Supporting Information

Photoinduced diversity-oriented synthesis of α-ketoester β-enamino esters, 3,3-difluoro-4-pyrrolin-2-ones, and 3-fluoro-3-pyrrolin-2-ones from bromodifluoroacetates and β-enamino esters

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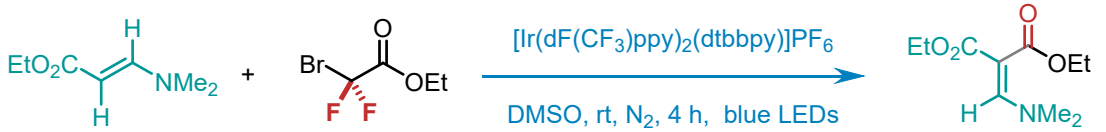
1. General information

All ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometer (400/100/376 MHz). Chemical shifts (δ) are given in parts per million relative to TMS or the residual of solvent signal (TMS, δ_H = 0.00 ppm; $CDCl_3$, δ_H = 7.26 ppm, δ_C = 77.0 ppm), and the coupling constants are given in Hertz (Hz). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. High resolution mass spectroscopy data of the product were collected on an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS (ESI). Crystallographic data of products **3q** and **5e** were collected on Bruker SMART APEX II (Mo target, voltage 50 KV, current 30 mA). The chemicals and solvents were purchased from commercial suppliers either Aldrich (USA), or Shanghai Chemical Company (P. R. China). Products were purified by flash chromatography on 200–300 mesh silica gels, SiO_2. The substrates enamines[1-9] and bromodifluoroacetates[10-12] were prepared according to previously described methods.

2. General procedures for the synthesis of products

2.1 General procedure for the synthesis of product 3 in 0.2 mmol scale (3a as an example)

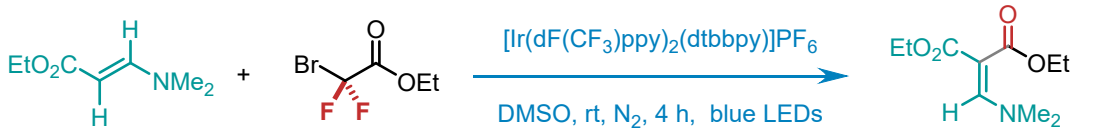


1a **2a** **3a**, 32.6 mg, 67%

A 10 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with ethyl (*E*)-3-(dimethylamino)acrylate **1a** (28.3 mg, 0.2 mmol), bromodifluoroacetate **2a** (121.8 mg, 0.6 mmol), $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (2.24 mg, 0.002 mmol, 1 mol%) and dimethyl sulfoxide (DMSO, 2.0 mL). The reaction vessel was exposed to blue LEDs (450–455 nm, 2×3 W) irradiation at room

temperature in N_2 with stirring for 4 h. After completion of the reaction, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether/ethyl acetate = 10:1~5:1, V/V) to give the corresponding product **3a** (32.6 mg, 67%).

2.2 General procedure for the synthesis of product 3a in 5.0 mmol scale



1a **2a** **3a**, 742 mg, 69%

A 100 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with ethyl (*E*)-3-(dimethylamino)acrylate **1a** (707.5 mg, 5.0 mmol), bromodifluoroacetate **2a** (3045 mg, 15.0 mmol), $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (28.05 mg, 0.025 mmol, 0.5 mol%) and dimethyl sulfoxide (DMSO, 50.0 mL). The reaction vessel was exposed to blue LEDs irradiation at room temperature in N_2 with stirring for 4 h. After completion of the reaction, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether : ethyl acetate = 2:1, V/V) to give the corresponding product **3a** (742 mg, 69%).

2.3 General procedure for the synthesis of product 4 in 0.2 mmol scale (4a as an example)

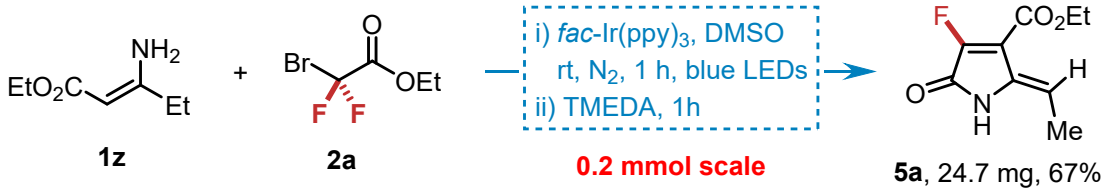
1n **2a** **4a**, 27.1 mg, 71%

A 10 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with methyl (*Z*)-3-aminobut-2-enoate **1n** (23.0 mg, 0.2 mmol), bromodifluoroacetate **2a** (81.2 mg, 0.4 mmol), *fac*-Ir(ppy)$_3$ (1.31 mg, 0.002 mmol, 1 mol%) and dimethyl sulfoxide (DMSO, 2.0 mL). The reaction vessel was exposed to blue LEDs (450–455 nm, 2×3 W) irradiation at room temperature in N_2 with stirring for 1 h. After completion of the reaction, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether/ethyl acetate = 10:1~5:1, V/V) to give the corresponding product **4a** (27.1 mg, 71%).

2.4 General procedure for the synthesis of product 4a in 5.0 mmol scale

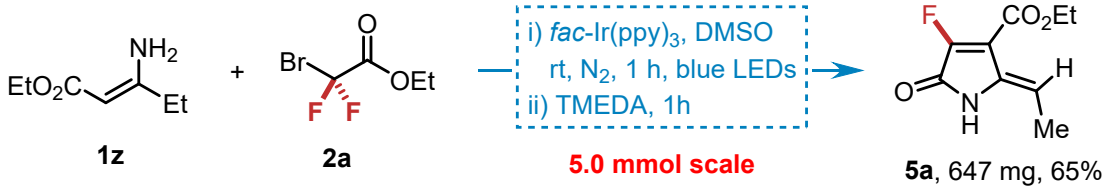
A 100 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with methyl (*Z*)-3-aminobut-2-enoate **1n** (575 mg, 5.0 mmol), bromodifluoroacetate **2a** (2030 mg, 10.0 mmol), *fac*-Ir(ppy)$_3$ (16.38 mg, 0.025 mmol, 0.5 mol%) and dimethyl sulfoxide (DMSO, 50.0 mL). The reaction vessel was exposed to blue LEDs irradiation at room temperature in N_2 with stirring for 1 h. After completion of the reaction, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether : ethyl acetate = 3:1, V/V) to give the corresponding product **4a** (593 mg, 62%).

2.5 General procedure for the synthesis of product 5 in 0.2 mmol scale (5a as an example)



A 10 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with ethyl (Z)-3-aminopent-2-enoate **1z** (28.6 mg, 0.20 mmol), bromodifluoroacetate **2a** (81.2 mg, 0.40 mmol), *fac*-Ir(ppy)$_3$ (1.31 mg, 0.002 mmol, 1 mol%) and dimethyl sulfoxide (DMSO, 2.0 mL). The reaction vessel was exposed to blue LEDs (450–455 nm, 2×3 W) irradiation at room temperature in N_2 with stirring for 1 h. After completion of the reaction (detected by TLC), TMEDA (23.2 mg, 0.2 mmol) is added and the reaction continues at room temperature for 1 h. Once the reaction is finished, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether/ethyl acetate = 10:1~5:1, V/V) to give the corresponding product **5a** (24.7 mg, 62%).

2.6 General procedure for the synthesis of product 5a in 5.0 mmol scale



A 100 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with ethyl (Z)-3-aminopent-2-enoate **1z** (715 mg, 5 mmol), bromodifluoroacetate **2a** (2030 mg, 10 mmol), *fac*-Ir(ppy)$_3$ (16.38 mg, 0.025 mmol, 0.5 mol%) and dimethyl sulfoxide (DMSO, 50 mL). The reaction vessel was exposed to blue LEDs irradiation at room temperature in N_2 with stirring for 1 h. After

completion of the reaction (detected by TLC), TMEDA (580 mg, 0.2 mmol) was added and the reaction was performed at room temperature for 1 h. Once the reaction was finished, the mixture was diluted with water and extracted with ethyl acetate, the organic layer was combined, dried over by anhydrous Na_2SO_4, and filtered, then concentrated to yield the crude product, which was further purified by flash chromatography (silica gel, petroleum ether : ethyl acetate = 3:1, V/V) to give the corresponding product **5a** (647 mg, 65%).

2.7 General photoreactor used in the reaction (Figure S1)

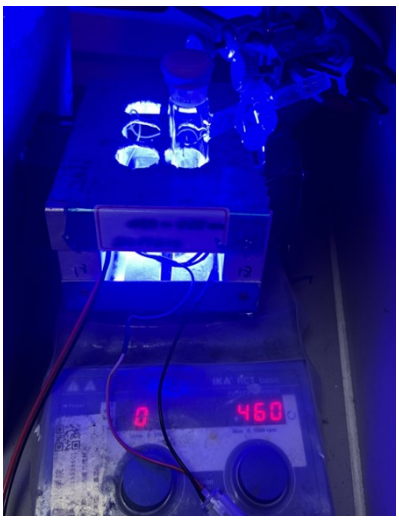
	Manufacturer: GeAo Chemical Company Model: 2×3 W, blue LEDs Broadband source: λ = 450–455 nm Material of the irradiation vessel: Borosilicate reaction tube Distance from the light source to the irradiation vessel: 3.0 cm No any filters

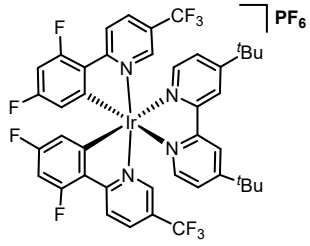
Figure S1. Photoreactor used in this research (2×3 W blue LEDs)

3. Optimization reaction conditions

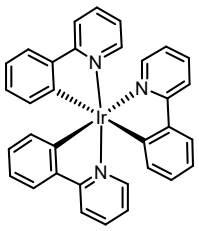
Table S1 Optimizing the reaction conditions for the formation of 3a[a]

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

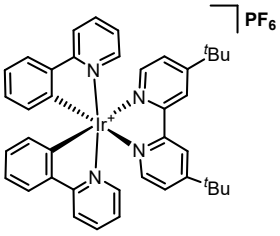
entry	solvent	photocatalyst (PC)	ratio of **1a**:**2a**	yield of **3a** (%)[b]
1	DMSO	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:2	50 (46)[c]
2	**DMSO**	**$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$**	**1a**:**2a = 1:3**	**70 (67)[c]**
3	DMSO	*fac*-$Ir(ppy)_3$	**1a**:**2a** = 1:3	30
4	DMSO	$[Ir(ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	trace
5	DMSO	4CzIPN	**1a**:**2a** = 1:3	15
6	DMSO	4DPAIPN	**1a**:**2a** = 1:3	33
7	DMSO	EosinY	**1a**:**2a** = 1:3	trace
8	DMSO	Rose Bengal	**1a**:**2a** = 1:3	trace
9	DMSO	–	**1a**:**2a** = 1:3	trace
10	DMA	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	61
11	THF	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	28
12	DCM	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	34
13	MeCN	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	37
14[d]	DMSO	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	trace
15[e]	DMSO	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	68
16[f]	DMSO	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	**1a**:**2a** = 1:3	65



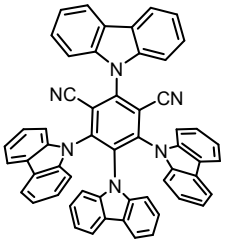
$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$



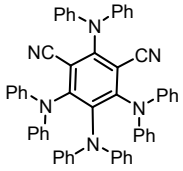
***fac*-Ir(ppy)$_3$**



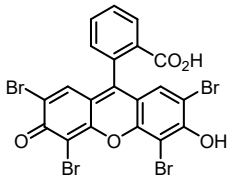
$[Ir(ppy)_2(dtbbpy)]PF_6$



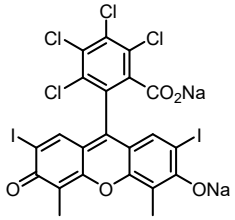
4CzIPN



4DPAIPN



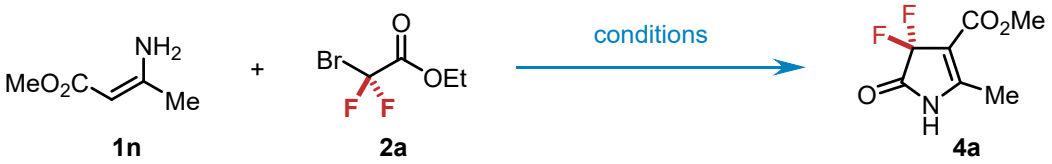
Eosin Y



Rose Bengal

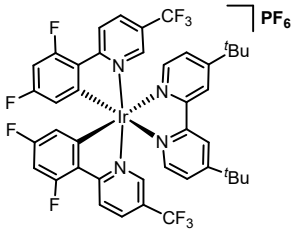
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (amount indicated in this Table), PC (1.0 mol%), DMSO (2.0 mL, 0.1 M), N_2, rt, 4 h, 450−455 nm blue LEDs. [b]Determined by ^1H NMR using dibromomethane as an internal standard. [c]Isolated yield. [d]In the absence of light. [e]H_2O (5.0 equiv). [f]H_2O (10.0 equiv).

Table S2 Optimizing the reaction conditions for the formation of 4a[a]

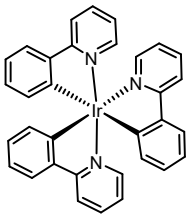


1n + **2a** → **4a**

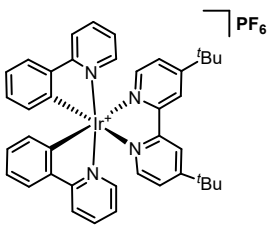
entry	solvent	PC	additive	ratio of **1n**:**2a**	yield of **4a** (%)[b]
1	DMF	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	25
2	DMA	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	38
3	NMP	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	<10%
4	**DMSO**	***fac*-Ir(ppy)$_3$**	–	**1n**:**2a** = 1:2	**80 (71)**[c]
5	1,4-Dioxane	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	trace
6	CH_3CN	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	trace
7	DMSO	[Ir(dF(CF_3)ppy)$_2$(dtbbpy)]PF_6	–	**1n**:**2a** = 1:2	60
8	DMSO	[Ir(ppy)$_2$(dtbbpy)]PF_6	–	**1n**:**2a** = 1:2	47
9	DMSO	Ru(bpy)$_3$(PF_6)$_2$	–	**1n**:**2a** = 1:2	trace
10	DMSO	*fac*-Ir(ppy)$_3$	Na_2CO_3	**1n**:**2a** = 1:2	N.D.
11	DMSO	*fac*-Ir(ppy)$_3$	K_3PO_4	**1n**:**2a** = 1:2	N.D.
12	DMSO	*fac*-Ir(ppy)$_3$	Et_3N	**1n**:**2a** = 1:2	N.D.
13	DMSO	*fac*-Ir(ppy)$_3$	DABCO	**1n**:**2a** = 1:2	N.D.
14	DMSO	*fac*-Ir(ppy)$_3$	$ZnCl_2$	**1n**:**2a** = 1:2	78
15	DMSO	*fac*-Ir(ppy)$_3$	HCOOH	**1n**:**2a** = 1:2	trace
16	DMSO	*fac*-Ir(ppy)$_3$	CF_3COOH	**1n**:**2a** = 1:2	52
17	DMSO	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:1.5	62
18	DMSO	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2.5	63
19	DMSO	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:3	53
20[d]	DMSO	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	N.D.
21	DMSO	–	–	**1n**:**2a** = 1:2	N.D.
22[e]	DMSO	*fac*-Ir(ppy)$_3$	–	**1n**:**2a** = 1:2	N.D.



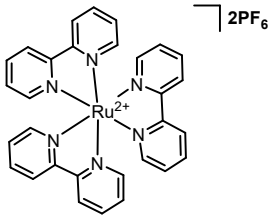
[Ir(dF(CF_3)ppy)$_2$(dtbbpy)]PF_6



fac-Ir(ppy)$_3$



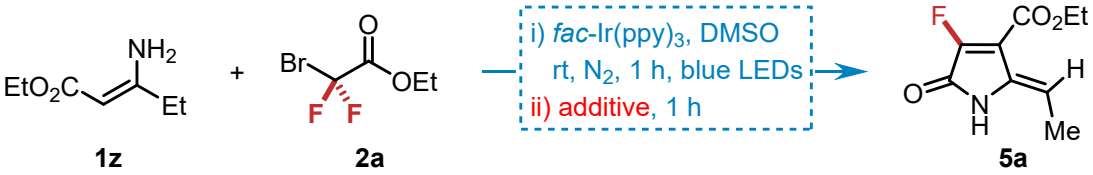
[Ir(ppy)$_2$(dtbbpy)]PF_6



[Ru(bpy)$_3$][2PF_6]

[a]Reaction conditions: **1n** (0.2 mmol), **2a** (amount indicated in this Table), PC (1.0 mol%), DMSO (2.0 mL, 0.1M), N_2, rt, 1 h, 450−455nm. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c]Isolated yield. [d]40 °C. [e]In the absence of light.

Table S3 Optimizing the reaction conditions for the formation of 5a[a]

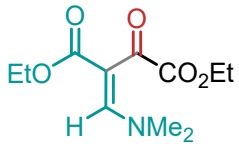


1z **2a** **5a**

entry	additive	yield of **5a** (%)[b]
1	Na_2CO_3	trace
2	K_3PO_4	trace
3	LiHMDS	20
4	CH_3COONa	trace
5	^{t}BuOK	trace
6	DBU	20
7	DABCO	trace
8	Py	trace
9	**TMEDA**	**70 (65)**[c]
10	DIPEA	15
11	Et_3N	37
12	*N,N,N′,N′*-Tetraethyl ethylened iamine	53
13	*N,N*-Dimethylethanolamine	51
14	Triisobutylamine	ND
15	Diethylamine	trace
16[d]	TMEDA	40
17[e]	TMEDA	43
18[f]	TMEDA	57
19[g]	TMEDA	55
20[h]	TMEDA	54
21[i]	TMEDA	52

[a]Reaction conditions: **1z** (0.2 mmol), **2a** (0.4 mmol), additive (0.2 mmol), *fac*-Ir(ppy)$_3$ (1.0 mol%), DMSO (2.0 mL, 0.1M), N_2, rt, 1 h, 450−455 nm blue LEDs. [b]Determined by ^{1}H NMR using dibromomethane as an internal standard. [c]Isolated yield. [d]TMEDA (0.5 equiv). [e]TMEDA (0.8 equiv). [f]TMEDA (1.2 equiv). [g]TMEDA (1.5 equiv). [h]TMEDA (2.0 equiv). [i]TMEDA (3.0 equiv).

4. Characterization data of products



3a

Diethyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

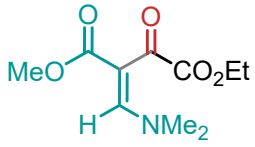
32.6 mg as oil (67% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 4.22 (q, J = 7.2 Hz, 2H), 4.09 (q, J = 7.2 Hz, 2H), 3.30 (s, 3H), 2.96 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 166.6, 166.0, 160.1, 97.2, 61.3, 60.2, 48.3, 43.2, 14.2, 14.0.

HRMS (ESI) *m/z*: Calcd for $C_{11}H_{18}NO_5^+$ $[M + H]^+$: 244.1179; found: 244.1177.

Spectral data obtained for the compound are in good agreement with the reported data.[12]



3b

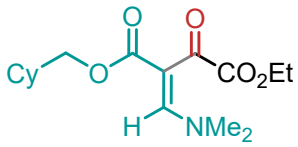
4-Ethyl 1-methyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

28.9 mg as oil (63% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 1/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 4.29 (q, J = 7.2 Hz, 2H), 3.68 (s, 3H), 3.34 (s, 3H), 3.02 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 167.1, 166.1, 160.2, 97.3, 61.5, 51.4, 48.5, 43.3, 14.2.

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{16}NO_5^+$ $[M + H]^+$: 230.1023; found: 230.1023.



3c

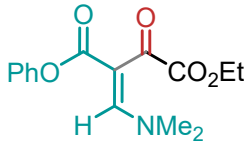
1-(Cyclohexylmethyl) 4-ethyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

39.5 mg as oil (64% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 1/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 3.90 (d, J = 6.8 Hz, 2H), 3.34 (s, 3H), 3.00 (s, 3H), 1.75–1.68 (m, 4H), 1.67–1.62 (m, 1H), 1.34 (t, J = 7.2 Hz, 3H), 1.24–1.08 (m, 4H), 0.98–0.87 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 167.0, 165.9, 160.1, 97.6, 69.7, 61.5, 48.5, 43.3, 37.3, 29.8, 26.4, 25.8, 14.1.

HRMS (ESI) *m/z*: Calcd for $C_{16}H_{26}NO_5^+$ $[M + H]^+$: 312.1805; found: 312.1803.



3d

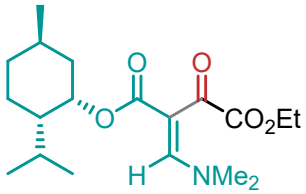
4-Ethyl 1-phenyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

40.4 mg as yellow solid, melting point: 60.2–62.5 ºC (70% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.20 (t, J = 7.6 Hz, 1H), 7.12–7.07 (m, 2H), 4.22 (q, J = 7.2 Hz, 2H), 3.38 (s, 3H), 3.09 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 166.0, 165.1, 161.0, 150.8, 129.5, 125.7, 121.8, 96.6, 61.7, 48.7, 43.6, 14.1.

HRMS (ESI) *m/z*: Calcd for $C_{15}H_{18}NO_5^+$ $[M + H]^+$: 292.1179; found: 292.1177.



3e

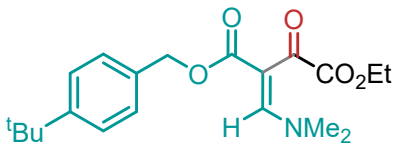
4-Ethyl-1-((1*R*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl)-(*E*)-2-((dimethylamino) methylene)-3-oxosuccinate

44.6 mg as oil (64% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 1/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 4.81–4.75 (m, 1H), 4.29–4.22 (m, 2H), 3.33 (s, 3H), 3.00 (s, 3H), 2.02–1.97 (m, 1H), 1.90–1.84 (m, 1H), 1.68–1.62 (m, 2H), 1.47–1.43 (m, 1H), 1.35 (t, J = 7.2 Hz, 3H), 1.33–1.25 (m, 2H), 0.99–0.88 (m, 2H), 0.88–0.83 (m, 6H), 0.73 (d, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 166.3, 166.1, 160.4, 97.6, 74.2, 61.4, 48.4, 47.4, 43.4, 41.0, 34.4, 31.5, 26.1, 23.4, 22.1, 21.0, 16.3, 14.1.

HRMS (ESI) *m/z*: Calcd for $C_{19}H_{32}NO_5^+$ $[M + H]^+$: 354.2275; found: 354.2271.



3f

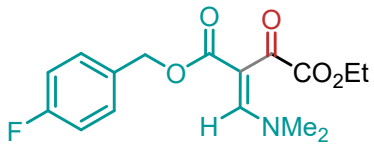
1-(4-(*tert*-Butyl)benzyl) 4-ethyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

51.4 mg as yellow solid, melting point: 84.3–86.7 ºC (72% yield, Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 5.10 (s, 2H), 3.93 (q, J = 7.2 Hz, 2H), 3.33 (s, 3H), 3.01 (s, 3H), 1.30 (s, 9H), 1.14 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 166.6, 166.0, 160.4, 151.4, 132.9, 128.6, 125.5, 97.1, 66.3, 61.4, 48.5, 43.4, 34.7, 31.4, 14.0.

HRMS (ESI) *m/z*: Calcd for $C_{20}H_{28}NO_5^+$ $[M + H]^+$: 362.1962; found: 362.1959.



3g

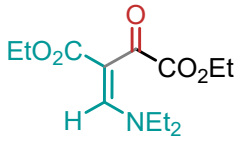
4-Ethyl-1-(4-fluorobenzyl) (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

40.2 mg as oil (63% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.33–7.28 (m, 2H), 7.00 (t, J = 8.8 Hz, 2H), 5.07 (s, 2H), 4.00 (q, J = 7.2 Hz, 2H), 3.31 (s, 3H), 2.97 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 166.4, 165.9, 162.6 (d, J = 246.7 Hz), 160.4, 131.9 (d, J = 3.2 Hz), 130.4 (d, J = 8.2 Hz), 115.4 (d, J = 21.5 Hz), 96.9, 65.5, 61.4, 48.4, 43.4, 13.9.

HRMS (ESI) *m/z*: Calcd for $C_{16}H_{19}FNO_5^+$ $[M + H]^+$: 324.1242; found:324.1241.



3h

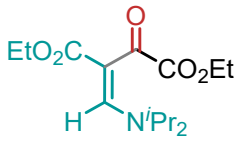
Diethyl (E)-2-((diethylamino)methylene)-3-oxosuccinate

50.3 mg as oil (47% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 4/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.56 (q, J = 7.2 Hz, 2H), 3.50 (q, J = 7.2 Hz, 2H), 1.38–1.26 (m, 6H), 1.23 (t, J = 7.2 Hz, 3H), 1.13 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.7, 167.0, 166.1, 157.0, 97.5, 61.4, 60.4, 54.4, 46.8, 14.9, 14.2, 14.1, 12.1.

HRMS (ESI) *m/z*: Calcd for $C_{13}H_{22}NO_5^+$ $[M + H]^+$: 272.1492; found: 272.1491.



3i

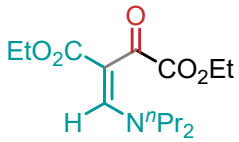
Diethyl (*E*)-2-((di-isopropylamino)methylene)-3-oxosuccinate

52 mg as oil (87% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 4.38–4.30 (m, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.82–3.71 (m, 1H), 1.35–1.31 (m, 9H), 1.29–1.22 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 167.4, 166.7, 155.4, 96.4, 61.3, 60.3, 55.7, 49.2, 24.1, 20.3, 14.2, 14.1.

HRMS (ESI) *m/z*: Calcd for $C_{15}H_{26}NO_5^+$ $[M + H]^+$: 300.1805; found: 300.1802



3j

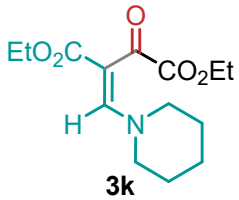
Diethyl (*E*)-2-((dipropylamino)methylene)-3-oxosuccinate

83.1 mg as oil (69% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H), 4.09 (q, J = 7.2 Hz, 2H), 3.55–3.26 (m, 4H), 1.71–1.59 (m, 2H), 1.53–1.42 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 0.87 (t, J = 7.6 Hz, 3H), 0.78 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 166.8, 166.0, 157.4, 97.3, 62.0, 61.3, 60.3, 53.8, 22.4, 19.6, 14.1, 14.0, 10.8, 10.7.

HRMS (ESI) *m/z*: Calcd for $C_{15}H_{26}NO_5^+$ $[M + H]^+$: 300.1805; found: 300.1805



3k

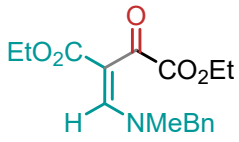
Diethyl (*E*)-2-oxo-3-(piperidin-1-ylmethylene)succinate

38.1 mg as oil (68% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.14 (q, J = 7.2 Hz, 2H), 3.64–3.51 (m, 2H), 3.50–3.39 (m, 2H), 1.81–1.66 (m, 6H), 1.33 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 167.0, 166.5, 158.6, 96.1, 61.4, 60.3, 58.3, 52.5, 26.7, 25.8, 23.2, 14.3, 14.1.

HRMS (ESI) *m/z*: Calcd for $C_{14}H_{22}NO_5^+$ $[M + H]^+$: 284.1492; found: 284.1490.



3l

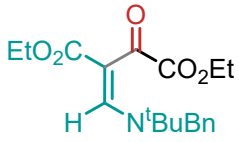
Diethyl (*E*)-2-((benzyl(methyl)amino)methylene)-3-oxosuccinate

81.4 mg as oil (64% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.38–7.28 (m, 3H), 7.20 (d, J = 6.8 Hz, 2H), 4.62 (d, J = 8.8 Hz, 2H), 4.26 (q, J = 7.2 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H), 2.90 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 166.6, 165.9, 159.6, 133.9, 129.2, 128.7, 127.4, 97.9, 64.9, 61.4, 60.3, 41.1, 14.2, 14.0.

HRMS (ESI) *m/z*: Calcd for $C_{17}H_{22}NO_5^+$ $[M + H]^+$: 320.1492; found: 320.1491.



3m

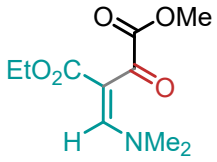
Diethyl *(E)*-2-((benzyl(*tert*-butyl)amino)methylene)-3-oxosuccinate

39.3 mg as oil (27% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.25–7.16 (m, 3H), 6.98 (d, J = 7.2 Hz, 2H), 4.93 (s, 2H), 4.11–4.05 (m, 2H), 3.94–3.78 (m, 2H), 1.49 (s, 9H), 1.21 (t, J = 7.2 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 167.1, 165.0, 152.2, 135.0, 128.5, 127.2, 126.6, 100.5, 63.5, 61.3, 60.4, 51.0, 29.3, 14.0, 13.9.

HRMS (ESI) *m/z*: Calcd for $C_{20}H_{28}NO_5^+$ $[M + H]^+$: 362.1962; found: 362.1960.



3n

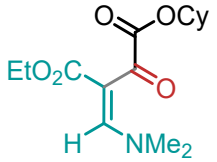
1-Ethyl-4-methyl (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

38.4 mg as oil (84% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 3.00 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 166.7, 166.4, 160.2, 97.4, 60.4, 52.2, 48.4, 43.3, 14.3.

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{16}NO_5^+$ $[M + H]^+$: 230.1023; found: 230.1023.



3o

1-Cyclohexyl-4-ethyl (*E*)-3-((dimethylamino)methylene)-2-oxosuccinate

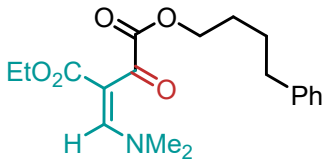
48.9 mg as oil (83% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 4.92–4.82 (m, 1H), 4.15 (q, J = 7.2 Hz,

2H), 3.33 (s, 3H), 3.00 (s, 3H), 1.97–1.90 (m, 2H), 1.77–1.70 (m, 2H), 1.56–1.45 (m, 3H), 1.43–1.26 (m, 3H), 1.24 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 166.8, 165.6, 160.0, 97.7, 74.2, 60.3, 48.4, 43.3, 31.5, 25.4, 23.9, 14.4.

HRMS (ESI) *m/z*: Calcd for $C_{15}H_{24}NO_5^+$ $[M + H]^+$: 298.1649; found: 298.1648.



3p

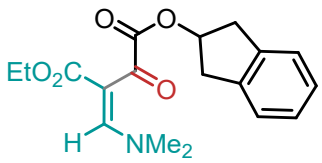
1-Ethyl-4-(4-phenylbutyl) (*E*)-2-((dimethylamino)methylene)-3-oxosuccinate

59.0 mg as oil (85% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.26-7.22 (m, 2H), 7.18–7.12 (m, 3H), 4.22 (t, J = 6.4 Hz, 2H), 4.11 (q, J = 7.2 Hz, 1H), 3.32 (s, 3H), 3.00 (s, 3H), 2.63 (t, J = 7.2 Hz, 2H), 1.88–1.54 (m, 6H), 1.21 (t, J = 7.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 166.2, 160.2, 142.1, 128.5, 128.4, 125.9, 97.6, 65.4, 60.4, 48.4, 43.4, 35.5, 28.1, 27.7, 14.4.

HRMS (ESI) *m/z*: Calcd for $C_{19}H_{26}NO_5^+$ $[M + H]^+$: 348.1805; found: 348.1801.



3q

1-(2,3-Dihydro-1*H*-inden-2-yl)-4-ethyl-(*E*)-3-((dimethylamino)methylene)-2-oxosuccinate

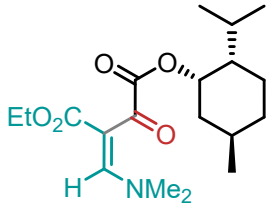
111.0 mg as yellow solid, melting point: 77.3–78.9 ºC (84% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.24–7.18 (m, 2H), 7.17–7.12 (m, 2H), 5.69–5.61 (m, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.35 (dd, J = 17.2, 6.8 Hz, 2H), 3.27 (s,

3H), 3.16 (dd, J = 17.2, 3.2 Hz, 2H), 2.96 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 166.6, 165.9, 160.1, 140.3, 126.7, 124.6, 97.2, 76.3, 60.2, 48.3, 43.3, 39.3, 14.4.

HRMS (ESI) *m/z*: Calcd for $C_{18}H_{22}NO_5^+$ $[M + H]^+$: 332.1492; found: 332.1489.



3r

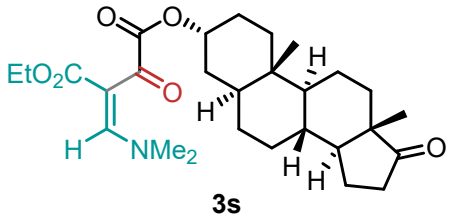
1-Ethyl-4-((1*R*,2*S*)-2-isopropyl-5-methylcyclohexyl)-(*E*)-2-((dimethylamino)methy-lene)-3-oxosuccinate

120.1 mg as yellow solid, melting point: 183.3–184.5 ºC (85% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 4.86–4.64 (m, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.30 (s, 3H), 2.98 (s, 3H), 2.14 (d, J = 12.0 Hz, 1H), 2.01–1.92 (m, 1H), 1.65 (d, J = 11.6 Hz, 2H), 1.52–1.37 (m, 2H), 1.23 (t, J = 7.2 Hz, 3H), 1.08–0.97 (m, 2H), 0.91–0.83 (m, 7H), 0.76 (d, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 166.7, 165.6, 159.7, 97.7, 75.6, 60.2, 48.3, 47.0, 43.1, 40.4, 34.2, 31.4, 25.9, 23.4, 22.1, 20.9, 16.4, 14.5.

HRMS (ESI) *m/z*: Calcd for $C_{19}H_{32}NO_5^+$ $[M + H]^+$: 354.2275; found: 354.2271.



3s

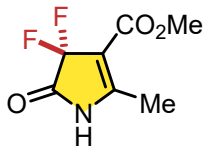
1-((3*R*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-Dimethyl-17-oxohexadecahydro-1*H*-cyclopen-ta[*a*]phenanthren-3-yl)-4-ethyl-(*E*)-3-((dimethylamino)methylene)-2-oxosuccinat-e

63.6 mg as oil (66% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 4.82-4.76 (m, 1H), 4.18–4.06 (m, 2H), 3.31 (s, 3H), 2.98 (s, 3H), 2.44–2.33 (m, 1H), 2.11–1.85 (m, 4H), 1.73 (s, 4H), 1.63-1.57 (m, 2H), 1.55–1.40 (m, 4H), 1.31–1.17 (m, 7H), 1.10–0.86 (m, 3H), 0.81 (s, 6H), 0.72–0.65 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 221.4, 183.6, 166.7, 165.6, 159.9, 97.5, 74.9, 60.3, 54.3, 51.4, 48.4, 47.8, 44.7, 43.2, 36.7, 35.9, 35.7, 35.0, 33.7, 31.5, 30.8, 28.3, 27.2, 21.8, 20.5, 14.3, 13.8, 12.3.

HRMS (ESI) *m/z*: Calcd for $C_{28}H_{42}NO_6^+$ $[M + H]^+$: 488.3007; found: 488.3005.



4a

Methyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

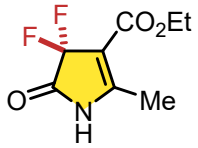
27.1 mg as a solid, melting point: 100.8–102.2 ºC (71% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 3.81 (s, 3H), 2.49 (t, J = 2.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (t, J = 30.3 Hz), 162.3, 162.2 (t, J = 6.8 Hz), 111.1 (t, J = 250.0 Hz), 102.8 (t, J = 21.9 Hz), 51.8, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.64 (s).

HRMS (ESI) *m/z*: Calcd for $C_7H_8F_2NO_3^+$ $[M + H]^+$: 192.0467; found: 192.0466.



4b

Ethyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

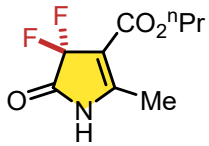
33.8 mg as a solid, melting point: 102.1–103.4 ºC (82% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 2.48 (t, J = 3.2 Hz, 3H), 1.32 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (t, J = 30.3 Hz), 162.0 (t, J = 7.4 Hz), 161.9 (t, J = 1.7 Hz), 111.1 (t, J = 249.7 Hz), 102.8 (t, J = 21.6 Hz), 60.8, 14.5, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.84 (t, J = 2.5 Hz).

HRMS (ESI) *m/z*: Calcd for $C_8H_{10}F_2NO_3^+$ $[M + H]^+$: 206.0623; found: 206.0623.



4c

Propyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

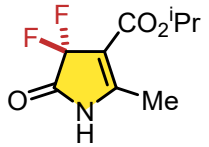
28.0 mg as a solid, melting point: 83.1–84.3 ºC (64% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 4.16 (t, J = 6.4 Hz, 2H), 2.48 (s, 3H), 1.75– 1.67(m, 2H), 0.97 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0 (t, J = 30.4 Hz), 161.8, 161.7 (t, J=7.0 Hz), 111.0 (t, J = 249.7 Hz), 102.9 (t, J = 21.7 Hz), 66.2, 21.9, 14.4, 10.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.80 (s).

HRMS (ESI) *m/z*: Calcd for $C_9H_{12}F_2NO_3^+$ $[M + H]^+$: 220.0780; found: 220.0779.



4d

Isopropyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

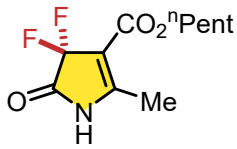
23.8 mg as a solid, melting point: 106.3–108.1 ºC (54% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 4/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 5.17–5.19 (m, 1H), 2.48 (t, J = 3.2 Hz, 3H), 1.31 (s, 3H), 1.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0 (t, J = 30.4 Hz), 161.3, 160.9 (t, J = 7.8 Hz), 111.1 (t, J = 250.0 Hz), 103.7 (t, J = 21.7 Hz), 68.4, 21.9, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.85 (s).

HRMS (ESI) *m/z*: Calcd for $C_9H_{12}F_2NO_3^+$ [M + H]$^+$: 220.0780; found: 220.0778.



4e

Pentyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

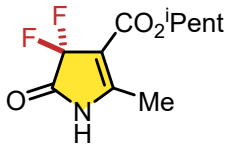
36.2 mg as an oil (73% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 4.20 (t, J = 6.8 Hz, 2H), 2.48 (t, J = 3.2 Hz, 3H), 1.71–1.66 (m, 2H), 1.36–1.33 (m, 4H), 0.90 (t, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (t, J = 30.4 Hz), 161.9, 161.6 (t, J = 7.4 Hz), 111.1 (t, J = 249.9 Hz), 103.2 (t, J = 21.7 Hz), 64.9, 28.3, 28.1, 22.4, 14.6, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.75 (d, J = 2.7 Hz).

HRMS (ESI) *m/z*: Calcd for $C_{11}H_{16}F_2NO_3^+$ [M + H]$^+$: 248.1093; found: 248.1091.



4f

Isopentyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

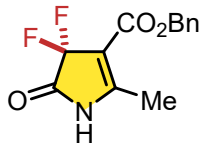
38.3 mg as a solid, melting point: 95.3–96.5 ºC (78% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 4.23 (t, J = 6.8 Hz, 2H), 2.48 (t, J = 3.2 Hz, 3H), 1.76–1.68 (m, 1H), 1.59 (q, J = 6.8 Hz, 2H), 0.92 (d, J = 6.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (t, J = 30.4 Hz), 161.9, 161.8 (t, J = 7.4 Hz), 111.1 (t, J = 249.8 Hz), 103.1 (t, J = 21.8 Hz), 63.4, 37.3, 25.2, 22.5, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.66 ~ –113.76 (m).

HRMS (ESI) *m/z*: Calcd for $C_{11}H_{16}F_2NO_3^+$ [M + H]$^+$: 248.1093; found: 248.1091.



4g

Benzyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

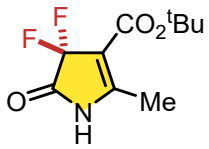
32.8 mg as a solid, melting point: 108.8–109.2 ºC (62% yield, flash column chromatography eluent, petroleum ether/ethyl acetate =3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.43–7.27 (m, 5H), 5.27 (s, 2H), 2.45 (t, J = 3.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8 (t, J = 30.4 Hz), 162.1 (t, J = 7.4 Hz), 161.5, 135.9, 128.7, 128.3, 127.8, 111.0 (t, J = 250.0 Hz), 102.9 (t, J = 21.9 Hz), 66.1, 14.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.32 (s).

HRMS (ESI) *m/z*: Calcd for $C_{13}H_{12}F_2NO_3^+$ $[M + H]^+$: 268.0780; found: 268.0781.



4h

Tert-butyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

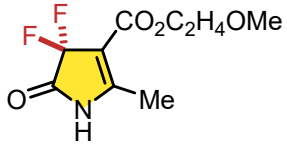
22.6 mg as a solid, melting point: 113.3–114.5 ºC (49% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 4/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 2.44 (t, J = 3.2 Hz, 3H), 1.51 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3 (t, J = 30.4 Hz), 161.0, 160.2 (t, J = 7.5 Hz), 111.2 (t, J = 249.8 Hz), 104.7 (t, J = 21.5 Hz), 82.0, 28.4, 14.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ –114.11~ –114.17 (m).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{14}F_2NO_3^+$ $[M + H]^+$: 234.0936; found: 234.0932.



4i

2-Methoxyethyl-4,4-difluoro-2-methyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxyl

a-te

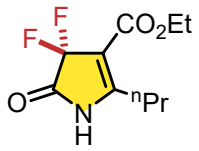
32.7 mg as a solid, melting point: 110.6–112.1 ºC (70% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 4.36 (t, J = 4.8 Hz, 2H), 3.67 (t, J = 4.8 Hz, 2H), 3.40 (s, 3H), 2.46 (t, J = 3.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9 (t, J = 30.3 Hz), 162.7 (t, J = 7.3 Hz), 161.7, 111.1 (t, J = 249.8 Hz), 102.5 (t, J = 21.7 Hz), 70.4, 63.5, 59.1, 14.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.47 ~ –113.67 (m).

HRMS (ESI) *m/z*: Calcd for $C_9H_{12}F_2NO_4^+$ $[M + H]^+$: 236.0729; found: 236.0728.



4j

Ethyl-4,4-difluoro-5-oxo-2-propyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate

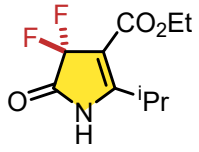
30 mg as an oil (65% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 2.94–2.84 (m, 2H), 1.68–1.64 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3 (t, J = 30.5 Hz), 165.2 (t, J = 7.1 Hz), 161.6, 111.3 (t, J = 250.1 Hz), 102.9 (t, J = 21.7 Hz), 60.6, 29.6, 20.3, 14.3, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.70 (s).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{14}F_2NO_3^+$ $[M + H]^+$: 234.0936; found:234.0932.



4k

Ethyl-4,4-difluoro-2-isopropyl-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

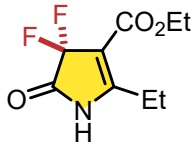
37.4 mg as yellow solid, melting point: 99.9–101.8 ºC (81% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.06–3.98 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H), 1.24 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6 (t, J = 7.0 Hz), 168.0 (t, J = 30.5 Hz), 161.5, 111.5 (t, J = 250.2 Hz), 101.4 (t, J = 21.5 Hz), 60.7, 26.3, 19.2, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.92 (d, J = 1.9 Hz).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{14}F_2NO_3^+$ $[M + H]^+$: 234.0936; found: 234.0931.



4l

Ethyl 2-ethyl-4,4-difluoro-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

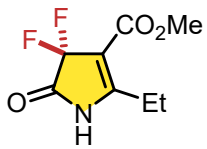
29.7 mg as yellow solid, melting point: 103.4–105.4 ºC (68% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 2.92 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6 (t, J = 30.4 Hz), 166.6 (t, J = 7.2 Hz), 161.6, 111.4 (t, J = 250.1 Hz), 102.1 (t, J = 21.6 Hz), 60.7, 21.4, 14.3, 10.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.87 ~ –113.88(m).

HRMS (ESI) *m/z*: Calcd for $C_9H_{12}F_2NO_3^+$ $[M + H]^+$: 220.0780; found: 220.0779.



4m

Methyl-2-ethyl-4,4-difluoro-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

30.4 mg as yellow solid, melting point: 94.5–96.6 ºC (75% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

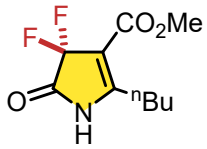
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 3.81 (s, 3H), 2.95–2.93 (m, 2H), 1.26 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5 (t, J = 30.5 Hz), 166.8 (t, J = 7.2 Hz), 162.0,

111.3 (t, J = 250.2 Hz), 101.9 (t, J = 21.7 Hz), 51.7, 21.4, 10.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.69 (s).

HRMS (ESI) *m/z*: Calcd for $C_8H_{10}F_2NO_3^+$ $[M + H]^+$: 206.0623; found: 206.0622.



4n

Methyl 2-butyl-4,4-difluoro-5-oxo-4,5-dihydro-1*H*-pyrrole-3-carboxylate

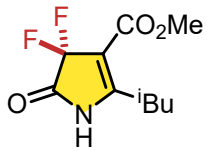
40.9 mg as oil (88% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 3.80 (s, 3H), 2.99–2.84 (m, 2H), 1.65–1.57 (m, 2H), 1.40–1.37 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4 (t, J = 30.3 Hz), 166.1 (t, J = 7.1 Hz), 162.1, 111.3 (t, J = 250.0 Hz), 102.3 (t, J = 21.7 Hz), 51.7, 28.7, 27.6, 22.5, 13.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.62 (d, J = 1.6 Hz).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{14}F_2NO_3^+$ $[M + H]^+$: 234.0936; found: 234.0934.



4o

Methyl 4,4-difluoro-2-isobutyl-5-oxopyrrolidine-3-carboxylate

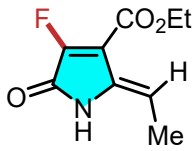
35.5 mg as yellow solid, melting point: 81.6–82.7 ºC (75% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 3.81 (s, 3H), 2.85–2.79 (m, 2H), 2.07–1.99 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3 (t, J = 30.5 Hz), 164.8 (t, J = 7.2 Hz), 162.0 (d, J = 1.8 Hz), 111.2 (t, J = 250.2 Hz), 103.4 (t, J = 21.7 Hz), 51.7, 36.4, 27.6, 22.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ –113.54 (d, J = 2.1 Hz).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{14}F_2NO_3^+$ $[M + H]^+$: 234.0936; found: 234.0935.



5a

Ethyl (*Z*)-2-ethylidene-4-fluoro-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate

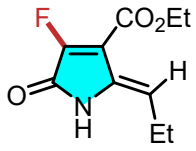
24.7 mg as a yellow solid, melting point: 129.5–131.1 ºC (62% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 6.43 (q, J = 7.6 Hz, 1H), 4.35 (q, J = 7.2 Hz, 2H), 2.06–1.97 (m, 3H), 1.36 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J = 28.2 Hz), 160.5 (d, J = 4.4 Hz), 154.1 (d, J = 296.7 Hz), 129.7 (d, J = 2.2 Hz), 118.1 (d, J = 13.2 Hz), 113.6 (d, J = 1.9 Hz), 61.8, 14.2, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ −125.86 (s).

HRMS (ESI) *m/z*: Calcd for $C_9H_{11}FNO_3^+$ $[M+H]^+$: 200.0717; found: 200.0715.



5b

Ethyl (*Z*)-4-fluoro-5-oxo-2-propylidene-2,5-dihydro-1*H*-pyrrole-3-carboxylate

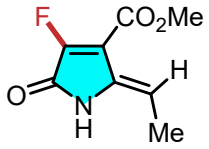
29.7 mg as a colorless solid, melting point: 126.1–127.5 ºC (68% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 6.37 (t, J = 8.0 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 2.43–2.36 (m, 2H), 1.38 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.92 (d, J = 28.1 Hz), 160.51 (d, J = 4.5 Hz), 154.10 (d, J = 296.7 Hz), 128.28 (d, J = 2.0 Hz), 125.00 (d, J = 13.1 Hz), 113.63 (d, J = 1.5 Hz), 61.78, 21.28, 14.24, 13.81.

^{19}F NMR (376 MHz, $CDCl_3$) δ −125.51 (s).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{13}FNO_3^+$ $[M + H]^+$: 214.0874; found: 214.0871.



5c

Methyl (*Z*)-2-ethylidene-4-fluoro-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate

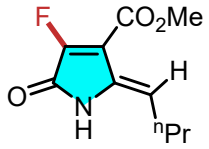
24.0 mg as a colorless solid, melting point: 81.6–84.1 ºC, (65% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 6.49–6.40 (m, 1H), 3.90 (s, 3H), 2.02 (d, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J = 28.1 Hz), 160.9 (d, J = 4.4 Hz), 154.2 (d, J = 296.9 Hz), δ 129.56 (d, J = 2.1 Hz), 118.4 (d, J = 13.1 Hz), 113.2, 52.5, 13.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ –125.52 (s).

HRMS (ESI) *m/z*: Calcd for $C_8H_9FNO_3^+$ $[M + H]^+$: 186.0561; found: 186.0559.



5d

Methyl (*Z*)-2-butylidene-4-fluoro-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate

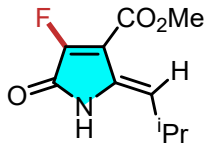
30.2 mg as a colorless solid, melting point: 124.5–125.6 ºC (71% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 6.40 (t, J = 8.4 Hz, 1H), 3.90 (s, 3H), 2.39–2.33 (m, 2H), 1.57–1.53 (m, 2H), 0.95 (t, J = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, J = 28.1 Hz), 160.9 (d, J = 4.4 Hz), 154.2 (d, J = 297.3 Hz), 128.8 (d, J = 2.1 Hz), 123.6 (d, J = 13.1 Hz), 113.2, 52.5, 29.7, 22.5, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ –125.29 (s).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{13}FNO_3^+$ $[M + H]^+$: 214.0874; found: 214.0875.



5e

Methyl (*Z*)-4-fluoro-2-(2-methylpropylidene)-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate

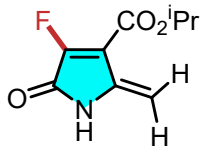
22.6 mg as a colorless solid, melting point: 169.7–171.3 ºC (63% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 6.25 (d, J = 10.4 Hz, 1H), 3.90 (s, 3H), 2.89-2.80 (m, 1H), 1.13 (d, J = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J = 28.1 Hz), 160.9 (d, J = 4.4 Hz), 154.2 (d, J = 297.2 Hz), 130.3 (d, J = 13.0 Hz), 126.9 (d, J = 2.1 Hz), 113.4 (d, J = 1.6 Hz), 52.5, 27.7, 22.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ −125.04 (s).

HRMS (ESI) *m/z*: Calcd for $C_{10}H_{13}FNO_3^+$ $[M + H]^+$: 214.0874; found: 214.0871.



5f

***iso*-Propyl 4-fluoro-2-methylene-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate**

22.1 mg as a colorless solid, melting point: 126.7–127.1 ºC (53% yield, flash column chromatography eluent, petroleum ether/ethyl acetate = 3/1, V/V).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 5.91 (d, J = 1.2 Hz, 1H), 5.28 (t, J = 1.6 Hz, 1H), 5.25–5.19 (m, 1H), 1.37-1.35 (d, J = 6.4 Hz, 6H).

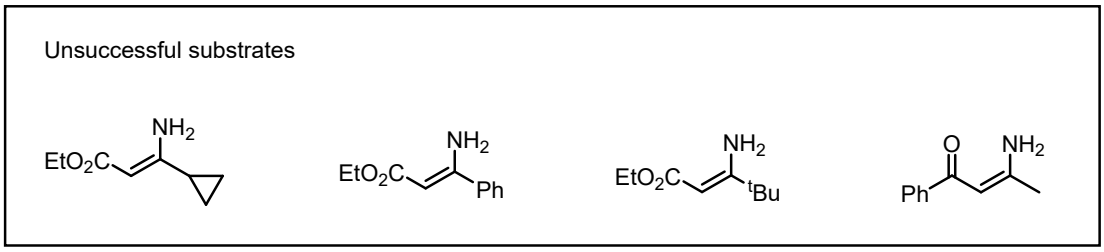
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (d, J = 29.2 Hz), 159.4 (d, J = 4.4 Hz), 155.1 (d, J = 300.9 Hz), 134.8 (d, J = 2.9 Hz), 113.7 (d, J = 1.5 Hz), 103.9 (d, J = 13.4 Hz), 69.8, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ −121.54 (s).

HRMS (ESI) *m/z*: Calcd for $C_9H_{11}FNO_3^+$ $[M + H]^+$: 200.0717; found: 200.0719.

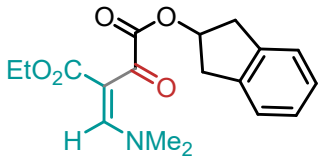
5. Unsuccessful substrates in the reaction

Unsuccessful substrates in the reaction are as shown in the following Scheme.



6. X-Ray structure and data for 3q and 5e

6.1 Crystallographic data and molecular structure of **3q** (CCDC: 2411565)



3q

General procedure for crystal culture of **3q**: To a test tube (15 mL) with added **3q** (20 mg), dichloromethane (1.0 mL) was added slowly to make it dissolve completely. After it dissolved, a mixture of petroleum ether (2.0 mL) and EtOAc (3.0 mL) was added. Then, the test tube was sealed with a rubber stopper, and connected to air with a syringe needle. Finally, the tube was put in a dry and ventilated place to make the organic solvent to volatilize slowly. After a few days, the crystal of **3q** was obtained. The X-ray crystal structure of **3q** was shown in Figure S2.

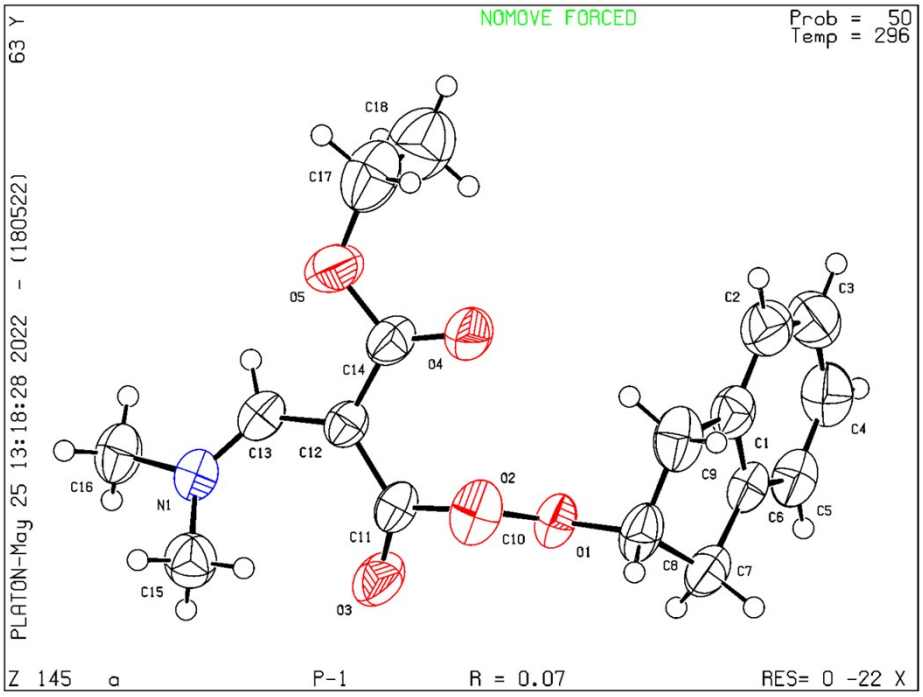
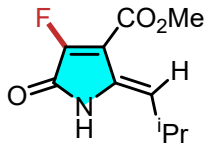


Figure S2 ORTEP diagram of **3q** with thermal displacement parameters drawn at 50% probability.

```
Bond precision:   C-C = 0.0061 A          Wavelength=0.71073

Cell:          a=8.385(6)          b=10.583(8)        c=11.061(8)
               alpha=104.306(12)   beta=104.375(12)   gamma=105.172(11)
Temperature:   296 K

                  Calculated                  Reported
Volume            865.0(11)                   865.0(11)
Space group       P -1                        P-1
Hall group        -P 1                        ?
Moiety formula    C18 H21 N O5                ?
Sum formula       C18 H21 N O5                C18 H21 N O5
Mr                331.36                      331.36
Dx,g cm-3         1.272                       1.272
Z                 2                           2
Mu (mm-1)         0.093                       0.093
F000              352.0                       352.0
F000'             352.19
h,k,lmax          9,12,13                     9,12,13
Nref              3052                        2998
Tmin,Tmax         0.976,0.981                 0.976,0.981
Tmin'             0.976

Correction method= # Reported T Limits: Tmin=0.976 Tmax=0.981
AbsCorr = MULTI-SCAN

Data completeness= 0.982            Theta(max)= 25.000

R(reflections)= 0.0678( 1720)                wR2(reflections)=
                                             0.1729( 2998)
S = 1.057                  Npar= 217
```

6.2 Crystallographic data and molecular structure of **5e** (CCDC: 2411690)



5e

General procedure for crystal culture of **5e**: To a test tube (15 mL) with added **5e** (30 mg), dichloromethane (1.0 mL) was added slowly to make it dissolve completely. After it dissolved, a mixture of petroleum ether (2.0 mL) and EtOAc (3.0 mL) was added. Then, the test tube was sealed with a rubber stopper, and connected to air with a syringe needle. Finally, the tube was put in a dry and ventilated place to make the organic solvent to volatilize slowly. After a few days, the crystal of **5e** was obtained The X-ray crystal structure of **5e** was shown in Figure **S3**.

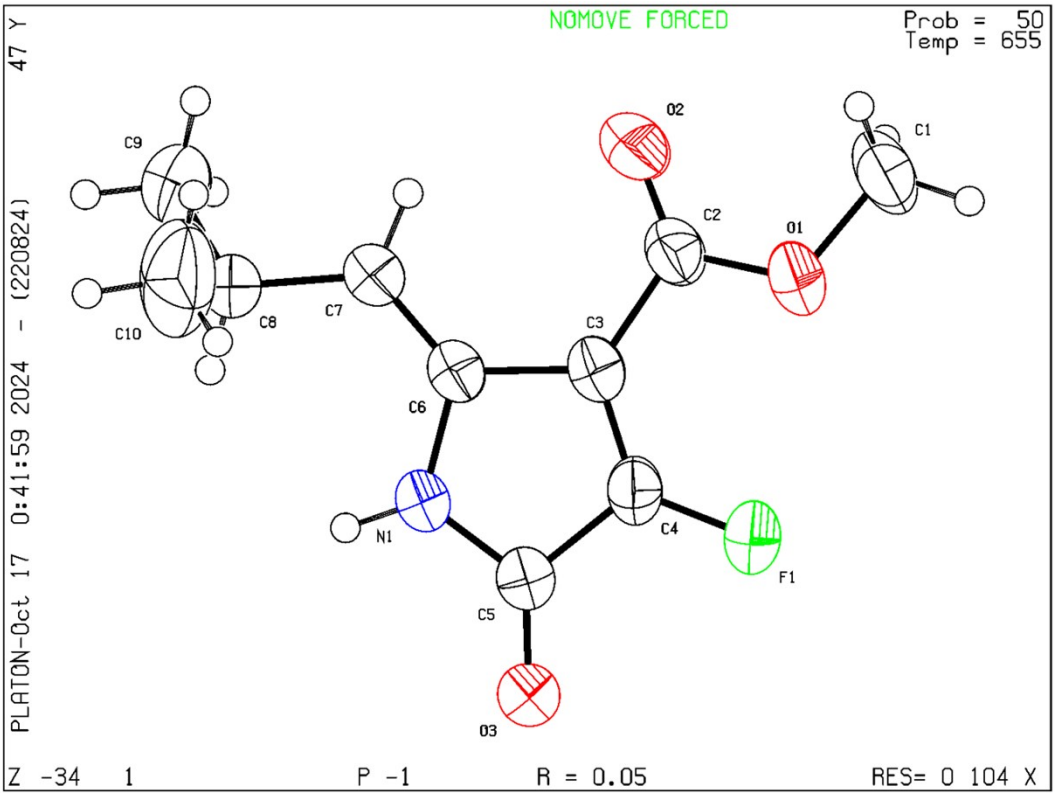


Figure S3 ORTEP diagram of **5e** with thermal displacement parameters drawn at 50% probability.

Bond precision: C-C = 0.0025 A Wavelength=1.54178

Cell: a=5.0040(1) b=9.2021(2) c=12.2894(3)
alpha=71.305(1) beta=80.810(1) gamma=83.848(1)
Temperature: 655 K

	Calculated	Reported
Volume	528.21(2)	528.21(2)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C10 H12 F N O3	C10 H12 F N O3
Sum formula	C10 H12 F N O3	C10 H12 F N O3
Mr	213.21	213.21
Dx,g cm-3	1.340	1.341
Z	2	2
Mu (mm-1)	0.943	0.943
F000	224.0	224.0
F000'	224.83	
h,k,lmax	6,11,14	6,11,14
Nref	1919	1864
Tmin,Tmax	0.805,0.820	0.577,0.753
Tmin'	0.805	

Correction method= # Reported T Limits: Tmin=0.577 Tmax=0.753
AbsCorr = ?

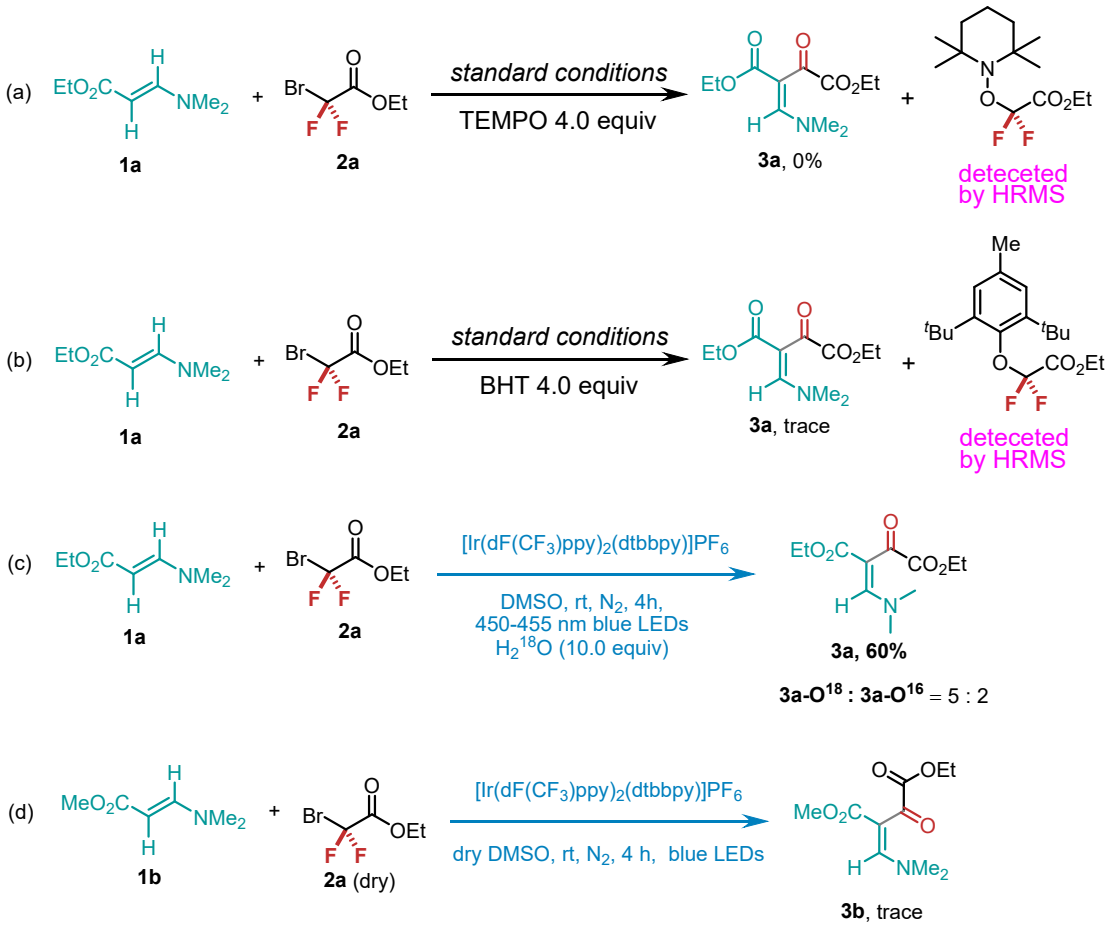
Data completeness= 0.971 Theta(max)= 68.227

R(reflections)= 0.0482(1716) wR2(reflections)= 0.1355(1864)

S = 1.045 Npar= 139

7. Mechanism investigation

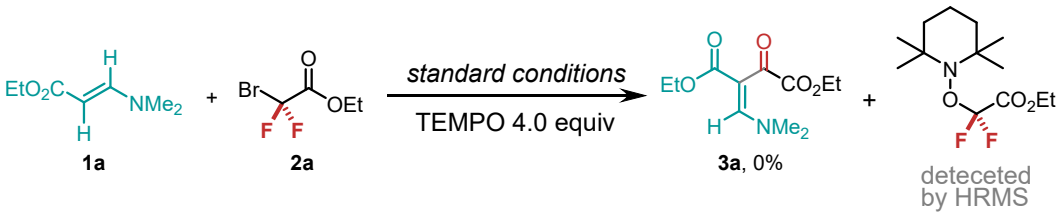
7.1 Control experiments (Scheme S1)

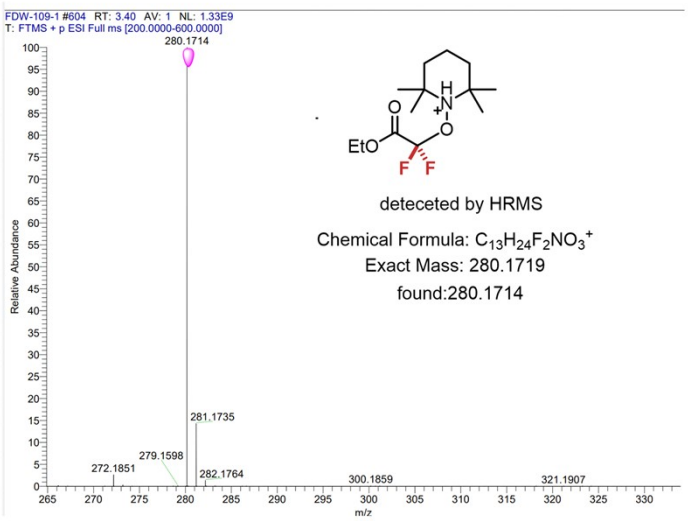


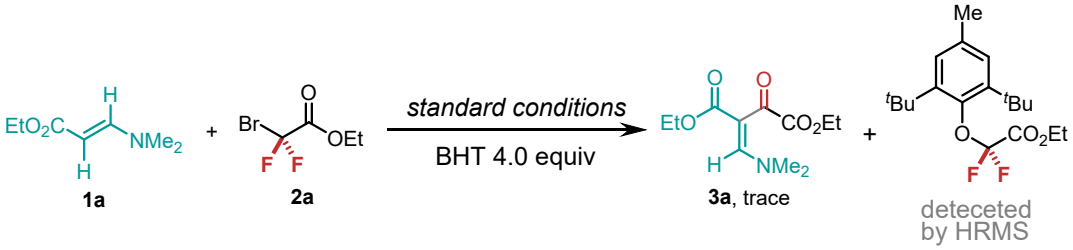
Scheme S1. Control experiments

7.2 Radical trapping experiments

A 10 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with ethyl (*E*)-3-(dimethylamino)acrylate **1a** (28.3 mg, 0.2 mmol), bromodifluoroacetate **2a** (121.8 mg, 0.6 mmol), $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (2.24 mg, 0.002 mmol, 1 mol%), TEMPO (126 mg, 0.8 mmol, 4.0 equiv) or BHT (176 mg, 0.8 mmol, 4.0 equiv) and dimethyl sulfoxide (DMSO, 2.0 mL). The reaction vessel was exposed to blue LEDs (450–455 nm, 2×3 W) irradiation at room temperature in N_2 with stirring for 4 h. After completion of the reaction, HRMS analysis of this reaction crude mixture showed that the corresponding TEMPO/ BHT-adduct was detected (Figure S4).







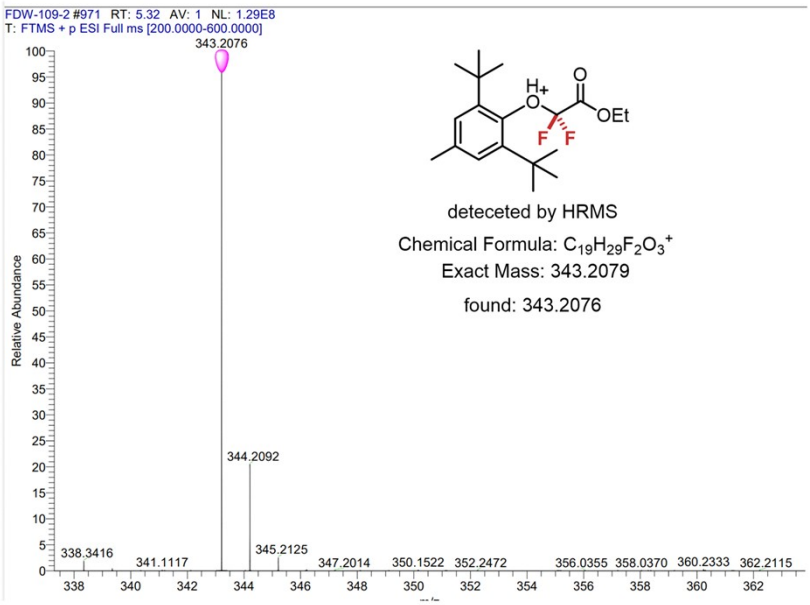


Figure S4. Radical trapping experiments

7.3 ^{18}O-Labeling experiments

For further study on the reaction mechanism, the ^{18}O isotope labeling experiment was conducted under the standard conditions with 10 equiv of $H_2{}^{18}O$. As expected, ^{18}O/^{16}O-labled product **3a** (**3a**-^{18}O:**3a**-^{16}O ≈ 5:2) was obtained (Figure S5). This result indicated that the oxygen atom in the newly constructed carbonyl group originated from water.

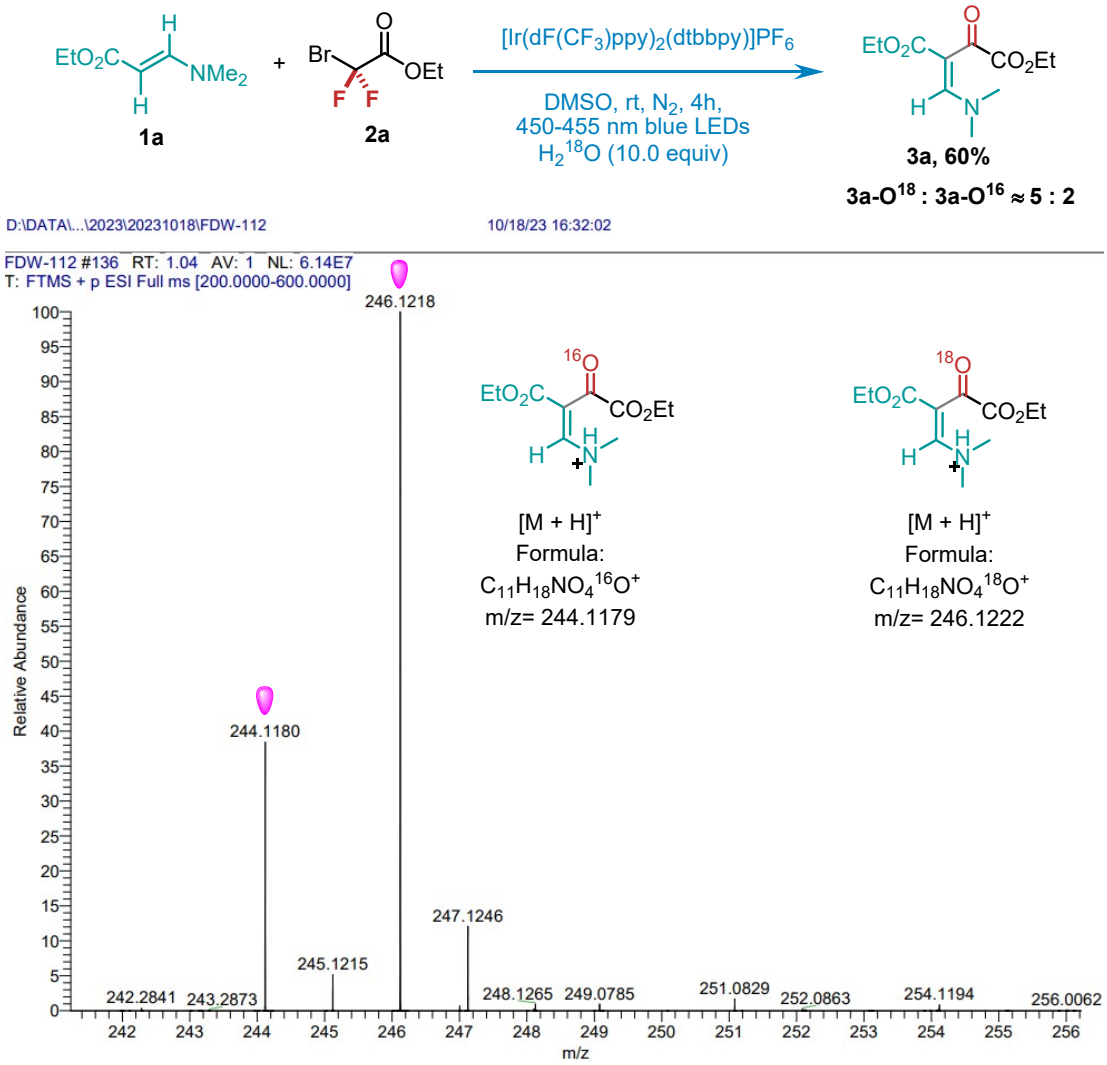


Figure S5. HRMS analysis of ^{18}O-labeling experiments

8. References

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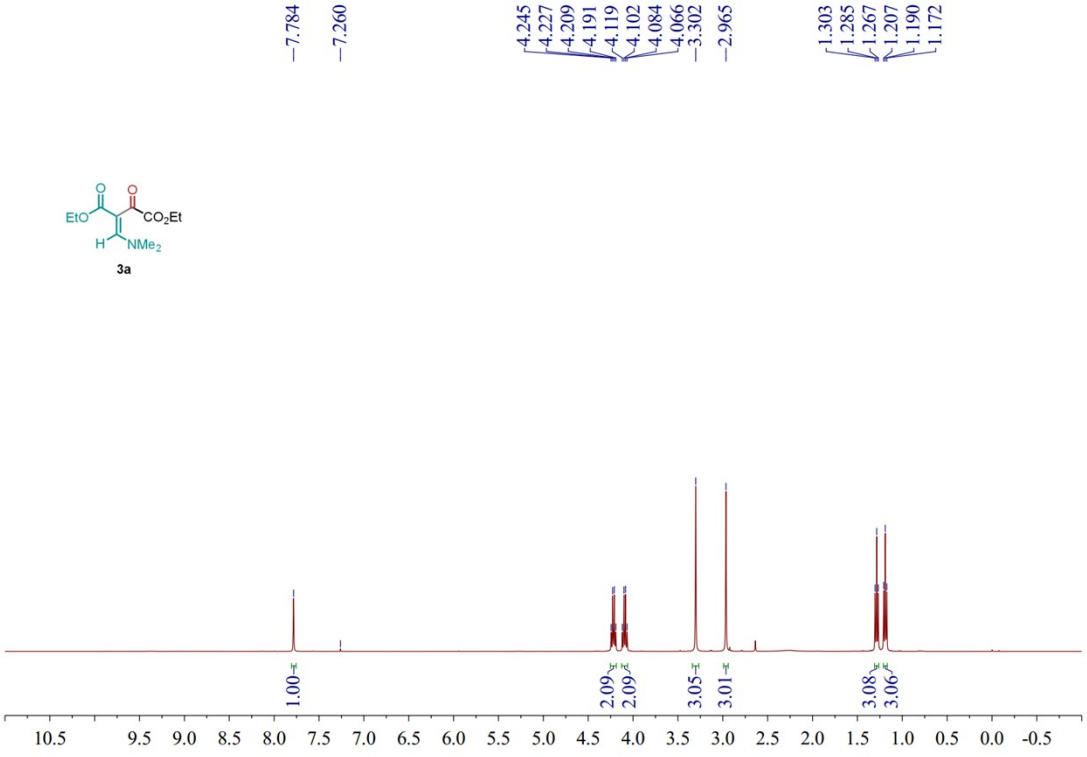
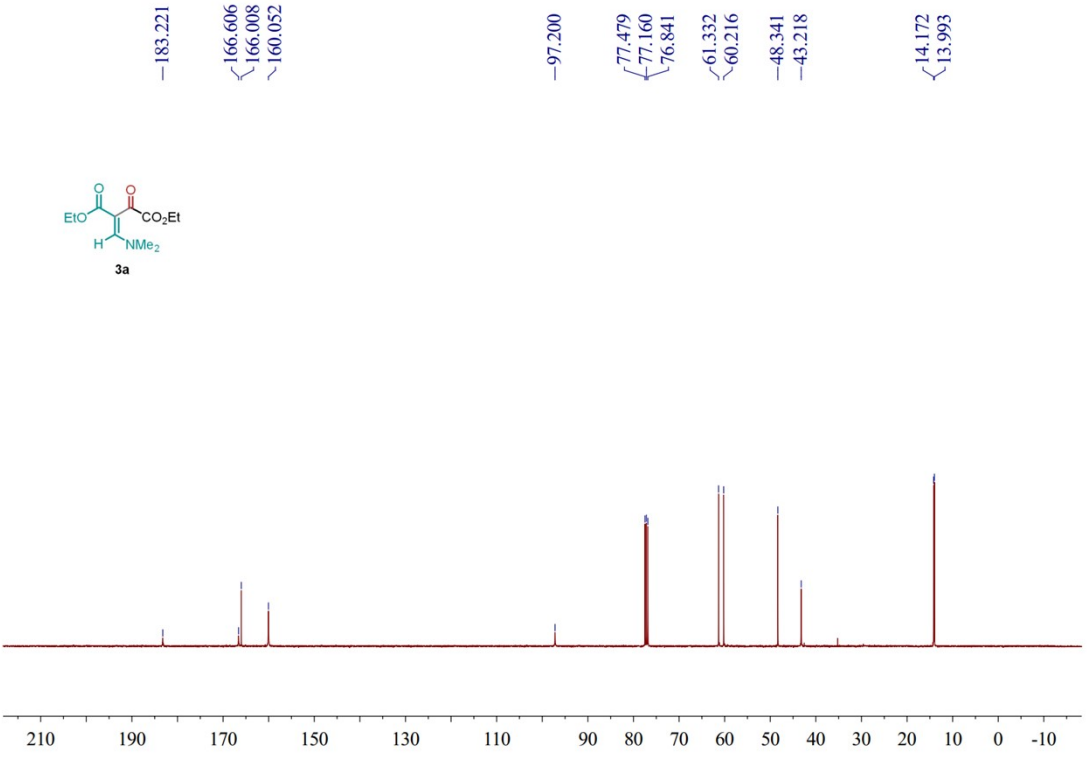
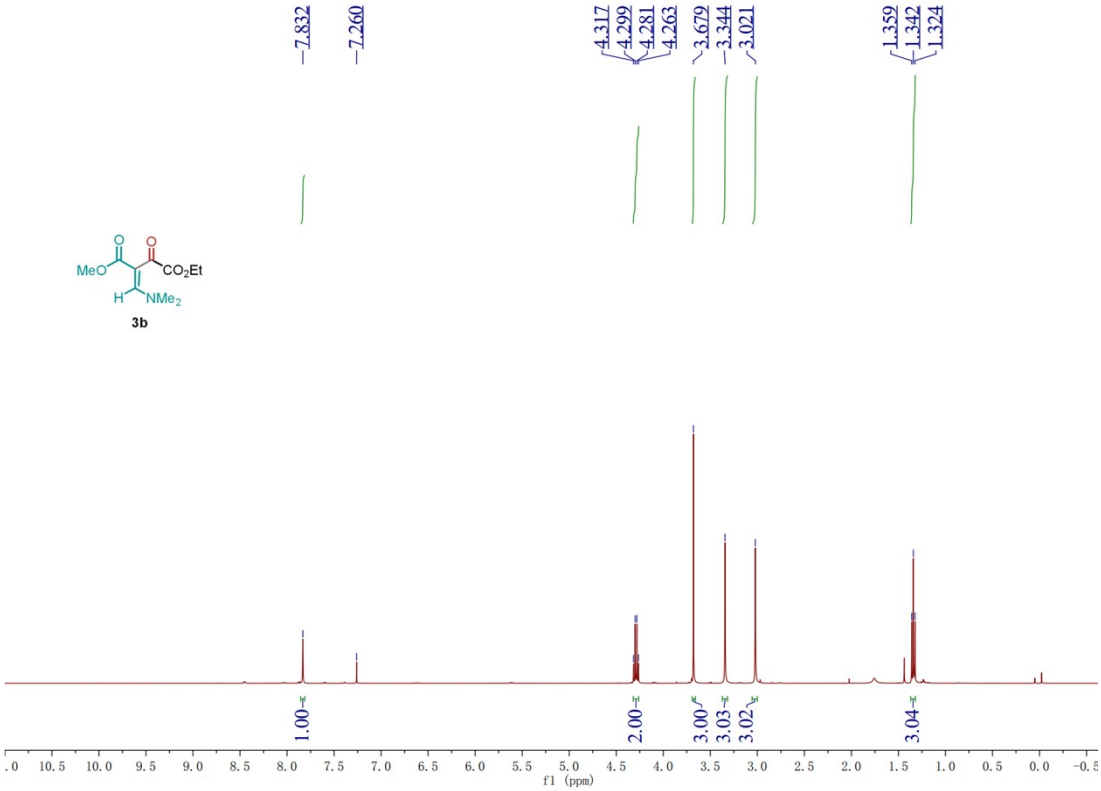
9. NMR Spectra of products



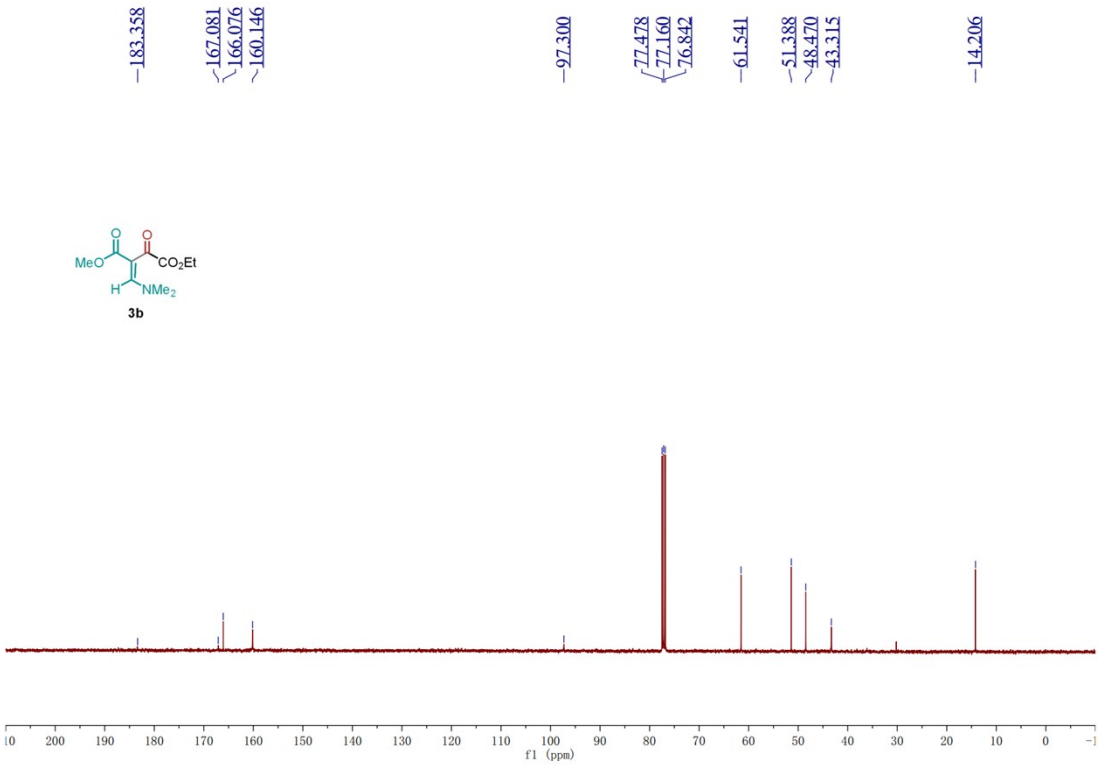
^{1}H NMR Spectrum of Compound **3a** (400 MHz, $CDCl_3$)



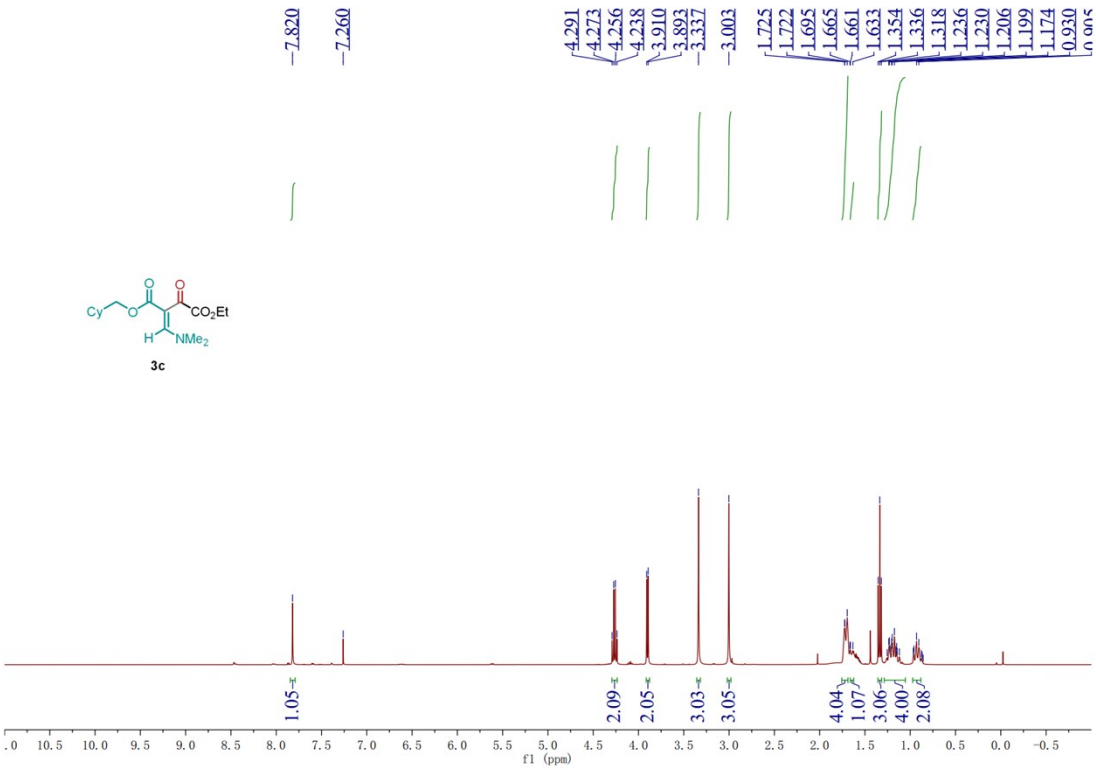
^{13}C{^{1}H} NMR Spectrum of Compound **3a** (100 MHz, $CDCl_3$)



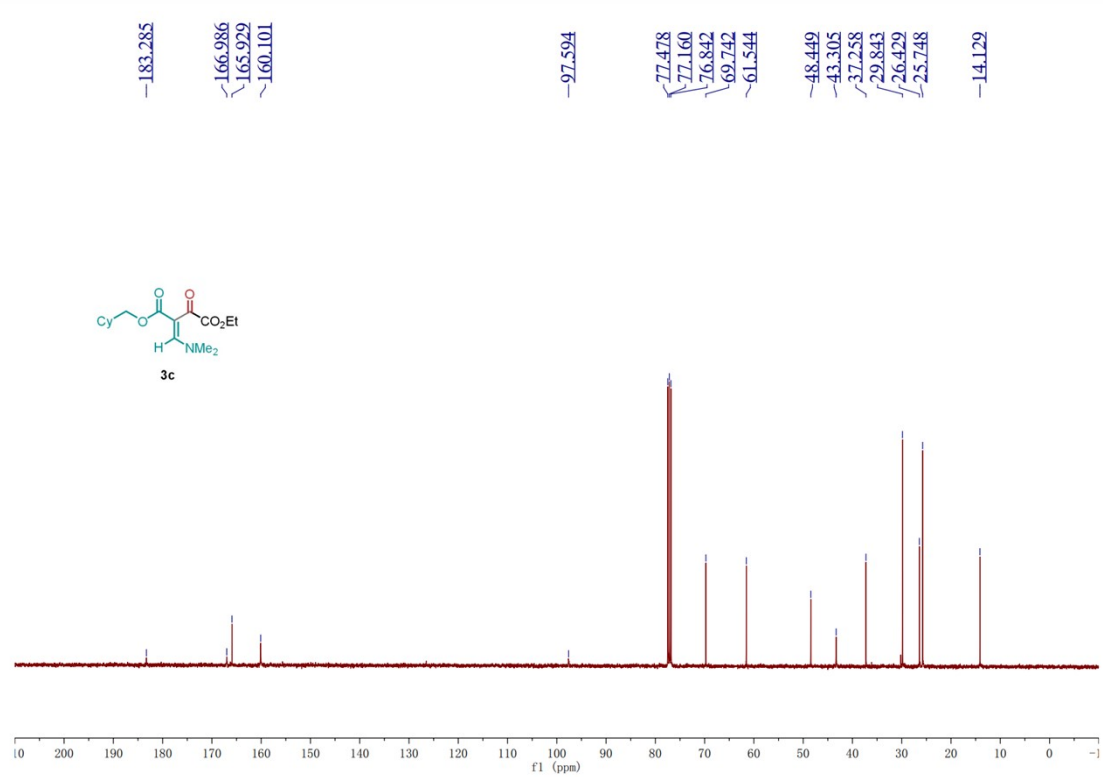
^{1}H NMR Spectrum of Compound **3b** (400 MHz, $CDCl_3$)



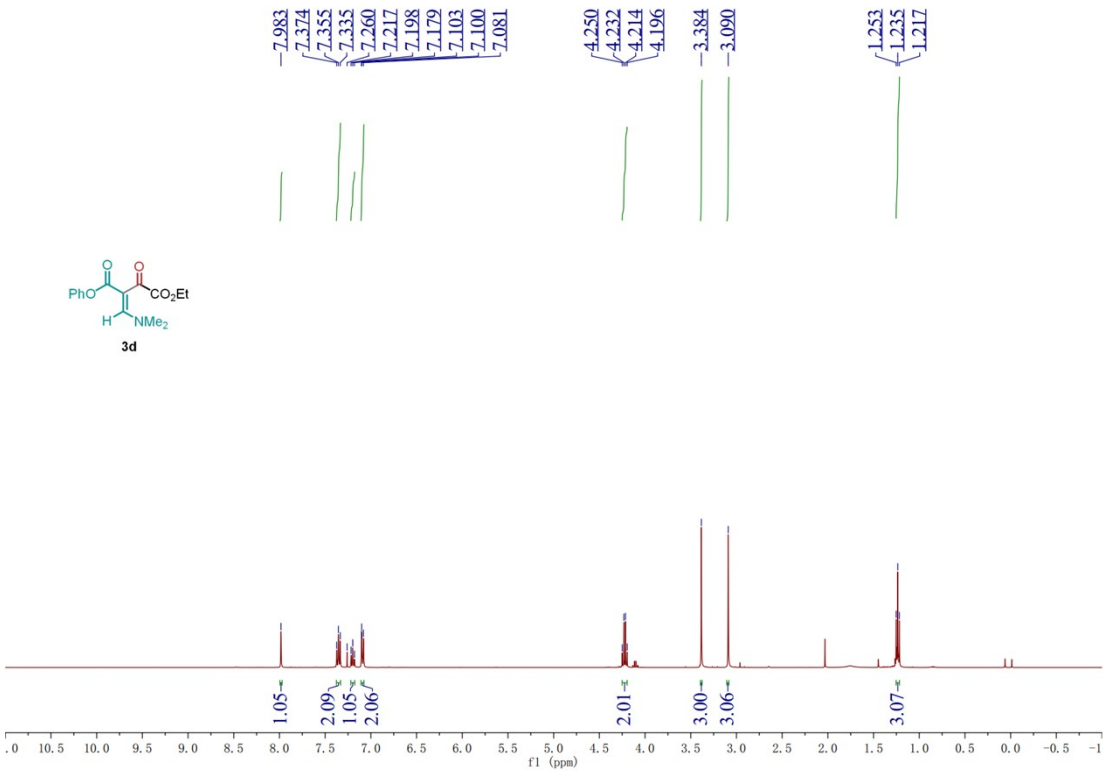
^{13}C{^{1}H} NMR Spectrum of Compound **3b** (100 MHz, $CDCl_3$)



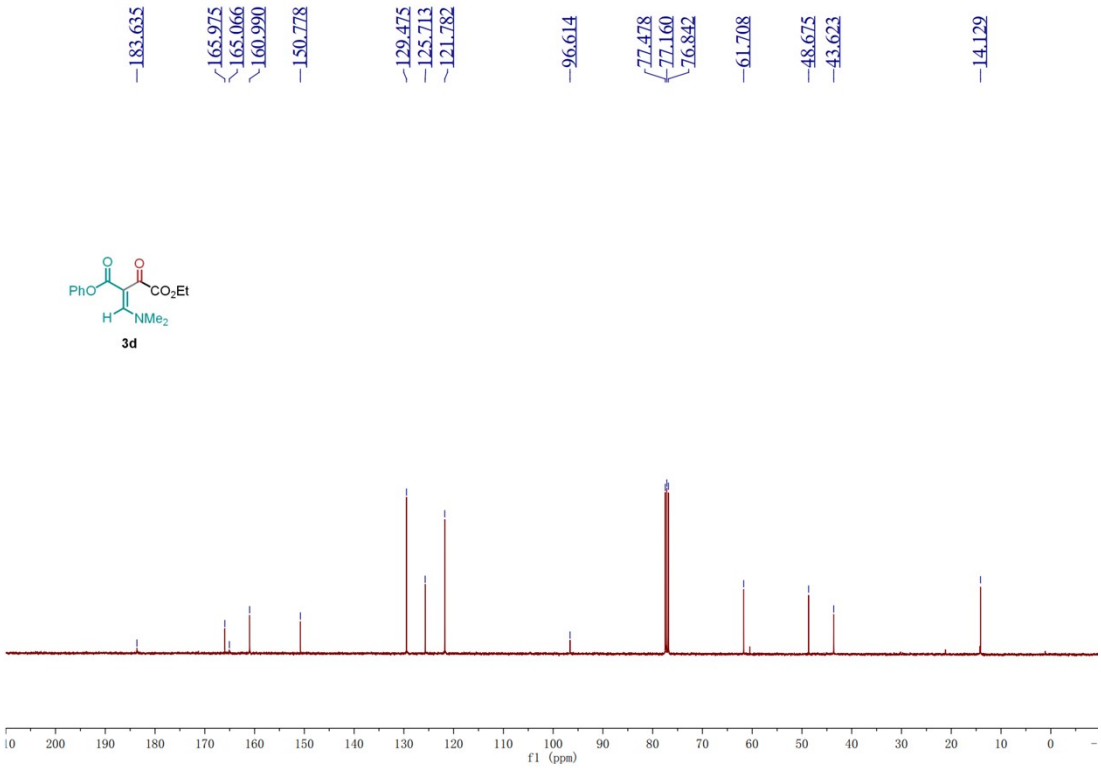
^{1}H NMR Spectrum of Compound **3c** (400 MHz, $CDCl_3$)



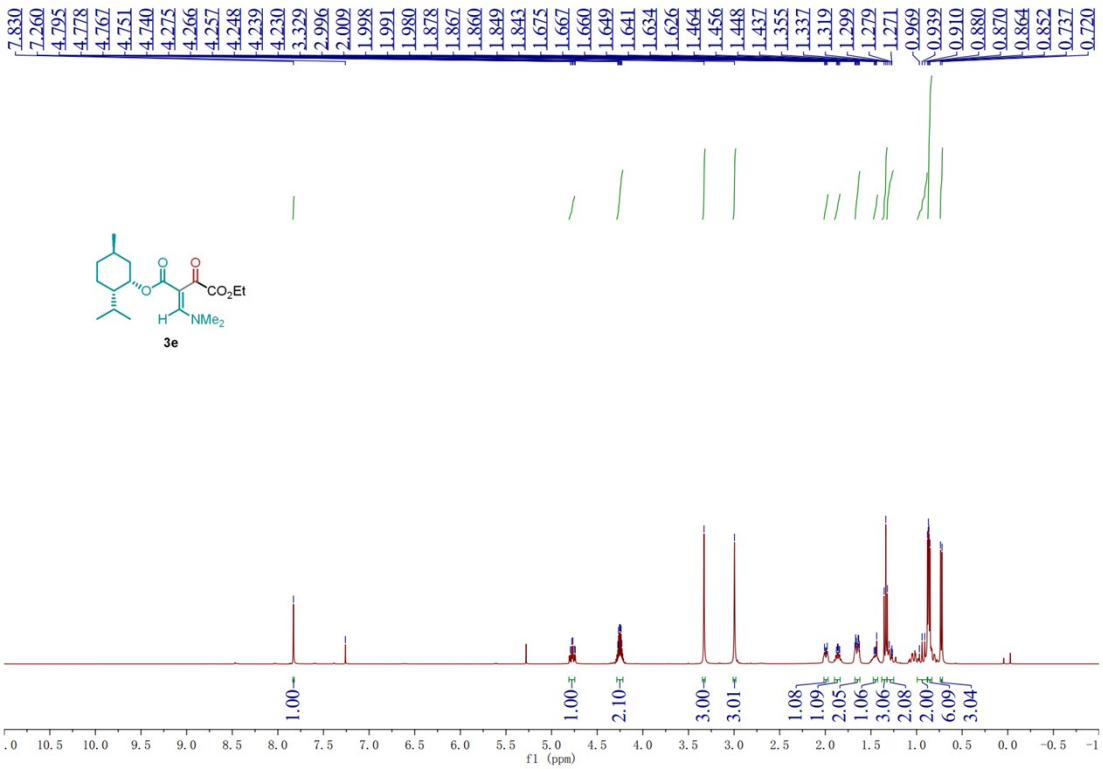
^{13}C{^{1}H} NMR Spectrum of Compound **3c** (100 MHz, $CDCl_3$)



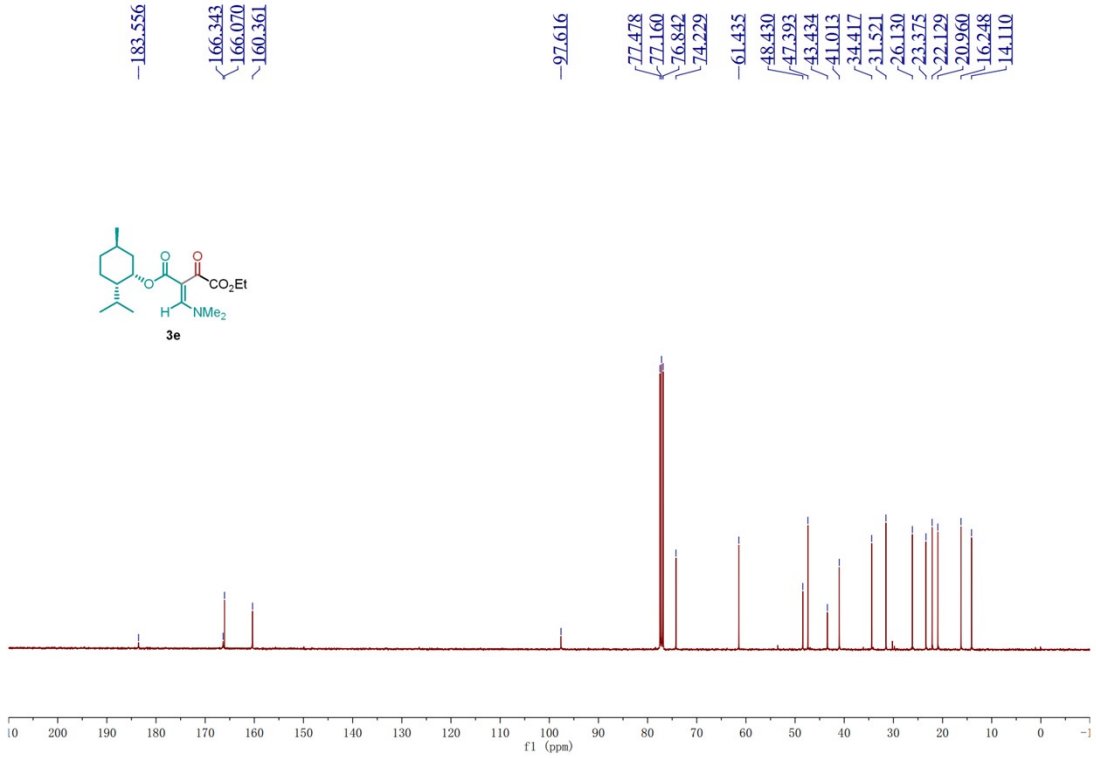
^{1}H NMR Spectrum of Compound **3d** (400 MHz, $CDCl_3$)



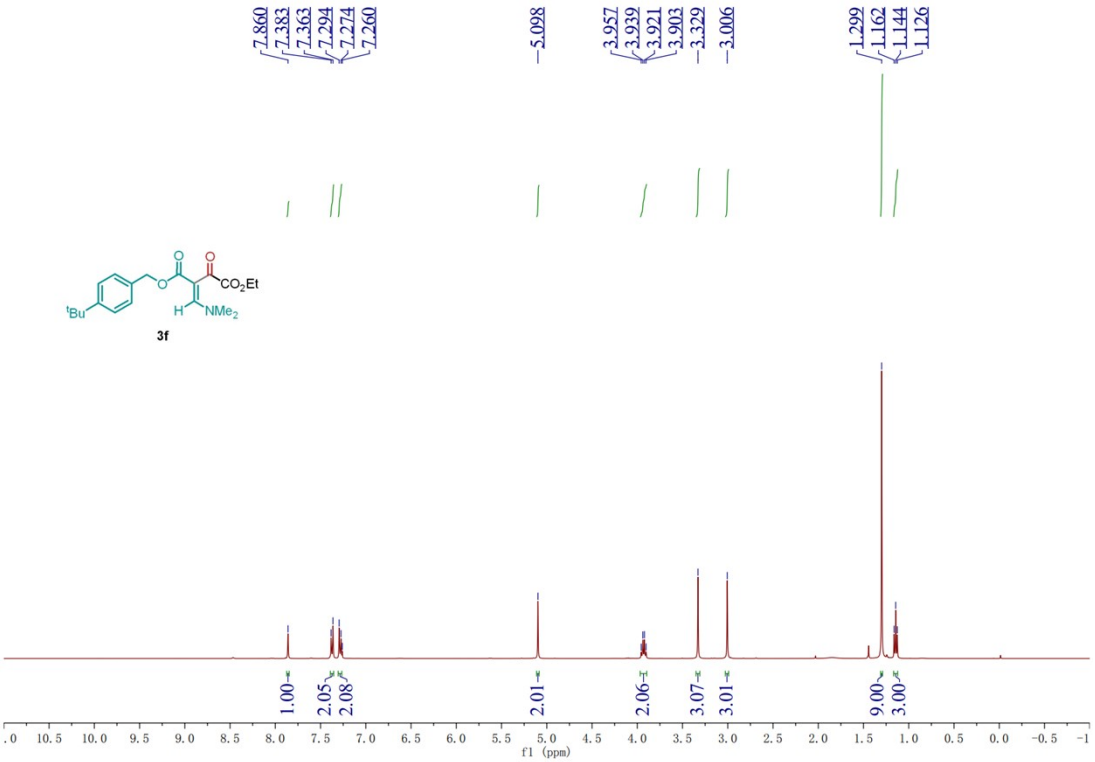
^{13}C{^{1}H} NMR Spectrum of Compound **3d** (100 MHz, $CDCl_3$)



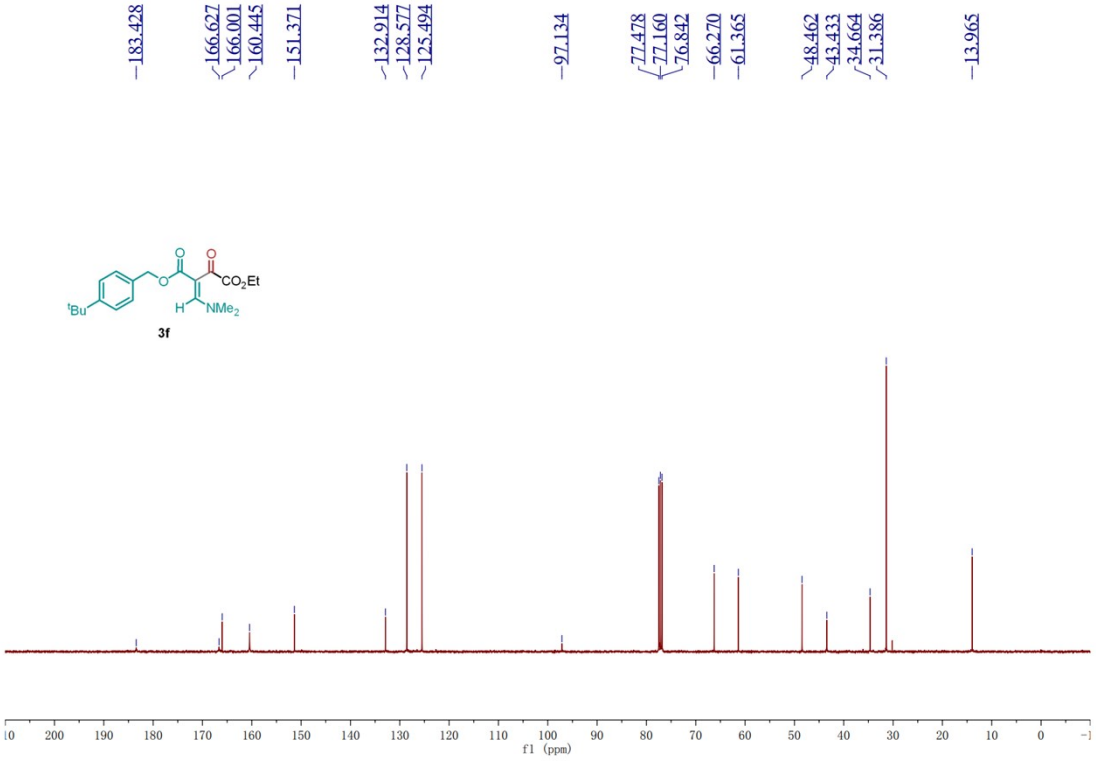
^{1}H NMR Spectrum of Compound **3e** (400 MHz, $CDCl_3$)



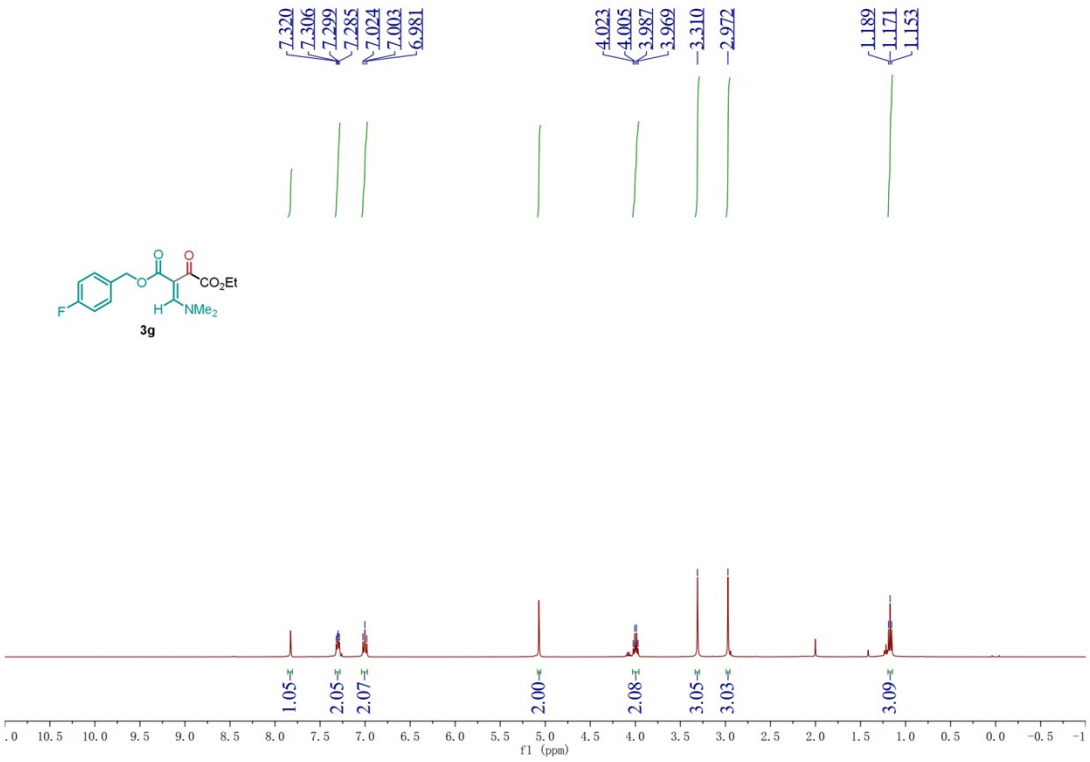
^{13}C{^{1}H} NMR Spectrum of Compound **3e** (100 MHz, $CDCl_3$)



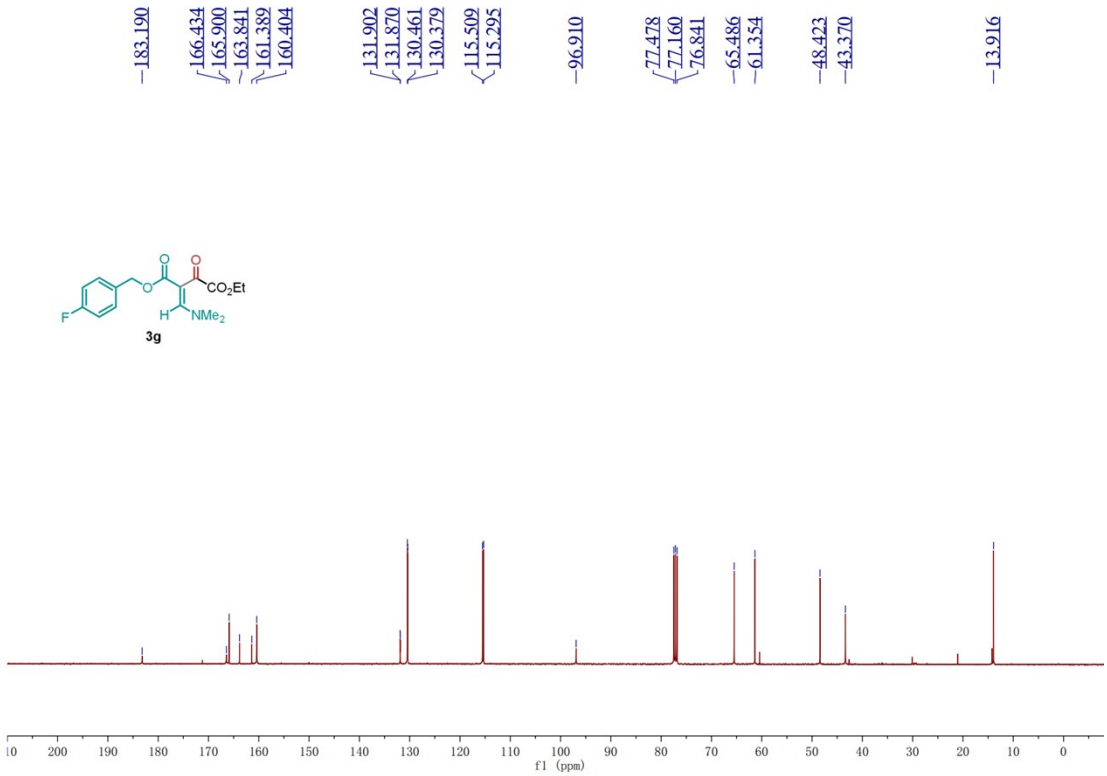
^{1}H NMR Spectrum of Compound **3f** (400 MHz, $CDCl_3$)



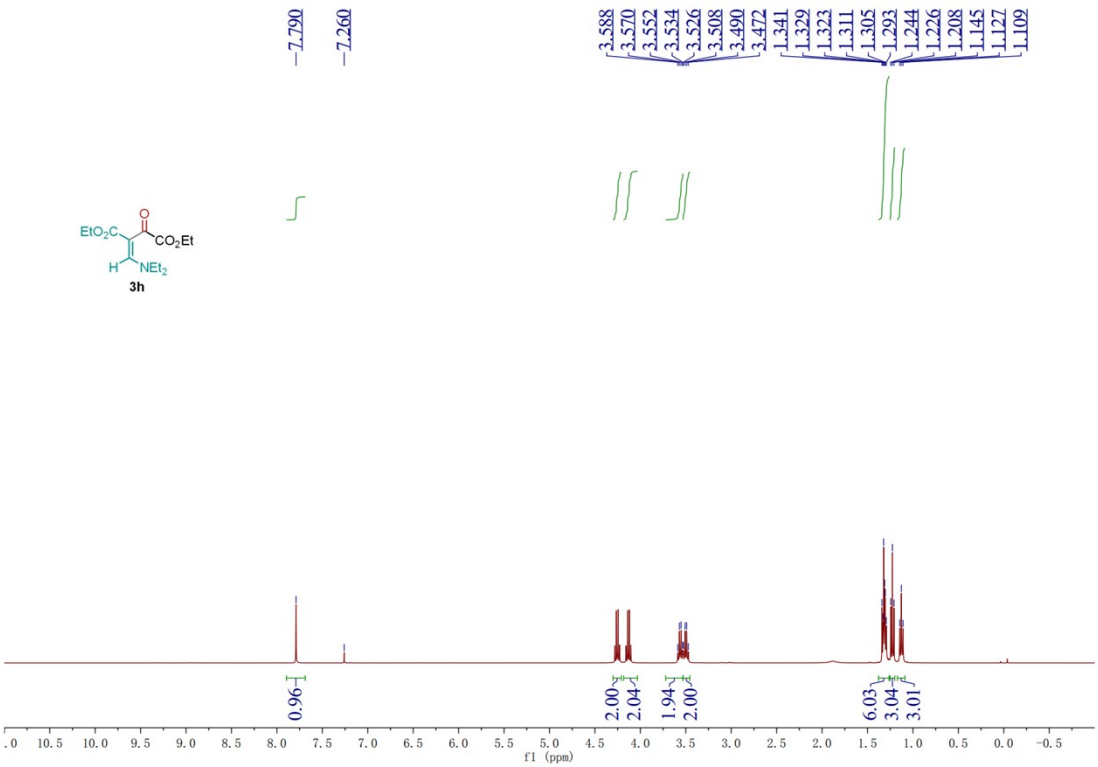
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **3f** (100 MHz, $CDCl_3$)



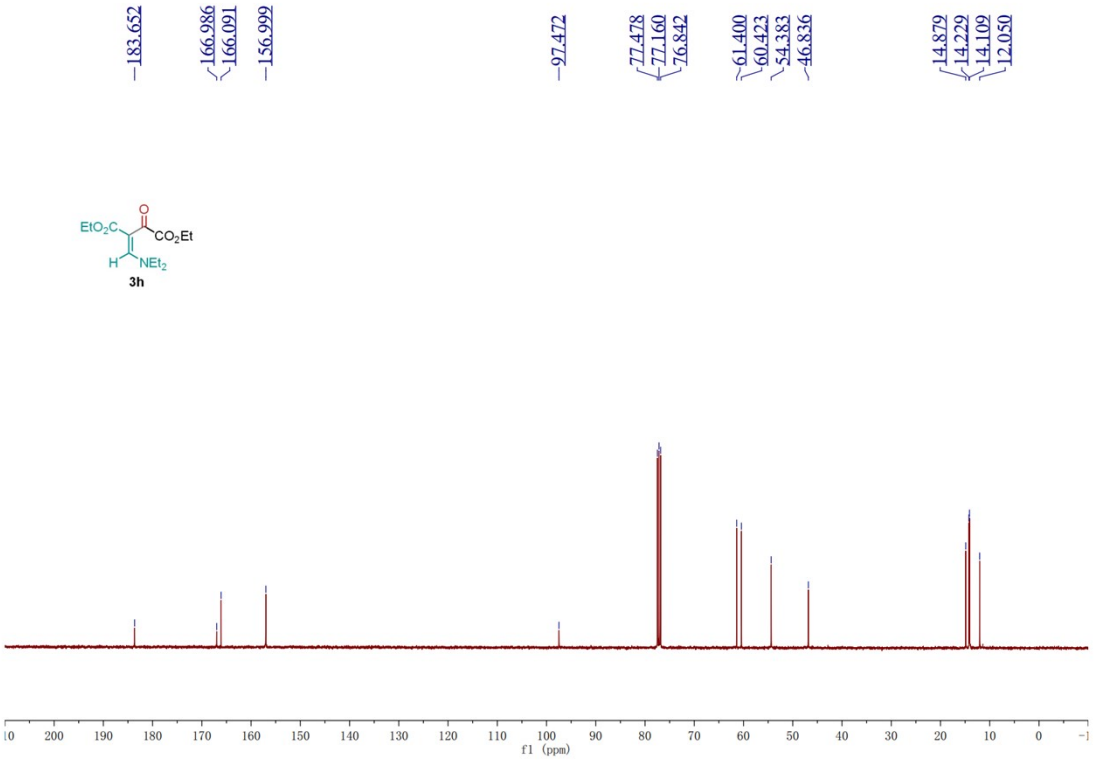
^{1}H NMR Spectrum of Compound **3g** (400 MHz, $CDCl_3$)



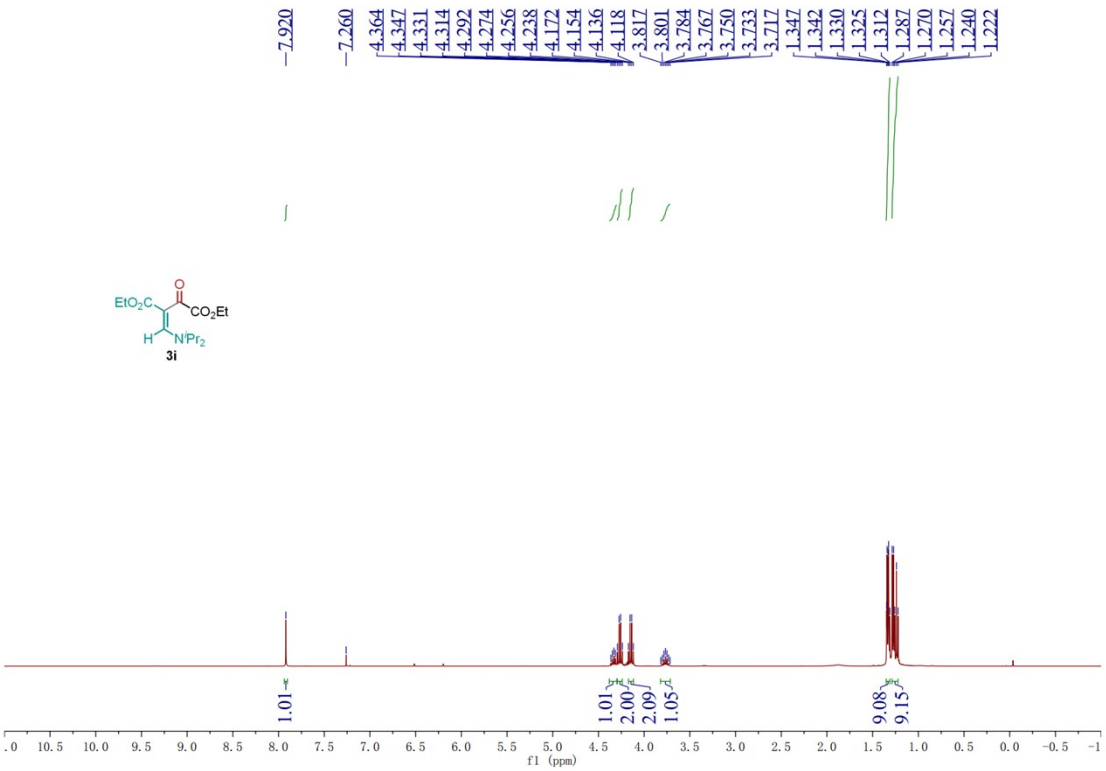
^{13}C{^{1}H} NMR Spectrum of Compound **3g** (100 MHz, $CDCl_3$)



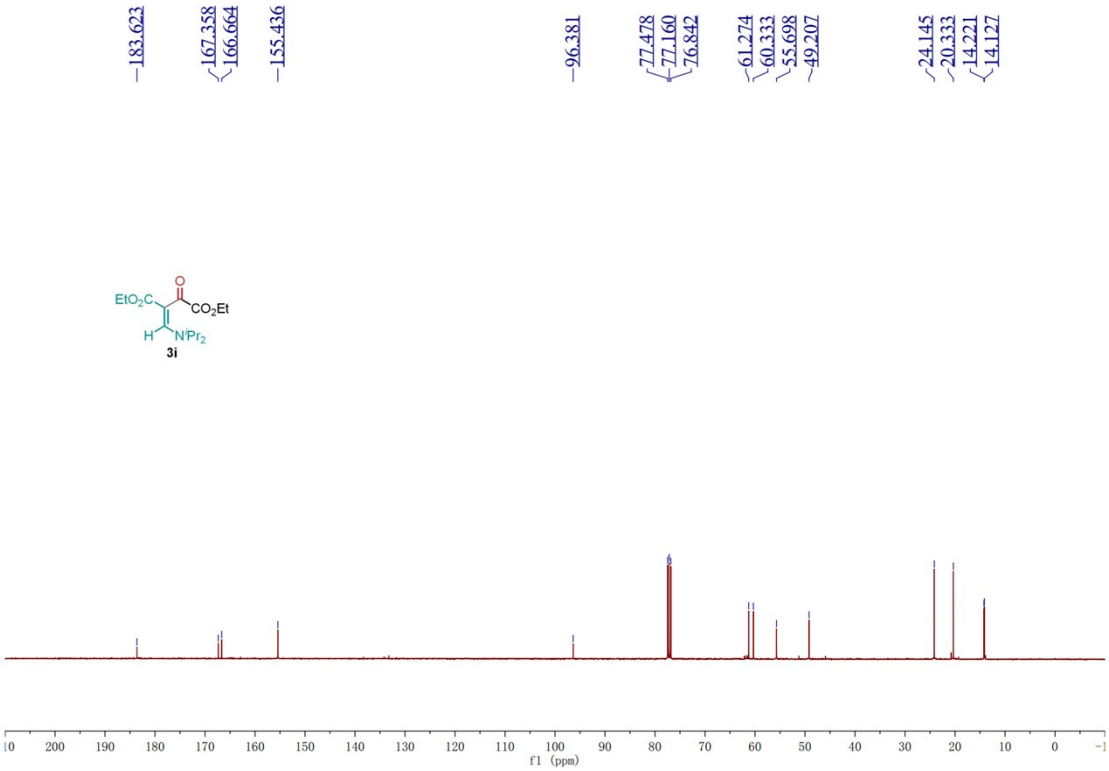
^{1}H NMR Spectrum of Compound **3h** (400 MHz, $CDCl_3$)



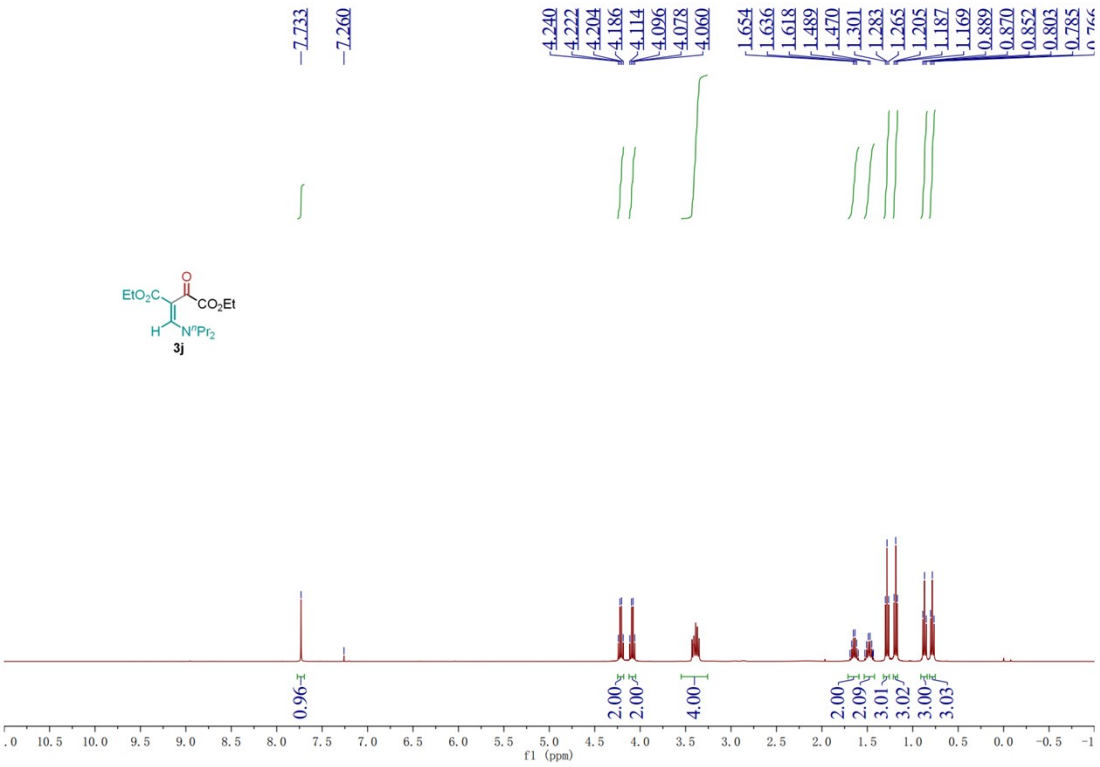
^{13}C{^{1}H} NMR Spectrum of Compound **3h** (100 MHz, $CDCl_3$)



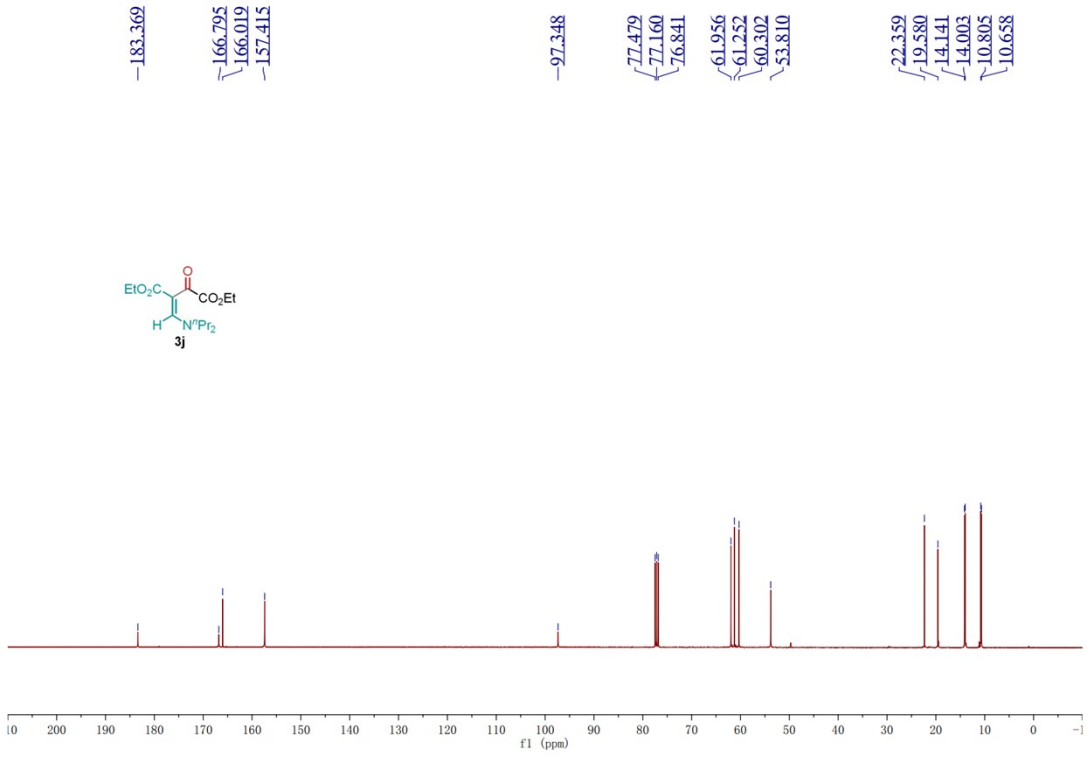
^{1}H NMR Spectrum of Compound **3i** (400 MHz, $CDCl_3$)



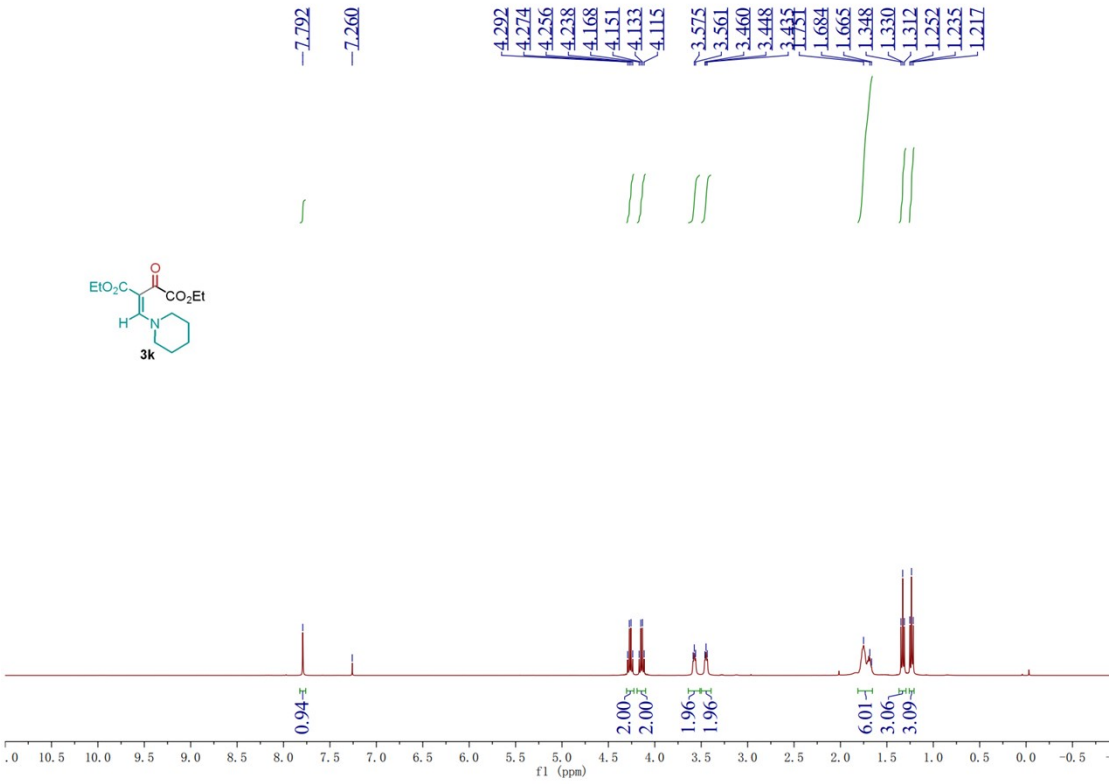
^{13}C{^{1}H} NMR Spectrum of Compound **3i** (100 MHz, $CDCl_3$)



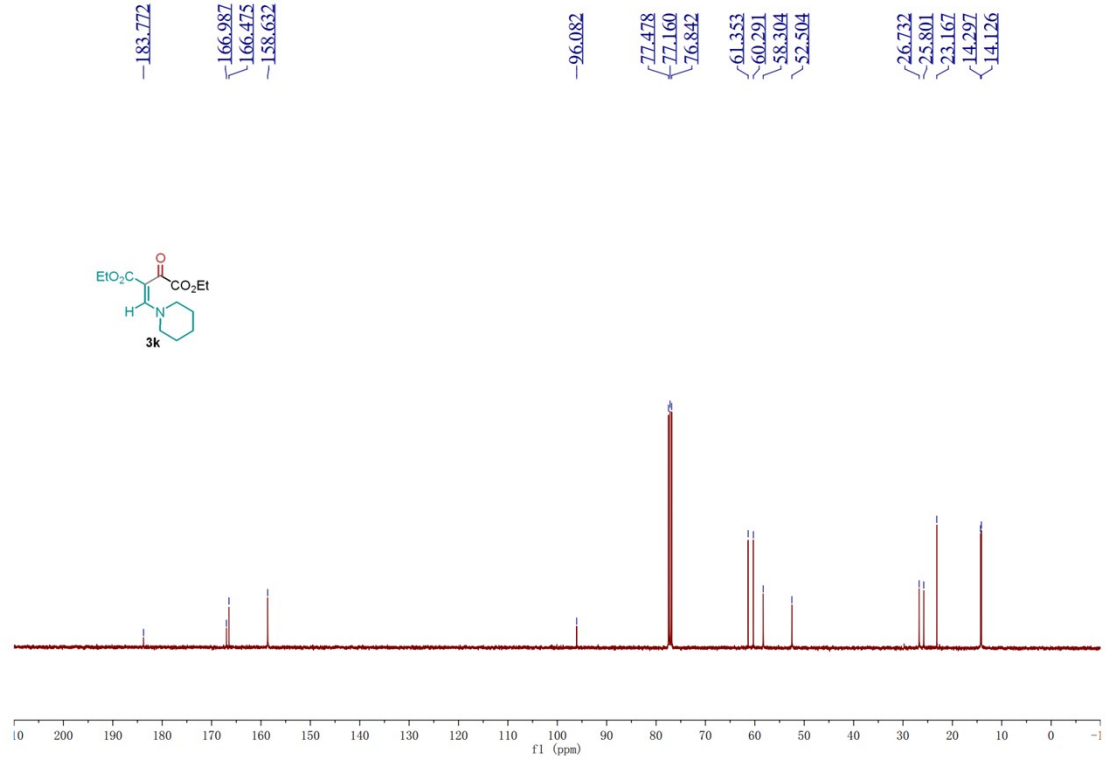
^{1}H NMR Spectrum of Compound **3j** (400 MHz, $CDCl_3$)



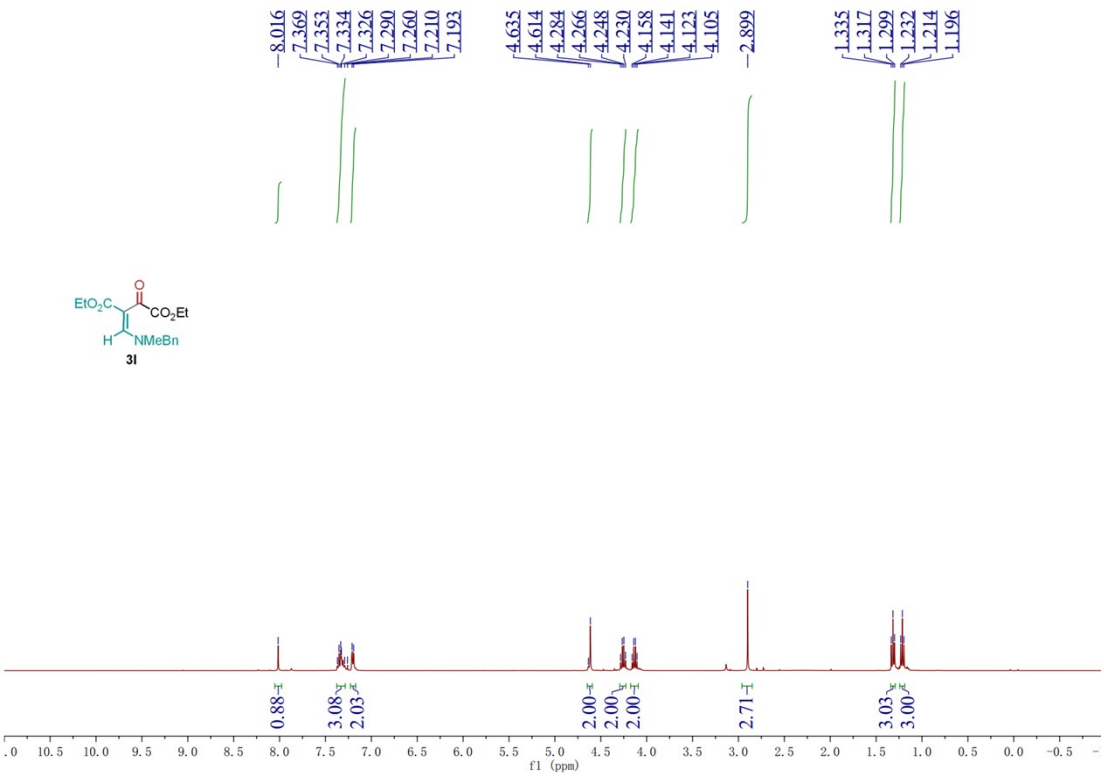
^{13}C{^{1}H} NMR Spectrum of Compound **3j** (100 MHz, $CDCl_3$)



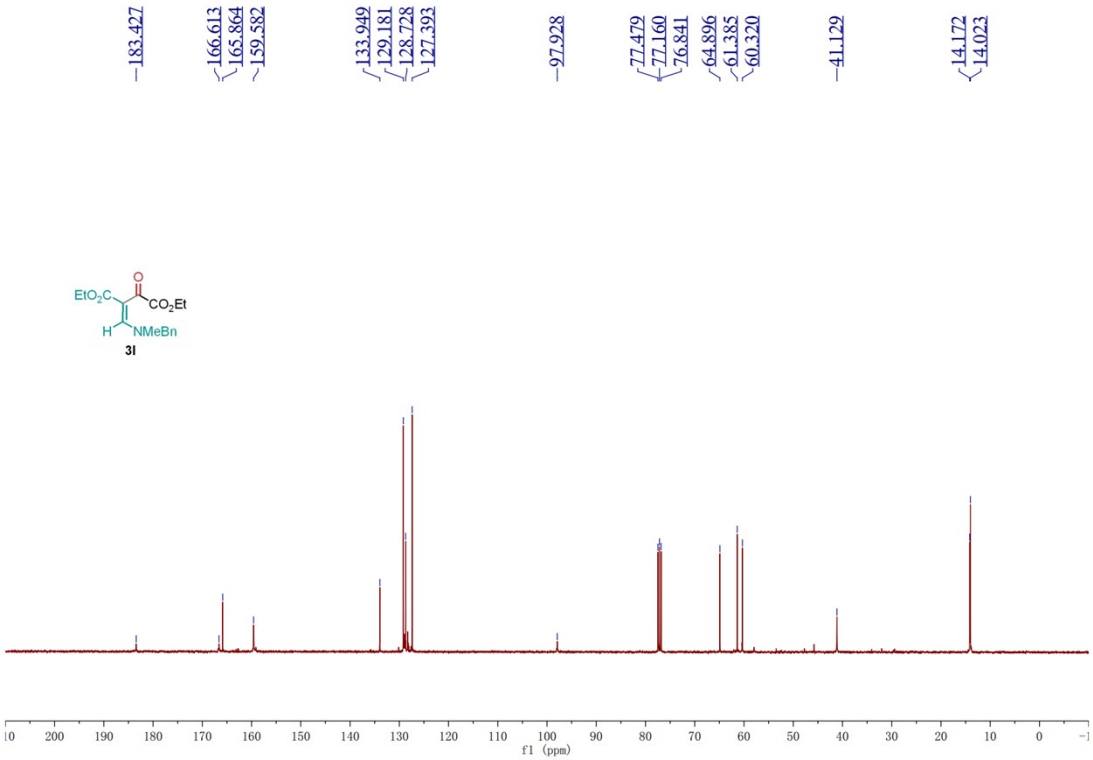
^{1}H NMR Spectrum of Compound **3k** (400 MHz, $CDCl_3$)



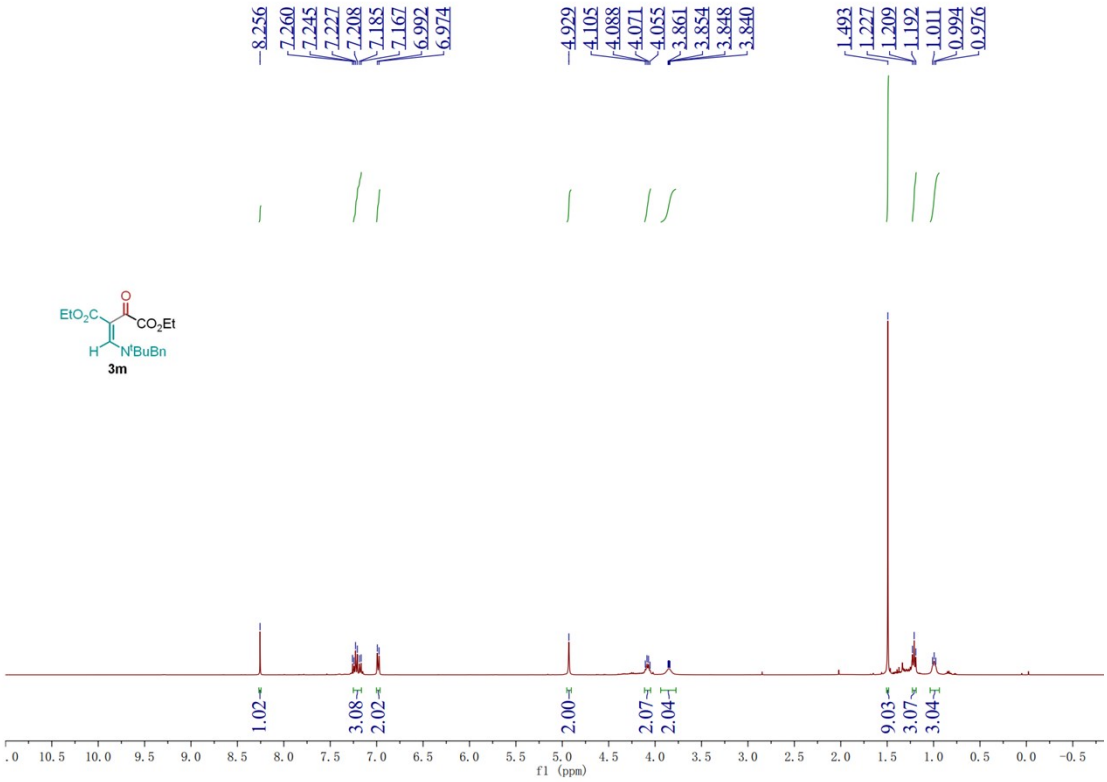
^{13}C{^{1}H} NMR Spectrum of Compound **3k** (100 MHz, $CDCl_3$)



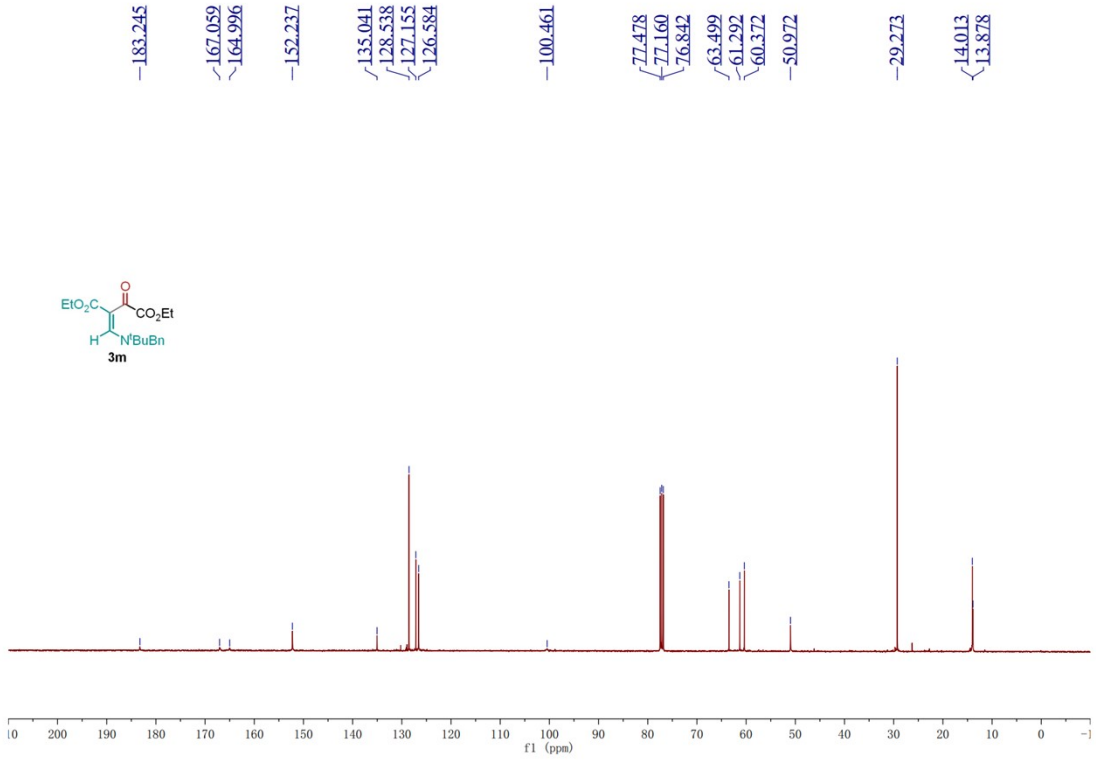
^{1}H NMR Spectrum of Compound **3l** (400 MHz, $CDCl_3$)



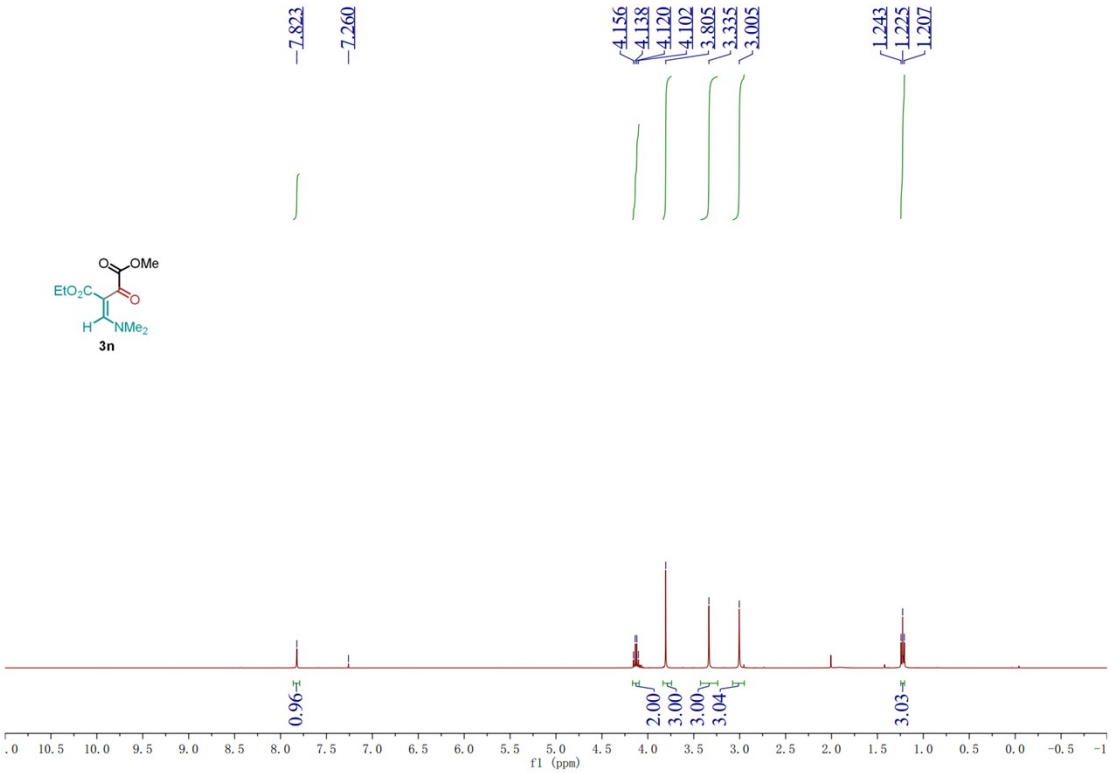
^{13}C{^{1}H} NMR Spectrum of Compound **3l** (100 MHz, $CDCl_3$)



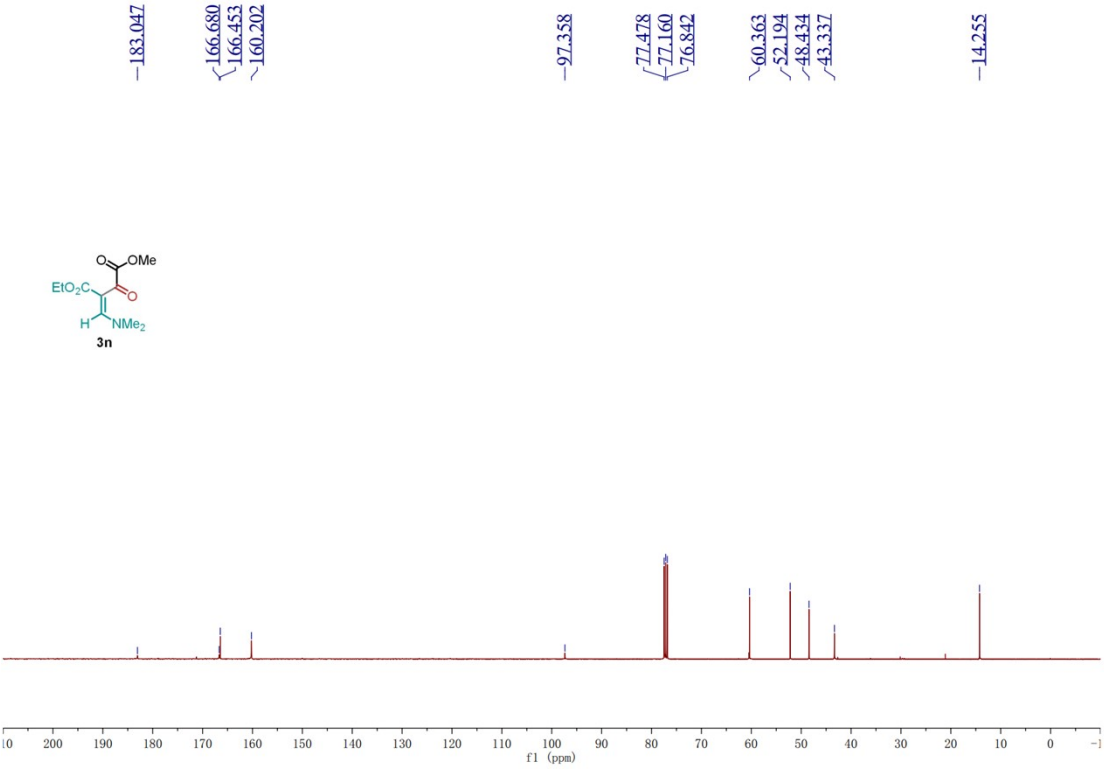
^{1}H NMR Spectrum of Compound **3m** (400 MHz, $CDCl_3$)



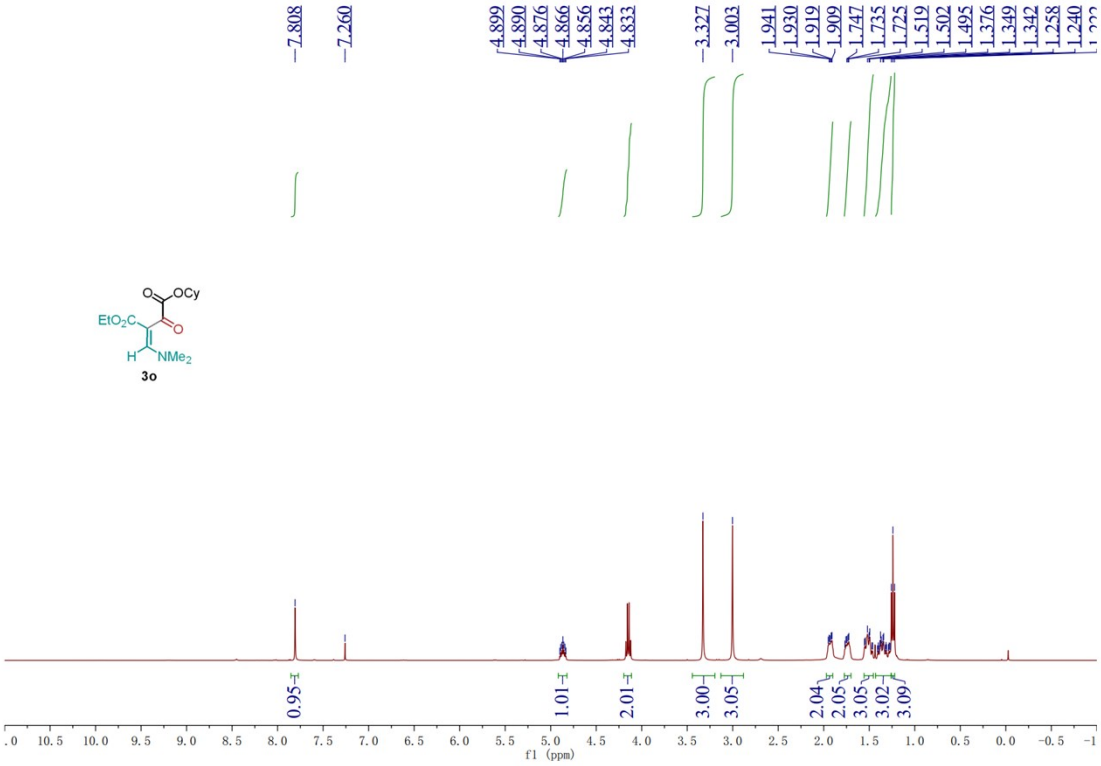
^{13}C{^{1}H} NMR Spectrum of Compound **3m** (100 MHz, $CDCl_3$)



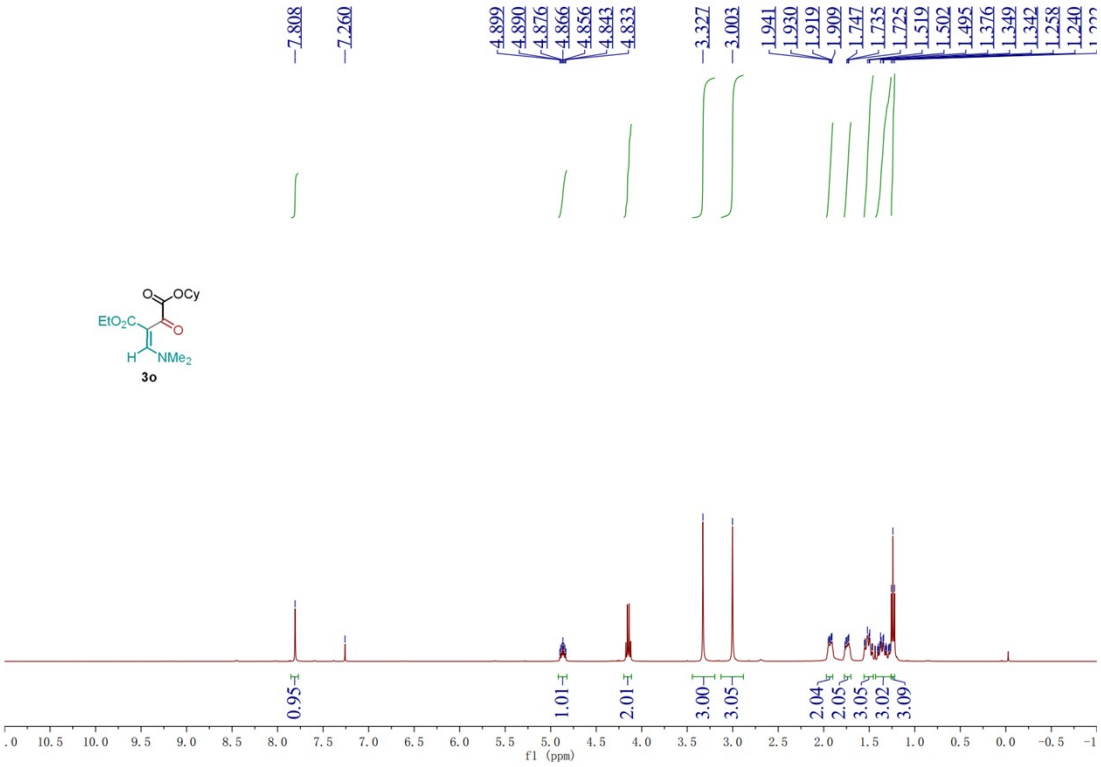
^{1}H NMR Spectrum of Compound **3n** (400 MHz, $CDCl_3$)



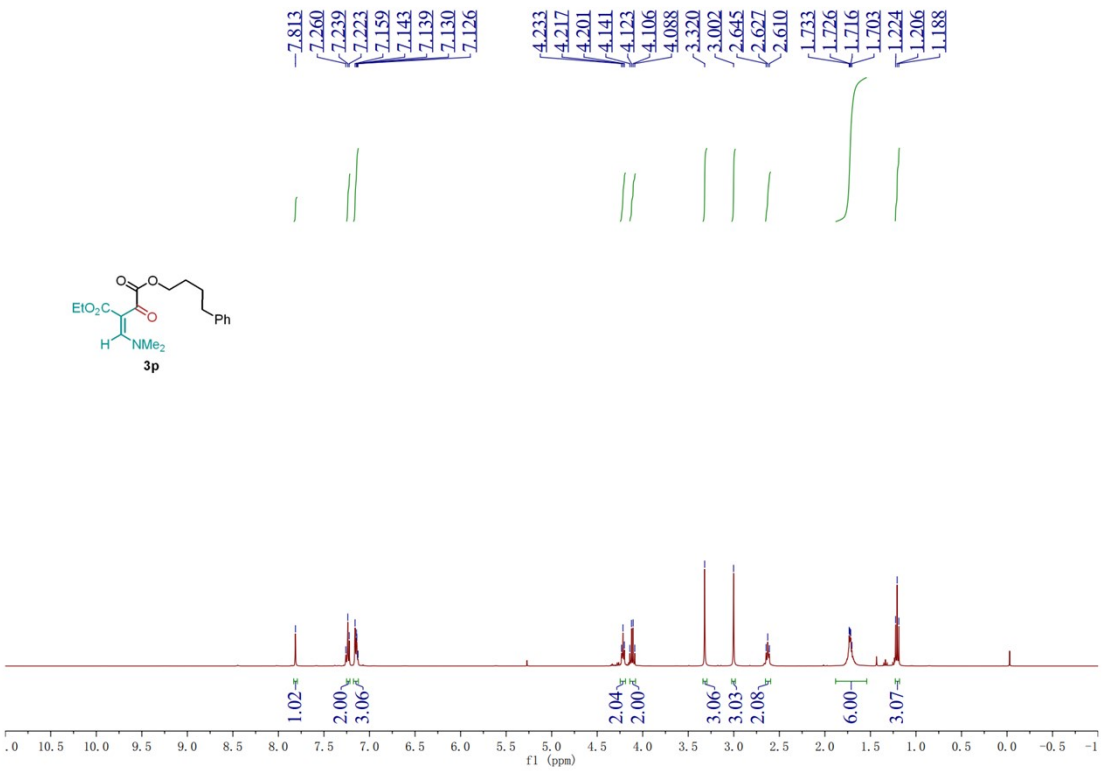
^{13}C{^{1}H} NMR Spectrum of Compound **3n** (100 MHz, $CDCl_3$)



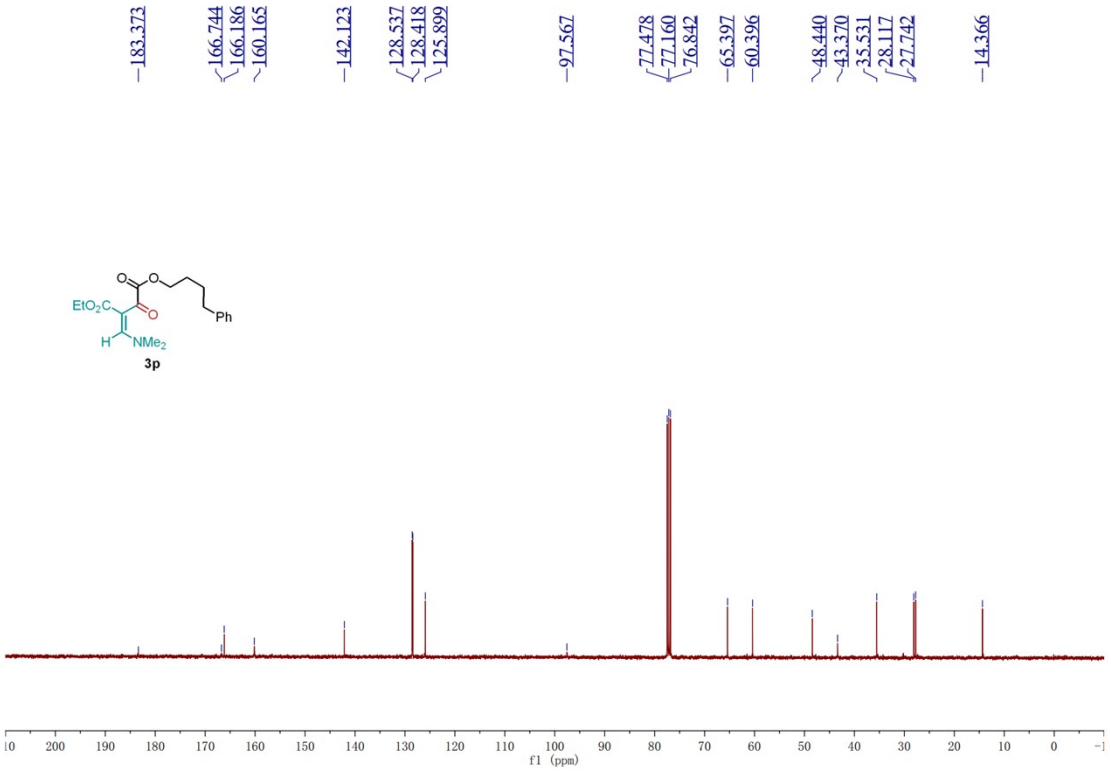
^{1}H NMR Spectrum of Compound **3o** (400 MHz, $CDCl_3$)



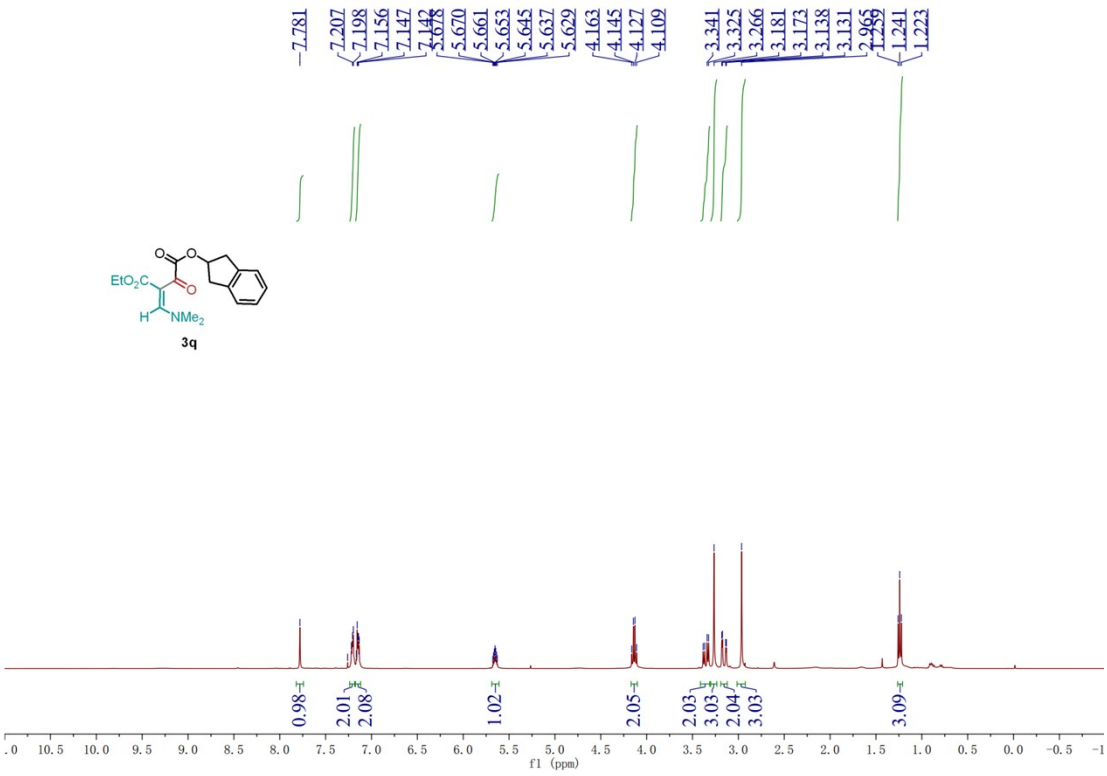
^{13}C{^{1}H} NMR Spectrum of Compound **3o** (100 MHz, $CDCl_3$)



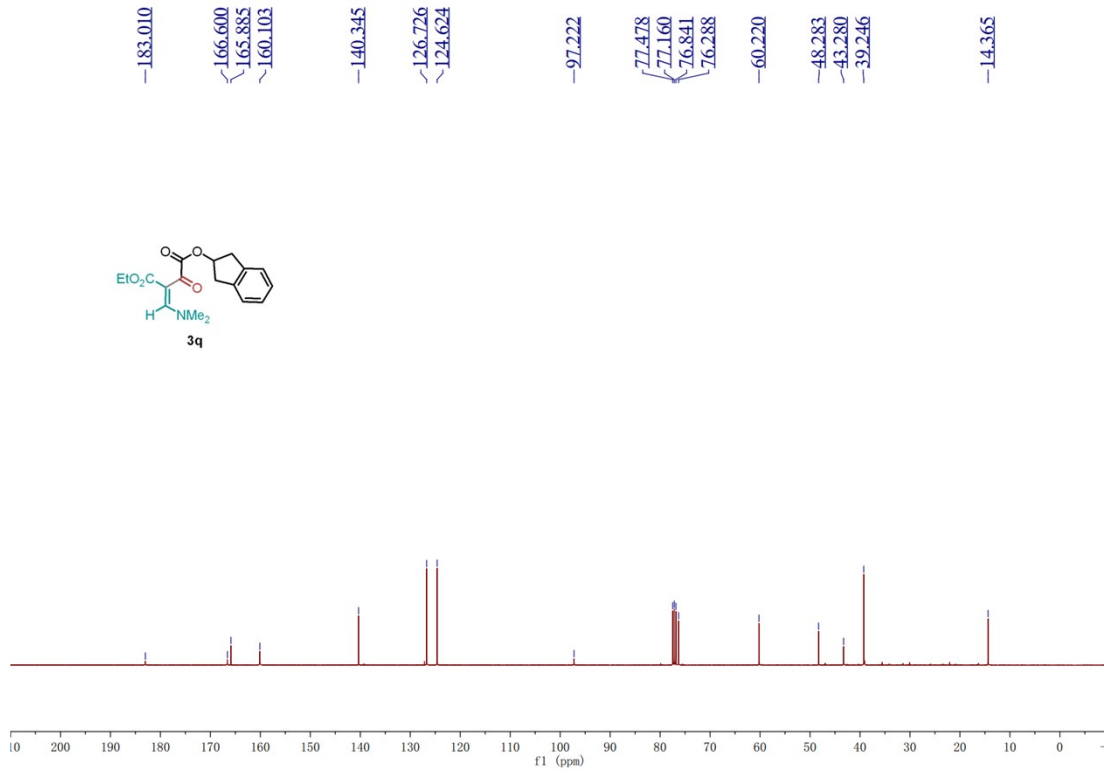
^{1}H NMR Spectrum of Compound **3p** (400 MHz, $CDCl_3$)



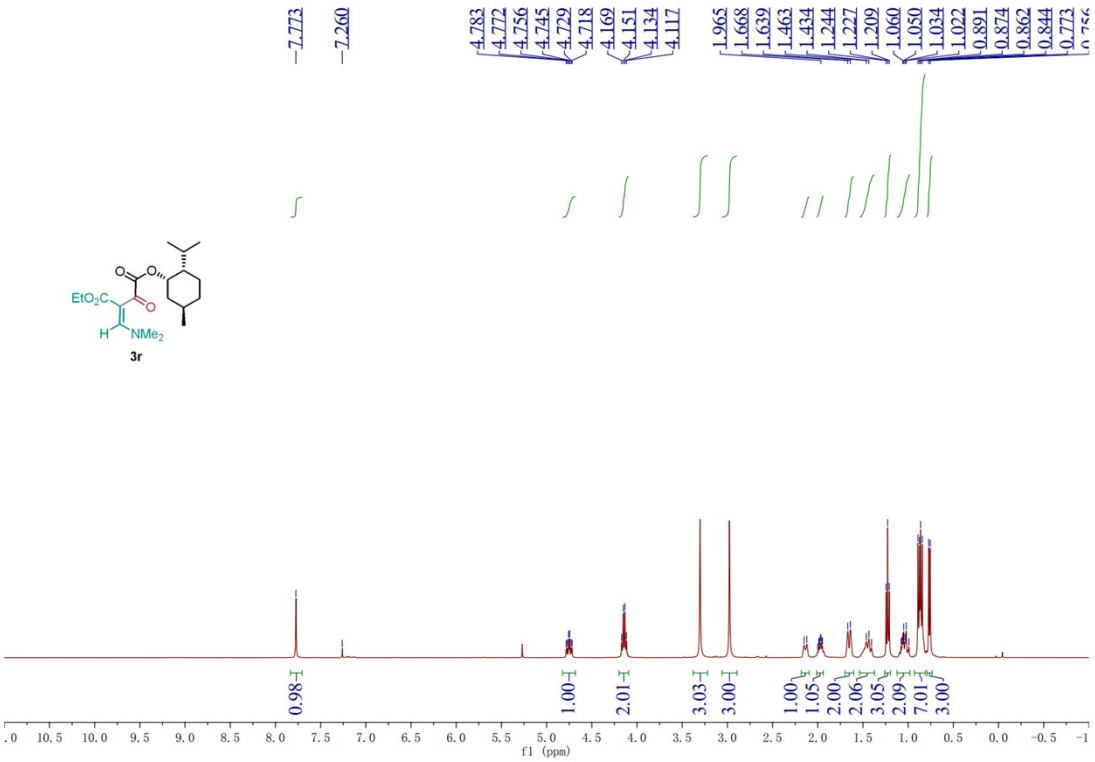
^{13}C{^{1}H} NMR Spectrum of Compound **3p** (100 MHz, $CDCl_3$)



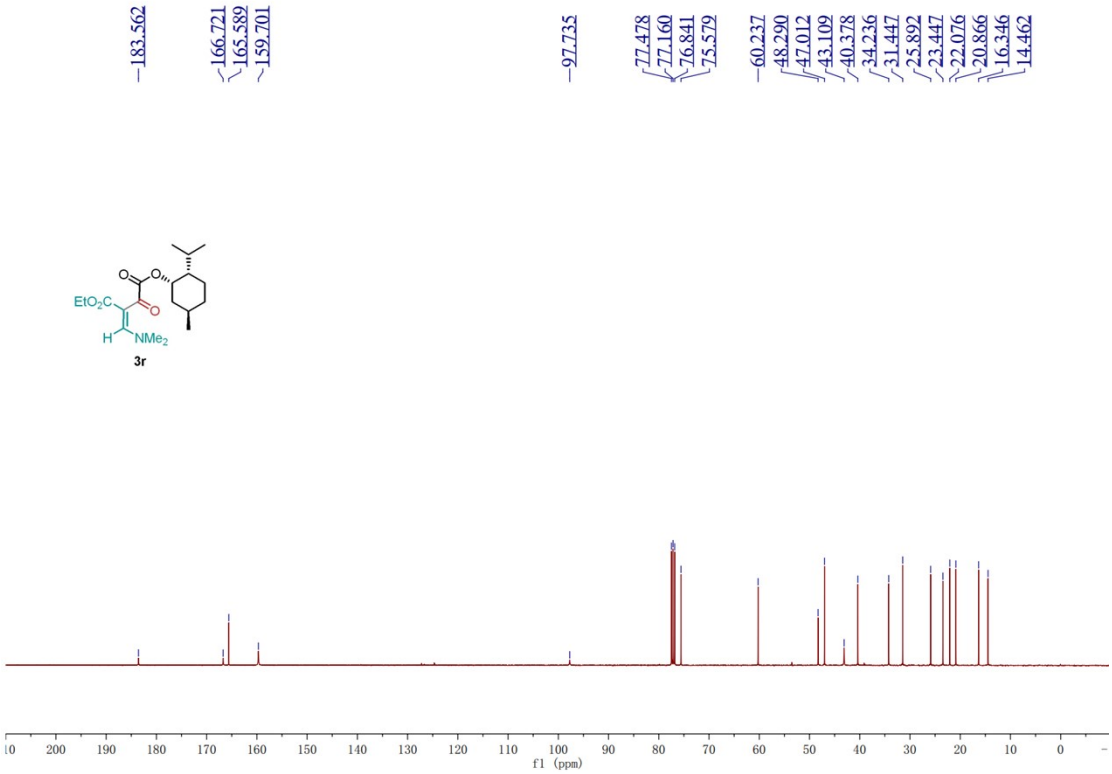
^{1}H NMR Spectrum of Compound **3q** (400 MHz, $CDCl_3$)



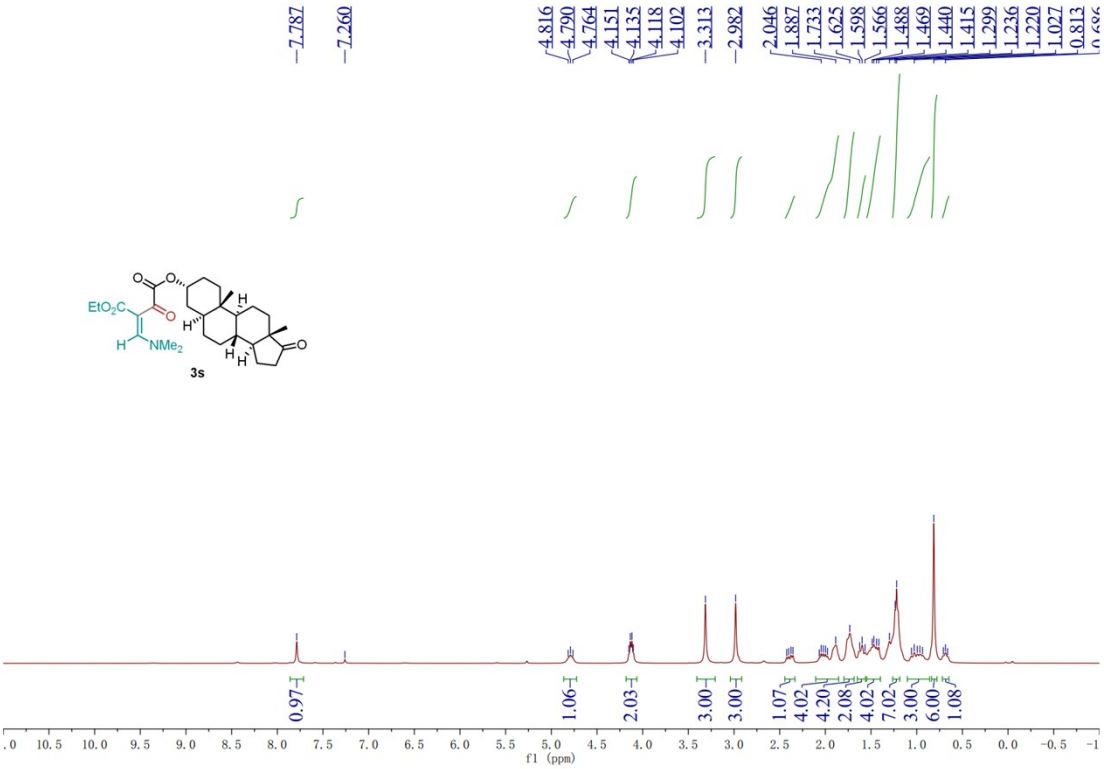
^{13}C{^{1}H} NMR Spectrum of Compound **3q** (100 MHz, $CDCl_3$)



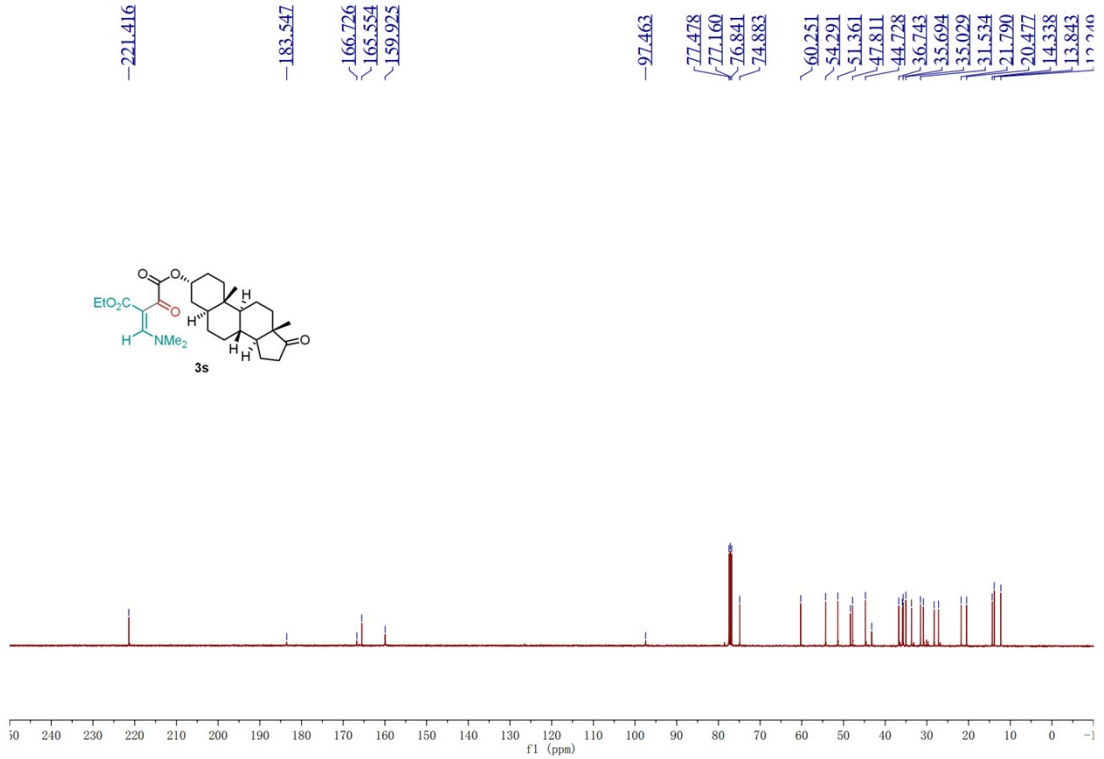
^{1}H NMR Spectrum of Compound **3r** (400 MHz, $CDCl_3$)



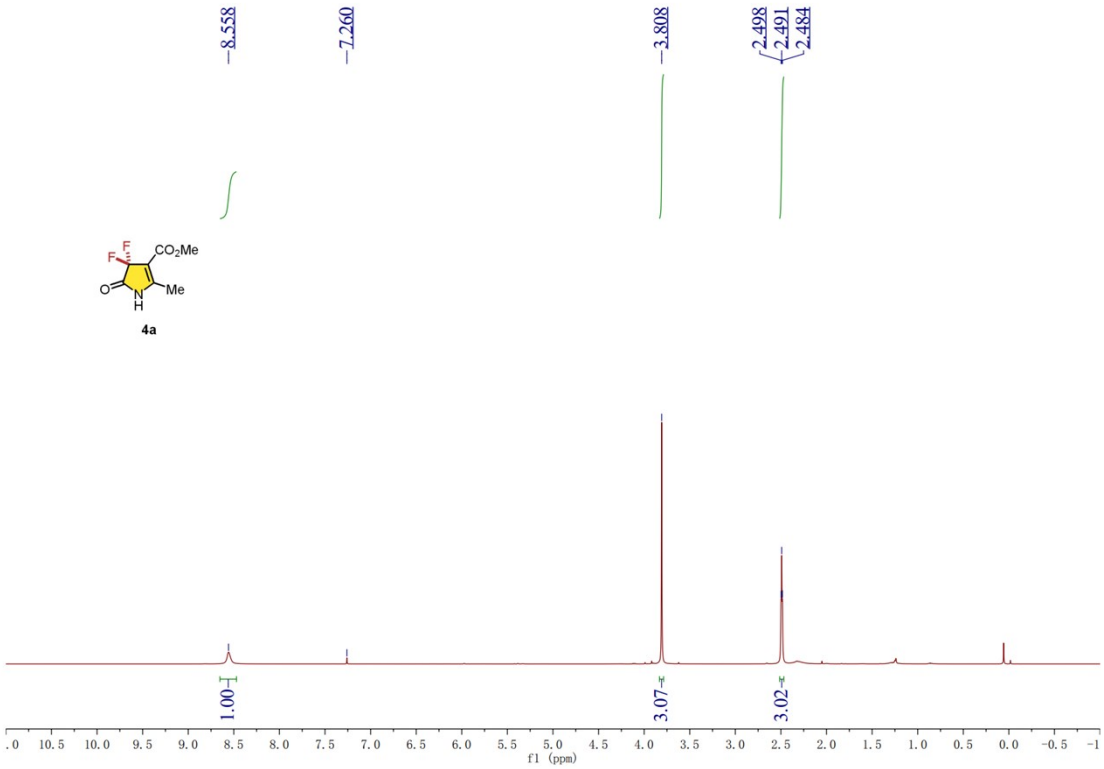
^{13}C{^{1}H} NMR Spectrum of Compound **3r** (100 MHz, $CDCl_3$)



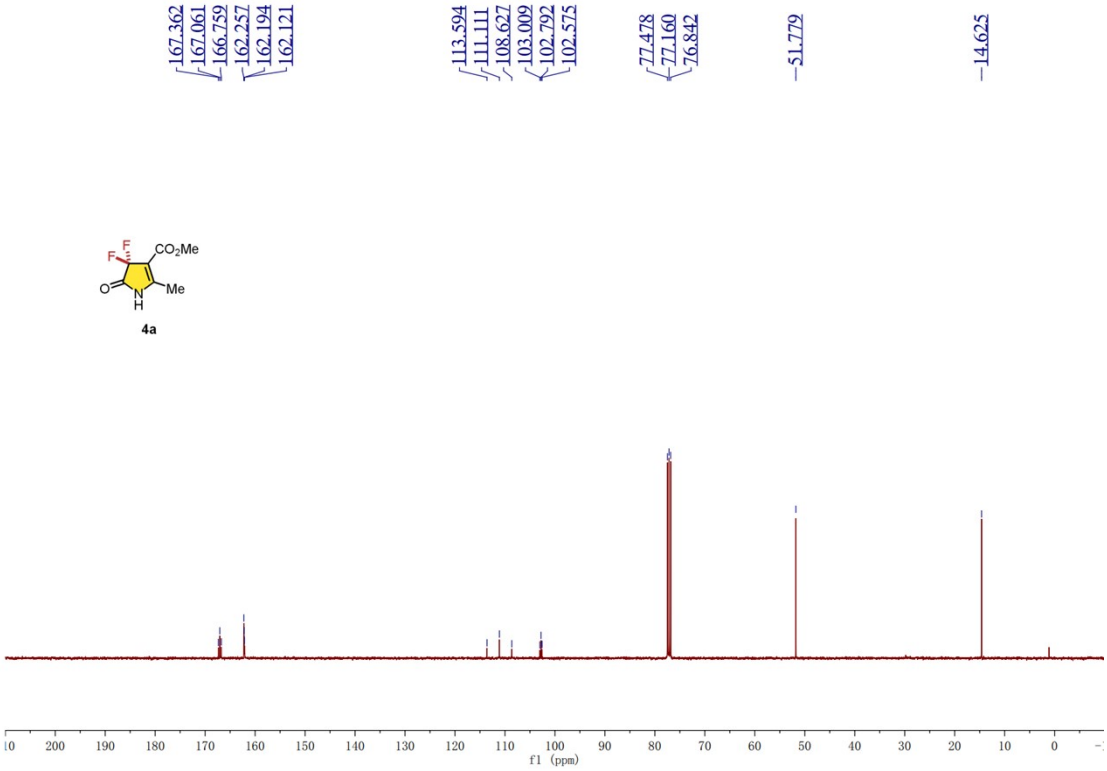
^{1}H NMR Spectrum of Compound **3s** (400 MHz, $CDCl_3$)



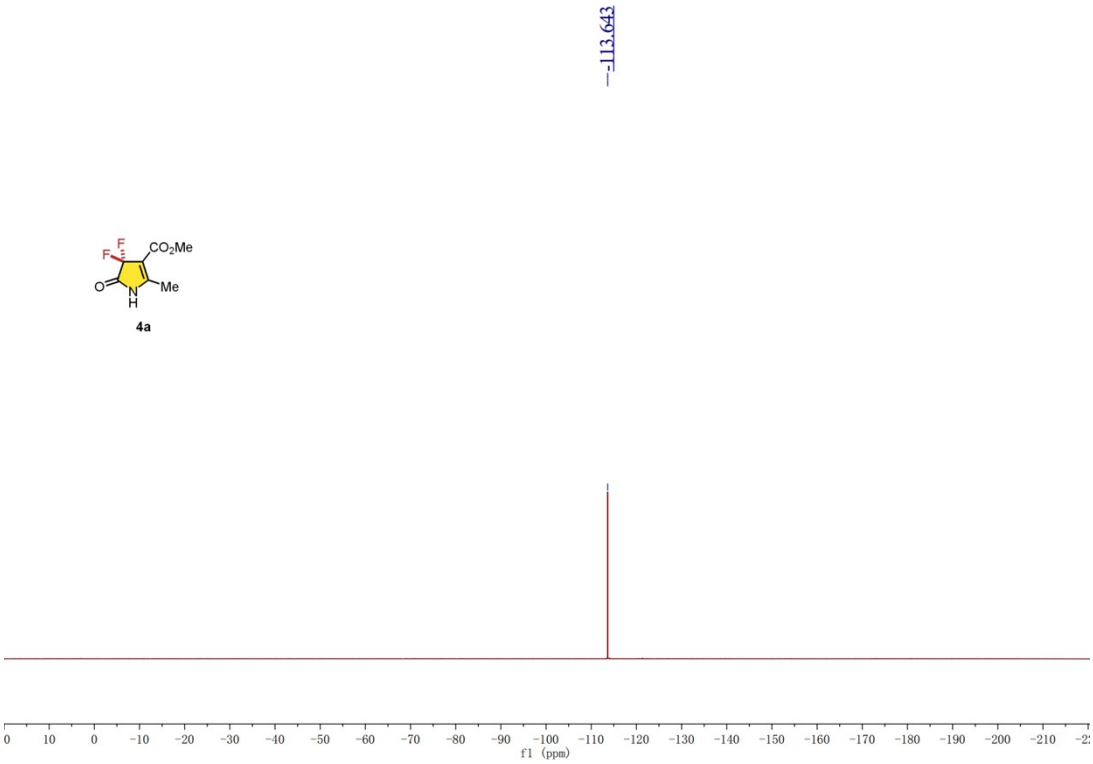
^{13}C{^{1}H} NMR Spectrum of Compound **3s** (100 MHz, $CDCl_3$)



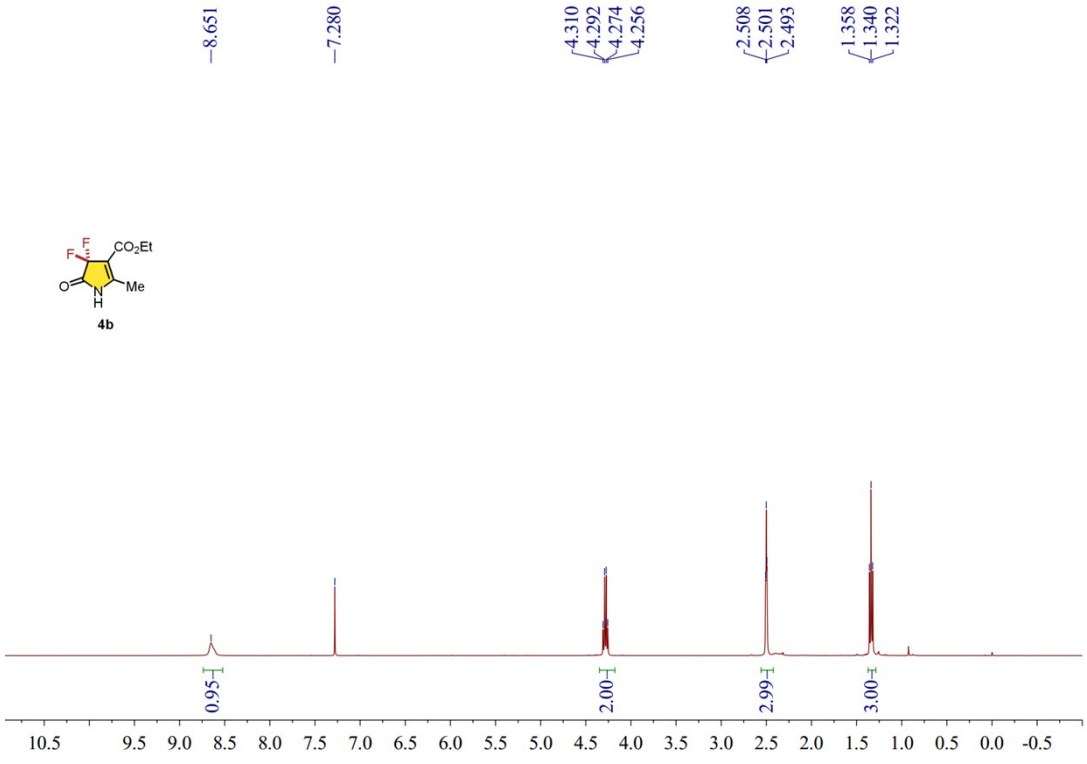
^{1}H NMR Spectrum of Compound **4a** (400 MHz, $CDCl_3$)



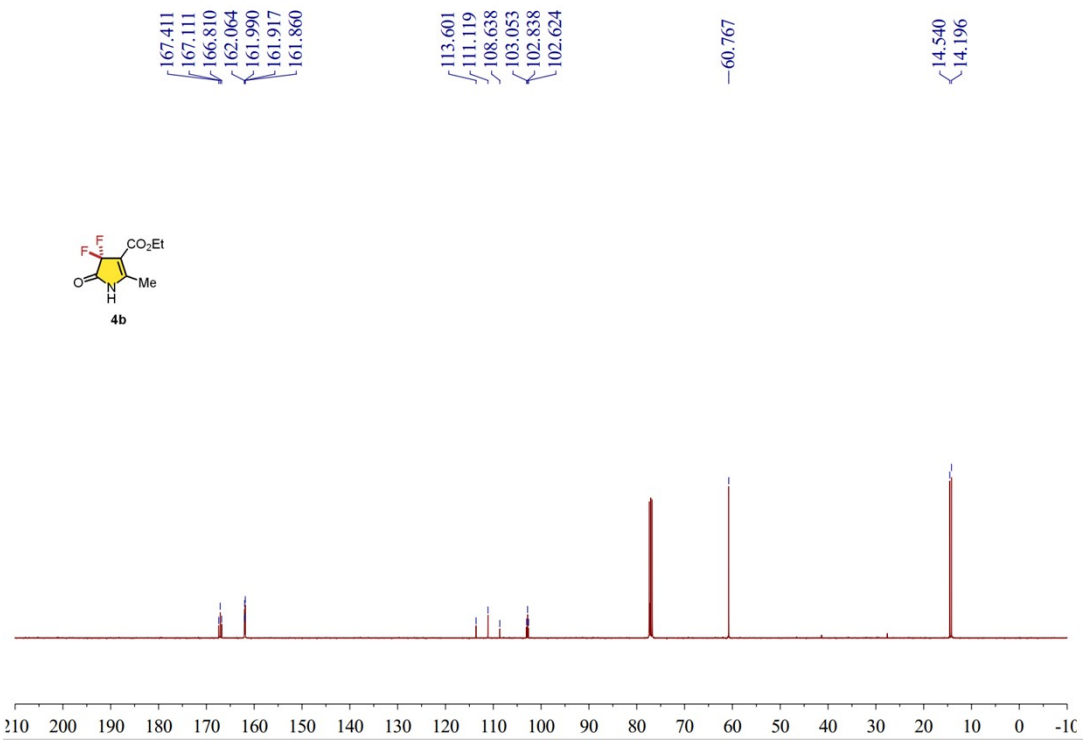
^{13}C{^{1}H} NMR Spectrum of Compound **4a** (100 MHz, $CDCl_3$)



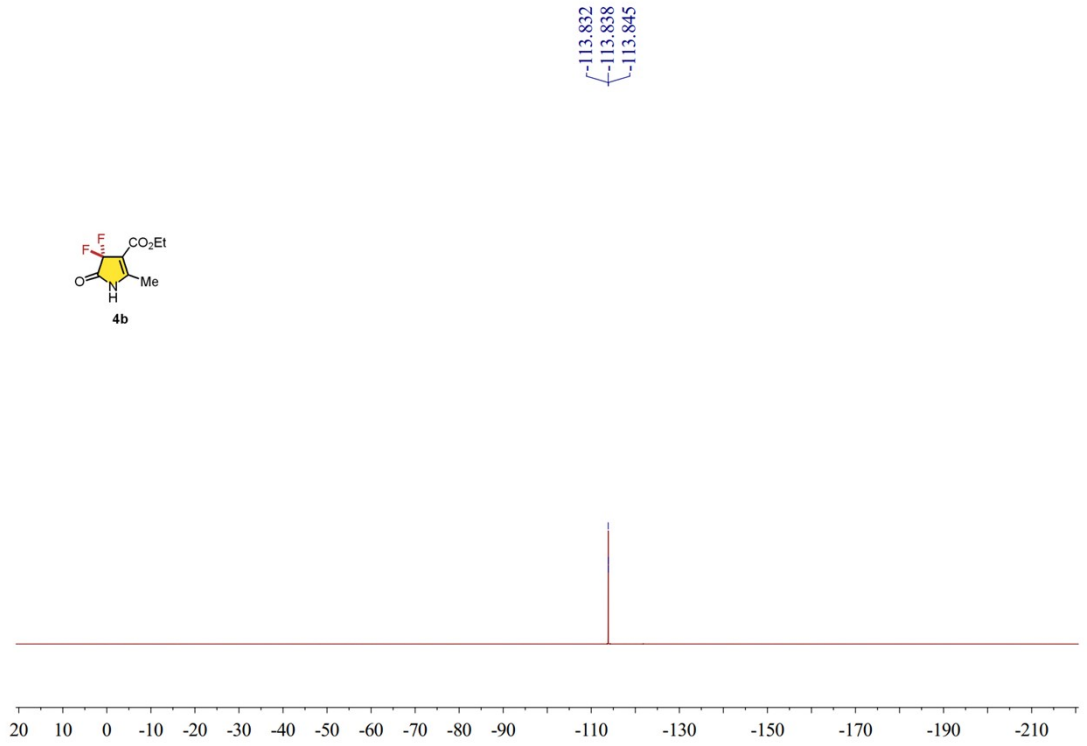
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4a** (376 MHz, $CDCl_3$)



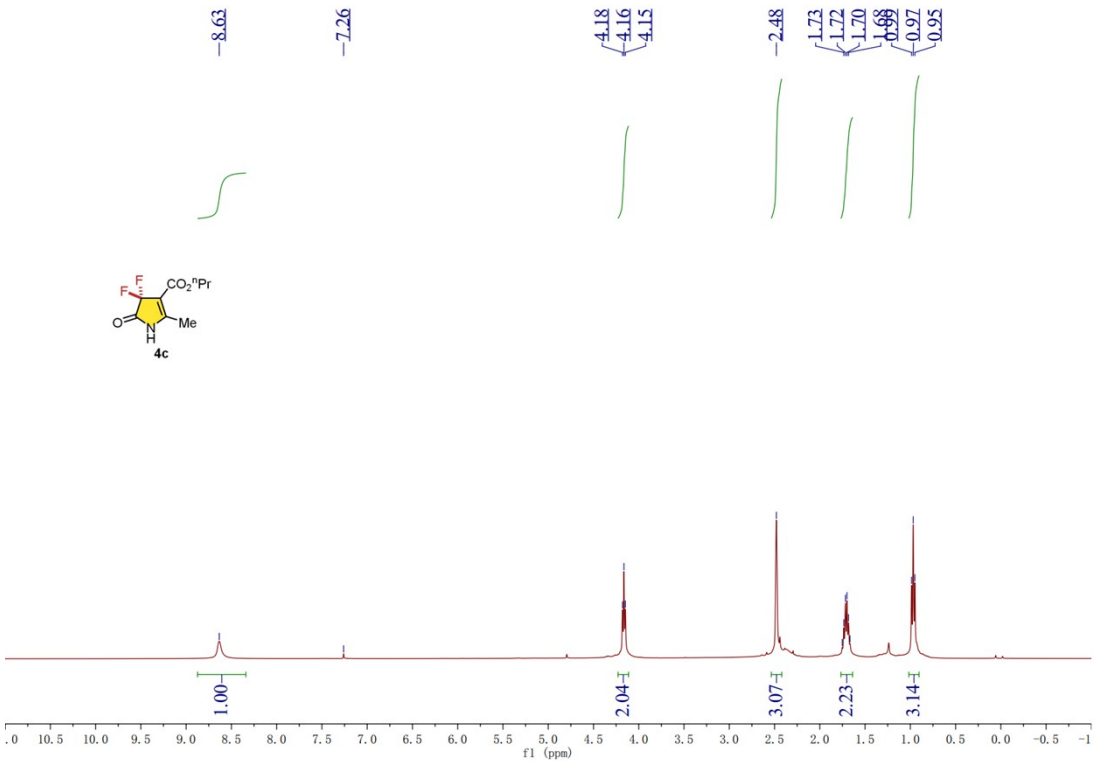
^{1}H NMR Spectrum of Compound **4b** (400 MHz, $CDCl_3$)



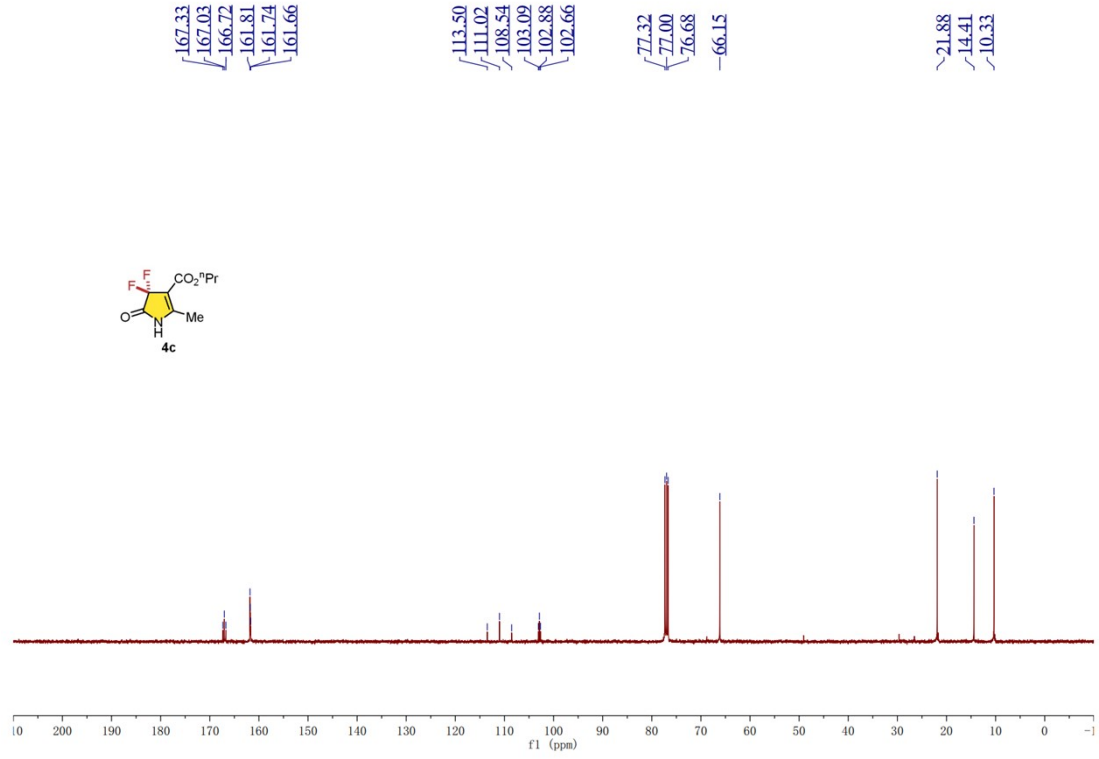
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4b** (100 MHz, $CDCl_3$)



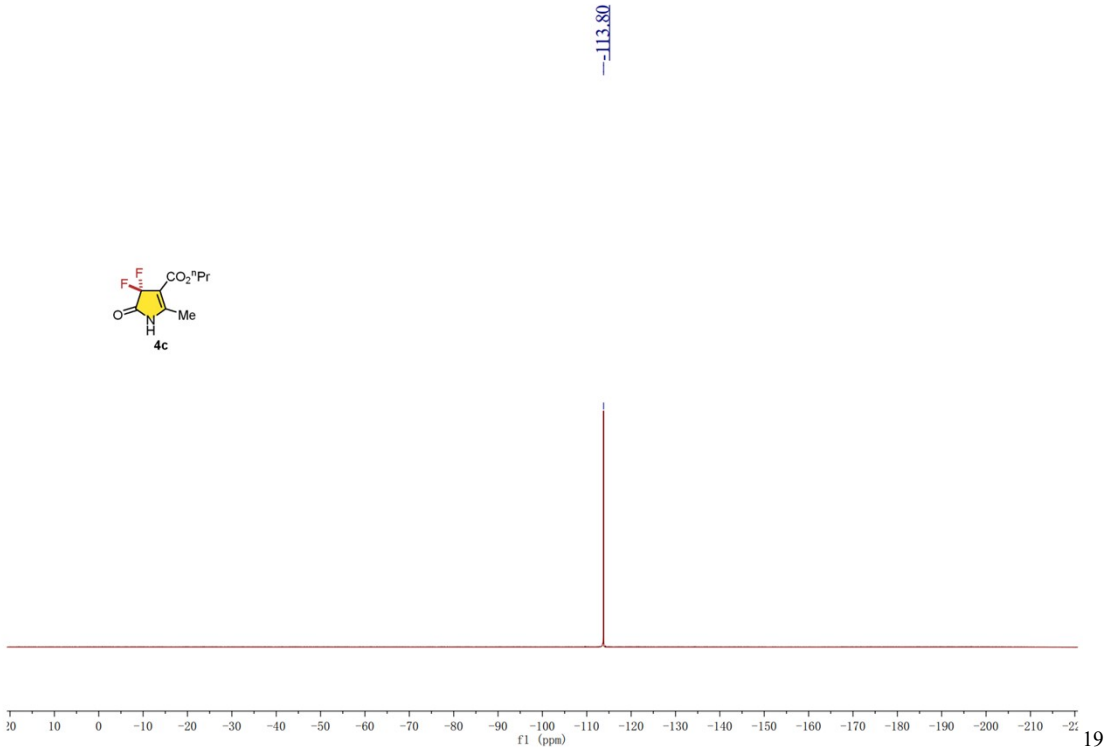
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4b** (376 MHz, $CDCl_3$)



^{1}H NMR Spectrum of Compound **4c** (400 MHz, $CDCl_3$)



^{13}C{^{1}H} NMR Spectrum of Compound **4c** (100 MHz, $CDCl_3$)



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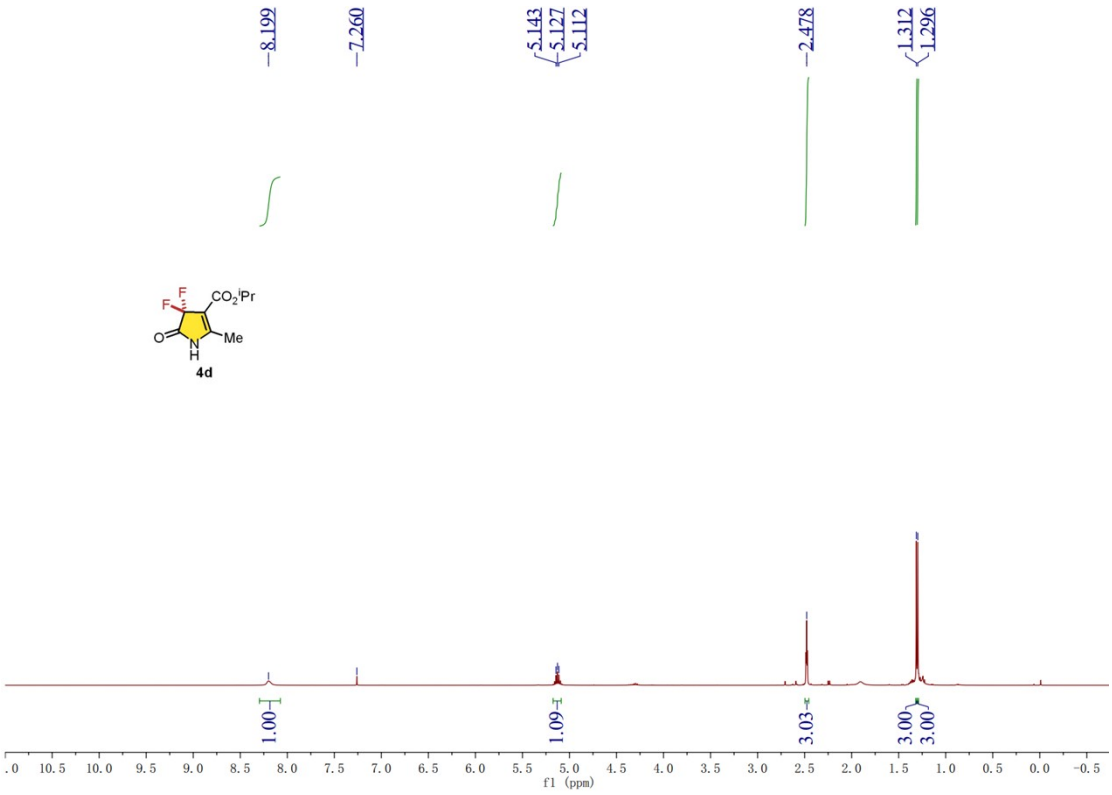
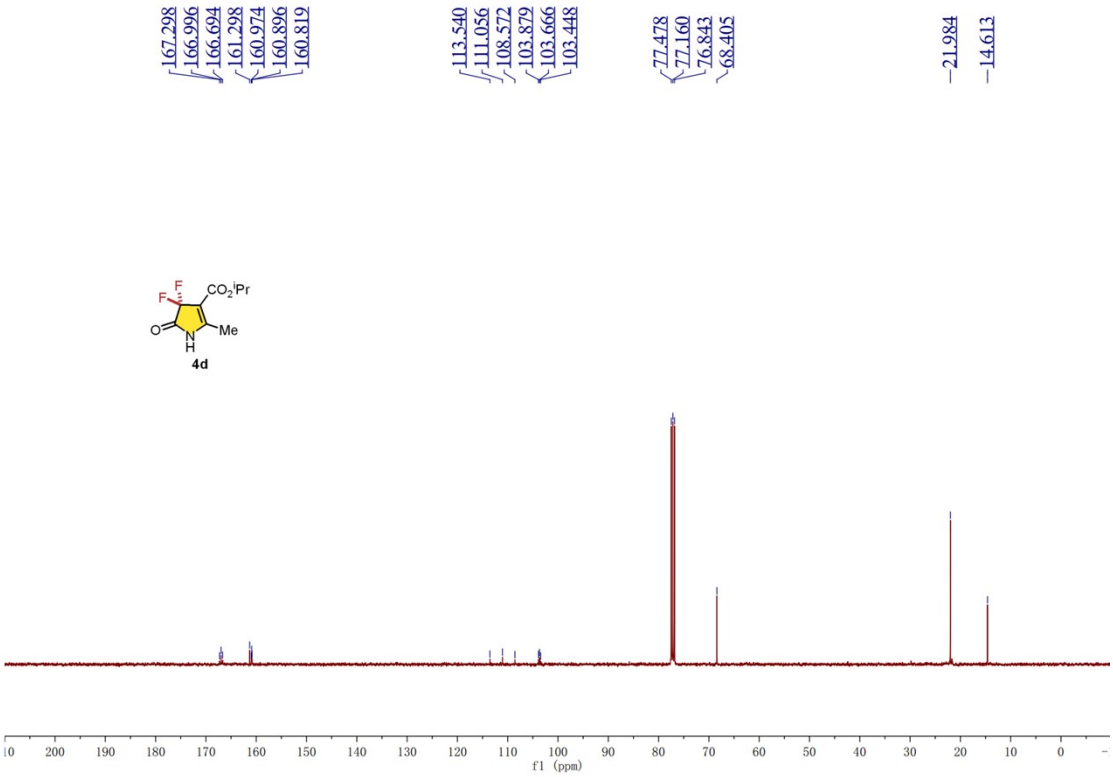
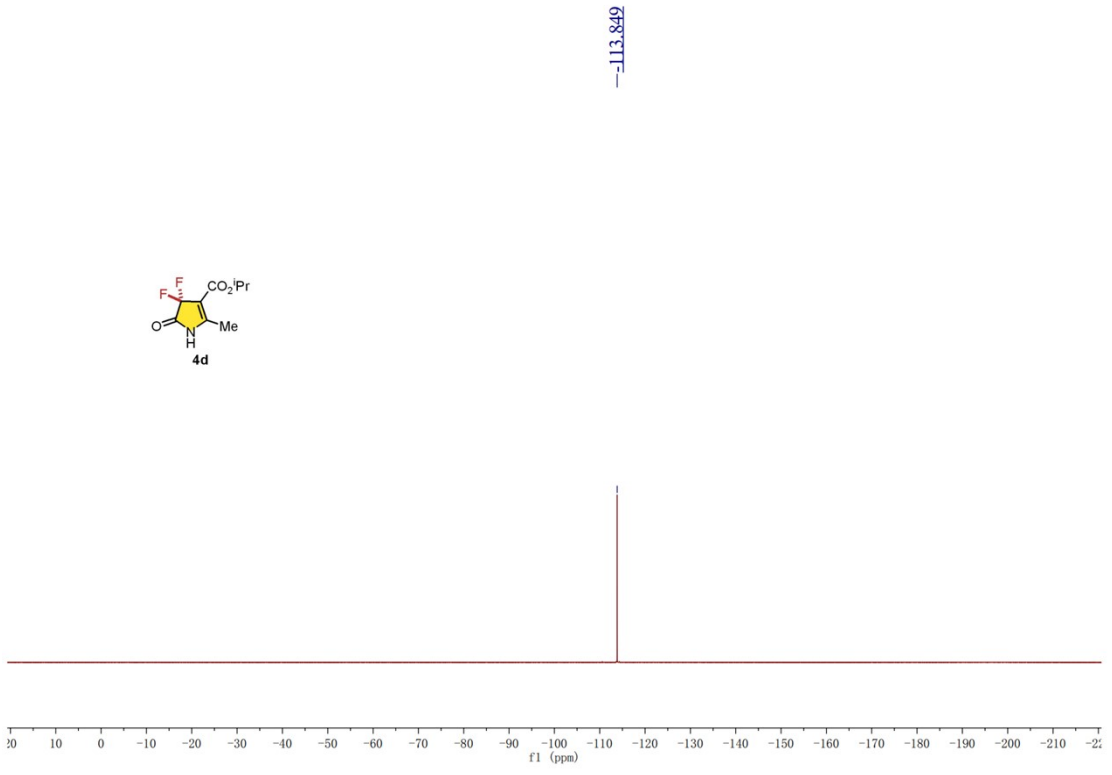
F{^{1}H} NMR Spectrum of Compound **4c** (376 MHz, $CDCl_3$)



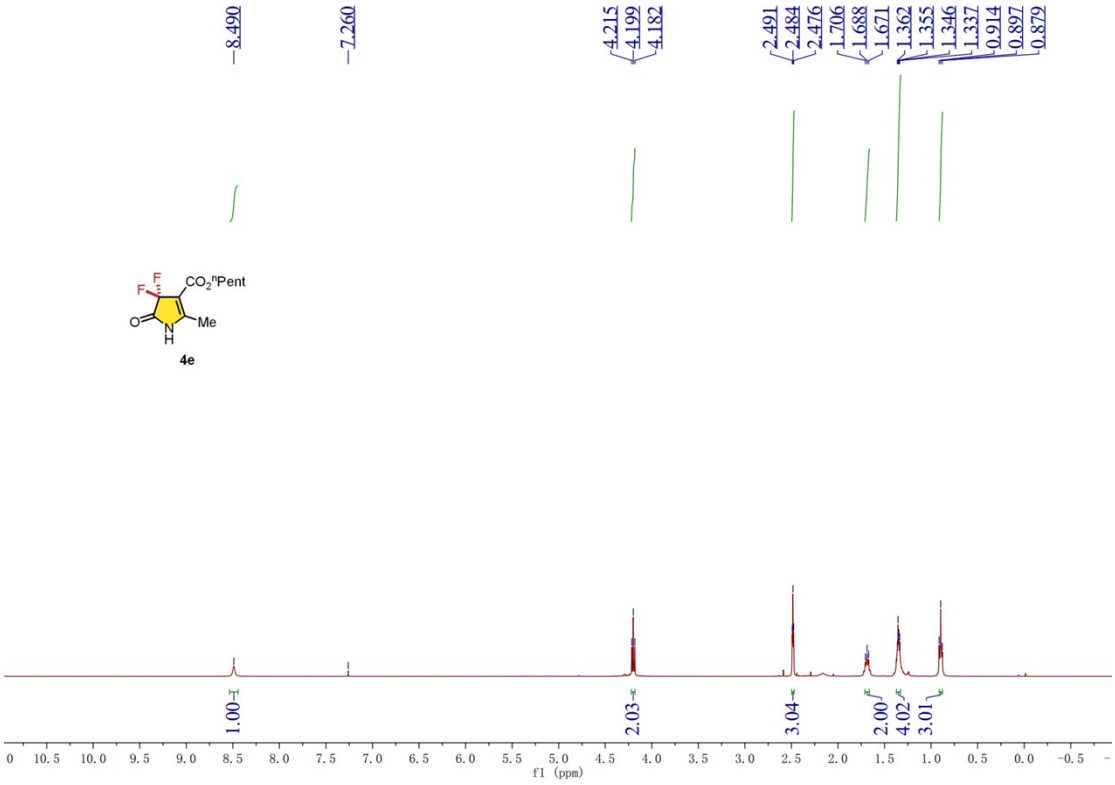
^{1}H NMR Spectrum of Compound **4d** (400 MHz, $CDCl_3$)



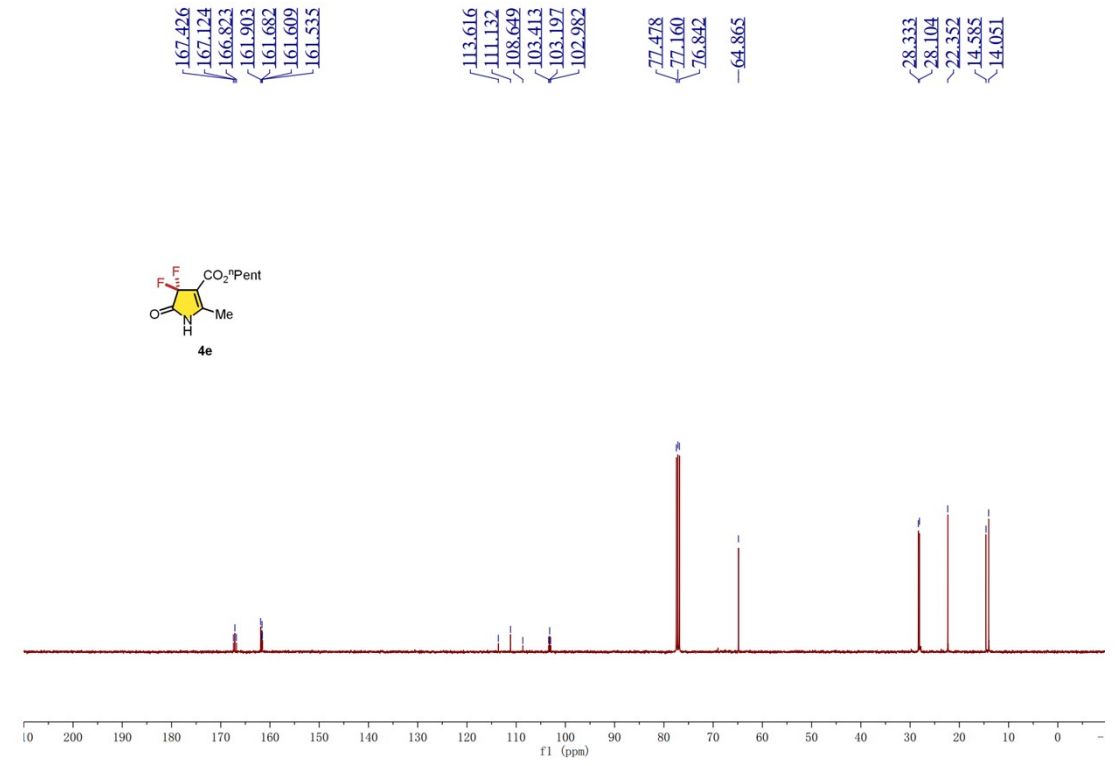
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4d** (100 MHz, $CDCl_3$)



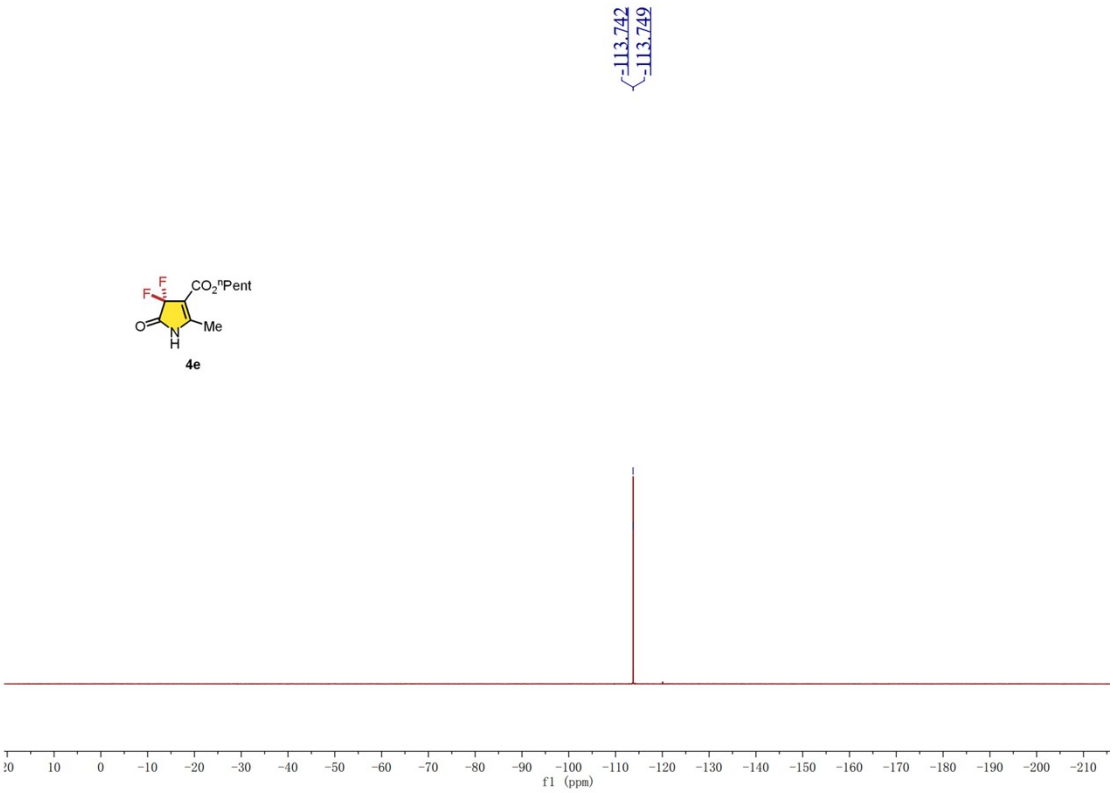
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4d** (376 MHz, $CDCl_3$)



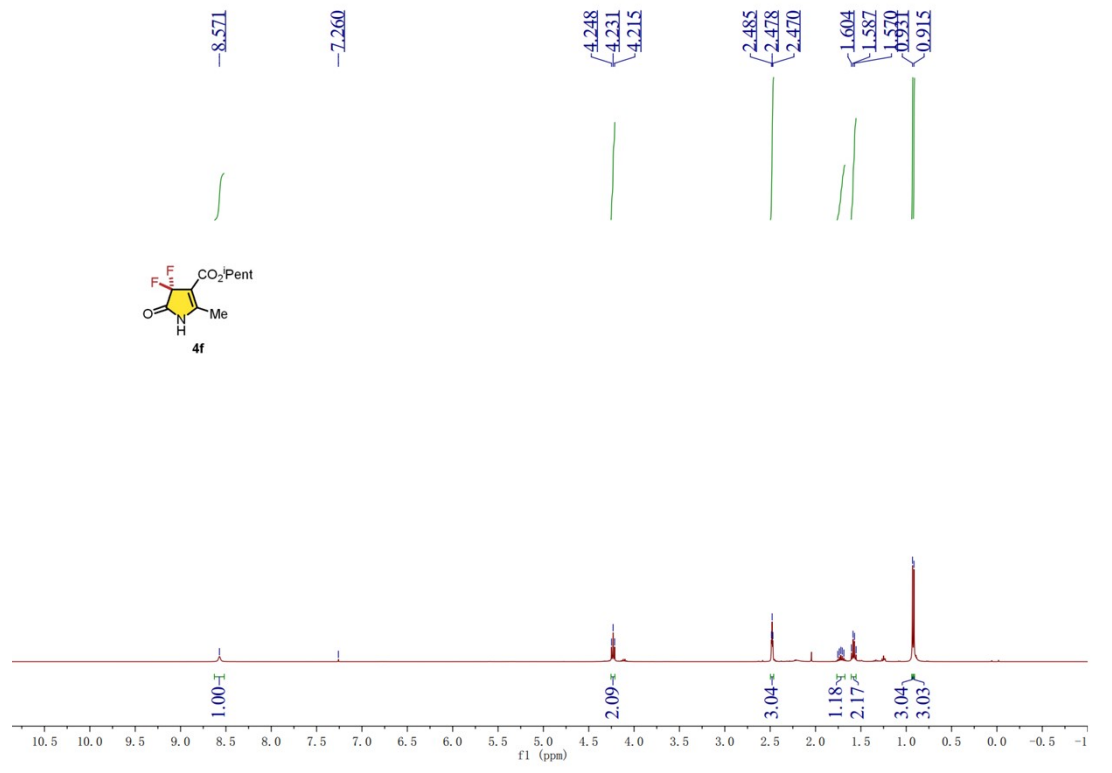
^{1}H NMR Spectrum of Compound **4e** (400 MHz, $CDCl_3$)



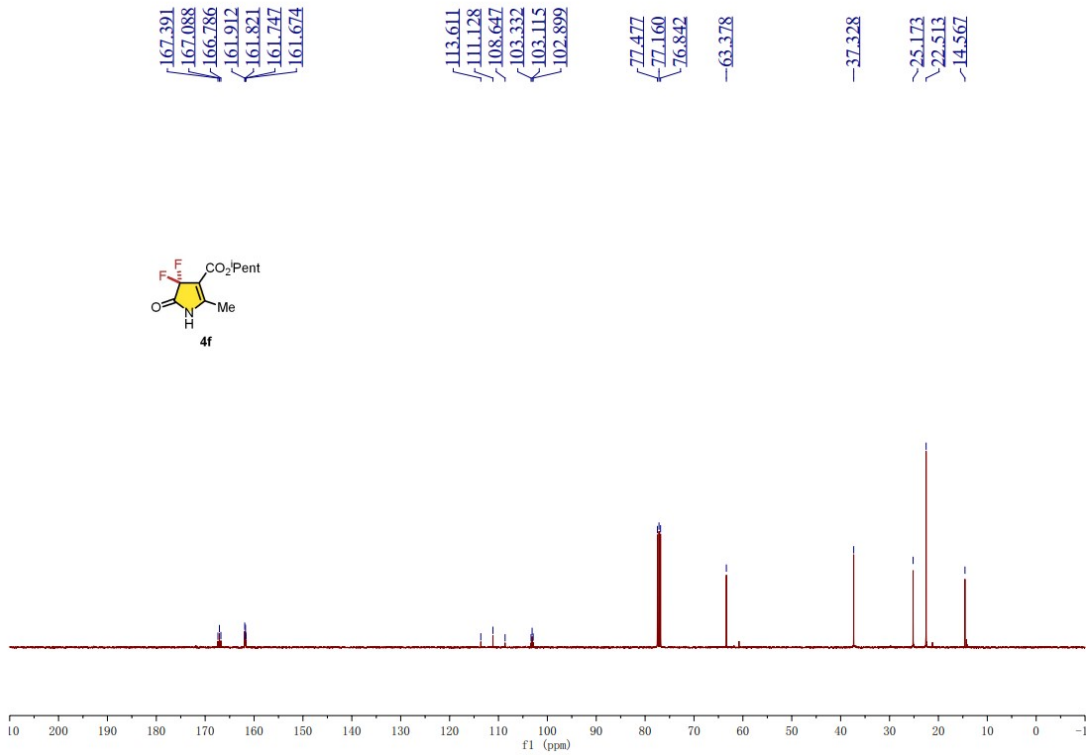
^{13}C{^{1}H} NMR Spectrum of Compound **4e** (100 MHz, $CDCl_3$)



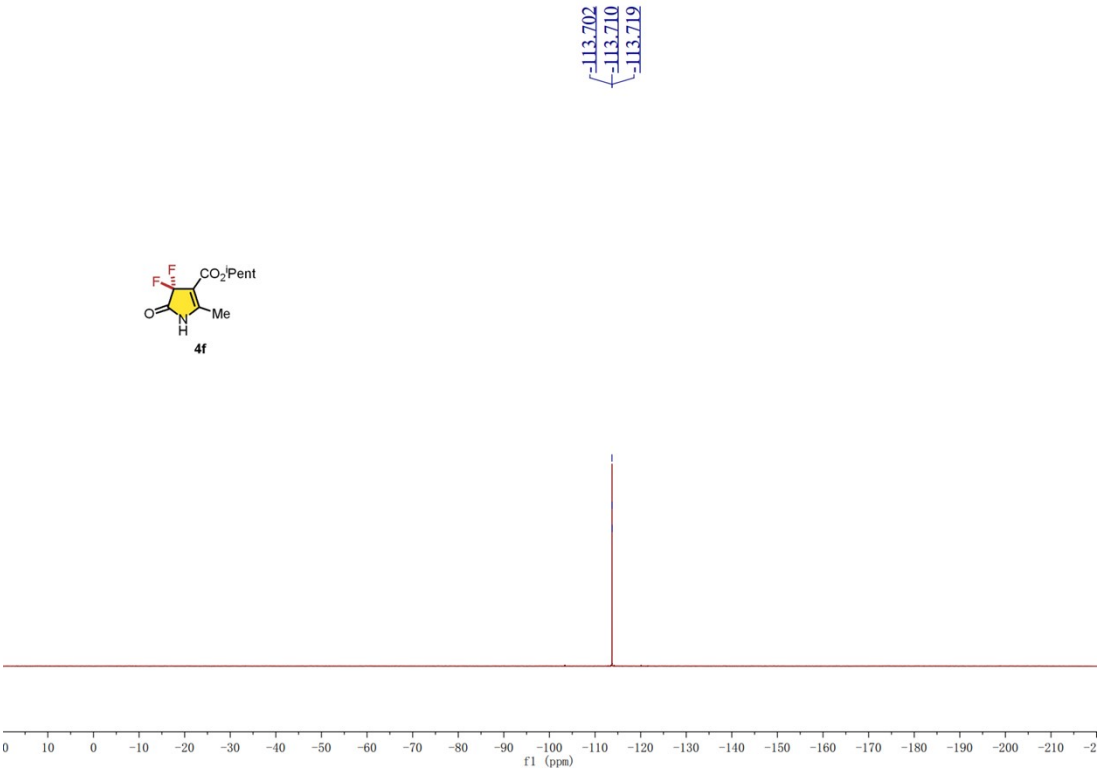
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4e** (376 MHz, $CDCl_3$)



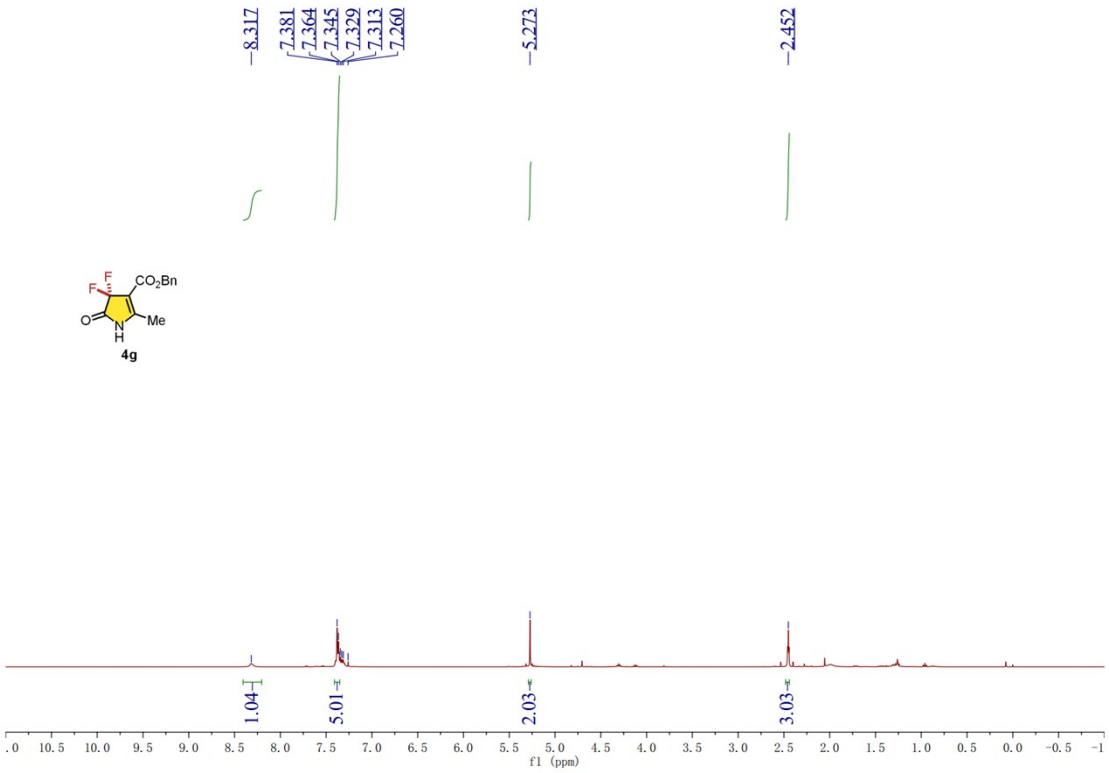
^{1}H NMR Spectrum of Compound **4f** (400 MHz, $CDCl_3$)



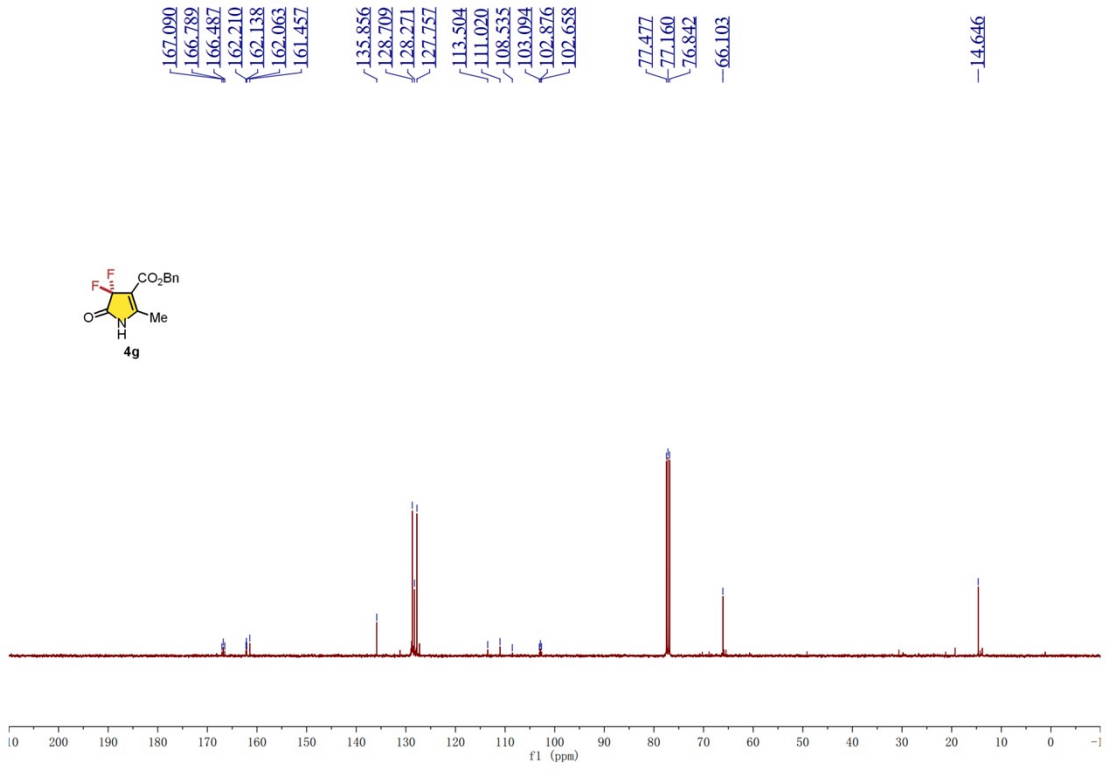
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4f** (100 MHz, $CDCl_3$)



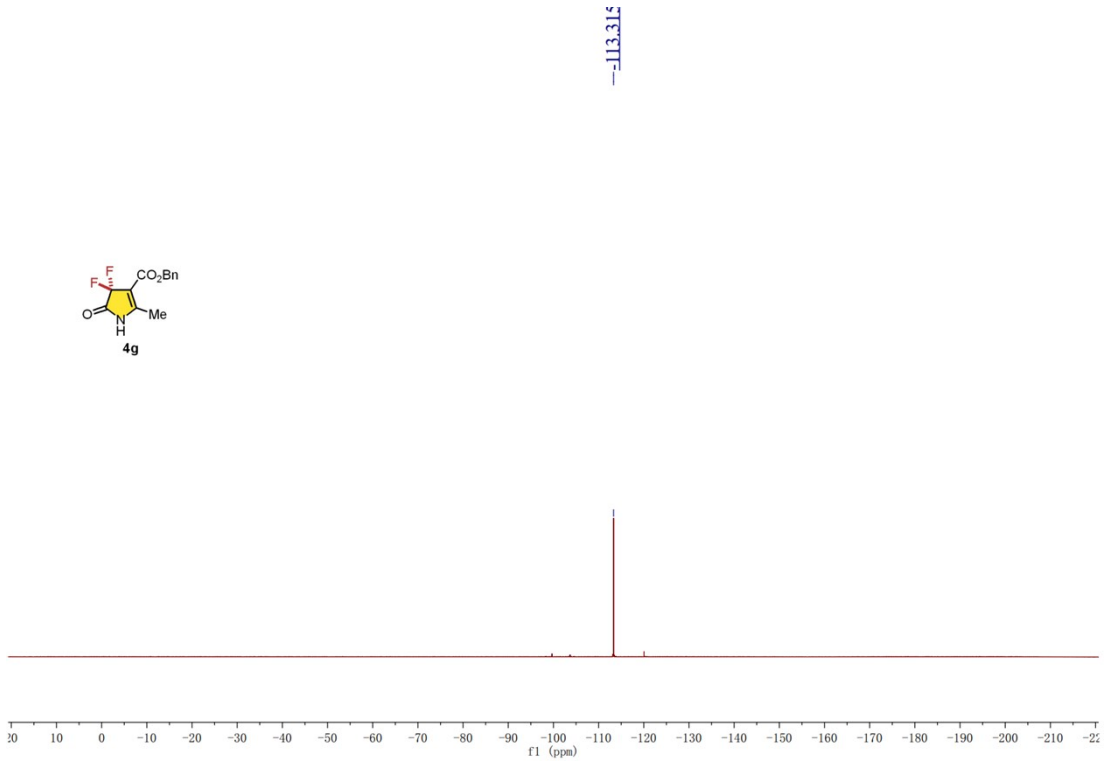
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4f** (376 MHz, $CDCl_3$)



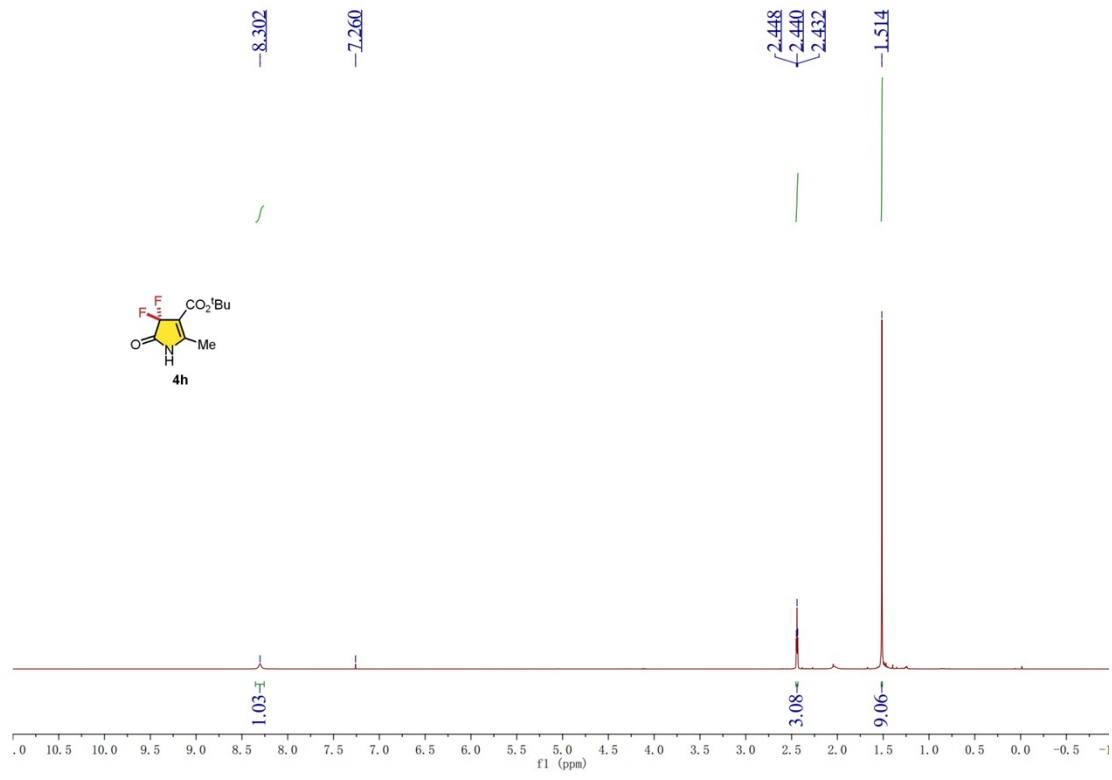
^{1}H NMR Spectrum of Compound **4g** (400 MHz, $CDCl_3$)



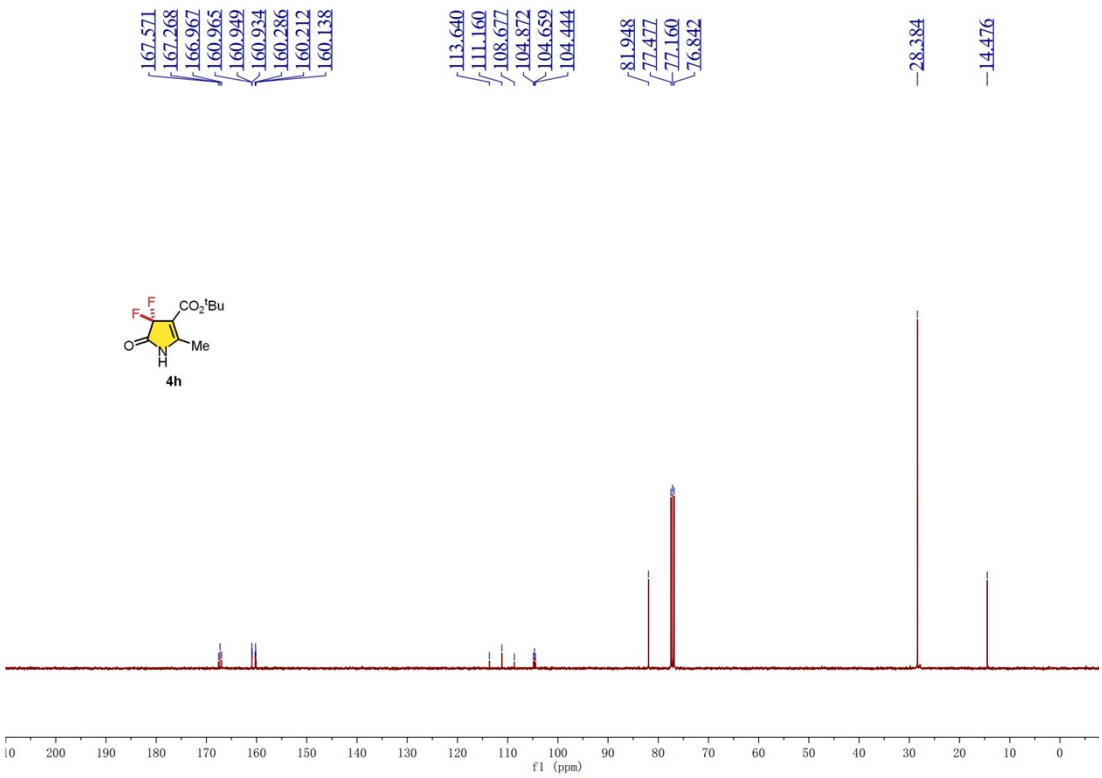
^{13}C{^{1}H} NMR Spectrum of Compound **4g** (100 MHz, $CDCl_3$)



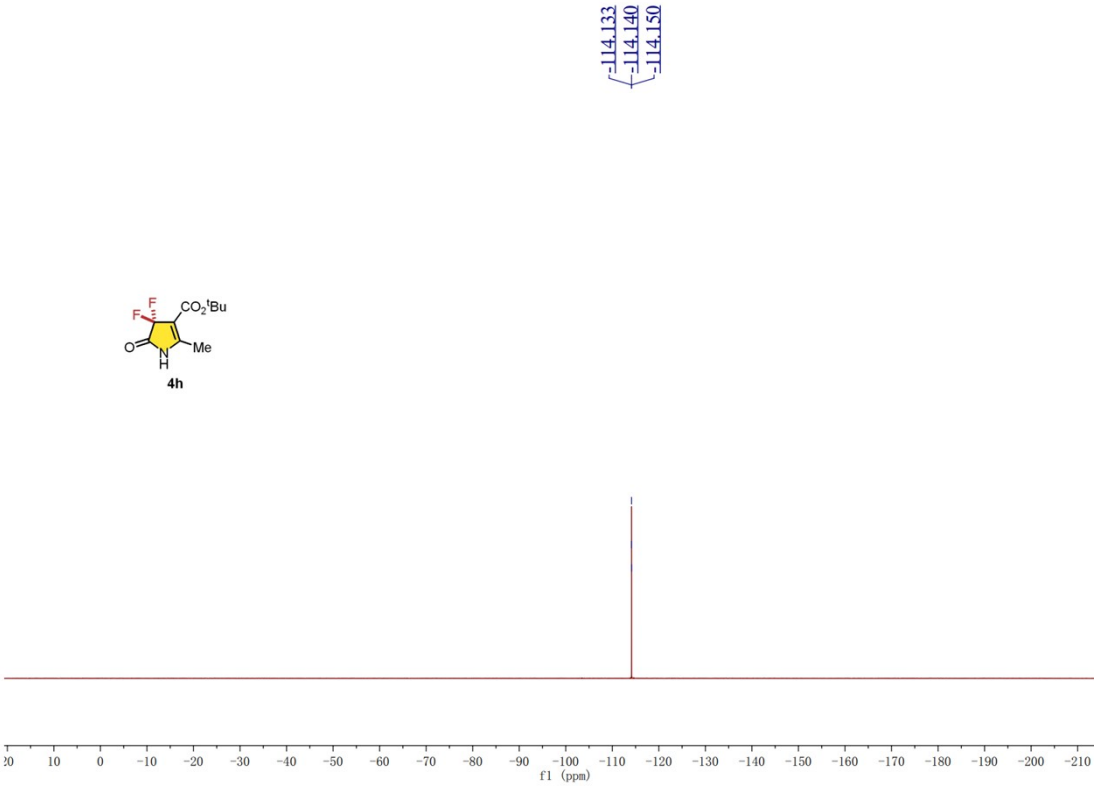
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4g** (376 MHz, $CDCl_3$)



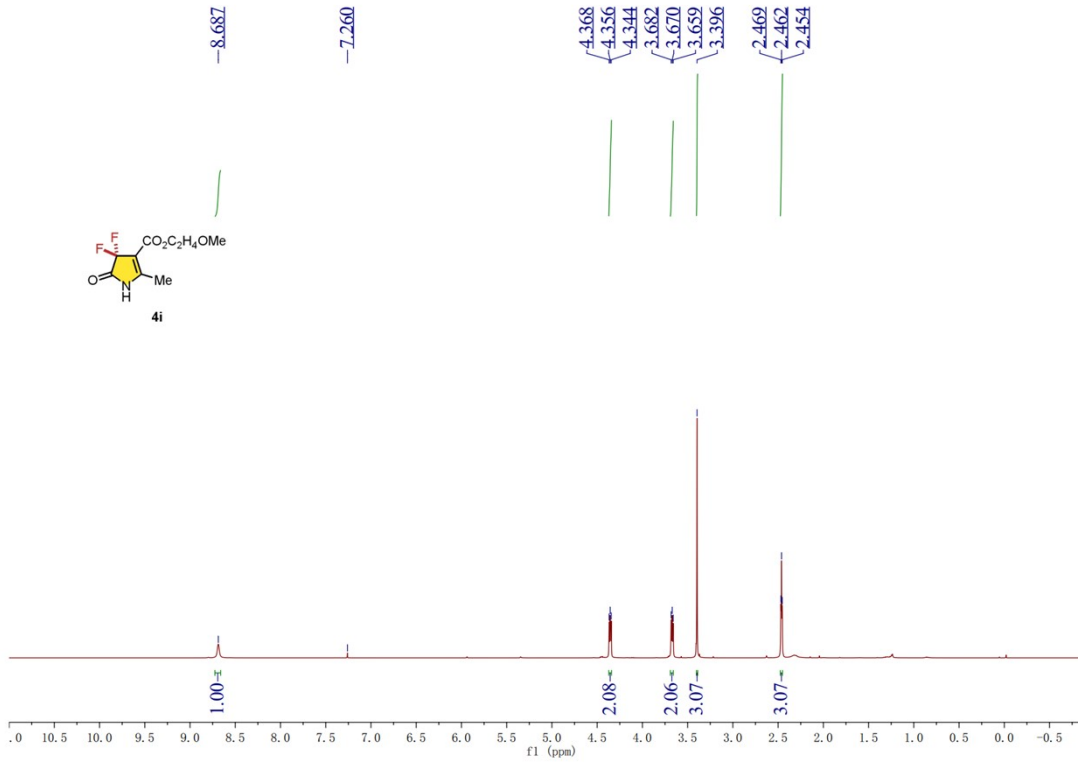
^{1}H NMR Spectrum of Compound **4h** (400 MHz, $CDCl_3$)



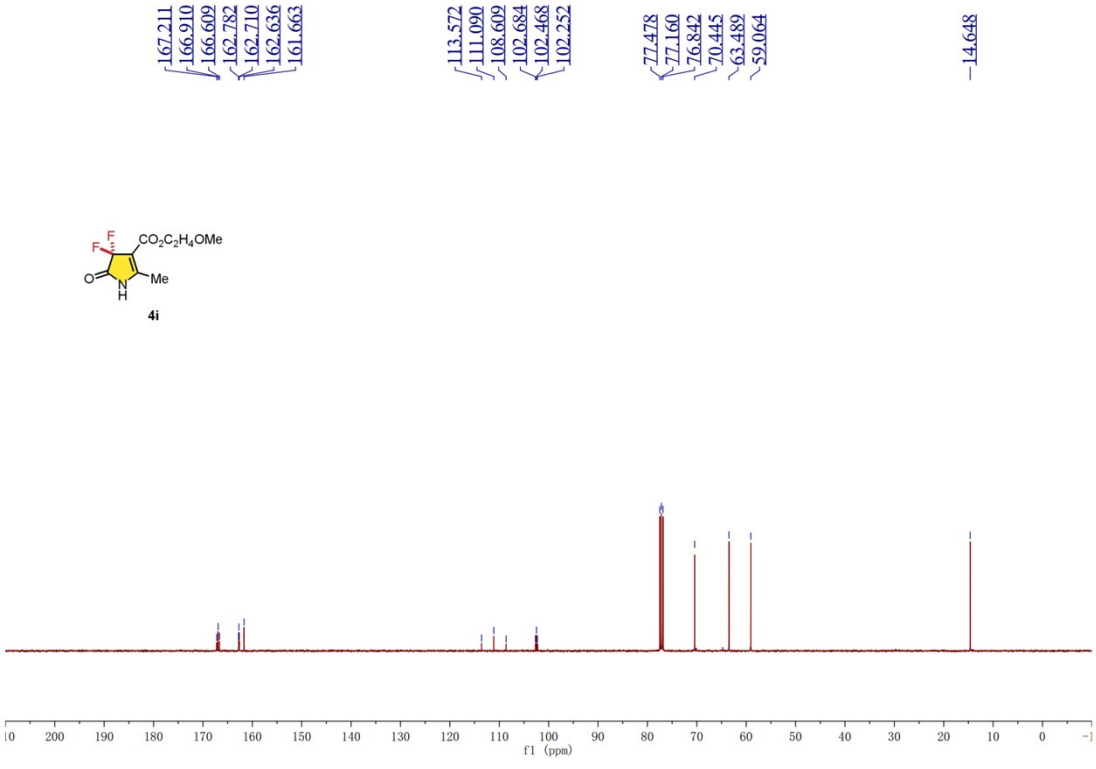
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4h** (100 MHz, $CDCl_3$)



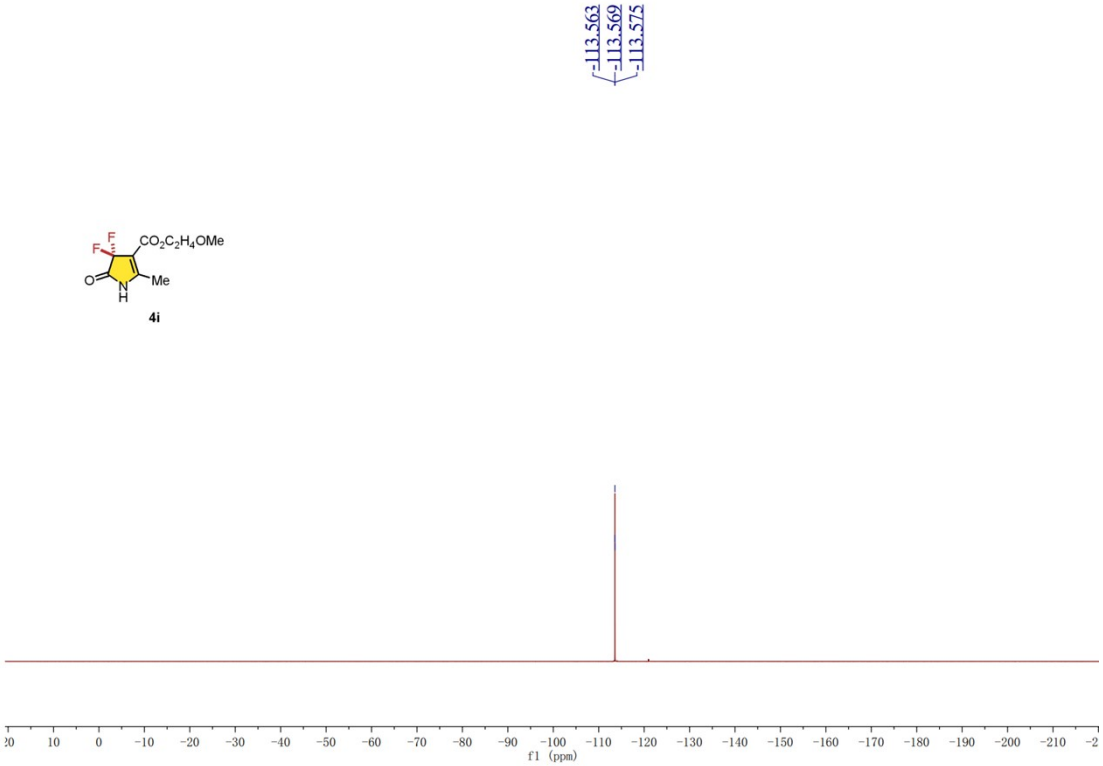
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4h** (376 MHz, $CDCl_3$)



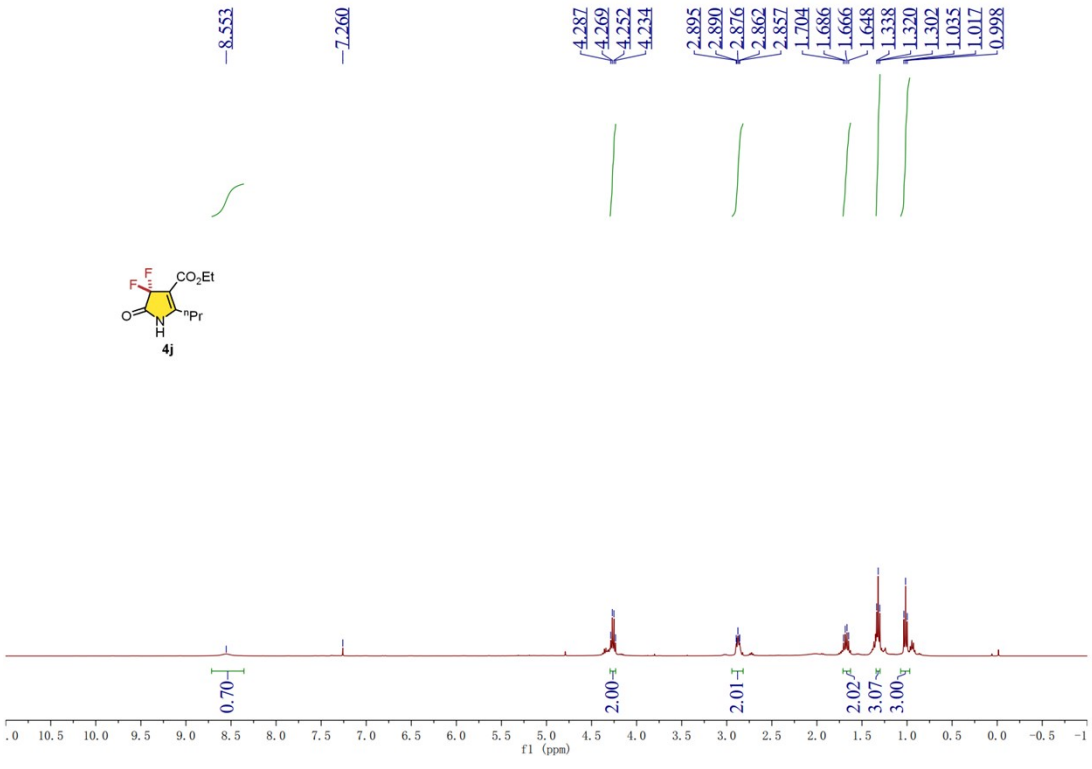
^{1}H NMR Spectrum of Compound **4i** (400 MHz, $CDCl_3$)



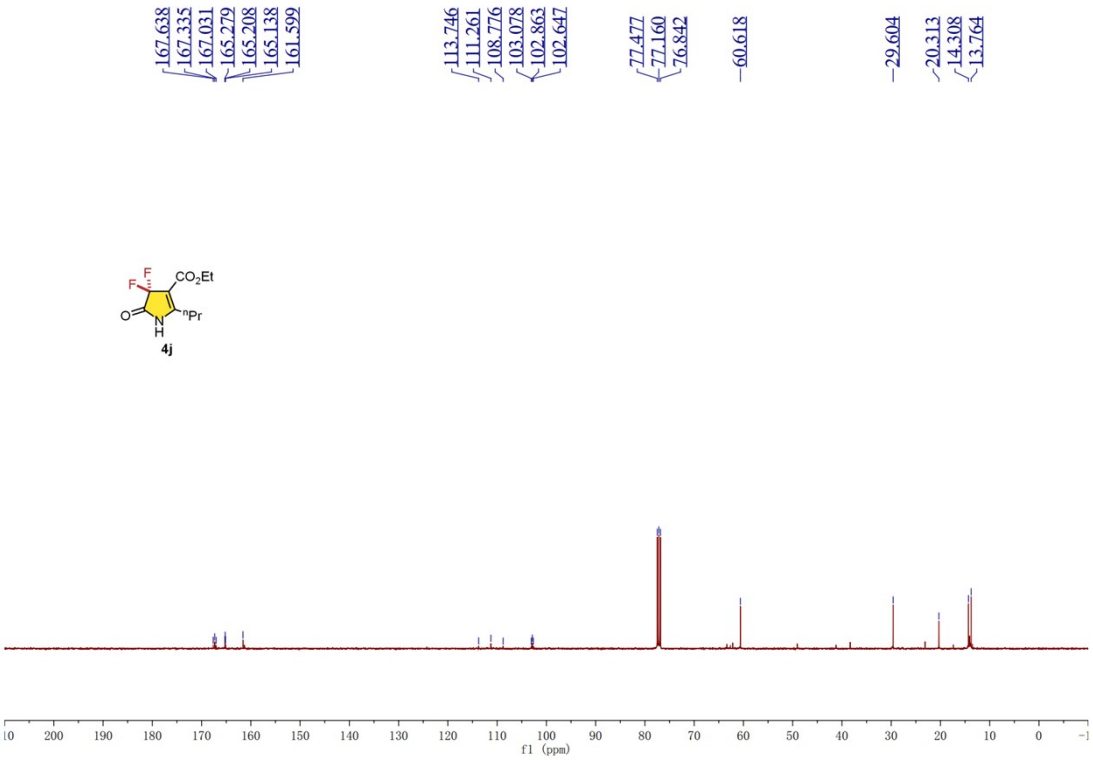
^{13}C{^{1}H} NMR Spectrum of Compound **4i** (100 MHz, $CDCl_3$)



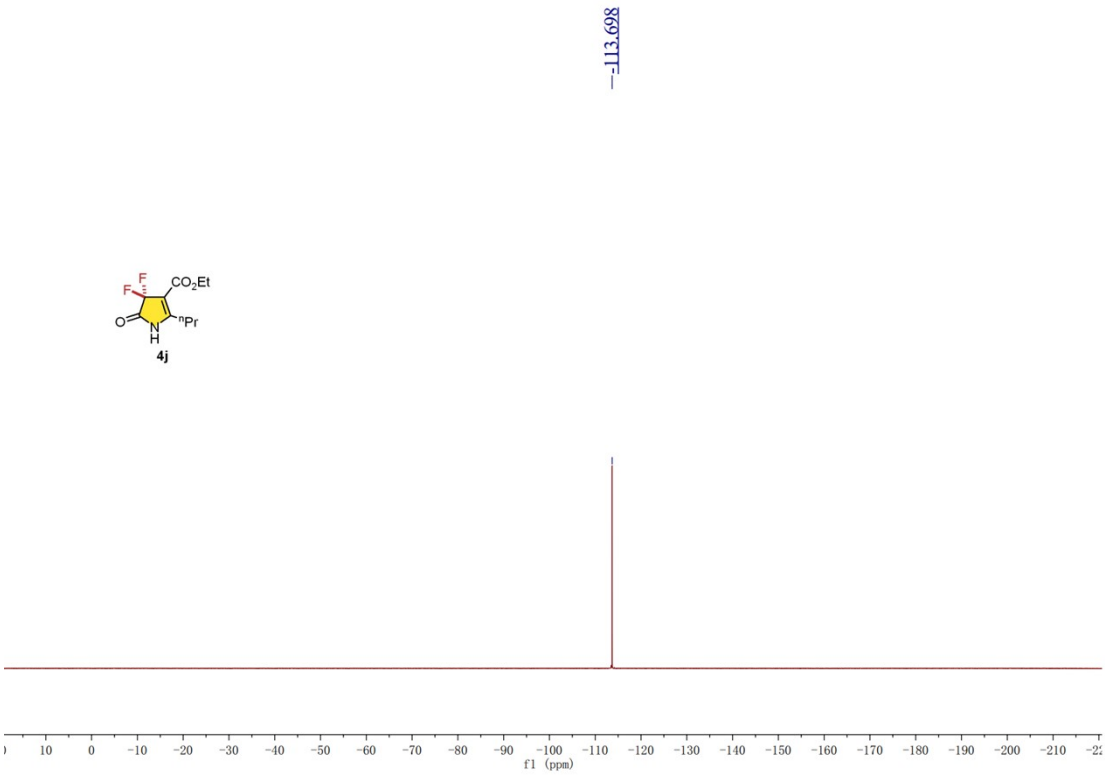
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4i** (376 MHz, $CDCl_3$)



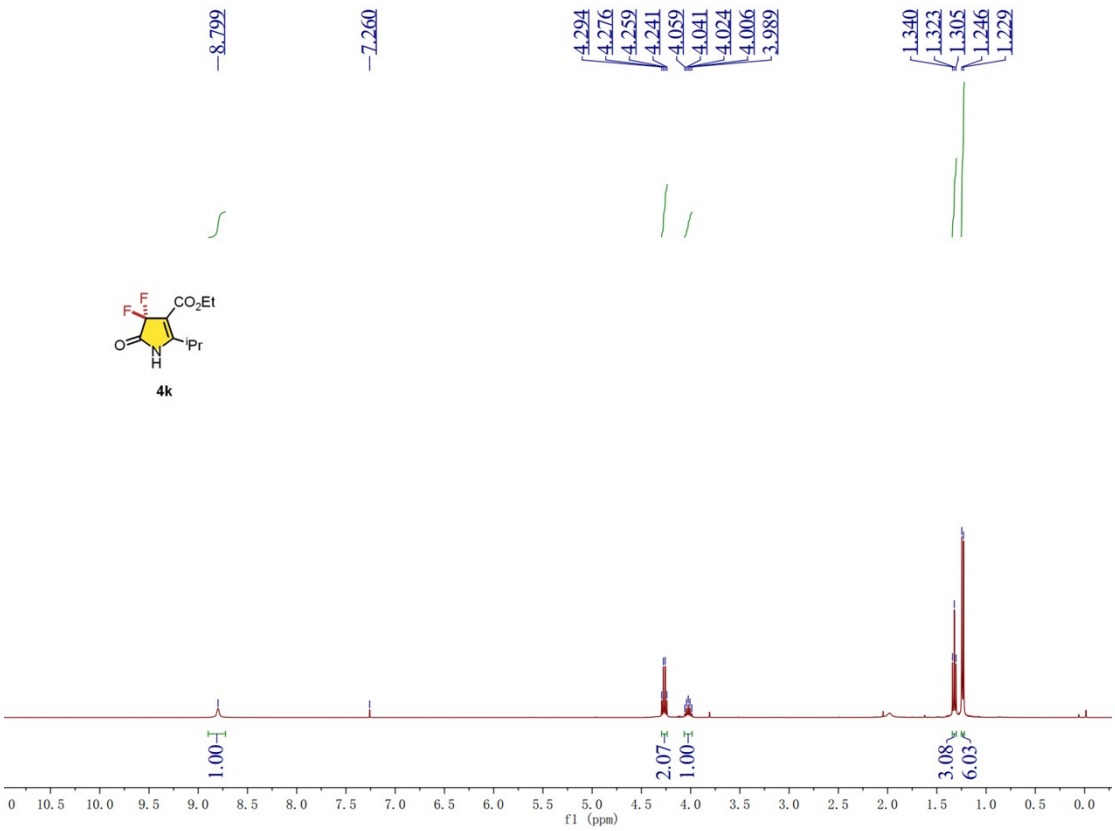
^{1}H NMR Spectrum of Compound **4j** (400 MHz, $CDCl_3$)



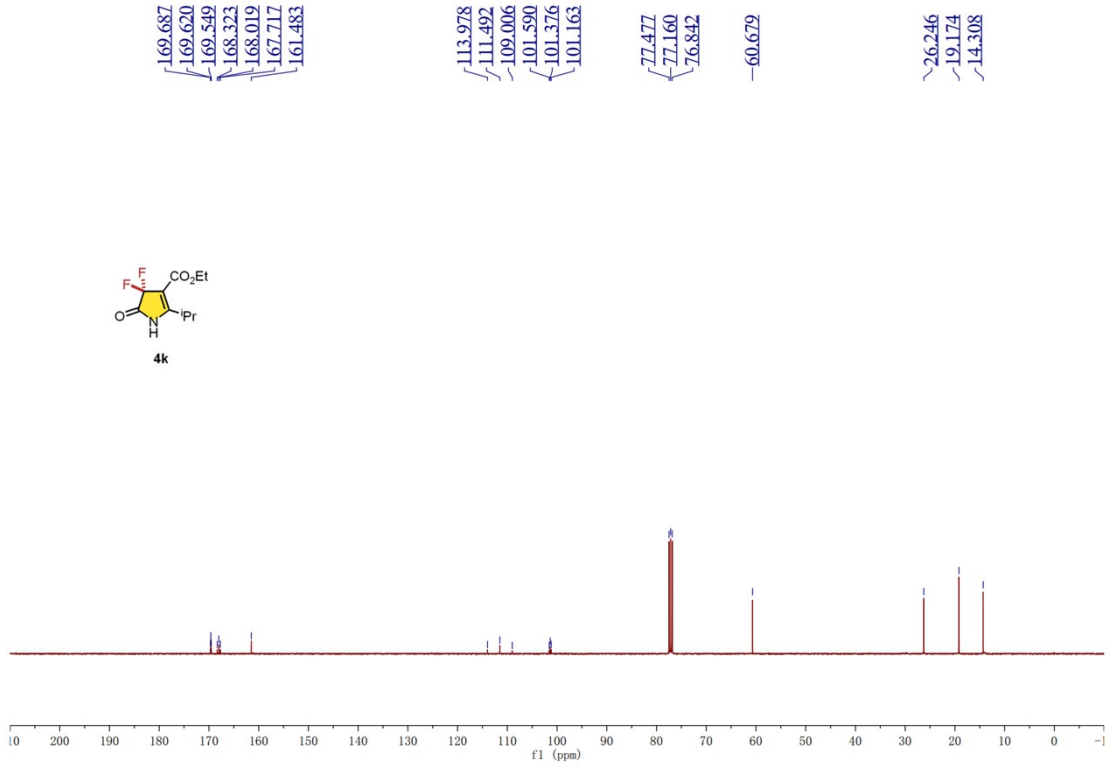
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4j** (100 MHz, $CDCl_3$)



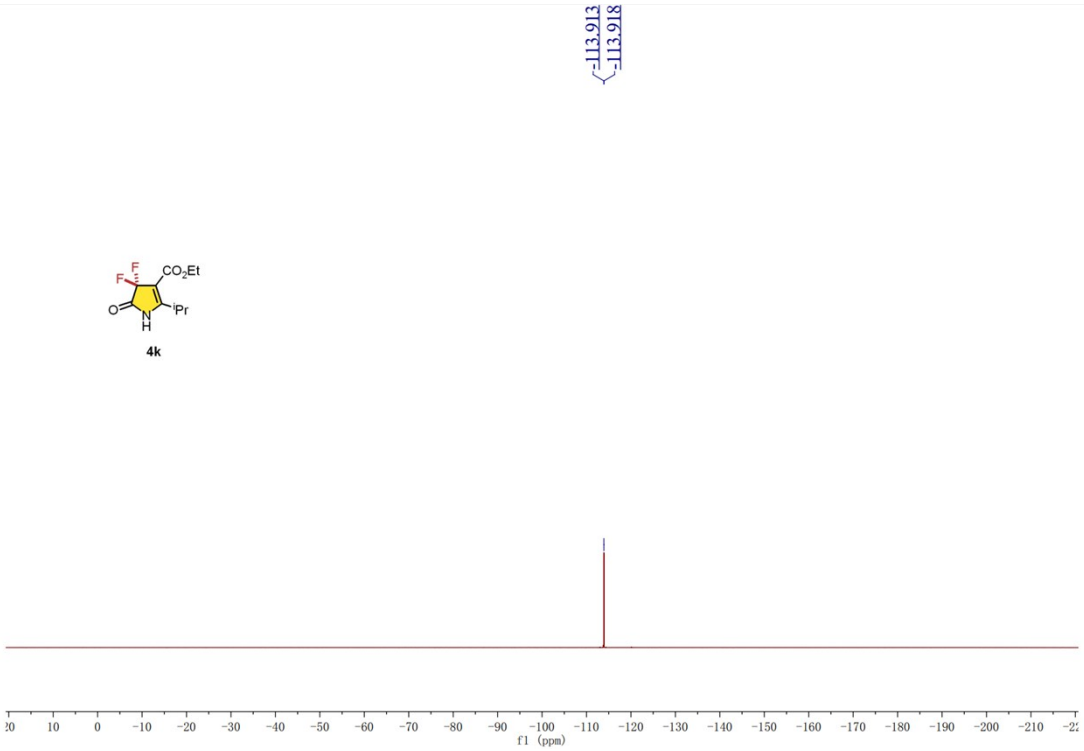
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4j** (376 MHz, $CDCl_3$)



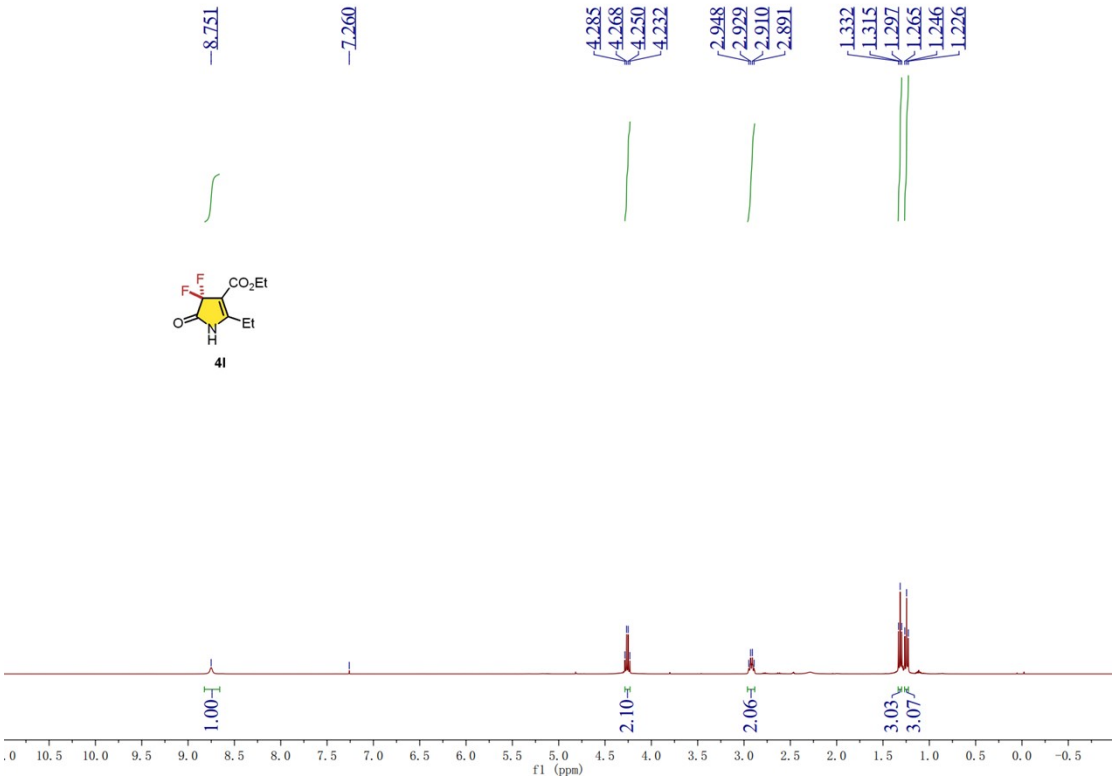
^{1}H NMR Spectrum of Compound **4k** (400 MHz, $CDCl_3$)



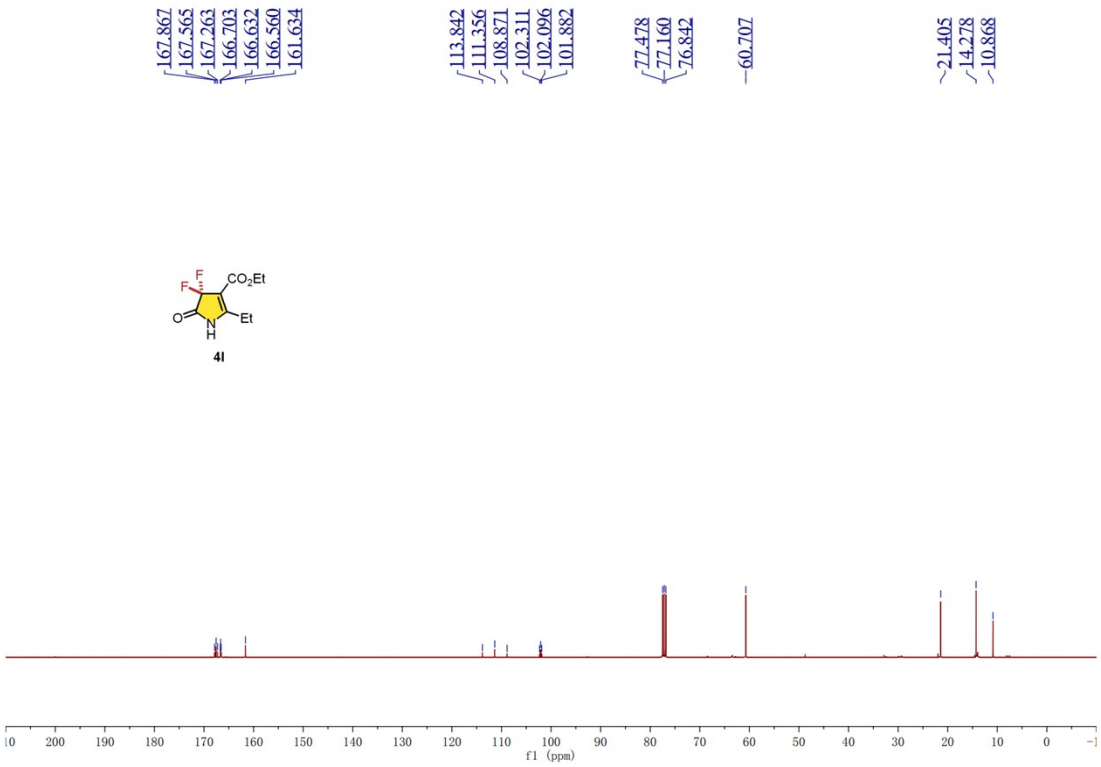
^{13}C{^{1}H} NMR Spectrum of Compound **4k** (100 MHz, $CDCl_3$)



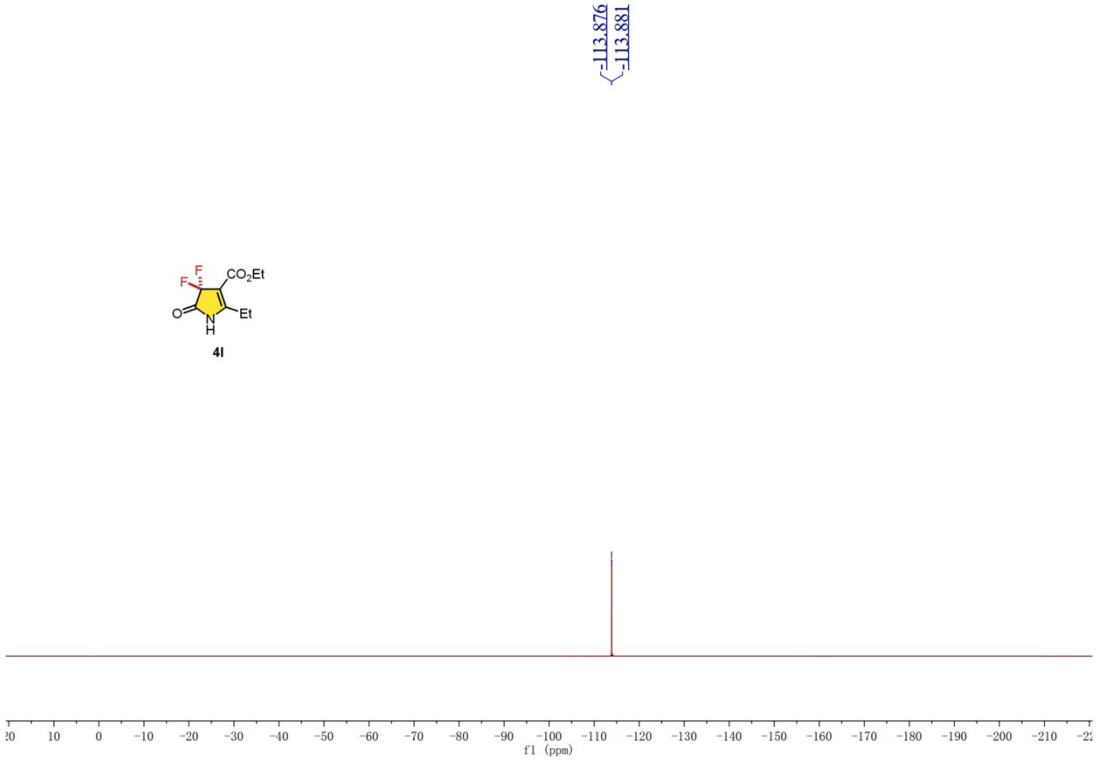
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4k** (376 MHz, $CDCl_3$)



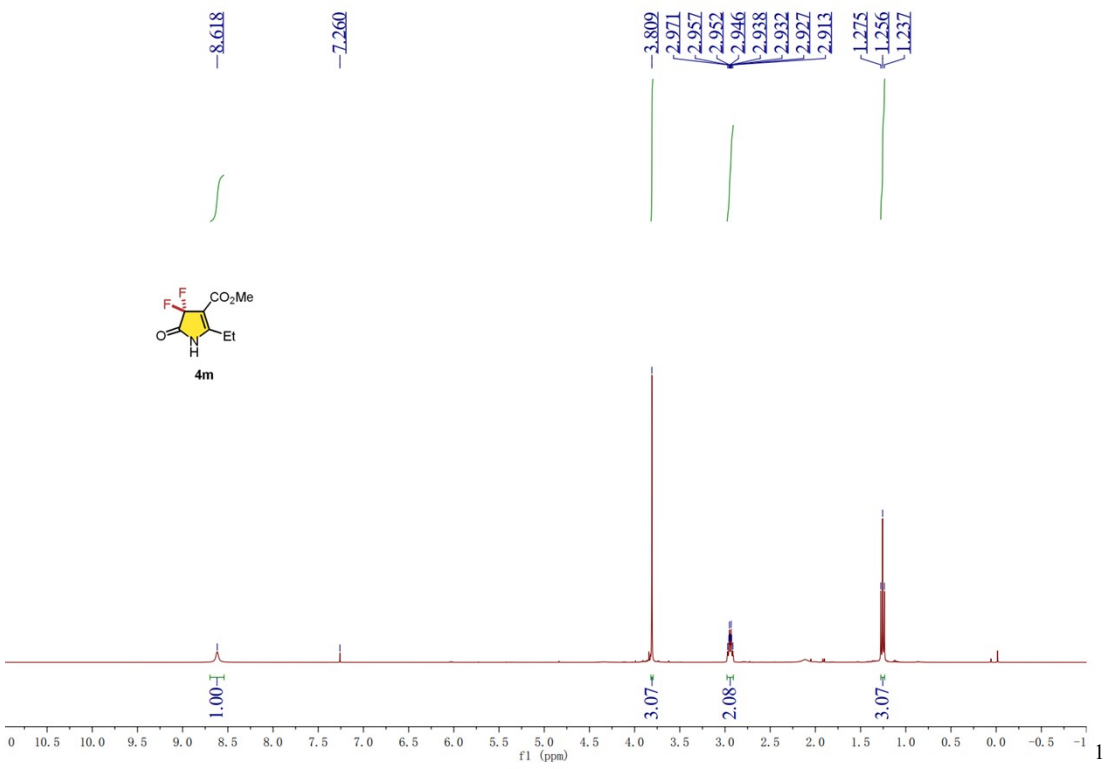
^{1}H NMR Spectrum of Compound **4l** (400 MHz, $CDCl_3$)



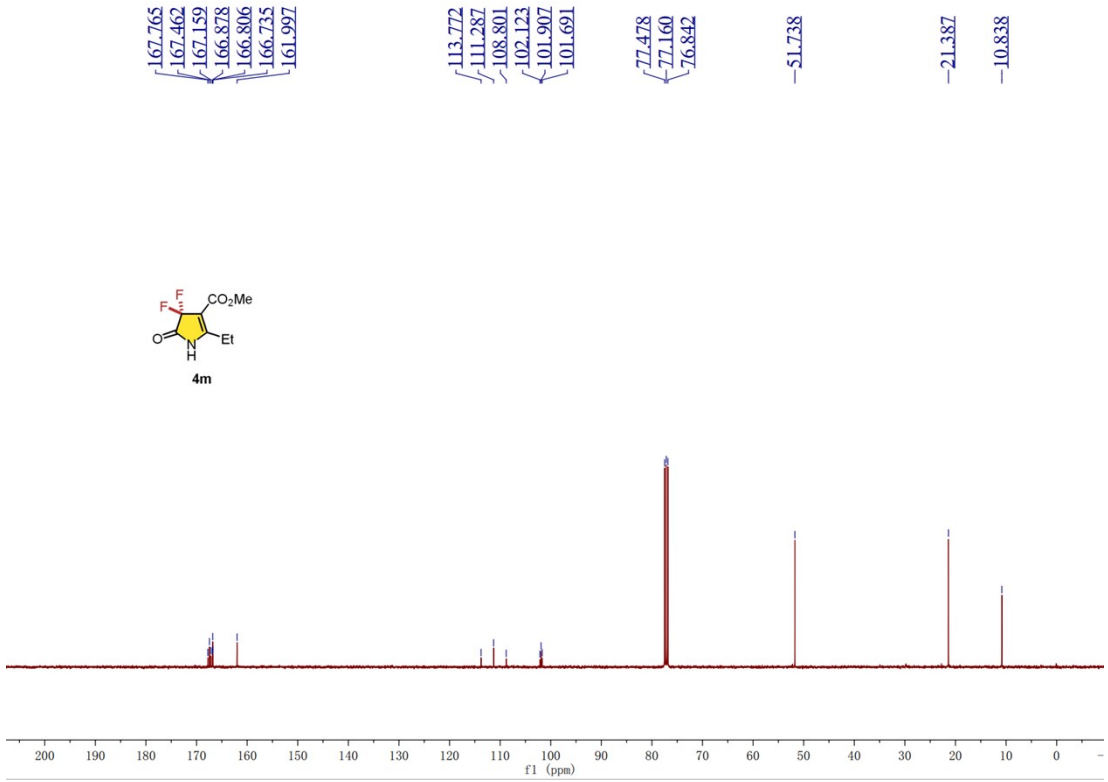
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4l** (100 MHz, $CDCl_3$)



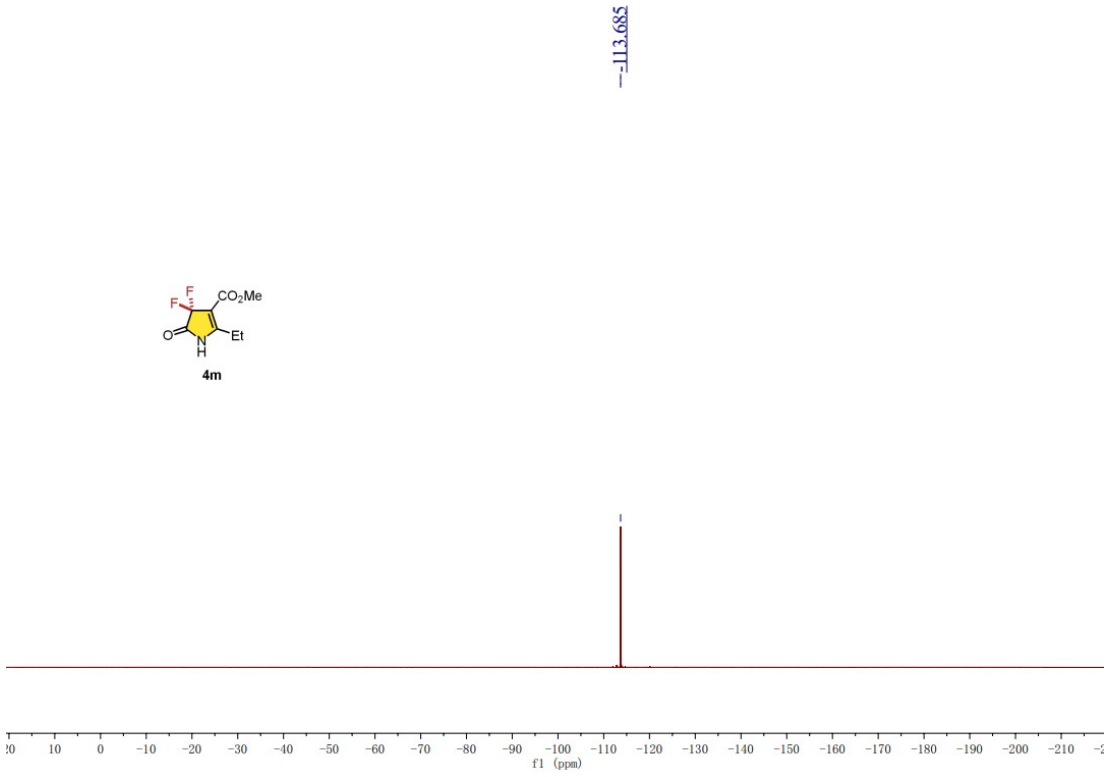
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4l** (376 MHz, $CDCl_3$)



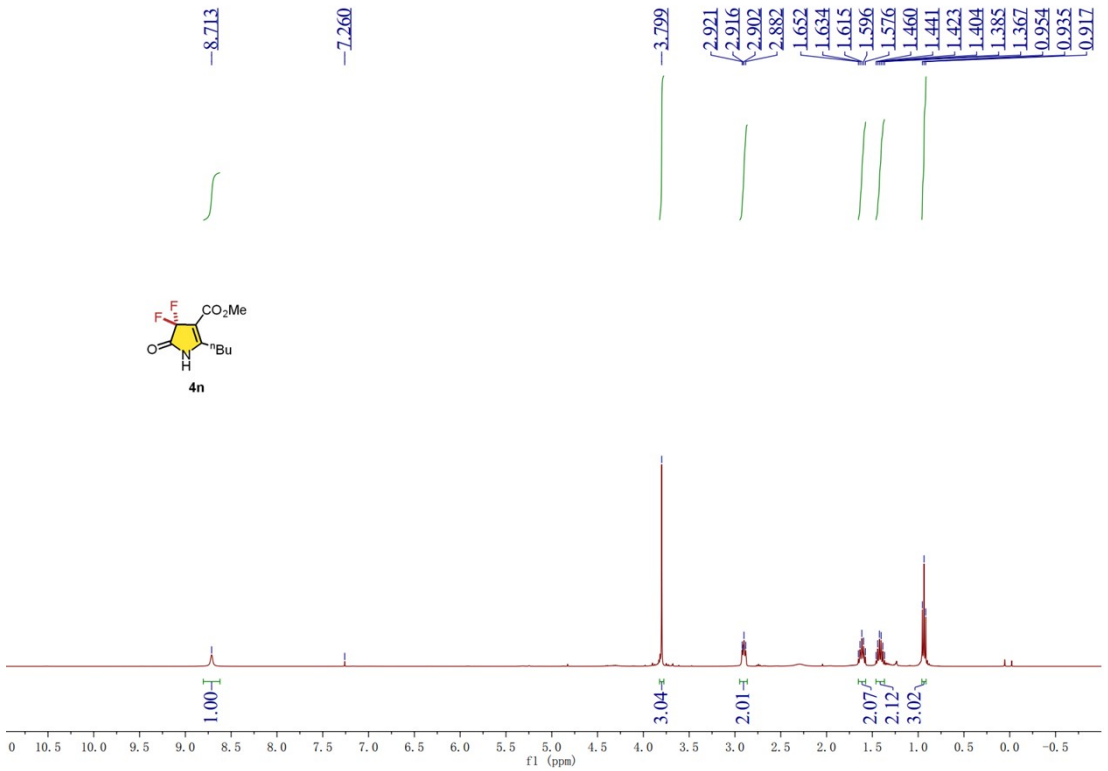
H NMR Spectrum of Compound **4m** (400 MHz, $CDCl_3$)



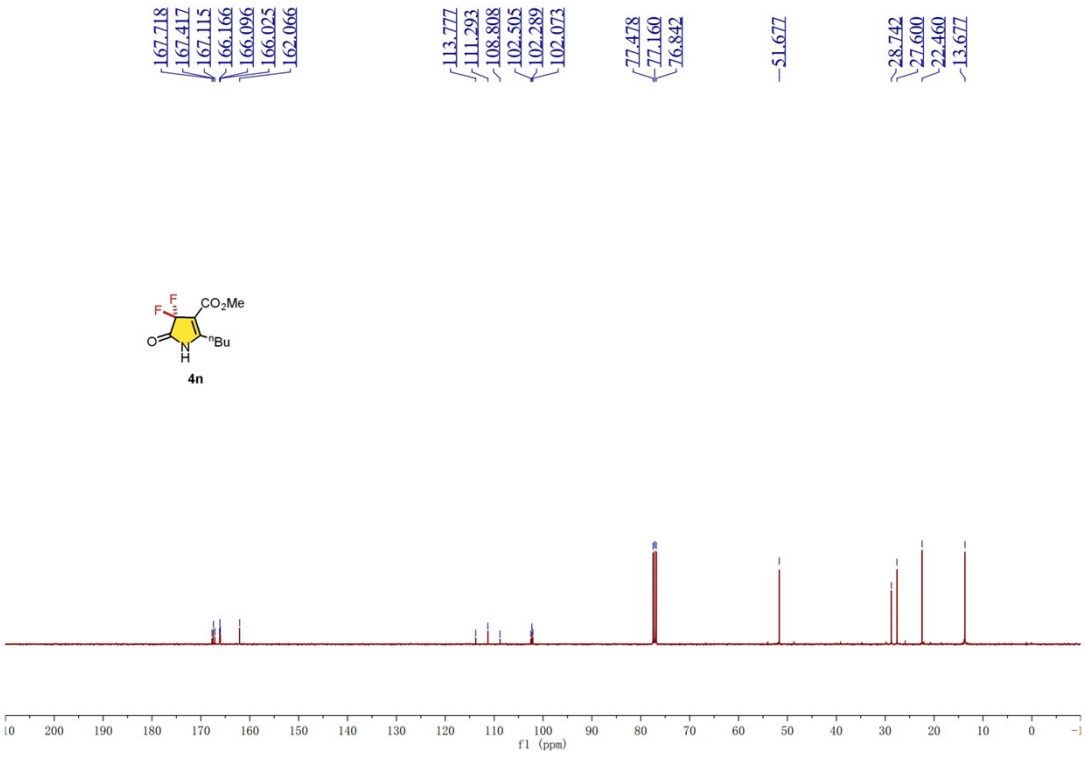
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4m** (100 MHz, $CDCl_3$)



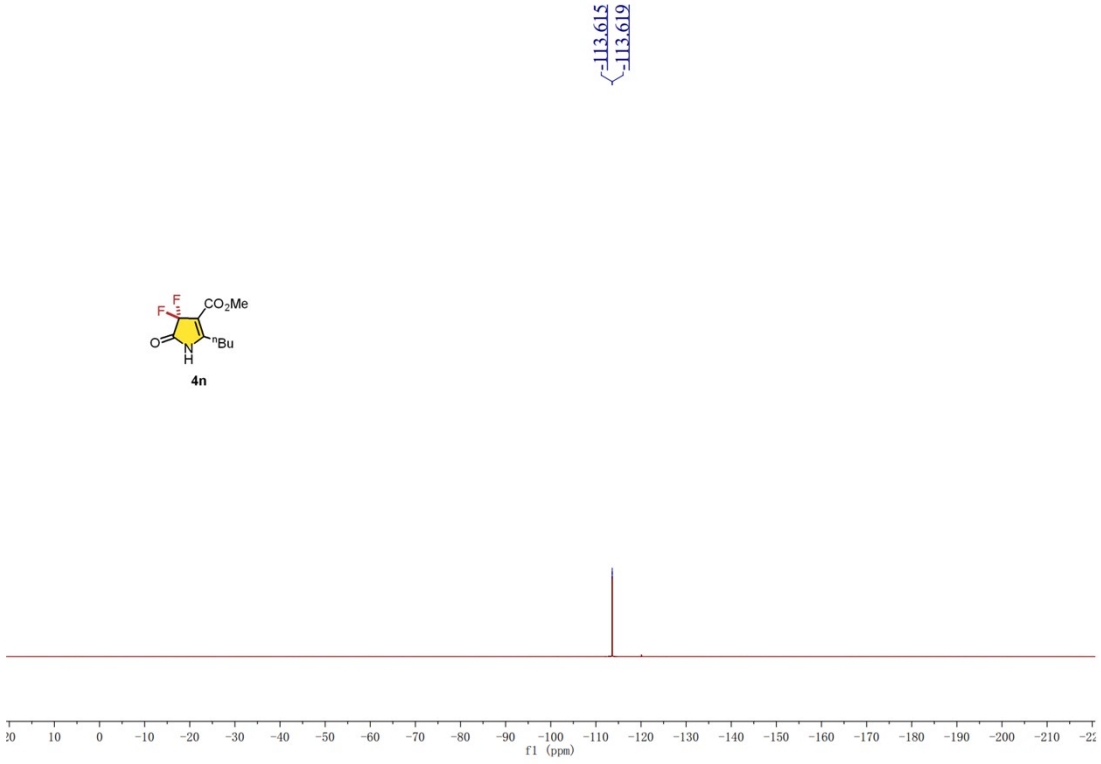
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4m** (376 MHz, $CDCl_3$)



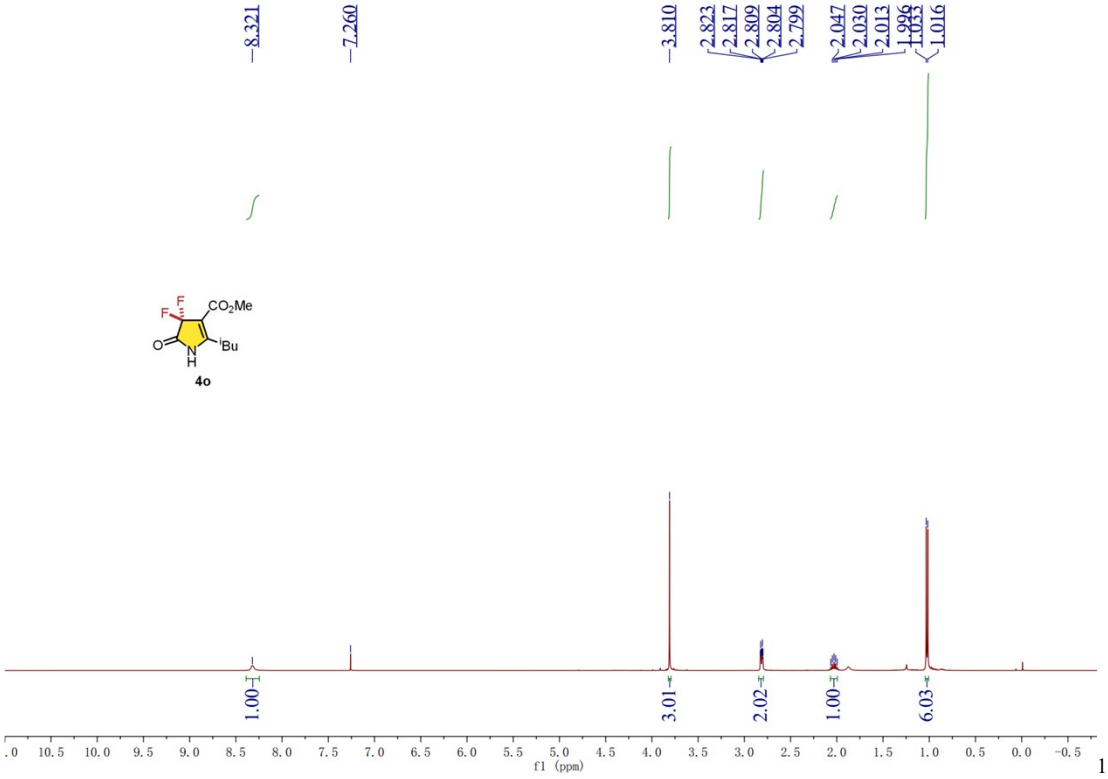
^{1}H NMR Spectrum of Compound **4n** (400 MHz, $CDCl_3$)



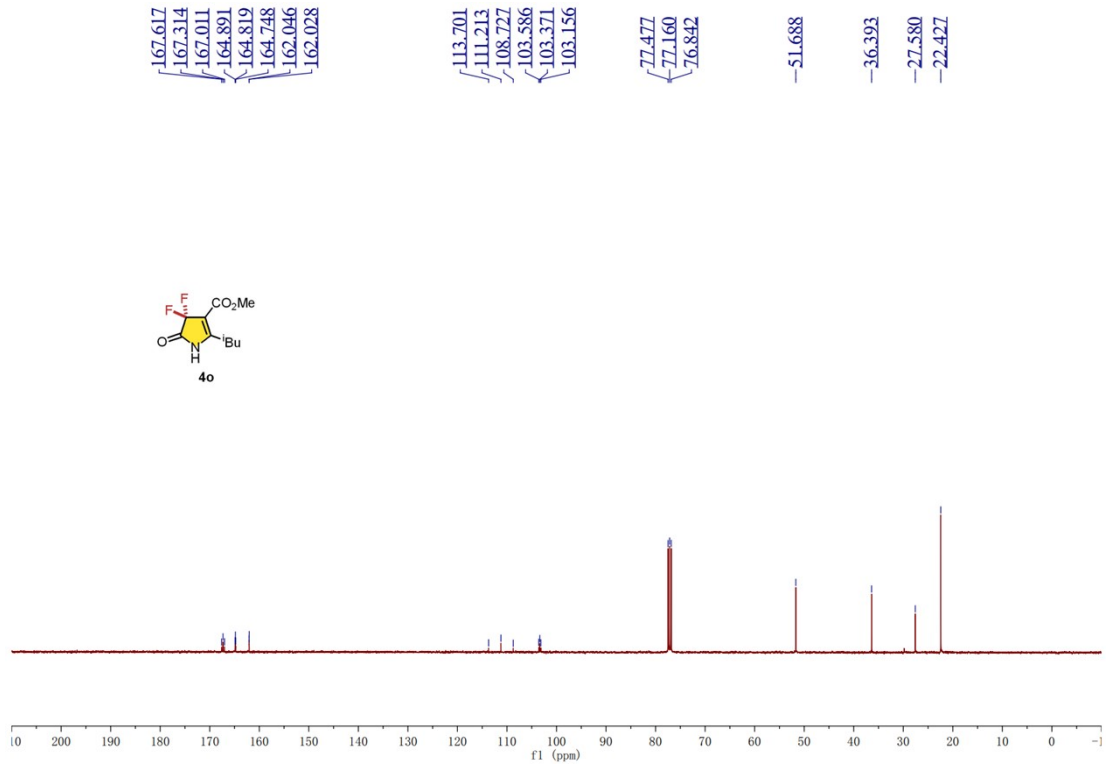
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **4n** (100 MHz, $CDCl_3$)



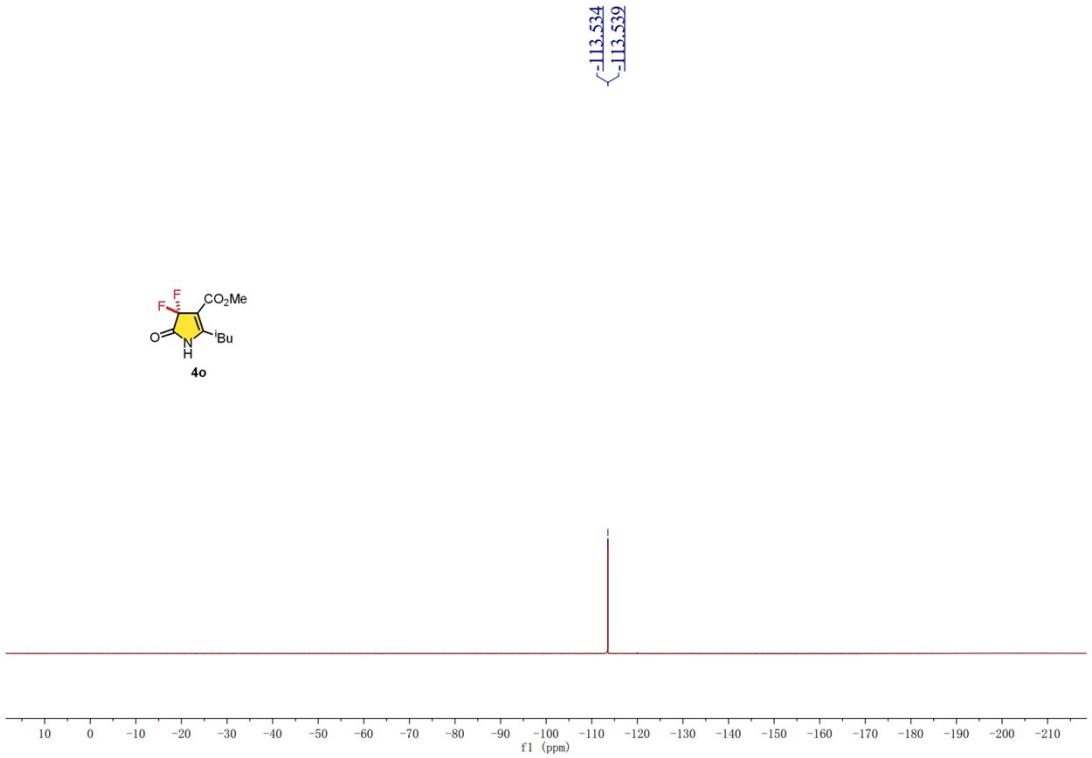
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4n** (376 MHz, $CDCl_3$)



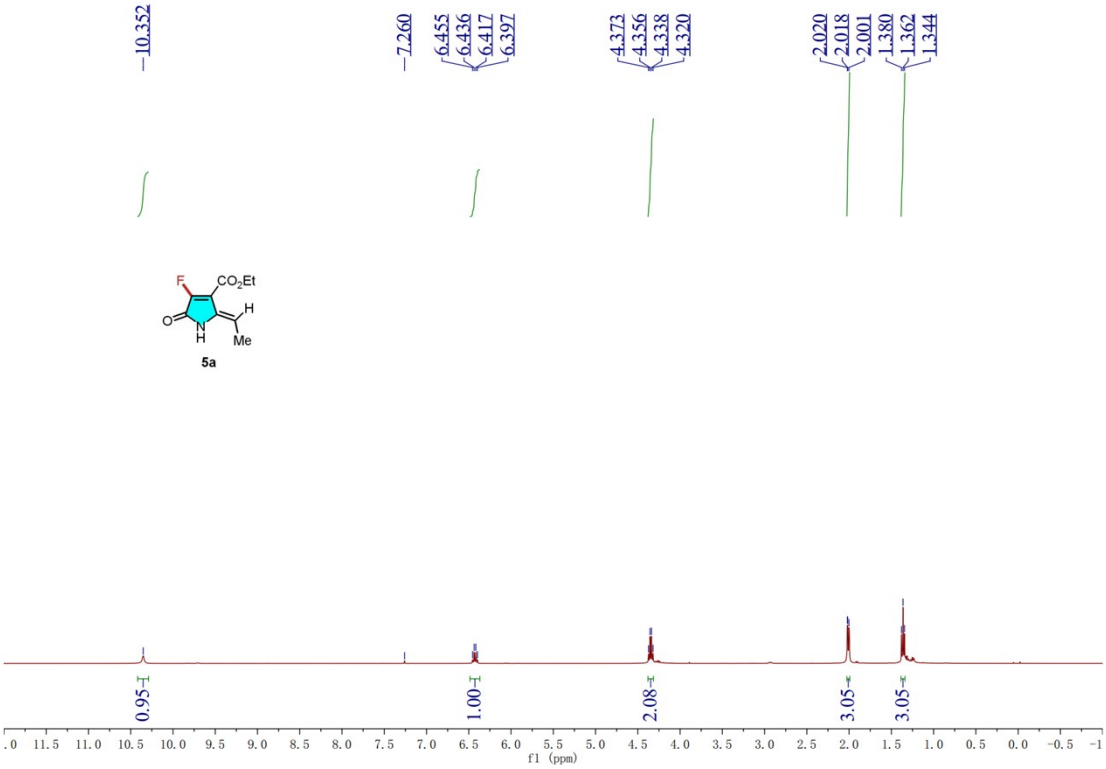
H NMR Spectrum of Compound **4o** (400 MHz, $CDCl_3$)



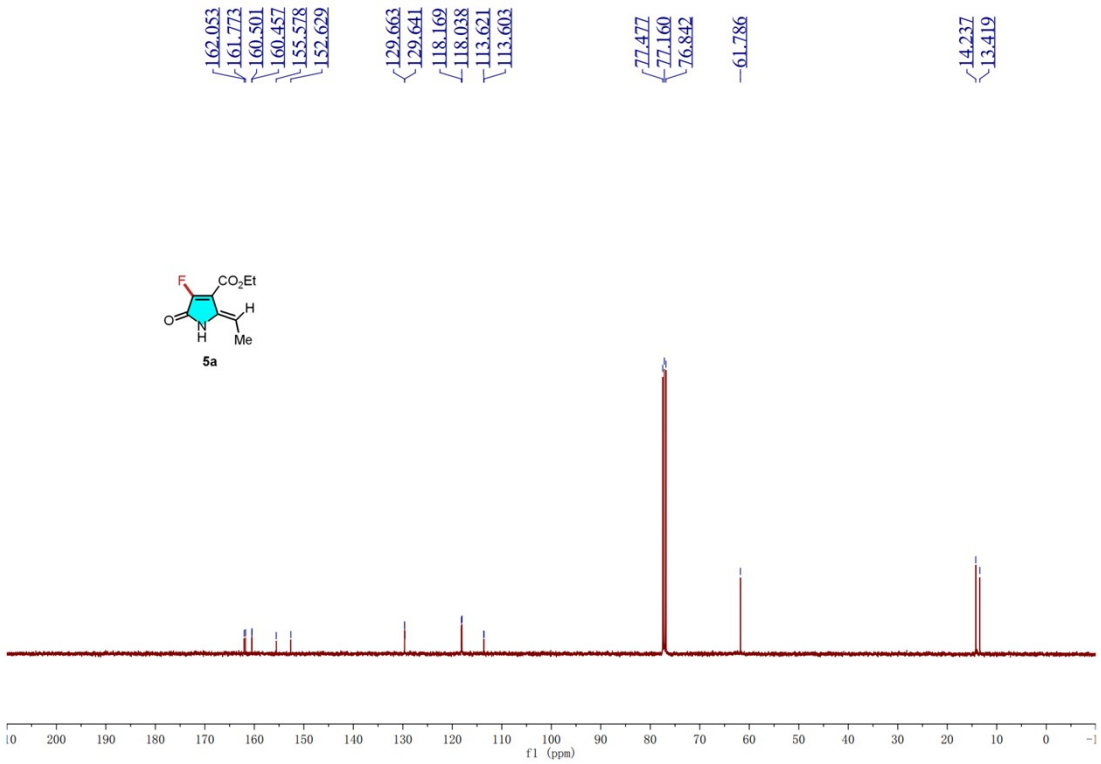
$^{13}C\{^1H\}$ NMR Spectrum of Compound **4o** (100 MHz, $CDCl_3$)



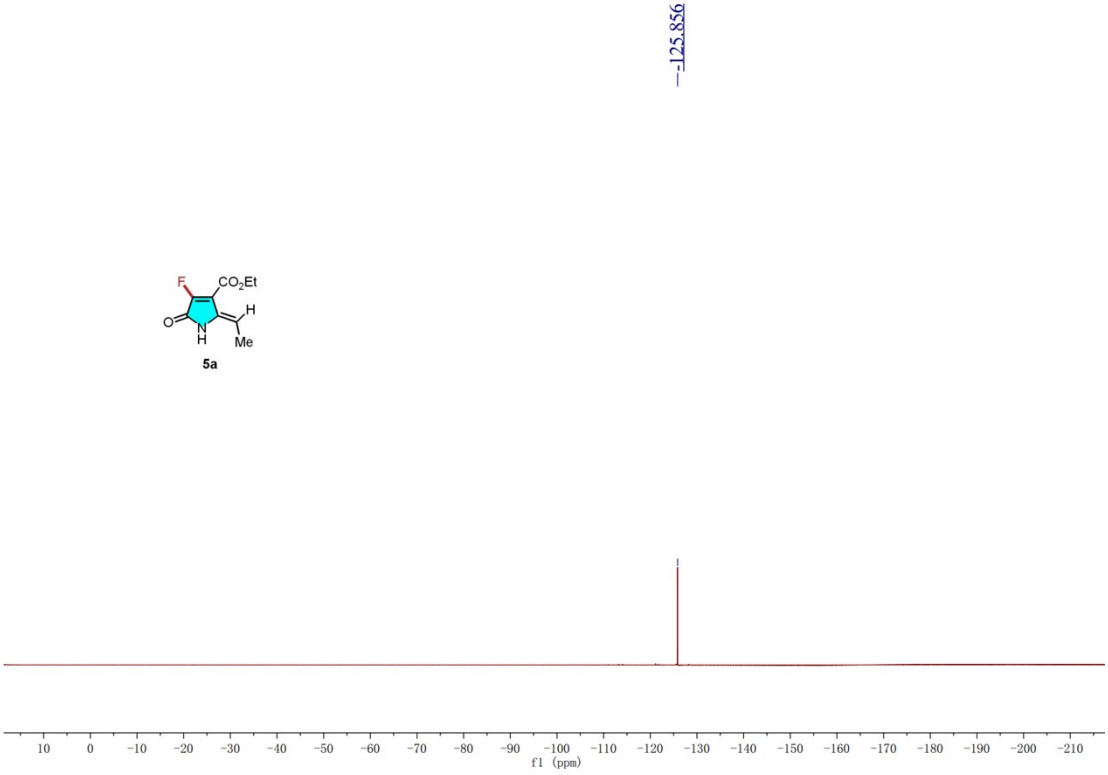
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **4o** (376 MHz, $CDCl_3$)



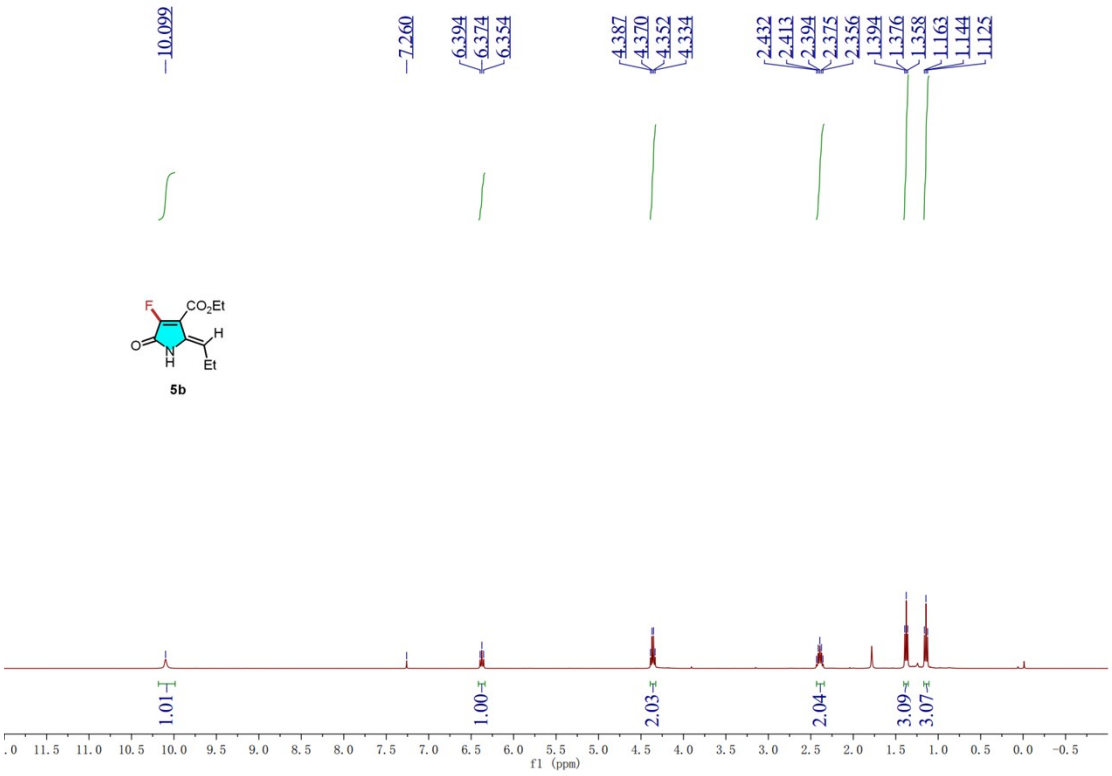
^{1}H NMR Spectrum of Compound **5a** (400 MHz, $CDCl_3$)



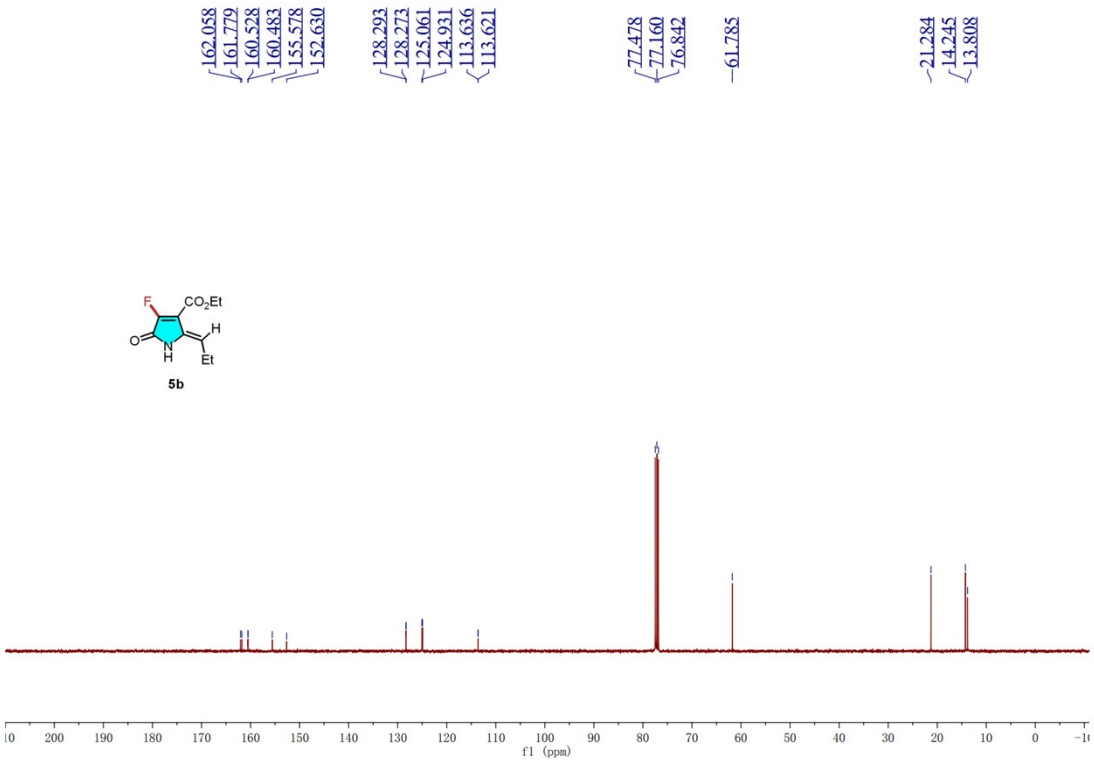
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5a** (100 MHz, $CDCl_3$)



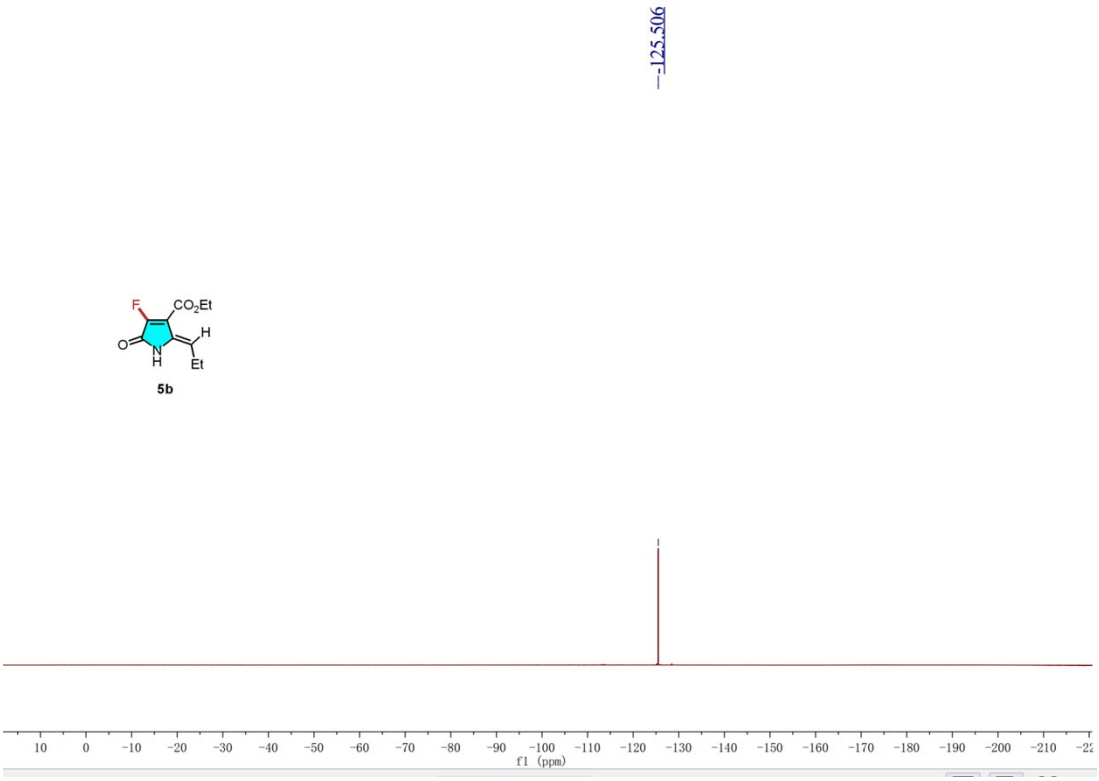
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5a** (376 MHz, $CDCl_3$)



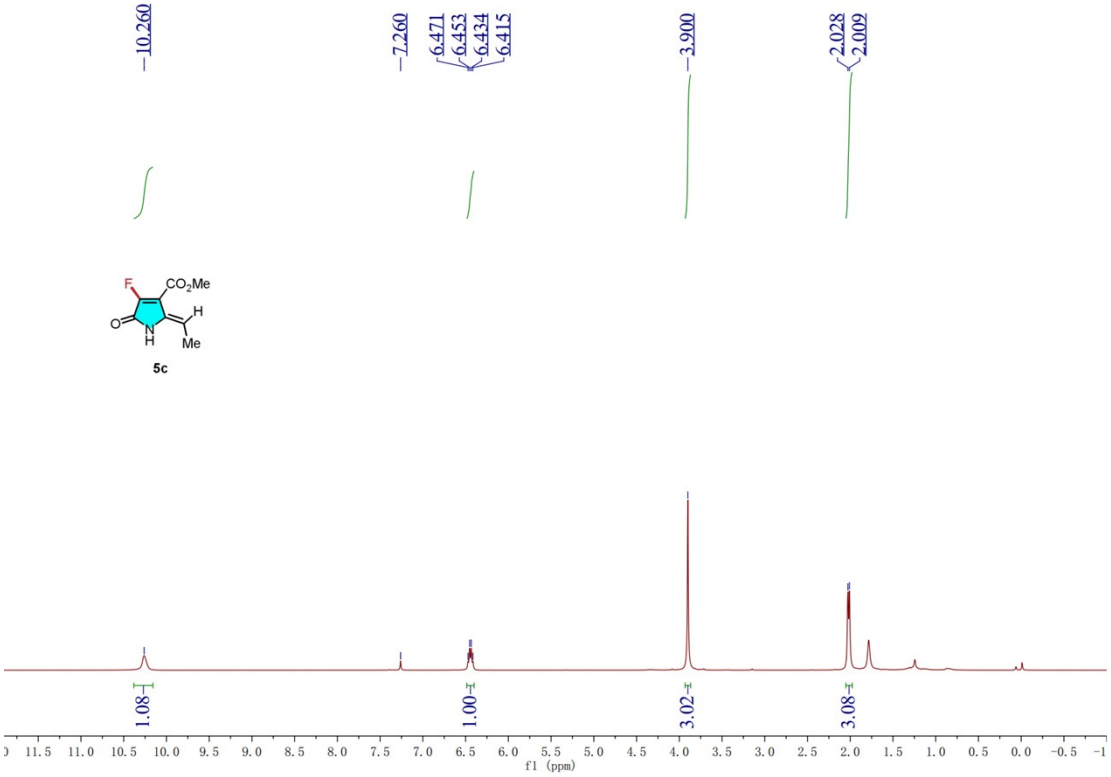
^{1}H NMR Spectrum of Compound **5b** (400 MHz, $CDCl_3$)



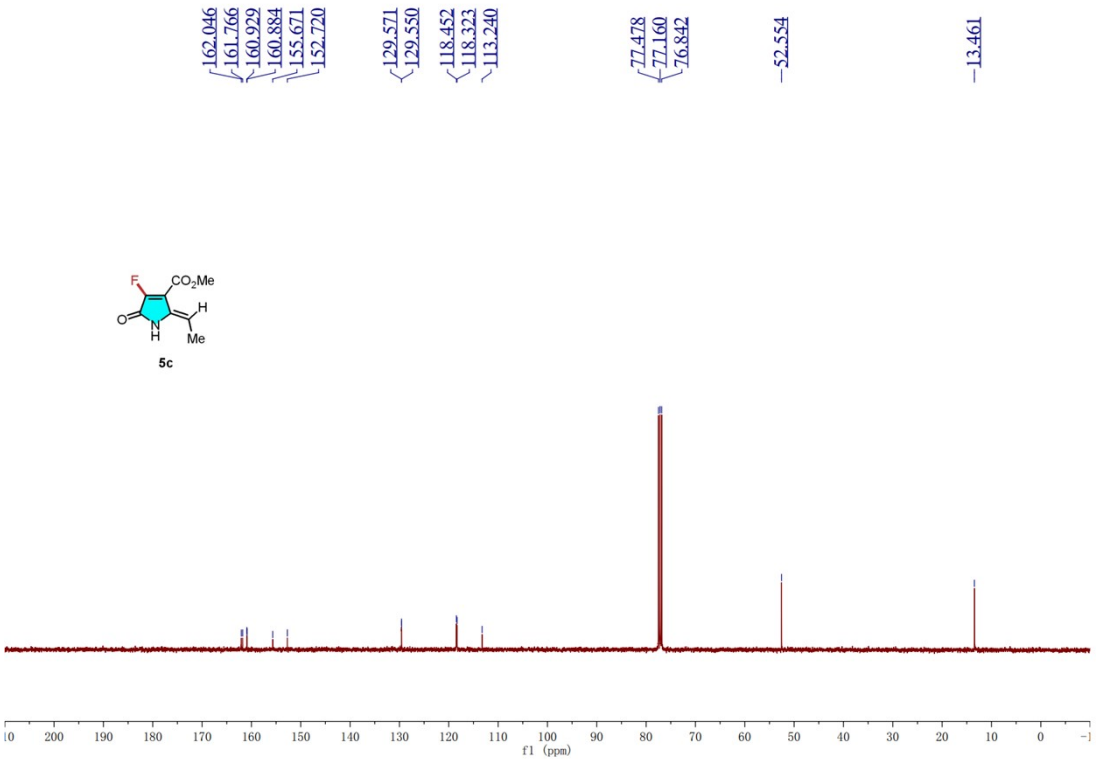
^{13}C{^{1}H} NMR Spectrum of Compound **5b** (100 MHz, $CDCl_3$)



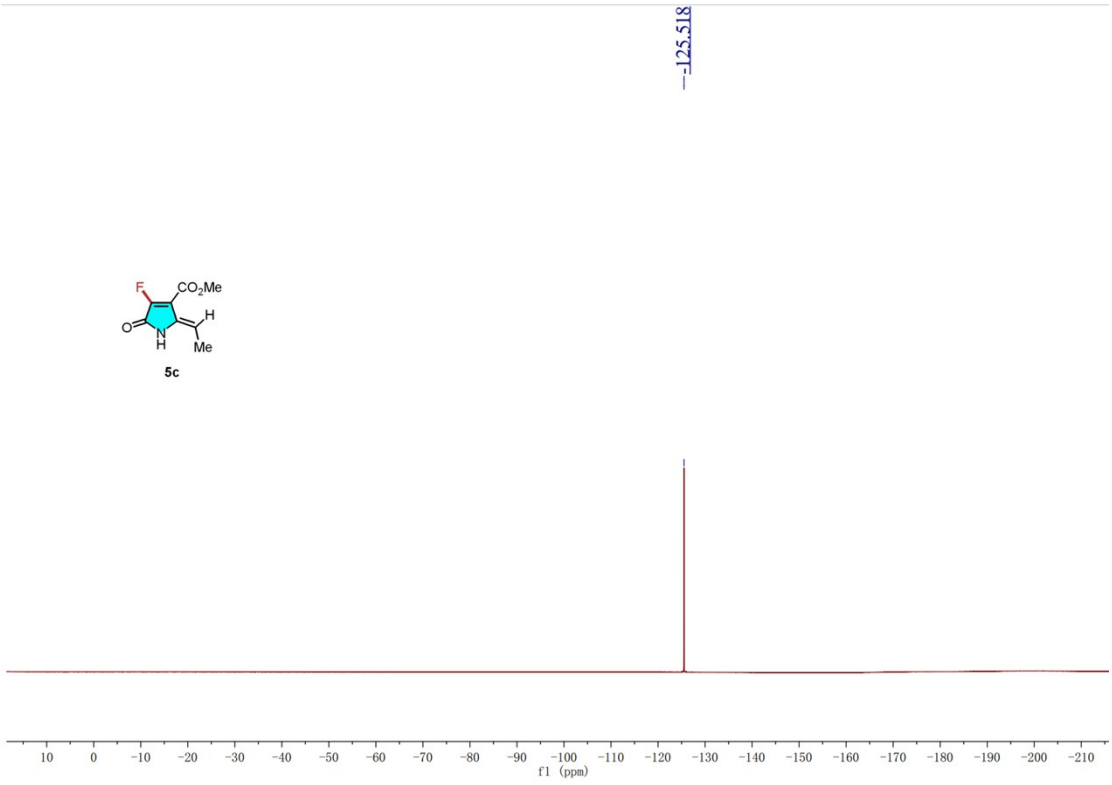
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5b** (376 MHz, $CDCl_3$)



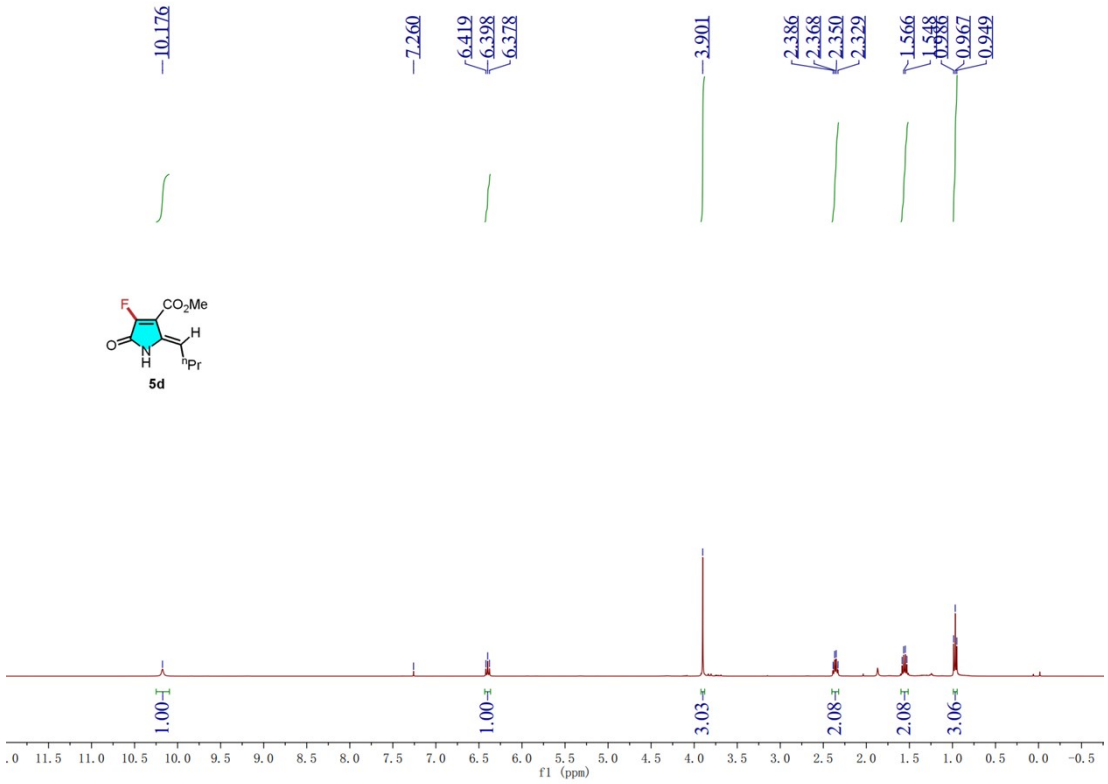
^{1}H NMR Spectrum of Compound **5c** (400 MHz, $CDCl_3$)



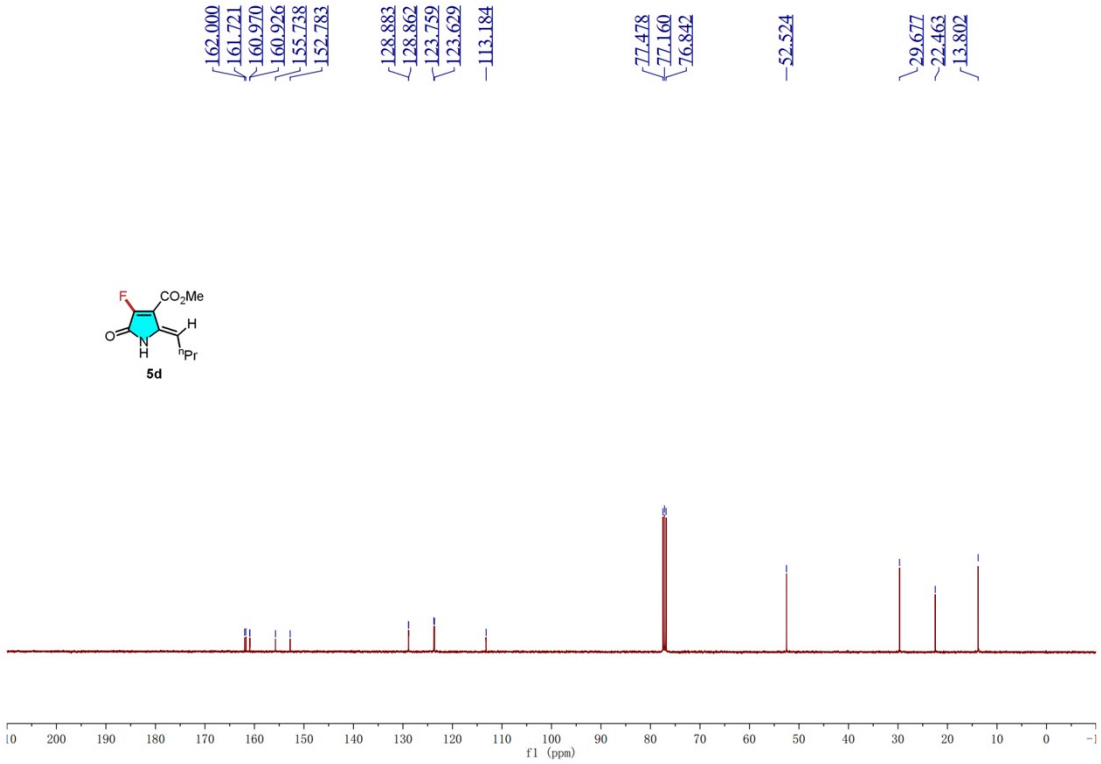
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5c** (100 MHz, $CDCl_3$)



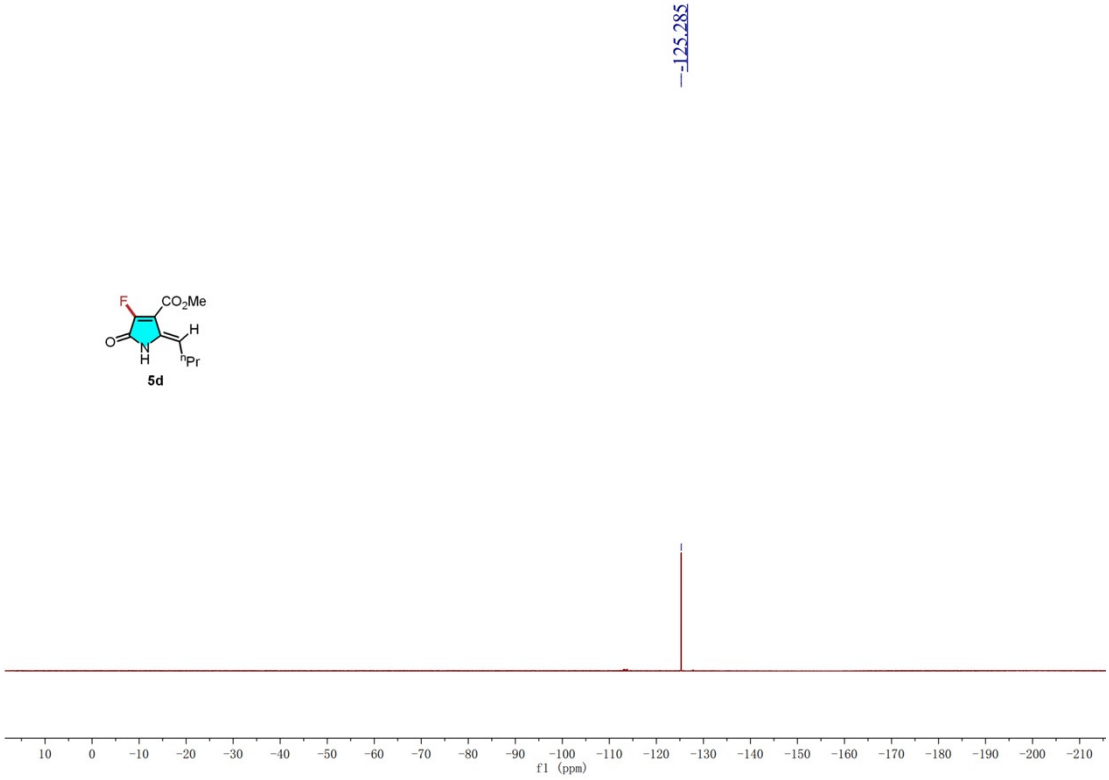
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5c** (376 MHz, $CDCl_3$)



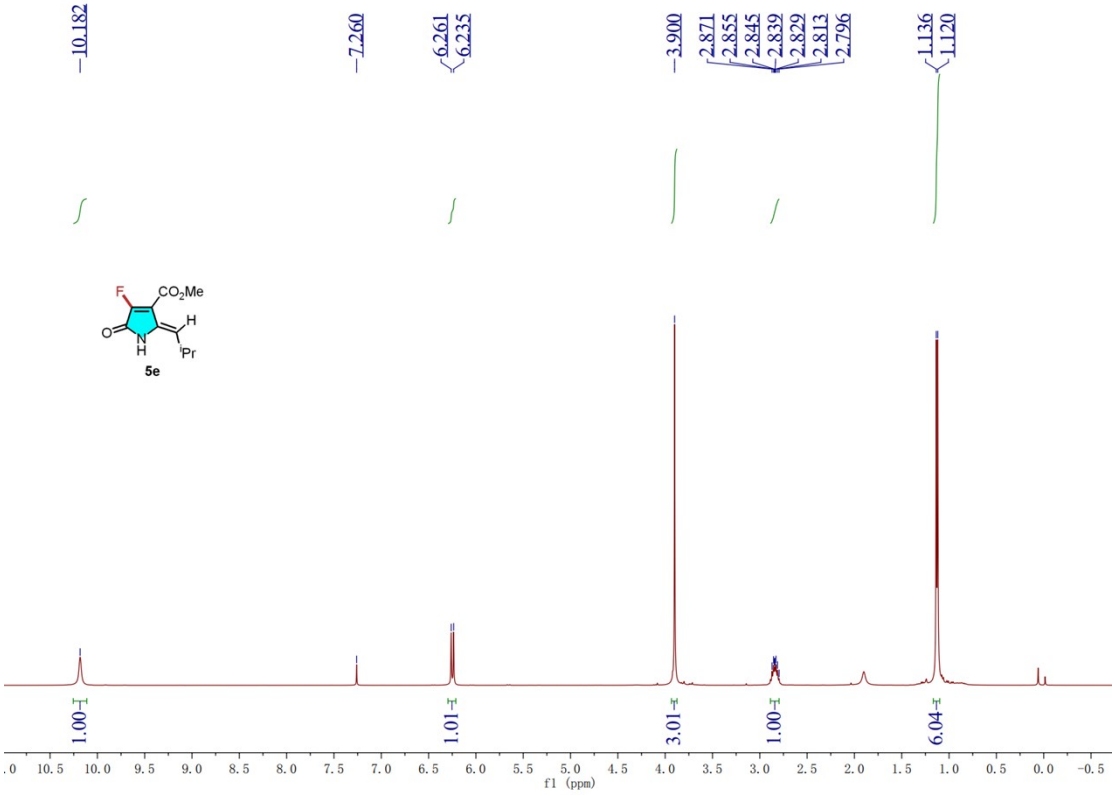
^{1}H NMR Spectrum of Compound **5d** (400 MHz, $CDCl_3$)



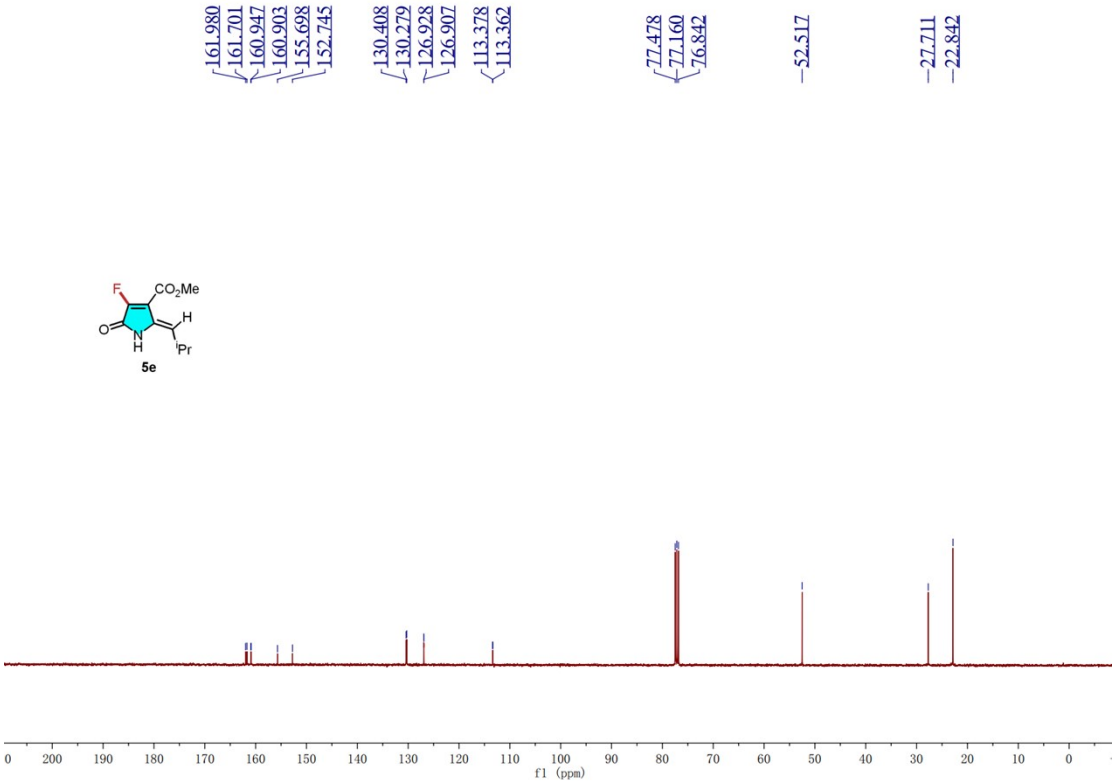
^{13}C{^{1}H} NMR Spectrum of Compound **5d** (100 MHz, $CDCl_3$)



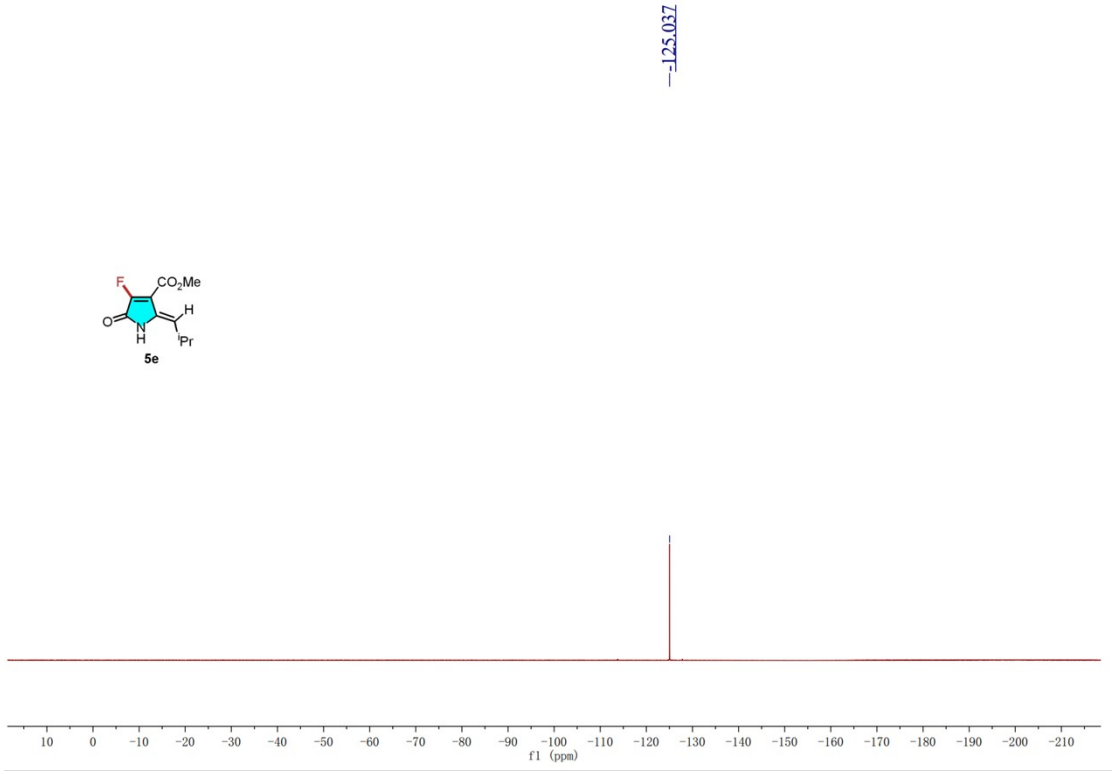
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5d** (376 MHz, $CDCl_3$)



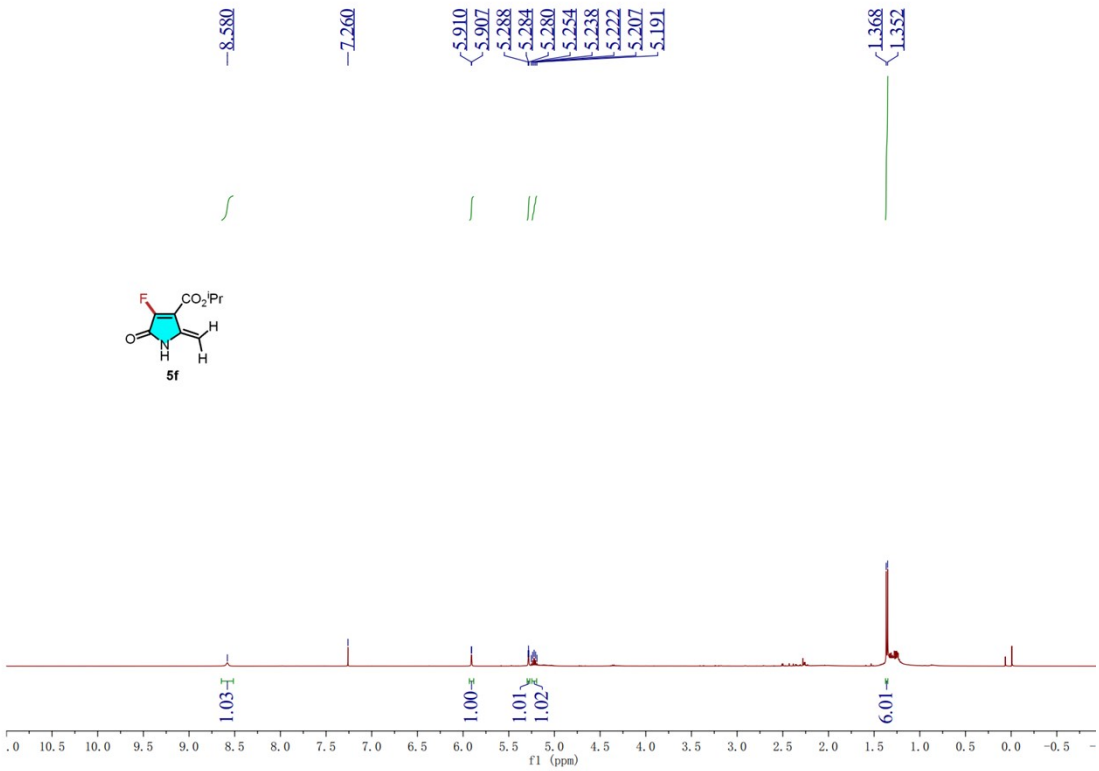
^{1}H NMR Spectrum of Compound **5e** (400 MHz, $CDCl_3$)



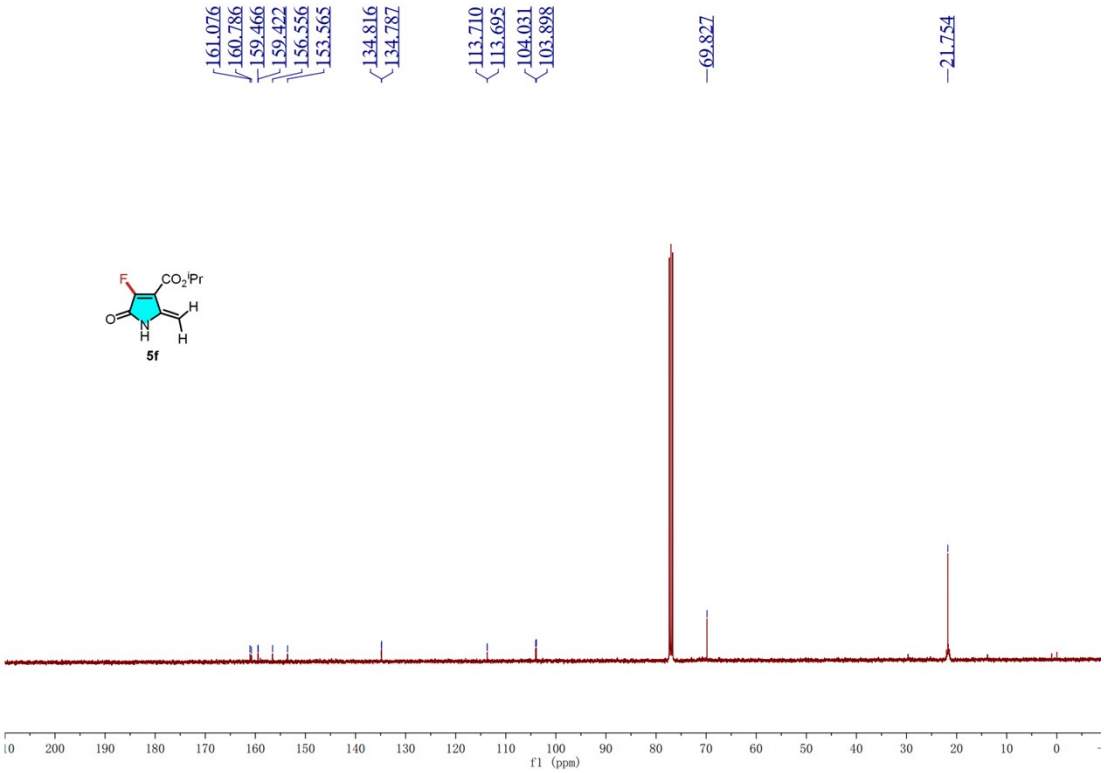
$^{13}C\{^{1}H\}$ NMR Spectrum of Compound **5e** (100 MHz, $CDCl_3$)



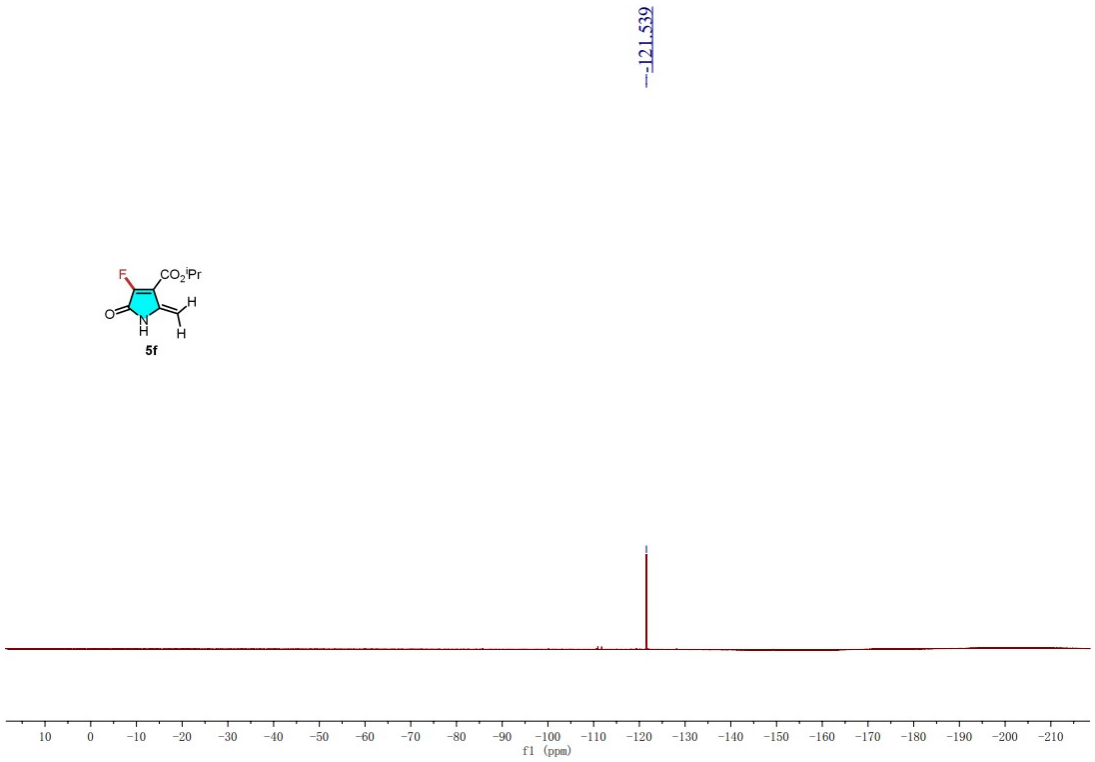
$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5e** (376 MHz, $CDCl_3$)



^{1}H NMR Spectrum of Compound **5f** (400 MHz, $CDCl_3$)



^{13}C{^{1}H} NMR Spectrum of Compound **5f** (100 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$ NMR Spectrum of Compound **5f** (376 MHz, $CDCl_3$)