Supporting Information

Access to Functionalized Pyrrolophenanthridines via an *ortho* C-H Amination/Interannular C-H Arylation Cascade of *N*-Arylpyrroles

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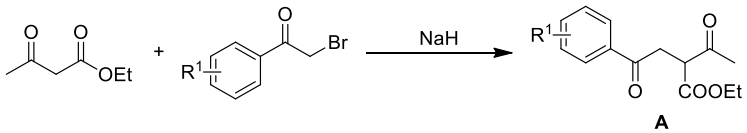
General Information and Procedure

1. General information

$Pd(OAc)_2$ (Energy Chemical) were purchased from above mentioned company and used without additional purification. Other chemical reagents were commercially available and directly used without any further purification.^{1}H NMR spectra were recorded at 400 MHz and 500 MHz NMR spectrometers using TMS as an internal standard, ^{13}C NMR spectra were recorded at 100 MHz and 125 MHz NMR spectrometers using TMS as an internal standard, and were fully decoupled by broad band proton decoupling. Data for ^{1}H NMR are reported as follows: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. Mass spectra were obtained on a Bruker Apex IV RTMS.

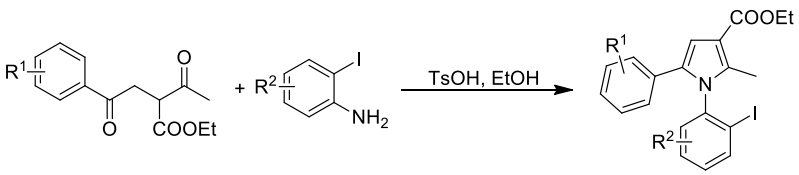
2. General procedure for the preparation of substrates

General Procedure of **1**[1]



A

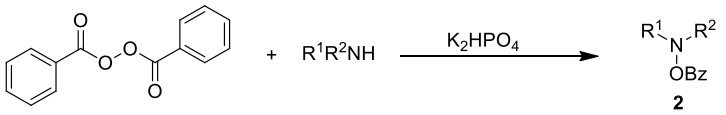
At 0 ℃, we add the tetrahydrofuran solution of active methylene compound dropwise to the anhydrous tetrahydrofuran suspension of sodium hydride. After stirring for 30 minutes, add dropwise the tetrahydrofuran solution of 2-bromoacetophenone. The slower the better in this step. The solution was stirred at 0 ℃ for 2 hours and then at room temperature for 8 hours. The reaction was quenched with HCl solution and extracted with ether (3×80 mL). The organic layers were combined, dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by silica gel flash chromatography, eluting with PE/EA, to give 1,4-dicarbonyl compound **A**.



A **1**

Subsequently, 0.1 equivalent of *p*-toluenesulfonic acid was added to the ethanol solution of 1,4-dicarbonyl compound **A** (1.1 equiv) and 2-iodoaniline. After refluxing for 24 hours, the solvent was removed in vacuo, the resulting mucus was dissolved in water, and Extraction with methyl chloride for three times, remove excess water with anhydrous sodium sulfate, concentrate and purify by fast silica gel column chromatography (PE/EA) to obtain reaction material **1**.

General Procedure of **2**[2]

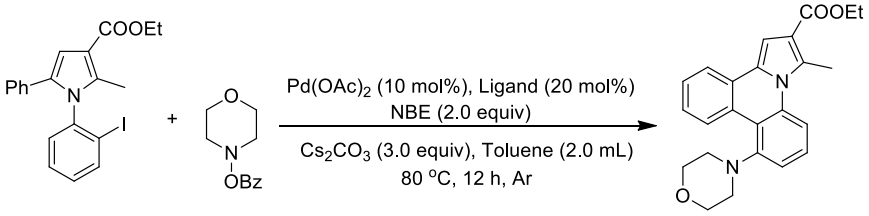


2

First, dissolve BPO and dipotassium hydrogen phosphate (1.5-2.0 equiv) in dichloromethane, add amine (1.2 equiv) to it, and stir the reaction at room temperature for about 2 hours (checked by TLC), add appropriate amount of water, and stir until the solution is clear Transparent. Extract with dichloromethane three times, remove excess water with anhydrous sodium sulfate, concentrate and purify by silica gel flash chromatography to obtain reaction material **2**.

3. Optimization of reaction conditions

Screening of Ligand



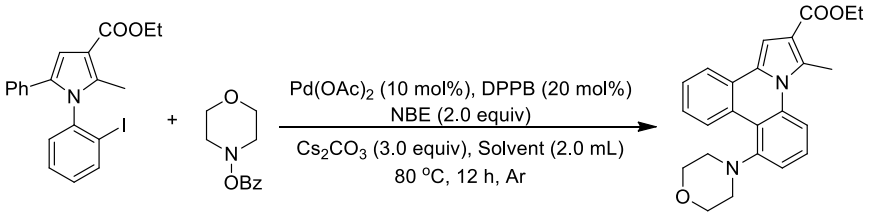
1a **2a** **3aa**

Entry[a]	Ligand	Yield(%)[b]
1	PPh_3	21
2	TFP	29
3	TCHP	<5
4	P(*o*-OMe-Ph)$_3$	<5
5	P(*o*-Me-Ph)$_3$	Trace
6	S-Phos	<5
7	DPPB	35
8	DPPF	13

9	BINAP	14
10	DPPE	11
11	DPPP	16
12	DPPM	<5

[a] Reactions conditons: **1a** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), Ligand (0.04 mmol), NBE (0.4 mmol), Cs_2CO_3 (0.6 mmol), Toluene (2.0 mL), 80 °C, 12 h. [b] Isolated yield by flash column chromatography.

Screening of Solvent

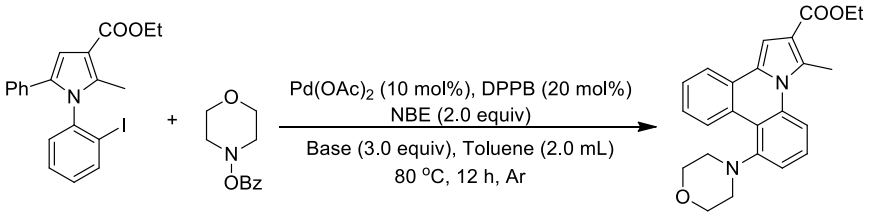


1a **2a** **3aa**

Entry[a]	Solvent	Yield(%)[b]
1	Dioxane	21
2	DME	17
3	TFE	n.d.
4	DCE	35
5	THF	19
6	HFIP	n.d.
7	MeCN	31
8	TBME	19
9	DMF	n.d.
10	NMP	<5
11	Xylene	20
12	*o*-Xylene	23
13	*p*-Xylene	17
14	$PhCF_3$	21
15	Mesitylene	20

[a] Reactions conditons: **1a** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), DPPB (0.04 mmol), NBE (0.4 mmol), Cs_2CO_3 (0.6 mmol), Solvent (2.0 mL), 80 °C, 12 h. [b] Isolated yield by flash column chromatography.

Screening of Base



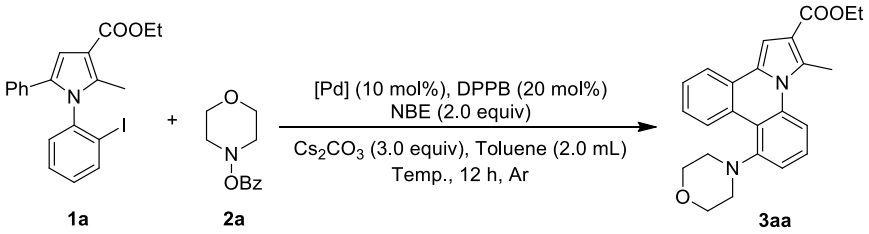
1a **2a** **3aa**

Entry[a]	Base	Yield(%)[b]
1	K_2CO_3	5
2	$KHCO_3$	<5

3	K_3PO_4	13
4	K_2HPO_4	<5
5	KH_2PO_4	Trace
6	KOAc	Trace
7	t-BuOK	n.d.
8	Na_2CO_3	5
9	$NaHCO_3$	<5
10	NaOAc	Trace
11	NaTFA	Trace
12	LiOAc	Trace

[a] Reactions conditons: **1a** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), DPPB (0.04 mmol), NBE (0.4 mmol), Base (0.6 mmol), Toluene (2.0 mL), 80 °C, 12 h. [b] Isolated yield by flash column chromatography.

Screening of Others



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

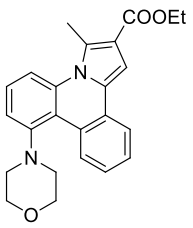
Entry[a]	[Pd]	Temperature(℃)	Yield(%)[b]
1	$Pd(OAc)_2$	60	13
2	$Pd(OAc)_2$	100	60
3	$Pd(OAc)_2$	120	74
4	$Pd(PPh_3)_4$	120	44
5	$PdCl_2$	120	26
6	$PdCl_2(MeCN)_2$	120	30
7	$Pd(TFA)_2$	120	19
8	$Pd_2(dba)_3$	120	9
9	$Pd(acac)_2$	120	31
10	$Pd_2Cl_2(CH_2CHCH_2)_2$	120	32
11[c]	$Pd(OAc)_2$	120	39
12[d]	$Pd(OAc)_2$	120	0

[a] Reactions conditons: **1a** (0.2 mmol), **2a** (0.4 mmol), [Pd] (0.02 mmol), DPPB (0.04 mmol), NBE (0.4 mmol), Base (0.6 mmol), Toluene (2.0 mL), Temperature, 12 h. [b] Isolated yield by flash column chromatography. [c]1.0 equiv. NBE was used. [d]In the absence of NBN.

4. General procedure for Palladium/Norbornene catalyzed C-H amination/cyclization cascade of *N*-aryl-pyrrole

To an oven-dried 25 mL Schlenk tube was added substrate **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), DPPB (0.04 mmol), NBE (0.4 mmol), Cs_2CO_3 (0.6 mmol), toluene (2.0 mL). The mixture was stirred in Ar for 12 h at 120 ºC followed by cooling. The resulting mixture was quenched by filtered through a celite pad and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to afford the product **3**.

5. Analytic data of products



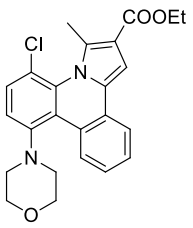
ethyl 3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3aa)

White solid. 74% yield; mp: 178-179 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.88-9.86 (m, 1H), 8.01-7.99 (m, 1H), 7.89-7.87 (m, 1H), 7.46-7.34 (m, 4H), 7.14-7.11 (m, 1H), 4.40 (q, J = 7.1 Hz, 2H), 4.02-3.96 (m, 4H), 3.29-3.24 (m, 2H), 3.16 (s, 3H), 3.02-2.96 (m, 2H), 1.45 (t, J = 6.9 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.1, 152.2, 136.8, 133.6, 129.7, 128.4, 127.7, 126.3, 126.2, 126.2, 126.0, 123.0, 117.7, 117.0, 115.1, 114.2, 102.9, 67.2, 60.3, 53.0, 17.1, 14.9.

HRMS m/z (ESI) calcd for $C_{24}H_{25}N_2O_3$ $(M+H)^+$: 389.1860, found: 389.1854.



ethyl

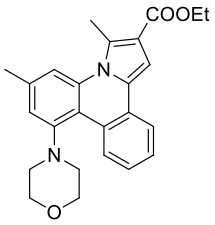
5-chloro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate(3ba)

White solid. 66% yield; mp: 140-142 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.68-9.66 (m, 1H), 7.96-7.94 (m, 1H), 7.49-7.45 (m, 1H), 7.38-7.33 (m, 3H), 7.00 (d, *J* = 8.6 Hz, 1H), 4.43-4.36 (m, 2H), 4.14-3.87 (m, 4H), 3.37-3.29 (m, 3H), 2.85-2.78 (m, 4H), 1.44 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.5, 148.9, 138.0, 132.0, 130.0, 128.9, 128.7, 126.3, 126.1, 125.7, 124.2, 122.3, 121.8, 119.7, 116.8, 114.7, 104.1, 66.7, 59.9, 55.3, 50.2, 17.0, 14.6.

HRMS m/z (ESI) calcd for $C_{24}H_{24}ClN_2O_3$ $(M+H)^+$: 423.1470, found: 423.1471.



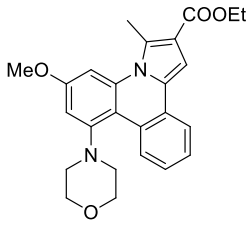
ethyl 3,6-dimethyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate(3ca)

White solid. 50% yield; mp: 186-187 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.81-9.79 (m, 1H), 7.99-7.97 (m, 1H), 7.68 (s, 1H), 7.43-7.32 (m, 3H), 6.93 (s, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.02-3.94 (m, 4H), 3.26-3.22 (m, 2H), 3.15 (s, 3H), 3.02-2.93 (m, 2H), 2.49 (s, 3H), 1.45 (t, *J* = 7.2, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 151.6, 137.4, 136.4, 133.0, 129.4, 127.5, 125.9, 125.6, 125.6, 125.5, 116.5, 115.8, 114.8, 114.4, 102.4, 66.9, 59.9, 52.7, 22.0, 16.8, 14.6.

HRMS m/z (ESI) calcd for $C_{25}H_{27}N_2O_3$ $(M+H)^+$: 403.2016, found: 403.2019.



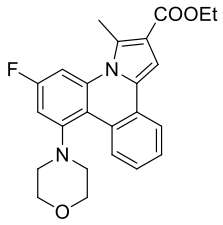
ethyl 6-methoxy-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate(3da)

White solid. 37% yield; mp: 190-191 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.69-9.67 (m, 1H), 7.98-7.95 (m, 1H), 7.41-7.31 (m, 4H), 6.69 (d, *J* = 2.5 Hz, 1H), 4.40 (q, *J* = 7.1 Hz), 4.01-3.93 (m, 7H), 3.26-3.23 (m, 2H), 3.17 (s, 3H), 2.99-2.91 (m, 2H),1.45 (t, *J* = 7.1Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 158.7, 153.1, 137.4, 132.5, 129.6, 126.9, 126.0, 125.7, 125.0, 124.9, 122.5, 116.8, 110.7, 102.3, 102.3, 98.7, 66.8, 59.9, 55.4, 52.6, 16.6, 14.6.

HRMS m/z (ESI) calcd for $C_{25}H_{27}N_2O_4$ $(M+H)^+$: 419.1965, found: 419.1959.



ethyl

6-fluoro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate

(3ea)

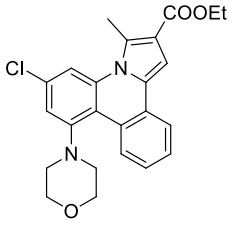
White solid. 56% yield; mp: 175-176 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.71-9.68 (m, 1H), 8.00-7.97 (m, 1H), 7.64-7.61 (m, 1H), 7.45-7.41 (m, 1H), 7.39-7.33 (m, 2H), 6.88-6.85 (m, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.01-3.94 (m, 4H), 3.28-3.24 (m, 2H), 3.16 (s, 3H), 2.98-2.91 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 161.5 (d, *J* = 244.4 Hz), 153.5 (d, *J* = 9.4 Hz), 137.2 (d, *J* = 12.1 Hz), 132.9, 129.4, 127.8, 125.8, 125.4 (d, *J* = 2.9 Hz), 125.2, 122.7, 117.1, 113.5 (d, *J* = 3.3 Hz), 102.7, 102.6, 102.4, 100.6 (d, *J* = 27.2 Hz), 66.6, 60.0, 52.5, 16.5, 14.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.68.

HRMS m/z (ESI) calcd for $C_{24}H_{24}FN_2O_3$ $(M+H)^+$: 407.1765, found: 407.1771.



ethyl

6-chloro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate

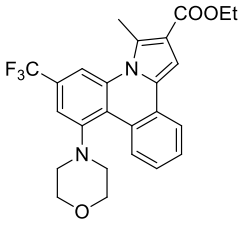
(3fa)

White solid. 39% yield; mp: 160-161 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.70-9.68 (m, 1H), 7.97-7.95 (m, 1H), 7.81 (d, *J* = 2.1 Hz, 1H), 7.46-7.42 (m, 1H), 7.38-7.33 (m, 1H), 7.31 (s, 1H), 7.05 (d, *J* = 2.1 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.97-3.92 (m, 4H), 3.26-3.22 (m, 2H), 3.12 (s, 3H), 2.98-2.91 (m, 2H), 1.45 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.5, 152.5, 136.8, 133.0, 133.0, 129.3, 128.2, 125.8, 125.7, 125.5, 125.1, 122.6, 117.0, 115.8, 115.0, 113.5, 102.8, 66.6, 60.0, 52.4, 16.6, 14.5.

HRMS m/z (ESI) calcd for $C_{24}H_{24}ClN_2O_3$ $(M+H)^+$: 423.1470, found: 423.1474.



ethyl 3-methyl-8-morpholino-6-(trifluoromethyl)pyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ga)

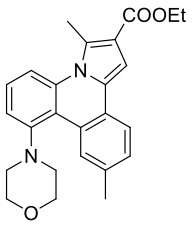
White solid. 29% yield; mp: 175-177 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.80-9.78 (m, 1H), 8.10 (s, 1H), 8.01-7.99 (m, 1H), 7.52-7.48 (m, 1H), 7.41-7.36 (m, 2H), 7.30 (s, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.01-3.94 (m, 4H), 3.32-3.29 (m, 2H), 3.15 (s, 3H), 3.06-2.98 (m, 2H), 1.45 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.5, 152.1, 136.2, 133.2, 129.2, 129.1, 128.7 (q, *J* = 32.6 Hz), 126.4, 125.9, 125.8, 124.8, 123.9 (q, *J* = 270.7 Hz), 122.8, 120.0, 117.3, 110.6 (q, *J* = 3.5 Hz), 110.3 (q, *J* = 4.3 Hz), 103.1, 66.6, 60.1, 52.4, 16.5, 14.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.78.

HRMS m/z (ESI) calcd for $C_{25}H_{24}F_3N_2O_3$ $(M+H)^+$: 457.1734, found: 457.1732.



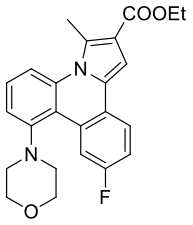
ethyl 3,10-dimethyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ja)

White solid. 41% yield; mp: 152-153 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.89-7.84 (m, 2H), 7.39-7.35 (m, 1H), 7.28-7.25 (m, 2H), 7.10-7.08 (m, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.00-3.94 (m, 4H), 3.28-3.24 (m, 2H), 3.14 (s, 3H), 3.03-2.95 (m, 2H), 1.45 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 151.7, 136.5, 135.1, 132.8, 129.5, 129.2, 127.2, 125.8, 125.8, 123.5, 122.5, 117.3, 116.5, 114.6, 113.8, 101.7, 67.0, 59.9, 52.7, 21.9, 16.7, 14.6.

HRMS m/z (ESI) calcd for $C_{25}H_{27}N_2O_3$ $(M+H)^+$: 403.2016, found: 403.2015.



ethyl

10-fluoro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ka)

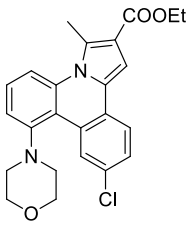
White solid. 25% yield; mp: 151-153 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.75-9.71 (m, 1H), 7.95-7.92 (m, 1H), 7.88-7.86 (m, 1H), 7.43 (t, *J* = 8.3 Hz, 1H), 7.25 (s, 1H), 7.19-7.13 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.05-3.96 (m, 4H), 3.25-3.21 (m, 2H), 3.13 (s, 3H), 3.04-2.97 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 161.0 (d, *J* = 240.0 Hz), 152.1, 136.7, 133.0, 128.7, 128.0, 127.3 (d, *J* = 9.6 Hz), 124.2 (d, *J* = 8.5 Hz), 122.5 (d, *J* = 2.2 Hz), 116.7, 116.6 (d, *J* = 3.0 Hz), 116.1, 115.8, 115.0, 114.0, 111.9, 111.7, 102.0, 66.7, 60.0, 52.8, 16.7, 14.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.15.

HRMS m/z (ESI) calcd for $C_{24}H_{24}FN_2O_3$ $(M+H)^+$: 407.1765, found: 407.1761.



ethyl

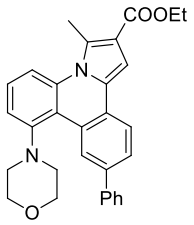
10-chloro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3la)

White solid. 33% yield; mp: 172-173 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.02 (d, 2.2 Hz, 1H), 7.87-7.84 (m, 2H), 7.42 (t, *J* = 8.2 Hz, 1H), 7.38-7.35 (m, 1H), 7.28 (s, 1H), 7.14-7.11 (m, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.07-3.96 (m, 4H), 3.23-3.20 (m, 2H), 3.13 (s, 3H), 3.03-2.97 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 152.0, 136.6, 133.4, 131.4, 128.5, 128.0, 128.0, 126.8, 125.6, 124.3, 123.7, 116.8, 116.2, 115.1, 113.9, 66.8, 60.0, 52.7, 16.7, 14.5.

HRMS m/z (ESI) calcd for $C_{24}H_{24}ClN_2O_3$ $(M+H)^+$: 423.1470, found:423.1476.



ethyl

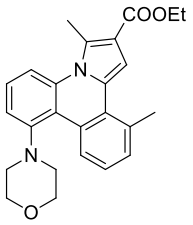
3-methyl-8-morpholino-10-phenylpyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ma)

White solid. 40% yield; mp: 169-171 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.29 (d, *J* = 1.8 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.89-7.87 (m, 1H), 7.76-7.74 (m, 2H), 7.72-7.69 (m, 1H), 7.54-7.50 (m, 2H), 7.43-7.38 (m, 2H), 7.36 (s, 2H), 7.16-7.14 (m, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 3.89-3.76 (m, 4H), 3.28-3.25 (m, 2H), 3.16 (s, 3H), 3.01-2.95 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 152.0, 140.9, 138.1, 136.6, 133.3, 129.1, 129.0, 127.4, 127.3, 126.8, 126.8, 126.1, 124.9, 124.4, 123.1, 117.5, 116.8, 115.0, 114.0, 102.7, 66.8, 60.0, 52.8, 16.8, 14.6.

HRMS m/z (ESI) calcd for $C_{30}H_{29}N_2O_3$ $(M+H)^+$: 465.2173, found: 465.2182.



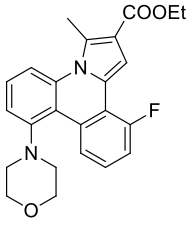
ethyl 3,12-dimethyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3na)

White solid. 20% yield; mp: 145-146 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.81 (d, J = 7.5 Hz, 1H), 7.73-7.70 (m, 1H), 7.42 (s, 1H), 7.40-7.34 (m, 2H), 7.31-7.27 (m, 1H), 7.08-7.06 (m, 1H), 4.41 (q, J = 7.1 Hz, 2H), 4.00-3.93 (m, 4H), 3.31-3.27 (m, 2H), 3.11 (s, 3H), 3.01-2.93 (m, 2H), 2.82 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 151.1, 135.7, 133.4, 133.0, 131.2, 138.4, 127.7, 127.0, 125.0, 122.9, 117.7, 116.3, 114.2, 113.8, 108.4, 66.8, 59.9, 52.4, 25.1, 16.8, 14.6.

HRMS m/z (ESI) calcd for $C_{25}H_{27}N_2O_3$ $(M+H)^+$: 403.2016, found: 403.2019.



ethyl 12-fluoro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3oa)

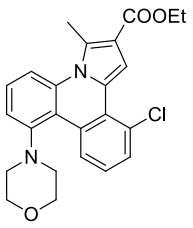
White solid. 33% yield; mp: 148-149 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.71 (d, J = 8.3 Hz, 1H), 7.82-7.80 (m, 1H), 7.58 (d, J = 4.8 Hz, 1H), 7.41 (t, J = 8.2 Hz, 1H), 7.33-7.28 (m, 1H), 7.22-7.17 (m, 1H), 7.12-7.10 (m, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.98-3.92 (m, 4H), 3.26-3.23 (m, 2H), 3.14 (s, 3H), 3.00-2.95 (m, 2H), 1.45 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 158.5 (d, J = 248.3 Hz), 151.8, 136.4, 133.3, 128.5 (d, J = 3.4 Hz), 127.8, 125.5 (d, J = 9.0 Hz), 123.7 (d, J = 2.8 Hz), 121.1 (d, J = 3.6 Hz), 117.1 (d, J = 3.0 Hz), 116.6 (d, J = 2.8 Hz), 115.3 (d, J = 12.4 Hz), 114.7, 114.2 (d, J = 21.1 Hz), 113.9, 108.3 (d, J = 17.6 Hz), 66.8, 60.0, 52.6, 16.7, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.82.

HRMS m/z (ESI) calcd for $C_{24}H_{24}FN_2O_3$ $(M+H)^+$: 407.1765, found: 407.1768.



ethyl

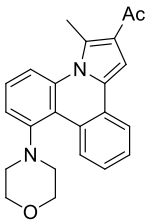
12-chloro-3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3pa)

White solid. 25% yield; mp: 168-169 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.88-9.86 (m, 1H), 8.21 (s, 1H), 7.72-7.70 (m, 1H), 7.55-7.53 (m, 1H), 7.40 (t, J = 8.1 Hz, 1H), 7.26 (t, J = 8.1 Hz, 1H), 7.10-7.07 (m, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.98-3.89 (m, 4H), 3.27-3.23 (m, 2H), 3.10 (s, 3H), 3.01-2.94 (m, 2H), 1.45 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 151.3, 135.9, 133.7, 130.7, 129.5, 129.2, 127.8, 126.0, 125.3, 123.6, 116.8, 116.5, 114.5, 113.9, 109.9, 66.8, 60.0, 52.4, 16.8, 14.6.

HRMS m/z (ESI) calcd for $C_{24}H_{24}ClN_2O_3$ $(M+H)^+$: 423.1470, found: 423.1472.



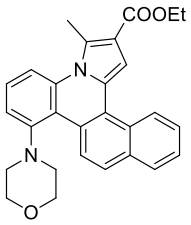
1-(3-methyl-8-morpholinopyrrolo[1,2-*f*]phenanthridin-2-yl)ethanone (3qa)

White solid. 40% yield; mp: 169-170 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.88 (d, J = 8.4 Hz, 1H), 8.00-7.98 (m, 1H), 7.86-7.83 (m, 1H), 7.48-7.44 (m, 1H), 7.42-7.36 (m, 2H), 7.26 (s, 1H), 7.14-7.12 (m, 1H), 4.02-3.95 (m, 4H), 3.28-3.24 (m, 2H), 3.13 (s, 3H), 3.02-2.95 (m, 2H), 2.63 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 196.2, 151.8, 136.1, 132.4, 129.3, 128.1, 127.3, 125.9, 125.9, 125.8, 125.8, 124.4, 122.4, 117.5, 114.9, 114.1, 102.7, 66.8, 52.6, 29.5, 17.2.

HRMS m/z (ESI) calcd for $C_{23}H_{23}N_2O_2$ $(M+H)^+$: 359.1754, found: 359.1750



ethyl

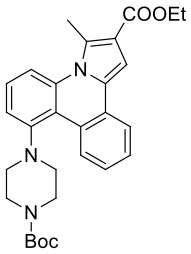
13-methyl-4-morpholinobenzo[i]pyrrolo[1,2-*f*]phenanthridine-12-carboxylate（3ra）

White solid. 18% yield; mp: 151-152 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.83 (d, J = 9.1 Hz, 1H), 9.01 (d, J = 8.5 Hz, 1H), 7.93-7.91 (m, 1H), 7.84-7.75 (m, 3H), 7.70-7.66 (m, 1H), 7.62-7.58 (m, 1H), 7.45 (t, J = 8.1 Hz, 1H), 7.18-7.16 (m, 1H), 4.43 (q, J = 7.1 Hz, 2H), 4.04-3.92 (m, 4H), 3.32-3.17 (m, 5H), 3.00-2.93 (m, 2H), 1.46 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 151.2, 135.2, 133.5, 133.3, 128.8, 128.3, 128.1, 127.3, 126.6, 126.4, 126.2, 125.2, 124.9, 123.6, 122.8, 118.2, 117.0, 115.3, 114.3, 108.1, 66.9, 60.0, 52.7, 16.6, 14.6.

HRMS m/z (ESI) calcd for $C_{28}H_{27}N_2O_3(M+H)^+$: 439.2016, found: 439.2017



ethyl

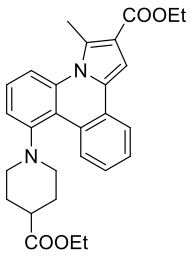
8-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-methylpyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ab)

White solid. 41% yield; mp: 196-197 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.86-9.84 (m, 1H), 8.00-7.98 (m, 1H), 7.88-7.86 (m, 1H), 7.45-7.32 (m, 4H), 7.10-7.08 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 4.15-4.10 (m, 2H), 3.36-3.30 (m, 2H), 3.15 (s, 3H), 2.82-2.77 (m, 2H), 1.51 (s, 9H), 1.45 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.7, 154.9, 151.8, 136.4, 133.1, 129.3, 128.1, 127.3, 126.0, 125.9, 125.8, 125.6, 122.6, 117.5, 116.6, 115.1, 113.9, 102.5, 80.0, 59.9, 52.3, 28.6, 16.8, 14.6.

HRMS m/z (ESI) calcd for $C_{29}H_{34}N_3O_4$ $(M+H)^+$: 488.2544, found: 488.2548.



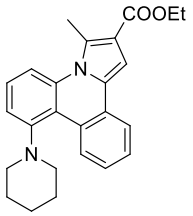
ethyl 8-(4-(ethoxycarbonyl)piperidin-1-yl)-3-methylpyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ac)

White solid. 32% yield; mp: 153-154 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.82-9.80 (m, 1H), 8.01-7.98 (m, 1H), 7.86-7.84 (m, 1H), 7.46-7.33 (m, 4H), 7.14-7.11 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 3.52-3.48 (m, 2H), 3.32-3.09 (m, 4H), 2.76-2.67 (m, 2H), 2.45-2.37 (m, 1H), 2.13-2.03 (m, 4H), 1.45 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.1, 165.8, 152.6, 136.3, 133.1, 129.4, 128.0, 127.1, 126.0, 125.9, 125.8, 125.8, 122.4, 117.7, 116.5, 115.2, 113.7, 102.4, 60.6, 59.9, 52.6, 41.3, 28.5, 16.8, 14.6, 14.3.

HRMS m/z (ESI) calcd for $C_{28}H_{31}N_2O_4$ $(M+H)^+$: 459.2278, found: 459.2276.



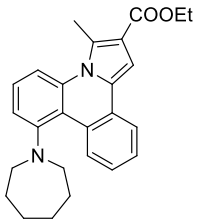
ethyl 3-methyl-8-(piperidin-1-yl)pyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ad)

White solid. 23% yield; mp: 79-80 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.90 (d, J = 8.4 Hz, 1H), 8.01-7.99 (m, 1H), 7.83-7.81 (m, 1H), 7.46-7.42 (m, 1H), 7.39-7.36 (m, 3H), 7.15-7.13 (m, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.43-3.39 (m, 2H), 3.15 (s, 3H), 2.73-2.67 (m, 2H), 1.95-1.90 (m, 2H), 1.80-1.75 (m, 2H), 1.45 (t, J = 7.1 Hz, 3H), 1.42-1.29 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.9, 153.4, 136.2, 133.0, 129.4, 127.8, 127.1, 126.3, 126.1, 125.6, 125.6, 122.3, 127.6, 116.5, 115.2, 113.2, 102.2, 59.9, 53.9, 26.0, 24.1, 16.7, 14.6.

HRMS m/z (ESI) calcd for $C_{25}H_{27}N_2O_2$ $(M+H)^+$: 387.2067, found: 387.2073.



ethyl 8-(azepan-1-yl)-3-methylpyrrolo[1,2-*f*]phenanthridine-2-carboxylate (3ae)

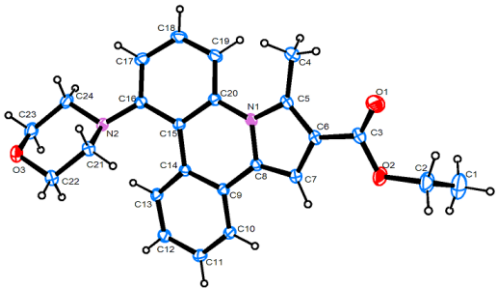
White solid. 11% yield; mp: 76-77 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.21-9.19 (m, 1H), 7.98-7.96 (m, 1H), 7.70-7.68 (m, 1H), 7.43-7.39 (m, 1H), 7.36-7.31 (m, 3H), 7.19-7.16 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.52-3.46 (m, 2H), 3.38-3.32 (m, 2H), 3.14 (s, 3H), 1.82-1.67 (m, 8H), 1.45 (t, *J* = 7.1 Hz, 3H).

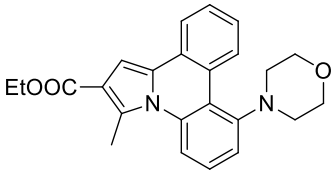
^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.9, 152.8, 136.2, 133.0, 129.4, 127.3, 126.8, 126.5, 125.7, 125.4, 125.4, 122.3, 116.8, 116.5, 116.3, 111.9, 102.2, 59.8, 55.3, 28.5, 28.5, 16.5, 14.6.

HRMS m/z (ESI) calcd for $C_{26}H_{29}N_2O_2$ $(M+H)^+$: 401.2224, found: 401.2229

6. X-ray crystallographic data

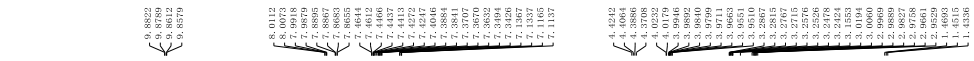


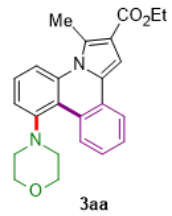
CCDC 2063259



3aa

7. Copies of ^{1}H and ^{13}C spectra





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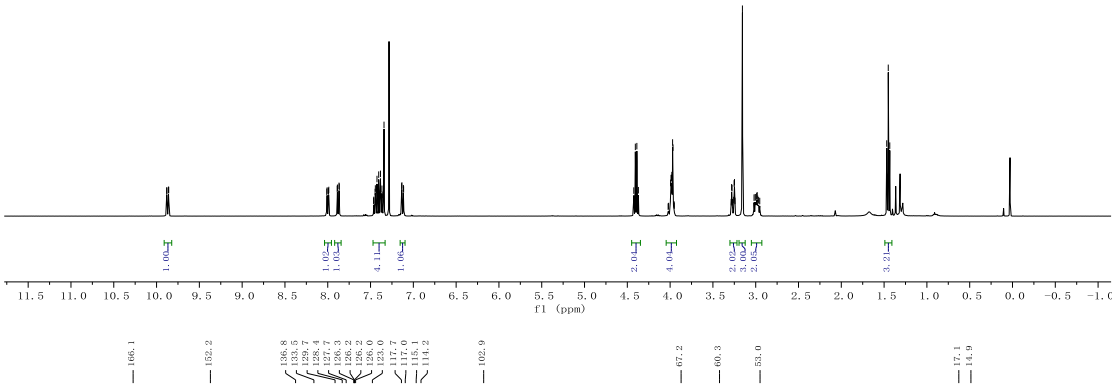
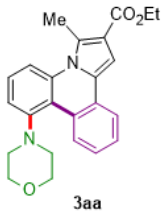
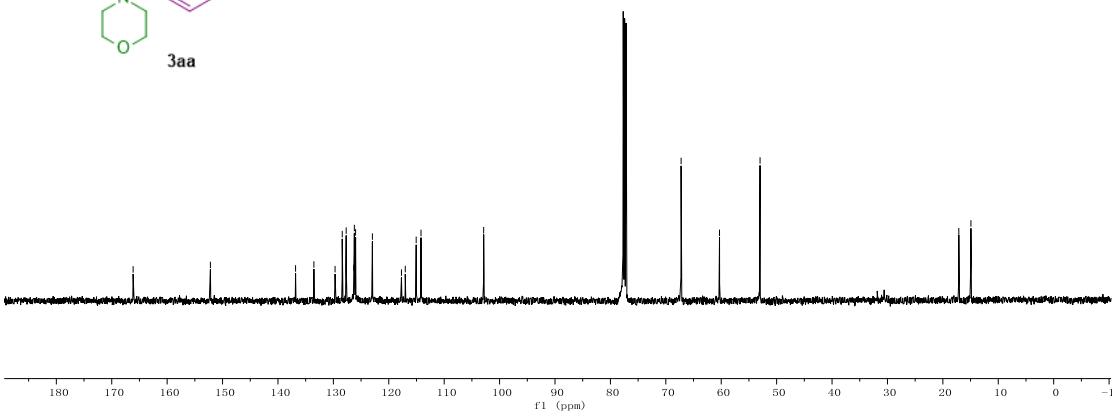
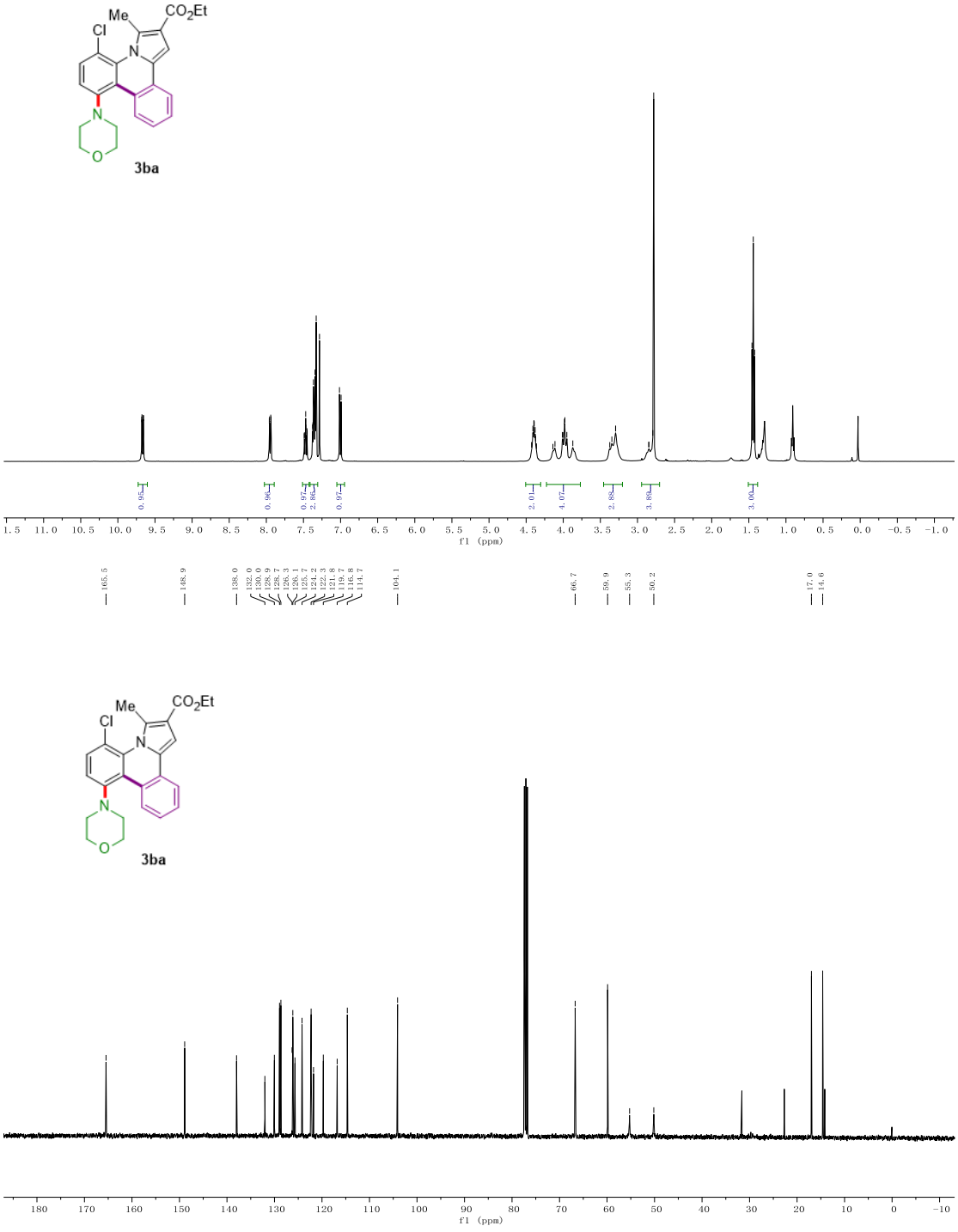




3aa

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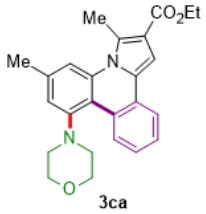
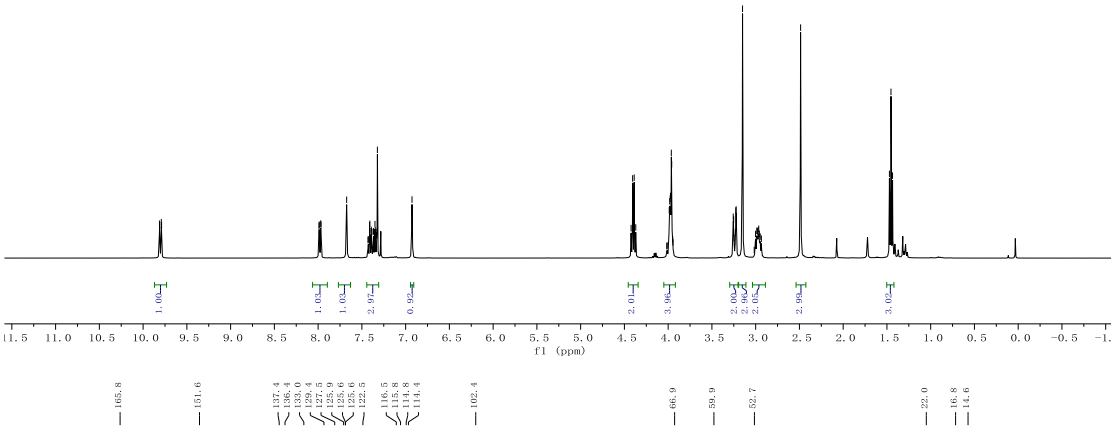
CO2Et
Cl
N
O
3ba
f1 (ppm)

Me
CO2Et
Cl
N
O
3ba
f1 (ppm)


Me
CO2Et
Me
N
N
O

3ca


1.00
1.03
1.02
2.97
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3.96
2.00
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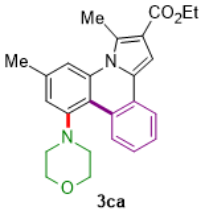
2.99
3.02
f1 (ppm)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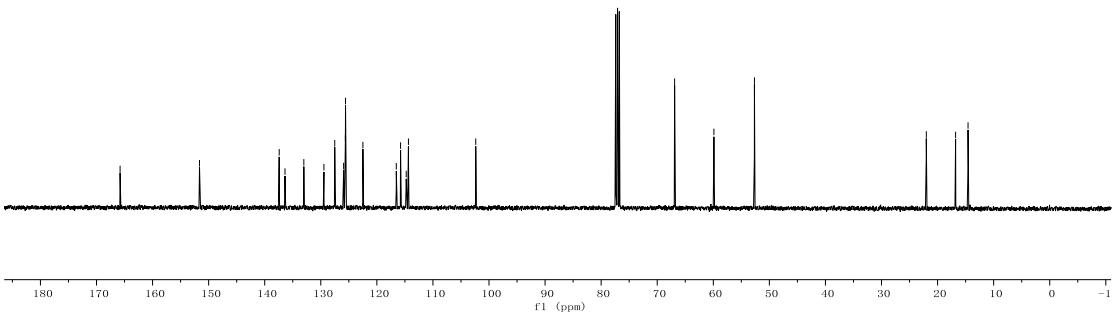
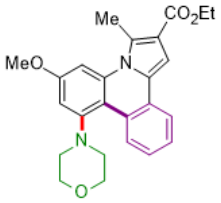

f1 (ppm)



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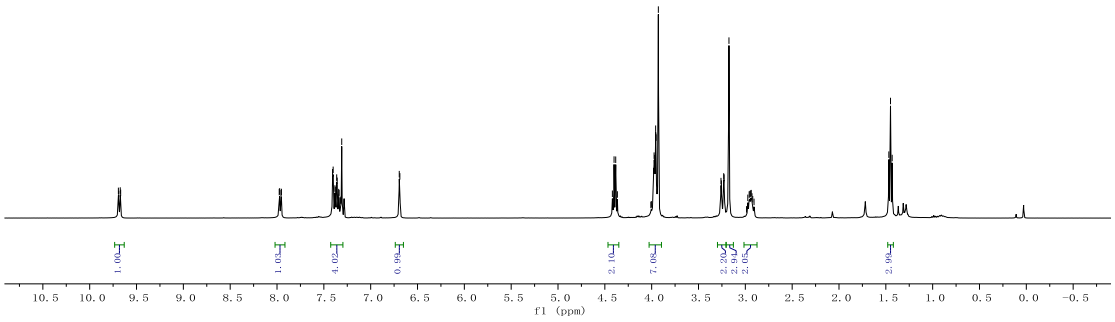

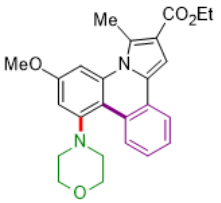

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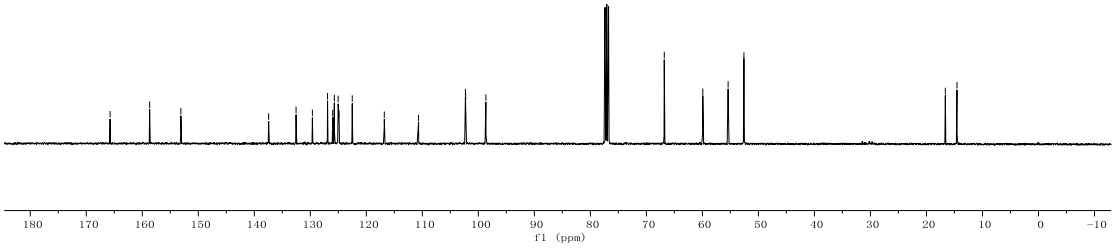

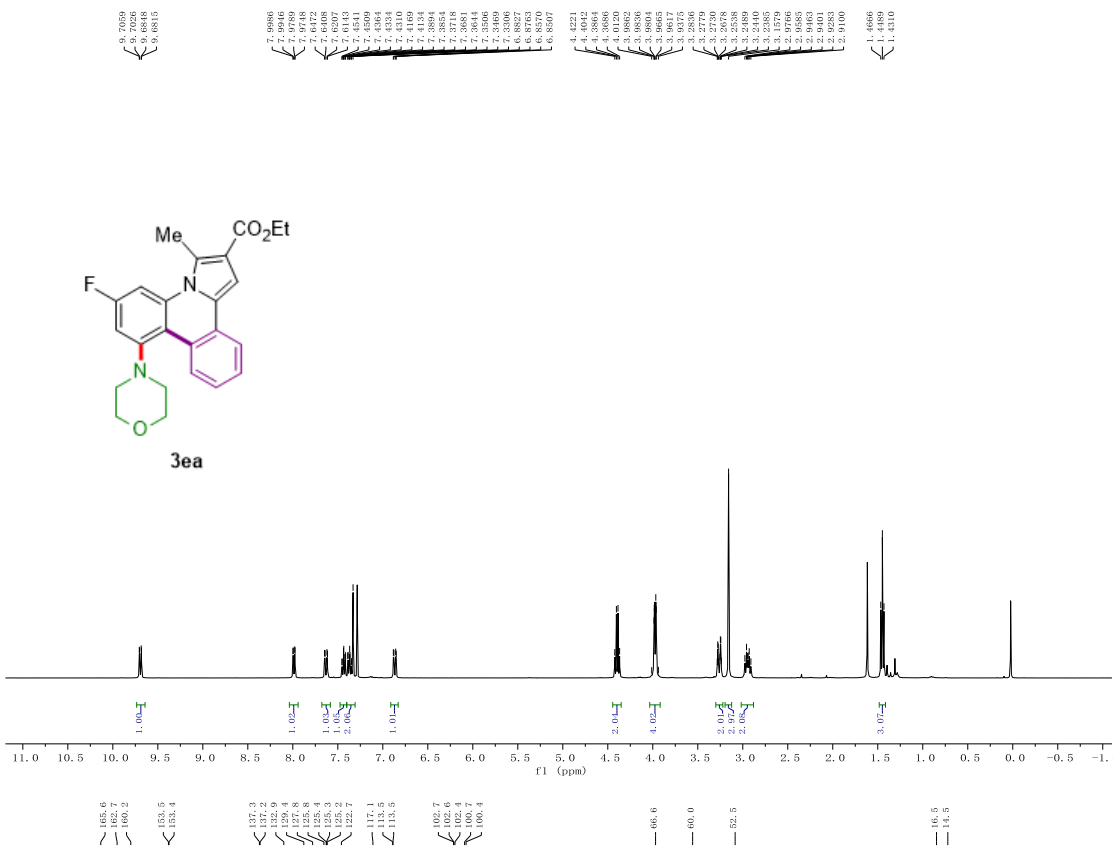
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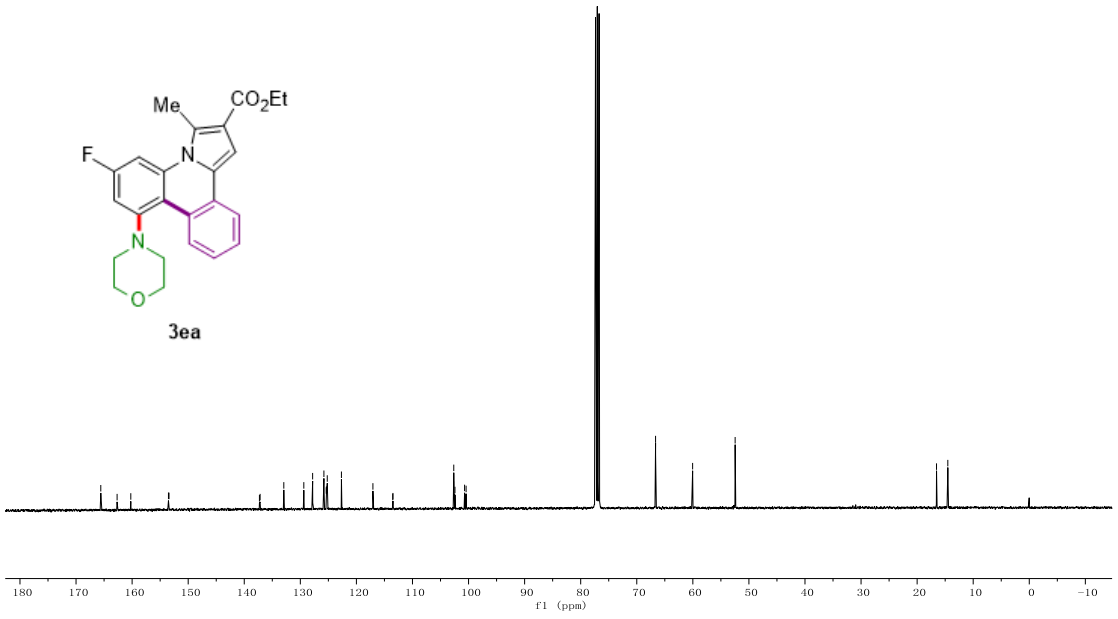
CO2Et
F
N
N
O
3ea
f1 (ppm)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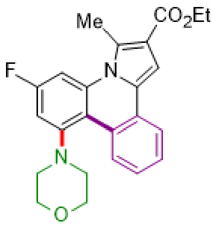
CO2Et
F
N
N
O
3ea
f1 (ppm)



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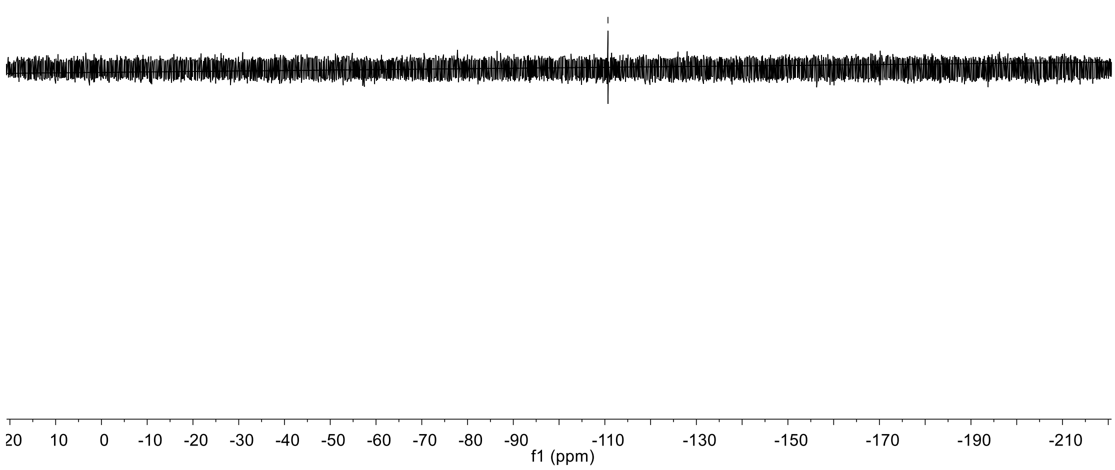
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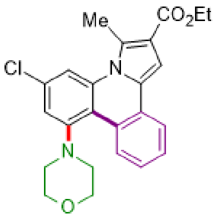
f1 (ppm)



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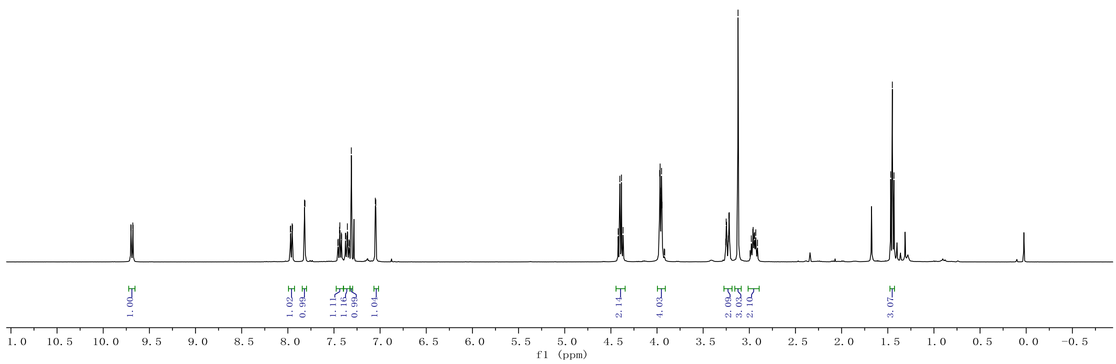
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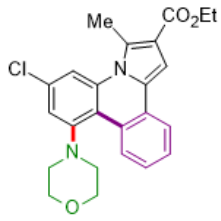
7.9726 7.9688 7.9528 7.9489 7.8194 7.8142 7.4575 7.4543 7.4397 7.4367 7.4341 7.4200 7.4167 7.3762 7.3724 7.3587 7.3550 7.3512 7.3375 7.3336 7.3122 7.0521 7.0469
4.4209 4.4031 4.3853 4.3675 3.9709 3.9661 3.9547 3.9506 3.9456 3.9220 3.9169 3.2561 3.2505 3.2455 3.2404 3.2268 3.2217 3.2168 3.1223 2.9915 2.9784 2.9619 2.9583 2.9481 2.9419 2.9302 2.9120
1.4683 1.4504 1.4327
1.00 1.02 0.99 1.11 1.16 0.99 1.04 2.14 4.03 2.09 3.03 2.10 3.07
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



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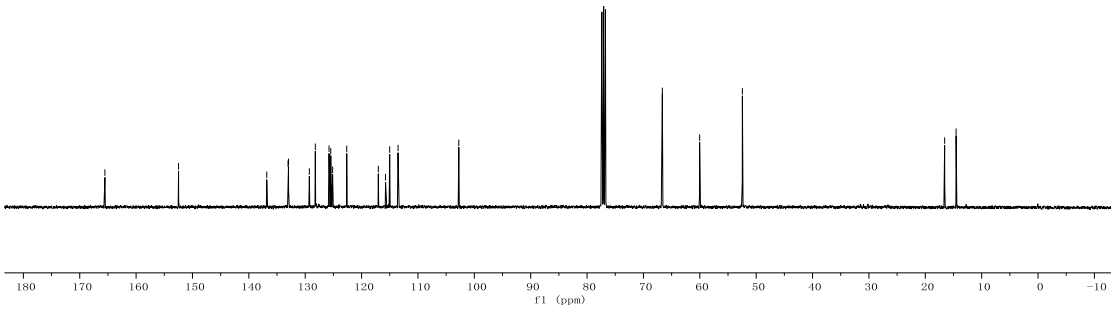

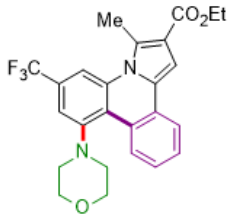

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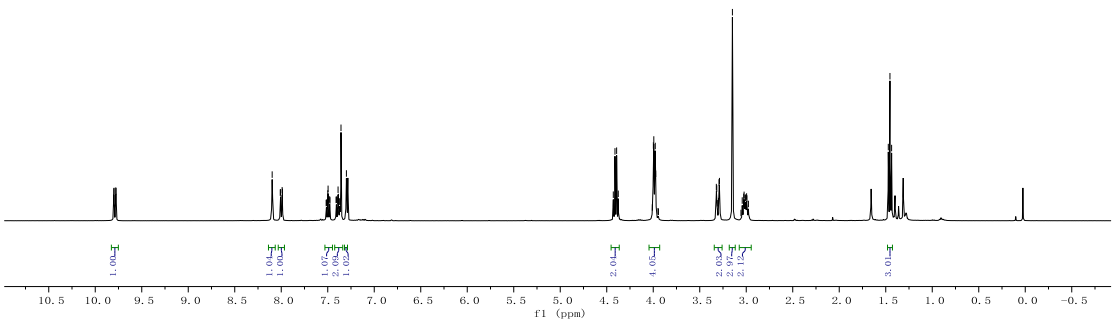

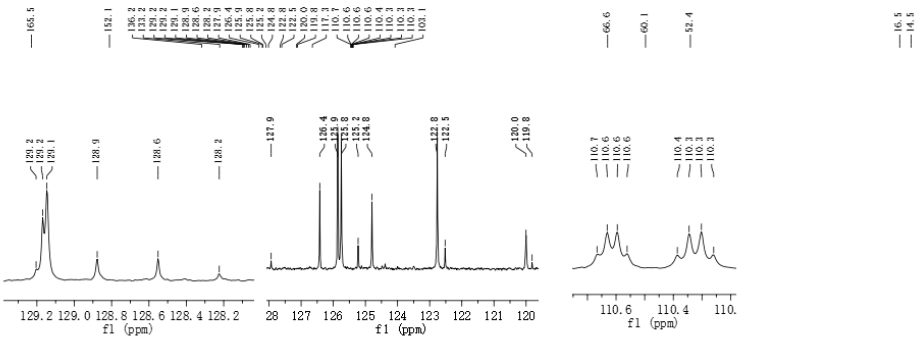
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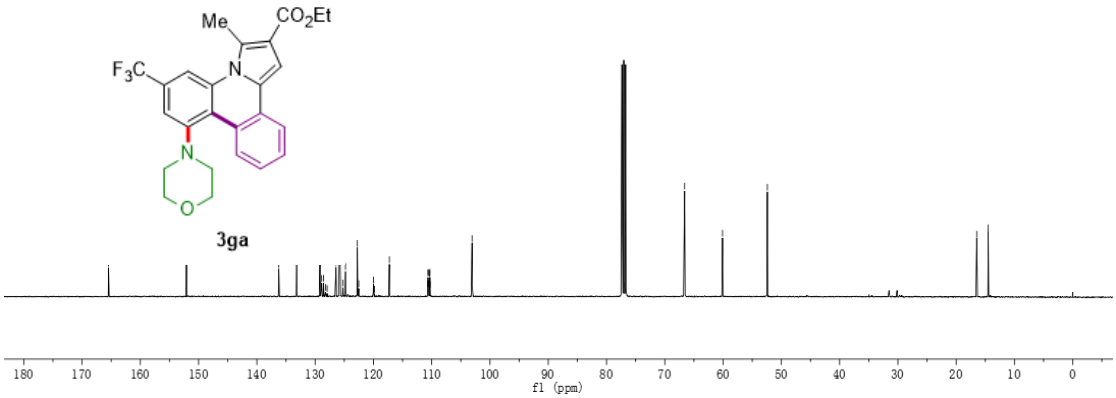
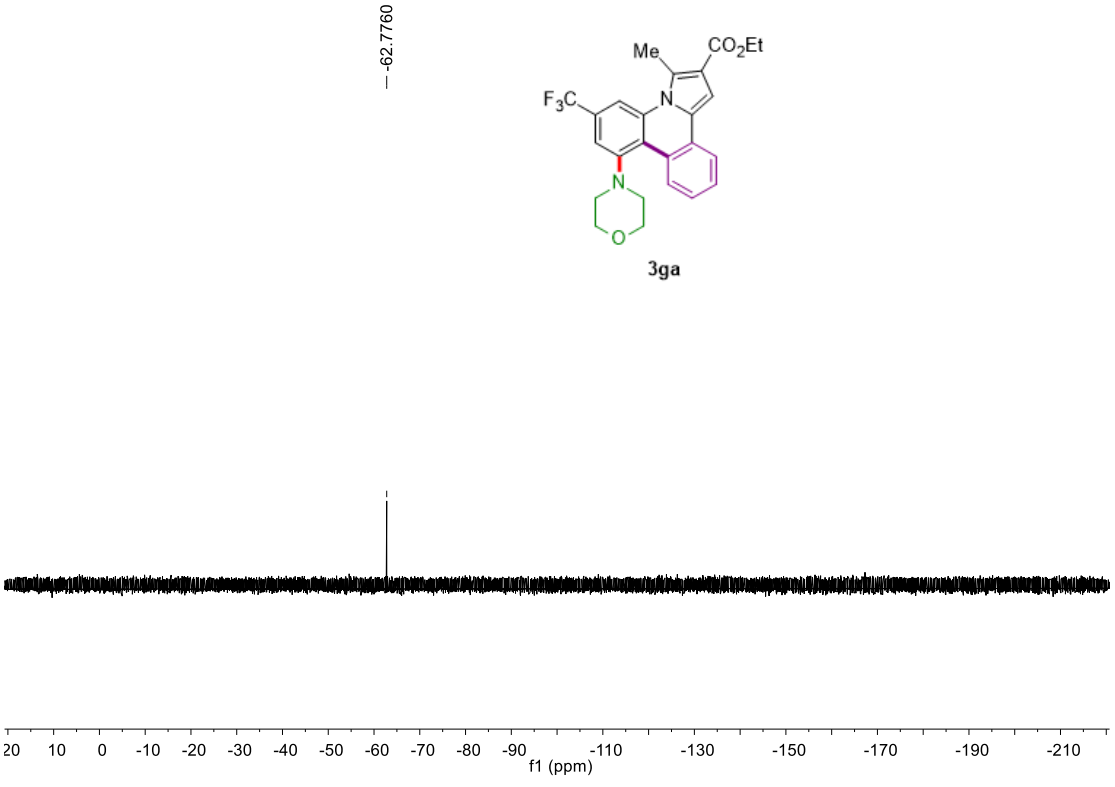
f1 (ppm)
128 127 126 125 124 123 122 121 120
f1 (ppm)
110.6 110.4 110.
f1 (ppm)


Me
CO2Et
F3C
N
O
3ga
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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F3C
N
O
3ga
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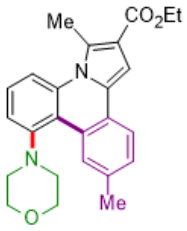
f1 (ppm)



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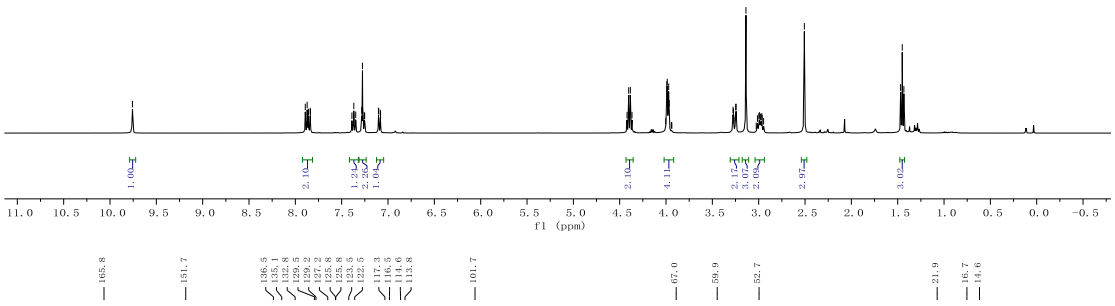

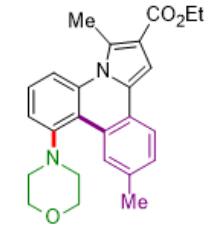

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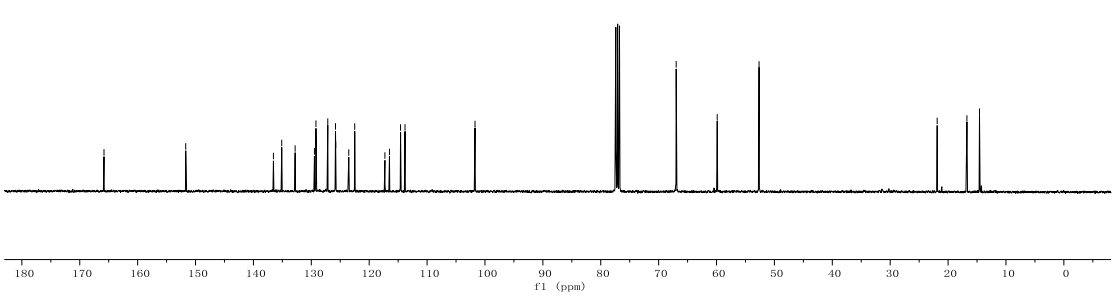

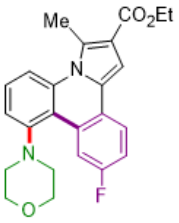

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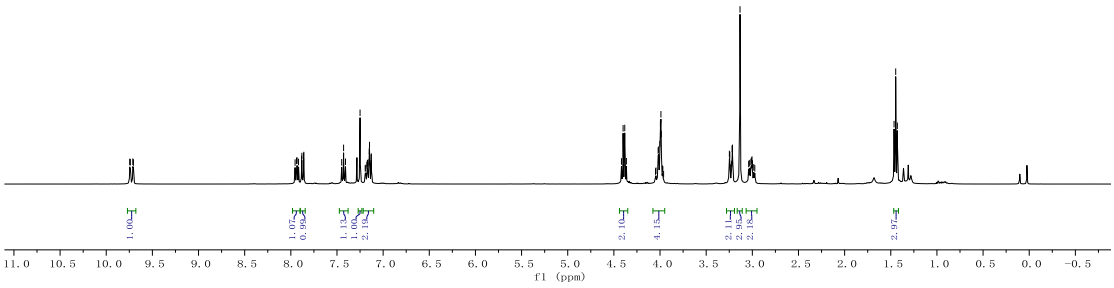

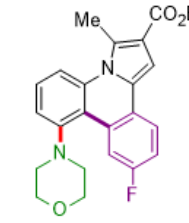

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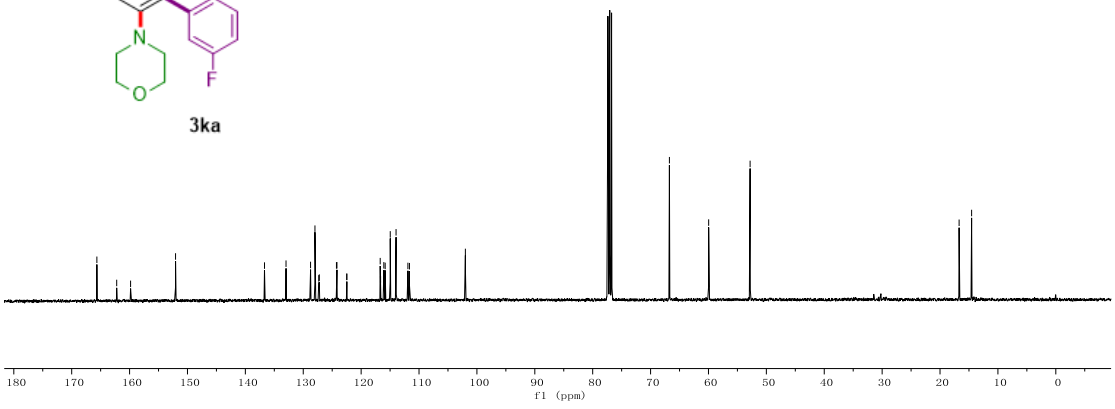

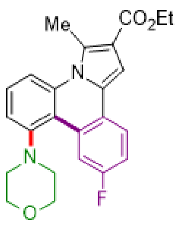

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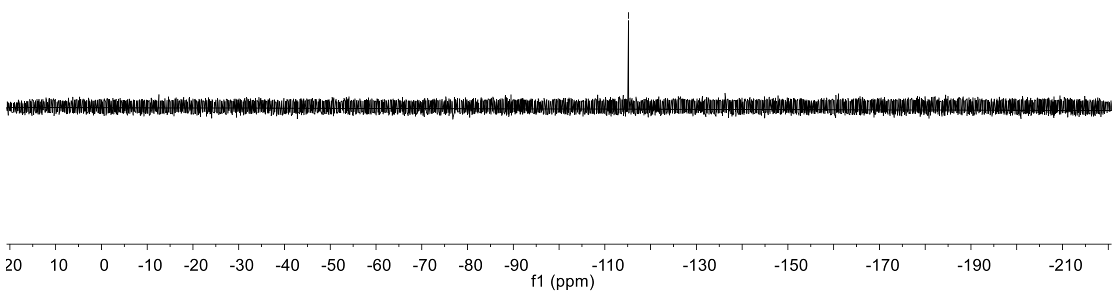
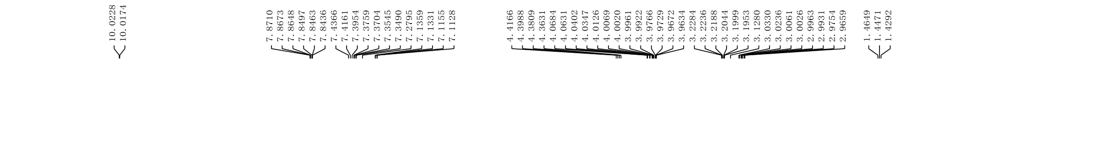
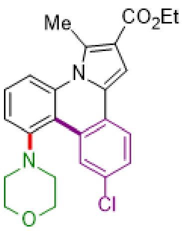
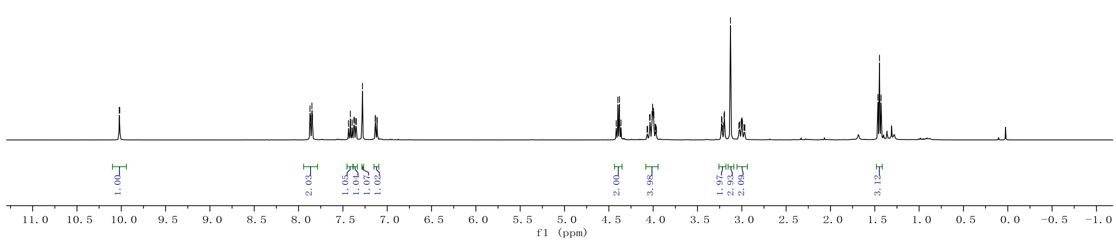
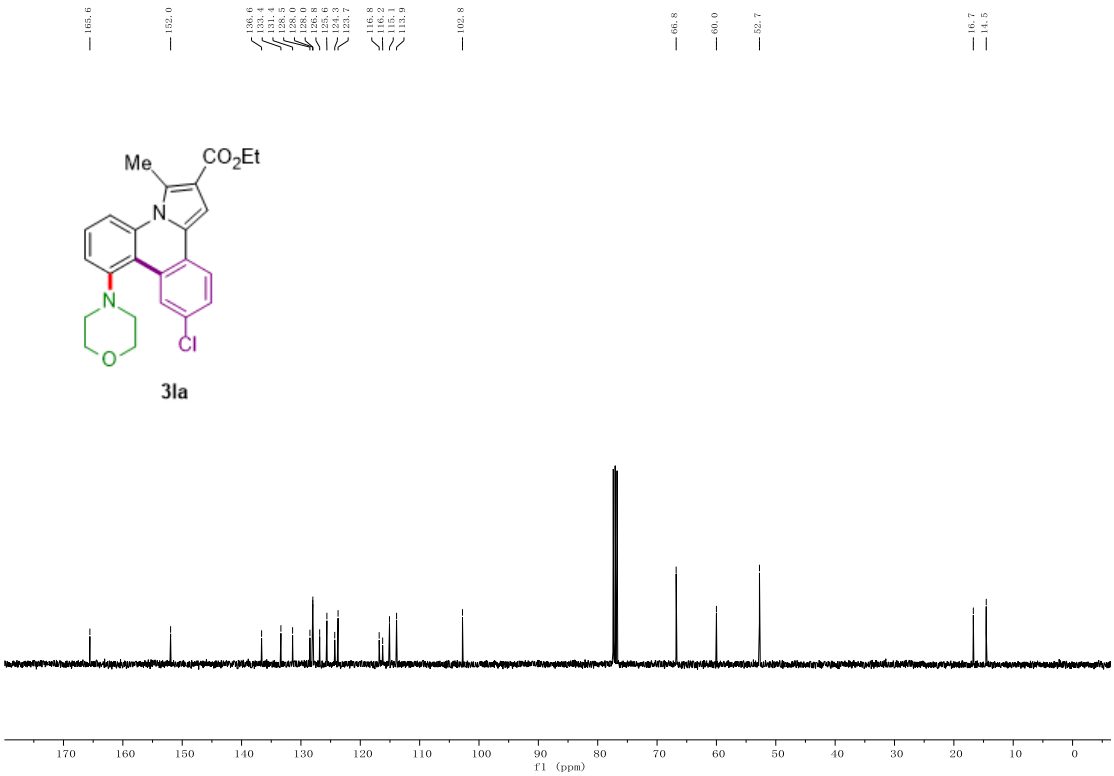






3la

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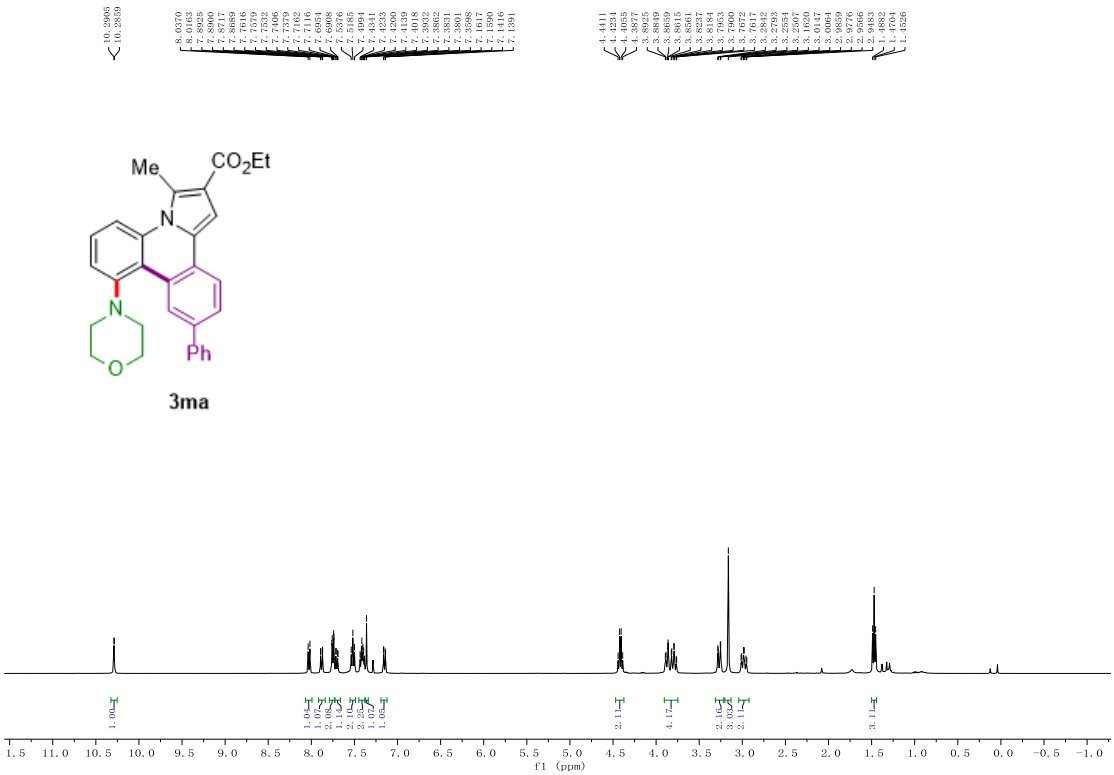
131.4
128.5
128.0
128.0
126.8
125.6
124.5
123.7
116.8
116.2
115.1
113.9
102.8
66.8
60.0
52.7
16.7
14.5
Me
CO2Et
N
N
O
Cl
3la
f1 (ppm)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7.7532
7.7406
7.7379
7.7162
7.7116
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7.6908
7.5376
7.5345
7.4994
7.4341
7.4233
7.4090
7.4139
7.4018
7.3932
7.3902
7.3851
7.3801
7.3598
7.1617
7.1490
7.1416
7.1391
4.4411
4.4234
4.4055
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3.8527
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3.7969
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3.7617
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3.2793
3.2554
3.2507
3.1620
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3.0064
2.9859
2.9776
2.9566
2.9483
2.9382
1.4704
1.4526
Me
CO2Et
N
N
O
Ph
3ma
1.00
1.04
1.07
2.08
1.14
2.14
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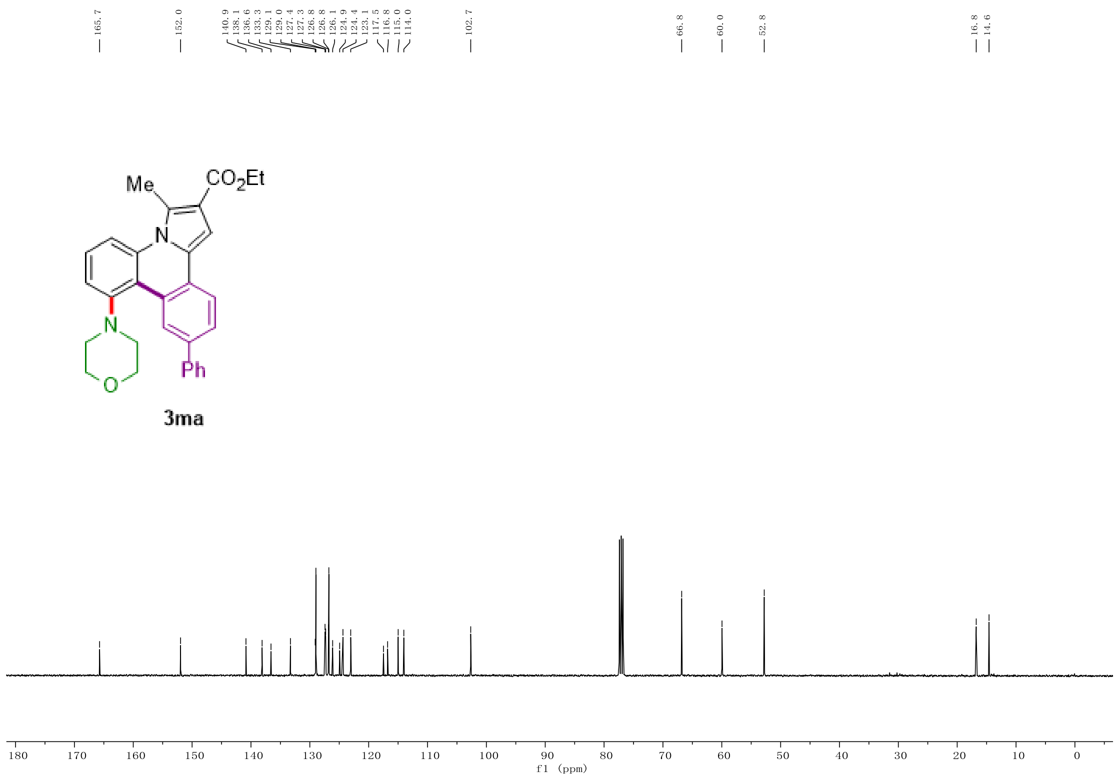
1.07
1.02
2.11
4.17
2.16
3.05
2.11
3.11
f1 (ppm)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126.8
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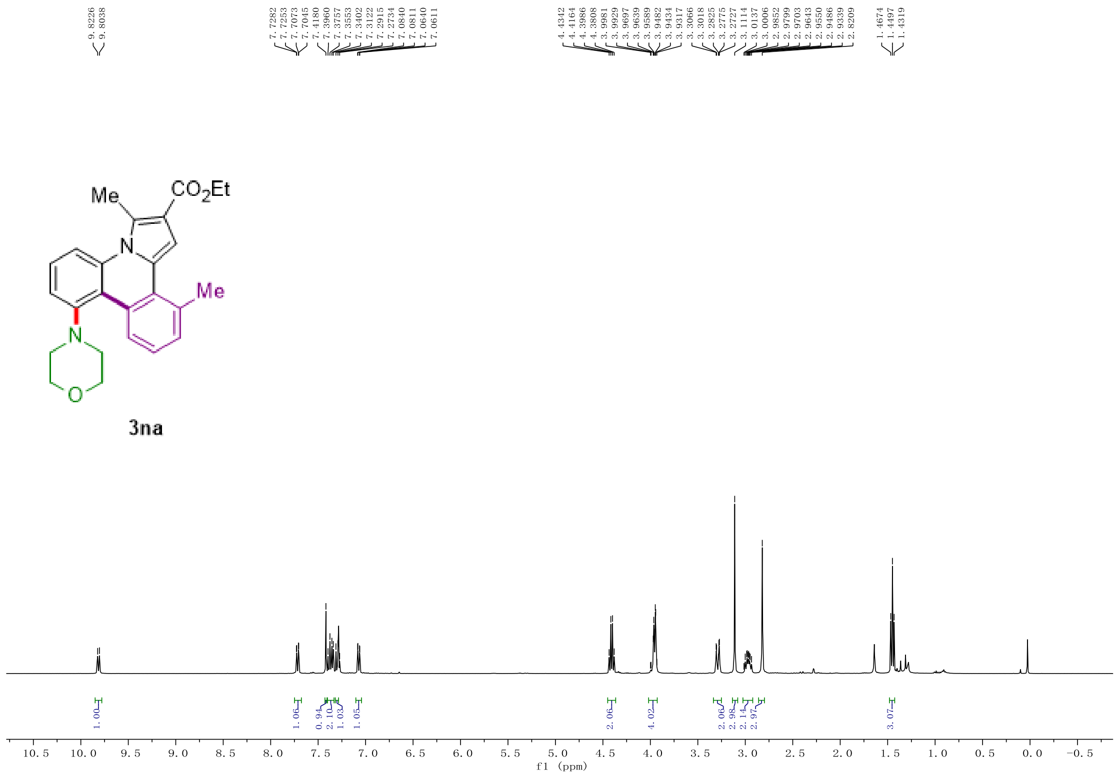
126.1
124.9
124.4
123.1
117.5
116.8
115.0
114.0
102.7
66.8
60.0
52.8
16.8
14.6
Me
CO2Et
N
O
Ph
f1 (ppm)

3ma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7.3402
7.3122
7.2915
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7.0840
7.0811
7.0640
7.0611
4.4342
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4.3986
4.3808
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3.9929
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3.9639
3.9589
3.9482
3.9434
3.9317
3.3066
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3.2727
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2.9550
2.9486
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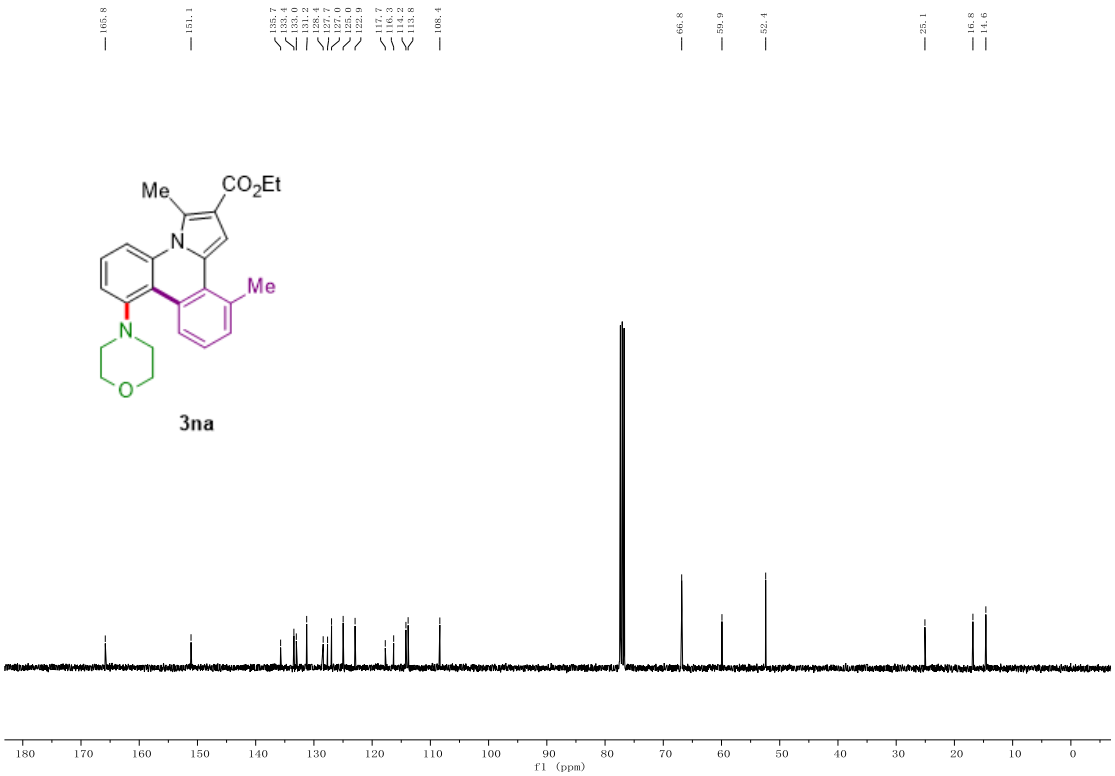
N
Me
N
O
f1 (ppm)

3na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131.2
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127.7
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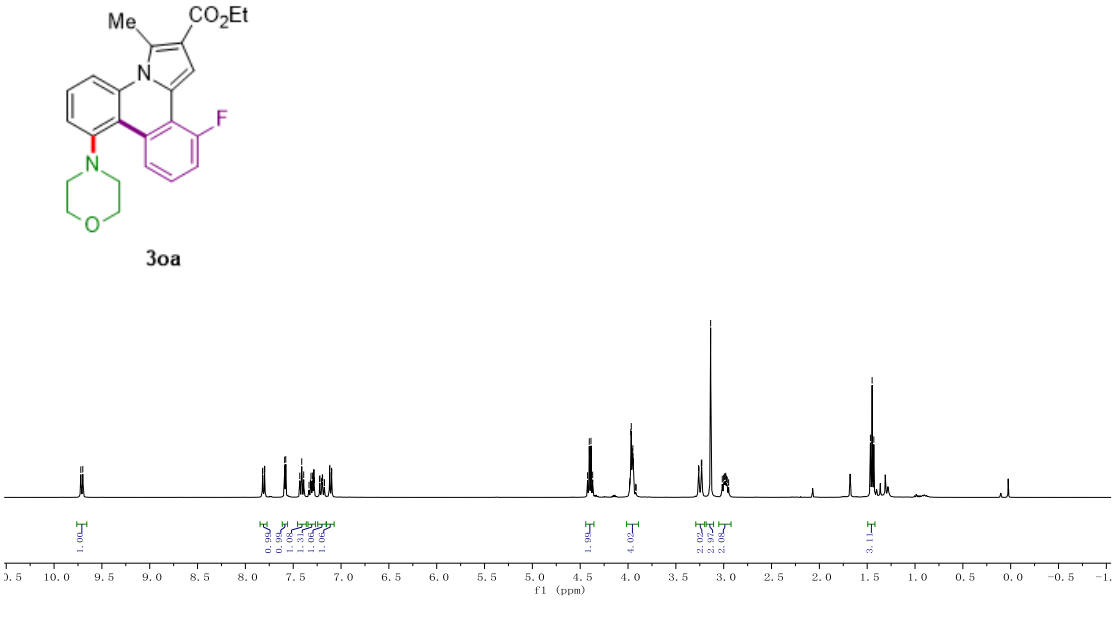
125.0
122.9
117.7
116.3
114.2
113.8
108.4
66.8
59.9
52.4
25.1
16.8
14.6
Me
CO2Et
N
Me
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3na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7.3143
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7.2211
7.2010
7.2012
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7.1758
7.1729
7.1199
7.1171
7.0997
7.0969
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3.9495
3.9435
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2.9630
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1.4455
1.4307
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CO2Et
N
F
N
O
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0.90
0.99
1.08
3.31
1.00
1.04
1.94
4.02
2.02
2.07
2.08
3.11
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

3oa


165.7
159.7
157.3
151.8
136.4
133.3
128.5
128.5
127.8
127.6
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123.7
123.7
121.1
121.0
117.1
117.1
116.6
116.6
115.4
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114.1
113.9
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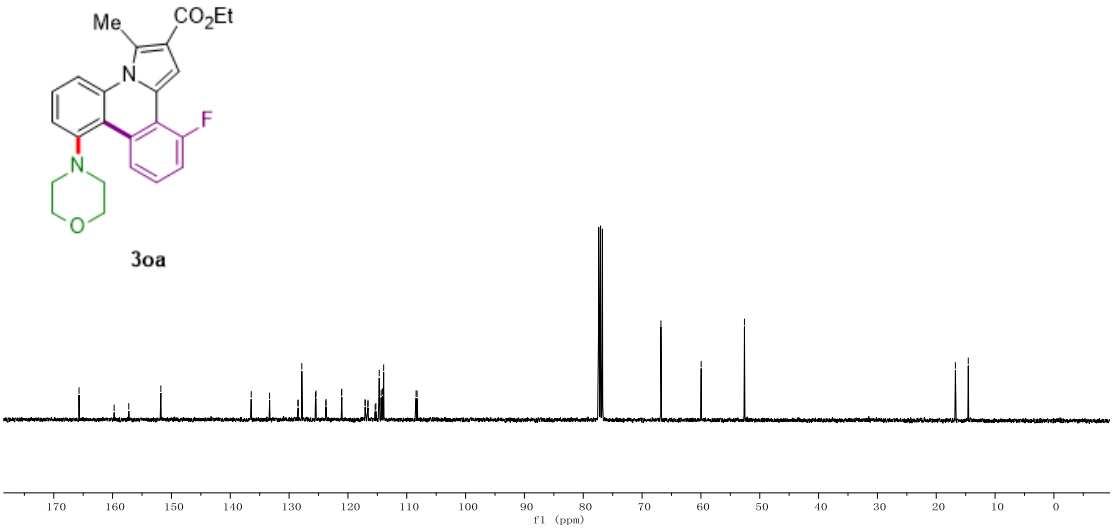
16.7
14.6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CO2Et
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F
N
O
3oa
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130
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100
90
80
70
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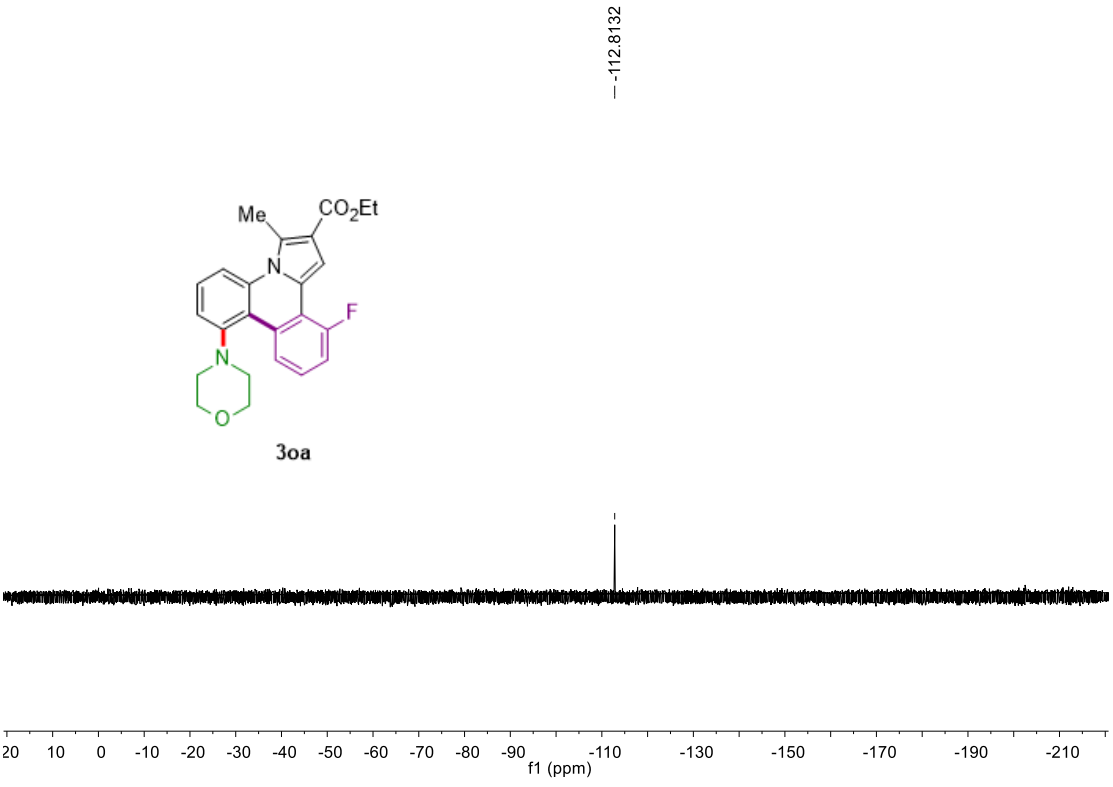
50
40
30
20
10
0
f1 (ppm)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-80
-90
-110
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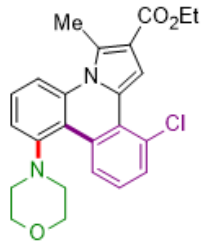
-150
-170
-190
-210
f1 (ppm)



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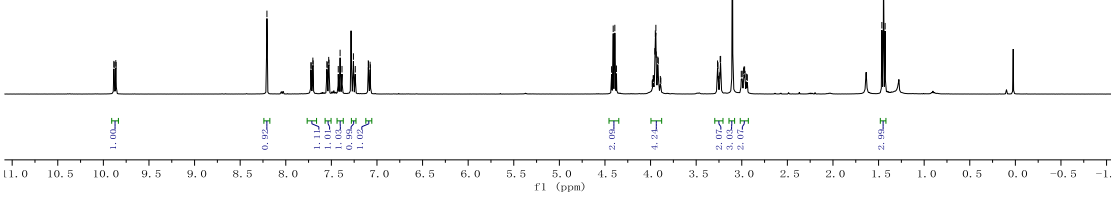

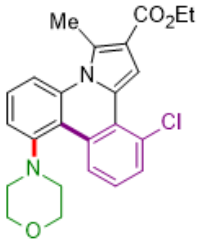

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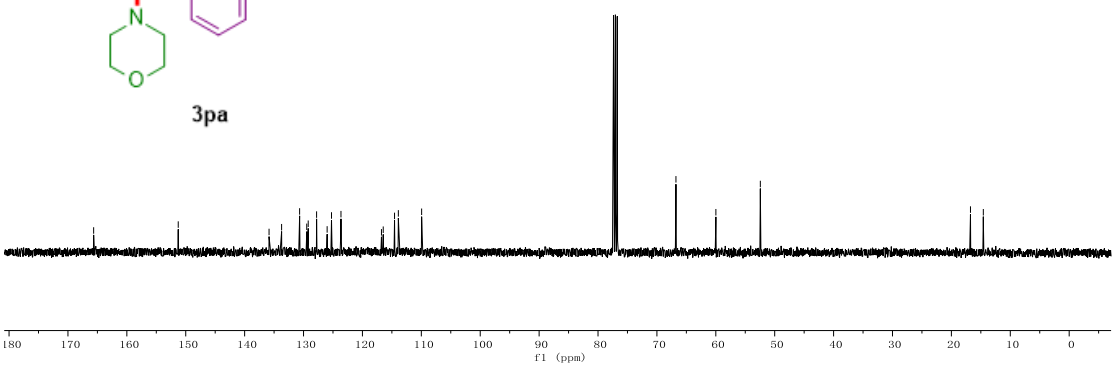

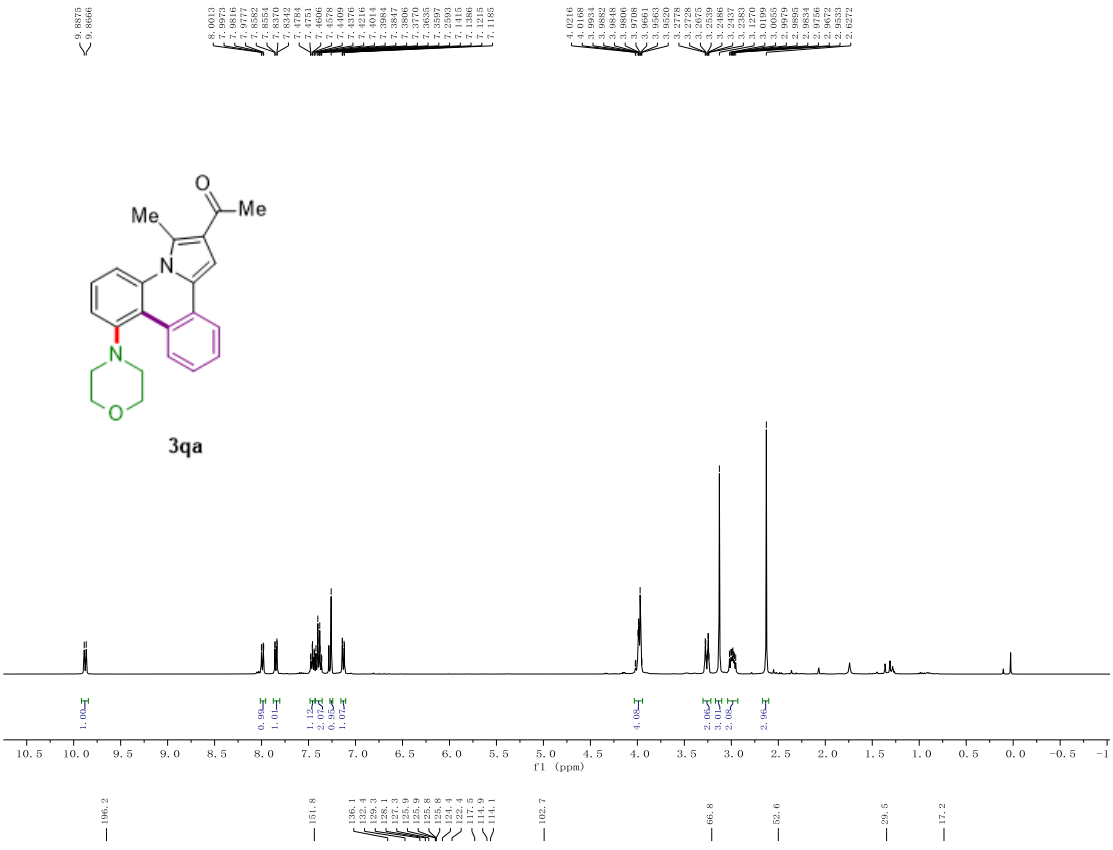
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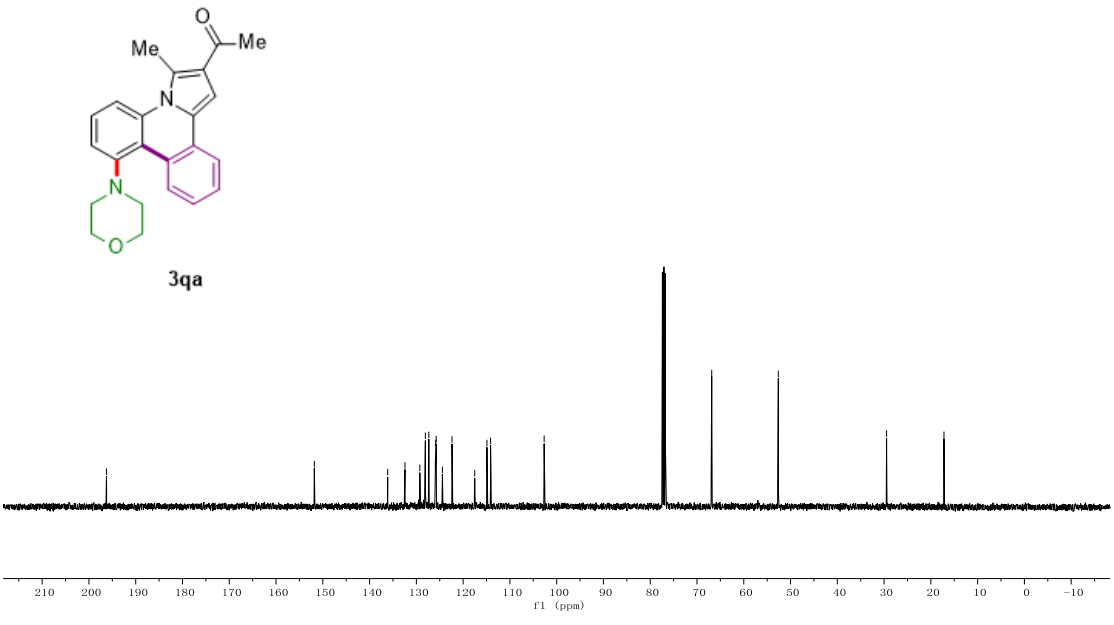
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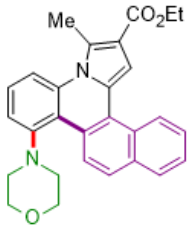

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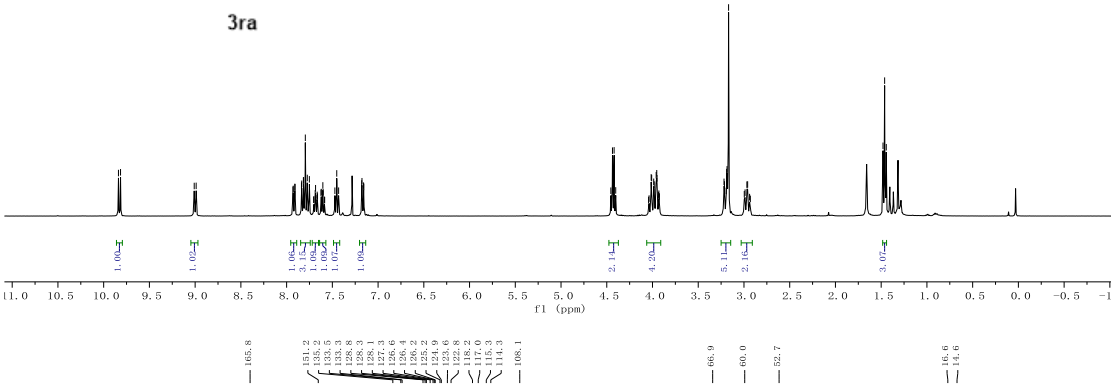

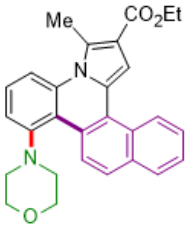

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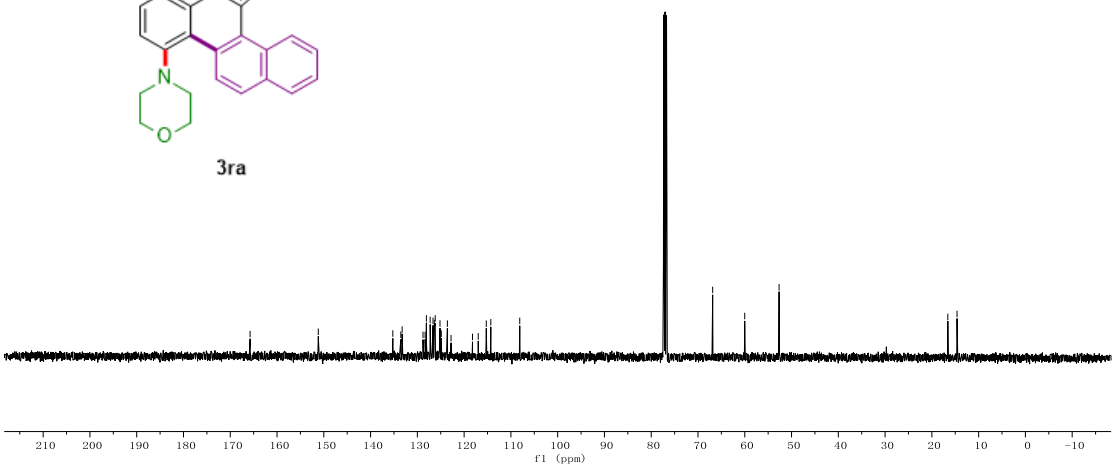

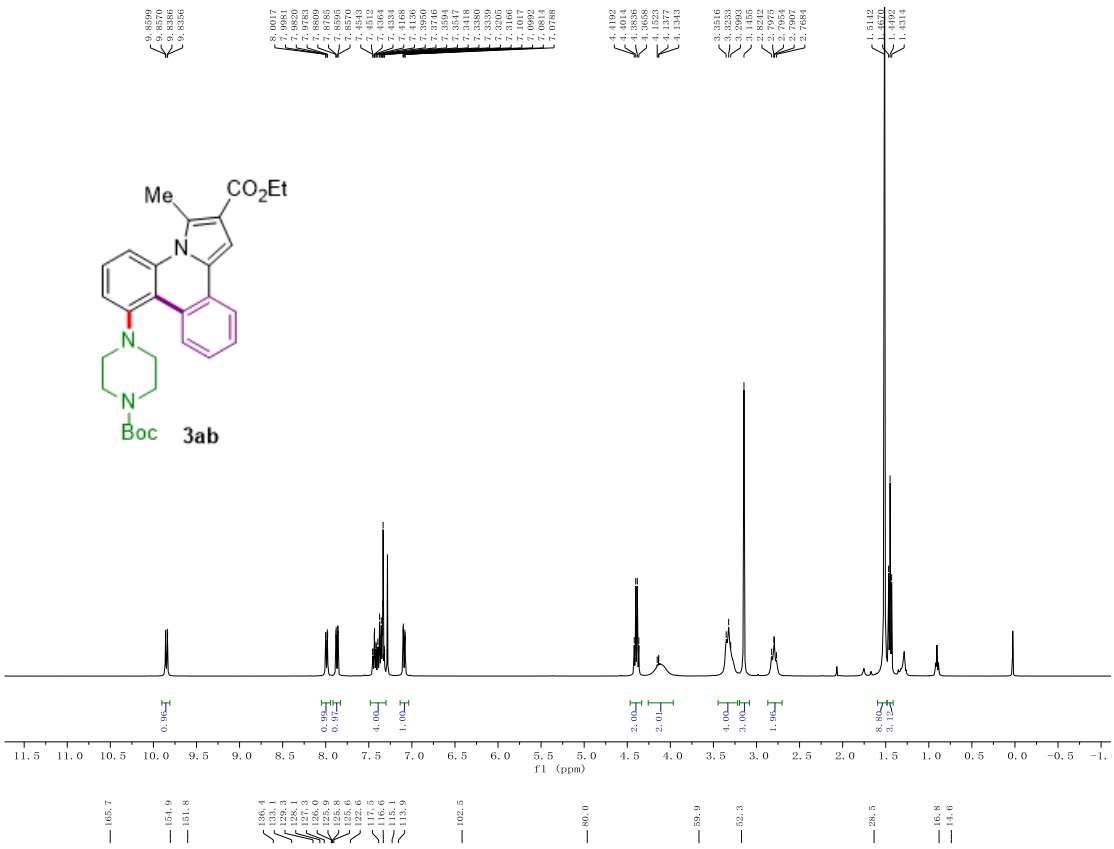
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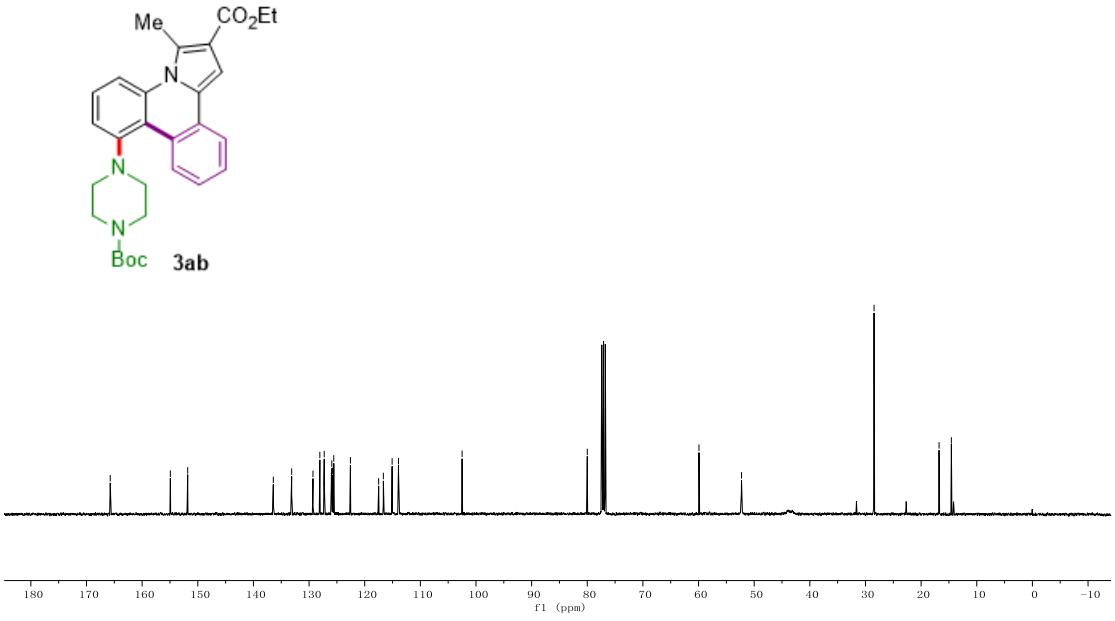
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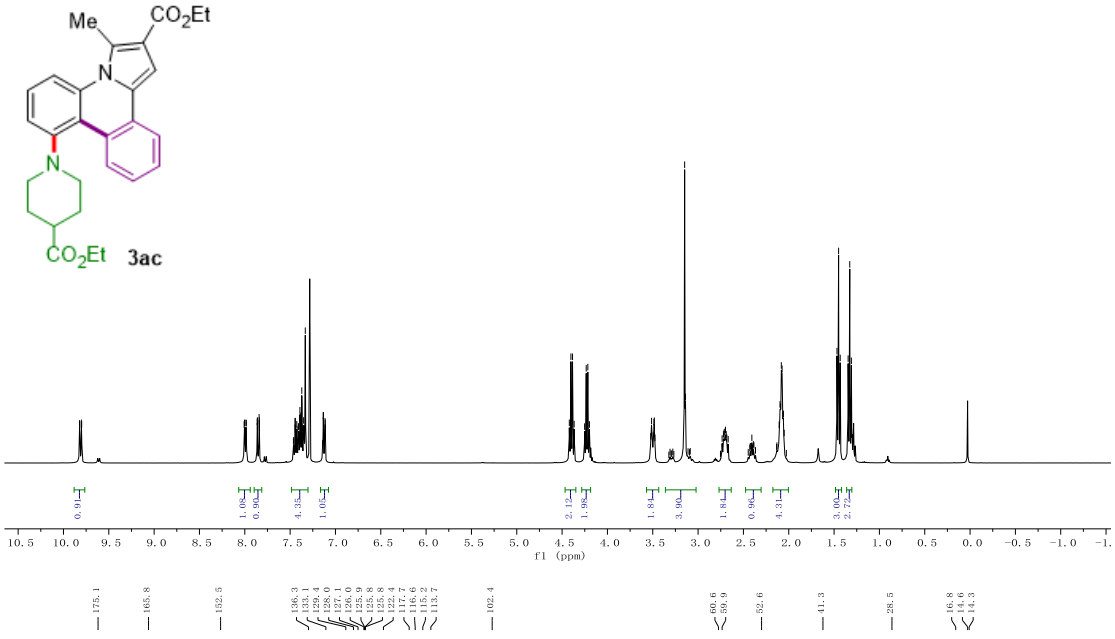
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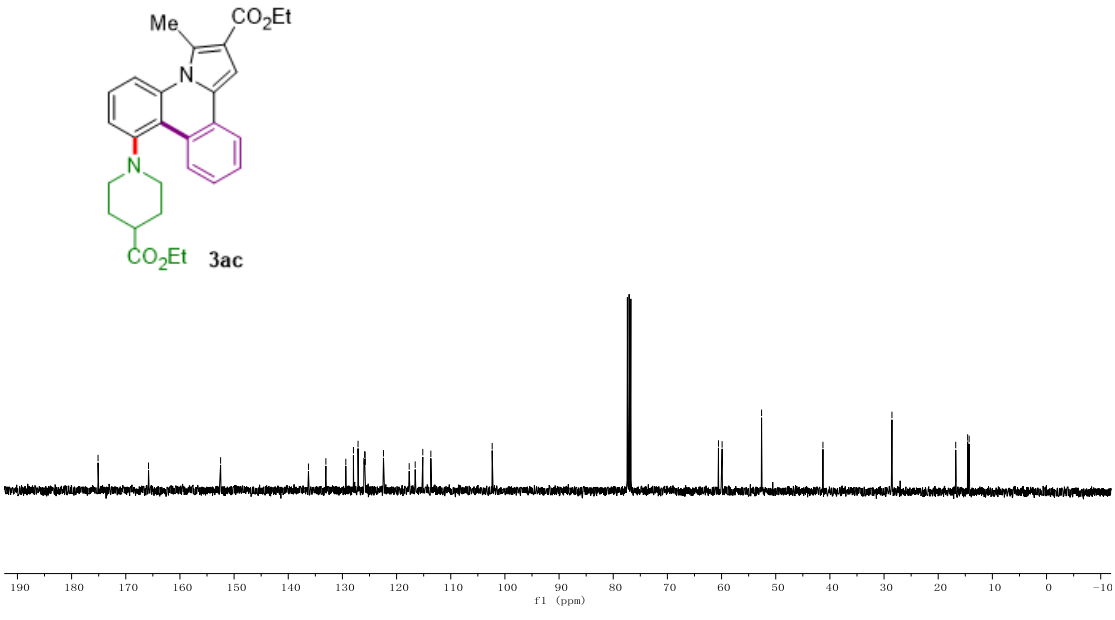
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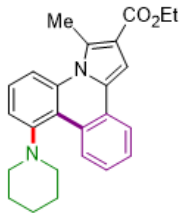

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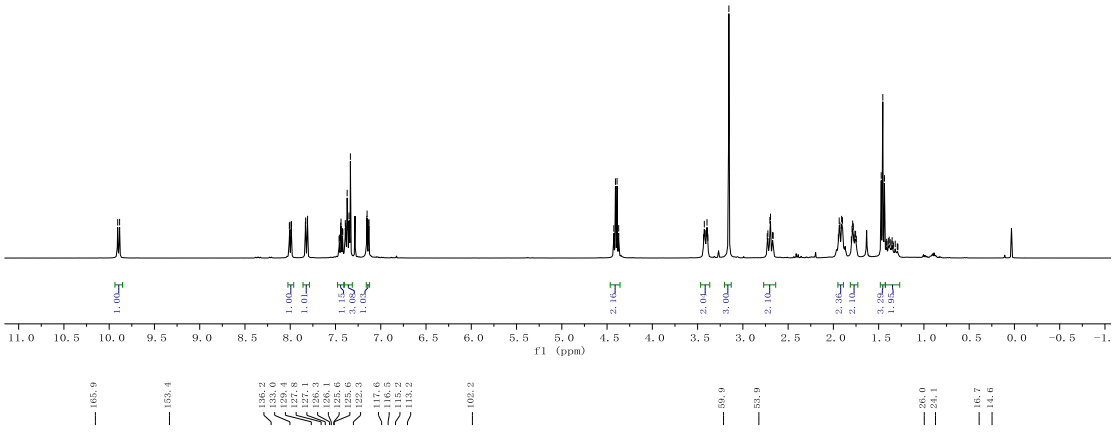

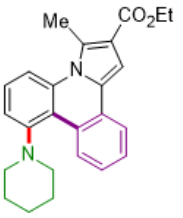

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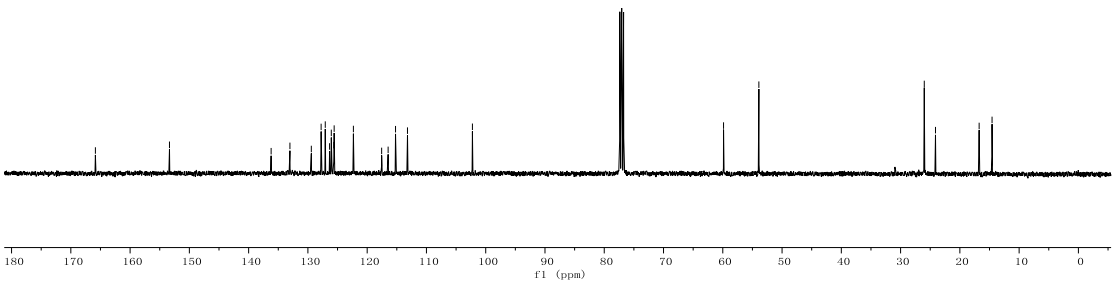

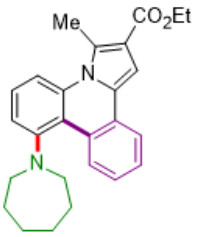

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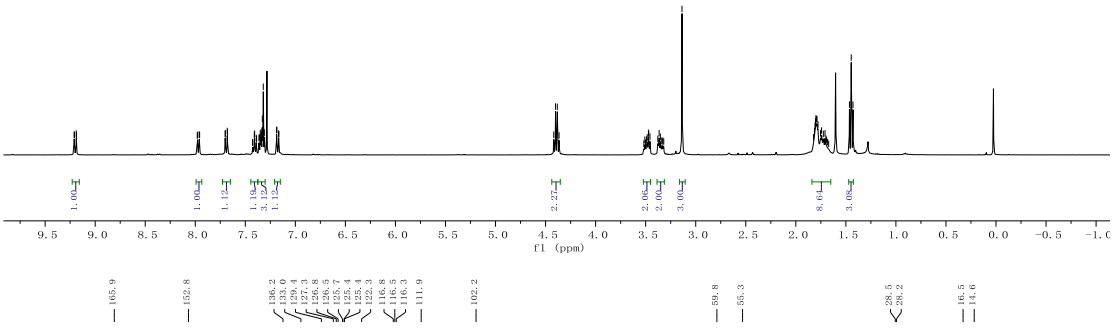

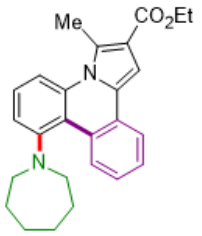

3ae

8. References

[1] Gluszok, S.; Frederick, R.; Foulon, C.; Klupsch, F.; Supuran, C. T.; Vullo, D.; Scozzafava, A.; Goossens, J. F.; Masereel, B.; Depreux, P.; Goossens, L., Design, Solid-Phase Synthesis, and Biological Evaluation of Novel 1,5-Diarylpyrrole-3-Carboxamides as Carbonic Anhydrase IX Inhibitors. *Bioorg. Med. Chem.* **2010**, *18*, 7392-401.

[2] Berman, A. M.; Johnson, J. S., Copper-Catalyzed Electrophilic Amination of Organozinc Nucleophiles: Documentation of O-Benzoyl Hydroxylamines as Broadly Useful $R_2N(+)$ and RHN(+) Synthons. *J. Org. Chem.* **2006**, *71*, 219-224.