Supporting Information

Pd-Catalyzed Domino Heck Cyclization/Cross-coupling of Indoles with *β*-Chlorovinyl Ketones: Synthesis of Antifungal Active Furan-bearing Indolo[2,1-α]isoquinolines

Yongqi Bai,[‡a] Xingrui Qi,[‡a] Hanjing Li,[a] Yihui Ban,[a] Rong Zhao,[a] Yian Wang,[a] Jingli Zhang,*[a] Taolei Sun[a,b] and Guanbin Gao*[a,b]

[a]Hubei Key Laboratory of Nanomedicine for Neurodegenerative Diseases, School of Chemistry, Chemical Engineering and Life Science, Wuhan University of Technology, Wuhan 430070, China

[b]State Key Laboratory of Advanced Technology for Materials Synthesis and Processing, Wuhan University of Technology, Wuhan 430070, China

[‡]Y. B. and X. Q. contributed equally.

Email: junniz@whut.edu.cn

Email: gbgao@whut.edu.cn

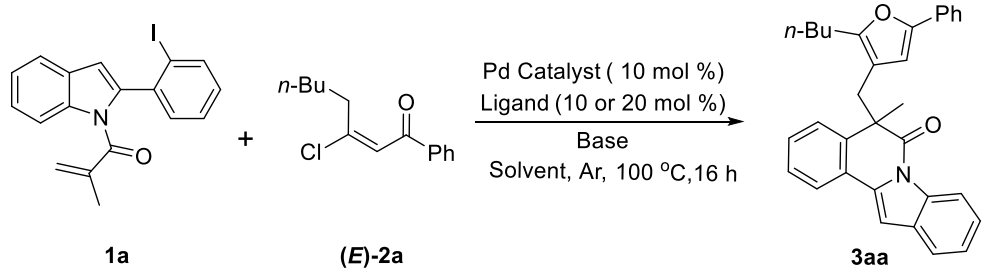
Table of contents

1) General considerations

Unless stated otherwise, all reactions were carried out under an inert atmosphere of dry argon, using oven-dried glassware (120 ºC), while work-up and isolation of products from catalytic reactions were performed open to air on a benchtop using general techniques. Reaction monitoring was performed using thin-layer chromatography (TLC) on Merck KGaA TLC Silica Gel 60 F_{254} plates. The developed plates were visualized with UV light (254 nm) or $KMnO_4$. Solvent evaporation was carried out by a rotary evaporator at the appropriate temperature and pressure. Toluene was distilled over sodium (1% w:v) and benzophenone (1% w:v); 1,4-dioxane was purchased from Energy Chemical and stored with molecular sieves; 1,2-DCE was purchased from Energy Chemical and stored with molecular sieves; THF was purchased from Energy Chemical and stored with molecular sieves; acetonitrile was purchased from Energy Chemical and stored with molecular sieves. Silica gel flash chromatography was performed on 200-300 mesh silica gel. NMR characterization data was collected at 298 K on a Bruker AVANCE III 500 operating at 500 MHz for ^{1}H-NMR, 126 MHz for ^{13}C-NMR, and 470 MHz for ^{19}F-NMR. ^{1}H-NMR chemical shifts were recorded in parts per million (ppm, δ) relative to TMS (δ = 0.00 ppm) with the solvent resonance as the internal standard ($CDCl_3$: δ = 7.26 ppm). Data for ^{1}H-NMR is reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. ^{13}C-NMR chemical shifts were reported in ppm with the solvent as the internal standard ($CDCl_3$: δ = 77.0 ppm). ^{19}F-NMR chemical shifts were reported in ppm with the PhF or $PhCF_3$ as the internal standard (PhF: δ = -112.96 ppm; $PhCF_3$: δ = -62.61 ppm).[1] High-resolution mass spectra were obtained from the following spectrometers: AB Sciex Triple TOF 5600+. The X-ray diffraction data were collected on Bruker SMART APEX CCD diffractometer. Melting points were obtained on a SGW® X-4 Melting Point Apparatus and uncorrected.

2) Optimization of Condition

Table S1. Optimization of the reaction conditions[a]



1a **(*E*)-2a** **3aa**

Entry	Pd Catalyst	Ligand	Base	Solvent	Yield (%)[b]
1	$Pd_2(dba)_3$	PPh_3	Cs_2CO_3	MeCN	80
2	$Pd_2(dba)_3$	PPh_3	K_2CO_3	MeCN	89
3	$Pd_2(dba)_3$	PPh_3	K_3PO_4	MeCN	82
4	$Pd_2(dba)_3$	PPh_3	$KHCO_3$	MeCN	85
5	$Pd_2(dba)_3$	PPh_3	Et_3N	MeCN	76
6	$PdCl_2$	PPh_3	K_2CO_3	MeCN	92
7	$Pd(OAc)_2$	PPh_3	K_2CO_3	MeCN	90
8	$PdCl_2$	P(*o*-Tol)$_3$	K_2CO_3	MeCN	90
9	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	MeCN	96
10	$PdCl_2$	Xphos	K_2CO_3	MeCN	71
11	$PdCl_2$	CyJohnphos	K_2CO_3	MeCN	60
12	$PdCl_2$	dppe	K_2CO_3	MeCN	71
13	$PdCl_2$	dppf	K_2CO_3	MeCN	81
14	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	Toluene	75
15	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	1,4-dioxane	73
16	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	1,2-DCE	55
17	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	THF	55
18[c]	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	MeCN	83
19[d]	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	MeCN	89
20[e]	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	MeCN	94
21[f]	$PdCl_2$	P(4-CF_3Ph)$_3$	K_2CO_3	MeCN	75

[a] Reaction conditions: **1a** (0.2 mmol), (*E*)-**2a** (2.0 equiv.), Pd catalyst (10 mol %), monodentate ligand (20 mol %) or bidentate ligand (10 mol %), base (2.5 equiv.) and solvent (2.0 mL) at 100 °C under Ar atmosphere for 16 h.

[b] Isolated yield.

[c] K_2CO_3 (2.0 equiv.) was used.

[d] Reaction run at 80 °C.

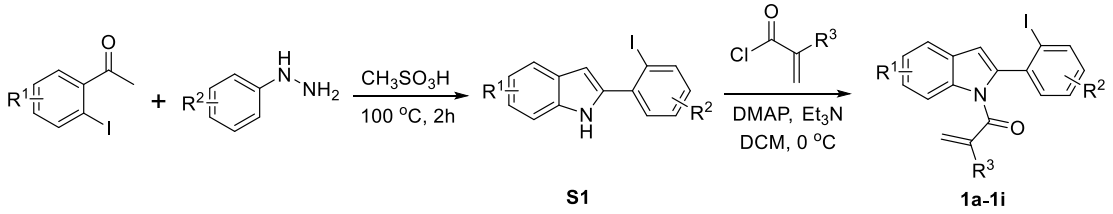
[e] Reaction run at 120 °C.

[f] (*Z*)-**2a** instead of (*E*)-**2a**.

3) General procedures

All standard reagents were purchased from Sigma Aldrich, TCI, Aladdin, Energy Chemical, and were used without further purification. Alkene-tethered indoles **1** and *β*-chlorovinyl ketones **2** were prepared according to literature procedures.

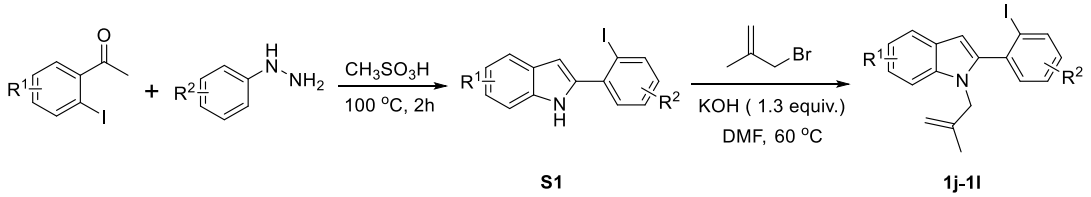
General Procedure 1: Synthesis of alkene-tethered indoles **1a-1i**[2,3,4]



Step I: A mixture of 2-iodoacetophenone (10 mmol), phenylhydrazine (10.5 mmol, 1.05 equiv.) was added to a round bottom flask and stirred at 100 °C for 1 h. After cooling the reaction to room temperature, methanesulfonic acid (12.5 equiv.) was added and the mixture was stirred at 100 °C for 1h. The reaction was cooled down to room temperature, then quenched with ice water and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered and concentrated in *vacuo*. The crude mixture was purified by silica gel flash column chromatography (0→5% EtOAc/petroleum ether) to give the corresponding substituted indole **S1**.

Step II: A solution of indole **S1** (7 mmol) and DMAP (0.2 equiv.) in DCM (0.5 M) was added Et_3N (2.0 equiv.) and acryloyl chloride (1.2 equiv.) at 0 °C. The reaction was warmed up to room temperature and stirred overnight. The mixture was filtered through a pad of silica, which was washed with EtOAc. The filtrate was concentrated in *vacuo* to give a residue, which was purified by silica gel flash column chromatography (0→2.5% EtOAc/petroleum ether) to afford the indoles **1a-1i**.

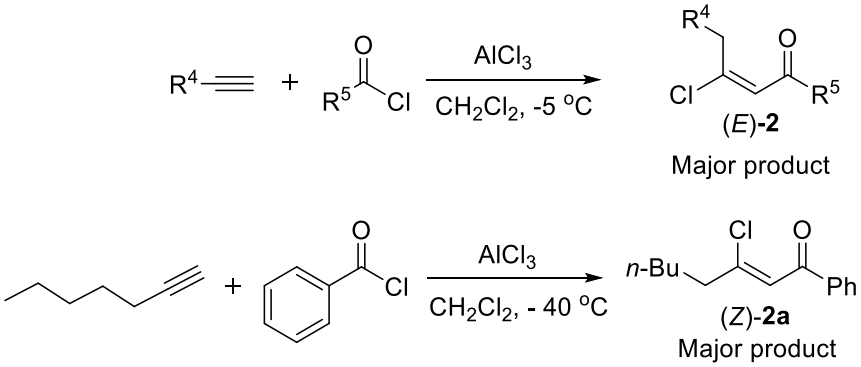
General Procedure 2: Synthesis of alkene-tethered indoles **1j-1l**[2,3]



Step I: A mixture of 2-iodoacetophenone (10 mmol), phenylhydrazine (10.5 mmol, 1.05 equiv.) was added to a round bottom flask and stirred at 100 °C for 1 h. After cooling the reaction to room temperature, methanesulfonic acid (12.5 equiv.) was added and the mixture was stirred at 100 °C for 1h. The reaction was cooled down to room temperature, then quenched with ice water and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered and concentrated in *vacuo*. The crude mixture was purified by silica gel flash column chromatography (0→5% EtOAc/petroleum ether) to give the corresponding substituted indole **S1**.

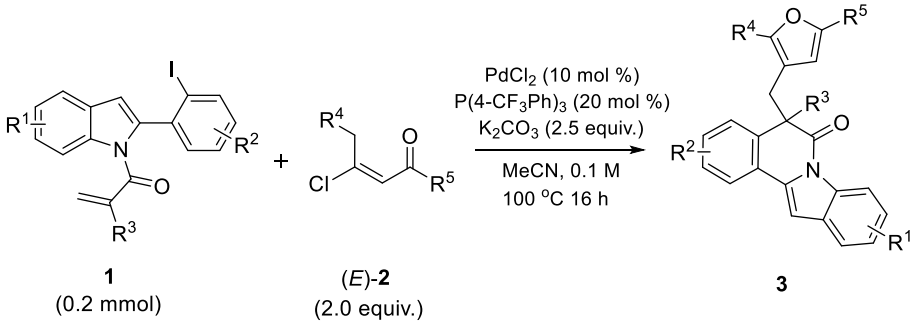
Step II: A solution of **S1** (6 mmol) in DMF (12 mL) and powdered KOH (1.3 equiv.) was stirred at 60 °C for 10 min, cooled to room temperature, and treated with 3-bromo-2-methylprop-1-ene (1.5 equiv.). The reaction mixture was stirred at 60 °C for 18 h, quenched with ice water and extracted with ethyl ether (3 x 15 mL). The combined organic layers were washed with H_2O, dried with Mg_2SO_4, concentrated in *vacuo* and purified by silica gel flash column chromatography (petroleum ether /EtOAc = 50:1) to afford the indoles **1j-1l**.

General Procedure 3: Synthesis of *β*-chlorovinyl ketones **2a-2t**[5,6,7]
The desired *β*-chlorovinyl ketone was prepared following literature procedure.



To a stirred suspension of aluminum chloride (1.47 g, 11 mmol, 1.1 equiv.) in dry dichloromethane (10 mL) at -5 °C (*E*-selective) or -40 °C (*Z*-selective) were added alkynes (10 mmol, 1.0 equiv.) and acyl chloride (10 mmol, 1.0 equiv.) dropwise at the same time. Stirring of the resulting solution was continued at the same temperature until the reaction was completed by TLC. The reaction was then quenched with H_2O, extracted with dichloromethane, and washed with brine. After drying over $MgSO_4$, the solution was concentrated under reduced pressure, and the crude product was purified by silica gel flash column chromatography (petroleum ether /DCM = 19:1) to afford *β*-chlorovinyl ketones **2a-2t**.

General Procedure 4: Synthesis of furan-containing indolo[2,1-*α*]isoquinolines **3**



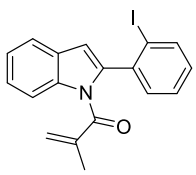
To a flame dried, 3-dram vial under argon atmosphere was added alkene-tethered indoles **1** (0.20 mmol, 1.0 equiv.), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol %), P(4-CF_3Ph)$_3$ (18.7 mg, 0.04 mmol, 20 mol %) and K_2CO_3 (69.1 mg, 0.5 mmol, 2.5 equiv.), and purged with argon for 5 minutes. Anhydrous and degassed MeCN (1.5 mL) were added and the mixture was stirred at room temperature for 5 minutes. (*E*)-*β*-chlorovinyl ketone

2 (0.4 mmol, 2.0 equiv.) was dissolved in anhydrous MeCN (0.5 mL) and transferred to the vial via syringe, and the mixture was stirred under argon for 5 minutes. A Teflon lined screw cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 ℃ for 16 hours. The reaction mixture was then cooled down to room temperature and was filtered through a plug of silica gel using EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash column chromatography using the indicated mobile phase.

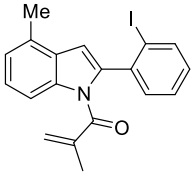
4) Synthesis of alkene-tethered indoles

All alkene-tethered indoles were synthesized according to literature procedures.

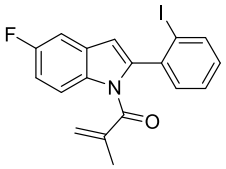
Suitable alkene-tethered indoles



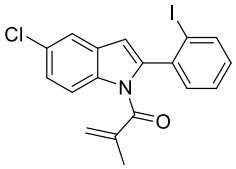
1a



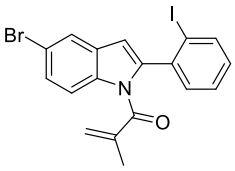
1b



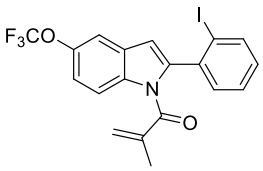
1c



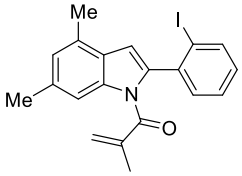
1d



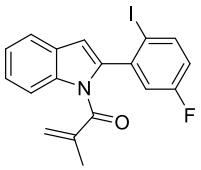
1e



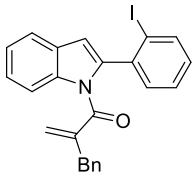
1f



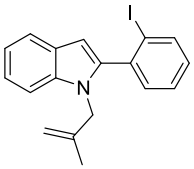
1g



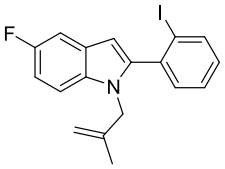
1h



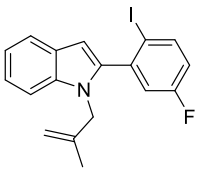
1i



1j

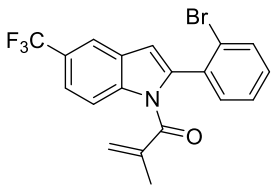


1k

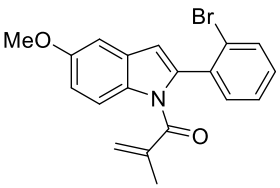


1l

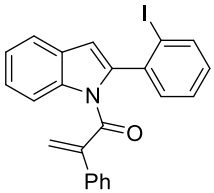
Unsuitable alkene-tethered indoles



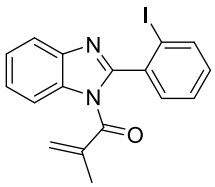
1m



1n



1o



1p

Alkene-tethered indoles **1m**,[3] **1n**,[3] **1o**,[8] and **1p**[8] were synthesized according to literature procedures. Indoles **1m**, **1n**, and **1o** afforded the desired products **3ma-3oa** in trace yields, respectively. Indole **1p** failed to generate bis-heterocyclic product **3pa**.

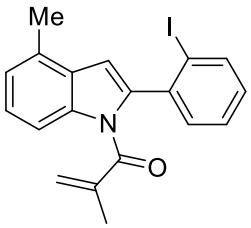
Known alkene-tethered indoles

1a, **1c**, **1d**, **1e**, **1g, 1h, 1j, 1k, 1m, 1n**, see: X. Yang, H. Lu, X. Zhu, L. Zhou, G. Deng, Y. Yang, and Y. Liang, *Org. Lett*. **2019**, *21*, 7284-7288.

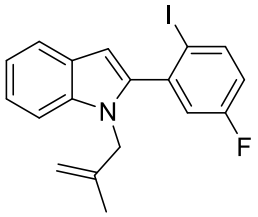
1f, **1i**, see: J.-S. Wang, J. Zhang, S. Wang, J. Ying, C.-Y. Li, and X.-F. Wu, *J. Catal*.

2022, *414*, 313-318.
1o, 1p, see: H. Qi, D. Chi, and S. Chen, *Org. Lett*. **2022**, *24*, 2910-2914.

Unknown alkene-tethered indoles



1-(2-(2-Iodophenyl)-4-methyl-1*H*-indol-1-yl)-2-methylprop-2-en-1-one (1b)
Synthesized according to **GP1** on a 3.0 mmol scale. Isolated by a flash column chromatography. **1b** was obtained as a yellow oil (782 mg, 65% yield).
Two rotamers were observed in a 2:1 ratio. The major rotamer is reported below.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.20 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 6.5 Hz, 1H), 6.65 (s, 1H), 5.30 (s, 1H), 5.29 (s, 1H), 2.49 (s, 3H), 1.81 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 141.0, 139.7, 137.4, 134.8, 131.5, 129.3, 127.8, 124.9, 124.8, 123.7, 120.5, 114.9, 112.3, 111.2, 109.7, 99.7, 22.0, 18.6.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{16}INONa$ 424.0169; found 424.0150.

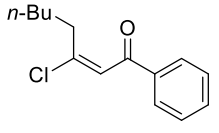


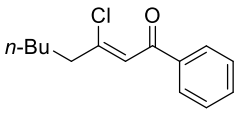
2-(5-Fluoro-2-iodophenyl)-1-(2-methylallyl)-1*H*-indole (1l)
Synthesized according to **GP2** on a 3.0 mmol scale. Isolated by a flash column chromatography. **1l** was obtained as a pale yellow oil (680 mg, 58% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 9.0, 5.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.17 – 7.10 (m, 2H), 6.89 (td, *J* = 8.5, 3.0 Hz, 1H), 6.52 (s, 1H), 4.77 (s, 1H), 4.64 – 4.30 (m, 2H), 4.41 (s, 1H), 1.53 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (d, *J* = 249.6 Hz), 140.9 (d, *J* = 1.5 Hz), 140.8, 140.4 (d, *J* = 7.9 Hz), 140.1 (d, *J* = 8.2 Hz), 136.9, 127.7, 122.1, 121.0, 120.1, 119.3 (d, *J* = 22.2 Hz), 117.5 (d, *J* = 21.8 Hz), 112.1, 110.5, 103.1, 94.4 (d, *J* = 3.4 Hz), 50.1, 20.0.
^{19}F NMR (470 MHz, $CDCl_3$): δ -114.05 – -114.10 (m, 1F).
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{16}FIN$ 392.0306; found 392.0262.

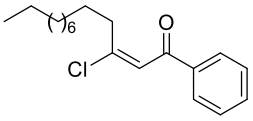
5) Synthesis of *β*-chlorovinyl ketones

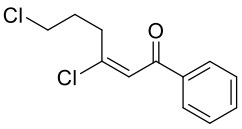
All *β-chlorovinyl ketones* were synthesized according to literature procedures.

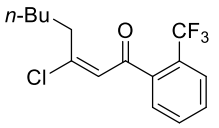
Suitable *β*-chlorovinyl ketones

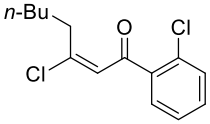

(*E*)-**2a**

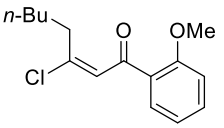

(*Z*)-**2a**

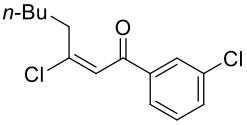

(*E*)-**2b**

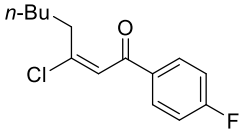

(*E*)-**2c**

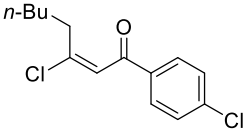

(*E*)-**2d**

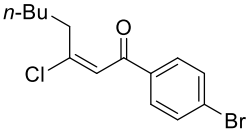

(*E*)-**2e**

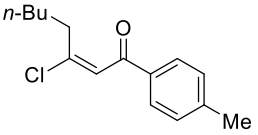

(*E*)-**2f**

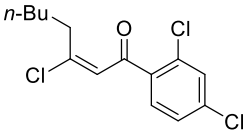

(*E*)-**2g**

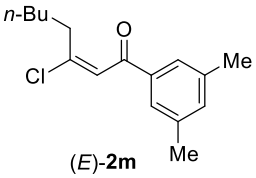

(*E*)-**2h**

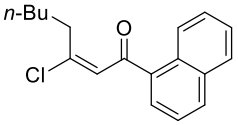

(*E*)-**2i**

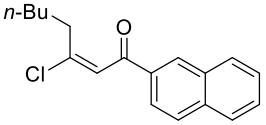

(*E*)-**2j**

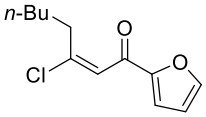

(*E*)-**2k**

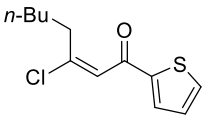

(*E*)-**2l**

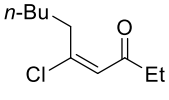

(*E*)-**2m**

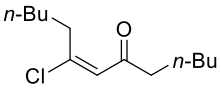

(*E*)-**2n**

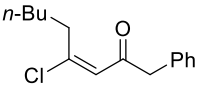

(*E*)-**2o**


(*E*)-**2p**

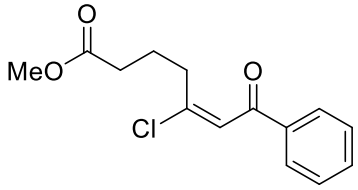

(*E*)-**2q**

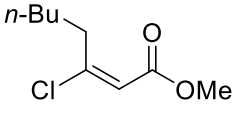

(*E*)-**2r**


(*E*)-**2s**


(*E*)-**2t**

Unsuitable *β*-chlorovinyl ketones


(*E*)-**2u**

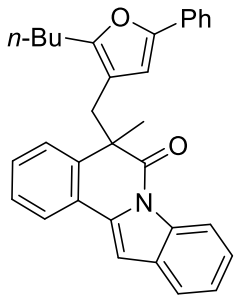

(*E*)-**2v**

β-chlorovinyl ketones (*E*)-**2u**[7] **and** (*E*)-**2v**[9] were synthesized according to literature procedures. *β*-chlorovinyl ketone (*E*)-**2u** yielded only trace product **3au** and no desired product **3av** was obtained upon employing (*E*)-**2v** as a substrate.

Known *β*-chlorovinyl ketones

(*E*)-**2a**, (*Z*)-**2a**, (*E*)-**2b**, (*E*)-**2c**, (*E*)-**2d**, (*E*)-**2g**, (*E*)-**2h**, (*E*)-**2i**, (*E*)-**2k**, (*E*)-**2m**, (*E*)-**2n**, (*E*)-**2o**, (*E*)-**2p**, (*E*)-**2q**, (*E*)-**2r**, (*E*)-**2s**, (*E*)-**2t**, see: F. Li, Y. Yuan, D. Lyu, Y. Yi, J. Zhang, T. Sun, G. Gao, *J. Org. Chem.*, **2024**, *89*, 7552-7560.
(*E*)-**2e**, (*E*)-**2f**, (*E*)-**2j**, see: S. Borra, H. Y. Kim, K. Oh, *Org. Lett*., **2023**, *25*, 288-292.
(*E*)-**2l**, (*E*)-**2u**, see: Y. Zhang, J. Zhang, Y. Yuan, L. Liu, B. Chen, T. Sun, *Eur. J. Org. Chem*., **2020**, 1976-1986.
(*E*)-**2v**, see: P. Yu, A. Bismuto, and B. Morandi, *Angew. Chem. Int. Ed*. **2020**, *59*, 2904-2910.

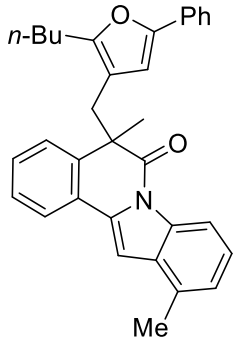
6) Characterization data of products 3



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3aa)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 88.5 mg, 96% yield, yellow solid, mp 96 – 98 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.5 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.37 (td, *J* = 7.5, 1.3 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.11 – 7.05 (m, 3H), 6.78 (s, 1H), 5.63 (s, 1H), 3.35 (d, *J* = 14.0 Hz, 1H), 2.89 (d, *J* = 14.0 Hz, 1H), 2.14 (t, *J* = 7.3 Hz, 2H), 1.92 (s, 3H), 1.38 – 1.20 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.4, 150.7, 137.8, 135.4, 135.3, 130.9, 130.7, 128.5, 128.3, 127.3, 126.7, 126.4, 125.7, 125.1, 124.4, 123.6, 123.2, 120.5, 116.5, 115.1, 106.9, 102.8, 49.7, 40.6, 30.3, 25.8, 25.2, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{29}NO_2Na$ 482.2091; found 482.2094.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-5,11-dimethylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ba)

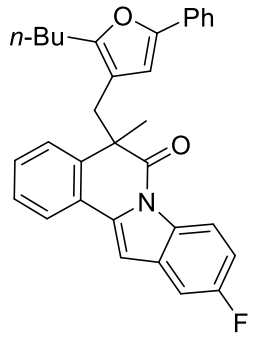
Prepared according to General Procedure **4** using starting material **1b** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 77.7 mg, 82% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.5 Hz, 1H), 7.75 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.42 – 7.32 (m, 3H), 7.16 (t, *J* = 7.5 Hz, 2H), 7.11 – 7.07 (m, 3H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.81 (s, 1H), 5.58 (s, 1H), 3.32 (d, *J* = 13.5 Hz, 1H),

2.87 (d, *J* = 14.0 Hz, 1H), 2.40 (s, 3H), 2.10 (t, *J* = 7.3 Hz, 2H), 1.92 (s, 3H), 1.36 – 1.19 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.3, 150.7, 137.6, 135.1, 134.8, 130.9, 130.0, 128.4, 128.2, 127.3, 126.6, 126.4, 125.9, 125.3, 124.9, 123.6, 123.1, 120.1, 116.8, 115.1, 106.8, 101.4, 49.7, 40.6, 30.3, 25.7, 25.1, 22.5, 18.4, 13.8.

HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{33}H_{32}NO_2$ 474.2428; found 474.2434.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-10-fluoro-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ca)

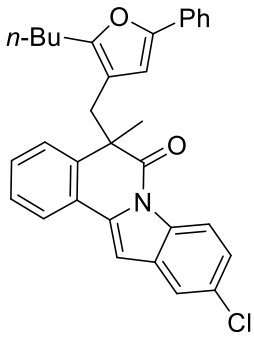
Prepared according to General Procedure **4** using starting material **1c** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 82.9 mg, 87% yield, yellow solid, mp 138 – 139 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.8, 4.8 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 2H), 7.11 – 7.03 (m, 5H), 6.72 (s, 1H), 5.56 (s, 1H), 3.31 (d, *J* = 14.0 Hz, 1H), 2.87 (d, *J* = 14.0 Hz, 1H), 2.07 (t, *J* = 7.0 Hz, 2H), 1.91 (s, 3H), 1.35 – 1.16 (m, 4H), 0.83 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 160.2 (d, *J* = 241.2 Hz), 153.3, 150.7, 138.0, 137.0, 131.8 (d, *J* = 10.3 Hz), 131.6, 130.8, 128.9, 128.3, 127.4, 126.7, 126.5, 125.3, 123.7, 123.1, 117.4 (d, *J* = 9.2 Hz), 115.0, 112.5 (d, *J* = 24.9 Hz), 106.7, 106.1 (d, *J* = 24.3 Hz), 102.3 (d, *J* = 3.9 Hz), 49.6, 40.7, 30.2, 25.7, 25.1, 22.4, 13.7.

^{19}F NMR (470 MHz, $CDCl_3$): δ -118.34 – -118.39 (m, 1F).

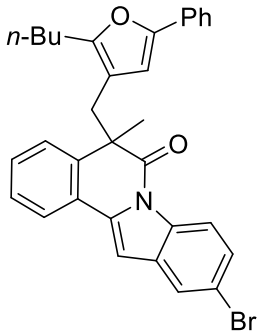
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{29}FNO_2$ 478.2177; found 478.2196.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-10-chloro-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3da)

Prepared according to General Procedure **4** using starting material **1d** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 69.1 mg, 70% yield, yellow solid, 126 – 128 ºC.

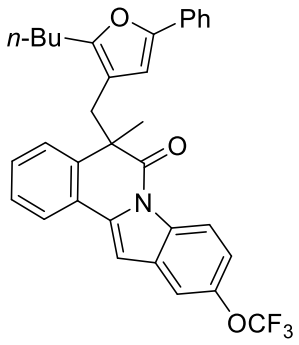
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.5 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.43 (td, *J* = 7.8, 1.5 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.18 (t, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.0 Hz, 2H), 6.67 (s, 1H), 5.55 (s, 1H), 3.29 (d, *J* = 13.5 Hz, 1H), 2.85 (d, *J* = 13.5 Hz, 1H), 2.05 (t, *J* = 7.3 Hz, 2H), 1.91 (s, 3H), 1.34 – 1.16 (m, 4H), 0.83 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.3, 150.8, 137.9, 136.8, 133.6, 132.0, 130.7, 130.0, 129.0, 128.3, 127.4, 126.6, 126.5, 125.3, 125.1, 123.8, 123.1, 120.1, 117.3, 114.9, 106.6, 101.8, 49.8, 40.9, 30.2, 25.5, 25.1, 22.4, 13.7.
HRMS (ESI) *m/z*: $[M+H]^+$calcd for $C_{32}H_{29}ClNO_2$ 494.1881; found 494.1878.



10-Bromo-5-((2-butyl-5-phenylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ea)

Prepared according to General Procedure **4** using starting material **1e** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 71.6 mg, 67% yield, yellow solid, mp 121 – 123 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.5 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 6.5 Hz, 2H), 7.47 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.66 (s, 1H), 5.54 (s,1H), 3.29 (d, *J* = 14.0 Hz, 1H), 2.85 (d, *J* = 14.0 Hz, 1H), 2.03 (t, *J* = 7.3 Hz, 2H), 1.91 (s, 3H), 1.34 – 1.16 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.3, 150.8, 137.9, 136.6, 133.9, 132.5, 130.7, 129.0, 128.3, 127.8, 127.5, 126.6, 126.5, 125.3, 123.8, 123.1, 117.75, 117.72, 114.9, 106.6, 101.7, 49.8, 40.9, 30.2, 25.5, 25.0, 22.4, 13.7.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{29}BrNO_2$ 538.1376; found 538.1375.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-5-methyl-10-(trifluoromethoxy)indolo[2,1-*a*]isoquinolin-6(5*H*)-one (3fa)

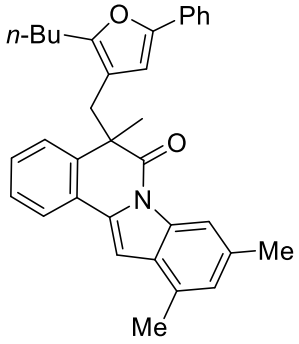
Prepared according to General Procedure **4** using starting material **1f** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 84.6 mg, 78% yield, yellow solid, mp 132 – 134 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 9.0 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* =7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.0 Hz, 2H), 6.74 (s, 1H), 5.58 (s, 1H), 3.32 (d, *J* = 14.0 Hz, 1H), 2.88 (d, *J* = 14.0 Hz, 1H), 2.08 (t, *J* = 7.3 Hz, 2H), 1.92 (s, 3H), 1.35 – 1.15 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.3, 150.8, 146.1, 138.0, 137.2, 133.4, 131.6, 130.7, 129.1, 128.3, 127.5, 126.7, 126.6, 125.2, 123.8, 123.1, 120.7 (q, *J* = 257.0 Hz), 118.1, 117.3, 114.9, 112.7, 106.6, 102.2, 49.7, 40.8, 30.2, 25.6, 25.1, 22.4, 13.7.

^{19}F NMR (470 MHz, $CDCl_3$) δ -57.80 (s, 3F).

HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{33}H_{28}F_3NO_3Na$ 566.1913; found 566.1926.

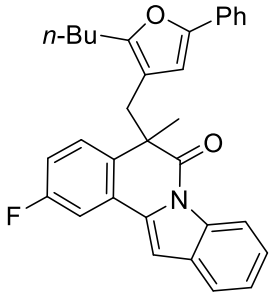


5-((2-Butyl-5-phenylfuran-3-yl)methyl)-5,9,11-trimethylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ga)

Prepared according to General Procedure **4** using starting material **1g** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 74.1 mg, 76% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.72 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.16 (t, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 2H), 6.92 (s, 1H), 6.77 (s, 1H), 5.58 (s, 1H), 3.30 (d, *J* = 14.0 Hz, 1H), 2.86 (d, *J* = 13.5 Hz, 1H), 2.51 (s, 3H), 2.36 (s, 3H), 2.13 (t, *J* = 7.5 Hz, 2H), 1.89 (s, 3H), 1.36 – 1.18 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H).

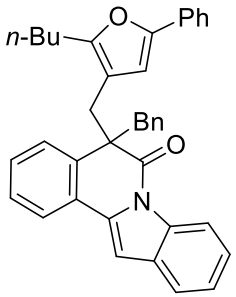
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.3, 150.7, 137.4, 135.5, 135.4, 134.3, 130.9, 129.5, 128.2, 128.1, 128.0, 127.2, 126.6, 126.3, 126.0, 123.4, 123.2, 115.2, 114.3, 107.0, 101.4, 49.7, 40.5, 30.3, 25.8, 25.2, 22.4, 21.9, 18.2, 13.8.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{34}H_{33}NO_2Na$ 510.2404; found 510.2413.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-2-fluoro-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ha)

Prepared according to General Procedure **3** using starting material **1h** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 74.3 mg, 78% yield, yellow solid, mp 120 – 122 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.5 Hz, 1H), 7.46 (d, *J* = 5.5 Hz, 1H), 7.45 (d, *J* = 5.5 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.14 – 7.09 (m, 2H), 7.07 (d, *J* = 7.0 Hz, 2H), 6.76 (s, 1H), 5.64 (s, 1H), 3.32 (d, *J* = 13.5 Hz, 1H), 2.84 (d, *J* = 14.0 Hz, 1H), 2.14 (t, *J* = 7.0 Hz, 2H), 1.90 (s, 3H), 1.40 – 1.20 (m, 4H), 0.86 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 161.9 (d, *J* = 246.6 Hz), 153.3, 150.3, 135.4, 134.3 (d, *J* = 3.3 Hz), 133.6 (d, *J* = 3.0 Hz), 130.8, 130.4, 128.7 (d, *J* = 8.4 Hz), 128.3, 127.5 (d, *J* = 8.6 Hz), 126.5, 125.6, 124.5, 123.2, 120.8, 116.5, 115.8 (d, *J* = 21.9 Hz), 115.0, 109.7 (d, *J* = 23.2 Hz), 106.7, 103.8, 49.5, 40.6, 30.3, 25.9, 25.2, 22.4, 13.8.
^{19}F NMR (470 MHz, $CDCl_3$): δ -114.83 – -114.88 (m, 1F).
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{28}FNO_2Na$ 500.1996; found 500.1999.



5-Benzyl-5-((2-butyl-5-phenylfuran-3-yl)methyl)indolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ia)

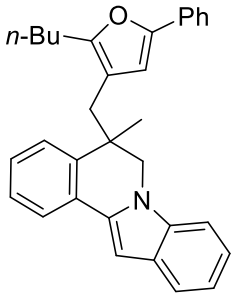
Prepared according to General Procedure **3** using starting material **1i** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 79.2 mg, 74% yield, yellow solid, 91 – 92 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.60

(d, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.16 (t, *J* = 7.3 Hz, 2H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.07 (t, *J* = 7.0 Hz, 1H), 6.94 – 6.86 (m, 3H), 6.81 (d, *J* = 5.5 Hz, 2H), 6.61 (s, 1H), 5.66 (s, 1H), 3.94 (d, *J* = 13.5 Hz, 1H), 3.67 (d, *J* = 16.0 Hz, 1H), 3.41 (d, *J* = 16.0 Hz, 1H), 3.16 (d, *J* = 14.0 Hz, 1H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.47 – 1.28 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 153.4, 150.8, 136.3, 135.4, 135.11, 135.07, 130.9, 130.5, 129.4, 128.3, 128.2, 127.8, 127.4, 127.3, 126.8, 126.44, 126.42, 125.0, 124.4, 123.6, 123.2, 120.3, 116.6, 115.1, 106.9, 102.8, 55.9, 47.3, 38.3, 30.5, 25.6, 22.5, 13.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{38}H_{33}NO_2Na$ 558.2404; found 558.2407.



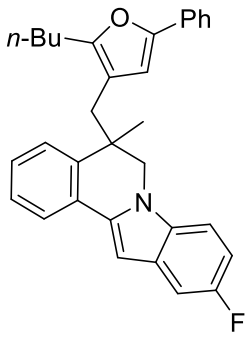
5-((2-Butyl-5-phenylfuran-3-yl)methyl)-5-methyl-5,6-dihydroindolo[2,1-*a*]isoquinoline (3ja)

Prepared according to General Procedure **4** using starting material **1j** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 61.3 mg, 69% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.33 (m, 4H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.93 (s, 1H), 6.16 (s, 1H), 4.27 (d, *J* = 12.5 Hz, 1H), 3.80 (d, *J* = 12.5 Hz, 1H), 2.52 (d, *J* = 14.5 Hz, 1H), 2.47 (d, *J* = 14.5 Hz, 1H), 2.20 – 2.08 (m, 2H), 1.53 (s, 3H), 1.48 – 1.40 (m, 2H), 1.24 – 1.15 (m, 2H), 0.82 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 150.8, 139.9, 136.9, 135.3, 131.6, 131.2, 128.9, 128.6, 128.1, 127.6, 127.3, 126.7, 125.5, 124.7, 123.2, 121.7, 120.9, 120.0, 116.1, 109.1, 108.9, 96.6, 49.2, 39.5, 35.3, 30.3, 25.6, 22.4, 13.7.

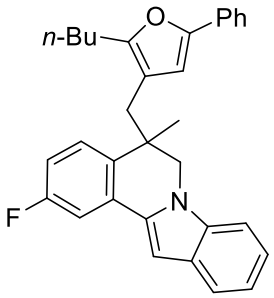
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{32}NO$ 446.2478; found 446.2495.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-10-fluoro-5-methyl-5,6-dihydroindolo[2,1-*a*]isoquinoline (3ka)

Prepared according to General Procedure **4** using starting material **1k** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 76 mg, 82% yield, yellow sticky oil.

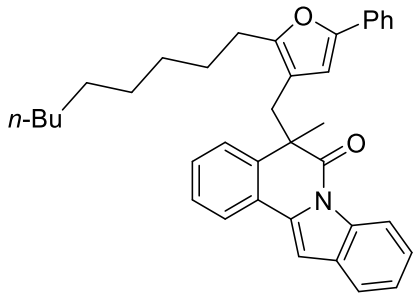
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.58 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.41 – 7.33 (m, 5H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.02 (td, *J* = 9.0, 2.5 Hz, 1H), 6.90 (s, 1H), 6.16 (s, 1H), 4.21 (d, *J* = 12.5 Hz, 1H), 3.76 (d, *J* = 12.0 Hz, 1H), 2.53 (d, *J* = 14.5 Hz, 1H), 2.48 (d, *J* = 14.5 Hz, 1H), 2.22 – 2.09 (m, 2H), 1.55 (s, 3H), 1.52 – 1.42 (m, 2H), 1.28 – 1.20 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2 (d, *J* = 234.7 Hz), 153.7, 150.9, 139.9, 136.8, 133.5, 131.1, 129.1 (d, *J* = 10.3 Hz), 128.6, 128.0, 127.8, 127.3, 126.8, 125.5, 124.8, 123.2, 115.9, 110.1, 109.9, 109.5 (d, *J* = 9.8 Hz), 108.7, 105.5 (d, *J* = 23.6 Hz), 96.5, 49.8, 39.5, 35.4, 30.3, 25.6, 22.4, 13.7.
^{19}F NMR (470 MHz, $CDCl_3$): δ -124.46 – -124.53 (m, 1F).
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{30}FNONa$ 486.2204; found 486.2214.



5-((2-Butyl-5-phenylfuran-3-yl)methyl)-2-fluoro-5-methyl-5,6-dihydroindolo[2,1-*a*]isoquinoline (3la)

Prepared according to General Procedure **4** using starting material **1l** and (*E*)-*β*-chlorovinyl ketone **2a**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 78.7 mg, 85% yield, yellow sticky oil.

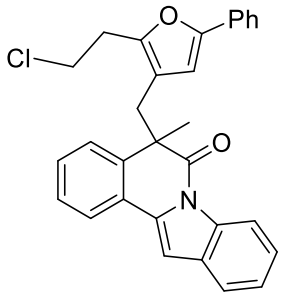
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 7.0 Hz, 2H), 7.49 (dd, *J* = 9.5, 3.0 Hz, 1H), 7.38 – 7.33 (m, 4H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.92 (s, 1H), 6.15 (s, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 3.78 (d, *J* = 12.5 Hz, 1H), 2.50 (d, *J* = 14.0 Hz, 1H), 2.44 (d, *J* = 14.5 Hz, 1H), 2.18 – 2.09 (m, 2H), 1.52 (s, 3H), 1.50 – 1.38 (m, 2H), 1.24 – 1.16 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.1 (d, *J* = 245.1 Hz), 154.1, 150.8, 136.9, 135.5 (d, *J* = 2.9 Hz), 134.3 (d, *J* = 3.0 Hz), 131.1, 130.0 (d, *J* = 8.7 Hz), 128.7, 128.6, 127.5 (d, *J* = 8.3 Hz), 126.7, 123.2, 122.2, 121.1, 120.2, 115.9, 114.2 (d, *J* = 21.4 Hz), 110.9 (d, *J* = 22.8 Hz), 109.2, 108.7, 97.4, 49.9, 39.3, 35.3, 30.3, 25.5, 22.4, 13.7.
^{19}F NMR (470 MHz, $CDCl_3$) δ -115.64 – -115.69 (m, 1F).
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{31}FNO$ 464.2384; found 464.2401.



5-Methyl-5-((2-nonyl-5-phenylfuran-3-yl)methyl)indolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ab)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2b**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 71.9 mg, 68% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.10 – 7.05 (m, 3H), 6.79 (s, 1H), 5.62 (s, 1H), 3.33 (d, *J* = 13.5 Hz, 1H), 2.89 (d, *J* = 13.5 Hz, 1H), 2.12 (t, *J* = 7.5 Hz, 2H), 1.92 (s, 3H), 1.36 – 1.18 (m, 14H), 0.92 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.4, 150.7, 137.8, 135.4, 135.3, 130.9, 130.7, 128.5, 128.2, 127.3, 126.7, 126.4, 125.7, 125.1, 124.4, 123.6, 123.2, 120.5, 116.5, 115.1, 106.9, 102.8, 49.7, 40.5, 31.9, 29.5, 29.34, 29.32, 28.1, 25.8, 25.5, 22.7, 14.1.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{37}H_{40}NO_2$ 530.3054; found 530.3069.

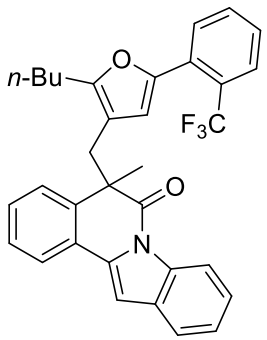


5-((2-(2-Chloroethyl)-5-phenylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ac)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2c**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 39.9 mg, 43% yield, pale green oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.0 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.48 – 7.37 (m, 4H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.78 (s, 1H), 5.65 (s, 1H), 3.50 – 3.43 (m, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.26 – 3.18 (m, 1H), 2.92 (d, *J* = 14.0 Hz, 1H), 2.79 – 2.73 (m, 1H), 2.66 – 2.61 (m, 1H), 1.92 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 151.9, 148.5, 137.6, 135.2, 130.7, 130.4, 128.8, 128.3, 127.5, 126.9, 126.6, 125.6, 125.3, 124.5, 123.6, 123.4, 120.6, 117.6, 116.5, 106.9, 103.0, 49.6, 41.9, 40.2, 29.3, 26.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{24}ClNO_2Na$ 488.1388; found 488.1392.



5-((2-Butyl-5-(2-(trifluoromethyl)phenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ad)

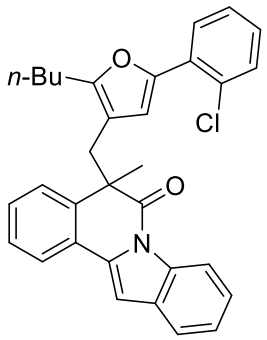
Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2d**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 47.6 mg, 45% yield, yellow sticky oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.25 (t, *J* = 7.0 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.82 (s, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.67 (s, 1H), 3.34 (d, *J* = 13.5 Hz, 1H), 2.89 (d, *J* = 13.5 Hz, 1H), 2.07 (t, *J* = 7.5 Hz, 2H), 1.91 (s, 3H), 1.35-1.25 (m, 2H), 1.22 – 1.14 (m, 2H), 0.82 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 154.4, 147.7, 138.1 (q, *J* = 6.3 Hz), 137.6, 135.5, 135.3, 131.3, 130.7, 129.6 (q, *J* = 2.3 Hz), 129.4, 128.6, 127.4, 126.8, 126.7, 126.3 (q, *J* = 5.8 Hz), 125.5, 125.1, 124.3, 123.6, 120.4, 116.6, 116.2 (q, *J* = 272.2 Hz), 115.1, 111.7 (q, *J* = 2.5 Hz), 102.7, 49.7, 40.5, 29.8, 25.8, 25.0, 22.3, 13.7.

^{19}F NMR (470 MHz, $CDCl_3$) δ -60.14 (s, 3F).

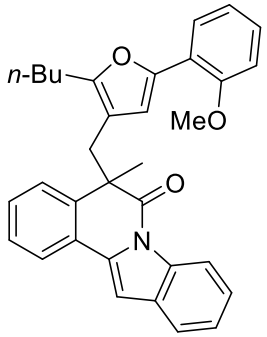
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{33}H_{28}F_3NO_2Na$ 550.1964; found 550.1968.



5-((2-Butyl-5-(2-chlorophenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ae)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2e**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 67.4 mg, 68% yield, yellow solid, mp 127 – 128 ºC.

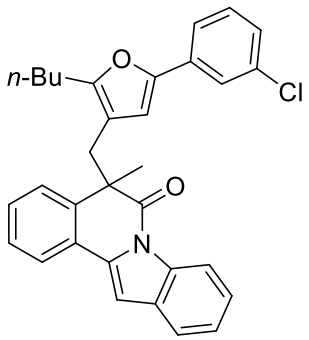
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.44-7.39 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.00 (td, *J* = 7.8, 1.5 Hz, 1H), 6.83 (s, 1H), 6.08 (s, 1H), 3.40 (d, *J* = 14.0 Hz, 1H), 2.94 (d, *J* = 14.0 Hz, 1H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.90 (s, 3H), 1.38 – 1.20 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.4, 147.0, 137.8, 135.5, 135.3, 130.7, 130.3, 129.5, 129.2, 128.6, 127.3, 127.2, 127.1, 126.7, 126.4, 125.5, 125.1, 124.4, 123.8, 120.4, 116.7, 115.4, 113.0, 102.9, 49.6, 40.1, 30.3, 26.5, 25.2, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{29}ClNO_2$ 494.1881; found 494.1905.



5-((2-Butyl-5-(2-methoxyphenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3af)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2f**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 84.2 mg, 86% yield, yellow sticky oil.

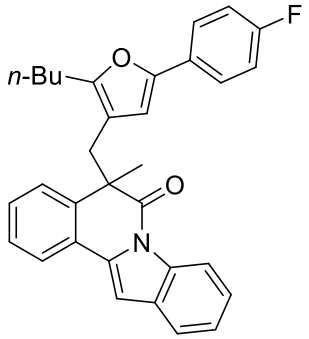
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.53 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.50 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.40 (td, *J* = 7.5, 1.5 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.26 (td, *J* = 7.5, 1.0 Hz, 1H), 7.06 (td, *J* = 7.8, 1.5 Hz, 1H), 6.86 (td, *J* = 7.5, 1.0 Hz, 1H), 6.82 (s, 1H), 6.73 (d, *J* = 8.5 Hz, 1H), 5.99 (s, 1H), 3.50 (s, 3H), 3.39 (d, *J* = 14.0 Hz, 1H), 2.95 (d, *J* = 14.0 Hz, 1H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.89 (s, 3H), 1.40 – 1.22 (m, 4H), 0.86 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 154.9, 152.1, 147.0, 138.0, 135.5, 135.3, 130.7, 128.4, 127.1, 126.9, 126.8, 125.5, 125.0, 124.9, 124.3, 123.7, 120.32, 120.29, 120.0, 116.7, 115.3, 111.9, 110.7, 102.7, 54.7, 49.6, 39.9, 30.4, 26.6, 25.2, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{33}H_{31}NO_3Na$ 512.2196; found 512.2197.



5-((2-Butyl-5-(3-chlorophenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ag)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2g**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 62.8 mg, 64% yield, yellow solid, 123 – 125 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 6.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 7.0 Hz, 2H), 7.40 – 7.38 (m, 1H), 7.36 (td, *J* = 7.5, 1.3 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.07 – 7.03 (m, 2H), 6.99 (s, 1H), 6.86 (dt, *J* = 7.0, 2.0 Hz, 1H), 6.76 (s, 1H), 5.62 (s, 1H), 3.30 (d, *J* = 14.0 Hz, 1H), 2.85 (d, *J* = 14.0 Hz, 1H), 2.06 (t, *J* = 7.3 Hz, 2H), 1.92 (s, 3H), 1.34 – 1.16 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 154.0, 149.3, 137.6, 135.35, 135.26, 134.3, 132.5, 130.6, 129.5, 128.6, 127.4, 126.6, 126.3, 125.7, 125.2, 124.5, 123.6, 123.1, 121.2, 120.5, 116.4, 115.4, 108.0, 102.8, 49.7, 40.7, 30.1, 25.6, 25.1, 22.4, 13.7.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{28}ClNO_2Na$ 516.1701; found 516.1721.

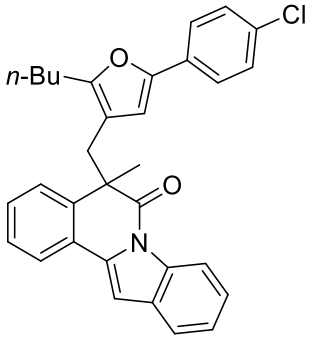


5-((2-Butyl-5-(4-fluorophenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ah)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2h**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 83.1 mg, 87% yield, yellow sticky oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.0 Hz, 1H), 7.72 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.34 (m, 4H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.83 (t, *J* = 8.8 Hz, 2H), 6.78 (s, 1H), 5.53 (s, 1H), 3.30 (d, *J* = 14.0 Hz, 1H), 2.85 (d, *J* = 14.0 Hz, 1H), 2.06 (t, *J* = 7.0 Hz, 2H), 1.91 (s, 3H), 1.32 – 1.14 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H).

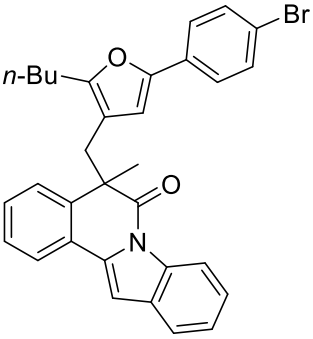
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 161.6 (d, *J* = 246.2 Hz), 153.3, 149.9, 137.7, 135.4 (d, *J* = 17.4 Hz), 130.7, 128.6, 127.3, 127.2 (d, *J* = 3.3 Hz), 126.6, 125.7, 125.1, 124.9, 124.8, 124.4, 123.6, 120.5, 116.4, 115.2 (d, *J* = 27.5 Hz), 115.1, 106.5, 102.7, 49.7, 40.6, 30.2, 25.7, 25.1, 22.4, 13.7.
^{19}F NMR (470 MHz, $CDCl_3$) δ -115.50 – -115.58 (m, 1F).
HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{32}H_{29}FNO_2$ 478.2177; found 478.2200.



5-((2-Butyl-5-(4-chlorophenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ai)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2i**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 88.8 mg, 90% yield, yellow solid, mp 118 – 119 °C.

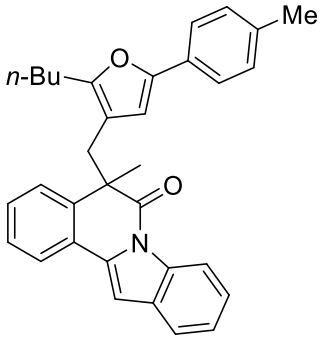
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.0 Hz, 1H), 7.71 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.40 – 7.34 (m, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.76 (s, 1H), 5.59 (s, 1H), 3.31 (d, *J* = 14.0 Hz, 1H), 2.86 (d, *J* = 14.0 Hz, 1H), 2.08 (t, *J* = 7.0 Hz, 2H), 1.91 (s, 3H), 1.34 – 1.16 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.7, 149.7, 137.7, 135.4, 135.3, 132.0, 130.7, 129.3, 128.6, 128.4, 127.4, 126.6, 125.7, 125.1, 124.41, 124.39, 123.6, 120.5, 116.5, 115.3, 107.3, 102.8, 49.7, 40.6, 30.2, 25.7, 25.1, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{32}H_{29}ClNO_2$ 494.1881; found 494.1899.



5-((5-(4-Bromophenyl)-2-butylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3aj)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2j**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 85.8 mg, 80% yield, yellow solid, mp 115 – 117 °C.

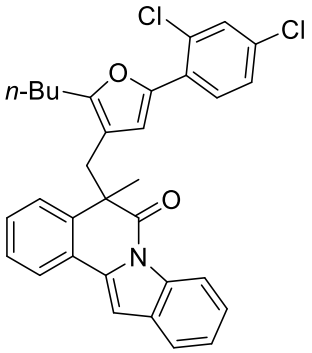
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.42-7.36 (m, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.78 (s, 1H), 5.61 (s, 1H), 3.32 (d, *J* = 13.5 Hz, 1H), 2.87 (d, *J* = 13.5 Hz, 1H), 2.08 (t, *J* = 7.0 Hz, 2H), 1.93 (s, 3H), 1.35 – 1.16 (m, 4H), 0.84 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.8, 149.7, 137.7, 135.4, 135.3, 131.3, 130.7, 129.7, 128.6, 127.4, 126.6, 125.7, 125.1, 124.7, 124.4, 123.6, 120.5, 120.0, 116.4, 115.3, 107.4, 102.8, 49.7, 40.6, 30.2, 25.7, 25.1, 22.4, 13.7.
HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{32}H_{29}BrNO_2$ 538.1376; found 538.1395.



5-((2-Butyl-5-(*p*-tolyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ak)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2k**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 90.7 mg, 96% yield, yellow solid, mp 90 – 91 °C.

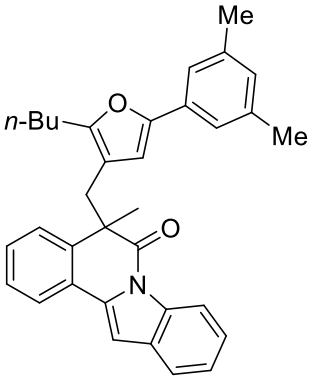
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.28 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.78 (s, 1H), 5.54 (s, 1H), 3.32 (d, *J* = 13.5 Hz, 1H), 2.88 (d, *J* = 13.5 Hz, 1H), 2.27 (s, 3H), 2.11 (t, *J* = 7.3 Hz, 2H), 1.91 (s, 3H), 1.34 – 1.18 (m, 4H), 0.83 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 152.9, 150.9, 137.8, 136.1, 135.4, 135.3, 130.7, 128.9, 128.5, 128.3, 127.3, 126.7, 125.7, 125.1, 124.4, 123.6, 123.2, 120.5, 116.5, 115.0, 106.1, 102.8, 49.7, 40.6, 30.3, 25.8, 25.2, 22.4, 21.1, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{33}H_{32}NO_2$ 474.2428; found 474.2249.



5-((2-Butyl-5-(2,4-dichlorophenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3al)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2l**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 69.5 mg, 66% yield, yellow sticky oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.41 (td, *J* = 7.5, 1.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.27 (td, *J* = 7.5, 1.0 Hz, 1H), 7.21 (d, *J* = 2.5 Hz, 1H), 7.07 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.82 (s, 1H), 6.07 (s, 1H), 3.40 (d, *J* = 14.0 Hz, 1H), 2.92 (d, *J* = 14.0 Hz, 1H), 2.21 (t, *J* = 7.8 Hz, 2H), 1.90 (s, 3H), 1.38 – 1.20 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.7, 146.1, 137.7, 135.4, 135.3, 131.9, 130.6, 130.0, 129.9, 128.6, 127.8, 127.7, 127.3, 126.74, 126.70, 125.5, 125.1, 124.4, 123.7, 120.4, 116.7, 115.6, 113.2, 102.9, 49.5, 40.1, 30.3, 26.5, 25.2, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{27}Cl_2NO_2Na$ 550.1311; found 550.1319.

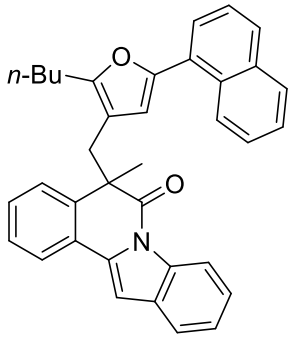


5-((2-Butyl-5-(3,5-dimethylphenyl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3am)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2m**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 92.5 mg, 95% yield, yellow solid, mp 116 – 118 ℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 9.5 Hz, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.36 (td, *J* = 7.5, 1.0 Hz, 1H), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H), 6.76 (s, 1H), 6.74 (s, 1H), 6.64 (s, 2H), 5.63 (s, 1H), 3.31 (d, *J* = 14.0 Hz, 1H), 2.87 (d, *J* = 14.0 Hz, 1H), 2.21 (s, 6H), 2.06 (t, *J* =

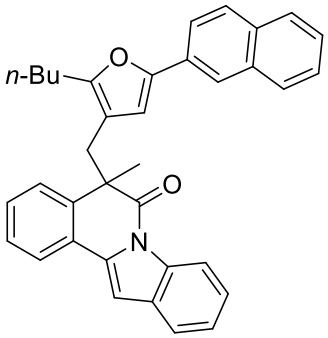
7.5 Hz, 2H), 1.93 (s, 3H), 1.33 – 1.17 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 153.1, 151.1, 137.74, 137.68, 135.4, 135.3, 130.7, 128.5, 128.3, 127.3, 126.6, 125.7, 125.0, 124.4, 123.6, 121.1, 120.5, 116.5, 114.9, 106.6, 102.8, 49.7, 40.9, 30.3, 25.5, 25.1, 22.5, 21.2, 13.8.
HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{34}H_{34}NO_2$ 488.2584; found 488.2602.



5-((2-Butyl-5-(naphthalen-1-yl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3an)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2n**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 56.9 mg, 56% yield, yellow solid, mp 112 – 114 ºC.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.85 (s, 1H), 5.70 (s, 1H), 3.45 (d, *J* = 13.5 Hz, 1H), 2.96 (d, *J* = 13.5 Hz, 1H), 2.24 – 2.18 (m, 2H), 1.95 (s, 3H), 1.42 – 1.22 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 153.5, 150.0, 138.0, 135.5, 135.3, 133.8, 130.7, 129.9, 128.7, 128.5, 128.2, 127.6, 127.3, 126.8, 126.0, 125.7, 125.52, 125.48, 125.2, 125.1, 124.5, 123.6, 120.5, 116.7, 114.9, 111.2, 102.8, 49.8, 40.7, 30.3, 26.2, 25.2, 22.5, 13.8.
HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{36}H_{31}NO_2Na$ 532.2247; found 532.2247.

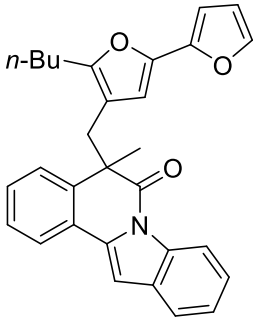


5-((2-Butyl-5-(naphthalen-2-yl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ao)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-

chlorovinyl ketone **2o**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 63.1 mg, 62% yield, yellow solid, mp 118 – 120 ºC.

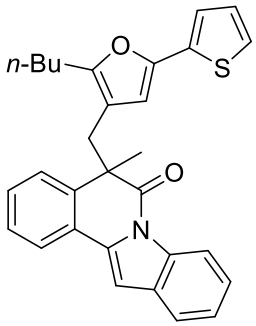
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.5 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.49 (s, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.39 (m, 3H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.10 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.74 (s, 1H), 5.74 (s, 1H), 3.35 (d, *J* = 14.0 Hz, 1H), 2.90 (d, *J* = 14.0 Hz, 1H), 2.13 (t, *J* = 7.3 Hz, 2H), 1.94 (s, 3H), 1.41 – 1.22 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.7, 150.8, 137.7, 135.4, 135.3, 133.4, 132.3, 130.7, 128.6, 128.2, 127.9, 127.8, 127.6, 127.3, 126.6, 126.1, 125.8, 125.4, 125.1, 124.4, 123.6, 122.1, 121.1, 120.5, 116.5, 115.3, 107.6, 102.8, 49.7, 40.8, 30.3, 25.6, 25.2, 22.5, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{36}H_{32}NO_2$ 510.2428; found 510.2432.



5-((5-Butyl-[2,2'-bifuran]-4-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ap)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2p**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 80 mg, 89% yield, yellow solid, mp 101 – 103 ºC.

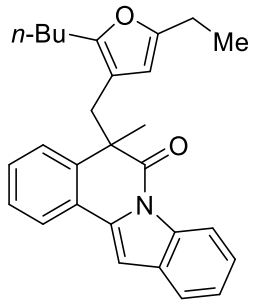
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 9.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.42 – 7.34 (m, 3H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.21 (s, 1H), 6.84 (s, 1H), 6.27 (dd, *J* = 3.5, 1.5 Hz, 1H), 6.06 (d, *J* = 3.0 Hz, 1H), 5.53 (s, 1H), 3.33 (d, *J* = 14.0 Hz, 1H), 2.90 (d, *J* = 14.0 Hz, 1H), 2.22 – 2.14 (m, 2H), 1.88 (s, 3H), 1.33 – 1.27 (m, 2H), 1.24 – 1.19 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.3, 146.5, 143.4, 141.0, 137.7, 135.4, 135.3, 130.6, 128.6, 127.4, 126.7, 125.5, 125.1, 124.4, 123.7, 120.4, 116.6, 114.9, 111.0, 107.2, 104.0, 102.9, 49.6, 39.8, 30.3, 26.3, 25.2, 22.4, 13.7.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{30}H_{28}NO_3$ 450.2064; found 450.2076.



5-((2-Butyl-5-(thiophen-2-yl)furan-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3aq)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2q**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 85.6 mg, 92% yield, orange sticky oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.43 – 7.34 (m, 3H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.02 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.84 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.82 (s, 1H), 6.67 (d, *J* = 4.0 Hz, 1H), 5.49 (s, 1H), 3.33 (d, *J* = 14.0 Hz, 1H), 2.88 (d, *J* = 14.0 Hz, 1H), 2.16 – 2.11 (m, 2H), 1.90 (s, 3H), 1.35 – 1.20 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 153.0, 146.3, 137.7, 135.4, 135.3, 133.9, 130.7, 128.6, 127.4, 127.2, 126.7, 125.6, 125.1, 124.4, 123.7, 123.2, 121.5, 120.5, 116.5, 115.1, 107.0, 102.9, 49.6, 40.3, 30.3, 25.9, 25.2, 22.4, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{30}H_{28}NO_2S$ 466.1835; found 466.1844.

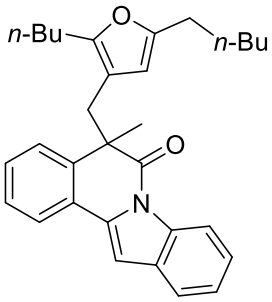


5-((2-Butyl-5-ethylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3ar)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2r**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 78 mg, 95% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.37 – 7.35 (m, 1H), 7.33 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.29 (td, *J* = 7.5, 1.5 Hz, 1H), 6.82 (s, 1H), 4.99 (s, 1H), 3.25 (d, *J* = 14.0 Hz, 1H), 2.81 (d, *J* = 13.5 Hz, 1H), 2.20 – 2.10 (m, 2H), 1.99 – 1.94 (m, 2H), 1.89 (s, 3H), 1.27 – 1.14 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H), 0.71 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 154.5, 151.2, 138.1, 135.7, 135.4, 130.6, 128.5, 127.2, 126.7, 125.6, 125.0, 124.3, 123.5, 120.2, 116.6, 113.2, 105.5, 102.4, 49.8, 40.9,

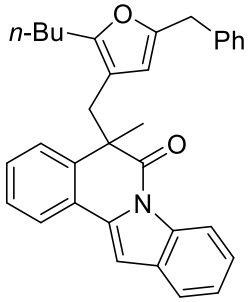
30.4, 25.6, 25.0, 22.4, 20.8, 13.8, 11.6.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{30}NO_2$ 412.2271; found 412.2280.



5-((2-Butyl-5-pentylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3as)

Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2s**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 86.9 mg, 96% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.52 (d, *J* = 7.0 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.33 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.28 (td, *J* = 7.0, 1.0 Hz, 1H), 6.83 (s, 1H), 4.96 (s, 1H), 3.26 (d, *J* = 14.0 Hz, 1H), 2.81 (d, *J* = 14.0 Hz, 1H), 2.14 – 2.09 (m, 2H), 2.02 – 1.97 (m, 2H), 1.87 (s, 3H), 1.25 – 1.06 (m, 8H), 1.02 – 0.95 (m, 2H), 0.82 (t, *J* = 7.0 Hz, 3H), 0.81 (t, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 153.3, 151.2, 138.1, 135.6, 135.3, 130.6, 128.5, 127.2, 126.7, 125.6, 125.0, 124.3, 123.5, 120.2, 116.6, 113.2, 106.2, 102.4, 49.7, 40.8, 31.0, 30.4, 27.4, 27.2, 25.8, 25.0, 22.4, 22.3, 13.9, 13.8.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{31}H_{32}NO_2$ 454.2741; found 454.2756.



5-((5-Benzyl-2-butylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (3at)

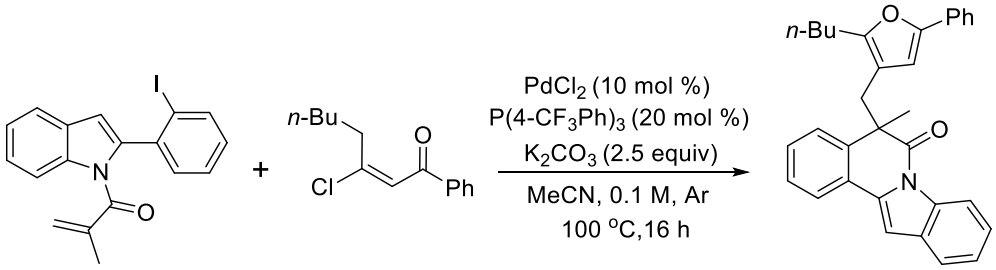
Prepared according to General Procedure **4** using starting material **1a** and (*E*)-*β*-chlorovinyl ketone **2t**. The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 71.8 mg, 76% yield, yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.29 (m, 5H), 7.14 – 7.11 (m, 2H), 6.82 (s, 1H), 6.75 – 6.72 (m, 2H), 4.91 (s, 1H), 3.51(d, *J* = 16.0 Hz, 1H), 3.46 (d, *J* = 16.5 Hz, 1H), 3.27 (d, *J* = 13.5 Hz, 1H), 2.81 (d, *J* = 14.0 Hz, 1H), 2.06 – 1.99 (m, 2H),

1.86 (s, 3H), 1.24 – 1.12 (m, 4H), 0.80 (t, J = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 152.2, 151.0, 138.2, 138.1, 135.6, 135.2, 130.6, 128.5, 128.4, 128.1, 127.2, 126.7, 126.0, 125.5, 125.1, 124.4, 123.5, 120.3, 116.7, 113.5, 108.2, 102.5, 49.7, 40.7, 34.0, 30.3, 26.0, 25.1, 22.4, 13.7.
HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{33}H_{32}NO_2$ 474.2428; found 474.2446.

7) Scale up and product derivatization experiments

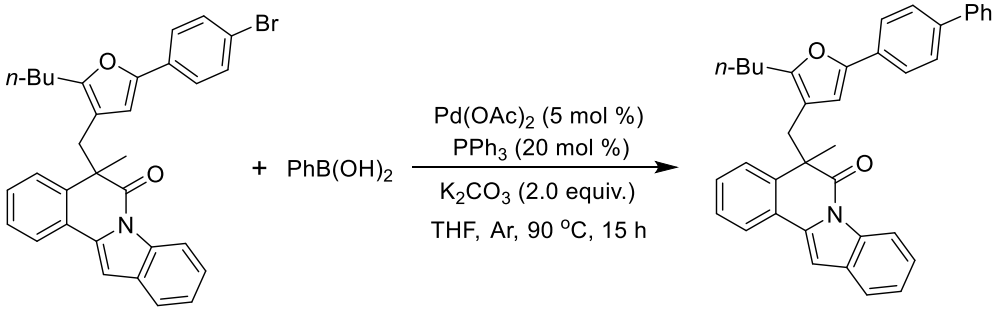
Scale up



1a, 3 mmol, 1.161 g (***E*)-2a** **3aa**, 76 % yield

A flame-dried, 9.5-dram vial under argon atmosphere was charged with alkene-tethered indole **1a** (1.161 g, 3.0 mmol, 1.0 equiv.), $PdCl_2$ (53.2 mg, 0.3 mmol, 10 mol %), P(4-$CF_3Ph)_3$ (280 mg, 0.6 mmol, 20 mol %) and K_2CO_3 (1.04 g, 7.5 mmol, 2.5 equiv.), and was purged with argon for 10 minutes. Anhydrous and degassed MeCN (15.0 mL) were added and the mixture was stirred at room temperature for 10 minutes. *β*-chlorovinyl ketone (*E*)-**2a** (1.42 g, 6.0 mmol, 2.0 equiv.) was dissolved in anhydrous MeCN (15.0 mL) and transferred to the vial via syringe, and the vial was then stirred under argon for 10 minutes. A Teflon lined screw cap was fitted on the 9.5-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 °C for 16 hours. The reaction mixture was then cooled down to room temperature and was filtered through a plug of silica gel using EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash column chromatography (petroleum ether/Et_2O = 25:1) to give the desired product **3aa** in 76% yield (1.047 g).

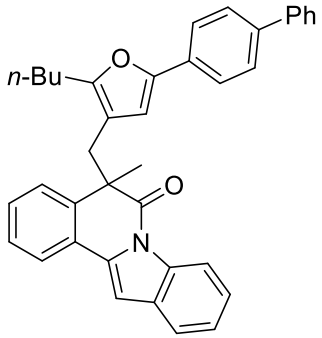
Product derivatization experiments



4, 81% yield

To a flame-dried, 3-dram vial containing a magnetic stirring bar under argon atmosphere were added Pd $(OAc)_2$ (2.24 mg, 0.01 mmol, 5 mol %), PPh_3 (10.5 mg, 0.04 mmol, 20 mol %), K_2CO_3 (55.3 mg, 0.4 mmol, 2.0 equiv.), phenylboronic acid (36.6 mg, 0.3 mmol, 1.5 equiv.), **3aj** (107.4 mg, 0.2 mmol, 1.0 equiv.), and THF (2.0 mL) sequentially, and the resulting mixture was stirred under argon for 10 min. A re-sealable silicone/PTFE crimp cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 90 °C for 15 hours. The reaction mixture was then cooled down to room temperature and was filtered through a plug of silica gel using EtOAc. The filtrate was concentrated under reduced pressure and the residue was

purified by silica gel flash column chromatography (petroleum ether/Et_2O = 25:1) to give the desired product **4** in 81% yield (86.7 mg).



5-((5-([1,1'-Biphenyl]-4-yl)-2-butylfuran-3-yl)methyl)-5-methylindolo[2,1-*a*]isoquinolin-6(5*H*)-one (4)

The product was purified by column chromatography (petroleum ether/Et_2O = 25:1), 86.7 mg, 81% yield, yellow oil.

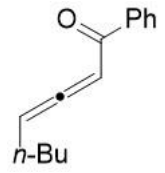
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.56 – 7.50 (m, 3H), 7.46 – 7.38 (m, 8H), 7.34 – 7.27 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.80 (s, 1H), 5.64 (s, 1H), 3.34 (d, *J* = 13.5 Hz, 1H), 2.89 (d, *J* = 14.0 Hz, 1H), 2.13 (t, *J* = 7.3 Hz, 2H), 1.92 (s, 3H), 1.36 – 1.20 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 153.5, 150.5, 140.8, 139.1, 137.7, 135.4, 135.3, 130.7, 129.9, 128.7, 128.5, 127.3, 127.1, 126.9, 126.8, 126.7, 125.7, 125.1, 124.4, 123.63, 123.56, 120.5, 116.5, 115.3, 107.1, 102.8, 49.7, 40.6, 30.3, 25.8, 25.2, 22.4, 13.8.

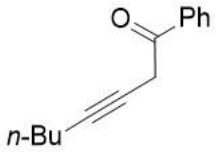
HRMS (ESI) *m/z*: $[M+Na]^+$calcd for $C_{38}H_{33}NO_2Na$ 558.2404; found 558.2388.

8) Mechanistic studies

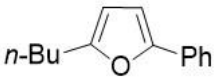
A. Synthesis of 5, 6, 7



Phenylocta-2,3-dien-1-one (5):
Prepared according to literature procedure.[10]



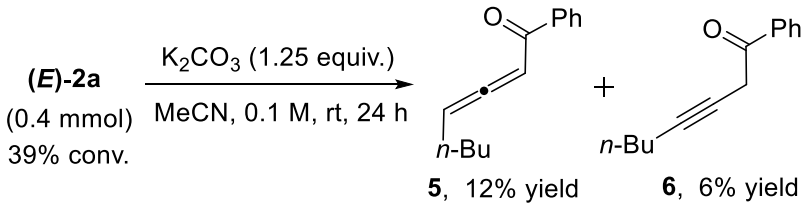
Phenyloct-3-yn-1-one (6):
Prepared according to literature procedure.[10]



2-Butyl-5-phenylfuran (7):
Prepared according to literature procedure.[10]

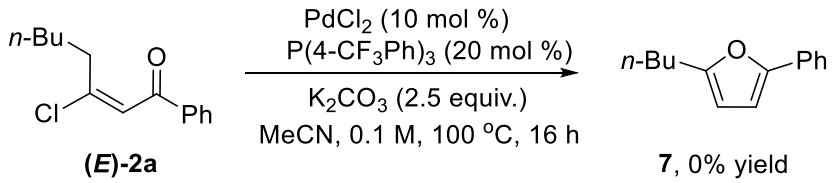
B. Control experiments

(1) Confirmation of (*E*)-2a as a precursor in the cascade cyclizations



To a flame-dried, 3-dram vial charged with (*E*)-*β*-chlorovinyl ketone **2a** (94.4 mg, 0.4 mmol, 1.0 equiv.) under argon were added dry MeCN (4.0 mL) and K_2CO_3 (69.1 mg, 0.5 mmol, 1.25 equiv.) at ambient temperature. The solution was stirred for 24 h and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography using 25:1 petroleum ether/Et_2O v:v as the mobile phase, affording the mixture of allenyl ketone **5** and alkynyl ketone **6** in 18% yield. The ratio of **5**/**6** was analyzed by ^{1}H NMR spectroscopy.

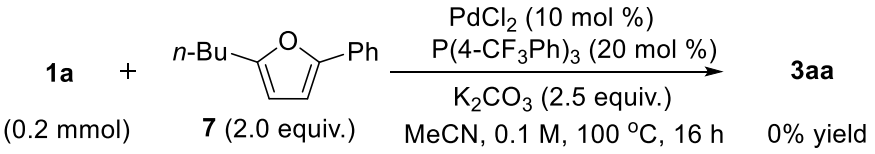
(2) Confirmation of Pd(0) is not the active species that produces furan



A flame-dried, 3-dram vial under argon atmosphere was charged with a stir bar, (*E*)-*β*-chlorovinyl ketone **2a** (47.2 mg, 0.20 mmol, 1.0 equiv.), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol %), P(4-CF_3Ph)$_3$ (18.7 mg, 0.04 mmol, 20 mol %) and K_2CO_3 (69.2 mg, 0.5 mmol,

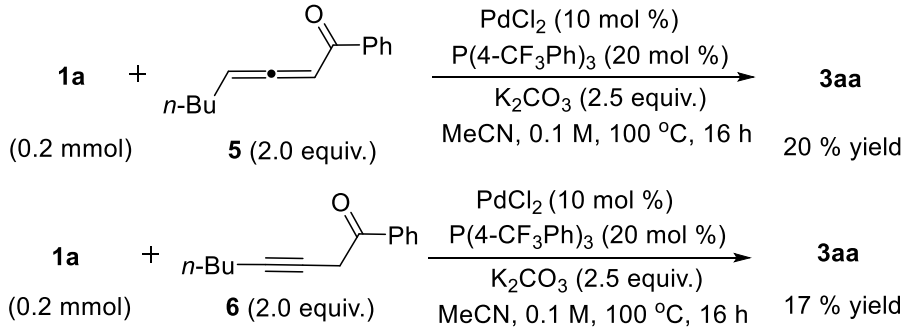
2.5 equiv.), and was purged with argon for 5 minutes. Anhydrous and degassed MeCN (2.0 mL) were added and the mixture was stirred at room temperature for 5 minutes. A Teflon lined screw cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 °C for 16 hours. The reaction mixture was then cooled down to room temperature and was monitored, no corresponding product **7** was obtained.

(3) Determining whether the cycloisomerized furan from (*E*)-2a was a catalytically active intermediate



A flame-dried, 3-dram vial under argon atmosphere was charged with a stir bar, 1-(2-(2-iodophenyl)-1*H*-indol-1-yl)-2-methylprop-2-en-1-one **1a** (77.4 mg, 0.20 mmol, 1.0 equiv.), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol %), $P(4\text{-}CF_3Ph)_3$ (18.7 mg, 0.04 mmol, 20 mol %) and K_2CO_3 (69.2 mg, 0.5 mmol, 2.5 equiv.), and was purged with argon for 5 minutes. Anhydrous and degassed MeCN (1.0 mL) were added and the mixture was stirred at room temperature for 5 minutes. 2-Butyl-5-phenylfuran **7** (80 mg, 0.4 mmol, 2.0 equiv.) was dissolved in anhydrous MeCN (1.0 mL) and transferred to the vial via syringe, and the vial was then purged with argon for 5 minutes. A Teflon lined screw cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 °C for 16 hours. The reaction mixture was then cooled down to room temperature and was monitored, no corresponding product **3aa** was obtained.

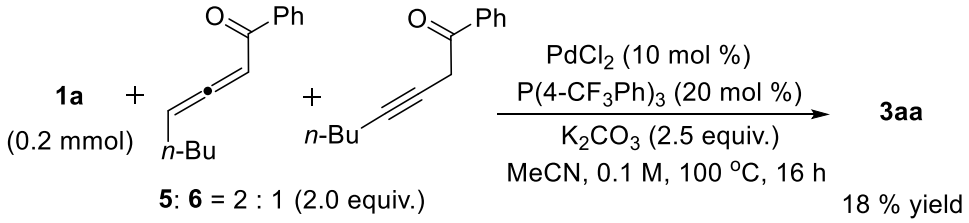
(4) Cascade cyclizations synthesized from allenyl ketone 5, alkynyl ketone 6



A flame-dried, 3-dram vial under argon atmosphere was charged with a stir bar, 1-(2-(2-iodophenyl)-1*H*-indol-1-yl)-2-methylprop-2-en-1-one **1a** (77.4 mg, 0.20 mmol, 1.0 equiv.), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol %), $P(4\text{-}CF_3Ph)_3$ (18.7 mg, 0.04 mmol, 20 mol %) and K_2CO_3 (69.2 mg, 0.5 mmol, 2.5 equiv.), and was purged with argon for 5 minutes. Anhydrous and degassed MeCN (1.0 mL) were added and the mixture was stirred at room temperature for 5 minutes. Allenyl ketone **5** (80 mg, 0.4 mmol, 2.0 equiv.) or alkynyl ketone **6** (80 mg, 0.4 mmol, 2.0 equiv.) was dissolved in anhydrous MeCN (1.0 mL) and transferred to the vial via syringe, and the vial was then purged with argon

for 5 minutes. A Teflon lined screw cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 ºC for 16 hours. The reaction mixture was then cooled down to room temperature and was filtered through a plug of silica gel using EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash column chromatography using 25:1 petroleum ether/Et_2O v:v as the mobile phase, affording the corresponding product **3aa** in 20% (18.4 mg), 17% (15.5 mg) yield, respectively.

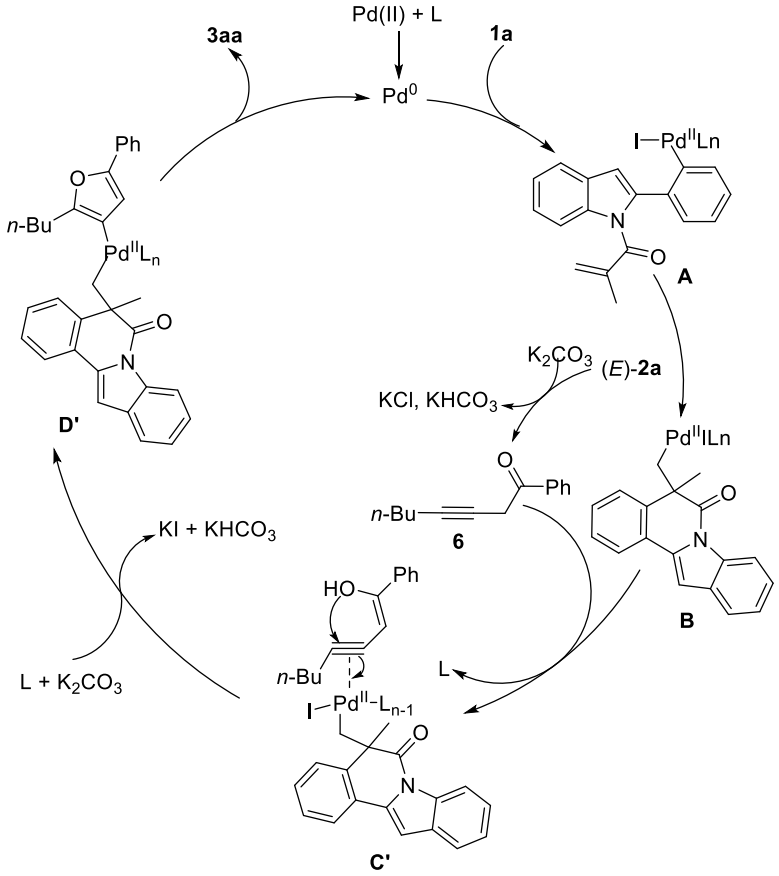
(5) Cascade cyclizations employing allenyl ketone 5 and alkynyl ketone 6



A flame-dried, 3-dram vial under argon atmosphere was charged with a stir bar, 1-(2-(2-iodophenyl)-1*H*-indol-1-yl)-2-methylprop-2-en-1-one **1a** (77.4 mg, 0.20 mmol, 1.0 equiv.), $PdCl_2$ (3.5 mg, 0.02 mmol, 10 mol %), $P(4\text{-}CF_3Ph)_3$ (18.7 mg, 0.04 mmol, 20 mol %), K_2CO_3 (69.2 mg, 0.5 mmol, 2.5 equiv.), and was purged with argon for 5 minutes. Anhydrous and degassed MeCN (1.0 mL) were added and the mixture was stirred at room temperature for 5 minutes. The mixture of allenyl ketone **5** and alkynyl ketone **6** (80 mg, 0.4 mmol, 2.0 equiv.) was dissolved in anhydrous MeCN (1.0 mL) and transferred to the vial via syringe, and the vial was then purged with argon for 5 minutes. A Teflon lined screw cap was fitted on the 3-dram vial. The vial was sealed with Teflon tape and placed in a preheated oil bath at 100 ºC for 16 hours. The reaction mixture was then cooled down to room temperature and was filtered through a plug of silica gel using EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash column chromatography using 25:1 petroleum ether/Et_2O v:v as the mobile phase, affording the corresponding product **3aa** in 18% (16.6 mg) yield.

C. The proposed mechanism from the intermediate alkynyl ketone 6

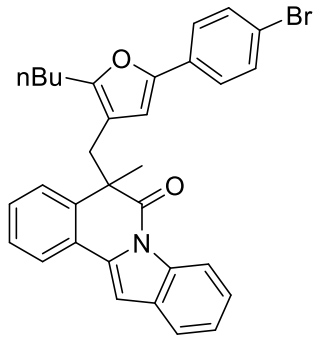
The experimental results indicate that alkynyl ketone **6** may also be the reactive intermediate in this cascade cyclization. There are two possible pathways involving alkynyl ketone **6** in the reaction: (1) **6** could be converted into allenyl ketone **5** to participate in the formation of furan ring (Scheme 4); (2) **6** directly participated in the reaction and the proposed pathway is shown in the Scheme S1.



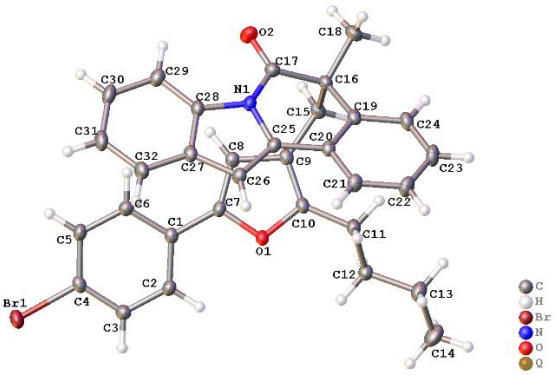
Scheme S1. The proposed mechanism from the intermediate alkynyl ketone **6**

The oxidation addition of **1a** to the Pd(0) catalyst followed by an intramolecular Heck reaction generates the alkylpalladium species **B**. Coordination of the triple bond of **6** to the intermediate **B** enables intramolecular nucleophilic attack of the oxygen atom onto the triple bond to produce the intermediate **C'**. In the presence of a base, intermediate **C'** could convert to the intermediate **D'**. Finally, the reductive elimination of intermediate **D'** affords the bis-heterocyclic product **3aa**. Although no Pd-carbene complex is generated in this pathway, it still cannot be completely ruled out.

9) X-Ray Crystal Structure



3aj



Product 3aj

Single crystal cultivation: the single crystal of **3aj** was obtained through solvent diffusion method.

Good solvent: THF; poor solvent: *n*-hexane.

Table S2. Crystal data and structure refinement for 240514h_0m.

Identification code	240514h_0m	
Empirical formula	C32 H28 Br N O2	
Formula weight	538.46	
Temperature	100(2) K	
Wavelength	1.34139 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 11.8884(10) Å	α= 90 °.
	b = 9.8535(8) Å	β= 92.855(2) °.
	c = 21.4916(18) Å	γ = 90 °.
Volume	2514.5(4) $Å^3$	
Z	4	
Density (calculated)	1.422 Mg/m^3	
Absorption coefficient	1.620 mm^{-1}	
F(000)	1112	
Crystal size	0.230 x 0.200 x 0.120 mm^3	
Theta range for data collection	3.583 to 61.700 °.	
Index ranges	-15<=h<=15, -10<=k<=12, -28<=l<=27	
Reflections collected	30775	
Independent reflections	5861 [R(int) = 0.0412]	
Completeness to theta = 53.594 °	99.6 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.986 and 0.826
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5861 / 0 / 328
Goodness-of-fit on F^2	1.034
Final R indices [I>2sigma(I)]	R1 = 0.0345, wR2 = 0.0906
R indices (all data)	R1 = 0.0355, wR2 = 0.0912
Extinction coefficient	0.0054(3)
Largest diff. peak and hole	0.478 and -0.871 e.$Å^{-3}$

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 240514h_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	9806(1)	1697(1)	6215(1)	26(1)
C(1)	6787(1)	4655(2)	6477(1)	17(1)
C(2)	6653(1)	3254(2)	6530(1)	19(1)
C(3)	7553(1)	2383(2)	6457(1)	20(1)
C(4)	8592(1)	2919(2)	6328(1)	20(1)
C(5)	8748(1)	4302(2)	6255(1)	21(1)
C(6)	7840(1)	5166(2)	6326(1)	20(1)
C(7)	5866(1)	5589(2)	6590(1)	17(1)
C(8)	5825(1)	6942(2)	6696(1)	18(1)
C(9)	4680(1)	7268(2)	6822(1)	17(1)
C(10)	4103(1)	6080(2)	6784(1)	18(1)
C(11)	2894(1)	5743(2)	6847(1)	20(1)
C(12)	2667(1)	4568(2)	7286(1)	20(1)
C(13)	1407(1)	4329(2)	7325(1)	27(1)
C(14)	1124(2)	3187(2)	7770(1)	35(1)
C(15)	4216(1)	8650(2)	6942(1)	19(1)
C(16)	3850(1)	9491(2)	6345(1)	18(1)
C(17)	4920(1)	9600(2)	5982(1)	19(1)
C(18)	3524(2)	10915(2)	6561(1)	25(1)
C(19)	2885(1)	8758(2)	5998(1)	18(1)
C(20)	3098(1)	7847(2)	5518(1)	17(1)
C(21)	2218(1)	7096(2)	5229(1)	21(1)
C(22)	1129(1)	7242(2)	5420(1)	25(1)
C(23)	910(1)	8146(2)	5895(1)	26(1)
C(24)	1780(1)	8889(2)	6182(1)	22(1)
C(25)	4243(1)	7684(2)	5322(1)	17(1)
C(26)	4721(1)	6738(2)	4960(1)	19(1)
C(27)	5895(1)	7076(2)	4929(1)	19(1)
C(28)	6091(1)	8277(2)	5268(1)	18(1)
C(29)	7150(1)	8886(2)	5326(1)	22(1)
C(30)	8026(1)	8223(2)	5044(1)	26(1)
C(31)	7854(1)	7003(2)	4720(1)	26(1)
C(32)	6793(1)	6424(2)	4654(1)	23(1)

N(1)	5061(1)	8648(1)	5519(1)	17(1)
O(1)	4811(1)	5032(1)	6642(1)	18(1)
O(2)	5665(1)	10396(1)	6127(1)	29(1)

Table S4. Bond lengths [Å] and angles [°] for 240514h_0m.

Br(1)-C(4)	1.9041(16)
C(1)-C(2)	1.395(2)
C(1)-C(6)	1.402(2)
C(1)-C(7)	1.460(2)
C(2)-C(3)	1.386(2)
C(2)-H(2)	0.9500
C(3)-C(4)	1.384(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.386(2)
C(5)-C(6)	1.390(2)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-C(8)	1.354(2)
C(7)-O(1)	1.3781(18)
C(8)-C(9)	1.437(2)
C(8)-H(8)	0.9500
C(9)-C(10)	1.358(2)
C(9)-C(15)	1.497(2)
C(10)-O(1)	1.3766(18)
C(10)-C(11)	1.488(2)
C(11)-C(12)	1.525(2)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.523(2)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.525(3)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-C(16)	1.571(2)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-C(19)	1.520(2)

C(16)-C(17)	1.529(2)
C(16)-C(18)	1.534(2)
C(17)-O(2)	1.212(2)
C(17)-N(1)	1.384(2)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-C(24)	1.397(2)
C(19)-C(20)	1.399(2)
C(20)-C(21)	1.402(2)
C(20)-C(25)	1.454(2)
C(21)-C(22)	1.384(2)
C(21)-H(21)	0.9500
C(22)-C(23)	1.390(3)
C(22)-H(22)	0.9500
C(23)-C(24)	1.387(3)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(25)-C(26)	1.357(2)
C(25)-N(1)	1.409(2)
C(26)-C(27)	1.439(2)
C(26)-H(26)	0.9500
C(27)-C(32)	1.402(2)
C(27)-C(28)	1.403(2)
C(28)-C(29)	1.394(2)
C(28)-N(1)	1.410(2)
C(29)-C(30)	1.394(2)
C(29)-H(29)	0.9500
C(30)-C(31)	1.399(3)
C(30)-H(30)	0.9500
C(31)-C(32)	1.386(2)
C(31)-H(31)	0.9500
C(32)-H(32)	0.9500

C(2)-C(1)-C(6)	118.79(14)
C(2)-C(1)-C(7)	121.32(14)
C(6)-C(1)-C(7)	119.87(14)
C(3)-C(2)-C(1)	120.74(15)

C(3)-C(2)-H(2)	119.6
C(1)-C(2)-H(2)	119.6
C(4)-C(3)-C(2)	119.23(15)
C(4)-C(3)-H(3)	120.4
C(2)-C(3)-H(3)	120.4
C(3)-C(4)-C(5)	121.58(15)
C(3)-C(4)-Br(1)	118.34(12)
C(5)-C(4)-Br(1)	120.02(12)
C(4)-C(5)-C(6)	118.72(15)
C(4)-C(5)-H(5)	120.6
C(6)-C(5)-H(5)	120.6
C(5)-C(6)-C(1)	120.87(15)
C(5)-C(6)-H(6)	119.6
C(1)-C(6)-H(6)	119.6
C(8)-C(7)-O(1)	109.76(13)
C(8)-C(7)-C(1)	132.98(15)
O(1)-C(7)-C(1)	117.11(14)
C(7)-C(8)-C(9)	107.10(14)
C(7)-C(8)-H(8)	126.5
C(9)-C(8)-H(8)	126.5
C(10)-C(9)-C(8)	106.07(14)
C(10)-C(9)-C(15)	127.23(14)
C(8)-C(9)-C(15)	126.64(14)
C(9)-C(10)-O(1)	110.31(13)
C(9)-C(10)-C(11)	132.46(15)
O(1)-C(10)-C(11)	117.20(14)
C(10)-C(11)-C(12)	115.30(13)
C(10)-C(11)-H(11A)	108.4
C(12)-C(11)-H(11A)	108.4
C(10)-C(11)-H(11B)	108.4
C(12)-C(11)-H(11B)	108.4
H(11A)-C(11)-H(11B)	107.5
C(13)-C(12)-C(11)	110.87(13)
C(13)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12A)	109.5
C(13)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	108.1

C(12)-C(13)-C(14)	113.44(15)
C(12)-C(13)-H(13A)	108.9
C(14)-C(13)-H(13A)	108.9
C(12)-C(13)-H(13B)	108.9
C(14)-C(13)-H(13B)	108.9
H(13A)-C(13)-H(13B)	107.7
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(9)-C(15)-C(16)	115.33(12)
C(9)-C(15)-H(15A)	108.4
C(16)-C(15)-H(15A)	108.4
C(9)-C(15)-H(15B)	108.4
C(16)-C(15)-H(15B)	108.4
H(15A)-C(15)-H(15B)	107.5
C(19)-C(16)-C(17)	114.21(13)
C(19)-C(16)-C(18)	112.79(13)
C(17)-C(16)-C(18)	108.61(13)
C(19)-C(16)-C(15)	108.77(13)
C(17)-C(16)-C(15)	104.51(12)
C(18)-C(16)-C(15)	107.43(13)
O(2)-C(17)-N(1)	120.70(15)
O(2)-C(17)-C(16)	122.01(15)
N(1)-C(17)-C(16)	116.93(13)
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(24)-C(19)-C(20)	118.37(15)
C(24)-C(19)-C(16)	121.00(14)
C(20)-C(19)-C(16)	120.42(14)
C(19)-C(20)-C(21)	120.43(14)
C(19)-C(20)-C(25)	119.42(14)

C(21)-C(20)-C(25)	120.15(14)
C(22)-C(21)-C(20)	120.17(16)
C(22)-C(21)-H(21)	119.9
C(20)-C(21)-H(21)	119.9
C(21)-C(22)-C(23)	119.76(16)
C(21)-C(22)-H(22)	120.1
C(23)-C(22)-H(22)	120.1
C(24)-C(23)-C(22)	120.15(16)
C(24)-C(23)-H(23)	119.9
C(22)-C(23)-H(23)	119.9
C(23)-C(24)-C(19)	121.10(16)
C(23)-C(24)-H(24)	119.5
C(19)-C(24)-H(24)	119.5
C(26)-C(25)-N(1)	109.42(13)
C(26)-C(25)-C(20)	131.85(15)
N(1)-C(25)-C(20)	118.72(14)
C(25)-C(26)-C(27)	107.59(14)
C(25)-C(26)-H(26)	126.2
C(27)-C(26)-H(26)	126.2
C(32)-C(27)-C(28)	119.71(15)
C(32)-C(27)-C(26)	132.35(16)
C(28)-C(27)-C(26)	107.90(14)
C(29)-C(28)-C(27)	122.33(15)
C(29)-C(28)-N(1)	130.65(15)
C(27)-C(28)-N(1)	107.00(13)
C(30)-C(29)-C(28)	116.80(16)
C(30)-C(29)-H(29)	121.6
C(28)-C(29)-H(29)	121.6
C(29)-C(30)-C(31)	121.69(16)
C(29)-C(30)-H(30)	119.2
C(31)-C(30)-H(30)	119.2
C(32)-C(31)-C(30)	120.96(16)
C(32)-C(31)-H(31)	119.5
C(30)-C(31)-H(31)	119.5
C(31)-C(32)-C(27)	118.46(16)
C(31)-C(32)-H(32)	120.8
C(27)-C(32)-H(32)	120.8
C(17)-N(1)-C(25)	124.50(13)

C(17)-N(1)-C(28)	126.11(14)
C(25)-N(1)-C(28)	108.05(13)
C(10)-O(1)-C(7)	106.76(12)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 240514h_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	20(1)	25(1)	34(1)	1(1)	7(1)	7(1)
C(1)	16(1)	19(1)	16(1)	-1(1)	2(1)	2(1)
C(2)	16(1)	20(1)	21(1)	-1(1)	3(1)	-1(1)
C(3)	20(1)	17(1)	23(1)	0(1)	4(1)	0(1)
C(4)	17(1)	21(1)	20(1)	-1(1)	2(1)	4(1)
C(5)	15(1)	23(1)	25(1)	-1(1)	4(1)	0(1)
C(6)	18(1)	18(1)	24(1)	0(1)	3(1)	-1(1)
C(7)	14(1)	20(1)	18(1)	1(1)	2(1)	0(1)
C(8)	16(1)	20(1)	18(1)	0(1)	1(1)	0(1)
C(9)	17(1)	20(1)	16(1)	0(1)	2(1)	3(1)
C(10)	16(1)	19(1)	18(1)	2(1)	4(1)	4(1)
C(11)	16(1)	22(1)	22(1)	3(1)	4(1)	3(1)
C(12)	18(1)	20(1)	23(1)	2(1)	4(1)	1(1)
C(13)	18(1)	32(1)	32(1)	6(1)	4(1)	-1(1)
C(14)	28(1)	40(1)	38(1)	11(1)	8(1)	-7(1)
C(15)	19(1)	20(1)	18(1)	-3(1)	2(1)	3(1)
C(16)	18(1)	16(1)	21(1)	-1(1)	4(1)	2(1)
C(17)	20(1)	16(1)	22(1)	0(1)	4(1)	1(1)
C(18)	28(1)	17(1)	30(1)	-2(1)	6(1)	5(1)
C(19)	17(1)	18(1)	19(1)	3(1)	2(1)	4(1)
C(20)	16(1)	19(1)	17(1)	3(1)	2(1)	2(1)
C(21)	17(1)	26(1)	20(1)	1(1)	1(1)	0(1)
C(22)	15(1)	35(1)	25(1)	2(1)	0(1)	-2(1)
C(23)	14(1)	36(1)	28(1)	3(1)	3(1)	4(1)
C(24)	19(1)	26(1)	23(1)	1(1)	5(1)	7(1)
C(25)	16(1)	18(1)	17(1)	2(1)	2(1)	-1(1)
C(26)	18(1)	21(1)	19(1)	-1(1)	4(1)	-1(1)
C(27)	18(1)	21(1)	18(1)	2(1)	5(1)	2(1)
C(28)	16(1)	20(1)	19(1)	2(1)	5(1)	2(1)
C(29)	18(1)	25(1)	23(1)	2(1)	4(1)	-2(1)
C(30)	15(1)	34(1)	28(1)	5(1)	5(1)	-1(1)
C(31)	19(1)	31(1)	28(1)	5(1)	9(1)	5(1)
C(32)	22(1)	24(1)	23(1)	0(1)	8(1)	4(1)

N(1)	15(1)	18(1)	19(1)	0(1)	4(1)	-1(1)
O(1)	14(1)	17(1)	22(1)	1(1)	4(1)	2(1)
O(2)	25(1)	24(1)	38(1)	-9(1)	8(1)	-7(1)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 240514h_0m.

	x	y	z	U(eq)
H(2)	5937	2893	6618	22
H(3)	7457	1430	6495	24
H(5)	9463	4653	6157	25
H(6)	7933	6115	6271	24
H(8)	6438	7560	6688	22
H(11A)	2556	5520	6429	24
H(11B)	2505	6560	6997	24
H(12A)	3028	3734	7134	24
H(12B)	3002	4774	7706	24
H(13A)	1082	4110	6904	33
H(13B)	1050	5177	7463	33
H(14A)	1481	2344	7639	52
H(14B)	305	3062	7763	52
H(14C)	1402	3420	8193	52
H(15A)	4792	9176	7188	23
H(15B)	3555	8550	7201	23
H(18A)	3213	11436	6203	37
H(18B)	4193	11378	6741	37
H(18C)	2958	10842	6875	37
H(21)	2368	6486	4901	25
H(22)	534	6725	5226	30
H(23)	162	8255	6023	31
H(24)	1621	9498	6509	27
H(26)	4349	5989	4763	23
H(29)	7268	9713	5547	27
H(30)	8759	8610	5073	31
H(31)	8475	6564	4544	31
H(32)	6676	5604	4428	27

Table S7. Torsion angles [°] for 240514h_0m.

C(6)-C(1)-C(2)-C(3)	2.2(2)
C(7)-C(1)-C(2)-C(3)	-176.26(14)
C(1)-C(2)-C(3)-C(4)	-0.1(2)
C(2)-C(3)-C(4)-C(5)	-1.7(2)
C(2)-C(3)-C(4)-Br(1)	-178.85(12)
C(3)-C(4)-C(5)-C(6)	1.3(2)
Br(1)-C(4)-C(5)-C(6)	178.46(12)
C(4)-C(5)-C(6)-C(1)	0.8(2)
C(2)-C(1)-C(6)-C(5)	-2.5(2)
C(7)-C(1)-C(6)-C(5)	175.94(14)
C(2)-C(1)-C(7)-C(8)	164.05(17)
C(6)-C(1)-C(7)-C(8)	-14.4(3)
C(2)-C(1)-C(7)-O(1)	-11.2(2)
C(6)-C(1)-C(7)-O(1)	170.39(13)
O(1)-C(7)-C(8)-C(9)	-0.14(17)
C(1)-C(7)-C(8)-C(9)	-175.62(15)
C(7)-C(8)-C(9)-C(10)	0.09(17)
C(7)-C(8)-C(9)-C(15)	-177.51(14)
C(8)-C(9)-C(10)-O(1)	-0.01(17)
C(15)-C(9)-C(10)-O(1)	177.57(13)
C(8)-C(9)-C(10)-C(11)	-178.00(16)
C(15)-C(9)-C(10)-C(11)	-0.4(3)
C(9)-C(10)-C(11)-C(12)	-130.51(18)
O(1)-C(10)-C(11)-C(12)	51.61(19)
C(10)-C(11)-C(12)-C(13)	178.93(14)
C(11)-C(12)-C(13)-C(14)	-178.59(16)
C(10)-C(9)-C(15)-C(16)	-92.26(19)
C(8)-C(9)-C(15)-C(16)	84.84(19)
C(9)-C(15)-C(16)-C(19)	63.71(17)
C(9)-C(15)-C(16)-C(17)	-58.66(17)
C(9)-C(15)-C(16)-C(18)	-173.92(14)
C(19)-C(16)-C(17)-O(2)	163.24(15)
C(18)-C(16)-C(17)-O(2)	36.4(2)
C(15)-C(16)-C(17)-O(2)	-78.02(19)
C(19)-C(16)-C(17)-N(1)	-23.6(2)
C(18)-C(16)-C(17)-N(1)	-150.42(14)

C(15)-C(16)-C(17)-N(1)	95.15(16)
C(17)-C(16)-C(19)-C(24)	-162.37(14)
C(18)-C(16)-C(19)-C(24)	-37.7(2)
C(15)-C(16)-C(19)-C(24)	81.34(18)
C(17)-C(16)-C(19)-C(20)	23.0(2)
C(18)-C(16)-C(19)-C(20)	147.60(15)
C(15)-C(16)-C(19)-C(20)	-93.33(16)
C(24)-C(19)-C(20)-C(21)	0.5(2)
C(16)-C(19)-C(20)-C(21)	175.31(14)
C(24)-C(19)-C(20)-C(25)	-179.50(14)
C(16)-C(19)-C(20)-C(25)	-4.7(2)
C(19)-C(20)-C(21)-C(22)	-0.6(2)
C(25)-C(20)-C(21)-C(22)	179.40(15)
C(20)-C(21)-C(22)-C(23)	0.7(3)
C(21)-C(22)-C(23)-C(24)	-0.7(3)
C(22)-C(23)-C(24)-C(19)	0.6(3)
C(20)-C(19)-C(24)-C(23)	-0.5(2)
C(16)-C(19)-C(24)-C(23)	-175.30(15)
C(19)-C(20)-C(25)-C(26)	166.80(16)
C(21)-C(20)-C(25)-C(26)	-13.2(3)
C(19)-C(20)-C(25)-N(1)	-13.8(2)
C(21)-C(20)-C(25)-N(1)	166.23(14)
N(1)-C(25)-C(26)-C(27)	1.18(18)
C(20)-C(25)-C(26)-C(27)	-179.34(16)
C(25)-C(26)-C(27)-C(32)	175.95(17)
C(25)-C(26)-C(27)-C(28)	-1.84(18)
C(32)-C(27)-C(28)-C(29)	2.4(2)
C(26)-C(27)-C(28)-C(29)	-179.52(15)
C(32)-C(27)-C(28)-N(1)	-176.36(14)
C(26)-C(27)-C(28)-N(1)	1.76(17)
C(27)-C(28)-C(29)-C(30)	-1.8(2)
N(1)-C(28)-C(29)-C(30)	176.57(16)
C(28)-C(29)-C(30)-C(31)	-0.2(3)
C(29)-C(30)-C(31)-C(32)	1.7(3)
C(30)-C(31)-C(32)-C(27)	-1.2(3)
C(28)-C(27)-C(32)-C(31)	-0.8(2)
C(26)-C(27)-C(32)-C(31)	-178.38(17)
O(2)-C(17)-N(1)-C(25)	179.88(15)

C(16)-C(17)-N(1)-C(25)	6.6(2)
O(2)-C(17)-N(1)-C(28)	14.7(3)
C(16)-C(17)-N(1)-C(28)	-158.56(14)
C(26)-C(25)-N(1)-C(17)	-167.54(15)
C(20)-C(25)-N(1)-C(17)	12.9(2)
C(26)-C(25)-N(1)-C(28)	-0.09(17)
C(20)-C(25)-N(1)-C(28)	-179.65(13)
C(29)-C(28)-N(1)-C(17)	-12.4(3)
C(27)-C(28)-N(1)-C(17)	166.13(15)
C(29)-C(28)-N(1)-C(25)	-179.63(16)
C(27)-C(28)-N(1)-C(25)	-1.06(17)
C(9)-C(10)-O(1)-C(7)	-0.08(16)
C(11)-C(10)-O(1)-C(7)	178.26(13)
C(8)-C(7)-O(1)-C(10)	0.14(16)
C(1)-C(7)-O(1)-C(10)	176.42(12)

Symmetry transformations used to generate equivalent atoms:

Table S8. Hydrogen bonds for 240514h_0m [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

10) Biological Assays

The bis-heterocyclic products were dissolved in 10 mL DMSO to generate a 50 μg/mL solution. DMSO was used as the negative control. The antifungal activities of bis-heterocyclic products were investigated against four phytopathogenic fungi (*Fusarium species*, *Botryosphaeria dothidea*, *Rhizotonia solani*, *Sclerotinia sclerotiorum*) at the concentration of 50 μg/mL using mycelial growth inhibitory rate methods on PDA,[11] with Osthole or Carbendazim used as the positive control (Table S9). The EC50 values of products **3** were further evaluated at different concentration by diluting the 50 μg/mL solution (Table S10).[11]

Table S9. Antifungal activity of bis-heterocyclic products **3** (inhibitory rate, %)[a]

Compound	inhibition rate (%) (50 μg/mL)			
	Fusarium species	*Botryosphaeria dothidea*	*Rhizoctonia solani*	*Sclerotinia sclerotiorum*
3aa	58.79	33.61	45.78	65.52
3ba	31.55	29.87	27.92	62.62
3ca	44.27	19.41	63.47	66.25
3da	57.16	**69.26**	45.67	72.97
3ea	67.07	51.19	30.74	66.62
3fa	68.68	48.41	54.77	48.22
3ga	51.53	36.86	40.95	56.48
3ha	16.41	14.43	42.44	53.54
3ia	46.45	64.88	59.27	**79.69**
3ja	38.37	27.12	70.77	62.17
3ka	55.65	57.79	53.07	62.73
3la	63.40	33.63	51.96	75.06
3ab	57.79	65.35	61.25	67.11
3ac	53.44	38.80	41.58	50.92
3ad	55.22	37.51	54.39	36.52
3ae	54.37	51.03	44.22	30.20
3af	16.64	31.44	29.61	58.29
3ag	54.90	40.61	52.44	53.21
3ah	66.14	51.02	49.73	52.58
3ai	61.15	56.55	49.71	55.98
3aj	46.60	56.94	38.36	66.97
3ak	**72.89**	30.88	72.48	60.23
3al	49.15	45.98	62.10	68.16
3am	66.01	48.47	62.08	49.94

3an	67.41	62.35	62.41	62.21
3ao	**72.50**	59.59	48.09	66.14
3ap	44.84	20.53	64.64	48.27
3aq	49.11	46.18	46.50	58.67
3ar	46.75	**68.72**	**79.38**	44.57
3as	40.91	48.10	60.13	72.21
3at	45.44	60.19	76.65	65.49
Osthole	96.45	96.66	98.05	95.61
Carbendazim	98.77	99.25	99.69	99.70

[a]All the data was the average value of three replications.

Table S10. EC_{50} determination of bis-heterocyclic compounds **3ao**, **3ak**, **3ar**, **3da**, **3ar** and **3ia**[a]

pathogen	compound	R	toxic regression	EC_{50} (μg/mL)	95% confidence interval
Fusarium species	**3ao**	0.9876	y = 1.6827x + 2.2740	41.6827	34.1657-53.7606
	3ak	0.9943	y = 1.2998x + 3.0292	32.8266	26.4270-42.9206
	Osthole	0.9400	y = 1.9505x + 5.4211	0.6083	0.2226-1.0424
	Carbendazim	0.9513	y = 2.3476x + 5.7305	0.4885	0.0785-1.0147
Botryosphaeria dothidea	**3ar**	0.9790	y = 0.9378x + 3.8046	18.8228	13.9987-25.0309
	3da	0.9864	y = 1.0005x + 3.7818	16.5014	12.3084-21.4472
	Osthole	0.9275	y = 1.6297x + 5.7149	0.3642	0.0712-0.7753
	Carbendazim	0.9507	y = 1.9876x + 5.9258	0.3421	0.0274-0.8421
Rhizoctonia solani	**3ar**	0.9713	y = 2.9401x + 1.2901	18.2751	14.0863-23.2702
	Osthole	0.9530	y = 2.1750x + 5.3899	0.6618	0.2478-1.1131
	Carbendazim	0.9559	y = 2.0448x + 5.8715	0.3748	0.0386-0.8761
Sclerotinia sclerotiorum	**3ia**	0.9811	y = 2.0842x + 1.9500	29.0680	25.1432-34.2875
	Osthole	0.9304	y = 1.7859x + 5.4863	0.5342	0.1764-0.9568
	Carbendazim	0.9499	y = 2.0577x + 5.9599	0.3416	0.0214-0.8641

[a]The EC_{50} value was the average value of three replications.

11) References

(1) C. P. Rosenau, B. J. Jelier, A. D. Gossert, and A. Togni, *Angew. Chem. Int. Ed*., **2018**, *57*, 9528-9533.

(2) X. Abel-Snape, C. E. Johnson, B. Imbriaco, and M. Lautens, *Chem. Sci*., **2023**, 14, 5650-5655.

(3) X. Yang, H. Lu, X. Zhu, L. Zhou, G. Deng, Y. Yang, and Y. Liang, *Org. Lett*., **2019**, 21, 7284-7288.

(4) J.-S. Wang, J. Zhang, S. Wang, J. Ying, C.-Y. Li, and X.-F. Wu, *J. Catal*. **2022**, *414*, 313-318.

(5) F. Li, Y. Yuan, D. Lyu, Y, Yi, J. Zhang, T. Sun and G. Gao, *J. Org. Chem*., **2024**, 89, 7552-7560.

(6) S. Borra, H. Y. Kim, and K. Oh, *Org. Lett*., **2023**, 25, 288-292.

(7) Y. Zhang, J. Zhang, Y. Yuan, L. Liu, B. Chen, and T. Sun, *Eur. J. Org. Chem*., **2020**, 1976-1986.

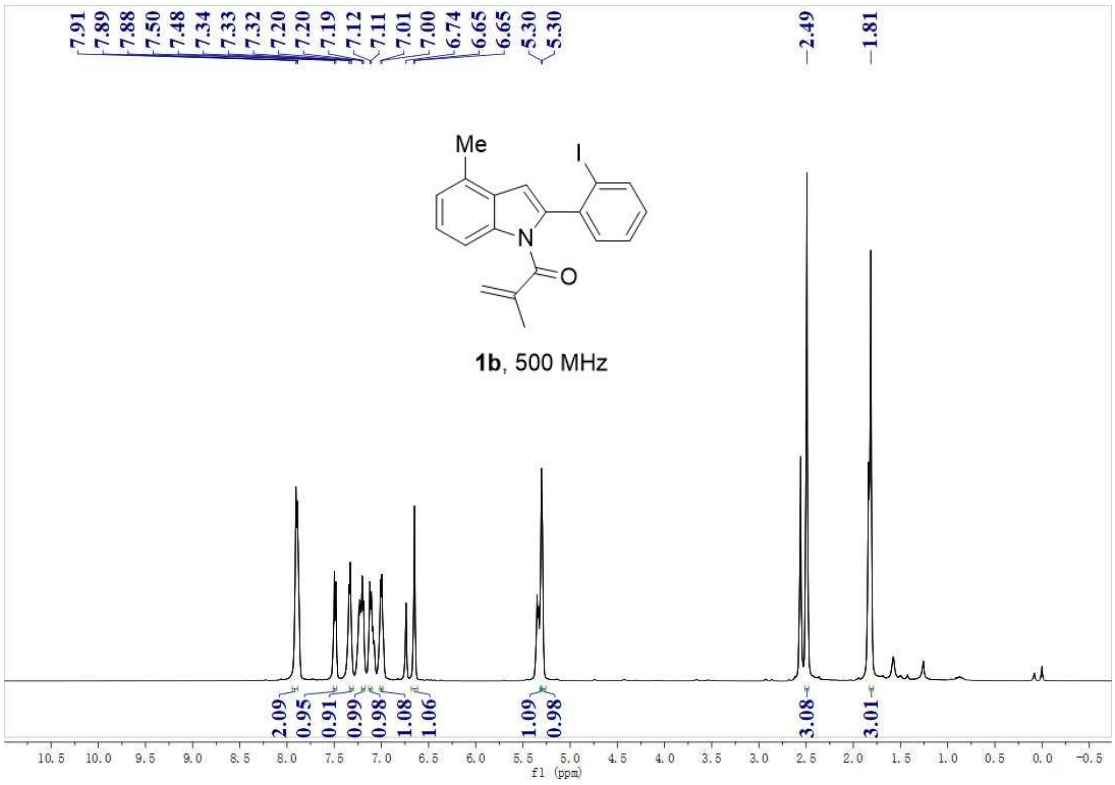
(8) H. Qi, D. Chi, and S. Chen, *Org. Lett*. **2022**, *24*, 2910-2914.

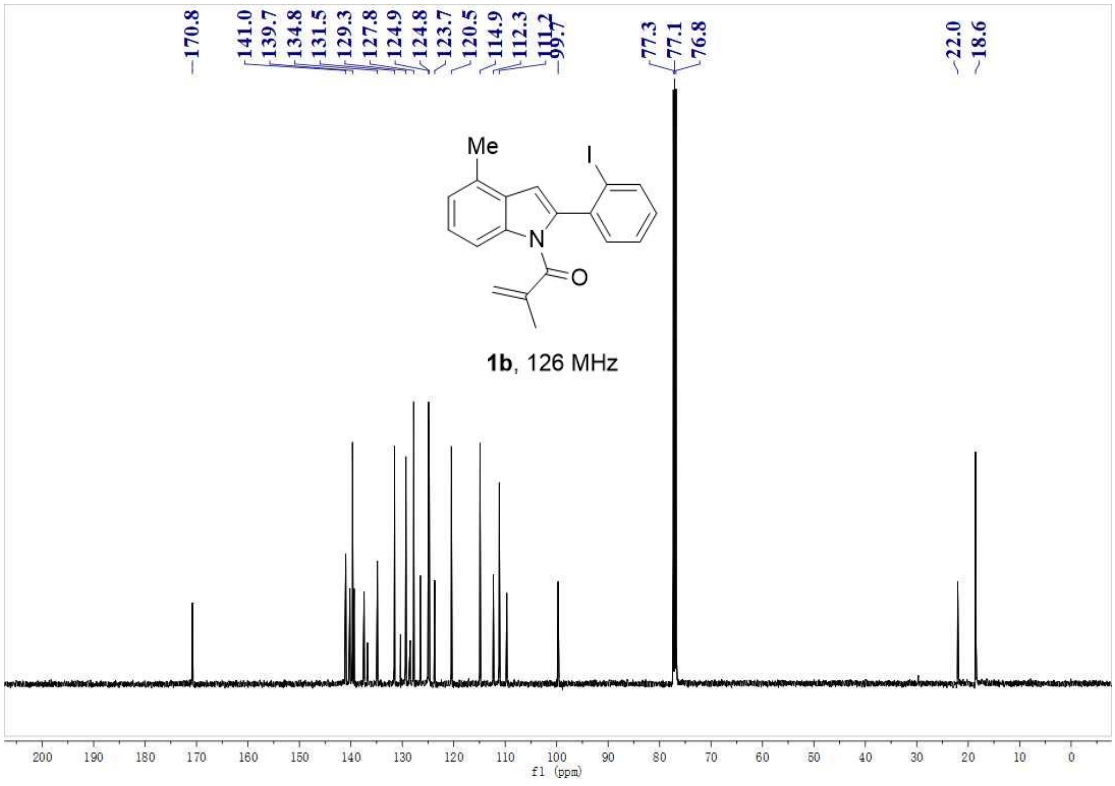
(9) P. Yu, A. Bismuto, and B. Morandi, *Angew. Chem. Int. Ed*. **2020**, *59*, 2904-2910.

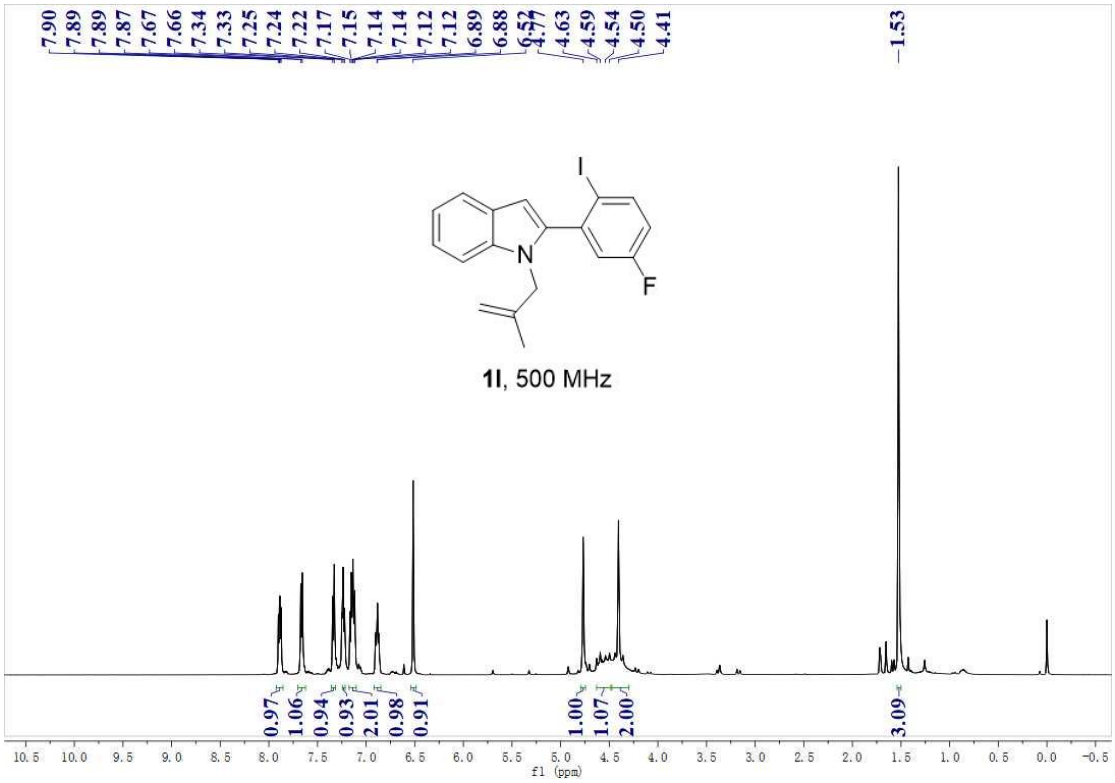
(10) H. Y. Kim, J.-Y. Li, and K. Oh, *J. Org. Chem.,* **2012**, *77*, 11132-11145.

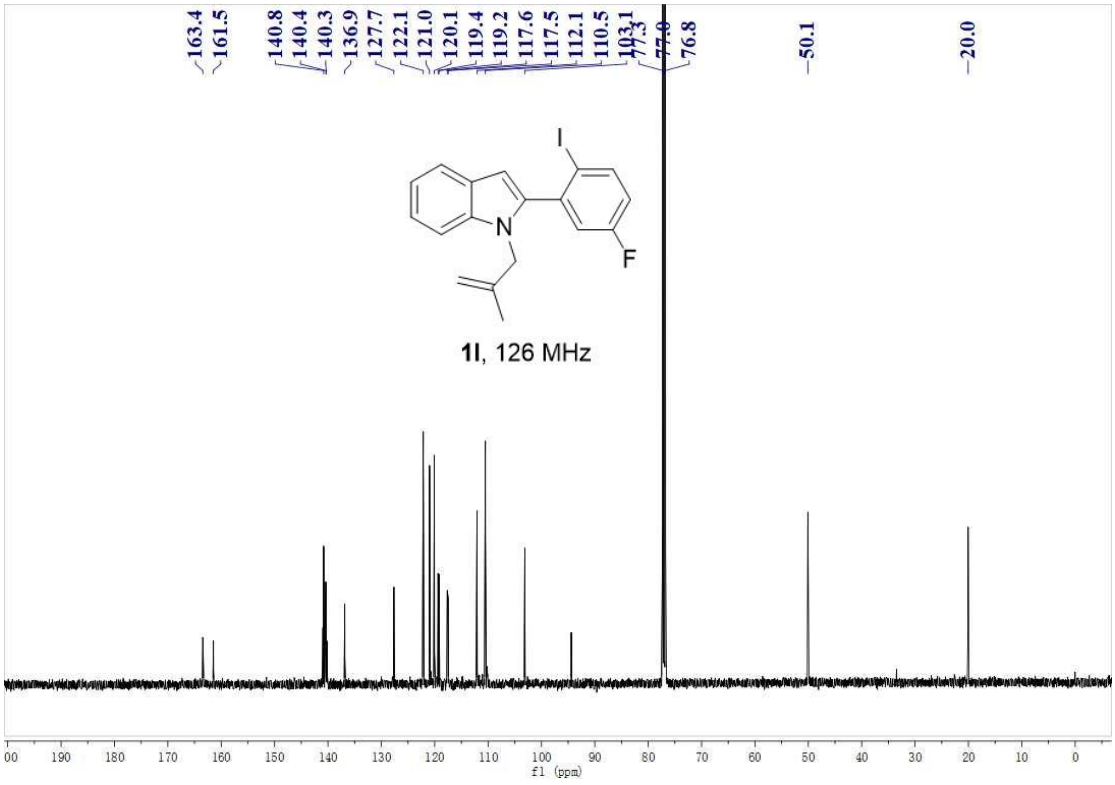
(11) (a) D. Du, C. Ji, S. Zheng, Y. Chen, H. Cai, Z. Li, D. Yan, and H. Teng, *Adv. Synth. Catal*., **2024**, *366*, 1738-1743; (b) P. Dai, K. Luo, X. Yu, W.-C. Yang, L. Wu, and W.-H. Zhang, *Adv. Synth. Catal*., **2018**, *360*, 468-473; (c) P. Dai, X. Yu, P. Teng, and W.-H. Zhang, C. Deng, *Org. Lett.*, **2018**, *20*, 6901-6905.

12) NMR Spectra

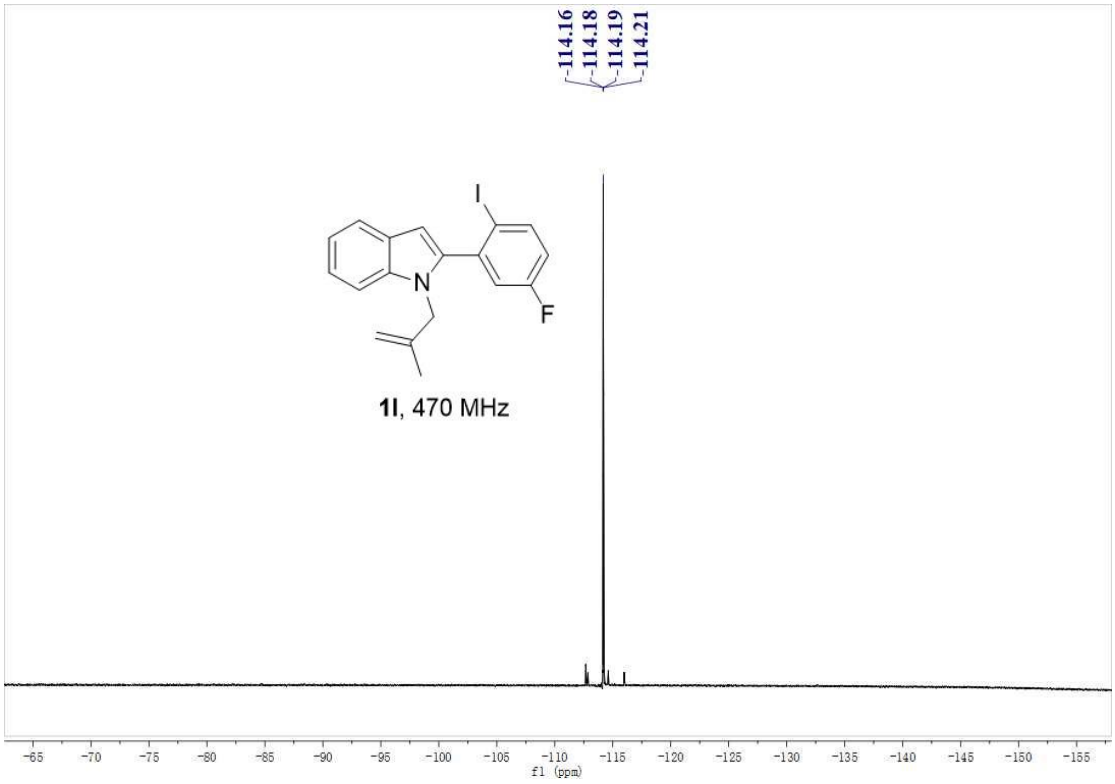




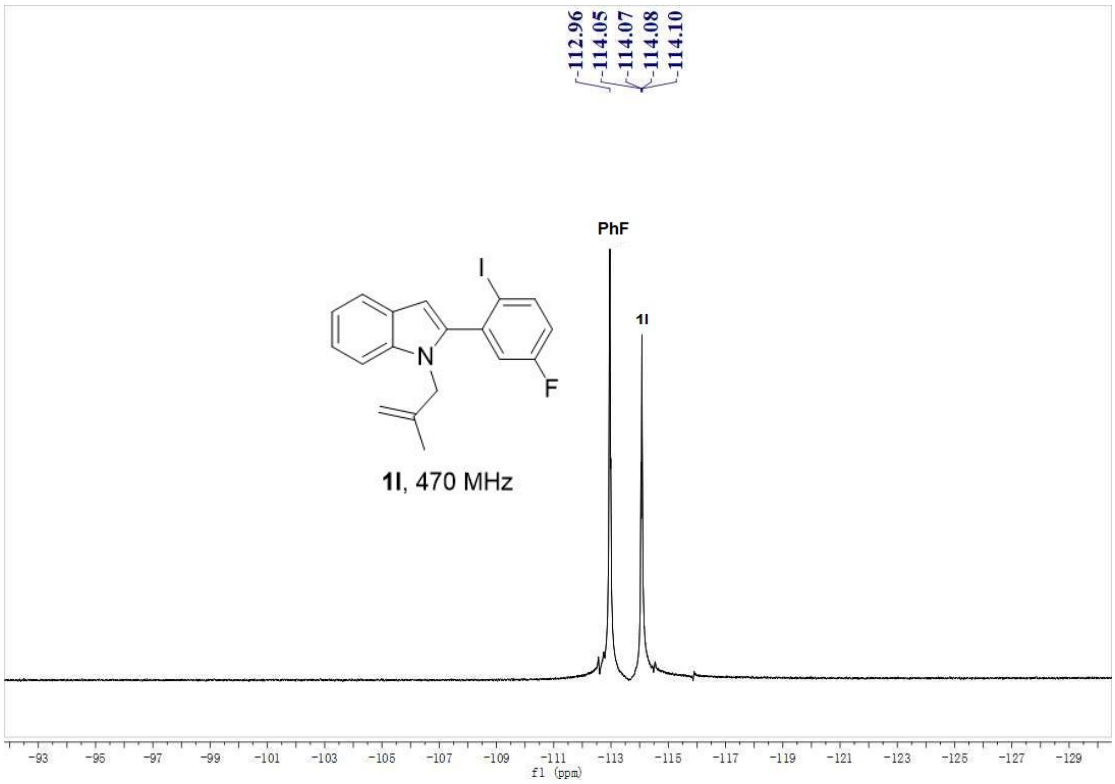

7.90
7.89
7.89
7.87
7.67
7.66
7.34
7.33
7.25
7.24
7.22
7.17
7.15
7.14
7.14
7.12
7.12
6.89
6.88
6.52
4.77
4.63
4.59
4.54
4.50
4.41
1.53
I
N
F
1I, 500 MHz
0.97
1.06
0.94
0.93
2.01
0.98
0.91
1.00
1.07
2.00
3.09
f1 (ppm)

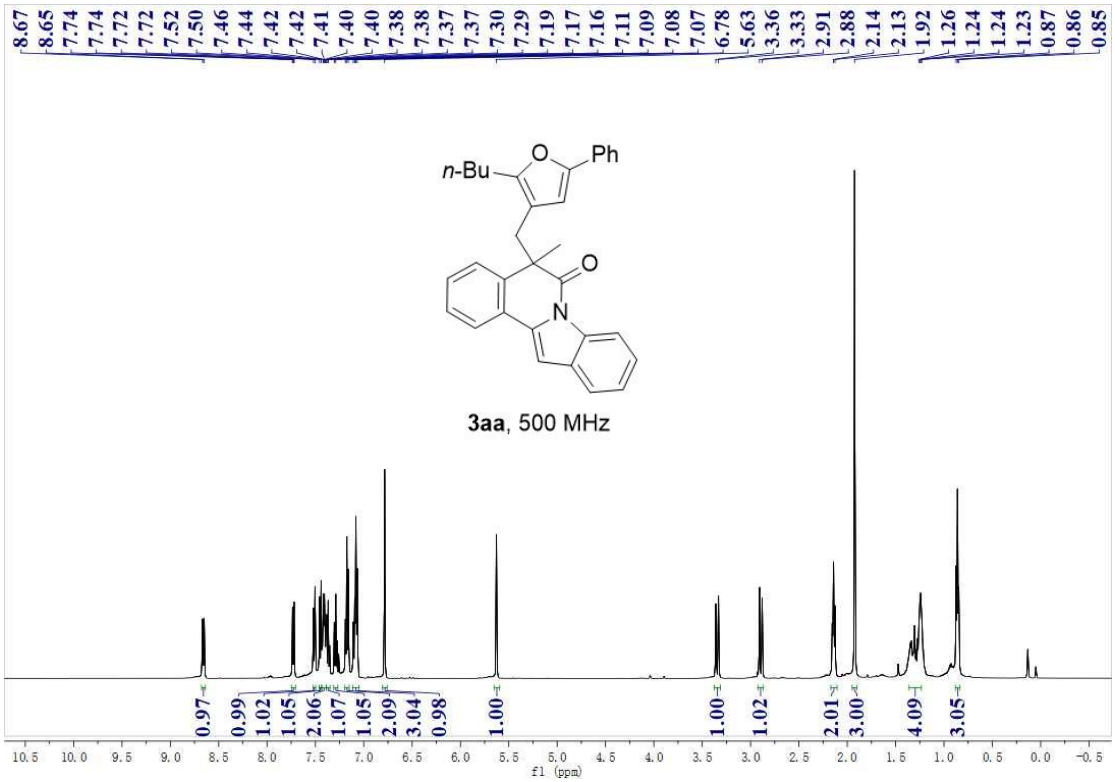

163.4
161.5
140.8
140.4
140.3
136.9
127.7
122.1
121.0
120.1
119.4
119.2
117.6
117.5
112.1
110.5
103.1
77.3
77.0
76.8
50.1
20.0
I
N
F
1I, 126 MHz
f1 (ppm)

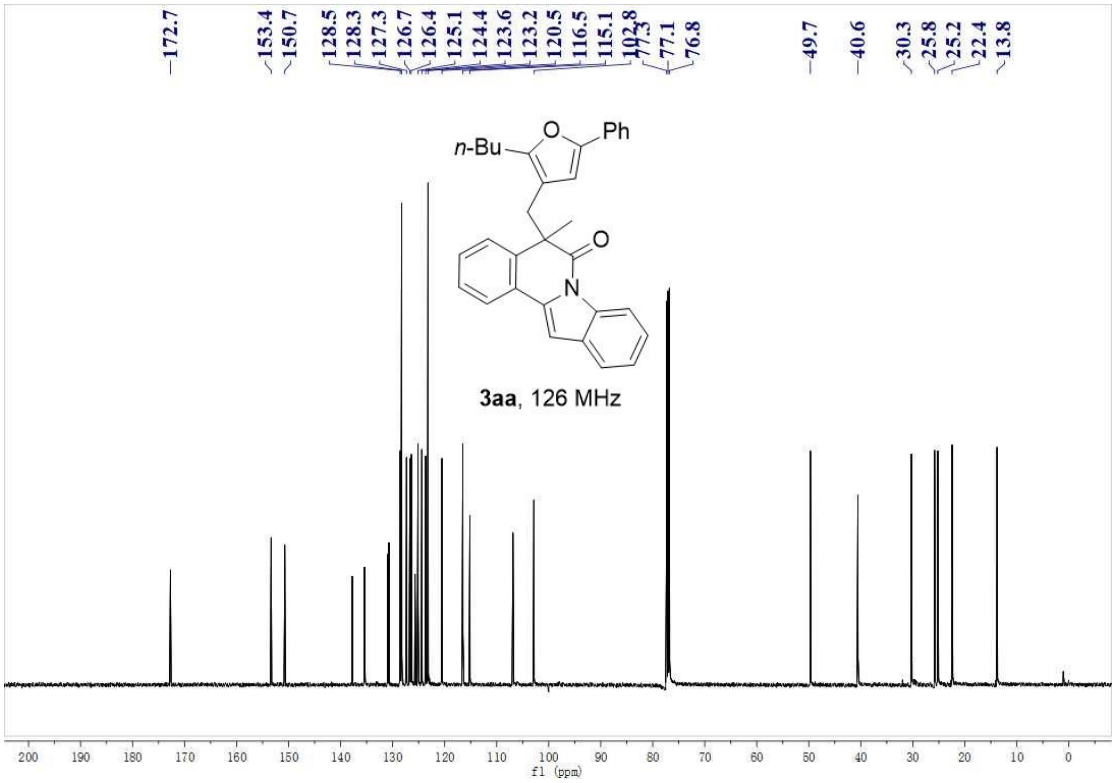
^{19}F NMR spectrum of **1l** without using internal reference compound

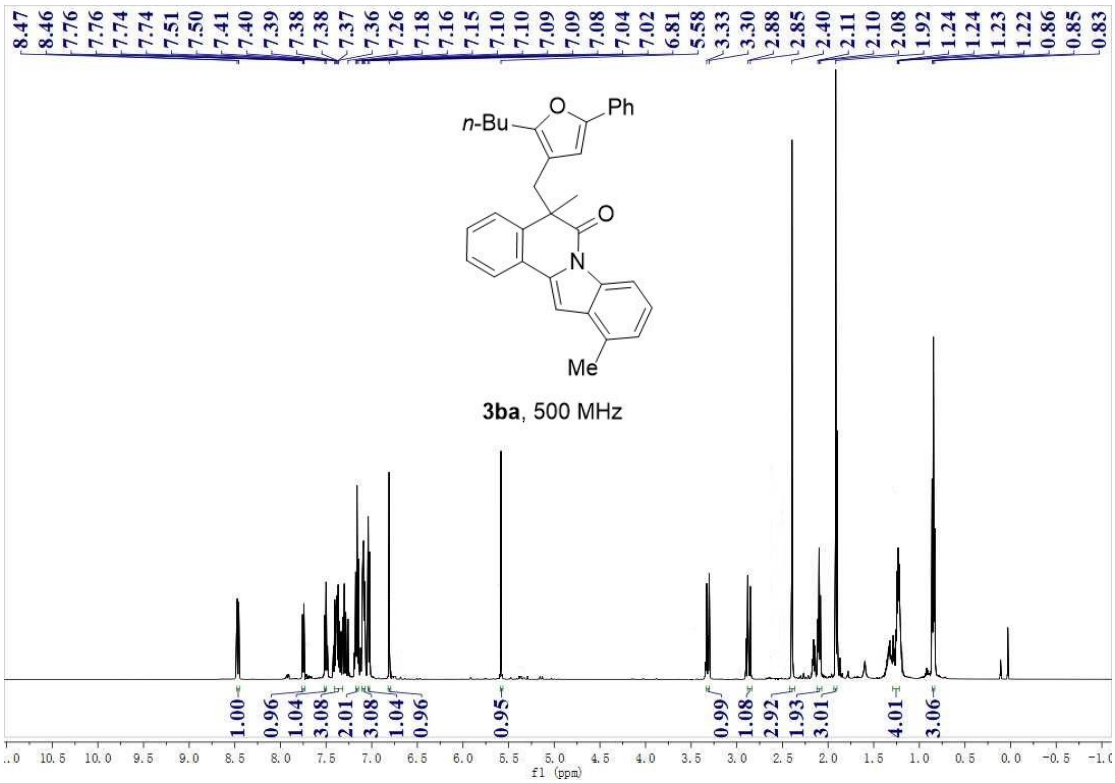


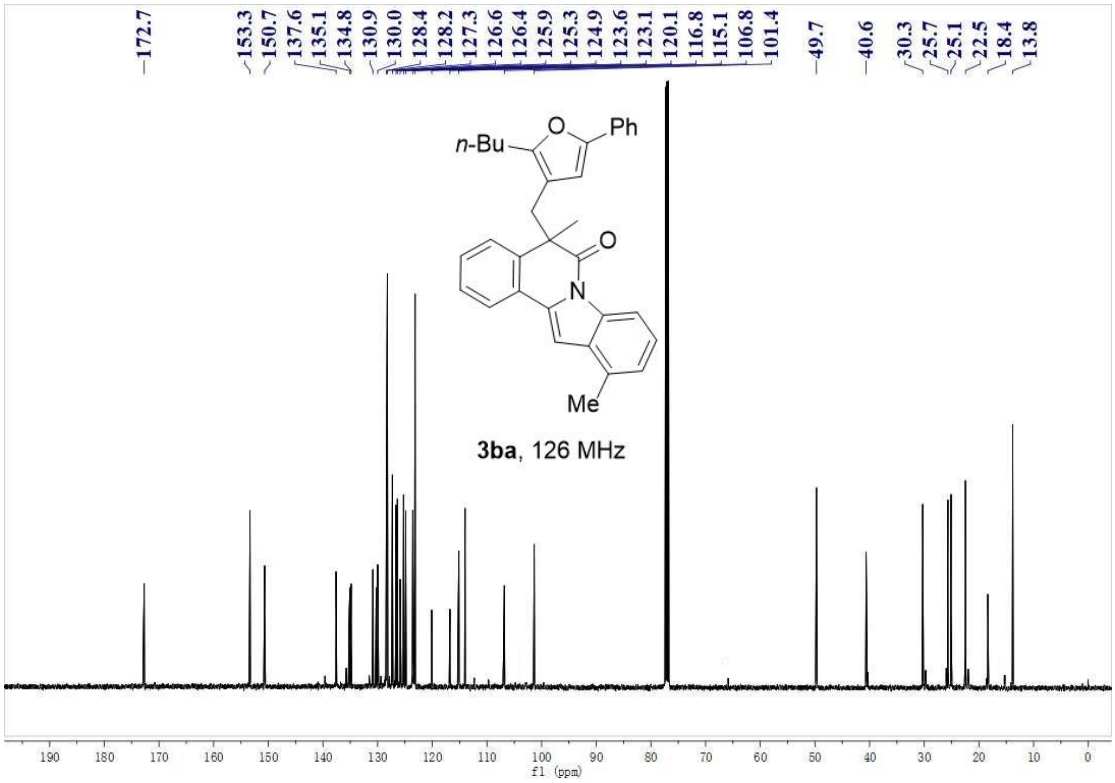
^{19}F NMR spectrum of **1l** referenced with PhF (-112.96) in $CDCl_3$

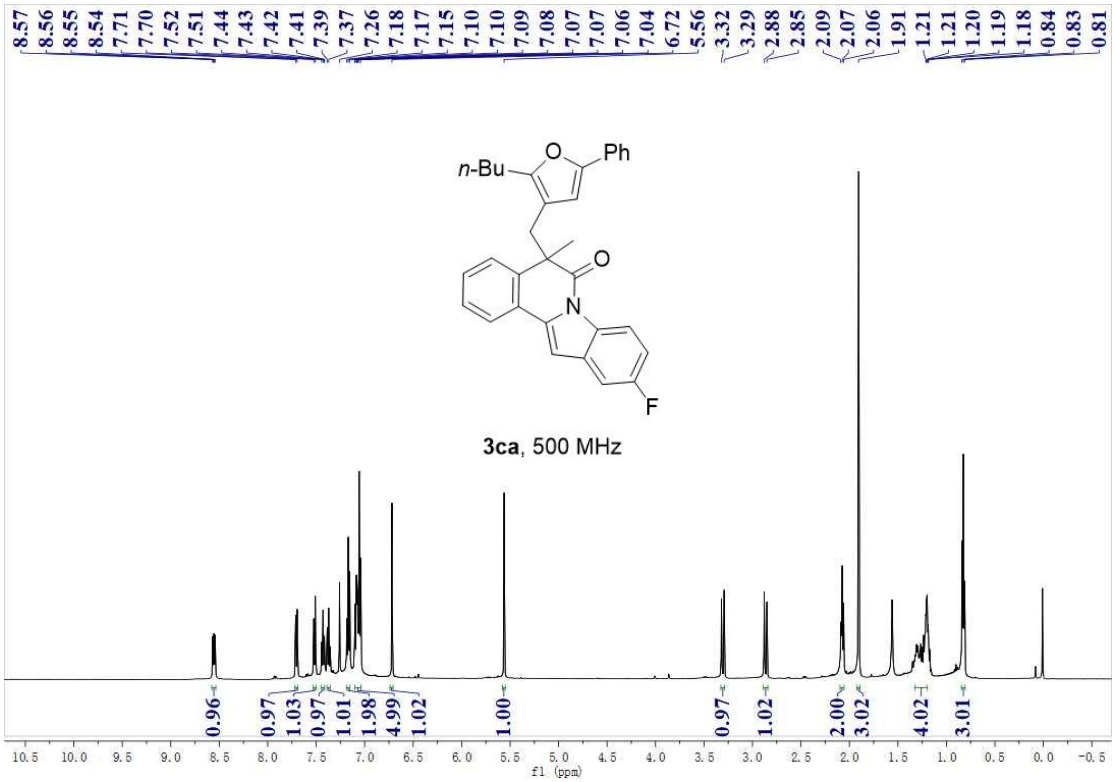


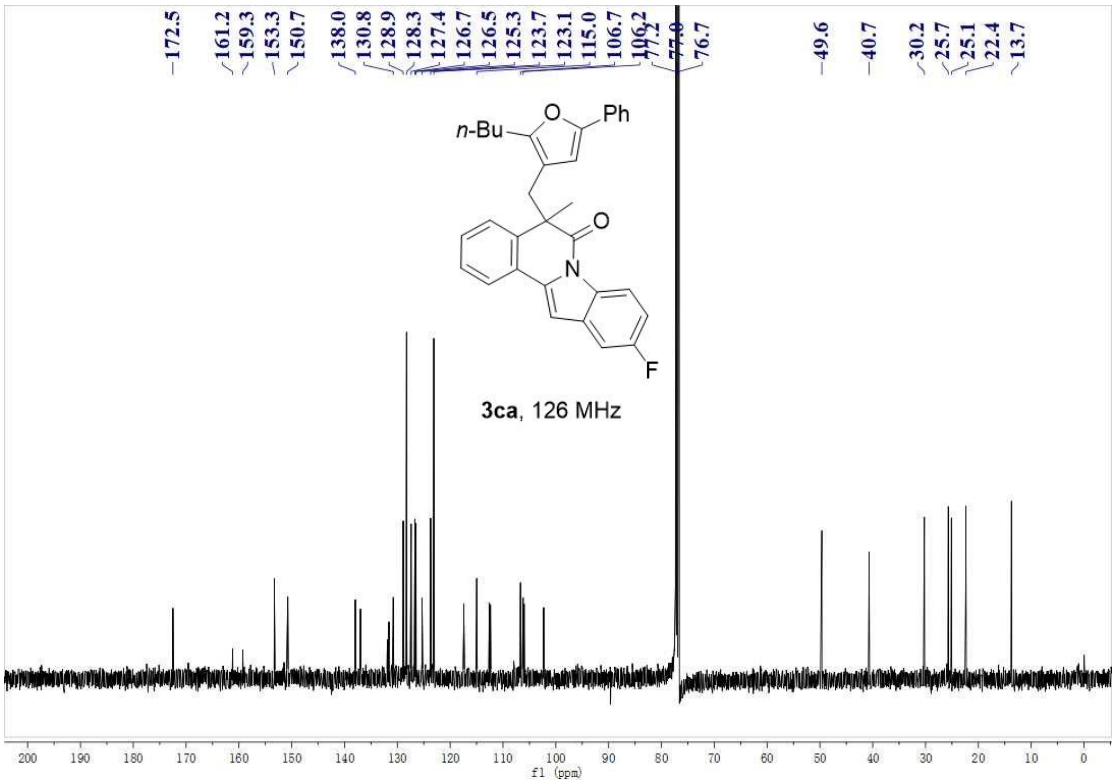

8.67 8.65 7.74 7.74 7.72 7.72 7.52 7.50 7.46 7.44 7.42 7.42 7.41 7.40 7.40 7.38 7.38 7.37 7.37 7.30 7.29 7.19 7.17 7.16 7.11 7.09 7.08 7.07 6.78 5.63 3.36 3.33 2.91 2.88 2.14 2.13 1.92 1.26 1.24 1.24 1.23 0.87 0.86 0.85
n-Bu
O
Ph
O
N
3aa, 500 MHz
0.97 0.99 1.02 1.05 2.06 1.07 1.05 2.09 3.04 0.98 1.00 1.00 1.02 2.01 3.00 4.09 3.05
f1 (ppm)


172.7
153.4 150.7
128.5 128.3 127.3 126.7 126.4 125.1 124.4 123.6 123.2 120.5 116.5 115.1 102.8 77.3 77.1 76.8
49.7 40.6 30.3 25.8 25.2 22.4 13.8
n-Bu
O
Ph
O
N
3aa, 126 MHz
f1 (ppm)

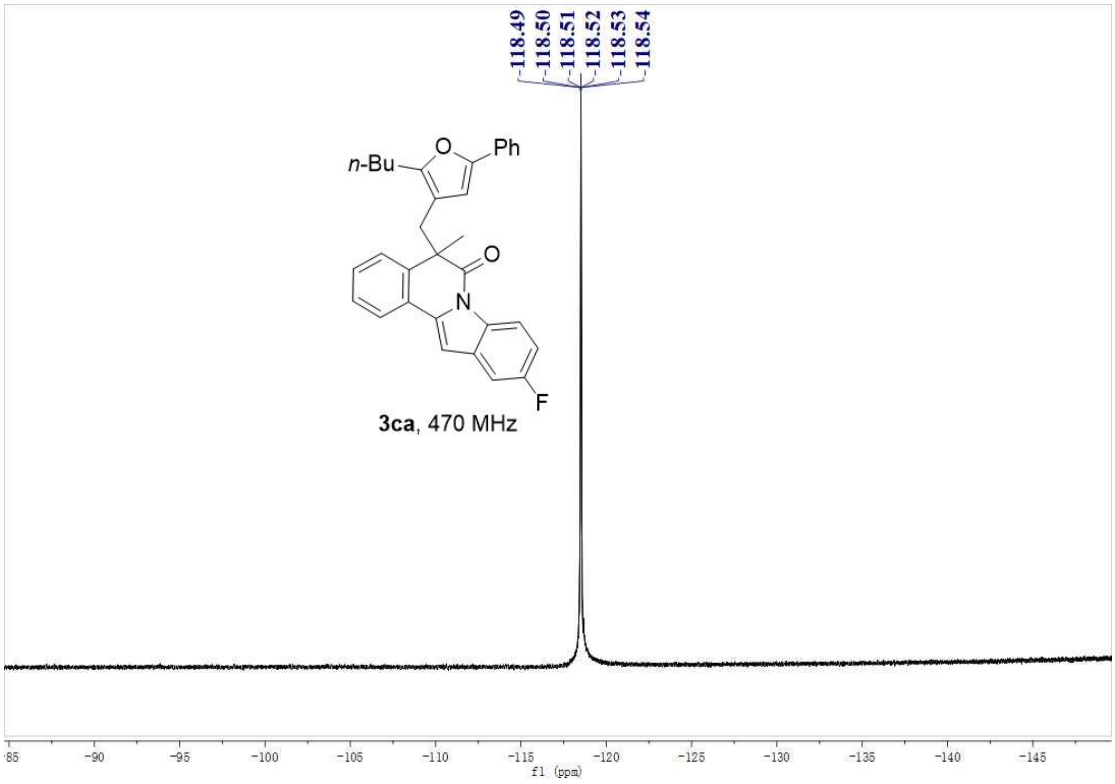

8.47 8.46 7.76 7.76 7.74 7.74 7.51 7.50 7.41 7.40 7.39 7.38 7.38 7.37 7.36 7.26 7.18 7.16 7.15 7.10 7.10 7.09 7.09 7.08 7.04 7.02 6.81 5.58 3.33 3.30 2.88 2.85 2.40 2.11 2.10 2.08 1.92 1.24 1.24 1.23 1.22 0.86 0.85 0.83
n-Bu
O
Ph
O
N
Me
3ba, 500 MHz
1.00 0.96 1.04 3.08 2.01 3.08 1.04 0.96 0.95 0.99 1.08 2.92 1.93 3.01 4.01 3.06
f1 (ppm)


172.7 153.3 150.7 137.6 135.1 134.8 130.9 130.0 128.4 128.2 127.3 126.6 126.4 125.9 125.3 124.9 123.6 123.1 120.1 116.8 115.1 106.8 101.4 49.7 40.6 30.3 25.7 25.1 22.5 18.4 13.8
n-Bu
O
Ph
O
N
Me
3ba, 126 MHz
f1 (ppm)

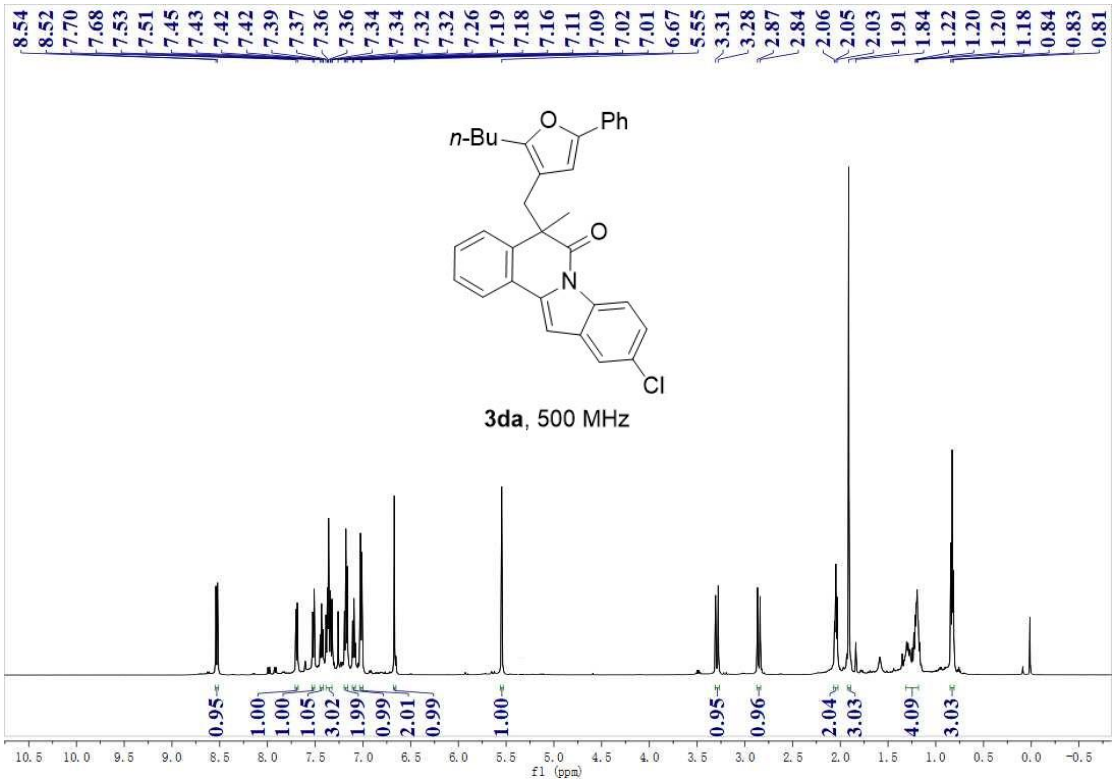

8.57 8.56 8.55 8.54 7.71 7.70 7.52 7.51 7.44 7.43 7.42 7.41 7.39 7.37 7.26 7.18 7.17 7.15 7.10 7.10 7.09 7.08 7.07 7.07 7.06 7.04 6.72 5.56 3.32 3.29 2.88 2.85 2.09 2.07 2.06 1.91 1.21 1.21 1.20 1.19 1.18 0.84 0.83 0.81
n-Bu
O
Ph
O
N
F
3ca, 500 MHz
0.96 0.97 1.03 0.97 1.01 1.98 4.99 1.02 1.00 0.97 1.02 2.00 3.02 4.02 3.01
f1 (ppm)

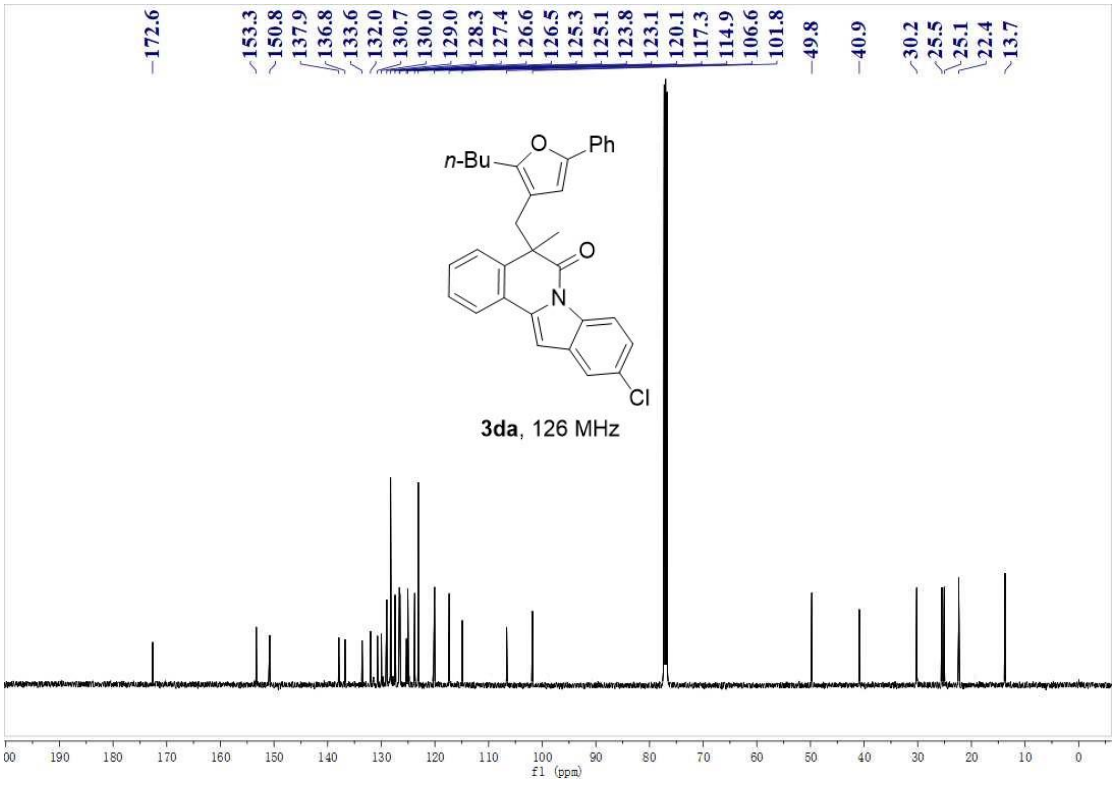

172.5 161.2 159.3 153.3 150.7 138.0 130.8 128.9 128.3 127.4 126.7 126.5 125.3 123.7 123.1 115.0 106.7 106.2 77.2 77.0 76.7 49.6 40.7 30.2 25.7 25.1 22.4 13.7
n-Bu
O
Ph
O
N
F
3ca, 126 MHz
f1 (ppm)

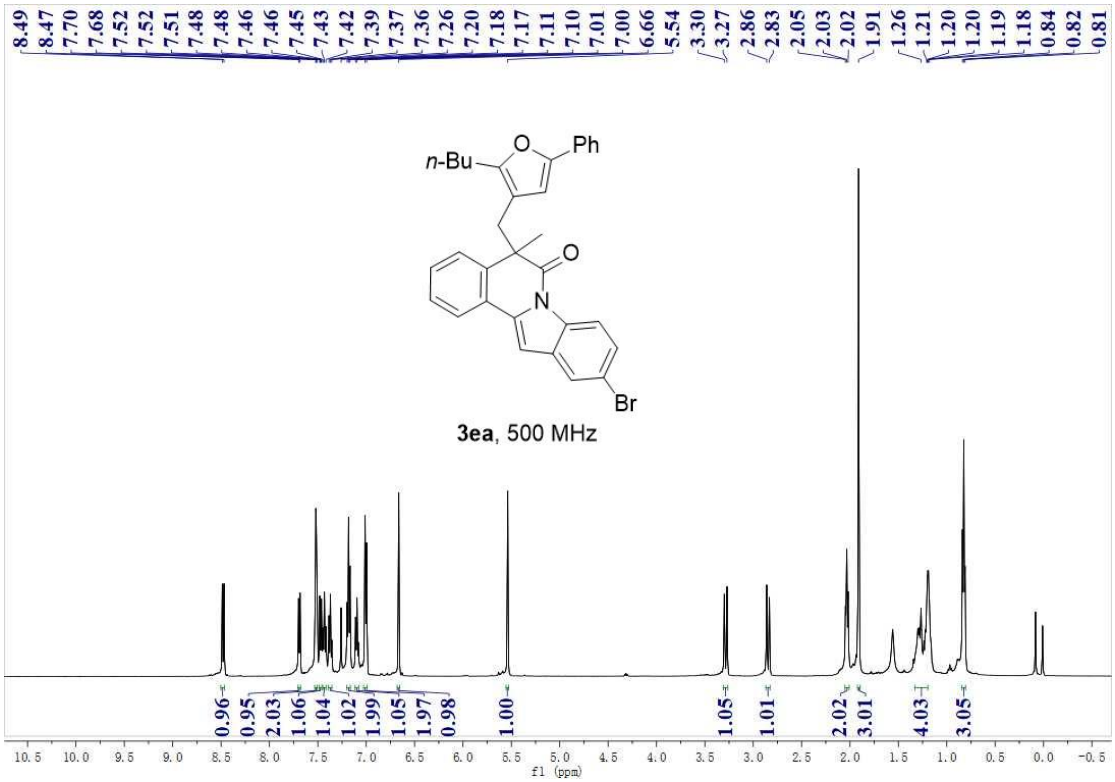
^{19}F NMR spectrum of **3ca** without using internal reference compound

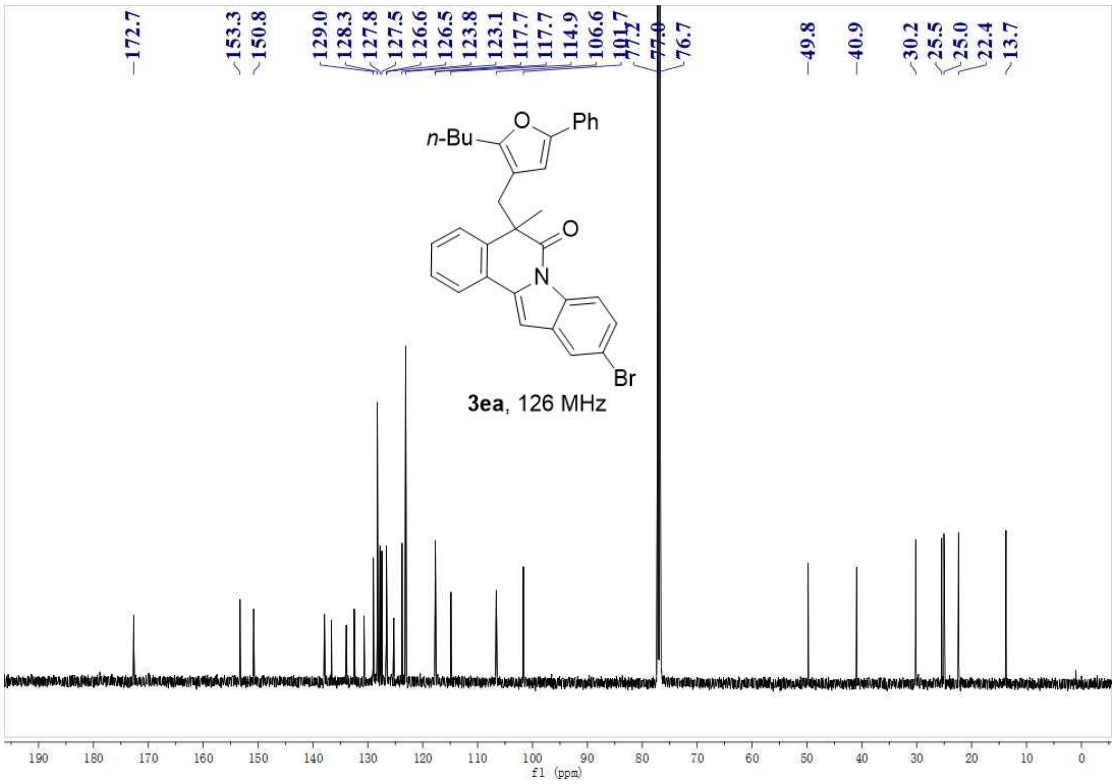


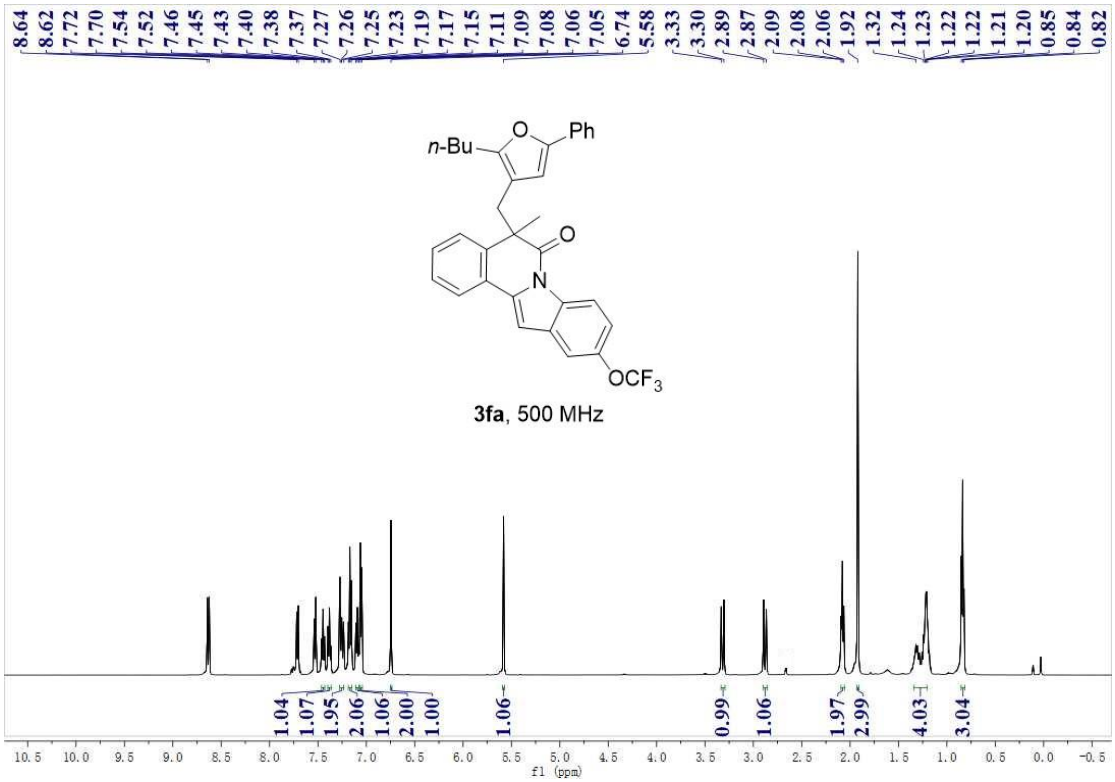
^{19}F NMR spectrum of **3ca** referenced with PhF (-112.96) in $CDCl_3$

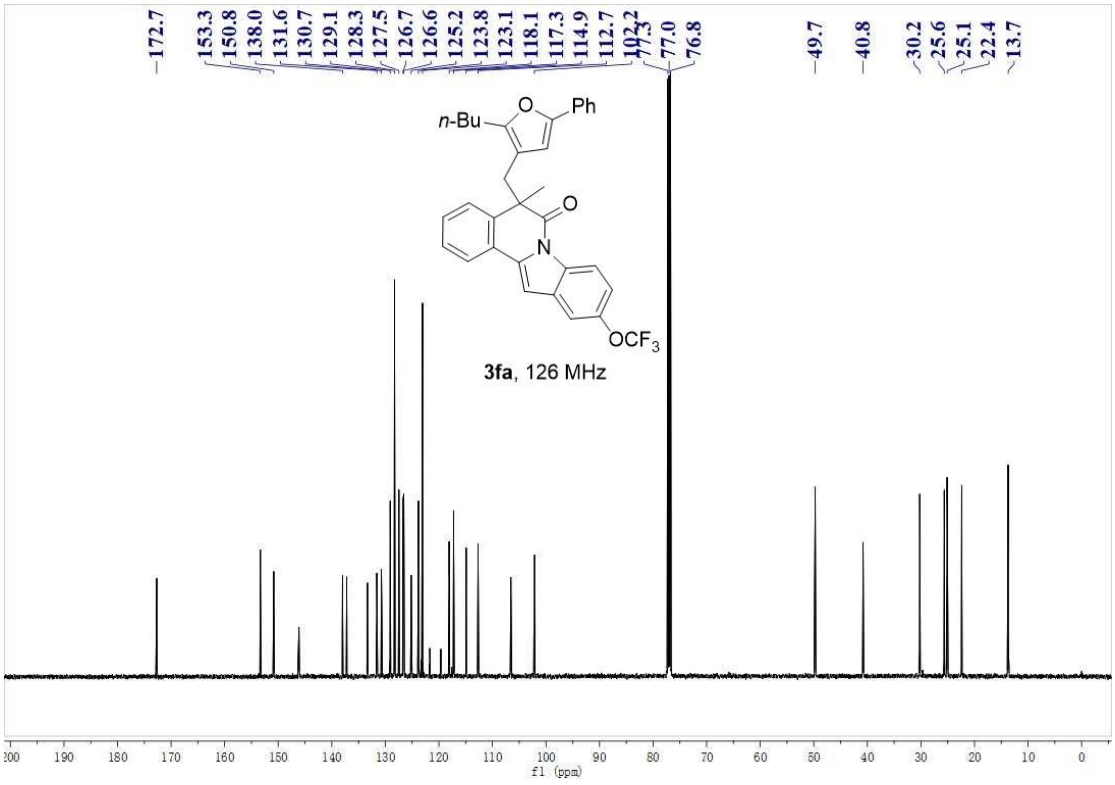

8.54 8.52 7.70 7.68 7.53 7.51 7.45 7.43 7.42 7.42 7.39 7.37 7.36 7.36 7.34 7.34 7.32 7.32 7.26 7.19 7.18 7.16 7.11 7.09 7.02 7.01 6.67 5.55 3.31 3.28 2.87 2.84 2.06 2.05 2.03 1.91 1.84 1.22 1.20 1.20 1.18 0.84 0.83 0.81
n-Bu
O
Ph
O
N
Cl
3da, 500 MHz
0.95 1.00 1.00 1.05 3.02 1.99 0.99 2.01 0.99 1.00 0.95 0.96 2.04 3.03 4.09 3.03
f1 (ppm)


172.6 153.3 150.8 137.9 136.8 133.6 132.0 130.7 130.0 129.0 128.3 127.4 126.6 126.5 125.3 125.1 123.8 123.1 120.1 117.3 114.9 106.6 101.8 49.8 40.9 30.2 25.5 25.1 22.4 13.7
n-Bu
O
Ph
O
N
Cl
3da, 126 MHz
f1 (ppm)

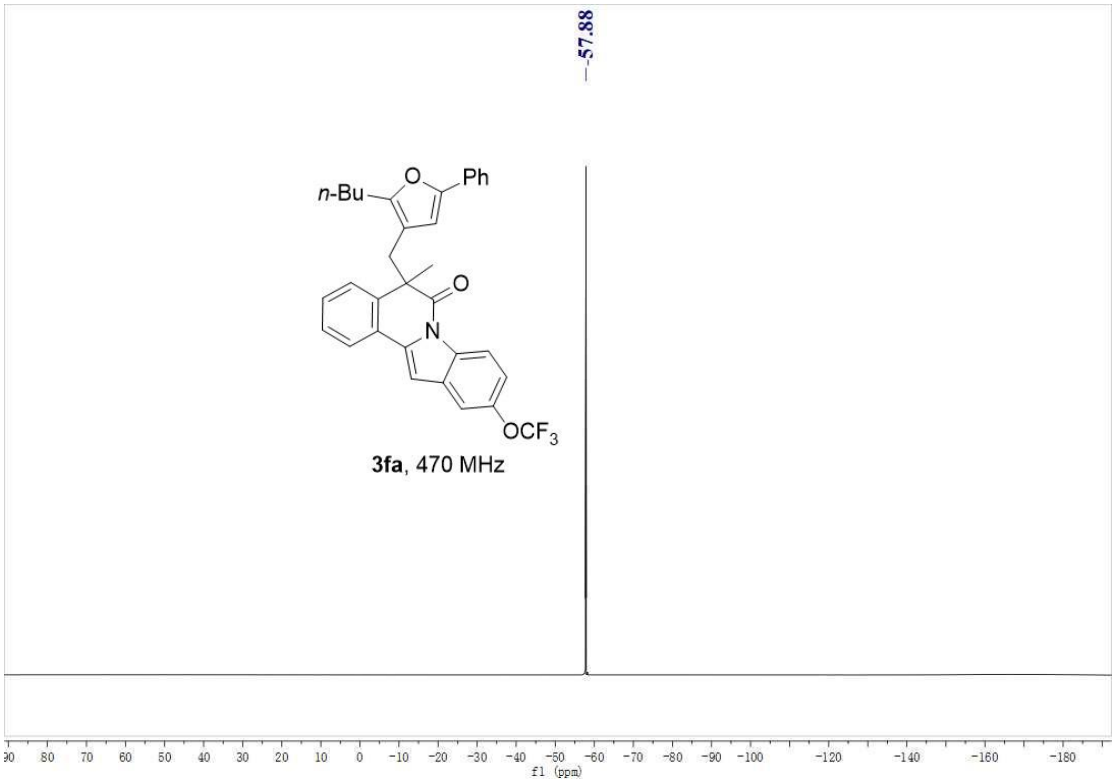

8.49 8.47 7.70 7.68 7.52 7.52 7.51 7.48 7.48 7.46 7.46 7.45 7.43 7.42 7.39 7.37 7.36 7.26 7.20 7.18 7.17 7.11 7.10 7.01 7.00 6.66 5.54 3.30 3.27 2.86 2.83 2.05 2.03 2.02 1.91 1.26 1.21 1.20 1.20 1.19 1.18 0.84 0.82 0.81
n-Bu
O
Ph
O
N
Br
3ea, 500 MHz
0.96 0.95 2.03 1.06 1.04 1.02 1.99 1.05 1.97 0.98 1.00 1.05 1.01 2.02 3.01 4.03 3.05
f1 (ppm)


172.7 153.3 150.8 129.0 128.3 127.8 127.5 126.6 126.5 123.8 123.1 117.7 117.7 114.9 106.6 101.7 77.2 77.0 76.7 49.8 40.9 30.2 25.5 25.0 22.4 13.7
n-Bu
O
Ph
O
N
Br
3ea, 126 MHz
f1 (ppm)

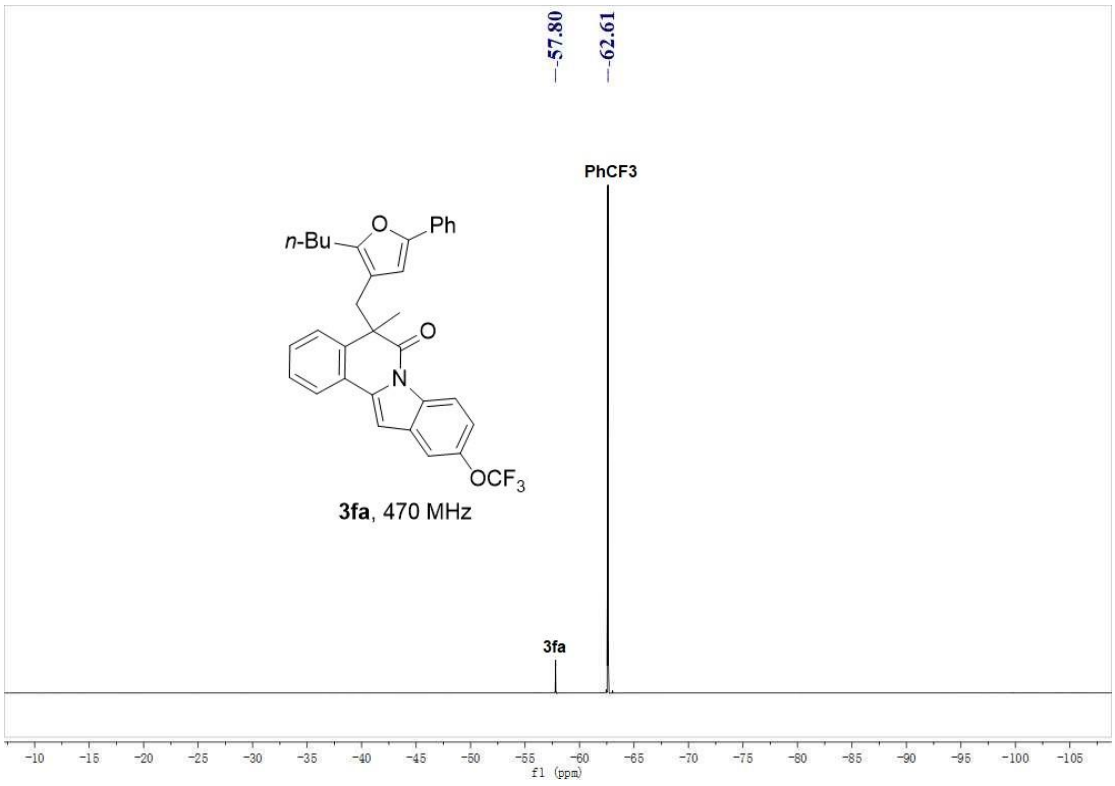

8.64 8.62 7.72 7.70 7.54 7.52 7.46 7.45 7.43 7.40 7.38 7.37 7.27 7.26 7.25 7.23 7.19 7.17 7.15 7.11 7.09 7.08 7.06 7.05 6.74 5.58 3.33 3.30 2.89 2.87 2.09 2.08 2.06 1.92 1.32 1.24 1.23 1.22 1.22 1.21 1.20 0.85 0.84 0.82
n-Bu
O
Ph
O
N
OCF3
3fa, 500 MHz
1.04 1.07 1.95 2.06 1.06 2.00 1.00 1.06 0.99 1.06 1.97 2.99 4.03 3.04
f1 (ppm)

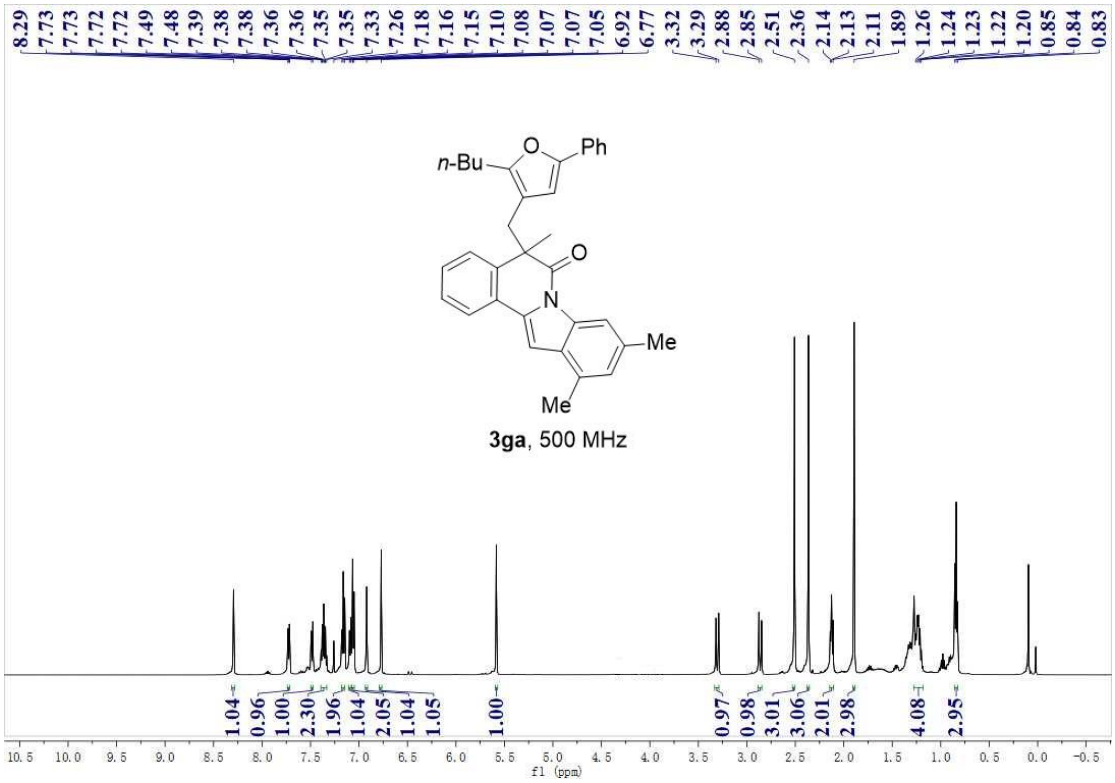

172.7 153.3 150.8 138.0 131.6 130.7 129.1 128.3 127.5 126.7 126.6 125.2 123.8 123.1 118.1 117.3 114.9 112.7 102.2 77.3 77.0 76.8 49.7 40.8 30.2 25.6 25.1 22.4 13.7
n-Bu
O
Ph
O
N
OCF3
3fa, 126 MHz
f1 (ppm)

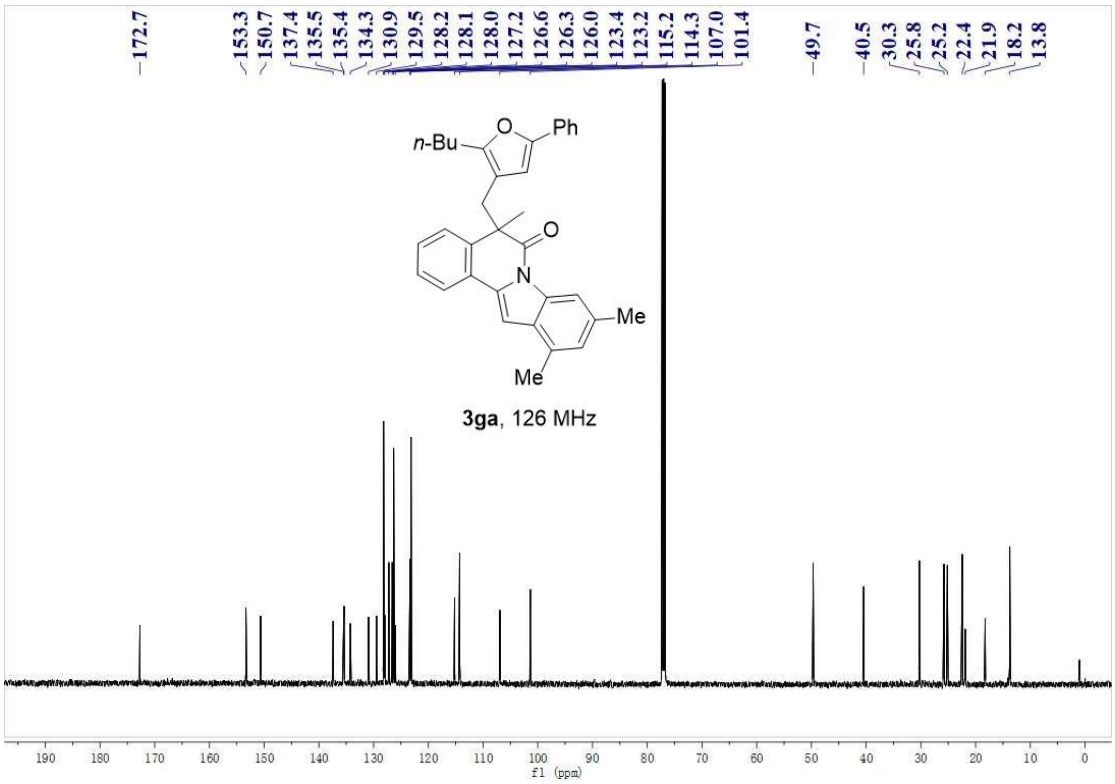
^{19}F NMR spectrum of **3fa** without using internal reference compound

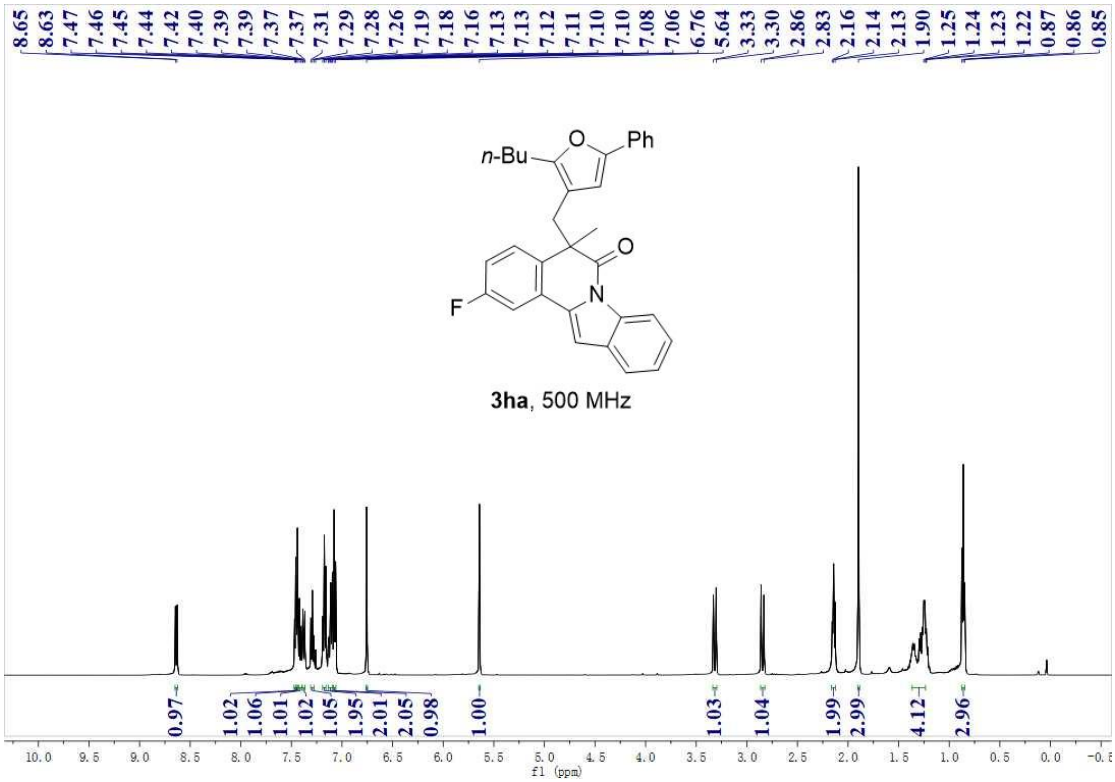


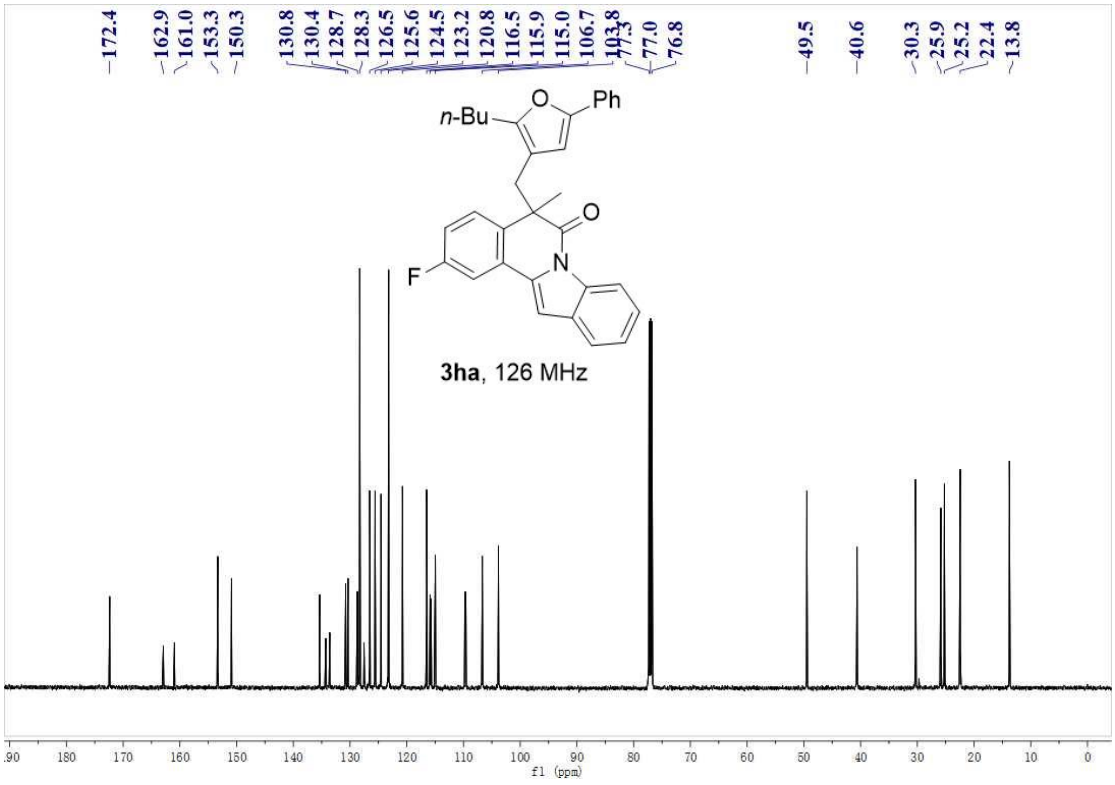
^{19}F NMR spectrum of **3fa** referenced with $PhCF_3$ (-62.61) in $CDCl_3$



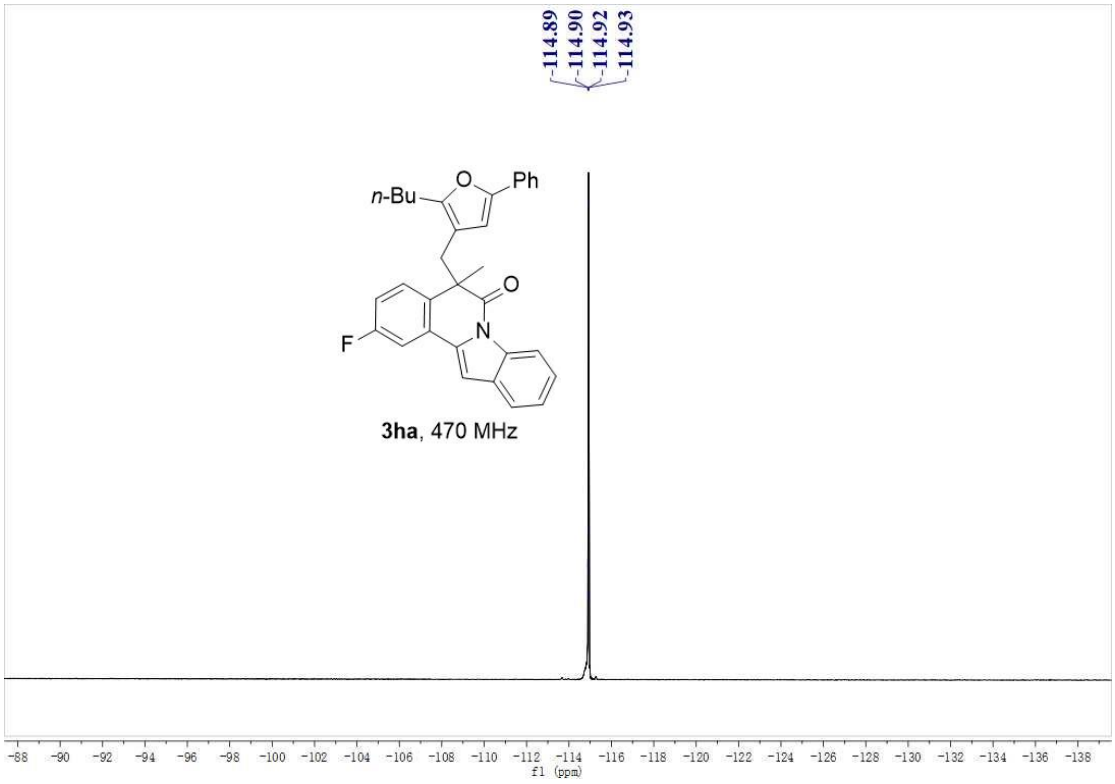

8.29 7.73 7.73 7.72 7.72 7.49 7.48 7.39 7.38 7.38 7.36 7.36 7.35 7.35 7.33 7.26 7.18 7.16 7.15 7.10 7.08 7.07 7.07 7.05 6.92 6.77 3.32 3.29 2.88 2.85 2.51 2.36 2.14 2.13 2.11 1.89 1.26 1.24 1.23 1.22 1.20 0.85 0.84 0.83
n-Bu
O
Ph
O
N
Me
Me
3ga, 500 MHz
1.04 0.96 1.00 2.30 1.96 1.04 2.05 1.04 1.05 1.00 0.97 0.98 3.01 3.06 2.01 2.98 4.08 2.95
f1 (ppm)


172.7 153.3 150.7 137.4 135.5 135.4 134.3 130.9 129.5 128.2 128.1 128.0 127.2 126.6 126.3 126.0 123.4 123.2 115.2 114.3 107.0 101.4 49.7 40.5 30.3 25.8 25.2 22.4 21.9 18.2 13.8
n-Bu
O
Ph
O
N
Me
Me
3ga, 126 MHz
f1 (ppm)

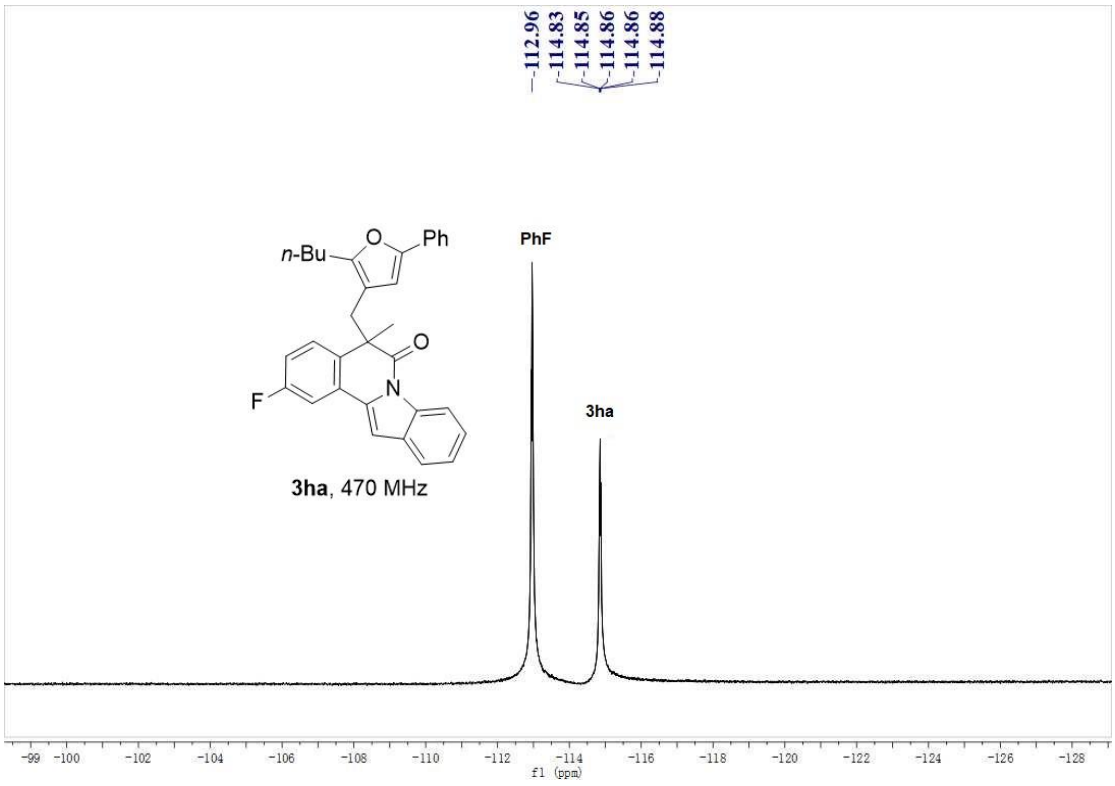

8.65 8.63 7.47 7.46 7.45 7.44 7.42 7.40 7.39 7.39 7.37 7.37 7.31 7.29 7.28 7.26 7.19 7.18 7.16 7.13 7.13 7.12 7.11 7.10 7.10 7.08 7.06 6.76 5.64 3.33 3.30 2.86 2.83 2.16 2.14 2.13 1.90 1.25 1.24 1.23 1.22 0.87 0.86 0.85
n-Bu
O
Ph
O
N
F
3ha, 500 MHz
0.97 1.02 1.06 1.01 1.02 1.05 1.95 2.01 2.05 0.98 1.00 1.03 1.04 1.99 2.99 4.12 2.96
f1 (ppm)

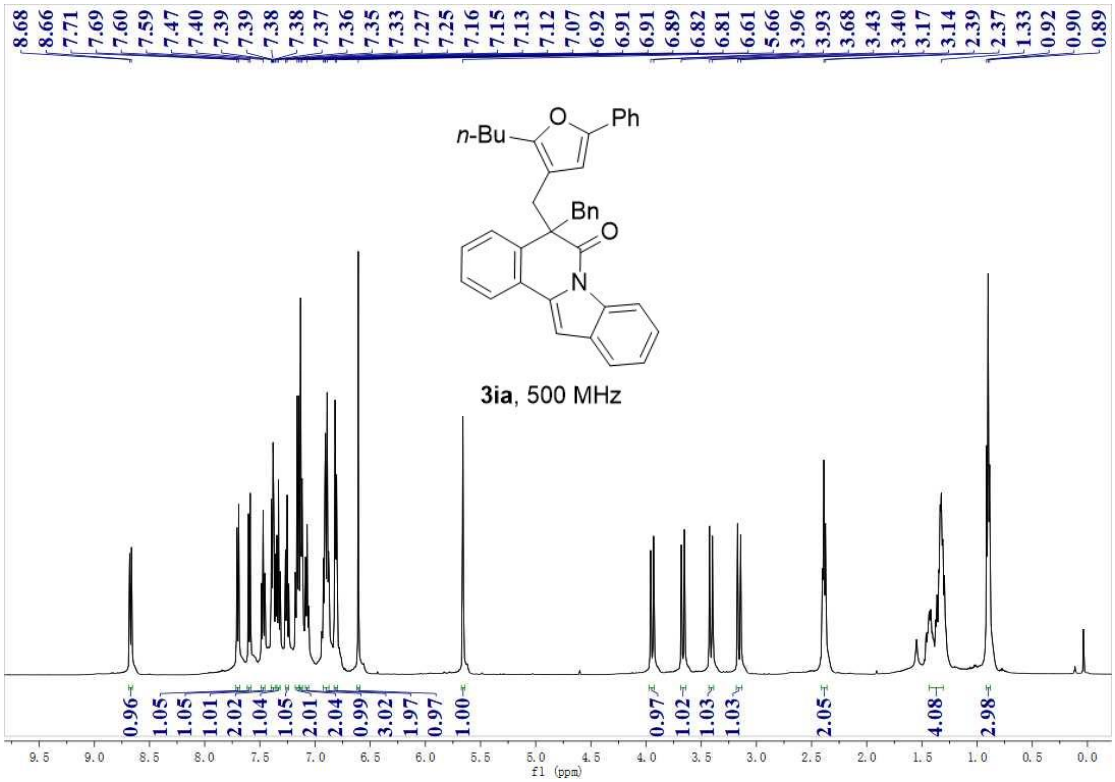

172.4 162.9 161.0 153.3 150.3 130.8 130.4 128.7 128.3 126.5 125.6 124.5 123.2 120.8 116.5 115.9 115.0 106.7 77.3 77.0 76.8 49.5 40.6 30.3 25.9 25.2 22.4 13.8
n-Bu
O
Ph
O
N
F
3ha, 126 MHz
f1 (ppm)

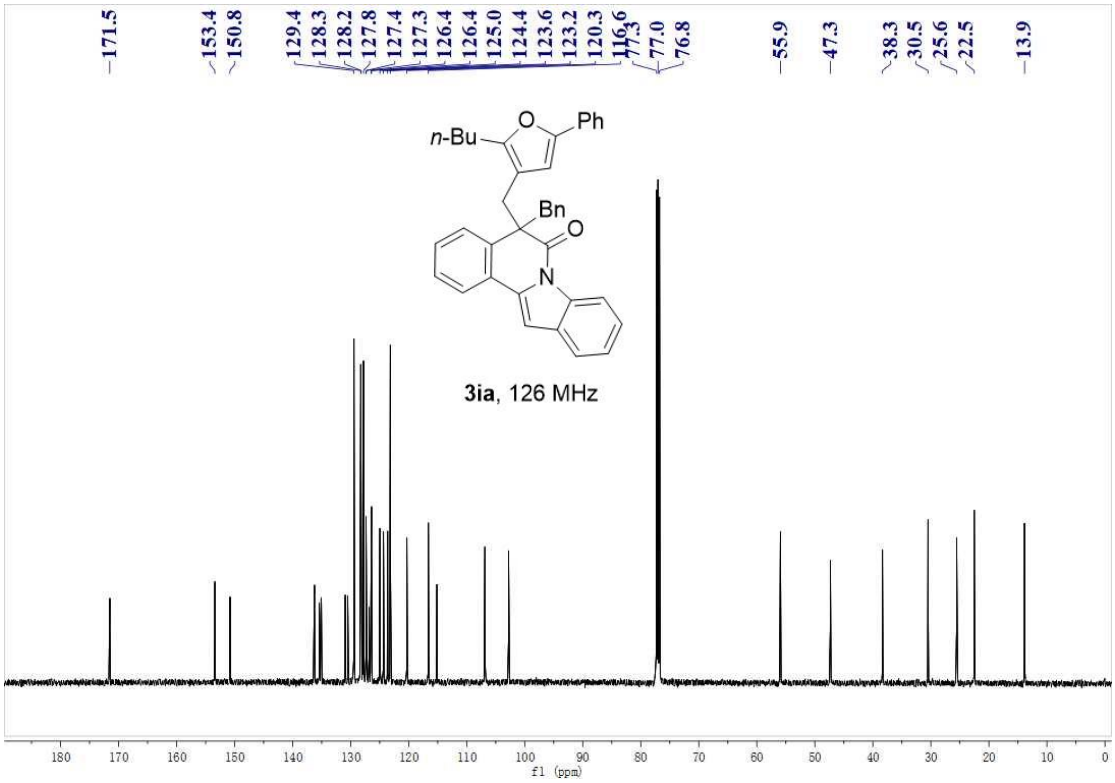
^{19}F NMR spectrum of **3ha** without using internal reference compound

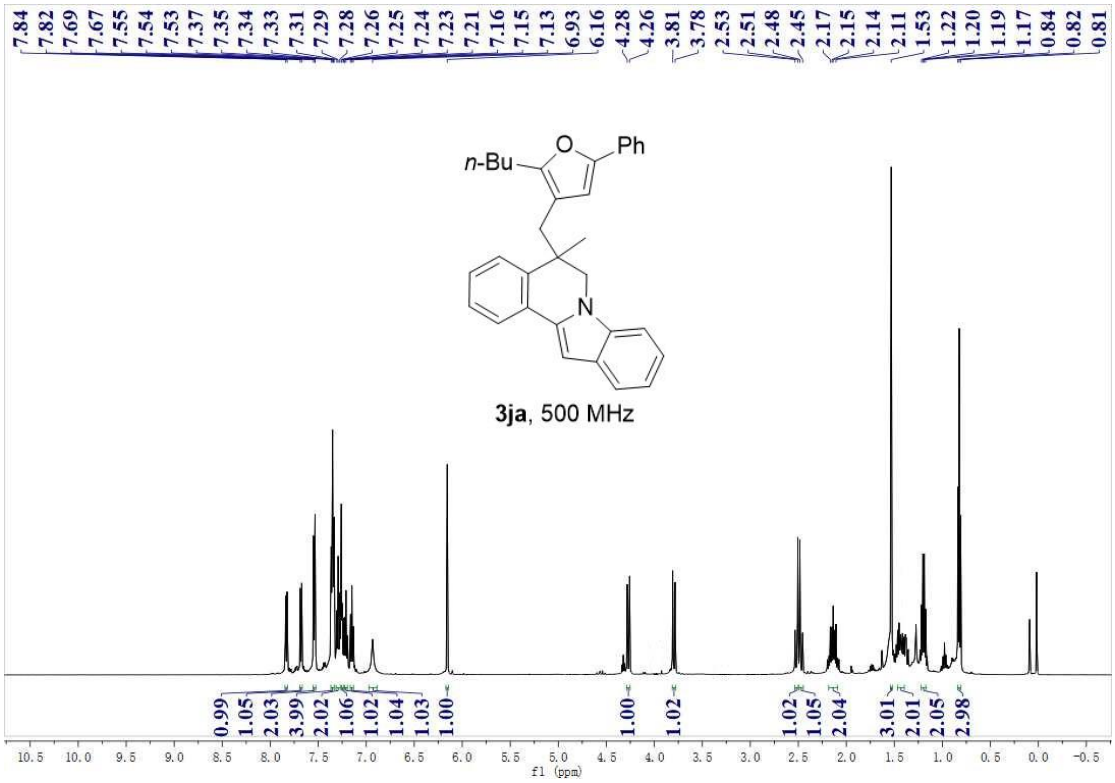


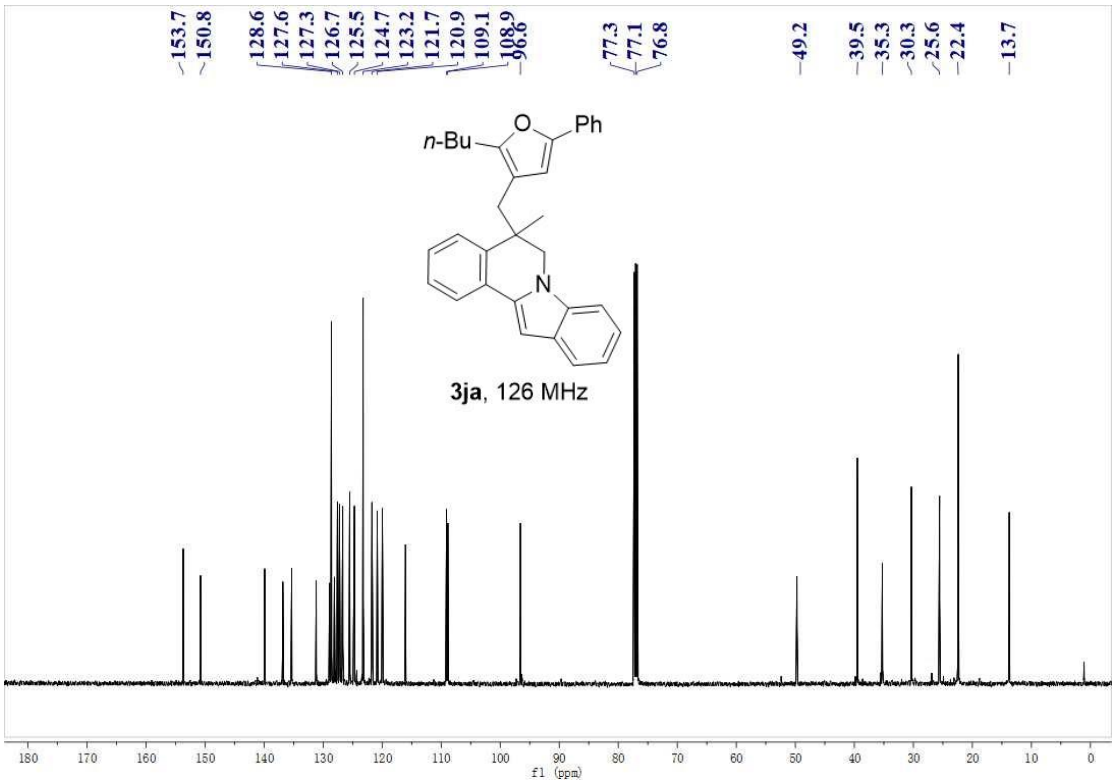
^{19}F NMR spectrum of **3ha** referenced with PhF (-112.96) in $CDCl_3$

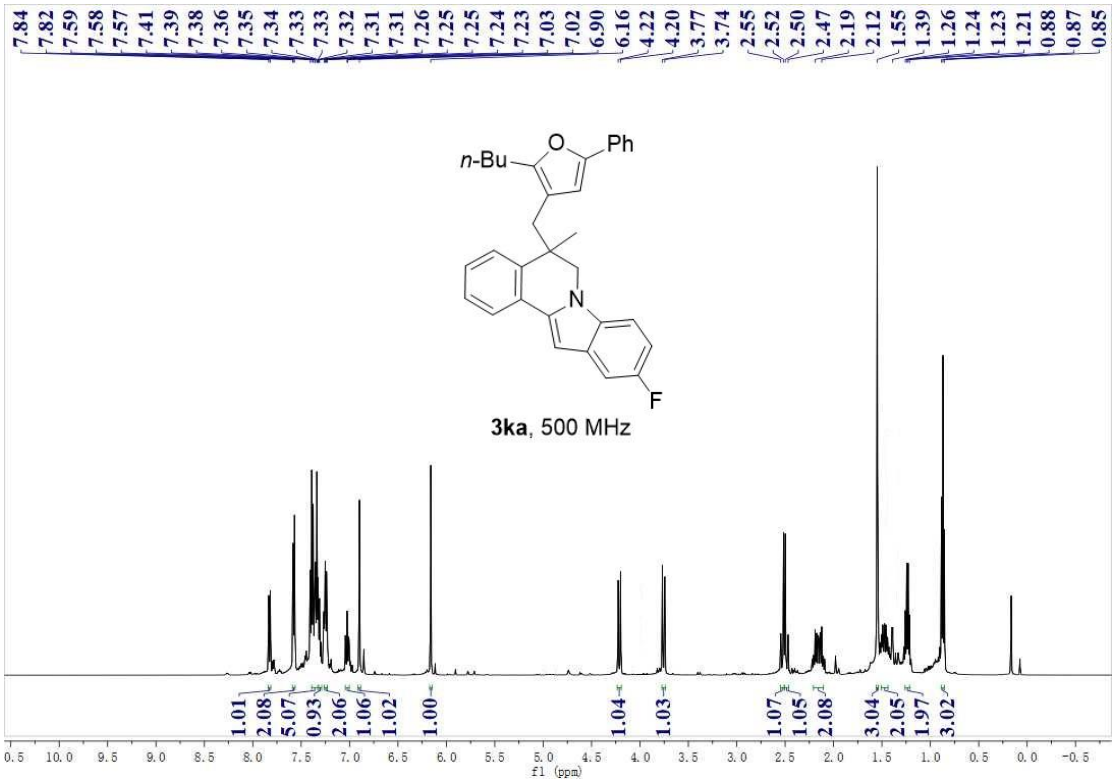


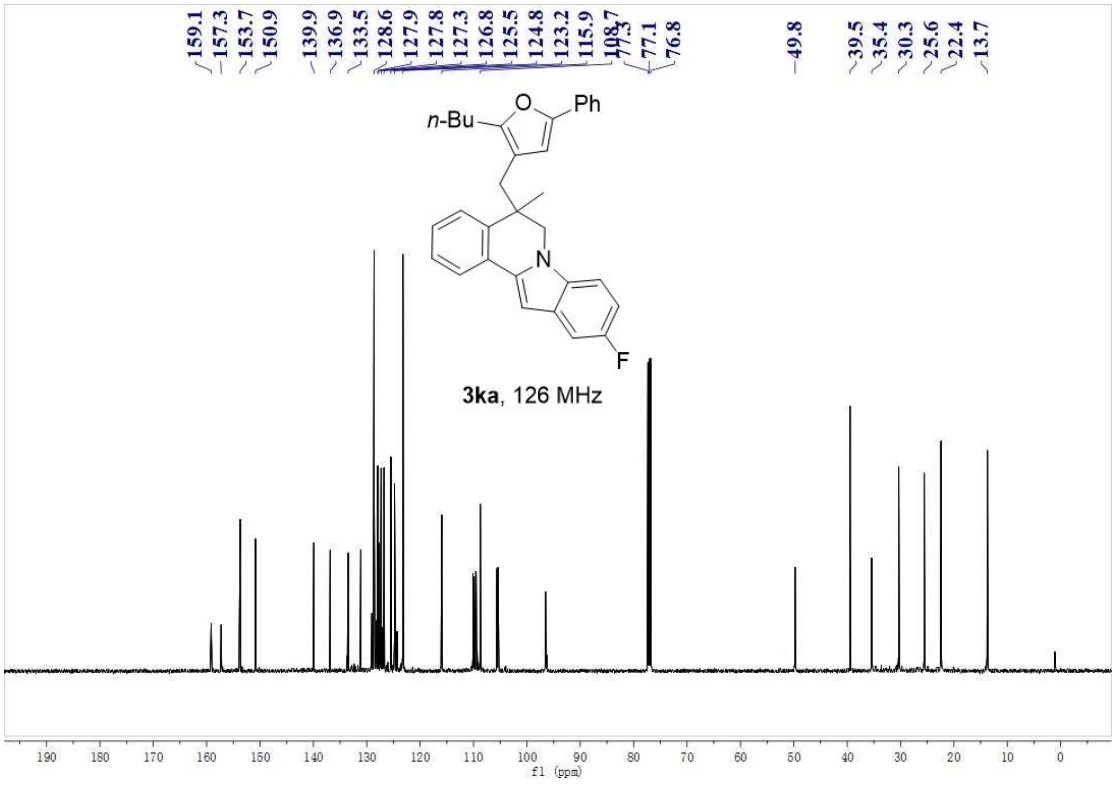

8.68 8.66 7.71 7.69 7.60 7.59 7.47 7.40 7.39 7.39 7.38 7.38 7.37 7.36 7.35 7.33 7.27 7.25 7.16 7.15 7.13 7.12 7.07 6.92 6.91 6.91 6.89 6.82 6.81 6.61 5.66 3.96 3.93 3.68 3.43 3.40 3.17 3.14 2.39 2.37 1.33 0.92 0.90 0.89
n-Bu
O
Ph
Bn
O
N
3ia, 500 MHz
0.96 1.05 1.05 1.01 2.02 1.04 1.05 2.01 2.04 0.99 3.02 1.97 0.97 1.00 0.97 1.02 1.03 1.03 2.05 4.08 2.98
f1 (ppm)


171.5 153.4 150.8 129.4 128.3 128.2 127.8 127.4 127.3 126.4 126.4 125.0 124.4 123.6 123.2 120.3 116.6 77.3 77.0 76.8 55.9 47.3 38.3 30.5 25.6 22.5 13.9
n-Bu
O
Ph
Bn
O
N
3ia, 126 MHz
f1 (ppm)

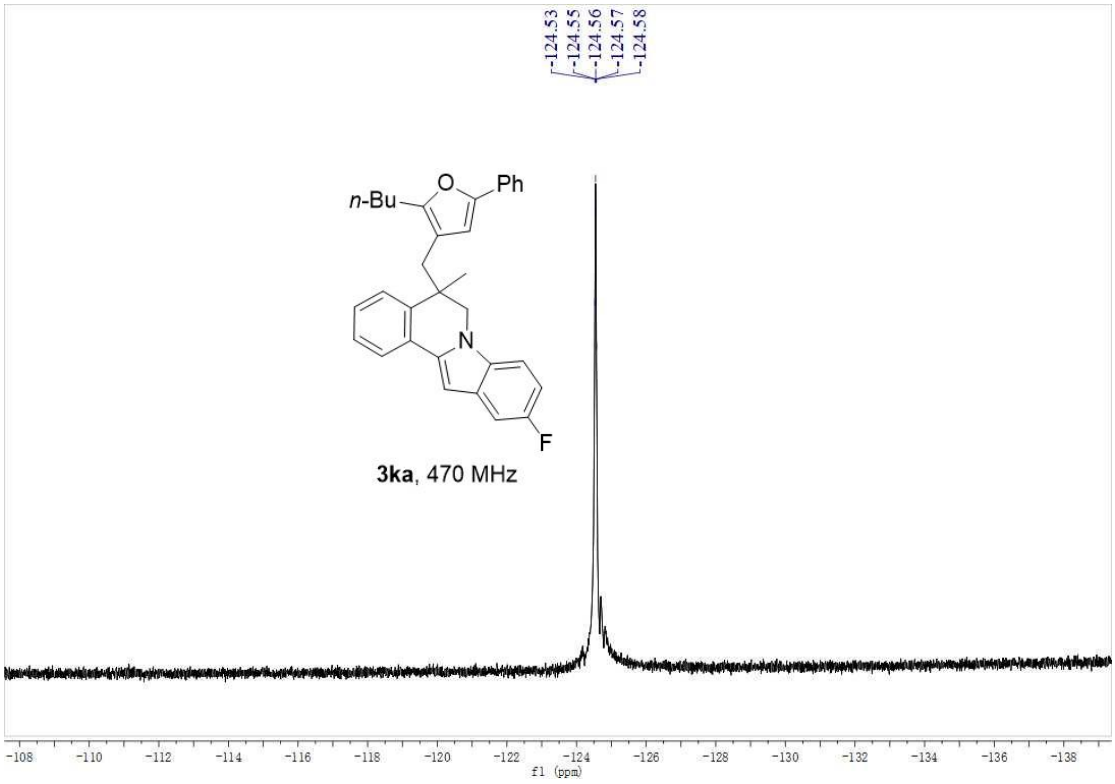

7.84 7.82 7.69 7.67 7.55 7.54 7.53 7.37 7.35 7.34 7.33 7.31 7.29 7.28 7.26 7.25 7.24 7.23 7.21 7.16 7.15 7.13 6.93 6.16 4.28 4.26 3.81 3.78 2.53 2.51 2.48 2.45 2.17 2.15 2.14 2.11 1.53 1.22 1.20 1.19 1.17 0.84 0.82 0.81
n-Bu
O
Ph
N
3ja, 500 MHz
0.99 1.05 2.03 3.99 2.02 1.06 1.02 1.04 1.03 1.00 1.00 1.02 1.02 1.05 2.04 3.01 2.01 2.05 2.98
f1 (ppm)


153.7 150.8 128.6 127.6 127.3 126.7 125.5 124.7 123.2 121.7 120.9 109.1 108.9 96.6 77.3 77.1 76.8 49.2 39.5 35.3 30.3 25.6 22.4 13.7
n-Bu
O
Ph
N
3ja, 126 MHz
f1 (ppm)

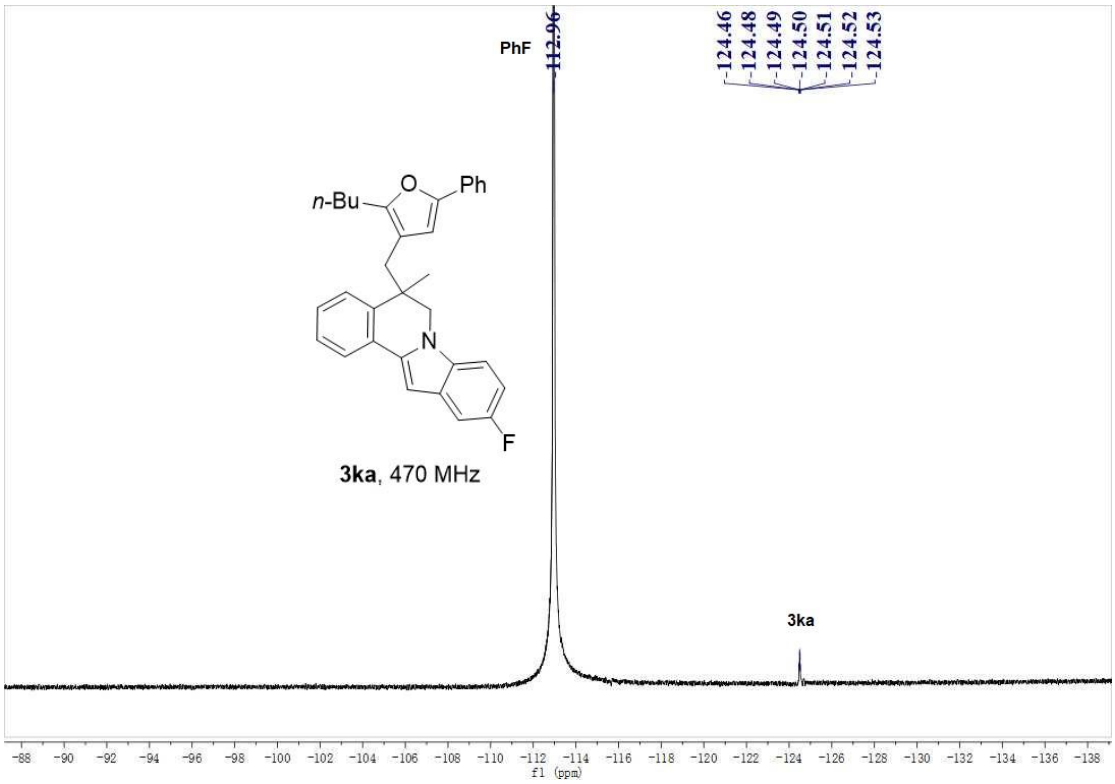

7.84 7.82 7.59 7.58 7.57 7.41 7.39 7.38 7.36 7.35 7.34 7.33 7.33 7.32 7.31 7.31 7.26 7.25 7.25 7.24 7.23 7.03 7.02 6.90 6.16 4.22 4.20 3.77 3.74 2.55 2.52 2.50 2.47 2.19 2.12 1.55 1.39 1.26 1.24 1.23 1.21 0.88 0.87 0.85
n-Bu
O
Ph
N
F
3ka, 500 MHz
1.01 2.08 5.07 0.93 2.06 1.06 1.02 1.00 1.04 1.03 1.07 1.05 2.08 3.04 2.05 1.97 3.02
f1 (ppm)

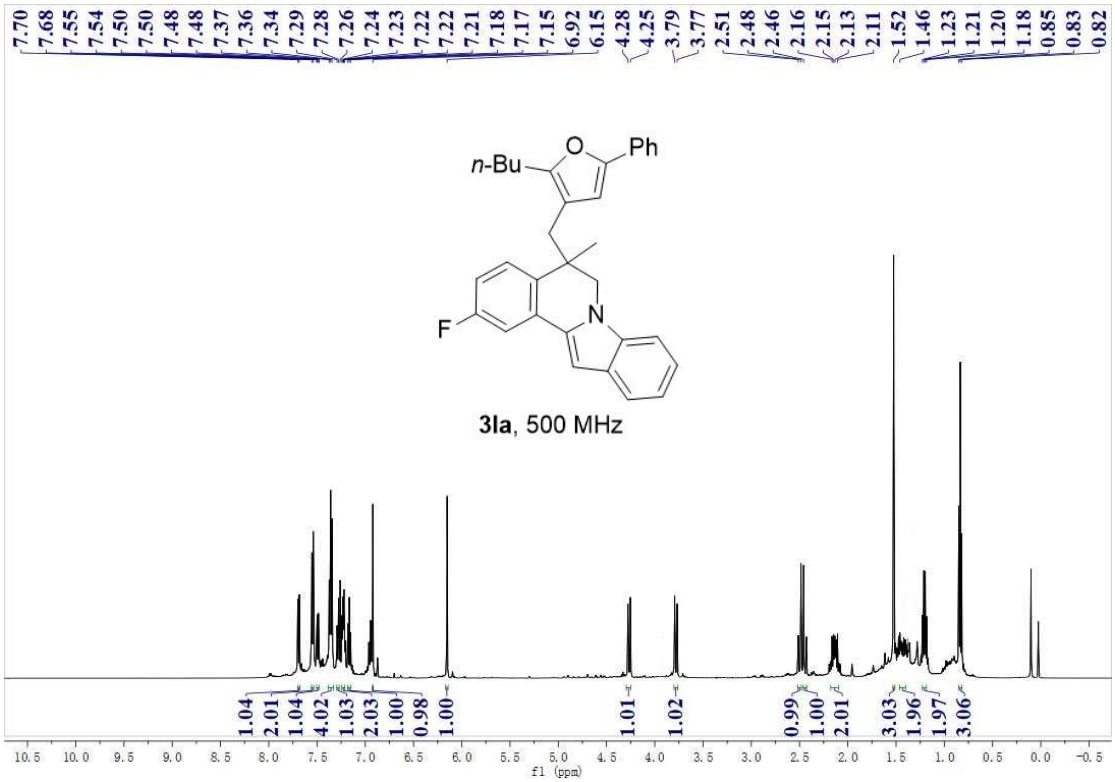

159.1 157.3 153.7 150.9 139.9 136.9 133.5 128.6 127.9 127.8 127.3 126.8 125.5 124.8 123.2 115.9 108.7 77.3 77.1 76.8 49.8 39.5 35.4 30.3 25.6 22.4 13.7
n-Bu
O
Ph
N
F
3ka, 126 MHz
f1 (ppm)

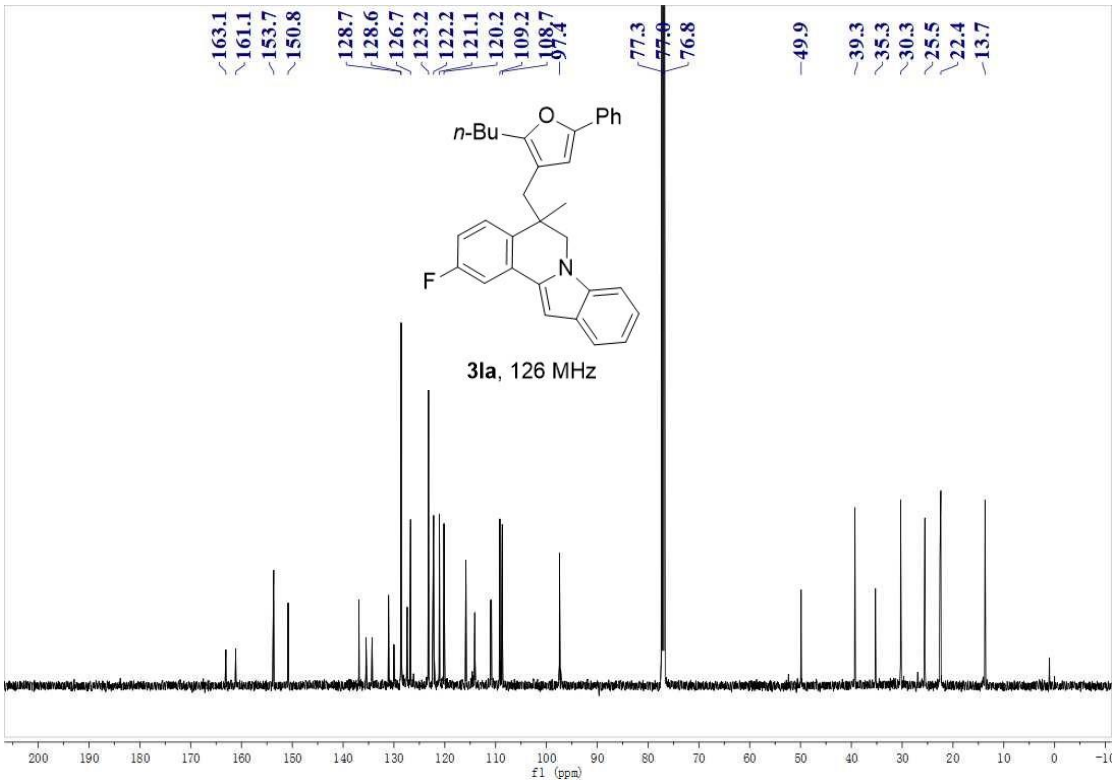
^{19}F NMR spectrum of **3ka** without using internal reference compound



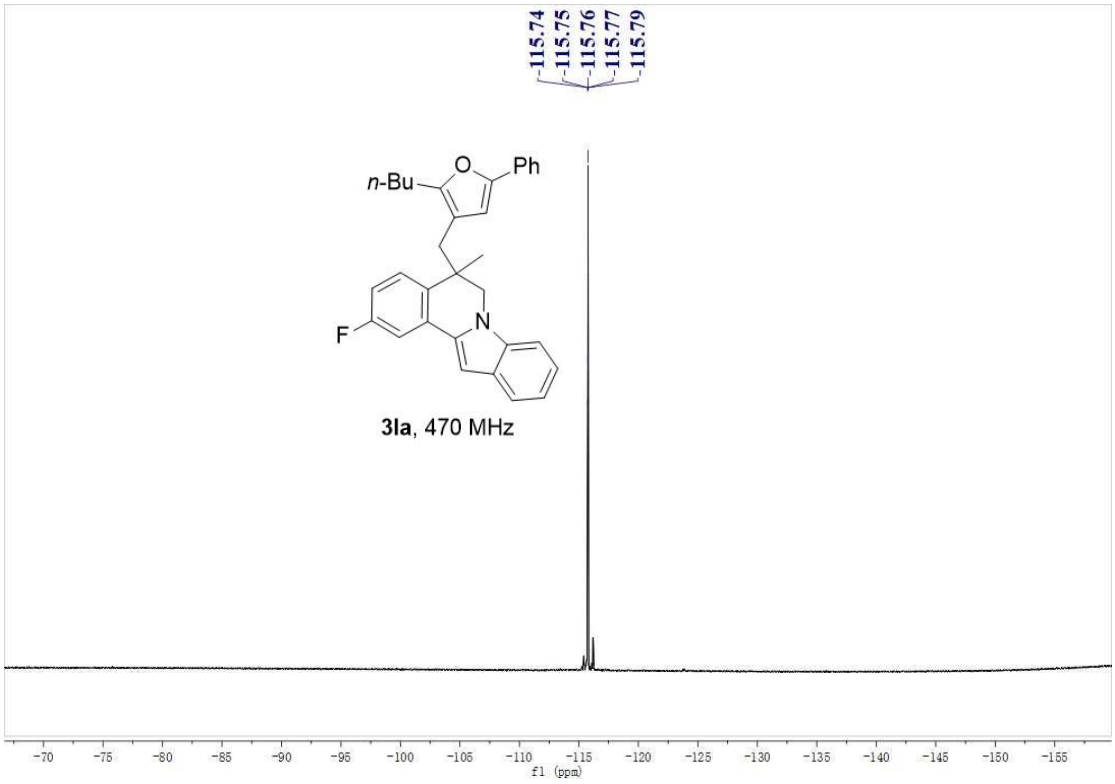
^{19}F NMR spectrum of **3ka** referenced with PhF (-112.96) in $CDCl_3$



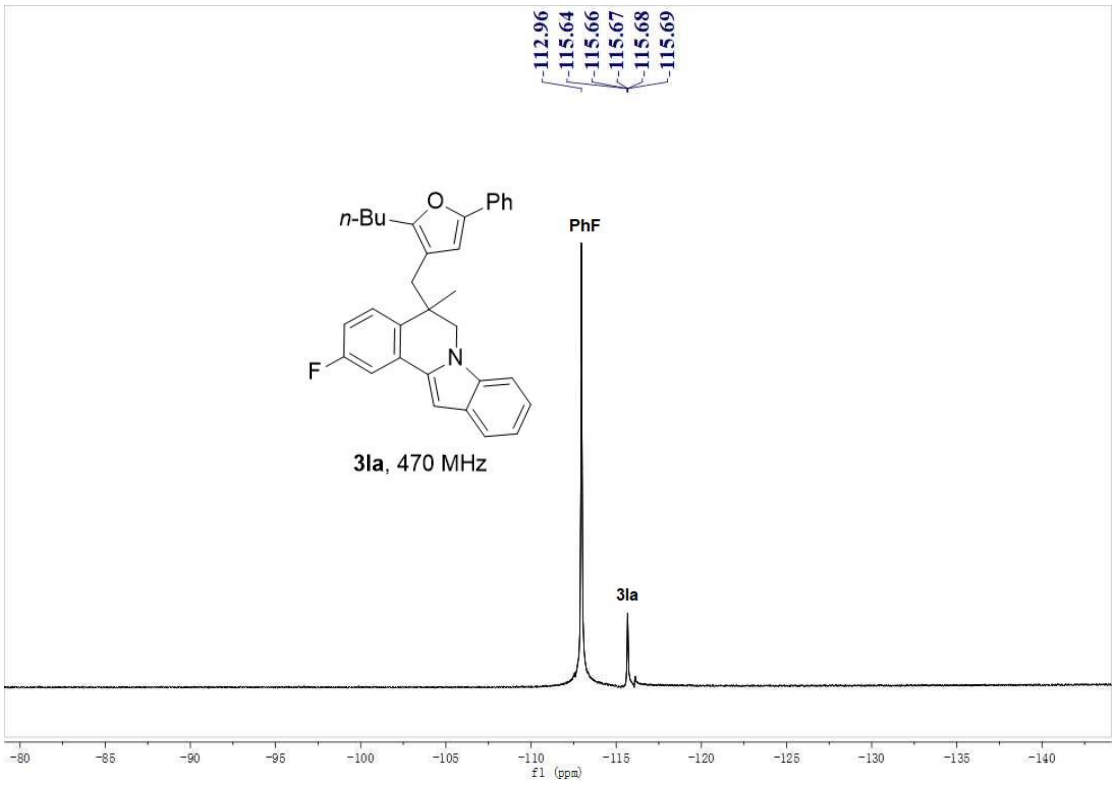

7.70 7.68 7.55 7.54 7.50 7.50 7.48 7.48 7.37 7.36 7.34 7.29 7.28 7.26 7.24 7.23 7.22 7.22 7.21 7.18 7.17 7.15 6.92 6.15 4.28 4.25 3.79 3.77 2.51 2.48 2.46 2.16 2.15 2.13 2.11 1.52 1.46 1.23 1.21 1.20 1.18 0.85 0.83 0.82
n-Bu
O
Ph
F
N
3la, 500 MHz
1.04 2.01 1.04 4.02 1.03 2.03 1.00 0.98 1.00 1.01 1.02 0.99 1.00 2.01 3.03 1.96 1.97 3.06
f1 (ppm)

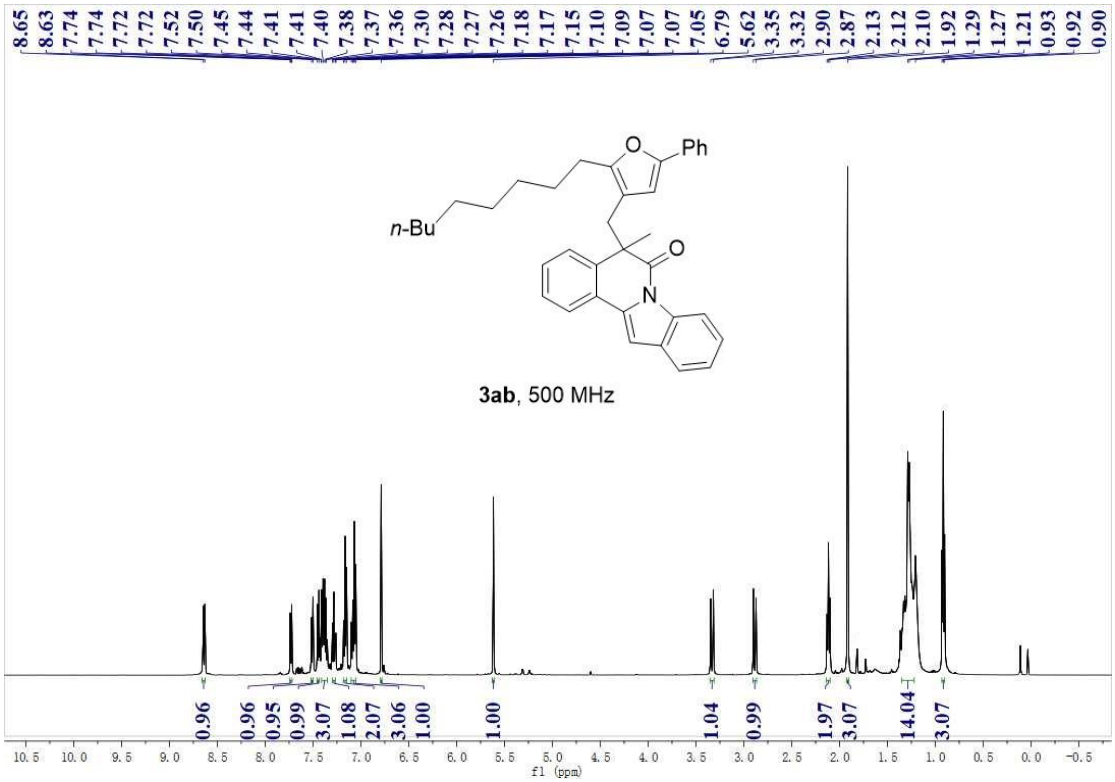

163.1 161.1 153.7 150.8 128.7 128.6 126.7 123.2 122.2 121.1 120.2 109.2 108.7 97.4 77.3 77.0 76.8 49.9 39.3 35.3 30.3 25.5 22.4 13.7
n-Bu
O
Ph
F
N
3la, 126 MHz
f1 (ppm)

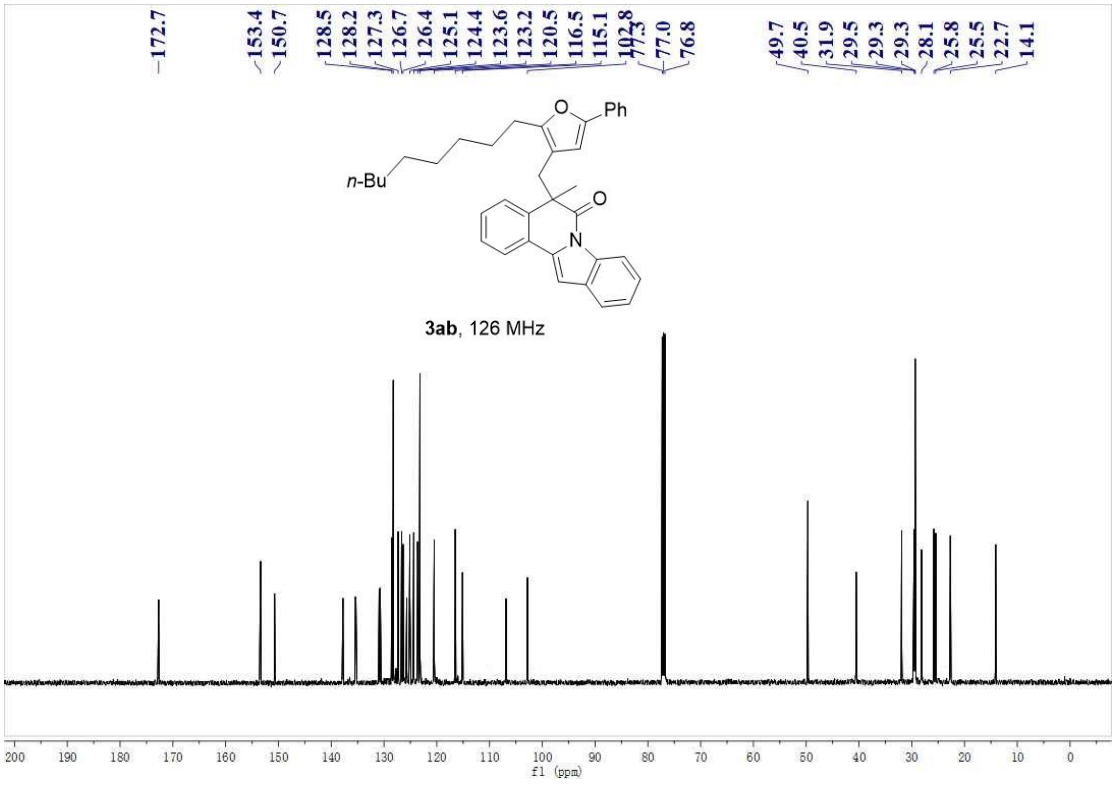
^{19}F NMR spectrum of **3la** without using internal reference compound

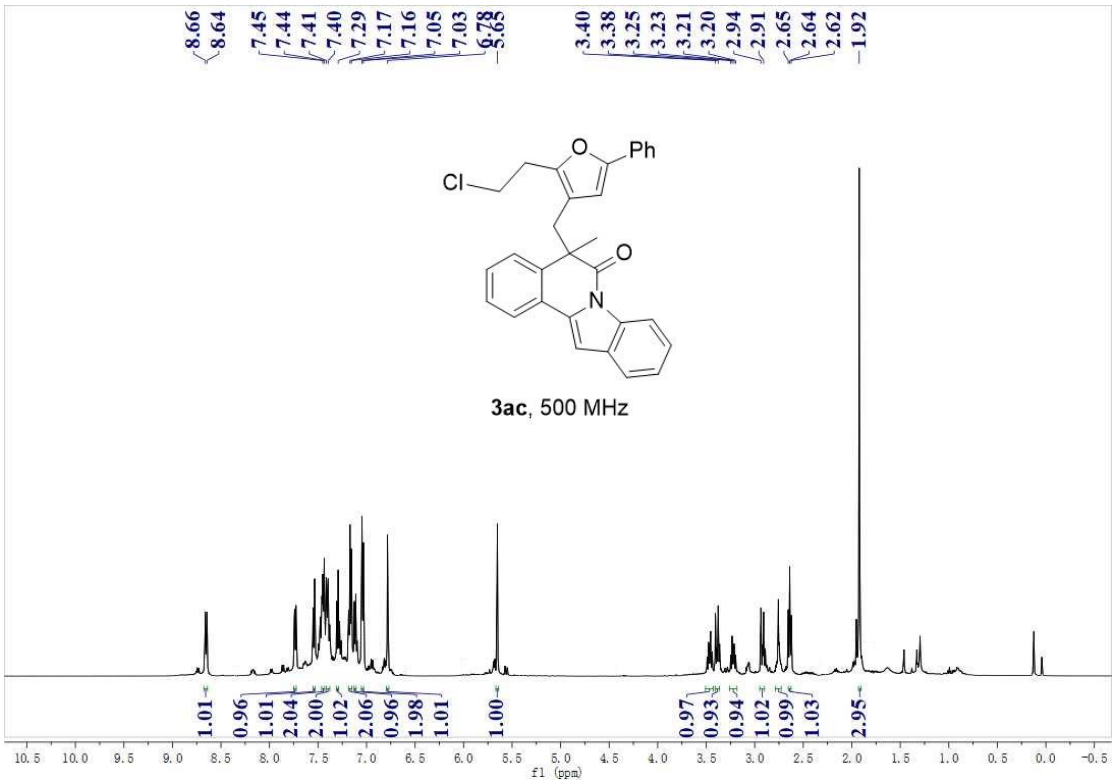


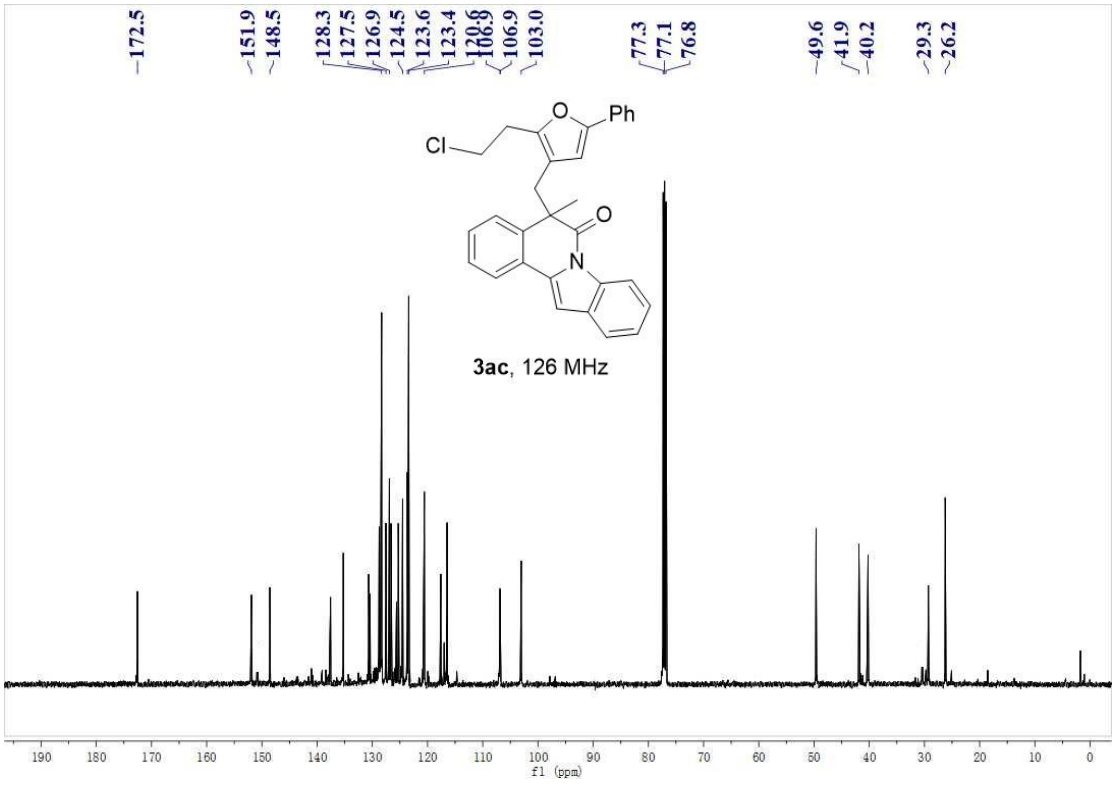
^{19}F NMR spectrum of **3la** referenced with PhF (-112.96) in $CDCl_3$

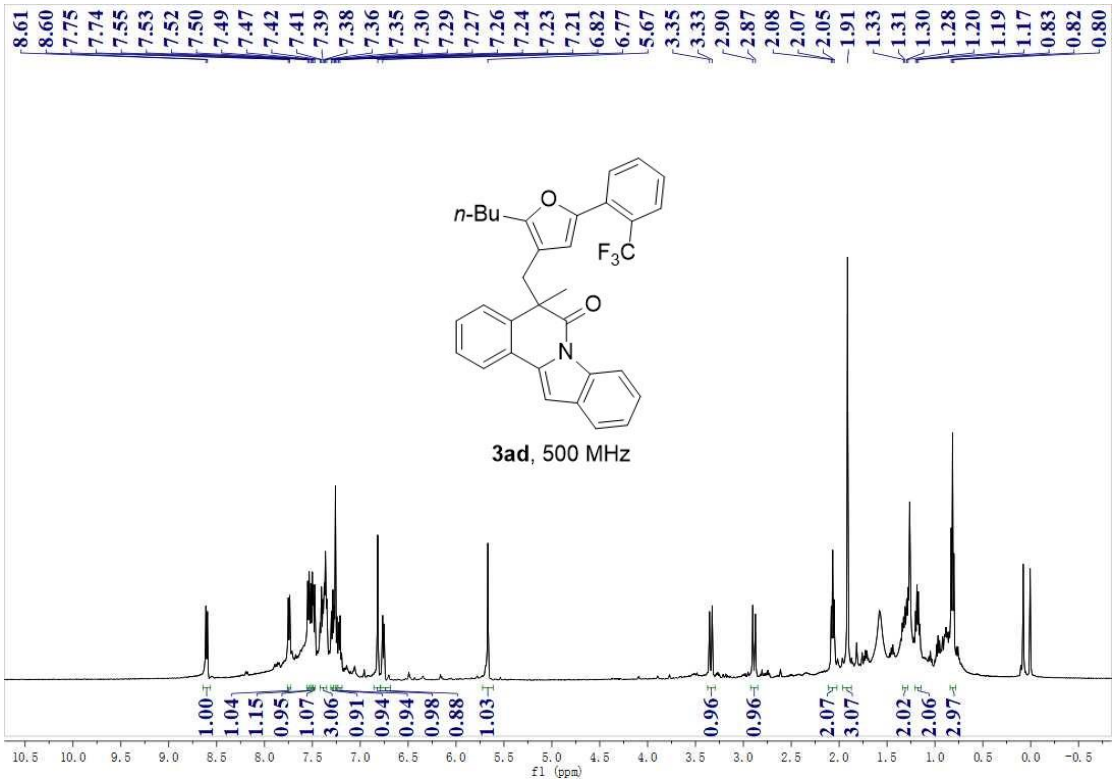


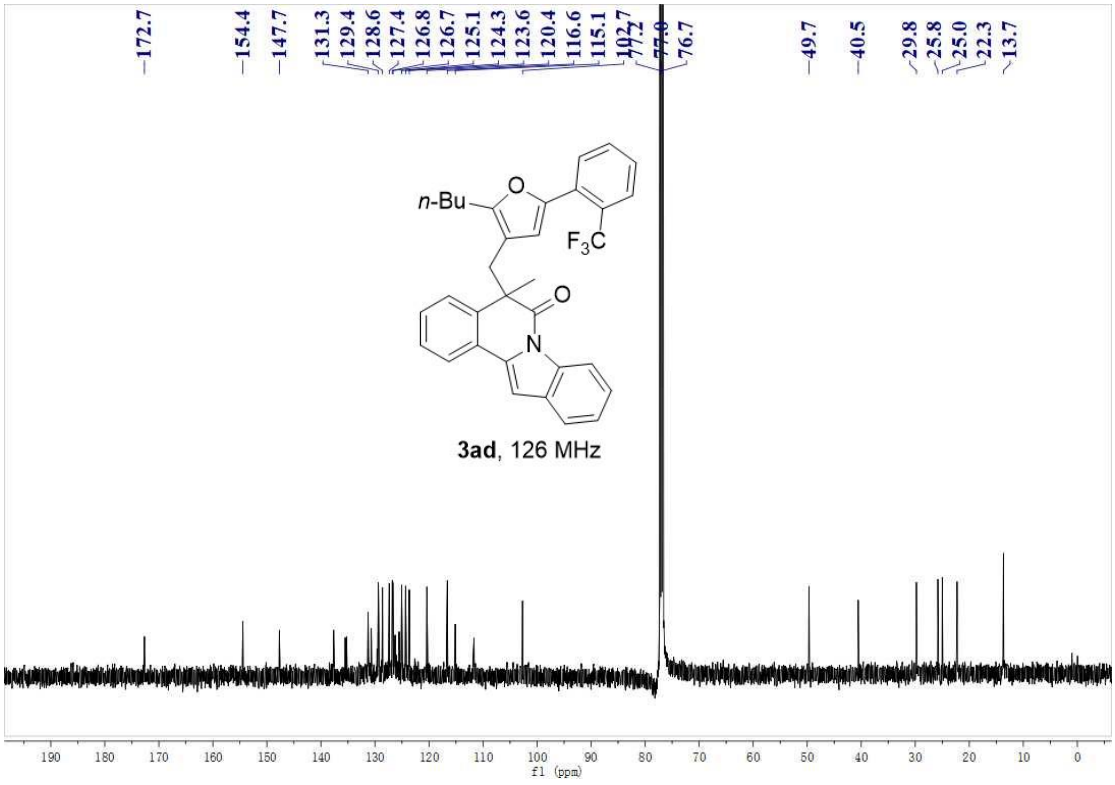

8.65 8.63 7.74 7.74 7.72 7.72 7.52 7.50 7.45 7.44 7.41 7.41 7.40 7.38 7.37 7.36 7.30 7.28 7.27 7.26 7.18 7.17 7.15 7.10 7.09 7.07 7.07 7.05 6.79 5.62 3.35 3.32 2.90 2.87 2.13 2.12 2.10 1.92 1.29 1.27 1.21 0.93 0.92 0.90
Ph
O
n-Bu
O
N
3ab, 500 MHz
0.96 0.96 0.95 0.99 3.07 1.08 2.07 3.06 1.00 1.00 1.04 0.99 1.97 3.07 14.04 3.07
f1 (ppm)


172.7
153.4 150.7
128.5 128.2 127.3 126.7 126.4 125.1 124.4 123.6 123.2 120.5 116.5 115.1 102.8 77.3 77.0 76.8
49.7 40.5 31.9 29.5 29.3 29.3 28.1 25.8 25.5 22.7 14.1
Ph
O
n-Bu
O
N
3ab, 126 MHz
f1 (ppm)

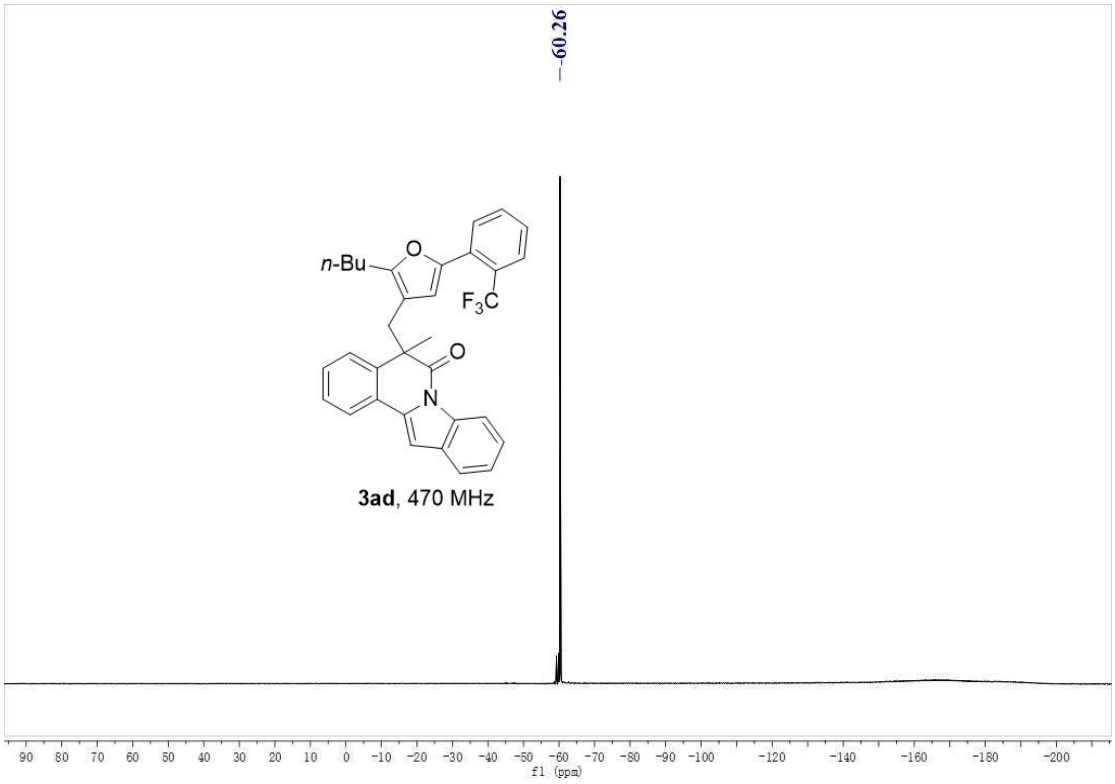

8.66
8.64
7.45
7.44
7.41
7.40
7.29
7.17
7.16
7.05
7.03
6.78
6.65
3.40
3.38
3.25
3.23
3.21
3.20
2.94
2.91
2.65
2.64
2.62
1.92
Cl
O
Ph
O
N
3ac, 500 MHz
1.01
0.96
1.01
2.04
2.00
1.02
2.06
0.96
1.98
1.01
1.00
0.97
0.93
0.94
1.02
0.99
1.03
2.95
f1 (ppm)


172.5
151.9
148.5
128.3
127.5
126.9
124.5
123.6
123.4
120.6
106.9
103.0
77.3
77.1
76.8
49.6
41.9
40.2
29.3
26.2
Cl
O
Ph
O
N
3ac, 126 MHz
f1 (ppm)

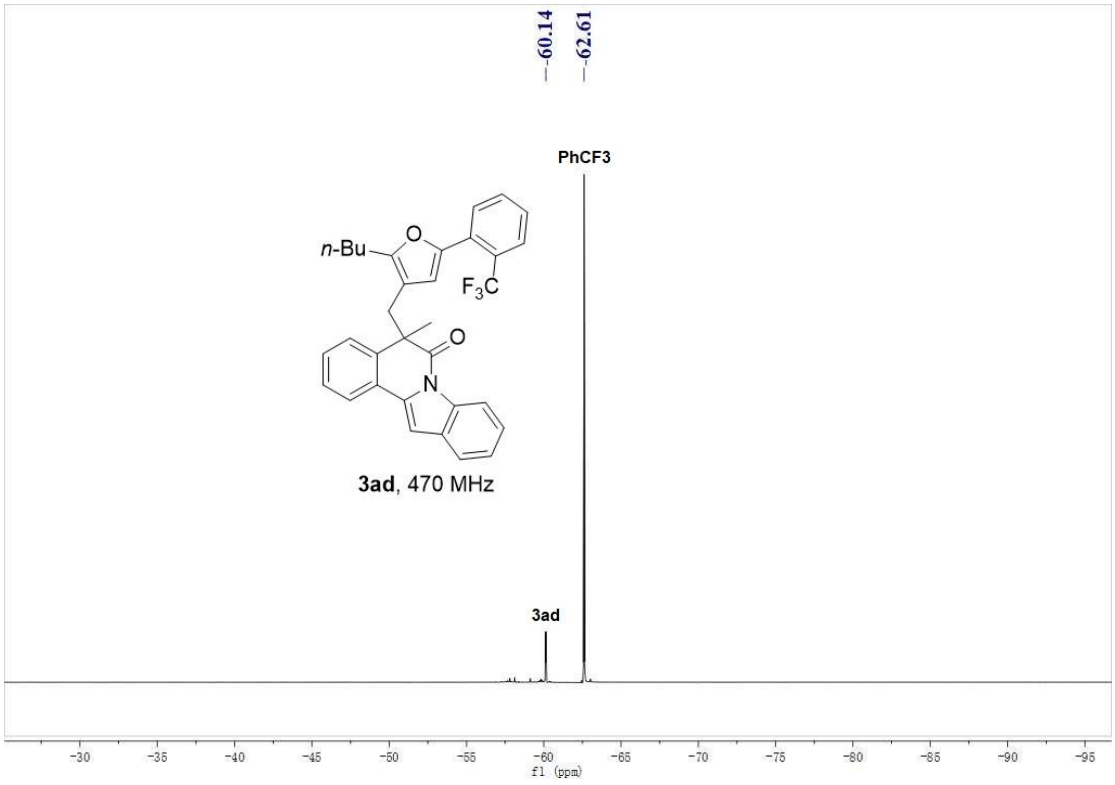

8.61 8.60 7.75 7.74 7.55 7.53 7.52 7.50 7.49 7.47 7.42 7.41 7.39 7.38 7.36 7.35 7.30 7.29 7.27 7.26 7.24 7.23 7.21 6.82 6.77 5.67 3.35 3.33 2.90 2.87 2.08 2.07 2.05 1.91 1.33 1.31 1.30 1.28 1.20 1.19 1.17 0.83 0.82 0.80
n-Bu
O
F3C
O
N
3ad, 500 MHz
1.00 1.04 1.15 0.95 1.07 3.06 0.91 0.94 0.94 0.98 0.88 1.03 0.96 0.96 2.07 3.07 2.02 2.06 2.97
f1 (ppm)

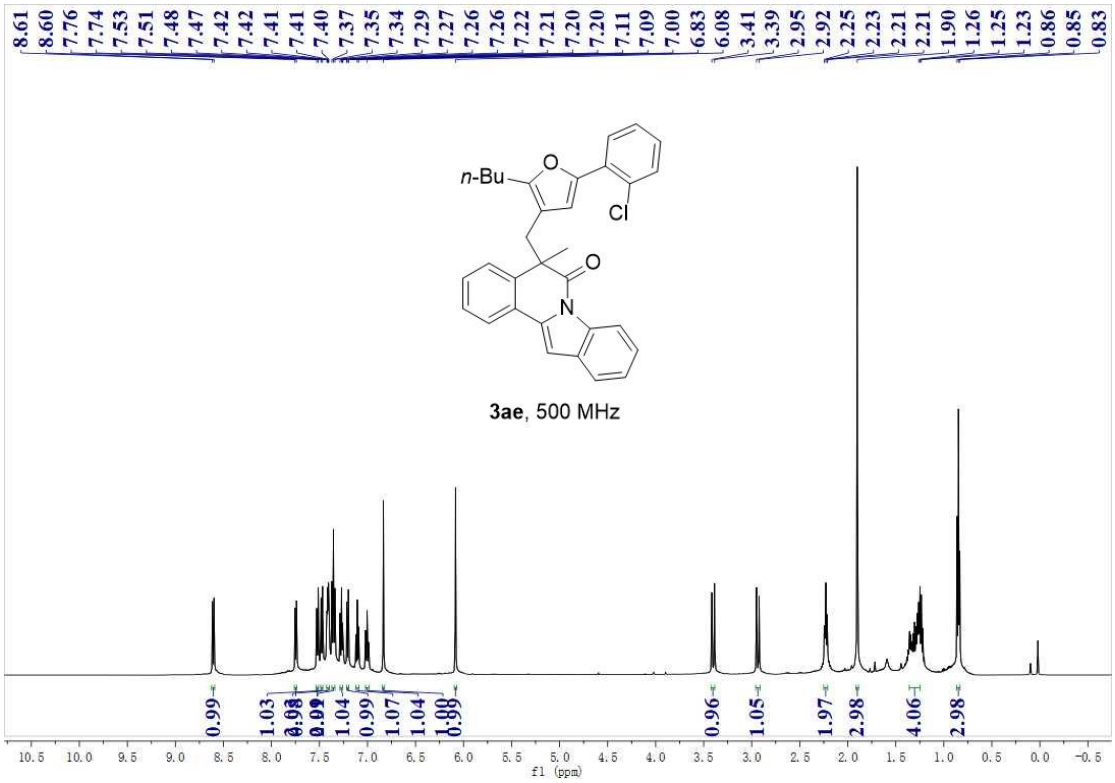

172.7 154.4 147.7 131.3 129.4 128.6 127.4 126.8 126.7 125.1 124.3 123.6 120.4 116.6 115.1 102.7 77.2 77.0 76.7 49.7 40.5 29.8 25.8 25.0 22.3 13.7
n-Bu
O
F3C
O
N
3ad, 126 MHz
f1 (ppm)

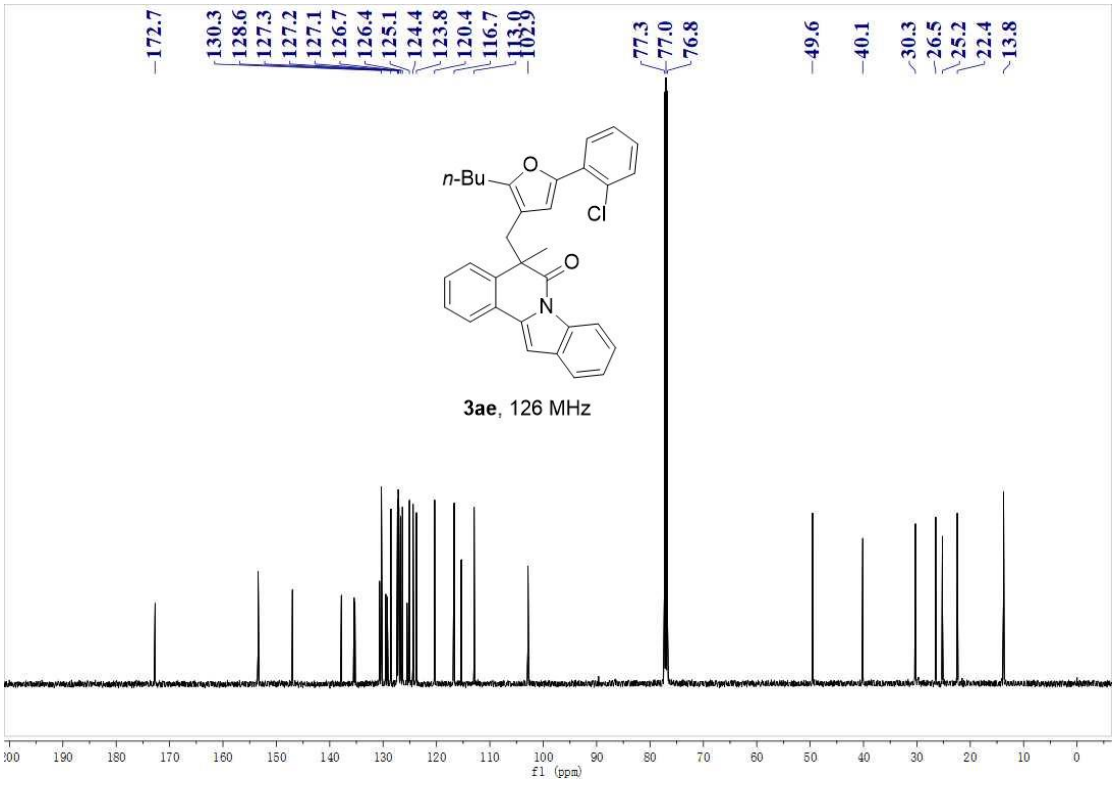
^{19}F NMR spectrum of **3ad** without using internal reference compound

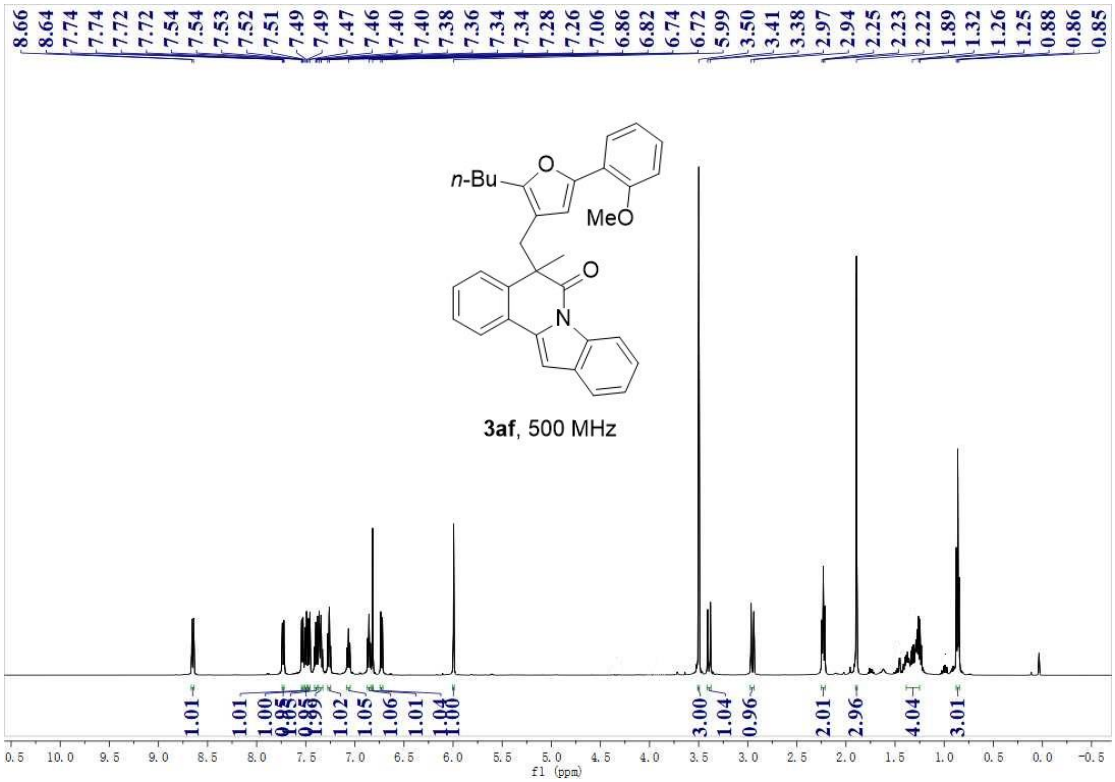


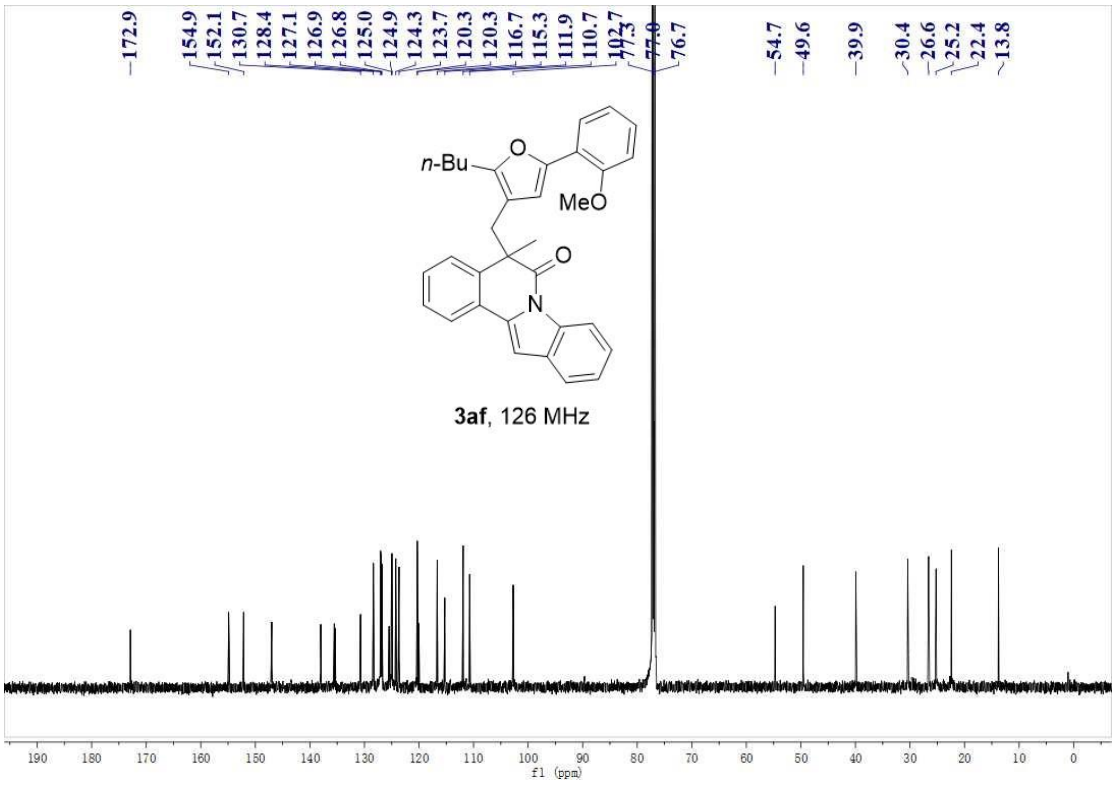
^{19}F NMR spectrum of **3ad** referenced with $PhCF_3$ (-62. 61) in $CDCl_3$

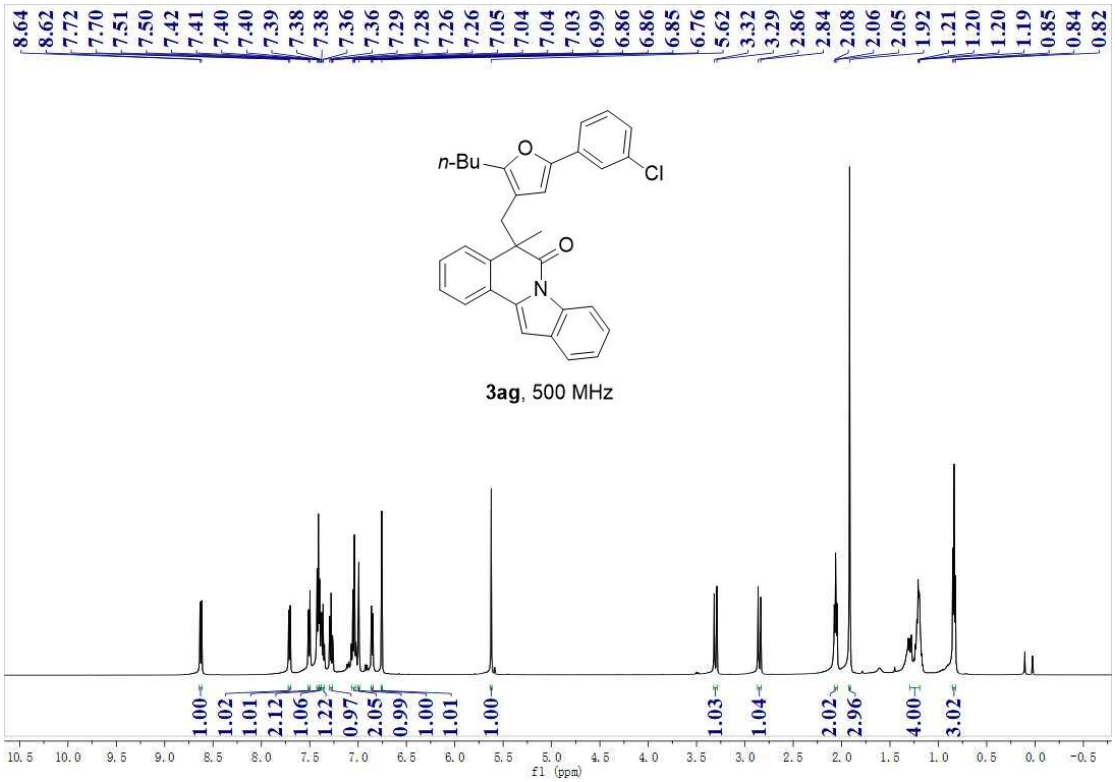


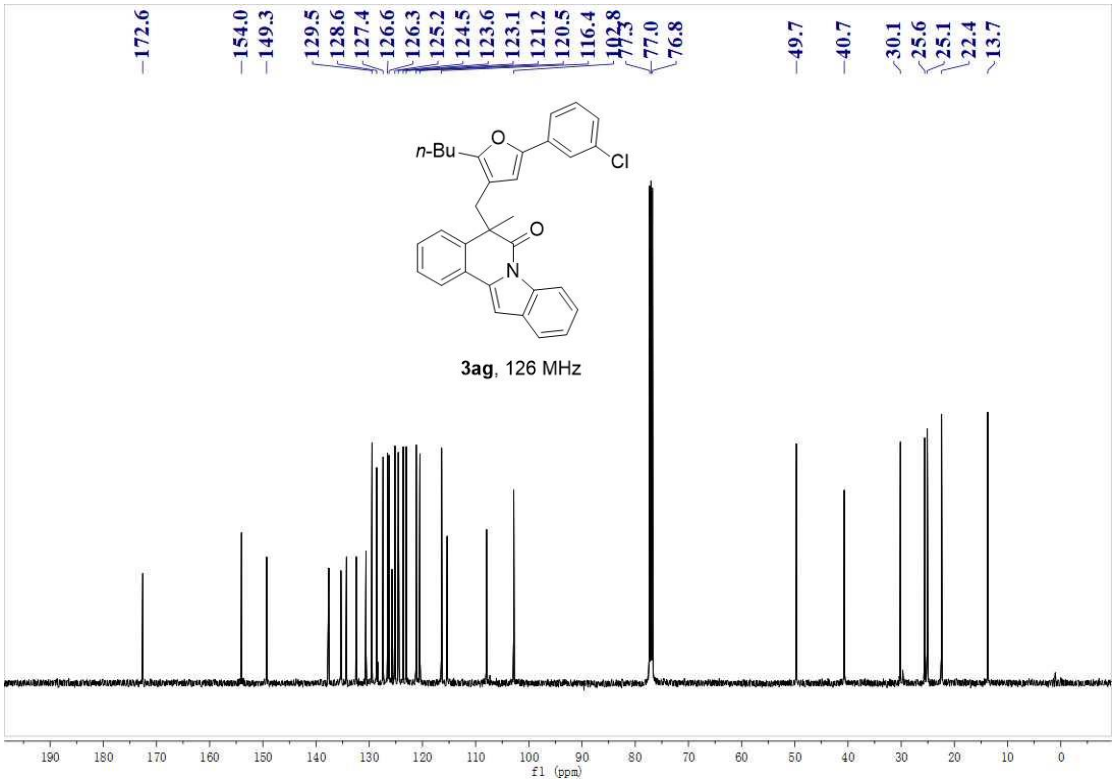

8.61
8.60
7.76
7.74
7.53
7.51
7.48
7.47
7.42
7.42
7.41
7.41
7.40
7.37
7.35
7.34
7.29
7.27
7.26
7.26
7.22
7.21
7.20
7.20
7.11
7.09
7.00
6.83
6.08
3.41
3.39
2.95
2.92
2.25
2.23
2.21
2.21
1.90
1.26
1.25
1.23
0.86
0.85
0.83
n-Bu
O
Cl
O
N
3ae, 500 MHz
0.99
1.03
1.04
0.99
1.07
1.04
0.96
1.05
1.97
2.98
4.06
2.98
f1 (ppm)

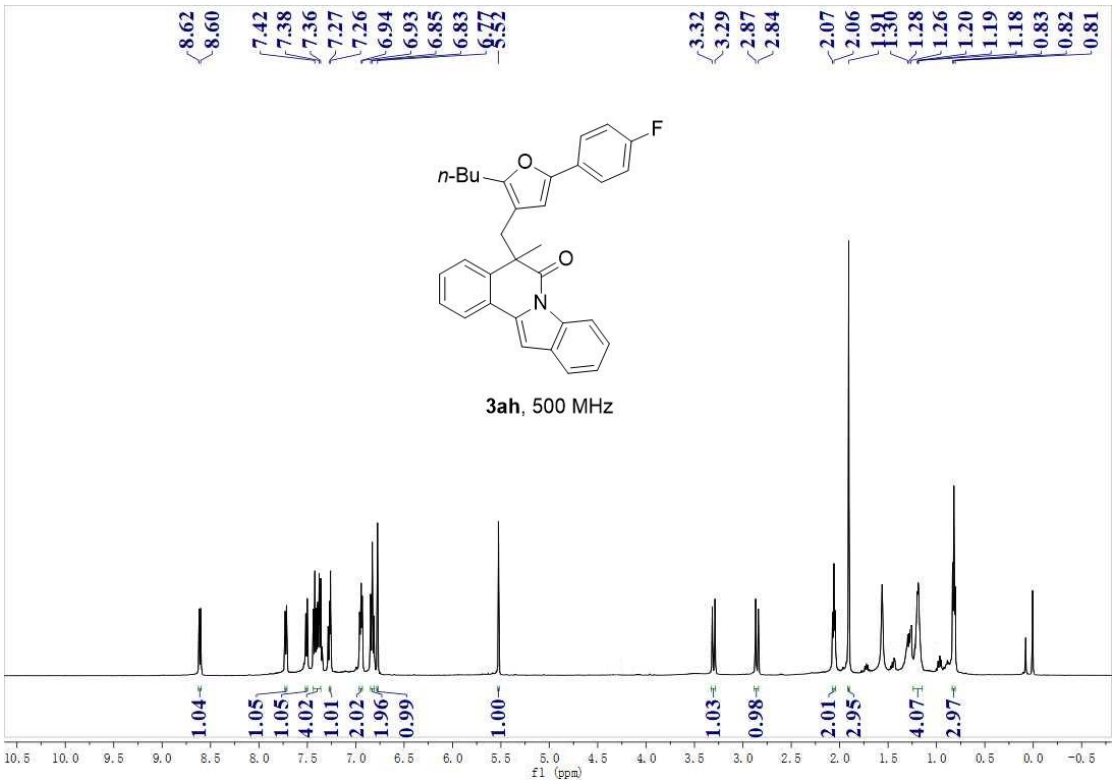

172.7
130.3
128.6
127.3
127.2
127.1
126.7
126.4
125.1
124.4
123.8
120.4
116.7
113.0
102.3
77.3
77.0
76.8
49.6
40.1
30.3
26.5
25.2
22.4
13.8
n-Bu
O
Cl
O
N
3ae, 126 MHz
f1 (ppm)


8.66 8.64 7.74 7.74 7.72 7.72 7.54 7.54 7.53 7.52 7.51 7.49 7.49 7.47 7.46 7.40 7.40 7.38 7.36 7.34 7.34 7.28 7.26 7.06 6.86 6.82 6.74 6.72 5.99 3.50 3.41 3.38 2.97 2.94 2.25 2.23 2.22 1.89 1.32 1.26 1.25 0.88 0.86 0.85
n-Bu
O
MeO
O
N
3af, 500 MHz
1.01 1.01 1.00 1.02 1.05 1.06 1.01 3.00 1.04 0.96 2.01 2.96 4.04 3.01
f1 (ppm)

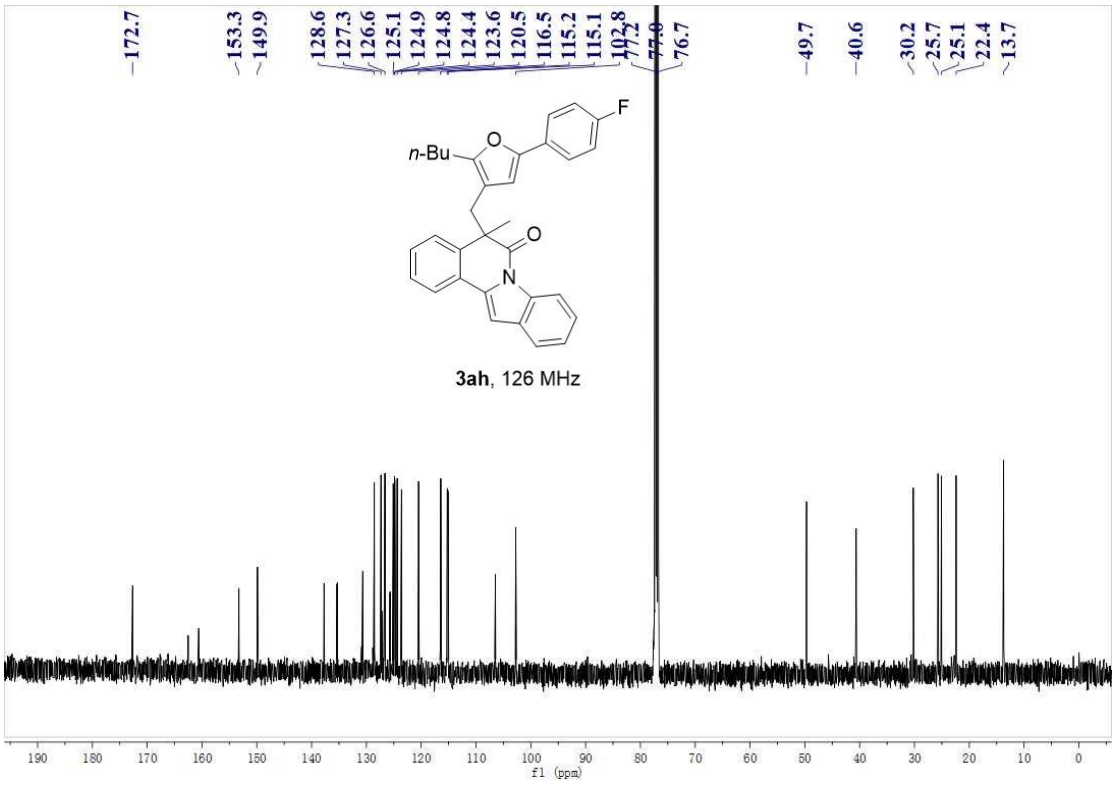

172.9 154.9 152.1 130.7 128.4 127.1 126.9 126.8 125.0 124.9 124.3 123.7 120.3 120.3 116.7 115.3 111.9 110.7 102.7 77.3 77.0 76.7 54.7 49.6 39.9 30.4 26.6 25.2 22.4 13.8
n-Bu
O
MeO
O
N
3af, 126 MHz
f1 (ppm)


8.64 8.62 7.72 7.70 7.51 7.50 7.42 7.41 7.40 7.40 7.39 7.38 7.38 7.36 7.36 7.29 7.28 7.26 7.26 7.05 7.04 7.04 7.03 6.99 6.86 6.86 6.85 6.76 5.62 3.32 3.29 2.86 2.84 2.08 2.06 2.05 1.92 1.21 1.20 1.20 1.19 0.85 0.84 0.82
n-Bu
O
Cl
O
N
3ag, 500 MHz
1.00 1.02 1.01 2.12 1.06 1.22 0.97 2.05 0.99 1.00 1.01 1.00 1.03 1.04 2.02 2.96 4.00 3.02
f1 (ppm)


172.6 154.0 149.3 129.5 128.6 127.4 126.6 126.3 125.2 124.5 123.6 123.1 121.2 120.5 116.4 77.3 77.0 76.8 49.7 40.7 30.1 25.6 25.1 22.4 13.7
n-Bu
O
Cl
O
N
3ag, 126 MHz
f1 (ppm)

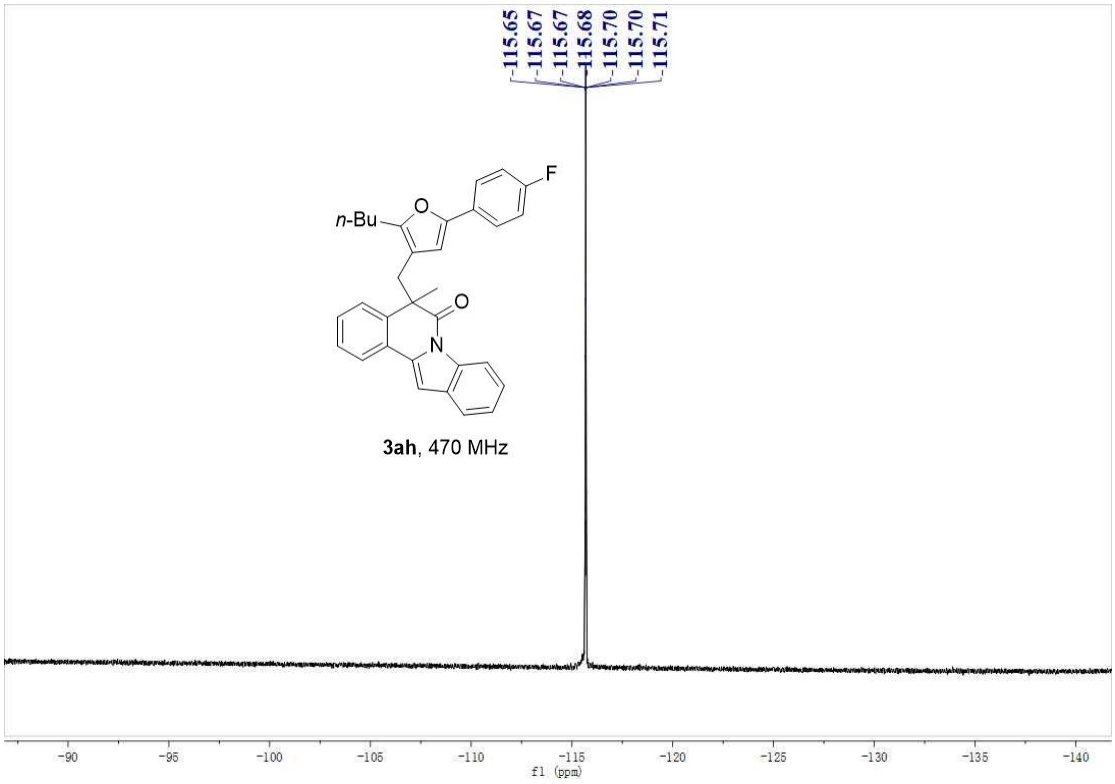


3ah, 500 MHz

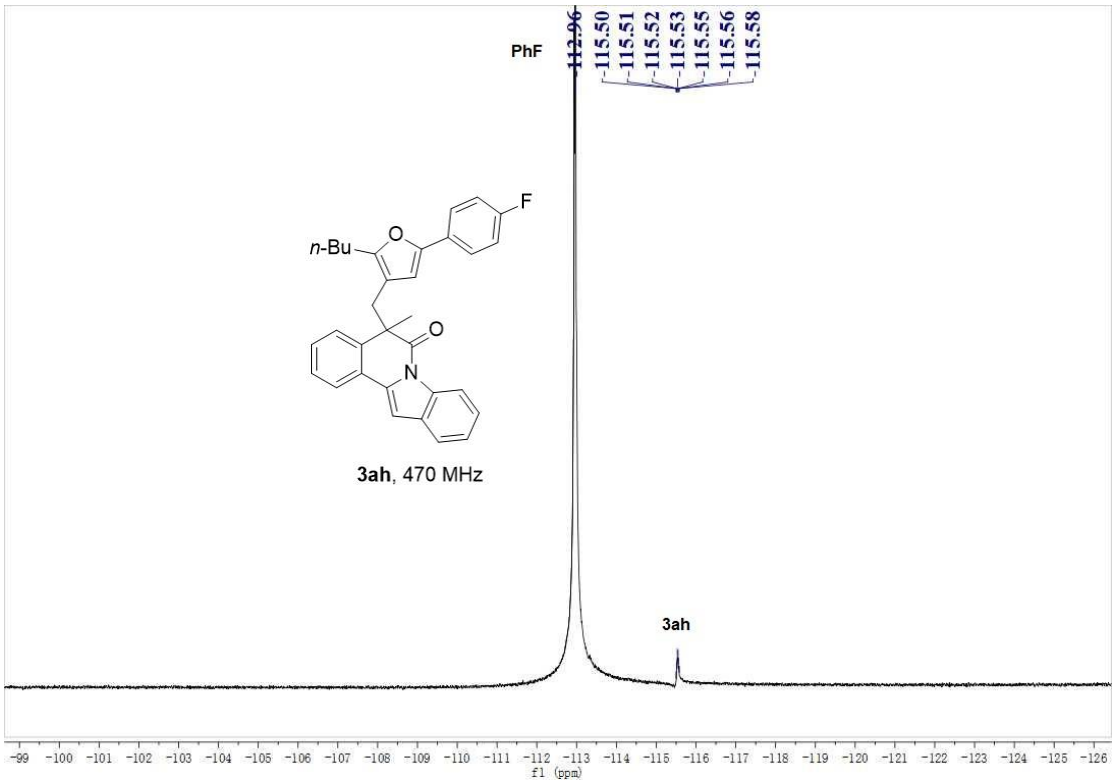


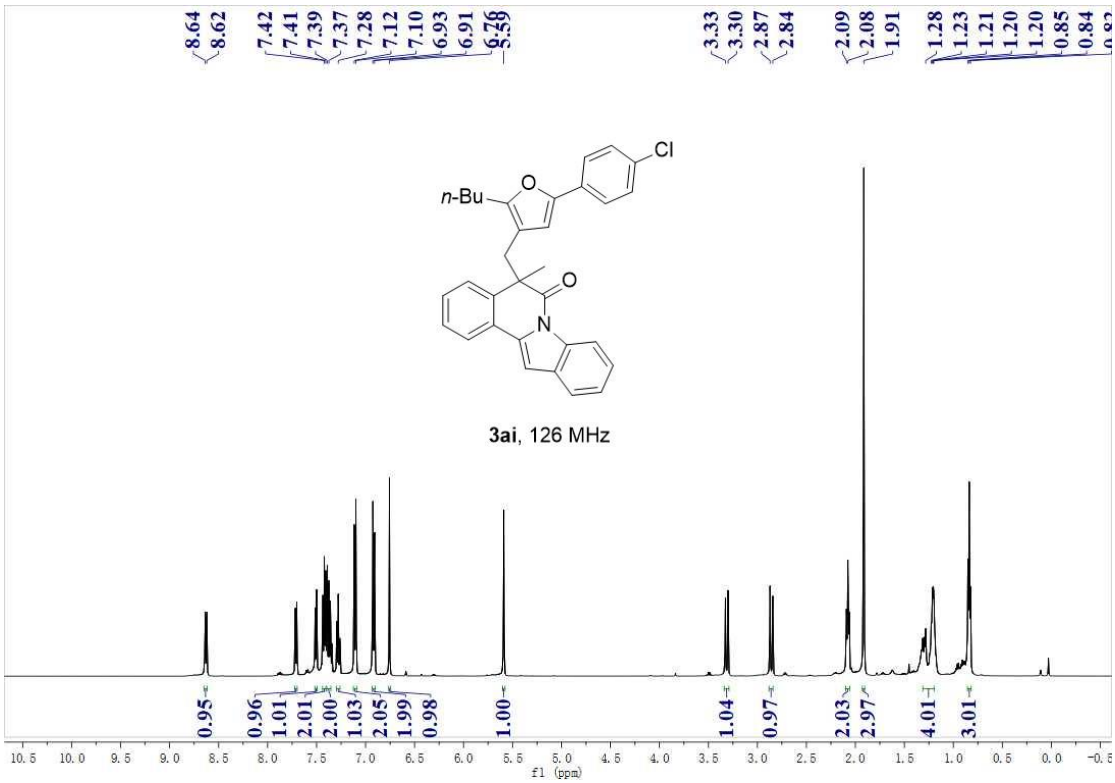
3ah, 126 MHz

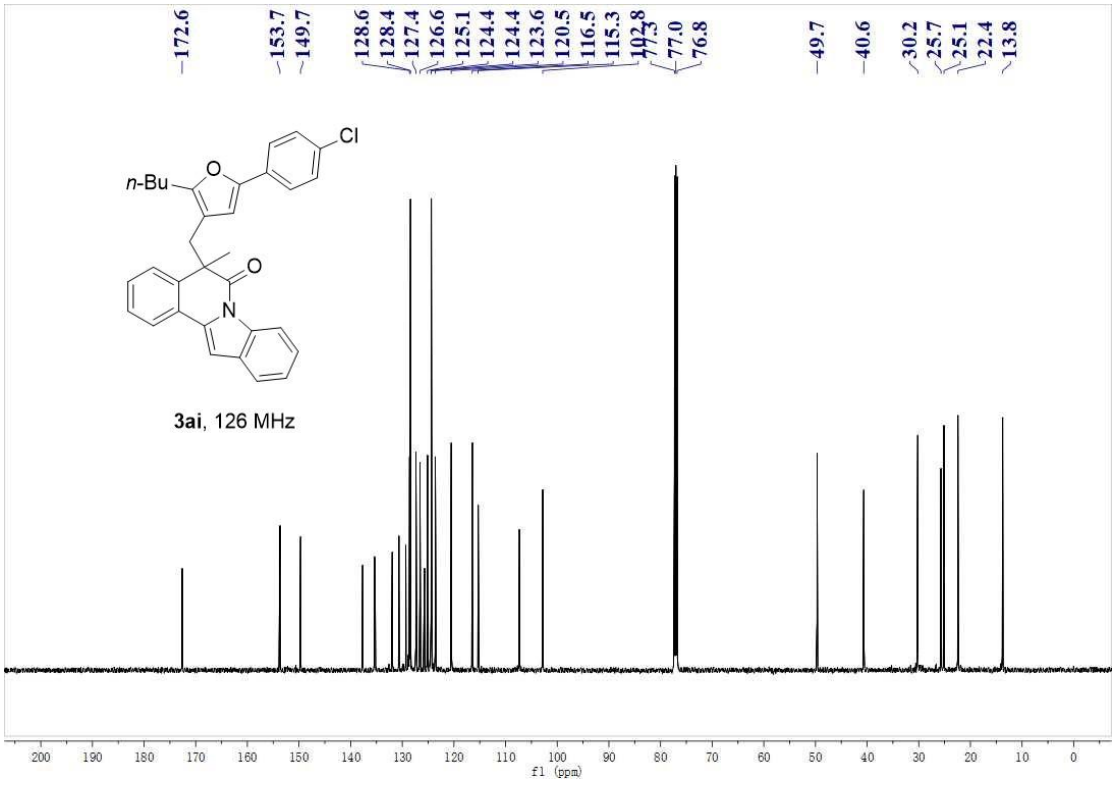
^{19}F NMR spectrum of **3ah** without using internal reference compound

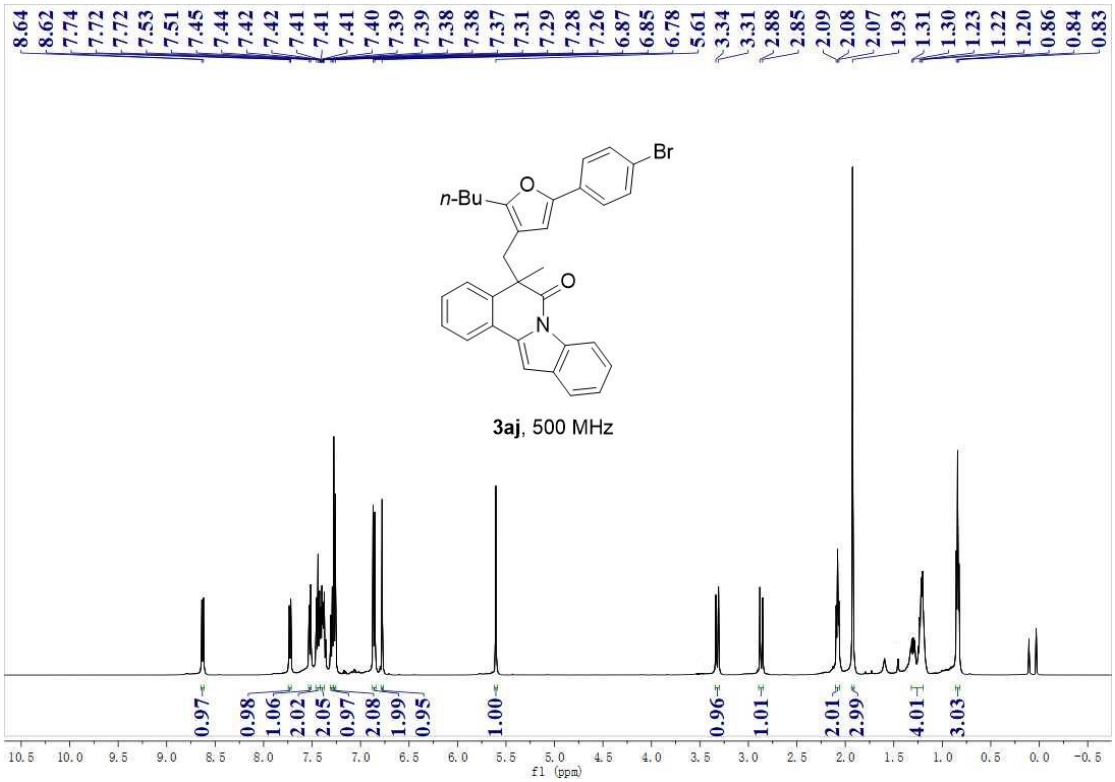


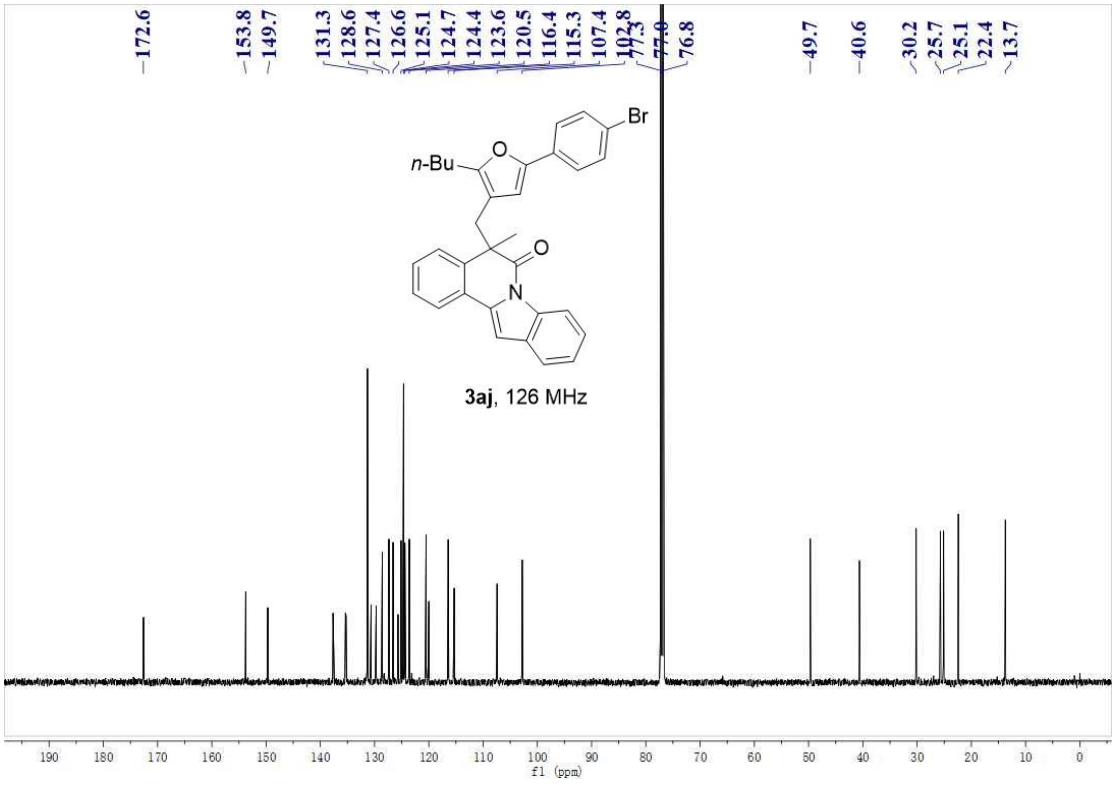
^{19}F NMR spectrum of **3ah** referenced with PhF (-112.96) in $CDCl_3$

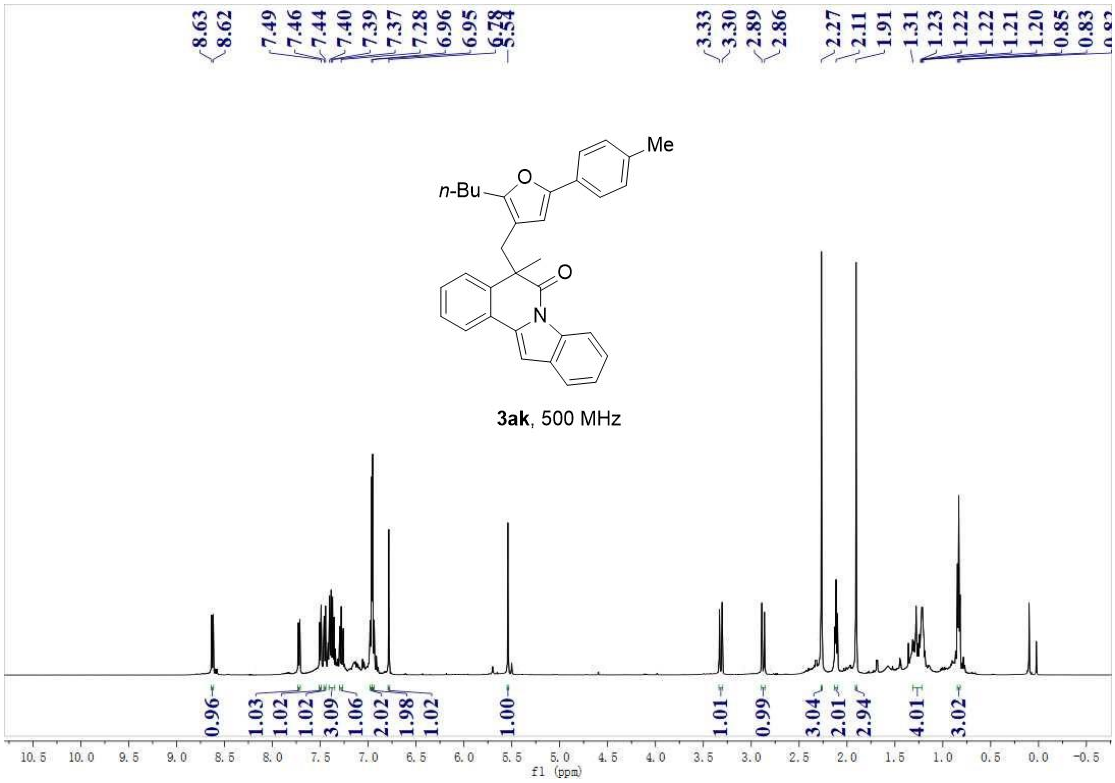



8.64
8.62
7.42
7.41
7.39
7.37
7.28
7.12
7.10
6.93
6.91
6.76
6.75
3.33
3.30
2.87
2.84
2.09
2.08
1.91
1.28
1.23
1.21
1.20
1.20
0.85
0.84
n-Bu
O
Cl
O
N
3ai, 126 MHz
0.95
0.96
1.01
2.01
2.00
1.03
2.05
1.99
0.98
1.00
1.04
0.97
2.03
2.97
4.01
3.01
f1 (ppm)

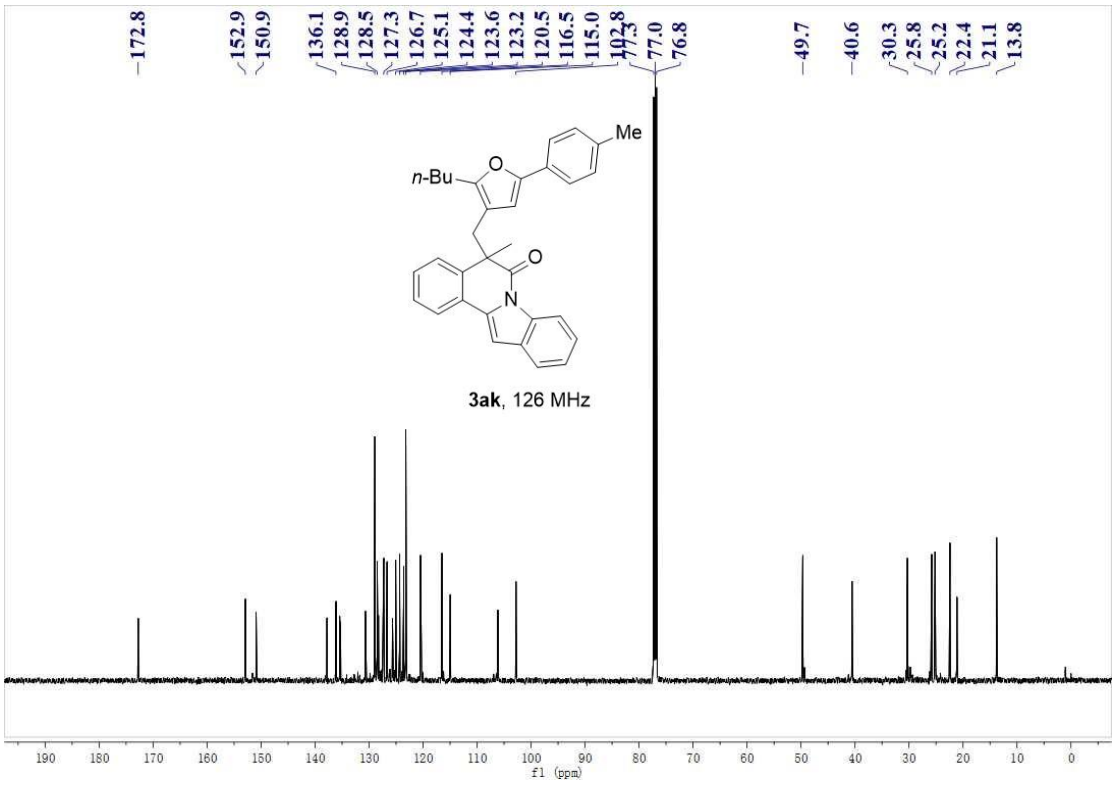

172.6
153.7
149.7
128.6
128.4
127.4
126.6
125.1
124.4
124.4
123.6
120.5
116.5
115.3
102.8
77.3
77.0
76.8
49.7
40.6
30.2
25.7
25.1
22.4
13.8
n-Bu
O
Cl
O
N
3ai, 126 MHz
f1 (ppm)


8.64 8.62 7.74 7.72 7.72 7.53 7.51 7.45 7.44 7.42 7.42 7.41 7.41 7.41 7.40 7.39 7.39 7.38 7.38 7.37 7.31 7.29 7.28 7.26 6.87 6.85 6.78 5.61 3.34 3.31 2.88 2.85 2.09 2.08 2.07 1.93 1.31 1.30 1.23 1.22 1.20 0.86 0.84 0.83
Br
n-Bu
O
O
N
3aj, 500 MHz
0.97 0.98 1.06 2.02 2.05 0.97 2.08 1.99 0.95 1.00 0.96 1.01 2.01 2.99 4.01 3.03
f1 (ppm)

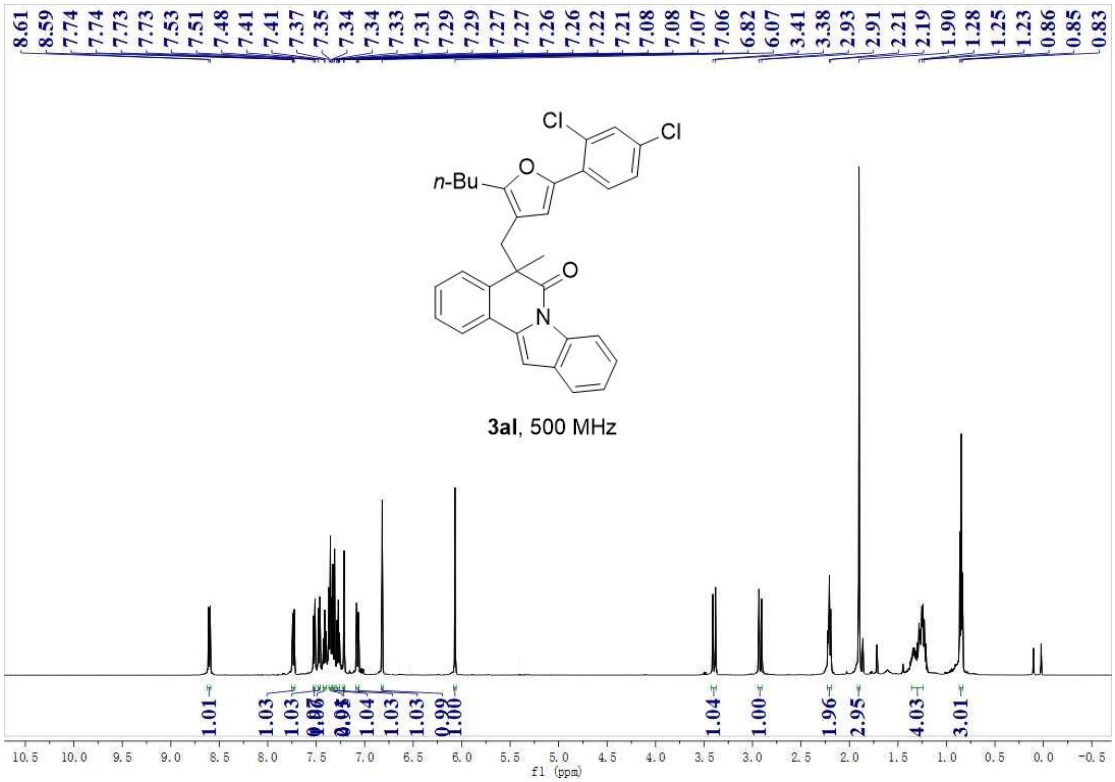

172.6 153.8 149.7 131.3 128.6 127.4 126.6 125.1 124.7 124.4 123.6 120.5 116.4 115.3 107.4 102.8 77.3 77.0 76.8 49.7 40.6 30.2 25.7 25.1 22.4 13.7
Br
n-Bu
O
O
N
3aj, 126 MHz
f1 (ppm)



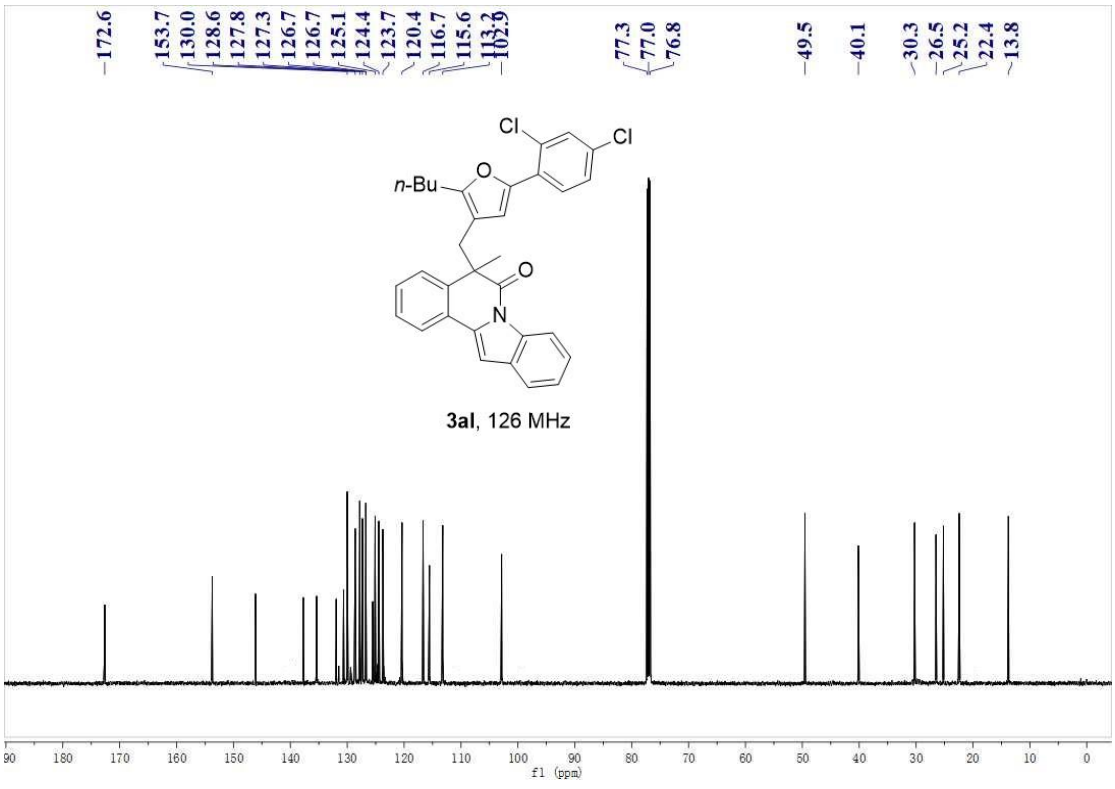
3ak, 500 MHz



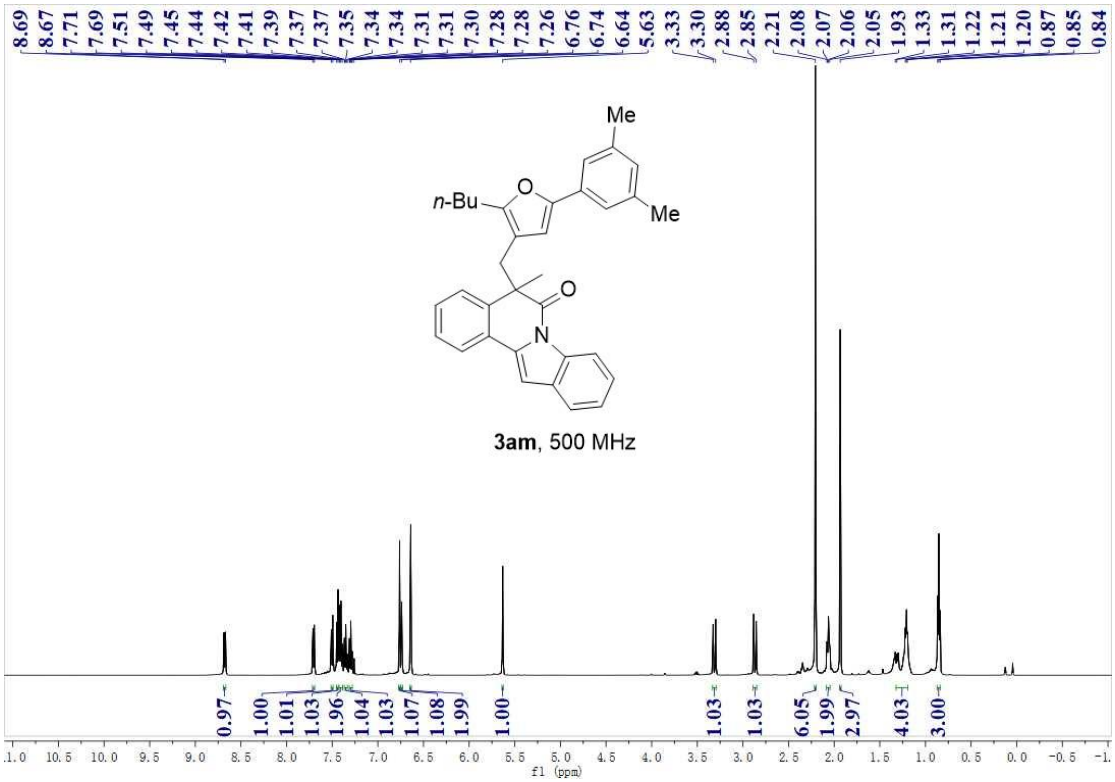
3ak, 126 MHz

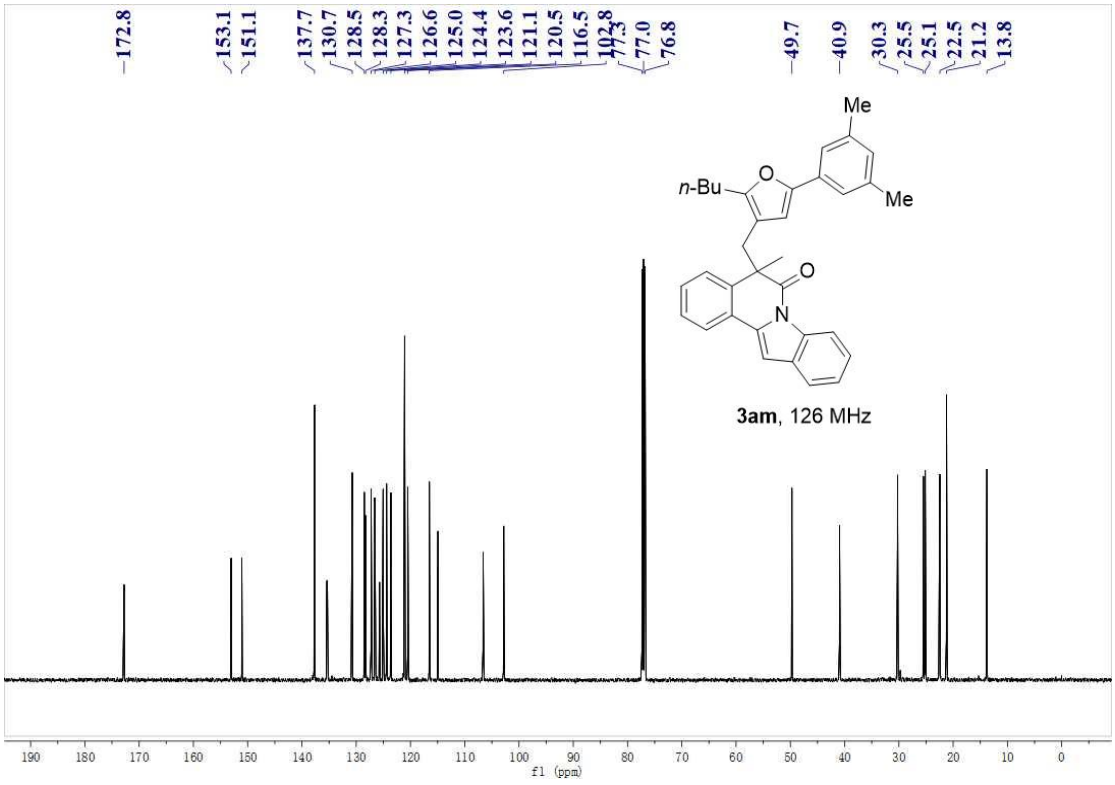


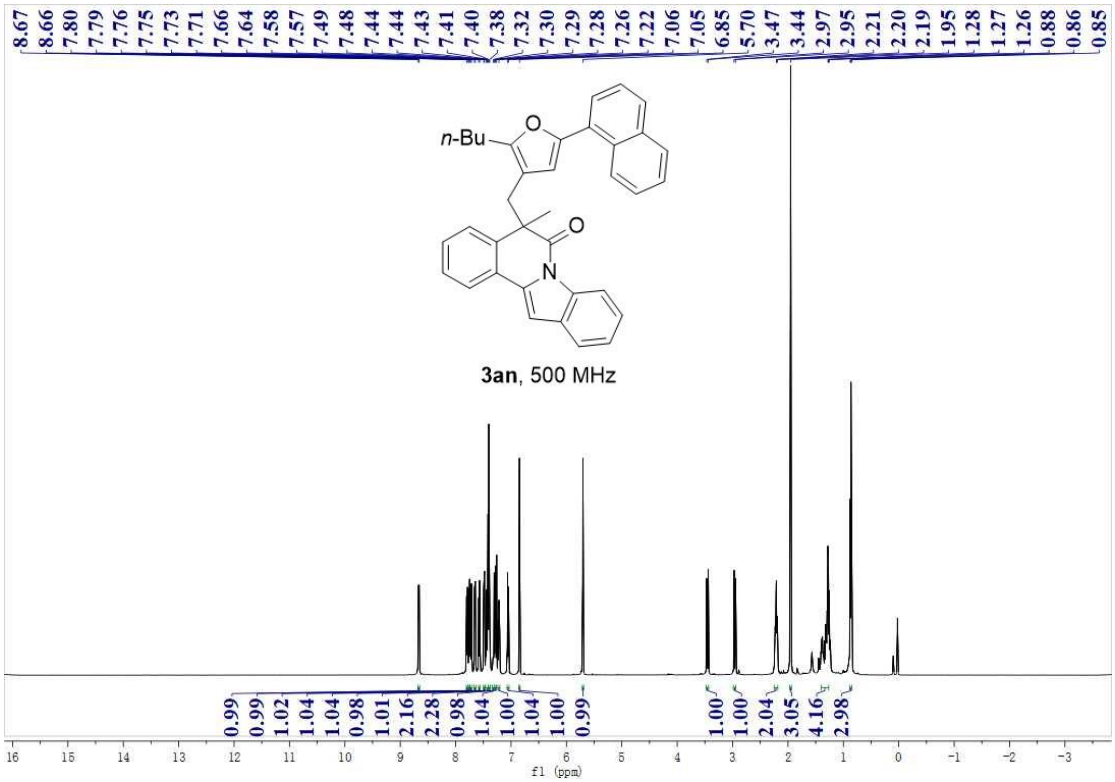
3al, 500 MHz

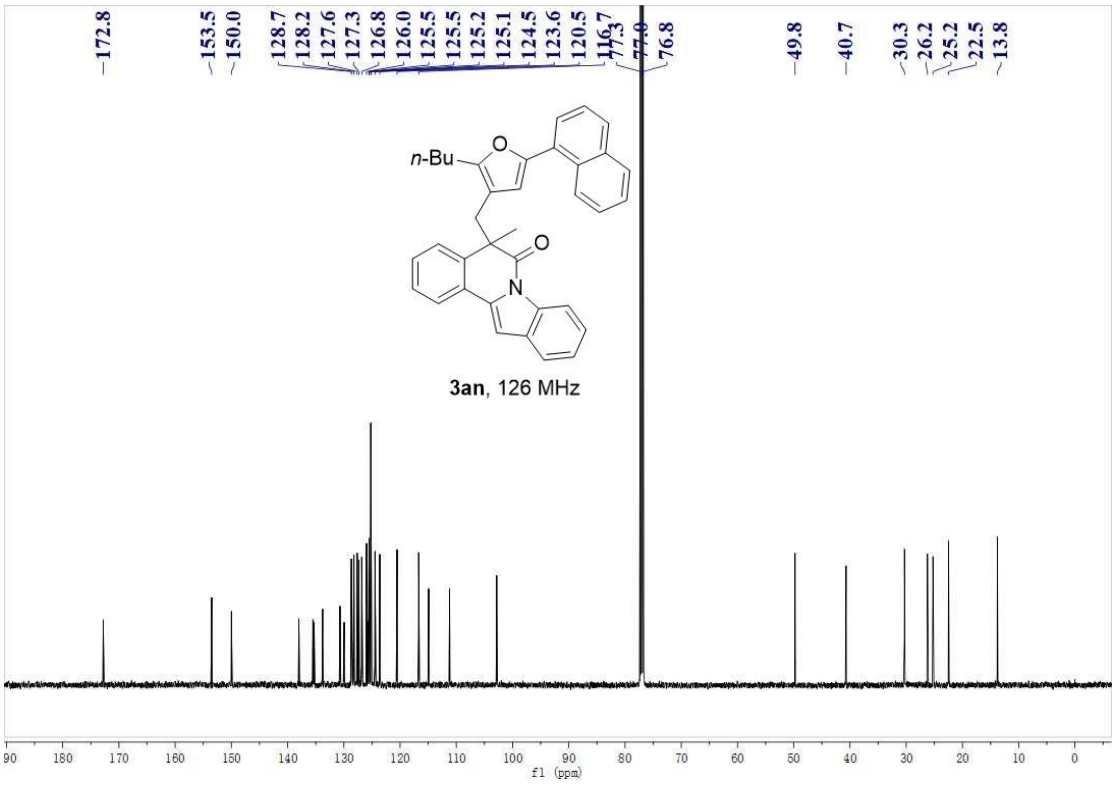


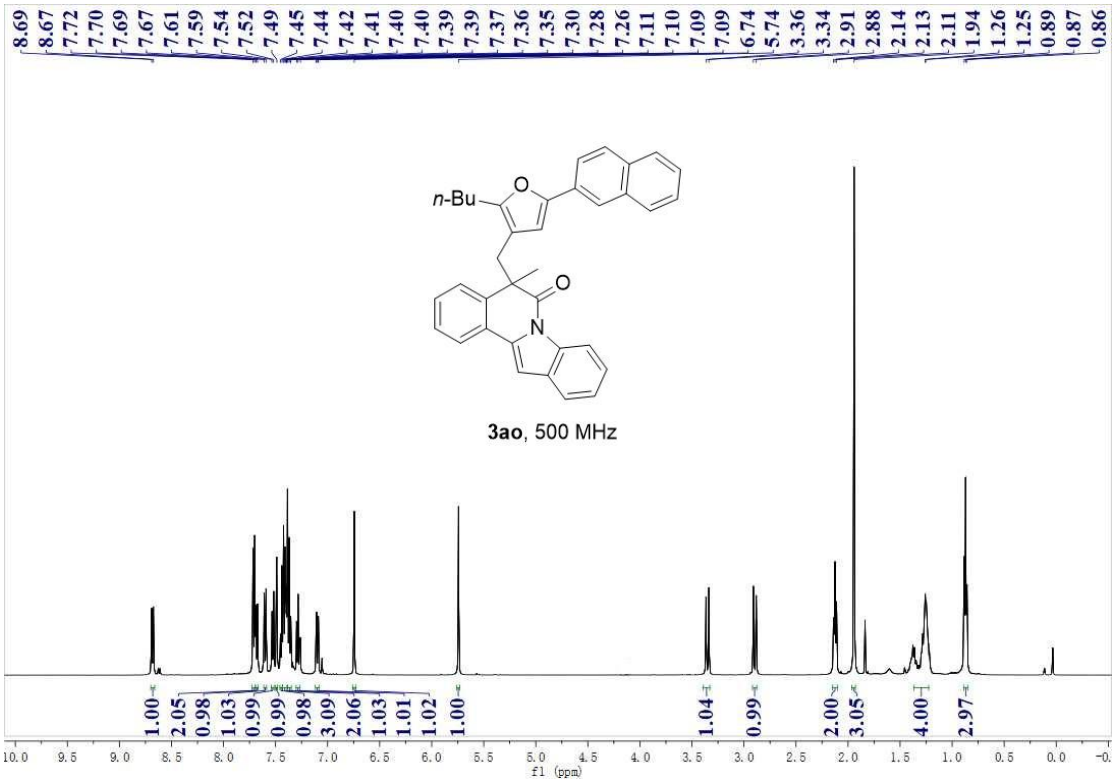
3al, 126 MHz

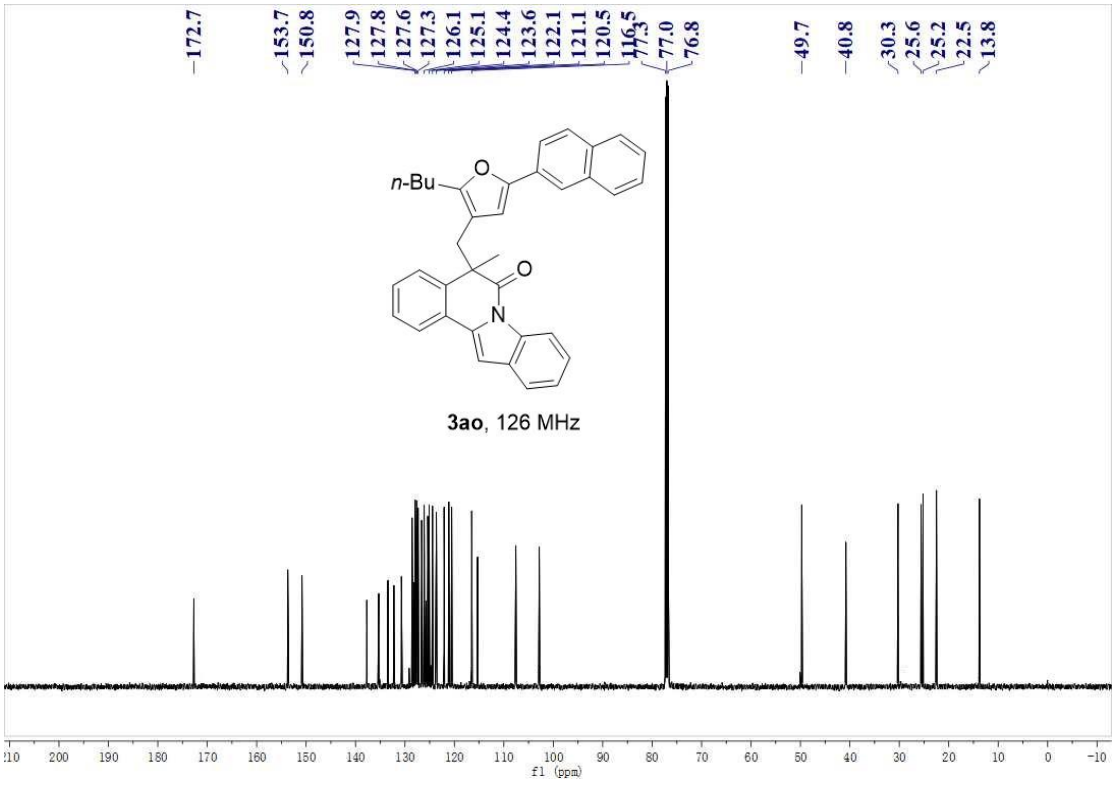

8.69 8.67 7.71 7.69 7.51 7.49 7.45 7.44 7.42 7.41 7.39 7.37 7.37 7.35 7.34 7.34 7.31 7.31 7.30 7.28 7.28 7.26 6.76 6.74 6.64 5.63 3.33 3.30 2.88 2.85 2.21 2.08 2.07 2.06 2.05 1.93 1.33 1.31 1.22 1.21 1.20 0.87 0.85 0.84
Me
n-Bu
O
Me
O
N
3am, 500 MHz
0.97 1.00 1.01 1.03 1.96 1.04 1.03 1.07 1.08 1.99 1.00 1.03 1.03 6.05 1.99 2.97 4.03 3.00
f1 (ppm)

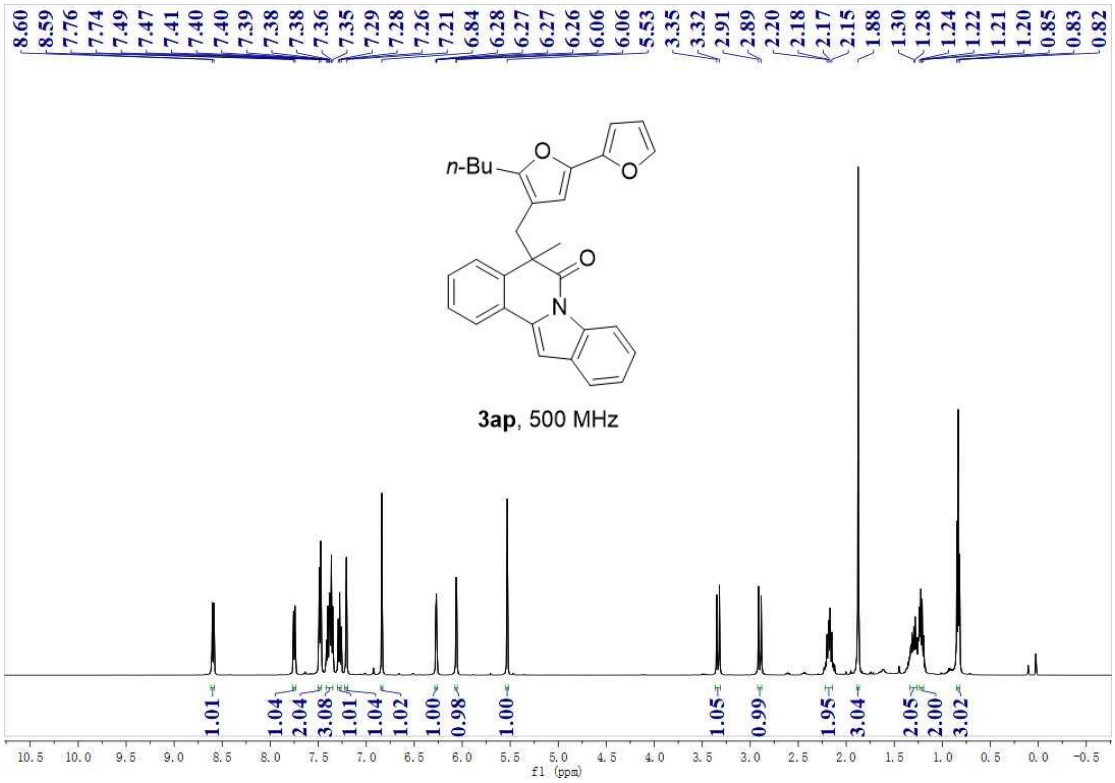

172.8 153.1 151.1 137.7 130.7 128.5 128.3 127.3 126.6 125.0 124.4 123.6 121.1 120.5 116.5 102.8 77.3 77.0 76.8 49.7 40.9 30.3 25.5 25.1 22.5 21.2 13.8
Me
n-Bu
O
Me
O
N
3am, 126 MHz
f1 (ppm)

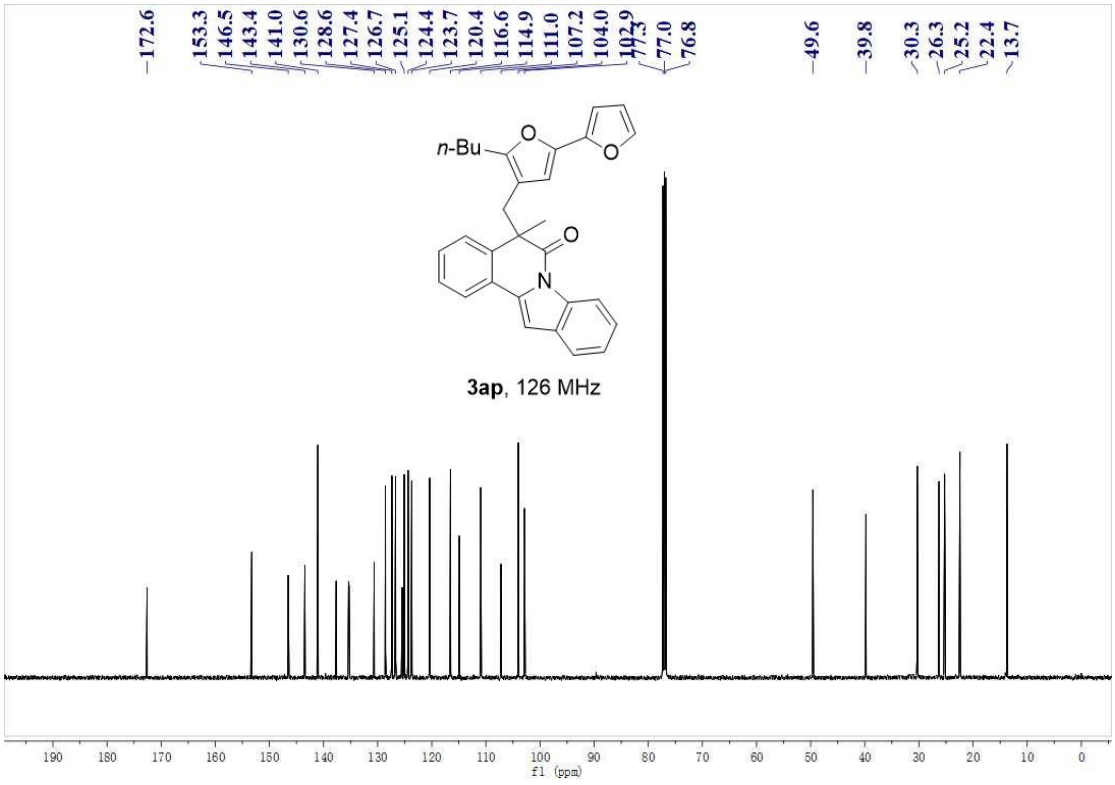

8.67 8.66 7.80 7.79 7.76 7.75 7.73 7.71 7.66 7.64 7.58 7.57 7.49 7.48 7.44 7.44 7.43 7.41 7.40 7.38 7.32 7.30 7.29 7.28 7.26 7.22 7.06 7.05 6.85 5.70 3.47 3.44 2.97 2.95 2.21 2.20 2.19 1.95 1.28 1.27 1.26 0.88 0.86 0.85
n-Bu
O
O
N
3an, 500 MHz
0.99 0.99 1.02 1.04 1.04 0.98 1.01 2.16 2.28 0.98 1.04 1.00 1.04 1.00 0.99 1.00 1.00 2.04 3.05 4.16 2.98
f1 (ppm)

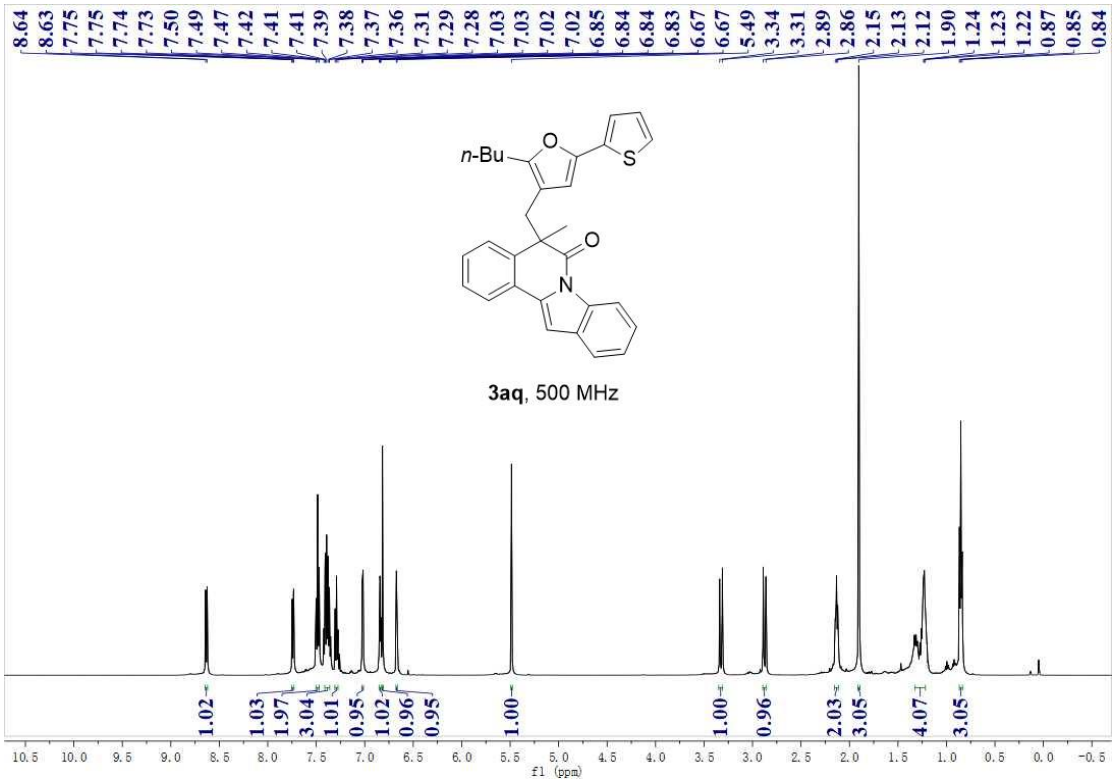

172.8 153.5 150.0 128.7 128.2 127.6 127.3 126.8 126.0 125.5 125.5 125.2 125.1 124.5 123.6 120.5 116.7 77.3 77.0 76.8 49.8 40.7 30.3 26.2 25.2 22.5 13.8
n-Bu
O
O
N
3an, 126 MHz
f1 (ppm)

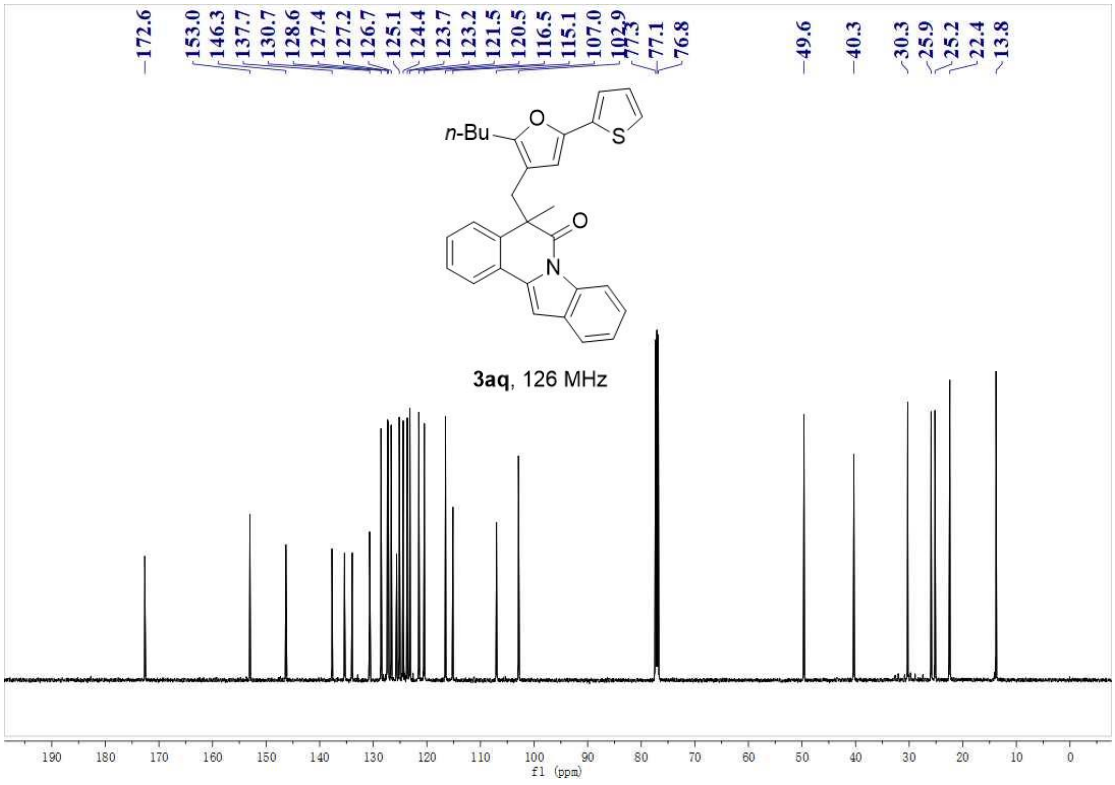

8.69
8.67
7.72
7.70
7.69
7.67
7.61
7.59
7.54
7.52
7.49
7.45
7.44
7.42
7.41
7.40
7.40
7.39
7.39
7.37
7.36
7.35
7.30
7.28
7.26
7.11
7.10
7.09
7.09
6.74
5.74
3.36
3.34
2.91
2.88
2.14
2.13
2.11
1.94
1.26
1.25
0.89
0.87
0.86
n-Bu
O
O
N
3ao, 500 MHz
1.00
2.05
0.98
1.03
0.99
0.99
0.98
3.09
2.06
1.03
1.01
1.02
1.00
1.04
0.99
2.00
3.05
4.00
2.97
f1 (ppm)

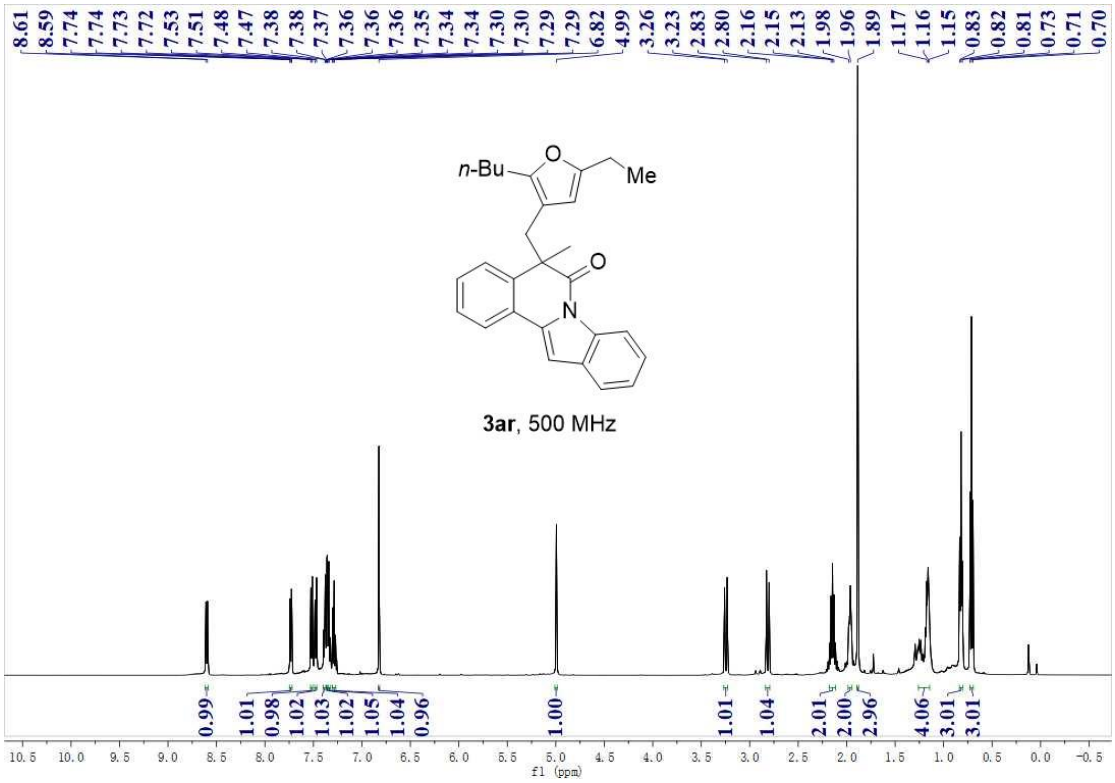

172.7
153.7
150.8
127.9
127.8
127.6
127.3
126.1
125.1
124.4
123.6
122.1
121.1
120.5
116.5
77.3
77.0
76.8
49.7
40.8
30.3
25.6
25.2
22.5
13.8
n-Bu
O
O
N
3ao, 126 MHz
f1 (ppm)


8.60 8.59 7.76 7.74 7.49 7.47 7.41 7.40 7.40 7.39 7.38 7.38 7.36 7.35 7.29 7.28 7.26 7.21 6.84 6.28 6.27 6.27 6.26 6.06 6.06 5.53 3.35 3.32 2.91 2.89 2.20 2.18 2.17 2.15 1.88 1.30 1.28 1.24 1.22 1.21 1.20 0.85 0.83 0.82
n-Bu
O
O
O
N
3ap, 500 MHz
1.01 1.04 2.04 3.08 1.01 1.04 1.02 1.00 0.98 1.00 1.05 0.99 1.95 3.04 2.05 2.00 3.02
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)

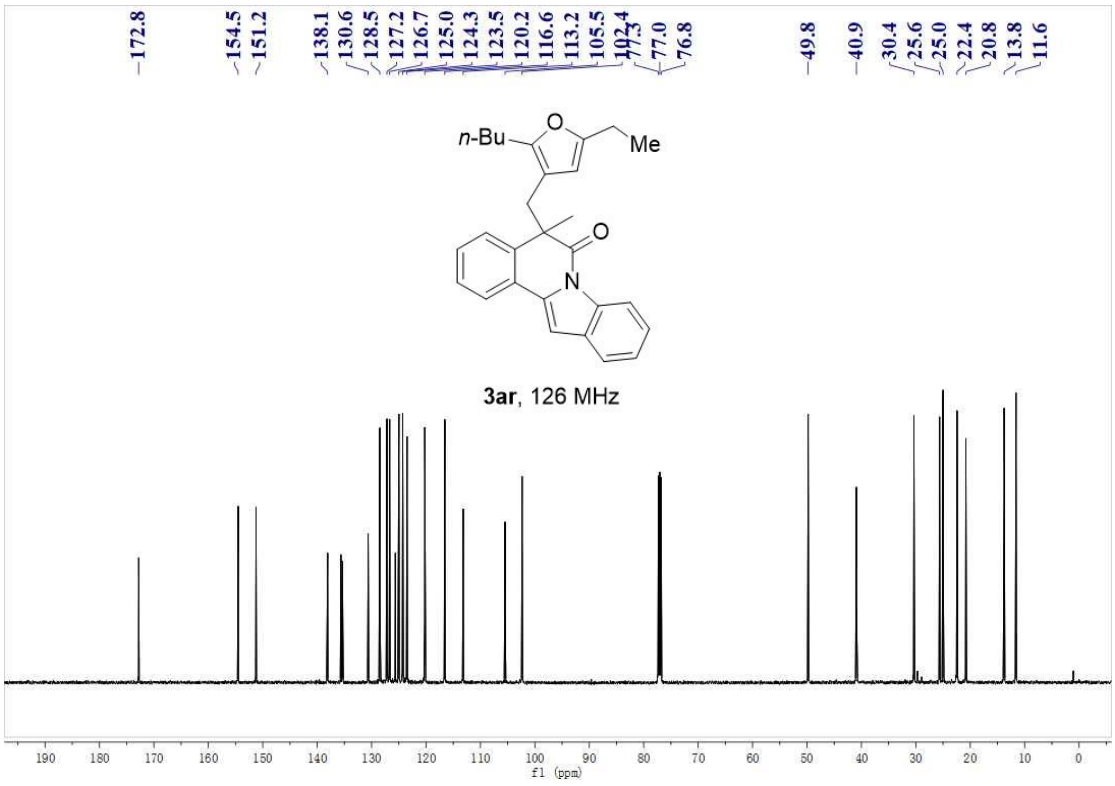

172.6 153.3 146.5 143.4 141.0 130.6 128.6 127.4 126.7 125.1 124.4 123.7 120.4 116.6 114.9 111.0 107.2 104.0 102.9 77.3 77.0 76.8 49.6 39.8 30.3 26.3 25.2 22.4 13.7
n-Bu
O
O
O
N
3ap, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.64 8.63 7.75 7.75 7.74 7.73 7.50 7.49 7.47 7.42 7.41 7.41 7.39 7.38 7.37 7.36 7.31 7.29 7.28 7.03 7.03 7.02 7.02 6.85 6.84 6.84 6.83 6.67 6.67 5.49 3.34 3.31 2.89 2.86 2.15 2.13 2.12 1.90 1.24 1.23 1.22 0.87 0.85 0.84
n-Bu
O
S
O
N
3aq, 500 MHz
1.02 1.03 1.97 3.04 1.01 0.95 1.02 0.96 0.95 1.00 1.00 0.96 2.03 3.05 4.07 3.05
f1 (ppm)

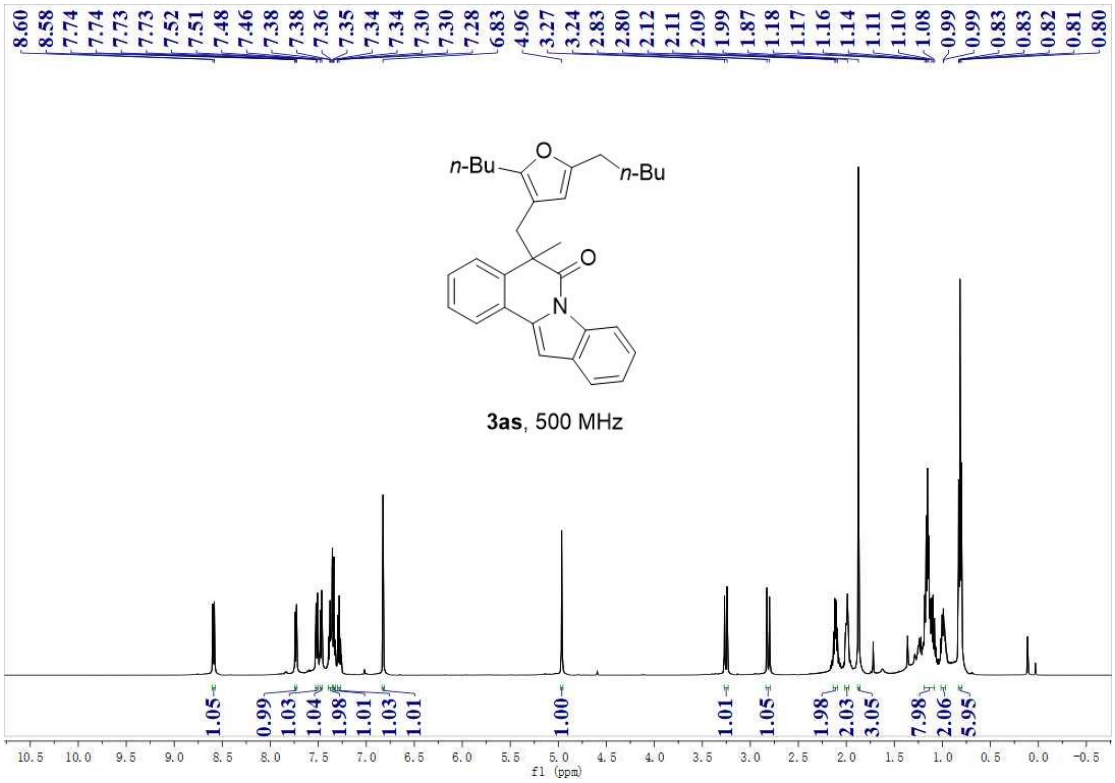

172.6 153.0 146.3 137.7 130.7 128.6 127.4 127.2 126.7 125.1 124.4 123.7 123.2 121.5 120.5 116.5 115.1 107.0 102.9 77.3 77.1 76.8 49.6 40.3 30.3 25.9 25.2 22.4 13.8
n-Bu
O
S
O
N
3aq, 126 MHz
f1 (ppm)

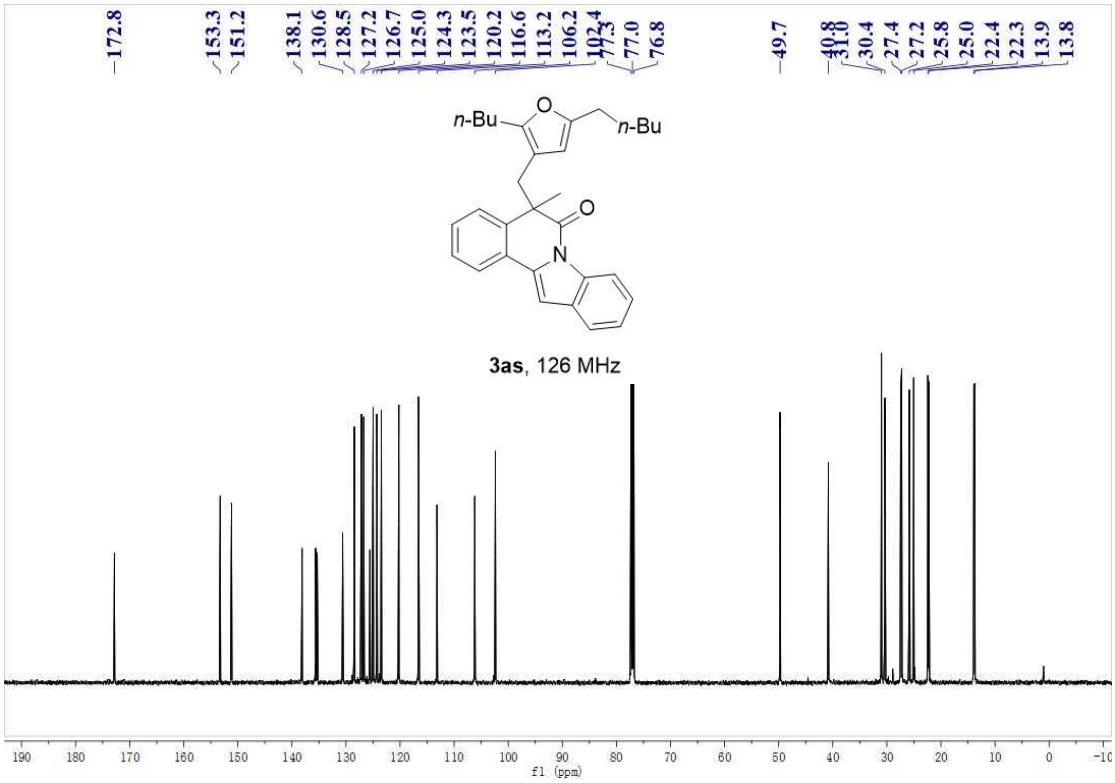


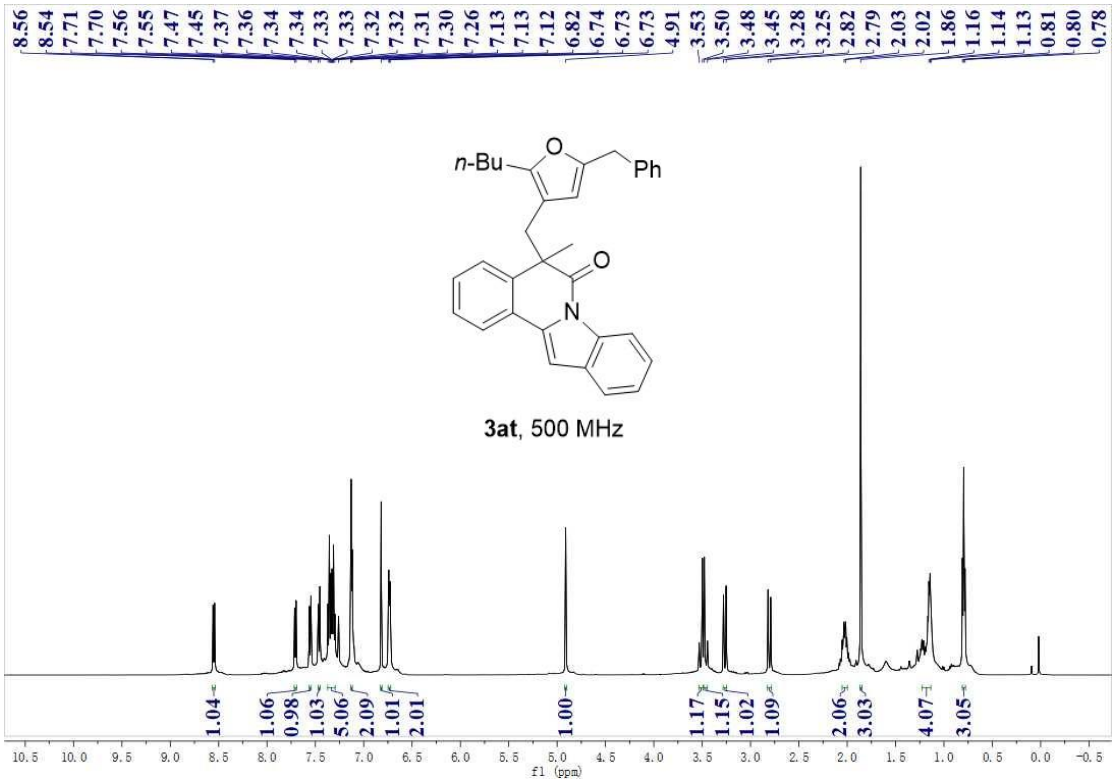
3ar, 500 MHz

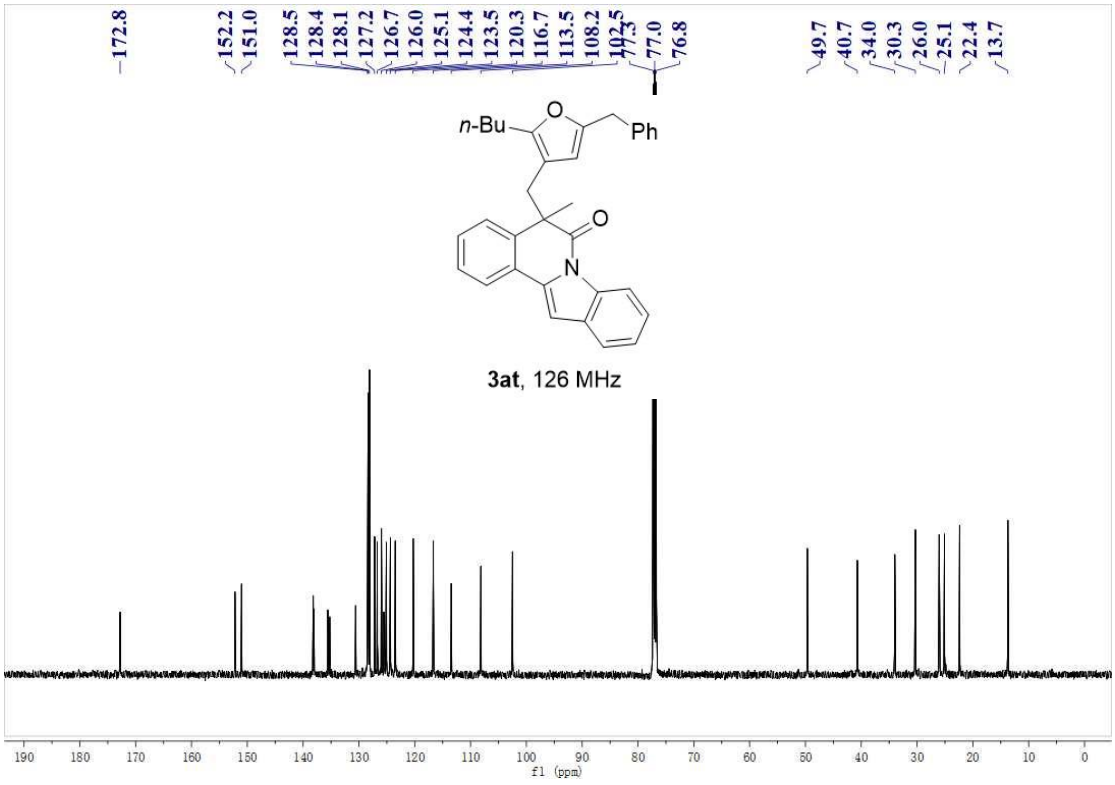


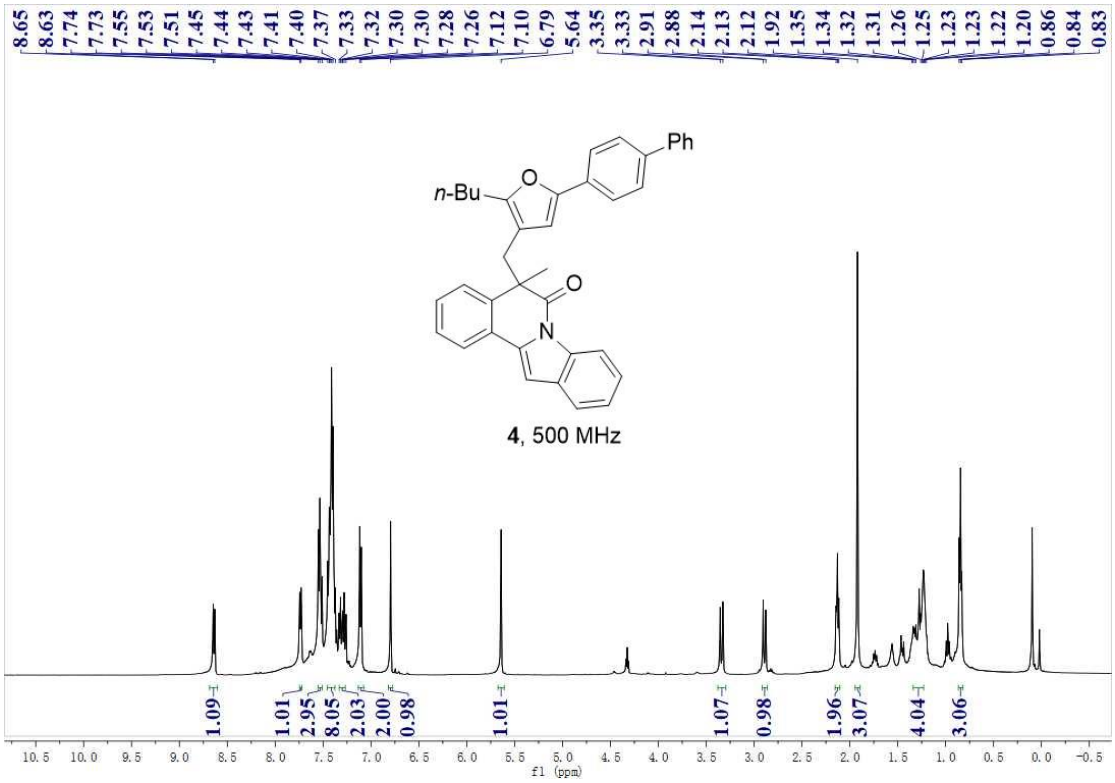
3ar, 126 MHz

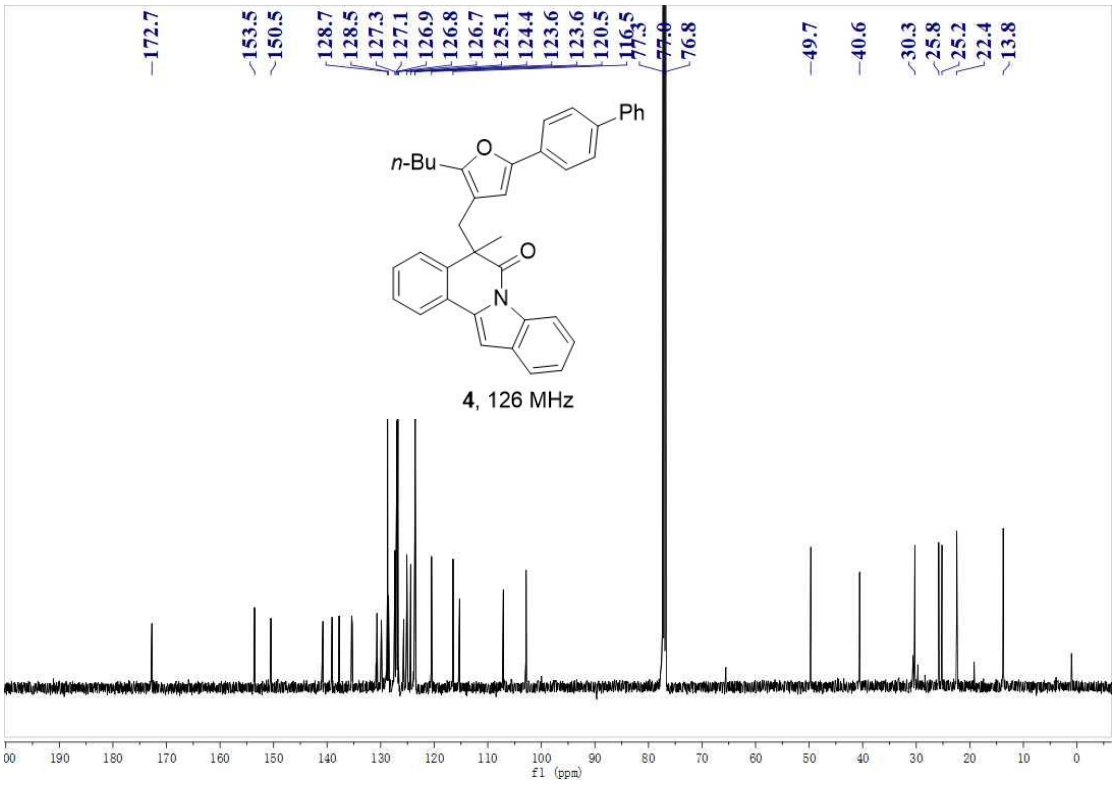

8.60 8.58 7.74 7.74 7.73 7.73 7.52 7.51 7.48 7.46 7.38 7.38 7.36 7.35 7.34 7.34 7.30 7.30 7.28 6.83 4.96 3.27 3.24 2.83 2.80 2.12 2.11 2.09 1.99 1.87 1.18 1.17 1.16 1.14 1.11 1.10 1.08 0.99 0.99 0.83 0.83 0.82 0.81 0.80
n-Bu
n-Bu
O
O
N
3as, 500 MHz
1.05 0.99 1.03 1.04 1.98 1.01 1.03 1.01 1.00 1.01 1.05 1.98 2.03 3.05 7.98 2.06 5.95
f1 (ppm)


172.8 153.3 151.2 138.1 130.6 128.5 127.2 126.7 125.0 124.3 123.5 120.2 116.6 113.2 106.2 102.4 77.3 77.0 76.8 49.7 40.8 31.0 30.4 27.4 27.2 25.8 25.0 22.4 22.3 13.9 13.8
n-Bu
n-Bu
O
O
N
3as, 126 MHz
f1 (ppm)


8.56 8.54 7.71 7.70 7.56 7.55 7.47 7.45 7.37 7.36 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.30 7.26 7.13 7.13 7.12 6.82 6.74 6.73 6.73 4.91 3.53 3.50 3.48 3.45 3.28 3.25 2.82 2.79 2.03 2.02 1.86 1.16 1.14 1.13 0.81 0.80 0.78
n-Bu
O
Ph
O
N
3at, 500 MHz
1.04 1.06 0.98 1.03 5.06 2.09 1.01 2.01 1.00 1.17 1.15 1.02 1.09 2.06 3.03 4.07 3.05
f1 (ppm)


172.8 152.2 151.0 128.5 128.4 128.1 127.2 126.7 126.0 125.1 124.4 123.5 120.3 116.7 113.5 108.2 77.3 77.0 76.8 49.7 40.7 34.0 30.3 26.0 25.1 22.4 13.7
n-Bu
O
Ph
O
N
3at, 126 MHz
f1 (ppm)


8.65
8.63
7.74
7.73
7.55
7.53
7.51
7.45
7.44
7.43
7.41
7.40
7.37
7.33
7.32
7.30
7.30
7.28
7.26
7.12
7.10
6.79
5.64
3.35
3.33
2.91
2.88
2.14
2.13
2.12
1.92
1.35
1.34
1.32
1.31
1.26
1.25
1.23
1.23
1.22
1.20
0.86
0.84
0.83
Ph
n-Bu
O
O
N
4, 500 MHz
1.09
1.01
2.95
8.05
2.03
2.00
0.98
1.01
1.07
0.98
1.96
3.07
4.04
3.06
f1 (ppm)


172.7
153.5
150.5
128.7
128.5
127.3
127.1
126.9
126.8
126.7
125.1
124.4
123.6
123.6
120.5
116.5
77.3
77.0
76.8
49.7
40.6
30.3
25.8
25.2
22.4
13.8
Ph
n-Bu
O
O
N
4, 126 MHz
f1 (ppm)