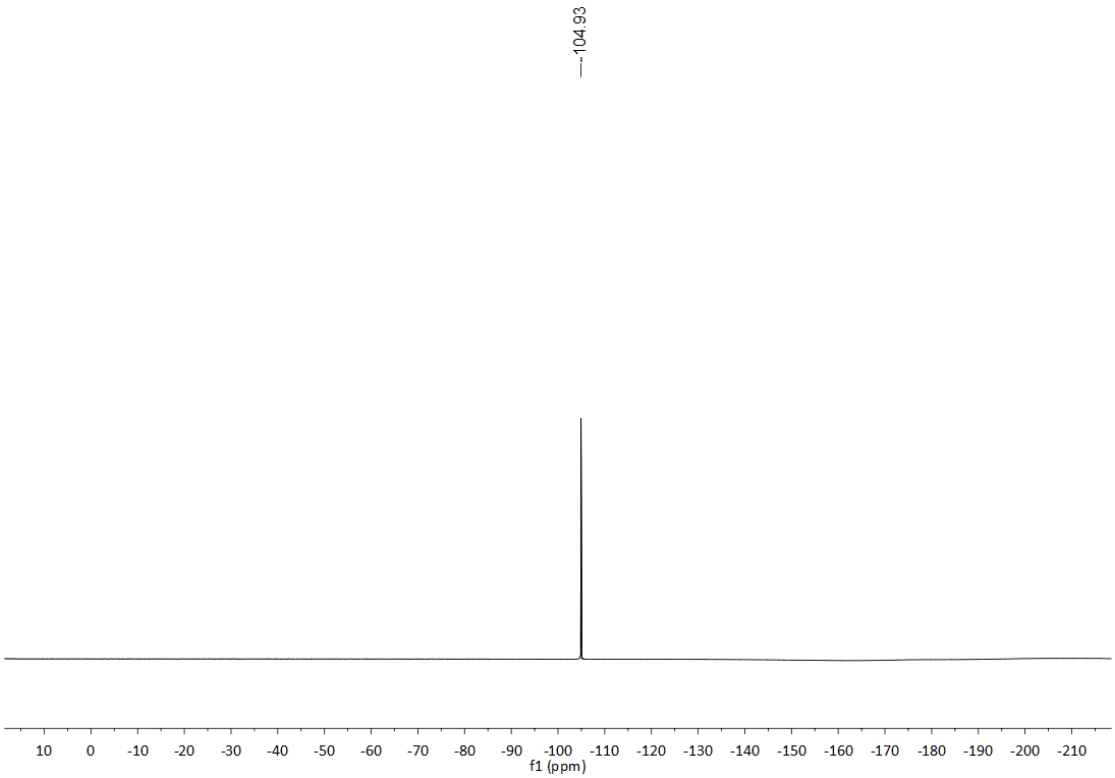


3-(2-(4-(*tert*-butyl)phenyl)-1,1-difluoro-2-oxoethyl)-6,7-dichloroquinoxalin-2(1*H*)-one (3va)

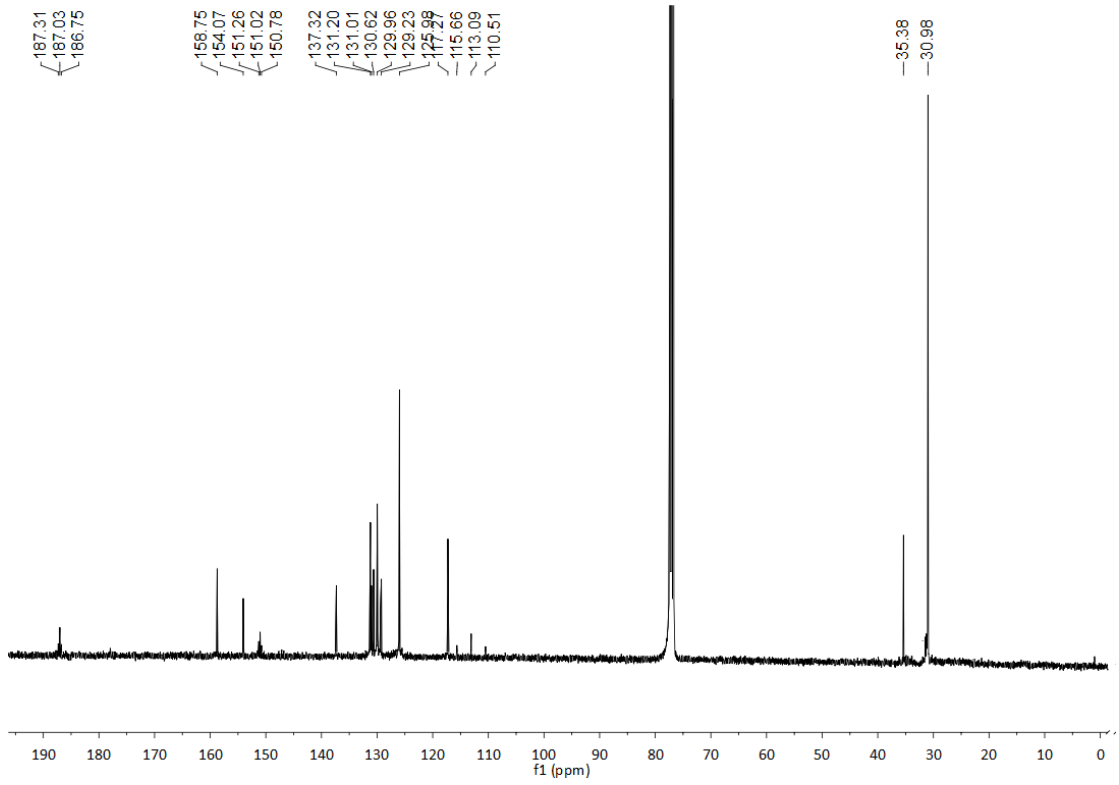
^{1}H NMR (400 MHz, $CDCl_3$):



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



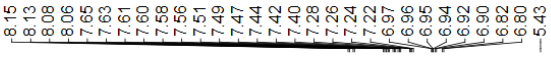
^{13}C NMR (100 MHz, $CDCl_3$):

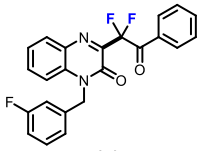


3-(1,1-difluoro-2-oxo-2-phenylethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one

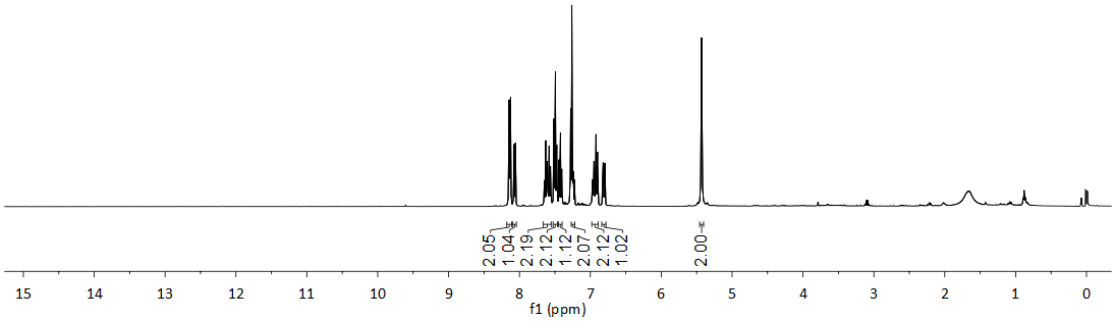
(3ab)

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

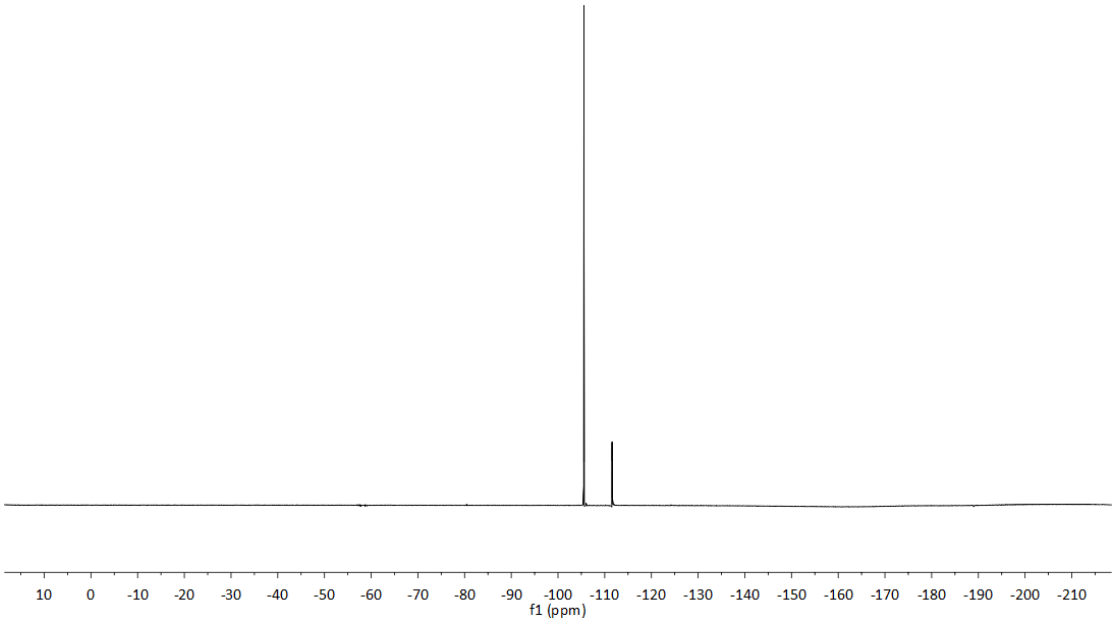




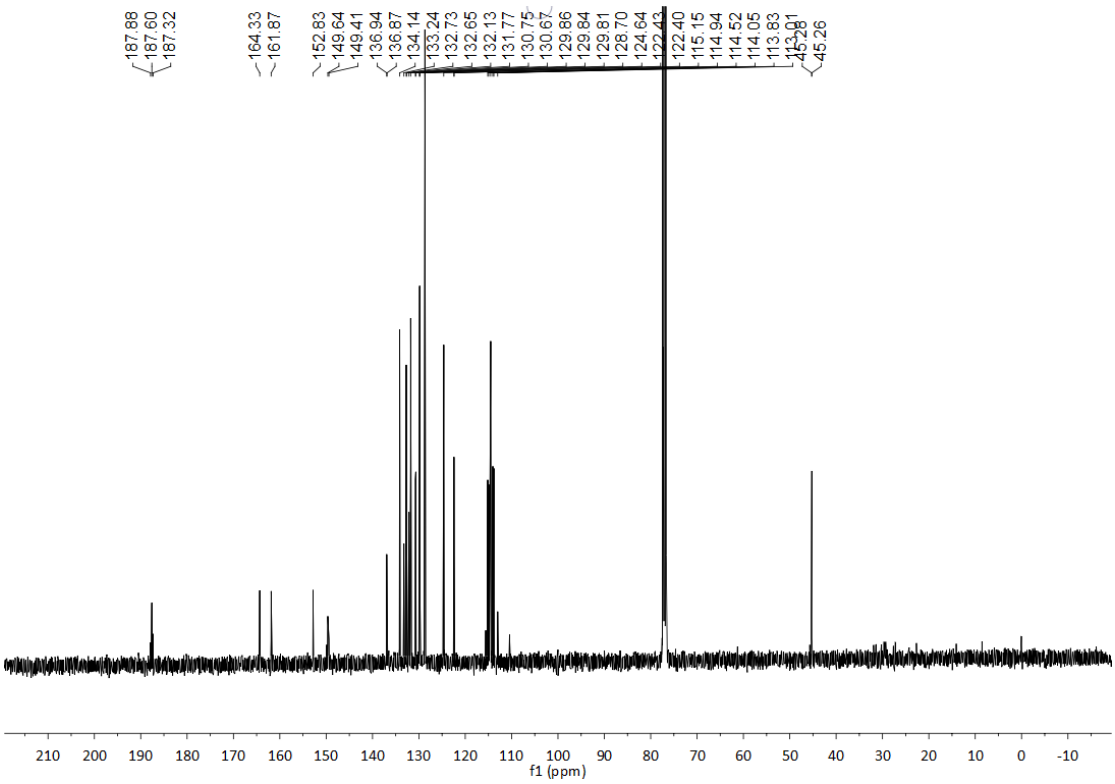
3ab



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

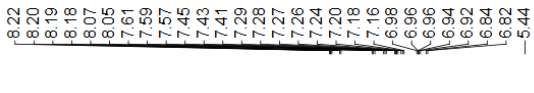


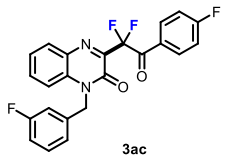
^{13}C NMR (100 MHz, $CDCl_3$):



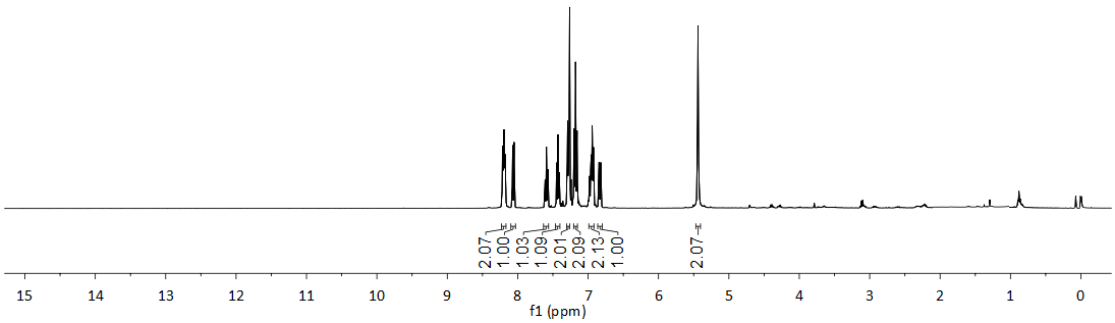
3-(1,1-difluoro-2-(4-fluorophenyl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3ac)

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

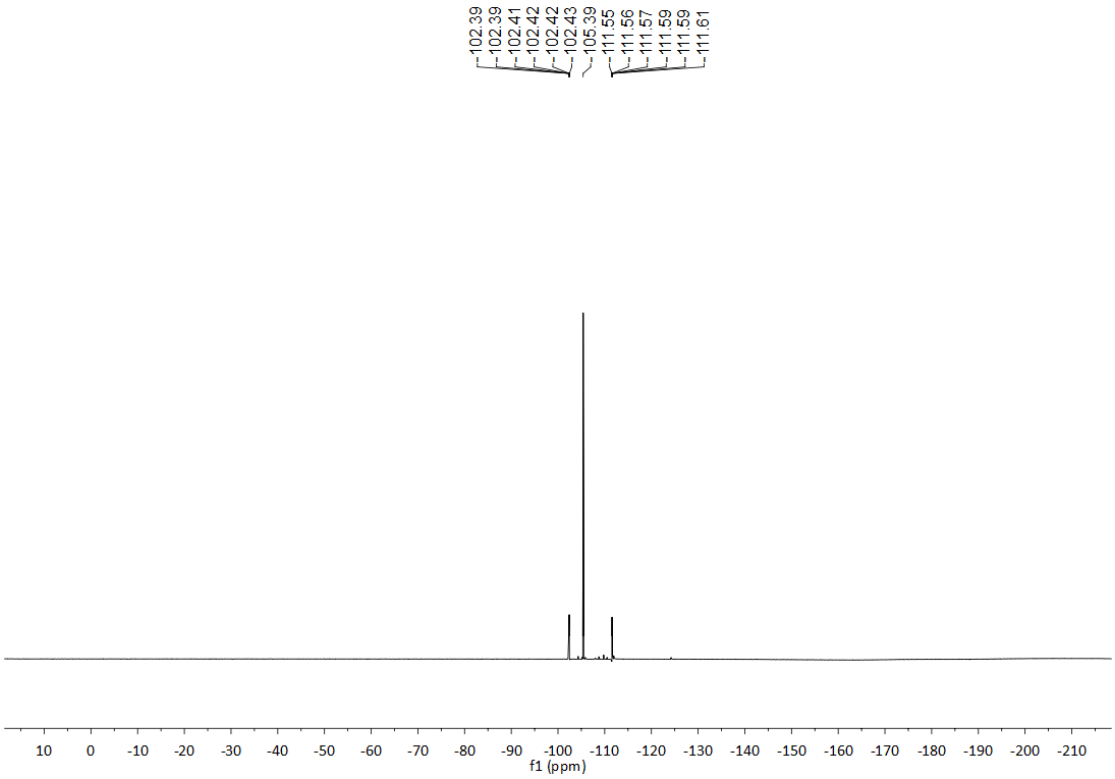




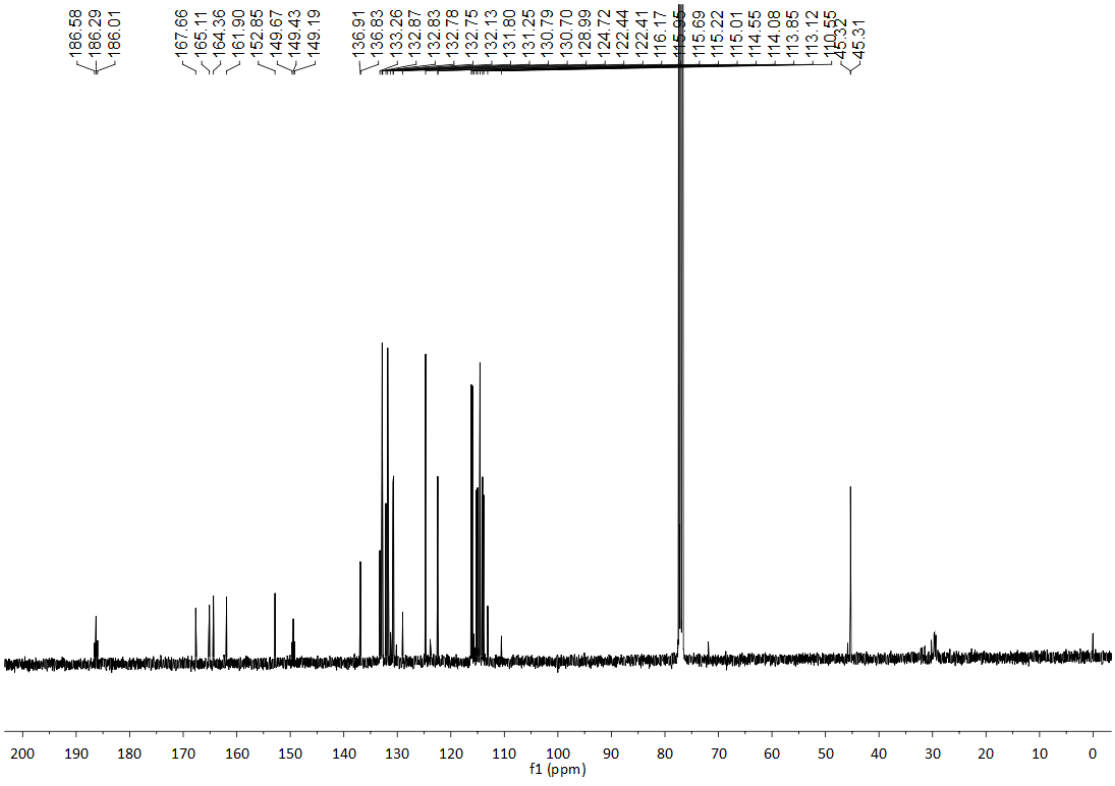
3ac



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

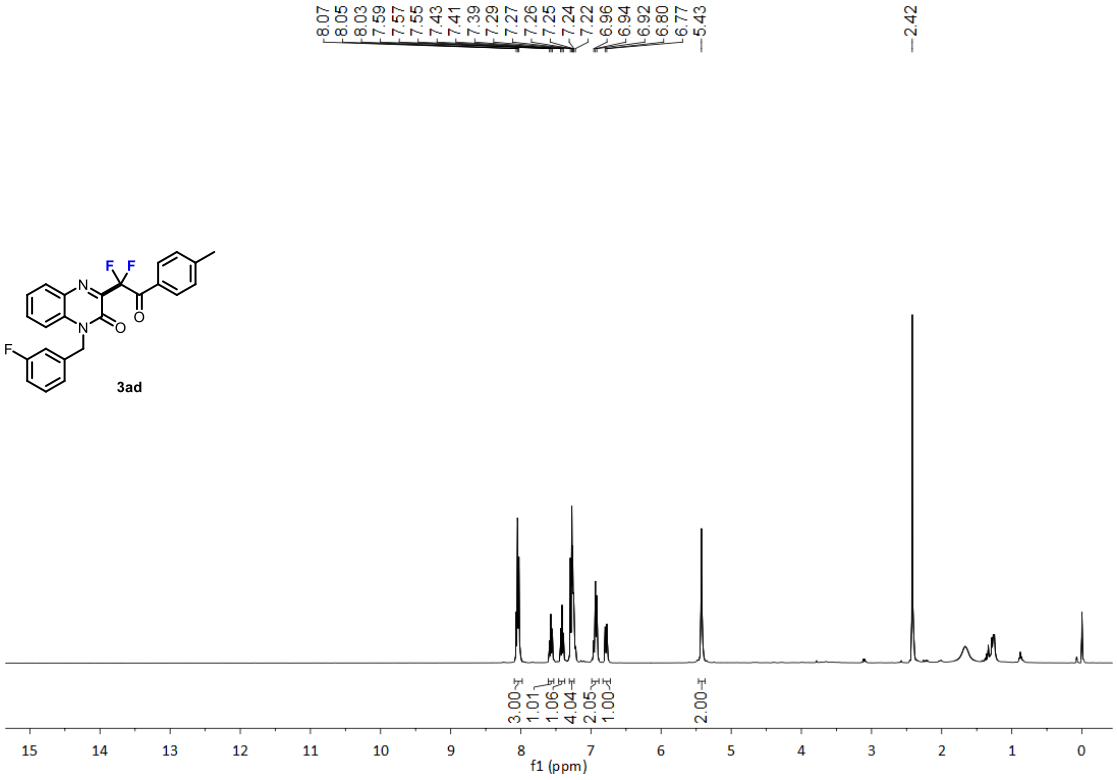


^{13}C NMR (100 MHz, $CDCl_3$):

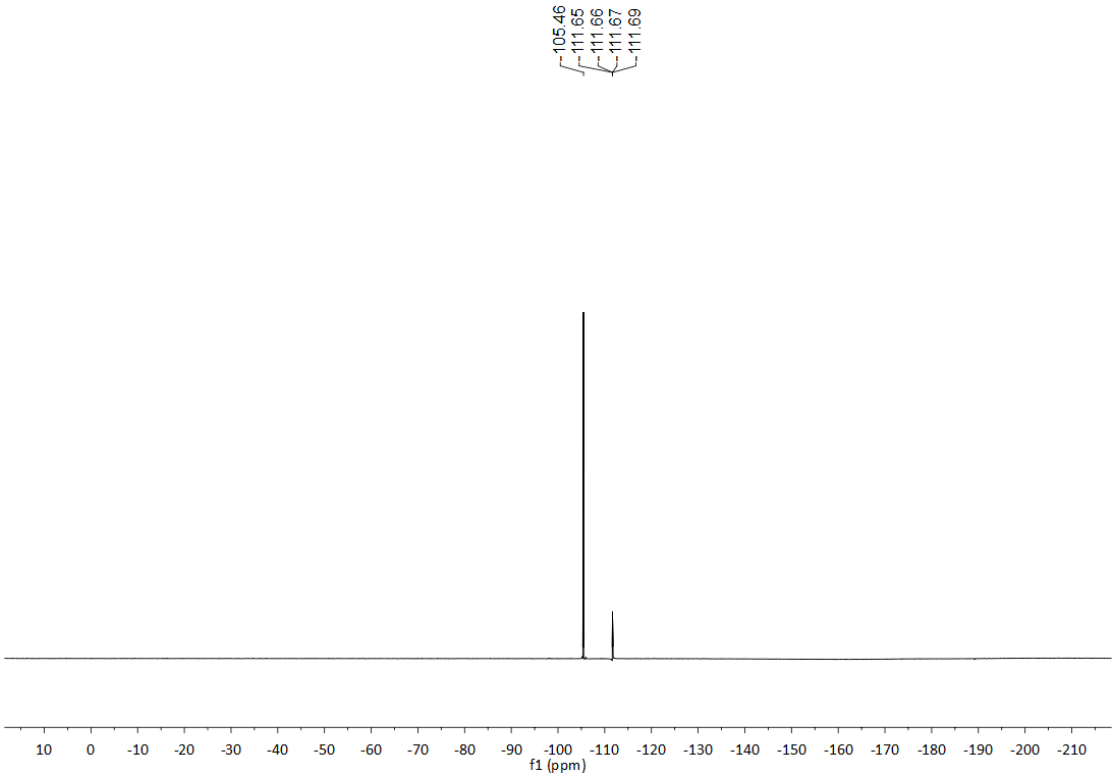


3-(1,1-difluoro-2-oxo-2-(p-tolyl)ethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3ad)

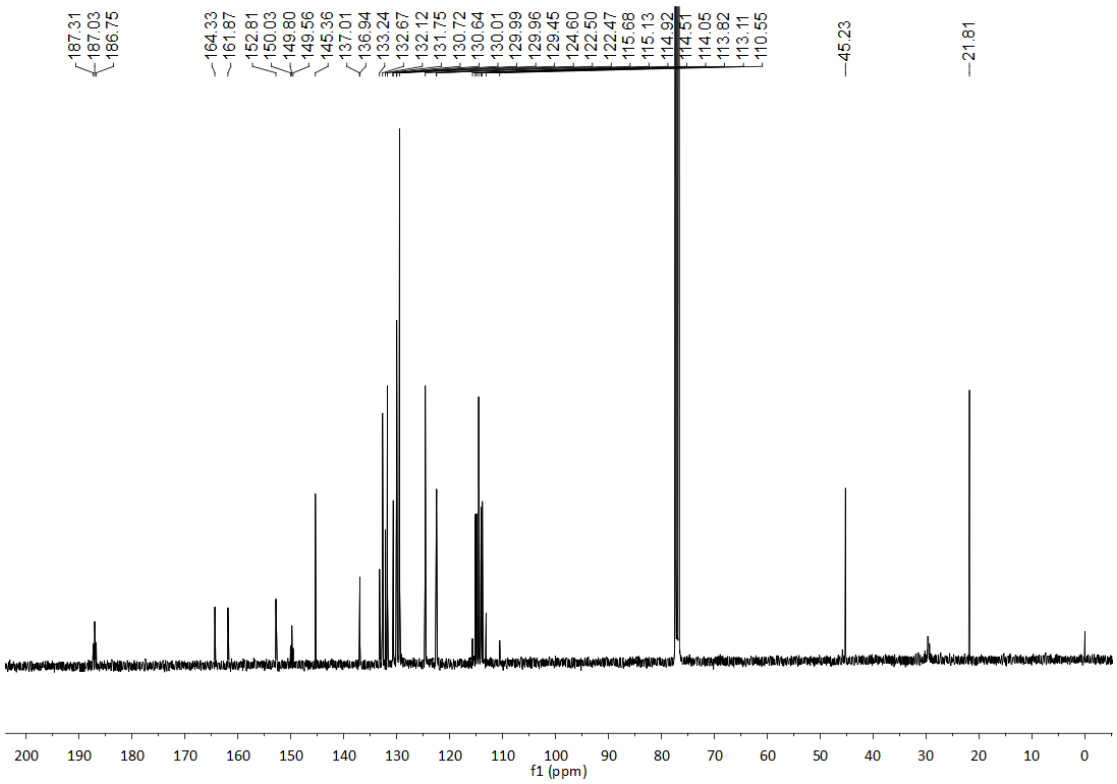
^{1}H NMR (400 MHz, $CDCl_3$):



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

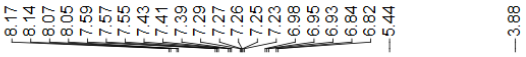


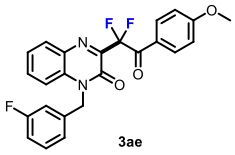
^{13}C NMR (100 MHz, $CDCl_3$):



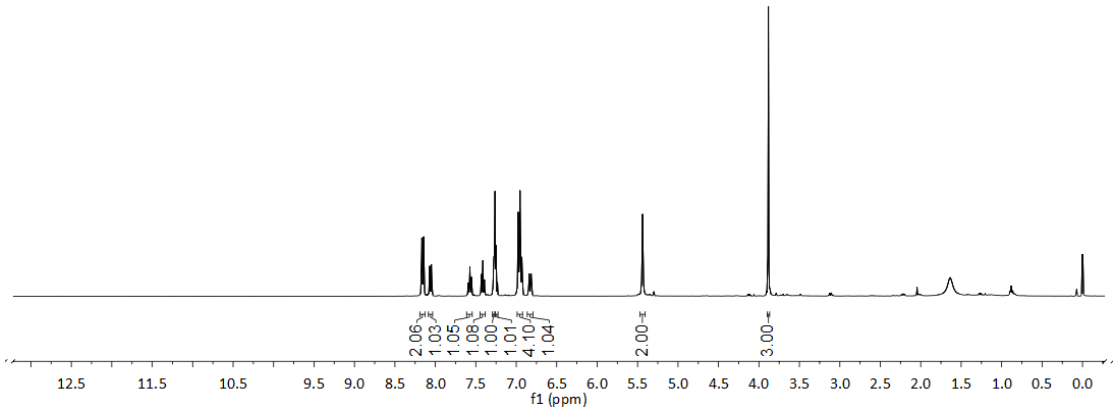
3-(1,1-difluoro-2-(4-methoxyphenyl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3ae)

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

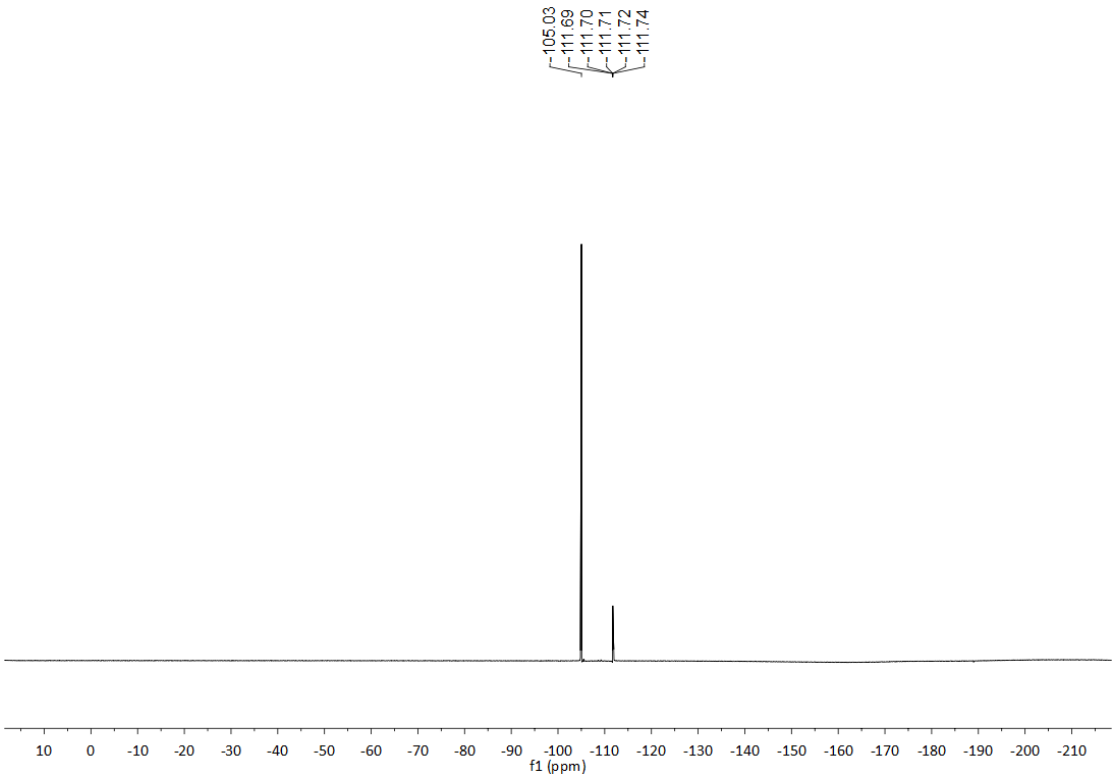




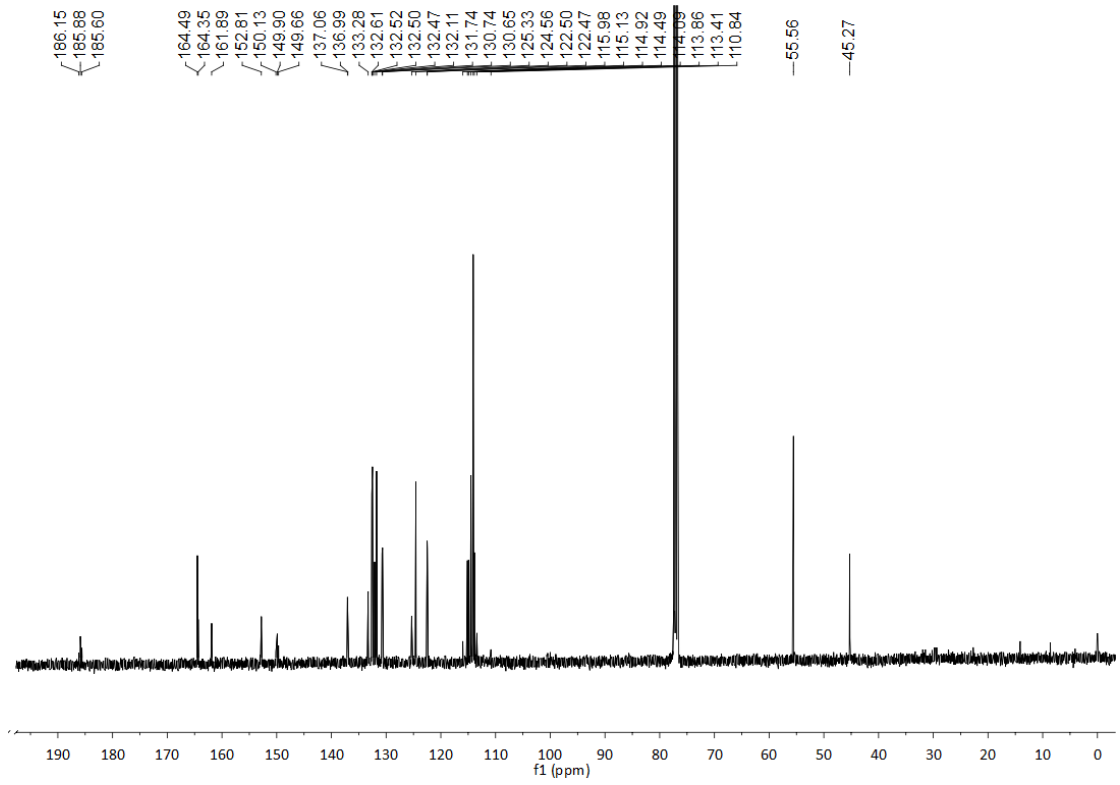
3ae



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

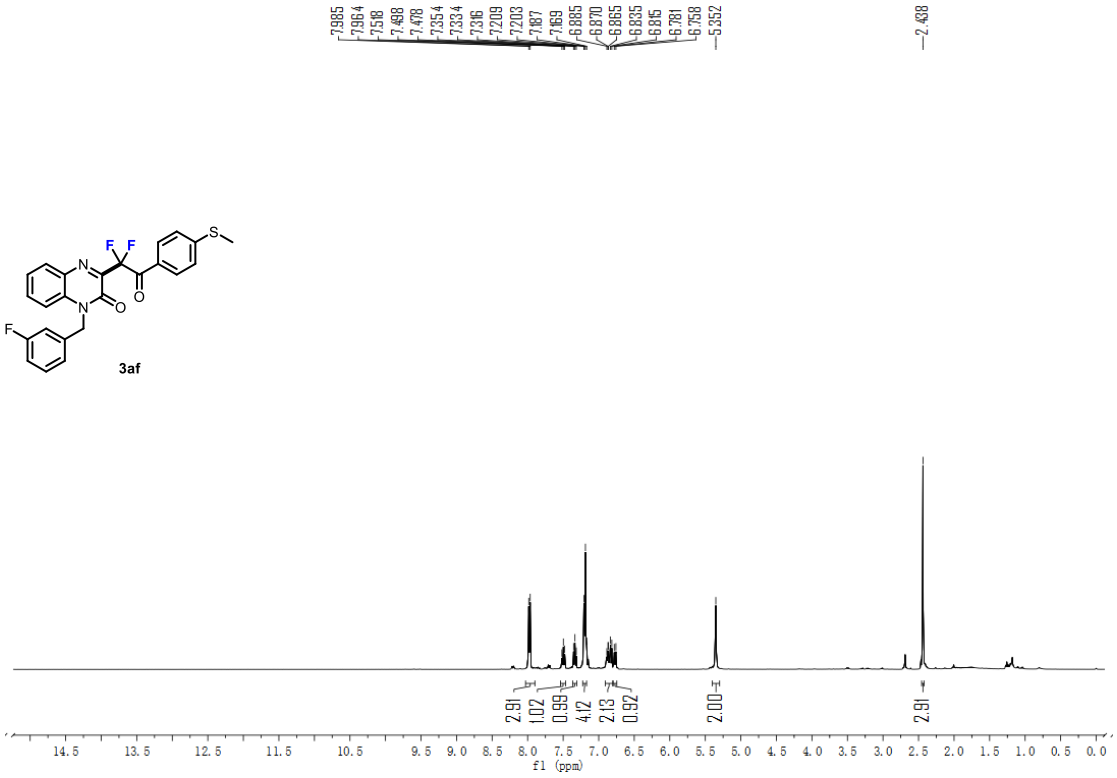


^{13}C NMR (100 MHz, $CDCl_3$):

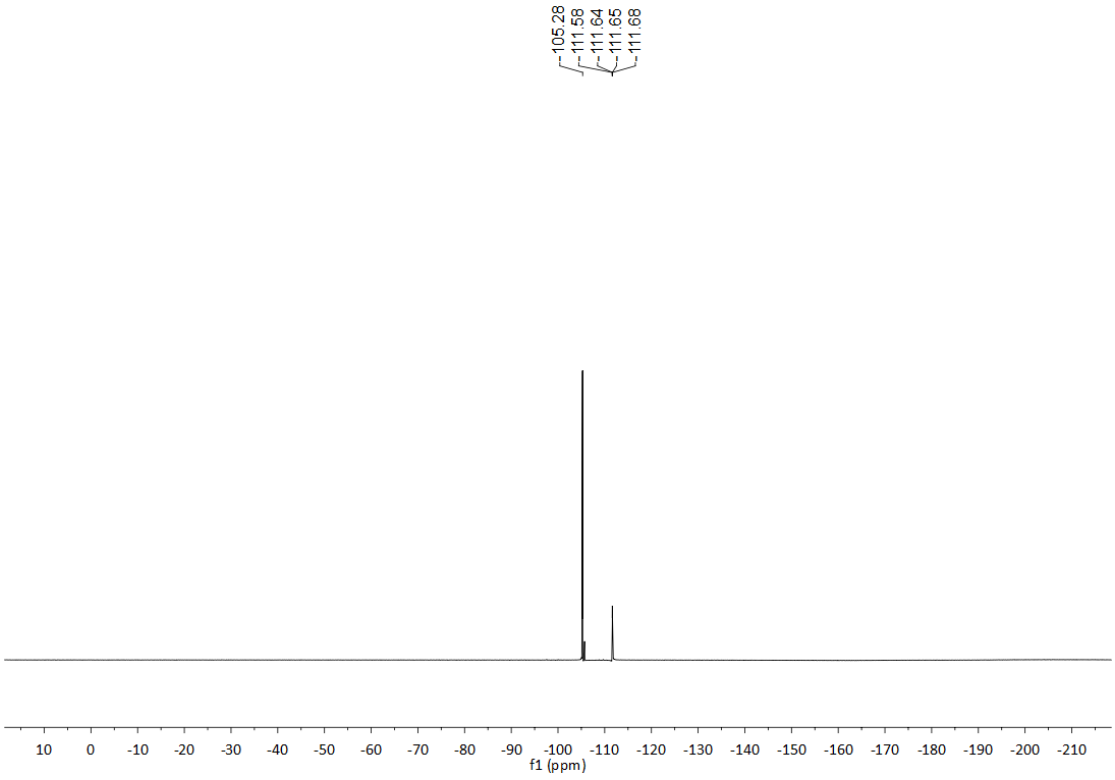


3-(1,1-difluoro-2-(4-(methylthio)phenyl)-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1*H*)-one (3af)

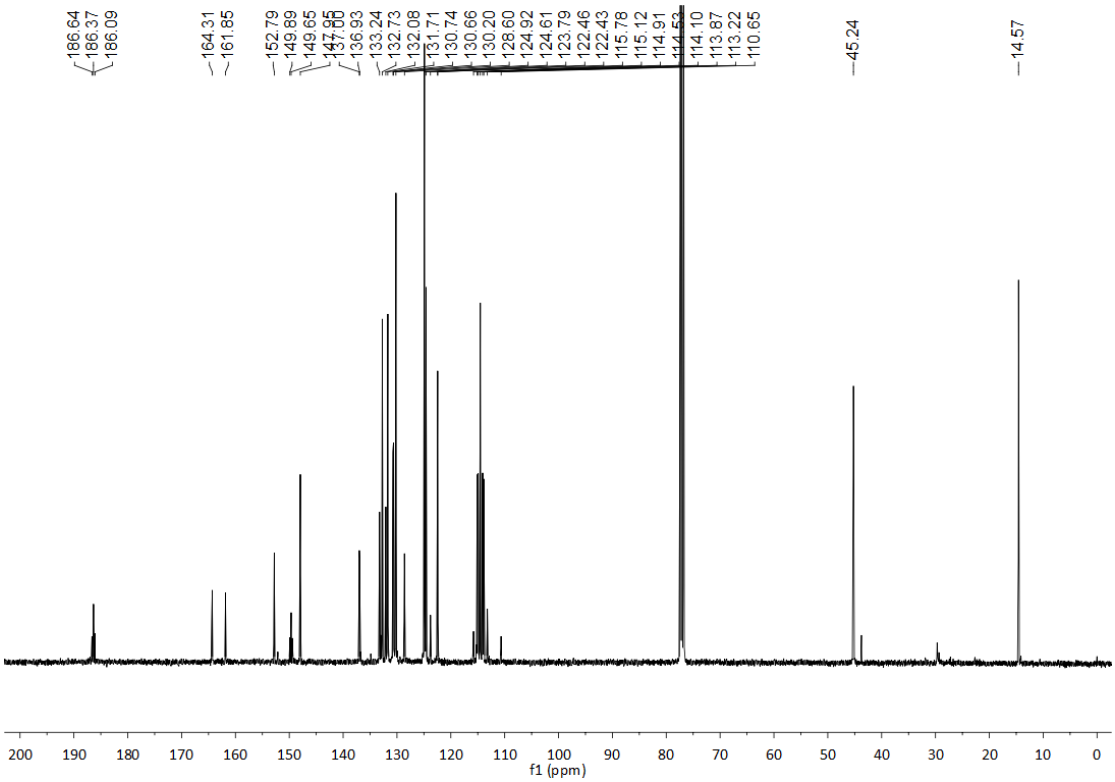
^{1}H NMR (400 MHz, $CDCl_3$):



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

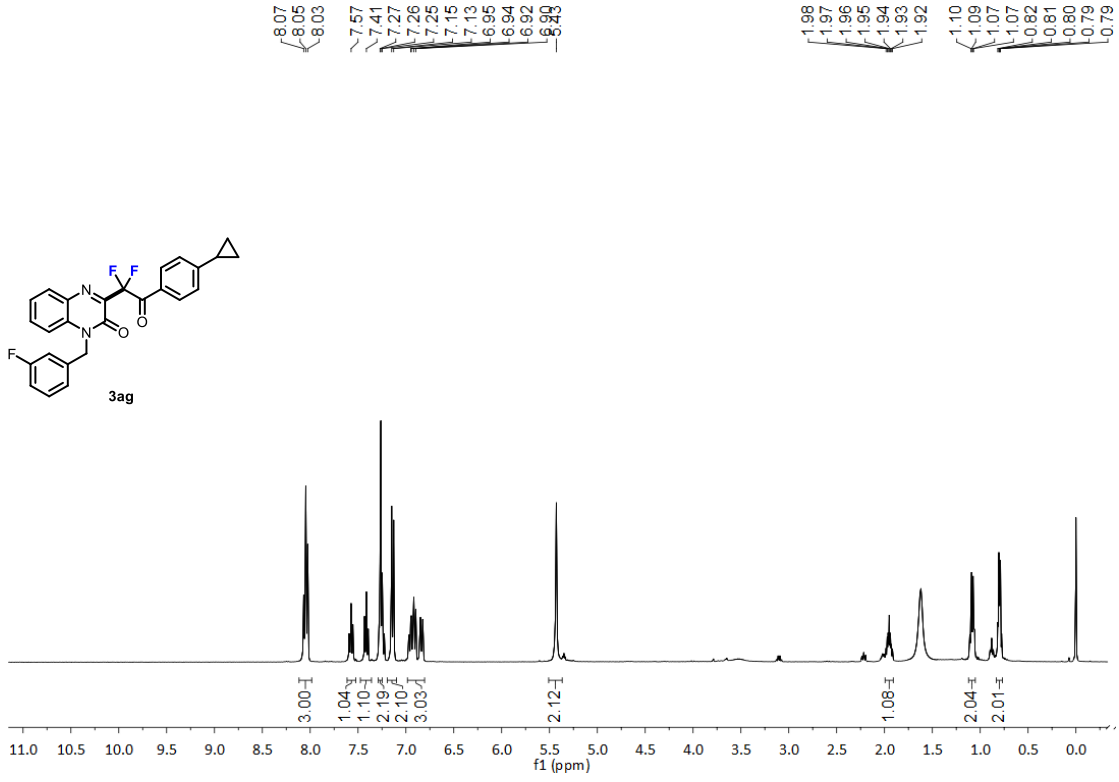


^{13}C NMR (100 MHz, $CDCl_3$):

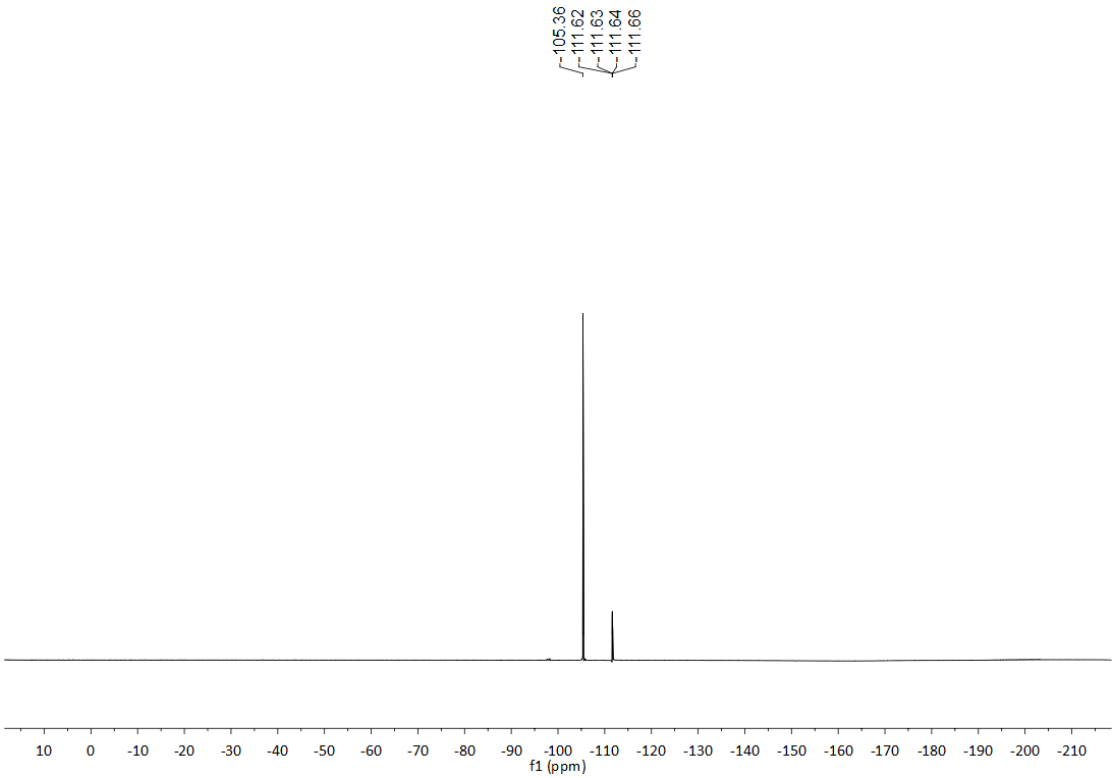


3-(2-(4-cyclopropylphenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1*H*)-one (3ag)

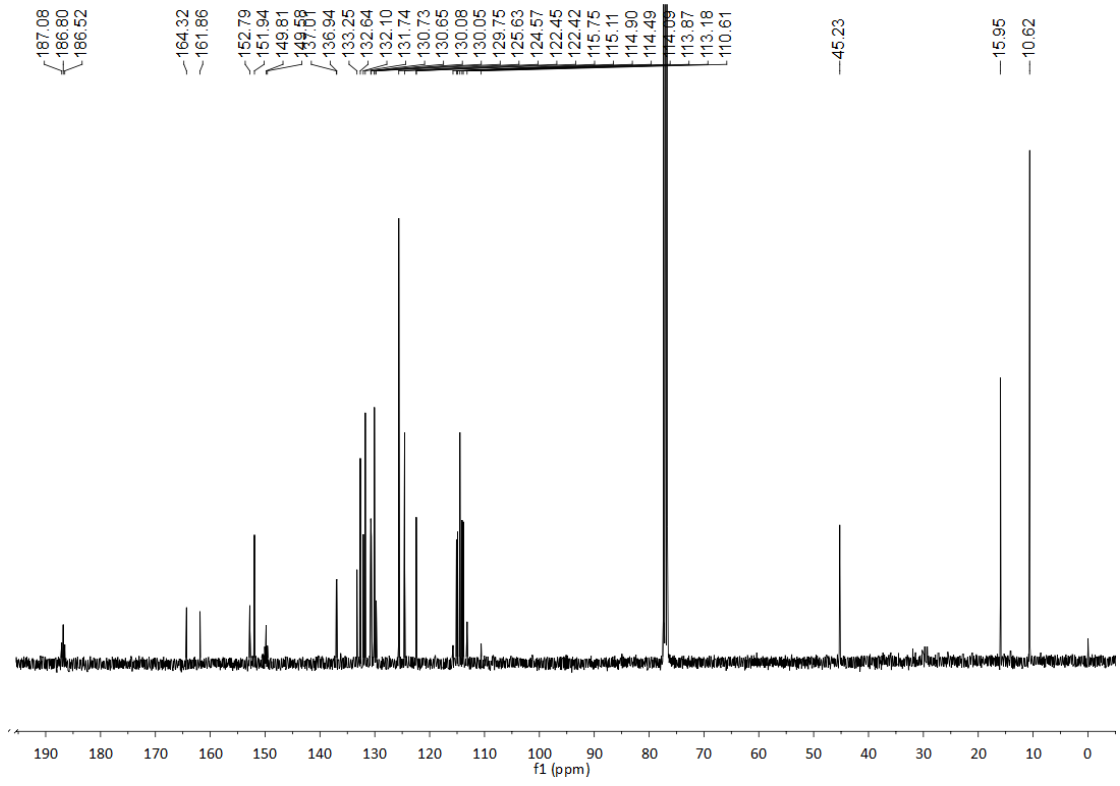
^{1}H NMR (400 MHz, $CDCl_3$):



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

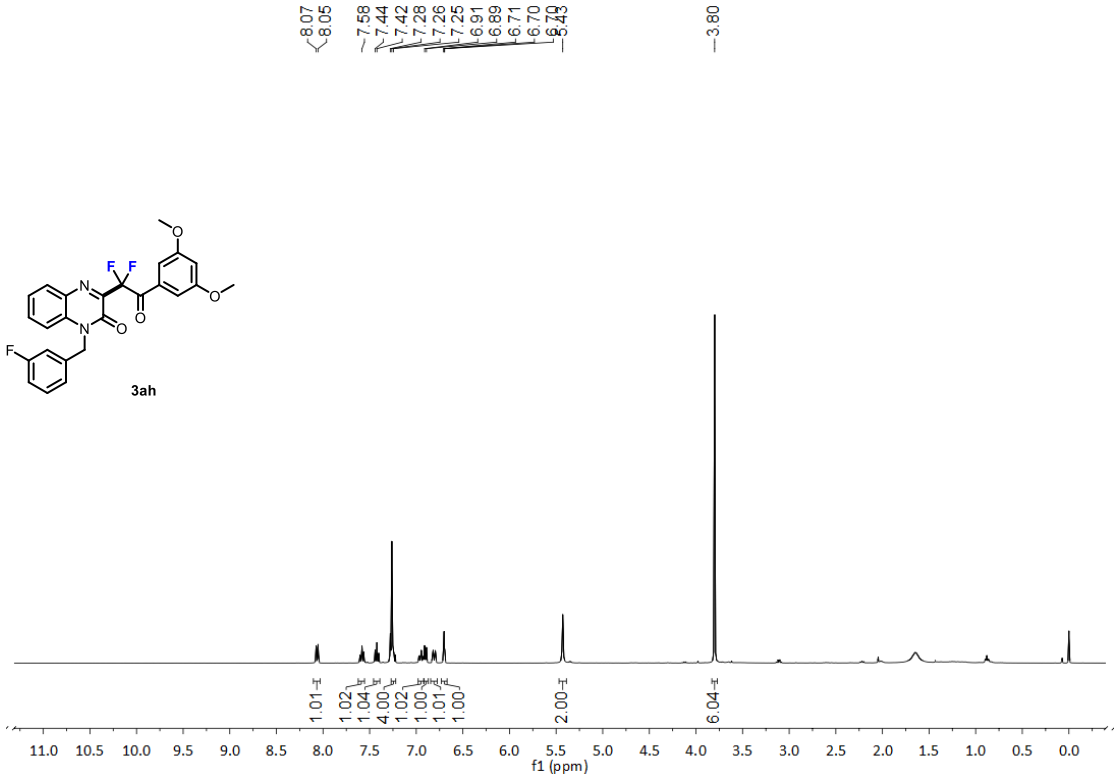


^{13}C NMR (100 MHz, $CDCl_3$):

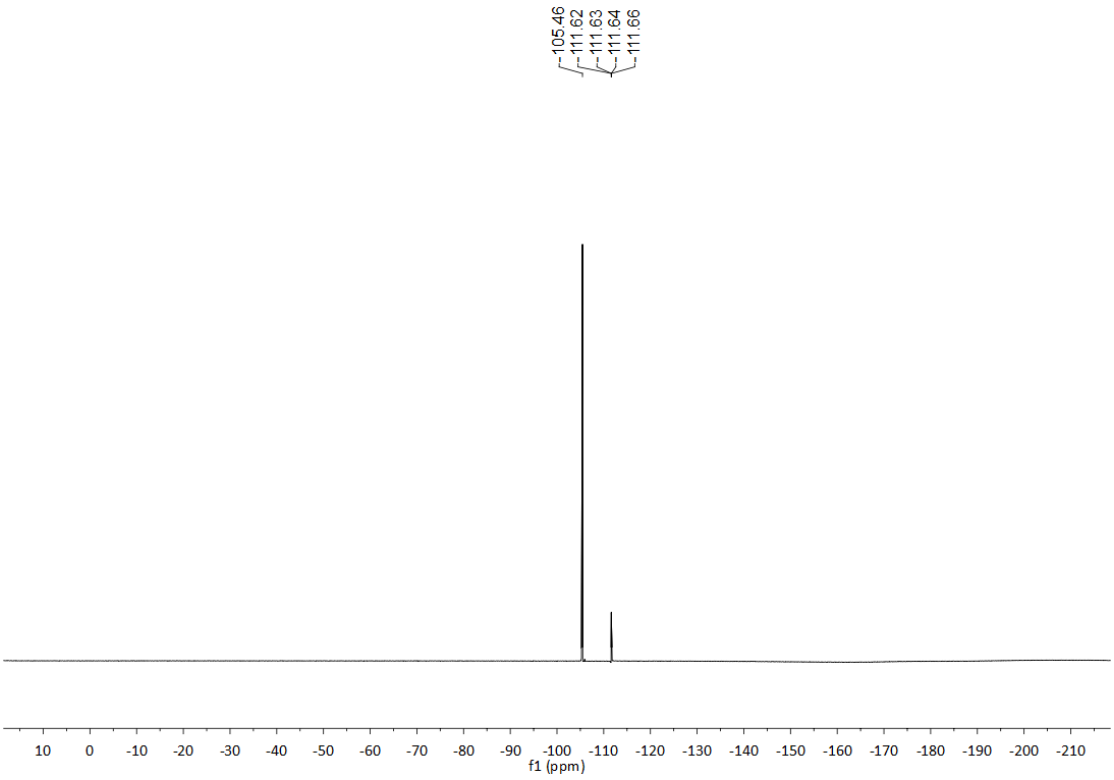


3-(2-(3,5-dimethoxyphenyl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1*H*)-one (3ah)

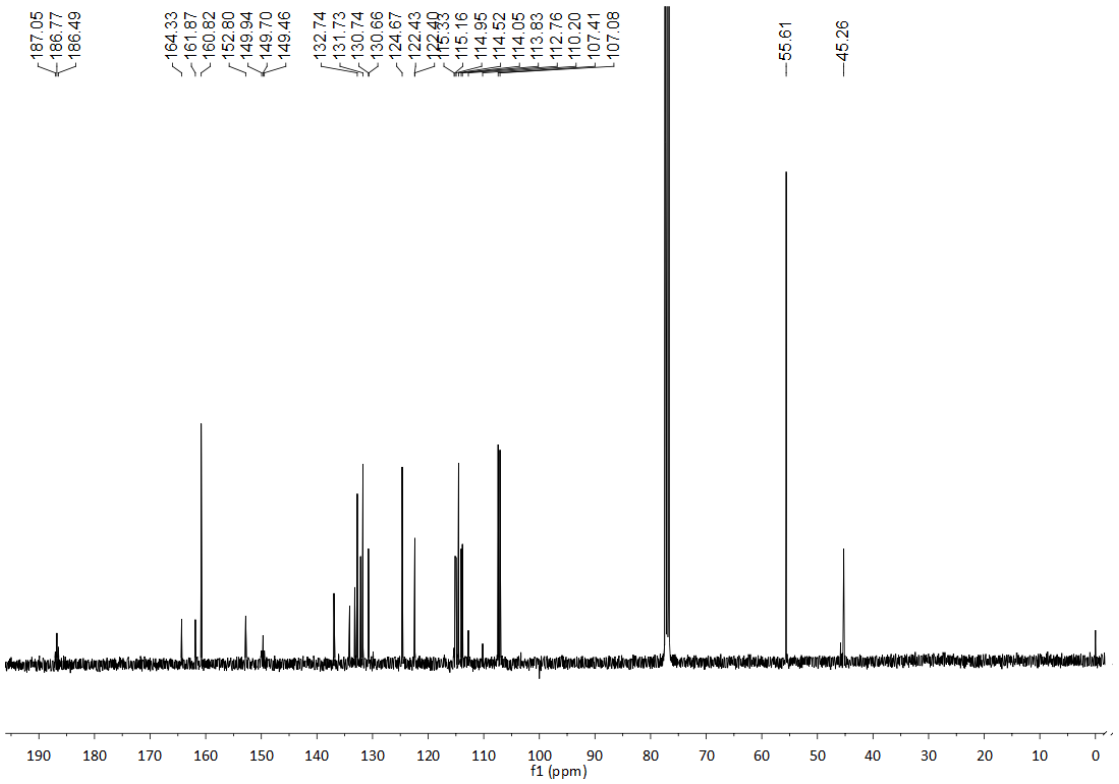
^{1}H NMR (400 MHz, $CDCl_3$):



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

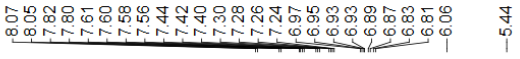


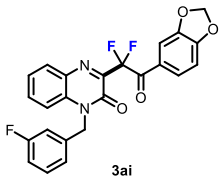
^{13}C NMR (100 MHz, $CDCl_3$):



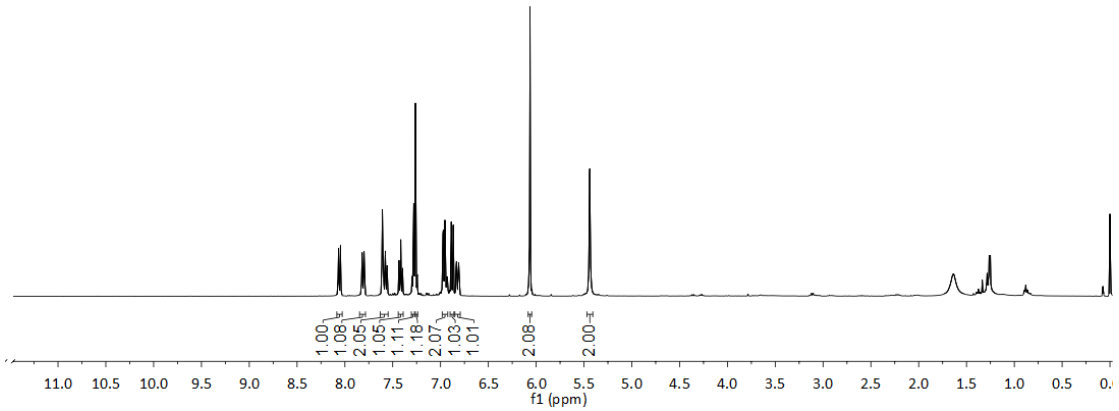
3-(2-(benzo[*d*][1,3]dioxol-5-yl)-1,1-difluoro-2-oxoethyl)-1-(3-fluorobenzyl) quinoxalin-2(1*H*)-one (3ai)

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

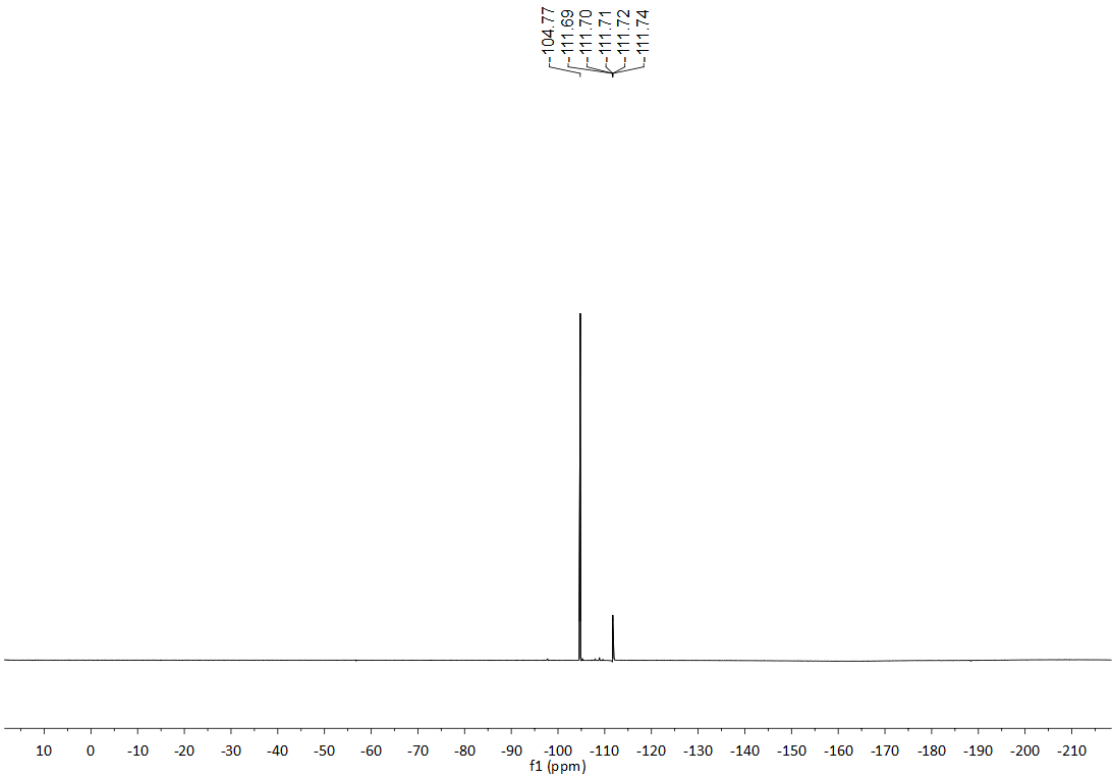




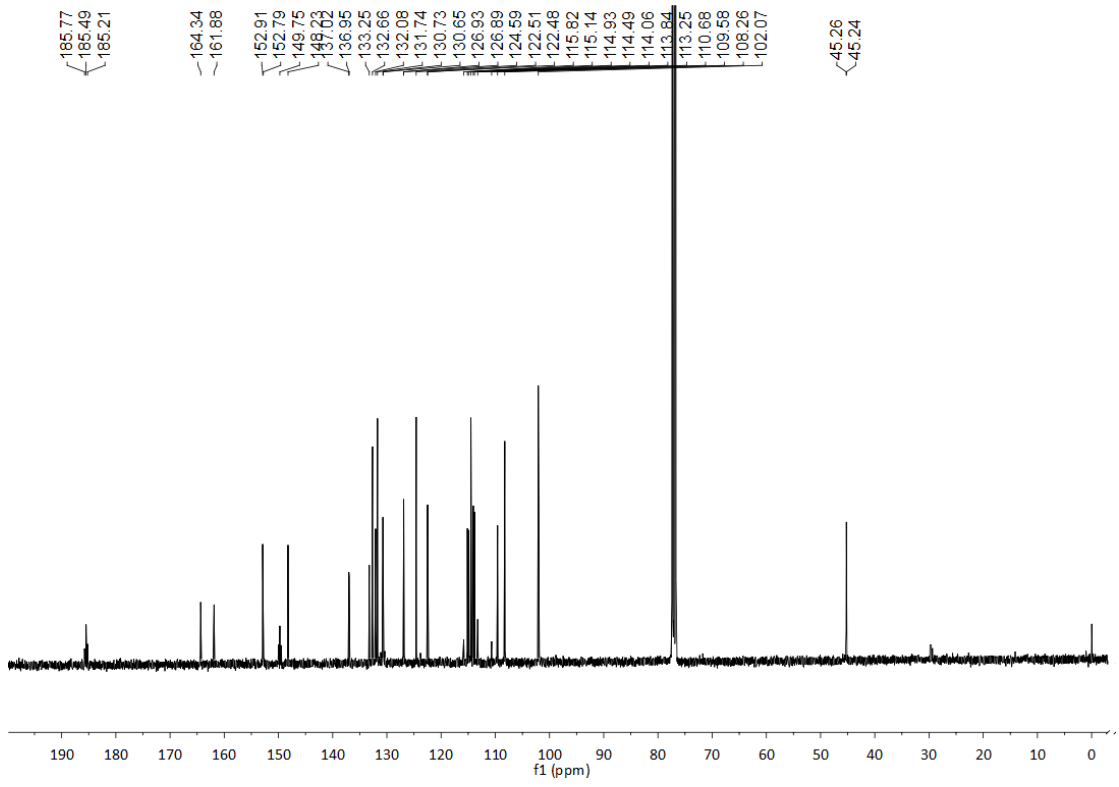
3ai



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

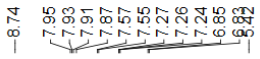


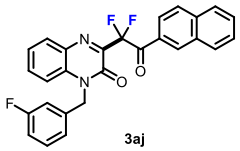
^{13}C NMR (100 MHz, $CDCl_3$):



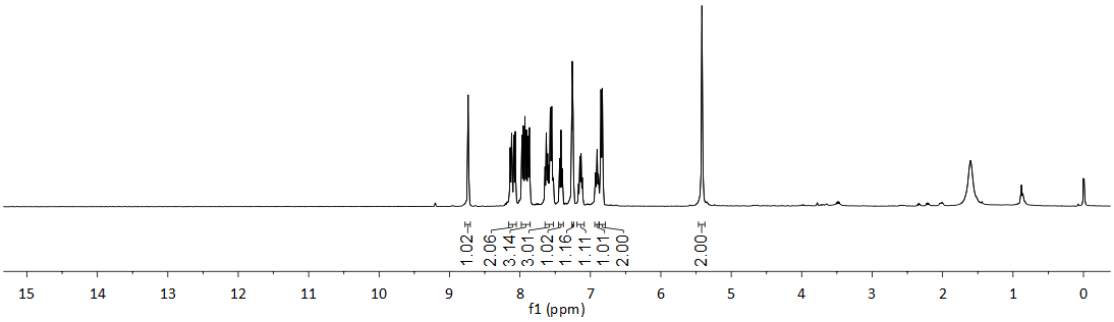
3-(1,1-difluoro-2-(naphthalen-2-yl)-2-oxoethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3aj)

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

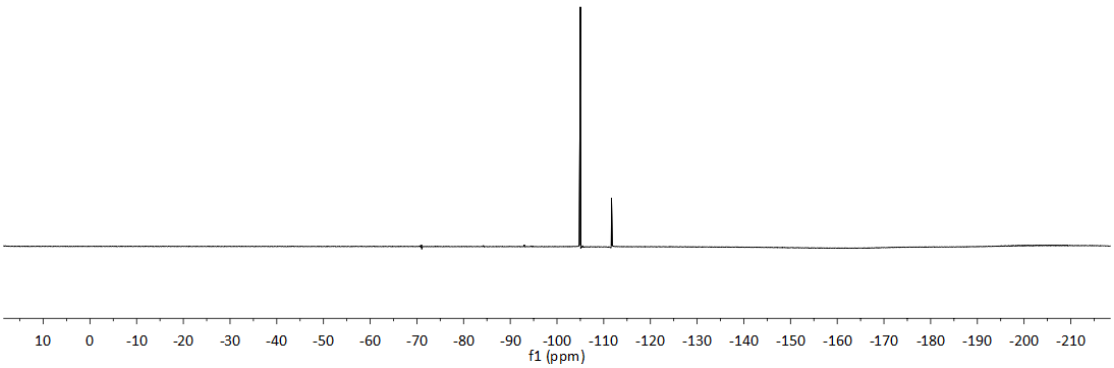




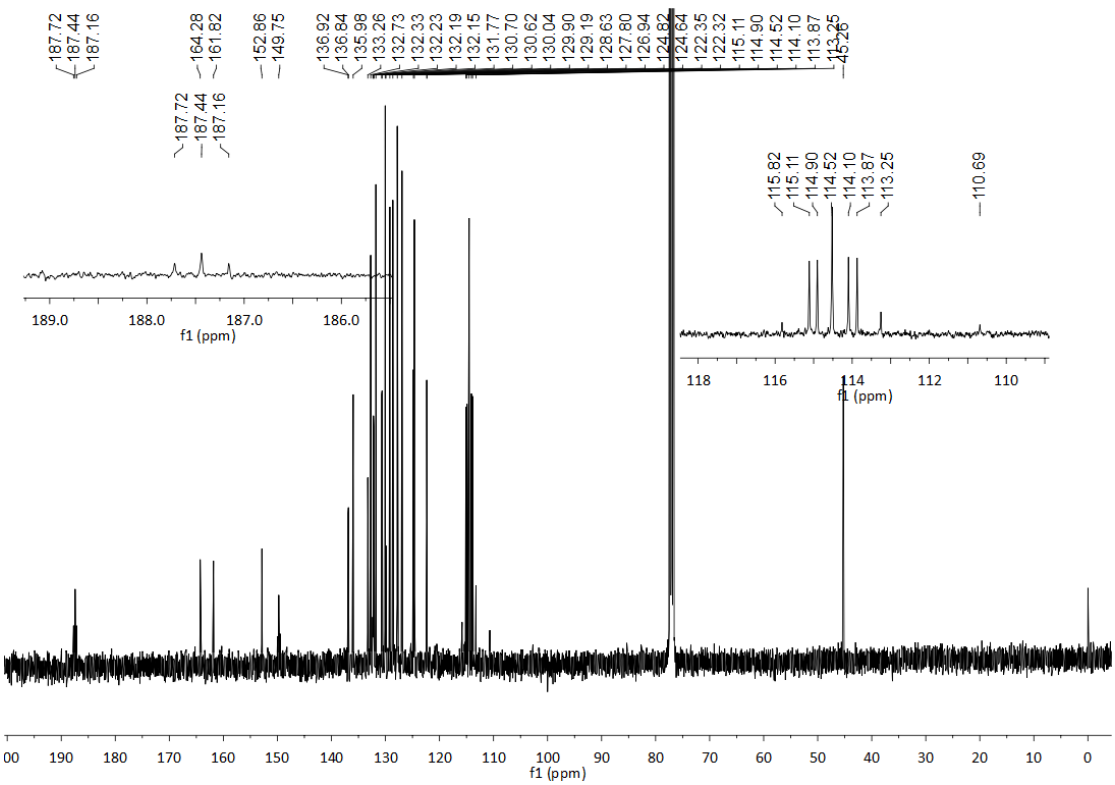
3aj



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

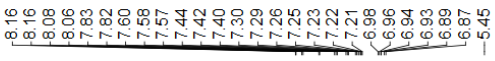


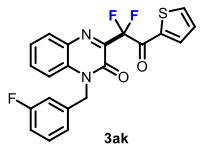
^{13}C NMR (100 MHz, $CDCl_3$):



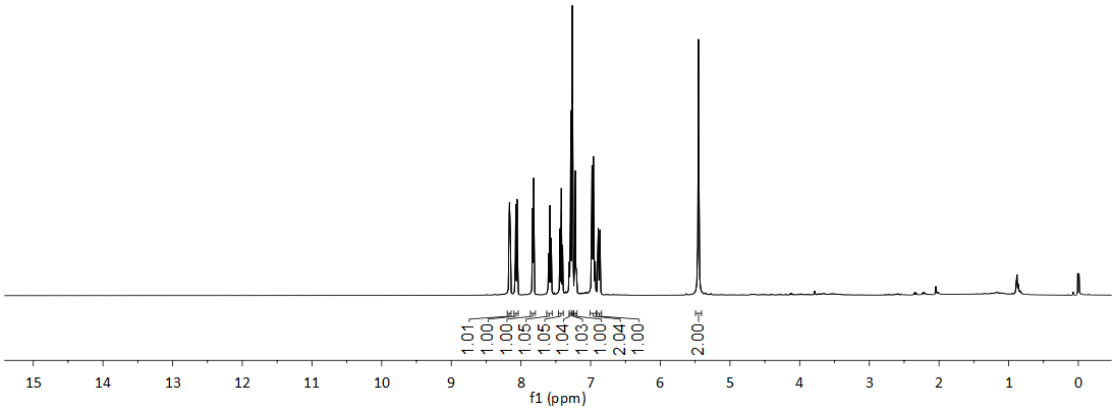
3-(1,1-difluoro-2-oxo-2-(thiophen-2-yl)ethyl)-1-(3-fluorobenzyl)quinoxalin-2(1*H*)-one (3ak)

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

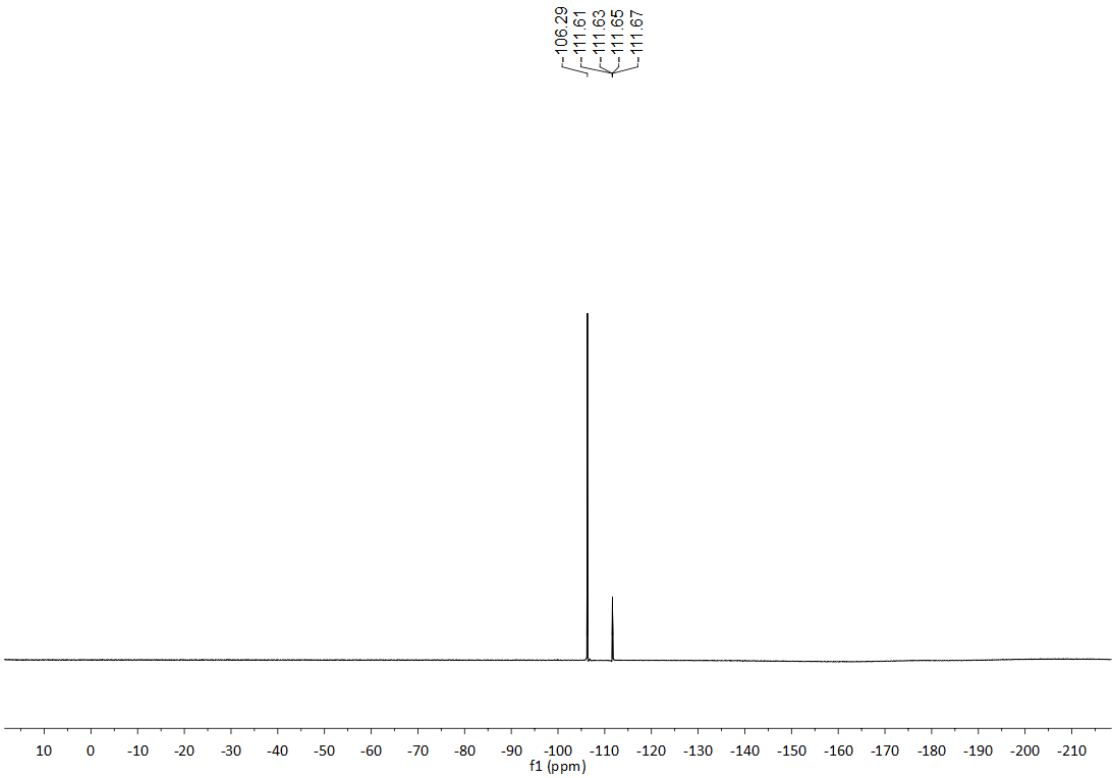




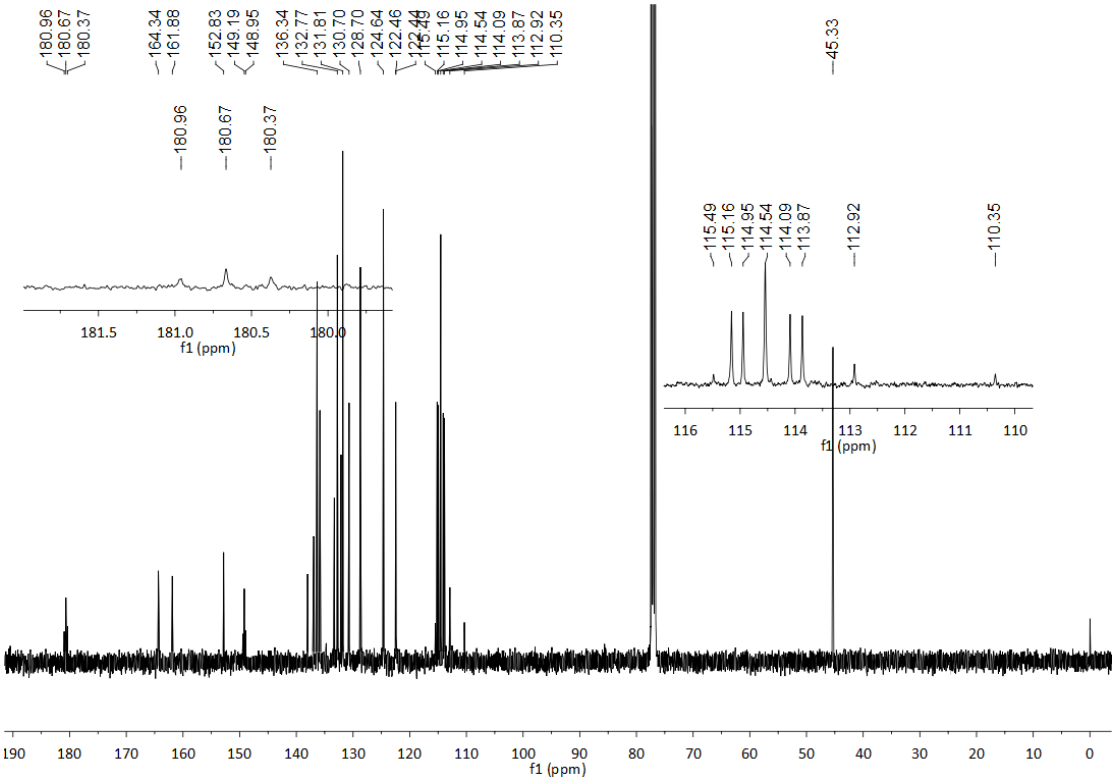
3ak



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

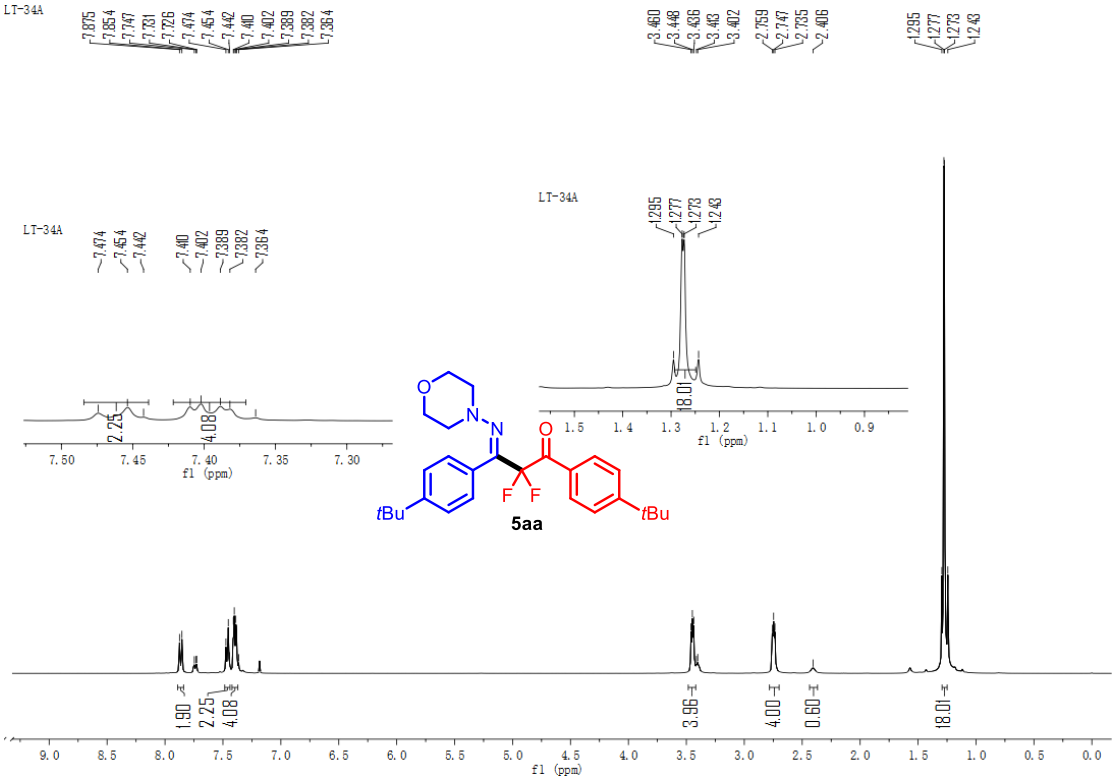


^{13}C NMR (100 MHz, $CDCl_3$):

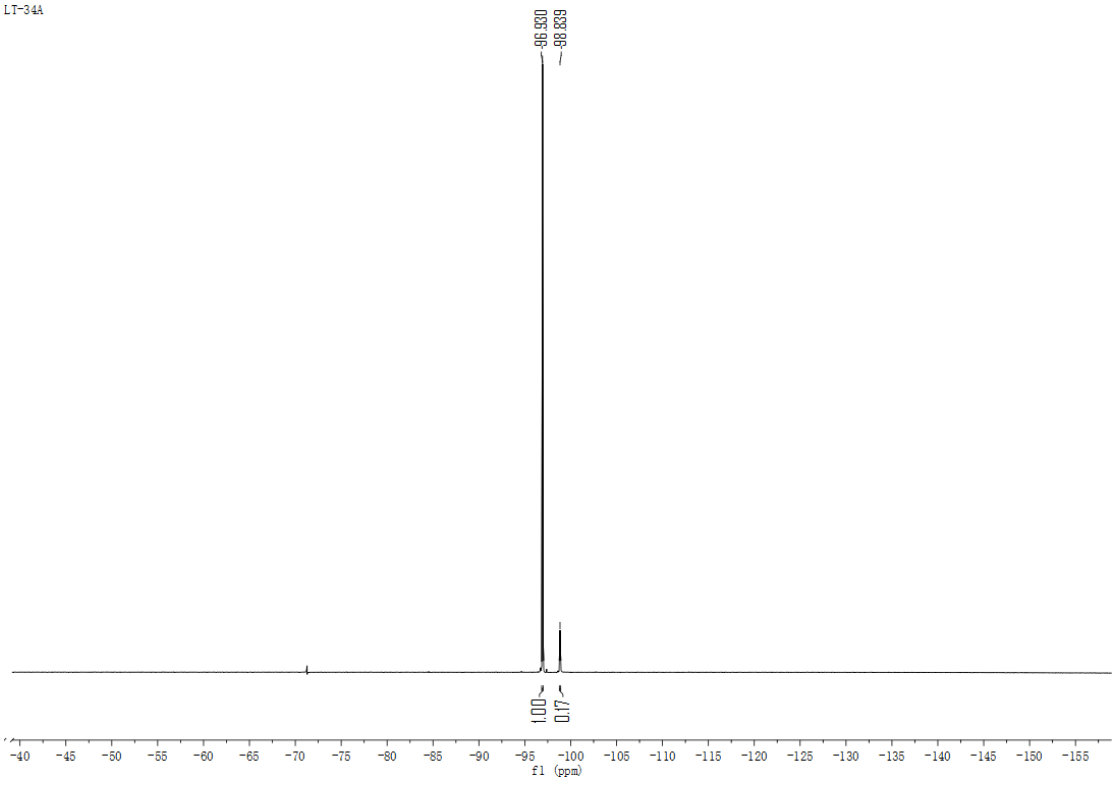


(E)-1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5aa)

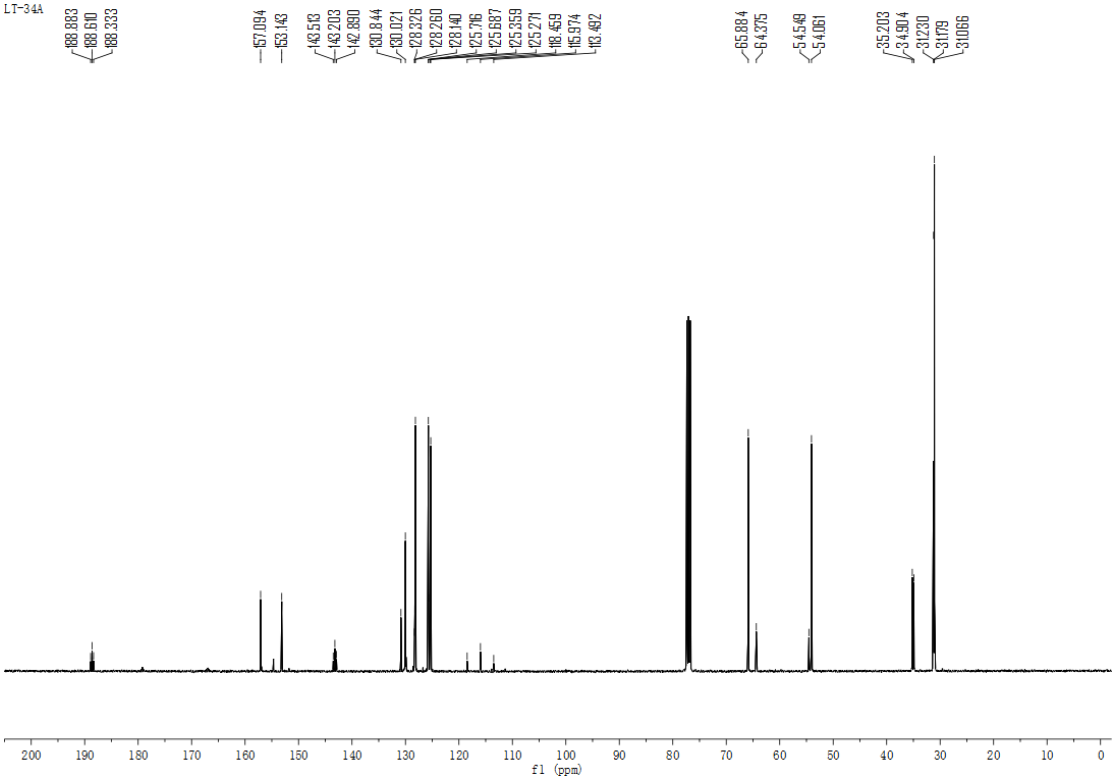
^{1}H NMR (400 MHz, $CDCl_3$):



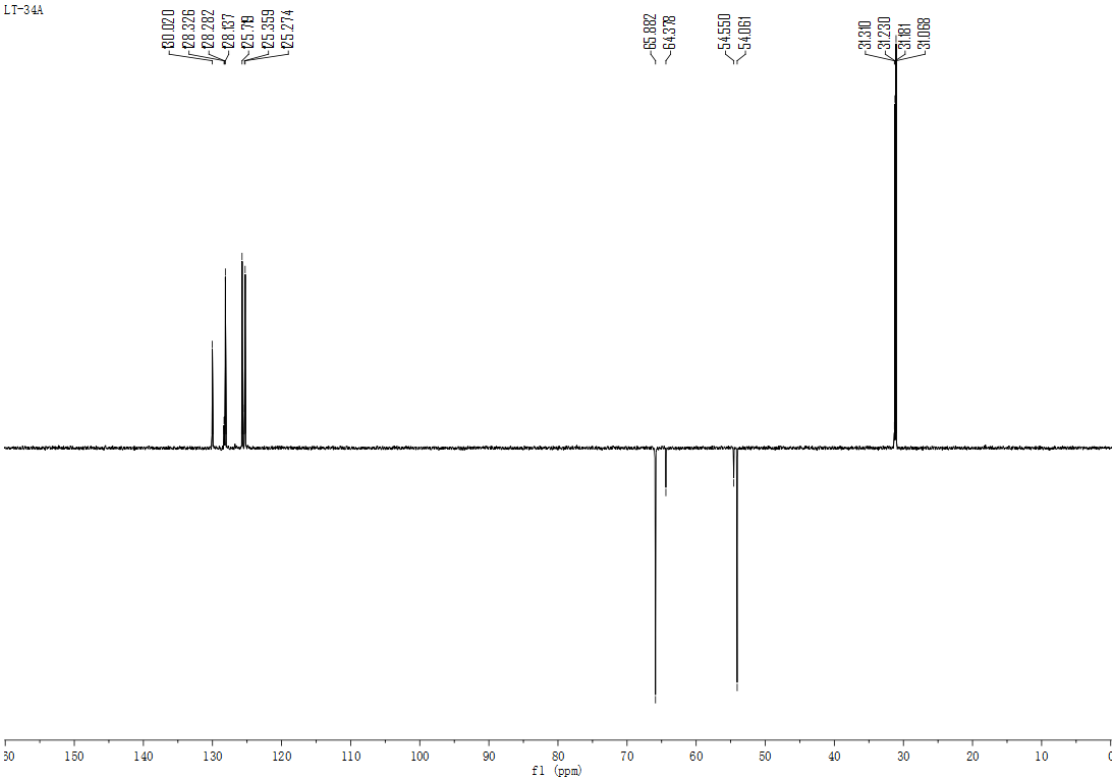
^{19}F NMR (376 MHz, $CDCl_3$):



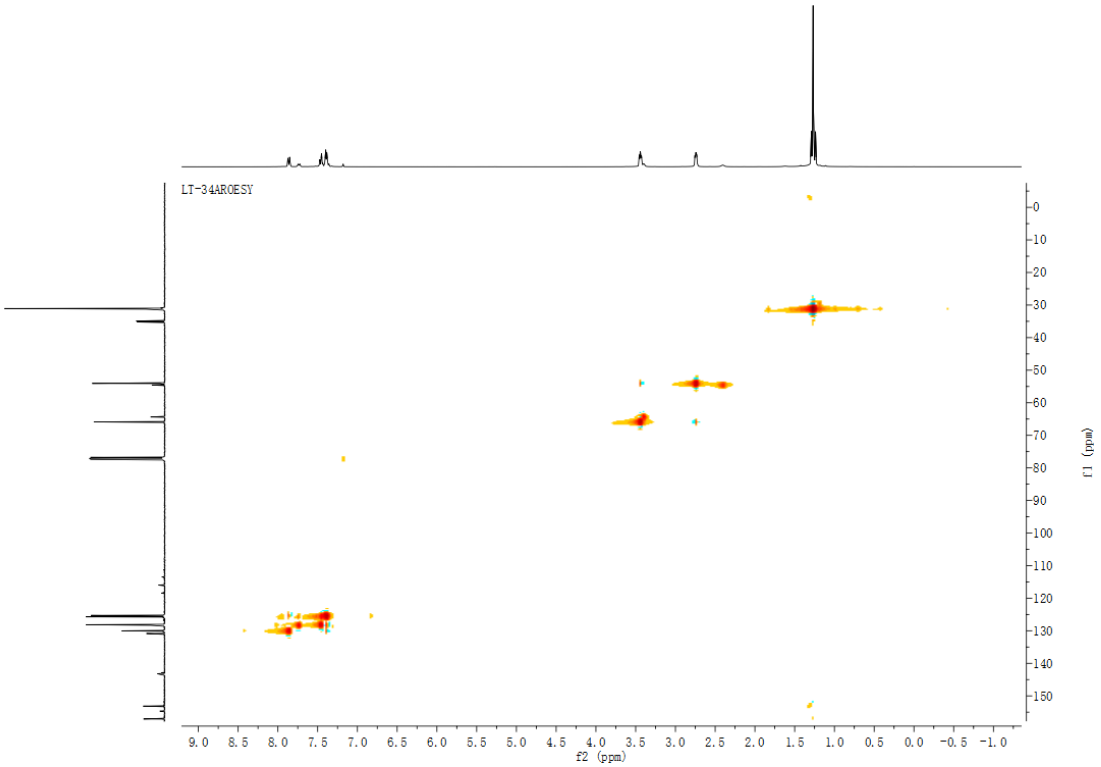
^{13}C NMR (100 MHz, $CDCl_3$):



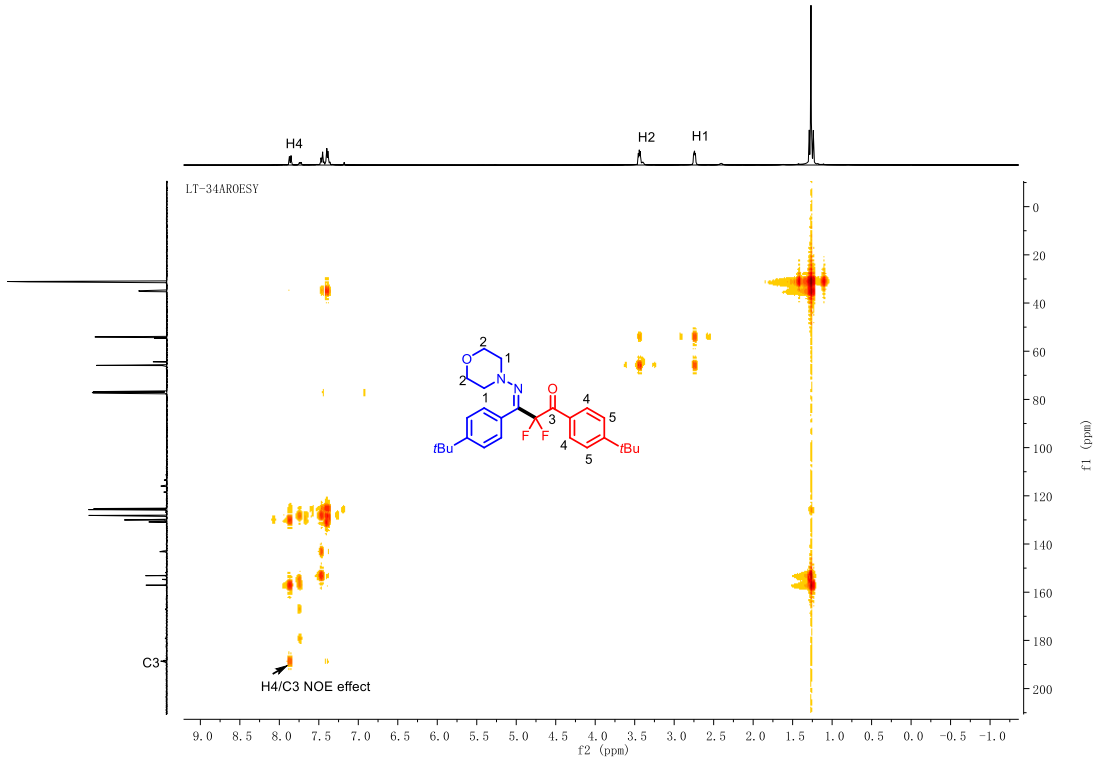
DEPT



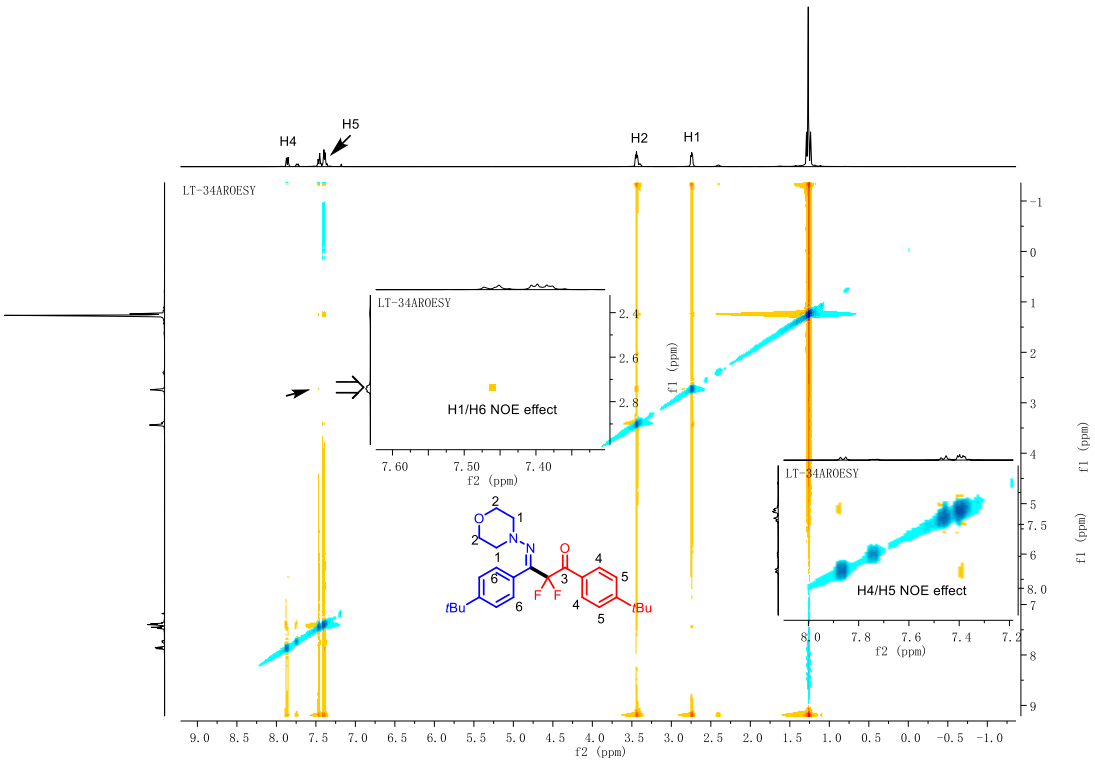
HSQC



HMBC

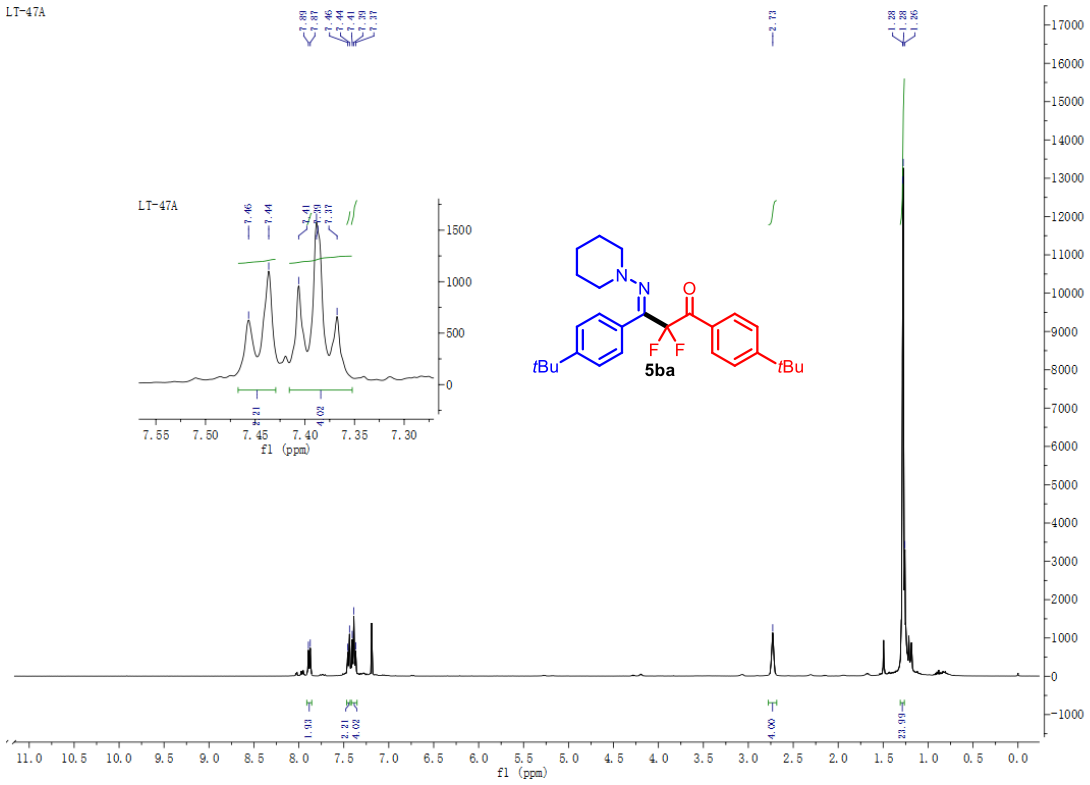


ROESY

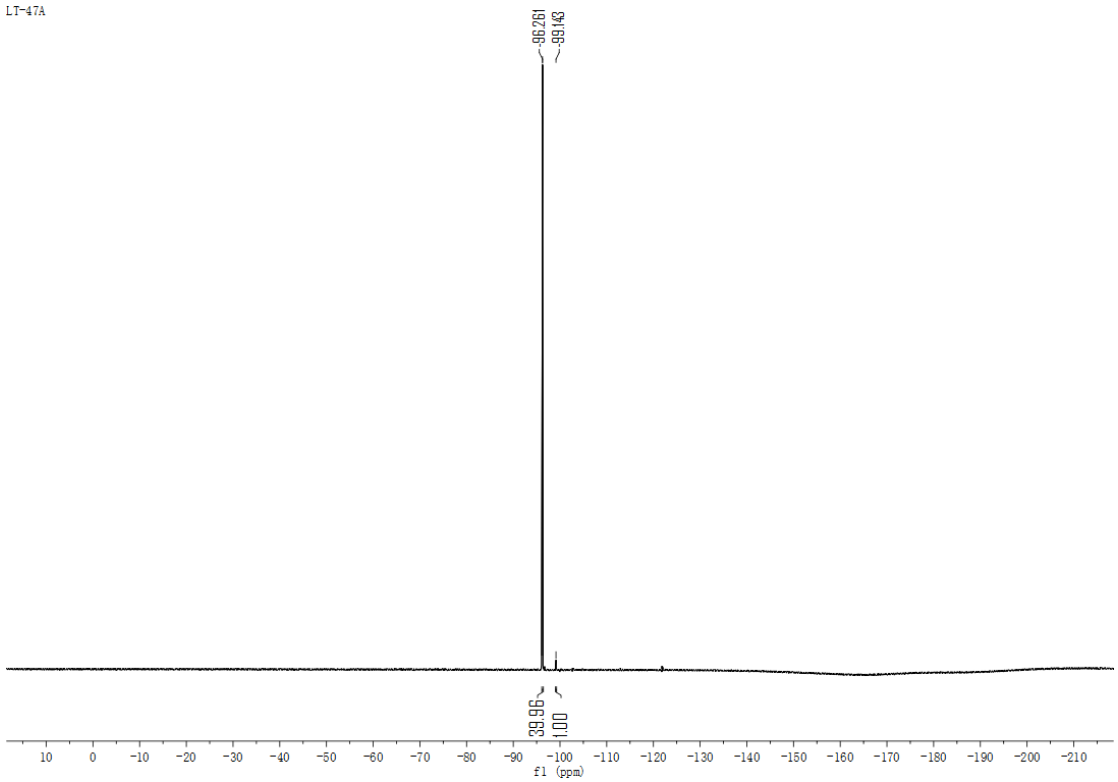


(E)-1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-(piperidin-1-ylimino)propan-1-one (5ba)

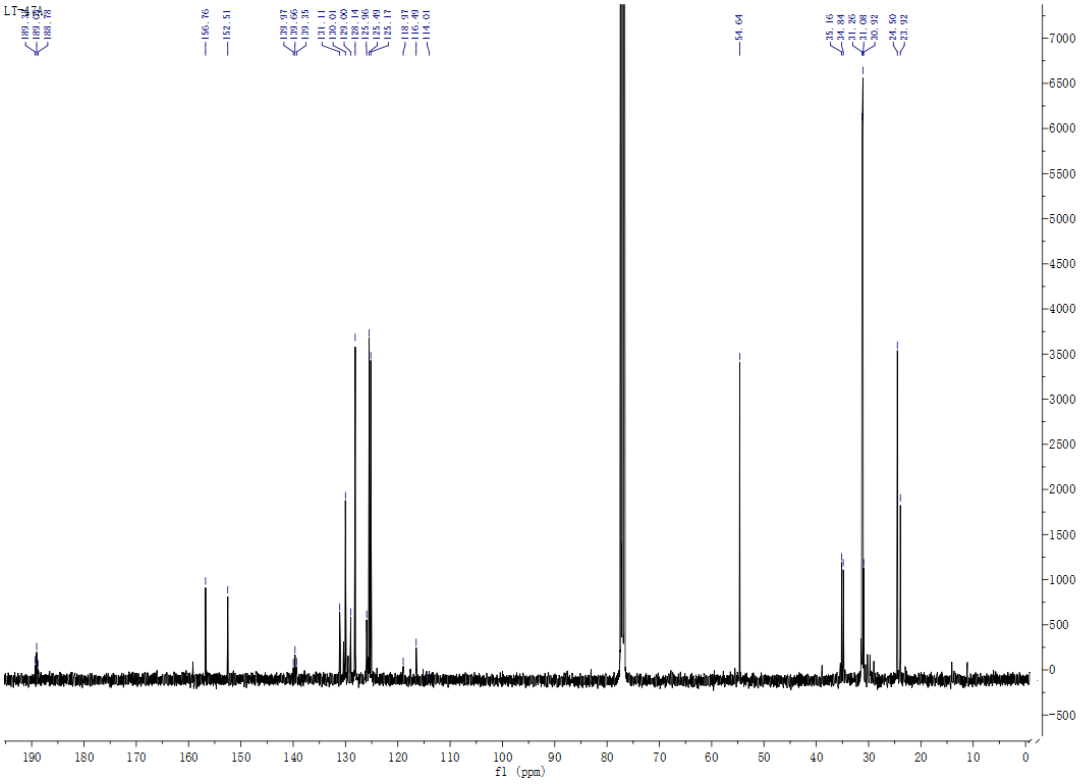
^{1}H NMR (400 MHz, $CDCl_3$):



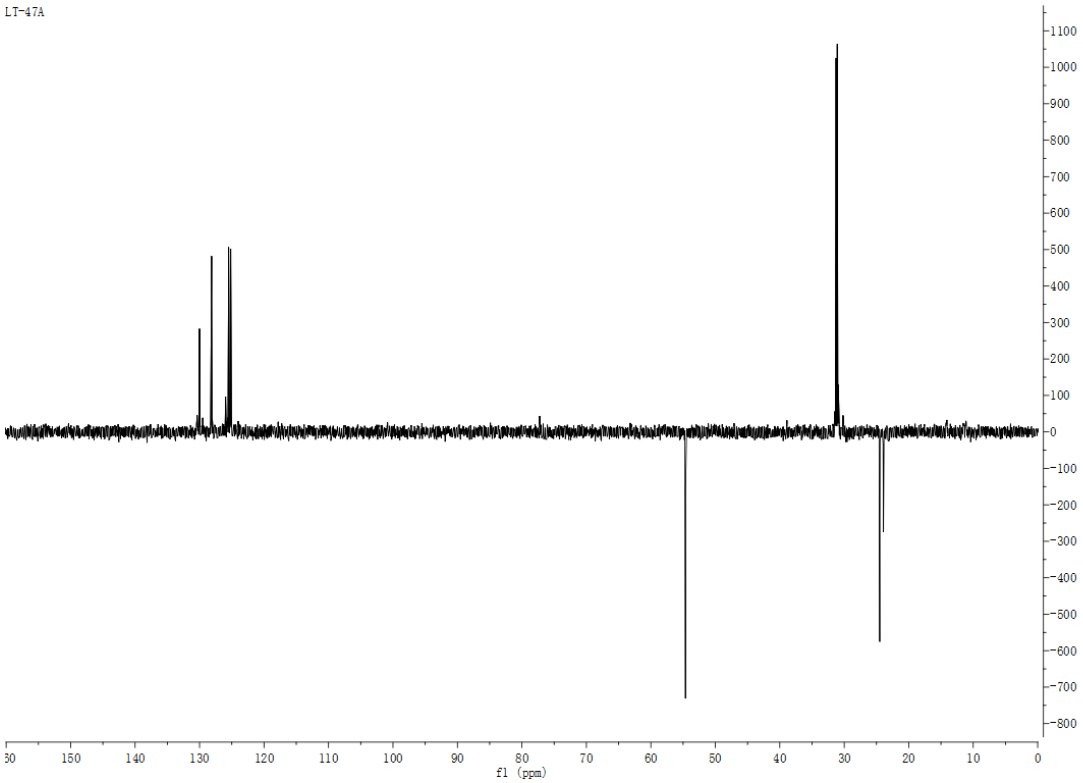
^{19}F NMR (376 MHz, $CDCl_3$):



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

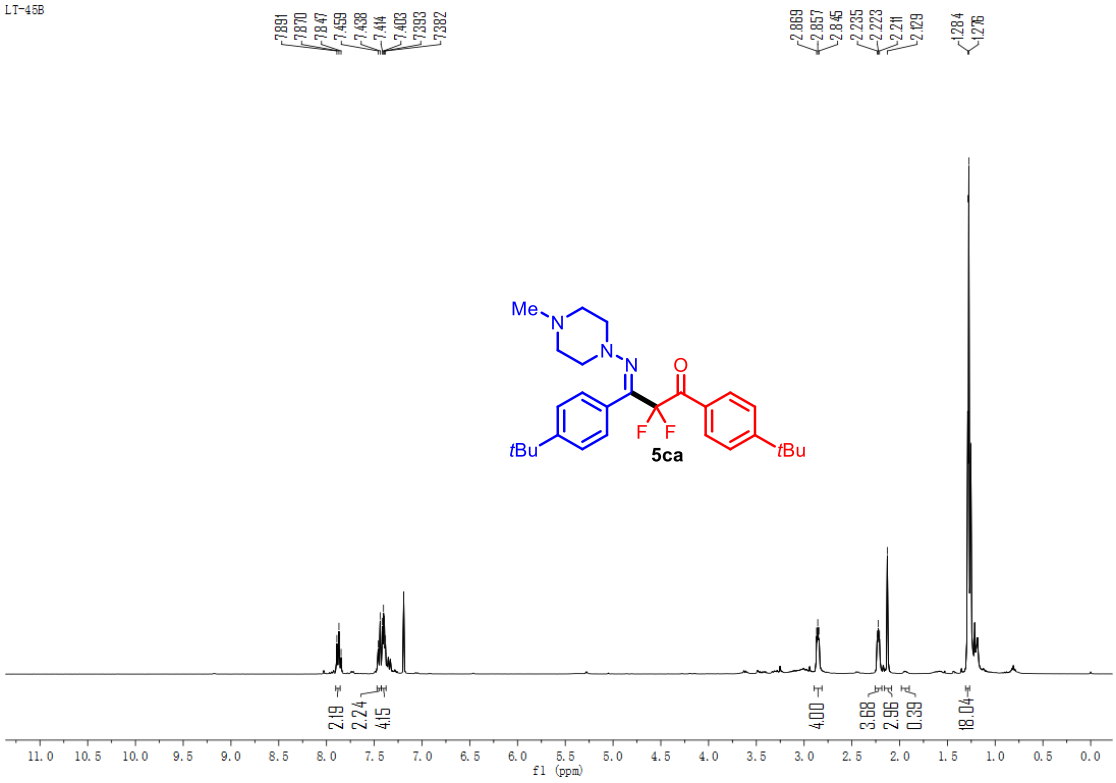


DEPT

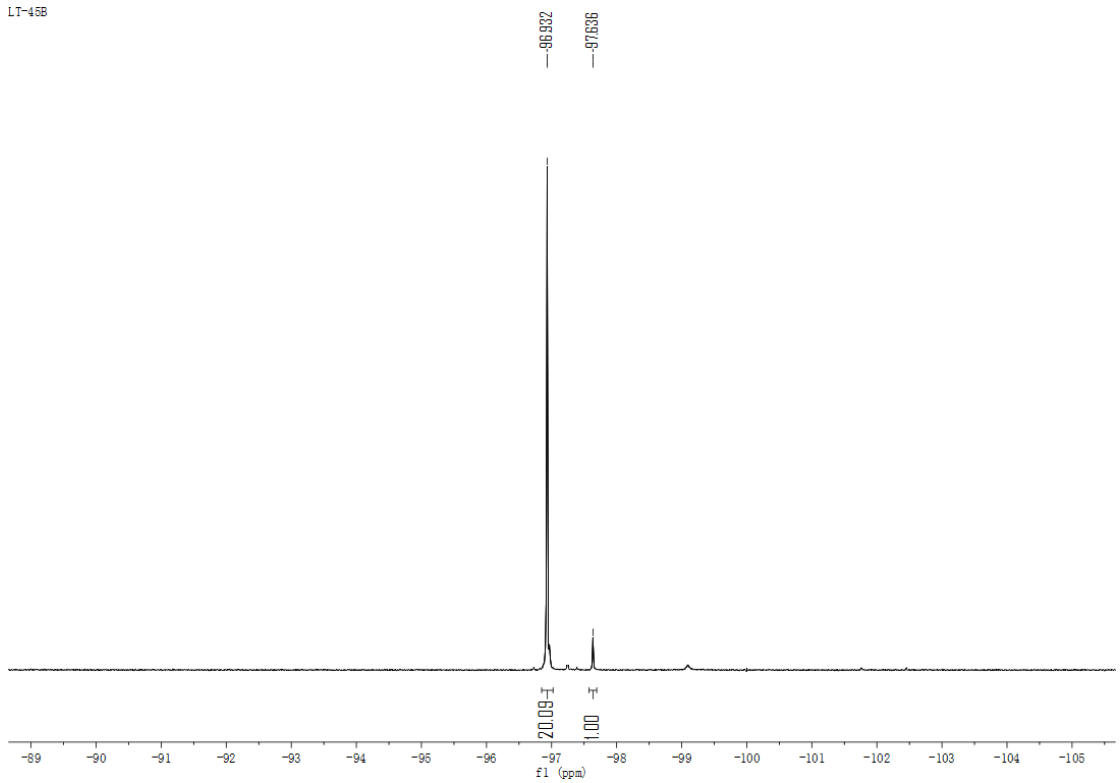


(E)-1,3-bis(4-(tert-butyl)phenyl)-2,2-difluoro-3-((4-methylpiperazin-1-yl)imino)propan-1-one (5ca)

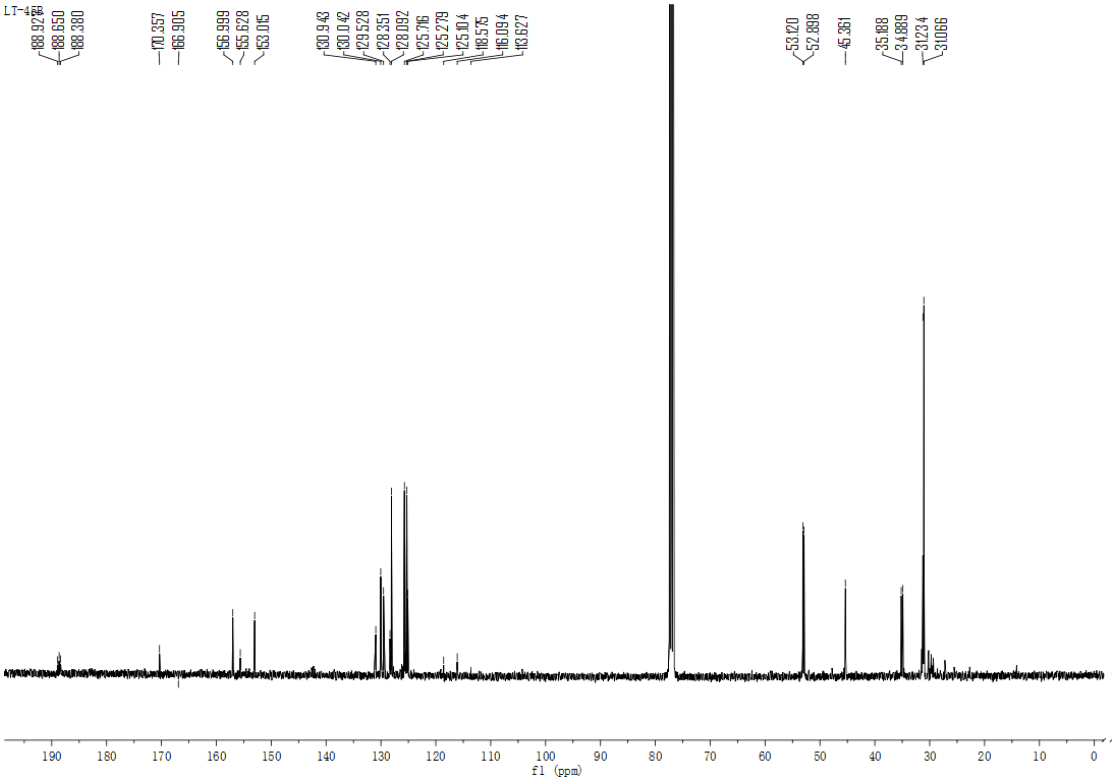
^{1}H NMR (400 MHz, $CDCl_3$):



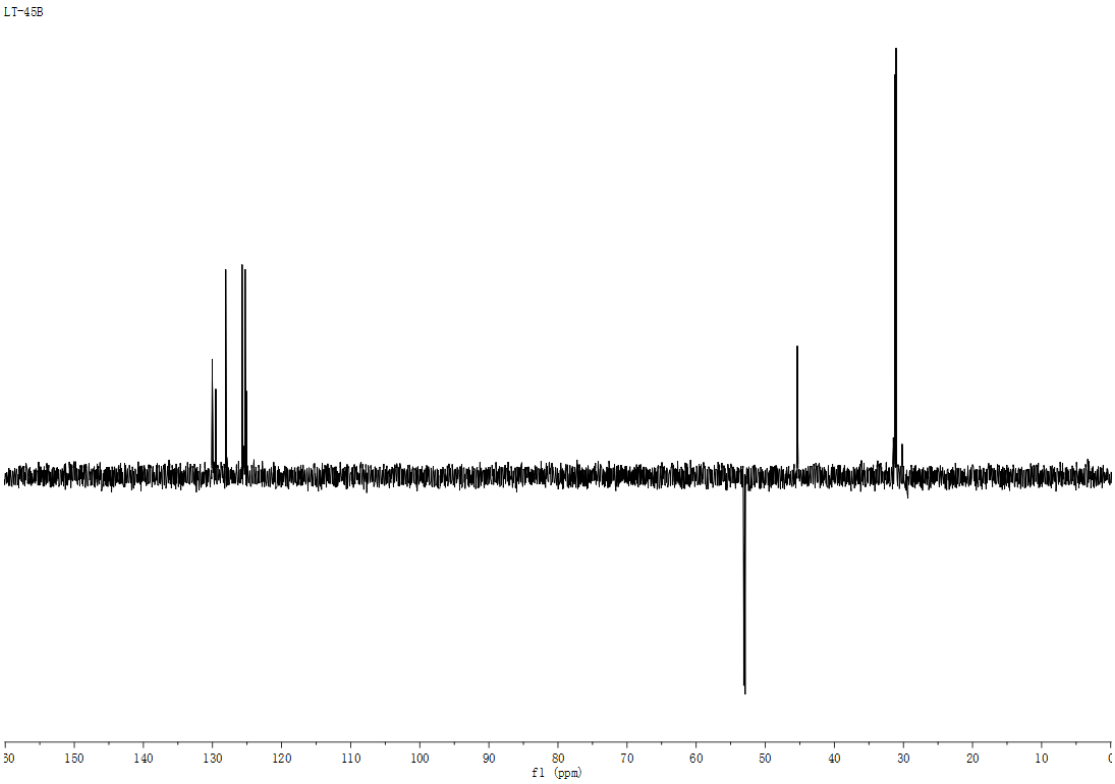
^{19}F NMR (376 MHz, $CDCl_3$):



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

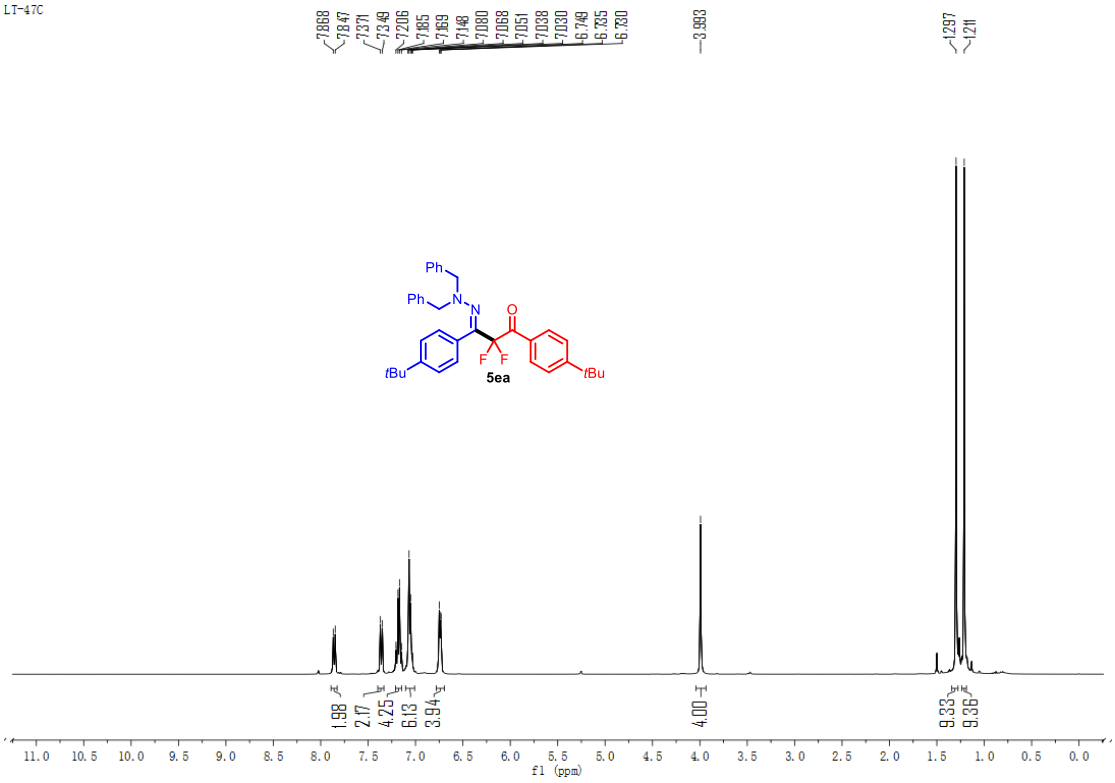


DEPT

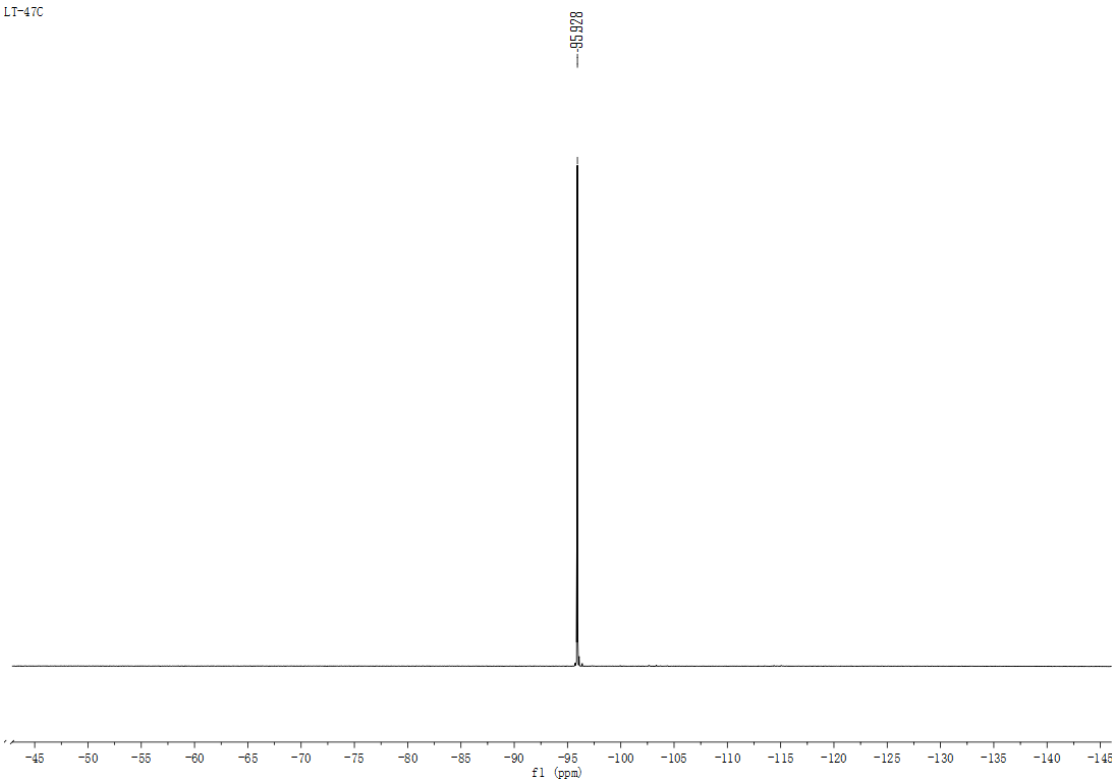


(E)-1,3-bis(4-(tert-butyl)phenyl)-3-(2,2-dibenzylhydrazono)-2,2-difluoropropan-1-one (5ea)

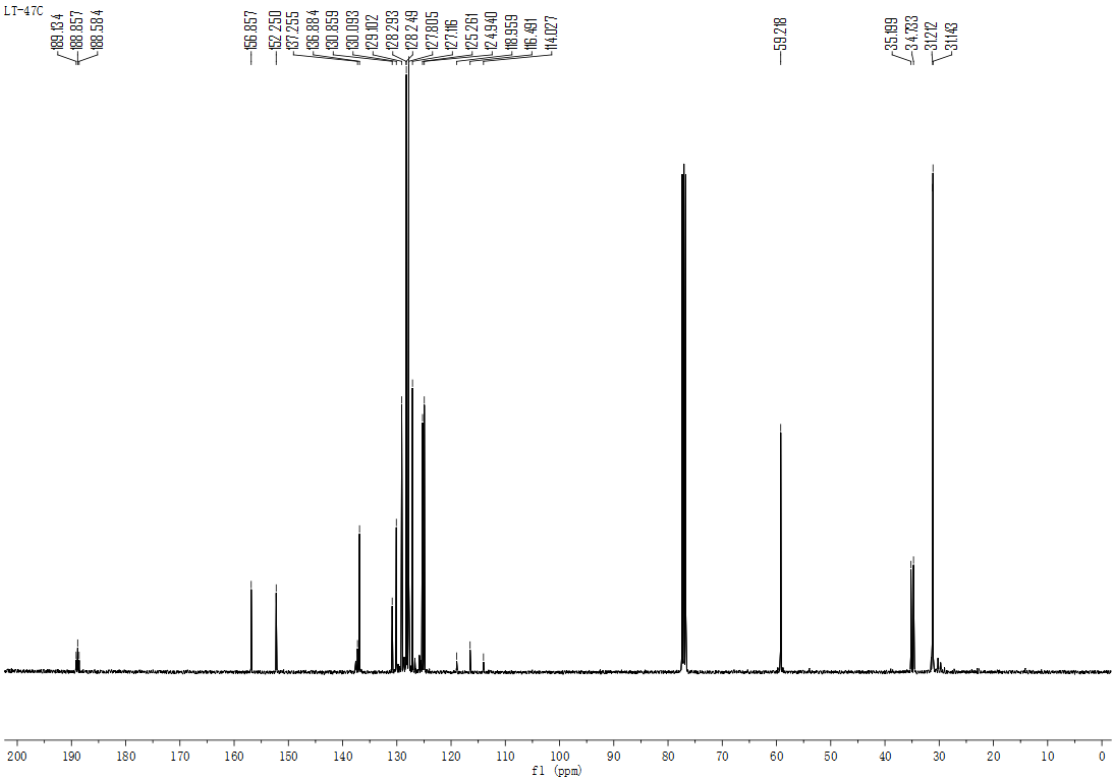
^{1}H NMR (400 MHz, $CDCl_3$):



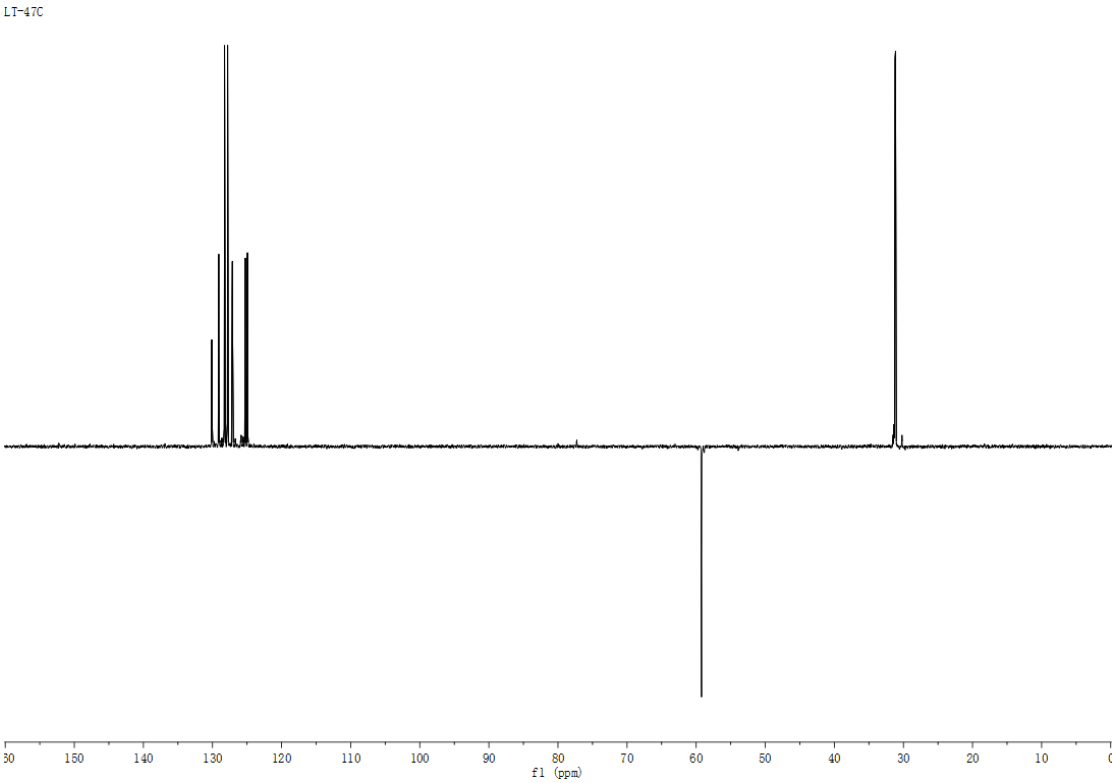
^{19}F NMR (376 MHz, $CDCl_3$):



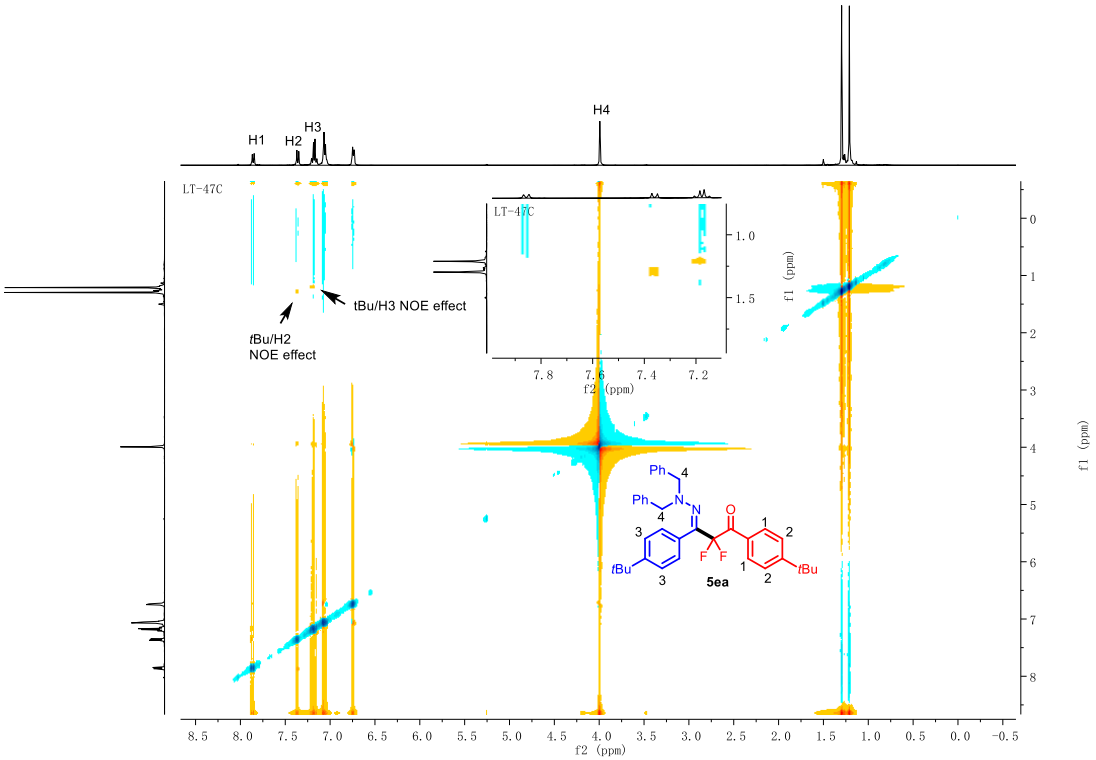
^{13}C NMR (100 MHz, $CDCl_3$):

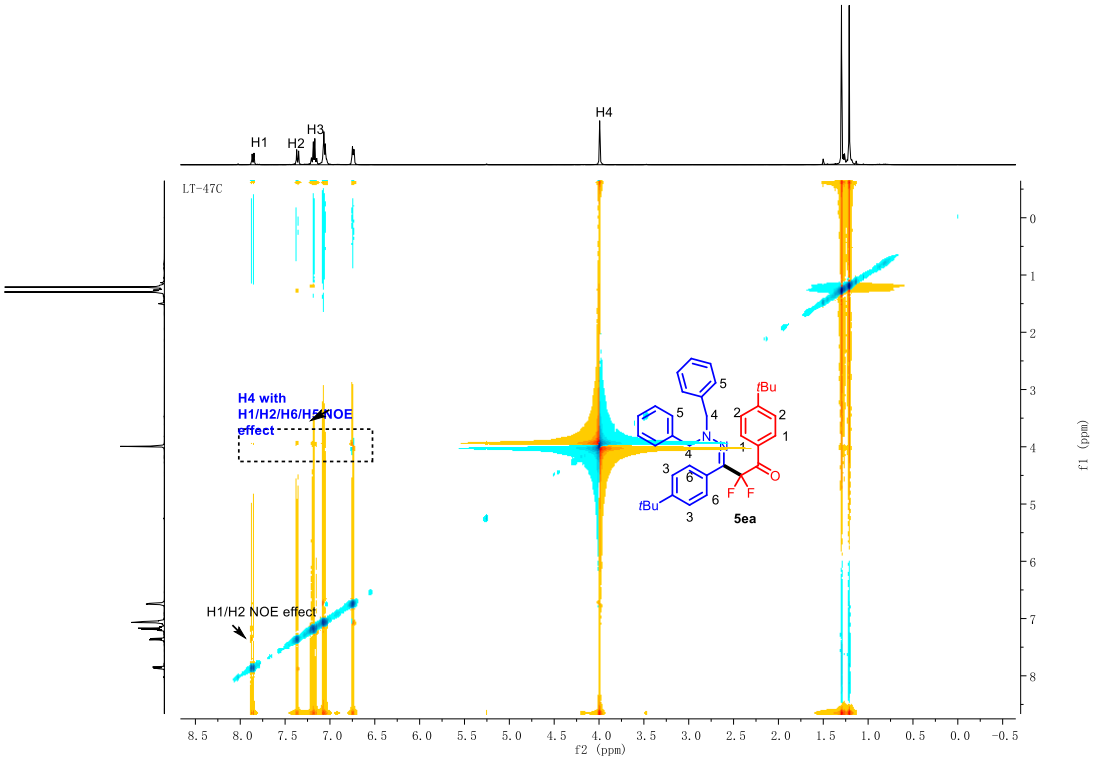


DEPT



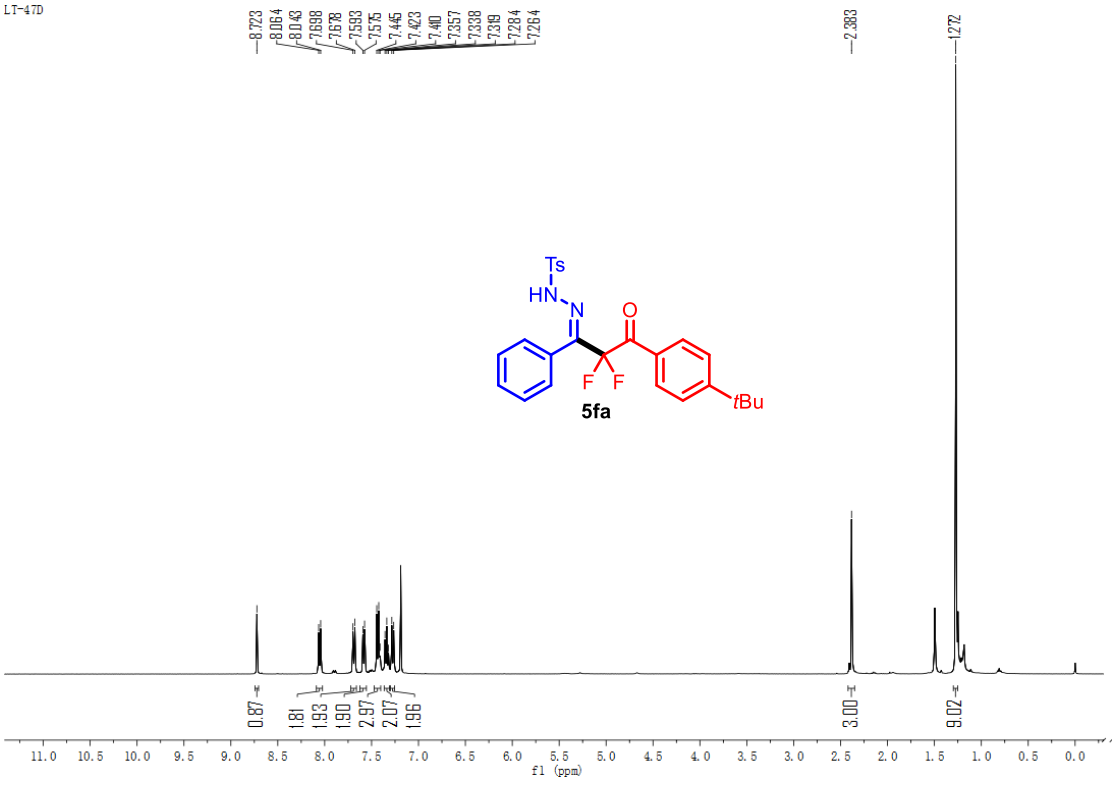
ROESY



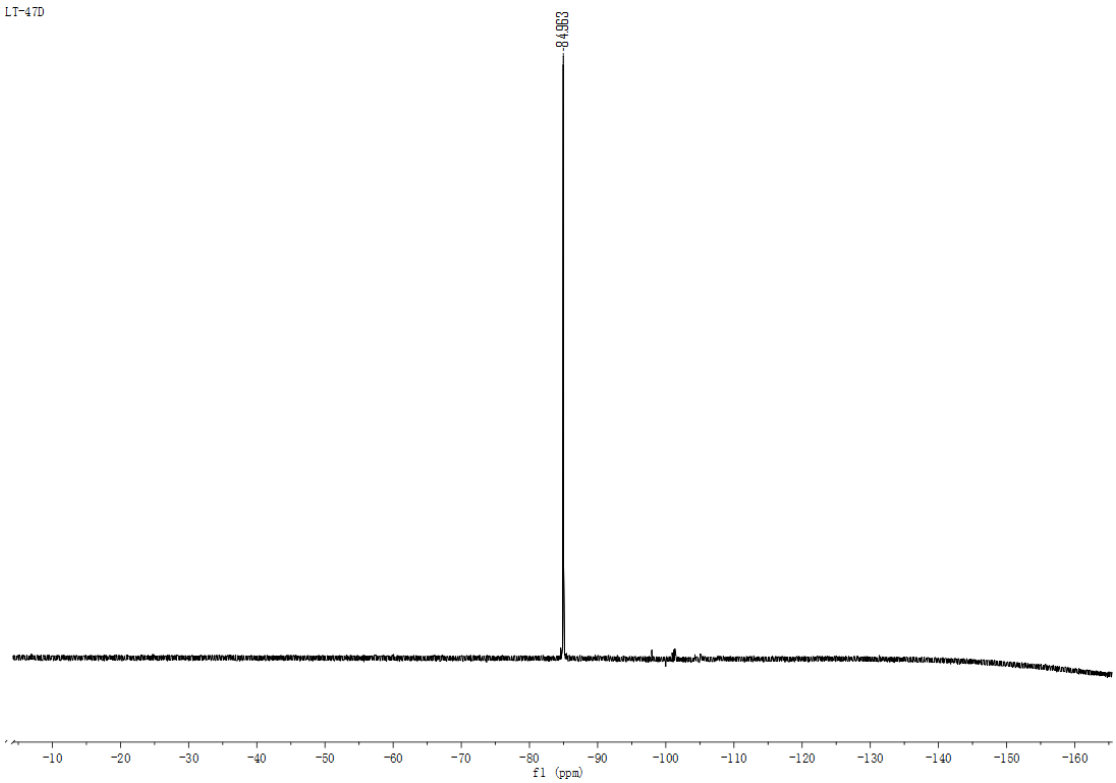


(E)-N'-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-oxo-1-phenylpropylidene)-4-methylbenzenesulfonohydrazide (5fa)

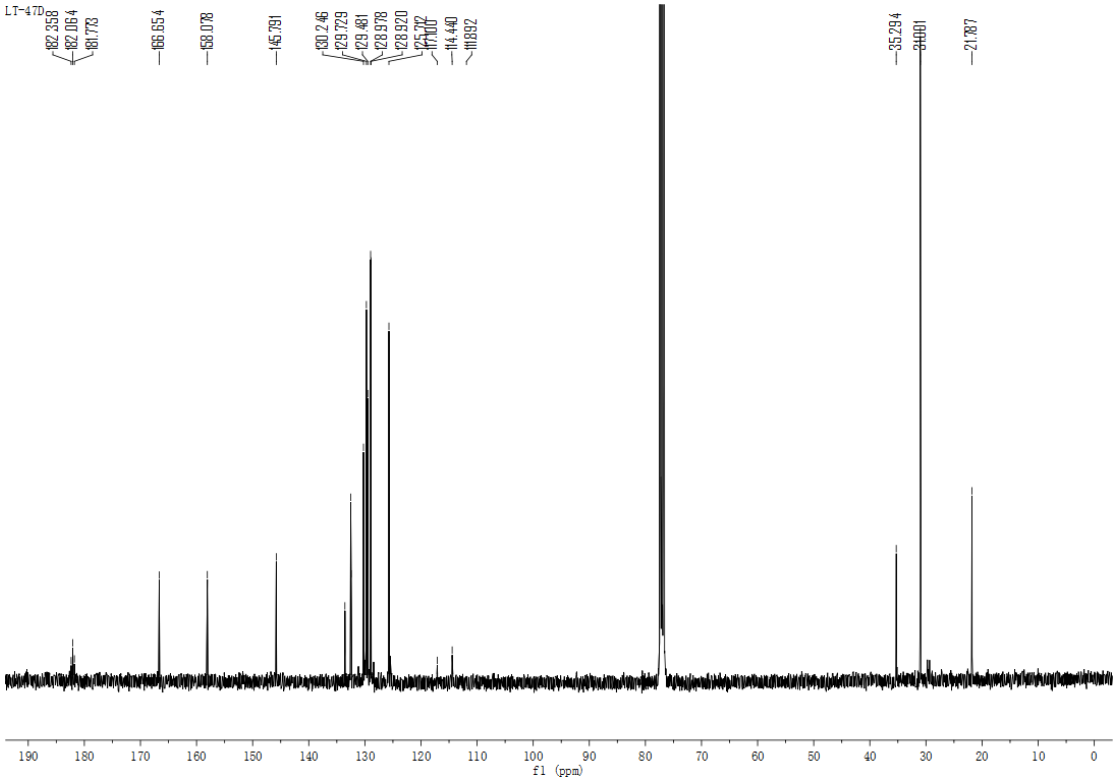
^{1}H NMR (400 MHz, $CDCl_3$):



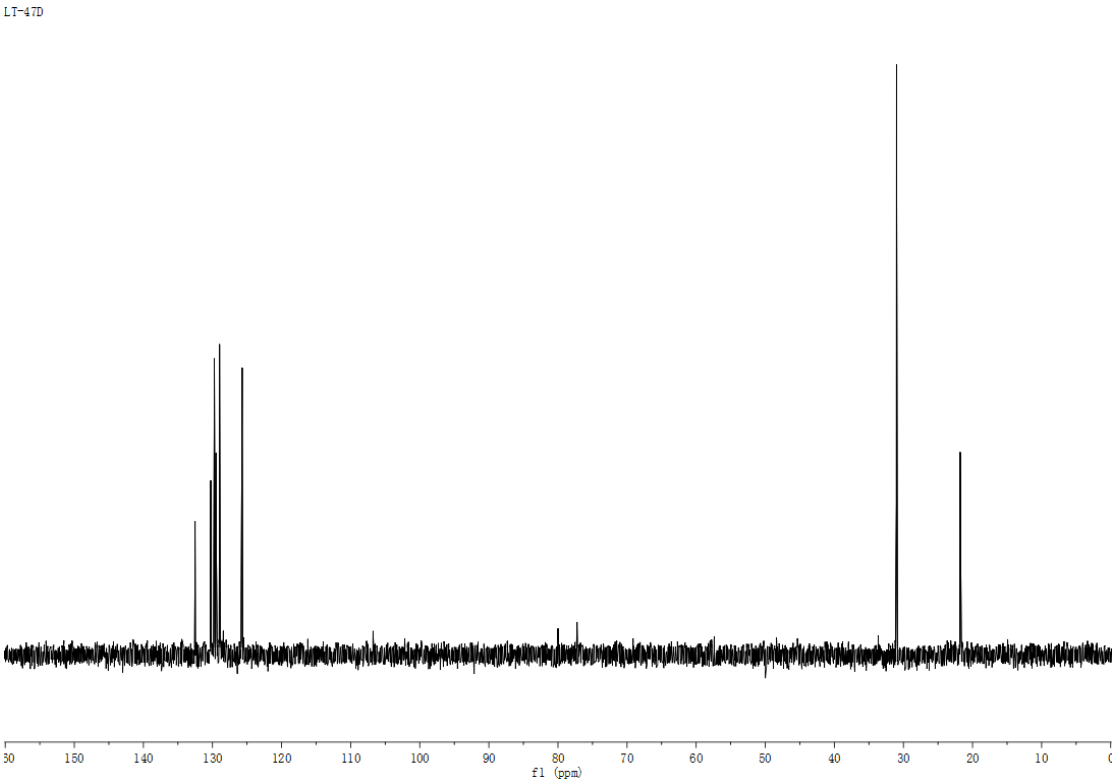
^{19}F NMR (376 MHz, $CDCl_3$):



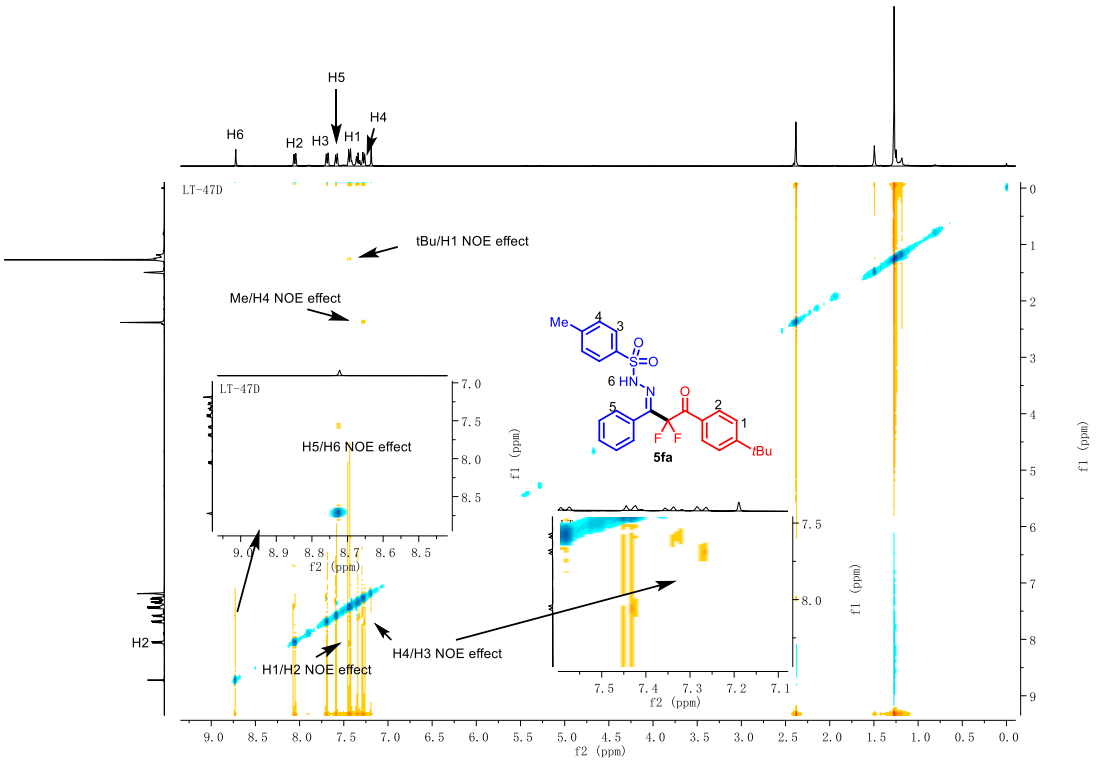
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

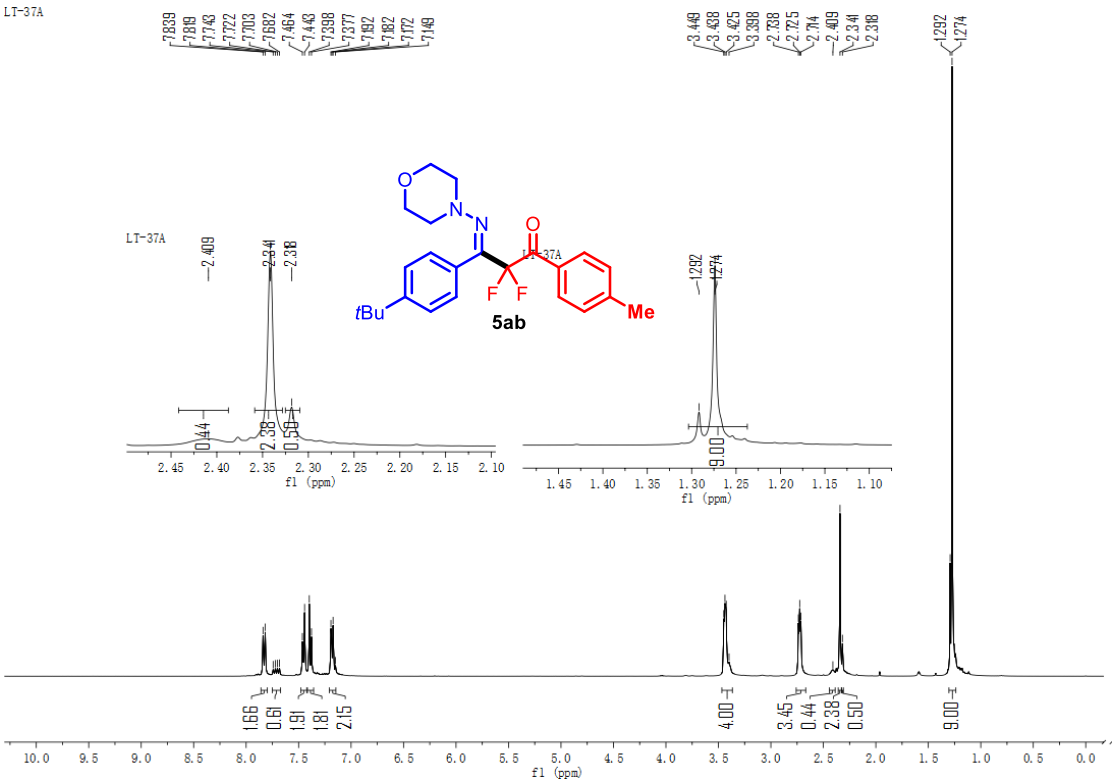


ROESY

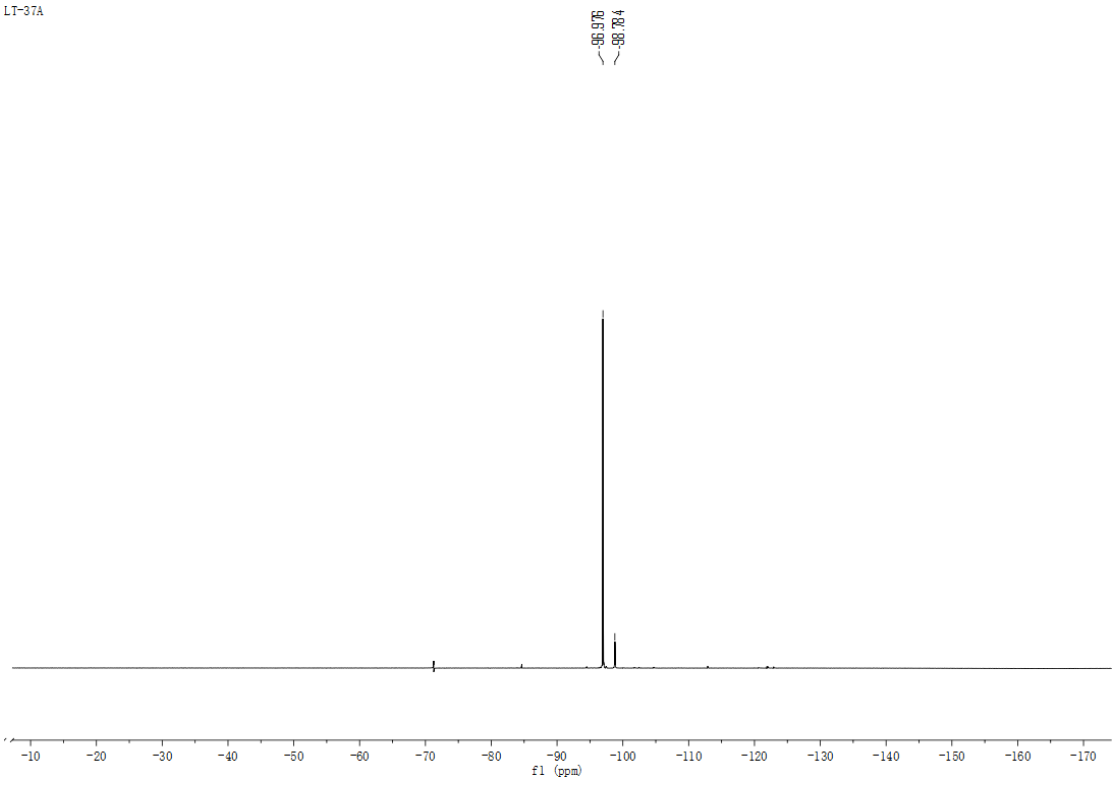


(E)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-1-(p-tolyl)propan-1-one (5ab)

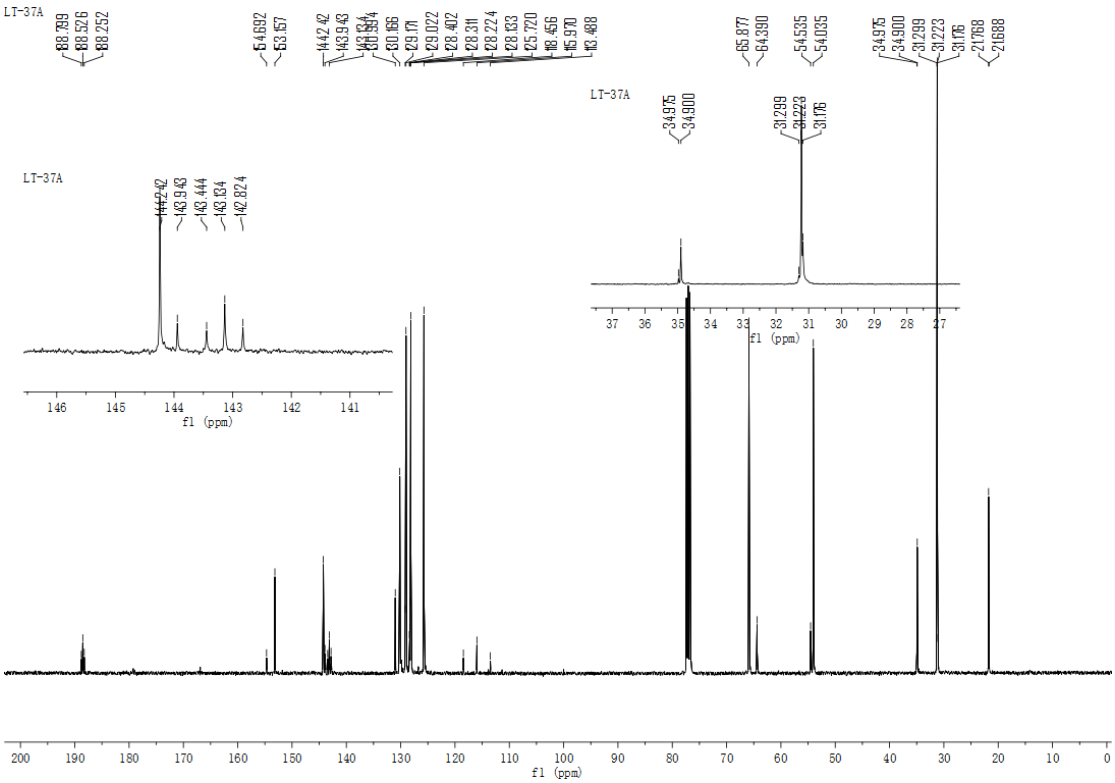
^{1}H NMR (400 MHz, $CDCl_3$):



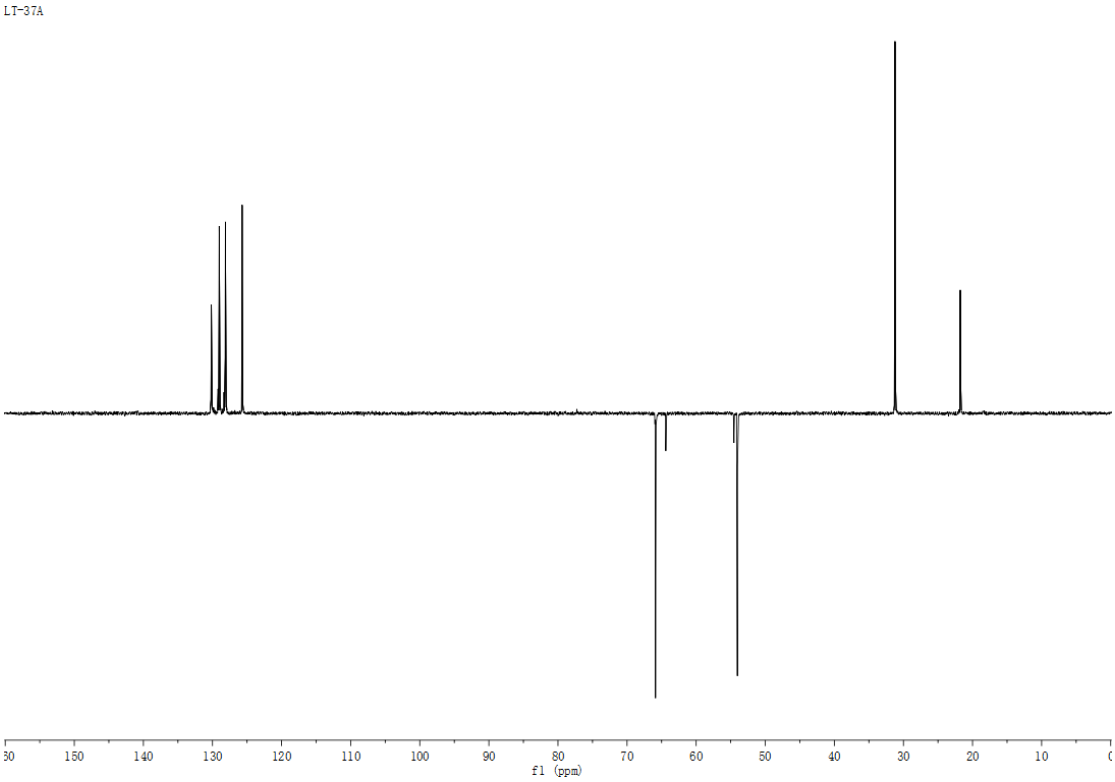
^{19}F NMR (376 MHz, $CDCl_3$):



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

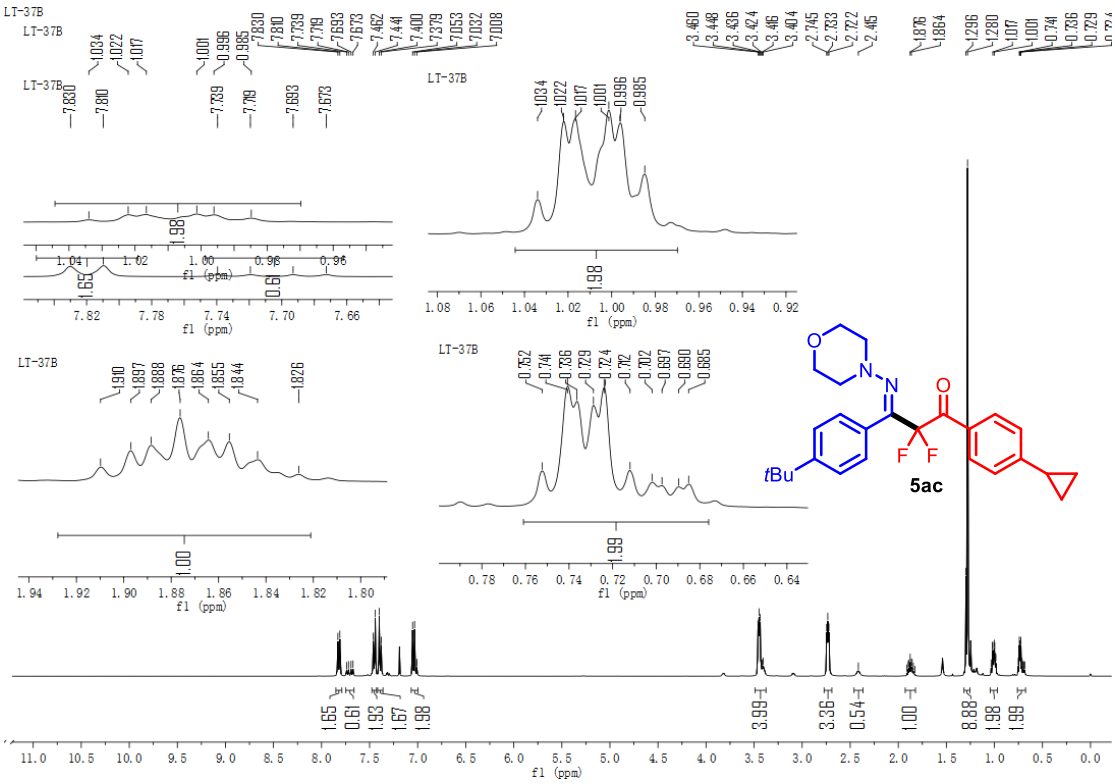


DEPT

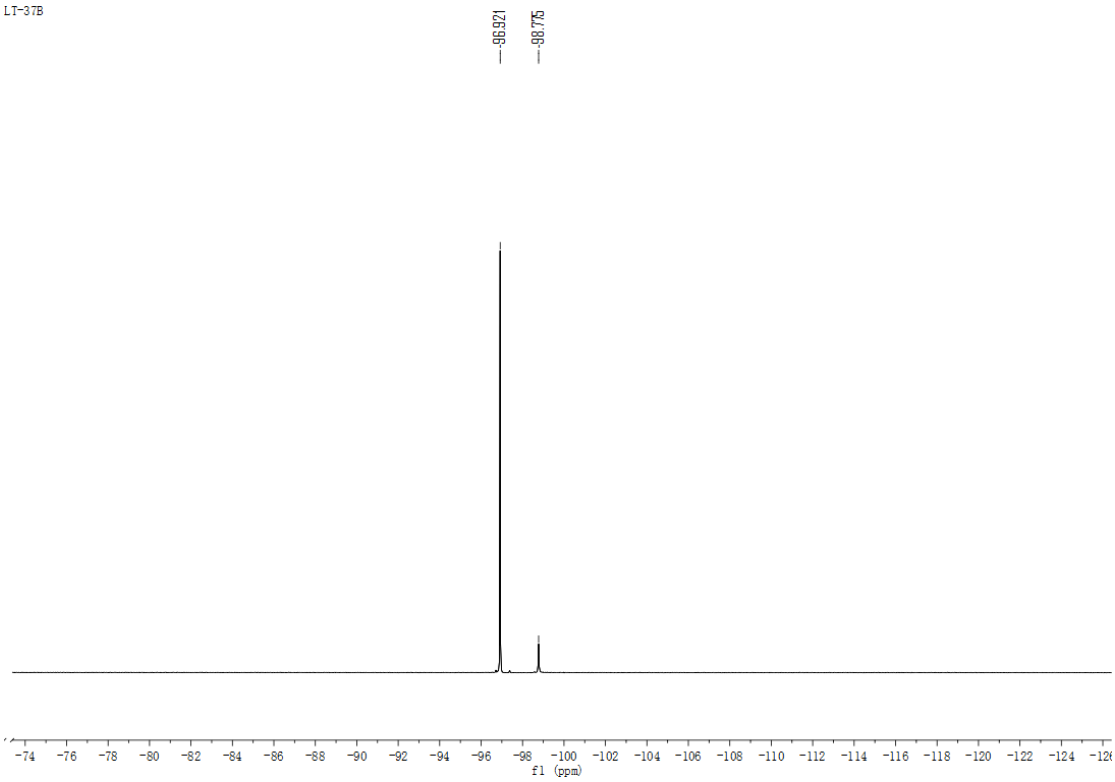


(E)-3-(4-(tert-butyl)phenyl)-1-(4-cyclopropylphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ac)

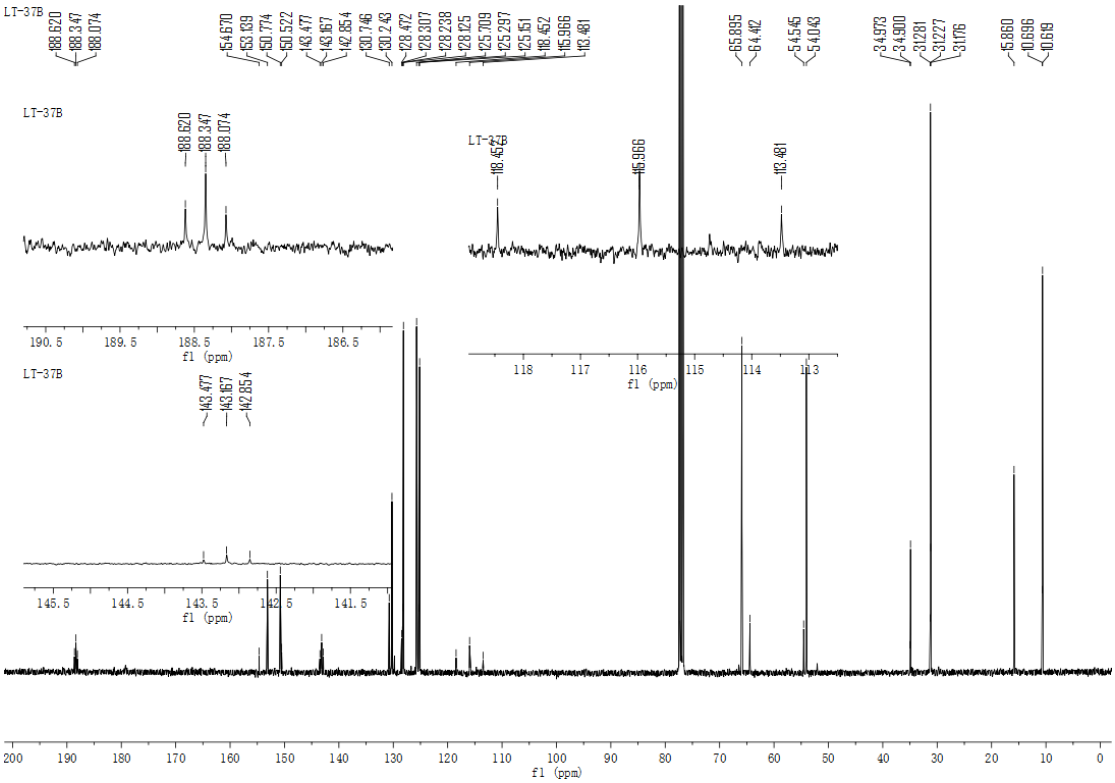
^{1}H NMR (400 MHz, $CDCl_3$):



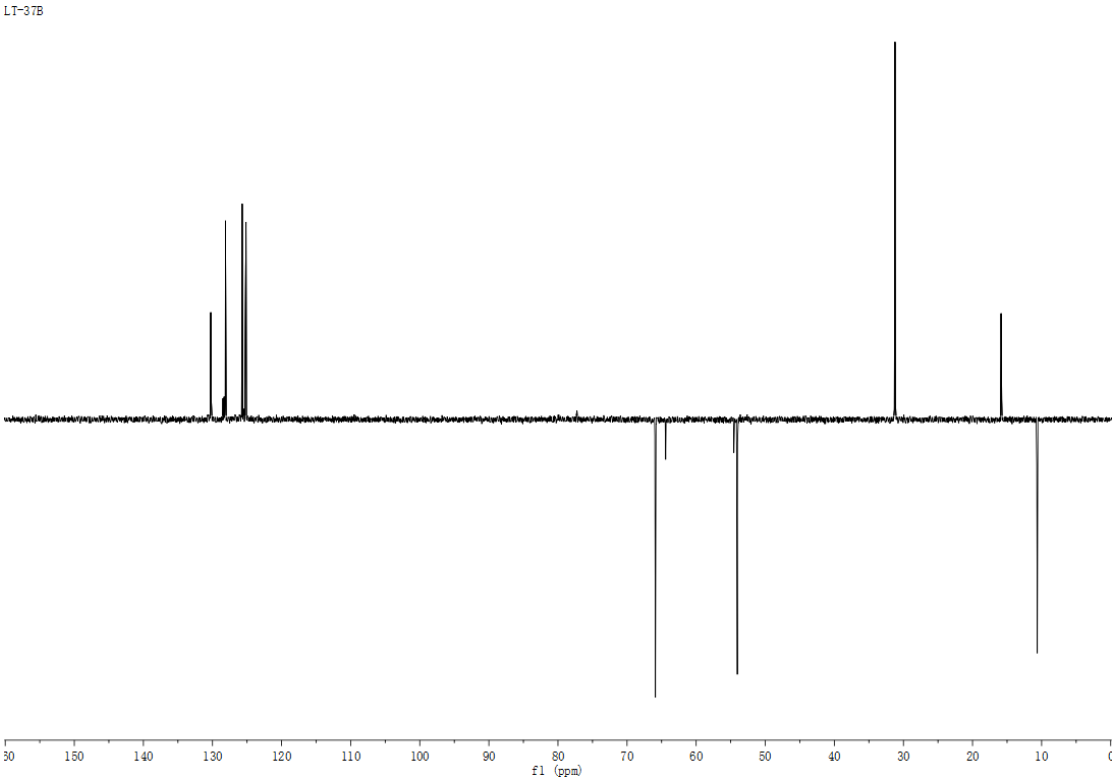
^{19}F NMR (376 MHz, $CDCl_3$):



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

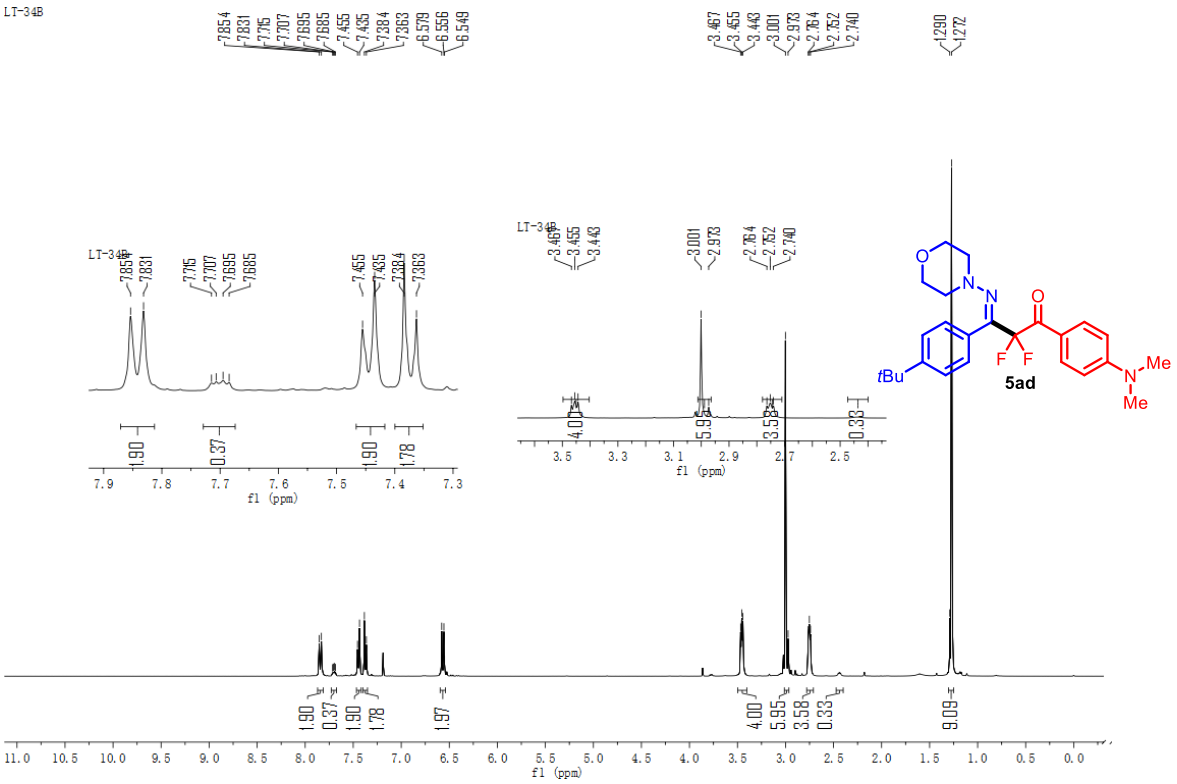


DEPT

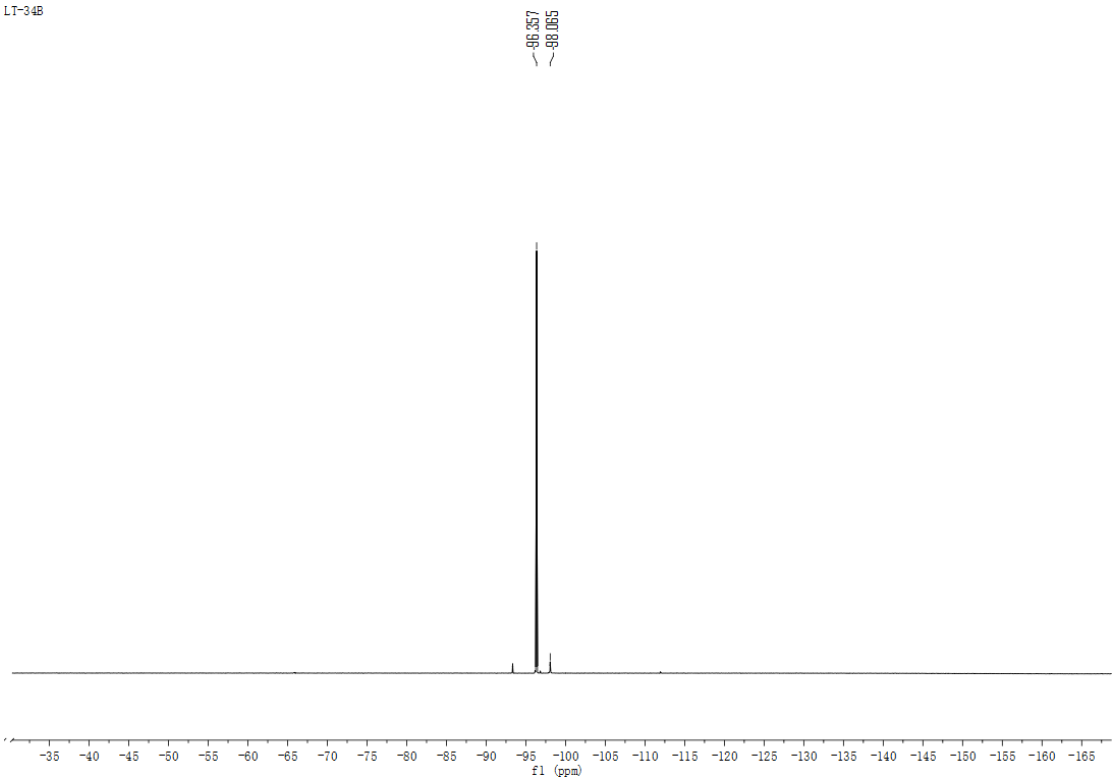


(E)-3-(4-(tert-butyl)phenyl)-1-(4-(dimethylamino)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ad)

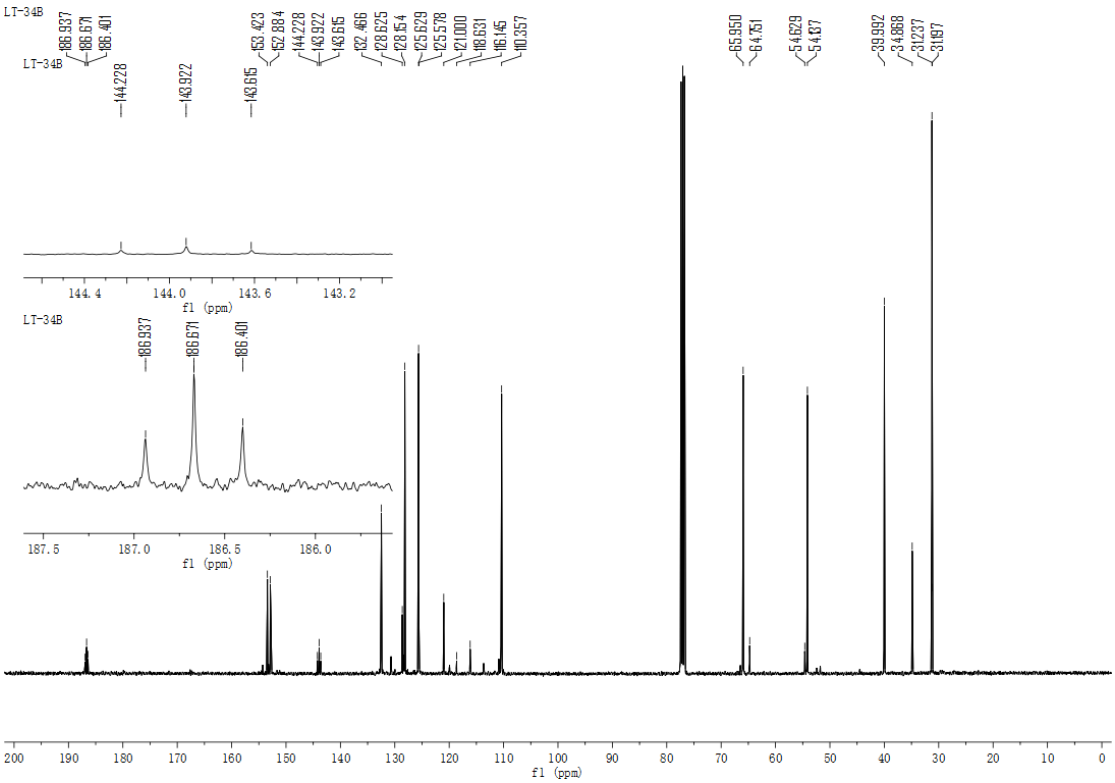
^{1}H NMR (400 MHz, $CDCl_3$):



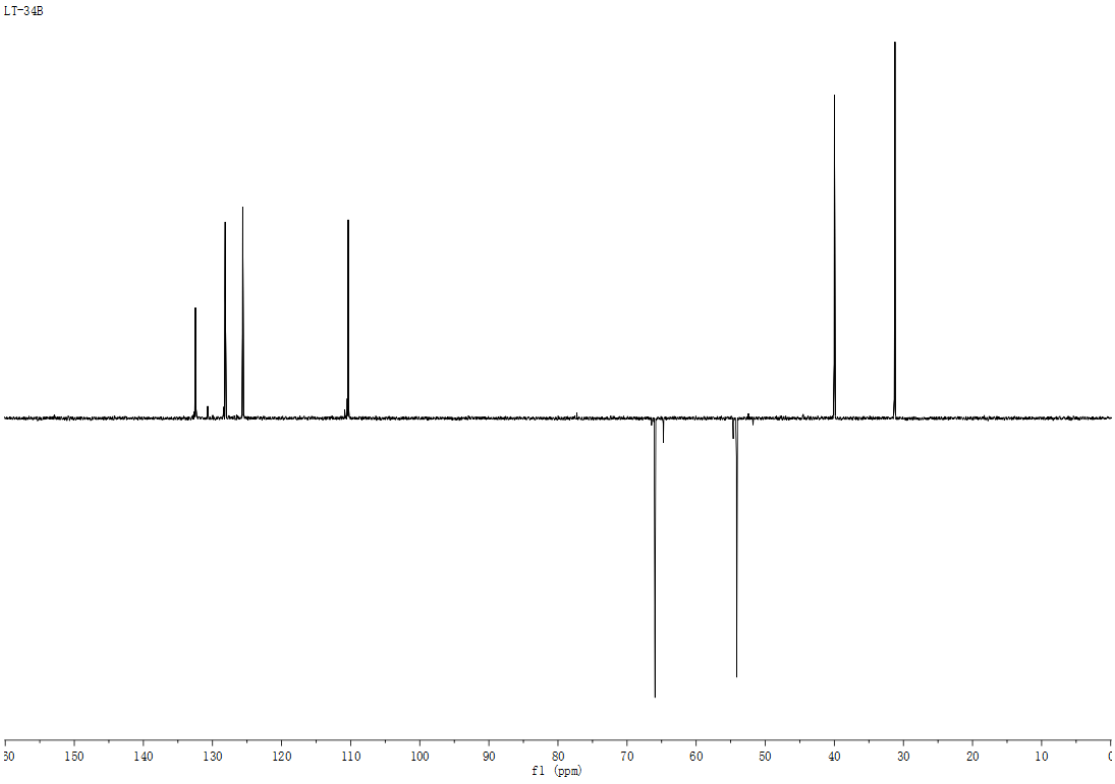
^{19}F NMR (376 MHz, $CDCl_3$):



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

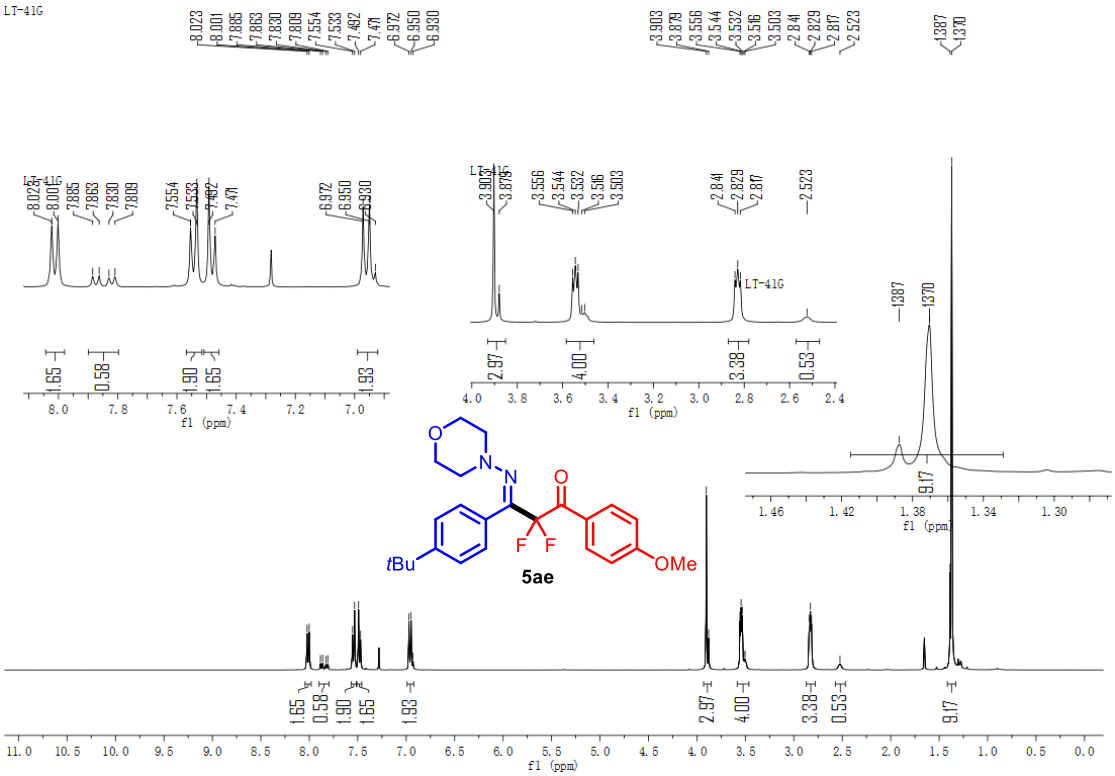


DEPT

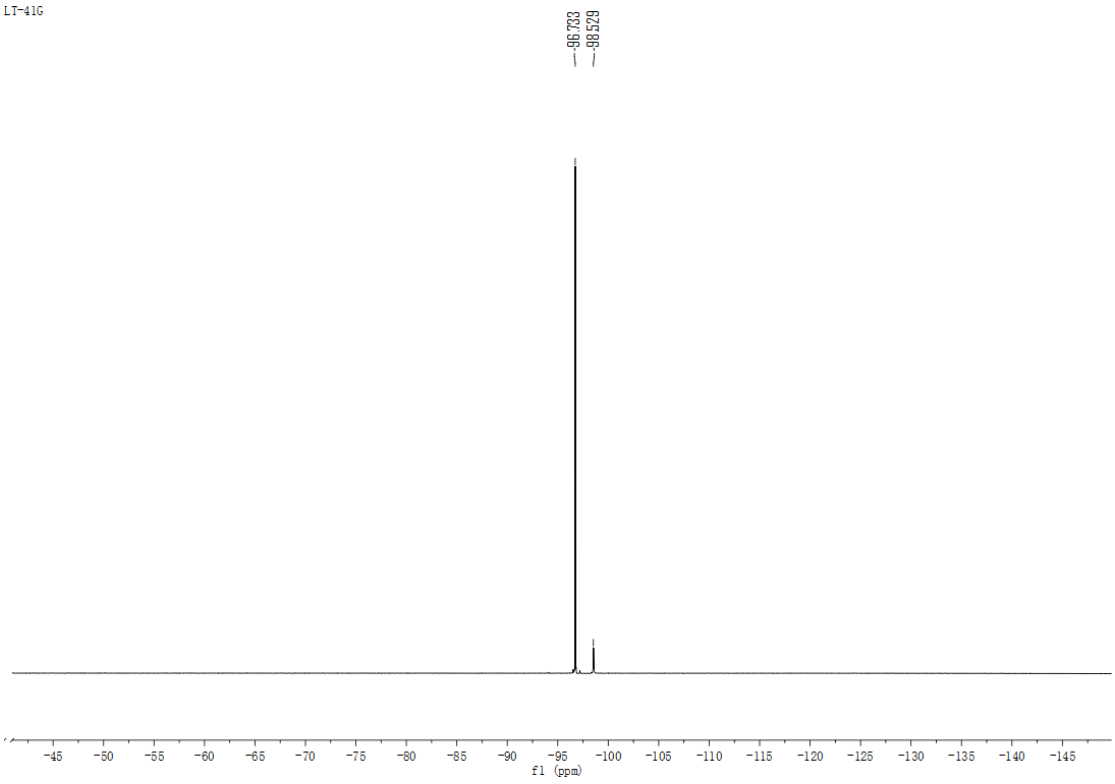


(E)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ae)

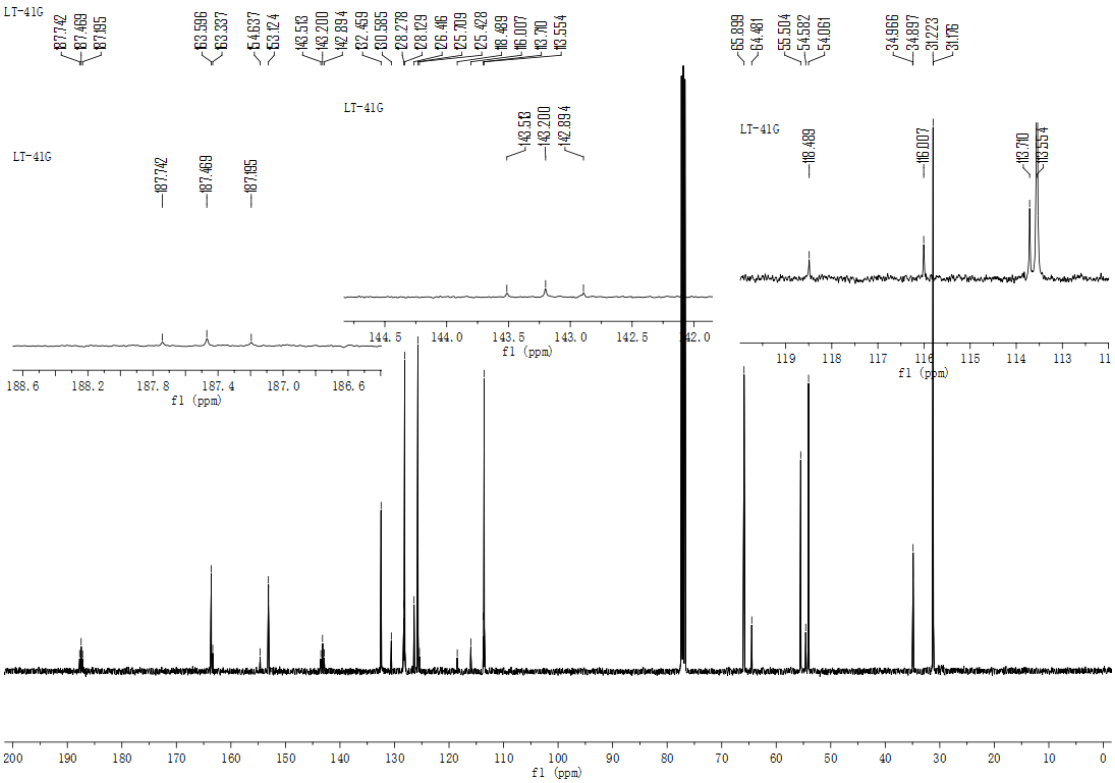
^{1}H NMR (400 MHz, $CDCl_3$):



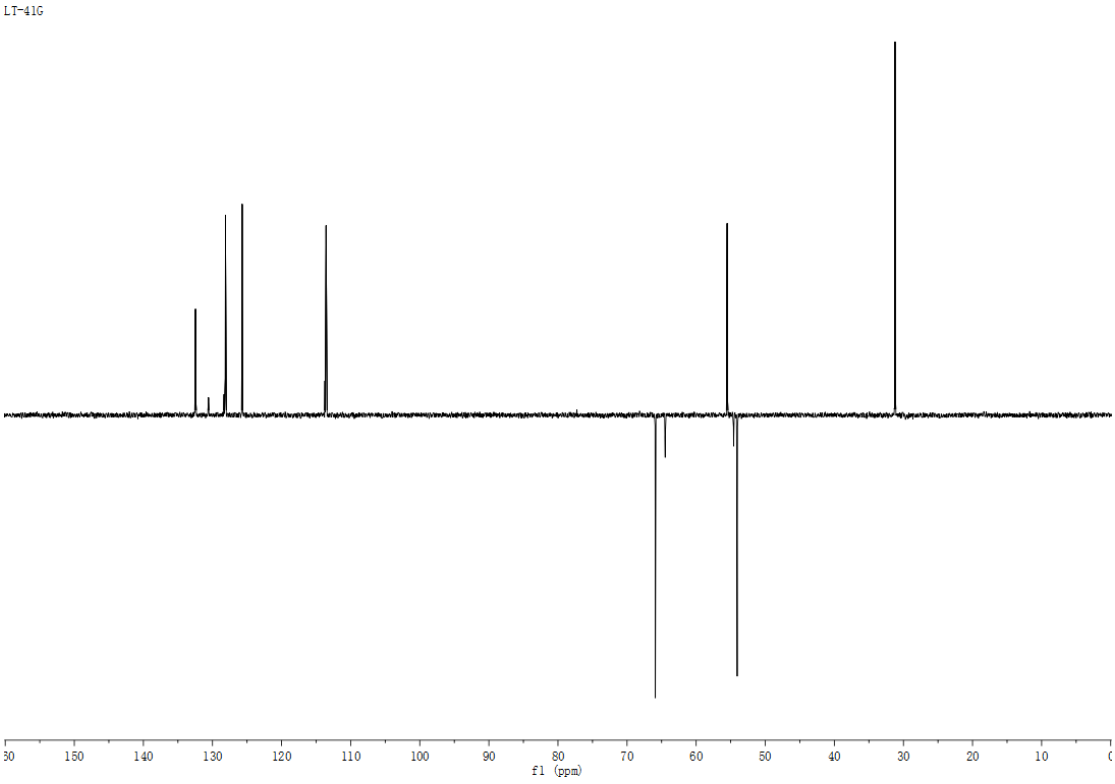
^{19}F NMR (376 MHz, $CDCl_3$):



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

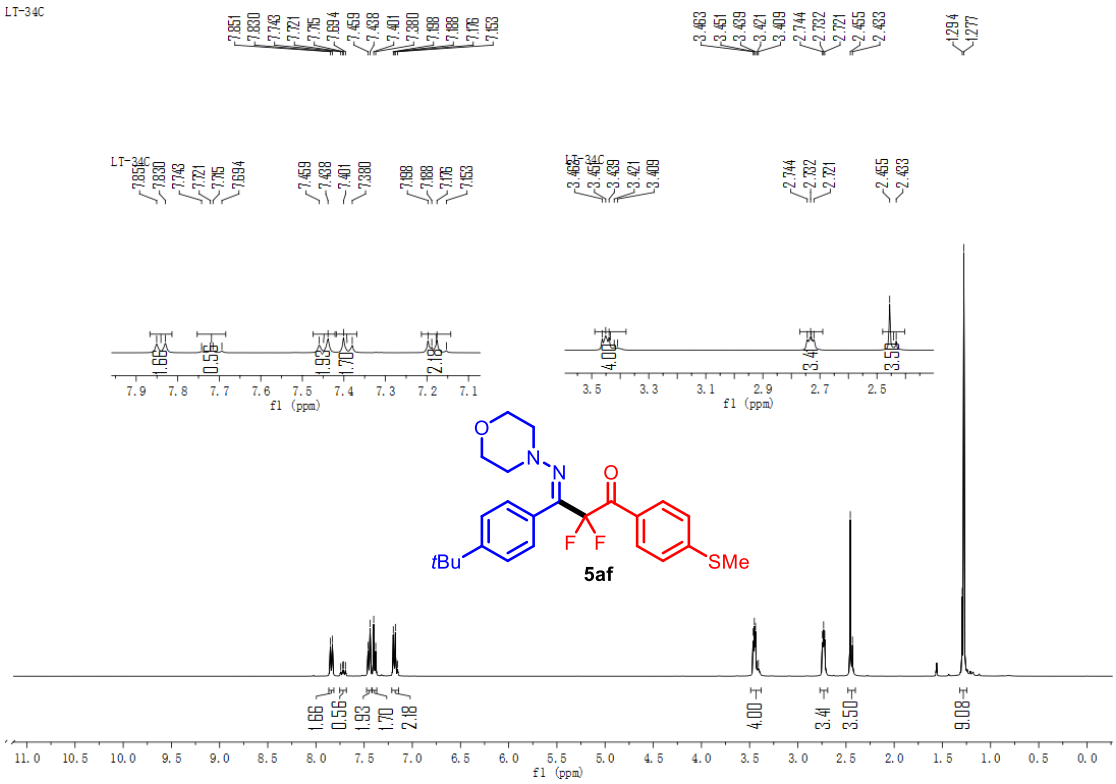


DEPT

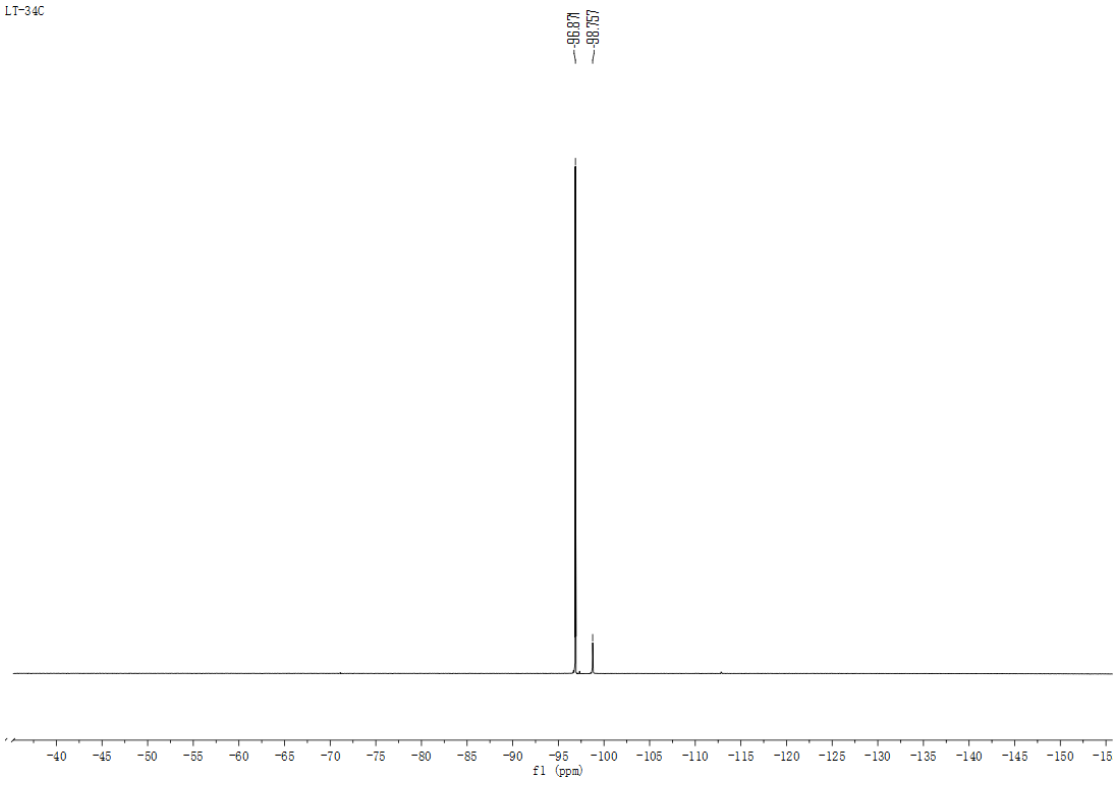


(E)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-(methylthio)phenyl)-3-(morpholino imino)propan-1-one (5af)

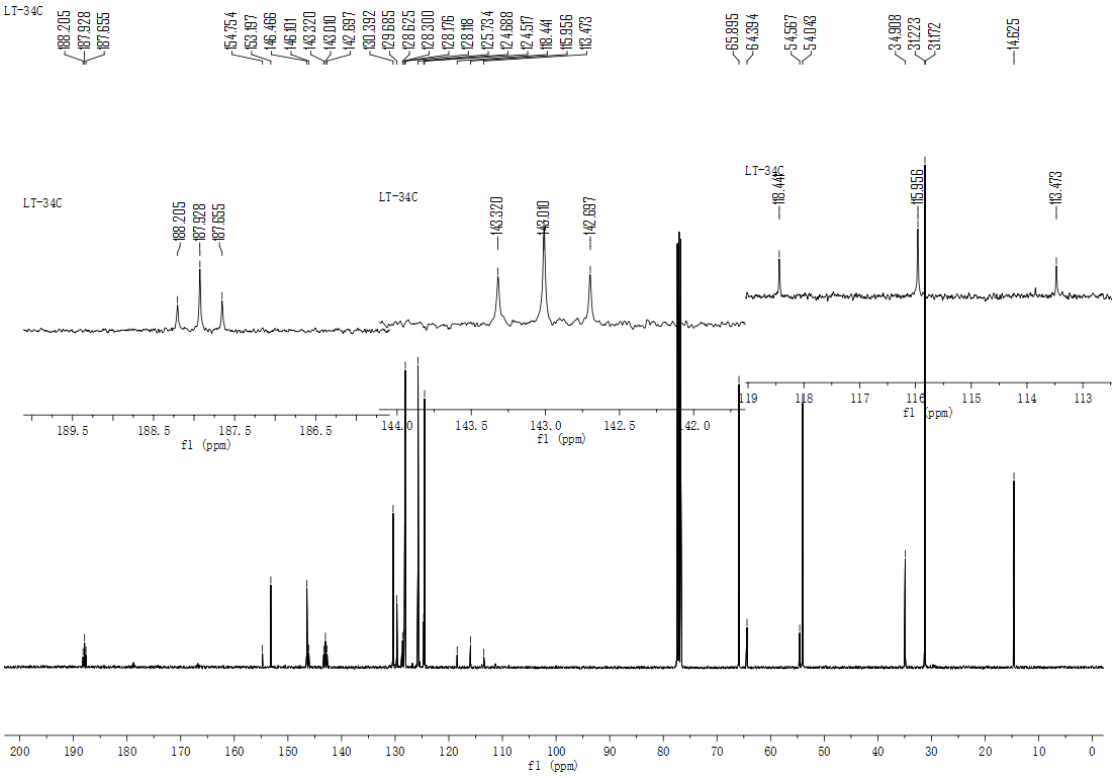
^{1}H NMR (400 MHz, $CDCl_3$):



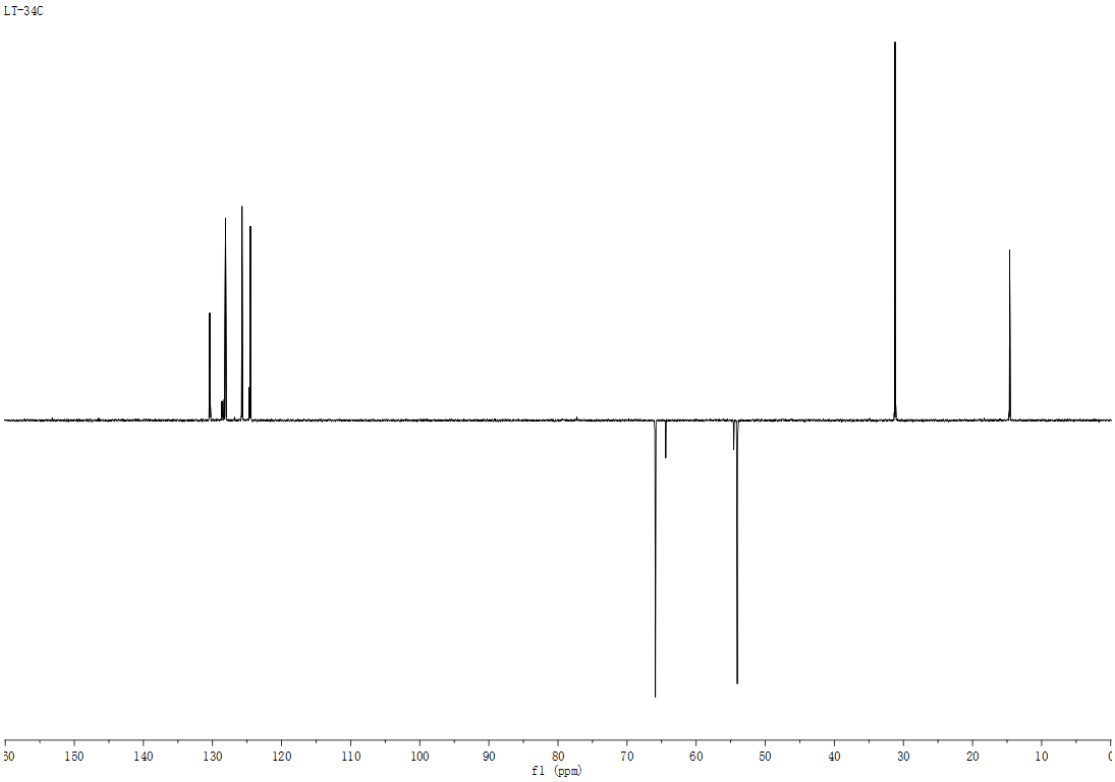
^{19}F NMR (376 MHz, $CDCl_3$):



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

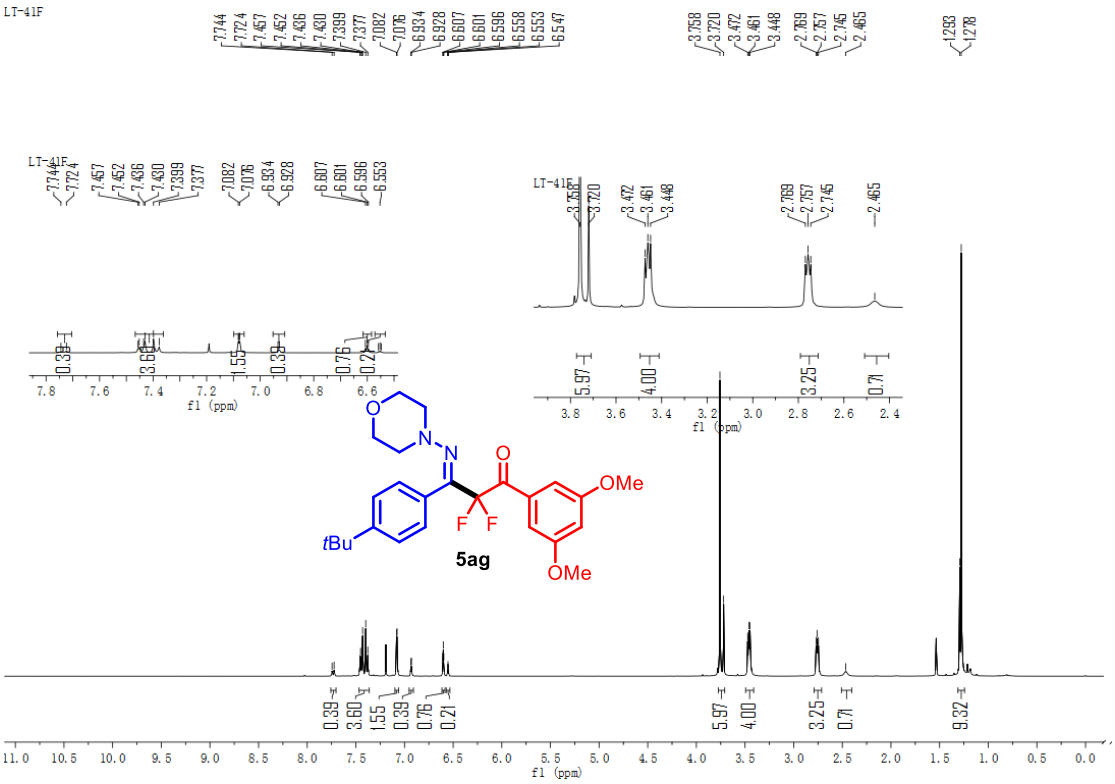


DEPT

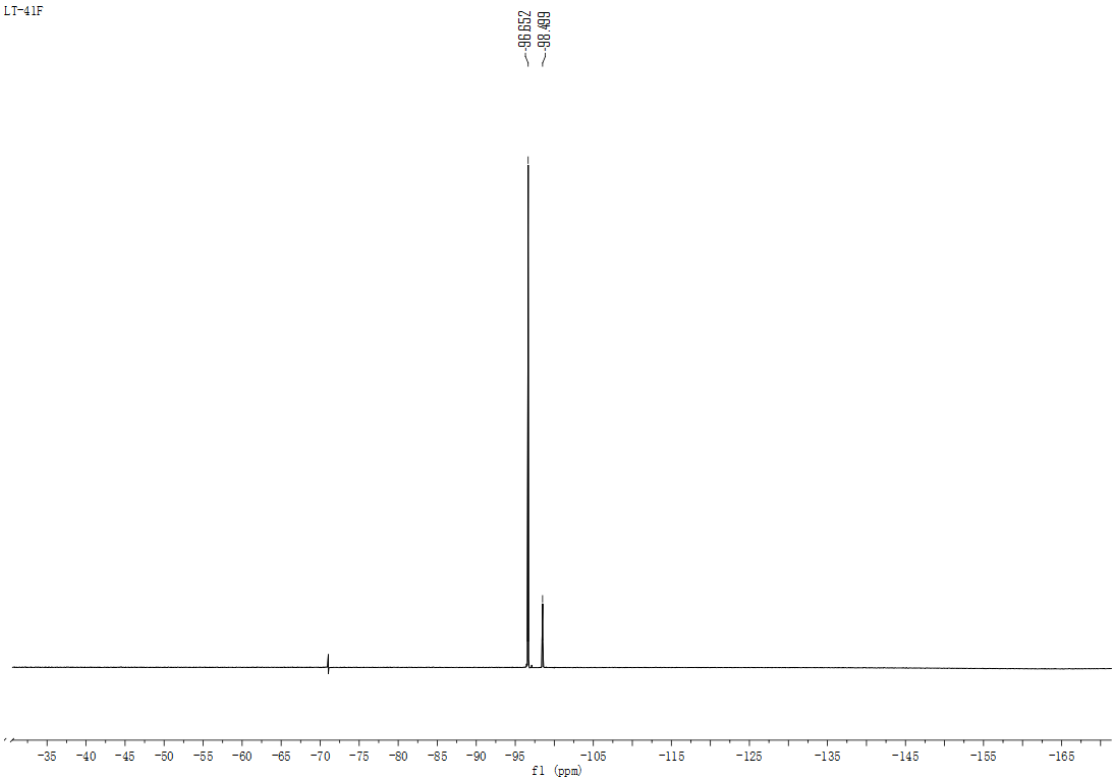


(E)-3-(4-(tert-butyl)phenyl)-1-(3,5-dimethoxyphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ag)

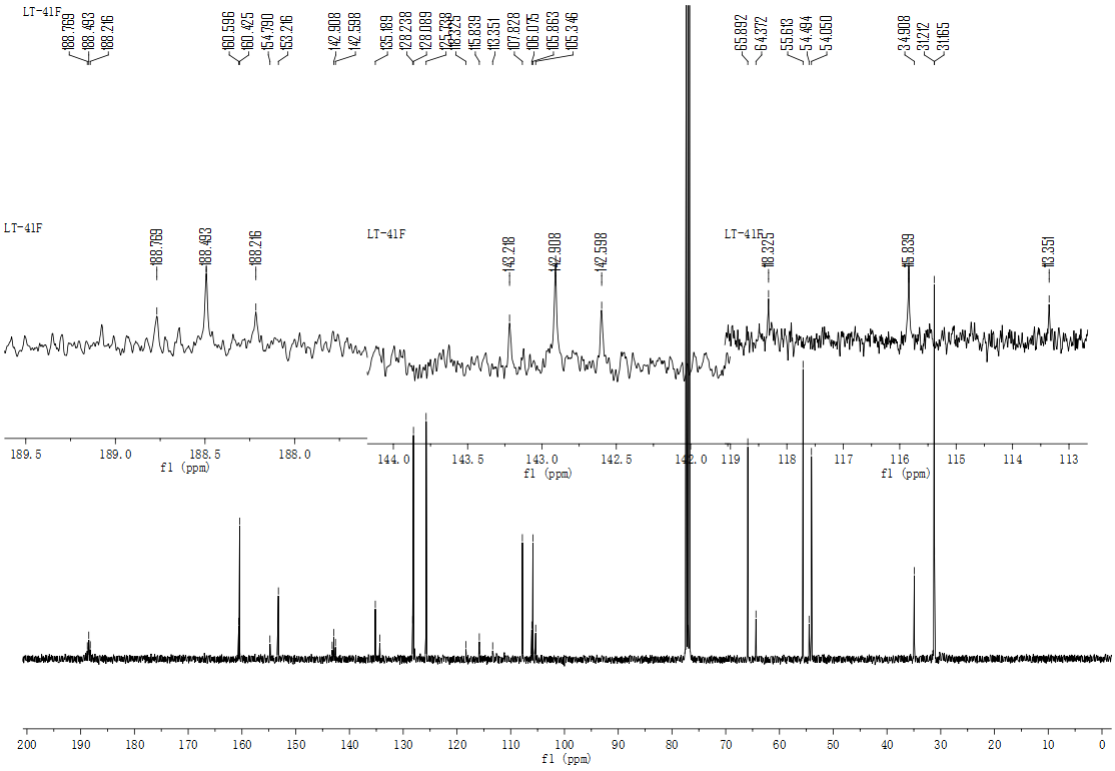
^{1}H NMR (400 MHz, $CDCl_3$)



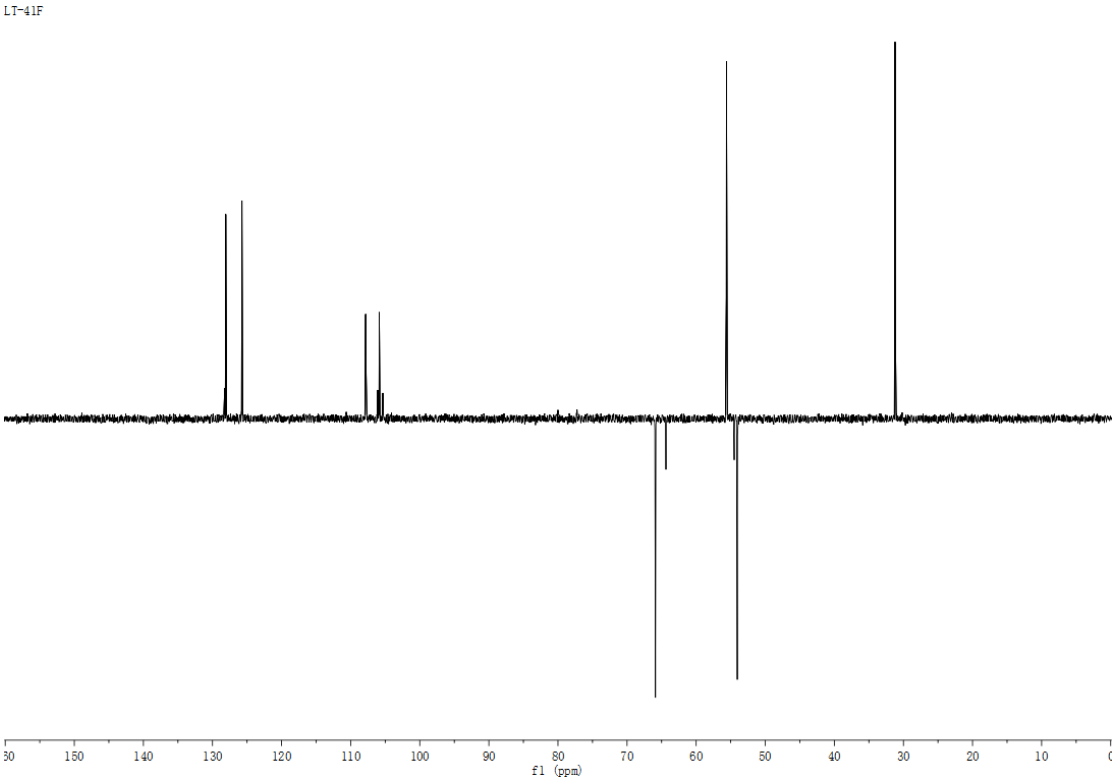
^{19}F NMR (376 MHz, $CDCl_3$):



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

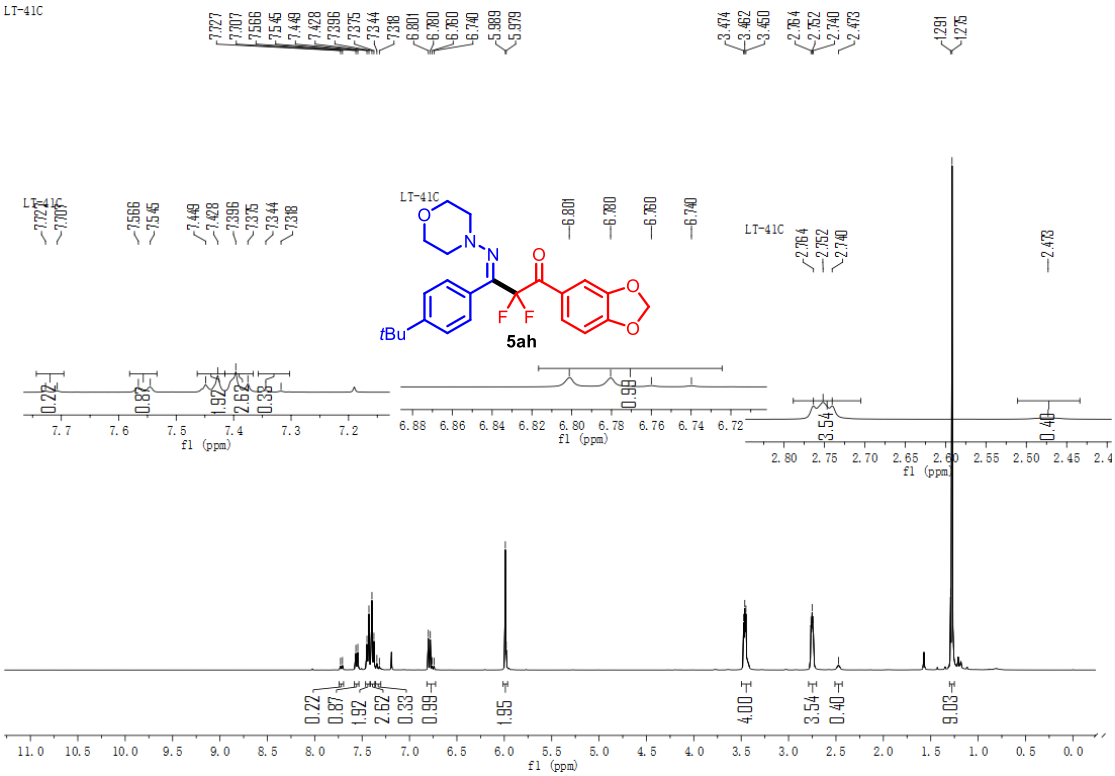


DEPT

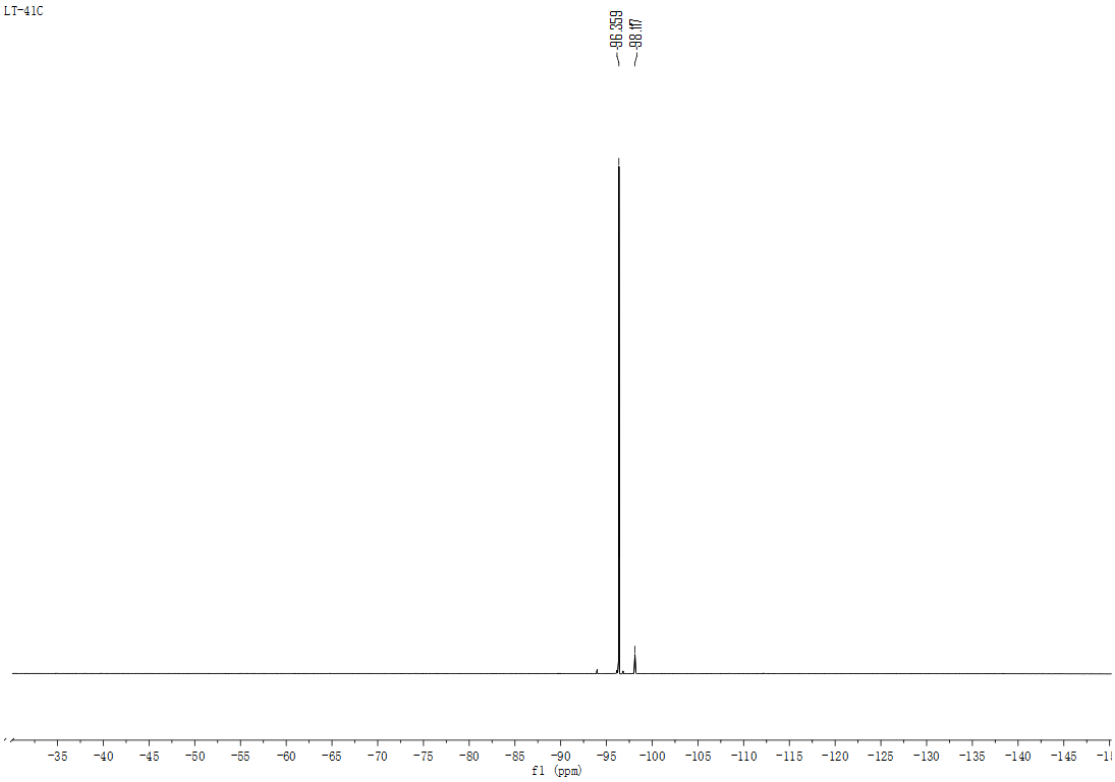


(E)-1-(benzo[d][1,3]dioxol-5-yl)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ah)

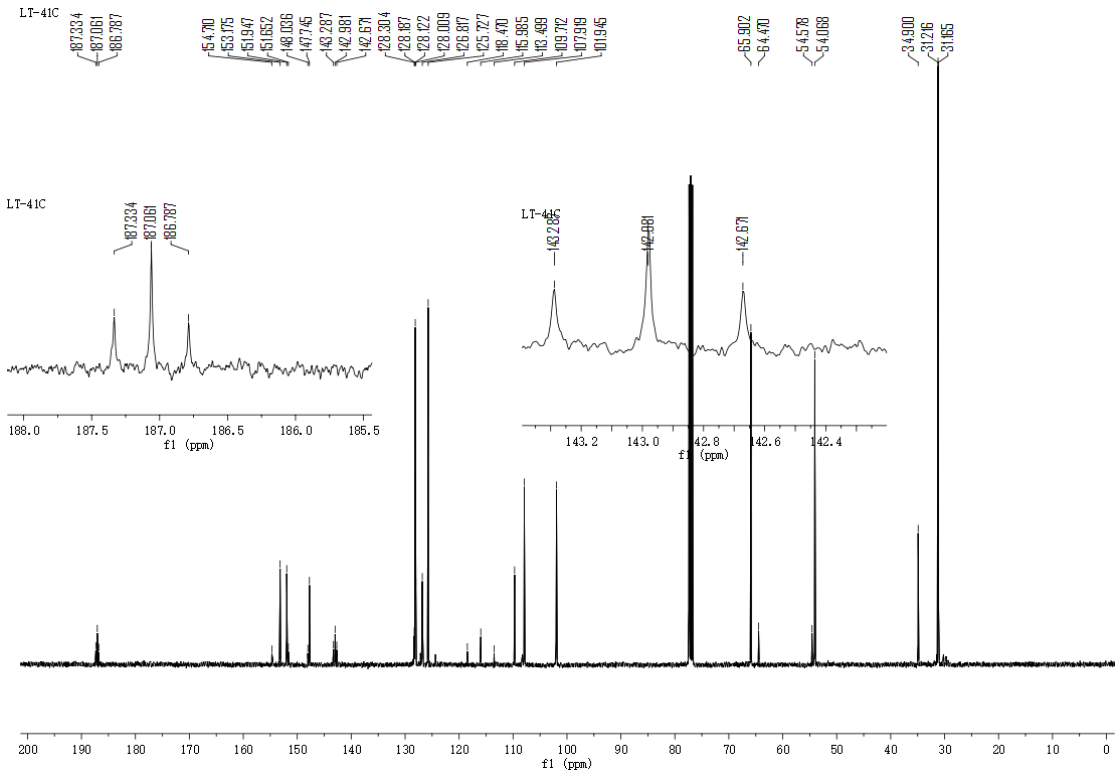
^{1}H NMR (400 MHz, $CDCl_3$)



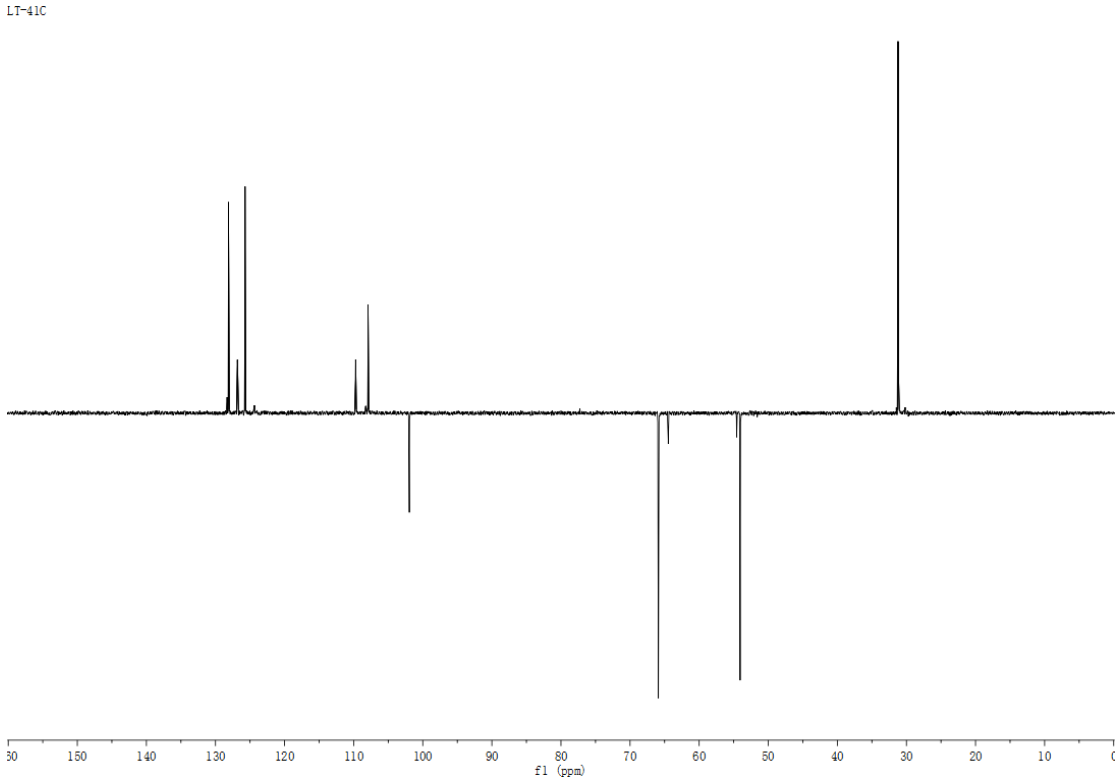
^{19}F NMR (376 MHz, $CDCl_3$):



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

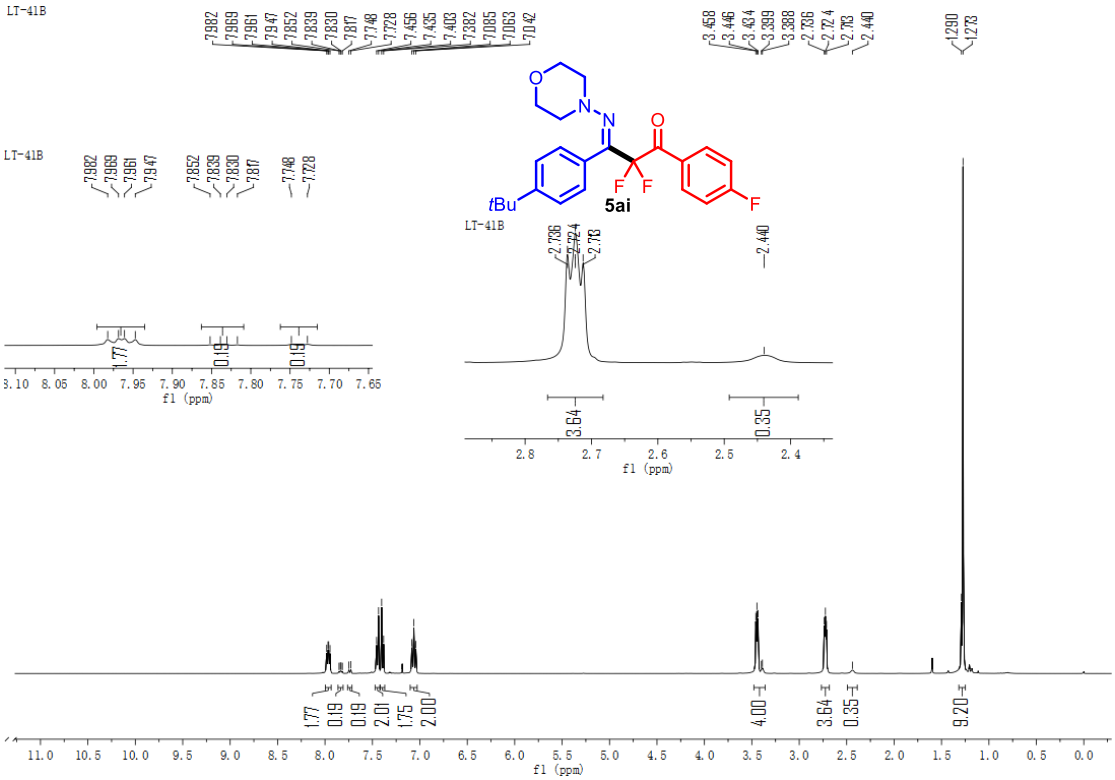


DEPT

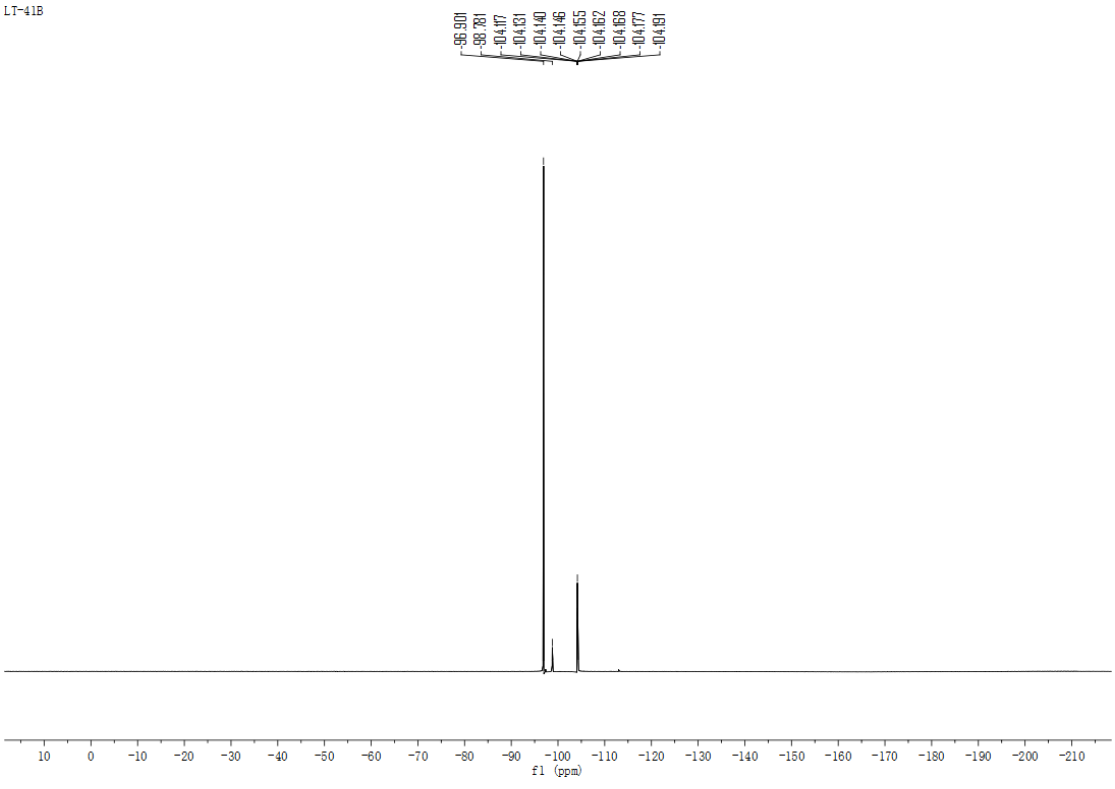


(E)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(4-fluorophenyl)-3-(morpholinoimino) propan-1-one (5ai)

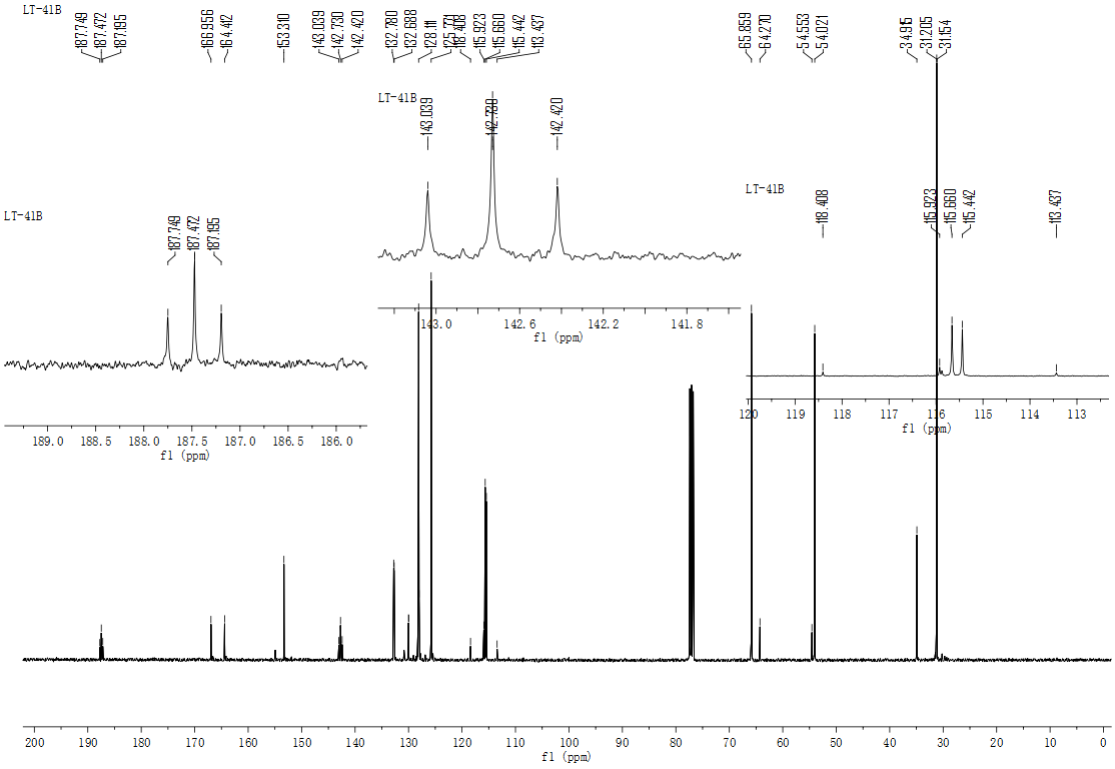
^{1}H NMR (400 MHz, $CDCl_3$)



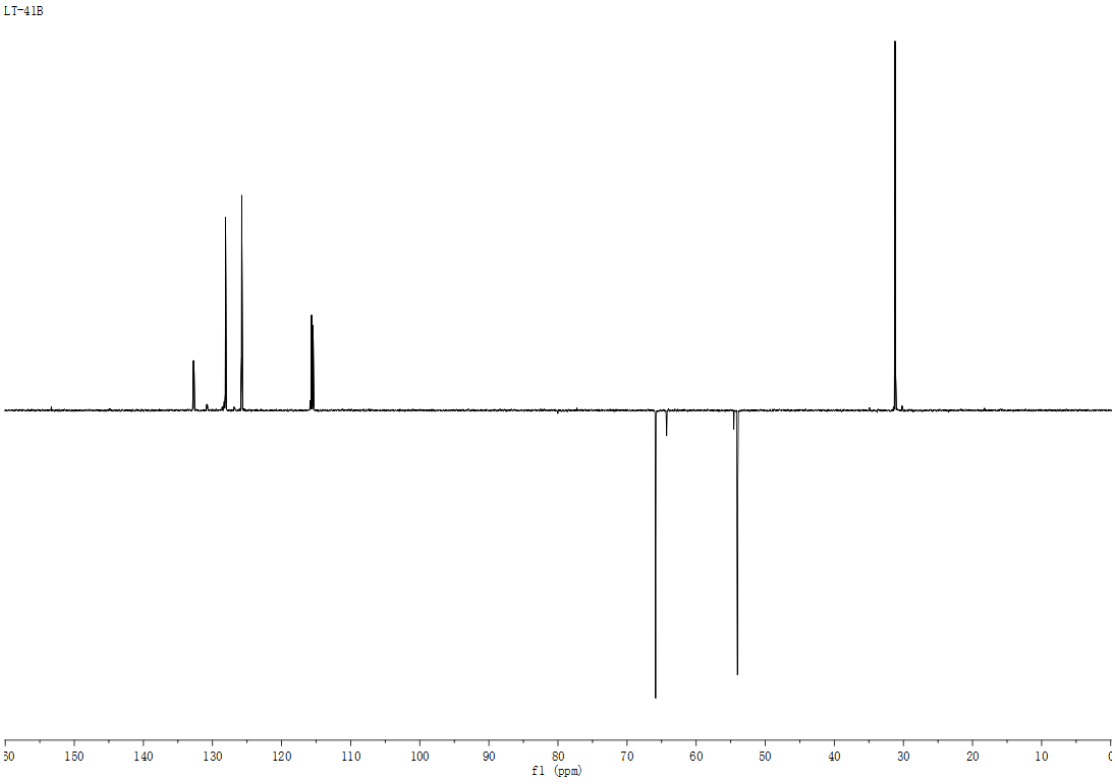
^{19}F NMR (376 MHz, $CDCl_3$):



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

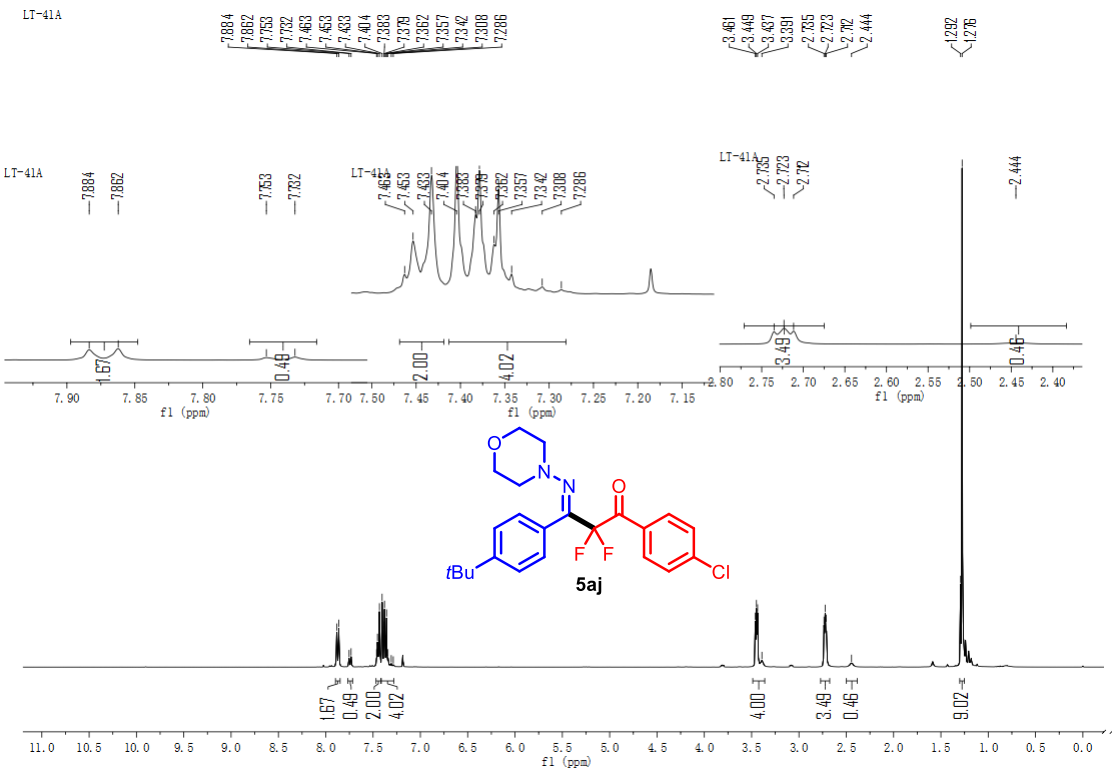


DEPT

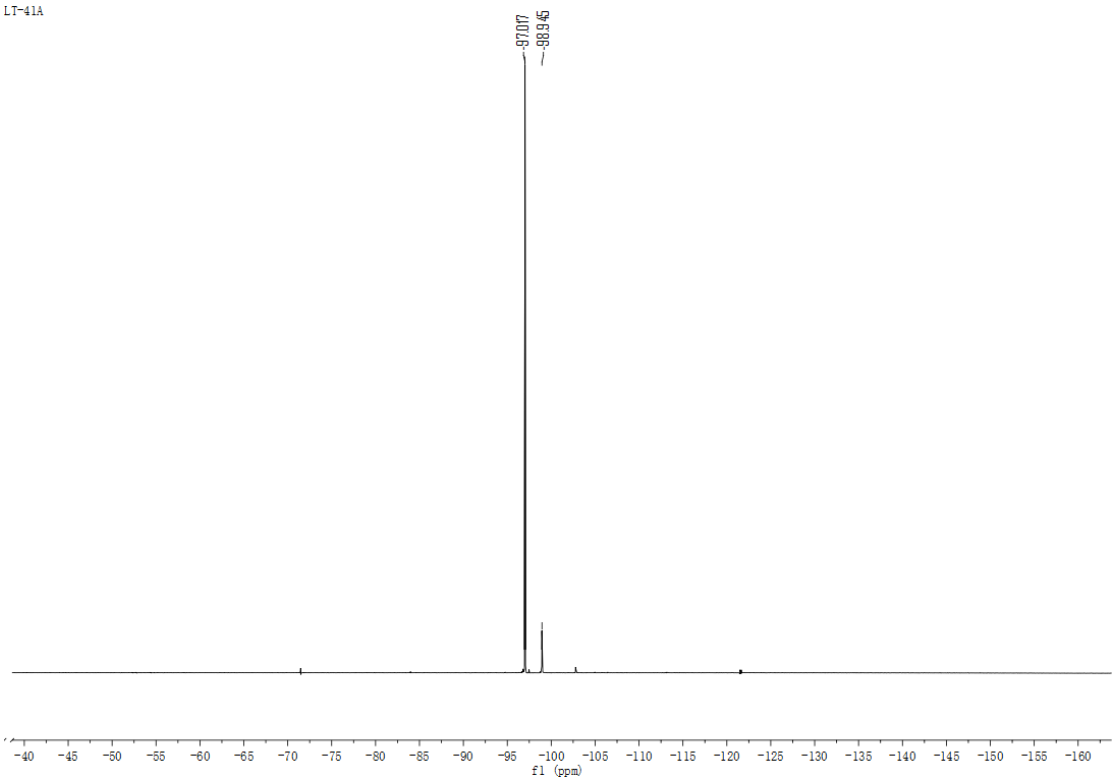


(E)-3-(4-(tert-butyl)phenyl)-1-(4-chlorophenyl)-2,2-difluoro-3-(morpholinoimino) propan-1-one (5aj)

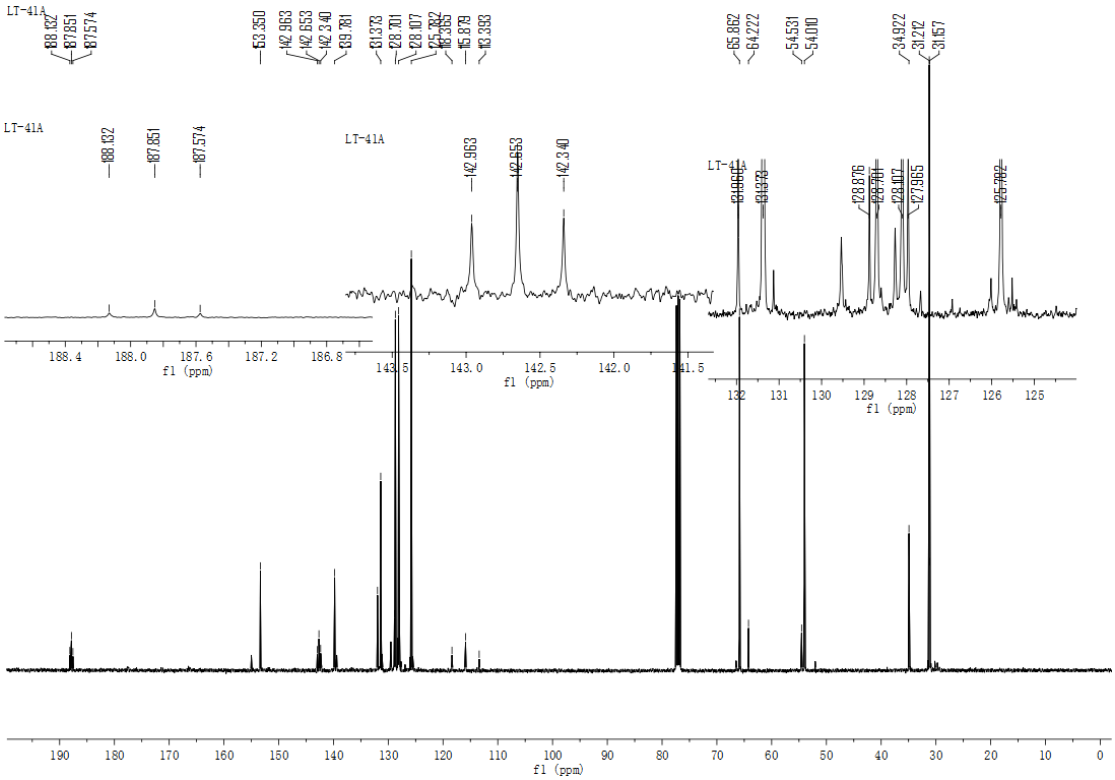
^{1}H NMR (400 MHz, $CDCl_3$)



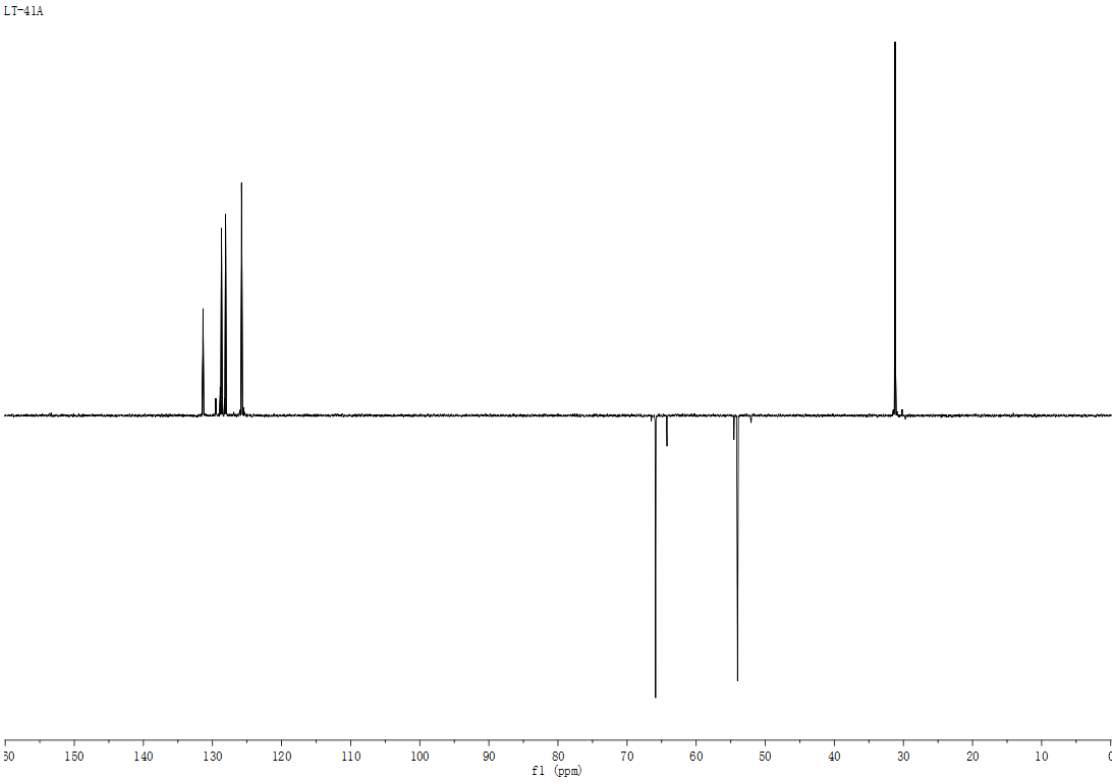
^{19}F NMR (376 MHz, $CDCl_3$):



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

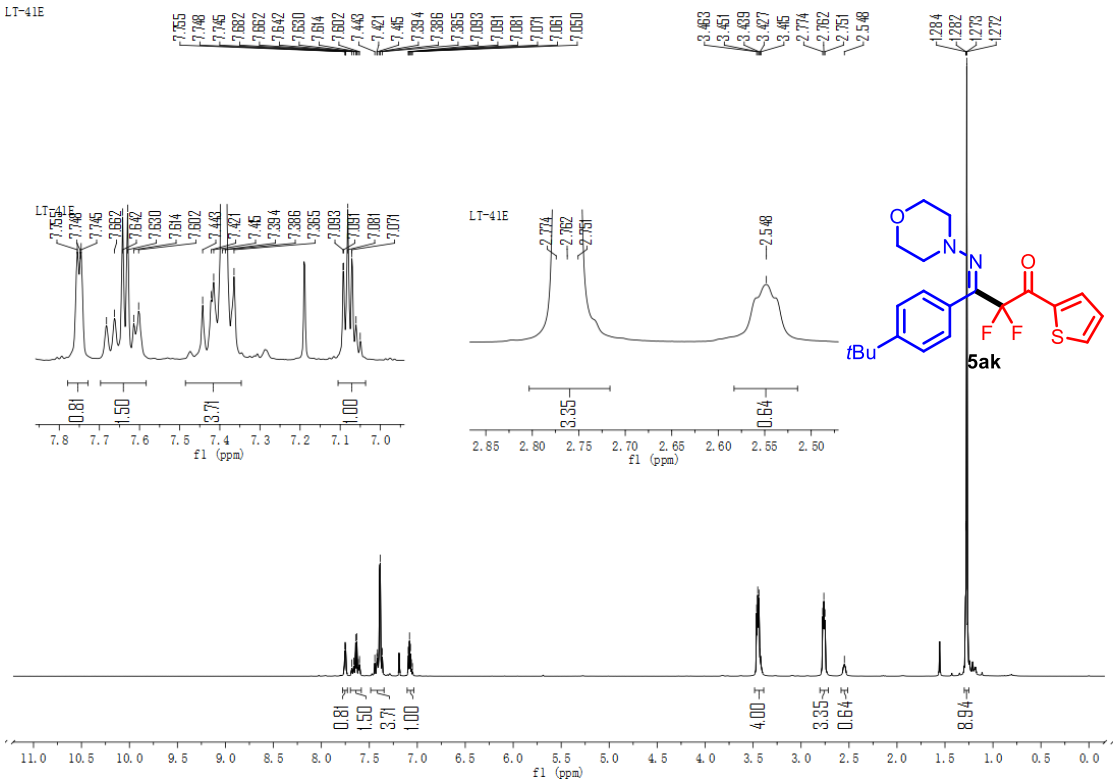


DEPT

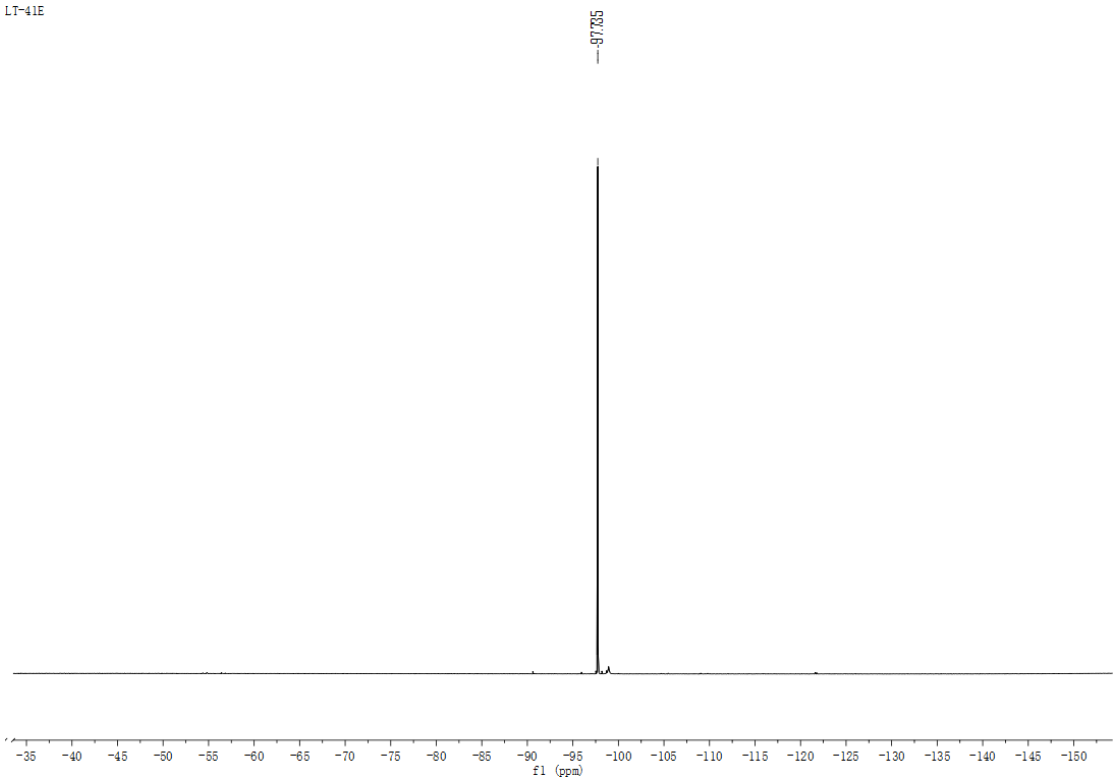


(E)-3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-1-(thiophen-2-yl)propan-1-one (5ak)

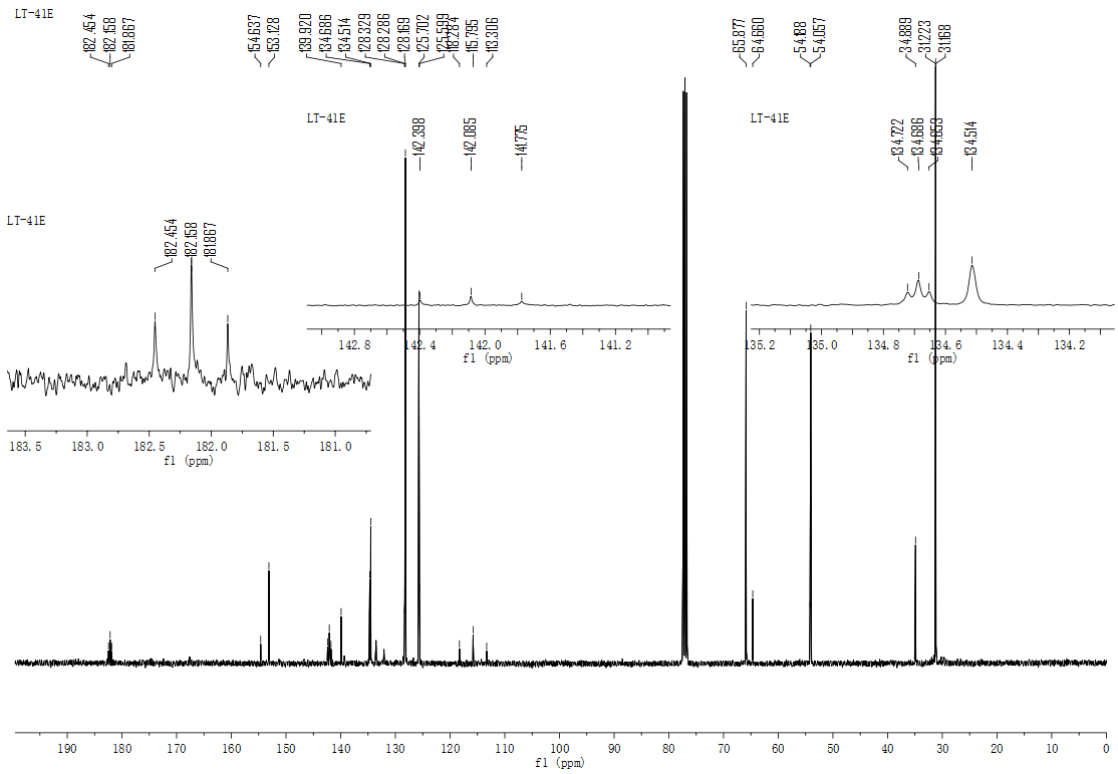
^{1}H NMR (400 MHz, $CDCl_3$)



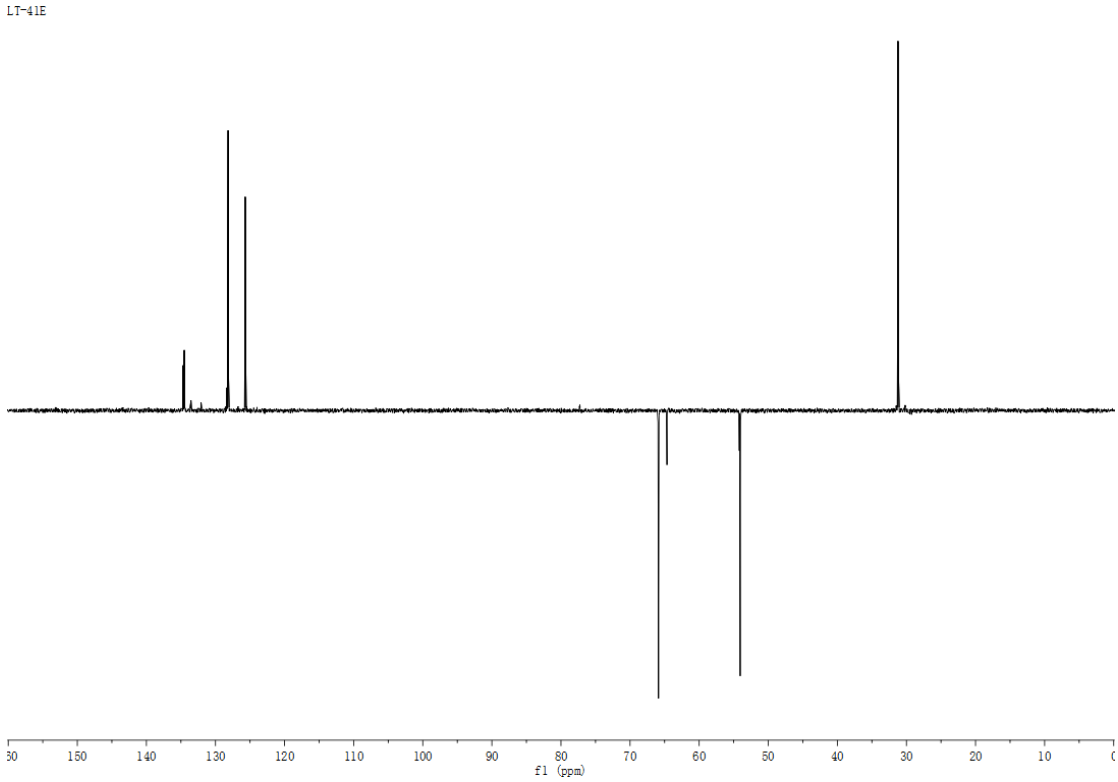
^{19}F NMR (376 MHz, $CDCl_3$):



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

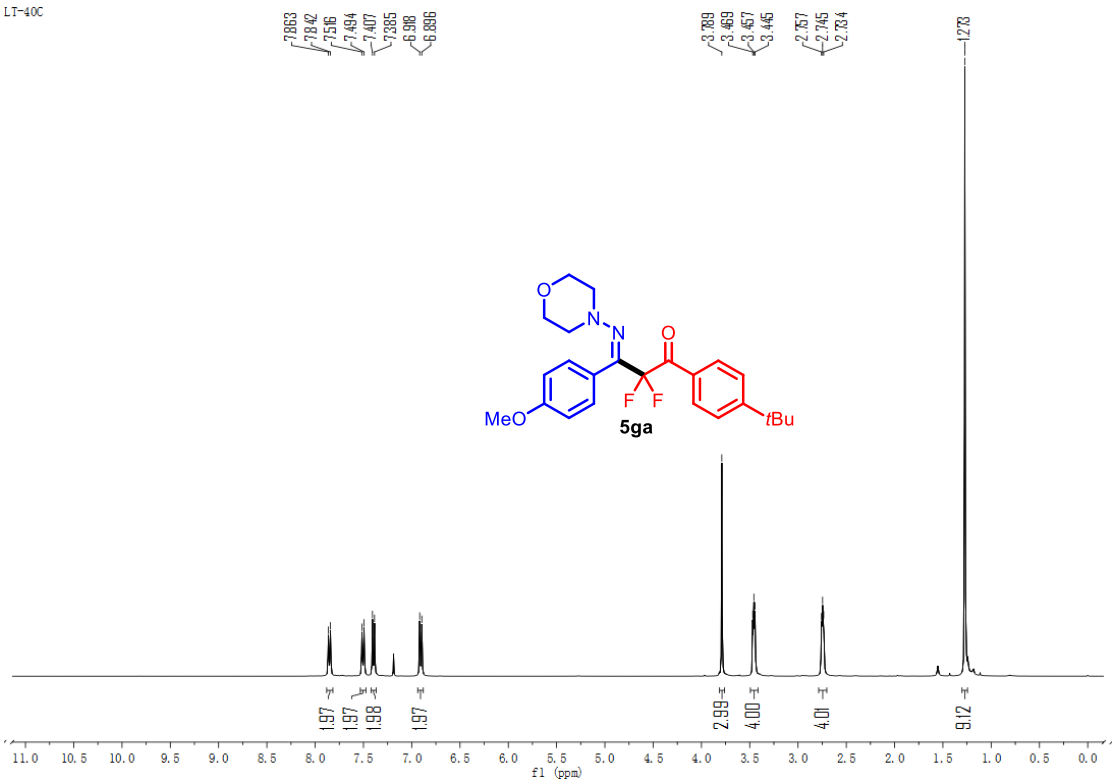


DEPT

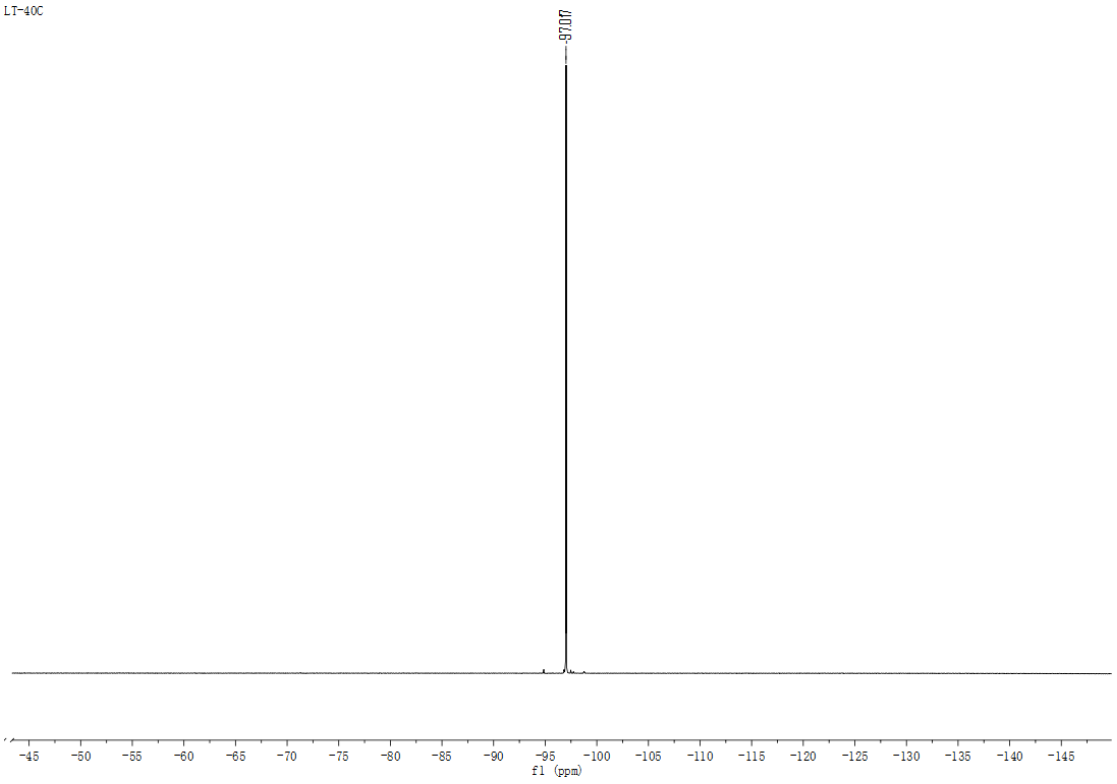


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(4-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ga)

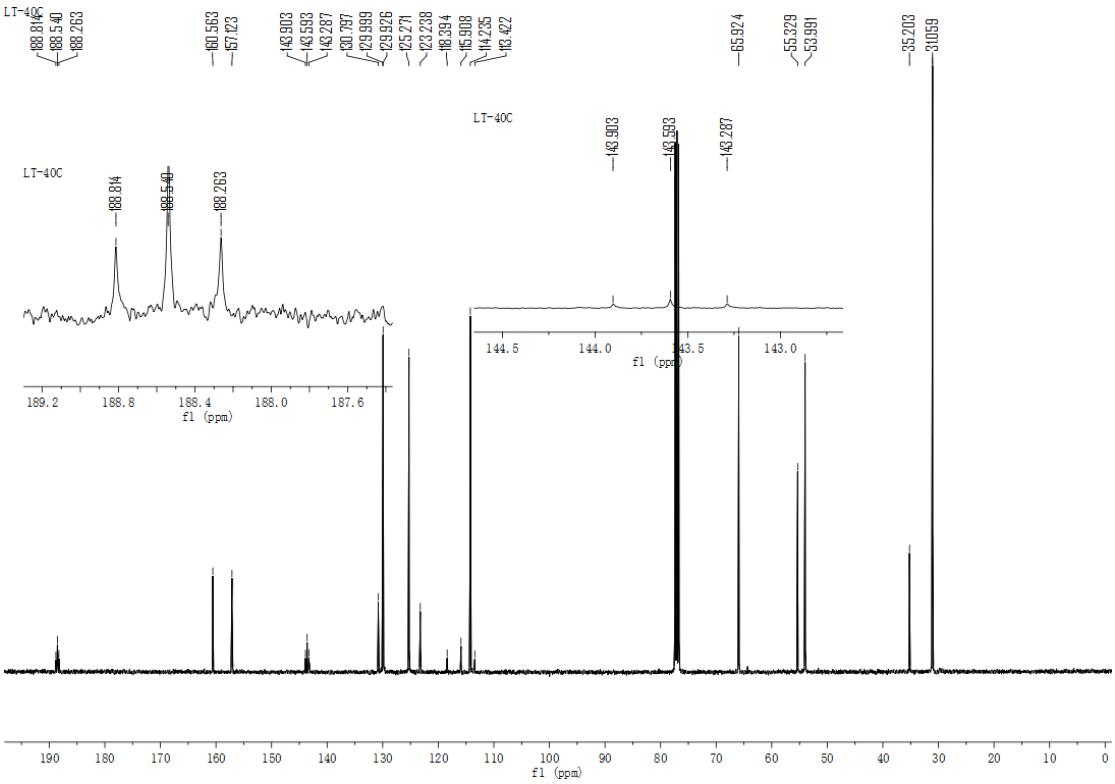
^{1}H NMR (400 MHz, $CDCl_3$)



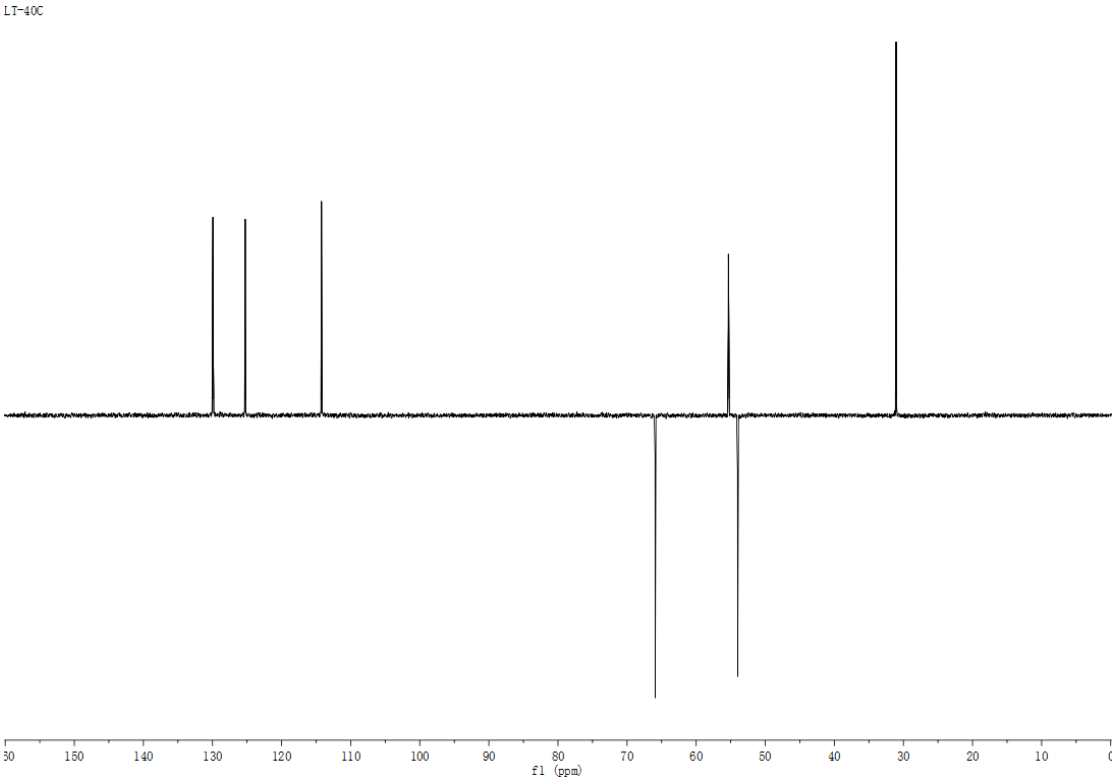
^{19}F NMR (376 MHz, $CDCl_3$):



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

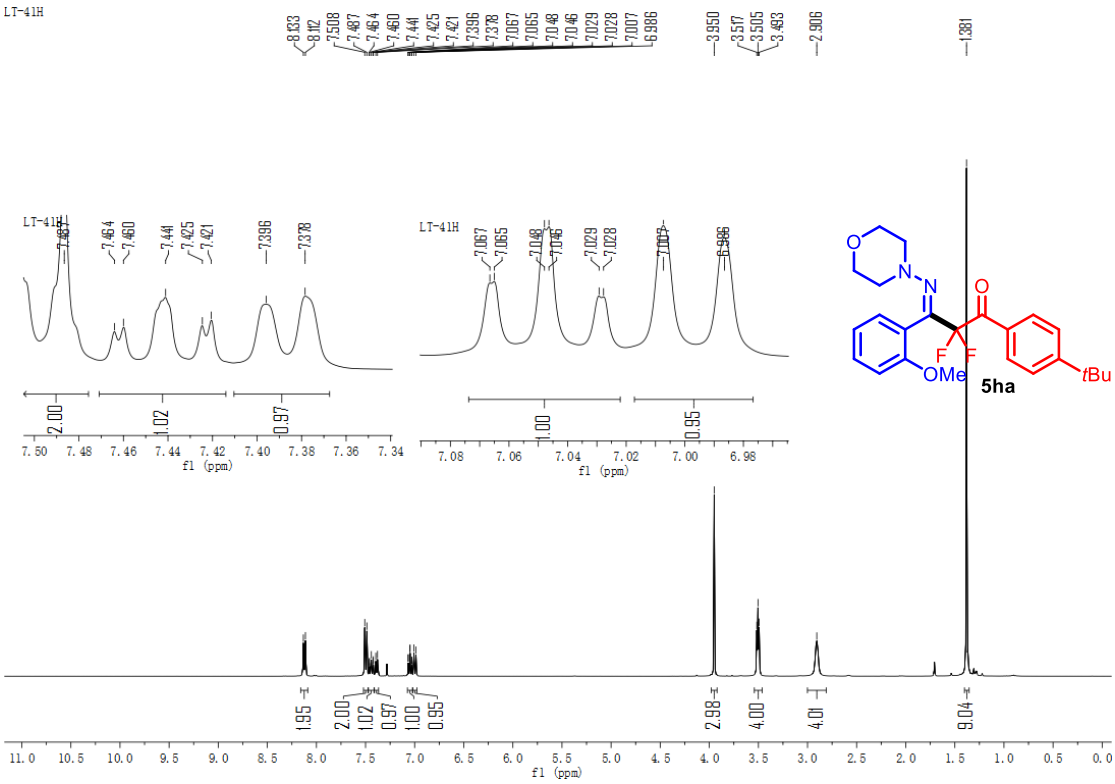


DEPT

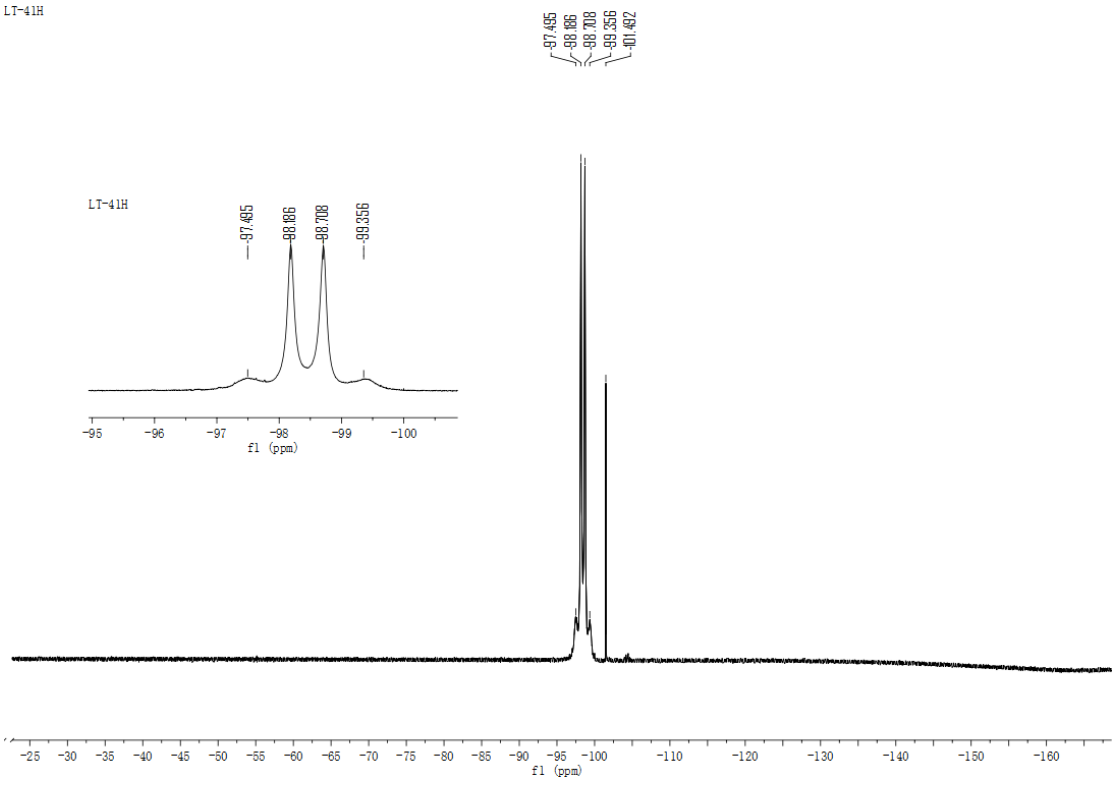


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(2-methoxyphenyl)-3-(morpholinoimino)propan-1-one (5ha)

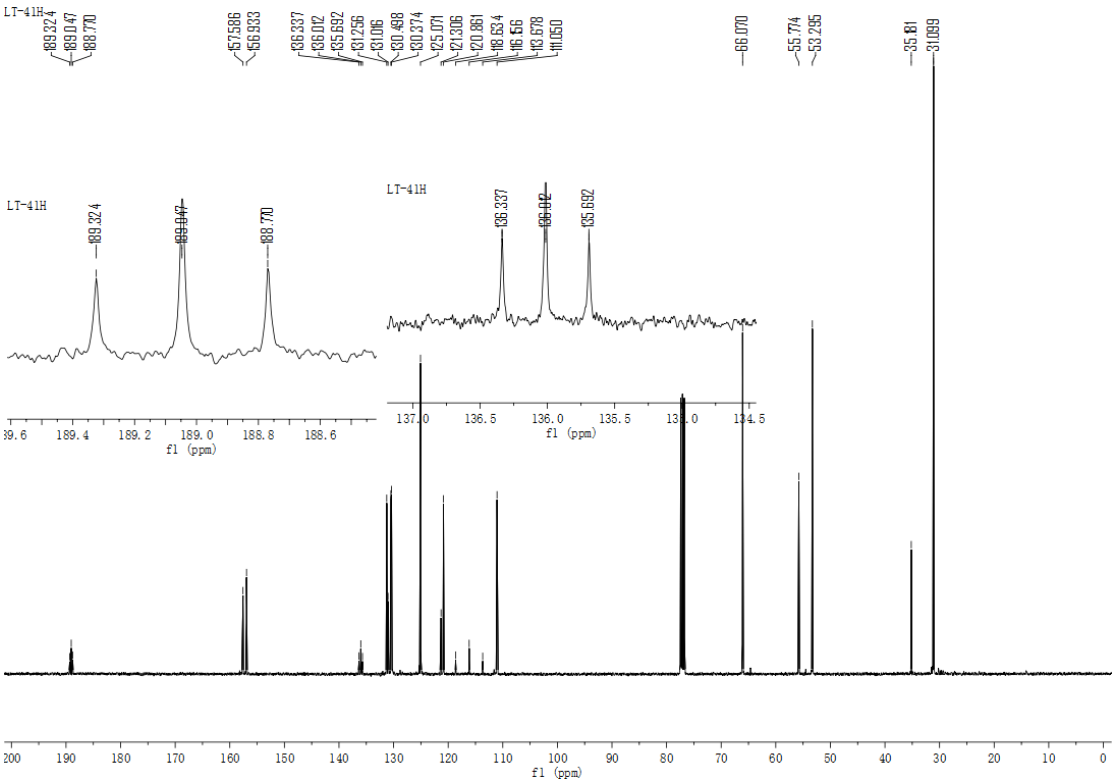
^{1}H NMR (400 MHz, $CDCl_3$)



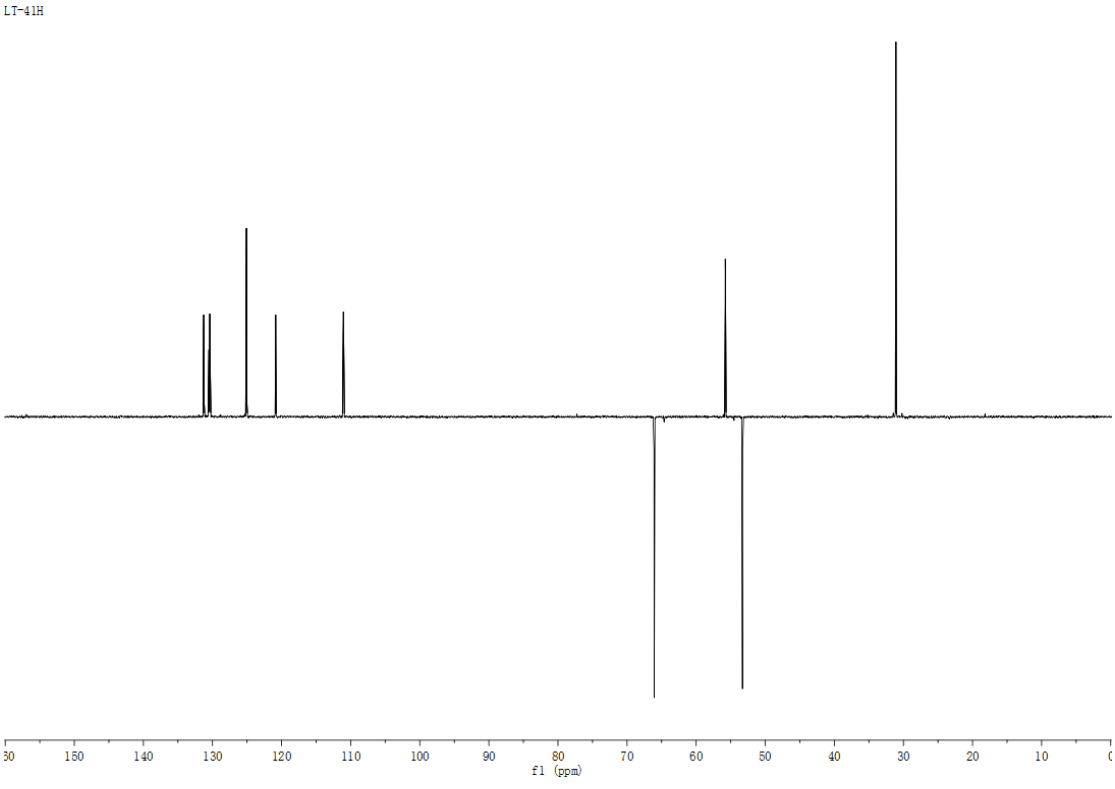
^{19}F NMR (376 MHz, $CDCl_3$):



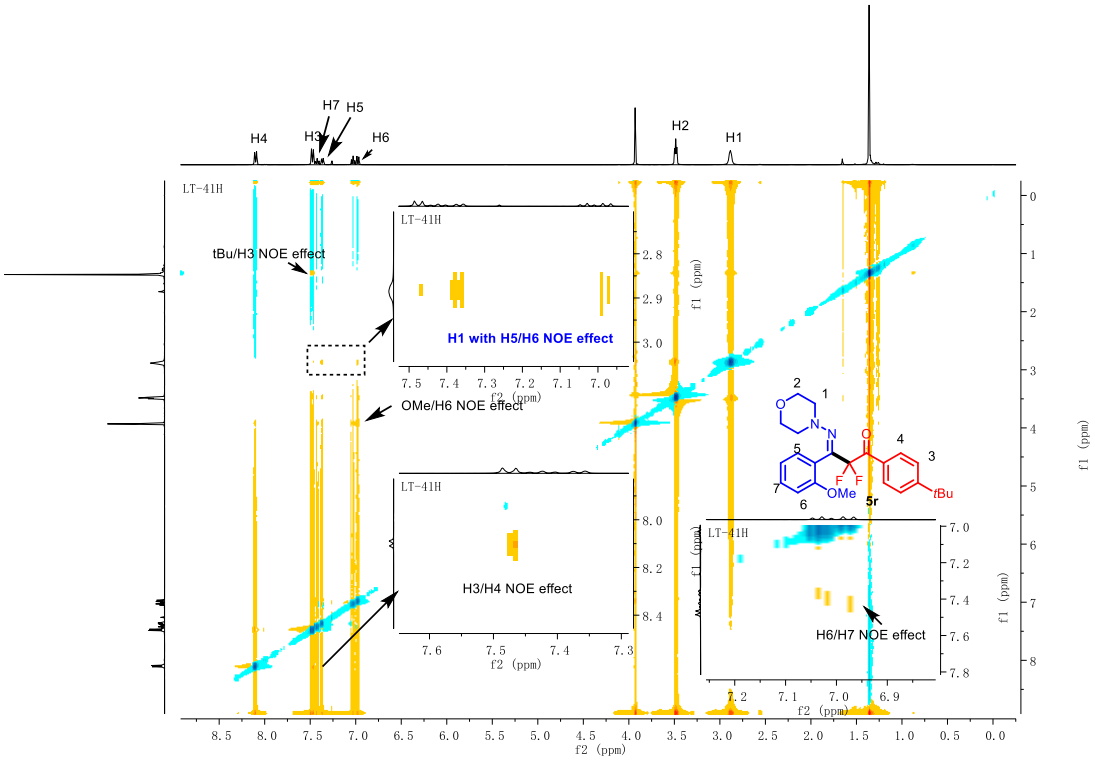
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

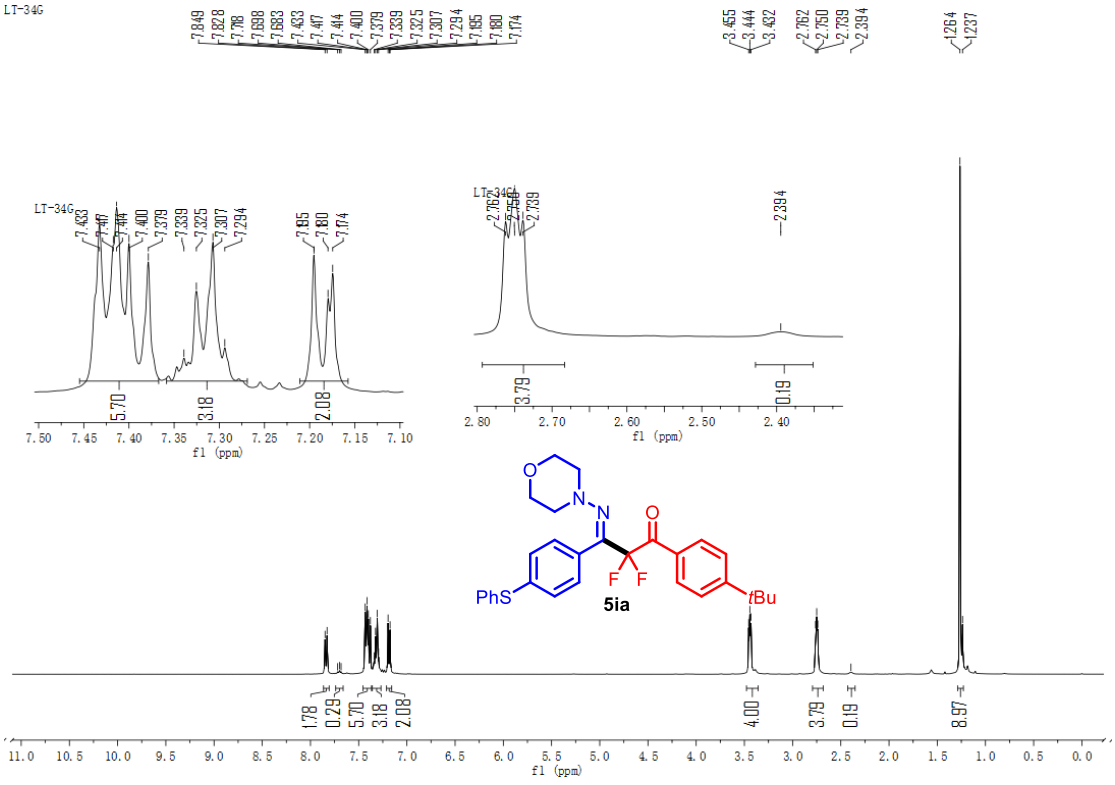


ROESY

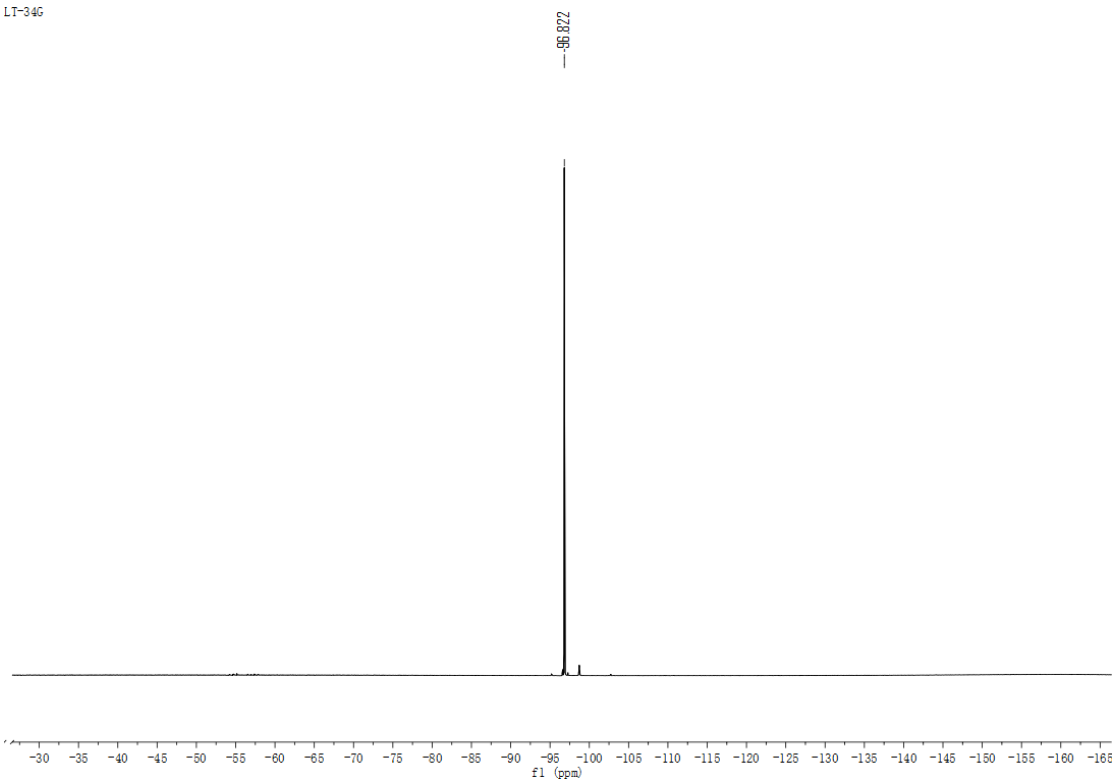


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(4-(phenylthio)phenyl)propan-1-one (5ia)

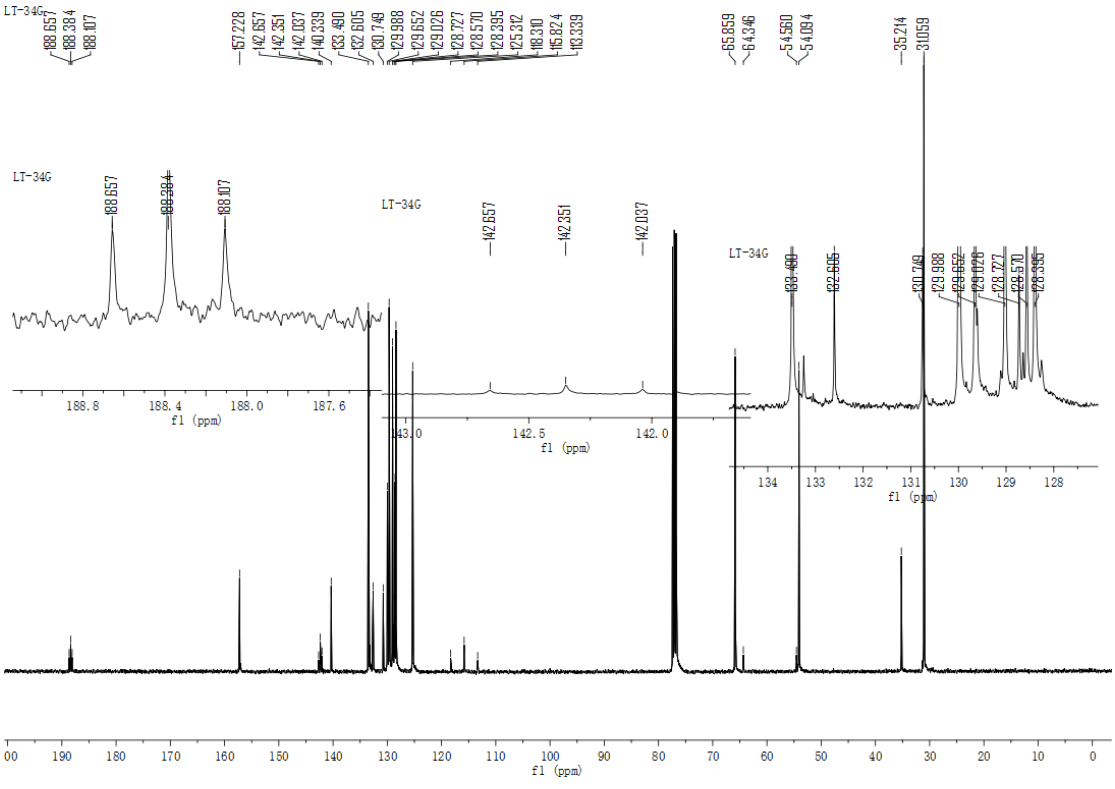
^{1}H NMR (400 MHz, $CDCl_3$)



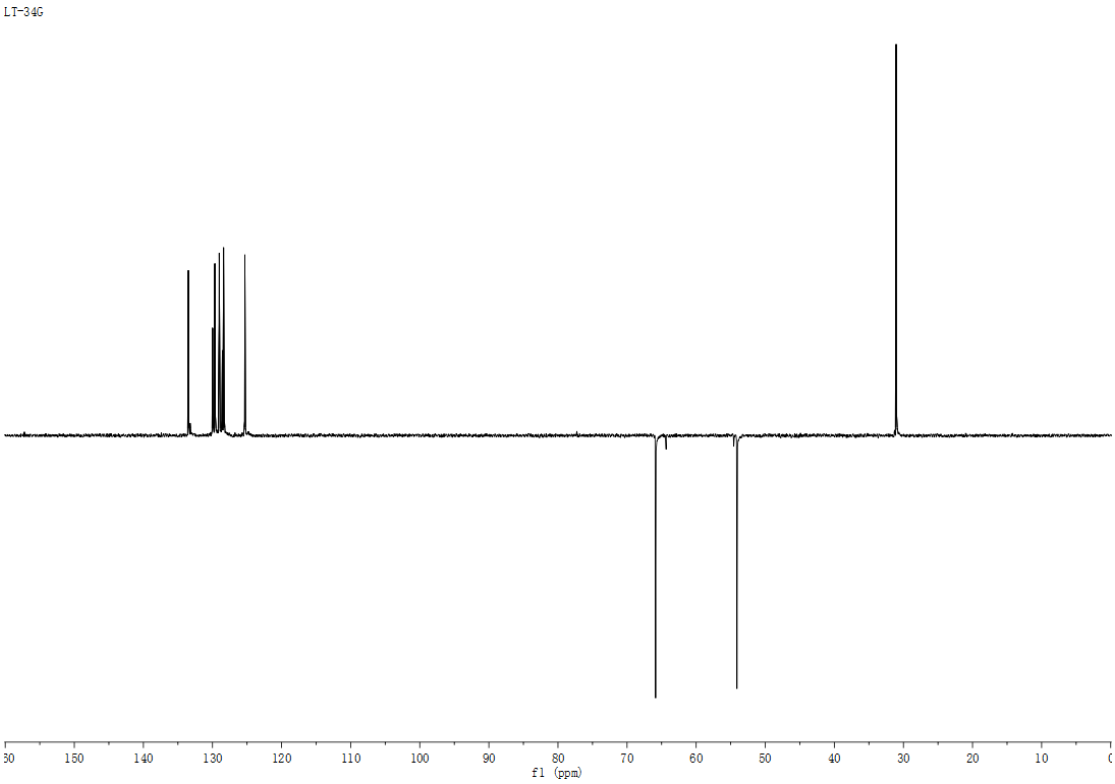
^{19}F NMR (376 MHz, $CDCl_3$):



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

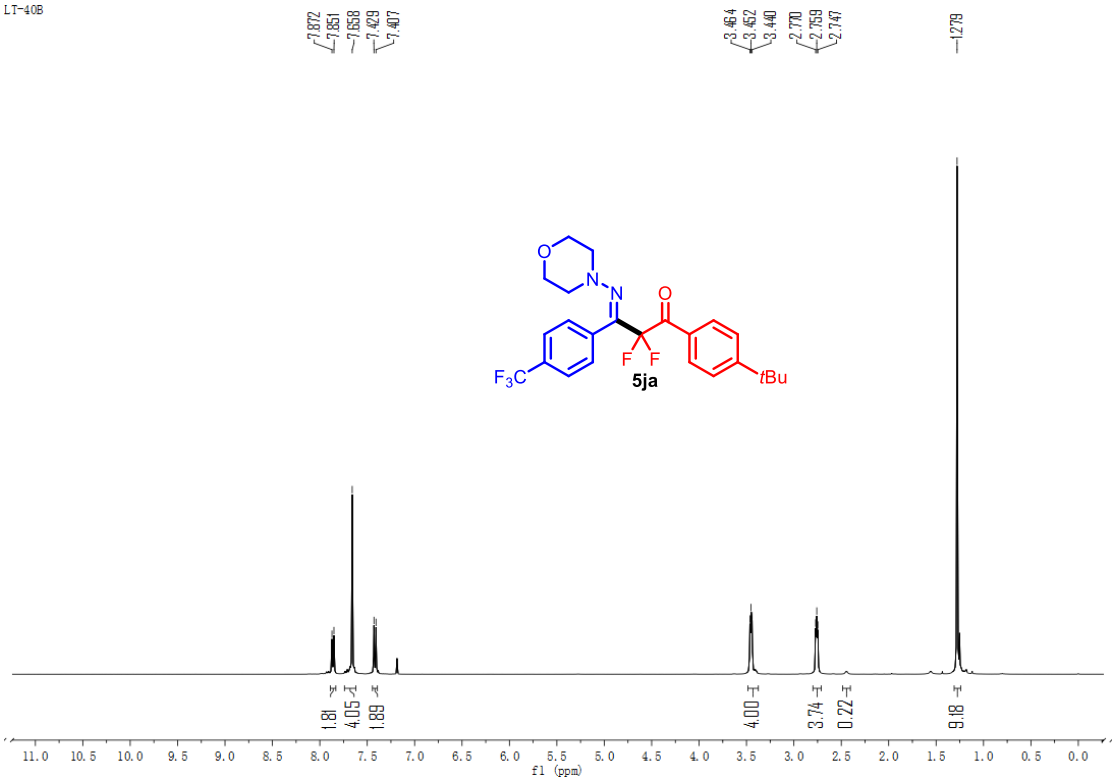


DEPT

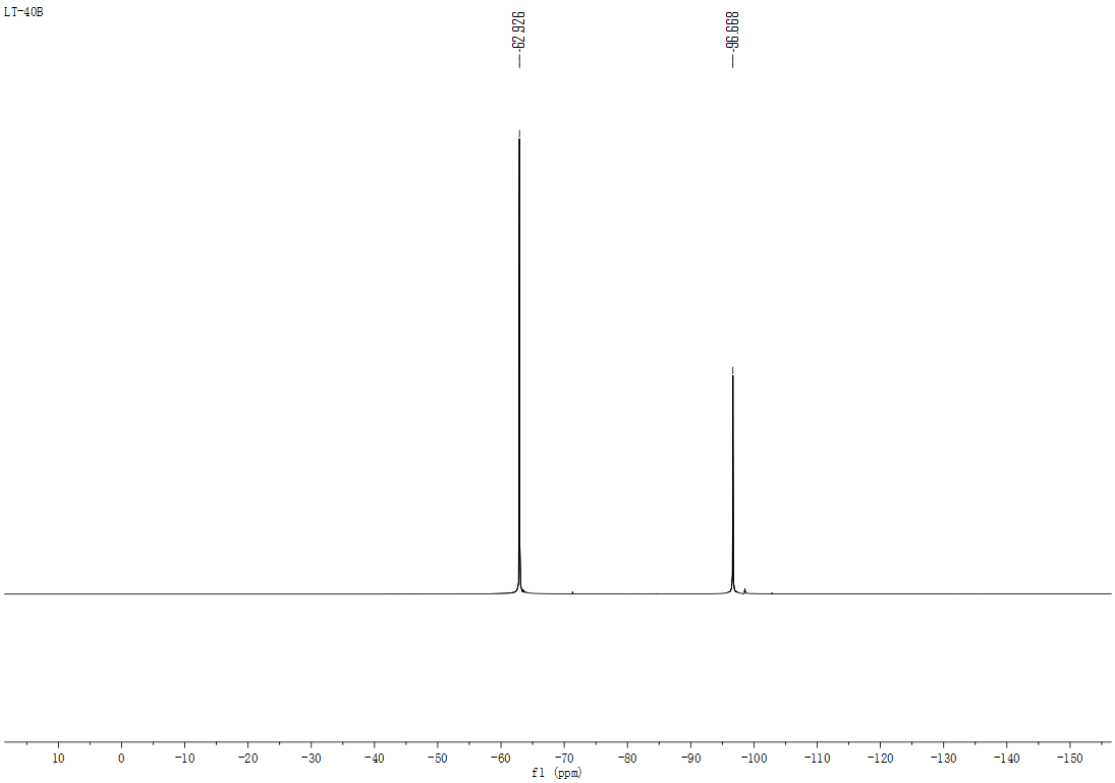


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(4-(trifluoromethyl)phenyl)propan-1-one (5ja)

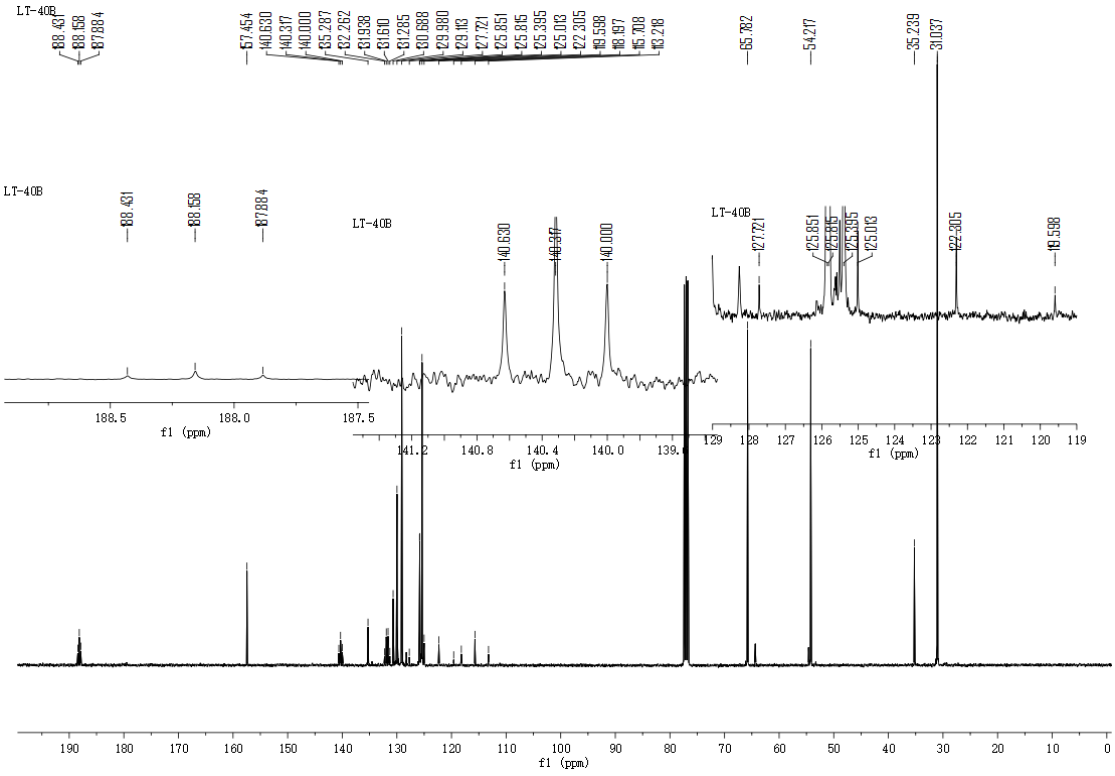
^{1}H NMR (400 MHz, $CDCl_3$)



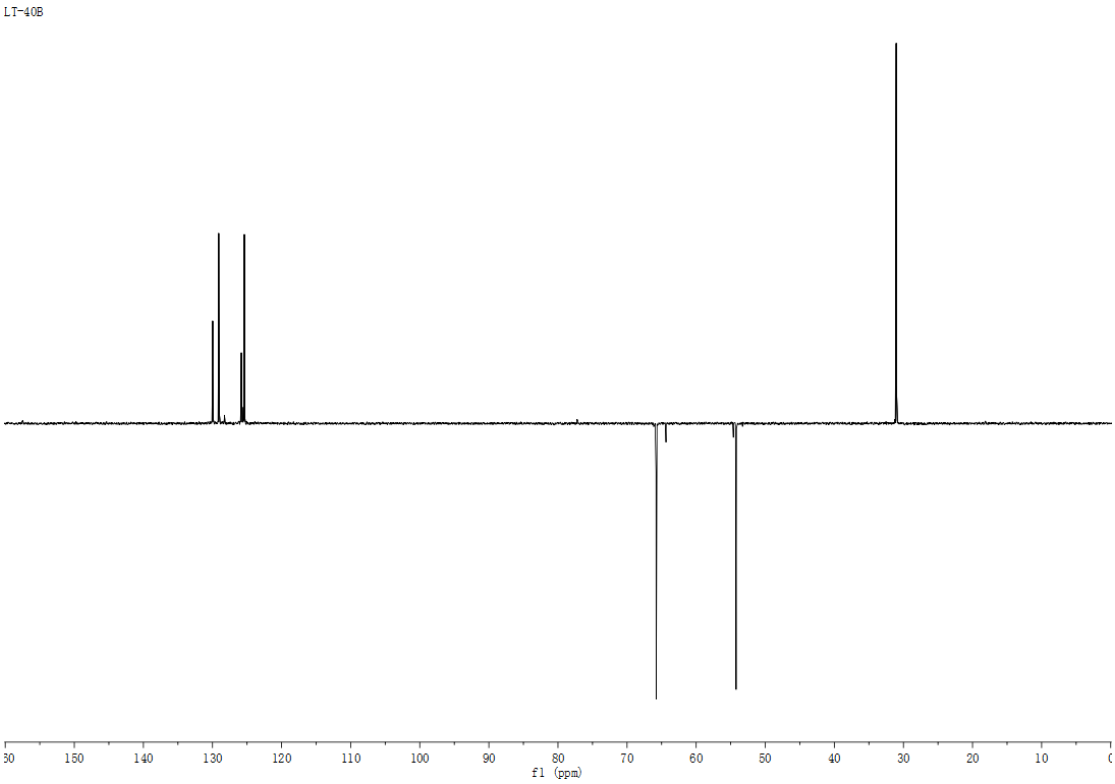
^{19}F NMR (376 MHz, $CDCl_3$):



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

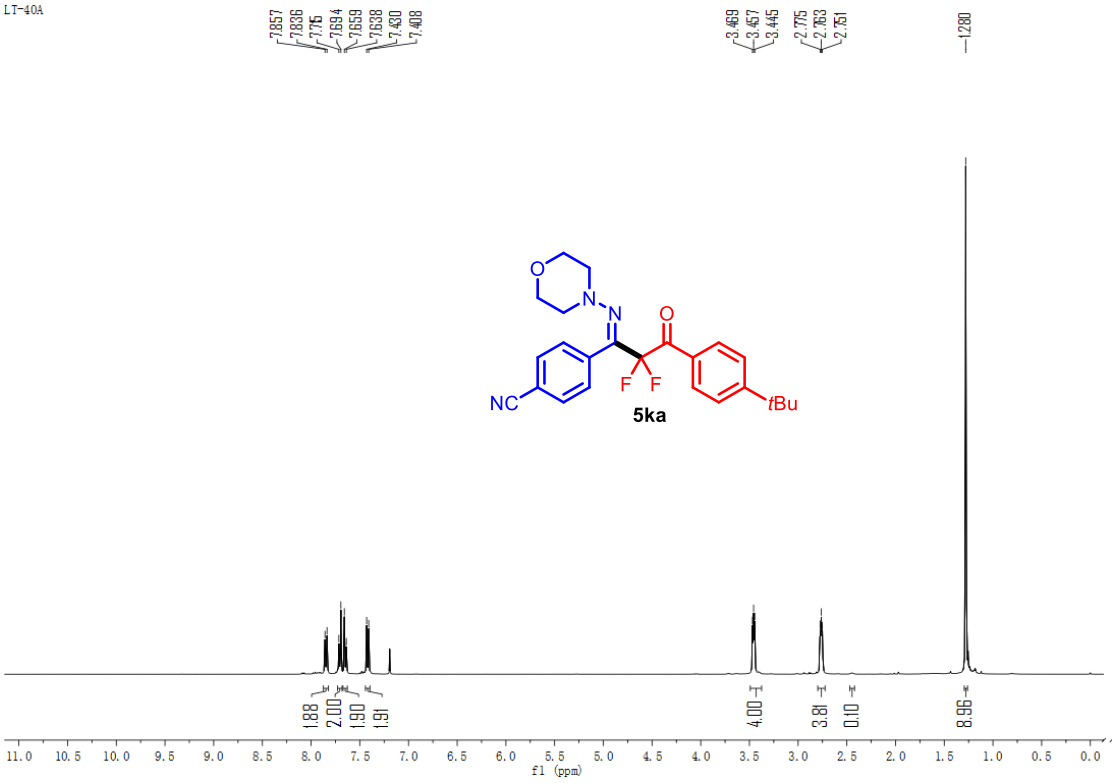


DEPT

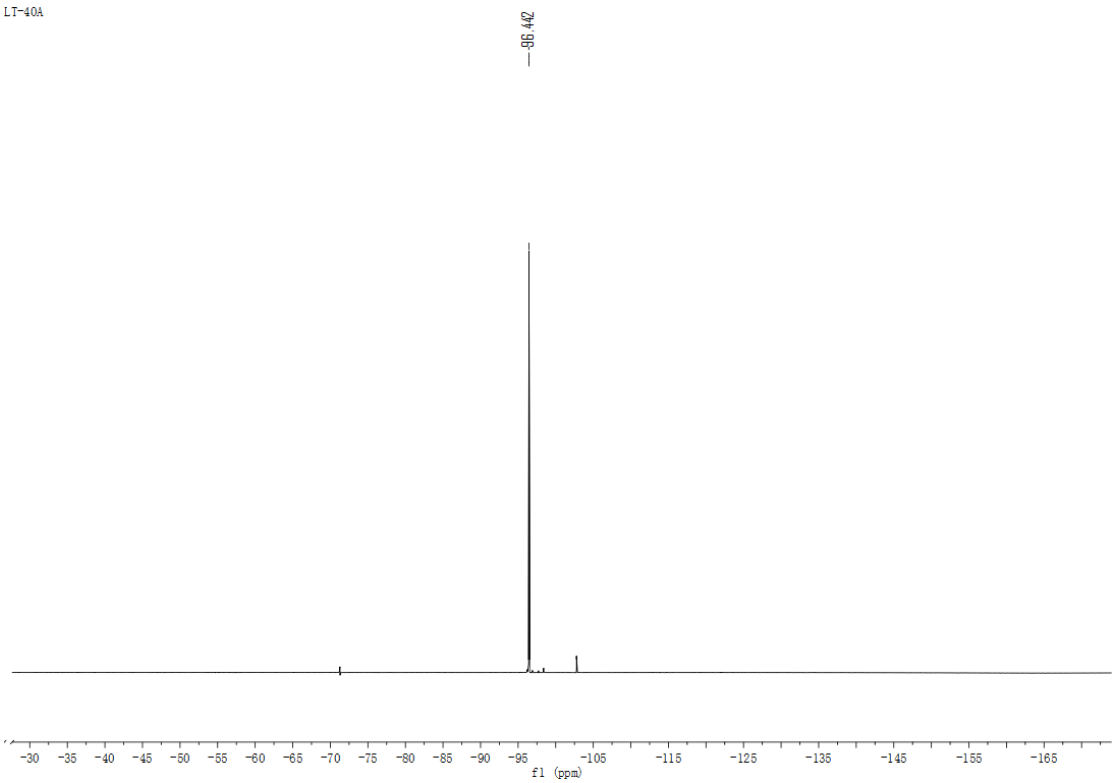


(E)-4-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)benzonitrile (5ka)

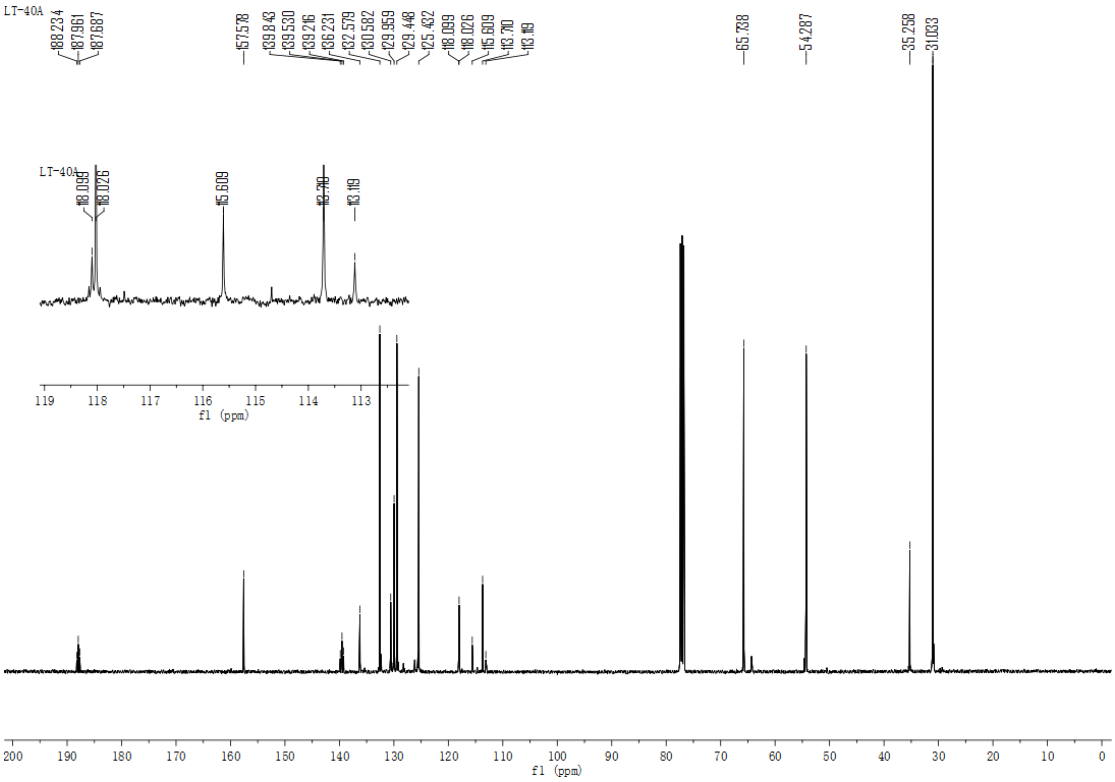
^{1}H NMR (400 MHz, $CDCl_3$)



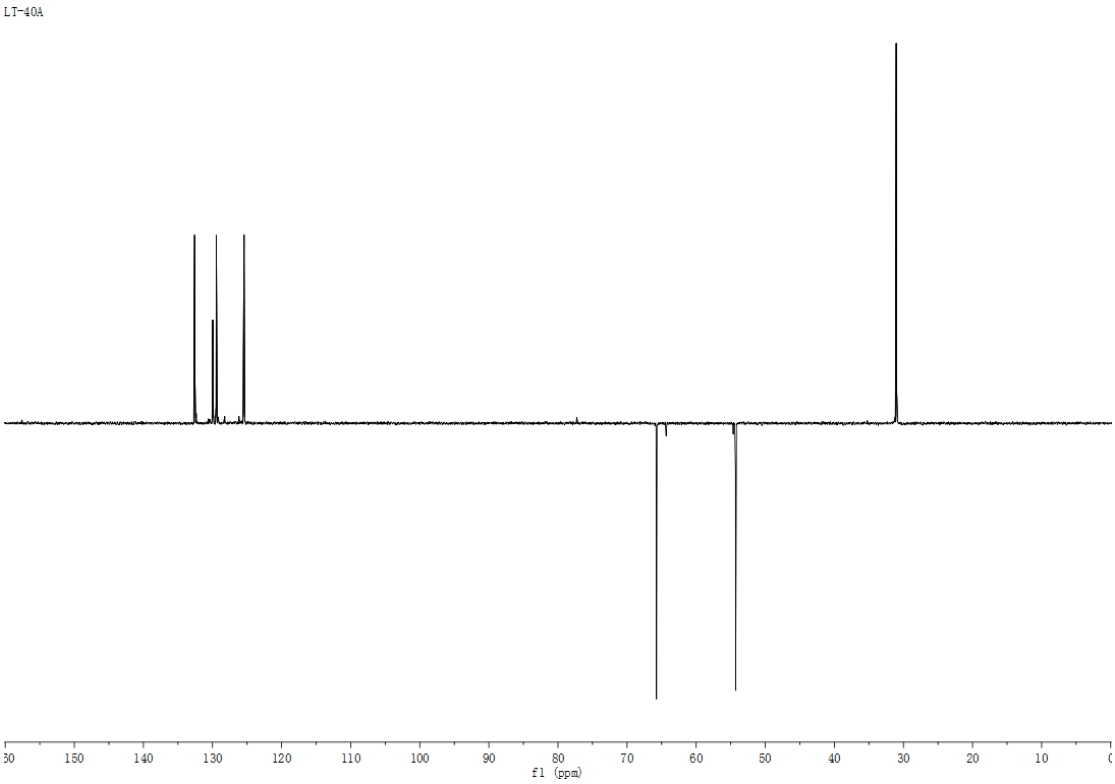
^{19}F NMR (376 MHz, $CDCl_3$):



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

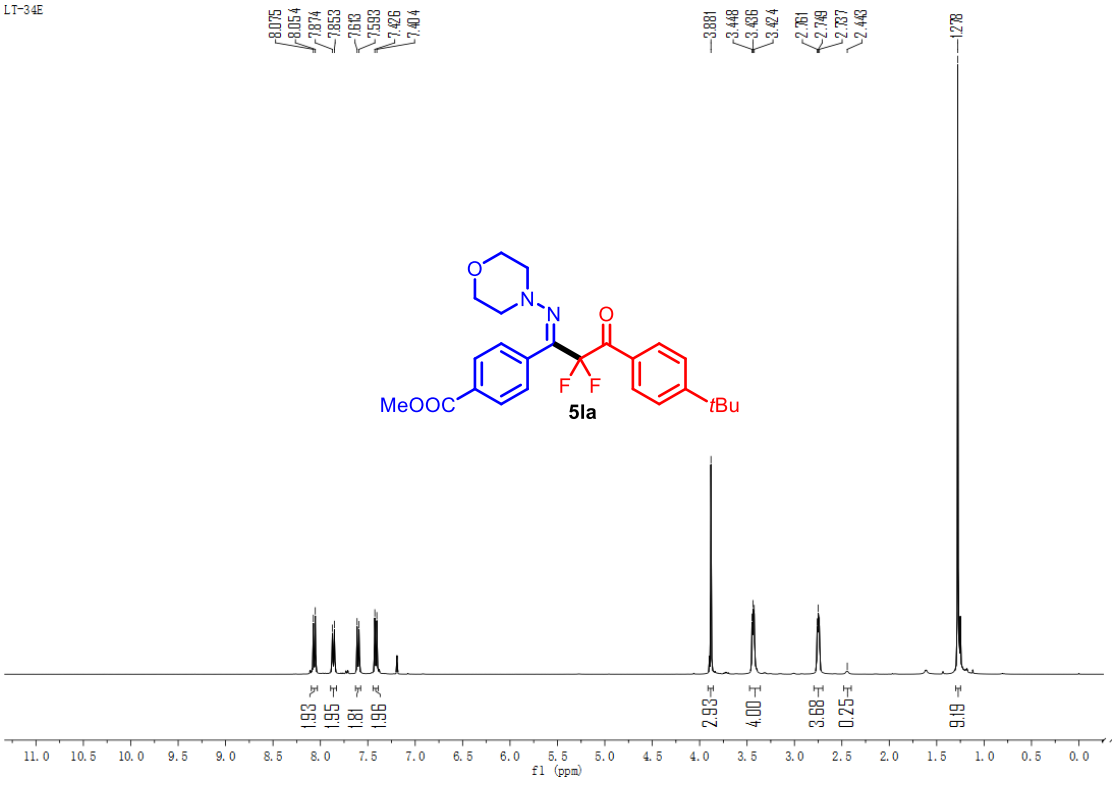


DEPT

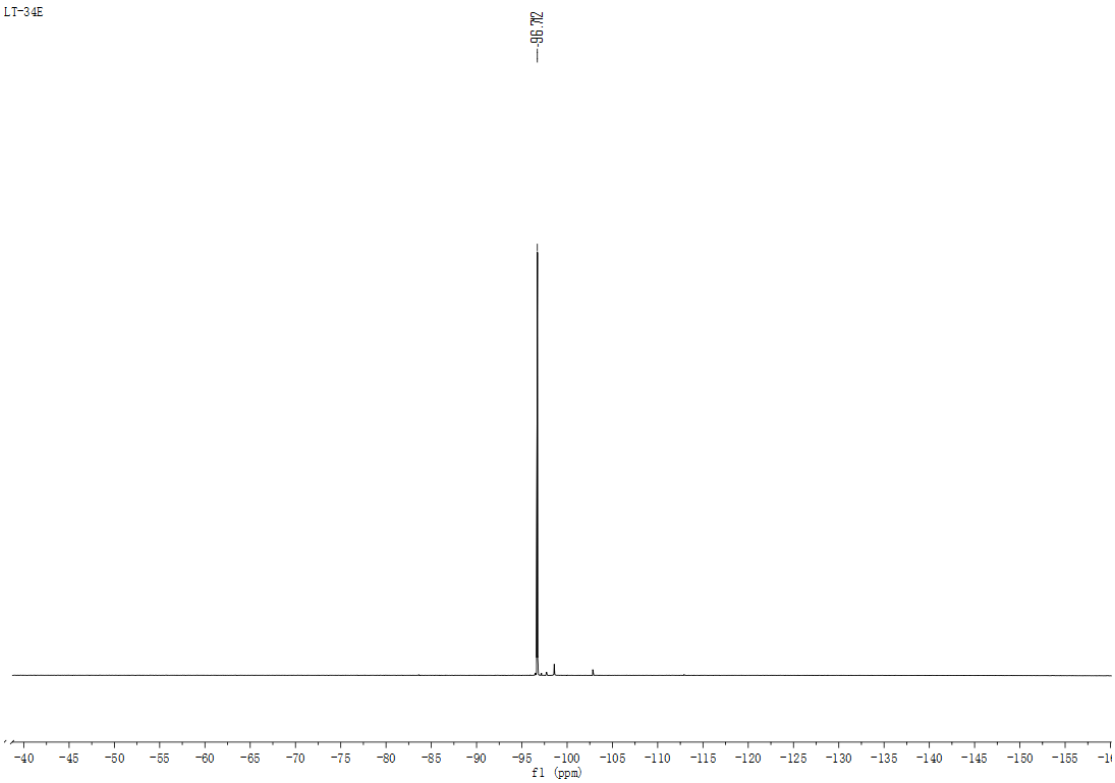


Methyl (E)-4-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)benzoate (5la)

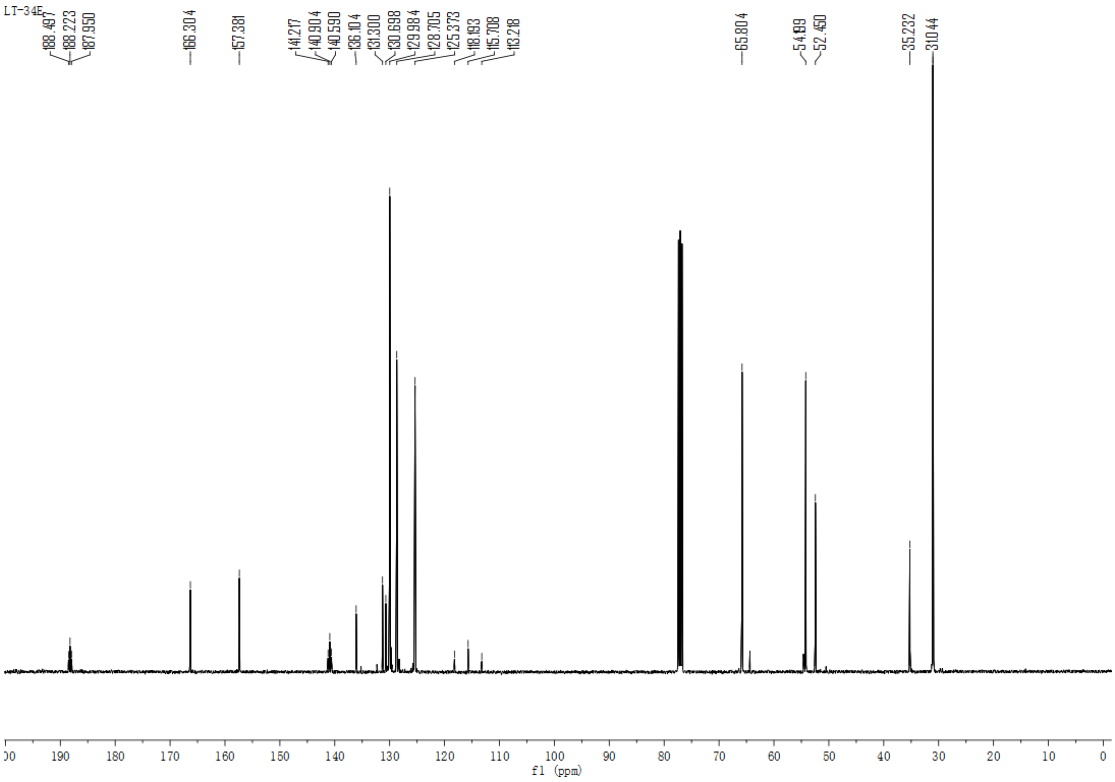
^{1}H NMR (400 MHz, $CDCl_3$)



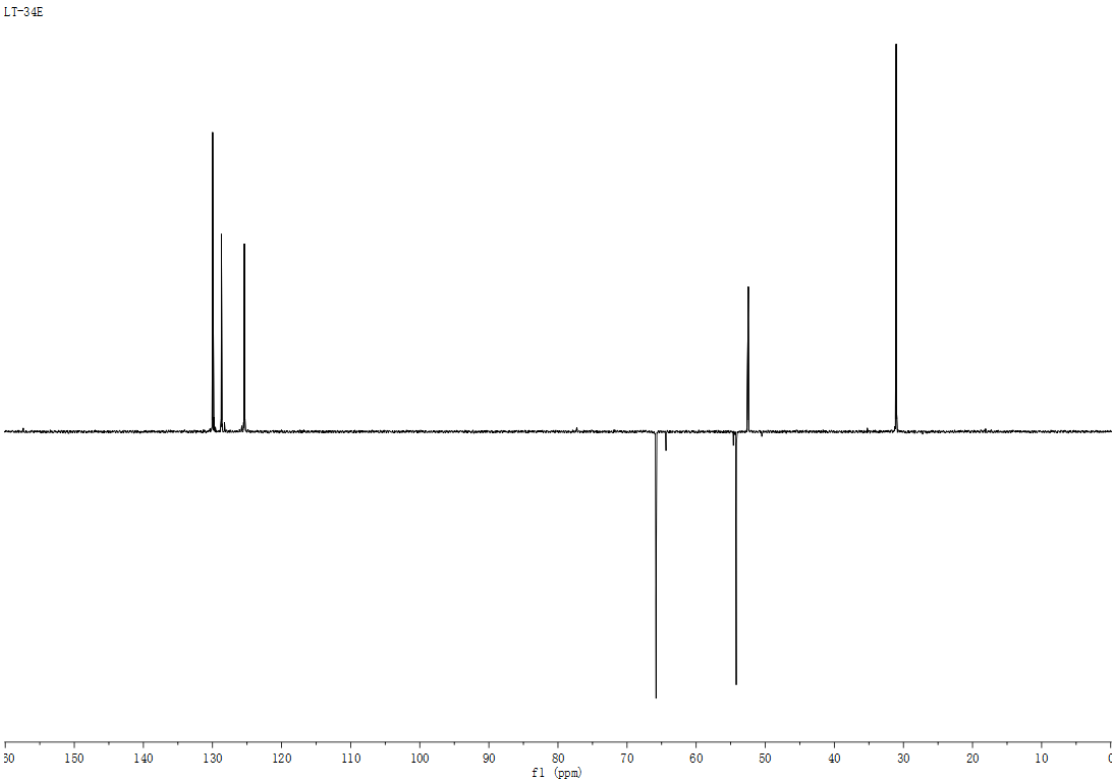
^{19}F NMR (376 MHz, $CDCl_3$):



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

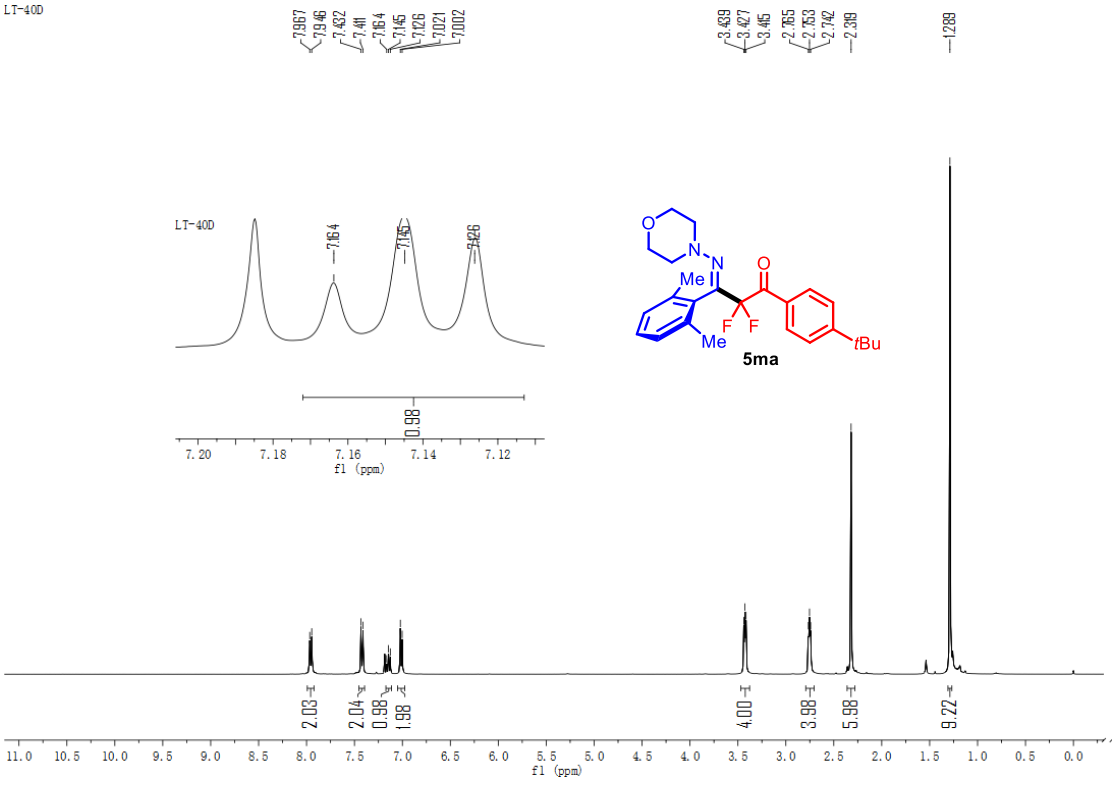


DEPT

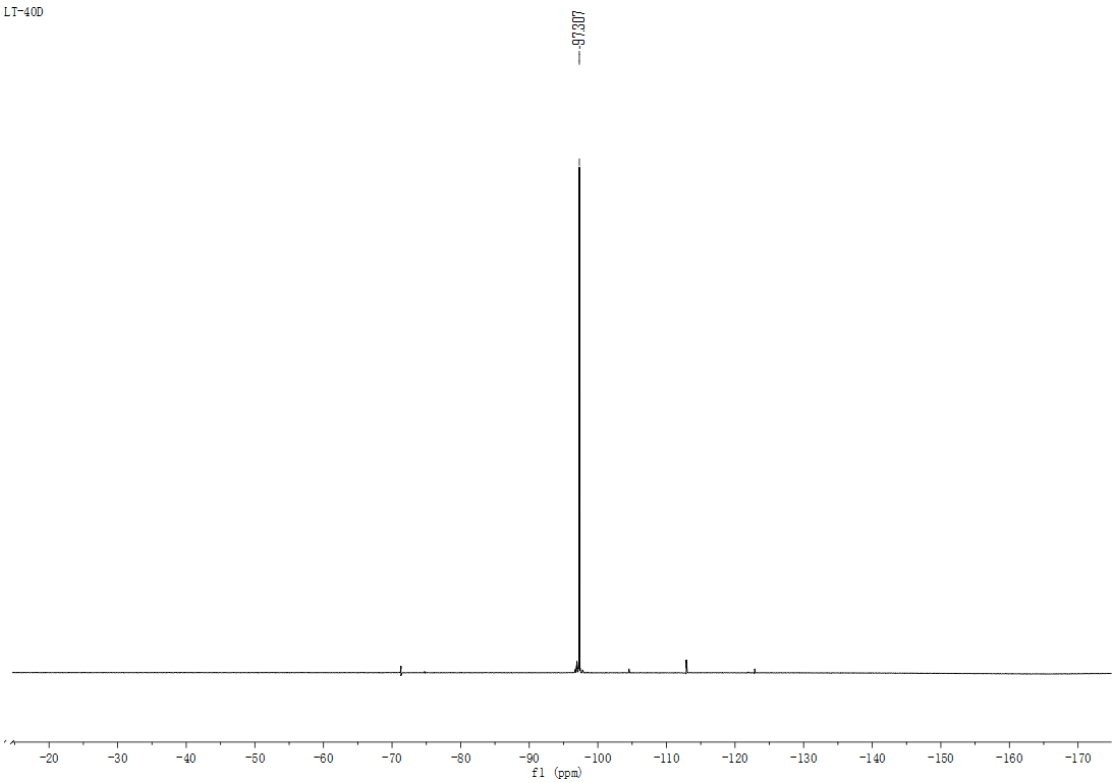


(E)-1-(4-(tert-butyl)phenyl)-3-(2,6-dimethylphenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5ma)

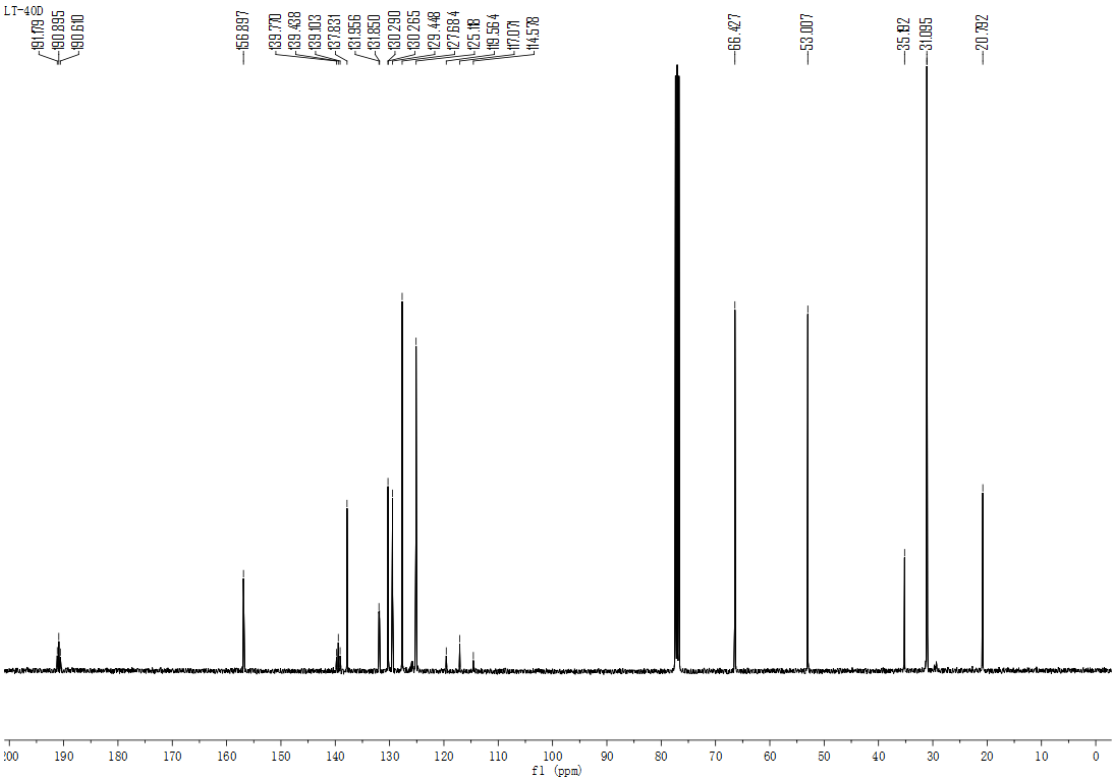
^{1}H NMR (400 MHz, $CDCl_3$)



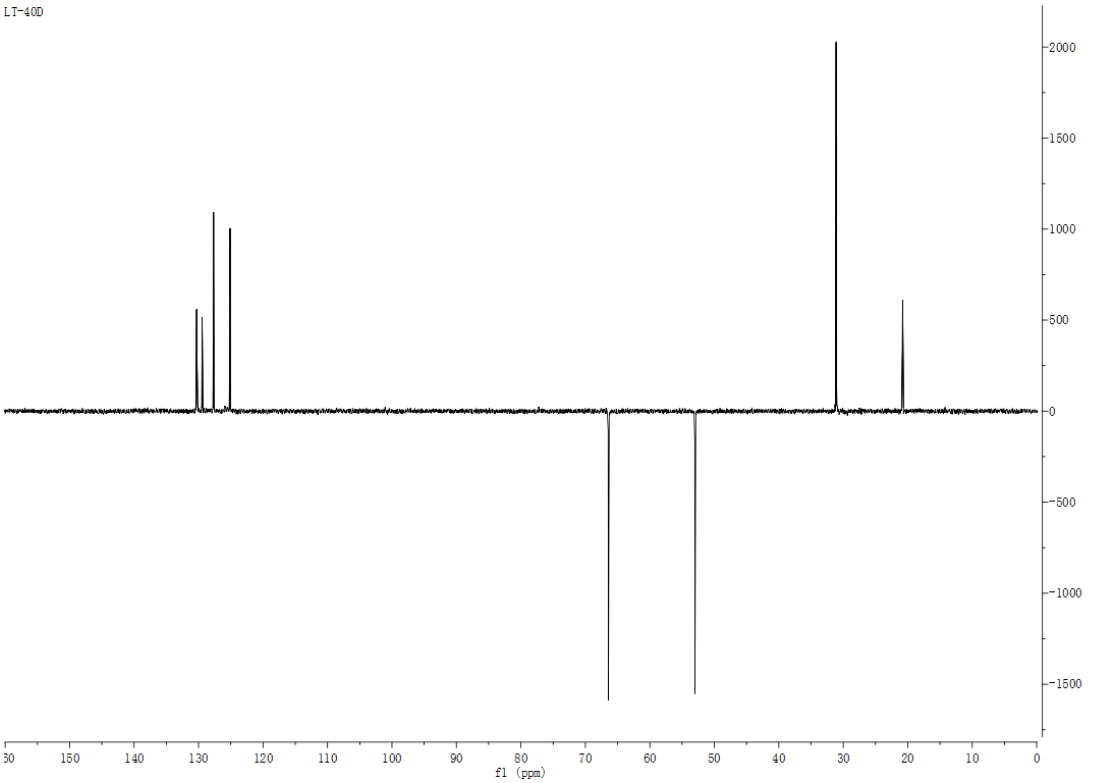
^{19}F NMR (376 MHz, $CDCl_3$):



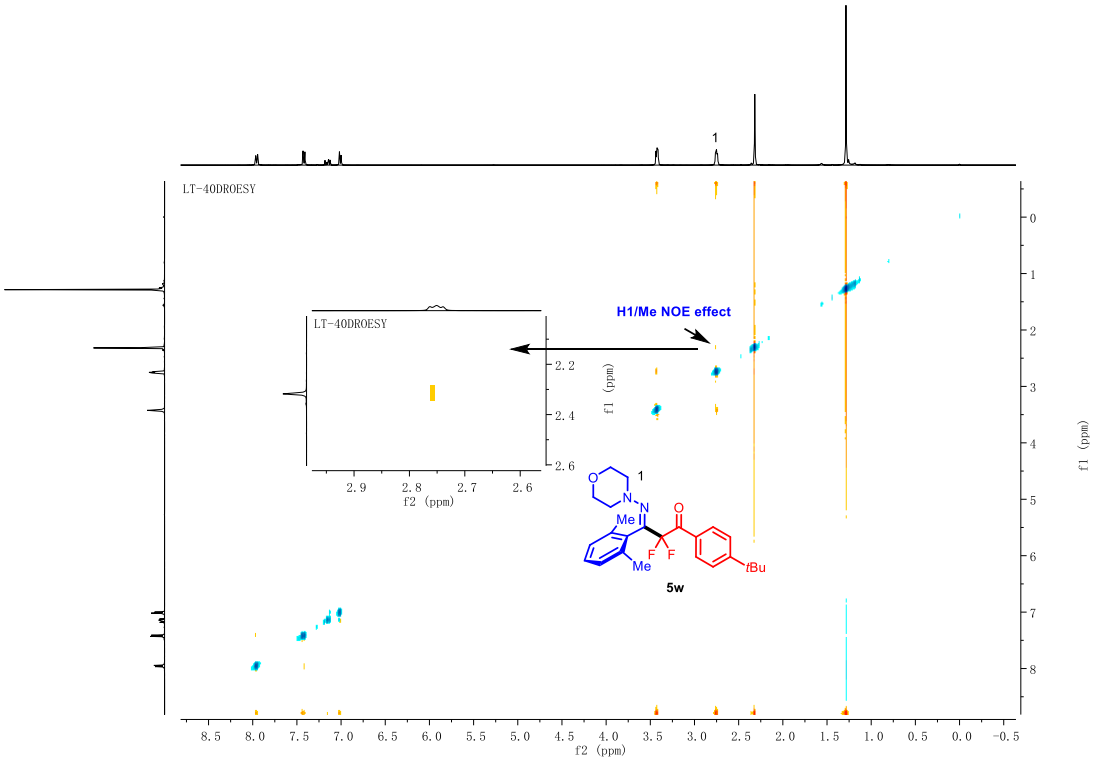
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

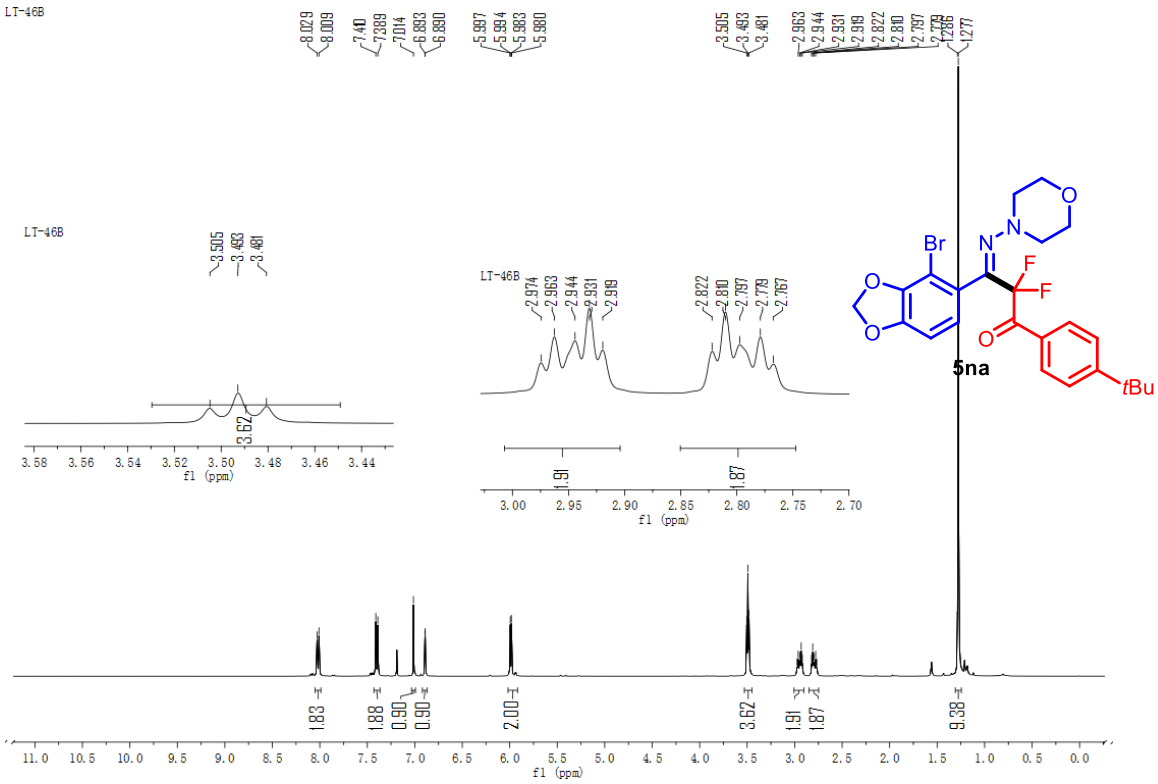


ROESY

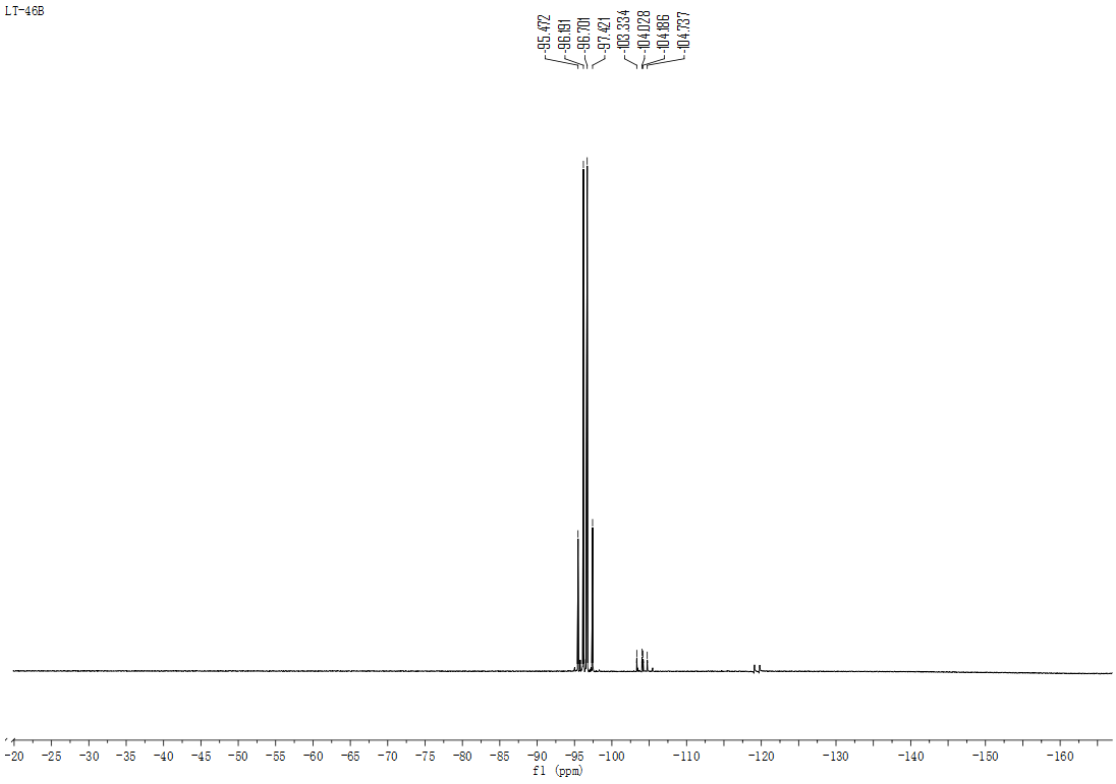


(Z)-3-(4-bromobenzo[d][1,3]dioxol-5-yl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5na)

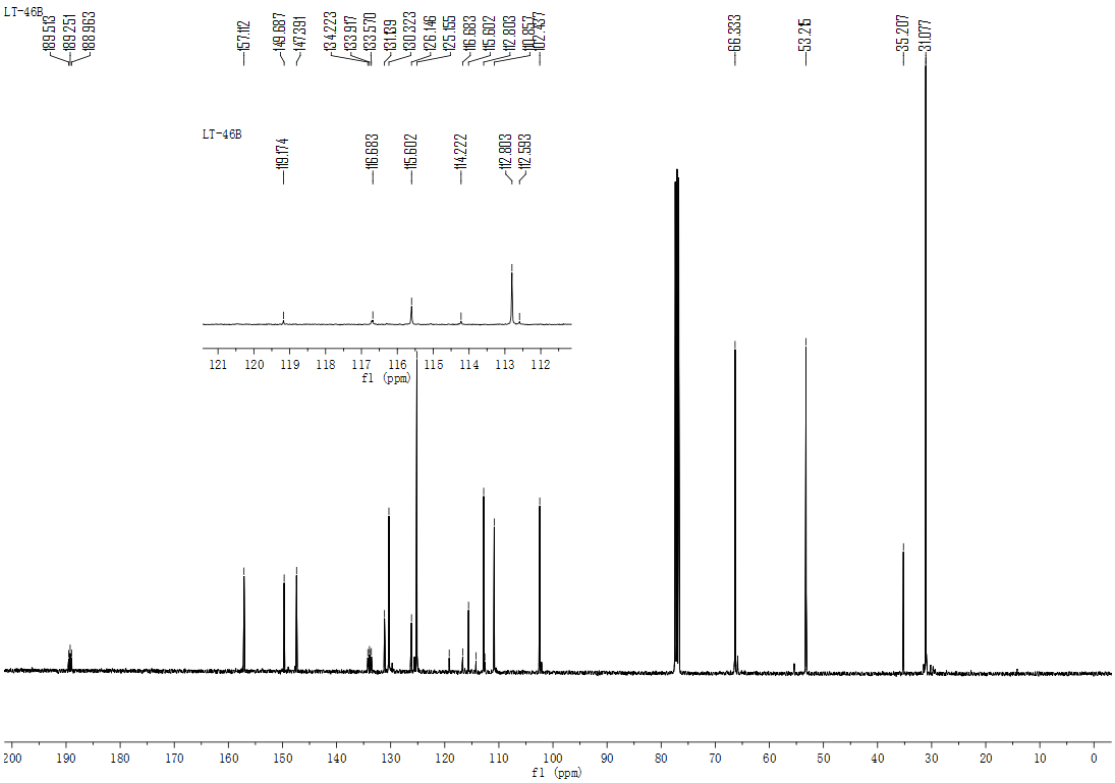
^{1}H NMR (400 MHz, $CDCl_3$)



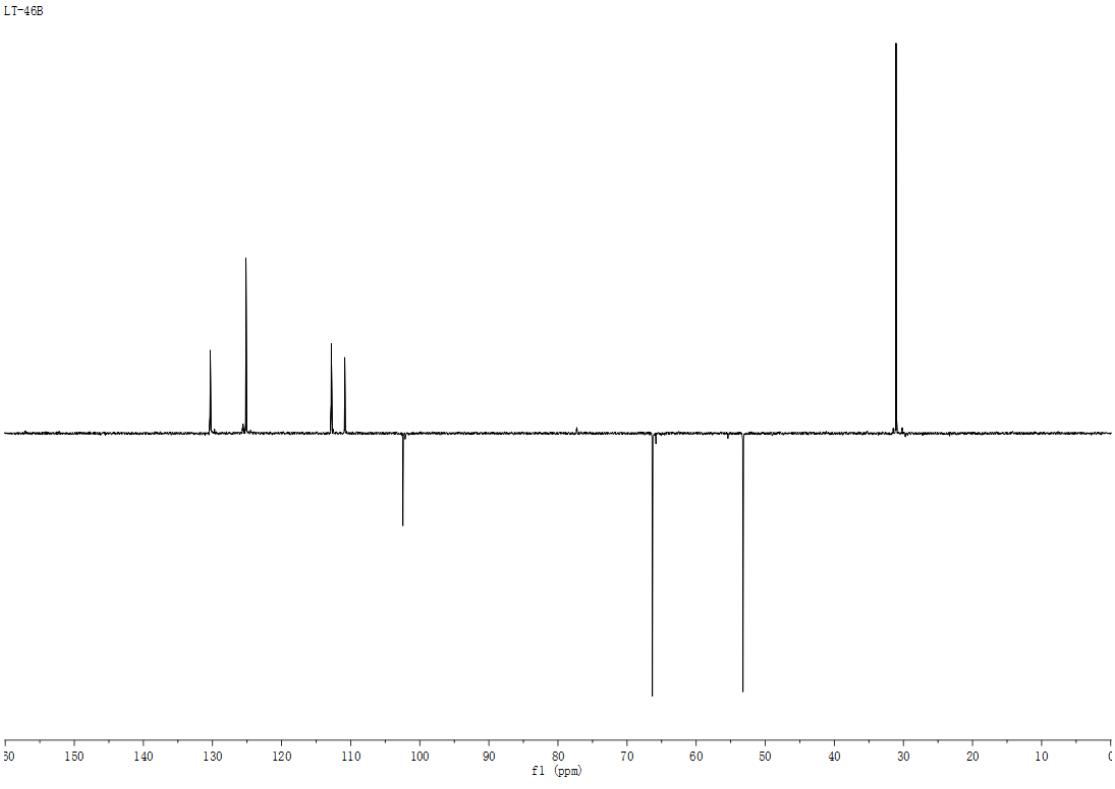
^{19}F NMR (376 MHz, $CDCl_3$):



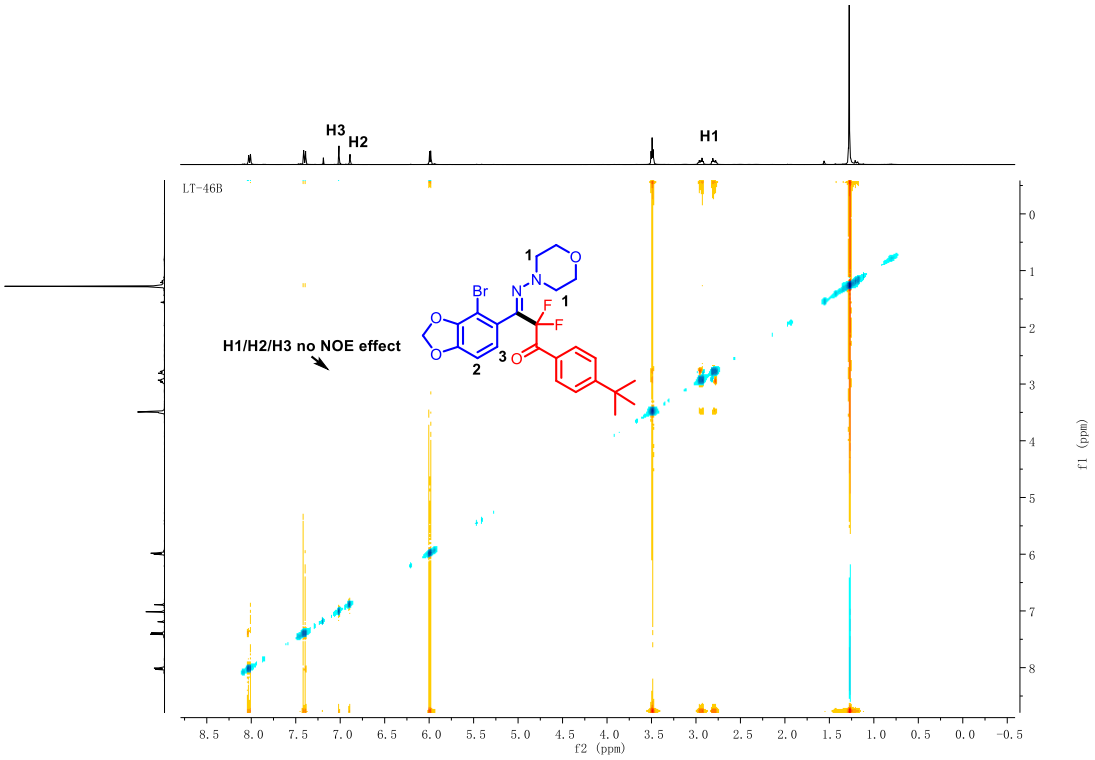
^{13}C NMR (100 MHz, $CDCl_3$):



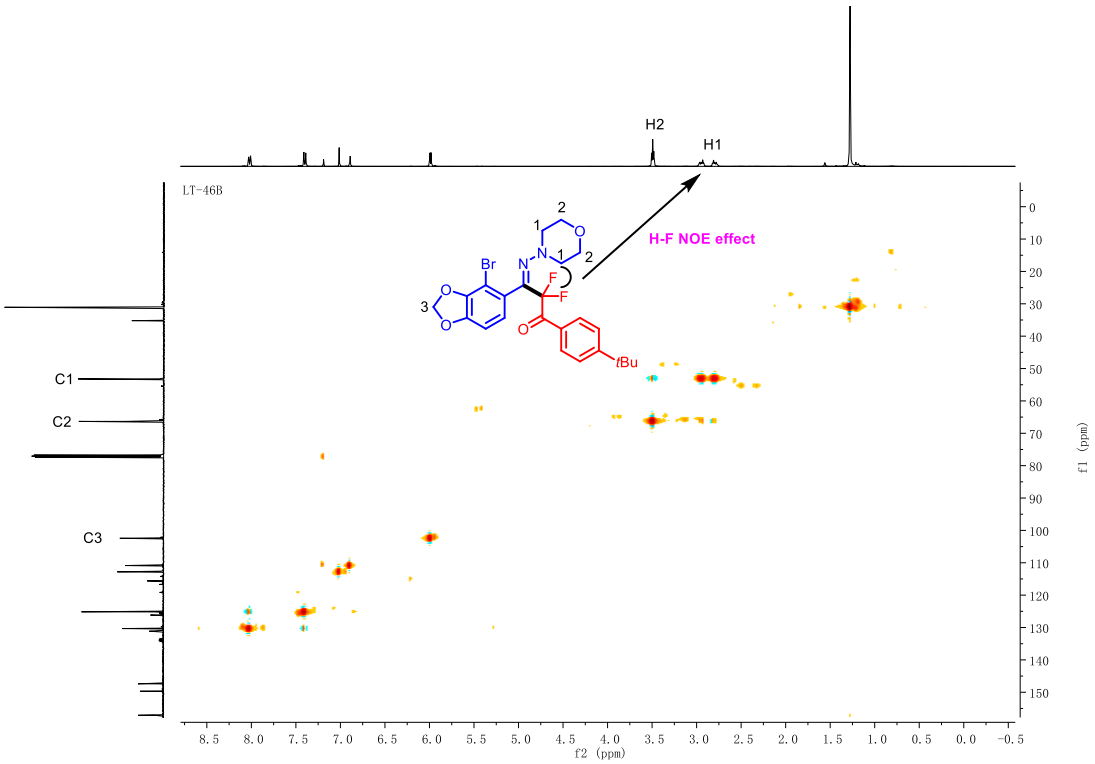
DEPT



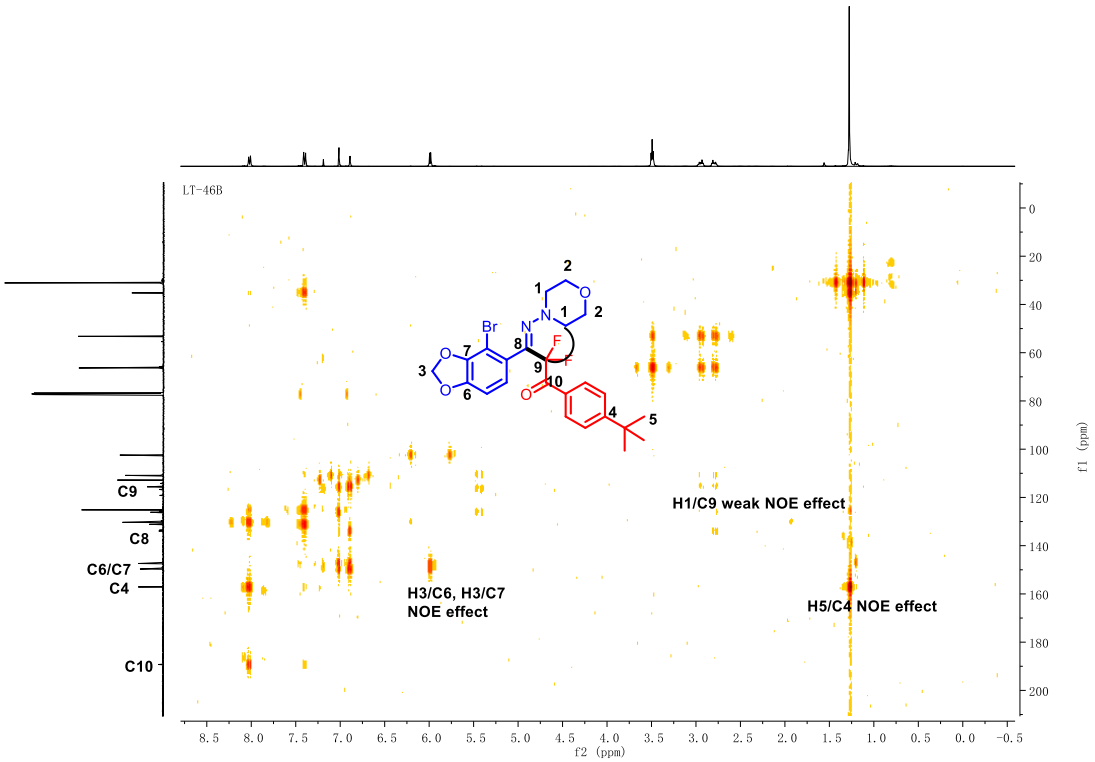
ROESY



HSQC

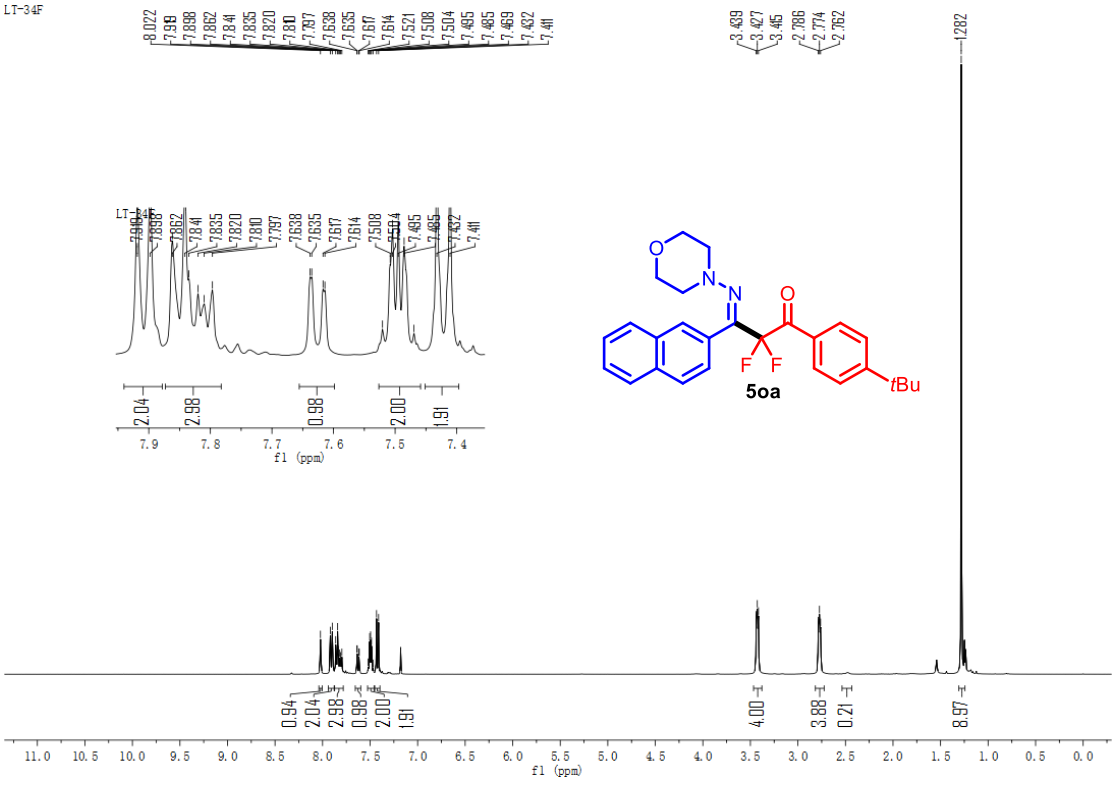


HMBC

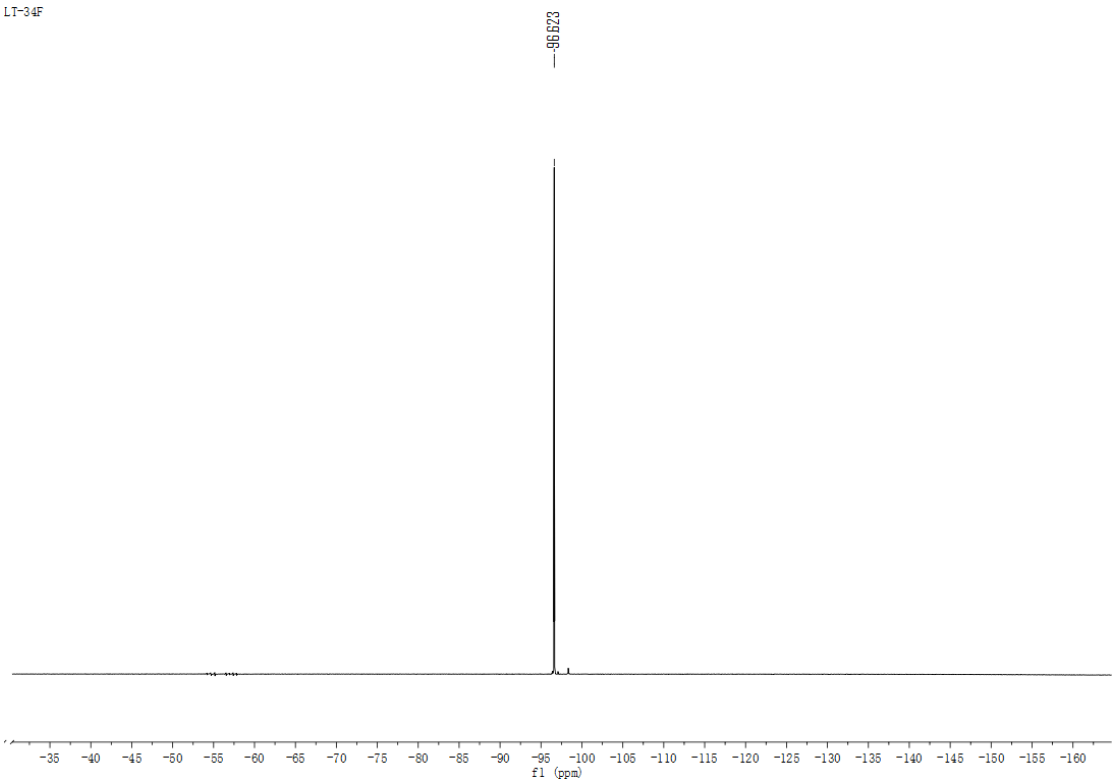


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(naphthalen-2-yl)propan-1-one (5oa)

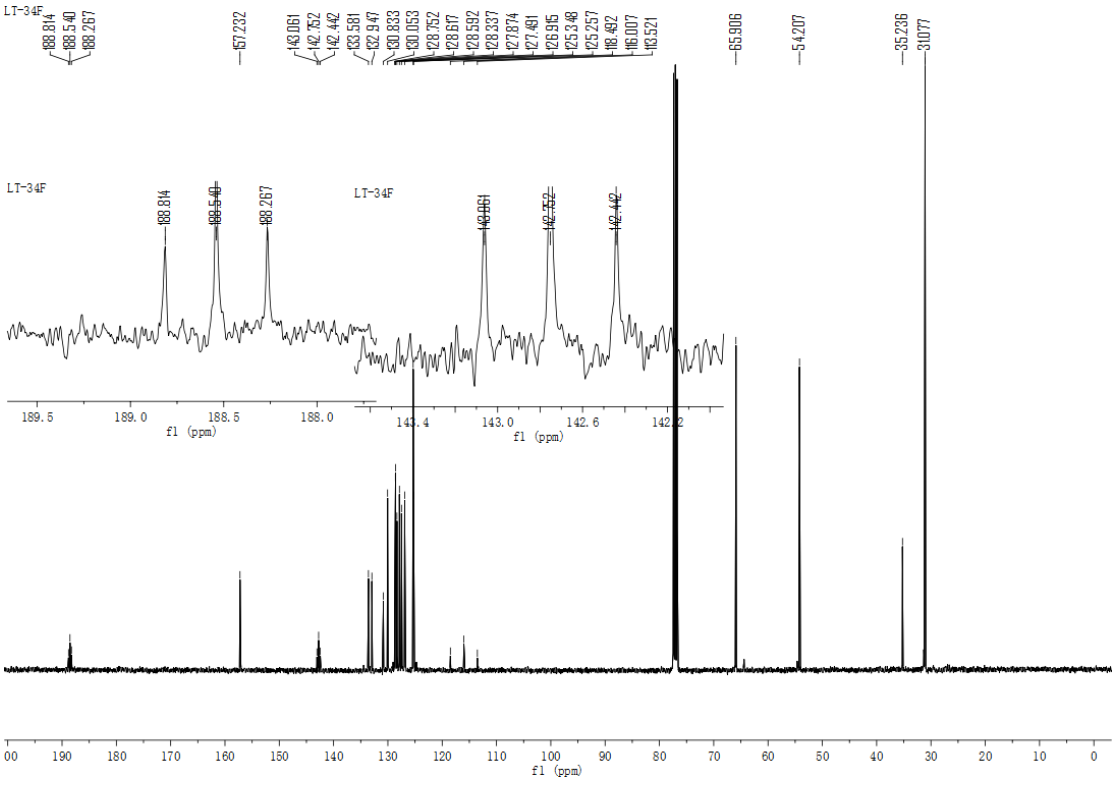
^{1}H NMR (400 MHz, $CDCl_3$)



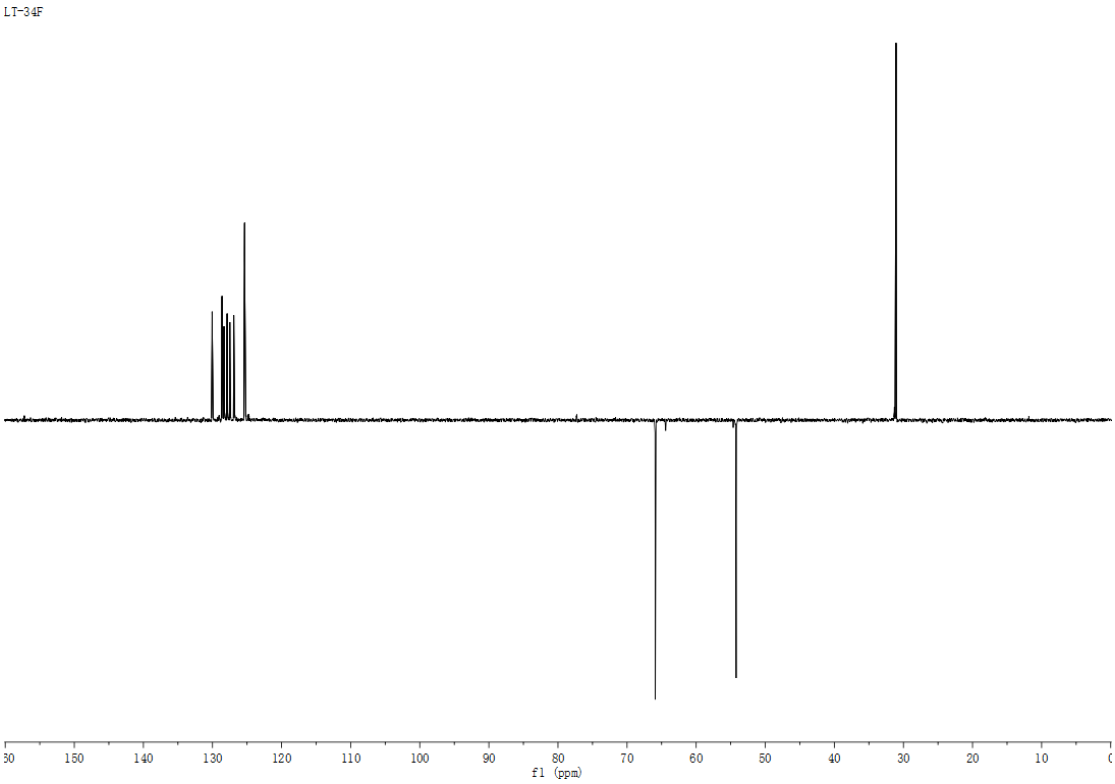
^{19}F NMR (376 MHz, $CDCl_3$):



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

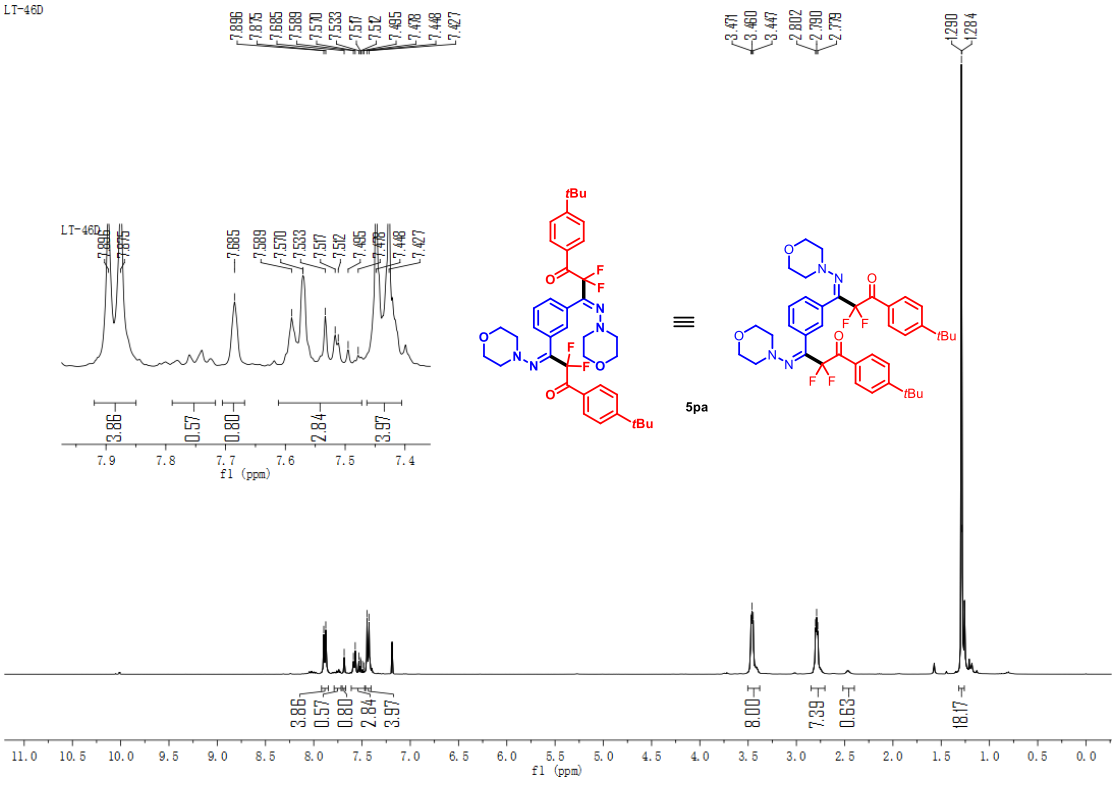


DEPT

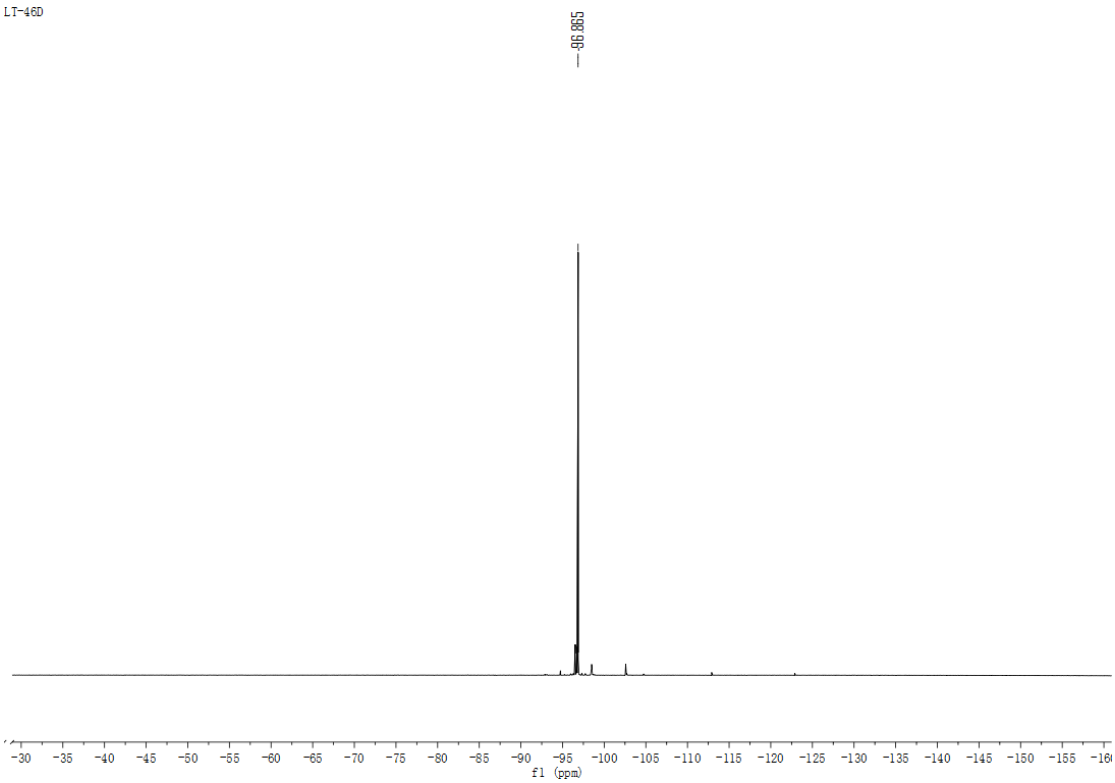


(3E,3'E)-3,3'-(1,3-phenylene)bis(1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one) (5pa)

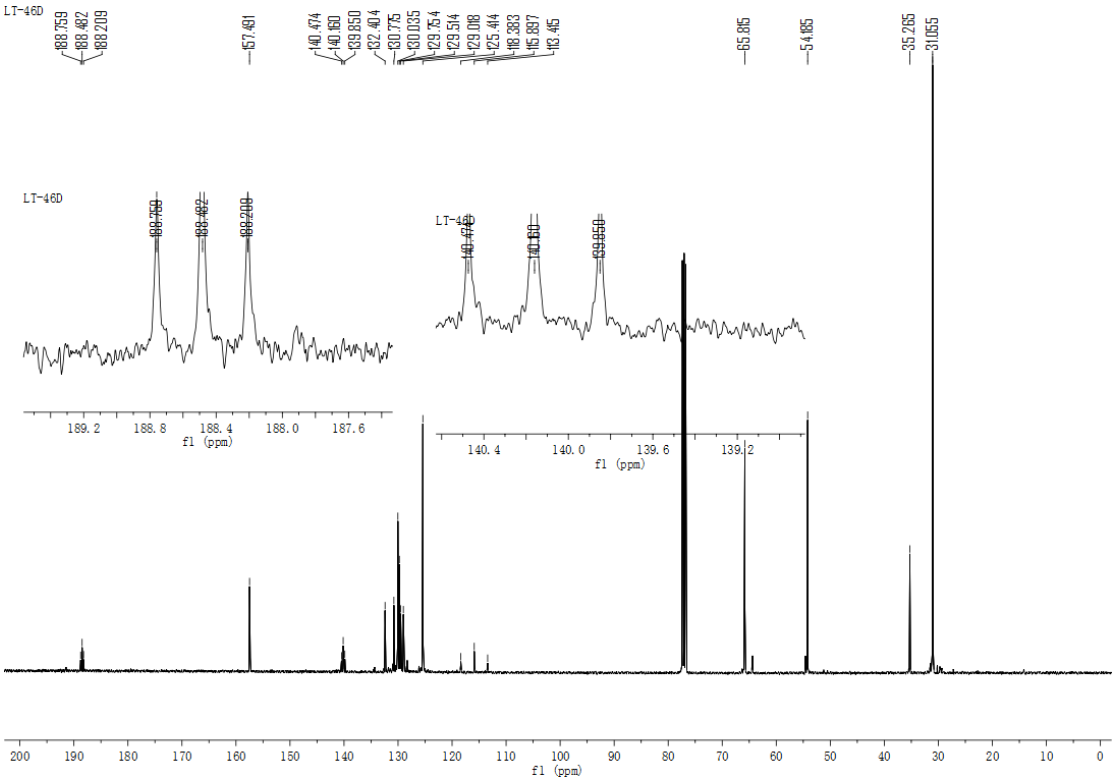
^{1}H NMR (400 MHz, $CDCl_3$)



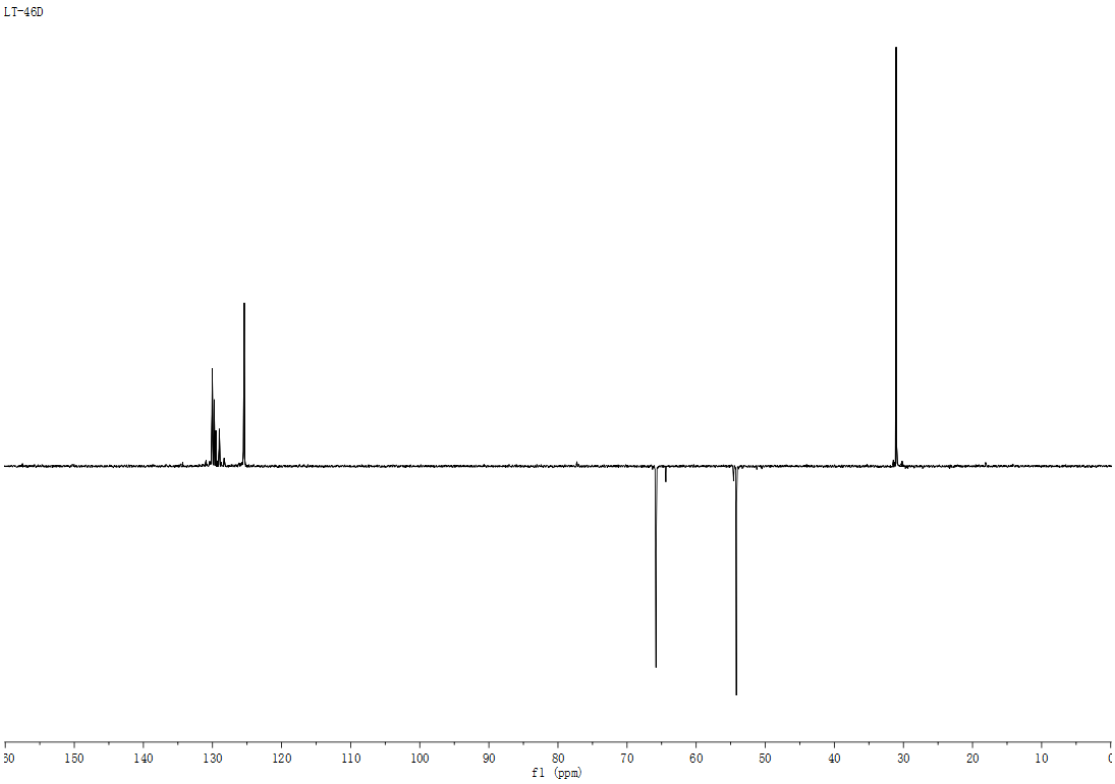
^{19}F NMR (376 MHz, $CDCl_3$):



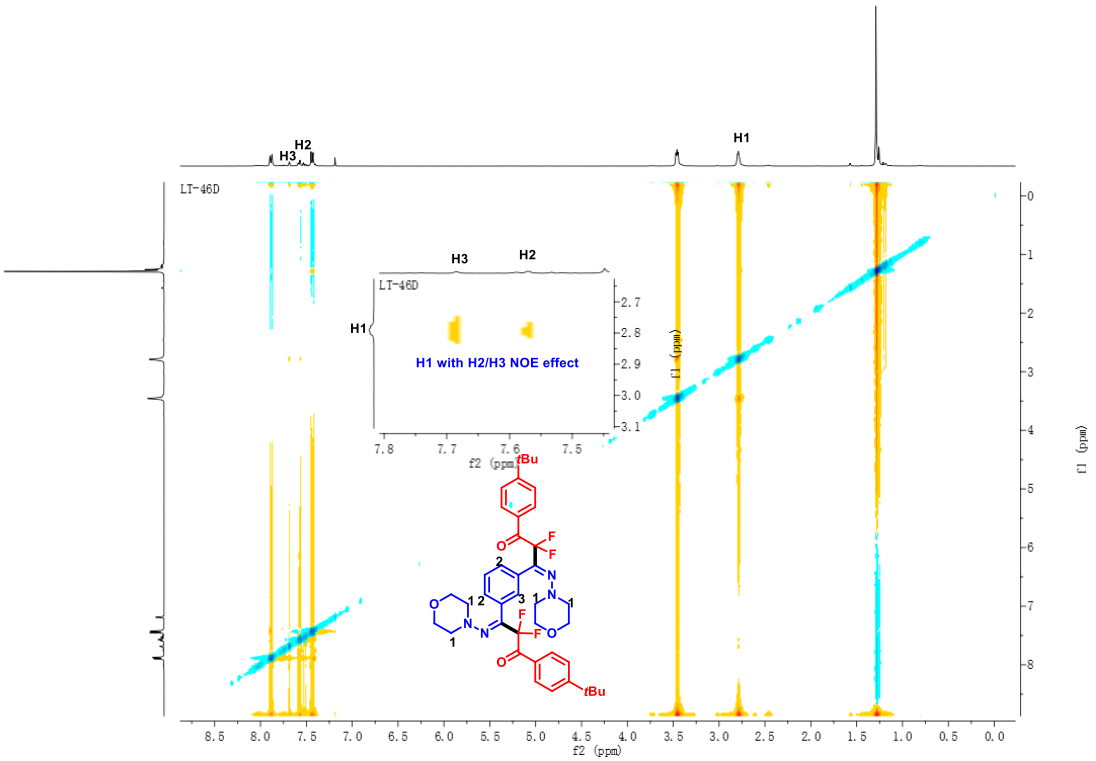
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

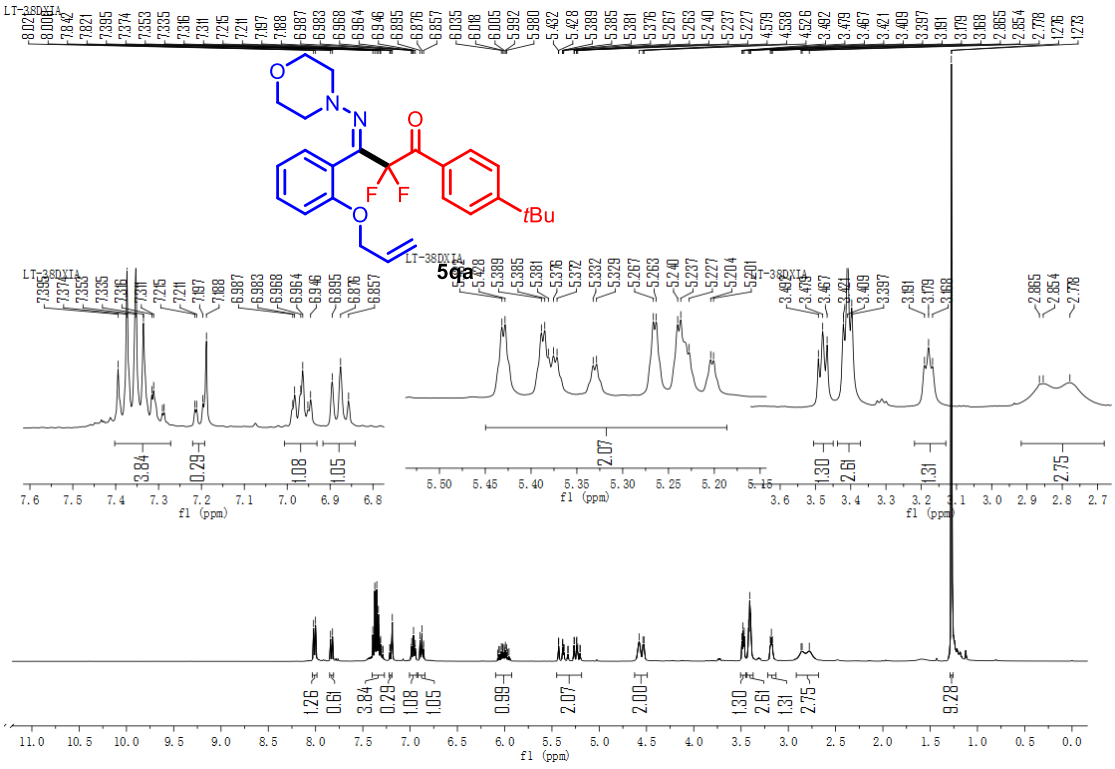


ROESY

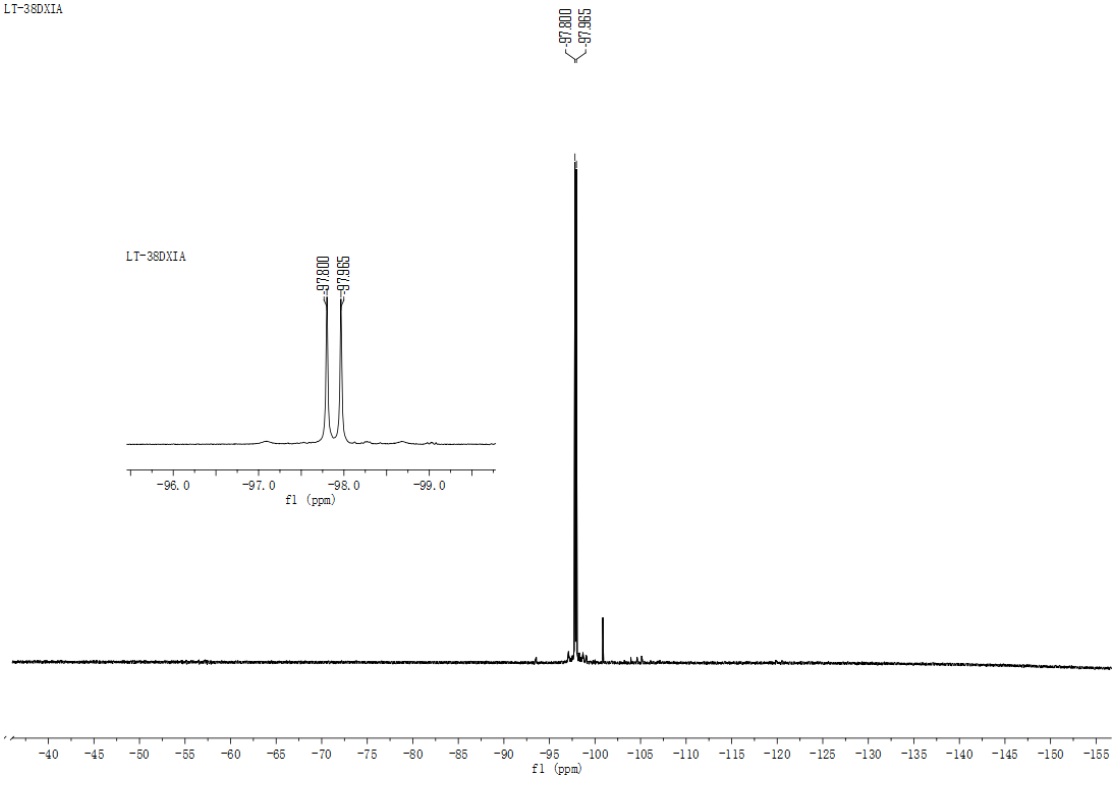


(E)-3-(2-(allyloxy)phenyl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)propan-1-one (5qa)

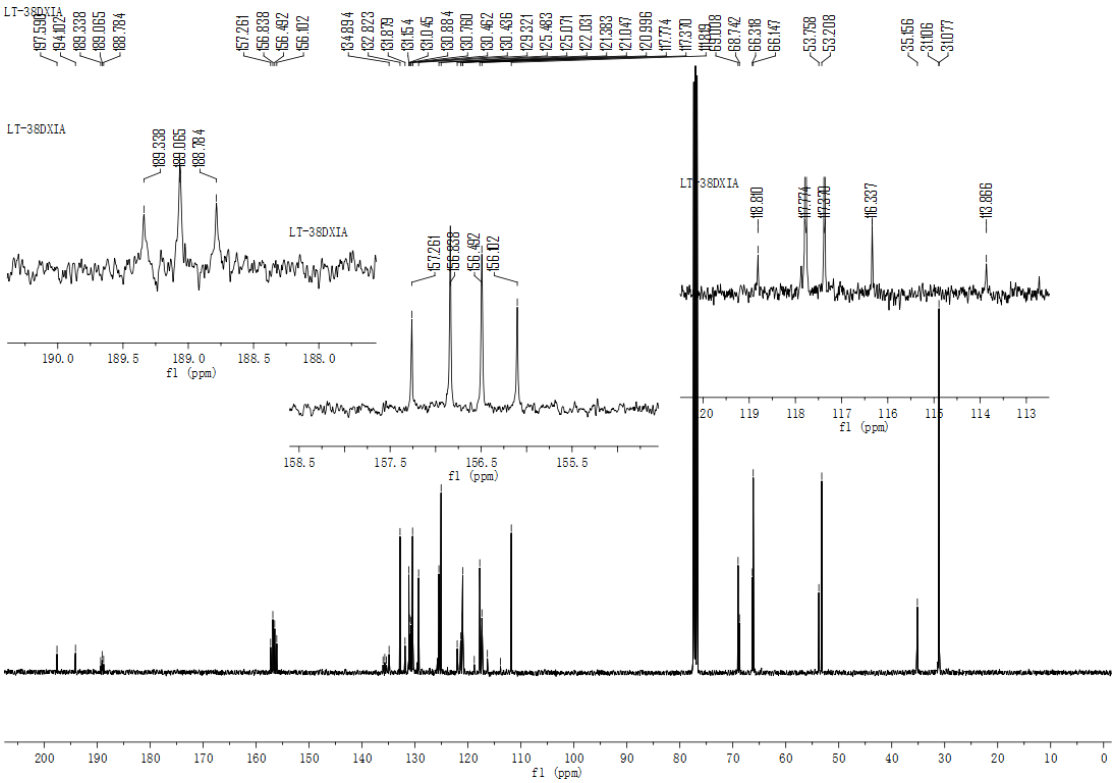
^{1}H NMR (400 MHz, $CDCl_3$)



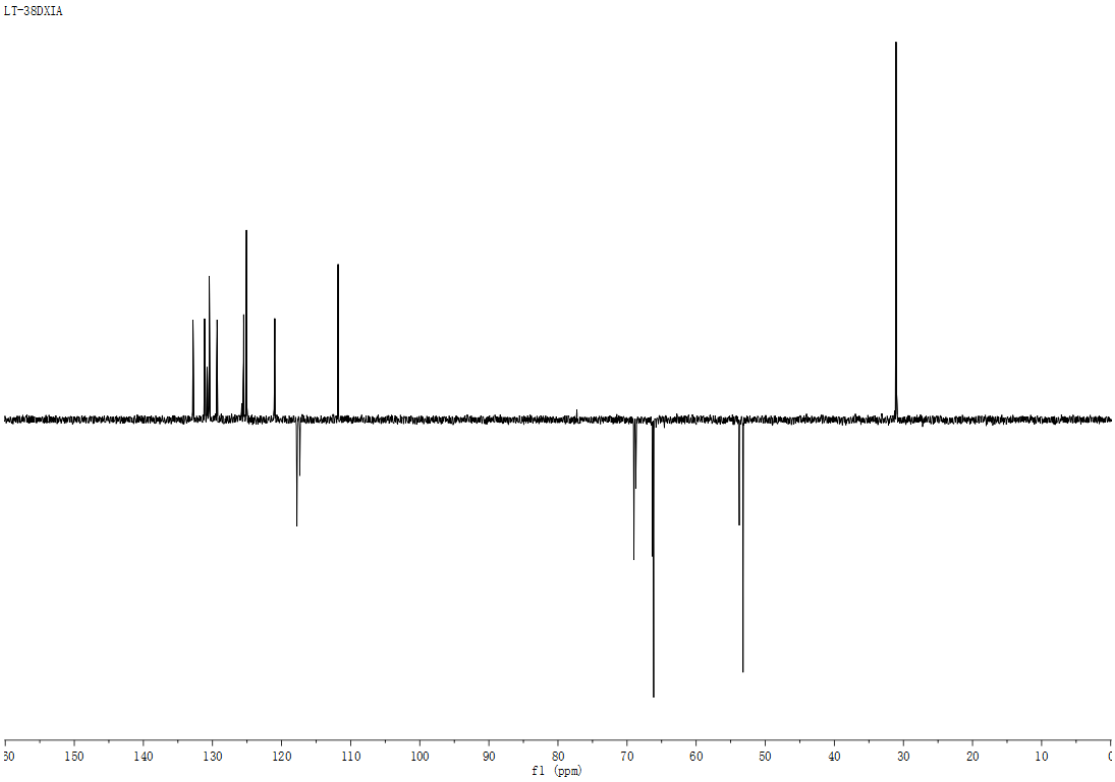
^{19}F NMR (376 MHz, $CDCl_3$):



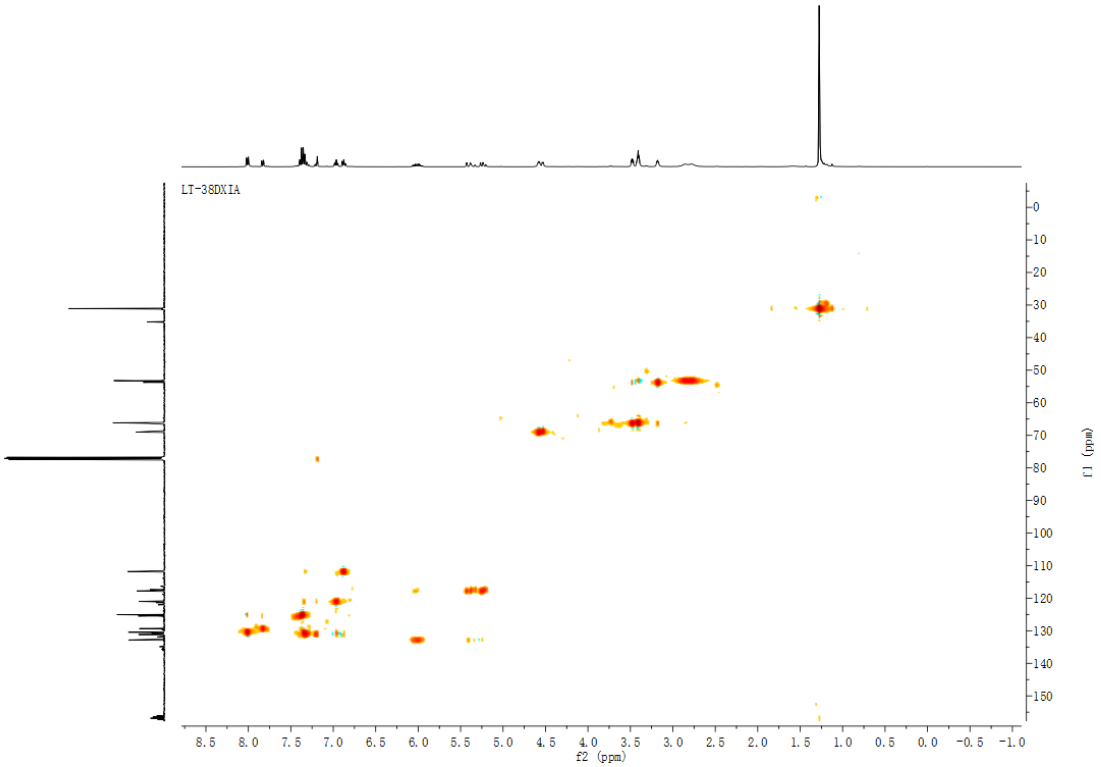
^{13}C NMR (100 MHz, $CDCl_3$):

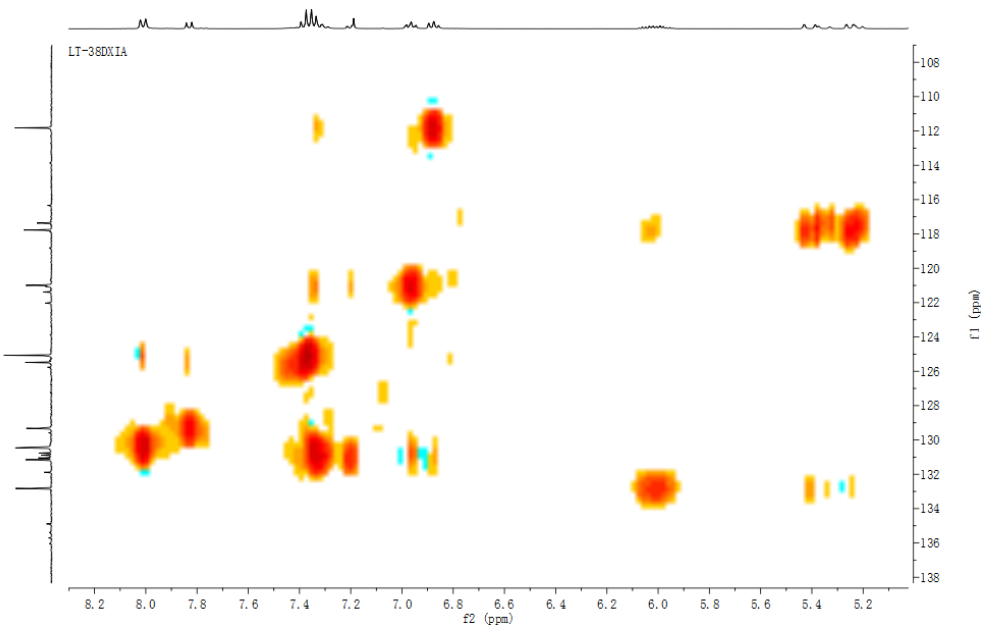


DEPT

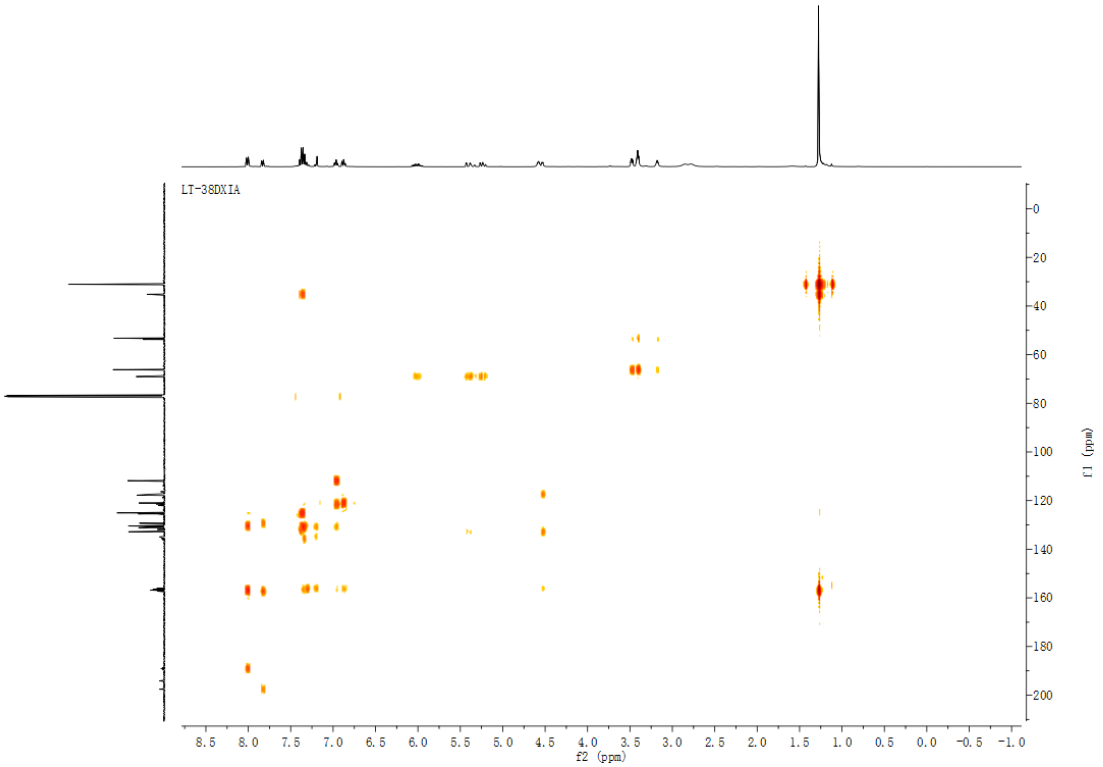


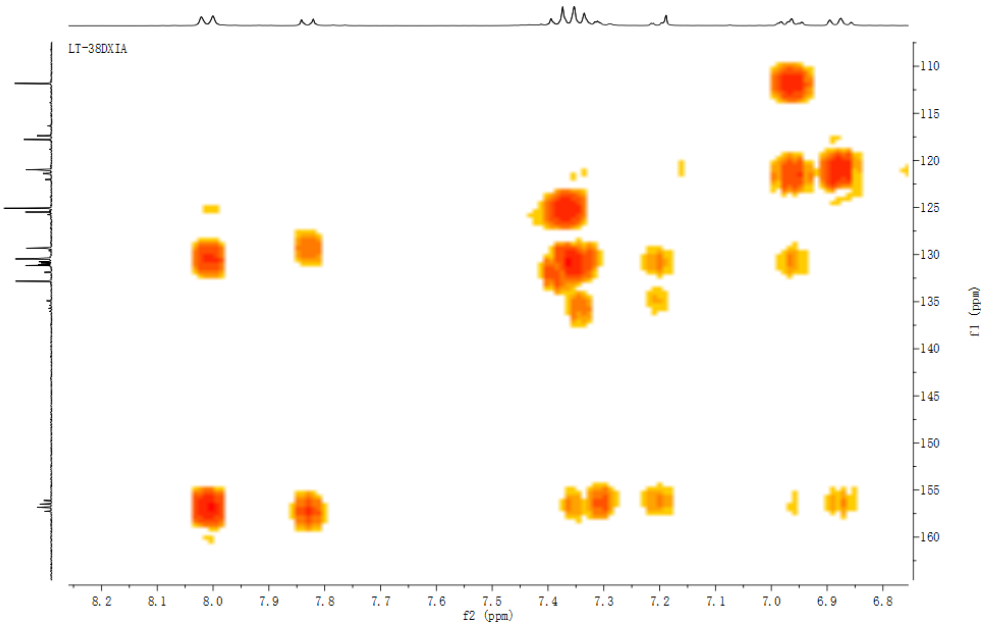
HSQC





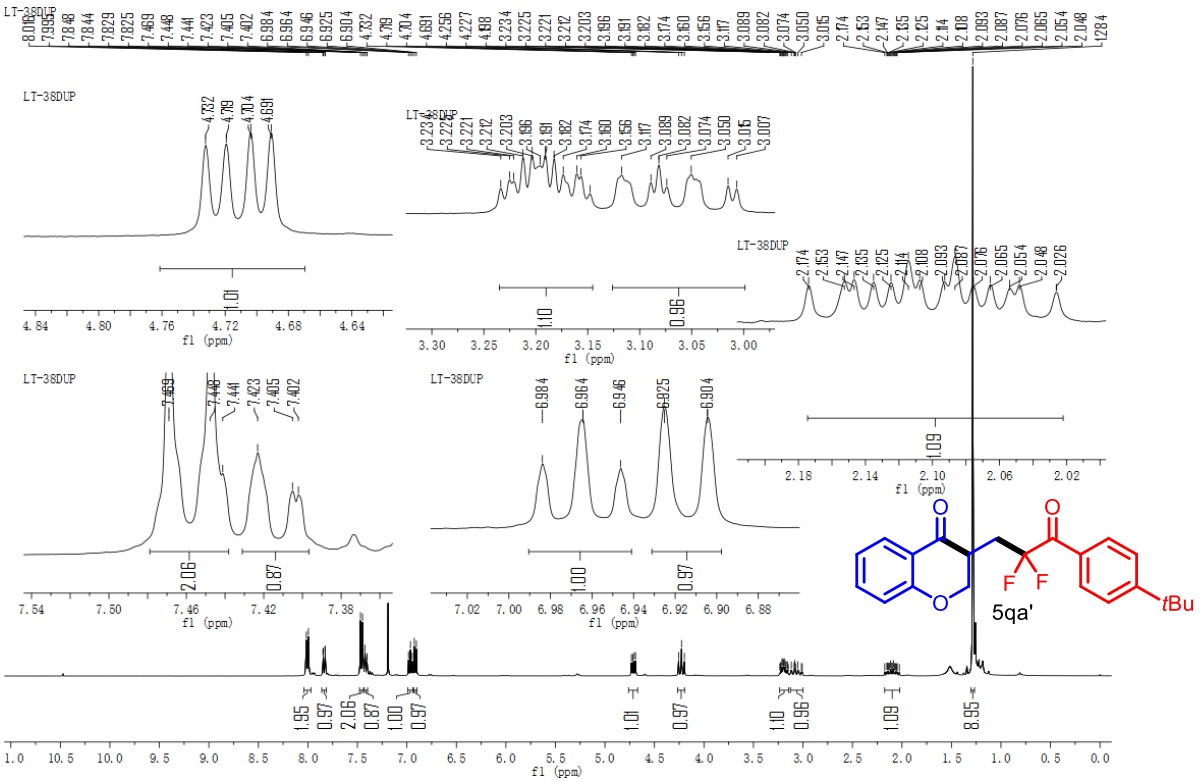
HMBC



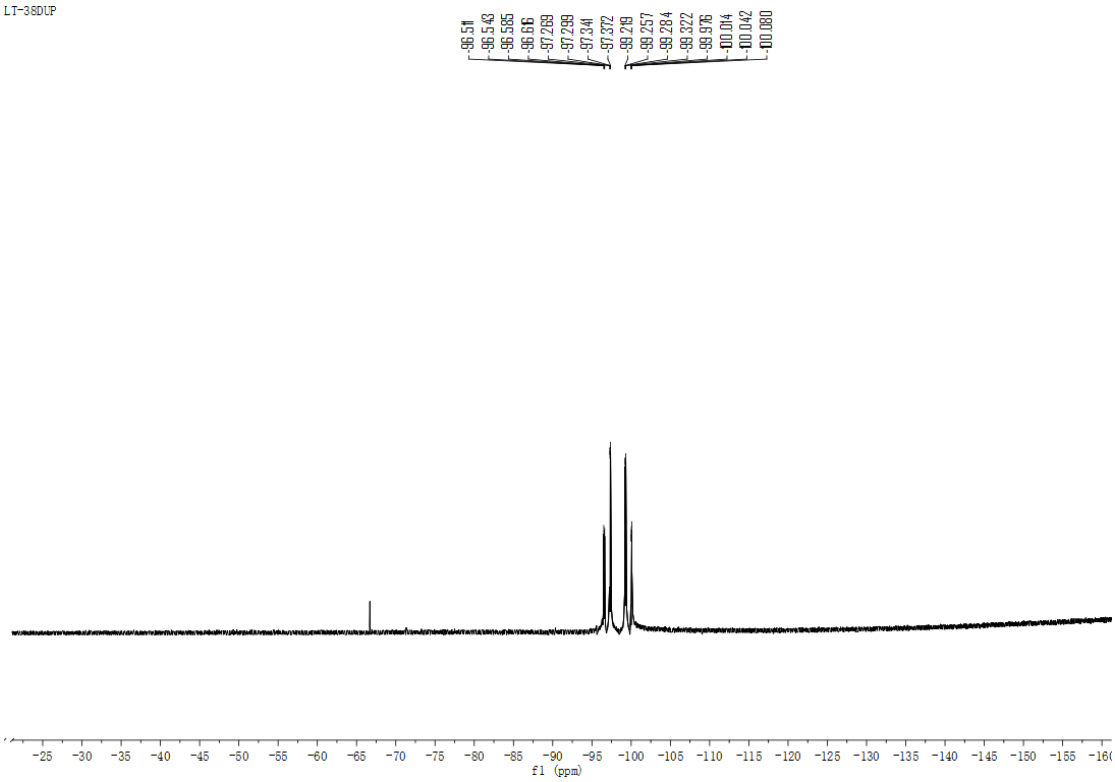


3-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-3-oxopropyl)chroman-4-one (5qa')

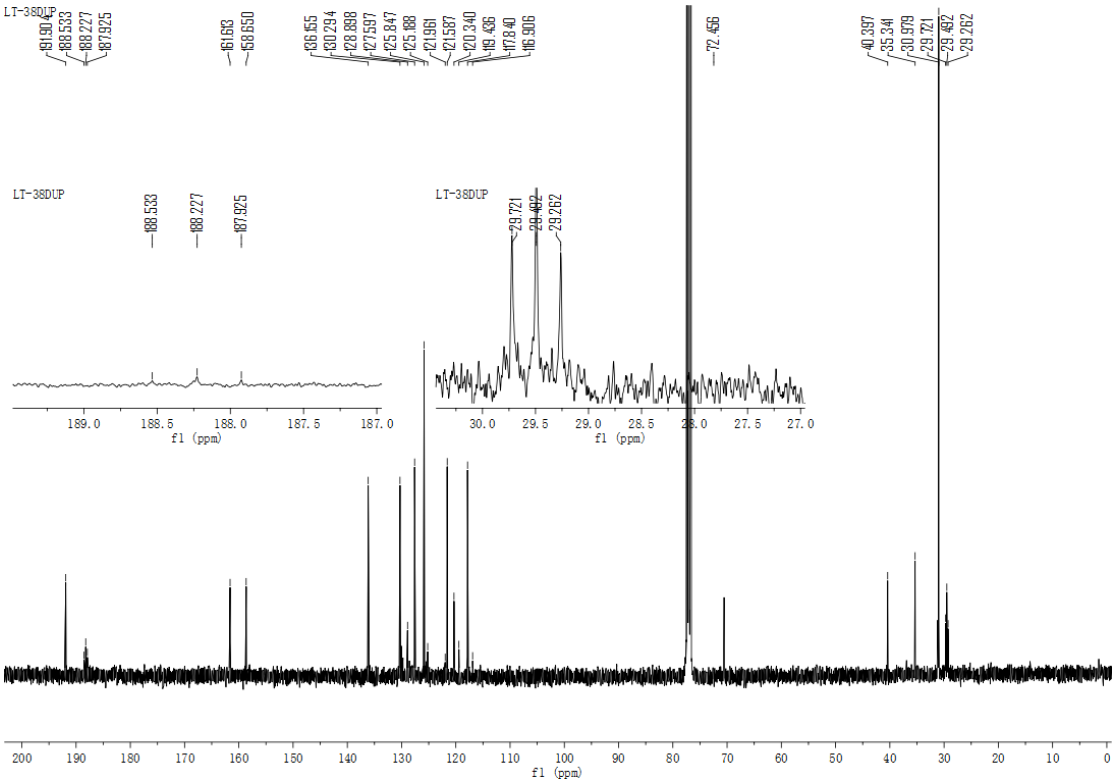
^{1}H NMR (400 MHz, $CDCl_3$)



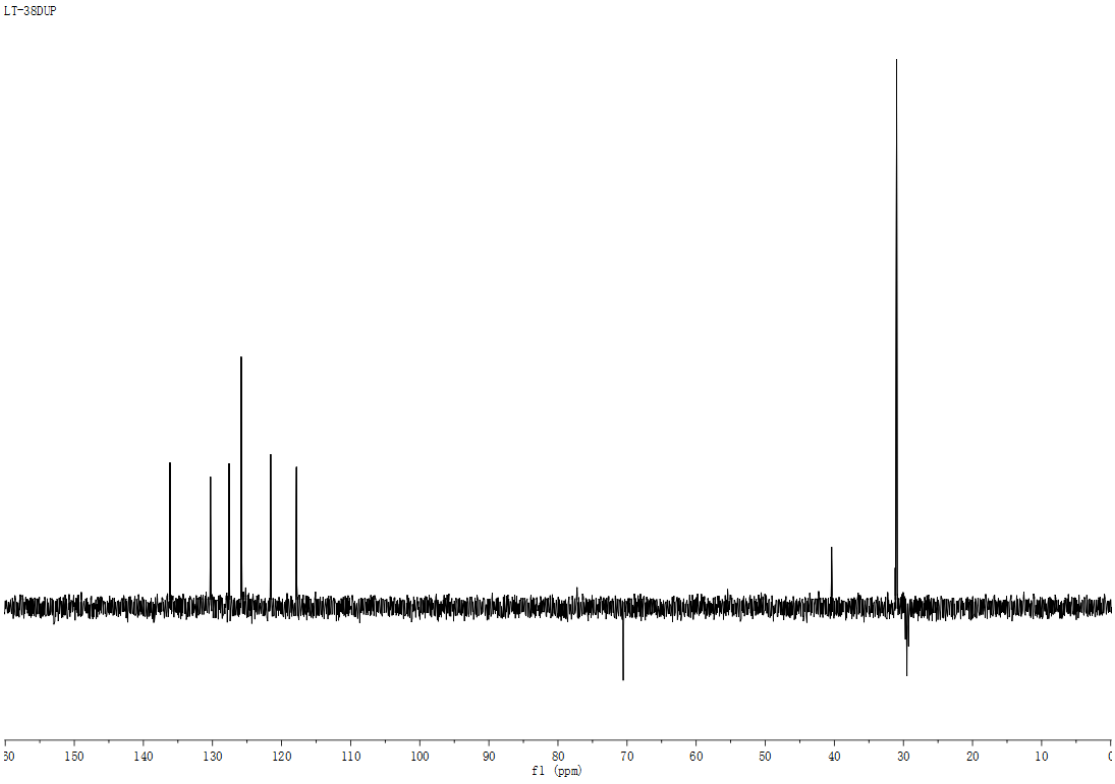
^{19}F NMR (376 MHz, $CDCl_3$):



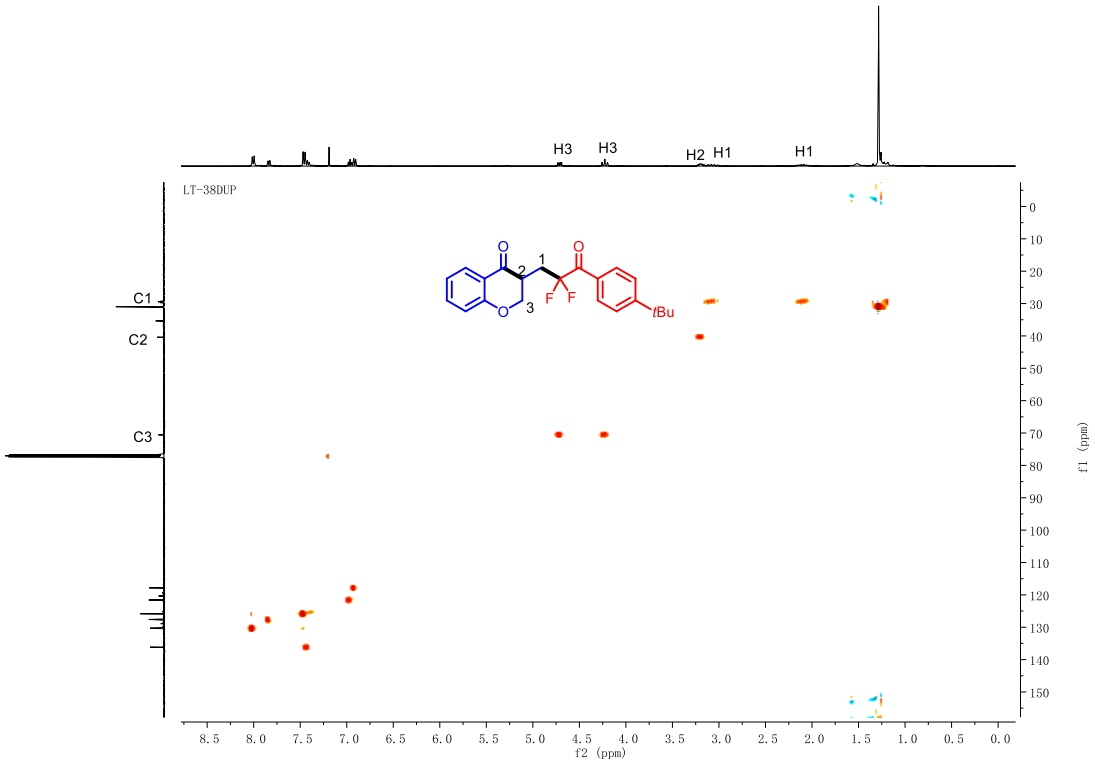
^{13}C NMR (100 MHz, $CDCl_3$):



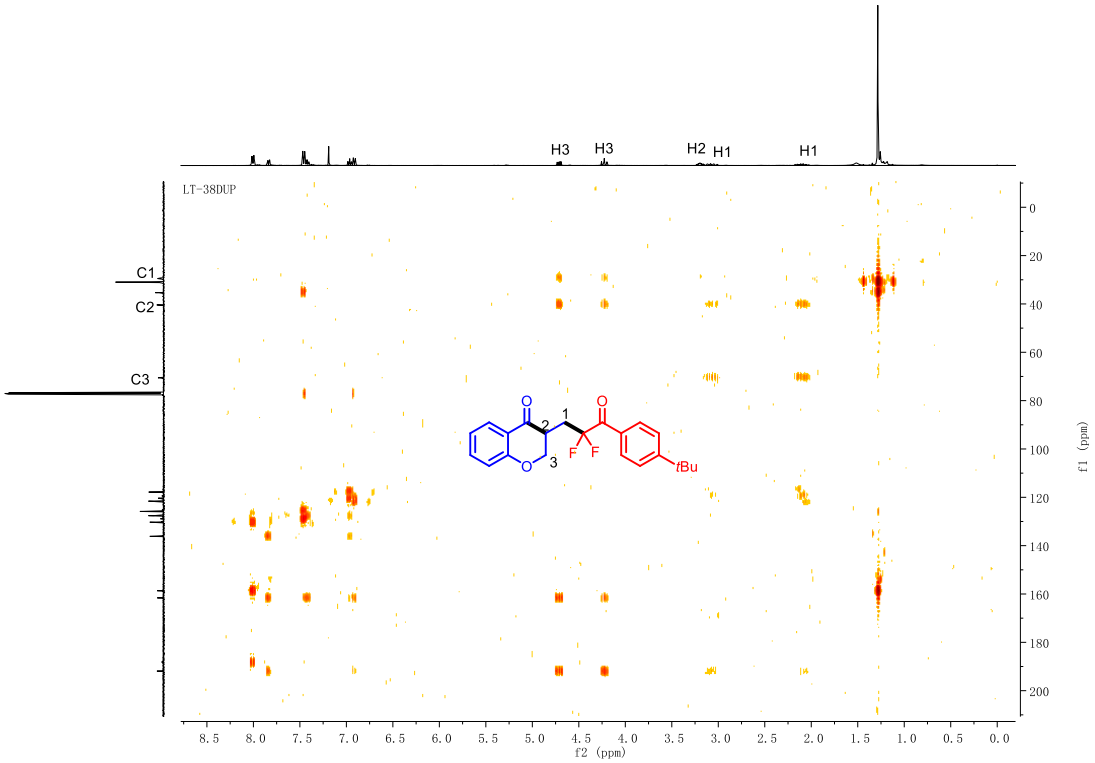
DEPT



HSQC

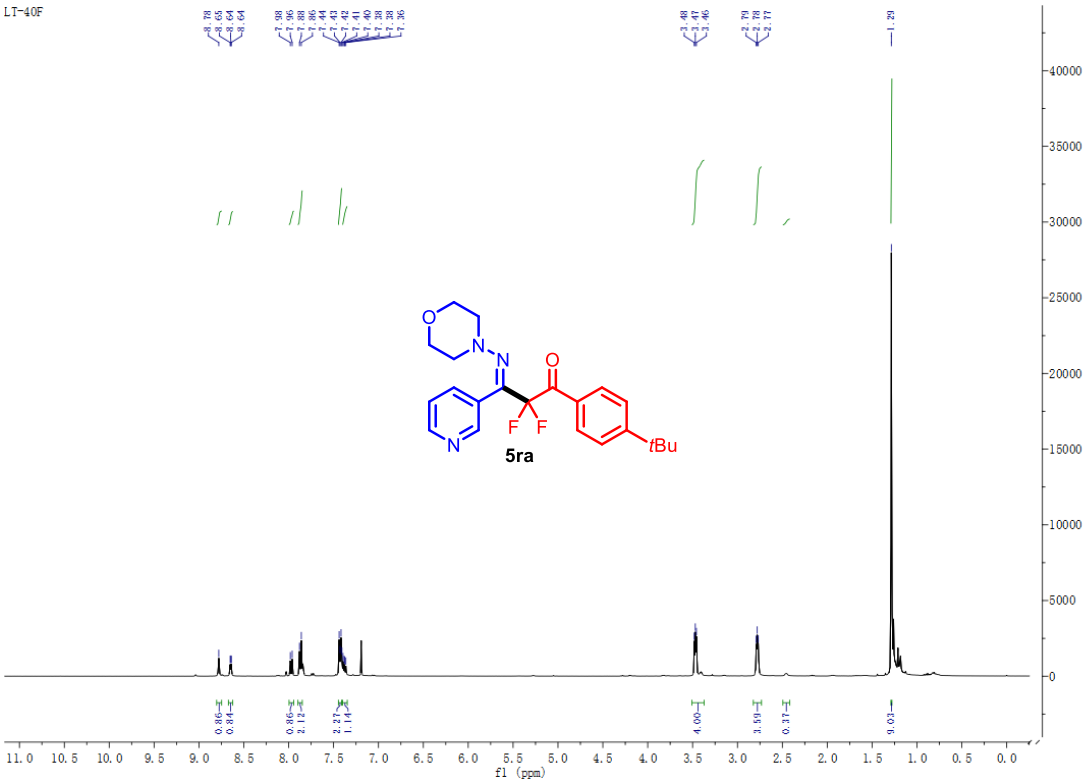


HMBC

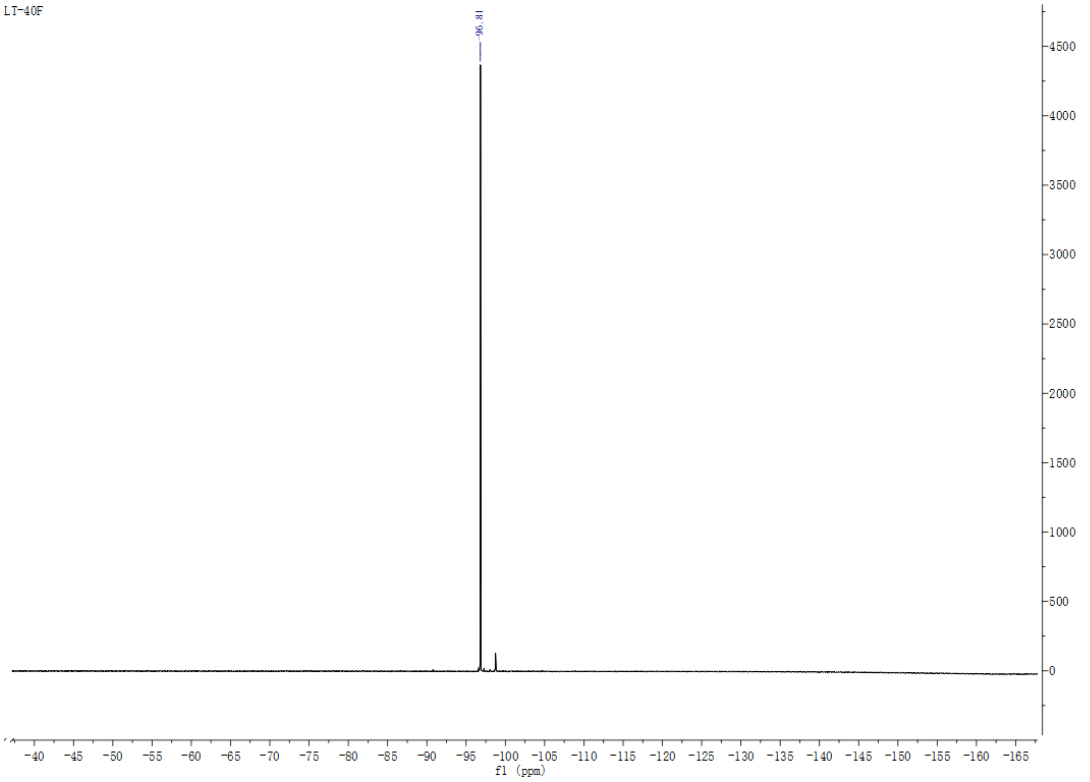


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-3-(pyridin-3-yl)propan-1-one (5ra)

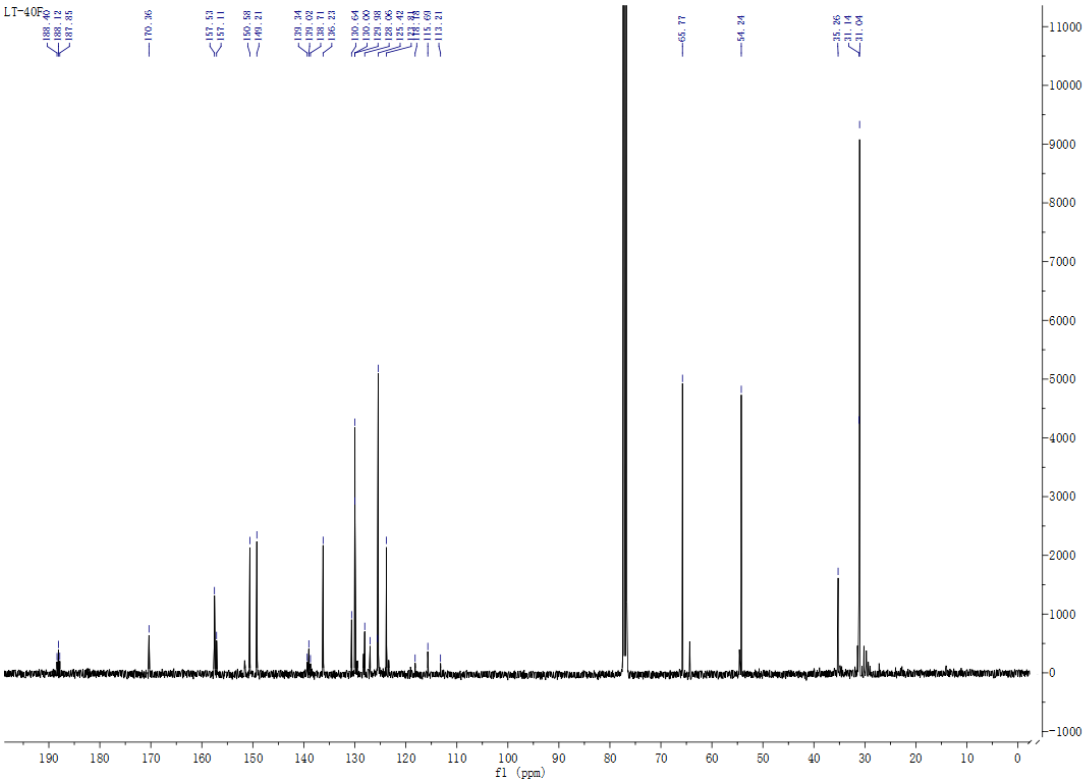
^{1}H NMR (400 MHz, $CDCl_3$)



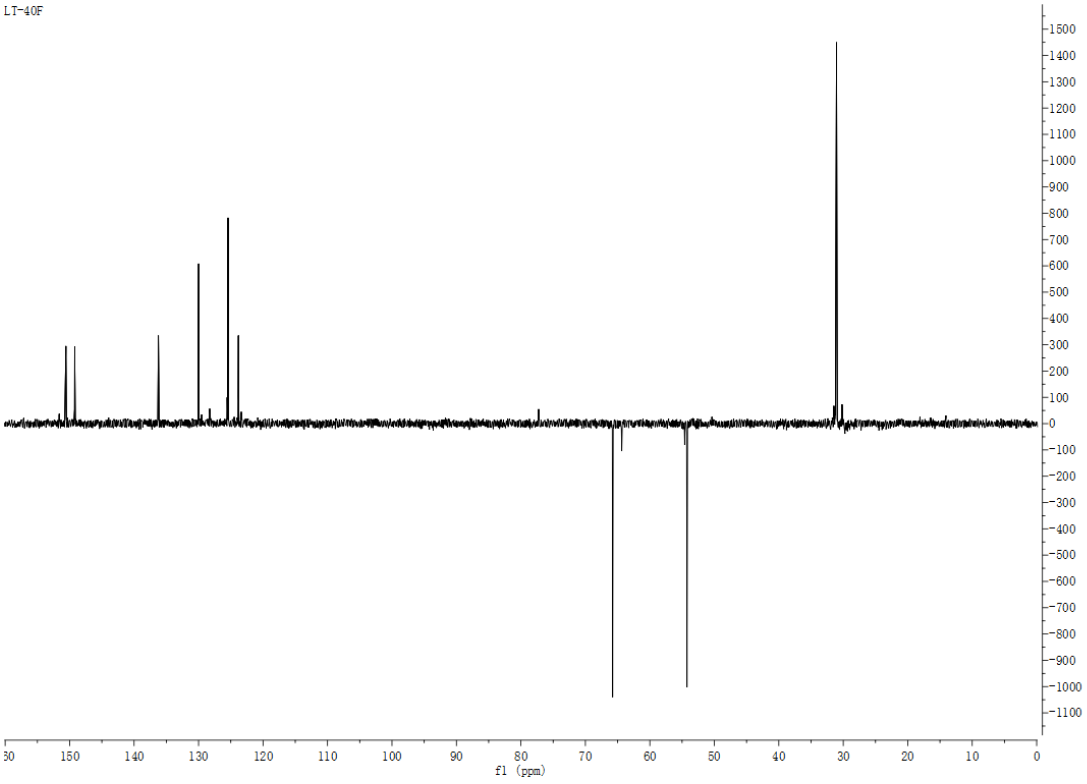
^{19}F NMR (376 MHz, $CDCl_3$):



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



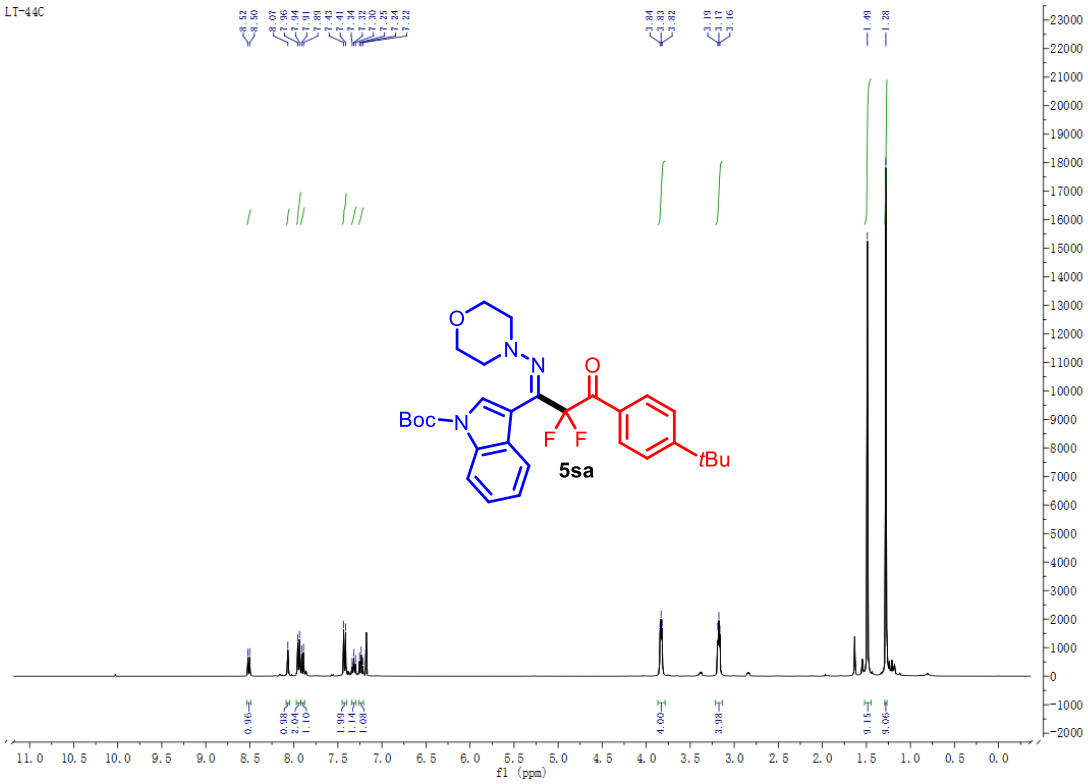
DEPT



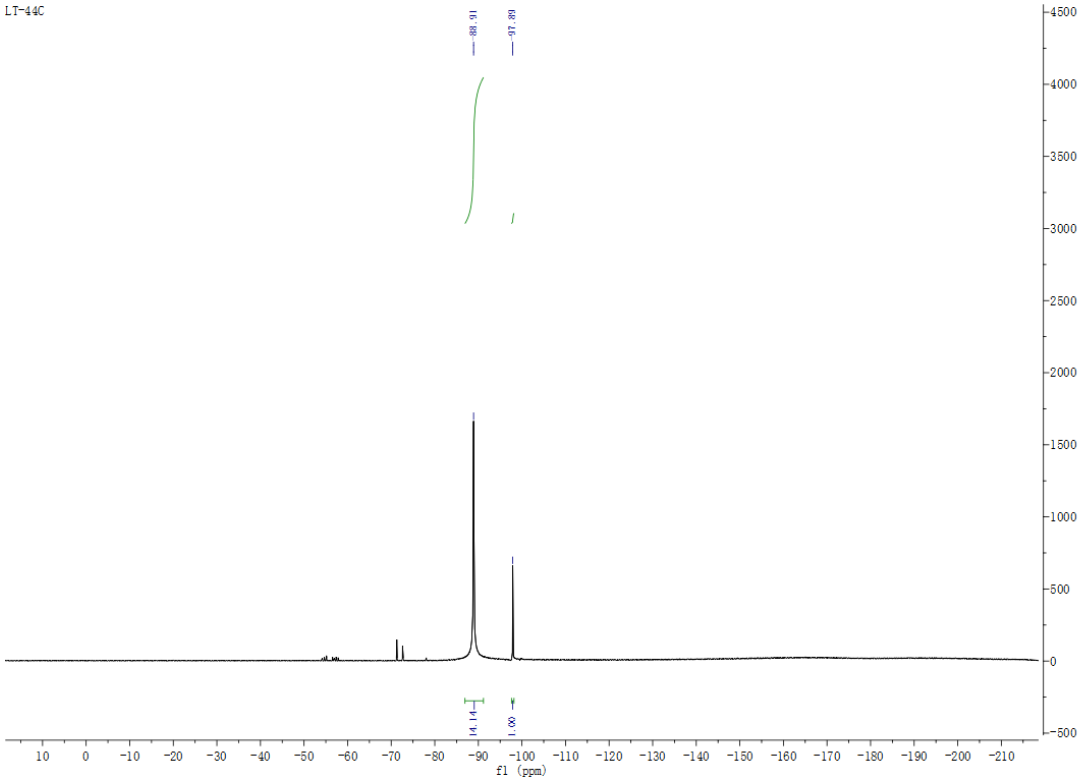
tert-butyl

(E)-3-(3-(4-(tert-butyl)phenyl)-2,2-difluoro-1-(morpholinoimino)-3-oxopropyl)-1H-indole-1-carboxylate (5sa)

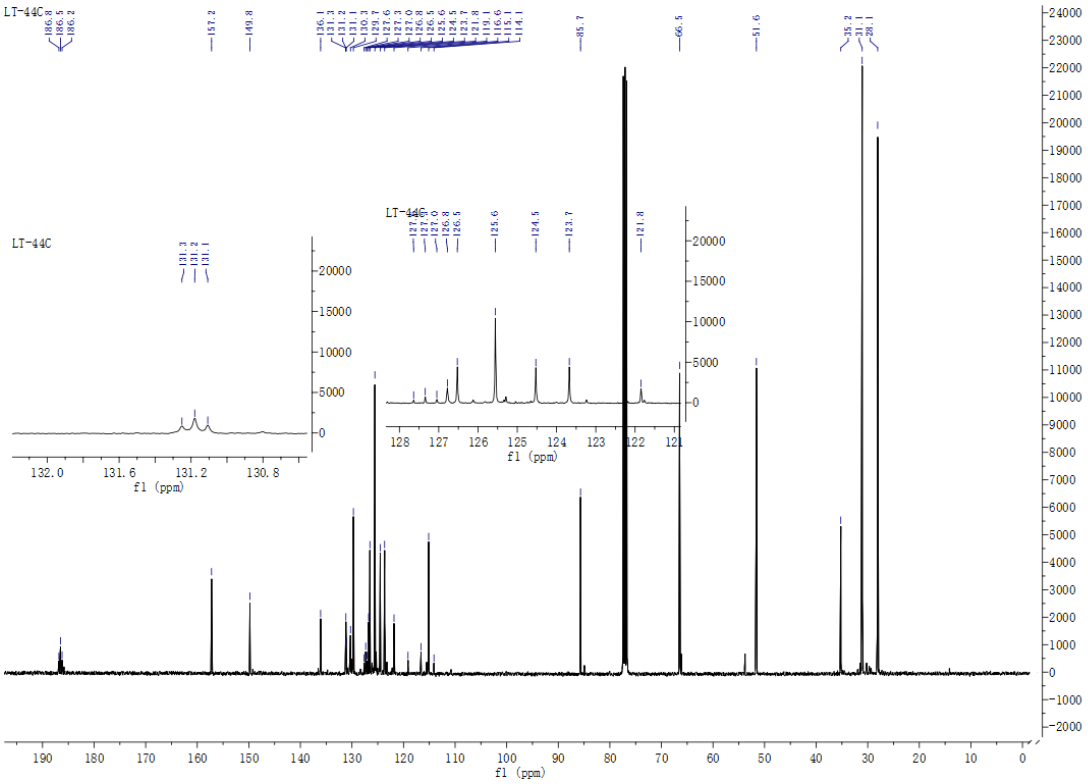
^{1}H NMR (400 MHz, $CDCl_3$)



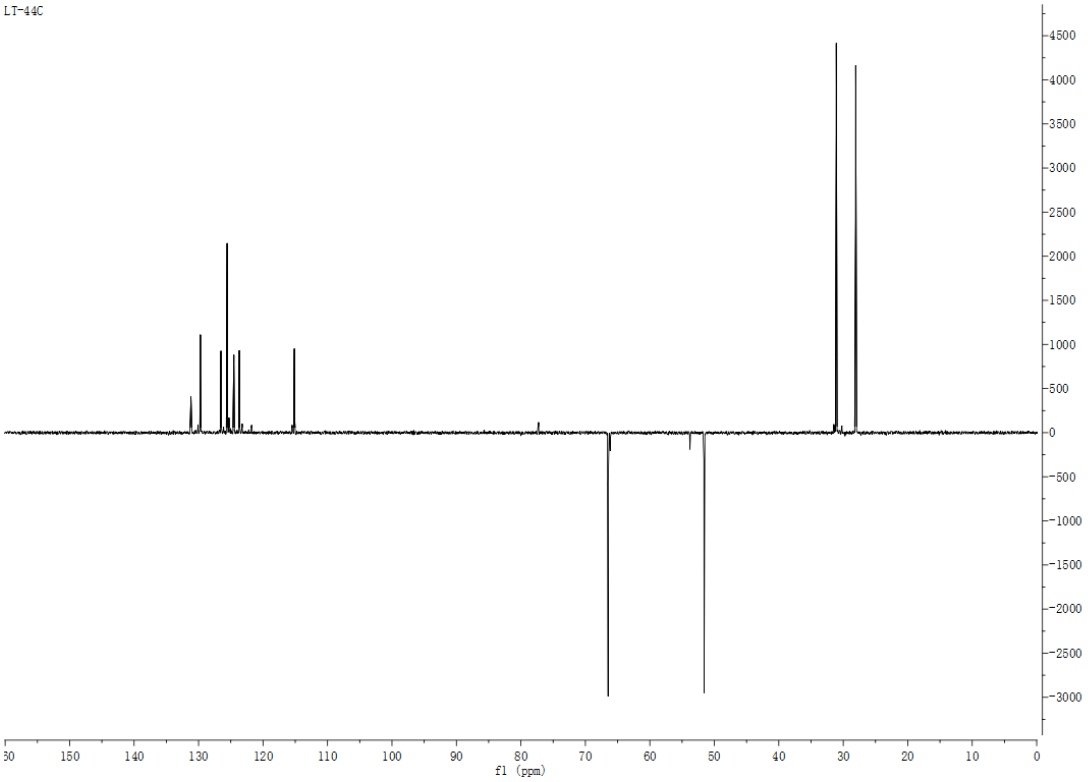
^{19}F NMR (376 MHz, $CDCl_3$):



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

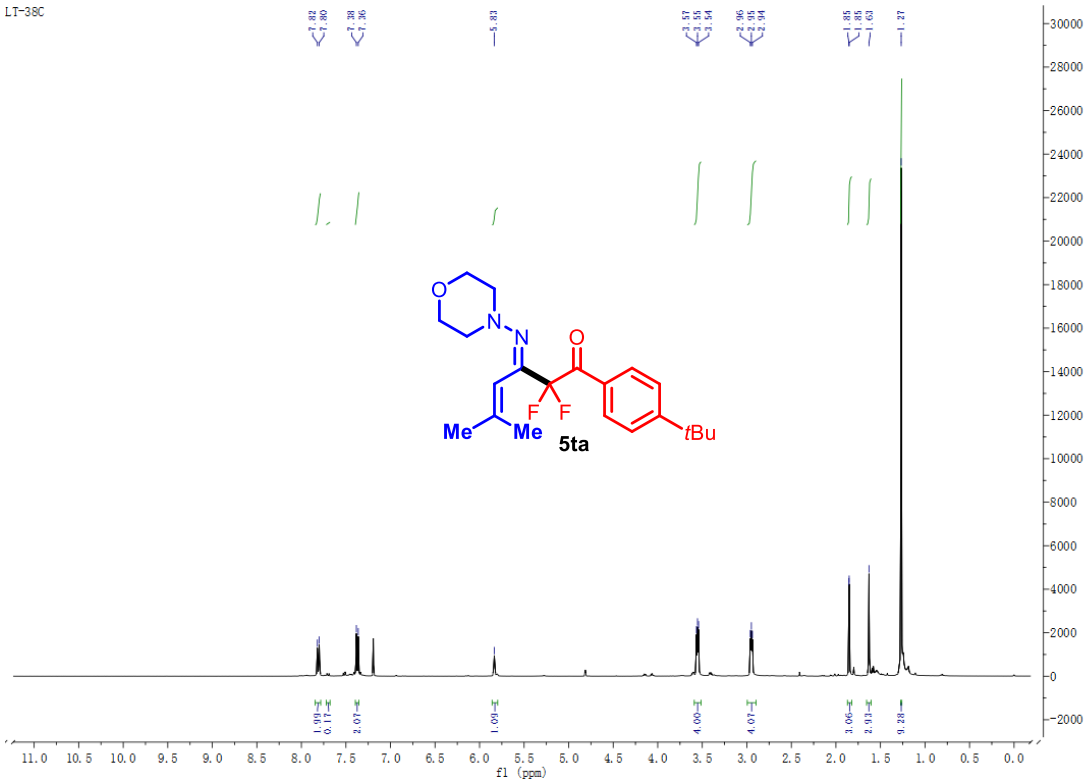


DEPT

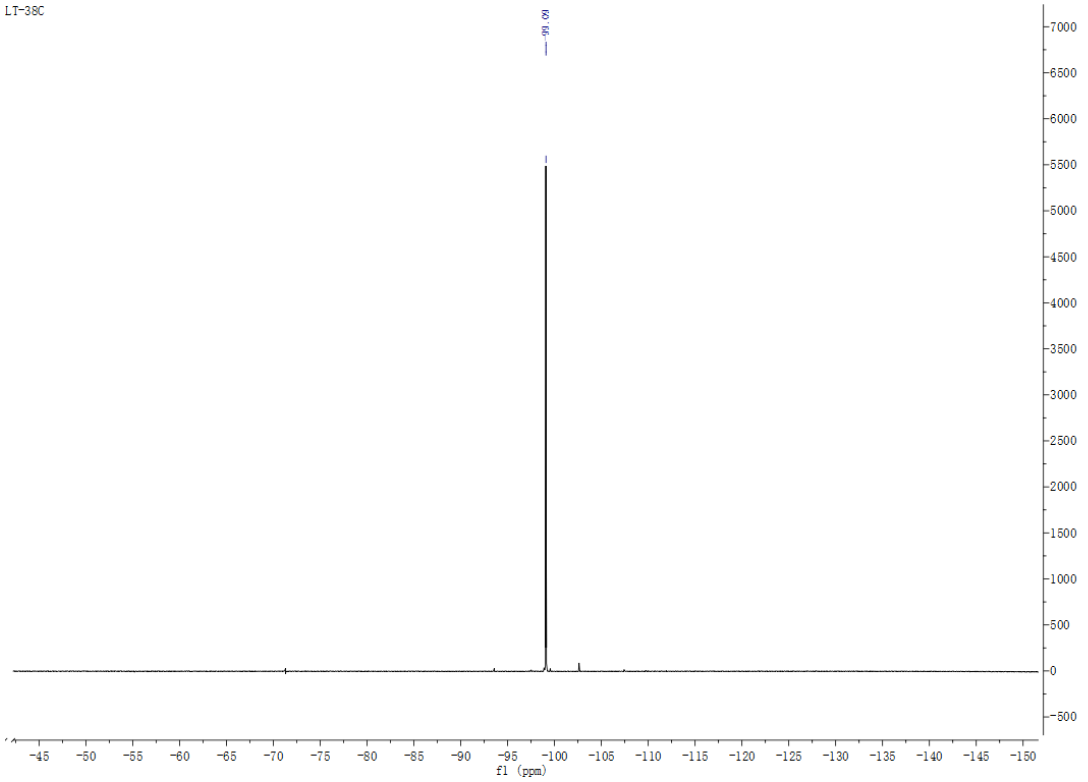


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-5-methyl-3-(morpholinoimino)hex-4-en-1-one (5ta)

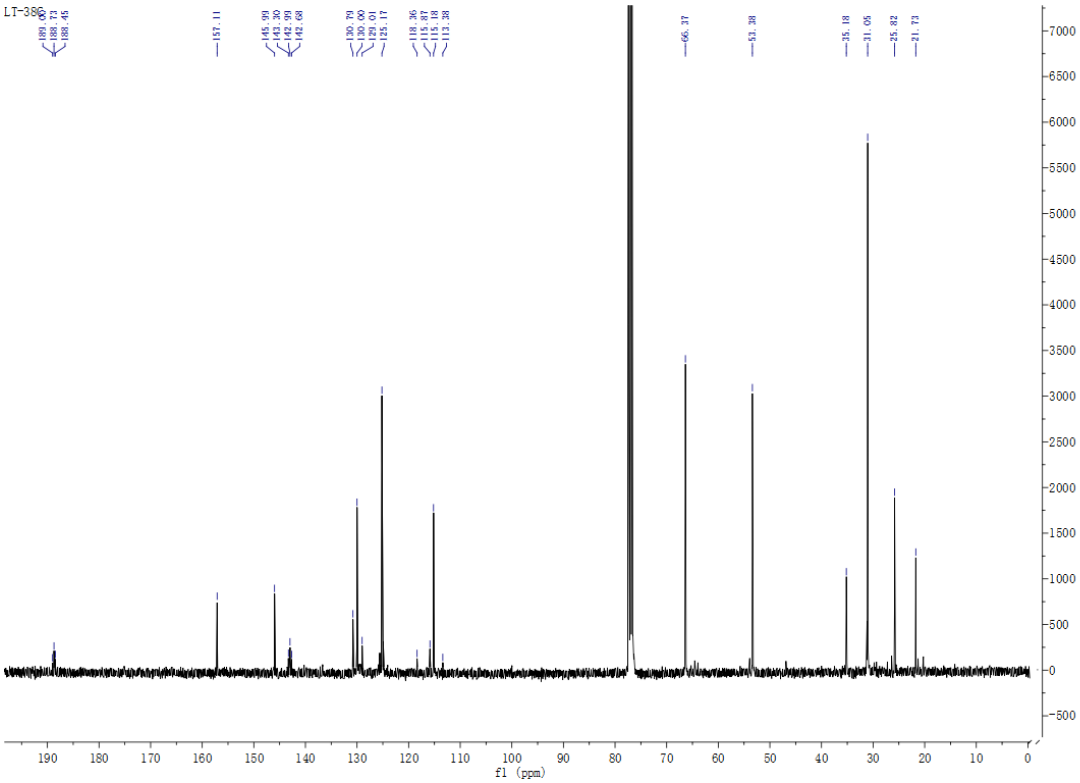
^{1}H NMR (400 MHz, $CDCl_3$)



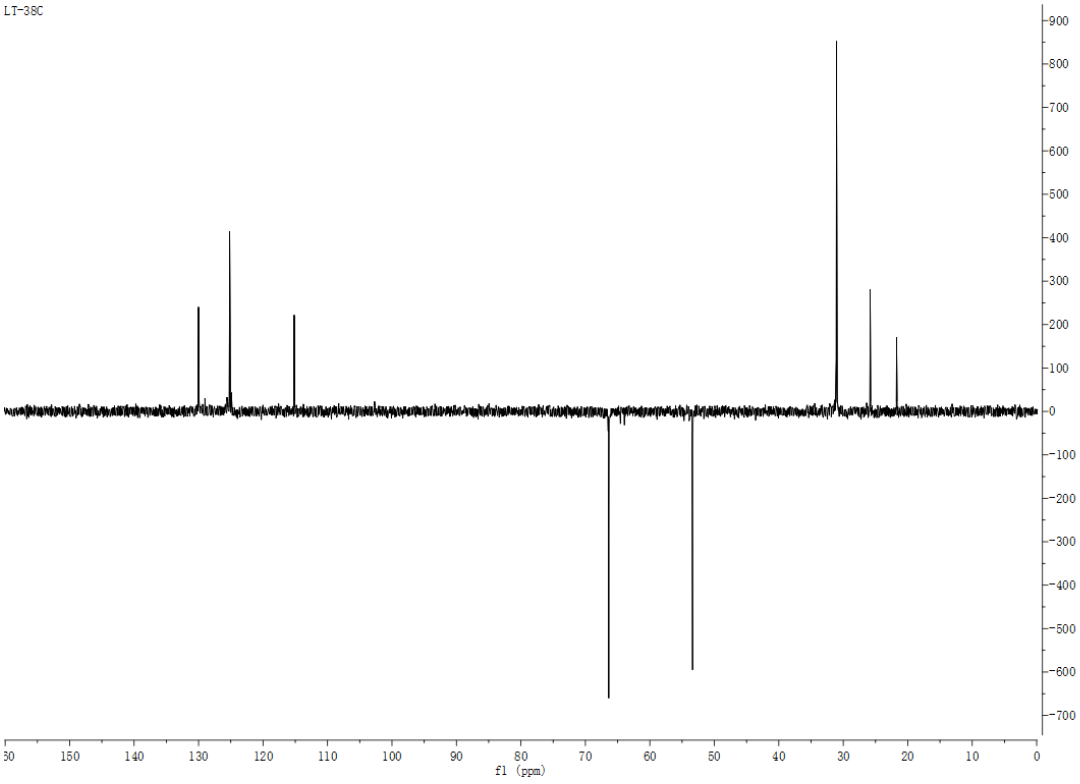
^{19}F NMR (376 MHz, $CDCl_3$):



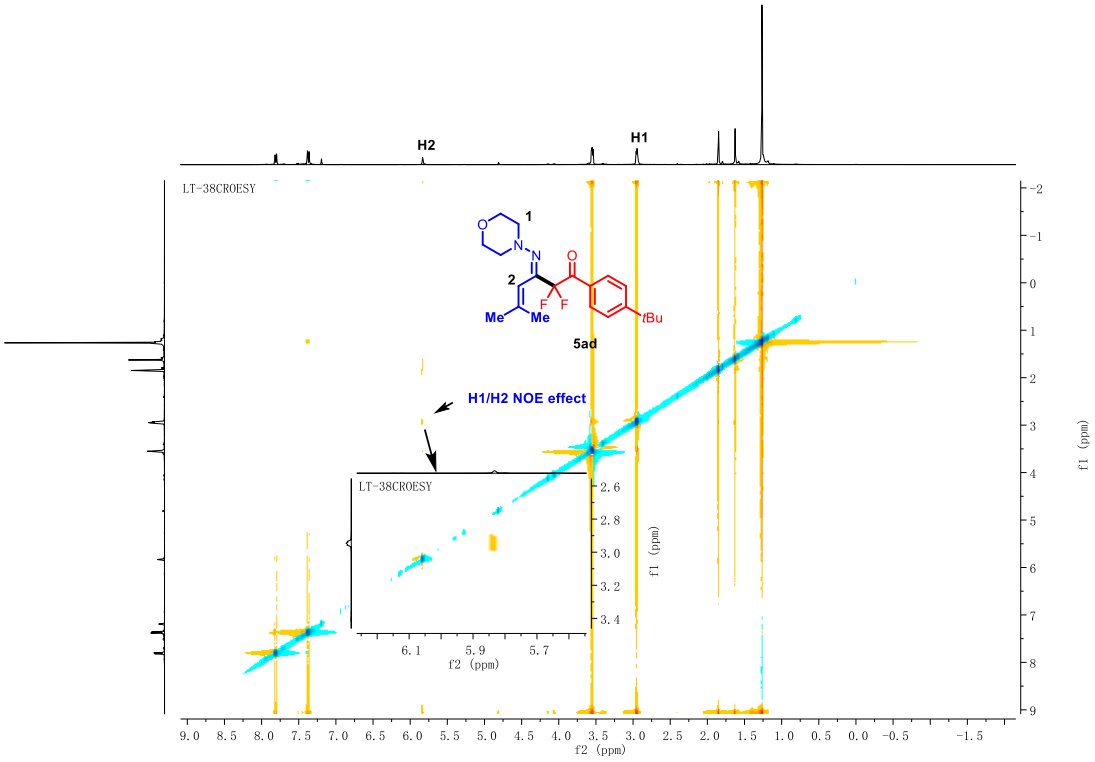
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

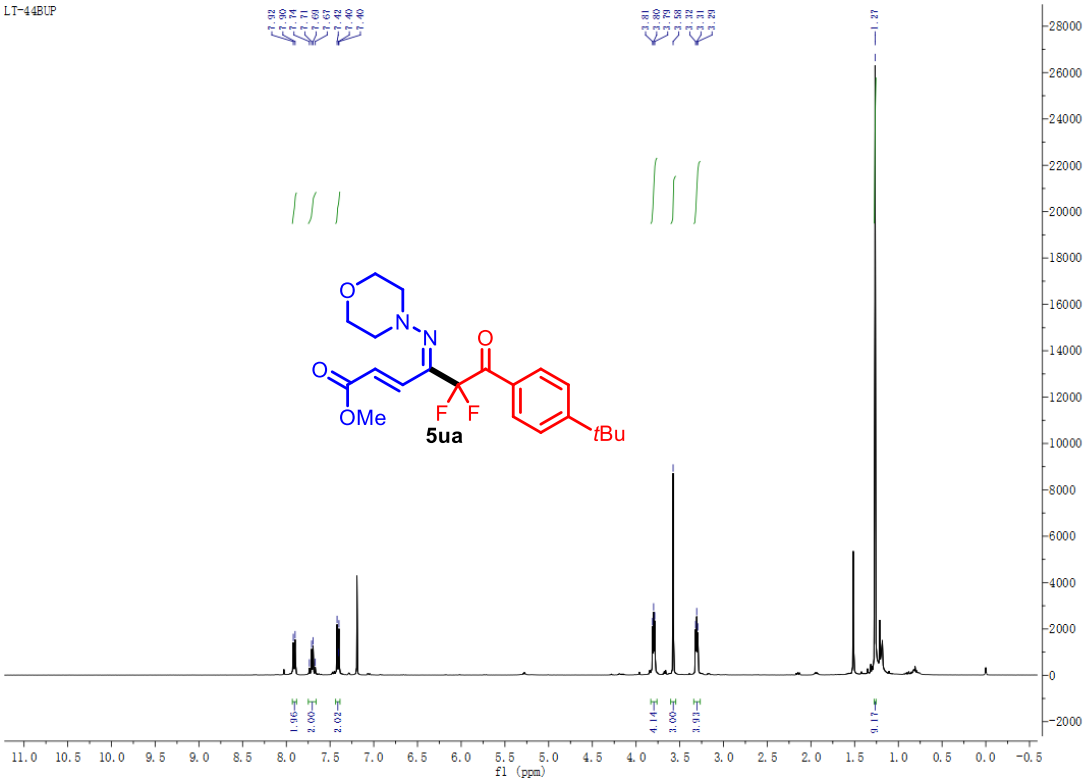


ROESY

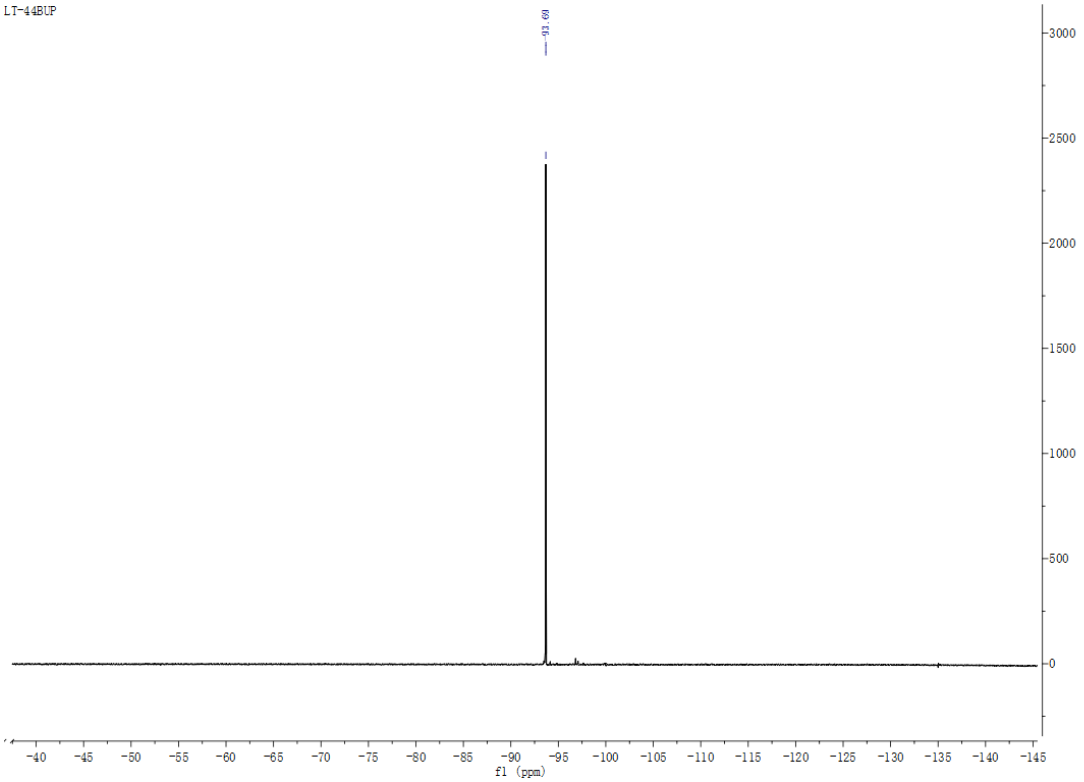


methyl (2E,4E)-6-(4-(tert-butyl)phenyl)-5,5-difluoro-4-(morpholinoimino)-6-oxohex-2-enoate (5ua)

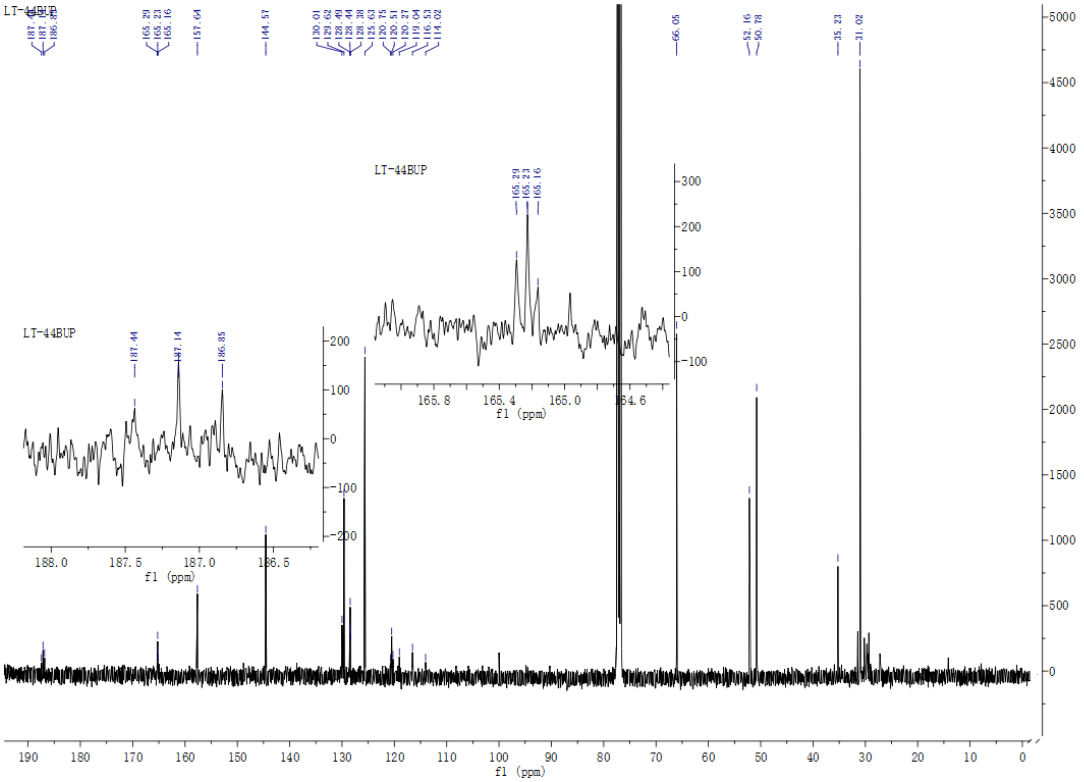
^{1}H NMR (400 MHz, $CDCl_3$)



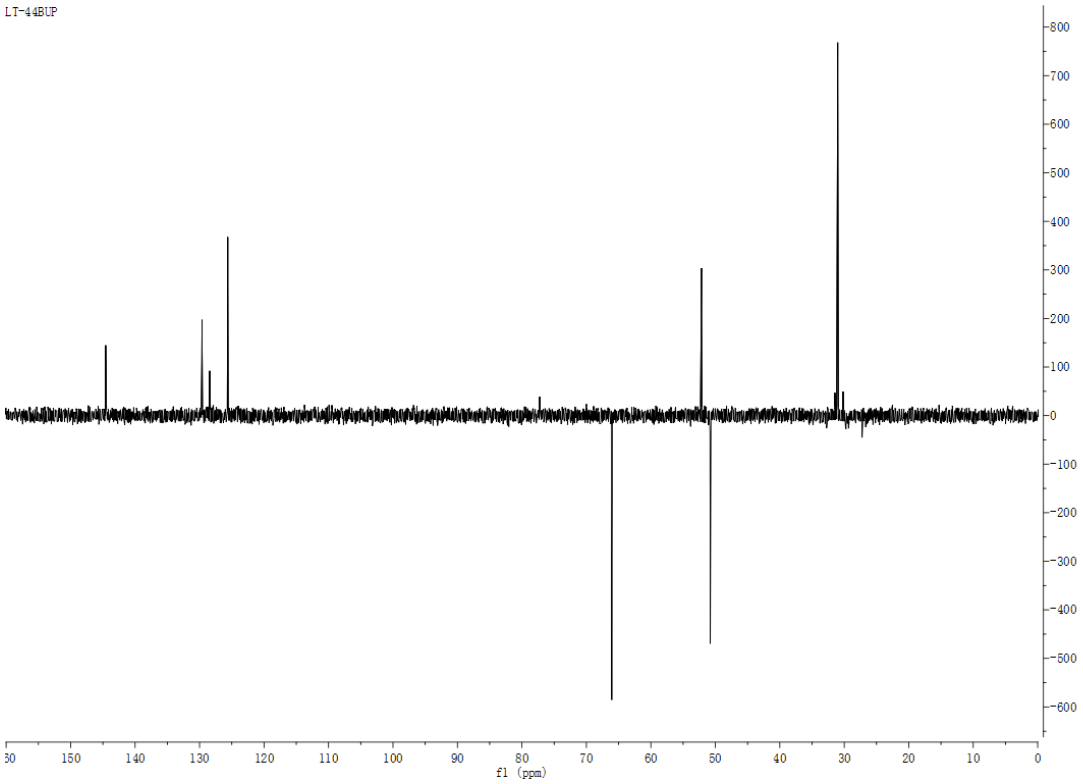
^{19}F NMR (376 MHz, $CDCl_3$):



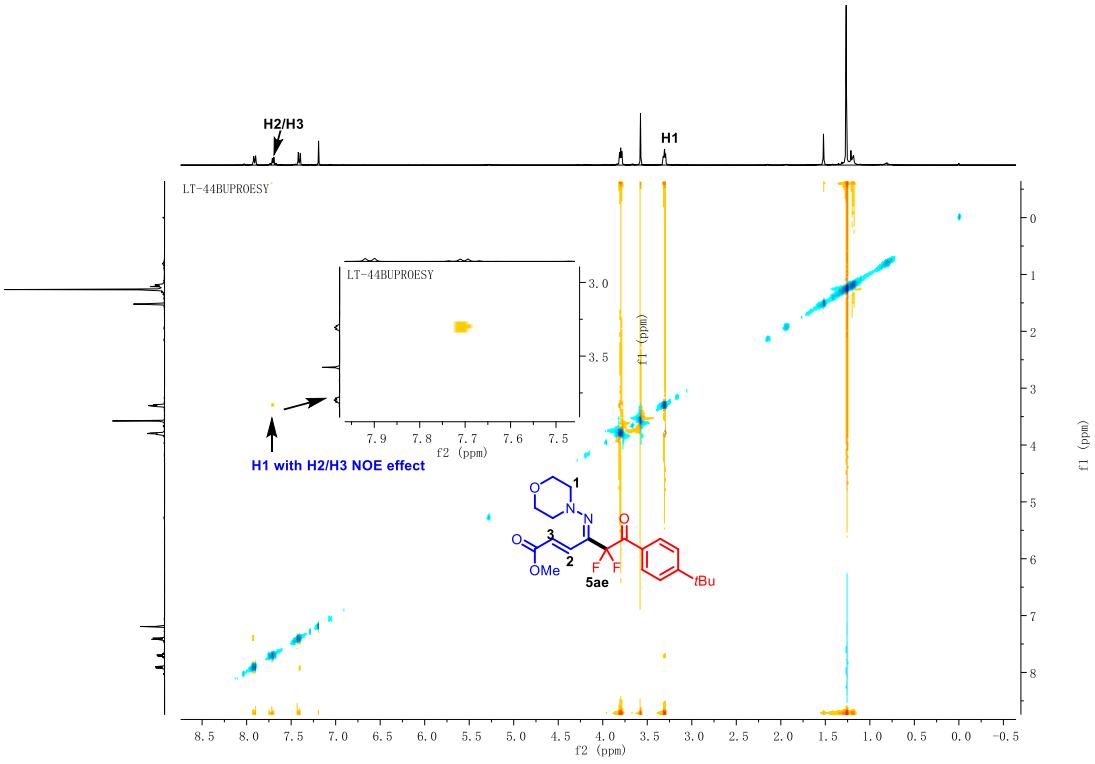
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

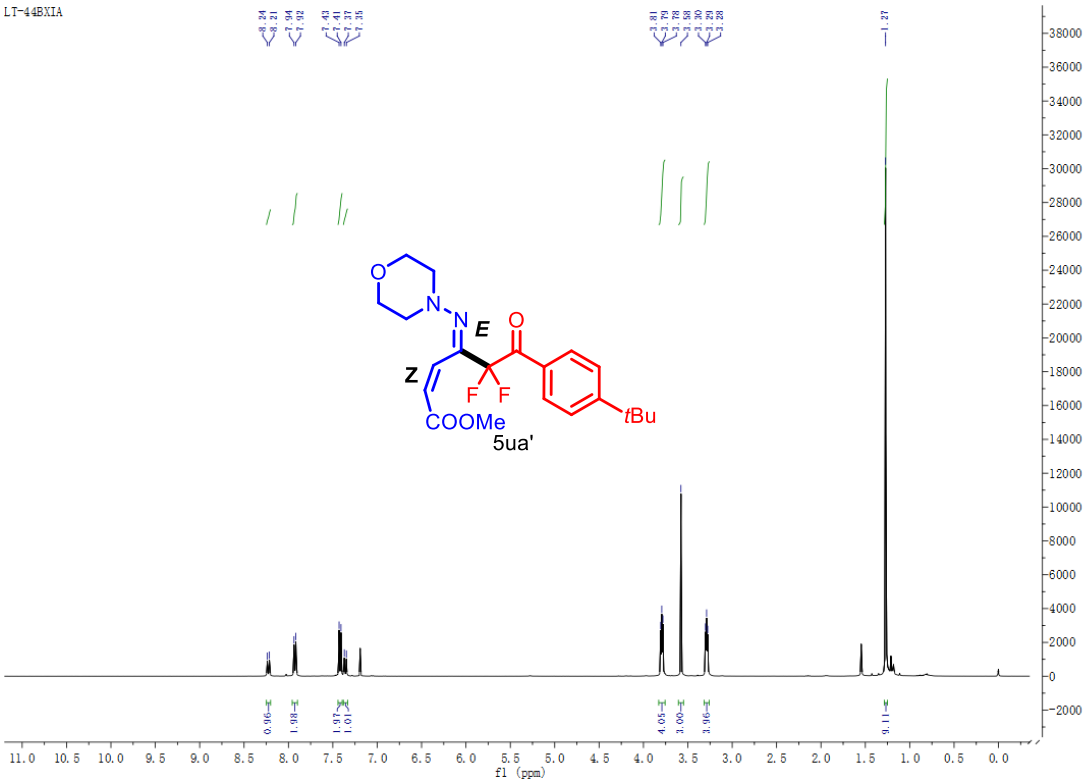


ROESY

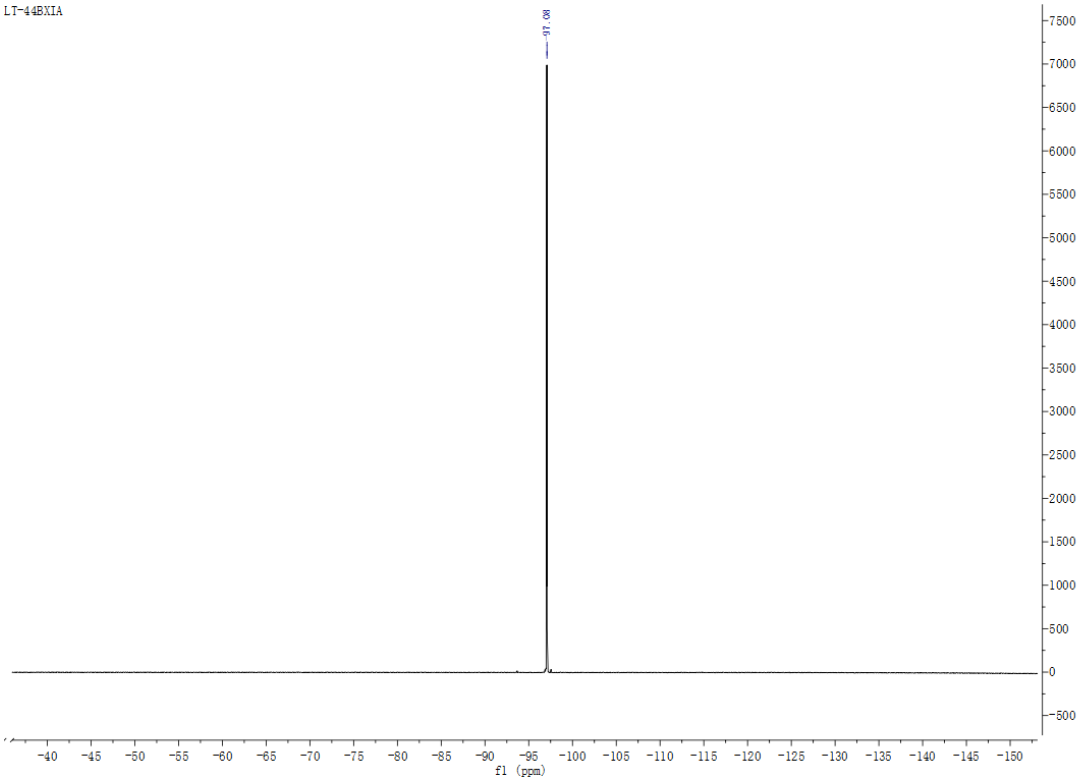


methyl (2Z,4E)-6-(4-(tert-butyl)phenyl)-5,5-difluoro-4-(morpholinoimino)-6-oxohex-2-enoate (5ua')

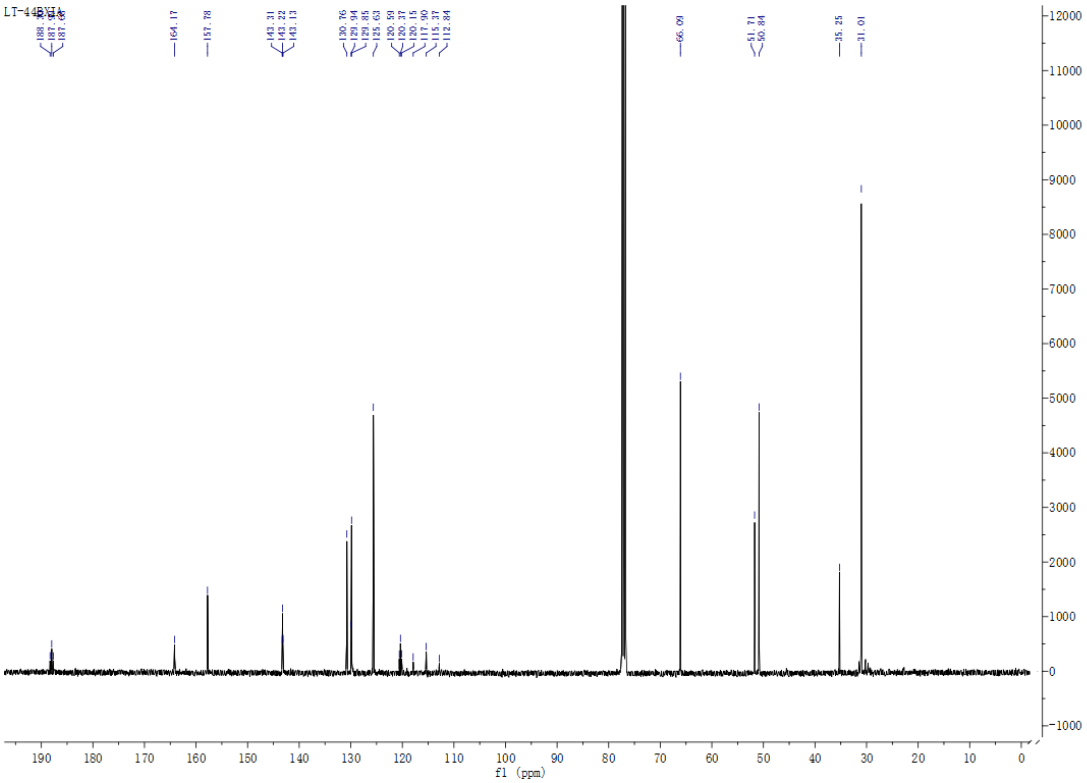
^{1}H NMR (400 MHz, $CDCl_3$)



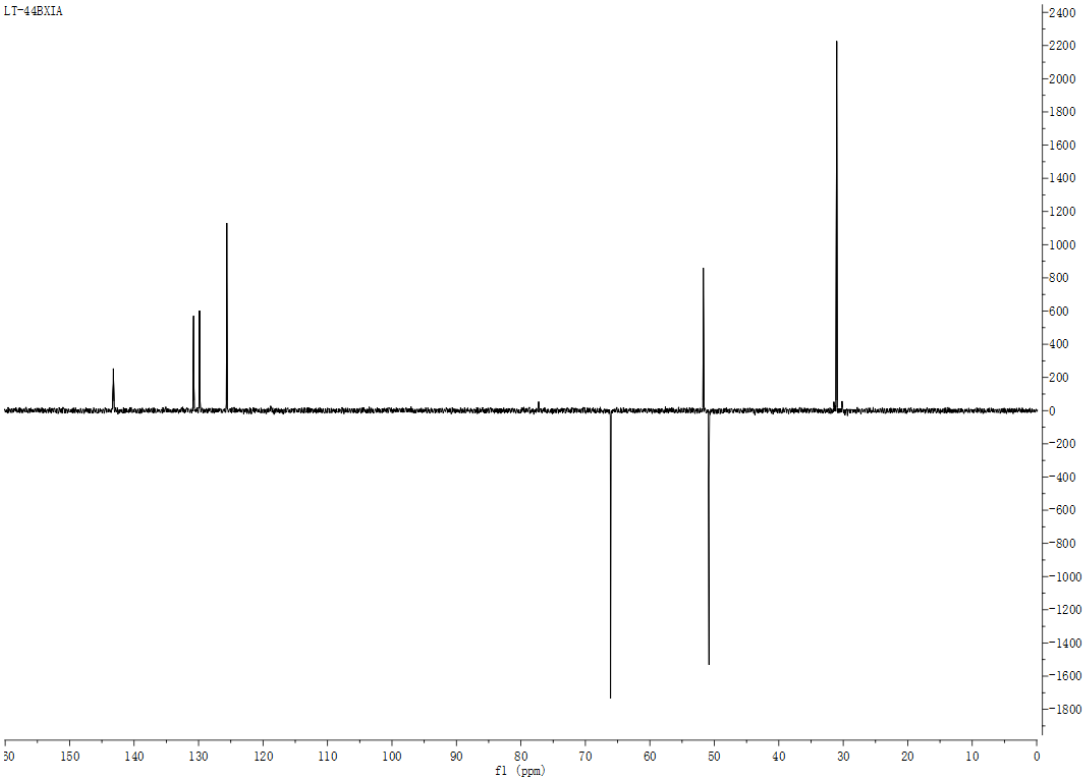
^{19}F NMR (376 MHz, $CDCl_3$):



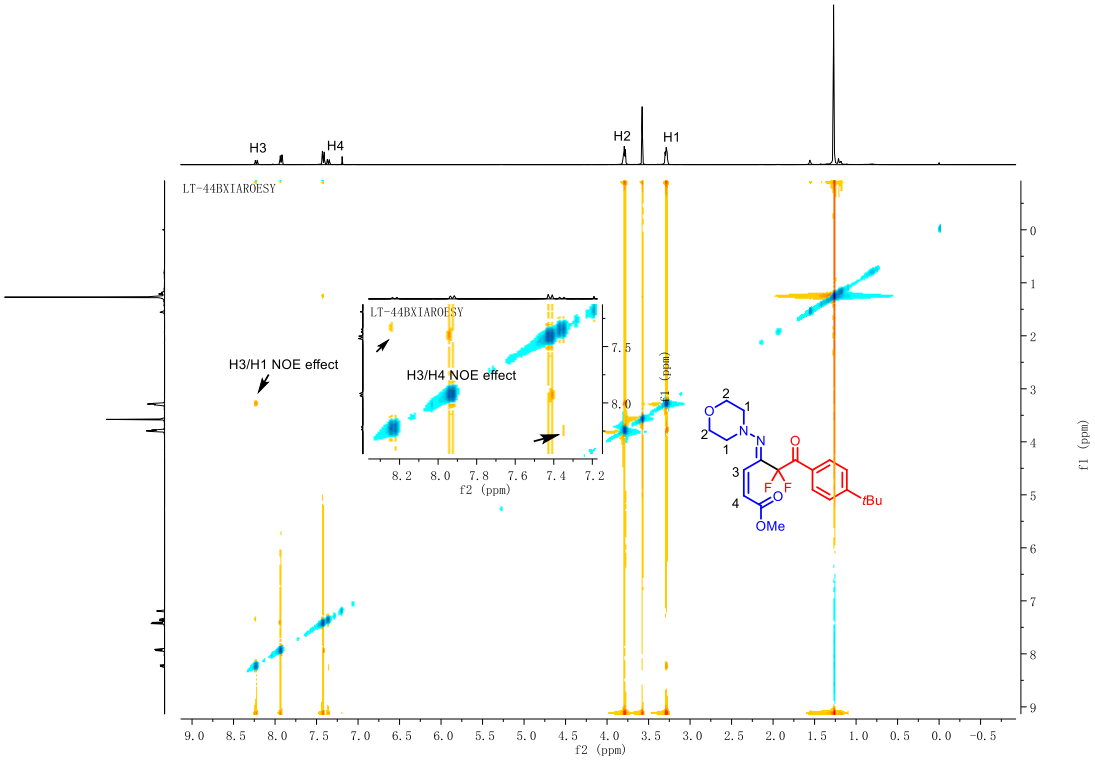
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

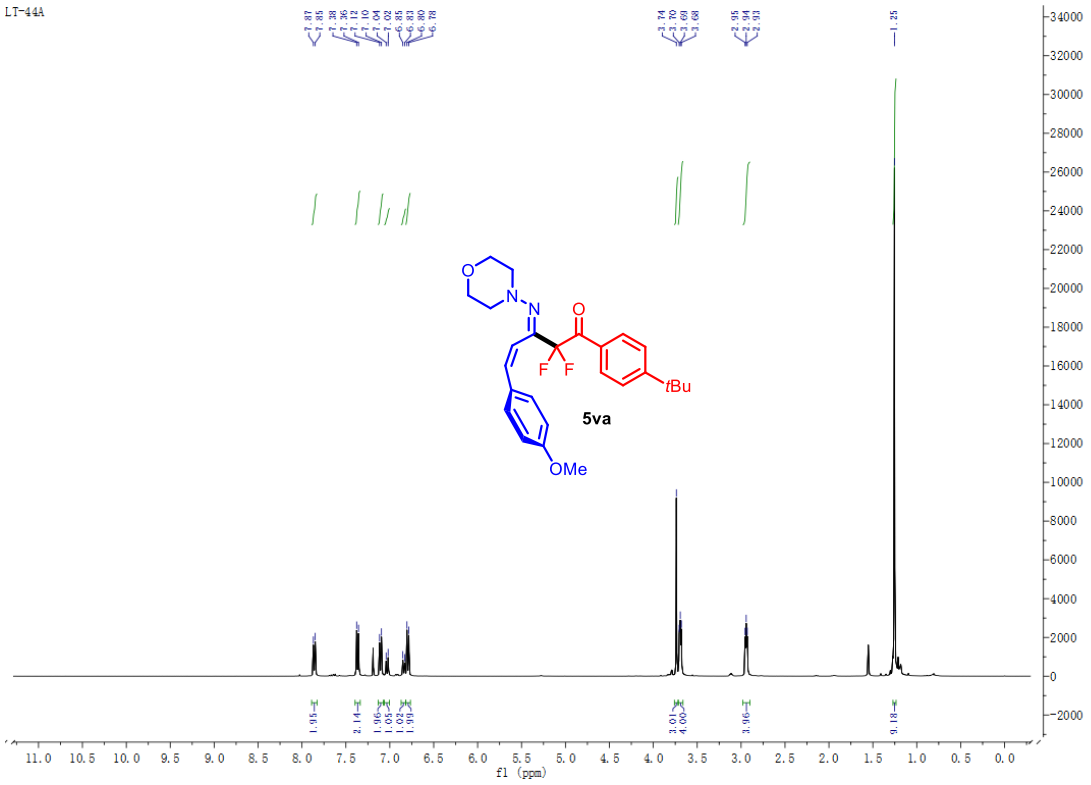


ROESY

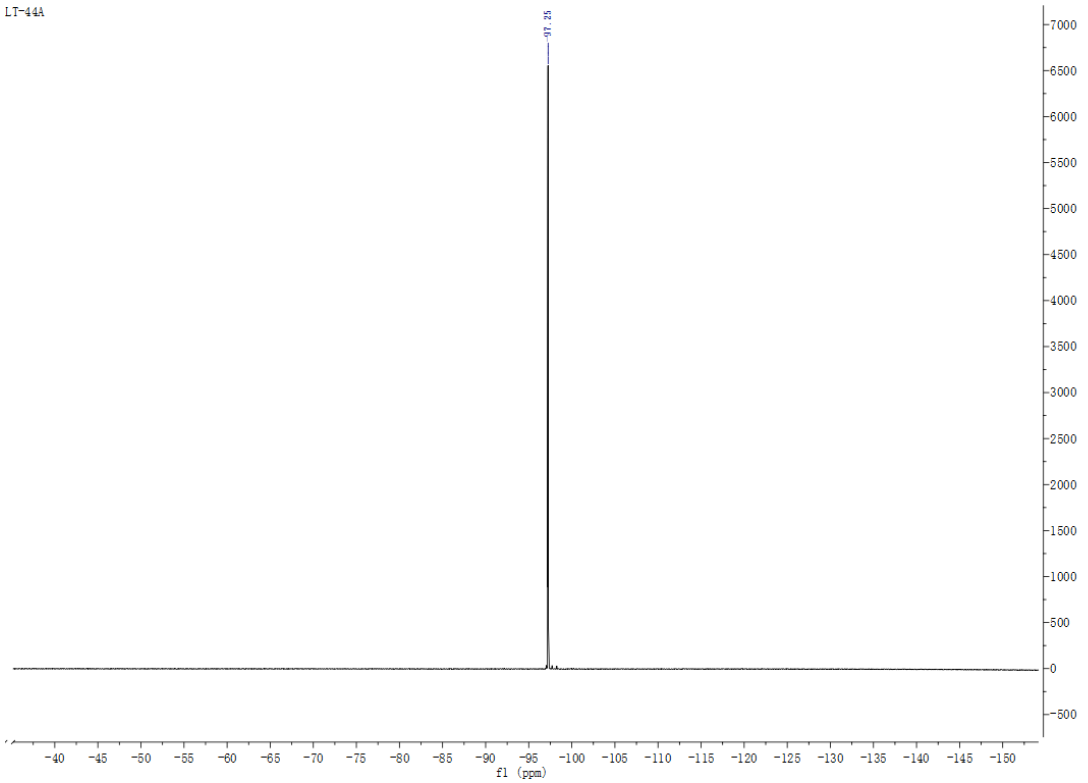


(3E,4Z)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-5-(4-methoxyphenyl)-3-(morpholinoimino)pent-4-en-1-one (5va)

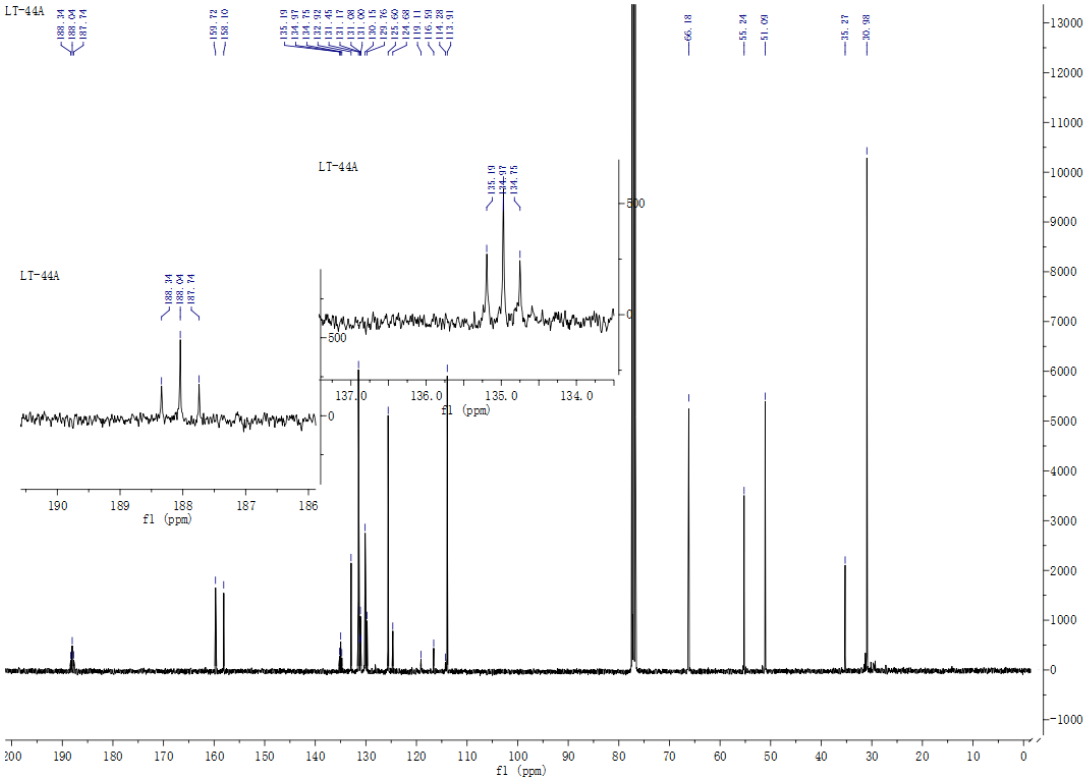
^{1}H NMR (400 MHz, $CDCl_3$)



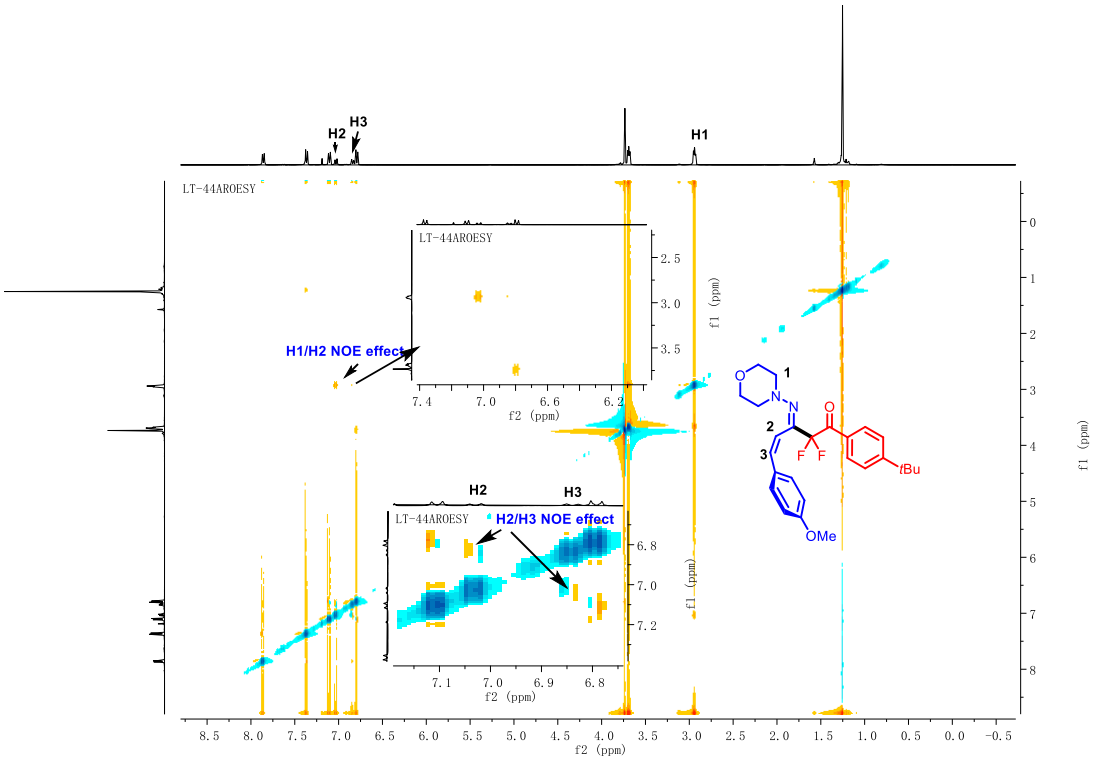
^{19}F NMR (376 MHz, $CDCl_3$):



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

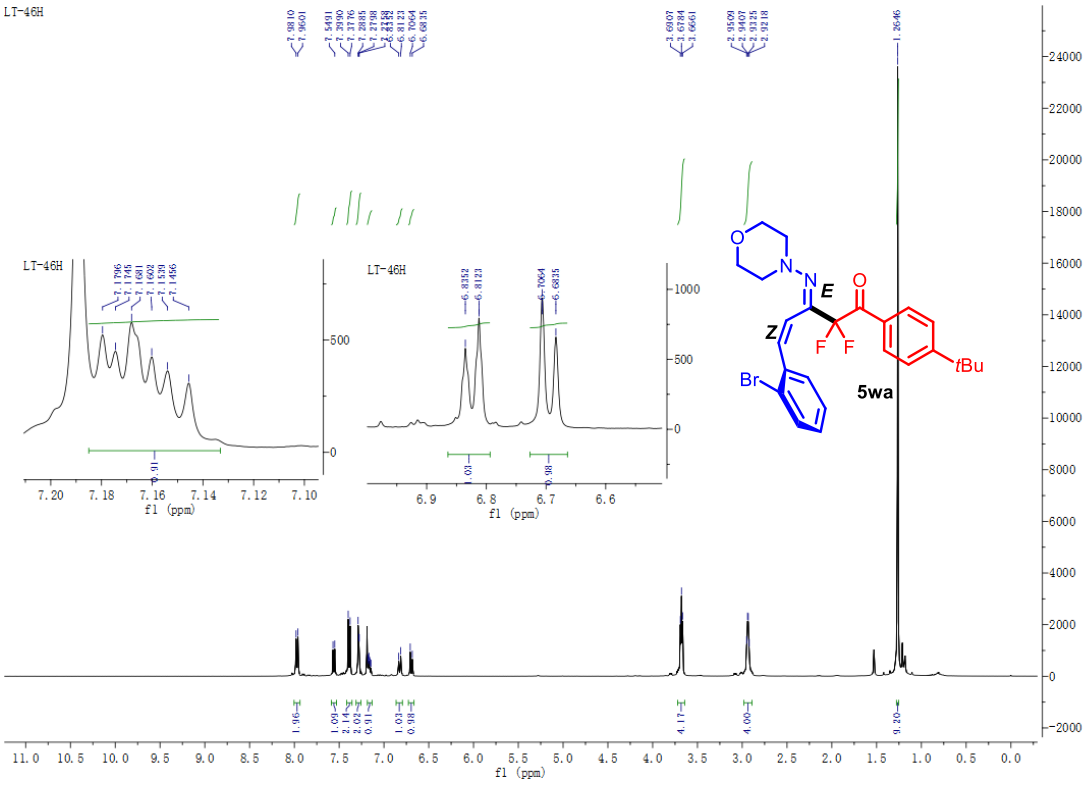


ROESY

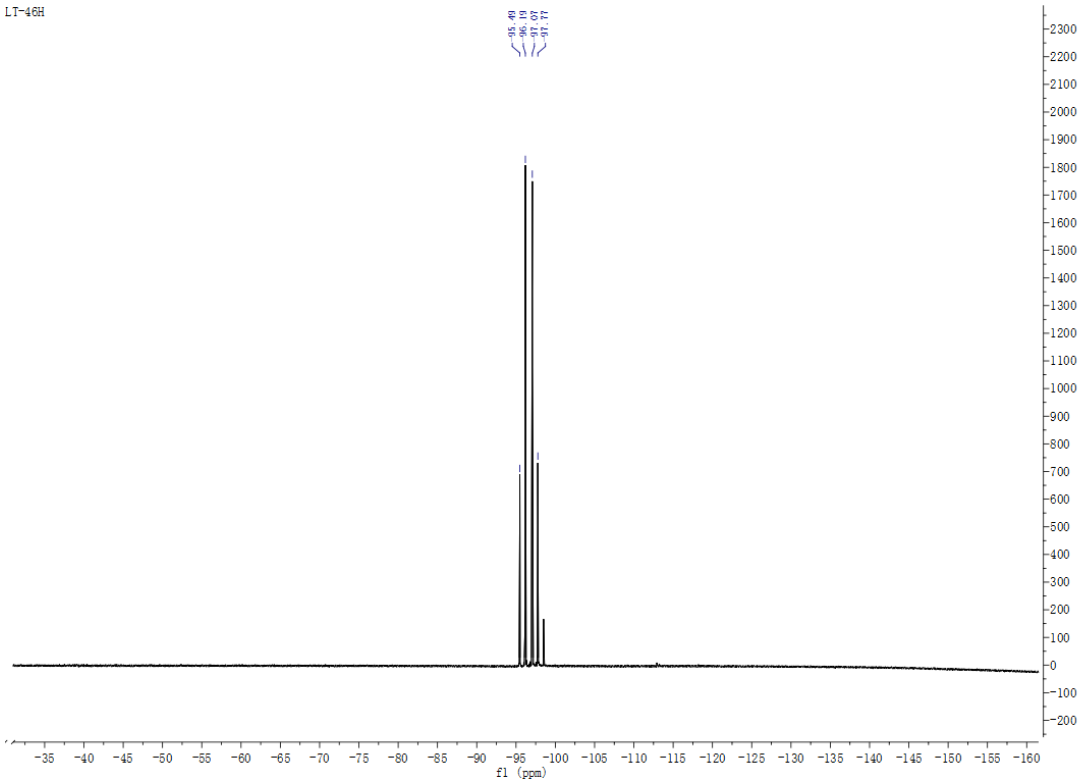


(3E,4Z)-5-(2-bromophenyl)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)pent-4-en-1-one (5wa)

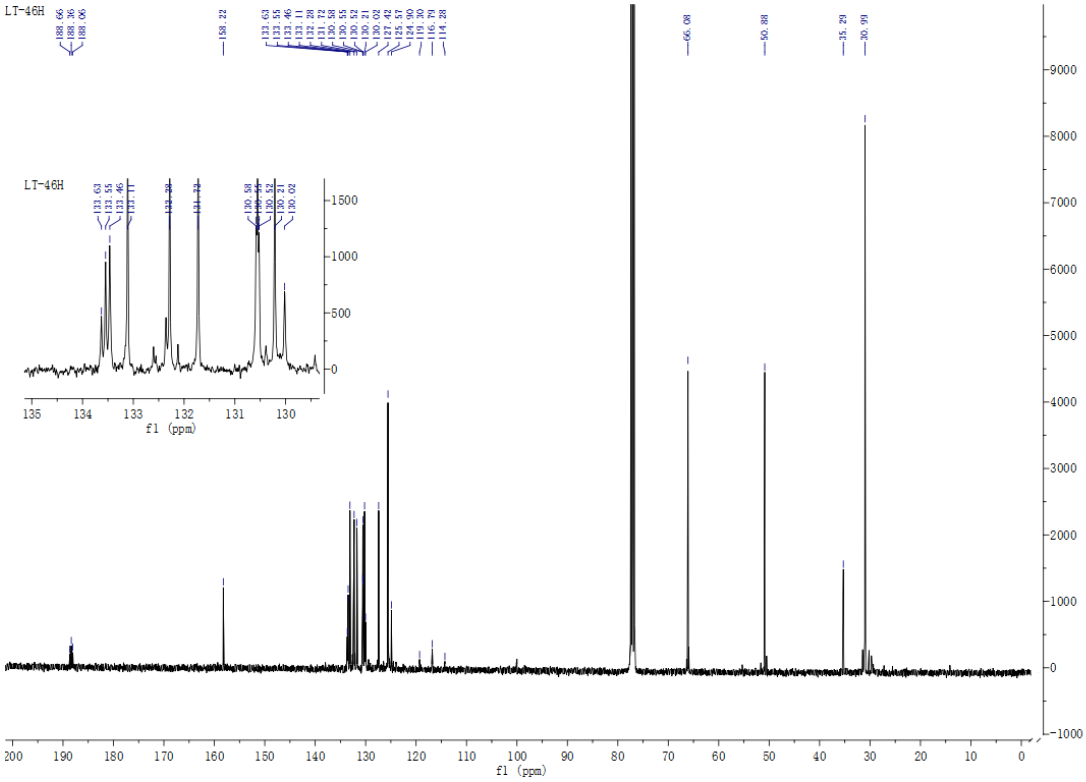
^{1}H NMR (400 MHz, $CDCl_3$)



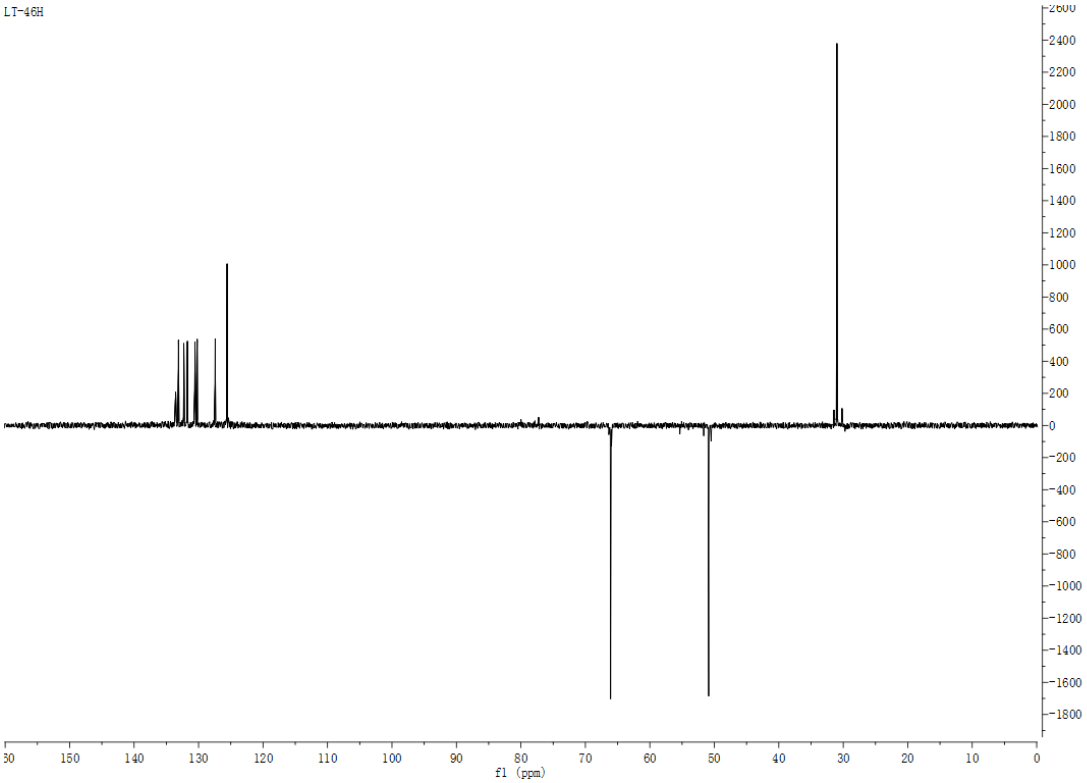
^{19}F NMR (376 MHz, $CDCl_3$):



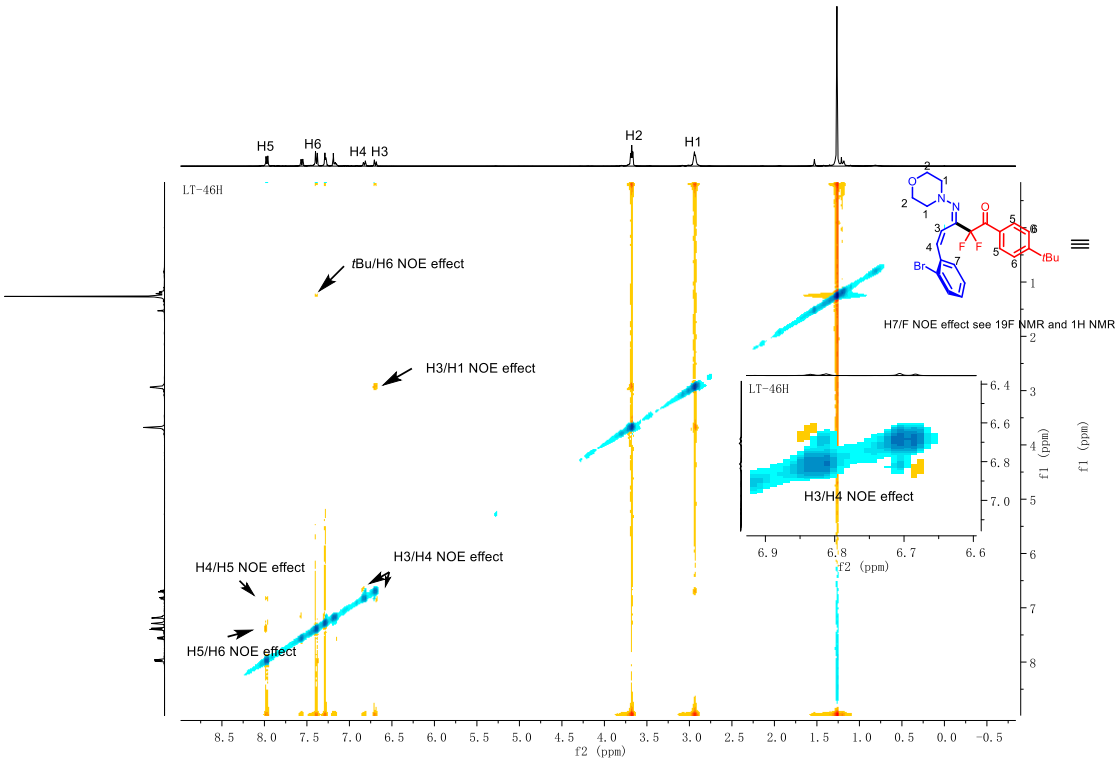
^{13}C NMR (100 MHz, $CDCl_3$):

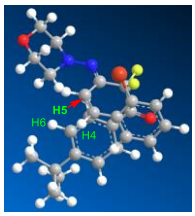


DEPT



ROESY

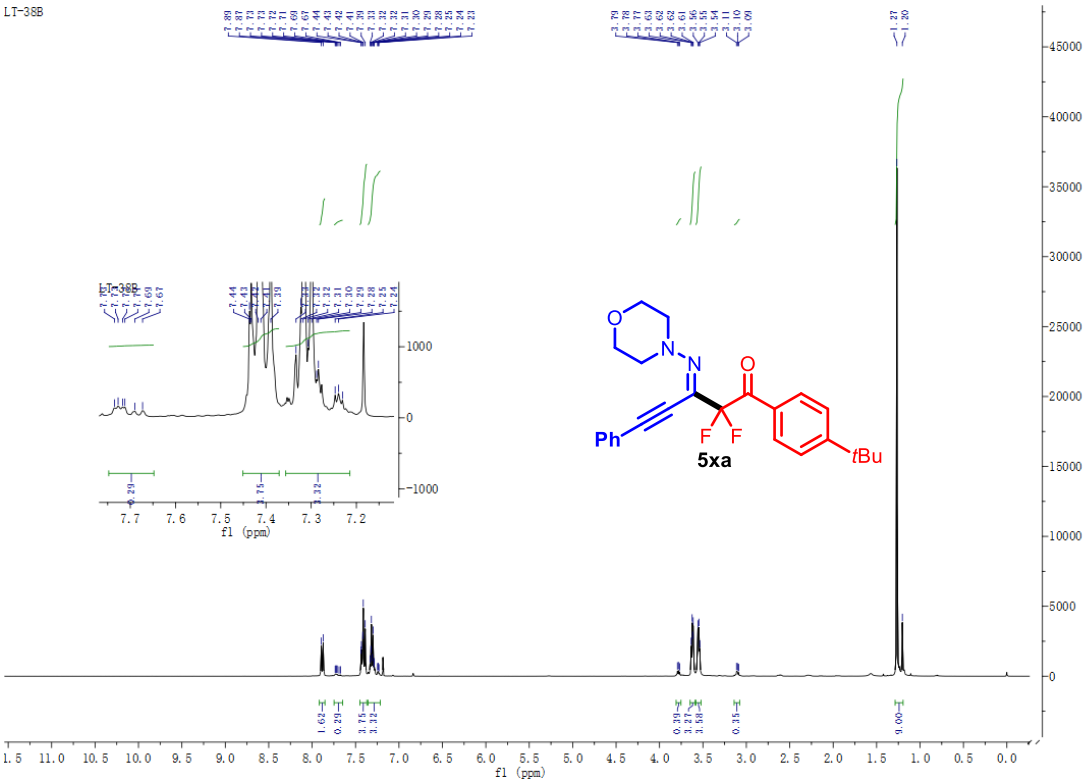




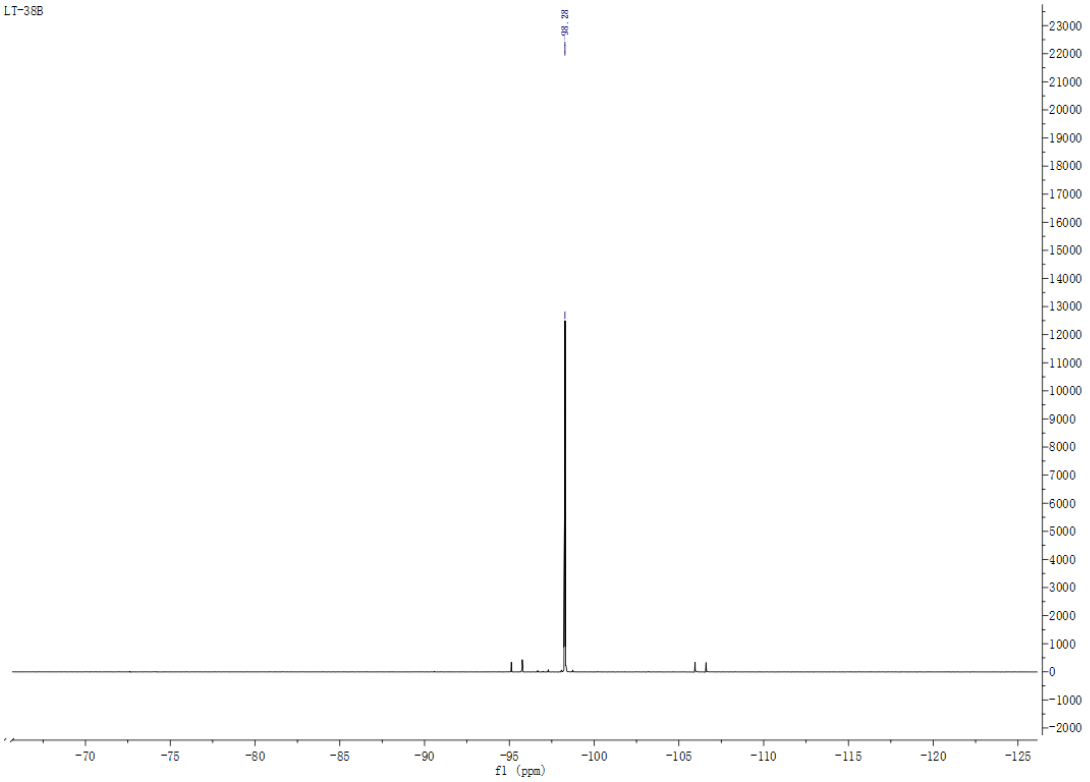
3D structure of **5wa**

(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-5-phenylpent-4-yn-1-one (5xa)

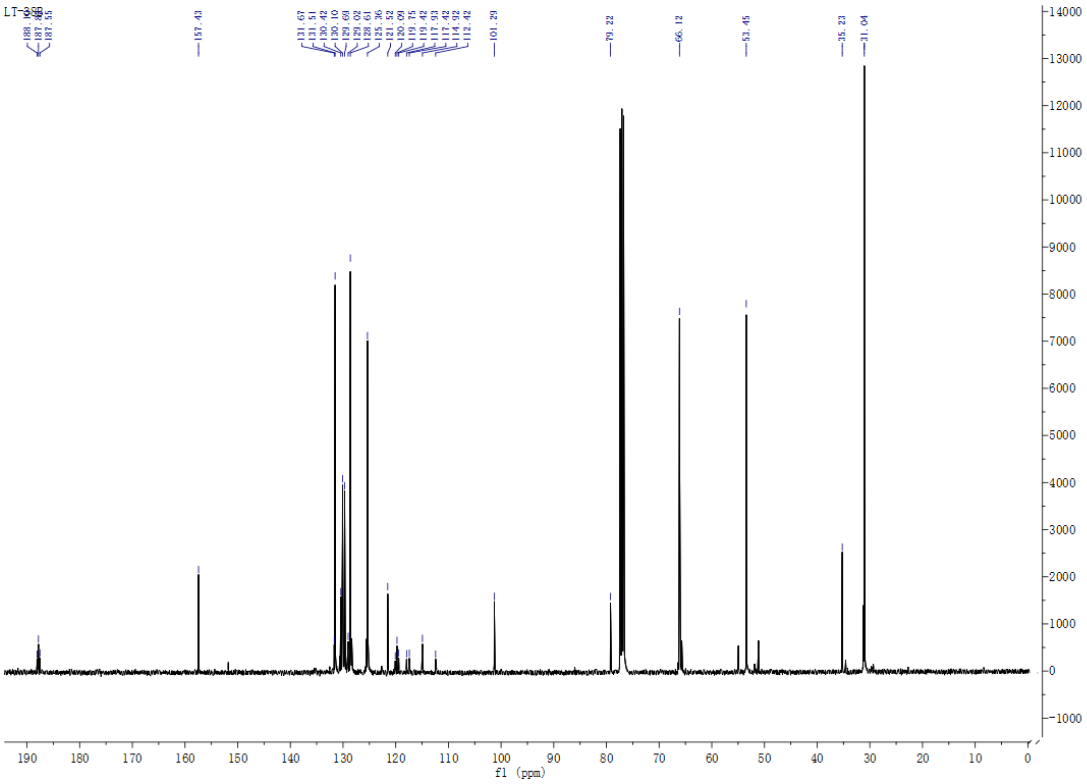
^{1}H NMR (400 MHz, $CDCl_3$)



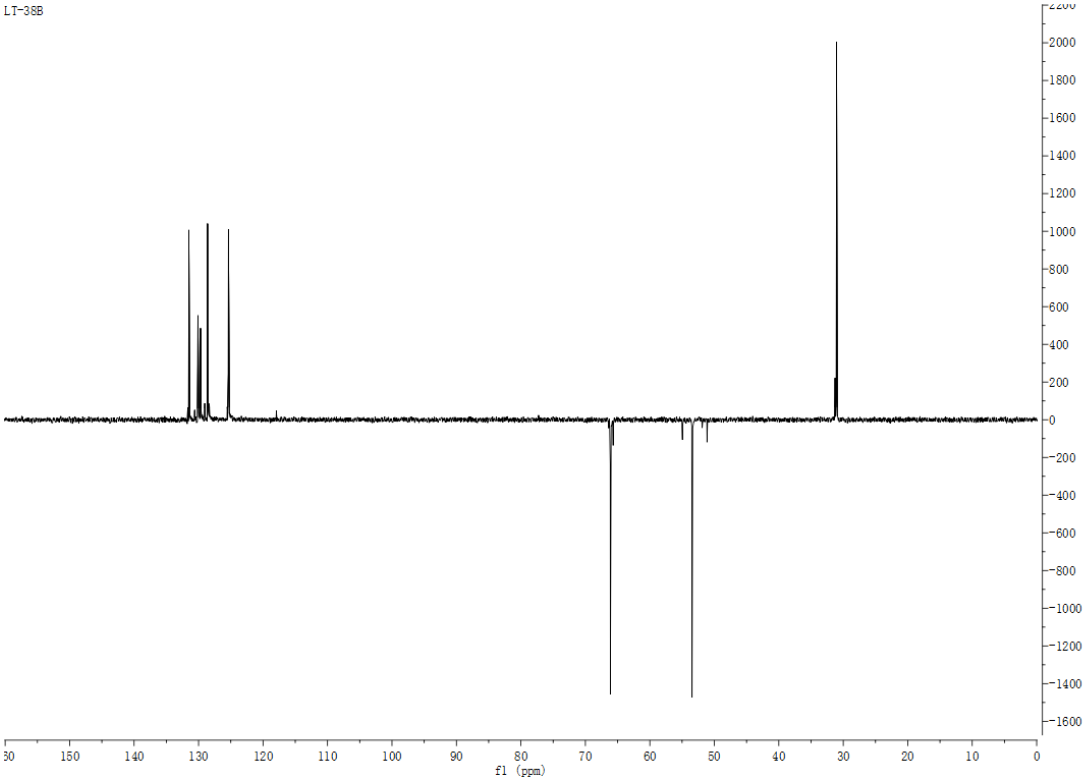
^{19}F NMR (376 MHz, $CDCl_3$):



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



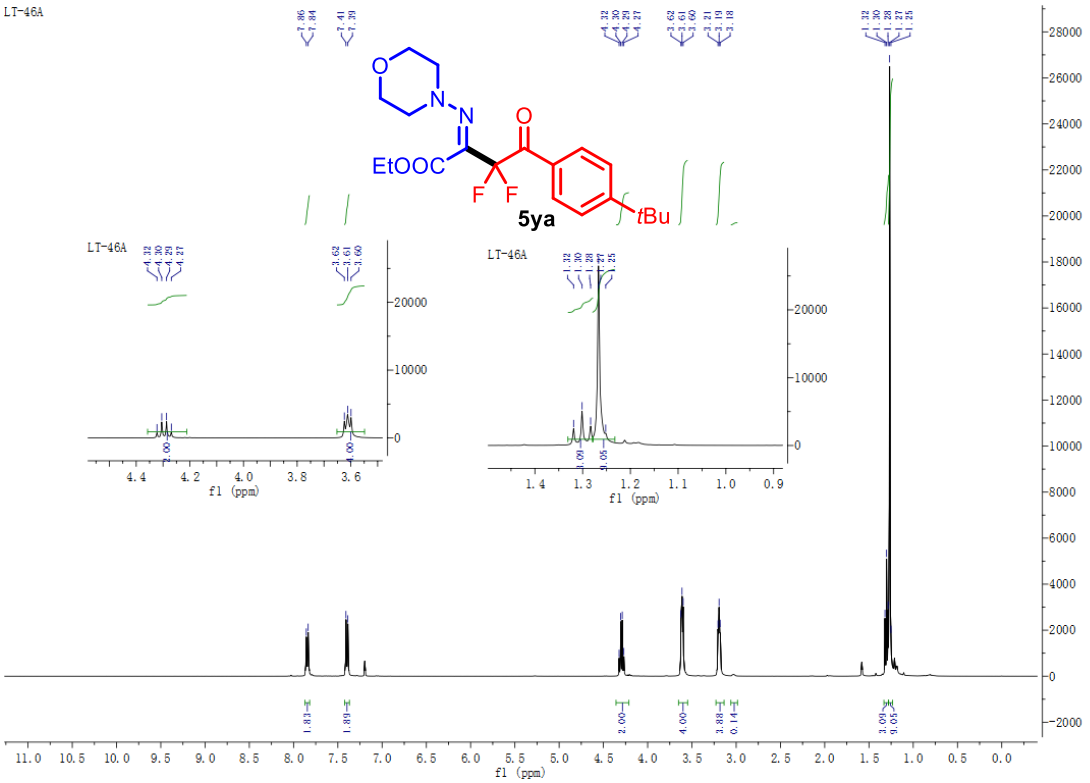
DEPT



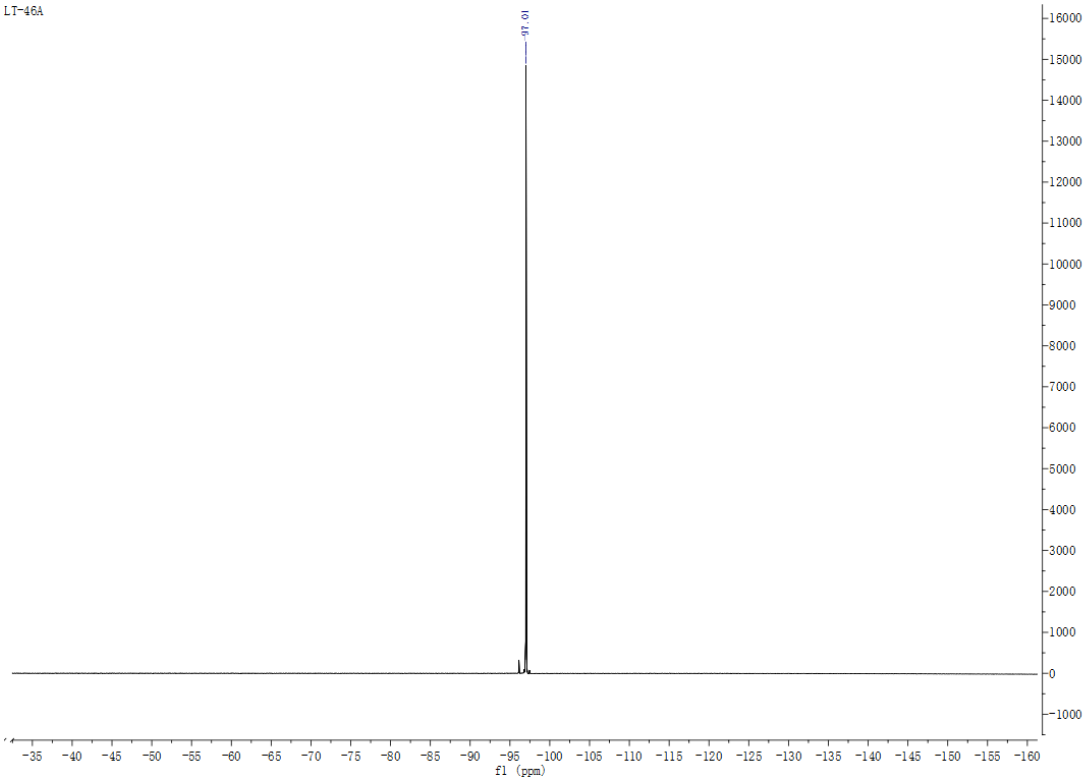
ethyl

(E)-4-(4-(tert-butyl)phenyl)-3,3-difluoro-2-(morpholinoimino)-4-oxobutanoate (5ya)

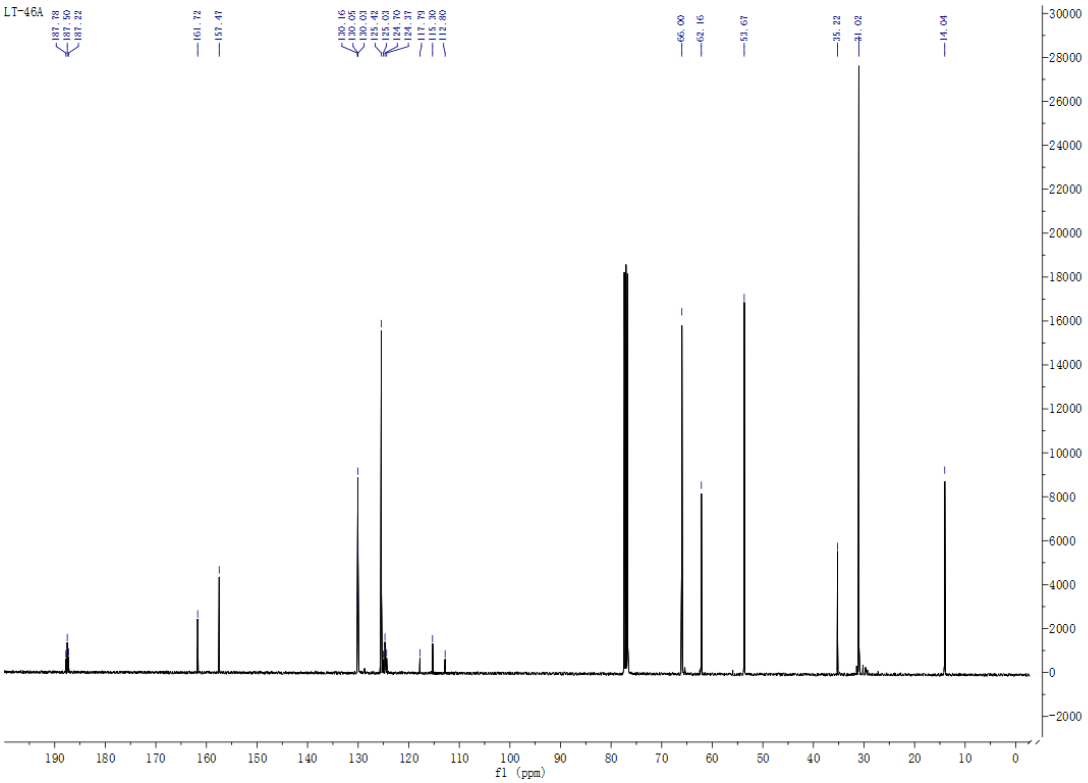
^{1}H NMR (400 MHz, $CDCl_3$)



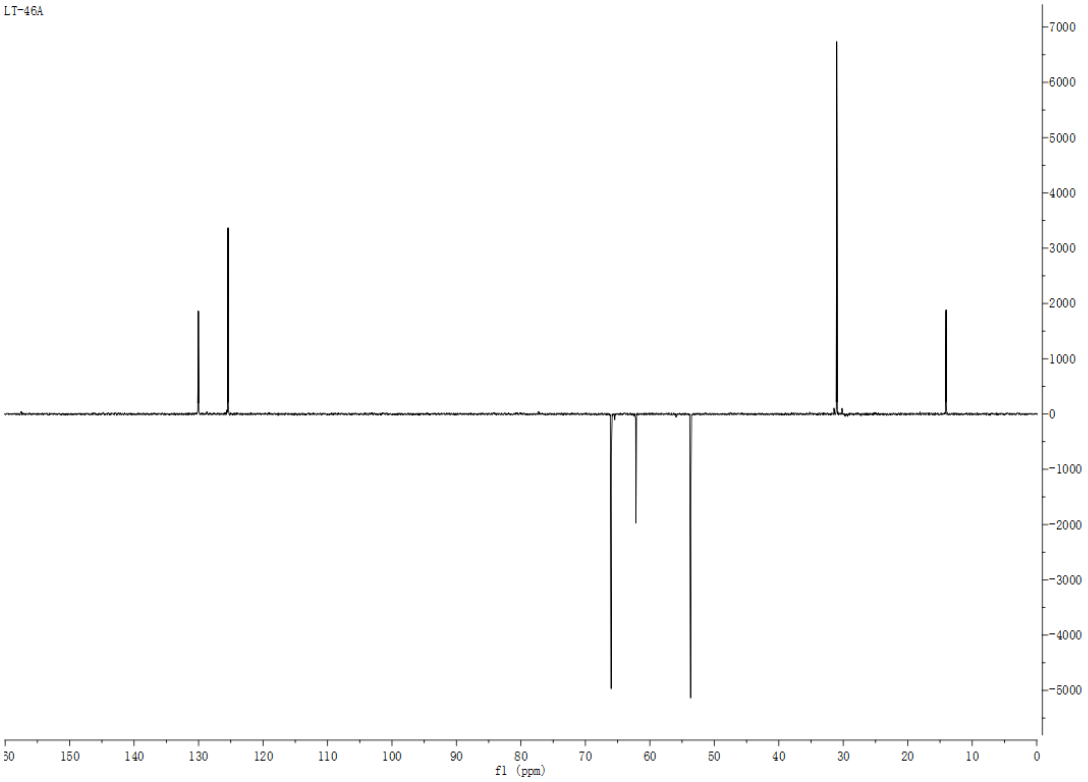
^{19}F NMR (376 MHz, $CDCl_3$):



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

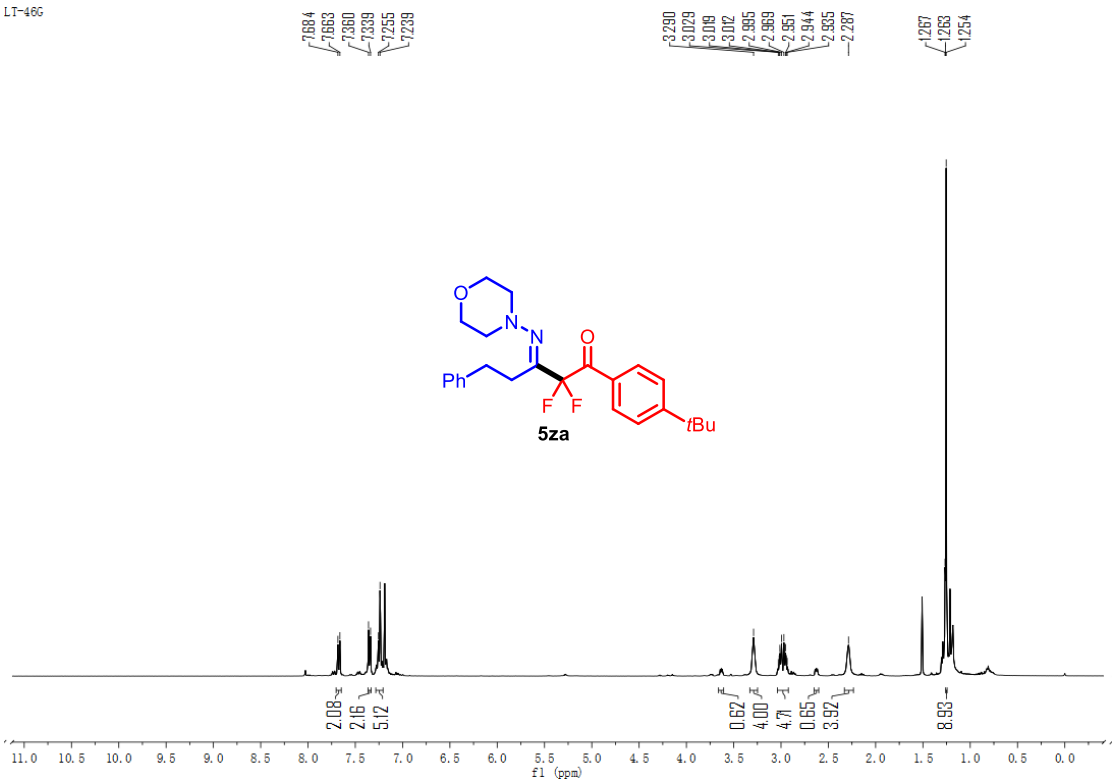


DEPT

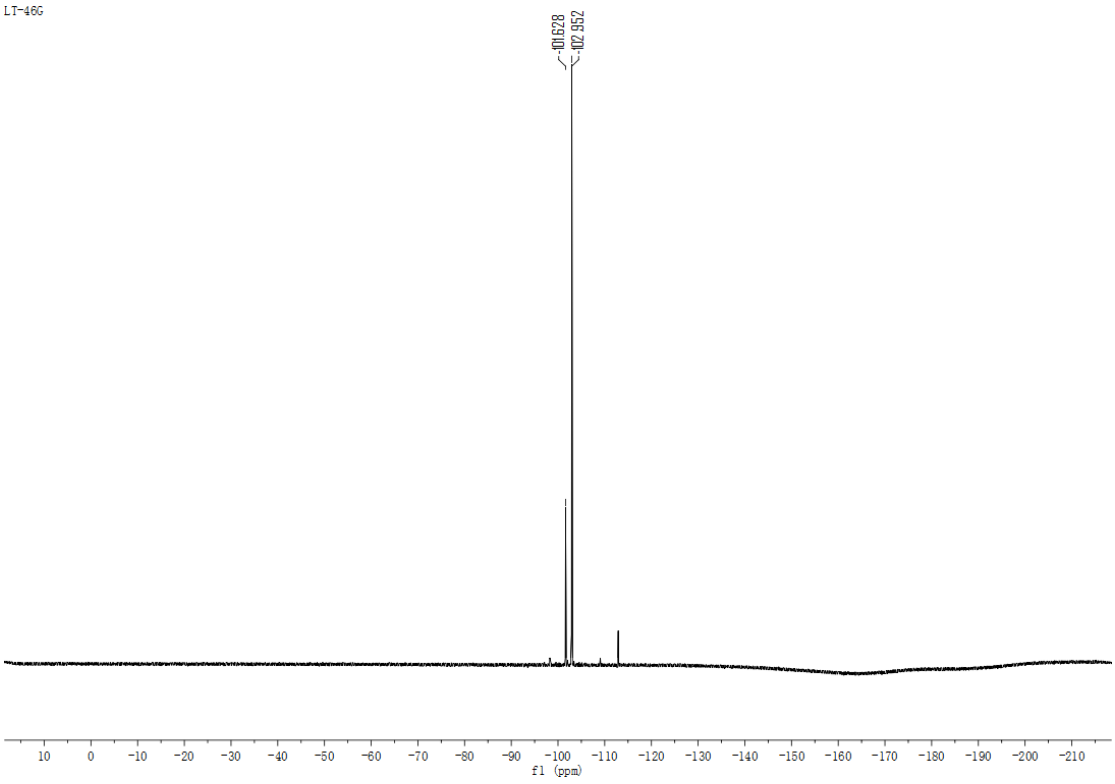


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(morpholinoimino)-5-phenylpentan-1-one (5za)

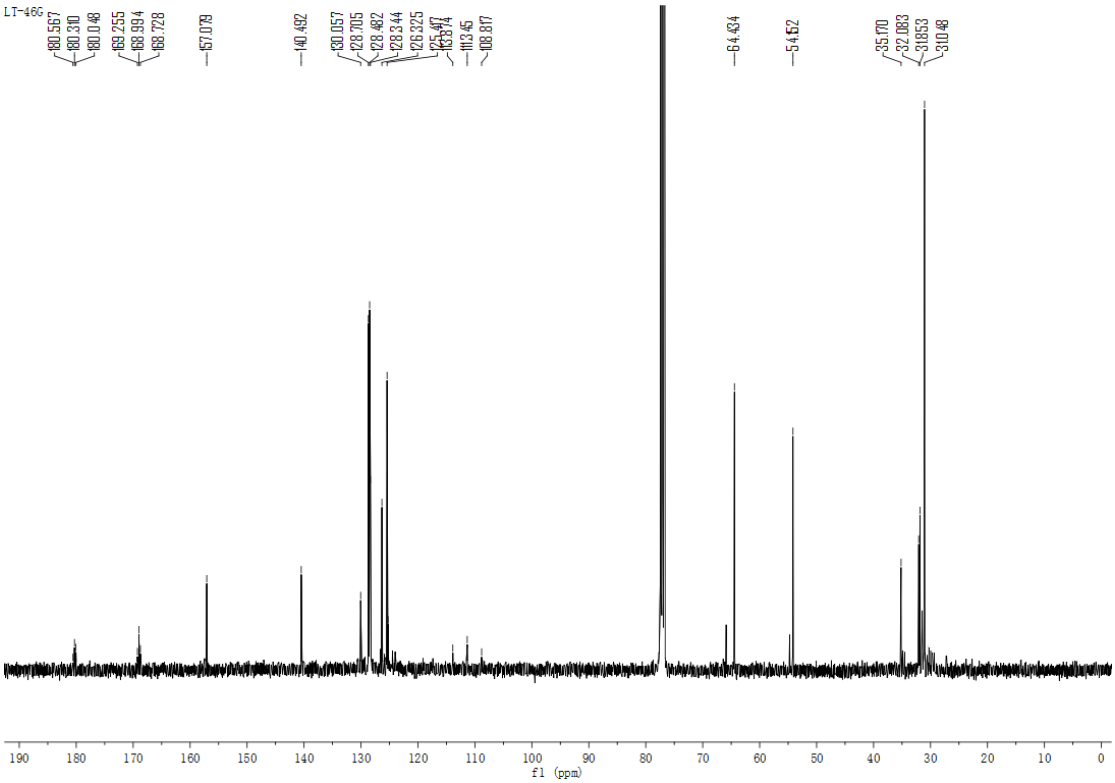
^{1}H NMR (400 MHz, $CDCl_3$)



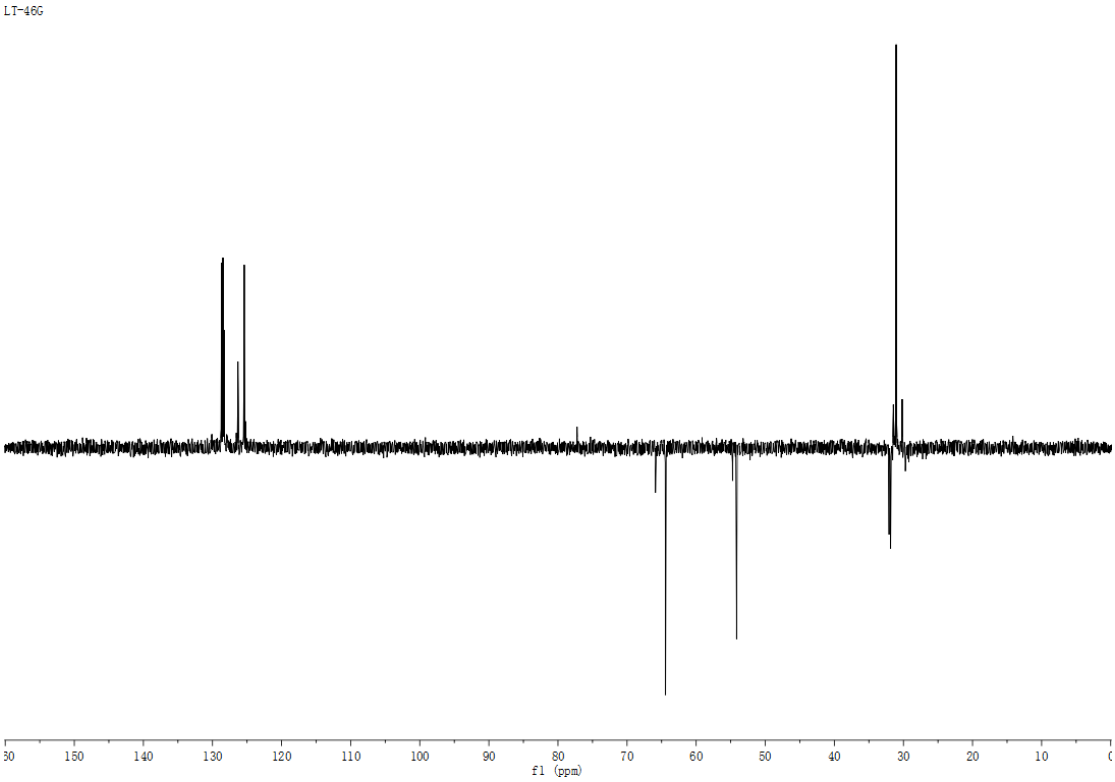
^{19}F NMR (376 MHz, $CDCl_3$):



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

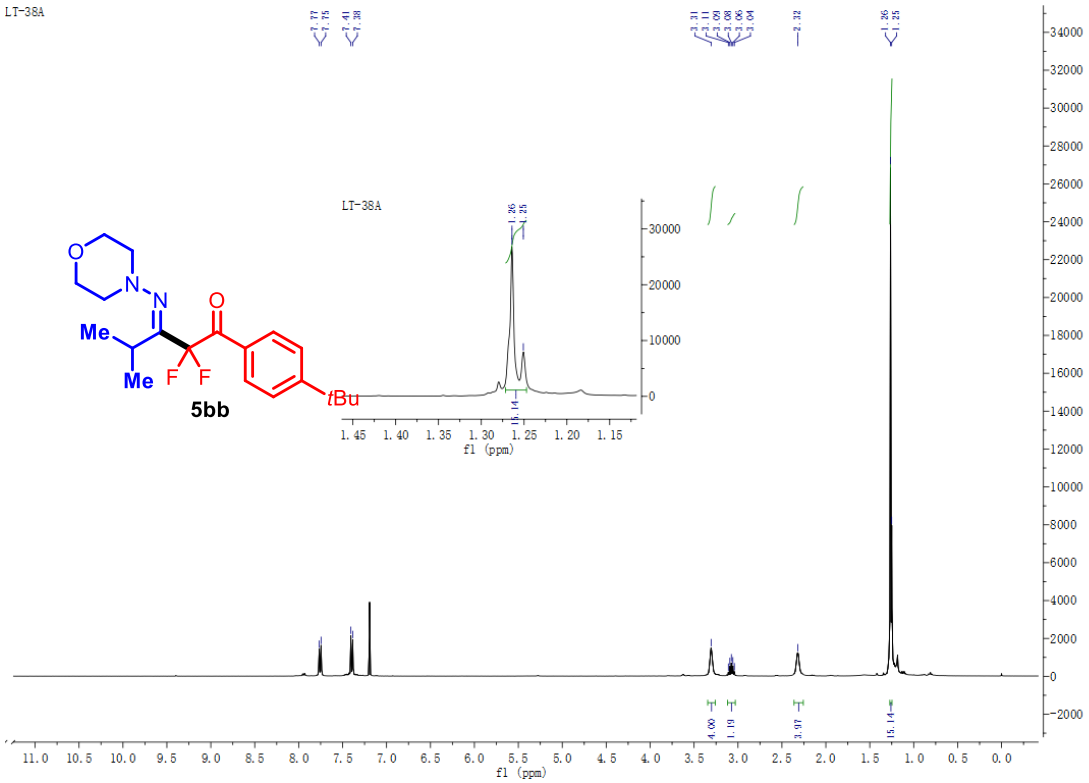


DEPT

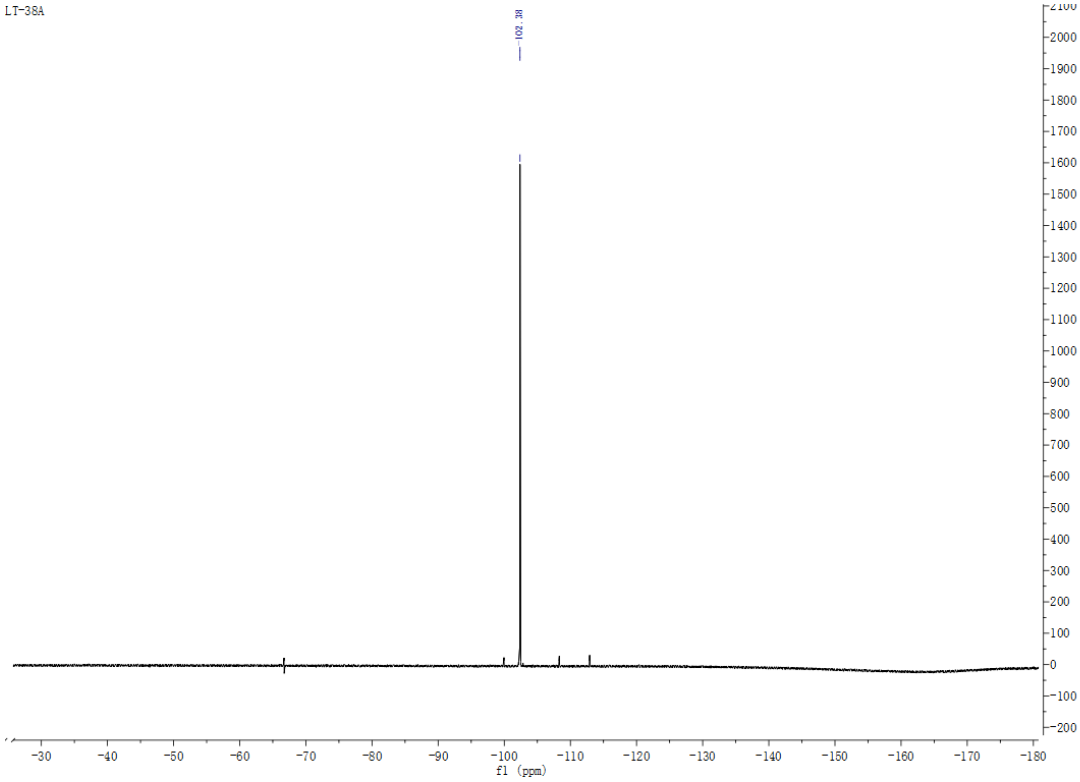


(E)-1-(4-(tert-butyl)phenyl)-2,2-difluoro-4-methyl-3-(morpholinoimino)pentan-1-one (5bb)

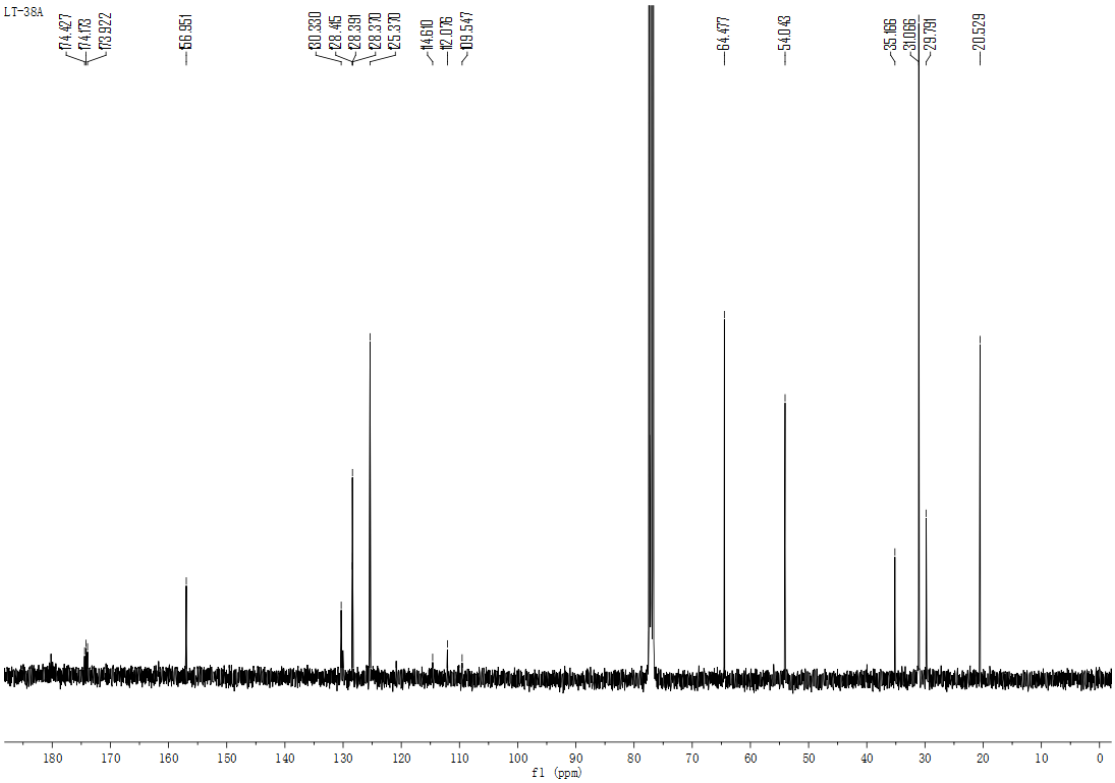
^{1}H NMR (400 MHz, $CDCl_3$)



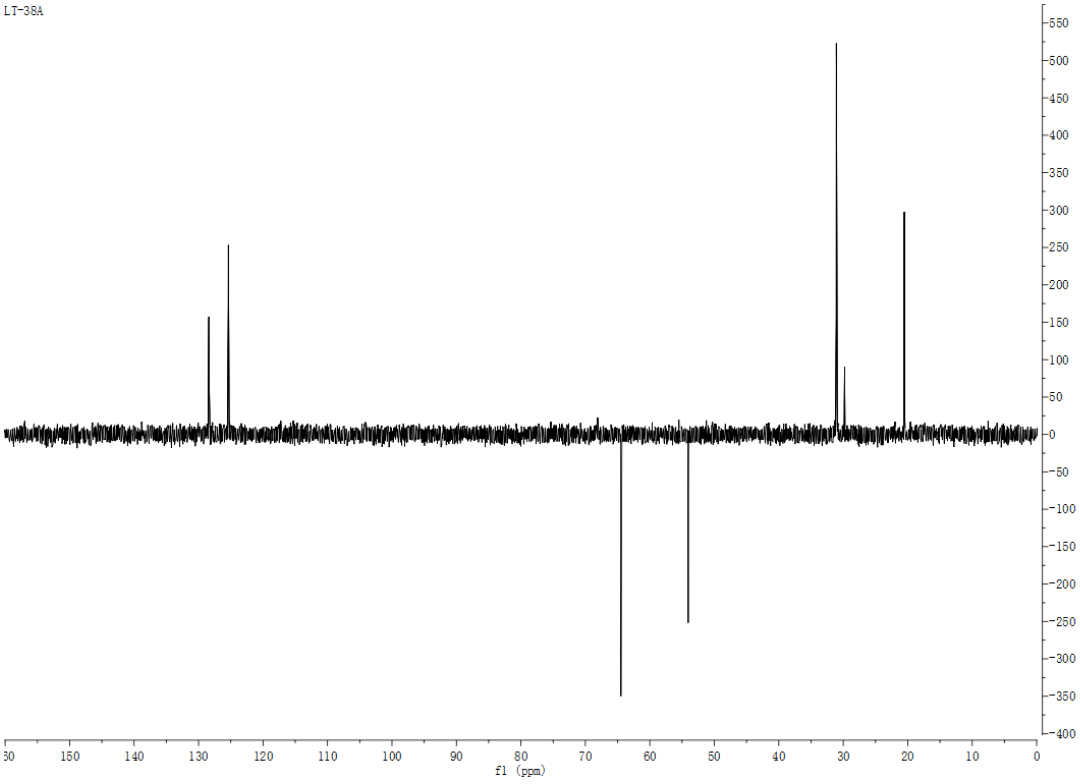
^{19}F NMR (376 MHz, $CDCl_3$):



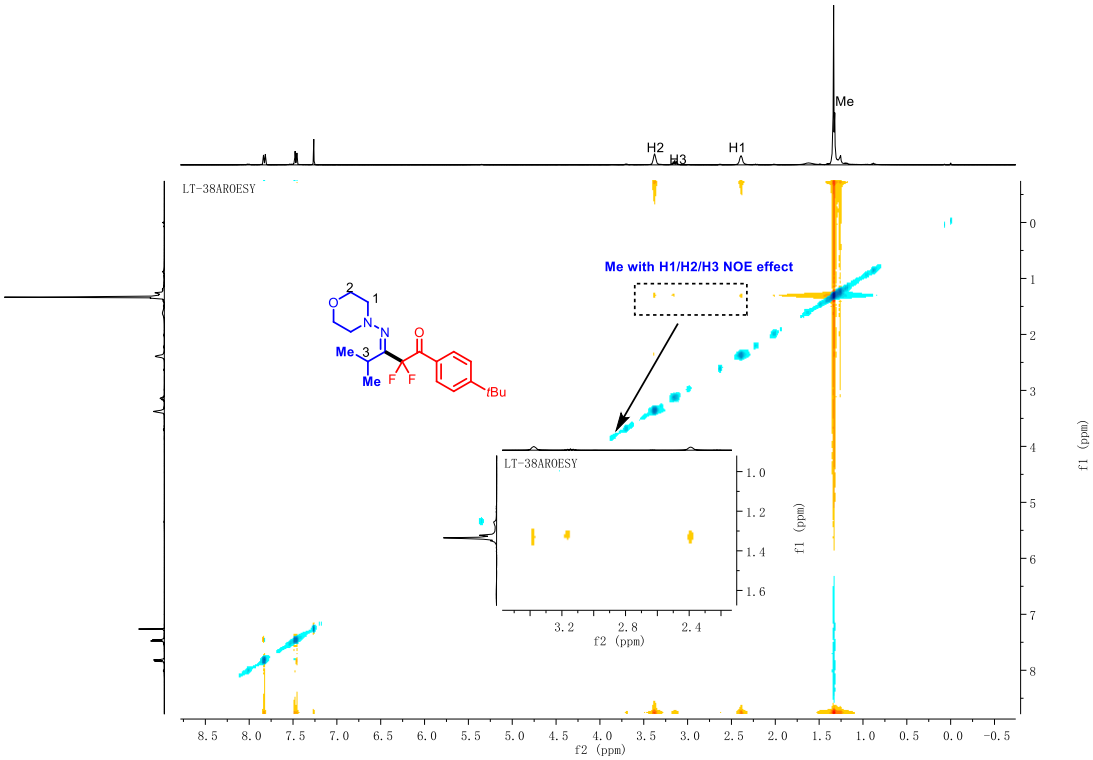
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

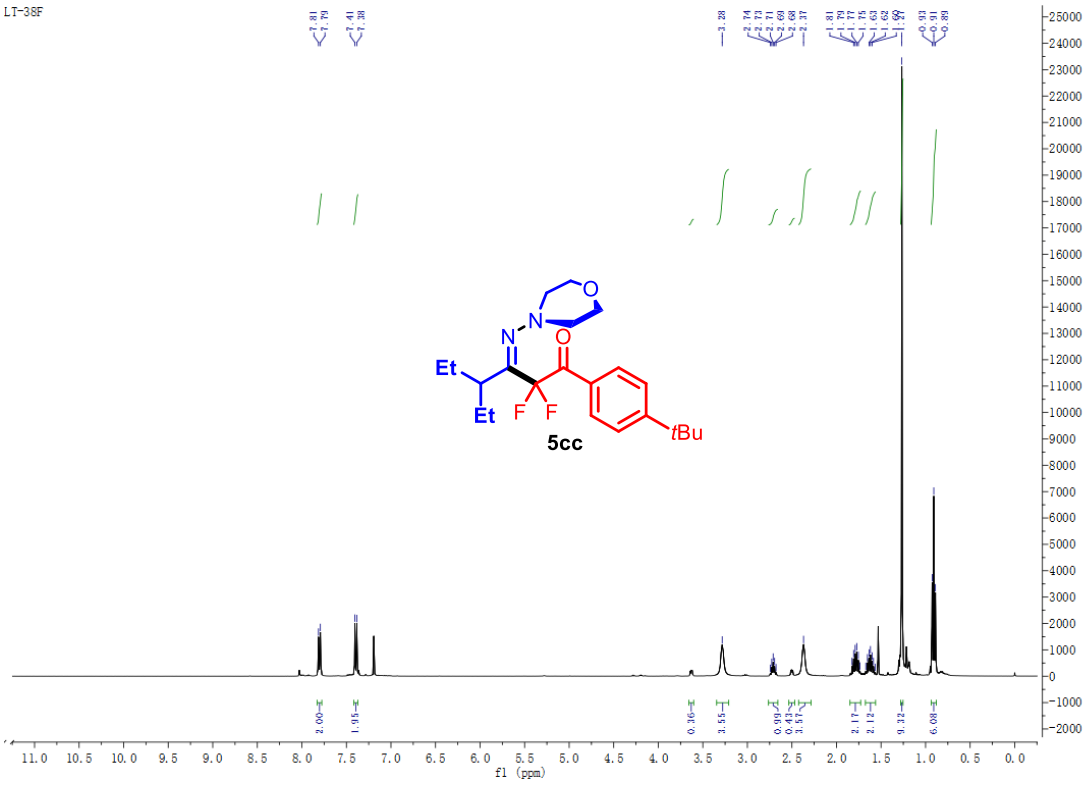


ROESY

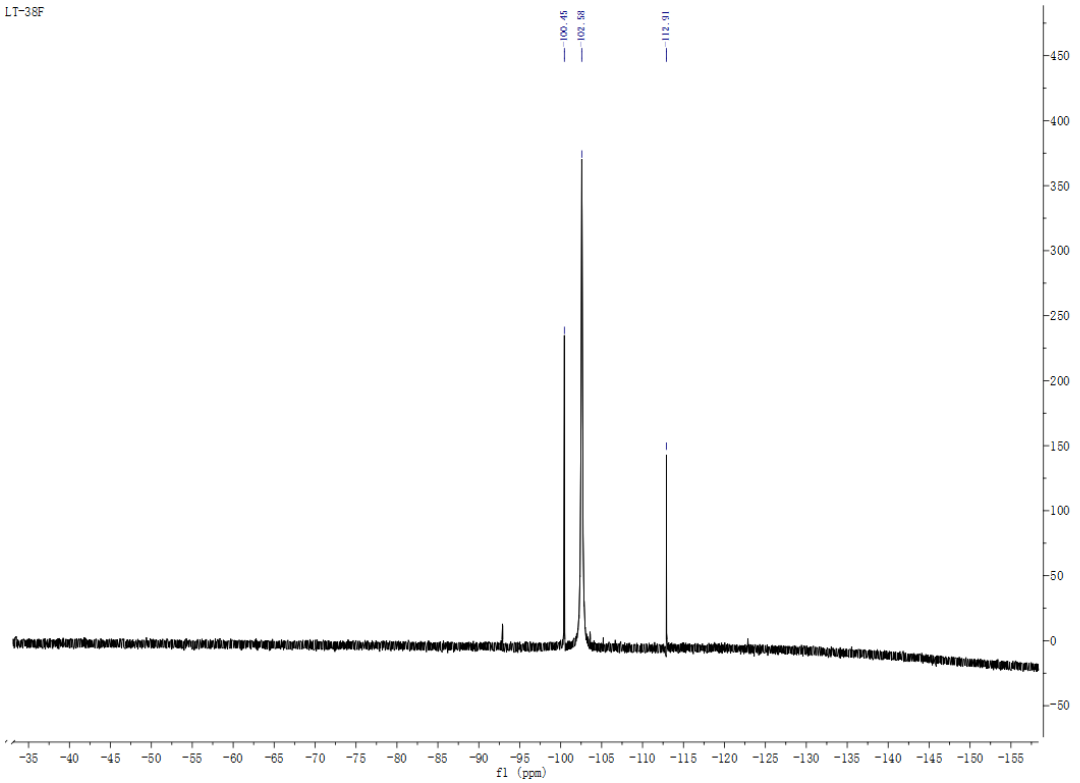


(Z)-1-(4-(tert-butyl)phenyl)-4-ethyl-2,2-difluoro-3-(morpholinoimino)hexan-1-one (5cc)

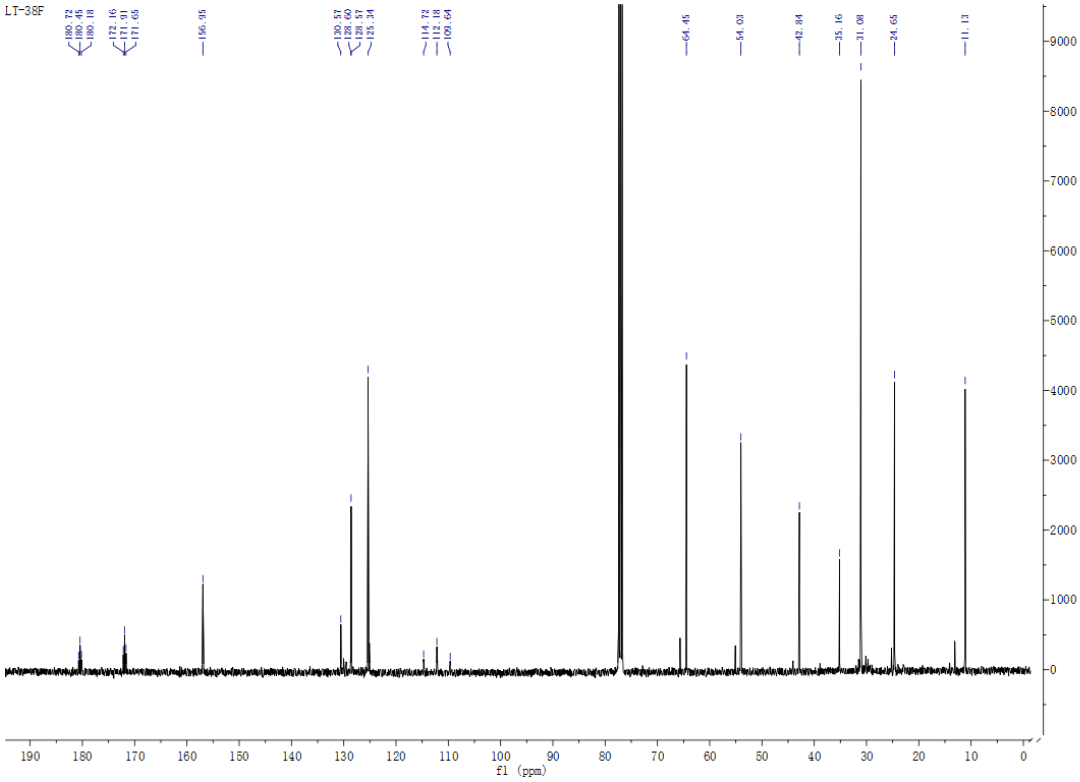
^{1}H NMR (400 MHz, $CDCl_3$)



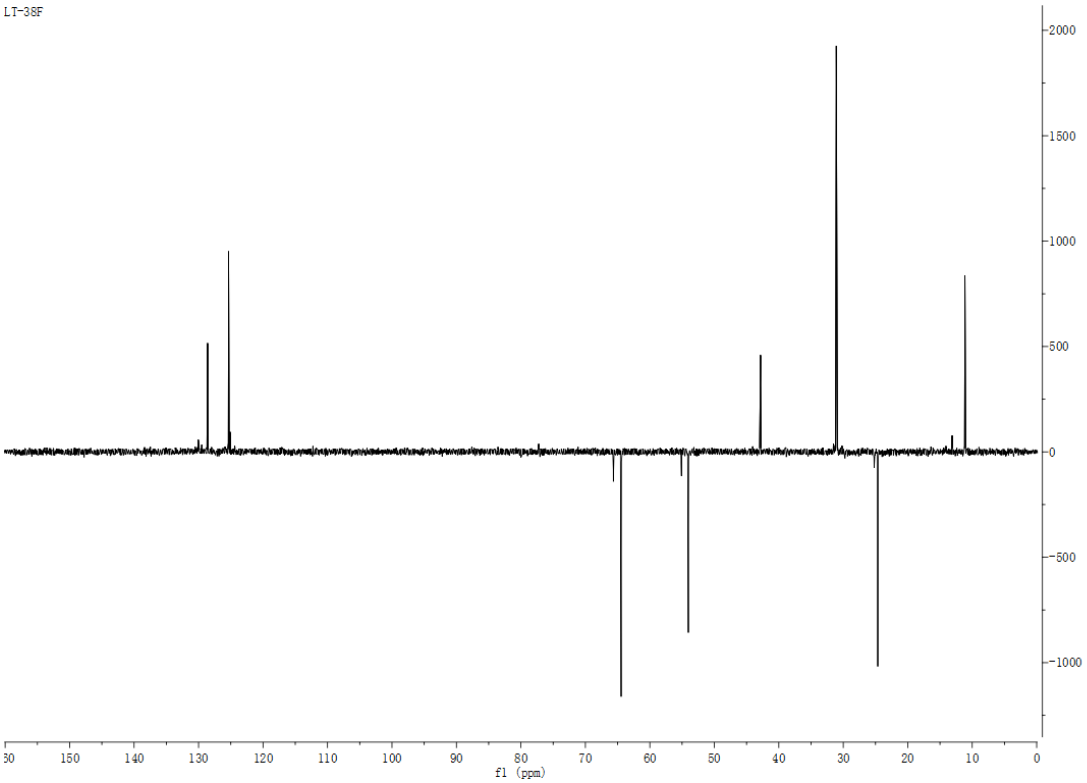
^{19}F NMR (376 MHz, $CDCl_3$):



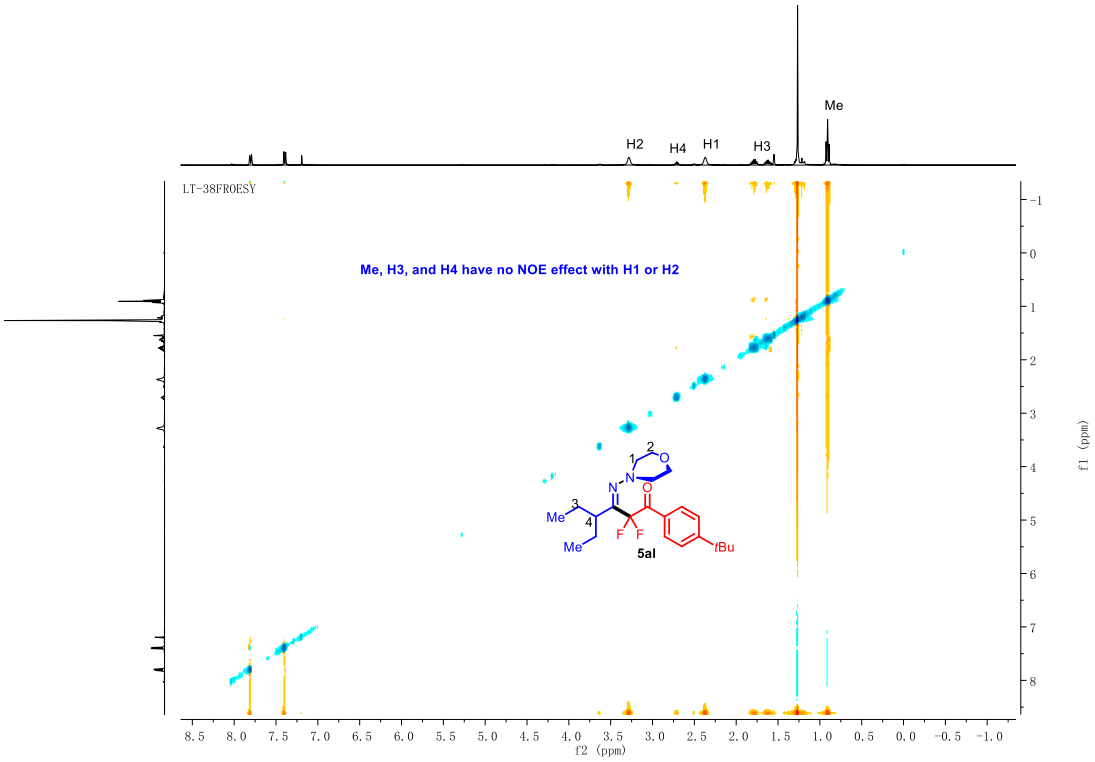
^{13}C NMR (100 MHz, $CDCl_3$):



DEPT

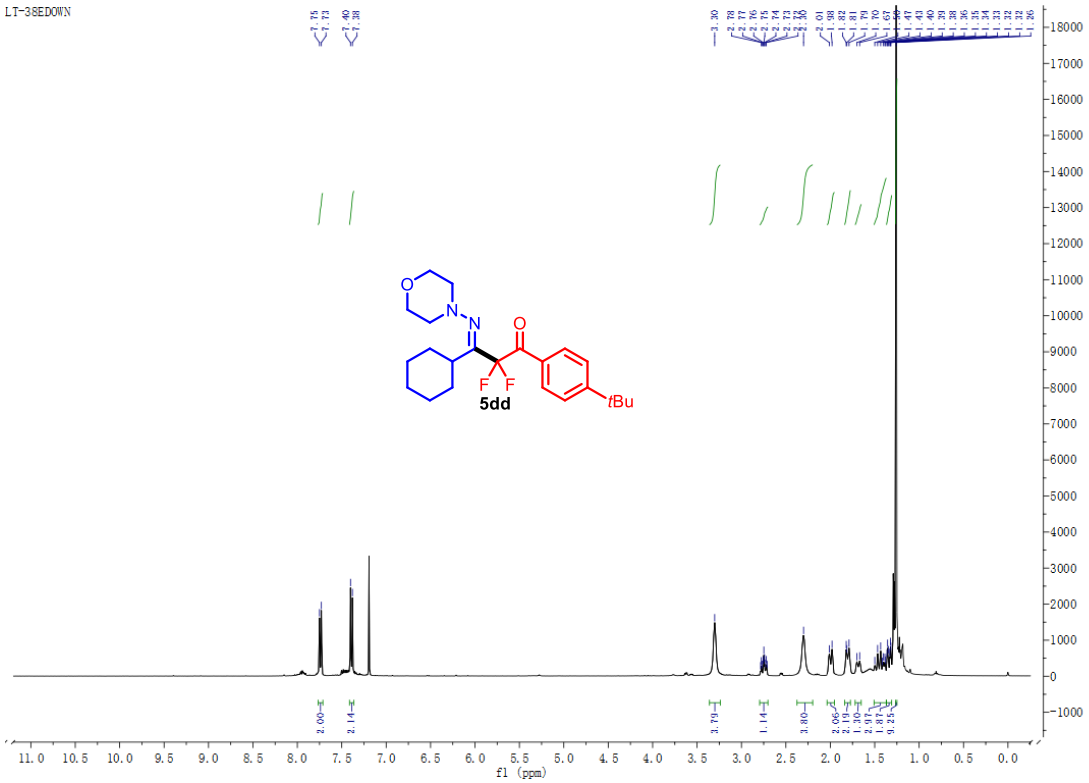


ROESY

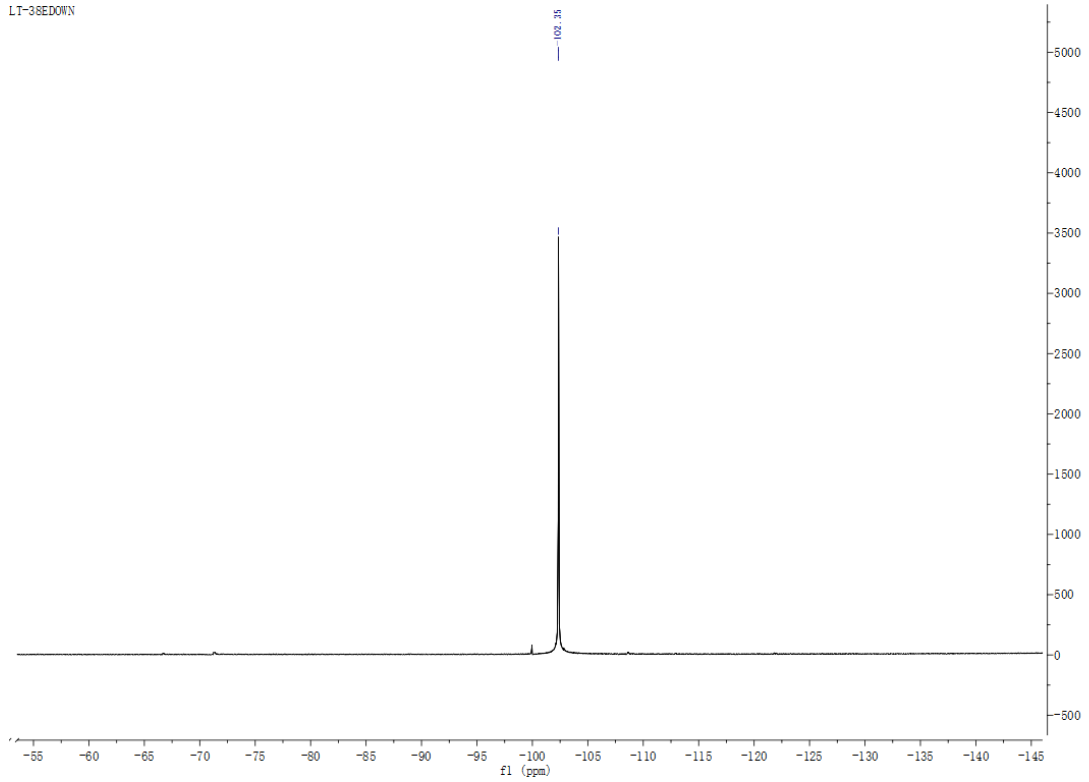


(E)-1-(4-(tert-butyl)phenyl)-3-cyclohexyl-2,2-difluoro-3-(morpholinoimino)propan-1-one (5dd)

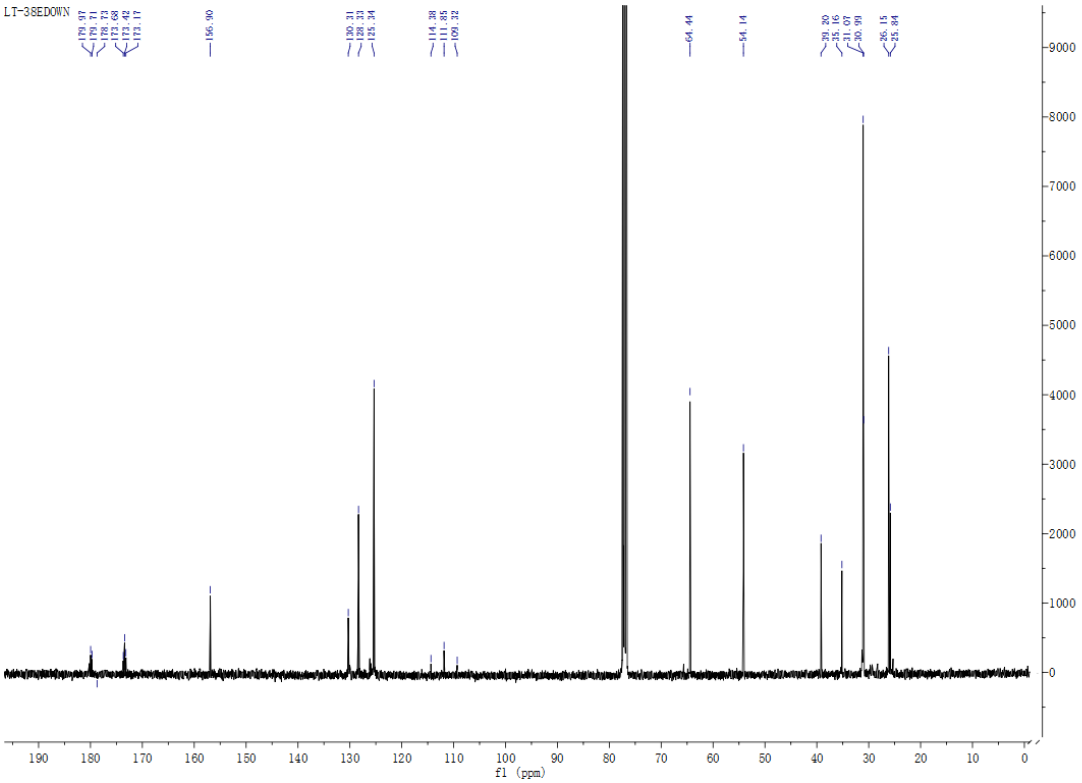
^{1}H NMR (400 MHz, $CDCl_3$)



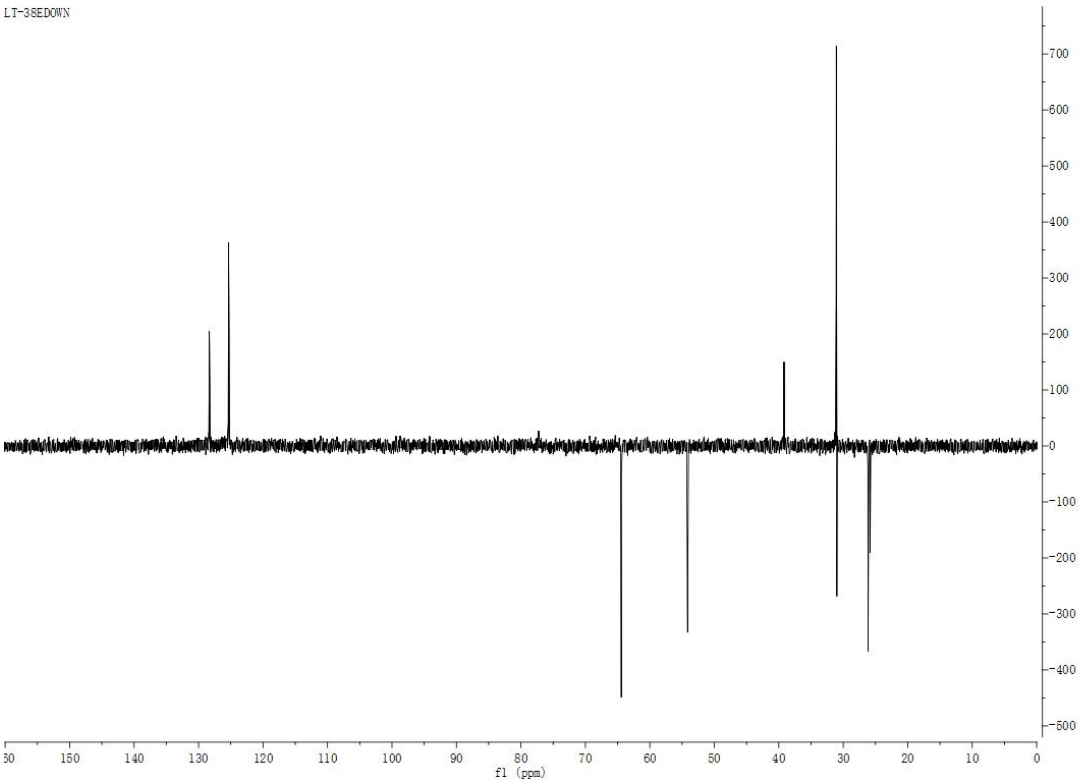
^{19}F NMR (376 MHz, $CDCl_3$):



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



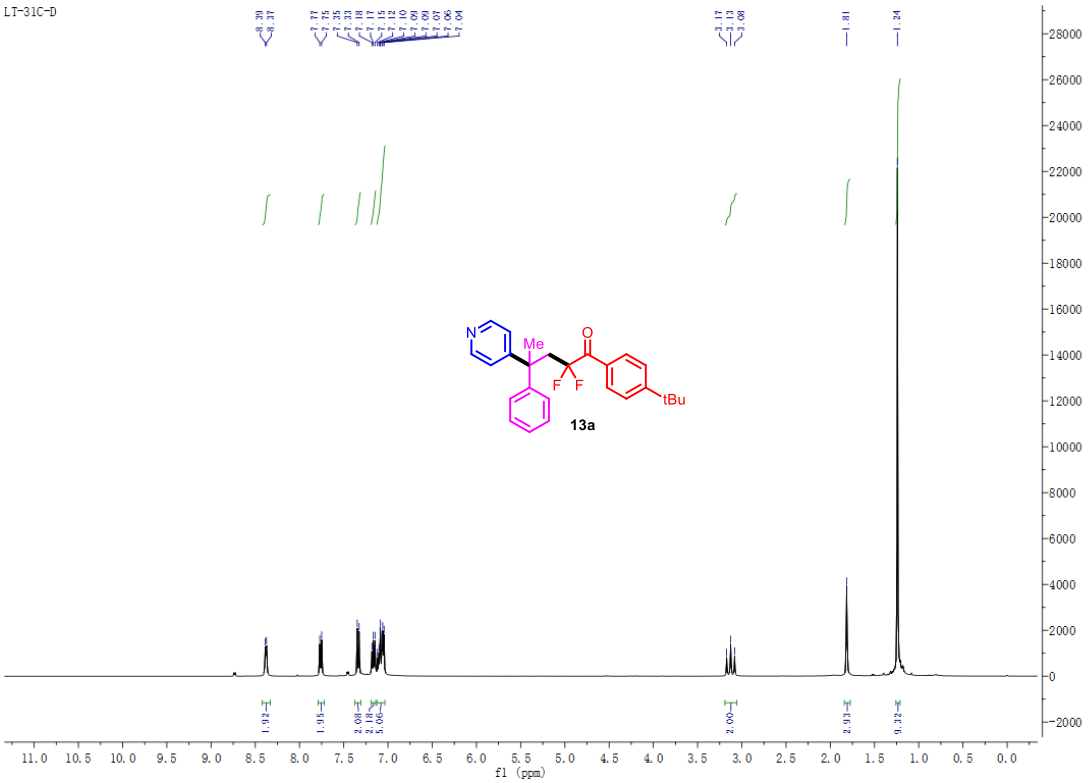
DEPT



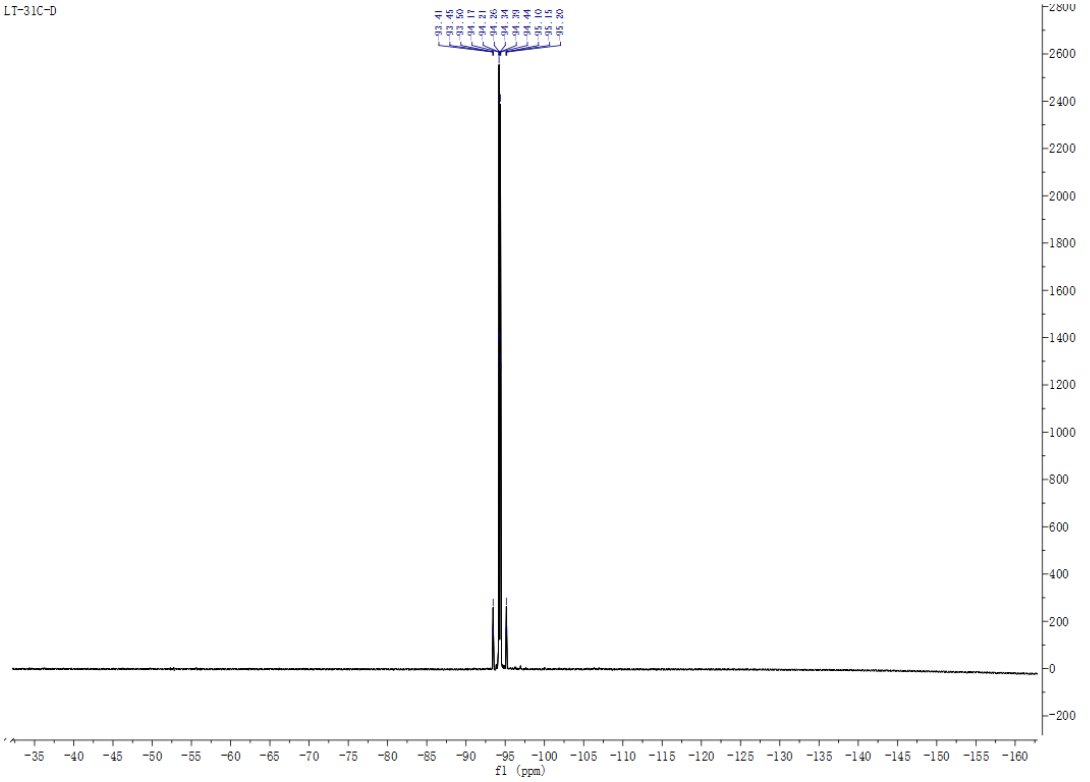
The fluorine spectrum has splits and generally has F-H coupling

1-(4-(tert-butyl)phenyl)-2,2-difluoro-4-phenyl-4-(pyridin-4-yl)pentan-1-one (13a)

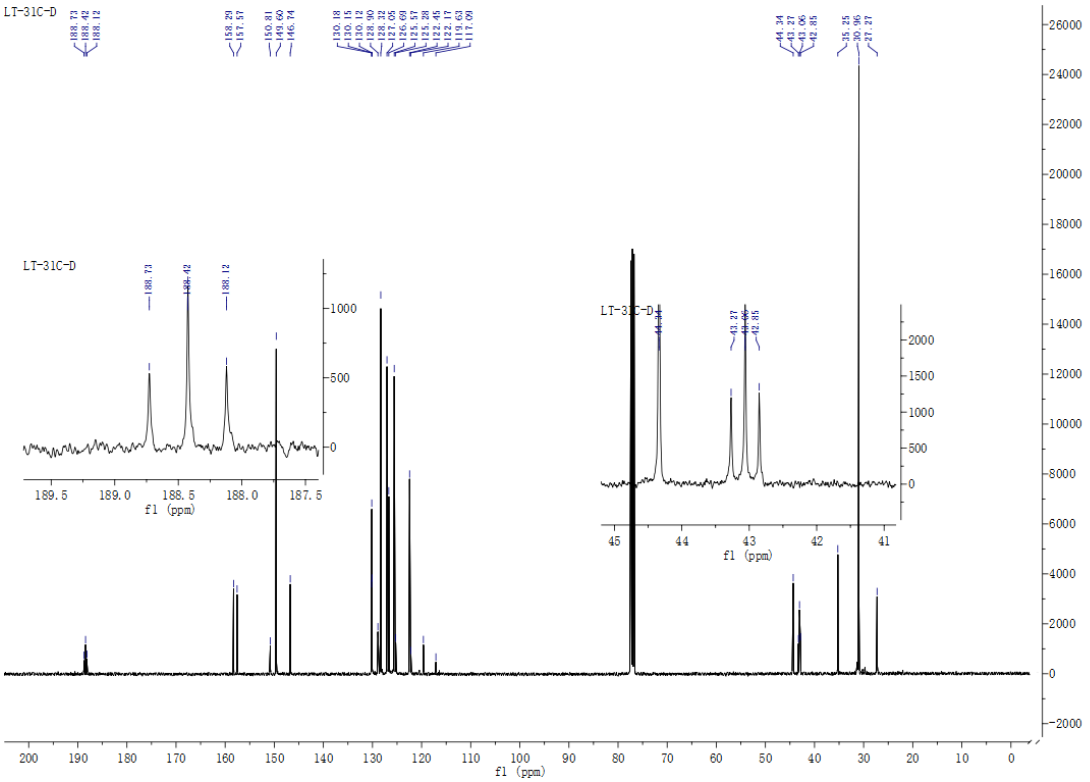
^{1}H NMR (400 MHz, $CDCl_3$)



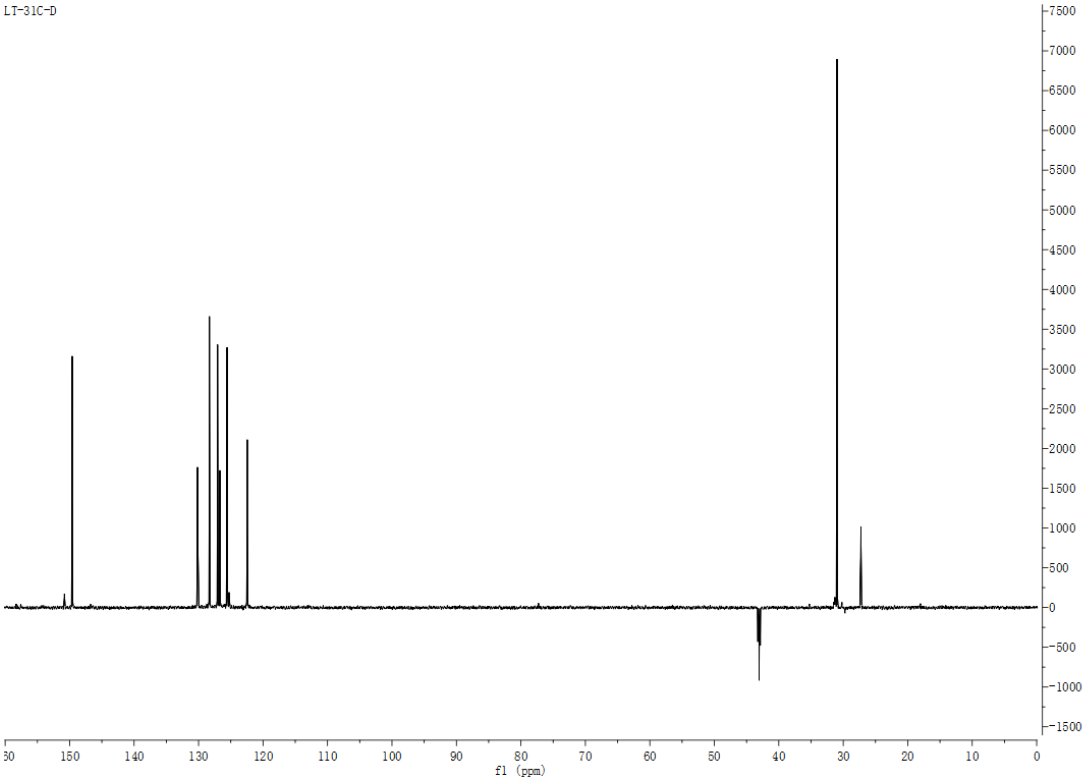
^{19}F NMR (376 MHz, $CDCl_3$):



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

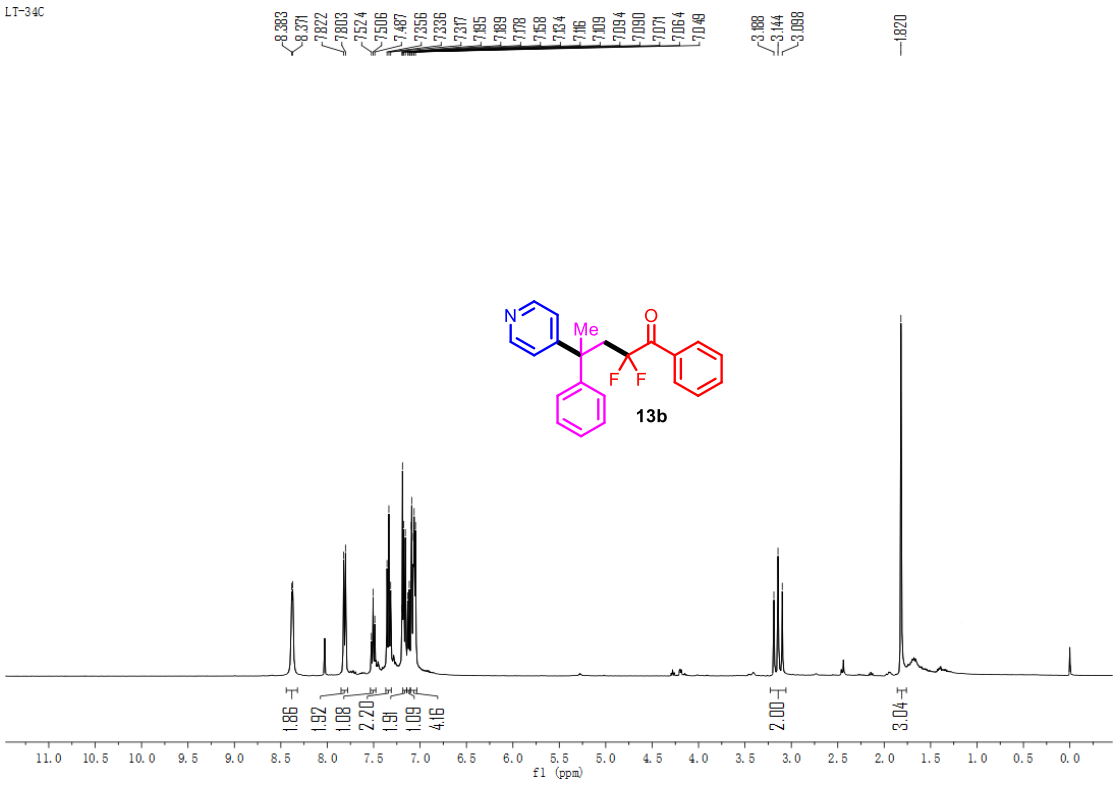


DEPT

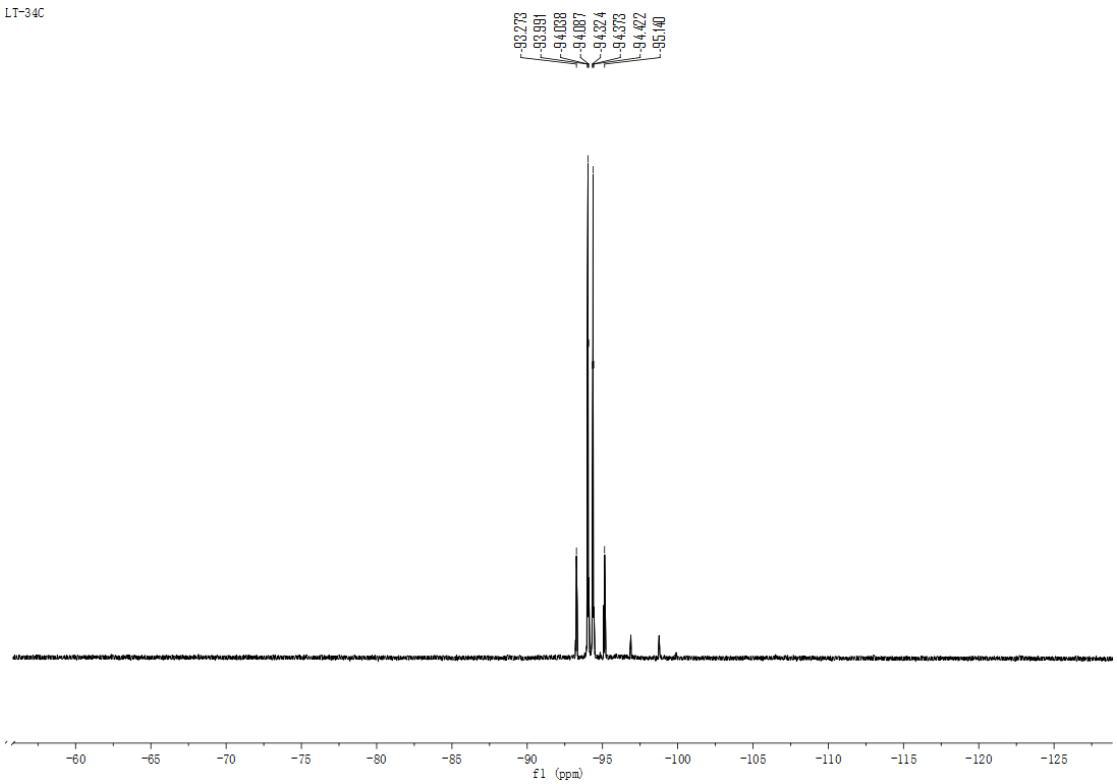


2,2-difluoro-1,4-diphenyl-4-(pyridin-4-yl)pentan-1-one (13b)

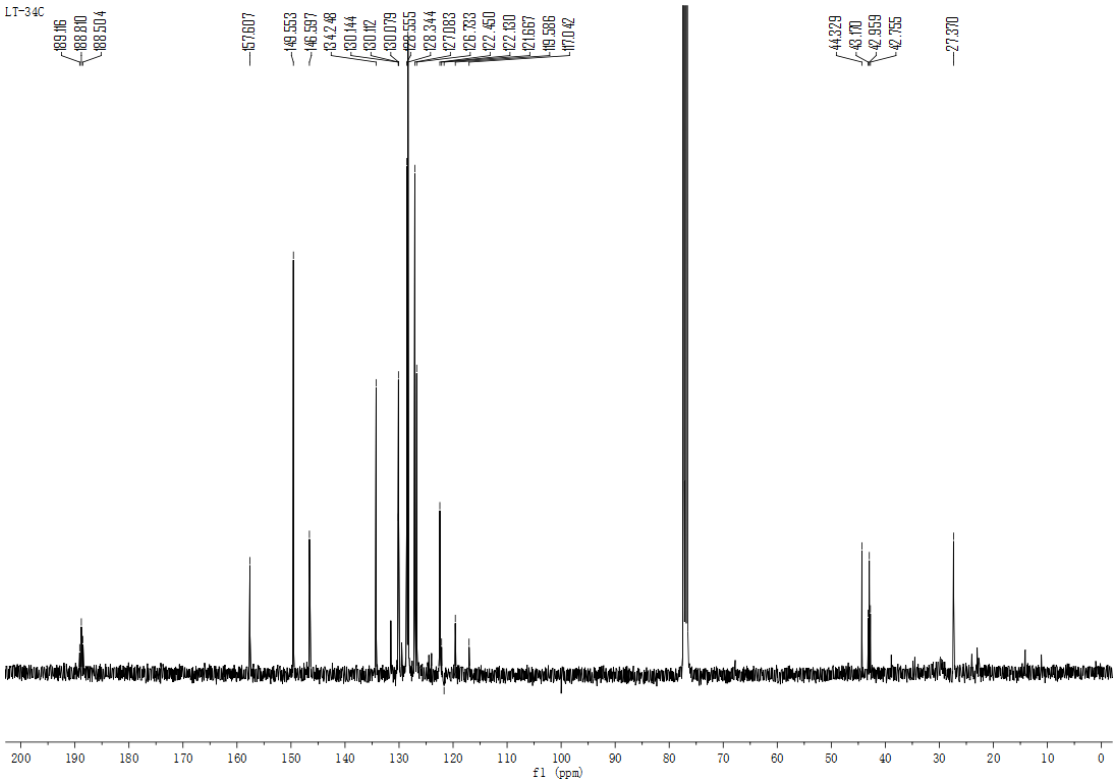
^{1}H NMR (400 MHz, $CDCl_3$)



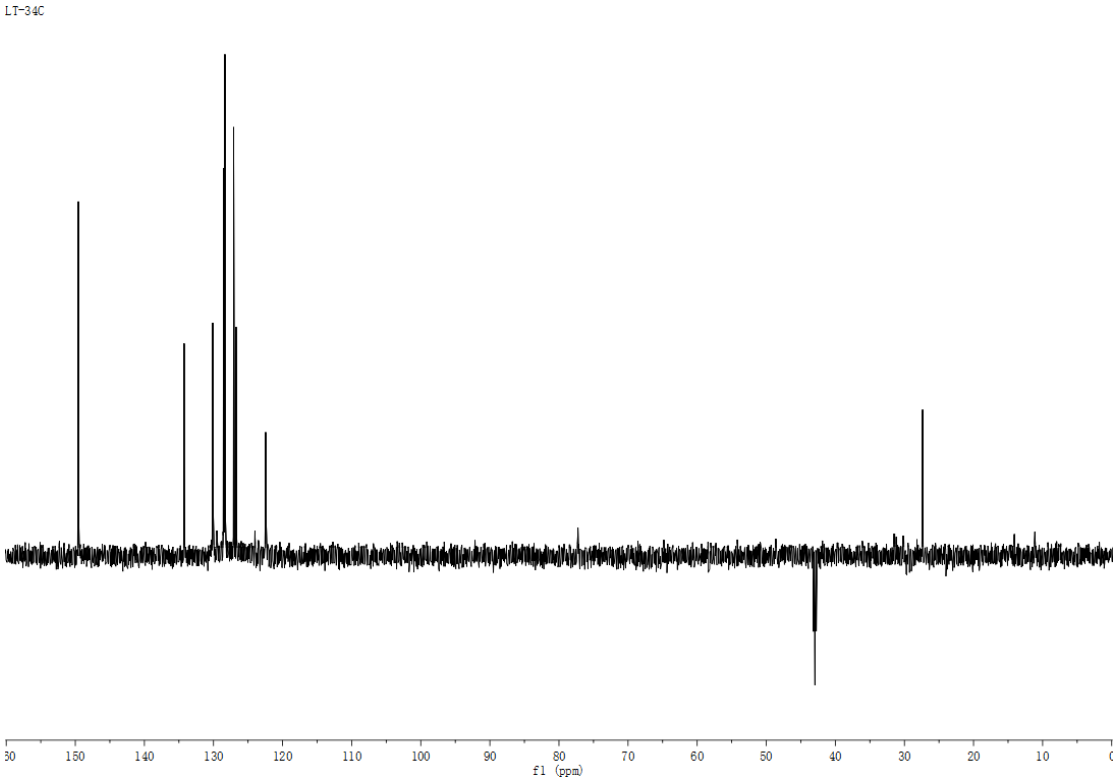
^{19}F NMR (376 MHz, $CDCl_3$):



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

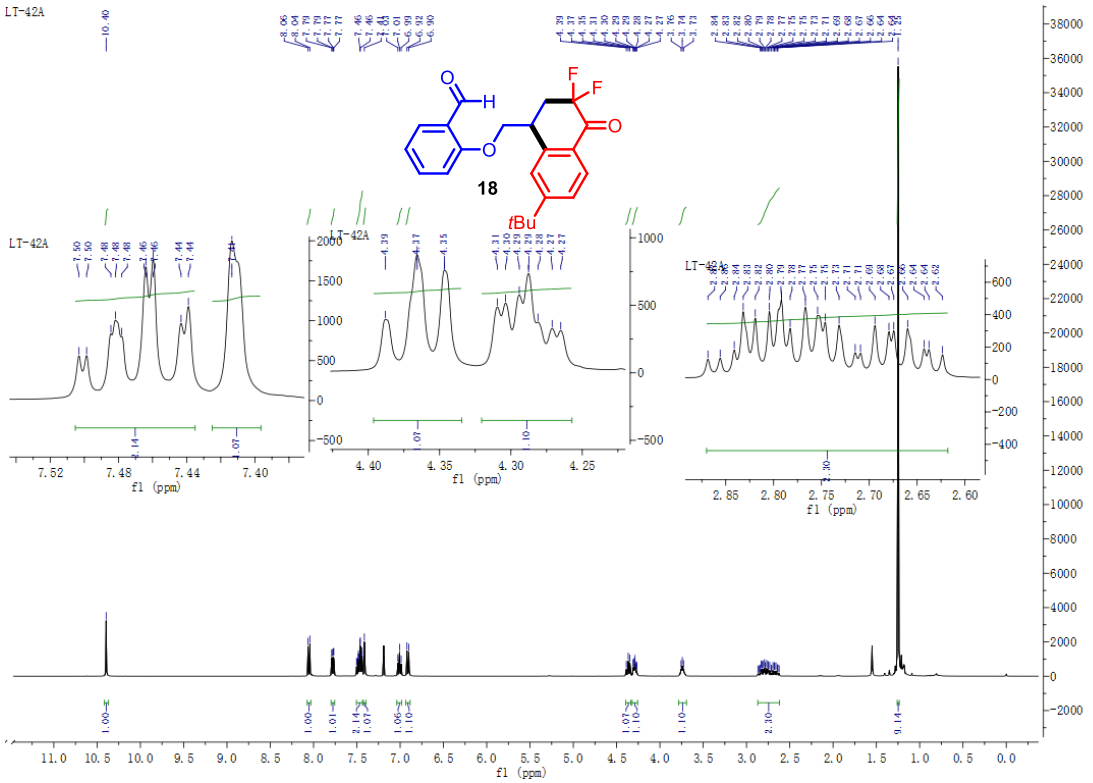


DEPT

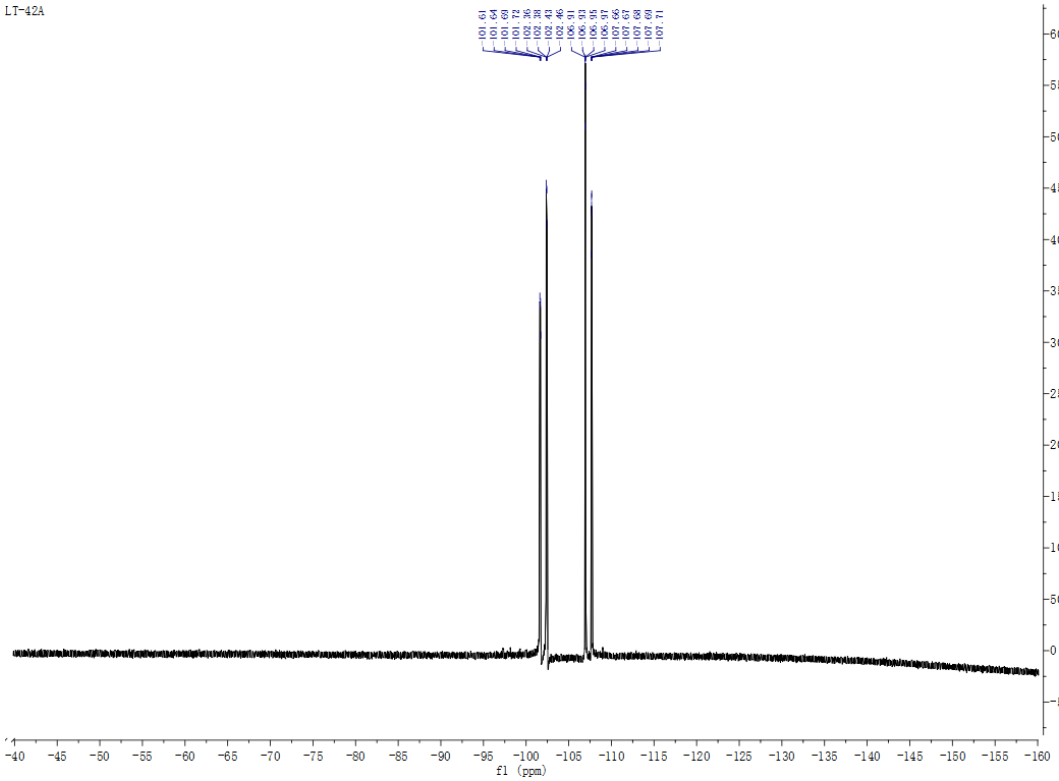


2-((7-(tert-butyl)-3,3-difluoro-4-oxo-1,2,3,4-tetrahydronaphthalen-1-yl)methoxy) benzaldehyde (18)

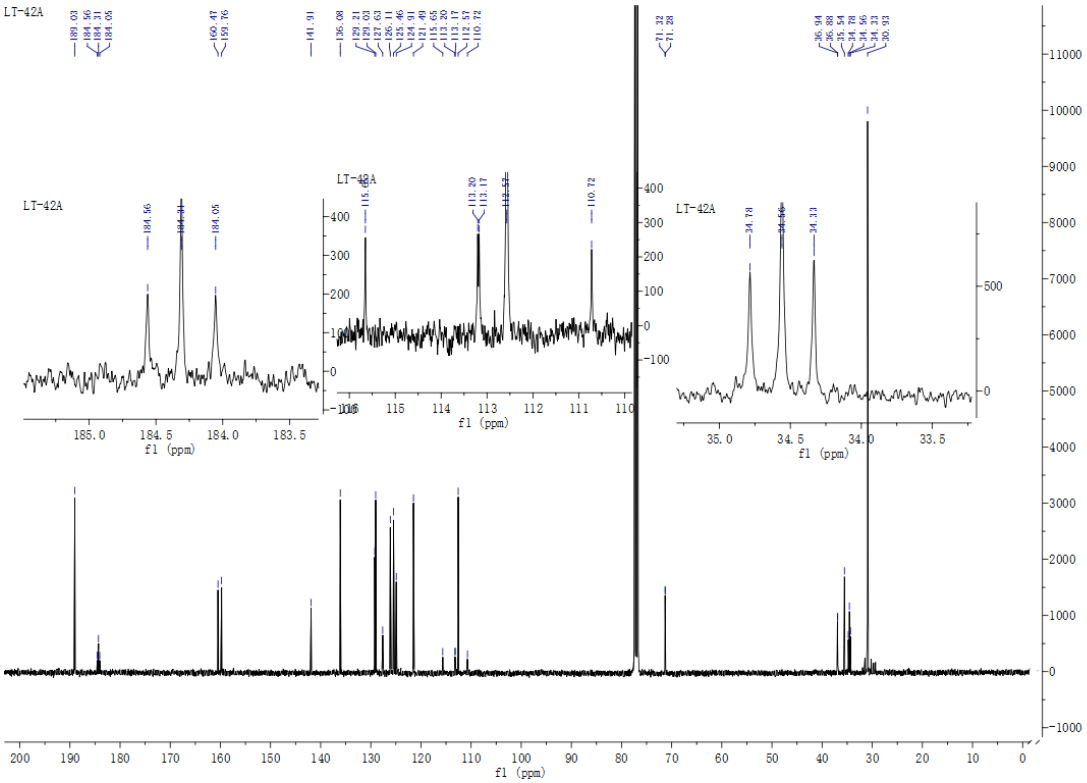
^{1}H NMR (400 MHz, $CDCl_3$)



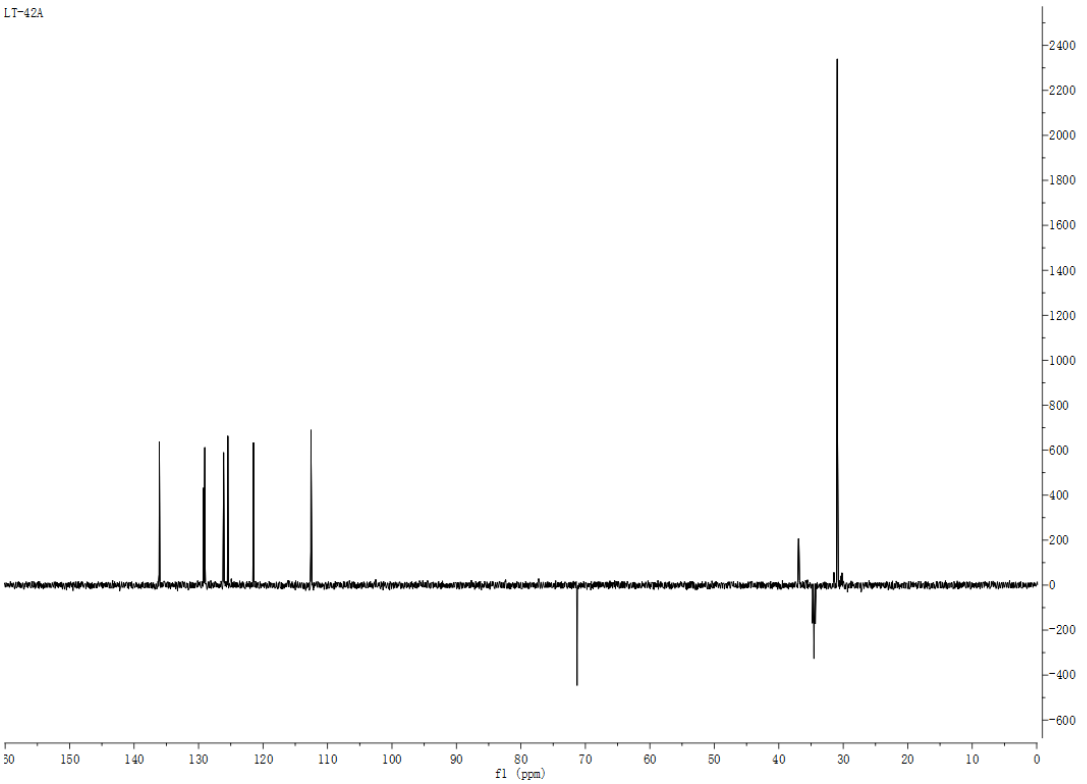
^{19}F NMR (376 MHz, $CDCl_3$):



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

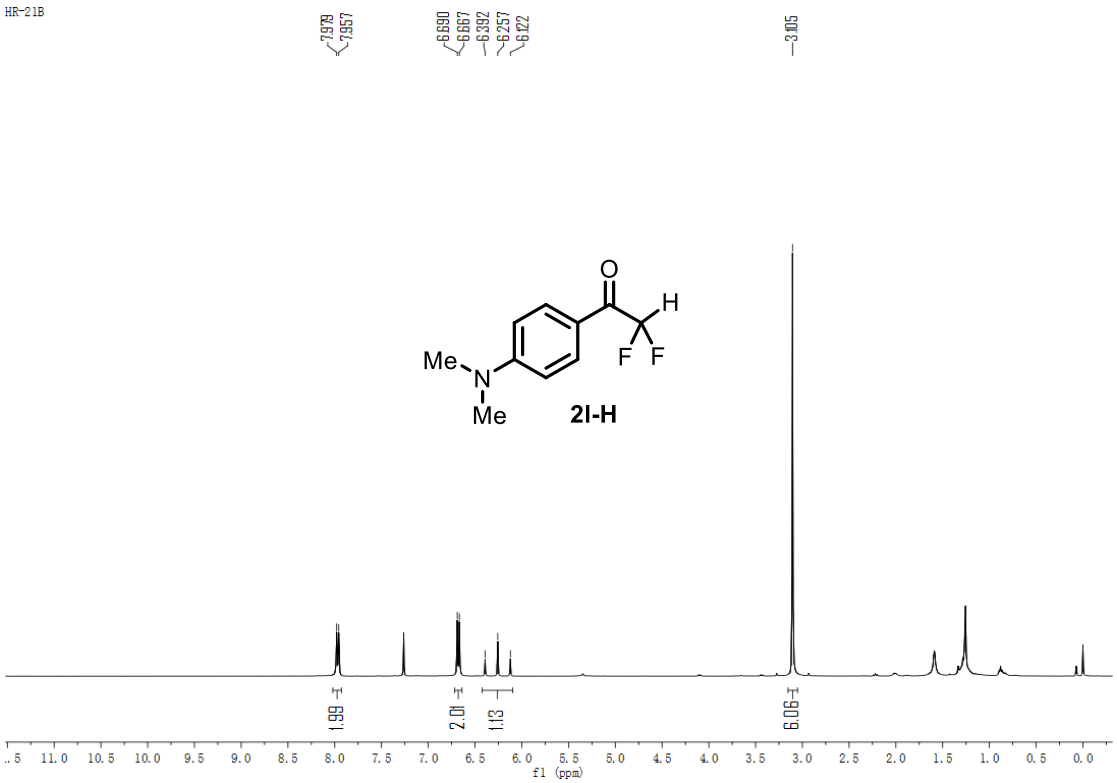


DEPT

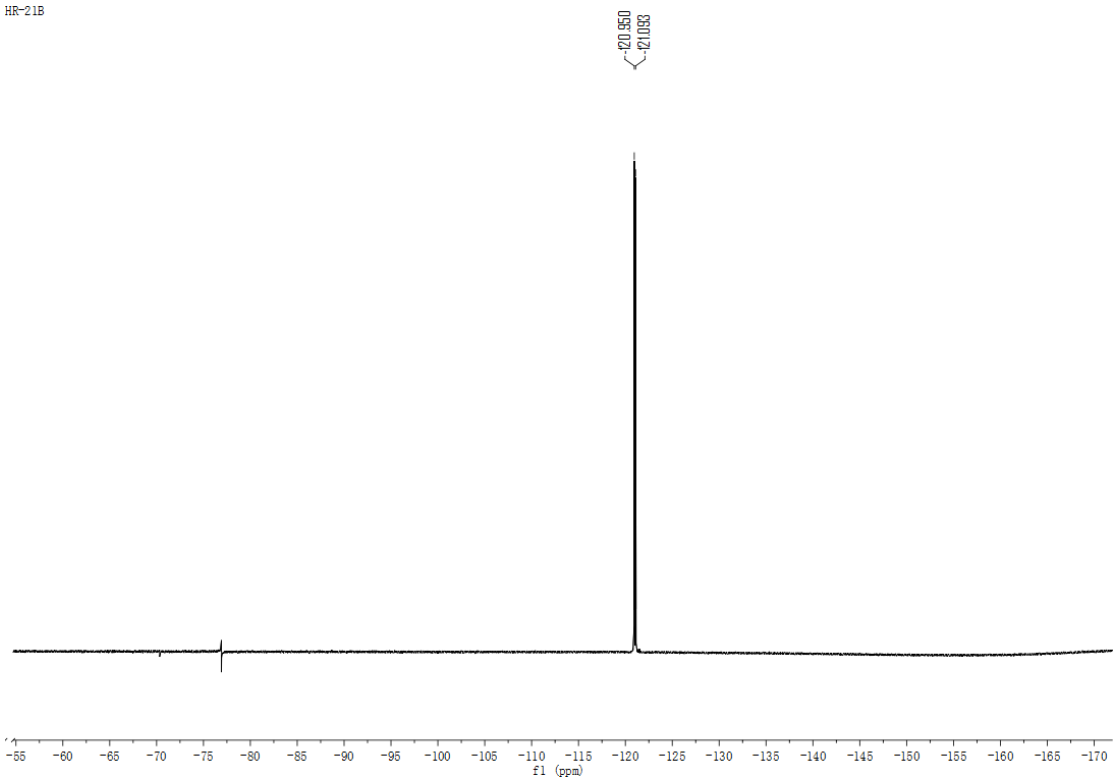


1-(4-(dimethylamino)phenyl)-2,2-difluoroethan-1-one (2l-H)

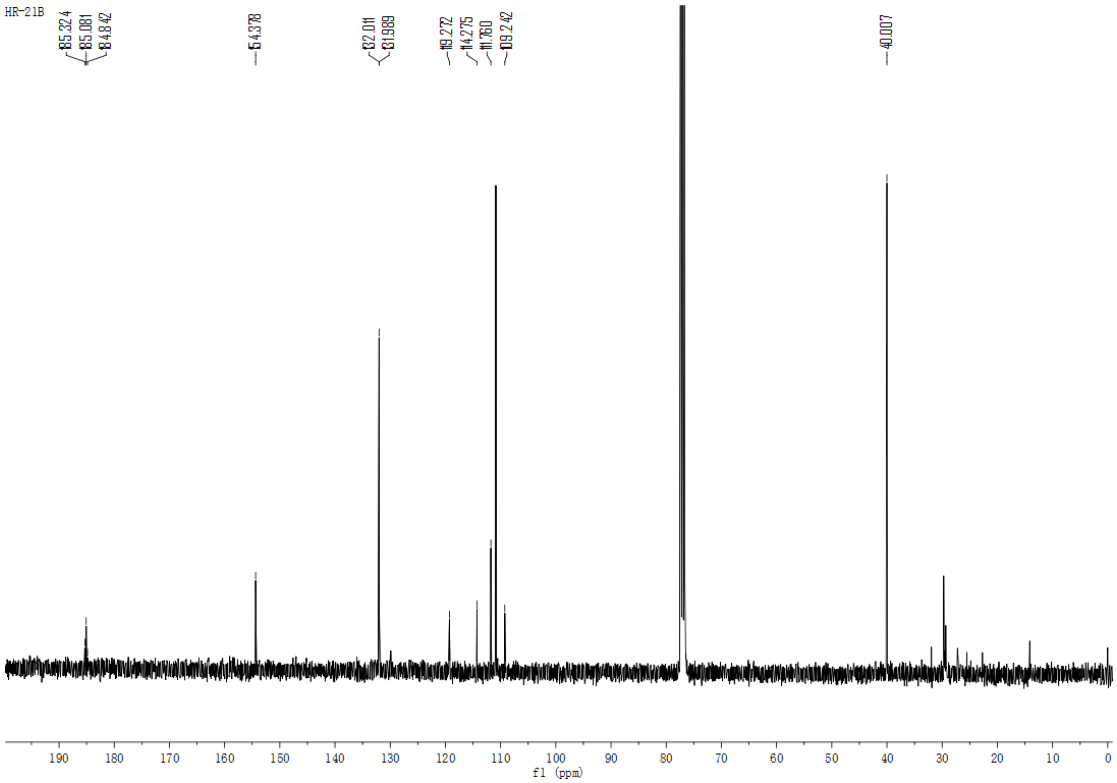
^{1}H NMR (400 MHz, $CDCl_3$)



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

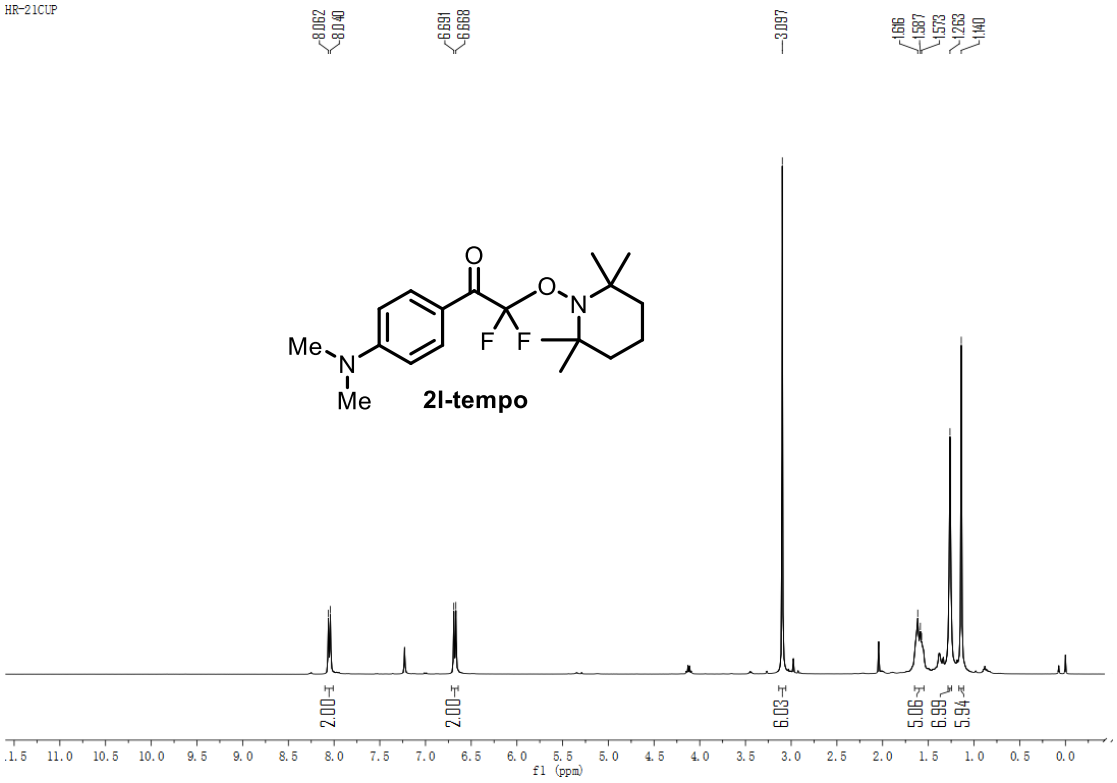


^{13}C NMR (100 MHz, $CDCl_3$):



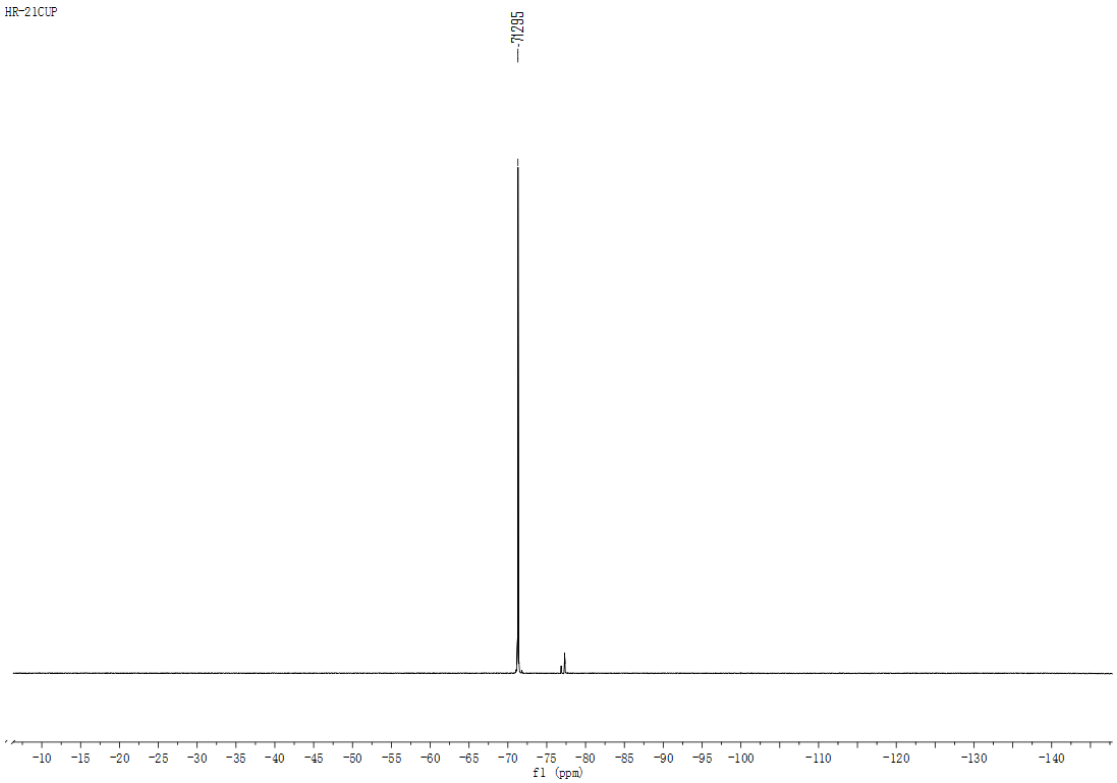
1-(4-(dimethylamino)phenyl)-2,2-difluoro-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethan-1-one (2l-tempo)

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

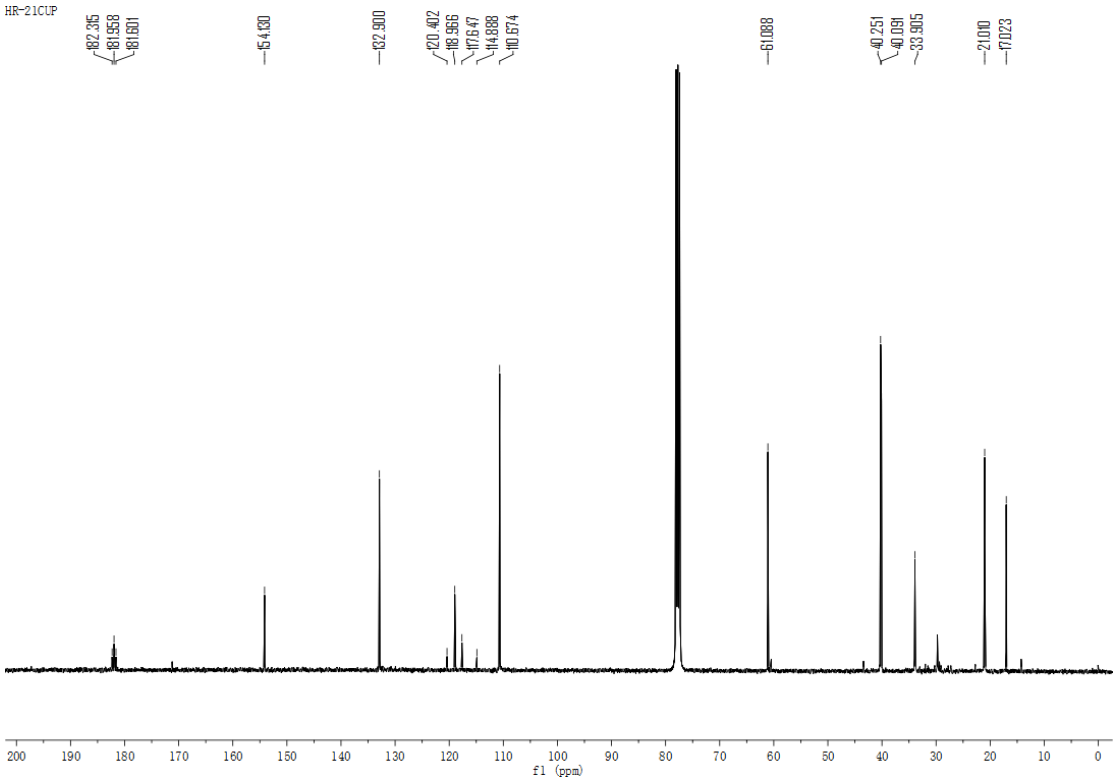


2l-tempo

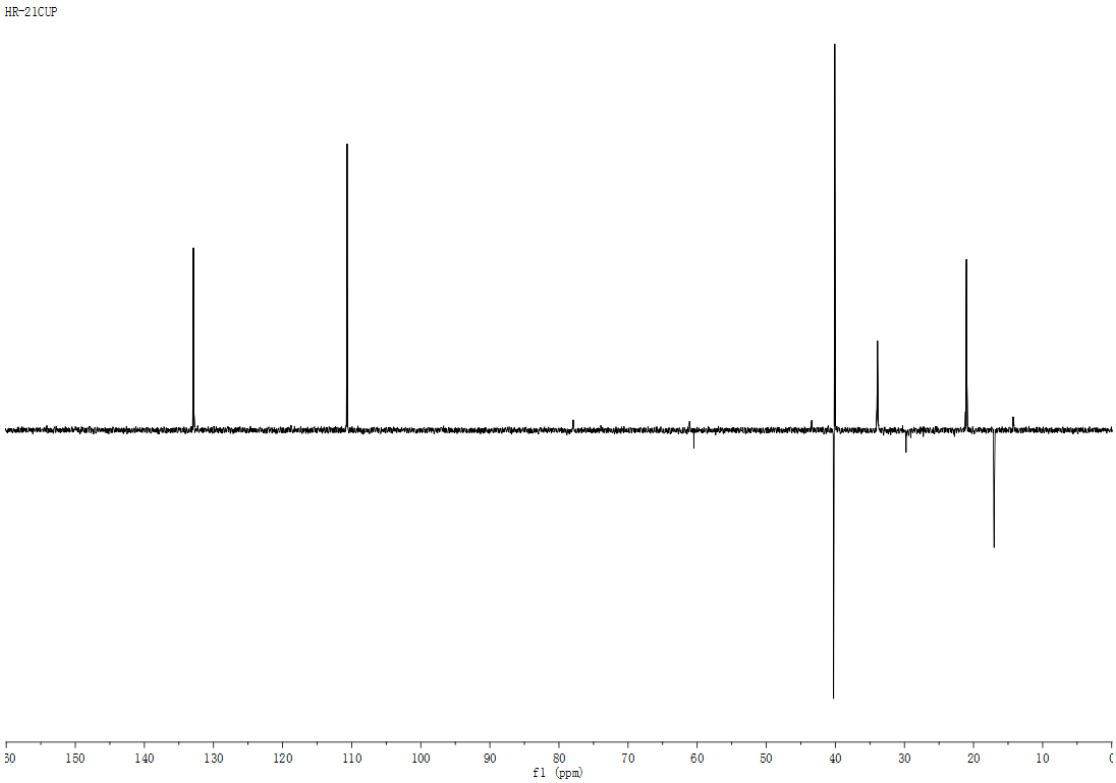
^{19}F NMR (376 MHz, $CDCl_3$):



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



dept



12. Reference:

1. T. Nihei, N. Iwai, T. Matsuda and T. Kitazume, *J. Org. Chem*., **2005**, *70*, 5912.

2. A. Carrër, J.-D. Brion, S. Messaoudi, and M. Alami, *Org. Lett.* **2013**, *15*, 5606.

3. P. Xu, G. Wang, Y. Zhu, W. Li, Y. Cheng, S. Li, C. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 2939.

4. J. Evenäs, F. Edfeldt, M. Lepistö, N. Svitacheva, A. Synnergren, B. Lundquist, M. Gränse, A. Rönnholm, M. Varga, J. Wright, M. Wei, S. Yue, J. Wang, C. Li, X. Li, G. Chen, Y. Liao, G. Lv, A. Tjörnebo, F. Narjes, *Bioorg. Med. Chem. Lett.* **2014**, *24*, 1315.

5. Y. Takeuchi, H. Ogura, A. Kanada, T. Koizumi, *J. Org. Chem.* **1992**, *57*, 2196.

6. Y. Wu, Y. Li, J. Deng, *J. Fluorine Chem.* **2005**, *126*, 791.

7. (a) C. Qu, Z. Wu, W. Li, H. Du, C. Zhu, *Adv. Synth. Catal.* **2017**, *359*, 1672-1677; (b) C. Qu, G. Song, J. Xu, W. Yan, C. Zhou, H. Li, Z. Chen, Z. Xu, *Org. Lett.* **2019**, *21*, 8169-8173.

8. E. Arceo, I. D. Jurberg, A. Alvarez-Fernandez, P. Melchiorre, *Nat. Chem.* **2013**, *5*, 750.

9. (a) L. Lin, Z. Yang, J. Liu, J. Wang, J. Zheng, J. Li, X. Zhang, X. Liu, H. Jiang, J. Li, *Green Chem.* **2021**, *23*, 5467; (b) S. Jung, S. Shin, S. Park, S. Hong, *J. Am. Chem. Soc.* **2020**, *142*, 11370; (c) L. Candish, M. Teders, F. Glorius, *J. Am. Chem. Soc.* **2017**, *139*, 7440.

10. For some examples on visible light-promoted transition metal-free protocol by iodination or direct use of iodoalkanes, see: (a) M. Silvi, C. Sandford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2017**, *139*, 5736. (b) Y. Cheng, C. Mück-Lichtenfeld, A. Studer, *J. Am. Chem. Soc.* **2018**, *140*, 6221. (c) X. Tang, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 814. (d) C. Gerleve, M. Kischkewtz, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 2441. (e) Y. Cheng, C. Mück-Lichtenfeld, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 16832. (f) M. Kischkewtz, C. Gerleve, A. Studer, *Org. Lett.* **2018**, *20*, 3666. (g) D. Zheng, A. Studer, *Org. Lett.* **2019**, *21*, 325; (h) K. Li, X. Zhang, J. Chen, Y. Gao, C. Yang, K. Zhang, Y. Zhou, B. Fan,

Org. Lett. **2019**, *21*, 9914; (i) T. Mao, M. Ma, L. Zhao, D. Xue, Y. Yu, J. Gu, C. He, *Chem. Commun.* **2020**, *56*, 1815; (j) K. Li, J. Chen, C. Yang, K. Zhang, C. Pan, B. Fan, *Org. Lett.* **2020**, *22*, 4261-4265.

11. (a) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765；(b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55*, 58.

12. (a) F. Juliá, T. Constantin, D. Leonori, *Chem. Rev.* **2022**, *122*, 2292; (b) T. Constantin, M. Zanini, A. Regni, N. S. Sheikh, F. Juliá, D. Leonori, *Science*, **2020**, *367*, 1021.

13. (a) M. Salamone, M. Bietti, *Acc. Chem. Res.* **2015**, *48*, 2895; (b) B. P. Roberts, *Chem. Soc. Rev.* **1999**, *28*, 25-35; (c) H. Cao, X. Tang, H. Tang, Y. Yuan, J. Wu, *Chem. Catal.* **2021**, *1*, 523.

14. (a) P. Zhang, C. Le, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2016**, *138*, 8084; (b) R. W. Pipal, K. T. Stout, P. Z. Musacchio, S. Ren, T. J. A. Graham, S. Verhoog, L. Gantert, T. G. Lohith, A. Schmitz, H. S. Lee, D. Hesk, E. D. Hostetler, lan W. Davies, D. W. C. MacMillan, *Nature*, **2021**, *589*, 542; (c) T. M. Faraggi, C. Rouget-Virbel, J. A. RincÓn, M. Barberis, C. Matros, S. Garcí a-Cerrada, J. Agejas, O. de, Frutos, D. W. C. MacMillan, *Org. Process Res. Dev.* **2021**, *25*, 1966; (d) H. Huang, P. Bellotti, J. E. Erchinger, T. O. Paulisch, F. Glorius, *J. Am. Chem. Soc.* **2022**, *144*, 1899; (e) A. EIMarrouni, C. B. Ritts, J. Balsells, *Chem. Sci.* **2018**, *9*, 6639; (f) S. Jung, S. Shin, S. Park, S. Hong, *J. Am. Chem. Soc.* **2020**, *142*, 11370; (g) T. Kerackian, A. Reina, D. Bouyssi, N. Monteiro, A. Amgoune, *Org. Lett.* **2020**, *22*, 2240; (h) J. Dong, X. Lyu, Z. Wang, X. Wang, H. Song, Y. Liu, Q. Wang, *Chem. Sci.* **2019**, *10*, 976; (i) Q. Zhou, S. J. S. DÜsel, L. Lu, B. KÖnig, W. Xiao, *Chem. Commun.* **2019**, *55*, 107; (j) M. S. Santos, M, Cybularczyk-Cecotka, B. KÖnig, M. Giedyl, *Chem. Eur. J.* **2020**, *26*, 15323; (k) Z. Zhang, X. Hu, *ACS Catal.* **2020**, *10*, 777; (l) Z. Wang, Q. Liu, X. Ji, G. Deng, H. Huang, *ACS Catal.* **2020**, *10*, 154.

15. (a) C. Liu, H. Liu, X. Zheng, S. Chen, Q. Lai, C. Zheng, M. Huang, K. Cai, Z. Cai, S. Cai, *ACS Catal.* **2022**, *12*, 1375; (b) S. K. Kariofillis, S. Jiang, A. M. Zurański, S. S. Gandhi, J. I. M. Alvarado, A. G. Doyle, *J. Am. Chem. Soc.* **2022**, *144*, 1045; (c) X. Shu, L. Huan, Q. Huang, H. Huo, *J. Am. Chem. Soc.* **2020**, *142*, 19058; (d) Z. Wang, X. Ji, T. Han, G. Deng, H. Huang, *Adv. Synth. Catal.* **2019**, *361*, 5643; (e) C. Cao, G. Zhang, F. Xue, H. Deng, *Org. Chem. Front.* **2022**, *9*, 959; (f) P. Jia, Q. Li, W. Poh, H. Jiang, H. Liu, H. Deng, J. Wu, *Chem.* **2020**, *6*, 1766; (g) Z. Li, W. Wang, J. Yang, Y. Wu, W. Zhang, *Org. Lett.* **2013**, 15, 3820; (h) J. M. Tanko, M. Sadeghipour, *Angew. Chem. Int. Ed.* **1999**, *38*, 159; (i) H. Yue, C. Zhu, L. Huang, A. Dewanji, M. Rueping, *Chem. Commun.* **2022**, *58*, 171; (j) O. M. Griffiths, H. A. Esteves, Y. Chen, K. Sowa, O. S. May, P. Morse, D. C. Blakemore, S. V. Ley, *J. Org. Chem.* **2021**, *86*, 13559; (k) T. Kawasaki, N. Ishida, M. Murakami, *J. Am. Chem. Soc.* **2020**, *141*, 3366; (l) Q. Wang, H, Huang, Z. Sun, Y. Chen, G. Deng, *Green, Chem.* **2021**, *23*, 7790; (m) T. Kawasaki, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed.* **2020**, *59*, 18267-18271; (n) X. Ji, Q. Liu, Z. Wang, P. Wang, G. Deng, H. Huang, *Green Chem.* **2020**, *22*, 8233-8237; (o) H. Wang, H. Liu, M. Wang, M. Huang, X. Shi, T. Wang, X. Cong, J. Yan, J. Wu, *iScience*, **2021**, *24*, 102693; (p) T. Kawasaki, T. Tosaki, N. Ishida, M. Murakami, *Org. Lett.* **2021**, *23*, 7683.

16. M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426.

17. (a) K. Li, J. Chen, C. Yang, K. Zhang, C. Pan, B. Fan, *Org. Lett.* **2020**, *22*, 4261; (b) G. Gu, M. Huang, J. Kim, J. Zhang, Y. Li, Y. Wu, *Green. Chem.* **2020**, *22*, 2543; (c) J. F. Franz, W. B. Kraus, K. Zeitler, *Chem. Commun.* **2015**, *51*, 8280; (d) C. Qu, Z. Wu, W. Li, H. Du, C. Zhu, *Adv. Synth. Catal.*

2017, *359*, 1672; (e) C. Qu, G. Song, J. Xu, W. Yan, C. Zhou, H. Li, Z. Chen, Z. Xu, *Org. Lett.* **2019**, *21*, 8169.