Supporting Information

Metal-free, visible-light driven *α*-C(sp^3)−H *gem*-difluoroallylation of glycine derivatives with trifluoromethyl alkenes and 1,3-enynes

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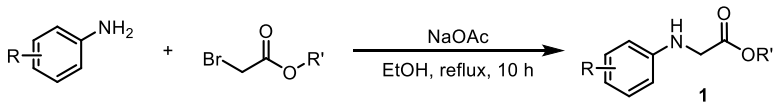
1. General Information

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

2. Starting Materials

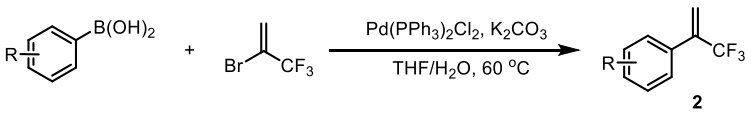
2.1 Preparation of Glycine Derivatives 1



Following the literature procedure:[1]a mixture of aniline (10 mmol), bromide acetate (1.2 equiv) and anhydrous sodium acetate (2.0 equiv) in 30 mL of ethanol was refluxed for 10 h (heating mantle). The mixture was then cooled down to the room temperature and filtered through celite. The celite was washed with DCM, the combined organic layer was evaporated to remove the solvent and the crude product was then purified by column chromatography (PE/EA = 10:1 to 1:1). . The pure product was obtained as solid or liquid.

Following the literature procedure:[1] to a 100 mL round-bottom flask, *N*-aryl glycines (10.0 mmol) and corresponding amines (10.0 mmol) were dissolved in 30 mL DCM, EDCI (16.0 mmol) HOBt (14.5 mmol) and Et_3N (20.0 mmol) were added. The reaction mixture stirred overnight. Subsequently, water was added to the roundbottom flask. The resulting mixture was extracted with DCM (three times), and the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography (PE/EA = 4:1 to 1:1). The pure product was obtained.

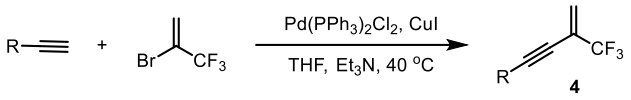
2.2 Preparation of Trifluoromethylalkenes 2



Following the literature procedure,[2] to an oven-dried 100 mL two-neck round bottom flask equipped with a stirring bar and a condenser was charged with arylboronic acid (3.0 mmol, 1.0 equiv), K_2CO_3 (12.0 mmol, 4.0 equiv), and $Pd(PPh_3)_2Cl_2$ (0.03 mmol, 1.0 mol%). The flask was purged with nitrogen three times. A mixture of degassed THF (10 mL) and H_2O (7 mL) were added via syringe, followed by 2-bromo-3,3,3-trifluoroprop-1-ene (6.0 mmol, 2.0 equiv). The reaction mixture was heated to 60 °C and stirred for 24 h. Then the reaction mixture was cooled to room temperature and diluted with diethyl ether (25 mL) and H_2O (25 mL). The layers were

separated, and the aqueous layer was extracted with Et_2O (2 × 25 mL). The combined organic layers were washed with H_2O (25 mL), brine (25 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20 : 1) to afford trifluoromethylalkenes **2**. All the spectra data are in agreement with the literature.

2.3 The preparation of 2-Trifluoromethyl-1, 3-Enynes 4

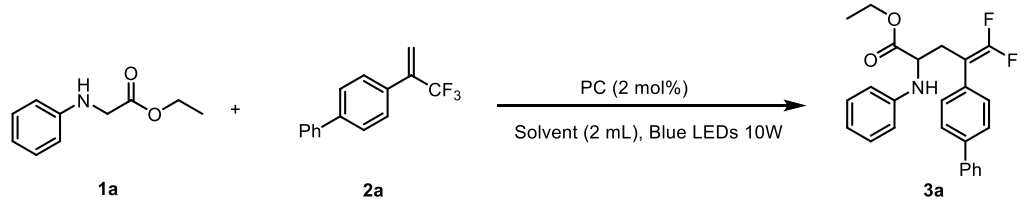


A Schlenk flask was charged with $Pd(PPh_3)_2Cl_2$ (2 mol %) and CuI (5 mol %) under N_2 atmosphere. Dry triethyamine and 2-bromo-3,3,3-trifluoro-1-propene (1.2 equiv) were added subsequently followed by dropwise addition of phenylacetylene (1.0 equiv). The reaction mixture was stirred at 40 °C until completion. The reaction was then quenched with saturated NH_4Cl solution and extracted with pentane. Combined extracts were dried over Na_2SO_4 and solvent was removed under vacuum. The residue was purified by column chromatography to afford the corresponding enyne.

Compounds **1**[1], **2**[2] and **4**[3] were prepared according to the literatures.

3 Optimization of Reaction conditions

3.1 General Procedure for the Reaction of ethyl *N*-phenylglycinate 1a with Trifluoromethyl alkene 2a

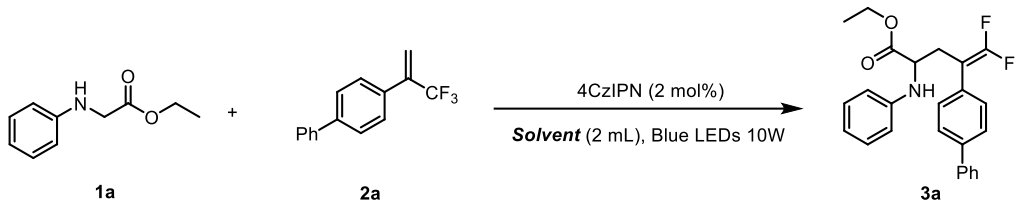


1a **2a** **3a**

To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with glycine derivatives **1a** (0.20 mmol, 1.0 equiv.) and photocatalyst. Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkenes **2a** (0.20 mmol, 1.0 equiv.) in solvent (2 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of a 10 W Blue LEDs (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the resulting mixture was quenched with H_2O and extracted with EtOAc (3 x 10 mL). The combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 30:1 to 2:1) furnishes the corresponding products **3a**.

3.2 Optimization of the Reaction 1a, 2a

Solvent

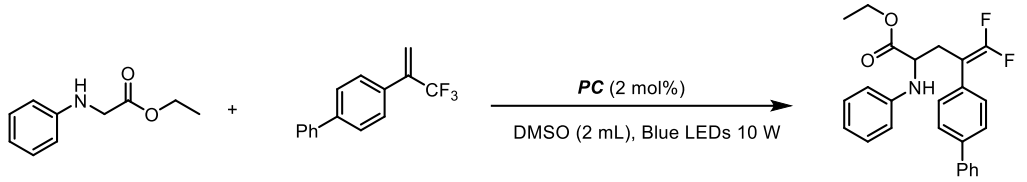


1a **2a** **3a**

Entry	Solvent	Yields (%) [a]
1	DMSO	35
2	DMF	21
3	DMAc	trace
4	NMP	trace
5	DCE	trace
6	MeCN	trace
7	Toluene	trace
8	EtOAc	trace

Reaction conditions: **1a** (1.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.), Solvent (2.0 mL), 4CzIPN (2 mol%), Blue LEDs 10 W, for 24 h, under N_2, isolated yield.

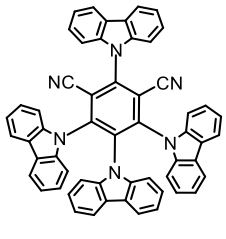
Photocatalyst



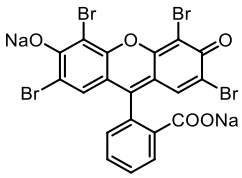
1a **2a** **3a**

Entry	PC	Yields (%) [a]
1	4CzIPN	35
2	Rhodamine B	19
3	EosinY	trace
4	Methlyene Blue	trace
5	Rose Bengale	trace
6	Ir(ppy)3	trace [b]

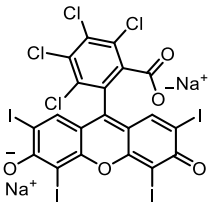
[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), PC (2 mol%), Blue LEDs 10 W, for 24 h, under N_2. [b] $Ir(ppy)_3$ as PC (2 mol%), for 24 h, under N_2, isolated yield.



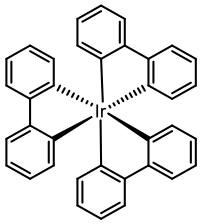
4CzIPN



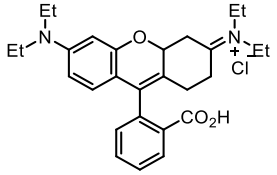
Eosin Y



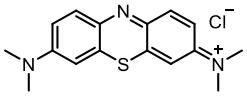
Rose Bengale



***fac*-Ir(ppy)$_3$**

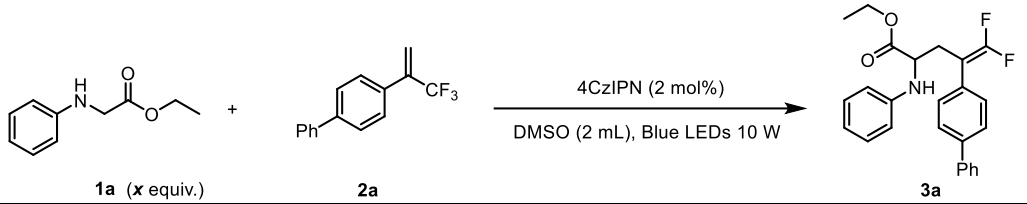


Rhodamine B



Methylene Blue

Ratio of 1a:2a



1a (***x*** equiv.) **2a** **3a**

Entry	**1a : 2a**	Yields (%) [a]
1	1:1	35
2	1.2:1	41
3	1.5:1	70
4	2.0:1	88
5	2.5:1	89

[a] Reaction conditions: **1a** (x equiv.), **2a** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), 4CzIPN (2 mol%), Blue LEDs 10 W, for 24 h, under N_2, isolated yield.

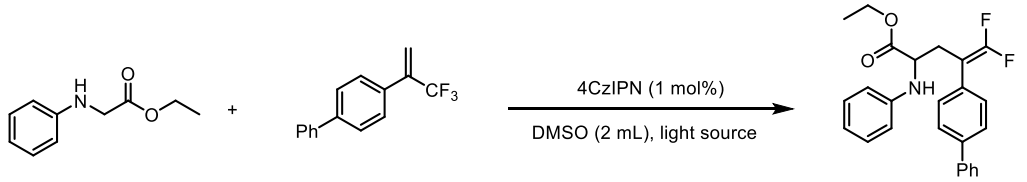
Ratio of 4CzIPN

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

Entry	4CzIPN (***x*** mol%)	Yields (%) [a]
1	1	89
2	2	88
3	3	86
4	0	0

[a] Reaction conditions: **1a** (0.4 mmol, 2.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), 4CzIPN (*x* mol%), Blue LEDs 10 W, for 24 h, under N_2, isolated yield.

Light source

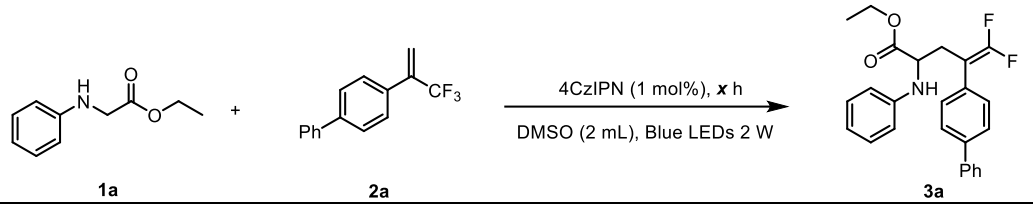


1a **2a** **3a**

Entry	**Light source**	Yields (%) [a]
1	Blue LEDs 2 W	92
2	Blue LEDs 6 W	90
3	Blue LEDs 10 W	88
4	White light 15 W	20
5[b]	Blue LEDs 2 W	0
6	dark	0

[a] Reaction conditions: **1a** (2.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), 4CzIPN (1 mol%), Light source, for 24 h, under N_2, isolated yield, [b] under air**.**

Time

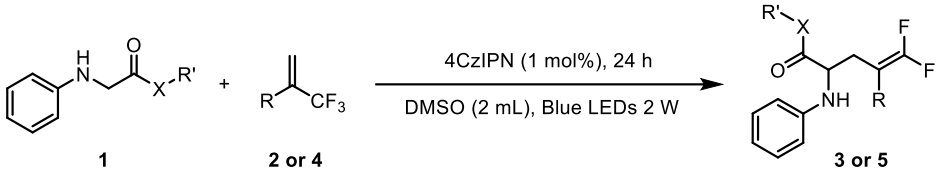


1a **2a** **3a**

Entry	*Time* (h)	Yields (%) [a]
1	12	45
2	18	77
3	24	92
4	30	90

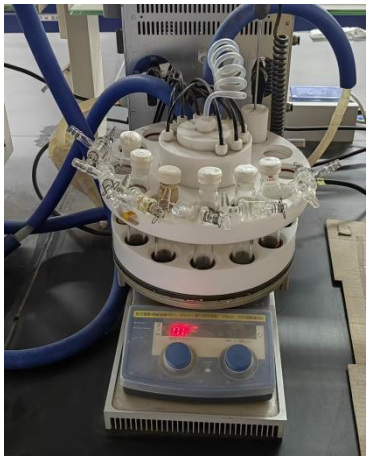
[a] Reaction conditions: **1a** (0.4 mmol, 2.0 equiv.), **2a** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), 4CzIPN (1 mol%), Blue LEDs 2 W, for ***x*** h, under N_2, isolated yield.

4. Representative Procedure for the Glycine Derivatives 1 with Trifluoromethyl Alkenes 2 or 4

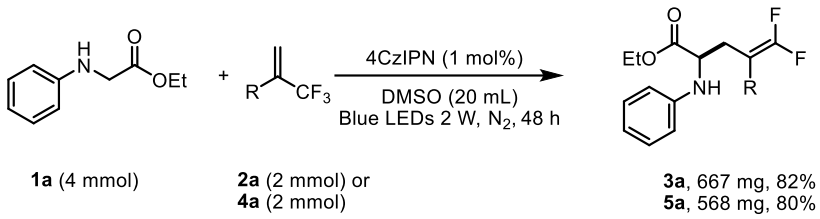


To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with glycine derivatives **1** (0.40 mmol, 2.0 equiv.) and 4CzIPN (1 mol%). Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkenes **2** (0.20 mmol, 1.0 equiv.) in DMSO (2 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of a 2 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the resulting mixture was quenched with H_2O and extracted with EtOAc (3 x 10 mL). The combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 30:1 to 2:1) furnishes the corresponding products **3** and **5**.

The Visible-Light Photoredox Catalysis Experimental Setup (photographed by author Li-Na Guo)



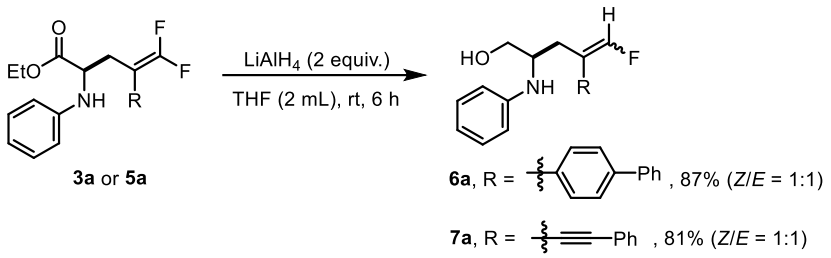
5. Large Scale synthesis of 3a and 5a



To a 50 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with glycine derivatives **1a** (4 mmol, 2.0 equiv.) and 4CzIPN (1 mol%). Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkenes **2a** or **4a** (2 mmol, 1.0 equiv.) in DMSO (20 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of 2 W blue LEDs (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the resulting mixture was quenched with H_2O and extracted with EtOAc (3 x 10 mL). The combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 20:1) furnishes the corresponding products **3a** and **5a**.

6. Derivatizations of Products

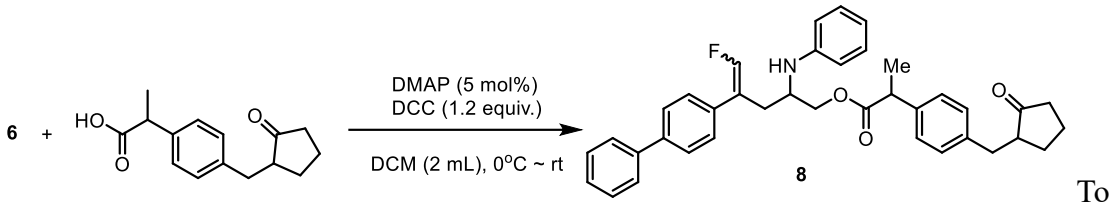
*Reductions of **3a** and **5a***



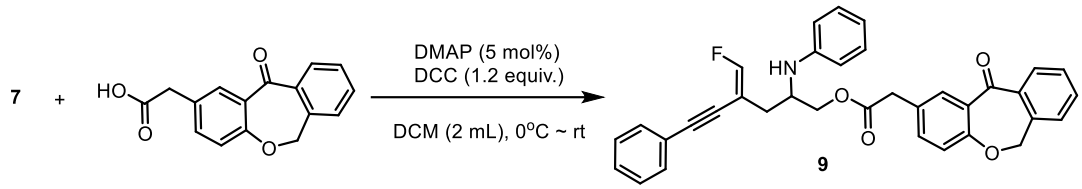
To a solution of product **3a** or **5a** (0.2 mmol, 1.0 equiv.) in THF (2 mL) was added lithium aluminium tetrahydride (0.42 mmol, 2.1 equiv.) at room temperature. The reaction mixture was stirred for 6 h. After completion as detected by TLC, the reaction was quenched with saturated NH_4Cl aqueous solution. The aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3 : 1) to afford

products **6a** or **7a**.

*Esterifications of **6** and 7*

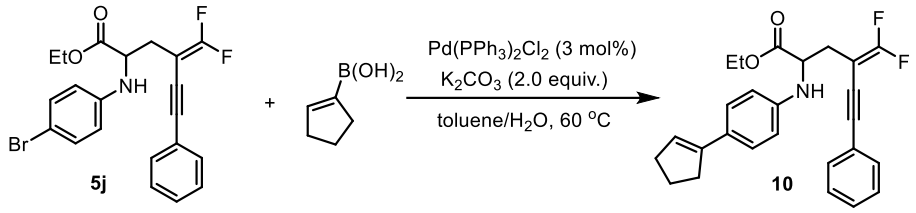


To A solution of **6** (0.2 mmol), Loxoprofen (0.24 mmol), and DMAP (5 mol%) in DCM (2 mL) at 0 ºC was added DCC (0.24 mmol) in one portion. A precipitate began to form almost immediately. The reaction was stirred at 0ºC for 10 min and then warmed to room temperature. After completion as detected by TLC, the reaction was then diluted with pentane (10 mL) and filtered through a short plug of silica. The aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to afford products **8**.



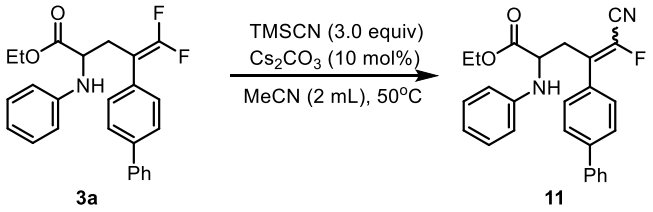
To a solution of **7** (0.2 mmol), Isoxepac (0.24 mmol), and DMAP (5 mol%) in DCM (2 mL) at 0 ºC was added DCC (0.24 mmol) in one portion. A precipitate began to form almost immediately. The reaction was stirred at 0ºC for 10 min and then warmed to room temperature. After completion as detected by TLC, the reaction was then diluted with pentane (10 mL) and filtered through a short plug of silica. The aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to afford products **9**.

Suzuki coupling of ***5j***



To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with1-cyclopentenylboronic acid (0.24 mmol), K_2CO_3 (2.0 equiv.) and $Pd(PPh_3)Cl_2$ (3 mol %) were added. The vessel was evacuated and filled with nitrogen (three times). **5j** (0.2 mmol), toluene (2.0 mL), H_2O (1.0 mL), and were added via syringe. The tube was put into a heating jacket and stirred at 60 °C overnight. The reaction mixture was cooled to room temperature. The aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 10:1) to give the desired coupling product **10** in 51% yield.

Nucleophilic substitution of ***3a***

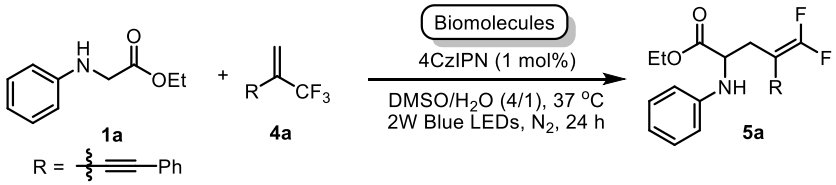


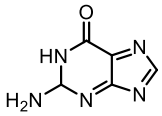
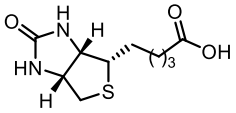
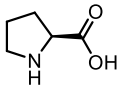
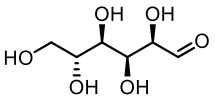
To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with **3a** (0.20 mmol), Cs_2CO_3 (10 mol%), TMSCN (3.0 equiv.) and anhydrous MeCN (2.0 mL). Then the reaction was stirred at 50 °C for 24 h. The aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over Na_2SO_4, filtered and concentrated under the reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 10:1) to give the desired coupling product **11** in 66% yield.

7. Compatibility with biomolecules

The glycine ester **1a** (0.4 mmol), 1, 3-enyne **4a** (0.2 mmol), 4CzIPN (1 mol%), DMSO (2.0 mL) and H_2O (0.5 mL) were added sequentially to a 10 mL oven-dried

Schlenk-tube equipped with a magnetic stirrer. Then, the tube was evacuated and backfilled with nitrogen (three times), the vial was sealed and exposed to Blue LEDs at 37 °C. The reaction mixture was monitored by TLC until the starting material *N*-alkoxyphthalimides were consumed.



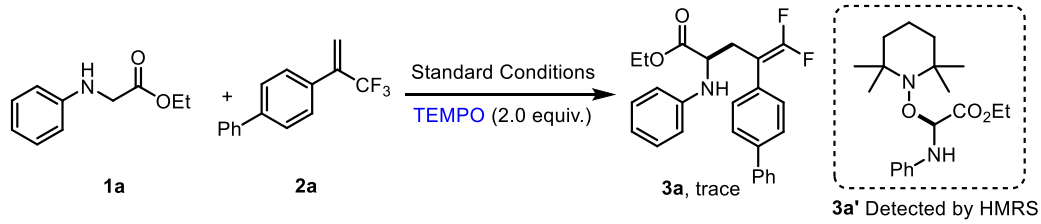
Entry	Biomolecules	Yield[a]	Entry	Biomolecules	Yield[a]
1	none	90%	4	10 mg ml^{-1} Lysozyme	65%
2	 Guanine (1.0 equiv.)	62%	5	 D-Biotin (1.0 equiv.)	73%
3	 L-Proline (1.0 equiv.)	79%	6	 D-(+)-Glucose (1.0 equiv.)	33%

[a]^{19}F NMR yields using $PhCF_3$ as an internal standard.

The reaction of **1a** and **4a** was performed in a mixed solvent system (DMSO:H_2O = 4:1) and biological temperature (37 °C). And 90% yield of **5a** was still obtained in this case. Then, a broad of biomolecules were examined as an extra additive for this reaction, including nucleobase, amino acid, lysozyme, biotin, and saccharide. All those reactions worked smoothly and gave desired products in satisfactory yields (entries 1-6).

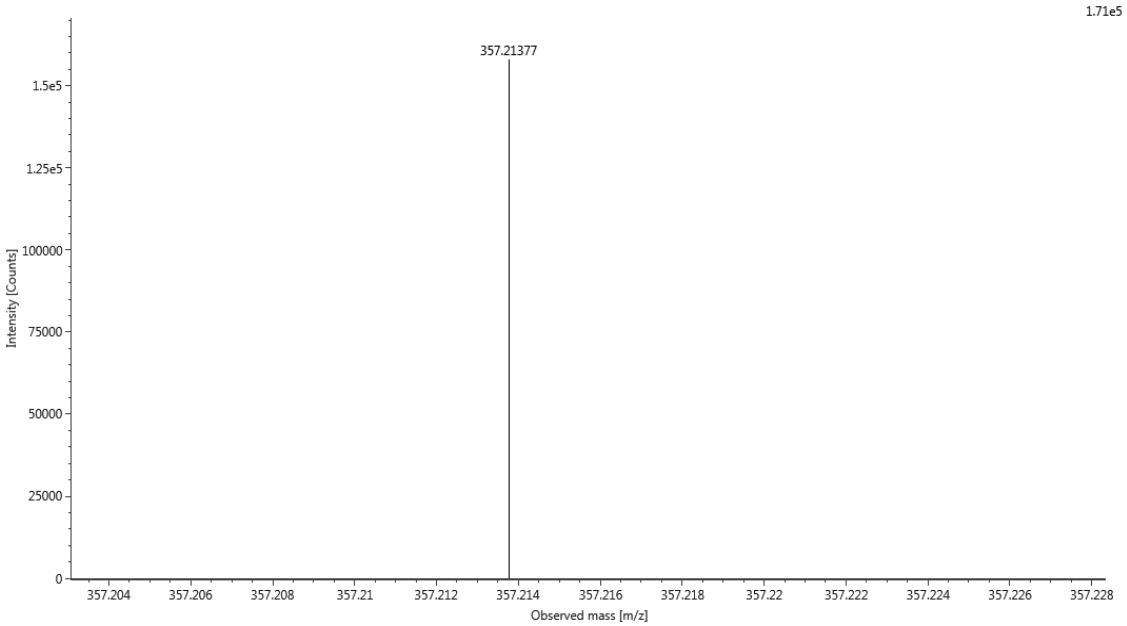
8. Mechanism Studies

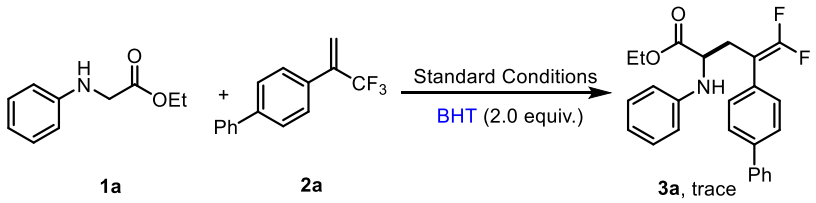
(1) Radical Inhibiting Experiment



i) To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with glycine derivatives **1a** (0.4 mmol, 2.0 equiv.), 4CzIPN (1 mol%). Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkenes **2a** (0.2 mmol, 1.0 equiv.) and TEMPO (0.4 mmol, 2.0 equiv.) in DMSO (2.0 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of 2 W Blue LEDs (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time.

When 2.0 equiv. of TEMPO was subjected into the reaction of **1a** with **2a** under the standard conditions, only a trace amount of **3a** was observed, along with the TEMPO adduct **3a'** was detected by LC-HRMS. **HRMS (ESI)** calcd for $C_{19}H_{31}N_2O_3Na$ $[M+Na]^+$ 357.2149, found 357.2138. This result indicates that a radical intermediate might be involved in this transformation.



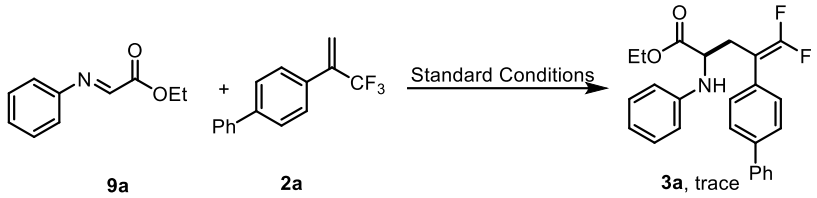


1a **2a** **3a**, trace

ii) To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with glycine derivative **1a** (0.4 mmol, 2.0 equiv.), 4CzIPN (1 mol%). Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkene **2a** (0.2 mmol, 1.0 equiv.) and BHT (0.4 mmol, 2.0 equiv.) in DMSO (2.0 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of 2 W Blue LEDs (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time.

When 2.0 equiv of BHT was subjected into the reaction of **1a** with **2a** under the standard conditions, only a trace amount of **3a** was observed. This result indicates that a radical pathway might be involved in this transformation.

(2) Control Experiments



To a 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with **9a** (0.40 mmol, 2.0 equiv.), 4CzIPN (1 mol%), Then, the tube was evacuated and backfilled with nitrogen (three times). Subsequently, a solution of trifluoromethyl alkene **2a** (0.20 mmol, 1.0 equiv.) in DMSO (2.0 mL) was added by a syringe. The reaction mixture was stirred under the irradiation of 2 W Blue LEDs (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. When ethyl-2-(phenylimino)acetate **9a** was used instead of **1a** under the standard conditions, only a trace amount of **3a** was observed. This result indicates that ethyl-2-(phenylimino) acetate **9a** was not the major intermediate in this transformation.

(3) Stern-Volmer Fluorescence Quenching Experiments

To a solution of 4CzIPN in anhydrous, N_2-saturated DMSO (5×10^{-4} mol/L) in a quartz cuvette, different amounts of glycine ester **1a** and trifluoromethyl alkenes **2a** were added, respectively, and the resulting changes in fluorescence intensity (concentration of **1a** and **2a**: 2.5×10^{-2} mol/L, 5×10^{-2} mol/L, 7.5×10^{-2} mol/L, 10×10^{-2} mol/L, 12.5×10^{-2} mol/L were collected. The emission intensity at 536 nm was collected with excited wavelength of 460 nm. The results are shown in Figure S1 and S2.

a) b)

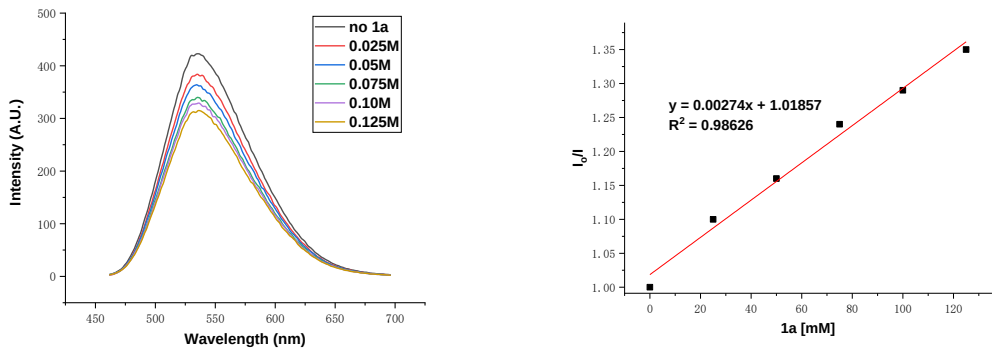


Figure S1. (a) The fluorescence emission spectra of 4CzIPN with different concentration of **1a**

added. (b) The Stern–Volmer emission quenching studies of **1a**. I_0 is the inherent fluorescence intensity of 4CzIPN. I is the fluorescence intensity of 4CzIPN in the presence of **1a**.

c) d)

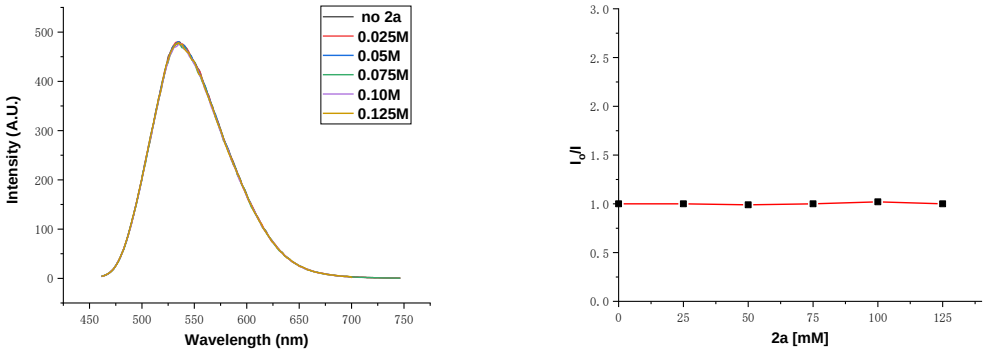


Figure S2. (c) The fluorescence emission spectra of 4CzIPN with different concentration of **2a** added. (d) The Stern–Volmer emission quenching studies of **2a**. I_0 is the inherent fluorescence intensity of 4CzIPN. I is the fluorescence intensity of 4CzIPN in the presence of **2a**.

(4) Light On-Off experiments

To further examine the impact of light, we conducted experiments under alternating periods of irradiation and darkness. The yield of **3a** was determined by crude ^{19}F NMR spectra using $PhCF_3$ as an internal standard.

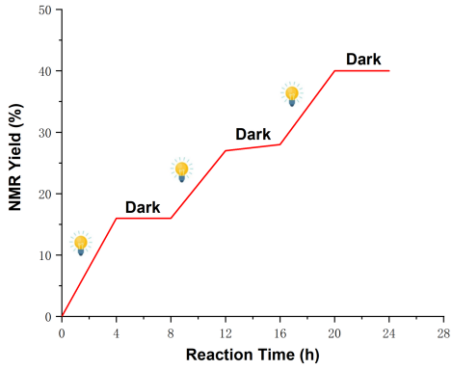


Figure S3 Yield of Light On-Off Experiments

The results of light on-off experiments indicated that the reaction proceeded only under the irradiation of light. Thus, the reaction maybe proceed via a catalytic process rather than a radical chain process.

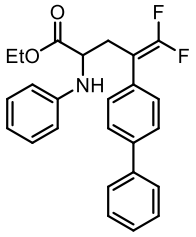
9. References

1 H. Xin, Z.-H. Yuan, M.-Y. Yang, M.-H. Wang, X.-H. Duan and L.-N. Guo., *Green Chem*., **2021**, *23*, 9549.

2 C. Zhu, M.-M. Sun, K. Chen, H. Liu and C. Feng, *Angew. Chem., Int. Ed.*, **2021**, *60*, 20237.

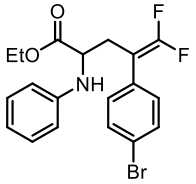
3 Z. Kuang, H. Chen, J. Qiu, Z. Ou, Y. Lan, and Q. Song, *Chem*., **2020**, *6*, 2347.

10. Characterization of Products



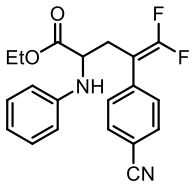
Ethyl 4-([1,1'-biphenyl]-4-yl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3a).

colorless oil (92%, 74.9 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 4H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.42 – 7.39 (m, 3H), 7.14 (dd, *J* = 8.4, 7.2 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 2H), 4.13 – 4.02 (m, 4H), 2.96 (s, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 154.7 (dd, *J* = 289.5, 287.0 Hz), 146.3, 140.7, 140.5, 131.6 (t, *J* = 3.3 Hz), 129.4, 129.0, 127.7, 127.4, 127.2, 118.6, 113.7, 88.8 (dd, *J* = 21.2, 16.3 Hz), 61.5, 55.3, 31.6, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.81 (d, *J* = 37.6 Hz), -89.16 (d, *J* = 37.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3390, 2923, 1731, 1602, 1504, 1377, 1192, 1028, 755 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}F_2NO_2$ $[M+H]^+$ 408.1769, found 408.1762.



Ethyl 4-(4-bromophenyl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3b).

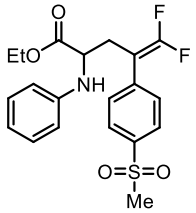
colorless oil (86%, 70.3 mg); R_f = 0.40 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.19 – 7.11 (m, 4H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 2H), 4.10 – 3.02 (m, 3H), 2.88 (s, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 154.6 (dd, *J* = 290.2, 287.6 Hz), 146.2, 131.9, 131.7 (t, *J* = 3.3 Hz), 130.3 (t, *J* = 2.9 Hz), 129.4, 121.9, 118.8, 113.7, 88.4 (dd, *J* = 21.8, 16.2 Hz), 61.6, 55.2, 31.5, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.49 (d, *J* = 36.5 Hz), -88.86 (d, *J* = 36.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3370, 2856, 1734, 1601, 1499, 1375, 1249, 822 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}BrF_2NO_2$ $[M+H]^+$ 410.0561, found 410.0547.



Ethyl 4-(4-cyanophenyl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3c).

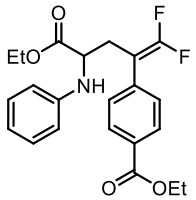
colorless oil (66%, 47.0 mg); R_f = 0.40 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 7.6 Hz, 2H), 4.15 – 3.99 (m, 3H), 2.98 – 2.88 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6,

154.8 (dd, *J* = 292.2, 289.4 Hz), 145.9, 137.8 (dd, *J* = 4.0, 3.0 Hz), 132.3, 129.4, 129.2 (t, *J* = 3.2 Hz), 118.8, 118.5, 113.6, 111.5, 88.5 (dd, *J* = 22.0, 15.0 Hz), 61.6, 55.2, 30.9, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.40 (d, *J* = 30.8 Hz), -86.56 (d, *J* = 30.8 Hz); IR (neat): υ_{max} (cm^{-1}) 3380, 3054, 2260, 1729, 1601, 1506, 1311, 840 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{19}F_2N_2O_2$ $[M+H]^+$ 357.1409, found 357.1411.



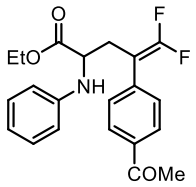
Ethyl 5,5-difluoro-4-(4-(methylsulfonyl)phenyl)-2-(phenylamino)pent-4-enoate (3d).

colorless oil (77%, 63.0 mg); R_f = 0.40 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 7.6 Hz, 1H), 6.44 (d, *J* = 8.0 Hz, 2H), 4.11 – 4.02 (m, 3H), 3.05 (s, 3H), 3.01 – 2.89 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 154.9 (dd, *J* = 292.1, 289.2 Hz), 145.9, 139.7, 138.7 (t, *J* = 3.2 Hz), 129.4 (t, *J* = 3.1 Hz), 129.4, 127.7, 118.7, 113.5, 88.4 (dd, *J* = 22.2, 15.5 Hz), 61.6, 55.1, 44.4, 31.1, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.50 (d, *J* = 31.2 Hz), -86.72 (d, *J* = 31.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3375, 2985, 2941, 2361, 1727, 1309, 1140, 774 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}F_2NO_4S$ $[M+H]^+$ 410.1232, found 410.1230.



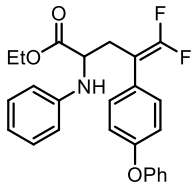
Ethyl 4-(5-ethoxy-1,1-difluoro-5-oxo-4-(phenylamino)pent-1-en-2-yl)benzoate (3e).

colorless oil (86%, 69.3 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 2H), 4.40 (q, *J* = 7.2 Hz, 2H), 4.11 – 4.01 (m, 3H), 2.94 (d, *J* = 4.0 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 166.2, 154.8 (dd, *J* = 291.6 288.1 Hz), 146.2, 137.4 (t, *J* = 3.8 Hz), 129.9, 129.4, 128.5 (t, *J* = 3.0 Hz), 118.8, 113.7, 88.8 (dd, *J* = 21.6, 15.7 Hz), 61.5, 61.2, 55.3 31.4, 14.4, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.46 (d, *J* = 33.9 Hz), -87.71 (d, *J* = 34.0 Hz); IR (neat): υ_{max} (cm^{-1}) 3377, 2986, 2877, 1714, 1274, 1022, 857 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}F_2NO_4$ $[M+H]^+$ 404.1668, found 404.1661.



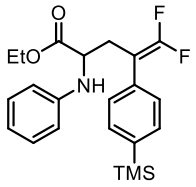
Ethyl 4-(4-acetylphenyl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3f).

colorless oil (77%, 57.4 mg); R_f = 0.60 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.87 (m, 2H), 7.52 – 7.45 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 7.6 Hz, 2H), 4.10 – 4.12 (m, 3H), 2.97 – 2.91 (m, 2H), 2.55 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 172.8, 154.8 (dd, *J* = 290.1, 287.8 Hz), 146.1, 137.5, 133.3, 129.4, 129.0, 128.4 (t, *J* = 2.8 Hz), 127.7, 118.7, 113.6, 88.6 (dd, *J* = 21.6, 16.2 Hz), 61.5, 55.1, 31.3, 26.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.59 (d, *J* = 36.5 Hz), -88.88 (d, *J* = 36.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3374, 2984, 2361, 1730, 1602, 1230, 1025, 796 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{22}F_2NO_3$ $[M+H]^+$ 374.1562, found 374.1551.



Ethyl 5,5-difluoro-4-(4-phenoxyphenyl)-2-(phenylamino)pent-4-enoate (3g).

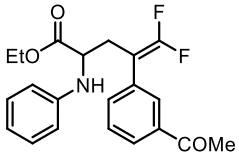
colorless oil (63%, 53.3 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.16 (t, *J* = 8.4 Hz, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 2H), 4.14 – 4.07 (m, 3H), 2.92 – 2.90 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.60 (d, *J* = 39.1 Hz), -90.07 (d, *J* = 39.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 157.1, 156.8, 154.6 (dd, *J* = 289.1, 286.8 Hz), 146.2, 130.1 (t, *J* = 2.8 Hz), 123.0, 129.4, 127.2 (dd, *J* = 3.7, 3.2 Hz), 123.8, 119.4, 118.7, 113.7, 88.4 (dd, *J* = 21.3, 16.4 Hz), 61.5, 55.3, 31.7, 14.2; IR (neat): υ_{max} (cm^{-1}) 3376, 2983, 1718, 1603, 1372, 1089, 752 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}F_2NO_3$ $[M+H]^+$ 424.1719, found 424.1722.



Ethyl 5,5-difluoro-2-(phenylamino)-4-(4-(trimethylsilyl)phenyl)pent-4-enoate (3h).

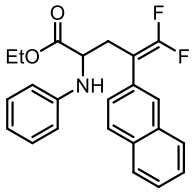
colorless oil (58%, 46.7 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 2H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 7.6 Hz, 2H), 4.09 – 3.96 (m, 3H), 2.92 – 2.90 (m, 2H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 154.7 (dd, *J* = 289.9, 286.8 Hz), 146.3, 140.3, 133.7, 133.1 (t, *J* = 3.4 Hz), 129.4, 127.9 (t, *J* = 3.4 Hz), 118.7 (s), 113.8, 89.0 (dd, *J* = 21.0, 16.2 Hz), 61.5, 55.4, 31.5, 14.2, -1.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.12 (d, *J* = 37.6 Hz), -89.47 (d, *J* =

37.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3386, 3057, 2816, 2360, 1730, 1602, 1181, 781 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{28}F_2NO_2Si$ $[M+H]^+$ 404.1852, found 404.1835.



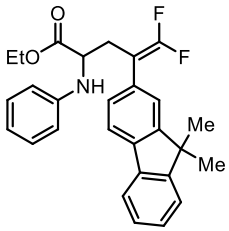
Ethyl 4-(3-acetylphenyl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3i).

colorless oil (60%, 44.8 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.86 (m, 2H), 7.52 – 7.45 (m, 2H), 7.11 (t, *J* = 8.4 Hz, 2H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 2H), 4.12 – 4.00 (m, 3H), 2.99 – 2.91 (m, 3H), 2.55 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.54 (d, *J* = 36.1 Hz), -88.82 (d, *J* = 36.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 172.8, 154.8 (dd, *J* = 289.7, 287.7 Hz), 146.0 (d, *J* = 4.8 Hz), 137.5, 133.3 (dd, *J* = 6.8, 4.2 Hz), 129.4, 129.0, 128.5 (t, *J* = 2.7 Hz), 127.8 , 118.8 (d, *J* = 6.2 Hz), 113.7 (d, *J* = 5.9 Hz), 88.6 (dd, *J* = 21.6, 16.3 Hz), 61.6 , 55.2, 31.4, 26.7, 14.2; IR (neat): υ_{max} (cm^{-1}) 3374, 2983, 1715, 1602, 1371, 1024, 750 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{22}F_2NO_3$ $[M+H]^+$ 374.1562, found 374.1555.



Ethyl 5,5-difluoro-4-(naphthalen-2-yl)-2-(phenylamino)pent-4-enoate (3j).

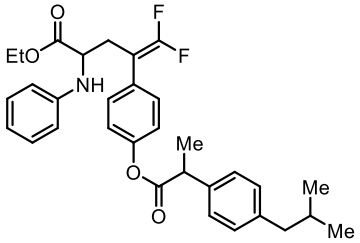
colorless oil (79%, 60.2 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.76 (m, 4H), 7.56 – 7.49 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 6.48 (d, *J* = 7.6 Hz, 2H), 4.17 – 3.96 (m, 4H), 3.03 (s, 2H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 154.8 (dd, *J* = 289.9, 287.1 Hz), 146.3, 133.3, 132.8, 130.0 (t, *J* = 3.0 Hz), 129.3, 128.4, 128.1, 127.9 (t, *J* = 3.0 Hz), 127.8, 126.6, 126.5, 126.3 (t, *J* = 2.9 Hz), 118.6, 113.7, 89.2 (dd, *J* = 21.2, 16.2 Hz), 61.4, 55.3, 31.8, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.01 (d, *J* = 37.6 Hz), -89.29 (d, *J* = 37.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3379, 3055, 2361, 1727, 1602, 1229, 1109, 818 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}F_2NO_2$ $[M+H]^+$ 382.1613, found 382.1601.



Ethyl 4-(9,9-dimethyl-9*H*-fluoren-2-yl)-5,5-difluoro-2-(phenylamino)pent-4-enoate (3k).

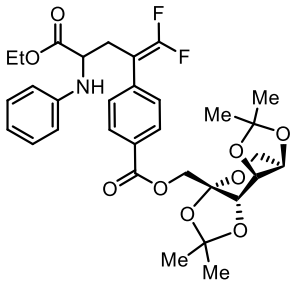
White solid (85%, 76.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H), 7.45 (d, *J* = 6.0 Hz, 1H), 7.39 – 7.28 (m, 5H), 7.10 (t, *J* = 7.2 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 2H), 4.12 –

4.03 (m, 3H), 2.96 (d, *J* = 6.0 Hz, 2H), 1.48 (s, 3H), 1.49 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 154.7 (dd, *J* = 289.6, 287.2 Hz), 154.1, 153.9, 146.3, 139.0, 138.7, 131.5 (t, *J* = 3.0 Hz), 129.4, 127.7, 127.6 (t, *J* = 2.7 Hz), 127.2, 122.9 (t, *J* = 2.7 Hz), 122.8, 120.3, 120.2, 118.7, 113.7, 89.5 (dd, *J* = 21.1, 15.7 Hz), 61.5, 55.4, 47.0, 32.0, 27.3, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.16 (d, *J* = 38.7 Hz), -89.89 (d, *J* = 38.7 Hz); IR (neat): υ_{max} (cm^{-1}) 3385, 3059, 2360, 1730, 1602, 1254, 1024, 831 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{28}F_2NO_2$ $[M+H]^+$ 448.2083, found 448.2071.



Ethyl 5,5-difluoro-4-(4-((2-(4-isobutylphenyl)propanoyl)oxy)phenyl)-2-(phenylamino)pent-4-en -oate (3l).

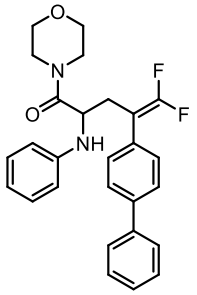
colorless oil (51%, 54.6 mg, d.r. = 1:1); R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 4H), 7.16 – 7.09 (m, 4H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 2H), 4.05 – 3.93 (m, 5H), 2.86 (s, 2H), 2.46 (d, *J* = 7.2 Hz, 2H), 1.90 – 1.83 (m, 1H), 1.60 (d, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 173.0, 154.6 (dd, *J* = 289.3, 287.2 Hz), 150.4, 146.3, 141.0, 137.2, 130.1 (t, *J* = 3.2 Hz), 129.7, 129.4, 127.3, 121.8, 118.7, 113.7, 88.4 (dd, *J* = 21.7, 16.3 Hz), 61.5, 55.2, 45.4, 45.2, 31.7, 30.3, 22.5, 18.6, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.00 (d, *J* = 37.6 Hz), -89.50 (d, *J* = 37.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3332, 3030, 2857, 1726, 1643, 1460, 1236, 764 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{36}F_2NO_4$ $[M+H]^+$ 536.2607, found 536.2587.



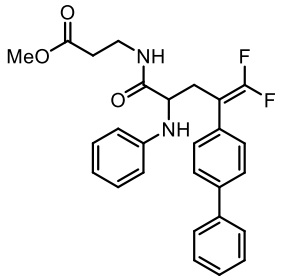
((3aS,5aR,8aR,8bS)-2,2,7,7-Tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-y l)methyl 4-(5-ethoxy-1,1-difluoro-5-oxo-4-(phenylamino)pent-1-en-2-yl)benzoate (3m).

white solid (67%, 82.7 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 2H), 4.71 – 4.64 (m, 2H), 4.47 (s, 1H), 4.35 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.27 (d, *J* = 7.6 Hz, 1H), 4.14 – 3.95 (m, 5H), 3.83 (t, *J* = 12.4 Hz, 1H), 2.93 (s, 2H), 1.56 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.20 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 165.6, 154.8 (dd, *J* = 291.8, 288.5 Hz), 146.1, 137.8, 130.1, 129.4, 128.5 (t, *J* = 2.9 Hz), 118.8, 113.6, 109.3, 109.0, 101.7, 88.8 (dd, *J* = 21.5, 15.8 Hz), 70.9, 70.7, 70.2, 65.6, 61.52, 61.46,

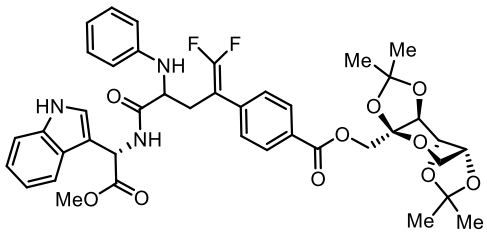
55.2, 31.3, 26.6, 26.0, 25.7, 24.1, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.17 (dd, *J* = 33.1, 9.6 Hz), -87.34 (dd, *J* = 33.1, 9.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3309, 3001, 2769, 2293, 1736, 1313, 1179, 843 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{38}F_2NO_9$ $[M+H]^+$ 618.2509, found 618.2499.



4-([1,1'-Biphenyl]-4-yl)-5,5-difluoro-1-morpholino-2-(phenylamino)pent-4-en-1-one (3n).
yellow solid (84%, 75.3 mg); m.p.: 130-131 °C; R_f = 0.5 (petroleum ether/ethyl acetate = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.55 (m, 4H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 3H), 7.14 (t, *J* = 8.0 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 2H), 4.40 (s, 2H), 3.61 – 3.54 (m, 5H), 3.47 – 3.33 (m, 3H), 2.09 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 154.6 (dd, *J* = 291.0, 287.2 Hz), 146.5, 140.6, 140.3, 131.8 (t, *J* = 3.8 Hz), 129.5, 129.0, 128.7 (t, *J* = 3.1 Hz), 127.8, 127.3, 127.1, 118.7, 114.0, 88.8 (dd, *J* = 21.2, 14.9 Hz), 66.8, 66.6, 51.7, 46.0, 42.5.0, 31.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.14 (d, *J* = 36.5 Hz), -88.44 (d, *J* = 36.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3386, 2956, 1732, 1603, 1372, 1168, 1018, 749 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}F_2N_2O_2$ $[M+H]^+$ 449.2035, found 449.2032.

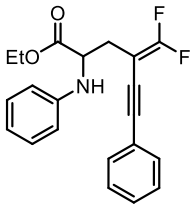


Methyl 3-(4-([1,1'-biphenyl]-4-yl)-5,5-difluoro-2-(phenylamino)pent-4-enamido)propanoate (3o).
white solid (75%, 69.6 mg); m.p.: 147-148 °C; R_f = 0.5 (petroleum ether/ethyl acetate = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 4H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 5.6 Hz, 3H), 7.14 (t, *J* = 8.4 Hz, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 2H), 3.91 (s, 1H), 3.74 – 3.72 (m, 1H), 3.53 (s, 3H), 3.51 – 3.41 (m, 2H), 3.17 – 3.13 (m, 1H), 2.90 – 2.84 (m, 1H), 2.45 (t, *J* = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 172.4, 154.6 (dd, *J* = 290.8, 286.5 Hz), 146.3, 140.8, 140.4, 131.0 (t, *J* = 3.7 Hz), 129.4, 128.9, 127.5, 127.1, 119.3, 113.7, 89.2 (dd, *J* = 20.7, 15.3 Hz), 57.9, 51.7, 34.7, 33.7, 31.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.08 (d, *J* = 38.7 Hz), -89.53 (d, *J* = 39.1 Hz); IR (neat): υ_{max} (cm^{-1}) 3394, 2958, 2870, 1739, 1604, 1072, 1023, 952 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}F_2N_2O_2$ $[M+H]^+$ 465.1984, found 465.1976.



((3aS,5aR,8aR,8bS)-2,2,7,7-Tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl-4-(5-(((S)-1-(1H-indol-3-yl)-2-methoxy-2-oxoethyl)amino)-1,1-difluoro-5-oxo-4-(phenylamino)pent-1-en-2-yl)benzoate (3p).

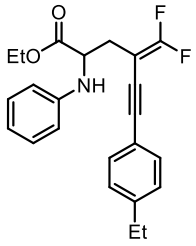
white solid (63%, 97.7 mg, d.r. = 1:1); m.p.: 210-211 ºC; R_f = 0.5 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 0.5H), 8.22 (s, 0.5H), 7.99 (dd, *J* = 13.2, 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 0.5H), 7.40 (dd, *J* = 8.0, 4.4 Hz, 0.5H), 7.32 – 7.28 (m, 1.5H), 7.24 – 7.20 (m, 1.5H), 7.16 – 7.12 (m, 3H), 7.07 – 6.98 (m, 1H), 6.87 – 6.77 (m, 2H), 6.42 – 6.36 (m, 2H), 4.92 – 4.89 (m, 0.5H), 4.86 – 4.81 (m, 0.5H), 4.75 (dd, *J* = 11.6, 8.4 Hz, 1H), 4.70 (d, *J* = 7.6 Hz, 1H), 4.49 (s, 1H), 4.38 (d, *J* = 11.6 Hz, 0.5H), 4.31 (d, *J* = 8.0 Hz, 0.5H), 4.16 (q, *J* = 7.2 Hz, 1H), 4.01 (d, *J* = 12.8 Hz, 0.5H), 3.85 (d, *J* = 13.2 Hz, 0.5H), 3.71 (s, 1.5H), 3.67 (s, 1.5H), 3.36 – 3.28 (m, 2H), 3.15 (dd, *J* = 14.8, 4.8 Hz, 1H), 3.08 (d, *J* = 15.2 Hz, 0.5H), 2.93 (d, *J* = 23.2 Hz, 0.5H), 2.82 (dd, *J* = 13.2, 10.0 Hz, 0.5H), 2.66 (dd, *J* = 13.2, 8.8 Hz, 0.5H), 2.08 (s, 1H), 1.60 (s, 3H), 1.50 (s, 3H), 1.42 (d, *J* = 4.8 Hz, 3H), 1.40 (s, 1H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 172.0, 171.9, 171.8, 171.3, 165.5, 165.5, 154.7 (t, *J* = 288.0 Hz), 154.6 (t, *J* = 286.4 Hz), 146.3, 146.2, 137.2 (t, *J* = 4.1 Hz), 136.2, 136.1, 130.1, 130.0, 129.4, 129.3, 129.2, 129.0, 128.5 (t, *J* = 2.8 Hz), 128.3 (t, *J* = 2.6 Hz), 127.7, 127.2, 123.1, 122.9, 122.3, 122.1, 119.6, 119.5, 119.4, 119.3, 118.4, 118.4, 114.0, 113.7, 111.6, 111.3, 109.6, 109.2, 109.1, 109.0, 108.9, 101.7, 101.6, 89.1 (dd, *J* = 21.4, 15.1 Hz), 89.0 (dd, *J* = 21.6, 15.0 Hz), 70.8, 70.7, 70.6, 70.1, 65.8, 65.6, 61.4, 60.5, 57.8, 57.5, 53.1, 52.4, 52.4, 52.2, 31.5, 31.1, 27.5, 27.3, 26.6, 25.9, 25.6, 24.0, 21.1, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.41 (d, *J* = 34.6 Hz), -86.64 (d, *J* = 33.8 Hz), -87.74 (d, *J* = 12.0 Hz), -87.83 (d, *J* = 12.4 Hz); IR (neat): υ_{max} (cm^{-1}) 3376, 2983, 1718, 1603, 1496, 1408, 1277, 1189, 1156, 1089, 1026 cm^{-1}; HRMS (ESI) calcd for $C_{41}H_{44}F_2N_3O_{10}$ $[M+H]^+$ 776.2989, found 776.2927.



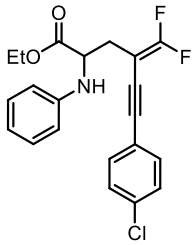
Ethyl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5a).

colorless oil (93%, 60.1 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H), 7.38 – 7.32 (m, 3H), 7.21 (t, *J* = 8.4 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 4.41 (t, *J* = 6.4 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.78 – 2.66 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 159.7 (dd, *J* = 295.9, 293.2 Hz), 146.4, 131.6, 129.5, 128.5, 128.5, 122.6, 118.7, 113.8, 94.4 (t, *J* = 5.7 Hz), 80.4 (dd, *J* = 7.6, 4.3 Hz), 75.3 (dd, *J* = 34.0,

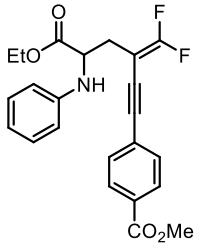
17.7 Hz), 61.7, 55.4, 30.8, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.29 (d, *J* = 11.3 Hz), -83.11 (d, *J* = 11.3 Hz); IR (neat): υ_{max} (cm^{-1}) 3385, 2983, 2875, 1716, 1599, 1491, 1016, 816 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}F_2NO_2$ $[M+H]^+$ 324.1205, found 324.1197.



Ethyl 4-(difluoromethylene)-6-(4-ethylphenyl)-2-(phenylamino)hex-5-ynoate (5b).
colorless oil (84%, 64.3 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.13 (m, 4H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 2H), 4.37 (t, *J* = 6.4 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 2.69 – 2.63 (m, 4H), 1.28 – 1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 159.7 (dd, *J* = 295.5, 292.7 Hz), 146.4, 145.3, 131.6, 129.5, 128.1, 119.9, 118.7, 113.8, 94.7 (t, *J* = 5.6 Hz), 79.7 (dd, *J* = 7.8, 4.4 Hz), 75.4 (dd, *J* = 34.0, 17.8 Hz), 61.7, 55.4, 31.0, 28.9, 15.5, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.68 (d, *J* = 12.2 Hz), -83.60 (d, *J* = 12.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3388, 2983, 1715, 1595, 1275, 1194, 1076, 909 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}F_2NO_2$ $[M+H]^+$ 384.1770, found 384.1767.

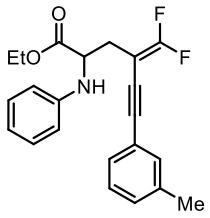


Ethyl 6-(4-chlorophenyl)-4-(difluoromethylene)-2-(phenylamino)hex-5-ynoate (5c).
colorless oil (87%, 67.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 4H), 7.18 (t, *J* = 8.4 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 2H), 4.35 (t, *J* = 6.4 Hz, 1H), 4.24 – 4.15 (m, 2H), 2.72 – 2.64 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 159.7 (dd, *J* = 295.8, 295.2 Hz), 146.2, 134.7, 132.7, 129.4, 128.8, 121.0, 118.6, 113.6, 93.2 (t, *J* = 5.6 Hz), 81.4 (dd, *J* = 7.5, 4.4 Hz), 75.0 (dd, *J* = 34.1, 17.6 Hz), 61.6, 55.3, 30.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.74 (d, *J* = 9.8 Hz), -82.44 (d, *J* = 9.8 Hz); IR (neat): υ_{max} (cm^{-1}) 3394, 2982, 1715, 1601, 1371, 1274, 1087, 916 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{19}ClF_2NO_2$ $[M+H]^+$ 390.1067, found 390.1075.



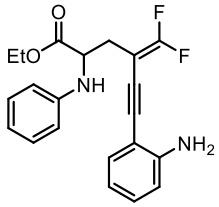
Methyl-4-(3-(difluoromethylene)-6-ethoxy-6-oxo-5-(phenylamino)hex-1-yn-1-yl)benzoate (5d).

colorless oil (69%, 58.9 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 2H), 4.37 (q, *J* = 6.4 Hz, 1H), 4.21 (t, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 2.71 (s, 2H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 166.6, 159.9 (dd, *J* = 296.9, 294.1 Hz), 146.3, 131.4, 129.9, 129.6, 129.5, 127.3, 118.8, 113.7, 93.6 (t, *J* = 5.8 Hz), 83.4 (dd, *J* = 7.8, 4.3 Hz), 75.2 (dd, *J* = 34.3, 17.5 Hz), 61.7, 55.3, 52.4, 30.7, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.00 (d, *J* = 7.9 Hz), -81.64 (d, *J* = 7.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3392, 3054, 1630, 1523, 1491, 1274, 1023, 863 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{24}F_2NO_4$ $[M+H]^+$ 428.1667, found 428.1646.

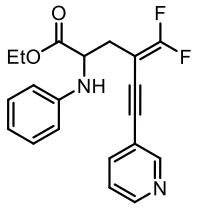


Ethyl 4-(difluoromethylene)-2-(phenylamino)-6-(m-tolyl)hex-5-ynoate (5e).

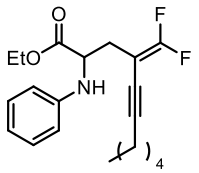
colorless oil (89%, 65.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.23 (m, 2H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 4.37 (t, *J* = 6.4 Hz, 1H), 4.27 – 4.12 (m, 3H), 2.68 (d, *J* = 5.6 Hz, 2H), 2.33 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 159.7 (dd, *J* = 295.7, 292.9 Hz), 146.4, 138.2, 132.2, 129.7, 129.5, 128.6, 128.4, 122.5, 118.7, 113.8, 94.7 (t, *J* = 5.7 Hz), 80.0 (dd, *J* = 7.6, 4.2 Hz), 75.3 (dd, *J* = 34.0, 17.7 Hz), 61.7, 55.4, 31.0, 21.3, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.47 (d, *J* = 11.7 Hz), -83.32 (d, *J* = 11.7 Hz); IR (neat): υ_{max} (cm^{-1}) 3547, 3165, 2821, 2293, 1631, 1174, 1035, 919 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{22}F_2NO_4$ $[M+H]^+$ 370.1613, found 370.1605.



Ethyl 6-(2-aminophenyl)-4-(difluoromethylene)-2-(phenylamino)hex-5-ynoate (5f).
yellow oil (76%, 56.2 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.36 (m, 1H), 7.31 – 7.22 (m, 3H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.81 – 6.78 (m, 4H), 4.49 – 4.39 (m, 3H), 4.31 (q, *J* = 7.2 Hz, 2H), 2.82 (s, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 159.5 (dd, *J* = 295.1, 293.7 Hz), 148.1, 146.3, 132.1, 130.2, 129.5, 118.8, 117.9, 114.5, 113.8, 107.1, 91.3 (t, *J* = 5.7 Hz), 85.3 (dd, *J* = 7.6, 4.3 Hz), 75.3 (dd, *J* = 33.9, 17.8 Hz), 61.8, 55.5, 30.9, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.48 (d, *J* = 11.3 Hz), -83.49 (d, *J* = 11.3 Hz); IR (neat): υ_{max} (cm^{-1}) 3384, 3009, 2881, 2253, 1718, 1276, 1032, 958, 833 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{21}F_2N_2O_2$ $[M+H]^+$ 371.1566, found 371.1559.

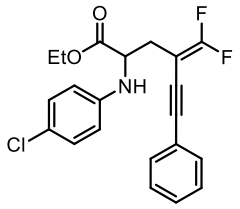


Ethyl 4-(difluoromethylene)-2-(phenylamino)-6-(pyridin-3-yl)hex-5-ynoate (5g).
yellow oil (52%, 37.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.20 (t, *J* = 7.2 Hz, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 4.39 (s, 1H), 4.25 – 4.21 (m, 2H), 2.73 (s, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 160.0 (dd, *J* = 296.9, 294.2 Hz), 152.1, 149.0, 146.3, 138.5, 129.5, 123.2, 119.9, 118.8, 113.7, 90.9 (t, *J* = 5.7 Hz), 83.8 (dd, *J* = 7.9, 4.4 Hz), 75.0 (dd, *J* = 34.3, 17.5 Hz), 61.7, 55.3, 30.7, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.91 (d, *J* = 7.9 Hz), -81.54 (d, *J* = 7.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3386, 2860, 2253, 1603, 1443, 1274, 1086, 997, 877 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{19}F_2N_2O_2$ $[M+H]^+$ 357.1409, found 357.1414.

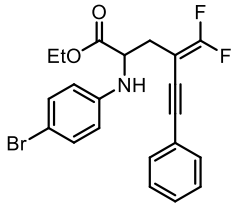


Ethyl 4-(difluoromethylene)-2-(phenylamino)undec-5-ynoate (5h).
colorless oil (66%, 46.1mg); R_f = 0.6 (petroleum ether/ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 8.4 Hz, 2H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 2H), 4.29 (t, *J* = 7.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 2.55 (d, *J* = 6.4 Hz, 2H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.59 – 1.52 (m, 2H), 1.40 – 1.30 (m, 6H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 160.0 (dd, *J* =

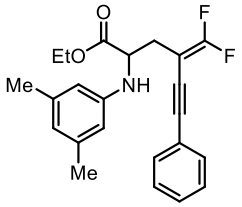
293.6, 290.8 Hz), 146.6, 129.4, 118.7, 113.8, 96.0 (t, *J* = 5.4 Hz), 75.2 (dd, *J* = 33.5, 18.2 Hz), 71.4 (dd, *J* = 7.5, 3.9 Hz), 61.6, 55.4, 31.3, 31.2, 28.4, 22.3, 19.6, 14.2, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.14 (d, *J* = 17.8 Hz), -85.64 (d, *J* = 17.8 Hz); IR (neat): υ_{max} (cm^{-1}) 3387, 3056, 1717, 1603, 1275, 1180, 995, 874 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}F_2NO_2$ $[M+H]^+$ 350.1926, found 350.1918.



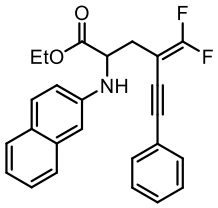
Ethyl 2-((4-chlorophenyl)amino)-4-(difluoromethylene)-6-phenylhex-5-ynoate (5i).
colorless oil (81%, 63.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.41 (m, 2H), 7.35 (s, 3H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 4.37 – 4.29 (m, 2H), 4.20 (q, *J* = 7.2, 2H), 2.68 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 159.7 (dd, *J* = 296.1, 293.4 Hz), 145.0, 131.6, 129.4, 128.9, 128.6, 123.3, 122.5, 114.9, 94.5 (t, *J* = 5.8 Hz), 80.2 (dd, *J* = 7.9, 4.6 Hz), 75.1 (dd, *J* = 34.0, 17.8 Hz), 61.9, 55.5, 30.8, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.99 (d, *J* = 10.8 Hz), -82.94 (d, *J* = 10.7 Hz); IR (neat): υ_{max} (cm^{-1}) 3387, 3058, 2942, 1716, 1443, 1277, 1082, 885 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{19}ClF_2NO_2$ $[M+H]^+$ 390.1067, found 390.1075.



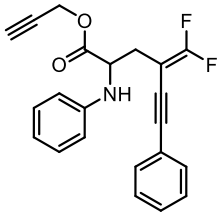
Ethyl 2-((4-bromophenyl)amino)-4-(difluoromethylene)-6-phenylhex-5-ynoate (5j).
colorless oil (83%, 71.9 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.36 (m, 2H), 7.30 – 7.28 (m, 3H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.51 (d, *J* = 8.8 Hz, 2H), 4.28 (t, *J* = 6.0 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.66 – 2.62 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 159.7 (dd, *J* = 296.1, 293.5 Hz), 145.4, 132.2, 131.5, 128.8, 128.5, 122.5, 115.3, 110.3, 94.5 (t, *J* = 5.6 Hz), 80.2 (dd, *J* = 7.6, 4.2 Hz), 75.1 (dd, *J* = 33.9, 17.7 Hz), 61.7, 55.3, 30.7, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.92 (d, *J* = 10.9 Hz), -82.84 (d, *J* = 10.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3546, 3165, 2943, 2293, 1632, 1376, 1035, 919 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{19}BrF_2NO_2$ $[M+H]^+$ 434.0517, found 434.0545.



Ethyl 4-(difluoromethylene)-2-((3,5-dimethylphenyl)amino)-6-phenylhex-5-ynoate (5k).
colorless oil (86%, 65.9 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 2H), 7.36 – 7.34 (m, 3H), 6.44 (s, 1H), 6.34 (s, 2H), 4.39 (t, *J* = 6.4 Hz, 1H), 4.26 – 4.18 (m, 3H), 2.69 (d, *J* = 6.4 Hz, 2H), 2.22 (s, 6H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 159.7 (dd, *J* = 295.8, 293.5 Hz), 146.5, 139.1, 131.6, 128.7, 128.5, 122.6, 120.7, 111.7, 94.4 (t, *J* = 5.7 Hz), 80.5 (dd, *J* = 7.7, 4.0 Hz), 75.4 (dd, *J* = 34.0, 17.6 Hz), 61.6, 55.4, 31.0, 21.6, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.26 (d, *J* = 11.7 Hz), -83.10 (d, *J* = 11.7 Hz); IR (neat): υ_{max} (cm^{-1}) 3547, 3003, 2864, 2293, 1645, 1493, 1116, 1035, 919 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}F_2NO_2$ $[M+H]^+$ 384.1770, found 384.1768.

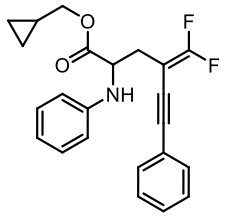


Ethyl 4-(difluoromethylene)-2-(naphthalen-2-ylamino)-6-phenylhex-5-ynoate (5l).
colorless oil (75%, 60.8 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 14.4, 8.0 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.39 – 7.33 (m, 4H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.92 (d, *J* = 2.0 Hz, 1H), 4.55 (t, *J* = 6.0 Hz, 1H), 4.29 – 4.20 (m, 2H), 2.80 – 2.78 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 159.8 (dd, *J* = 296.0, 293.5 Hz), 144.0, 135.0, 131.6, 129.3, 128.8, 128.5, 128.1, 127.7, 126.5, 126.2, 122.6, 118.3, 105.7, 94.5 (t, *J* = 5.8 Hz), 80.4 (dd, *J* = 7.5, 4.0 Hz), 75.3 (dd, *J* = 34.2, 17.9 Hz), 61.8, 55.3, 30.6, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.01 (d, *J* = 11.3 Hz), -82.86 (d, *J* = 11.3 Hz); IR (neat): υ_{max} (cm^{-1}) 3362, 2944, 2409, 2253, 1661, 1198, 1033, 995 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}F_2NO_2$ $[M+H]^+$ 406.1613, found 406.1611.

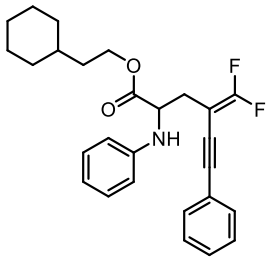


Prop-2-yn-1-yl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5m).
colorless oil (77%, 56.2 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.43 (m, 2H), 7.35 – 7.33 (m, 3H), 7.21 – 7.17 (m, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 2H), 4.73 (t, *J* = 2.4 Hz, 1H), 4.45 (dd, *J*

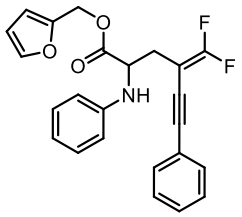
= 14.8, 6.4 Hz, 1H), 4.30 (d, *J* = 8.4 Hz, 1H), 2.74 – 2.71 (m, 2H), 2.48 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 159.8 (dd, *J* = 295.9, 292.0Hz), 146.3, 131.6, 129.6, 128.8, 128.5, 122.6, 119.0, 113.9, 94.6 (t, *J* = 5.0 Hz), 80.2 (dd, *J* = 17.8, 9.5 Hz), 75.6, 75.0 (dd, *J* = 34.2, 17.3 Hz), 55.4, 53.0, 30.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.78 (d, *J* = 10.5 Hz), -82.62 (d, *J* = 10.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3460, 2940, 1667, 1427, 1264, 1113, 927 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}F_2NO_2$ $[M+H]^+$ 366.1300, found 366.1302.



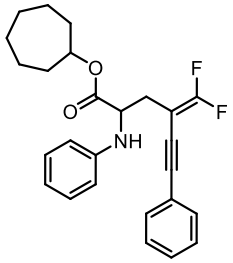
Cyclopropylmethyl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5n).
colorless oil (73%, 55.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.35 – 7.34 (m, 3H), 7.19 (t, *J* = 7.8 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 2H), 4.43 – 4.36 (m, 2H), 4.02 – 3.94 (m, 2H), 2.73 – 2.70 (m, 2H), 1.18 – 1.08 (m, 1H), 0.57 – 0.53 (m, 2H), 0.27 – 0.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 159.6 (dd, *J* = 295.9, 293.2 Hz), 146.3, 131.5, 129.4, 128.7, 128.4, 122.6, 118.6, 113.7, 94.3 (t, *J* = 5.6 Hz), 80.3 (dd, *J* = 7.7, 4.2 Hz), 75.2 (dd, *J* = 34.1, 17.7 Hz), 70.4, 55.3, 30.9, 9.7, 3.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.24 (d, *J* = 11.2 Hz), -83.00 (d, *J* = 11.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3340, 2982, 2831, 1665, 1278, 1023, 755 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}F_2NO_2$ $[M+H]^+$ 382.1613, found 382.1623.



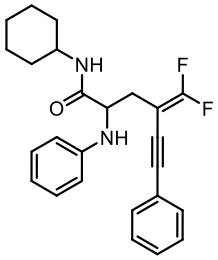
2-cyclohexylethyl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5o).
colorless oil (81%, 70.8 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.45 (m, 2H), 7.36 – 7.34 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 2H), 5.02 – 4.96 (m, 1H), 4.36 (t, *J* = 6.4 Hz, 1H), 2.69 (d, *J* = 6.0 Hz, 2H), 1.91 – 1.82 (m, 2H), 1.68 – 1.60 (m, 3H), 1.55 – 1.53 (m, 3H), 1.44 – 1.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 159.7 (dd, *J* = 296.0, 293.4 Hz), 146.4, 131.5, 129.4, 128.7, 128.4, 122.6, 118.6, 113.7, 94.4 (t, *J* = 5.7 Hz), 80.3 (dd, *J* = 7.7, 4.3 Hz), 76.7, 75.3 (dd, *J* = 34.1, 17.7 Hz), 55.5, 33.7, 33.6, 30.8, 28.22, 28.18, 22.73, 22.70; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.41 (d, *J* = 11.9 Hz), -83.00 (d, *J* = 11.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3387, 2983, 1715, 1602, 1274, 1183, 1026, 871 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{30}F_2NO_2$ $[M+H]^+$ 438.2239, found 438.2242.



Furan-2-ylmethyl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5p).
colorless oil (66%, 53.7 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.42 (m, 3H), 7.35 – 7.33 (m, 3H), 7.18 (t, *J* = 7.6 Hz, 2H), 6.77 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 6.38-6.35 (m, 2H), 5.13 (q, *J* = 13.2 Hz, 2H), 4.42 (t, *J* = 6.4 Hz, 1H), 2.70 – 2.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 159.7 (dd, *J* = 295.9, 293.3 Hz), 148.9, 146.3, 143.6, 131.6, 129.5 , 128.8, 128.5, 122.6, 118.8, 113.8, 111.2, 110.7, 94.5 (t, *J* = 5.7 Hz), 80.2 (dd, *J* = 7.7, 4.3 Hz), 75.1 (dd, *J* = 33.9, 17.9 Hz), 59.0, 55.4, 30.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.00 (d, *J* = 10.8 Hz), -82.95 (d, *J* = 10.8 Hz); IR (neat): υ_{max} (cm^{-1}) 3375, 2970, 2875, 1737, 1680, 1496, 1183, 1033 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{20}F_2NO_3$ $[M+H]^+$ 408.1405, found 408.1423.

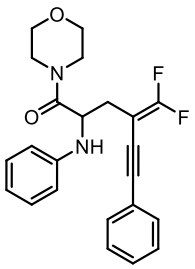


Cyclohexyl 4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (5q).
colorless oil (78%, 66.0 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.43 (m, 2H), 7.35 – 7.33 (m, 3H), 7.18 (t, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 2H), 4.39 – 4.32 (m, 2H), 4.16 (t, *J* = 8.4 Hz, 2H), 2.71 – 2.68 (m, 2H), 1.66 – 1.64 (m, 4H), 1.50 (q, *J* = 6.8 Hz, 2H), 1.29 – 1.22 (m, 2H), 1.20 – 1.15 (m, 2H), 0.93-0.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 159.6 (dd, *J* = 295.6, 292.5 Hz), 146.4, 131.6, 129.5, 128.8, 128.5, 122.7, 118.7, 113.8, 94.5 (t, *J* = 5.6 Hz), 80.4 (dd, *J* = 7.7, 4.2 Hz), 75.3 (dd, *J* = 34.1, 17.7 Hz), 64.0, 55.5, 36.0, 34.5, 33.2, 31.0, 26.6, 26.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.19 (d, *J* = 10.9 Hz), -83.10 (d, *J* = 10.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3347, 3057, 2958, 1745, 1511, 1276, 1033, 916 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{28}F_2NO_2$ $[M+H]^+$ 424.2082, found 424.2083.



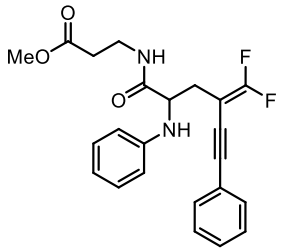
***N*-cyclohexyl-4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynamide (5r).**

colorless oil (80%, 51.7 mg); R_f = 0.3 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 3H), 7.22 – 7.15 (m, 2H), 6.82 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 2H), 4.03 – 3.93 (m, 1H), 3.85 – 3.71 (m, 1H), 2.95 – 2.83 (m, 1H), 2.71 – 2.55 (m, 1H), 1.89 – 1.77 (m, 2H), 1.67 – 1.52 (m, 3H), 1.39 – 1.27 (m, 2H), 1.10 – 1.05 (m, 2H), 0.87 – 0.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 159.7 (dd, *J* = 296.6, 294.2 Hz), 146.5, 131.6, 129.5, 128.9, 128.5, 122.3, 119.6, 114.2, 95.1 (t, *J* = 5.7 Hz), 80.2 (dd, *J* = 7.6, 4.2 Hz), 75.5 (dd, *J* = 33.8, 17.1 Hz), 58.8, 48.2, 33.0, 32.9, 30.7, 25.5, 24.9, 24.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.50 (d, *J* = 8.5 Hz), -82.14 (d, *J* = 10.1 Hz); IR (neat): υ_{max} (cm^{-1}) 3697, 3394, 2958, 2208, 1725, 1601, 1277, 1055 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}F_2NO_2$ $[M+H]^+$ 324.1205, found 324.1197.

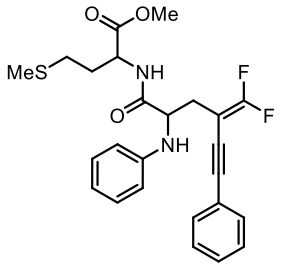


4-(difluoromethylene)-1-morpholino-6-phenyl-2-(phenylamino)hex-5-yn-1-one (5s).

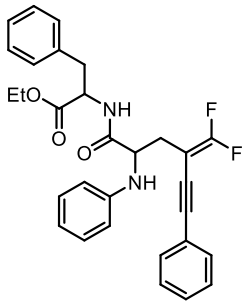
yellow solid (80%, 63.4 mg); m.p.: 141-142 °C; R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.38 – 7.36 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 2H), 4.67 (t, *J* = 6.4 Hz, 1H), 3.73 – 3.54 (m, 8H), 2.62 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 159.6 (dd, *J* = 296.2, 294.0 Hz), 146.5, 131.5, 129.6, 129.0, 128.7, 122.4, 118.8, 114.0, 94.5 (t, *J* = 5.5 Hz), 80.7 (dd, *J* = 7.8, 4.2 Hz), 75.3 (dd, *J* = 34.4, 17.1 Hz), 66.9, 66.7, 51.7, 46.3, 42.7, 31.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.72 (d, *J* = 9.8 Hz), -82.51 (d, *J* = 9.8 Hz); IR (neat): υ_{max} (cm^{-1}) 3387, 2983, 1735, 1603, 1234, 1140, 1043, 938 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{23}F_2N_2O_2$ $[M+H]^+$ 397.1722, found 397.1729.



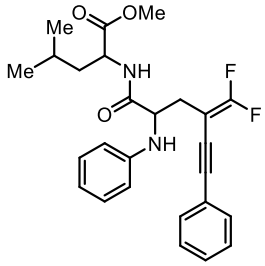
Methyl 3-(4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynamido)propanoate (5t). colorless oil (82%, 67.6 mg, d.r. = 1:1); m.p.: 111-112 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 5H), 7.18 (t, *J* = 8.4 Hz, 2H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 2H), 4.02 – 3.98 (m, 1H), 3.58 – 3.45 (m, 5H), 2.89 – 2.83 (m, 1H), 2.64 – 2.58 (m, 1H), 2.50 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 172.1, 159.7 (dd, *J* = 296.6, 293.8 Hz), 146.4, 131.6, 129.5, 128.9, 128.5, 122.3, 119.4, 113.9, 95.1 (t, *J* = 5.8 Hz), 80.0 (dd, *J* = 7.6, 4.3 Hz), 75.5 (dd, *J* = 33.8, 17.2 Hz), 58.4, 51.8, 34.9, 33.8, 30.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.45 (d, *J* = 10.5 Hz), -82.32 (d, *J* = 10.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3373, 2823, 1716, 1933, 1214, 1157, 1031, 856 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{23}F_2N_2O_3$ $[M+H]^+$ 413.1617, found 413.1606.



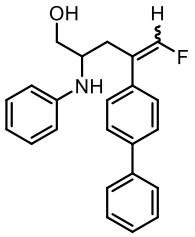
Methyl (4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoyl)methioninate (5u). yellow solid (62%, 58.5 mg, d.r. = 1:1); m.p.: 121-122 °C; R_f = 0.6 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 0.5H), 7.42 (d, *J* = 8.0 Hz, 0.5H), 7.34 – 7.30 (m 5H), 7.19 (t, *J* = 8.0 Hz, 2H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.65 (dd, *J* = 15.2, 8.0 Hz, 2H), 4.77 – 4.67 (m, 1H), 4.37 (s, 1H), 4.11 – 4.06 (m, 1H), 3.69 (s, 1H), 3.65 (s, 1H), 2.92 – 2.83 (m, 1H), 2.71 – 2.63 (m, 1H), 2.46 – 2.42 (m, 1H), 2.33 – 2.29 (m, 1H), 2.16 – 2.08 (m, 1H), 2.01 (s, 1.5H), 1.92 (s, 2.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 172.04, 172.02, 171.7, 159.6 (dd, *J* = 296.1, 293.6 Hz), 146.3, 146.3, 131.5, 129.4, 129.4, 128.8, 128.8, 128.4, 128.4, 122.1, 119.5, 114.2, 113.8, 95.0 (t, *J* = 5.4 Hz), 80.0 (dd, *J* = 9.9, 4.2 Hz), 79.9 (dd, *J* = 9.9, 4.2 Hz), 75.3 (dd, *J* = 33.9, 17.6 Hz), 75.3 (dd, *J* = 33.9, 17.6 Hz), 58.4 (t, *J* = 2.2 Hz), 58.3 (t, *J* = 2.2 Hz), 52.5, 52.4, 51.6, 51.2, 31.2, 31.2, 30.5, 30.4, 30.0, 29.7, 15.4, 15.2; ^{19}F NMR (376 MHz,) δ -76.54 (dd, *J* = 19.6, 9.8 Hz), -82.29 (dd, *J* = 26.3, 9.4 Hz); IR (neat): υ_{max} (cm^{-1}) 3358, 2983, 2831, 1716, 1602, 1497, 1190, 1023, 807cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{27}F_2N_2O_3$ $[M+H]^+$ 473.1705, found 473.1682.



Ethyl (4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoyl)phenylalaninate (5v).
white solid (75%, 75.3 mg, d.r. = 1:1); m.p.: 105-106 ºC; R_f = 0.5 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 5H), 7.21 – 7.12 (m, 4H), 7.07 (t, *J* = 7.6 Hz, 2H), 6.88 – 6.82 (m, 3H), 6.56 (d, *J* = 8.0 Hz, 2H), 4.94 – 4.89 (m, 1H), 4.13 (q, *J* = 14.4, 7.2 Hz, 2H), 4.00 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.02 (dd, *J* = 29.6, 13.6 Hz, 2H), 2.90 – 2.85 (m, 1H), 2.60 – 2.54 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 171.3, 159.7 (dd, *J* = 298.2.0, 293.3 Hz), 146.5, 135.5, 131.6, 129.6, 129.4, 128.9, 128.6, 128.5, 127.1, 122.3, 119.6, 114.0, 95.2 (t, *J* = 4.9 Hz), 79.9 (dd, *J* = 14.9, 7.1 Hz), 75.5 (dd, *J* = 34.3, 17.9 Hz), 61.7, 58.5, 52.7, 38.1, 30.8, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.26 (d, *J* = 10.5 Hz), -82.19 (d, *J* = 10.5 Hz); IR (neat): υ_{max} (cm^{-1}) 3381, 2934, 2861, 1719, 1603, 1371, 1253, 1142, 1026, 862 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{29}F_2N_2O_3$ $[M+H]^+$ 503.2140, found 503.2129.

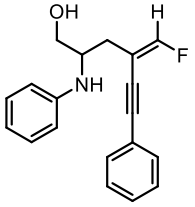


Methyl (4-(difluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoyl)leucinate (5w).
White solid (71%, 64.5 mg, d.r. = 1:1); m.p.: 80-81ºC; R_f = 0.3 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.32 (m, 4H), 7.23 – 7.17 (m, 3H), 6.83 (dd, *J* = 12.8, 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.67 – 4.61 (m, 1H), 4.07 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.69 (s, 1.5H), 3.65 (s, 1.5H), 2.93 – 2.84 (m, 1H), 2.70 – 2.62 (m, 1H), 1.65 – 1.55 (m, 1.5H), 1.50 – 1.41 (m, 1.5H), 0.90 (d, *J* = 6.0 Hz, 2H), 0.88 (d, *J* = 6.4 Hz, 2H), 0.81 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 172.8, 172.1, 172.0, 159.7 (t, *J* = 295.3 Hz), 146.5, 146.4, 132.1, 132.0, 131.6, 129.4, 128.9, 128.8, 128.5, 128.4, 122.2, 119.7, 119.6, 114.5, 114.0, 95.1 (t, *J* = 5.5 Hz), 80.1 (dd, *J* = 11.6, 7.5 Hz), 75.4 (dd, *J* = 33.8, 17.4 Hz), 75.3 (dd, *J* = 33.8, 17.4Hz), 75.1, 58.8, 58.5, 57.8, 52.4, 52.3, 50.8, 50.5, 41.3, 41.1, 30.6, 30.5, 25.0, 24.8, 22.9, 21.7, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.78 (dd, *J* = 23.5, 8.0 Hz), -71.23 (dd, *J* = 15.2, 8.0 Hz), -76.24 (dd, *J* = 23.5, 10.3 Hz), -81.99 (dd, *J* = 40.9, 10.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3641, 2821, 2349, 1785, 1711, 1581, 1271, 1049, 917 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{29}F_2N_2O_3$ $[M+H]^+$ 455.2141, found 455.2147.



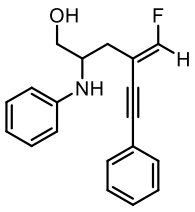
4-([1,1'-biphenyl]-4-yl)-5-fluoro-2-(phenylamino)pent-4-en-1-ol (6a).

colorless oil (87%, 60.4 mg, *Z/E* = 1:1); R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 4H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 2H), 6.90 (d, *J* = 85.4 Hz, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 2H), 3.75 – 3.71 (m, 1H), 3.60 – 3.58 (m, 2H), 2.94 – 2.91 (m, 1H), 2.83 – 2.78 (m, 1H), 2.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 147.3, 146.1, 140.7 (d, *J* = 40.0 Hz), 134.8 (d, *J* = 9.0 Hz), 129.4, 129.0, 127.6, 127.4 (d, *J* = 3.0 Hz), 127.1, 121.8 (d, *J* = 9.0 Hz), 118.2, 114.0, 64.1, 53.7, 29.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -128.19 (d, *J* = 85.4 Hz); IR (neat): υ_{max} (cm^{-1}) 3360, 2982, 1716, 1497, 1478, 1280, 1190, 1023 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{23}FNO$ $[M+H]^+$ 348.1758, found 348.1746.



(Z)-4-(fluoromethylene)-6-phenyl-2-(phenylamino)hex-5-yn-1-ol (7a).

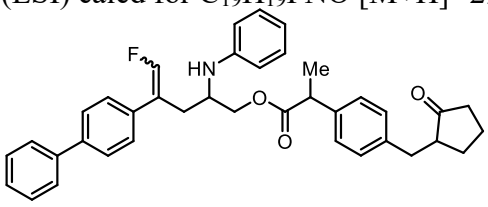
colorless oil (40%, 23.6 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46– 7.43 (m, *2*H), 7.37 – 7.35 (m, 3H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 83.6 Hz, 1H), 6.79 – 6.74 (m, 3H), 3.85 (d, *J* = 9.2 Hz, 2H), 3.72– 3.67 (m, 1H), 2.65 – 2.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2 (d, *J* = 270.1 Hz), 147.2, 131.5, 129.5, 128.5, 122.7, 118.1, 113.9, 106.1 (d, *J* = 19.4 Hz), 91.6 (d, *J* = 9.5 Hz), 84.3 (d, *J* = 15.1 Hz), 63.8, 53.6, 29.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.00 (d, *J* = 292.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3740, 2983, 2821, 2264, 1964, 1756, 1194, 1055, 1003 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}FNO$ $[M+H]^+$ 296.1445, found 296.1453.



(E)-4-(Fluoromethylene)-6-phenyl-2-(phenylamino)hex-5-yn-1-ol (7a').

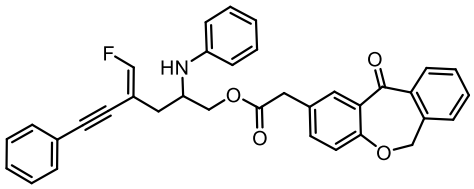
colorless oil (41%, 24.2 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 2H), 7.36 (s, 3H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.04 (d, *J* = 116.8 Hz, 1H), 6.79 – 6.67 (m, 3H), 3.85 (s, 2H), 3.78 – 3.65 (m, 1H), 2.45 – 2.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8 (d, *J* = 271.1 Hz), 147.0, 129.6,

128.9, 128.5, 122.7, 118.3, 114.0, 103.9 (d, J = 5.2 Hz), 96.9 (d, J = 7.9 Hz), 82.3 (d, J = 2.7 Hz), 63.2, 53.5, 31.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.55 (d, J = 81.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3389, 2984, 1737, 1603, 1238, 1095, 1043, 939 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}FNO$ $[M+H]^+$ 296.1445, found 296.1455.



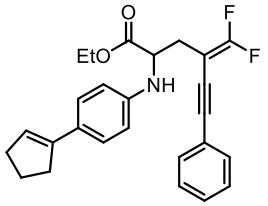
4-([1,1'-Biphenyl]-4-yl)-5-fluoro-2-(phenylamino)pent-4-en-1-yl-2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoate (8)

colorless oil (80%, 92.0 mg, Z/E = 1:1); R_f = 0.6 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.54 (m, 3H), 7.48 (t, J = 7.2 Hz, 2H), 7.41 – 7.37 (m, 1H), 7.28 – 7.22 (m, 5H), 7.16 – 7.09 (m, 5H), 6.97 (d, J = 9.2 Hz, 1H), 6.78 – 6.67 (m, 1H), 6.45 – 6.40 (m, 1H), 4.23 – 4.04 (m, 1H), 3.73 – 3.68 (m, 4H), 3.15 (dd, J = 14.0, 3.6 Hz, 1H), 2.82 – 2.72 (m, 1H), 2.56 – 2.48 (m,1H), 2.40 – 2.33 (m, 2H), 2.18 – 2.09 (m, 2H), 2.00 – 1.94 (m, 1H), 1.79 – 1.71 (m, 1H), 1.66 (s, 3H), 1.52 – 1.47 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 174.4, 148.7, 146.7, 146.1, 140.4, 139.0, 138.9, 138.4, 138.4, 134.5 (dd, J = 8.8, 2.7 Hz), 129.24, 129.16, 128.9, 127.6, 127.5, 127.5), 127.3, 127.0, 117.8, 113.4, 65.3, 62.7, 52.0, 51.0, 50.7, 45.1, 45.0, 38.2, 35.2, 29.3, 20.6, 18.6, 18.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -127.92 (d, J = 85.4 Hz), -127.96 (d, J = 84.6 Hz); IR (neat): υ_{max} (cm^{-1}) 3788, 2697, 2958, 2349, 1601, 1372, 1277, 1033, 860 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{39}FNO_3$ $[M+H]^+$ 576.2909, found 576.2906.



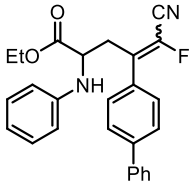
(*Z*)-4-(Fluoromethylene)-6-phenyl-2-(phenylamino)hex-5-yn-1-yl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetate (9)

colorless oil (92%, 100.3 mg); R_f = 0.6 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.59 – 7.43 (m, 4H), 7.42 – 7.34 (m, 3H), 7.33 – 7.30 (m, 2H), 7.18 – 7.12 (m, 2H), 7.00 – 6.91 (m, 2H), 6.73 – 6.66 (m, 3H), 5.16 (s, 2H), 4.40 (dd, J = 11.2, 4.8 Hz, 1H), 4.15 (dd, J = 11.2, 4.8 Hz, 1H), 4.05 – 3.99 (m, 1H), 3.65 (s, 2H), 2.60 – 2.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9, 171.4, 160.6, 155.7, 153.0, 146.8, 140.5, 136.4, 135.7, 132.9, 132.6, 131.6, 129.6, 129.5, 129.4, 128.7, 128.5, 127.9, 127.7, 125.2, 121.2, 118.0, 113.5, 105.7 (d, J = 19.2 Hz), 91.74 (d, J = 9.3 Hz), 84.01 (d, J = 14.9 Hz), 73.7, 65.7, 50.9, 40.2, 29.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.49 (d, J = 83.2 Hz); IR (neat): υ_{max} (cm^{-1}) 3376, 2983, 1716, 1496, 1208, 1189, 1026, 752 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{29}FNO_4$ $[M+H]^+$ 546.2075, found 546.2071.



Ethyl 2-((4-(cyclopent-1-en-1-yl)phenyl)amino)-4-(difluoromethylene)-6-phenylhex-5-ynoate (10)

colorless oil (51%, 42.9 mg); R_f = 0.5 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 5.2 Hz, 2H), 7.36 (s, 3H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.67 (d, *J* = 8.0 Hz, 2H), 6.01 (s, 1H), 4.40 (t, *J* = 6.0 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 2.73 – 2.67 (m, 2H), 2.52 (s, 1H), 2.07 – 1.94 (m, 1H), 1.28 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 159.60 (dd, *J* = 295.6 , 292.5 Hz), 145.0, 142.0, 131.5, 128.7, 128.4, 127.9, 126.7, 122.7, 122.5, 113.6, 94.3 (t, *J* = 5.4 Hz), 80.3 (dd, *J* = 6.5, 4.4 Hz), 75.3 (dd, *J* = 34.4, 19.3 Hz), 61.6, 55.4, 54.0, 33.2, 30.7, 23.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.21 (d, *J* = 10.9 Hz), -83.03 (d, *J* = 10.9 Hz); IR (neat): υ_{max} (cm^{-1}) 3373, 2883, 2823, 1719, 1633, 1434, 1277, 1031, 806 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{26}F_2NO_2$ $[M+H]^+$ 422.1926, found 422.1922.

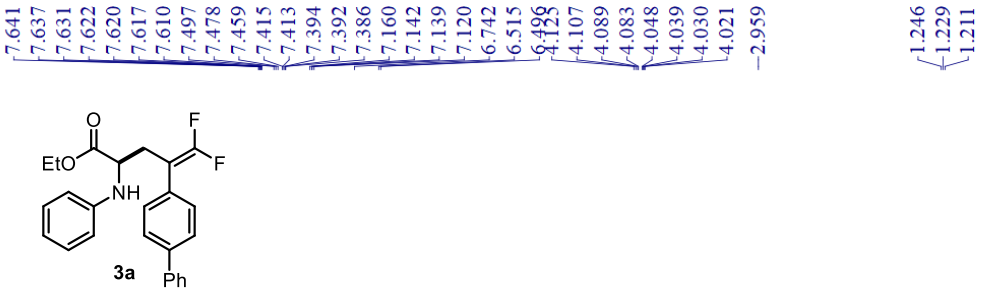


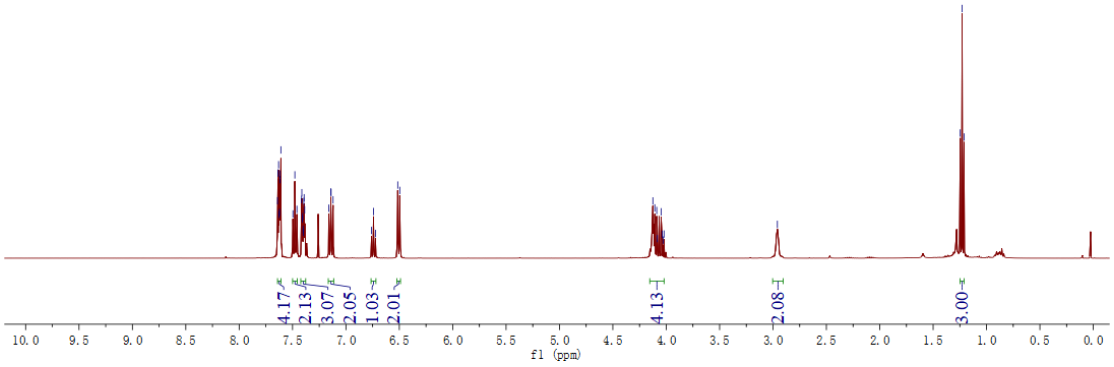
Ethyl 4-(cyanofluoromethylene)-6-phenyl-2-(phenylamino)hex-5-ynoate (11)

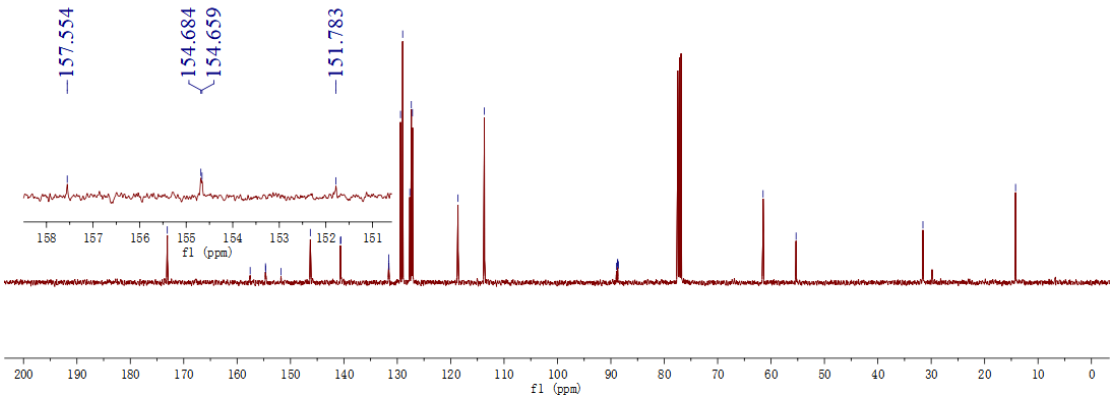
colorless oil (66%, 47.8 mg); R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 7.2 Hz, 2H), 7.51 – 7.40 (m, 5H), 7.14 (t, *J* = 8.0 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 2H), 4.19 – 4.05 (m, 4H), 3.18 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 145.8, 143.1, 134.0, 136.2 (d, *J* = 14.9 Hz), 132.4, 130.9, 13.0, 129.5, 129.1, 129.0, 128.1, 127.9, 127.2, 119.0, 113.8, 112.3 (d, *J* = 47.1 Hz), 61.9, 54.7, 33.5, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.62 (s); IR (neat): υ_{max} (cm^{-1}) 3360, 2982, 2941, 1716, 1497, 1372, 1118, 807 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{24}FN_2O_2$ $[M+H]^+$ 415.1816, found 415.1818.

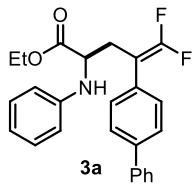
11. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra of Products 3 and 5 - 11

^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3a (Chloroform-d)

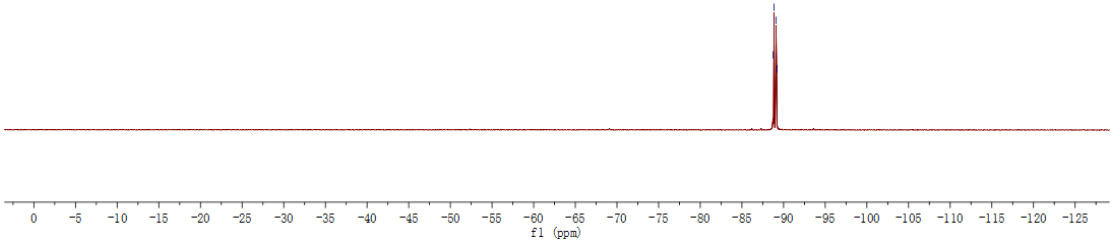




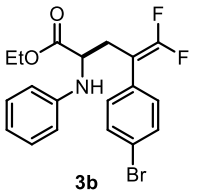




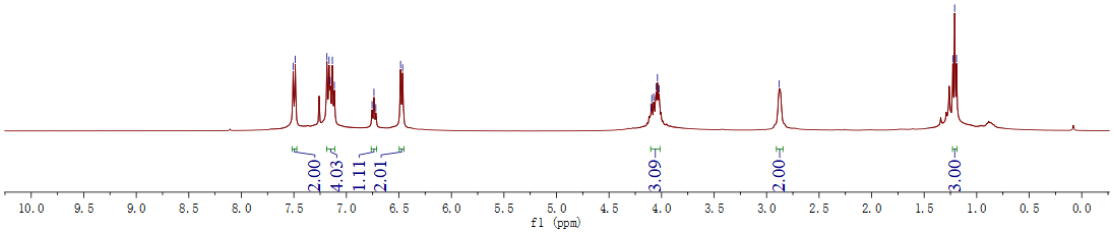
3a

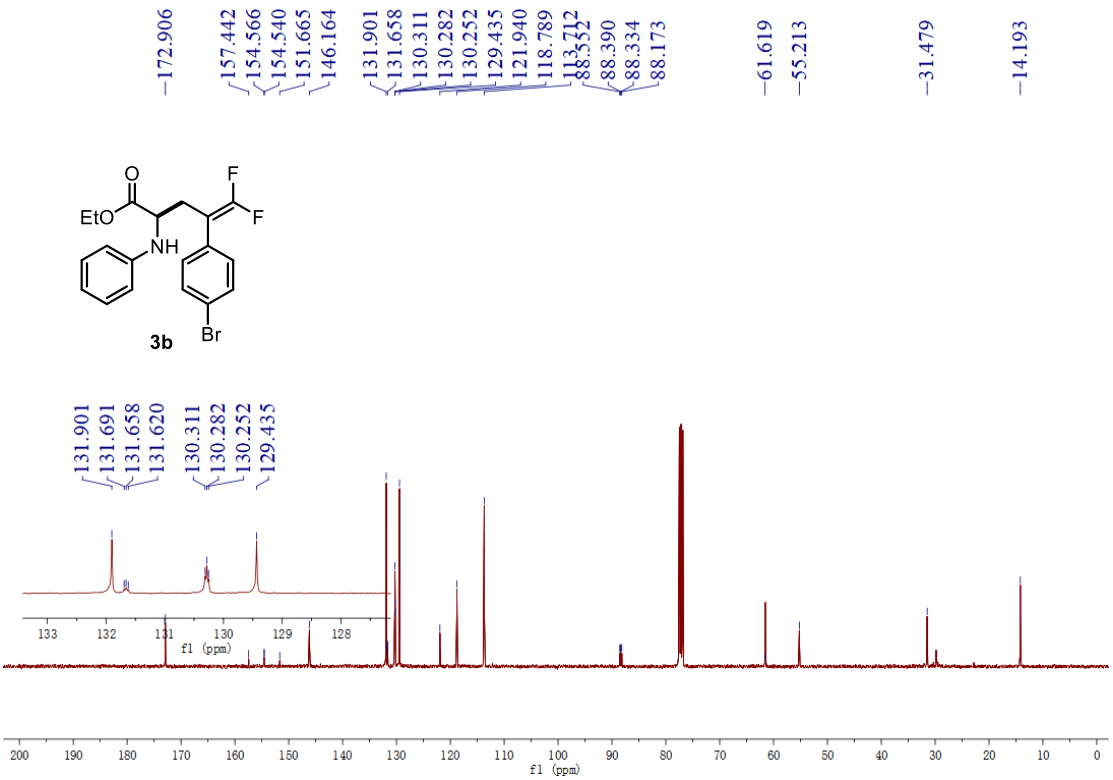


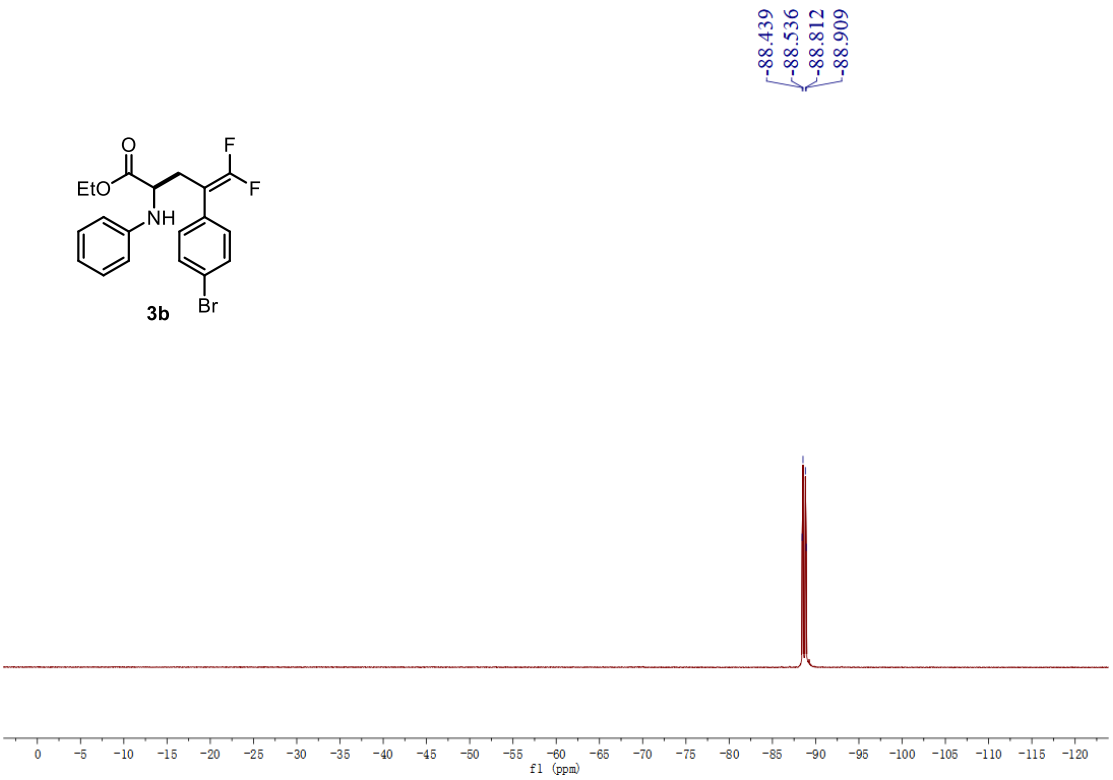
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3b (Chloroform-d)



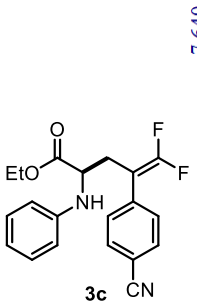
3b

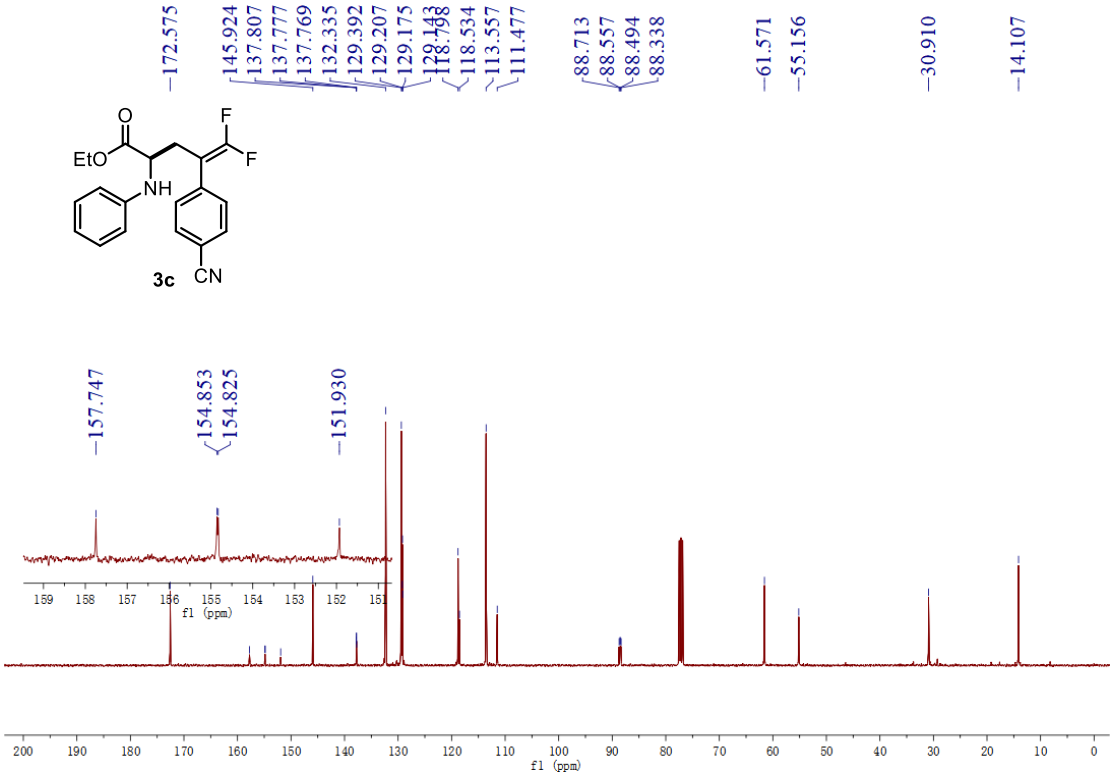


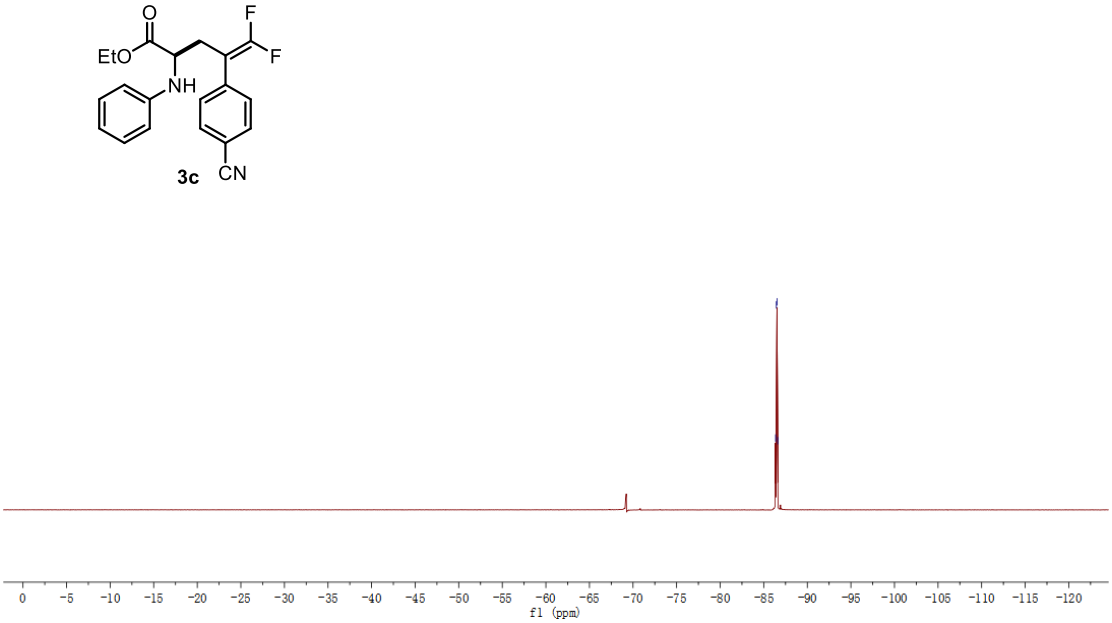

172.906
157.442
154.566
154.540
151.665
146.164
131.901
131.658
130.311
130.282
130.252
129.435
121.940
118.789
113.712
88.552
88.390
88.334
88.173
61.619
55.213
31.479
14.193
EtO
O
F
F
NH
Br
3b
131.901
131.691
131.658
131.620
130.311
130.282
130.252
129.435
f1 (ppm)


88.439
88.536
88.812
88.909
EtO
O
F
F
NH
Br
3b
f1 (ppm)

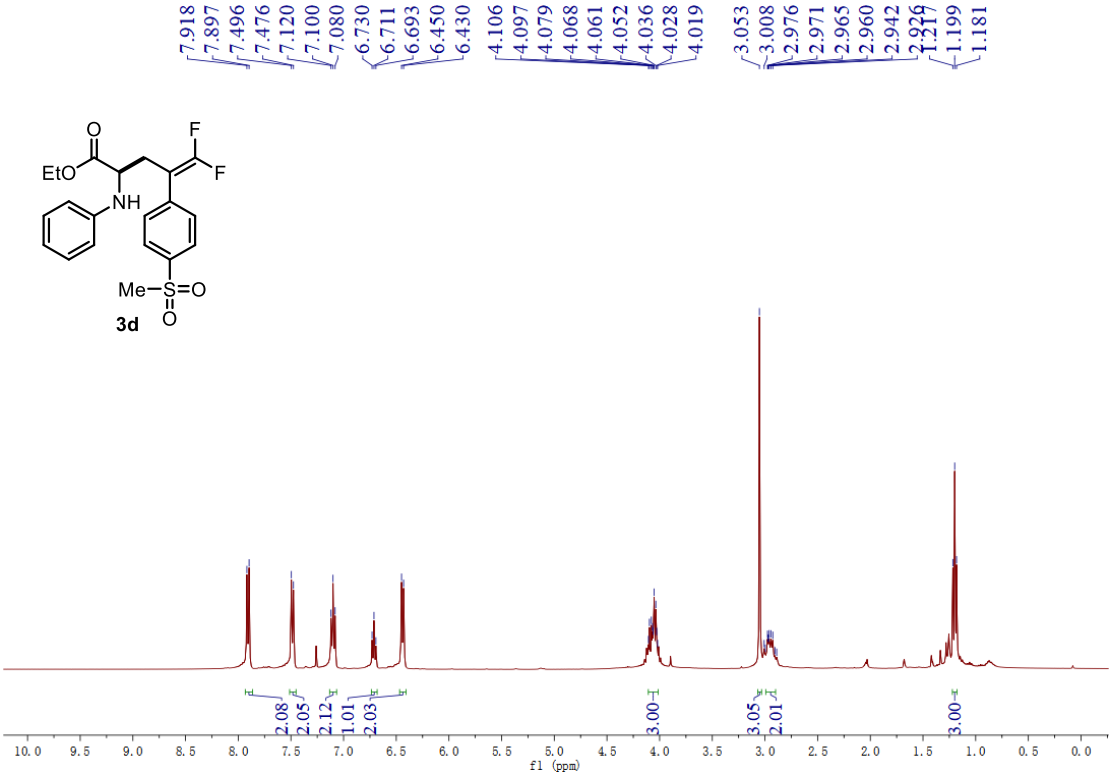
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3c (Chloroform-d)

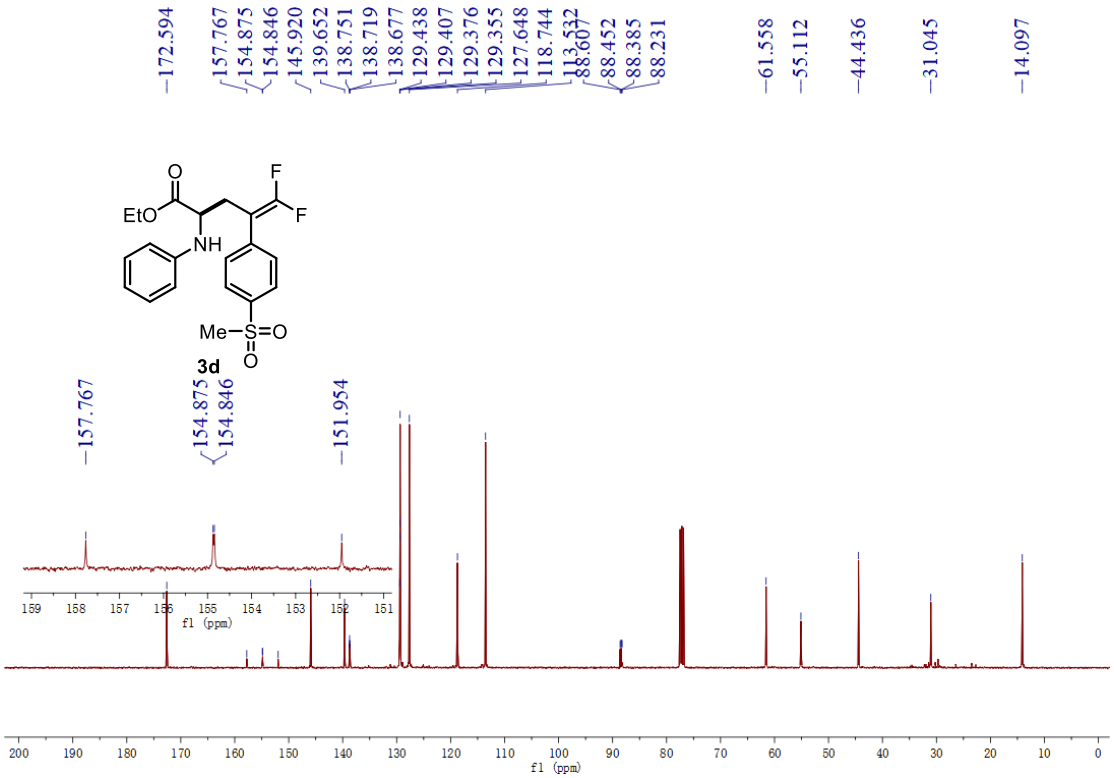






^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3d (Chloroform-d)

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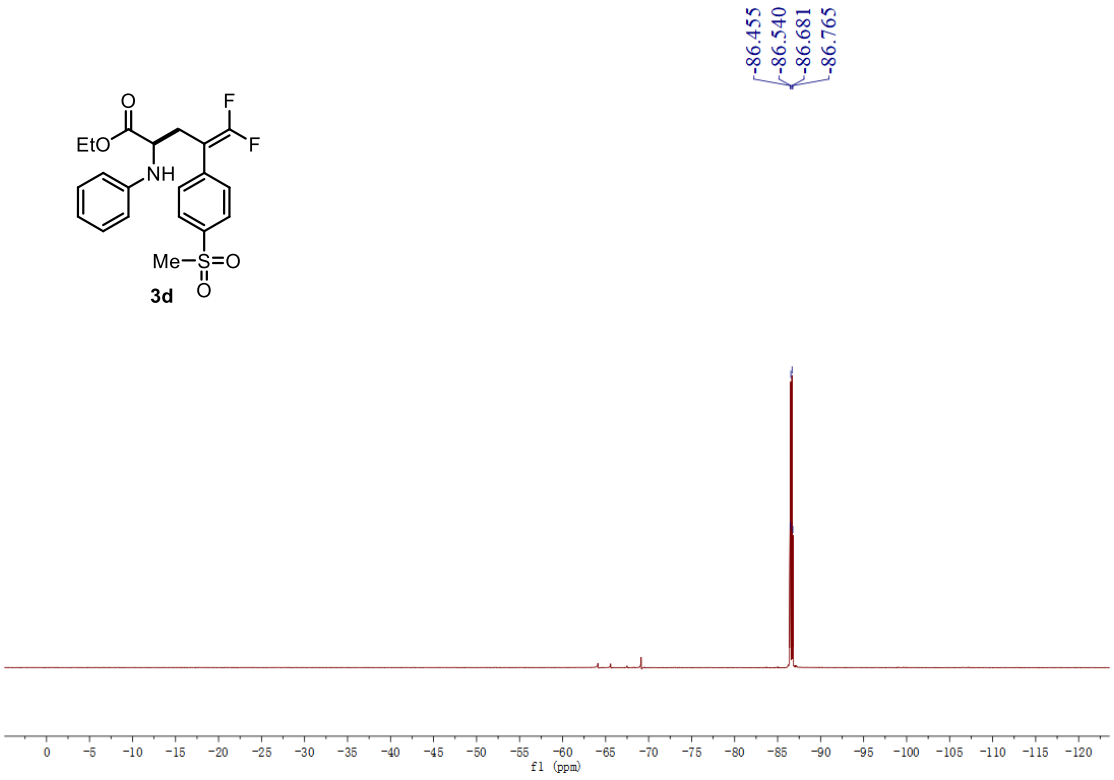
154.875
154.846
145.920
139.652
138.751
138.719
138.677
129.438
129.407
129.376
129.355
127.648
118.744
113.532
88.607
88.452
88.385
88.231
61.558
55.112
44.436
31.045
14.097
EtO
NH
F
F
Me—S=O
O
3d
157.767
154.875
154.846
151.954
f1 (ppm)


86.455
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86.765
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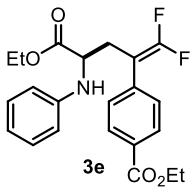
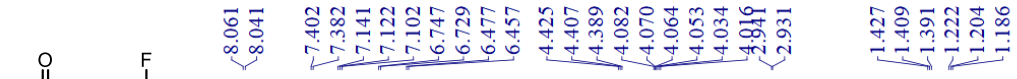
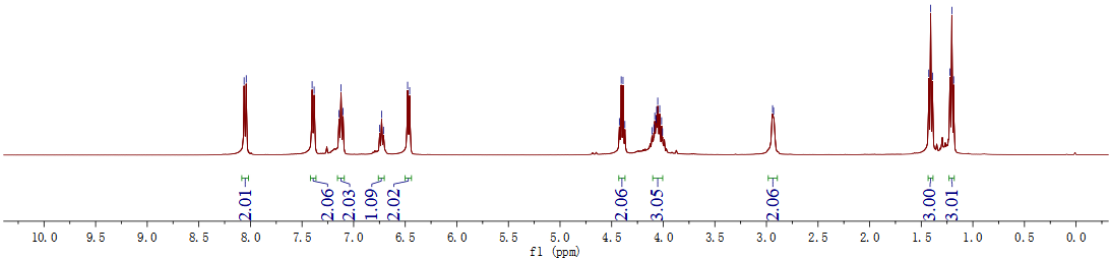
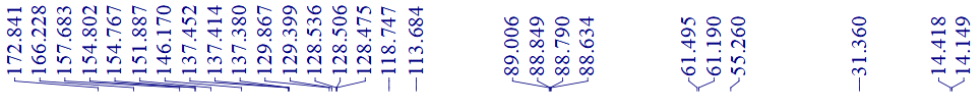
NH
F
F
Me—S=O
O
3d
f1 (ppm)

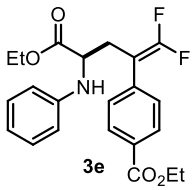
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3e (Chloroform-d)

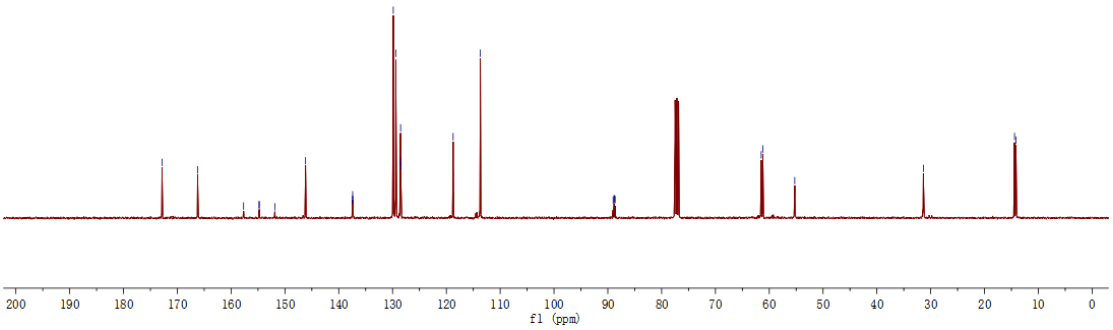


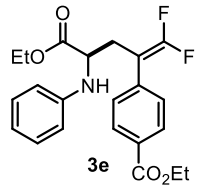


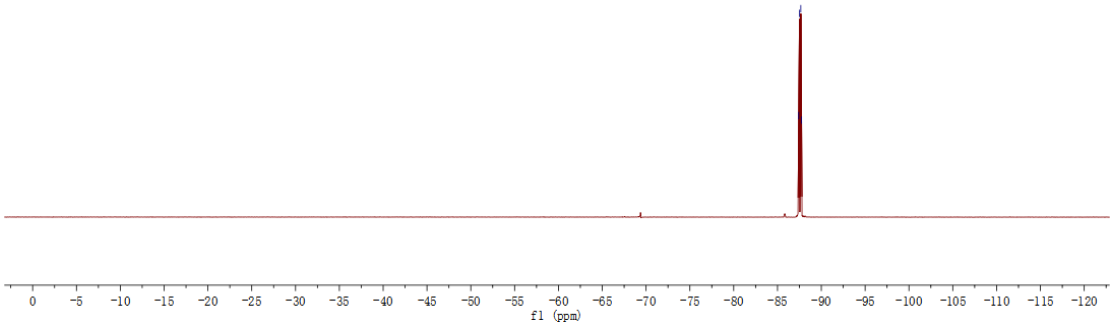




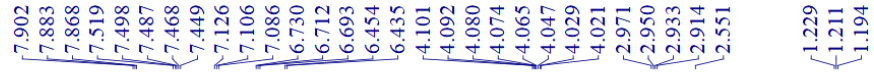


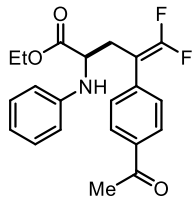


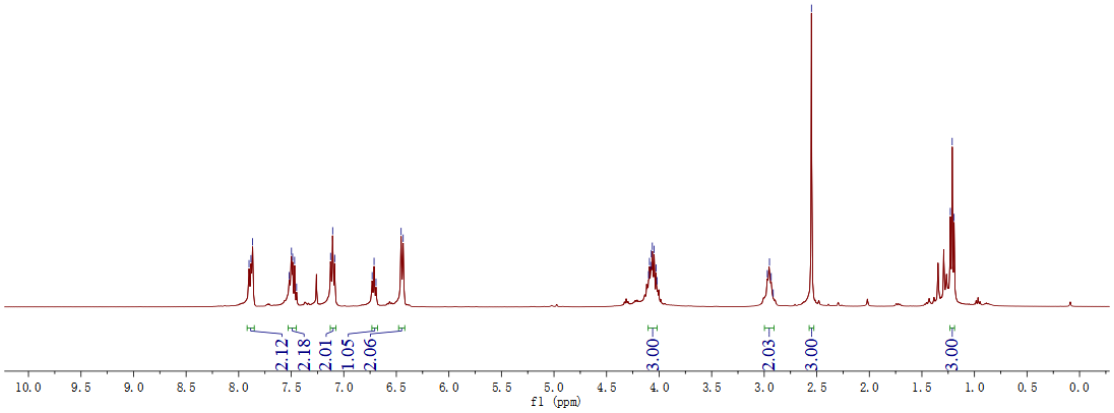


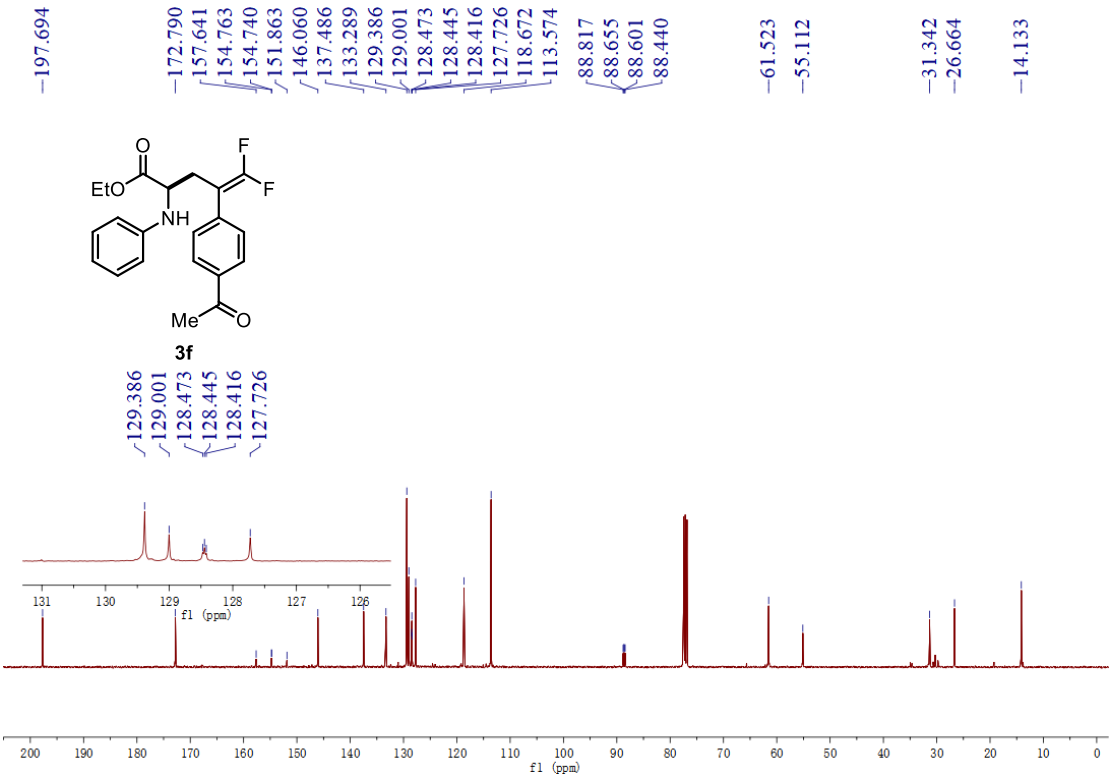


^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3f (Chloroform-d)





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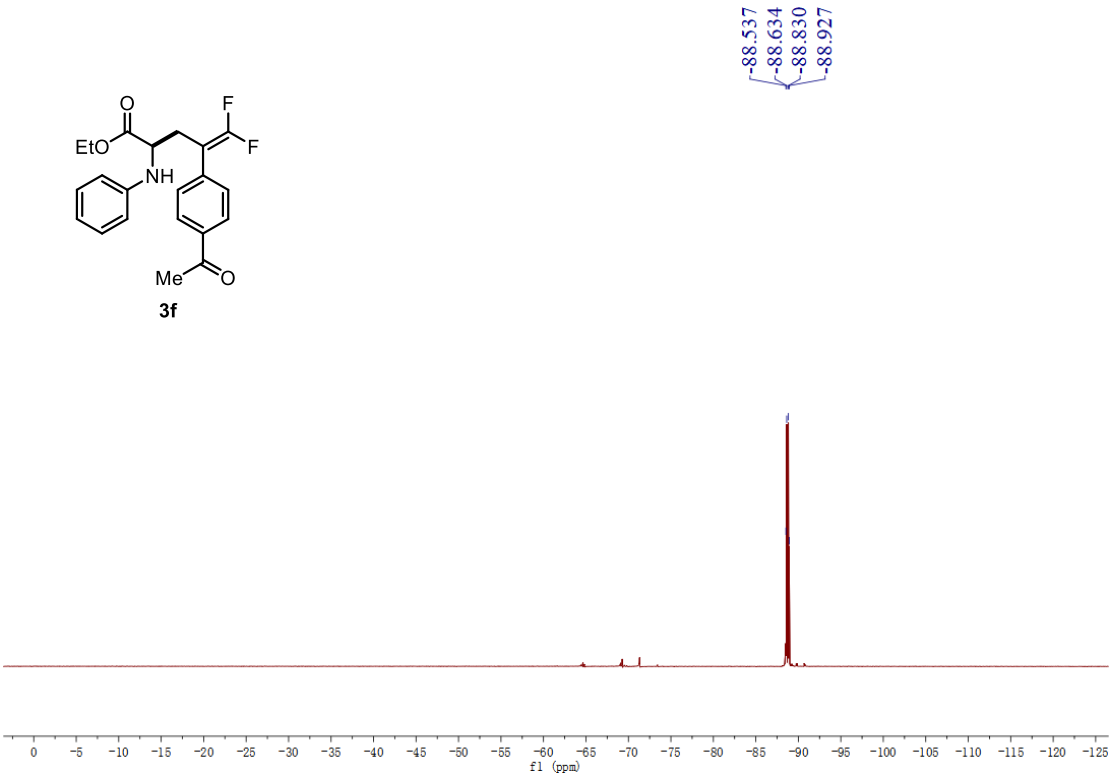
154.740
151.863
146.060
137.486
133.289
129.386
129.001
128.473
128.445
128.416
127.726
118.672
113.574
88.817
88.655
88.601
88.440
61.523
55.112
31.342
26.664
14.133
O
EtO
NH
F
F
Me
O
3f
129.386
129.001
128.473
128.445
128.416
127.726
131
130
129
128
127
126
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


88.537
88.634
88.830
88.927
O
EtO
NH
F
F
Me
O
3f
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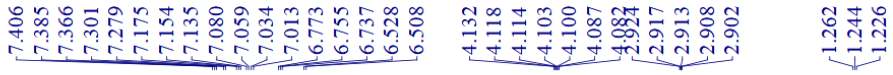
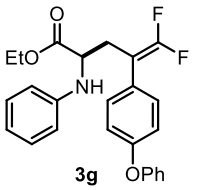
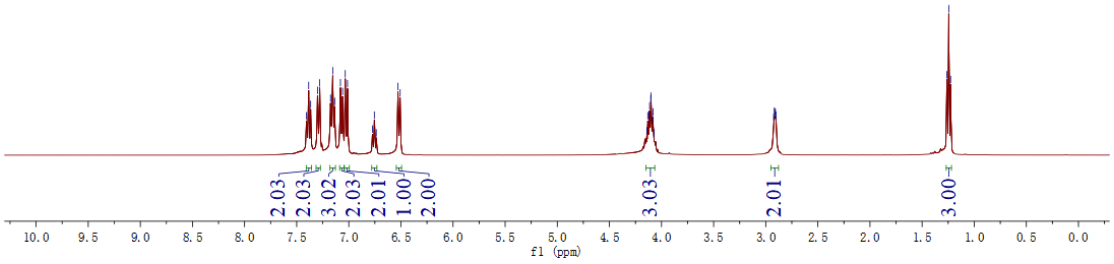
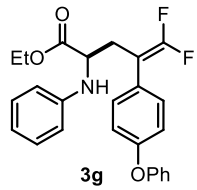
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
f1 (ppm)

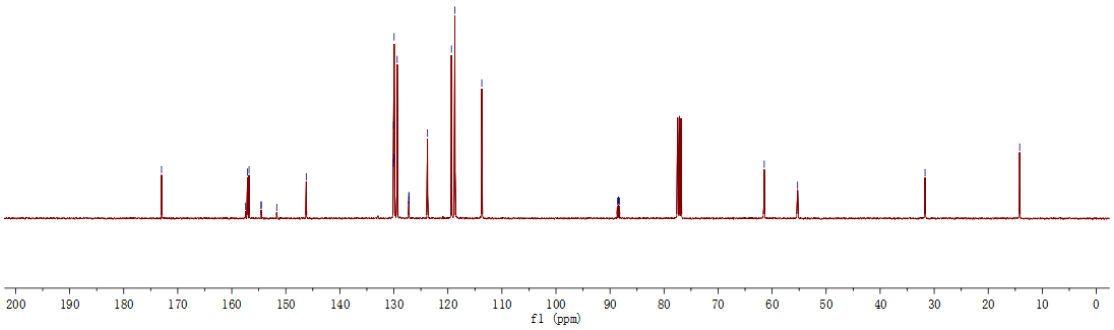
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3g (Chloroform-d)

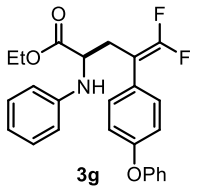




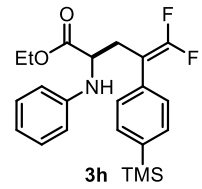


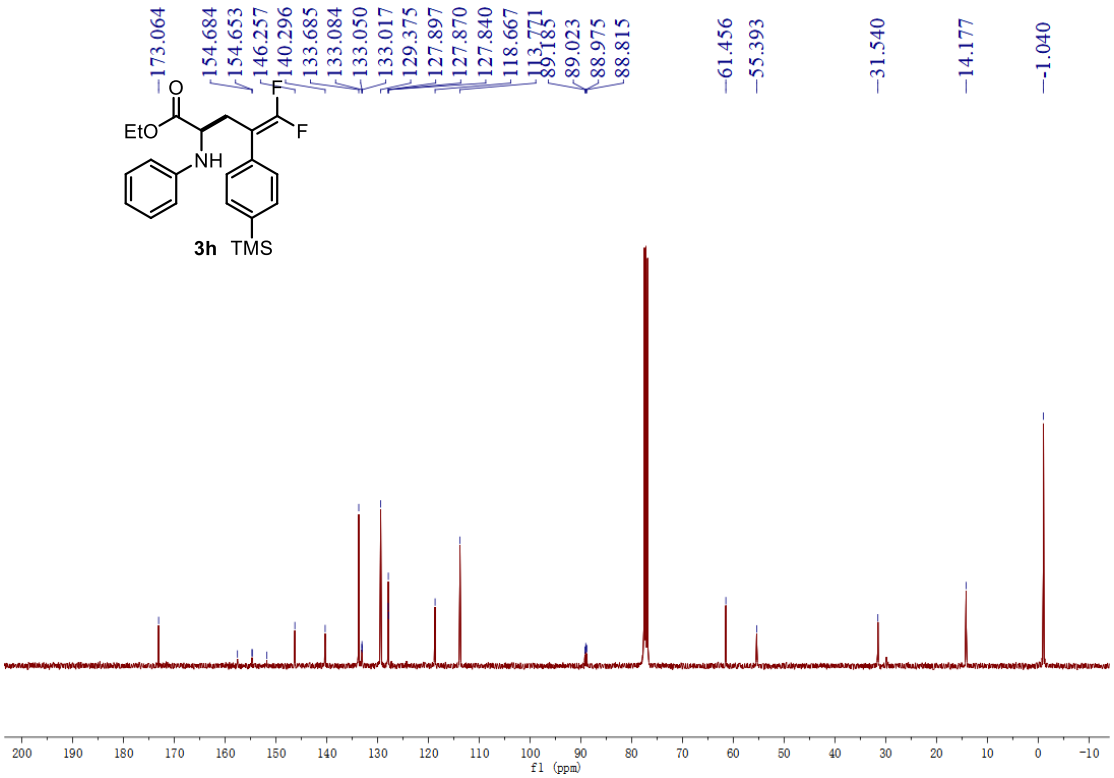


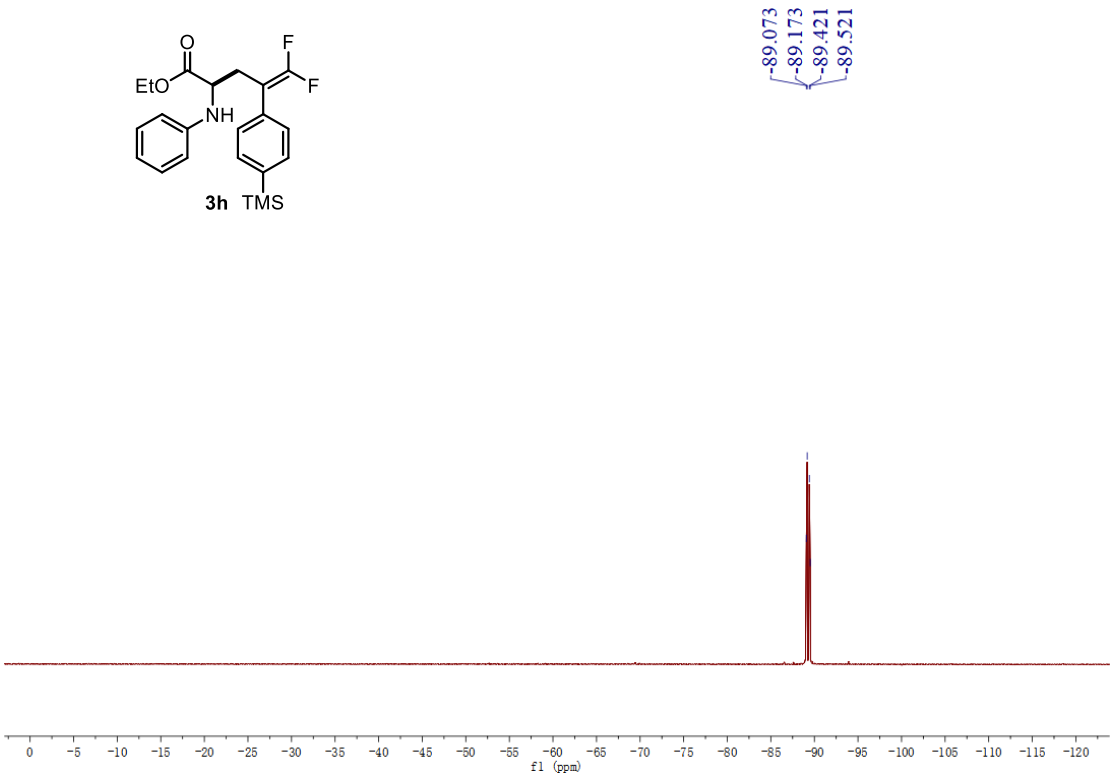




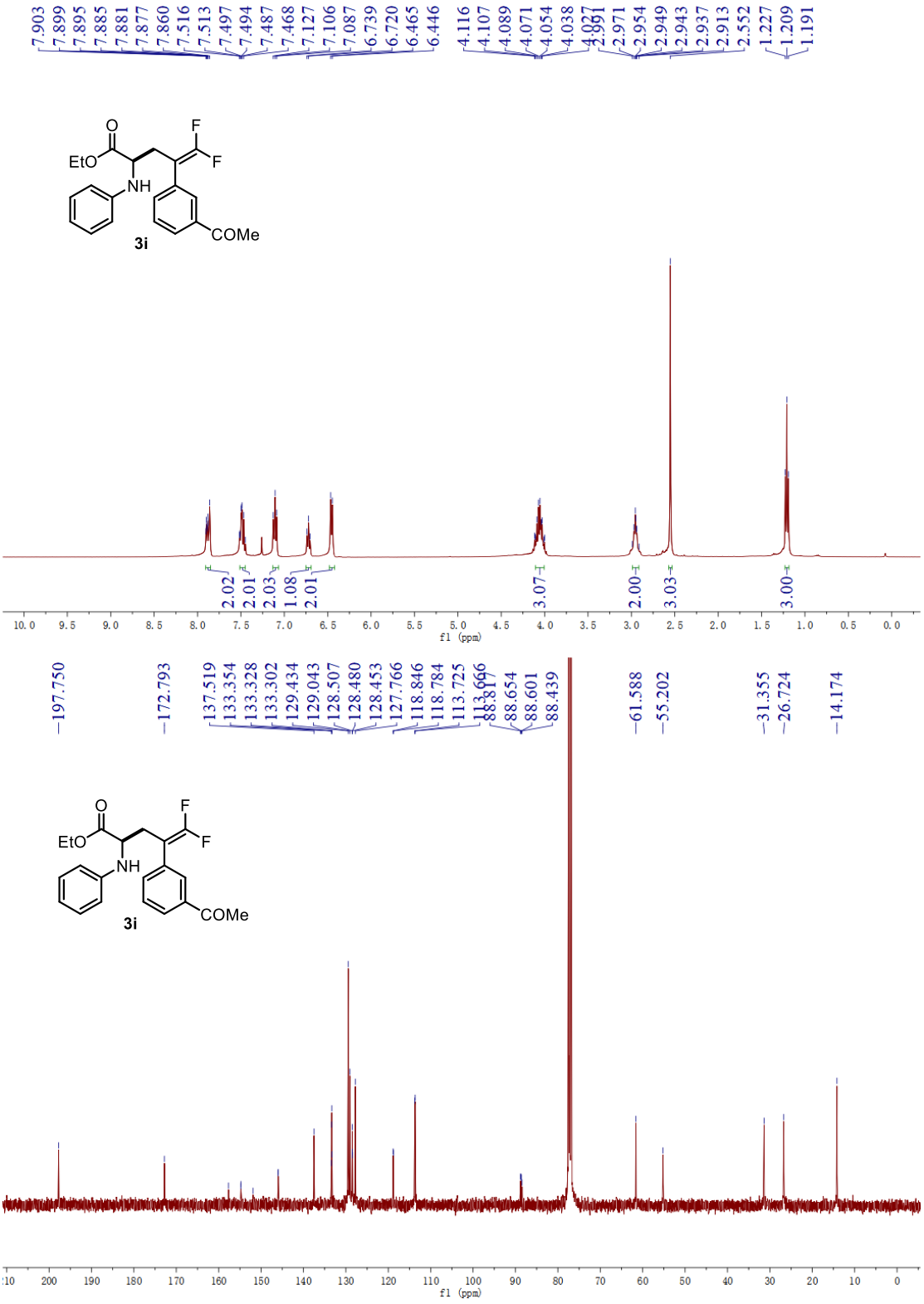
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3h (Chloroform-d)

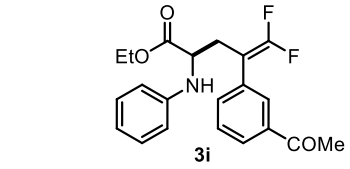



173.064
154.684
154.653
146.257
140.296
133.685
133.084
133.050
133.017
129.375
127.897
127.870
127.840
118.667
113.771
89.185
89.023
88.975
88.815
61.456
55.393
31.540
14.177
1.040
O
EtO
NH
F
F
3h TMS
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

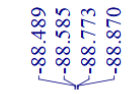

89.073
89.173
89.421
89.521
O
EtO
NH
F
F
3h TMS
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120
f1 (ppm)

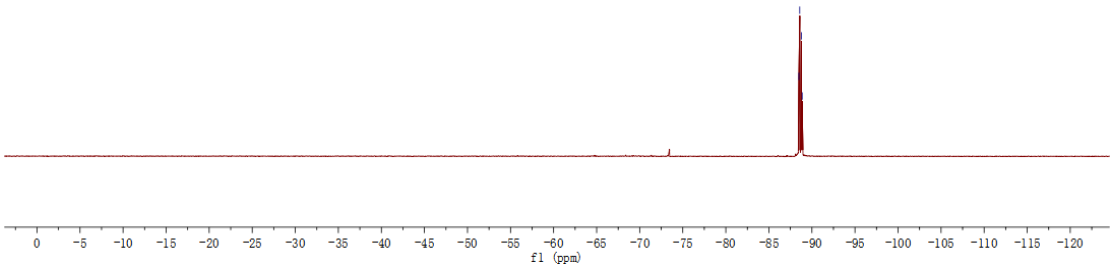
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3i (Chloroform-d)



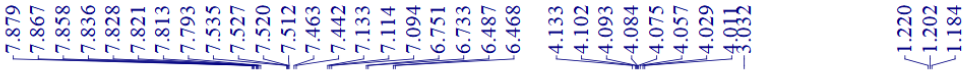


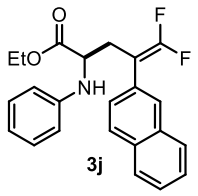
3i



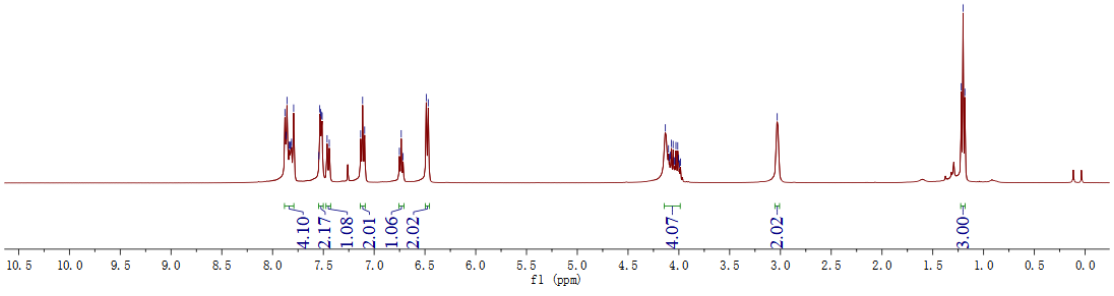


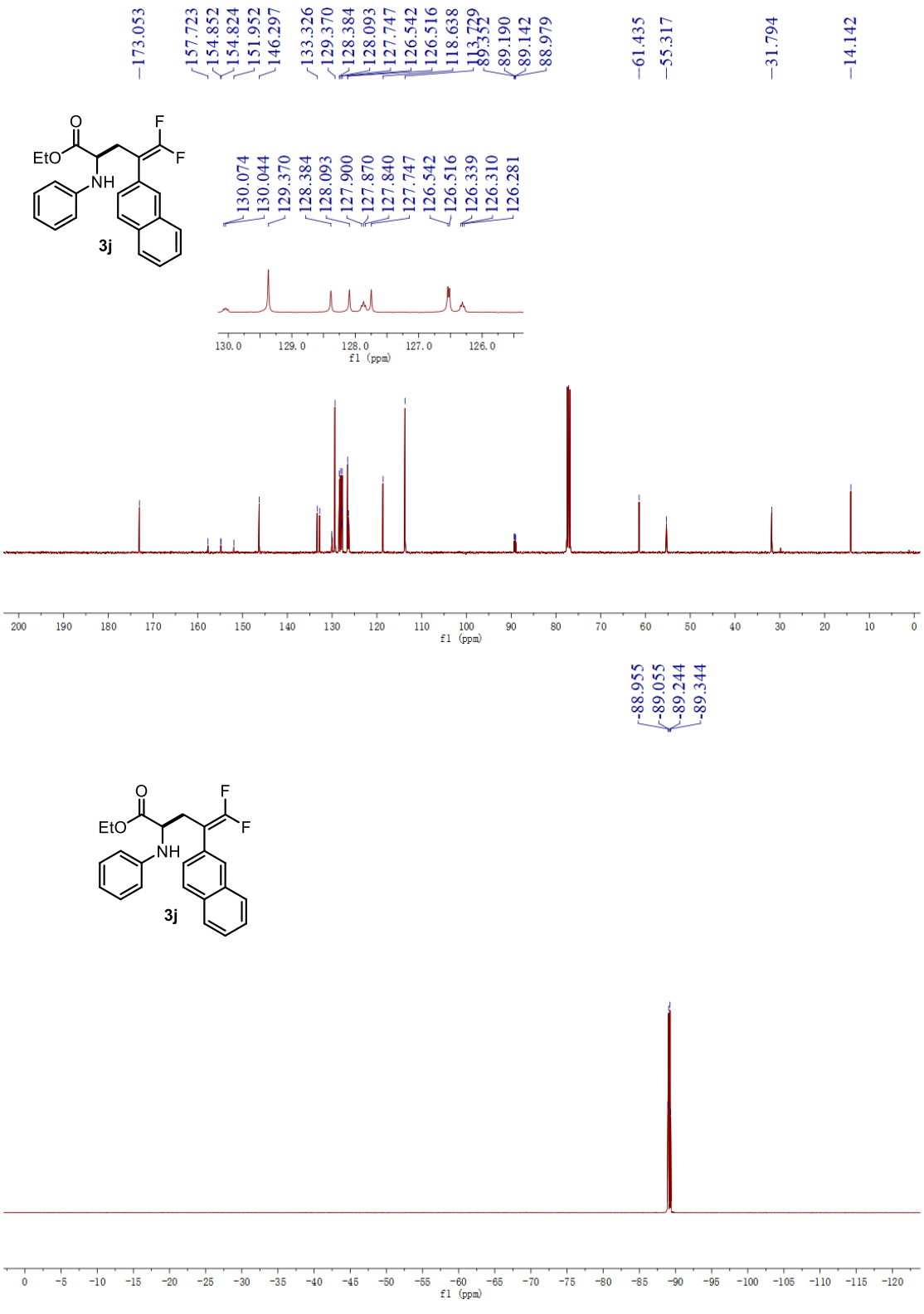
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3j (Chloroform-d)



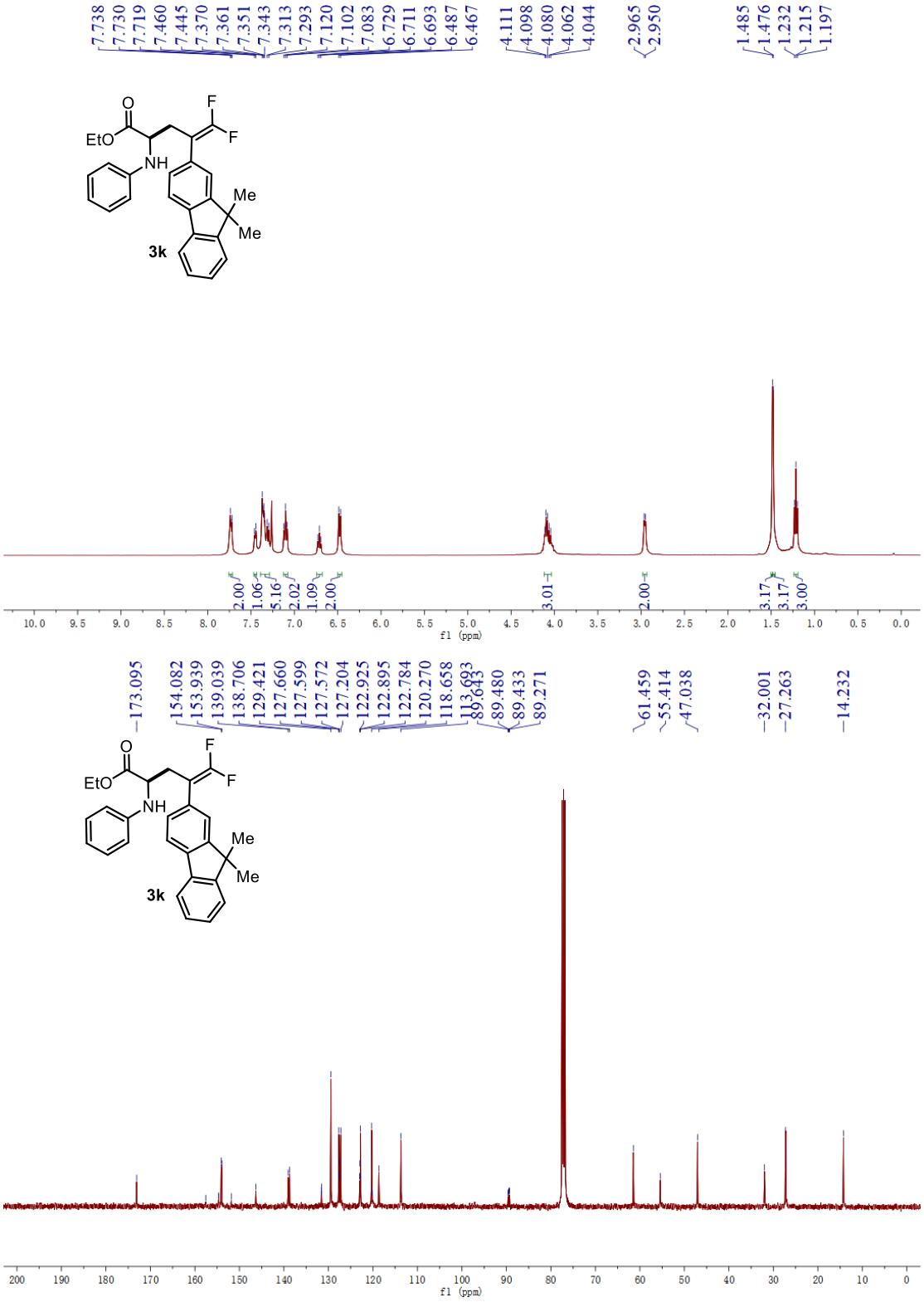


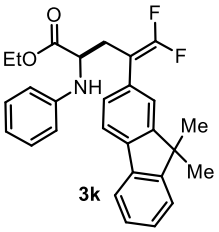
3j



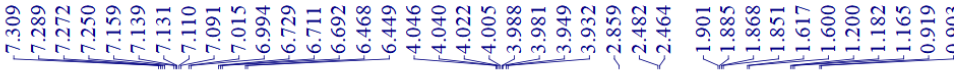

173.053
157.723
154.852
154.824
151.952
146.297
133.326
129.370
128.384
128.093
127.747
126.542
126.516
118.638
113.729
89.352
89.190
89.142
88.979
61.435
55.317
31.794
14.142
O
EtO
F
F
NH
3j
130.074
130.044
129.370
128.384
128.093
127.900
127.870
127.840
127.747
126.542
126.516
126.339
126.310
126.281
130.0
129.0
128.0
127.0
126.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
-88.955
-89.055
-89.244
-89.344
O
EtO
F
F
NH
3j
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
f1 (ppm)

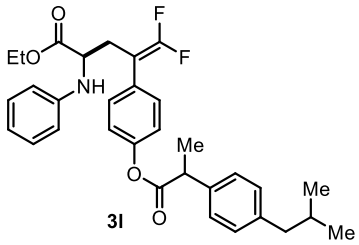
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3k (Chloroform-d)

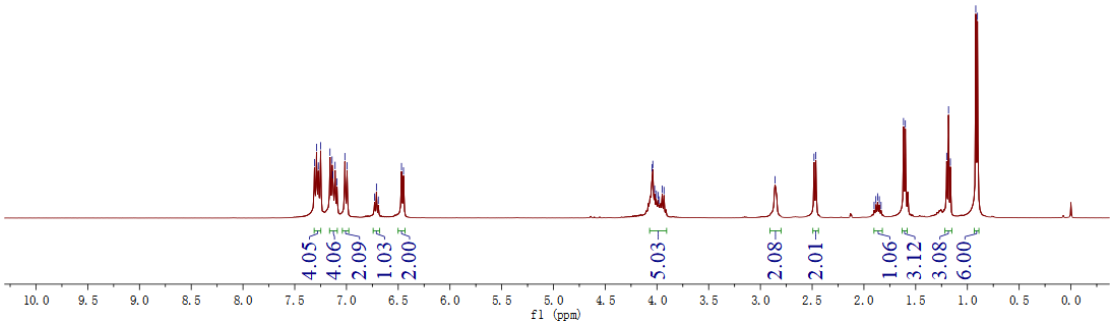


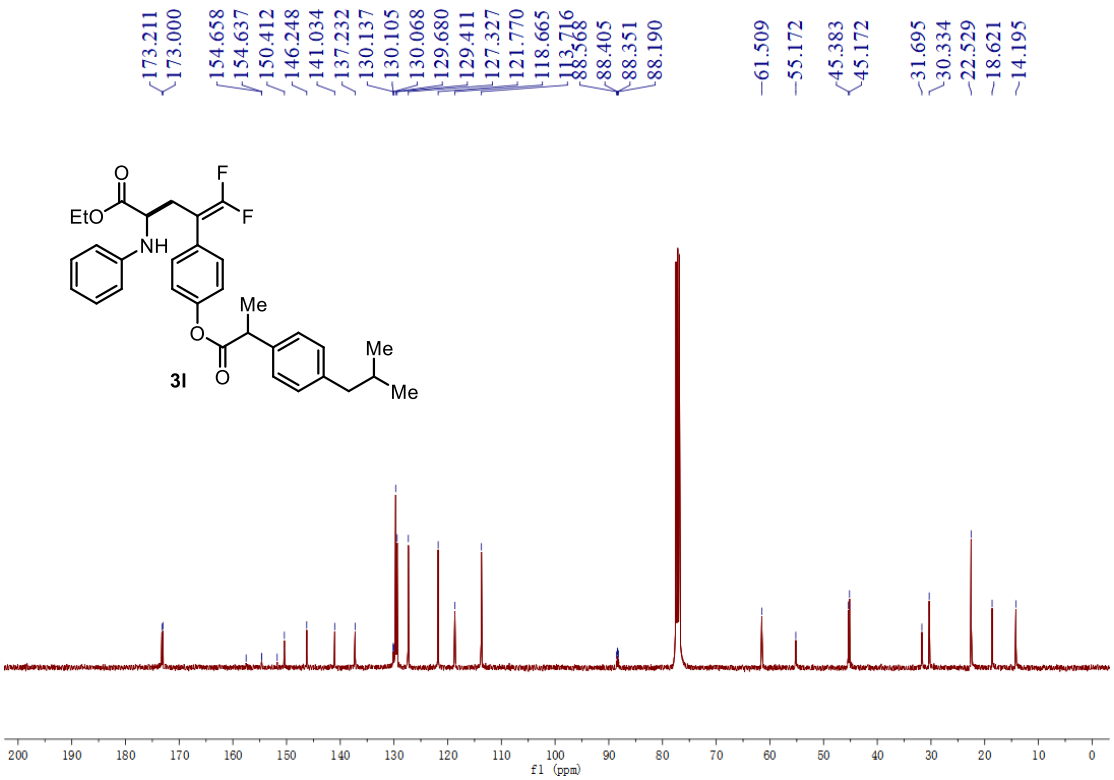


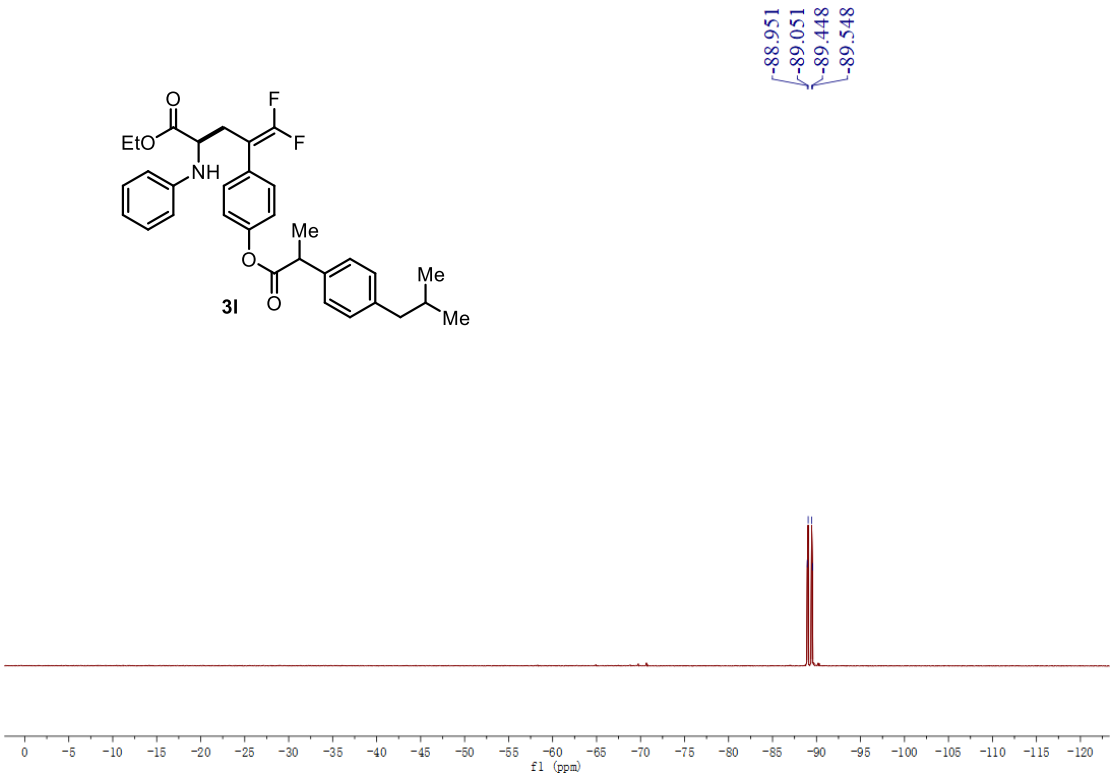
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3l (Chloroform-d)



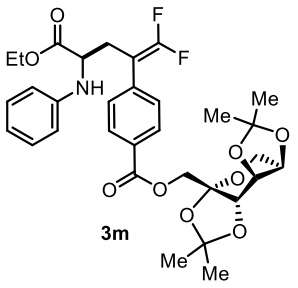




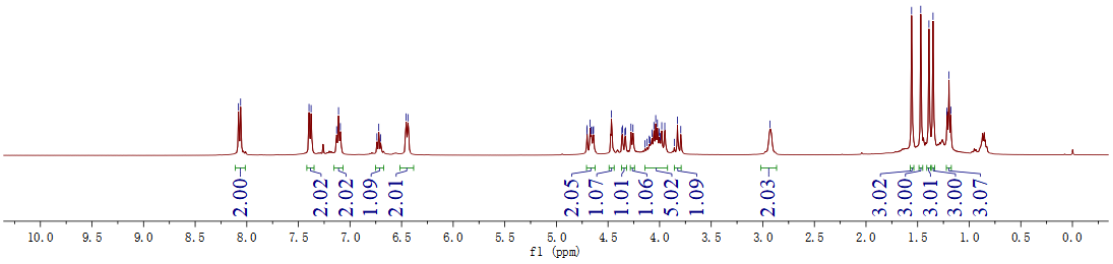

173.211
173.000
154.658
154.637
150.412
146.248
141.034
137.232
130.137
130.105
130.068
129.680
129.411
127.327
121.770
118.665
113.716
88.568
88.405
88.351
88.190
61.509
55.172
45.383
45.172
31.695
30.334
22.529
18.621
14.195
EtO
NH
F
F
O
Me
Me
Me
O
O
3l
f1 (ppm)

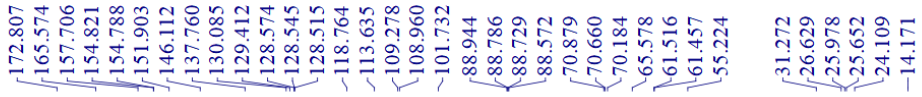

88.951
89.051
89.448
89.548
EtO
NH
F
F
O
Me
Me
Me
O
O
3l
f1 (ppm)

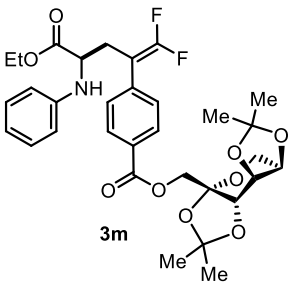
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3m (Chloroform-d)



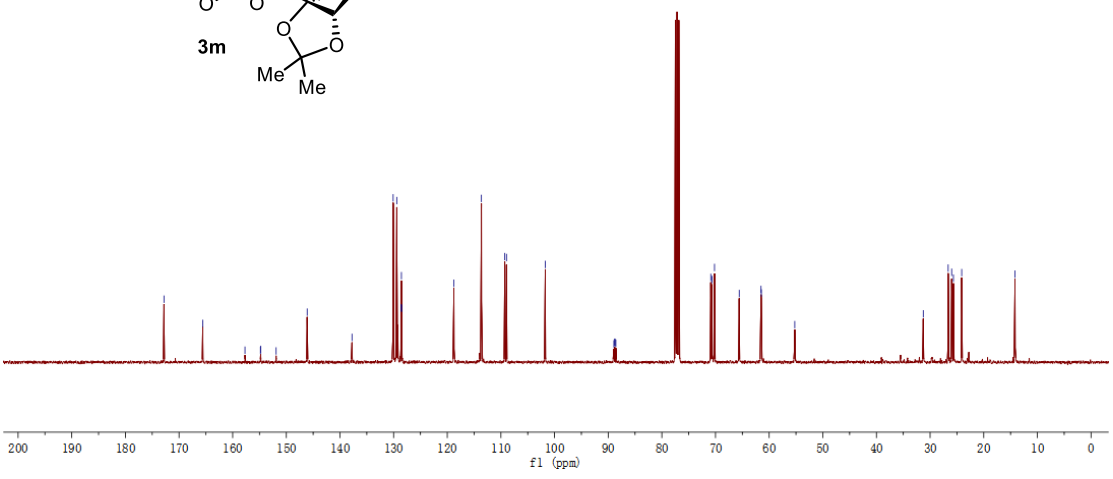
3m

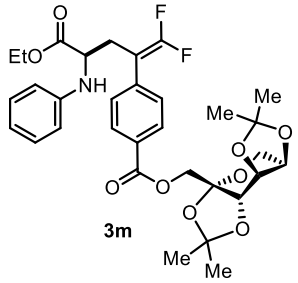




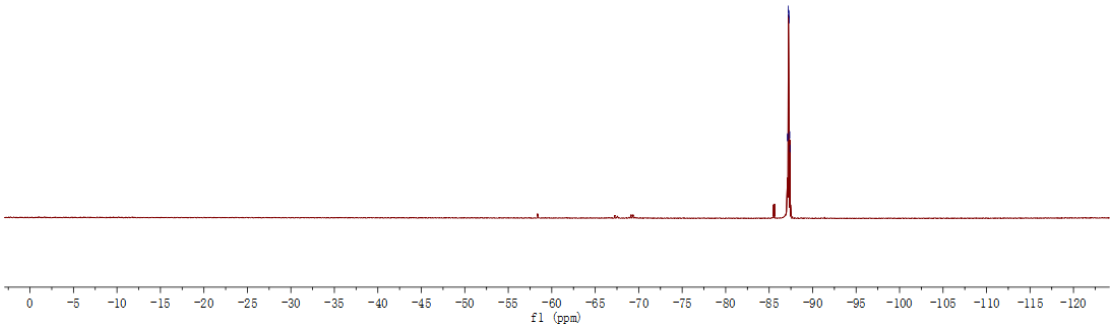


3m

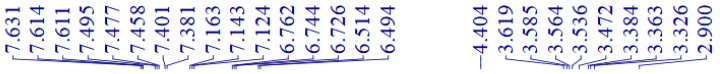


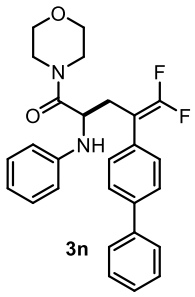


3m

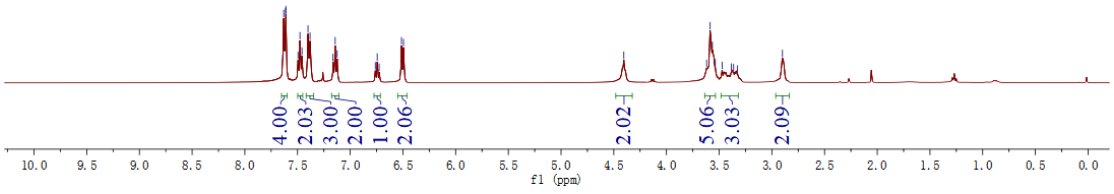


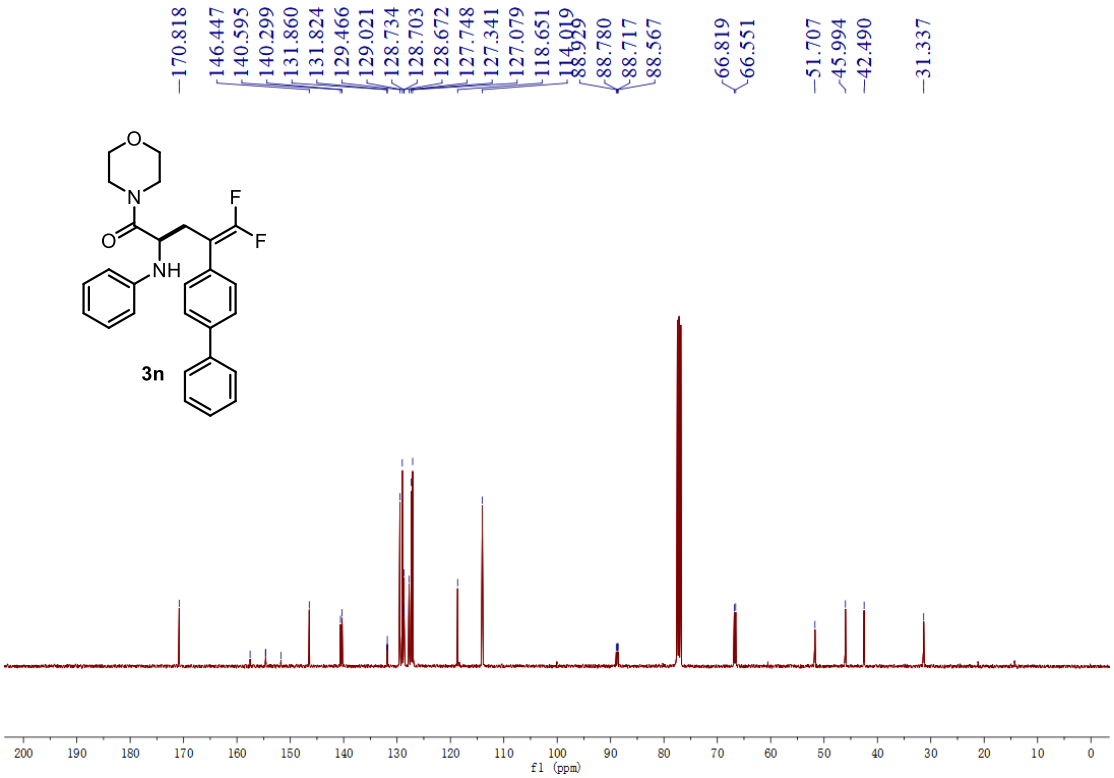
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3n (Chloroform-d)

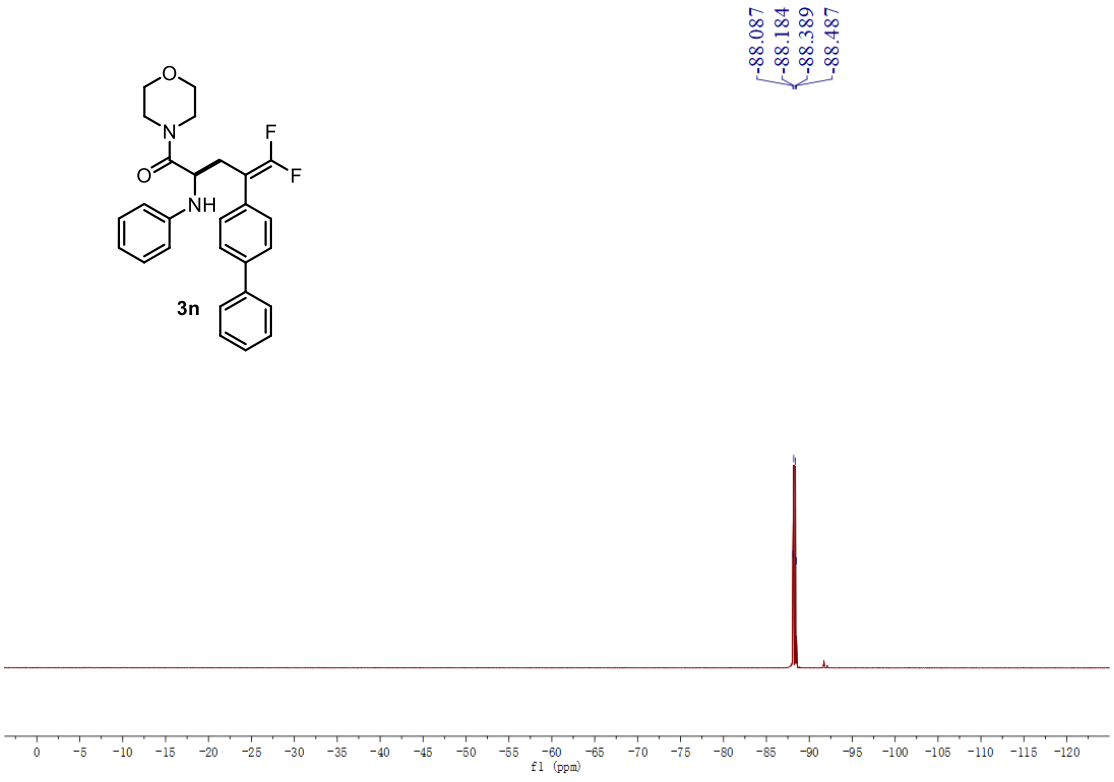




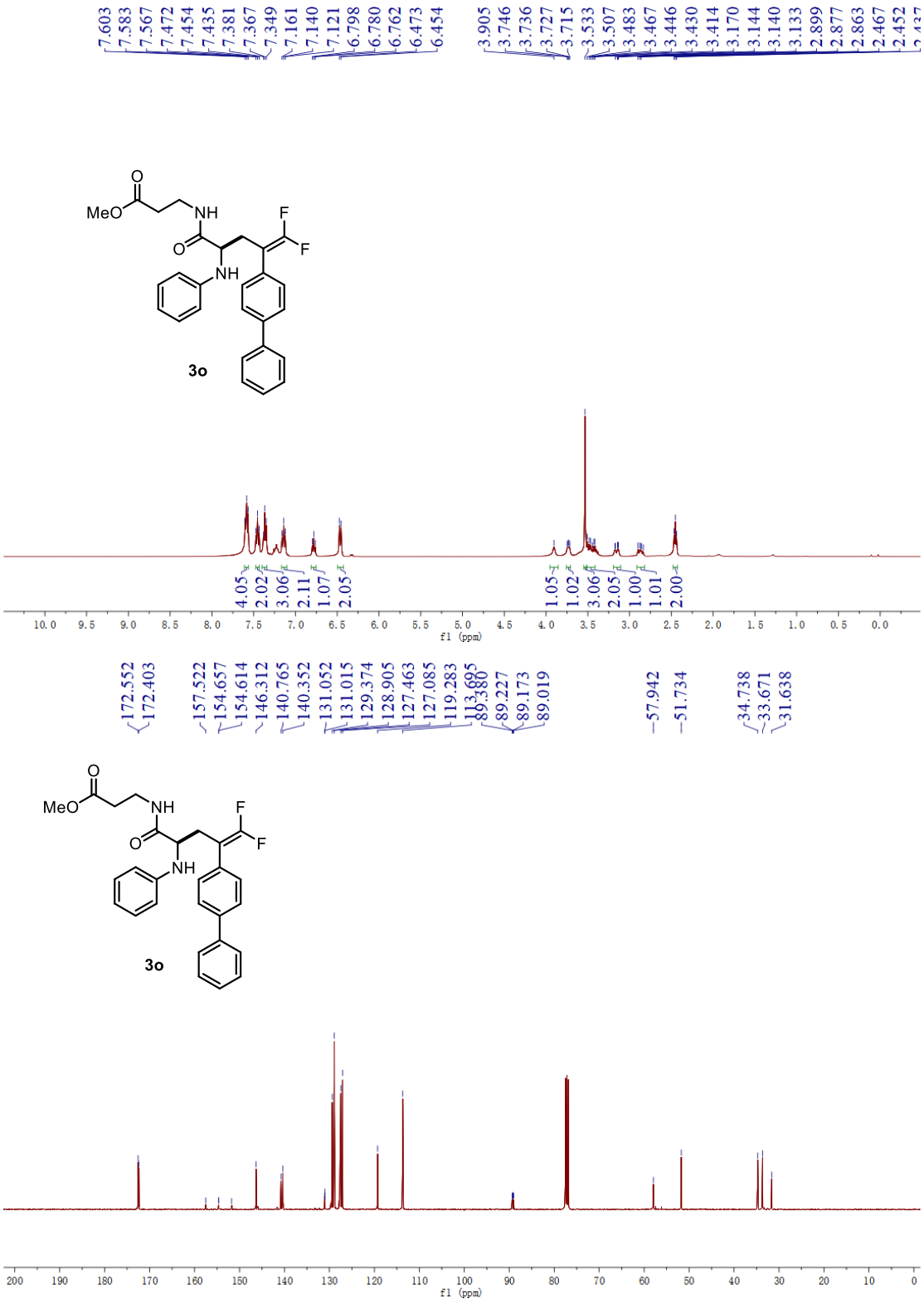
3n

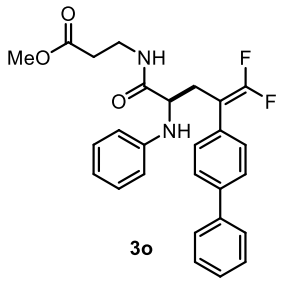



170.818
146.447
140.595
140.299
131.860
131.824
129.466
129.021
128.734
128.703
128.672
127.748
127.341
127.079
118.651
114.019
88.929
88.780
88.717
88.567
66.819
66.551
51.707
45.994
42.490
31.337
O
N
O
NH
F
F
3n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

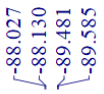

-88.087
-88.184
-88.389
-88.487
O
N
O
NH
F
F
3n
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120
f1 (ppm)

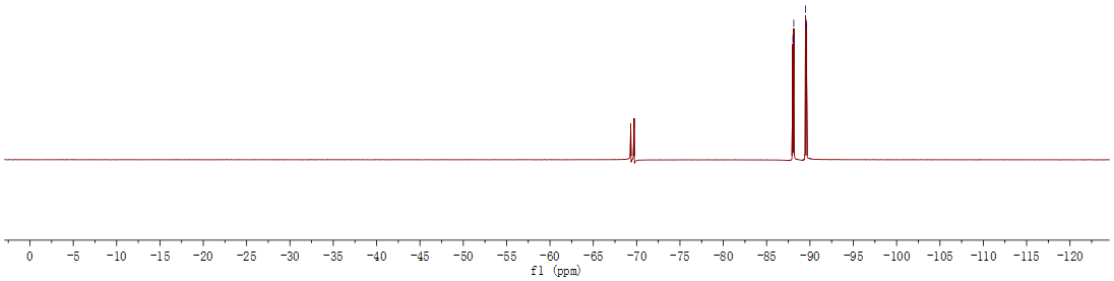
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3o (Chloroform-d)



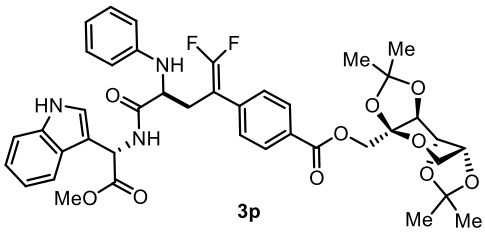


3o

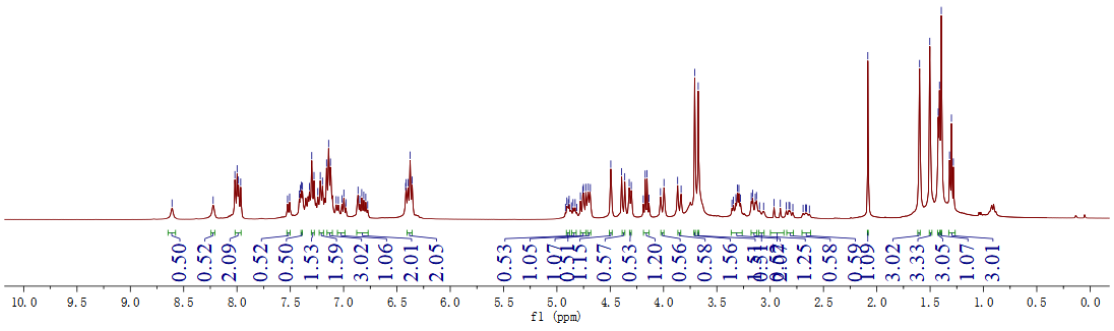


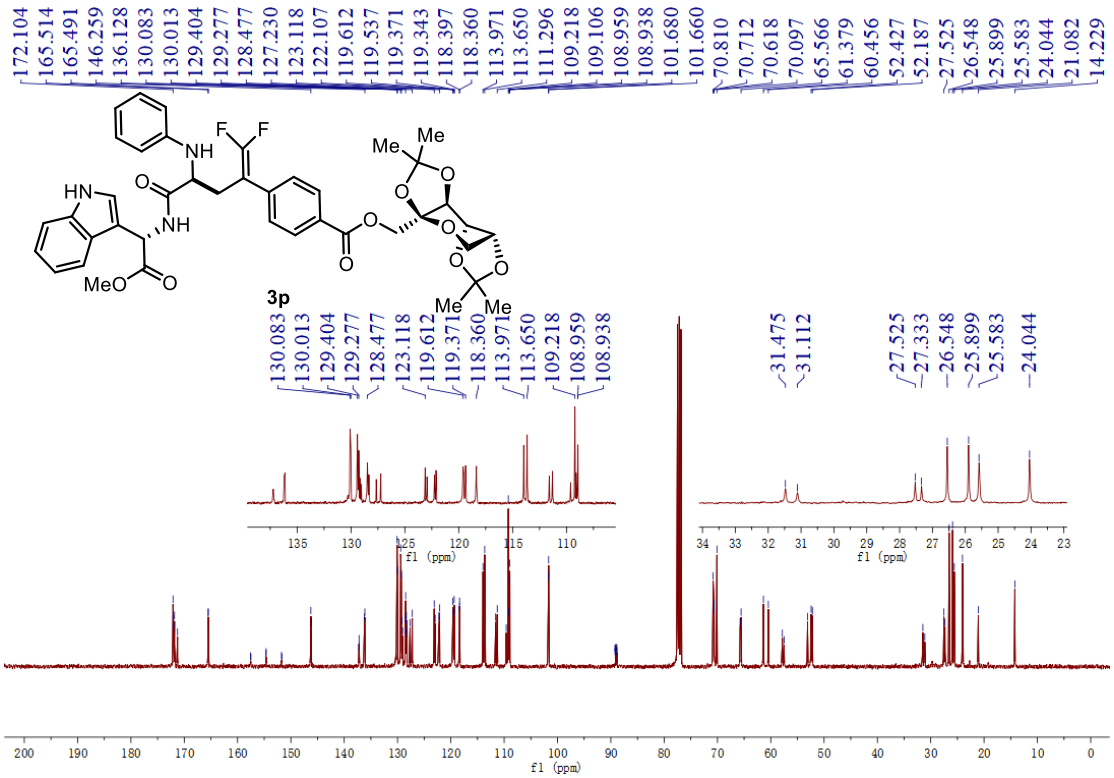


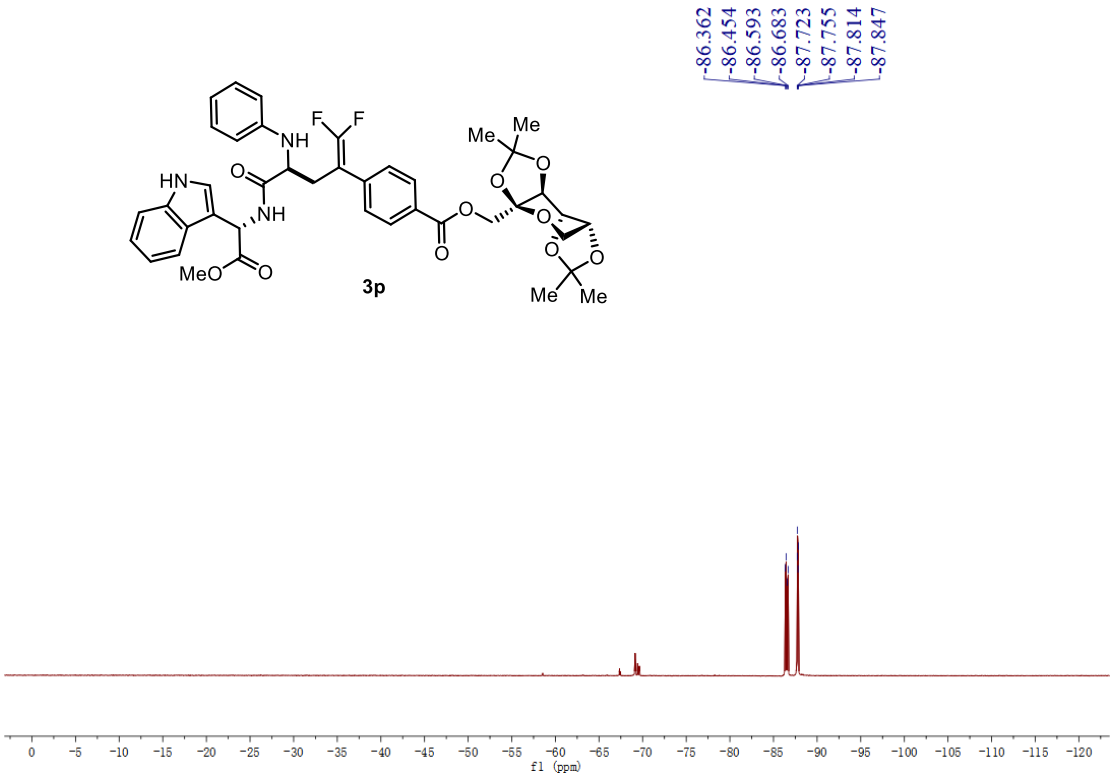
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 3p (Chloroform-d)



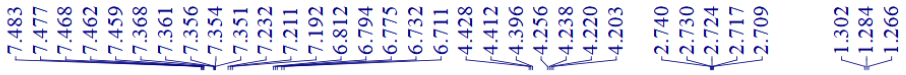
3p

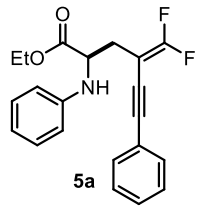


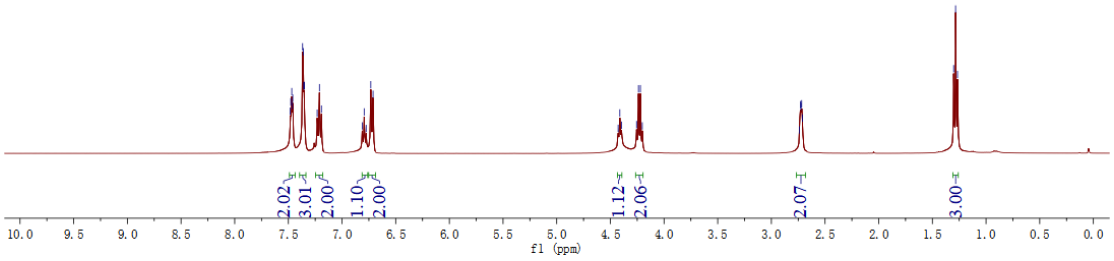

172.104
165.514
165.491
146.259
136.128
130.083
130.013
129.404
129.277
128.477
127.230
123.118
122.107
119.612
119.537
119.371
119.343
118.397
118.360
113.971
113.650
111.296
109.218
109.106
108.959
108.938
101.680
101.660
70.810
70.712
70.618
70.097
65.566
61.379
60.456
52.427
52.187
27.525
26.548
25.899
25.583
24.044
21.082
14.229
3p
31.475
31.112
27.525
27.333
26.548
25.899
25.583
24.044
f1 (ppm)

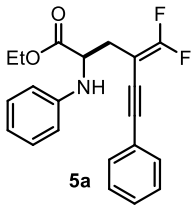

-86.362
-86.454
-86.593
-86.683
-87.723
-87.755
-87.814
-87.847
3p
f1 (ppm)

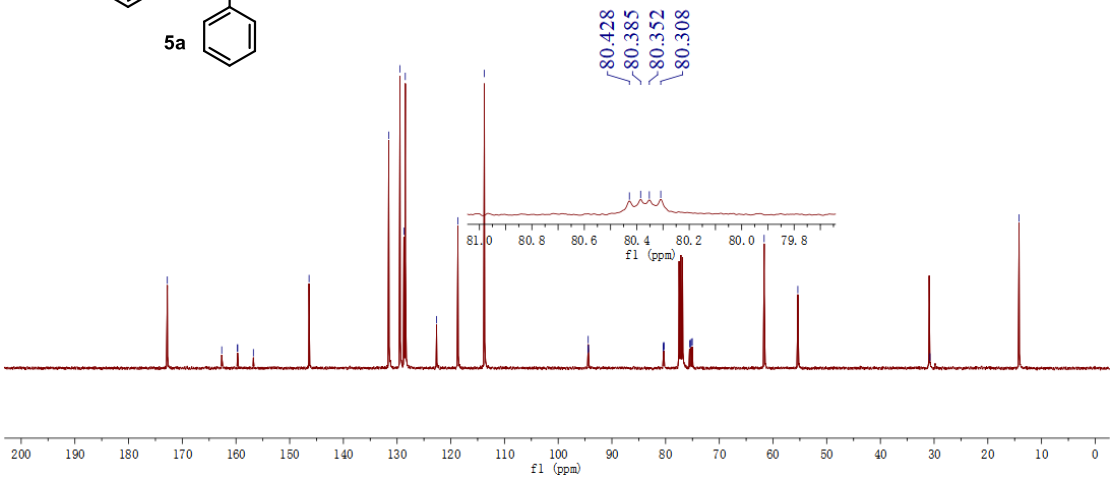
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5a (Chloroform-d)

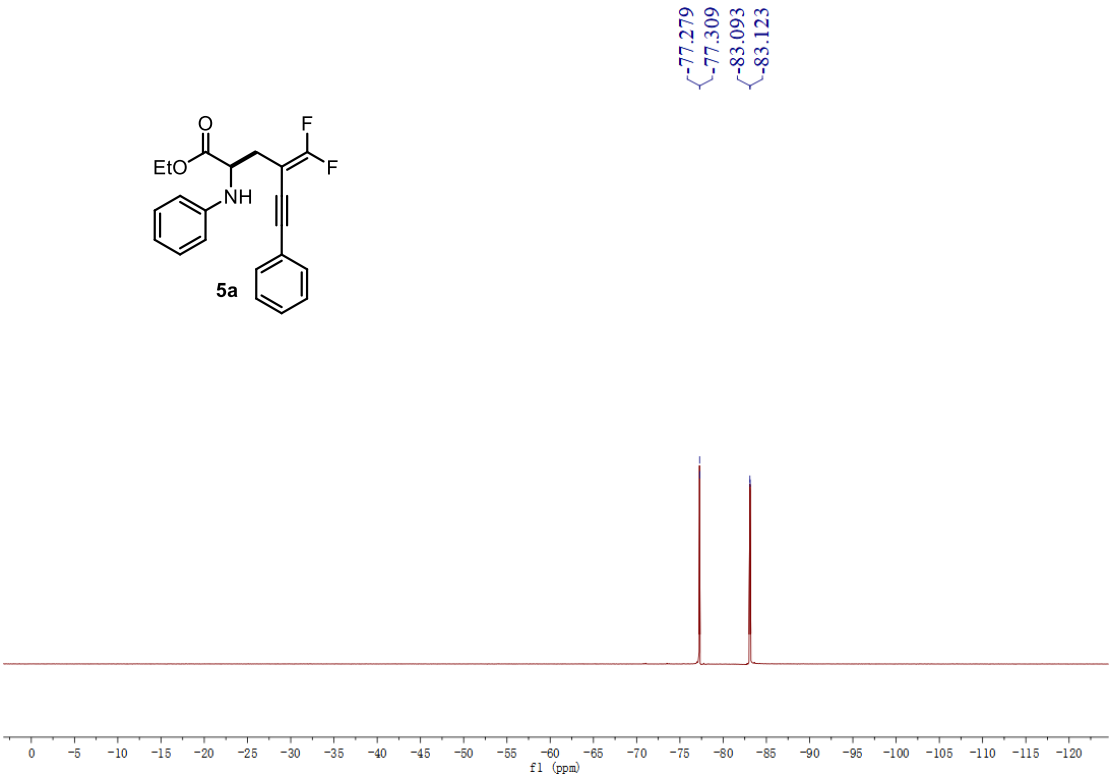




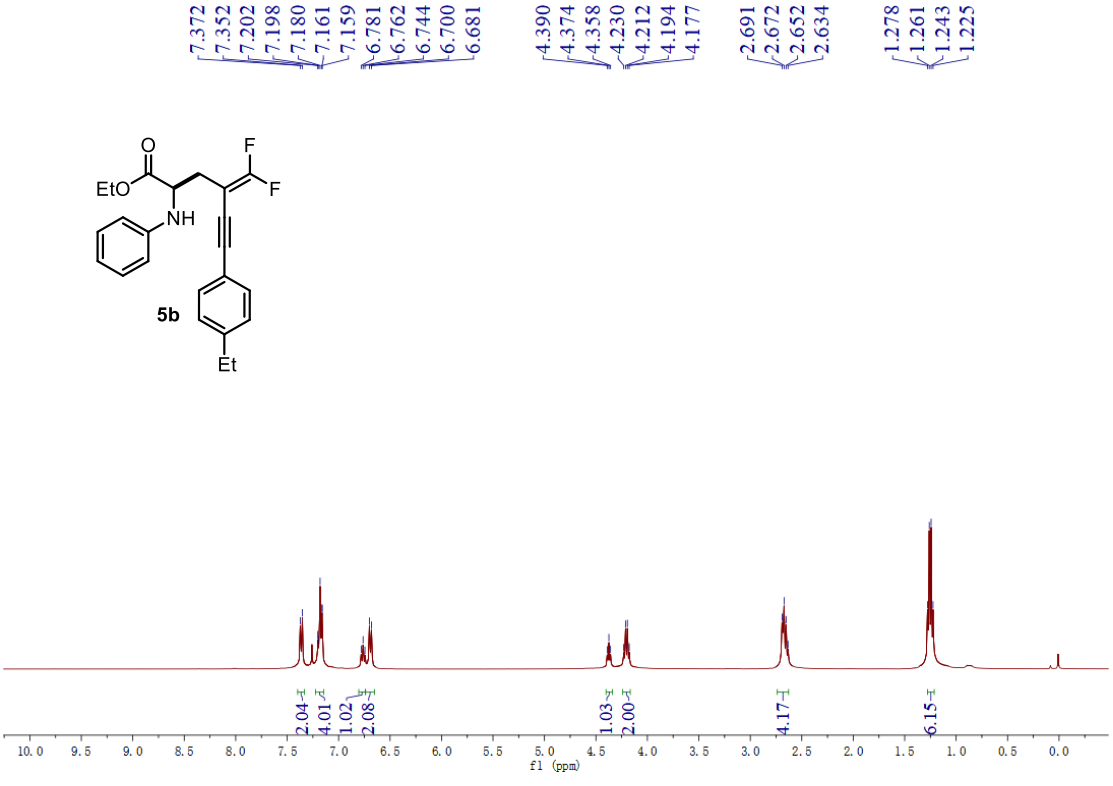


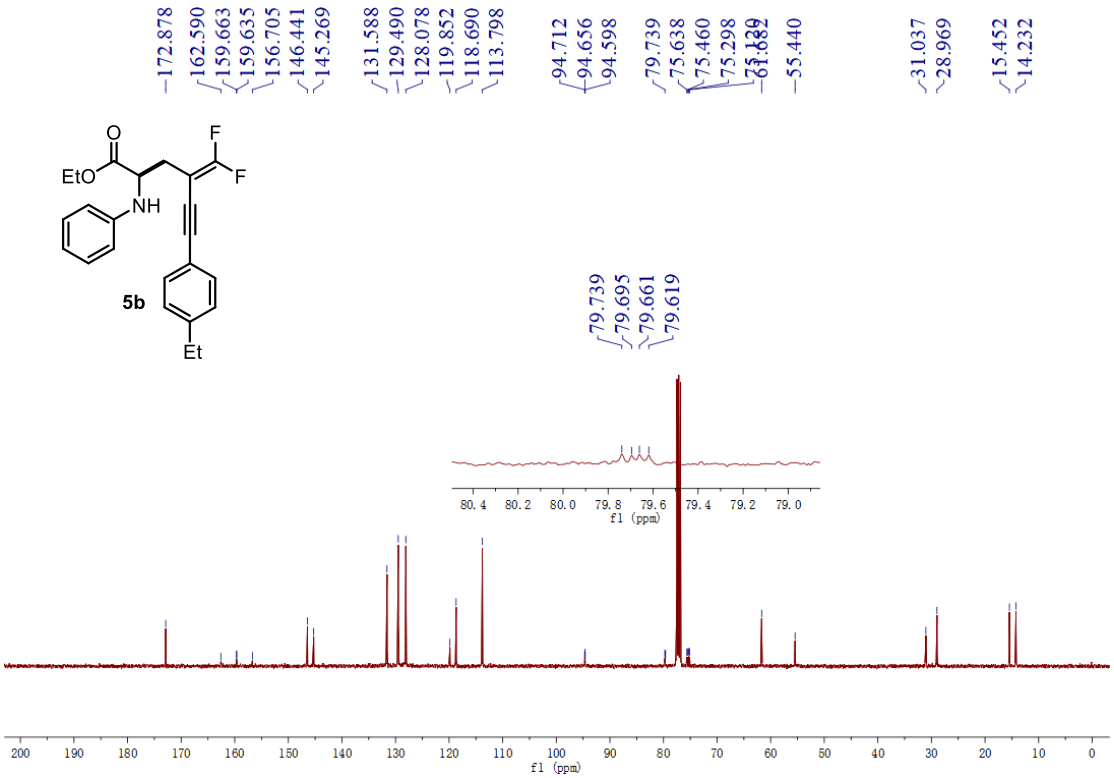


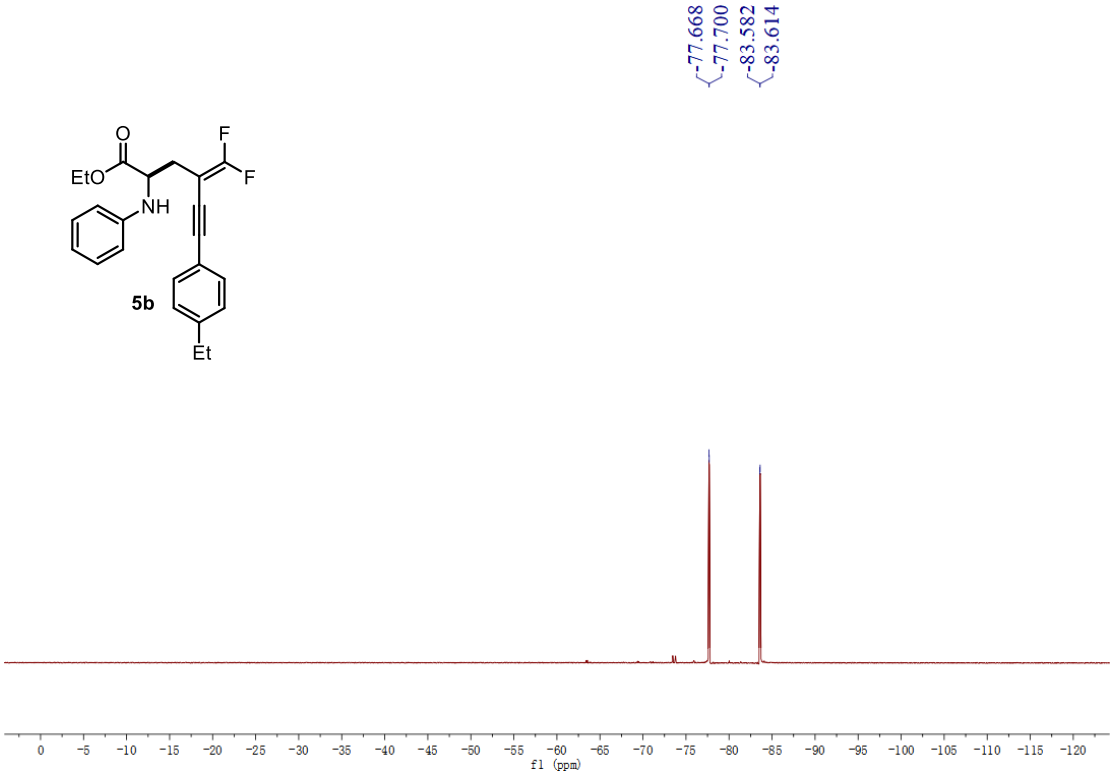




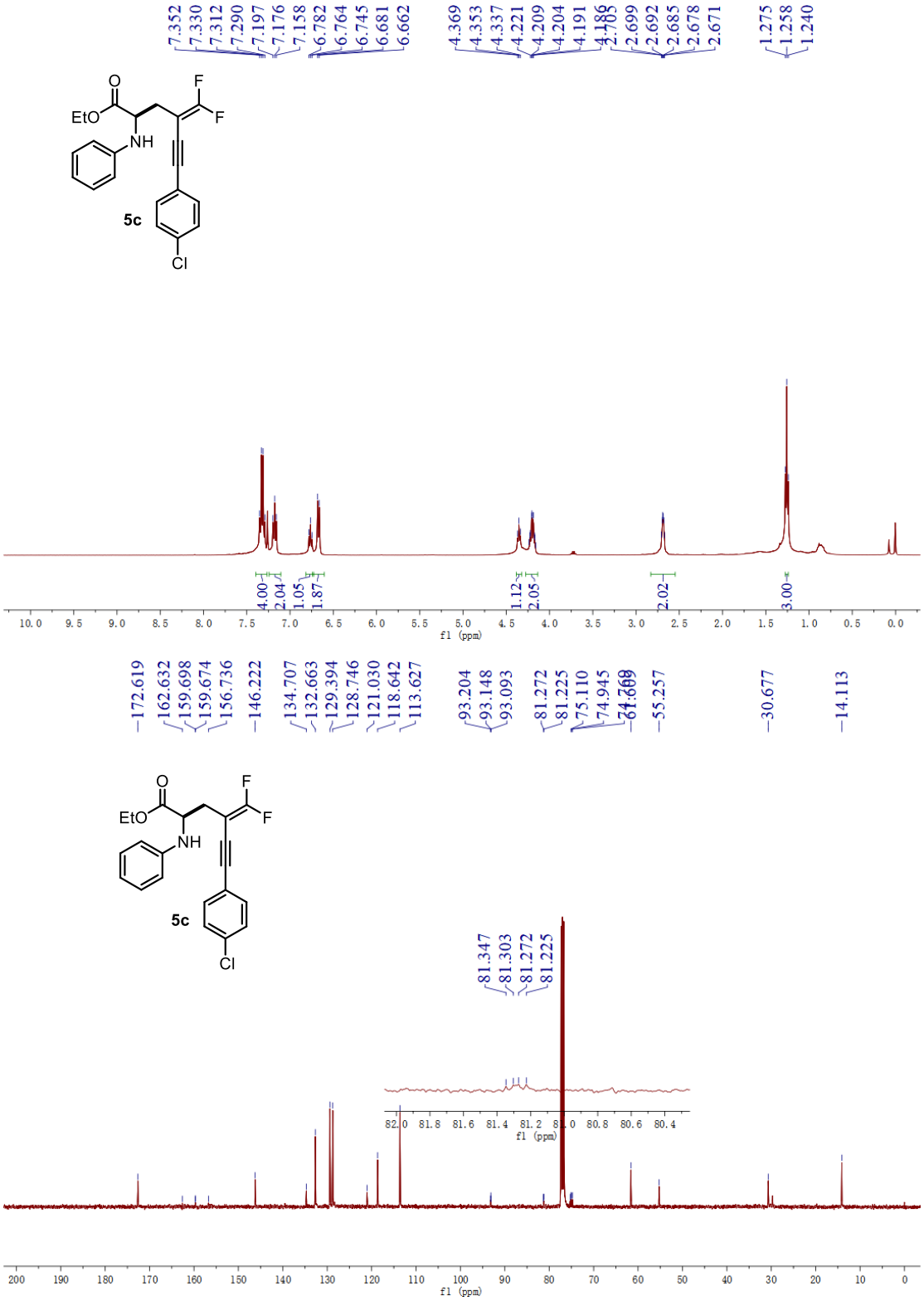
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5b (Chloroform-d)

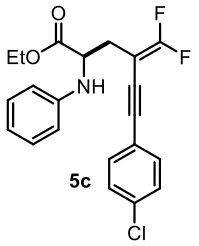



172.878
162.590
159.663
159.635
156.705
146.441
145.269
131.588
129.490
128.078
119.852
118.690
113.798
94.712
94.656
94.598
79.739
75.638
75.460
75.298
55.440
31.037
28.969
15.452
14.232
O
EtO
F
F
NH
5b
Et
79.739
79.695
79.661
79.619
80.4
80.2
80.0
79.8
79.6
79.4
79.2
79.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

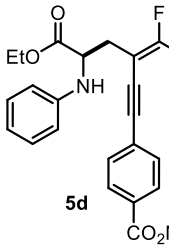

-77.668
-77.700
-83.582
-83.614
O
EtO
F
F
NH
5b
Et
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
f1 (ppm)

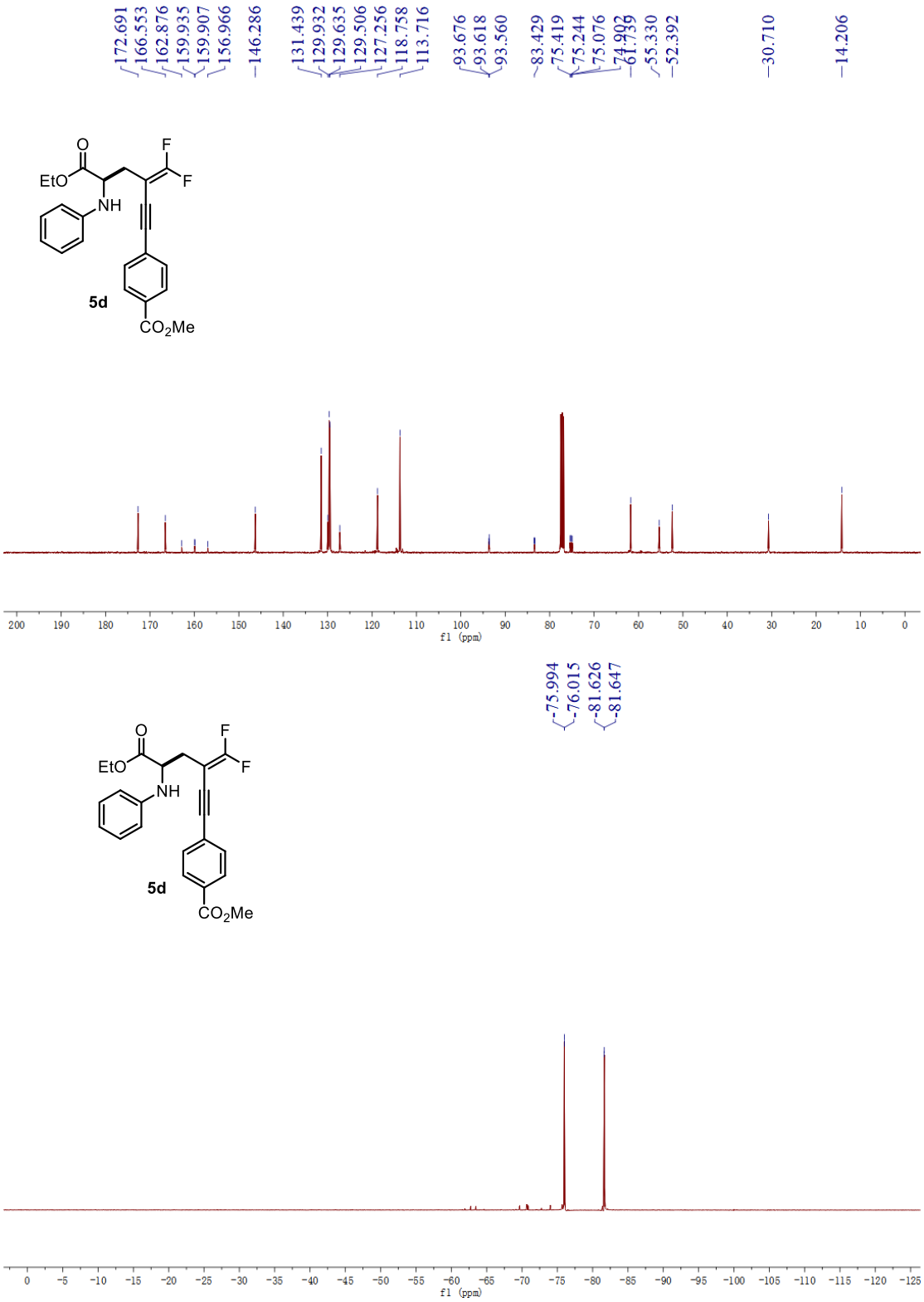
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5c (Chloroform-d)



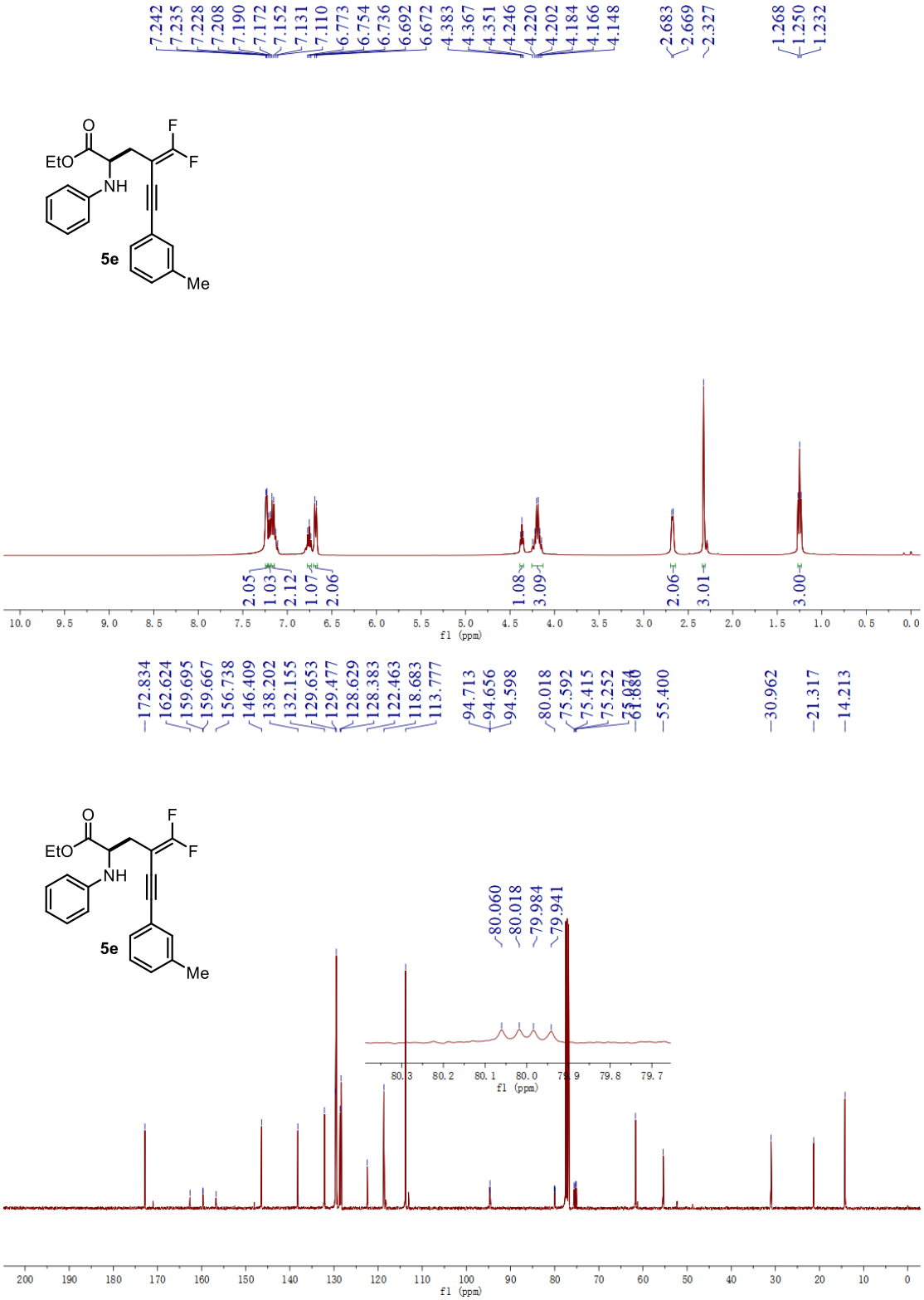


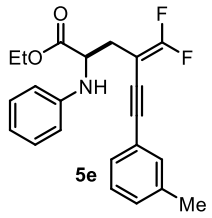
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5d (Chloroform-d)

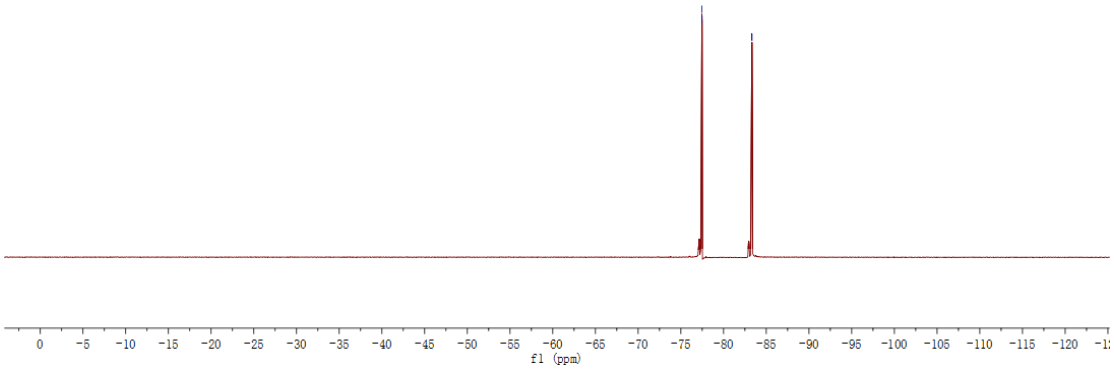



172.691
166.553
162.876
159.935
159.907
156.966
146.286
131.439
129.932
129.635
129.506
127.256
118.758
113.716
93.676
93.618
93.560
83.429
75.419
75.244
75.076
74.902
61.739
55.330
52.392
30.710
14.206
O
EtO
F
F
NH
5d
CO2Me
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
-75.994
-76.015
-81.626
-81.647
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125
f1 (ppm)

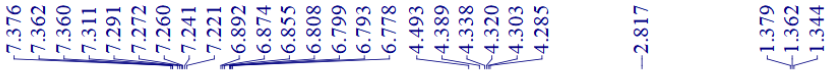
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5e (Chloroform-d)

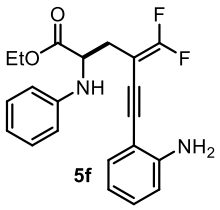


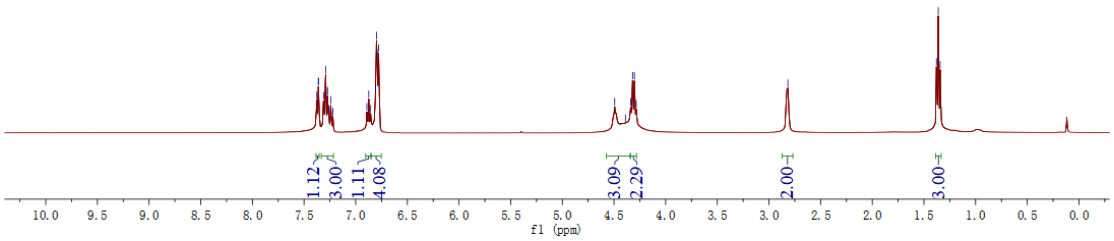


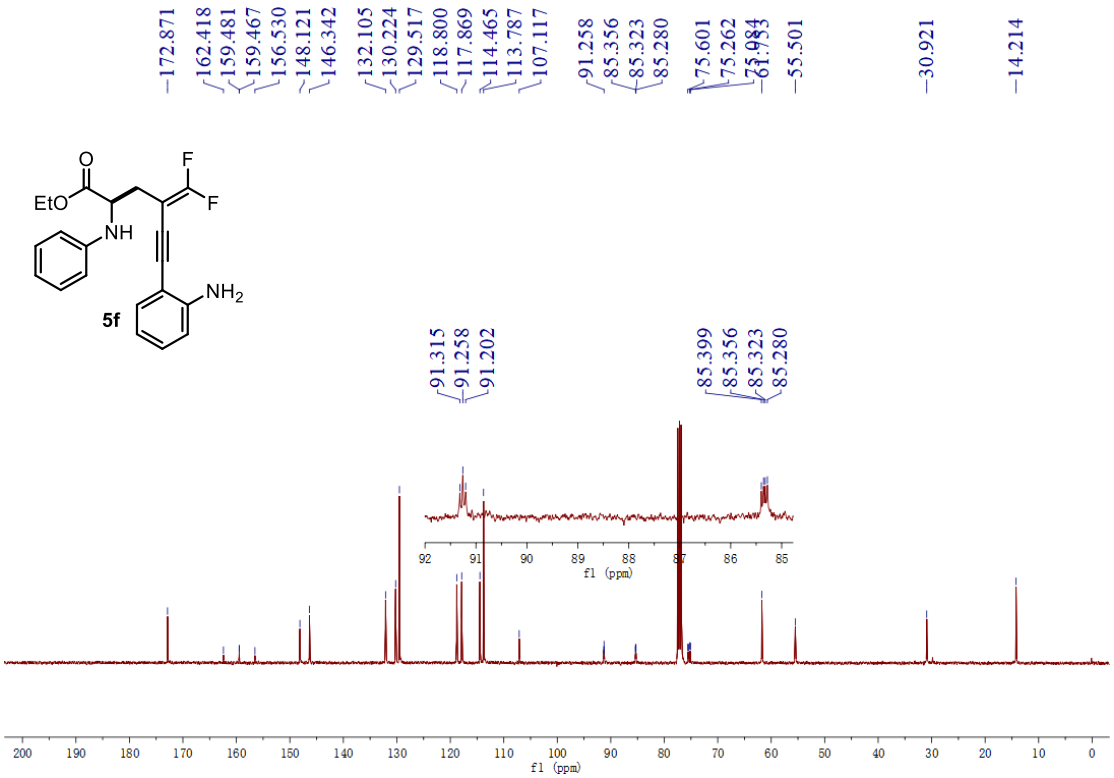


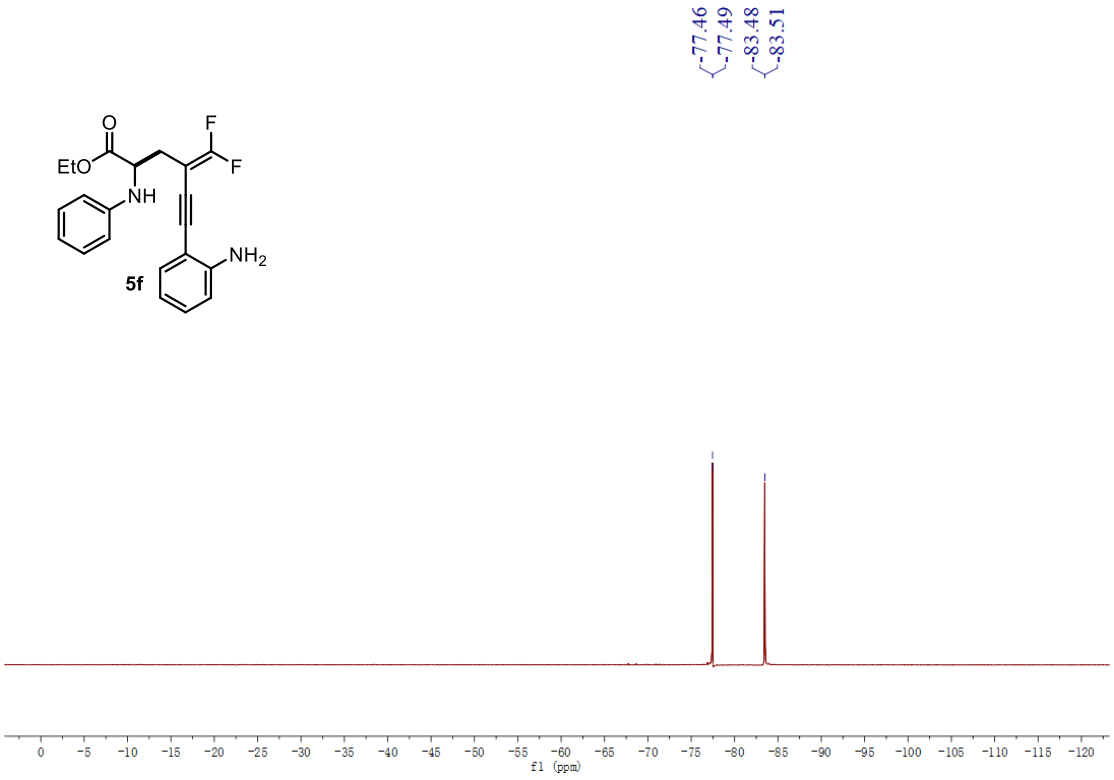
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5f (Chloroform-d)



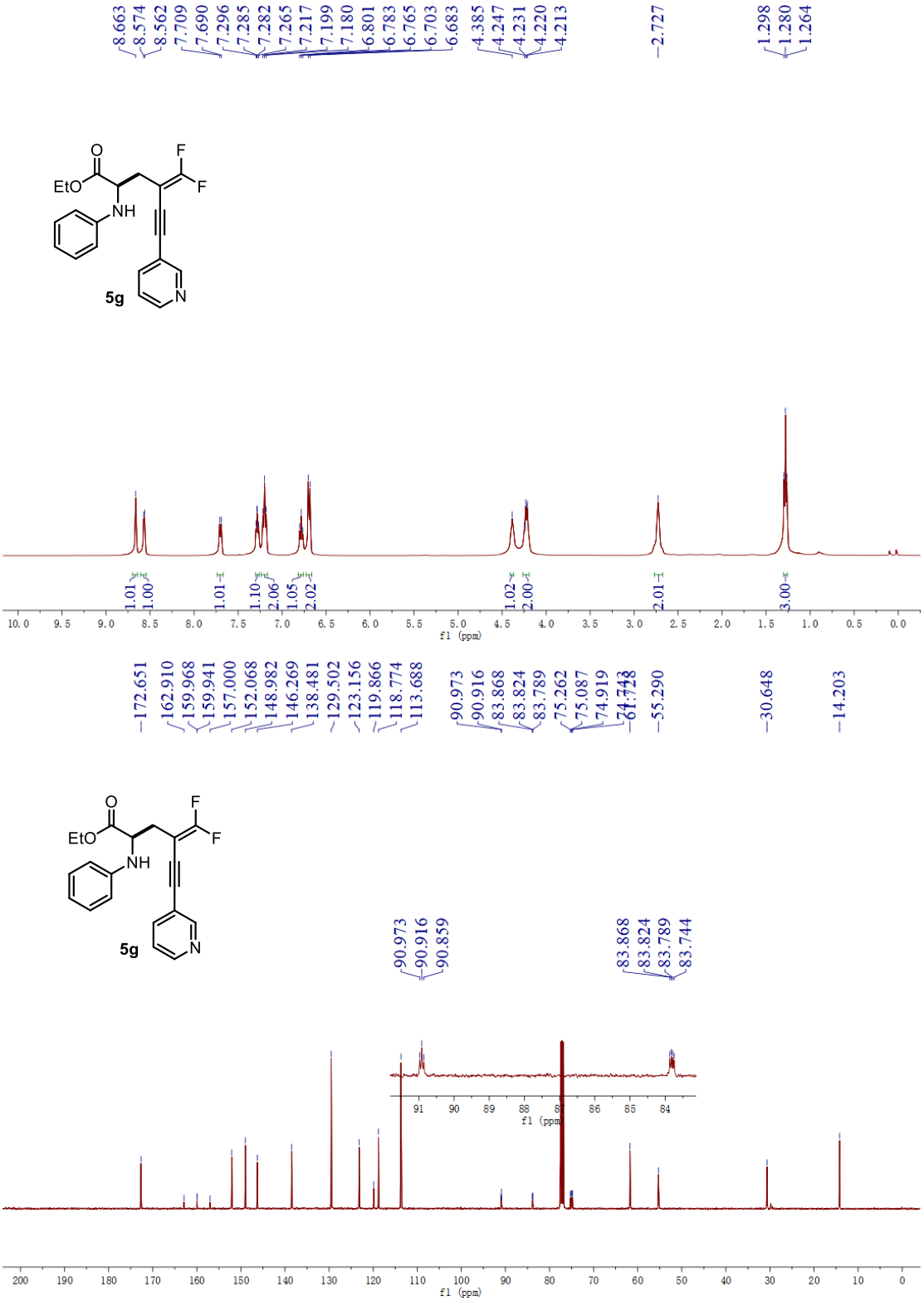


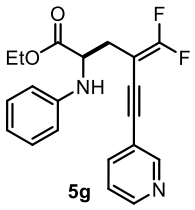



172.871
162.418
159.481
159.467
156.530
148.121
146.342
132.105
130.224
129.517
118.800
117.869
114.465
113.787
107.117
91.258
85.356
85.323
85.280
75.601
75.262
61.953
55.501
30.921
14.214
O
EtO
F
F
NH
NH2
5f
91.315
91.258
91.202
85.399
85.356
85.323
85.280
f1 (ppm)


-77.46
-77.49
-83.48
-83.51
O
EtO
F
F
NH
NH2
5f
f1 (ppm)

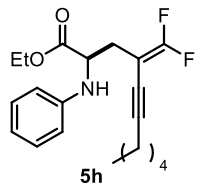
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5g (Chloroform-d)



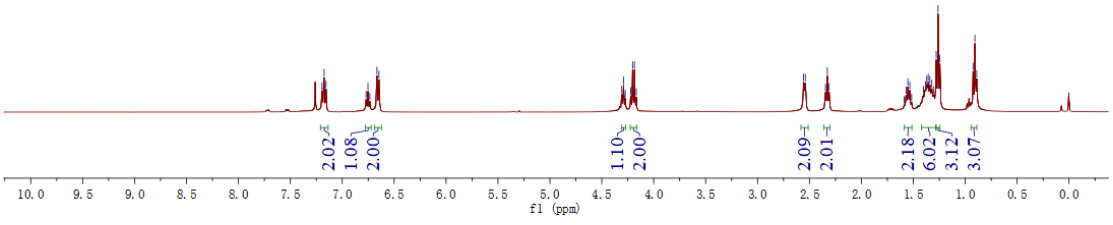


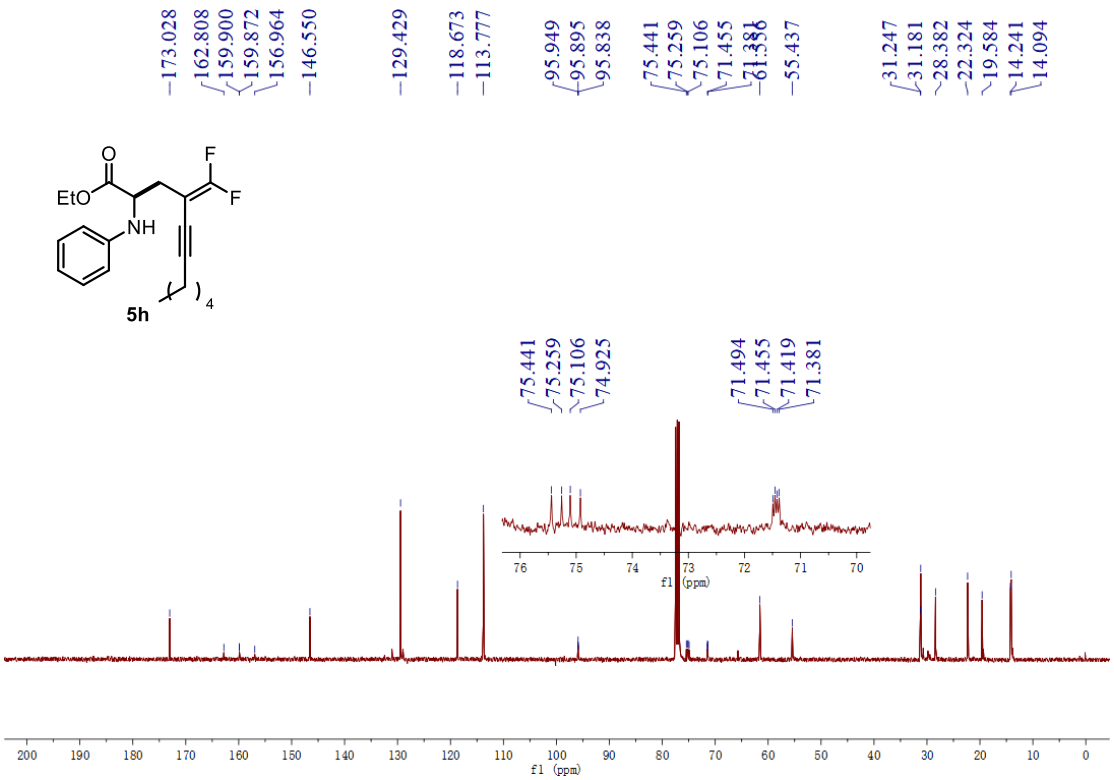
5g

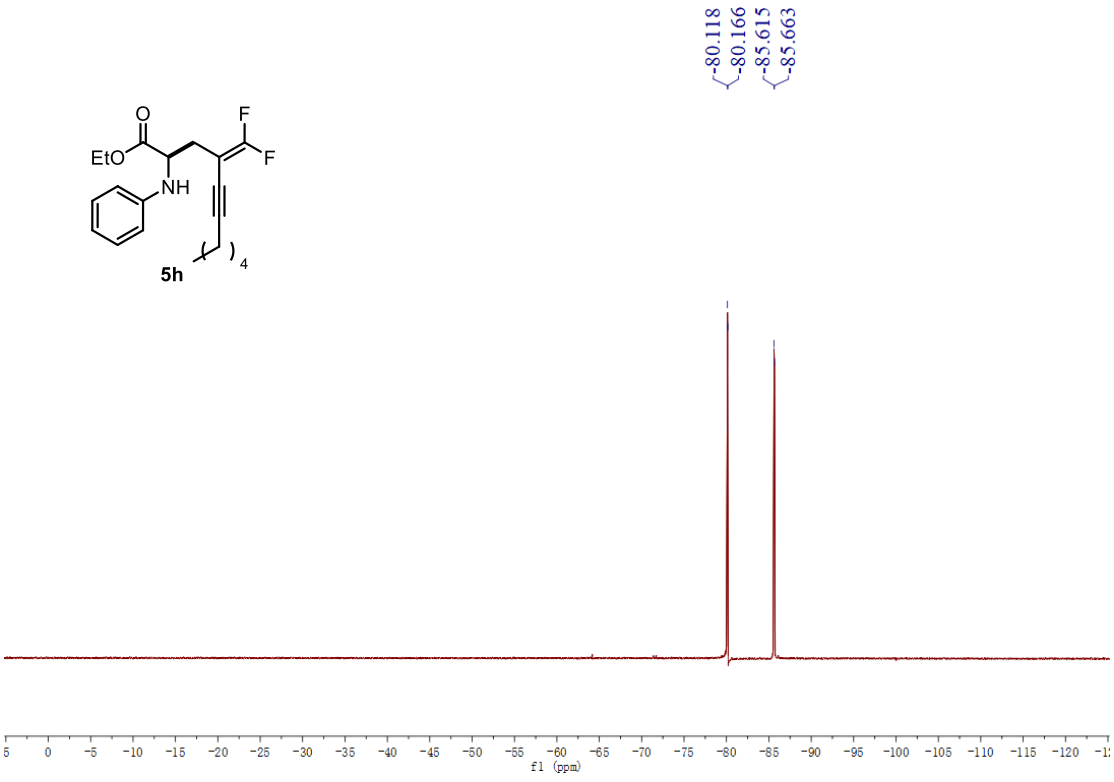
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5h (Chloroform-d)



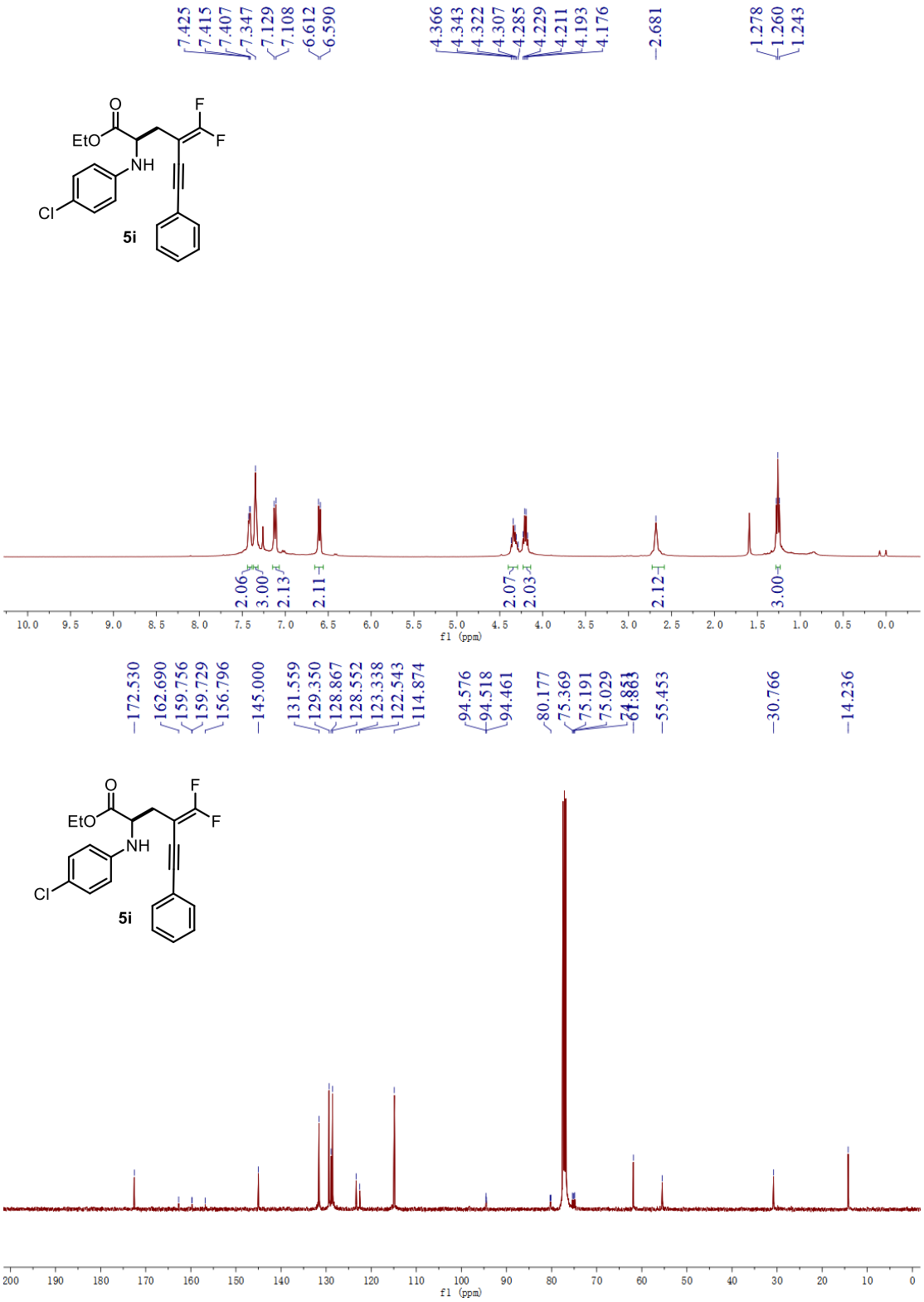
5h

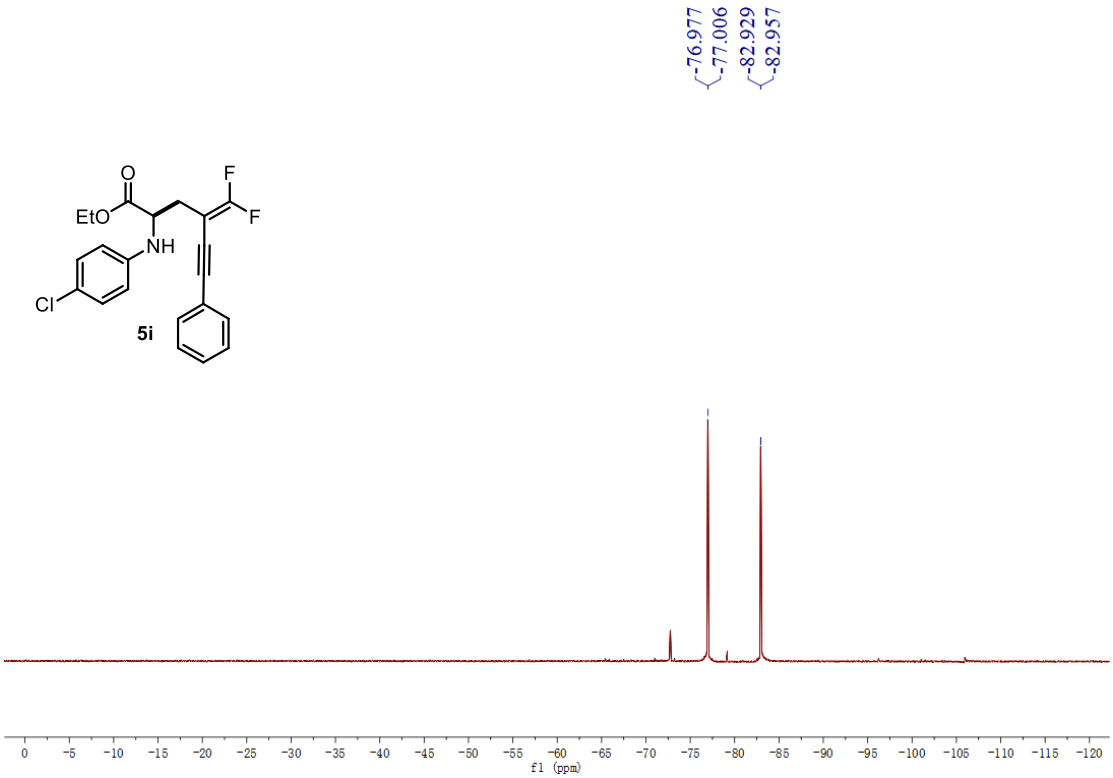



173.028
162.808
159.900
159.872
156.964
146.550
129.429
118.673
113.777
95.949
95.895
95.838
75.441
75.259
75.106
71.455
71.381
55.437
31.247
31.181
28.382
22.324
19.584
14.241
14.094
EtO
NH
F
F
O
4
5h
75.441
75.259
75.106
74.925
71.494
71.455
71.419
71.381
f1 (ppm)

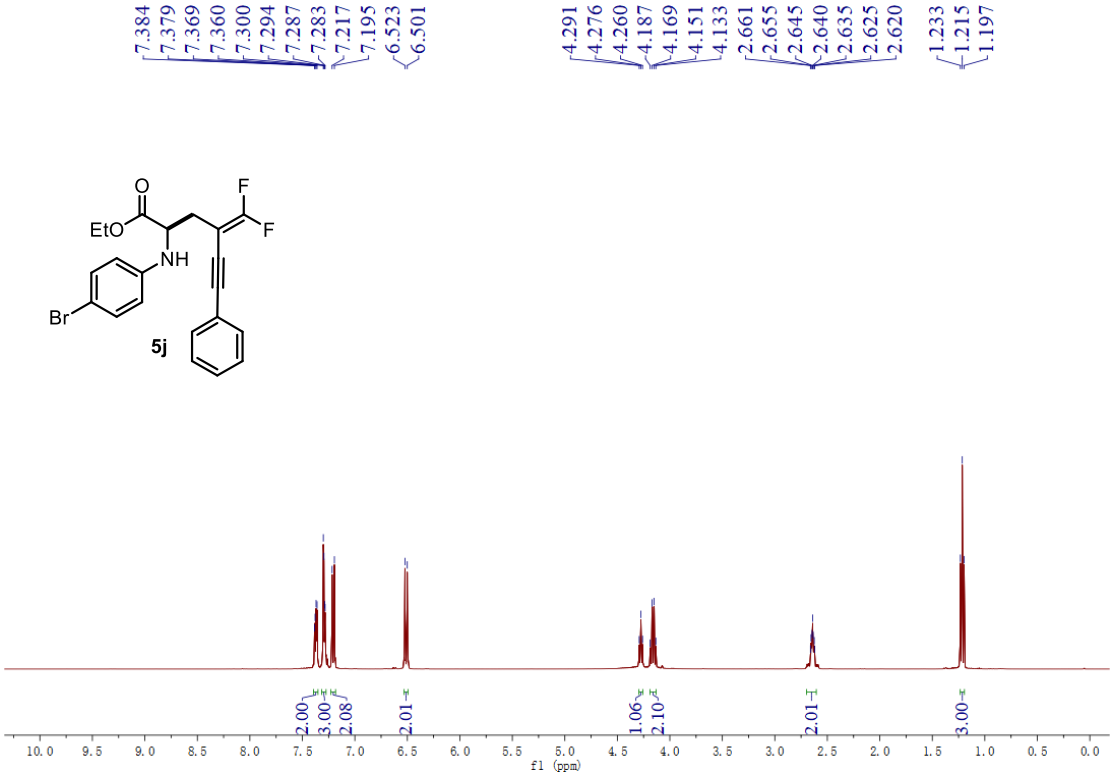

-80.118
-80.166
-85.615
-85.663
EtO
NH
F
F
O
4
5h
f1 (ppm)

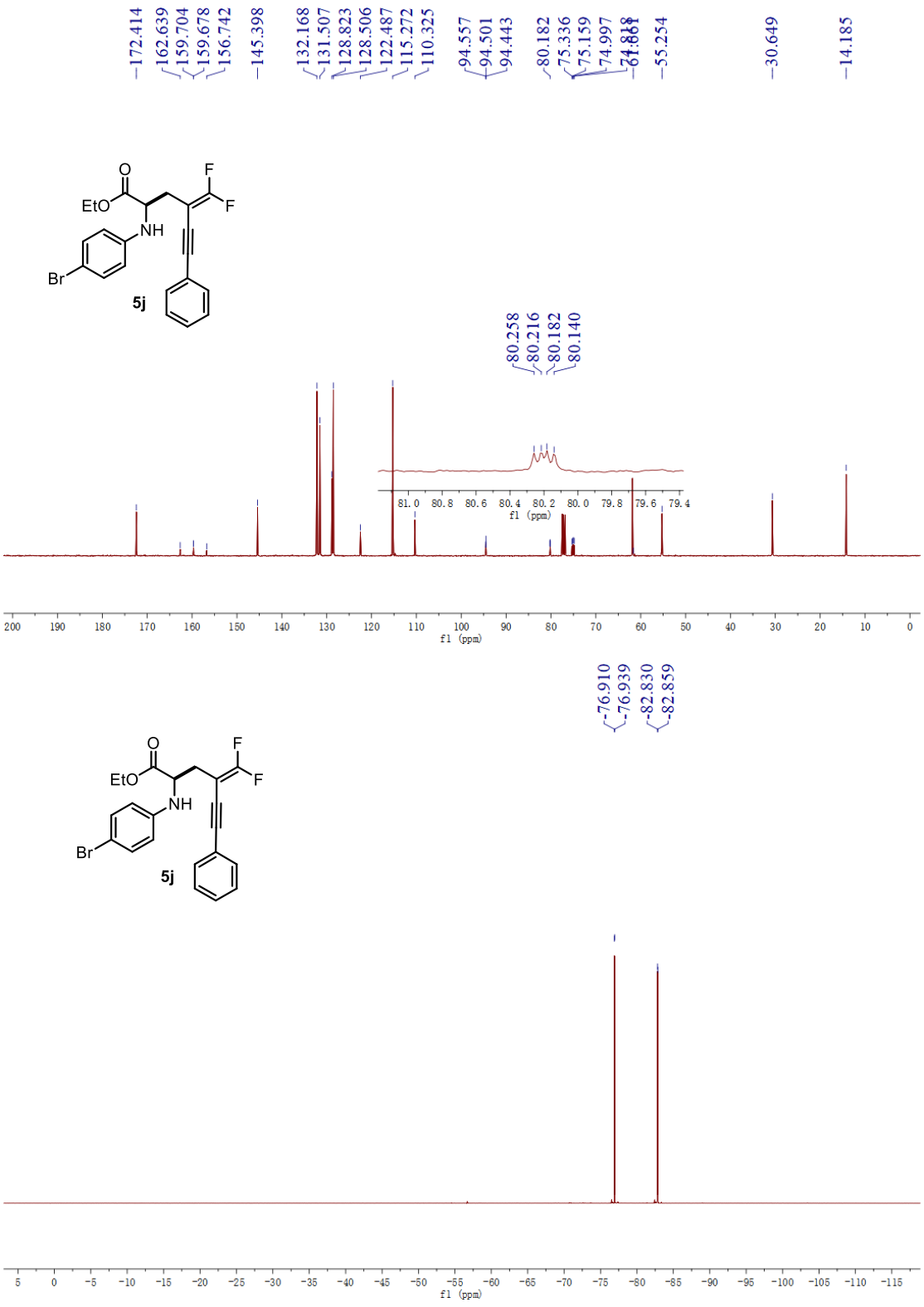
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5i (Chloroform-d)



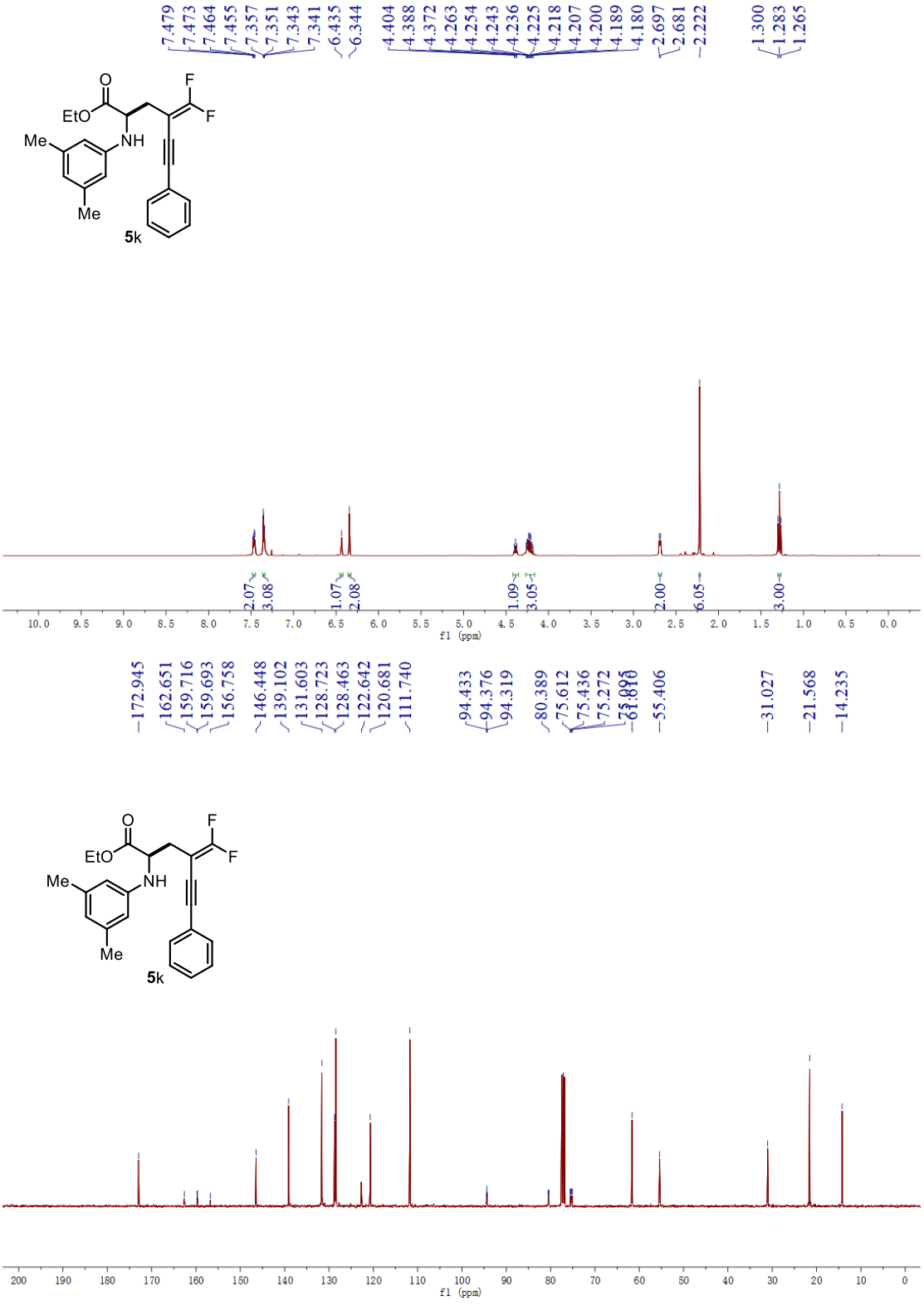


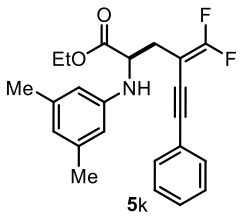
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5j (Chloroform-d)




172.414
162.639
159.704
159.678
156.742
145.398
132.168
131.507
128.823
128.506
122.487
115.272
110.325
94.557
94.501
94.443
80.182
75.336
75.159
74.997
55.254
30.649
14.185
80.258
80.216
80.182
80.140
81.0 80.8 80.6 80.4 80.2 80.0 79.8 79.6 79.4
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
O
EtO
NH
F
F
Br
5j
-76.910
-76.939
-82.830
-82.859
5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115
f1 (ppm)

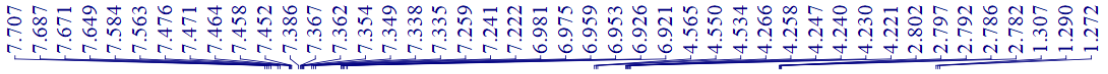
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5k (Chloroform-d)

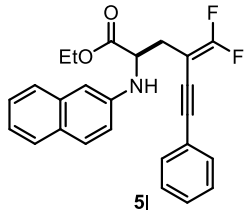




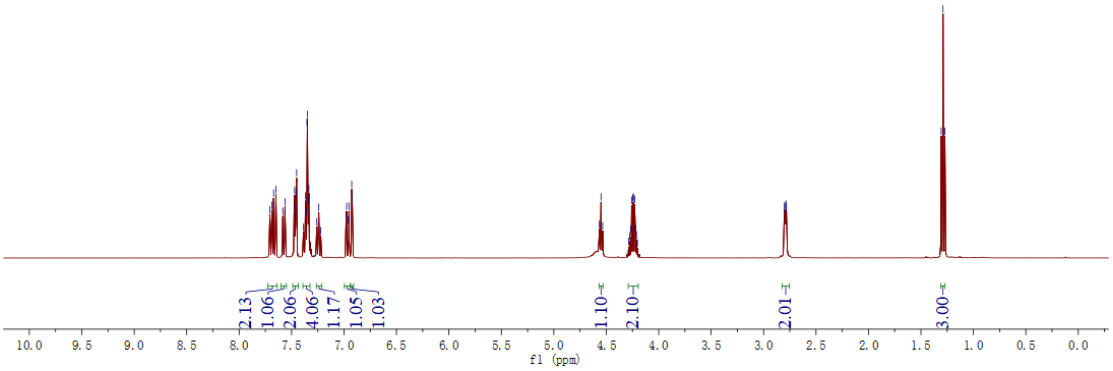
5k

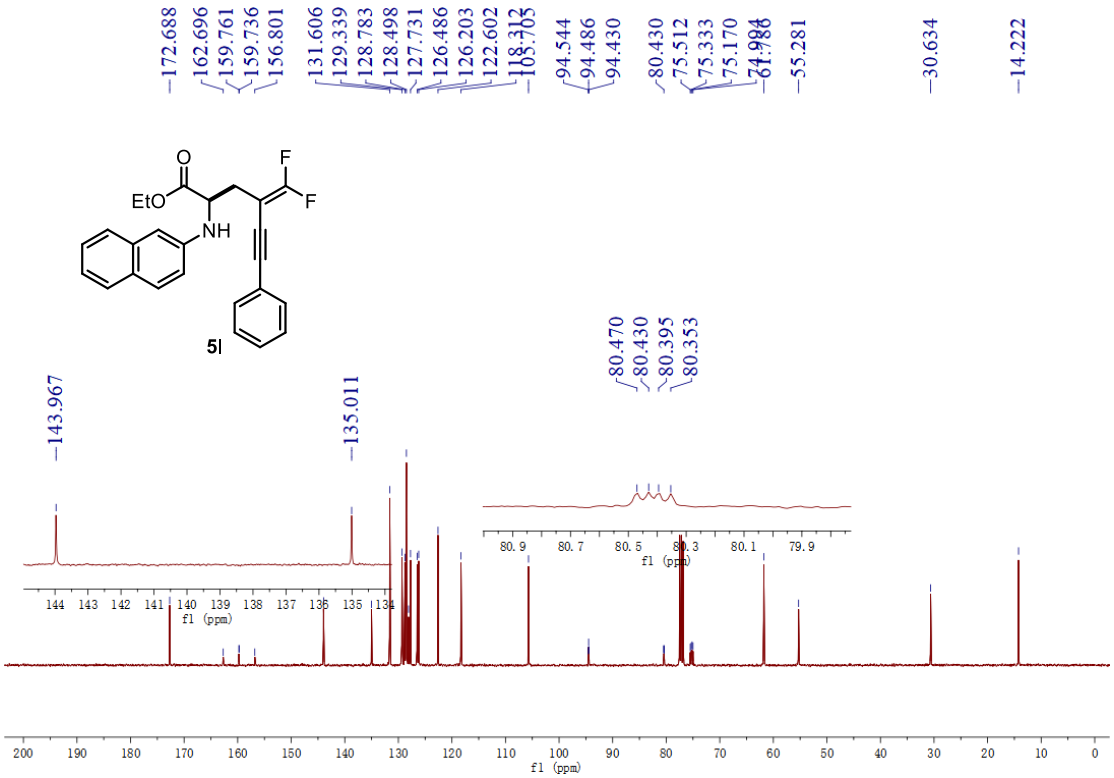
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5l (Chloroform-d)

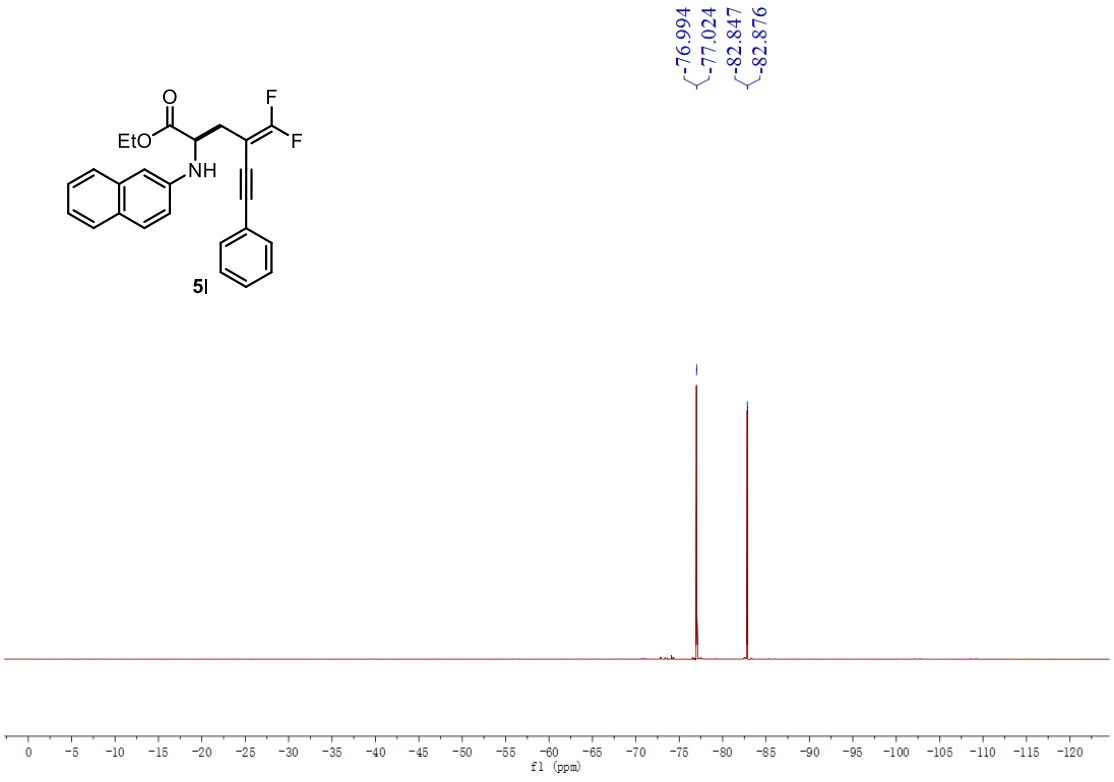




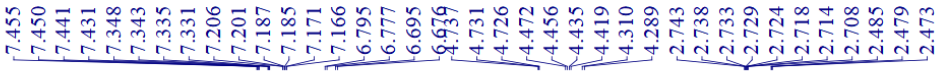
5l

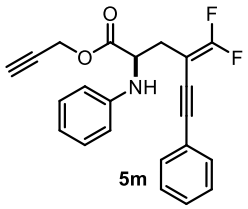


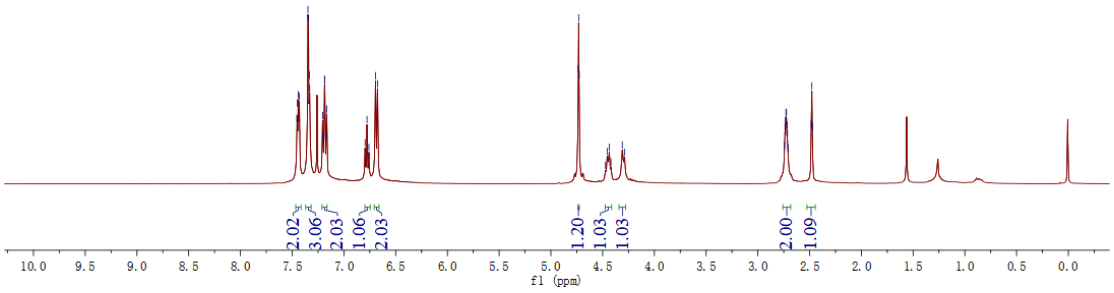

172.688
162.696
159.761
159.736
156.801
131.606
129.339
128.783
128.498
127.731
126.486
126.203
122.602
118.312
105.705
94.544
94.486
94.430
80.430
75.512
75.333
75.170
55.281
30.634
14.222
O
EtO
NH
F
F
5l
143.967
135.011
80.470
80.430
80.395
80.353
f1 (ppm)

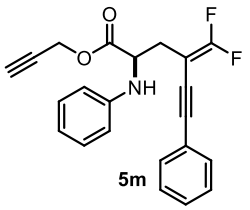

76.994
77.024
82.847
82.876
O
EtO
NH
F
F
5l
f1 (ppm)

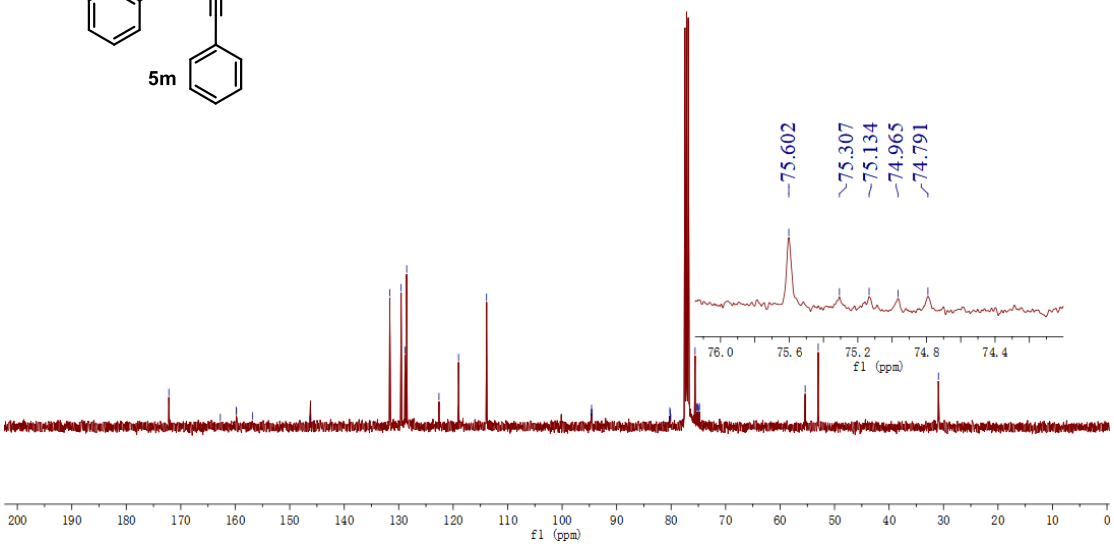
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5m (Chloroform-d)

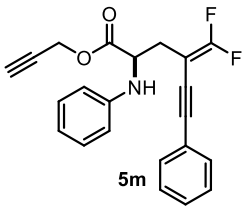


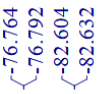


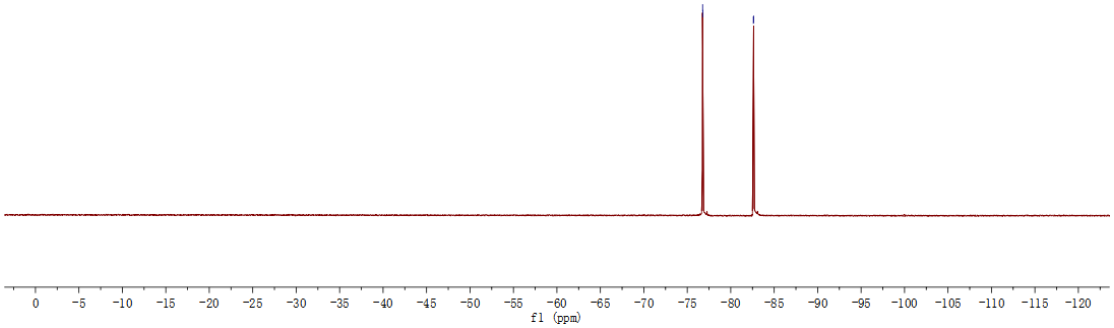




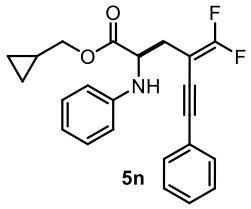


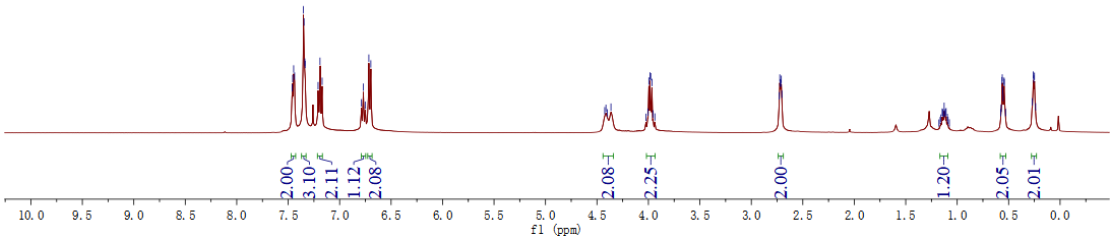


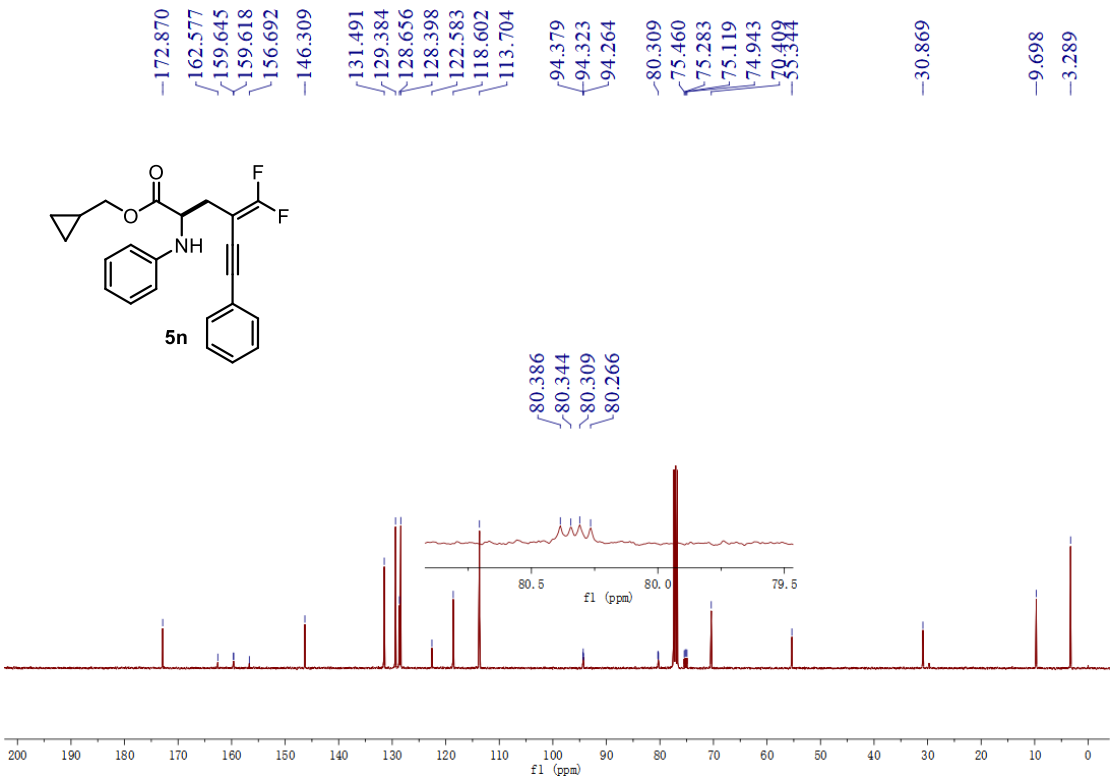


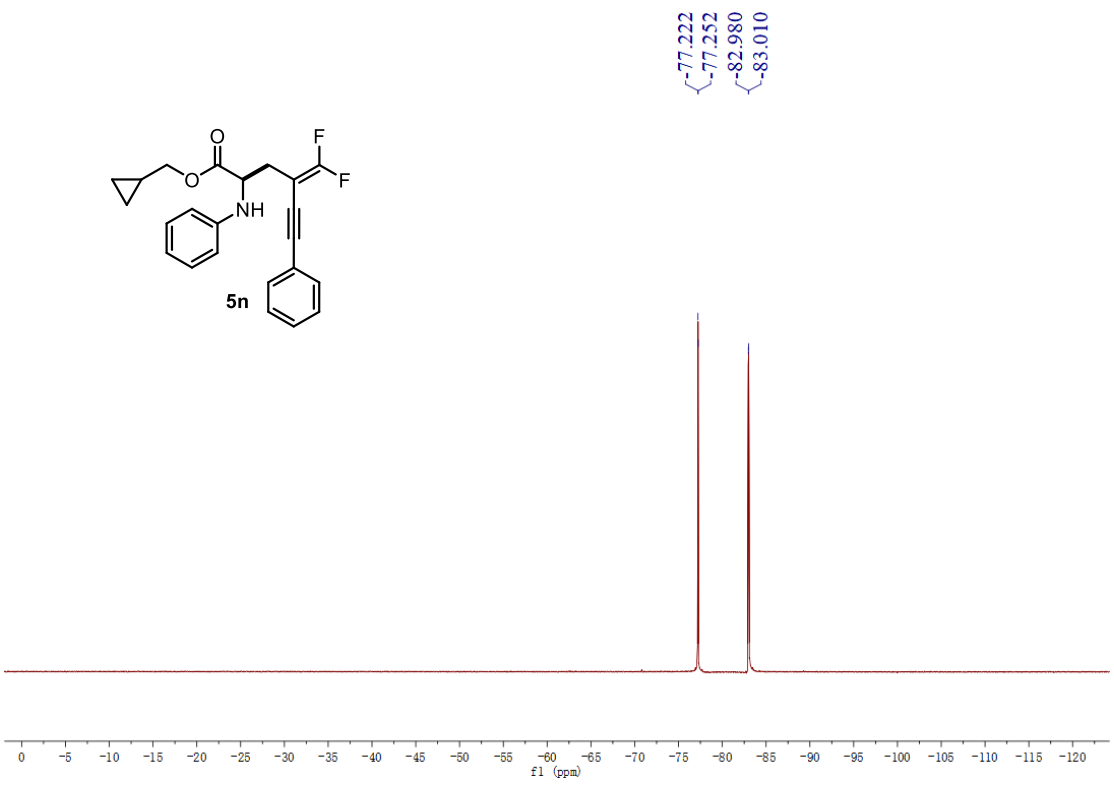


^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5n (Chloroform-d)

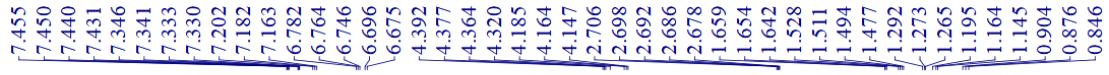


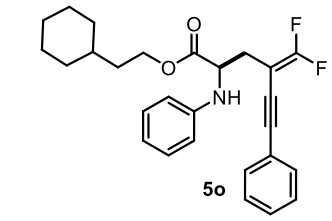


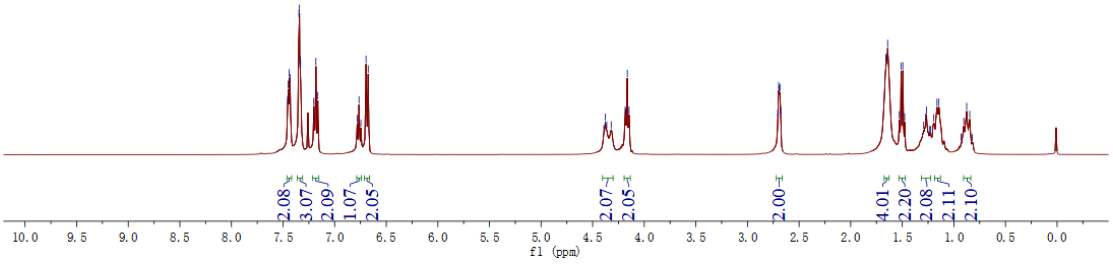

172.870
162.577
159.645
159.618
156.692
146.309
131.491
129.384
128.656
128.398
122.583
118.602
113.704
94.379
94.323
94.264
80.309
75.460
75.283
75.119
74.943
70.409
55.344
30.869
9.698
3.289
O
O
NH
F
F
5n
80.386
80.344
80.309
80.266
80.5
80.0
79.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

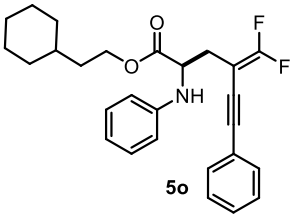

77.222
77.252
82.980
83.010
O
O
NH
F
F
5n
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120
f1 (ppm)

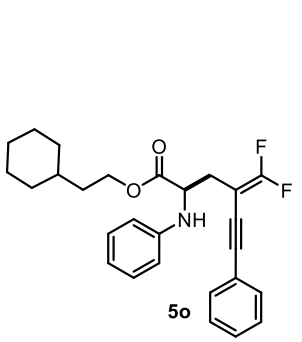
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5o (Chloroform-d)



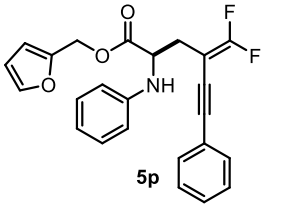


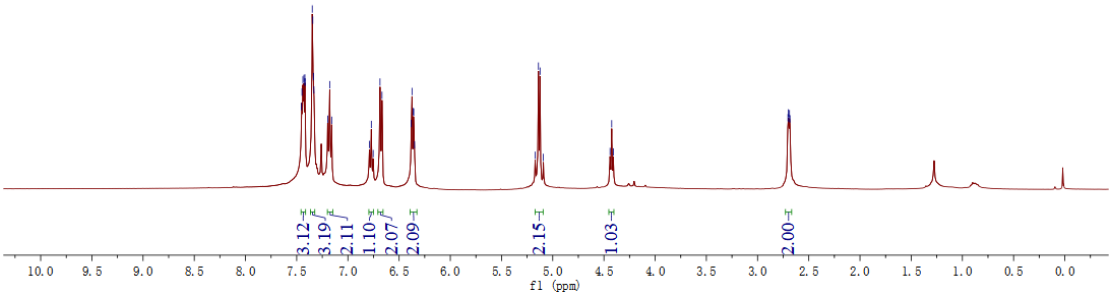


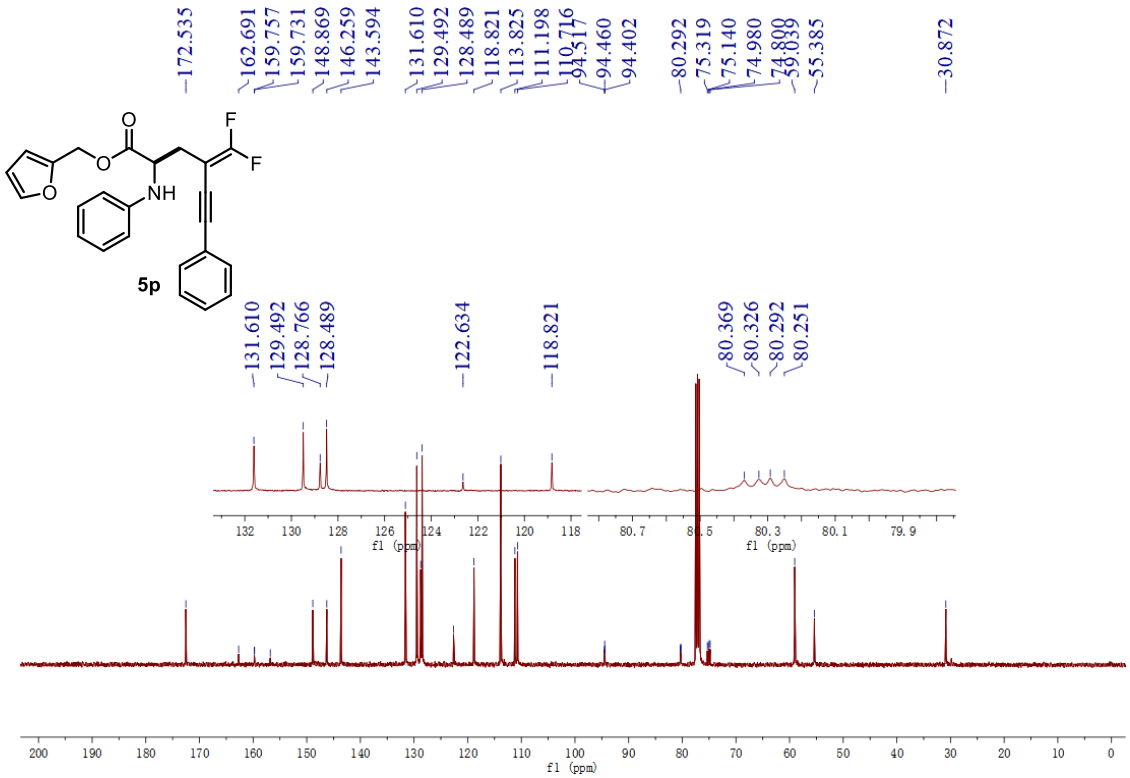


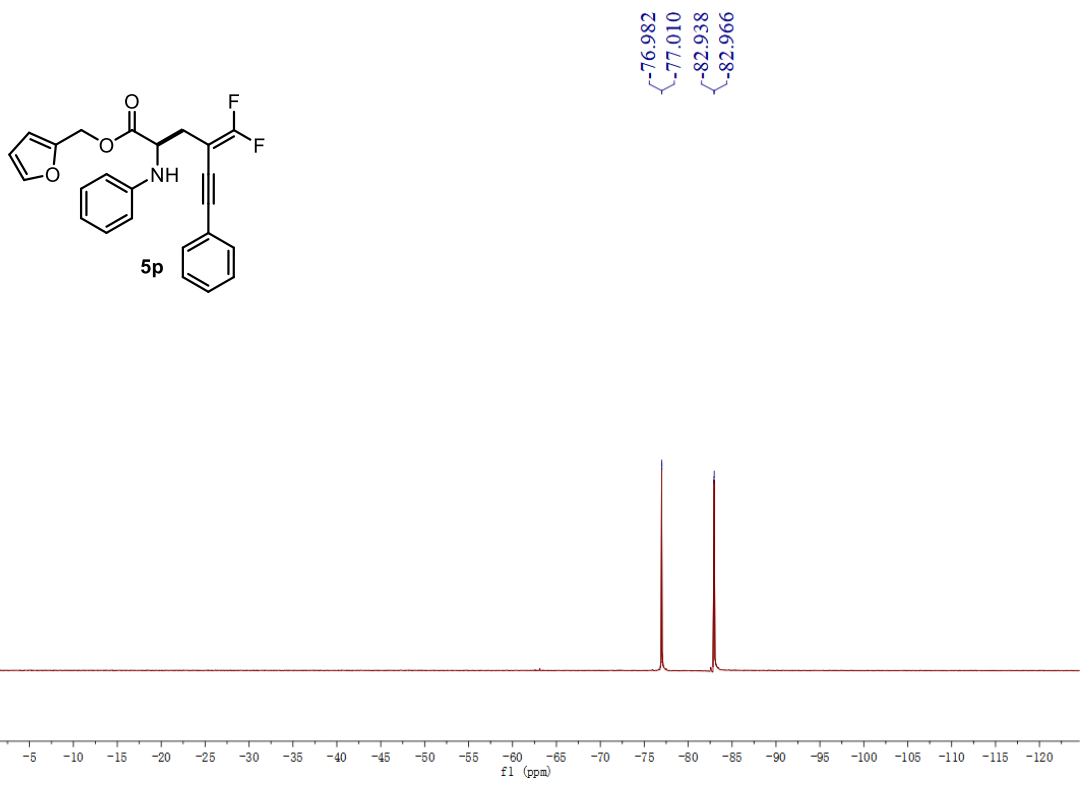


^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5p (Chloroform-d)

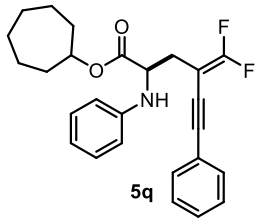


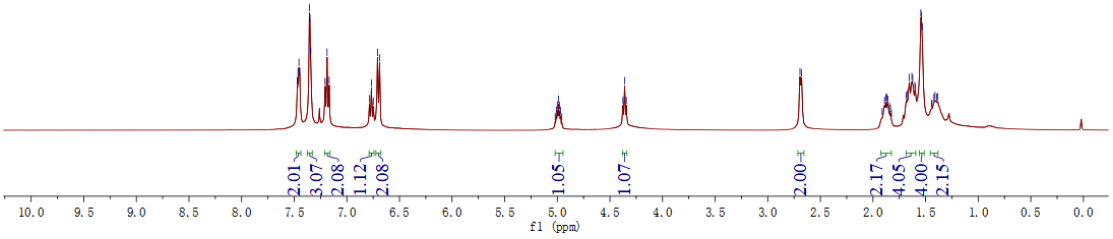


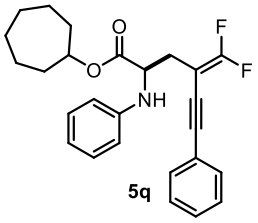

172.535
162.691
159.757
159.731
148.869
146.259
143.594
131.610
129.492
128.489
118.821
113.825
111.198
110.716
94.517
94.460
94.402
80.292
75.319
75.140
74.980
74.800
59.039
55.385
30.872
O
O
NH
F
F
5p
131.610
129.492
128.766
128.489
122.634
118.821
80.369
80.326
80.292
80.251
f1 (ppm)
f1 (ppm)

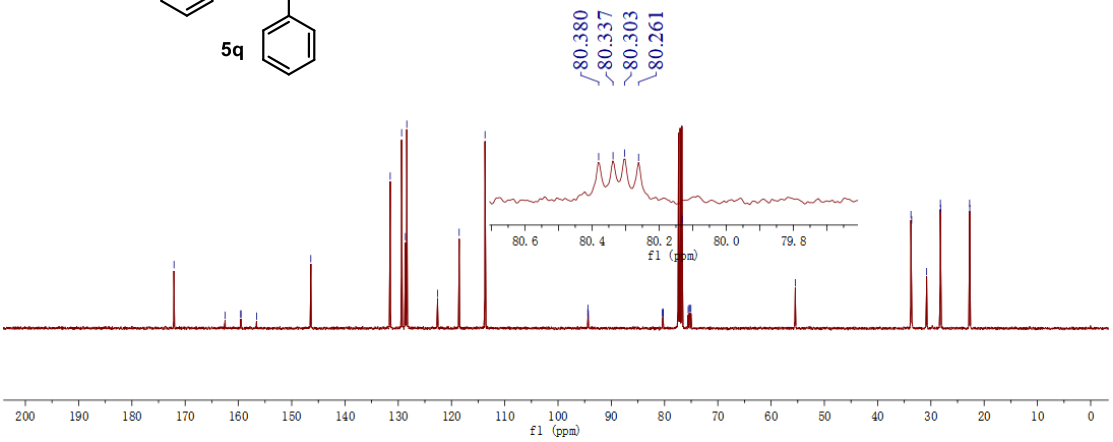

76.982
77.010
82.938
82.966
O
O
NH
F
F
5p
f1 (ppm)

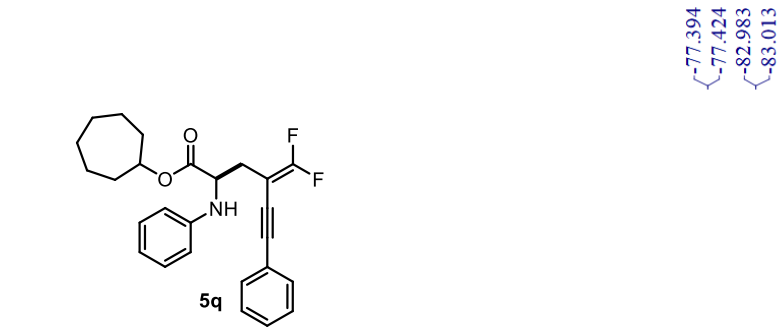
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5q (Chloroform-d)

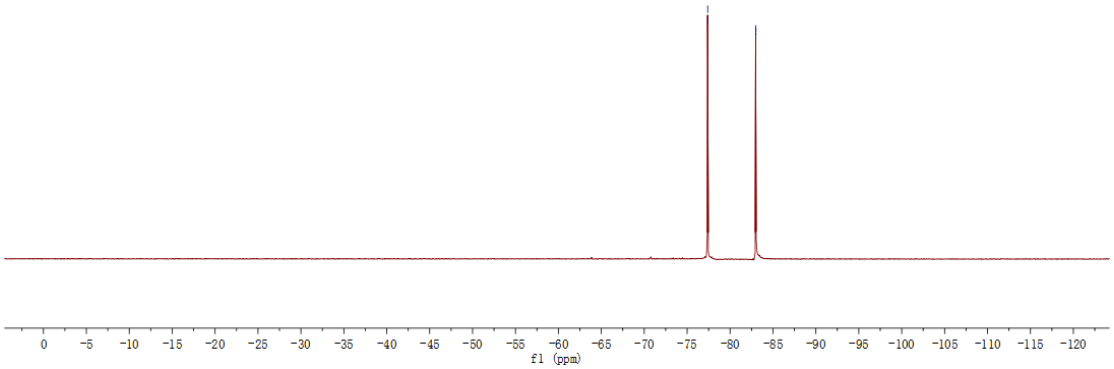




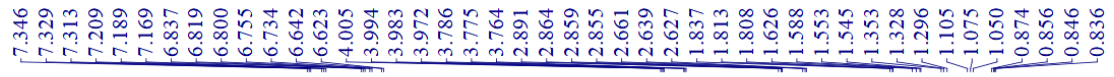


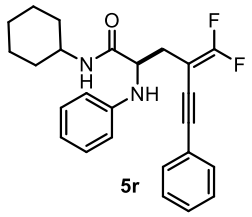


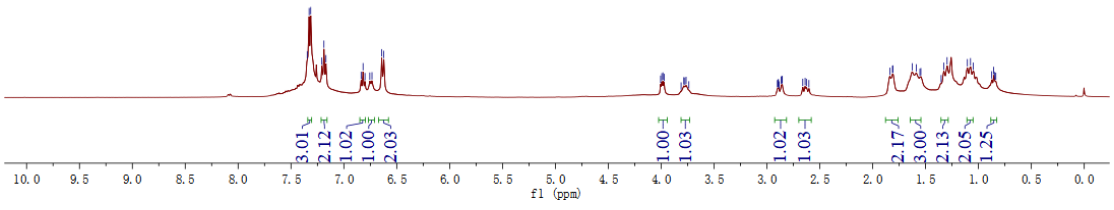


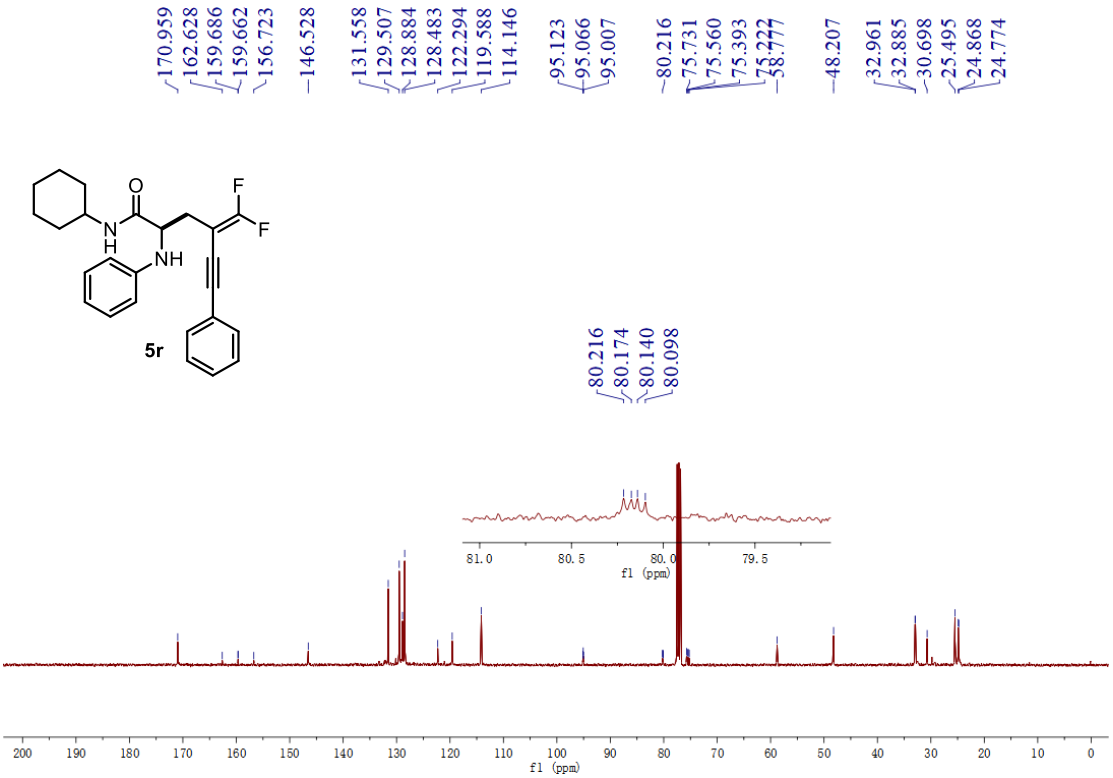


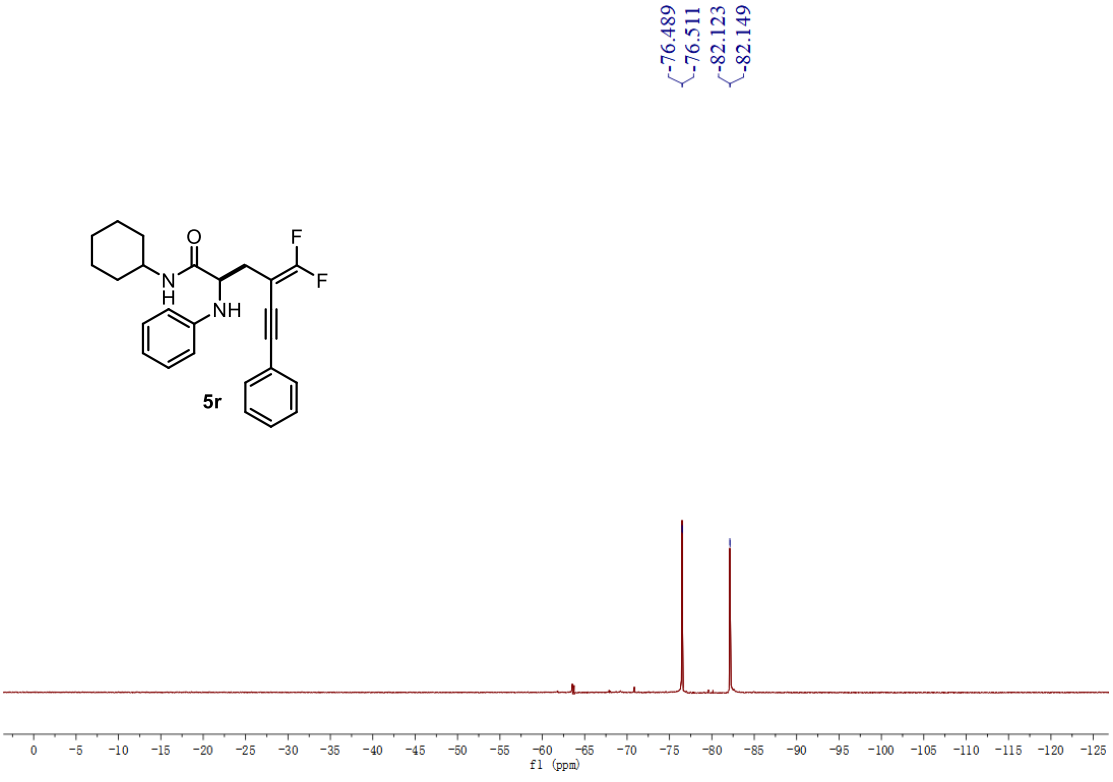
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5r (Chloroform-d)



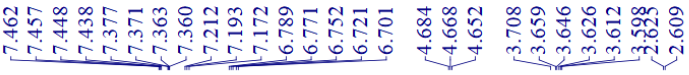


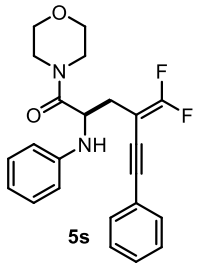


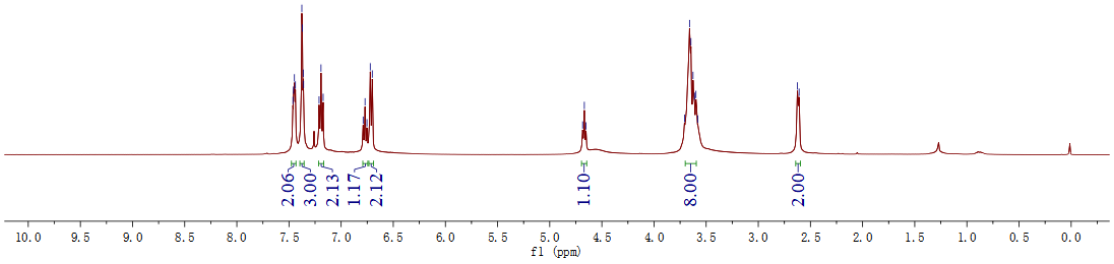

170.959
162.628
159.686
159.662
156.723
146.528
131.558
129.507
128.884
128.483
122.294
119.588
114.146
95.123
95.066
95.007
80.216
75.731
75.560
75.393
75.222
58.777
48.207
32.961
32.885
30.698
25.495
24.868
24.774
5r
80.216
80.174
80.140
80.098
81.0
80.5
80.0
79.5
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

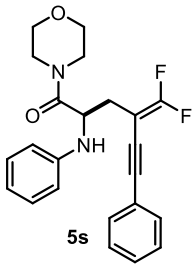

-76.489
-76.511
-82.123
-82.149
5r
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
f1 (ppm)

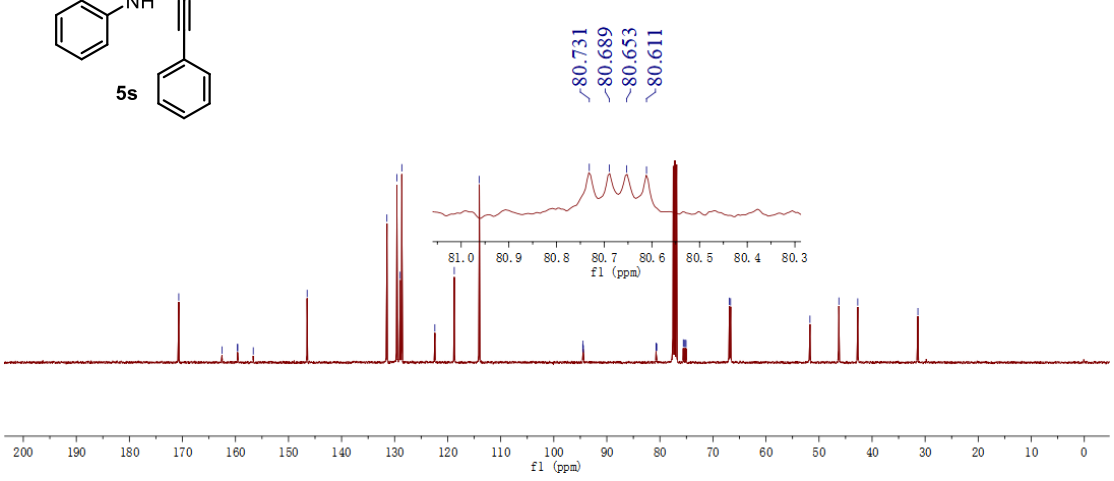
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5s (Chloroform-d)

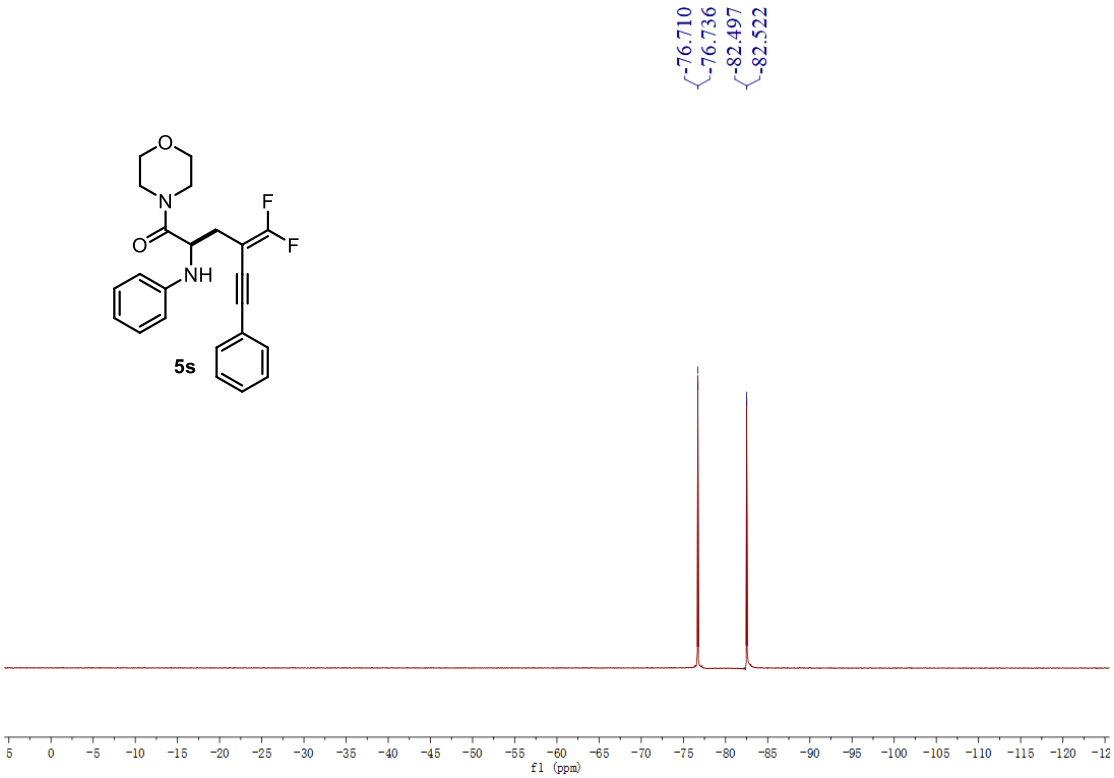




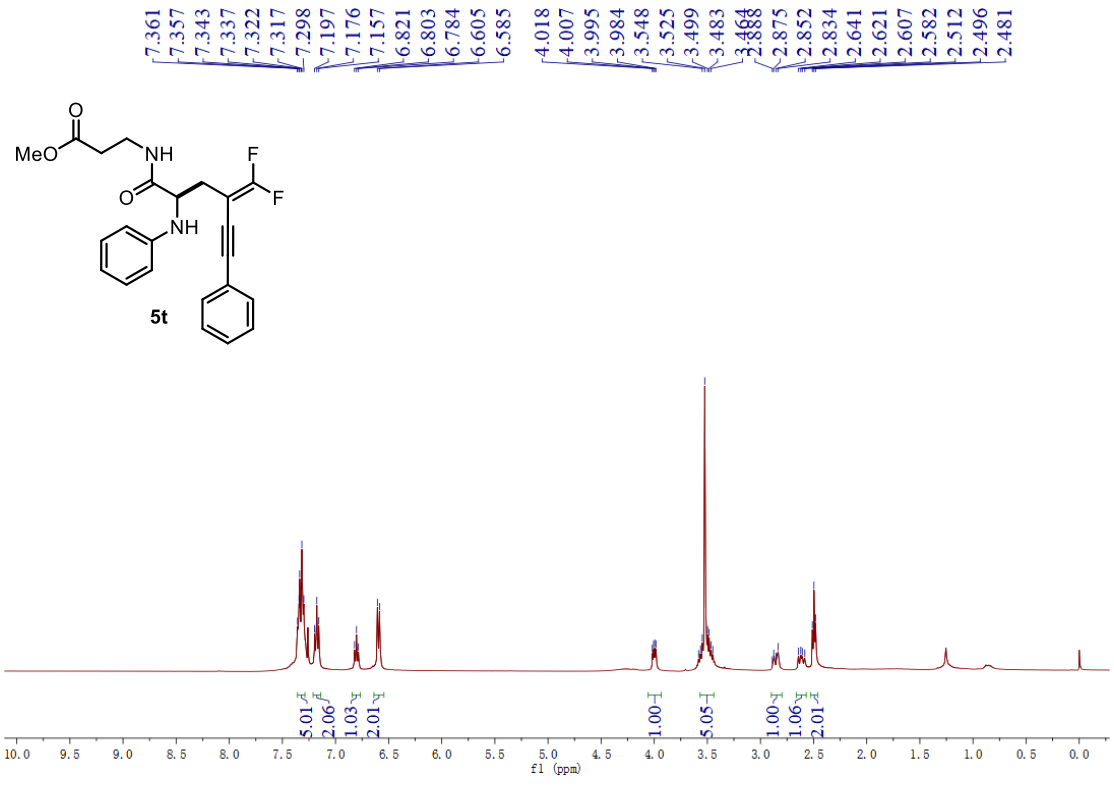


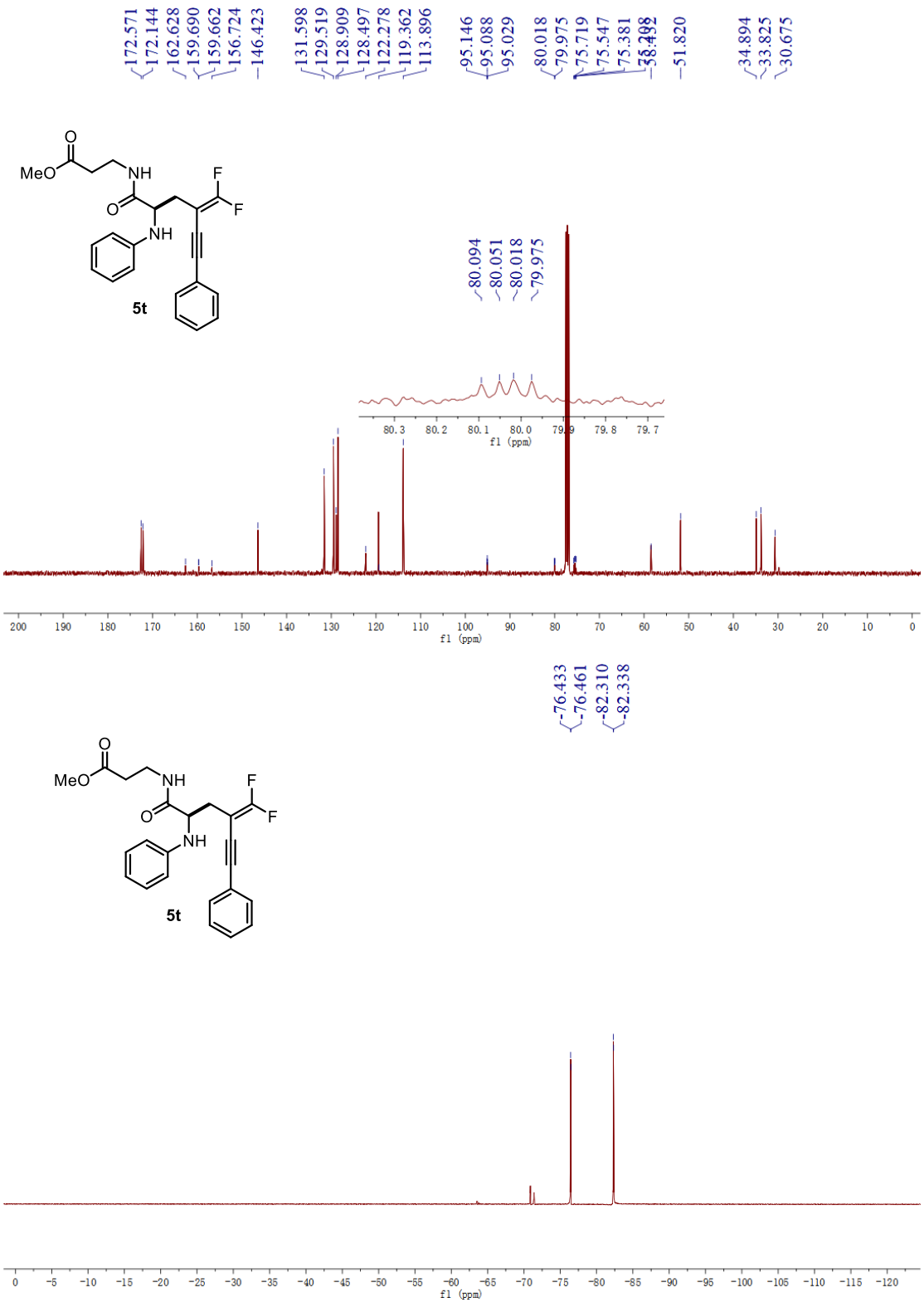




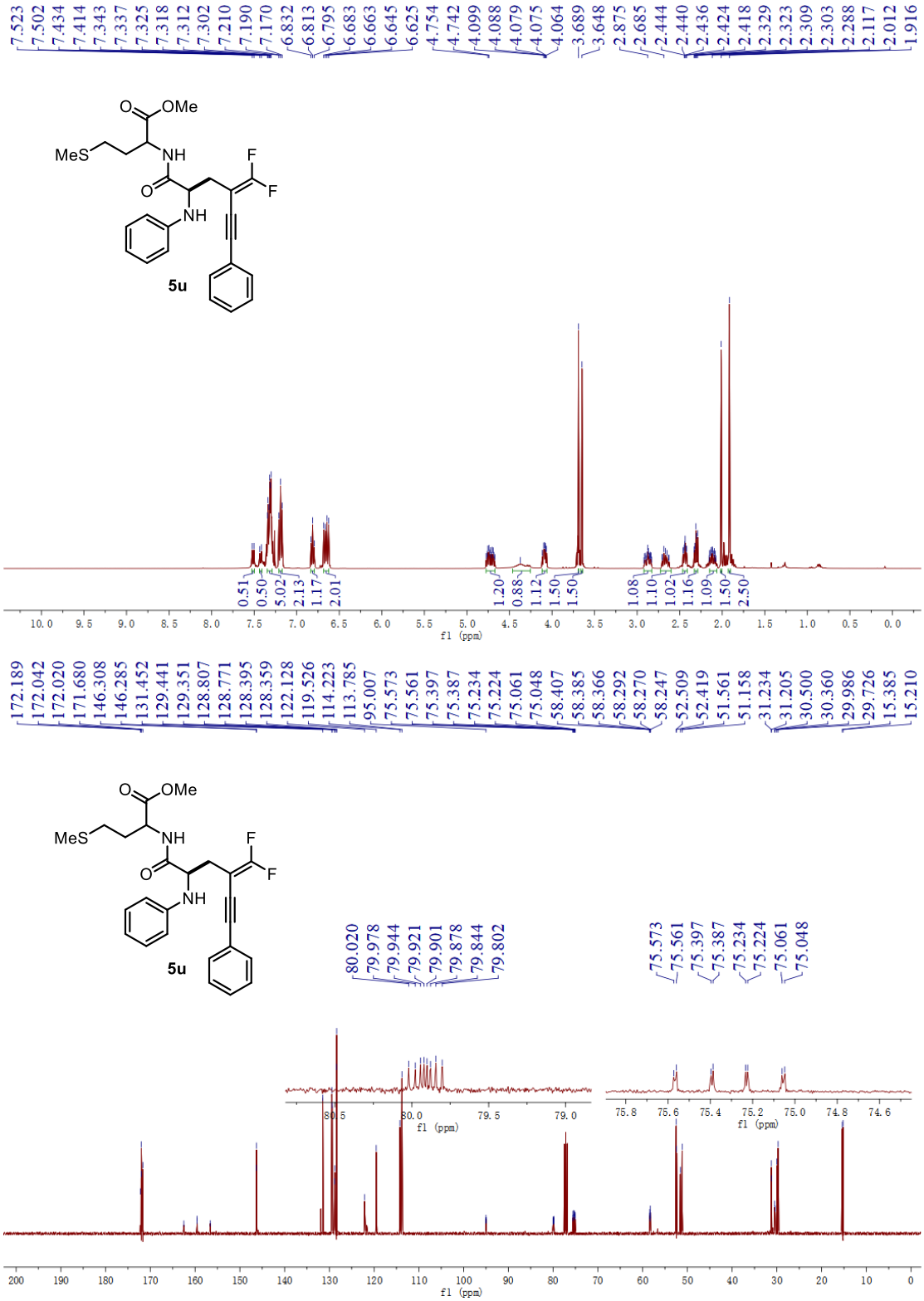


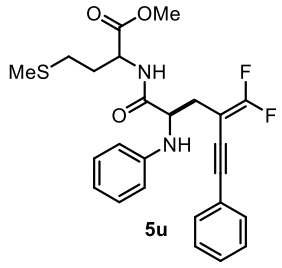
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5t (Chloroform-d)

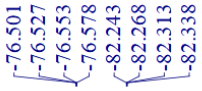


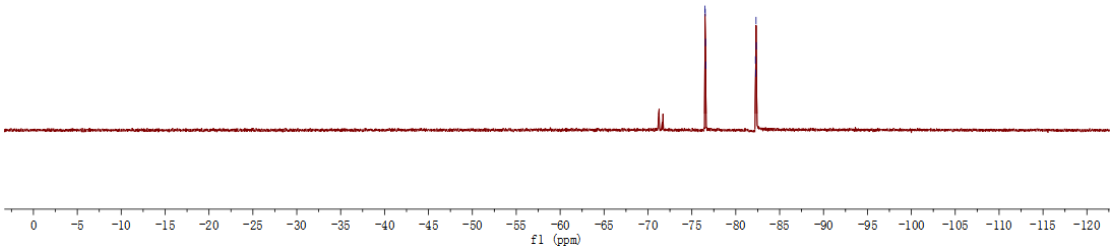

172.571
172.144
162.628
159.690
159.662
156.724
146.423
131.598
129.519
128.909
128.497
122.278
119.362
113.896
95.146
95.088
95.029
80.018
79.975
75.719
75.547
75.381
51.820
34.894
33.825
30.675
MeO
NH
O
F
F
NH
5t
80.094
80.051
80.018
79.975
f1 (ppm)
-76.433
-76.461
-82.310
-82.338
f1 (ppm)

^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5u (Chloroform-d)

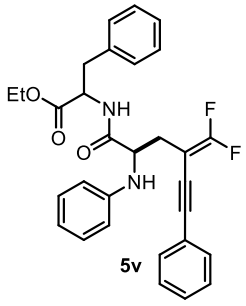


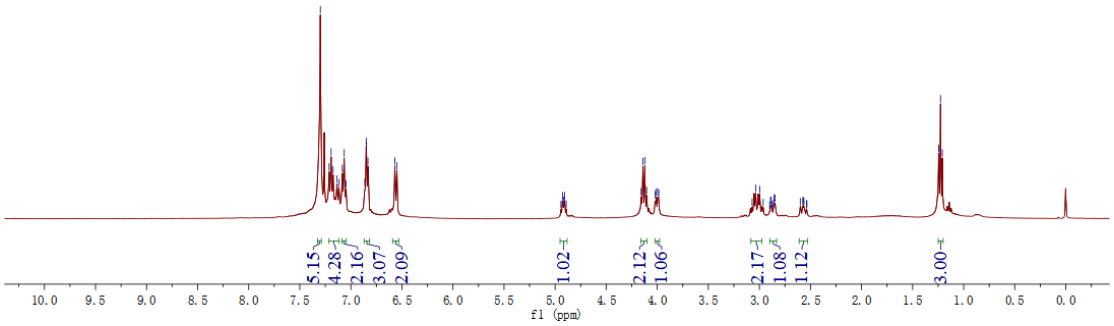


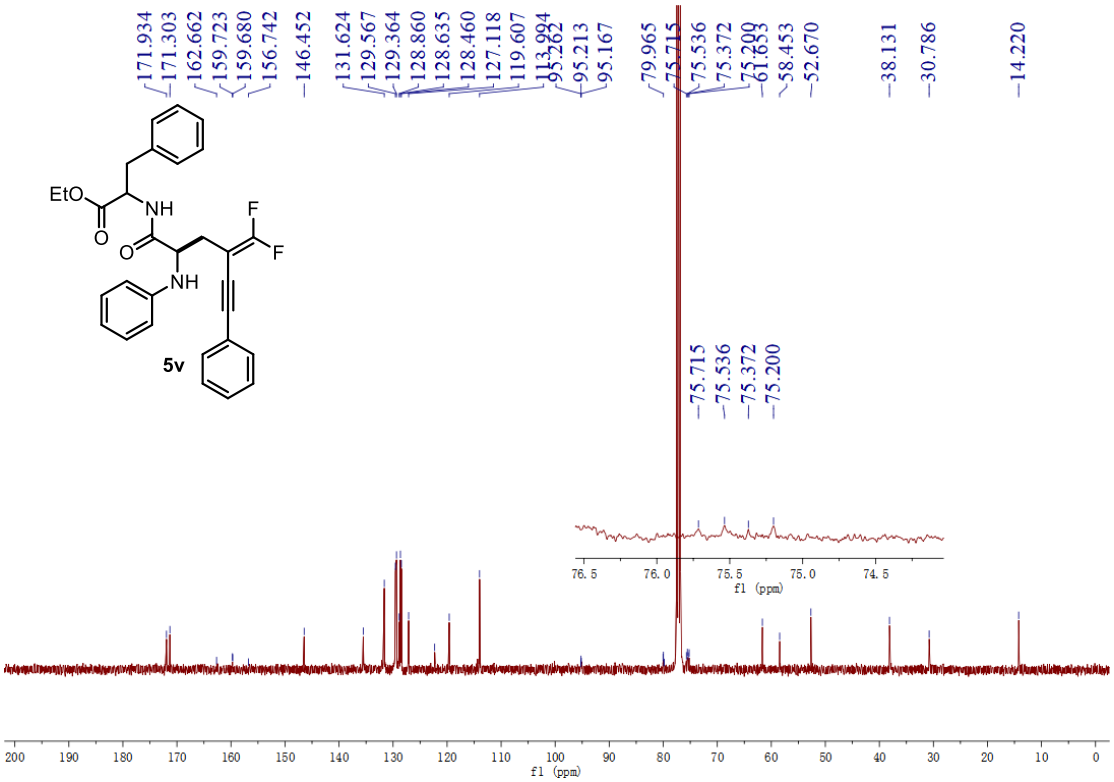


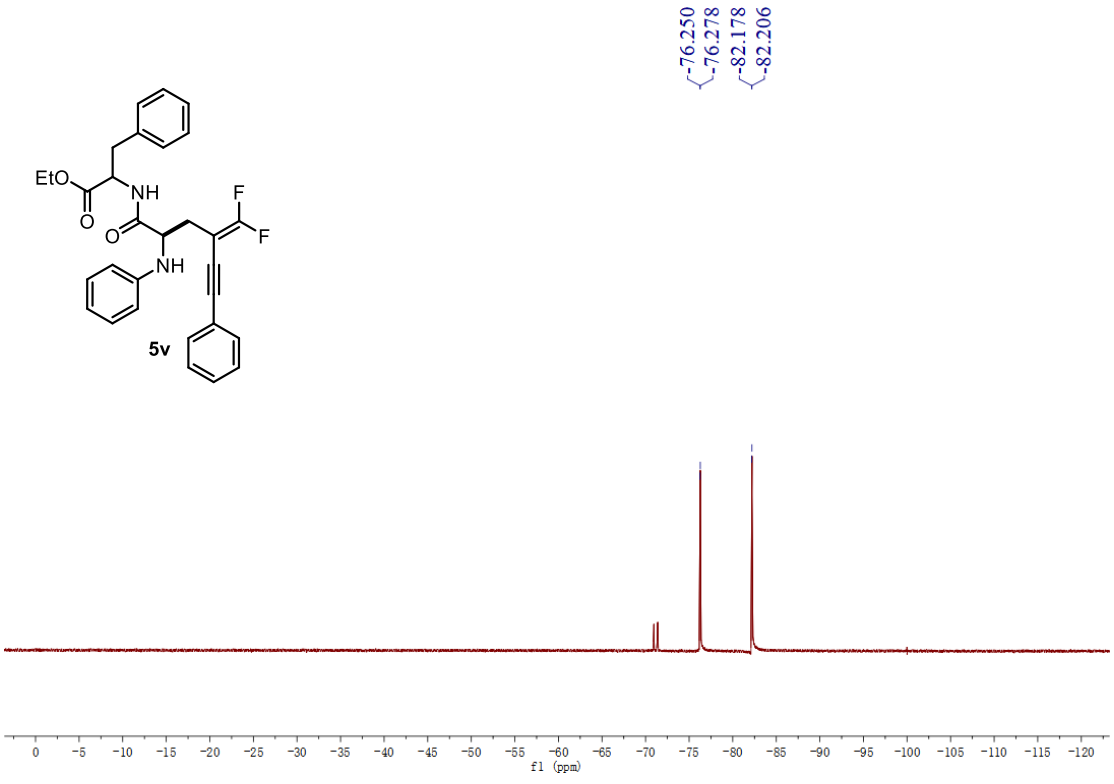


^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5v (Chloroform-d)

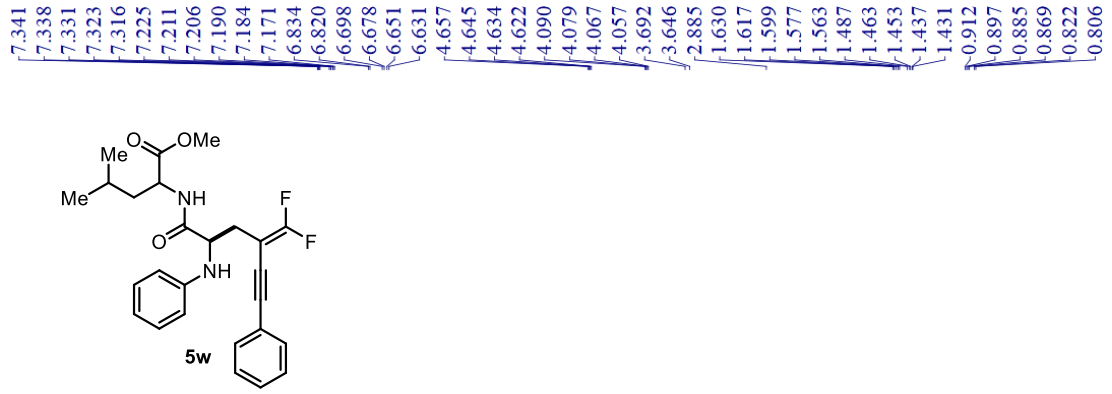


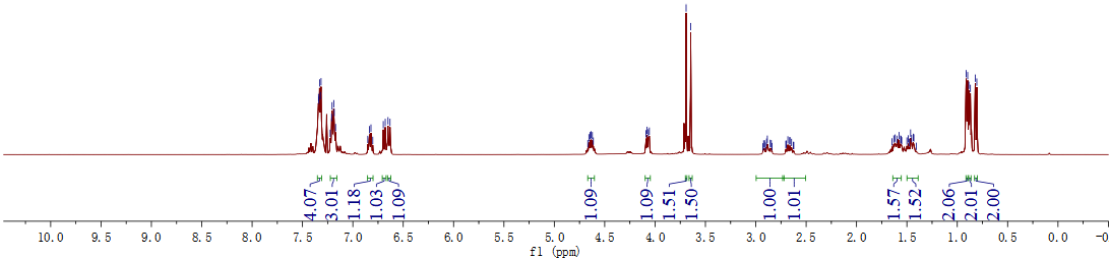


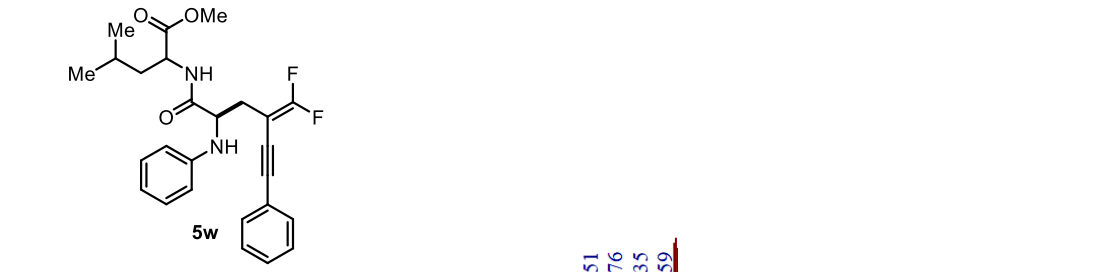

171.934
171.303
162.662
159.723
159.680
156.742
146.452
131.624
129.567
129.364
128.860
128.635
128.460
127.118
119.607
113.994
95.262
95.213
95.167
79.965
75.715
75.536
75.372
75.200
61.653
58.453
52.670
38.131
30.786
14.220
EtO
NH
O
F
F
NH
5v
f1 (ppm)

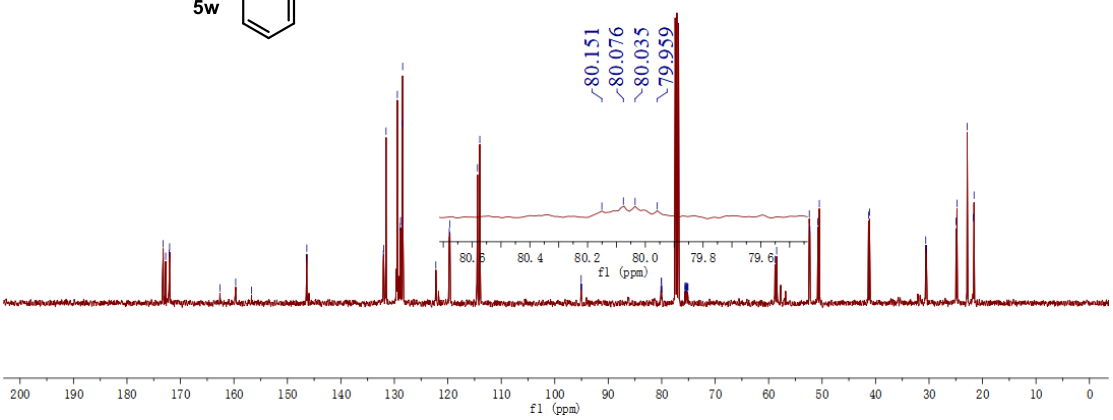

-76.250
-76.278
-82.178
-82.206
EtO
NH
O
F
F
NH
5v
f1 (ppm)

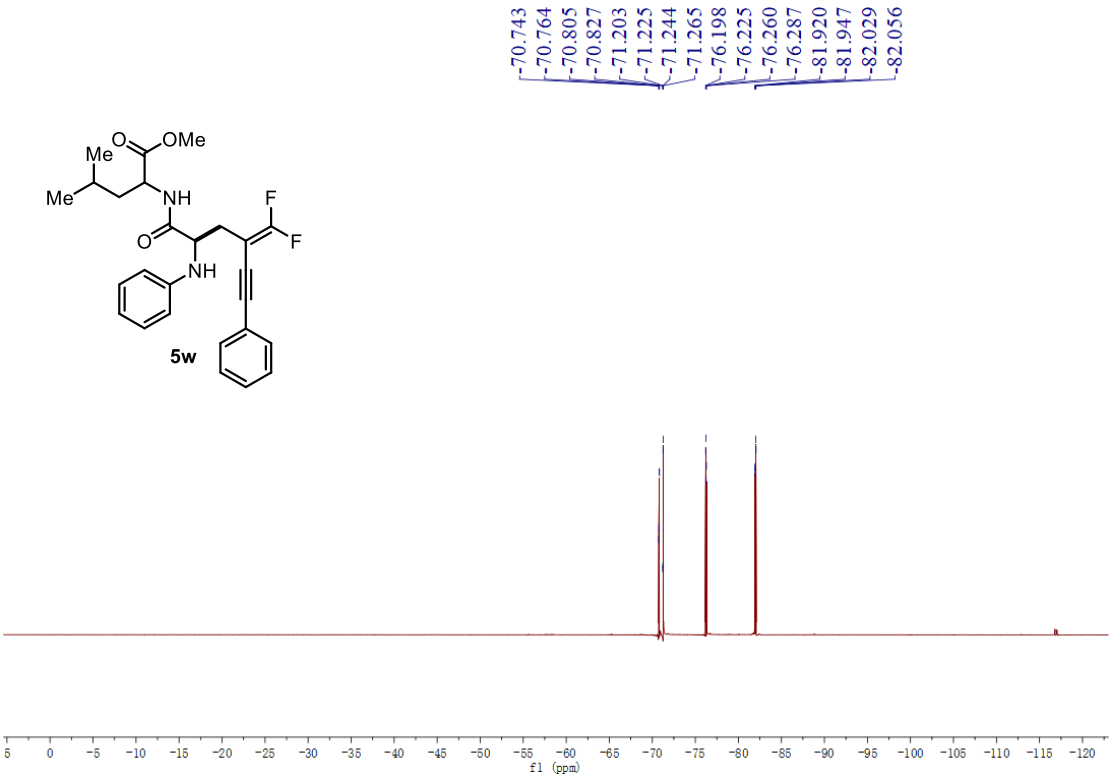
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 5w (Chloroform-d)



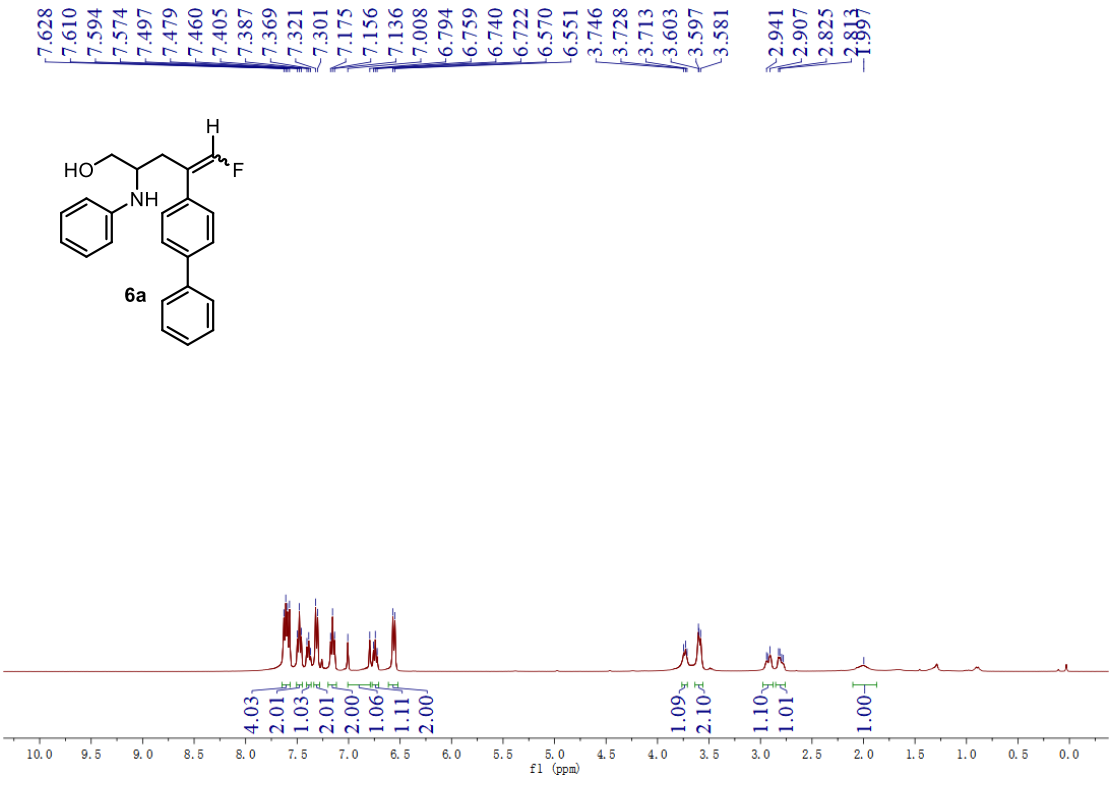


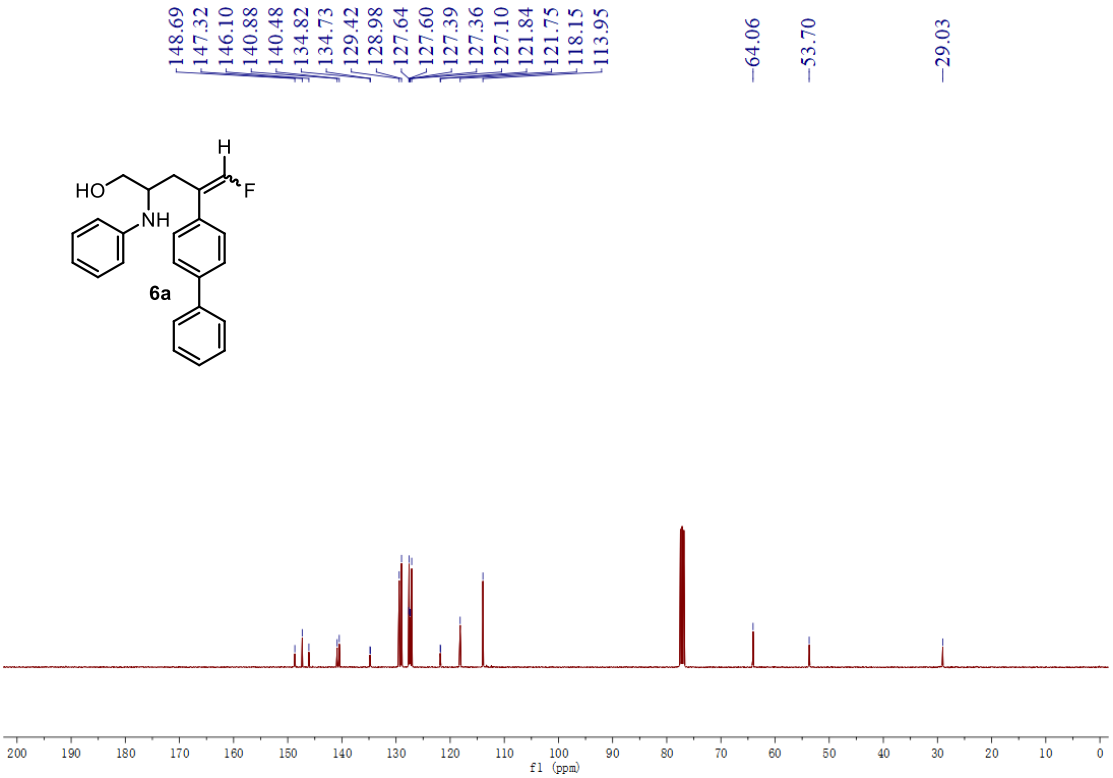


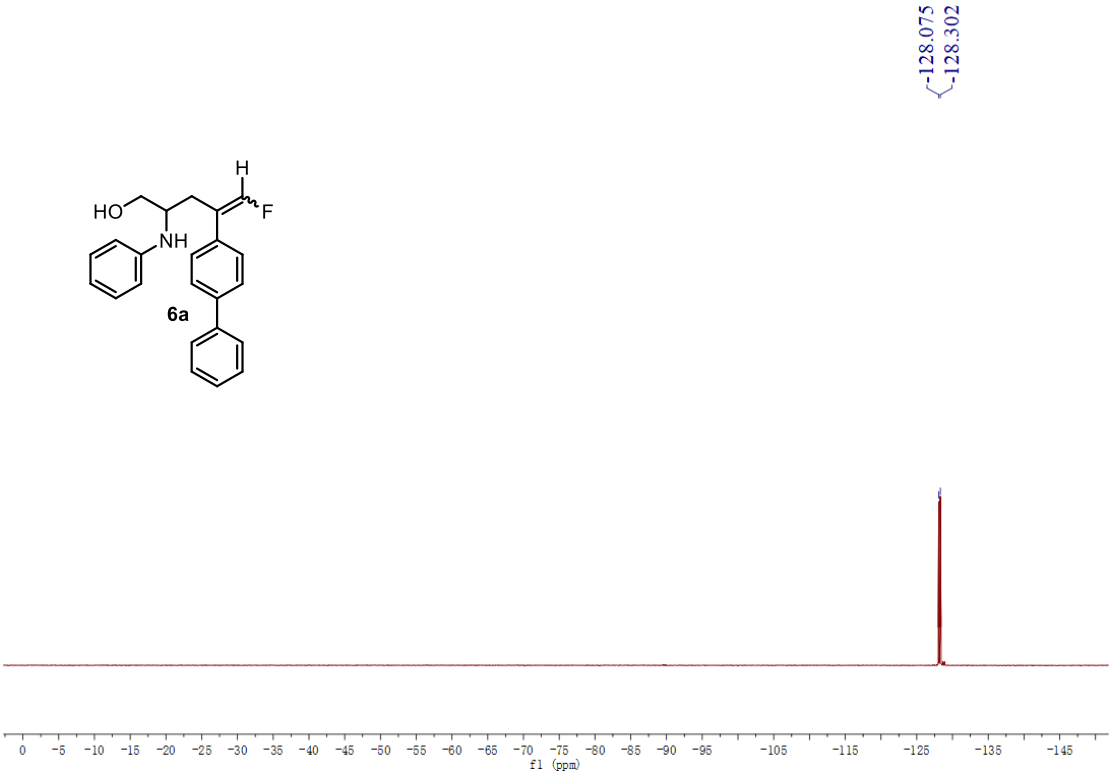




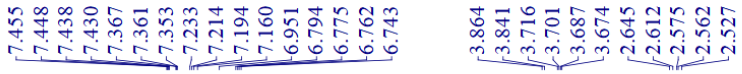
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 6a (Chloroform-d)

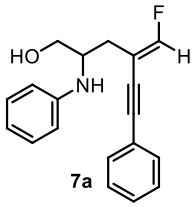


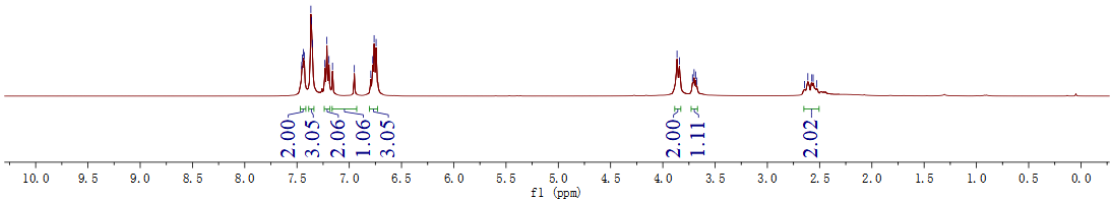

148.69
147.32
146.10
140.88
140.48
134.82
134.73
129.42
128.98
127.64
127.60
127.39
127.36
127.10
121.84
121.75
118.15
113.95
64.06
53.70
29.03
H
HO
F
NH
6a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

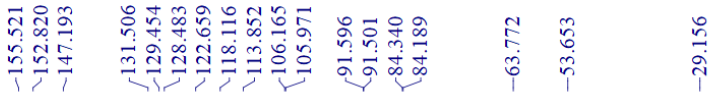

-128.075
-128.302
H
HO
F
NH
6a
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145
f1 (ppm)

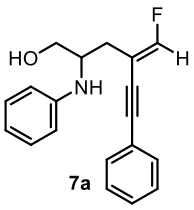
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 7a (Chloroform-d)

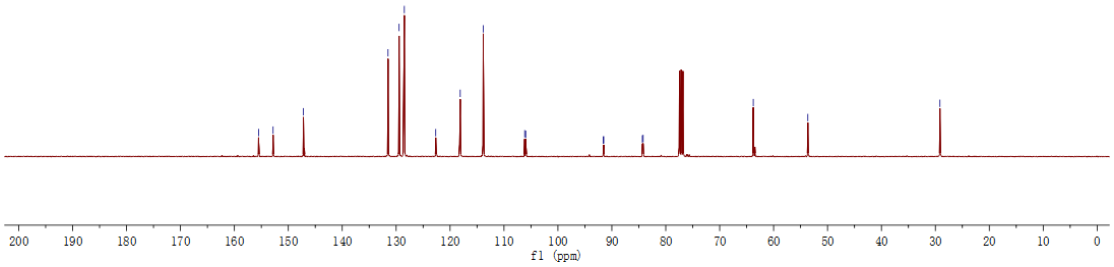


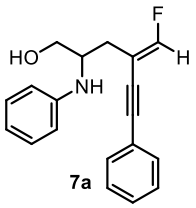




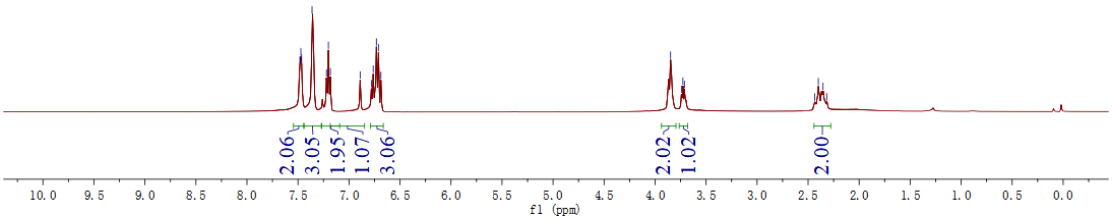


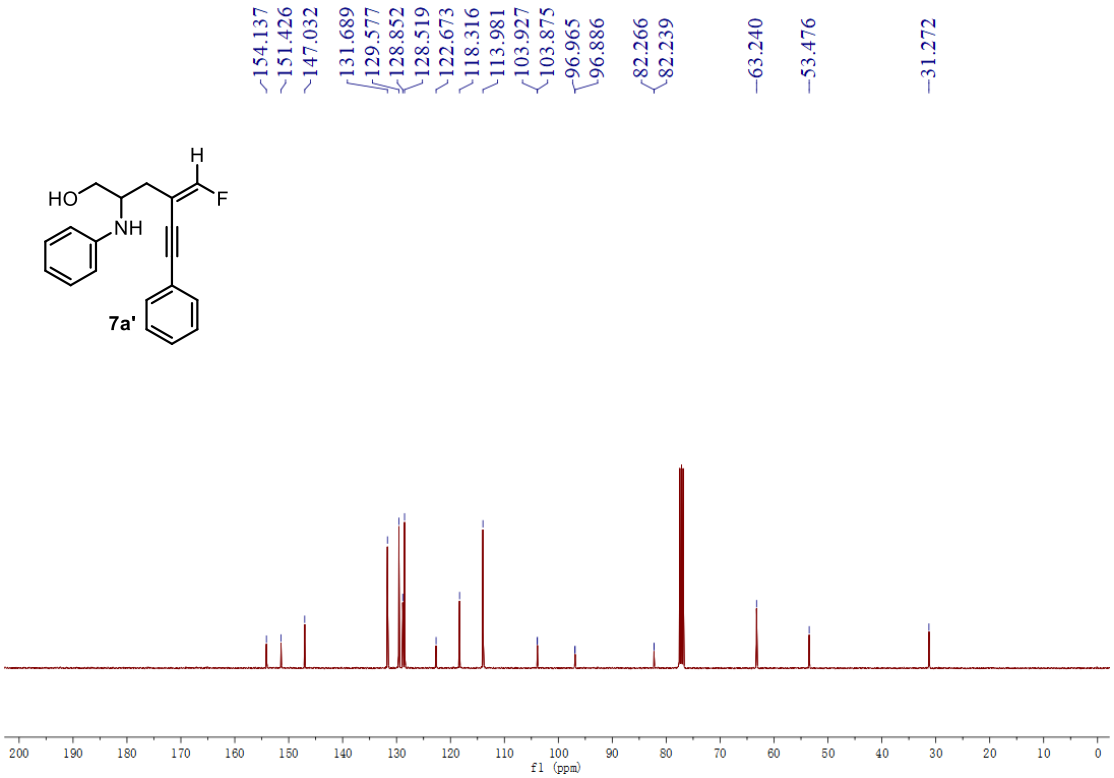


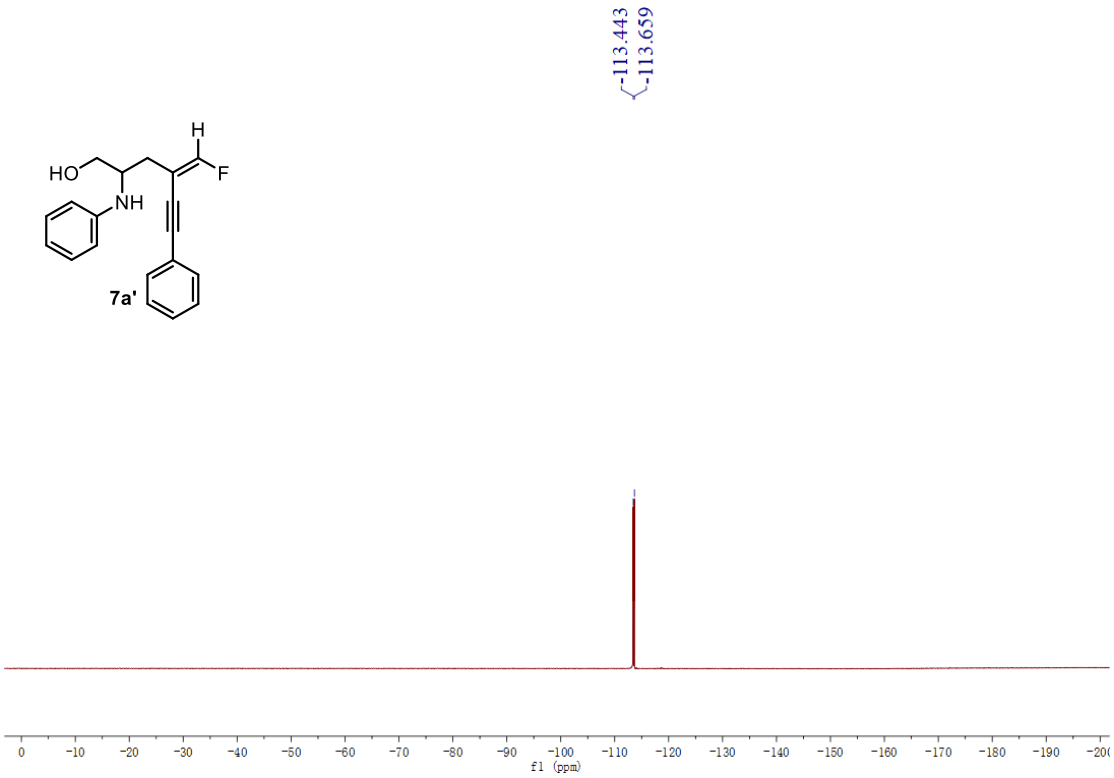




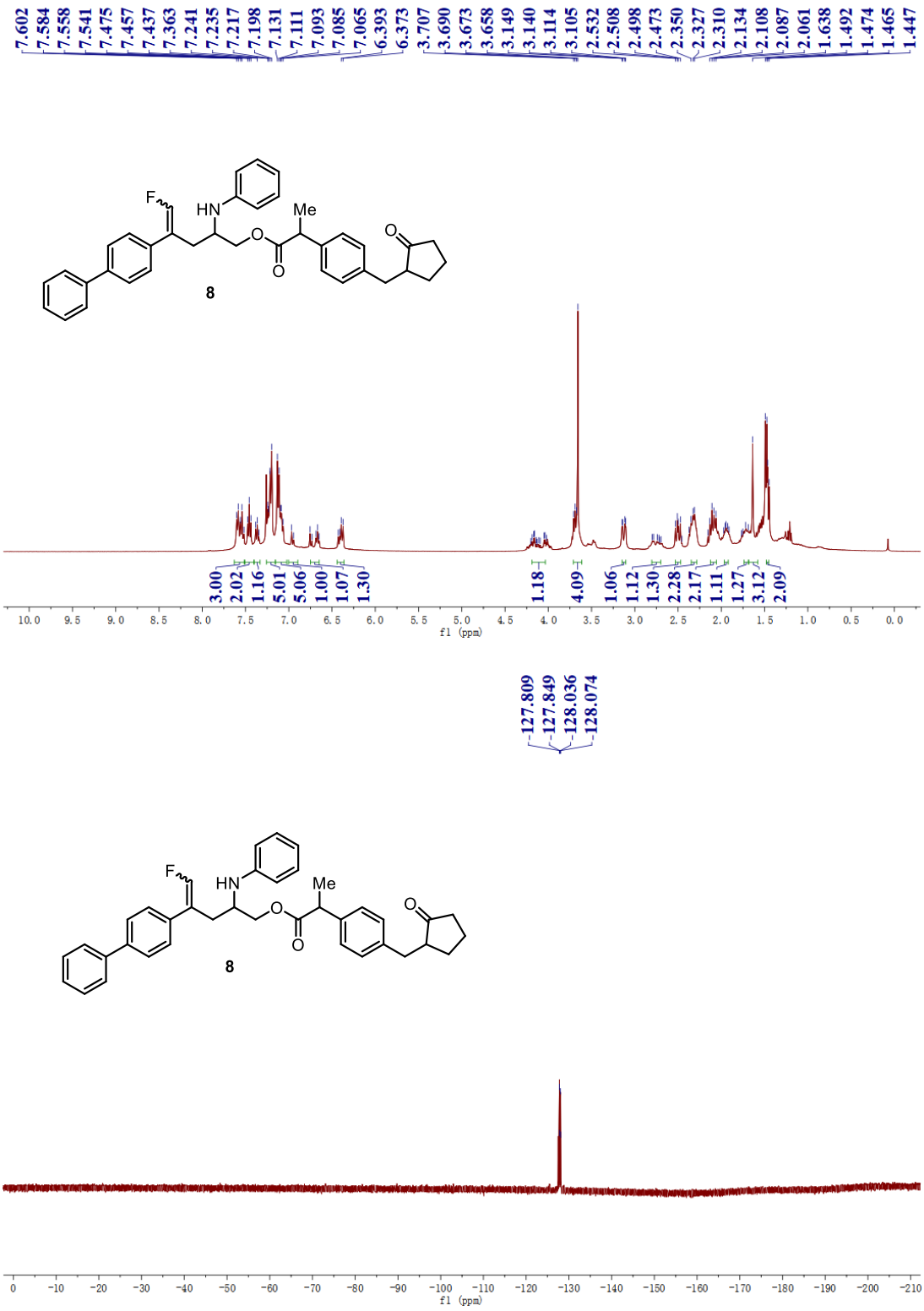
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 7a' (Chloroform-d)

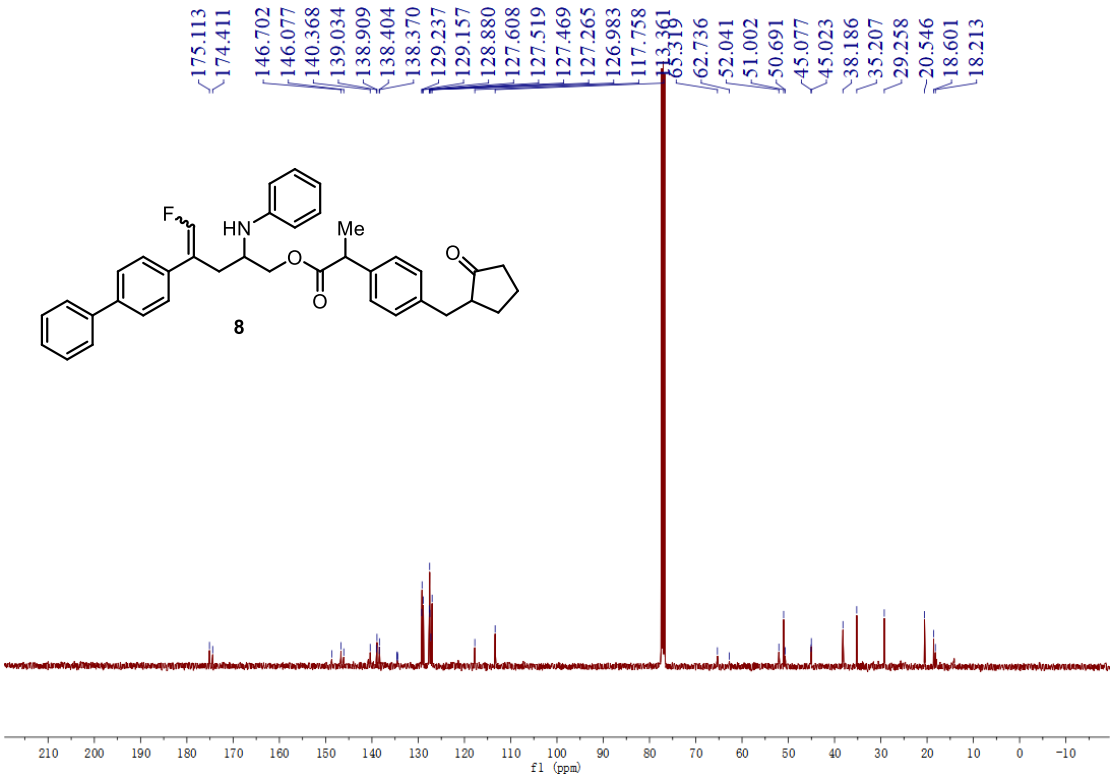



154.137
151.426
147.032
131.689
129.577
128.852
128.519
122.673
118.316
113.981
103.927
103.875
96.965
96.886
82.266
82.239
63.240
53.476
31.272
HO
NH
H
F
7a'
f1 (ppm)

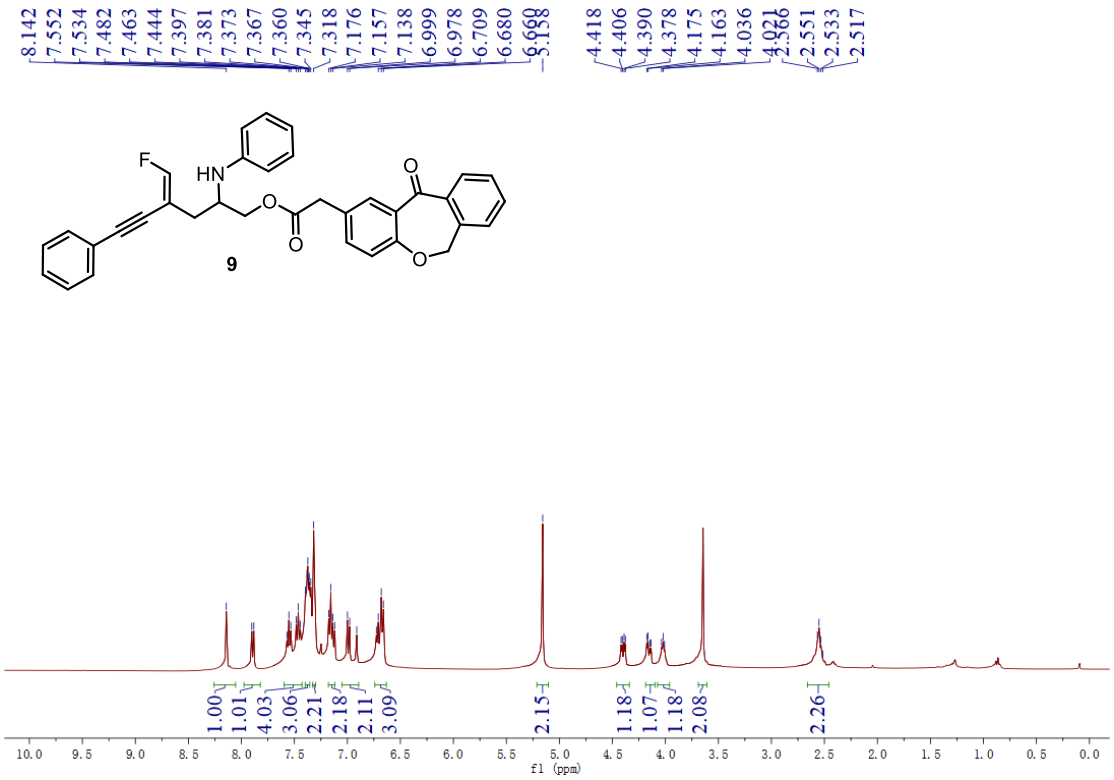

-113.443
-113.659
HO
NH
H
F
7a'
f1 (ppm)

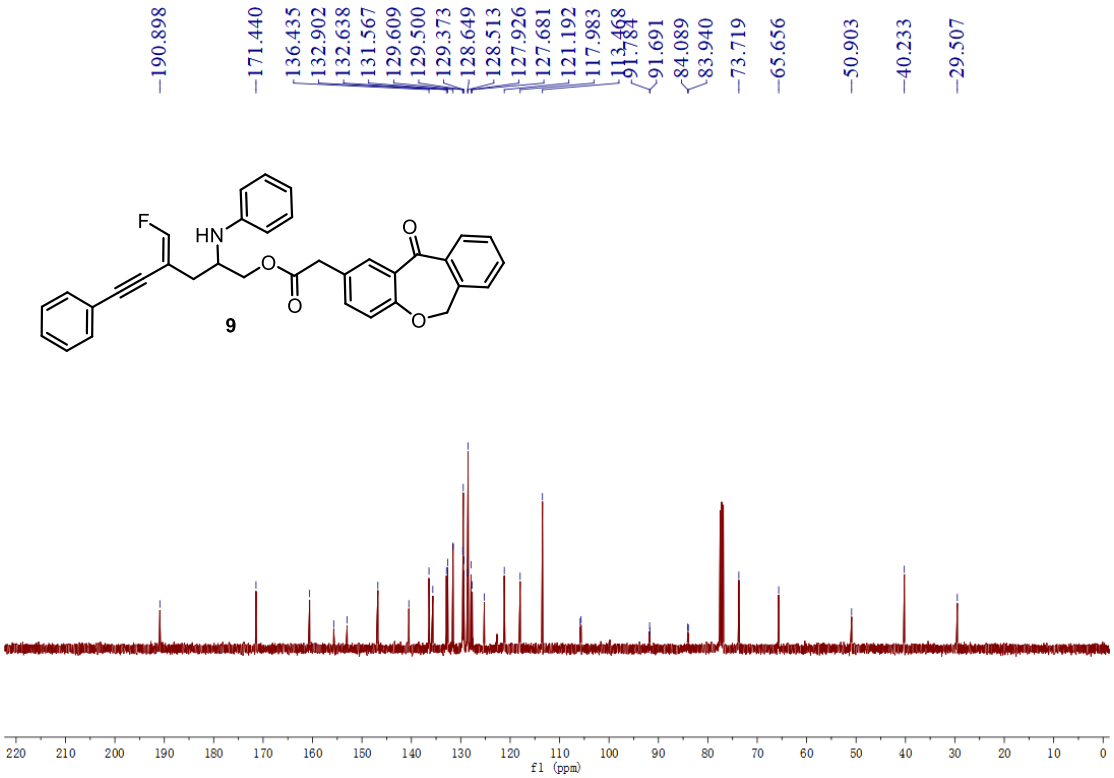
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 8 (Chloroform-d)

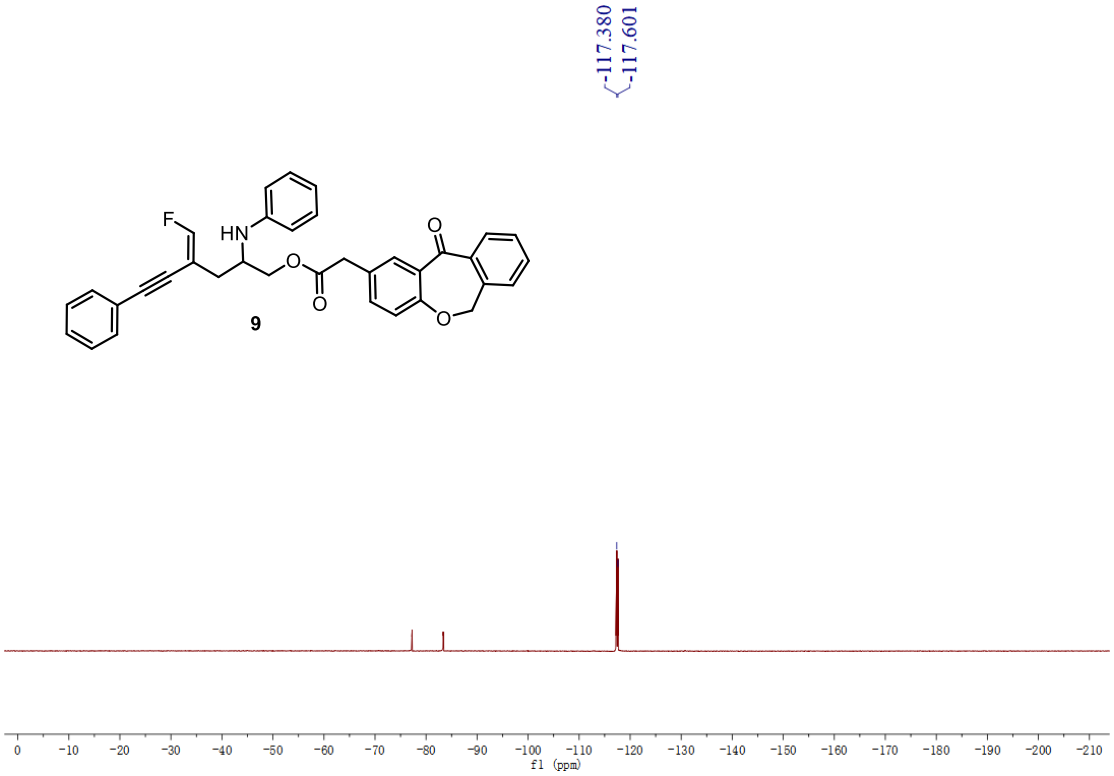




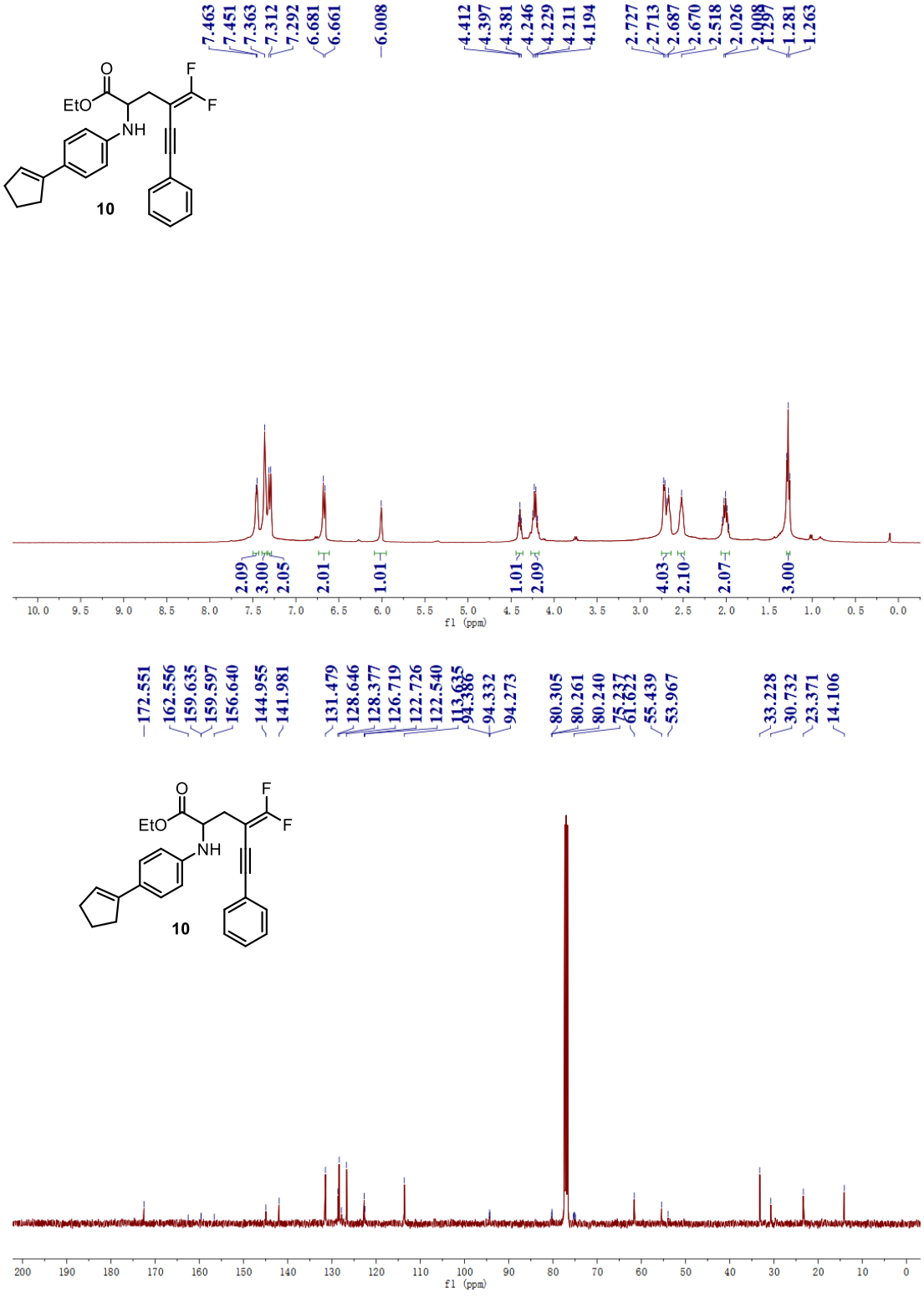
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 9 (Chloroform-d)

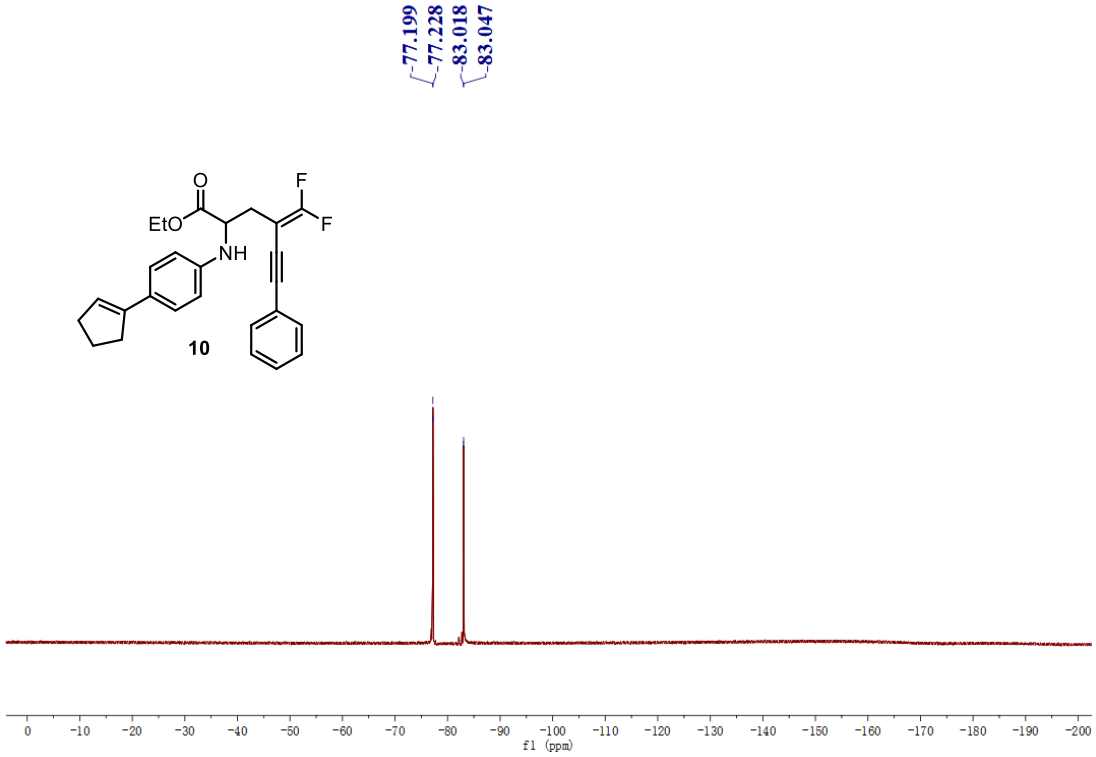



190.898
171.440
136.435
132.902
132.638
131.567
129.609
129.500
129.373
128.649
128.513
127.926
127.681
121.192
117.983
113.468
91.784
91.691
84.089
83.940
73.719
65.656
50.903
40.233
29.507
F
HN
O
O
O
O
9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

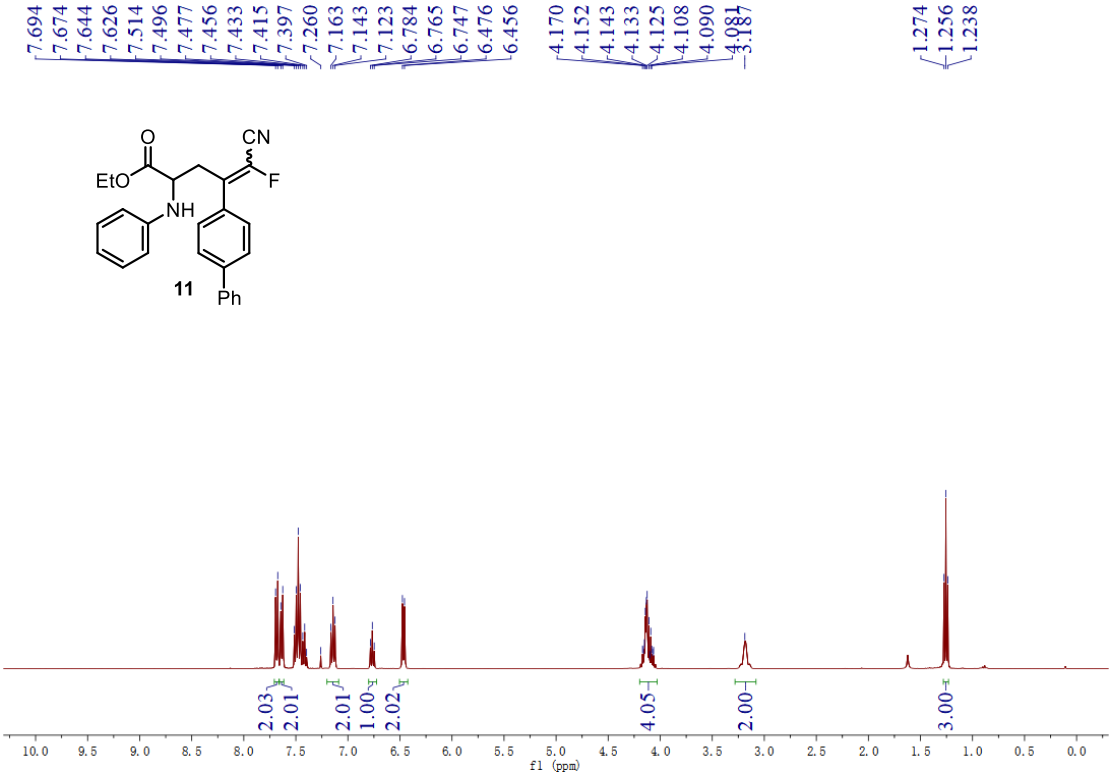

-117.380
-117.601
F
HN
O
O
O
O
9
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

^{1}H, ^{13}C NMR and ^{19}F spectra for compound 10 (Chloroform-d)

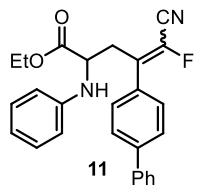




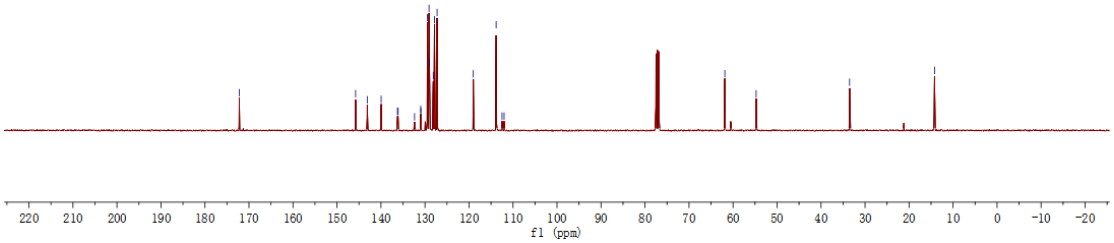
^{1}H, ^{13}C NMR and ^{19}F spectra for compound 11 (Chloroform-d)



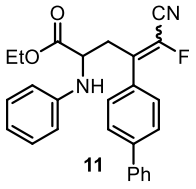

172.204
145.769
143.118
139.959
136.252
136.104
132.371
130.969
130.937
129.457
129.082
128.976
128.117
127.856
127.244
119.023
113.832
112.488
112.020
61.862
54.750
33.511
14.206


O
CN
EtO
F
NH
Ph

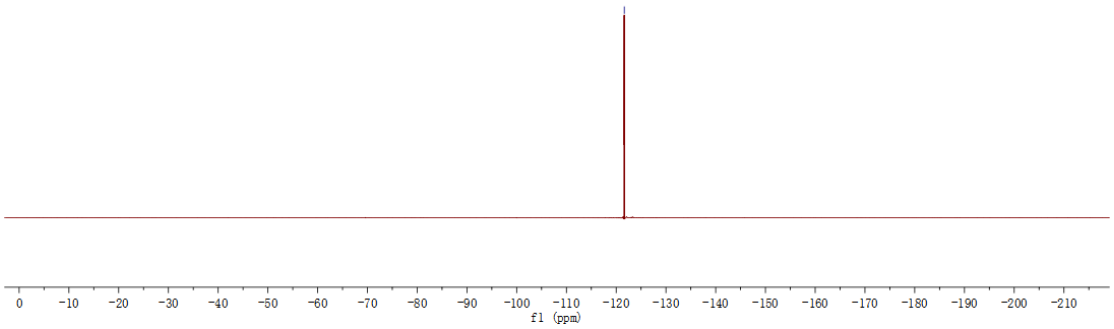
11


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-121.630


O
CN
EtO
F
NH
Ph

11


0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)