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Atom-economic metal free mediated difunctionalization of isocyanides with 3-methyleneoxindoles and 3-methylenebenofuranones

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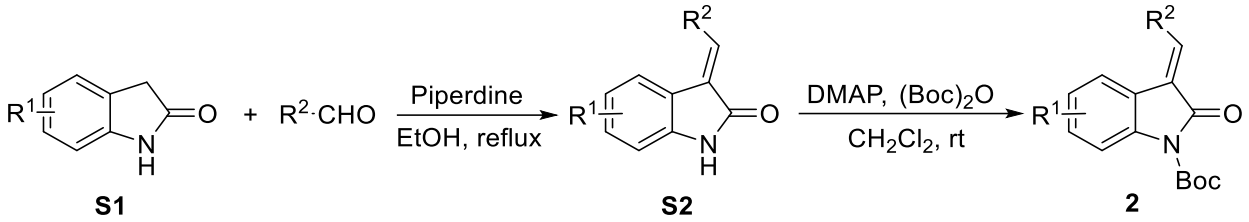
1. General Information

Reactions were carried out using commercial reagents in over-dried apparatus. ^{1}H NMR spectra were recorded on commercial instruments (400 MHz and 600 MHz). Chemical shifts are recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26 ppm; DMSO-d_6, δ = 2.50 ppm). Spectra are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR data were collected on commercial instruments (101 MHz and 151 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0; DMSO-d_6, δ = 39.5 ppm). ^{19}F NMR data were collected on commercial instruments (565 MHz) with complete proton decoupling. Melting points (m.p.) were measured on the electrothermal digital melting point apparatus. HRMS was recorded on a commercial apparatus (ESI source). All isocyanides **1**,[1] 3-methyleneoxindoles **2**[2] and 3-methylene-benofuranones **4**[3] were prepared according to the literature.

2. Preparing of 3-methyleneoxindoles 2.



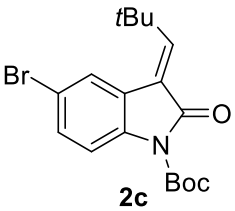
S1 S2 2

S1 to S2: The aldehyde (1.2 equiv.) was added to a solution of **S1** (1.0 equiv., 133 mg) in EtOH (5 mL), finally piperidine (10 mol%) was added. The reaction was refluxed for 24 h, then it was cooled to room temperature and the solvent was removed under reduced pressure. The product **S2** was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4/1).

S2 to 2: The **S2** was dissolved in CH_2Cl_2 (5 mL), and DMAP (5 mol%) was added. Then $(Boc)_2O$ (1.1 equiv.) was added. The reaction mixture was stirred at room temperature for 1 h. After the reaction was completed, the solvent was removed under reduced pressure and the product **2** was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30/1).

3-methyleneoxindoles **2a**,[2b] **2b**,[2b] **2h**,[2a] 2**i**,[2d] **2l,**[2e] **2m**,[2c] **2o**[2a] and **2p**[2a] are known compounds.

Tert-butyl (*E*)-5-bromo-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2c



2c

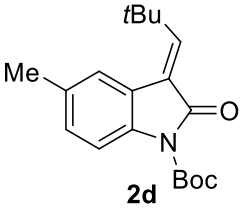
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 60–62 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.79 (m, 2H), 7.42 (dt, *J* = 8.8, 2.0 Hz, 1H), 7.27 (d, *J* = 1.8 Hz, 1H), 1.62 (s, 9H), 1.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 156.0, 149.1, 139.0, 131.6, 128.7, 124.6, 122.8, 116.7, 116.5, 84.3, 32.9, 29.1, 28.0.

HRMS (ESI–TOF) calcd for $C_{18}H_{22}BrNNaO_3^+$ ([M+Na^+]) = 402.0675, Found 402.0671.

Tert-butyl (*E*)-3-(2,2-dimethylpropylidene)-5-methyl-2-oxoindoline-1 carboxylate 2d



2d

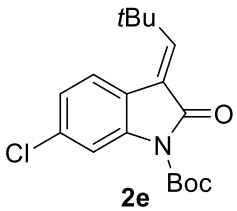
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 62–64 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.26 (s, 1H), 7.16 (dd, *J* = 8.3, 1.8 Hz, 1H), 2.43 (s, 3H), 1.69 (s, 9H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 153.8, 149.4, 137.9, 132.9, 129.5, 126.6, 125.7, 121.0, 114.7, 83.7, 32.6, 29.1, 28.1, 21.2.

HRMS (ESI–TOF) calcd for $C_{19}H_{25}NNaO_3^+$ ([M+Na^+]) = 338.1727, Found 338.1722.

Tert-butyl (*E*)-6-chloro-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2e



2e

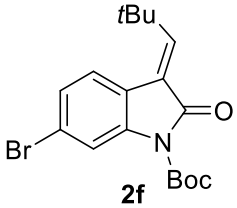
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 105–107 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.1 Hz, 1H), 7.65 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.25 (s, 1H), 7.16 (dt, *J* = 8.3, 2.1 Hz, 1H), 1.65 (s, 9H), 1.38 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 154.8, 149.1, 140.9, 135.0, 126.6, 124.7, 123.7, 119.4, 115.7, 84.5, 32.8, 29.1, 28.0.

HRMS (ESI–TOF) calcd for $C_{18}H_{22}ClNNaO_3^+$ ([M+Na$^+$]) = 358.1180, Found 358.1178.

Tert-butyl (*E*)-6-bromo-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2f



2f

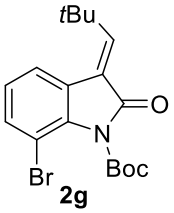
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 128–129 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 1.8 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.33 (dt, *J* = 8.3, 1.3 Hz, 1H), 7.28 (s, 1H), 1.66 (s, 9H), 1.39 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 155.1, 149.1, 141.0, 126.9, 126.7, 124.8, 123.1, 119.9, 118.5, 84.5, 32.9, 29.1, 28.1.

HRMS (ESI–TOF) calcd for $C_{18}H_{22}BrNNaO_3^+$ ([M+Na$^+$]) = 402.0675, Found 402.0673.

Tert-butyl (*E*)-7-bromo-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2g



2g

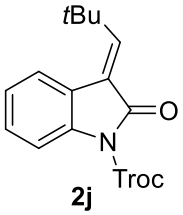
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 51–52 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.25 (s, 1H), 7.02 (t, *J* = 8.0 Hz, 1H), 1.64 (s, 9H), 1.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 156.0, 148.3, 139.1, 133.6, 125.4, 125.1, 124.5, 124.2, 106.9, 85.2, 32.9, 29.1, 27.7.

HRMS (ESI–TOF) calcd for $C_{18}H_{23}BrNO_3^+$ ([M+H$^+$]) = 380.0856, Found 380.0854.

2,2,2-trichloroethyl (*E*)-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2j



2j

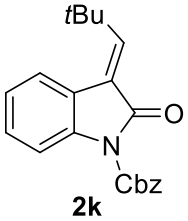
White solid. R_f = 0.4 (PE:EA = 30:1), m.p. 77–78 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.80 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.27 – 7.21 (m, 1H), 5.05 (s, 2H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 155.4, 149.4, 138.9, 129.2, 126.2, 124.9, 124.4, 121.3, 115.3, 94.2, 75.6, 32.8, 29.0.

HRMS (ESI–TOF) calcd for $C_{16}H_{17}Cl_3NO_3^+$ ([M+H$^+$]) = 376.0269, Found 376.0268.

Benzyl (*E*)-3-(2,2-dimethylpropylidene)-2-oxoindoline-1-carboxylate 2k



2k

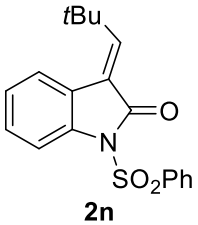
Yellow solid. R_f = 0.4 (PE:EA = 30:1), m.p. 89–91 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.36 – 7.31 (m, 2H), 7.31 – 7.28 (m, 1H), 7.19 (dt, *J* = 7.7, 1.2 Hz, 1H), 5.47 (s, 2H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 154.6, 150.8, 139.6, 135.1, 129.0, 128.5, 128.2, 127.8, 126.0, 125.2, 123.9, 121.0, 115.1, 68.3, 32.7, 29.0.

HRMS (ESI–TOF) calcd for $C_{21}H_{22}NO_3^+$ ([M+H$^+$]) = 336.1594, Found 336.1597.

***E*-3-(2,2-dimethylpropylidene)-1-(phenylsulfonyl)indolin-2-one 2n**



2n

Yellow solid. R_f = 0.4 (PE:EA = 30:1), m.p. 75.2–76.9 °C.

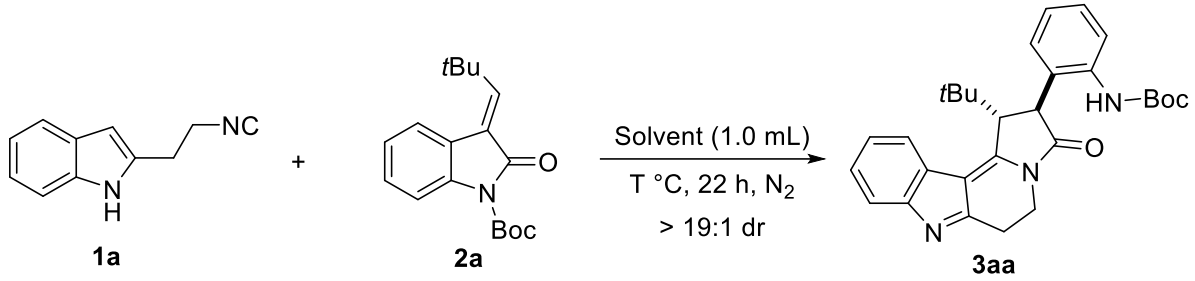
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 2H), 8.03 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.50 (td, *J* = 7.9, 2.4 Hz, 2H), 7.37 – 7.30 (m, 1H), 7.20 – 7.15 (m, 1H), 7.14 (d, *J* = 2.2 Hz, 1H), 1.32 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 155.6, 139.3, 138.6, 134.2, 129.4, 129.0, 127.9, 126.5, 124.6, 124.1, 121.1, 113.6, 77.3, 77.0, 76.7, 32.9, 28.9.

HRMS (ESI-TOF) calcd for $C_{19}H_{20}NO_3S^+$ ([M+H$^+$]) = 342.1158, Found 342.1157.

3. Optimization of the reaction conditions

Table 1 Screening of reaction solvents and temperature

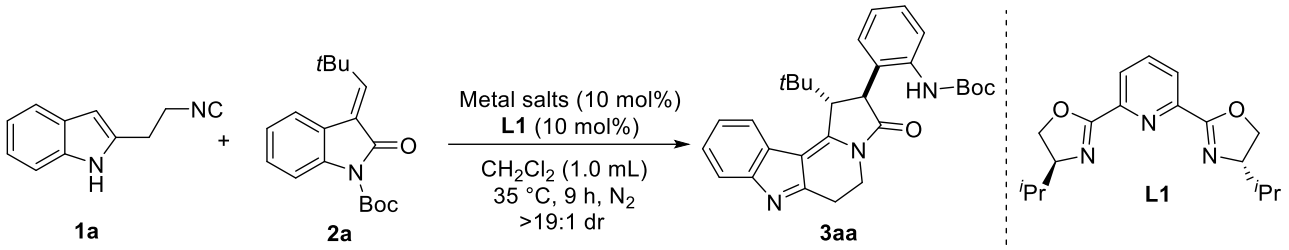


Entry[a]	Solvent	T (°C)	Yield (%)[b] **3aa**
1	CH_2Cl_2	70	85
2	$CHCl_3$	70	78
3	$ClCH_2CH_2Cl$	70	92
4	THF	70	30
5	Toluene	70	31
6	EtOAc	70	47
7	Et_2O	70	37
8	CH_3CN	70	64
9	EtOH	70	21
10	MeOH	70	0
11	$ClCH_2CH_2Cl$	rt	36
12	$ClCH_2CH_2Cl$	40	61
13[c]	$ClCH_2CH_2Cl$	70	72

[a]Unless otherwise noted, the reactions were performed **1a** (0.10 mmol) and **2a** (0.10 mmol) in indicated solvent (1.0 mL) and indicated temperature in sealed tube under N_2 for 22 h. [b]The yield of isolated product for **3aa**. [c]with $ClCH_2CH_2Cl$ (0.5 mL).

4. Catalytic enantioselective variant

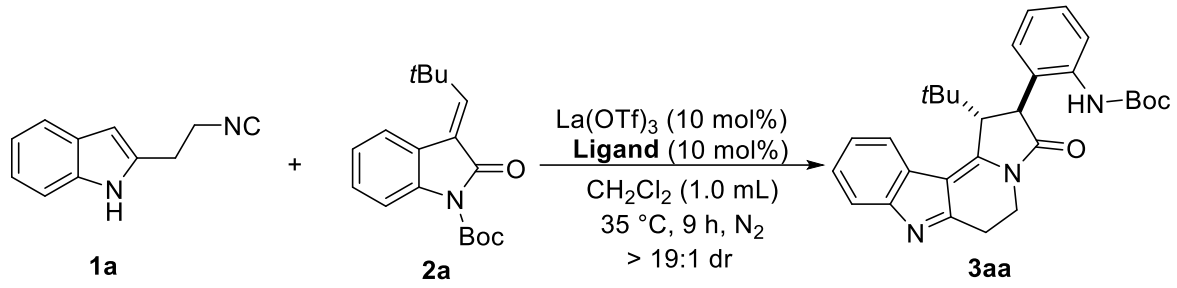
Table 2 Screening of the metal salts

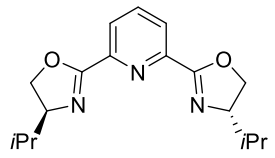


Entry[a]	Metal salts	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	$Ni(OTf)_2$	0	n.d.
2	$Al(OTf)_3$	60	0
3	$Fe(OTf)_3$	43	0
4	$Zn(OTf)_2$	56	0
5	$Cu(OTf)_2$	56	0
6	$Al(OTf)_3$	31	0
7	$Mg(OTf)_2$	52	0
8	$In(OTf)_3$	55	0
9	$Sc(OTf)_3$	37	0
10	$Y(OTf)_3$	89	20
11	$La(OTf)_3$	85	70
12	$Pr(OTf)_3$	86	60
13	$Nd(OTf)_3$	88	44
14	$Sm(OTf)_3$	90	40
15	$Eu(OTf)_3$	83	20
16	$Gd(OTf)_3$	92	26
17	$Dy(OTf)_3$	83	24
18	$Ho(OTf)_3$	80	28
19	$Er(OTf)_3$	74	24
20	$Tm(OTf)_3$	88	18
21	$Yb(OTf)_3$	85	10
22	$Lu(OTf)_3$	93	20

[a]Unless otherwise noted, the reactions were performed with Lewis acid (10 mol%), **L1** (10 mol%), **1a** (0.10 mmol) and **2a** (0.10 mmol) in CH_2Cl_2 (1.0 mL) at 35 ℃ under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis. n.d. = not detected.

Table 3 Screening of the chiral ligands





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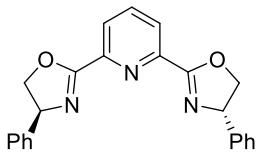
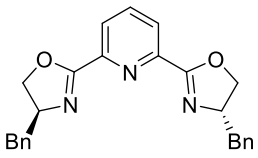
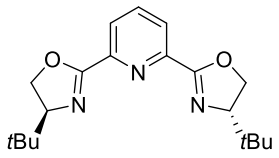


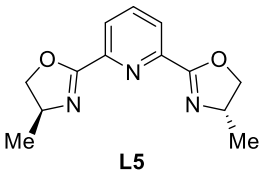
L2



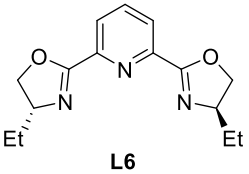
L3



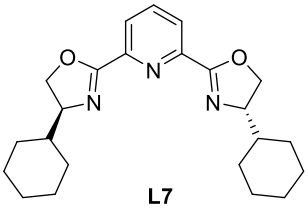
L4



L5



L6



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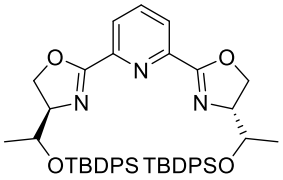
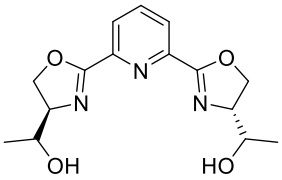
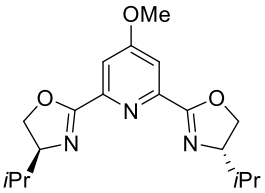


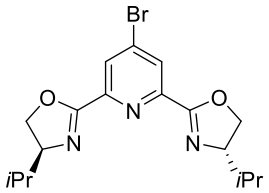
L8



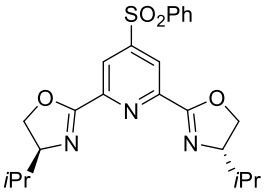
L9



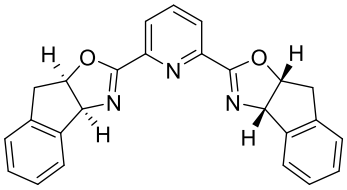
L10



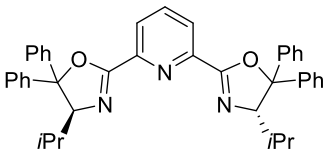
L11



L12



L13



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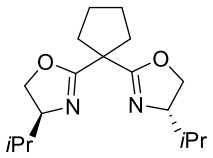

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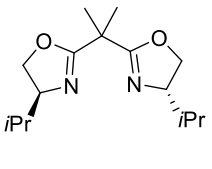

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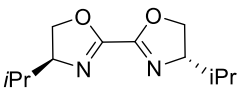
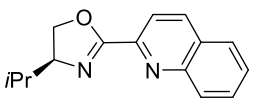


L17



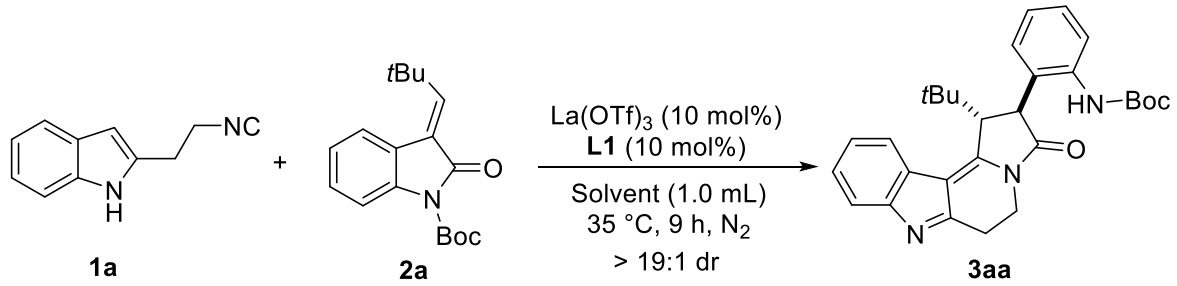
L18

Entry[a]	Ligand	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	**L1**	85	70
2	**L2**	65	28
3	**L3**	54	37
4	**L4**	86	0
5	**L5**	82	60
6	**L6**	91	42

7	**L7**	87	58
8	**L8**	90	0
9	**L9**	87	0
10	**L10**	92	67
11	**L11**	81	45
12	**L12**	82	27
13	**L13**	88	30
14	**L14**	78	0
15	**L15**	75	0
16	**L16**	68	0
17	**L17**	75	0
18	**L18**	82	0

[a]Unless otherwise noted, the reactions were performed with $La(OTf)_3$ (10 mol%), **Ligand** (10 mol%), **1a** (0.10 mmol) and **2a** (0.10 mmol) in CH_2Cl_2 (1.0 mL) at 35 ℃ under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis.

Table 4 Screening of the solvent

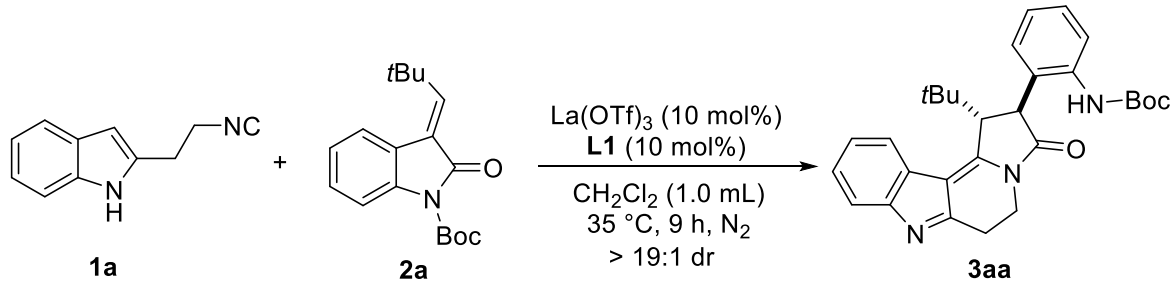


1a **2a** **3aa**

Entry[a]	Solvent	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	CH_2Cl_2	85	70
2	$ClCH_2CH_2Cl$	86	57
3	$CHCl_3$	88	38
4	THF	70	50
5	Toluene	78	45
6	CH_3CN	50	39
7	EtOAc	60	38
8	MeOH	0	n.d.
9	1,4-dioxane	0	n.d.

[a]Unless otherwise noted, the reactions were performed with $La(OTf)_3$ (10 mol%), **L1** (10 mol%), **1a** (0.10 mmol) and **2a** (0.10 mmol) in indicated solvent (1.0 mL) at 35 ℃ under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis.

Table 5 Screening of the ratio of the substrates

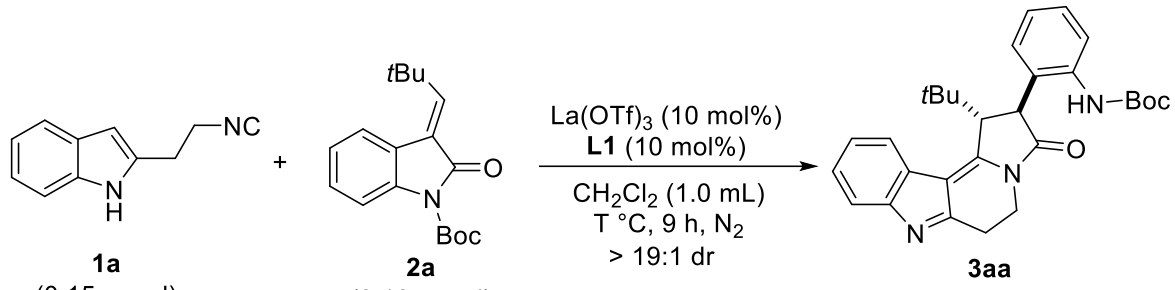


1a **2a** **3aa**

Entry[a]	**1a** (x mmol)	**2a** (y mmol)	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	0.1	0.1	85	70
2	0.15	0.1	90	74
3	0.2	0.1	81	67
4	0.1	0.15	91	61
5	0.1	0.2	91	49

[a]Unless otherwise noted, the reactions were performed with $La(OTf)_3$ (10 mol%), **L1**(10 mol%), **1a** (x mmol) and **2a** (y mmol) in CH_2Cl_2 (1.0 mL) at 35 ℃ under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis.

Table 6 Screening of the reaction temperature

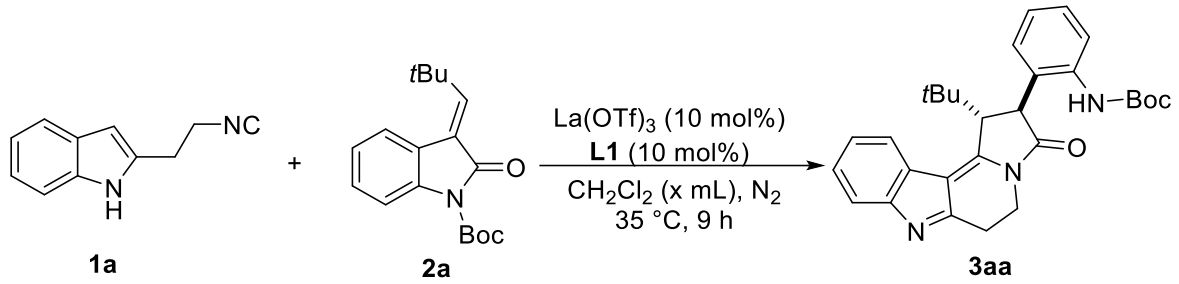


1a (0.15 mmol) **2a** (0.10 mmol) **3aa**

Entry[a]	T (℃)	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	50	65	60
2	40	74	68
3	35	90	74
4	30	85	70
5	rt	81	62
6[d]	0	51	44
7[e]	–10	31	14

[a]Unless otherwise noted, the reactions were performed with $La(OTf)_3$ (10 mol%), **L1** (10 mol%), **1a** (0.15 mmol) and **2a** (0.10 mmol) in CH_2Cl_2 (1.0 mL) at indicated temperature under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis. [d]with 36 h. [e]with 48 h.

Table 7 Screening of the reaction concentration



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

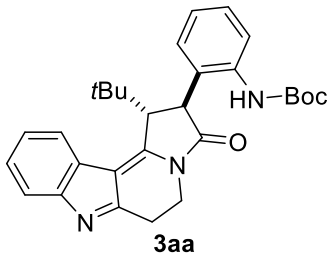
Entry[a]	CH_2Cl_2 (x mL)	Yield (%)[b] **3aa**	*ee*[c] **(3aa)**
1	0.5	89	54
2	1.0	90	74
3	1.5	96	70
4	2.0	91	67

[a]Unless otherwise noted, the reactions were performed with $La(OTf)_3$ (10 mol%), **L1**(10 mol%), **1a** (0.15 mmol) and **2a** (0.10 mmol) in CH_2Cl_2 (x mL) at 35 ℃ under N_2 for 9 h. [b]The yield of isolated product for **3aa**. [c]*ee* (**3aa**) determined by chiral HPLC analysis.

5. General procedure and spectral data of products 3

A dry sealed tube was charged with isocyanide **1** (0.1 mmol), 3-alkenyl-oxindoles **2** (0.1 mmol), and $ClCH_2CH_2Cl$ (1.0 mL). The reaction mixture continued stirring at 70 ℃ under N_2 for 22 h. The residue was directly purified by flash chromatography on silica gel by using petroleum ether/ethyl acetate = 1/2 as eluent to afford the desired products **3**.

Tert-butyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl) carbamate 3aa



3aa

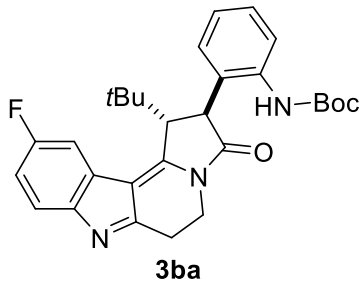
The reaction was run at 70 ℃ for 22 h, affording product **3aa** in 92% yield (43.4 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 110.8–111.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.79 – 7.68 (m, 2H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.33 (td, *J* = 7.7, 1.2 Hz, 1H), 7.29 – 7.20 (m, 2H), 7.03 – 6.93 (m, 2H), 4.17 (s, 1H), 4.00 – 3.87 (m, 2H), 3.62 (s, 1H), 3.22 – 3.04 (m, 2H), 1.54 (s, 9H), 1.14 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 163.4, 155.9, 155.1, 153.8, 137.1, 128.8, 128.6, 128.2, 127.2, 125.4, 125.4, 125.1, 124.1, 121.9, 120.3, 117.9, 80.6, 53.8, 46.5, 38.9, 38.7, 28.4, 28.1, 25.4.

HRMS (ESI–TOF) calcd for $C_{29}H_{34}N_3O_3^+$ ([M+H$^+$]) = 472.2595, Found 472.2579.

Tert-butyl(2-(1-(tert-butyl)-10-fluoro-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3ba



3ba

The reaction was run at 70 ℃ for 22 h, affording product **3ba** in 75% yield (36.8 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 118.7–119.2 °C.

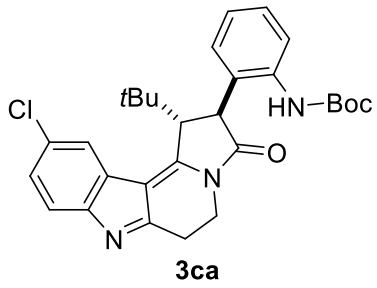
^{1}H NMR (600 MHz,$CDCl_3$) δ 7.86 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.53 (dd, *J* = 8.6, 4.8 Hz, 1H), 7.39 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.28 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.07 – 6.99 (m, 2H), 6.93 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.18 (s, 1H), 4.01 – 3.87 (m, 2H), 3.56 (s, 1H), 3.18 – 3.06 (m, 2H), 1.53 (s, 9H), 1.14 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 163.3 (d, *J* = 3.0 Hz), 161.1 (d, *J* = 241.6 Hz), 159.5, 156.4, 153.8, 152.0, 137.0, 129.3 (d, *J* = 10.6 Hz), 128.7, 125.5, 125.4, 125.0, 120.7 (d, *J* = 9.1 Hz), 117.6, 113.8 (d, *J* = 24.2 Hz), 108.9 (d, *J* = 25.6 Hz), 80.7, 53.8, 46.5, 38.9, 38.7, 28.3, 28.0, 25.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ –118.54.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}FN_3O_3^+$ ([M+H$^+$]) = 490.2500, Found 490.2498.

Tert-butyl(2-(1-(tert-butyl)-10-chloro-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3ca



3ca

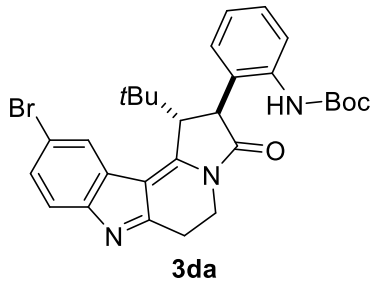
The reaction was run at 70 ℃ for 22 h, affording product **3ca** in 85% yield (43.1 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 110.6–112.3 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.28 (td, *J* = 8.5, 1.8 Hz, 2H), 7.03 (td, *J* = 7.6, 1.3 Hz, 1H), 6.94 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.18 (s, 1H), 4.01 – 3.88 (m, 2H), 3.57 (s, 1H), 3.18 – 3.07 (m, 2H), 1.53 (s, 9H), 1.14 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 163.7, 156.8, 154.2, 153.8, 137.0, 129.7, 129.6, 128.7, 128.6, 127.0, 125.6, 125.5, 125.0, 121.7, 121.0, 117.1, 80.7, 53.9, 46.5, 38.8, 38.7, 28.3, 28.0, 25.2.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}ClN_3O_3^+$ ([M+H$^+$]) = 506.2205, Found 506.2209.

Tert-butyl(2-(10-bromo-1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3da



3da

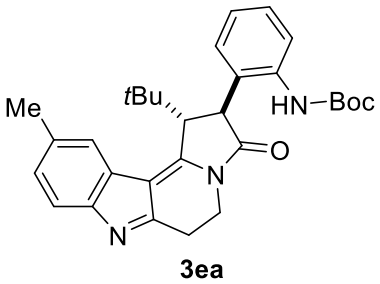
The reaction was run at 70 ℃ for 22 h, affording product **3da** in 90% yield (49.6 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 120.3–121.3 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.66 (m, 3H), 7.53 – 7.38 (m, 2H), 7.28 (td, *J* = 7.7, 1.5 Hz, 1H), 7.04 (td, *J* = 7.6, 1.3 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 4.18 (s, 1H), 4.00 – 3.88 (m, 2H), 3.57 (s, 1H), 3.17 – 3.07 (m, 2H), 1.53 (s, 9H), 1.13 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 163.3, 155.8, 153.8, 153.5, 136.3, 131.6, 130.6, 128.3, 128.0, 127.3, 126.7, 124.2, 121.8, 120.3, 118.3, 117.9, 81.0, 53.3, 46.3, 38.9, 38.8, 28.2, 28.0, 25.2.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}BrN_3O_3^+$ ([M+H$^+$]) = 550.1700, Found 550.1700.

Tert-butyl(2-(1-(tert-butyl)-10-methyl-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamatev 3ea



3ea

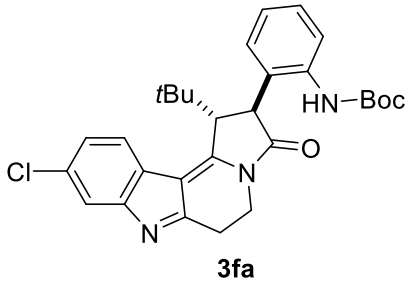
The reaction was run at 70 ℃ for 22 h, affording product **3ea** in 93% yield (45.2 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 118.9–122.2 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.29 – 7.24 (m, 1H), 7.16 – 7.12 (m, 1H), 7.03 – 6.95 (m, 2H), 4.16 (s, 1H), 3.92 (t, *J* = 7.4 Hz, 2H), 3.60 (s, 1H), 3.16 – 3.04 (m, 2H), 2.46 (s, 3H), 1.54 (s, 9H), 1.13 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.1, 163.4, 155.7, 155.4, 154.0, 135.2, 134.2, 129.3, 129.2, 128.2, 127.0, 125.8, 125.7, 124.1, 121.7, 120.2, 117.8, 80.4, 53.7, 46.5, 38.9, 38.7, 28.3, 28.0, 25.3, 21.1.

HRMS (ESI–TOF) calcd for $C_{30}H_{36}N_3O_3^+$ ([M+H$^+$]) = 486.2751, Found 486.2750.

Tert-butyl(2-(1-(tert-butyl)-9-chloro-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3fa



3fa

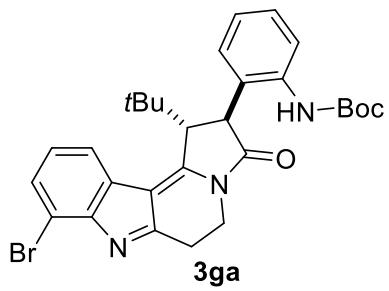
The reaction was run at 70 ℃ for 22 h, affording product **3fa** in 78% yield (39.5 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 117.2–118.4 °C.

^{1}H NMR (600 MHz,$CDCl_3$) δ 7.83 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.27 (td, *J* = 7.7, 1.5 Hz, 1H), 7.20 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.00 (td, *J* = 7.6, 1.3 Hz, 1H), 6.93 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.17 (s, 1H), 4.01 – 3.86 (m, 2H), 3.57 (s, 1H), 3.19 – 3.07 (m, 2H), 1.52 (s, 9H), 1.12 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 164.9, 156.8, 156.2, 153.8, 137.0, 132.6, 128.8, 128.7, 126.6, 125.7, 125.4, 125.0, 124.0, 122.1, 120.6, 117.1, 80.7, 53.9, 46.5, 38.8, 38.7, 28.3, 28.0, 25.3.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}ClN_3O_3^+$ ([M+H$^+$]) = 506.2205, Found 506.2204.

Tert-butyl(2-(8-bromo-1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3ga



3ga

The reaction was run at 70 ℃ for 22 h, affording product **3ga** in 60% yield (33.0 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 111.3–113.1 °C.

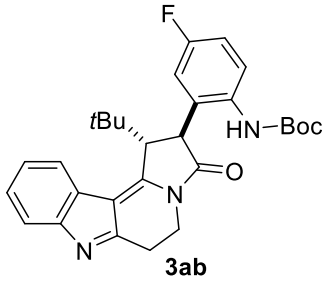
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.66 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.49 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.28

(dd, *J* = 7.6, 1.5 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.00 (td, *J* = 7.6, 1.3 Hz, 1H), 6.92 (dd, *J* = 7.9, 1.5 Hz, 1H), 4.18 (s, 1H), 4.04 – 3.85 (m, 2H), 3.61 (s, 1H), 3.21 (t, *J* = 7.4 Hz, 2H), 1.52 (s, 9H), 1.12 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 164.1, 157.6, 153.8, 153.6, 136.9, 130.1, 129.8, 128.7, 125.8, 125.7, 125.5, 125.1, 125.0, 120.7, 118.1, 114.3, 80.7, 53.9, 46.5, 38.9, 38.7, 28.3, 28.0, 25.4.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}BrN_3O_3^+$ ([M+H$^+$]) = 550.1700, Found 550.1703.

Tert-butyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)-4-fluorophenyl)carbamate 3ab



3ab

The reaction was run at 70 ℃ for 22 h, affording product **3ab** in 65% yield (32.0 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 140.3–141.7 °C.

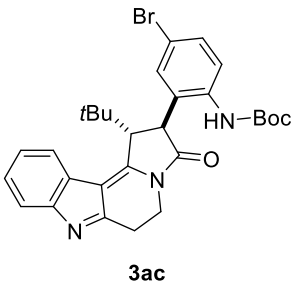
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.72 – 7.64 (m, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.23 (td, *J* = 7.5, 1.1 Hz, 1H), 6.99 – 6.94(m, 1H), 6.67 (dd, *J* = 9.2, 2.9 Hz, 1H), 4.15 (s, 1H), 4.02 – 3.87 (m, 2H), 3.54 (s, 1H), 3.18 – 3.11 (m, 2H), 1.51 (s, 9H), 1.13 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 163.3, 159.9 (d, *J* = 247.5 Hz), 155.9, 154.1, 154.0, 132.9 (d, *J* = 1.5 Hz), 131.4, 128.0, 127.7, 127.4, 124.2, 121.9, 120.4, 118.3, 115.4 (d, *J* = 22.2 Hz), 112.3 (d, *J* = 24.4 Hz), 80.8, 53.7, 46.5, 39.0, 38.8, 28.3, 28.0, 25.3.

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

HRMS (ESI–TOF) calcd for $C_{29}H_{33}FN_3O_3^+$ ([M+H$^+$]) = 490.2500, Found 490.2504.

Tert-butyl(4-bromo-2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3ac



3ac

The reaction was run at 70 ℃ for 22 h, affording product **3ac** in 88% yield (48.4 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 146.2–147.5 °C.

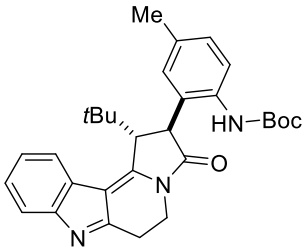
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.69 (dd, *J* = 15.1, 8.1 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.37 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 7.23 (td, *J* = 7.5, 1.1 Hz, 1H), 7.07 (d, *J* = 2.2 Hz, 1H), 4.10 (s, 1H), 4.04 – 3.84 (m, 2H), 3.56 (s, 1H), 3.23 – 3.06 (m, 2H), 1.51 (s, 9H), 1.11 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 163.3, 155.8, 153.9, 153.5, 136.3, 131.6, 130.6, 128.3, 128.0,

127.3, 126.7, 124.2, 121.8, 120.3, 118.3, 117.9, 81.0, 53.3, 46.3, 38.9, 38.8, 28.2, 27.9, 25.2.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}BrN_3O_3^+$ ([M+H$^+$]) = 550.1700, Found 550.1702.

Tert-butyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)-4-methylphenyl)carbamate 3ad



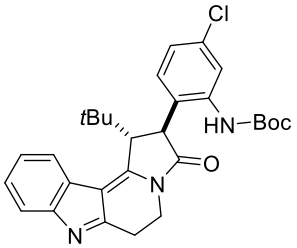
3ad

The reaction was run at 70 ℃ for 22 h, affording product **3ad** in 47% yield (22.7 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 137.4–138.6 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (t, *J* = 16.6 Hz, 2H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.57 (s, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.74 (s, 1H), 4.14 (s, 1H), 4.01 (dt, *J* = 14.2, 7.3 Hz, 1H), 3.87 (dt, *J* = 14.0, 7.6 Hz, 1H), 3.60 (s, 1H), 3.15 (t, *J* = 7.5 Hz, 2H), 2.15 (s, 3H), 1.50 (s, 9H), 1.12 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.1, 163.4, 155.7, 155.4, 154.0, 135.2, 134.2, 129.3, 129.2, 128.2, 127.0, 125.8, 125.7, 124.1, 121.7, 120.2, 117.8, 80.4, 53.7, 46.5, 38.9, 38.7, 28.3, 28.0, 25.3, 21.1.

HRMS (ESI–TOF) calcd for $C_{30}H_{36}N_3O_3^+$ ([M+H$^+$]) =486.2751, Found 486.2752.

Tert-butyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)-5-chlorophenyl)carbamate 3ae



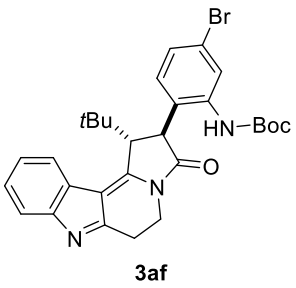
3ae

The reaction was run at 70 ℃ for 22 h, affording product **3ae** in 64% yield (32.6 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 121.6–123.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.94 – 7.81 (m, 1H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 7.23 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.95 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 1H), 4.08 (s, 1H), 4.00 – 3.85 (m, 2H), 3.57 (s, 1H), 3.22 – 3.04 (m, 2H), 1.55 (s, 9H), 1.13 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 163.3, 155.9, 154.3, 153.4, 138.4, 134.4, 128.0, 127.4, 126.3, 126.0, 125.0, 124.6, 124.2, 121.8, 120.4, 118.2, 81.1, 53.6, 46.2, 38.9, 38.7, 28.3, 28.0, 25.3.

HRMS (ESI–TOF) calcd for $C_{29}H_{33}ClN_3O_3^+$ ([M+H$^+$]) = 506.2205, Found 506.2205.

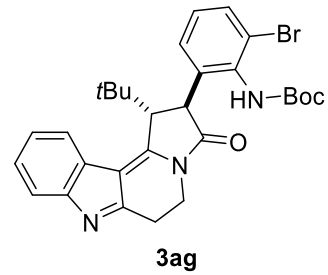
Tert-butyl(5-bromo-2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3af



3af

The reaction was run at 70 ℃ for 22 h, affording product **3af** in 83% yield (45.9 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 142.9–143.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.05 – 7.98 (m, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 7.23 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.11 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 1H), 4.07 (s, 1H), 4.00 – 3.87 (m, 2H), 3.56 (s, 1H), 3.21 – 3.04 (m, 2H), 1.55 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 163.3, 155.9, 154.2, 153.3, 138.5, 128.0, 127.9, 127.5, 127.4, 126.9, 126.3, 124.2, 122.2, 121.8, 120.4, 118.2, 81.1, 53.5, 46.2, 38.9, 38.7, 28.3, 28.0, 25.3. HRMS (ESI–TOF) calcd for $C_{29}H_{33}BrN_3O_3^+$ ([M+H$^+$]) = 550.1700, Found 550.1702.

Tert-butyl(2-bromo-6-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3ag

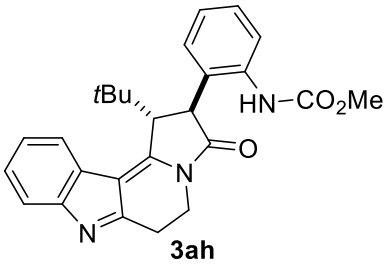


3ag

The reaction was run at 70 ℃ for 22 h, affording product **3ag** in 62% yield (34.1 mg) as a yellow solid. R_f = 0.3 (PE:EA = 1:2), m.p. 147.3–149.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.45 (m, 3H), 7.33 – 7.22 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10 – 6.87 (m, 2H), 6.49 (s, 1H), 4.28 (s, 1H), 4.13 – 4.07 (m, 1H), 3.88 – 3.80 (m, 1H), 3.46 (s, 1H), 3.26 – 3.02 (m, 2H), 1.36 (s, 9H), 1.10 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.3, 163.4, 155.8, 155.7, 153.9, 139.2, 134.7, 132.8, 129.5, 128.4, 126.8, 126.5, 126.1, 123.8, 122.1, 120.0, 117.9, 81.0, 55.1, 47.9, 39.2, 38.7, 28.1, 27.9, 25.3. HRMS (ESI-TOF) calcd for $C_{29}H_{33}BrN_3O_3^+$ ([M+H$^+$]) = 550.1700, Found 550.1703.

Methyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl) carbamate 3ah



3ah

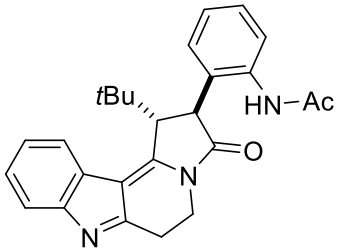
The reaction was run at 70 ℃ for 22 h, affording product **3ah** in 89% yield (38 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 160.1–162.3 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.23 (td, *J* = 7.5, 1.1 Hz, 1H), 7.06 – 6.98 (m, 2H), 4.16 (s, 1H), 3.97 – 3.88 (m, 2H), 3.73 (s, 3H), 3.63 (s, 1H), 3.18 – 3.06 (m, 2H), 1.13 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 163.4, 155.8, 155.0, 154.9, 136.6, 129.1, 129.0, 128.7, 128.1, 127.2, 125.7, 125.4, 124.1, 121.9, 120.2, 117.9, 53.5, 52.4, 46.7, 38.9, 38.6, 27.9, 25.2.

HRMS (ESI–TOF) calcd for $C_{26}H_{28}N_3O_3^+$ ([M+H$^+$]) = 430.2125, Found 430.2125.

N-(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)acetamide 3ai



3ai

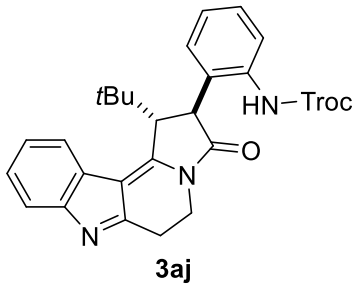
The reaction was run at 70 ℃ for 22 h, affording product **3ai** in 78% yield (32.2 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 123.2–124.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.75 (t, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.27 (m, 2H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.03 (dt, *J* = 15.6, 7.6 Hz, 2H), 4.15 (s, 1H), 3.98 – 3.88 (m, 2H), 3.65 (s, 1H), 3.12 (td, *J* = 11.3, 10.6, 5.5 Hz, 2H), 2.26 (s, 3H), 1.12 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 169.1, 163.3, 155.6, 154.8, 136.4, 128.9, 128.6, 127.9, 127.3, 126.5, 126.2, 125.0, 124.2, 121.8, 120.2, 118.1, 53.3, 46.6, 38.8, 38.6, 27.9, 25.1, 24.2.

HRMS (ESI–TOF) calcd for $C_{26}H_{28}N_3O_2^+$ ([M+H$^+$]) = 414.2176, Found 414.2178.

2,2,2-trichloroethyl(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)carbamate 3aj



3aj

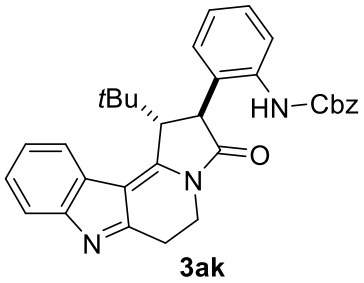
The reaction was run at 70 ℃ for 22 h, affording product **3aj** in 76% yield (41.2 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p.144.5–145.7 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.24 (td, *J* = 7.5, 1.0 Hz, 1H), 7.10 (td, *J* = 7.6, 1.3 Hz, 1H), 7.04 (dd, *J* = 7.9, 1.5 Hz, 1H), 4.84 (d, *J* = 12.1 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.19 (s, 1H), 3.99 – 3.89 (m, 2H), 3.64 (s, 1H), 3.19 – 3.05 (m, 2H), 1.13 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.9, 163.4, 155.8, 154.7, 152.9, 135.8, 129.8, 128.9, 128.0, 127.3, 126.6, 126.0, 125.5, 124.1, 121.9, 120.3, 118.1, 95.4, 74.5, 53.4, 46.7, 38.9, 38.7, 27.9, 25.3.

HRMS (ESI–TOF) calcd for $C_{27}H_{27}Cl_3N_3O_3^+$ ([M+H$^+$]) = 546.1113, Found 546.1116.

Benzyl(2-1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl) carbamate 3ak



3ak

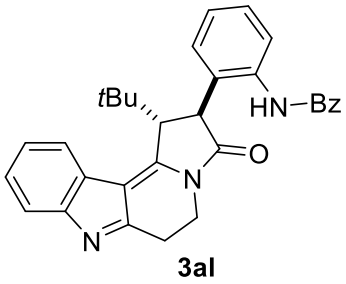
The reaction was run at 70 ℃ for 22 h, affording product **3ak** in 82% yield (41.4 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 129.4–130.2 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.73 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.45 – 7.36 (m, 4H), 7.36 – 7.27 (m, 3H), 7.24 (td, *J* = 7.5, 1.1 Hz, 1H), 7.08 – 6.98 (m, 2H), 5.19 (d, *J* = 12.3 Hz, 1H), 5.14 – 5.08 (m, 1H), 4.16 (s, 1H), 3.96 – 3.84 (m, 2H), 3.63 (s, 1H), 3.16 – 3.03 (m, 2H), 1.11 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.9, 163.4, 155.7, 155.1, 155.0, 154.5, 154.5, 136.4, 136.1, 129.4, 128.9, 128.7, 128.5, 128.2, 128.2, 128.0, 127.1, 125.9, 125.4, 124.0, 121.9, 120.2, 117.8, 67.0, 53.6, 53.5, 46.7, 38.8, 38.6, 27.9, 25.2.

HRMS (ESI–TOF) calcd for $C_{32}H_{32}N_3O_3^+$ ([M+H$^+$]) = 506.2438, Found 506.2439.

N-(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)benzamide 3al



3al

The reaction was run at 70 ℃ for 22 h, affording product **3al** in 89% yield (42.4 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 151.5-153.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.16 – 8.09 (m, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.66 – 7.50 (m, 4H), 7.36 (tt, *J* = 8.4, 2.5 Hz, 2H), 7.29 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.12 – 7.04 (m, 2H), 4.23 (s, 1H), 4.05 – 3.87 (m, 2H), 3.73 (s, 1H), 3.23 – 3.02 (m, 2H), 1.11 (s, 9H).

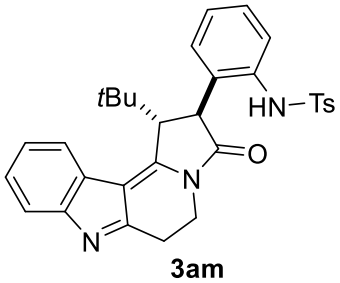
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 165.6, 163.3, 155.8, 154.3, 137.0, 134.1, 132.0, 128.8, 128.7, 128.5, 128.0, 127.4, 127.4, 126.3, 126.1, 125.0, 124.2, 121.9, 120.3, 118.3, 53.0, 46.9, 38.8, 38.6, 28.0, 25.3.

HRMS (ESI–TOF) calcd for $C_{31}H_{30}N_3O_2^+$ ([M+H$^+$]) = 476.2333, Found 476.2334.

N-(2-1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl)-4-methyl benzenesulfonamide 3am

The reaction was run at 70 ℃ for 22 h, affording product **3am** in 86% yield (45.1 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 145.2–146.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.41 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.36 – 7.26 (m, 3H), 7.22 (q, *J* = 8.1 Hz, 2H), 7.06



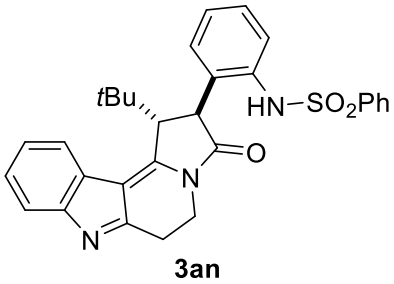
3am

(td, *J* = 7.7, 1.4 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.04 (s, 1H), 3.97 – 3.83 (m, 2H), 3.56 (s, 1H), 3.19 – 2.97 (m, 2H), 2.40 (s, 3H), 0.96 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 163.4, 155.8, 154.4, 143.7, 138.2, 135.9, 130.3, 129.9, 128.9, 128.0, 127.3, 126.9, 126.9, 126.5, 125.2, 124.1, 121.7, 120.3, 118.0, 52.7, 46.4, 38.8, 38.4, 27.7, 25.2, 21.5.

HRMS (ESI–TOF) calcd for $C_{31}H_{32}N_3O_3S^+$ ([M+H$^+$]) = 526.2159, Found 526.2161.

N-(2-(1-(tert-butyl)-3-oxo-2,3,5,6-tetrahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl) benzene sulfonamide 3an



3an

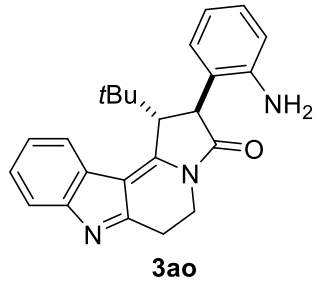
The reaction was run at 70 ℃ for 22 h, affording product **3an** in 87% yield (44.4 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 104.6–105.2 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.58 (dd, *J* = 22.1, 7.6 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (dt, *J* = 12.9, 7.6 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 4.07 (s, 1H), 3.96 – 3.83 (m, 2H), 3.56 (s, 1H), 3.17 – 3.01 (m, 2H), 0.97 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 163.4, 155.8, 154.4, 141.2, 135.8, 132.9, 130.4, 129.3, 128.9, 128.0, 127.3, 127.0, 126.9, 126.4, 125.3, 124.1, 121.7, 120.3, 118.1, 52.7, 46.4, 38.8, 38.5, 27.8, 25.2.

HRMS (ESI–TOF) calcd for $C_{30}H_{29}N_3O_3S^+$ ([M+H$^+$]) = 512.2002, Found 512.2004.

2-(2-aminophenyl)-1-(tert-butyl)-1,2,5,6-tetrahydro-3H-indolizino[7,8-b]indol-3-one 3ao



3ao

The reaction was run at 70 ℃ for 22 h, affording product **3ao** in 75% yield (27.8 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 180.5–181.7 °C.

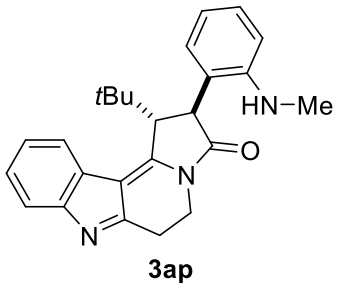
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.21 (s, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.14 – 6.91 (m, 4H), 6.75 (s, 1H), 6.59 (dt, *J* = 7.6, 3.3 Hz, 2H), 4.12 – 3.96 (m, 1H), 3.47 (s, 1H), 3.05 (dt, *J* = 13.6, 7.9 Hz, 1H), 2.91 – 2.77 (m, 2H), 2.62 (s, 1H), 0.69 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 170.5, 142.7, 135.7, 134.7, 127.5, 126.6, 126.3, 121.7, 120.9, 120.3, 118.9, 116.9, 114.7, 111.0, 108.6, 74.8, 54.3, 48.8, 32.5, 32.1, 28.6, 22.5.

HRMS (ESI–TOF) calcd for $C_{24}H_{26}N_3O^+$ ([M+H$^+$]) = 372.2070, Found 372.2070.

1-(tert-butyl)-2-(2-(methylamino)phenyl)-1,2,5,6-tetrahydro-3H-indolizino[7,8-b]indol-3-one

3ap



3ap

The reaction was run at 70 ℃ for 22 h, affording product **3ap** in 13% yield (5.0 mg) as a white solid. R_f = 0.4 (PE:EA = 1:1), m.p. 120.3–121.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.24 – 7.16 (m, 3H), 7.15 – 7.11 (m, 1H), 6.79 (t, *J* = 7.5 Hz, 2H), 4.48 – 4.38 (m, 1H), 3.57 (s, 1H), 3.12 – 2.96 (m, 2H), 2.91 – 2.77 (m, 2H), 2.73 (s, 3H), 0.68 (s, 9H).

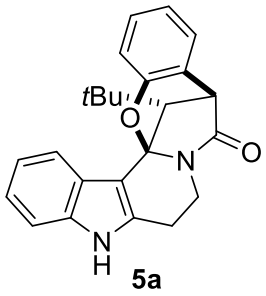
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 144.9, 135.7, 134.3, 128.4, 127.0, 126.5, 123.6, 122.4, 120.7, 120.5, 118.5, 114.6, 110.9, 109.0, 80.8, 56.8, 49.9, 35.6, 35.3, 33.0, 28.7, 22.9.

HRMS (ESI–TOF) calcd for $C_{25}H_{28}N_3O^+$ ([M+H$^+$]) = 386.2227, Found 386.2221.

6. General procedure and spectral data of products 5

A sealed tube was charged with isocyanide **1a** (0.15 mmol), 3-alkenyl-benzofuran-2-one **4** (0.1 mmol), and DBU (0.3 mmol), $ClCH_2CH_2Cl$ (1.0 mL) was then added. The reaction mixture continued stirring at 80 ℃ for 24 h under N_2. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate/dichloromethane= 2/1/1 as eluent to afford the desired products **5**.

16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2]pyrido[4,3-b]indol-9(10H)-one 5a



5a

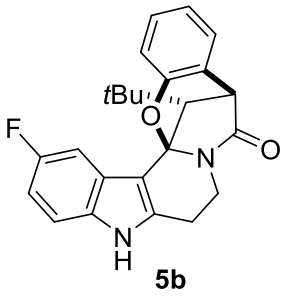
The reaction was run at rt for 24 h, affording product **5a** in 72% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 252.7–254.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.35 (s, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.17 (td, *J* = 7.8, 1.7 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 4.11 (dt, *J* = 12.7, 3.2 Hz, 1H), 3.69 (s, 1H), 3.07 – 3.00 (m, 1H), 2.94 – 2.85 (m, 2H), 2.81 (s, 1H), 0.72 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.6, 153.0, 135.7, 135.4, 128.6, 127.0, 126.1, 123.9, 121.1, 120.3, 119.9, 119.3, 116.2, 111.1, 106.9, 93.5, 54.4, 46.7, 33.6, 32.2, 28.2, 21.9.

HRMS (ESI–TOF) calcd for $C_{24}H_{25}N_2O_2^+$ ([M+H$^+$]) = 373.1911, Found 373.1907.

2-fluoro-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2]pyrido[4,3-b]indol-9(10H)-one 5b



5b

The reaction was run at rt for 24 h, affording product **5b** in 67% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 258.2–258.9 °C.

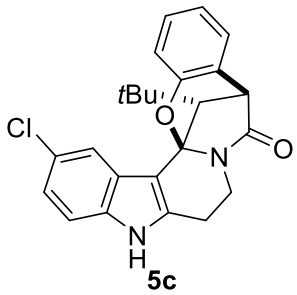
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.46 (s, 1H), 7.46 – 7.25 (m, 3H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.02 – 6.86 (m, 2H), 6.76 (t, *J* = 8.3 Hz, 1H), 4.15 – 4.04 (m, 1H), 3.68 (s, 1H), 3.10 – 2.98 (m, 1H), 2.95 – 2.85 (m, 3H), 0.73 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.6, 156.3 (*J* = 226.5 Hz), 153.0, 137.5, 132.4, 128.6, 127.0, 126.4, 123.8, 120.3, 116.2, 112.2, 109.2 (*J* = 15.1 Hz), 107.3, 104.9 (*J* = 30.2 Hz), 93.3, 53.9, 46.6, 33.5, 32.2, 28.1, 22.0.

^{19}F NMR (565 MHz, DMSO-d_6) δ –124.25.

HRMS (ESI–TOF) calcd for $C_{24}H_{24}FN_2O_2^+$ ([M+H$^+$]) = 391.1816, Found 391.1816.

2-chloro-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2] pyrido[4,3-b]indol-9(10H)-one 5c



5c

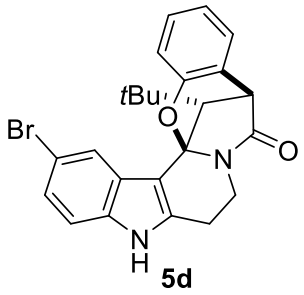
The reaction was run at rt for 24 h, affording product **5c** in 60% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 256.2–257.0 °C.

^{1}H NMR (600 MHz, DMSO-d_6) δ 11.58 (s, 1H), 7.61 (s, 1H), 7.40 (d, J = 8.6 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.24 – 7.03 (m, 2H), 6.90 (t, J = 7.6 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 4.10 (d, J = 11.9 Hz, 1H), 3.68 (s, 1H), 3.13 – 2.77 (m, 4H), 0.72 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.5, 152.8, 137.3, 134.2, 128.6, 127.2, 126.9, 124.0, 123.8, 121.1, 120.3, 118.9, 116.2, 112.7, 106.9, 93.2, 54.0, 46.6, 33.4, 32.2, 28.1, 21.9.

HRMS (ESI–TOF) calcd for $C_{24}H_{24}ClN_2O_2^+$ ([M+H$^+$]) = 407.1521, Found 407.1518.

2-bromo-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2] pyrido[4,3-b]indol-9(10H)-one 5d



5d

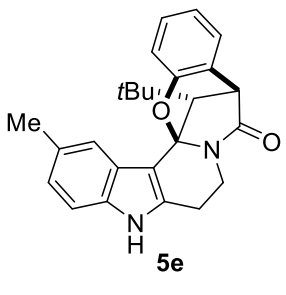
The reaction was run at rt for 24 h, affording product **5d** in 72% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 259.2–260.2 °C.

^{1}H NMR (600 MHz, DMSO-d_6) δ 11.59 (s, 1H), 7.75 (s, 1H), 7.36 (d, J = 8.6 Hz, 1H), 7.28 (d, J = 7.5 Hz, 1H), 7.22 (d, J = 8.6 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 4.10 (dd, J = 12.0, 4.6 Hz, 1H), 3.68 (s, 1H), 3.05 – 2.98 (m, 1H), 2.93 – 2.88 (m, 3H), 0.71 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.6, 152.9, 137.2, 134.5, 128.6, 127.9, 127.0, 123.8, 123.7, 121.9, 120.4, 116.3, 113.2, 112.0, 106.8, 93.2, 54.0, 46.6, 33.5, 32.2, 28.1, 21.9.

HRMS (ESI–TOF) calcd for $C_{24}H_{24}BrN_2O_2^+$ ([M+H$^+$]) = 451.1016, Found 451.1014.

2-methyl-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2] pyrido[4,3-b]indol-9(10H)-one 5e



5e

The reaction was run at rt for 24 h, affording product **5e** in 53% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 243.2–244.8 °C.

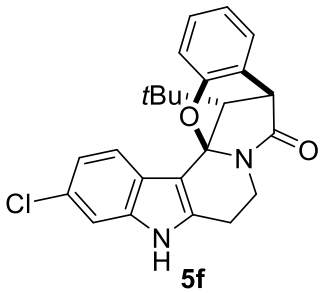
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 7.36 (s, 1H), 7.30 – 7.22 (m, 2H), 7.17 (dd, J = 8.6, 6.8 Hz, 1H), 6.90 (q, J = 7.6 Hz, 2H), 6.76 (d, J = 7.9 Hz, 1H), 4.09 (dt, J = 12.8, 2.9 Hz, 1H), 3.68 (s, 1H), 3.08 – 2.94 (m,

1H), 2.87 (q, *J* = 4.1 Hz, 2H), 2.79 (s, 1H), 2.36 (s, 3H), 0.72 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 172.5, 153.0, 135.3, 134.0, 128.6, 127.8, 126.9, 126.4, 123.9, 122.6, 120.3, 119.6, 116.2, 110.8, 106.4, 93.6, 54.3, 46.7, 33.6, 32.3, 28.2, 21.9, 21.2.

HRMS (ESI–TOF) calcd for $C_{25}H_{27}N_2O_2^+$ ([M+H$^+$]) = 387.2067, Found 387.2066.

3-chloro-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2] pyrido[4,3-b]indol-9(10H)-one 5f



5f

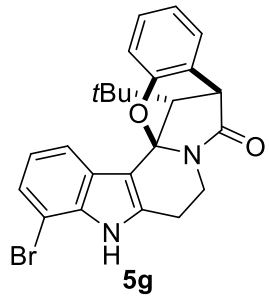
The reaction was run at rt for 24 h, affording product **5f** in 65% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 257.2–258.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.54 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 1.9 Hz, 1H), 7.29 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.17 (td, *J* = 7.7, 1.6 Hz, 1H), 7.06 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.90 (td, *J* = 7.5, 1.2 Hz, 1H), 6.75 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.16 – 4.09 (m, 1H), 3.70 (s, 1H), 3.08 – 3.00 (m, 1H), 2.95 – 2.87 (m, 2H), 2.82 (s, 1H), 0.71 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.5, 152.9, 136.7, 136.2, 128.6, 127.0, 125.8, 124.9, 123.8, 121.1, 120.4, 119.7, 116.2, 110.9, 107.2, 93.2, 54.3, 46.6, 33.5, 32.2, 28.1, 21.8.

HRMS (ESI–TOF) calcd for $C_{24}H_{24}ClN_2O_2^+$ ([M+H$^+$]) = 407.1521, Found 407.1517.

4-bromo-16-(tert-butyl)-6,7-dihydro-5H-10,15a-methanobenzo[6',7'][1,3]oxazepino[3',2':1,2] pyrido[4,3-b]indol-9(10H)-one 5g



5g

The reaction was run at rt for 24 h, affording product **5g** in 72% yield as a white solid. R_f = 0.4 (PE:EA:DCM = 2:1:1), m.p. 255.2–256.9 °C.

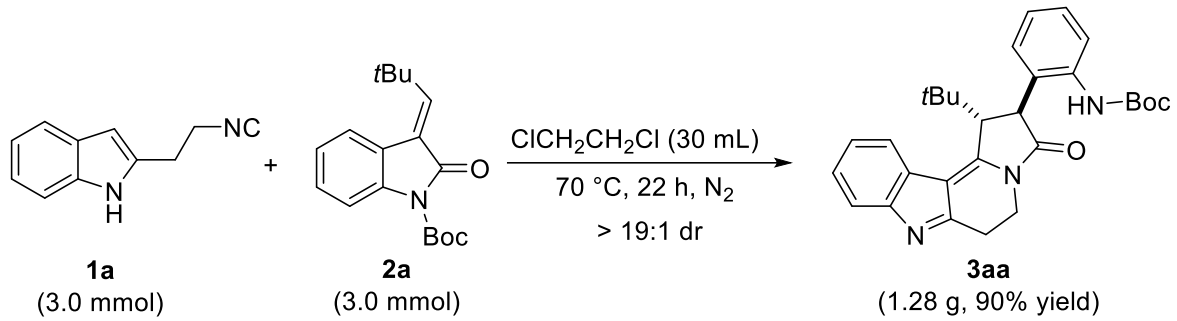
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.58 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.32 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.28 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.16 (td, *J* = 7.7, 1.7 Hz, 1H), 6.99 (t, *J* = 7.7 Hz, 1H), 6.89 (td, *J* = 7.5, 1.2 Hz, 1H), 6.74 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.11 (dd, *J* = 12.2, 5.9 Hz, 1H), 3.69 (s, 1H), 3.08 – 2.96 (m, 2H), 2.93 – 2.84 (m, 1H), 2.82 (s, 1H), 0.70 (s, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.6, 152.9, 137.1, 134.3, 128.7, 127.8, 127.1, 123.8, 121.0, 120.5, 119.5, 119.2, 116.2, 108.4, 103.9, 93.3, 54.3, 46.6, 33.6, 32.3, 28.2, 21.9.

HRMS (ESI–TOF) calcd for $C_{24}H_{24}BrN_2O_2^+$ ([M+H$^+$]) = 451.1016, Found 451.1008.

7. Experimental procedure for the scale-up reaction and transformation of the product 3aa

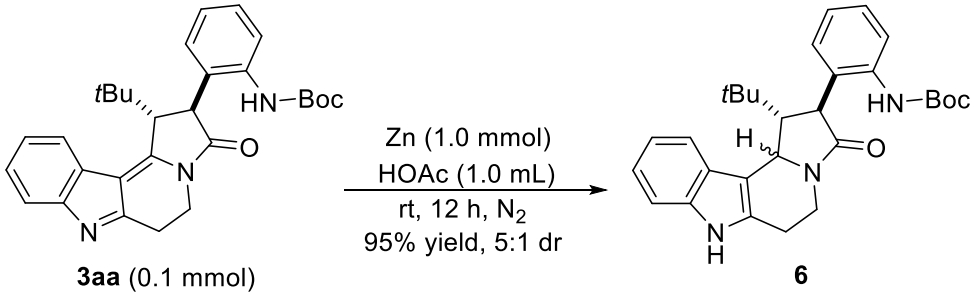
a) Scale-up version of the reaction



1a (3.0 mmol) **2a** (3.0 mmol) **3aa** (1.28 g, 90% yield)

Procedure: A dry round bottle was charged with **1a** (3.0 mmol, 510 mg) and **2a** (3.0 mmol, 900 mg). Then $ClCH_2CH_2Cl$ (30 mL) was added. The reaction mixture was stirred at 70 ℃ for 22 h under N_2. TLC monitored the reaction. The $ClCH_2CH_2Cl$ was removed under reduced pressure after the starting material was completed. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate= 1/2 as eluent to afford the desired product **3aa** in 90% yield.

b) Transformation of the product 3aa

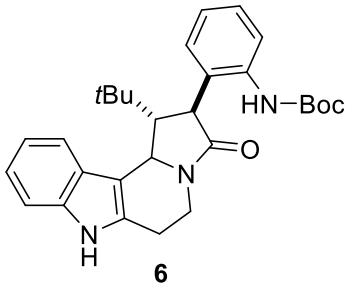


3aa (0.1 mmol) **6**

Procedure: A dry round bottle was charged with **3aa** (0.1 mmol) and Zn (1.0 mmol). Then HOAc (1.0 mL) was added under N_2. The reaction mixture was stirred at room temperature for 12 h. After the starting material was consumed, the reaction is quenched with $NaHCO_3$ and filtered. The filtrate was extracted with EtOAc, washed with water, dried over anhydrous Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by flash silica gel column chromatography using petroleum ether/ethyl acetate = 2/1 as eluent to afford the desired product **6** in 95% yield, with 5:1 dr.

(2-(1-(tert-butyl)-3-oxo-2,3,5,6,6a,7-hexahydro-1H-indolizino[7,8-b]indol-2-yl)phenyl) carbamate 6

The reaction was run at rt for 12 h, affording product **6** in 95% yield as a white solid. R_f = 0.6 (PE:EA = 1:2), m.p. 170.3–171.8 °C.



6

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.00 (s, 1H), 9.09 (s, 1H), 7.69 – 7.39 (m, 2H), 7.39 – 7.07 (m, 4H), 7.07 – 6.88 (m, 2H), 5.28 (d, J = 5.5 Hz, 1H), 4.39 (d, J = 11.5 Hz, 1H), 4.03 (s, 1H), 3.09 – 2.74 (m, 3H), 2.68 (d, J = 5.5 Hz, 1H), 1.47 (s, 9H), 0.79 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 173.7, 153.5, 137.0, 135.7, 132.8, 132.1, 127.1, 126.5, 126.5, 126.1, 124.8, 120.7, 118.7, 118.6, 110.9, 106.6, 78.7, 55.6, 53.5, 48.3, 36.9, 33.6, 28.3, 28.0, 22.6.

HRMS (ESI–TOF) calcd for $C_{29}H_{36}N_3O_3^+$ ([M+H$^+$]) = 474.2751, Found 474.2742.

8. Quantum chemical calculations

The exchange and correlation electronic effects are considered by employing the density functional theory (DFT)[4] at the M06-2X-D3 level,[5] which included Grimme's zero-damping D3-dispersion correction.[6] The ultrafine grid (99,590), having 99 radial shells and 590 angular points per shell, is used to evaluate the numerical integration accuracy. Geometry optimizations are performed with the double-zeta basis set 6-31G(d,p) in the dichloroethane medium while using Truhlar's SMD solvation model.[7] The temperature is set to 343.15 K for thermochemistry analysis. Based on the optimized structures, the electronic energy (E_{electron}) and solvation free energy (ΔG_{solv}) are calculated at the same level of theory. The harmonic vibrational frequencies are analyzed after the geometry optimizations to characterize the nature of the stationary point as a minimum with all positive frequencies or as a transition state with only one imaginary frequency and to provide the zero-point energy (E_{ZPE}), total entropy (S_{tot}) and thermal correction to enthalpy (H_{corr}) at the same theoretical level. The Gibbs free energies of free substrates (G_i) are defined as reference-point. In addition, the intrinsic reaction coordinate (IRC)[8] calculations are carried out to verify the transition state (TS) associated with the correct reactant complexes (RC), intermediate (IM) and product complexes (PC) at the same level of theory. All calculations were carried out with Gaussian 16 program.[9]

$$G = E_{\text{electron}} + \Delta G_{\text{solv}} + E_{\text{ZPE}} + H_{\text{corr}} - TS_{\text{tot}} \qquad (1)$$

$$\Delta G = G - \sum_i G_i \qquad (2)$$

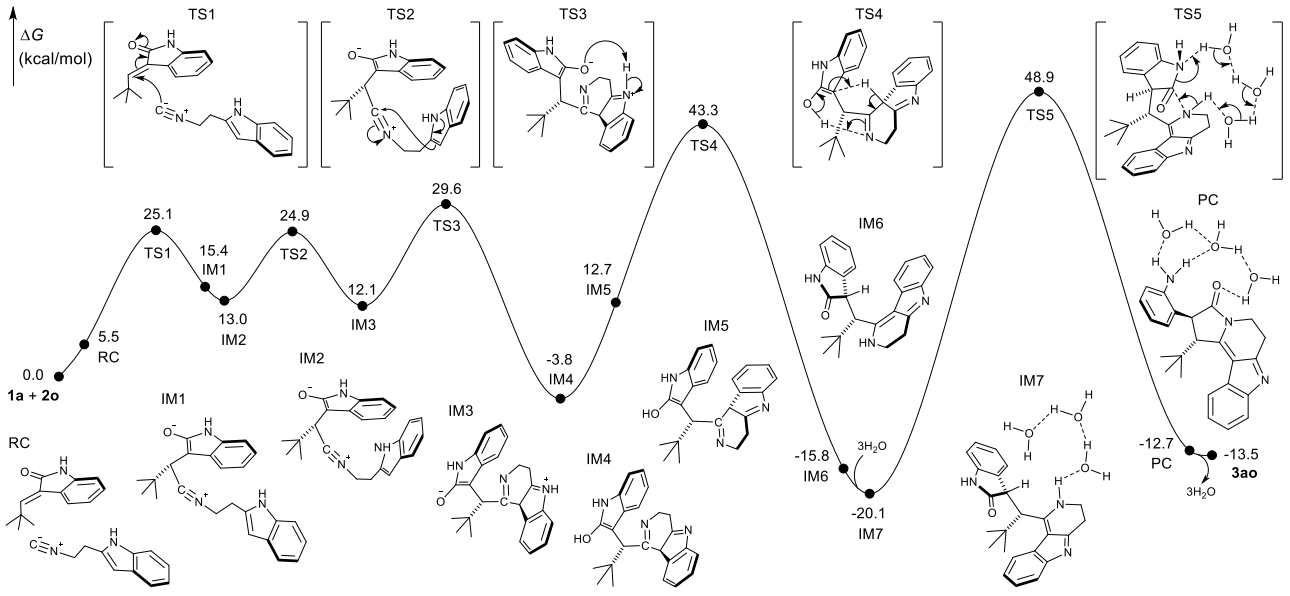


Figure 1. The relative energy profiles (kcal/mol) of reaction pathways at the M06-2X-D3/6-31G(d,p)/SMD(Dichloroethane) level of theory.

Cartesian coordinate for theoretical calculation

1a

C	-1.33778900	0.69150000	0.00016900
C	-1.50949700	-0.71597900	0.00003700
C	-2.77277600	-1.31668700	-0.00024400
C	-3.87651500	-0.47841600	-0.00038500
C	-3.73085900	0.92374200	-0.00025200
C	-2.47738100	1.51358600	0.00001900
C	0.07812300	0.93606100	0.00045200
H	-2.88052500	-2.39683200	-0.00034600
H	-4.87252300	-0.91005500	-0.00059900
H	-4.61865100	1.54839200	-0.00036400
H	-2.37377800	2.59483600	0.00012200
N	-0.25624200	-1.27939900	0.00022100
C	0.69876000	-0.28699700	0.00044200
H	0.56753100	1.89997700	0.00060000
C	2.15079400	-0.64681300	0.00070100
H	2.38715300	-1.25236800	0.88282600
H	2.38702600	-1.25396700	-0.88035500
H	-0.05789200	-2.27046200	0.00011800
C	3.02796100	0.60253000	-0.00049400
H	2.83661000	1.21306900	0.88578600
H	2.83639000	1.21151400	-0.88779200
C	5.53497600	-0.07474100	-0.00028000
N	4.40965300	0.24071100	-0.00036200

2o

C	-0.89756000	-0.24396100	0.00009900
C	-2.09677700	0.50351400	0.00005400
C	-3.34963700	-0.08883400	0.00019000
C	-3.40820800	-1.48366000	0.00039300
C	-2.24299600	-2.24740300	0.00045500
C	-0.98704900	-1.63448100	0.00031000
C	0.20798800	0.73481600	-0.00006900
H	-4.25004600	0.51653000	0.00014600
H	-4.37606500	-1.97488800	0.00050600
H	-2.30626900	-3.33027700	0.00062000
H	-0.09916000	-2.25483800	0.00037000
C	-0.45099600	2.09528300	-0.00017400
O	0.08603900	3.18862200	-0.00032400
N	-1.80508500	1.86612900	-0.00014100
H	-2.49327400	2.60702100	-0.00014400
C	1.55152300	0.70959200	-0.00015800
H	1.99823400	1.70627600	-0.00026400
C	2.52233700	-0.44980400	-0.00013600

C	2.33139700	-1.29610000	1.26907000
H	3.01515600	-2.15153000	1.25165800
H	2.55290700	-0.70076700	2.16038500
H	1.31140700	-1.67340500	1.36670700
C	2.33127100	-1.29628200	-1.26919800
H	2.55276000	-0.70109600	-2.16061700
H	3.01498600	-2.15174500	-1.25169900
H	1.31125800	-1.67354900	-1.36672300
C	3.95126500	0.10876100	-0.00025500
H	4.13060800	0.72546600	0.88658600
H	4.67888800	-0.70899600	-0.00019800
H	4.13053400	0.72527600	-0.88724300

RC

C	1.61555500	-1.15435400	0.56748100
C	0.35349700	-1.38384800	1.16476500
C	-0.39228100	-2.53292100	0.93928400
C	0.12571300	-3.48396800	0.05719500
C	1.35572600	-3.27662800	-0.56242100
C	2.10304300	-2.12233200	-0.30855600
C	2.07787000	0.16577800	1.05700600
H	-1.34433500	-2.68122400	1.44109300
H	-0.43759100	-4.38992300	-0.14226800
H	1.74710700	-4.01915700	-1.24947300
H	3.05205600	-1.99779700	-0.80884300
C	0.96476300	0.67164500	1.95629100
O	0.91158400	1.72404400	2.56592500
N	-0.00228800	-0.30314200	1.96390500
H	-0.86814300	-0.22188100	2.48113700
C	3.13221200	0.99484600	0.94504700
H	2.98091500	1.91421900	1.51796500
C	4.46701600	0.99048700	0.25154900
C	4.83394200	-0.29805300	-0.47625500
H	5.86056600	-0.22195400	-0.84929000
H	4.18290500	-0.45968000	-1.33909500
H	4.78250700	-1.16312000	0.19204900
C	5.52373400	1.27700400	1.33478500
H	5.30255300	2.20603500	1.86971900
H	6.50975600	1.37574800	0.86941900
H	5.56743200	0.46215700	2.06435000
C	4.45134500	2.15779000	-0.75288800
H	3.70570300	1.98577100	-1.53548700
H	5.43431200	2.24747900	-1.22740200
H	4.22253700	3.10608200	-0.25610200
C	-4.14788400	1.25797600	-0.44738300

C	-3.77081600	-0.03579300	-0.00543700
C	-4.66060300	-0.89453200	0.64926400
C	-5.94929800	-0.43325200	0.86327900
C	-6.34705500	0.85049600	0.43623400
C	-5.46324800	1.69555200	-0.21418000
C	-2.99066500	1.83294500	-1.07368100
H	-4.35026600	-1.88285900	0.97461600
H	-6.66663400	-1.07201600	1.36894400
H	-7.36518200	1.17789100	0.62209200
H	-5.77891300	2.68239100	-0.54013400
N	-2.45137600	-0.21593100	-0.34401100
C	-1.98178300	0.90939900	-0.98895500
H	-2.90808200	2.81130200	-1.52590600
C	-0.56559700	0.99666500	-1.45786600
H	0.12089900	1.07817200	-0.60693200
H	-0.44980200	1.90224500	-2.05807900
H	-1.91590000	-1.05893000	-0.18064500
C	-0.15875900	-0.22217200	-2.29466300
H	-0.21124200	-1.14814900	-1.71118200
H	-0.80269000	-0.32498200	-3.17176400
C	2.28866400	0.05434800	-3.11514400
N	1.18885200	-0.08130400	-2.74485300

TS1

C	-1.49130600	1.15748900	-0.12588800
C	-0.75777100	1.94436900	0.80742200
C	0.33091600	2.72025800	0.44267900
C	0.73704700	2.69505800	-0.89688300
C	0.08185400	1.87802700	-1.81998300
C	-1.02110600	1.10315000	-1.44120400
C	-2.52086900	0.46541000	0.62995800
H	0.86009200	3.31450800	1.18093500
H	1.58084900	3.30188800	-1.21074500
H	0.42734600	1.84294200	-2.84842100
H	-1.49944600	0.46620600	-2.17540100
C	-2.30473500	0.79256300	2.04544300
O	-2.89229300	0.37932400	3.04260300
N	-1.28386900	1.73665100	2.07192100
H	-0.92607400	2.14030300	2.92662600
C	-3.46803300	-0.52560400	0.33144500
H	-3.89412900	-0.91853600	1.26014700
C	-4.53053500	-0.53792900	-0.76949100
C	-4.00336700	-0.20345100	-2.16161100
H	-4.82054200	-0.26947700	-2.88719200
H	-3.22461000	-0.91032100	-2.47093400

H	-3.60116200	0.81189500	-2.20170700
C	-5.54275200	0.54063800	-0.33922400
H	-5.94667700	0.33098400	0.65674500
H	-6.37625300	0.56270300	-1.04860300
H	-5.07606300	1.52936800	-0.31954900
C	-5.23828000	-1.89446500	-0.79790100
H	-4.57309800	-2.68274200	-1.16363600
H	-6.10536600	-1.84655900	-1.46359400
H	-5.58871300	-2.17879200	0.20015300
C	4.49704800	-1.09080700	0.40596300
C	3.94860700	0.02425300	-0.27962700
C	4.74846200	0.98239900	-0.91287000
C	6.12100400	0.80582000	-0.85426400
C	6.68943500	-0.29595400	-0.18152000
C	5.89449600	-1.24023500	0.44619800
C	3.38862000	-1.84075200	0.92679000
H	4.30537500	1.82804100	-1.42964400
H	6.77222400	1.52898600	-1.33520800
H	7.76956200	-0.40132700	-0.15747800
H	6.34125900	-2.08484700	0.96278400
N	2.58254600	-0.06053500	-0.17441100
C	2.24651700	-1.17887900	0.55738400
H	3.42772900	-2.75365200	1.50457200
C	0.80910900	-1.51641900	0.77689300
H	0.24521800	-0.60740200	1.01527200
H	0.70880800	-2.20857800	1.61551900
H	1.91894200	0.61803500	-0.53399400
C	0.20657700	-2.15268800	-0.48716400
H	0.44243200	-1.55987000	-1.37540800
H	0.57728900	-3.16915300	-0.63265700
C	-2.34727900	-1.98753300	-0.15014200
N	-1.21990600	-2.18861600	-0.37234400

IM1

C	1.59986300	1.13240000	0.29833100
C	1.24021100	2.34235300	-0.37821800
C	0.16325300	3.12034700	0.01482800
C	-0.60155800	2.69715500	1.11107500
C	-0.27587600	1.51681800	1.78587800
C	0.81193700	0.73164200	1.38841000
C	2.71571000	0.58082400	-0.40924800
H	-0.08619700	4.03017300	-0.52337100
H	-1.44586200	3.29591400	1.43868000
H	-0.87279600	1.20398400	2.63854600
H	1.04736200	-0.17727500	1.93561500

C	2.99472600	1.41617700	-1.53899500
O	3.82096600	1.28055500	-2.45489900
N	2.11096600	2.50388200	-1.43706100
H	2.07391900	3.24625000	-2.12060100
C	3.33099300	-0.78290600	-0.33623100
H	3.81536800	-0.96002600	-1.30843600
C	4.35193500	-1.15011100	0.78037500
C	3.74611800	-0.94030700	2.16719500
H	4.48834500	-1.17565000	2.93664000
H	2.88085900	-1.59474300	2.33033800
H	3.42876600	0.09773700	2.30441600
C	5.55649800	-0.22689000	0.59220200
H	6.00319300	-0.35880600	-0.39896600
H	6.31790200	-0.45124400	1.34565300
H	5.26336300	0.82166300	0.69833300
C	4.77333700	-2.60992100	0.60283500
H	3.92178800	-3.29032700	0.72598500
H	5.52423300	-2.88101900	1.35123400
H	5.20484200	-2.77815600	-0.38963400
C	-4.66815000	-1.00351800	-0.58871100
C	-4.13557700	0.05642000	0.19047100
C	-4.94309900	0.89747400	0.96517900
C	-6.30673000	0.65704800	0.95431700
C	-6.85944100	-0.39308900	0.19100600
C	-6.05764200	-1.22032200	-0.57683500
C	-3.55702300	-1.63039700	-1.24756900
H	-4.51115900	1.70432600	1.54935900
H	-6.96366300	1.28838400	1.54437900
H	-7.93331500	-0.55066000	0.20812200
H	-6.49247900	-2.02474100	-1.16301600
N	-2.77534800	0.05539700	0.01026500
C	-2.42911800	-0.95222200	-0.86287400
H	-3.58629800	-2.47345000	-1.92385600
C	-0.98922300	-1.18516000	-1.18421900
H	-0.44290800	-0.23776500	-1.11876000
H	-0.87764400	-1.57651100	-2.19733100
H	-2.12211500	0.72765000	0.40141100
C	-0.37039500	-2.17643000	-0.18213200
H	-0.65093300	-1.92741500	0.84502800
H	-0.64923400	-3.20871600	-0.39502100
C	2.12758200	-1.62402300	-0.30846500
N	1.06251800	-2.06130700	-0.23708900

IM2

C	-0.88815100	-1.07733200	0.89106900

C	0.06880000	-2.14227200	0.82734100
C	0.78001100	-2.56708300	1.93874300
C	0.56439500	-1.91454700	3.16172500
C	-0.35923300	-0.86998000	3.24935700
C	-1.09014400	-0.45145300	2.13123900
C	-1.36494400	-0.87579000	-0.43840500
H	1.49897400	-3.37779000	1.85711700
H	1.11781800	-2.22723000	4.04109700
H	-0.51845100	-0.37383800	4.20260000
H	-1.80422900	0.36227300	2.22941200
C	-0.67438400	-1.76942500	-1.31440000
O	-0.72995400	-1.89242500	-2.54897500
N	0.14393600	-2.55850100	-0.48513700
H	0.79178600	-3.24254200	-0.84846900
C	-2.20048200	0.22088800	-1.01823900
H	-1.95881300	0.26004300	-2.09216200
C	-3.75628600	0.18467400	-0.88556600
C	-4.17402300	0.15642000	0.58403900
H	-5.26448500	0.09858300	0.66086500
H	-3.85231100	1.06365200	1.11051200
H	-3.74785700	-0.71148500	1.09612900
C	-4.22739200	-1.08938300	-1.58745100
H	-3.92420200	-1.09474100	-2.63952700
H	-5.31907600	-1.15438100	-1.54259000
H	-3.80763700	-1.97728100	-1.10635300
C	-4.34541000	1.41409200	-1.58047400
H	-4.02277100	2.34383100	-1.09620200
H	-5.43850000	1.38374600	-1.53964100
H	-4.04465600	1.45395200	-2.63279700
C	3.13666300	1.26494400	-0.80161800
C	2.77669200	0.15697000	0.00859400
C	3.29512800	-1.12631500	-0.20669300
C	4.18149000	-1.28767900	-1.25775600
C	4.55206600	-0.20080100	-2.07817600
C	4.04206200	1.06689300	-1.86006600
C	2.42335100	2.39880900	-0.29038800
H	3.00821700	-1.95606600	0.43122900
H	4.60063700	-2.26948300	-1.45486400
H	5.24961100	-0.36699000	-2.89320600
H	4.33335100	1.89846200	-2.49529200
N	1.89390900	0.61102800	0.95679200
C	1.68024500	1.95784400	0.77655100
H	2.45662800	3.41349400	-0.66310900
C	0.71702300	2.70436500	1.64856400
H	1.21716000	3.52764800	2.16714700

H	0.30064300	2.03482500	2.40604400
H	1.43497800	0.03975600	1.65913500
C	-0.42523900	3.33049900	0.84211100
H	-1.14827000	3.83213200	1.48805700
H	-0.05370000	4.03875800	0.09877400
C	-1.63968700	1.44534800	-0.44110300
N	-1.13792100	2.31346700	0.12176000

TS2

C	0.03959800	0.98462200	-1.24827400
C	-1.16770000	0.86167400	-2.01431400
C	-1.94377200	1.95665800	-2.35964200
C	-1.52244700	3.23155000	-1.95447400
C	-0.33199200	3.38301100	-1.23800200
C	0.45484800	2.27984100	-0.89221300
C	0.51651400	-0.33798900	-1.01725200
H	-2.85970900	1.82470200	-2.92970200
H	-2.11628600	4.10185500	-2.21541500
H	-0.00244700	4.37850800	-0.95190200
H	1.38480400	2.43174700	-0.34987700
C	-0.38221100	-1.26228600	-1.62839700
O	-0.37103800	-2.50617700	-1.65536300
N	-1.35850500	-0.47875000	-2.27444800
H	-2.17869300	-0.88139800	-2.70366300
C	1.57686900	-0.84817000	-0.09695000
H	1.25400000	-1.84657500	0.23284600
C	3.03451900	-1.00613300	-0.67096800
C	3.56670600	0.32579300	-1.19879400
H	4.54000500	0.17181400	-1.67659100
H	3.70290800	1.05790000	-0.39594700
H	2.88393200	0.74698000	-1.94337600
C	2.92599400	-2.00717600	-1.82583300
H	2.51924600	-2.96314300	-1.48273600
H	3.91937100	-2.18171700	-2.25246200
H	2.26887400	-1.62642900	-2.61157500
C	3.96907200	-1.57278400	0.40072300
H	4.11739500	-0.87145600	1.22789100
H	4.95137400	-1.78253300	-0.03444800
H	3.57470400	-2.51031400	0.80849300
C	-1.34464300	-1.14120900	1.67107100
C	-2.19353000	-0.16500400	1.10451400
C	-3.34292400	-0.49198700	0.38649300
C	-3.63571400	-1.84163700	0.25048700
C	-2.80924800	-2.83199100	0.81311500
C	-1.66488000	-2.49689400	1.52002100

C	-0.27318200	-0.42872200	2.32621800
H	-3.97167300	0.27841200	-0.04854100
H	-4.52196200	-2.13989300	-0.30077200
H	-3.07239600	-3.87671500	0.68287600
H	-1.02851300	-3.26572300	1.94768000
N	-1.67545500	1.07749600	1.42581100
C	-0.55182000	0.93370600	2.16761800
H	0.41957500	-0.84190500	3.04951700
C	0.24658900	2.09634100	2.63684400
H	-0.10775000	2.43191300	3.61750100
H	0.12438100	2.92489200	1.93266100
H	-1.98491700	1.95502200	1.02348800
C	1.73299600	1.73916700	2.79572400
H	2.34539400	2.63983200	2.80686900
H	1.92144300	1.18014800	3.71655400
C	1.60843600	0.01744500	1.09945200
N	2.15349900	0.89361500	1.69585500

IM3

C	0.09408800	0.75674400	1.34930000
C	1.32538300	0.47565300	2.03235000
C	2.15530000	1.47440400	2.51981500
C	1.76855500	2.81008300	2.34775100
C	0.56214400	3.11411200	1.70874300
C	-0.27736900	2.10925000	1.22056300
C	-0.46302200	-0.49561300	0.94902200
H	3.08295900	1.22057200	3.02625300
H	2.40232700	3.60658800	2.72494900
H	0.26099200	4.15313000	1.60087400
H	-1.21787900	2.37202200	0.74348400
C	0.40579800	-1.53385200	1.40506500
O	0.33096800	-2.77042200	1.27615200
N	1.47135300	-0.89354100	2.06751900
H	2.24562600	-1.39623200	2.47550400
C	-1.56968600	-0.80752600	-0.01824400
H	-1.32293100	-1.80982900	-0.40364100
C	-3.00715500	-0.92544100	0.56789200
C	-3.44717400	0.33877800	1.31305900
H	-4.42030600	0.16942700	1.78925600
H	-3.53854700	1.19166600	0.63723500
H	-2.72835600	0.59196100	2.09966400
C	-2.98310600	-2.08969900	1.56758300
H	-2.66976400	-3.02121000	1.08453100
H	-3.98092600	-2.24011200	1.99483200
H	-2.28293900	-1.88946900	2.38370900

C	-4.01166300	-1.26141600	-0.54066100
H	-4.12976600	-0.43335600	-1.24335600
H	-4.99391300	-1.48208200	-0.10782500
H	-3.69010100	-2.14731400	-1.10190700
C	1.04210600	-0.90442000	-1.60199600
C	2.13476800	-0.09195800	-1.27367100
C	3.36412600	-0.57388800	-0.86582500
C	3.48879500	-1.96287900	-0.80427300
C	2.42485900	-2.79841400	-1.15317100
C	1.19430600	-2.28236500	-1.56354200
C	-0.08261600	-0.00837900	-2.02979300
H	4.18136700	0.09227000	-0.61154900
H	4.43078800	-2.39802300	-0.48794800
H	2.55507600	-3.87389500	-1.09688900
H	0.37588500	-2.94363300	-1.82573000
N	1.74314500	1.25676600	-1.47083400
C	0.53429500	1.34273300	-1.93902000
H	-0.42475500	-0.19904200	-3.05777700
C	-0.26345600	2.55280100	-2.20988400
H	0.12014400	3.05669500	-3.10412900
H	-0.16479700	3.24316800	-1.36504100
H	2.32065200	2.06015500	-1.22627900
C	-1.72229300	2.10996200	-2.41972600
H	-2.37639500	2.98150900	-2.37841000
H	-1.82634900	1.66579600	-3.41864900
C	-1.38996700	0.15400400	-1.17417500
N	-2.14563000	1.14771400	-1.40573400

TS3

C	-2.43456500	0.09515400	-0.38137700
C	-3.02533900	-1.00207900	-1.08047800
C	-4.38477100	-1.29299400	-1.04016600
C	-5.20231600	-0.49820700	-0.23976600
C	-4.64875200	0.54734100	0.50939600
C	-3.28848200	0.84173400	0.45193500
C	-1.02199600	0.08947200	-0.68577100
H	-4.78557100	-2.13055900	-1.60400100
H	-6.26658800	-0.70477100	-0.18328400
H	-5.28950000	1.13766400	1.15809800
H	-2.88963100	1.62883400	1.07812900
C	-0.78336000	-1.07510900	-1.45678100
O	0.29717500	-1.63858000	-1.84424100
N	-2.01456500	-1.67383200	-1.72169700
H	-2.10551500	-2.52714200	-2.25320600
C	0.11557000	0.93666600	-0.16332400

H	0.99387200	0.57601800	-0.71357400
C	0.12209700	2.47381200	-0.41666200
C	-1.00035600	3.22847800	0.29739300
H	-0.83148900	4.30731200	0.20461600
H	-1.03878900	2.98308600	1.36414600
H	-1.97237600	3.00825400	-0.14825400
C	0.00109600	2.70823200	-1.92496900
H	0.80586100	2.19941100	-2.46795500
H	0.06285500	3.77903300	-2.14848800
H	-0.95381700	2.33313600	-2.30478600
C	1.46788600	3.02980600	0.06432600
H	1.61344500	2.85673700	1.13828800
H	1.51403600	4.11064600	-0.10590200
H	2.30041200	2.56623800	-0.47410100
C	2.84543800	-0.21887600	0.66963300
C	2.65873800	-1.30944600	-0.17941800
C	3.46248700	-1.55744500	-1.28150800
C	4.52336500	-0.67884800	-1.48713800
C	4.75342900	0.39960700	-0.62345800
C	3.91328700	0.64686100	0.46142300
C	1.73935300	-0.25899600	1.65719600
H	3.27251400	-2.39507000	-1.94314000
H	5.18764400	-0.83635800	-2.33041500
H	5.59623900	1.05754900	-0.80754300
H	4.08297200	1.49493800	1.11696000
N	1.54232500	-2.06487200	0.26768200
C	1.08854700	-1.55824900	1.39571600
H	1.97095900	-0.00864600	2.69261500
C	-0.03447200	-1.97642200	2.27733500
H	0.32333300	-2.76518400	2.94907100
H	-0.86942500	-2.37630700	1.69509600
H	0.91597100	-2.39875300	-0.53670900
C	-0.45839100	-0.72169900	3.08258900
H	-1.42072100	-0.89276000	3.56567000
H	0.27643000	-0.50619800	3.86918900
C	0.35390400	0.50283100	1.29481200
N	-0.59131800	0.38181600	2.13084200

IM4

C	-0.07316000	0.84876800	-1.33593600
C	-1.23885900	0.65659100	-2.12341100
C	-1.97309100	1.71173300	-2.66205000
C	-1.52661700	3.00111500	-2.40509600
C	-0.36803200	3.22241700	-1.64051600
C	0.36254500	2.16681000	-1.11149300

C	0.40668900	-0.45974400	-0.94904700
H	-2.86114600	1.52473200	-3.25776600
H	-2.07638600	3.84704900	-2.80502200
H	-0.03408500	4.24058300	-1.46465000
H	1.26099400	2.35529700	-0.53257700
C	-0.46881700	-1.34914800	-1.52989900
O	-0.50869600	-2.69000800	-1.52119400
N	-1.45009400	-0.70351200	-2.22369700
H	-2.19432300	-1.16359700	-2.72952300
C	1.49190900	-0.83855000	0.03372700
H	1.23702700	-1.84178700	0.41458000
C	2.91671200	-0.98248900	-0.57602800
C	3.37332100	0.27934600	-1.31521700
H	4.35198900	0.10231600	-1.77580200
H	3.46043900	1.12756000	-0.63330300
H	2.67075900	0.54195800	-2.11296400
C	2.86212500	-2.14320900	-1.57989800
H	2.57167000	-3.07970900	-1.08584700
H	3.84742500	-2.29931700	-2.03107400
H	2.15103600	-1.94259300	-2.38788100
C	3.92627200	-1.34550000	0.51913000
H	4.08056800	-0.51714200	1.21305800
H	4.89162100	-1.59965000	0.06814900
H	3.58667000	-2.21751700	1.09132400
C	-1.09065200	-0.92558800	1.65277700
C	-2.14899700	-0.02965800	1.41212400
C	-3.38023900	-0.47341300	0.94955900
C	-3.54832100	-1.84707600	0.75564600
C	-2.51703700	-2.74449500	1.03686300
C	-1.27624300	-2.29017300	1.49665800
C	0.06811200	-0.09085600	2.10362300
H	-4.18163000	0.23150100	0.75260200
H	-4.50028500	-2.22320900	0.39391600
H	-2.67714200	-3.80799100	0.89027300
H	-0.47737400	-2.99504500	1.71261400
N	-1.78784200	1.31536900	1.68927400
C	-0.57295200	1.28594300	2.10775700
H	0.41332100	-0.35461200	3.11447300
C	0.30397300	2.44619400	2.43907500
H	-0.01653300	2.91730300	3.37424000
H	0.22232400	3.19729600	1.64686100
H	0.18682200	-3.02541600	-0.93497400
C	1.75166400	1.94112500	2.57446200
H	2.44522500	2.78353400	2.58584800
H	1.86331400	1.41280800	3.53127600

C	1.32698500	0.08139200	1.23299400
N	2.12415300	1.04192800	1.47969200

IM5

C	2.41711200	0.50855600	-0.14042800
C	3.46389600	0.01671400	-0.97525300
C	4.42589200	0.82931100	-1.57146600
C	4.35012000	2.19541100	-1.34453900
C	3.33267700	2.72018300	-0.53309800
C	2.38307100	1.90244300	0.06483900
C	1.64505800	-0.64582500	0.28995000
H	5.20212000	0.39613400	-2.19482200
H	5.08029400	2.85899400	-1.79613300
H	3.28539800	3.79130200	-0.36277400
H	1.62815400	2.35628400	0.69199800
C	2.24627300	-1.72633300	-0.33256800
O	1.92828100	-3.02841900	-0.30771400
N	3.32615000	-1.35039000	-1.07041300
H	3.90542100	-1.97965200	-1.60911400
C	0.39958500	-0.96936200	1.09737400
H	0.61408300	-1.97304300	1.47722800
C	0.03680800	-0.25997500	2.45168000
C	0.31880100	1.23661000	2.56536200
H	-0.01384100	1.58129400	3.55087300
H	-0.21074600	1.82843800	1.81962800
H	1.39086000	1.43696500	2.49605900
C	0.89365500	-0.94507300	3.53114800
H	0.63044900	-2.00331400	3.63363400
H	0.74658500	-0.46153800	4.50243200
H	1.95805400	-0.88046800	3.27816300
C	-1.44221600	-0.52309900	2.75812300
H	-2.09656700	0.00222700	2.05209800
H	-1.68318600	-0.16948800	3.76602000
H	-1.67464000	-1.59216700	2.70776900
C	-1.87626600	0.99074800	-0.56595700
C	-3.26525900	0.95334400	-0.77967400
C	-4.06501900	2.07179100	-0.58777500
C	-3.44048100	3.26412700	-0.21641500
C	-2.05290700	3.33211900	-0.08635300
C	-1.25863700	2.19675800	-0.28039000
C	-1.35273200	-0.37574600	-0.92323800
H	-5.13608300	2.01745000	-0.75365400
H	-4.03796500	4.15707000	-0.06177400
H	-1.58034800	4.27949900	0.15271100
H	-0.17829400	2.26814900	-0.23459300

N	-3.69301700	-0.30054900	-1.29008600
C	-2.63331500	-1.01540700	-1.42206700
H	-0.60901300	-0.30543900	-1.73003800
C	-2.56649800	-2.42033200	-1.88099700
H	-1.89468800	-2.47816200	-2.74444000
H	-3.55058400	-2.79361400	-2.16982800
H	0.99413100	-3.13348200	-0.03542400
C	-1.98145900	-3.24914700	-0.72433700
H	-2.78514100	-3.53115900	-0.03445700
H	-1.55447000	-4.18139000	-1.10315100
C	-0.72990200	-1.34100100	0.11477800
N	-0.96824300	-2.59826600	0.09065500

TS4

C	2.18194600	-0.00364000	-0.20758800
C	2.86586300	-0.11925900	-1.43835700
C	4.01749400	0.58508300	-1.76538700
C	4.52568900	1.45066000	-0.80639900
C	3.87481800	1.59910900	0.42375700
C	2.71367900	0.89541100	0.72561200
C	0.96001400	-0.84432700	-0.30694800
H	4.49078500	0.45545100	-2.73297700
H	5.42652600	2.01758600	-1.01581100
H	4.27791700	2.28518700	1.16150000
H	2.23977500	1.06298600	1.68147600
C	1.10770600	-1.47280200	-1.58820600
O	0.32695200	-2.35754200	-2.17222400
N	2.17788500	-1.02805400	-2.24254500
H	2.41086200	-1.27596700	-3.19814400
C	0.02653400	-1.67011800	0.62467700
H	0.17581000	-2.70574300	0.30420100
C	0.08146100	-1.77836900	2.19859300
C	1.35134000	-1.20338000	2.82457400
H	1.45187200	-1.58554300	3.84610400
H	1.31014200	-0.11508300	2.89547000
H	2.24960300	-1.48755800	2.26780100
C	0.04049700	-3.28524900	2.51057800
H	-0.82906400	-3.75563700	2.03849500
H	-0.02606200	-3.44791900	3.59109200
H	0.94307300	-3.78562600	2.14245700
C	-1.15087900	-1.15214000	2.86847700
H	-1.26097900	-0.08832500	2.65165200
H	-1.06440000	-1.26539700	3.95431900
H	-2.06921800	-1.65888800	2.55408900
C	-1.34791700	1.44308800	0.32991600

C	-2.13711800	2.32537200	-0.45713900
C	-2.14829300	3.69853900	-0.20805800
C	-1.36448000	4.19613900	0.82745900
C	-0.57135800	3.33455500	1.59789200
C	-0.54949200	1.96427900	1.35115000
C	-1.53360500	0.12746400	-0.29630100
H	-2.76035000	4.35399300	-0.82078200
H	-1.36233800	5.26083800	1.03957800
H	0.03839200	3.74007700	2.39964400
H	0.07596500	1.31617300	1.95417000
N	-2.85273300	1.65473700	-1.45295500
C	-2.51197900	0.39645900	-1.33210900
H	-0.12022500	-0.01536300	-0.68878100
C	-3.10668800	-0.75186500	-2.08221700
H	-2.41713000	-1.10139800	-2.86248700
H	-4.04184900	-0.45846000	-2.56424300
H	-0.44742400	-2.58555600	-1.61217900
C	-3.33177500	-1.88031100	-1.06734900
H	-4.07121900	-1.56205000	-0.32073400
H	-3.72194000	-2.77287900	-1.56104000
C	-1.35571400	-1.29244000	0.07238900
N	-2.08809300	-2.24641400	-0.37895200

IM6

C	2.53805800	0.41511700	-0.23395100
C	3.31163600	0.11910400	-1.36740000
C	4.63560500	0.51241100	-1.49857500
C	5.19394400	1.25639100	-0.45831400
C	4.43389000	1.60882900	0.65485700
C	3.10025000	1.20106900	0.76276200
C	1.12994200	-0.09834700	-0.46730800
H	5.20606700	0.26144500	-2.38664700
H	6.22836200	1.57724000	-0.52980700
H	4.87482900	2.20901000	1.44355300
H	2.52230700	1.49651200	1.63158400
C	1.23095400	-0.68963600	-1.88963400
O	0.33941500	-1.22642900	-2.51813300
N	2.52842000	-0.55677700	-2.30416100
H	2.84557400	-0.86187500	-3.21561300
C	0.46058300	-1.21400000	0.39949700
H	0.90368100	-2.15809800	0.05441600
C	0.64625600	-1.29309300	1.95993800
C	2.10182100	-1.66054400	2.28227600
H	2.19944800	-1.83454200	3.35899300
H	2.80939200	-0.87972700	2.00625700

H	2.39301700	-2.58232600	1.76619100
C	-0.22534100	-2.44043000	2.50237400
H	-1.29472100	-2.22888500	2.40440800
H	-0.00843200	-2.57455900	3.56646500
H	-0.01062900	-3.38824600	1.99628400
C	0.24200400	-0.02508300	2.71027000
H	0.86655500	0.83081700	2.44996900
H	0.35318700	-0.19476800	3.78665300
H	-0.80273900	0.23582200	2.51811600
C	-1.95544800	1.19692500	0.13457800
C	-3.24403000	1.60080200	-0.32197000
C	-3.66415000	2.92944600	-0.26173100
C	-2.79402900	3.88461600	0.24961000
C	-1.52126400	3.50843500	0.69620700
C	-1.09923600	2.18237000	0.64951700
C	-1.93489300	-0.24814900	-0.08806500
H	-4.65496600	3.19542800	-0.61823400
H	-3.09863000	4.92536500	0.30136300
H	-0.84598500	4.26197900	1.09001000
H	-0.10816700	1.94233600	1.01425800
N	-3.99222400	0.53593800	-0.82483800
C	-3.22898000	-0.51696800	-0.68338500
H	0.45201100	0.75603400	-0.53485100
C	-3.57602600	-1.88203400	-1.18849800
H	-3.25020500	-1.96828200	-2.23346500
H	-4.65449700	-2.05026100	-1.15472600
H	-0.75693300	-3.29072400	-0.20154800
C	-2.84150800	-2.90245900	-0.33491300
H	-3.26873400	-2.91367500	0.67851700
H	-2.90674400	-3.90759900	-0.75147500
C	-1.01138200	-1.29674400	0.00853500
N	-1.43338300	-2.54132500	-0.24181200

IM7

C	2.41226800	-0.93395400	-0.07698300
C	2.34804100	-1.81258400	-1.17135000
C	3.24153800	-2.86024800	-1.34584900
C	4.25522200	-3.00980600	-0.39622000
C	4.37334200	-2.11920800	0.66805400
C	3.45844100	-1.07116200	0.82397500
C	1.31912600	0.10676700	-0.23358300
H	3.16336100	-3.52296000	-2.20143900
H	4.96913900	-3.82028900	-0.50475400
H	5.18390300	-2.23177500	1.38023300
H	3.57928200	-0.37192200	1.64364000

C	0.81707100	-0.18388400	-1.66794300
O	0.05844500	0.48276400	-2.34042400
N	1.34095200	-1.39837800	-2.04174100
H	1.18523800	-1.78823200	-2.96254400
C	0.07987500	-0.00039200	0.71872200
H	-0.31978600	-1.01137500	0.58995900
C	0.33619400	0.19645500	2.25903100
C	-0.98201700	0.55602400	2.96755300
H	-0.81136100	0.58073000	4.04882200
H	-1.76331400	-0.18462100	2.76621700
H	-1.35571400	1.53947200	2.66626200
C	1.34219500	1.31718500	2.54248000
H	2.29999400	1.17968700	2.03377200
H	1.53164400	1.37037400	3.62002300
H	0.94494300	2.28792100	2.22999000
C	0.80815800	-1.12953000	2.87340900
H	0.04227000	-1.90250400	2.74168700
H	0.96865300	-0.99895400	3.94889400
H	1.73468600	-1.50086500	2.43785600
C	-3.01906200	-0.73505400	0.10777500
C	-4.24151000	-0.51911000	-0.59521300
C	-5.22777300	-1.50578700	-0.64364000
C	-5.00022200	-2.71156400	0.01125200
C	-3.80692700	-2.92804200	0.71596100
C	-2.81891400	-1.94910200	0.77871200
C	-2.29923200	0.51089900	-0.05417000
H	-6.15142500	-1.32187000	-1.18510800
H	-5.75435600	-3.49228800	-0.01797500
H	-3.65194700	-3.87350000	1.22717000
H	-1.91368700	-2.13892600	1.34898100
N	-4.29921700	0.74560600	-1.18576600
C	-3.17123500	1.32986200	-0.84933400
H	1.73274000	1.11853100	-0.20367200
C	-2.69137000	2.66767000	-1.32234500
H	-3.52071600	3.36375400	-1.46823700
H	-2.17728200	2.54263000	-2.28391900
H	0.26309000	2.57197900	0.13640400
C	-1.71907500	3.21239600	-0.28038700
H	-1.20697700	4.10940800	-0.63100700
H	-2.27442200	3.46271700	0.63471200
C	-1.00203100	0.94196300	0.22499800
N	-0.69709100	2.22409700	0.05636800
O	1.74144000	3.68226900	0.16806500
H	1.71181800	4.17707500	0.99718000
H	3.88828200	1.26047100	-2.93164100

O	3.65341300	0.79485700	-2.11726600
H	4.07988500	-0.07186100	-2.17575400
H	2.57991200	3.17002700	0.21128700
O	3.92540900	2.06428800	0.28648100
H	4.78850100	2.48953300	0.37214700
H	3.93888500	1.59615900	-0.57550600

TS5

C	-2.86443800	0.61059200	-0.83002000
C	-3.51686100	-0.63538600	-0.65342300
C	-4.85999900	-0.80465100	-0.94976100
C	-5.57003700	0.28755000	-1.46141200
C	-4.93988600	1.50988100	-1.66336200
C	-3.58514500	1.67723500	-1.34199300
C	-1.47787200	0.38593400	-0.27790600
H	-5.34068800	-1.76820200	-0.80541500
H	-6.62051600	0.17167100	-1.71003100
H	-5.49874100	2.34643900	-2.07038000
H	-3.11734500	2.64128500	-1.50111200
C	-1.31072200	-1.11287100	-0.66171600
O	-1.07308300	-1.45168600	-1.86988500
N	-2.63533600	-1.63283500	-0.12313100
H	-2.83083800	-2.53862000	-0.55063200
C	-0.07907200	0.92584400	-0.56950800
H	0.04904400	0.97600300	-1.65856800
C	0.28696300	2.30523100	0.04335200
C	0.73913600	2.15039200	1.50242500
H	1.04334300	3.11978900	1.91135700
H	1.57529100	1.45585900	1.62218500
H	-0.09469100	1.78370100	2.11391000
C	-0.93949400	3.22589500	0.04831500
H	-1.30516600	3.38762700	-0.96927000
H	-0.65667600	4.20283500	0.45603500
H	-1.75477700	2.82663900	0.66032400
C	1.33140000	2.98007900	-0.86092800
H	2.11556800	2.29544900	-1.18394600
H	1.79814100	3.83738000	-0.36341800
H	0.83671300	3.34659400	-1.76681000
C	3.43075100	0.16315800	-0.18610000
C	4.39258400	-0.82126400	-0.53354400
C	5.75691200	-0.55301900	-0.55335200
C	6.18868300	0.71712300	-0.18263300
C	5.26299700	1.68170800	0.22304800
C	3.89425100	1.41337100	0.23864700
C	2.14564300	-0.55833600	-0.20676700

H	6.45587400	-1.33451300	-0.83457800
H	7.24821800	0.95305900	-0.18787200
H	5.61004500	2.66045900	0.53908100
H	3.22169100	2.18398900	0.58830500
N	3.81395300	-2.07327400	-0.79714600
C	2.54765700	-1.93648100	-0.55564800
H	-1.61363400	0.42202700	0.81671100
C	1.51523700	-2.98699200	-0.78004100
H	1.95071700	-3.98370700	-0.68443900
H	1.08721500	-2.87329200	-1.78114000
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H	0.81003500	-2.97161400	1.25397100
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H	0.67902400	-0.53218700	2.93547500
H	-3.23784400	-1.50364400	1.54338800
O	-3.71734900	-1.22279100	2.37205700
H	-4.55177200	-0.84814400	2.05620400
H	-0.99147200	-0.31475600	3.08344500
O	-2.07790300	0.40352900	3.40274100
H	-2.20231500	0.52184400	4.35597100
H	-2.83858000	-0.17911800	3.05125300

PC

C	-2.55306400	-0.56992600	-1.02084000
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C	-4.91760900	-0.42868500	-1.52999200
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C	-2.37807700	-1.27349800	-2.21415500
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H	-5.56077500	-1.31181200	-3.37030100
H	-3.27092900	-2.09767000	-3.99209200
H	-1.38221800	-1.62415400	-2.47614900
C	-0.96144300	-1.60425300	0.60147400
O	-1.67927000	-2.41129100	1.15902400
N	-4.11163900	0.45792100	0.55677300
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3ao

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C	4.25214600	0.50346800	0.37306200
C	5.54646000	0.00839400	0.49879200
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C	3.38726100	-1.69315600	-0.12560300
C	1.99900700	0.60175000	-0.00654200
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H	6.75748200	-1.76668100	0.41041800
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C	2.63476500	1.91391900	0.20974200
H	-1.79795900	-0.18745400	-1.58147300

C	1.83187100	3.17239500	0.24733200
H	2.45639800	4.03077100	-0.00613800
H	1.43424200	3.32617700	1.25826600
H	-3.39184200	-1.00165700	-2.28572700
C	0.69057400	3.01907500	-0.73808600
H	-0.04305400	3.82160100	-0.66777700
H	1.07201300	2.97465000	-1.76548000
C	0.62412300	0.58089400	-0.14594300
N	-0.00904000	1.77025300	-0.45463100

9. References

1. a) J. F. Zheng, J. Z. Bi, L. Ma, L. L. Chen, L. H. Tang, D. Xiong and Y. Tian, *Chem. Commun.,* **2023**, *59*, 8572−8575; b) X. H. Zhao, X. H. Liu, H. J. Mei, J. Guo, L. L. Lin, X. M. Feng. *Angew. Chem. Int. Ed.*, **2015**, *54*, 4032–4035; c) H. Liu, A. Domling, *J. Or*g. Chem., **2009**, *74*, 6895–6898.

2. a) X. H. Zhao, X. H. Liu, Q. Xiong, H. J. Mei, B. W. Ma, L. L. Lin and X. M. Feng, *Chem. Commun*., **2015**, *51*, 16076−16079; b) G. Wang, X. H. Liu, T. Y. Huang, Y. L. Kuang, L. L. Lin and X. M. Feng, *Org. Lett.*, **2013**, *15*, 76–79; c) S. H. Li, W. M. Yuan and S. M. Ma, *Angew. Chem. Int. Ed*., **2011**, *50*, 2578–2582; d) G. Tacconi, L. D. Maggi, P. Righetti, G. Desimoni, O. Azzolina and V. Ghislandi, *J. Chem. Soc*., Perkin Trans. 2, **1976**, 150–154; e) A. L. Gerten, M. C. Slade, K. M. Pugh and L. M. Stanley, *Org. Biomol. Chem.* **2013**, *11 (45)*, 7834–7837.

3. T. K. Heiss, R. S. Dorn, A. J. Ferreira, A. C. Love, and J. A. Prescher, *J. Am. Chem. Soc*. **2022**, *144*, 7871–7880.

4. a) P. Hohenberg, W. Kohn, *Phys. Rev.* **1964**, *136*, B864−B871; b) W. Kohn, L. J. Sham, *Phys. Rev.* **1965**, *140*, A1133−A1138.

5. Y. Zhao, D. G. Truhlar, Theor. *Chem. Acc.* **2008**, *120*, 215−241.

6. S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104.

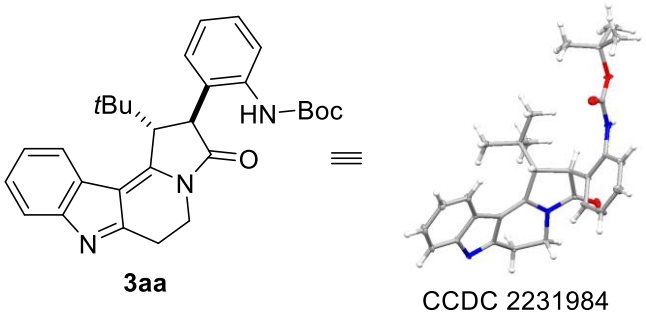
7. A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378−6396.

8. a) K. Fukui, *J. Chem. Phys.* **1970**, *74*, 4161−4163; b) K. Fukui, *Acc. Chem. Res.* **1981**, *14*, 363−368.

9. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Jr. Montgomery, J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, Gaussian 16, revision B.01, Gaussian, Inc.: Wallingford, CT, 2016.

10. X-ray crystallographic data

10.1 X-ray crystallographic data of **3aa**:



3aa ≡ CCDC 2231984

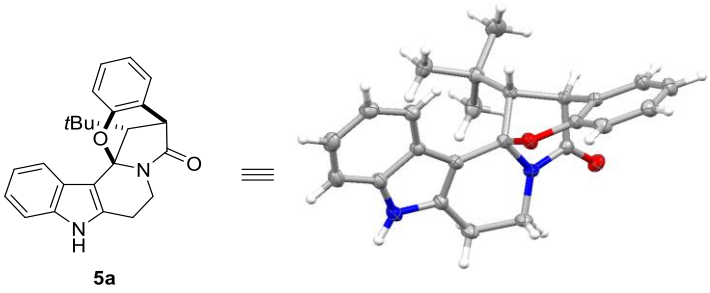
The single crystal for compound **3aa** was obtained by vaporization of a mixture solvent of Petroleum ether and ethyl acetate (v/v = 1/2). The data were collected on a Xcalibur Eos diffractometer equipped with MoKα X-ray sources (λ = 1.54178 Å).

X-ray derived ORTEP of **3aa** with thermal ellipsoids shown at the 30% probability level. Structure deposited at the Cambridge Crystallographic Data Centre. CCDC 2231984 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/

Empirical formula	$C_{27}H_{24}N_4O$
Formula weight	471.58
Temperature/K	173 (2)
Crystal system	trigonal
Space group	R-3
a/Å	25.3489 (3)
b/Å	25.3489 (3)
c/Å	27.6292 (6)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	15375.1 (5)
Z	18
ρcalcg/cm^3	0.917
μ/mm-1	0.475
F(000)	4536
Crystal size/mm^3	0.174 × 0.159 × 0.150
adiation	MoKα (λ = 1.54178)
2Θ range for data collection/°	5.142 to 136.568
Reflections collected	20003
Independent reflections	4710 [R_{int} = 0.0641, R_{sigma} = 0.0648]

Data/restraints/parameters	6042/0/327
Goodness-of-fit on F^2	1.286
Final R indexes [I>=2σ (I)]	R_1 = 0.1171, wR_2 = 0.2895
Final R indexes [all data]	R_1 = 0.1319, wR_2 = 0.3069
Largest diff. peak/hole/e $Å^{-3}$	0.78/-0.49

10.2 X-ray crystallographic data of **5a**:



5a

CCDC 2335020

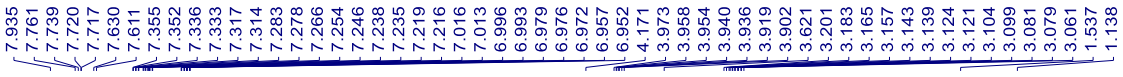
The single crystal for compound **5a** was obtained by vaporization of a mixture solvent of Ethanol and Dichloromethane (v/v = 2:3). The data were collected on a Xcalibur Eos diffractometer equipped with MoKα X-ray sources (λ = 0.71073 Å).

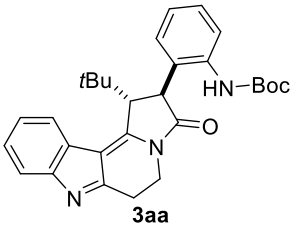
X-ray derived ORTEP of **5a** with thermal ellipsoids shown at the 30% probability level. Structure deposited at the Cambridge Crystallographic Data Centre. CCDC 2335020 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/.

Empirical formula	$C_{24}H_{24}N_2O_2$
Formula weight	372.45
Temperature/K	293.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.0963 (4)
b/Å	10.5857 (4)
c/Å	18.6757 (8)
α/°	90
β/°	104.516 (4)
γ/°	90
Volume/$Å^3$	1932.27 (14)
Z	4
ρcalcg/cm^3	1.280
μ/mm^{-1}	0.082
F(000)	792.0

Crystal size/mm^3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.48 to 52.742
Reflections collected	8350
Independent reflections	3952 [R_{int} = 0.0263, R_{sigma} = 0.0533]
Data/restraints/parameters	3952/0/260
Goodness-of-fit on F^2	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.0529, wR_2 = 0.1080
Final R indexes [all data]	R_1 = 0.0840, wR_2 = 0.1259
Largest diff. peak/hole/e $Å^{-3}$	0.17/-0.21

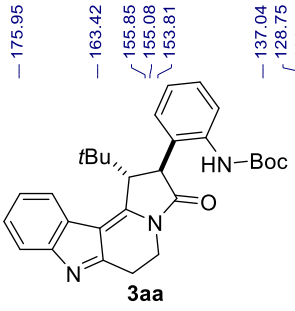
11. Copy of NMR spectra





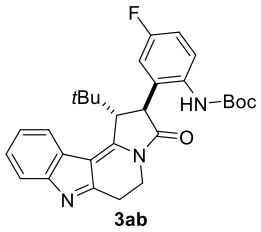
3aa

^{1}H NMR (400 MHz, $CDCl_3$)



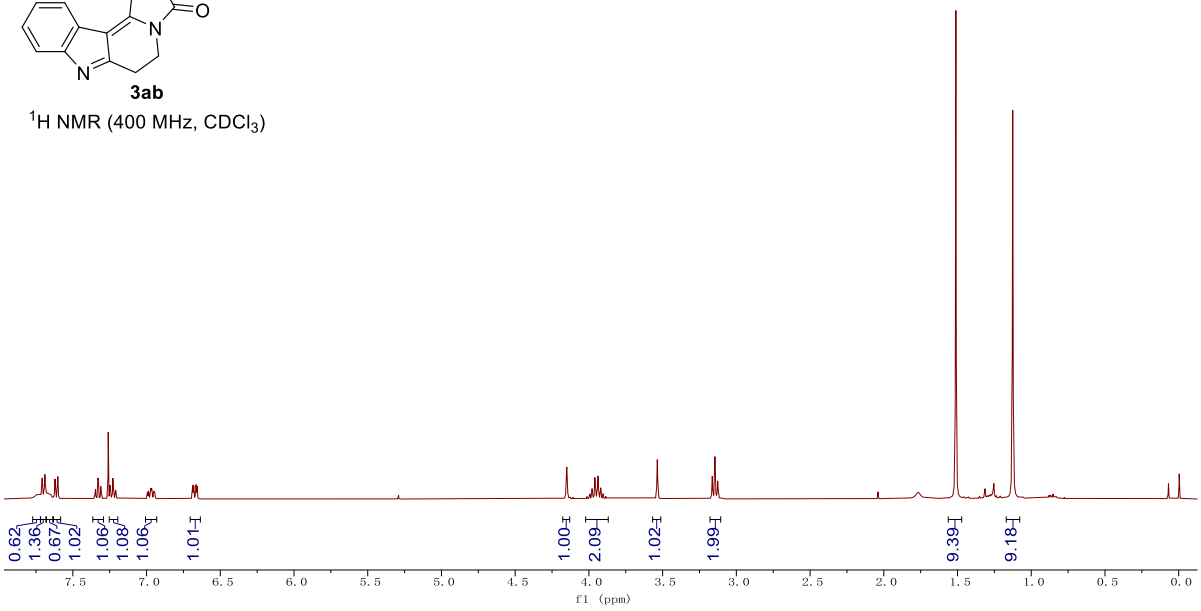
3aa

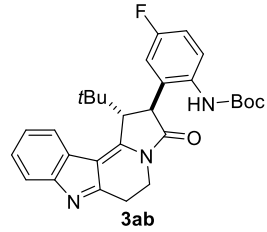
^{13}C NMR (101 MHz, $CDCl_3$)



3ab

^{1}H NMR (400 MHz, $CDCl_3$)





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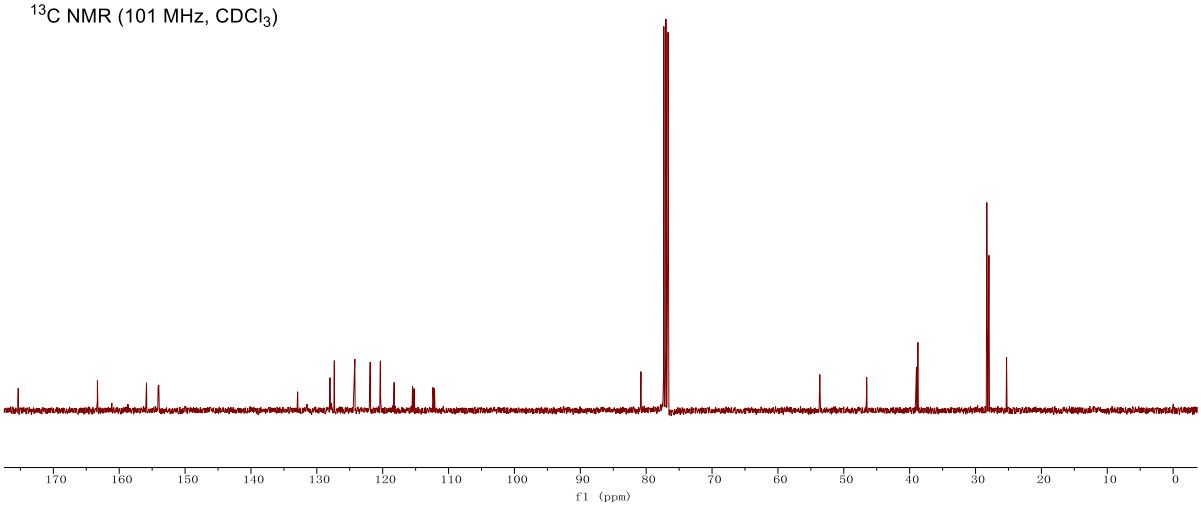
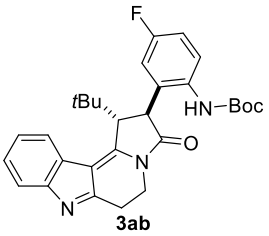
^{13}C NMR (101 MHz, $CDCl_3$)





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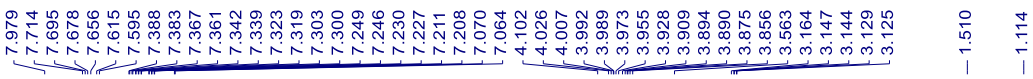
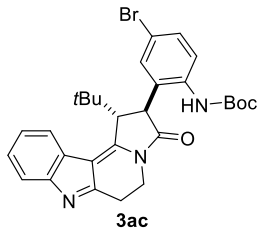
^{19}F NMR (376 MHz, $CDCl_3$)





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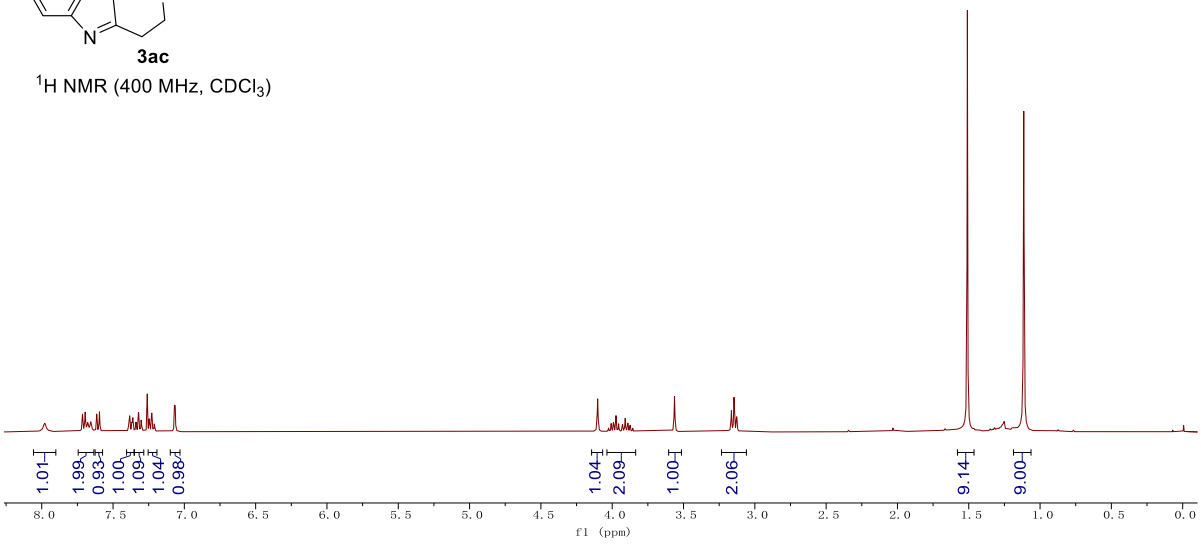

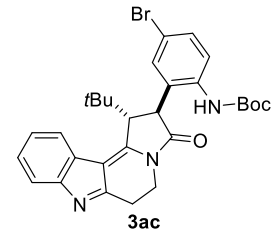

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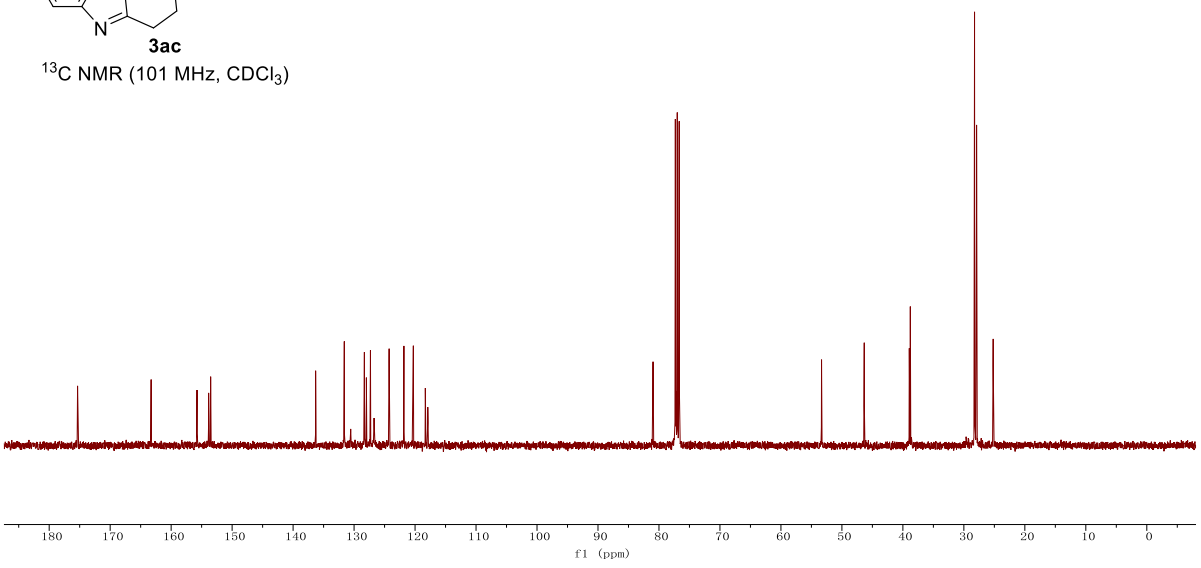

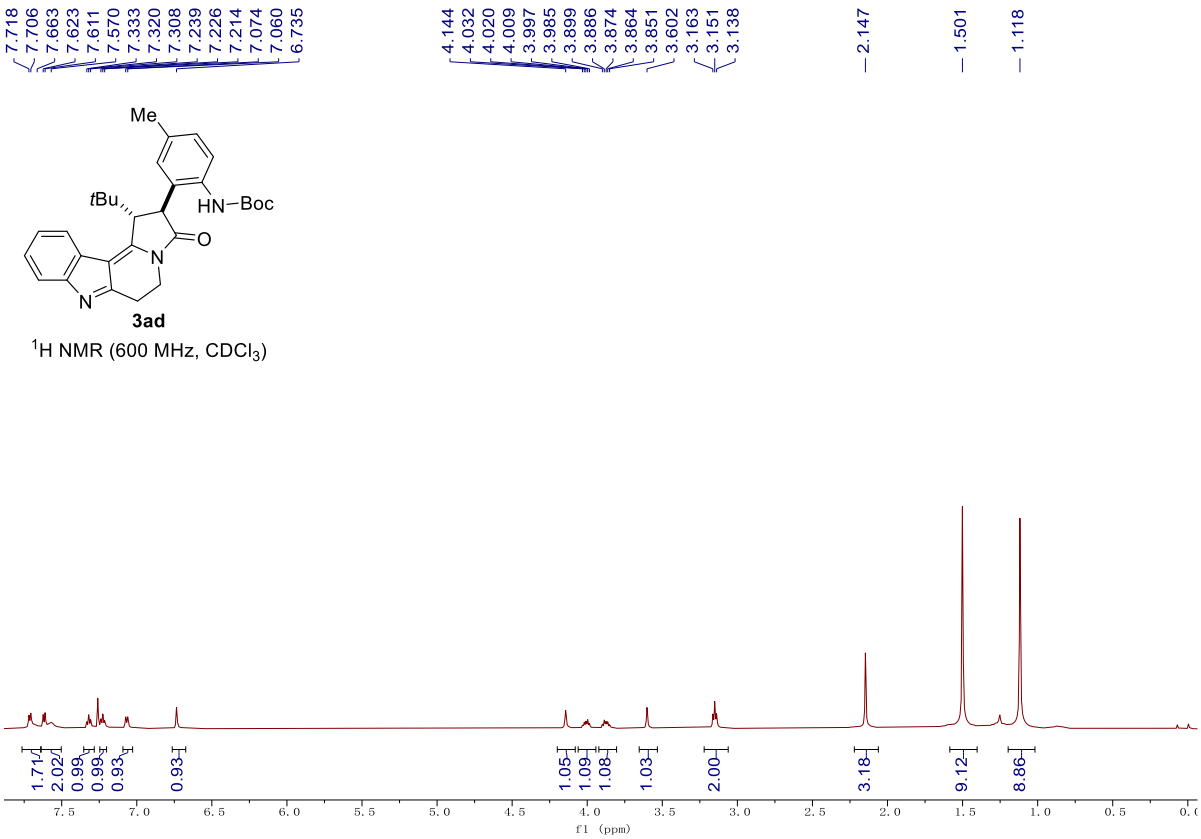
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7.239
7.226
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7.060
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3.874
3.864
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1.118
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tBu
HN–Boc
O
N
N
3ad
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0.99
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1.08
1.03
2.00
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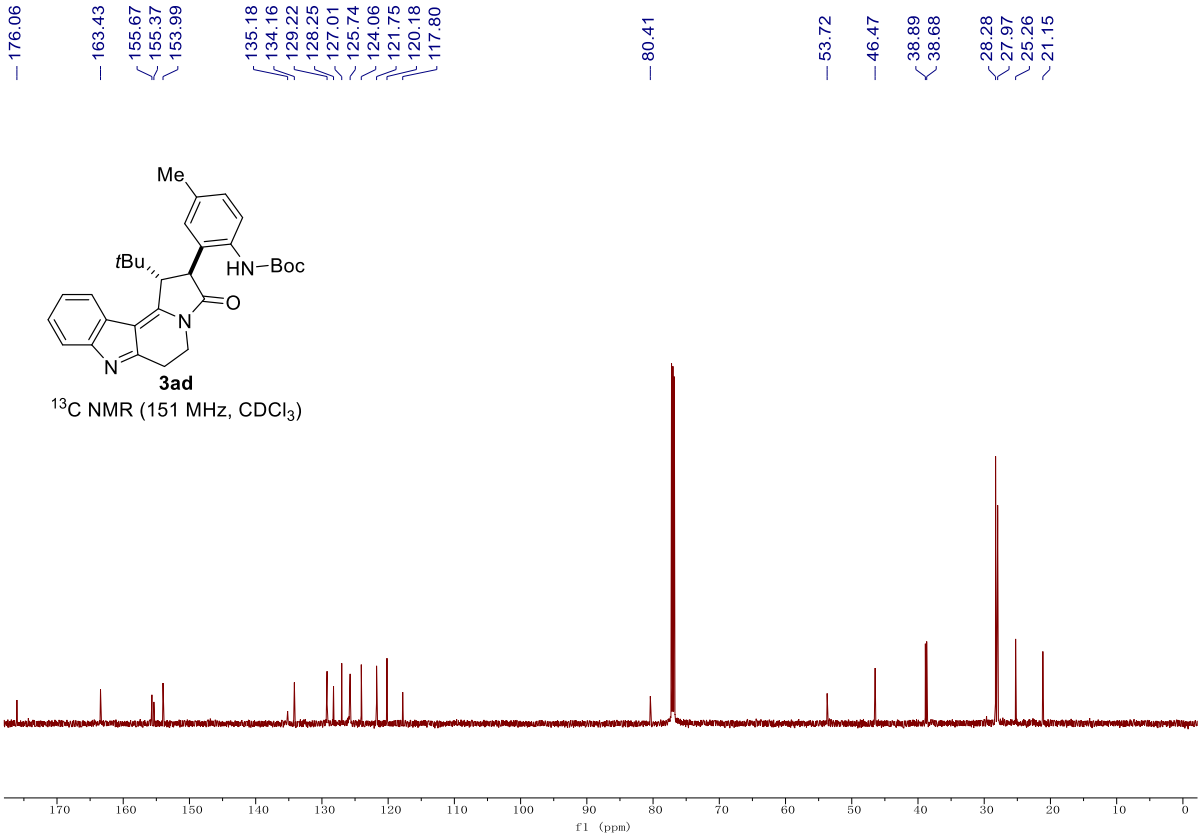
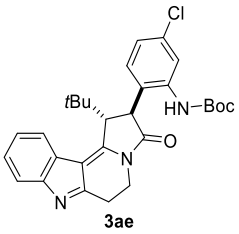
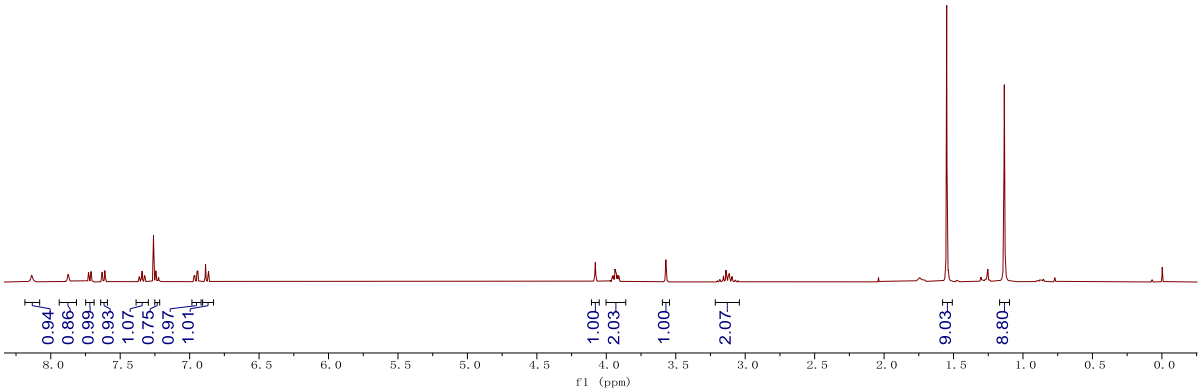
8.86
f1 (ppm)

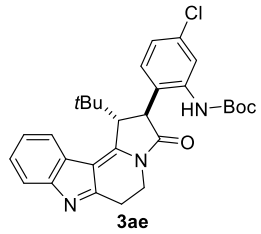

176.06
163.43
155.67
155.37
153.99
135.18
134.16
129.22
128.25
127.01
125.74
124.06
121.75
120.18
117.80
80.41
53.72
46.47
38.89
38.68
28.28
27.97
25.26
21.15
Me
tBu
HN–Boc
O
N
N
3ad
13C NMR (151 MHz, CDCl3)
f1 (ppm)



3ae

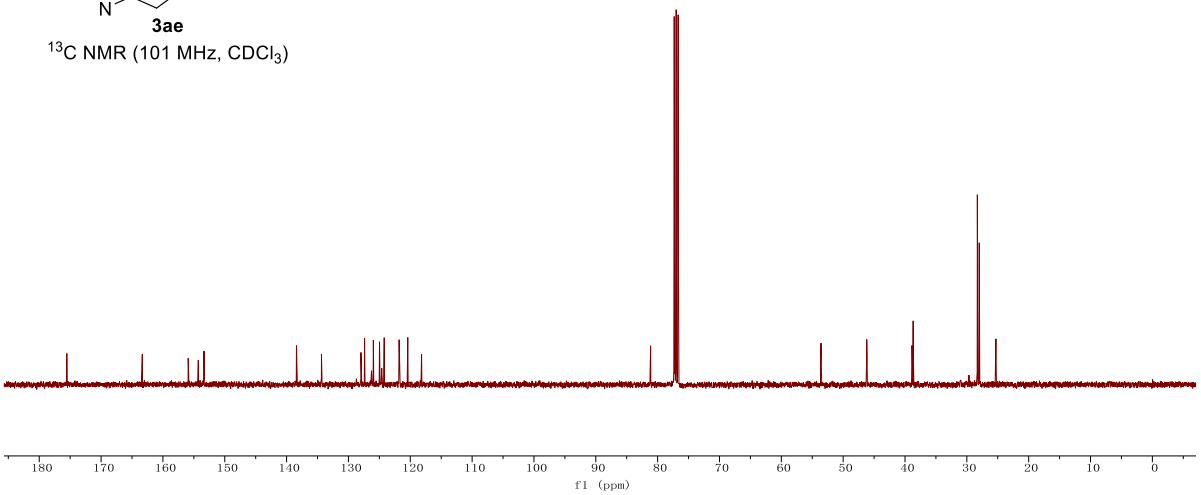
^{1}H NMR (400 MHz, $CDCl_3$)

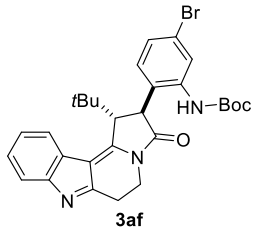




3ae

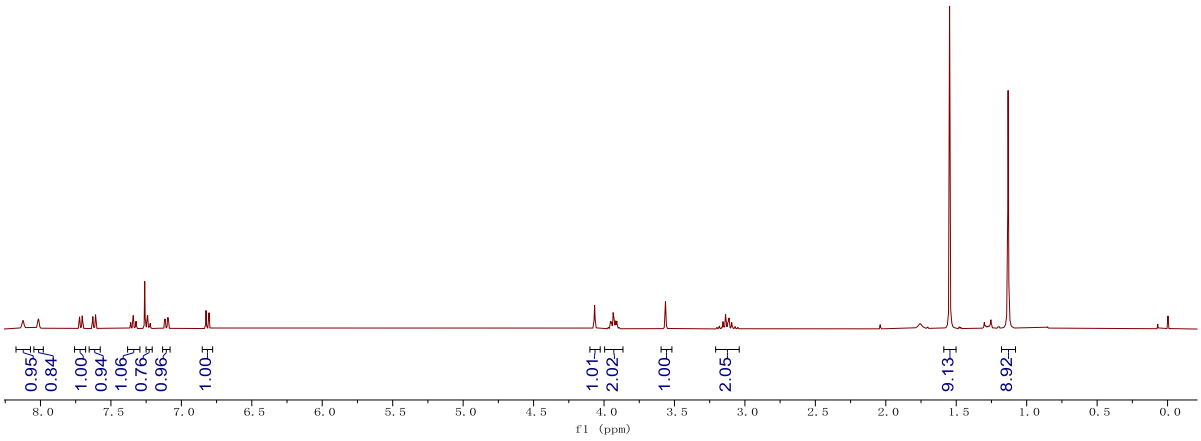
^{13}C NMR (101 MHz, $CDCl_3$)

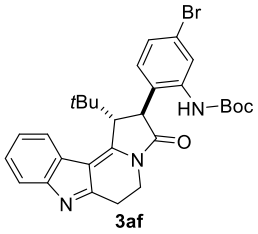




3af

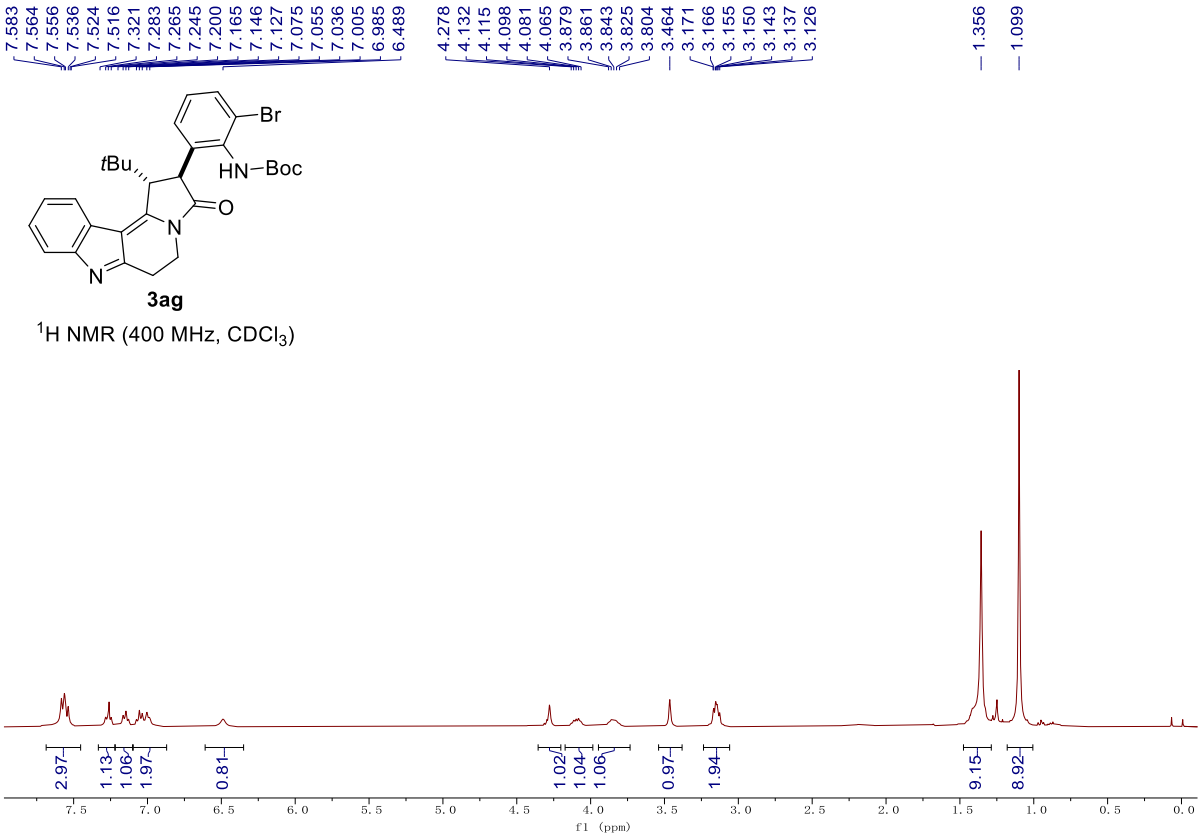
^{1}H NMR (400 MHz, $CDCl_3$)





3af

^{13}C NMR (101 MHz, $CDCl_3$)


7.583
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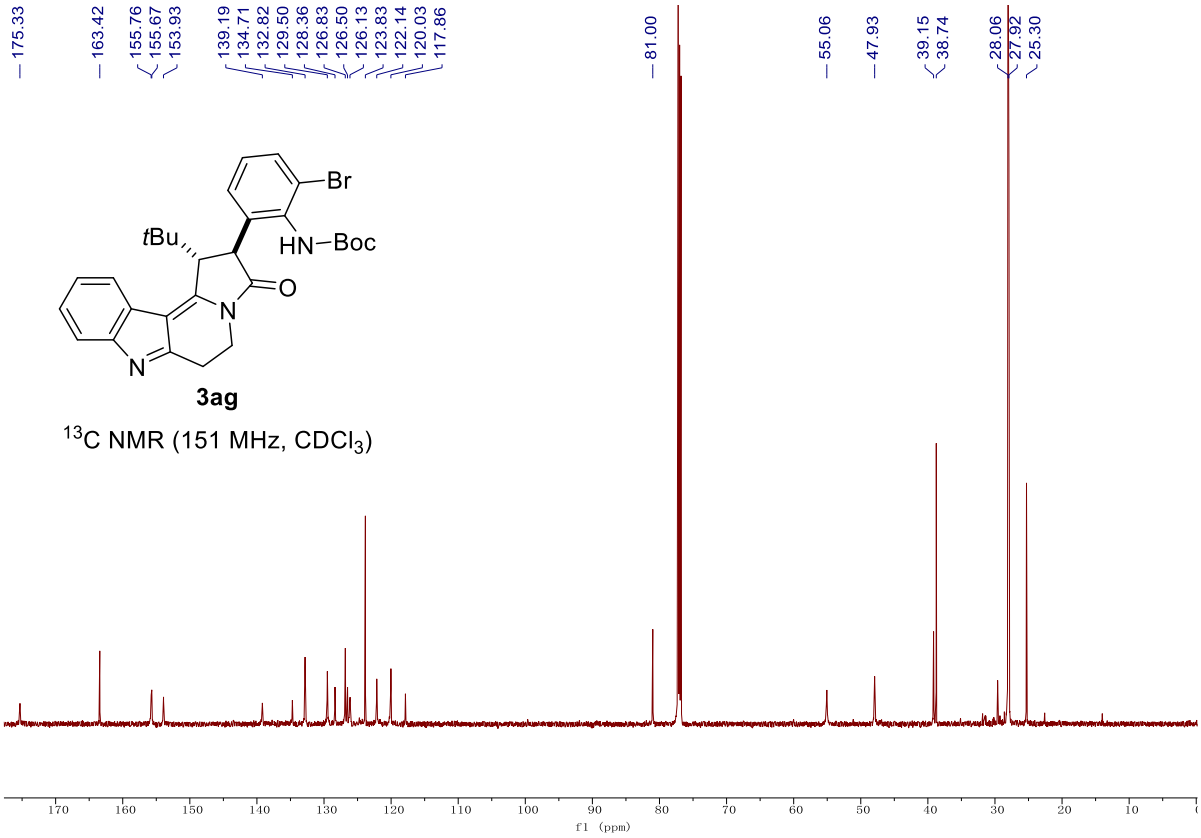
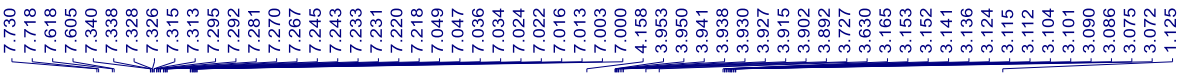
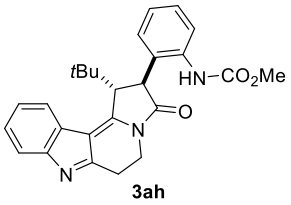
7.556
7.536
7.524
7.516
7.321
7.283
7.265
7.245
7.200
7.165
7.146
7.127
7.075
7.055
7.036
7.005
6.985
6.489
4.278
4.132
4.115
4.098
4.081
4.065
3.879
3.861
3.843
3.825
3.804
3.464
3.171
3.166
3.155
3.150
3.143
3.137
3.126
1.356
1.099
Br
tBu
HN−Boc
O
N
N
3ag
1H NMR (400 MHz, CDCl3)
2.97
1.13
1.06
1.97
0.81
1.02
1.04
1.06
0.97
1.94
9.15
8.92
f1 (ppm)

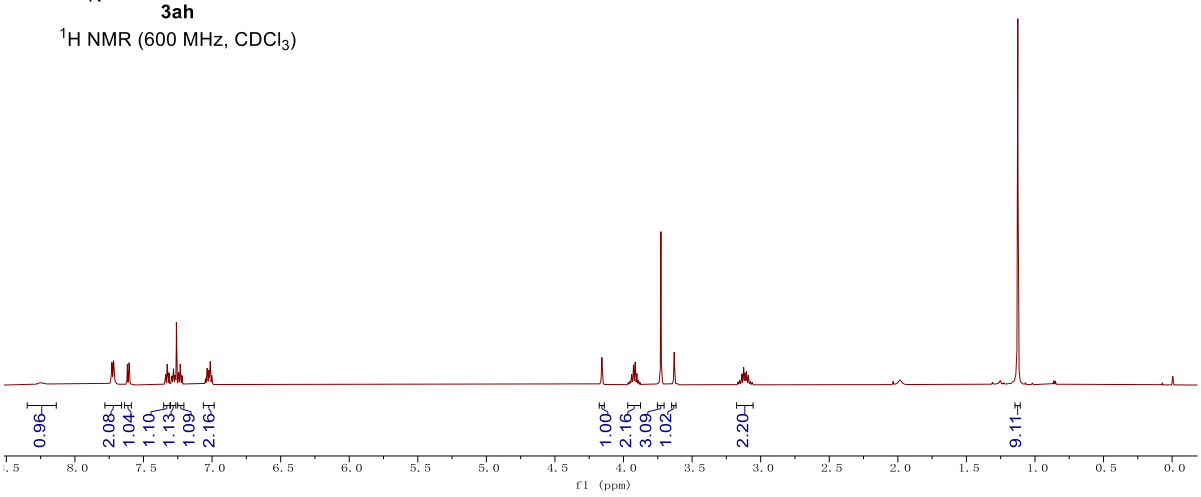

175.33
163.42
155.76
155.67
153.93
139.19
134.71
132.82
129.50
128.36
126.83
126.50
126.13
123.83
122.14
120.03
117.86
81.00
55.06
47.93
39.15
38.74
28.06
27.92
25.30
Br
tBu
HN−Boc
O
N
N
3ag
13C NMR (151 MHz, CDCl3)
f1 (ppm)

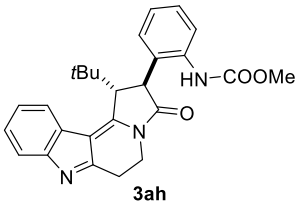




3ah

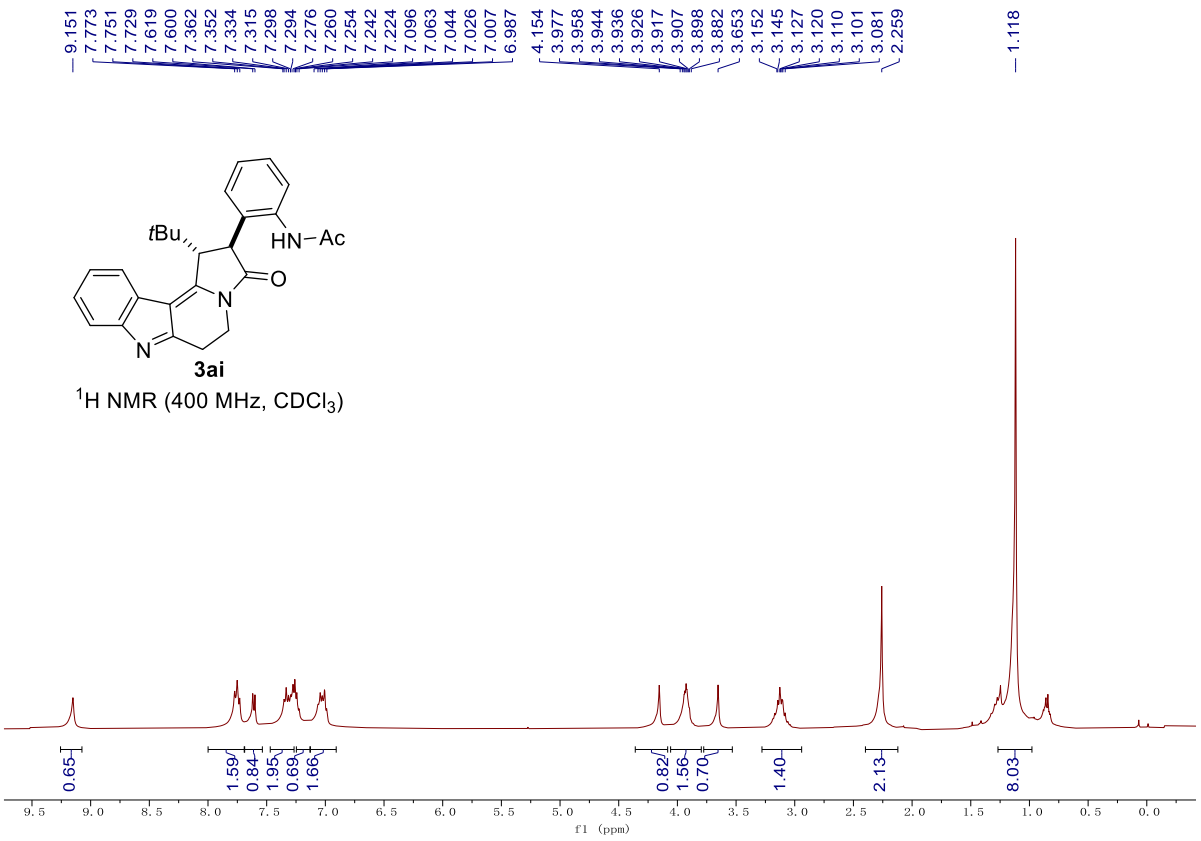
^{1}H NMR (600 MHz, $CDCl_3$)



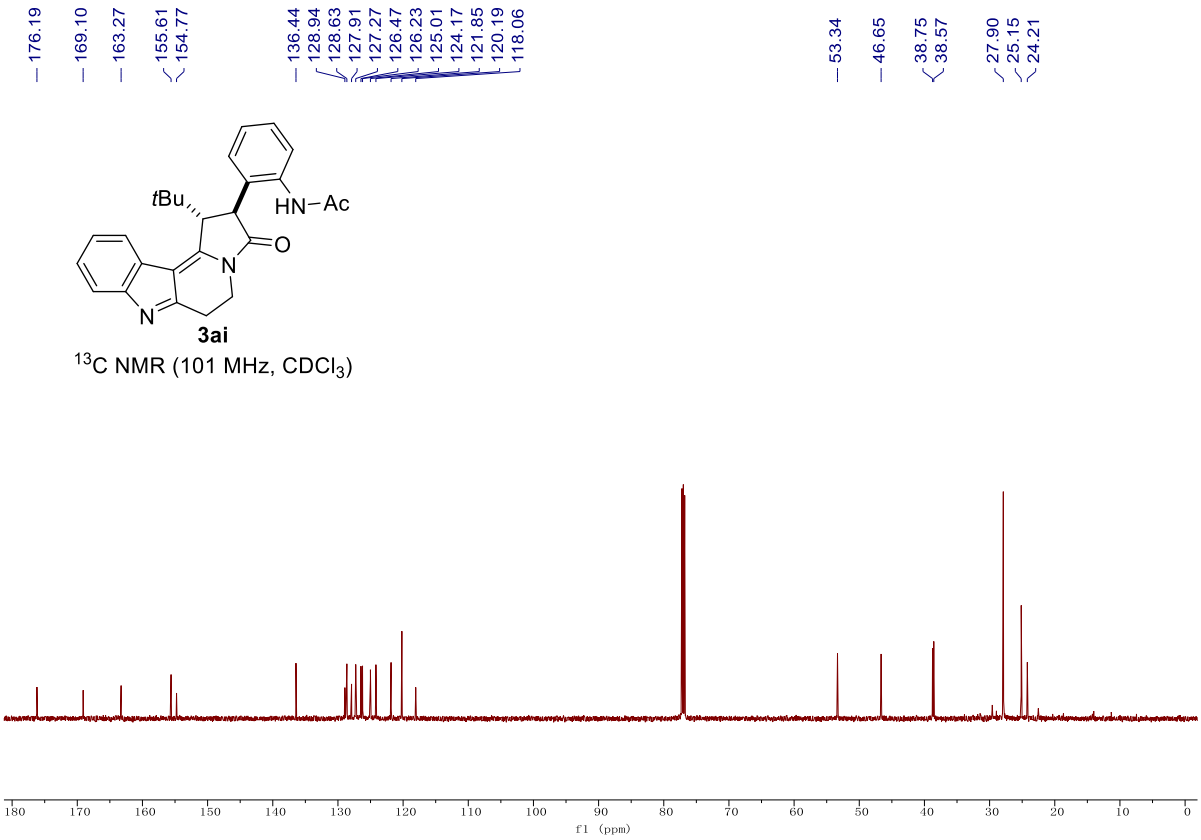


3ah

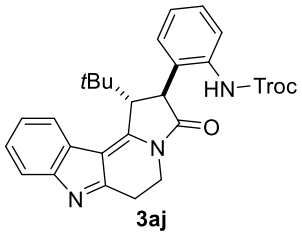
^{13}C NMR (151 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

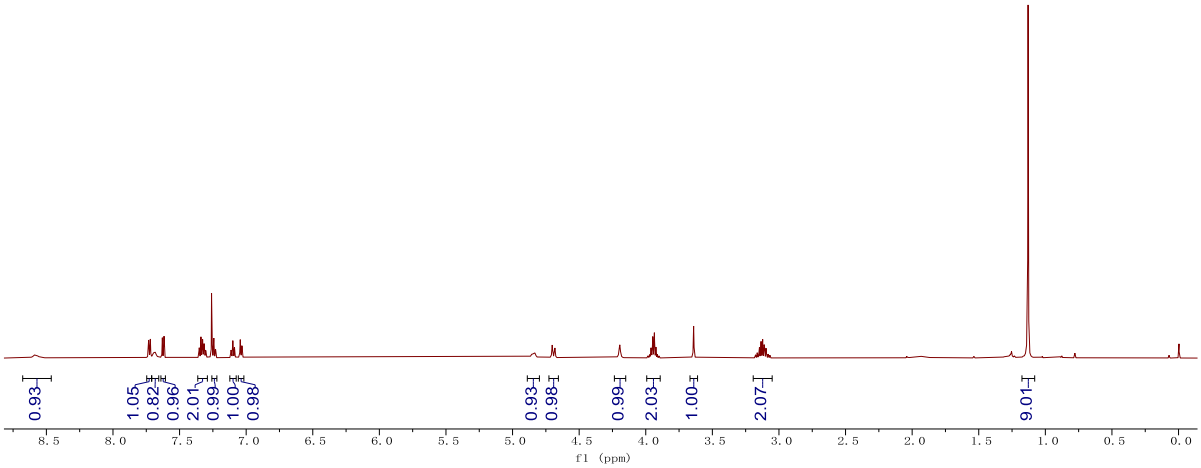


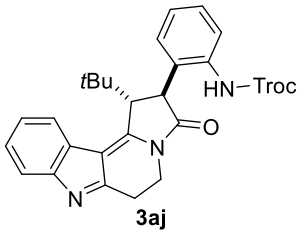
^{13}C NMR (101 MHz, $CDCl_3$)



3aj

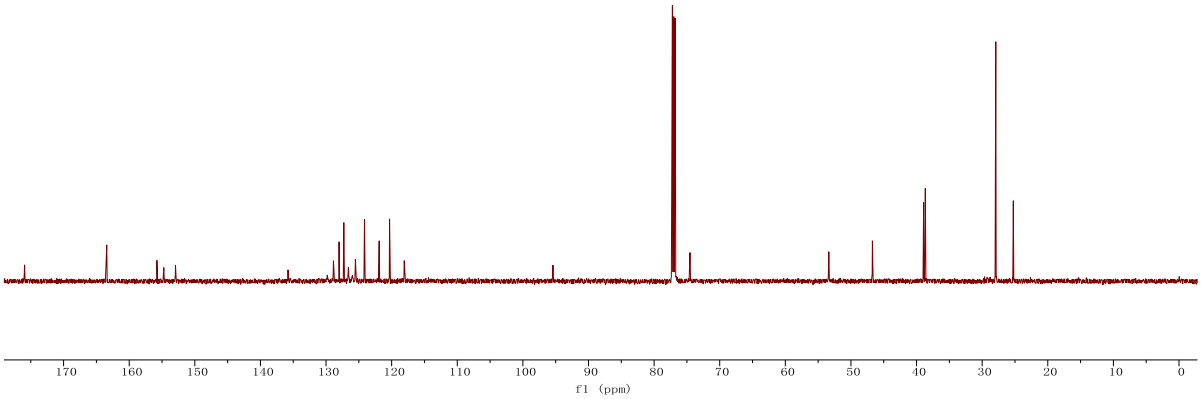
^{1}H NMR (600 MHz, $CDCl_3$)

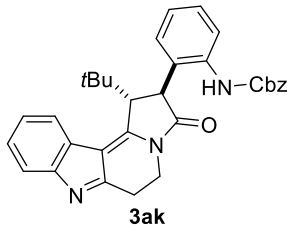




3aj

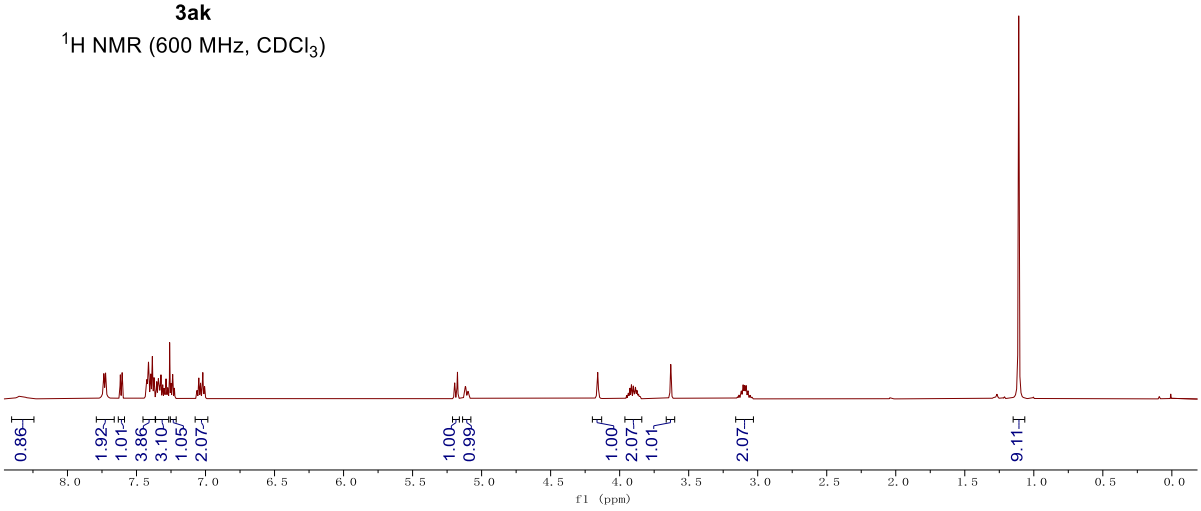
^{13}C NMR (151 MHz, $CDCl_3$)

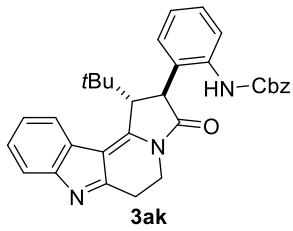




3ak

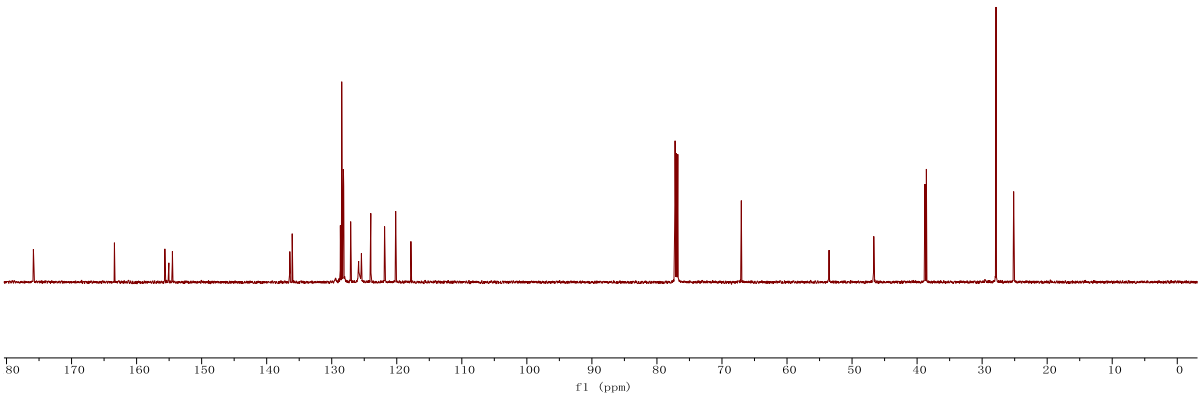
^{1}H NMR (600 MHz, $CDCl_3$)

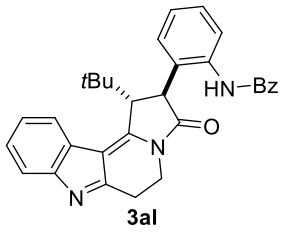




3ak

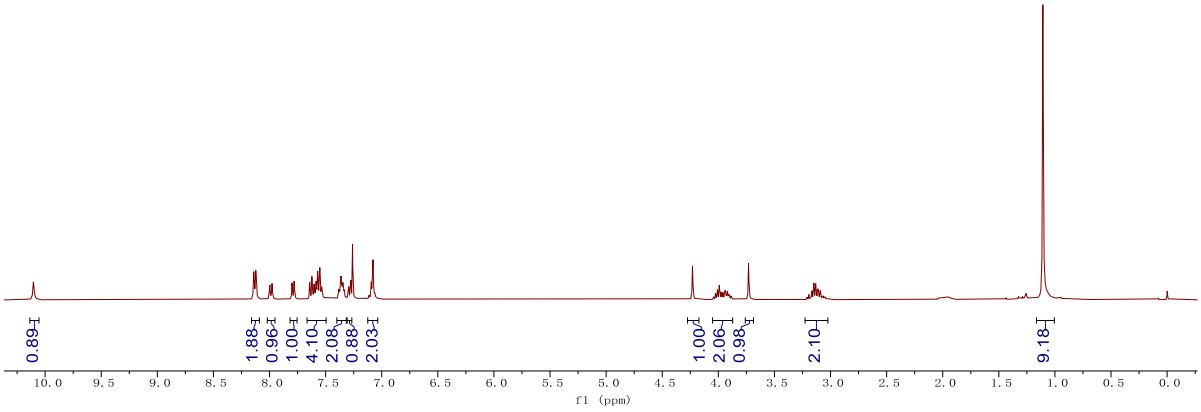
^{13}C NMR (151 MHz, $CDCl_3$)

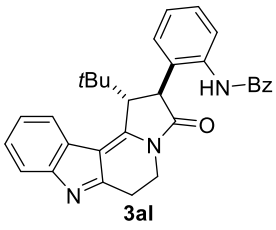




3al

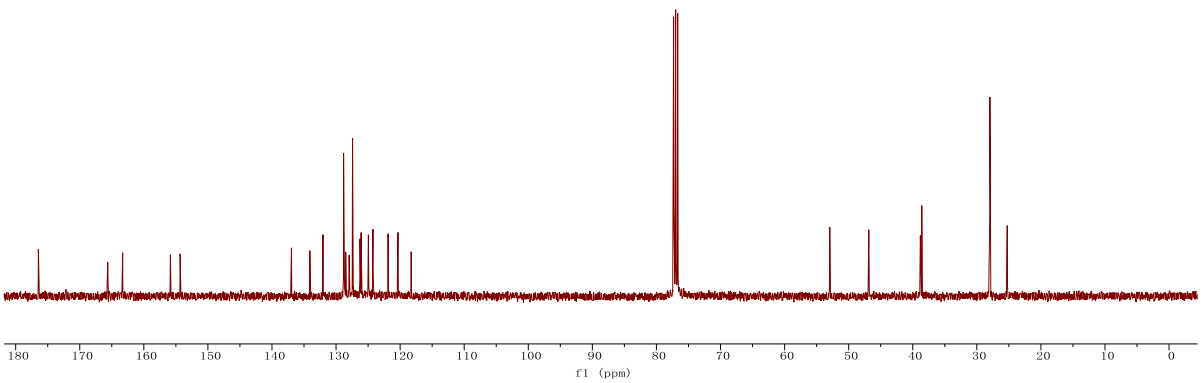
^{1}H NMR (400 MHz, $CDCl_3$)

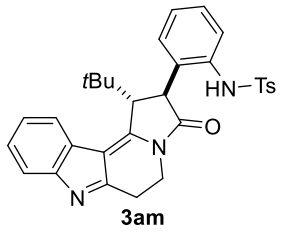




3al

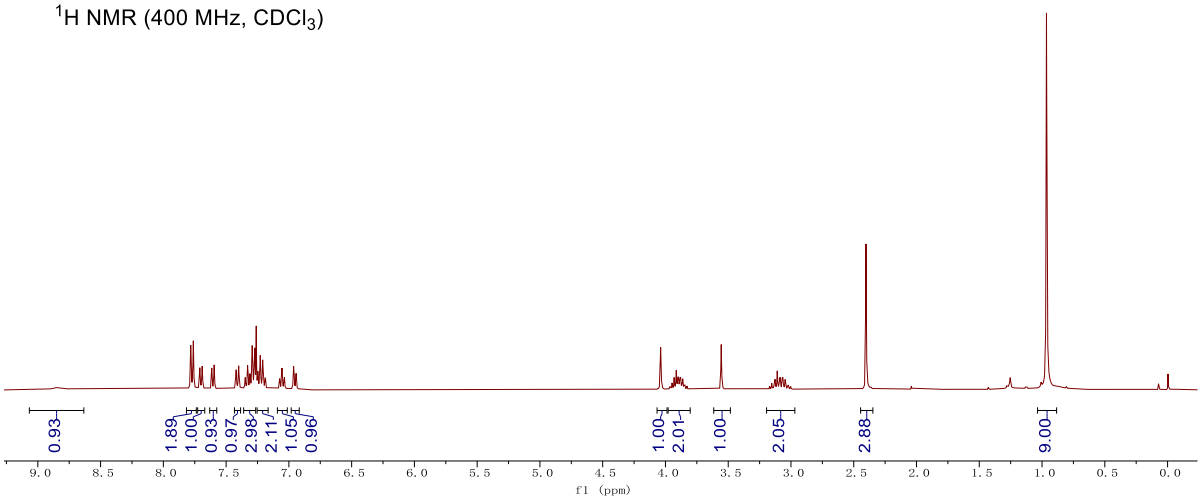
^{13}C NMR (101 MHz, $CDCl_3$)

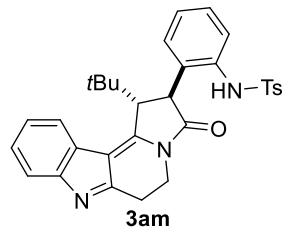




3am

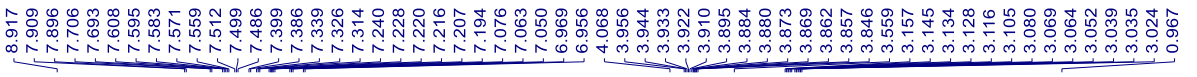
^{1}H NMR (400 MHz, $CDCl_3$)

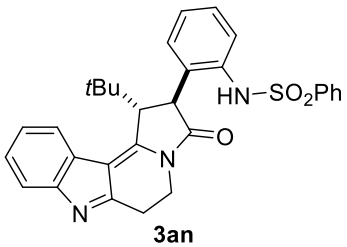




3am

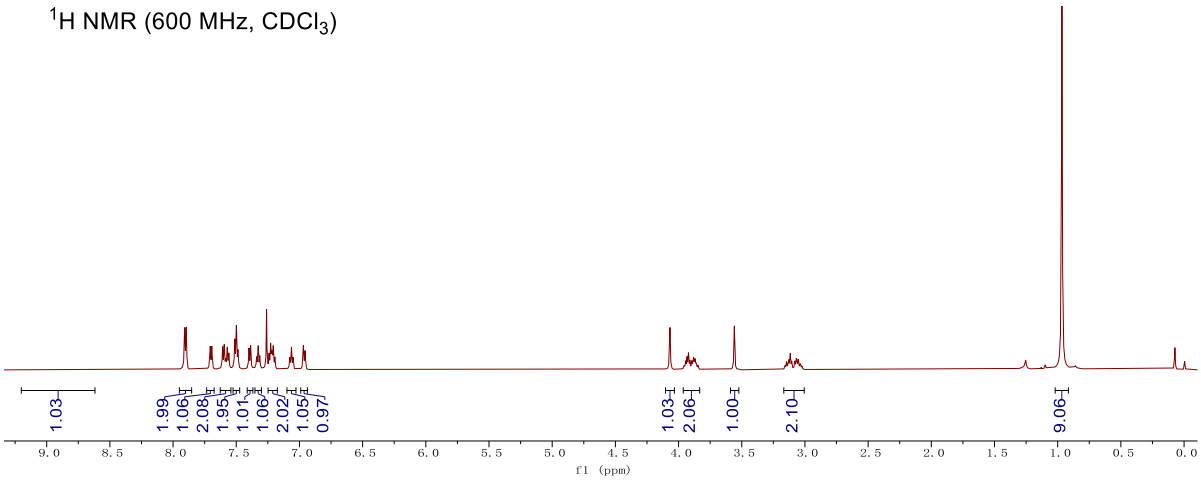
^{13}C NMR (101 MHz, $CDCl_3$)

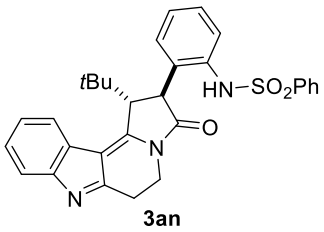




3an

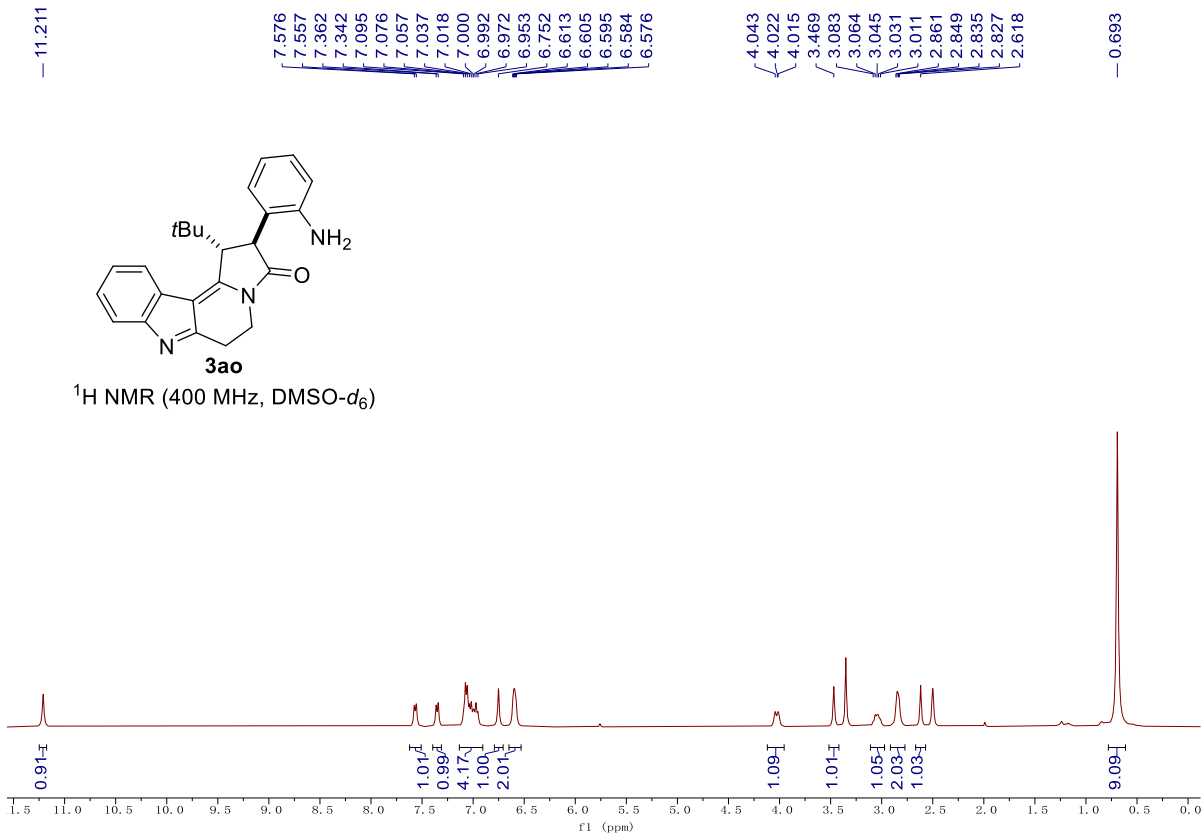
^{1}H NMR (600 MHz, $CDCl_3$)



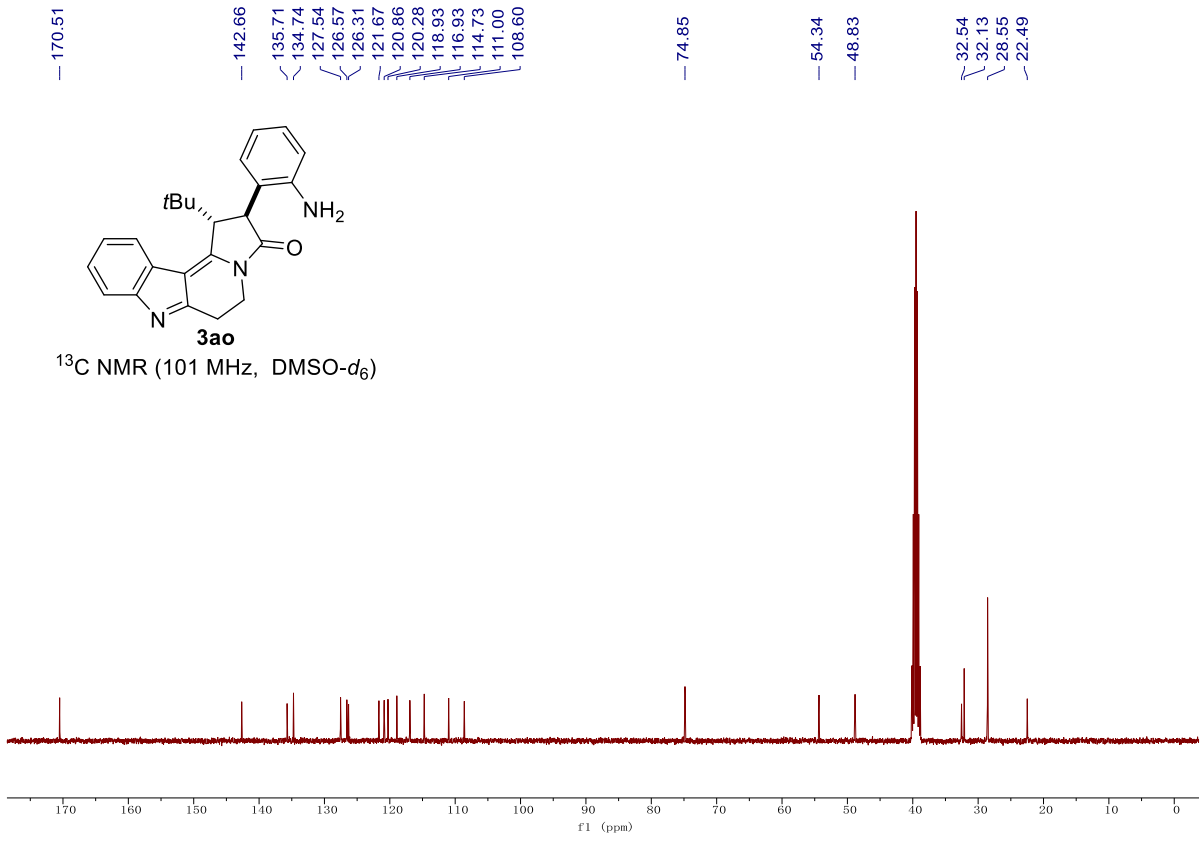


3an

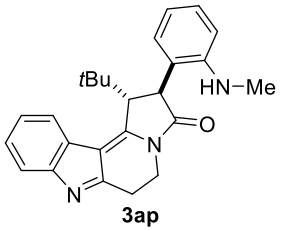
^{13}C NMR (151 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, DMSO-d_6)

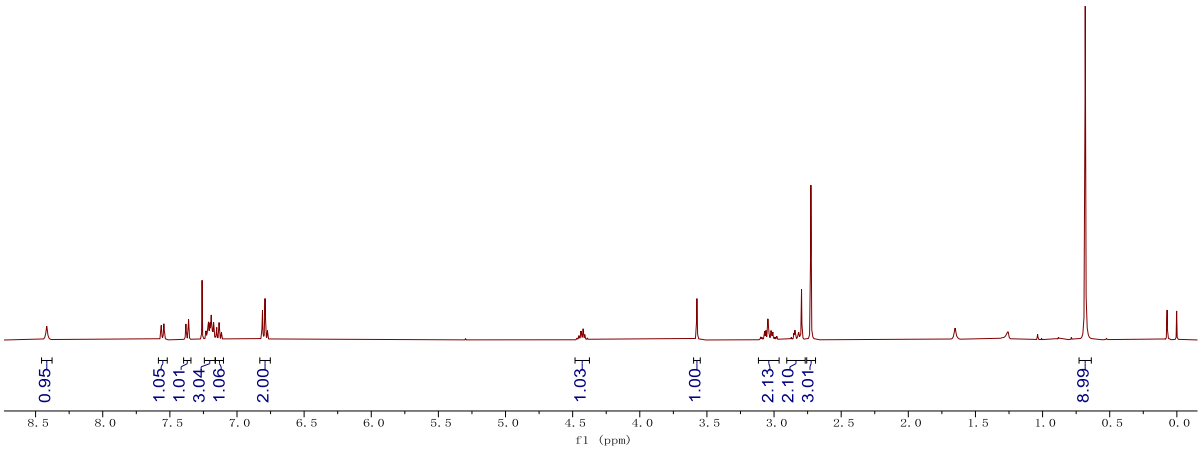


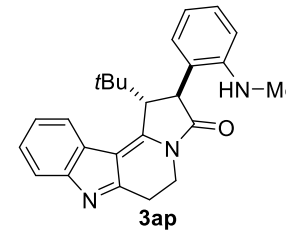
^{13}C NMR (101 MHz, DMSO-d_6)



3ap

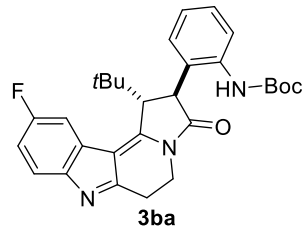
^{1}H NMR (400 MHz, $CDCl_3$)





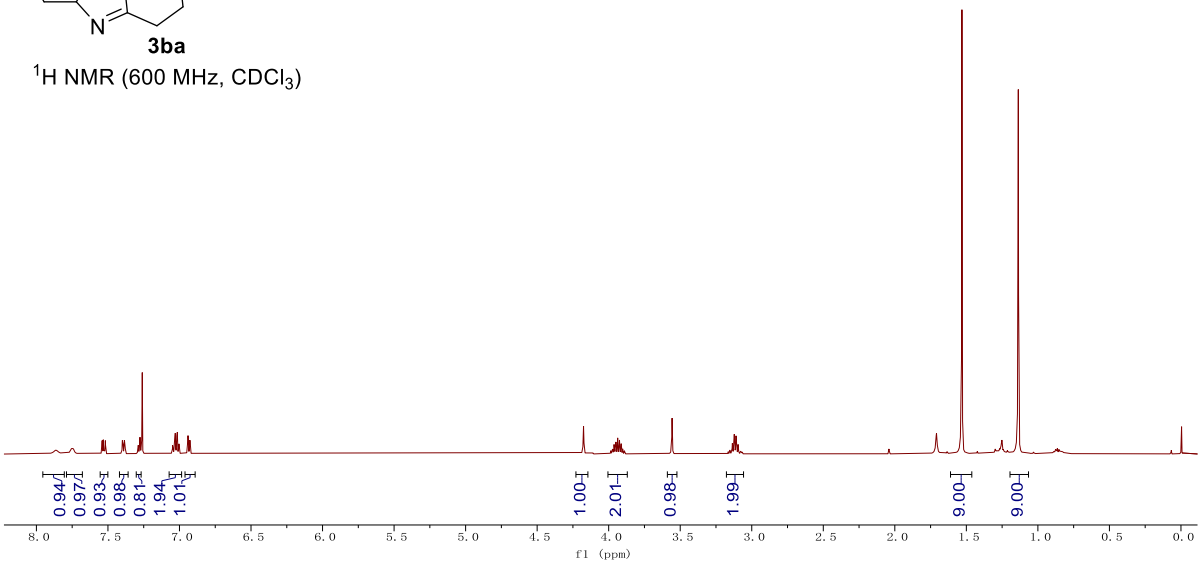
3ap

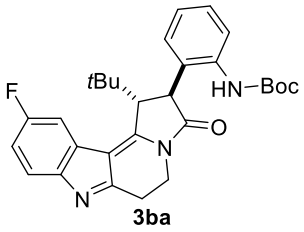
^{13}C NMR (151 MHz, $CDCl_3$)



3ba

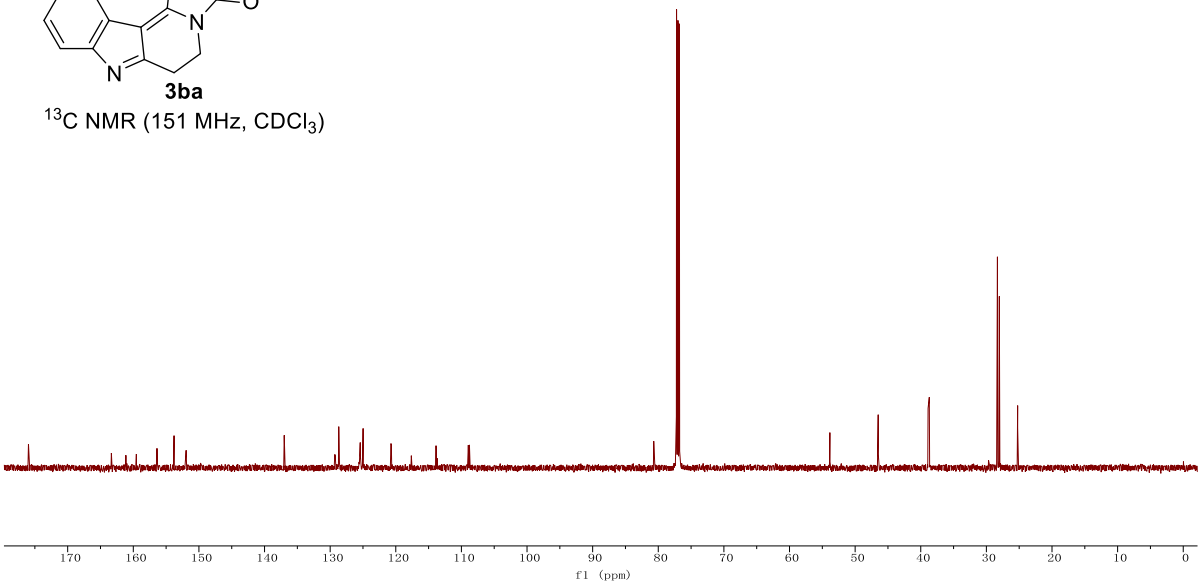
^{1}H NMR (600 MHz, $CDCl_3$)

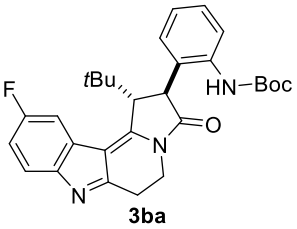




3ba

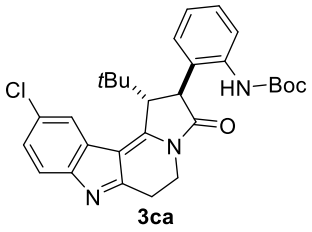
^{13}C NMR (151 MHz, $CDCl_3$)





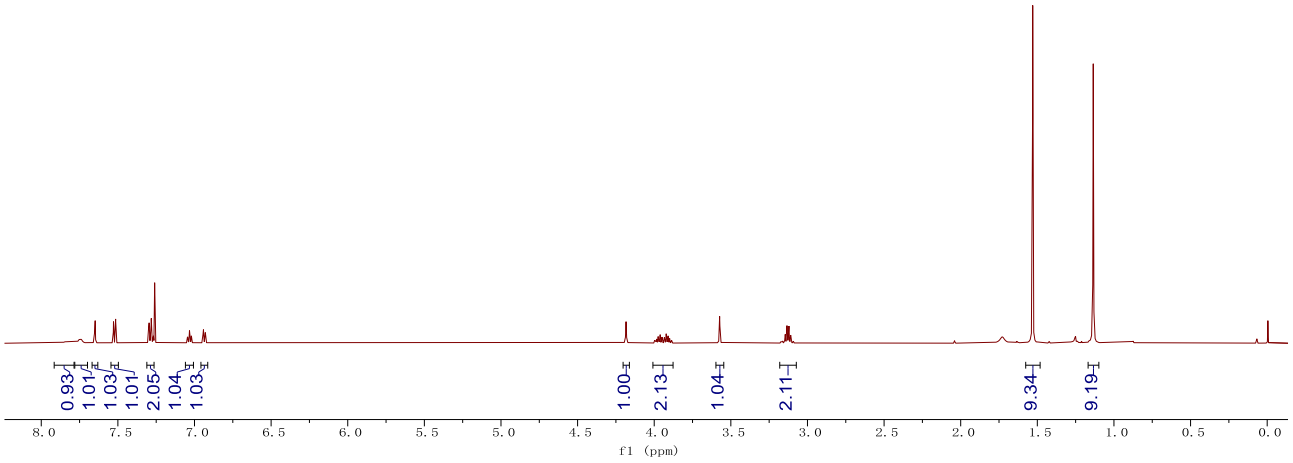
3ba

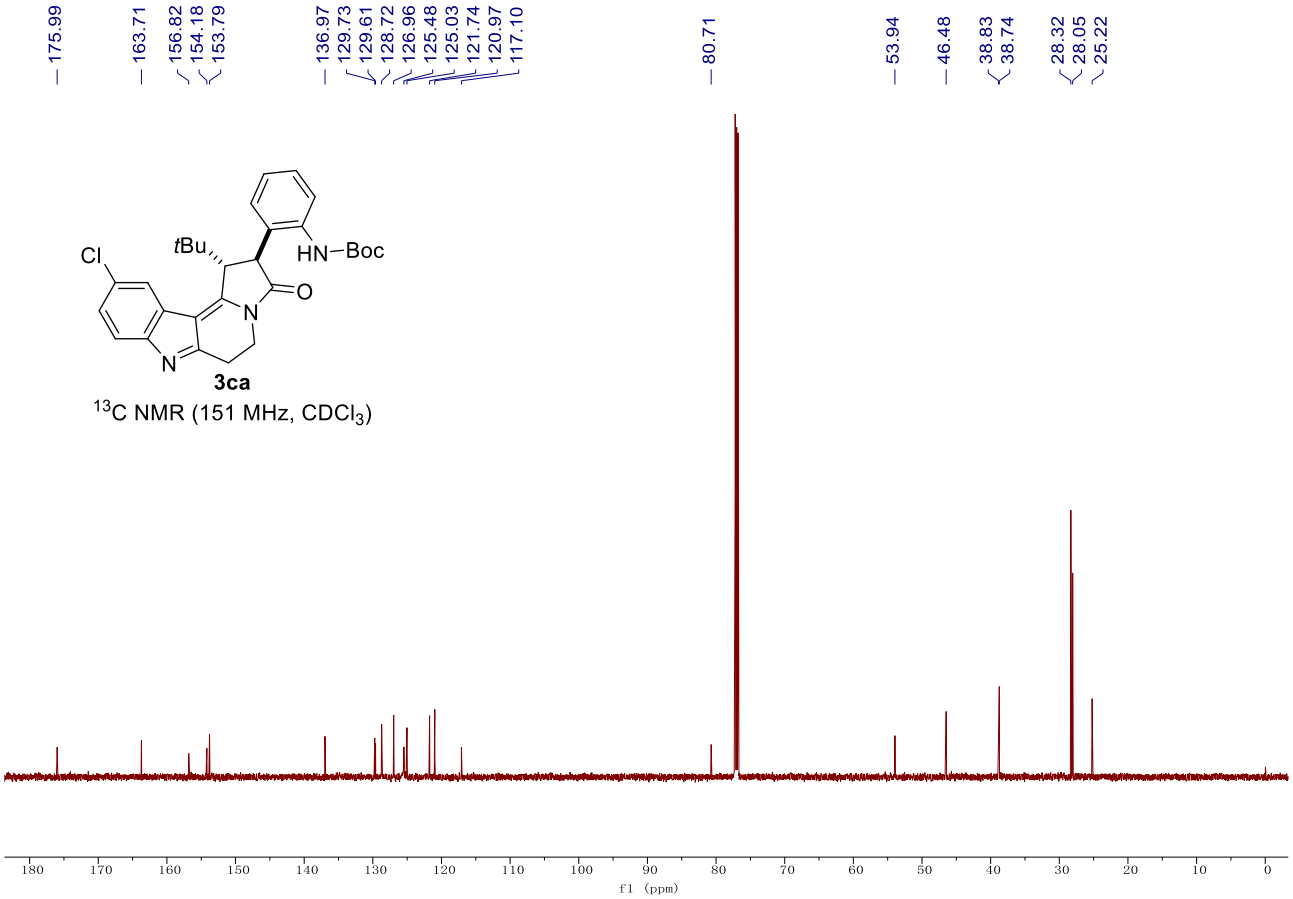
^{19}F NMR (565 MHz, $CDCl_3$)



3ca

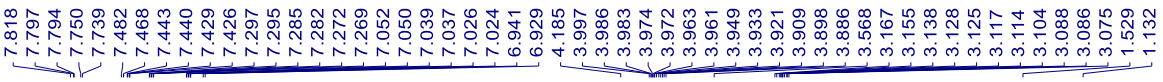
^{1}H NMR (600 MHz, $CDCl_3$)

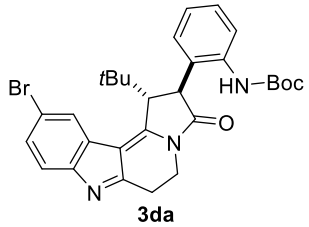




3ca

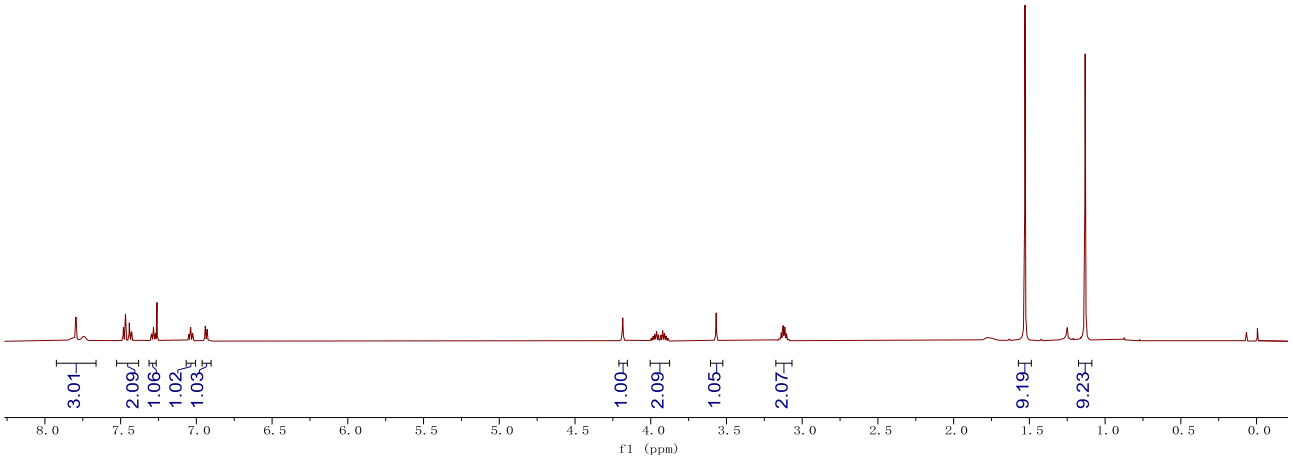
^{13}C NMR (151 MHz, $CDCl_3$)

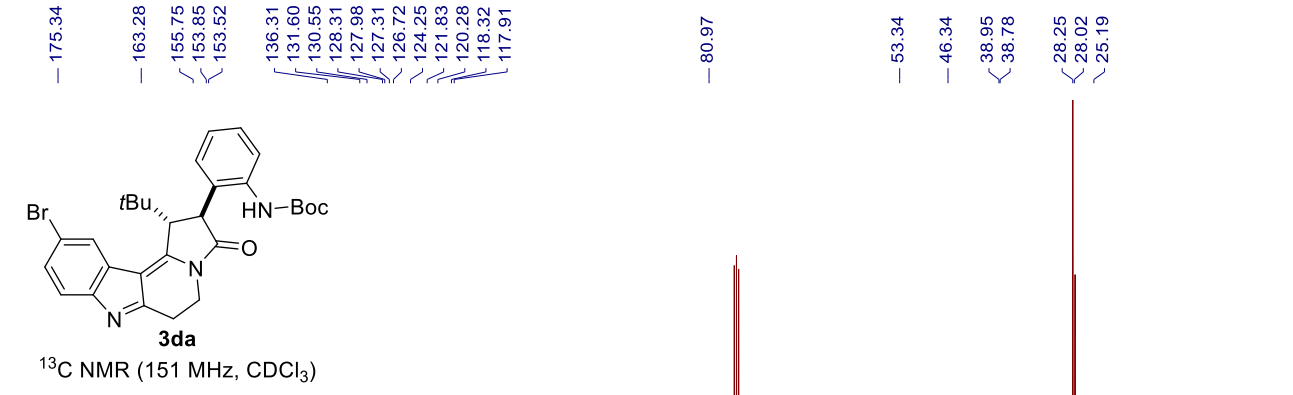




3da

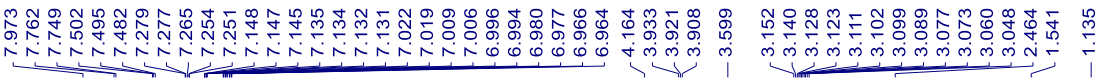
^{1}H NMR (600 MHz, $CDCl_3$)

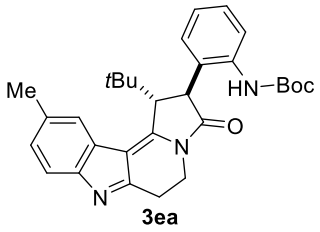




3da

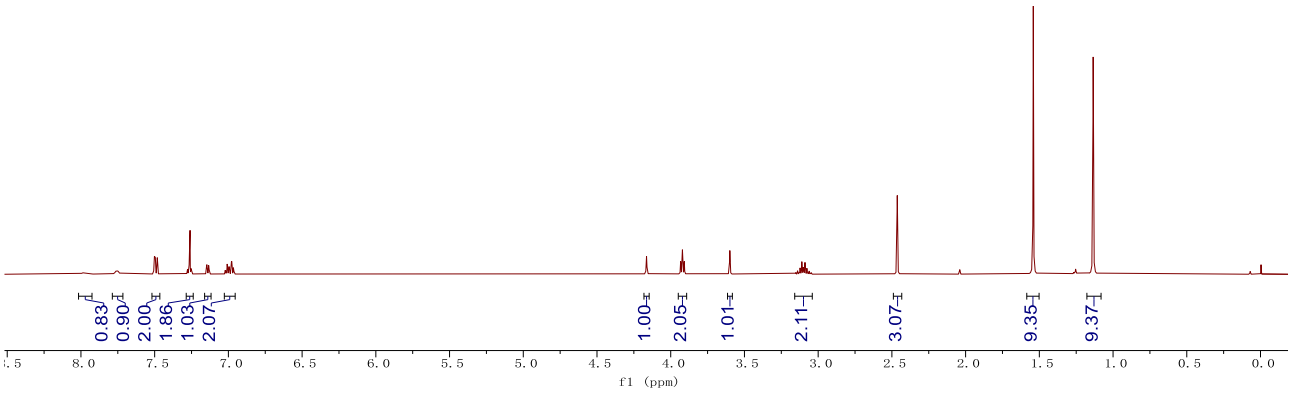
^{13}C NMR (151 MHz, $CDCl_3$)

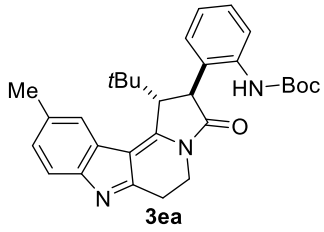




3ea

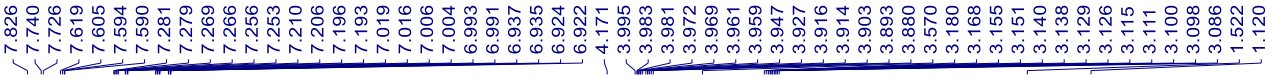
^{1}H NMR (600 MHz, $CDCl_3$)

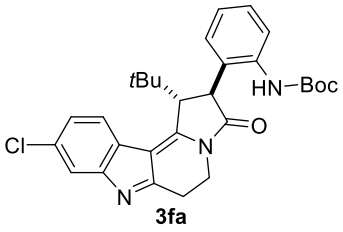




3ea

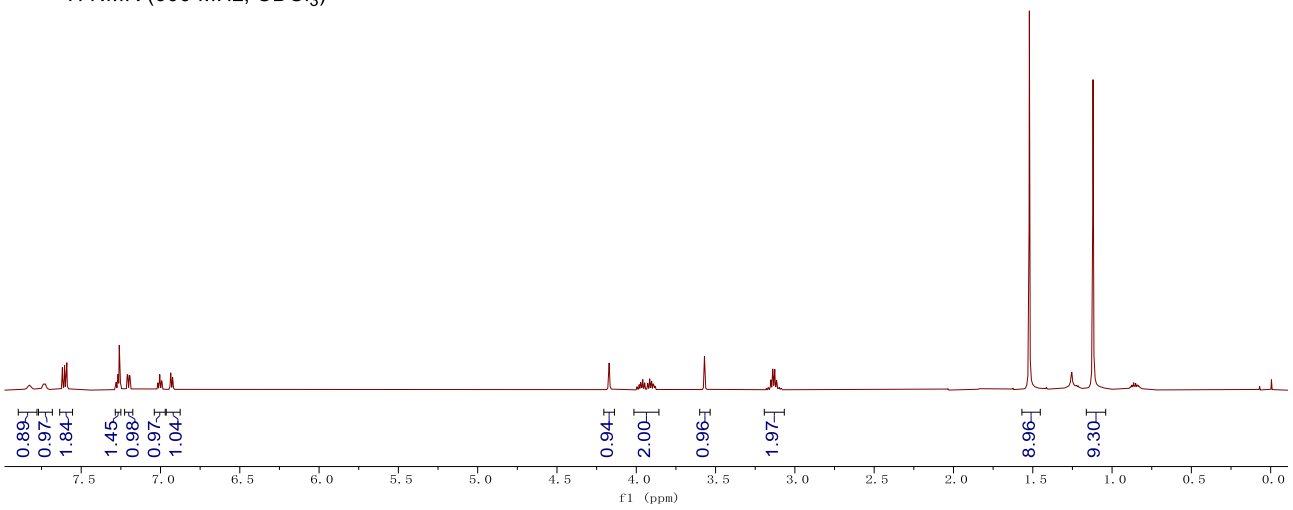
^{13}C NMR (151 MHz, $CDCl_3$)

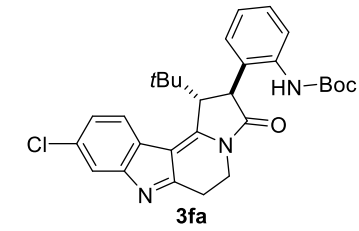




3fa

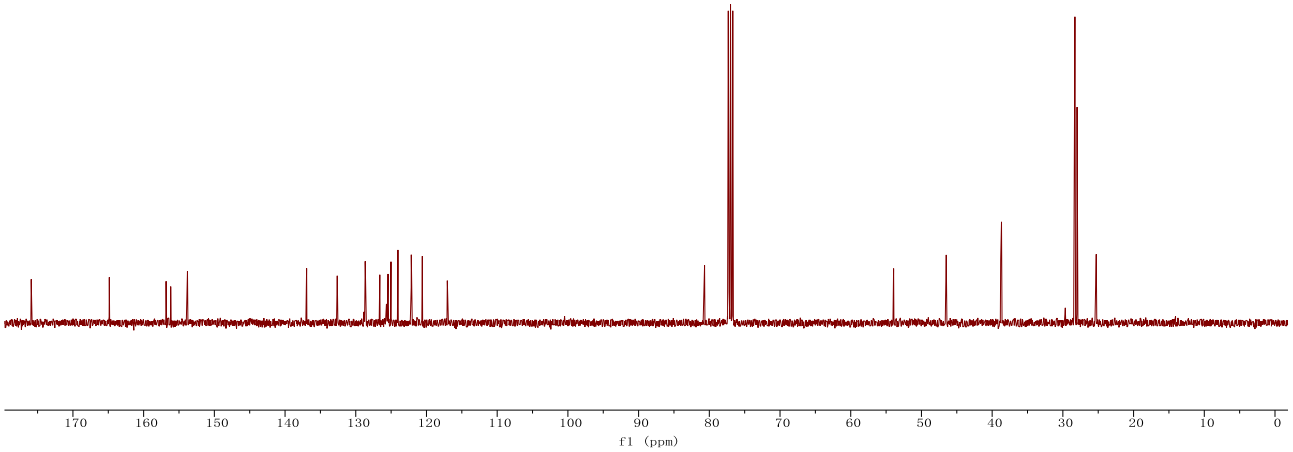
^{1}H NMR (600 MHz, $CDCl_3$)

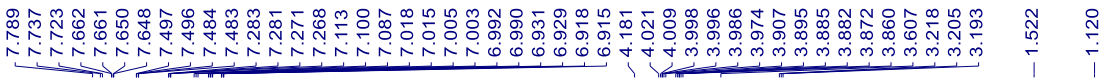


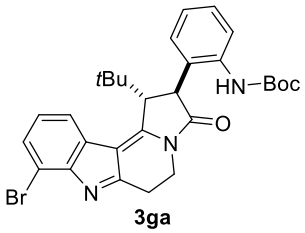


3fa

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

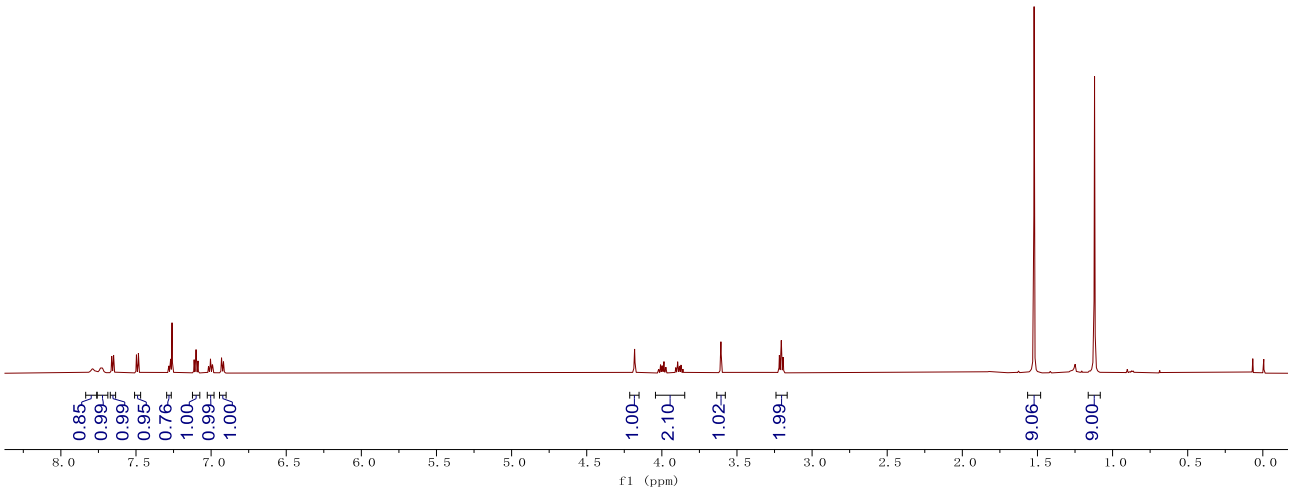


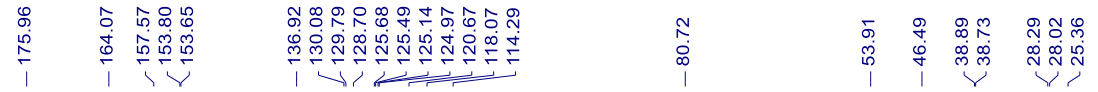


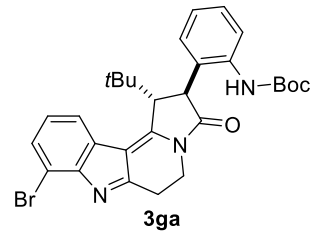


3ga

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

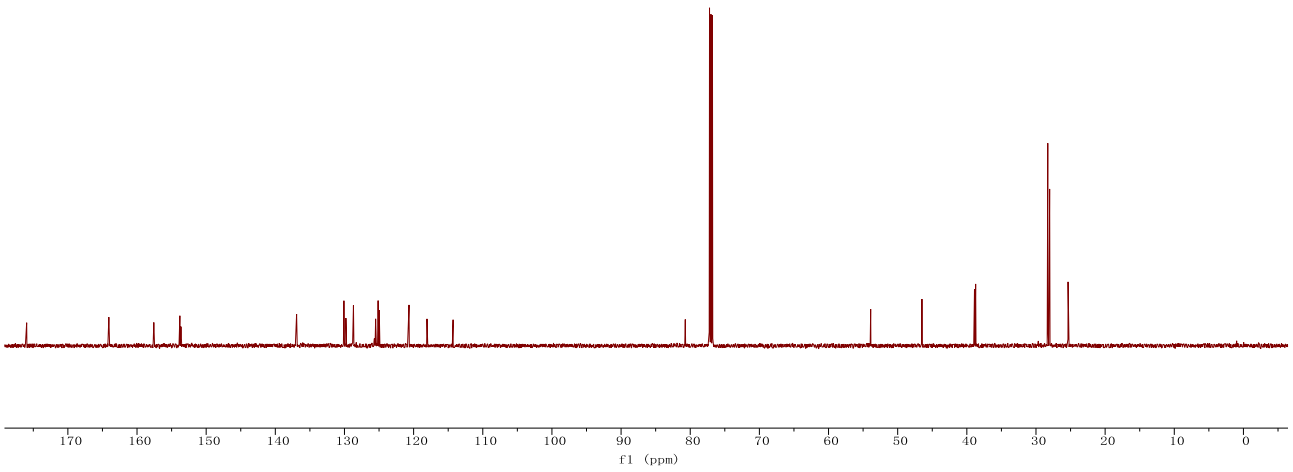


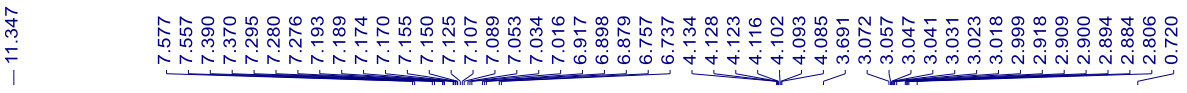


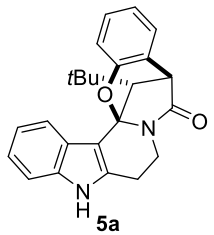


3ga

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

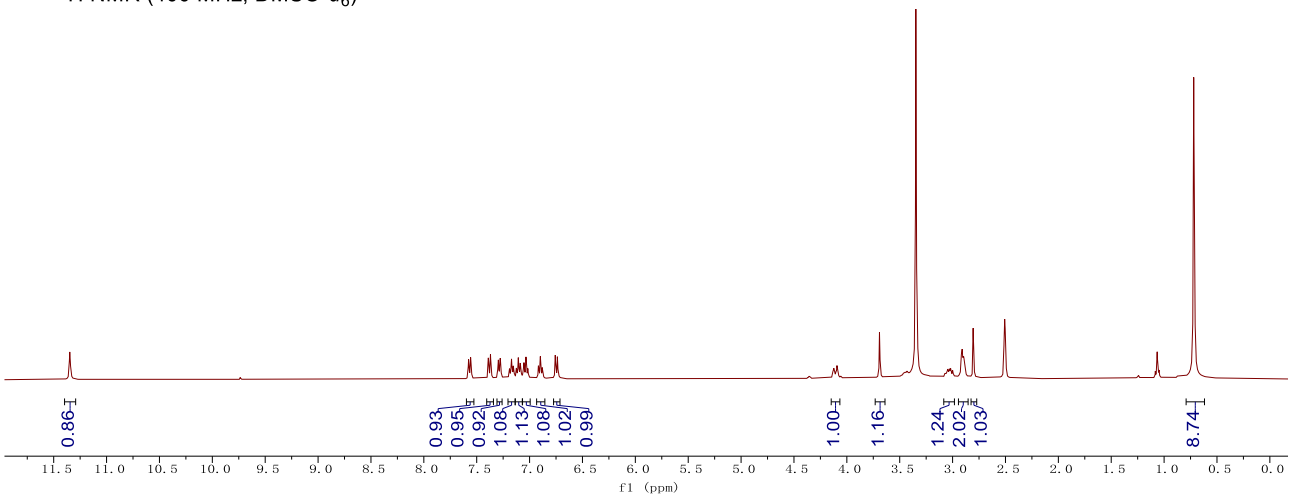


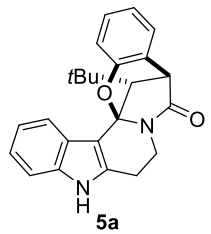




5a

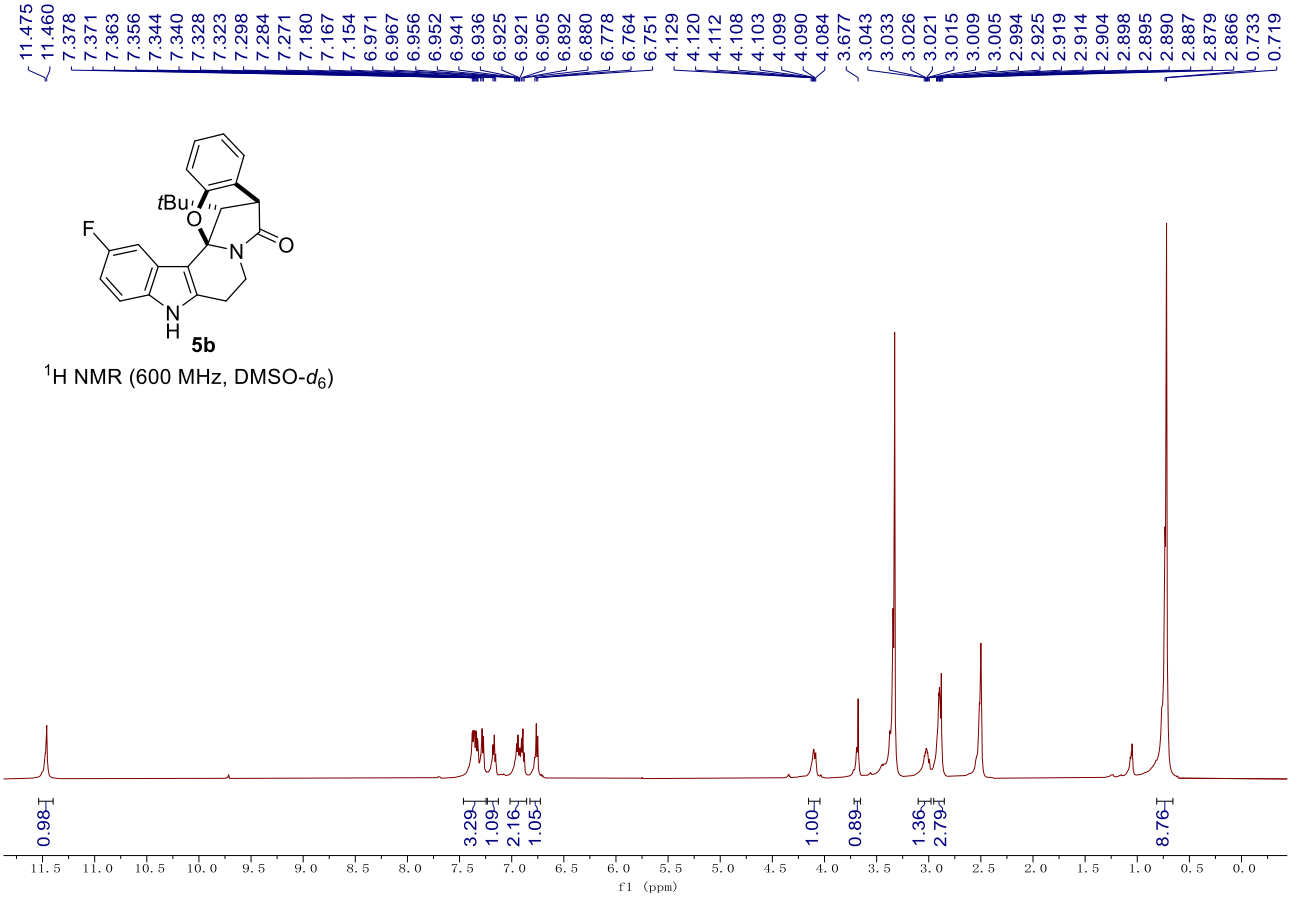
^{1}H NMR (400 MHz, DMSO-d_6)





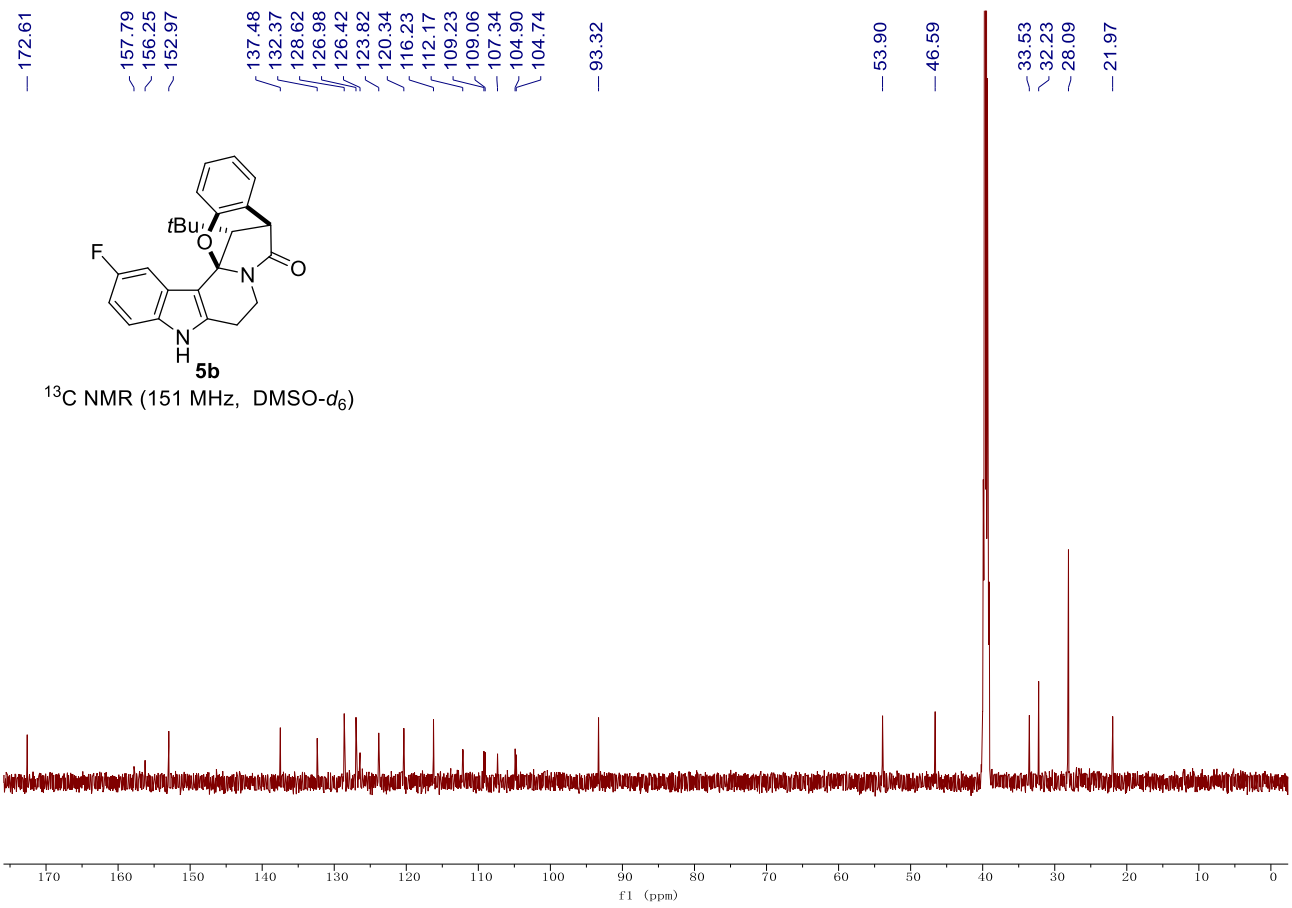
5a

^{13}C NMR (151 MHz, DMSO-d_6)



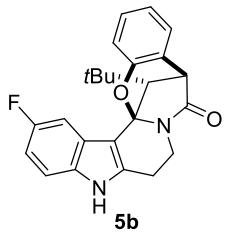
5b

^{1}H NMR (600 MHz, DMSO-d_6)



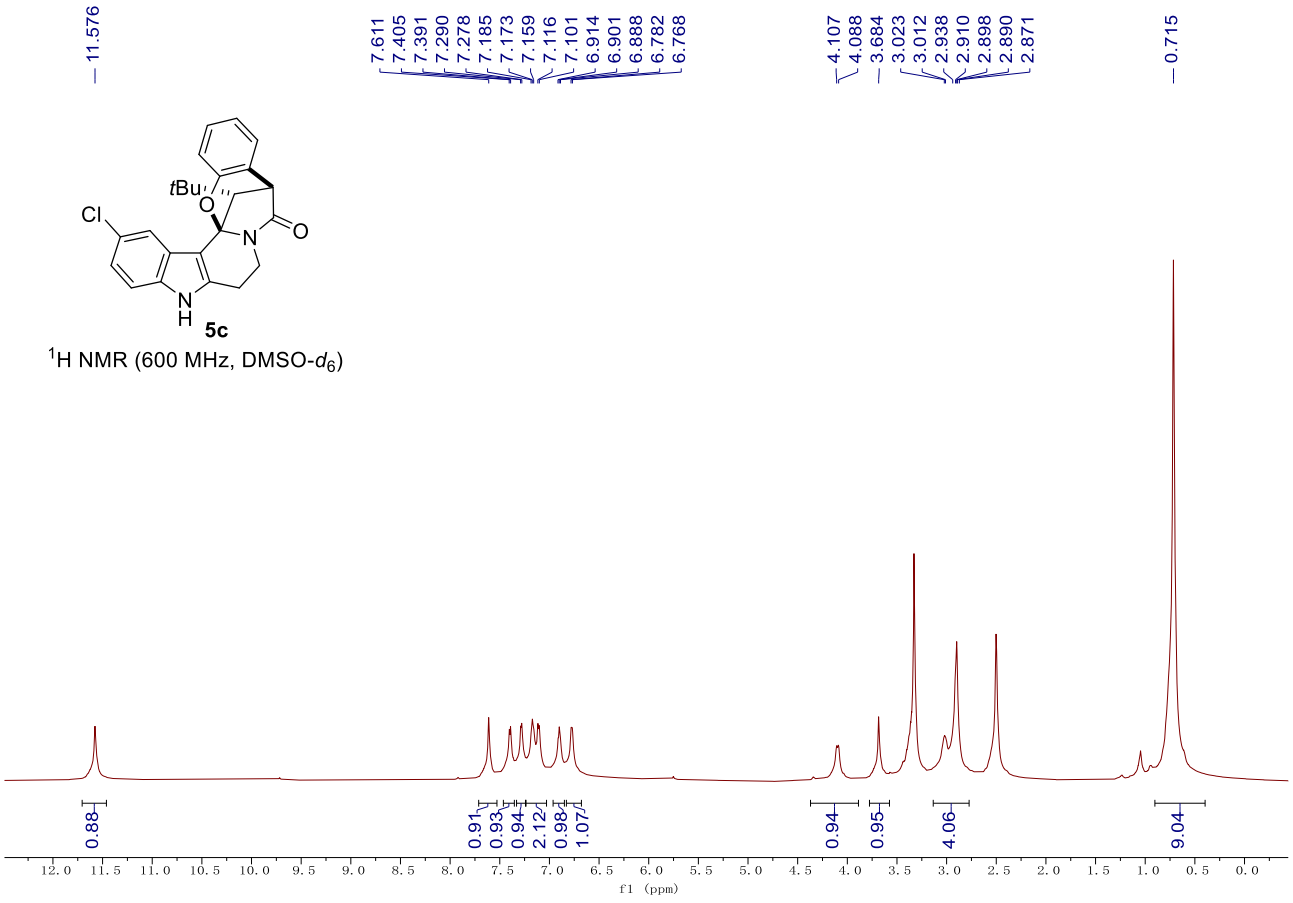
5b

^{13}C NMR (151 MHz, DMSO-d_6)



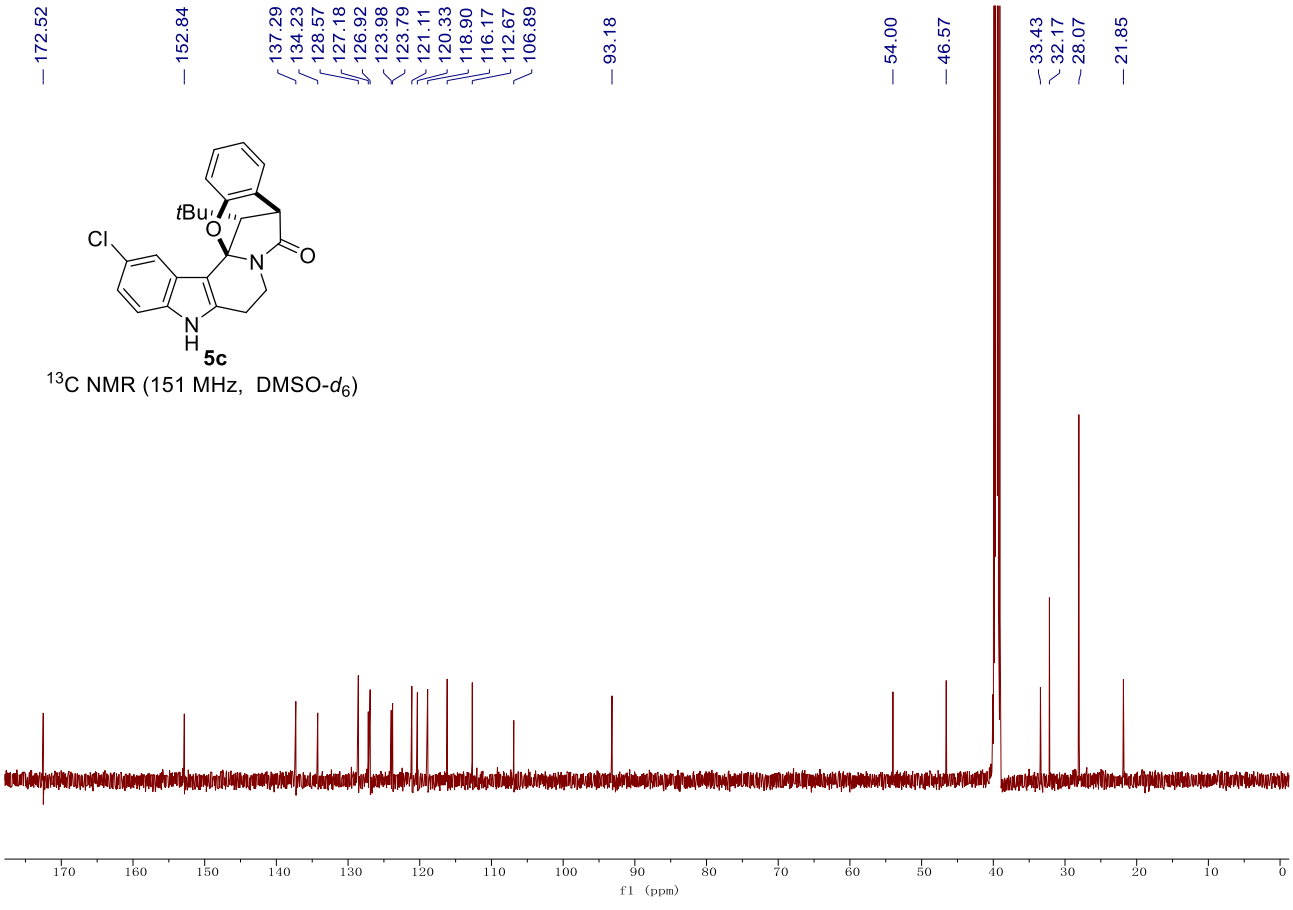
5b

^{19}F NMR (565 MHz, DMSO-d_6)



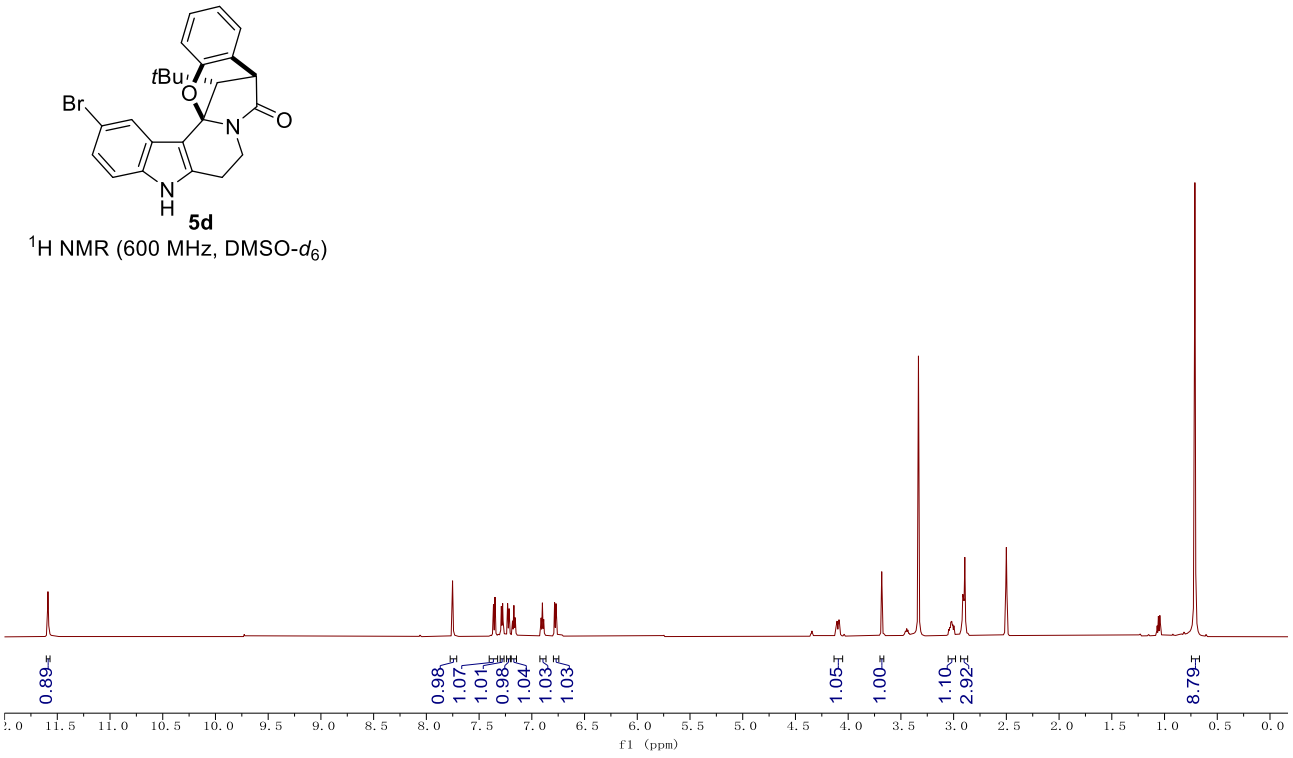
5c

^{1}H NMR (600 MHz, DMSO-d_6)



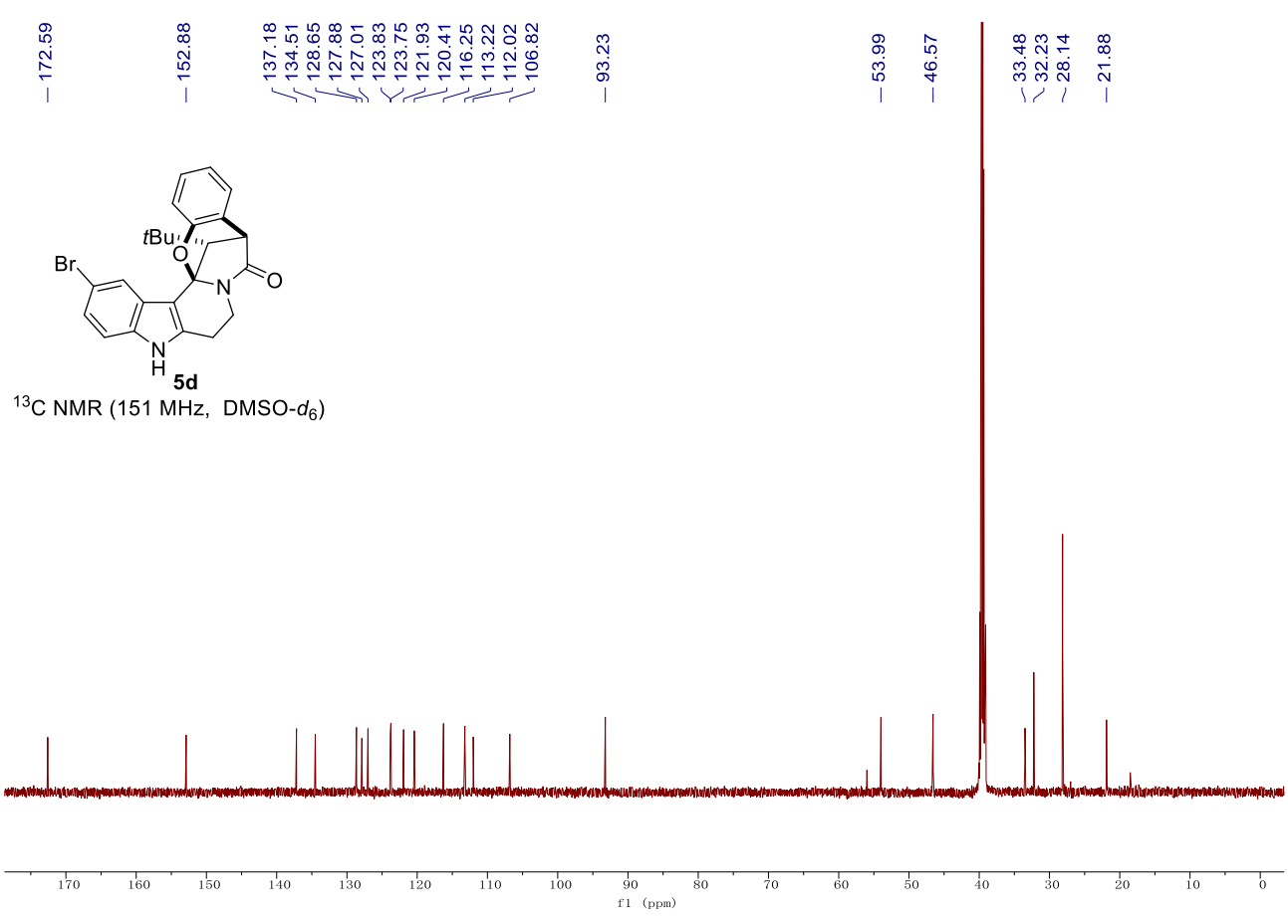
5c

^{13}C NMR (151 MHz, DMSO-d_6)



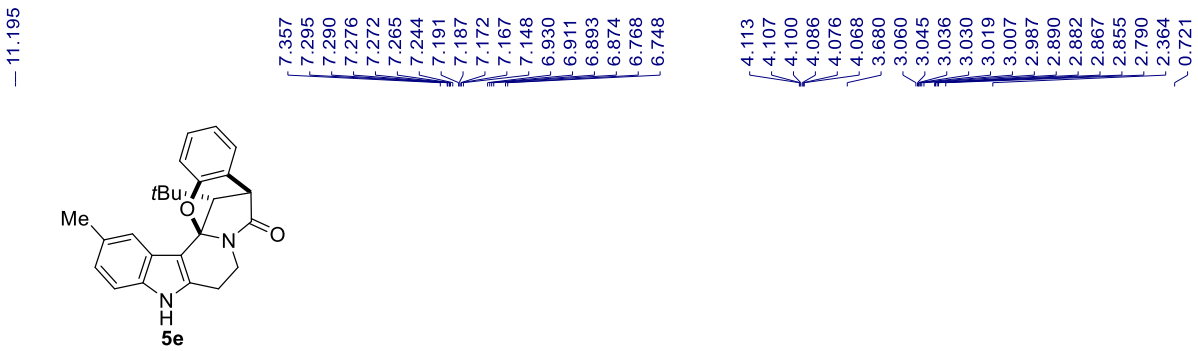
5d

^{1}H NMR (600 MHz, DMSO-d_6)



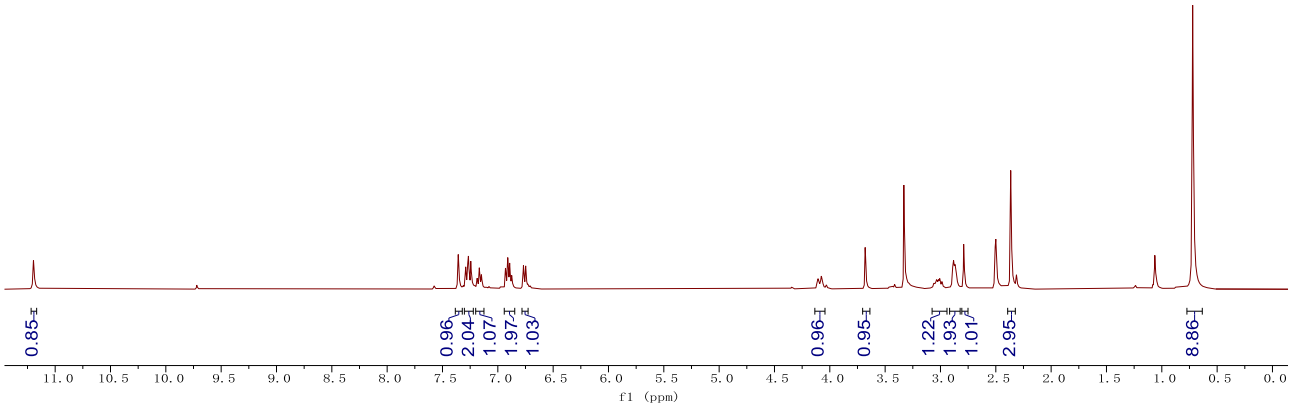
5d

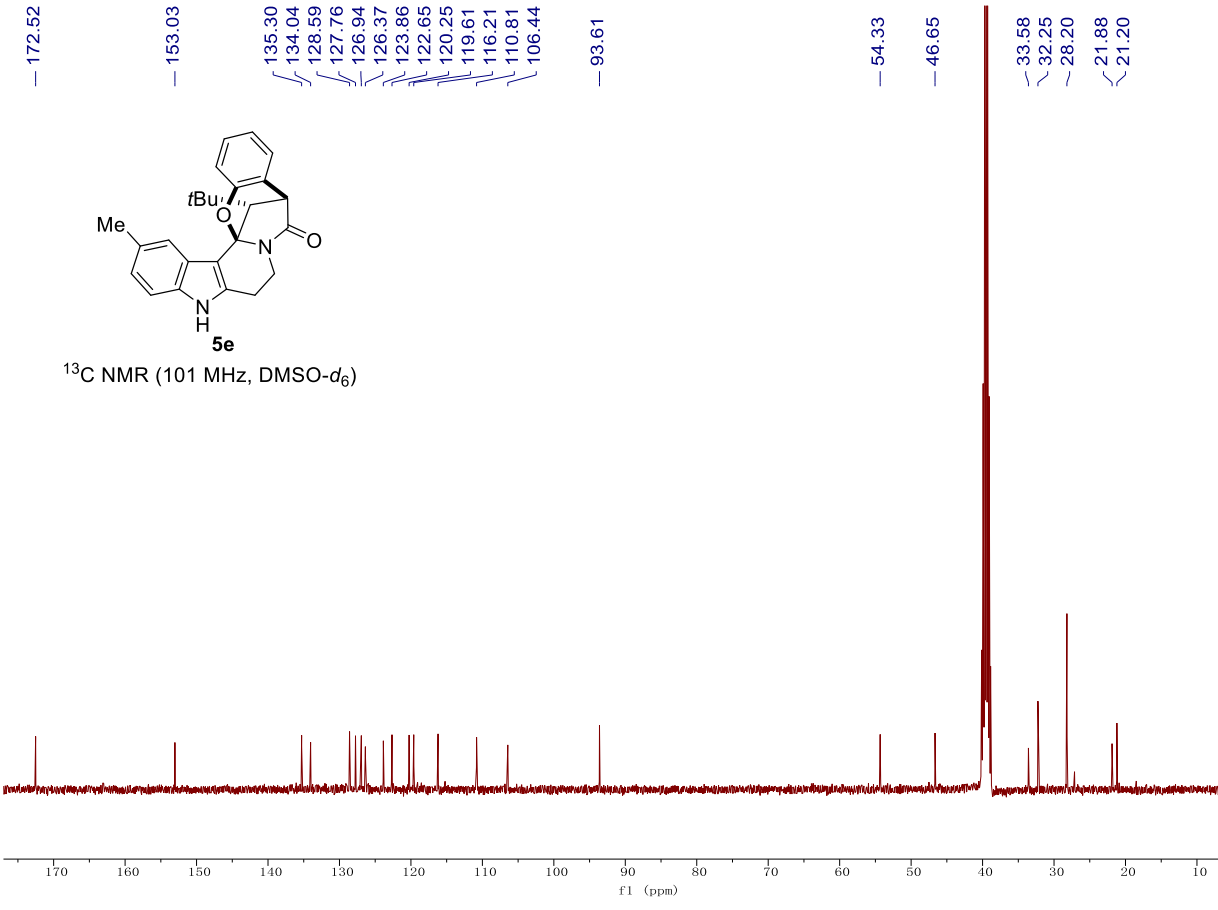
^{13}C NMR (151 MHz, DMSO-d_6)



5e

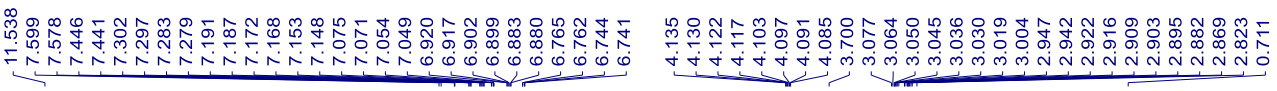
^{1}H NMR (400 MHz, DMSO-d_6)

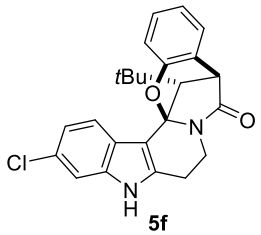




5e

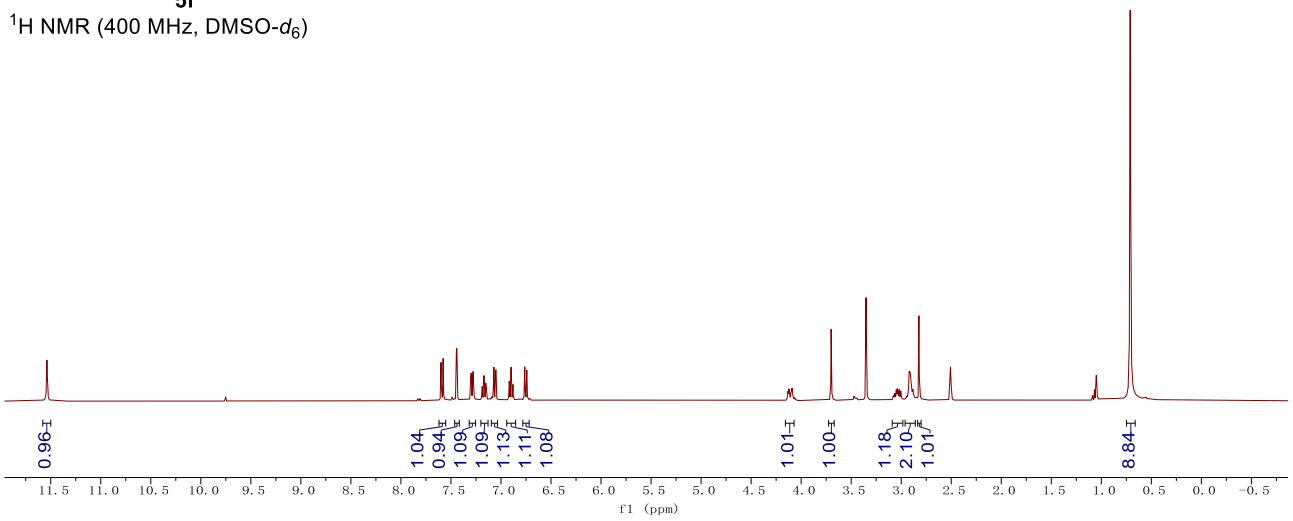
^{13}C NMR (101 MHz, DMSO-d_6)

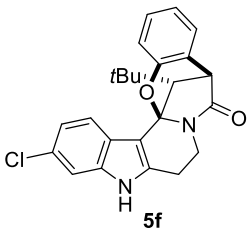




5f

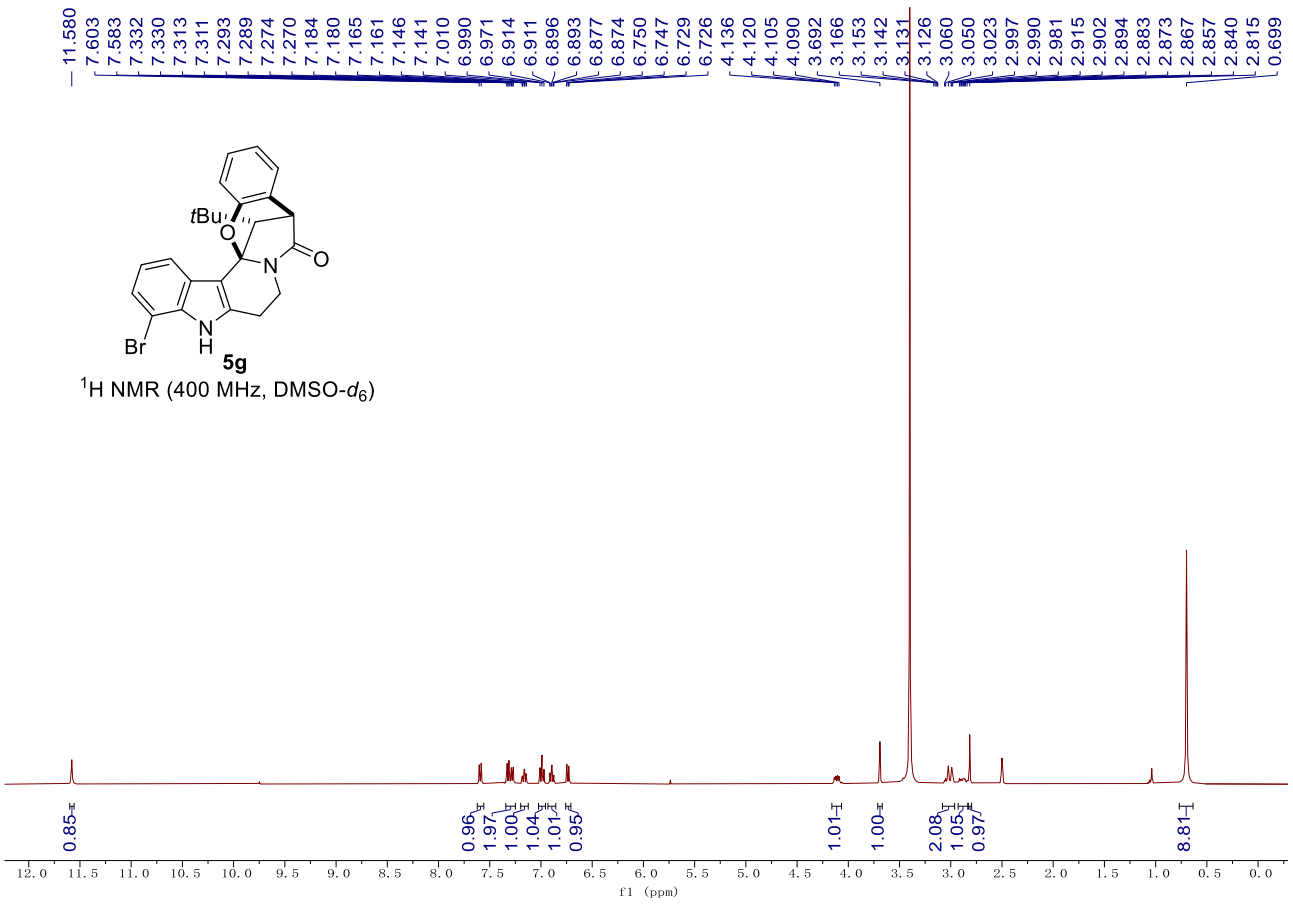
^{1}H NMR (400 MHz, DMSO-d_6)





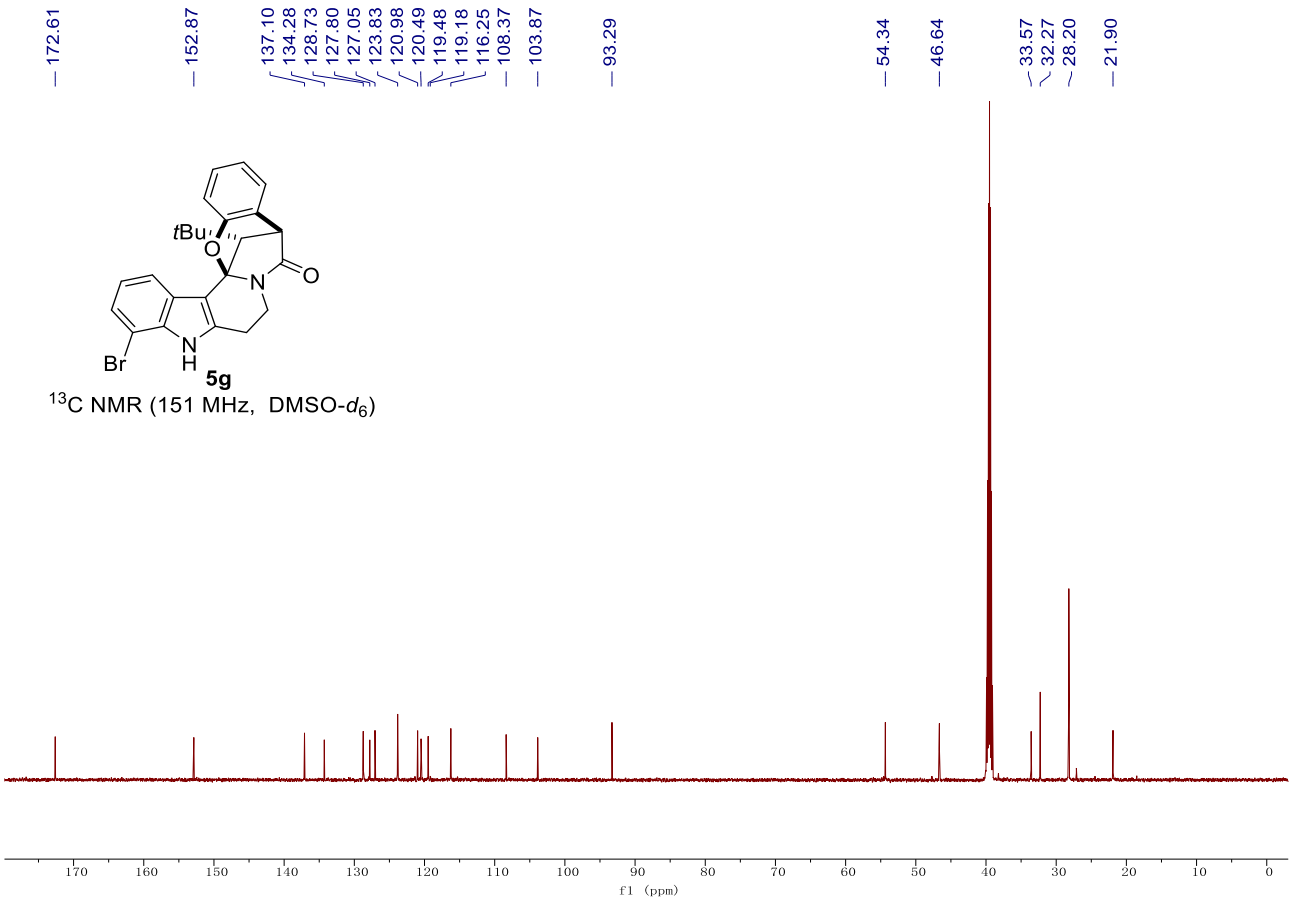
5f

^{13}C NMR (151 MHz, DMSO-d_6)



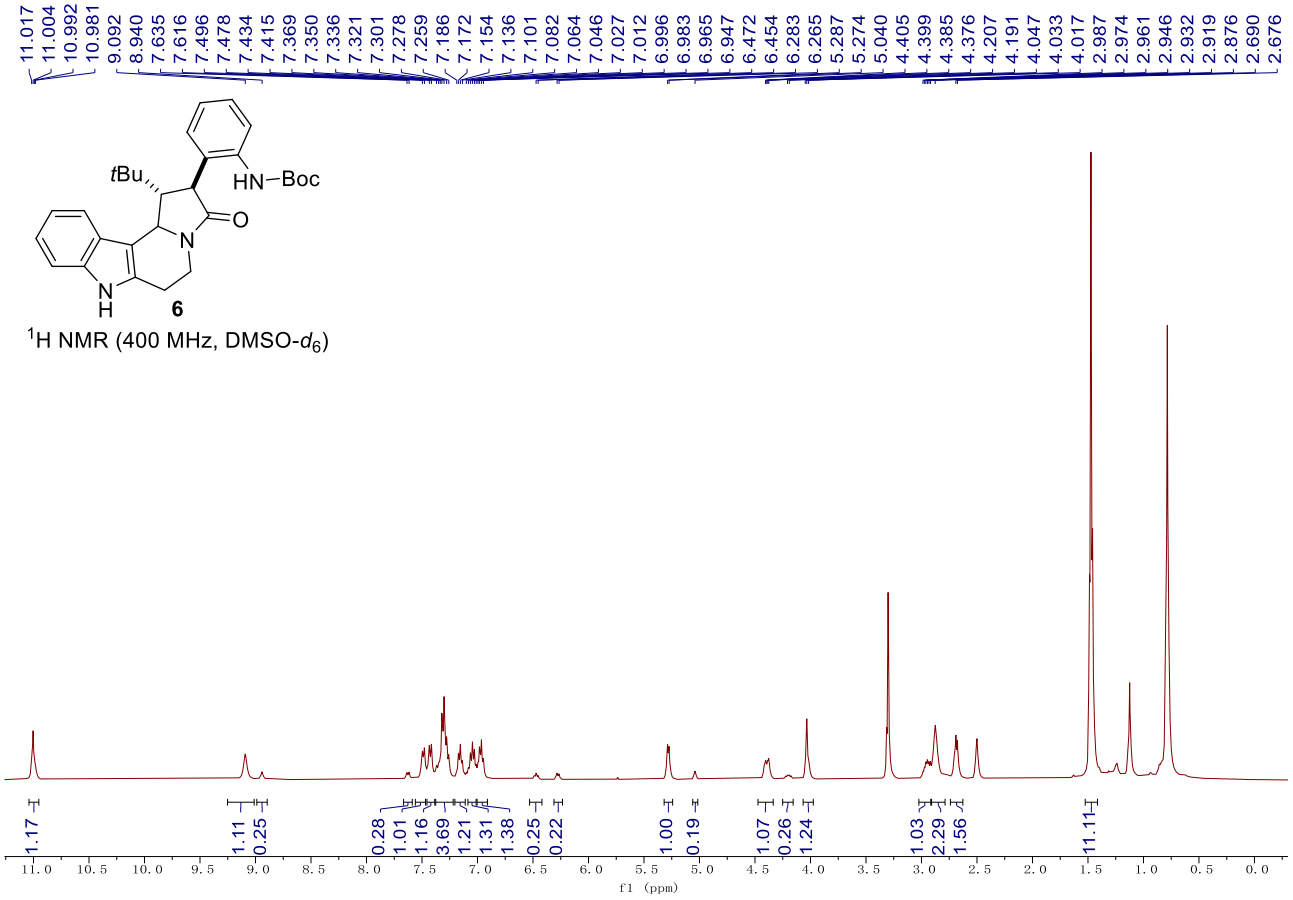
5g

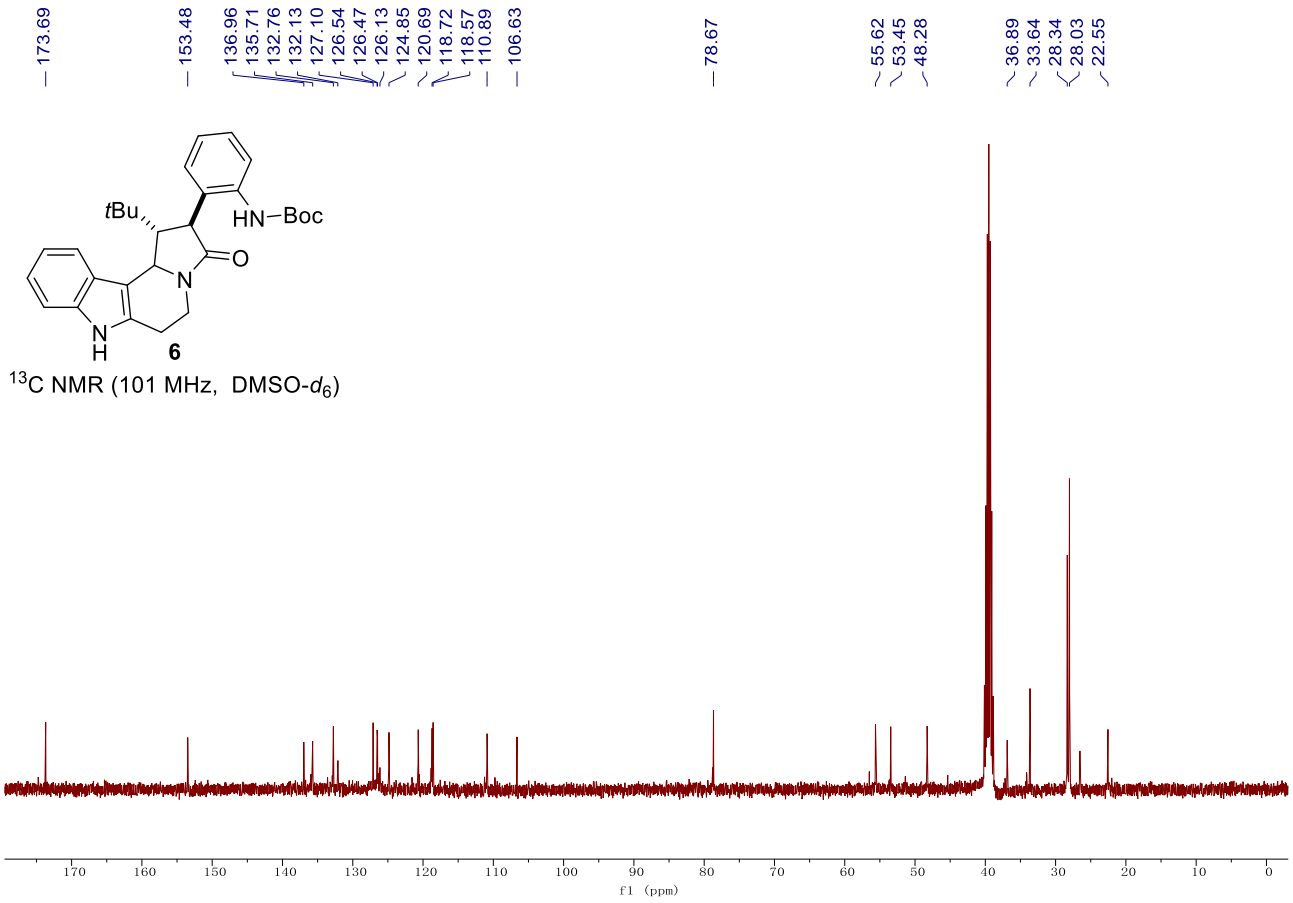
^{1}H NMR (400 MHz, DMSO-d_6)



5g

^{13}C NMR (151 MHz, DMSO-d_6)


11.017
11.004
10.992
10.981
9.092
8.940
7.635
7.616
7.496
7.478
7.434
7.415
7.369
7.350
7.336
7.321
7.301
7.278
7.259
7.186
7.172
7.154
7.136
7.101
7.082
7.064
7.046
7.027
7.012
6.996
6.983
6.965
6.947
6.472
6.454
6.283
6.265
5.287
5.274
5.040
4.405
4.399
4.385
4.376
4.207
4.191
4.047
4.033
4.017
2.987
2.974
2.961
2.946
2.932
2.919
2.876
2.690
2.676
tBu
HN−Boc
O
N
N
H
6
1H NMR (400 MHz, DMSO-d6)
1.17
1.11
0.25
0.28
1.01
1.16
3.69
1.21
1.31
1.38
0.25
0.22
1.00
0.19
1.07
0.26
1.24
1.03
2.29
1.56
11.11
f1 (ppm)


173.69
153.48
136.96
135.71
132.76
132.13
127.10
126.54
126.47
126.13
124.85
120.69
118.72
118.57
110.89
106.63
78.67
55.62
53.45
48.28
36.89
33.64
28.34
28.03
22.55
tBu
HN−Boc
O
N
N
H
6
13C NMR (101 MHz, DMSO-d6)
f1 (ppm)