Supporting Information

Pd-Catalyzed Cascade Heck Cyclization/Carbonylation of Indoles with Aryl Formates: Enantioselective Construction of Indolo[2,1-a]isoquinolines

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Contents

1. General Information

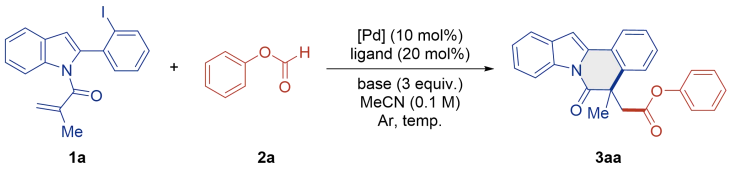
All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under argon. NMR spectra were recorded on a Bruker AV 600MHz NMR. Chemical shifts are reported in δ (ppm) referenced to the residual peaks of $CHCl_3$ (δ 7.26) for ^1H NMR, $CHCl_3$ (δ 77.00) for ^{13}C NMR. The following abbreviations are used to describe the multiplicities; s: singlet, d: doublet, t: triplet, q: quartet, quint: quintet, sext: sextet, hept: heptet, m: multiplet. Coupling constants are reported in Hertz (Hz). IR spectra were recorded on a FT-IR instrument. The HRMS analysis was obtained on a QTOF mass spectrometer. X-ray diffraction data were collected at 150 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation. For thin layer chromatography (TLC), NUO TAI precoated TLC plates (SHF254) were used, and compounds were visualized with a UV light at 254 nm. Flash column chromatography was performed with Silica gel (SANPONT). Enantiomeric excesses (ee) were determined by HPLC analysis on Shimazu (LC-2050) HPLC with Daicel chiral columns. Melting points were determined with melting points apparatus and are uncorrected.

2. Materials

All commercially available reagents were used directly without purification unless otherwise stated. All solvents were purified following standard procedures. Substrates **1**[1-2], **2b**-**2l**, **2n** and **2o**[2-4] were synthesized in the lab by the reported procedures. **2a** and **2m** were purchased from commercial sources and used directly without further purification unless otherwise stated.

3. Deoptimization Table

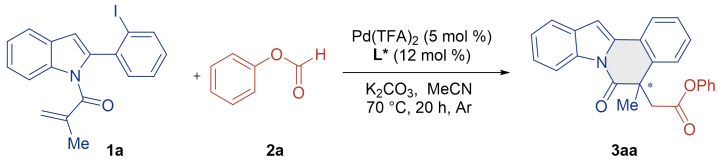
Table S1. Optimization of the Reaction Conditions[a]

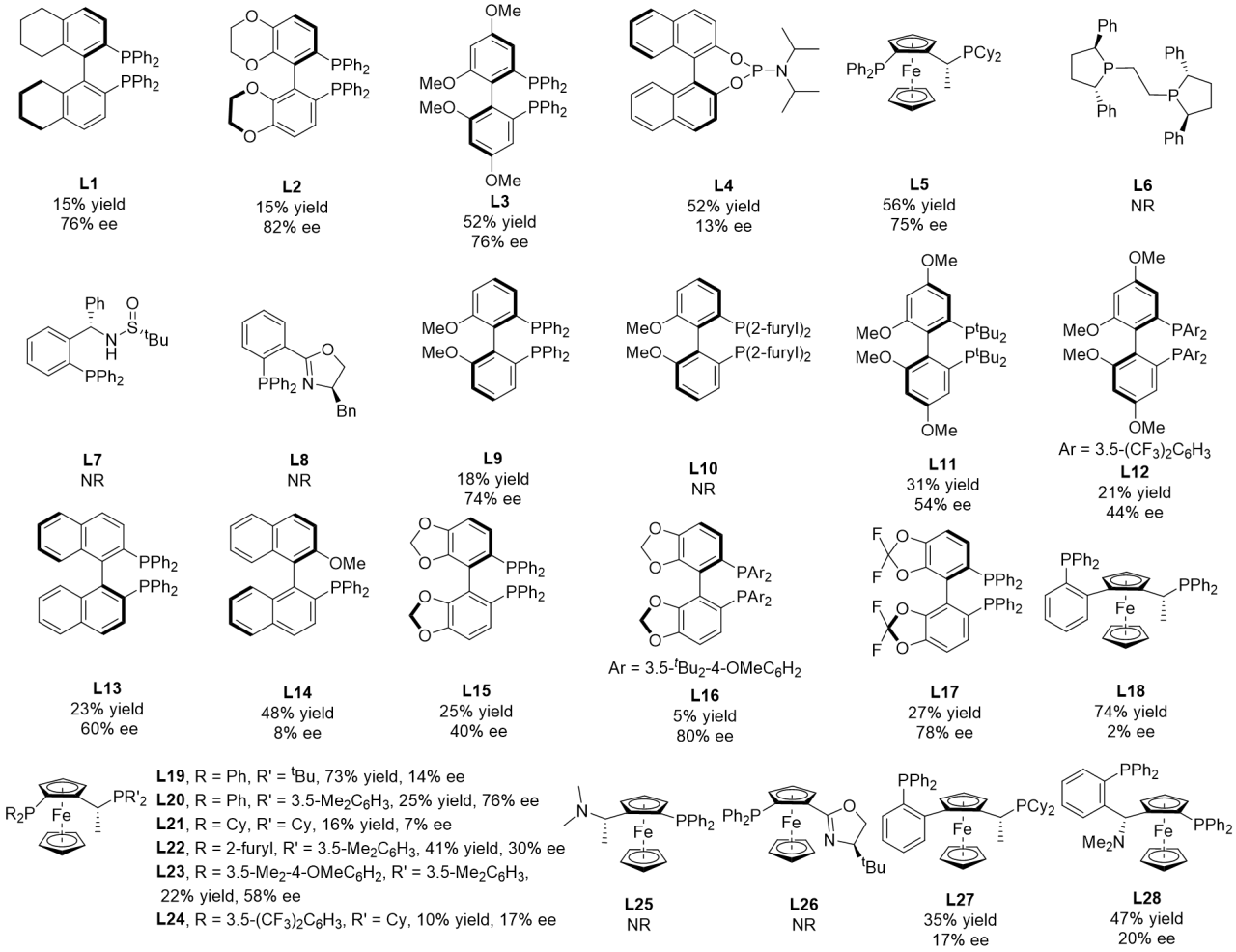


Entry	Catalyst	Ligand	Base	Solvent	Yield[b] (%)
1	$Pd(OAc)_2$	PPh_3	K_2CO_3	MeCN	64
2	$Pd(OAc)_2$	PPh_3	K_2CO_3	DCE	0
3	$Pd(OAc)_2$	PPh_3	K_2CO_3	Toluene	0
4	$Pd(TFA)_2$	PPh_3	K_2CO_3	MeCN	82
5	$Pd_2(dba)_3$	PPh_3	K_2CO_3	MeCN	73
6	$Pd(PhCN)_2Cl_2$	PPh_3	K_2CO_3	MeCN	74
7	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	K_2CO_3	MeCN	87
8	$Pd(TFA)_2$	P(*p*-anisyl)$_3$	K_2CO_3	MeCN	76
9	$Pd(TFA)_2$	PCy_3	K_2CO_3	MeCN	34
10	$Pd(TFA)_2$	BINAP	K_2CO_3	MeCN	73
11	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	Na_2CO_3	MeCN	27
12	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	Cs_2CO_3	MeCN	27
13	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	*t*-BuOK	MeCN	0
14	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	K_3PO_4	MeCN	76
15	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	K_2CO_3	MeCN	94[c]
16	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	K_2CO_3	MeCN	94[c,d]
17	$Pd(TFA)_2$	P(*p*-tolyl)$_3$	K_2CO_3	MeCN	97[c,d,e]

[a]Reaction conditions unless otherwise noted: **1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (10.0 mol %), ligand (20.0 mol %), MeCN (1 mL, 0.1 M), base (0.3 mmol), 80 °C, 20 h under an argon atmosphere. [b]Isolated yields. [c]70°C. [d]**2a** (0.15 mmol). [e] K_2CO_3 (0.2 mmol).

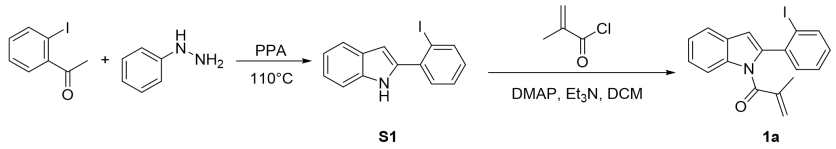
Table S2. Screening of the chiral ligands under optimal racemic reaction conditions.[a]





[a]Reaction conditions unless otherwise noted: **1a** (0.1 mmol), **2a** (0.15 mmol), $Pd(TFA)_2$ (5.0 mol %), ligand (12.0 mol %), MeCN (1.0 mL, 0.1 M), K_2CO_3 (0.2 mmol), 70 °C, 20 h under an argon atmosphere. Isolated yields. Determined by HPLC analysis.

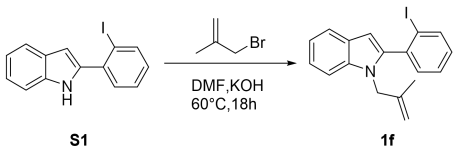
4. Preparation of Substrates 1



Scheme S1

Step I: A mixture of 2-iodoacetophenone (10.0 mmol, 2.5 g, 1.0 equiv.), phenylhydrazine (12.0 mmol, 1.3 g, 1.2 equiv.) and polyphosphoric acid (PPA, 30.0 g) was added to a round bottom flask and stirred at 110°C in an oil bath for 6 h. After the completion of the reaction, the residue was quenched with ice water and extracted with ethyl acetate. The organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1, v/v) to give the corresponding substituted indole **S1** as a yellow oil (65%, 2.3 g).

Step II: To the solution of indole **S1** (7.2 mmol, 1.0 equiv., 2.3 g) and DMAP (1.5 mmol, 0.2 equiv., 183 mg) in DCM (15.0 mL) was added Et_3N (14.4 mmol, 2.0 equiv., 1.5 g) and methacryloyl chloride (8.7 mmol, 1.2 equiv., 910 mg) at 0 °C. The solution was warmed up to room temperature and stirred for overnight. The mixture was diluted with DCM and saturated Na_2CO_3 solution. The organic and aqueous layers were separated. The aqueous layer was extracted with DCM. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a residue, which was purified by flash chromatography (petroleum ether/ethyl acetate = 10:1, v/v) and then recrystallized from *n*-hexane/EtOAc to afford the product **1a** as a yellow solid (46%, 1.3g) (Scheme S1). Procedure for the synthesis of substrates **1b-1e, 1j** is similar to **1a**.

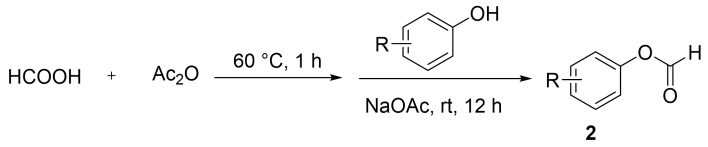


Scheme S2

A solution of **S1** (6.0 mmol, 1.91 g, 1.0 equiv.) in 10.0 mL of DMF and powdered KOH (7.8 mmol, 437 mg, 1.3 equiv.) was stirred at 60 °C in an oil bath for 10 min, cooled to room temperature, and treated with 3-bromo-2-methylprop-1-ene (8.9 mmol, 1.20 g, 1.5 equiv.). The reaction mixture was stirred at 60 °C in an oil bath for 18 h, and then poured onto ice and diluted with 15 mL of EtOAc. The combined organic layers were washed with H_2O, brine, dried over Na_2SO_4, concentrated under reduced pressure and purified by chromatography (petroleum ether/ethyl acetate = 20:1, v/v) to afford the desired product **1g** as a yellow oil (60%, 1.3 g) (Scheme S2). Procedure for the synthesis of substrates

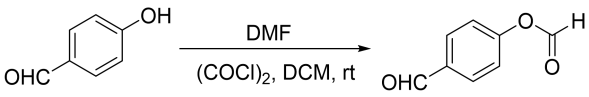
1g-1i is similar to **1f**.

5. Preparation of Substrates 2



Scheme S3

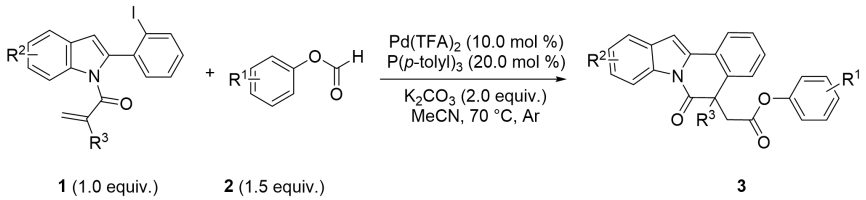
Formic acid (23 mL, 600 mmol, 6.0 equiv.) was added to acetic anhydride (38 mL, 400 mmol, 4.0 equiv.) at rt. The mixture was stirred at 60 °C (oil bath) for 1 h and cooled to rt. The resulting solution was poured to the flask containing phenol (9.4 g, 100 mmol) and NaOAc (8.2 g, 100 mmol, 1.0 equiv.). The mixture was stirred at room temperature for 12 h. Then, CH_2Cl_2 and water was added to the mixture and the organic layer was extracted with CH_2Cl_2 (three times), washed with saturated $NaHCO_3$ solution (three times) and brine (one time), and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. Then the filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20:1, v/v) on silica gel to provide the desired products **2b-g**, **2i-2l**, **2n**, and **2o** (Scheme S3)[3].



Scheme S4

To a solution of phenolic substrate (5 mmol) in DCM, oxalyl chloride (15 mmol) was added at 0 °C and after that DMF (7.5 mmol) was added in a dropwise manner. The reaction was allowed to reach room temperature slowly and stirring for 6 h. A saturated solution of sodium bicarbonate (15 mL) was added to the reaction mixture to quench of excess oxalyl chloride. The reaction mixture was extracted with ethyl acetate (3x10 mL), dried over anhydrous Na_2SO_4, and evaporated to dryness under vacuum. The crude product was purified by column chromatography over silica gel (petroleum ether/ethyl acetate = 10:1, v/v) to give the products **2h** as colorless oil (70%, 0.53 g) (Scheme S4)[4].

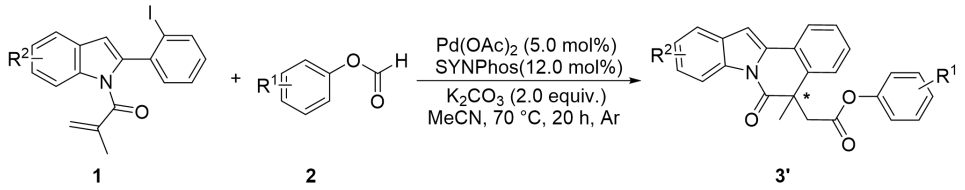
6. A Typical Procedure for the Synthesis of Products 3 and Asymmetric Products 3



Scheme S5

Compounds **1** (0.1 mmol, 1.0 equiv.), compounds **2** (0.15 mmol, 1.5 equiv.), $Pd(TFA)_2$ (3.3 mg,

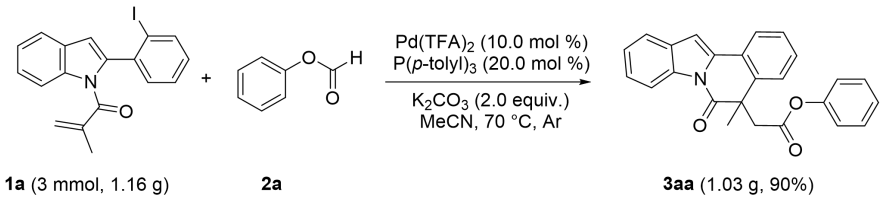
10.0 mol %), P(*p*-tolyl)$_3$ (6.1 mg, 20.0 mol %) and K_2CO_3 (27.6 mg, 0.2 mmol, 2.0 equiv.) were added to a reaction tube successively under an argon atmosphere, and then MeCN (1.0 mL) was added via syringe. The resulting mixture was stirred at 70°C in an oil bath for 20 h. After cooling at room temperature, the mixture was concentrated under reduced pressure. The residue was purified on a silica gel column (petroleum ether/ethyl acetate = 15: 1, v/v) to afford the products **3** (Scheme S5).



Scheme S6

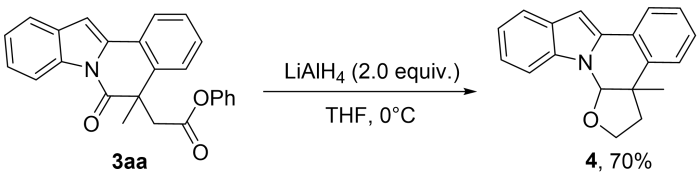
Compounds **1** (0.1 mmol, 1.0 equiv.), compounds **2** (0.20 mmol, 2.0 equiv.), Pd(OAc)$_2$ (1.2 mg, 5.0 mol %), SYNPhos (7.7 mg, 12.0 mol %) and K_2CO_3 (27.6 mg, 0.2 mmol, 2.0 equiv.) were added to a reaction tube successively under an argon atmosphere, and then MeCN (1.0 mL) was added via syringe. The resulting mixture was stirred at 70°C in an oil bath for 20 h. After cooling at room temperature, the mixture was concentrated under reduced pressure. The residue was purified on a silica gel column (petroleum ether/ethyl acetate = 15: 1, v/v) to afford the asymmetric products **3** (Scheme S6).

7. Scale-Up Reaction and Derivatizations



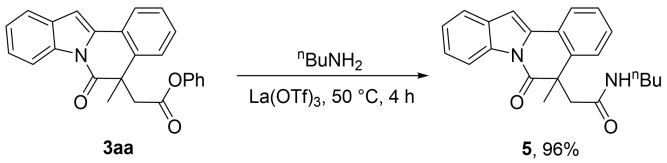
Scheme S7

Scale-up reaction: Compound **1a** (3.0 mmol, 1.16 g, 1.0 equiv.), **2a** (4.5 mmol, 550 mg, 1.5 equiv.), Pd(TFA)$_2$ (0.3 mmol, 100 mg), P(*p*-tolyl)$_3$ (0.6 mmol, 182 mg) and K_2CO_3 (6.0 mmol, 828 mg, 2.0 equiv.) were added to a sealed tube, and MeCN (30.0 mL) was added via syringe under an argon atmosphere. The reaction mixture was stirred at 70°C until completion (monitored by TLC). After cooling at room temperature, the mixture was concentrated under reduced pressure. The residue was purified on a silica gel column (petroleum ether/ethyl acetate = 20: 1, v/v) to afford the product **3aa** (1.03 g, 90%) (Scheme S7).



Scheme S8

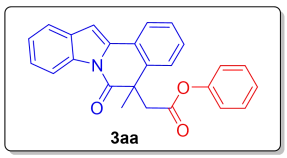
$LiAlH_4$ (15.2 mg, 0.4 mmol, 2.0 equiv.) was added in a solution of product **3aa** (77 mg, 0.2 mmol, 1.0 equiv.) in THF (2.0 mL) at 0˚C. After stirring at 0˚C for 8 h, the mixture was quenched with 5.0 mL H_2O and extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2: 1, v/v) to afford the corresponding product **4** (39 mg, 70%) (Scheme S8).



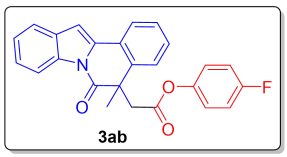
Scheme S9

To a solution of **3aa** (77 mg, 0.2 mmol, 1.0 equiv.) in 1 mL $^{n}BuNH_2$ was added $La(OTf)_3$ (6 mg, 5.0 mol%). The reaction mixture was stirred at 50°C for 4 h. After cooling at room temperature, the mixture was extracted with ethyl acetate, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified through silica gel chromatography (petroleum ether/EtOAc = 10:1) to give amide **5** with 96% yield (Scheme S9).

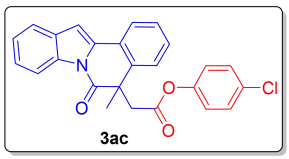
8. Characterization of the Products



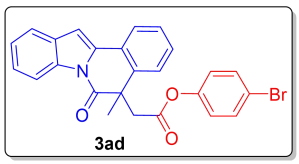
*Phenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3aa**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (37 mg, 97% yield). Mp: 70−75 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.48 – 7.28 (m, 5H), 7.21 - 7.14 (m, 2H), 7.10 – 7.01 (m, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 4.02 (d, *J* = 17.0 Hz, 1H), 3.36 (d, *J* = 17.0 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.8, 150.1, 137.4, 135.4, 135.3, 130.6, 129.1, 128.9, 127.5, 125.7, 125.2, 125.2, 124.7, 124.4, 124.1, 121.1, 120.4, 116.6, 103.3, 46.4, 44.3, 30.3. IR: 1756, 1696, 1596, 1449, 1379, 1343, 1268, 1161, 1084, 932, 813, 755 cm^{-1}. HRMS (ESI) *m/z*: Calcd for $C_{25}H_{19}NO_3Na$ $[M + Na]^+$, 404.1257; Found, 404.1255



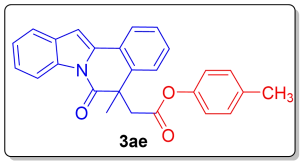
4-Fluorophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ab)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (40 mg, 88% yield). Mp: 91−94 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, J = 8.2 Hz, 1H), 7.91 – 7.88 (m, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.45 – 7.36 (m, 4H), 7.33 – 7.30 (m, 1H), 7.05 (s, 1H), 6.87 – 6.83 (m, 2H), 6.64 – 6.59 (m, 2H), 4.01 (d, J = 17.0 Hz, 1H), 3.35 (d, J = 16.9 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.9, 160.0 (d, $J_{C\text{-}F}$ = 244.2 Hz), 145.9 (d, $J_{C\text{-}F}$ = 3.0 Hz)., 137.3, 135.4, 135.2, 130.6, 128.9, 127.6, 125.3, 124.7, 124.6, 124.1, 122.5 (d, $J_{C\text{-}F}$ = 8.4 Hz)., 120.5, 116.7, 115.8 (d, $J_{C\text{-}F}$ = 23.5 Hz), 103.4, 46.5, 44.2, 30.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -116.91(s, 1F). IR: 1756, 1698, 1600, 1504, 1450, 1383, 1342, 1185, 1091, 838, 752 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{18}FNO_3Na$ $[M + Na]^+$, 422.1163; found, 422.1148.



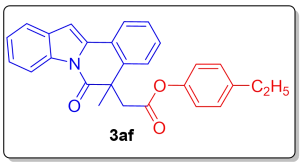
4-Chlorophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ac)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (39 mg, 93% yield). Mp: 97-98 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, J = 8.2 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.46 – 7.36 (m, 4H), 7.35 – 7.30 (m, 1H), 7.13 (d, J = 8.9 Hz, 2H), 7.06 (s, 1H), 6.60 (d, J = 8.9 Hz, 2H), 4.01 (d, J = 17.0 Hz, 1H), 3.35 (d, J = 17.0 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.7, 148.5, 137.2, 135.4, 135.2, 131.1, 130.6, 129.2, 128.9,127.7, 125.3, 125.2, 124.7, 124.6, 124.1, 122.5, 120.5, 116.6, 103.5, 46.4, 44.3, 30.3. IR: 1756, 1697, 1600, 1486, 1448, 1380, 1343, 1197, 1164, 1085, 813, 758 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{19}ClNO_3$ $[M + H]^+$, 416.1048; found, 416.1022



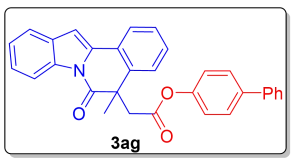
4-*Bromophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate* ***(3ad)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (32 mg, 67% yield). Mp: 79-81 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.4 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.44 – 7.26 (m, 7H), 7.05 (s, 1H), 6.57 – 6.50 (m, 2H), 4.00 (d, *J* = 17.0 Hz, 1H), 3.34 (d, *J* = 17.0 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1, 168.6, 149.1, 137.3, 135.4, 135.2, 132.2, 130.6, 128.9, 127.7, 125.3, 124.7, 124.6, 124.1, 122.9, 120.5, 118.9, 116.7, 103.4, 46.5, 44.3, 30.3. IR: 1758, 1698, 1645, 1450, 1381, 1340, 1198, 1161, 1071, 825, 757 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{18}BrNO_3Na$ $[M + H]^+$, 482.0362; found, 482.0365.



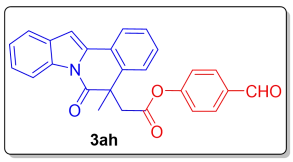
P-Tolyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ae)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (36 mg, 90% yield). Mp: 79−82 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 9.3 Hz, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.46 – 7.34 (m, 4H), 7.32 – 7.29 (m, 1H), 7.04 (s, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.53 (d, *J* = 8.5 Hz, 2H), 4.01 (d, *J* = 16.9 Hz, 1H), 3.35 (d, *J* = 16.9 Hz, 1H), 2.20 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 169.0, 147.9, 137.5, 135.5, 135.4, 135.3, 130.6, 129.6, 128.9, 127.5, 125.3, 125.2, 124.8, 124.5, 124.1, 120.8, 120.4, 116.7, 103.3, 46.5, 44.4, 30.3, 20.7. IR: 1756, 1696, 1506, 1450, 1381, 1342, 1196, 1165, 1018, 813, 754 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{26}H_{21}NO_3Na$ $[M + Na]^+$, 418.1414; found, 418.1406.



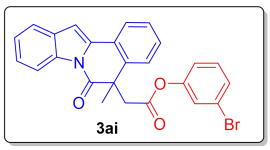
4-Ethylphenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3af)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (39 mg, 96% yield). Mp: 68−72 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.84 (m, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.48 – 7.28 (m, 5H), 7.04 (s, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 8.5 Hz, 2H), 4.01 (d, *J* = 16.9 Hz, 1H), 3.35 (d, *J* = 16.9 Hz, 1H), 2.51 (q, *J* = 7.6 Hz, 2H), 1.71 (s, 3H), 1.17 – 1.06 (m, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 169.0, 148.1, 141.7, 137.5, 135.5, 135.3, 130.6, 128.9, 128.5, 127.5, 125.3, 125.2, 124.8, 124.5, 124.1, 120.9, 120.4, 116.7, 103.3, 46.5, 44.4, 30.3, 28.1, 15.4. IR: 1756, 1696, 1643, 1506, 1452, 1381, 1342, 1200, 1158, 815, 750 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{27}H_{23}NO_3Na$ $[M + Na]^+$, 432.1570; found, 432.1579.



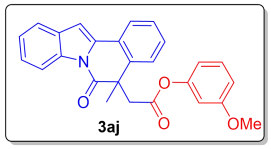
[1,1'-Biphenyl]-4-yl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ag)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (33 mg, 71% yield). Mp: 101−107 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.88 (m, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.48 – 7.46 (m, 1H), 7.44 – 7.35 (m, 9H), 7.33 – 7.28 (m, 2H), 7.06 (s, 1H), 6.74 (d, *J* = 8.8 Hz, 2H), 4.05 (d, *J* = 17.0 Hz, 1H), 3.39 (d, *J* = 16.9 Hz, 1H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 169.0, 149.5, 140.2, 138.9, 137.4, 135.5, 135.3, 130.6, 128.9, 128.7, 127.9, 127.6, 127.2, 127.0, 125.3, 125.2, 124.8, 124.5, 124.1, 121.4, 120.5, 116.7, 103.4, 46.5, 44.4, 30.3. IR: 1757, 1698, 1602, 1486, 1449, 1382, 1343,1262, 1172, 1085, 831, 755 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{31}H_{23}NO_3Na$ $[M + Na]^+$, 480.1570; found, 480.1569.



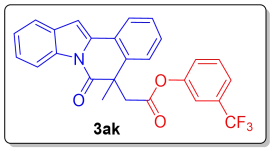
*4-Formylphenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3ah**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1, v/v) afforded the title compound as a yellow solid (30 mg, 73% yield). Mp: 92−95 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.59 (d, *J* = 5.4 Hz, 1H), 7.92 (s, 1H), 7.81 – 7.71 (m, 2H), 7.61 (d, *J* = 7.3 Hz, 1H), 7.45 – 7.28 (m, 4H), 7.07 (d, *J* = 2.9 Hz, 1H), 7.00 – 6.83 (m, 3H), 4.05 (d, *J* = 17.0 Hz, 1H), 3.40 (d, *J* = 16.9 Hz, 1H), 1.74 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.8, 172.1, 168.2, 154.7, 137.2, 135.4, 135.1, 133.9, 131.0, 130.6, 129.0, 127.7, 125.3, 125.2, 124.7, 124.6, 124.2, 121.9, 120.5, 116.6, 115.9, 103.5, 46.5, 44.3, 30.3. IR: 1760, 1694, 1595, 1506, 1452, 1381, 1344, 1208, 1158, 1089, 837, 758 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{26}H_{20}NO_4$ $[M + H]^+$, 410.1387; found, 410.1368.



*3-Bromophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3ai**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.1 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.45 – 7.30 (m, 5H), 7.21 (d, *J* = 7.1 Hz, 1H), 7.06 – 7.01 (m, 2H), 6.83 (s, 1H), 6.63 (d, *J* = 10.5 Hz, 1H), 4.00 (d, *J* = 17.0 Hz, 1H), 3.35 (d, *J* = 17.0 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.5, 150.5, 137.2, 135.4, 135.2, 130.6, 130.2, 129.0, 128.9, 127.7, 125.3, 125.2, 124.7, 124.7, 124.6, 124.1, 122.1, 120.5, 120.1, 118.8, 116.7, 103.5, 46.4, 44.2, 30.3. IR: 1762, 1693, 1588, 1453, 1379, 1343, 1193, 1151, 1083, 756, 674 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{18}BrNO_3Na$ $[M + Na]^+$, 482.0362; found, 482.0365.

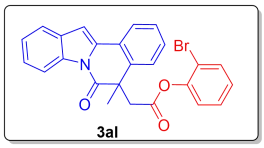


*3-Methoxyphenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3aj**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (31 mg, 74% yield). Mp: 81−85 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 7.90 – 7.87 (m, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.35 (m, 4H), 7.33 – 7.29 (m, 1H), 7.08 – 7.02 (m, 2H), 6.63 – 6.59 (m, 1H), 6.30 – 6.26 (m, 1H), 6.14 (t, *J* = 2.3 Hz, 1H), 4.01 (d, *J* = 16.9 Hz, 1H), 3.60 (s, 3H), 3.35 (d, *J* = 16.8 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.7, 160.2, 151.0, 137.4, 135.4, 135.3, 130.6, 129.5, 128.9, 127.6, 125.4, 125.2, 124.8, 124.5, 124.1, 120.4, 116.7, 113.3, 111.9, 106.8, 103.3, 55.2, 46.5, 44.4, 30.3. IR: 1757, 1695, 1601, 1488, 1451, 1381, 1343, 1264, 1063, 1149, 1036, 814, 754 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{26}H_{21}NO_4Na$ $[M + Na]^+$, 434.1363; found, 434.1373.

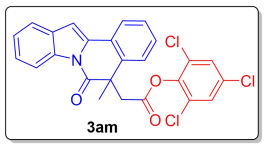


*3-(Trifluoromethyl)phenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3ak**)*. Purification by column chromatography on

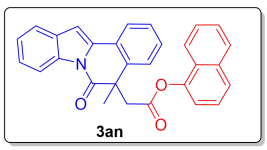
silica gel (petroleum ether/ethyl acetate = 10:1, v/v) afforded the title compound as a yellow solid (35 mg, 70% yield). Mp: 75−80 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.7 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.50 – 7.40 (m, 4H), 7.38 – 7.29 (m, 3H), 7.09 (s, 1H), 6.91 (d, J = 6.2 Hz, 2H), 4.07 (d, J = 16.9 Hz, 1H), 3.40 (d, J = 16.9 Hz, 1H), 1.75 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1, 168.5, 150.1, 137.2, 135.4, 135.1, 131.7 (d, J_{C-F} = 32.8 Hz), 130.6, 129.7, 129.0, 127.8, 125.3 (d, J_{C-F} = 4.5 Hz), 124.8, 124.7, 124.6, 124.1, 122.6, 120.5, 118.4 (d, J_{C-F} = 4.0 Hz), 116.7, 103.5, 46.5, 44.3, 30.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.79. IR: 1763, 1697, 1599, 1450, 1380, 1329, 1283, 1165, 1131, 1087, 806, 756 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{26}H_{19}NO_3$ $[M + H]^+$, 450.1312; found, 450.1304.



*2-Bromophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3al**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (35 mg, 75% yield). Mp: 102−108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 (d, J = 8.2 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.48 (d, J = 9.1 Hz, 1H), 7.44 – 7.33 (m, 4H), 7.30 (t, J = 7.9 Hz, 1H), 7.16 – 7.10 (m, 1H), 7.03 (s, 1H), 6.99 – 6.93 (m, 1H), 6.77 (d, J = 8.2 Hz, 1H), 4.06 (d, J = 17.3 Hz, 1H), 3.47 (d, J = 17.3 Hz, 1H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1, 168.1, 147.8, 137.3, 135.5, 135.3, 133.1, 130.6, 128.9, 128.2, 127.6, 127.2, 125.5, 125.2, 124.9, 124.5, 124.1, 123.4, 120.4, 116.7, 115.9, 103.3, 46.3, 43.9, 30.4. IR: 1765, 1694, 1599, 1449, 1379, 1341, 1258, 1206, 1138, 808, 752 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{18}BrNO_3Na$ $[M + Na]^+$, 482.0362; found, 482.0365.

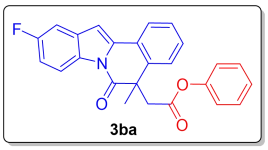


*2,4,6-Trichlorophenyl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3am**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (34 mg, 70% yield). Mp: 74−77 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, J = 8.2 Hz, 1H), 7.91 – 7.82 (m, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.46 (d, J = 6.6 Hz, 1H), 7.42 – 7.34 (m, 3H), 7.31 (s, 1H), 7.17 (s, 2H), 7.03 (s, 1H), 4.11 (d, J = 17.4 Hz, 1H), 3.49 (d, J = 17.4 Hz, 1H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.7, 166.7, 147.0, 142.4, 136.9, 135.4, 135.2, 131.9, 130.6, 129.3, 128.8, 128.2, 128.0, 127.6, 125.5, 125.2, 124.9, 124.5, 124.1, 121.6, 120.4, 116.7, 103.4, 46.2, 43.3, 30.5. IR: 1773, 1697, 1562, 1451, 1382, 1342, 1269, 1116, 1082, 814, 756 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{17}Cl_3NO_3$ $[M + H]^+$, 484.0269; found, 484.0278.

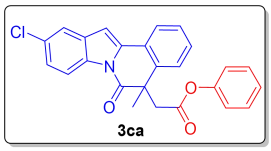


*Naphthalen-1-yl 2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate (**3an**)*. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (33

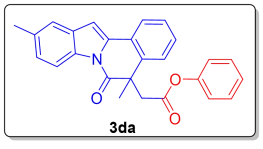
mg, 76% yield). Mp: 70−75 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.2 Hz, 1H), 7.90 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.66 – 7.55 (m, 3H), 7.51 – 7.28 (m, 7H), 7.13 (s, 1H), 7.04 (s, 1H), 6.78 (d, *J* = 11.3 Hz, 1H), 4.07 (d, *J* = 16.9 Hz, 1H), 3.42 (d, *J* = 16.9 Hz, 1H), 1.74 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 169.0, 147.8, 137.5, 135.5, 135.3, 133.4, 131.3, 130.6, 129.1, 129.0, 127.6, 127.6, 127.5, 126.4, 125.6, 125.4, 125.2, 124.8, 124.5, 124.1, 120.6, 120.5, 118.2, 116.7, 103.4, 46.5, 44.5, 30.3. IR: 1752, 1690, 1641, 1512, 1454, 1384, 1344, 1263, 1160, 810, 750 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{29}H_{21}NO_3Na$ [M + Na]$^+$, 454.1414; found, 454.1401.



Phenyl 2-(10-fluoro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ba)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (28 mg, 70% yield). Mp: 97−103 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 – 8.50 (m, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.49 – 7.38 (m, 3H), 7.24 – 7.16 (m, 3H), 7.11 – 7.05 (m, 2H), 6.99 (s, 1H), 6.68 (d, *J* = 7.9 Hz, 2H), 4.01 (d, *J* = 17.1 Hz, 1H), 3.38 (d, *J* = 16.9 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1, 168.8, 160.2 (d, J_{C-F} = 240.9 Hz)， 150.1, 137.7, 136.8, 131.8, 131.7, 129.2, 129.1, 127.6, 125.8, 125.3, 124.4, 124.2, 121.1, 117.7 (d, J_{C-F} = 9.2 Hz), 112.6 (d, J_{C-F} = 24.9 Hz), 106.0 (d, J_{C-F} = 24.1 Hz), 102.8 (d, J_{C-F} = 4.1 Hz), 46.3, 44.4, 30.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -118.12. IR: 1753, 1696, 1651, 1597, 1456, 1379, 1338, 1164, 962, 869, 766 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{18}FNO_3Na$ [M + Na]$^+$, 422.1163; found, 422.1167.

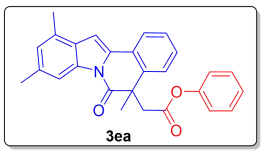


Phenyl 2-(10-chloro-5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ca)***. Mp: 88−91 °C. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow oil (19 mg, 46% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 2.1 Hz, 1H), 7.47 – 7.37 (m, 3H), 7.32 – 7.28 (m, 1H), 7.17 (t, *J* = 7.9 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 6.68 – 6.63 (m, 2H), 3.98 (d, *J* = 17.0 Hz, 1H), 3.36 (d, *J* = 17.0 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 168.8, 150.1, 137.7, 136.6, 133.8, 131.9, 130.1, 129.4, 129.2, 127.7, 125.8, 125.4, 125.2, 124.4, 124.3, 121.1, 120.0, 117.7, 102.4, 46.4, 44.5, 30.3. IR: 1755, 1699, 1643, 1595, 1446, 1371, 1185, 1165, 1070, 811, 687 cm^{-1}. HR MS (ESI) *m/z*: calcd for $C_{25}H_{18}ClNO_3Na$ [M + Na]$^+$, 438.0873; found, 438.0881.

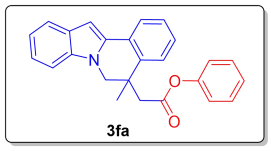


Phenyl 2-(5,10-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3da)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (18 mg, 44% yield). Mp: 110−115 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.4 Hz, 1H), 7.89 – 7.85

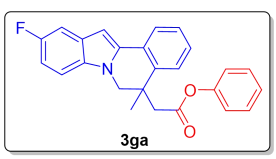
(m, 1H), 7.46 – 7.42 (m, 1H), 7.41 – 7.35 (m, 3H), 7.20 – 7.14 (m, 3H), 7.07 – 7.04 (m, 1H), 6.97 (s, 1H), 6.68 – 6.61 (m, 2H), 4.01 (d, J = 16.9 Hz, 1H), 3.34 (d, J = 16.9 Hz, 1H), 2.45 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.0, 168.9, 155.7, 150.1, 137.4, 135.3, 134.1, 133.6, 130.8, 129.6, 129.1, 128.8, 127.5, 126.5, 125.7, 125.3, 124.9, 124.0, 121.2, 120.5, 120.4, 116.3, 115.3, 103.2, 46.4, 44.3, 30.3, 21.4. IR: 1756, 1694, 1646, 1595, 1456, 1377, 1161, 1084, 967, 863, 691 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{26}H_{21}NO_3Na$ $[M + Na]^+$, 418.1414; found, 418.1406.



Phenyl 2-(5,9,11-trimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ea)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (36 mg, 87% yield). Mp: 110−117 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.90 (s, 1H), 7.46 – 7.41 (m, 1H), 7.40 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 7.09 – 7.04 (m, 2H), 6.97 (s, 1H), 6.66 (d, J = 7.5 Hz, 2H), 4.02 (d, J = 16.9 Hz, 1H), 3.35 (d, J = 16.9 Hz, 1H), 2.50 (d, J = 30.8 Hz, 6H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 168.8, 150.1, 137.1, 135.6, 135.6, 134.1, 129.4, 129.1, 128.5, 127.9, 127.5, 126.4, 125.7, 125.2, 125.1, 123.8, 121.2, 114.5, 101.9, 46.5, 44.3, 30.4, 21.9, 18.4. IR: 1758, 1694, 1647, 1591, 1492, 1413, 1382, 1334, 1267, 1189, 1086, 856, 721 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{27}H_{23}NO_3Na$ $[M + Na]^+$, 432.1570; found, 432.1579.

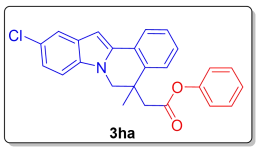


Phenyl 2-(5-methyl-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3fa)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1, v/v) afforded the title compound as yellow liquid (25 mg, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.44 – 7.34 (m, 5H), 7.28 – 7.21 (m, 2H), 7.19 – 7.14 (m, 1H), 6.96 (s, 1H), 6.95 – 6.90 (m, 2H), 4.73 (d, J = 12.4 Hz, 1H), 3.96 (d, J = 12.4 Hz, 1H), 2.80 – 2.71 (m, 2H), 1.78 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.4, 150.3, 138.5, 137.0, 134.8, 129.3, 128.7, 128.0, 127.9, 127.7, 125.9, 125.0, 124.9, 121.9, 121.4, 120.7, 120.0, 109.1, 97.0, 49.3, 42.6, 38.0, 22.6. IR: 1747, 1650, 1591, 1462, 1338, 1189, 1106, 1026, 939, 797, 689 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{25}H_{22}NO_2$ $[M + H]^+$, 368.1645; found, 368.1643.

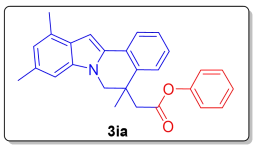


Phenyl 2-(10-fluoro-5-methyl-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ga)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as yellow liquid (23 mg, 59% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 1H), 7.55 – 7.50 (m, 1H), 7.43 – 7.34 (m, 4H), 7.34 – 7.27 (m, 3H), 7.27 – 7.21 (m, 1H), 7.01 – 6.94 (m, 1H), 6.95 – 6.88 (m, 3H), 4.69 (d, J = 12.4 Hz, 1H), 3.92 (d, J = 12.4 Hz, 1H), 2.73 (d, J = 9.5 Hz, 2H), 1.77 (s, 3H). ^{13}C NMR (151 MHz,

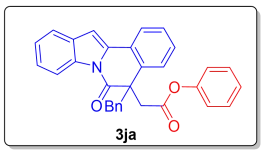
$CDCl_3$) δ 169.4, 158.1 (d, J_{C-F} = 234.5 Hz), 150.2, 138.5, 136.3, 133.6, 129.4, 128.9 (d, J_{C-F} = 10.7 Hz),128.2, 127.8, 127.7, 125.9, 125.0, 124.9, 121.4, 110.4, 110.2, 109.7 (d, J_{C-F} = 9.7 Hz), 105.4 (d, J_{C-F} = 23.7 Hz), 96.9 (d, J_{C-F} = 4.9 Hz), 49.4, 42.6, 38.0, 22.5. ^{19}F NMR (565 MHz, $CDCl_3$) δ -124.38. IR: 1746, 1647, 1485 1458, 1344, 1196, 1114, 1064, 936, 857, 791 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{21}FNO_2$ $[M + H]^+$, 386.1551; found, 386.1554.



Phenyl 2-(10-chloro-5-methyl-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ha)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as yellow liquid (22 mg, 55% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.4 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.40 – 7.31 (m, 4H), 7.30 – 7.20 (m, 2H), 7.18 – 7.13 (m, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.85 (s, 1H), 4.67 (d, *J* = 12.4 Hz, 1H), 3.89 (d, *J* = 12.4 Hz, 1H), 2.69 (d, *J* = 7.3 Hz, 2H), 1.74 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.4, 150.2, 138.6, 136.0, 135.3, 129.6, 129.4, 128.3, 127.8, 127.6, 125.9, 125.6, 125.0, 124.9, 122.2, 121.4, 120.0, 110.1, 96.5, 49.3, 42.6, 38.0, 22.5. IR: 1746, 1639, 1593, 1455, 1336, 1190, 1102, 1063, 937, 865, 795 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{25}H_{21}ClNO_2$ $[M + H]^+$, 402.1255; found, 402.1243.

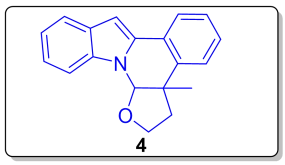


Phenyl 2-(5,9,11-trimethyl-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ia)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v) afforded the title compound as a yellow solid (23 mg, 56% yield). Mp: 82−84 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.4 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.47 – 7.32 (m, 4H), 7.30 – 7.23 (m, 1H), 7.09 (s, 1H), 6.96 (d, *J* = 5.9 Hz, 3H), 6.85 (s, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 3.93 (d, *J* = 12.4 Hz, 1H), 2.83 – 2.72 (m, 2H), 2.64 (s, 3H), 2.52 (s, 3H), 1.80 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.5, 150.3, 138.2, 137.1, 133.7, 132.1, 129.9, 129.3, 128.3, 127.7, 127.5, 126.5, 125.8, 125.0, 124.6, 122.2, 121.5, 106.7, 95.5, 49.4, 42.6, 38.0, 22.5, 21.8, 18.7. IR: 1753, 1595, 1457, 1336, 1297, 1239, 1185, 1103, 1023, 939, 811, 696 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1958; found, 396.1952.

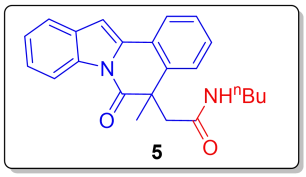


Phenyl 2-(5-benzyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetate ***(3ja)*** . Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1, v/v) afforded the title compound as a yellow solid (40 mg, 89% yield). Mp: 86−95 ˚C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.66 (m, 1H), 7.50 – 7.40 (m, 3H), 7.40 – 7.32 (m, 2H), 7.29 – 7.23 (m, 1H), 7.21 – 7.14 (m, 2H), 7.10 – 7.04 (m, 1H), 6.96 – 6.90 (m, 1H), 6.85 – 6.79 (m, 2H), 6.73 – 6.65 (m, 3H), 6.60 – 6.55 (m, 2H), 4.22 (d, *J* = 17.0 Hz, 1H), 3.55 – 3.49 (m, 2H), 3.14 (d, *J* = 12.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.1, 168.9, 155.7,

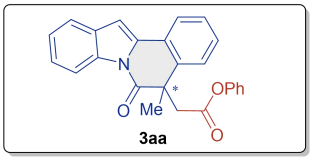
150.1, 135.0, 134.9, 134.8, 134.1, 130.3, 129.6, 129.4, 129.1, 128.5, 127.7, 127.5, 126.9, 126.5, 125.7, 125.6, 125.0, 124.3, 123.7, 121.1, 120.5, 120.3, 116.4, 115.3, 103.0, 52.4, 49.8, 43.1 IR: 1758, 1690, 1595, 1490, 1449, 1378, 1344, 1265, 1194, 1153, 1019, 935, 814, 755 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{31}H_{23}NO_3Na$ $[M + Na]^+$, 480.1570; found, 480.1569.



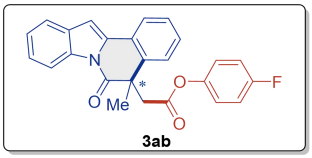
3a-Methyl-2,3,3a,13a-tetrahydrofuro[2,3-c]indolo[2,1-a]isoquinoline ***(4)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1, v/v) afforded the title compound as a white solid (39 mg, 70% yield). Mp: 82−89 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 – 7.80 (m, 1H), 7.61 (d, *J* = 5.5 Hz, 2H), 7.47 – 7.42 (m, 1H), 7.32 – 7.27 (m, 2H), 7.23 – 7.20 (m, 1H), 7.15 – 7.12 (m, 1H), 6.93 (s, 1H), 5.87 (s, 1H), 4.03 – 3.98 (m, 1H), 3.77 – 3.71 (m, 1H), 2.59 – 2.54 (m, 1H), 2.32 – 2.26 (m, 1H), 1.48 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.5, 136.7, 135.1, 128.7, 128.0, 127.7, 127.2, 125.0, 124.8, 121.7, 120.7, 119.9, 108.9, 96.5, 59.4, 50.7, 42.0, 37.7, 23.6. IR: 1459, 1376, 1316, 1269, 1045, 1007, 919, 757 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{19}H_{18}NO$ $[M + H]^+$, 276.1383; found, 276.1384.



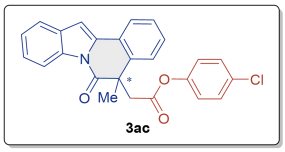
N-Butyl-2-(5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)acetamide ***(5)***. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1, v/v) afforded the title compound as a white solid (69 mg, 96%). Mp: 101−107 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 9.3 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.37 – 7.29 (m, 5H), 7.03 (s, 1H), 5.75 (s, 1H), 3.53 (d, *J* = 15.3 Hz, 1H), 2.94 – 2.84 (m, 3H), 1.59 (s, 3H), 1.15 – 1.09 (m, 2H), 1.06 – 1.00 (m, 2H), 0.70 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.0, 169.2, 137.8, 135.5, 135.4, 130.7, 128.6, 127.1, 125.5, 124.9, 124.5, 124.3, 123.9, 120.4, 116.6, 102.9, 46.7, 46.2, 38.9, 31.2, 29.9, 19.7, 13.5. IR: 1700, 1641, 1596, 1556, 1451, 1372, 1341, 1263, 1176, 1077, 951, 803, 754 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{23}H_{24}N_2O_2Na$ $[M + Na]^+$, 383.1735; found, 383.1750.



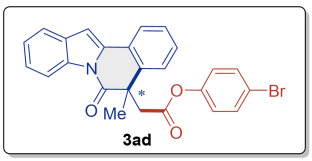
(3aa). Yellow solid (34 mg, 87% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -49.9° (*c* = 1.0 in $CHCl_3$) for 87% *ee*. HPLC (Chiralpak-IC column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 25.969 min; t_{minor} = 20.944 min.



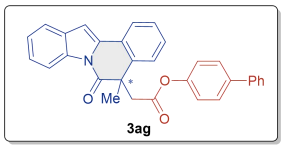
(3ab). Yellow solid (19 mg, 47% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -81.6° (*c* = 1.0 in $CHCl_3$) for 82% *ee*. HPLC (Chiralpak-IC column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 19.287 min; t_{minor} = 16.972 min.



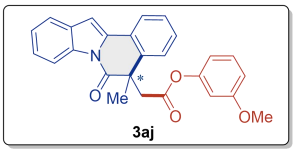
(3ac). Yellow solid (18 mg, 43% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -116° (*c* = 1.0 in $CHCl_3$) for 82% ee. HPLC (Chiralpak-IC column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 17.616 min; t_{minor} = 15.842 min.



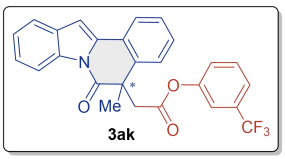
(3ad). Yellow solid (38 mg, 83% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -93.8° (*c* = 1.0 in $CHCl_3$) for 78% *ee*. HPLC (Chiralpak-IC column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 22.477 min; t_{minor} = 20.527 min.



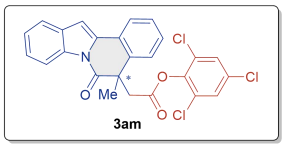
(3ag). Yellow solid (27 mg, 61% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -77.1° (*c* = 1.0 in $CHCl_3$) for 84% ee. HPLC (Chiralpak-IB column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 18.294 min; t_{minor} = 19.509 min.



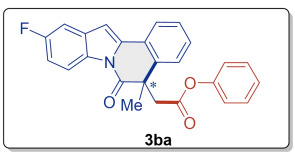
(3aj). Yellow solid (34 mg, 84% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -91.5° (*c* = 1.0 in $CHCl_3$) for 81% *ee*. HPLC (Chiralpak-IC column, hexane/isopropanol = 80/20, flow rate: 0.8 mL/min): t_{major} = 19.500 min; t_{minor} = 16.451 min.



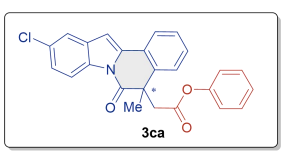
(3ak). Yellow solid (27 mg, 60% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -84.0° (*c* = 1.0 in $CHCl_3$) for 78% ee. HPLC (Chiralpak-IC column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 7.660 min; t_{minor} = 7.042 min.



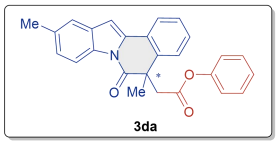
(3am). Yellow solid (38 mg, 80% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -14.4° (*c* = 1.0 in $CHCl_3$) for 80% ee. HPLC (Chiralpak-IC column, hexane/isopropanol = 98/2, flow rate: 0.8 mL/min): t_{major} = 16.344 min; t_{minor} = 14.585 min.



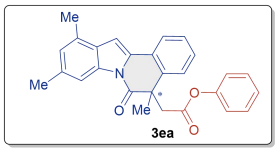
(3ba). Yellow solid (18 mg, 44% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -47.5° (*c* = 1.0 in $CHCl_3$) for 81% *ee*. HPLC (Chiralpak-AD column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 21.654 min; t_{minor} = 24.537 min.



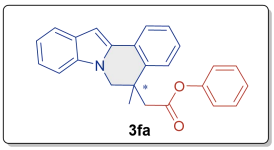
(3ca). Yellow solid (17 mg, 43% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -20.1° (*c* = 1.0 in $CHCl_3$) for 80% ee. HPLC (Chiralpak-AD column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 17.851 min; t_{minor} = 21.584 min.



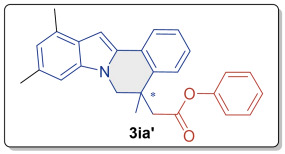
(3da). Yellow solid (20 mg, 52% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -57.4° (*c* = 1.0 in $CHCl_3$) for 80% ee. HPLC (Chiralpak-IC column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 18.426 min; t_{minor} = 14.974 min.



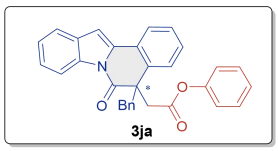
(3ea). Yellow solid (27 mg, 67% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -144.5° (*c* = 1.0 in $CHCl_3$) for 86% ee. HPLC (Chiralpak-IC column, hexane/isopropanol = 90/10, flow rate: 0.8 mL/min): t_{major} = 10.980 min; t_{minor} = 12.080 min.



(3fa'). Yellow liquid (29 mg, 79% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -119.4° (*c* = 1.0 in $CHCl_3$) for 64% ee. HPLC (Chiralpak-AD column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 11.178 min; t_{minor} = 13.292 min.



(3ia'). Yellow solid (25 mg, 64% yield). Specific Rotation $[\alpha]^{25}_{D}$ = -93.9° (*c* = 1.0 in $CHCl_3$) for 70% ee. HPLC (Chiralpak-IB column, hexane/isopropanol = 95/5, flow rate: 0.8 mL/min): t_{major} = 9.872 min; t_{minor} = 11.215 min.



(3ja). Yellow solid (26 mg, 57% yield). Specific Rotation $[\alpha]^{25}_{D}$ = 57° (*c* = 1.0 in $CHCl_3$) for 84% ee. HPLC (Chiralpak-AD column, hexane/isopropanol = 85/15, flow rate: 0.8 mL/min): t_{major} = 22.246 min; t_{minor} = 15.702 min.

9. X-Ray Analysis Data of Single Crystal 3aa (CCDC 2295989)

The crystal of product **3aa** was obtained by slow evaporation in *n*-hexane and dichloromethane. The single crystal X-ray analysis determined the structure of product **3aa** (**Fig. S1**) as expected.

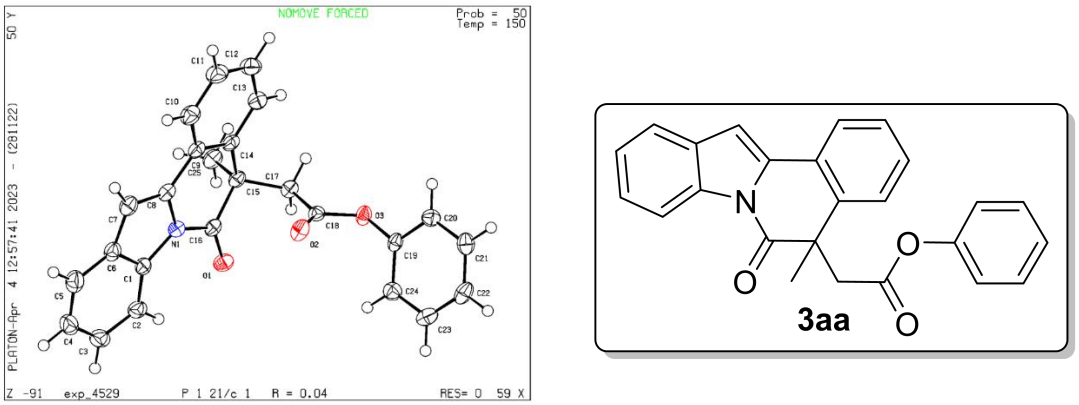


Fig. S1. X-ray structure of 3aa. Thermal ellipsoids shown at 50% probability.

Bond precision:	C-C = 0.0021 A		Wavelength=0.71073
Cell:	a=11.8280(9)	b=14.9837(9)	c=11.0984(9)
	alpha=90	beta=106.250(8)	gamma=90
Temperature:	150 K		
	Calculated		Reported
Volume	1888.4(3)		1888.4(2)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2ybc		-P 2ybc
Moiety formula	C25 H19 N O3		C25 H19 N O3
Sum formula	C25 H19 N O3		C25 H19 N O3
Mr	381.41		381.41
Dx,g cm-3	1.342		1.342
Z	4		4
Mu (mm-1)	0.088		0.088
F000	800.0		800.0
F000’	800.37		
h,k,lmax	14,17,13		14,17,13
Nref	3321		3320

Tmin,Tmax	0.988,0.991	0.502,1.000
Tmin’	0.988	

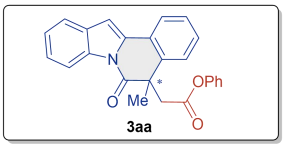
Correction method= # Reported T Limits: Tmin=0.502 Tmax=1.000
AbsCorr = MULTI-SCAN		

Data completeness= 1.000	T heta(max)= 24.997	
R(reflections)= 0.0385(2840)	wR2(reflections)= 0.0953(3320)	
S = 1.030	Npar= 263	

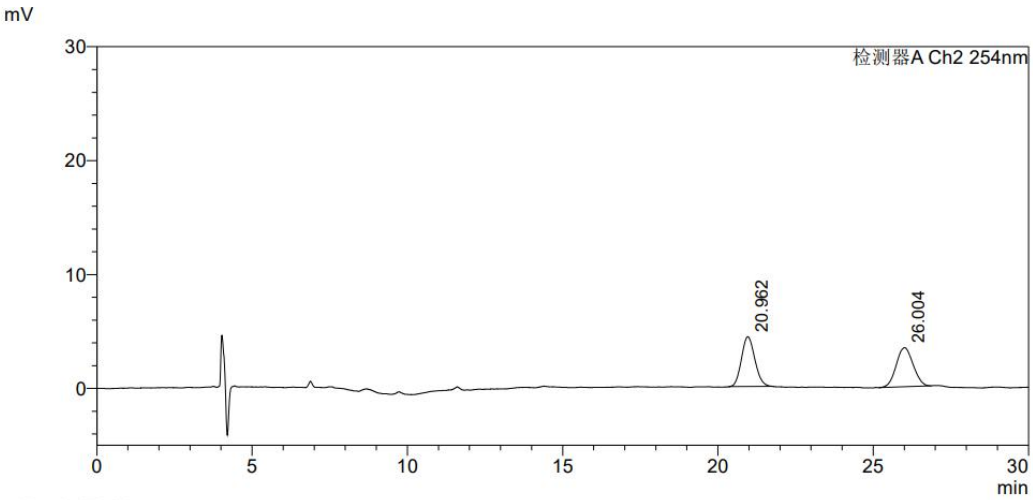
10. References

1. Qi, H.; Chi, D.; Chen, S. *Org. Lett.* **2022**, *24*, 2910-2914.
2. Lu, H.; Yang, X.; Zhou, L.; Li, W.; Deng, G.; Yang, Y.; Liang, Y. *Org. Chem. Front.* **2020**, *7*, 2016-2021.
3. (a) Katafuchi, Y.; Fujihara, T.; Iwai, T.; Terao, J.; Tsuji, Y. *Adv. Synth.* **2011**, *353*, 475-482. (b) Álvarez-Calero, J. M.; Jorge, Z. D.; Massanet, G. M. *Org. Lett.* **2016**, *18*, 6344-6347. (c) Ruble, J. C.; Maddocks, C. J.; Aathimanikandan, S. V.; Richardson, J. *Synlett* **2020**, *31*, 1608-1612.
4. Batuta, S.; Ali, M. A.; Chatterjee, A.; Alam, M. N.; Das, S.; Mandal, D.; Begum, N. A. *Synth. Commun.* **2016**, *46*, 692-700.

11. Chiral HPLC Charts and NMR Spectra



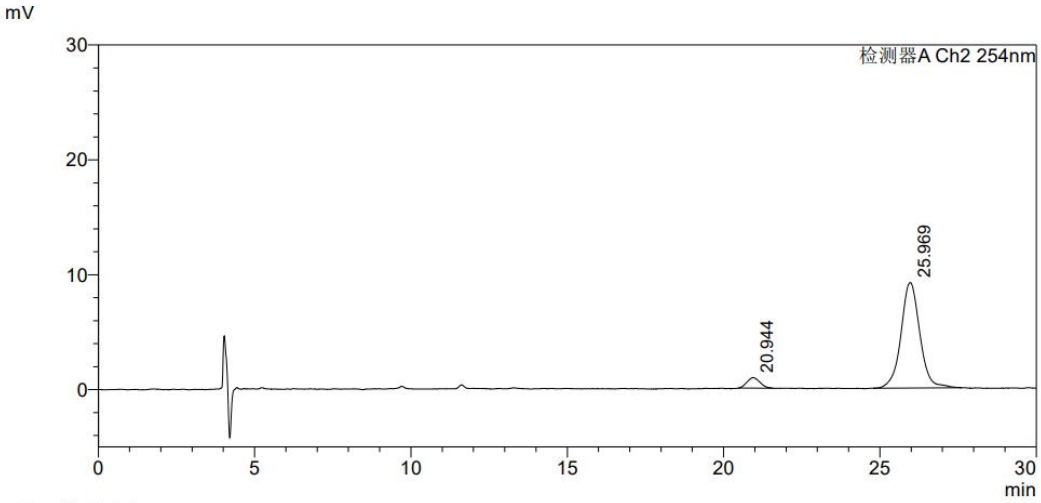
3aa



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	20.962	132230	4378	50.712
2	26.004	128518	3422	49.288
总计		260748	7800	100.000



<Peak Table>

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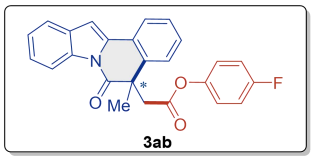
Peak#	Ret. Time	Area	Height	Area%
1	20.944	26082	911	6.400
2	25.969	381418	9180	93.600
总计		407500	10090	100.000



3ab

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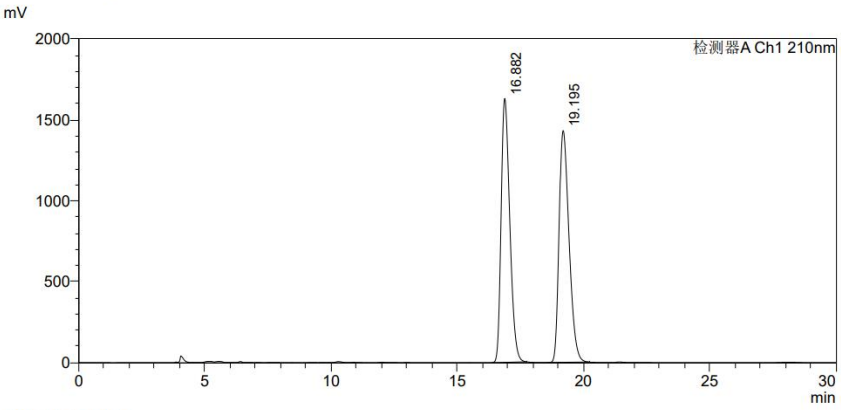

<Peak Table>

检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	16.882	39063908	1630798	49.937
2	19.195	39162956	1433140	50.063
总计		78226864	3063938	100.000

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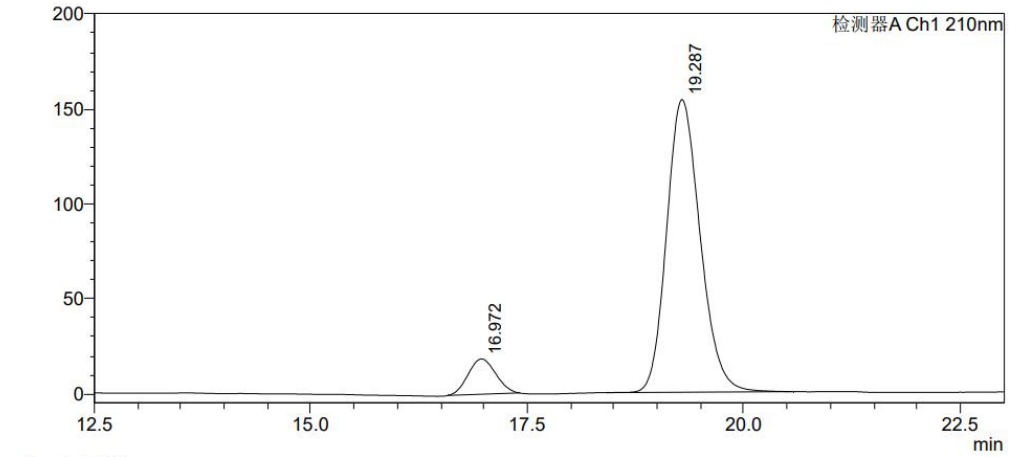
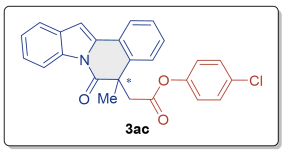
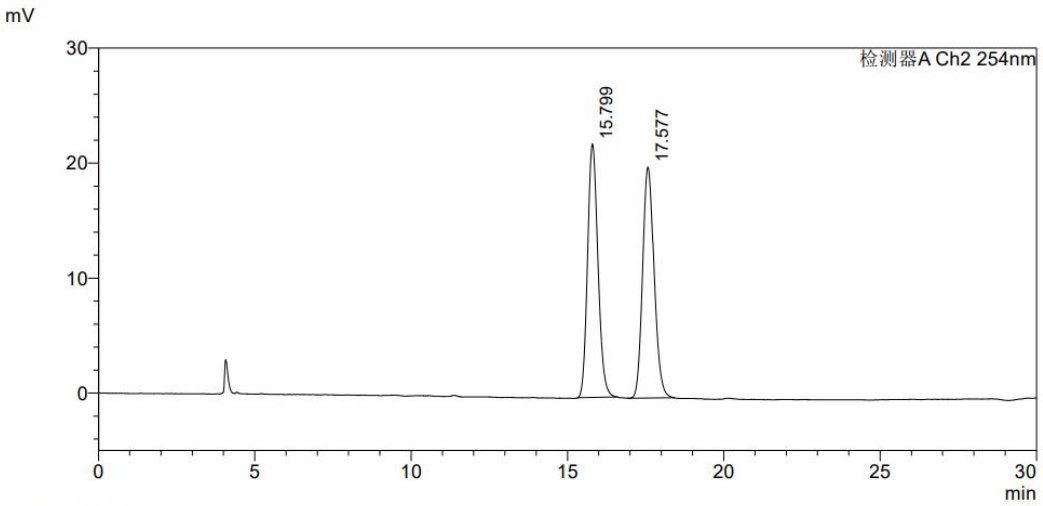


<Peak Table>

检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	16.972	412453	18617	9.023
2	19.287	4158657	154158	90.977
总计		4571110	172776	100.000





<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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2	17.577	512555	20076	49.991
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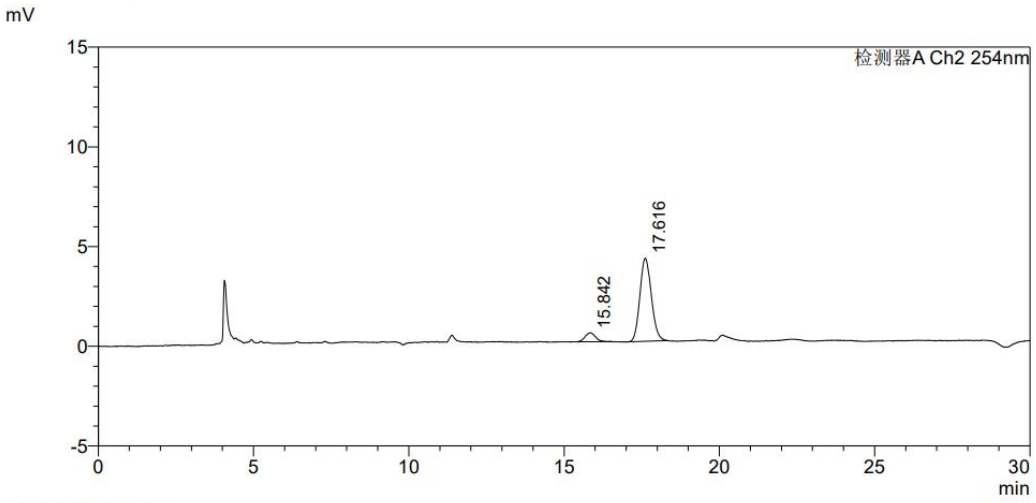

<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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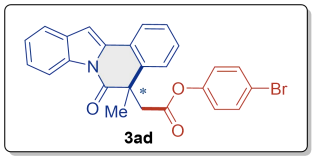
2	17.616	105899	4162	91.064
总计		116291	4609	100.000



3ad

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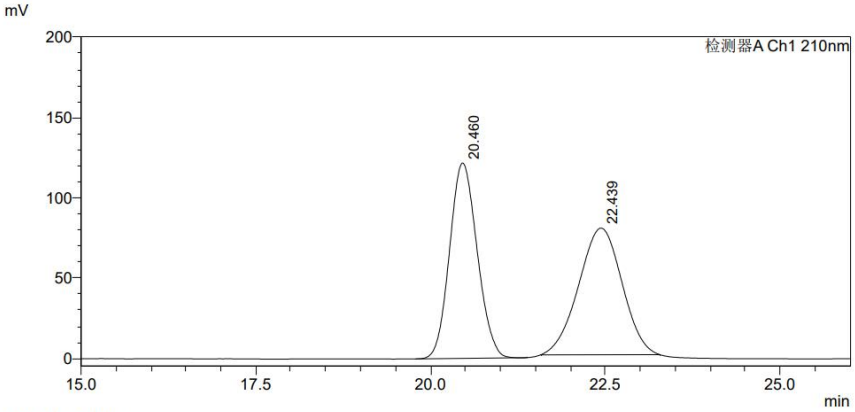

<Peak Table>

检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	20.460	3339370	121659	49.501
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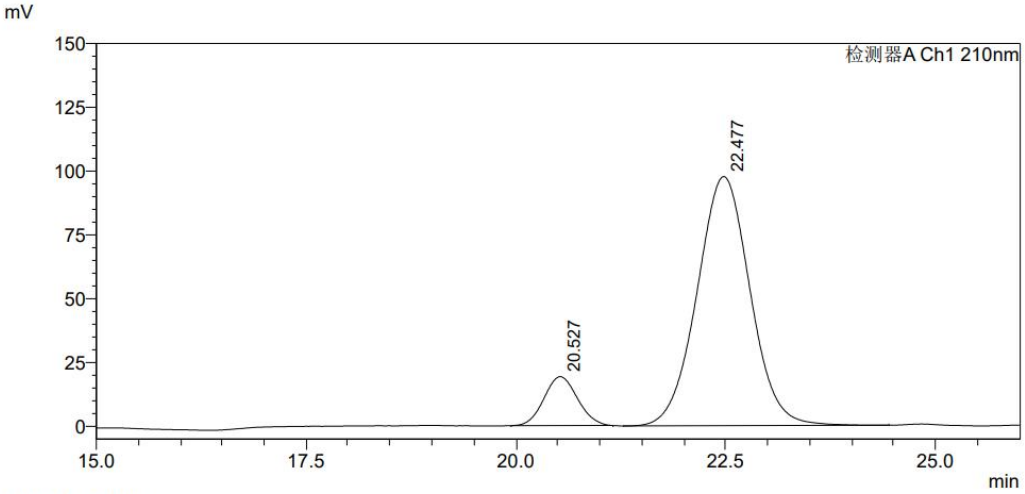

<Peak Table>

检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	20.527	532770	19181	11.062
2	22.477	4283570	97627	88.938
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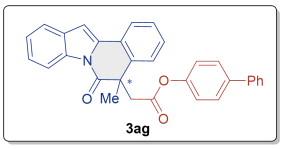

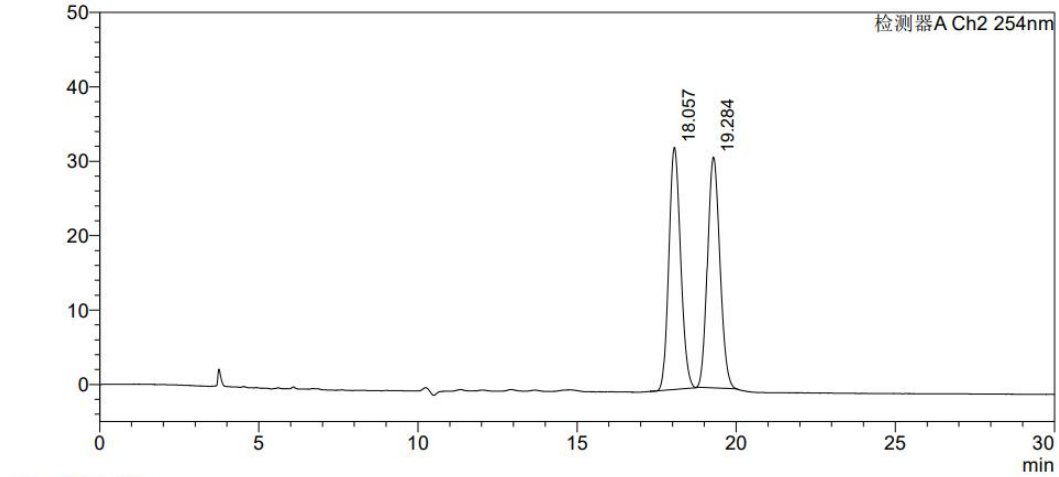

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2	19.284	840222	31022	50.051
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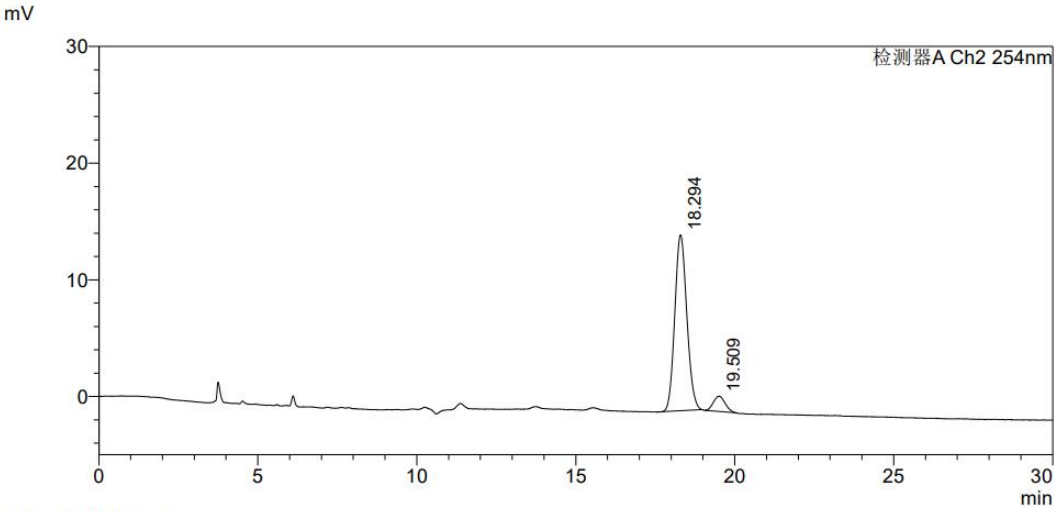

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检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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2	19.509	33532	1304	7.752
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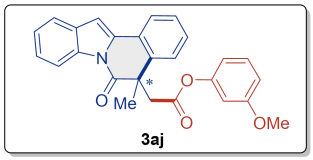

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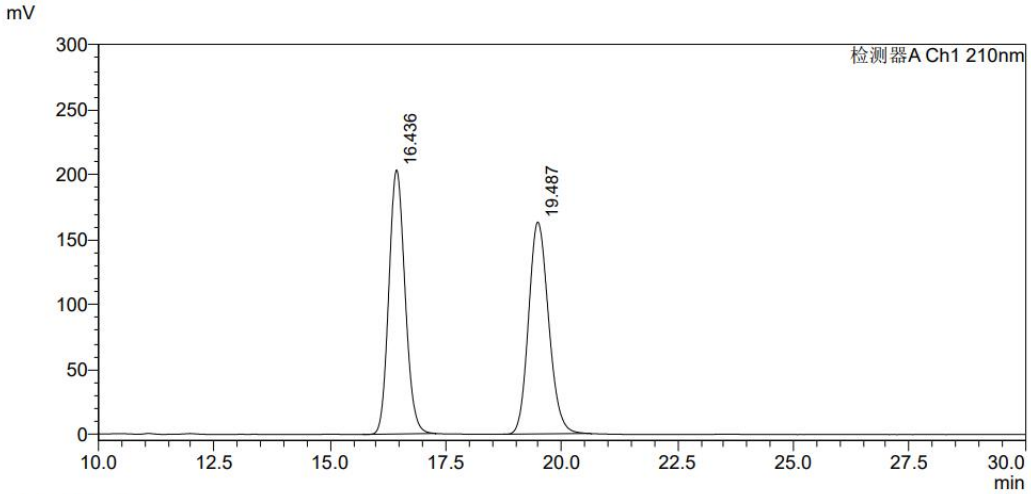

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检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	16.436	4932773	203399	50.061
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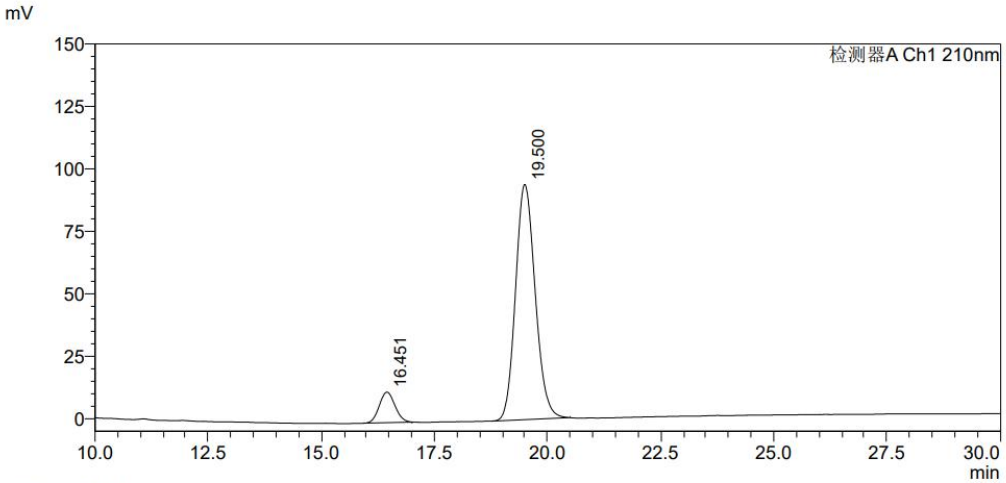

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检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
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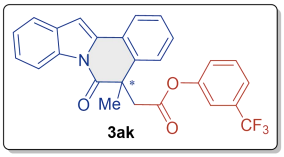
2	19.500	2845990	94187	90.587
总计		3141719	106431	100.000



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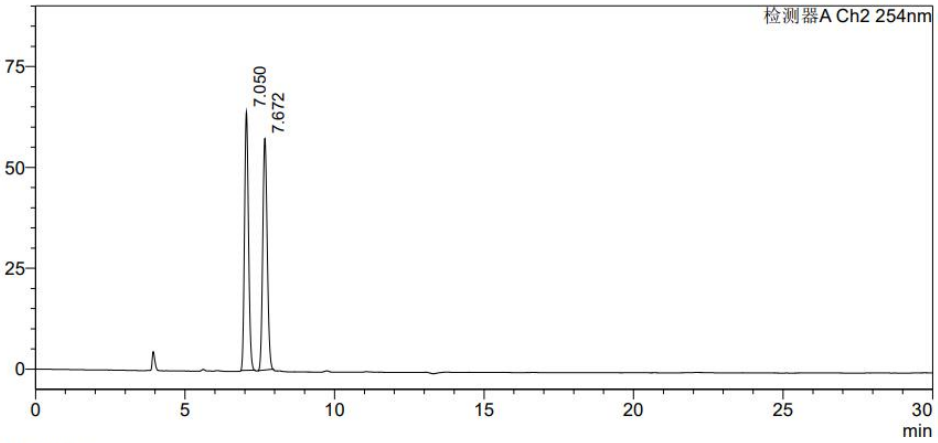

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检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.050	599489	64016	50.141
2	7.672	596106	57358	49.859
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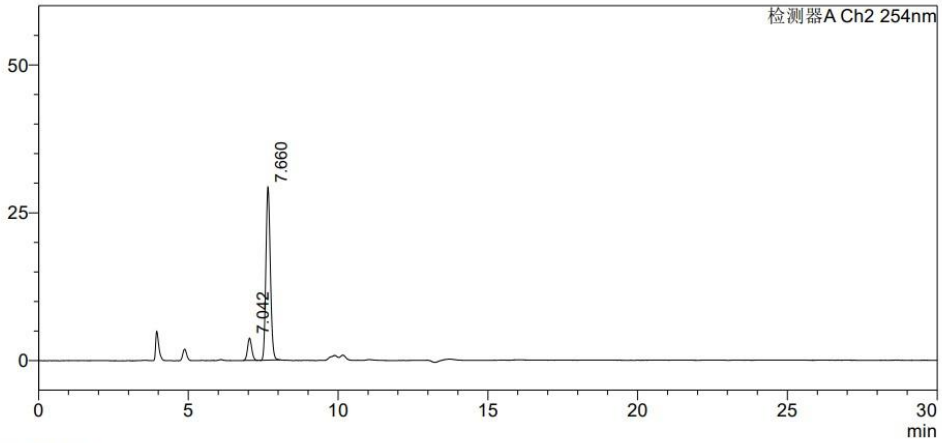

<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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2	7.660	306360	29203	89.254
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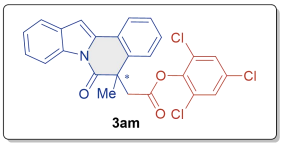

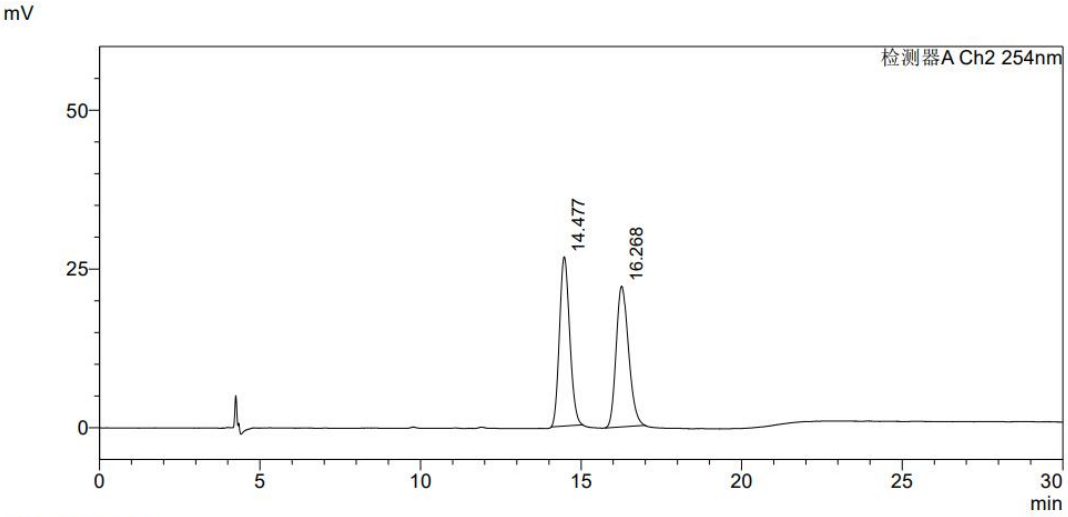

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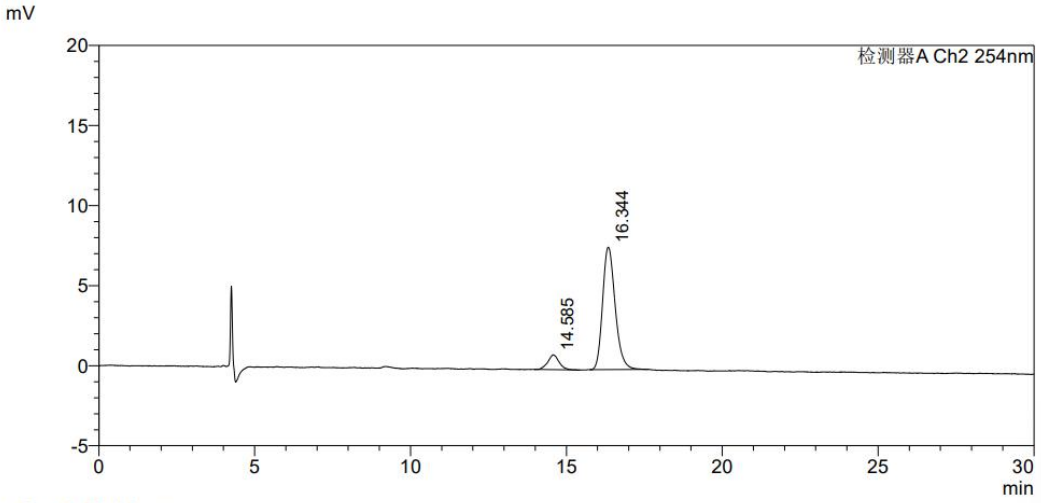
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.477	594406	26638	50.148
2	16.268	590892	22142	49.852
总计		1185298	48780	100.000



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检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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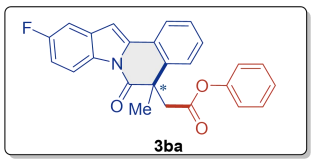
2	16.344	212153	7655	90.063
总计		235562	8576	100.000



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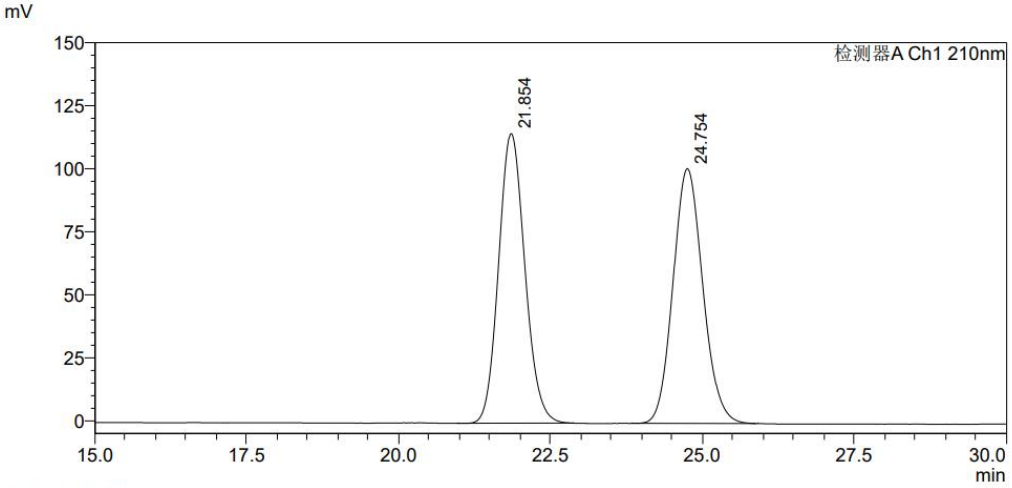

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检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	21.854	3454113	114902	49.977
2	24.754	3457273	101093	50.023
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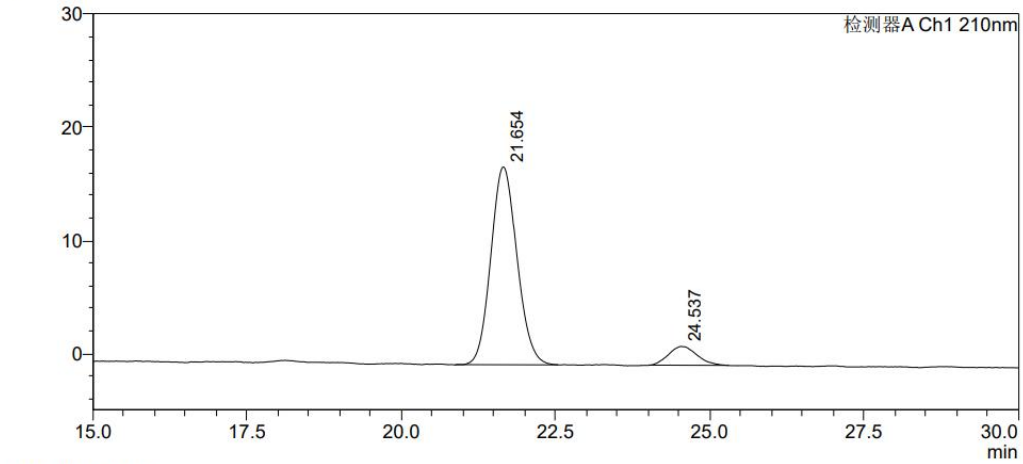

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检测器A Ch1 210nm

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2	24.537	54005	1672	9.461
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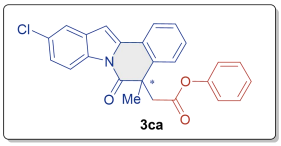

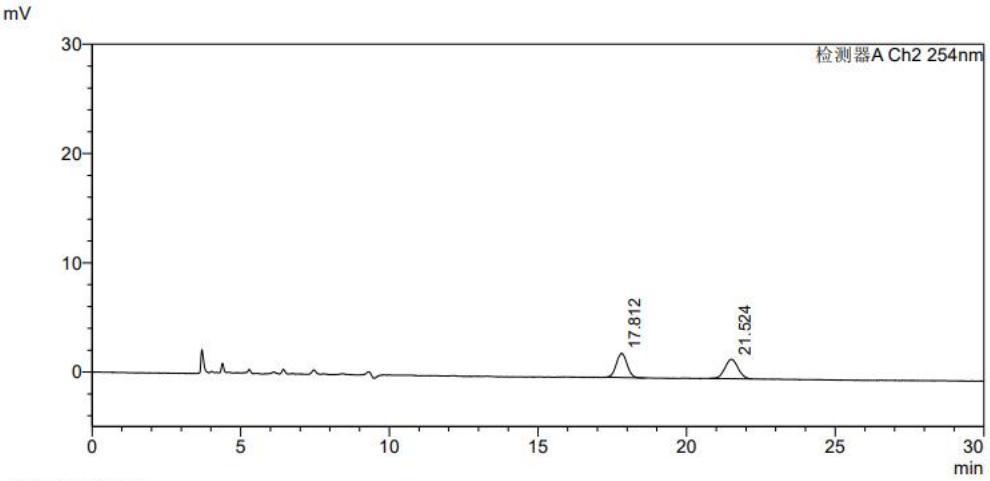

<Peak Table>

检测器A Ch2 254nm

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1	17.812	54318	2204	50.118
2	21.524	54062	1770	49.882
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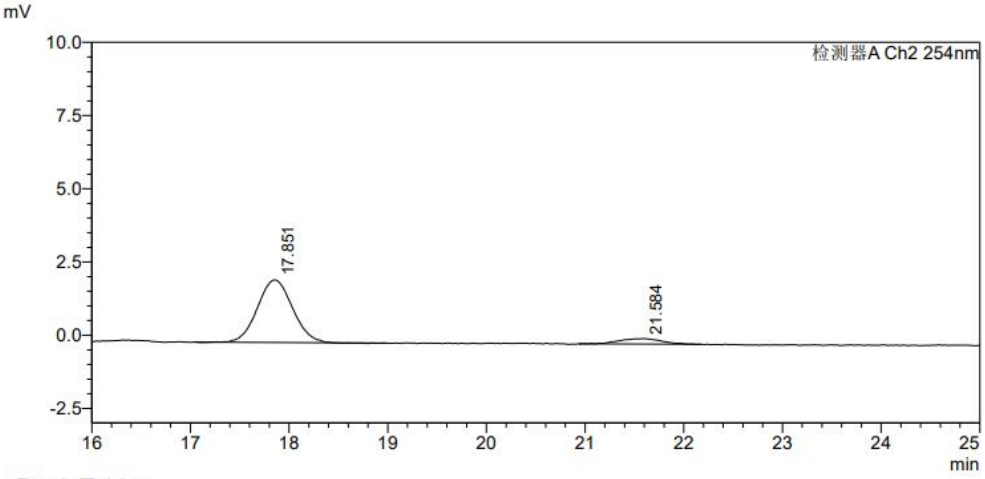

<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
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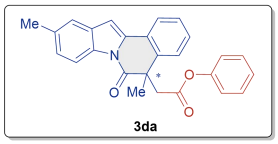
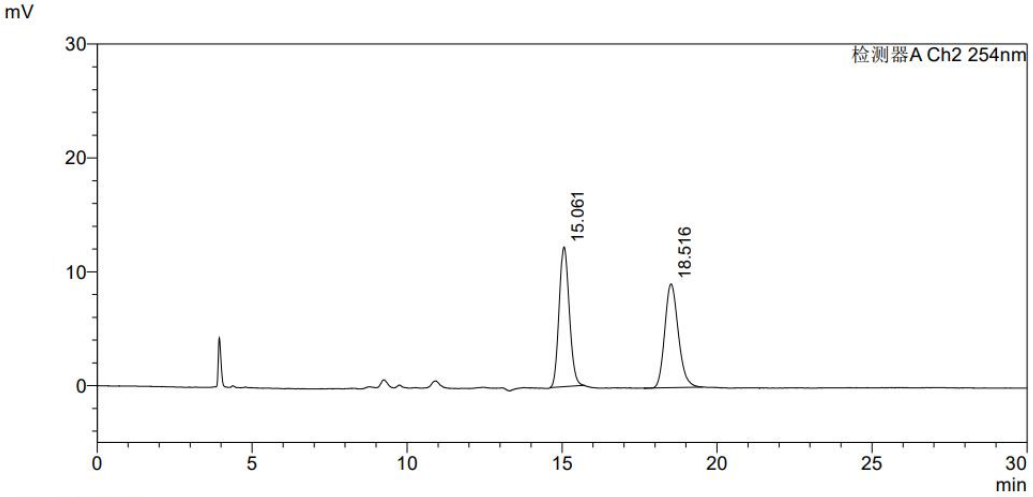
2	21.584	5586	191	9.638
总计		57951	2323	100.000

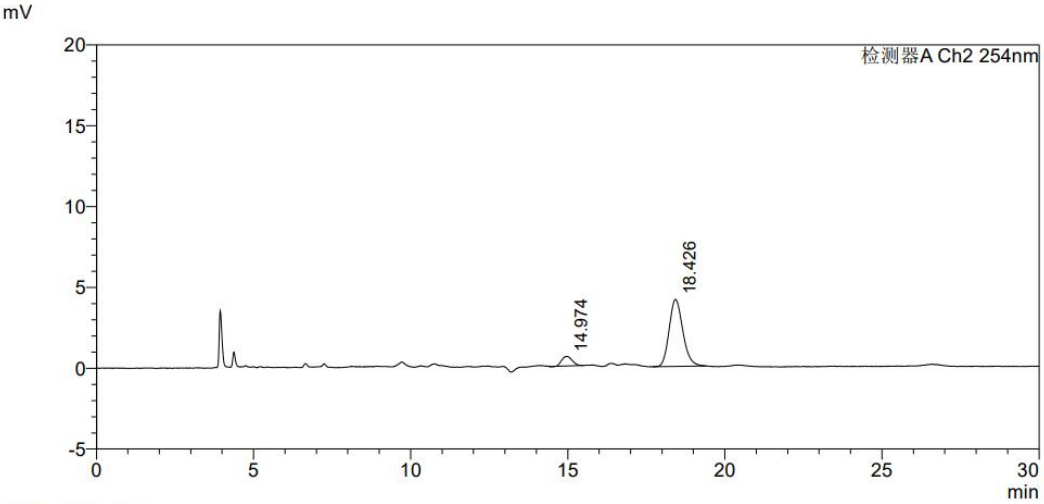




<Peak Table>

检测器A Ch2 254nm

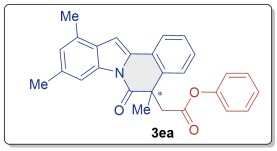
Peak#	Ret. Time	Area	Height	Area%
1	15.061	277374	12277	49.982
2	18.516	277574	9108	50.018
总计		554948	21385	100.000

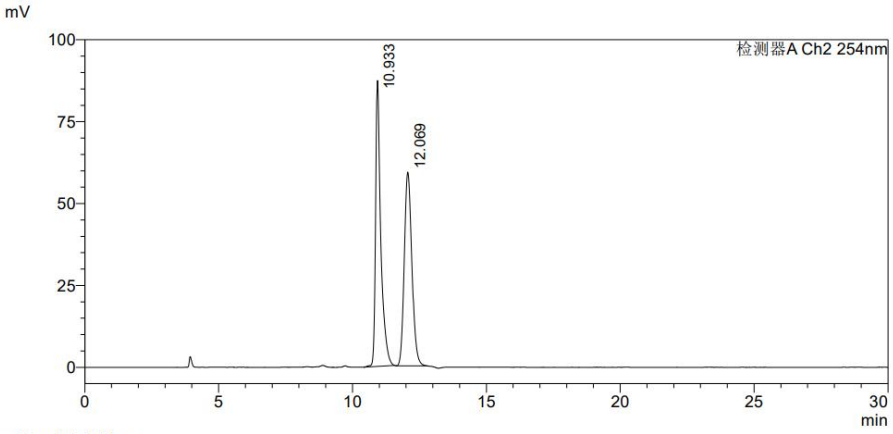


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.974	13612	594	9.724
2	18.426	126374	4145	90.276
总计		139987	4739	100.000

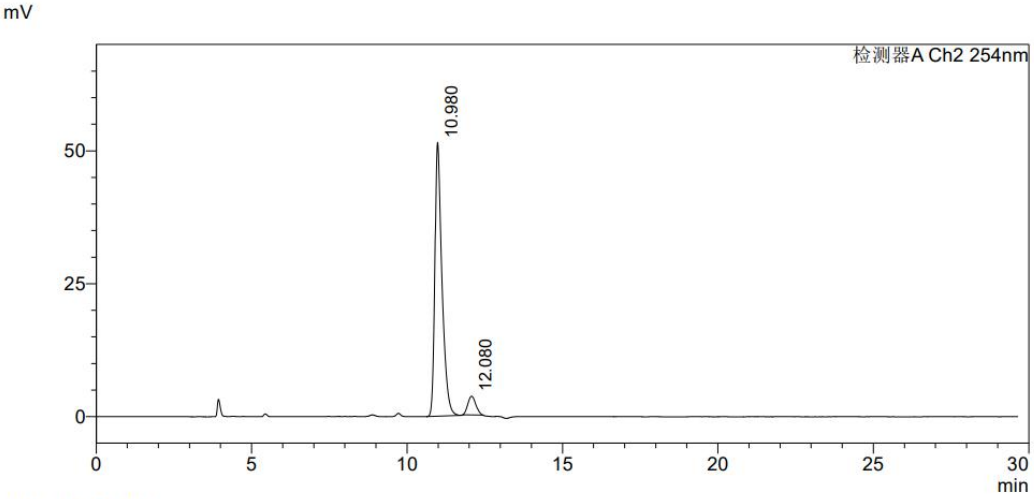




<Peak Table>

检测器A Ch2 254nm

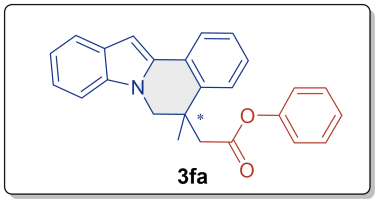
Peak#	Ret. Time	Area	Height	Area%
1	10.933	1152452	87352	49.789
2	12.069	1162205	59110	50.211
总计		2314657	146462	100.000



<Peak Table>

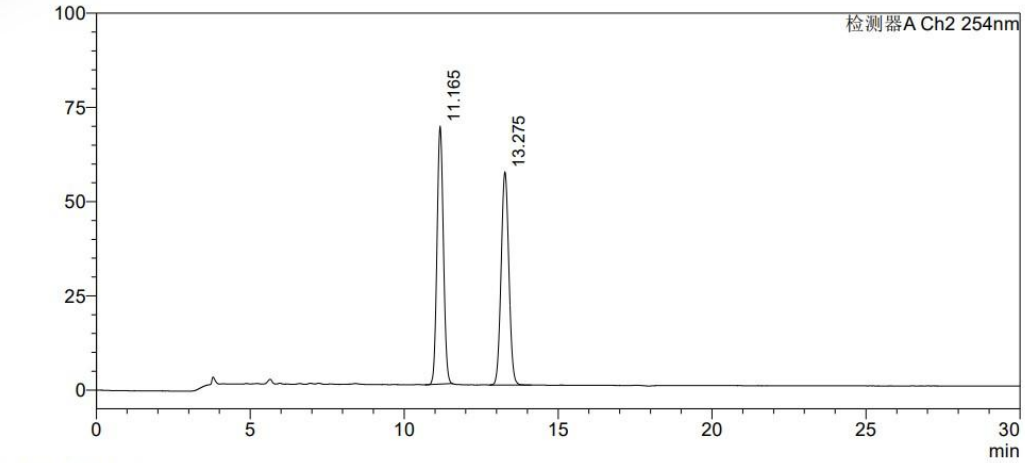
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.980	805829	51410	92.770
2	12.080	62799	3511	7.230
总计		868629	54921	100.000



3fa

<Chromatogram>

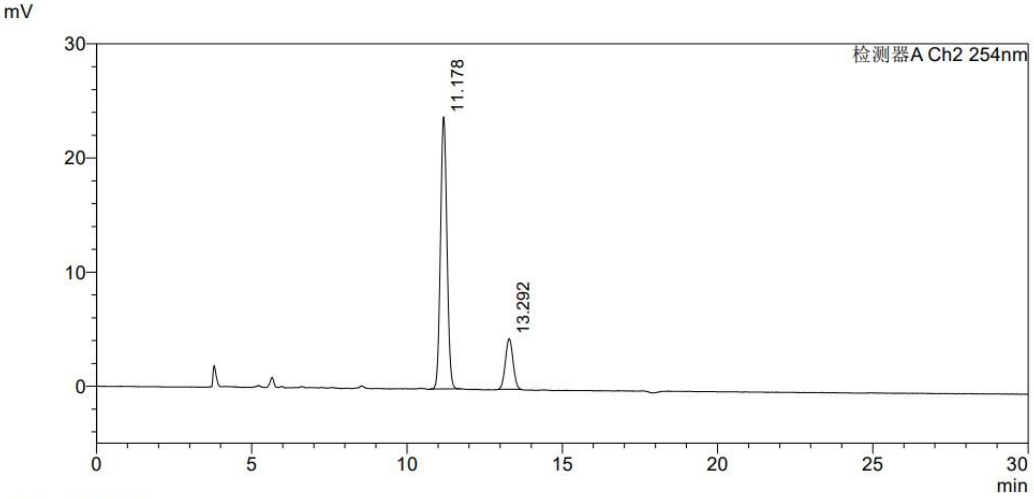


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.165	985522	68242	49.782
2	13.275	994154	56544	50.218
总计		1979676	124785	100.000

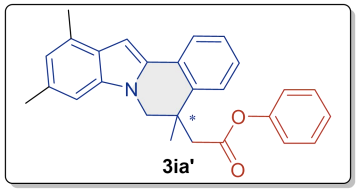
<Chromatogram>



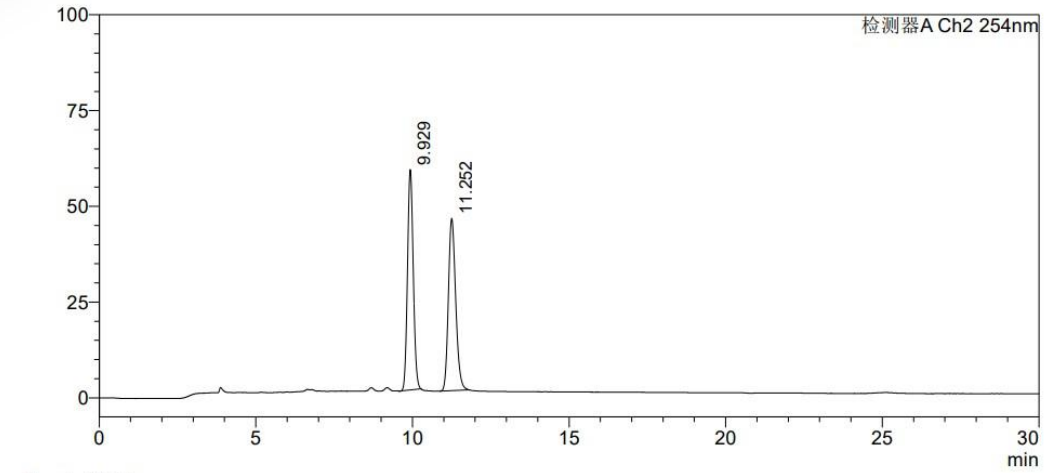
<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.178	346274	23839	81.968
2	13.292	76179	4430	18.032
总计		422452	28270	100.000



<Chromatogram>

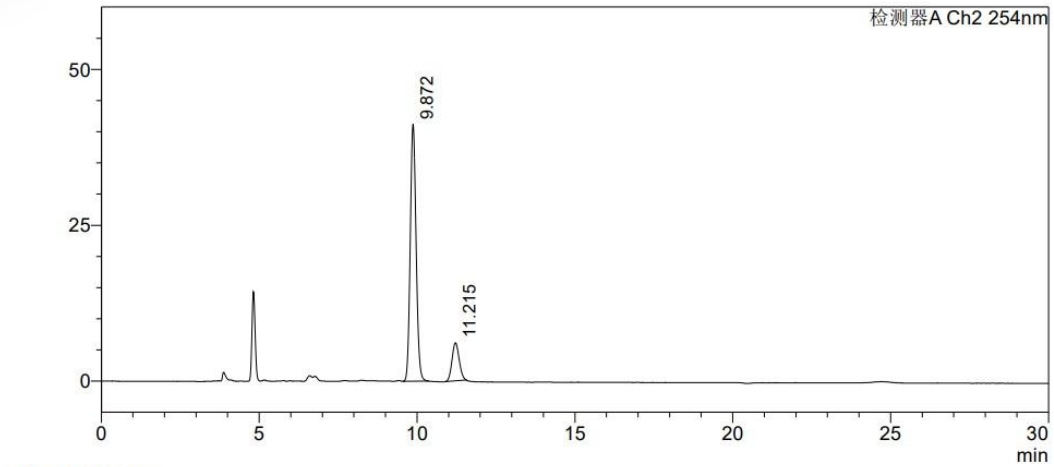


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.929	737519	57505	50.165
2	11.252	732677	44928	49.835
总计		1470196	102433	100.000

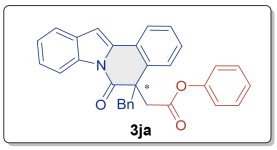
<Chromatogram>

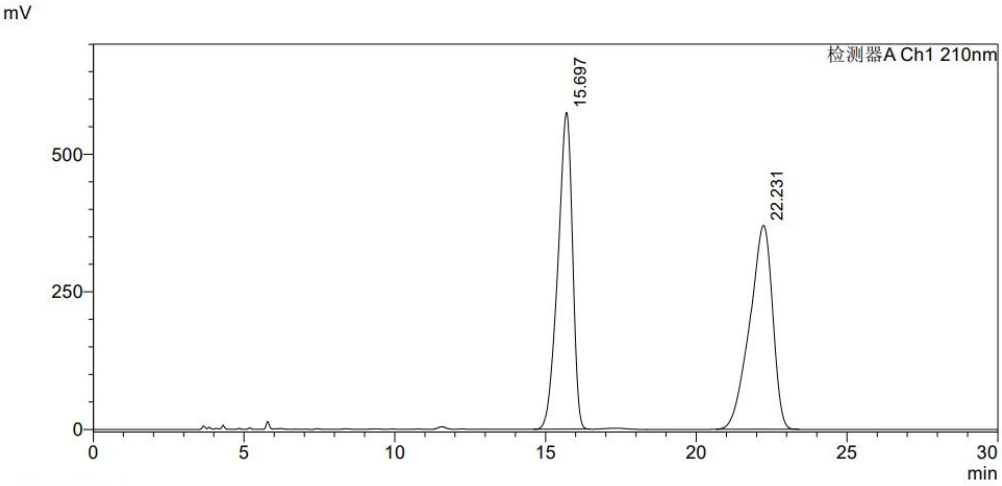


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.872	532672	41191	84.711
2	11.215	96142	6089	15.289
总计		628813	47279	100.000

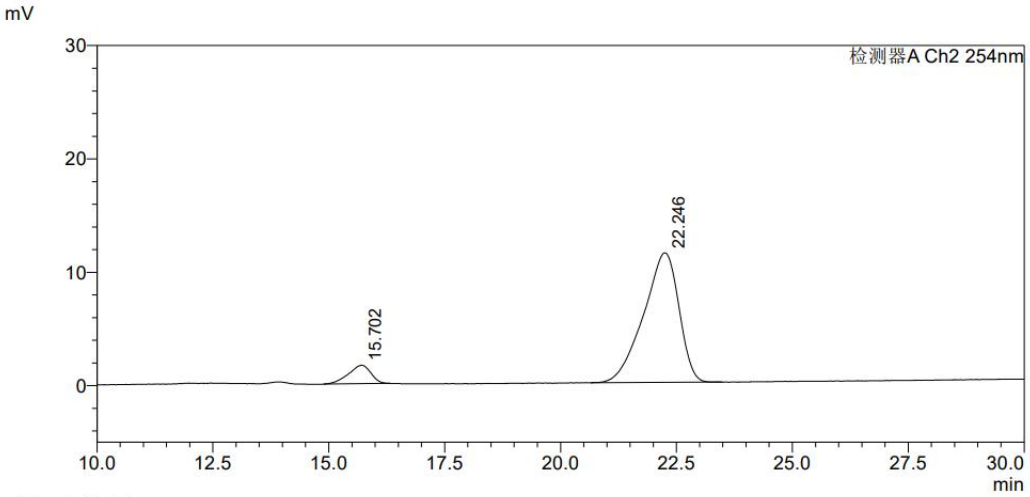




<Peak Table>

检测器A Ch1 210nm

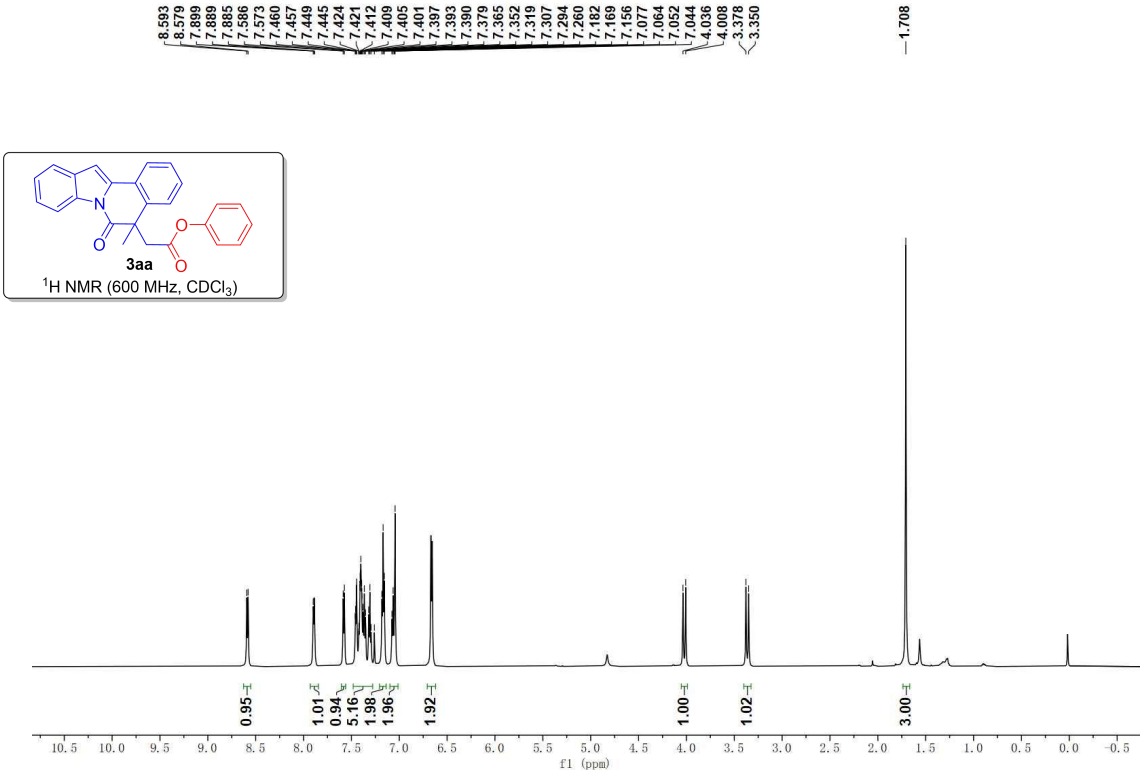
Peak#	Ret. Time	Area	Height	Area%
1	15.697	19475083	575757	49.818
2	22.231	19617234	370721	50.182
总计		39092317	946478	100.000

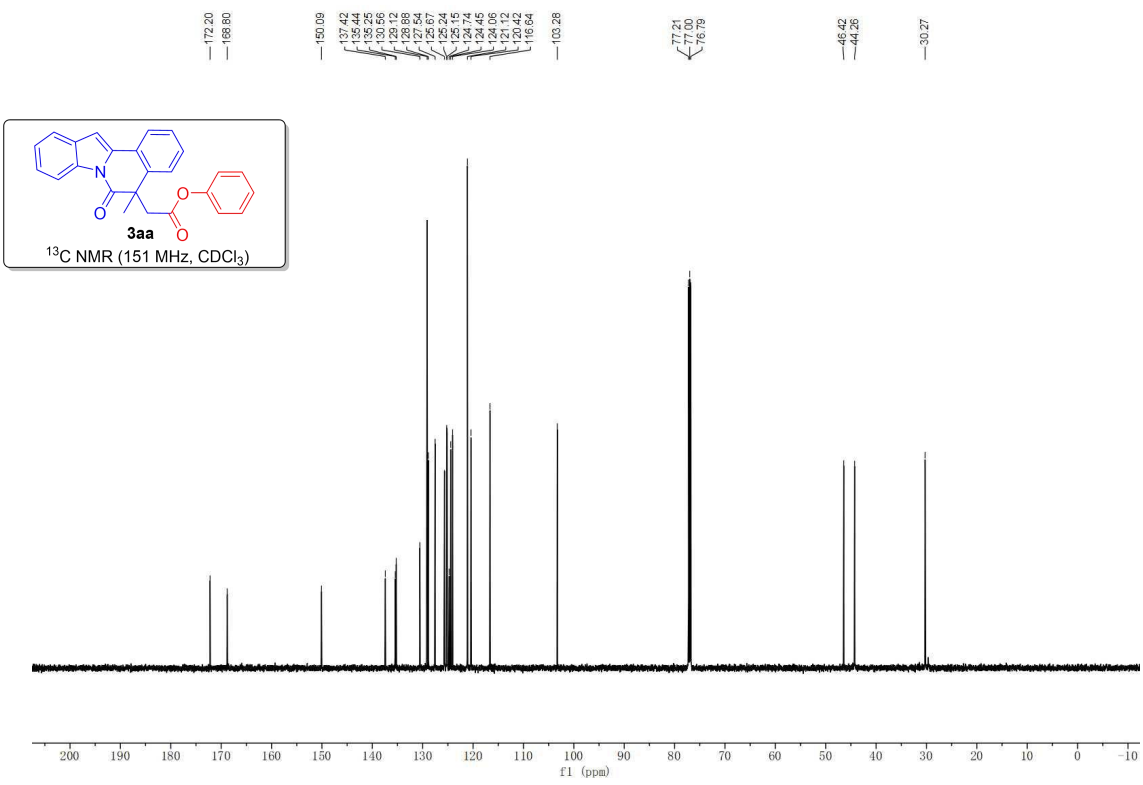


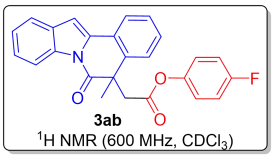
<Peak Table>

检测器A Ch2 254nm

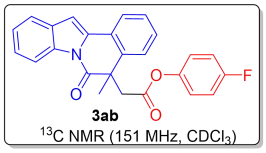
Peak#	Ret. Time	Area	Height	Area%
1	15.702	54705	1630	8.291
2	22.246	605122	11423	91.709
总计		659827	13053	100.000


8.593
8.579
7.899
7.889
7.885
7.586
7.573
7.460
7.457
7.449
7.445
7.424
7.421
7.412
7.409
7.405
7.401
7.397
7.393
7.390
7.379
7.365
7.352
7.319
7.307
7.294
7.260
7.182
7.169
7.156
7.077
7.064
7.052
7.044
4.036
4.008
3.378
3.350
1.708
3aa
1H NMR (600 MHz, CDCl3)
0.95
1.01
0.94
5.16
1.98
1.96
1.92
1.00
1.02
3.00
f1 (ppm)

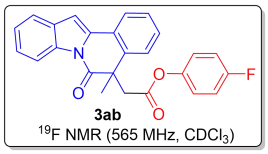

172.20
168.80
150.09
137.42
135.44
135.25
130.56
129.12
128.88
127.54
125.67
125.24
125.15
124.74
124.45
124.16
121.12
120.42
116.64
103.28
77.21
77.00
76.79
46.42
44.26
30.27
3aa
13C NMR (151 MHz, CDCl3)
f1 (ppm)


3ab
^{1}H NMR (600 MHz, $CDCl_3$)

8.594
8.581
7.903
7.896
7.892
7.887
7.597
7.584
7.447
7.443
7.434
7.432
7.411
7.407
7.401
7.395
7.376
7.362
7.330
7.317
7.305
7.259
7.054
6.863
6.848
6.834
6.627
6.616
6.612
6.604
4.023
3.995
3.365
3.337
1.709
1.00
1.05
1.05
4.32
1.05
1.04
2.01
2.02
1.07
1.08
3.11
f1 (ppm)

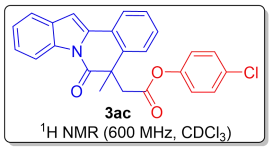

3ab
^{13}C NMR (151 MHz, $CDCl_3$)

172.20
168.92
160.87
159.25
145.88
145.86
137.33
135.43
135.19
130.57
128.94
127.64
125.25
124.74
124.55
124.10
122.57
122.52
120.49
116.65
115.87
115.71
103.41
77.21
77.00
76.79
46.45
44.21
30.29
f1 (ppm)



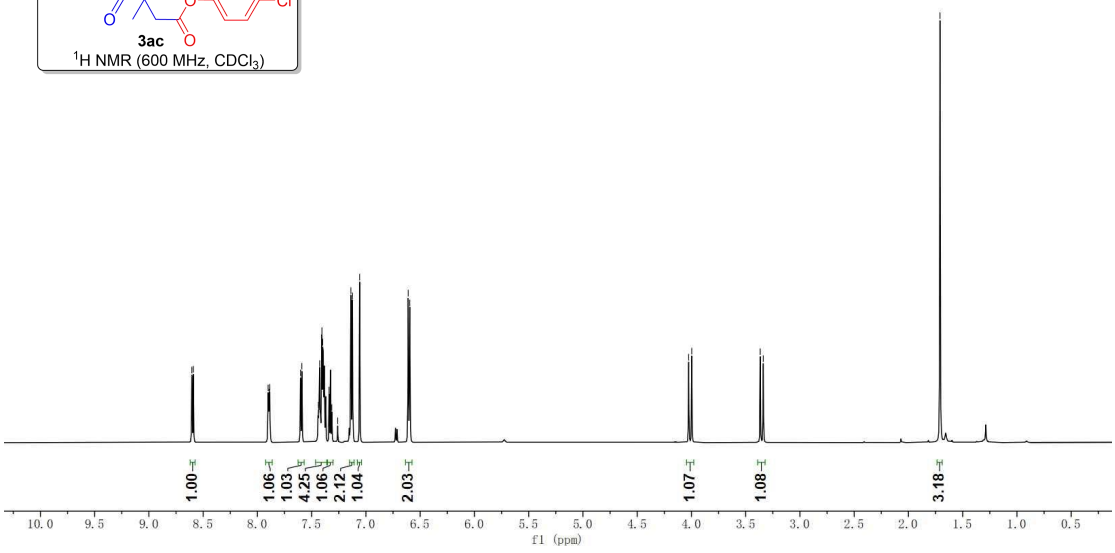
3ab

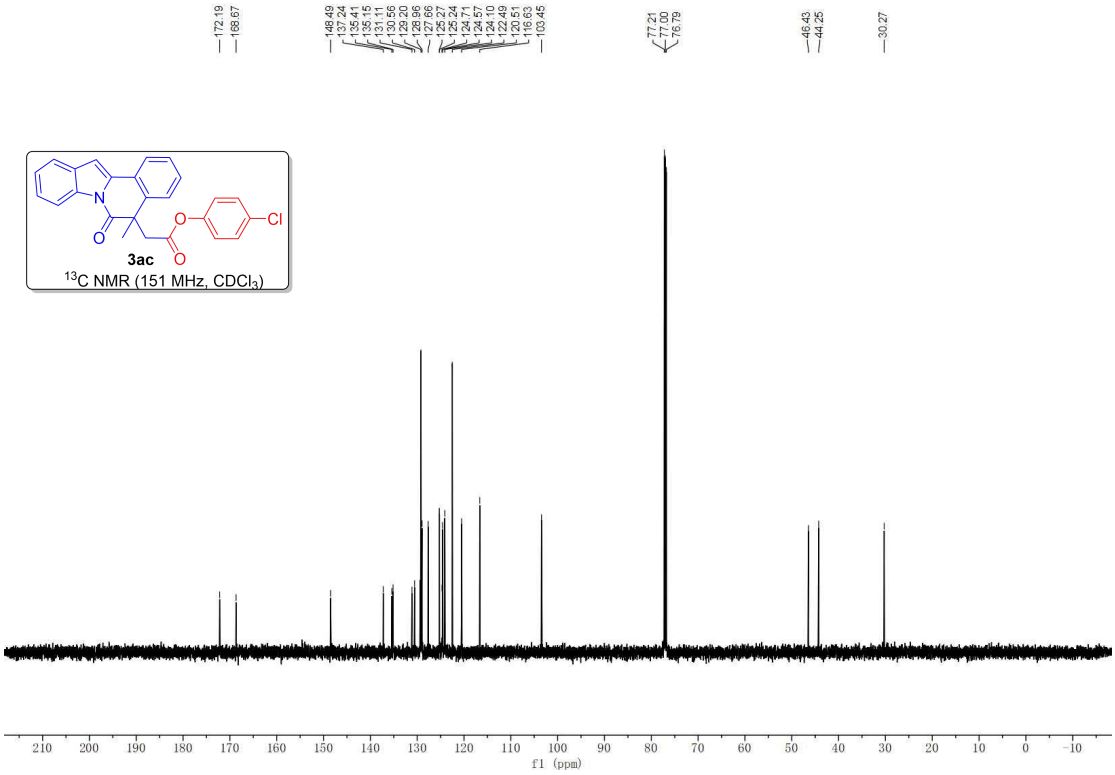
^{19}F NMR (565 MHz, $CDCl_3$)

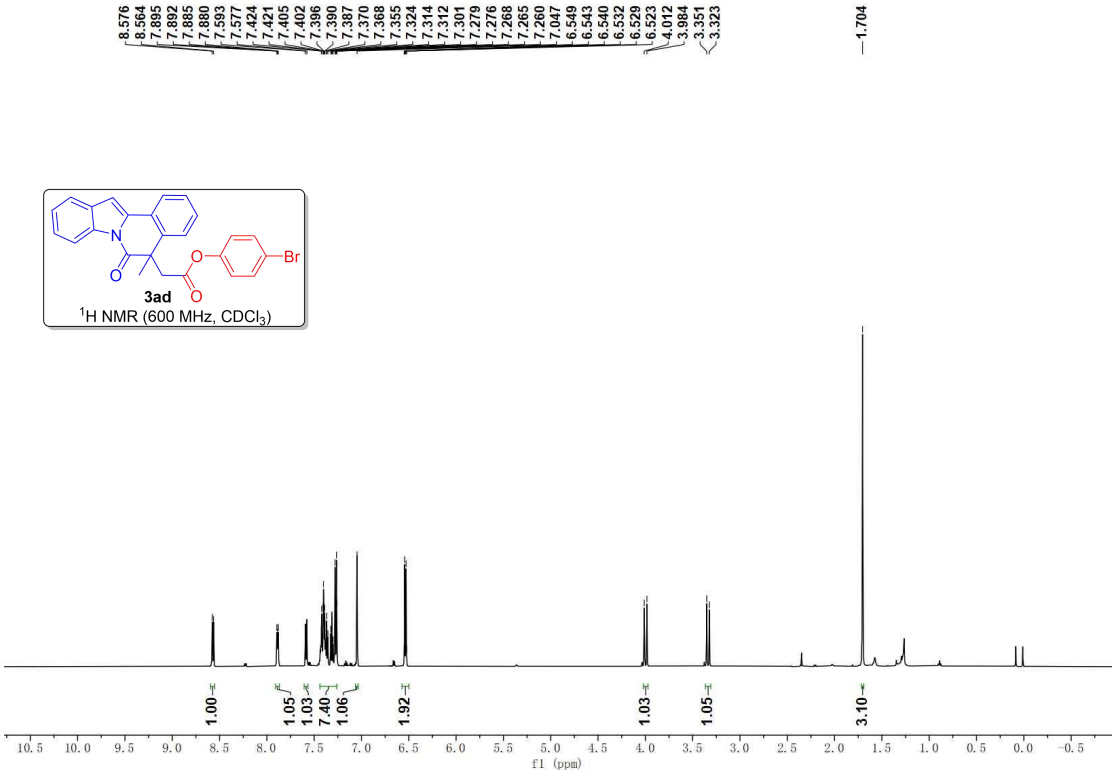


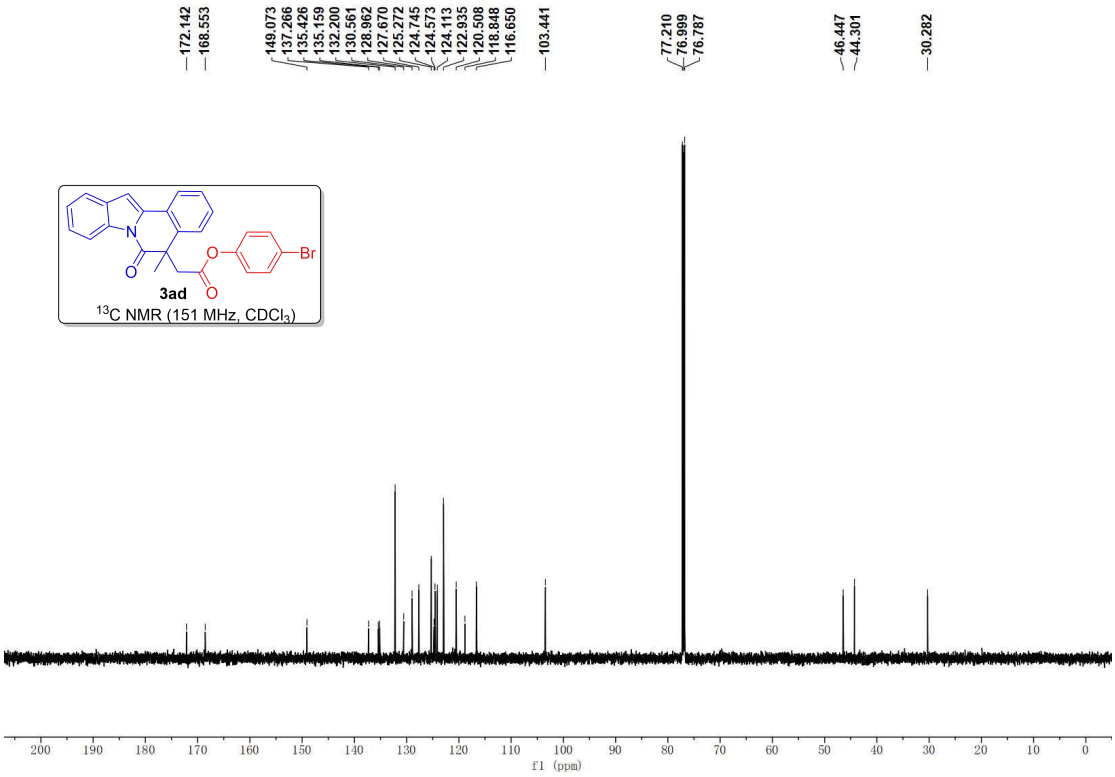
3ac

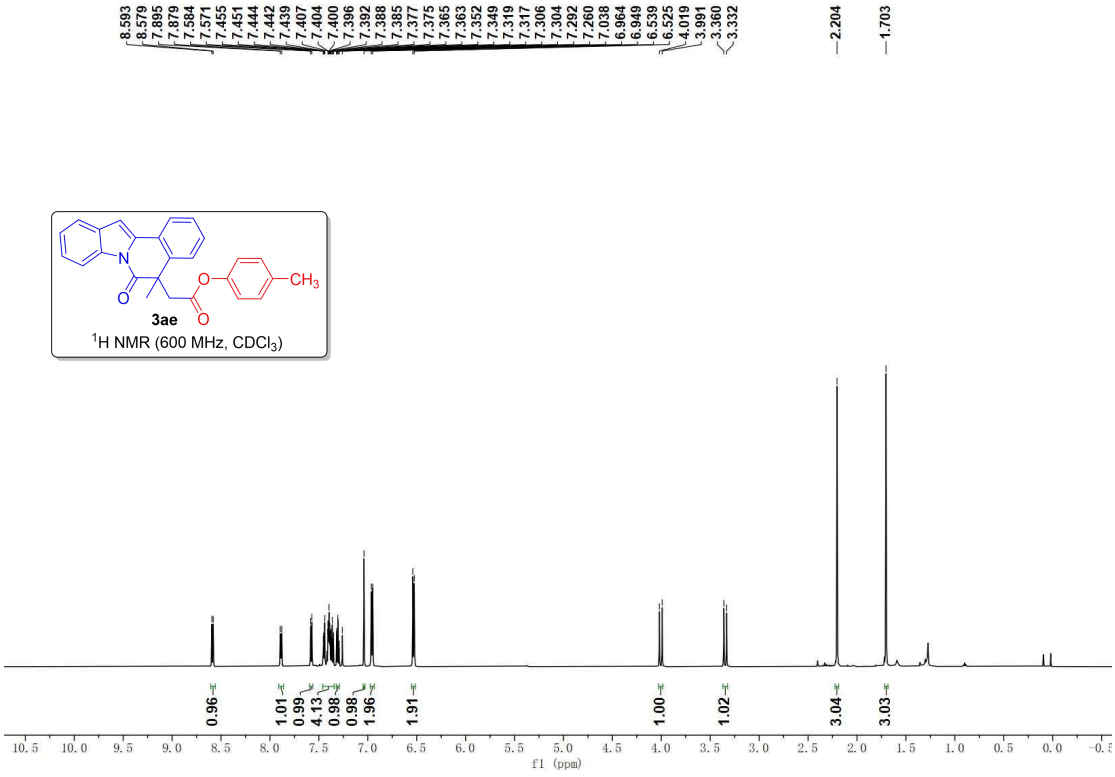
^{1}H NMR (600 MHz, $CDCl_3$)

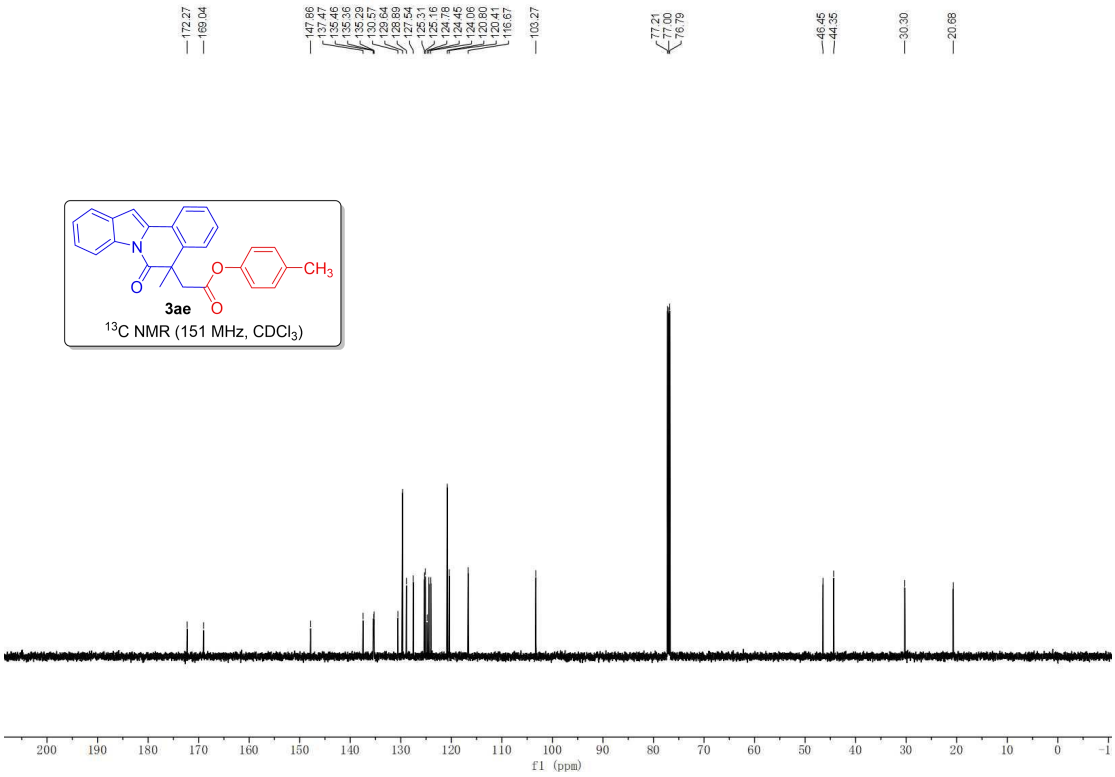


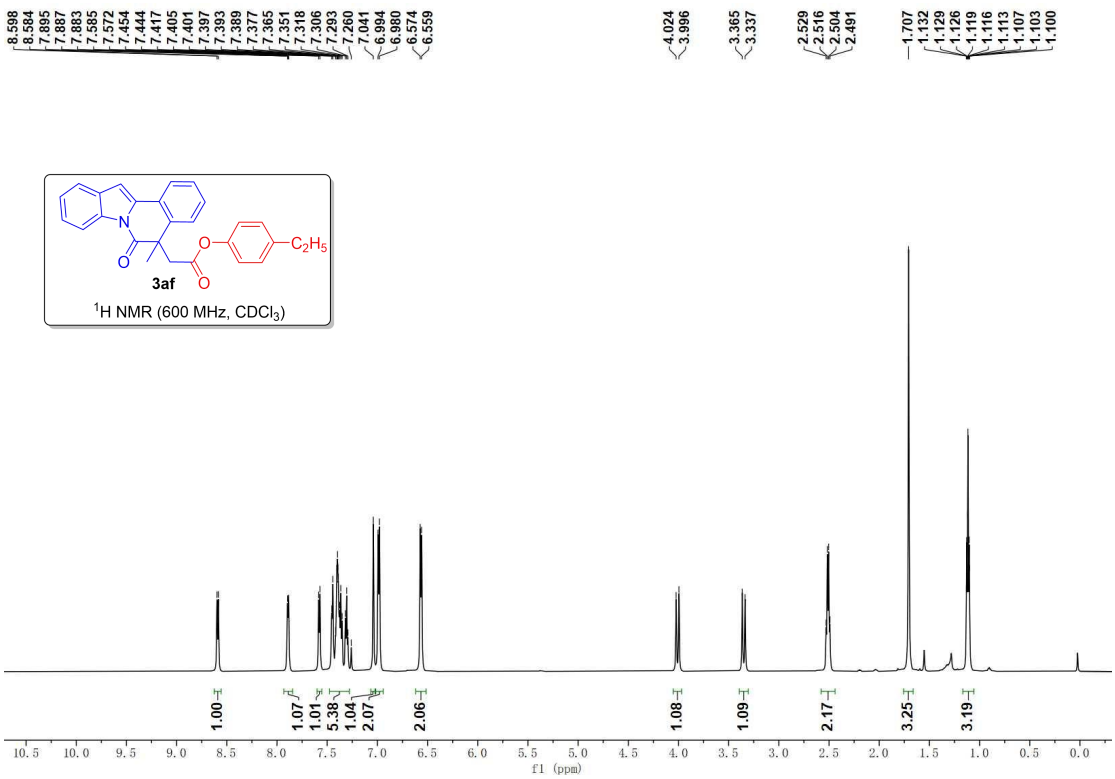

172.19
168.67
148.49
137.24
135.41
135.15
131.11
130.56
129.20
128.96
127.66
125.27
125.24
124.71
124.57
124.10
122.49
120.51
116.63
103.45
77.21
77.00
76.79
46.43
44.25
30.27
3ac
13C NMR (151 MHz, CDCl3)
f1 (ppm)

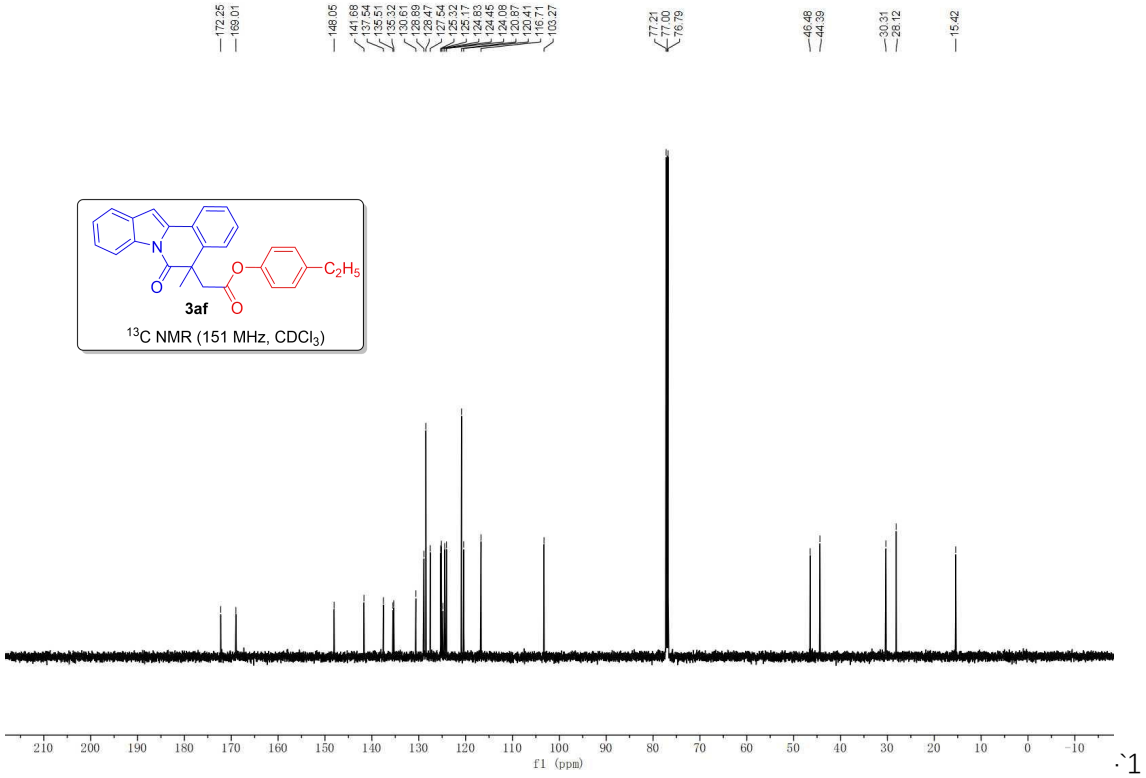

8.576
8.564
7.895
7.892
7.885
7.880
7.593
7.577
7.424
7.421
7.405
7.402
7.396
7.390
7.387
7.370
7.368
7.355
7.324
7.314
7.312
7.301
7.279
7.276
7.268
7.265
7.260
7.047
6.549
6.543
6.540
6.532
6.529
6.523
4.012
3.984
3.351
3.323
1.704
3ad
1H NMR (600 MHz, CDCl3)
1.00
1.05
1.03
7.40
1.06
1.92
1.03
1.05
3.10
f1 (ppm)

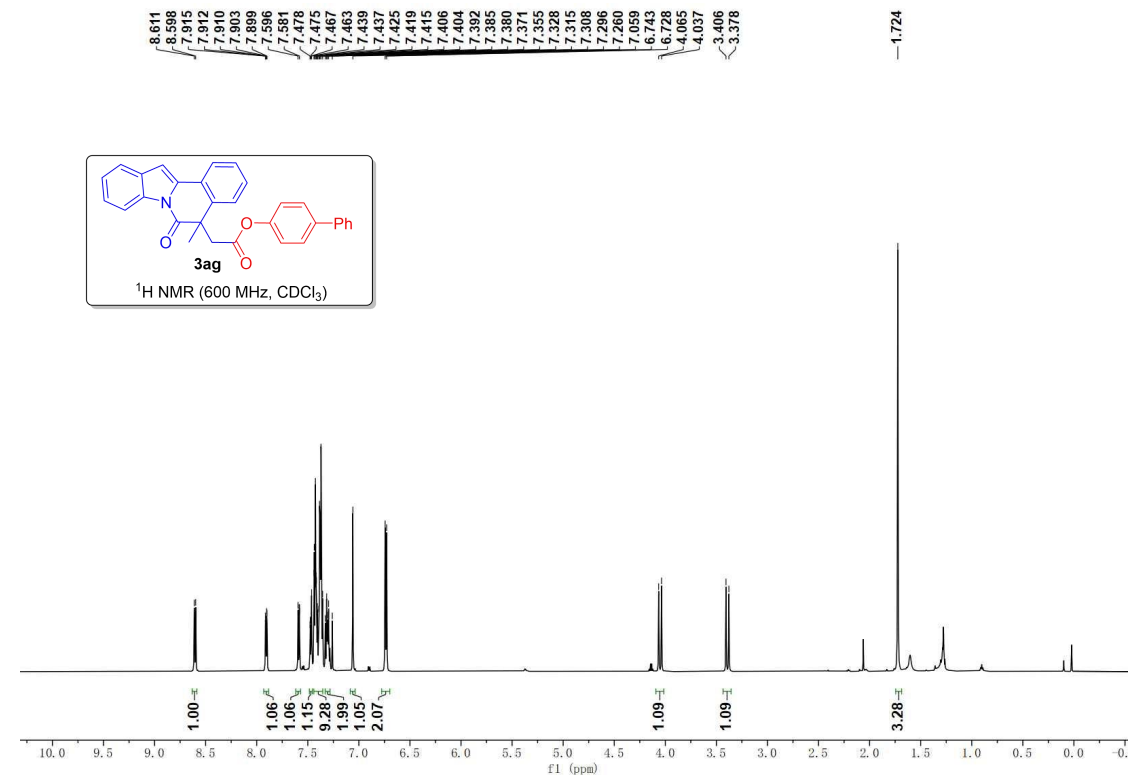

172.142
168.553
149.073
137.266
135.426
135.159
132.200
130.561
128.962
127.670
125.272
124.745
124.573
124.113
122.935
120.508
118.848
116.650
103.441
77.210
76.999
76.787
46.447
44.301
30.282
Br
O
N
O
O
3ad
13C NMR (151 MHz, CDCl3)
f1 (ppm)

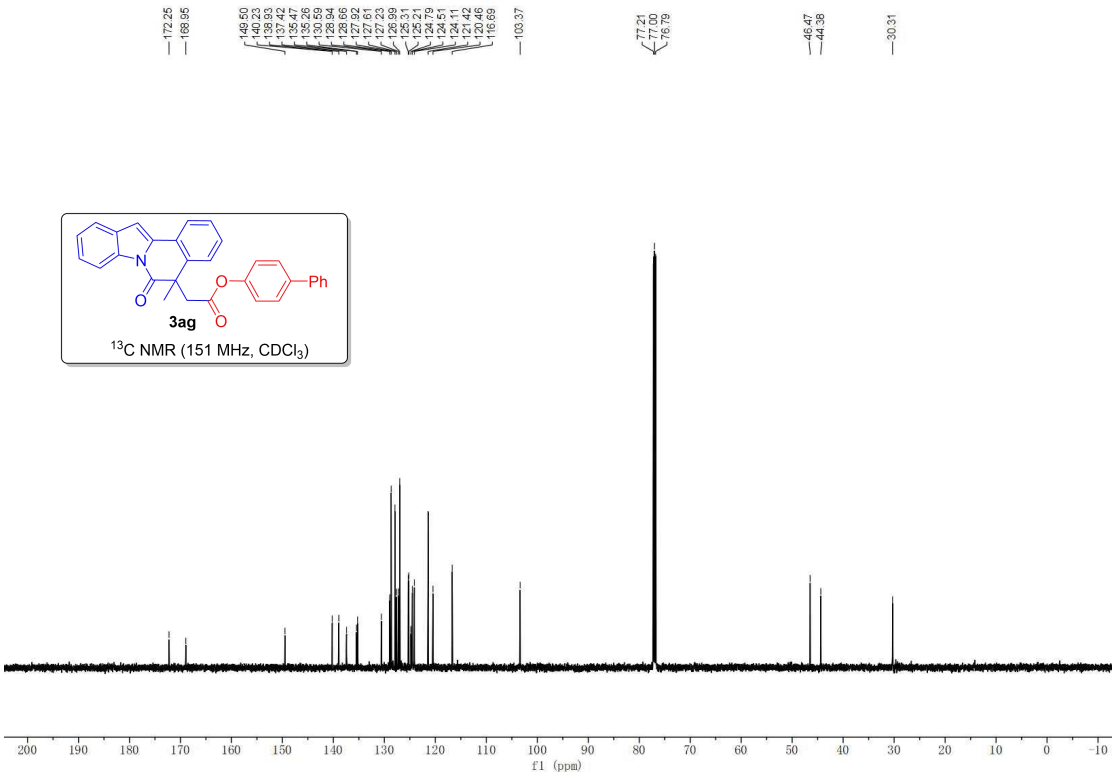

8.593
8.579
7.895
7.879
7.584
7.571
7.455
7.451
7.444
7.442
7.439
7.407
7.404
7.400
7.396
7.392
7.388
7.385
7.377
7.375
7.365
7.363
7.352
7.349
7.319
7.317
7.306
7.304
7.292
7.260
7.038
6.964
6.949
6.539
6.525
4.019
3.991
3.360
3.332
2.204
1.703
CH3
O
N
O
O
3ae
1H NMR (600 MHz, CDCl3)
0.96
1.01
0.99
4.13
0.98
0.98
1.96
1.91
1.00
1.02
3.04
3.03
f1 (ppm)

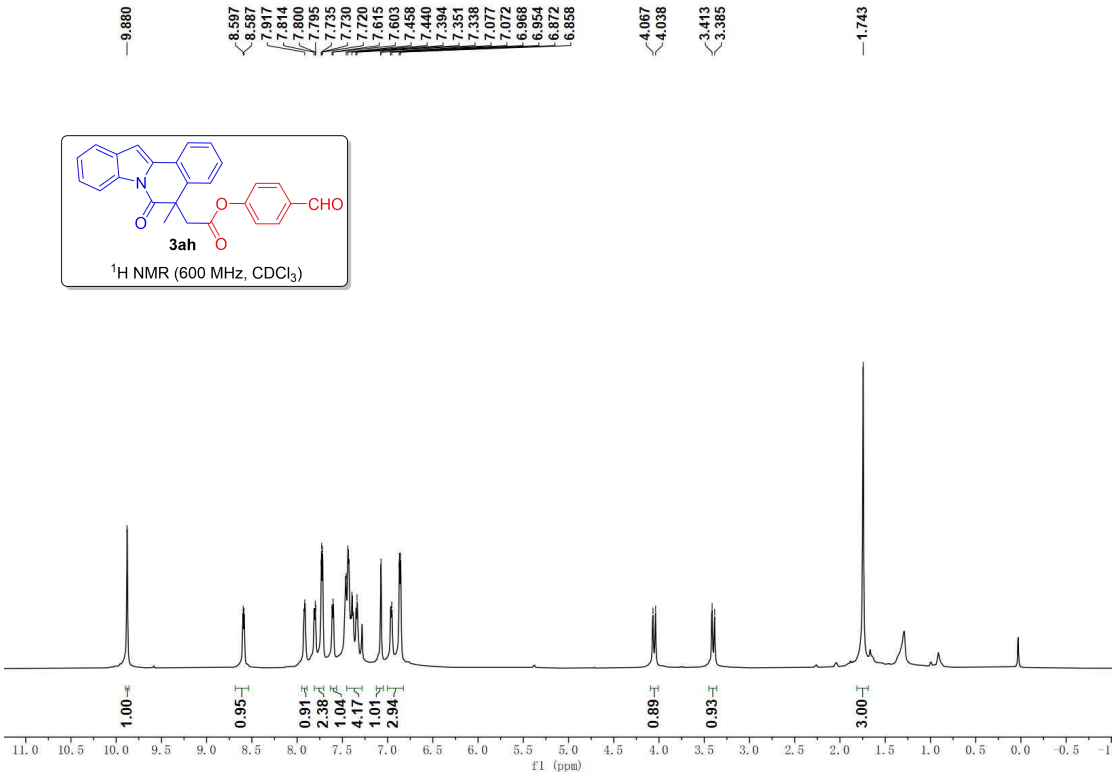

172.27
169.04
147.86
137.47
135.46
135.36
135.29
130.57
129.64
128.89
127.54
127.31
125.16
124.78
124.45
124.06
120.80
120.41
116.67
103.27
77.21
77.00
76.79
46.45
44.35
30.30
20.68
CH3
O
O
O
N
3ae
13C NMR (151 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

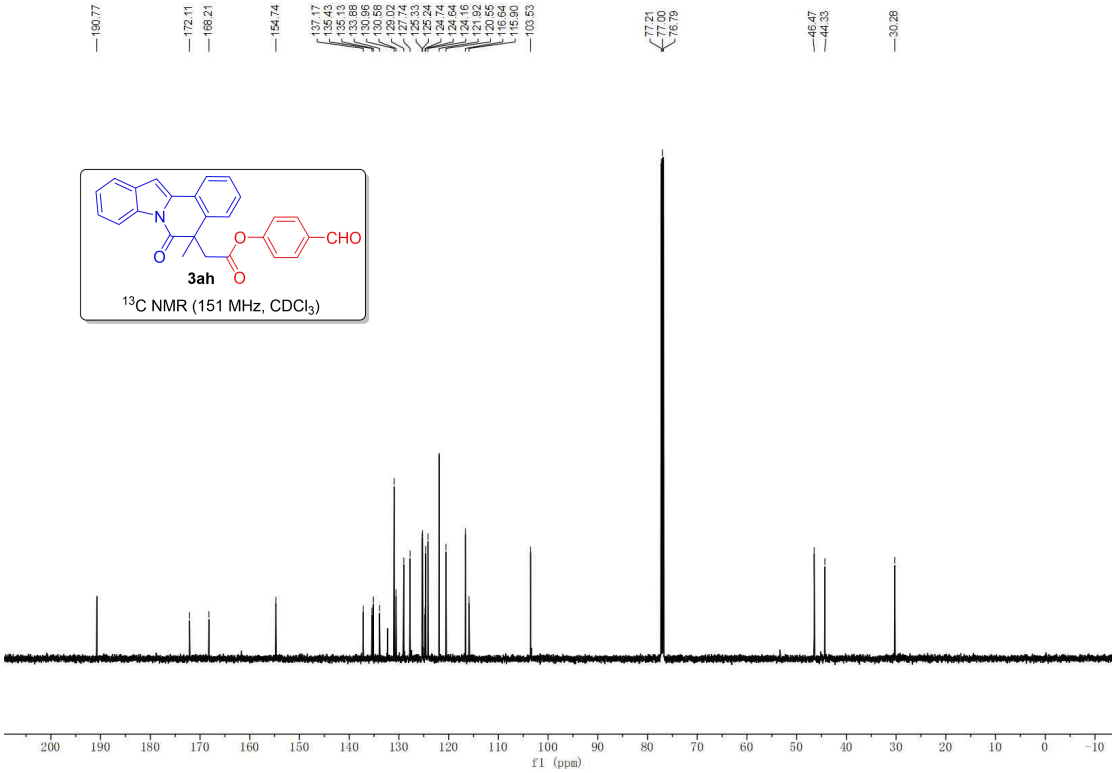

8.598
8.584
7.895
7.887
7.883
7.585
7.572
7.454
7.444
7.417
7.405
7.401
7.397
7.393
7.389
7.377
7.365
7.351
7.318
7.306
7.293
7.260
7.041
6.994
6.980
6.574
6.559
4.024
3.996
3.365
3.337
2.529
2.516
2.504
2.491
1.707
1.132
1.129
1.126
1.119
1.116
1.113
1.107
1.103
1.100
C2H5
O
O
O
N
3af
1H NMR (600 MHz, CDCl3)
1.00
1.07
1.01
5.38
1.04
2.07
2.06
1.08
1.09
2.17
3.25
3.19
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
f1 (ppm)

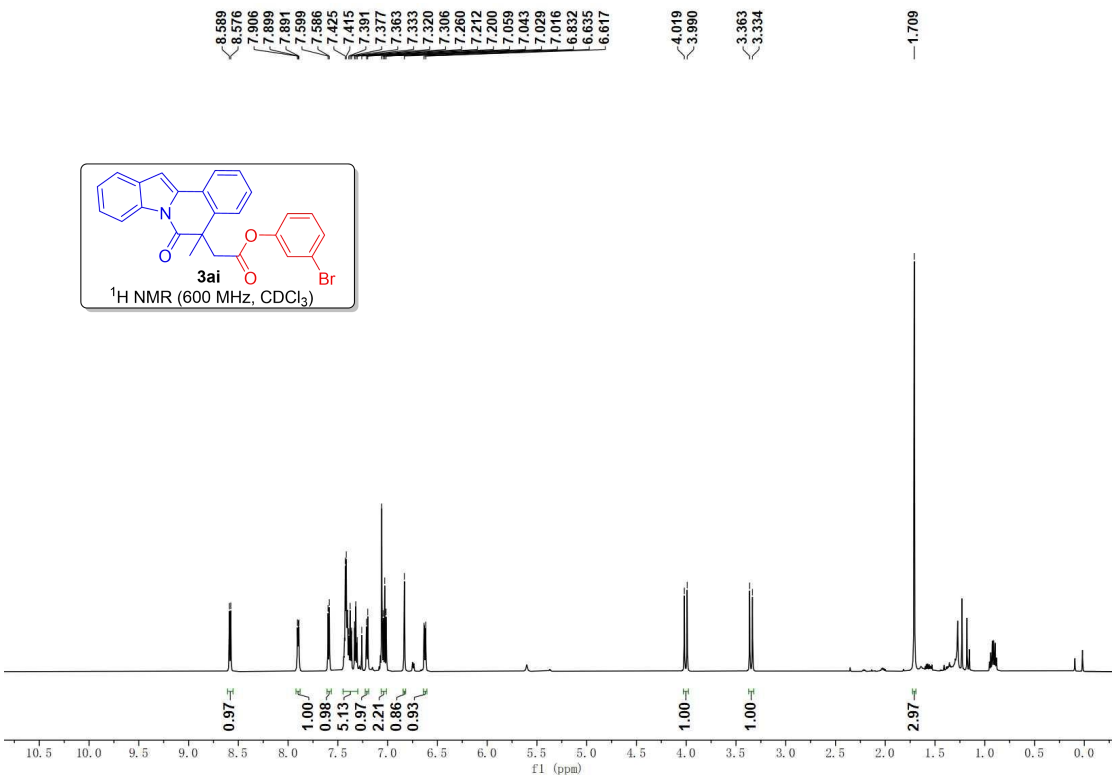

172.25
169.01
148.05
141.68
137.54
135.51
135.32
130.61
128.89
128.47
127.54
125.32
124.83
124.45
124.08
120.87
120.41
116.71
103.27
77.21
77.00
76.79
46.48
44.39
30.31
28.12
15.42
3af
13C NMR (151 MHz, CDCl3)
f1 (ppm)

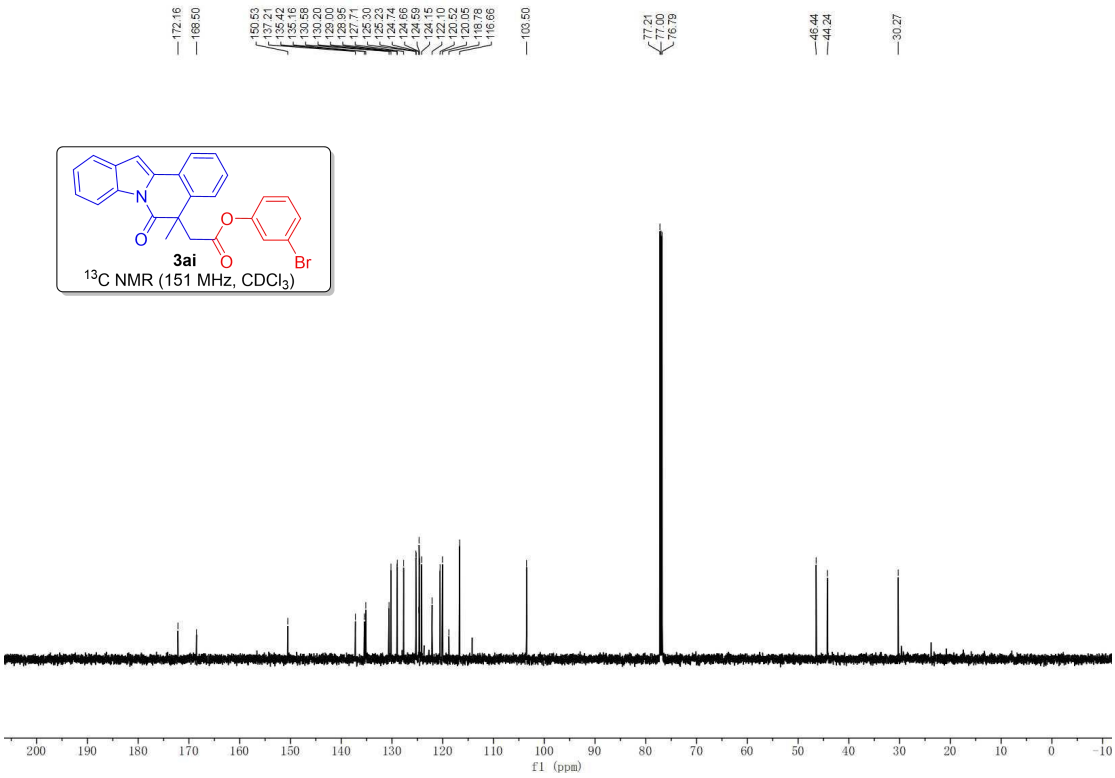

8.611
8.598
7.915
7.912
7.910
7.903
7.899
7.596
7.581
7.478
7.475
7.467
7.463
7.439
7.437
7.425
7.419
7.415
7.406
7.404
7.392
7.385
7.380
7.371
7.355
7.328
7.315
7.308
7.296
7.260
7.059
6.743
6.728
4.065
4.037
3.406
3.378
1.724
3ag
1H NMR (600 MHz, CDCl3)
1.00
1.06
1.06
1.15
9.28
1.99
1.05
2.07
1.09
1.09
3.28
f1 (ppm)

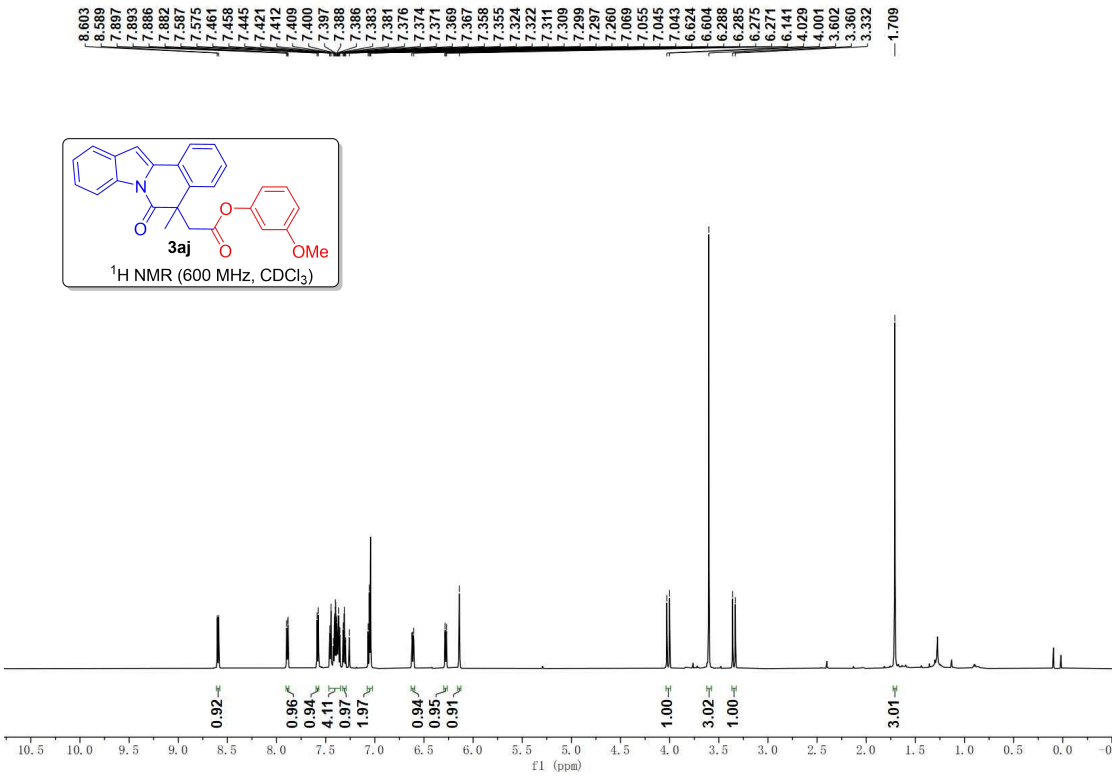

172.25
168.95
149.50
140.23
139.83
137.42
135.47
135.26
130.59
128.94
128.66
127.92
127.51
127.23
126.69
125.31
125.21
124.79
124.51
124.11
121.42
120.46
116.69
103.37
77.21
77.00
76.79
46.47
44.38
30.31
Ph
O
O
N
O
3ag
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

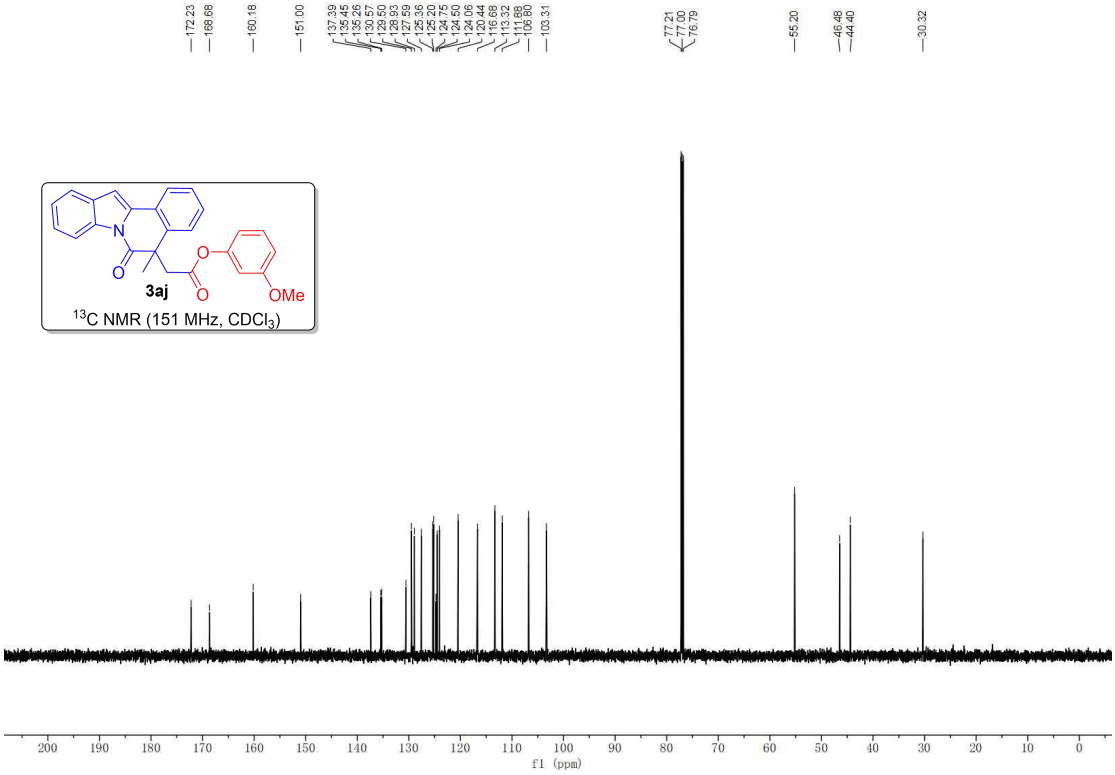

9.880
8.597
8.587
7.917
7.814
7.800
7.795
7.735
7.730
7.720
7.615
7.603
7.458
7.440
7.394
7.351
7.338
7.077
7.072
6.968
6.954
6.872
6.858
4.067
4.038
3.413
3.385
1.743
CHO
O
O
N
O
3ah
1H NMR (600 MHz, CDCl3)
1.00
0.95
0.91
2.38
1.04
4.17
1.01
2.94
0.89
0.93
3.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1
f1 (ppm)

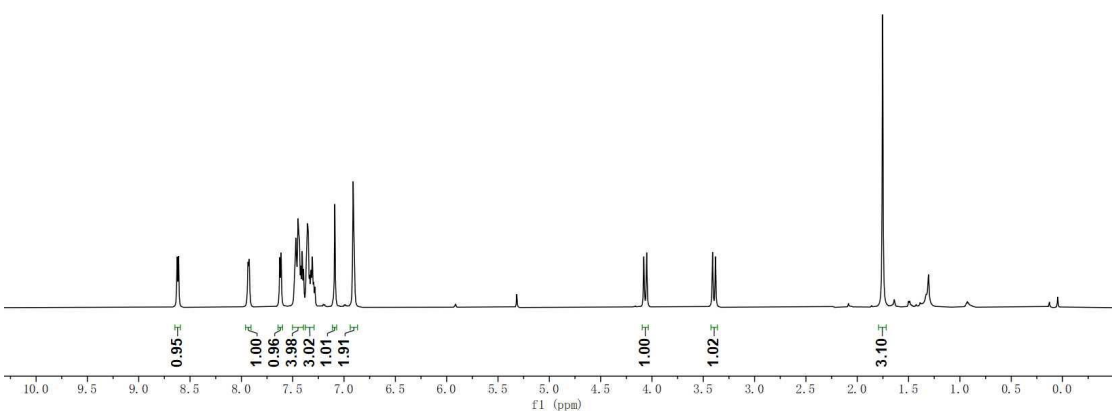

190.77
172.11
168.21
154.74
137.17
135.43
135.13
130.88
130.66
130.58
129.02
127.74
125.33
125.24
124.74
124.64
124.16
121.92
120.55
116.64
115.90
103.53
77.21
77.00
76.79
46.47
44.33
30.28
CHO
O
N
O
O
3ah
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

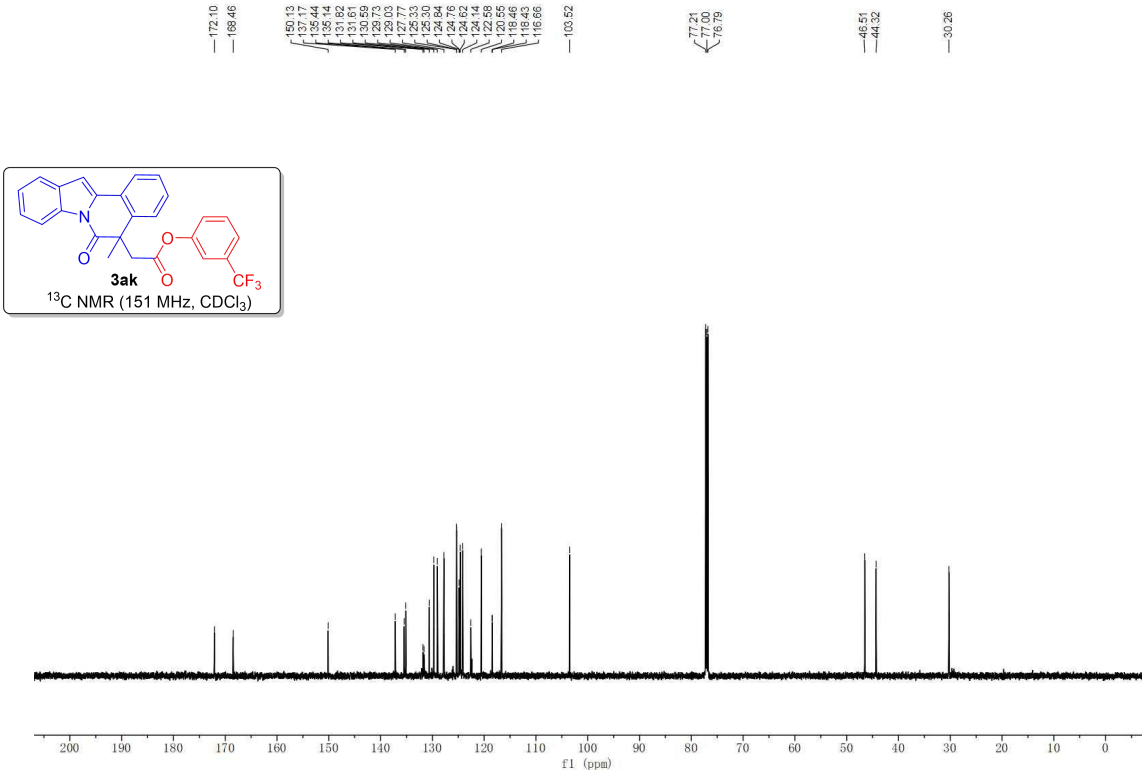

8.589
8.576
7.906
7.899
7.891
7.599
7.586
7.425
7.415
7.391
7.377
7.363
7.333
7.320
7.306
7.260
7.212
7.200
7.059
7.043
7.029
7.016
6.832
6.635
6.617
4.019
3.990
3.363
3.334
1.709
Br
O
N
O
O
3ai
1H NMR (600 MHz, CDCl3)
0.97
1.00
0.98
5.13
0.97
2.21
0.86
0.93
1.00
1.00
2.97
10.5
10.0
9.5
9.0
8.5
8.0
7.5
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
f1 (ppm)

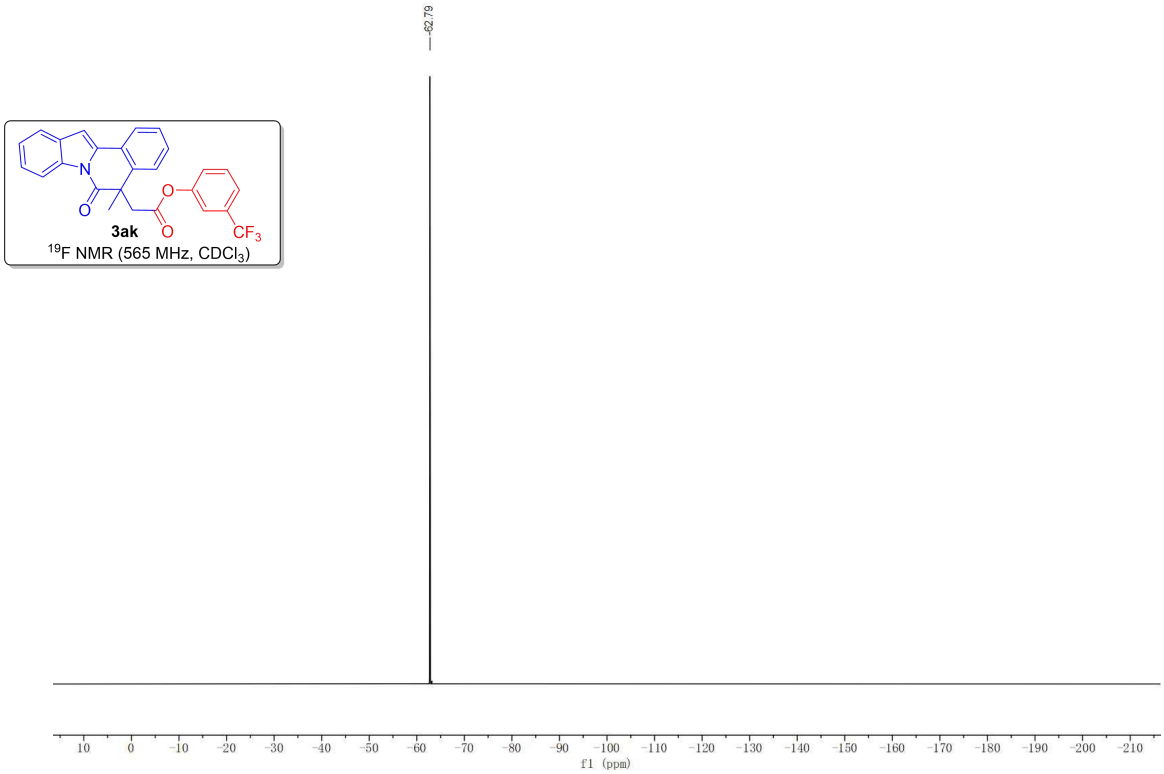

172.16
168.50
150.53
137.21
135.42
135.16
130.58
130.20
129.00
128.95
127.71
125.30
125.23
124.74
124.66
124.59
124.15
122.10
120.52
120.05
115.78
115.66
103.50
77.21
77.00
76.79
46.44
44.24
30.27
3ai
13C NMR (151 MHz, CDCl3)
O
N
O
O
Br
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

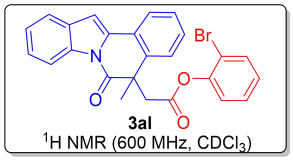

8.603
8.589
7.897
7.893
7.886
7.882
7.587
7.575
7.461
7.458
7.445
7.421
7.412
7.409
7.400
7.397
7.388
7.386
7.383
7.381
7.376
7.374
7.371
7.369
7.367
7.358
7.355
7.324
7.322
7.311
7.309
7.299
7.297
7.260
7.069
7.055
7.045
7.043
6.624
6.604
6.288
6.285
6.275
6.271
6.141
4.029
4.001
3.602
3.360
3.332
1.709
3aj
1H NMR (600 MHz, CDCl3)
O
N
O
O
OMe
0.92
0.96
0.94
4.11
0.97
1.97
0.94
0.95
0.91
1.00
3.02
1.00
3.01
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
f1 (ppm)


172.23
169.68
160.18
151.00
137.39
135.45
135.26
130.57
129.50
128.93
127.53
125.36
125.20
124.75
124.50
124.06
120.44
116.68
113.32
111.85
106.80
103.31
77.21
77.00
76.79
55.20
46.48
44.40
30.32
3aj
13C NMR (151 MHz, CDCl3)
f1 (ppm)

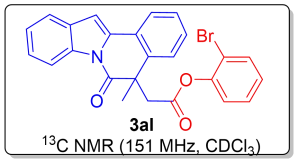

3ak
1H NMR (600 MHz, CDCl3)
0.95
1.00
0.96
3.98
3.02
1.01
1.91
1.00
1.02
3.10
f1 (ppm)


172.10
168.46
150.13
137.17
135.44
135.14
131.82
131.61
130.59
129.73
129.03
127.77
125.33
125.30
124.84
124.75
124.62
124.14
122.58
120.55
118.46
118.43
116.66
103.52
77.21
77.00
76.79
46.51
44.32
30.26
3ak
O
O
O
CF3
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

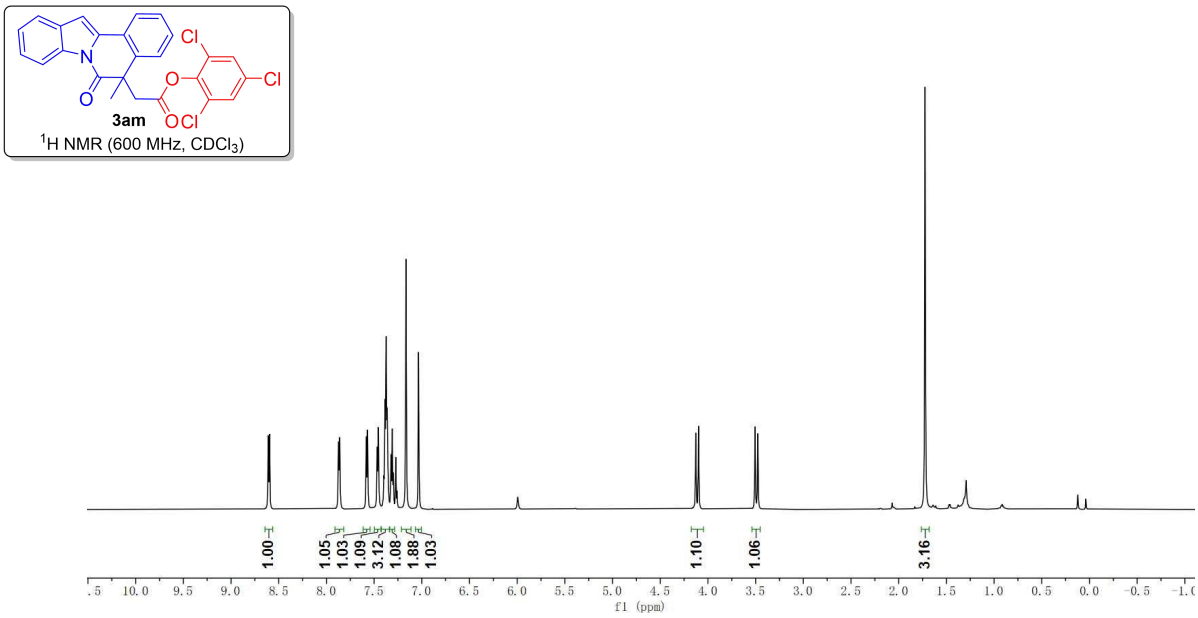

-62.79
3ak
O
O
O
CF3
19F NMR (565 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

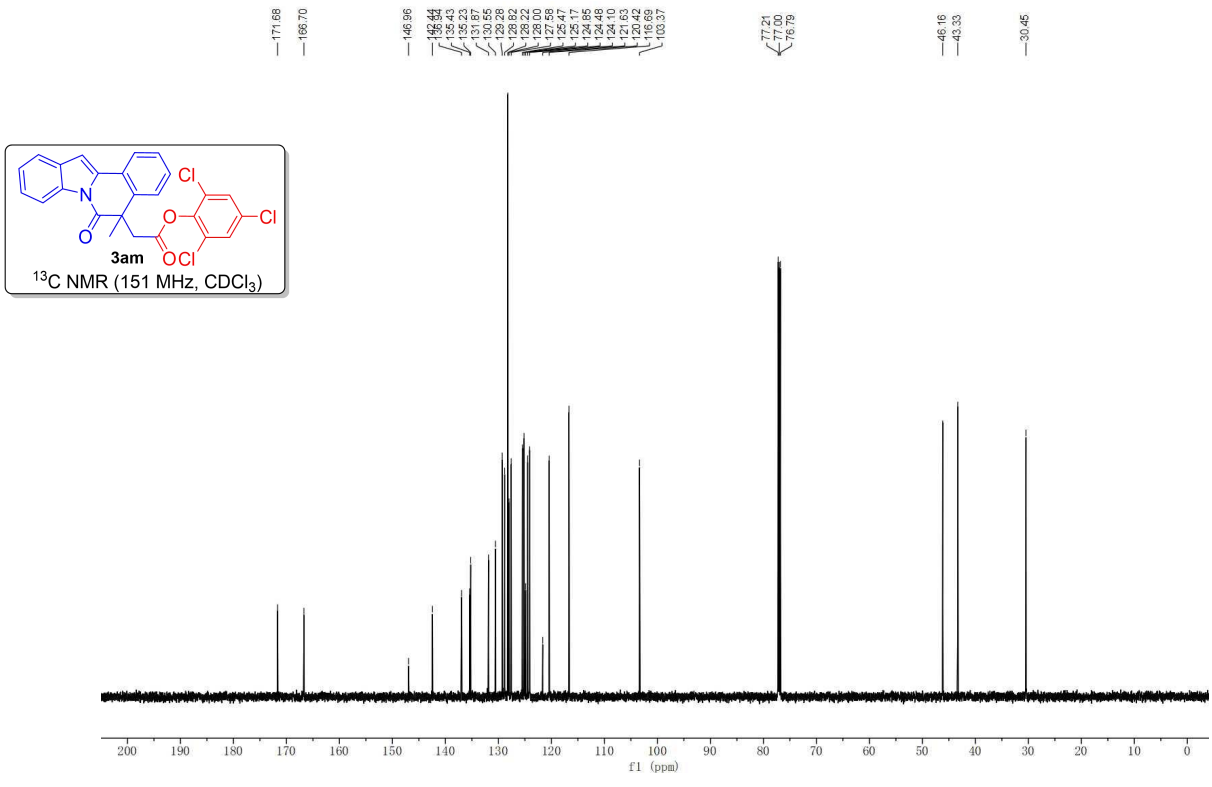

Br
O
N
O
O
3al
1H NMR (600 MHz, CDCl3)

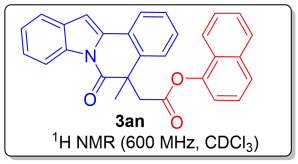
8.588
8.575
7.882
7.880
7.869
7.867
7.575
7.563
7.488
7.473
7.421
7.410
7.398
7.385
7.371
7.359
7.344
7.311
7.299
7.285
7.260
7.141
7.129
7.118
7.031
6.976
6.963
6.950
6.776
6.762
4.074
4.045
3.486
3.457
1.718
0.96
1.03
1.00
1.02
4.08
1.01
0.99
1.01
0.97
0.96
1.00
1.00
3.02
f1 (ppm)


Br
O
N
O
O
3al
13C NMR (151 MHz, CDCl3)

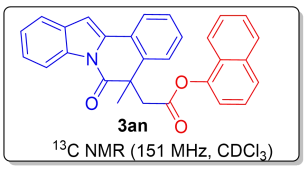
172.08
168.12
147.77
137.30
135.48
135.33
133.11
130.60
128.85
128.71
127.56
127.24
125.51
125.15
124.89
124.46
124.11
120.43
120.42
116.70
115.93
103.32
77.21
77.00
76.79
46.26
43.90
30.36
f1 (ppm)


8.610
8.596
7.873
7.862
7.859
7.581
7.569
7.469
7.466
7.455
7.399
7.386
7.374
7.365
7.361
7.352
7.310
7.260
7.166
7.034
4.127
4.098
3.506
3.477
1.724
3am
1H NMR (600 MHz, CDCl3)
1.00
1.05
1.03
1.09
3.12
1.08
1.88
1.03
1.10
1.06
3.16
f1 (ppm)

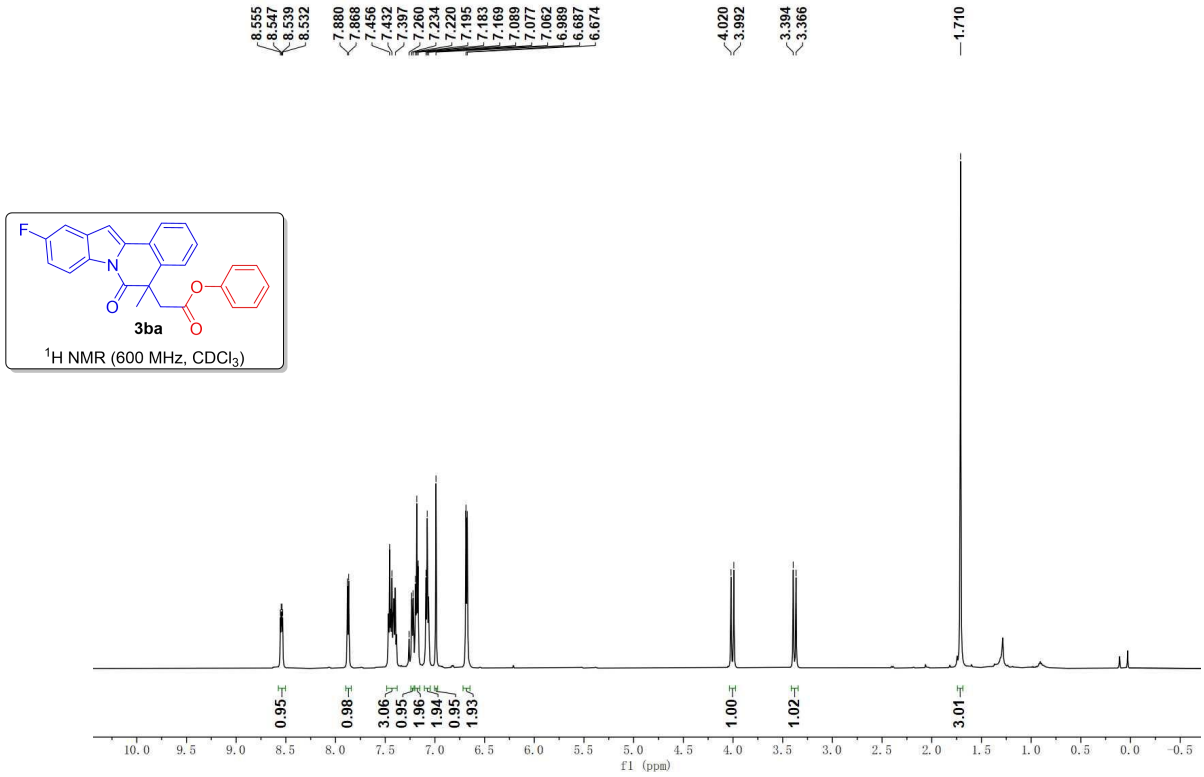

171.68
166.70
146.96
142.44
136.94
135.43
133.23
131.67
130.55
129.28
128.82
128.22
128.00
127.58
125.47
125.17
124.85
124.48
124.10
121.63
120.42
116.69
103.37
77.21
77.00
76.79
46.16
43.33
30.45
3am
13C NMR (151 MHz, CDCl3)
f1 (ppm)

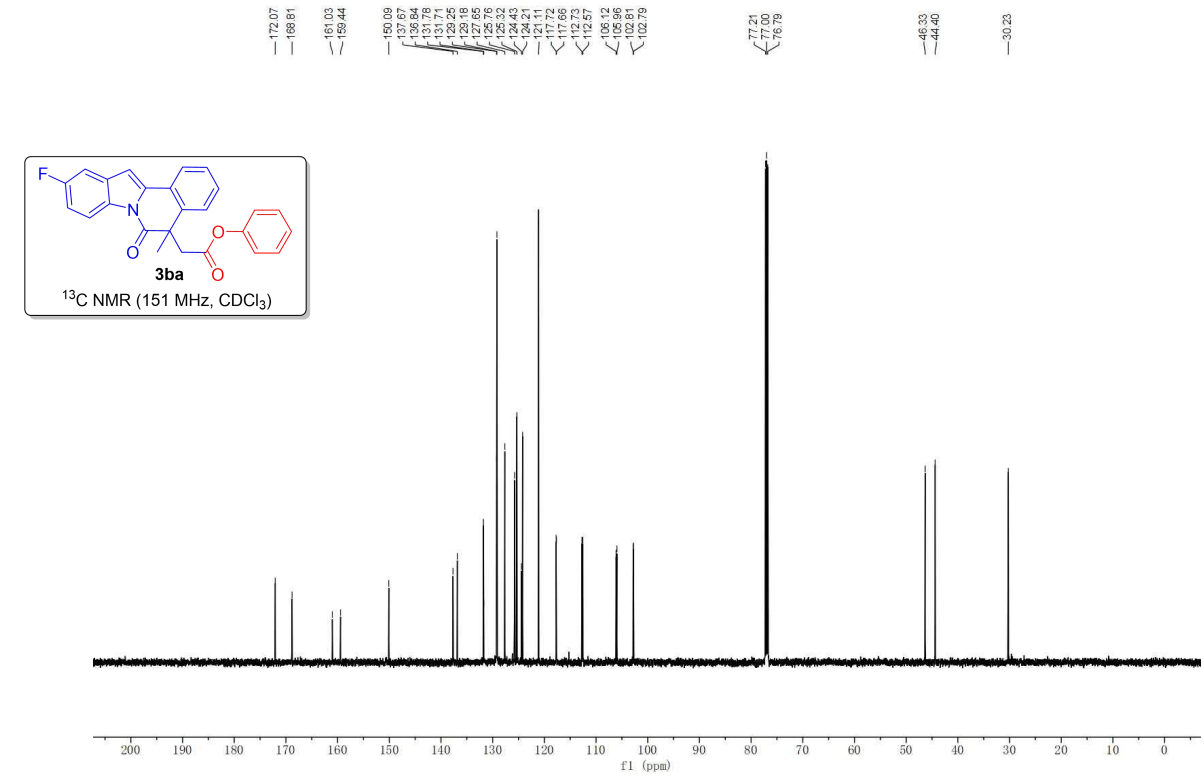

3an
^{1}H NMR (600 MHz, $CDCl_3$)

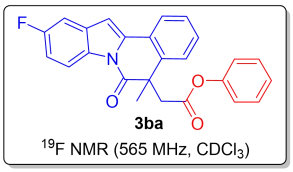
8.614
8.600
7.910
7.898
7.714
7.699
7.644
7.629
7.611
7.598
7.580
7.567
7.494
7.482
7.450
7.438
7.424
7.412
7.380
7.317
7.305
7.292
7.260
7.132
7.044
6.791
6.772
4.089
4.060
3.430
3.402
1.738
0.93
0.96
1.02
2.98
7.11
0.93
0.92
0.92
1.00
1.01
3.03
f1 (ppm)


3an
^{13}C NMR (151 MHz, $CDCl_3$)

172.26
168.97
147.76
137.48
135.49
135.29
133.45
131.30
130.60
129.14
128.88
127.82
127.56
127.53
126.36
125.58
125.36
125.23
124.84
124.51
124.14
120.58
120.46
118.18
116.70
103.37
77.21
77.00
76.79
46.52
44.50
30.32
f1 (ppm)

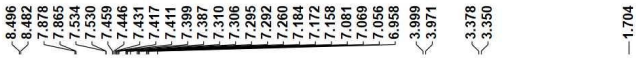

8.555
8.547
8.539
8.532
7.880
7.868
7.456
7.432
7.397
7.260
7.234
7.220
7.195
7.183
7.169
7.089
7.077
7.062
6.989
6.687
6.674
4.020
3.992
3.394
3.366
1.710
F
N
O
O
O
3ba
1H NMR (600 MHz, CDCl3)
0.95
0.98
3.06
0.95
1.96
1.94
0.95
1.93
1.00
1.02
3.01
f1 (ppm)

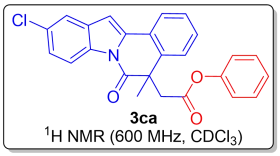

172.07
168.81
161.03
159.44
150.09
137.67
136.84
131.78
131.71
129.25
129.18
127.65
125.76
125.32
124.43
124.21
123.11
117.72
117.66
112.73
112.57
106.12
105.96
102.81
102.79
77.21
77.00
76.79
46.33
44.40
30.23
F
N
O
O
O
3ba
13C NMR (151 MHz, CDCl3)
f1 (ppm)



3ba

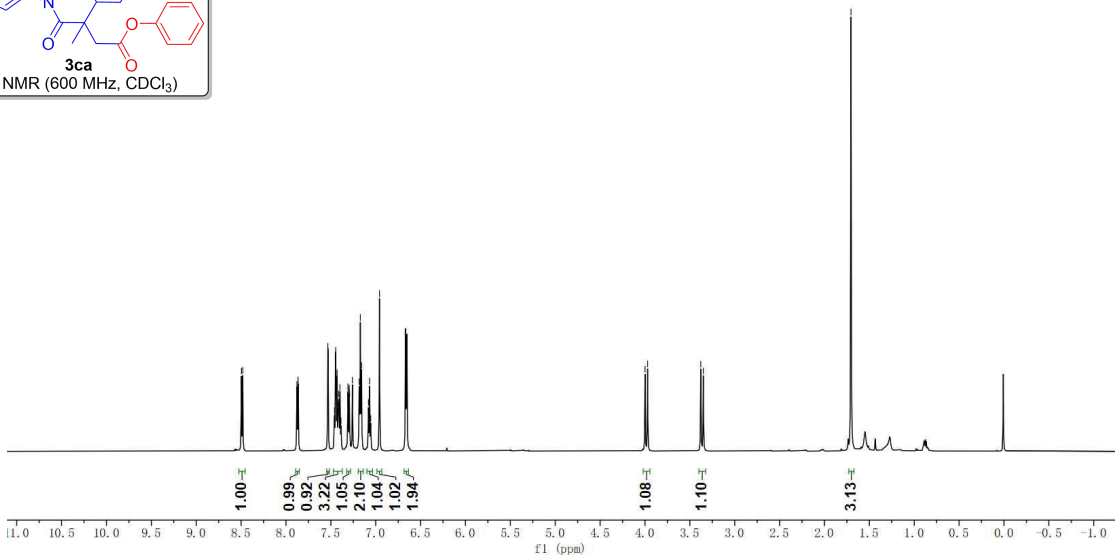
^{19}F NMR (565 MHz, $CDCl_3$)

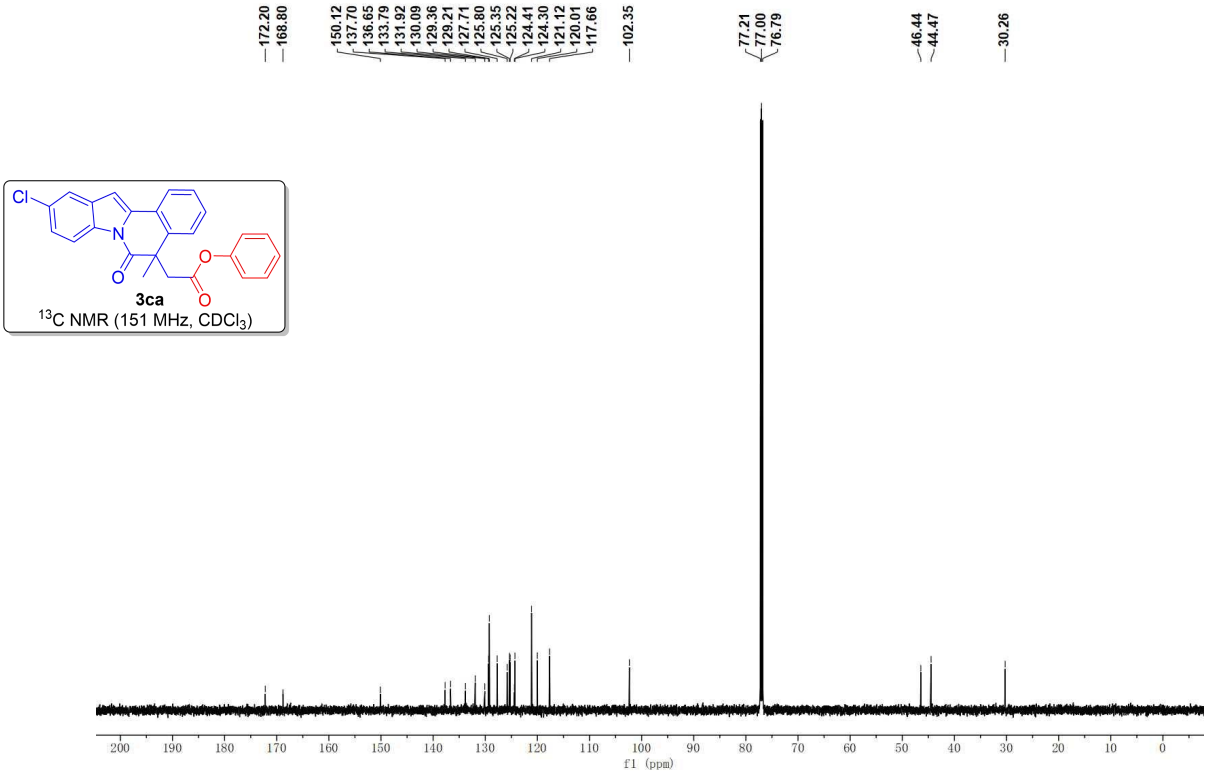


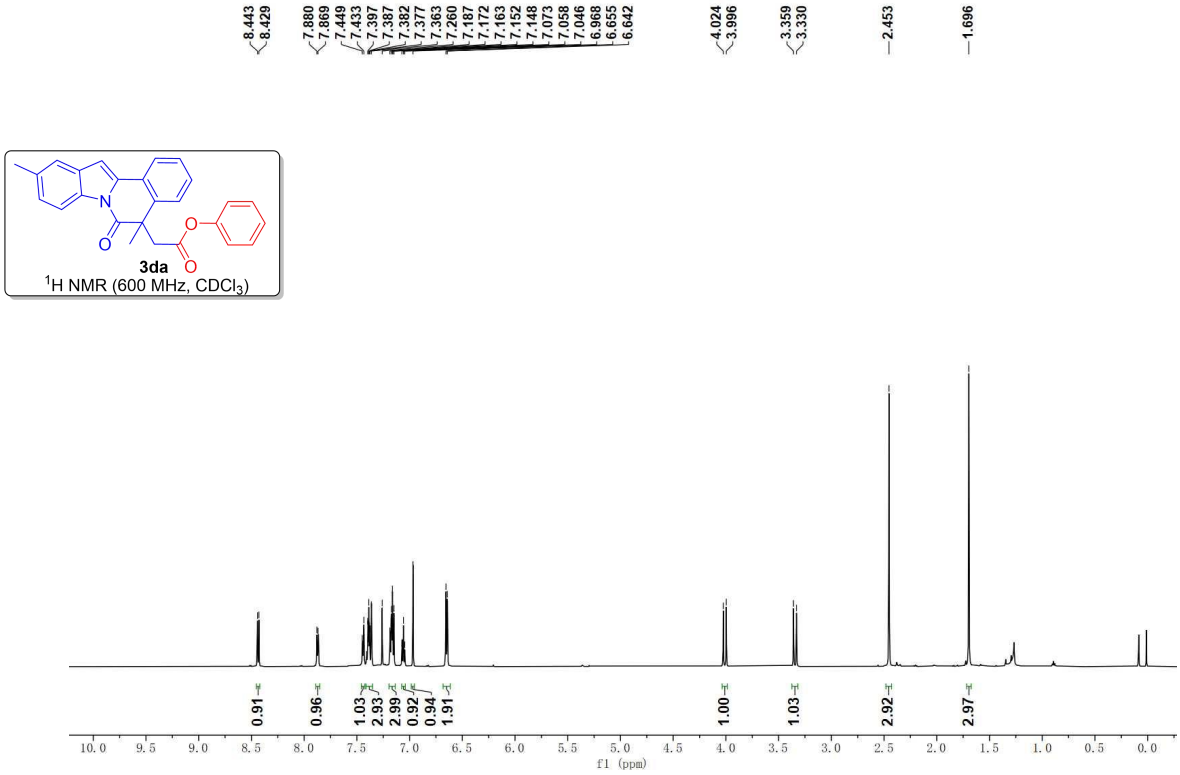


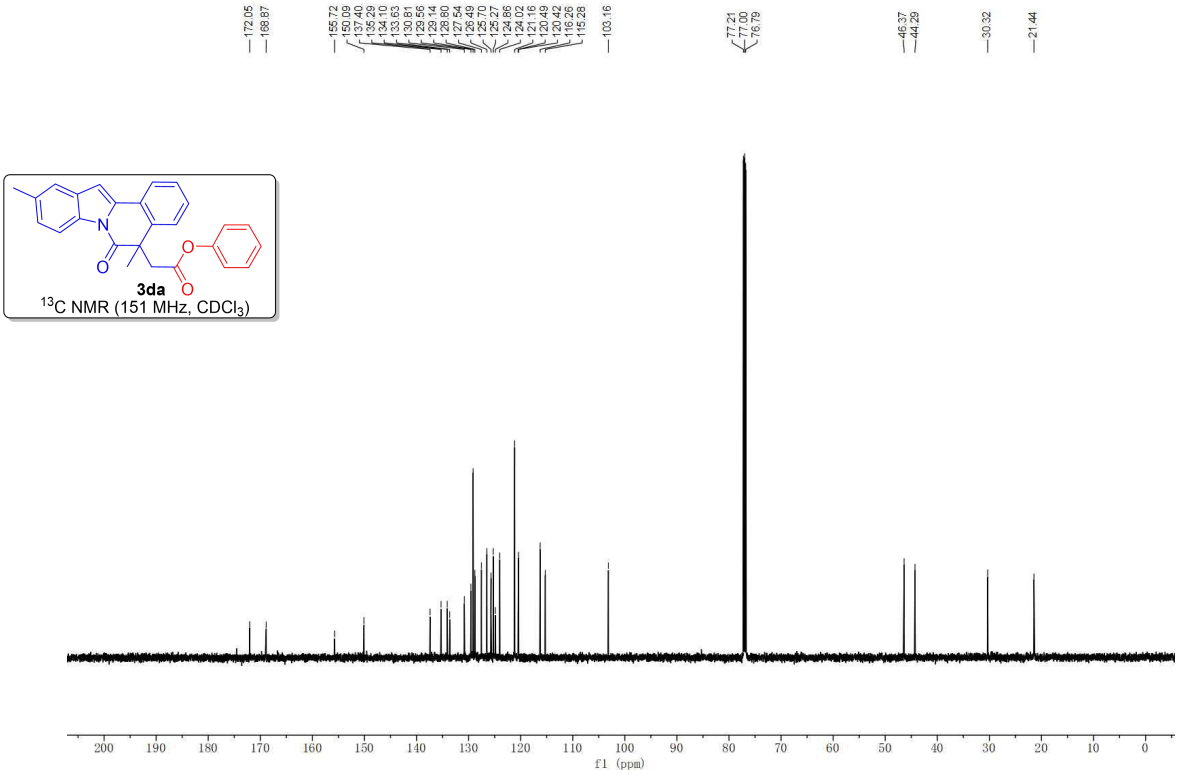
3ca

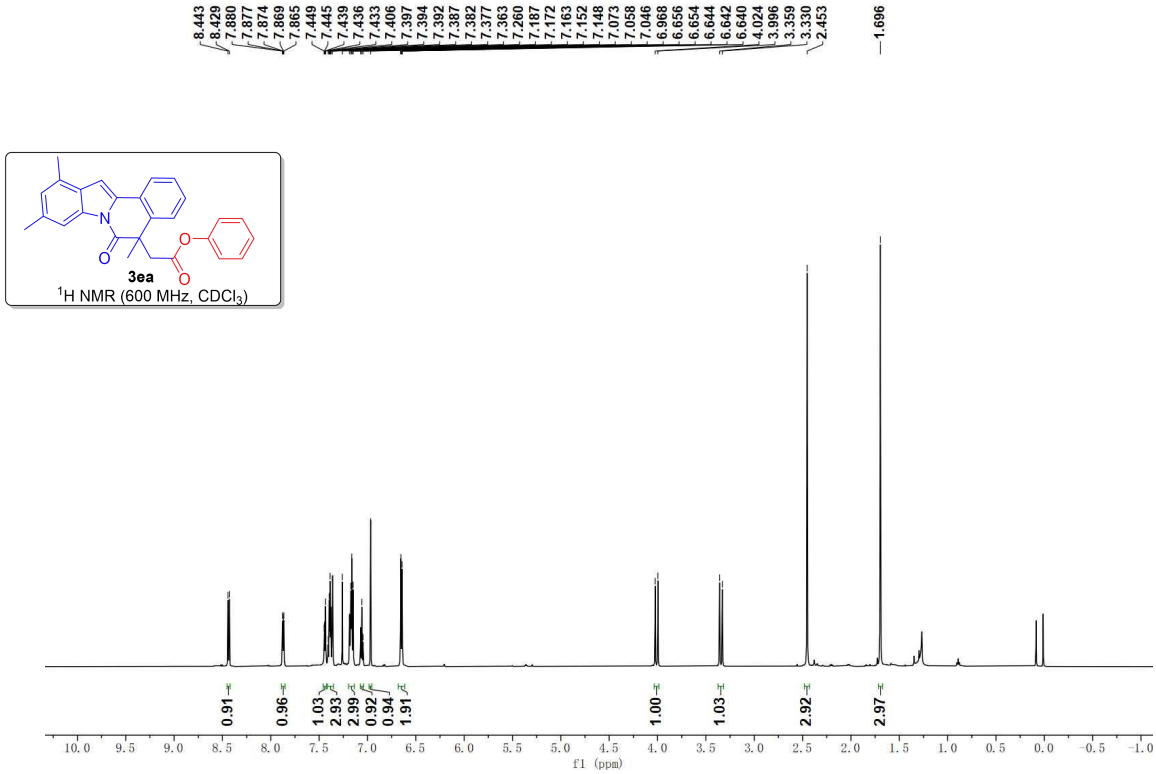
^{1}H NMR (600 MHz, $CDCl_3$)



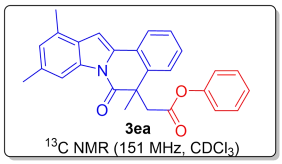

172.20
168.80
150.12
137.70
136.65
133.79
131.92
130.09
129.36
129.21
127.71
125.80
125.35
125.22
124.41
124.30
121.12
120.01
117.66
102.35
77.21
77.00
76.79
46.44
44.47
30.26
Cl
N
O
O
O
3ca
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

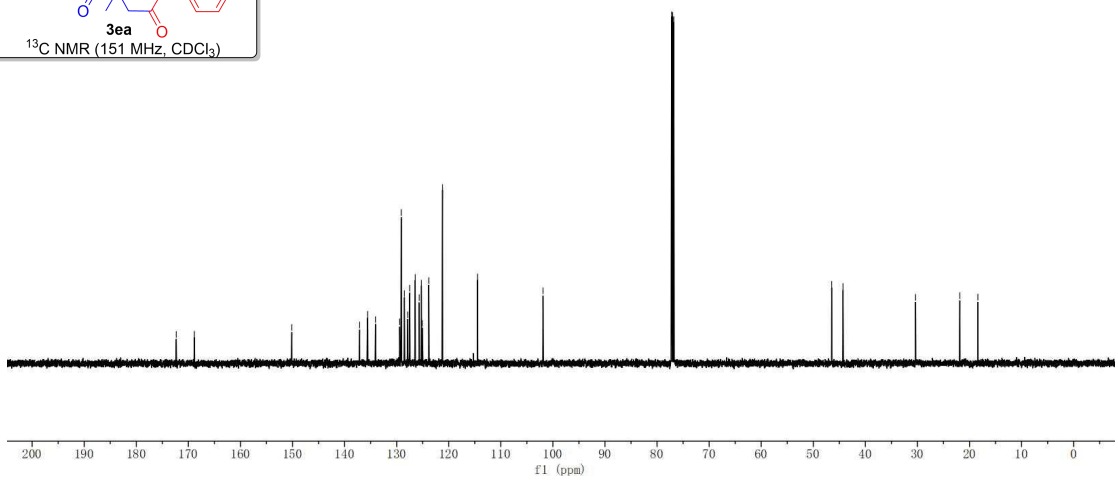

8.443
8.429
7.880
7.869
7.449
7.433
7.397
7.387
7.382
7.377
7.363
7.260
7.187
7.172
7.163
7.152
7.148
7.073
7.058
7.046
6.968
6.655
6.642
4.024
3.996
3.359
3.330
2.453
1.696
N
O
O
O
3da
1H NMR (600 MHz, CDCl3)
0.91
0.96
1.03
2.93
2.99
0.92
0.94
1.91
1.00
1.03
2.92
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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
f1 (ppm)


172.05
168.87
155.72
150.09
137.40
135.29
134.10
133.63
130.81
129.56
129.14
128.80
127.54
126.49
125.70
125.27
124.86
124.02
121.16
120.49
120.42
115.26
115.28
103.16
77.21
77.00
76.79
46.37
44.29
30.32
21.44
3da
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

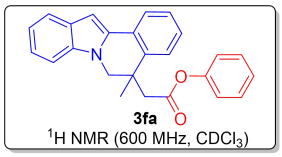

8.443
8.429
7.880
7.877
7.874
7.869
7.865
7.449
7.445
7.439
7.436
7.433
7.406
7.397
7.394
7.392
7.387
7.382
7.377
7.363
7.260
7.187
7.172
7.163
7.152
7.148
7.073
7.058
7.046
6.968
6.656
6.654
6.644
6.642
6.640
4.024
3.996
3.359
3.330
2.453
1.696
3ea
1H NMR (600 MHz, CDCl3)
0.91
0.96
1.03
2.93
2.99
0.92
0.94
1.91
1.00
1.03
2.92
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)


172.33
168.84
150.13
137.10
135.65
135.57
134.07
129.42
129.12
128.51
127.86
127.50
126.44
125.67
125.25
125.09
123.83
121.19
114.46
101.90
77.21
77.00
76.79
46.47
44.29
30.35
21.86
18.39

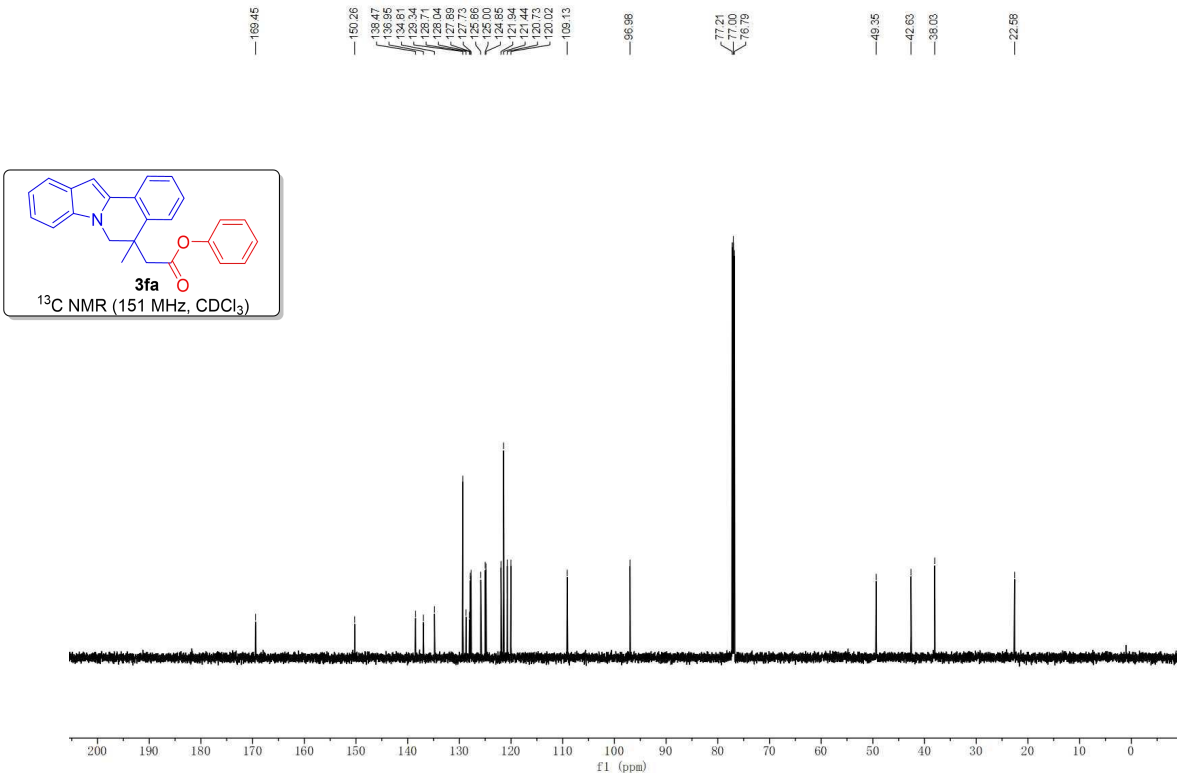

3ea
13C NMR (151 MHz, CDCl3)

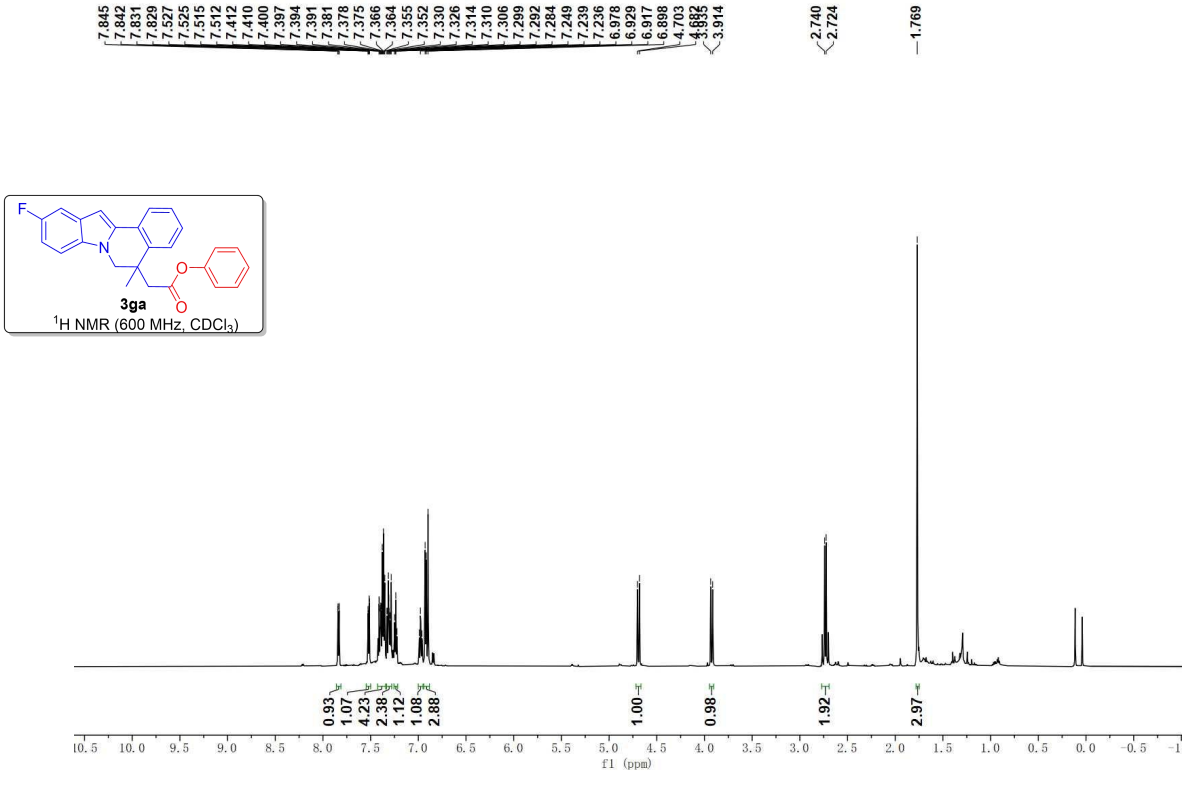

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

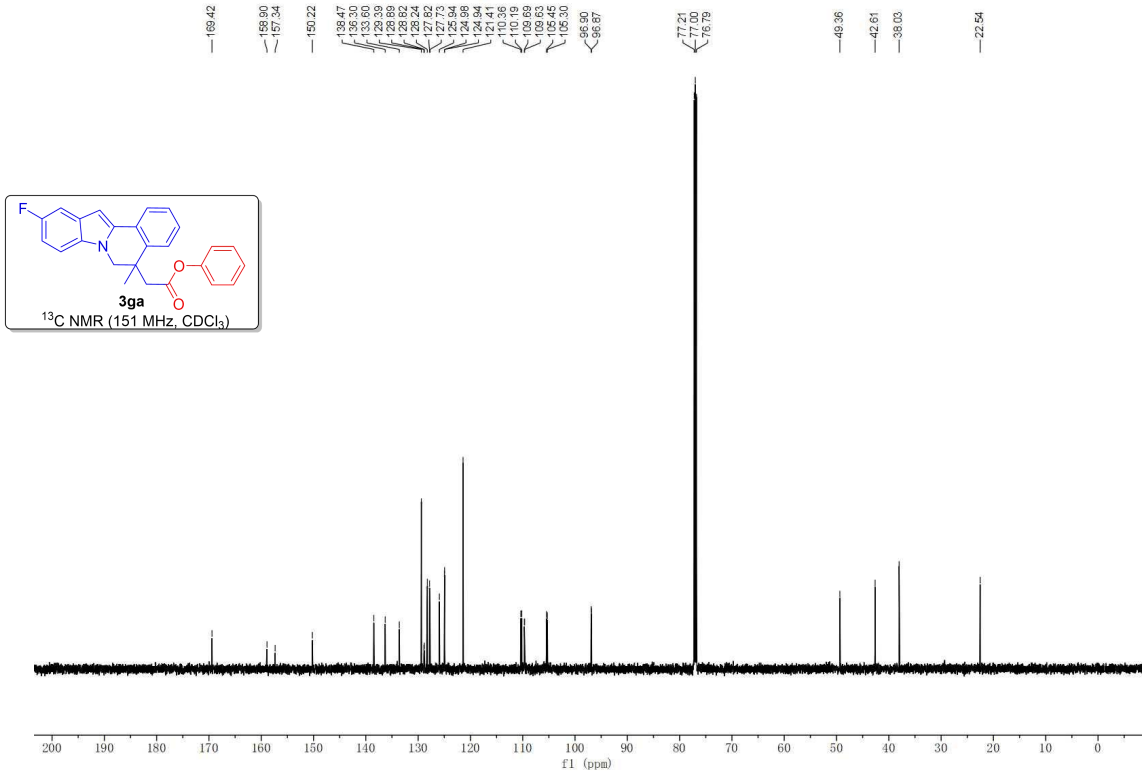

7.877
7.875
7.865
7.862
7.709
7.696
7.531
7.518
7.427
7.414
7.412
7.401
7.399
7.385
7.383
7.380
7.373
7.370
7.368
7.366
7.360
7.357
7.354
7.284
7.266
7.253
7.239
7.177
7.164
6.964
6.937
6.935
6.924
6.922
6.921
4.740
4.719
3.967
3.947
2.788
2.764
2.749
2.724
1.784

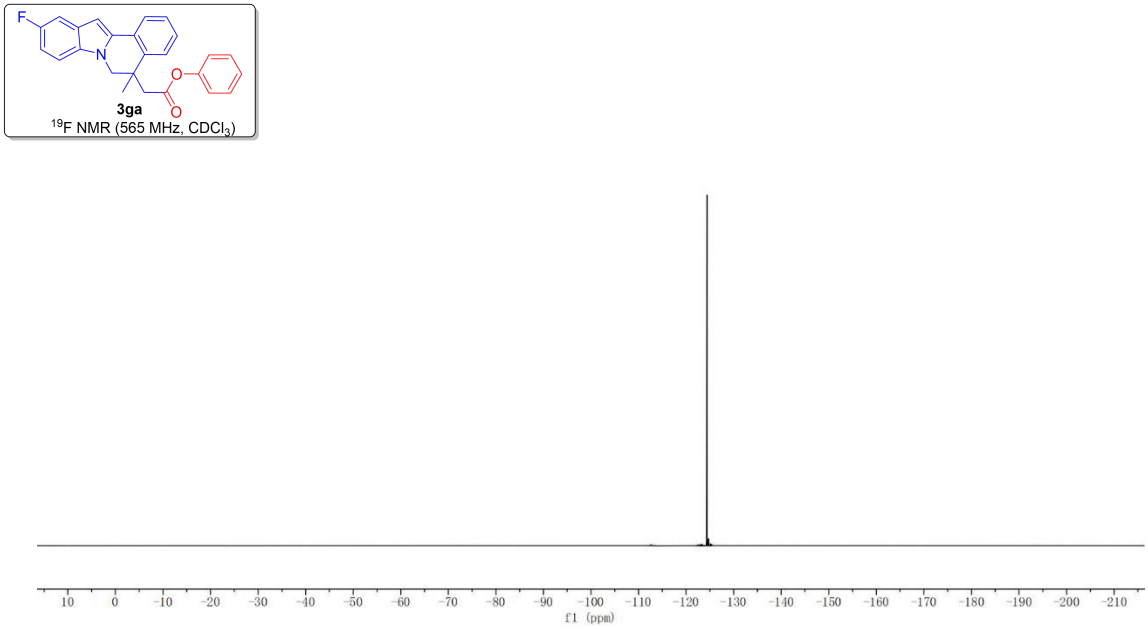

3fa
1H NMR (600 MHz, CDCl3)

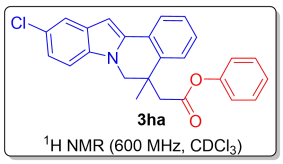
0.92
0.95
1.00
5.09
1.95
1.01
0.94
1.92
1.00
0.97
2.01
3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


169.45
150.26
138.47
135.95
134.81
129.34
128.71
128.04
127.89
127.73
125.86
125.00
124.85
121.94
121.44
120.73
120.02
109.13
96.98
77.21
77.00
76.79
49.35
42.63
38.03
22.58
3fa
13C NMR (151 MHz, CDCl3)
f1 (ppm)

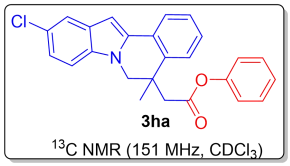

7.845
7.842
7.831
7.829
7.527
7.525
7.515
7.512
7.412
7.410
7.400
7.397
7.394
7.391
7.381
7.378
7.375
7.366
7.364
7.355
7.352
7.330
7.326
7.314
7.310
7.306
7.299
7.292
7.284
7.249
7.239
7.236
6.978
6.929
6.917
6.898
4.703
3.935
3.914
2.740
2.724
1.769
3ga
1H NMR (600 MHz, CDCl3)
0.93
1.07
4.23
2.38
1.12
1.08
2.88
1.00
0.98
1.92
2.97
f1 (ppm)


169.42
158.90
157.34
150.22
138.47
136.00
133.60
129.39
128.89
128.82
128.24
127.82
127.73
125.94
125.88
124.94
121.41
110.36
110.19
109.69
109.63
105.45
105.30
96.90
96.87
77.21
77.00
76.79
49.36
42.61
38.03
22.54
F
N
O
O
3ga
13C NMR (151 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

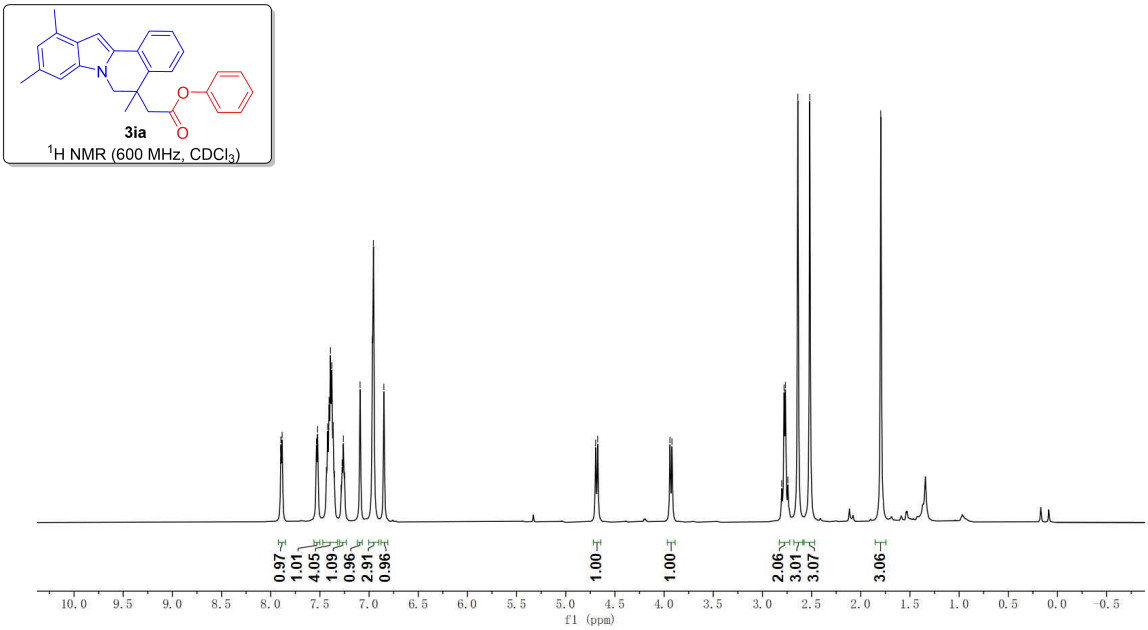

124.38
F
N
O
O
3ga
19F NMR (565 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

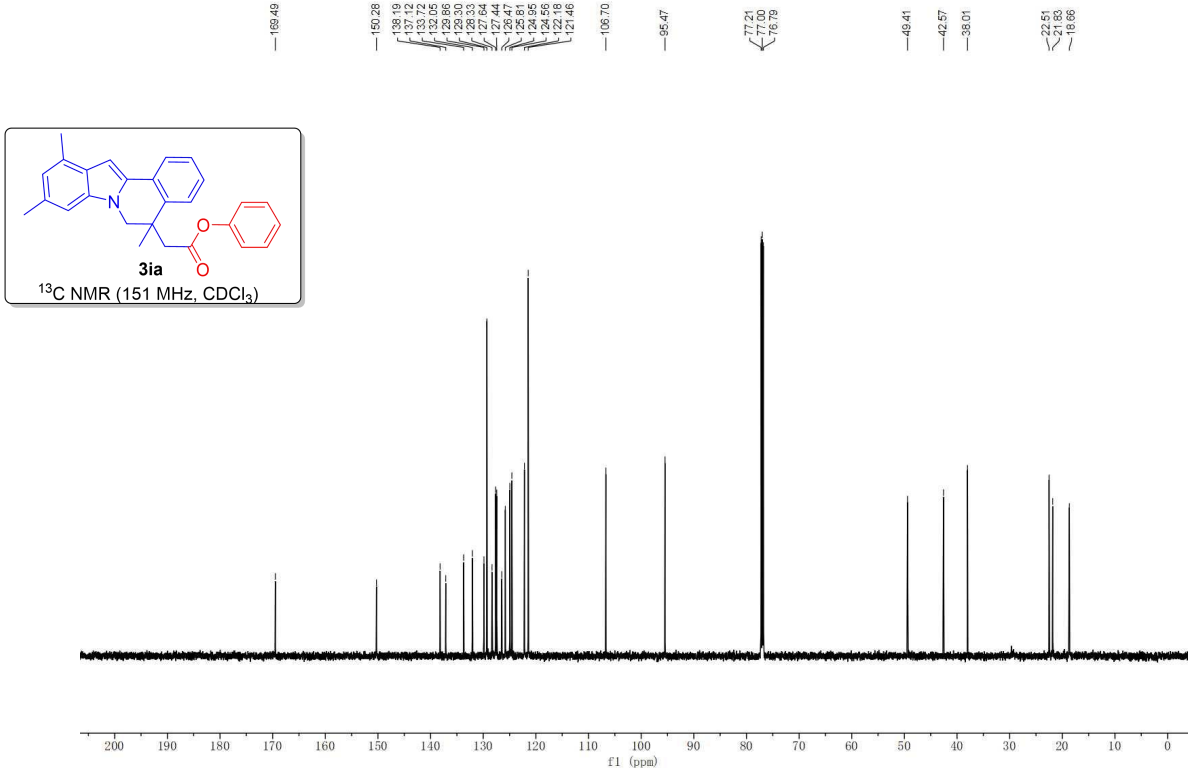


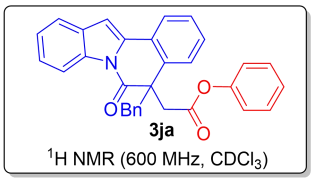
^{1}H NMR (600 MHz, $CDCl_3$)



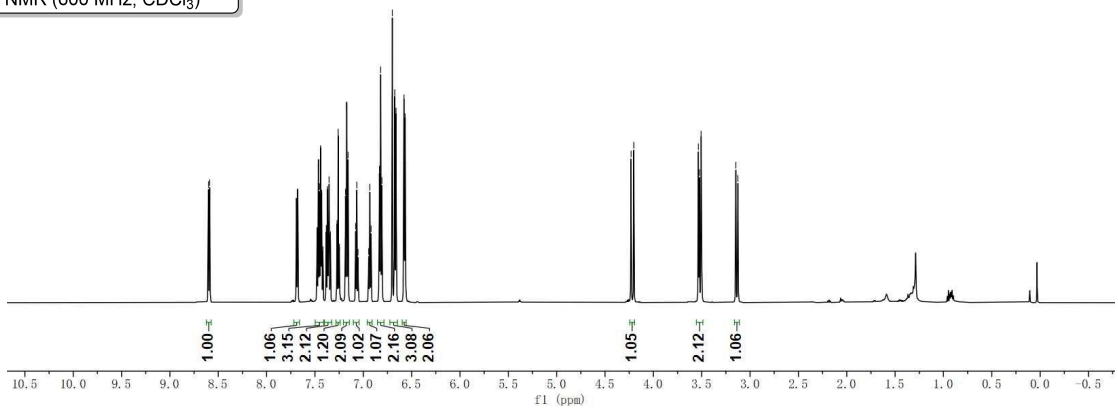
^{13}C NMR (151 MHz, $CDCl_3$)

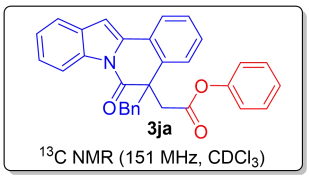

7.896
7.884
7.536
7.523
7.434
7.422
7.407
7.392
7.379
7.365
7.353
7.284
7.274
7.261
7.249
7.092
6.966
6.956
6.850
4.696
4.676
3.941
3.920
2.804
2.780
2.766
2.741
2.640
2.519
1.797
3ia
1H NMR (600 MHz, CDCl3)
0.97
1.01
4.05
1.09
0.96
2.91
0.96
1.00
1.00
2.06
3.01
3.07
3.06
f1 (ppm)


169.49
150.28
138.19
137.12
133.72
132.05
129.86
129.30
128.83
127.74
127.44
126.47
125.81
124.95
124.56
122.18
121.46
106.70
95.47
77.21
77.00
76.79
49.41
42.57
38.01
22.51
21.83
18.66
3ia
13C NMR (151 MHz, CDCl3)
f1 (ppm)

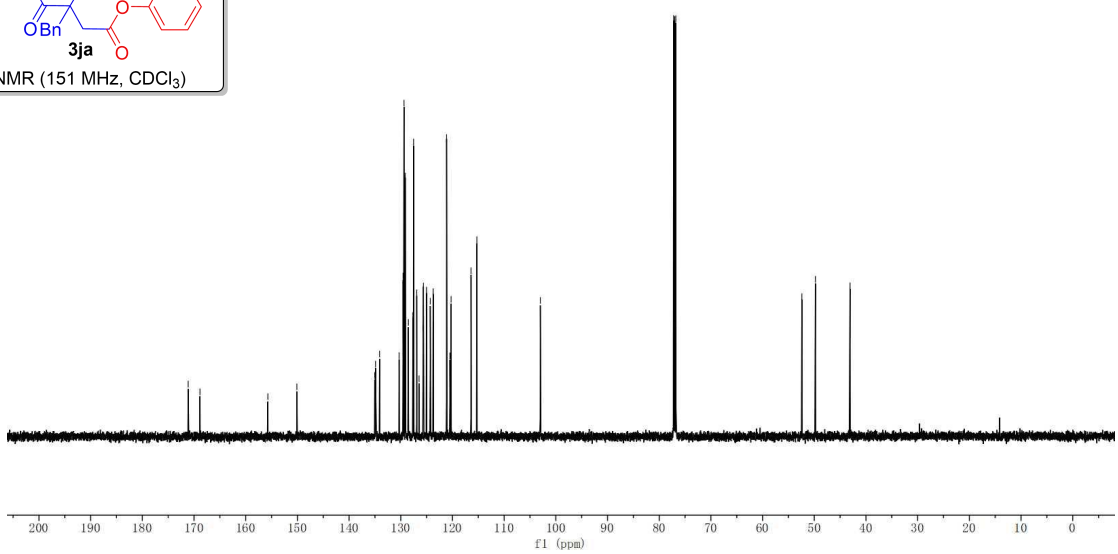


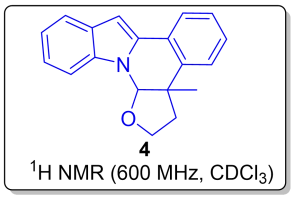
^{1}H NMR (600 MHz, $CDCl_3$)





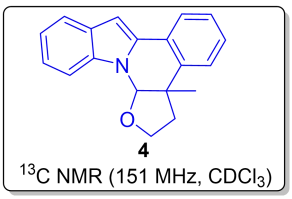
^{13}C NMR (151 MHz, $CDCl_3$)





4

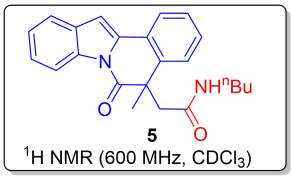
^{1}H NMR (600 MHz, $CDCl_3$)

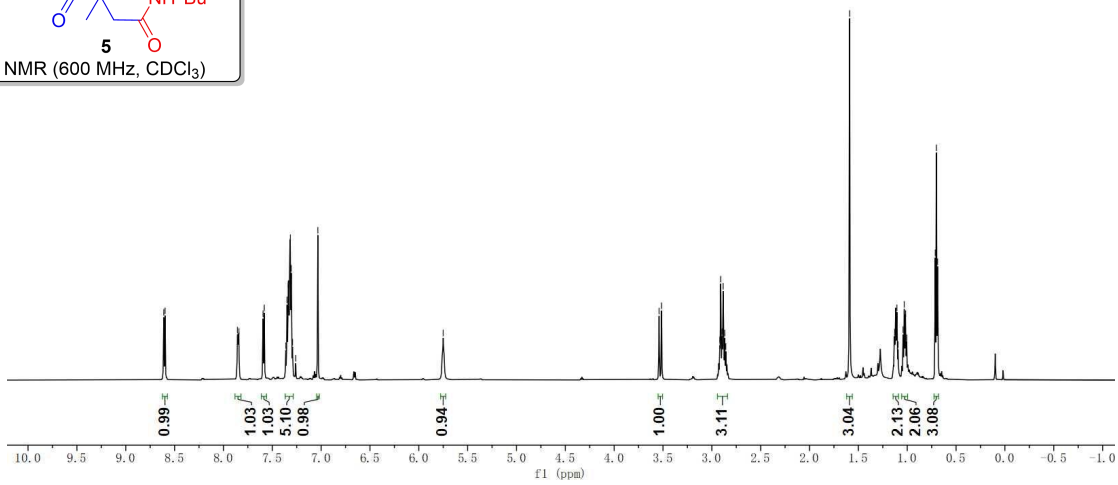


4

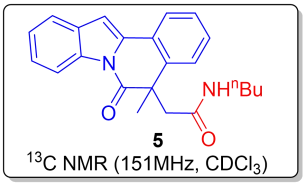
^{13}C NMR (151 MHz, $CDCl_3$)

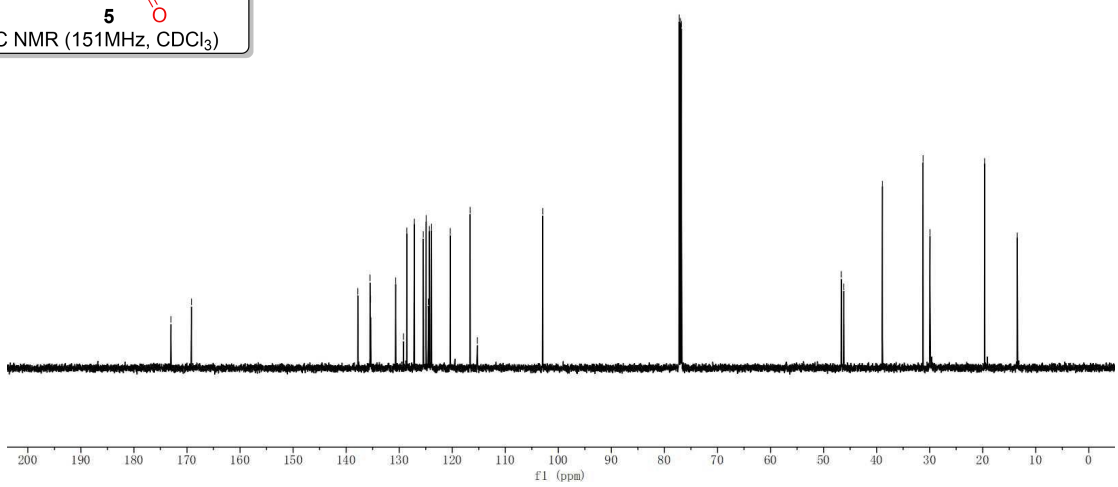

8.611
8.597
7.857
7.841
7.595
7.582
7.361
7.349
7.337
7.315
7.306
7.293
7.260
7.034
5.751
3.540
3.515
2.918
2.910
2.896
2.884
2.868
2.857
1.590
1.129
1.121
1.105
1.094
1.043
1.031
1.016
1.005
0.713
0.701
0.689


NH^{n}Bu
O
O
5
^{1}H NMR (600 MHz, CDCl$_3$)


0.99
1.03
1.03
5.10
0.98
0.94
1.00
3.11
3.04
2.13
2.06
3.08
f1 (ppm)


173.03
169.17
137.80
135.50
135.39
130.66
129.19
128.57
127.44
125.46
124.91
124.51
124.31
123.90
120.37
116.63
115.28
102.95
77.21
77.00
76.79
46.67
46.19
38.91
31.24
29.94
19.65
13.49


NH^{n}Bu
O
O
5
^{13}C NMR (151MHz, CDCl$_3$)


f1 (ppm)