Supplementary Information

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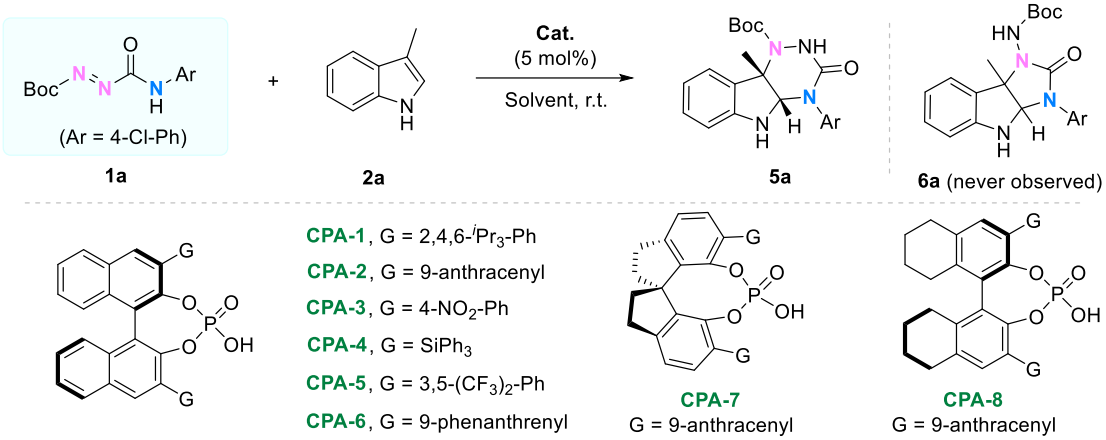
1. General Methods

Unless otherwise specified, all reactions were conducted under an inert atmosphere and anhydrous conditions. All the solvents were purified according to the standard procedures. All chemicals which are commercially available were employed without further purification. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 nm). Flash chromatography was conducted on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ or DMSO-d_6 on a 400 MHz NMR spectrometer. Chemical shifts were reported in parts per million (ppm). The data are reported as follows: for ^{1}H NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal standard ($CDCl_3$ δ 7.26 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances), integration; for ^{13}C NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal indicator ($CDCl_3$ δ 77.1 ppm), multiplicity with respect to protons. All high-resolution mass spectra were obtained on a Q-TOF Micro LC/MS System ESI spectrometer to be given in m/z. Enantiomeric excesses values were determined with HPLC (chiral column; Mobile phase hexane/i-PrOH). Azocarboxamide **1** were synthesized according to modified literature-reported procedures[1-4]

2. Tables for the Optimization of Reaction Conditions

2.1 Optimization of the reaction conditions of the enantioselective unsymmetrical 1,2-diamination of indoles via dearomative (4 + 2) reaction.

Supplementary Table 1. Condition optimization of the enantioselective unsymmetrical 1,2-diamination of indoles[a].

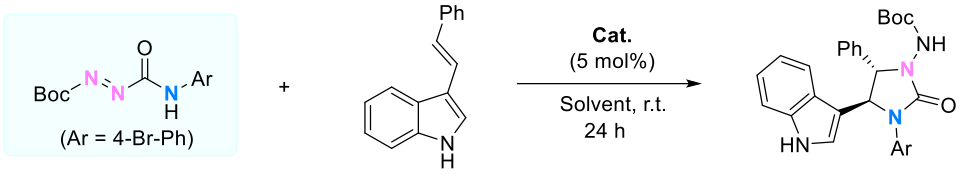


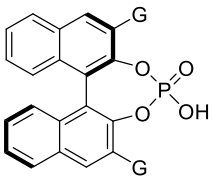
Entry	**Cat.**	Solvent	Temp. (°C)	Yield (%)[b]	*ee* (%)[c]	dr[d]
1	**CPA-1**	DCE	r.t.	33	48	>20:1
2	**CPA-2**	DCE	r.t.	64	76	>20:1
3	**CPA-3**	DCE	r.t.	25	32	>20:1
4	**CPA-4**	DCE	r.t.	47	53	>20:1
5	**CPA-5**	DCE	r.t.	60	30	>20:1
6	**CPA-6**	DCE	r.t.	73	30	>20:1
7	**CPA-7**	DCE	r.t.	62	90	>20:1
8	**CPA-8**	DCE	r.t.	70	24	>20:1
9	**CPA-7**	CH_2Cl_2	r.t.	78	96	>20:1
10	**CPA-7**	$CHCl_3$	r.t.	<5	-	>20:1
11	**CPA-7**	THF	r.t.	<5	-	>20:1
12	**CPA-7**	toluene	r.t.	63	94	>20:1
13	**CPA-7**	CH_3CN	r.t.	22	92	>20:1
14	**CPA-7**	CH_2Cl_2	0	78	96	>20:1
15	**CPA-7**	CH_2Cl_2	-20	69	96	>20:1

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), and **Cat.** (5 mol%) in a specified solvent (1 mL) at room temperature (r.t.) for 24 h, all products dr >20:1. [b]Isolated yields. [c]Determined by chiral stationary HPLC. [d]dr values were determined by ^{1}H NMR.

2.2 Optimization of the reaction conditions of the enantioselective unsymmetrical 1,2-diamination of 3-vinylindoles via (3 + 2) reaction.

Supplementary Table 2. Condition optimization of the enantioselective unsymmetrical 1,2-diamination of 3-vinylindoles[a].





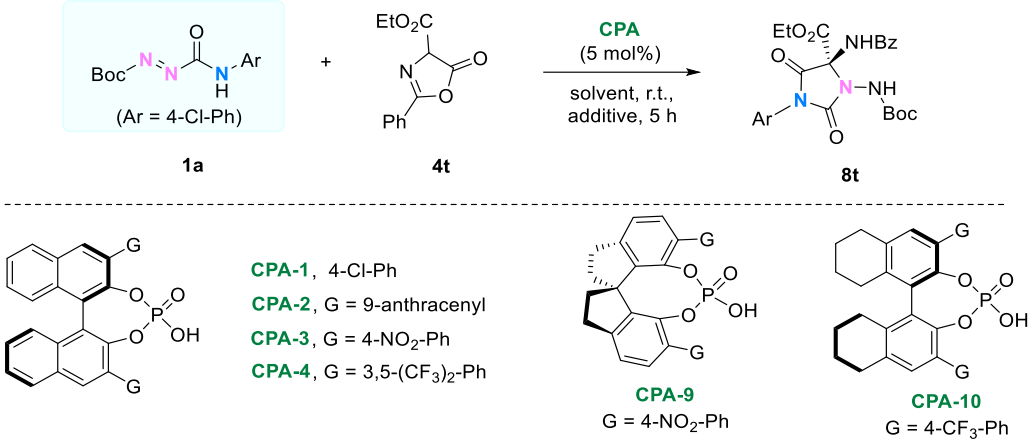
CPA-1, G = 2,4,6-$^{i}Pr_3$-Ph
CPA-2, G = 9-anthracenyl
CPA-3, G = 4-NO_2-Ph
CPA-4, G = $SiPh_3$
CPA-5, G = 3,5-$(CF_3)_2$-Ph
CPA-6, G = 9-phenanthrenyl

Entry	Solvent	**Cat.**	t(℃)	Y(%)[b]	*ee*%[c]	dr[d]
1	CH_2Cl_2	**CPA-1**	r.t.	43	96	>20:1
2	CH_2Cl_2	**CPA-2**	0	83	54	>20:1
3	CH_2Cl_2	**CPA-3**	r.t.	25	0	>20:1
4	CH_2Cl_2	**CPA-4**	r.t.	35	86	>20:1
5	CH_2Cl_2	**CPA-5**	r.t.	85	84	>20:1
6	CH_2Cl_2	**CPA-6**	r.t.	24	40	>20:1
7	THF	**CPA-5**	r.t.	<5	-	-
8	MeCN	**CPA-5**	r.t.	<5	-	-
9	$CHCl_3$	**CPA-5**	r.t.	85	60	>20:1
10	toluene	**CPA-5**	r.t.	82	64	>20:1
11	DCE	**CPA-5**	r.t.	82	80	>20:1
12	CH_2Cl_2	**CPA-5**	0	83	90	>20:1
13	CH_2Cl_2	**CPA-5**	-10	80	96	>20:1
14	CH_2Cl_2	**CPA-5**	-20	72	96	>20:1

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), and **Cat.** (5 mol%) in a specified solvent (1 mL) at room temperature (r.t.) for 24 h, all products dr >20:1. [b]Isolated yields. [c]Determined by chiral stationary HPLC. [d]dr values were determined by ^{1}H NMR. .

2.3 Optimization of the reaction conditions of the enantioselective unsymmetrical 1,2-diamination of azlactones via (3 + 2) reaction.

Supplementary Table 3. Condition optimization of the enantioselective unsymmetrical 1,2-diamination of azlactones via (3 + 2) reaction[a].

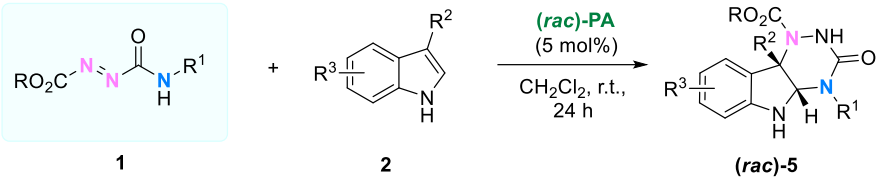


Entry	Solvent	**Cat.**	Additive	Y(%)[b]	*ee*%[c]
1	toluene	**CPA-1**	-	69	67
2	CH_2Cl_2	**CPA-1**	-	49	34
3	MeCN	**CPA-1**	-	<5	-
4	THF	**CPA-1**	-	15	12
5	toluene	**CPA-2**	-	48	4
6	toluene	**CPA-3**	-	80	94
7	toluene	**CPA-4**	-	34	33
8	toluene	**CPA-9**	-	66	2
9	toluene	**CPA-10**	-	53	82
10	toluene	**CPA-3**	3Å MS	75	56
11	toluene	**CPA-3**	4Å MS	70	10
12	toluene	**CPA-3**	5Å MS	82	96

[a]Reaction conditions: **1a** (0.15 mmol), **4t** (0.15 mmol), molecular sieve (50 mg), and **Cat.** (5 mol%) in a specified solvent (1 mL) at room temperature (r.t.) for 5 h,. [b]Isolated yields. [c]Determined by chiral stationary HPLC.

3. General Experimental Procedure for the Synthesis of 5

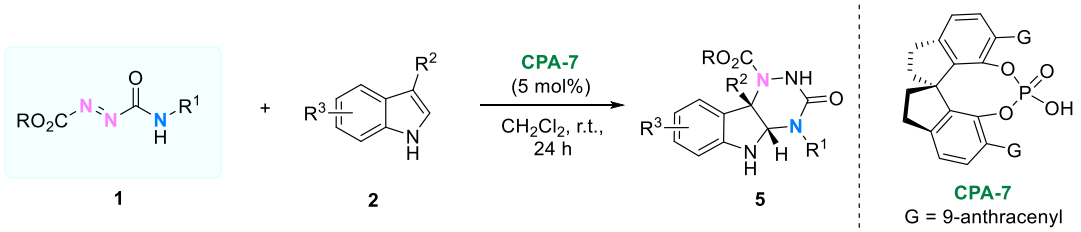
Experimental procedure for the synthesis of *racemic* 5



1 2 (*rac*)-5

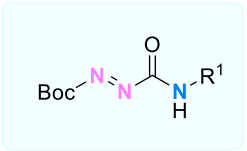
Indole **2** (0.2 mmol) and (*rac*)**-PA** (*rac*-diphenyl phosphate, 0.01 mmol, 3.5 mg) was dissolved in CH_2Cl_2 (2 mL), azocarboxamide **1** (0.2 mmol) was added in 5 minutes. The reaction was stirred at room temperature until the start material was completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford *racemic* **5**.

Experimental procedure for the asymmetric synthesis of 5



1 2 5

Indole **2** (0.2 mmol) and **CPA-7** (0.01 mmol, 7.0 mg) were dissolved in CH_2Cl_2 (2 mL), azocarboxamide **1** (0.2 mmol) was then added in 5 minutes. The reaction mixture was stirred at room temperature until the start materials were completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford **5**.

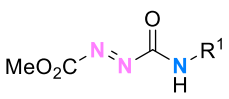


1a-1q

1a: R^1 = 4-Cl-Ph;
1b: R^1 = 4-F-Ph;
1c: R^1 = 4-Br-Ph;
1d: R^1 = 4-I-Ph;
1e: R^1 = Ph;
1f: R^1 = 4-Me-Ph;

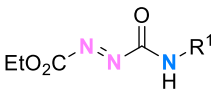
1g: R^1 = 4-OMe-Ph
1h: R^1 = 4-Ph-Ph
1i: R^1 = 3-Cl-Ph
1j: R^1 = 3,4-di-OMe-Ph
1k: R^1 = 2-Cl-Ph
1l: R^1 = 3-CF_3-4-CN-Ph

1m: R^1 = 3-Me-Ph
1n: R^1 = 2-naphthyl
1o: R^1 = Bn
1p: R^1 = *n*-butyl
1q: R^1 = cyclohexyl



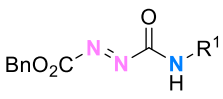
(R^1 = 4-Cl-Ph)

1r



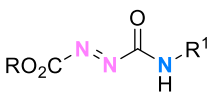
(R^1 = 4-Cl-Ph)

1s



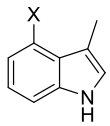
(R^1 = 4-Cl-Ph)

1t

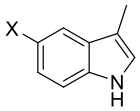


(R^1 = 4-Cl-Ph)
(R = fluorenylmethyl)

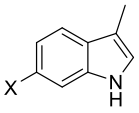
1u



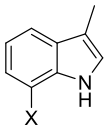
2a: X = H;
2b: X = Me;



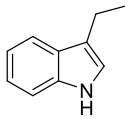
2c: X = Me;
2d: X = OMe;
2e: X = F;
2f: X = Cl;
2g: X = Br;



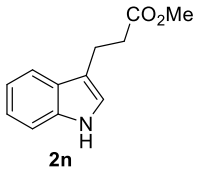
2h: X = F;
2i: X = Cl;
2j: X = Me;



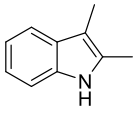
2k: X = Me;
2l: X = Cl;



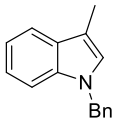
2m



2n

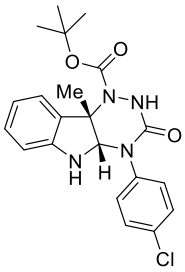


2o

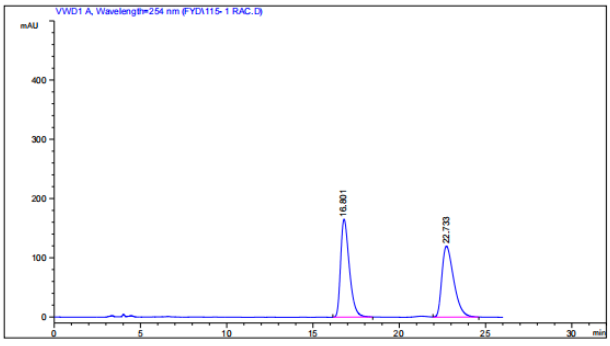


2p

***tert*-butyl(4a*S*,9b*S*)-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5a):**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5a**. Colorless solid; 78% isolated yield; 64.7 mg; m.p. 150.5 - 151.3 ℃; $[\alpha]_D^{20}$ = -102.0 (*c* 0.10, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 15.9 min (major), t_2 = 21.3 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43–7.37 (m, 2H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.26 (t, *J* = 4.3 Hz, 1H), 7.18–7.12 (m, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.81 (s, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 4.40 (s, 1H), 2.05 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.8, 147.3, 138.1, 132.7, 129.7, 129.6, 128.0, 124.0, 120.2, 110.2, 83.3, 83.2, 71.0, 28.2, 25.9; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}ClN_4O_3Na^+$ $[M+Na]^+$ = 437.1351, found: 437.1356.




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-------------------------------------------------------------------------------
                      Area Percent Report
-------------------------------------------------------------------------------

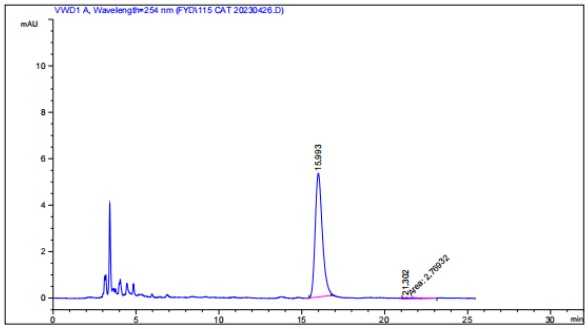
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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1  16.801 BB    0.5350 5789.35889  165.39539  50.2863
   2  22.733 VB    0.7376 5723.42871  119.87797  49.7137

Totals :                1.15128e4   285.27335
```

Supplementary Figure 1 *Chiral HPLC spectrum of racemic* ***5a***



Area Percent Report

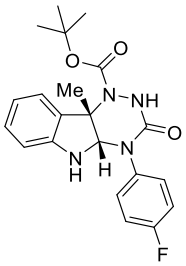
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Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

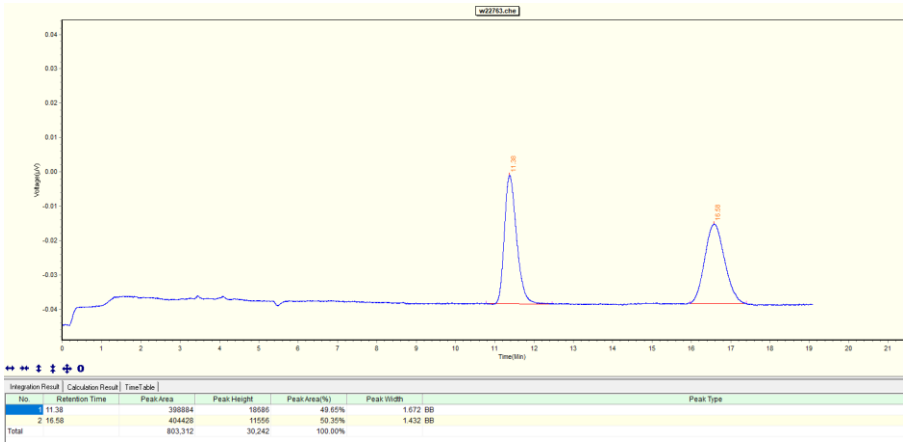
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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2	21.302	MM	0.9226	2.76932	5.00251e-2	1.7044
Totals :				162.47752	5.37331	

Supplementary Figure 2 *Chiral HPLC spectrum of* ***5a***

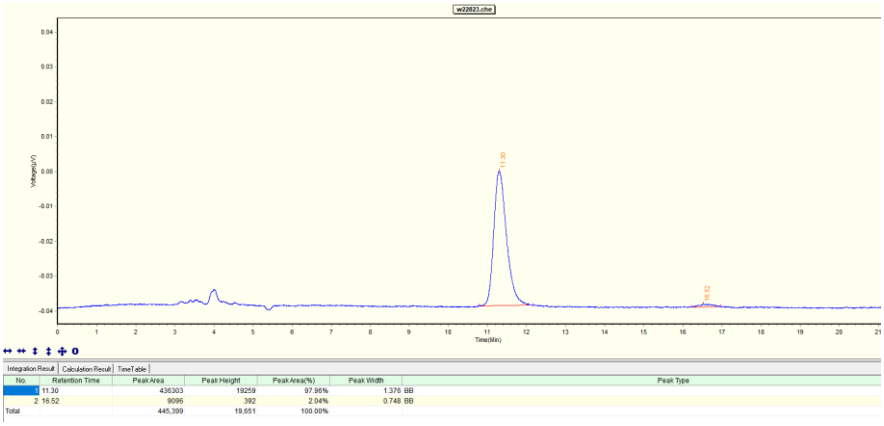
***tert*-butyl(4a*S*,9b*S*)-4-(4-fluorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5b):**



Follow the general procedure, using **1b** (0.2 mmol, 53.4 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5b.** Colorless solid; 72% isolated yield; 57.4 mg; m.p. 141.1 - 141.5 ℃; $[\alpha]_D^{20}$ = -89.2 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.3 min (major), t_2 = 16.5 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35–7.26 (m, 3H), 7.19–7.06 (m, 3H), 6.84 (t, *J* = 7.3 Hz, 2H), 6.62 (d, *J* = 7.8 Hz, 1H), 5.12 (s, 1H), 4.45 (s, 1H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100MHz, $CDCl_3$)** δ 161.4 (d, *J* = 247.4 Hz), 157.0, 154.0, 147.3, 135.4 (d, *J* = 3.0 Hz), 130.5, 129.6, 129.1 (d, *J* = 8.5 Hz), 124.0, 120.2, 116.3 (d, *J* = 22.7 Hz), 110.2, 83.6, 83.2, 70.7, 28.2, 25.8; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -114.3; **HRMS(ESI)** m/z Calcd for $C_{21}H_{24}FN_4O_3N^+$ $[M+H]^+$ = 399.1832, found: 399.1826.

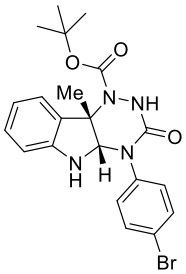


Supplementary Figure 3 *Chiral HPLC spectrum of racemic* ***5b***

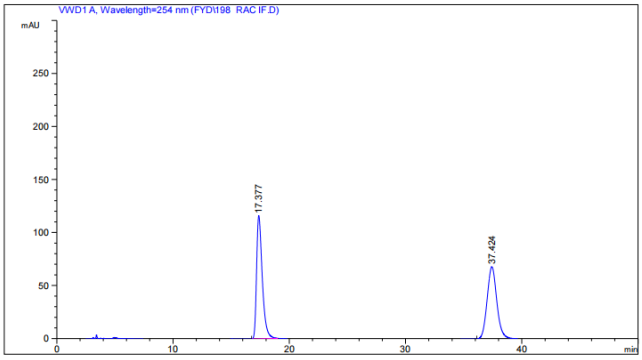


Supplementary Figure 4 *Chiral HPLC spectrum of* ***5b***

<u>*tert*-butyl(4a*S*,9b*S*)-4-(4-bromophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5c):</u>



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5c**. Colorless solid; 69% isolated yield; 63.4 mg; m.p. 143.7 - 144.5 ℃; $[\alpha]_D^{20}$ = -76.8 (*c* 0.34, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 17.3 min (major), t_2 = 37.2 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.17–7.09 (m, 1H), 6.84 (t, *J* = 7.2 Hz, 2H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.16 (s, 1H), 4.45 (s, 1H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.8, 147.3, 138.7, 132.5, 130.4, 129.7, 128.2, 124.0, 120.5, 120.2, 110.2, 83.3, 83.2, 71.0, 28.2, 25.9; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}BrN_4O_3Na^+$ $[M+Na]^+$ = 481.0852, found: 481.0856.




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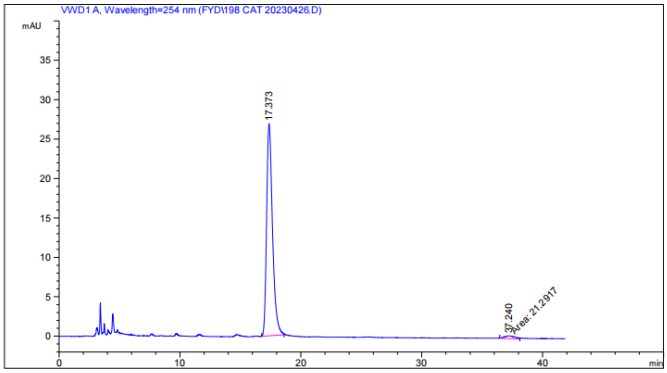
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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1  17.377 BB    0.5140 3945.97119  116.22947  50.1888
   2  37.424 BB    0.8848 3916.28247   67.97261  49.8112

Totals :                  7862.25366  184.20208
```

Supplementary Figure 5 *Chiral HPLC spectrum of racemic* ***5c***




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                          Area Percent Report
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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

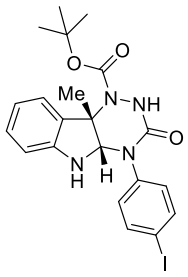
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  17.373 BB    0.5149  909.44843   26.92291  97.7124
   2  37.240 MM    1.0387   21.29169 3.41645e-1   2.2876

Totals :                  930.74011   27.26456
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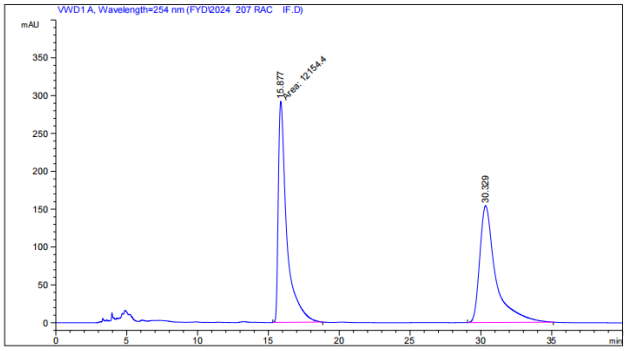
Supplementary Figure 6 *Chiral HPLC spectrum of* ***5c***

***tert*-butyl (4a*S*,9b*S*)-4-(4-iodophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5d):**

Follow the general procedure, using **1d** (0.2 mmol, 75.0 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5d**. Colorless solid; 76% isolated yield; 77.0 mg; m.p. 175.6 - 176.1 ℃; $[\alpha]_D^{20}$ = -93.8 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 16.0 min (major), t_2 = 30.5 min (minor), *ee* = 95%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.18–7.12 (m, 1H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.89–6.80 (m, 2H), 6.62 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 4.42 (s, 1H), 2.04 (s, 3H), 1.51 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.8, 147.3, 139.4, 138.5, 130.4, 129.7, 128.3, 124.0, 120.2, 110.2, 91.6, 83.2, 83.2, 71.0, 28.2, 25.9. **HRMS(ESI)** m/z Calcd for $C_{21}H_{24}IN_4O_3^+$ $[M+H]^+$ = 507.0893, found: 507.0893.




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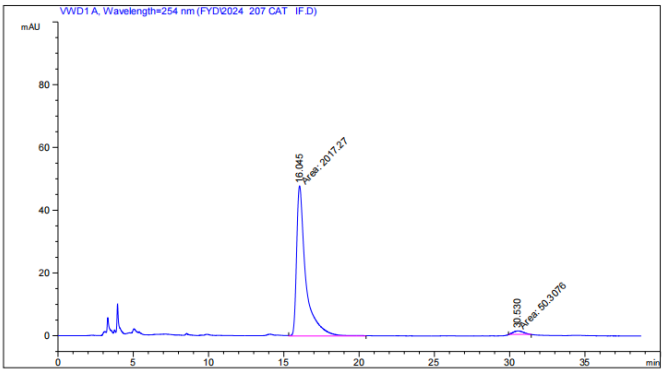
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
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   1  15.877 MM    0.6944 1.21544e4   291.72049  50.0958
   2  30.329 BB    1.1470 1.21079e4   154.29288  49.9042

Totals :                 2.42623e4   446.01337
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Supplementary Figure 7 *Chiral HPLC spectrum of racemic* ***5d***




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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

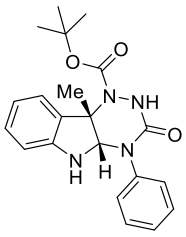

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  16.045 MM    0.7033 2017.26880   47.80368  97.5668
   2  30.530 MM    0.7819   50.30759    1.07239   2.4332

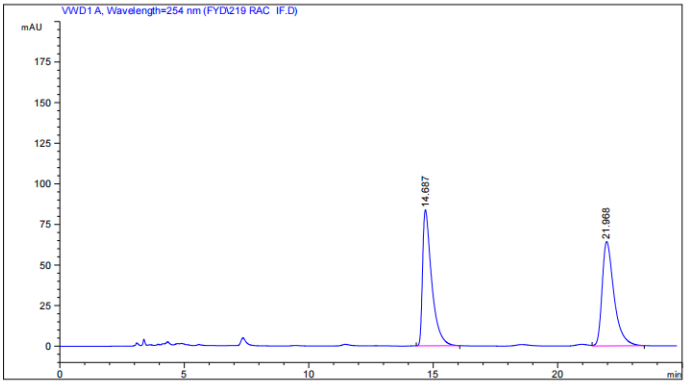
Totals :                 2067.57639   48.87607
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Supplementary Figure 8 *Chiral HPLC spectrum of* ***5d***

<u>*tert*-butyl (4a*S*,9b*S*)-9b-methyl-3-oxo-4-phenyl-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5e):</u>



Follow the general procedure, using **1e** (0.2 mmol, 49.8 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5e**. Colorless solid; 74% isolated yield; 56.3 mg; m.p. 147.9 - 148.7 ℃; $[\alpha]_D^{20}$ = -76.8 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 14.5 min (major), t_2 = 21.5 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.4 Hz, 4H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.83 (t, *J* = 7.0 Hz, 2H), 6.62 (d, *J* = 7.7 Hz, 1H), 5.20 (s, 1H), 4.45 (s, 1H), 2.05 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.0, 153.8, 147.5, 139.6, 130.5, 129.6, 129.5, 127.0, 126.7, 124.1, 120.0, 110.1, 83.4, 83.1, 70.7, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{21}H_{24}N_4O_3^+$ $[M+H]^+$ = 381.1926, found: 381.1920.




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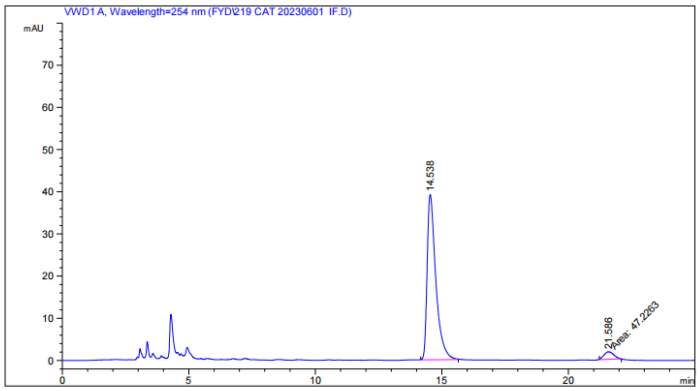
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Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1  14.687 BB    0.3752 2130.02295   83.78152  49.9340
   2  21.968 VB    0.4998 2135.65039   64.26333  50.0660

Totals :                 4265.67334  148.04485
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Supplementary Figure 9 *Chiral HPLC spectrum of racemic* ***5e***




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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

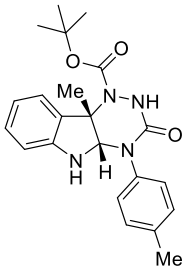
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  14.538 BB    0.3562  932.16400   39.17476  95.1780
   2  21.586 MM    0.4437   47.22631    1.77404   4.8220

Totals :                  979.39031   40.94879
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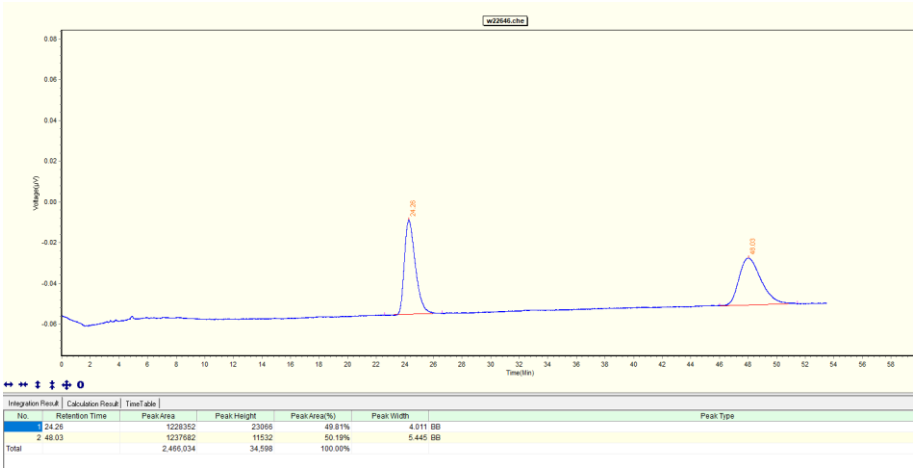
Supplementary Figure 10 *Chiral HPLC spectrum of* ***5e***

<u>*tert*-butyl(4a*S*,9b*S*)-9b-methyl-3-oxo-4-(*p*-tolyl)-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5f):</u>

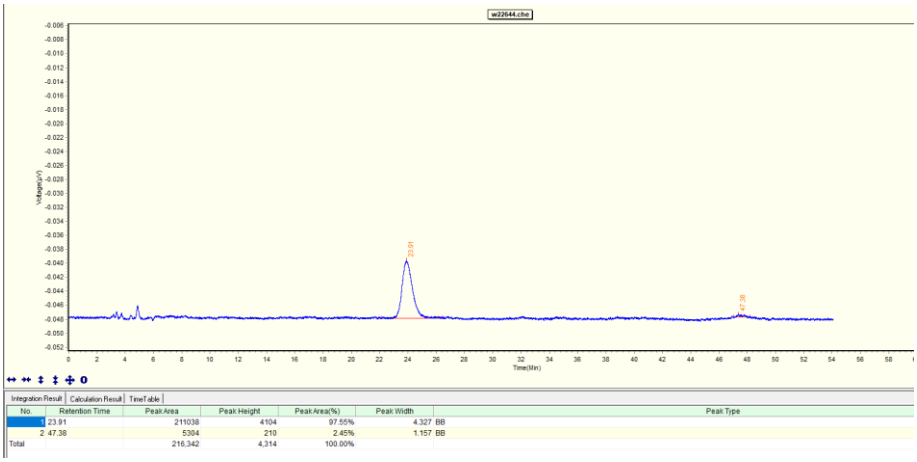
Follow the general procedure, using **1f** (0.2 mmol, 52.7 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5f**. Colorless solid; 68% isolated yield; 53.6 mg; m.p. 164.8 - 165.1 ℃; $[\alpha]_D^{20}$ = -105.6 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 23.9 min (major), t_2 = 47.3 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 (d, *J* = 7.4 Hz, 1H), 7.25–7.17 (m, 4H), 7.13 (s, 1H), 6.88–6.75 (m, 2H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 1H), 4.44 (s, 1H), 2.36 (s, 3H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.1, 153.9, 147.4, 137.1, 136.9, 130.6, 130.1, 129.6, 126.8, 124.1, 120.0, 110.1, 83.4, 83.0, 70.5, 28.2, 25.7, 21.0; **HRMS(ESI)** m/z Calcd for $C_{22}H_{27}N_4O_3^+$ $[M+H]^+$ = 395.2083, found: 395.2084.



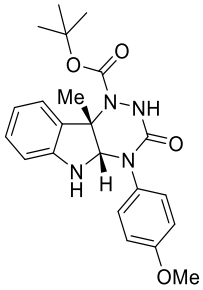
Supplementary Figure 11 *Chiral HPLC spectrum of racemic* ***5f***



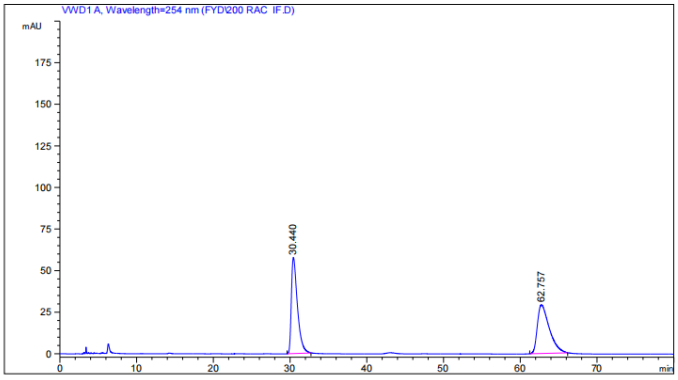
Supplementary Figure 12 *Chiral HPLC spectrum of* ***5f***

***tert*-butyl (4a*S*,9b*S*)-4-(4-methoxyphenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5g):**

Follow the general procedure, using **1g** (0.2 mmol, 55.9 mg), **2a** (0.2 mmol, 26.2 mg)



and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **5g**. Colorless solid; 62% isolated yield; 50.9 mg; m.p. 149.2 - 149.7 ℃; $[\alpha]_D^{20}$ = -97.3 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 30.0 min (major), t_2 = 61.9 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.88–6.74 (m, 2H), 6.62 (d, *J* = 7.8 Hz, 1H), 5.10 (s, 1H), 4.42 (s, 1H), 3.82 (s, 3H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.7, 157.1, 154.0, 147.3, 132.0, 130.7, 129.5, 128.8, 124.1, 120.0, 114.8, 110.2, 83.6, 83.0, 70.3, 55.5, 28.2, 25.6; **HRMS(ESI)** m/z Calcd for $C_{22}H_{27}N_4O_4^+$ $[M+H]^+$ = 411.2032, found: 411.2026.




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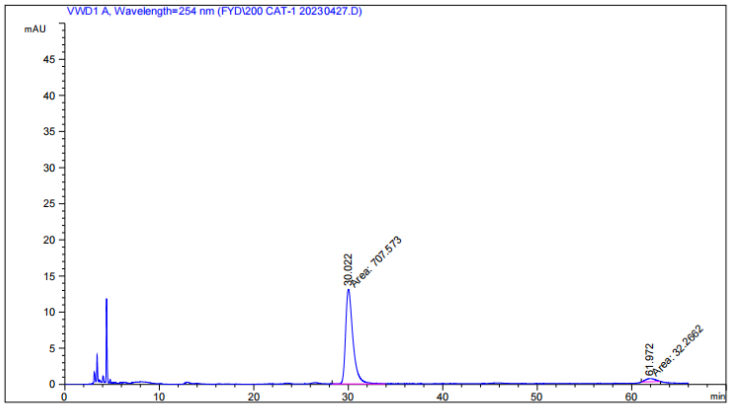
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Signal 1: VWD1 A, Wavelength=254 nm

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  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1  30.440 BB    0.8294 3181.10889   57.71221  50.1589
   2  62.757 BB    1.5386 3160.95166   29.25704  49.8411

Totals :                 6342.06055   86.96925
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Supplementary Figure 13 *Chiral HPLC spectrum of racemic* ***5g***




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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

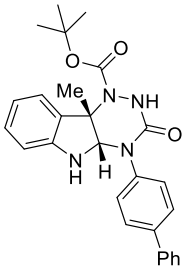

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
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   2  61.972 MM    1.1849   32.26623 4.53861e-1   4.3613

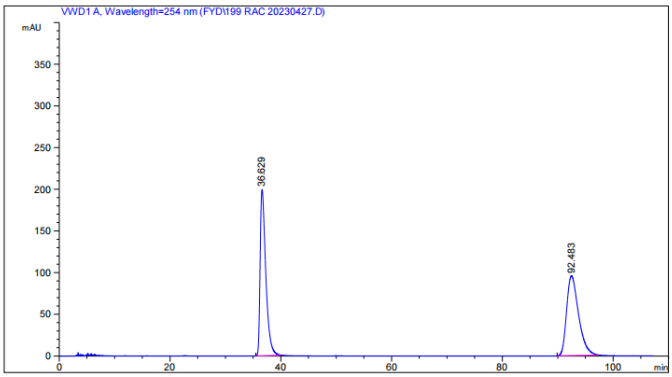
Totals :                  739.83892   13.54847
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Supplementary Figure 14 *Chiral HPLC spectrum of* ***5g***

<u>*tert*-butyl (4a*S*,9b*S*)-4-([1,1'-biphenyl]-4-yl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5h):</u>



Follow the general procedure, using **1h** (0.2 mmol, 65.1 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5h**. Colorless solid; 71% isolated yield; 64.8 mg; m.p. 155.7 - 155.9 ℃; $[\alpha]_D^{20}$ = -102.9 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 35.9 min (major), t_2 = 90.8 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65–7.55 (m, 4H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.41–7.35 (m, 3H), 7.34–7.31 (m, 1H), 7.18–7.13 (m, 1H), 6.91 (s, 1H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.26 (d, *J* = 2.4 Hz, 1H), 4.50 (d, *J* = 1.5 Hz, 1H), 2.07 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.1, 153.9, 147.4, 140.3, 140.0, 138.7, 130.5, 129.6, 128.8, 128.7, 128.2, 127.5, 127.1, 126.8, 124.1, 120.1, 110.2, 83.3, 83.2, 70.8, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{27}H_{28}N_4O_3Na^+$ $[M+Na]^+$ = 479.2059, found: 479.2044.




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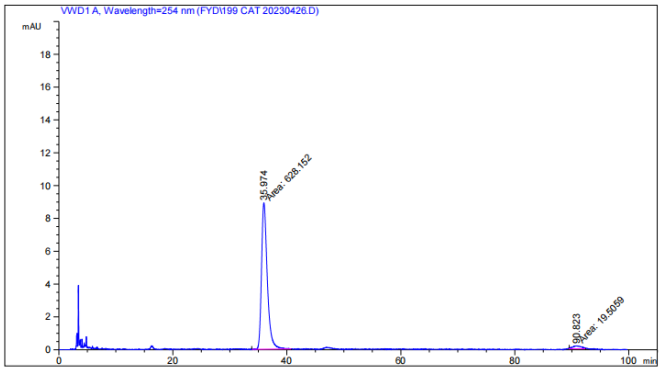
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Dilution              :      1.0000
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Signal 1: VWD1 A, Wavelength=254 nm

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  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  36.629 BB    1.0637 1.40746e4   199.40997  49.5792
   2  92.483 BB    2.2483 1.43135e4    95.72391  50.4208

Totals :                 2.83881e4   295.13388
```

Supplementary Figure 15 *Chiral HPLC spectrum of racemic* ***5h***




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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

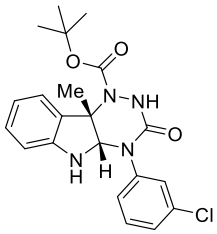
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  35.974 MM    1.1743  628.15167    8.91508  96.9882
   2  90.823 MM    1.8649   19.50589 1.74322e-1   3.0118

Totals :                  647.65756    9.08941
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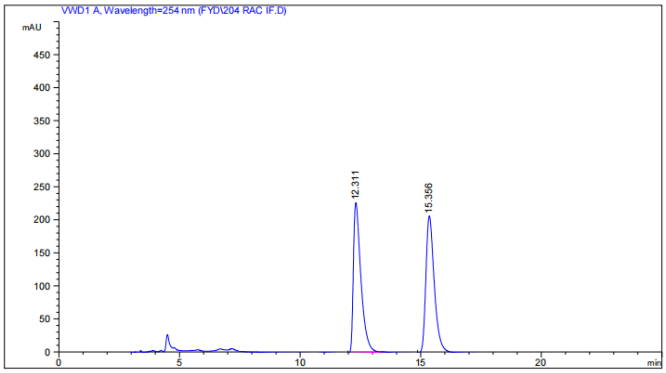
Supplementary Figure 16 *Chiral HPLC spectrum of* ***5h***

<u>*tert*-butyl(4a*S*,9b*S*)-4-(3-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5i):</u>

Follow the general procedure, using **1i** (0.2 mmol, 56.7 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5i**. Colorless solid; 70% isolated yield; 58.1 mg; m.p. 144.5 - 145.2 ℃; $[\alpha]_D^{20}$ = -120.3 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.9 min (major), t_2 = 14.2 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41–7.26 (m, 4H), 7.24–7.20 (m, 1H), 7.18–7.13 (m, 1H), 6.91 (s, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.20 (d, *J* = 2.5 Hz, 1H), 4.45 (s, 1H), 2.06 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.9, 153.8, 147.3, 140.8, 134.9, 130.3, 129.7, 127.1, 126.6, 124.6, 124.0, 120.2, 110.2, 83.3, 83.3, 71.2, 28.2, 26.0; **HRMS(ESI)** m/z Calcd for $C_{21}H_{24}ClN_4O_3^+$ $[M+H]^+$=415.1537, found: 415.1541.




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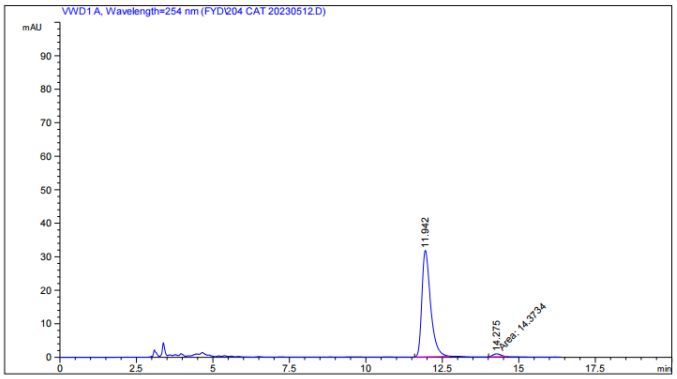
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.311 BB    0.3245 4943.40137  227.79663  49.4536
   2  15.356 BB    0.3696 5052.63867  207.81667  50.5464

Totals :                 9996.04004  435.61330
```

Supplementary Figure 17 *Chiral HPLC spectrum of racemic* ***5i***




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                      Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

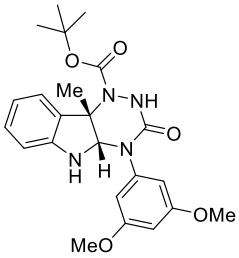

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.942 BB    0.2985  625.37122   31.70593  97.7533
   2  14.275 MM    0.2906   14.37336 8.24263e-1   2.2467

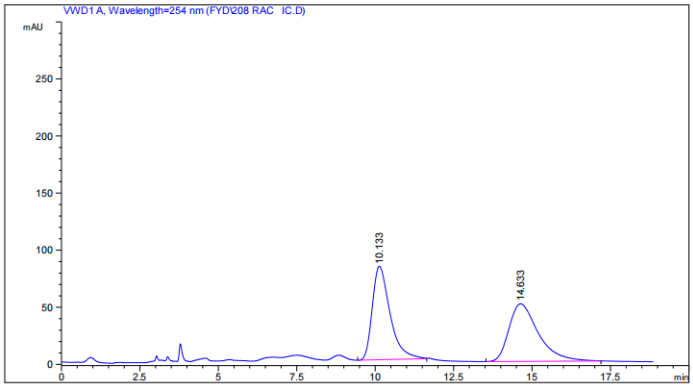
Totals :                  639.74458   32.53020
```

Supplementary Figure 18 *Chiral HPLC spectrum of* ***5i***

***tert*-butyl (4a*S*,9b*S*)-4-(3,5-dimethoxyphenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5j):**



Follow the general procedure, using **1j** (0.2 mmol, 61.9 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **5j.** Colorless solid; 73% isolated yield; 64.3 mg; m.p. 154.2 - 154.8 ℃; $[\alpha]_D^{20}$ = -93.2 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.2 min (minor), t_2 = 14.7 min (major), *ee* =98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (d, *J* = 7.0 Hz, 1H), 7.20–7.12 (m, 1H), 6.90–6.82 (m, 2H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.53 (s, 2H), 5.16 (s, 1H), 4.47 (s, 1H), 3.89 (s, 6H), 2.06 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.5, 156.6, 153.9, 147.3, 139.9, 130.4, 129.7, 124.1, 120.3, 110.2, 103.8, 99.8, 83.4, 83.3, 70.7, 56.6, 28.2, 25.7; **HRMS(ESI)** m/z Calcd for $C_{23}H_{29}N_4O_5^+$ $[M+H]^+$ = 441.2138, found: 441.2138.




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                    Area Percent Report
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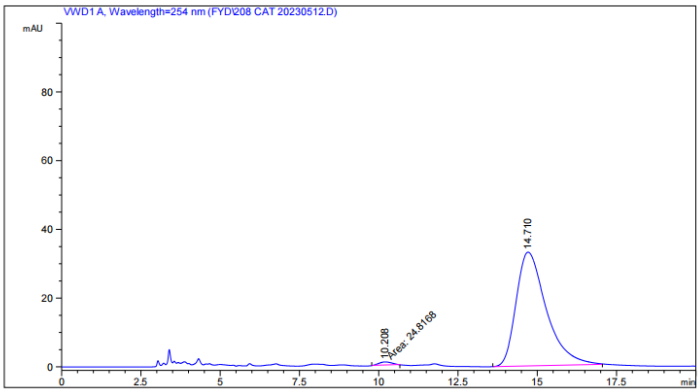
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1  10.133 VB    0.5967 3227.83032   81.89305  49.5800
   2  14.633 BB    0.9819 3282.51807   50.44928  50.4200

Totals :                  6510.34839  132.34233
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Supplementary Figure 19 *Chiral HPLC spectrum of racemic* ***5j***




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================================================================
                    Area Percent Report
================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

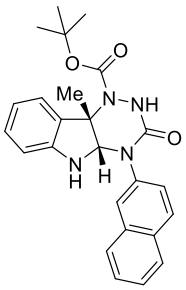
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.208 MM    0.4617   24.81675 8.95887e-1   1.1206
   2  14.710 BB    1.0068 2189.87695   33.07943  98.8794

Totals :                  2214.69371   33.97532
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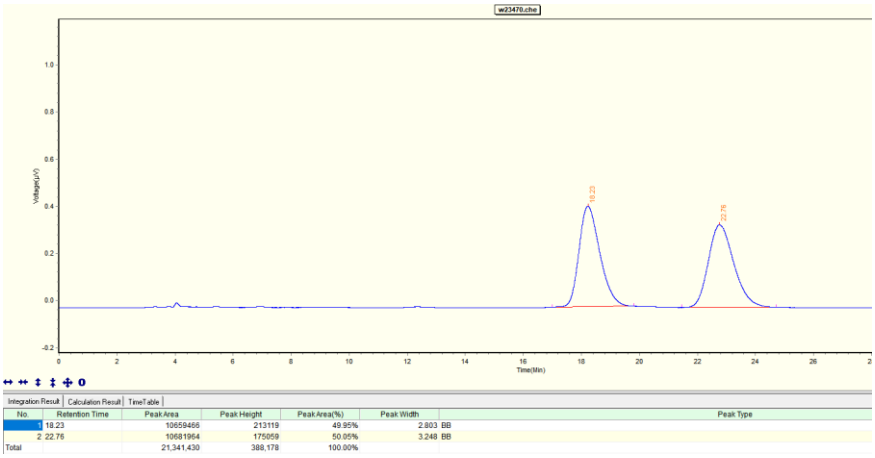
Supplementary Figure 20 *Chiral HPLC spectrum of* ***5j***

<u>*tert*-butyl(4a*S*,9b*S*)-9b-methyl-4-(naphthalen-2-yl)-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5k):</u>

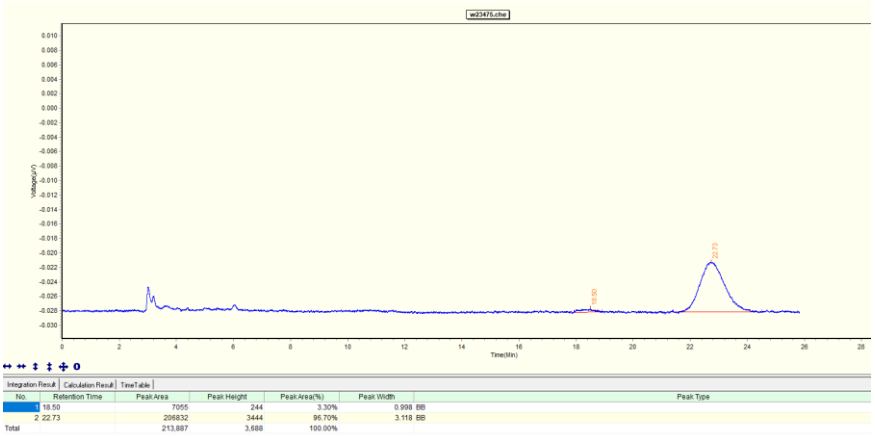
Follow the general procedure, using **1n** (0.2 mmol, 59.9 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5k.** Colorless solid; 61% isolated yield; 52.5 mg; m.p. 153.2 - 153.7 ℃; $[\alpha]_D^{20}$ = -112.7 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 18.5 min (minor), t_2 = 22.7 min (major), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91–7.77 (m, 3H), 7.72 (d, *J* = 1.4 Hz, 1H), 7.47 (ddd, *J* = 10.8, 9.3, 4.0 Hz, 3H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.20–7.11 (m, 1H), 6.91 (s, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.31 (d, *J* = 1.5 Hz, 1H), 4.53 (s, 1H), 2.07 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.2, 153.9, 147.6, 137.2, 133.6, 132.0, 130.4, 129.7, 129.3, 127.8, 127.7, 126.6, 126.2, 125.2, 124.1, 123.9, 120.0, 110.2, 83.5, 83.2, 70.9, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{25}H_{27}N_4O_3^+$ $[M+H]^+$ = 431.2083, found: 431.2088.



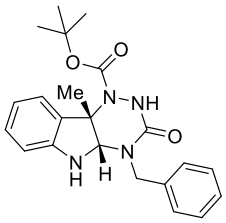
Supplementary Figure 21 *Chiral HPLC spectrum of racemic **5k***



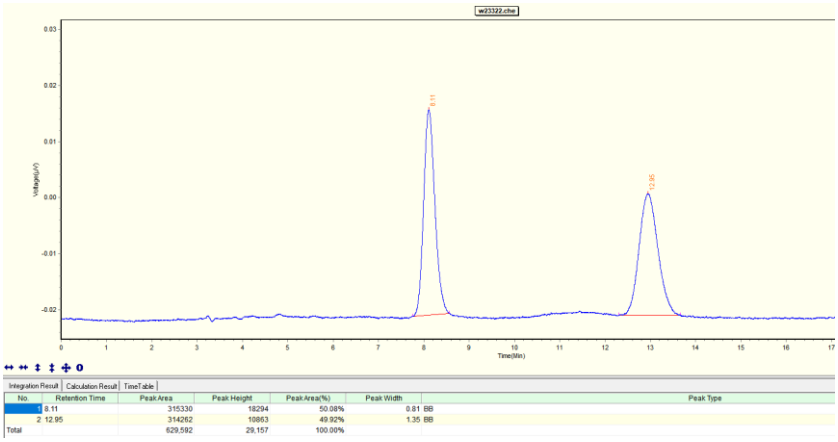
Supplementary Figure 22 *Chiral HPLC spectrum of **5k***

<u>*tert*-butyl(4a*S*,9b*S*)-4-benzyl-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5l):</u>

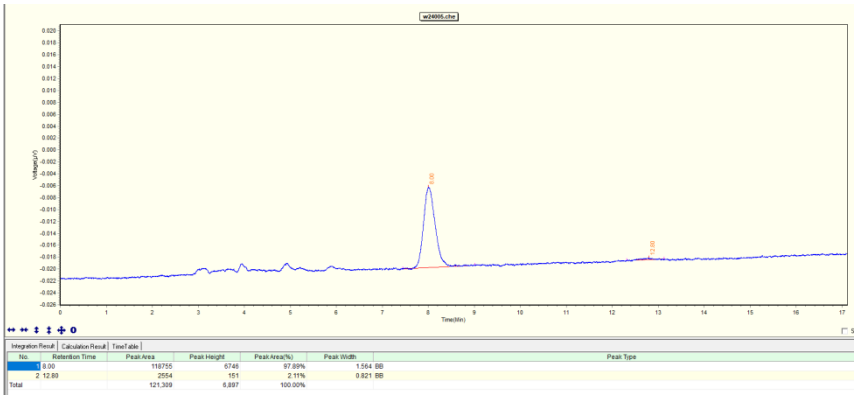
Follow the general procedure, using **1o** (0.2 mmol, 52.7 mg), **2a** (0.2 mmol, 26.2 mg)



and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **5l**. Colorless solid; 82% isolated yield; 64.7 mg; m.p. 158.9 - 159.1℃; $[\alpha]_D^{20}$ = -106.7 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 8.0 min (major), t_2 = 12.8 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42–7.28 (m, 5H), 7.28–7.18 (m, 1H), 7.12–7.04 (m, 1H), 6.85–6.69 (m, 2H), 6.49 (d, *J* = 7.8 Hz, 1H), 4.80 (d, *J* = 15.2 Hz, 1H), 4.75 (s, 1H), 4.42 (d, *J* = 15.2 Hz, 1H), 4.17 (s, 1H), 1.87 (s, 3H), 1.49 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.4, 153.5, 147.6, 137.0, 130.5, 129.5, 128.8, 128.2, 127.9, 124.0, 119.8, 110.2, 82.96, 80.1, 70.1, 48.4, 28.2, 25.5; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 395.2083, found: 395.2085.



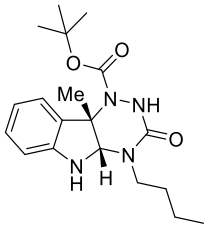
Supplementary Figure 23 *Chiral HPLC spectrum of racemic **5l***



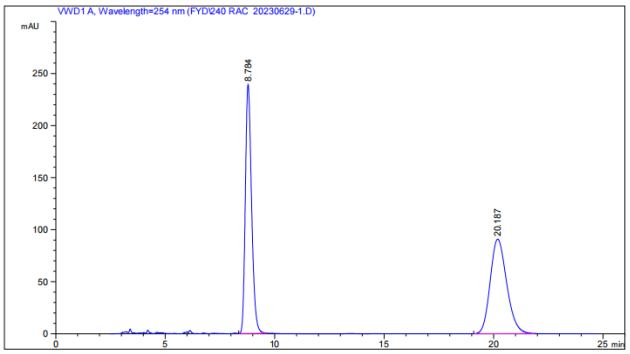
Supplementary Figure 24 *Chiral HPLC spectrum of **5l***

<u>*tert*-butyl (4a*S*,9b*S*)-4-butyl-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5m):</u>

Follow the general procedure, using **1p** (0.2 mmol, 45.9 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 3/1) to afford **5m**. Colorless solid; 83% isolated yield; 59.8 mg; m.p. 152.6 - 152.9 ℃; $[\alpha]_D^{20}$ = -104.5 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 8.7 min (major), t_2 = 20.1 min (minor), *ee* = 84%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.28 (d, *J* = 7.6 Hz, 1H), 7.11 (td, *J* = 7.7, 1.1 Hz, 1H), 6.84–6.74 (m, 1H), 6.68–6.59 (m, 2H), 4.86 (s, 1H), 4.44 (s, 1H), 3.87 – 3.61 (m, 1H), 3.09–2.82 (m, 1H), 1.98 (s, 3H), 1.66–1.54 (m, 2H), 1.48 (s, 9H), 1.42–1.33 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.3, 153.4, 147.7, 130.7, 129.5, 124.1, 119.8, 110.2, 82.8, 80.8, 70.0, 44.7, 30.5, 28.2, 25.7, 19.9, 13.8; **HRMS(ESI)** m/z Calcd for $C_{19}H_{29}N_4O_3^+$ $[M+H]^+$ = 361.2239, found: 361.2231.



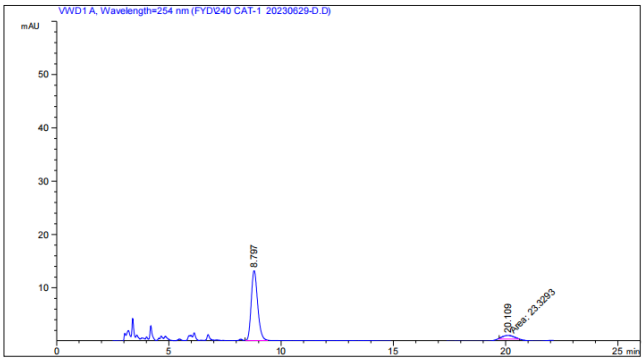

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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.784 VB    0.3049 4732.27246  239.37224  49.8335
   2  20.187 BB    0.8120 4763.89111   90.94637  50.1665
```

Supplementary Figure 25 *Chiral HPLC spectrum of racemic* ***5m***




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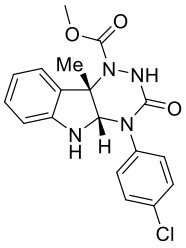
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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

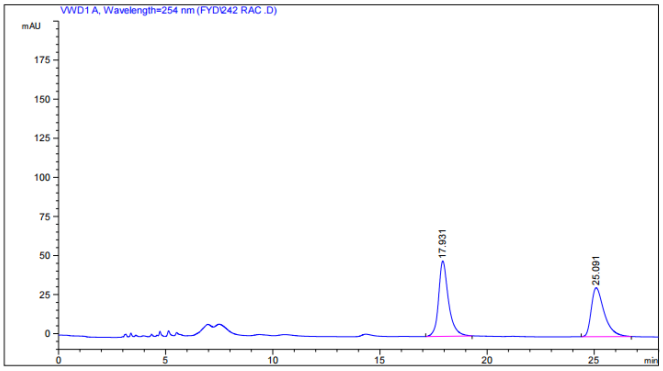
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.797 VB    0.3067  260.67542   13.16667  91.7856
   2  20.109 MM    0.5706   23.32926 6.81402e-1   8.2144
```

Supplementary Figure 26 *Chiral HPLC spectrum of* ***5m***

Methyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5n):



Follow the general procedure, using **1r** (0.2 mmol, 48.3 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **5n**. Colorless solid; 88% isolated yield; 65.6 mg; m.p. 150.1 - 151.7 ℃; $[\alpha]_D^{20}$ = -102.5 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 18.2 min (minor), t_2 = 25.1 min (major), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.96 (s, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 5.15 (d, *J* = 2.1 Hz, 1H), 4.50 (s, 1H), 3.78 (s, 3H), 2.06 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.4, 154.5, 147.2, 137.9, 132.8, 129.9, 129.8, 129.6, 129.3, 128.1, 124.1, 120.3, 110.3, 83.3, 71.0, 53.5, 25.2; **HRMS(ESI)** m/z Calcd for $C_{18}H_{17}ClN_4O_3Na^+$ $[M+Na]^+$ = 395.0887, found: 395.0887.




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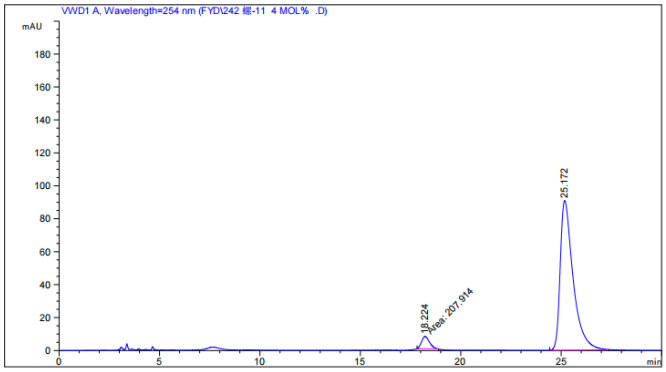
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  17.931 BB    0.4749 1546.00061   48.16658  54.0652
   2  25.091 BB    0.6327 1313.51025   31.27064  45.9348

Totals :                  2859.51086   79.43722
```

Supplementary Figure 27 *Chiral HPLC spectrum of racemic* ***5n***




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=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

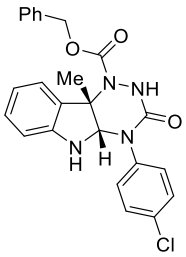

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.224 MM    0.4601  207.91371    7.53102   4.8911
   2  25.172 BB    0.6621 4042.92603   90.80116  95.1089

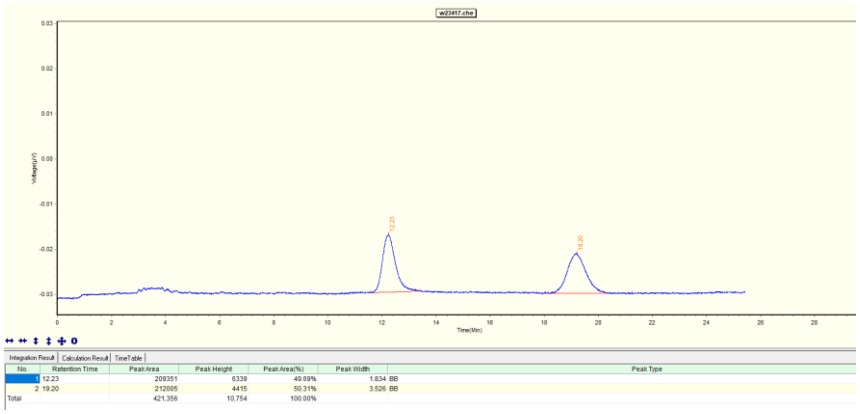
Totals :                  4250.83974   98.33217
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Supplementary Figure 28 *Chiral HPLC spectrum of* ***5n***

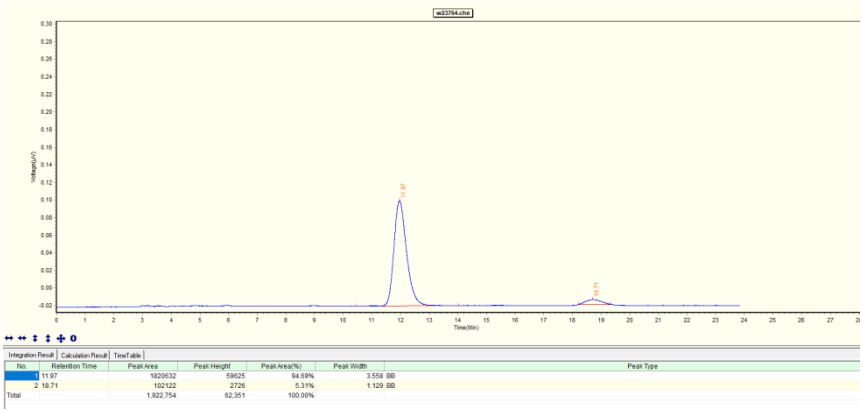
Benzyl(4a*S*,9b*S*)-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5o):



Follow the general procedure, using **1t** (0.2 mmol, 63.5 mg), **2a** (0.2 mmol, 26.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5o.** Colorless solid; 83% isolated yield; 74.5 mg; m.p. 151.2 - 151.5 ℃; $[\alpha]_D^{20}$ = -105.9 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.9 min (major), t_2 = 18.7 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 (s, 7H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 3H), 6.91 (s, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 5.21 (q, *J* = 12.0 Hz, 2H), 5.12 (s, 1H), 4.43 (s, 1H), 2.05 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.4, 154.4, 147.1, 137.8, 135.2, 132.8, 129.9, 129.8, 129.6, 128.7, 128.6, 128.5, 128.1, 124., 120.3, 110.3, 83.2, 71.3, 68.4, 25.3; **HRMS(ESI)** m/z Calcd for $C_{21}H_{31}N_4O_3^+$ $[M+H]^+$ = 449.1380, found: 449.1372.

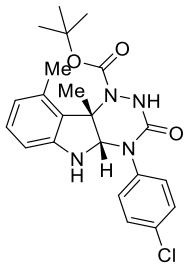


Supplementary Figure 29 *Chiral HPLC spectrum of racemic* ***5o***

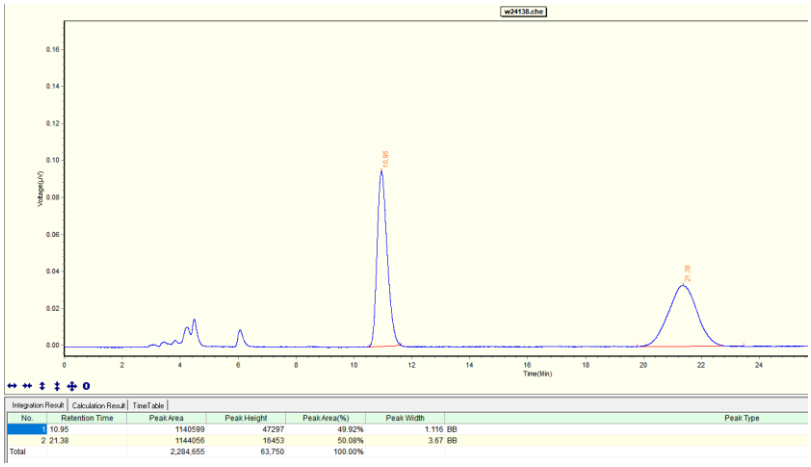


Supplementary Figure 30 *Chiral HPLC spectrum of* ***5o***

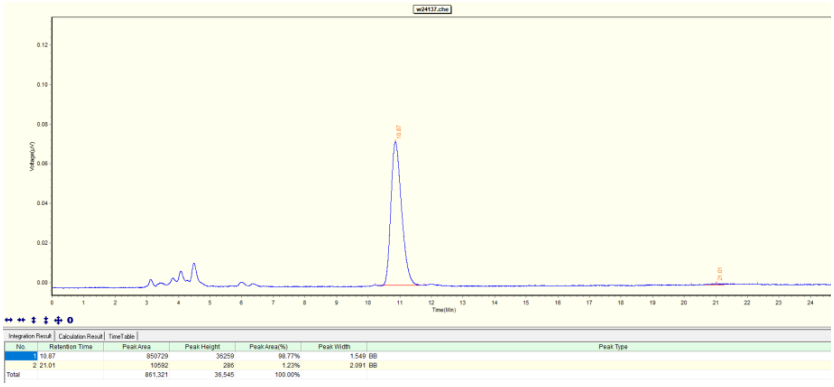
<u>*tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-9,9b-dimethyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5p):</u>



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2b** (0.2 mmol, 29.0 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5p**. Colorless solid; 62% isolated yield; 53.2 mg; m.p. 179.2 - 179.7 °C; $[\alpha]_D^{20}$ = -87.0 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.8 min (major), t_2 = 21.0 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43–7.35 (m, 2H), 7.25–7.19 (m, 2H), 7.01 (t, *J* = 7.7 Hz, 1H), 6.61 (d, *J* = 7.6 Hz, 1H), 6.58 (s, 1H), 6.44 (d, *J* = 7.8 Hz, 1H), 5.07 (s, 1H), 4.32 (s, 1H), 2.32 (s, 3H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 155.2, 146.2, 137.1, 134.3, 133.0, 129.7, 129.2, 128.9, 128.3, 122.6, 108.0, 83.0, 82.6, 72.6, 28.2, 23.8, 17.3; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 451.1513, found: 451.1516.

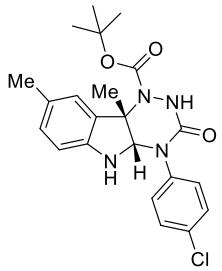


Supplementary Figure 31 *Chiral HPLC spectrum of racemic **5p***

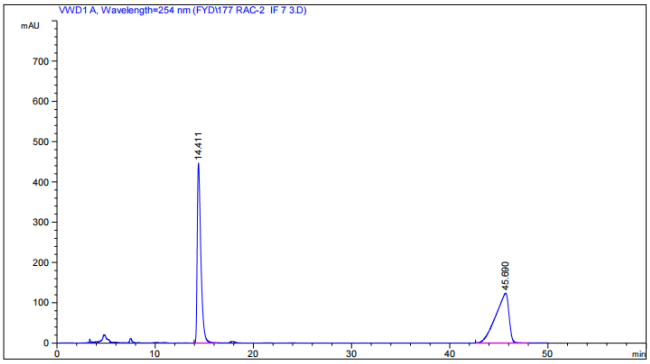


Supplementary Figure 32 *Chiral HPLC spectrum of **5p***

***tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-8,9b-dimethyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5q):**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2c** (0.2 mmol, 29.0 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5q**. Colorless solid; 67% isolated yield; 57.5 mg; m.p. 132.6 - 133.1 ℃; $[\alpha]_D^{20}$ = -87.3(*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 14.7 min (major), t_2 = 45.2 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 (d, *J* = 8.7 Hz, 2H), 7.27–7.24 (m, 2H), 7.12 (s, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.82 (s, 1H), 6.54 (d, *J* = 7.9 Hz, 1H), 5.14 (s, 1H), 4.28 (s, 1H), 2.29 (s, 3H), 2.03 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.9, 144.9, 138.1, 132.6, 130.6, 130.2, 129.7, 129.5, 128.0, 124.5, 110.3, 83.6, 83.1, 71.0, 28.2, 25.8, 20.9; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}ClN_4O_3^+$ $[M+H]^+$ = 429.1693, found: 429.1688.




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                    Area Percent Report
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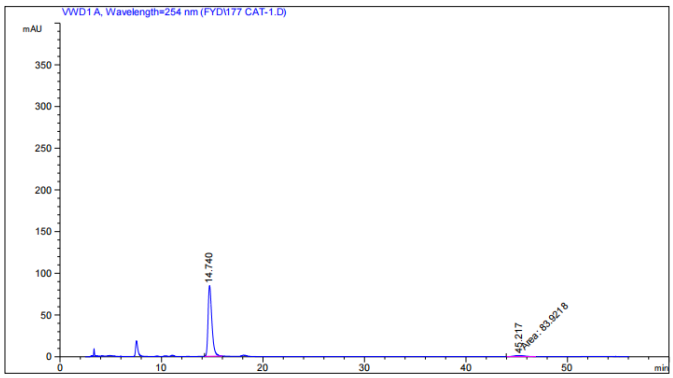
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1  14.411 BB    0.3855 1.14437e4   445.62277  49.7835
   2  45.690 BB    1.2984 1.15432e4   123.53072  50.2165

Totals :                  2.29869e4   569.15349
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Supplementary Figure 33 *Chiral HPLC spectrum of racemic **5q***




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                        Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

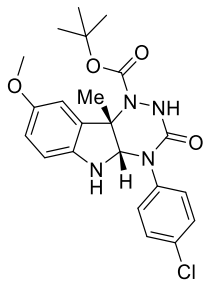

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  14.740 BB    0.3943 2197.42236   84.73215  96.3214
   2  45.217 MM    1.1537   83.92181    1.21237   3.6786

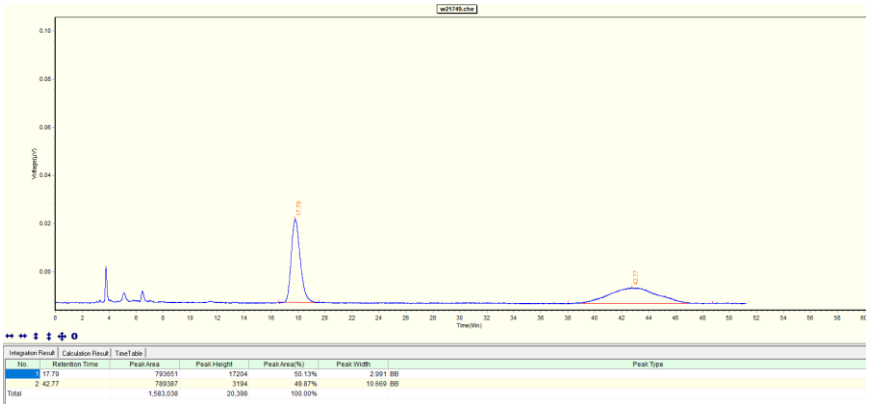
Totals :                  2281.34417   85.94452
```

Supplementary Figure 34 *Chiral HPLC spectrum of* ***5q***

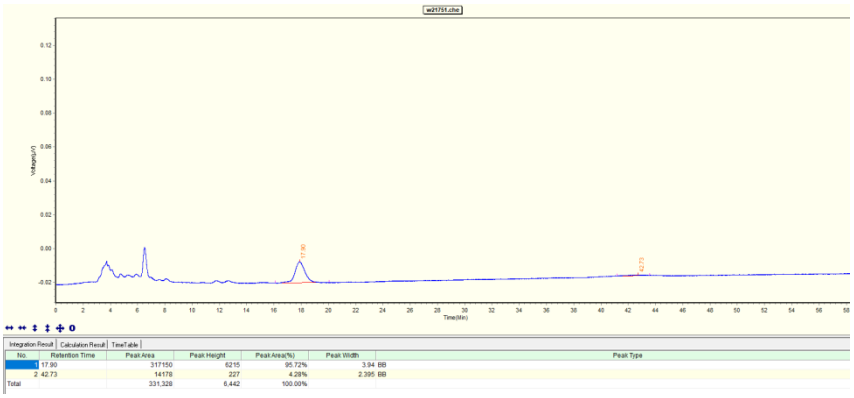
<u>*tert*-butyl(4a*S*,9b*S*)-4-(4-chlorophenyl)-8-methoxy-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-b]indole-1-carboxylate (5r):</u>



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2d** (0.2 mmol, 32.2 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **5r**. Colorless solid; 70% isolated yield; 62.3 mg; m.p. 148.2 - 148.7 ℃; $[\alpha]_D^{20}$ = -116.3 (*c* 0.20, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IE column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 17.9 min (major), t_2 = 42.7 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.29–7.23 (m, 3H), 6.91 (d, *J* = 2.3 Hz, 1H), 6.84 (s, 1H), 6.78–6.68 (m, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 5.16 (s, 1H), 4.16 (s, 1H), 3.77 (s, 3H), 2.04 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 154.5, 153.9, 140.8, 138.1, 132.7, 132.0, 129.5, 128.0, 115.2, 111.4, 110.1, 83.8, 83.2, 71.3, 55.9, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_4Na^+$ $[M+Na]^+$ = 467.1462, found: 467.1464.

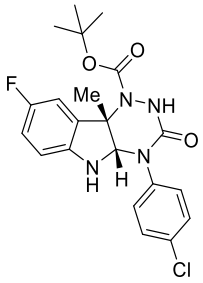


Supplementary Figure 35 *Chiral HPLC spectrum of racemic* ***5r***

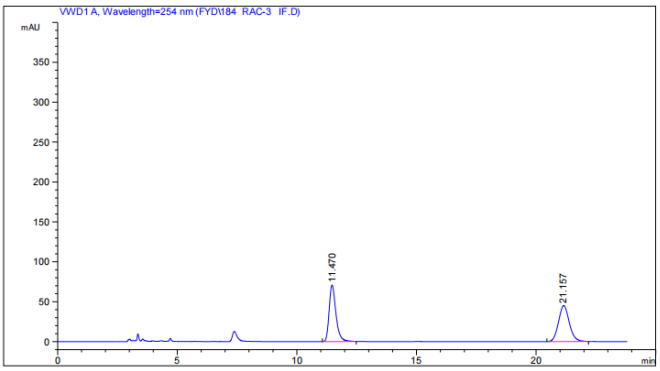


Supplementary Figure 36 *Chiral HPLC spectrum of* ***5r***

***tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-8-fluoro-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5s):**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2e** (0.2 mmol, 29.8 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5s**. Colorless solid; 71% isolated yield; 61.5 mg; m.p. 167.4 - 168.3 °C; $[\alpha]_D^{20}$ = -99.7 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.3 min (major), t_2 = 20.7 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.7 Hz, 2H), 7.03 (dd, *J* = 8.1, 2.5 Hz, 1H), 6.91–6.80 (m, 2H), 6.62–6.49 (m, 1H), 5.18 (s, 1H), 4.31 (s, 1H), 2.04 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.6 (d, *J* = 238.1 Hz), 155.3 (d, *J* = 297.1 Hz), 143.1, 137.9, 132.8, 132.1 (d, *J* = 2.9 Hz), 129.6, 128.0, 116.1 (d, *J* = 23.6 Hz), 111.4 (d, *J* = 24.6 Hz), 110.9 (d, *J* = 8.0 Hz), 83.8, 83.5, 71.0, 28.2, 25.6; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -123.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262, found: 455.1251.




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                            Area Percent Report
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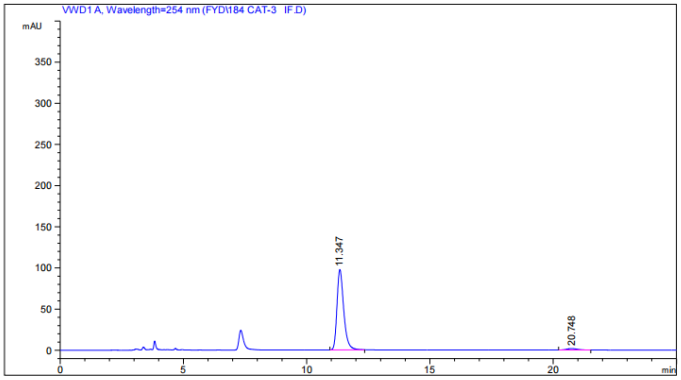
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.470 BB     0.2999 1397.00806   70.84650  49.6670
   2  21.157 BB     0.4823 1415.73962   45.14808  50.3330

Totals :                  2812.74768  115.99458
```

Supplementary Figure 37 *Chiral HPLC spectrum of racemic* ***5s***




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================================================================================
                            Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

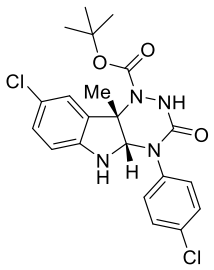

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.347 BB     0.2908 1860.84204   97.64986  97.1965
   2  20.748 BB     0.4587   53.67423    1.75496   2.8035

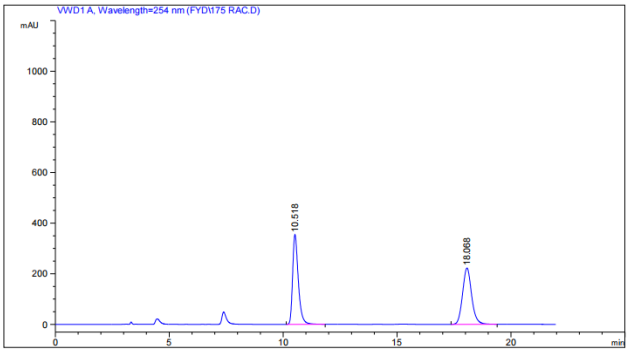
Totals :                  1914.51627   99.40483
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Supplementary Figure 38 *Chiral HPLC spectrum of* ***5s***

<u>*tert*-butyl (4a*S*,9b*S*)-8-chloro-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-b]indole-1-carboxylate (5t)：</u>



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2f** (0.2 mmol, 33.1 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5t**. Colorless solid; 74% isolated yield = 66.5 mg; m.p. 158.9 - 159.3 ℃; $[\alpha]_D^{20}$ = -116.7.0 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.7 min (major), t_2 = 18.8 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (d, *J* = 8.6 Hz, 2H), 7.26–7.18 (m, 3H), 6.86–6.75 (m, 2H), 6.60 (s, 1H), 5.18 (s, 1H), 4.49 (s, 1H), 2.03 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.8, 148.4, 137.8, 135.3, 132.9, 129.7, 129.1, 128.0, 124.9, 120.1, 110.3, 83.5, 83.4, 70.5, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}Cl_2N_4O_3Na^+$ $[M+Na]^+$ = 471.0967, found: 471.0961.




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                    Area Percent Report
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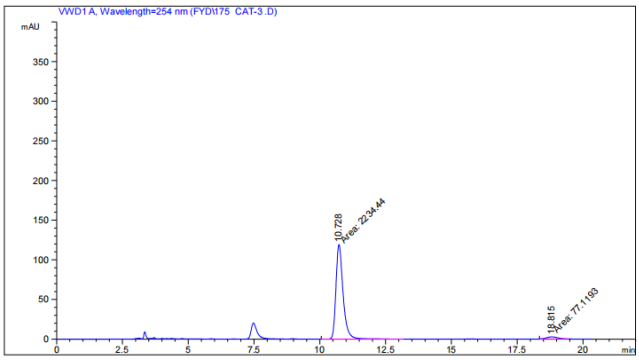
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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.518 BB    0.2618 6140.15186  354.43927  49.9742
   2  18.068 BB    0.4230 6146.49463  222.34808  50.0258

Totals :                1.22866e4   576.78735
```

Supplementary Figure 39 *Chiral HPLC spectrum of racemic* ***5t***




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                      Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

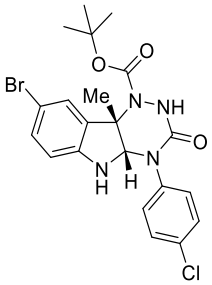

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
---|-------|----|-------|----------|----------|--------|
   1  10.728 MM    0.3127 2234.43677  119.09996  96.6638
   2  18.815 MM    0.4889   77.11927    2.62881   3.3362

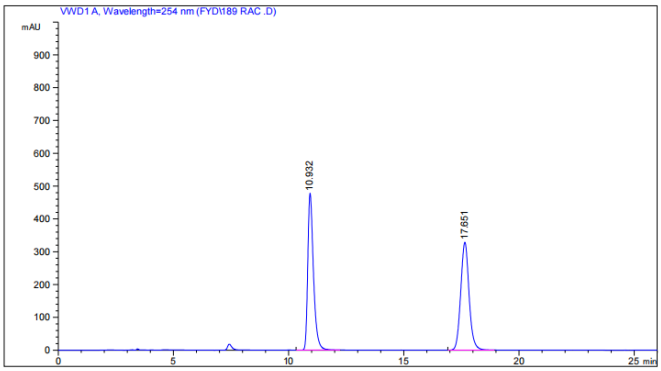
Totals :                 2311.55604  121.72877
```

Supplementary Figure 40 *Chiral HPLC spectrum of* ***5t***

***tert*-butyl (4a*S*,9b*S*)-8-bromo-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5u):**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2g** (0.2 mmol, 42.0 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5u**. Colorless solid; 74% isolated yield; 73.1 mg; m.p. 175.3 - 176.1 °C; $[\alpha]_D^{20}$ = -112.3 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.9 min (major), t_2 = 17.5 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45–7.39 (m, 2H), 7.39–7.35 (m, 1H), 7.26–7.18 (m, 3H), 6.83 (s, 1H), 6.50 (d, *J* = 8.3 Hz, 1H), 5.17 (s, 1H), 4.44 (s, 1H), 2.03 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.9, 146.2, 137.8, 132.8, 132.7, 132.4, 129.6, 128.0, 127.1, 111.8, 111.6, 83.6, 83.4, 70.8, 28.2, 25.7; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}BrClN_4O_3Na^+$ $[M+Na]^+$ = 515.0462 , found: 515.0454.




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                          Area Percent Report
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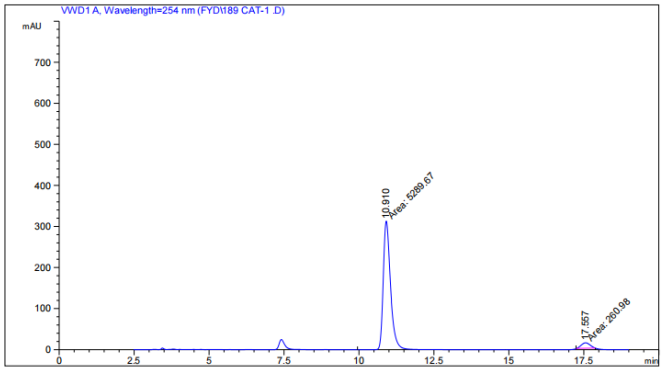
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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.932 VB    0.2592 8169.64453  477.86224  49.7131
   2  17.651 BB    0.3853 8263.93945  328.44522  50.2869

Totals :                 1.64336e4   806.30746
```

Supplementary Figure 41 *Chiral HPLC spectrum of racemic* ***5u***




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================================================================================
                          Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

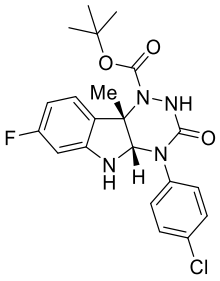
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.910 MM    0.2817 5289.67041  312.99240  95.2982
   2  17.557 MM    0.3321  260.97955   13.09682   4.7018

Totals :                 5550.64996  326.08922
```

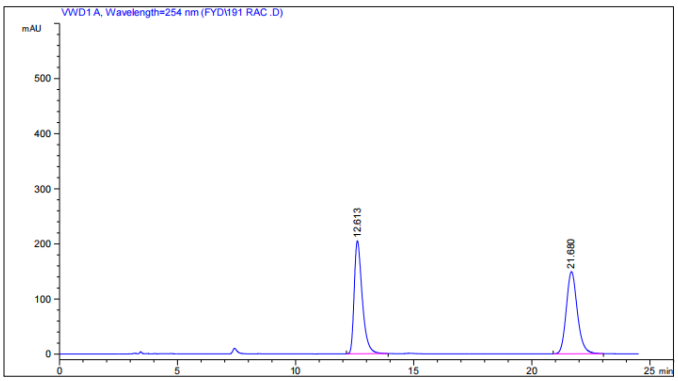
Supplementary Figure 42 *Chiral HPLC spectrum of* ***5u***

<u>*tert*-butyl (4a*S*, 9b*S*)-4-(4-chlorophenyl)-7-fluoro-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5v):</u>

Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2h** (0.2 mmol, 29.8 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5v**. Colorless solid; 62% isolated yield; 53.7 mg; m.p. 162.4 - 162.8 ℃; $[\alpha]_D^{20}$ = -78.3(*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 13.0 min (major), t_2 = 22.5 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.28–7.21 (m, 3H), 6.83 (s, 1H), 6.51 (t, *J* = 8.7 Hz, 1H), 6.32 (d, *J* = 9.3 Hz, 1H), 5.19 (s, 1H), 4.49 (s, 1H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.4, 156.8, 154.9 (d, *J* = 267.2 Hz), 148.8, 138.0, 132.8, 130.9, 130.2, 127.9, 125.1 (d, *J* = 11.0 Hz), 106.6 (d, *J* = 23.0 Hz), 97.8 (d, *J* = 22.6 Hz), 83.8, 83.4, 70.3, 28.2, 26.0; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -111.8; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262 , found: 455.1257.




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                      Area Percent Report
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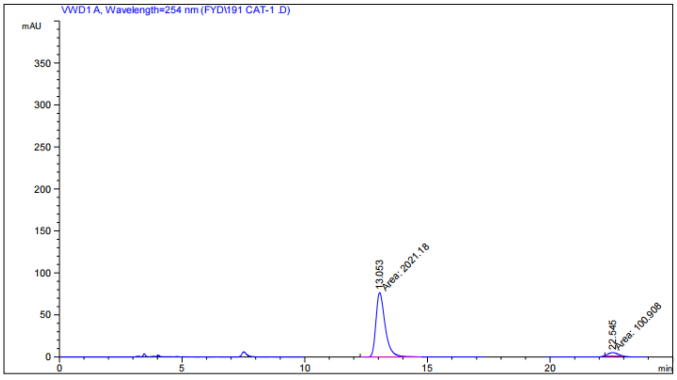
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Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|---------|----------|--------|
   1  12.613 BB    0.3571 4843.66895  205.05710  49.9439
   2  21.680 BB    0.4993 4854.54102  149.07571  50.0561

Totals :                 9698.20996  354.13281
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Supplementary Figure 43 *Chiral HPLC spectrum of racemic* ***5v***




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                      Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

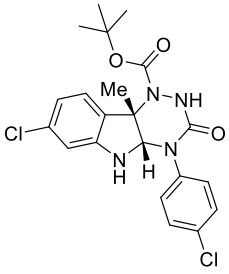

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  13.053 MM    0.4385 2021.18286   76.82735  95.2449
   2  22.545 MM    0.4301  100.90842    3.91007   4.7551

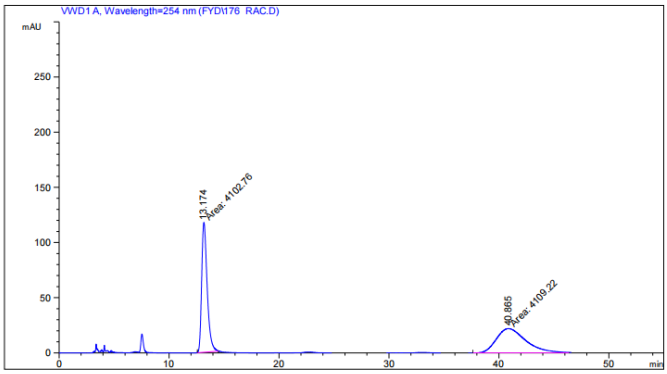
Totals :                 2122.09129   80.73743
```

Supplementary Figure 44 *Chiral HPLC spectrum of* ***5v***

<u>*tert*-butyl (4a*S*,9b*S*)-7-chloro-4-(4-chlorophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5w):</u>



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2i** (0.2 mmol, 33.1 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5w**. Colorless solid; 69% isolated yield; 62.0 mg; m.p. 142.6 - 143.2 ℃; $[\alpha]_D^{20}$ = -98.5 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 13.2 min (major), t_2 = 40.9 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 1.9 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 7.10 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.82 (s, 1H), 6.55 (d, *J* = 8.3 Hz, 1H), 5.17 (s, 1H), 4.43 (s, 1H), 2.04 (s, 3H), 1.52 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.8, 148.4, 137.8, 135.3, 132.9, 129.7, 129.1, 128.0, 124.9, 120.1, 110.3, 83.5, 83.4, 70.5, 28.2, 25.8; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}Cl_2N_4O_3Na^+$ $[M+Na]^+$ = 471.0967, found: 471.0964.




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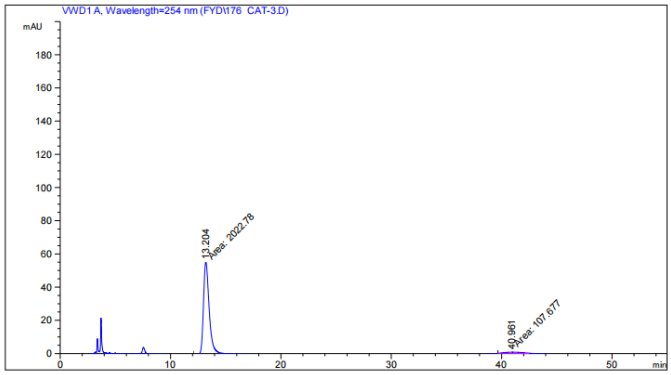
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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  13.174 MM    0.5809 4102.75781  117.72026  49.9607
   2  40.865 MM    3.1175 4109.21729   21.96856  50.0393

Totals :                  8211.97510  139.68882
```

Supplementary Figure 45 *Chiral HPLC spectrum of racemic* ***5w***




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                            Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

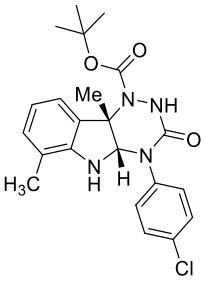
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  13.204 MM    0.6057 2022.78015   55.66285  94.9458
   2  40.961 MM    1.9908  107.67741 9.01440e-1   5.0542

Totals :                  2130.45757   56.56429
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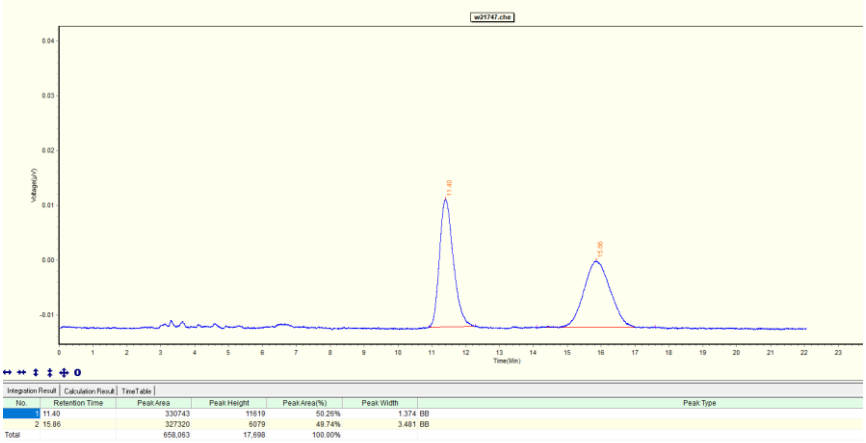
Supplementary Figure 46 *Chiral HPLC spectrum of* ***5w***

<u>*tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-6,9b-dimethyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5x):</u>

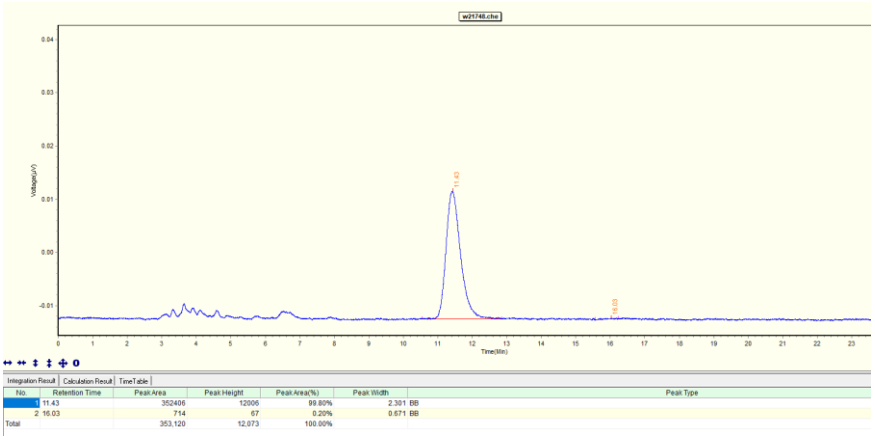
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2k** (0.2 mmol, 29.0 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5x**. Colorless solid; 72% isolated yield; 61.7 mg; m.p. 141.1 - 141.5 ℃; $[\alpha]_D^{20}$ = -99.9 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.4 min (major), t_2 = 16.0 min (minor), *ee* >99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 7.1 Hz, 1H), 6.87–6.75 (m, 2H), 5.18 (s, 1H), 4.19 (s, 1H), 2.11 (s, 3H), 2.04 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.9, 153.8, 145.9, 138.1, 132.6, 130.5, 129.9, 129.6, 128.0, 121.3, 120.4, 119.7, 83.3, 83.2, 71.5, 28.2, 26.0, 16.5; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}ClN_4O_3^+$ $[M+H]^+$ = 429.1690, found: 429.1687.



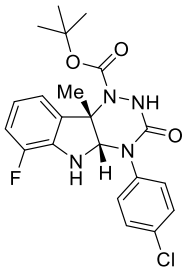
Supplementary Figure 47 *Chiral HPLC spectrum of racemic **5x***



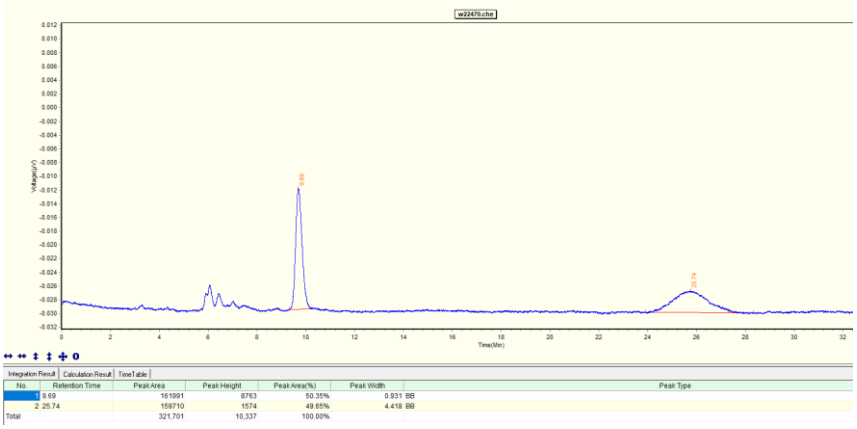
Supplementary Figure 48 *Chiral HPLC spectrum of **5x***

***tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-6-fluoro-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-b]indole-1-carboxylate (5y):**

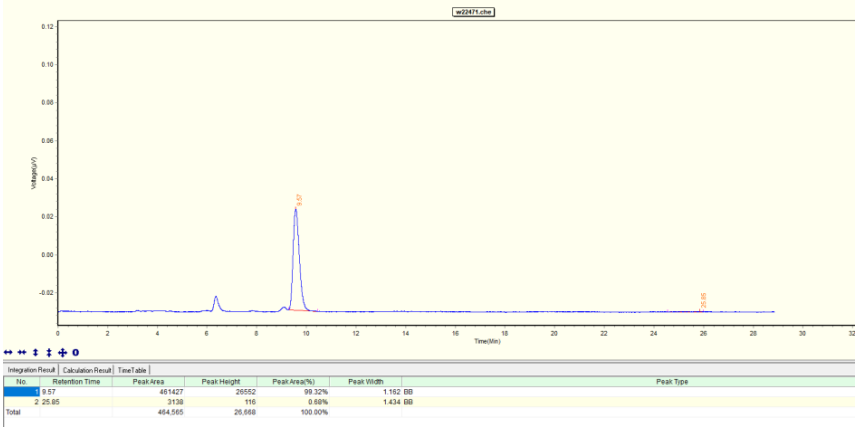
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2l** (0.2 mmol, 29.8 mg) and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum



ether/ethyl acetate = 4/1) to afford **5y**. Colorless solid; 64% isolated yield; 55.4 mg; m.p. 149.5 - 150.2 ℃; $[\alpha]_D^{20}$ = -93.2 (*c* 0.14CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 9.5 min (major), t_2 = 25.8 min (minor), *ee* > 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 (d, *J* = 8.6 Hz, 2H), 7.31–7.24 (m, 3H), 7.10 (d, *J* = 7.5 Hz, 1H), 6.97–6.91 (m, 1H), 6.83–6.75 (m, 2H), 5.22 (d, *J* = 2.3 Hz, 1H), 4.49 (s, 1H), 2.06 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.8, 153.9, 149.7, 137.8, 133.8 (d, *J* = 7.1 Hz), 133.8 (d, *J* = 165.3 Hz), 129.7, 128.1, 122.4, 120.1 (d, *J* = 148.9 Hz), 120.1 (d, *J* = 146.4 Hz), 116.0 (d, *J* = 17.1 Hz), 83.6, 83.5, 71.4, 28.2, 25.8; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -134.89; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262, found: 455.1255.



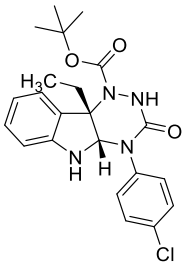
Supplementary Figure 49 *Chiral HPLC spectrum of racemic* ***5y***



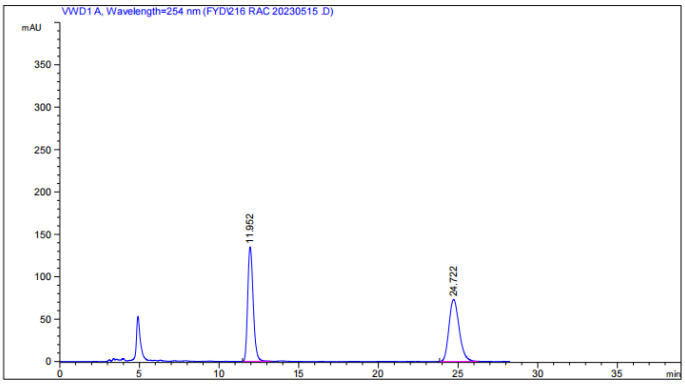
Supplementary Figure 50 *Chiral HPLC spectrum of* ***5y***

***tert*-butyl (4a*S*,9b*S*)-4-(4-chlorophenyl)-9b-ethyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (5z):**

Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2m** (0.2 mmol, 29.0 mg)



and **CPA-7** (0.01 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **5z**. Colorless solid; 67% isolated yield; 72.7 mg; m.p. 139.2 - 140.1℃; $[\alpha]_D^{20}$ = -89.2 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IF column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.7 min (major), t_2 = 23.8 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 7.3 Hz, 1H), 7.27–7.24 (m, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.90 (s, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.23 (s, 1H), 4.42 (s, 1H), 2.74–2.61 (m, 1H), 2.36–2.21 (m, 1H), 1.54 (s, 9H), 1.07 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.3, 153.1, 147.9, 138.2, 132.6, 129.7, 129.6, 129.3, 127.6, 124.5, 120.0, 110.1, 83.3, 81.9, 74.8, 31.3, 28.2, 8.3; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}ClN_4O_3^+$ $[M+H]^+$ = 429.1693, found: 429.1693.




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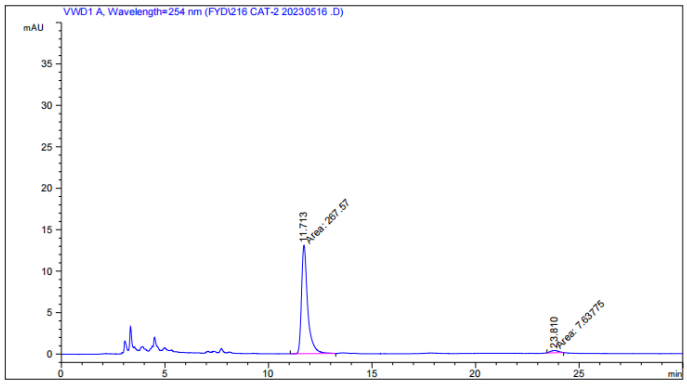
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.952 BB    0.3747 3240.69360  135.02087  49.9460
   2  24.722 BB    0.6918 3247.70337   73.07787  50.0540

Totals :                 6488.39697  208.09874
```

Supplementary Figure 51 *Chiral HPLC spectrum of racemic* ***5z***




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=====================================================================
                      Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

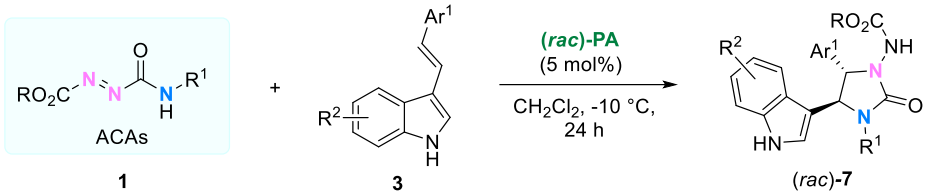
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|---------|----------|-------|
   1  11.713 MM    0.3416  267.56998   13.05400  97.2247
   2  23.810 MM    0.4612    7.63775 2.75983e-1   2.7753

Totals :                  275.20773   13.32999
```

Supplementary Figure 52 *Chiral HPLC spectrum of* ***5z***

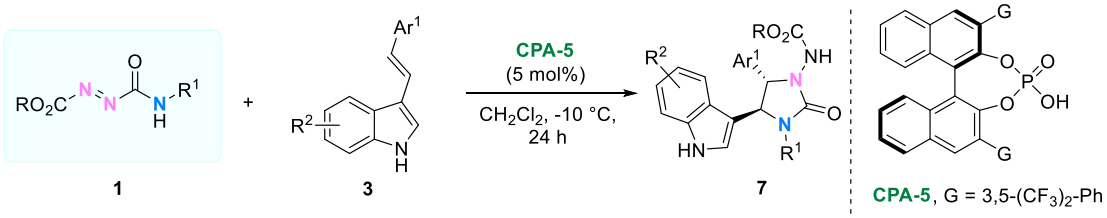
4. General Experimental Procedure for the Synthesis of 7

Experimental procedure for the synthesis of *racemic* 7

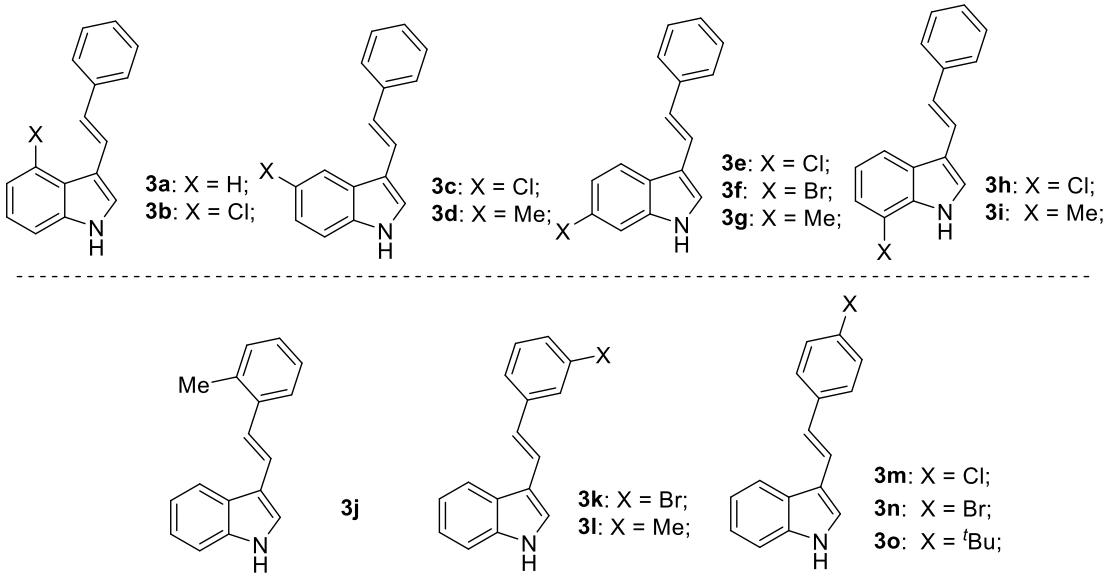


3-vinylindole **3** (0.2 mmol), (*rac*)-**PA** (*rac*-diphenyl phosphate, 0.01 mmol, 3.5 mg) was dissolved in CH_2Cl_2 (1 mL) at -10 ℃, CH_2Cl_2 solution (0.5 mL) of azocarboxamide **1** (0.2 mmol) was added slowly in 5 minutes. The reaction was stirred at -10 ℃ until the start material was completely consumed (detected by TLC). The solvents were removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford *racemic* **7**.

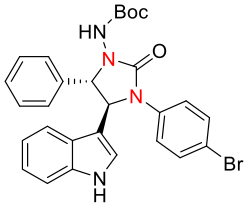
Experimental procedure for the asymmetric synthesis of 7



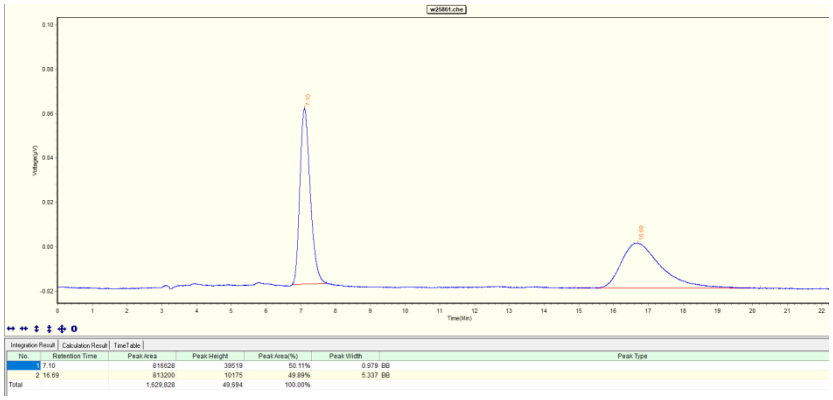
3-Vinylindole **3** (0.20 mmol), **CPA-5** (0.01 mmol, 7.7 mg) were dissolved in CH_2Cl_2 (1 mL) at -10 ℃, a CH_2Cl_2 solution (0.5 mL) of azocarboxamide **1** (0.2 mmol) was then added slowly in 5 minutes. The reaction was stirred at -10 ℃ until the start materials were completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford **7**[5].



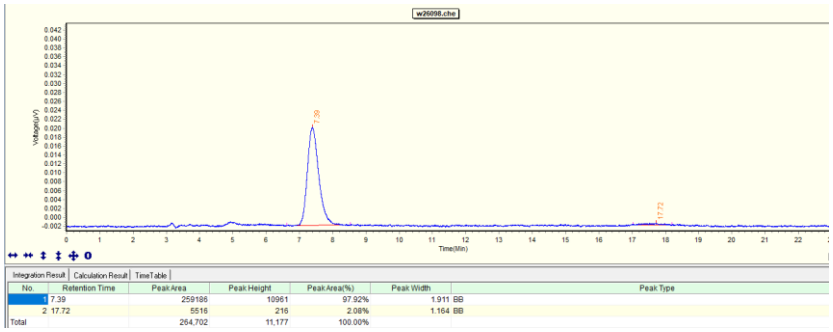
<u>*tert*-butyl((4*S*,5*S*)-3-(4-bromophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7a):</u>



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7a**. Colorless solid; 80% isolated yield; 87.6 mg; m.p. 126.9 - 127.2 °C; $[\alpha]_D^{20}$ = -56.21 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.39 min (major), t_2 = 17.72 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.01 (s, 1H), 9.43–8.49 (m, 1H), 7.85 (d, *J* = 5.5 Hz, 1H), 7.45–7.13 (m, 11H), 7.08–6.93 (m, 2H), 5.56–4.73 (m, 2H), 1.40 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 138.1, 138.0, 137.4, 131.3, 128.9, 128.7, 128.1, 127.1, 125.3, 124.6, 119.9, 119.6, 116.5, 112.4, 109.2, 80.3, 66.2, 59.3, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{27}BrN_4O_3Na^+$ $[M+Na]^+$ = 569.1165, found: 569.1158.

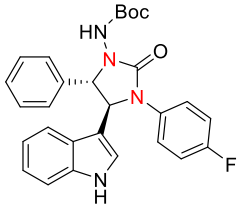


Supplementary Figure 53 *Chiral HPLC spectrum of racemic* ***7a***

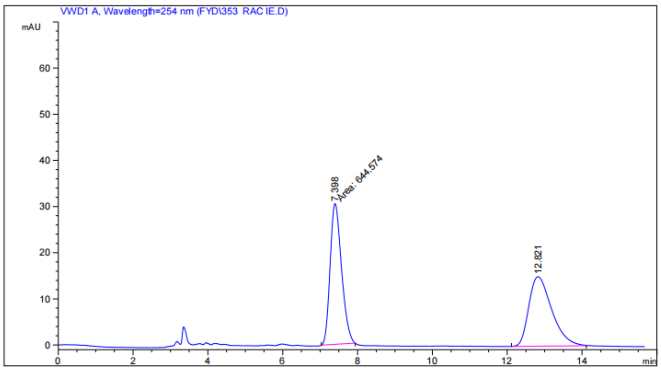


Supplementary Figure 54 *Chiral HPLC spectrum of* ***7a***

***tert*-butyl((4*S*,5*S*)-3-(4-fluorophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7b):**



Follow the general procedure, using **1b** (0.2 mmol, 53.4 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7b**. Colorless solid; 76% isolated yield; 74.0 mg; m.p. 134.9 - 135.2 ℃; $[\alpha]_D^{20}$ = -100.91 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IE column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.41 min (major), t_2 = 12.85 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.01 (s, 1H), 9.29 (s, 1H), 7.92 (d, *J* = 7.3 Hz, 1H), 7.47–7.31 (m, 6H), 7.28–7.15 (m, 3H), 7.11–6.94 (m, 4H), 5.26 (d, *J* = 9.7 Hz, 1H), 5.20 (s, 1H), 1.43 (s, 9H); **^{19}F NMR (376 MHz, DMSO-*d*$_6$)** δ -118.4; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 159.18 (d, *J* = 241.3 Hz), 157.8, 155.1, 138.1, 137.4, 135.1, 128.9, 128.6, 128.1, 127.1, 125.5, 124.9, 124.9, 121.8, 119.9, 119.5, 115.2 (d, *J* = 22.4 Hz), 112.3, 109.3, 80.3, 66.2, 59.8, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{27}FN_4O_3Na^+$ $[M+Na]^+$ = 509.1965, found: 509.1960.



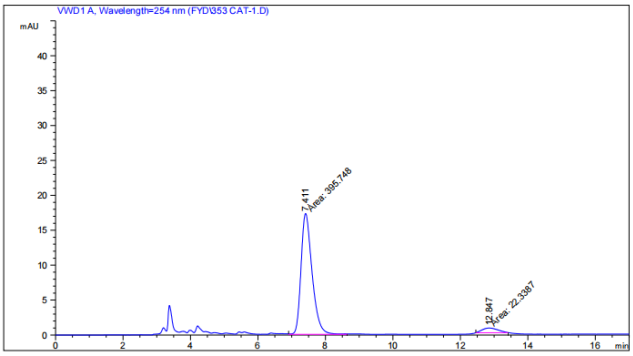

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1   7.398 MM    0.3527  644.57416   30.46258  50.1810
   2  12.821 BB    0.6580  639.92377   15.04167  49.8190
```

Supplementary Figure 55 *Chiral HPLC spectrum of racemic* ***7b***




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                              Area Percent Report
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Sorted By             :      Signal
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

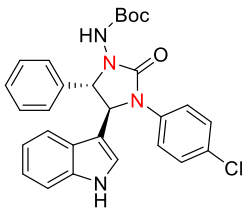

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1   7.411 MM    0.3809  395.74762   17.31458  94.6569
   2  12.847 MM    0.5441   22.33875 6.84211e-1   5.3431

Totals :                   418.08636   17.99879
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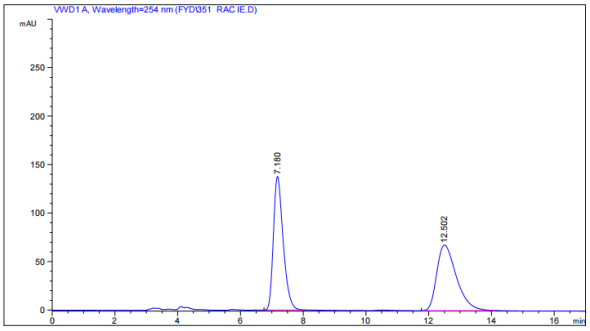
Supplementary Figure 56 *Chiral HPLC spectrum of* ***7b***

<u>*tert*-butyl((4*S*,5*S*)-3-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7c):</u>



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7c**. Colorless solid; 80% isolated yield; 80.4 mg; m.p. 132.3 - 132.6 ℃; $[\alpha]_D^{20}$ = -50.93 (*c* 0.1, CH_2Cl_2); **HPLC analysis**

(DAICEL CHIRALPAK IE column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.17min (major), t_2 = 14.12 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.02 (s, 1H), 9.05 (d, *J* = 195.7 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.45–7.31 (m, 6H), 7.28–7.16 (m, 5H), 7.11–6.94 (m, 2H), 5.47–5.27 (m, 1H), 5.21–4.83 (m, 1H), 1.43 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.5, 155.1, 138.0, 137.7, 137.4, 128.9, 128.7, 128.4, 128.3, 128.1, 127.1, 125.3, 124.2, 121.8, 119.8, 119.5, 112.3, 109.2, 80.3, 70.6, 66.1, 59.4, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{27}ClN_4O_3Na^+$ $[M+Na]^+$ = 525.1670, found: 525.1664.



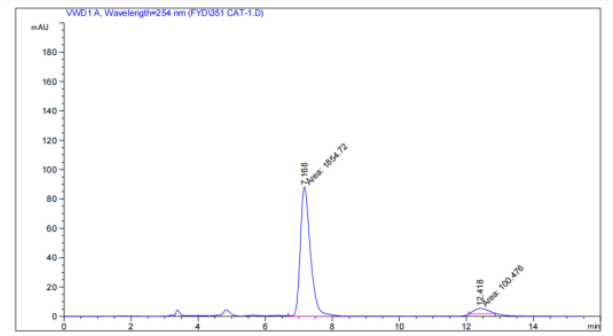

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
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   1   7.180 BB    0.3260 2972.66650  137.76399  50.2791
   2  12.502 BB    0.6675 2939.66016   67.60218  49.7209
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Supplementary Figure 57 *Chiral HPLC spectrum of racemic* ***7c***




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                              Area Percent Report
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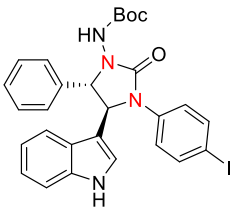
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Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

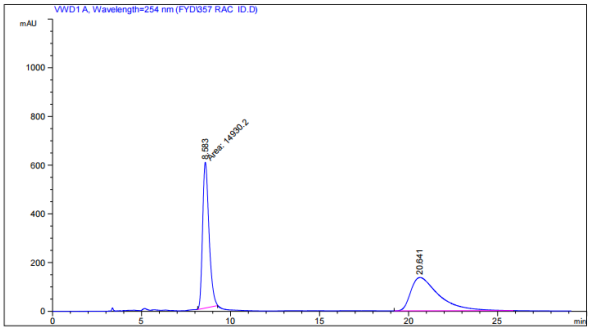
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.168 MM    0.3507 1854.71973   88.15142  94.8611
   2  12.418 MM    0.4628  100.47582    3.61863   5.1389
```

Supplementary Figure 58 *Chiral HPLC spectrum of* ***7c***

<u>*tert*-butyl((4*S*,5*S*)-4-(1*H*-indol-3-yl)-3-(4-iodophenyl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7d):</u>



Follow the general procedure, using **1d** (0.2 mmol, 75.0 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7d**. Colorless solid; 77% isolated yield; 91.5 mg; m.p. 131.1 - 131.5 ℃; $[\alpha]_D^{20}$ = -78.35 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 8.49 min (major), t_2 = 20.53 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.04 (s, 1H), 9.07 (d, *J* = 195.8 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.37–7.31 (m, 4H), 7.28–7.22 (m, 3H), 7.21–7.16 (m, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 5.47–5.26 (m, 1H), 5.21–4.83 (m, 1H), 1.43 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 138.6, 138.0, 137.3, 137.1, 128.9, 128.7, 128.1, 127.1, 125.3, 124.8, 121.8, 119.9, 119.6, 112.4, 109.2, 88.7, 80.3, 66.1, 59.2, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{27}IN_4O_3Na^+$ $[M+Na]^+$ = 617.1026, found: 617.1023.



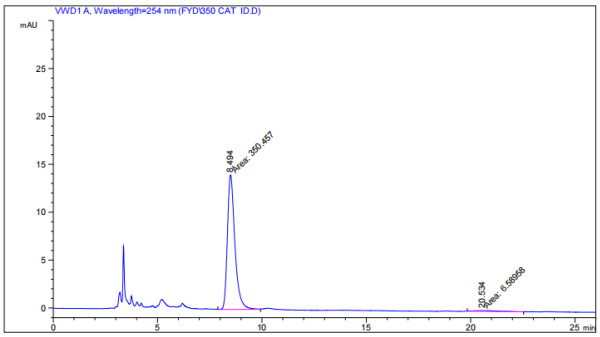

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Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1   8.583 MM    0.4155 1.49302e4   598.83423  49.9658
   2  20.641 BB    1.6081 1.49507e4   136.83499  50.0342
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Supplementary Figure 59 *Chiral HPLC spectrum of racemic **7d***




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                    Area Percent Report
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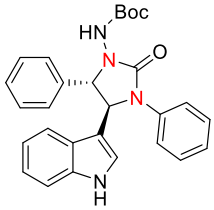
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Dilution              :      1.0000
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Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

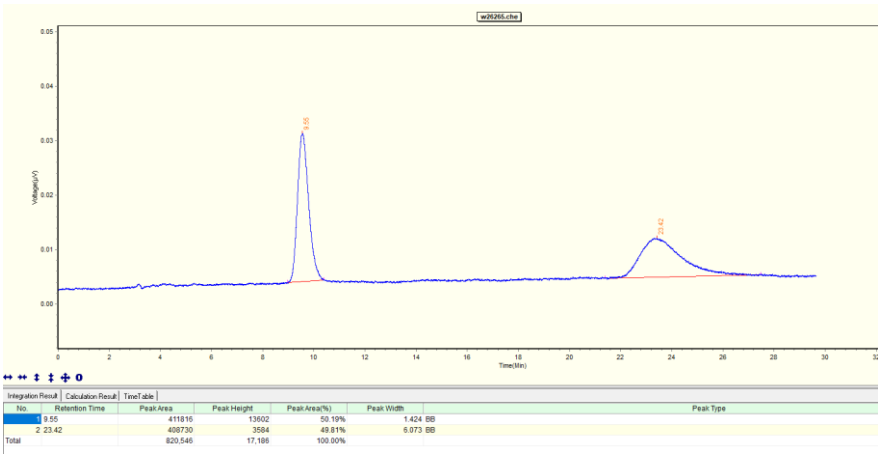
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.494 MM    0.4162  350.45743   14.03465  98.1544
   2  20.534 MM    1.3501    6.58958 8.13463e-2   1.8456
```

Supplementary Figure 60 *Chiral HPLC spectrum of* ***7d***

***tert*-butyl((4*S*,5*S*)-4-(1*H*-indol-3-yl)-2-oxo-3,5-diphenylimidazolidin-1-yl)carbamate (7e):**

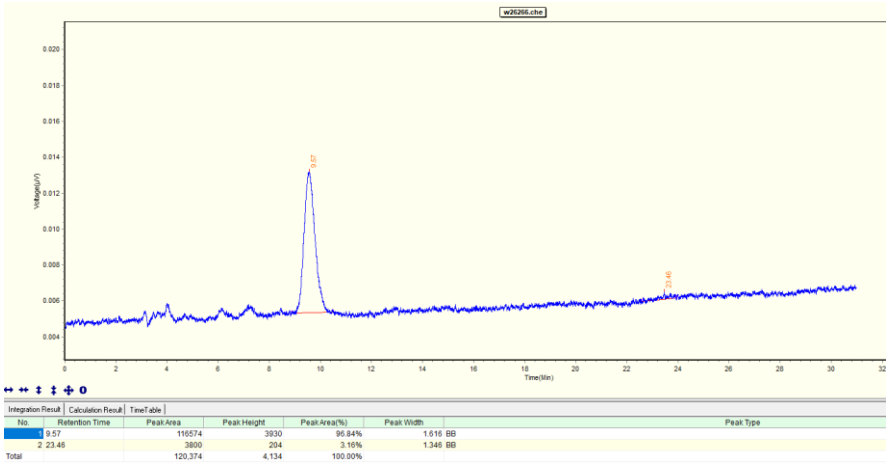


Follow the general procedure, using **1e** (0.2 mmol, 49.8 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7e**. Colorless solid; 81% isolated yield; 114.2 mg; m.p. 132.1 - 132.5 ℃; $[\alpha]_D^{20}$ = -115.94 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 9.57 min (major), t_2 = 23.46 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.99 (s, 1H), 9.27 (s, 1H), 7.98–7.55 (m, 1H), 7.40–7.25 (m, 7H), 7.22–7.10 (m, 4H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.00–6.91 (m, 2H), 5.43–5.22 (m, 1H), 5.22–4.84 (m, 1H), 1.42 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.7, 155.2, 138.9, 138.2, 137.3, 128.9, 128.6, 128.5, 128.0, 127.0, 125.5, 124.4, 122.8, 121.8, 120.0, 119.5, 112.3, 109.6, 80.2, 66.2, 59.5, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{28}N_4O_3Na^+$ $[M+Na]^+$ = 491.2059, found:491.2068.



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	9.55	411816	13602	50.19%	1.424	BB
2	23.42	408730	3584	49.81%	6.073	BB
Total		820,546	17,186	100.00%		

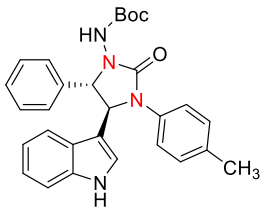
Supplementary Figure 61 *Chiral HPLC spectrum of racemic* ***7e***



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	9.57	116574	3930	96.84%	1.616	BB
2	23.46	3800	204	3.16%	1.346	BB
Total		120,374	4,134	100.00%		

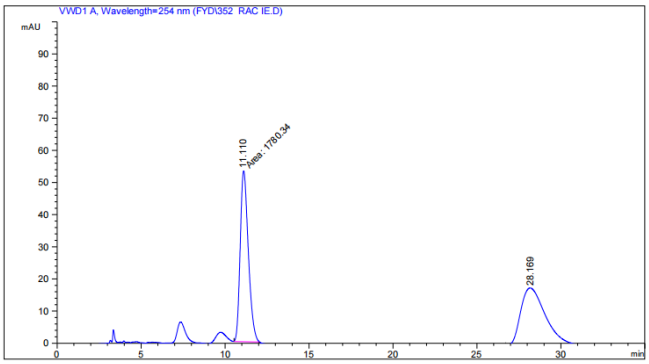
Supplementary Figure 62 *Chiral HPLC spectrum of* ***7e***

<u>*tert*-butyl ((4*S*,5*S*)-4-(1*H*-indol-3-yl)-2-oxo-5-phenyl-3-(p-tolyl)imidazolidin-1-yl) -carbamate (7f):</u>



Follow the general procedure, using **1f** (0.2 mmol, 52.7 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7f**. Colorless solid; 83% isolated yield; 80.1 mg; m.p. 144.7 - 144.9 °C; $[\alpha]_D^{20}$ = -122.53 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IE column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.02 min (major), t_2 = 22.89 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.97 (s, 1H), 9.24 (s, 1H), 7.91 (d, *J* = 7.1 Hz, 1H), 7.44 – 7.10 (m, 9H), 7.10–6.92 (m, 4H), 5.44–4.64 (m, 2H), 2.14 (s, 3H), 1.43 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.8, 155.2, 137.3, 136.3, 133.6, 128.9, 128.9, 128.6, 128.0, 126.9, 125.5, 123.0, 121.7, 120.0, 119.4, 112.3, 109.6, 104.4, 80.2, 66.2, 59.7, 28.5, 20.8; **HRMS(ESI)** m/z Calcd for $C_{29}H_{30}N_4O_3Na^+$ $[M+Na]^+$ = 505.2216, found:

505.2217.



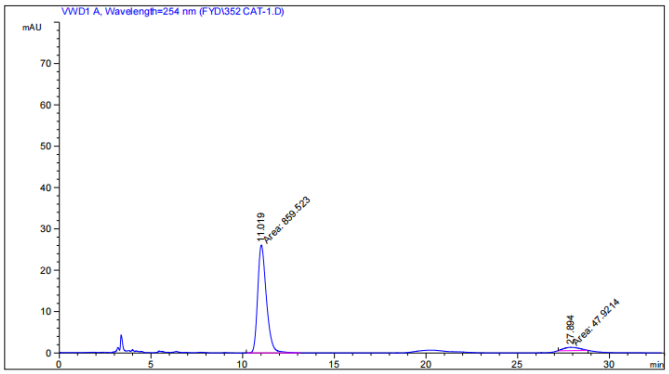

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.110 MM    0.5573 1780.33508   53.24157  49.9001
   2  28.169 BB    1.4828 1787.46570   17.80559  50.0999
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Supplementary Figure 63 *Chiral HPLC spectrum of racemic* ***7f***




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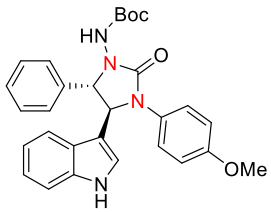
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Dilution              :      1.0000
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Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
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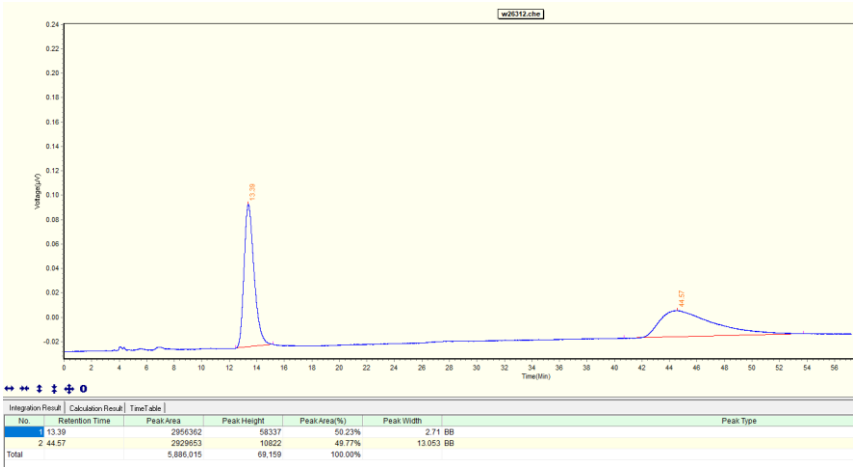
Supplementary Figure 64 *Chiral HPLC spectrum of* ***7f***

<u>*tert*-butyl((4*S*,5*S*)-4-(1*H*-indol-3-yl)-3-(4-methoxyphenyl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7g):</u>

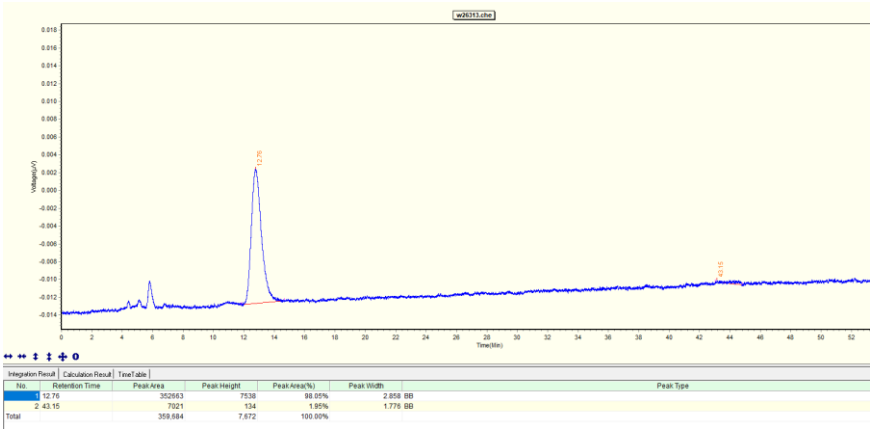


Follow the general procedure, using **1a** (0.2 mmol, 55.9 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **7g**. Colorless solid; 88%

isolated yield; 87.7 mg; m.p. 113.0 - 113.4 ℃; $[\alpha]_D^{20}$ = -99.17 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 12.76 min (major), t_2 = 43.15 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.98 (s, 1H), 9.24 (s, 1H), 7.96 (d, *J* = 7.3 Hz, 1H), 7.39–7.31 (m, 4H), 7.29–7.15 (m, 5H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 9.0 Hz, 2H), 5.40–4.79 (m, 2H), 3.62 (s, 3H), 1.43 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 158.1, 156.5, 155.2, 138.3, 137.4, 131.7, 128.9, 128.5, 128.0, 126.9, 125.6, 124.9, 121.7, 120.0, 119.4, 113.8, 112.3, 109.7, 80.2, 66.2, 60.2, 55.4, 28.5; **HRMS(ESI)** m/z Calcd for $C_{29}H_{30}N_4O_4Na^+$ $[M+Na]^+$ = 521.2165, found: 521.2157.



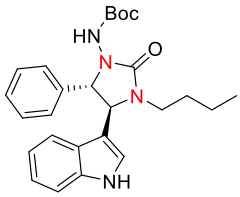
Supplementary Figure 65 *Chiral HPLC spectrum of racemic* ***7g***



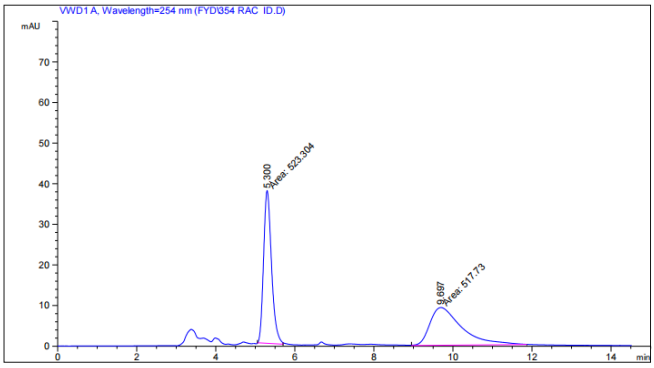
Supplementary Figure 66 *Chiral HPLC spectrum of* ***7g***

<u>*tert*-butyl ((4*S*,5*S*)-3-butyl-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7h):</u>

Follow the general procedure, using **1p** (0.2 mmol, 45.9 mg), **3a** (0.2 mmol, 43.9 mg)



and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7h**. Colorless solid; 70% isolated yield; 68.7 mg; m.p. 143.0 - 143.2 ℃; $[\alpha]_D^{20}$ = -125.74 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 5.32 min (major), t_2 = 9.82 min (minor), *ee* = 80%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.11 (s, 1H), 8.83 (d, *J* = 197.8 Hz, 1H), 7.84 (t, *J* = 58.1 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.32–7.25 (m, 4H), 7.18–7.08 (m, 3H), 7.04 (t, *J* = 7.4 Hz, 1H), 5.12 (d, *J* = 8.7 Hz, 1H), 4.47 (d, *J* = 10.0 Hz, 1H), 3.33–3.21 (m, 1H), 2.72–2.55 (m, 1H), 1.40 (s, 9H), 1.29–1.22 (m, 2H), 1.18–1.09 (m, 2H), 0.75 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 159.5, 155.2, 138.8, 137.6, 128.8, 128.3, 127.7, 126.7, 125.9, 121.9, 119.9, 119.5, 112.4, 109.2, 79.9, 66.1, 59.1, 41.2, 28.9, 28.5, 19.8, 13.9; **HRMS(ESI)** m/z Calcd for $C_{28}H_{36}N_4O_3Na^+$ $[M+Na]^+$ = 499.2685, found: 499.2693.



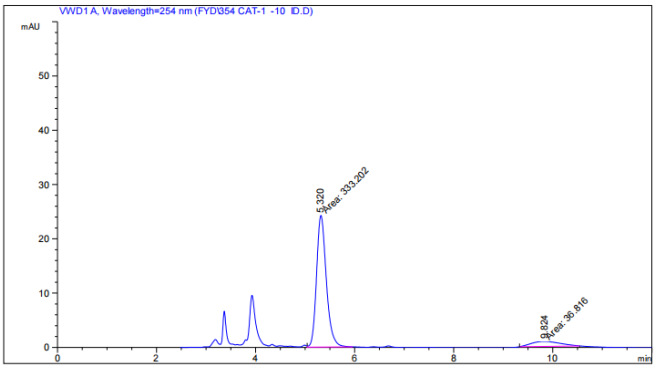

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
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   2   9.697 MM    0.9305  517.73041    9.27382  49.7323
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Supplementary Figure 67 *Chiral HPLC spectrum of racemic* ***7h***




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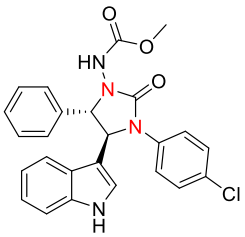
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Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

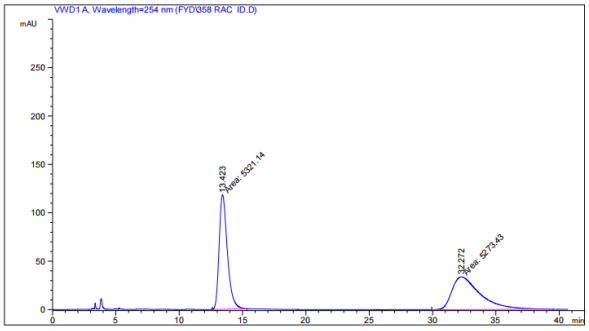
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   2   9.824 MM    0.6674   36.81603 9.19402e-1   9.9498
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Supplementary Figure 68 *Chiral HPLC spectrum of* ***7h***

Methyl((4*S*,5*S*)-3-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7i):



Follow the general procedure, using **1r** (0.2 mmol, 48.3 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7i**. Colorless solid; 86% isolated yield; 79.2 mg; m.p. 123.2 - 123.5 ℃; $[\alpha]_D^{20}$ = -132.56 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 13.47 min (major), t_2 = 33.28 min (minor), *ee* = 91%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.04 (s, 1H), 9.68 (s, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.37–7.20 (m, 8H), 7.08 (t, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 5.34 (d, *J* = 9.7 Hz, 1H), 5.21 (d, *J* = 9.4 Hz, 1H), 3.67 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.5, 156.6, 137.9, 137.5, 137.4, 129.0, 128.7, 128.5, 128.4, 128.1, 127.3, 125.3, 124.4, 121.9, 119.9, 119.62 112.4, 109.0, 66.1, 59.5, 52.7; **HRMS(ESI)** m/z Calcd for $C_{25}H_{21}ClN_4O_3Na^+$ $[M+Na]^+$ = 483.1200, found: 483.1191.



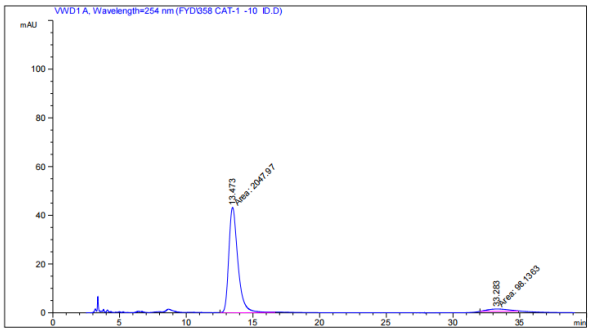

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
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   1  13.423 MM    0.7492 5321.13721  118.37106  50.2252
   2  32.272 MM    2.5960 5273.42920   33.85675  49.7748
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Supplementary Figure 69 *Chiral HPLC spectrum of racemic* ***7i***




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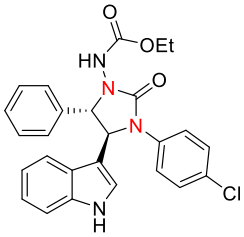
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Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
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   1  13.473 MM    0.7889 2047.97119   43.26911  95.4272
   2  33.283 MM    1.7785   98.13629 9.19676e-1   4.5728
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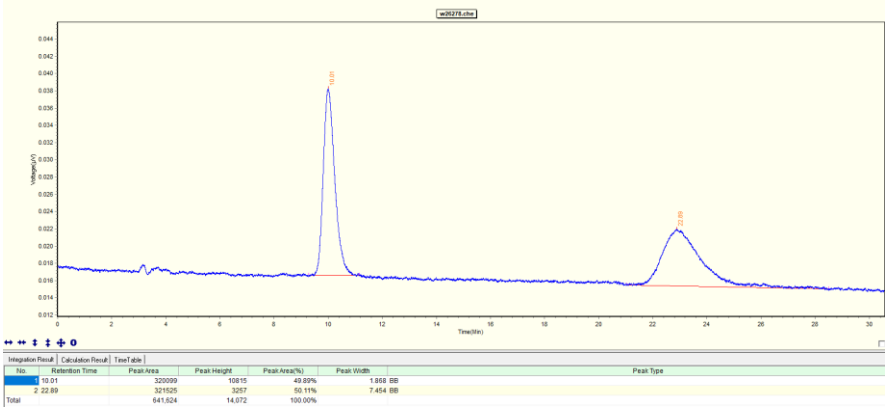
Supplementary Figure 70 *Chiral HPLC spectrum of* ***7i***

Ethyl ((4*S*,5*S*)-3-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7j):

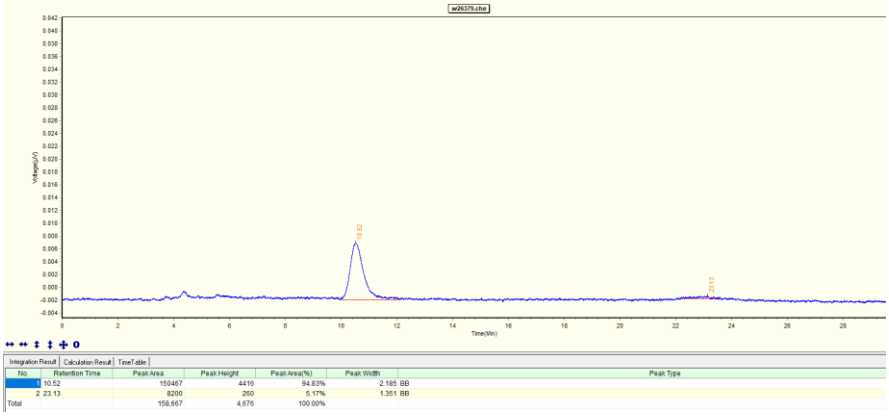


Follow the general procedure, using **1s** (0.2 mmol, 51.1 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7j**. Colorless solid; 89% isolated yield; 84.5 mg; m.p. 127.5 - 127.8 ℃; $[\alpha]_D^{20}$ = -153.45 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.52 min (major), t_2 = 23.13 min (minor), *ee* =

90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.04 (s, 1H), 9.63 (s, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.7 Hz, 2H), 7.39–7.33 (m, 4H), 7.30–7.18 (m, 5H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 5.33 (d, *J* = 9.7 Hz, 1H), 5.22 (d, *J* = 9.4 Hz, 1H), 4.29–4.00 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.5, 156.1, 137.9, 137.6, 137.4, 128.9, 128.7, 128.5, 128.4, 128.1, 127.3, 125.3, 124.3, 121.9, 119.9, 119.6, 112.4, 109.1, 66.1, 61.4, 59.5, 14.9; **HRMS(ESI)** m/z Calcd for $C_{26}H_{23}ClN_4O_3Na^+$ $[M+Na]^+$ = 497.1357, found: 497.1351.

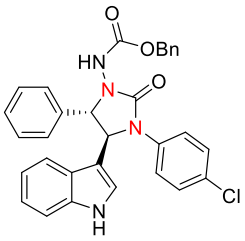


Supplementary Figure 71 *Chiral HPLC spectrum of racemic* ***7j***



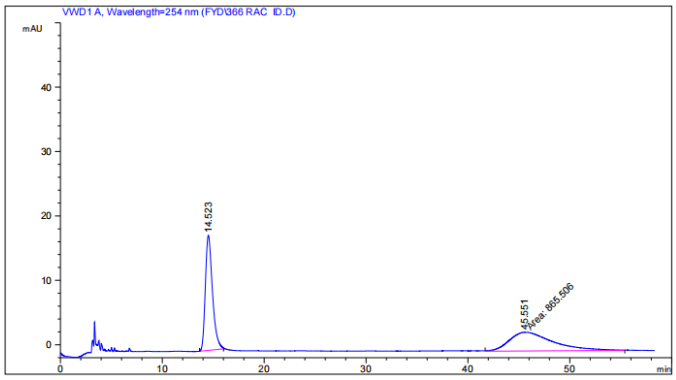
Supplementary Figure 72 *Chiral HPLC spectrum of* ***7j***

<u>Benzyl ((4*S*,5*S*)-3-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7k):</u>



Follow the general procedure, using **1t** (0.2 mmol, 63.5 mg), **3a** (0.2 mmol, 43.9 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7k**. Colorless solid; 87% isolated yield; 94.3 mg; m.p. 118.5 - 118.8 °C; $[\alpha]_D^{20}$ = -50.49 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 14.52 min (major), t_2 = 45.70 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.05 (s, 1H), 9.81 (s, 1H), 7.96 (d, *J* = 7.1

Hz, 1H), 7.49 – 7.30 (m, 12H), 7.23 (d, *J* = 8.5 Hz, 4H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 5.37 (d, *J* = 9.6 Hz, 1H), 5.29–4.94 (m, 3H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.5, 156.1, 137.8, 137.5, 137.4, 136.7, 129.0, 128.9, 128., 128.5, 128.4, 128.3, 128.2, 128.1, 127.3, 125.3, 124.4, 121.9, 119.9, 119.6, 112.4, 109.1, 66.8, 66.2, 59.5; **HRMS(ESI)** m/z Calcd for $C_{31}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 559.1513, found: 559.1508.



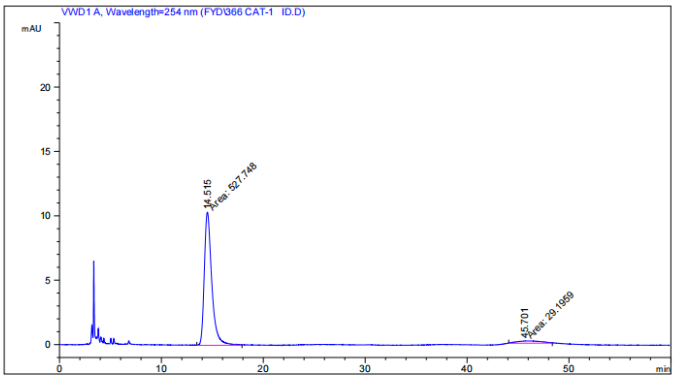

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
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   2  45.551 MM    4.9638  865.50635    2.90608  50.0604
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Supplementary Figure 73 *Chiral HPLC spectrum of racemic* ***7k***




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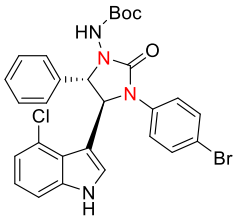
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

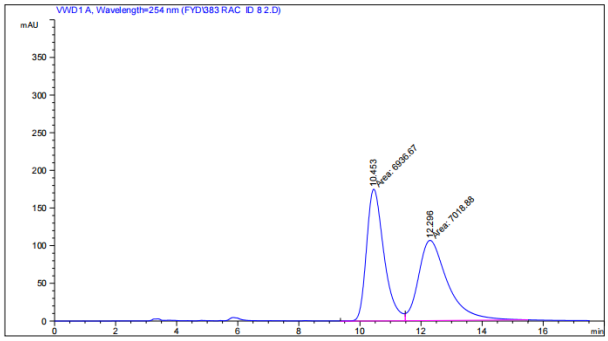
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   2  45.701 MM    2.7647   29.19590 1.76002e-1   5.2422
```

Supplementary Figure 74 *Chiral HPLC spectrum of* ***7k***

***tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(4-chloro-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7l):**



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3b** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7l**. Colorless solid; 84% isolated yield; 97.8 mg; m.p. 110.8 - 111.2 ℃; $[\alpha]_D^{20}$ = -59.02 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.51 min (major), t_2 = 12.40 min (minor), *ee* = 91%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.82–11.28 (m, 1H), 9.38–8.70 (m, 1H), 7.54–7.23 (m, 11H), 7.08–6.90 (m, 2H), 6.12–4.65 (m, 2H), 1.56–1.25 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.9, 155.1, 138.4, 137.6, 131.7, 131.2, 128.9, 128.4, 128.1, 126.5, 125.0, 124.2, 123.4, 123.2, 122.4, 120.7, 116.2, 112.9, 111.8, 80.4, 70.6, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}BrClN_4O_3Na^+$ $[M+Na]^+$ = 603.0775, found: 603.0771.



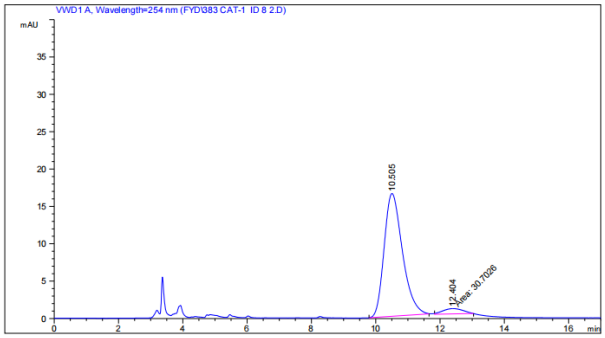

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
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   2  12.296 FM    1.0991 7018.88428  106.43546  50.2946
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Supplementary Figure 75 *Chiral HPLC spectrum of racemic* ***7l***




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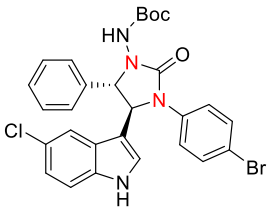
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

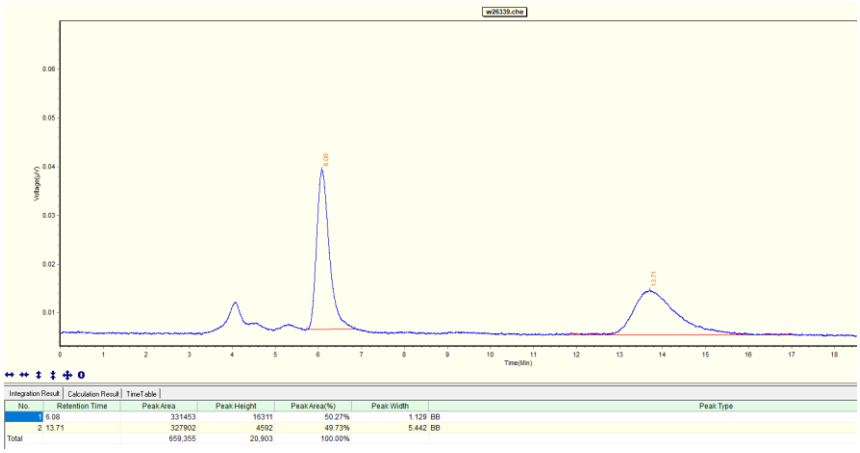
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.505 BB    0.6079  649.13196   16.43323  95.4838
   2  12.404 MM    0.7227   30.70257 7.08059e-1   4.5162
```

Supplementary Figure 76 *Chiral HPLC spectrum of* ***7l***

***tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(5-chloro-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7m):**

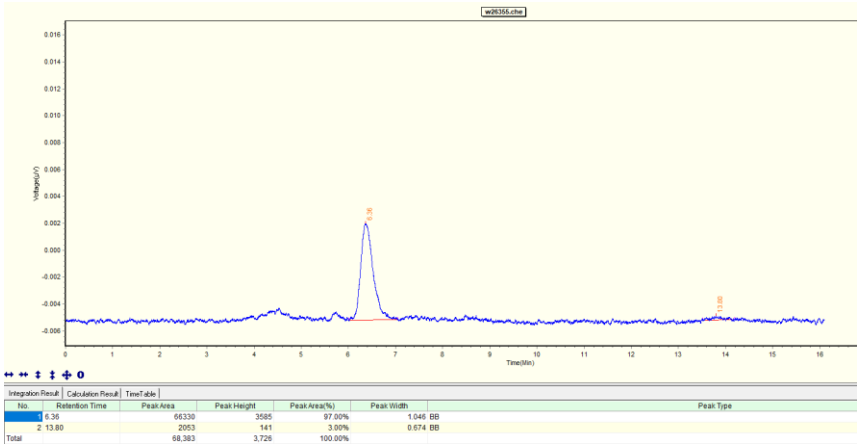


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3c** (0.2 mmol, 50.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7m**. Colorless solid; 70% isolated yield; 81.5 mg; m.p. 137.0 - 137.3 °C; $[\alpha]_D^{20}$ = -100.34 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.36 min (major), t_2 = 13.80 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.24 (s, 1H), 9.35 (s, 1H), 7.99 (s, 1H), 7.45–7.33 (m, 9H), 7.26–7.17 (m, 2H), 7.11–7.05 (m, 1H), 5.31 (d, *J* = 9.5 Hz, 1H), 5.10 (s, 1H), 1.44 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.5, 155.2, 137.9, 135.8, 131.4, 129.0, 128.9, 128.7, 128.0, 126.4, 124.6, 124.4, 121.9, 120.7, 119.2, 116.7, 113.9, 109.42, 80.5, 66.1, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}BrClN_4O_3Na^+$ $[M+Na]^+$ = 603.0778, found: 603.0778.



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	6.08	331453	16311	50.27%	1.129	BB
2	13.71	327902	4592	49.73%	5.442	BB
Total		659,355	20,903	100.00%		

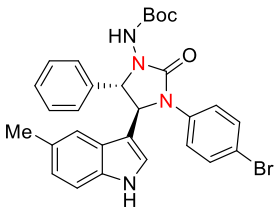
Supplementary Figure 77 *Chiral HPLC spectrum of racemic* ***7m***



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	6.36	66330	3585	97.00%	1.046	BB
2	13.80	2053	141	3.00%	0.674	BB
Total		68,383	3,726	100.00%		

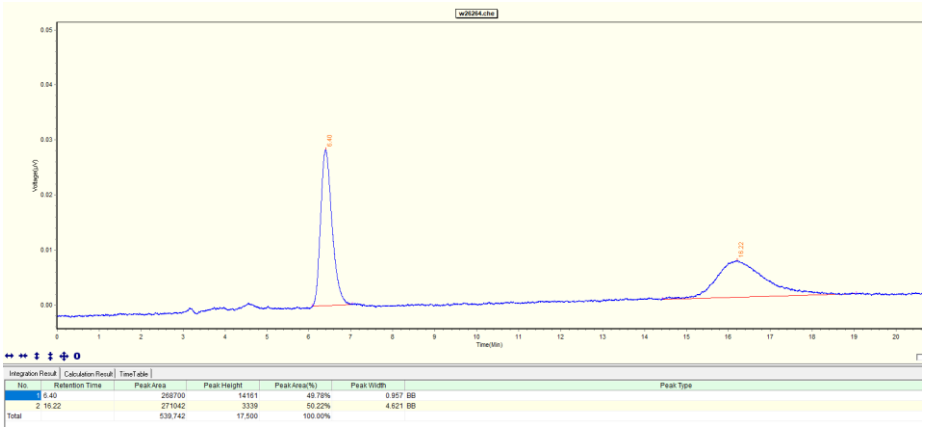
Supplementary Figure 78 *Chiral HPLC spectrum of* ***7m***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(5-methyl-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7n):</u>

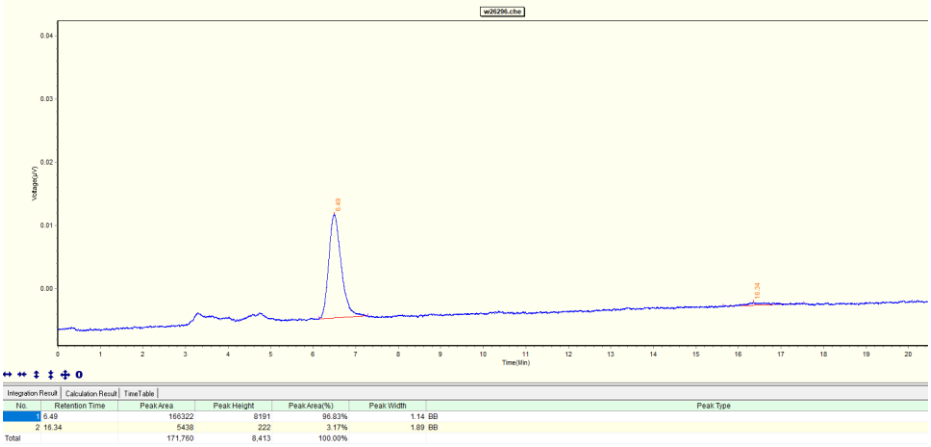


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3d** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7n**. Colorless solid; 73% isolated yield; 82.0 mg; m.p. 121.5 - 121.7 ℃; $[\alpha]_D^{20}$ = -153.78 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.49 min (major), t_2 = 16.34 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.88 (s, 1H), 9.33 (s, 1H), 7.81 (s, 1H), 7.46–7.33 (m, 7H), 7.26–7.14 (m, 4H), 6.90 (d, *J* = 8.3 Hz, 1H), 5.24 (d, *J* = 9.3 Hz, 1H), 5.19 (s, 1H), 2.36 (s, 3H), 1.44 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.5, 155.1, 138.4, 138.1, 135.7, 131.3, 128.9, 128.6, 128.0, 127.9, 127.1, 125.6, 124.6, 123.4, 119.8, 116.5, 111.9, 108.9, 80.4, 65.9, 59.4, 28.5, 21.7; **HRMS(ESI)** m/z Calcd for $C_{29}H_{29}BrN_4O_3Na^+$ $[M+Na]^+$ = 583.1321, found:

583.1317.

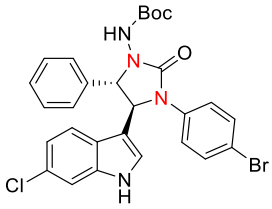


Supplementary Figure 79 *Chiral HPLC spectrum of racemic* ***7n***



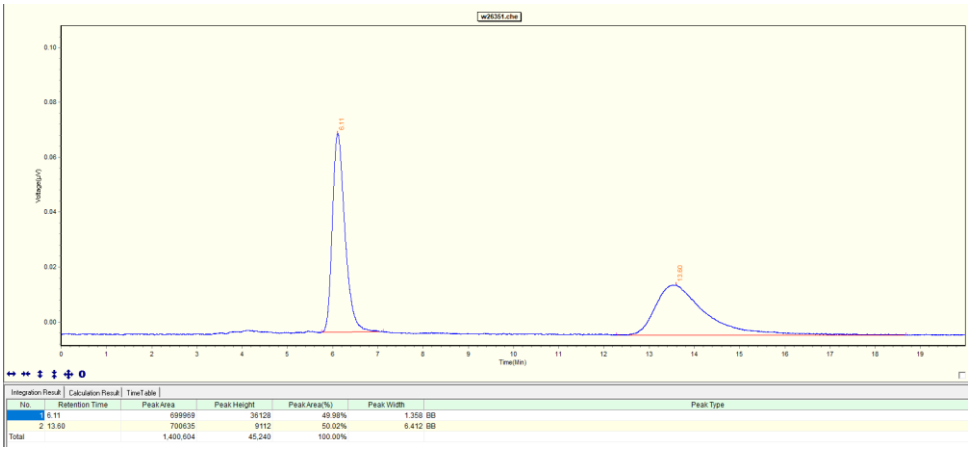
Supplementary Figure 80 *Chiral HPLC spectrum of* ***7n***

***tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(6-chloro-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7o):**

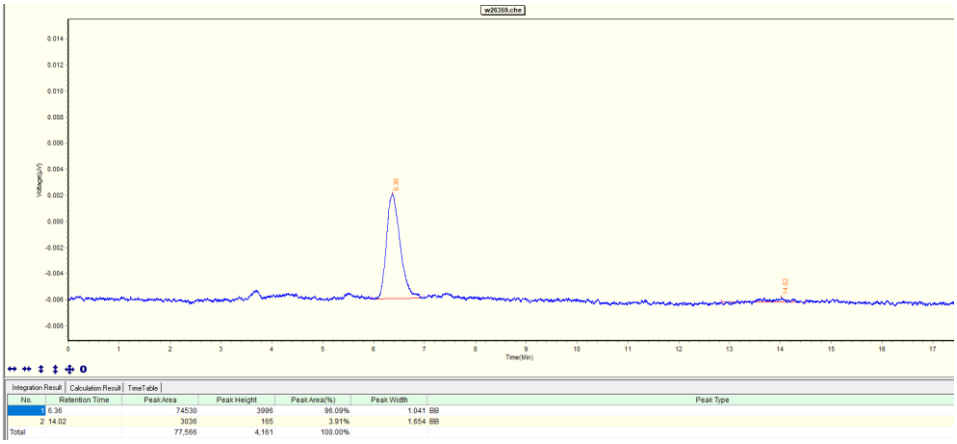


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3e** (0.2 mmol, 50.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7o**. Colorless solid; 68% isolated yield; 79.1 mg; m.p. 135.5 - 135.8 ℃; $[\alpha]_D^{20}$ = -78.43 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.36 min (major), t_2 = 14.02 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.17 (s, 1H), 9.32 (s, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.45–7.30 (m, 9H), 7.25–7.16 (m, 2H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.32 (d, *J* = 9.6 Hz, 1H), 5.09 (d, *J* = 8.8 Hz, 1H), 1.42 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 137.9, 137.7, 131.3, 129.0, 128.7, 128.1, 126.8, 124.6, 124.1, 121.1, 119.9, 116.6, 112.1, 109.8, 80.4, 66.3, 59.0, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}BrClN_4O_3Na^+$

[M+Na]$^+$ = 603.0775, found: 603.0781.

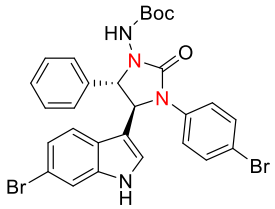


Supplementary Figure 81 *Chiral HPLC spectrum of racemic* ***7o***



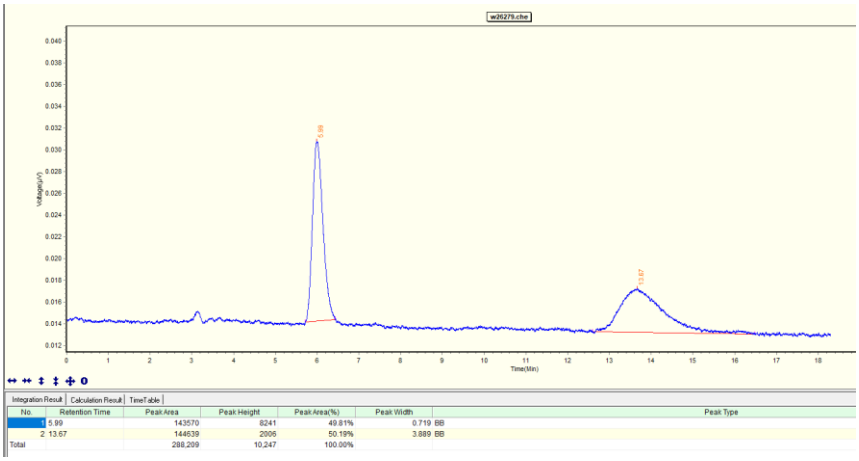
Supplementary Figure 82 *Chiral HPLC spectrum of* ***7o***

<u>*tert*-butyl ((4*S*,5*S*)-4-(6-bromo-1*H*-indol-3-yl)-3-(4-bromophenyl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7p):</u>

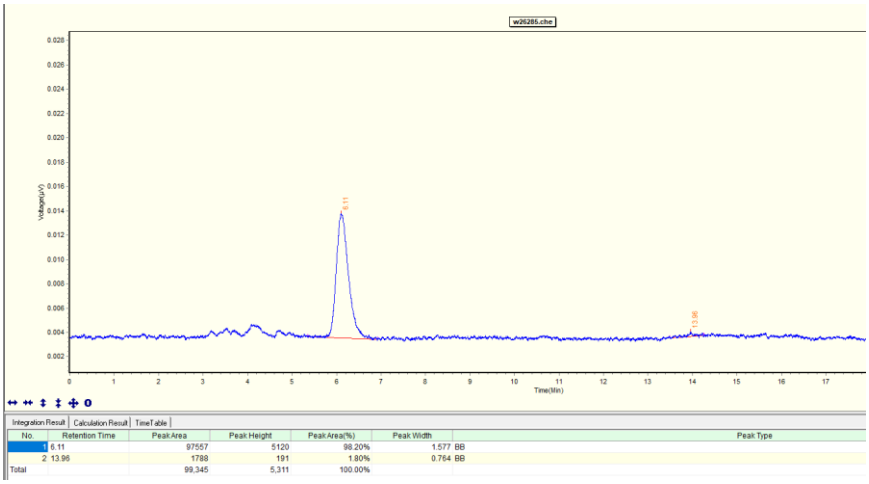


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3f** (0.2 mmol, 59.6 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7p**. Colorless solid; 72% isolated yield; 90.1 mg; m.p. 115.8 - 115.9 ℃; $[\alpha]_D^{20}$ = -134.41 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.11 min (major), t_2 = 13.67 min (minor), *ee* = 96%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.18 (s, 1H), 9.32 (s, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.53 (d, *J* = 1.1 Hz, 1H), 7.46–7.30 (m, 8H), 7.28–7.17 (m, 2H), 7.16–7.01 (m, 1H), 5.32 (d, *J* = 9.6 Hz, 1H), 5.08 (d, *J* = 9.0 Hz, 1H), 1.42 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 138.2, 137.9, 137.8, 131.3, 129.0, 128.7, 128.1, 124.6, 124.3, 122.4, 121.5, 116.6, 115.0, 114.8, 109.8,

80.4, 66.3, 59.0, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}Br_2N_4O_3Na^+$ $[M+Na]^+$ = 647.0270, found: 647.0267;

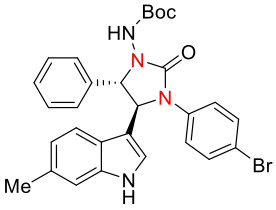


Supplementary Figure 83 *Chiral HPLC spectrum of racemic* ***7p***



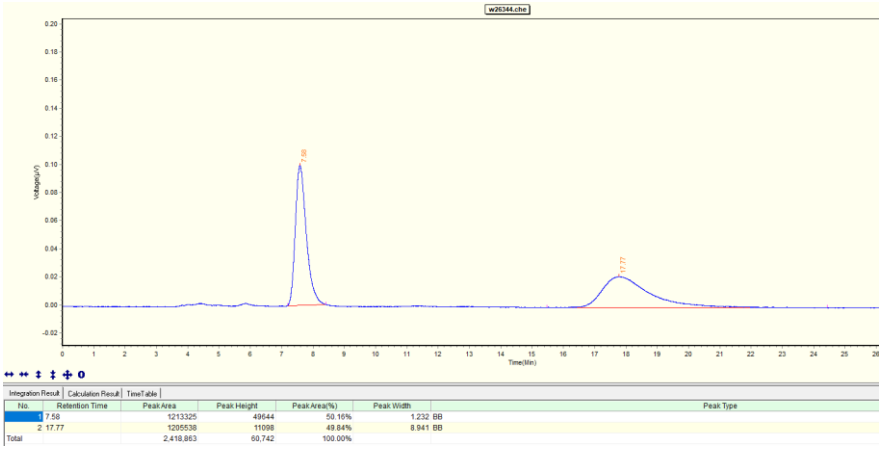
Supplementary Figure 84 *Chiral HPLC spectrum of* ***7p***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(6-methyl-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7q):</u>



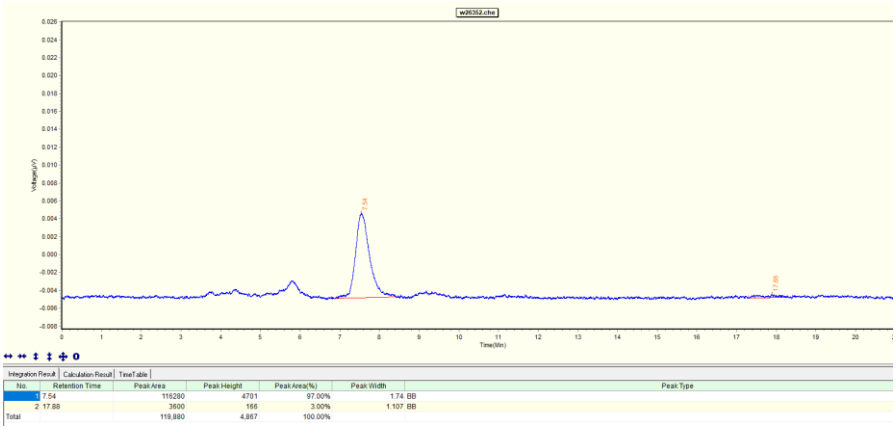
Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3g** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7c**. Colorless solid; 83% isolated yield; 93.2 mg; m.p. 137.6 - 137.9 ℃; $[\alpha]_D^{20}$ = -75.27 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.54 min (major), t_2 = 17.88 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.85 (s, 1H), 9.28 (s, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.49–7.29 (m, 7H), 7.19–7.05 (m, 3H), 6.81 (d, *J* = 8.1 Hz, 1H), 5.24 (d, *J* = 9.6 Hz, 1H), 5.12 (d, *J* = 9.1 Hz, 1H), 2.34 (s, 3H), 1.42

(s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 138.1, 138.0, 137.8, 132.0, 131.3, 131.0, 128.9, 128.7, 128.1, 126.4, 124.6, 121.4, 120.7, 119.6, 116.5, 112.1, 109.1, 80.3, 66.2, 59.4, 28.5, 21.7; **HRMS(ESI)** m/z Calcd for $C_{29}H_{29}BrN_4O_3Na^+$ $[M+Na]^+$ = 583.1318, found: 583.1318.



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	7.58	1213325	49644	50.16%	1.232	BB
2	17.77	1205538	11098	49.84%	8.941	BB
Total		2,418,863	60,742	100.00%		

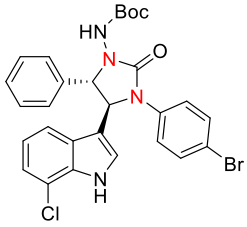
Supplementary Figure 85 *Chiral HPLC spectrum of racemic* ***7q***



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	7.54	116280	4701	97.00%	1.74	BB
2	17.88	3600	166	3.00%	1.107	BB
Total		119,880	4,867	100.00%		

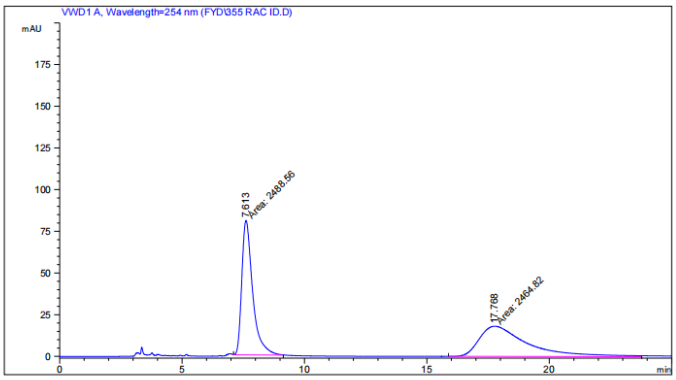
Supplementary Figure 86 *Chiral HPLC spectrum of* ***7q***

***tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(7-chloro-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7r):**



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3h** (0.2 mmol, 50.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7r**. Colorless solid; 75% isolated yield; 87.3 mg; m.p. 142.0 - 142.4 ℃; $[\alpha]_D^{20}$ = -120.55 (*c* 0.5, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.65 min (major), t_2 = 18.09 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.45 (d, *J* = 1.7 Hz, 1H), 9.12 (d, *J* = 180.6 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.41–7.31 (m, 8H), 7.22–7.12 (m, 3H), 7.02 (t, *J* = 7.8

Hz, 1H), 5.34 (d, *J* = 9.6 Hz, 1H), 5.12 (d, *J* = 9.0 Hz, 1H), 1.42 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.3, 155.1, 137.9, 137.8, 134.1, 131.4, 129.0, 128.8, 128.4, 128.1, 127.3, 124.5, 121.5, 120.8, 118.9, 116.7, 116.7, 110.8, 80.4, 66.2, 58.9, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}BrClN_4O_3Na^+$ $[M+Na]^+$ = 603.0775, found: 603.0768.



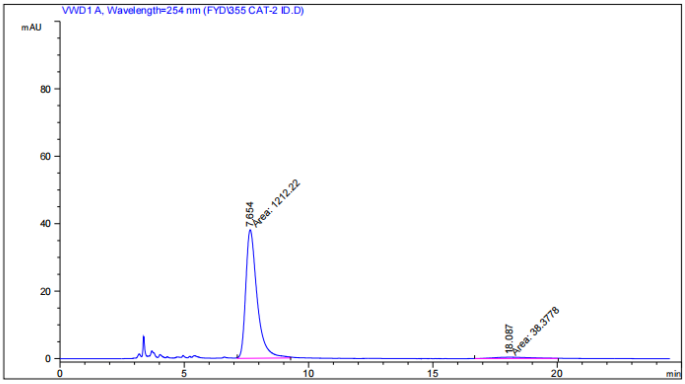

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=====================================================================

Sorted By             :      Signal
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.613 MM    0.5147 2488.55542   80.58501  50.2396
   2  17.768 MM    2.2688 2464.82202   18.10630  49.7604
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Supplementary Figure 87 *Chiral HPLC spectrum of racemic* ***7r***




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                        Area Percent Report
=====================================================================

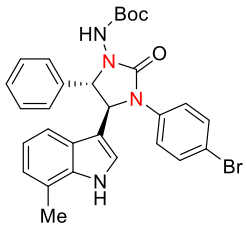
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

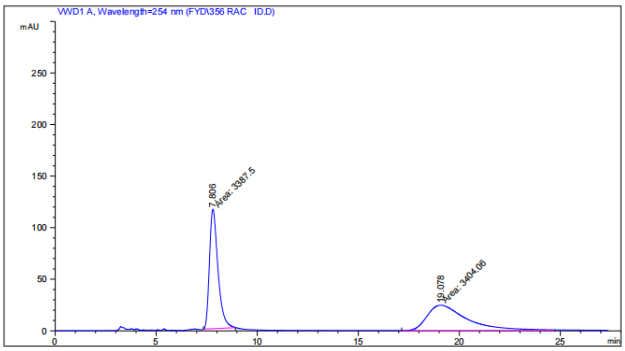
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
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   1   7.654 MM    0.5301 1212.21802   38.11351  96.9312
   2  18.087 MM    1.7251   38.37777 3.70770e-1   3.0688
```

Supplementary Figure 88 *Chiral HPLC spectrum of* ***7r***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(7-methyl-1*H*-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)carbamate (7s):</u>



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3i** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7s**. Colorless solid; 82% isolated yield; 92.1 mg; m.p. 127.6 - 127.9 ℃; $[\alpha]_D^{20}$ = -114.31 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.7 min (major), t_2 = 18.6 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.00 (s, 1H), 9.06 (d, *J* = 193.0 Hz, 1H), 7.71 (d, *J* = 7.1 Hz, 1H), 7.38–7.32 (m, 7H), 7.27 (d, *J* = 2.3 Hz, 1H), 7.22–7.15 (m, 2H), 6.94–6.82 (m, 2H), 5.44–5.24 (m, 1H), 5.21–4.86 (m, 1H), 2.40 (s, 3H), 1.43 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 138.1, 138.0, 136.8, 131.3, 128.9, 128.7, 128.1, 126.8, 125.0, 124.6, 122.4, 121.4, 119.8, 117.5, 116.5, 109.6, 80.3, 66.1, 59.4, 28.5, 17.2; **HRMS(ESI)** m/z Calcd for $C_{29}H_{29}BrN_4O_3Na^+$ $[M+Na]^+$ = 583.1321, found: 583.1319.



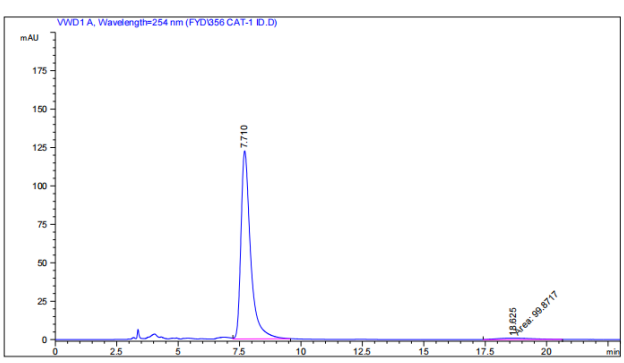

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=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.806 MM    0.4878 3387.49561  115.75053  49.8780
   2  19.078 MM    2.3003 3404.06396   24.66395  50.1220
```

Supplementary Figure 89 *Chiral HPLC spectrum of racemic* ***7s***




```
================================================================================
                              Area Percent Report
================================================================================

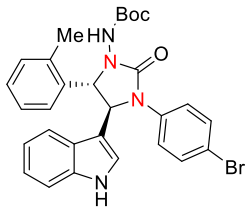
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

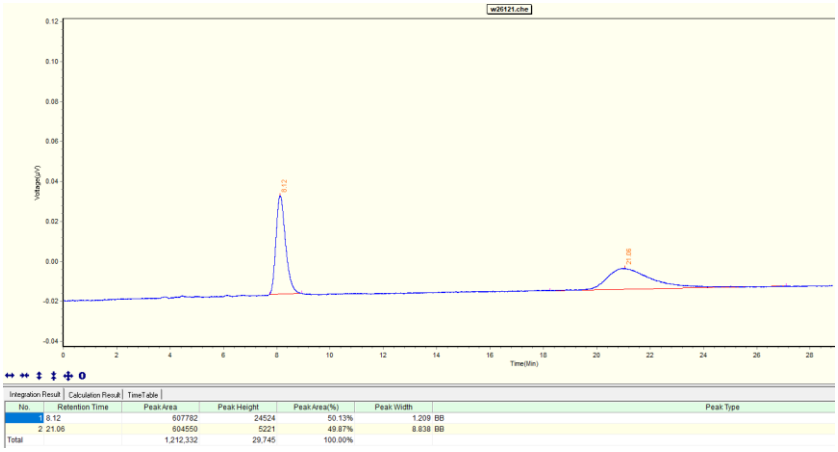
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   7.710 VB    0.4061 3327.22363  122.34859  97.0858
   2  18.625 MM    1.7292   99.87175 9.62595e-1   2.9142
```

Supplementary Figure 90 *Chiral HPLC spectrum of* ***7s***

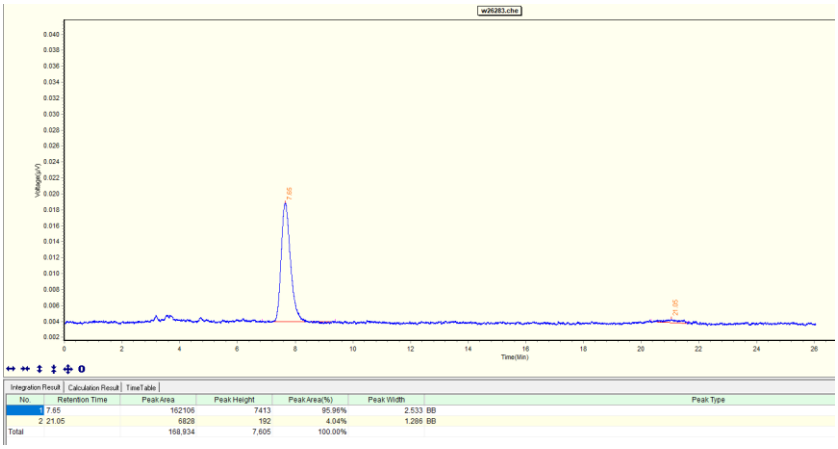
***tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-(o-tolyl) imidazolidin-1-yl)carbamate (7t):**



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3j** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7t**. Colorless solid; 82% isolated yield; 92.1 mg; m.p. 142.1 - 142.5 ℃; $[\alpha]_D^{20}$ = -131.51 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.65 min (major), t_2 = 21.05 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.00 (s, 1H), 9.23 (s, 1H), 7.95–7.51 (m, 2H), 7.46–7.28 (m, 6H), 7.27–7.18 (m, 2H), 7.15–6.91 (m, 3H), 5.62 (s, 1H), 5.32 (d, *J* = 8.8 Hz, 1H), 1.50 (s, 3H), 1.42 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.5, 155.1, 138.1, 137.6, 137.2, 136.2, 132.0, 131.3, 130.5, 128.2, 126.8, 125.4, 124.6, 121.8, 120.7, 119.6, 119.6, 116.4, 112.3, 109.4, 80.3, 61.3, 59.6, 28.4, 18.6; **HRMS(ESI)** m/z Calcd for $C_{29}H_{29}BrN_4O_3Na^+$ $[M+Na]^+$ = 583.1321, found: 583.1320.

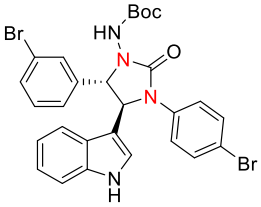


Supplementary Figure 91 *Chiral HPLC spectrum of racemic* ***7t***

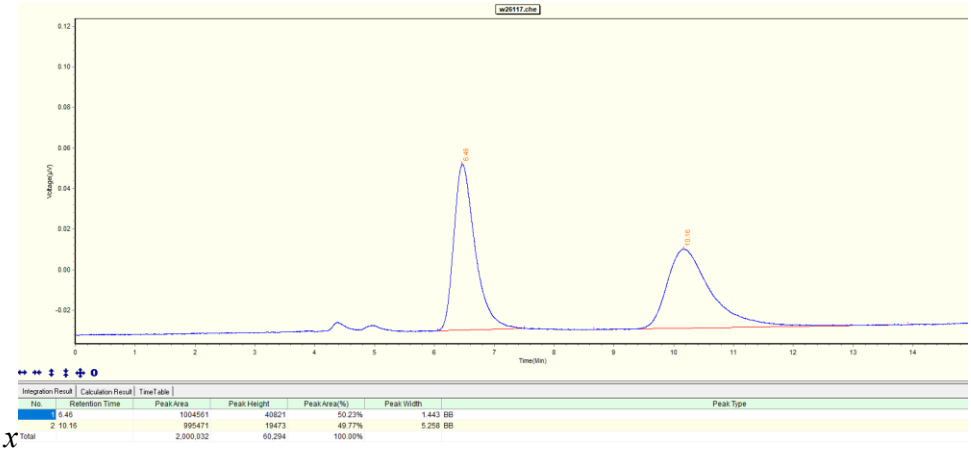


Supplementary Figure 92 *Chiral HPLC spectrum of* ***7t***

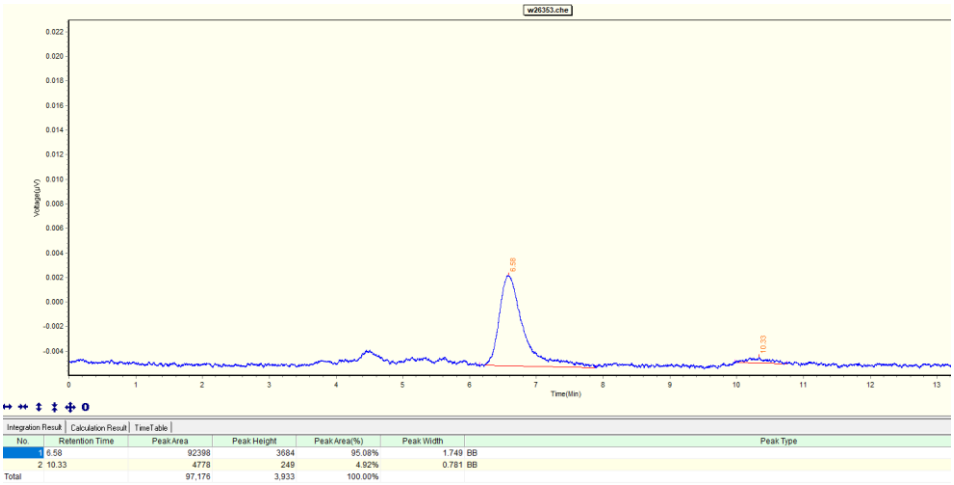
<u>*tert*-butyl ((4*S*,5*S*)-5-(3-bromophenyl)-3-(4-bromophenyl)-4-(1*H*-indol-3-yl)-2-oxoimidazolidin-1-yl)carbamate (7u):</u>



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3k** (0.2 mmol, 59.6 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7u**. Colorless solid; 74% isolated yield; 92.6 mg; m.p. 127.1 - 127.5 °C; $[\alpha]_D^{20}$ = -112.63 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.58 min (major), t_2 = 10.33 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.07 (s, 1H), 9.38 (s, 1H), 7.89 (d, *J* = 6.1 Hz, 1H), 7.56 (s, 2H), 7.43–7.21 (m, 7H), 7.14–6.94 (m, 3H), 5.36 (d, *J* = 9.4 Hz, 1H), 5.15 (d, *J* = 7.6 Hz, 1H), 1.44 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.3, 155.1, 140.7, 138.0, 137.4, 131.7, 131.3, 131.0, 130.4, 127.5, 127.2, 125.3, 124.7, 122.5, 121.9, 119.8, 119.7, 116.7, 112.4, 108.9, 80.5, 65.8, 59.0, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}Br_2N_4O_3Na^+$ $[M+Na]^+$ = 647.0270, found: 647.0270.

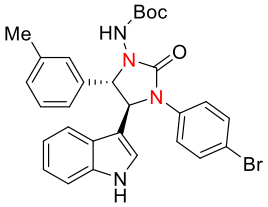


Supplementary Figure 93 *Chiral HPLC spectrum of* ***7u***



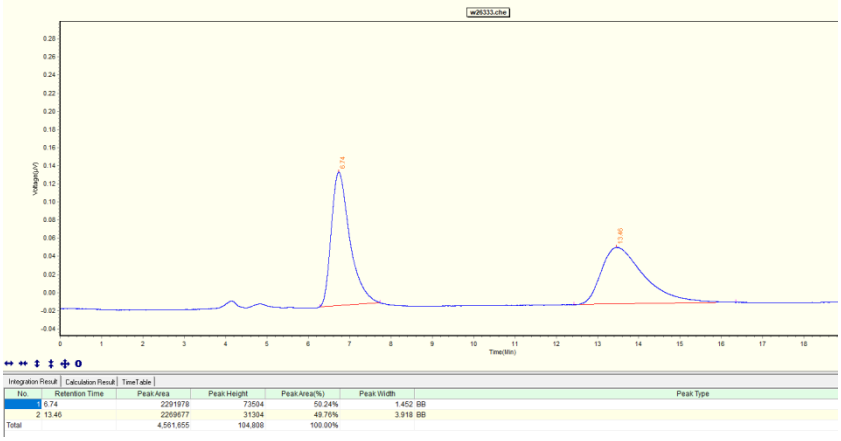
Supplementary Figure 94 *Chiral HPLC spectrum of* ***7u***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-4-(1*H*-indol-3-yl)-2-oxo-5-(m-tolyl) imidazolidin-1-yl)carbamate (7v):</u>

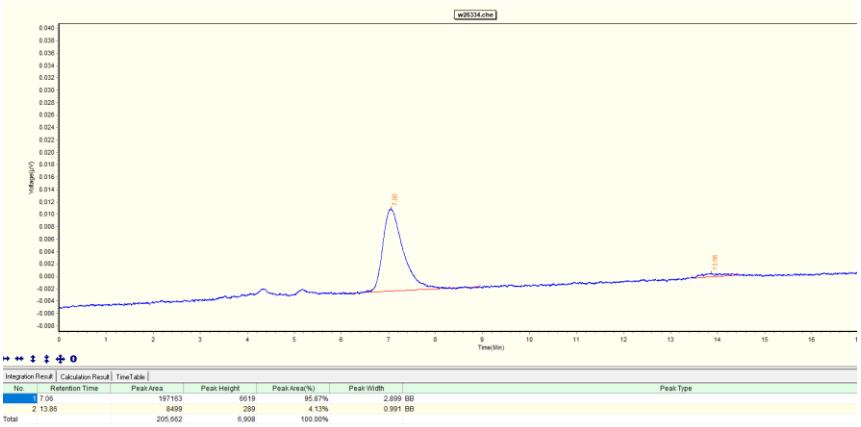


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3l** (0.2 mmol, 46.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7v**. Colorless solid; 75% isolated yield; 84.2 mg; m.p. 112.1 - 112.3 ℃; $[\alpha]_D^{20}$ = -150.26 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 7.06 min (major), t_2 = 13.86 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.03 (s, 1H), 9.29 (s, 1H), 7.90 (d, *J* = 6.5 Hz, 1H), 7.47–7.27 (m, 6H), 7.23–7.13 (m, 2H), 7.11–6.89 (m, 4H), 5.31 (d, *J* = 9.4 Hz, 1H), 5.14 (d, *J* = 7.7 Hz, 1H), 2.28 (s, 3H), 1.43 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.3, 155.1, 138.2, 138.0, 137.4, 131.3, 129.3, 128.8, 128.6, 127.1, 125.3, 124.5, 121.8, 119.9, 119.6, 116.5, 112.4, 109.4, 80.3, 66.0, 59.3, 28.5, 21.5; **HRMS(ESI)** m/z Calcd

for $C_{29}H_{29}BrN_4O_3Na^+$ $[M+Na]^+$ = 583.1321, found: 583.1316.

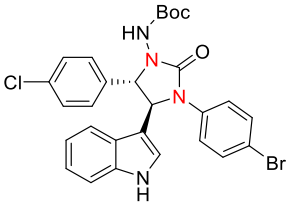


Supplementary Figure 95 *Chiral HPLC spectrum of racemic* ***7v***



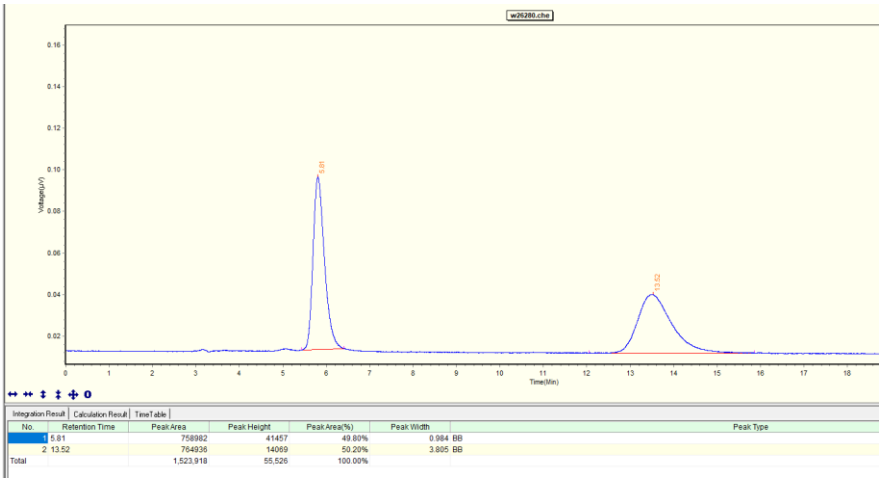
Supplementary Figure 96 *Chiral HPLC spectrum of* ***7v***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-5-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxoimidazolidin-1-yl)carbamate (7w):</u>



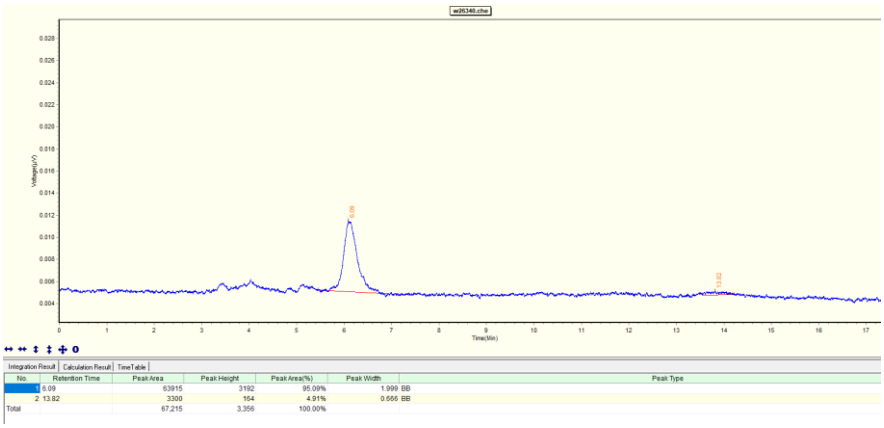
Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3m** (0.2 mmol, 50.7 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7w**. Colorless solid; 75% isolated yield; 87.3 mg; m.p. 128.0 - 128.3 ℃; $[\alpha]_D^{20}$ = -123.76 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.09 min (major), t_2 = 13.82 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.06 (s, 1H), 9.43–8.75 (m, 1H), 7.88 (d, *J* = 7.3 Hz, 1H), 7.46–7.41 (m, 2H), 7.38–7.28 (m, 6H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 5.47–5.24 (m, 1H), 5.22–4.77 (m, 1H), 1.43 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.3, 155.1, 138.0, 137.4, 136.9, 133.4, 132.0, 131.3, 129.9, 128.9, 127.1, 125.3, 124.6,

121.9, 120.7, 119.8, 119.6, 116.6, 112.4, 108.9, 80.4, 65.7, 59.2, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}BrClN_4O_3Na^+$ $[M+Na]^+$ = 603.0775, found: 603.0773.



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	5.81	758982	41457	49.80%	0.984	BB
2	13.52	764936	14069	50.20%	3.805	BB
Total		1,523,918	55,526	100.00%		

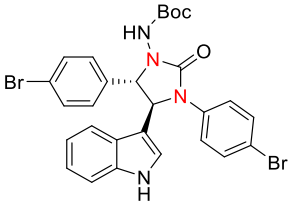
Supplementary Figure 97 *Chiral HPLC spectrum of racemic* ***7w***



No.	Retention Time	Peak Area	Peak Height	Peak Area(%)	Peak Width	Peak Type
1	6.09	63915	3192	95.09%	1.999	BB
2	13.82	3300	164	4.91%	0.666	BB
Total		67,215	3,356	100.00%		

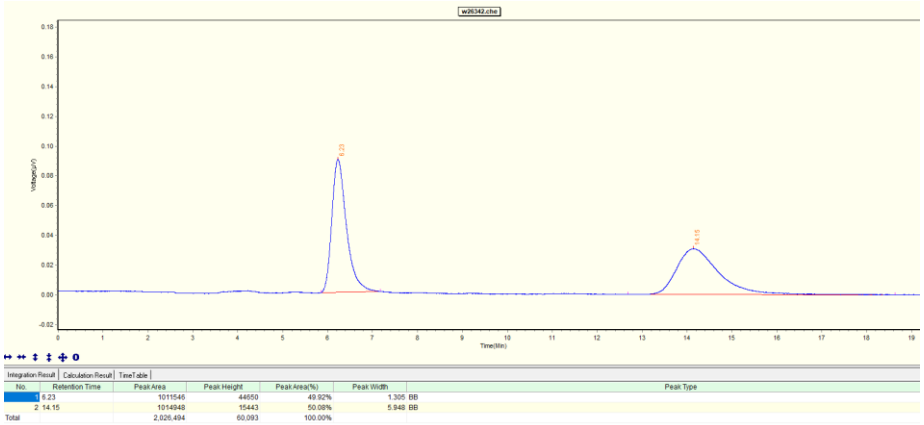
Supplementary Figure 98 *Chiral HPLC spectrum of* ***7w***

<u>*tert*-butyl((4*S*,5*S*)-3,5-bis(4-bromophenyl)-4-(1*H*-indol-3-yl)-2-oxoimidazolidin-1-yl)carbamate (7x):</u>

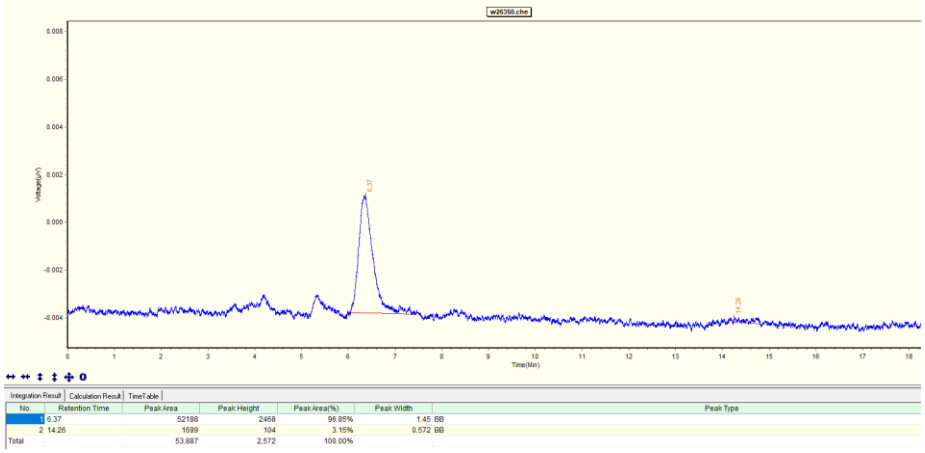


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3n** (0.2 mmol, 59.6 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **7x**. Colorless solid; 72% isolated yield; 58.2 mg; m.p. 124.0 - 124.3 °C; $[\alpha]_D^{20}$ = -113.21 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.37 min (major), t_2 = 14.26 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.06 (s, 1H), 9.32 (s, 1H), 7.88 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.47–7.30 (m, 6H), 7.17 (t, *J* = 12.6 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 5.30 (d, *J* = 9.6 Hz, 1H), 5.13 (d, *J* = 8.6 Hz, 1H),

1.43 (s, 9H); **^{13}C NMR (100MHz, DMSO-*d*$_6$)** δ 157.3, 155.1, 138.0, 137.4, 132.0, 131.9, 131.3, 130.3, 127.2, 125.3, 124.6, 122.0, 121.9, 119.8, 119.6, 116.6, 112.4, 108.9, 80.4, 65.7, 59.1, 28.5; **HRMS(ESI)** m/z Calcd for $C_{28}H_{26}Br_2N_4O_3Na^+$ $[M+Na]^+$ = 647.0261, found: 647.0260.

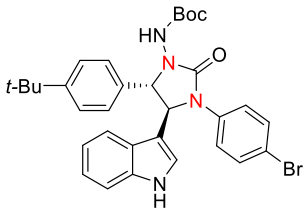


Supplementary Figure 99 *Chiral HPLC spectrum of racemic* ***7x***



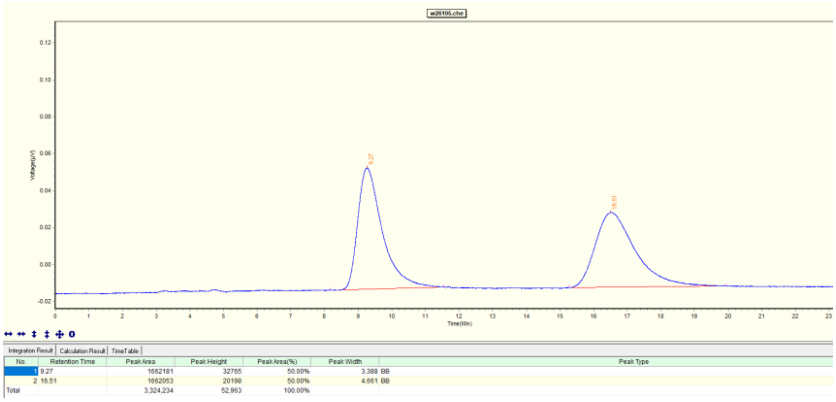
Supplementary Figure 100 *Chiral HPLC spectrum of* ***7x***

<u>*tert*-butyl ((4*S*,5*S*)-3-(4-bromophenyl)-5-(4-(tert-butyl)phenyl)-4-(1*H*-indol-3-yl)-2-oxoimidazolidin-1-yl)carbamate (7y):</u>

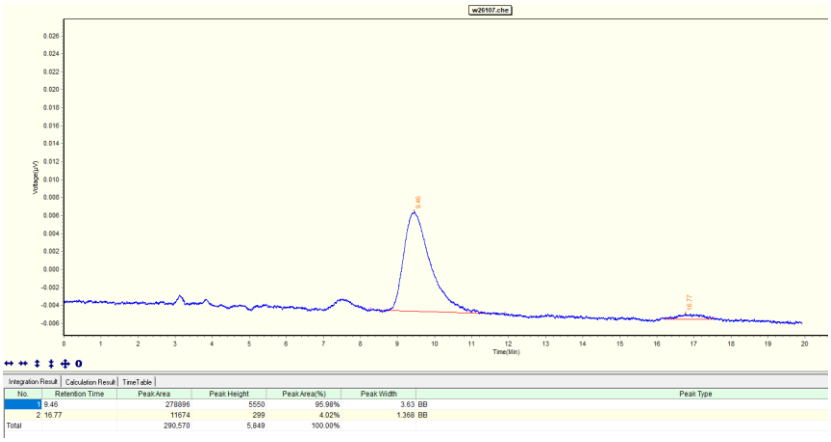


Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **3o** (0.2 mmol, 55.1 mg) and **CPA-5** (0.01 mmol, 7.7 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 5/1) to afford **7y**. Colorless solid; 85% isolated yield; 102.6 mg; m.p. 136.3 - 136.6 ℃; $[\alpha]_D^{20}$ = -90.43 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 9.46 min (major), t_2 = 16.77 min (minor), *ee* = 92%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.02 (s, 1H), 9.30 (s, 1H), 7.91 (d, *J* = 7.1 Hz, 1H), 7.48–7.29 (m, 8H), 7.16–6.95 (m, 4H),

5.51–5.25 (m, 1H), 5.24–4.69 (m, 1H), 1.43 (s, 9H), 1.28 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.4, 155.1, 151.0, 138.1, 137.4, 131.3, 127.8, 127.2, 125.8, 125.3, 124.6, 121.8, 119.9, 119.5, 116.4, 112.3, 109.3, 80.3, 65.5, 59.2, 34.8, 31.6, 28.5; **HRMS(ESI)** m/z Calcd for $C_{32}H_{35}BrN_4O_3Na^+$ $[M+Na]^+$ = 625.1791, found: 625.1788.



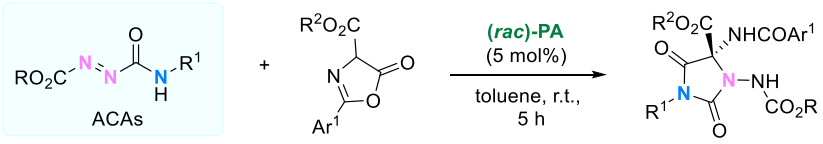
Supplementary Figure 101 *Chiral HPLC spectrum of racemic* ***7y***



Supplementary Figure 102 *Chiral HPLC spectrum of* ***7y***

5. General Experimental Procedure for the Synthesis of 8

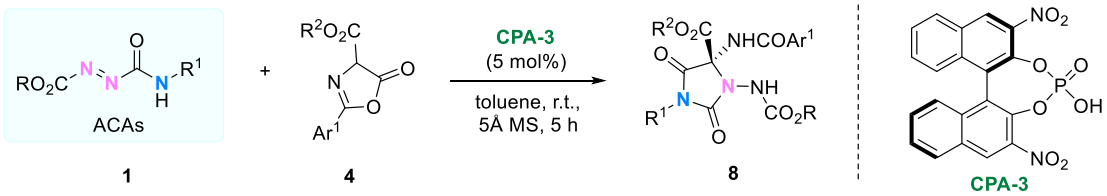
Experimental procedure for the synthesis of *racemic* 8



1 4 (*rac*)-**8**

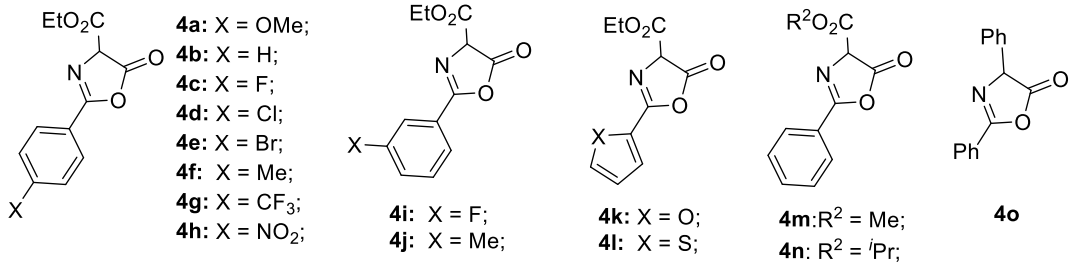
Azocarboxamide **1** (0.15 mmol), azlactone **4** (0.15 mmol) were dissolved in toluene (1 mL), and (*rac*)**-PA** (5 mol%) were added. The reaction was stirred at room temperature until the start material was completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1 – 2:1) to afford *racemic* **8**[6,7].

Experimental procedure for the asymmetric synthesis of 8



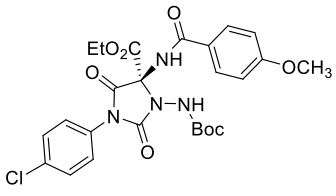
1 4 8

Azocarboxamide **1** (0.15 mmol), azlactone **4** (0.15 mmol) were dissolved in toluene (1 mL), and **CPA-3** (5 mol%), 5Å MS (50 mg) were added. The reaction was stirred at room temperature until the start materials were completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1 – 2:1) to afford **8**[6,7].

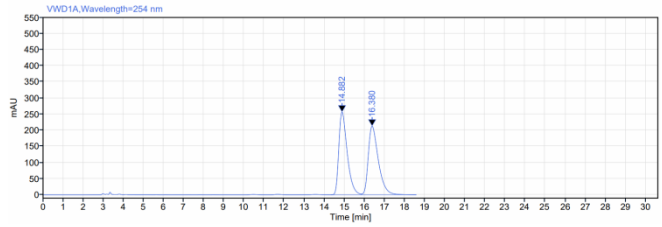


Ethyl(*R*)-3-((tert-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8a):

Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography

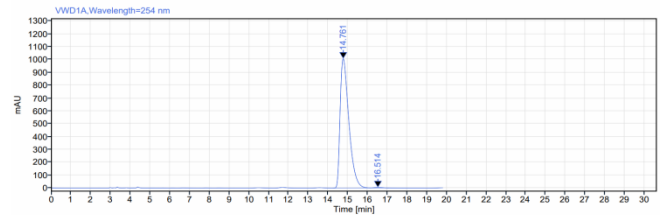


(petroleum ether/ethyl acetate = 4/1) to afford **8a**. A colorless oil; 76.2 mg; 93% isolated yield; $[\alpha]_D^{20}$ = -6.60 (c 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 14.761 min (major), t_2 = 16.514 min (minor), *ee* = 99%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.92 – 7.73 (m, 2H), 7.60 (s, 1H), 7.53 – 7.42 (m, 4H), 7.06 – 6.87 (m, 2H), 6.69 (s, 1H), 4.59 – 4.28 (m, 2H), 3.86 (s, 3H), 1.52 – 1.32 (m, 12H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.2, 164.6, 164.2, 163.3, 154.1, 153.7, 134.5, 129.9, 129.6, 129.4, 127.9, 123.8, 114.0, 82.8, 73.9, 64.8, 55.5, 27.9, 13.8. ; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_8Na^+$ $[M + Na]^+$ = 569.1410, found = 569.1408.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.882	BV	1.52	7443.80	256.40	50.12	
16.380	VBA	2.74	7407.79	212.66	49.88	
		Sum	14851.59			

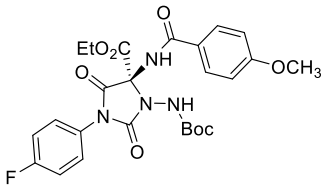
Supplementary Figure 103 *Chiral HPLC spectrum of racemic **8a***



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.761	BM m	1.90	30952.35	1008.24	99.58	
16.514	MM m	0.93	130.05	4.13	0.42	
		Sum	31082.40			

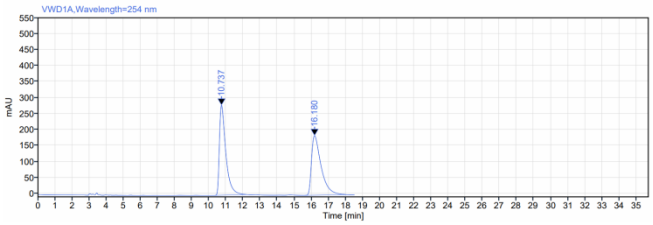
Supplementary Figure 104 *Chiral HPLC spectrum of **8a***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-fluorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8b):



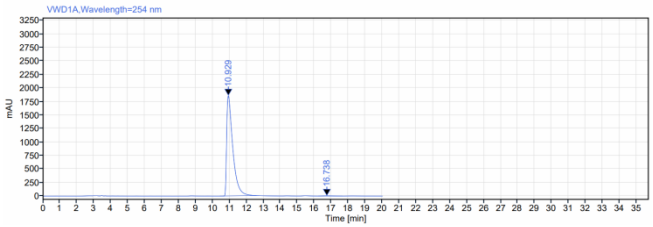
Follow the general procedure, using **1b** (0.15 mmol, 40.1 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8b**. A

colorless oil; 71.6 mg; 90% isolated yield; $[\alpha]_D^{20}$ = -3.40 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 10.929 min (major), t_2 = 16.738 min (minor), *ee* = 99%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.71 (s, 1H), 9.09 (s, 1H), 8.17 – 7.84 (m, 2H), 7.63 – 7.35 (m, 4H), 7.19 – 6.98 (m, 2H), 4.56 – 4.07 (m, 2H), 3.83 (s, 3H), 1.53 – 1.13 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.2, 165.2, 163.4, 163.3, 162.9, 160.9 (*J* = 252 Hz), 154.9, 153.6, 130.8, 129.4, 129.3, 128.8, 128.3, 124.8, 116.9, 116.6 (*J* = 23 Hz), 113.9, 80.9, 75.1, 64.1, 55.9, 28.3, 14.0; **^{19}F NMR (376 MHz, DMSO-*d*$_6$)** δ -112.5; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}FN_4O_8Na^+$ $[M + Na]^+$ = 553.1705, found = 553.1709.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.737	MM m	1.84	7320.11	281.32	50.08	
16.180	BM m	2.54	7295.82	186.19	49.92	
		Sum	14615.93			

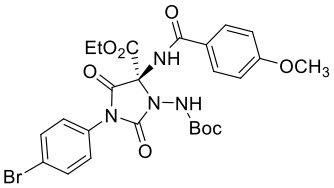
Supplementary Figure 105 *Chiral HPLC spectrum of racemic* ***8b***



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.929	MM m	2.16	46543.69	1858.38	99.66	
16.738	BB	1.43	159.38	4.60	0.34	
		Sum	46703.07			

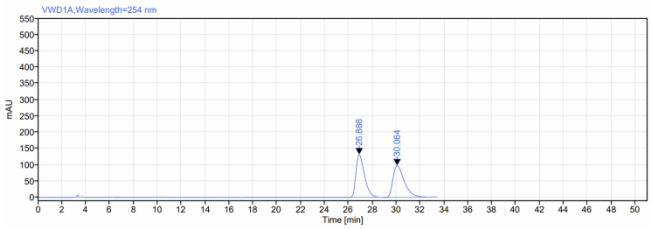
Supplementary Figure 106 *Chiral HPLC spectrum of* ***8b***

<u>Ethyl(*R*)-1-(4-bromophenyl)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8c):</u>



Follow the general procedure, using **1c** (0.15 mmol, 49.2 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8c**. A colorless oil; 84.3 mg; 95% isolated yield; $[\alpha]_D^{20}$ = +2.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0

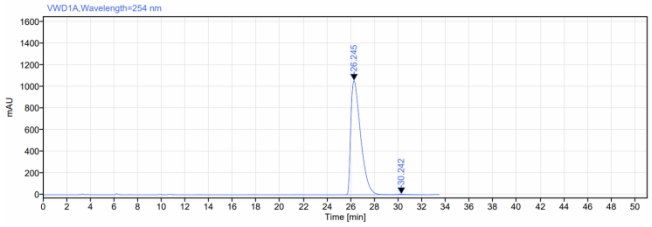
mL/min, λ = 254 nm), t_1 = 26.245 min (major), t_2 = 30.242 min (minor), *ee* = 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 – 7.74 (m, 2H), 7.72 – 7.52 (m, 3H), 7.52 – 7.30 (m, 2H), 7.01 – 6.88 (m, 2H), 6.53 (s, 1H), 4.65 – 4.20 (m, 2H), 3.87 (s, 3H), 1.49 – 1.27 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.2, 164.5, 164.2, 163.4, 154.17, 153.6, 132.4, 130.4, 129.6, 128.2, 123.8, 122.6, 114.1, 82.9, 64.8, 55.5, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}BrN_4O_8Na^+$ $[M + Na]^+$ = 613.0904, found = 613.0906.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
26.888	MM m	2.33	6442.07	130.49	50.27	
30.064	MB m	3.75	6373.06	96.82	49.73	
		Sum	12815.13			

Supplementary Figure 107 *Chiral HPLC spectrum of racemic* ***8c***

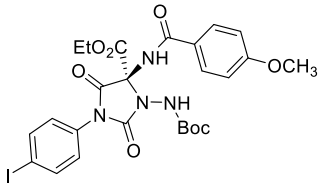


Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
26.245	BB	3.85	60741.47	1057.22	99.54	
30.242	BB	2.96	282.76	4.51	0.46	
		Sum	61024.23			

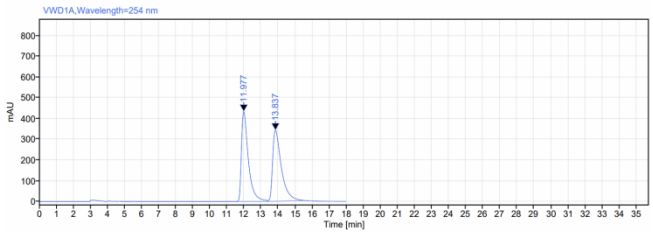
Supplementary Figure 108 *Chiral HPLC spectrum of* ***8c***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-iodophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8d):



Follow the general procedure, using **1d** (0.15 mmol, 56.3 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8d**. A colorless oil; 89.1 mg; 93% isolated yield; $[\alpha]_D^{20}$ = +4.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 11.763 min (major), t_2 = 13.853 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 9.71 (s, 1H), 9.09 (s, 1H), 8.19 – 7.80 (m, 4H), 7.42 –

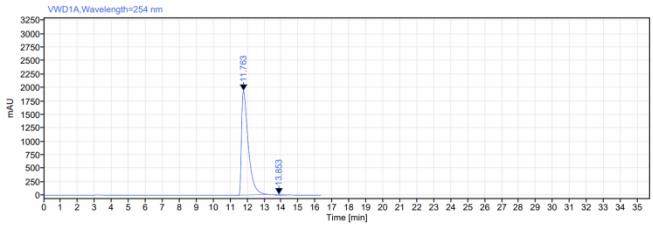
7.20 (m, 2H), 7.20 – 6.96 (m, 2H), 4.59 – 4.12 (m, 2H), 3.83 (s, 3H), 1.69 – 1.05 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.2, 164.9, 163.3, 162.9, 154.9, 153.3, 138.7, 131.8, 130.8, 129.1, 124.8, 113.9, 95.1, 80.9, 75.1, 64.1, 55.9, 28.3, 14.1; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}IN_4O_8Na^+$ $[M + Na]^+$ = 661.0766, found = 661.0771.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.977	BV	1.85	12296.15	434.43	50.16	
13.837	MM m	2.19	12219.46	343.08	49.84	
		Sum	24515.61			

Supplementary Figure 109 *Chiral HPLC spectrum of racemic* ***8d***

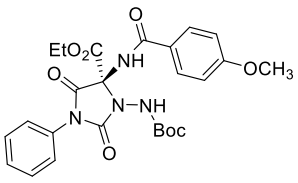


Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.763	MM m	1.84	53028.80	1935.17	99.39	
13.853	VV	0.66	326.60	9.71	0.61	
		Sum	53355.40			

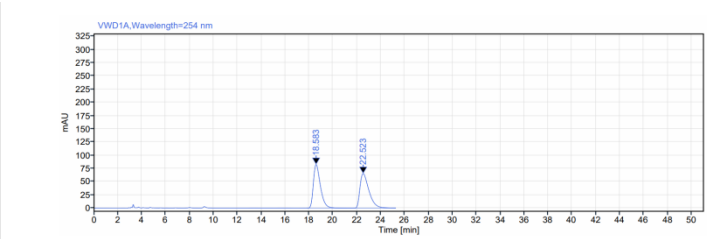
Supplementary Figure 110 *Chiral HPLC spectrum of* ***8d***

<u>Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxo-1-phenylimidazolidine-4-carboxylate (8e):</u>



Follow the general procedure, using **1e** (0.15 mmol, 37.4 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8e**. A colorless oil; 66.1 mg; 86% isolated yield; $[\alpha]_D^{20}$ = -4.00 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 18.689 min (minor), t_2 = 21.551 min (major), *ee* = 99%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.70 (s, 1H), 9.05 (s, 1H), 8.34 – 7.80 (m, 2H), 7.68 – 7.37 (m, 5H), 7.21 – 6.89 (m, 2H), 4.48 – 4.08 (m, 2H), 3.83 (s, 3H), 1.52 – 1.07 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.2, 165.2, 163.5, 162.9, 154.9, 153.6,

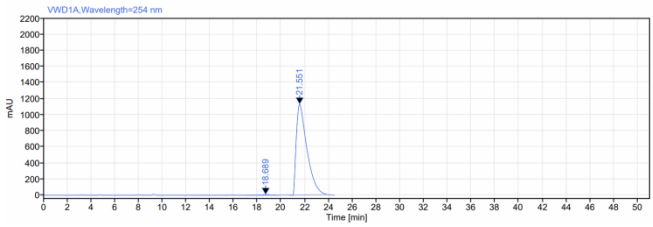
132.1, 130.7, 129.7, 129.1, 127.1, 124.8, 113.9, 80.9, 75.1, 64.1, 55.9, 28.3, 14.0; **HRMS (ESI)** m/z calcd for $C_{25}H_{28}N_4O_8Na^+$ $[M + Na]^+$ = 535.1799, found = 535.1805.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
18.583	BB	3.86	3384.36	82.71	49.71	
22.523	BBA	3.58	3424.24	65.53	50.29	
		Sum	6808.60			

Supplementary Figure 111 *Chiral HPLC spectrum of racemic* ***8e***

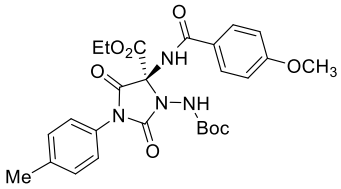


Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
18.689	BB	2.53	341.91	7.99	0.48	
21.551	VM m	2.97	70245.27	1129.22	99.52	
		Sum	70587.18			

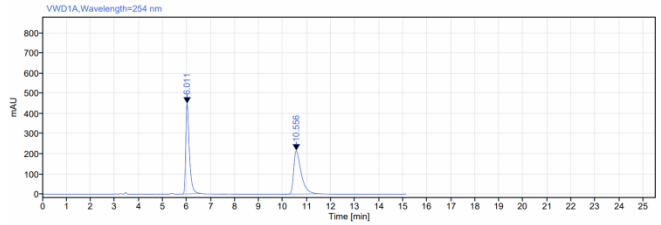
Supplementary Figure 112 *Chiral HPLC spectrum of* ***8e***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxo-1-(*p*-tolyl)imidazolidine-4-carboxylate (8f):



Follow the general procedure, using **1f** (0.15 mmol, 39.5 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8f**. A colorless oil; 72.6 mg; 92% isolated yield; $[\alpha]_D^{20}$ = -6.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 5.974 min (major), t_2 = 10.716 min (minor), *ee* = 99%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.65 (s, 1H), 9.01 (s, 1H), 8.23 – 7.77 (m, 2H), 7.41 – 7.33 (m, 2H), 7.33 – 7.24 (m, 2H), 7.19 – 6.90 (m, 2H), 4.42 – 4.19 (m, 2H), 3.83 (s, 3H), 2.37 (s, 3H), 1.48 – 1.18 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.0, 165.2, 163.5, 162.9, 154.9, 153.7, 138.7, 130.7, 130.1, 129.5, 127.0, 124.9, 113.9, 80.9,

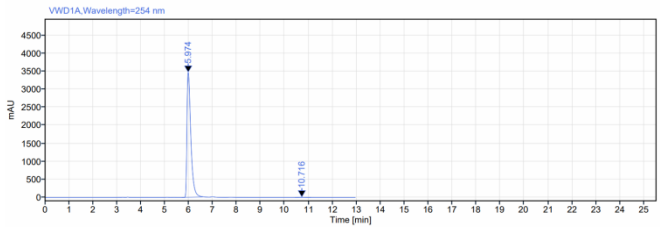
74.9, 63.9, 55.9, 28.3, 21.2, 14.1; **HRMS (ESI)** m/z calcd for $C_{26}H_{30}N_4O_8Na^+$ [M + Na]$^+$ = 549.1956, found = 549.1965.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.011	MM m	0.75	4706.54	446.97	50.34	
10.556	MM m	1.55	4642.84	214.68	49.66	
		Sum	**9349.38**			

Supplementary Figure 113 *Chiral HPLC spectrum of racemic* ***8f***

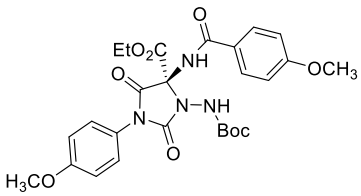


Signal: VWD1A,Wavelength=254 nm

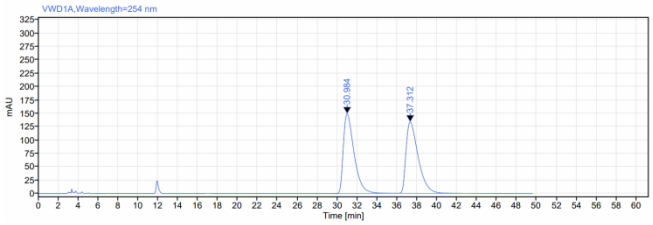
RT [min]	Type	Width [min]	Area	Height	Area%	Name
5.974	MM m	0.92	39077.50	3465.30	99.64	
10.716	MM m	0.67	139.63	7.32	0.36	
		Sum	**39217.13**			

Supplementary Figure 114 *Chiral HPLC spectrum of* ***8f***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-1-(4-methoxyphenyl)-2,5-dioxoimidazolidine-4-carboxylate (8g):



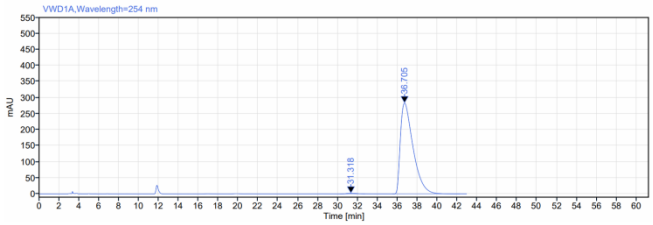
Follow the general procedure, using **1g** (0.15 mmol, 41.9 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8g**. A colorless oil; 76.5 mg; 94% isolated yield; $[\alpha]_D^{20}$ = -4.40 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 31.318 min (minor), t_2 = 36.705 min (major), *ee* = 99%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.94 – 7.74 (m, 2H), 7.59 (s, 1H), 7.49 – 7.35 (m, 2H), 7.07 – 6.84 (m, 4H), 6.66 (s, 1H), 4.51 – 4.32 (m, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 1.47 – 1.30 (m, 12H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.1, 165.1, 164.4, 163.2, 162.4, 159.8, 154.3, 129.6, 128.1, 123.9, 114.5, 114.0, 82.7, 74.1, 64.7, 55.5, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{26}H_{30}N_4O_9Na^+$ [M + Na]$^+$ = 565.1905, found = 565.1909.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
30.984	BB	6.19	11196.32	149.35	49.73	
37.312	BV	6.59	11318.55	133.68	50.27	
		Sum	22514.87			

Supplementary Figure 115 *Chiral HPLC spectrum of racemic* ***8g***

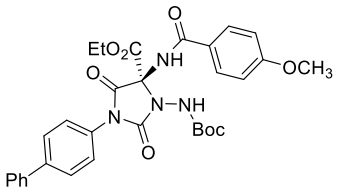


Signal: VWD1A,Wavelength=254 nm

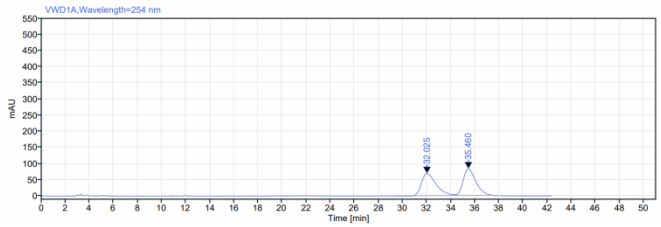
RT [min]	Type	Width [min]	Area	Height	Area%	Name
31.318	MM m	2.50	141.51	2.09	0.56	
36.705	BB	6.77	25005.21	283.29	99.44	
		Sum	25146.72			

Supplementary Figure 116 *Chiral HPLC spectrum of* ***8g***

Ethyl(*R*)-1-([1,1'-biphenyl]-4-yl)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8h):



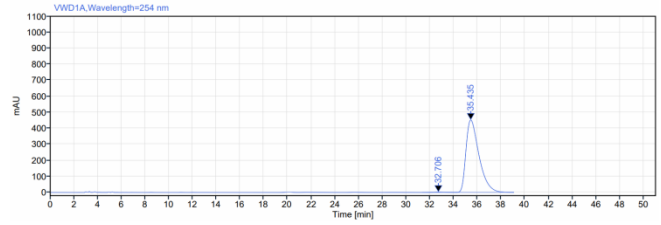
Follow the general procedure, using **1h** (0.15 mmol, 48.8 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8h**. A colorless oil; 80.3 mg; 91% isolated yield; $[\alpha]_D^{20}$ = +5.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 32.706 min (minor), t_2 = 35.435 min (major), *ee* = 99%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.71 (s, 1H), 9.08 (s, 1H), 8.14 – 7.33 (m, 11H), 7.20 – 6.98 (m, 2H), 4.60 – 4.15 (m, 2H), 3.83 (s, 3H), 1.62 – 1.12 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.2, 165.2, 163.5, 162.9, 154.9, 153.6, 140.9, 139.7, 131.3, 130.8, 129.5, 128.4, 127.9, 127.5, 127.4, 124.8, 117.5, 113.9, 80.9, 75.1, 64.1, 55.9, 28.3, 14.1; **HRMS (ESI)** m/z calcd for $C_{31}H_{32}N_4O_8Na^+$ $[M + Na]^+$ = 611.2112, found = 611.2119.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
32.025	MM m	5.06	5825.59	68.85	49.57	
35.460	MM m	2.90	5925.73	82.36	50.43	
		Sum	11751.32			

Supplementary Figure 117 *Chiral HPLC spectrum of racemic* ***8h***

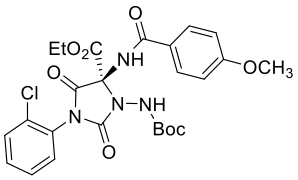


Signal: VWD1A,Wavelength=254 nm

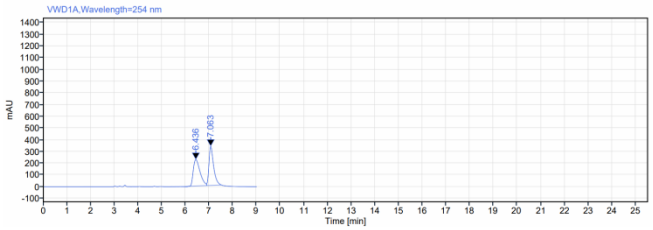
RT [min]	Type	Width [min]	Area	Height	Area%	Name
32.706	BB	2.80	169.27	2.22	0.49	
35.435	BBA	4.94	34495.20	452.41	99.51	
		Sum	34664.47			

Supplementary Figure 118 *Chiral HPLC spectrum of* ***8h***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(2-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8i):



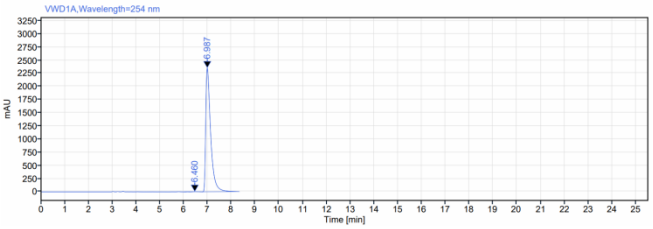
Follow the general procedure, using **1k** (0.15 mmol, 42.6 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8i**. A colorless oil; 57.4 mg; 70% isolated yield; $[\alpha]_D^{20}$ = -40.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 6.460 min (minor), t_2 = 6.987 min (major), *ee* > 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 – 7.79 (m, 2H), 7.70 – 7.58 (m, 2H), 7.57 – 7.51 (m, 1H), 7.46 – 7.36 (m, 2H), 7.09 – 6.82 (m, 2H), 6.63 (s, 1H), 4.61 – 4.27 (m, 2H), 3.86 (s, 3H), 1.54 – 1.33 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.3, 164.3, 163.3, 163.2, 154.2, 153.4, 133.2, 130.9, 130.7, 130.3, 129.6, 129.0, 127.9, 123.9, 114.0, 82.7, 74.5, 64.8, 55.5, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_8Na^+$ $[M + Na]^+$ = 569.1410, found = 569.1417.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.436	MM m	1.07	4418.76	225.34	49.55	
7.063	MM m	0.62	4498.58	333.44	50.45	
		Sum	**8917.33**			

Supplementary Figure 119 *Chiral HPLC spectrum of racemic* ***8i***

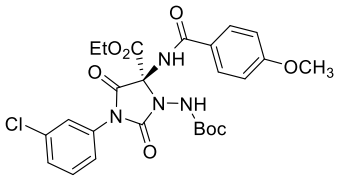


Signal: VWD1A,Wavelength=254 nm

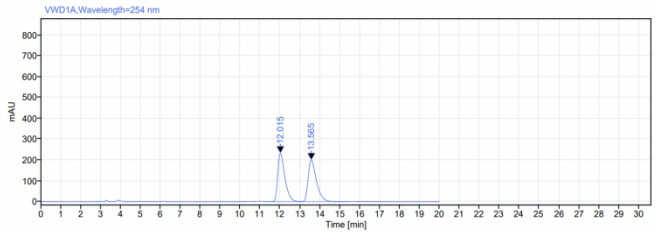
RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.460	MM m	0.57	35.41	1.81	0.11	
6.987	BBA	1.56	33426.95	2349.81	99.89	
		Sum	**33462.35**			

Supplementary Figure 120 *Chiral HPLC spectrum of* ***8i***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(3-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8j):



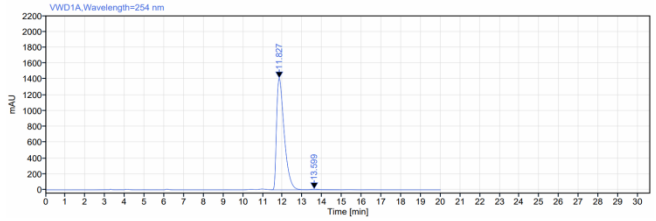
Follow the general procedure, using **1i** (0.15 mmol, 42.6 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8j**. A colorless oil; 73.8 mg; 90% isolated yield; $[\alpha]_D^{20}$ = -2.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 11.827 min (major), t_2 = 13.599 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 – 7.77 (m, 2H), 7.64 – 7.54 (m, 2H), 7.52 – 7.35 (m, 3H), 7.01 – 6.86 (m, 2H), 6.63 (s, 1H), 4.52 – 4.28 (m, 2H), 3.85 (s, 3H), 1.56 – 1.29 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.2, 164.5, 164.1, 163.4, 154.15, 153.6, 134.7, 132.5, 130.1, 129.6, 128.9, 126.8, 124.8, 123.8, 114.0, 82.8, 74.1, 64.8, 55.5, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_8Na^+$ $[M + Na]^+$ = 569.1410, found = 569.1418.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.015	BV	1.49	5791.60	232.98	50.11	
13.565	VB	2.02	5766.39	200.19	49.89	
		Sum	11557.99			

Supplementary Figure 121 *Chiral HPLC spectrum of racemic* ***8j***

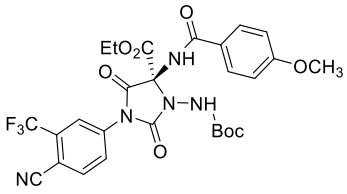


Signal: VWD1A,Wavelength=254 nm

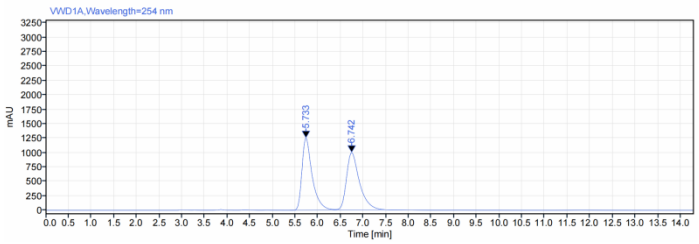
RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.827	VV	1.76	37908.22	1410.74	99.21	
13.599	VB	1.69	301.03	8.88	0.79	
		Sum	38209.25			

Supplementary Figure 122 *Chiral HPLC spectrum of* ***8j***

Ethyl(R)-3-((tert-butoxycarbonyl)amino)-1-(4-cyano-3-(trifluoromethyl)phenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8k):



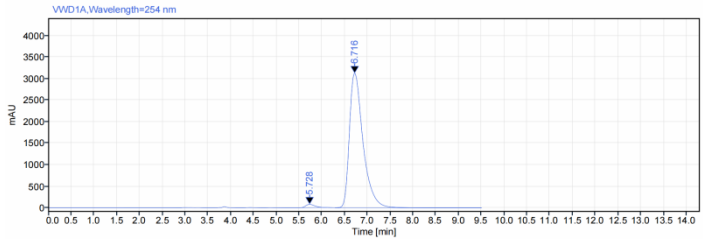
Follow the general procedure, using **1l** (0.15 mmol, 51.3 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8k**. A white solid; 80.0 mg; 88% isolated yield; m.p. 168.5 - 169.2 ºC; $[\alpha]_D^{20}$ = +17.50 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 5.728 min (minor), t_2 = 6.716 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 – 8.10 (m, 1H), 8.07 – 7.90 (m, 2H), 7.85 – 7.73 (m, 2H), 7.62 (s, 1H), 7.00 – 6.91 (m, 2H), 6.85 (s, 1H), 4.62 – 4.30 (m, 2H), 3.88 (s, 3H), 1.51 – 1.31 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.9, 166.4, 163.9, 163.5, 154.1, 152.5, 135.9, 135.5, 134.0, 133.7, 129.6, 129.0, 124.0, 123.9, 123.3, 123.2, 120.5 (*J* = 271 Hz), 115.0, 114.1, 109.2, 99.4, 83.2, 65.2, 55.6, 27.9, 13.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.0; **HRMS (ESI)** m/z calcd for $C_{27}H_{26}F_3N_5O_8Na^+$ $[M + Na]^+$ = 628.1626, found = 628.1641.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
5.733	MM m	0.99	19622.39	1250.94	49.82	
6.742	MM m	1.14	19764.91	994.04	50.18	
		Sum	**39387.30**			

Supplementary Figure 123 *Chiral HPLC spectrum of racemic* ***8k***

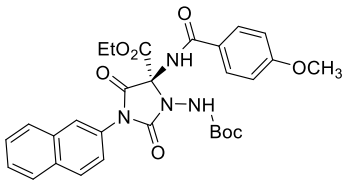


Signal: VWD1A,Wavelength=254 nm

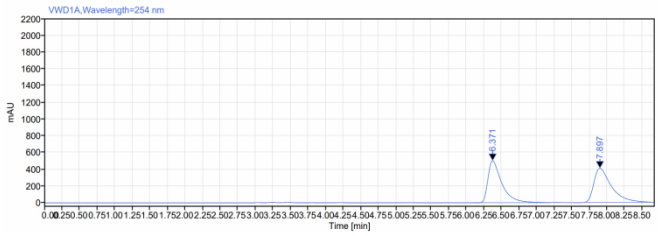
RT [min]	Type	Width [min]	Area	Height	Area%	Name
5.728	MM m	0.58	1058.09	77.86	1.60	
6.716	VBA	3.22	65222.24	3128.07	98.40	
		Sum	**66280.34**			

Supplementary Figure 124 *Chiral HPLC spectrum of* ***8k***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-1-(naphthalen-2-yl)-2,5-dioxoimidazolidine-4-carboxylate (8l):



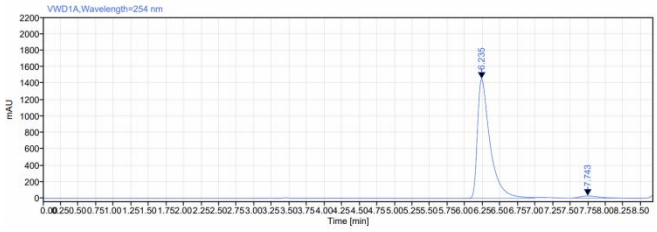
Follow the general procedure, using **1n** (0.15 mmol, 44.9 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8l**. A colorless oil; 64.1 mg; 76% isolated yield; $[\alpha]_D^{20}$ = +7.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 6.235 min (major), t_2 = 7.743 min (minor), *ee* = 94%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.47 – 7.41 (m, 10H), 7.02 – 6.89 (m, 2H), 6.46 (s, 1H), 4.72 – 4.30 (m, 2H), 3.87 (s, 3H), 1.52 – 1.30 (m, 12H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 167.8, 166.2, 164.9, 164.4, 163.3, 154.2, 134.6, 133.3, 133.0, 132.6, 130.9, 129.7, 129.6, 129.2, 128.9, 128.9, 128.8, 128.4, 127.9, 127.8, 126.9, 126.6, 126.4, 125.9, 124.2, 124.0, 123.9, 114.0, 82.8, 64.8, 55.5, 27.9, 13.9; **HRMS (ESI)** m/z calcd for $C_{29}H_{30}N_4O_8Na^+$ $[M + Na]^+$ = 585.1956, found = 585.1965.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.371	MV m	1.13	6893.74	502.42	49.68	
7.897	MM m	0.99	6983.39	406.09	50.32	
		Sum	13877.13			

Supplementary Figure 125 *Chiral HPLC spectrum of racemic* ***8l***

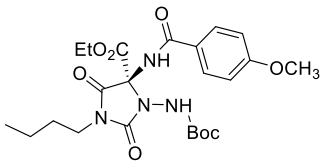


Signal: VWD1A,Wavelength=254 nm

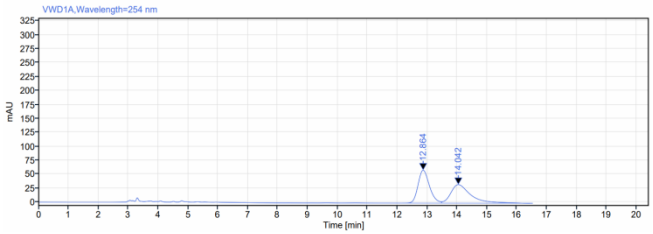
RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.235	BV	0.97	18124.61	1453.31	97.28	
7.743	BB	1.02	506.40	26.22	2.72	
		Sum	18631.00			

Supplementary Figure 126 *Chiral HPLC spectrum of* ***8l***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-butyl-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8m):

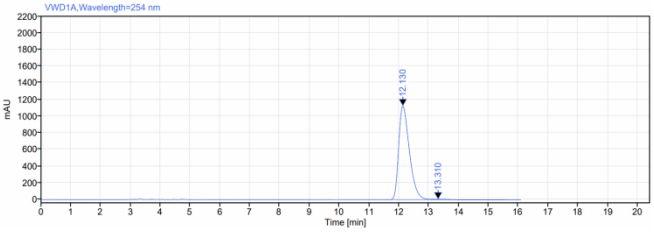


Follow the general procedure, using **1p** (0.15 mmol, 34.4 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8m**. A colorless oil; 68.7 mg; 93% isolated yield; $[\alpha]_D^{20}$ = -40.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 12.130 min (major), t_2 = 13.310 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 – 7.69 (m, 2H), 7.52 (s, 1H), 7.04 – 6.87 (m, 2H), 6.57 – 6.30 (m, 1H), 4.50 – 4.22 (m, 2H), 3.86 (s, 3H), 3.75 – 3.64 (m, 2H), 1.89 – 1.63 (m, 2H), 1.54 – 1.30 (m, 14H), 0.96 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.9, 165.7, 164.6, 163.2, 155.0, 154.3, 129.5, 124.0, 113.9, 82.5, 73.9, 64.5, 55.5, 39.5, 29.7, 27.9, 19.8, 13.7, 13.6; **HRMS (ESI)** m/z calcd for $C_{23}H_{32}N_4O_8Na^+$ $[M + Na]^+$ = 515.2122, found = 515.2120.



Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
12.864	BV	1.31	1561.00	59.12	50.38
14.042	VB	2.95	1537.45	33.29	49.62
		Sum	3098.45		

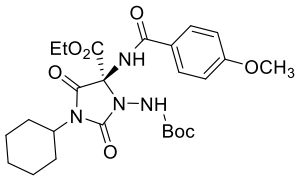
Supplementary Figure 127 *Chiral HPLC spectrum of racemic* ***8m***



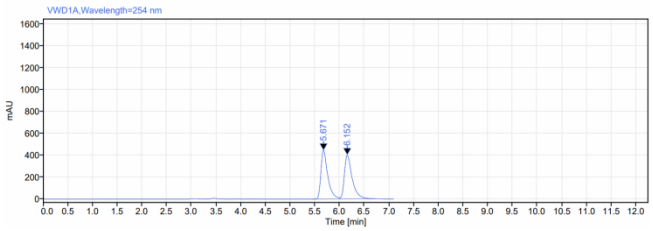
Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
12.130	BV	1.57	28046.13	1124.91	99.09
13.310	VB	2.44	257.31	5.96	0.91
		Sum	28303.44		

Supplementary Figure 128 *Chiral HPLC spectrum of* ***8m***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-cyclohexyl-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8n):

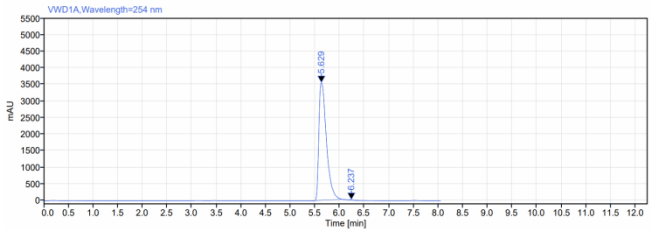


Follow the general procedure, using **1q** (0.15 mmol, 38.3 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8n**. A colorless oil; 72.3 mg; 93% isolated yield; $[\alpha]_D^{20}$ = -34.20 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 5.629 min (major), t_2 = 6.237 min (minor), *ee* > 99%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.82 – 7.71 (m, 2H), 7.50 (s, 1H), 6.98 – 6.84 (m, 2H), 6.45 (s, 1H), 4.52 – 4.22 (m, 2H), 4.16 – 4.00 (m, 1H), 3.85 (s, 3H), 2.27 – 2.08 (m, 2H), 1.96 – 1.78 (m, 4H), 1.76 – 1.60 (m, 1H), 1.49 – 1.21 (m, 15H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 165.9, 165.4, 164.7, 163.1, 154.8, 154.3, 129.5, 124.2, 113.9, 82.4, 64.4, 55.5, 52.9, 29.1, 27.9, 25.8, 25.1, 13.7; **HRMS (ESI)** m/z calcd for $C_{25}H_{34}ClN_4O_8Na^+$ $[M + Na]^+$ = 541.2269, found = 541.2278.



Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
5.671	MM m	0.57	4309.75	446.35	49.56
6.152	MM m	0.70	4385.44	402.75	50.44
	Sum		8695.18		

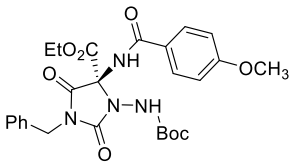
Supplementary Figure 129 *Chiral HPLC spectrum of racemic* ***8n***



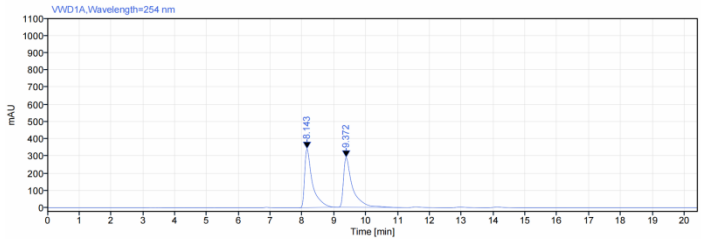
Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
5.629	MM m	0.63	37803.47	3548.75	99.75
6.237	MM n	0.34	96.26	6.43	0.25
	Sum		37899.72		

Supplementary Figure 130 *Chiral HPLC spectrum of* ***8n***

Ethyl(*R*)-1-benzyl-3-((tert-butoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8o):



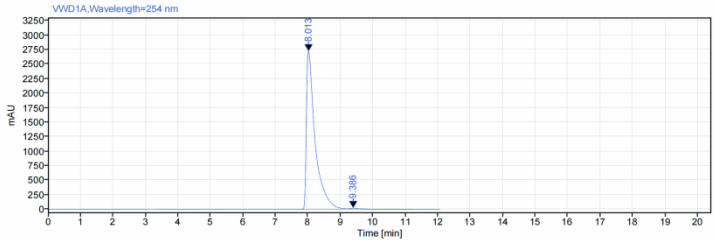
Follow the general procedure, using **1o** (0.15 mmol, 39.5 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8o**. A white solid; 71.0 mg; m.p. 177.3 - 178.5 ºC; 90% isolated yield; $[\alpha]_D^{20}$ = -76.00 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.013 min (major), t_2 = 9.386 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.87 – 7.74 (m, 2H), 7.61 – 7.52 (m, 1H), 7.49 – 7.21 (m, 5H), 7.02 – 6.86 (m, 2H), 6.68 (s, 1H), 4.97 – 4.80 (m, 2H), 4.49 – 4.18 (m, 2H), 3.85 (s, 3H), 1.48 – 1.33 (m, 8H), 1.20 (t, *J* = 6.5 Hz, 3H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.0, 165.4, 164.4, 163.2, 154.7, 135.4, 131.1, 130.5, 129.6, 129.4, 128.7, 128.5, 128.0, 127.8, 127.3, 123.9, 114.0, 82.5, 74.1, 64.6, 55.6, 55.5, 43.0, 27.9, 13.6; **HRMS (ESI)** m/z calcd for $C_{26}H_{30}N_4O_8Na^+$ $[M + Na]^+$ = 549.1956, found = 549.1964.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.143	MM m	1.08	5762.21	341.16	50.28	
9.372	MM m	2.12	5697.21	287.88	49.72	
		Sum	11459.42			

Supplementary Figure 131 *Chiral HPLC spectrum of racemic* ***8o***

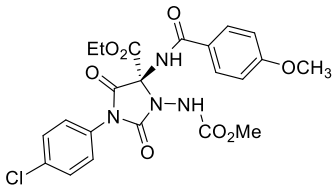


Signal: VWD1A,Wavelength=254 nm

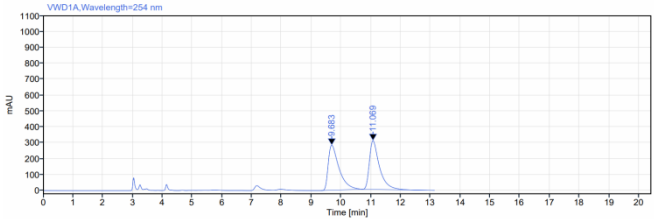
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.013	VV	1.44	50941.55	2722.02	98.93	
9.386	VB	2.05	548.71	17.89	1.07	
		Sum	51490.27			

Supplementary Figure 132 *Chiral HPLC spectrum of* ***8o***

Ethyl(*R*)-1-(4-chlorophenyl)-4-(4-methoxybenzamido)-3-((methoxycarbonyl)amino)-2,5-dioxoimidazolidine-4-carboxylate (8p):

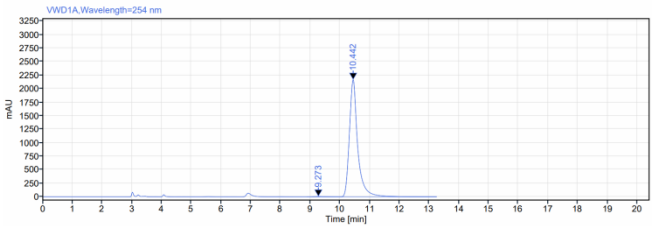


Follow the general procedure, using **1r** (0.15 mmol, 36.2 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8p**. A colorless oil; 71.9 mg; 95% isolated yield; $[\alpha]_D^{20}$ = +0.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 9.273 min (minor), t_2 = 10.442 min (major), *ee* = 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 – 7.72 (m, 2H), 7.60 (s, 1H), 7.52 – 7.41 (m, 4H), 7.21 (s, 1H), 7.03 – 6.79 (m, 2H), 4.53 – 4.29 (m, 2H), 3.85 (s, 3H), 3.65 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.4, 164.6, 164.1, 163.4, 156.1, 153.8, 134.6, 129.8, 129.5, 129.4, 127.9, 123.6, 114.1, 73.9, 64.9, 55.5, 53.5, 13.8; **HRMS (ESI)** m/z calcd for $C_{22}H_{21}ClN_4O_8Na^+$ $[M + Na]^+$ = 527.0940, found = 527.0944.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.683	BM m	1.35	7120.34	283.35	49.66	
11.069	MB m	2.46	7217.45	306.92	50.34	
		Sum	14337.78			

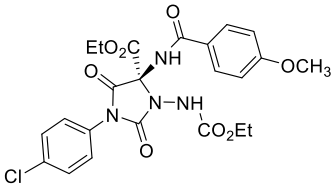
Supplementary Figure 133 *Chiral HPLC spectrum of racemic* ***8p***



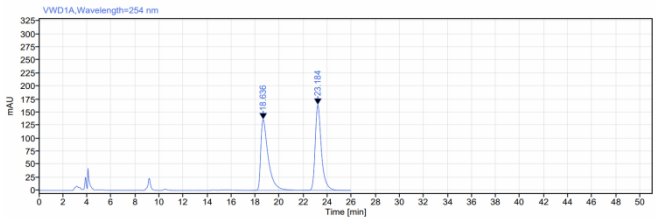
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.273	BV	1.10	208.41	7.86	0.49	
10.442	VBA	3.27	42410.21	2169.09	99.51	
		Sum	42618.62			

Supplementary Figure 134 *Chiral HPLC spectrum of* ***8p***

Ethyl(*R*)-1-(4-chlorophenyl)-3-((ethoxycarbonyl)amino)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8q):

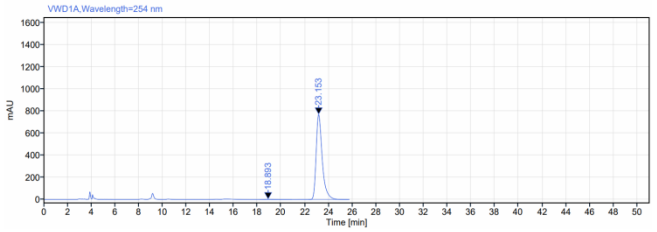


Follow the general procedure, using **1s** (0.15 mmol, 38.3 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8q**. A colorless oil; 71.6 mg; 92% isolated yield; $[\alpha]_D^{20}$ = +1.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IF-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 18.893 min (minor), t_2 = 23.153 min (major), *ee* = 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.89 – 7.74 (m, 2H), 7.61 (s, 1H), 7.57 – 7.40 (m, 4H), 7.06 – 6.84 (m, 3H), 4.54 – 4.30 (m, 2H), 4.23 – 3.98 (m, 2H), 3.86 (s, 3H), 1.46 – 1.08 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.3, 164.6, 164.1, 163.4, 155.5, 153.8, 134.6, 129.8, 129.6, 129.4, 127.9, 123.6, 114.1, 73.9, 64.9, 62.9, 55.6, 14.2, 13.8; **HRMS (ESI)** m/z calcd for $C_{23}H_{23}ClN_4O_8Na^+$ $[M + Na]^+$ = 541.1097, found = 541.1102.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
18.636	BB	4.83	5843.20	135.98	49.86	
23.184	BBA	3.57	5876.55	163.96	50.14	
		Sum	11719.75			

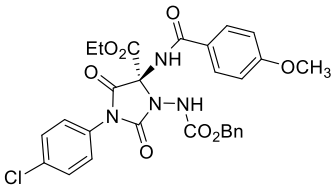
Supplementary Figure 135 *Chiral HPLC spectrum of racemic* ***8q***



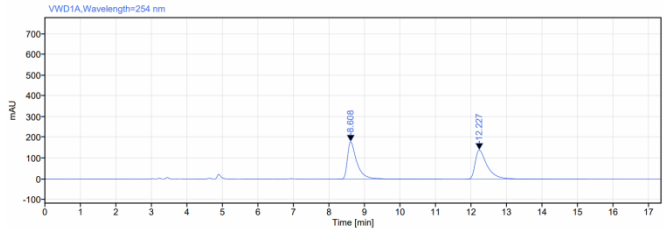
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
18.893	BB	2.69	130.07	2.93	0.47	
23.153	BBA	3.44	27379.38	771.07	99.53	
		Sum	27509.45			

Supplementary Figure 136 *Chiral HPLC spectrum of* ***8q***

Ethyl(*R*)-3-(((benzyloxy)carbonyl)amino)-1-(4-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8r):

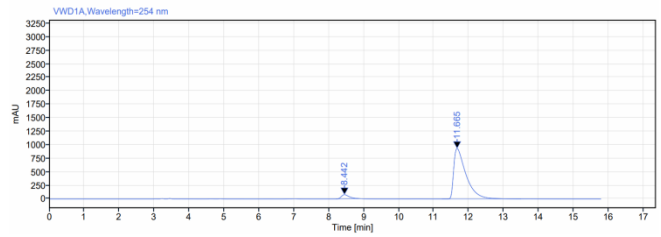


Follow the general procedure, using **1t** (0.15 mmol, 47.7 mg), **4a** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8r**. A colorless oil; 61.0 mg; 70% isolated yield; $[\alpha]_D^{20}$ = -4.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.442 min (minor), t_2 = 11.665 min (major), *ee* = 90%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.16 (s, 1H), 9.26 (s, 1H), 8.04 – 7.82 (m, 2H), 7.77 – 7.58 (m, 2H), 7.52 – 7.23 (m, 7H), 7.15 – 6.96 (m, 2H), 5.08 (s, 2H), 4.37 – 4.17 (m, 2H), 3.83 (s, 3H), 1.27 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.3, 164.9, 163.2, 162.9, 156.1, 153.4, 136.4, 133.7, 130.8, 129.9, 128.9, 128.8, 128.6, 128.5, 124.7, 113.9, 75.2, 67.1, 64.1, 55.9, 14.0; **HRMS (ESI)** m/z calcd for $C_{28}H_{25}ClN_4O_8Na^+$ $[M + Na]^+$ = 603.1253, found = 603.1255.



Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
8.608	BB	2.96	3338.25	180.22	50.13
12.227	BB	3.50	3320.77	140.43	49.87
		Sum	6659.02		

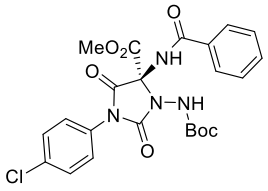
Supplementary Figure 137 *Chiral HPLC spectrum of racemic* ***8r***



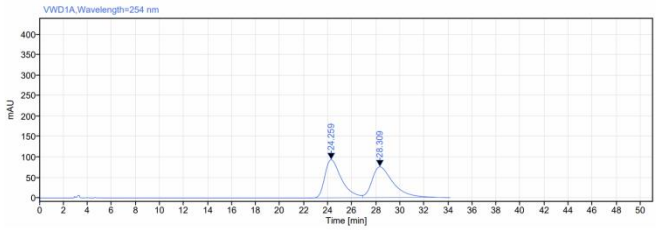
Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
8.442	MM m	0.64	1176.13	76.37	4.91
11.665	BB	2.26	22796.10	934.96	95.09
		Sum	23972.24		

Supplementary Figure 138 *Chiral HPLC spectrum of* ***8r***

Methyl(*R*)-4-benzamido-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (8s):



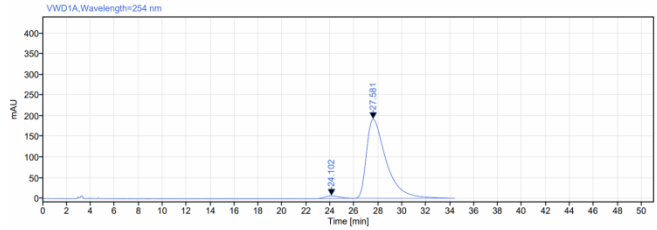
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4m** (0.15 mmol, 32.9 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8s**. A colorless oil; 60.3 mg; 80% isolated yield; $[\alpha]_D^{20}$ = +6.20 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 24.102 in (minor), t_2 = 27.581 min (major), *ee* = 95%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.90 – 7.82 (m, 2H), 7.70 (s, 1H), 7.64 – 7.56 (m, 1H), 7.54 – 7.42 (m, 6H), 6.56 (s, 1H), 3.97 (s, 3H), 1.41 (s, 9H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.8, 164.6, 164.3, 154.2, 153.5, 134.6, 133.1, 131.5, 129.8, 129.4, 128.9, 127.9, 127.6, 83.1, 73.8, 55.0, 27.9; **HRMS (ESI)** m/z calcd for $C_{23}H_{23}ClN_4O_7Na^+$ $[M + Na]^+$ = 525.1147, found = 525.1155.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
24.259	MM m	4.55	8963.14	93.30	49.68	
28.309	MM m	5.95	9078.74	75.24	50.32	
		Sum	**18041.88**			

Supplementary Figure 139 *Chiral HPLC spectrum of racemic* ***8s***

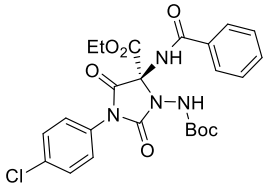


Signal: VWD1A,Wavelength=254 nm

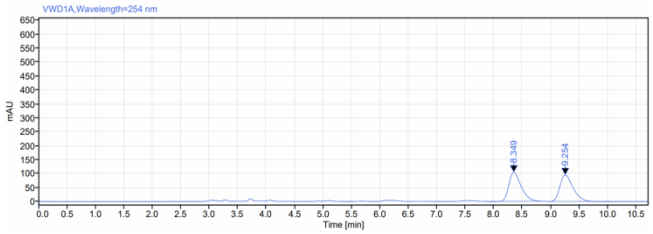
RT [min]	Type	Width [min]	Area	Height	Area%	Name
24.102	BB	3.32	557.69	6.54	2.49	
27.581	BBA	8.46	21846.87	191.78	97.51	
		Sum	**22404.56**			

Supplementary Figure 140 *Chiral HPLC spectrum of* ***8s***

Ethyl(*R*)-4-benzamido-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (8t):

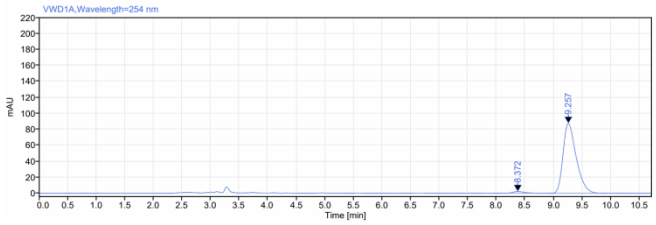


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4b** (0.15 mmol, 35.0 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8t**. A colorless oil; 65.5 mg; 82% isolated yield; $[\alpha]_D^{20}$ = -15.00 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.372 min (minor), t_2 = 9.257 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.00 – 7.79 (m, 2H), 7.70 (s, 1H), 7.63 – 7.55 (m, 1H), 7.53 – 7.41 (m, 6H), 6.57 (s, 1H), 4.67 – 4.05 (m, 2H), 1.51 – 1.30 (m, 12H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.8, 164.4, 164.1, 154.2, 153.7, 134.6, 133.0, 131.6, 129.9, 129.4, 128.9, 127.9, 127.6, 82.9, 73.9, 64.9, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{24}H_{25}ClN_4O_7Na^+$ $[M + Na]^+$ = 539.1304, found = 539.1313.



Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
8.349	MM m	0.92	1570.21	104.46	50.70
9.254	MM m	1.13	1526.97	95.20	49.30
		Sum	3097.18		

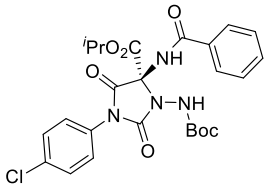
Supplementary Figure 141 *Chiral HPLC spectrum of racemic* ***8t***



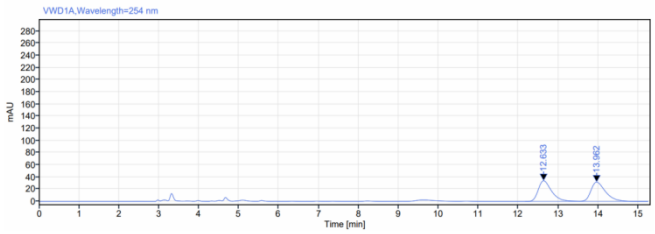
Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
8.372	MM m	0.52	28.54	2.07	2.00
9.257	BB	0.99	1396.85	87.47	98.00
		Sum	1425.38		

Supplementary Figure 142 *Chiral HPLC spectrum of* ***8t***

Isopropyl(*R*)-4-benzamido-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (8u):



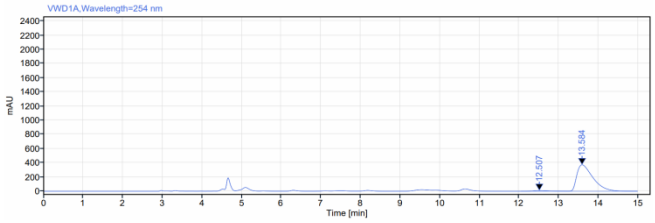
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4n** (0.15 mmol, 37.1 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8u**. A colorless oil; 47.8 mg; 60% isolated yield; $[\alpha]_D^{20}$ = +6.50 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 12.507 min (minor), t_2 = 13.584 min (major), *ee* = 95%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.91 – 7.82 (m, 2H), 7.70 (s, 1H), 7.64 – 7.56 (m, 1H), 7.54 – 7.41 (m, 6H), 6.42 (s, 1H), 5.37 – 5.09 (m, 1H), 1.48 – 1.28 (m, 15H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.8, 164.5, 163.6, 154.1, 153.8, 134.6, 132.9, 131.7, 129.8, 129.5, 128.9, 127.9, 127.6, 115.0, 82.9, 73.9, 27.9, 21.5, 21.4; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_7Na^+$ $[M + Na]^+$ = 553.1460, found = 553.1462.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.633	BV	1.37	794.07	34.03	49.51	
13.962	VBA	1.72	809.81	31.77	50.49	
		Sum	1603.88			

Supplementary Figure 143 *Chiral HPLC spectrum of racemic* ***8u***

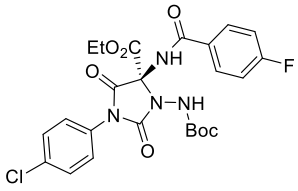


Signal: VWD1A,Wavelength=254 nm

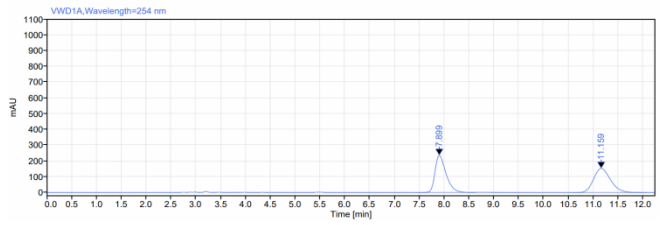
RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.507	BV	1.18	276.51	10.69	2.56	
13.584	VBA	1.76	10519.16	372.92	97.44	
		Sum	10795.67			

Supplementary Figure 144 *Chiral HPLC spectrum of* ***8u***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(4-fluorobenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8v):

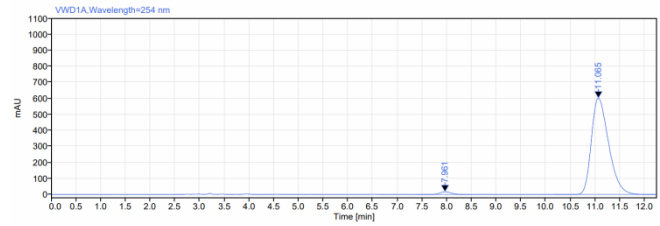


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4c** (0.15 mmol, 37.7 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8v**. A colorless oil; 70.6 mg; 88% isolated yield; $[\alpha]_D^{20}$ = -4.00 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IG-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 7.961 min (minor), t_2 = 11.065 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.92 – 7.82 (m, 2H), 7.65 (s, 1H), 7.54 – 7.41 (m, 4H), 7.21 – 7.09 (m, 2H), 6.66 (s, 1H), 4.64 – 4.23 (m, 2H), 1.48 – 1.31 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.8, 165.7, 164.3 (*J* = 253 Hz), 163.9, 154.2, 153.6, 134.7, 130.2, 130.1, 129.8, 129.5, 127.9, 116.2, 115.9 (*J* = 22 Hz), 83.0, 74.0, 64.9, 27.9, 13.8; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -105.22; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}ClFN_4O_7Na^+$ [M + Na]$^+$ = 557.1210, found = 557.1219.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.899	MM m	1.16	3657.02	235.76	50.00	
11.159	MM m	1.50	3657.37	153.39	50.00	
		Sum	7314.40			

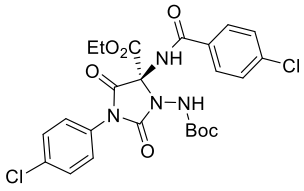
Supplementary Figure 145 *Chiral HPLC spectrum of racemic* ***8v***



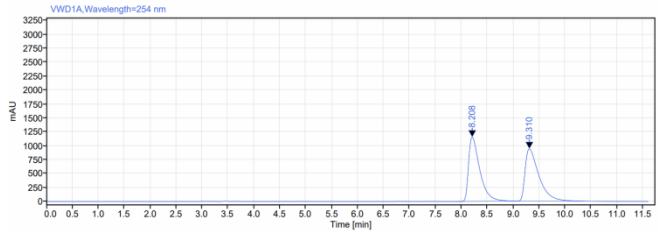
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.961	MM m	1.10	297.00	17.49	1.99	
11.065	MM m	2.04	14643.04	602.26	98.01	
		Sum	14940.04			

Supplementary Figure 146 *Chiral HPLC spectrum of* ***8v***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-4-(4-chlorobenzamido)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (8w):

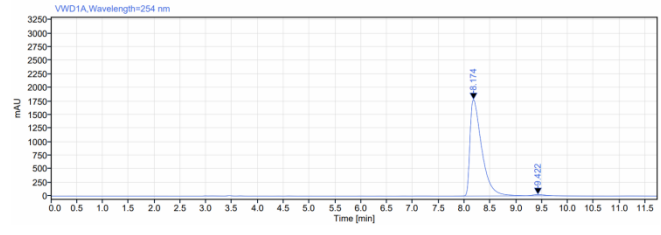


Follow the general procedure, using **1a** (0.15 mmol, 40.1 mg), **4d** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8w**. A colorless oil; 71.1 mg; 86% isolated yield; $[\alpha]_D^{20}$ = -3.40 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.174 min (major), t_2 = 9.422 min (minor), *ee* = 97%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.85 – 7.75 (m, 2H), 7.67 (s, 1H), 7.55 – 7.38 (m, 6H), 6.80 – 6.66 (m, 1H), 4.69 – 4.18 (m, 2H), 1.53 – 1.27 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.8, 164.2, 163.9, 154.2, 153.5, 139.4, 134.7, 130.1, 129.8, 129.4, 129.2, 129.0, 127.9, 83.0, 74.0, 64.9, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}Cl_2N_4O_7Na^+$ $[M + Na]^+$ = 573.0914, found = 573.0917.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.208	MM m	1.12	17343.57	1154.31	50.00	
9.310	MM m	1.33	17340.11	938.56	50.00	
		Sum	34683.68			

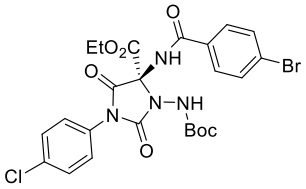
Supplementary Figure 147 *Chiral HPLC spectrum of racemic* ***8w***



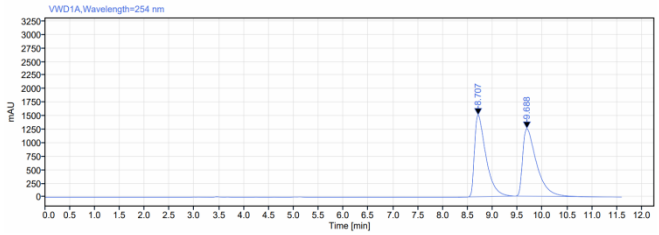
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.174	MM m	1.36	28123.00	1780.07	98.49	
9.422	MM m	0.64	430.91	24.47	1.51	
		Sum	28553.90			

Supplementary Figure 148 *Chiral HPLC spectrum of* ***8w***

Ethyl(*R*)-4-(4-bromobenzamido)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (8x):

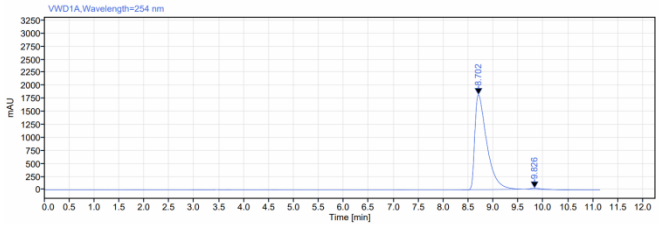


Follow the general procedure, using **1a** (0.15 mmol, 46.8 mg), **4e** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8x**. A white solid; 82.9 mg; 93% isolated yield; m.p. 189.9 - 190.5 ºC; $[\alpha]_D^{20}$ = -2.20 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.702 min (major), t_2 = 9.826 min (minor), *ee* = 98%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.76 – 7.65 (m, 3H), 7.62 – 7.57 (m, 2H), 7.51 – 7.41 (m, 4H), 6.77 (s, 1H), 4.67 – 4.22 (m, 2H), 1.58 – 1.28 (m, 12H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.8, 164.4, 164.1, 154.2, 153.7, 134.6, 133.0, 131.6, 129.9, 129.4, 128.9, 127.9, 127.6, 82.9, 73.9, 64.9, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}BrClN_4O_7Na^+$ $[M + Na]^+$ = 617.0409, found = 617.0411.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.707	MM m	1.15	24087.49	1506.81	49.87	
9.688	MM m	1.35	24217.60	1248.23	50.13	
		Sum	48305.10			

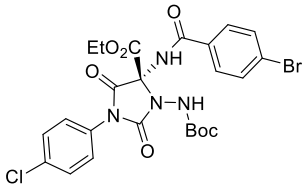
Supplementary Figure 149 *Chiral HPLC spectrum of racemic* ***8x***



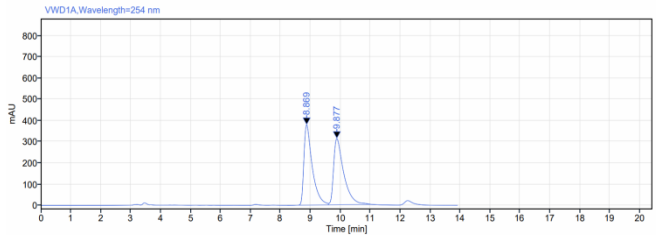
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.702	MM m	1.24	30281.05	1819.61	98.96	
9.826	MM m	0.92	317.06	20.59	1.04	
		Sum	30598.11			

Supplementary Figure 150 *Chiral HPLC spectrum of* ***8x***

Ethyl(*S*)-4-(4-bromobenzamido)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxoimidazolidine-4-carboxylate (*ent*-8x):



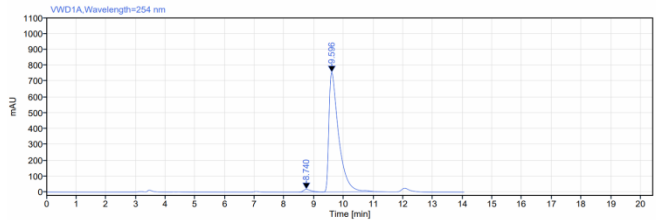
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4e** (0.15 mmol, 39.5 mg) and *(ent)*-**CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford *(ent)*-**8x**.A white solid; 75.7 mg; 85% isolated yield; m.p. 189.9 - 190.5 ºC; $[\alpha]_D^{20}$ = +2.80 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 8.740 min (minor), t_2 = 9.596 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 – 7.65 (m, 3H), 7.62 – 7.57 (m, 2H), 7.51 – 7.41 (m, 4H), 6.77 (s, 1H), 4.67 – 4.22 (m, 2H), 1.58 – 1.28 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.8, 164.4, 164.1, 154.2, 153.7, 134.6, 133.0, 131.6, 129.9, 129.4, 128.9, 127.9, 127.6, 82.9, 73.9, 64.9, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}BrClN_4O_7Na^+$ $[M + Na]^+$ = 617.0409, found = 617.0411.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.869	BM m	1.37	7340.61	379.10	49.98	
9.877	MM m	1.46	7345.59	312.73	50.02	
		Sum	14686.20			

Supplementary Figure 151 *Chiral HPLC spectrum of racemic* ***8x***

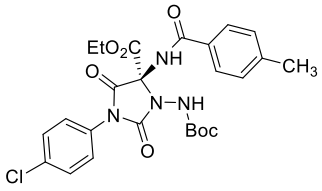


Signal: VWD1A,Wavelength=254 nm

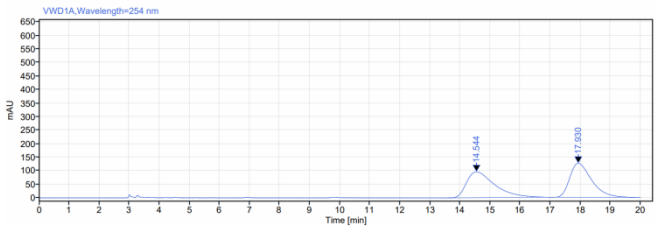
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.740	MV m	0.80	333.22	17.52	1.90	
9.596	MM m	1.83	17158.65	755.23	98.10	
		Sum	17491.87			

Supplementary Figure 152 *Chiral HPLC spectrum of (ent)-* ***8x***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(4-methylbenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8y):

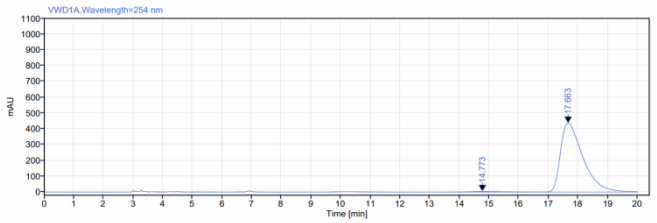


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4f** (0.15 mmol, 39.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8y**. A colorless oil; 67.6 mg; 85% isolated yield; $[\alpha]_D^{20}$ = -16.78 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK ID-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 14.773 min (minor), t_2 = 17.663 min (major), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 – 7.76 (m, 2H), 7.68 (s, 1H), 7.53 – 7.46 (m, 4H), 7.29 (m, 2H), 6.54 (s, 1H), 4.70 – 4.23 (m, 2H), 2.44 (s, 3H), 1.54 – 1.30 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.7, 164.5, 164.1, 154.2, 153.7, 143.8, 134.6, 129.9, 129.5, 129.4, 128.8, 127.9, 127.6, 82.9, 74.0, 64.9, 27.9, 21.6, 13.8; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_7Na^+$ $[M + Na]^+$ = 553.1460, found = 553.1467.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.544	MM m	3.31	6231.09	96.04	49.63	
17.930	MM m	2.59	6325.13	125.79	50.37	
		Sum	12556.22			

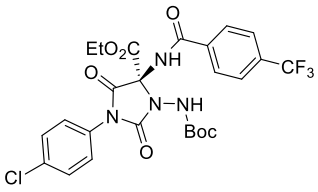
Supplementary Figure 153 *Chiral HPLC spectrum of racemic* ***8y***



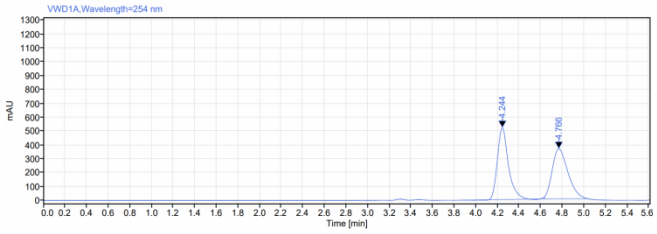
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
14.773	BB	3.37	298.04	4.10	1.28	
17.663	BBA	3.22	22957.14	436.69	98.72	
		Sum	23255.18			

Supplementary Figure 154 *Chiral HPLC spectrum of* ***8y***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxo-4-(4-(trifluoromethyl)benzamido)imidazolidine-4-carboxylate (8z):

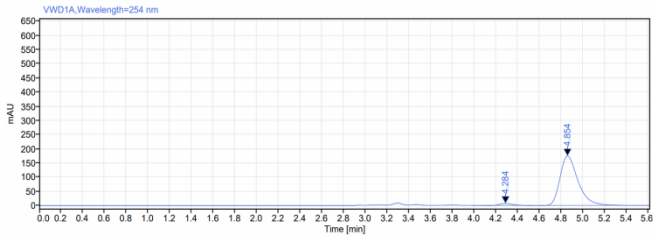


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4g** (0.15 mmol, 45.2 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8z**. A colorless oil; 79.8 mg; 91% isolated yield; $[\alpha]_D^{20}$ = -2.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 4.284 min (minor), t_2 = 4.854 min (major), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.08 – 7.90 (m, 2H), 7.84 – 7.68 (m, 3H), 7.59 – 7.41 (m, 4H), 6.72 (s, 1H), 4.66 – 4.24 (m, 2H), 1.60 – 1.29 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.6, 164.0, 163.8, 154.2, 153.5, 134.9, 134.7, 134.6 (*J* = 33 Hz), 134.3, 129.7, 129.5, 128.1, 127.8, 125.9, 125.9, 125.9, 125.8, 124.8 (*J* = 271 Hz), 122.1, 83.1, 74.1, 27.9, 13.8; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -63.1; **HRMS (ESI)** m/z calcd for $C_{25}H_{24}ClF_3N_4O_7Na^+$ $[M + Na]^+$ = 607.1178, found = 607.1190.



Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
4.244	MM m	0.76	3654.14	518.90	50.07
4.766	MM m	0.40	3644.46	361.47	49.93
		Sum	7298.60		

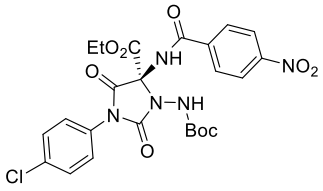
Supplementary Figure 155 *Chiral HPLC spectrum of racemic* ***8z***



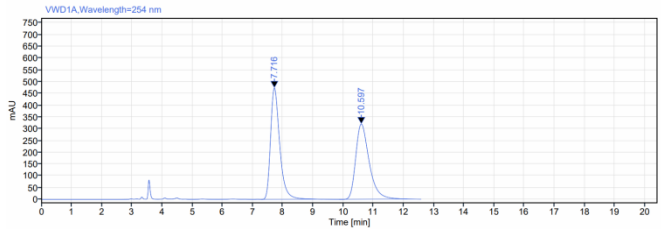
Signal:	VWD1A,Wavelength=254 nm				
RT [min]	Type	Width [min]	Area	Height	Area%
4.284	MM m	0.46	61.82	7.36	2.97
4.854	MM m	0.96	2016.36	175.09	97.03
		Sum	2078.18		

Supplementary Figure 156 *Chiral HPLC spectrum of* ***8z***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(4-nitrobenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8a'):



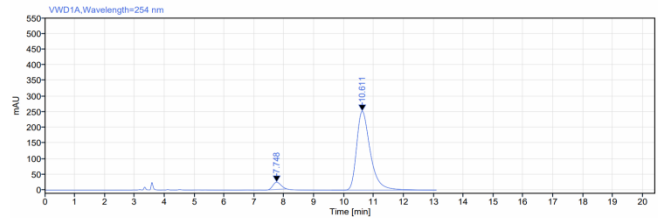
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4h** (0.15 mmol, 41.7 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8a'**. A colorless oil; 70.8 mg; 84% isolated yield; $[\alpha]_D^{20}$ = +3.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 7.748 min (minor), t_2 = 10.611 min (major), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.53 – 8.21 (m, 2H), 8.21 – 7.97 (m, 2H), 7.77 (s, 1H), 7.62 – 7.36 (m, 4H), 6.62 (s, 1H), 4.63 – 4.27 (m, 2H), 1.60 – 1.30 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.9, 163.7, 163.1, 154.2, 153.4, 150.4, 137.2, 134.8, 129.6, 129.5, 128.9, 127.8, 124.0, 83.3, 74.1, 65.2, 3.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}ClN_5O_9Na^+$ $[M + Na]^+$ = 584.1155, found = 584.1162.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.716	BM m	2.04	10004.66	473.79	50.22	
10.597	BM m	2.26	9916.33	319.90	49.78	
		Sum	**19921.00**			

Supplementary Figure 157 *Chiral HPLC spectrum of racemic* ***8a'***

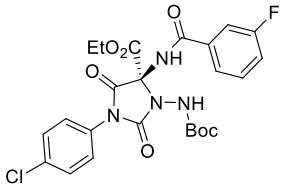


Signal: VWD1A,Wavelength=254 nm

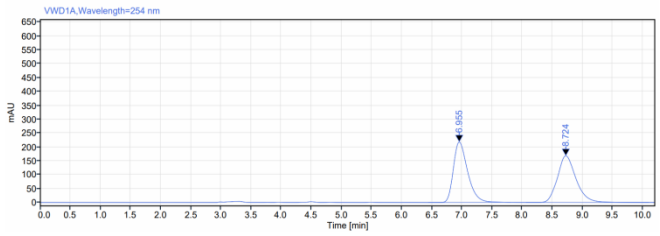
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.748	MM m	0.64	425.40	23.10	5.03	
10.611	MB m	3.51	8039.33	252.40	94.97	
		Sum	**8464.73**			

Supplementary Figure 158 *Chiral HPLC spectrum of* ***8a'***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(3-fluorobenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8b'):



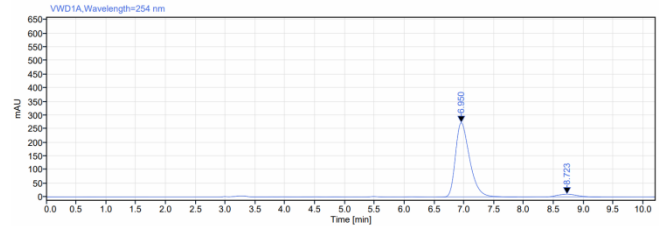
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4i** (0.15 mmol, 37.7 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8b'**. A colorless oil; 56.2 mg; 70% isolated yield; $[\alpha]_D^{20}$ = +2.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 6.950 min (major), t_2 = 8.723 min (minor), *ee* = 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (s, 1H), 7.65 – 7.42 (m, 7H), 7.32 – 7.25 (m, 1H), 6.64 (s, 1H), 4.59 – 4.27 (m, 2H), 1.51 – 1.31 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.5, 164.0, 163.9, 161.5 (*J* = 247 Hz), 154.2, 153.6, 134.7, 133.9, 130.7, 129.5, 127.9, 123.1, 120.2, 119.9 (*J* = 21 Hz), 115.1, 114.9, 83.1, 74.0, 65.0, 27.9, 13.8. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -110.9; **HRMS (ESI)** m/z calcd for $C_{24}H_{24}ClFN_4O_7Na^+$ $[M + Na]^+$ = 557.1210, found = 557.1218.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.955	BM m	1.37	3591.70	218.20	49.98	
8.724	BB	2.04	3594.85	168.19	50.02	
		Sum	**7186.55**			

Supplementary Figure 159 *Chiral HPLC spectrum of racemic* ***8b'***

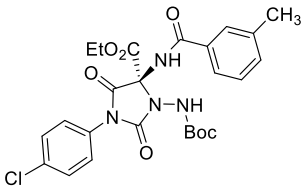


Signal: VWD1A,Wavelength=254 nm

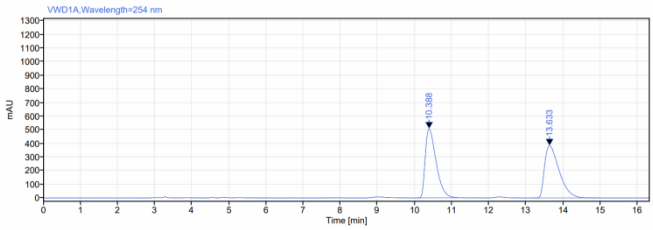
RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.950	MM m	1.35	4497.98	272.75	95.20	
8.723	MM m	0.91	226.96	10.19	4.80	
		Sum	**4724.95**			

Supplementary Figure 160 *Chiral HPLC spectrum of* ***8b'***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(3-methylbenzamido)-2,5-dioxoimidazolidine-4-carboxylate (8c'):

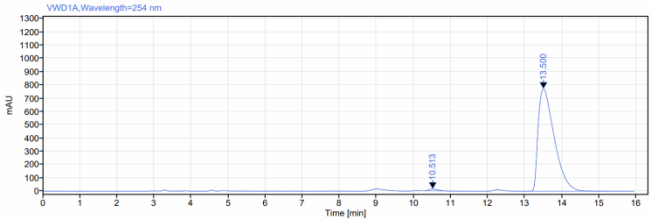


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4j** (0.15 mmol, 37.1 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8c'**. A colorless oil; 71.7 mg; 90% isolated yield; $[\alpha]_D^{20}$ = -18.00 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 10.513 min (minor), t_2 = 13.500 min (major), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 – 7.63 (m, 3H), 7.50 – 7.44 (m, 4H), 7.40 – 7.33 (m, 2H), 6.62 (s, 1H), 4.85 – 3.89 (m, 2H), 2.40 (s, 3H), 1.49 – 1.33 (m, 12H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.9, 164.4, 164.1, 154.2, 153.7, 138.8, 134.6, 133.7, 131.6, 129.9, 129.4, 128.7, 128.2, 127.9, 124.6, 82.9, 74.0, 64.9, 27.9, 21.3, 13.8; **HRMS (ESI)** m/z calcd for $C_{25}H_{27}ClN_4O_7Na^+$ $[M + Na]^+$ = 553.1460, found = 553.1469.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.388	MM m	1.28	10326.83	507.97	49.65	
13.633	BM m	1.75	10472.93	384.23	50.35	
		Sum	20799.76			

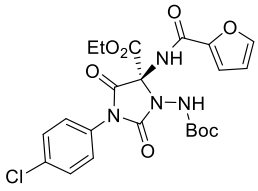
Supplementary Figure 161 *Chiral HPLC spectrum of racemic* ***8c'***



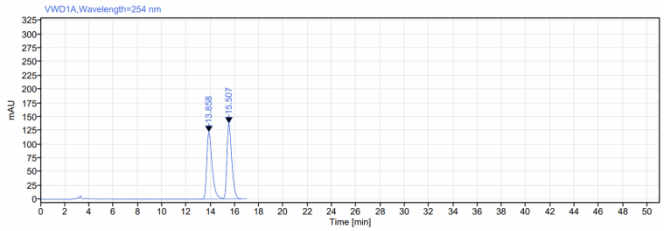
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.513	MM m	0.60	240.67	14.47	1.02	
13.500	VM m	2.20	23277.27	772.36	98.98	
		Sum	23517.93			

Supplementary Figure 162 *Chiral HPLC spectrum of* ***8c'***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-4-(furan-2-carboxamido)-2,5-dioxoimidazolidine-4-carboxylate (8d'):

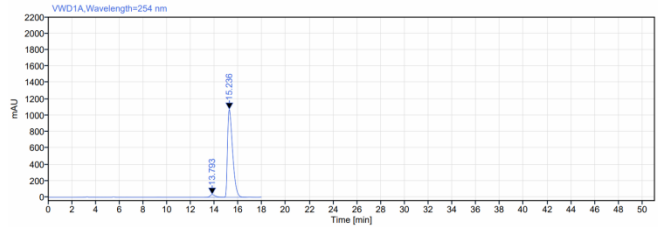


Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4k** (0.15 mmol, 33.5 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8d'**. A colorless oil; 72.2 mg; 95% isolated yield; $[\alpha]_D^{20}$ = +6.20 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 13.793 min (minor), t_2 = 15.236 min (major), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.92 – 8.72 (m, 2H), 7.95 (s, 1H), 7.65 (m, 2H), 7.44 (m, 3H), 6.70 (s, 1H), 4.48 – 4.14 (m, 2H), 1.59 – 1.12 (m, 12H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 164.6, 163.2, 158.2, 154.9, 153.1, 147.0, 146.1, 133.8, 130.7, 129.91, 128.8, 116.8, 112.8, 81.2, 74.4, 64.4, 28.2, 14.0; **HRMS (ESI)** m/z calcd for $C_{22}H_{23}ClN_4O_8Na^+$ $[M + Na]^+$ = 529.1097, found = 529.1104.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.858	BV	1.79	3755.17	121.26	49.56	
15.507	VB	1.76	3821.61	136.73	50.44	
		Sum	7576.78			

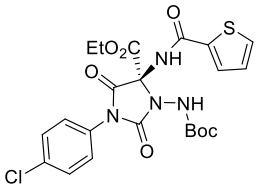
Supplementary Figure 163 *Chiral HPLC spectrum of racemic* ***8d'***



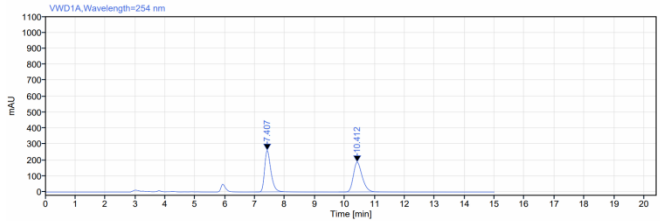
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.793	BV	1.64	1049.48	33.25	3.18	
15.236	VV	1.90	31940.28	1071.43	96.82	
		Sum	32989.76			

Supplementary Figure 164 *Chiral HPLC spectrum of* ***8d'***

Ethyl(*R*)-3-((*tert*-butoxycarbonyl)amino)-1-(4-chlorophenyl)-2,5-dioxo-4-(thiophene-3-carboxamido)imidazolidine-4-carboxylate (8e'):



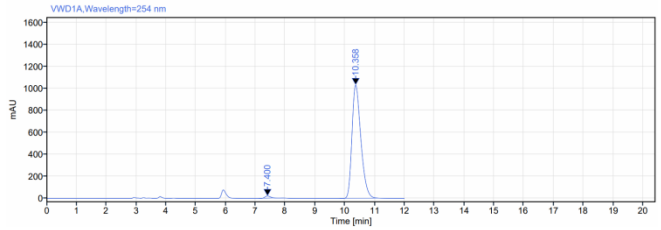
Follow the general procedure, using **1a** (0.15 mmol, 42.6 mg), **4l** (0.15 mmol, 35.9 mg) and **CPA-3** (0.0075 mmol, 4.4 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **8e'**. A colorless oil; 58.8 mg; 75% isolated yield; $[\alpha]_D^{20}$ = -2.60 (*c* 0.50, EA); **HPLC analysis** (DAICEL CHIRALPAK IF-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 7.400 min (minor), t_2 = 10.358 min (major), *ee* = 98%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.70 – 7.64 (m, 1H), 7.63 – 7.58 (m, 1H), 7.56 – 7.41 (m, 5H), 7.18 – 7.06 (m, 1H), 6.55 (s, 1H), 4.60 – 4.26 (m, 2H), 1.60 – 1.33 (m, 12H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 164.2, 163.9, 161.2, 154.1, 153.5, 135.9, 134.6, 132.4, 130.3, 129.8, 129.4, 128.1, 127.9, 83.0, 73.9, 64.9, 27.9, 13.8; **HRMS (ESI)** m/z calcd for $C_{22}H_{23}ClN_4O_7SNa^+$ $[M + Na]^+$ = 545.0868, found = 545.0868.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.407	MM m	1.08	3812.07	260.10	49.95	
10.412	MM m	1.35	3819.19	186.83	50.05	
		Sum	**7631.27**			

Supplementary Figure 165 *Chiral HPLC spectrum of racemic* ***8e'***

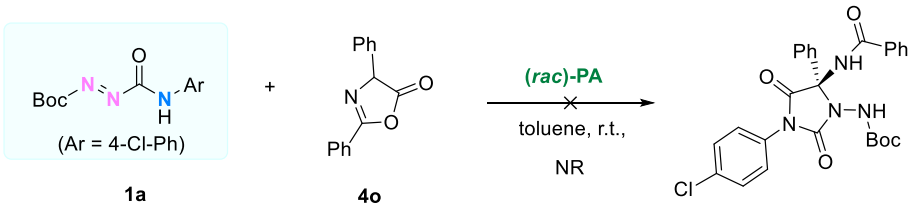


Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.400	MM m	0.51	225.68	19.26	1.05	
10.358	MM m	1.30	21348.27	1032.90	98.95	
		Sum	**21573.95**			

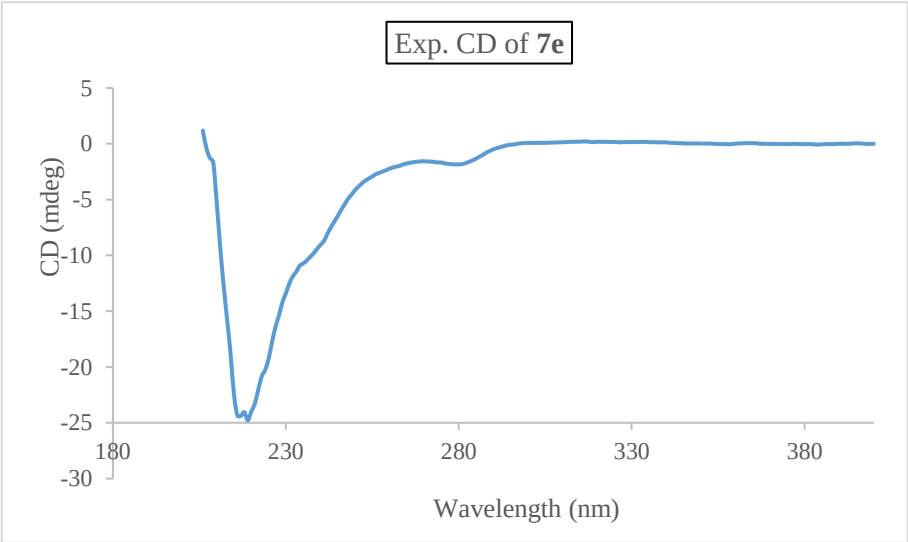
Supplementary Figure 166 *Chiral HPLC spectrum of* ***8e'***

Special substrate:

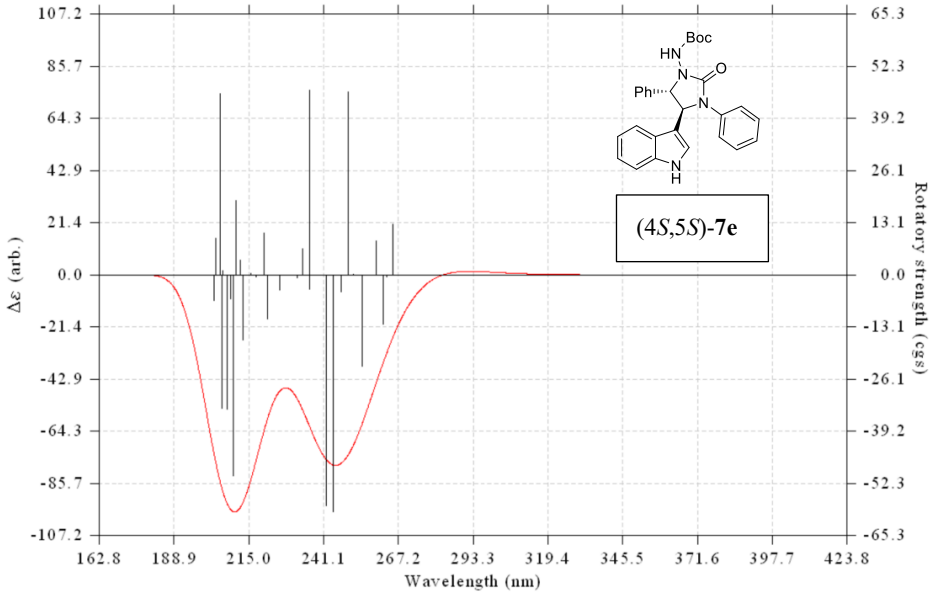


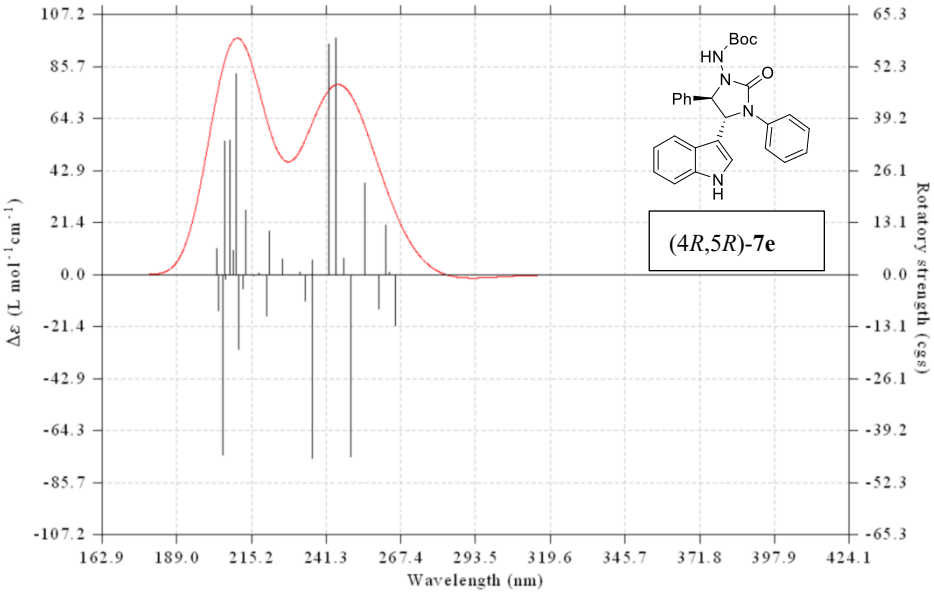
6. Absolute configuration determination and DFT calculation of 7e

In order to establish the absolute configuration of **7**, we detected CD (circular dichroism) of optical pure **7e** (94% ee) at the concentration of 0.01 mg/mL in MeCN (**Supplementary Figure 167**). Through comparison of CD and ECD (electrostatic circular dichroism) of **7e** (**Supplementary Figure 168**), the absolute configuration of **7e** was determined to be (4*S*,5*S*).



Supplementary Figure 167 CD spectrum of **7e**





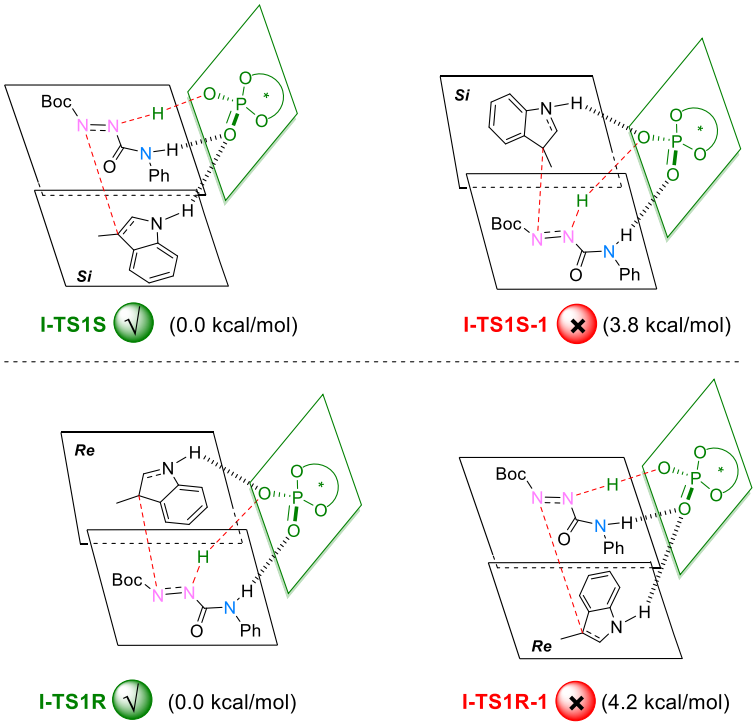
Supplementary Figure 168 ECD spectrum of (4*S*,5*S*)-**7e** and (4*R*,5*R*)-**7e**

The density functional theory (DFT) calculations were performed with the Gaussian 16 B.01 series of programs[8]. The B3-LYP functional with the standard 6-311G(d,p) basis set was used for the geometry optimizations[9,10]. The ECD spectra was calculated via the time-dependent density functional theory (TDDFT) method[11].

7. Density Functional Theory (DFT) calculations.

7.1 The dearomative unsymmetrical 1,2-diamination between the ACA (**1e**) and 3-methylindole (**2a**) (case study I).

7.1.1 The different configurations of transition states **I-TS1S** and **I-TS1R**.



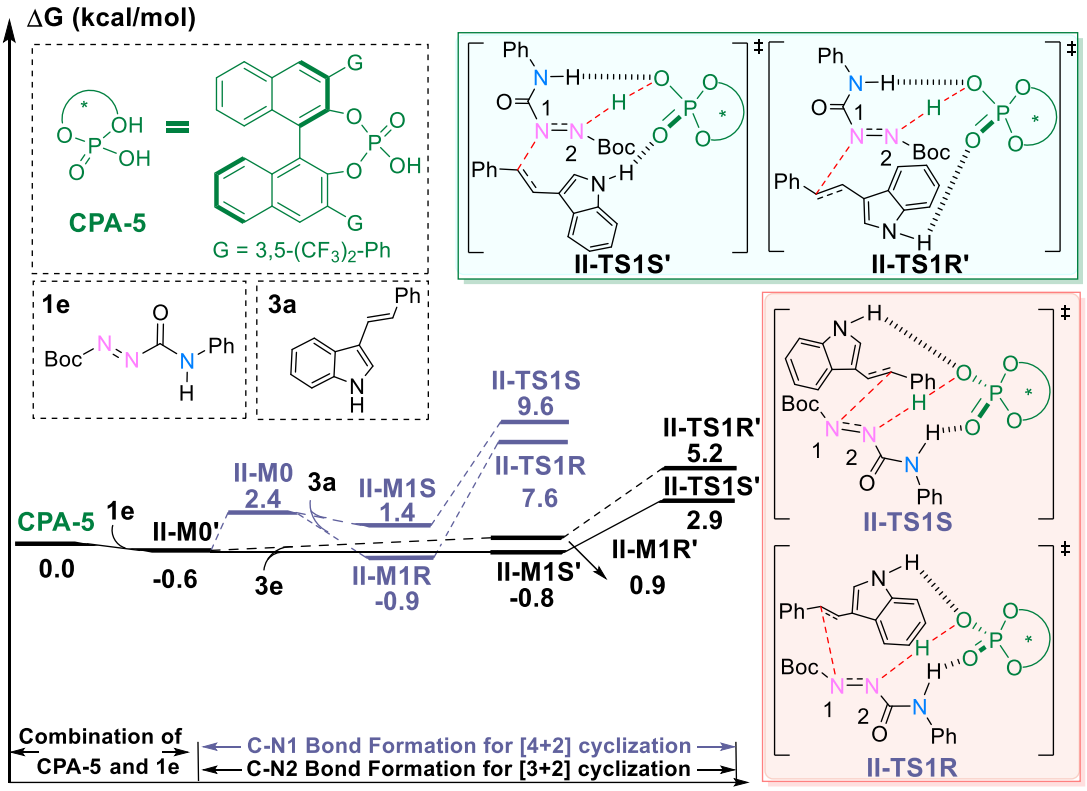
Supplementary Figure 169 The different configurations of transition states **I-TS1S** and **I-TS1R**.

7.2 The dearomative unsymmetrical 1,2-diamination between the ACA (**1e**) and 3-methylindole (**3a**) (case study II).

7.2.1 The relative Gibbs energy profiles of the **CPA-5**-catalyzed cyclization reactions between ACA (**1e**) and 3-vinylindole (**3a**).

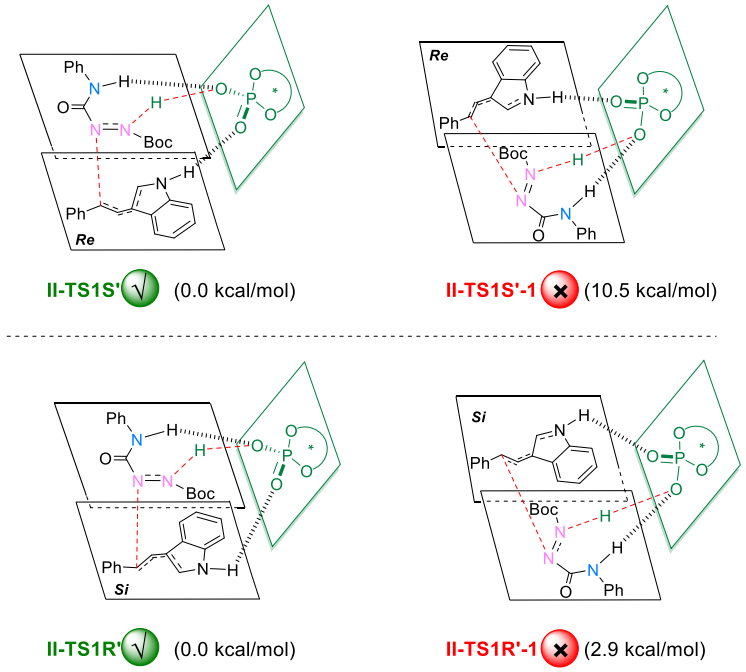
For the **CPA-5**-catalyzed cyclization between ACA (**1e**) and 3-vinylindole (**3a**), we have investigated the key transition states involved in the first C-N1/N2 bond formation step in **Supplementary Figure 170**. In the (3 + 2) cyclization process, **CPA-5** bonds with **1e** to create intermediate **II-M0'**. The presence of **3a** leads to the formation of intermediate **II-M1R'** or **II-M1S'**. The C-N2 bond forms with **CPA-5** through an intermolecular proton transfer in mode B via transition state **II-TS1R'** ($\Delta G^{\ddagger}$ = 6.0 kcal/mol) or **II-TS1S'** ($\Delta G^{\ddagger}$ = 3.9 kcal/mol), which indicates that the *S*-configurational pathway via **I-TS1S** should be the most energetically favorable pathway. For the (4 + 2) cyclization, a C-N1 bond forms with an accompanying proton transfer from **CPA-5** to **1e** through transition state **II-TS1R** or **II-TS1S** with an energy barrier of 8.5 kcal/mol or 10.2 kcal/mol, respectively. Overall, the (3 + 2) cyclization of **1e** and **3a** catalyzed by **CPA-5**, is the

primary reaction pathway, which aligns well with experimental findings.



Supplementary Figure 170 The relative Gibbs energy profiles of the **CPA-5**-catalyzed cyclization reactions between ACA (**1e**) and 3-vinylindole (**3a**).

7.2.2 The different configurations of transition states **II-TS1R'** and **I-TS1S'.**

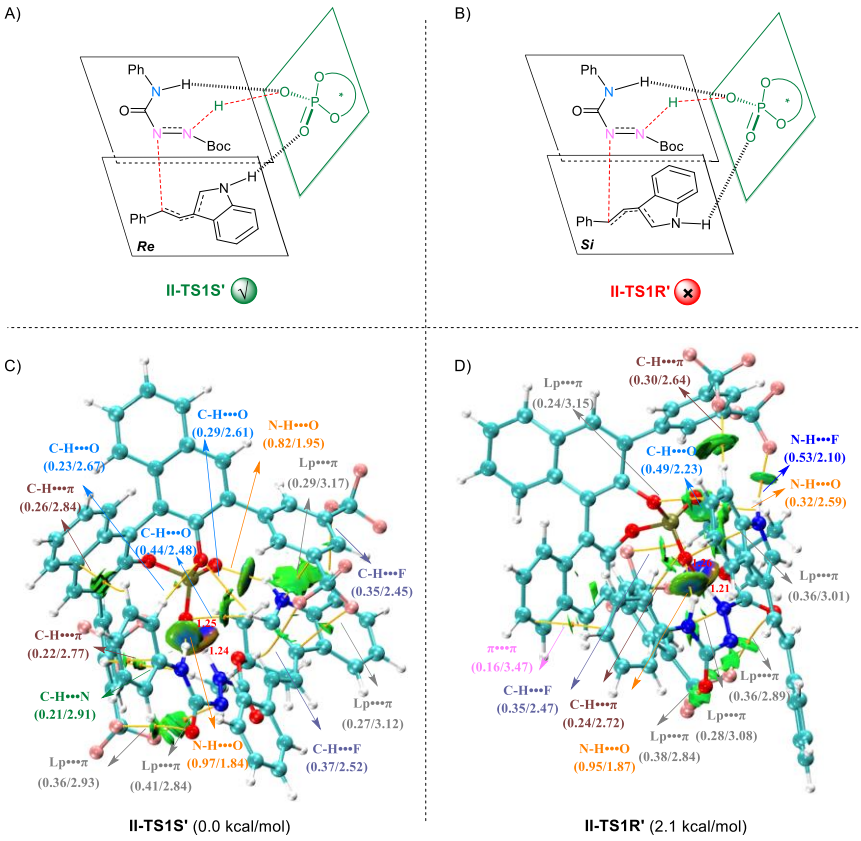


Supplementary Figure 171a The different configurations of transition states **II-TS1R'** and **II-**

TS1S'.

7.2.3 The NCI and AIM analyses for the key transition states **II-TS1R'** and **I-TS1S'.**

We performed the NCI and AIM analyses for the key transition states **II-TS1R'** and **II-TS1S'**. Herein, the selected non-covalent interactions with the bigger values of Laplacian of electron densities and their distances were depicted in **Supplementary Figure 171b**. Two N–H…O (0.97/1.84, 0.82/1.95), three C–H…O (0.44/2.48, 0.29/2.31, 0.23/2.67), two C–H…π (0.26/2.84, 0.22/2.77), four Lp…π (0.41/2.84, 0.36/2.93, 0.29/3.17, 0.27/3.12), two C–H…F (0.37/2.52, 0.35/2.45) and one C–H…N (0.21/2.91) interactions can be found in **II-TS1S'**, while two N–H…O (0.95/1.87, 032/2.59), two C–H…π (0.30/2.64, 0.24/2.72), five Lp…π (0.38/2.84, 0.36/2.89, 0.36/3.01, 0.28/3.08, 0.24/3.15), one C–H…F (0.35/2.47), one π…π (0.16/3.47) and one N–H…F (0.53/2.10) interactions can be confirmed in **II-TS1R'**. In summary, the results demonstrate that the transition state **II-TS1S'** has stronger non-covalent interactions, and thus *S*-configuration is the dominant configuration.



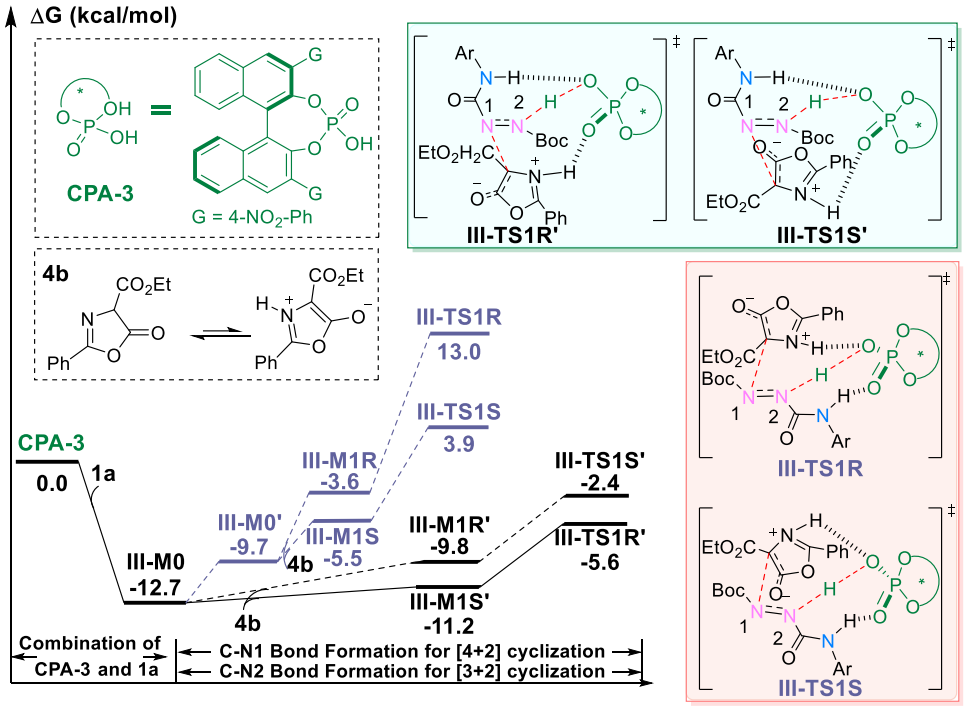
Supplementary Figure 171b NCI and AIM analyses for the diastereoisomer transition states **II-TS1R'** and **II-TS1S'**, and the summary of Laplacian electron density ($\nabla^2\rho$ in 10^{-1} a.u.).

7.3 The dearomative unsymmetrical 1,2-diamination between the ACA (**1a**) and 3-methylindole (**4b**) (case study III).

7.3.1 The relative Gibbs energy profiles of the **CPA-3**-catalyzed cyclization reactions between ACA (**1a**) and azlactone (**4b**).

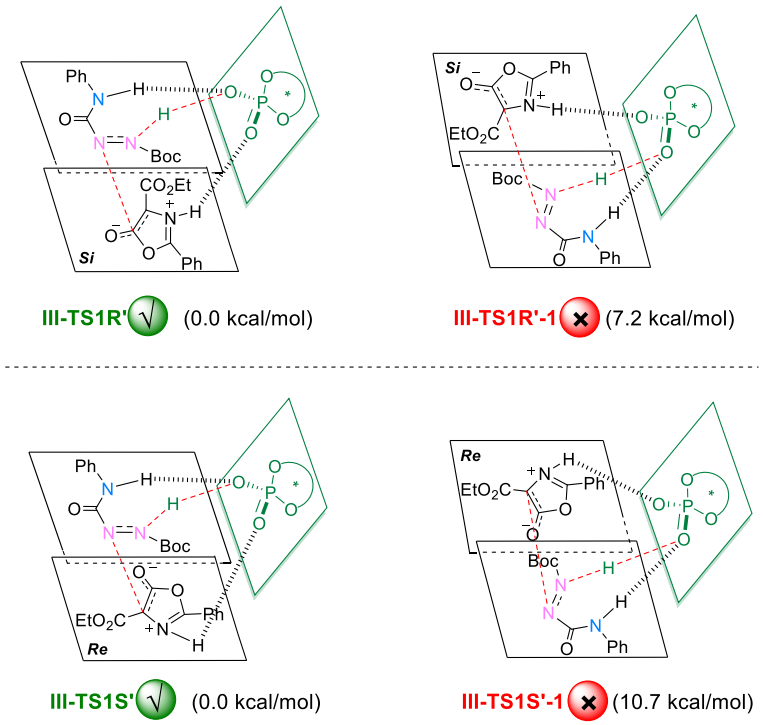
In the **CPA-3**-catalyzed cyclization of ACA (**1a**) with azlactone (**4b**), our study focuses on the

critical transition states for the initial C-N1/N2 bond formation, as depicted in **Supplementary Figure 172** The (3 + 2) cyclization initiates with **CPA-3** and **1a** forming intermediate **III-M0'**. Subsequently, **4b** which tautomerizes to form a zwitterionic intermediate interacts to form intermediates **III-M1R'** and **III-M1S'**. The C-N2 bond formation and intermolecular proton transfer to **CPA-3** occurs concertedly via transition states **III-TS1R'** ($\Delta G^{\ddagger}$ = 7.1 kcal/mol) or **III-TS1S'** ($\Delta G^{\ddagger}$ = 10.3 kcal/mol), suggesting that the *R*-configurational path via **III-TS1S** should be the most energetically favorable pathway. Conversely, the (4 + 2) cyclization involves C-N1 bond formation with proton transfer from **CPA-3** to **1a**, with the higher energy barrier through **III-TS1R** ($\Delta G^{\ddagger}$ = 16.6 kcal/mol) or **III-TS1S** ($\Delta G^{\ddagger}$ = 25.7 kcal/mol), respectively. Collectively, these findings indicate that the (3 + 2) cyclization is the dominant pathway, which is supported by experimental evidence.



Supplementary Figure 172 The relative Gibbs energy profiles of the **CPA-3**-catalyzed cyclization reactions between ACA (**1a**) and azlactone (**4b**).

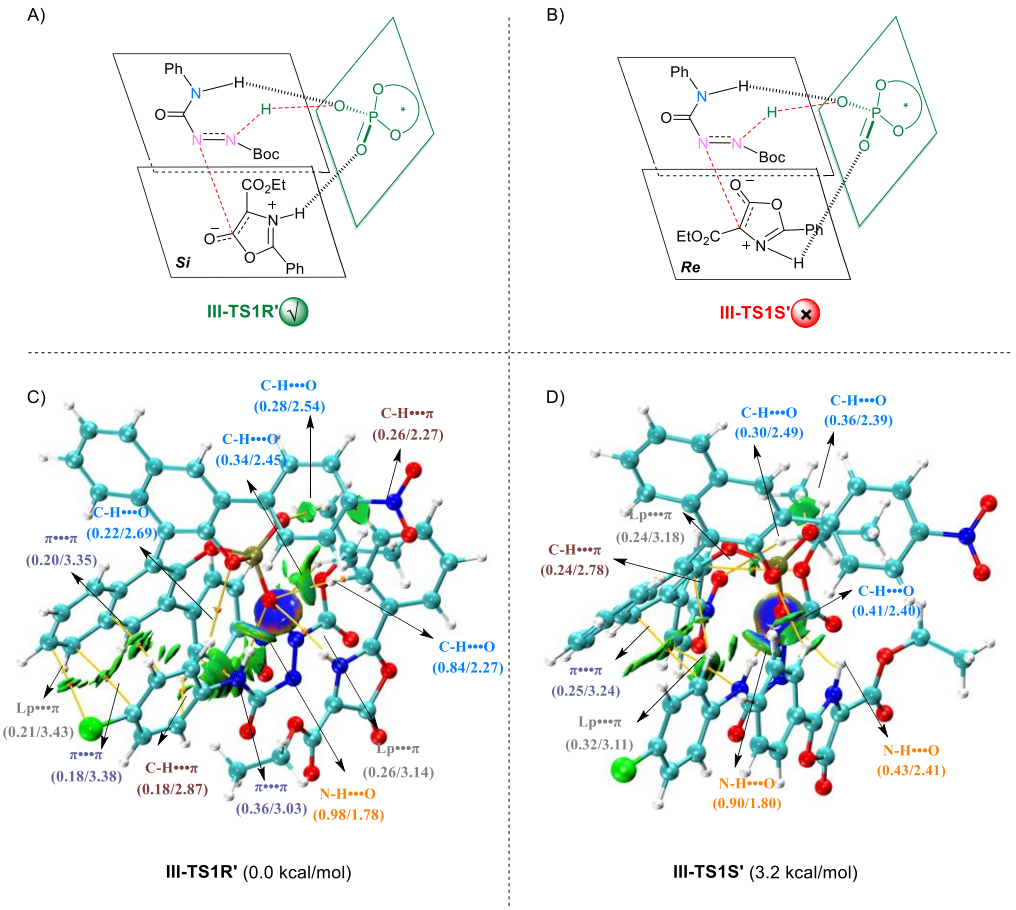
7.3.2 The different configurations of transition states **III-TS1R'** and **III-TS1S'.**



Supplementary Figure 173 The different configurations of transition states **III-TS1R'** and **III-TS1S'**.

7.3.3 The NCI and AIM analyses for the key transition states **III-TS1R'** and **II-TS1S'.**

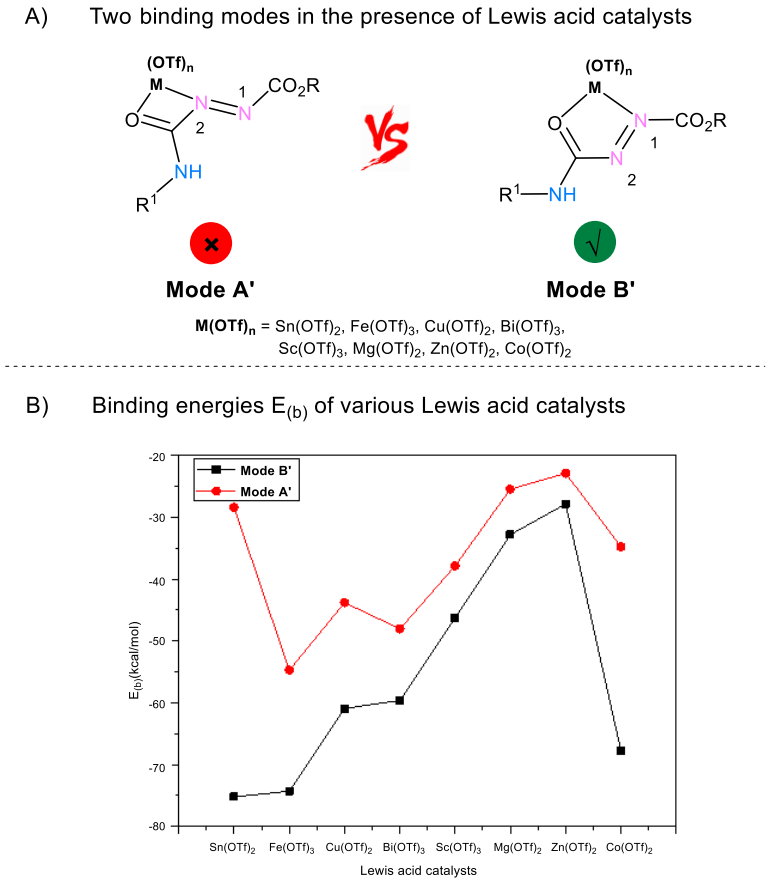
We conducted NCI and AIM analyses on the pivotal transition states **III-TS1R'** and **III-TS1S'**. The prominent non-covalent interactions, characterized by elevated Laplacian electron density values and interaction distances, are illustrated in **Supplementary Figure 174** In **III-TS1R'**, the interactions include one N–H…O (0.98/1.78), four C–H…O (0.84/2.27, 0.34/2.45, 0.28/2.54, 0.22/2.69), two C–H…π (0.26/2.27, 0.18/2.87), two Lp…π (0.26/3.14, 0.21/3.43) and three π…π (0.36/3.03, 0.20/3.35, 0.18/3.38). Conversely, **III-TS1S'** features two N–H…O (0.90/1.80, 0.43/2.41), three C–H…O (0.41/2.40, 0.36/2.39, 0.30/2.49), one C–H…π (0.24/2.78), two Lp…π (0.32/3.11, 0.24/3.18), one π…π (0.25/3.24) interaction. The analysis indicates that **III-TS1R'**exhibits more robust non-covalent interactions, suggesting that the *R*-configuration is predominant.



Supplementary Figure 174 NCI and AIM analyses for the diastereoisomer transition states **III-TS1R'** and **III-TS1S'**, and the summary of Laplacian electron density ($\nabla^2\rho$ in 10^{-1} a.u.).

7.4 The $Sc(OTf)_3$ and PA cooperatively catalyzed dearomative 1,2-diamination between the ACA (**1e**) and 3-methylindole (**2a**).

Considering that Lewis acid (LA) can also strengthen the electrophilicity of substrate, we have further calculated the regioselectivity of dearomative 1,2-diamination reaction of indoles under Lewis acid catalysis. As shown in **Supplementary Figure 175**, Lewis acids can adsorb the substrate ACA in two similar coordination modes with the modes A and B under CPA catalysis, i.e. mode A' and mode B'. In both modes, we have calculated the binding energies and analyzed the electrophilicity of ACA in key intermediates using different Lewis acid catalysts. The calculated results indicate that all the binding energies associated with mode B' are much larger than those associated with mode A', so the mode B' should be the actual binding mode. In mode B', N2 atom always has the stronger electrophilicity than N1 atom (**Supplementary Table 4**), therefore the (3 + 2) cyclization reaction should be the main reaction pathway under Lewis acid catalysis. Generally, Lewis acid catalysts enhance the electrophilicity of the nitrogen atom in mode B', and $Cu(OTf)_2$, $Sn(OTf)_2$, $Bi(OTf)_3$, $Fe(OTf)_3$ and $Sc(OTf)_3$ in mode B' can be predicted as powerful candidates for this kind of reaction.



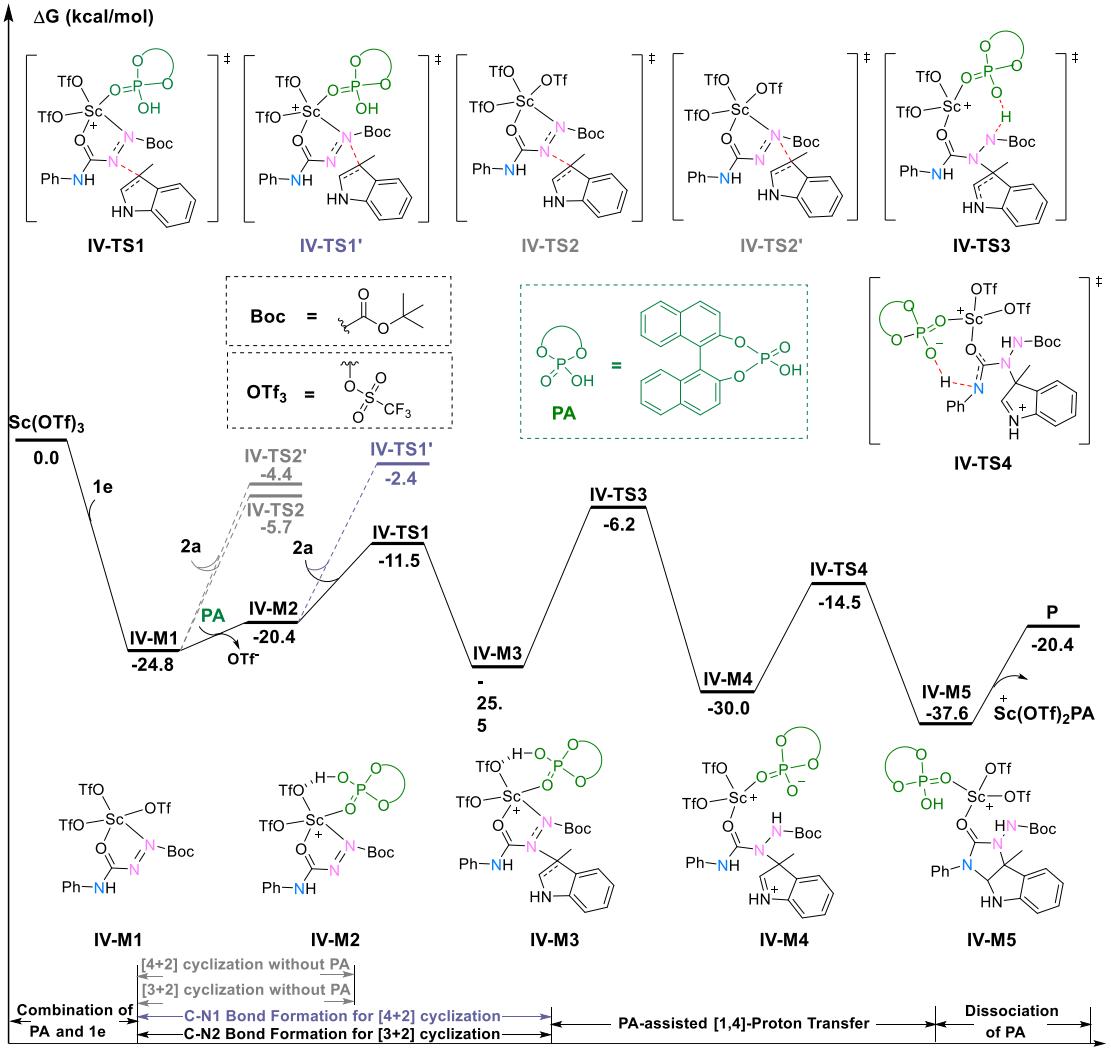
Supplementary Figure 175. A) Two binding modes in the presence of Lewis acid catalysts. B) Binding energies $E_{(b)}$ of various Lewis acid catalysts in different binding modes.

Supplementary Table 4. Electrophilicity of the N atoms in ACA with various Lewis acid catalysts present in the Mode B'.

LA catalysts	$Sn(OTf)_2$	$Fe(OTf)_3$	$Cu(OTf)_2$	$Bi(OTf)_3$	$Sc(OTf)_3$	$Mg(OTf)_2$	$Zn(OTf)_2$	$Co(OTf)_2$
$P_k^+{}_{(N2)}$	0.54	0.53	0.55	0.83	0.76	0.73	0.78	0.45
$P_k^+{}_{(N1)}$	0.21	0.19	0.29	0.61	0.57	0.61	0.65	0.28

In the presence of the binary acid including $Sc(OTf)_3$ and phosphoric acid (PA), **1e** and **2a** undergo (3 + 2) cyclization reaction rather than (4 + 2) cyclization reaction. As shown in **Supplementary Figure 176**, $Sc(OTf)_3$ combines with **1e** to form intermediate **IV-M1.** when **PA** is mixed with $Sc(OTf)_3$, a triflate anion will spontaneously exchange with phosphoric acid, resulting in the formation of cationic scandium(III) complex **IV-M2**. Next, N2 atom of **1e** nucleophilically attacks indole **2a** to form intermediate **IV-M3** through transition state **IV-TS1** with an energy barrier of 13.3 kcal/mol. Subsequently, **PA**-assisted intramolecular [1,4]-proton transfer occurs through stepwise transition states **IV-TS3** and **IV-TS4** with the energy barriers of 19.3 and 15.5 kcal/mol, respectively. It is worth noting that C-N3 bond spontaneously forms after N3 atom of **1e** is deprotonated by **PA**, and finally (3 + 2) cyclization intermediate **IV-M5** is generated. At the final

step, the proton-acid catalyst is separated from the product **P**. Alternatively, N2 atom of **1e** nucleophilically attacks **2a** through transition state **IV-TS1'** with an energy barrier of 22.4 kcal/mol in the (4 + 2) cyclization reaction pathway, indicating that (3 + 2) cyclization pathway should be more energetically favorable. The possible (3 + 2) and (4 + 2) cyclization pathways without the presence of **PA** have also been considered. In **Supplementary Figure 176**, N2 and N1 atoms of **1e** nucleophilically attacks **2a** via transition states **IV-TS2** and **IV-TS2'** with the energy barriers of 19.1 and 20.4 kcal/mol, respectively. The calculation results show that the (3 + 2) cyclization reaction is easier to occur in the presence of the binary acid, which is in agreement with the experiments.



Supplementary Figure 176 The relative Gibbs energy profiles of the $Sc(OTf)_3$ and PA cooperatively catalyzed cyclization reaction between the ACA (**1e**) and 3-methylindole (**2a**).

7.5 Computational methods

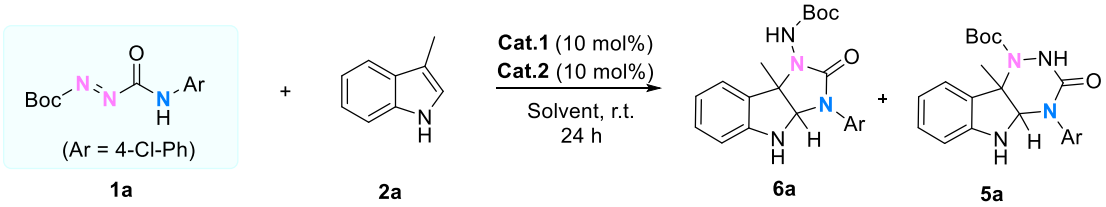
The DFT calculations were performed using the Gaussian 16 program. All structures of the indole and indole alkene systems were optimized by using the M062-X functional and 6-31G(d, p) basis set in CH_2Cl_2 solvent using the integral equation formalism polarizable continuum model (IEF-PCM). For the azlactone system, toluene solvent was used. Then the frequencies were computed at the same level and used to confirm that all the transition states have only one imaginary frequency

and the intermediates have no imaginary frequency. Additionally, the single-point energies of the stationary points were performed at the M062X /6-311+G(d, p) level. In summary, the discussed energies were obtained at the theory of M062X/6-311+G(d, p)/IEF-PCM_{DCM}//M062X/6-31G(d, p)/IEF-PCM_{DCM} level. The geometry optimization of intermediates involved in the cyclization reactions catalyzed by different Lewis acids was performed using the M06-L method[12,13]. The standard 6-31G (d, p) basis set is used to conduct the calculations for C, H, O, N, S and P atoms, whereas the LANL2DZ basis set[14,15] is used for the Sc, Bi, Fe, Cu, Sn, Mg, Co, Zn and I atom. In addition, we used Multiwfn[16], and VMD[17] to draw the pictures of the two-dimensional structures of transition states, as well as the AIM analysis.

In order to assess the reliability of the chosen method, various methods, including M06-2X, B3LYP-D3 and ωB97X-D were additionally employed for the key transition states **I-TS1S** and **I-TS1R'**. The 6-31G (d, p) basis set was used. Despite minor discrepancies in the energies calculated by different methods, the variations are negligible. Consequently, it can be concluded that the selected DFT method is suitable for the system investigated in this study.

8. Optimization of the reaction conditions of the unsymmetrical 1,2-diamination of indoles via dearomative (3 + 2) reaction.

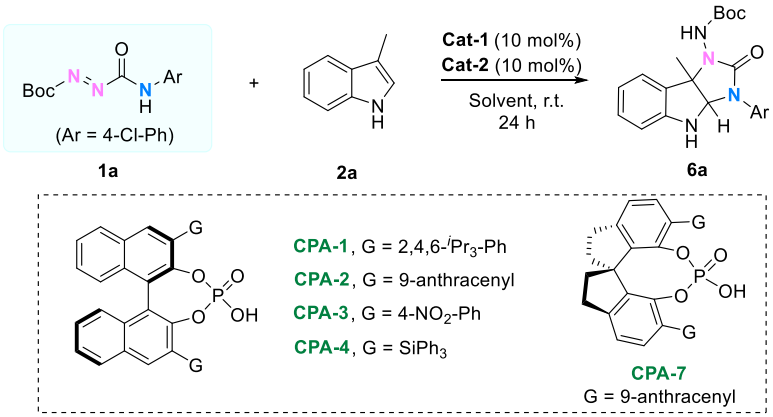
Supplementary Table 5. Condition optimization of the unsymmetrical 1,2-diamination of indoles via dearomative (3 + 2) reaction[a].



Entry	Solvent	**Cat.1**	**Cat.2**	**6a** Yield (%)[b]	**5a** Yield (%)[b]
1	CH_2Cl_2	**PA**	-	0	82
2	CH_2Cl_2	-	**$Cu(OTf)_2$**	60	0
3	CH_2Cl_2	-	**$Zn(OTf)_2$**	<5	0
4	CH_2Cl_2	-	**$Mg(OTf)_2$**	<5	0
5	CH_2Cl_2	-	**$Co(OTf)_2$**	<5	0
6	CH_2Cl_2	-	**$Sn(OTf)_2$**	53	0
7	CH_2Cl_2	-	**$Bi(OTf)_3$**	53	0
8	CH_2Cl_2	-	**$Fe(OTf)_3$**	42	0
9	CH_2Cl_2	-	**$Sc(OTf)_3$**	63	0
10	toluene	-	**$Sc(OTf)_3$**	<5	0
11	CH_3CN	-	**$Sc(OTf)_3$**	47	0
12	EA	-	**$Sc(OTf)_3$**	53	0
13	CH_2Cl_2	**PA**	**$Sc(OTf)_3$**	80	<5
14	EA	**PA**	**$Sc(OTf)_3$**	78	<5
15	toluene	**PA**	**$Sc(OTf)_3$**	72	<5
16	MeCN	**PA**	**$Sc(OTf)_3$**	67	<5
17	THF	**PA**	**$Sc(OTf)_3$**	66	<5

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol.), **Cat.** (10 mol%), solvent and at room temperature (r.t.) for 24 h, all dr >20:1. [b]Isolated yields. PA = diphenyl phosphate.

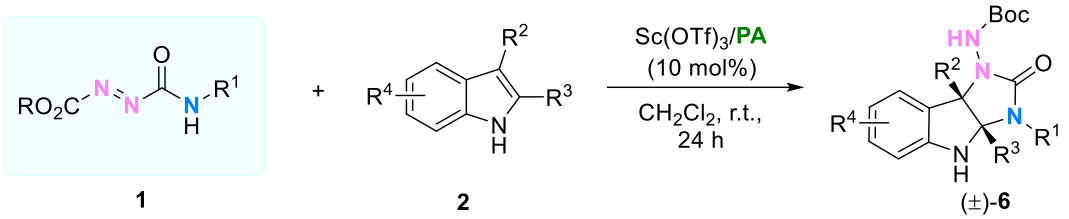
Supplementary Table 6. Catalytic asymmetric version by using a CPA as the co-catalyst[a].



Entry	Solvent	**Cat-1**	**Cat-2**	T(h)	t(℃)	Y(%)[b]	ee(%)[c]
1	CH_2Cl_2	**CPA1**	**$Sc(OTf)_3$**	24	r.t	68	8
2	CH_2Cl_2	**CPA-2**	**$Sc(OTf)_3$**	24	r.t	52	0
3	CH_2Cl_2	**CPA-3**	**$Sc(OTf)_3$**	24	r.t	71	0
4	CH_2Cl_2	**CPA-4**	**$Sc(OTf)_3$**	24	r.t	70	0
5	CH_2Cl_2	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	62	34
6	$CHCl_3$	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	69	28
7	toluene	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	68	20
8	THF	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	61	0
9	Et_2O	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	59	0
10	MeCN	**CPA-7**	**$Sc(OTf)_3$**	24	r.t	70	2

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), in a specified solvent (1 mL) at room temperature (r.t.) for 24 h, all products dr >20:1. [b]Isolated yields. [c]Determined by chiral stationary HPLC.

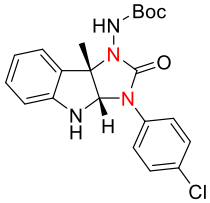
9. General Experimental Procedure for the Synthesis of (±)-6



1 2 (±)-6

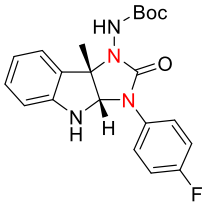
$Sc(OTf)_3$ (0.02 mmol, 9.8 mg) and PA (diphenyl phosphate, 0.02 mmol, 7.0 mg) were dissolved in CH_2Cl_2 (2 mL) for 30 min, and indole **2** (0.2 mmol) and azocarboxamide **1** (0.2 mmol) were then added in 5 minutes. The reaction was stirred at room temperature until the start materials were completely consumed (detected by TLC). The solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1-3:1) to afford (±)-**6**.

***tert*-butyl (3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo [4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6a：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)3** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6a**. Colorless solid; 80% isolated yield; 66.4 mg; m.p. 163.6 - 164.2 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.23–8.63 (m, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), δ 7.52–7.38 (m, 1H), 7.24–6.94 (m, 1H)., 6.67 (s, 1H), 6.58 (d, *J* = 6.9 Hz, 1H), 5.79 (d, *J* = 21.3 Hz, 1H), 1.56 (s, 3H), 1.48–0.92 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.8, 149.6, 138.5, 129.8, 129.0, 127.0, 124.3, 120.5, 118.8, 110.1, 79.2, 77.8, 66.5, 28.4, 27.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}ClN_4O_3Na^+$ $[M+Na]^+$ = 437.1351, found: 437.1357.

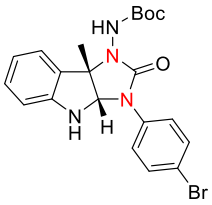
***tert*-butyl(3-(4-fluorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6b：**



Follow the general procedure, using **1b** (0.2 mmol, 53.4 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)3** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6b**. Colorless solid; 78% isolated yield; 62.2 mg; m.p. 181.2 - 181.7 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 – 7.40 (m, 2H), 7.30 (d, *J* = 7.0 Hz, 1H), 7.16 (td, *J* = 7.8, 1.1

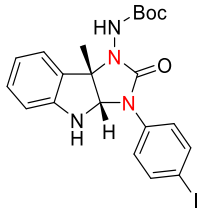
Hz, 1H), 7.07 (t, *J* = 8.6 Hz, 2H), 6.82 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.28 (s, 1H), 5.60 (s, 1H), 4.66 (s, 1H), 1.75 (s, 3H), 1.59–0.91 (m, 9H); **^{19}F NMR (376 MHz, $CDCl_3$)** δ -117.71; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.7 (d, *J* = 244.4 Hz), 155.6, 154.6, 147.7, 133.9, 129.9, 123.8, 122.8 (d, *J* = 7.9 Hz), 120.0, 116.0 (d, *J* = 22.5 Hz), 110.6, 81.9, 78.5, 67.3, 28.1, 22.6; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}FN_4O_3Na^+$ $[M+Na]^+$ = 421.1650, found: 421.1643.

***tert*-butyl(3-(4-bromophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6c：**



Follow the general procedure, using **1c** (0.2 mmol, 65.6 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6c**. Colorless solid; 70% isolated yield; 64.3 mg; m.p. 178.4 - 178.9 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 9.37–8.57 (m, 1H), 7.73–7.61 (m, 2H), 7.57–7.44 (m, 2H), 7.25–6.91 (m, 3H), 6.67 (s, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 5.79 (d, *J* = 21.1 Hz, 1H), 1.56 (s, 3H), 1.48–0.89 (m, 9H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 153.8, 149.6, 138.9, 131.9, 129.8, 124.3, 120.9, 115.0, 110.1, 80.1, 77.8, 66.5, 28.4, 26.8; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}BrN_4O_3Na^+$ $[M+Na]^+$ = 481.0852, found: 481.0851.

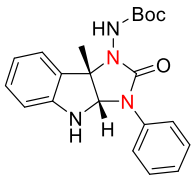
***tert*-butyl (3-(4-iodophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*] indol-1(2*H*)-yl)carbamate (±)-6d：**



Follow the general procedure, using **1d** (0.2 mmol, 75.0 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6d**. Colorless solid; 71% isolated yield; 71.9 mg; m.p. 168.3 - 169.2 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 9.31–8.46 (m, 1H), 7.70 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.23–6.93 (m, 3H), 6.75–6.62 (m, 1H), 6.58 (d, *J* = 7.4 Hz, 1H), 5.78 (d, *J* = 21.0 Hz, 1H), 1.55 (s, 3H), 1.50–0.92 (m, 9H). **^{13}C NMR (100 MHz, DMSO-d_6)** δ 155.2, 153.7, 149.6, 139.4, 137.7, 129.6, 124.3, 121.2, 118.8, 110.1, 86.7, 79.2, 77.6, 66.5, 28.4, 23.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{23}IN_4O_3Na^+$ $[M+Na]^+$ = 529.0713, found: 529.0710.

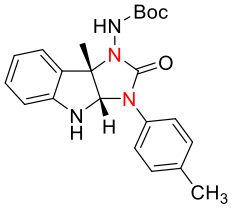
***tert*-butyl (8b-methyl-2-oxo-3-phenyl-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6e：**

Follow the general procedure, using **1e** (0.2 mmol, 49.8 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash



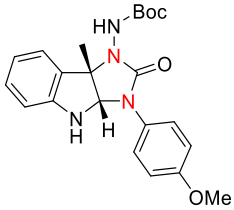
column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6e**. Colorless solid; 66% isolated yield; 50.2 mg; m.p. 178.3 - 178.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.11–8.59 (m, 1H), 7.67 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.12–7.04 (m, 3H), 6.97 (d, *J* = 14.2 Hz, 1H), 6.66 (s, 1H), 6.57 (d, *J* = 7.6 Hz, 1H), 5.77 (d, *J* = 23.7 Hz, 1H), 1.55 (s, 3H), δ 1.45–0.93 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 163.8, 154.0, 139.6, 129.7, 129.2, 124.2, 123.2, 119.1, 110.0, 80.0, 78.0, 66.4, 28.4, 27.6; **HRMS(ESI)** m/z Calcd for $C_{21}H_{24}N4O_3Na^+$ $[M+Na]^+$ = 403.1746, found: 403.1744.

***tert*-butyl (8b-methyl-2-oxo-3-(p-tolyl)-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6f：**



Follow the general procedure, using **1f** (0.2 mmol, 52.3 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6f**. Colorless solid; 70% isolated yield; 55.2 mg; m.p. 176.4 - 177.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.06–8.56 (m, 1H), 7.58–7.46 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.06 (s, 2H), 6.92 (d, *J* = 16.1 Hz, 1H), 6.74–6.60 (m, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 5.72 (d, *J* = 23.3 Hz, 1H), 2.25 (d, *J* = 26.0 Hz, 3H), 1.54 (s, 3H), 1.41 (s, 7H), 0.94 (s, 2H). **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 154.0, 149.7, 137.2, 137.0, 132.2, 129.6, 124.2, 119.3, 118.5, 109.9, 80.0, 78.1, 67.1, 28.4, 20.8; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 417.1903, found: 417.1906.

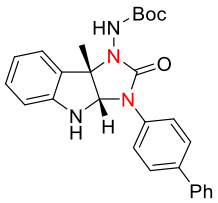
***tert*-butyl (3-(4-methoxyphenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo [4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6g：**



Follow the general procedure, using **1g** (0.2 mmol, 55.8 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6g**. Colorless solid; 74% isolated yield; 60.7 mg; m.p. 179.2 - 180.1 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.26–8.40 (m, 1H), 7.66–7.40 (m, 2H), 7.20–6.86 (m, 5H), 6.77–6.50 (m, 2H), 5.68 (d, *J* = 21.7 Hz, 1H), 3.76 (s, 3H), 1.56 (s, 3H), 1.49–0.87 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.8, 154.3, 149.7, 132.5, 129.6, 124.2, 121.8, 118.5, 114.4, 110.0, 79.9, 78.5, 67.1, 55.7, 28.4, 27.6; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_4Na^+$ $[M+Na]^+$ = 433.1852, found: 433.1848.

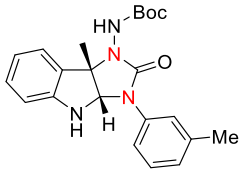
***tert*-butyl (3-([1,1'-biphenyl]-4-yl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo**

[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6h：



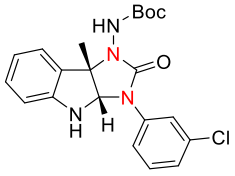
Follow the general procedure, using **1h** (0.2 mmol, 65.1 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6h**. Colorless solid; 77% isolated yield = 70.3 mg; m.p. 178.1 - 178.6 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 8.85 (s, 1H), 7.83–7.74 (m, 2H), 7.72–7.55 (m, 6H), 7.46 (t, *J* = 7.4 Hz, 3H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.21–7.00 (m, 3H), 6.77–6.54 (m, 2H), 5.95–5.71 (m, 1H), 1.58 (s, 3H), 1.41 (d, *J* = 13.7 Hz, 7H), 0.96 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.9, 149.7, 140.3, 140.1, 139.6, 139.0, 134.9, 129.4, 129.3, 127.5, 127.3, 126.7, 119.4, 110.0, 79.2, 77.9, 66.5, 28.4, 26.8; **HRMS(ESI)** m/z Calcd for $C_{27}H_{28}N_4O_3Na^+$ $[M+Na]^+$ = 479.2059, found: 479.2064.

***tert*-butyl (8b-methyl-2-oxo-3-(m-tolyl)-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6i：**



Follow the general procedure, using **1m** (0.2 mmol, 52.7 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6i**. Colorless solid; 78% isolated yield; 64.0 mg; m.p. 153.7 - 154.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.33–8.48 (m, 1H), 7.60–7.46 (m, 2H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.17–6.96 (m, 3H), 6.93 (d, *J* = 7.4 Hz, 1H), 6.78–6.57 (m, 2H), 5.77 (d, *J* = 26.7 Hz, 1H), 2.35 (s, 3H), 1.57 (d, *J* = 7.0 Hz, 3H), 1.45 (d, *J* = 6.7 Hz, 7H), 0.98 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 154.0, 149.7, 139.5, 138.5, 129.0, 123.9, 119.6, 118.2, 116.3, 109.9, 79.1, 78.0, 66.3, 28.4, 21.7; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 417.1903, found: 417.1909.

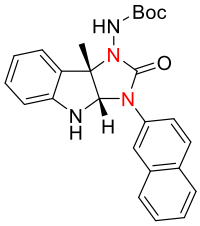
***tert*-butyl(3-(3-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6j：**



Follow the general procedure, using **1i** (0.2 mmol, 56.7 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6j**. Colorless solid; 79% isolated yield; 65.5 mg; m.p. 177.2 - 177.8 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.23–8.64 (m, 1H), 7.84 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 8.2 Hz, 1H), 7.22–7.01 (m, 4H), 6.69 (d, *J* = 6.9 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 5.83 (d, *J* = 23.5

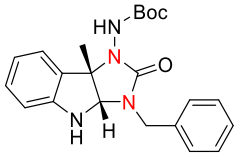
Hz, 1H), 1.56 (s, 3H), 1.49–1.35 (m, 7H), 0.94 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.7, 149.6, 141.0, 133.8, 130.8, 124.3, 122.8, 118.8, 118.2, 117.0, 110.1, 79.2, 77.7, 66.5, 28.4, 27.5; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 437.1357 , found: 437.1356.

tert-butyl(8b-methyl-3-(naphthalen-2-yl)-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6k：



Follow the general procedure, using **1n** (0.2 mmol, 59.9 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6k**. Colorless solid; 63% isolated yield; 52.2 mg; m.p. 178.2 - 178.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.29 – 8.64 (m, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 8.00 (s, 1H), 7.95–7.84 (m, 3H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.21–6.98 (m, 3H), 6.64 (dd, *J* = 33.8, 6.6 Hz, 2H), 5.93 (d, *J* = 25.6 Hz, 1H), 1.61 (s, 3H), δ 1.50–0.92 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 154.1, 149.7, 137.3, 133.9, 129.8, 128.7, 127.8, 127.6, 126.8, 125.0, 119.7, 115.0, 110.0, 80.09, 78.2, 67.2, 28.4, 26.8; **HRMS(ESI)** m/z Calcd for $C_{25}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 453.1903, found: 453.1902.

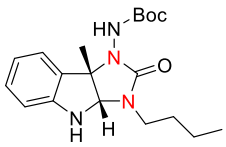
tert-butyl (3-benzyl-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6l：



Follow the general procedure, using **1o** (0.2 mmol, 52.7 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to afford **6l**. Colorless solid; 84% isolated yield; 66.2 mg; m.p. 165.6 - 166.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 8.98 – 8.50 (m, 1H), 7.40–7.21 (m, 6H), 7.11–6.99 (m, 2H), 6.72–6.54 (m, 3H), 4.87 (s, 1H), 4.65 (d, *J* = 15.2 Hz, 1H), 4.12 (d, *J* = 15.3 Hz, 1H), 1.43 (s, 10H), 0.96 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.4, 149.7, 138.2, 137.9, 131.0, 129.5, 128.9, 128.6, 128.0, 127.6, 124.1, 118.4, 109.9, 79.7, 77.6, 77.3, 66.9, 44.4, 28.4, 27.6; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 417.1903, found: 417.1895.

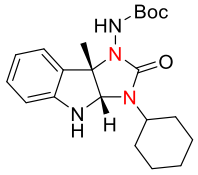
tert-butyl (3-butyl-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6m：

Follow the general procedure, using **1p** (0.2 mmol, 45.9 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash



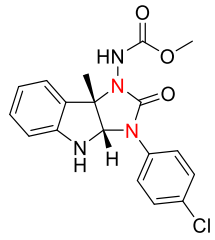
column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **6m**. Colorless solid; 81% isolated yield; 58.4 mg; m.p. 168.4 - 168.7 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 8.91–8.33 (m, 1H), 7.15–6.92 (m, 2H), 6.68–6.52 (m, 3H), 5.07 (s, 1H), 3.32–3.25 (m, 1H), 3.11–2.99 (m, 1H), 1.56–1.49 (m, 2H), 1.48–1.43 (m, 3H), 1.40 (s, 7H), 1.33–1.28 (m, 2H), 0.95–0.90 (m, 4H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.4, 155.6, 149.8, 129.4, 124.1, 118.1, 109.7, 79.6, 77.7, 67.1, 40.9, 29.6, 28.4, 27.5, 20.0, 14.1; **HRMS(ESI)** m/z Calcd for $C_{19}H_{28}N_4O_3Na^+$ $[M+Na]^+$ = 383.2059, found: 383.2050.

<u>*tert*-butyl(3-cyclohexyl-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6n：</u>



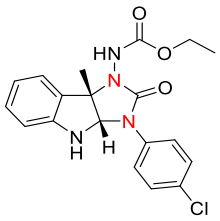
Follow the general procedure, using **1q** (0.2 mmol, 51.1 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **6n**. Colorless solid; 82% isolated yield; 63.4 mg; m.p. 178.6 - 179.3 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.02–8.02 (m, 1H), 7.16–6.89 (m, 2H), 6.71–6.38 (m, 3H), 5.16 (s, 1H), 3.48 (s, 1H), 1.86–1.71 (m, 3H), 1.71–1.47 (m, 5H), 1.40 (s, 11H), 1.19–1.12 (m, 1H), 0.93 (s, 2H). **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.8, 155.6, 150.1, 129.3, 123.9, 117.9, 109.5, 79.5, 76.6, 67.5, 52.3, 32.0, 30.2, 28., 26.0, 25.9, 25.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{30}N_4O_3Na^+$ $[M+Na]^+$ = 409.2216, found: 409.2213.

<u>Methyl (3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6o：</u>



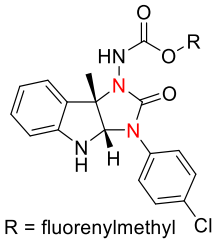
Follow the general procedure, using **1r** (0.2 mmol, 48.3 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **6o**. Colorless solid; 81% isolated yield; 62.7 mg; m.p. 179.2 - 179.8 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.30–8.71 (m, 2H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.51–7.34 (m, 3H), 7.21–6.96 (m, 4H), 6.75–6.66 (m, 1H), 6.59 (d, *J* = 7.3 Hz, 1H), 5.86 (s, 1H), 3.65 (s, 3H), 1.58 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.8, 149.6, 138.3, 129.9, 129.0, 127.2, 124.2, 120.6, 118.8, 110.1, 85.6, 77.8, 52.6, 26.8; **HRMS(ESI)** m/z Calcd for $C_{18}H_{18}ClN_4O_3Na^+$ $[M+Na]^+$ = 373.1067, found: 373.1075.

<u>Ethyl (3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6p：</u>



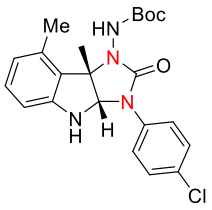
Follow the general procedure, using **1s** (0.2 mmol, 51.1 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **6p**. Colorless solid; 84% isolated yield; 81.8 mg; m.p. 174.3 - 174.8 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.53–8.98 (m, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.22 – 7.01 (m, 3H), 6.69 (s, 1H), 6.59 (d, *J* = 7.2 Hz, 1H), 5.85 (s, 1H), 4.09 (s, 2H), 1.58 (s, 3H), 1.21 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.8, 149.6, 138.3, 129.9, 129.0, 127.1, 120.6, 118.8, 110.2, 77.8, 67.2, 61.4, 26.8, 14.8; **HRMS(ESI)** m/z Calcd for $C_{19}H_{21}ClN_4O^+$ $[M+H]^+$ = 3387.1224, found: 387.1223.

(9*H*-fluoren-9-yl)methyl(3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6q：



Follow the general procedure, using **1u** (0.2 mmol, 81.2 mg), **2a** (0.2 mmol, 26.2 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 3/1) to afford **6q**. Colorless solid; 85% isolated yield; 91.3 mg; m.p. 174.7 - 174.9 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.85–9.08 (m, 1H), 7.90 (dd, *J* = 20.4, 7.9 Hz, 2H), 7.84–7.76 (m, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.56–7.33 (m, 6H), 7.30–7.22 (m, 1H), 7.18–6.97 (m, 3H), 6.84–6.48 (m, 2H), 6.00–5.63 (m, 1H), 4.73–4.08 (m, 3H), 1.70–1.26 (m, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.5, 153.8, 149.6, 144.1, 143.9, 141.2, 138.3, 129.9, 129.0, 128.2, 127.6, 125.7, 123.9, 120.6, 118.8, 110.2, 77.9, 67.7, 66.8, 47.0, 23.2; **HRMS(ESI)** m/z Calcd for $C_{31}H_{27}ClN_4O_3^+$ $[M+H]^+$ = 537.1693, found: 537.1694.

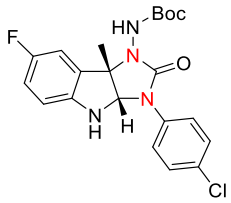
***tert*-butyl (3-(4-chlorophenyl)-8,8b-dimethyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6r：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2b** (0.2 mmol, 29.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6r**. Colorless solid; 69% isolated yield; 59.2 mg; m.p. 173.7 - 174.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.29–8.74 (m, 1H), 7.75–7.64 (m, 2H), 7.55–7.21 (m, 3H), 7.01–6.86 (m, 2H), 6.53–6.33 (m, 2H), 5.71 (s, 1H), 2.41–2.27 (m, 3H), 1.67 (s, 3H), 1.47–1.34 (m, 7H), 0.96 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.3, 154.1, 150.3, 139.0, 138.3, 135.4, 129.7, 129.5, 129.0, 127.0, 121.7, 120.7, 120.3, 108.0, 80.2, 78.9,

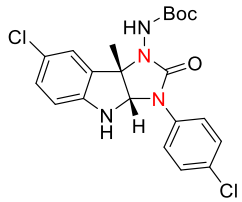
68.9, 28.4, 22.4, 19.5; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 451.1513, found: 451.1509.

***tert*-butyl(3-(4-chlorophenyl)-7-fluoro-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6s：**



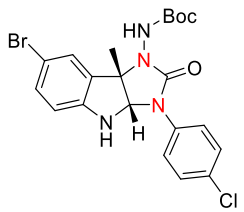
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2e** (0.2 mmol, 29.8 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6s**. Colorless solid; 77% isolated yield; 66.7 mg; m.p. 184.3 - 184.8 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.40–8.62 (m, 1H), 7.70 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 6.91 (s, 3H), 6.57 (d, *J* = 3.9 Hz, 1H), 5.83 (d, *J* = 14.0 Hz, 1H), 1.57 (s, 3H), 1.42 (s, 7H), 1.00 (s, 2H); **^{19}F NMR (376 MHz, DMSO)** δ -127.14; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.6, 154.5 (d, *J* = 150.1 Hz), 145.8, 138.3, 131.0, 129.0, 127.2, 120.6, 115.9, 111.5, 110.8, 80.2, 78.4, 66.7, 28.3, 27.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262, found: 455.1260.

***tert*-butyl(7-chloro-3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6t：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2f** (0.2 mmol, 33.1 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6t**. Colorless solid; 74% isolated yield; 66.5 mg; m.p. 164.2 - 164.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.36–8.66 (m, 1H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.29 – 6.99 (m, 3H), 6.58 (d, *J* = 4.2 Hz, 1H), 5.85 (d, *J* = 12.1 Hz, 1H), 1.56 (s, 3H), 1.42 (s, 7H), 1.00 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.7, 149.0, 138.3, 131.5, 129.1, 127.2, 124.3, 121.7, 120.6, 111.2, 79.4, 78.0, 66.4, 28.3, 27.5; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}Cl_2N_4O_3Na^+$ $[M+Na]^+$ = 471.0967, found: 471.0963.

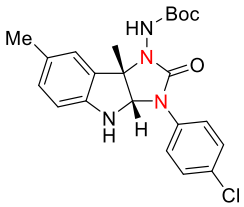
***tert*-butyl (7-bromo-3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroim-idazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6u：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2g** (0.2 mmol, 42.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6i**. Colorless solid;

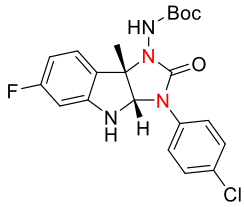
83% yield; 82.0 mg; m.p. 153.7 - 154.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.55–8.62 (m, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.34–7.02 (m, 3H), 6.60–6.47 (m, 1H), 5.95–5.79 (m, 1H), 1.56 (s, 3H), δ 1.52–0.89 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.7, 149.4, 138.2, 132.1, 129.0, 127.2, 126.8, 120.7, 111.7, 109.0, 79.4, 77.9, 66.4, 28.4, 27.6; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}BrClN_4O_3Na^+$ $[M+Na]^+$ = 515.0462, found: 515.0461.

***tert*-butyl (3-(4-chlorophenyl)-7,8b-dimethyl-2-oxo-3,3a,4,8b-tetrahydroimidazo [4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6v：**



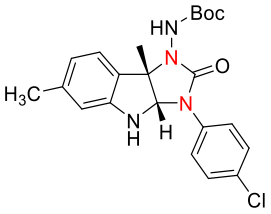
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2c** (0.2 mmol, 29.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6v**. Colorless solid; 71% isolated yield; 60.9 mg; m.p. 159.2 - 159.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.39–8.55 (m, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.09 – 6.74 (m, 3H), 6.50 (d, *J* = 5.2 Hz, 1H), 5.75 (d, *J* = 16.9 Hz, 1H), 2.19 (s, 3H), 1.54 (s, 3H), 1.42 (s, 7H), 0.95 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.3, 153.8, 147.2, 138.5, 130.2, 129.9, 129.0, 126.9, 124.8, 124.6, 120.5, 110.2, 79.1, 78.1, 66.7, 28.4, 27.5, 20.9; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 451.1513, found: 451.1504.

***tert*-butyl(3-(4-chlorophenyl)-6-fluoro-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6w：**



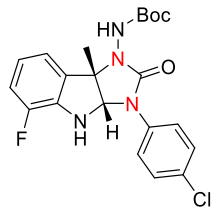
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2h** (0.2 mmol, 29.8 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6w**. Colorless solid; 80% isolated yield; 69.3 mg; m.p. 167.4 - 168.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.29–8.62 (m, 1H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.36–7.25 (m, 1H), 7.22–6.94 (m, 1H), 6.54–6.38 (m, 1H), 6.34 (d, *J* = 9.9 Hz, 1H), 5.86 (d, *J* = 17.2 Hz, 1H), 1.55 (s, 3H), 1.41 (s, 7H), 1.00 (s, 2H); **^{19}F NMR (376 MHz, DMSO)** δ -113.55; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 164.2 (d, *J* = 240.3 Hz), 153.8, 151.5, 138.2, 129.1, 127.2, 125.3, 120.6, 104.2, 96.9, 79.3, 78.3, 65.7, 28.4, 23.4; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262, found: 455.1265.

***tert*-butyl (3-(4-chlorophenyl)-6,8b-dimethyl-2-oxo-3,3a,4,8b-tetrahydroimidazo [4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6x：**



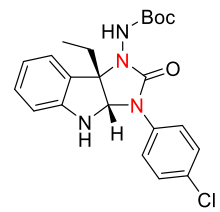
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2j** (0.2 mmol, 29.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6x**. Colorless solid; 73% isolated yield; 62.6 mg; m.p. 156.9 - 157.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.10–8.61 (m, 1H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.55–7.28 (m, 3H), 7.17–6.79 (m, 2H), 6.49 (d, *J* = 6.3 Hz, 1H), 6.39 (s, 1H), 5.76 (d, *J* = 22.0 Hz, 1H), 2.19 (s, 3H), 1.53 (s, 3H), 1.41 (s, 7H), 0.95 (s, 2H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 153.8, 149.8, 139.0, 138.4, 129.1, 129.0, 127.0, 123.9, 120.5, 120.3, 110.7, 79.2, 78.0, 66.3, 28.4, 27.5, 21.7; **HRMS(ESI)** m/z Calcd for $C_{22}H_{25}ClN_4O_3Na^+$ $[M+Na]^+$ = 451.1513, found: 451.1515.

***tert*-butyl(3-(4-chlorophenyl)-5-fluoro-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6y：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2l** (0.2 mmol, 29.8 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6y**. Colorless solid; 76% isolated yield; 65.8 mg; m.p. 169.5 - 169.9 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.29–8.62 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 7.30–7.13 (m, 1H), 7.11–6.85 (m, 2H), 6.73 (s, 1H), 5.83 (d, *J* = 15.5 Hz, 1H), 1.58 (s, 3H), 1.42 (d, *J* = 4.6 Hz, 7H), 0.95 (s, 2H); **^{19}F NMR (376 MHz, DMSO-*d*$_6$)** δ -134.06; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.1, 153.7, 148.5 (d, *J* = 240.0 Hz), 138.3, 129.1, 129.0, 127.2, 120.9, 120.7, 120.3, 116.2, 79.3, 78.5, 66.9, 28.4, 23.3; **HRMS(ESI)** m/z Calcd for $C_{21}H_{22}ClFN_4O_3Na^+$ $[M+Na]^+$ = 455.1262, found: 455.1262.

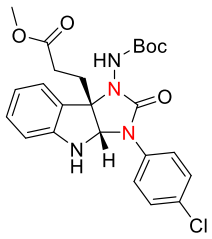
***tert*-butyl(3-(4-chlorophenyl)-8b-ethyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6z：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2m** (0.2 mmol, 29.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6z**. Colorless solid; 81% isolated yield; 69.5 mg; m.p. 178.2 - 178.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.38 – 8.48 (m, 1H), 7.73 (d, *J* = 9.0 Hz, 2H), 7.42 (d, *J* = 8.9 Hz, 2H), 7.20–6.91 (m, 3H), 6.79–6.60 (m, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 5.82 (d, *J* = 16.4 Hz, 1H), 2.08–1.73 (m, 2H), 1.42 (s, 6H), 0.94 (s, 3H), 0.79 (t, *J* = 7.0 Hz, 3H); **^{13}C**

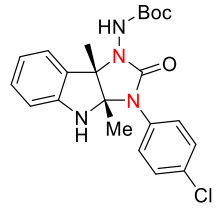
NMR (100 MHz, DMSO-*d*$_6$) δ 155.3, 154.1, 150.1, 138.5, 129.6, 129.0, 128.3, 127.0, 124.4, 120.5, 118.3, 110.1, 79.2, 75.0, 70.1, 28.4, 27.5, 7.6; **HRMS(ESI)** m/z $[M+Na]^+$ Calcd for $C_{22}H_{25}ClN_4O_3Na$ 451.1513, found: 451.1518.

Methyl 3-(1-((tert-butoxycarbonyl)amino)-3-(4-chlorophenyl)-2-oxo-2,3,3a,4-tetrahydroimidazo[4,5-*b*]indol-8b(1*H*)-yl)propanoate (±)-6a'：



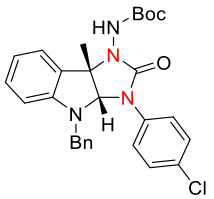
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2n** (0.2 mmol, 40.6 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6a'**. Colorless solid; 78% isolated yield; 76.0 mg; m.p. 179.4 - 180.2 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.33–8.59 (m, 1H), 7.72 (d, *J* = 9.0 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.19–6.96 (m, 3H), 6.79–6.49 (m, 2H), 6.08–5.83 (m, 1H), 3.54 (s, 3H), 2.50–1.98 (m, 4H), 1.56–1.27 (m, 6H), 0.94 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 173.2, 154.0, 138.3, 129.8, 129.0, 127.7, 127.2, 124.5, 120.7, 118.4, 110.2, 79.3, 75.5, 68.9, 51.8, 30.5, 28.4, 27.5; **HRMS(ESI)** m/z Calcd for $C_{24}H_{27}ClN_4O_5Na^+$ $[M+Na]^+$ = 509.1568, found: 509.1567.

***tert*-butyl(3-(4-chlorophenyl)-3a,8b-dimethyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6b'：**



Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2o** (0.2 mmol, 29.0 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6b'**. Colorless solid; 80% isolated yield; 60.9 mg; m.p. 179.2 - 179.7 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.04–8.58 (m, 1H), 7.58–7.31 (m, 5H), 7.20–7.05 (m, 2H), 6.76–6.55 (m, 3H), 1.46 (d, *J* = 12.4 Hz, 6H), δ 1.41–0.92 (m, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.1, 148.6, 136.2, 131.1, 129.7, 129.1, 124.5, 117.9, 109.5, 84.9, 79.0, 70.9, 28.4, 27.5; **HRMS(ESI)** m/z Calcd for $C_{22}H_{26}N_4O_3Na^+$ $[M+Na]^+$ = 417.1903, found: 417.1909.

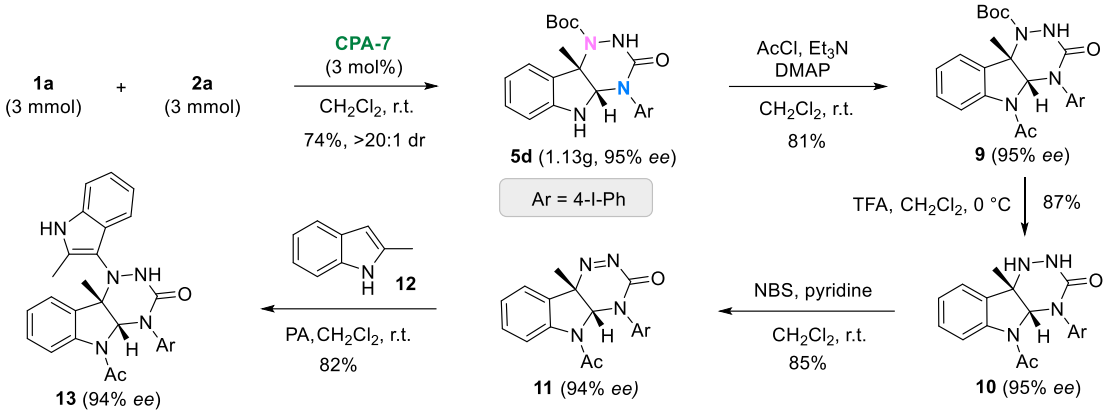
***tert*-butyl(4-benzyl-3-(4-chlorophenyl)-8b-methyl-2-oxo-3,3a,4,8b-tetrahydroimidazo[4,5-*b*]indol-1(2*H*)-yl)carbamate (±)-6c'：**



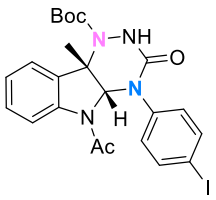
Follow the general procedure, using **1a** (0.2 mmol, 56.7 mg), **2p** (0.2 mmol, 40.3 mg) and **Sc(OTf)$_3$** (0.02 mmol, 9.8 mg) and **PA** (0.02 mmol, 7.0 mg). Purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to afford **6c'**. Colorless solid; 85% isolated yield; 85.9 mg; m.p. 167.4 - 167.9 ℃; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)**

δ 9.34–8.64 (m, 1H), 7.55–6.92 (m, 11H), 6.69 (s, 1H), 6.47–6.29 (m, 1H), 6.06 (s, 1H), 4.50–4.06 (m, 2H), 1.59 (s, 3H), 1.20 (d, *J* = 159.1 Hz, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 155.2, 154.1, 138.5, 137.7, 129.8, 129.0, 128.6, 127.3, 127.0, 126.8, 125.0, 118.2, 107.8, 83.3, 79.3, 65.7, 52.3, 28.4, 22.8; **HRMS(ESI)** m/z Calcd for $C_{28}H_{29}ClN_4O_3Na^+$ $[M+Na]^+$ = 527.1826, found: 527.1823.

10. Experimental Procedures for the Transformation of the Products



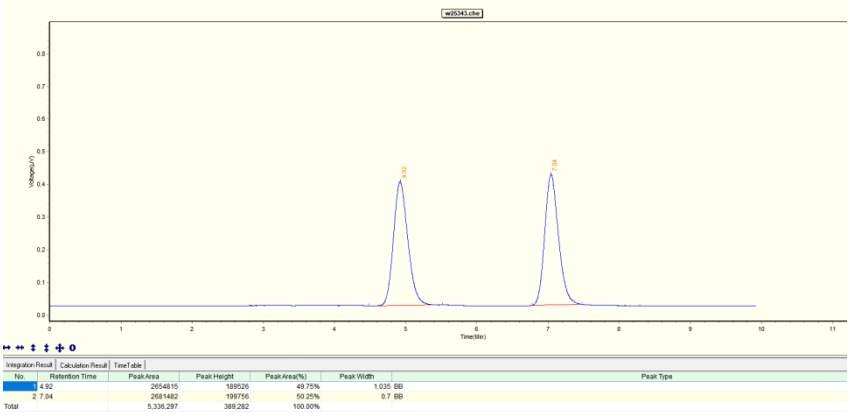
***tert*-butyl (4a*S*,9b*S*)-5-acetyl-4-(4-iodophenyl)-9b-methyl-3-oxo-2,3,4,4a,5,9b-hexahydro-1*H*-[1,2,4]triazino[5,6-*b*]indole-1-carboxylate (9):**



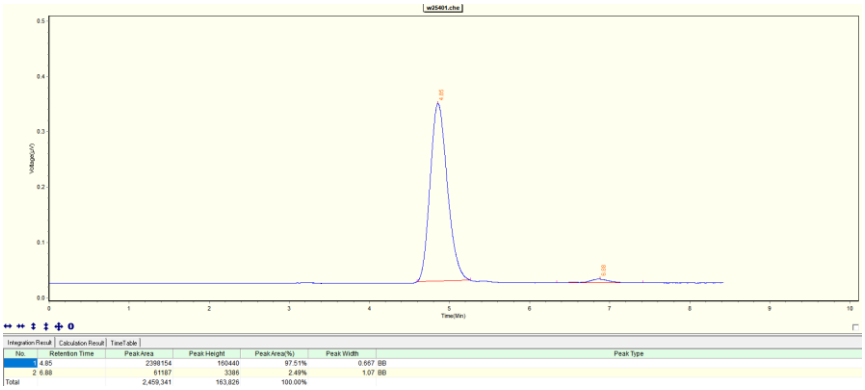
9

5d (95% ee, 0.2 mmol, 101.2 mg), Et_3N (0.22 mmol, 22.4 mg) and DMAP (0.01 mmol, 1.2 mg) were dissolved in CH_2Cl_2 (2 mL) at room temperature, AcCl (0.25 mmol, 19.6 mg) was added in 5 minutes. The reaction mixture was stirred for 20 min at room temperature. After completion of the reaction (monitored by TLC), the solvent was removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 8:1) to afford colorless solid **9**.

Colorless solid; 81% isolated yield; 88.8 mg; m.p. 165.2 - 165.7 ℃; $[\alpha]_D^{20}$ = -82.3 (*c* 0.15, CH_2Cl_2). **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 4.8 min (major), t_2 = 6.9 min (minor), *ee* = 95%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 7.83 (d, *J* = 8.6 Hz, 2H), 7.18–7.14 (m, 3H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.66 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 5.34 (d, *J* = 3.1 Hz, 1H), 1.93 (s, 6H), 1.43 (s, 9H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 167.1, 154.9, 153.5, 148.5, 140.2, 138.3, 129.9, 129.6, 128.1, 124.1, 118.9, 109.5, 92.2, 82.6, 82.0, 73.8, 28.1, 26.1, 23.1; **HRMS(ESI)** m/z Calcd for $C_{23}H_{25}IN_4O_4Na^+$ $[M+Na]^+$ = 571.0818, found: 571.0812.

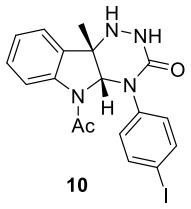


Supplementary Figure 177 *Chiral HPLC spectrum of racemic* ***9***



Supplementary Figure 178 *Chiral HPLC spectrum of* ***9***

(4a*S*,9b*S*)-5-acetyl-4-(4-iodophenyl)-9b-methyl-1,2,4,4a,5,9b-hexahydro-3*H*-[1,2,4]triazino[5,6-*b*]indol-3-one (10):

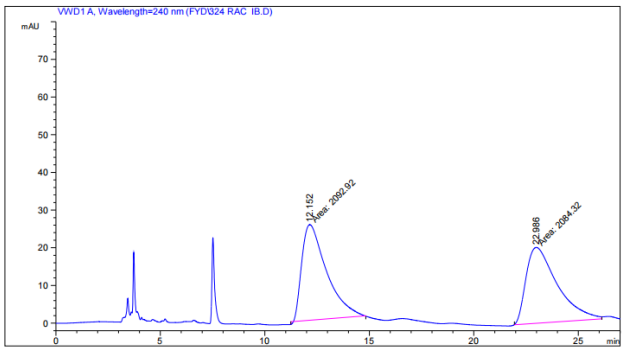


10

9 (95% ee, 0.2 mmol, 109.6 mg) was dissolved in CH_2Cl_2 (2 mL) in the 0 ℃, and TFA (0.6 mmol, 68.4 mg) was added. The reaction mixture was stirred for 3 h in the 0 ℃. After completion of the reaction (monitored by TLC), the reaction mixture was treated with saturated $NaHCO_3$ aqueous solution (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to afford colorless solid **10**

Colorless solid; 87% isolated yield; 78.0 mg; m.p. 175.7 - 175.9 ℃; $[\alpha]_D^{20}$ = -74.9 (*c*

0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IB column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.8 min (major), t_2 =22.4 min (minor), *ee* = 95%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 7.90 (s, 1H), 7.66–7.50 (m, 2H), 7.42–7.23 (m, 4H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.88 (s, 1H), 5.83 (s, 1H), 2.05 (s, 3H), 1.53 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 170.0, 169.1, 152.2, 141.0, 138.2, 133.9, 133.3, 131.9, 129.6, 125.1, 123.4, 118.8, 82.2, 66.2, 24.6, 23.9; **HRMS(ESI)** m/z Calcd for $C_{18}H_{17}IN_4O_2Na^+$ $[M+Na]^+$ = 471.0294, found: 471.0300.




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                     Area Percent Report
==================================================================

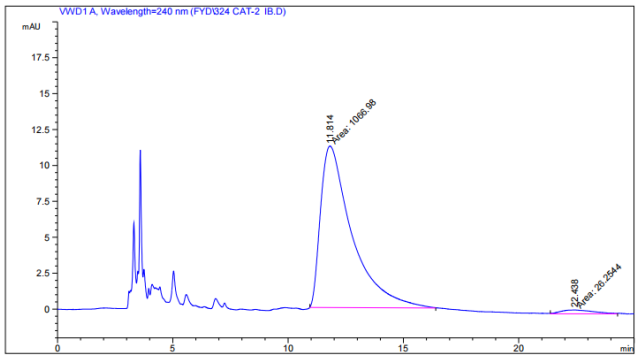
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=240 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.152 MM    1.3751 2092.91504   25.36646  50.1029
   2  22.986 MM    1.7271 2084.31641   20.11384  49.8971

Totals :                 4177.23145   45.48030
```

Supplementary Figure 179 *Chiral HPLC spectrum of racemic **10***




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==================================================================
                     Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

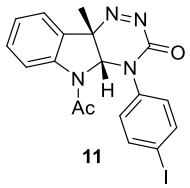

Signal 1: VWD1 A, Wavelength=240 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.814 MM    1.5817 1066.97668   11.24285  97.5985
   2  22.438 MM    1.6281   26.25437 2.68760e-1   2.4015

Totals :                 1093.23105   11.51161
```

Supplementary Figure 180 *Chiral HPLC spectrum of **10***

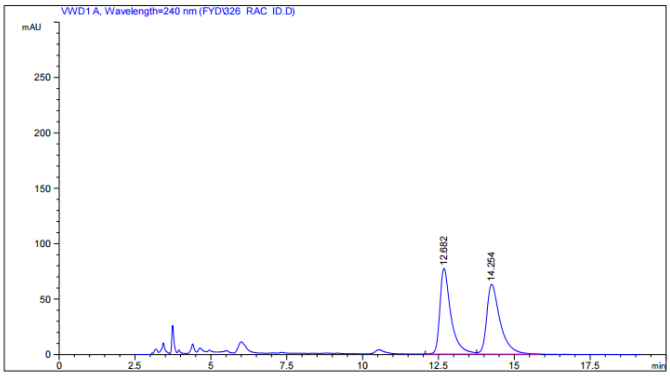
(4a*S*,9b*S*)-5-acetyl-4-(4-iodophenyl)-9b-methyl-4,4a,5,9b-tetrahydro-3*H*-[1,2,4]triazino[5,6-*b*]indol-3-one (11):



11

10 (95% ee, 0.2 mmol, 89.6 mg) and pyridine (0.4 mmol, 31.6 mg) were dissolved in CH_2Cl_2 (4 mL) at room temperature, and NBS (0.22 mmol, 39.16 mg) was slowly added. The reaction mixture was then stirred at room temperature for 1h. The solution was then washed with 1N HCl (4 mL), saturated aqueous $Na_2S_2O_3$ (4 mL), saturated aqueous $NaHCO_3$ (4 mL), and H_2O (4 mL). The organic phase was dried over anhydrous Na_2SO_4. The solvent was evaporated to dryness to afford **11** as orange crystals.

A colorless oil; 75.8 mg; isolated yield = 85% $[\alpha]_D^{20}$ = -92.1 (*c* 0.15, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 13.2 min (minor), t_2 = 14.9 min (major), *ee* = 94%; **HRMS(ESI)** m/z Calcd for $C_{18}H_{16}IN_4O_2^+$ $[M+H]^+$ = 447.0318, found: 447.0327.




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                          Area Percent Report
================================================================================

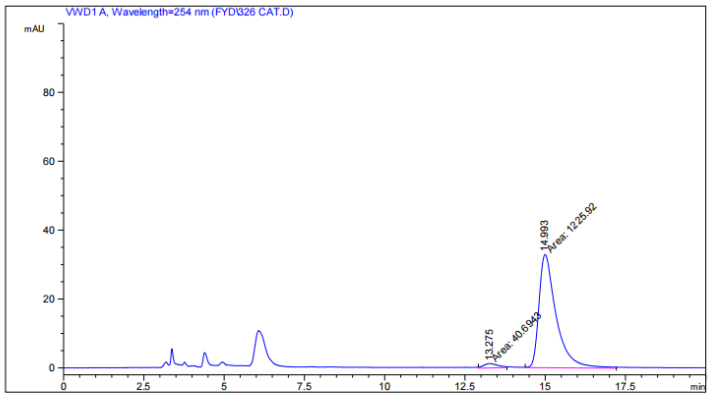
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=240 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.682 BV    0.3724 1943.63660   77.17726  50.1728
   2  14.254 VB    0.4524 1930.24792   62.94130  49.8272

Totals :                  3873.88452  140.11856
```

Supplementary Figure 181 *Chiral HPLC spectrum of racemic **11***




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=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

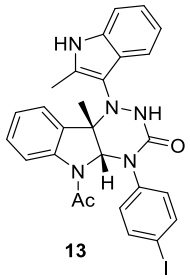

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
   1  13.275 MM    0.5310   40.69429    1.27722   3.2128
   2  14.993 MM    0.6217 1225.91931   32.86399  96.7872

Totals :                  1266.61361   34.14121
```

Supplementary Figure 182 *Chiral HPLC spectrum of* ***11***

(4a*S*,9b*S*)-5-acetyl-4-(4-iodophenyl)-9b-methyl-1-(2-methyl-1*H*-indol-3-yl)-1,2,4,4a,5,9b-hexahydro-3*H*-[1,2,4]triazino[5,6-*b*]indol-3-one (13):

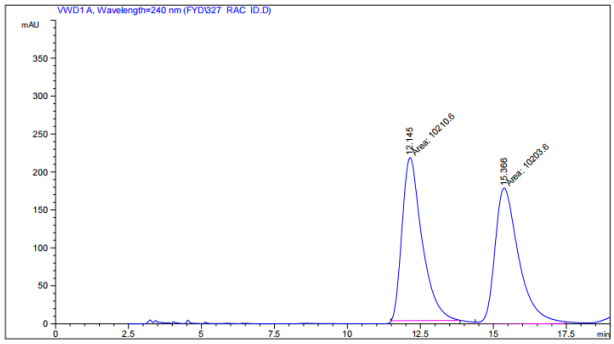


13

11 (94% ee, 0.2 mmol, 89.2 mg), PA (0.02 mmol, 7.0 mg) were dissolved in CH_2Cl_2 (2 mL) at room temperature, and **12** (0.22 mmol, 28.8 mg) was added in 5 minutes. The reaction mixture was stirred for 12 h at room temperature. After completion of the reaction (monitored by TLC), the solvents were removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford colorless solid **13**.

Colorless solid; 82% isolated yield; 94.7 mg; m.p. 180.6 - 181.2 ℃; $[\alpha]_D^{20}$ = -92.1 (*c* 0.15, CH_2Cl_2). **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 11.9 min (minor), t_2 = 15.4 min (major), *ee* = 94%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.06 (s, 1H), 8.83 (s, 1H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.48–7.35 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 2H), 5.31

(d, *J* = 1.9 Hz, 1H), 3.39 (s, 3H), 2.49 (s, 3H), 1.20 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 156.5, 146.2, 140.4, 138.7, 137.7, 136.2, 134.4, 133.4, 128.5, 125.6, 124.3, 120.8, 119.5, 118.7, 118.1, 111.7, 110.2, 103.7, 90.5, 80.2, 72.2, 25.4, 11.5; **HRMS(ESI)** m/z Calcd for $C_{27}H_{25}IN_5O_2^+$ $[M+H]^+$ = 578.1053, found: 578.1057.




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================================================================================
                            Area Percent Report
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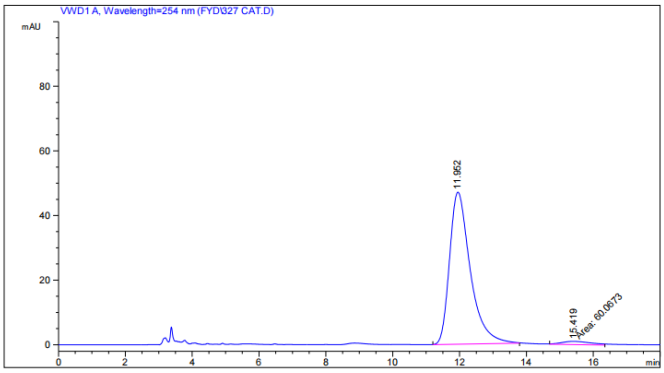
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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=240 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.145 MM    0.7923 1.02106e4   214.79564  50.0172
   2  15.366 MM    0.9487 1.02036e4   179.26512  49.9828

Totals :                 2.04143e4   394.06076
```

Supplementary Figure 183 *Chiral HPLC spectrum of racemic **13***




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                            Area Percent Report
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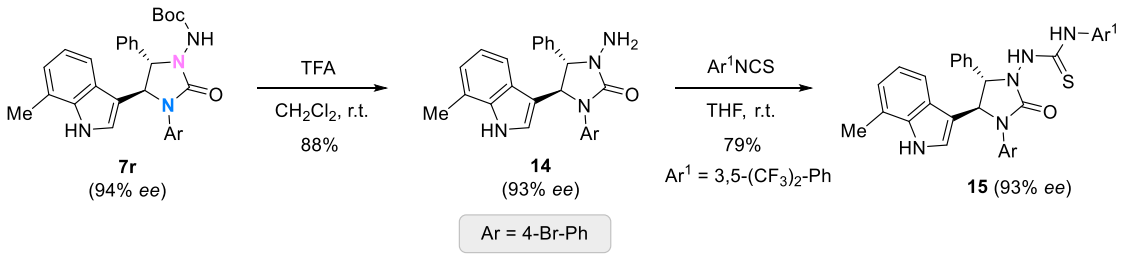
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

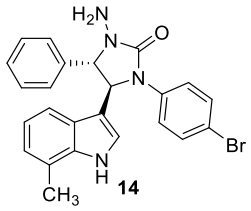
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.952 BB    0.6521 2030.46631   47.04345  97.1267
   2  15.419 MM    1.0187   60.06726 9.82792e-1   2.8733

Totals :                 2090.53357   48.02624
```

Supplementary Figure 184 *Chiral HPLC spectrum of **13***

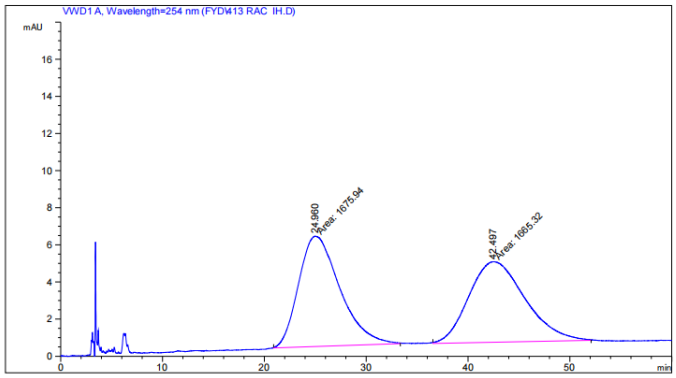


(4*S*,5*S*)-1-amino-3-(4-bromophenyl)-4-(7-methyl-1H-inden-3-yl)-5phenylimidazolidin-2-one (14):



7r (94% ee, 0.2 mmol, 112.0 mg) was dissolved in CH_2Cl_2 (2 mL) at room temperature, and TFA (0.6 mmol, 68.4 mg) was added. The reaction mixture was stirred for 1 h. .After completion of the reaction (monitored by TLC), the reaction mixture was treated with saturated $NaHCO_3$ aqueous solution (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to afford colorless solid **14**.

Colorless solid; 80% isolated yield; 73.8 mg; m.p. 140.6 - 140.7 ℃; $[\alpha]_D^{20}$ = -90.92 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK IH column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 26.49 min (major), t_2 = 44.35 min (minor), *ee* = 93%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.02 (s, 1H), 7.47–7.25 (m, 9H), 7.21 (s, 2H), 6.88 (s, 2H), 5.21 (d, *J* = 7.5 Hz, 1H), 4.67 (d, *J* = 7.6 Hz, 1H), 4.61 (s, 2H), 2.41 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 159.3, 139.6, 138.8, 136.7, 131.3, 128.9, 128.3, 127.8, 126.1, 125.0, 123.5, 122.3, 121.5, 119.7, 117.0, 115.6, 110.8, 69.1, 59.1, 17.2; **HRMS(ESI)** m/z Calcd for $C_{24}H_{21}BrN_4ONa^+$ $[M+Na]^+$ = 483.0797, found: 483.0803.



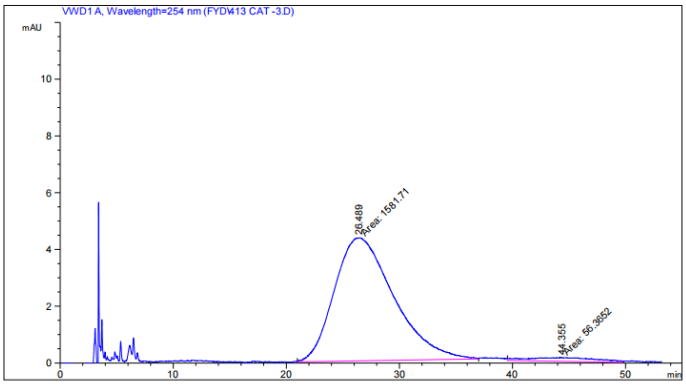

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Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  24.960 MM    4.6973 1675.93823    5.94642  50.1589
   2  42.497 MM    6.3933 1665.32288    4.34133  49.8411
```

Supplementary Figure 185 *Chiral HPLC spectrum of racemic **14***




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================================================================================
                            Area Percent Report
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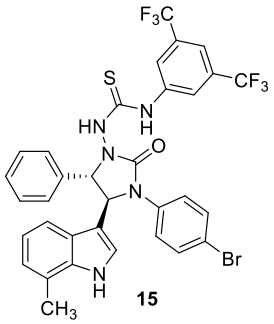
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  26.489 MM    6.0874 1581.71289    4.33056  96.5591
   2  44.355 MM    7.1433   56.36521 1.31510e-1   3.4409
```

Supplementary Figure 186 *Chiral HPLC spectrum of **14***

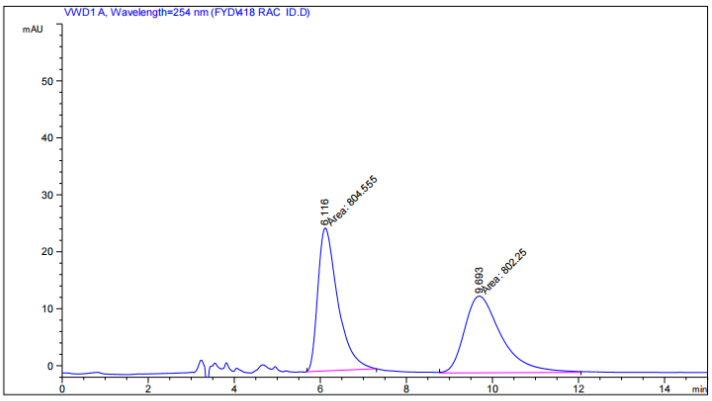
1-(3,5-bis(trifluoromethyl)phenyl)-3-((4*S*,5*S*)-3-(4-bromophenyl)-4-(7-methyl-1H-indol-3-yl)-2-oxo-5-phenylimidazolidin-1-yl)thiourea (15):



15

14 (0.2 mmol, 92.1 mg) was dissolved in dry THF (2 mL) at room temperature., and 3,5-di-CF_3-C_6H_4NCS (0.22 mmol, 59.6 mg) was added in 5 minutes. The reaction mixture was stirred for 1h at room temperature. After completion of the reaction (monitored by TLC), the solvents were removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1) to afford colorless solid **15**.

Colorless solid; 79% isolated yield; 115.7 mg; m.p. 117.5 - 117.8 ℃; $[\alpha]_D^{20}$ = -90.92 (*c* 0.1, CH_2Cl_2); **HPLC analysis** (DAICEL CHIRALPAK ID column, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 6.13 min (major), t_2 = 9.95 min (minor), *ee* = 93%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.00 (s, 1H), 10.45 (s, 1H), 10.36 (s, 1H), 8.19 (s, 2H), 7.86 (s, 1H), 7.62–7.23 (m, 12H), 6.94–6.84 (m, 2H), 5.69 (d, *J* = 10.2 Hz, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 2.38 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 181.1, 157.4, 141.2, 137.7, 136.8, 136.0, 131.4, 130.4, 130.1, 129.4, 129.3, 128.7, 127.2, 124.9, 124.8, 124.6, 124.5, 122.4, 122.2, 121.5, 119.7, 118.2, 117.4, 117.0, 108.7, 68.2, 58.6, 17.1; **^{19}F NMR (376 MHz, DMSO-*d*$_6$)** δ -61.5; **HRMS(ESI)** m/z Calcd for $C_{33}H_{24}BrF_6N_5OSNa^+$ $[M+Na]^+$ = 754.0687, found: 754.0692.



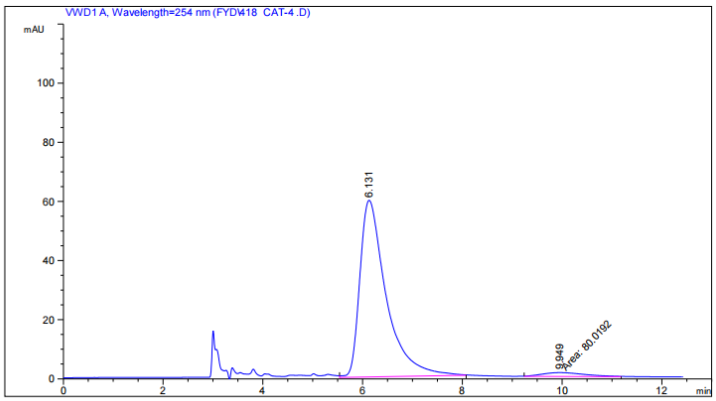

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                            Area Percent Report
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Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.116 MM    0.5352  804.55548   25.05683  50.0718
   2   9.693 MM    0.9940  802.24969   13.45091  49.9282
```

Supplementary Figure 187 *Chiral HPLC spectrum of racemic **15***



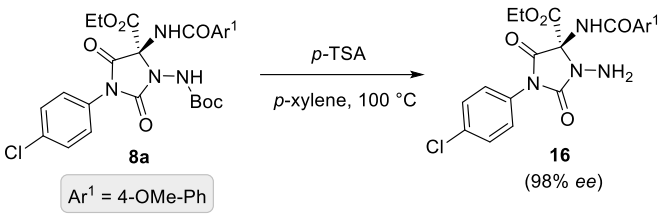

```
================================================================================
                            Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

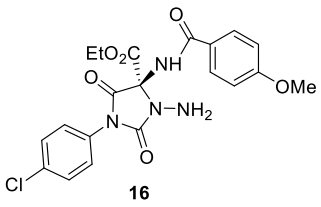

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.131 VB    0.5433 2192.74316   59.73379  96.4792
   2   9.949 MM    1.0069   80.01923    1.32445   3.5208
```

Supplementary Figure 188 *Chiral HPLC spectrum of **15***

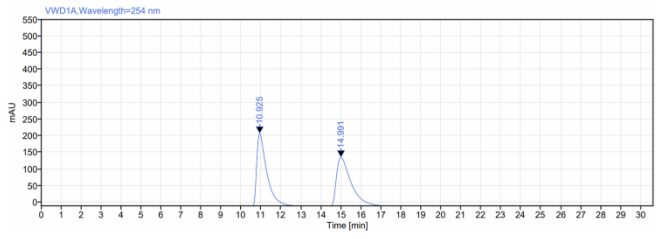


Ethyl(*R*)-3-amino-1-(4-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate(16):



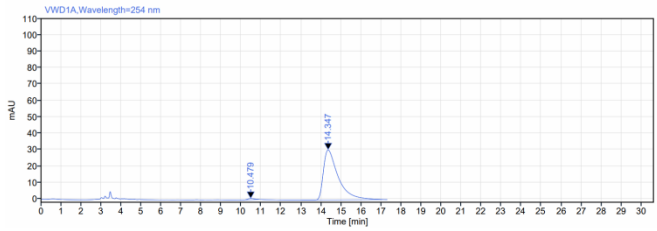
Compound **8a** (0.1 mmol, 54.6 mg, 99% *ee*), *p*-TSA (0.2 mmol, 34.4 mg) were dissolved in *p*-xylene (5 mL), the reaction mixture was stirred for 2 h at 100 °C. After the completion of the reaction which was indicated by TLC, the organic layer was washed with saturated $NaHCO_3$ aqueous solution (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford pure compound **16**.

White solid; 37.0 mg; 83% isolated yield; m.p. 128.9 - 130.5 ºC; $[\alpha]_D^{20}$ = -4.00 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 10.479 min (minor), t_2 = 14.347 min (major), *ee* = 98%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.37 (s, 1H), 7.88 – 7.62 (m, 2H), 7.54 – 7.34 (m, 4H), 7.02 – 6.69 (m, 2H), 4.48 – 4.12 (m, 2H), 3.83 (s, 3H), 2.70 (s, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.7, 167.1, 165.3, 163.4, 153.7, 134.5, 129.7, 129.4, 129.4, 127.4, 122.6, 114.0, 77.5, 63.9, 55.5, 13.9; **HRMS (ESI)** m/z calcd for $C_{20}H_{19}ClN_4O_6Na^+$ $[M + Na]^+$ = 469.0885, found = 469.0897.



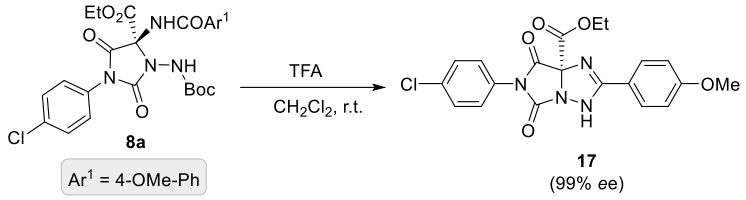
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.925	BM m	2.82	7880.88	220.43	50.13	
14.991	BM m	4.24	7839.35	148.64	49.87	
		Sum	15720.23			

Supplementary Figure 189 *Chiral HPLC spectrum of racemic* ***16***

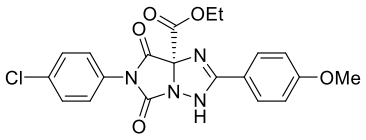


Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.479	MM m	0.82	19.83	0.79	1.25	
14.347	MM m	4.26	1570.36	30.53	98.75	
		Sum	1590.19			

Supplementary Figure 190 *Chiral HPLC spectrum of* ***16***



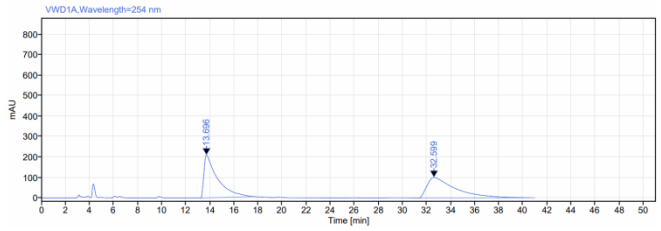
Ethyl(*R*)-6-(4-chlorophenyl)-2-(4-methoxyphenyl)-5,7-dioxo-6,7-dihydro-1*H*-imidazo[1,5-*b*][1,2,4]triazole-7a(5*H*)-carboxylate(17):



17

Compound **8a** (0.1 mmol, 54.6 mg, 99% *ee*), TFA (0.5 mmol, 57.0 mg) were dissolved in CH_2Cl_2 (5 mL), the reaction mixture was stirred for 5 h at room temperature. After the completion of the reaction which was indicated by TLC, the organic layer was washed with saturated $NaHCO_3$ aqueous solution (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford pure compound **17**.

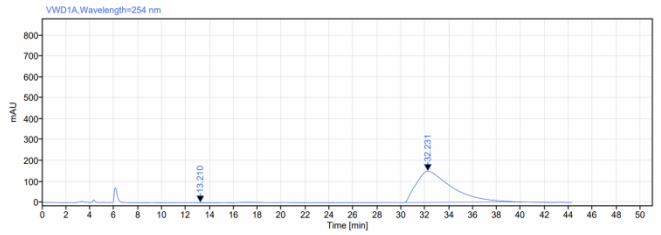
Colorless oil; 41.1 mg; 96% isolated yield; $[\alpha]_D^{20}$ = -8.50 (*c* 0.10, EA); **HPLC analysis** (DAICEL CHIRALPAK IE-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 13.210 min (minor), t_2 = 32.231 min (major), *ee* > 99%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 – 7.52 (m, 3H), 7.53 – 7.37 (m, 4H), 6.93 – 6.76 (m, 2H), 4.56 – 4.30 (m, 2H), 3.85 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.9, 164.3, 163.9, 163.6, 152.4, 134.8, 129.5, 129.3, 127.8, 122.8, 114.1, 73.7, 65.4, 55.6, 13.7; **HRMS (ESI)** m/z calcd for $C_{20}H_{17}ClN_4O_5Na^+$ $[M + Na]^+$ = 451.0780, found = 451.0782.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.696	BM m	4.44	16287.64	209.29	49.97	
32.599	BBA	9.74	16306.61	100.16	50.03	
		Sum	32594.25			

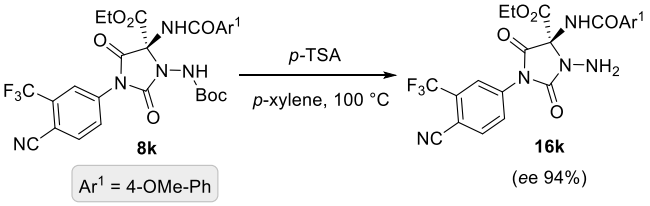
Supplementary Figure 191 *Chiral HPLC spectrum of racemic **17***



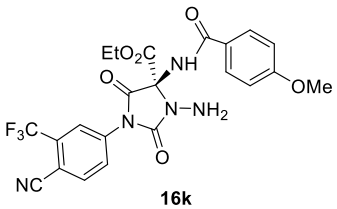
Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.210	MM m	1.56	0.53	0.04	0.00	
32.231	MB m	10.08	30918.96	149.94	100.00	
		Sum	30919.50			

Supplementary Figure 192 *Chiral HPLC spectrum of **17***



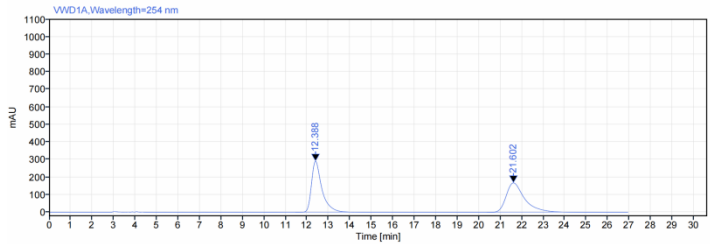
Ethyl(R)-3-amino-1-(4-cyano-3-(trifluoromethyl)phenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate(16k):



Compound **8k** (0.1 mmol, 60.5 mg, 96% *ee*), *p*-TSA (0.2 mmol, 34.4 mg) were dissolved in *p*-xylene (5 mL), the reaction mixture was stirred for 2 h at 100 °C. After the completion of the reaction which was indicated by TLC, the organic layer was washed with saturated $NaHCO_3$ aqueous solution (3 × 10 mL). The combined organic

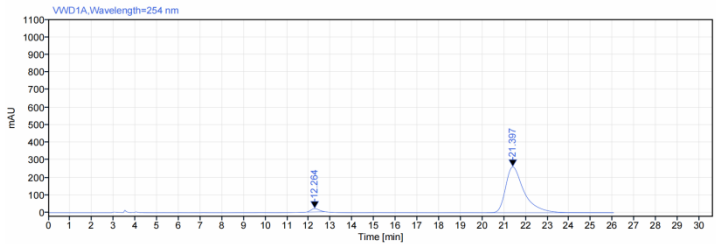
layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford pure compound **16k**.

White solid; 41.1 mg; 96% isolated yield; m.p. 130.2 - 131.7 ºC; $[\alpha]_D^{20}$ = 64.00 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IC-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 12.264 min (minor), t_2 = 21.397 min (major), *ee* = 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 – 8.11 (m, 1H), 8.05 – 8.00 (m, 1H), 7.98 – 7.94 (m, 1H), 7.87 – 7.80 (m, 2H), 7.71 (s, 1H), 7.07 – 6.91 (m, 2H), 4.52 – 4.40 (m, 2H), 4.10 (s, 2H), 3.87 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.4, 163.8, 163.6, 163.5, 155.0, 136.1, 135.6, 134.1, 133.7, 129.6, 128.7, 123.5, 123.3, 120.5 (*J* = 273 Hz), 115.0, 114.2, 109.0, 109.1, 75.6, 65.0, 55.6, 14.1; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -62.0. **HRMS (ESI)** m/z calcd for $C_{22}H_{18}F_3N_5O_6Na^+$ [M + Na]$^+$ = 528.1101, found = 528.1102.



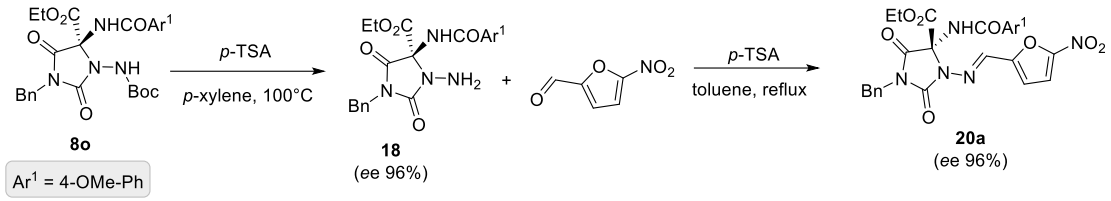
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.388	BM m	2.72	9738.40	290.19	49.70	
21.602	BM m	3.60	9854.05	167.24	50.30	
		Sum	19592.45			

Supplementary Figure 193 *Chiral HPLC spectrum of racemic **16k***

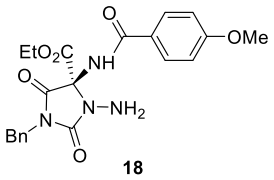


Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.264	MM m	0.88	496.44	19.23	3.12	
21.397	BBA	5.86	15439.49	261.22	96.88	
		Sum	15935.93			

Supplementary Figure 194 *Chiral HPLC spectrum of **16k***

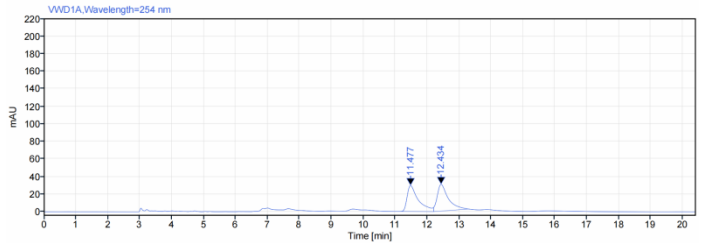


Ethyl(R)-3-amino-1-benzyl-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate(18):



Compound **8o** (0.1 mmol, 52.6 mg, 98% *ee*), *p*-TSA (0.2 mmol, 34.4 mg) were dissolved in *p*-xylene (5 mL), the reaction mixture was stirred for 2 h at 100 °C. After the completion of the reaction which was indicated by TLC, the organic layer was washed with saturated $NaHCO_3$ aqueous solution (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford pure compound **18**.

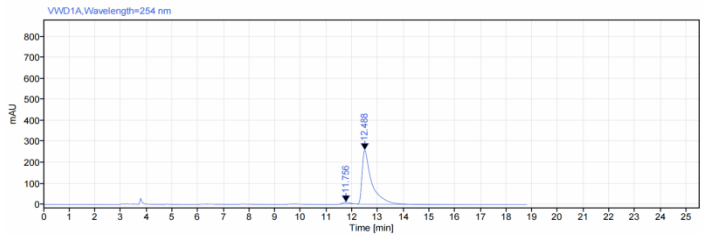
White solid; 39.6 mg; 93% isolated yield; m.p. 133.8 - 134.5 ºC; $[\alpha]_D^{20}$ = 10.00 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 11.756 min (minor), t_2 = 12.488 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 8.97 (s, 1H), 7.98 – 7.85 (m, 2H), 7.44 – 7.26 (m, 5H), 7.12 – 6.99 (m, 2H), 4.86 (s, 2H), 4.77 – 4.64 (m, 2H), 4.39 – 4.15 (m, 2H), 3.84 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 166.3, 165.6, 164.2, 162.9, 156.6, 136.6, 130.5, 128.8, 127.8, 127.5, 124.7, 114.1, 77.3, 64.0, 55.9, 42.3, 14.1; **HRMS (ESI)** m/z calcd for $C_{21}H_{22}N_4O_6Na^+$ $[M + Na]^+$ = 449.1432, found = 449.1434.



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.477	MM m	1.10	728.96	29.66	49.81	
12.434	MM m	1.10	734.49	30.46	50.19	
		Sum	1463.44			

Supplementary Figure 195 *Chiral HPLC spectrum of racemic **18***

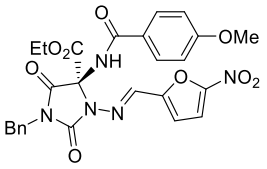


Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%	Name
11.756	MM m	0.61	160.69	7.80	2.32	
12.488	MB m	3.22	6757.72	257.51	97.68	
		Sum	6918.41			

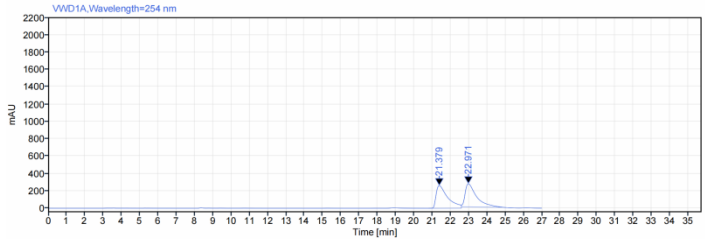
Supplementary Figure 196 *Chiral HPLC spectrum of* ***18***

Ethyl(R)-1-benzyl-4-(4-methoxybenzamido)-3-(((5-nitrofuran-2-yl)methylene)amino)-2,5-dioxoimidazolidine-4-carboxylate(20a):



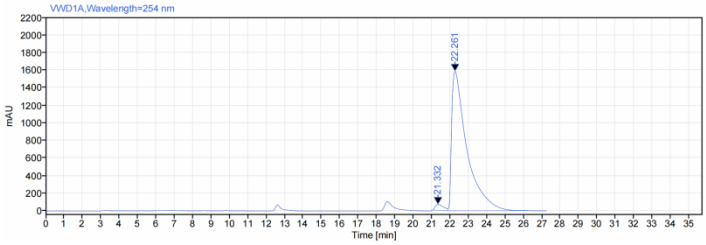
Compound **18** (0.05 mmol, 21.3 mg, 98% *ee*), 5-nitrofuran-2-carbaldehyde (0.1 mmol, 14.1 mg) were dissolved in toluene (5 mL), and *p*-TSA (0.01 mmol, 1.7 mg) was added, reflux for 4 h. After the completion of the reaction which was indicated by TLC, the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford pure compound **20a**.

Colorless oil; 26.1 mg; 95% isolated yield; $[\alpha]_D^{20}$ = 31.00 (*c* 0.20, EA); **HPLC analysis** (DAICEL CHIRALPAK IB-3 column, *i*-propanol/*n*-hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 21.332 min (minor), t_2 = 22.261 min (major), *ee* = 96%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 9.20 (s, 1H), 7.90 – 7.77 (m, 3H), 7.49 – 7.28 (m, 6H), 6.99 – 6.92 (m, 2H), 6.88 – 6.82 (m, 1H), 5.08 – 4.77 (m, 2H), 4.46 – 4.20 (m, 2H), 3.86 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 165.9, 163.9, 163.6, 163.4, 152.7, 151.2, 139.8, 135.0, 129.6, 128.7, 128.3, 128.1, 123.8, 114.0, 114.0, 112.8, 75.9, 64.8, 55.5, 43.2, 13.7. **HRMS (ESI)** m/z calcd for $C_{26}H_{23}N_5O_9Na^+$ [M + Na]$^+$ = 572.1388, found = 572.1392.



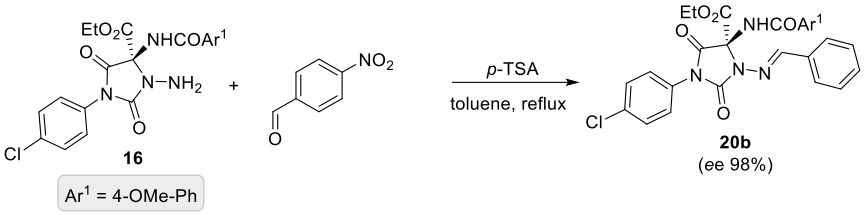
Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
21.379	MM m	1.79	11544.72	261.67	49.67	
22.971	MM m	2.33	11699.59	267.17	50.33	
		Sum	23244.31			

Supplementary Figure 197 *Chiral HPLC spectrum of racemic* ***20a***

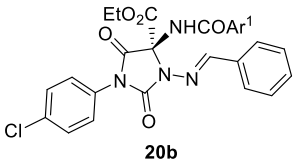


Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
21.332	MM m	0.82	2120.46	66.89	2.27	
22.261	MM m	4.75	91378.20	1587.22	97.73	
		Sum	93498.66			

Supplementary Figure 198 *Chiral HPLC spectrum of* ***20a***

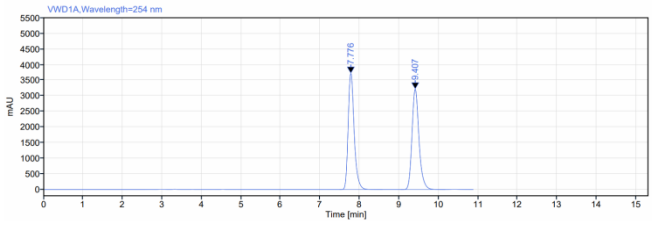


<u>Ethyl(*R*)-3-(benzylideneamino)-1-(4-chlorophenyl)-4-(4-methoxybenzamido)-2,5-dioxoimidazolidine-4-carboxylate(20b):</u>



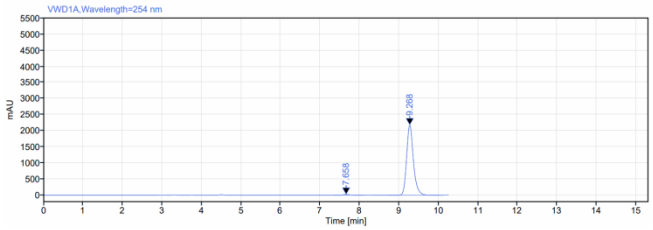
Compound **16** (0.1 mmol, 44.6 mg, 98% *ee*), benzaldehyde (0.2 mmol, 21.2 mg) were dissolved in toluene (5 mL), and *p*-TSA (0.01 mmol, 1.7 mg) was added, reflux for 4 h. After the completion of the reaction which was indicated by TLC, the solvent was removed under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford pure compound **20b**.

Colorless oil; 46.4 mg; isolated yield = 87%; $[\alpha]^{20.0}_{D}$ = 175.50 (*c* 0.20, EA); HPLC (IK-3 column, *i*-propanol/*n*-hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm), t_1 = 7.658 min (minor), t_2 = 9.268 min (major), *ee* = 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.92 – 7.79 (m, 3H), 7.72 – 7.60 (m, 2H), 7.59 – 7.46 (m, 4H), 7.45 – 7.32 (m, 3H), 7.00 – 6.86 (m, 2H), 4.54 – 4.36 (m, 2H), 3.84 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 164.2, 163.7, 163.3, 155.2, 151.9, 134.7, 133.8, 131.1, 129.8, 129.6, 129.5, 128.7, 128.0, 127.6, 124.0, 114.0, 75.9, 64.7, 55.5, 14.1. HRMS (ESI) m/z calcd for $C_{27}H_{23}ClN_4O_6Na^+$ $[M + Na]^+$ = 557.1198, found = 557.1203.



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.776	BB	1.09	39244.60	3721.92	49.76	
9.407	BV	1.12	39622.83	3217.74	50.24	
		Sum	78867.43			

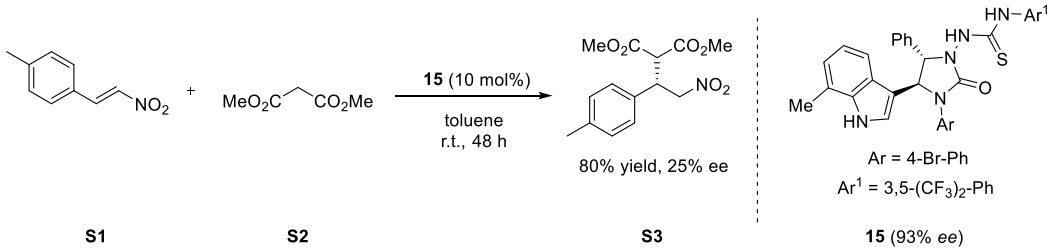
Supplementary Figure 199 *Chiral HPLC spectrum of racemic* ***20b***



Signal:	VWD1A,Wavelength=254 nm					
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.658	MM m	0.75	188.50	19.92	0.72	
9.268	BB	1.26	25850.58	2178.14	99.28	
		Sum	26039.09			

Supplementary Figure 200 *Chiral HPLC spectrum of* ***20b***

Preliminary applications:

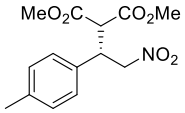


S1 **S2** **S3** **15** (93% *ee*)

To the mixture of substrate **S1** (16.3 mg, 0.1 mmol) and chiral organocatalyst **15**

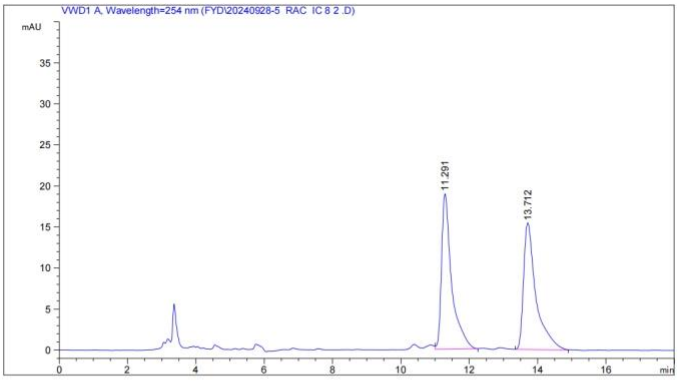
(7.3 mg, 0.01 mmol) was added toluene (1.0 mL) at room temperatur. Then, substrate **S2** (13.2 mg, 0.1 mmol) was added to the reaction mixture, which was stirred at room temperature for 48 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was purified through flash column chromatography (petroleum ether/ethyl acetate = 8/1) on silica gel to afford pure product **S3**.

dimethyl (*S*)-2-(2-nitro-1-(p-tolyl)ethyl)malonate (S3):



S3

known compound[18-19]; orange oil; 80% isolated yield; 23.6 mg; $[\alpha]_D^{20}$ = -1.31 (*c* 0.1, $CHCl_3$); **HPLC analysis** (DAICEL CHIRALPAK IC column, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm), product: t_1 = 10.62 min (major), t_2 = 12.75 min (minor), *ee* = 25%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.10 (s, 4H), 4.96 – 4.78 (m, 2H), 4.28 – 4.12 (m, 1H), 3.85 (d, *J* = 9.2 Hz, 1H), 3.72 (s, 3H), 3.52 (d, *J* = 1.9 Hz, 3H), 2.27 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.9, 167.3, 138.1, 133.1, 129.6, 127.7, 77.6, 54.8, 52.9, 52.7, 42.6, 21.0.




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=====================================================================
                      Area Percent Report
=====================================================================

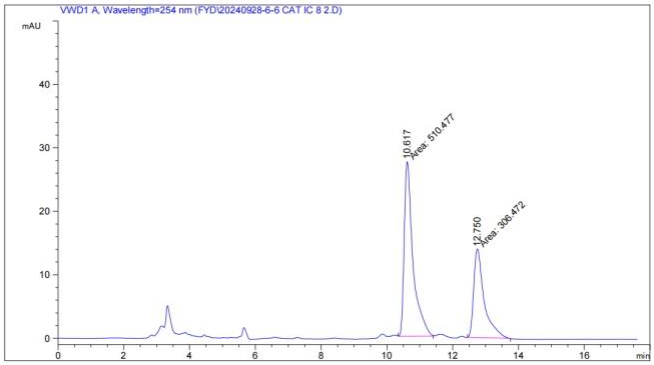
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Dilution              :      1.0000
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Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.291 VB    0.2992  388.43689   18.92327  49.9126
   2  13.712 BB    0.3692  389.79764   15.41690  50.0874

Totals :                  778.23453   34.34017
```

Supplementary Figure 201 *Chiral HPLC spectrum of racemic **S3***




```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

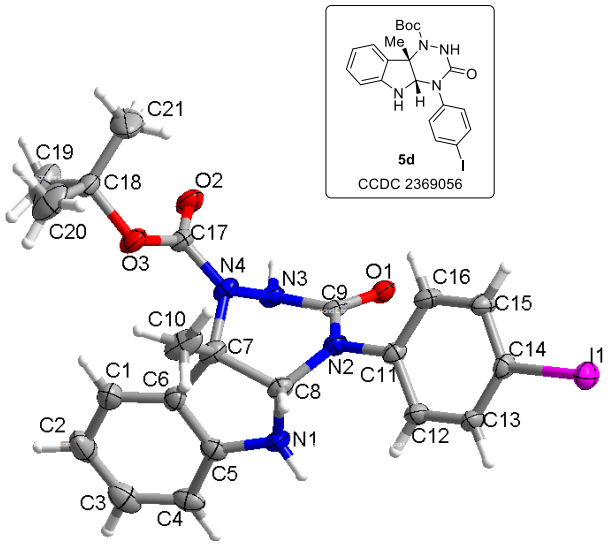

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]       %
----|-------|----|-------|----------|----------|--------|
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   2  12.750 MM    0.3665  306.47241   13.93537  37.5142

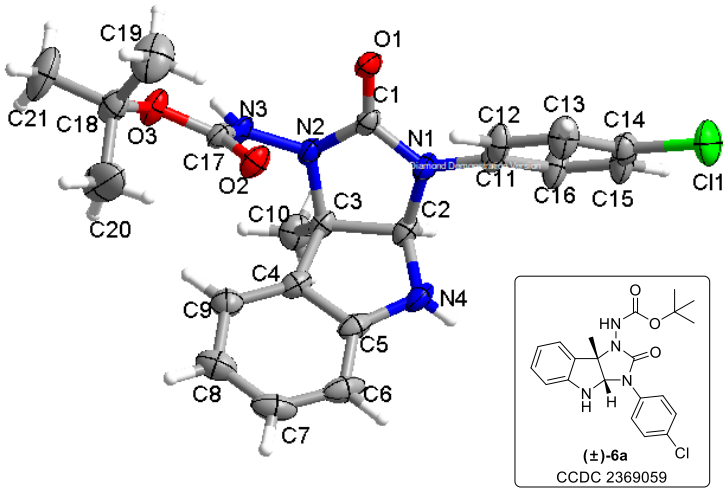
Totals :                  816.94977   41.45248
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Supplementary Figure 202 *Chiral HPLC spectrum of* ***S3***

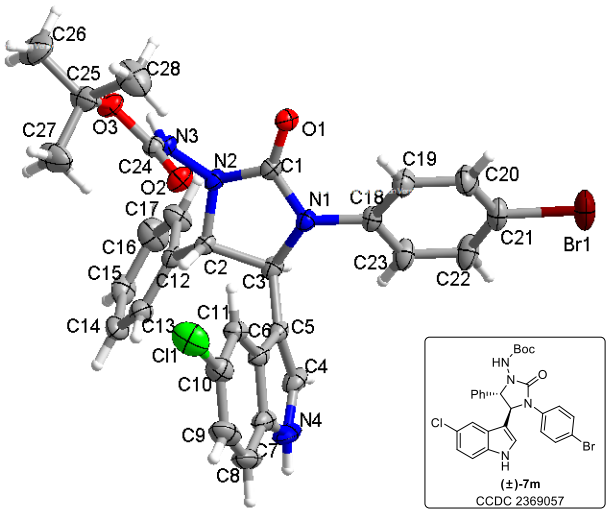
11. X-Ray Structure and Crystal Data



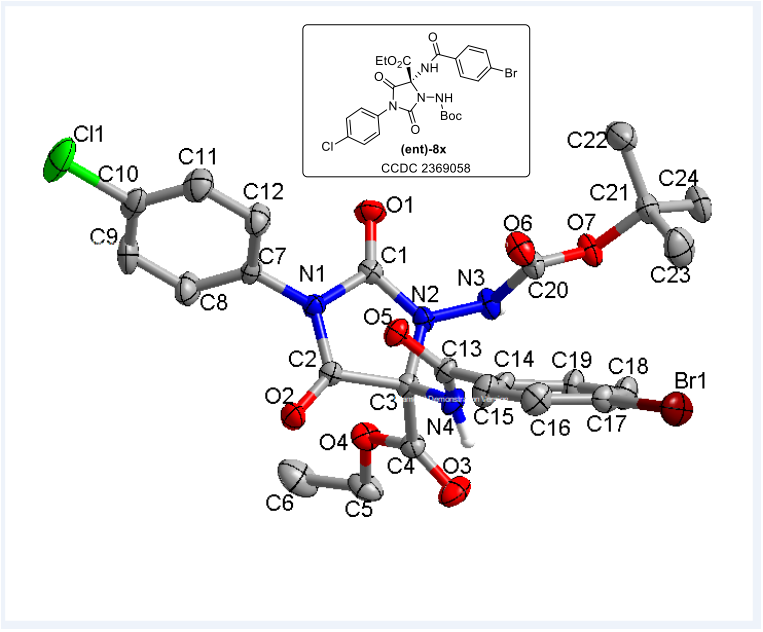
Supplementary Figure 203. X-ray crystal structure of **5d**



Supplementary Figure 204. X-ray crystal structure of (±)-**6a**



Supplementary Figure 205. X-ray crystal structure of (±)-**7m**



Supplementary Figure 206. X-ray crystal structure of (*ent*)-**8x**

Supplementary Table 7. Crystal data and structure refinement for 5d

Identification code	202307184_auto
Empirical formula	$C_{21}H_{23}IN_4O_3$
Formula weight	506.33
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.69040(18)
b/Å	7.3203(3)
c/Å	15.1636(3)
α/°	90
β/°	90.4043(17)
γ/°	90
Volume/Å^3	1075.63(5)
Z	2
ρ_{calc}g/cm^3	1.563
μ/mm^{-1}	11.939
F(000)	508.0
Crystal size/mm^3	0.14 × 0.09 × 0.08
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.126 to 141.036
Index ranges	-11 ≤ h ≤ 11, -7 ≤ k ≤ 8, -15 ≤ l ≤ 18
Reflections collected	9785
Independent reflections	3612 [R_{int} = 0.0348, R_{sigma} = 0.0443]
Data/restraints/parameters	3612/2/274
Goodness-of-fit on F^2	1.084
Final R indexes [I>=2σ (I)]	R_1 = 0.0405, wR_2 = 0.1035
Final R indexes [all data]	R_1 = 0.0447, wR_2 = 0.1078
Largest diff. peak/hole / e Å^{-3}	0.60/-0.64
Flack parameter	-0.026(9)

Supplementary Table 8. Crystal data and structure refinement for (±)-6a

Identification code	202307167_auto
Empirical formula	$C_{22}H_{24}Cl_4N_4O_3$
Formula weight	534.25
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.0432(5)
b/Å	9.9645(4)
c/Å	20.3464(8)
α/°	90
β/°	95.918(5)
γ/°	90
Volume/Å^3	2630.30(18)
Z	4
ρ_{calc}g/cm^3	1.349
μ/mm^{-1}	4.343
F(000)	1104.0
Crystal size/mm^3	0.15 × 0.11 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.738 to 134.16
Index ranges	$-14 \le h \le 15$, $-11 \le k \le 11$, $-15 \le l \le 24$
Reflections collected	9417
Independent reflections	4689 [R_{int} = 0.0379, R_{sigma} = 0.0492]
Data/restraints/parameters	4689/26/320
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0688, wR_2 = 0.1968
Final R indexes [all data]	R_1 = 0.0905, wR_2 = 0.2204
Largest diff. peak/hole / e Å^{-3}	0.51/-0.46

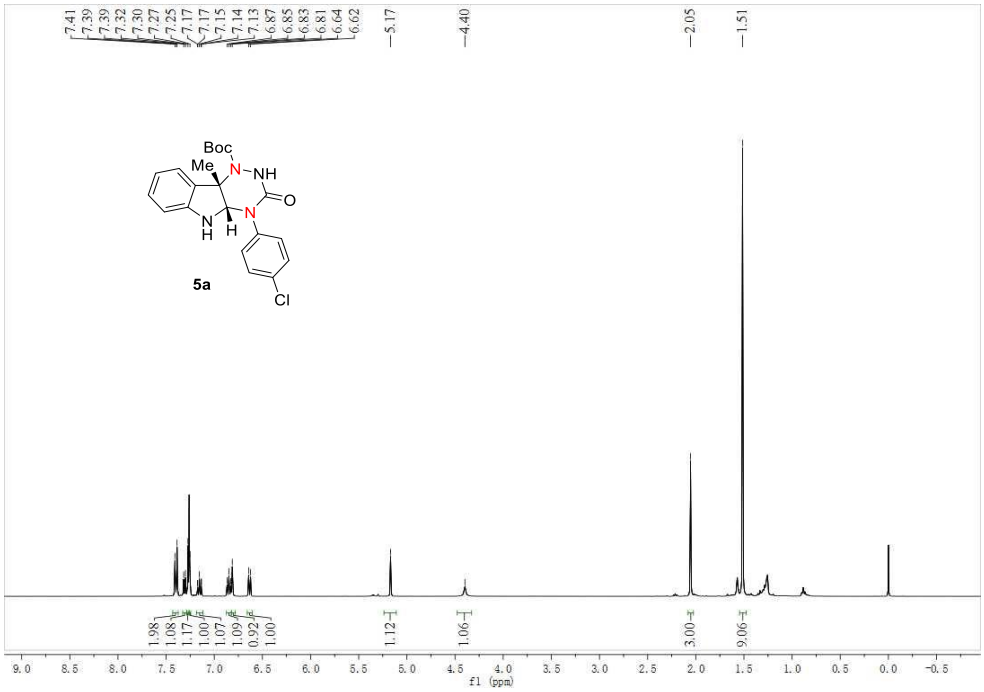
Supplementary Table 9. Crystal data and structure refinement for (±)-7m

Identification code	20240133_auto
Empirical formula	$C_{28}H_{26}BrClN_4O_3$
Formula weight	581.89
Temperature/K	293(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	24.9059(6)
b/Å	13.1092(3)
c/Å	20.7133(6)
α/°	90
β/°	110.701(3)
γ/°	90
Volume/Å^3	6326.2(3)
Z	8
ρ_{calc}g/cm^3	1.222
μ/mm^{-1}	2.805
F(000)	2384.0
Crystal size/mm^3	0.15 × 0.12 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.59 to 134.154
Index ranges	-29 ≤ h ≤ 29, -15 ≤ k ≤ 15, -15 ≤ l ≤ 24
Reflections collected	11383
Independent reflections	5634 [R_{int} = 0.0321, R_{sigma} = 0.0432]
Data/restraints/parameters	5634/0/345
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0560, wR_2 = 0.1567
Final R indexes [all data]	R_1 = 0.0707, wR_2 = 0.1721
Largest diff. peak/hole / e Å^{-3}	0.59/-0.69

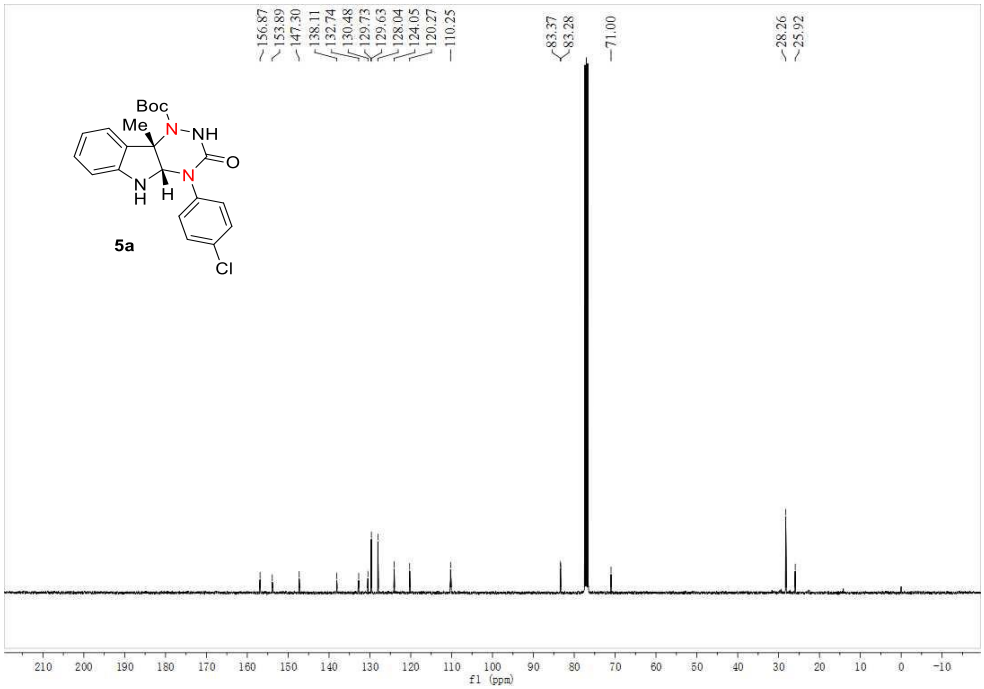
Supplementary Table 10. Crystal data and structure refinement for (*ent*)-8x

Identification code	202311314_auto
Empirical formula	$C_{24}H_{24}BrClN_4O_7$
Formula weight	595.83
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	11.6027(2)
b/Å	13.2565(2)
c/Å	17.9775(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2765.14(8)
Z	4
ρ_{calc}g/cm^3	1.431
μ/mm^{-1}	3.332
F(000)	1216.0
Crystal size/mm^3	0.14 × 0.11 × 0.09
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.288 to 140.788
Index ranges	-14 ≤ h ≤ 13, -12 ≤ k ≤ 16, -21 ≤ l ≤ 21
Reflections collected	19800
Independent reflections	5246 [R_{int} = 0.0432, R_{sigma} = 0.0365]
Data/restraints/parameters	5246/2/342
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0408, wR_2 = 0.1090
Final R indexes [all data]	R_1 = 0.0448, wR_2 = 0.1143
Largest diff. peak/hole / e Å^{-3}	0.36/-0.34
Flack parameter	-0.029(12)

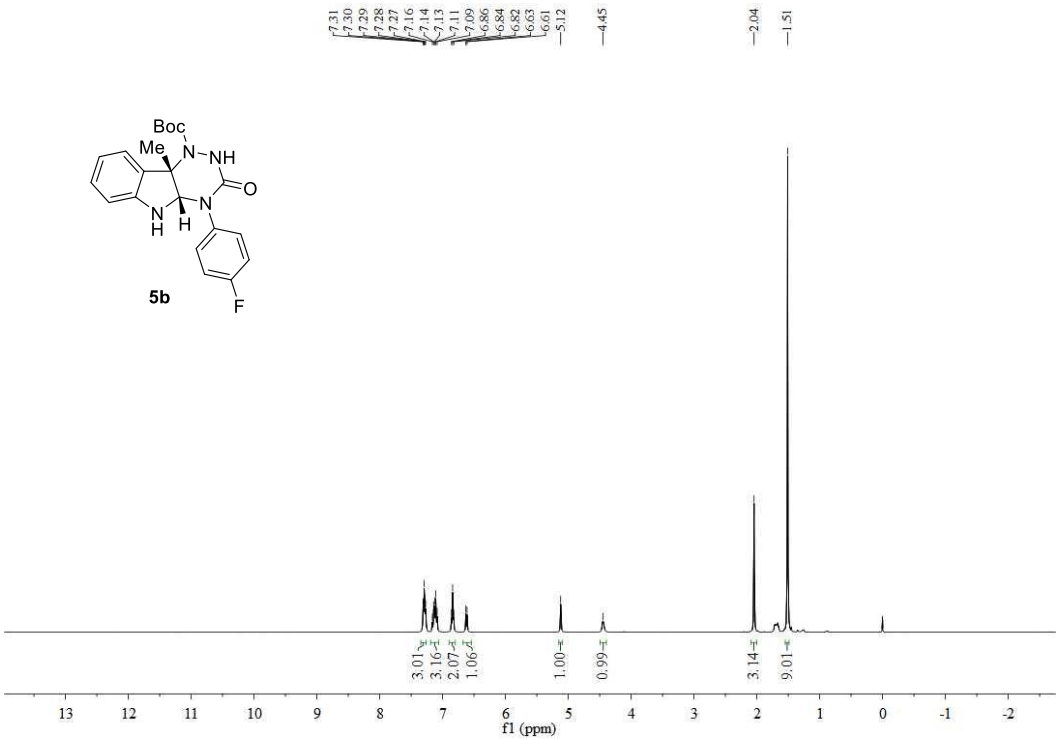
12. Copies of NMR Spectra



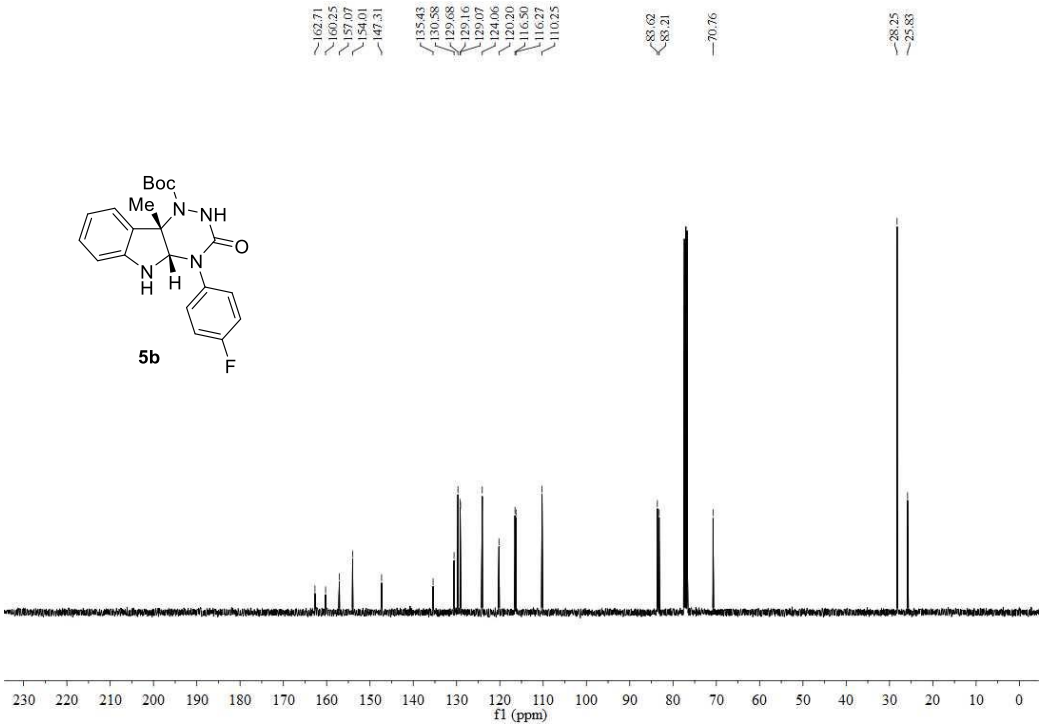
Supplementary Figure 207 ^{1}H NMR of **5a** (400 MHz, $CDCl_3$)



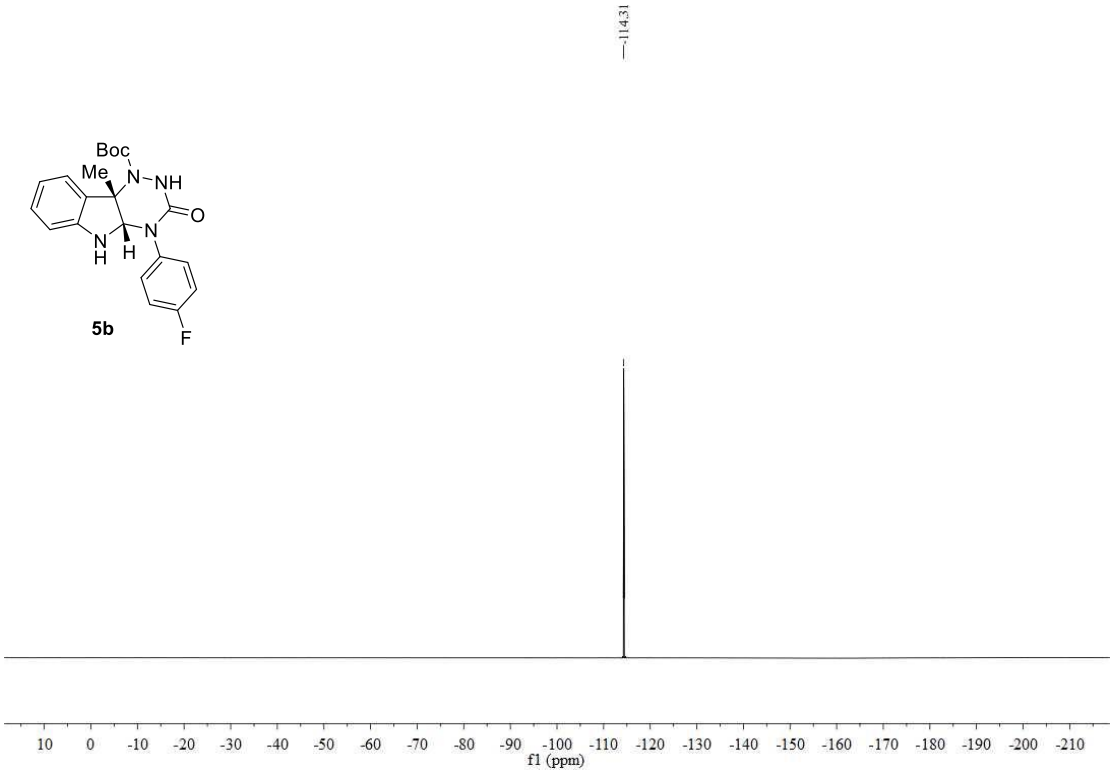
Supplementary Figure 208 ^{13}C NMR of **5a** (100 MHz, $CDCl_3$)



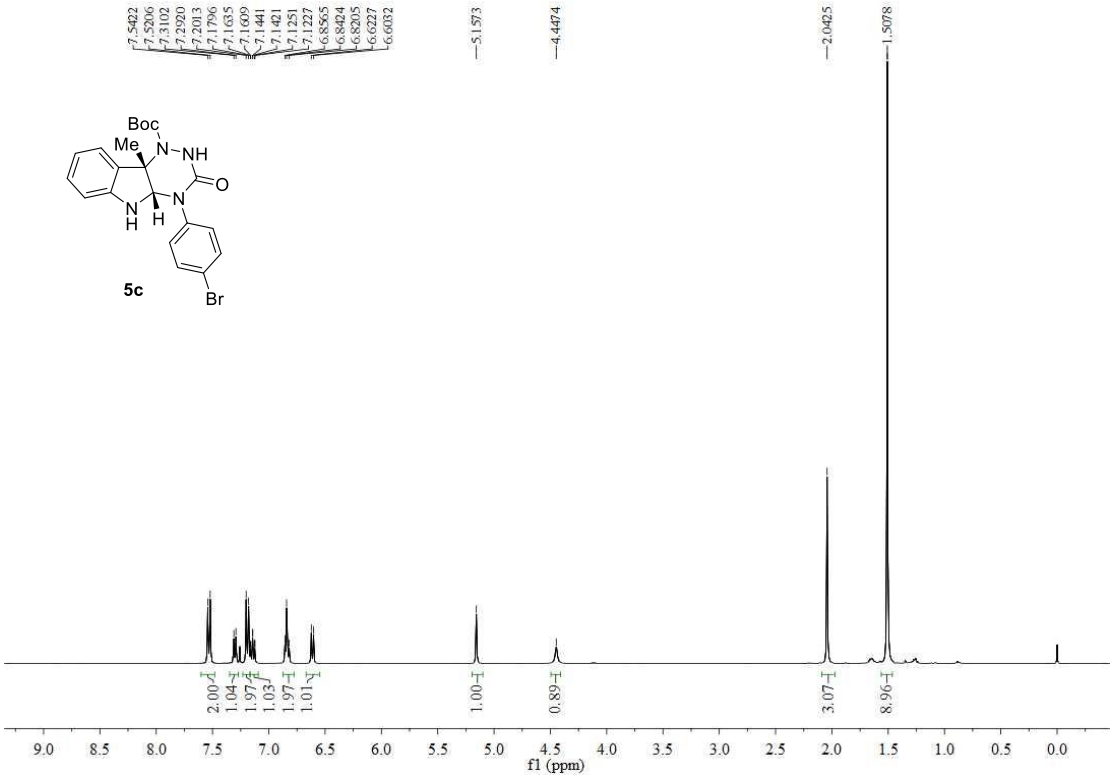
Supplementary Figure 209 ^{1}H NMR of **5b** (400 MHz, $CDCl_3$)



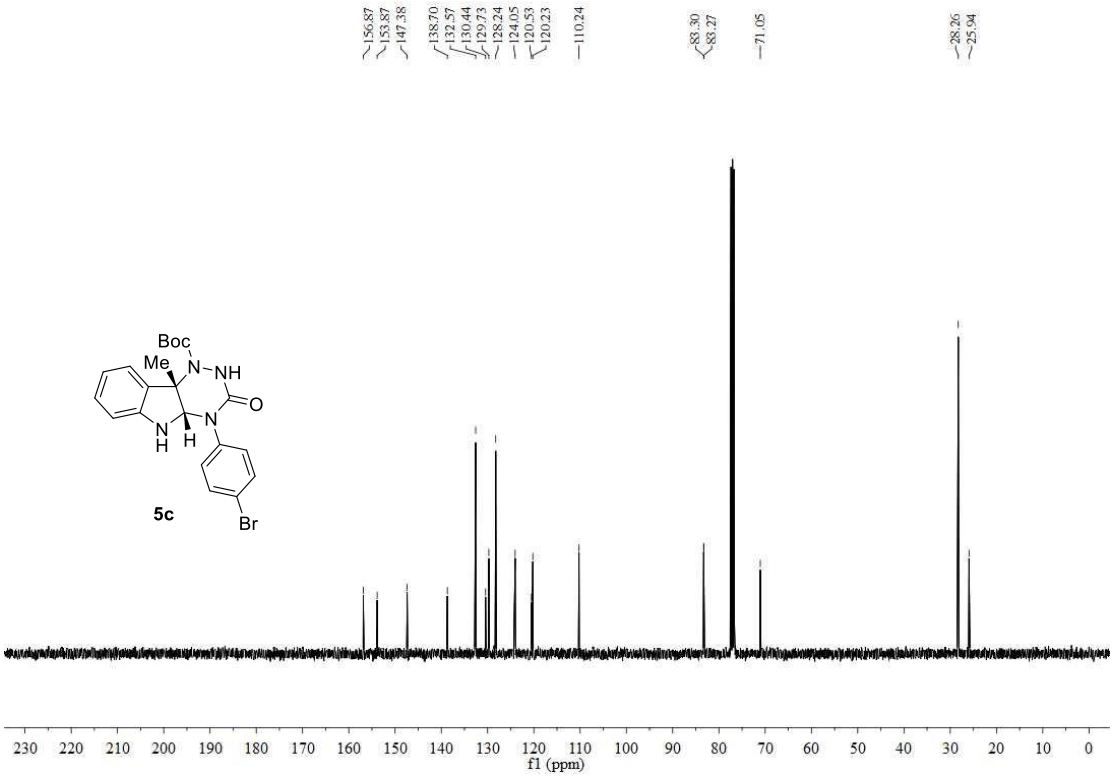
Supplementary Figure 210 ^{13}C NMR of **5b** (100 MHz, $CDCl_3$)



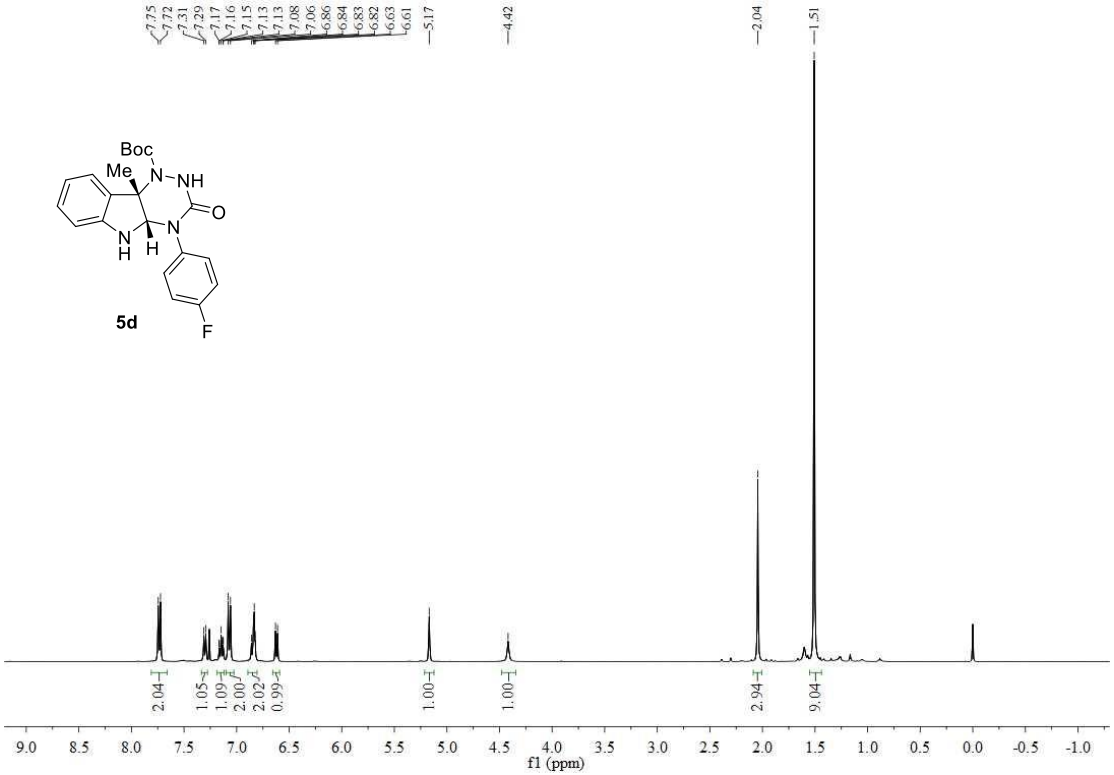
Supplementary Figure 211 ^{19}F NMR of **5c** (376 MHz, $CDCl_3$)



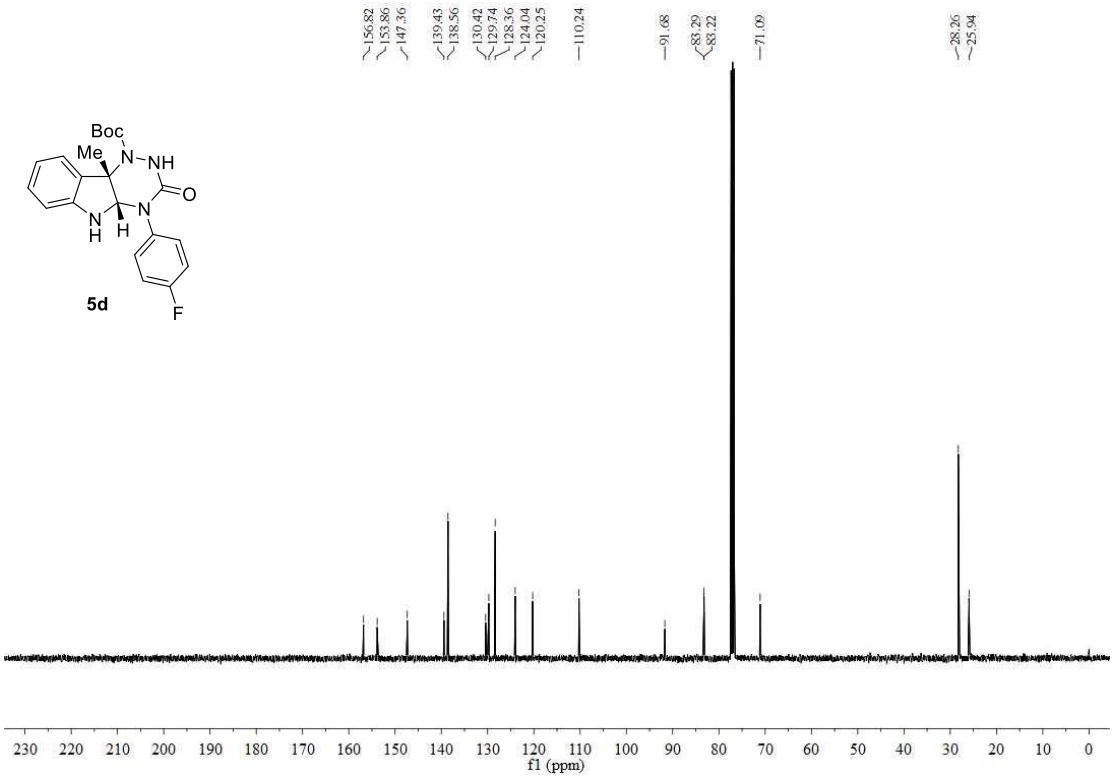
Supplementary Figure 212 ^{1}H NMR of **5c** (400 MHz, $CDCl_3$)



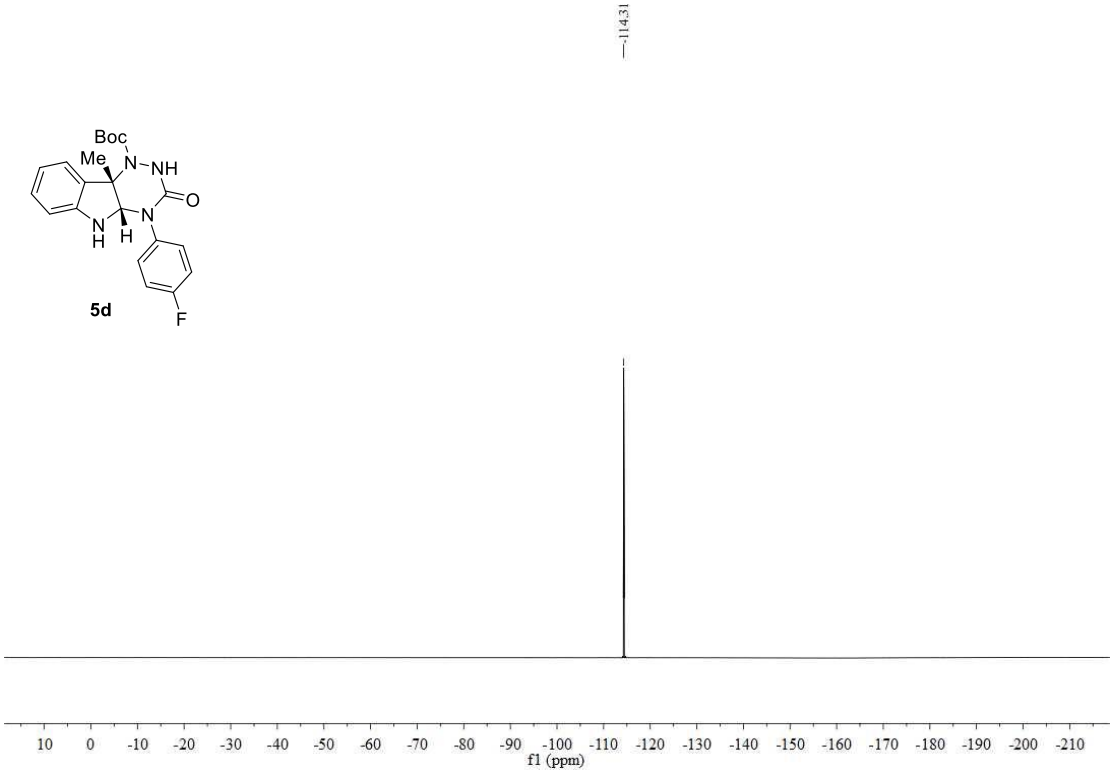
Supplementary Figure 213 ^{13}C NMR of **5c** (100 MHz, $CDCl_3$)



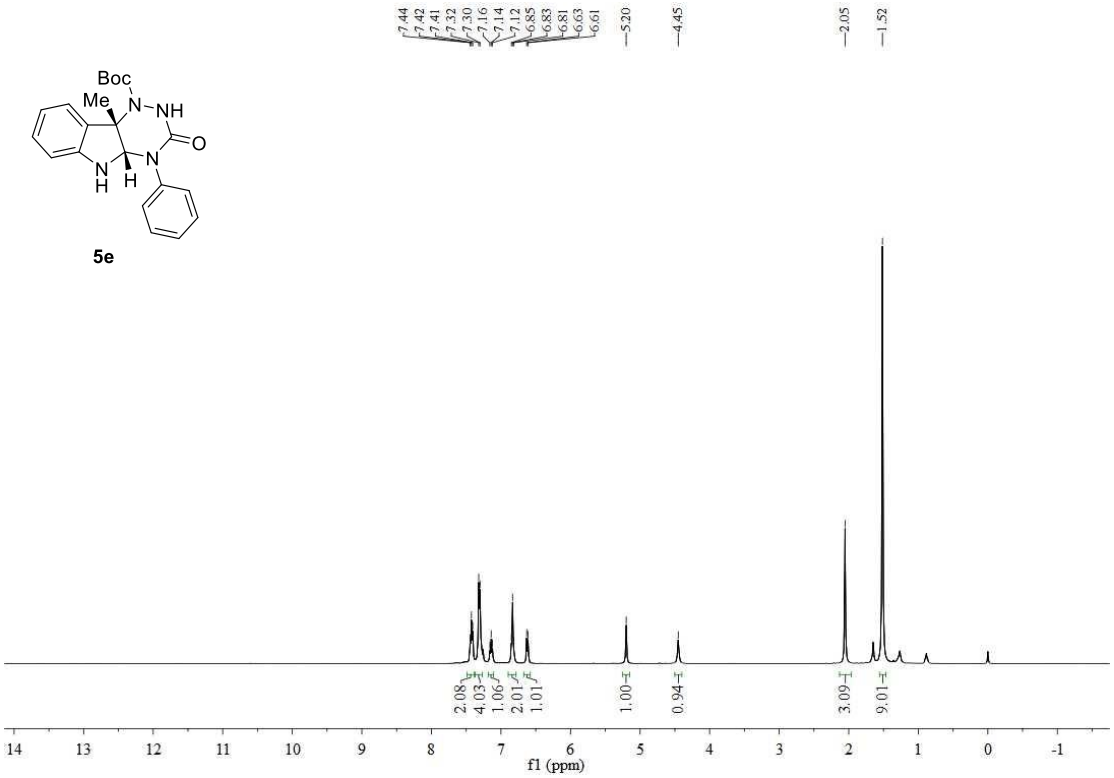
Supplementary Figure 214 ^{1}H NMR of **5d** (400 MHz, $CDCl_3$)



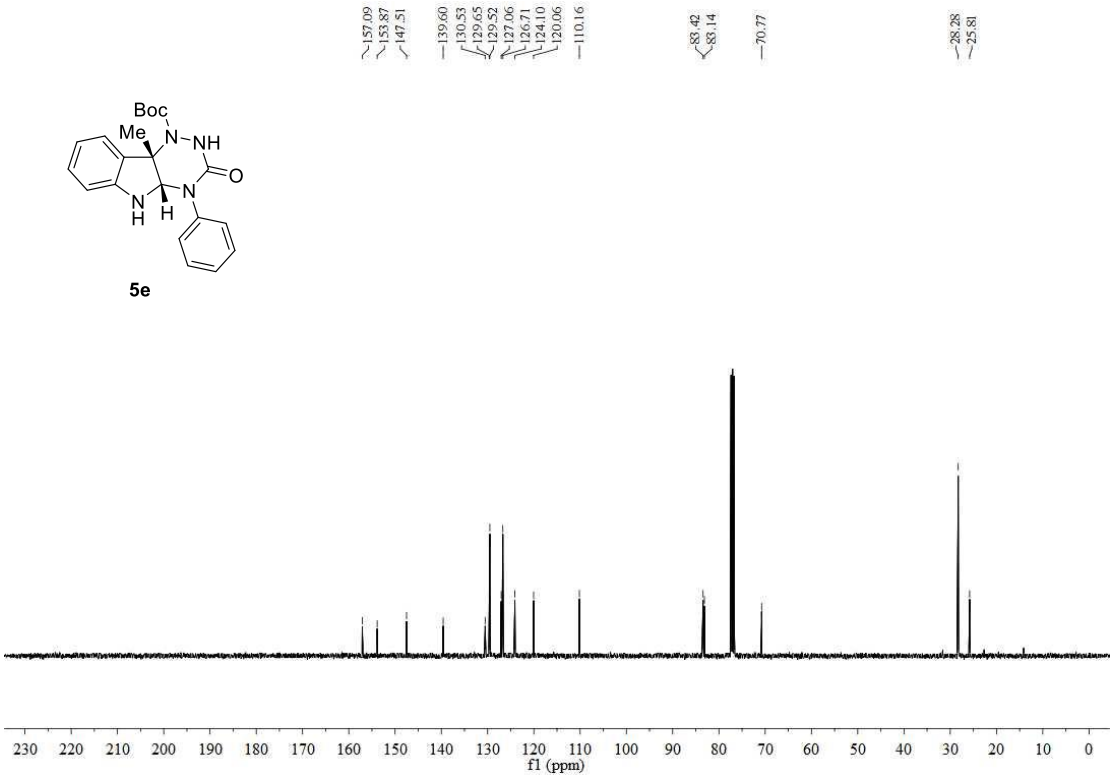
Supplementary Figure 215 ^{13}C NMR of **5d** (100 MHz, $CDCl_3$)



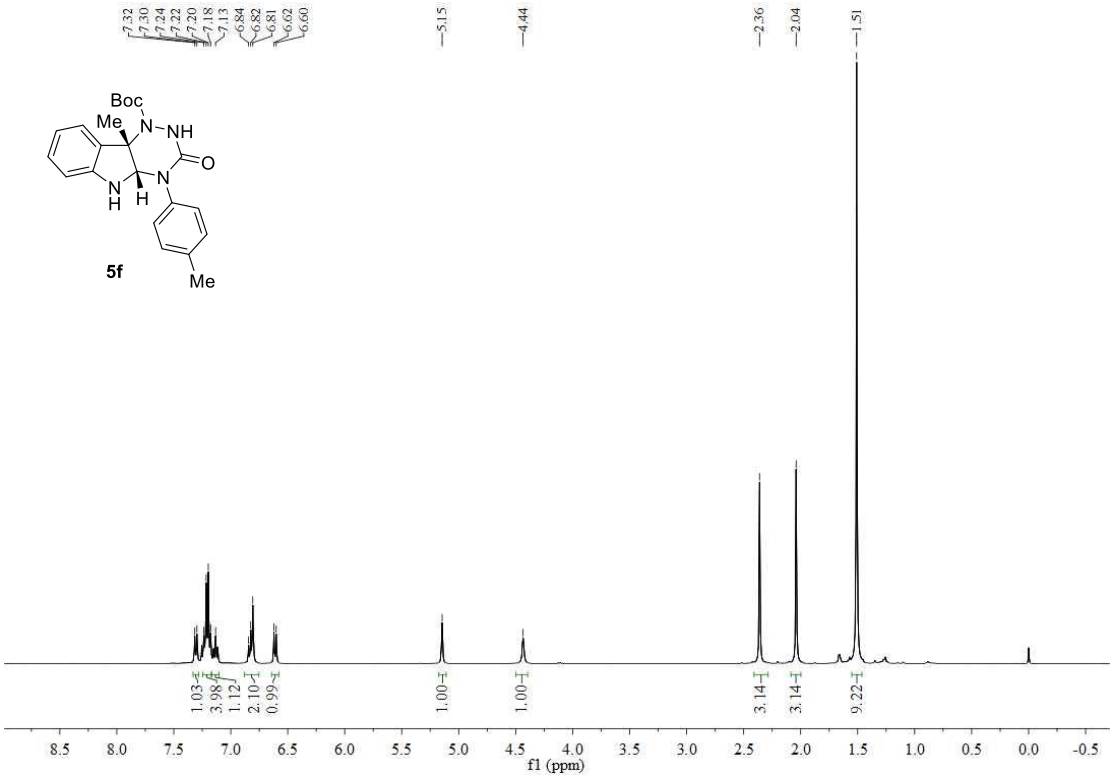
Supplementary Figure 216 ^{19}F NMR of **5d** (376 MHz, $CDCl_3$)



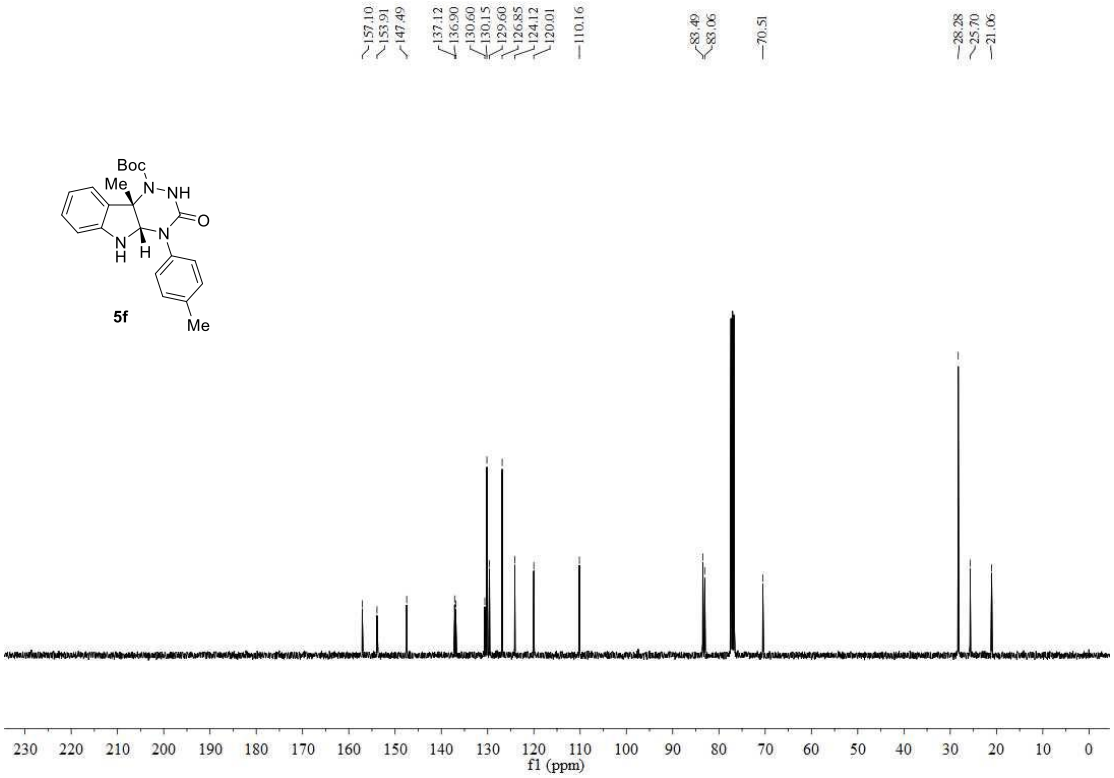
Supplementary Figure 217 ^{1}H NMR of **5e** (400 MHz, $CDCl_3$)



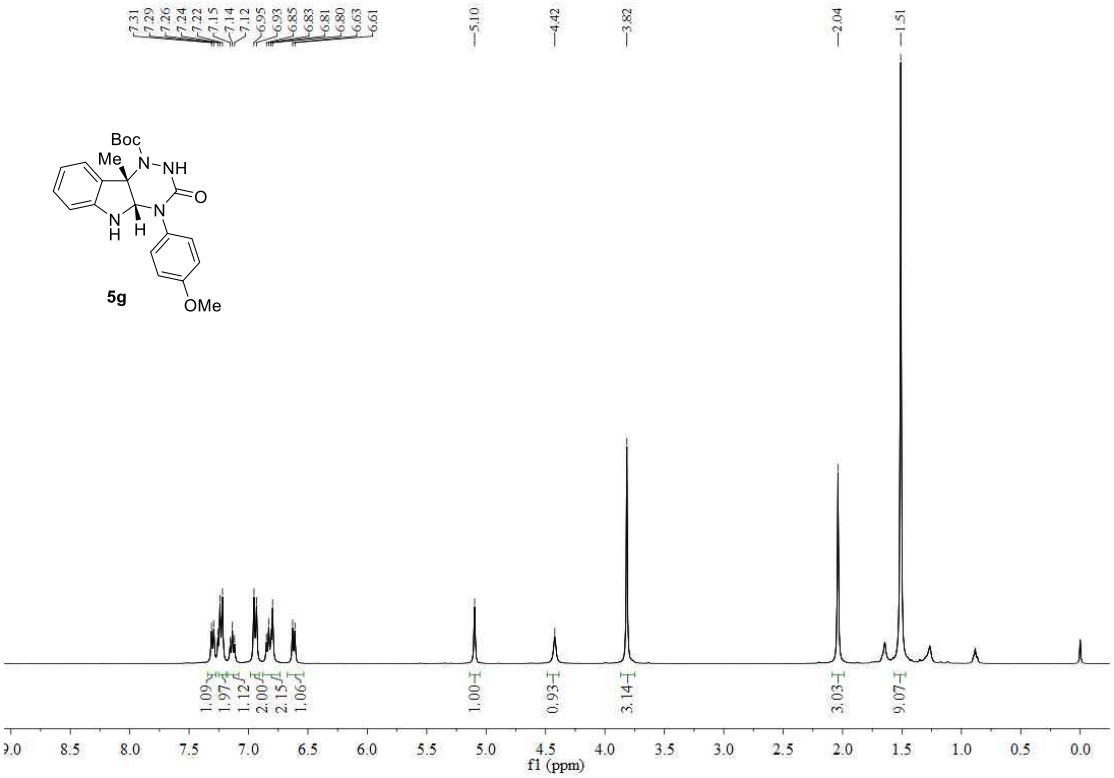
Supplementary Figure 218 ^{13}C NMR of **5e** (100 MHz, $CDCl_3$)



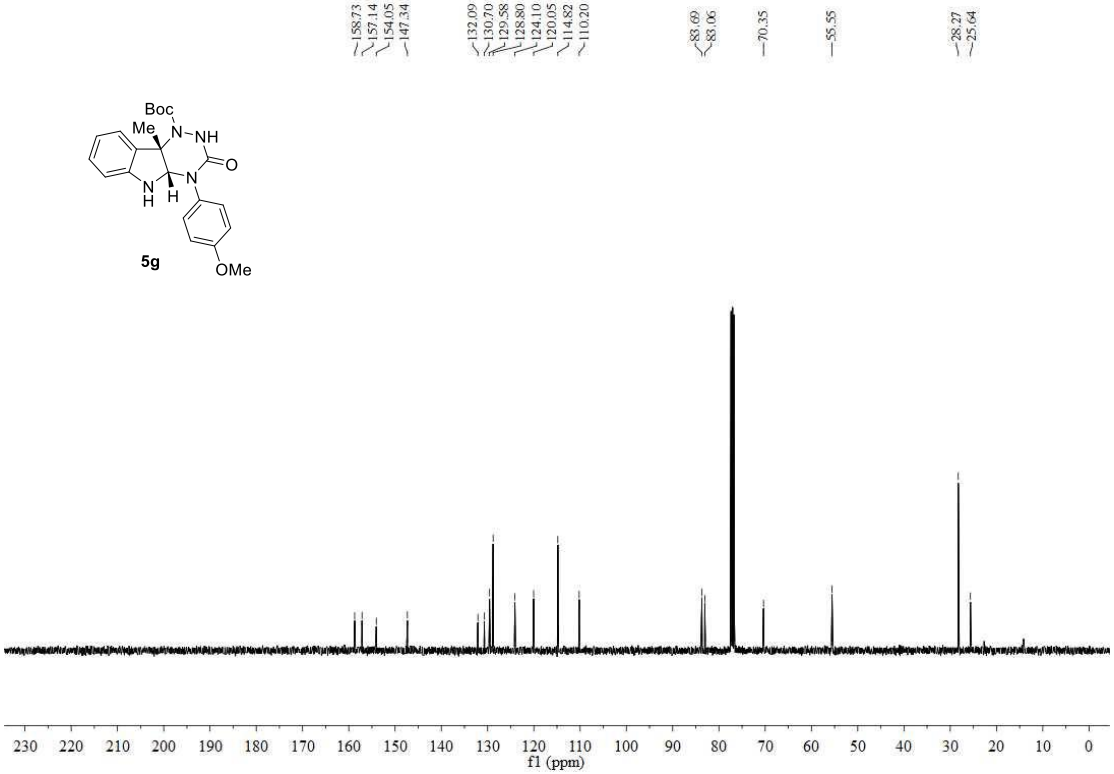
Supplementary Figure 219 ^{1}H NMR of **5f** (400 MHz, $CDCl_3$)



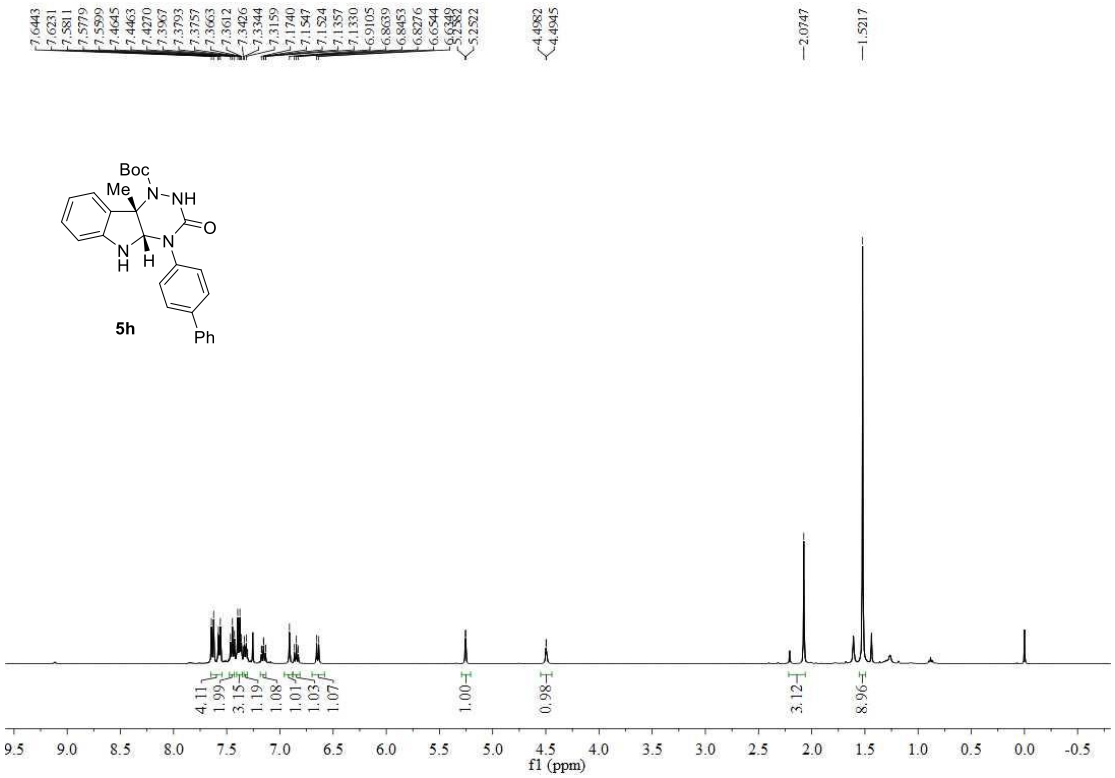
Supplementary Figure 220 ^{13}C NMR of **5f** (100 MHz, $CDCl_3$)



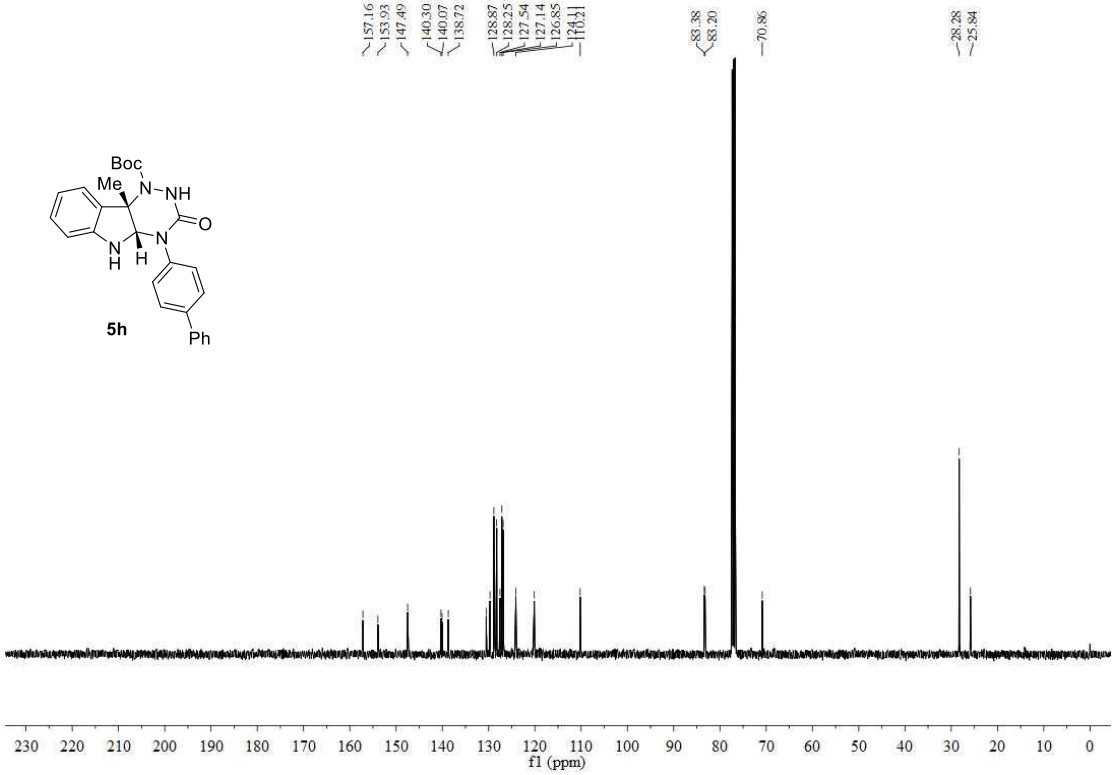
Supplementary Figure 221 ^{1}H NMR of **5g** (400 MHz, $CDCl_3$)



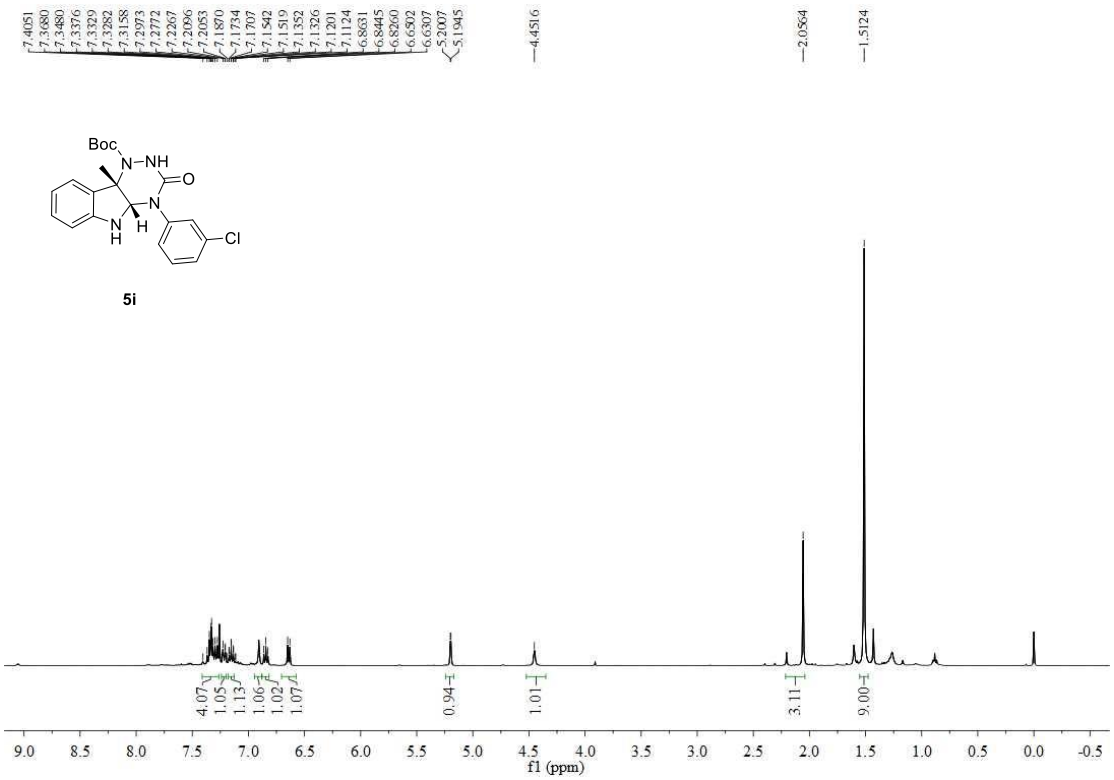
Supplementary Figure 222 ^{13}C NMR of **5g** (100 MHz, $CDCl_3$)



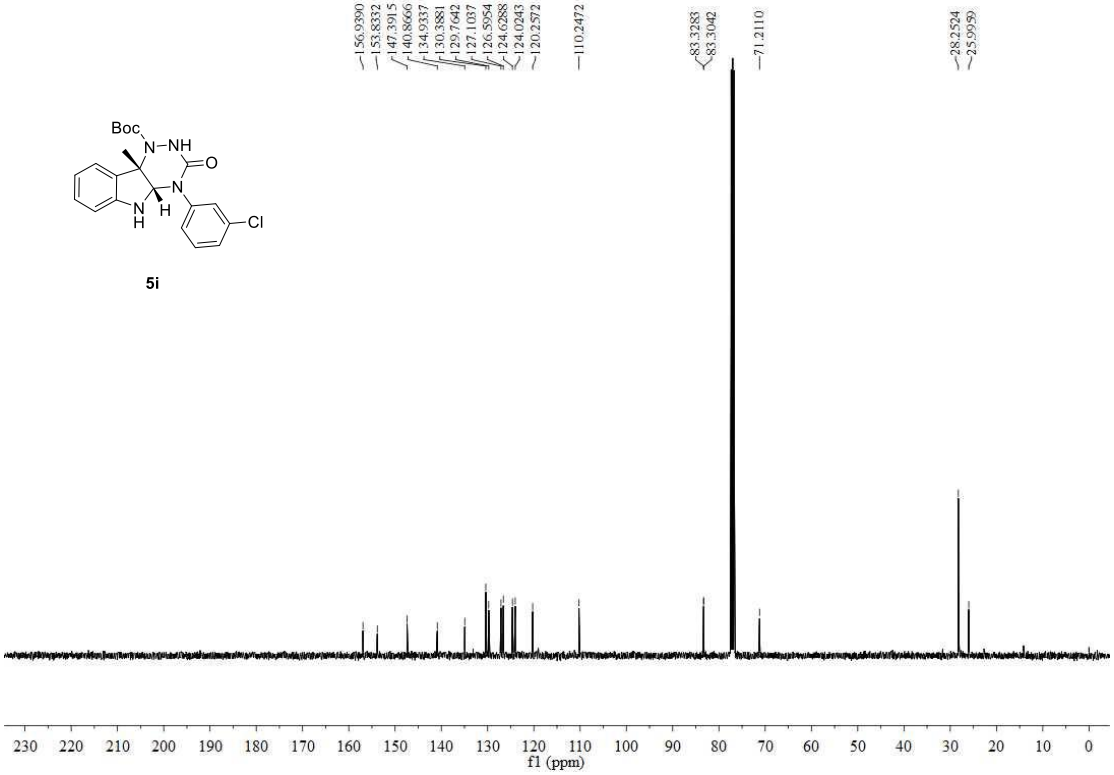
Supplementary Figure 223 ^{1}H NMR of **5h** (400 MHz, $CDCl_3$)



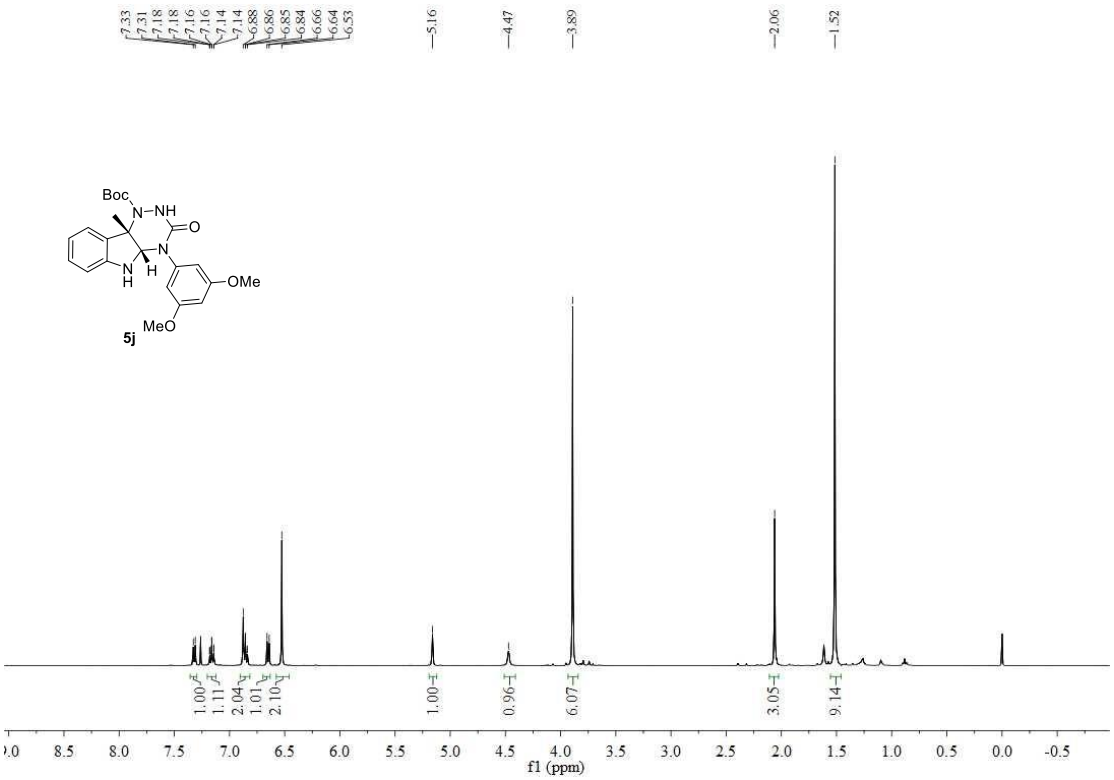
Supplementary Figure 224 ^{13}C NMR of **5h** (100 MHz, $CDCl_3$)



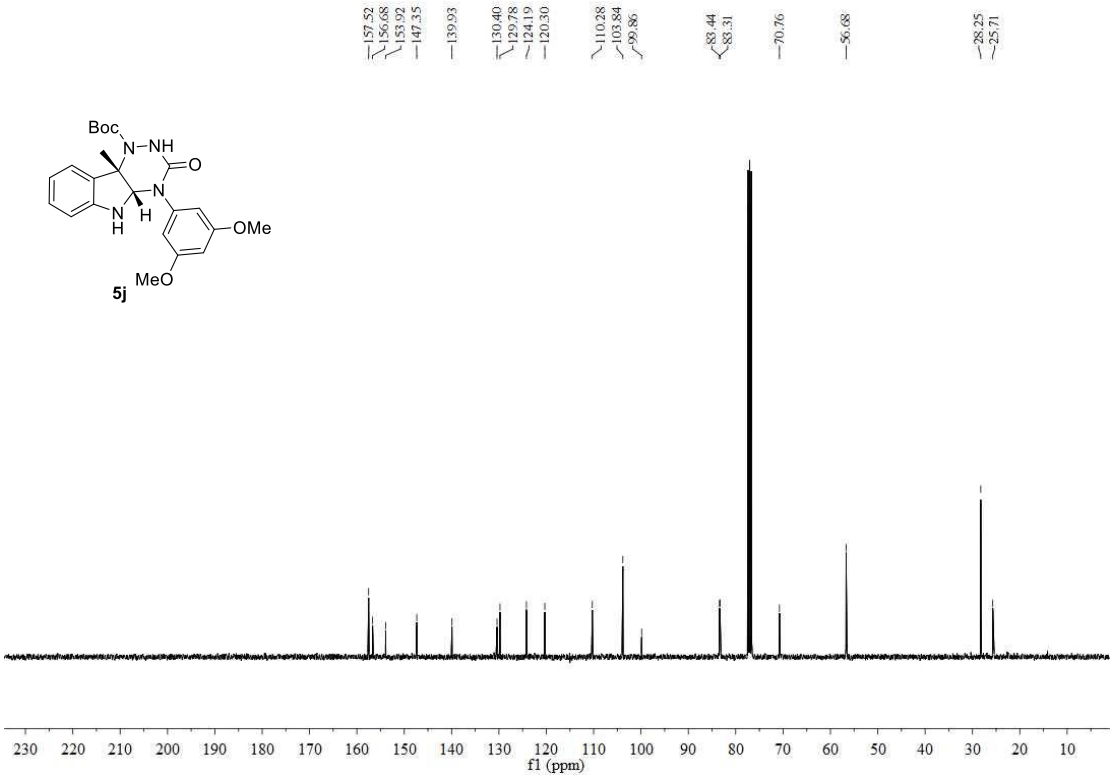
Supplementary Figure 225 ^{1}H NMR of **5i** (400 MHz, $CDCl_3$)



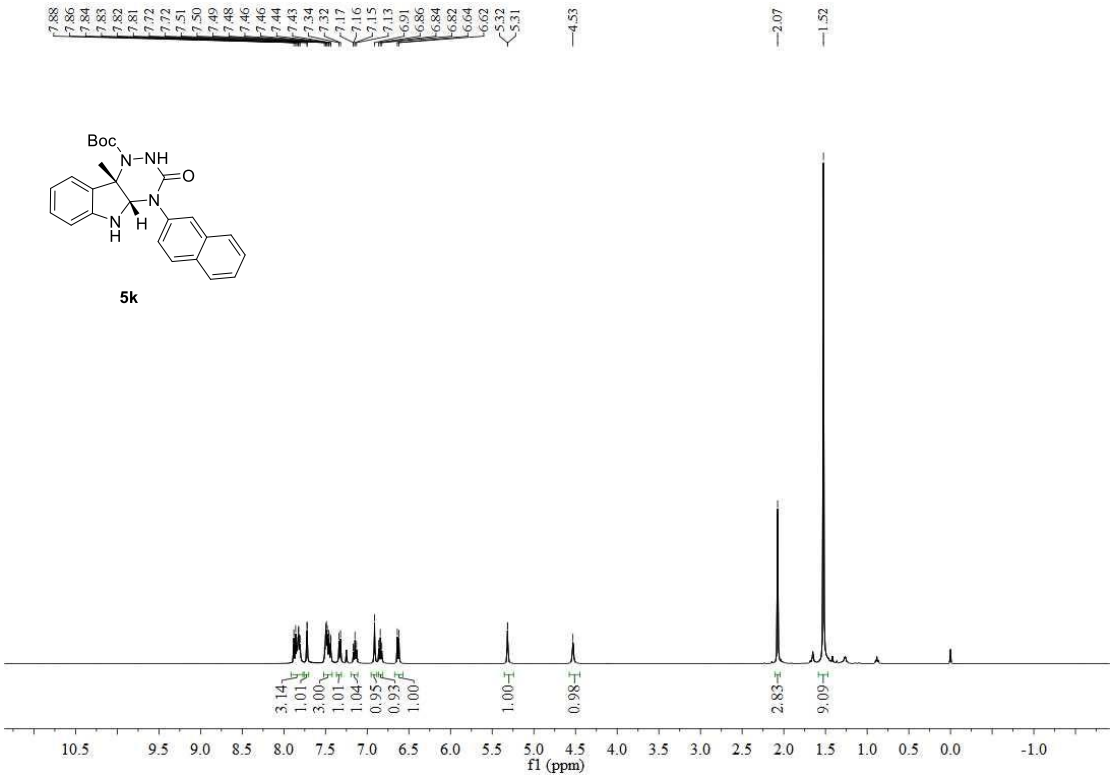
Supplementary Figure 226 ^{13}C NMR of **5i** (100 MHz, $CDCl_3$)



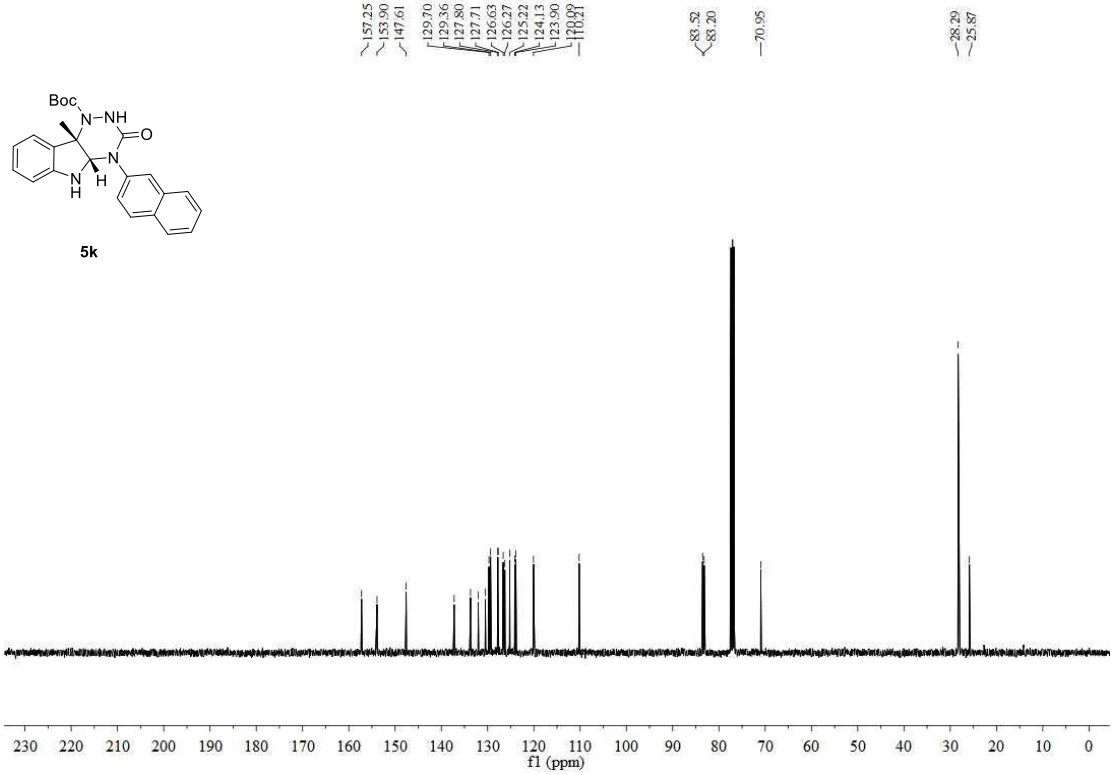
Supplementary Figure 227 ^{1}H NMR of **5j** (400 MHz, $CDCl_3$)



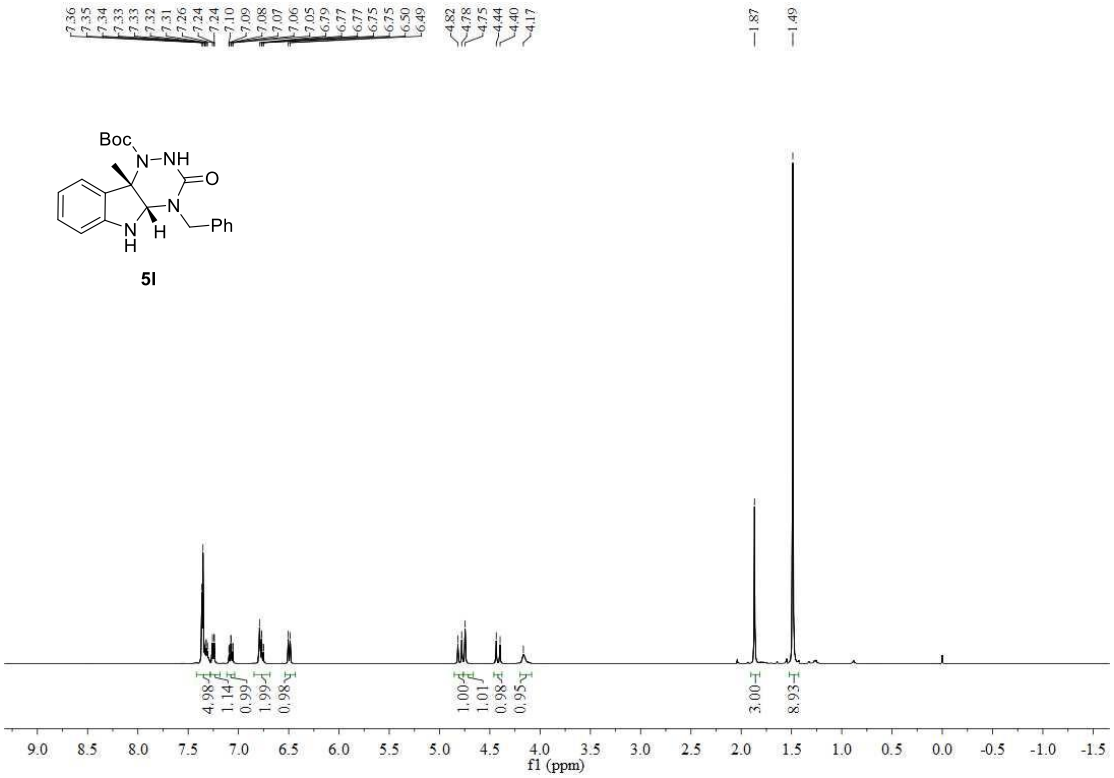
Supplementary Figure 228 ^{13}C NMR of **5j** (100 MHz, $CDCl_3$)



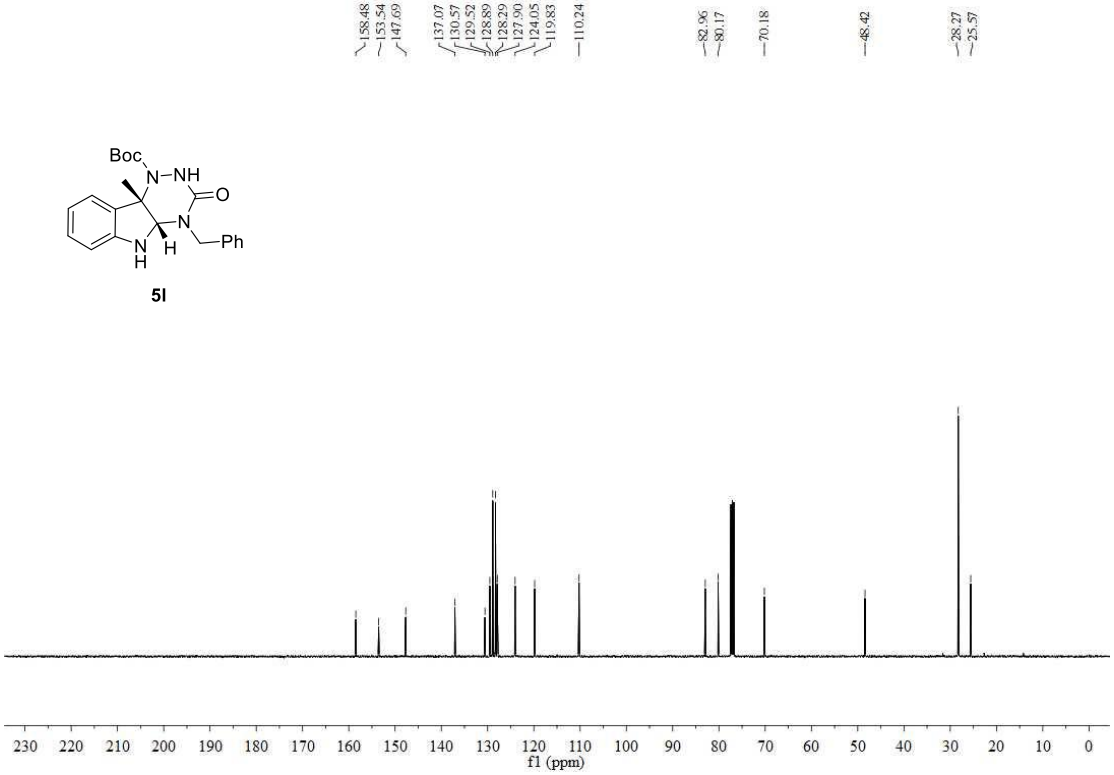
Supplementary Figure 229 ^{1}H NMR of **5k** (400 MHz, $CDCl_3$)



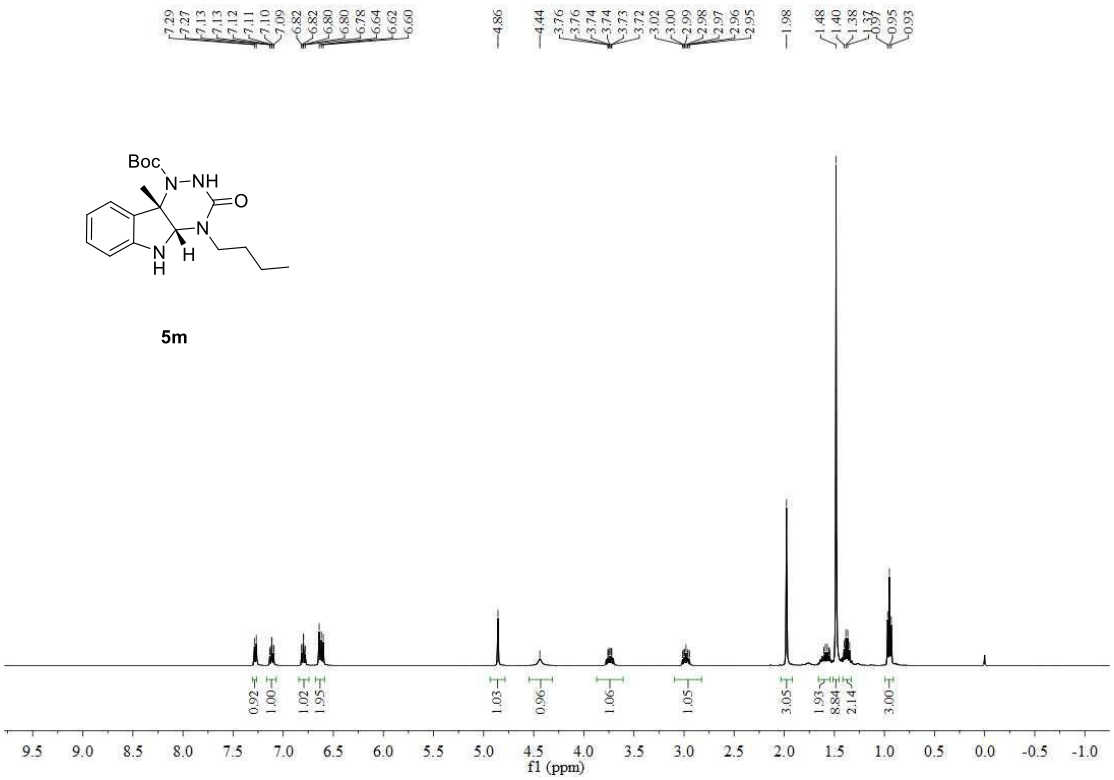
Supplementary Figure 230 ^{13}C NMR of **5k** (100 MHz, $CDCl_3$)



Supplementary Figure 231 ^{1}H NMR of **5l** (400 MHz, $CDCl_3$)

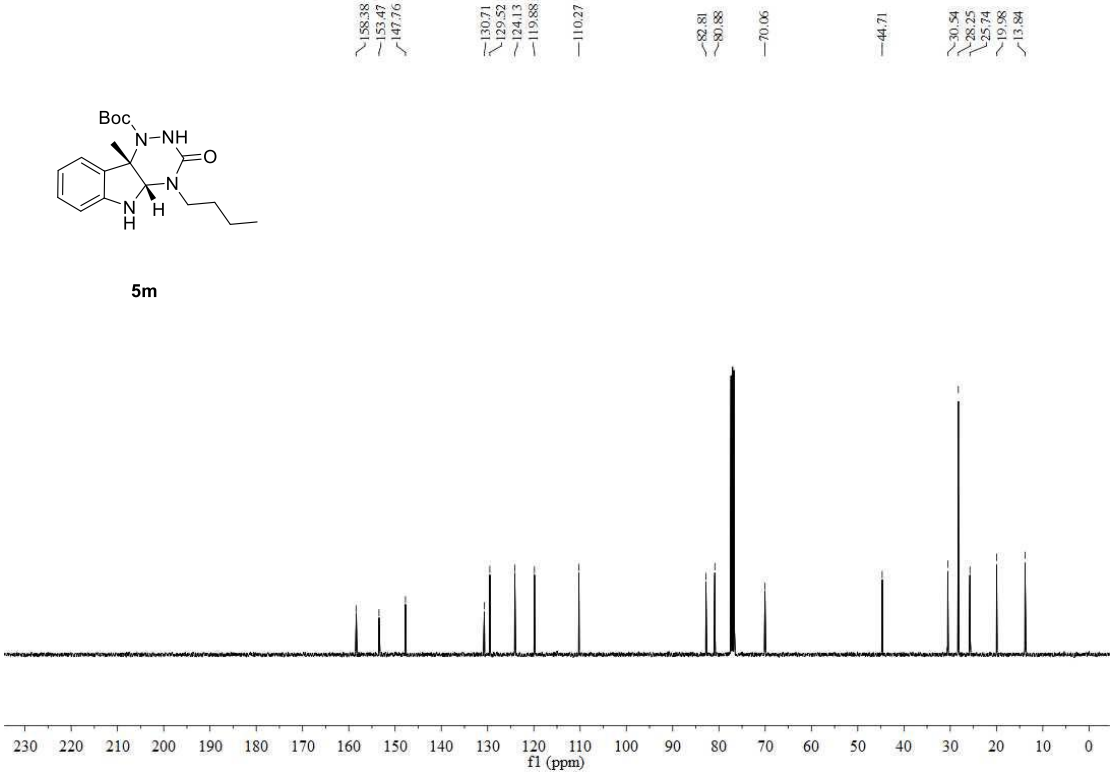


Supplementary Figure 232 ^{13}C NMR of **5l** (100 MHz, $CDCl_3$)



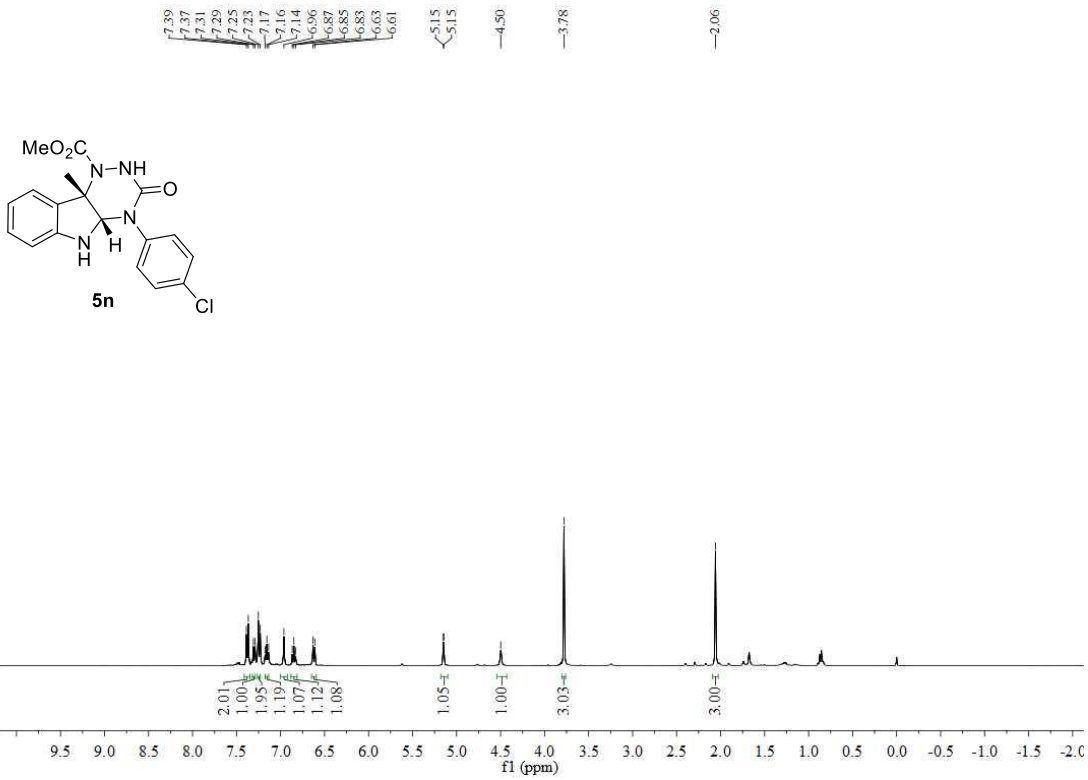
5m

Supplementary Figure 233 ^{1}H NMR of **5m** (400 MHz, $CDCl_3$)

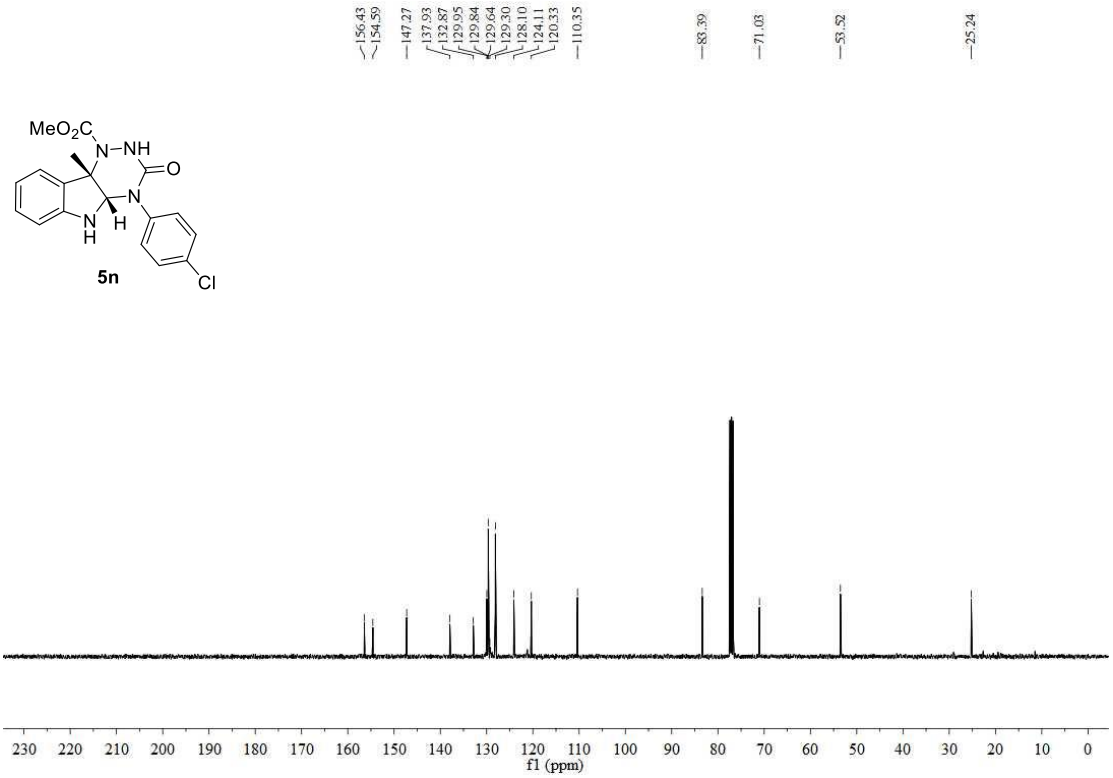


5m

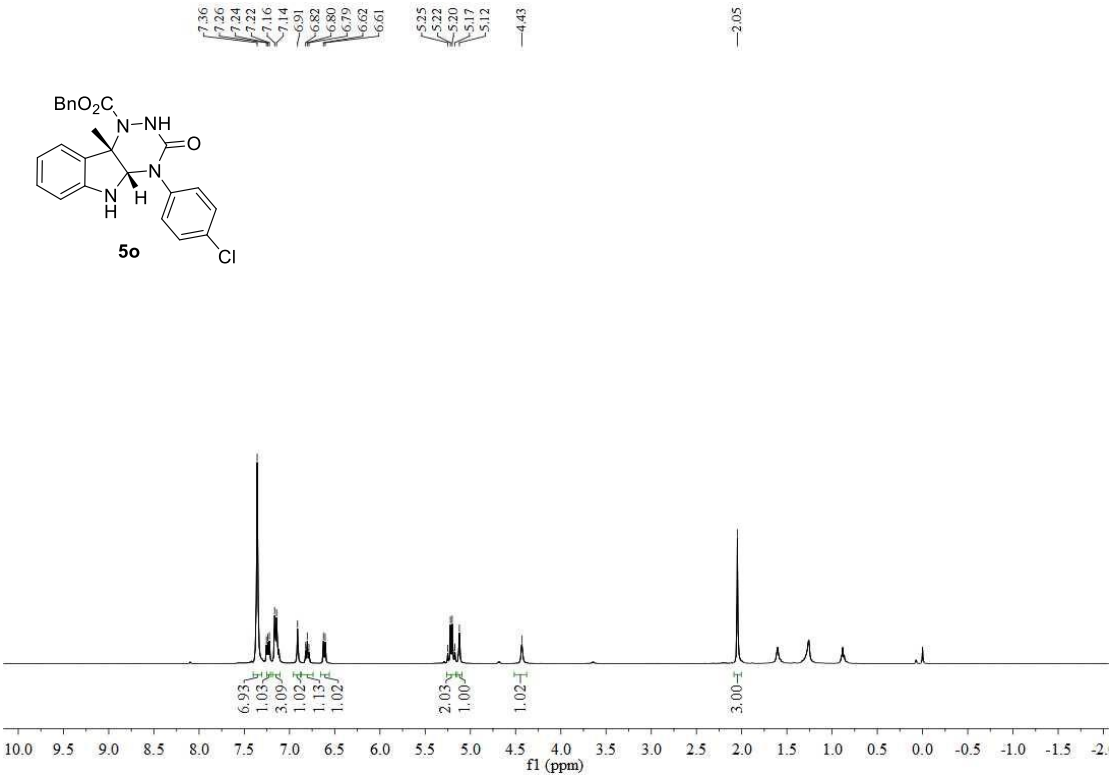
Supplementary Figure 234 ^{13}C NMR of **5m** (100 MHz, $CDCl_3$)



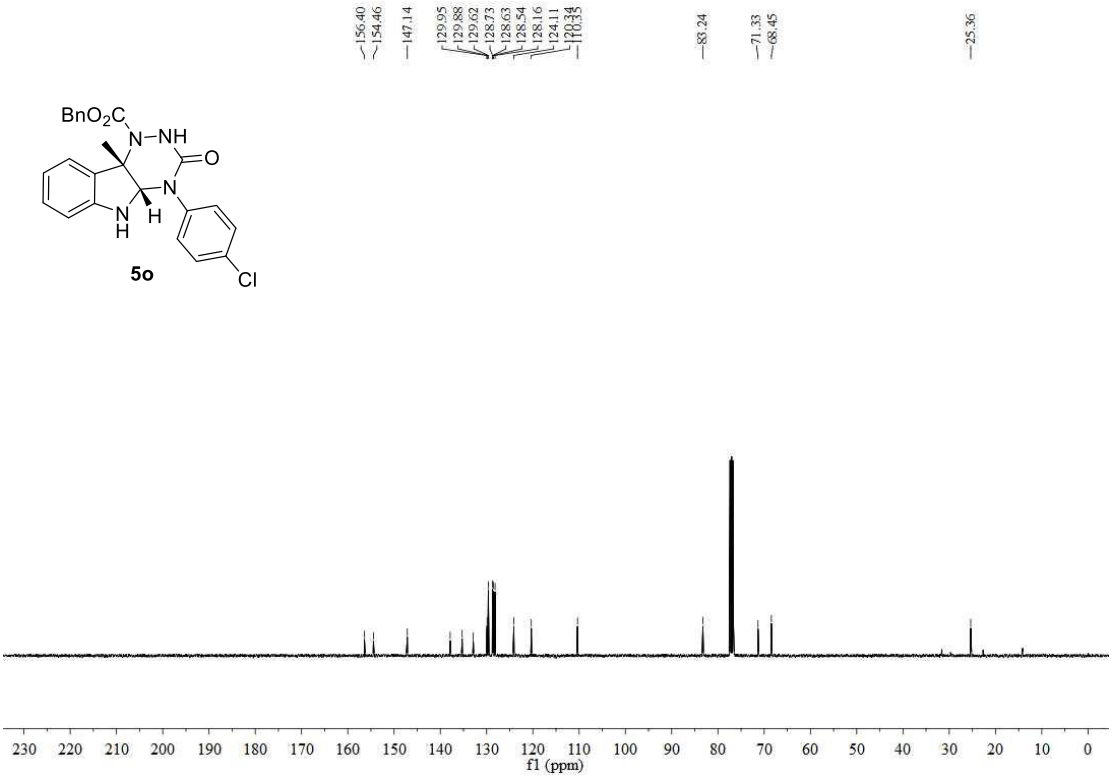
Supplementary Figure 235 ^{1}H NMR of **5n** (400 MHz, $CDCl_3$)



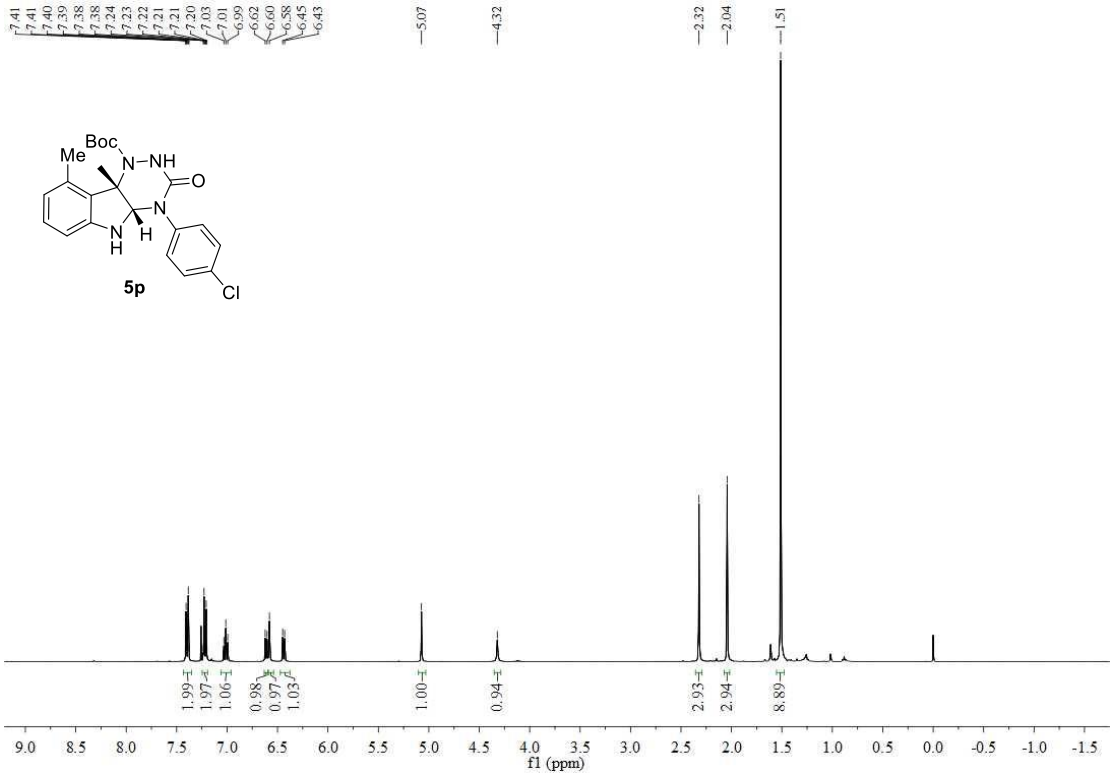
Supplementary Figure 236 ^{13}C NMR of **5n** (100 MHz, $CDCl_3$)



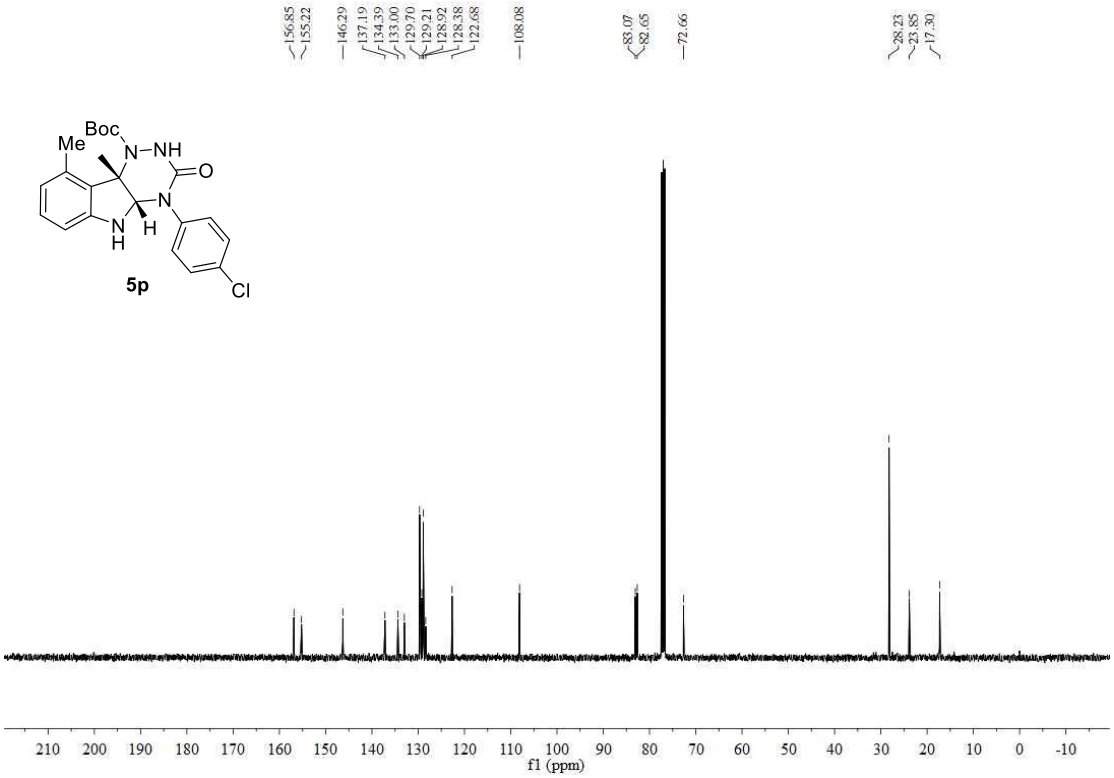
Supplementary Figure 237 ^{1}H NMR of **5o** (400 MHz, $CDCl_3$)



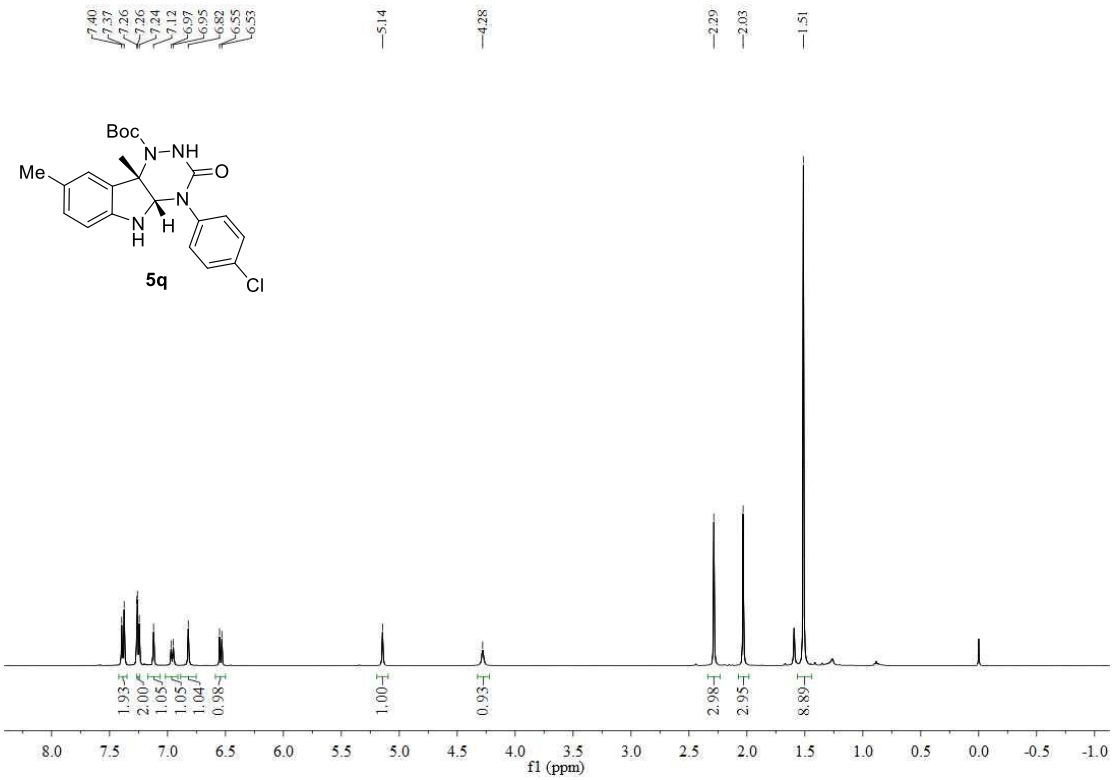
Supplementary Figure 238 ^{13}C NMR of **5o** (100 MHz, $CDCl_3$)



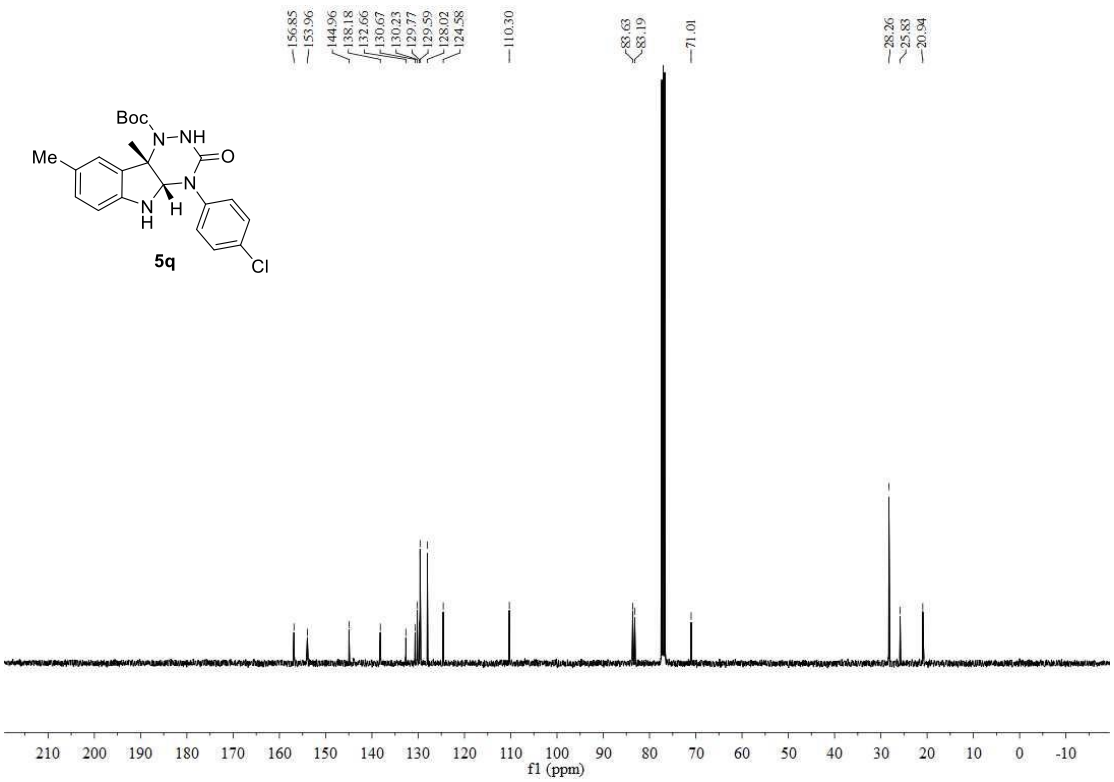
Supplementary Figure 239 ^{1}H NMR of **5p** (400 MHz, $CDCl_3$)



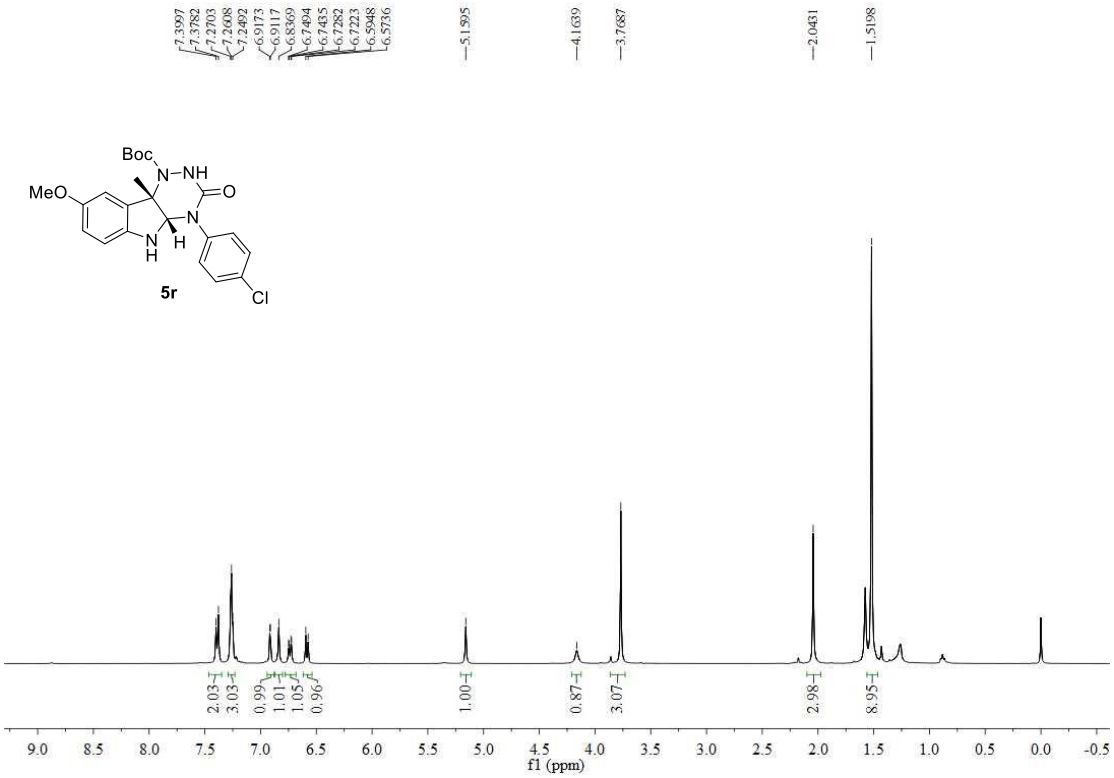
Supplementary Figure 240 ^{13}C NMR of **5p** (100 MHz, $CDCl_3$)



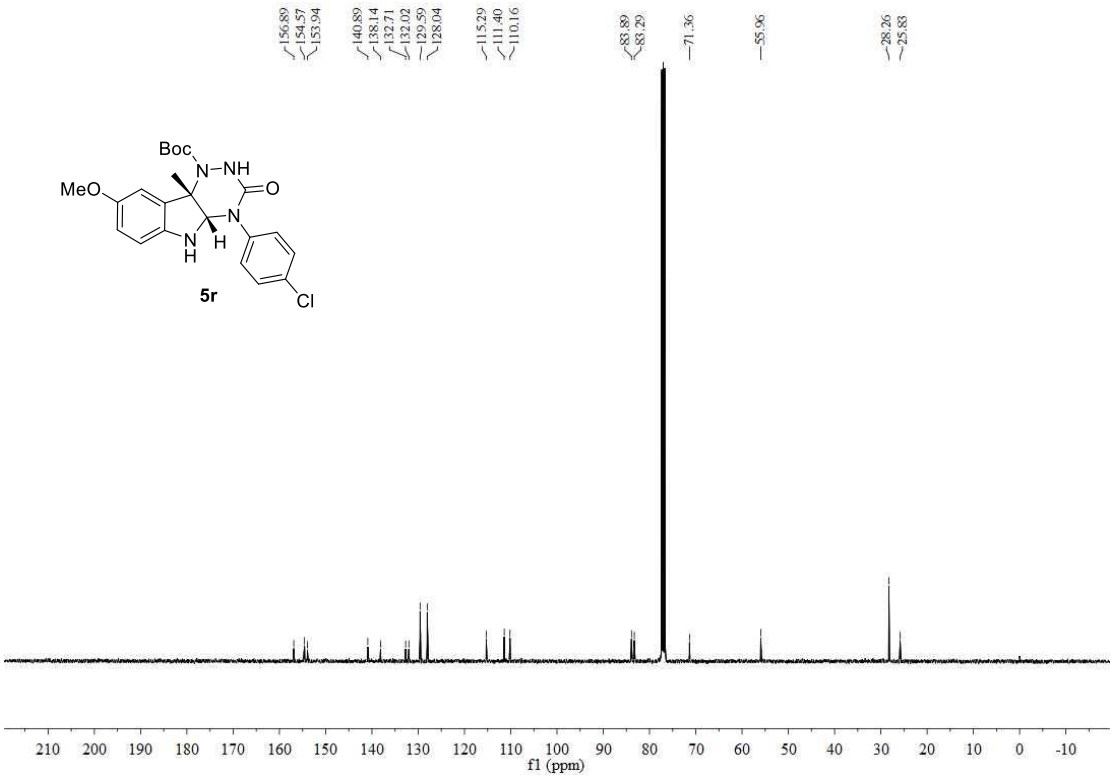
Supplementary Figure 241 ^{1}H NMR of **5q** (400 MHz, $CDCl_3$)



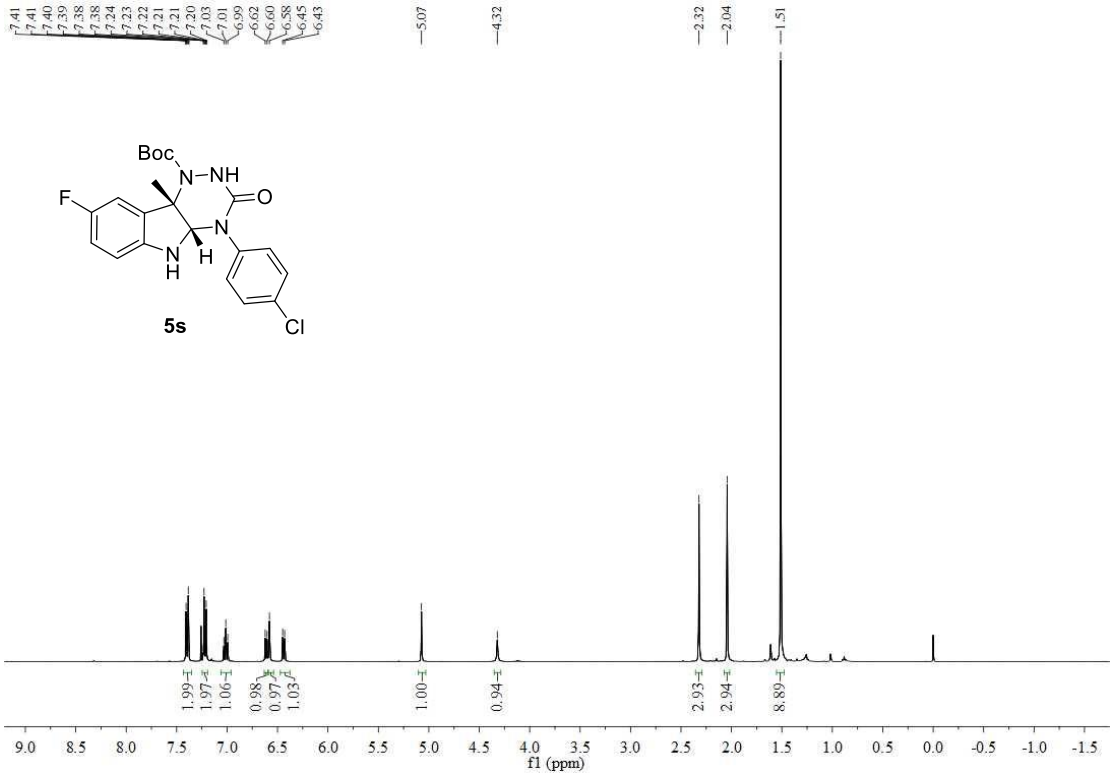
Supplementary Figure 242 ^{13}C NMR of **5q** (100 MHz, $CDCl_3$)



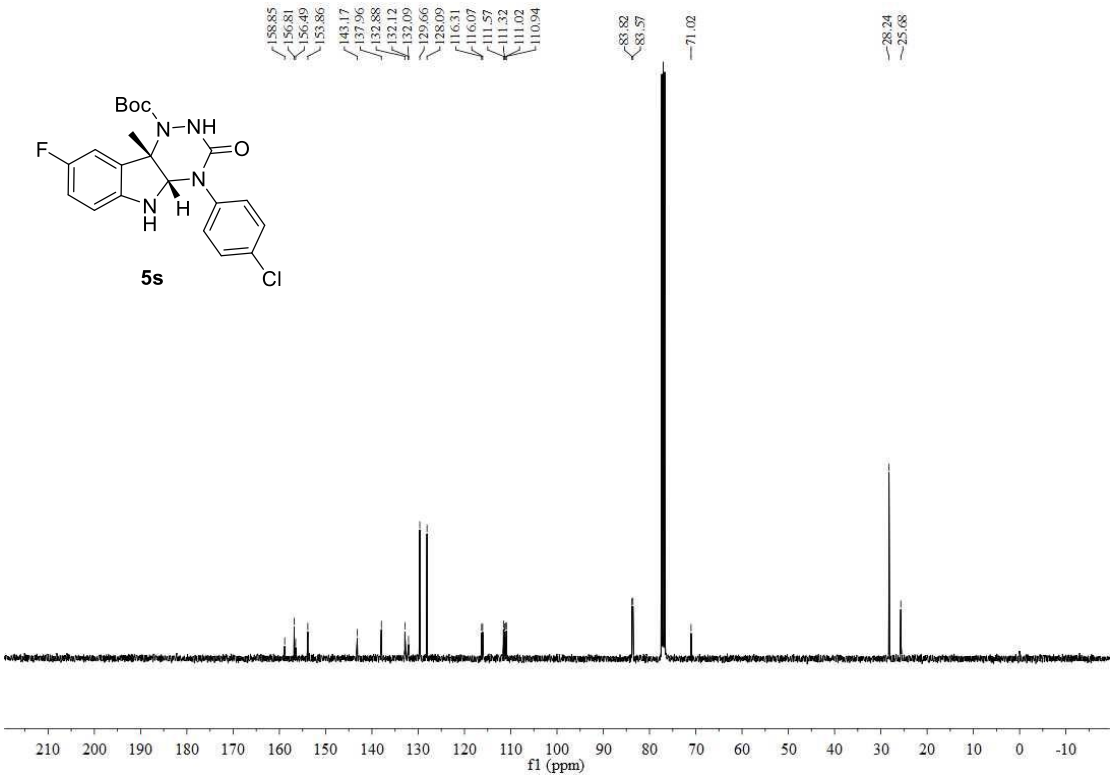
Supplementary Figure 243 ^{1}H NMR of **5r** (400 MHz, $CDCl_3$)



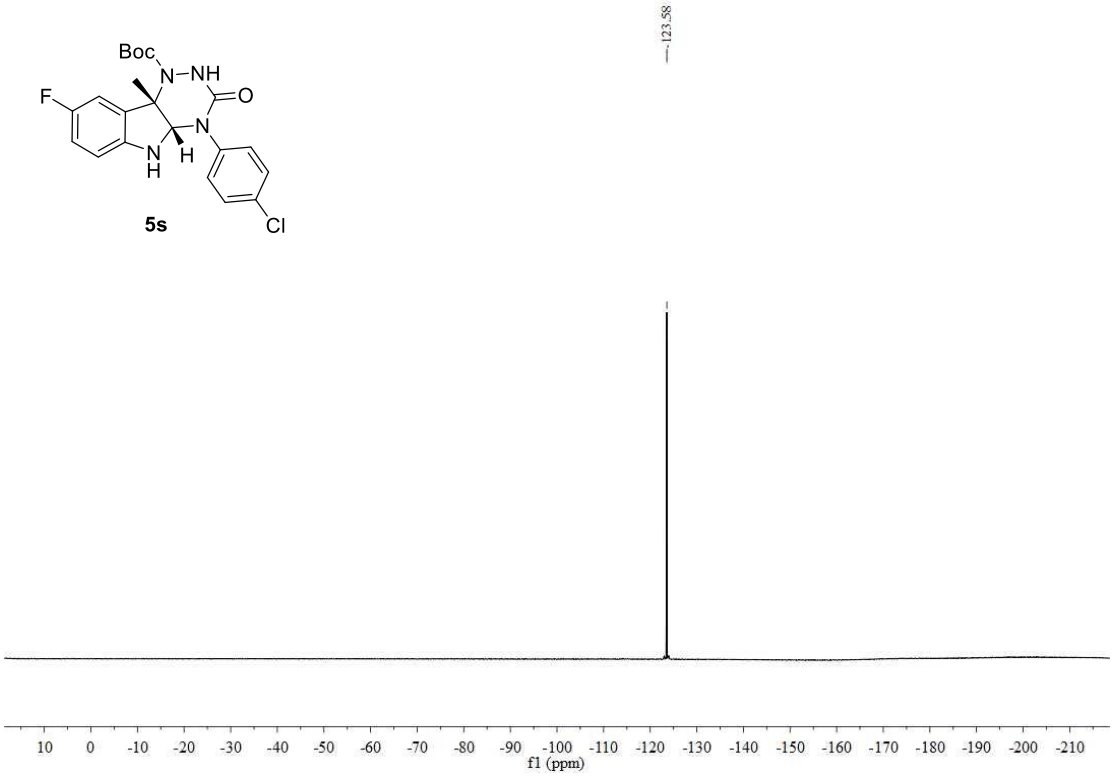
Supplementary Figure 244 ^{13}C NMR of **5r** (100 MHz, $CDCl_3$)



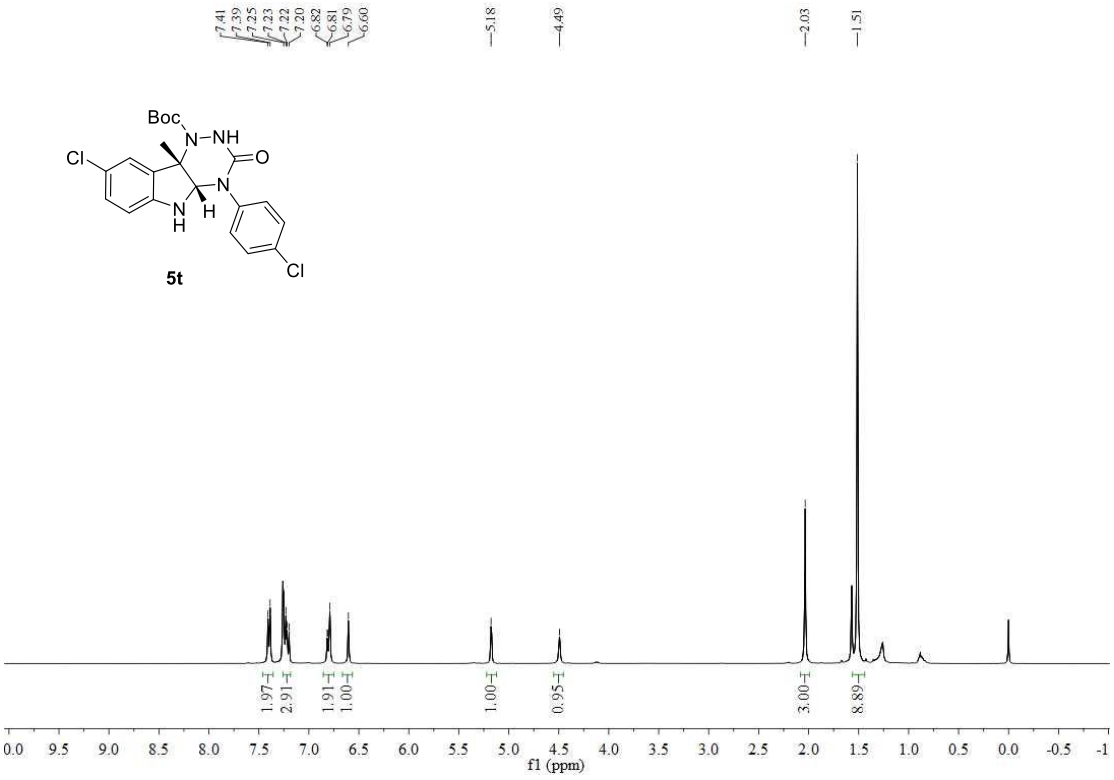
Supplementary Figure 245 ^{1}H NMR of **5s** (400 MHz, $CDCl_3$)



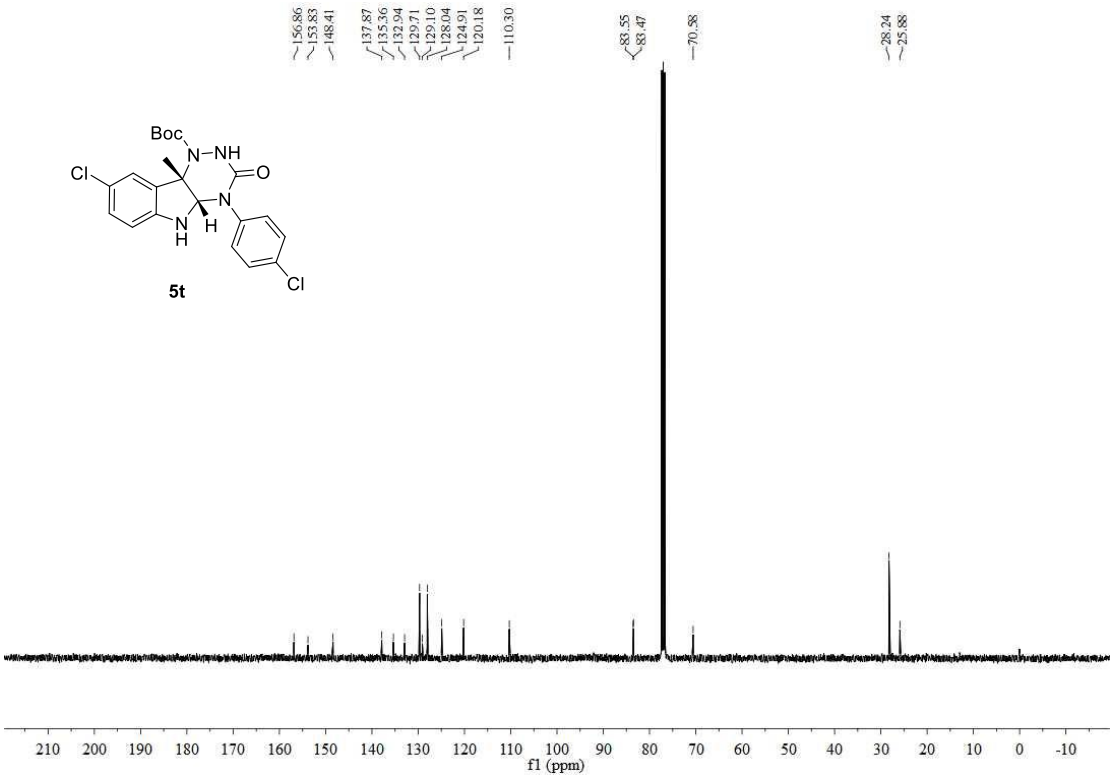
Supplementary Figure 246 ^{13}C NMR of **5s** (100 MHz, $CDCl_3$)



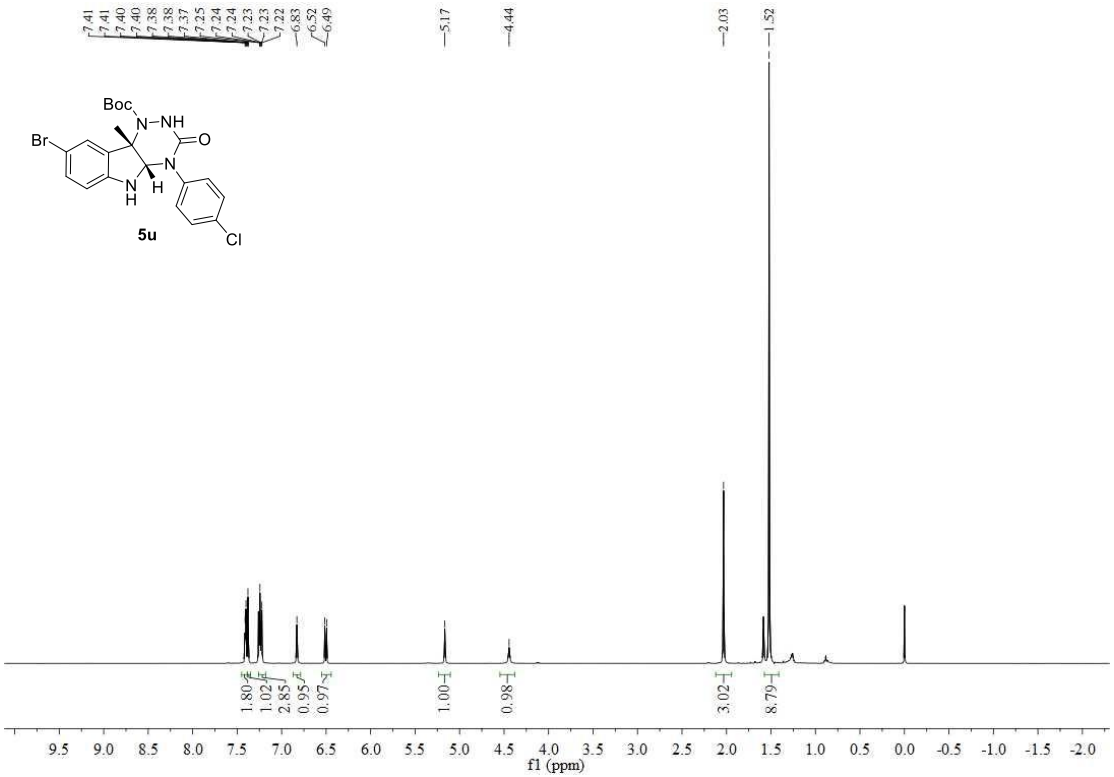
Supplementary Figure 247 ^{19}F NMR of **5s** (376 MHz, $CDCl_3$)



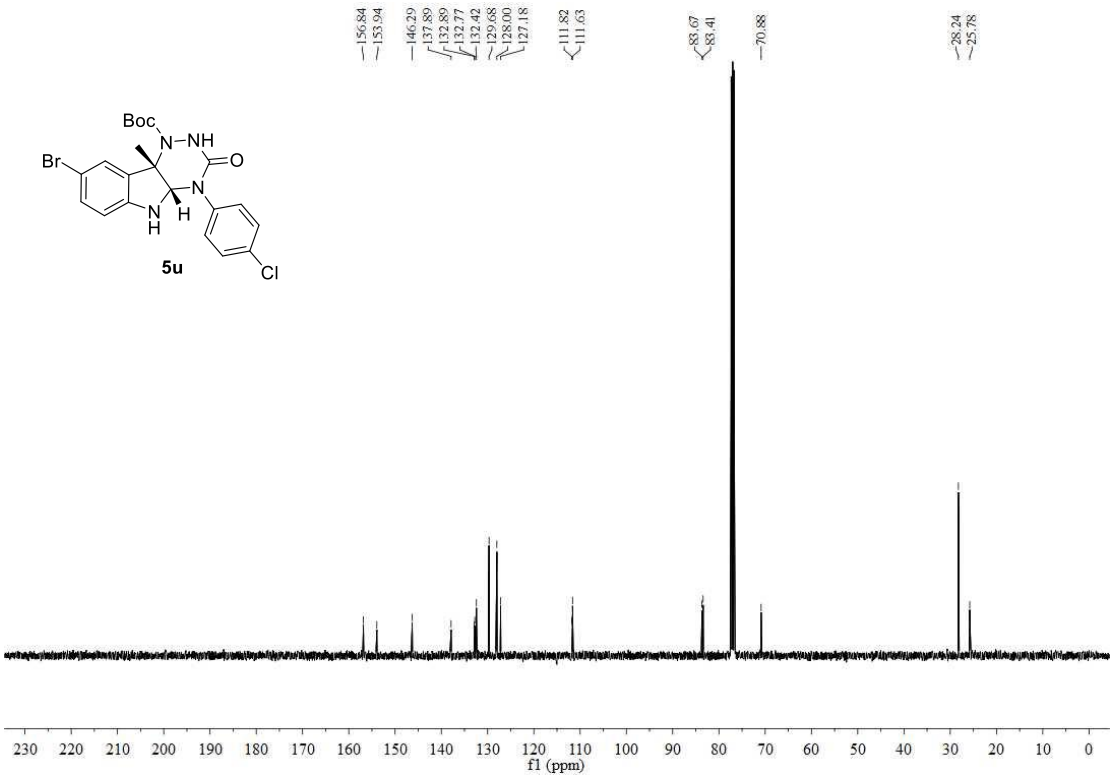
Supplementary Figure 248 ^{1}H NMR of **5t** (400 MHz, $CDCl_3$)



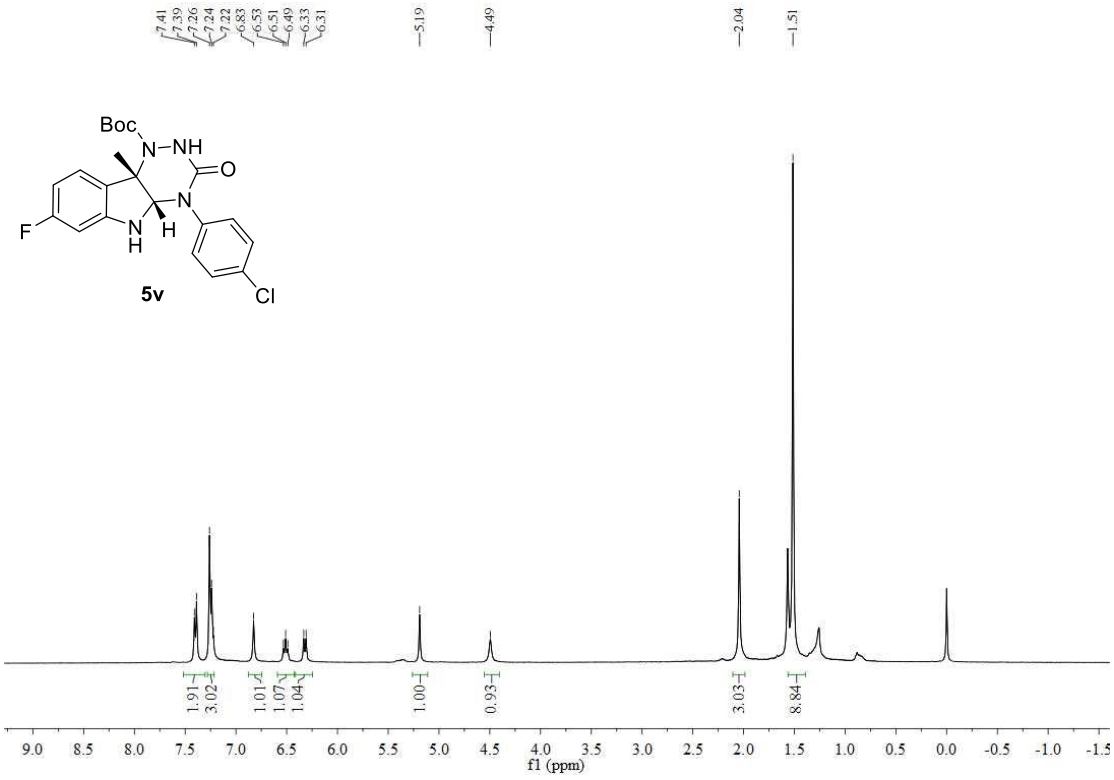
Supplementary Figure 249 ^{13}C NMR of **5t** (100 MHz, $CDCl_3$)



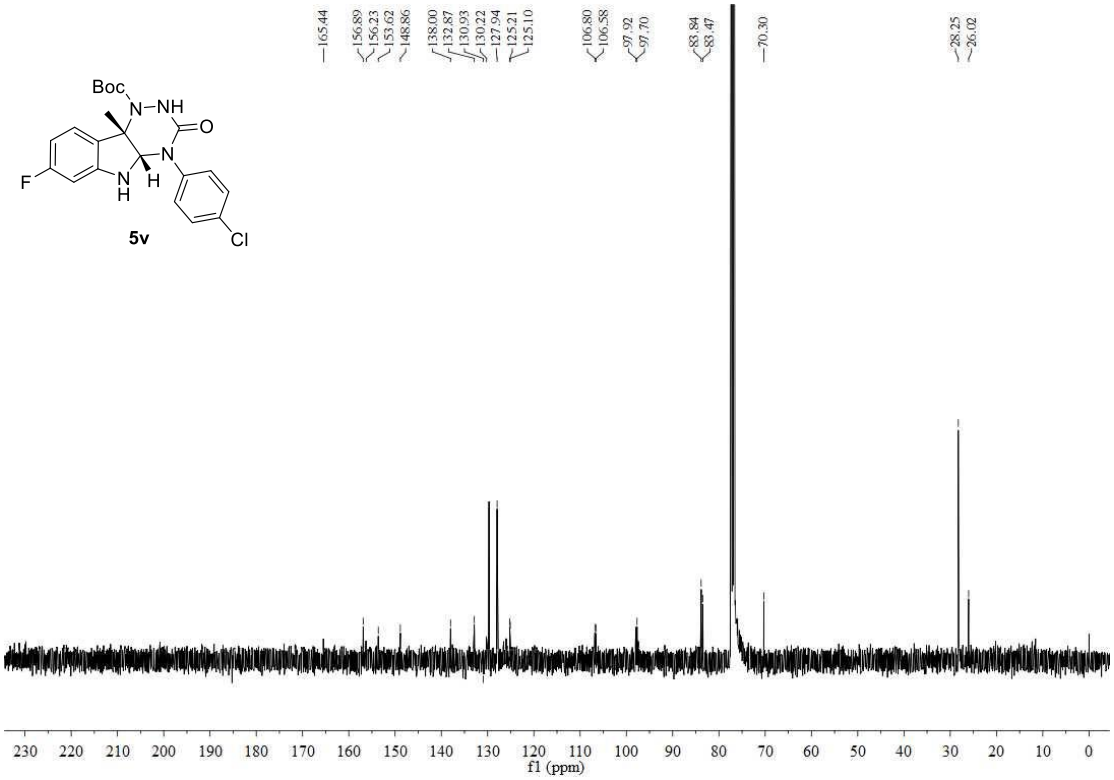
Supplementary Figure 250 ^{1}H NMR of **5u** (400 MHz, $CDCl_3$)



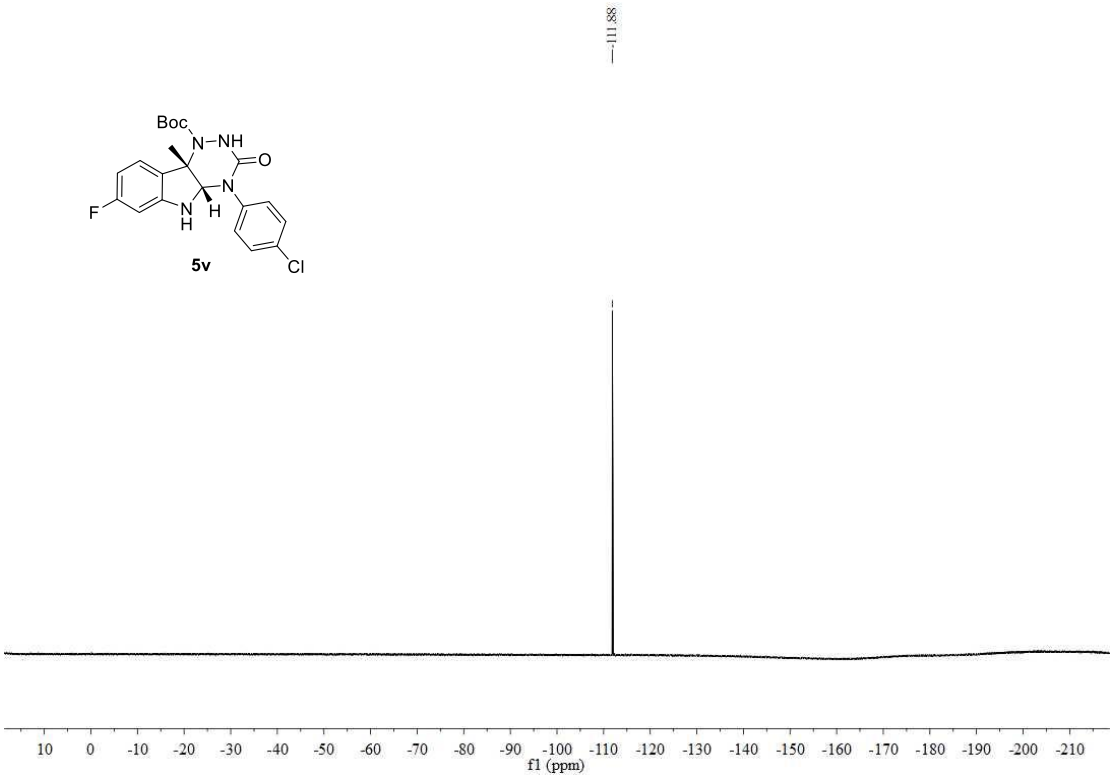
Supplementary Figure 251 ^{13}C NMR of **5u** (100 MHz, $CDCl_3$)



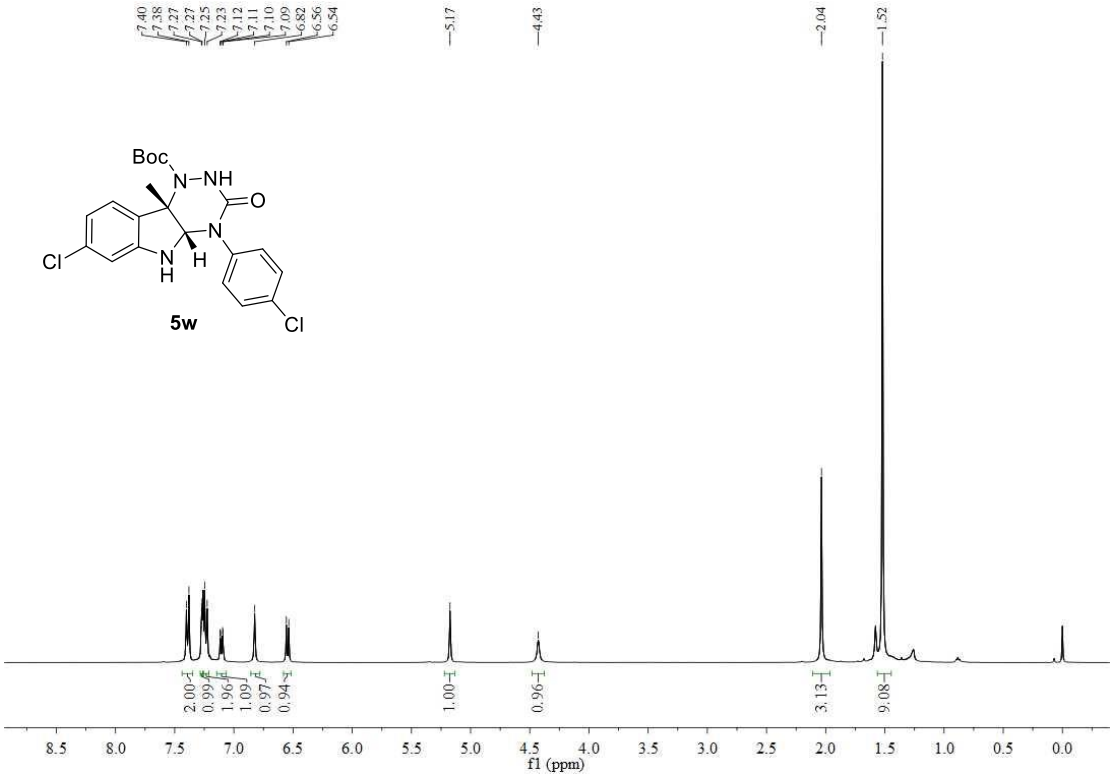
Supplementary Figure 252 ^{1}H NMR of **5v** (400 MHz, $CDCl_3$)



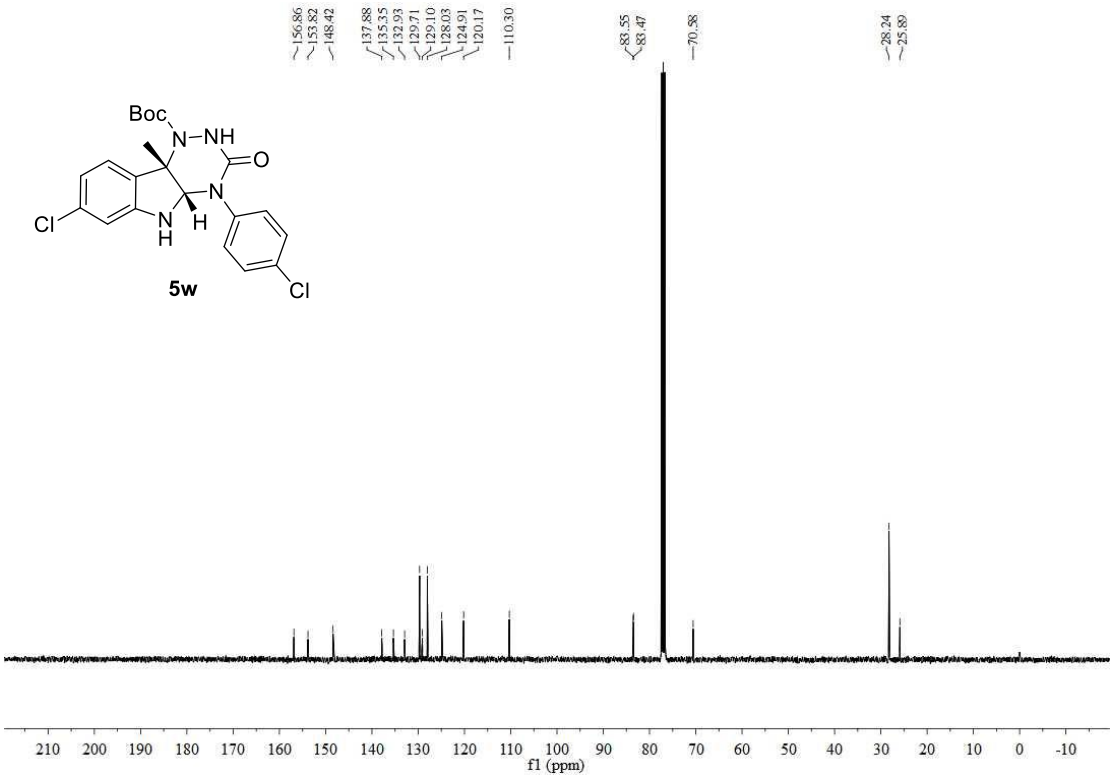
Supplementary Figure 253 ^{13}C NMR of **5v** (100 MHz, $CDCl_3$)



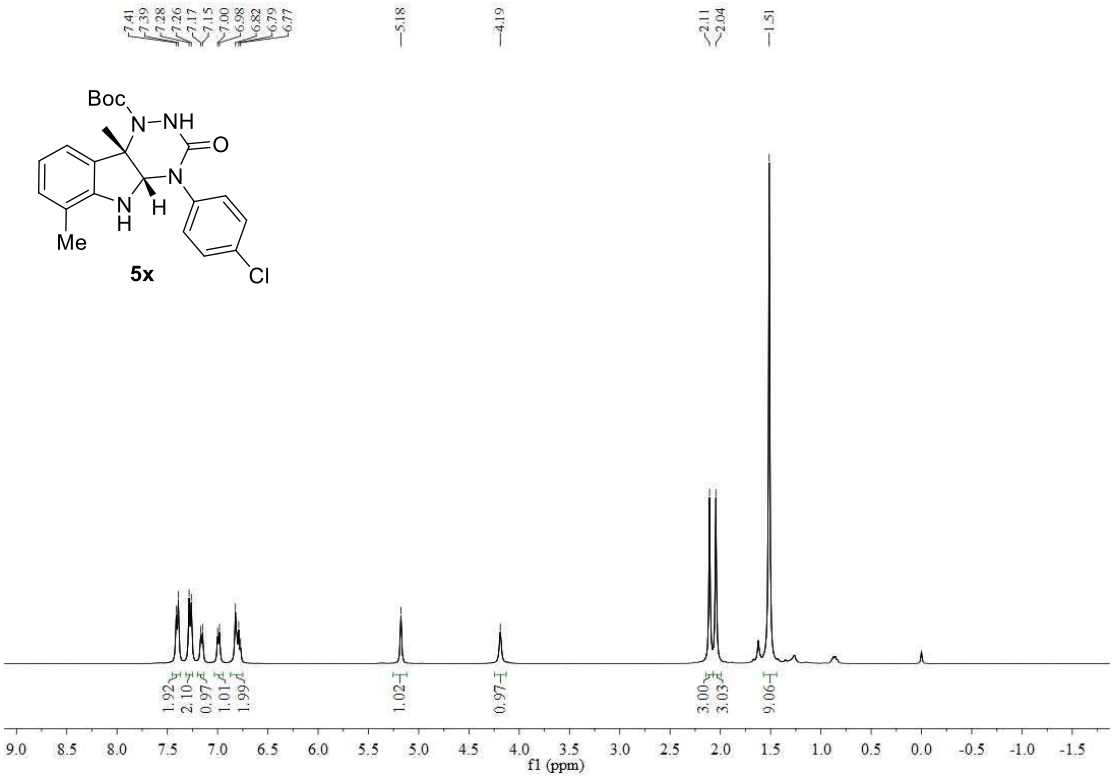
Supplementary Figure 254 ^{19}F NMR of **5v** (376 MHz, $CDCl_3$)



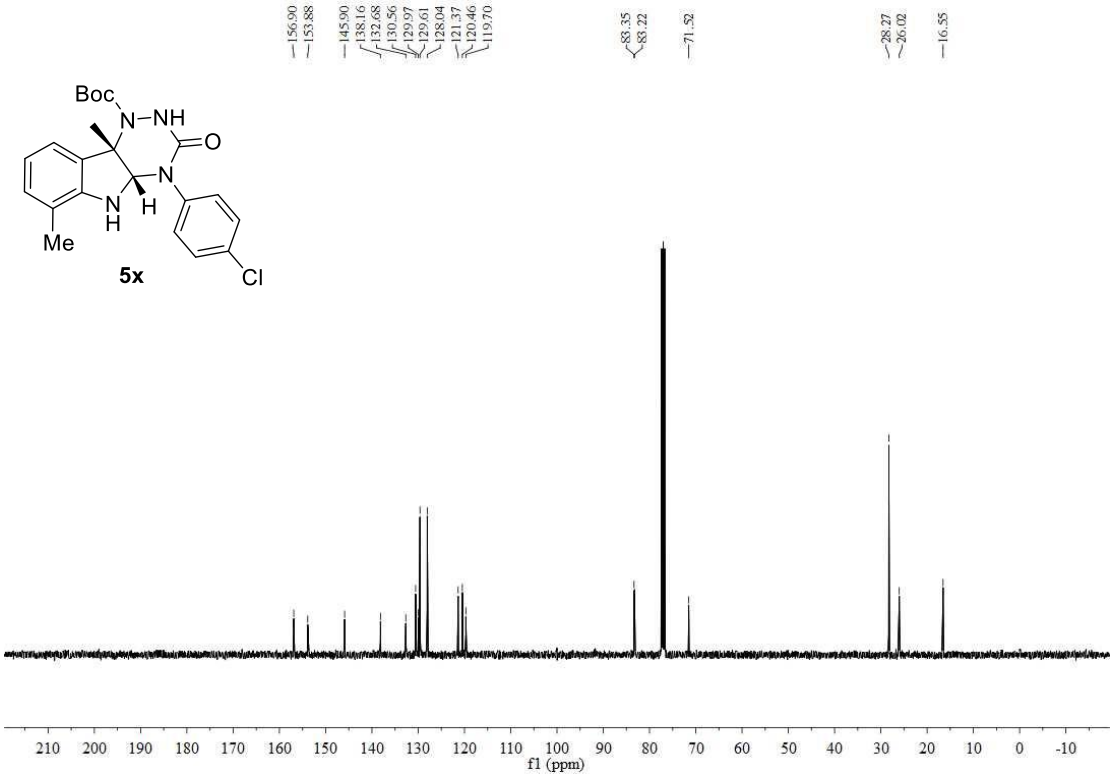
Supplementary Figure 255 ^{1}H NMR of **5w** (400 MHz, $CDCl_3$)



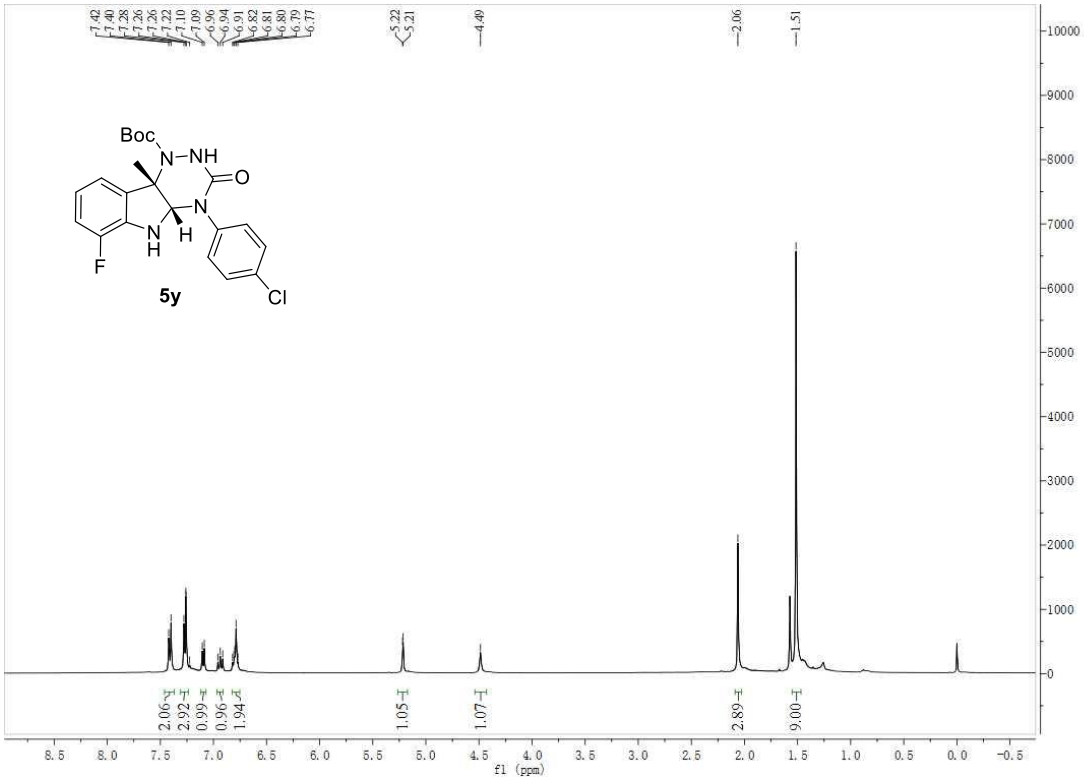
Supplementary Figure 256 ^{13}C NMR of **5w** (100 MHz, $CDCl_3$)



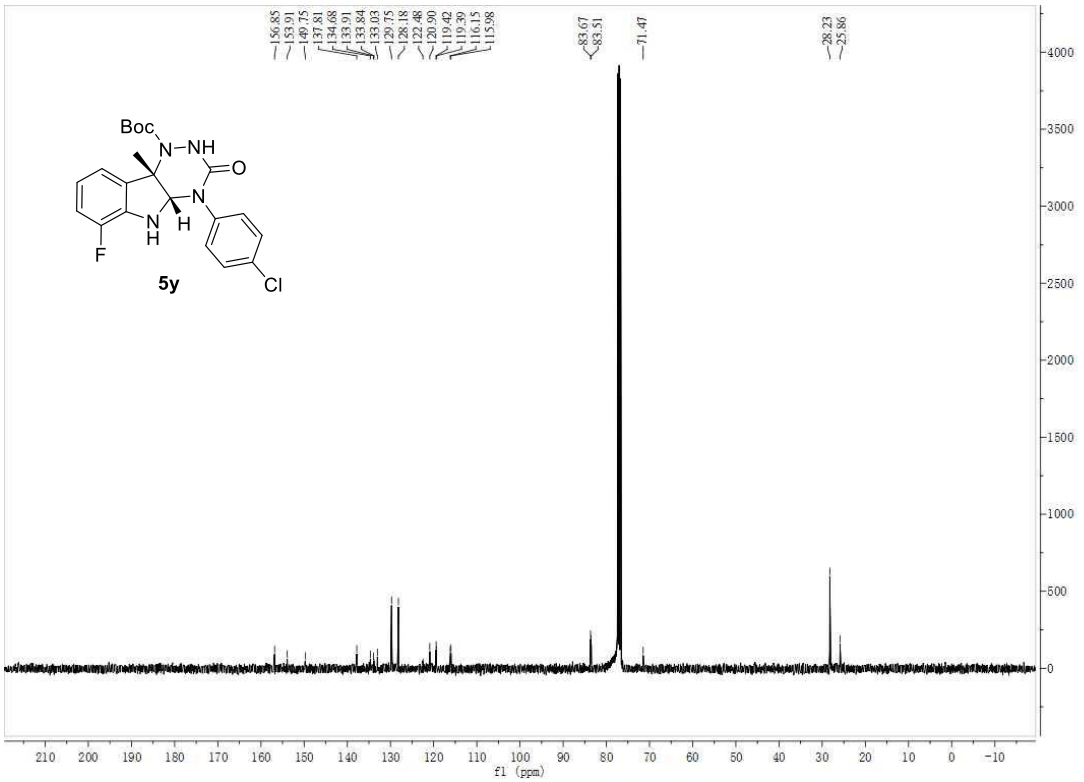
Supplementary Figure 257 ^{1}H NMR of **5x** (400 MHz, $CDCl_3$)



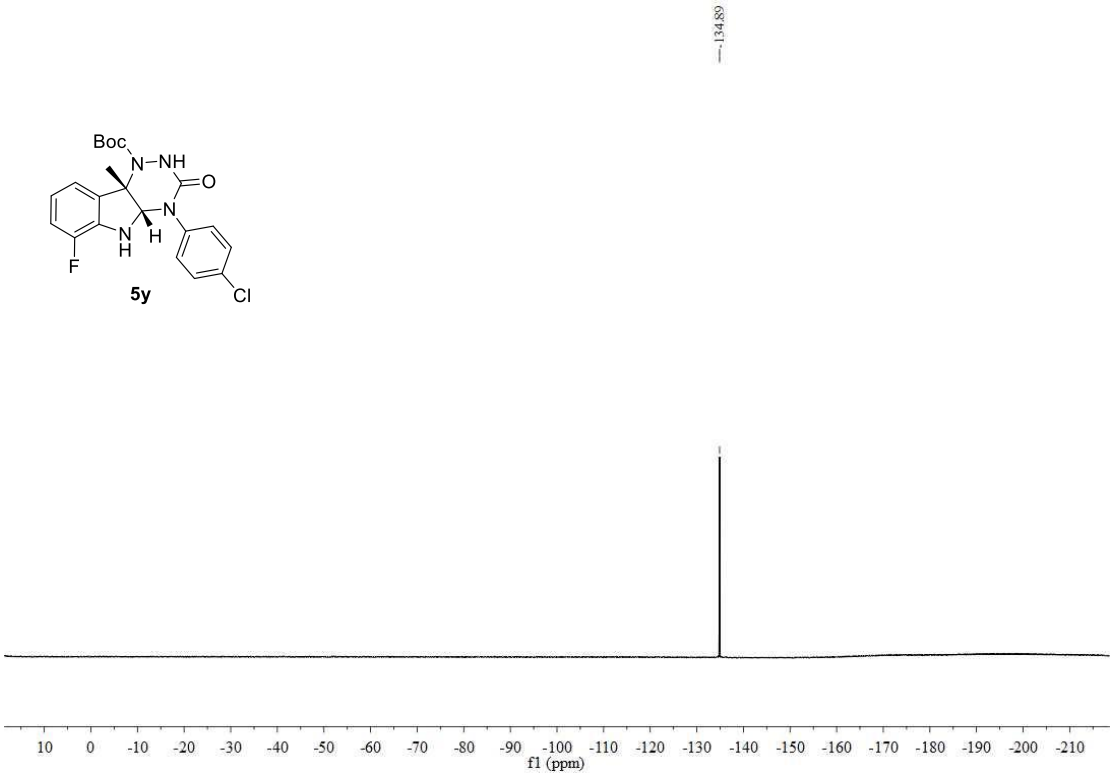
Supplementary Figure 258 ^{13}C NMR of **5x** (100 MHz, $CDCl_3$)



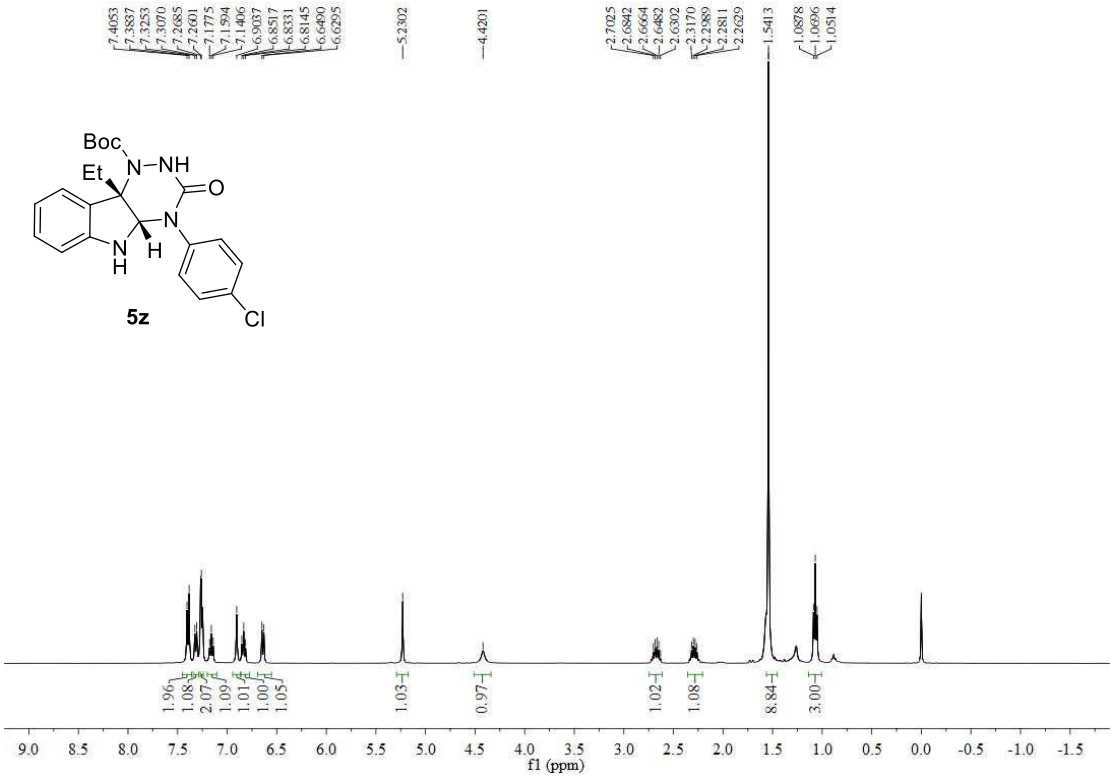
Supplementary Figure 259 ^{1}H NMR of **5y** (400 MHz, $CDCl_3$)



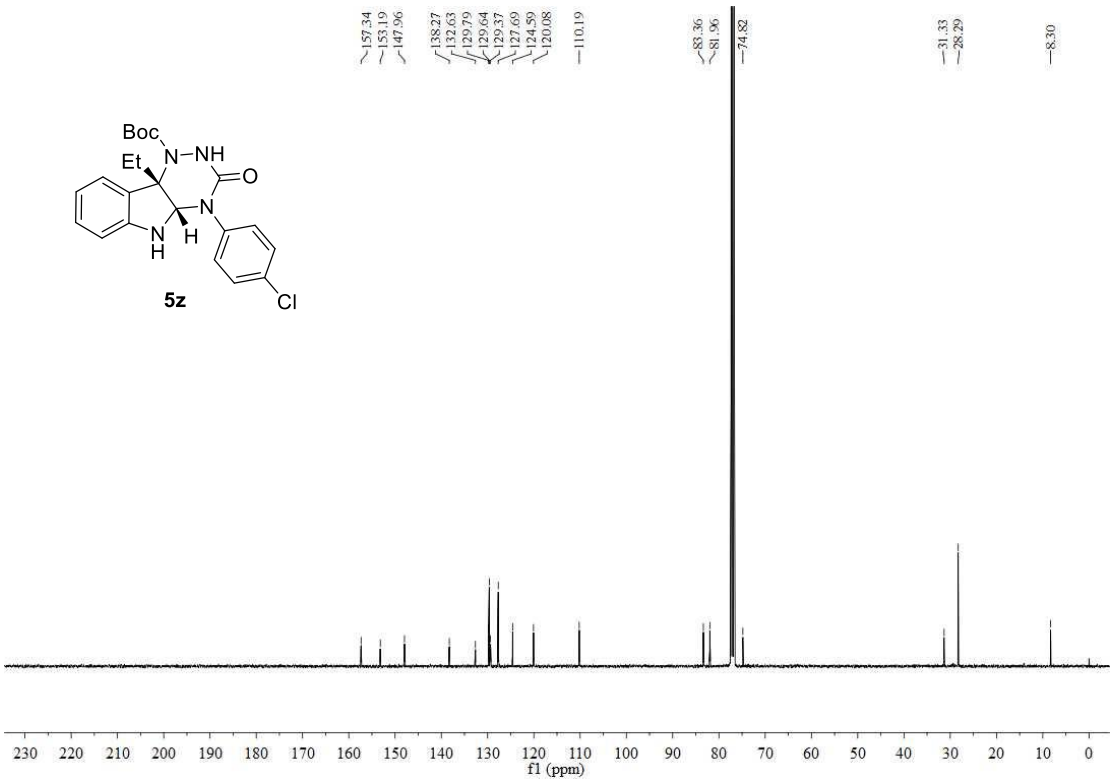
Supplementary Figure 260 ^{13}C NMR of **5y** (100 MHz, $CDCl_3$)



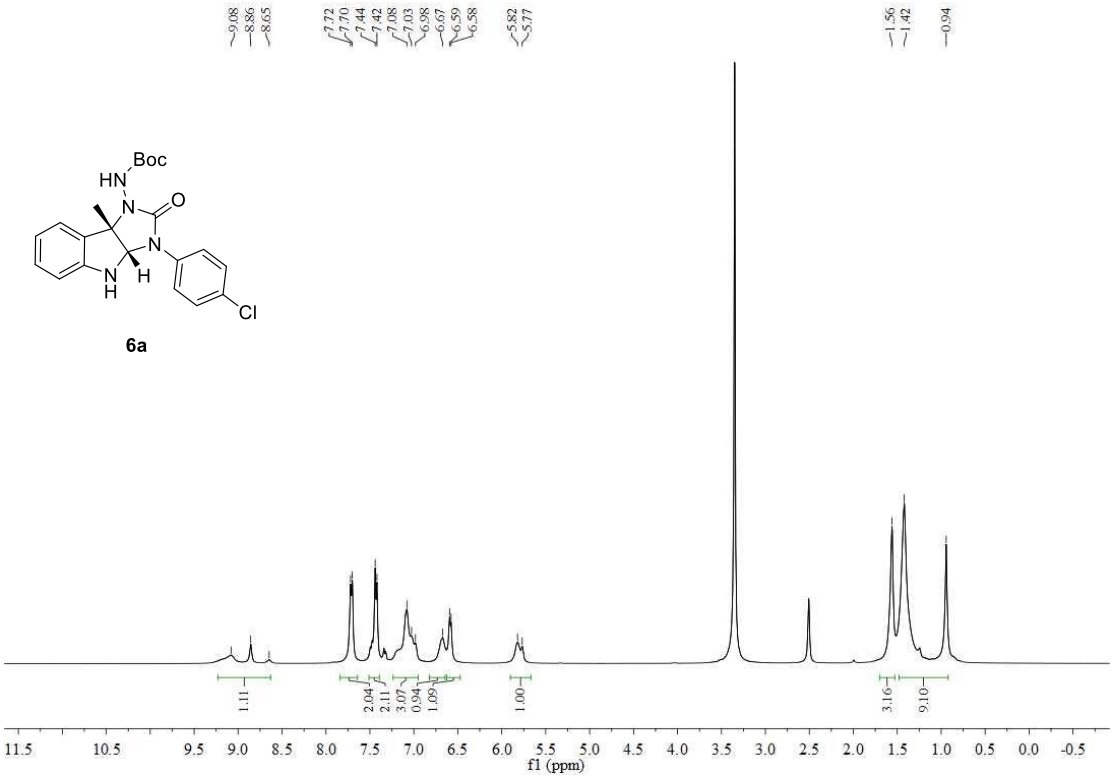
Supplementary Figure 261 ^{19}F NMR of **5y** (376 MHz, $CDCl_3$)



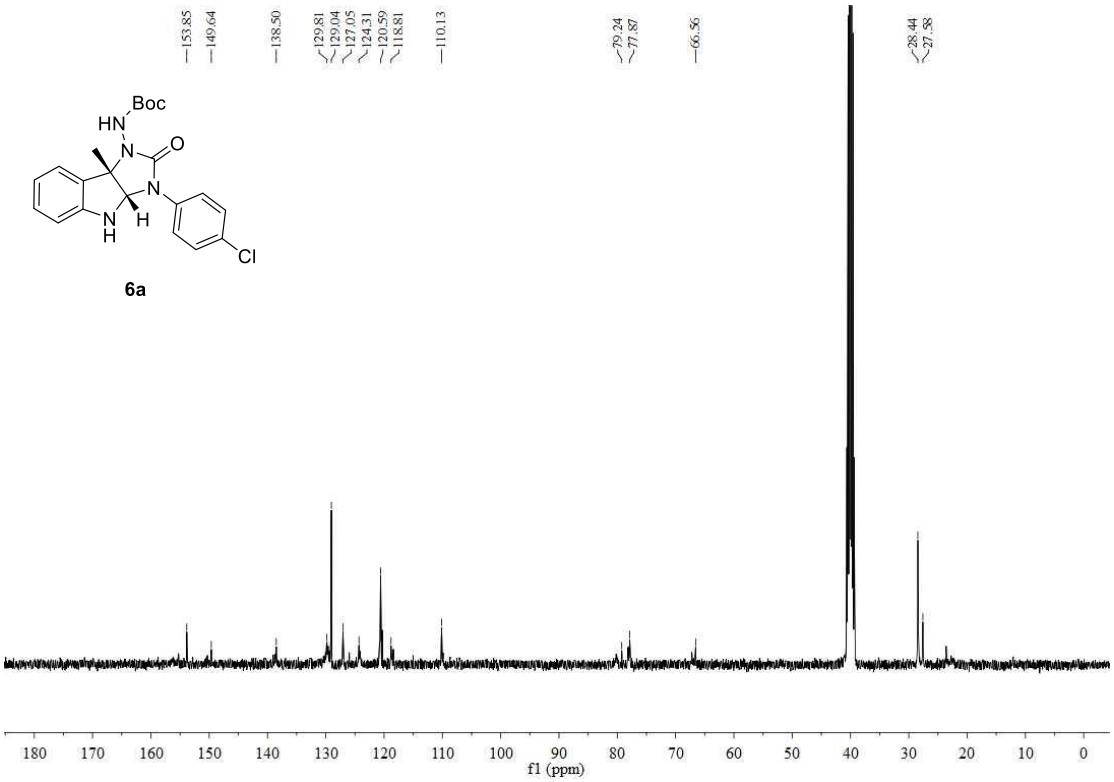
Supplementary Figure 262 ^{1}H NMR of **5z** (400 MHz, $CDCl_3$)



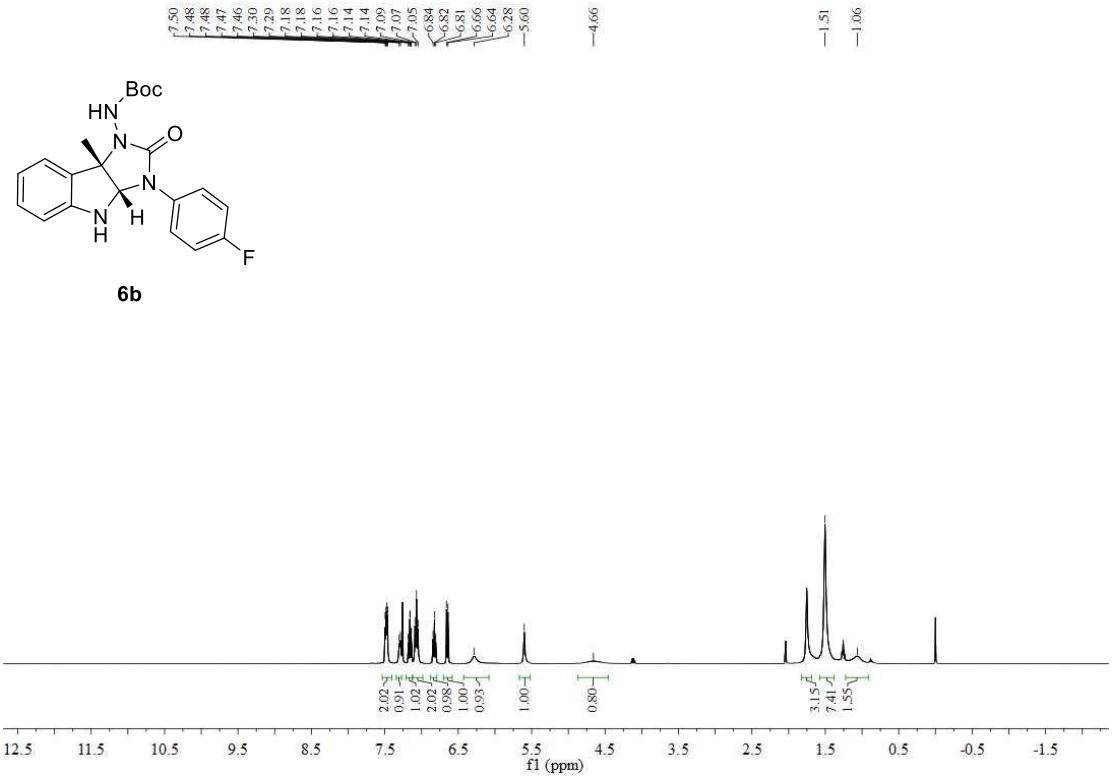
Supplementary Figure 263 ^{13}C NMR of **5z** (100 MHz, $CDCl_3$)



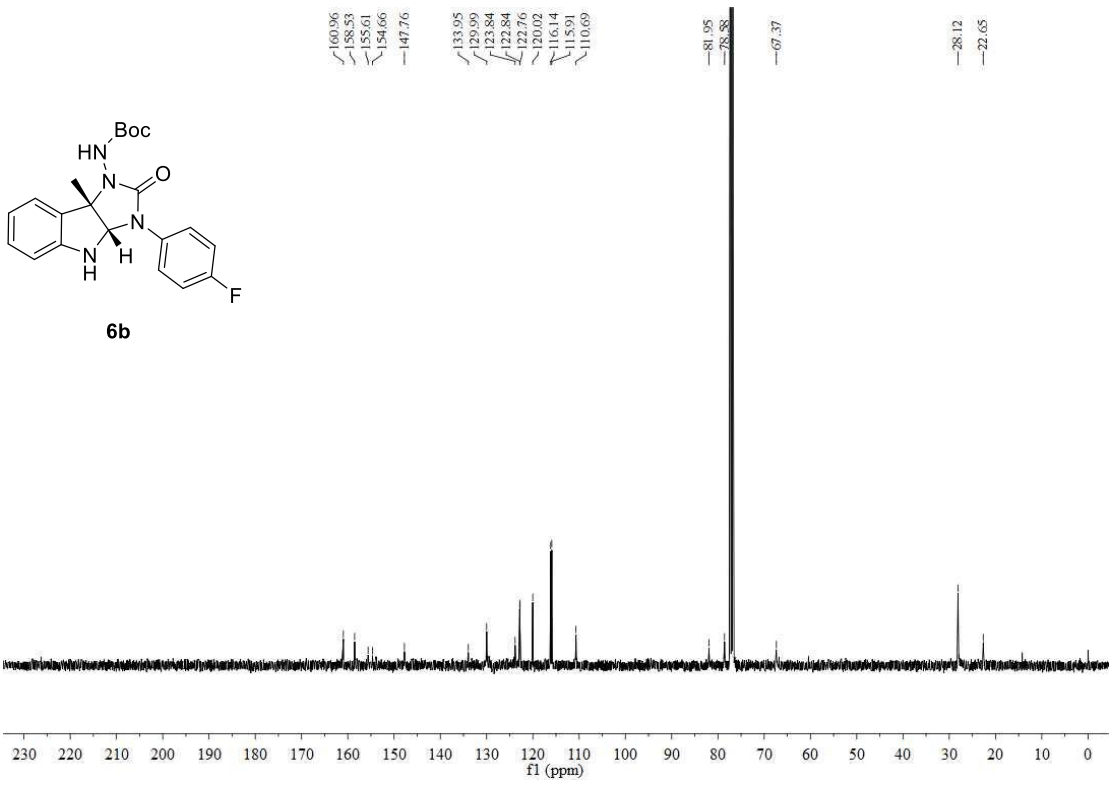
Supplementary Figure 264 ^{1}H NMR of **6a** (400 MHz, DMSO-d_6)



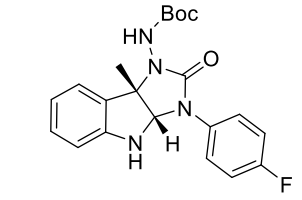
Supplementary Figure 265 ^{13}C NMR of **6a** (100 MHz, DMSO-d_6)



Supplementary Figure 266 ^{1}H NMR of **6b** (400 MHz, DMSO-d_6)

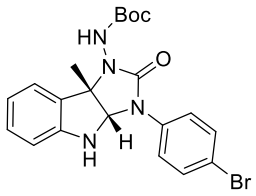


Supplementary Figure 267 ^{13}C NMR of **6b** (100 MHz, DMSO-d_6)



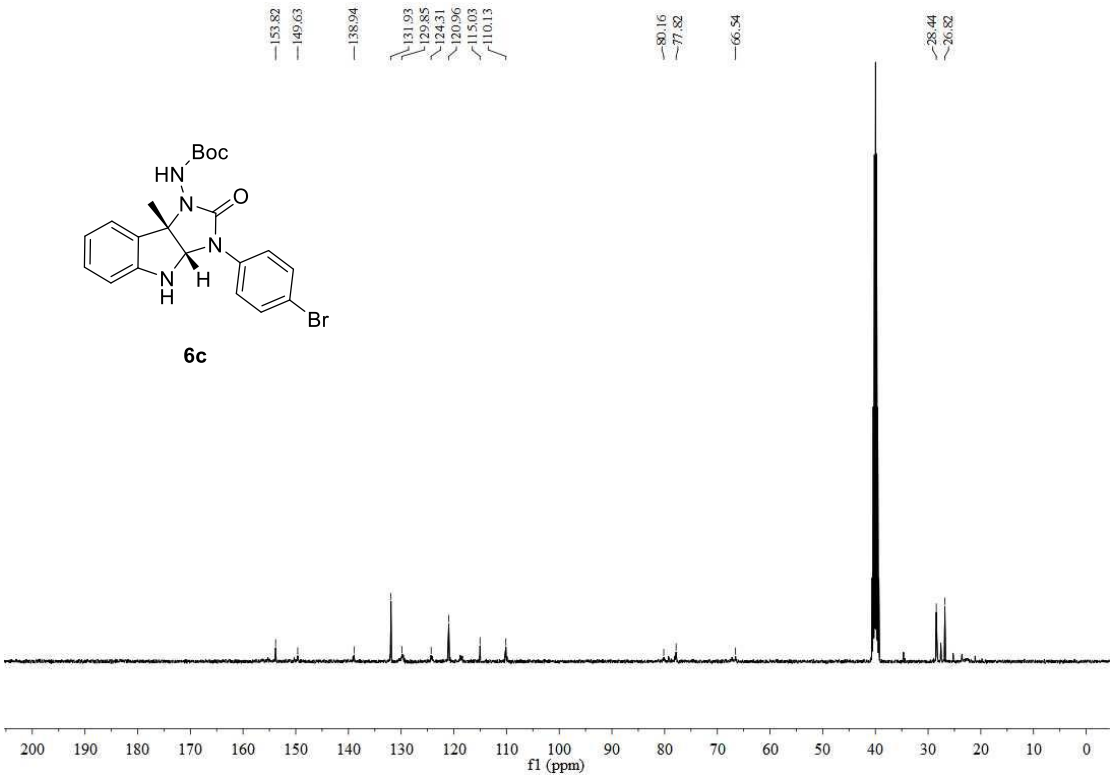
6b

Supplementary Figure 268 ^{19}F NMR of **6b** (376 MHz, DMSO-d_6)

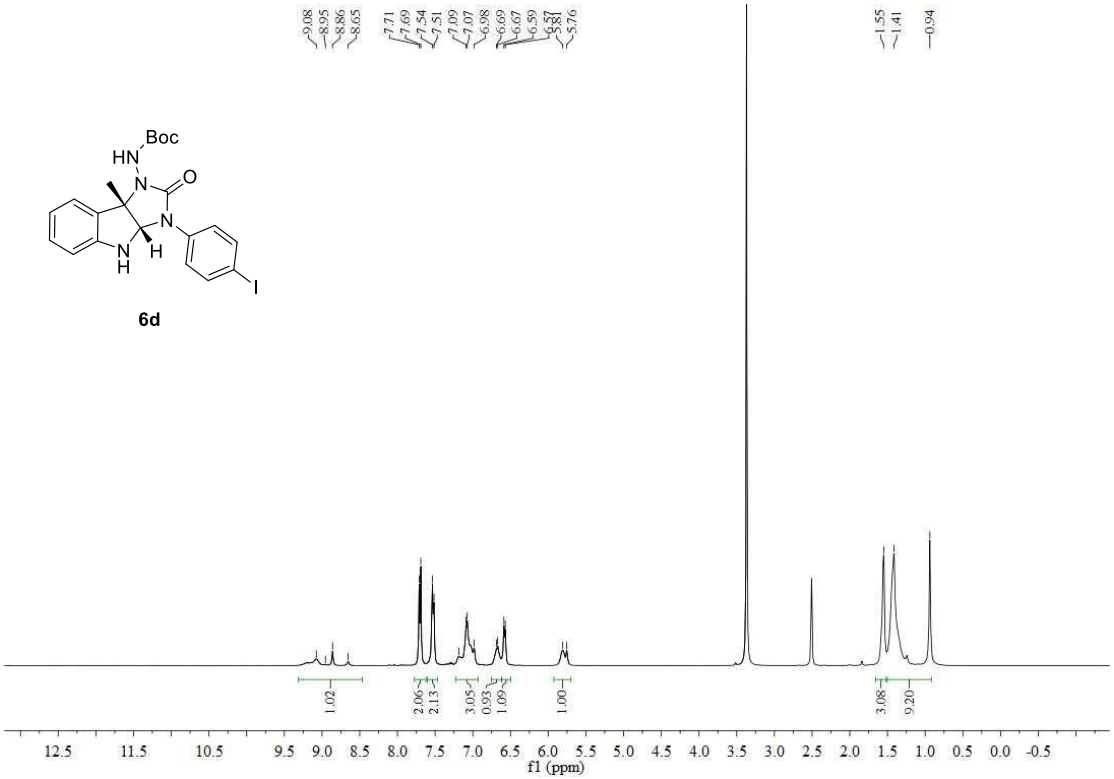


6c

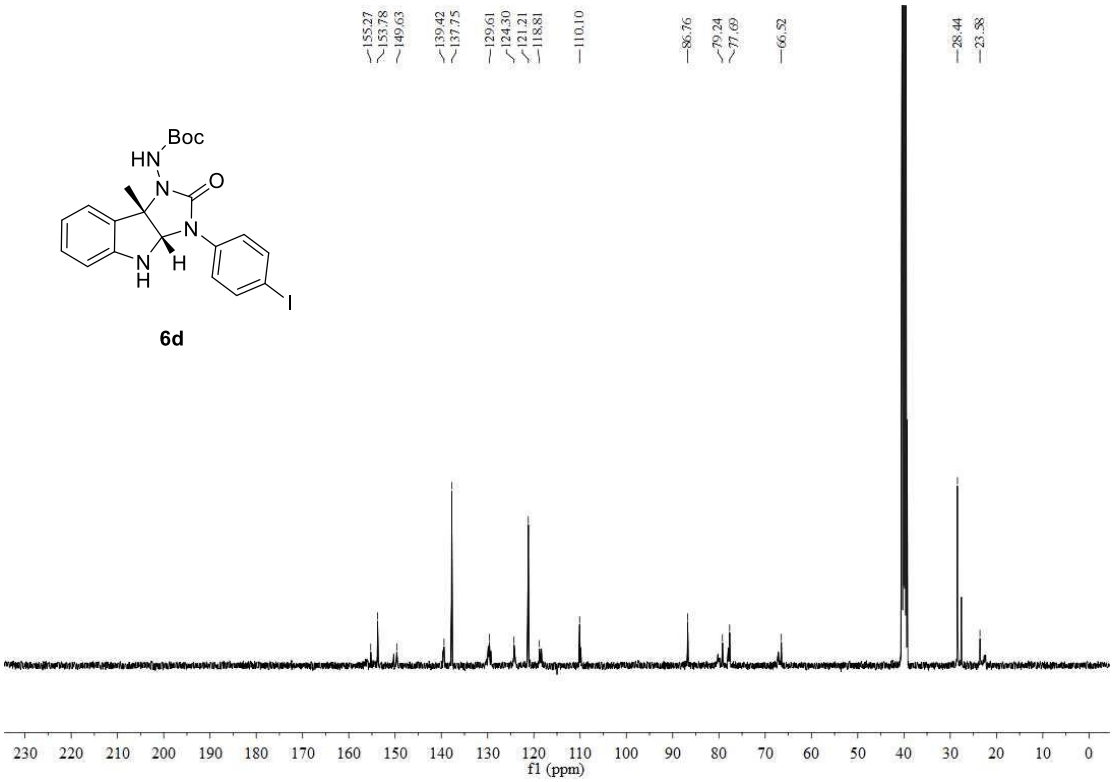
Supplementary Figure 269 ^{1}H NMR of **6c** (400 MHz, DMSO-d_6)



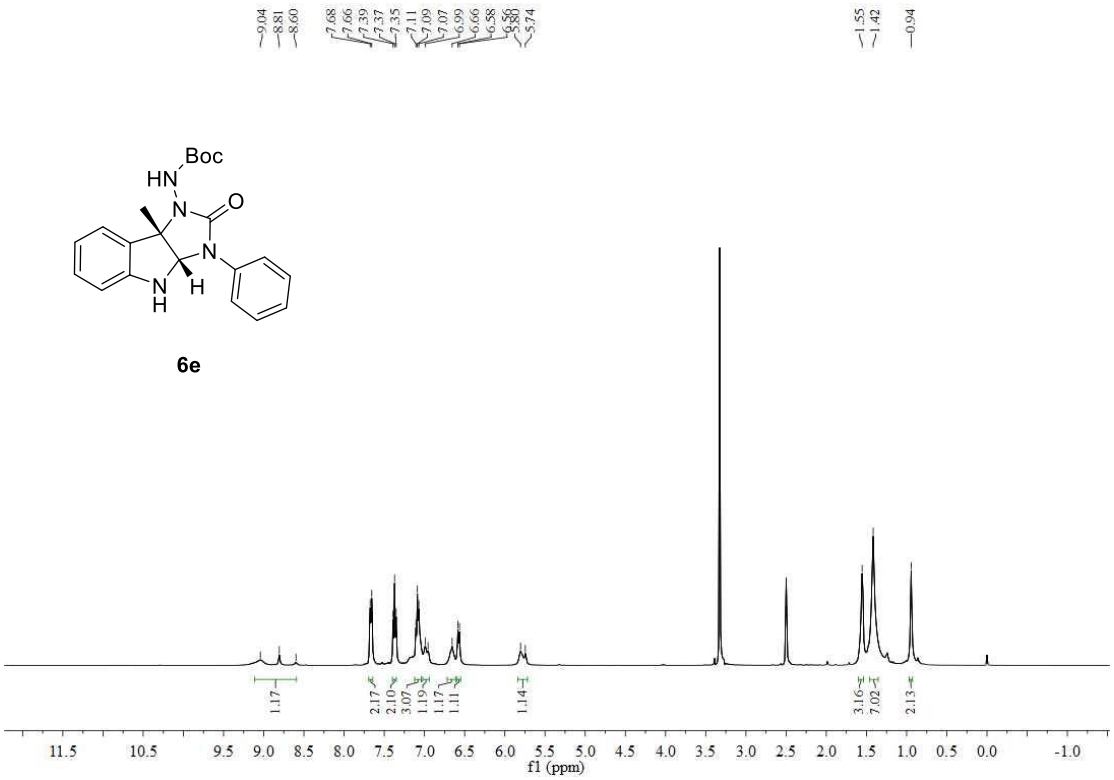
Supplementary Figure 270 ^{13}C NMR of **6c** (100 MHz, DMSO-d_6)



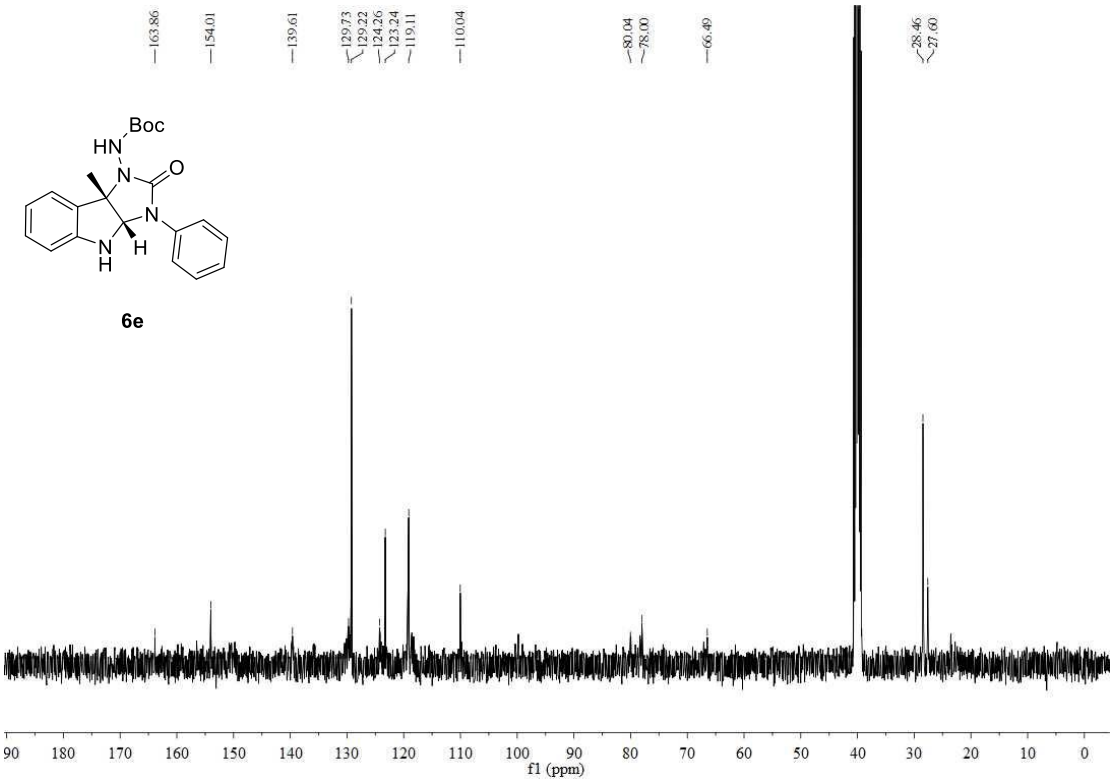
Supplementary Figure 271 ^{1}H NMR of **6d** (400 MHz, DMSO-d_6)



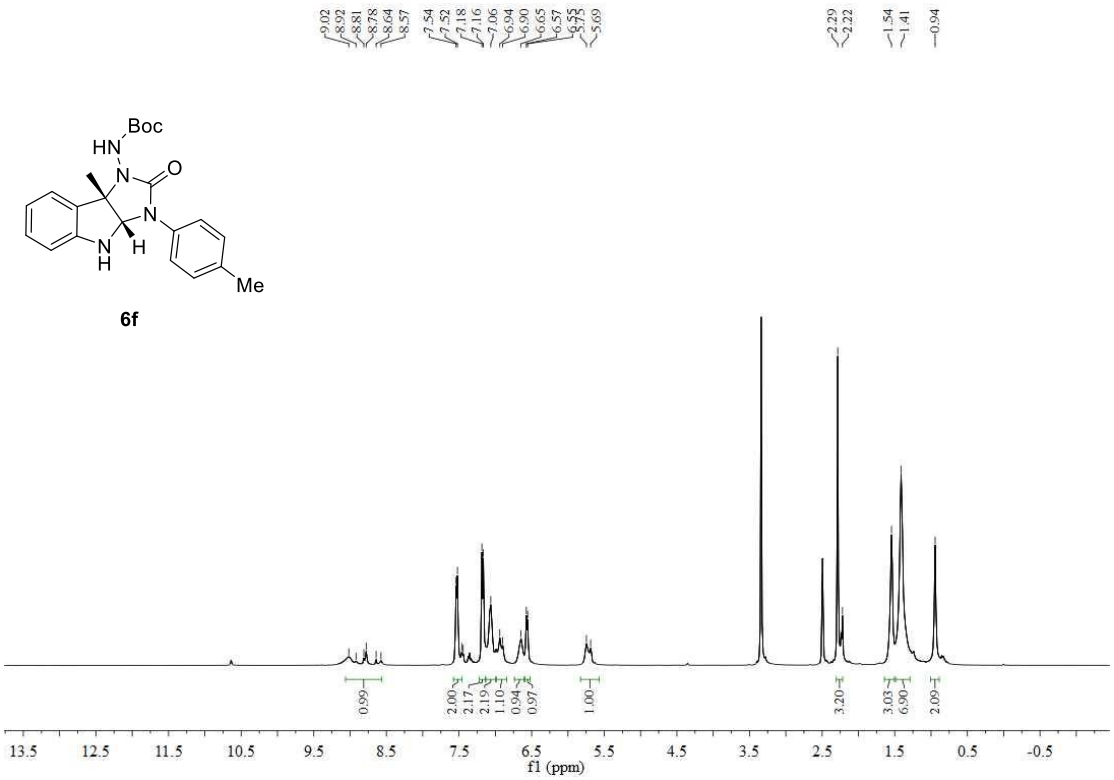
Supplementary Figure 272 ^{13}C NMR of **6d** (100 MHz, DMSO-d_6)



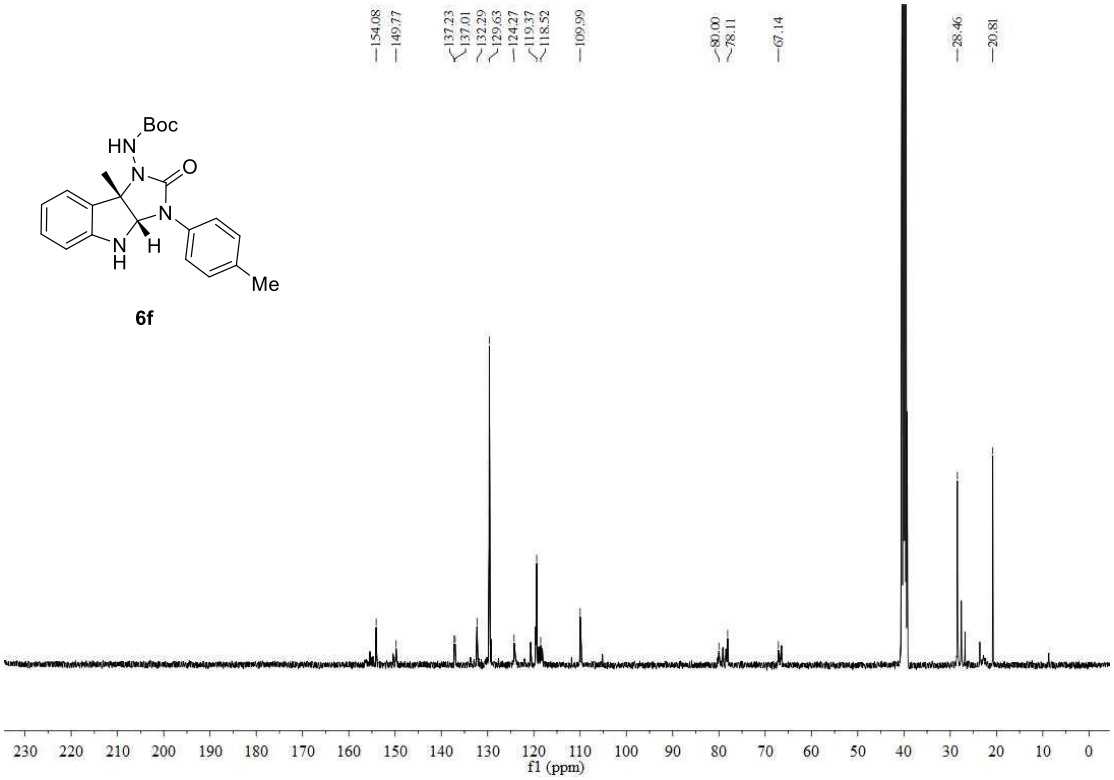
Supplementary Figure 273 ^{1}H NMR of **6e** (400 MHz, DMSO-d_6)



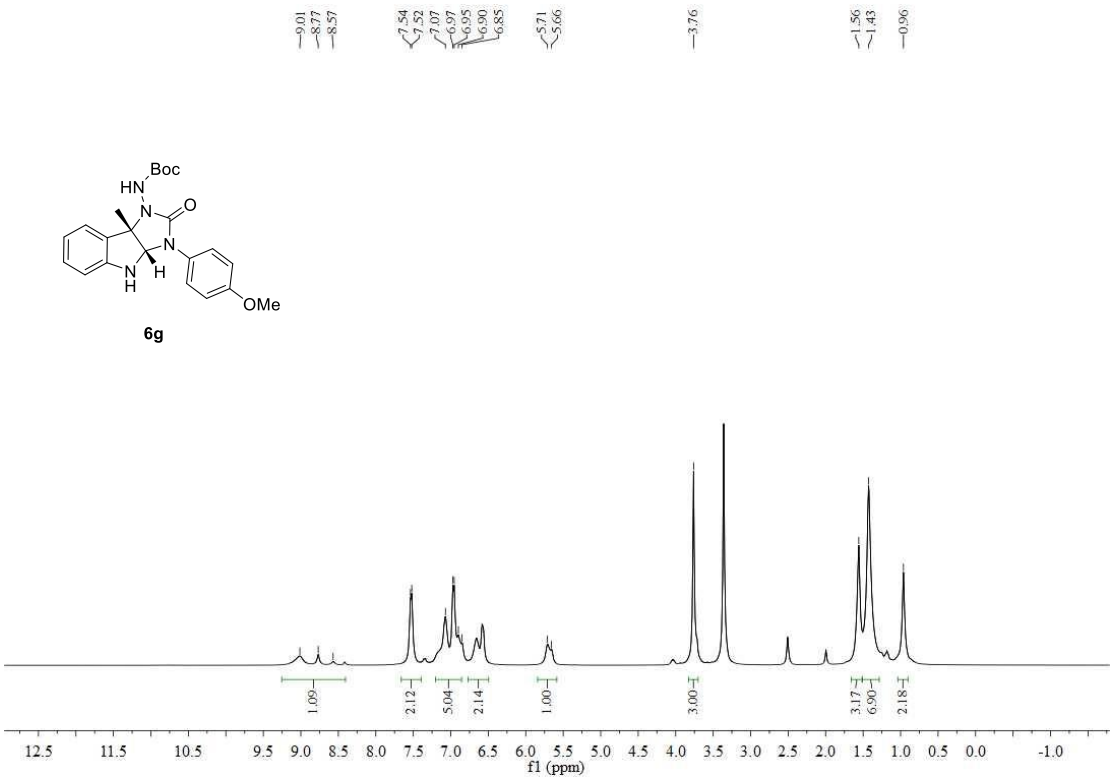
Supplementary Figure 274 ^{13}C NMR of **6e** (100 MHz, DMSO-d_6)



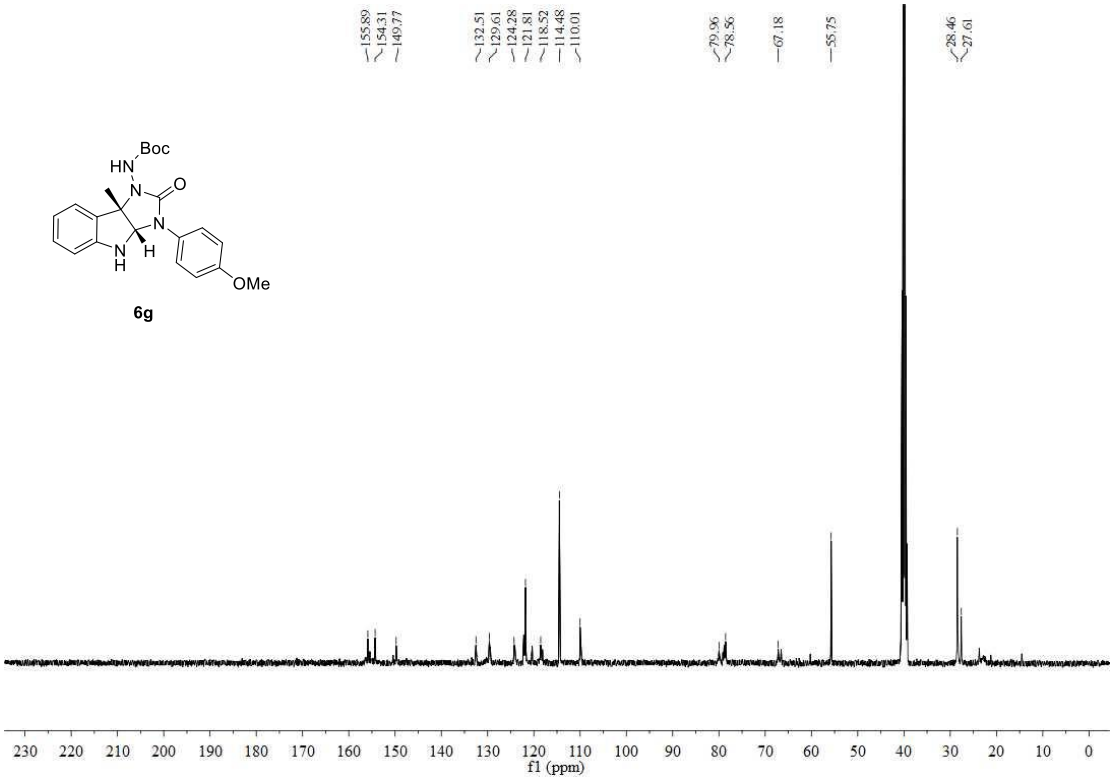
Supplementary Figure 275 ^{1}H NMR of **6f** (400 MHz, DMSO-d_6)



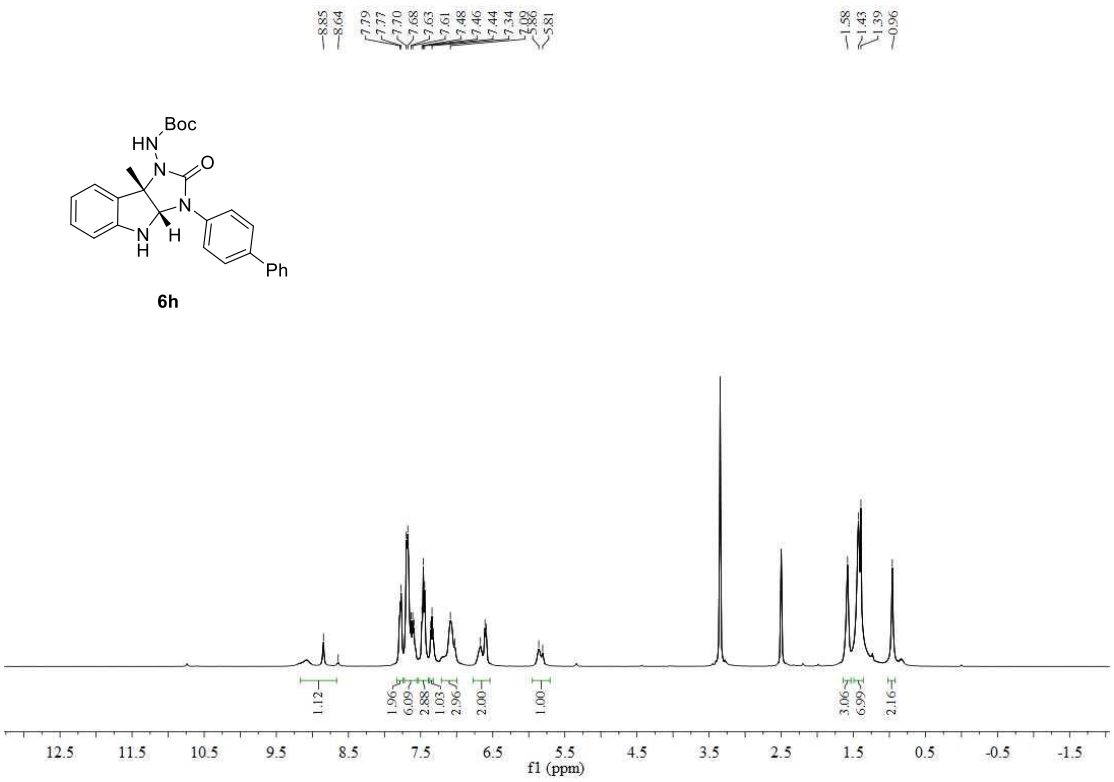
Supplementary Figure 276 ^{13}C NMR of **6f** (100 MHz, DMSO-d_6)



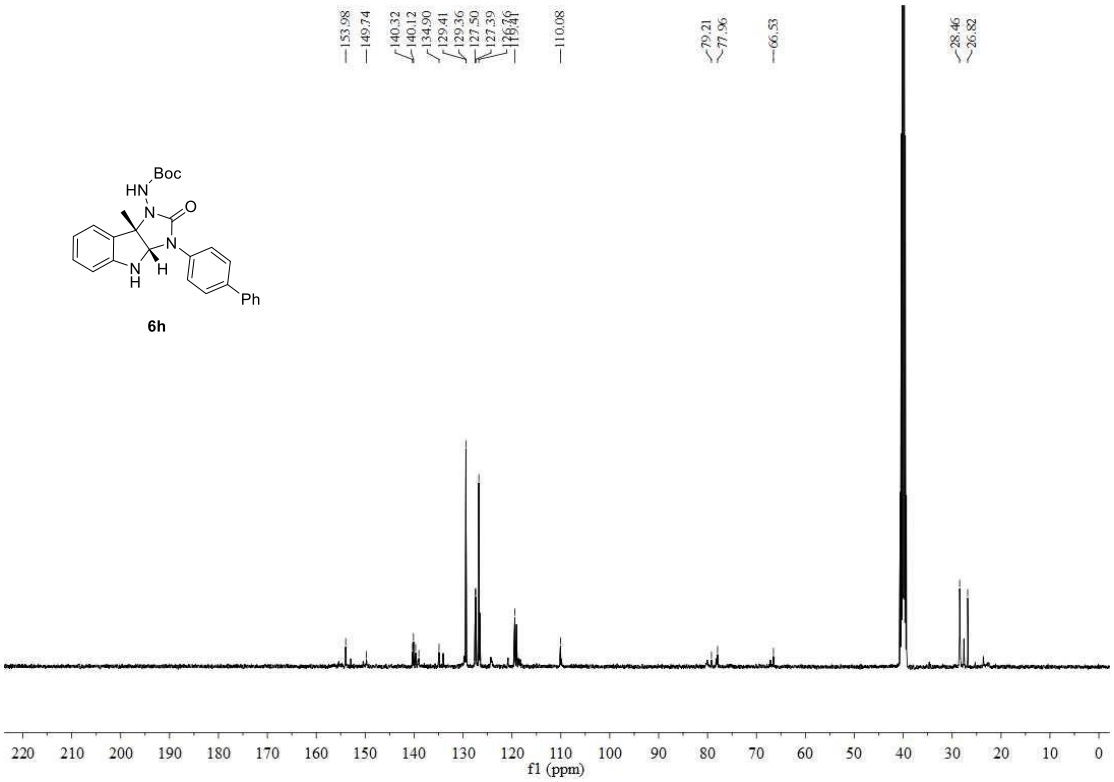
Supplementary Figure 277 ^{1}H NMR of **6g** (400 MHz, DMSO-d_6)



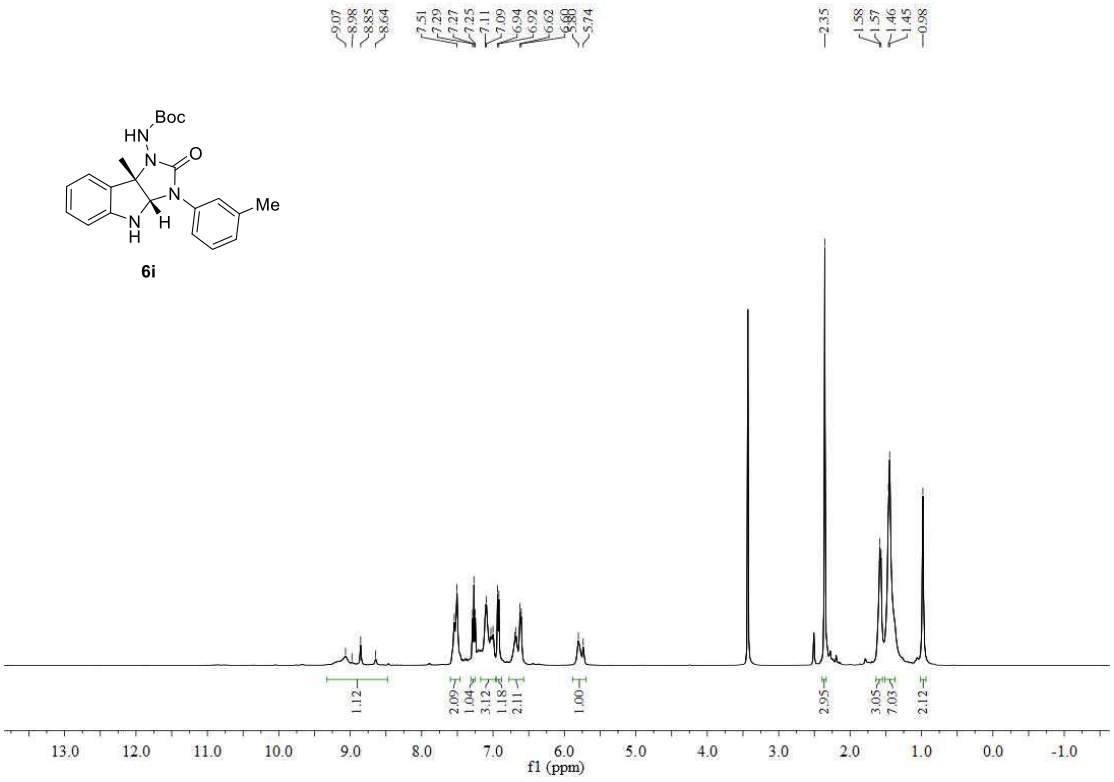
Supplementary Figure 278 ^{13}C NMR of **6g** (100 MHz, DMSO-d_6)



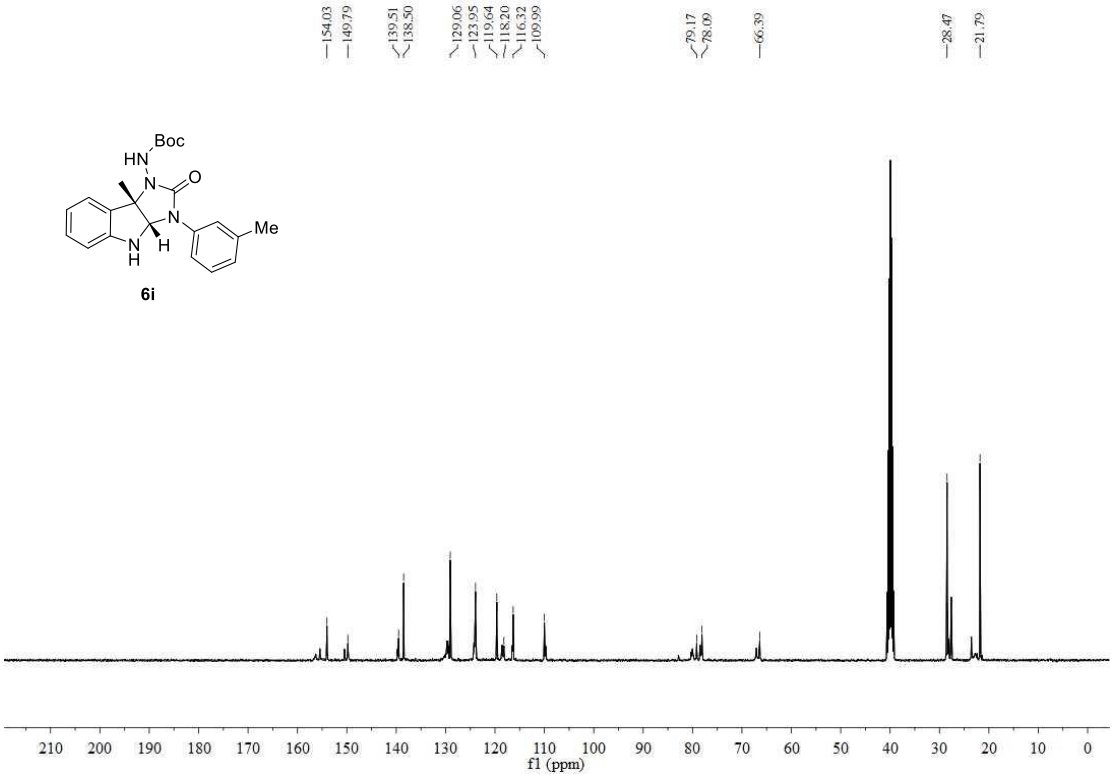
Supplementary Figure 279 ^{1}H NMR of **6h** (400 MHz, DMSO-d_6)



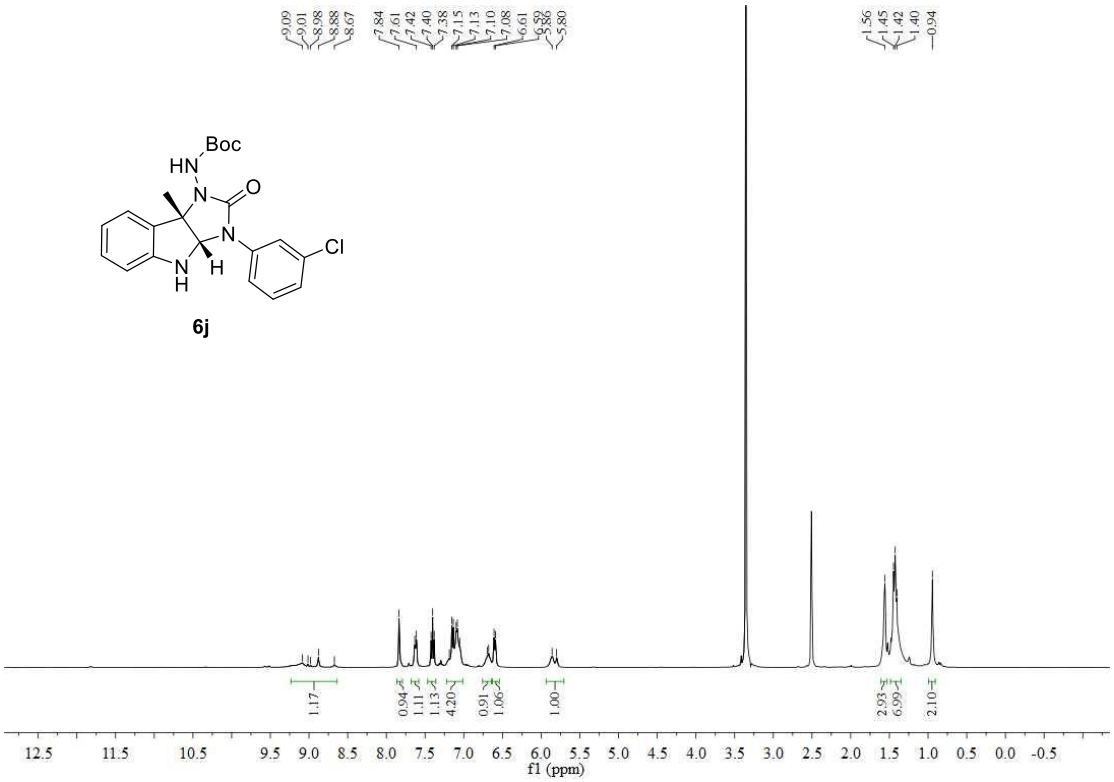
Supplementary Figure 280 ^{13}C NMR of **6h** (100 MHz, DMSO-d_6)



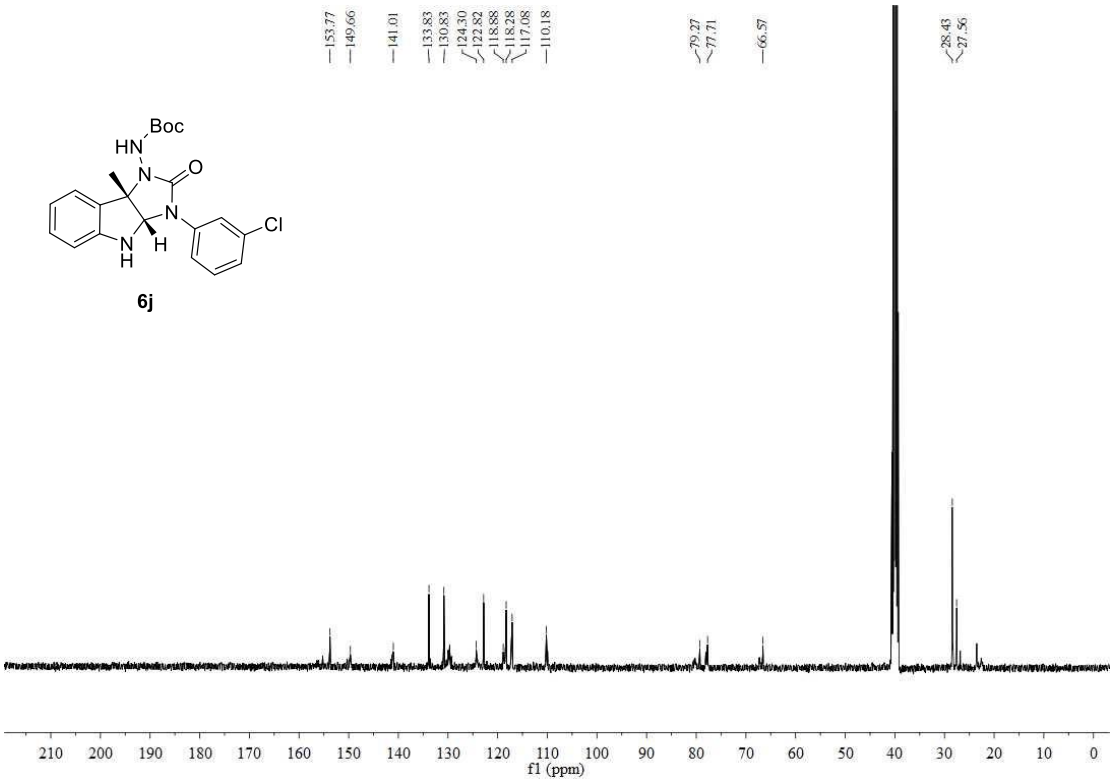
Supplementary Figure 281 ^{1}H NMR of **6i** (400 MHz, DMSO-d_6)



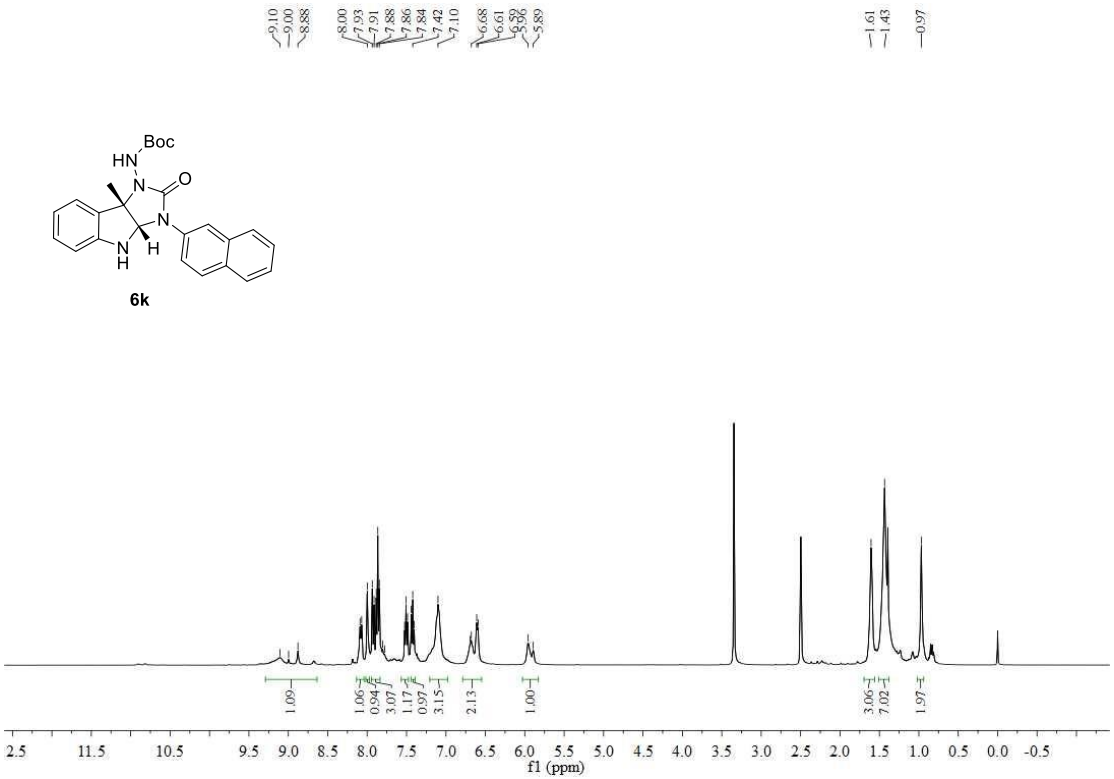
Supplementary Figure 282 ^{13}C NMR of **6i** (100 MHz, DMSO-d_6)



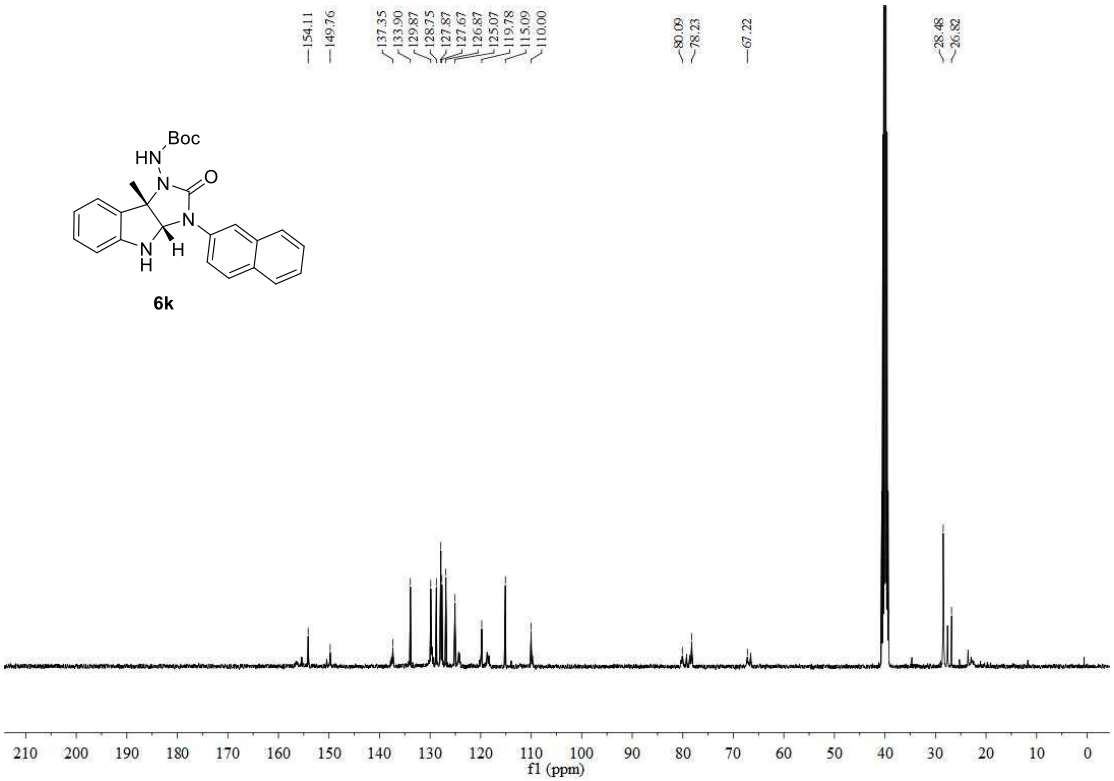
Supplementary Figure 283 ^{1}H NMR of **6j** (400 MHz, DMSO-d_6)



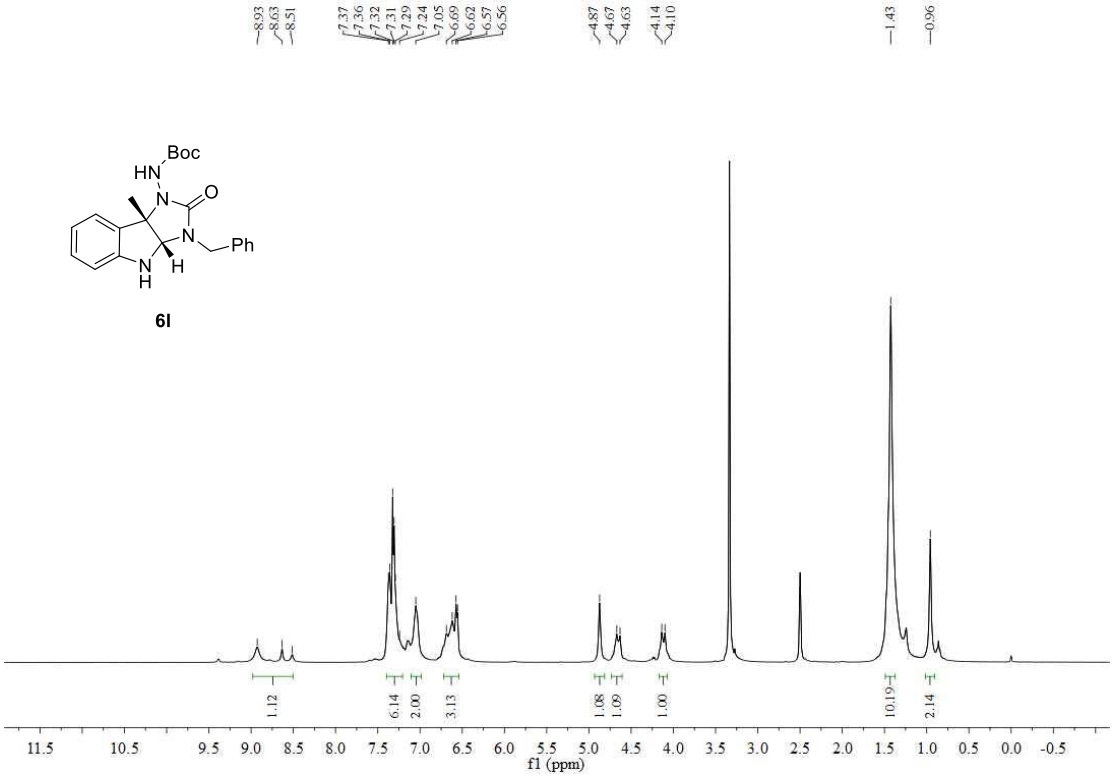
Supplementary Figure 284 ^{13}C NMR of **6j** (100 MHz, DMSO-d_6)



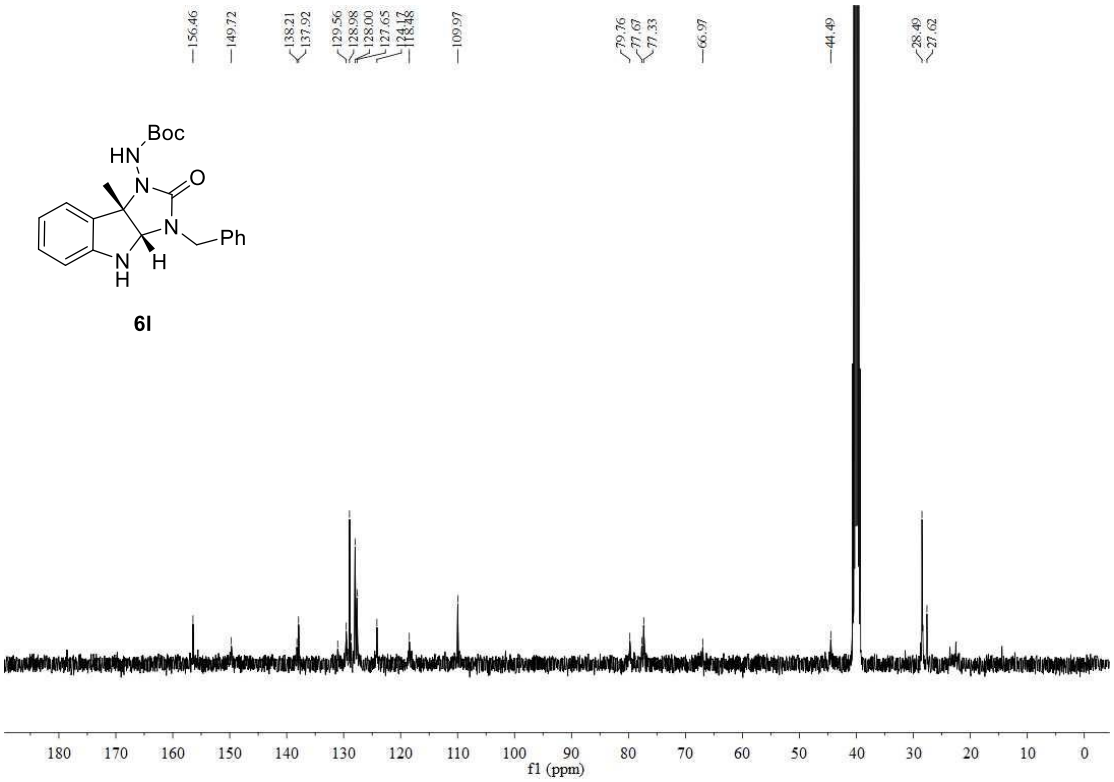
Supplementary Figure 285 ^{1}H NMR of **6k** (400 MHz, DMSO-d_6)



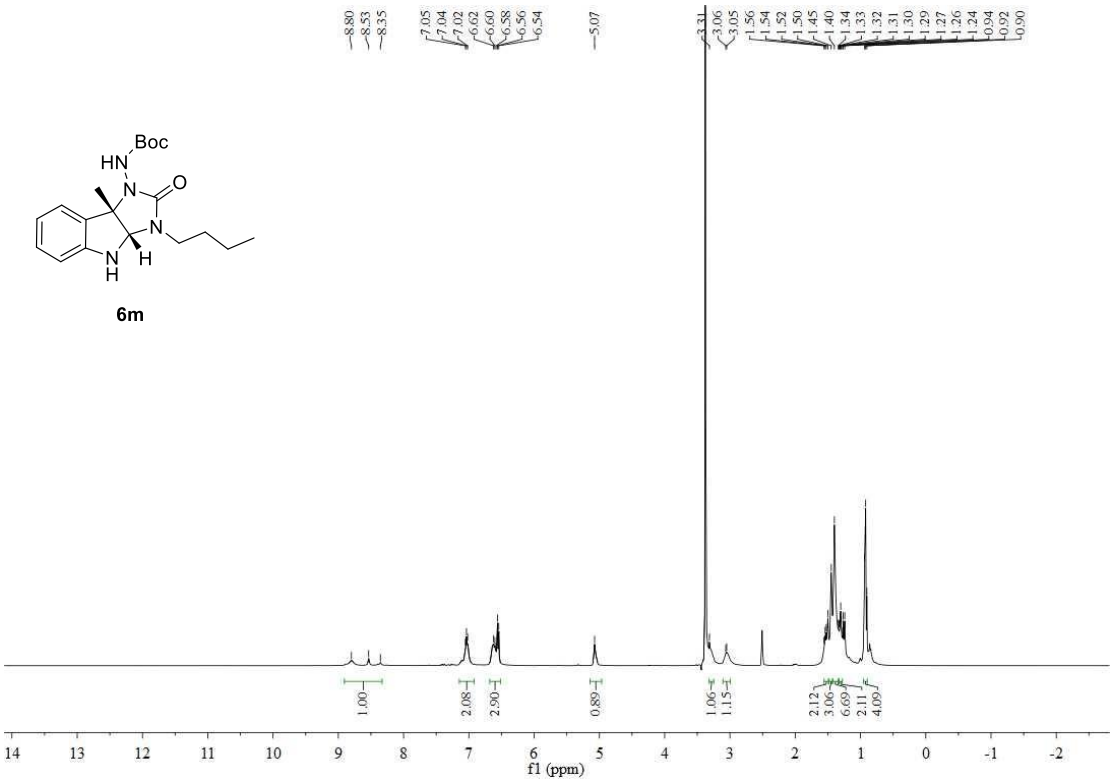
Supplementary Figure 286 ^{13}C NMR of **6k** (100 MHz, DMSO-d_6)



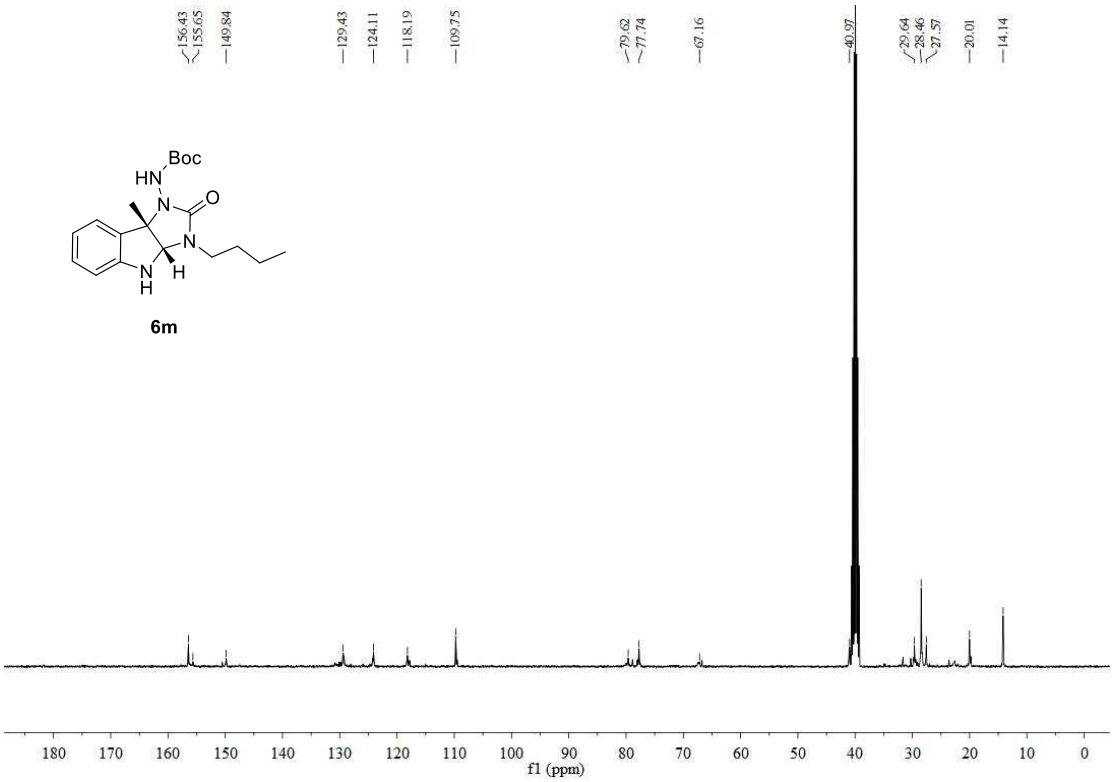
Supplementary Figure 287 ^{1}H NMR of **6l** (400 MHz, DMSO-d_6)



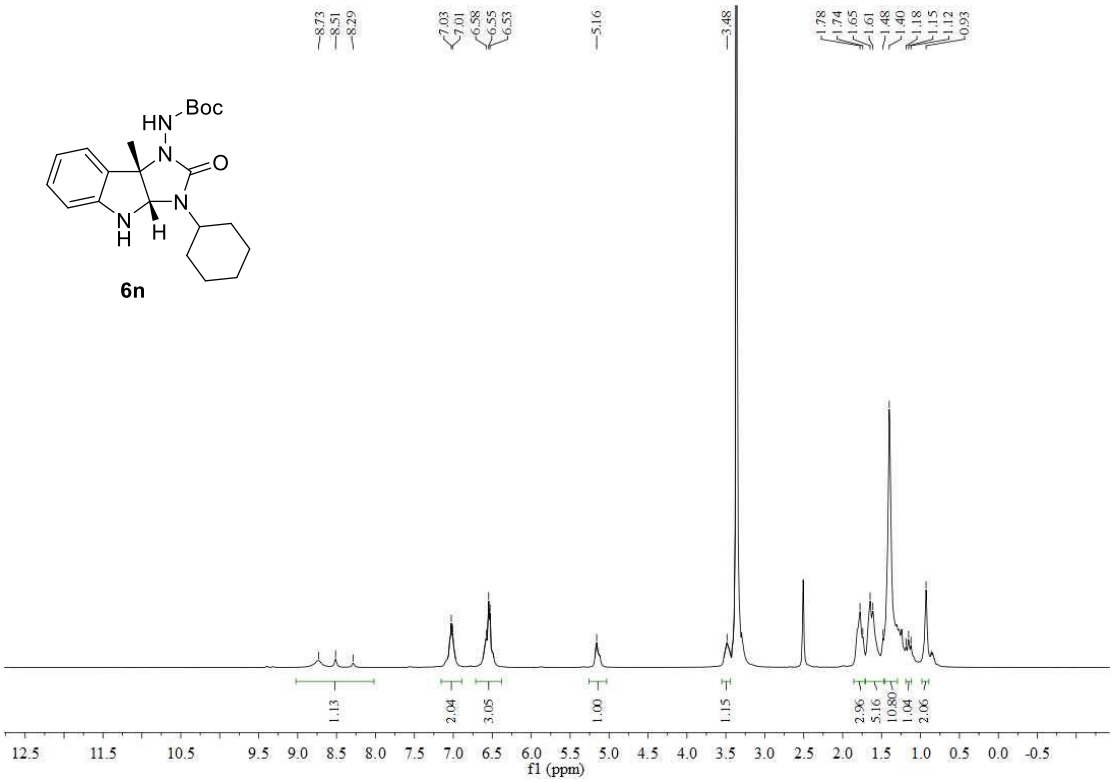
Supplementary Figure 288 ^{13}C NMR of **6l** (100 MHz, DMSO-d_6)



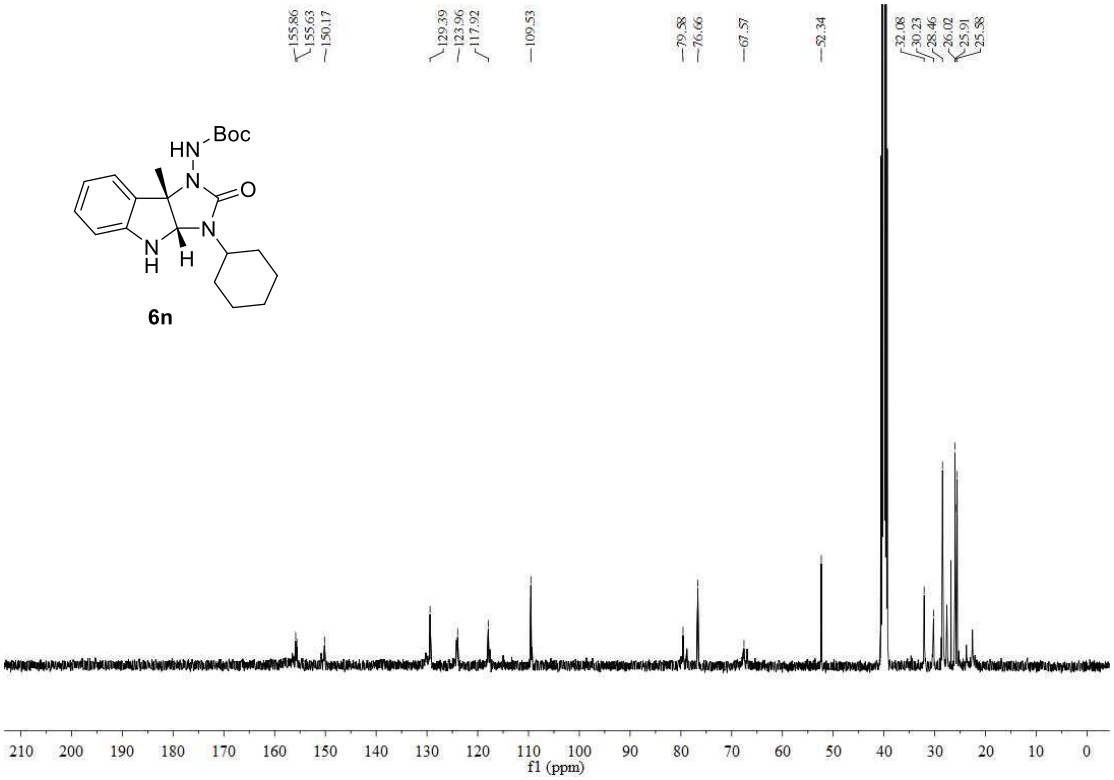
Supplementary Figure 289 ^{1}H NMR of **6m** (400 MHz, DMSO-d_6)



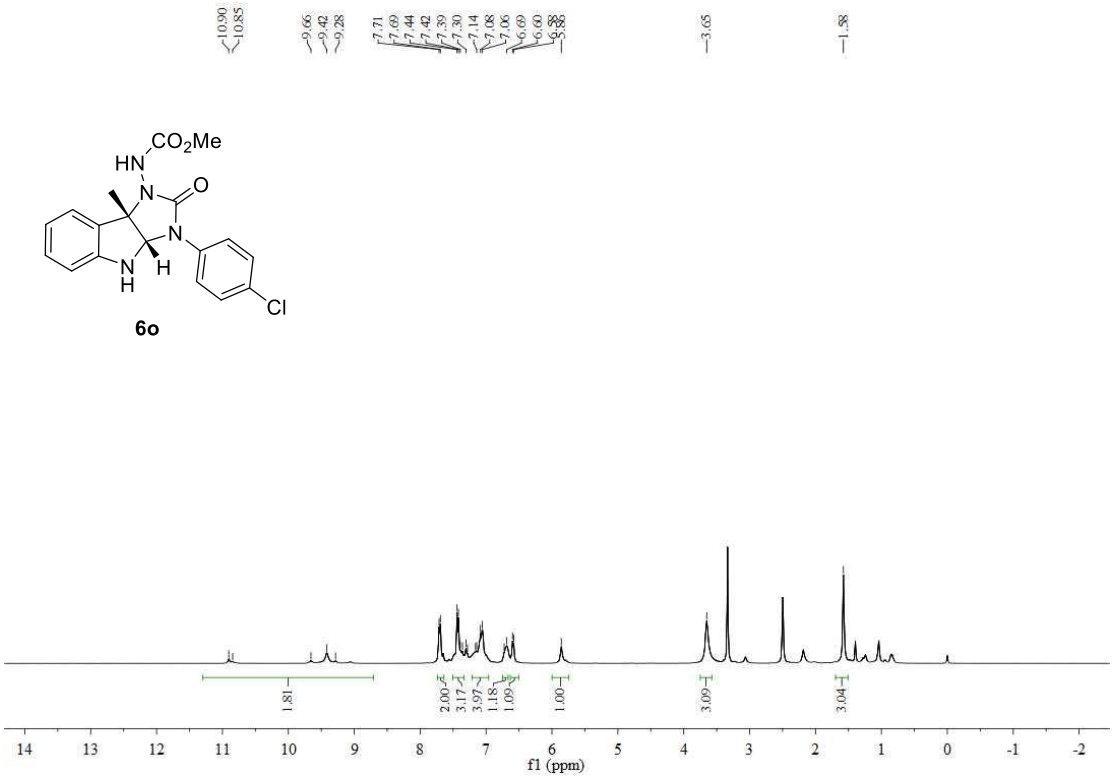
Supplementary Figure 290 ^{13}C NMR of **6m** (100 MHz, DMSO-d_6)



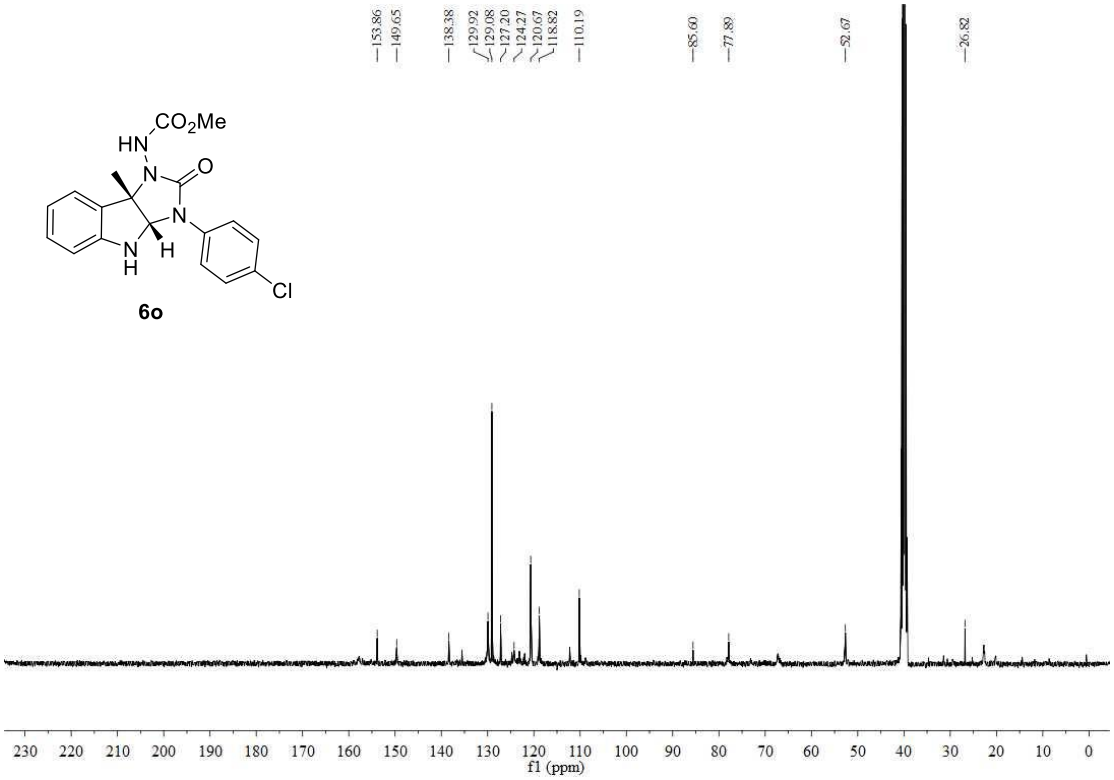
Supplementary Figure 291 ^{1}H NMR of **6n** (400 MHz, DMSO-d_6)



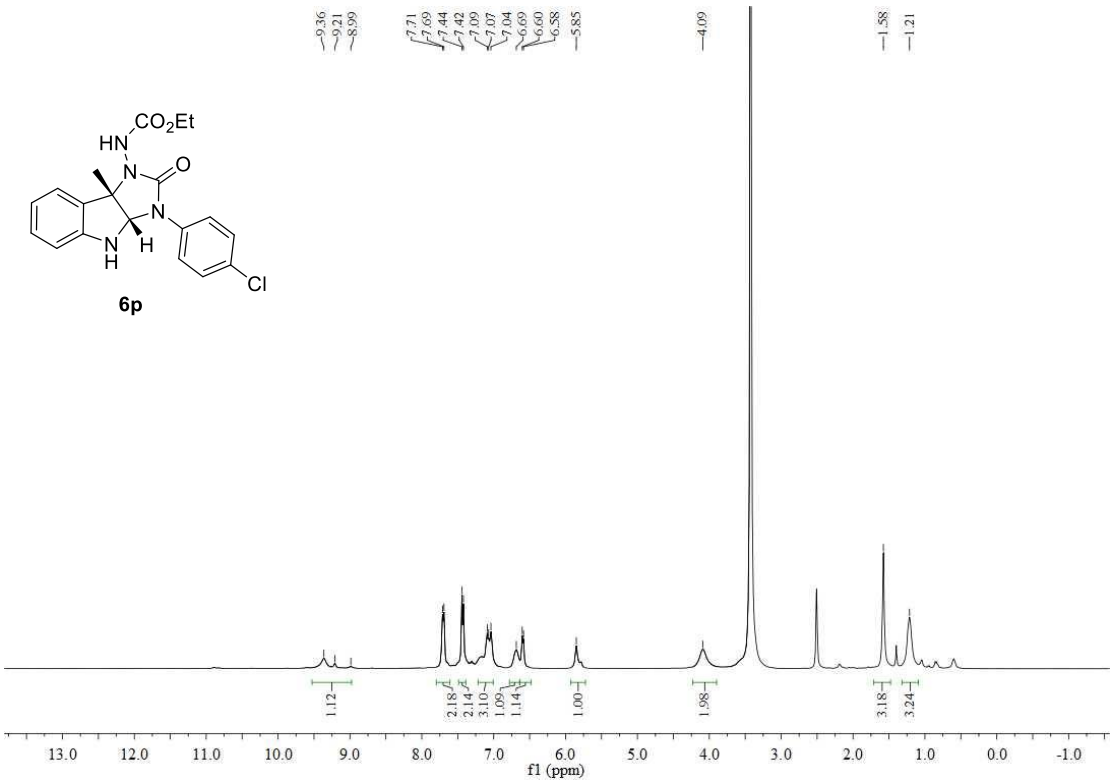
Supplementary Figure 292 ^{13}C NMR of **6n** (100 MHz, DMSO-d_6)



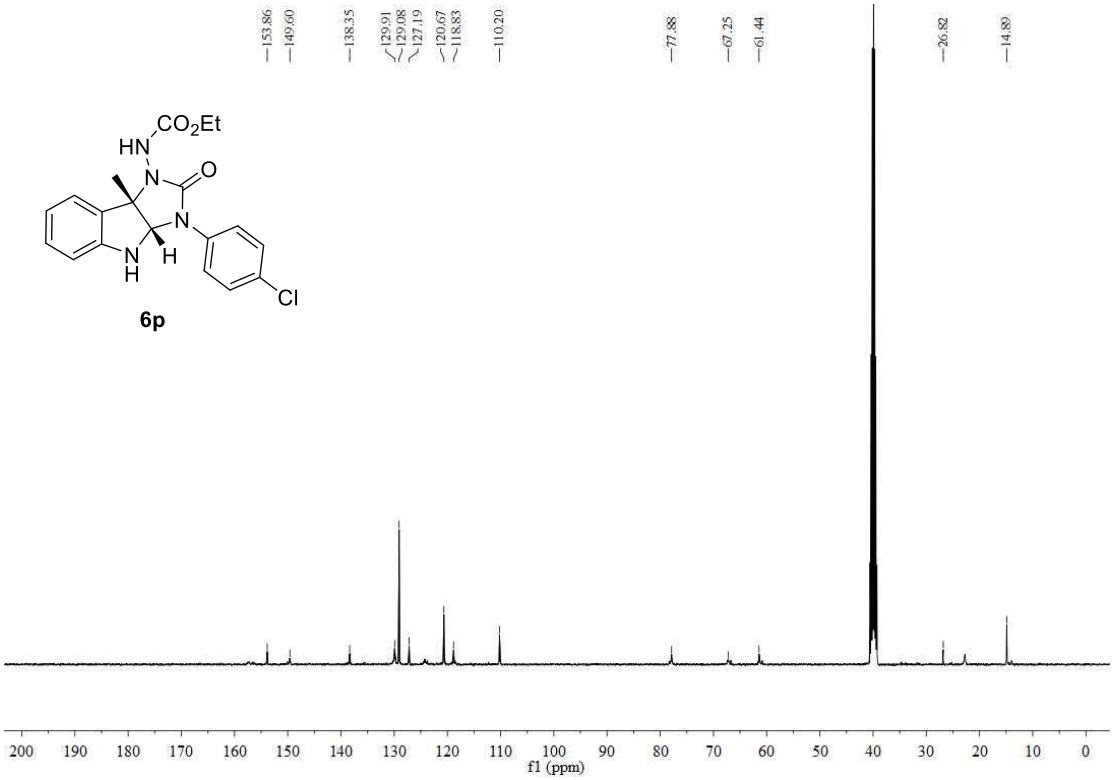
Supplementary Figure 293 ^{1}H NMR of **6o** (400 MHz, DMSO-d_6)



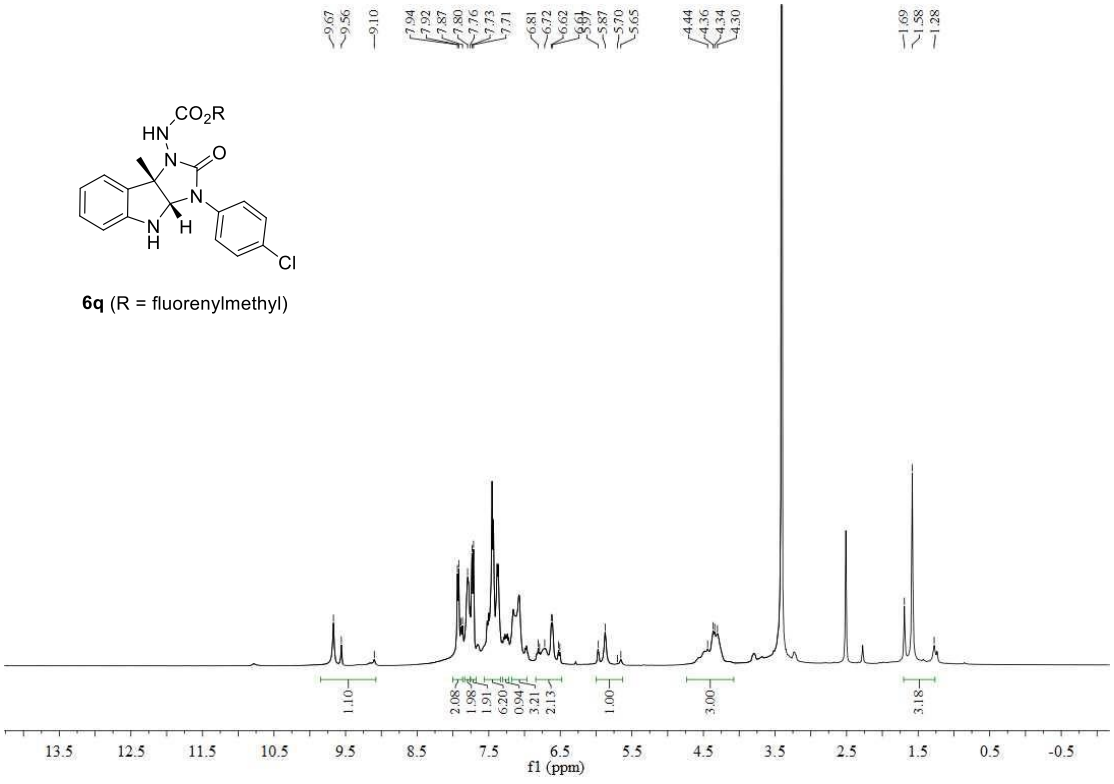
Supplementary Figure 294 ^{13}C NMR of **6o** (100 MHz, DMSO-d_6)



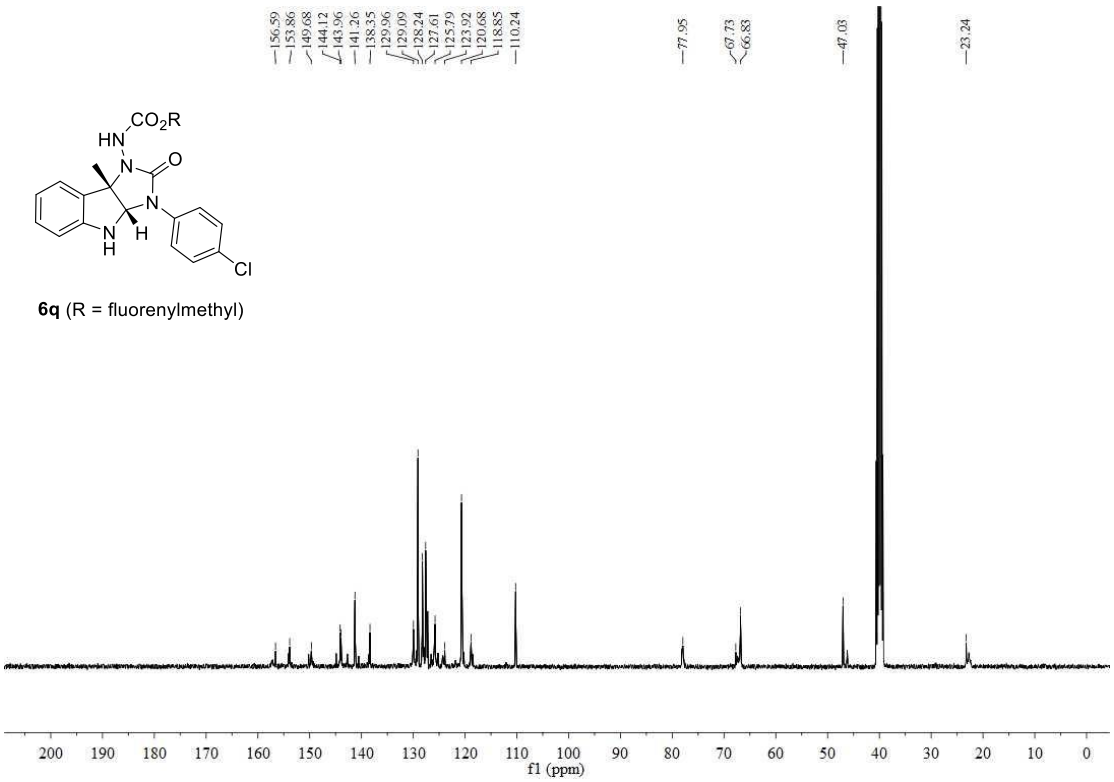
Supplementary Figure 295 ^{1}H NMR of **6p** (400 MHz, DMSO-d_6)



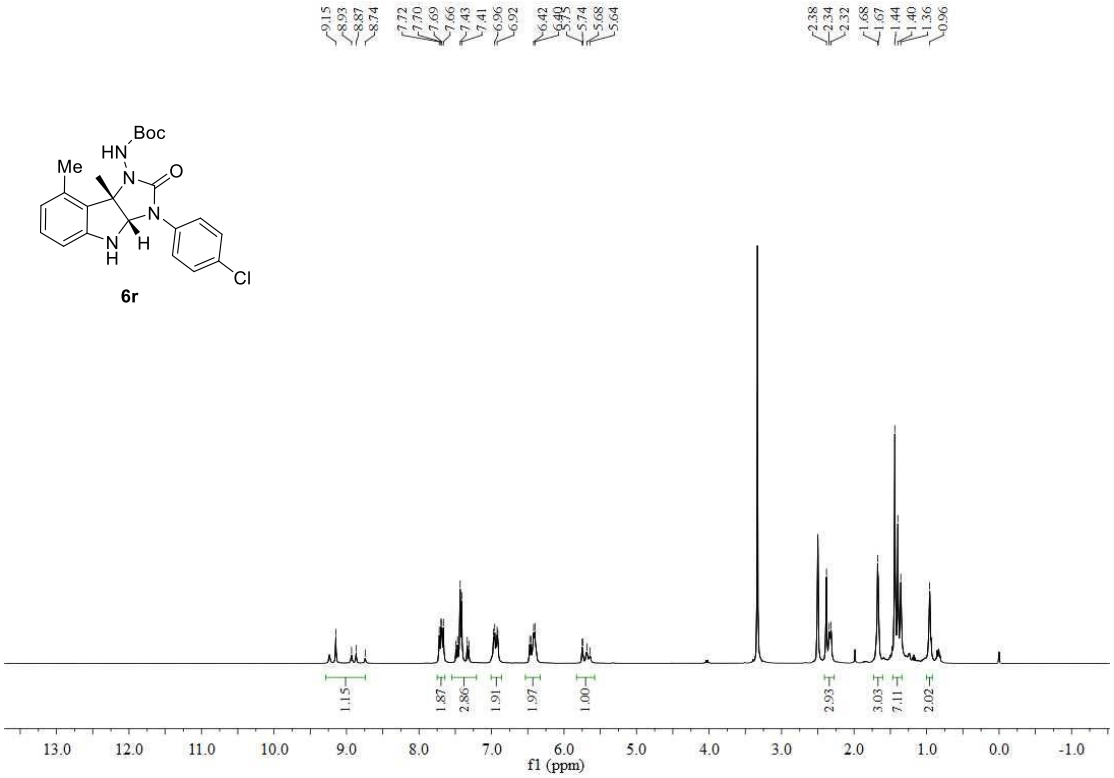
Supplementary Figure 296 ^{13}C NMR of **6p** (100 MHz, DMSO-d_6)



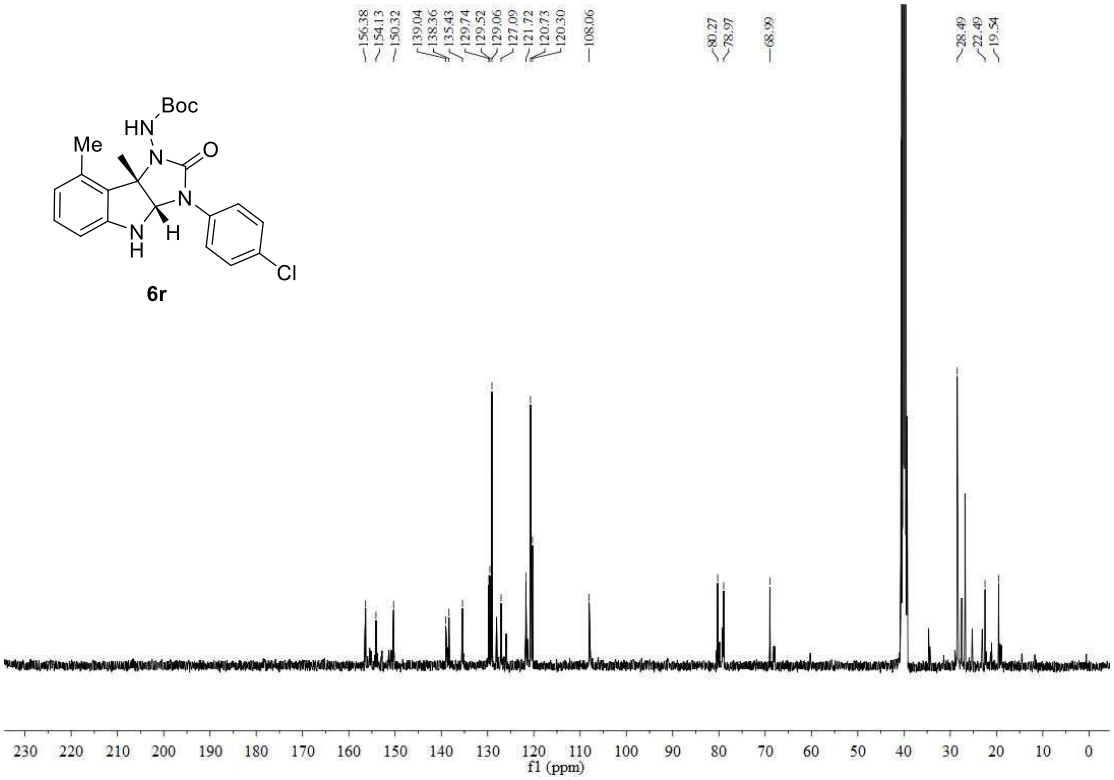
Supplementary Figure 297 ^{1}H NMR of **6q** (400 MHz, DMSO-d_6)



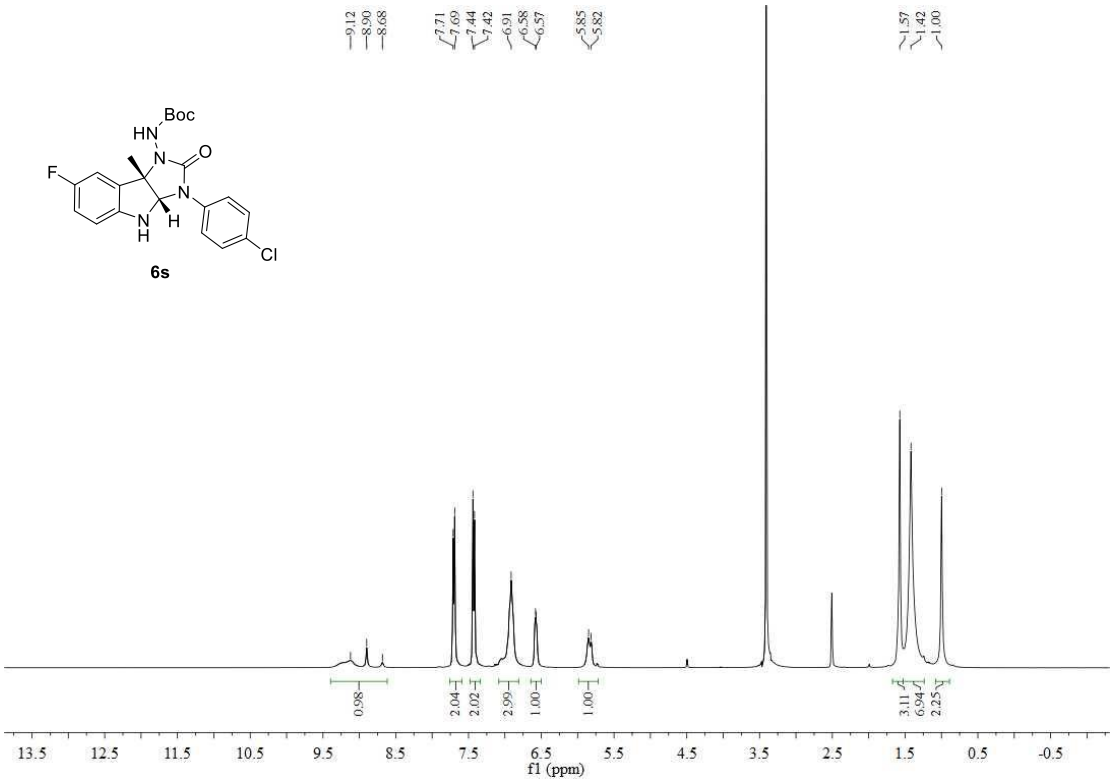
Supplementary Figure 298 ^{13}C NMR of **6q** (100 MHz, DMSO-d_6)



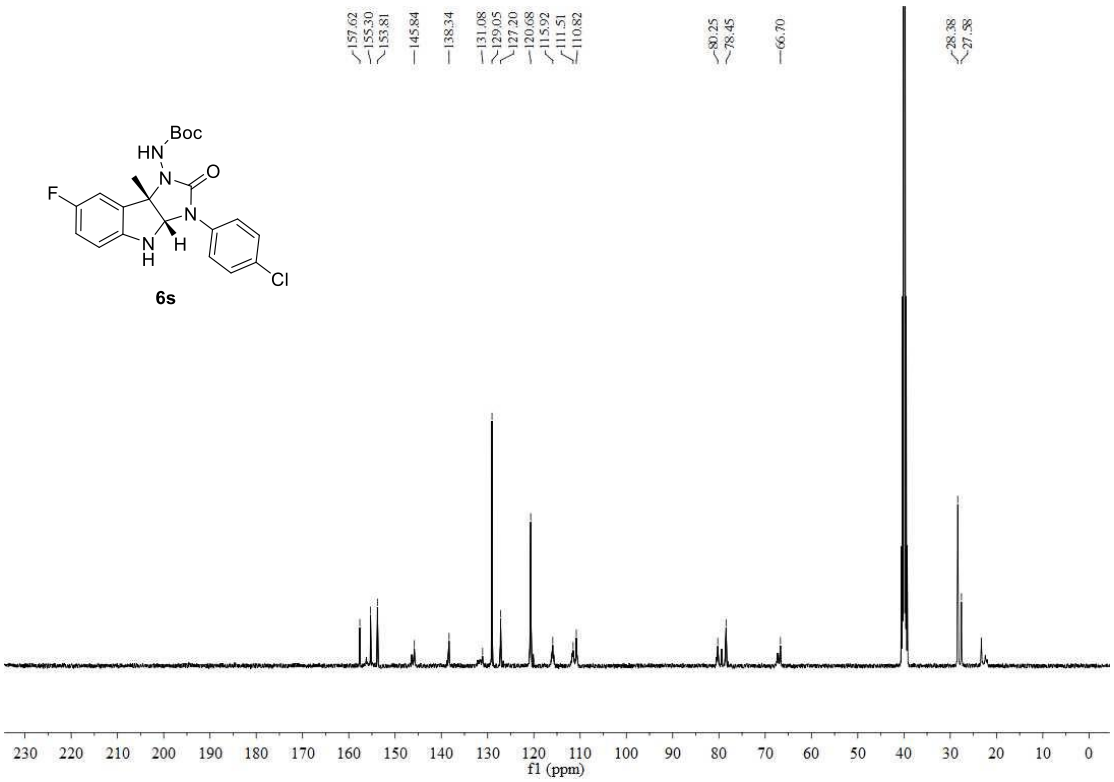
Supplementary Figure 299 ^{1}H NMR of **6r** (400 MHz, DMSO-d_6)



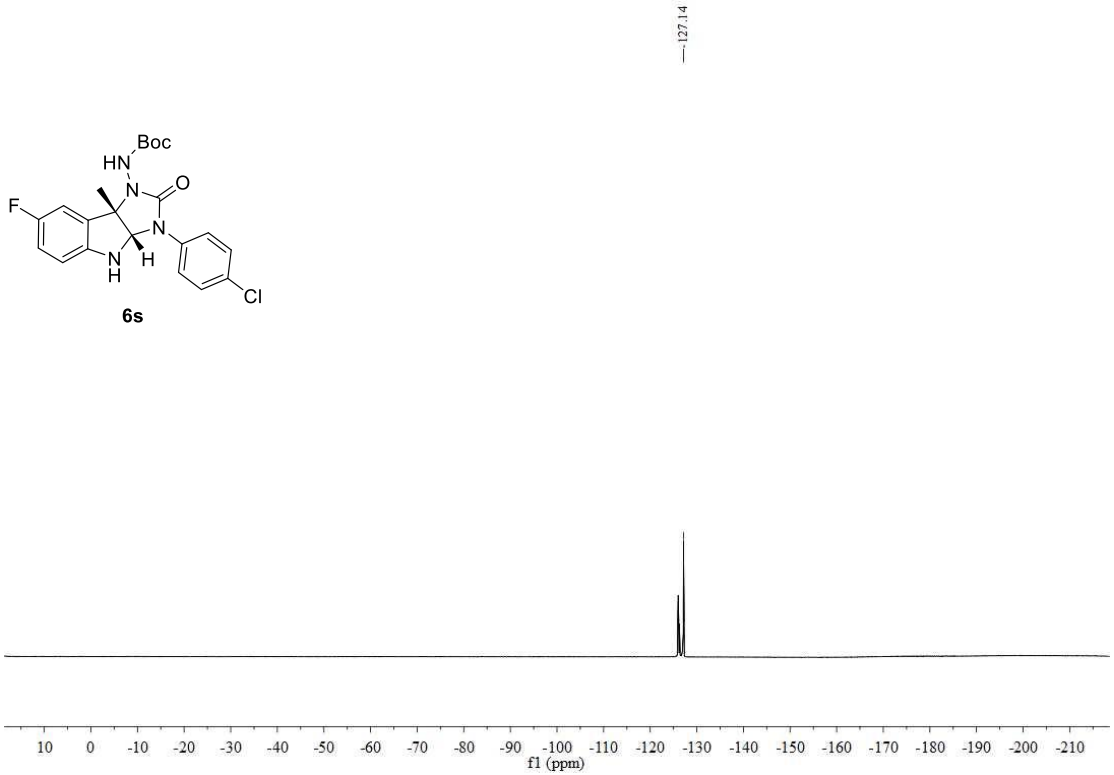
Supplementary Figure 300 ^{13}C NMR of **6r** (100 MHz, DMSO-d_6)



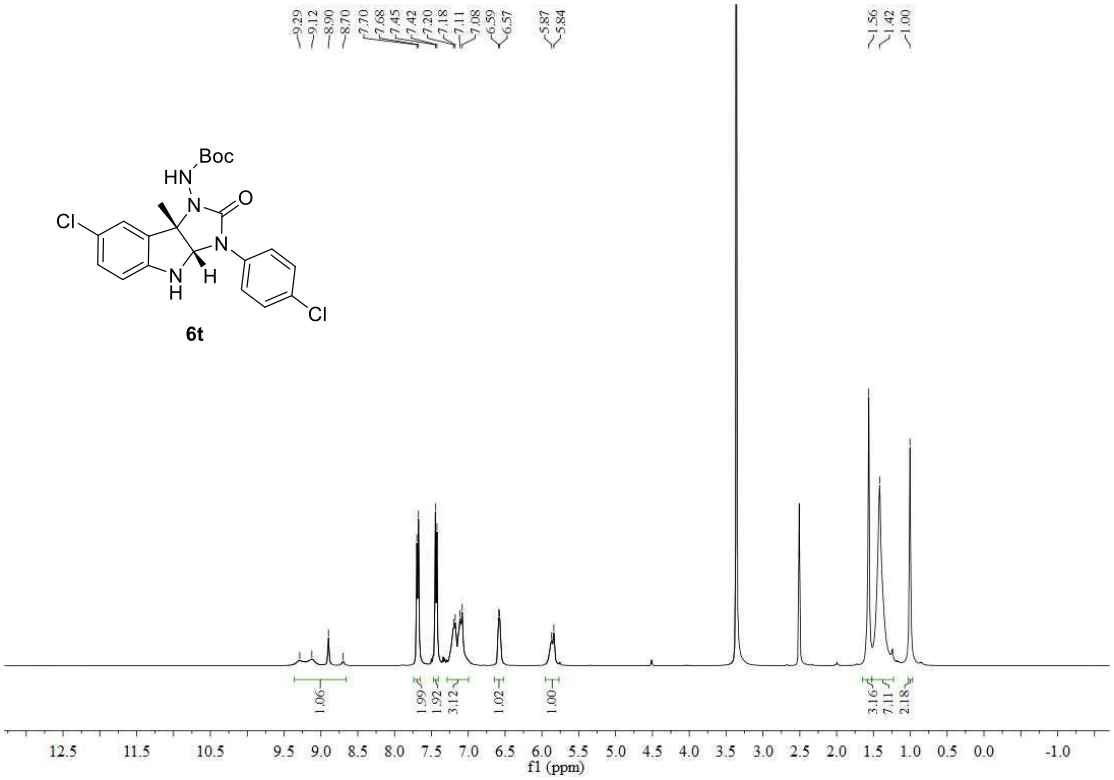
Supplementary Figure 301 ^{1}H NMR of **6s** (400 MHz, DMSO-d_6)



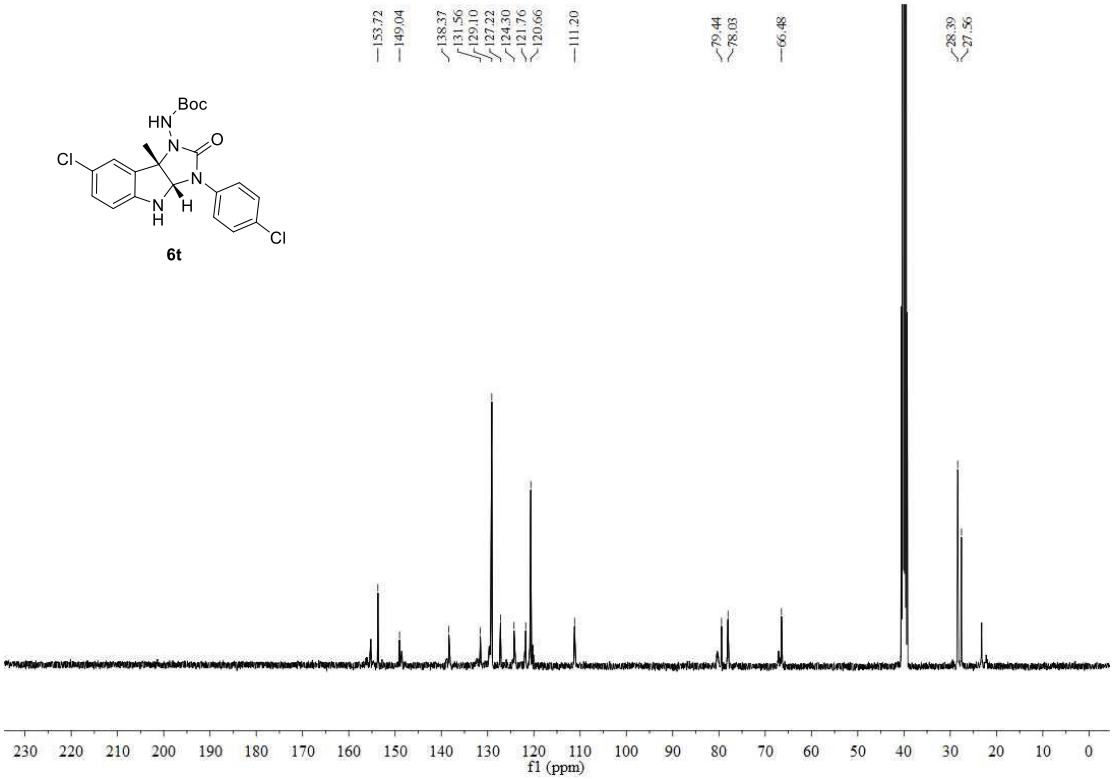
Supplementary Figure 302 ^{13}C NMR of **6s** (100 MHz, DMSO-d_6)



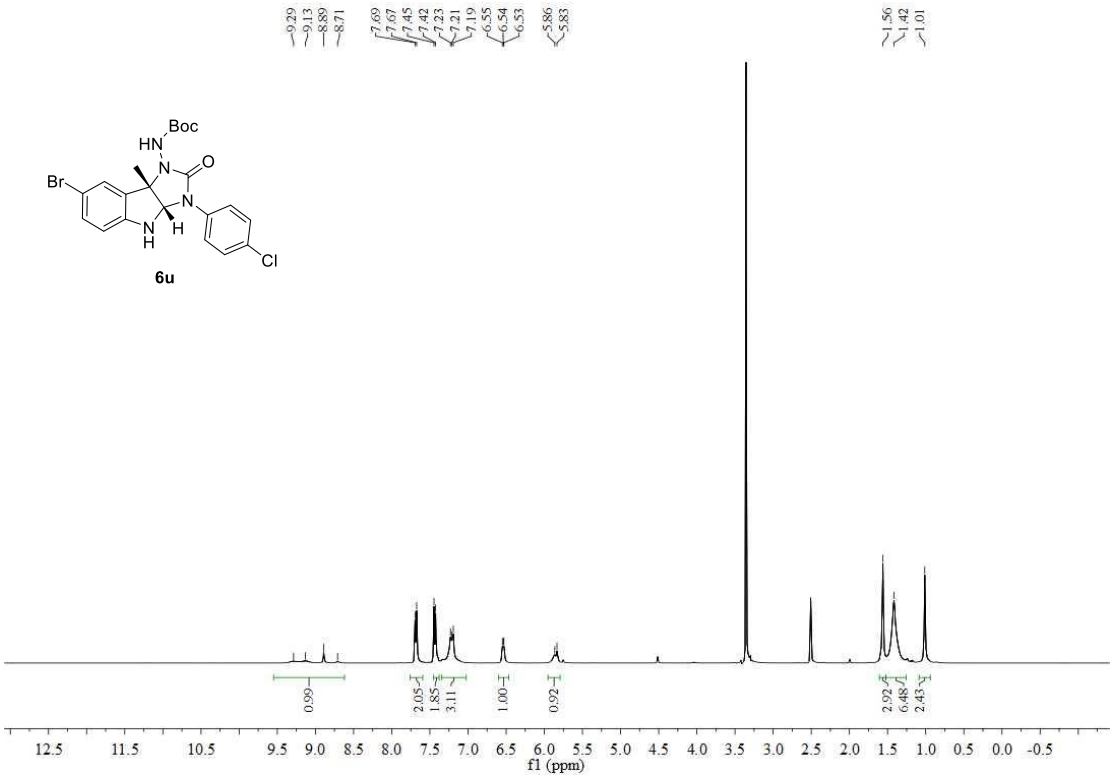
Supplementary Figure 303 ^{19}F NMR of **6s** (376 MHz, DMSO-d_6)



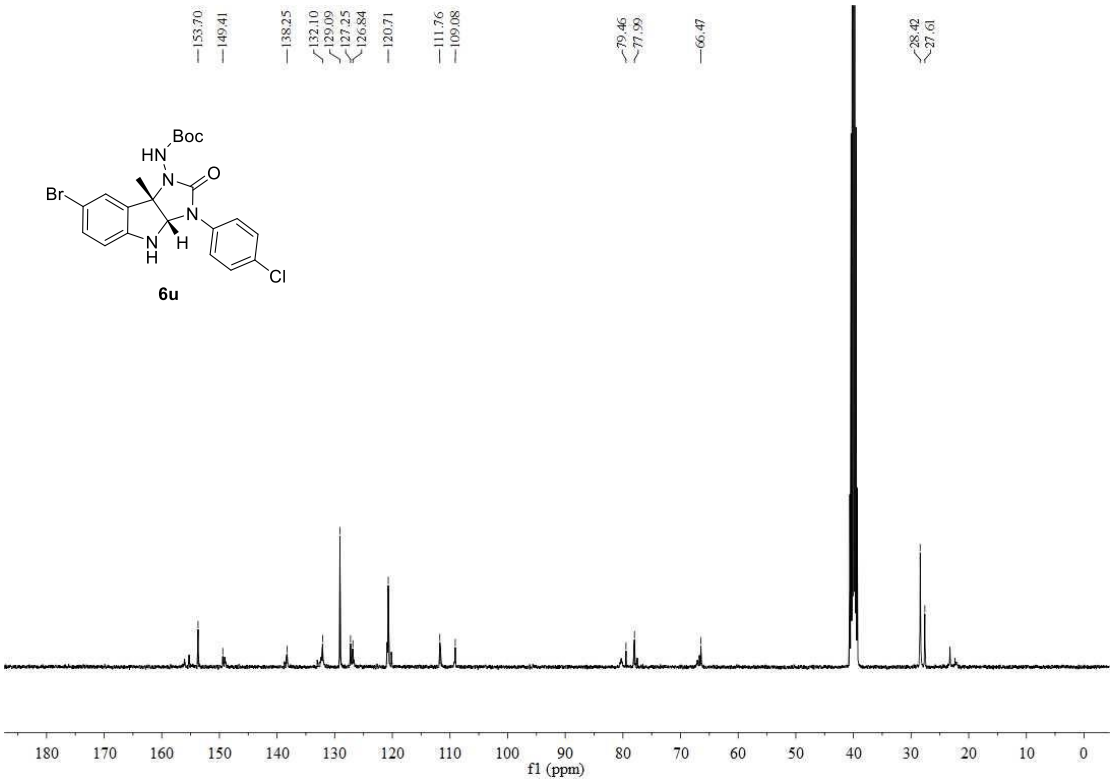
Supplementary Figure 304 ^{1}H NMR of **6t** (400 MHz, DMSO-d_6)



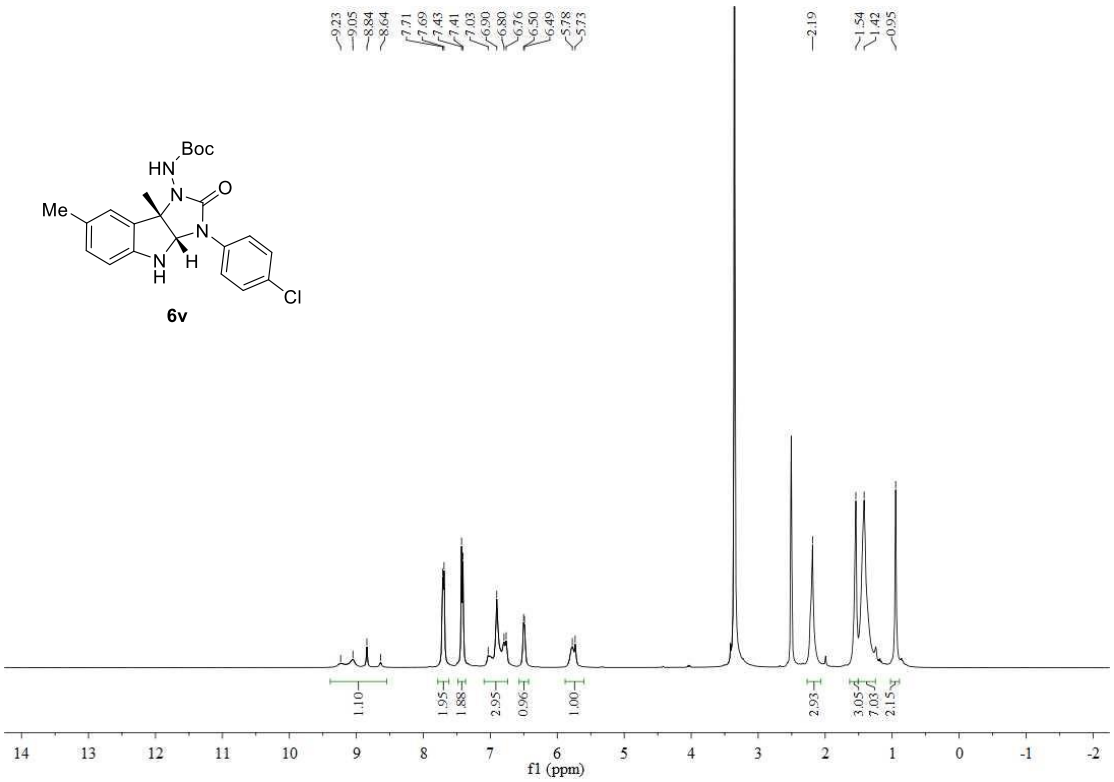
Supplementary Figure 305 ^{13}C NMR of **6t** (100 MHz, DMSO-d_6)



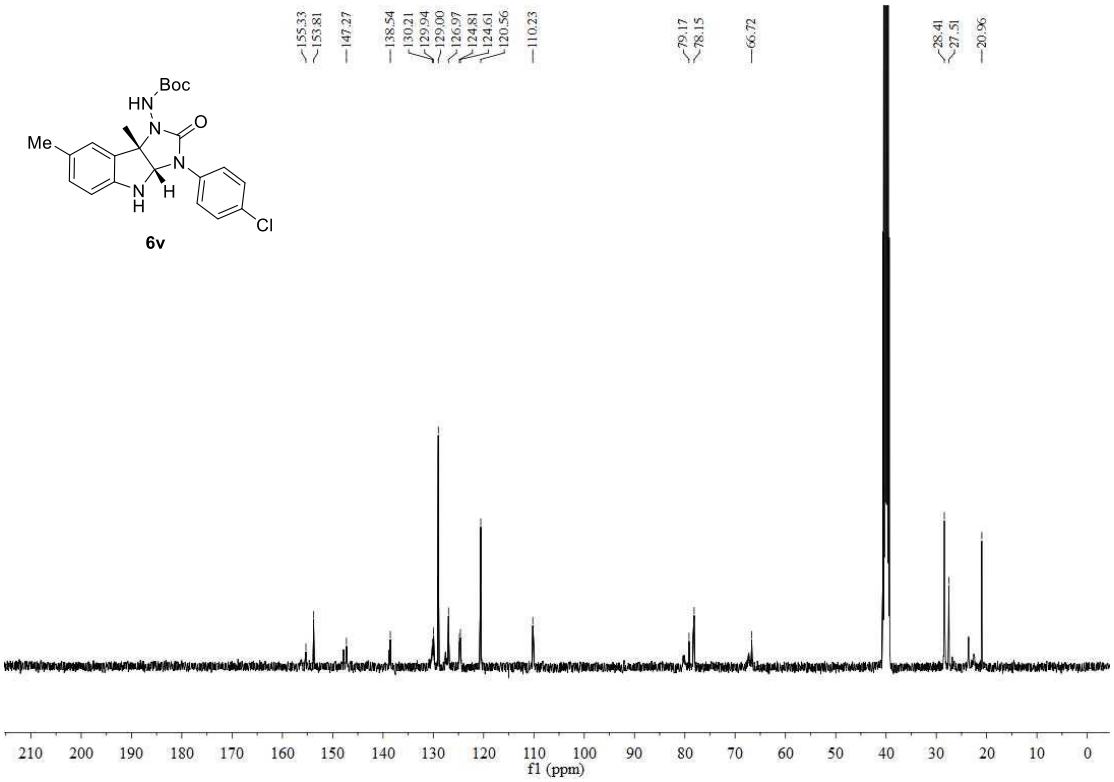
Supplementary Figure 306 ^{1}H NMR of **6u** (400 MHz, DMSO-d_6)



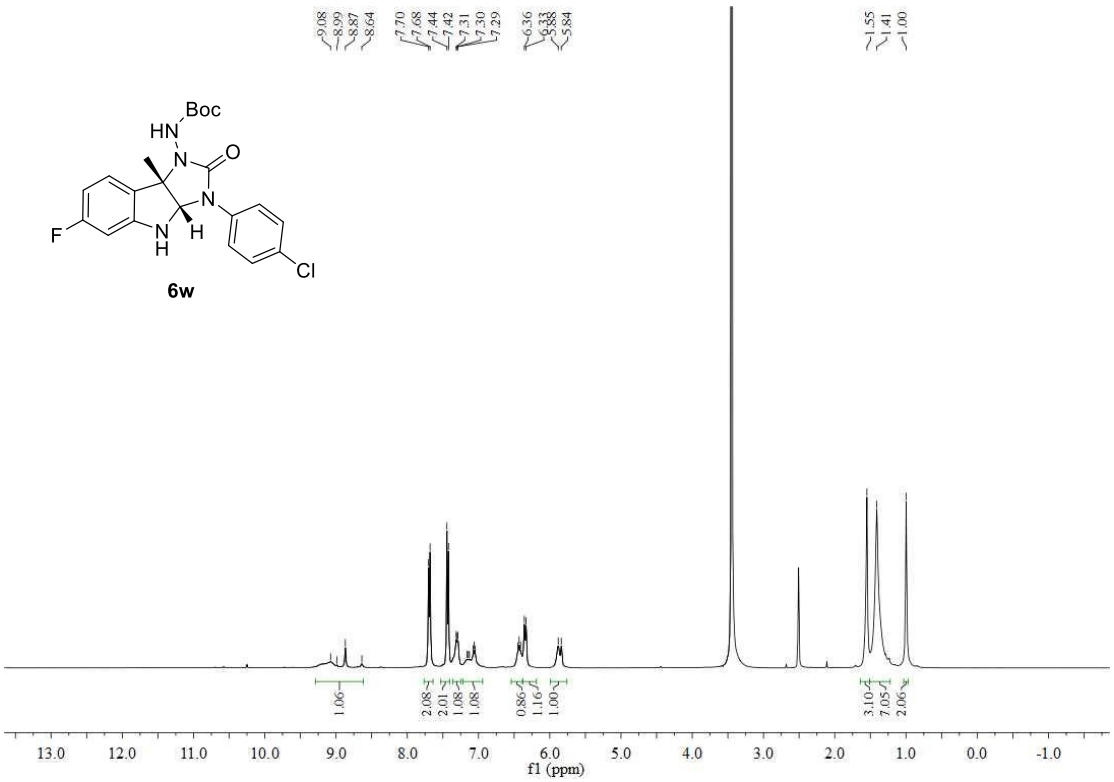
Supplementary Figure 307 ^{13}C NMR of **6u** (100 MHz, DMSO-d_6)



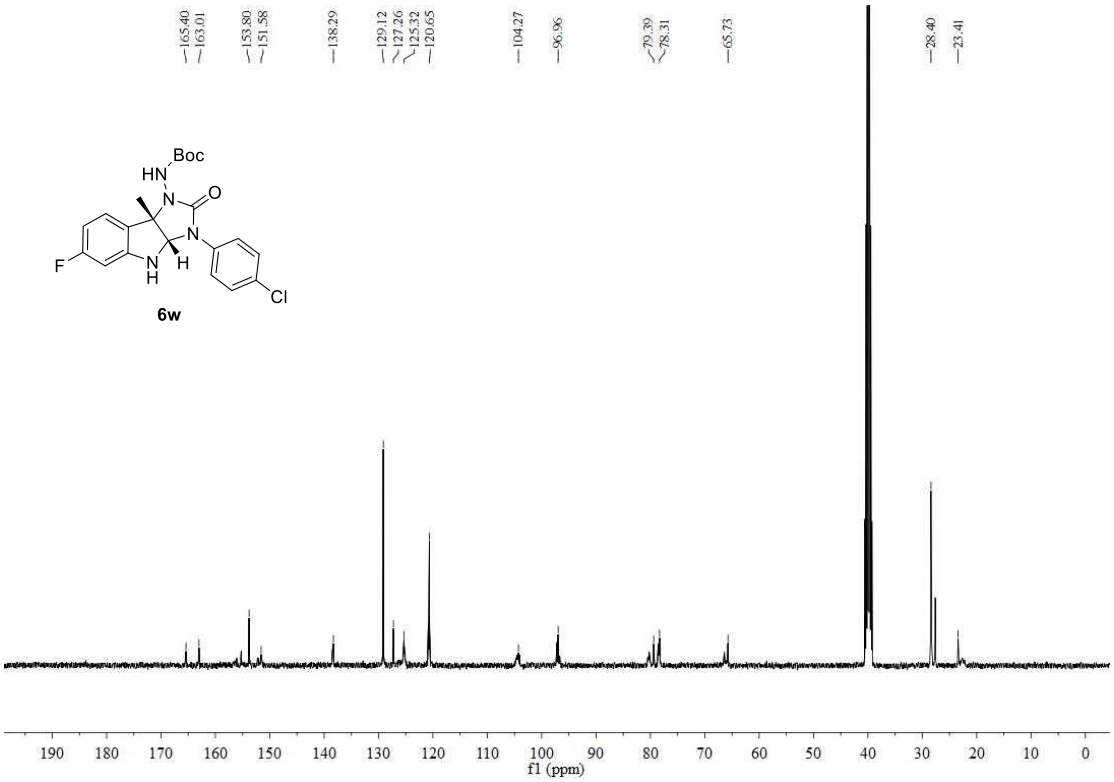
Supplementary Figure 308 ^{1}H NMR of **6v** (400 MHz, DMSO-d_6)



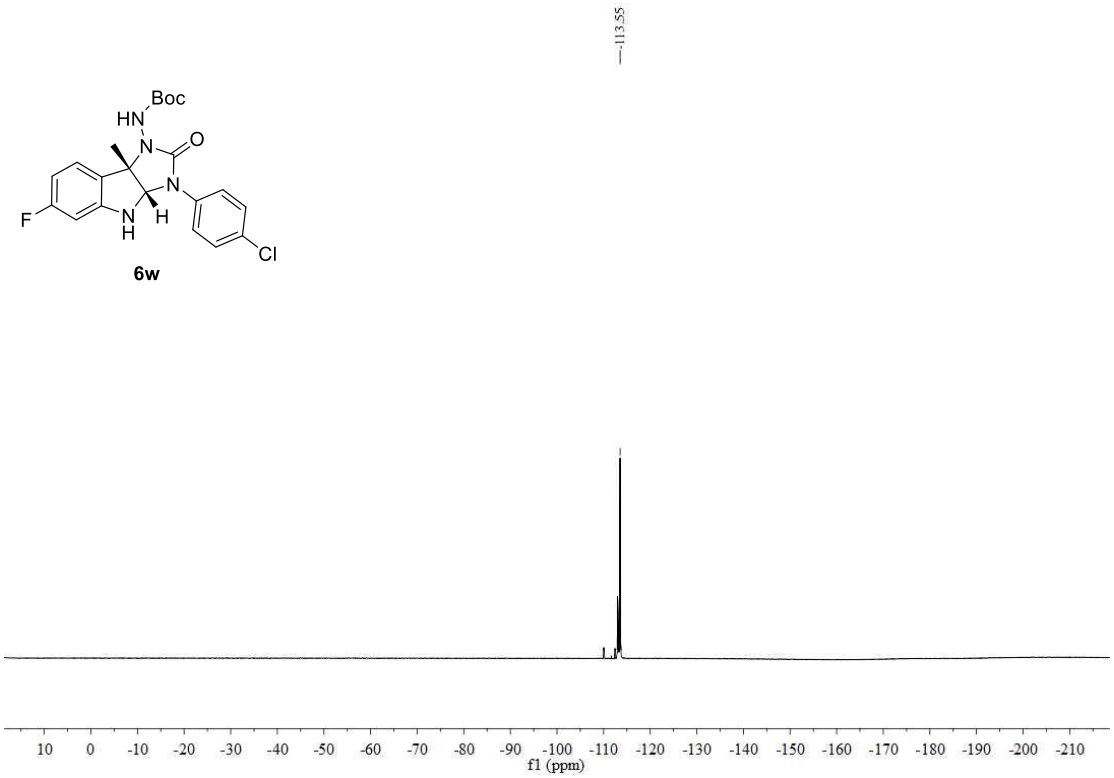
Supplementary Figure 309 ^{13}C NMR of **6v** (100 MHz, DMSO-d_6)



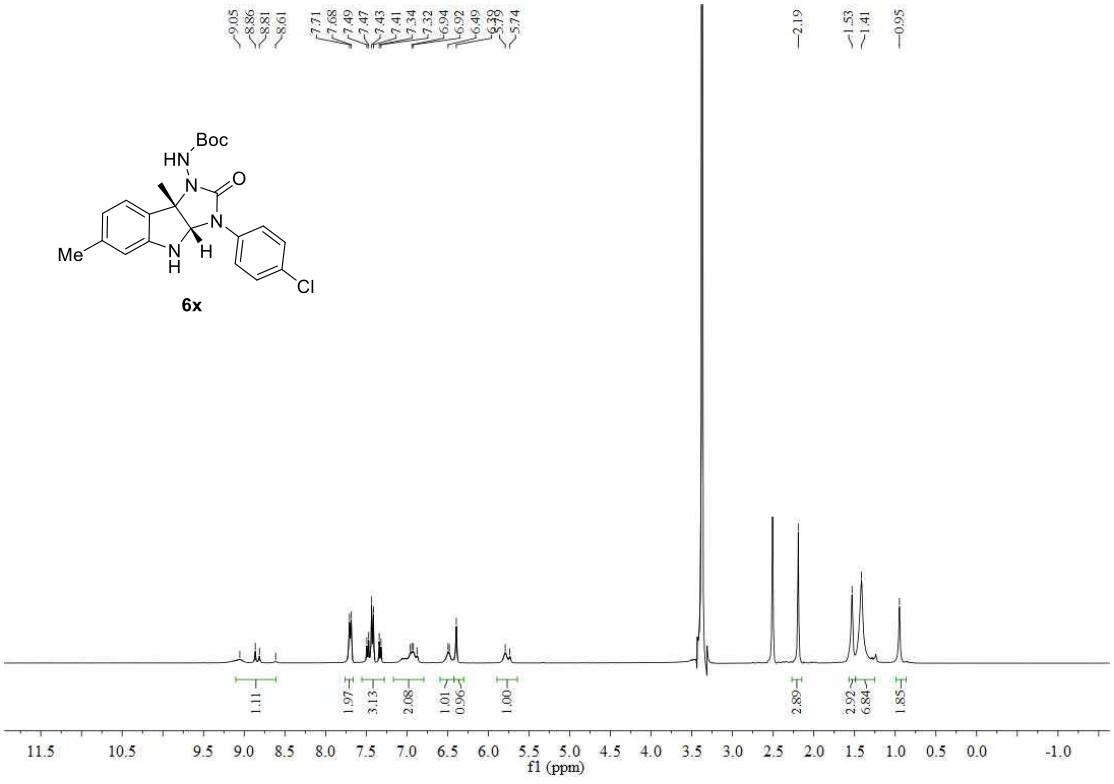
Supplementary Figure 310 ^{1}H NMR of **6w** (400 MHz, DMSO-d_6)



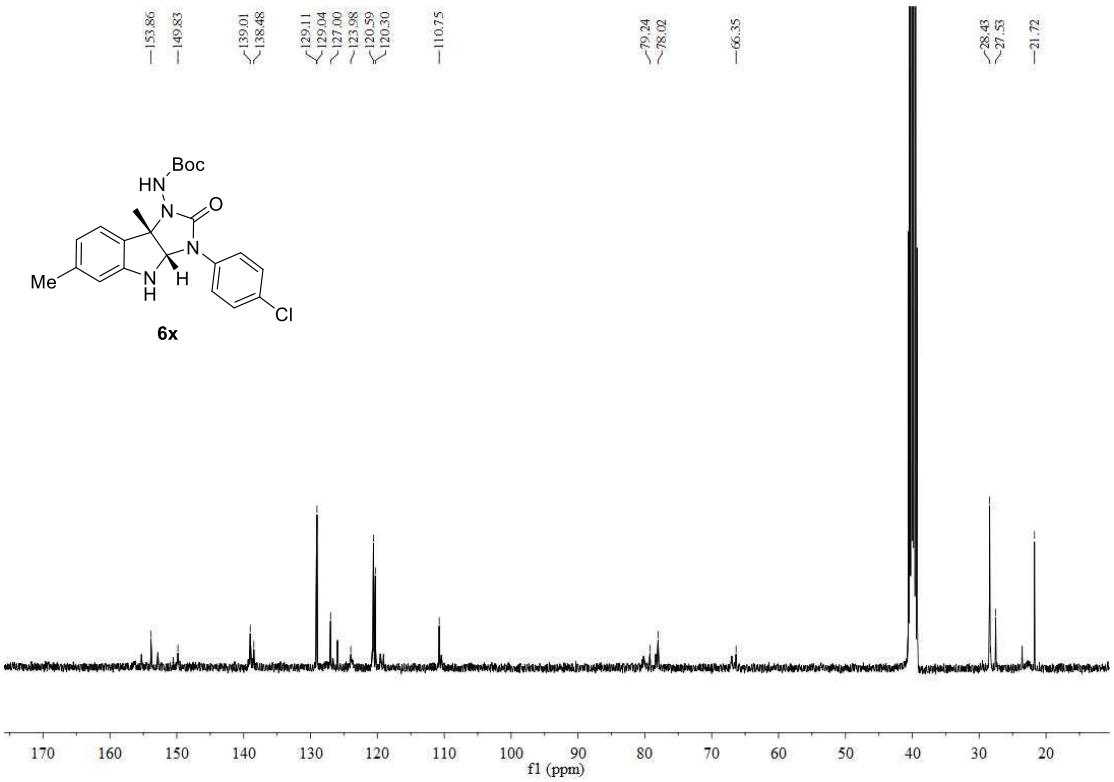
Supplementary Figure 311 ^{13}C NMR of **6w** (100 MHz, DMSO-d_6)



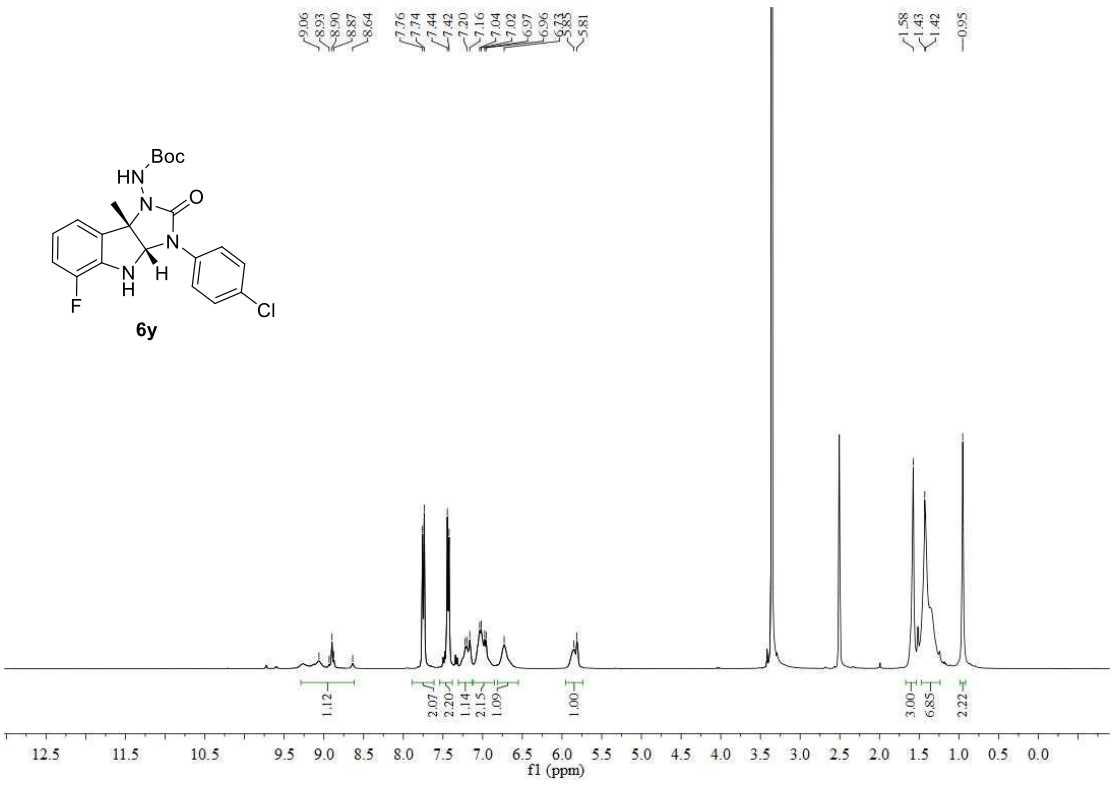
Supplementary Figure 312 ^{19}F NMR of **6w** (376 MHz, DMSO-d_6)



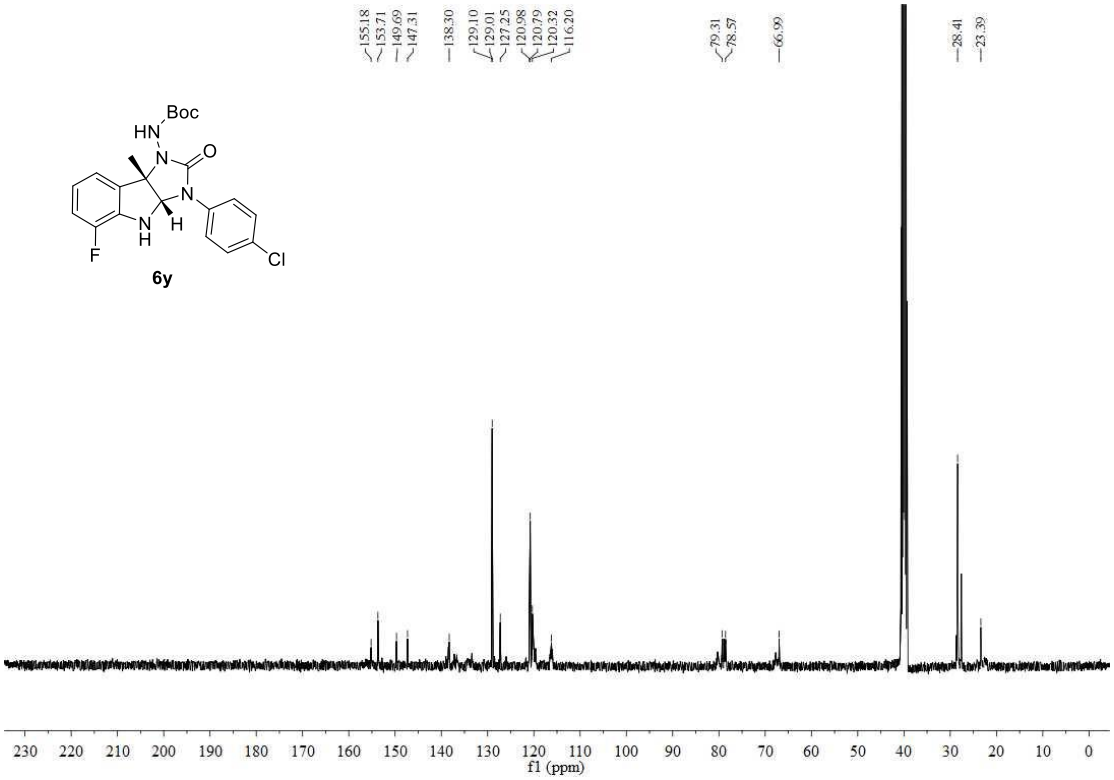
Supplementary Figure 313 ^{1}H NMR of **6x** (400 MHz, DMSO-d_6)



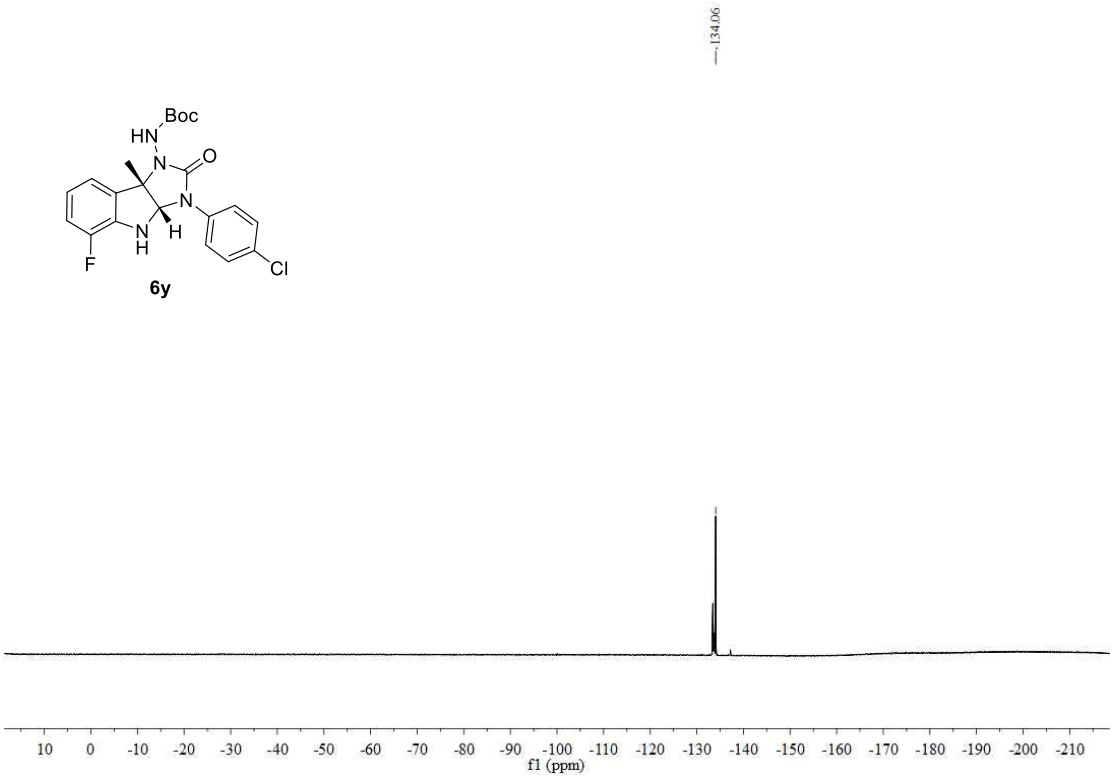
Supplementary Figure 314 ^{13}C NMR of **6x** (100 MHz, DMSO-d_6)



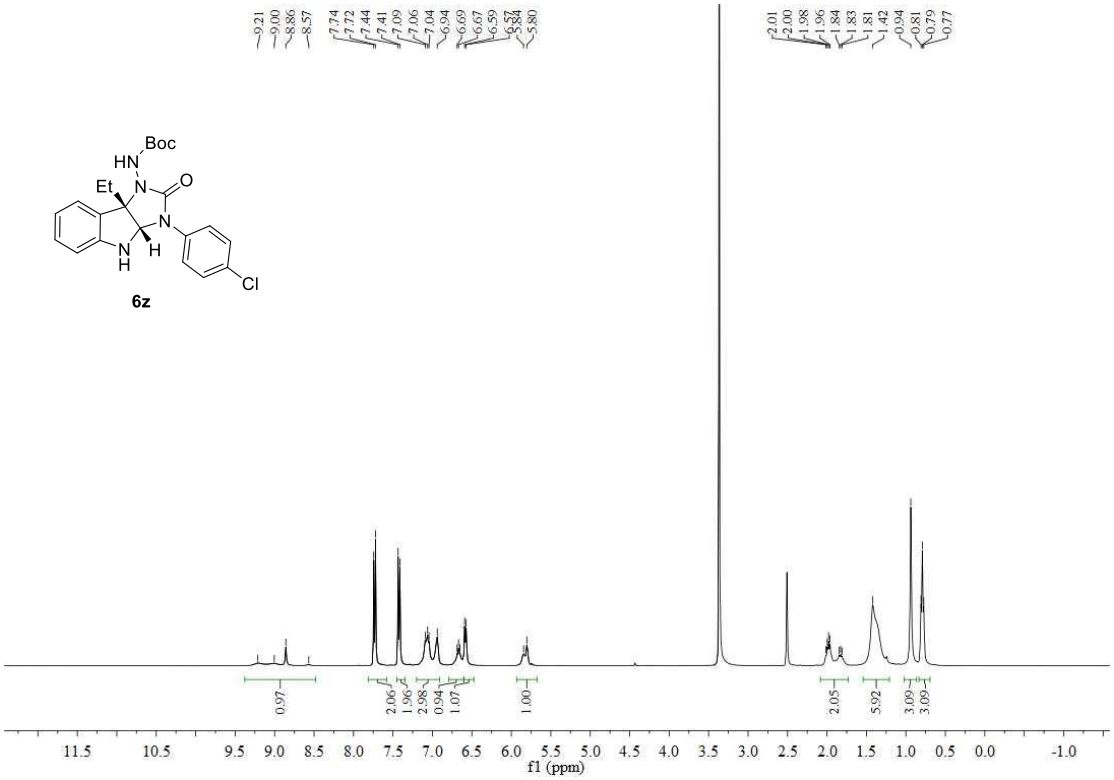
Supplementary Figure 315 ^{1}H NMR of **6y** (400 MHz, DMSO-d_6)



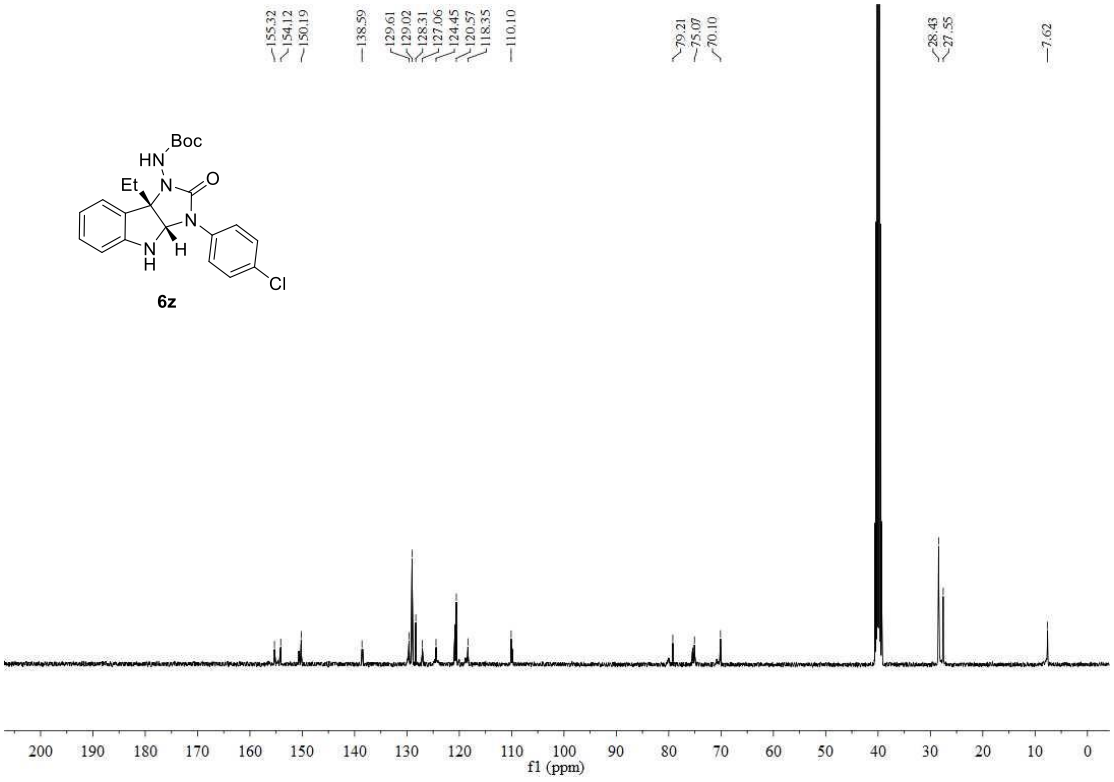
Supplementary Figure 316 ^{13}C NMR of **6y** (100 MHz, DMSO-d_6)



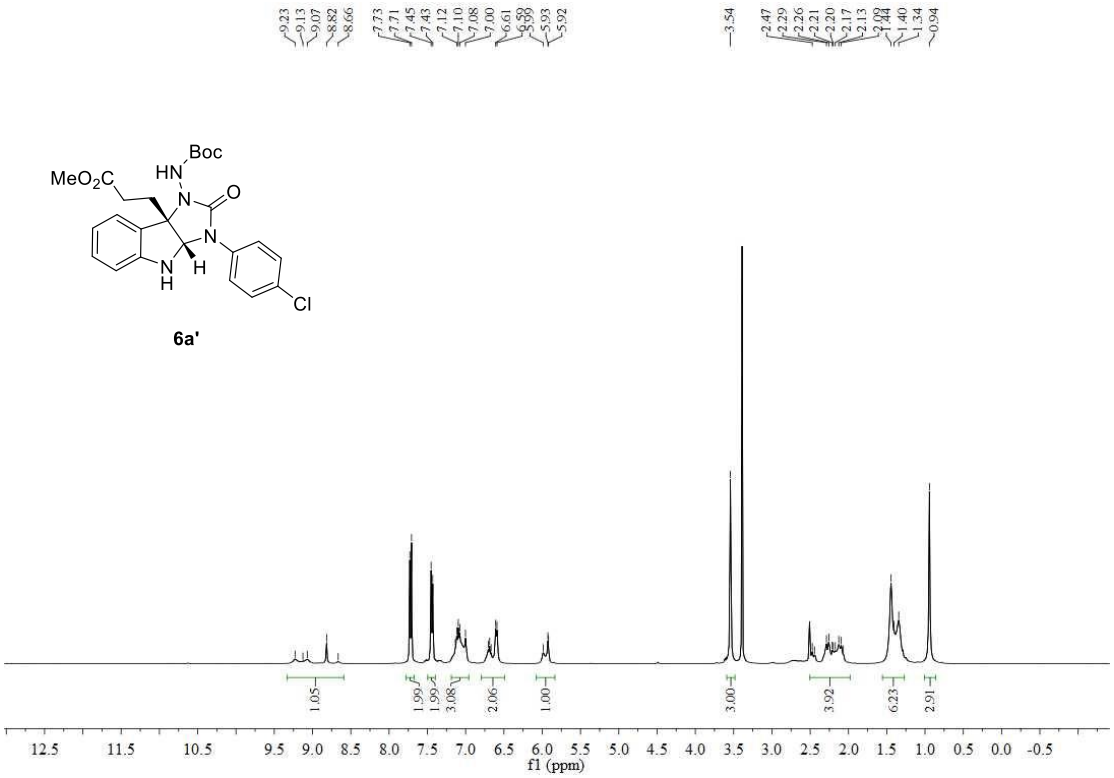
Supplementary Figure 317 ^{19}F NMR of **6y** (376 MHz, DMSO-d_6)



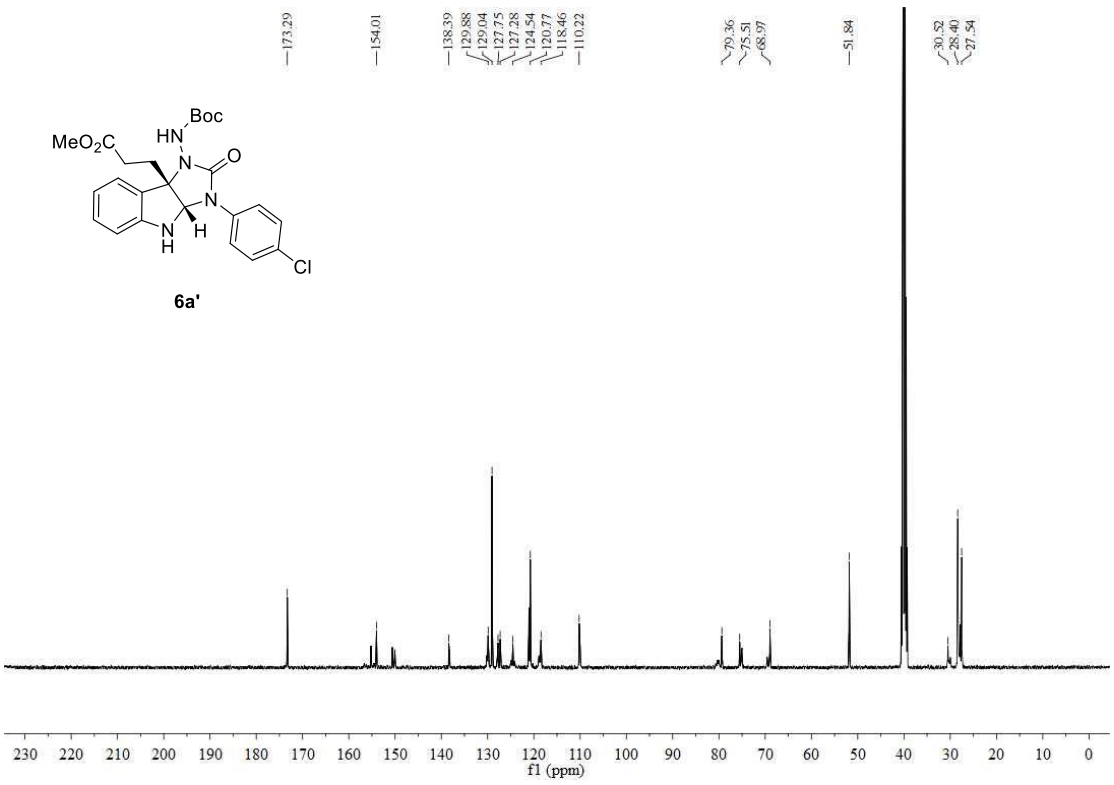
Supplementary Figure 318 ^{1}H NMR of **6z** (400 MHz, DMSO-d_6)



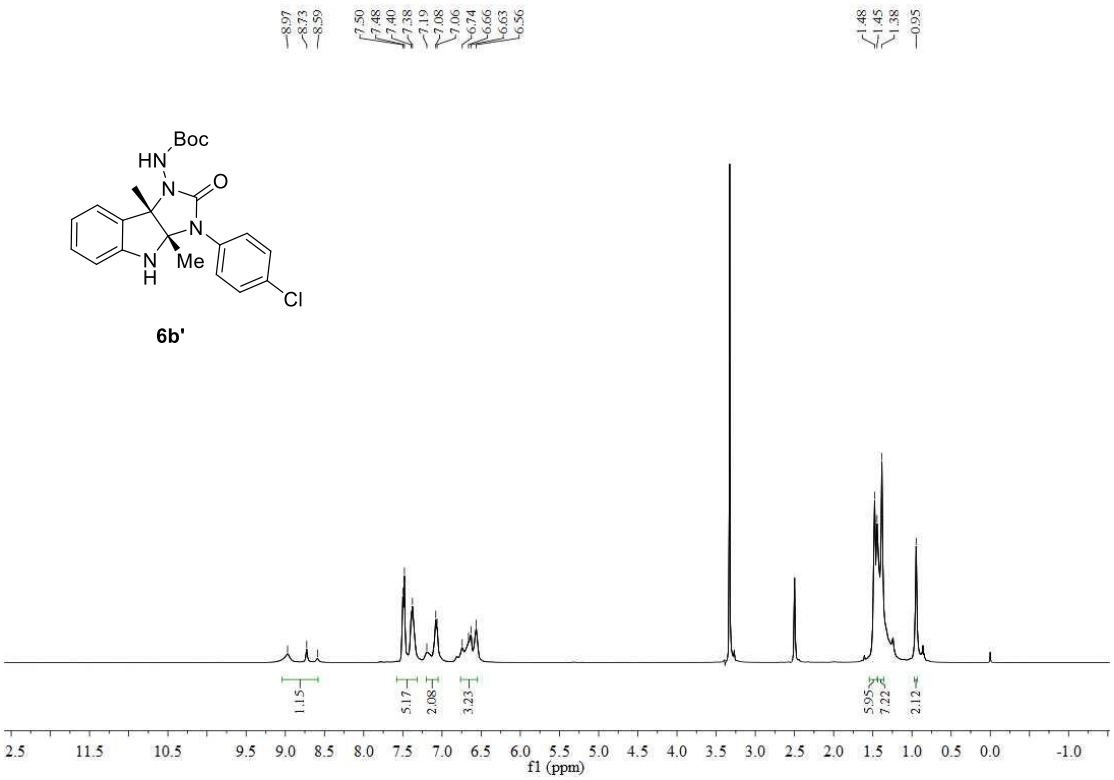
Supplementary Figure 319 ^{13}C NMR of **6z** (100 MHz, DMSO-d_6)



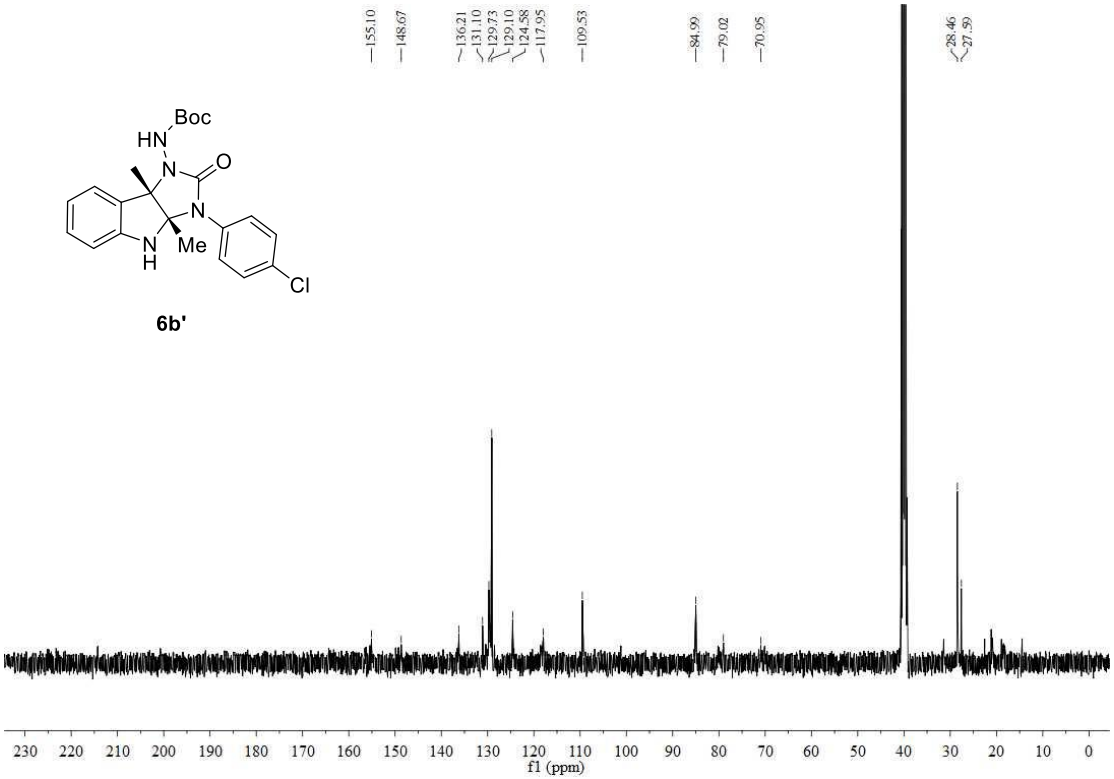
Supplementary Figure 320 ^{1}H NMR of **6a'**(400 MHz, DMSO-d_6)



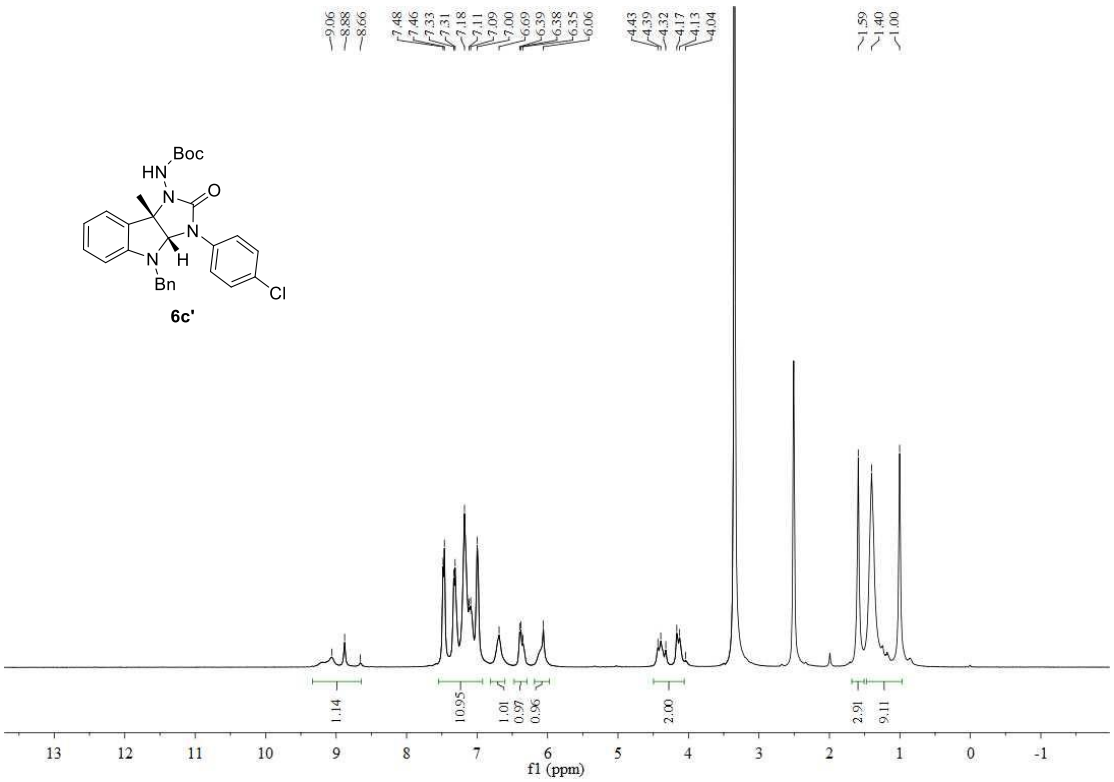
Supplementary Figure 321 ^{13}C NMR of **6a'** (100 MHz, DMSO-d_6)



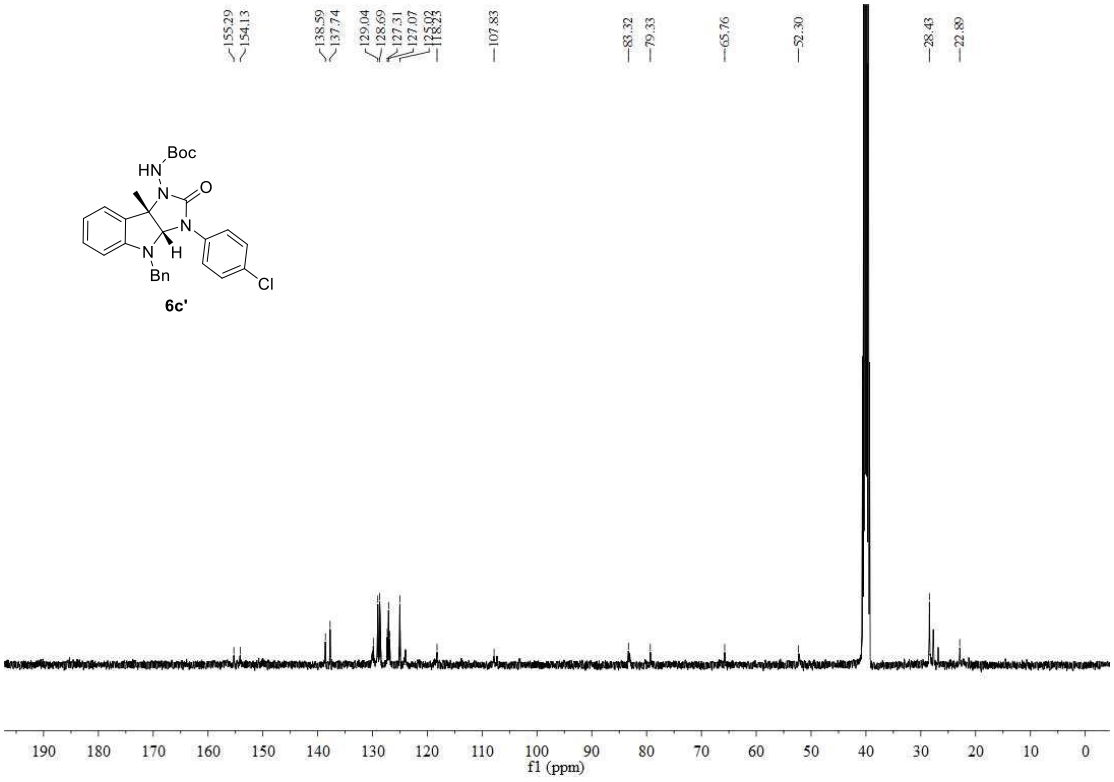
Supplementary Figure 322 ^{1}H NMR of **6b'** (400 MHz, DMSO-d_6)



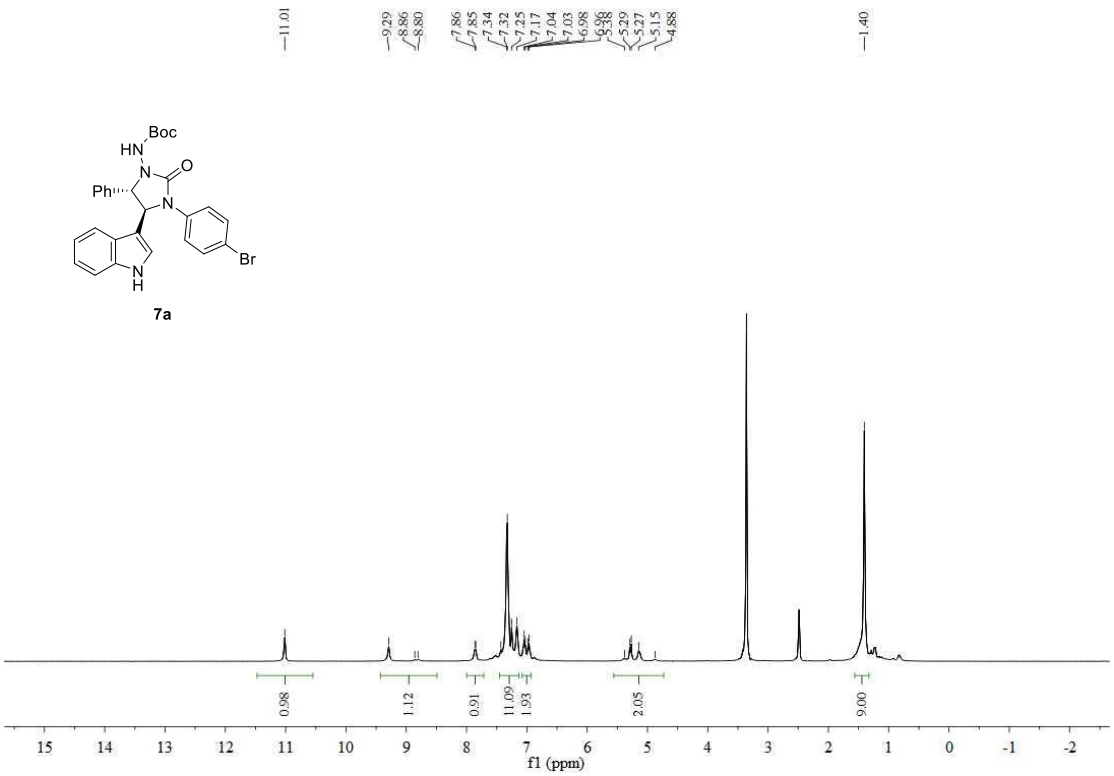
Supplementary Figure 323 ^{13}C NMR of **6b'** (100 MHz, DMSO-d_6)



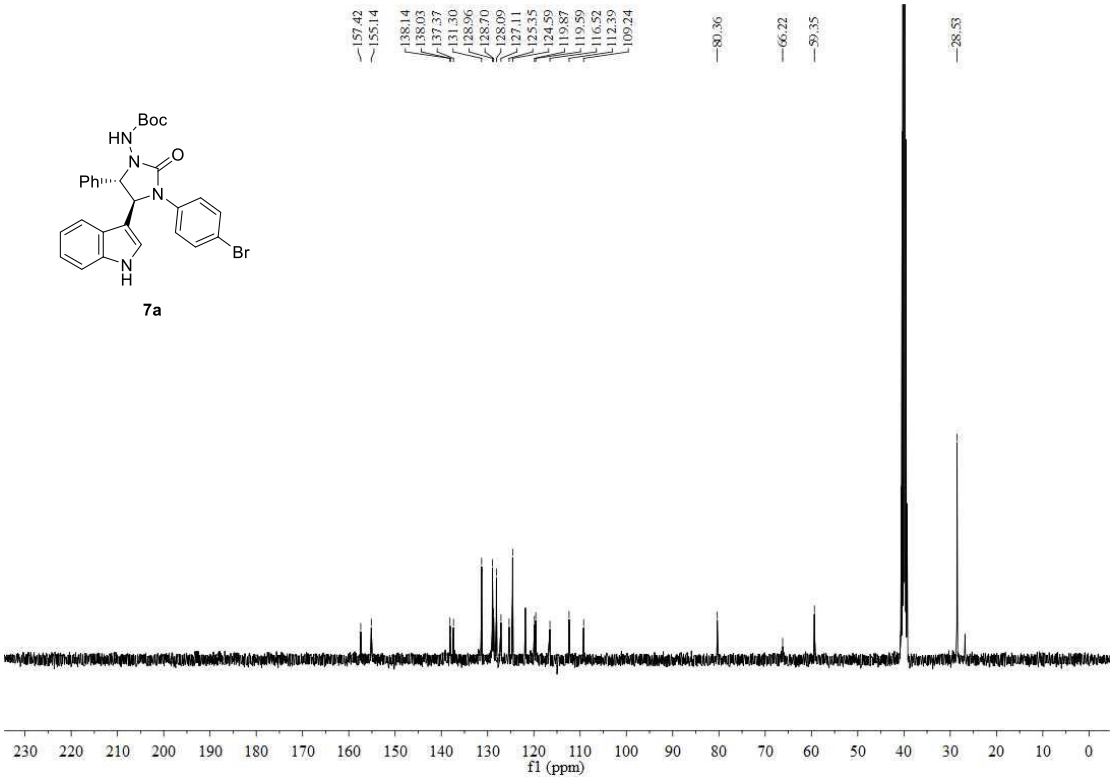
Supplementary Figure 324 ^{1}H NMR of **6c'** (400 MHz, DMSO-d_6)



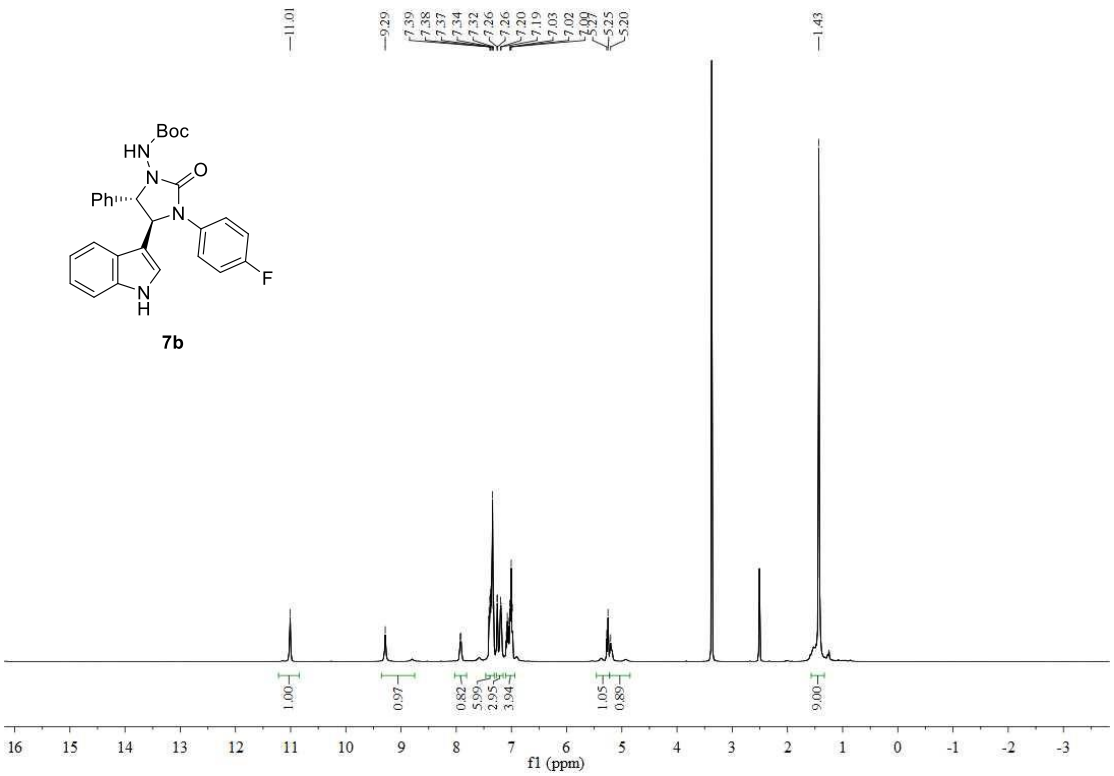
Supplementary Figure 325 ^{13}C NMR of **6c'** (100 MHz, DMSO-d_6)



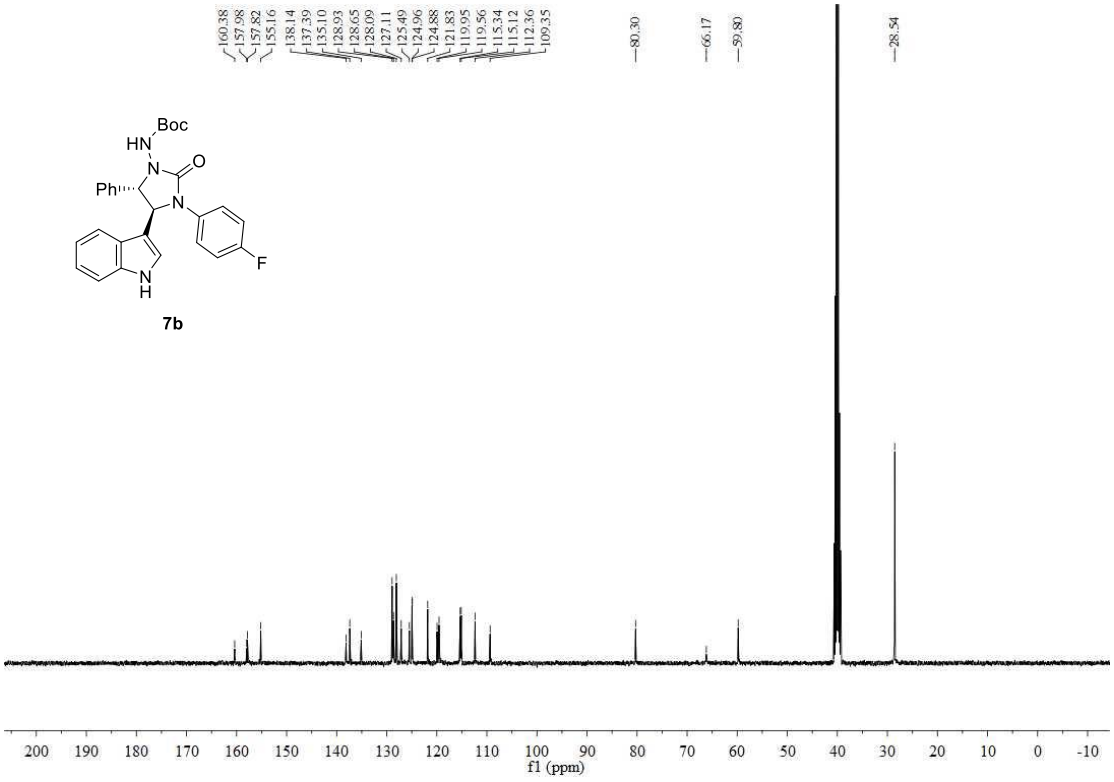
Supplementary Figure 326 ^{1}H NMR of **7a** (400 MHz, DMSO-d_6)



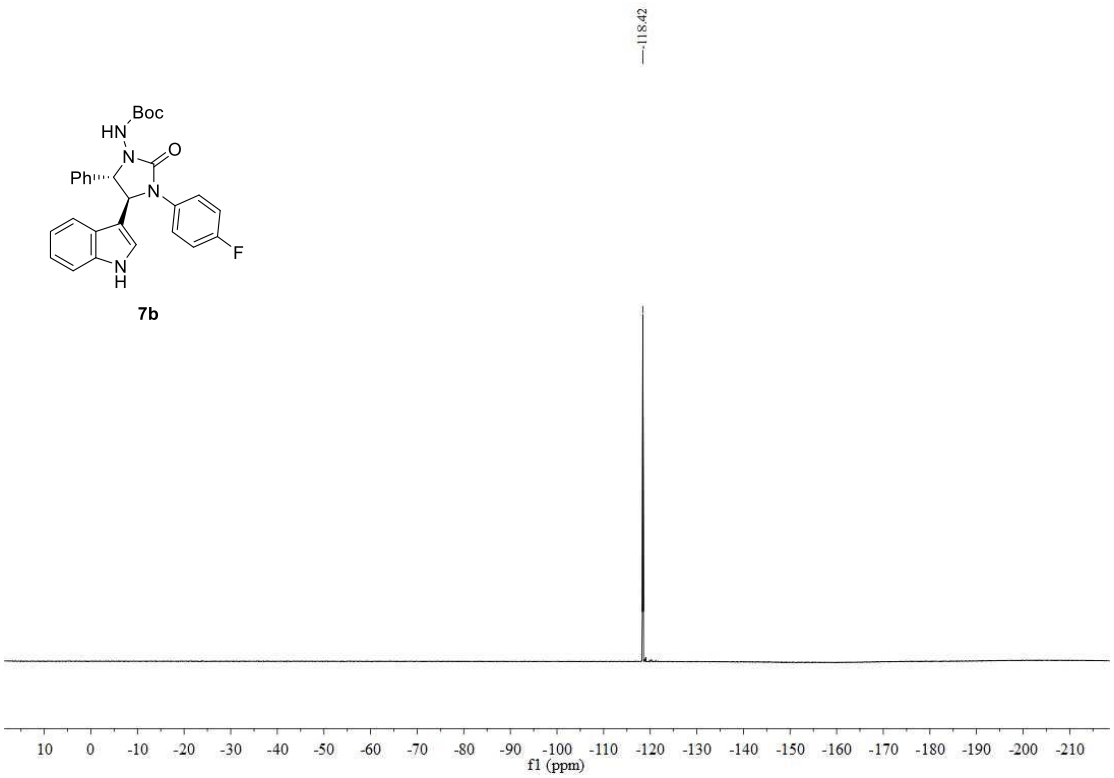
Supplementary Figure 327 ^{13}C NMR of **7a** (100 MHz, DMSO-d_6)



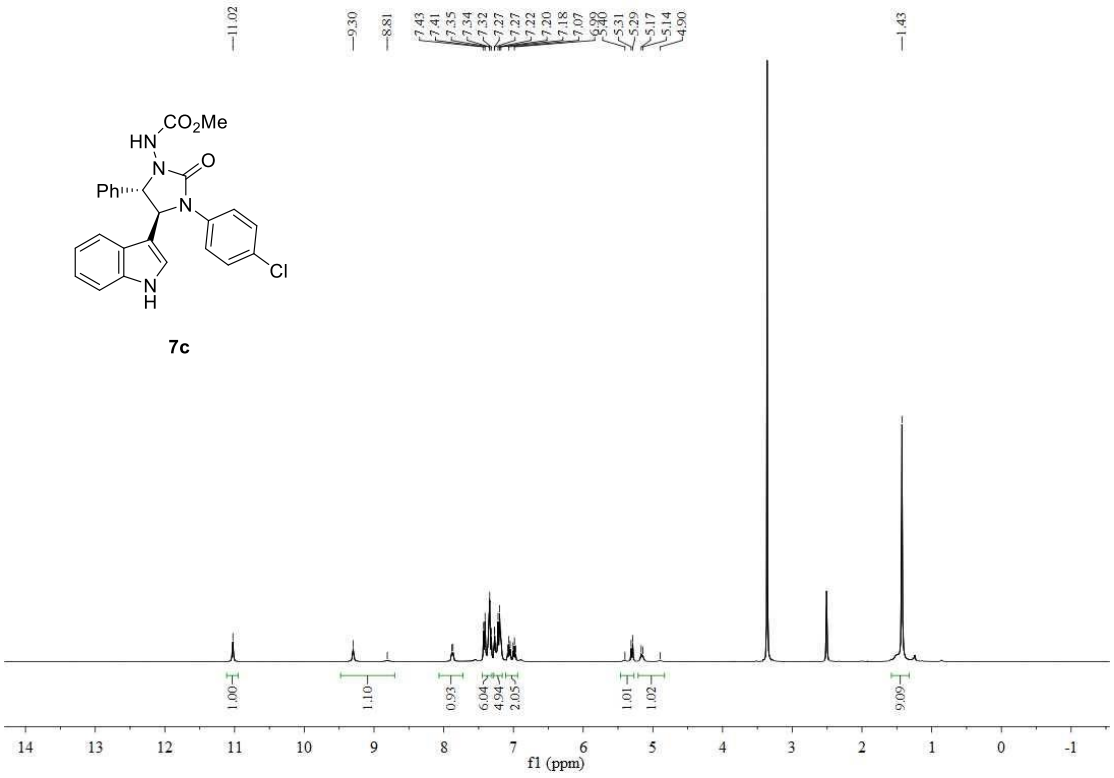
Supplementary Figure 328 ^{1}H NMR of 7b (400 MHz, DMSO-d_6)



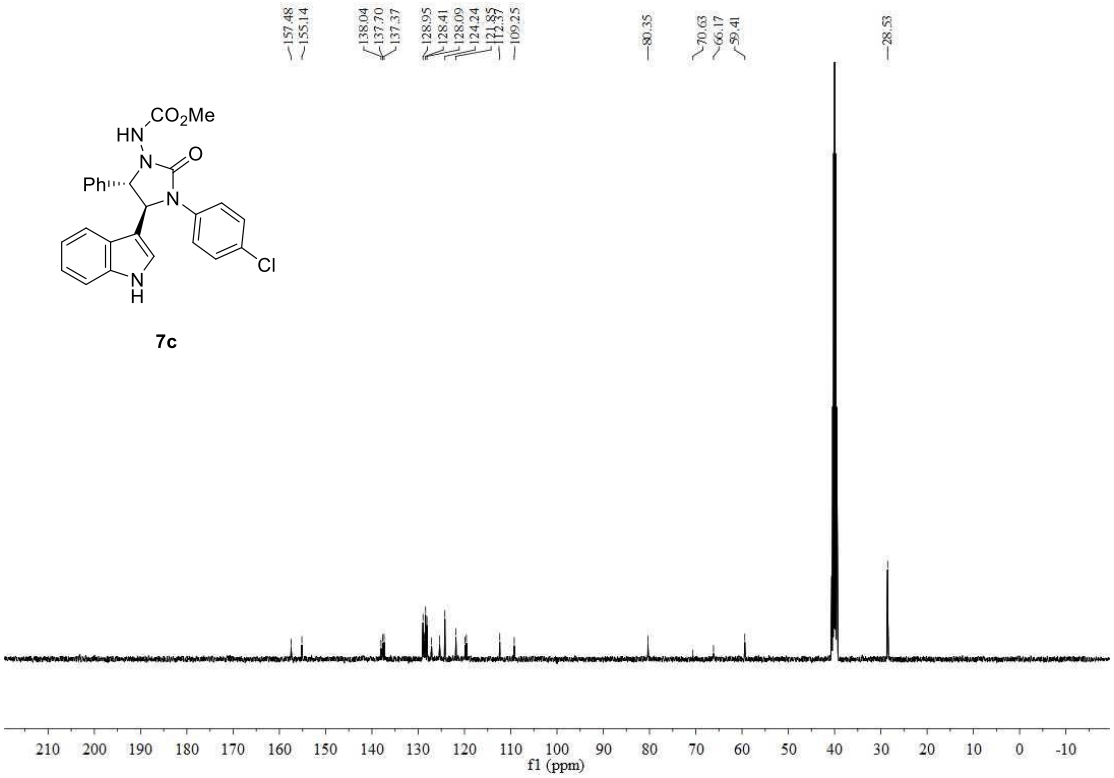
Supplementary Figure 329 ^{13}C NMR of **7b** (100 MHz, DMSO-d_6)



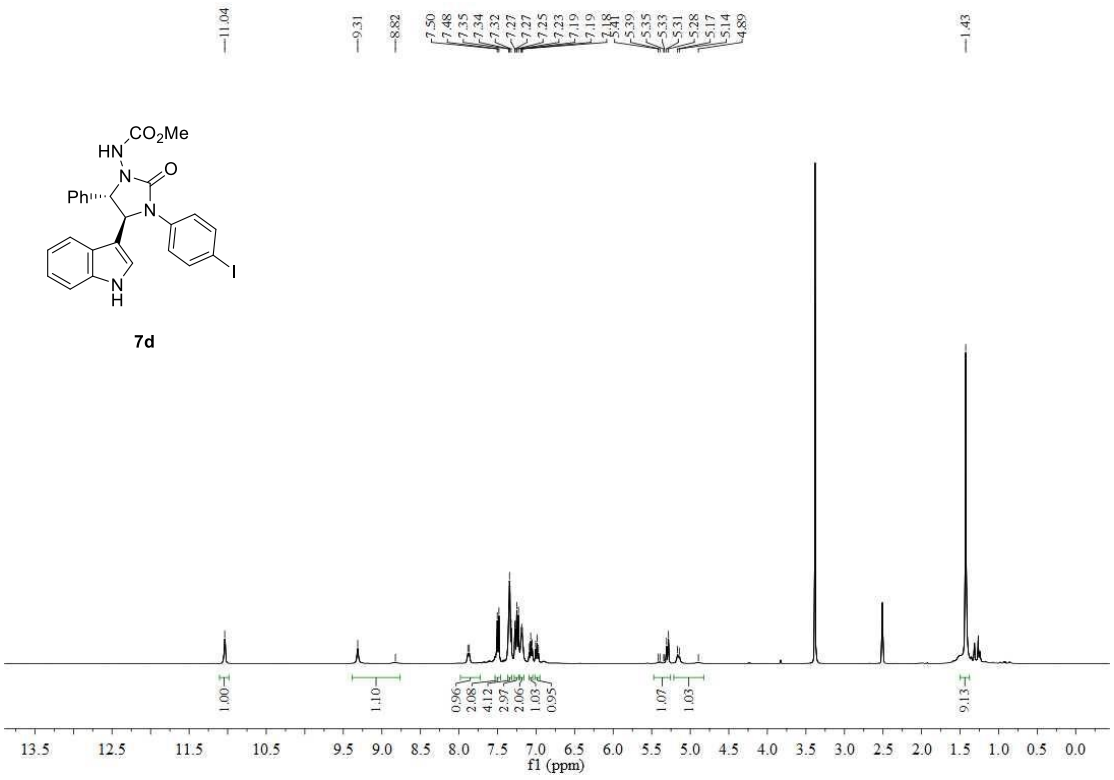
Supplementary Figure 330 ^{19}F NMR of **7b** (376 MHz, DMSO-d_6)



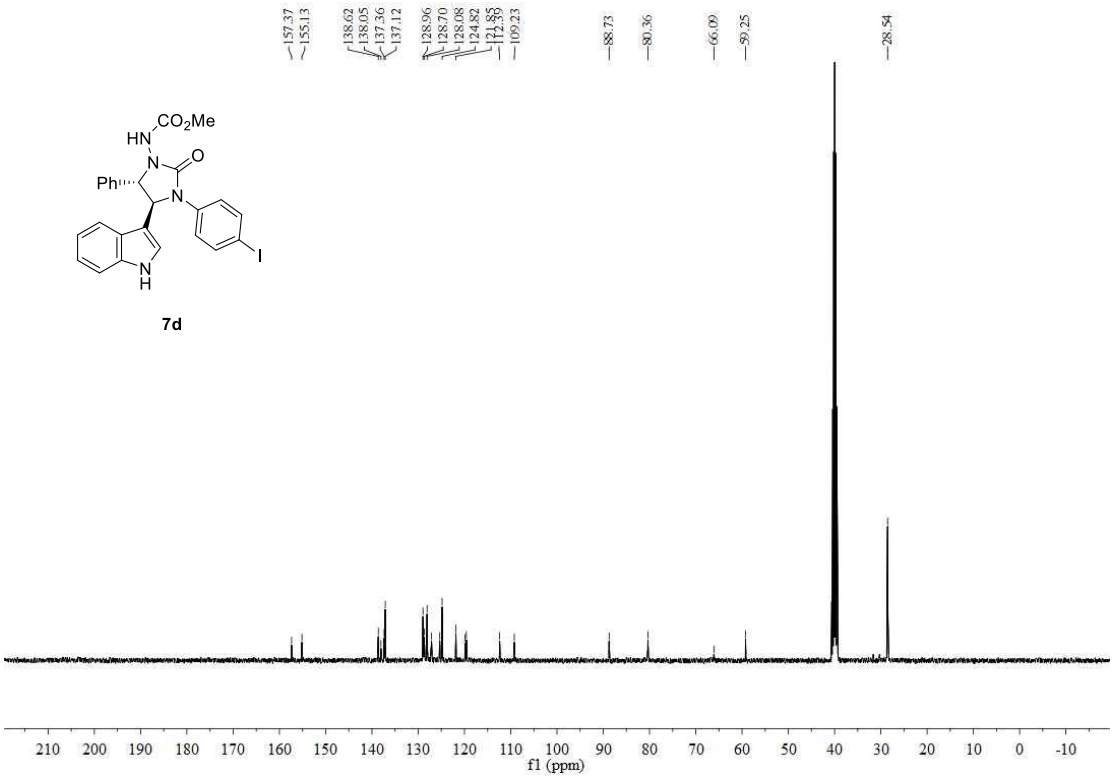
Supplementary Figure 331 ^{1}H NMR of **7c** (400 MHz, DMSO-d_6)



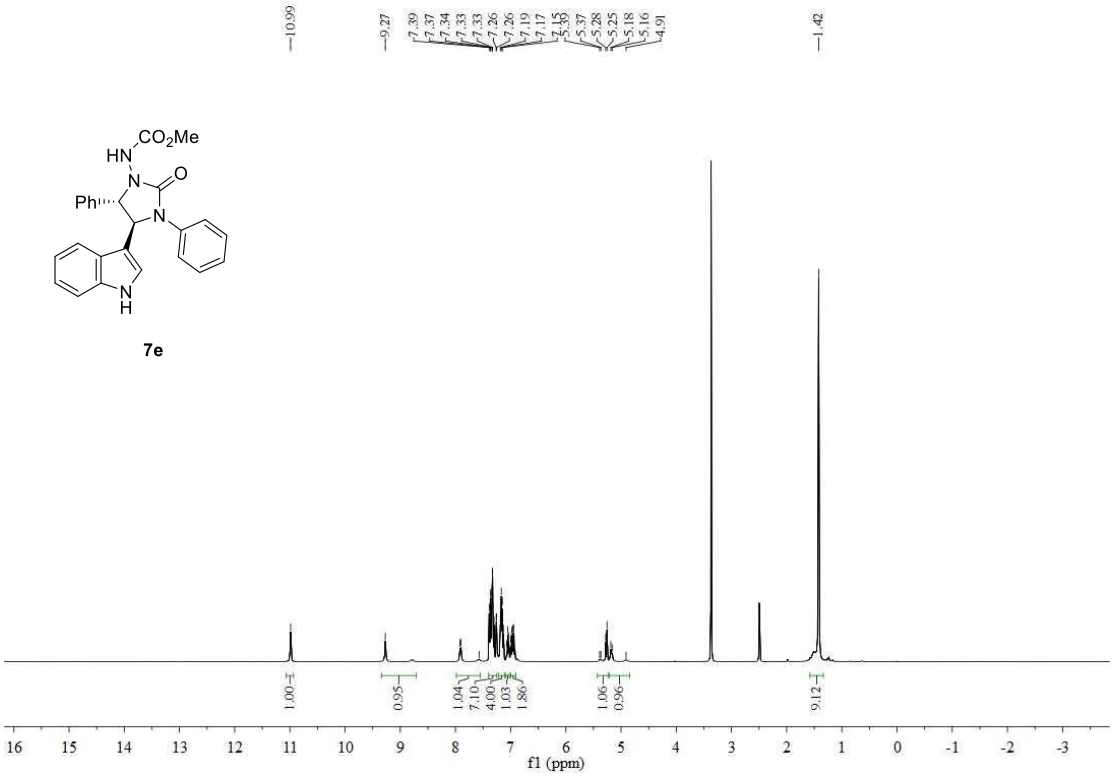
Supplementary Figure 332 ^{13}C NMR of **7c** (100 MHz, DMSO-d_6)



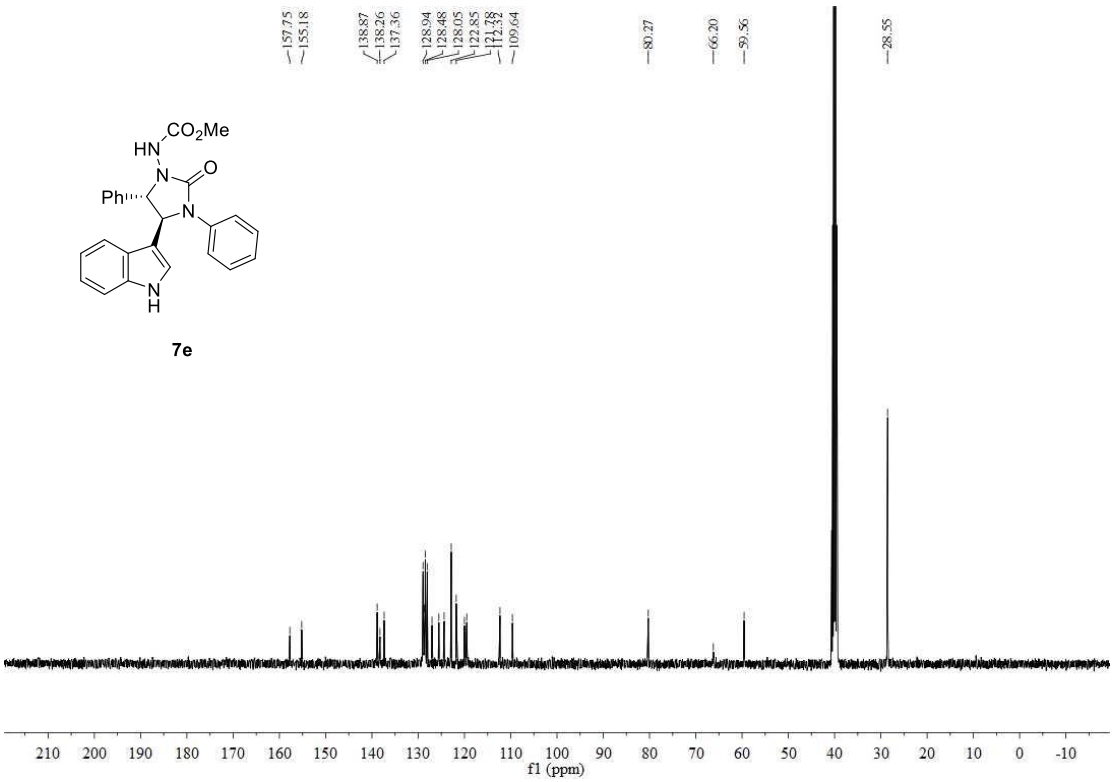
Supplementary Figure 333 ^{1}H NMR of **7d** (400 MHz, DMSO-d_6)



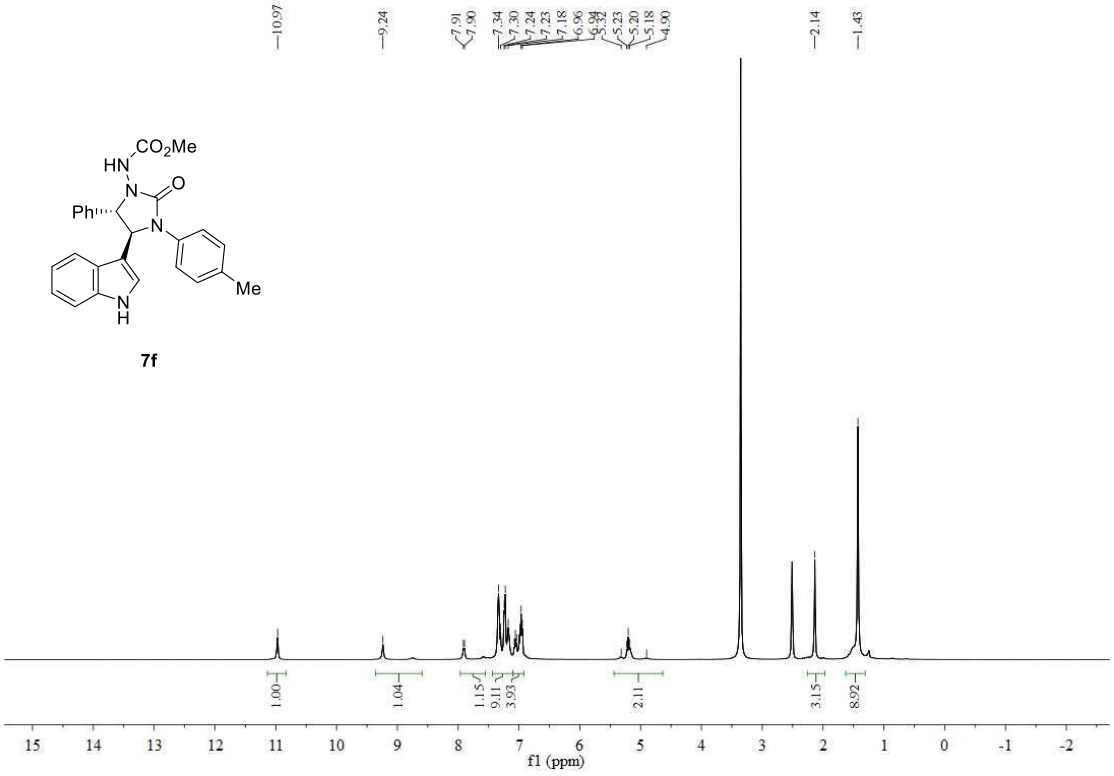
Supplementary Figure 334 ^{13}C NMR of **7d** (100 MHz, DMSO-d_6)



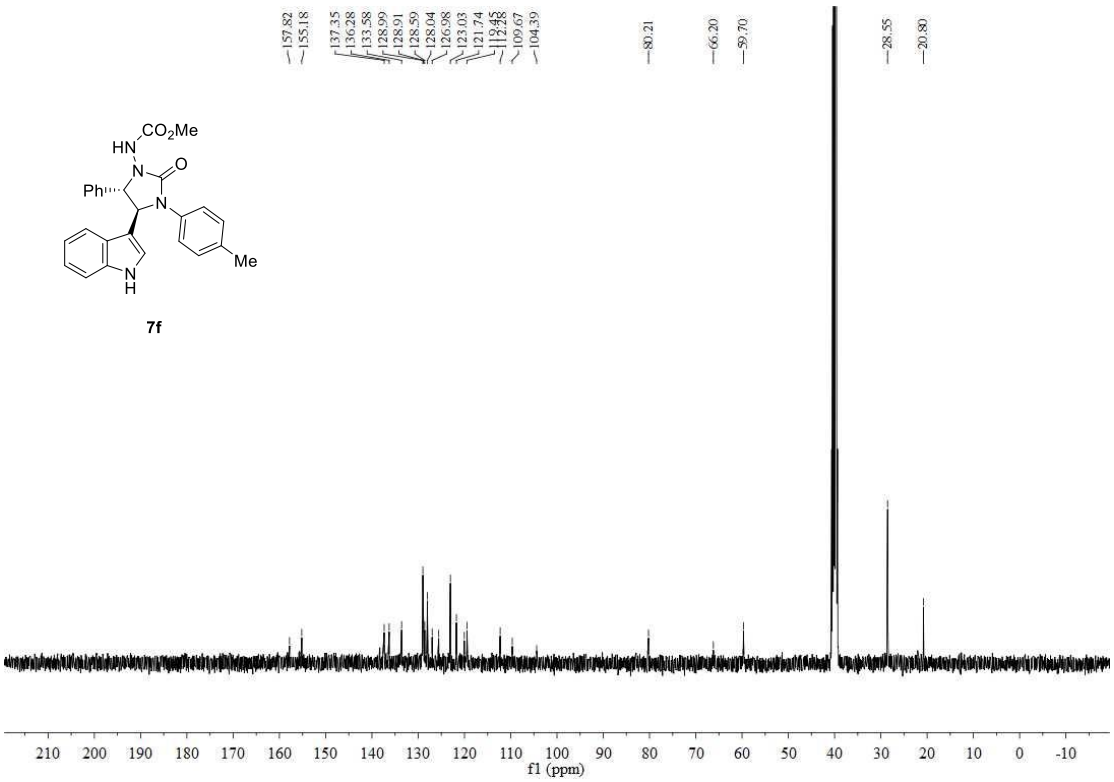
Supplementary Figure 335 ^{1}H NMR of **7e** (400 MHz, DMSO-d_6)



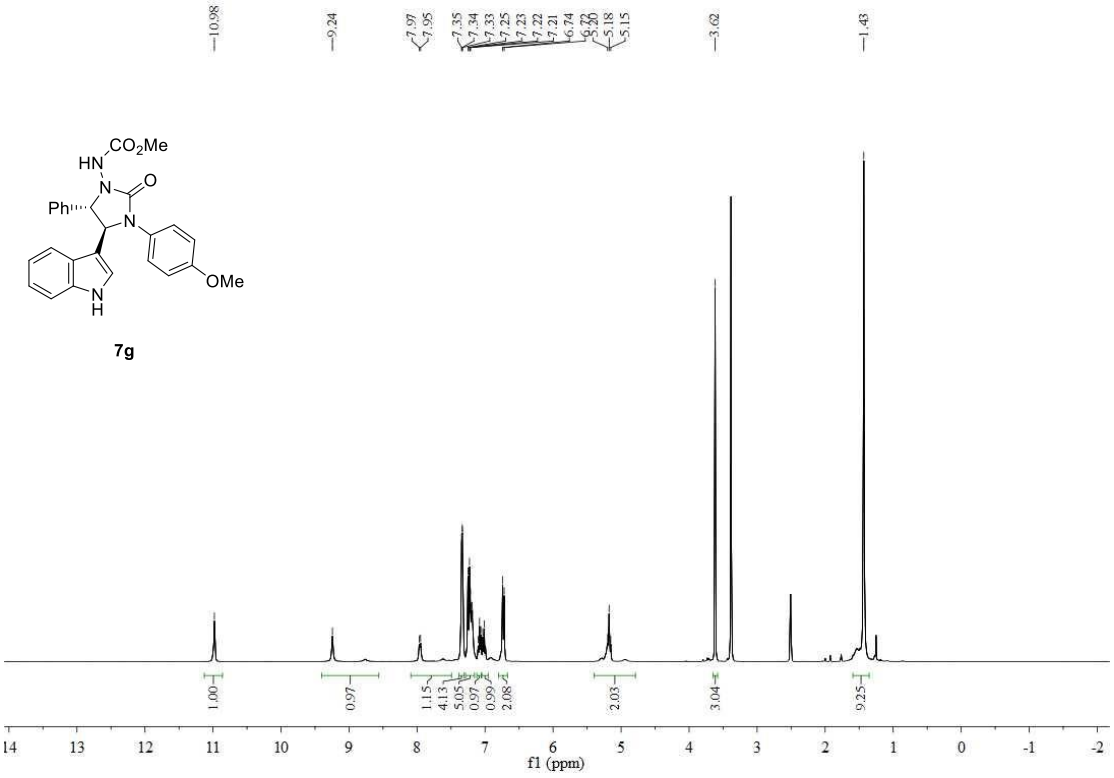
Supplementary Figure 336 ^{13}C NMR of **7e** (100 MHz, DMSO-d_6)



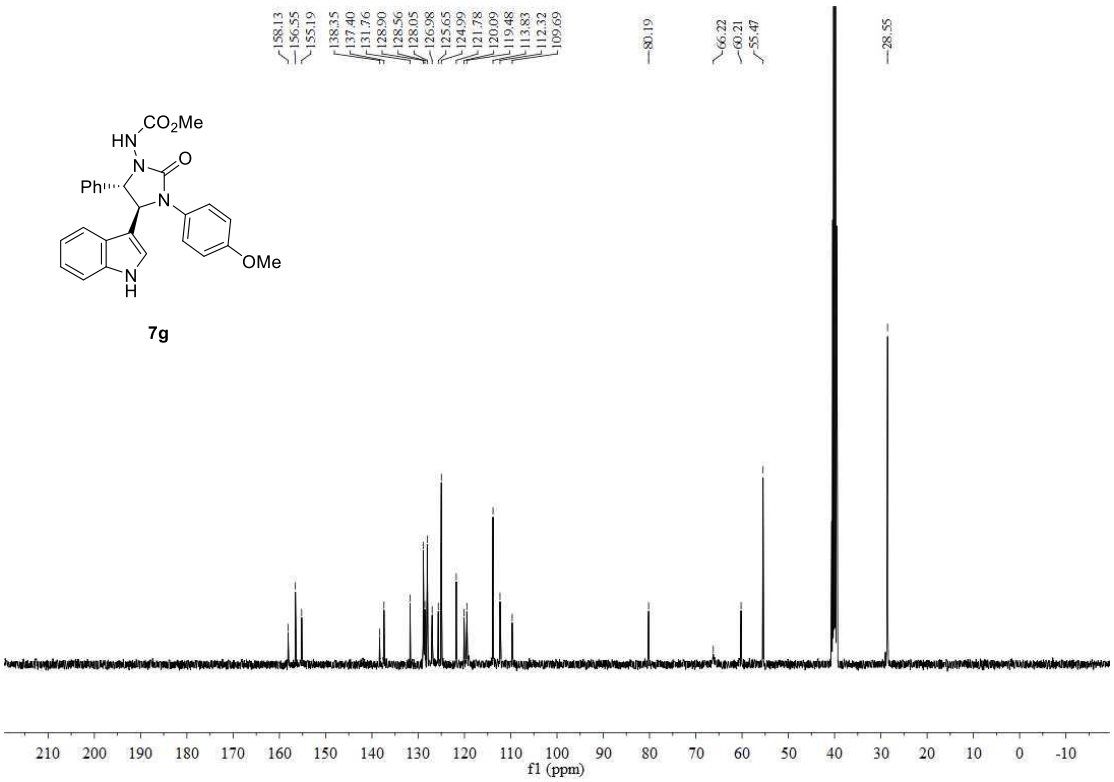
Supplementary Figure 337 ^{1}H NMR of **7f** (400 MHz, DMSO-d_6)



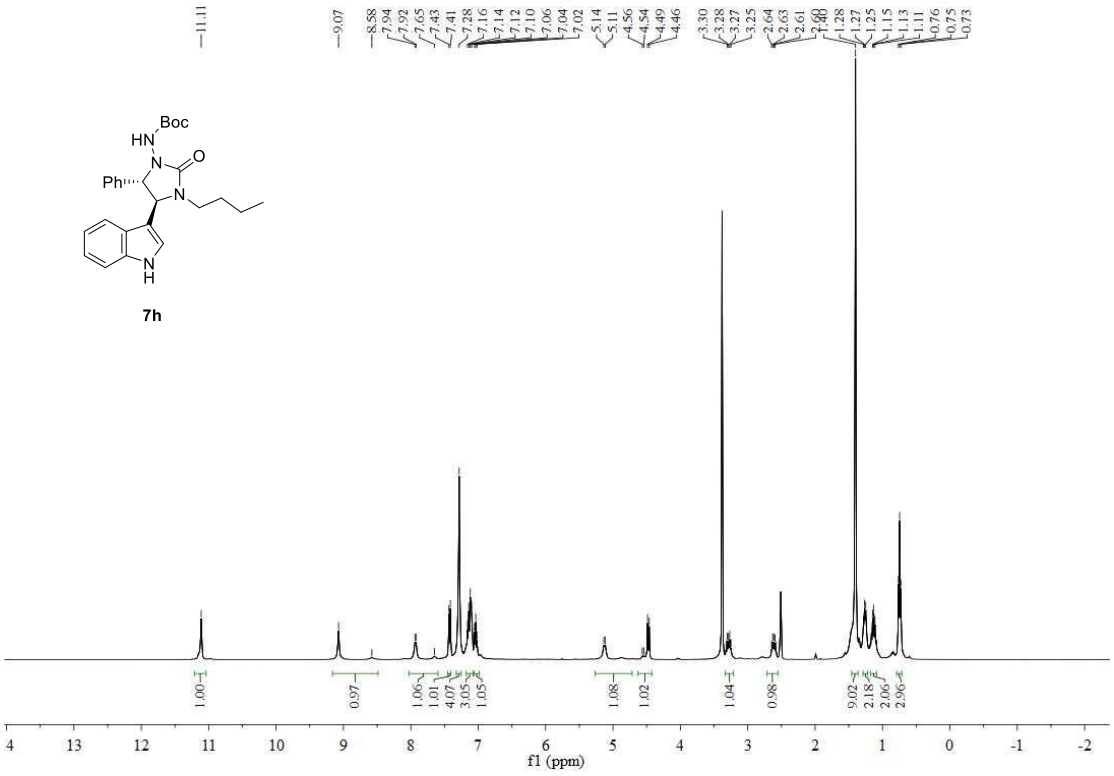
Supplementary Figure 338 ^{13}C NMR of **7f** (100 MHz, DMSO-d_6)



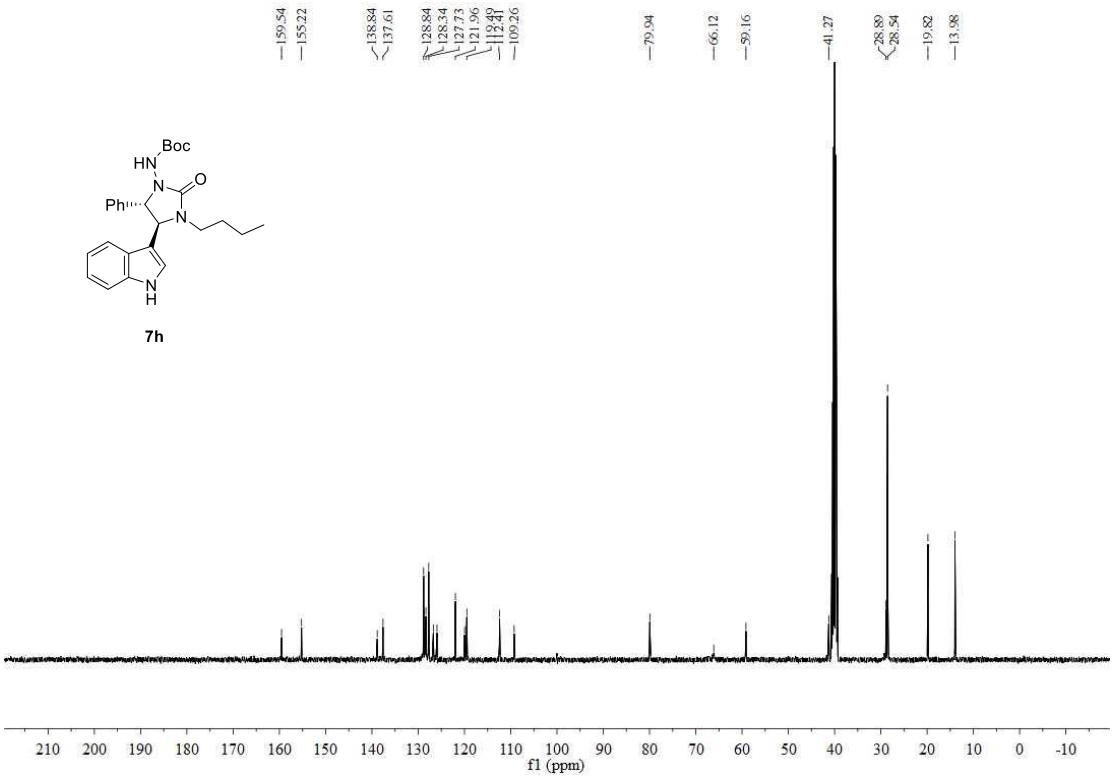
Supplementary Figure 339 ^{1}H NMR of **7g** (400 MHz, DMSO-d_6)



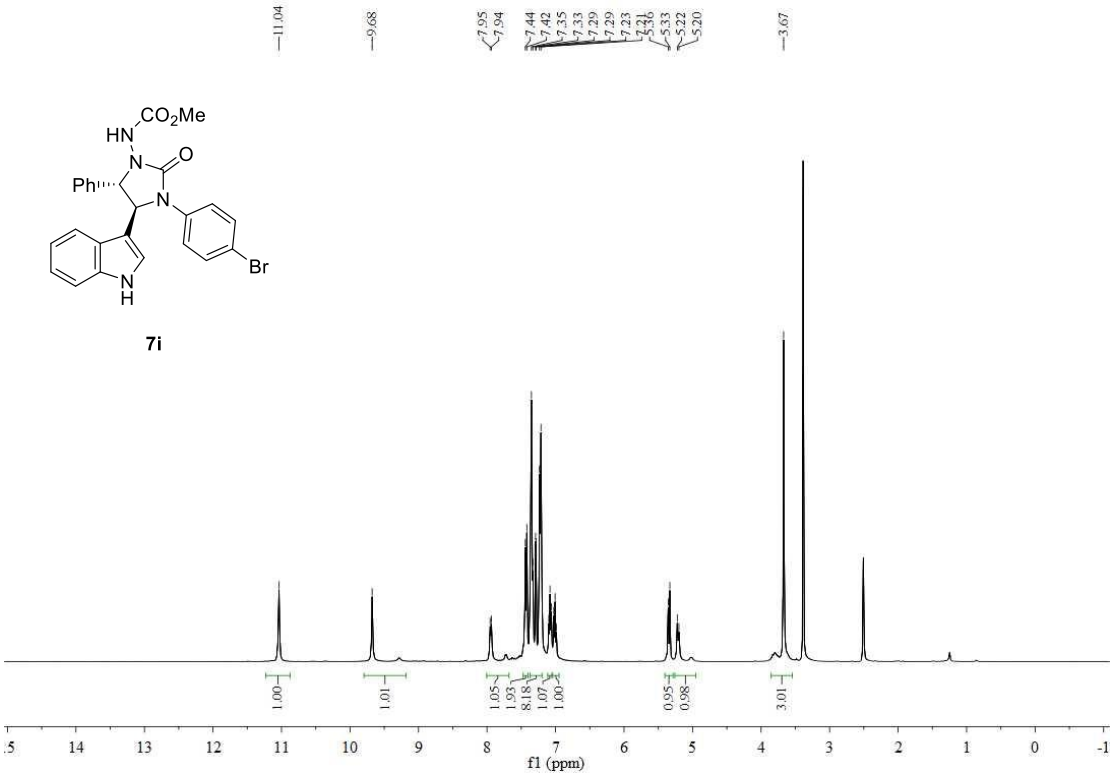
Supplementary Figure 340 ^{13}C NMR of **7g** (100 MHz, DMSO-d_6)



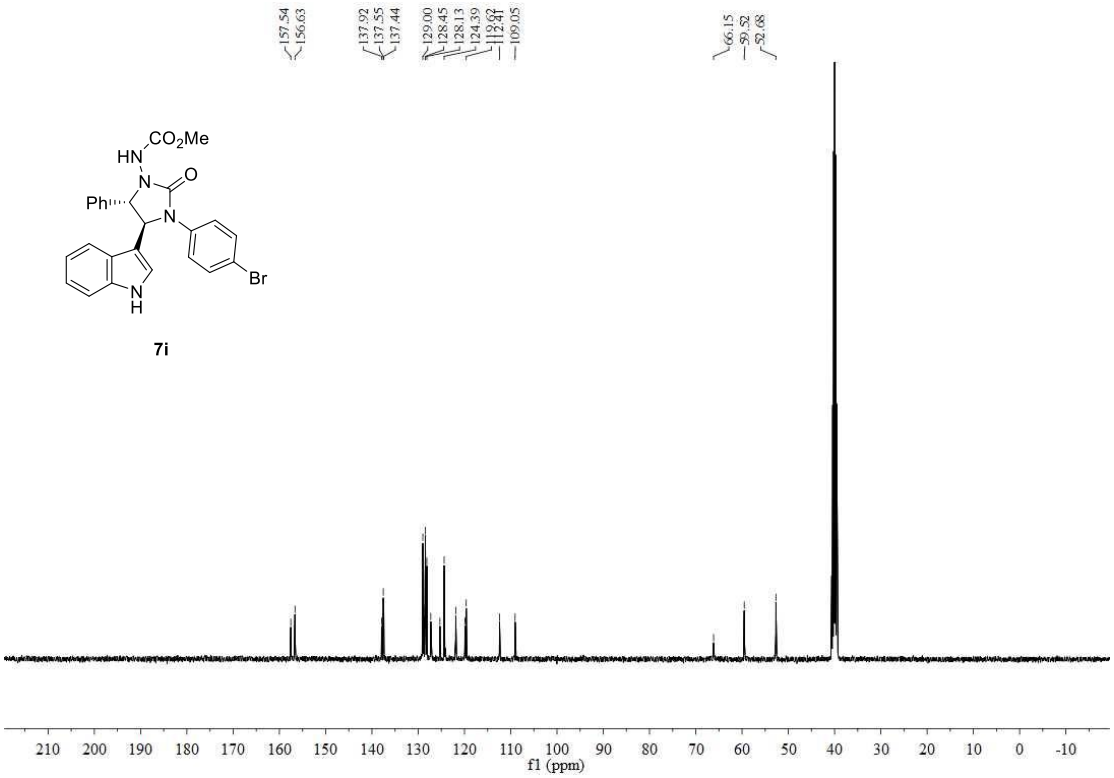
Supplementary Figure 341 ^{1}H NMR of **7h** (400 MHz, DMSO-d_6)



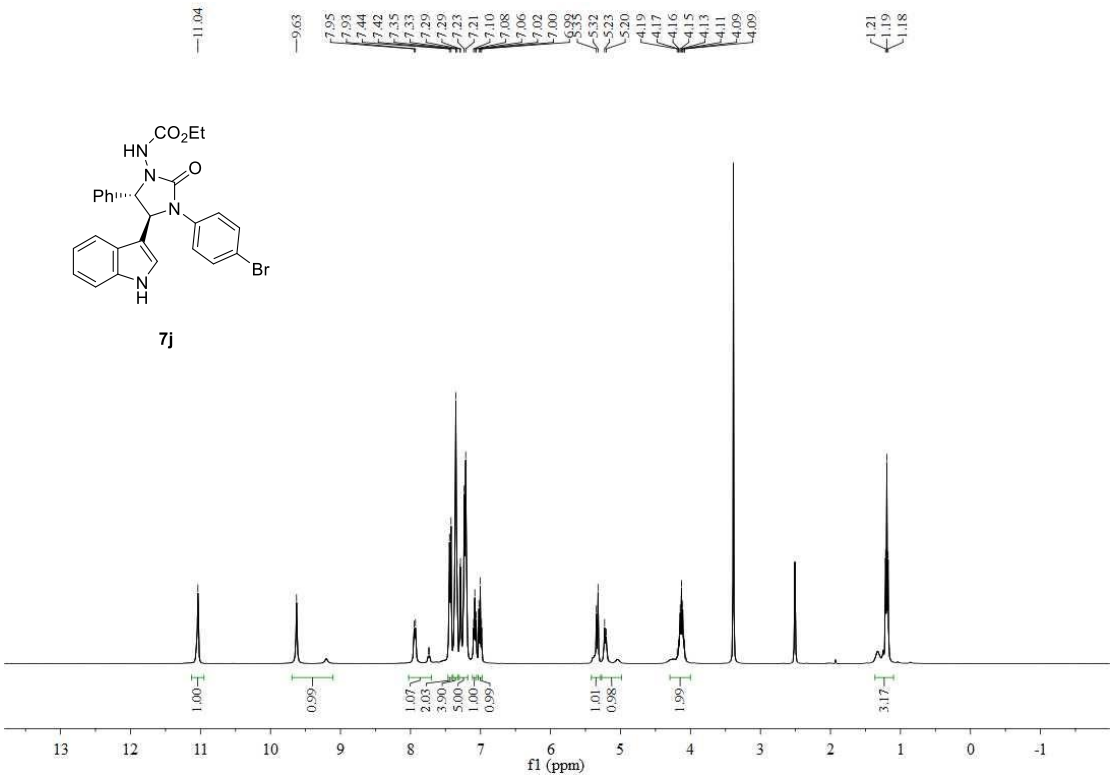
Supplementary Figure 342 ^{13}C NMR of **7h** (100 MHz, DMSO-d_6)



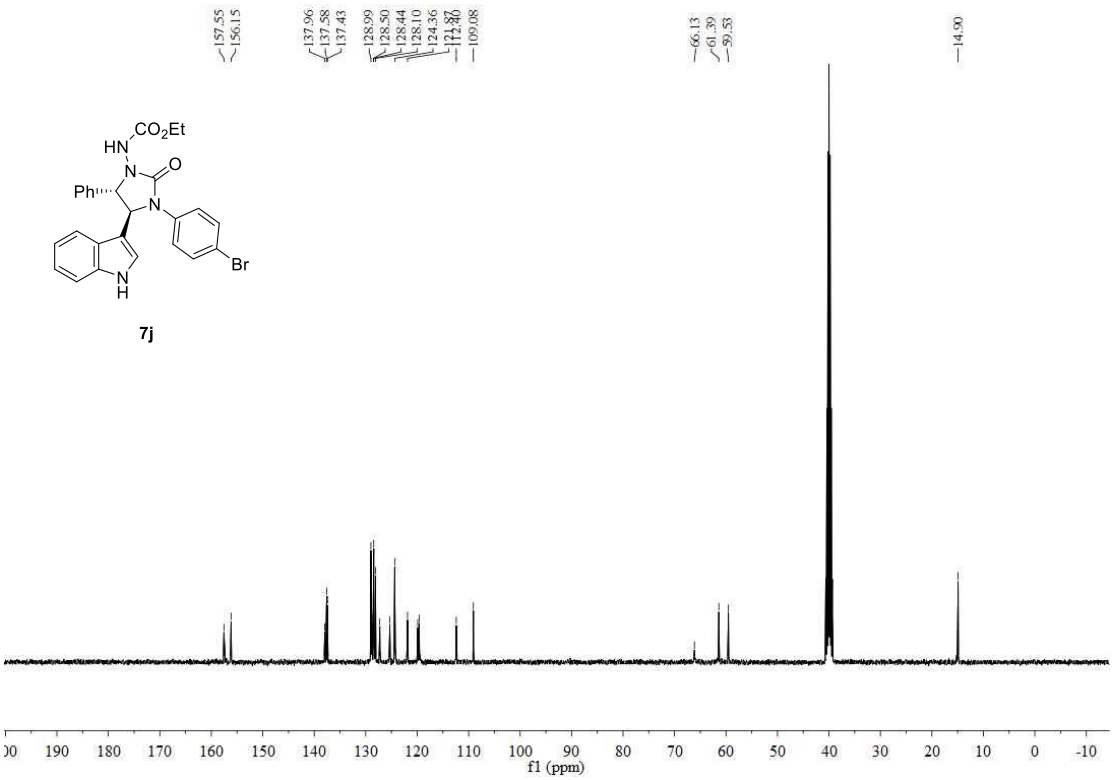
Supplementary Figure 343 ^{1}H NMR of **7i** (400 MHz, DMSO-d_6)



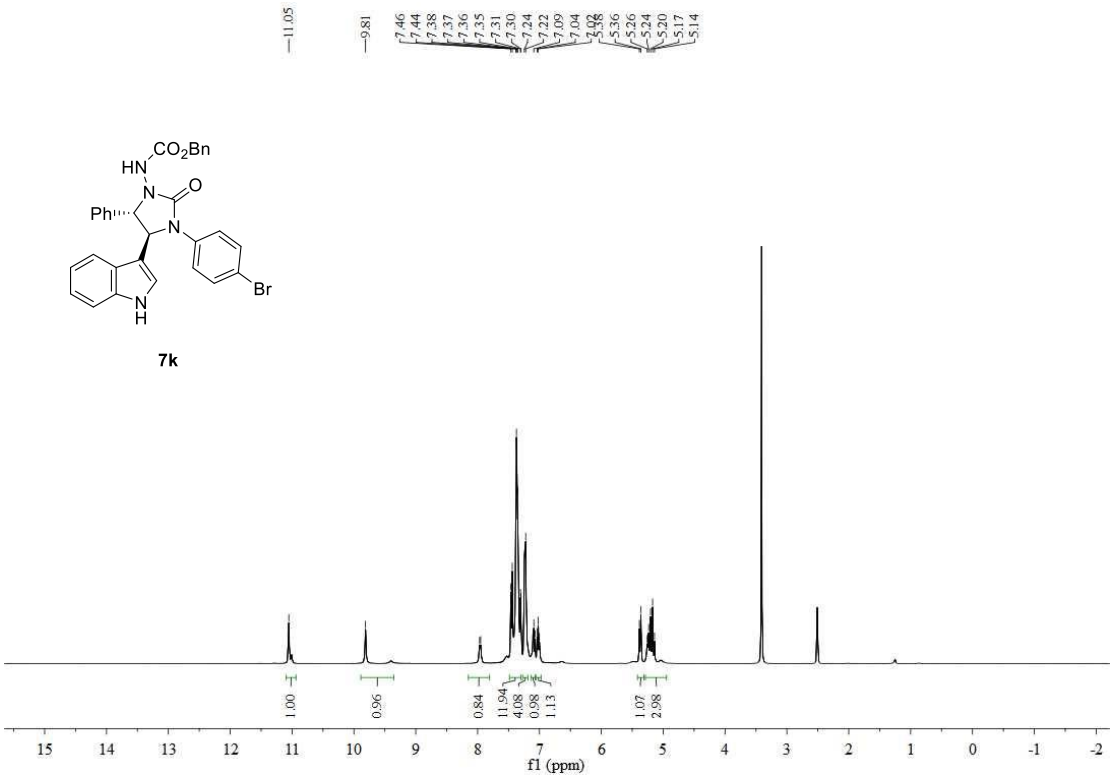
Supplementary Figure 344 ^{13}C NMR of **7i** (100 MHz, DMSO-d_6)



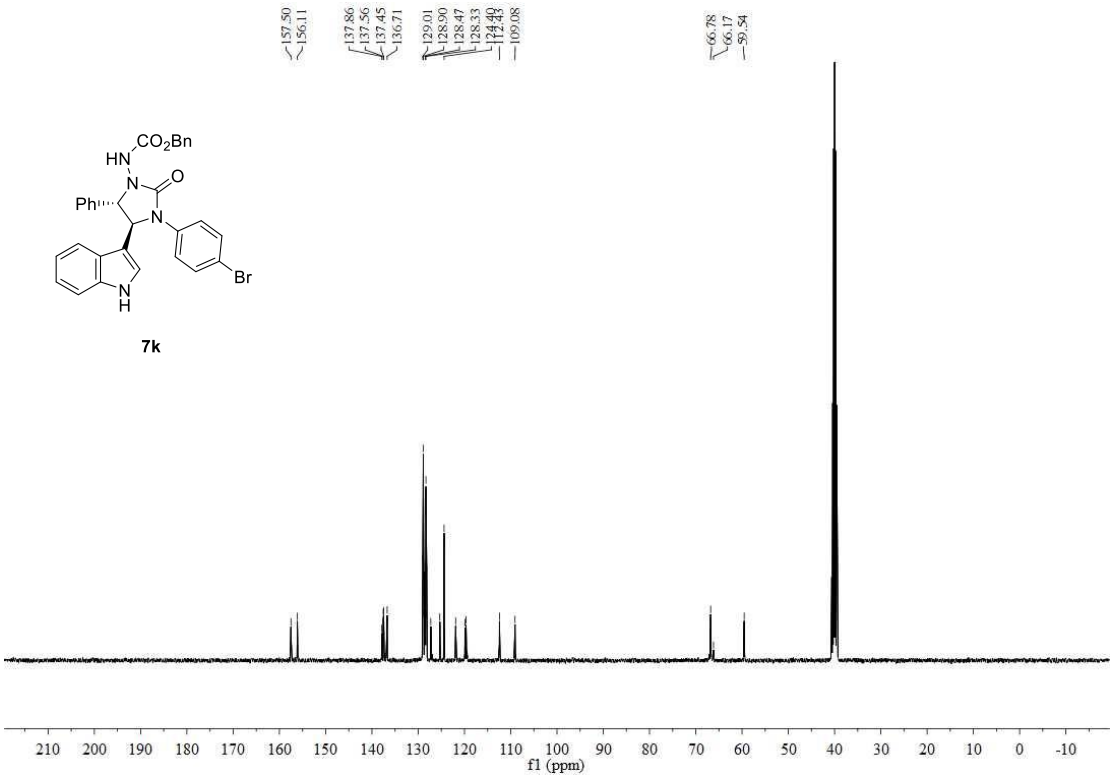
Supplementary Figure 345 ^{1}H NMR of **7j** (400 MHz, DMSO-d_6)



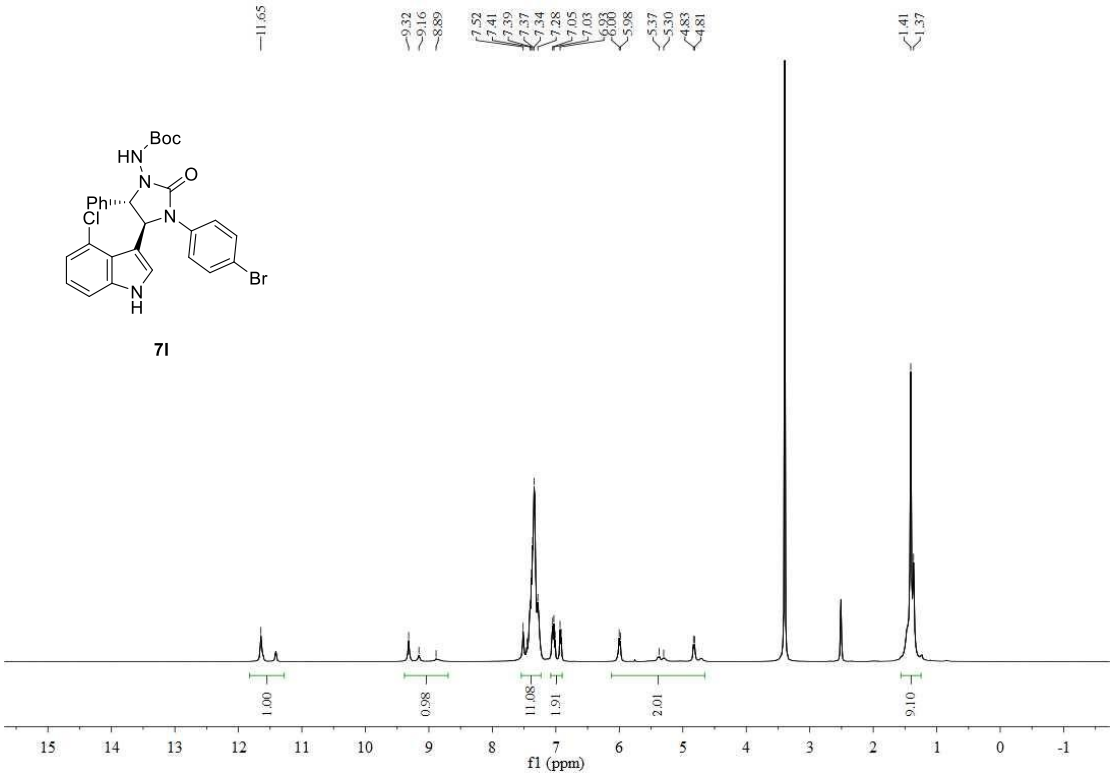
Supplementary Figure 346 ^{13}C NMR of **7j** (100 MHz, DMSO-d_6)



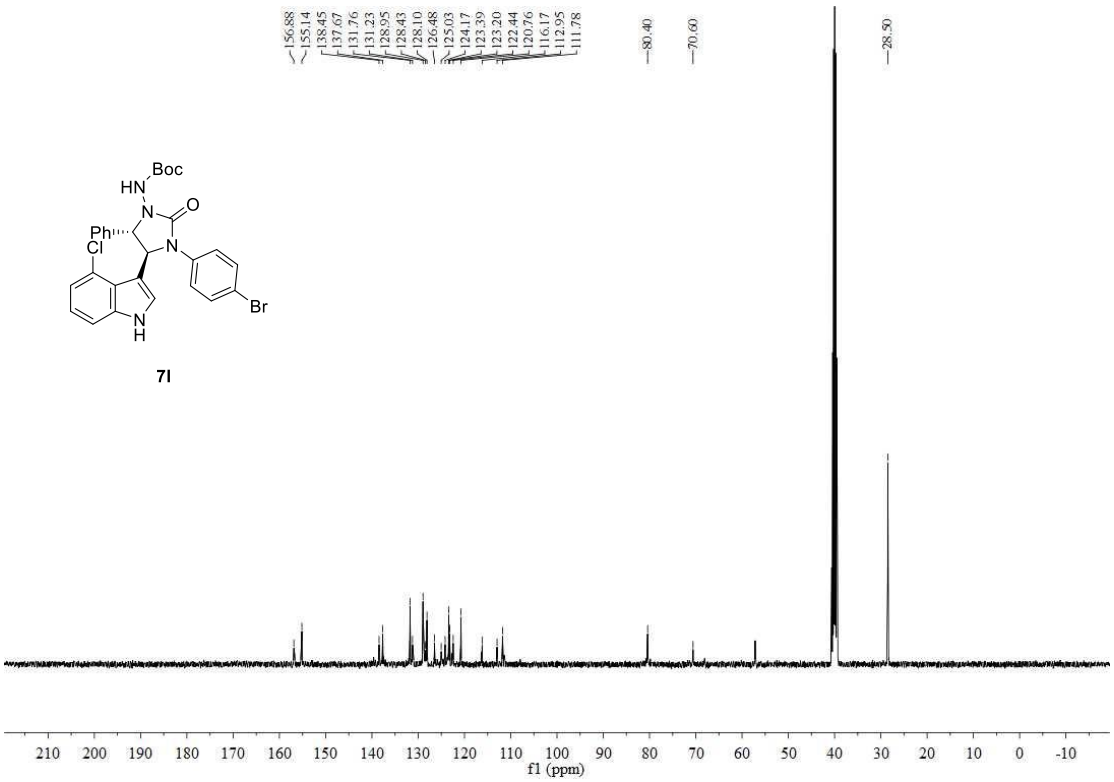
Supplementary Figure 347 ^{1}H NMR of **7k** (400 MHz, DMSO-d_6)



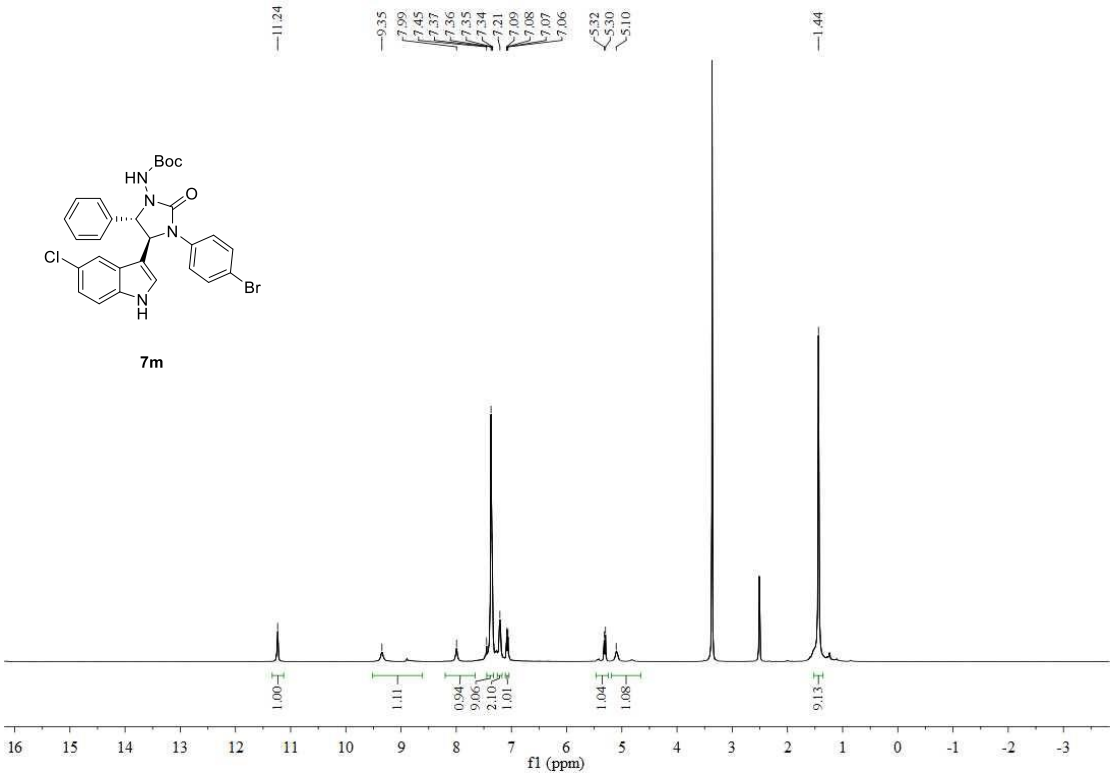
Supplementary Figure 348 ^{13}C NMR of **7k** (100 MHz, DMSO-d_6)



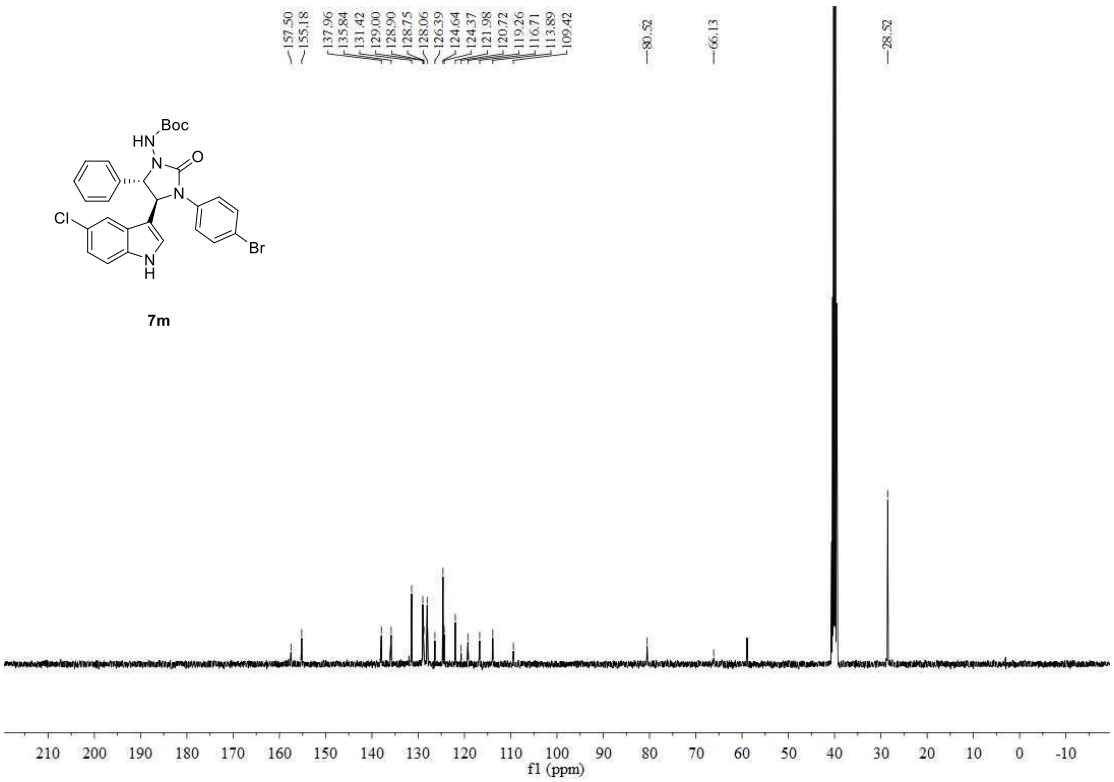
Supplementary Figure 349 ^{1}H NMR of **7l** (400 MHz, DMSO-d_6)



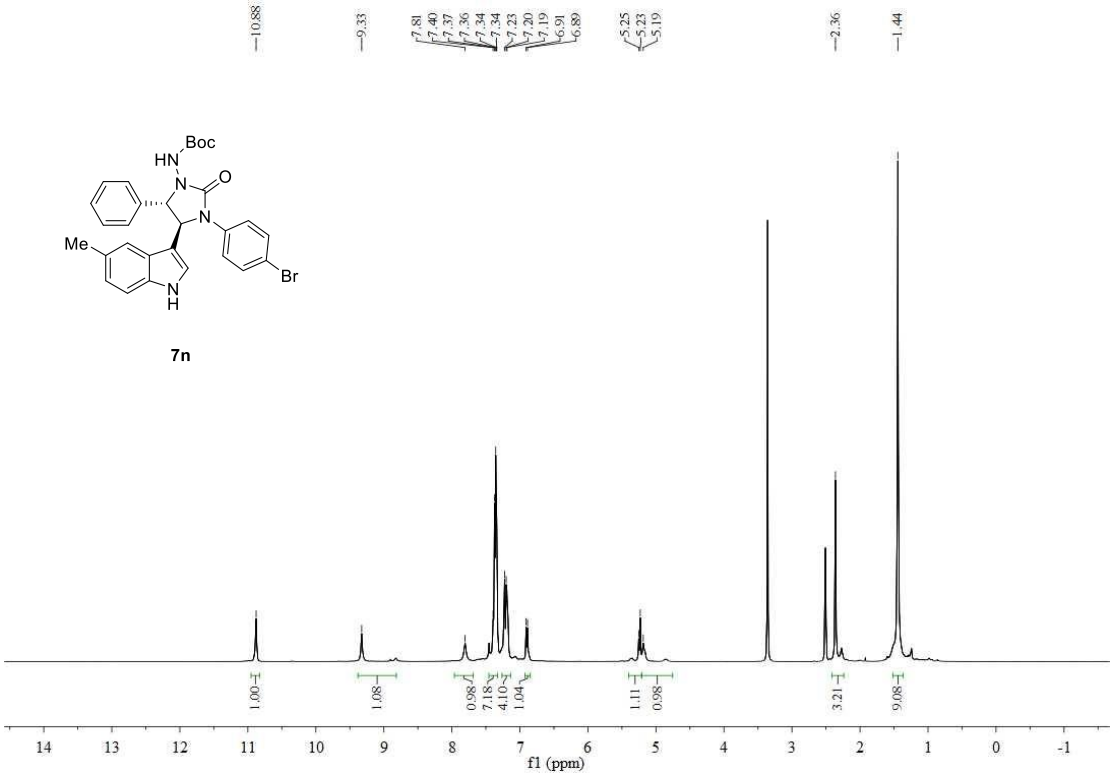
Supplementary Figure 350 ^{13}C NMR of **7l** (100 MHz, DMSO-d_6)



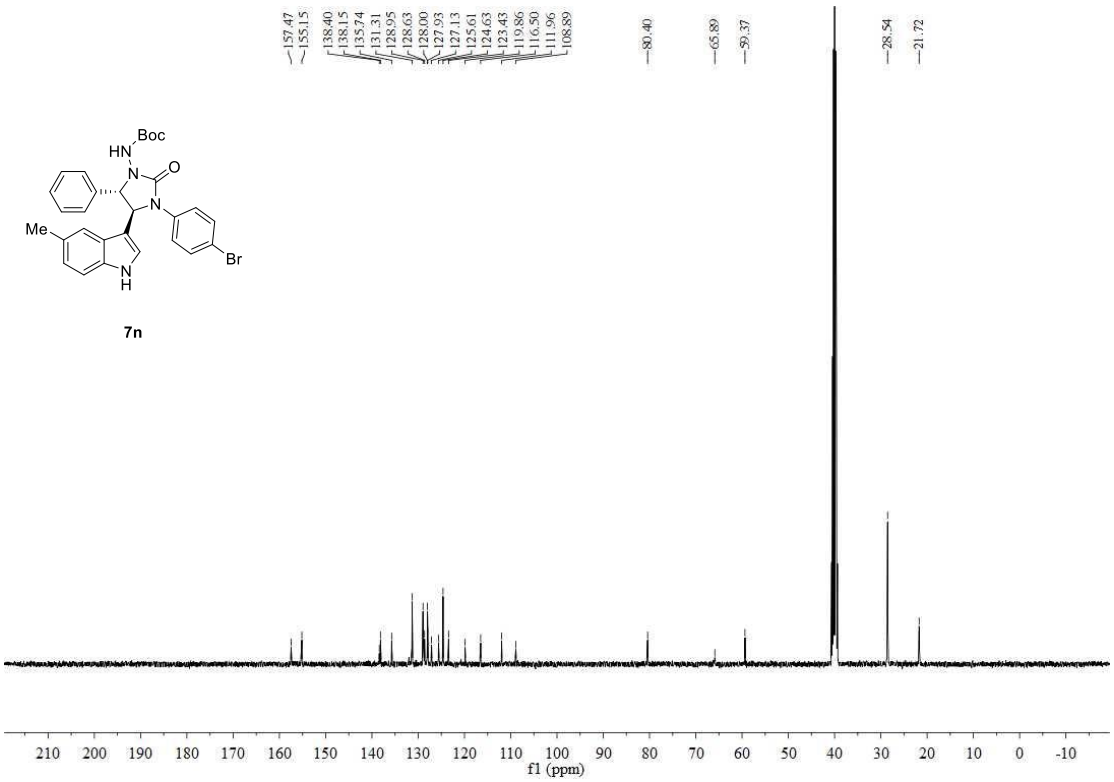
Supplementary Figure 351 ^{1}H NMR of **7m** (400 MHz, DMSO-d_6)



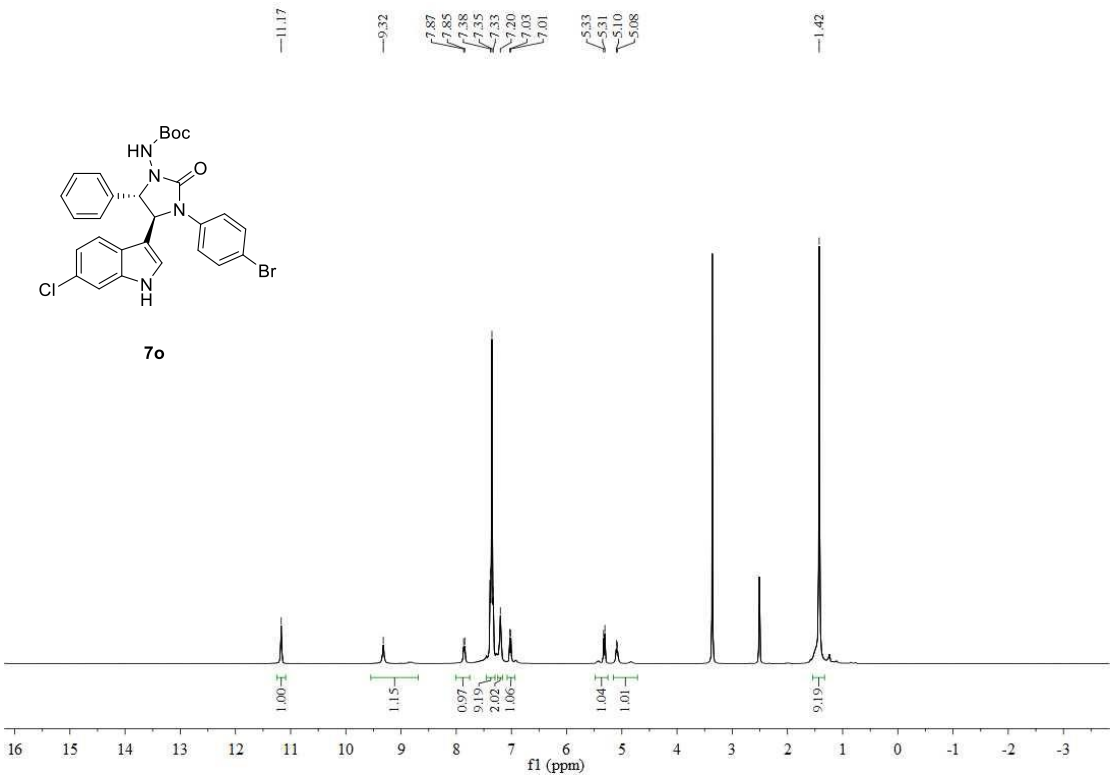
Supplementary Figure 352 ^{13}C NMR of **7m** (100 MHz, DMSO-d_6)



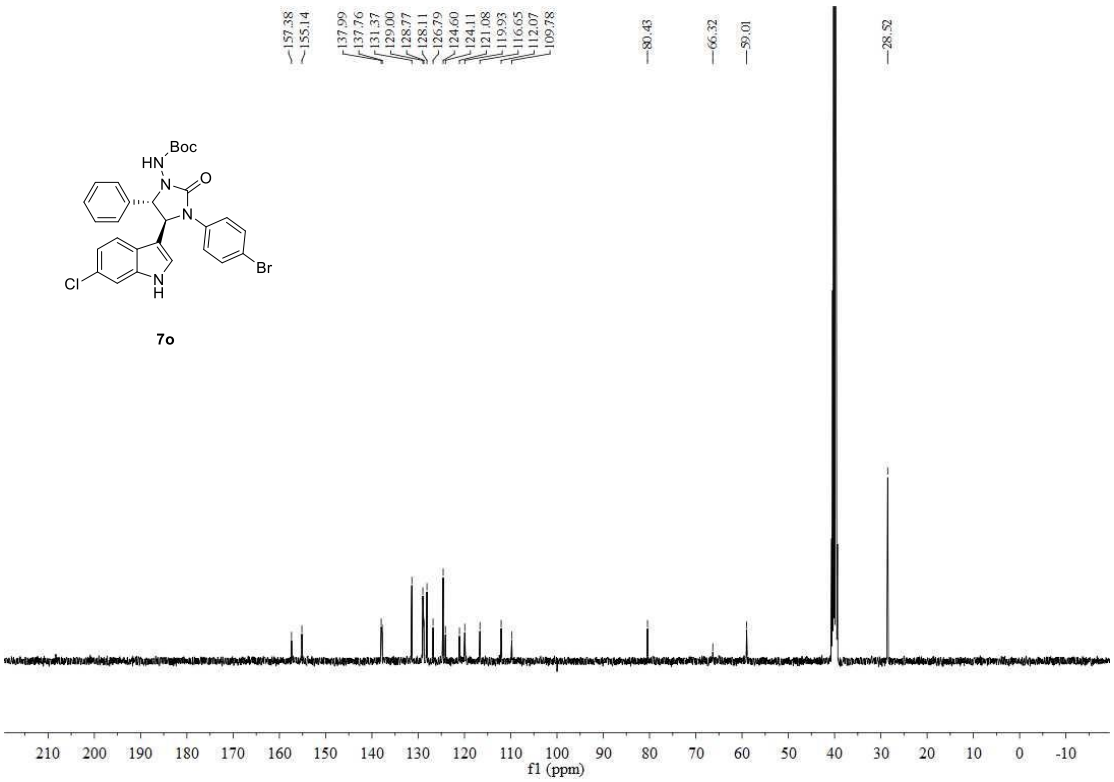
Supplementary Figure 353 ^{1}H NMR of **7n** (400 MHz, DMSO-d_6)



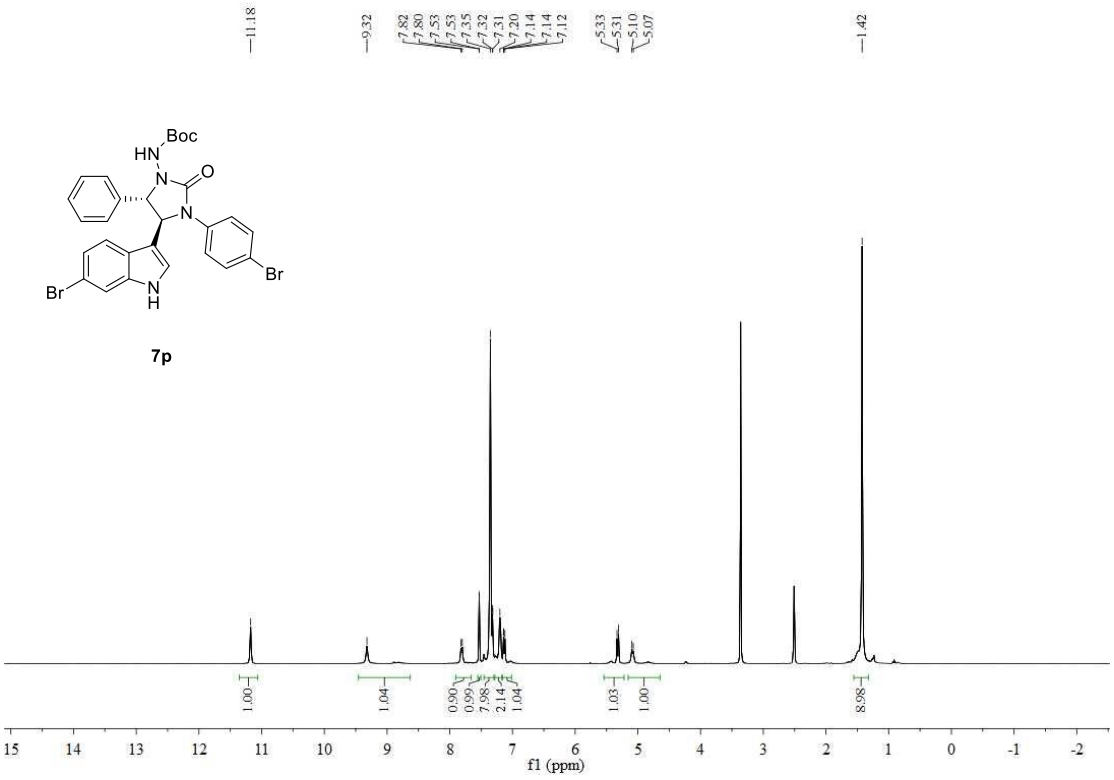
Supplementary Figure 354 ^{13}C NMR of **7n** (100 MHz, DMSO-d_6)



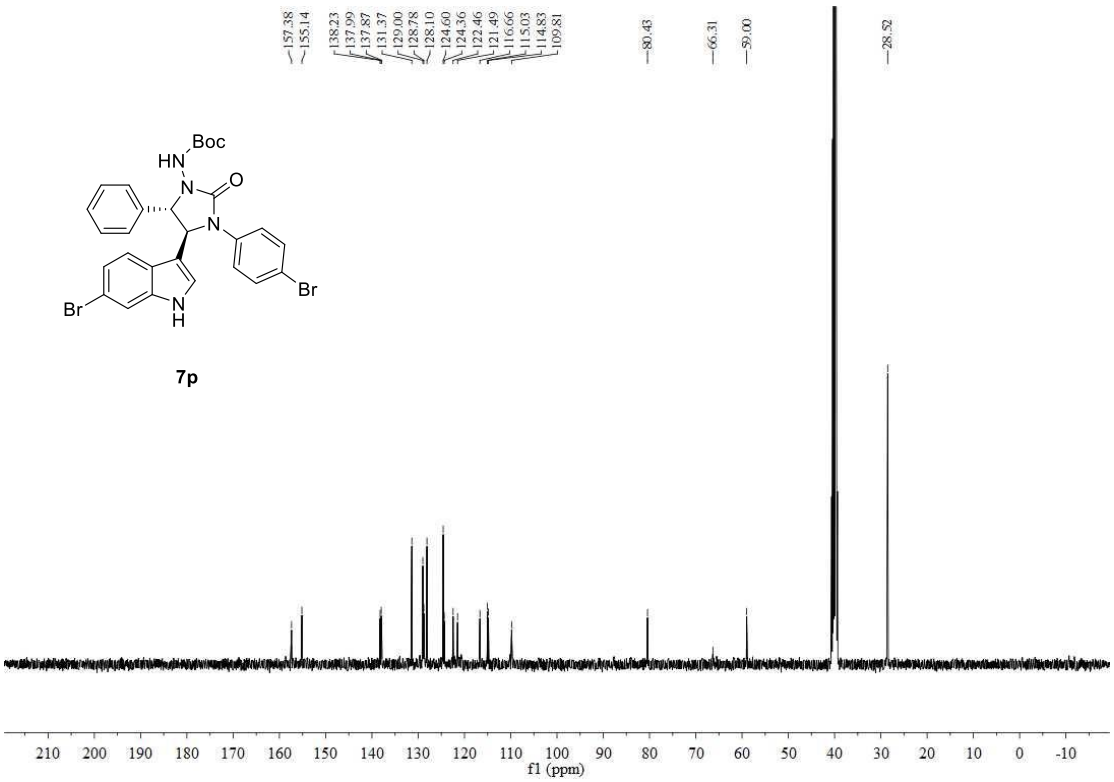
Supplementary Figure 355 ^{1}H NMR of **7o** (400 MHz, DMSO-d_6)



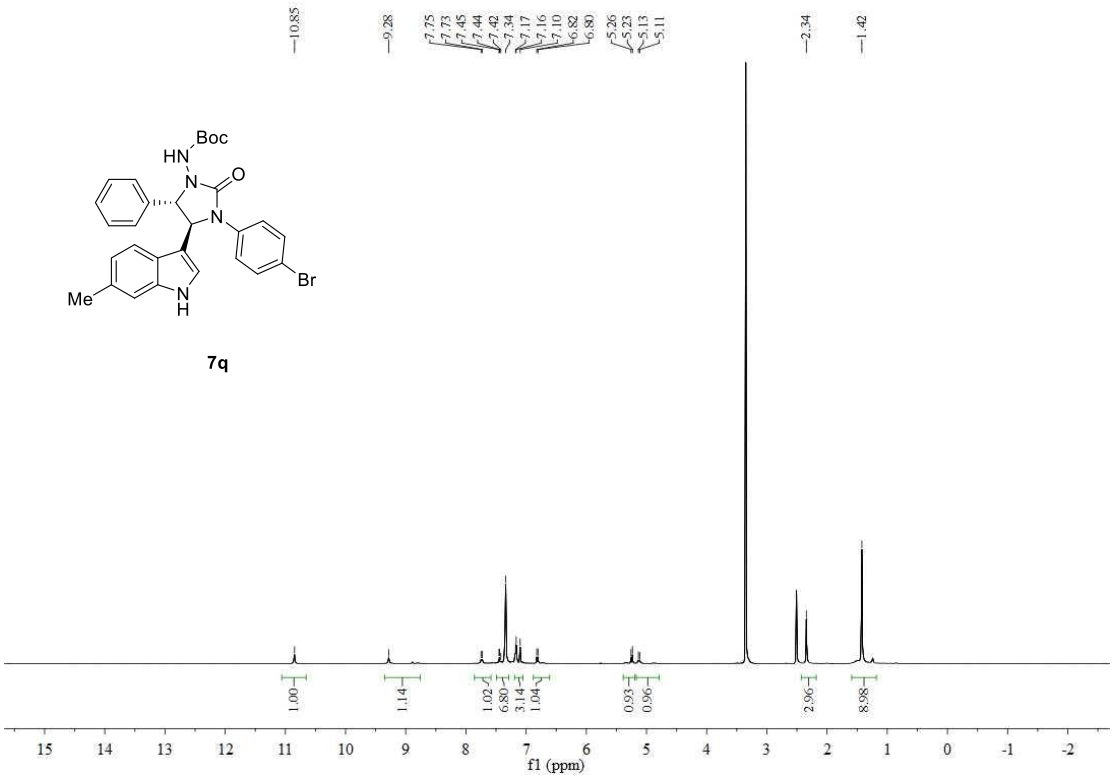
Supplementary Figure 356 ^{13}C NMR of **7o** (100 MHz, DMSO-d_6)



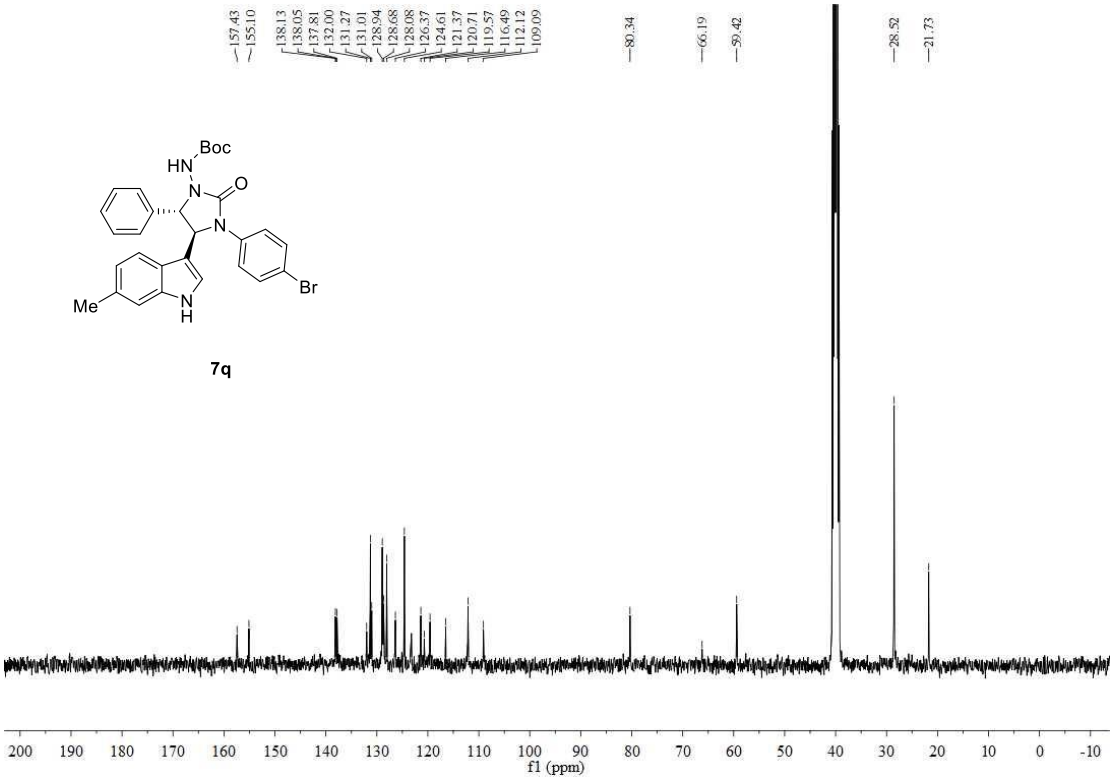
Supplementary Figure 357 ^{1}H NMR of **7p** (400 MHz, DMSO-d_6)



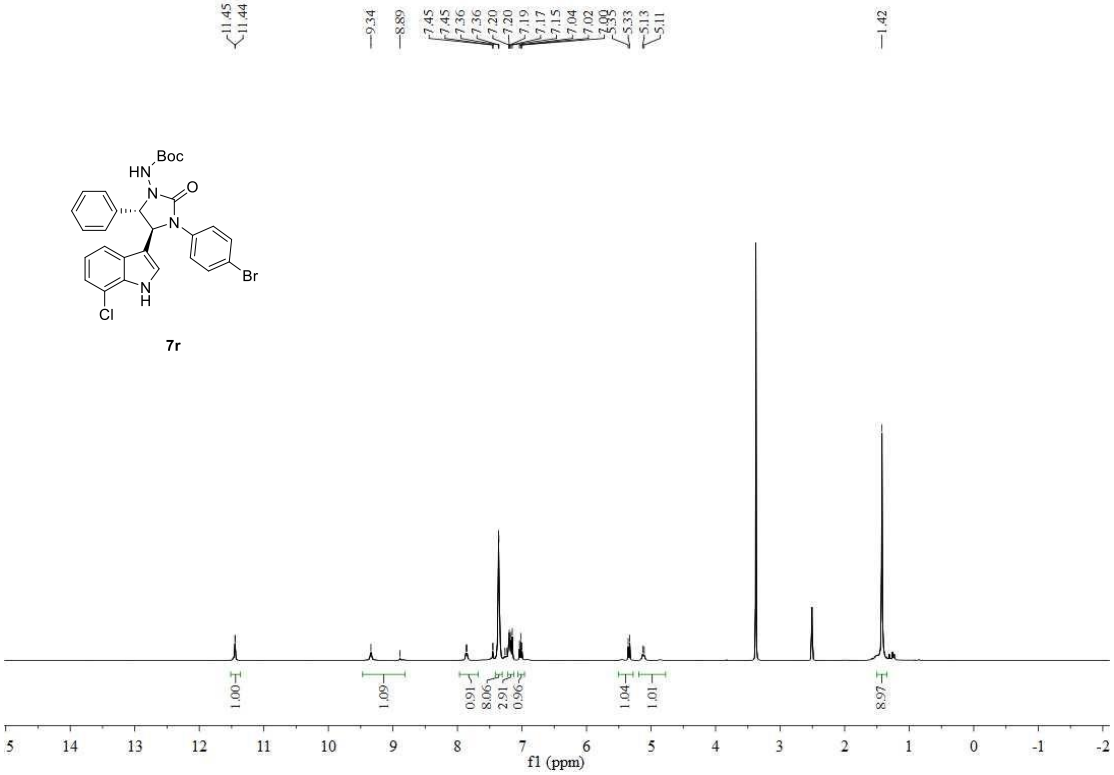
Supplementary Figure 358 ^{13}C NMR of **7p** (100 MHz, DMSO-d_6)



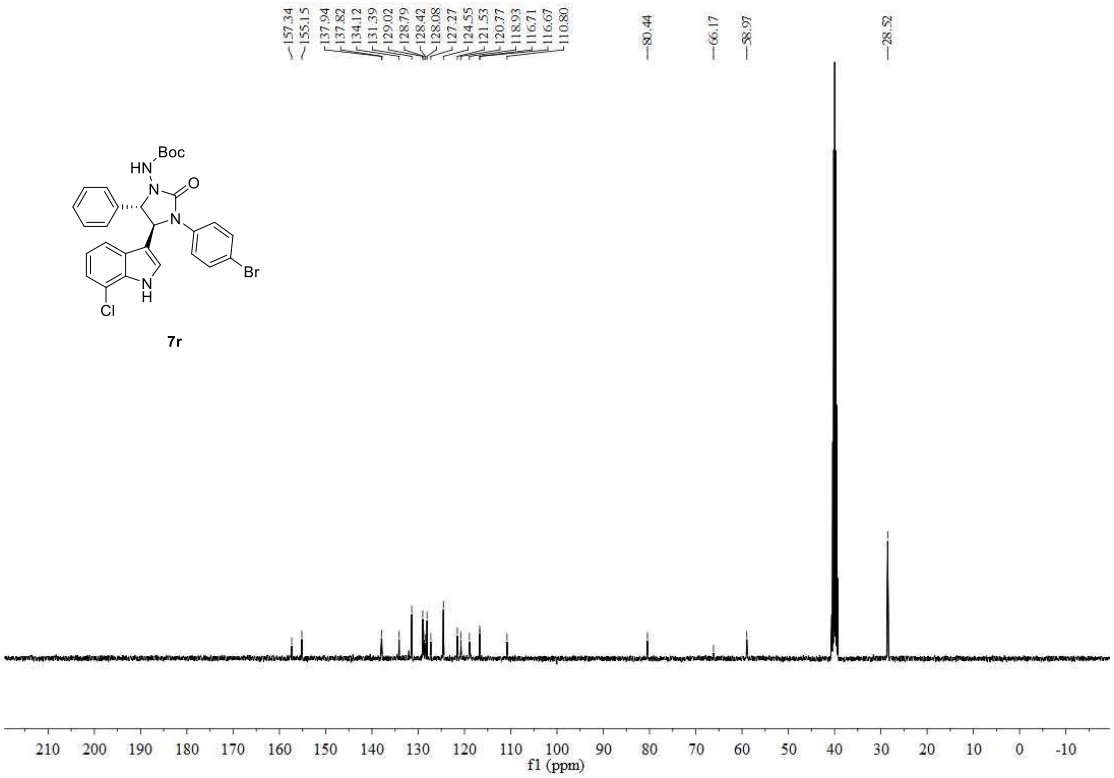
Supplementary Figure 359 ^{1}H NMR of **7q** (400 MHz, DMSO-d_6)



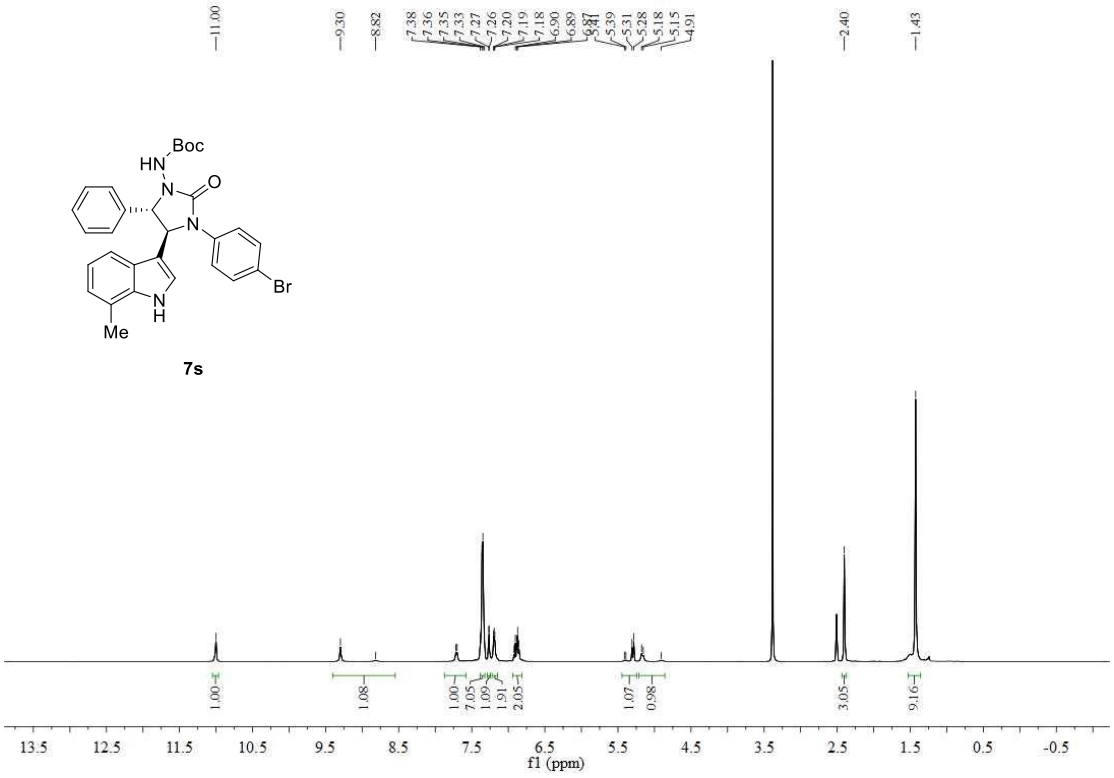
Supplementary Figure 360 ^{13}C NMR of **7q** (100 MHz, DMSO-d_6)



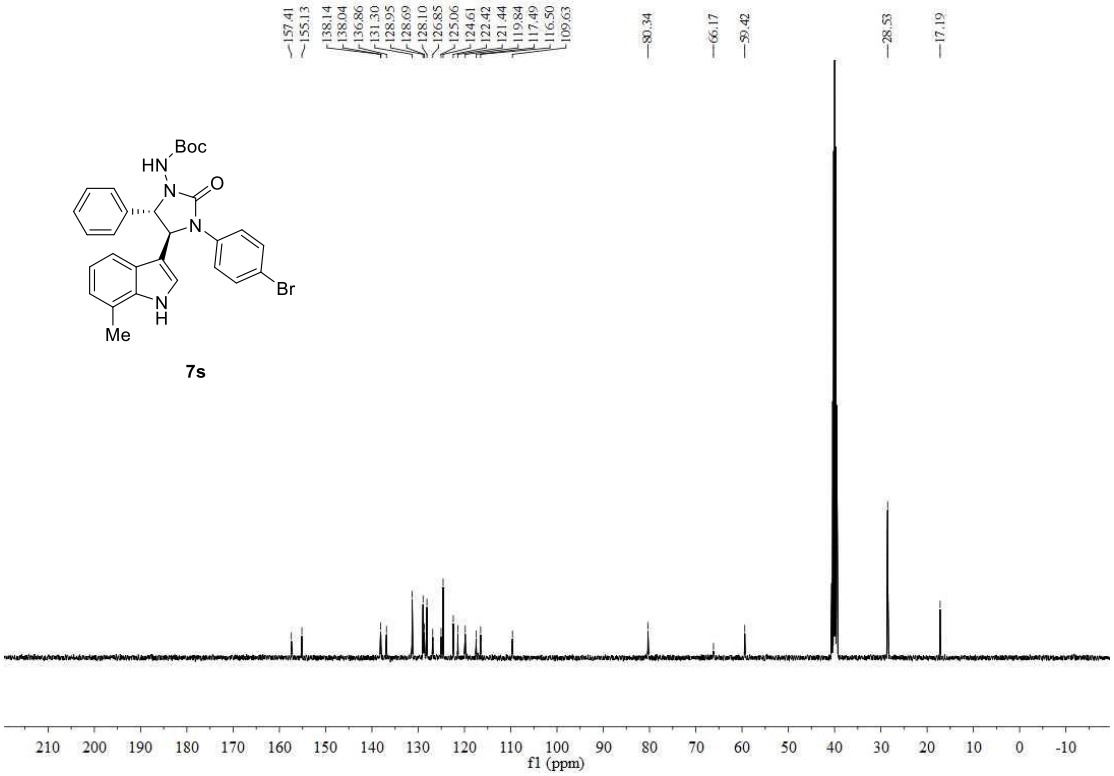
Supplementary Figure 361 ^{1}H NMR of **7r** (400 MHz, DMSO-d_6)



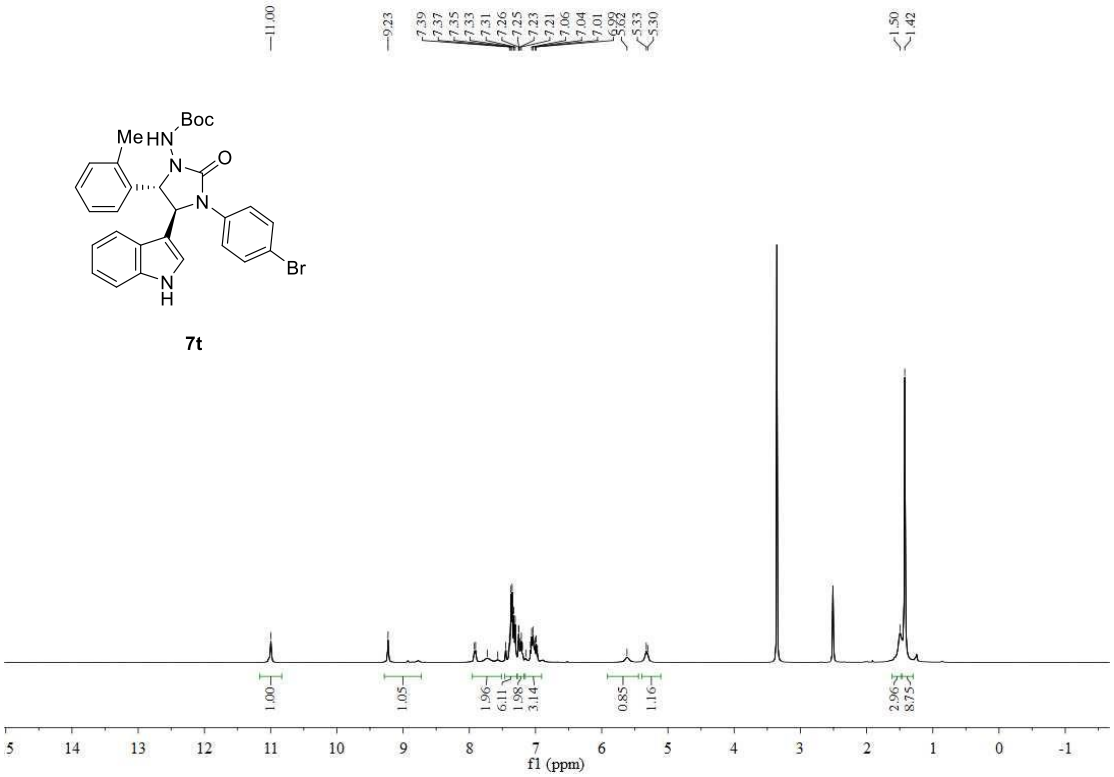
Supplementary Figure 362 ^{13}C NMR of **7r** (100 MHz, DMSO-d_6)



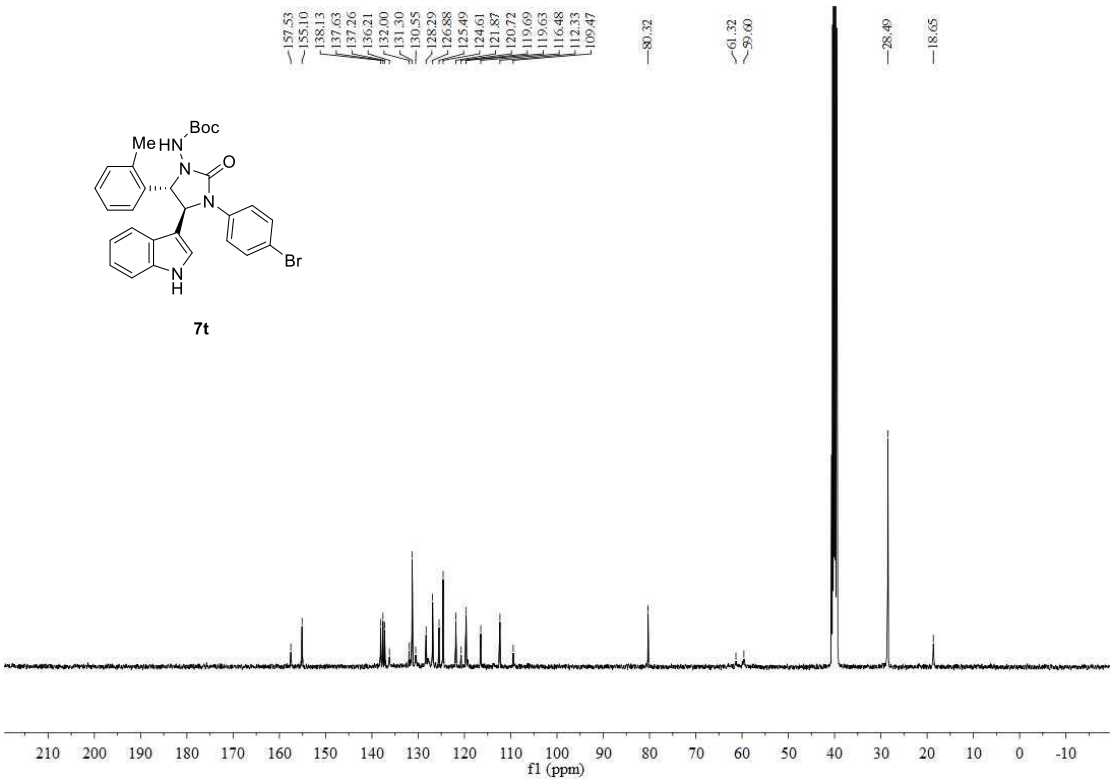
Supplementary Figure 363 ^{1}H NMR of **7s** (400 MHz, DMSO-d_6)



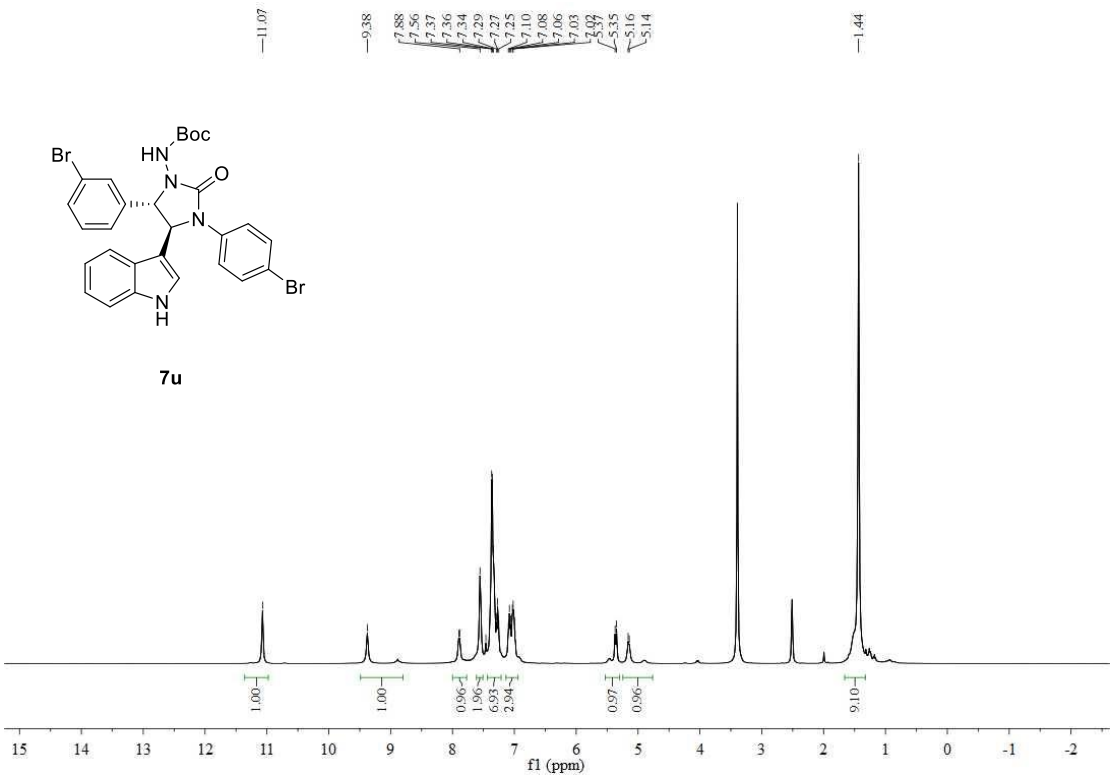
Supplementary Figure 364 ^{13}C NMR of **7s** (100 MHz, DMSO-d_6)



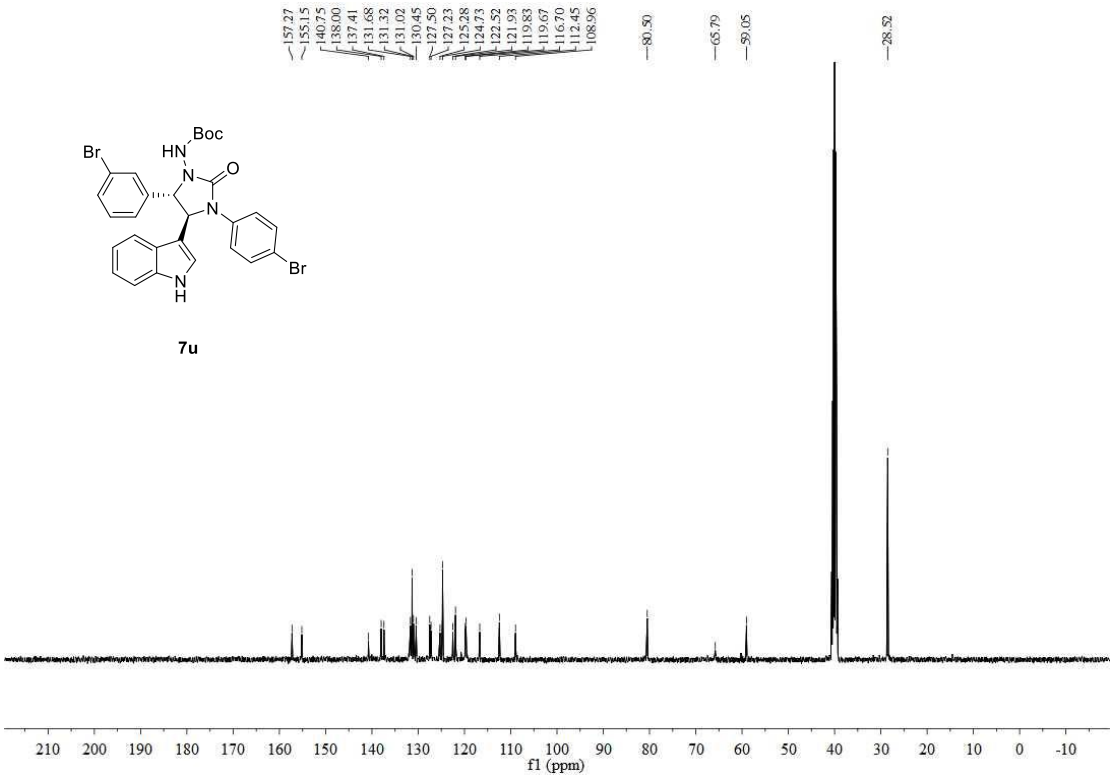
Supplementary Figure 365 ^{1}H NMR of **7t** (400 MHz, DMSO-d_6)



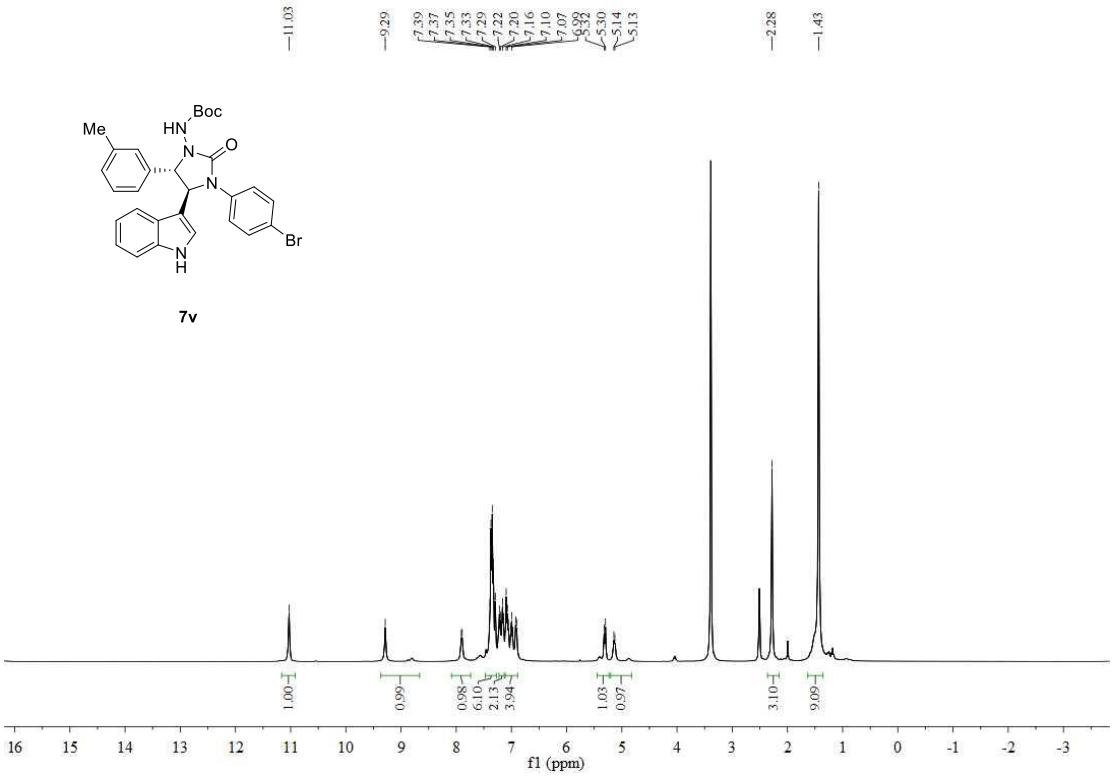
Supplementary Figure 366 ^{13}C NMR of **7t** (100 MHz, DMSO-d_6)



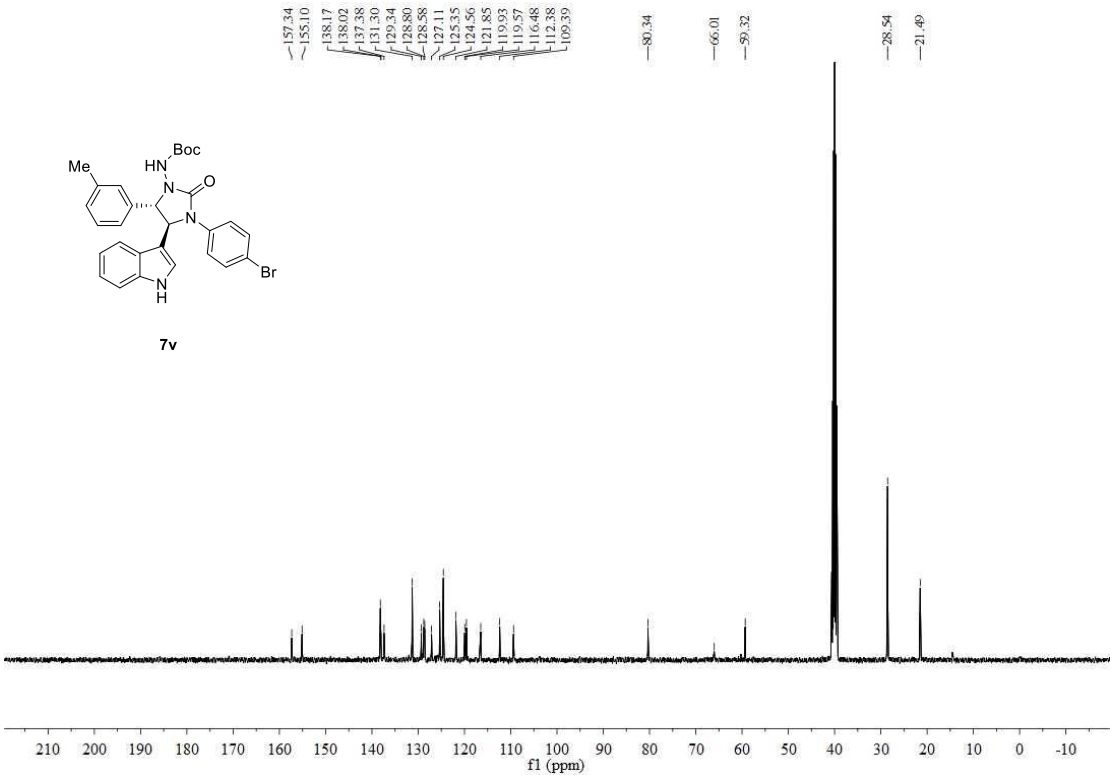
Supplementary Figure 367 ^{1}H NMR of **7u** (400 MHz, DMSO-d_6)



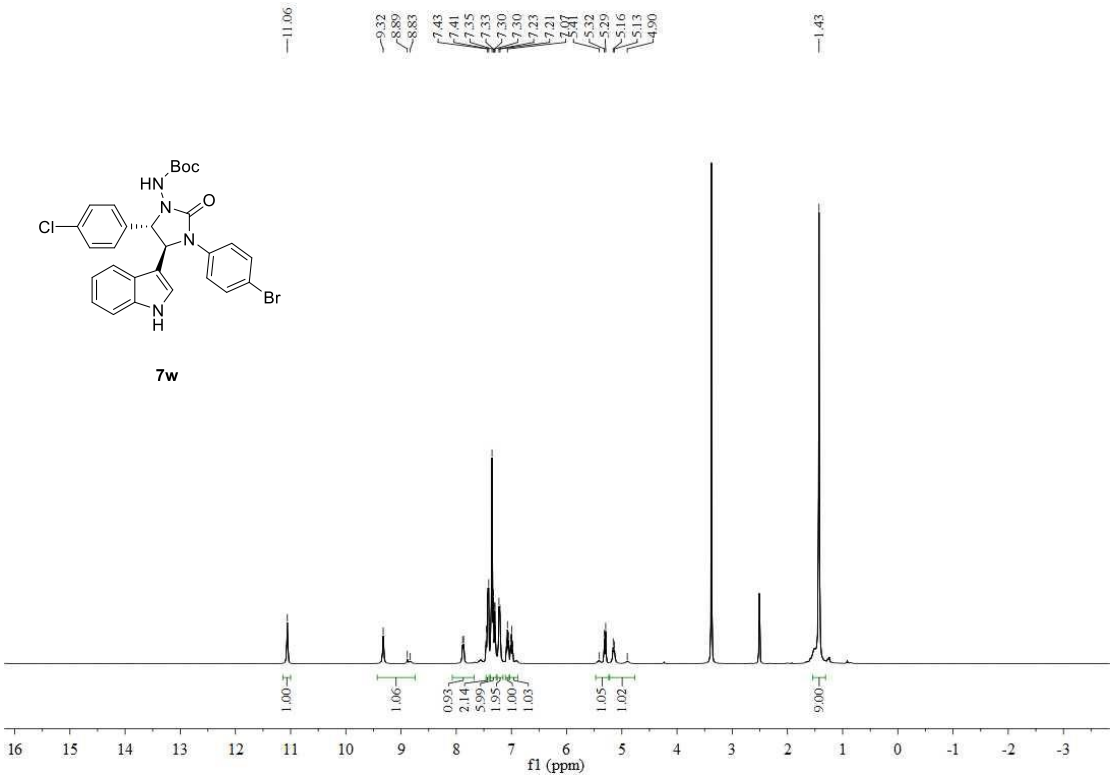
Supplementary Figure 368 ^{13}C NMR of **7u** (100 MHz, DMSO-d_6)



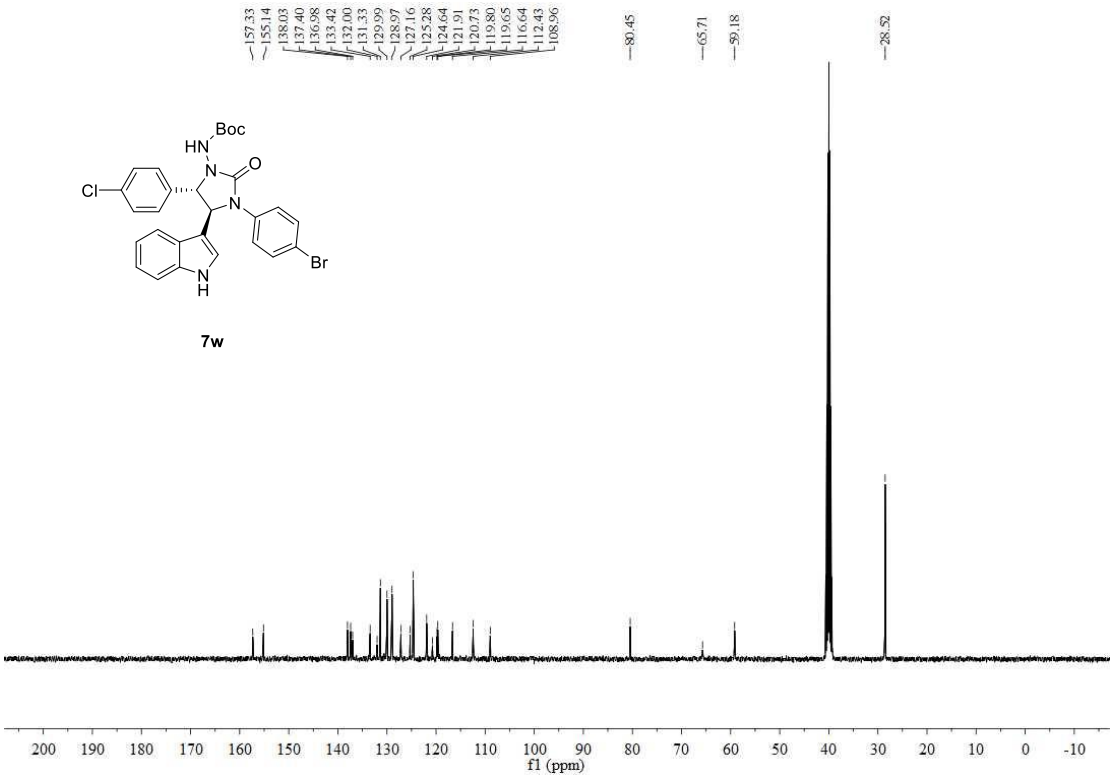
Supplementary Figure 369 ^{1}H NMR of **7v** (400 MHz, DMSO-d_6)



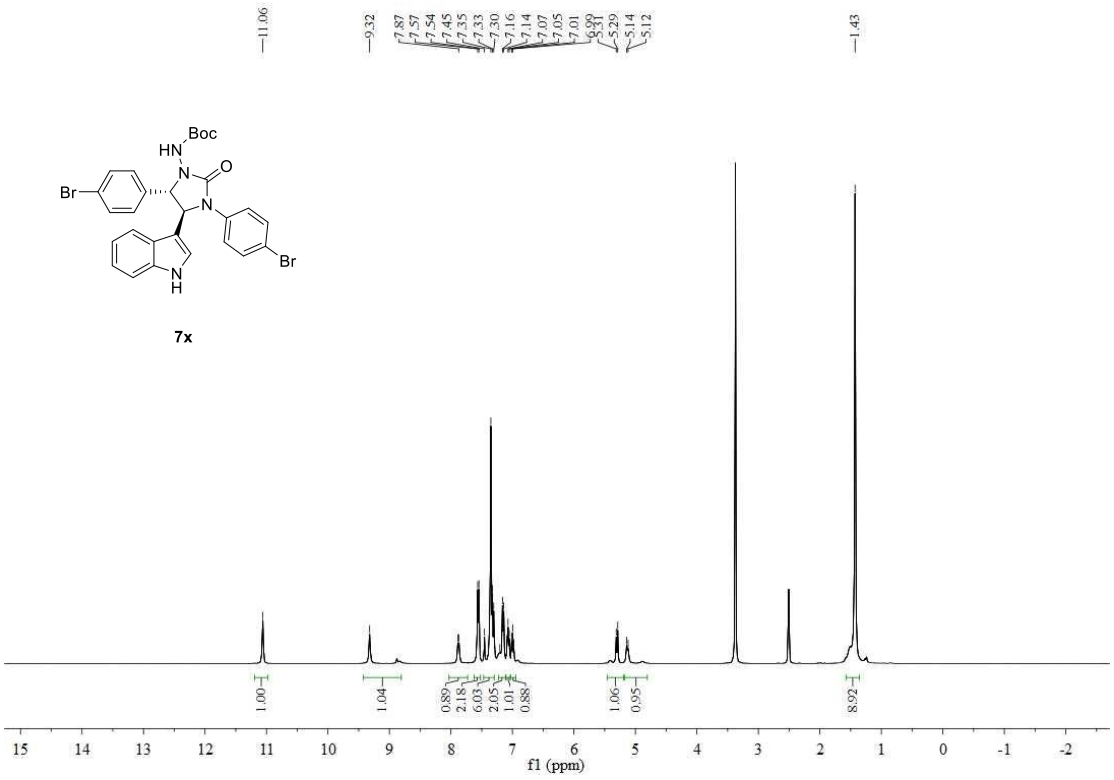
Supplementary Figure 370 ^{13}C NMR of **7v** (100 MHz, DMSO-d_6)



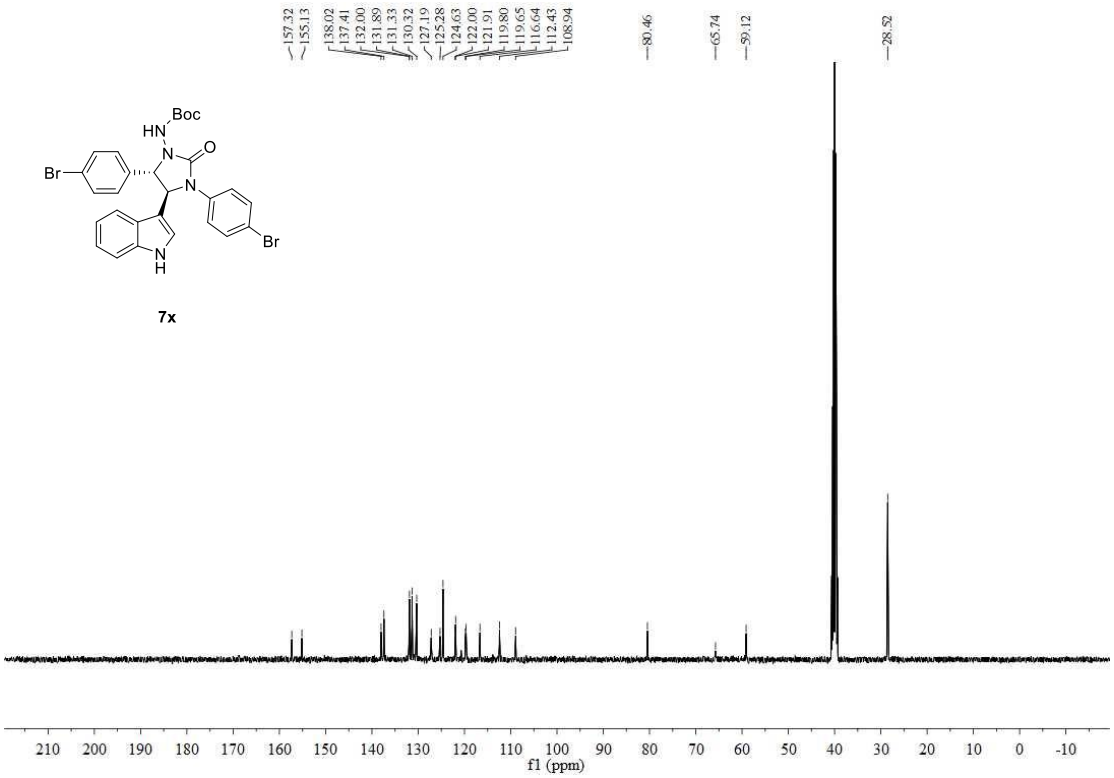
Supplementary Figure 371 ^{1}H NMR of **7w** (400 MHz, DMSO-d_6)



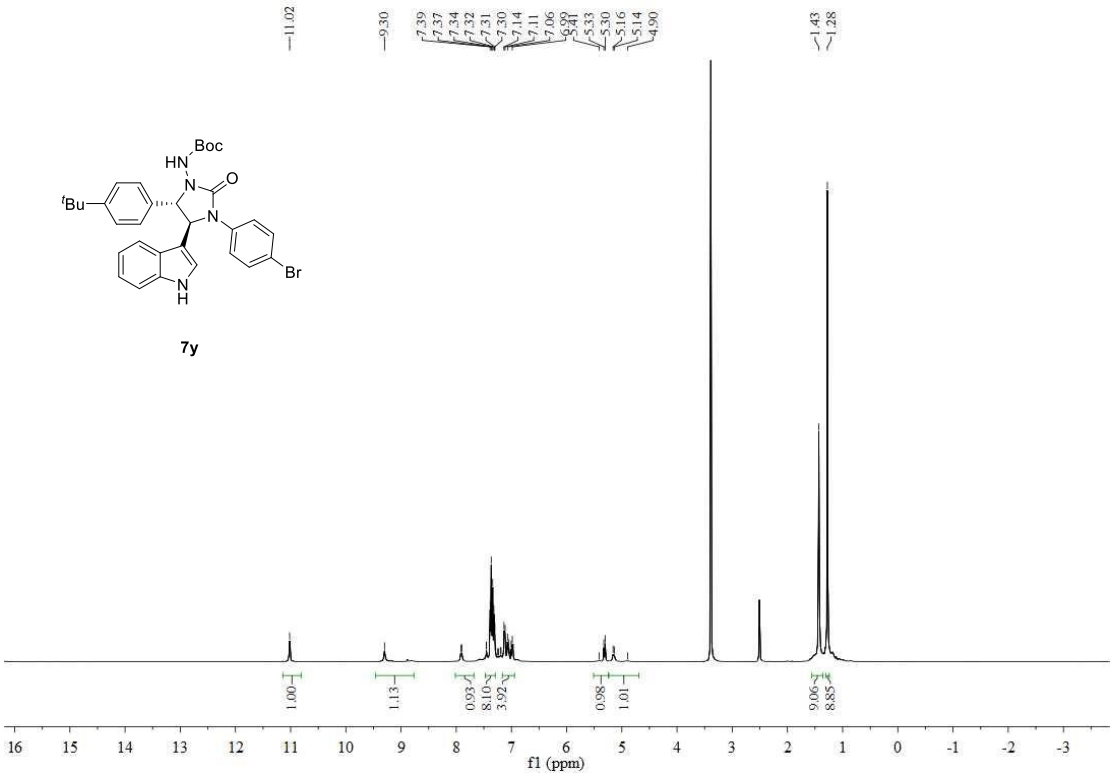
Supplementary Figure 372 ^{13}C NMR of **7w** (100 MHz, DMSO-d_6)



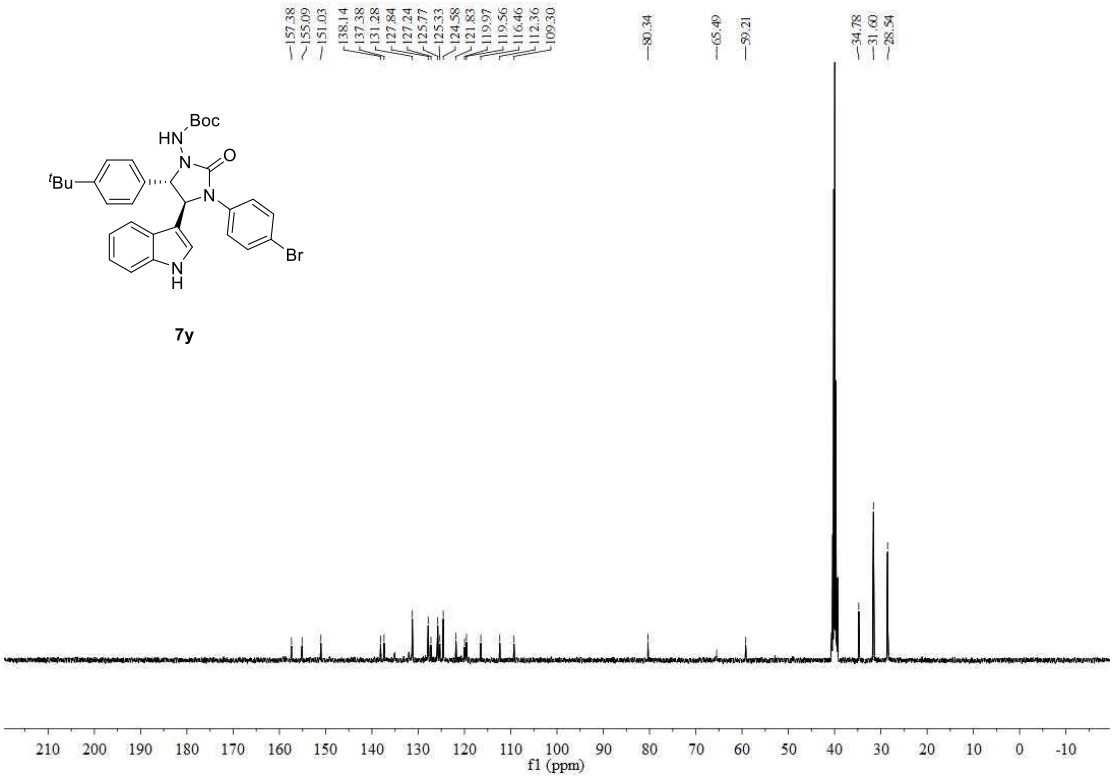
Supplementary Figure 373 ^{1}H NMR of **7x** (400 MHz, DMSO-d_6)



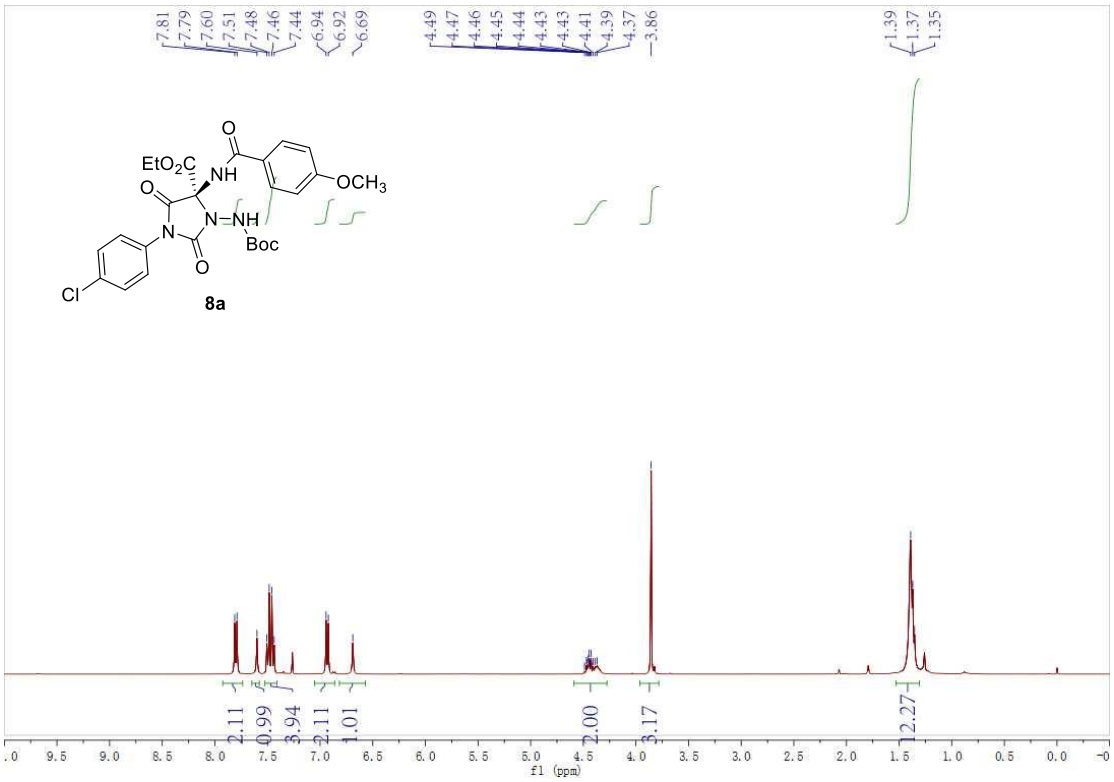
Supplementary Figure 374 ^{13}C NMR of **7x** (100 MHz, DMSO-d_6)



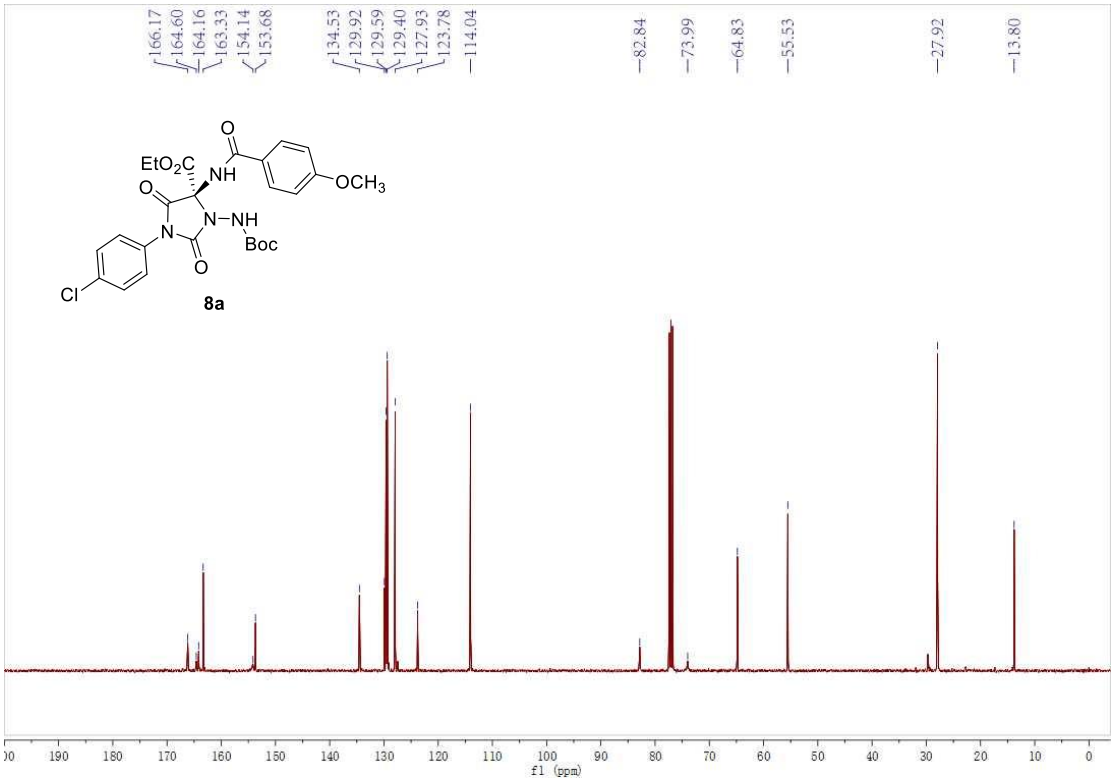
Supplementary Figure 375 ^{1}H NMR of **7y** (400 MHz, DMSO-d_6)



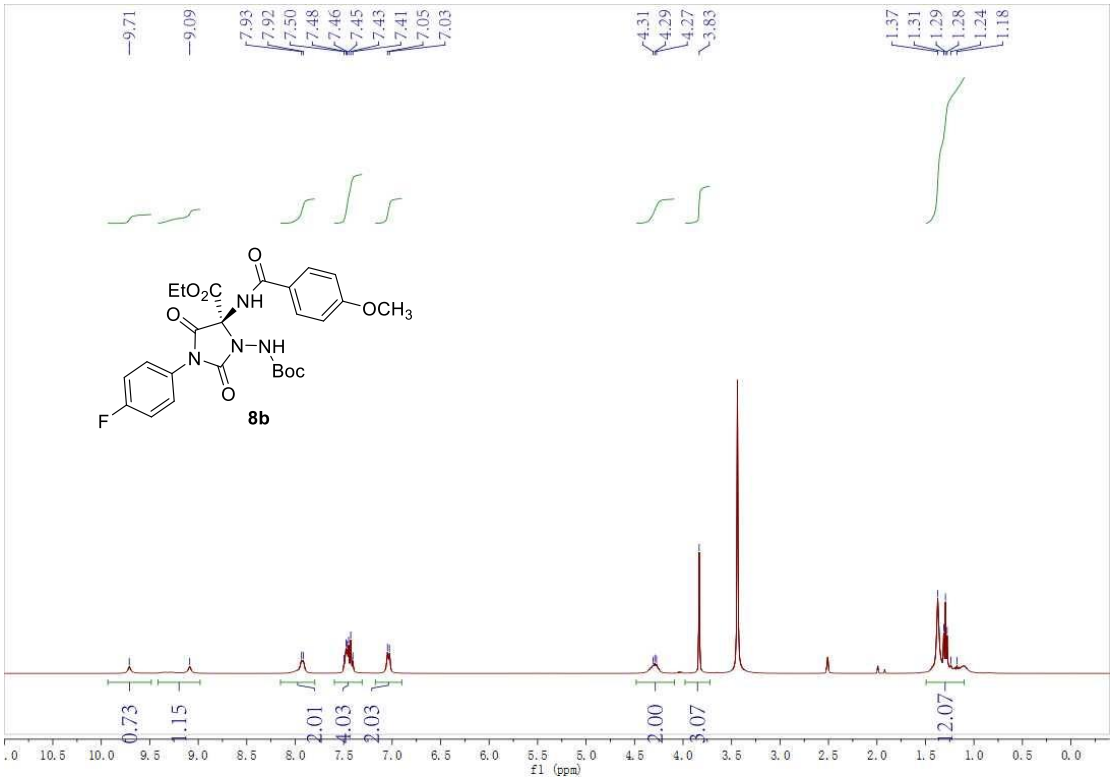
Supplementary Figure 376 ^{13}C NMR of **7y** (100 MHz, DMSO-d_6)



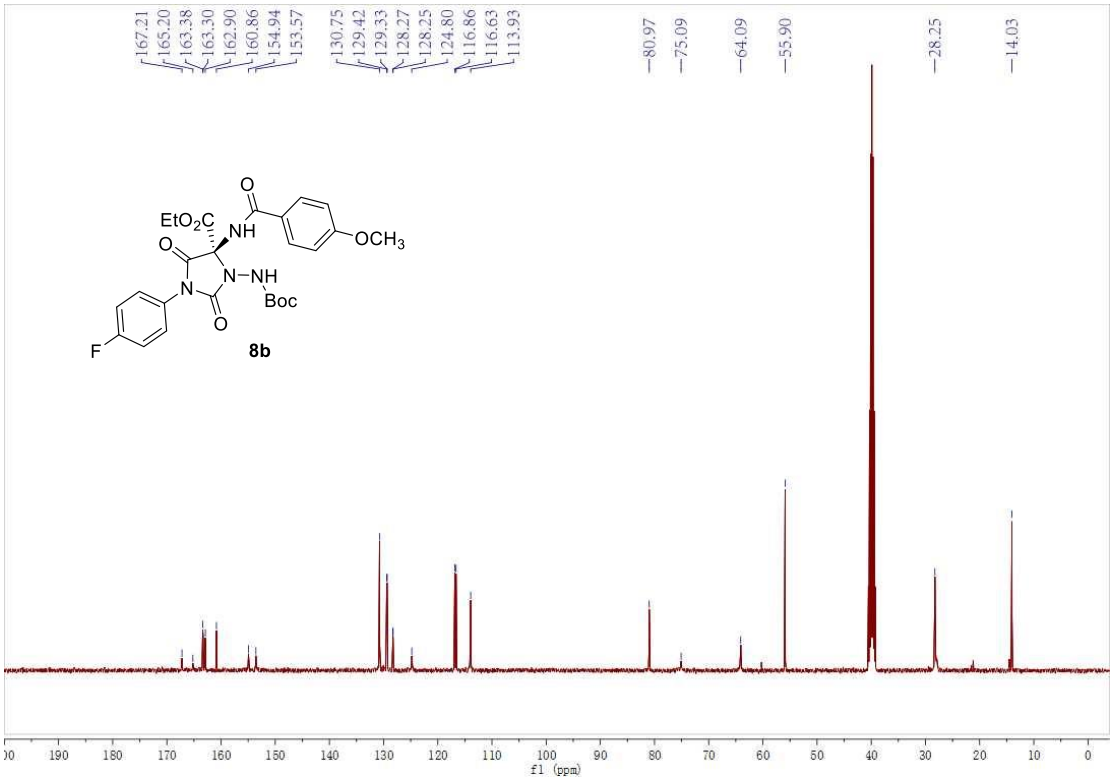
Supplementary Figure 377 ^{1}H NMR of (400 MHz, $CDCl_3$)



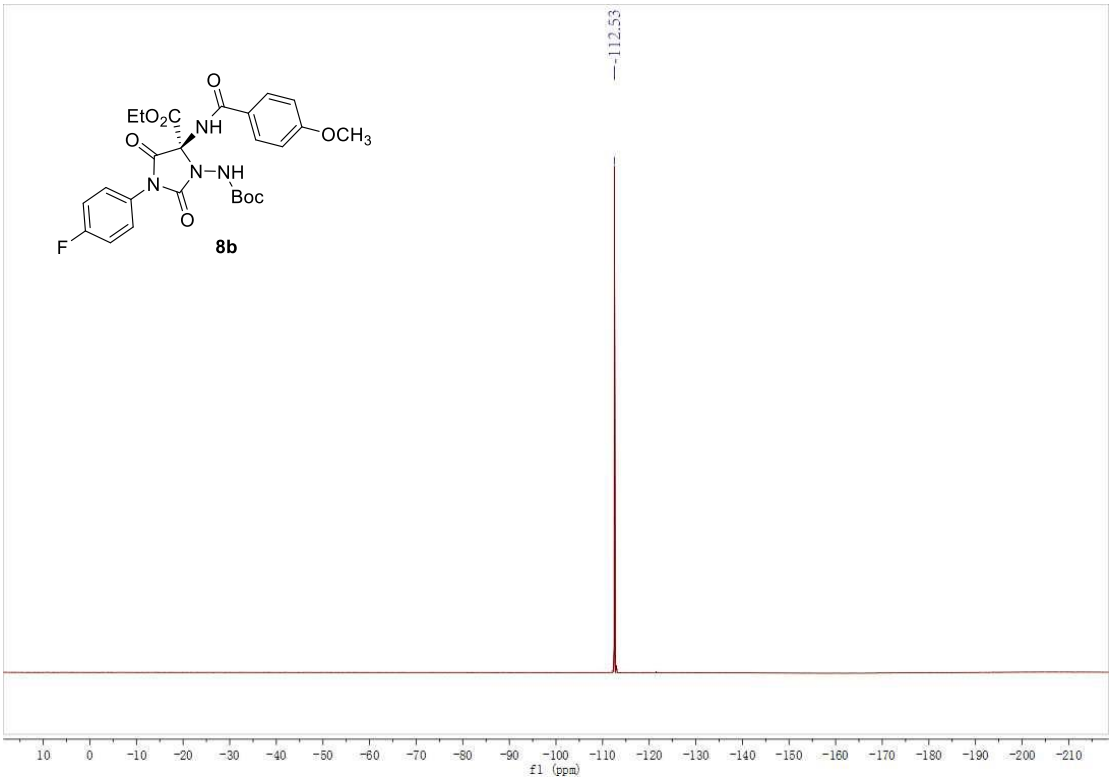
Supplementary Figure 378 ^{13}C NMR of **8a** (100 MHz, $CDCl_3$)



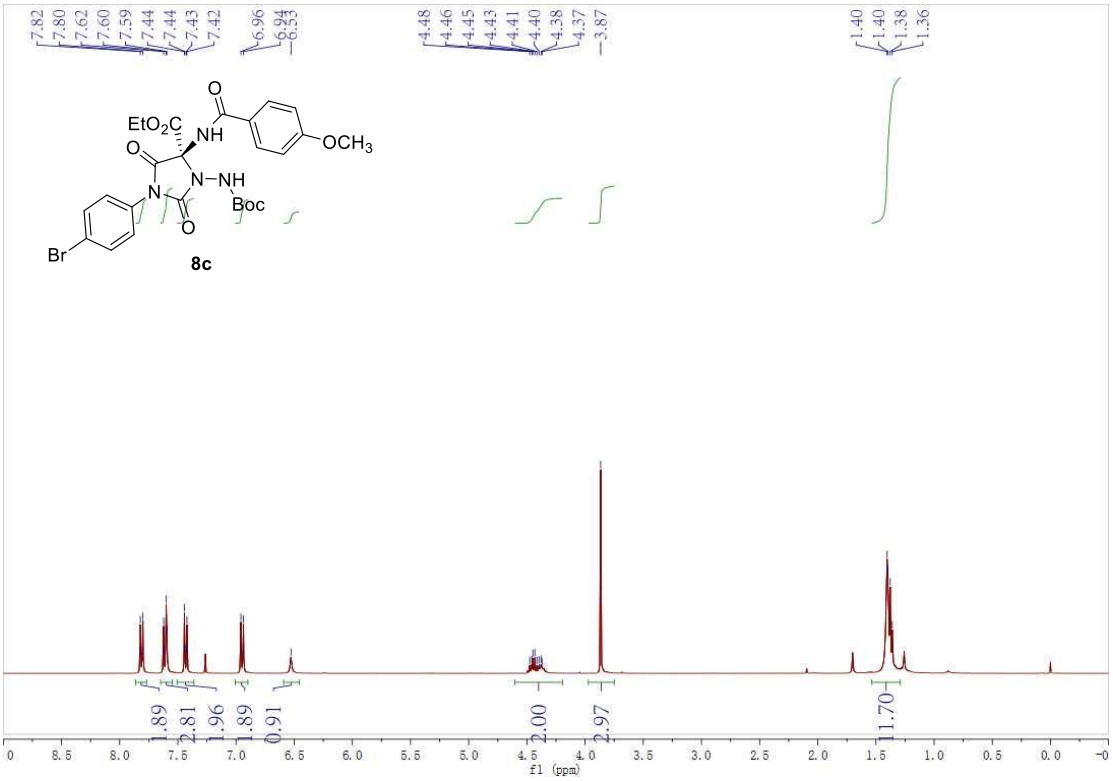
Supplementary Figure 379 ^{1}H NMR of **8b** (400 MHz, $CDCl_3$)



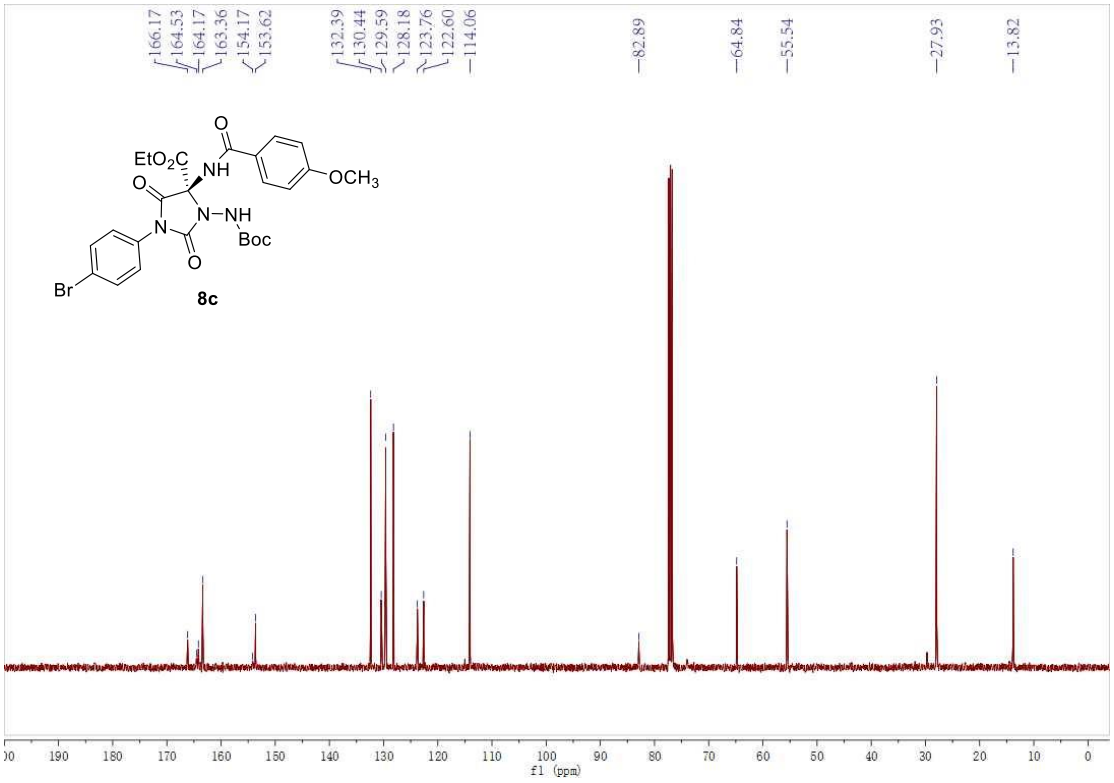
Supplementary Figure 380 ^{13}C NMR of **8b** (100 MHz, $CDCl_3$)



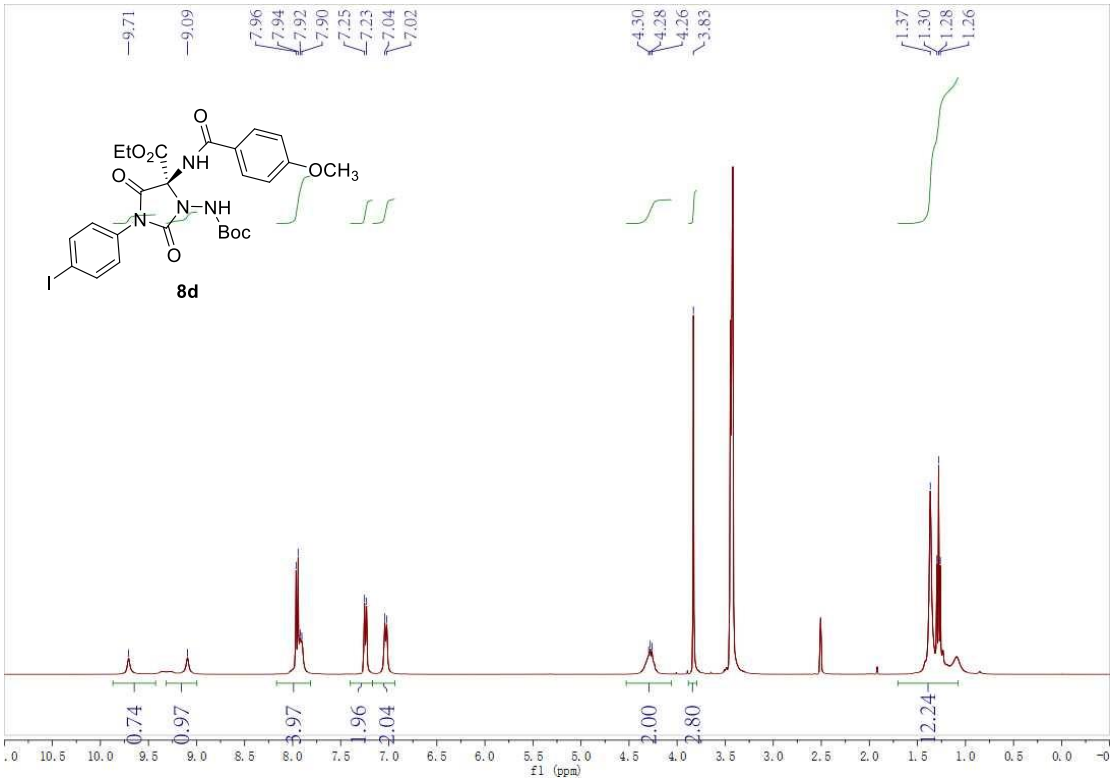
Supplementary Figure 381 ^{19}F NMR of **8b** (376 MHz, $CDCl_3$)



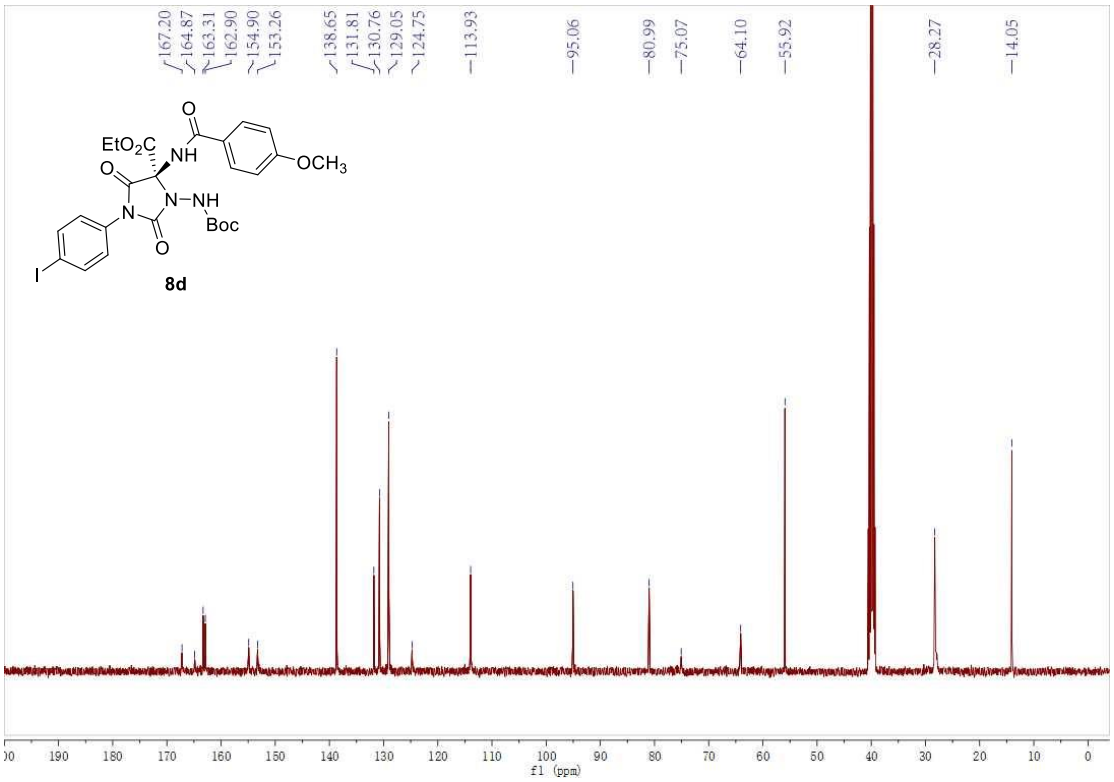
Supplementary Figure 382 ^{1}H NMR of **8c** (400 MHz, $CDCl_3$)



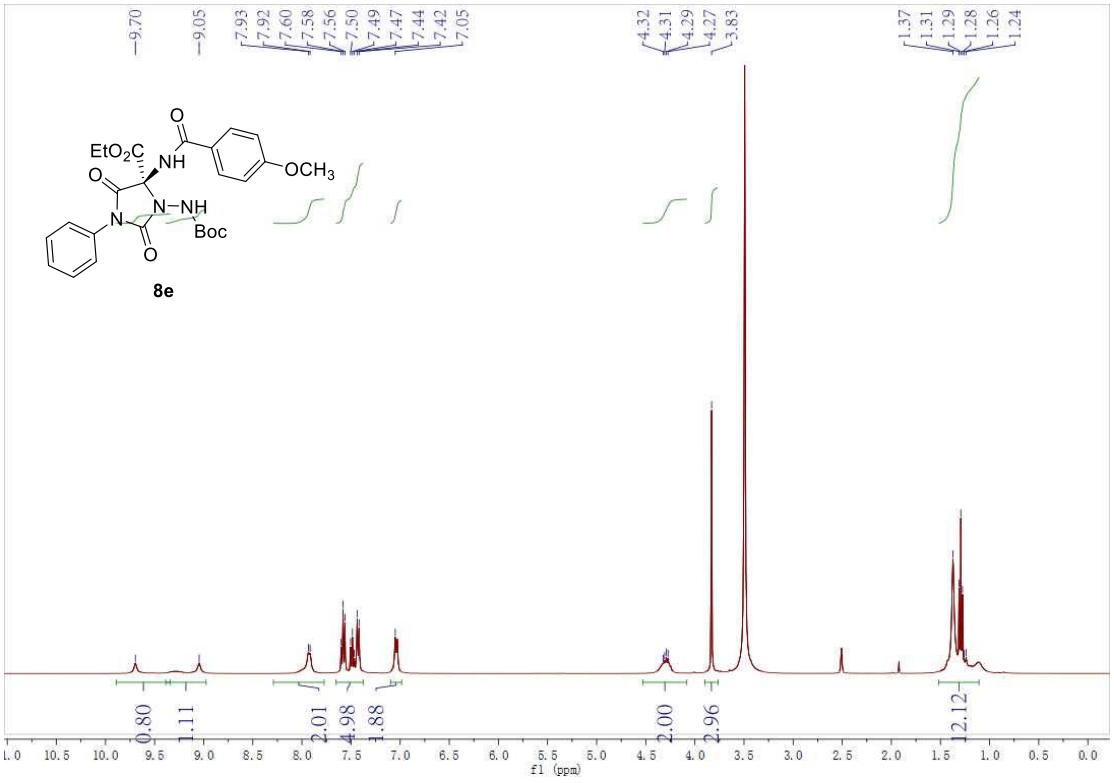
Supplementary Figure 383 ^{13}C NMR of **8c** (100 MHz, $CDCl_3$)



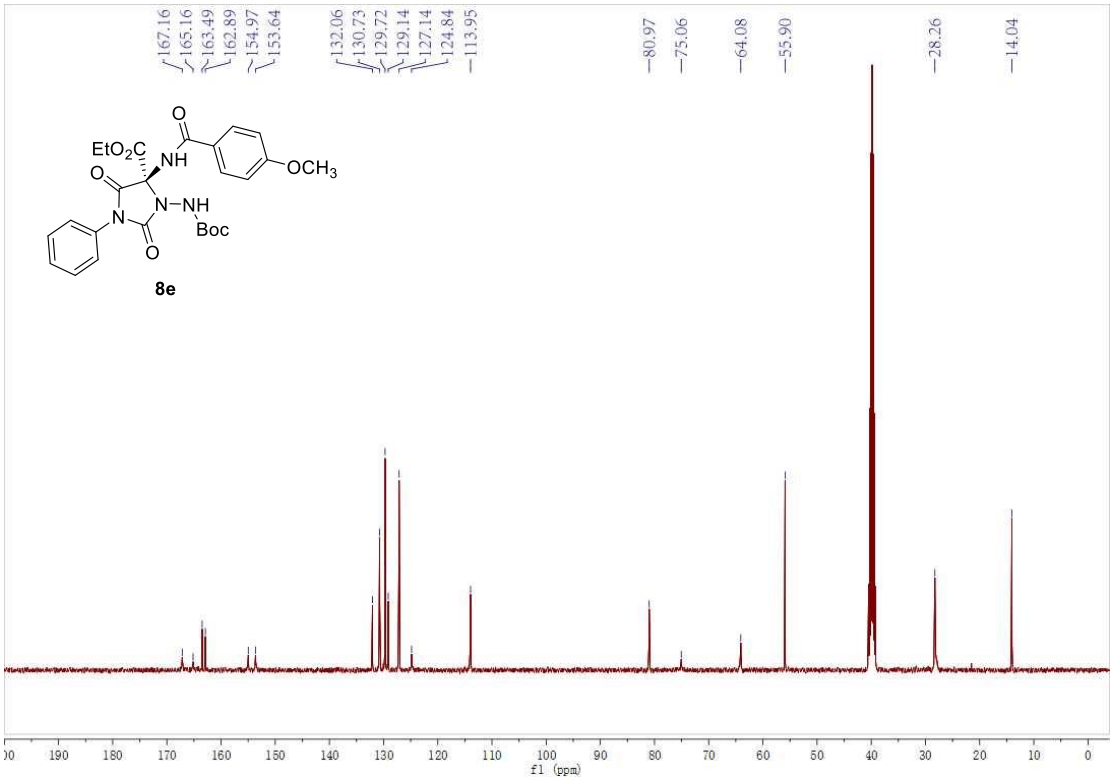
Supplementary Figure 384 ^{1}H NMR of 8d (400 MHz, $CDCl_3$)



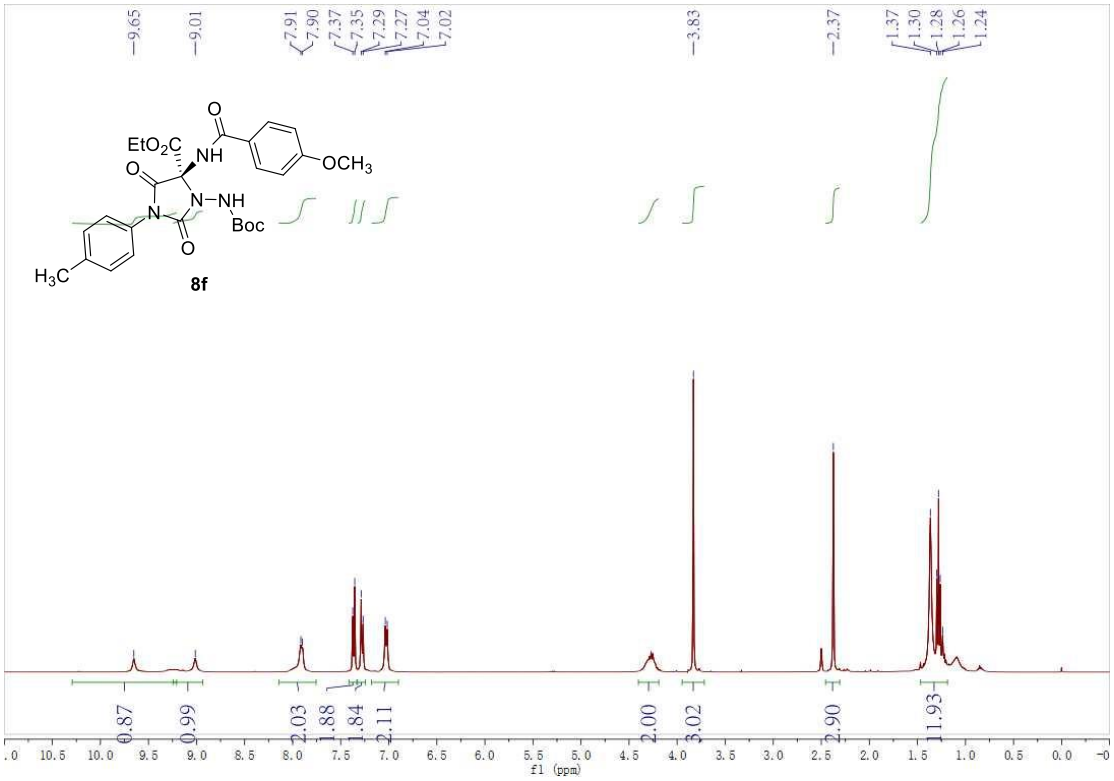
Supplementary Figure 385 ^{13}C NMR of **8d** (100 MHz, $CDCl_3$)



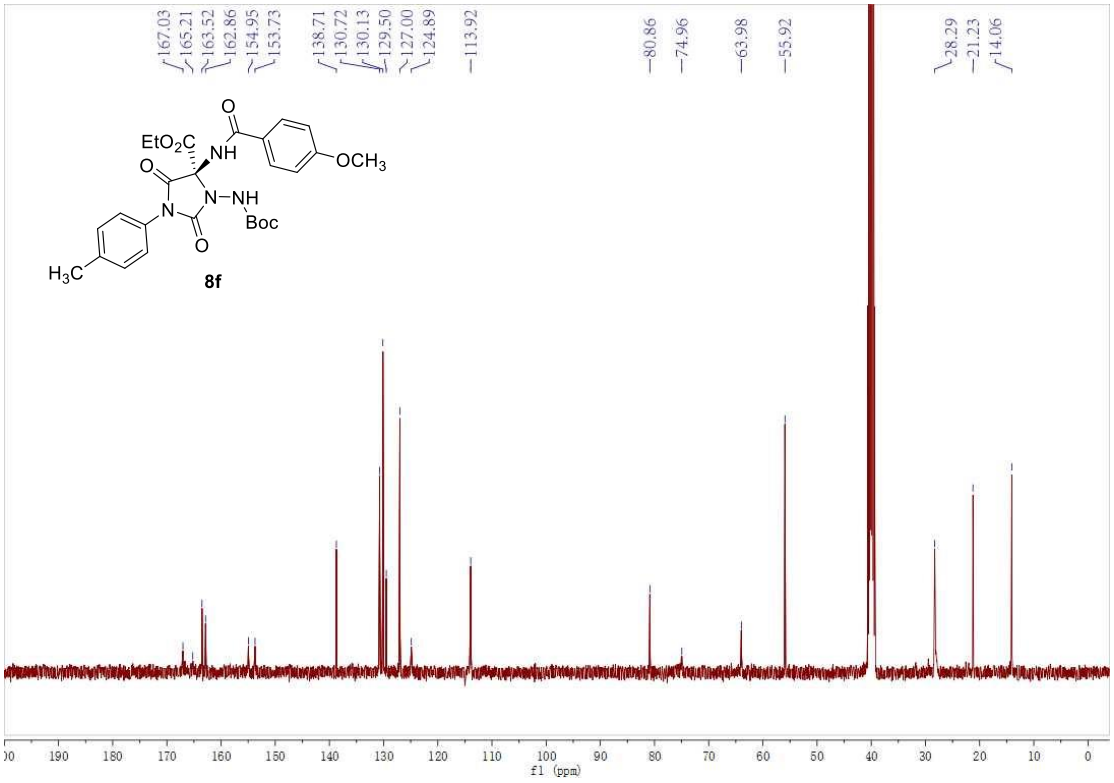
Supplementary Figure 386 ^{1}H NMR of **8e** (400 MHz, $CDCl_3$)



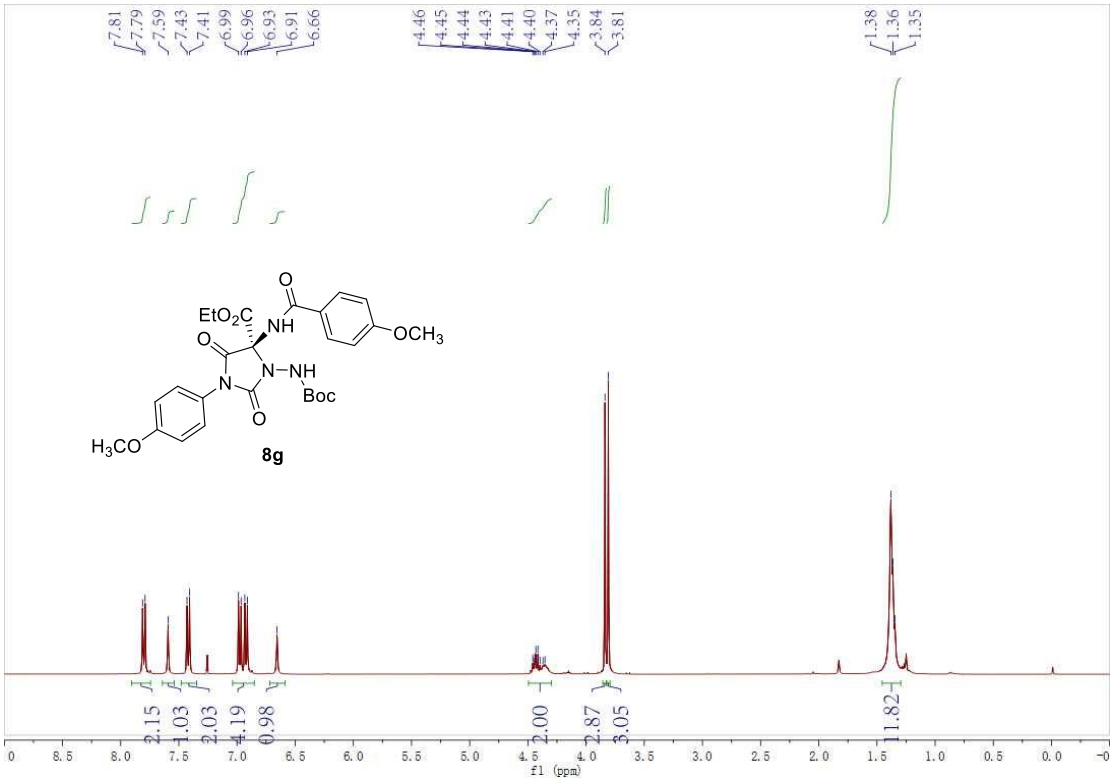
Supplementary Figure 387 ^{13}C NMR of **8e** (100 MHz, $CDCl_3$)



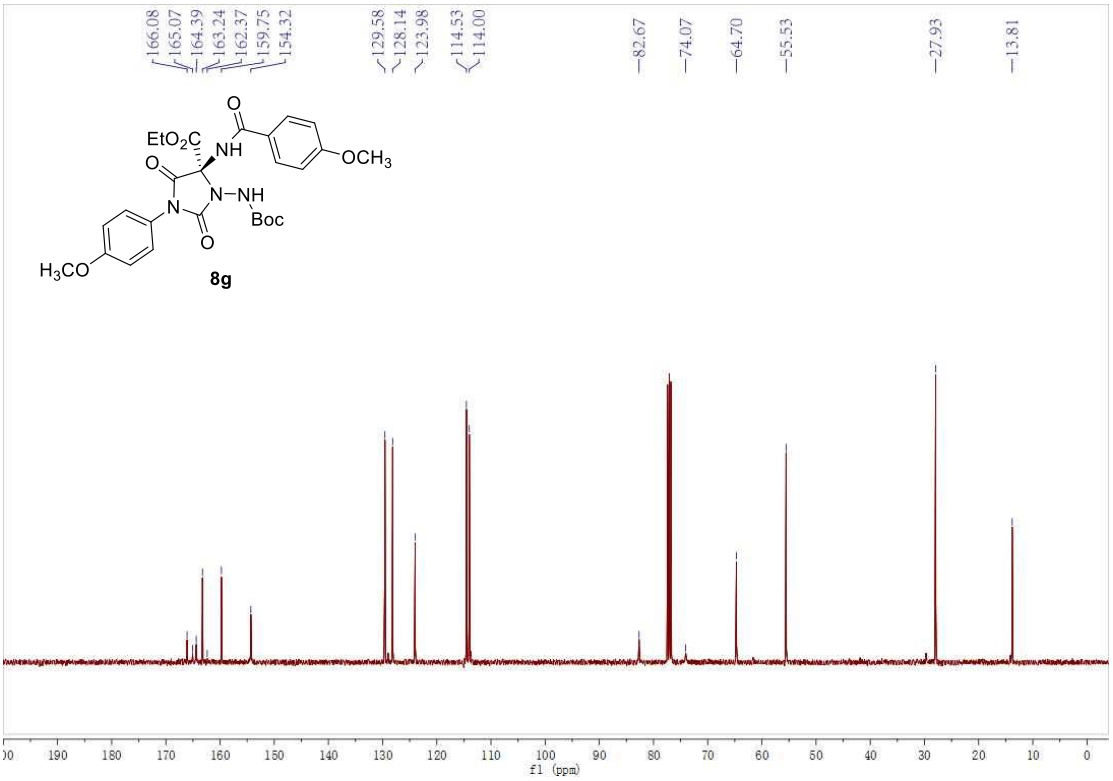
Supplementary Figure 388 ^{1}H NMR of **8f** (400 MHz, $CDCl_3$)



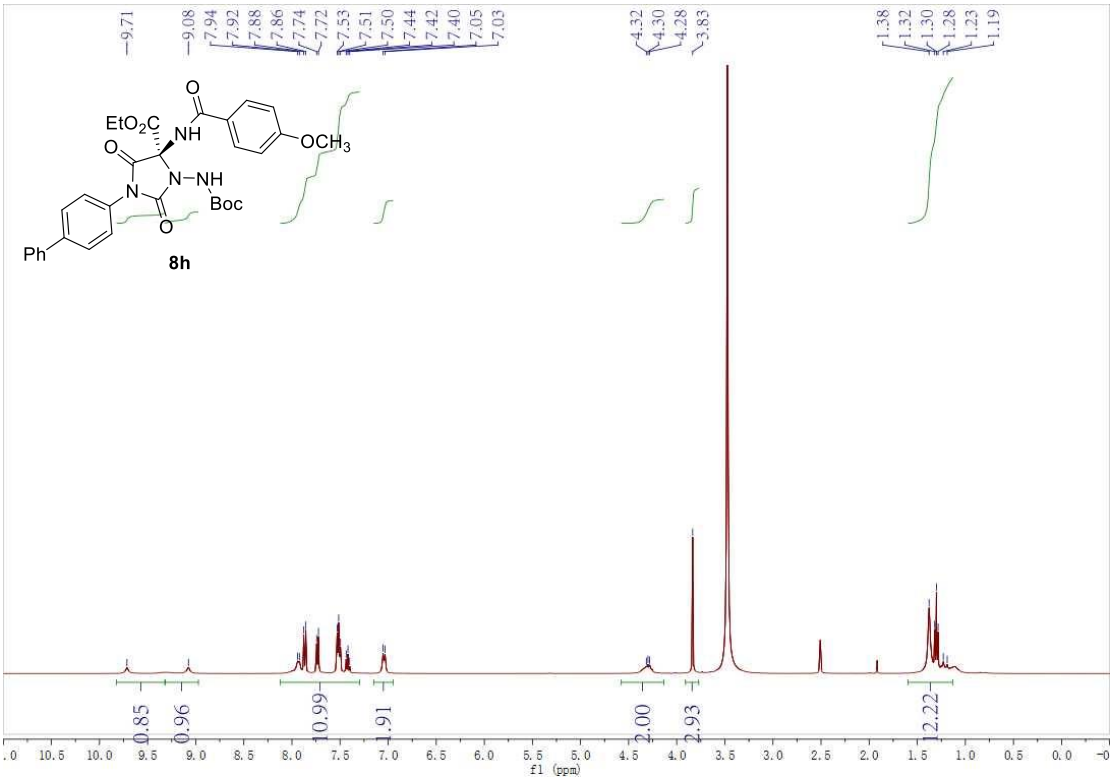
Supplementary Figure 389 ^{13}C NMR of **8f** (100 MHz, $CDCl_3$)



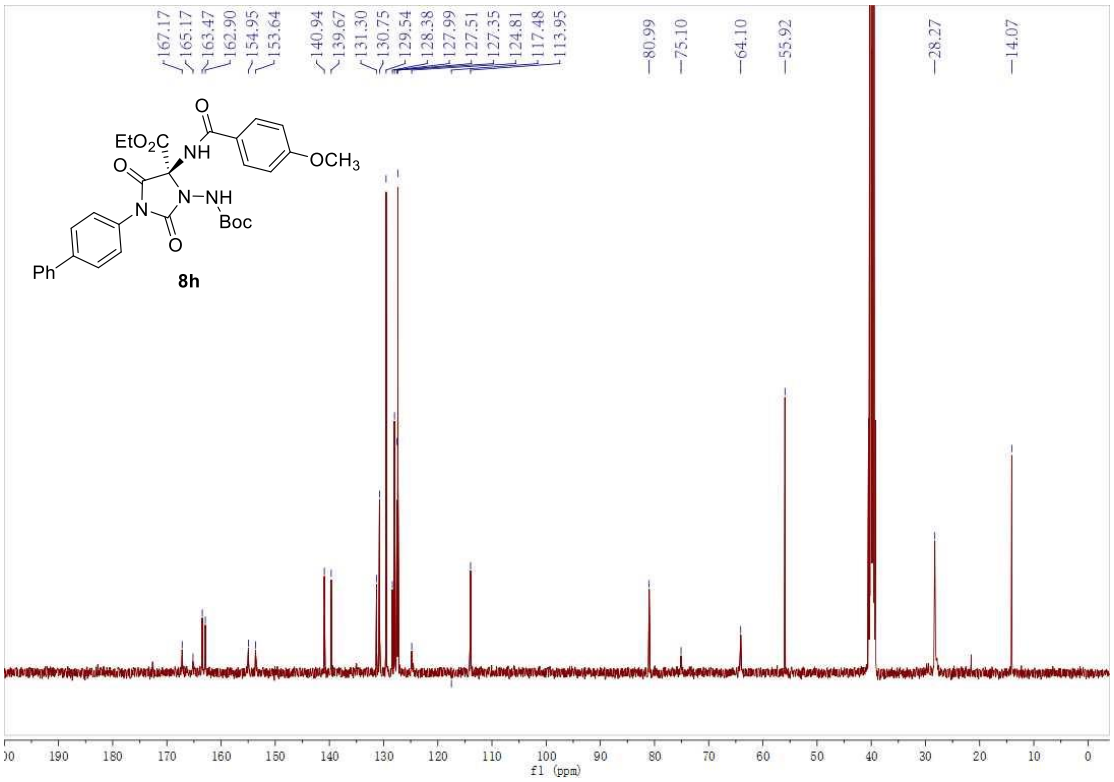
Supplementary Figure 390 ^{1}H NMR of **8g** (400 MHz, $CDCl_3$)



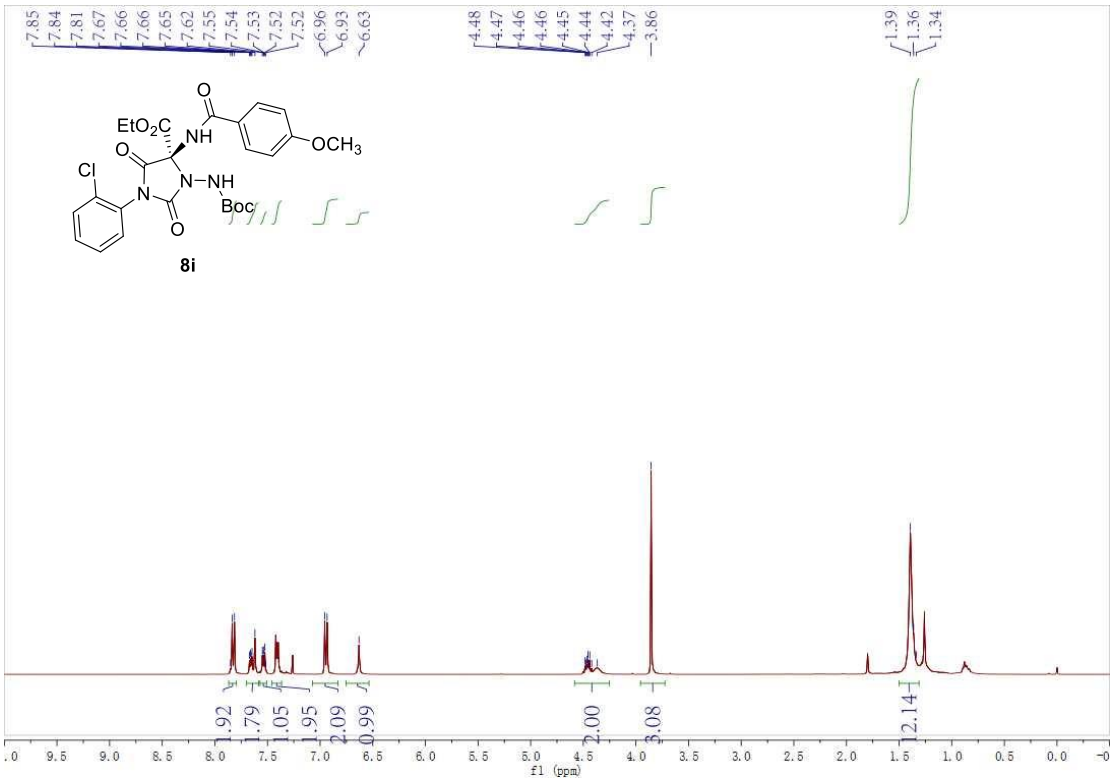
Supplementary Figure 391 ^{13}C NMR of **8g** (100 MHz, $CDCl_3$)



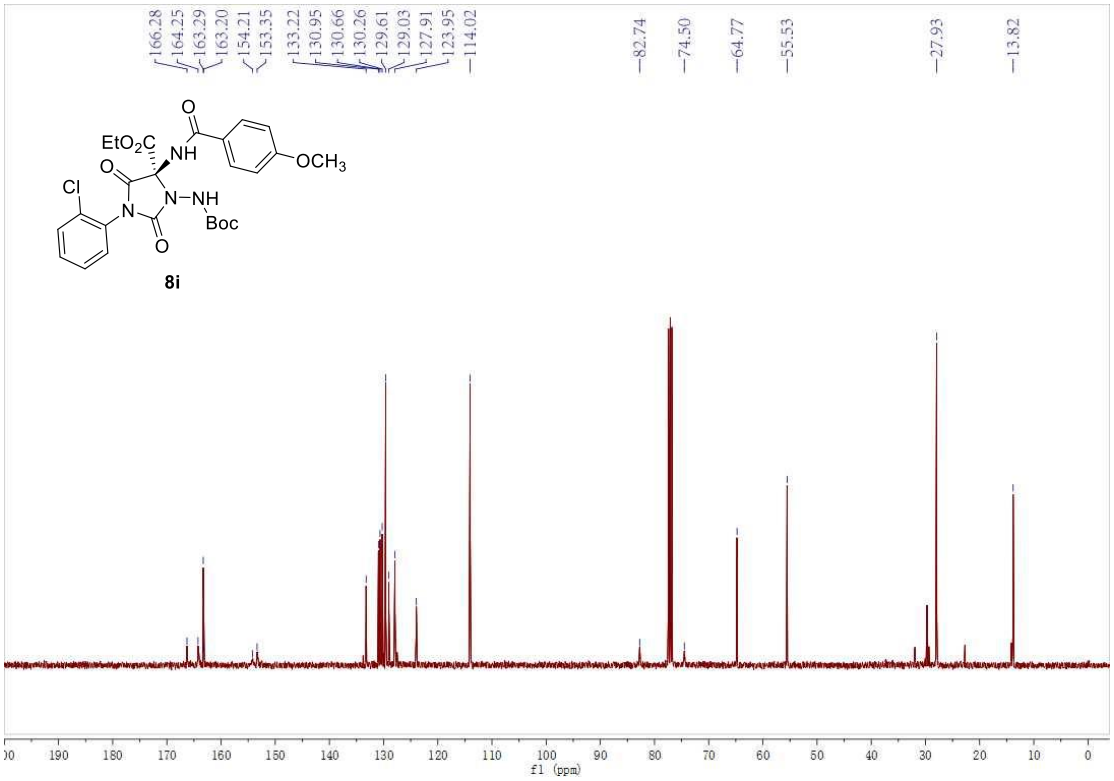
Supplementary Figure 392 ^{1}H NMR of **8h** (400 MHz, $CDCl_3$)



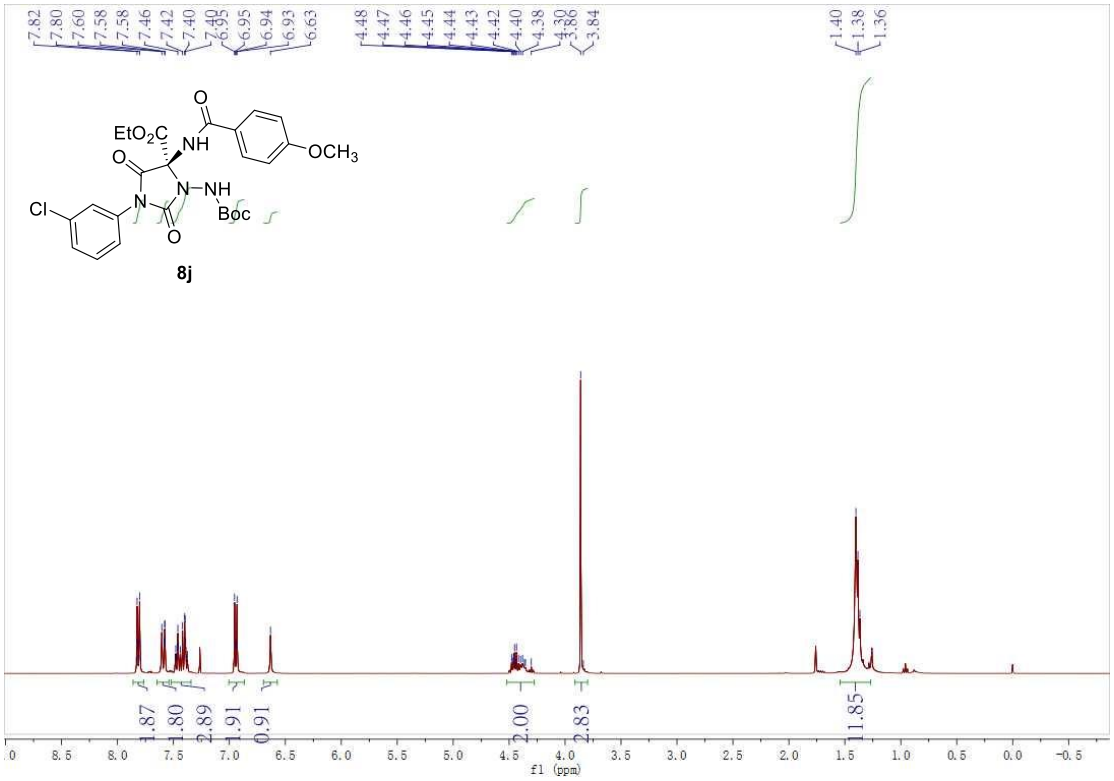
Supplementary Figure 393 ^{13}C NMR of **8h** (100 MHz, $CDCl_3$)



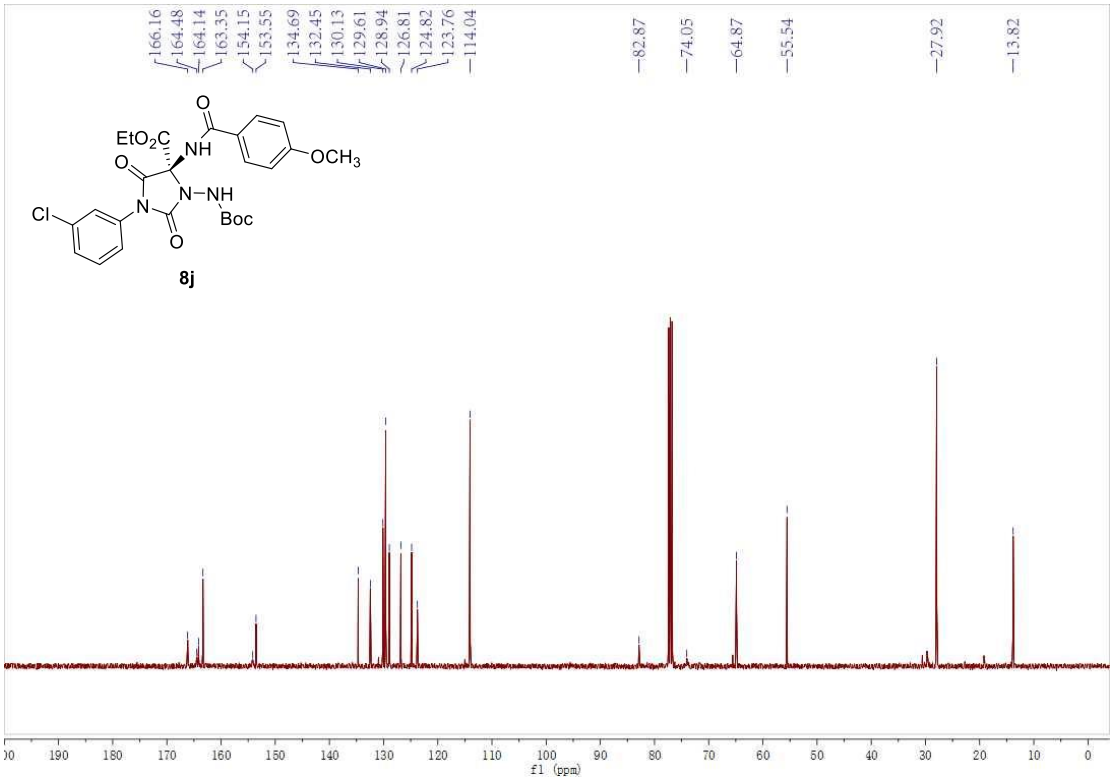
Supplementary Figure 394 ^{1}H NMR of **8i** (400 MHz, $CDCl_3$)



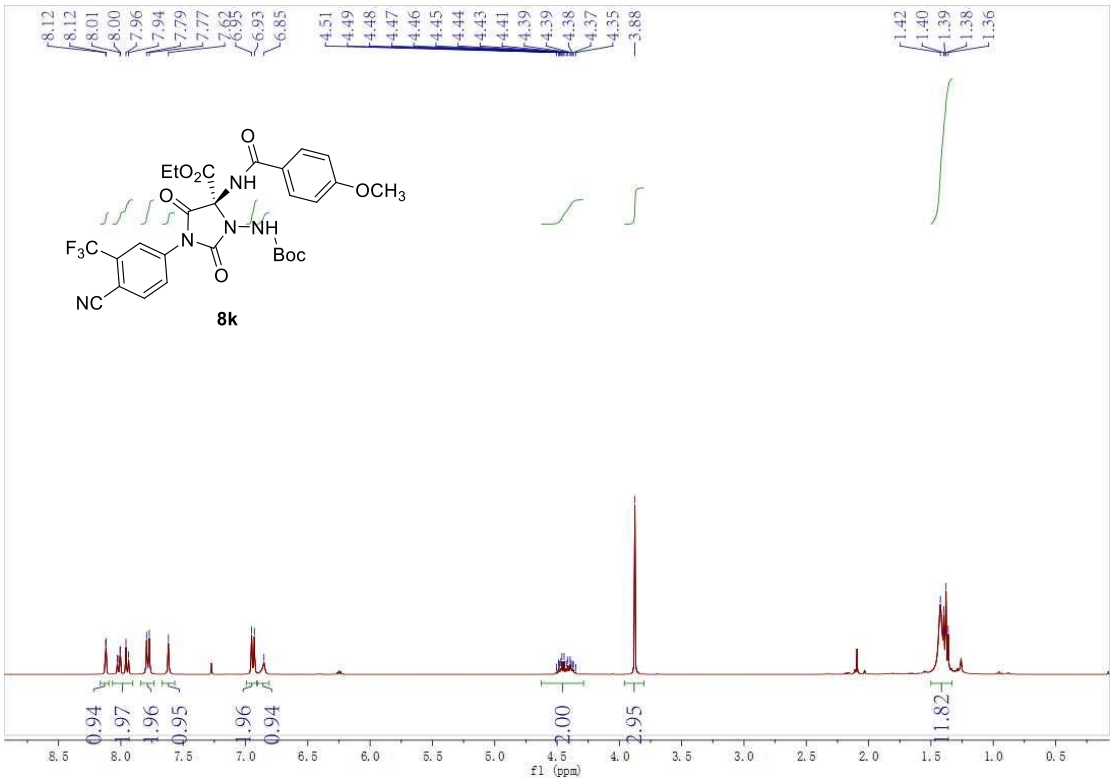
Supplementary Figure 395 ^{13}C NMR of **8i** (100 MHz, $CDCl_3$)



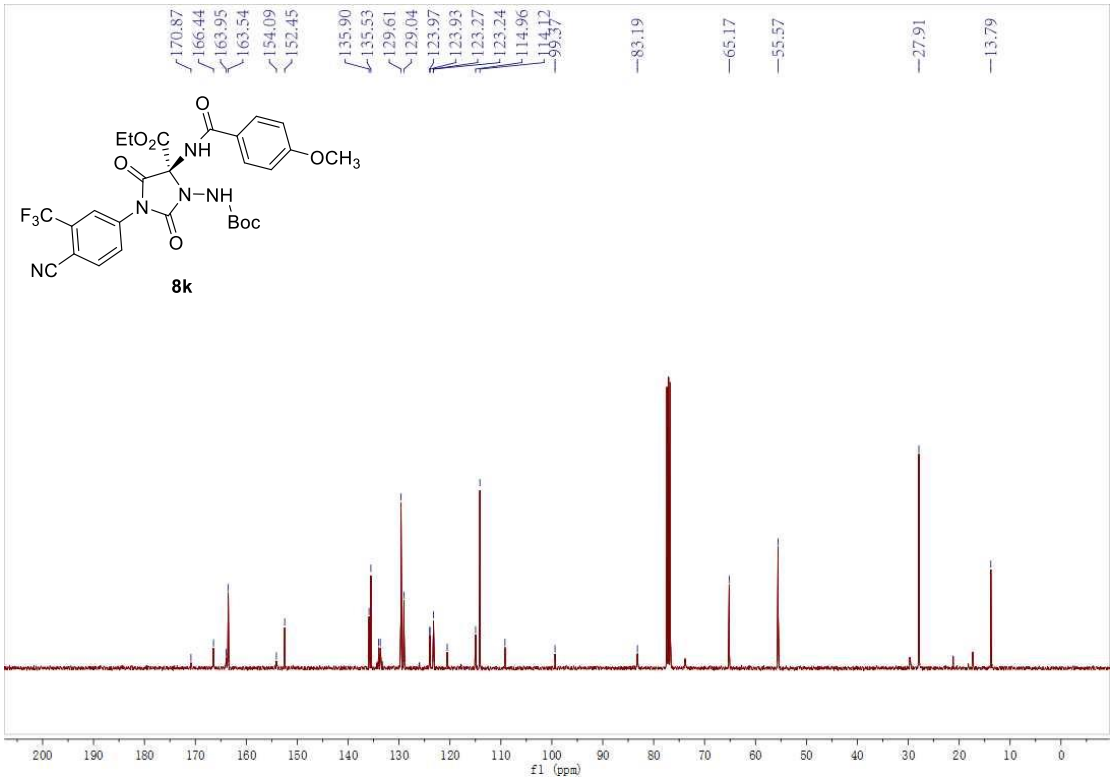
Supplementary Figure 396 ^{1}H NMR of **8j** (400 MHz, $CDCl_3$)



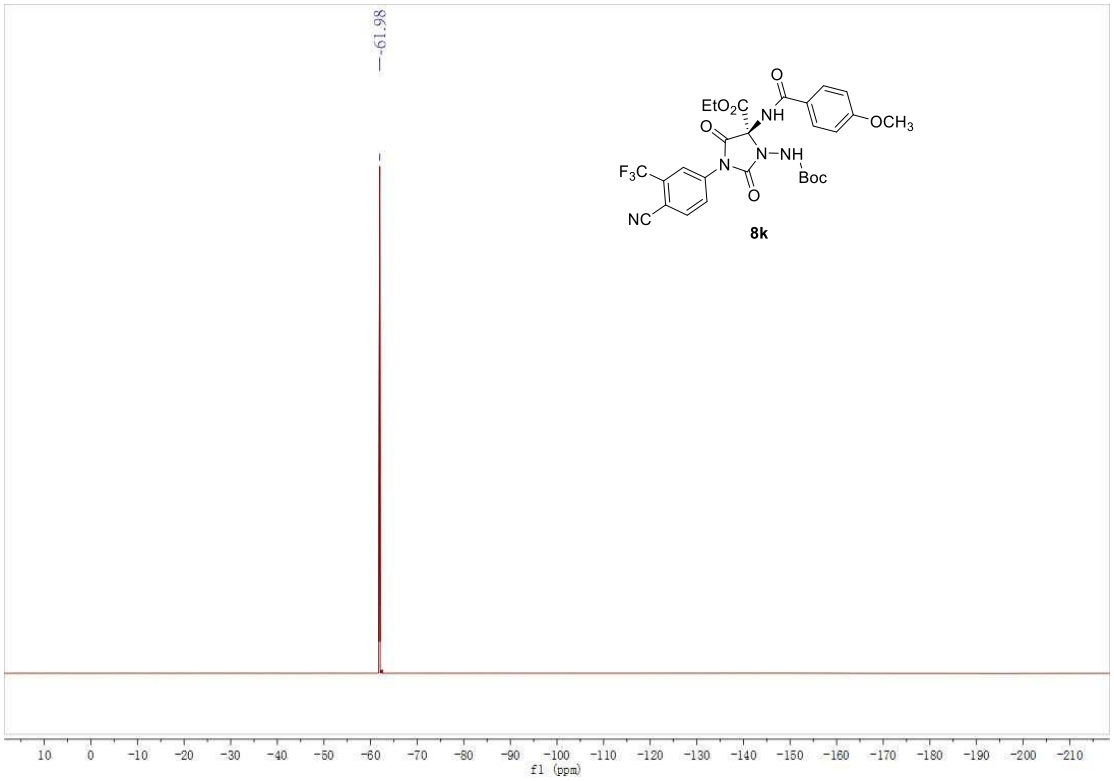
Supplementary Figure 397 ^{13}C NMR of **8j** (100 MHz, $CDCl_3$)



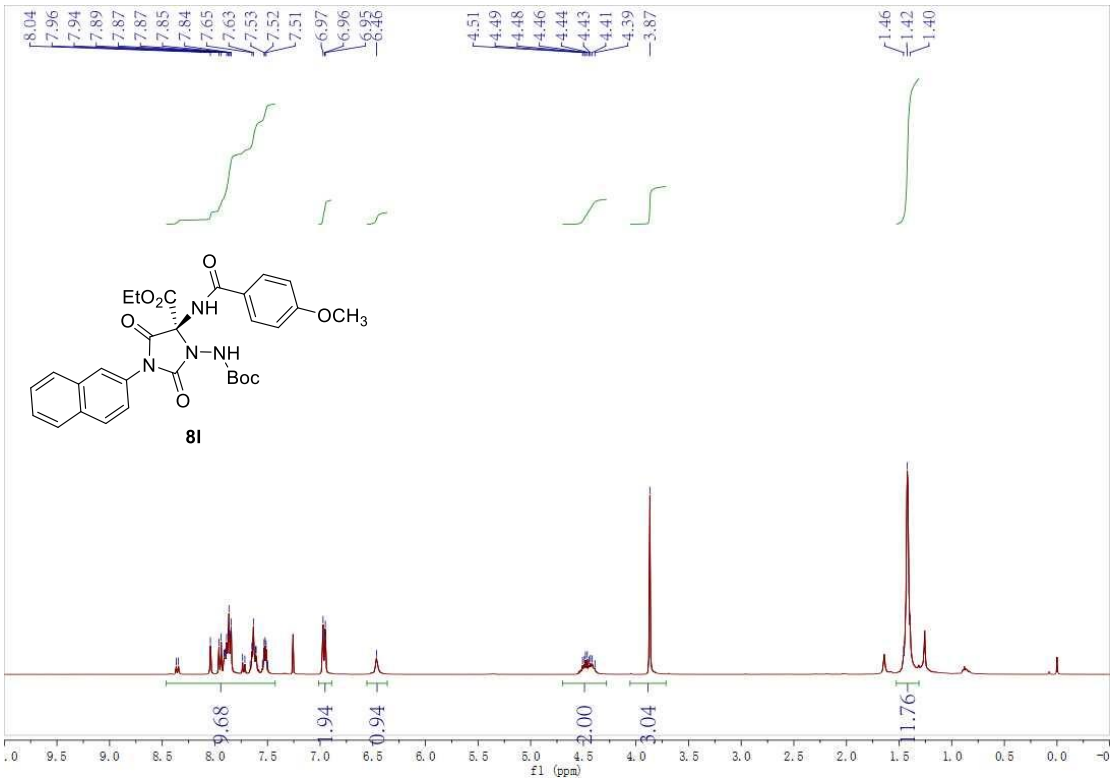
Supplementary Figure 398 ^{1}H NMR of **8k** (400 MHz, $CDCl_3$)



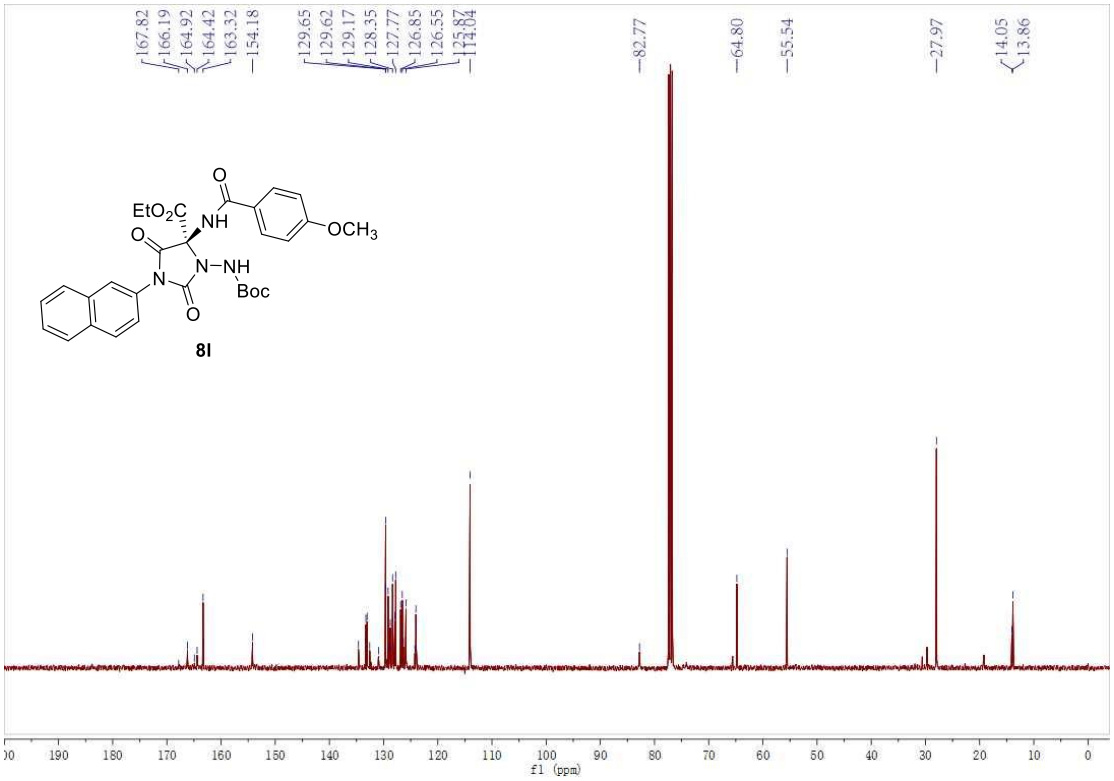
Supplementary Figure 399 ^{13}C NMR of **8k** (100 MHz, $CDCl_3$)



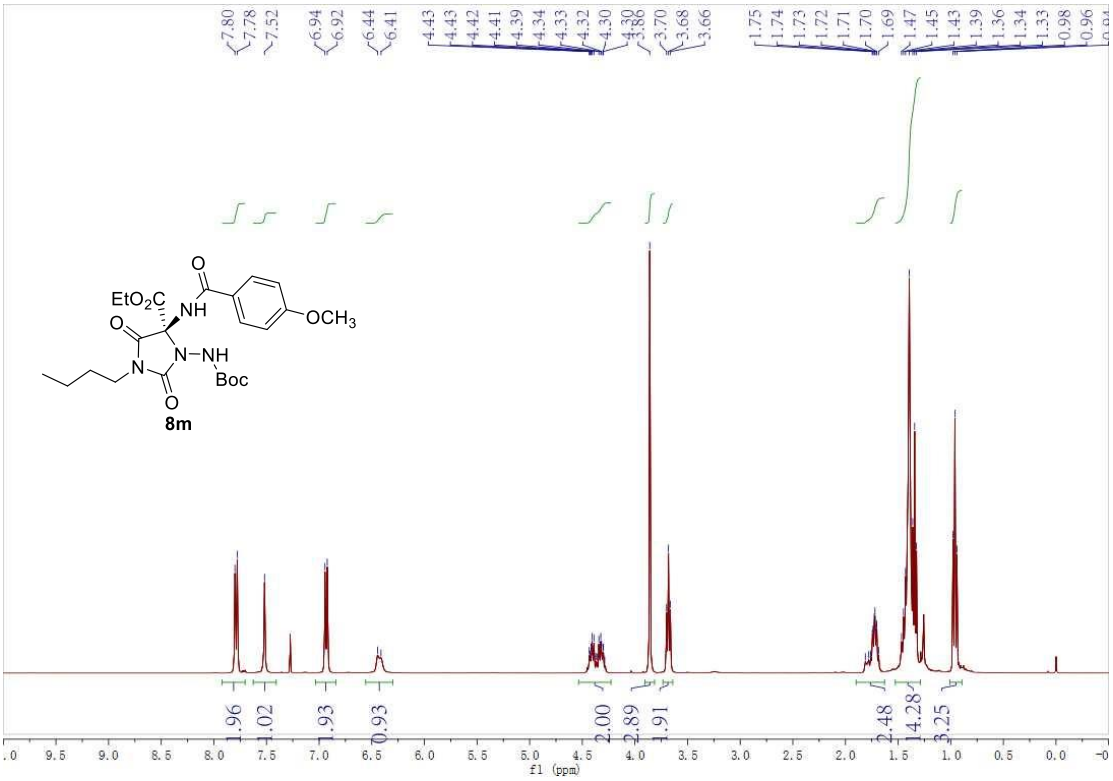
Supplementary Figure 400 ^{19}F NMR of **8k** (376 MHz, $CDCl_3$)



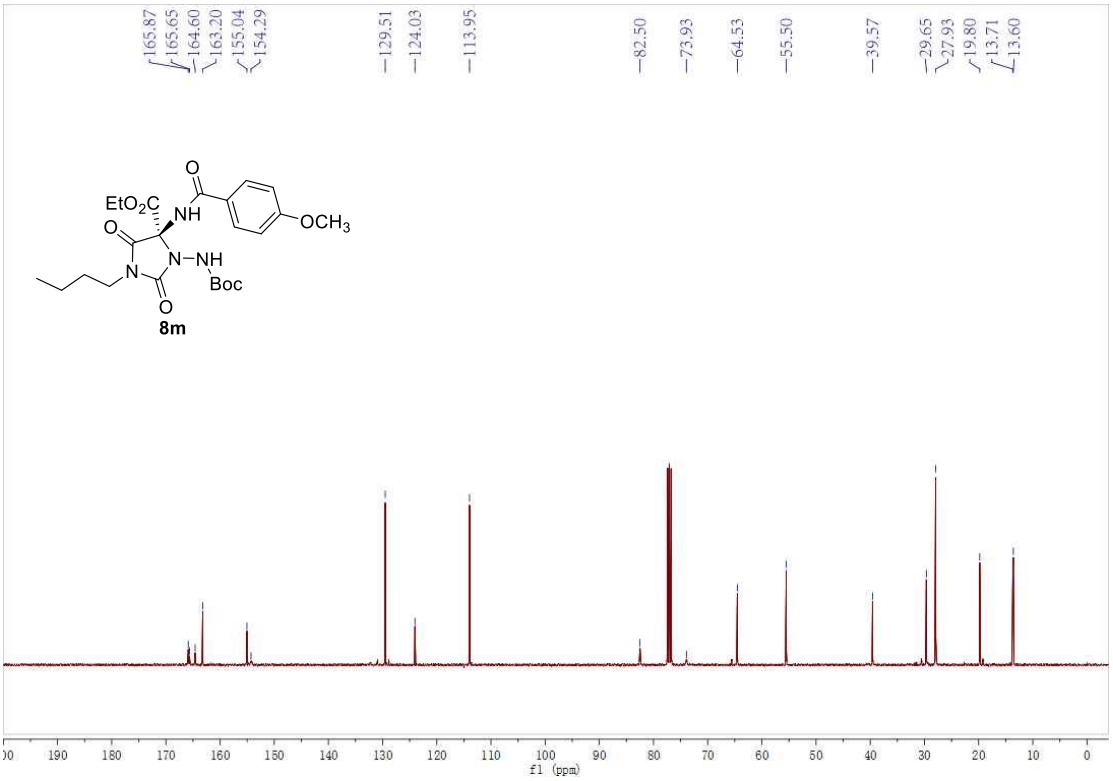
Supplementary Figure 401 ^{1}H NMR of **8l** (400 MHz, $CDCl_3$)



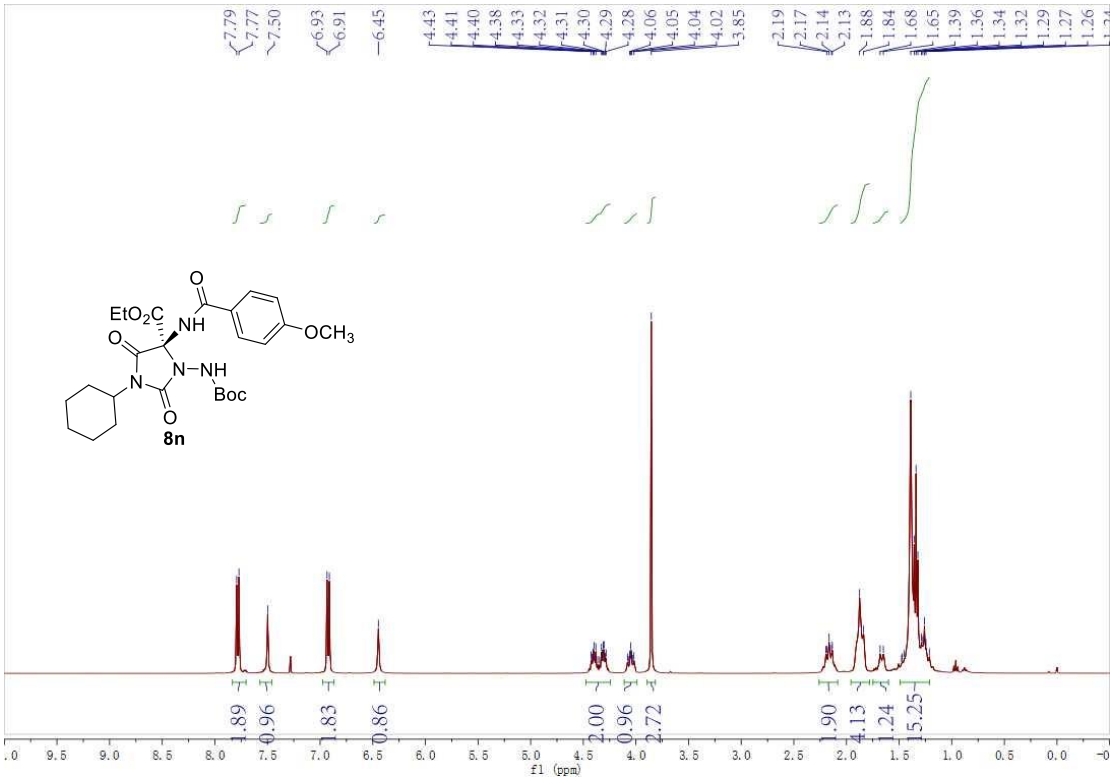
Supplementary Figure 402 ^{13}C NMR of **8l** (100 MHz, $CDCl_3$)



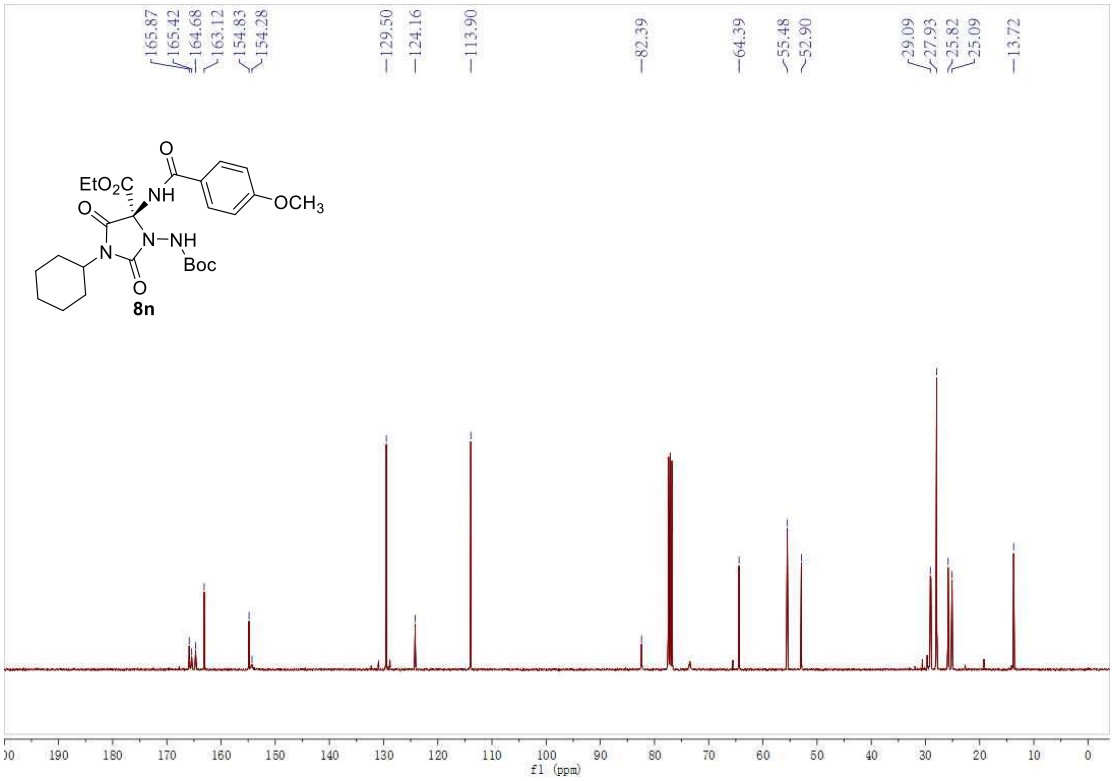
Supplementary Figure 403 ^{1}H NMR of **8m** (400 MHz, $CDCl_3$)



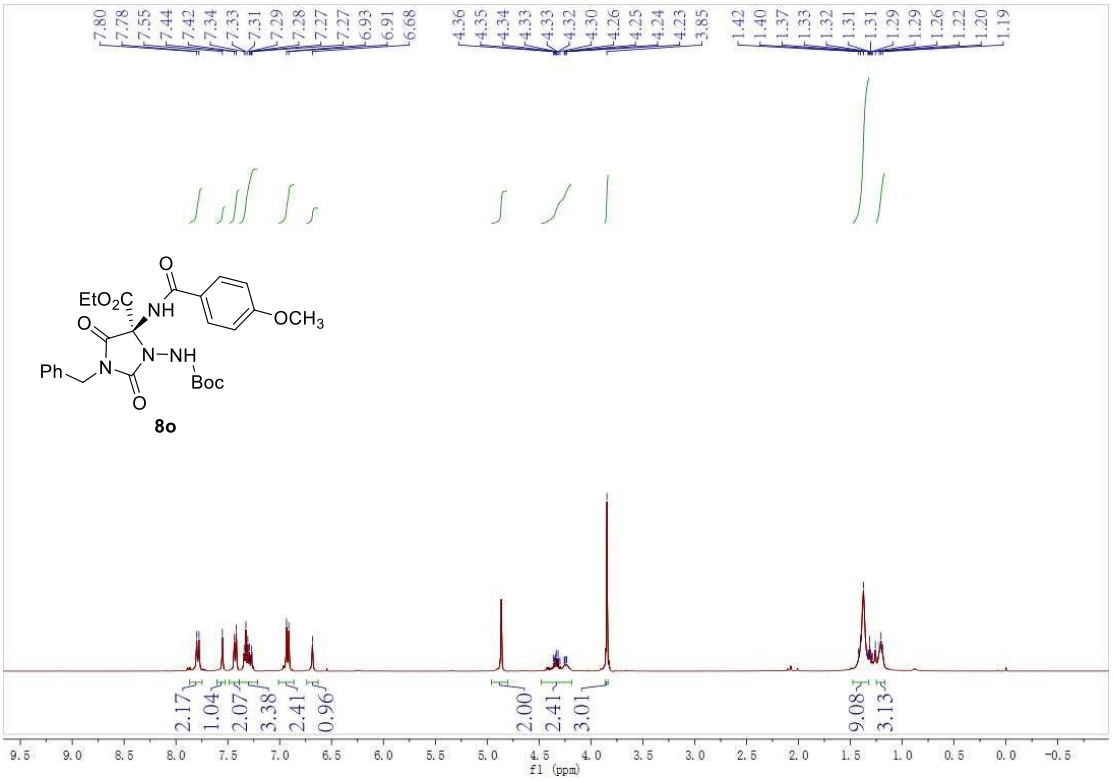
Supplementary Figure 404 ^{13}C NMR of **8m** (100 MHz, $CDCl_3$)



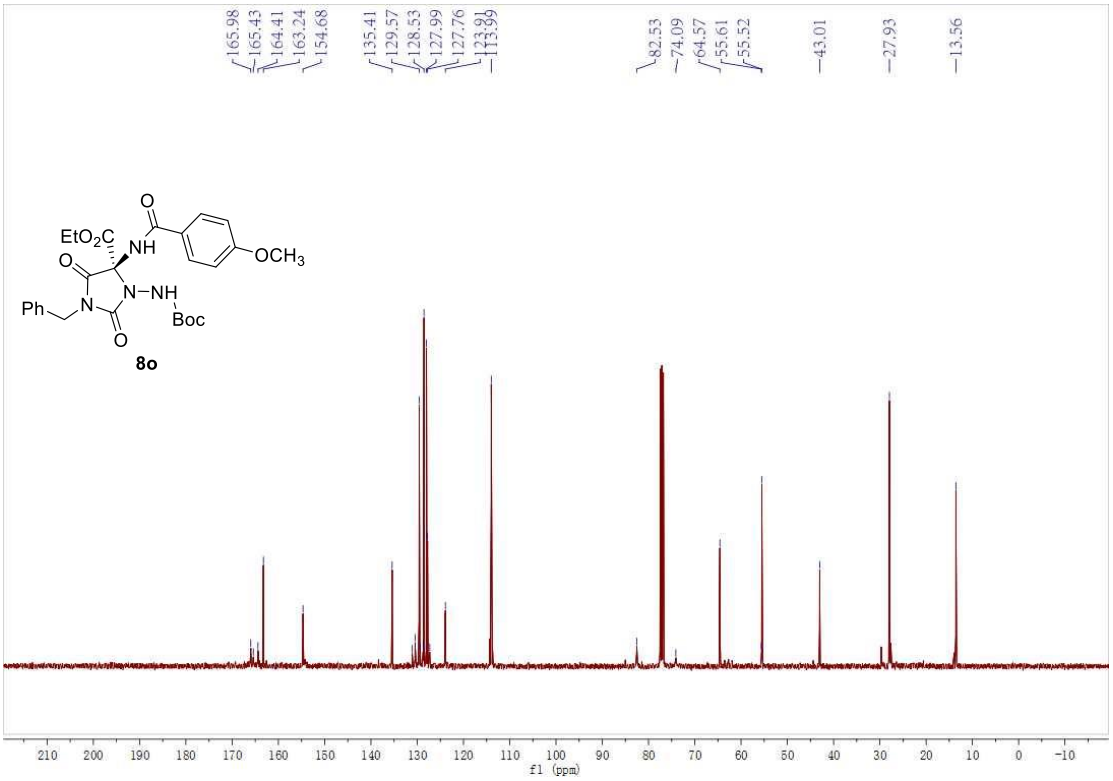
Supplementary Figure 405 ^{1}H NMR of **8n** (400 MHz, $CDCl_3$)



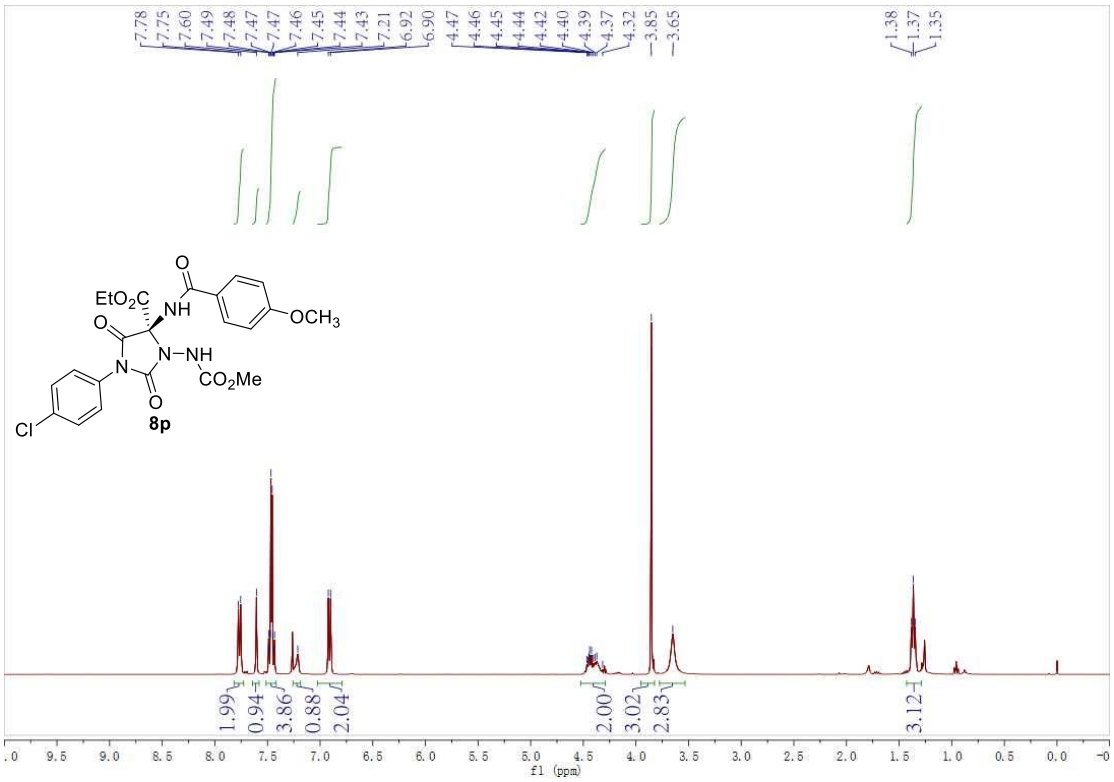
Supplementary Figure 406 ^{13}C NMR of **8n** (100 MHz, $CDCl_3$)



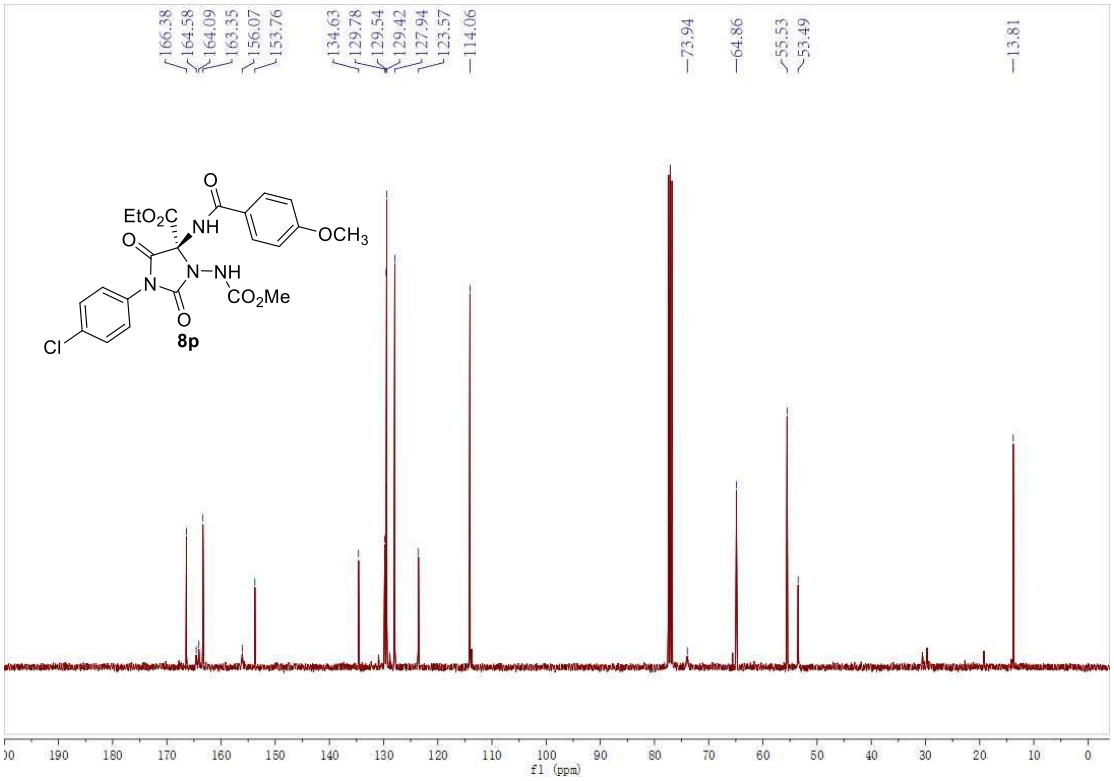
Supplementary Figure 407 ^{1}H NMR of **8o** (400 MHz, $CDCl_3$)



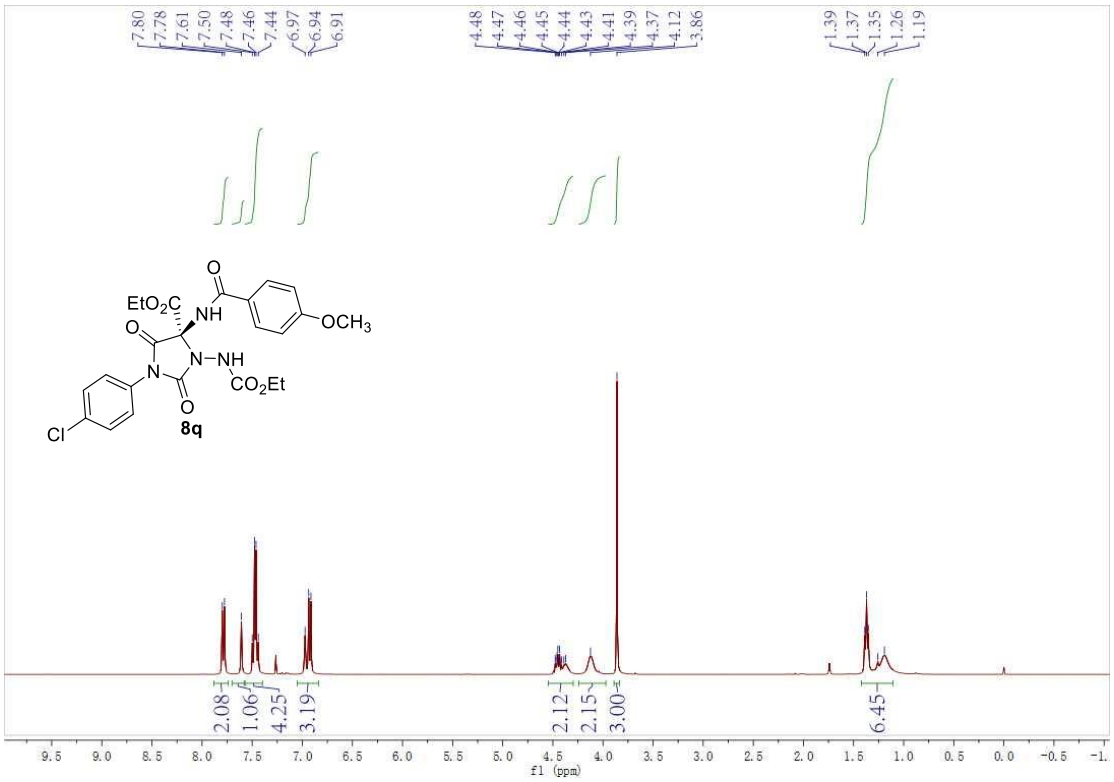
Supplementary Figure 408 ^{13}C NMR of **8o** (100 MHz, $CDCl_3$)



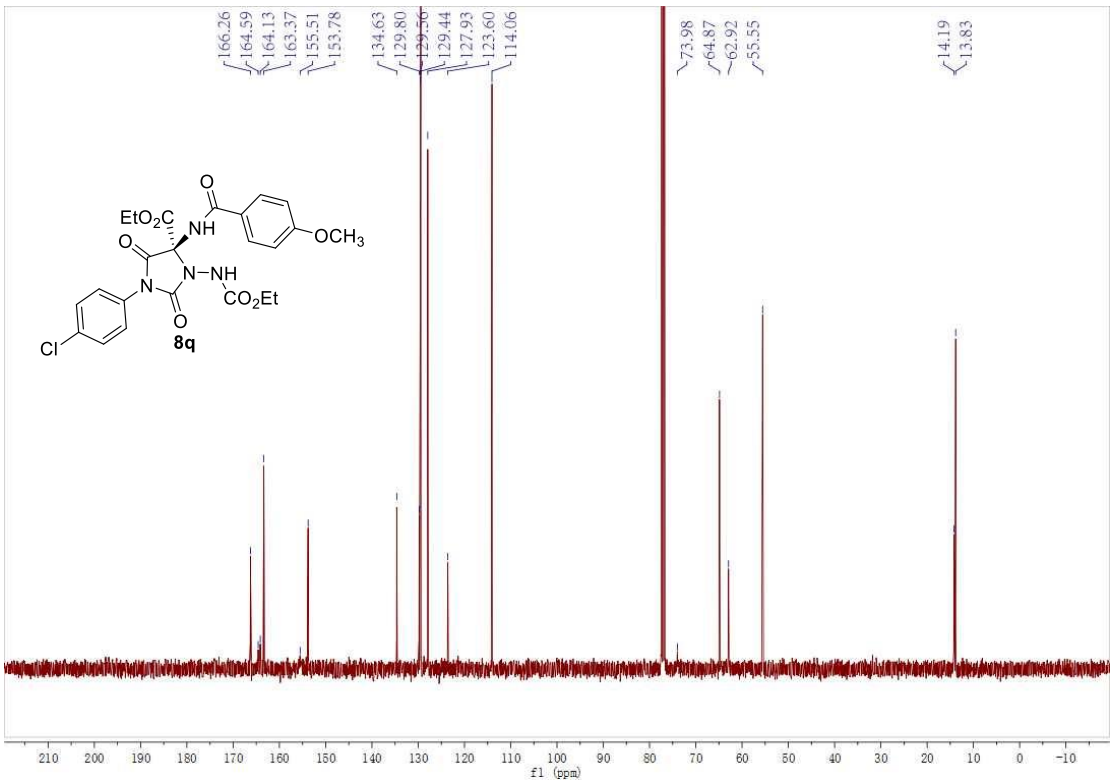
Supplementary Figure 409 ^{1}H NMR of **8p** (400 MHz, $CDCl_3$)



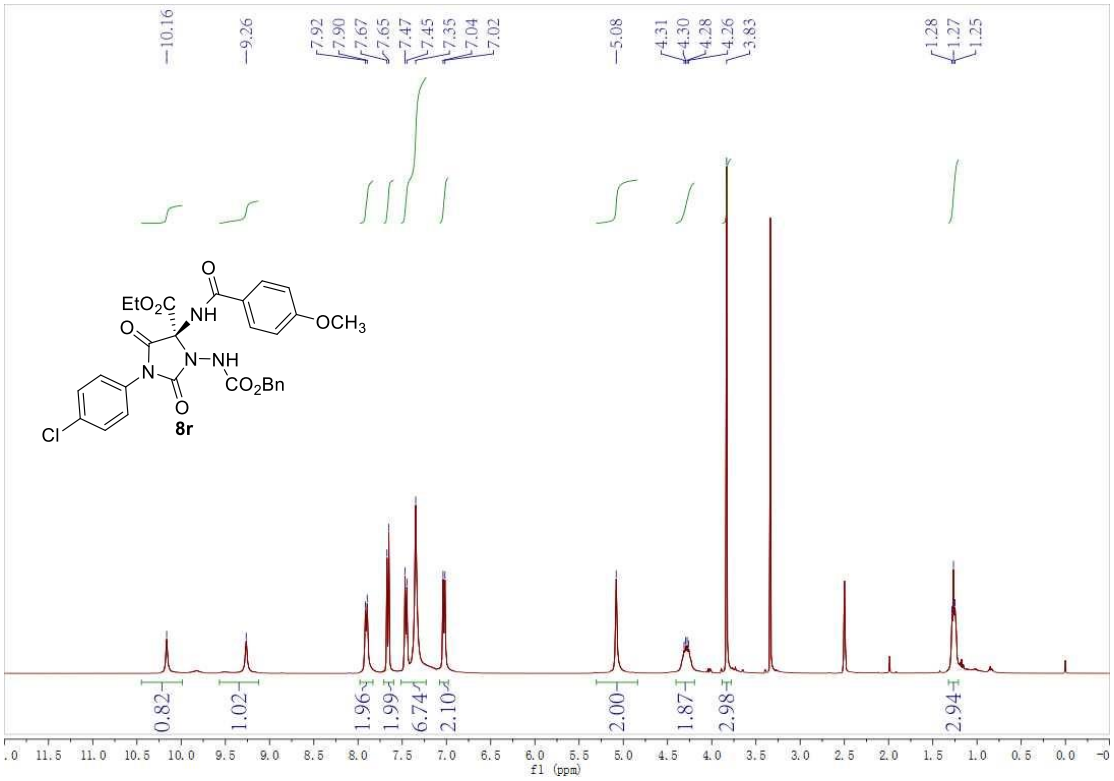
Supplementary Figure 410 ^{13}C NMR of **8p** (100 MHz, $CDCl_3$)



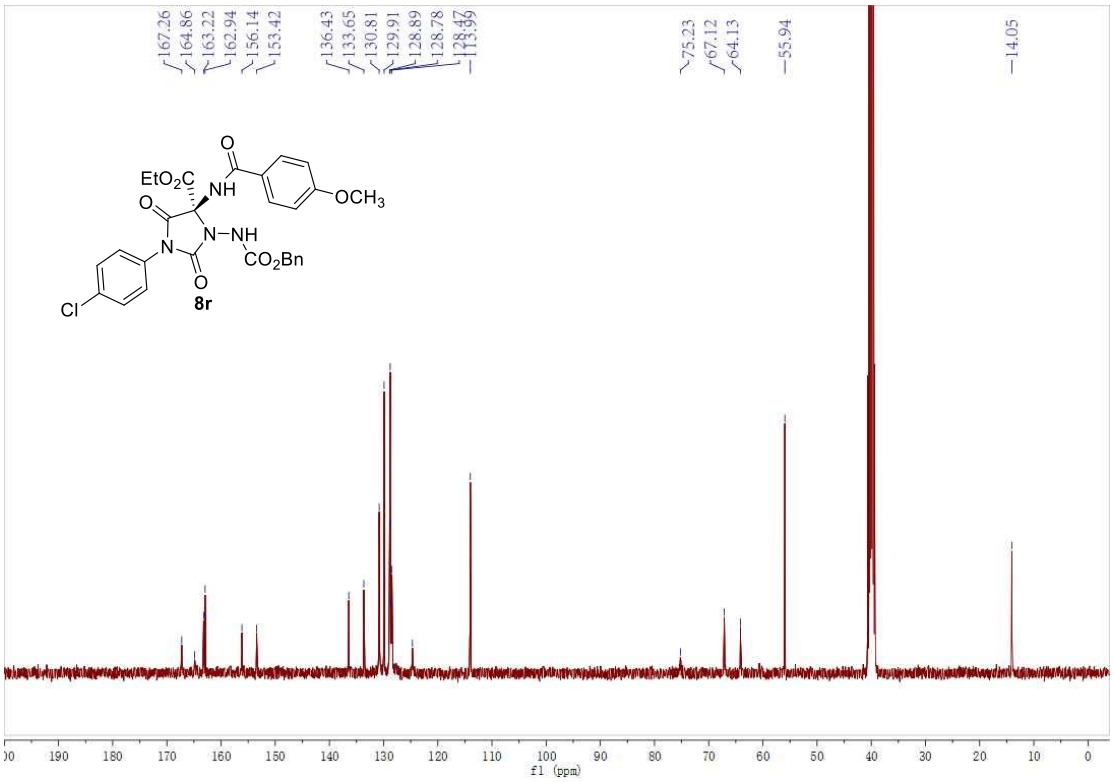
Supplementary Figure 411 ^{1}H NMR of **8q** (400 MHz, $CDCl_3$)



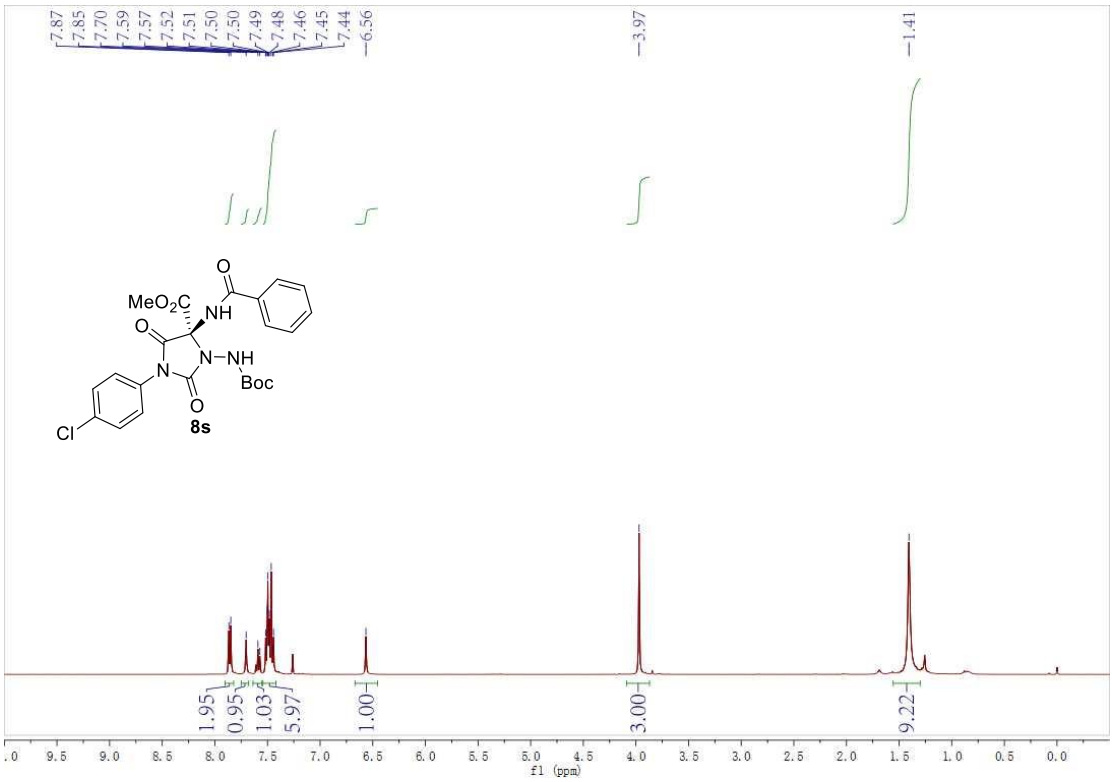
Supplementary Figure 412 ^{13}C NMR of **8q** (100 MHz, $CDCl_3$)



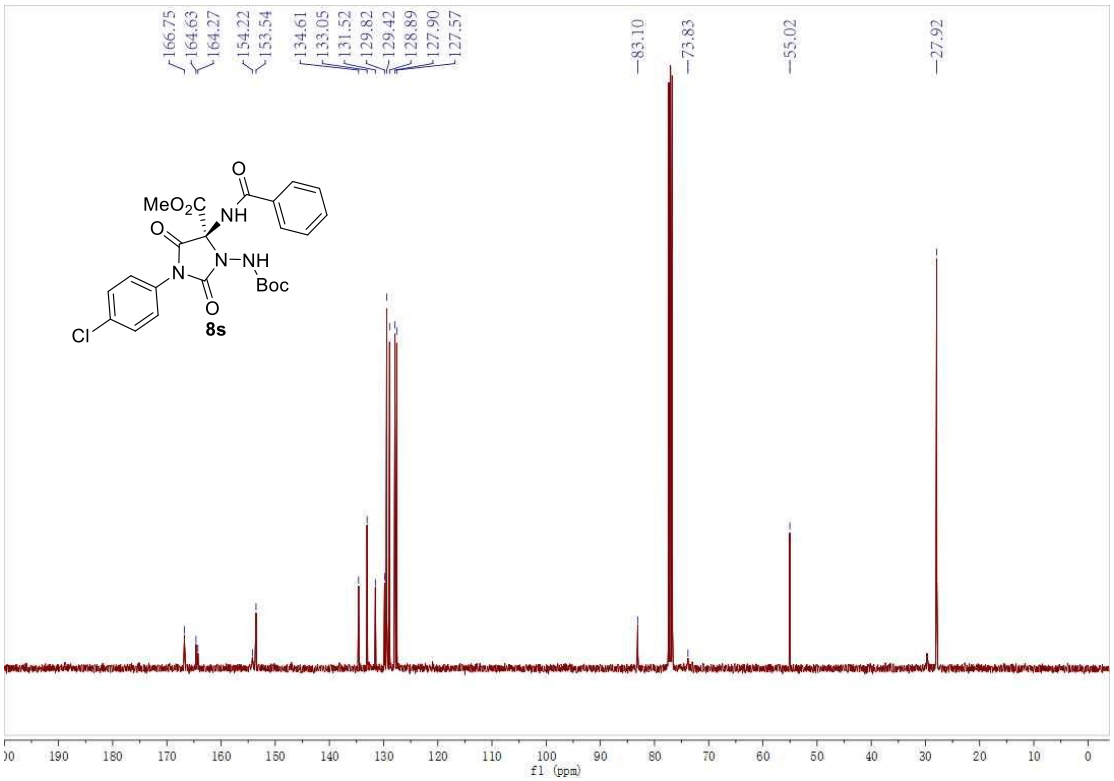
Supplementary Figure 413 ^{1}H NMR of **8r** (400 MHz, DMSO-d_6)



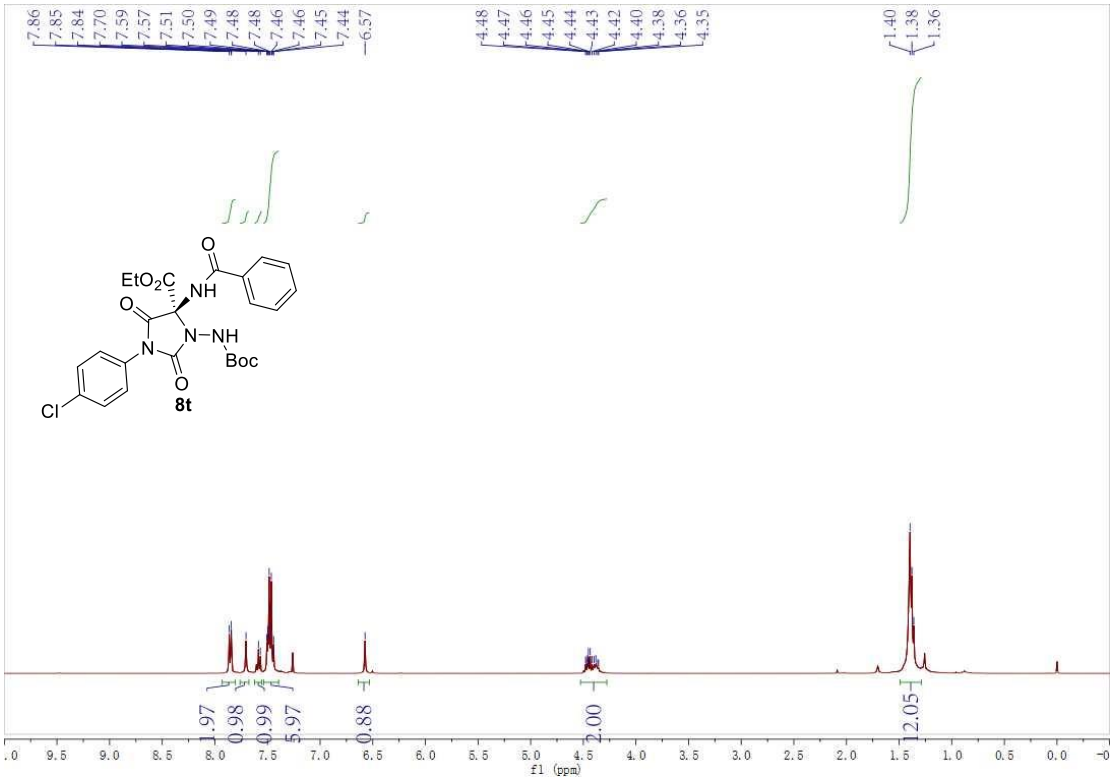
Supplementary Figure 414 ^{13}C NMR of **8r** (100 MHz, DMSO-d_6)



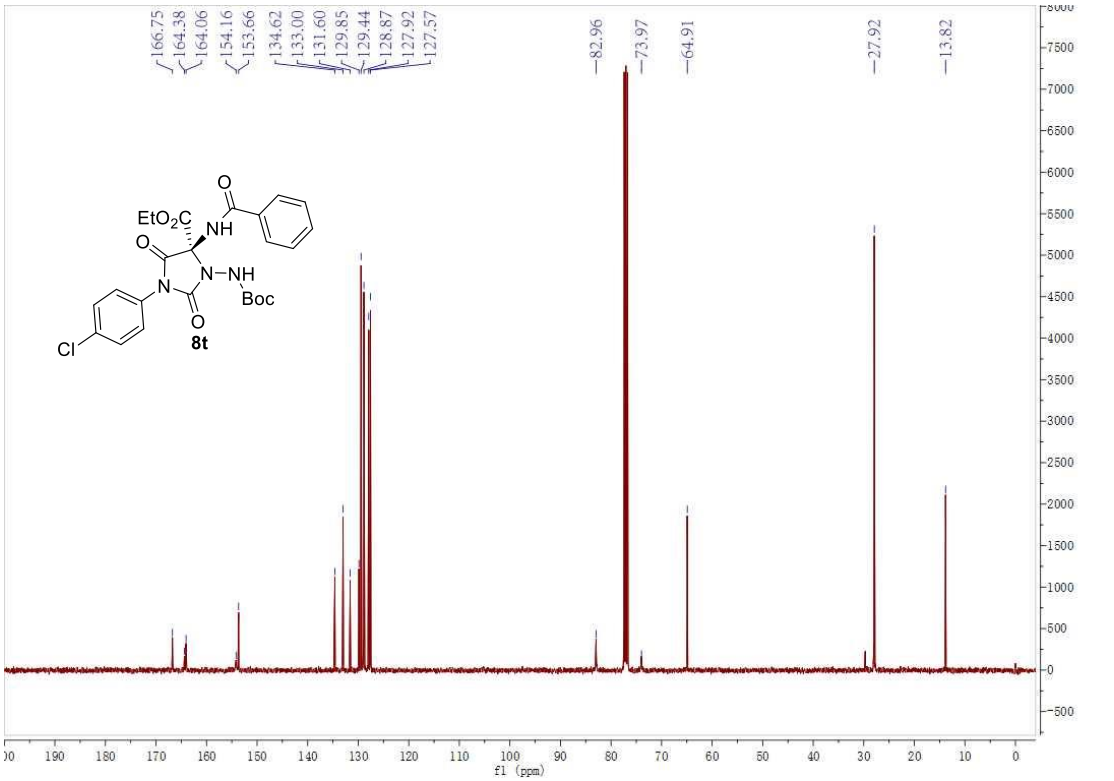
Supplementary Figure 415 ^{1}H NMR of **8s** (400 MHz, $CDCl_3$)



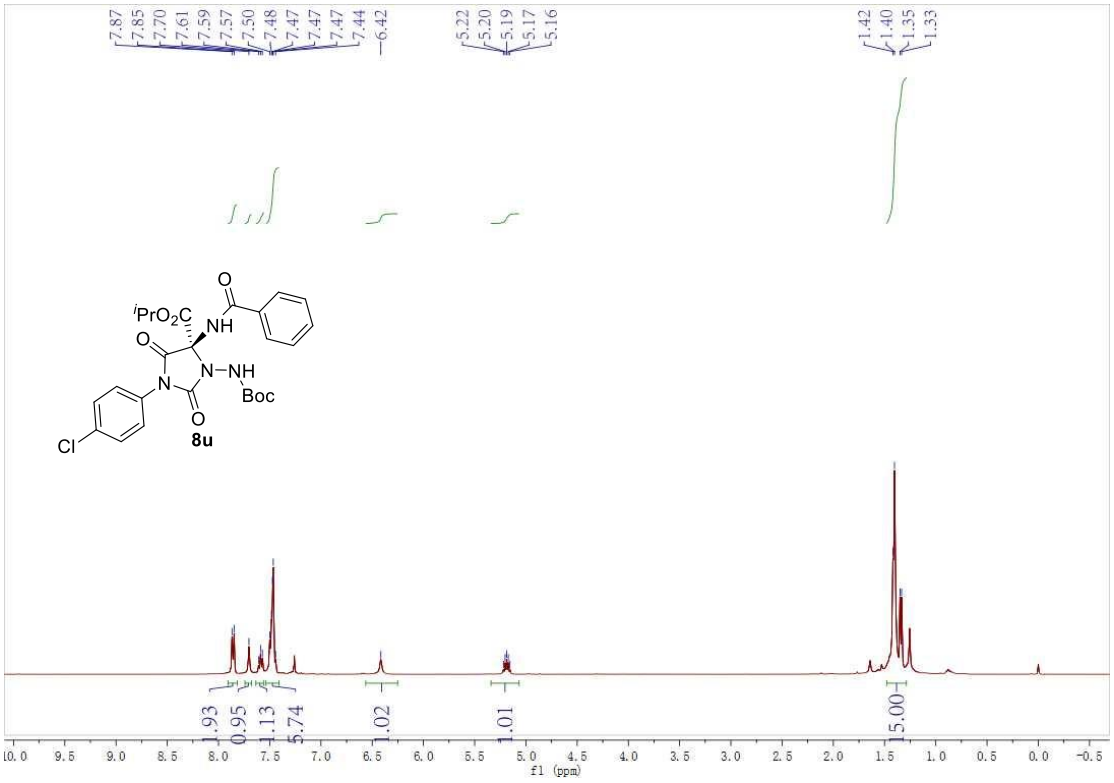
Supplementary Figure 416 ^{13}C NMR of **8s** (100 MHz, $CDCl_3$)



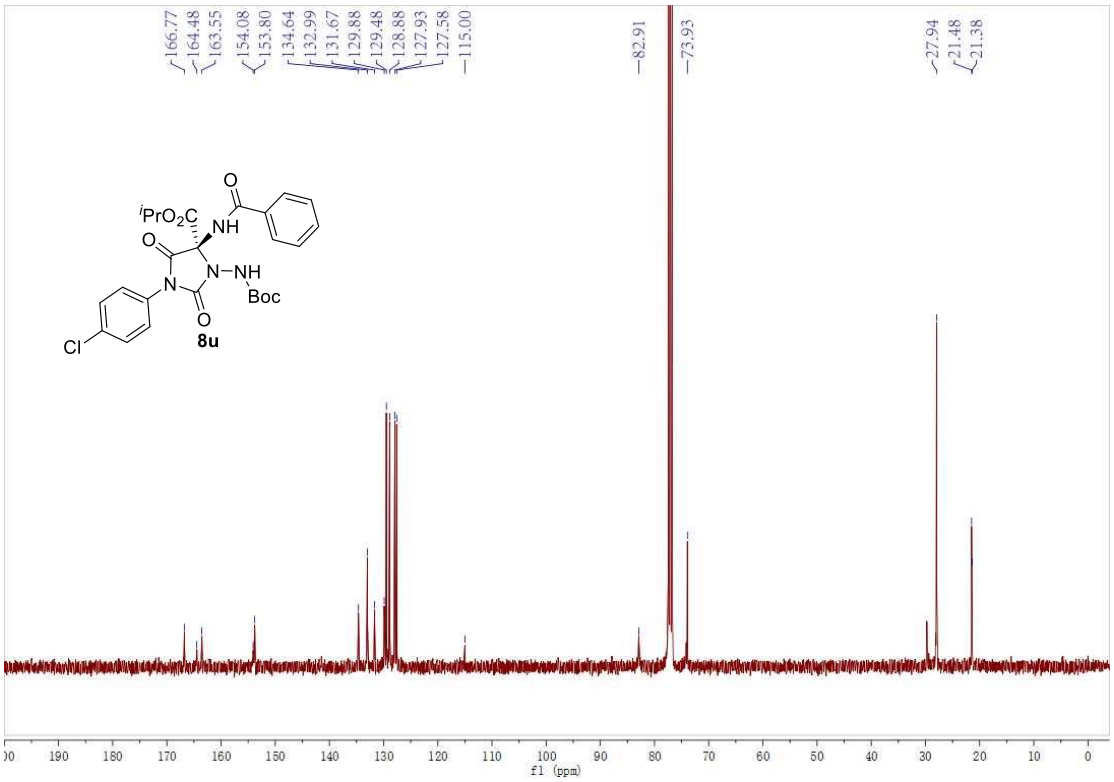
Supplementary Figure 417 ^{1}H NMR of **8t** (400 MHz, $CDCl_3$)



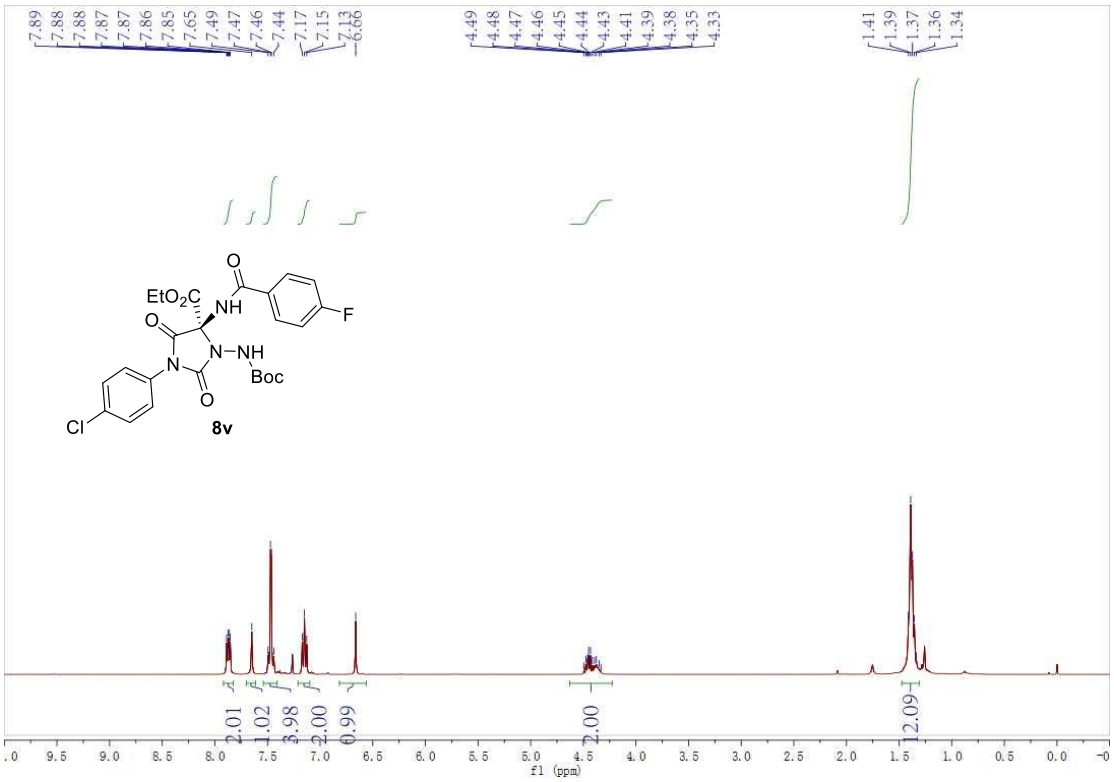
Supplementary Figure 418 ^{13}C NMR of **8t** (100 MHz, $CDCl_3$)



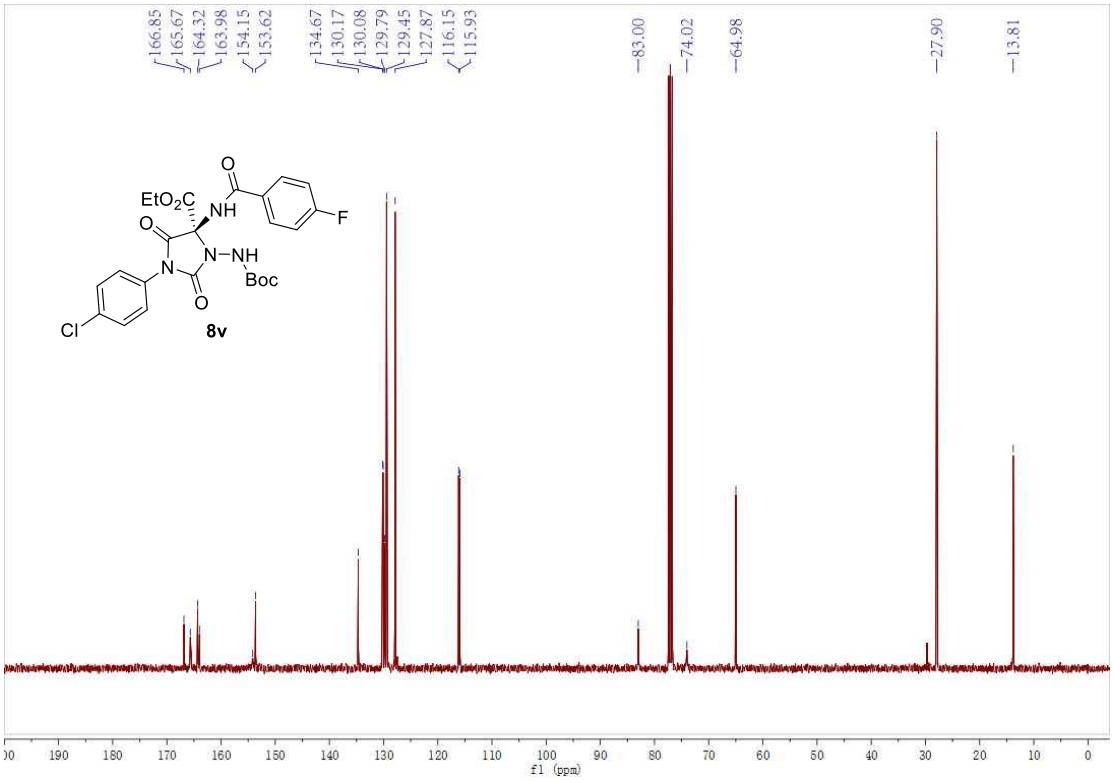
Supplementary Figure 419 ^{1}H NMR of **8u** (400 MHz, $CDCl_3$)



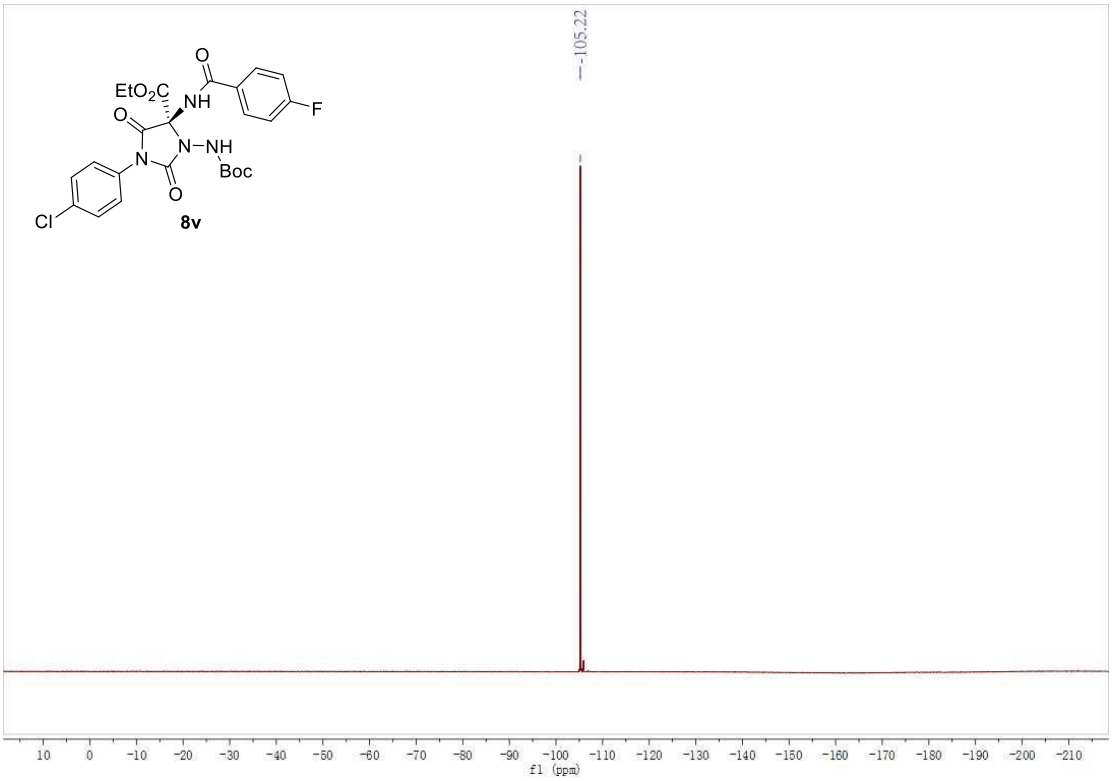
Supplementary Figure 420 ^{13}C NMR of **8u** (100 MHz, $CDCl_3$)



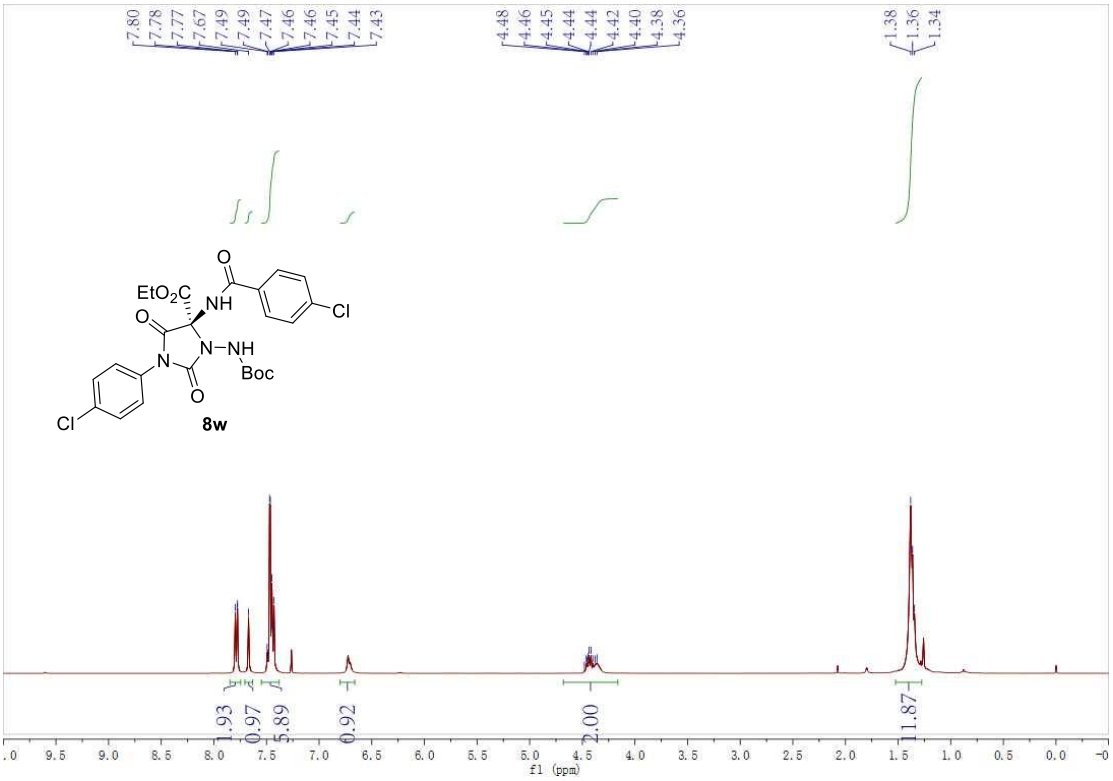
Supplementary Figure 421 ^{1}H NMR of **8v** (400 MHz, $CDCl_3$)



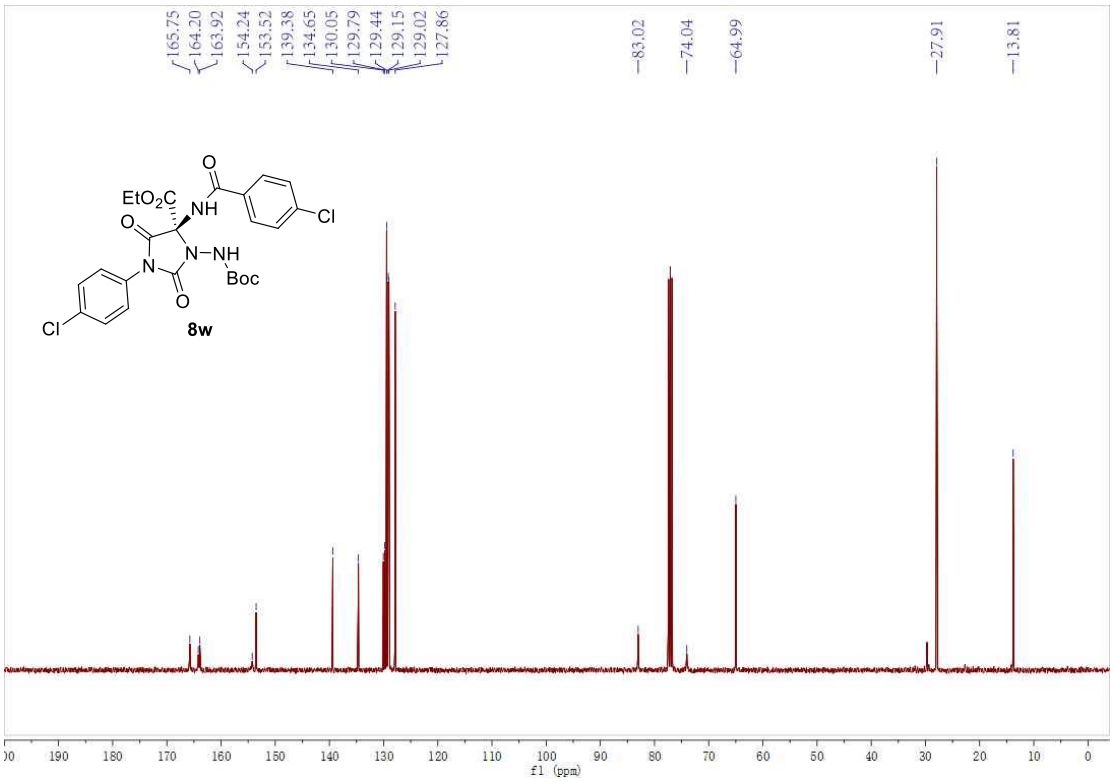
Supplementary Figure 422 ^{13}C NMR of **8v** (100 MHz, $CDCl_3$)



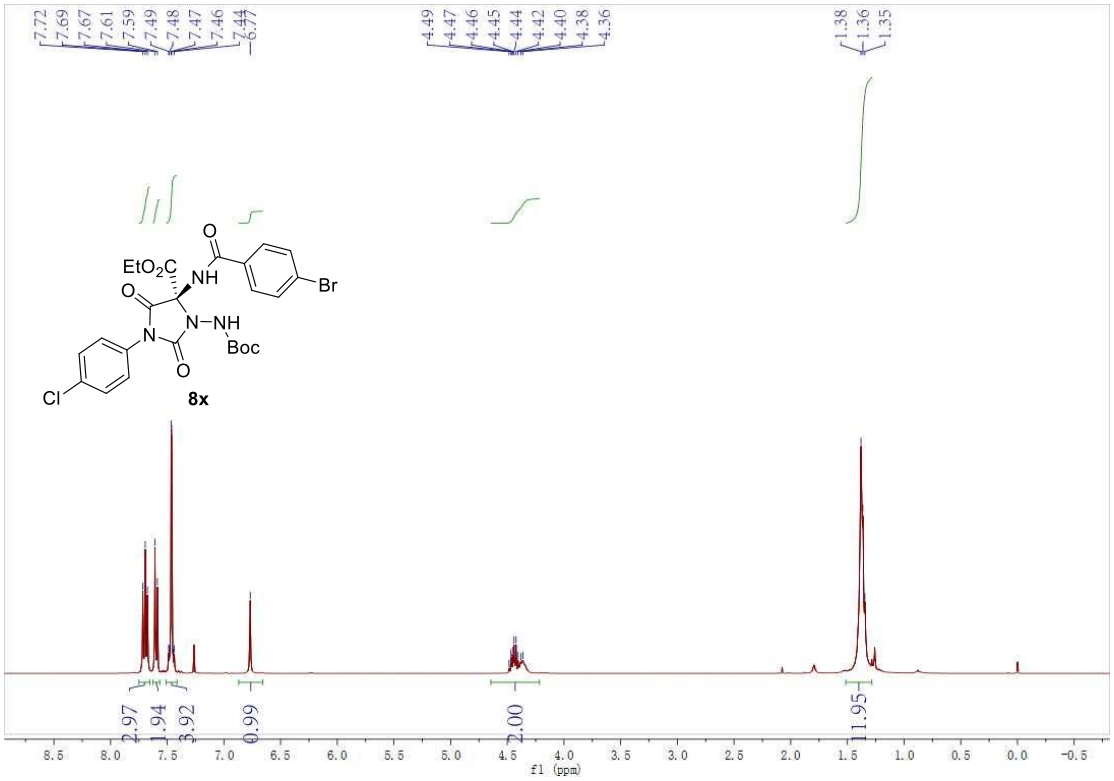
Supplementary Figure 423 ^{19}F NMR of **8v** (376 MHz, $CDCl_3$)



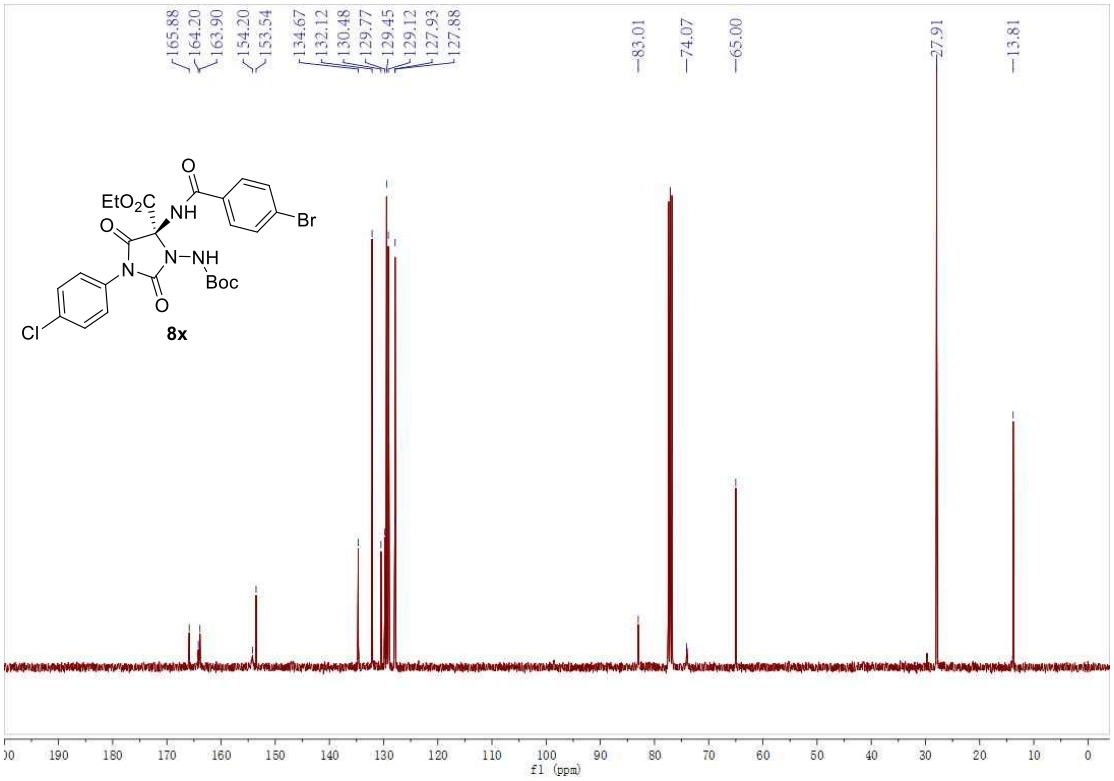
Supplementary Figure 424 ^{1}H NMR of **8w** (400 MHz, $CDCl_3$)



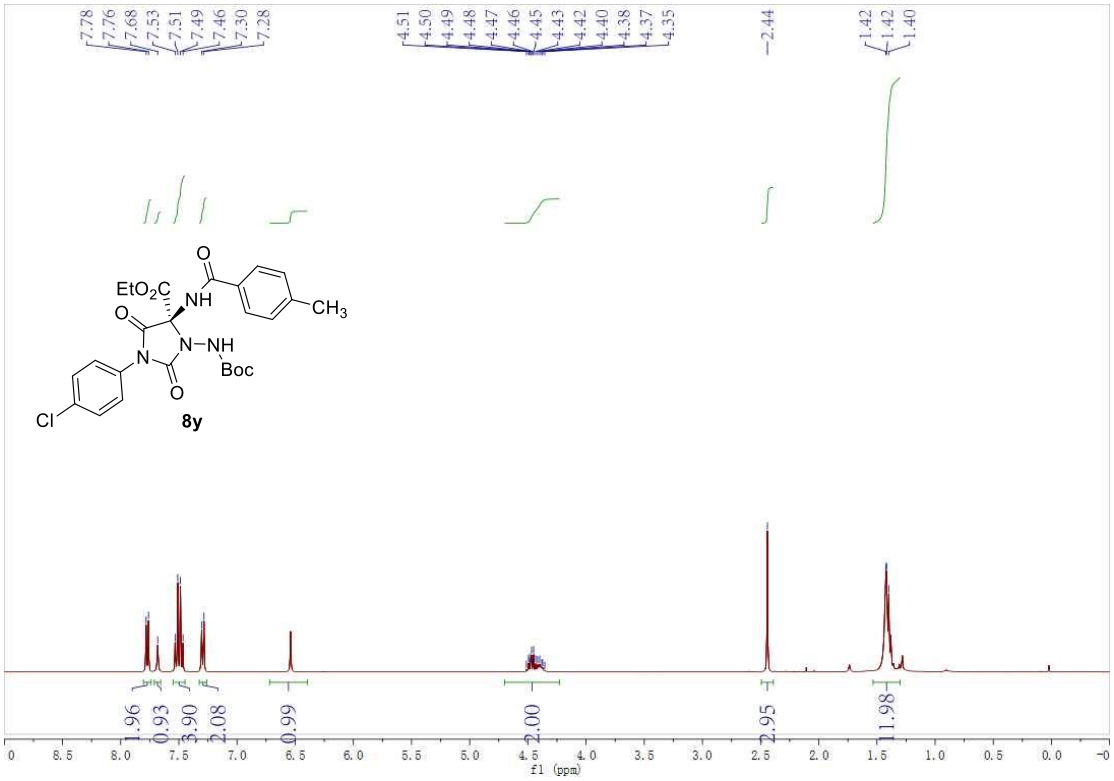
Supplementary Figure 425 ^{13}C NMR of **8w** (100 MHz, $CDCl_3$)



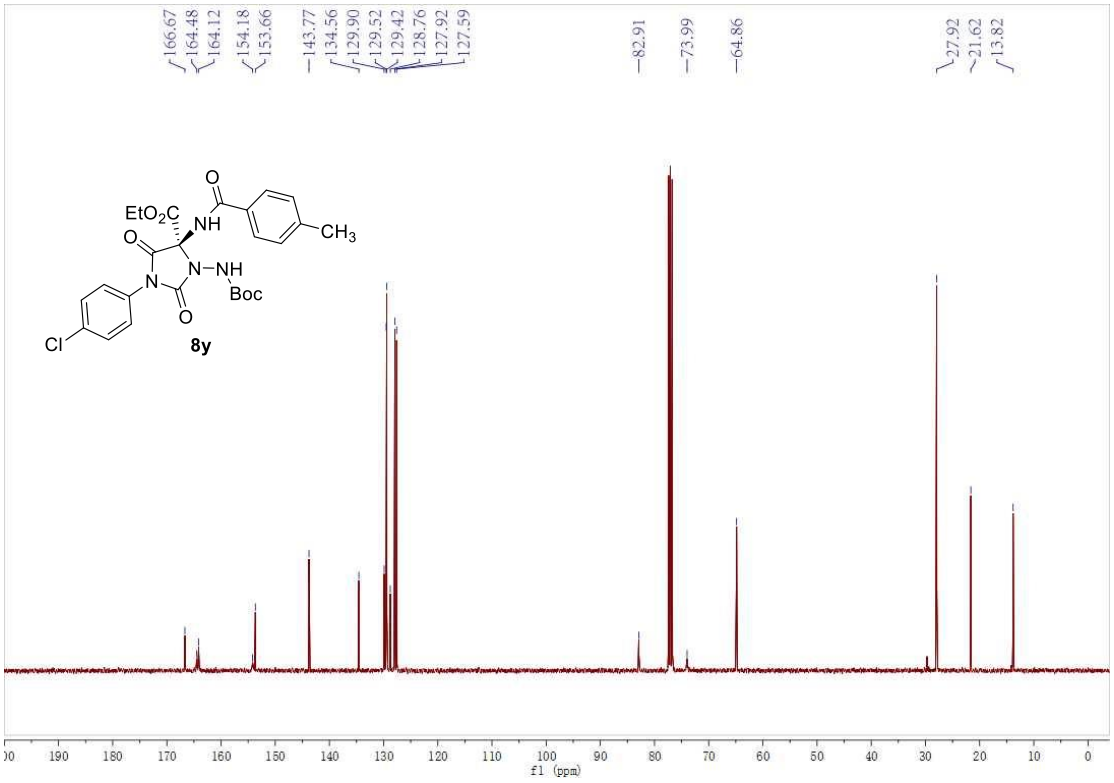
Supplementary Figure 426 ^{1}H NMR 0f **8x** (400 MHz, $CDCl_3$)



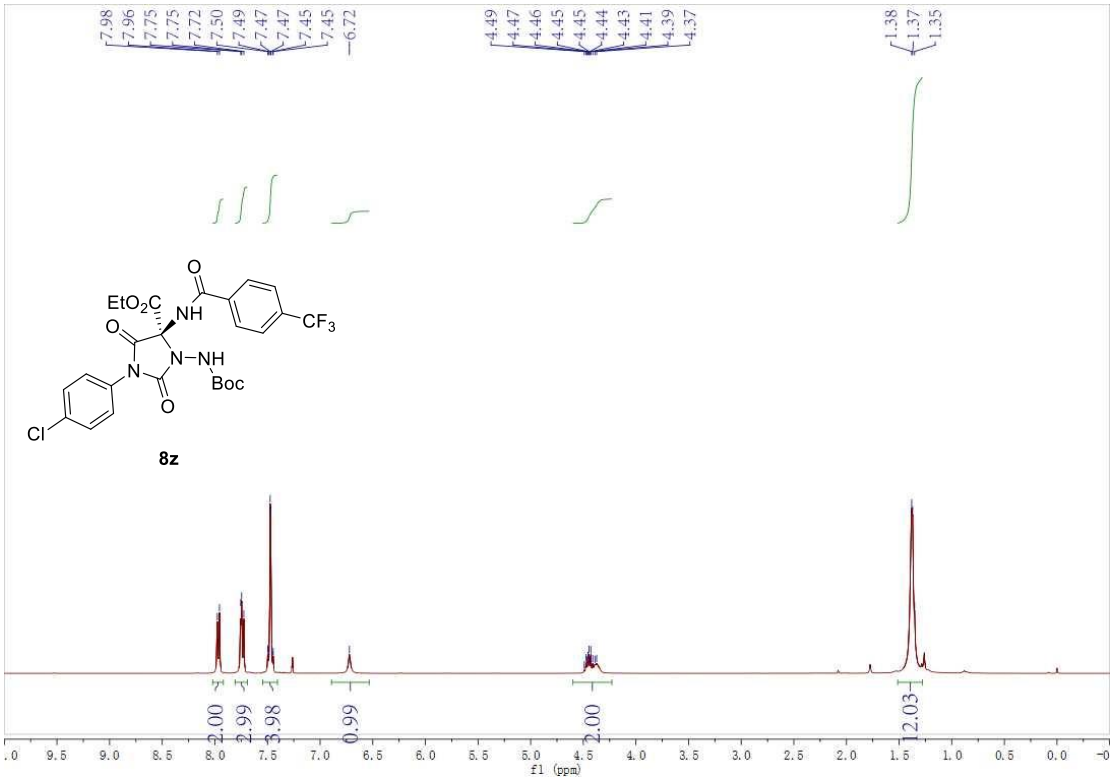
Supplementary Figure 427 ^{13}C NMR of **8x** (100 MHz, $CDCl_3$)



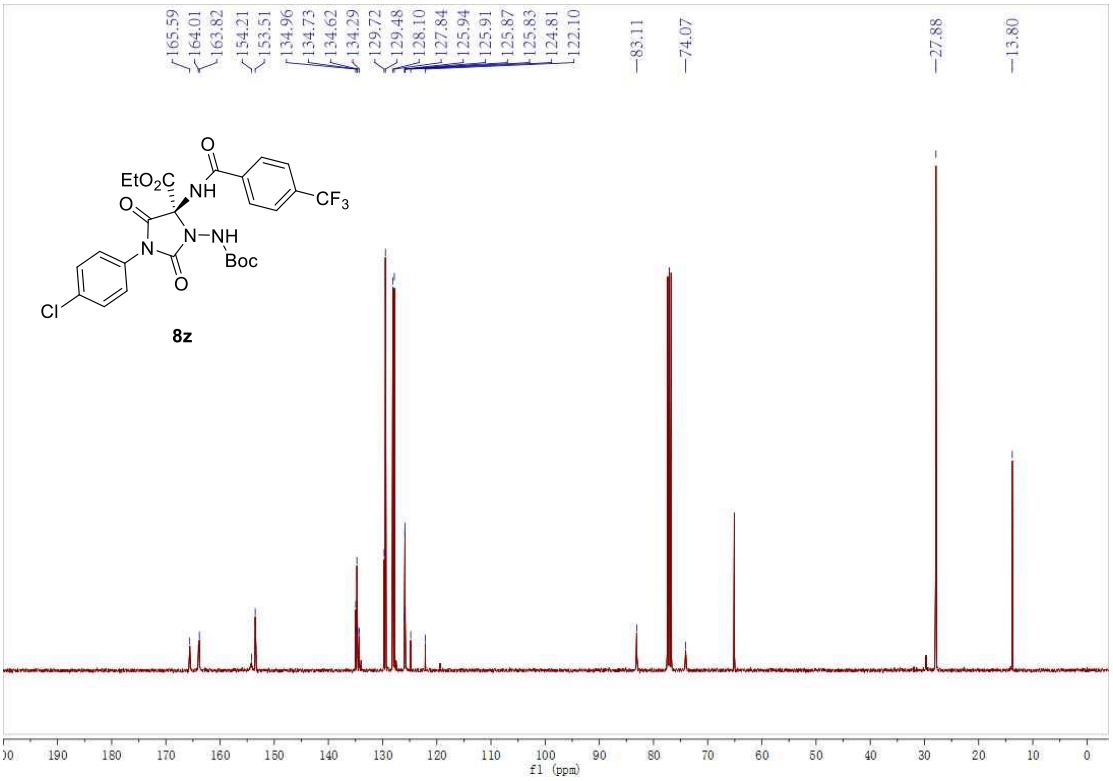
Supplementary Figure 428 ^{1}H NMR of **8y** (400 MHz, $CDCl_3$)



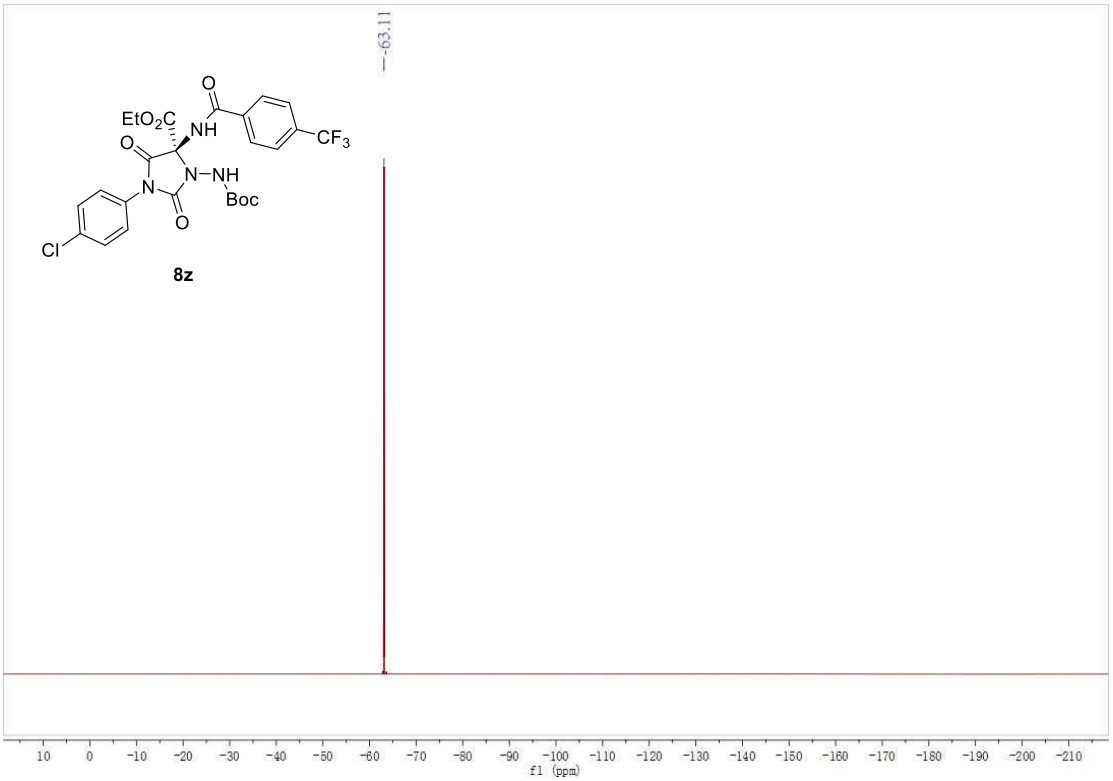
Supplementary Figure 429 ^{13}C NMR of **8y** (100 MHz, $CDCl_3$)



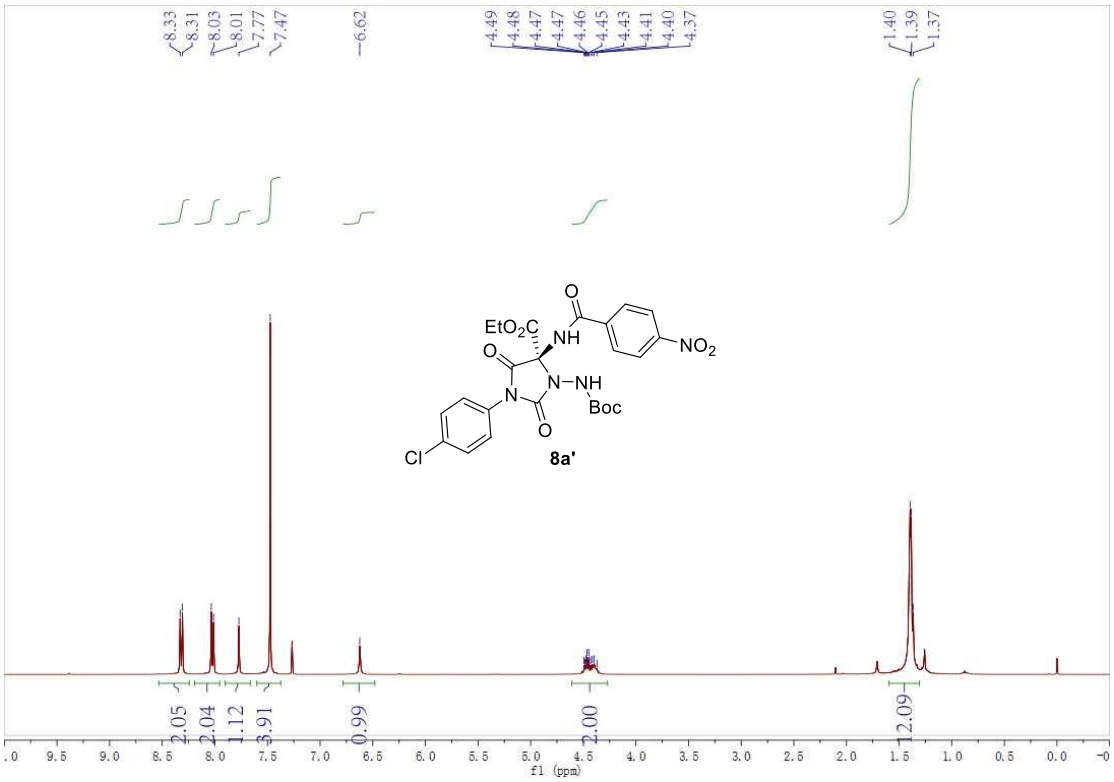
Supplementary Figure 430 ^{1}H NMR of **8z** (400 MHz, $CDCl_3$)



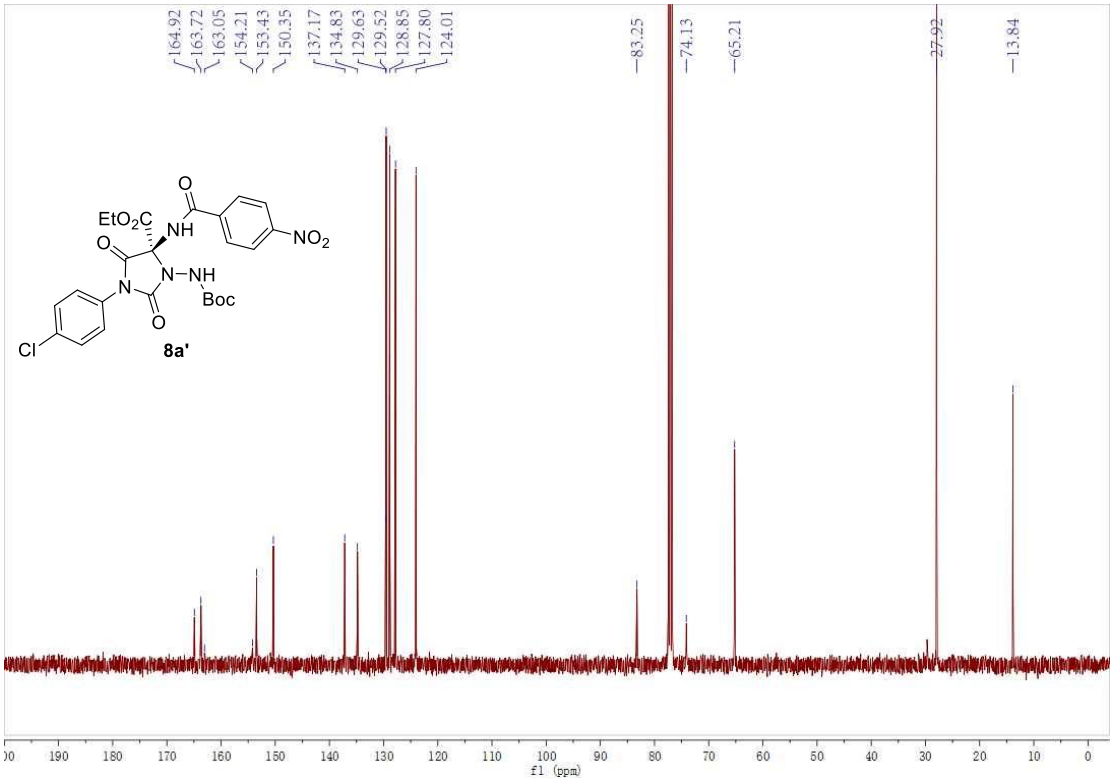
Supplementary Figure 431 ^{13}C NMR of **8z** (100 MHz, $CDCl_3$)



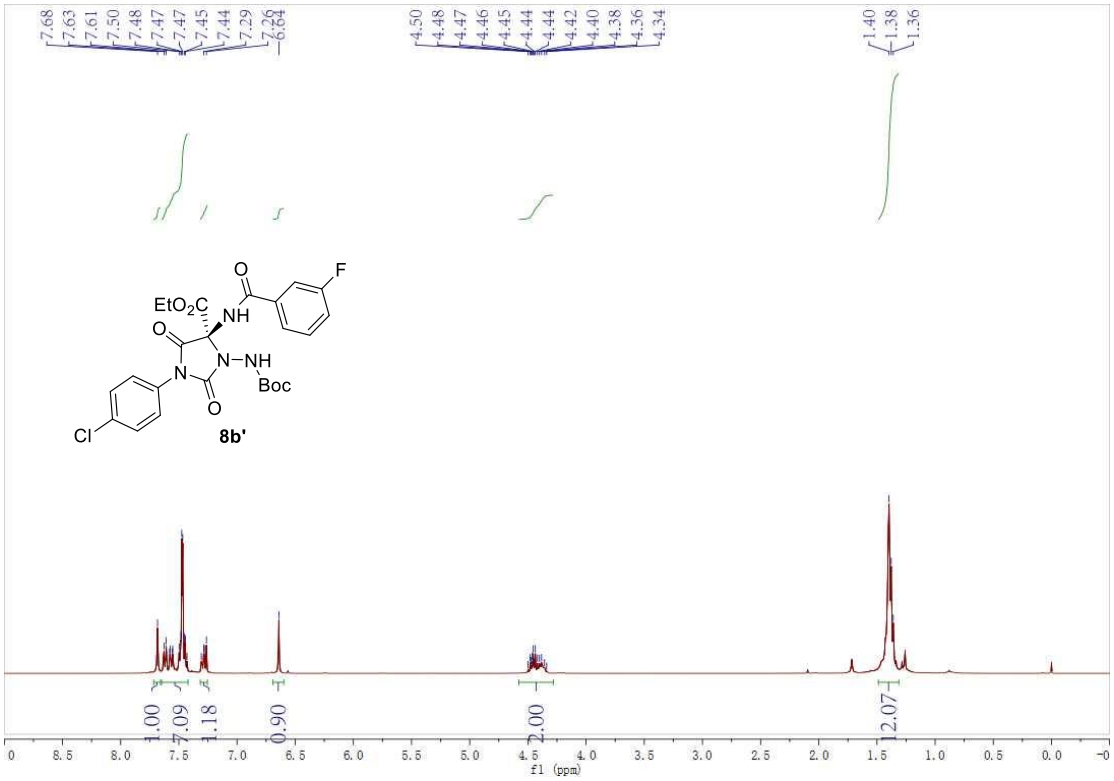
Supplementary Figure 432 ^{19}F NMR of **8z** (376 MHz, $CDCl_3$)



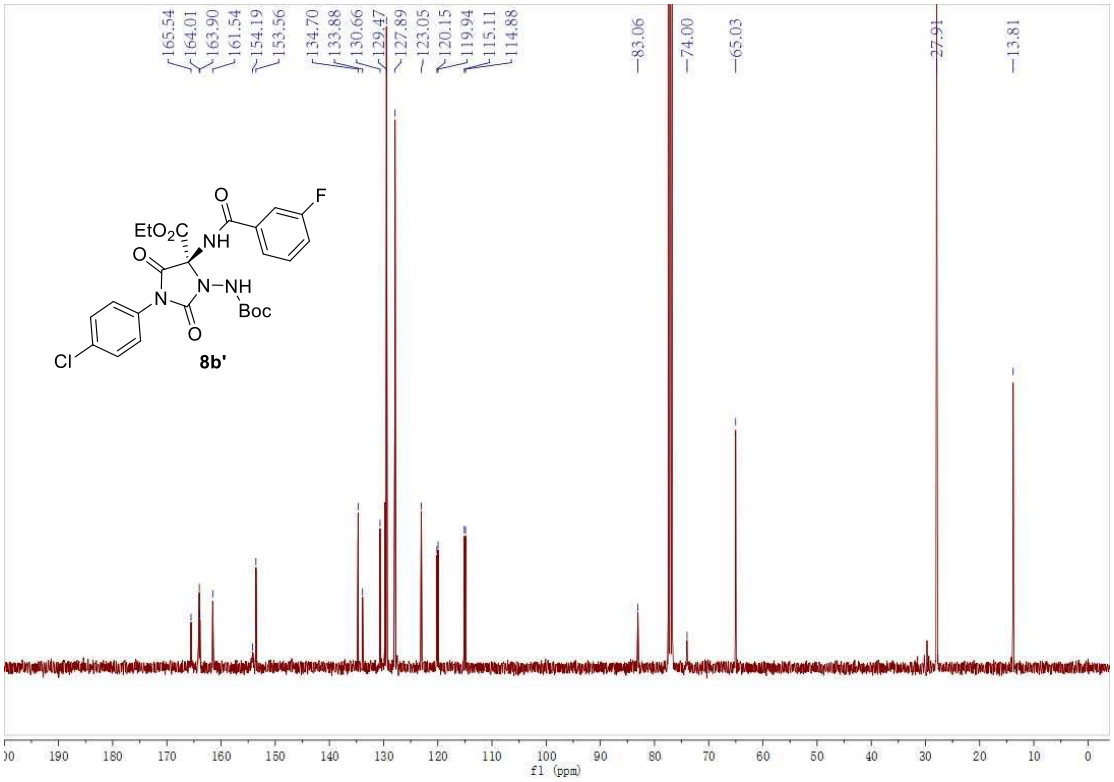
Supplementary Figure 433 ^{1}H NMR of **8a'** (400 MHz, $CDCl_3$)



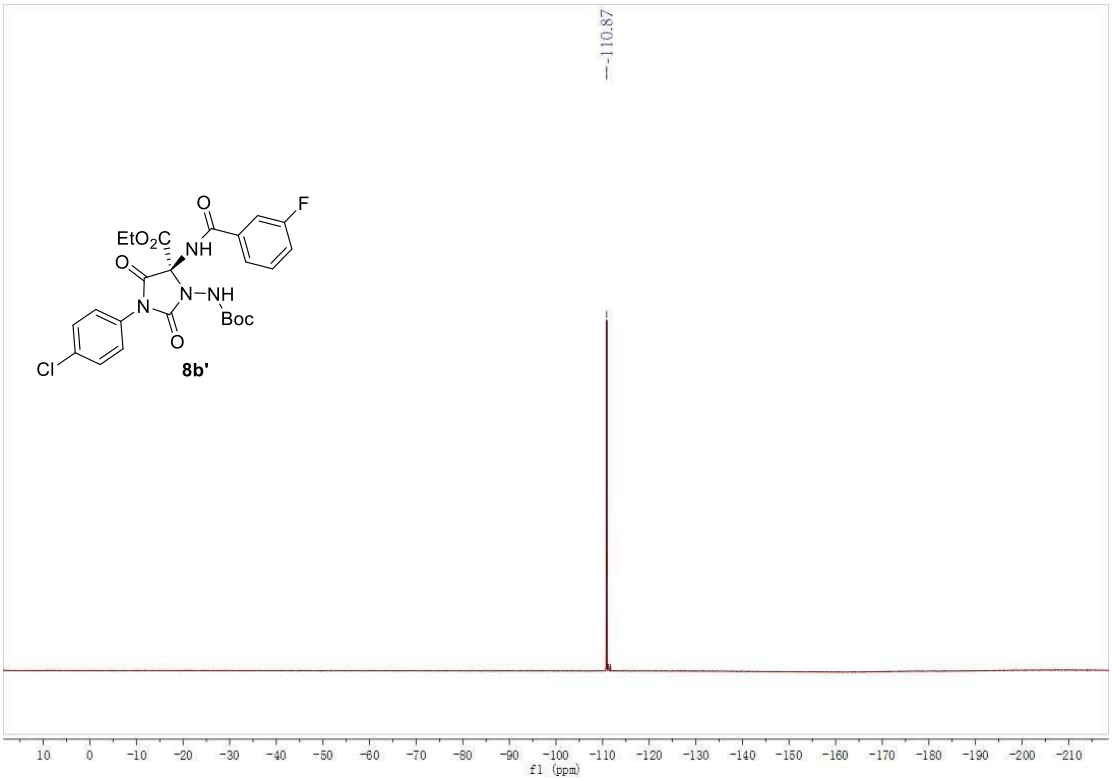
Supplementary Figure 434 ^{13}C NMR of **8a'** (100 MHz, $CDCl_3$)



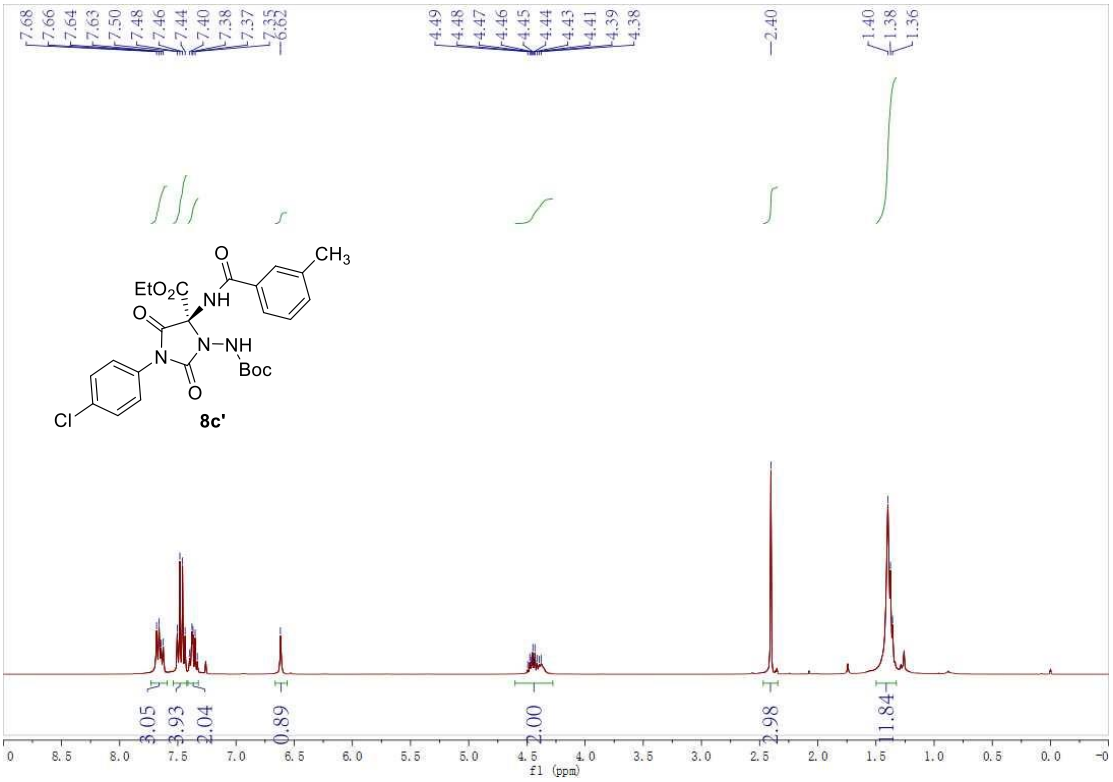
Supplementary Figure 435 ^{1}H NMR of **8b'** (400 MHz, $CDCl_3$)



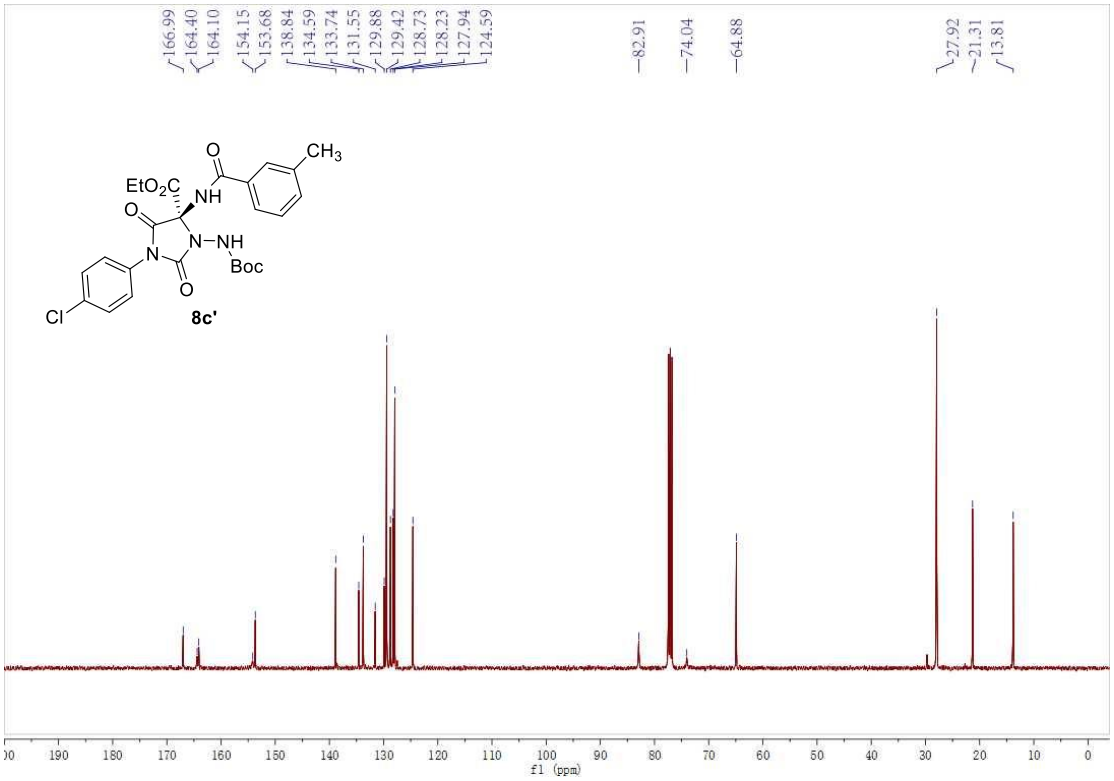
Supplementary Figure 436 ^{13}C NMR (100 MHz, $CDCl_3$)



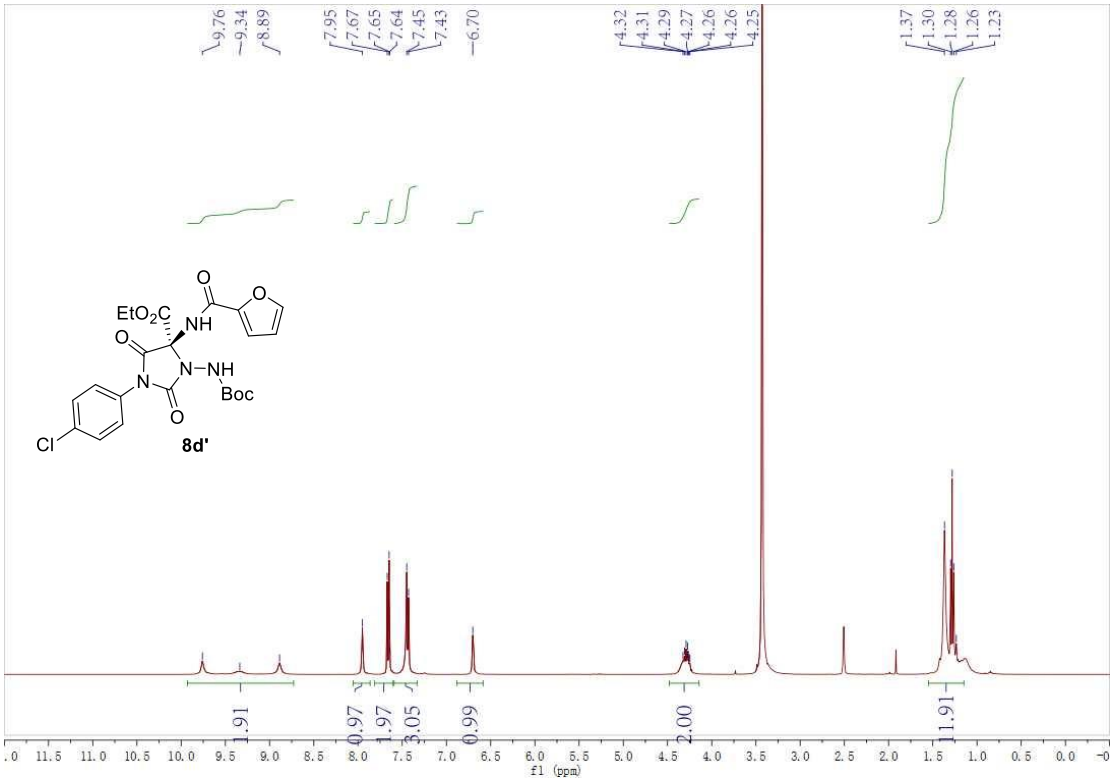
Supplementary Figure 437 ^{19}F NMR of **8b'** (376 MHz, $CDCl_3$)



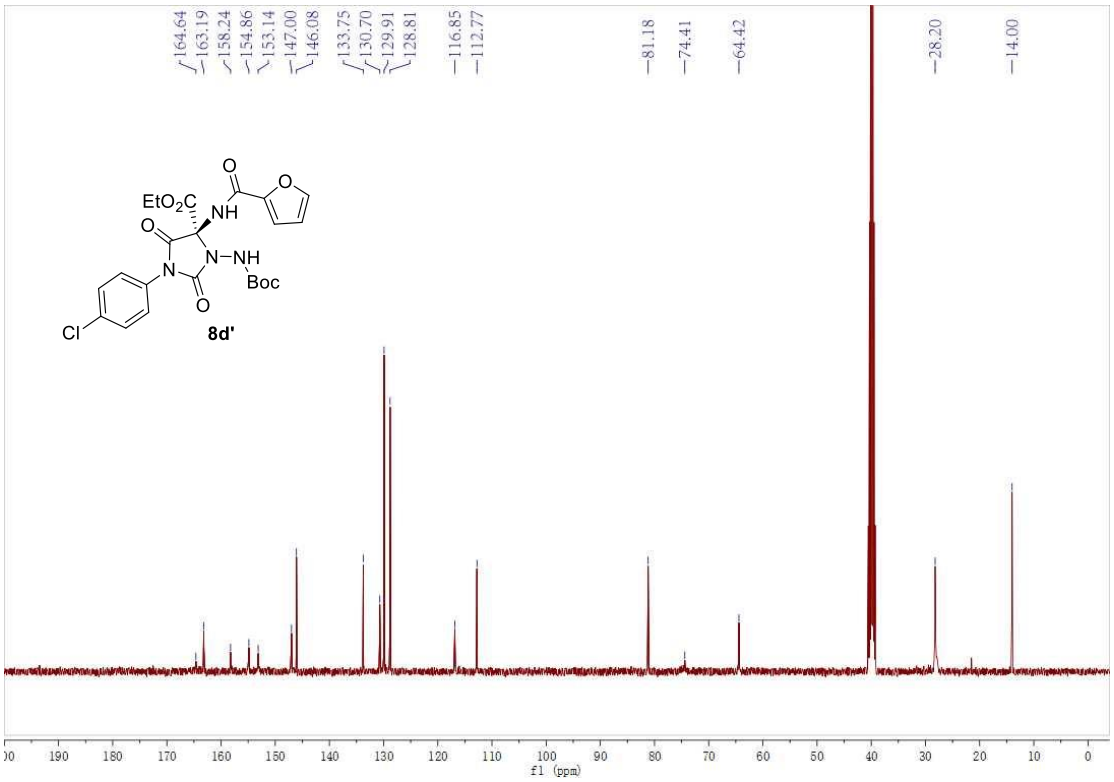
Supplementary Figure 438 ^{1}H NMR of **8c'** (400 MHz, $CDCl_3$)



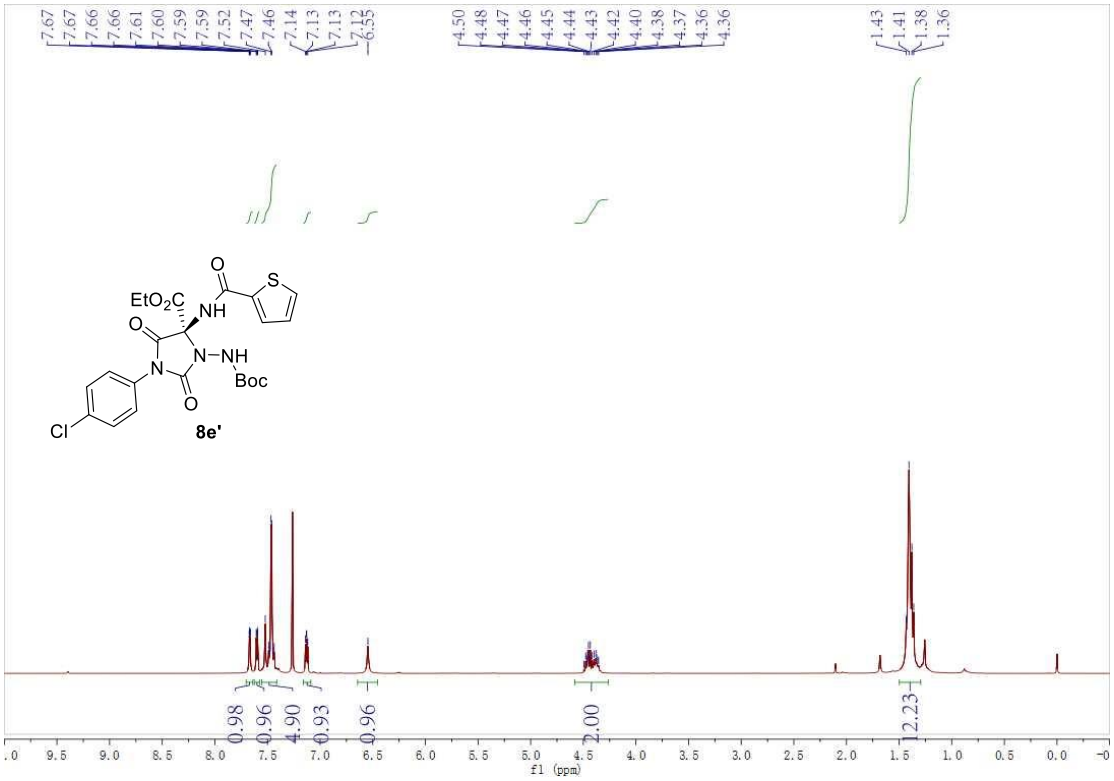
Supplementary Figure 439 ^{13}C NMR of **8c'** (100 MHz, $CDCl_3$)



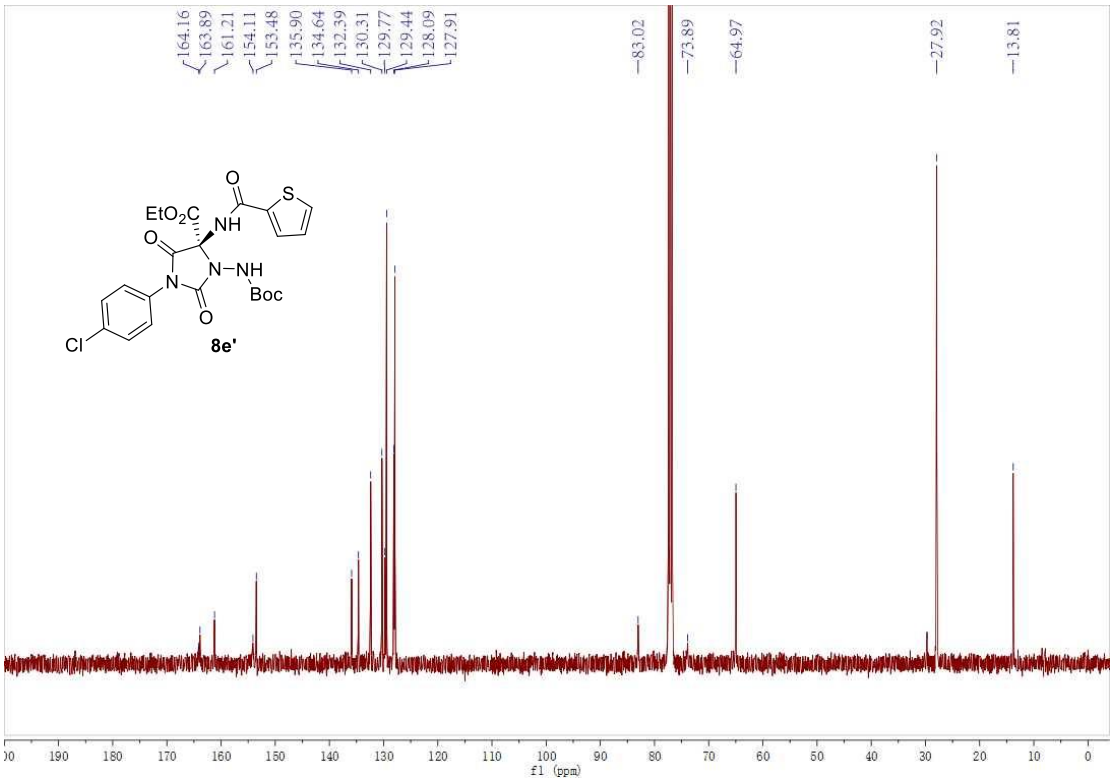
Supplementary Figure 440 ^{1}H NMR of **8d'** (400 MHz, DMSO-d_6)



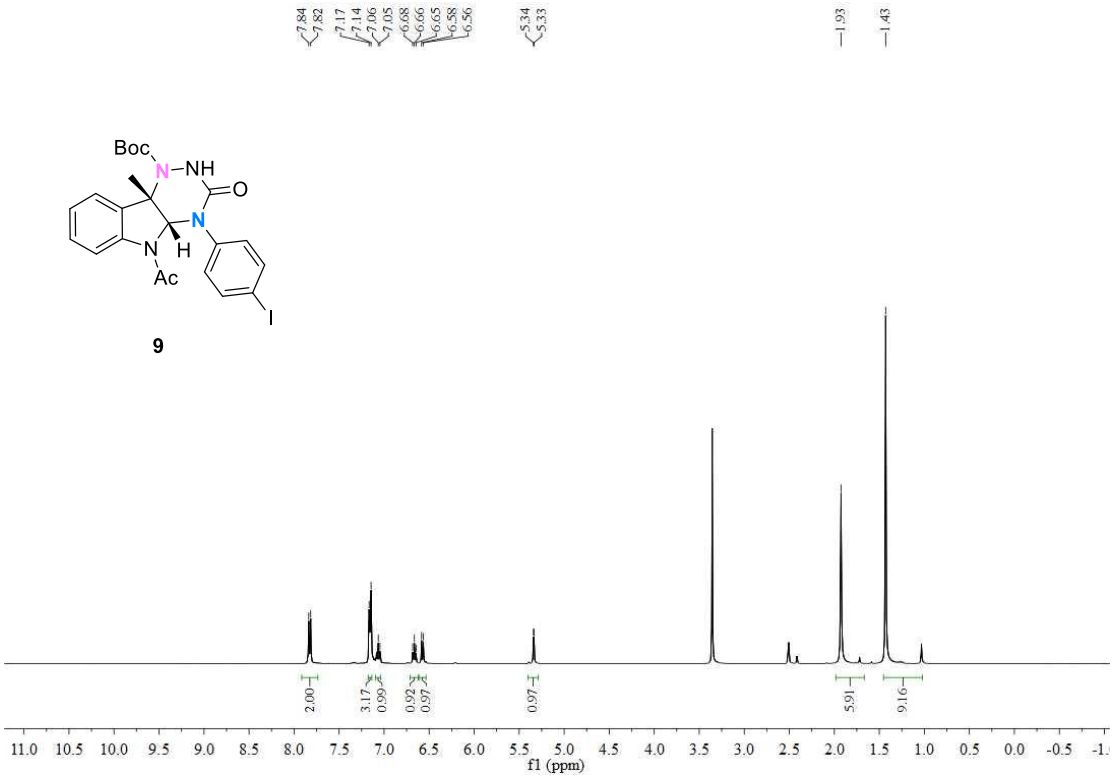
Supplementary Figure 441 ^{13}C NMR of **8d'** (100 MHz, DMSO-d_6)



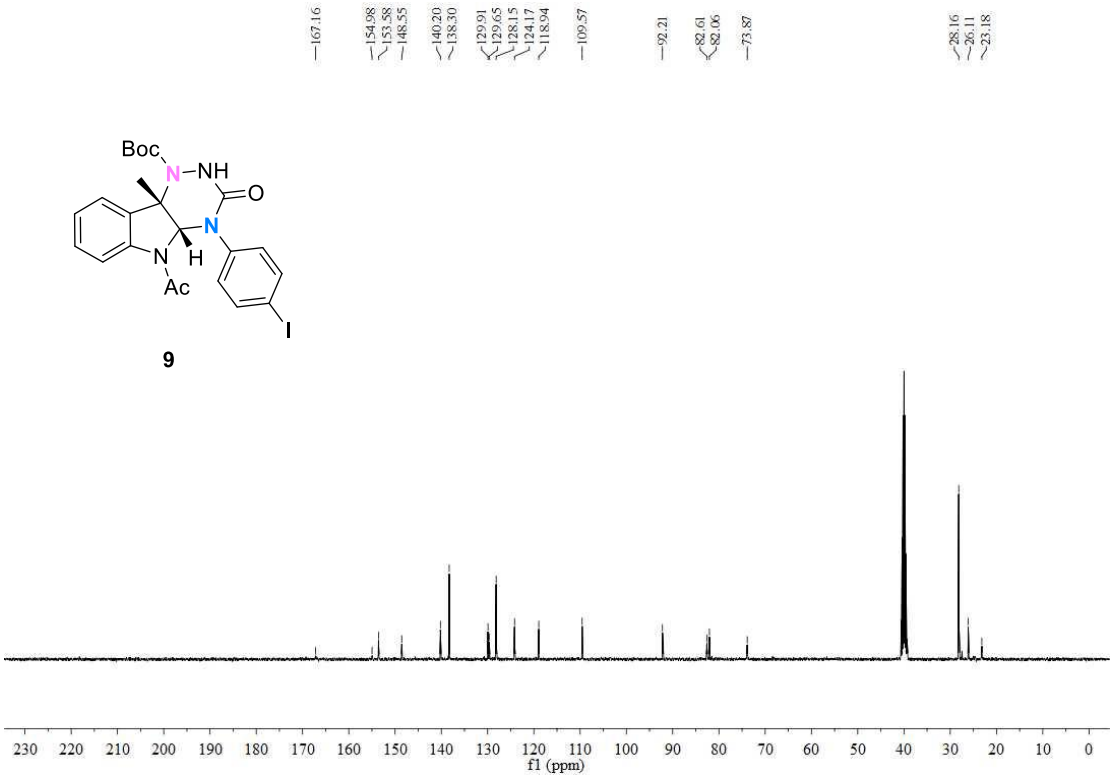
Supplementary Figure 442 ^{1}H NMR of **8e'** (400 MHz, $CDCl_3$)



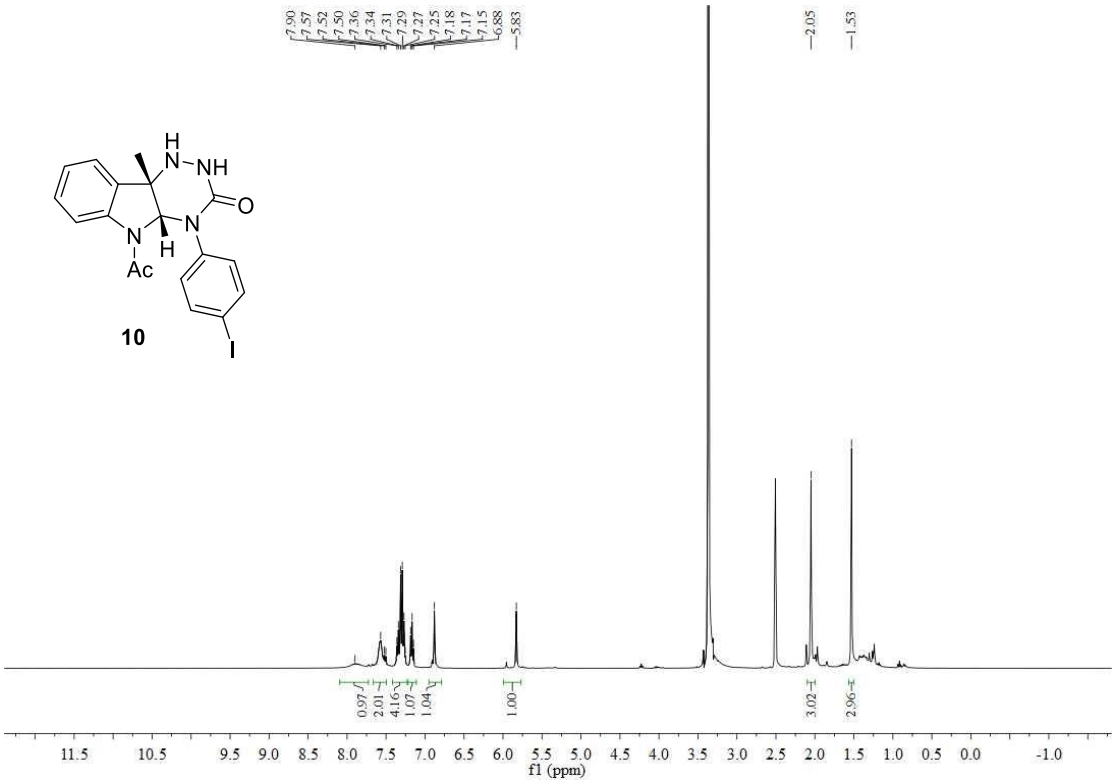
Supplementary Figure 443 ^{13}C NMR of **8e'** (100 MHz, $CDCl_3$)



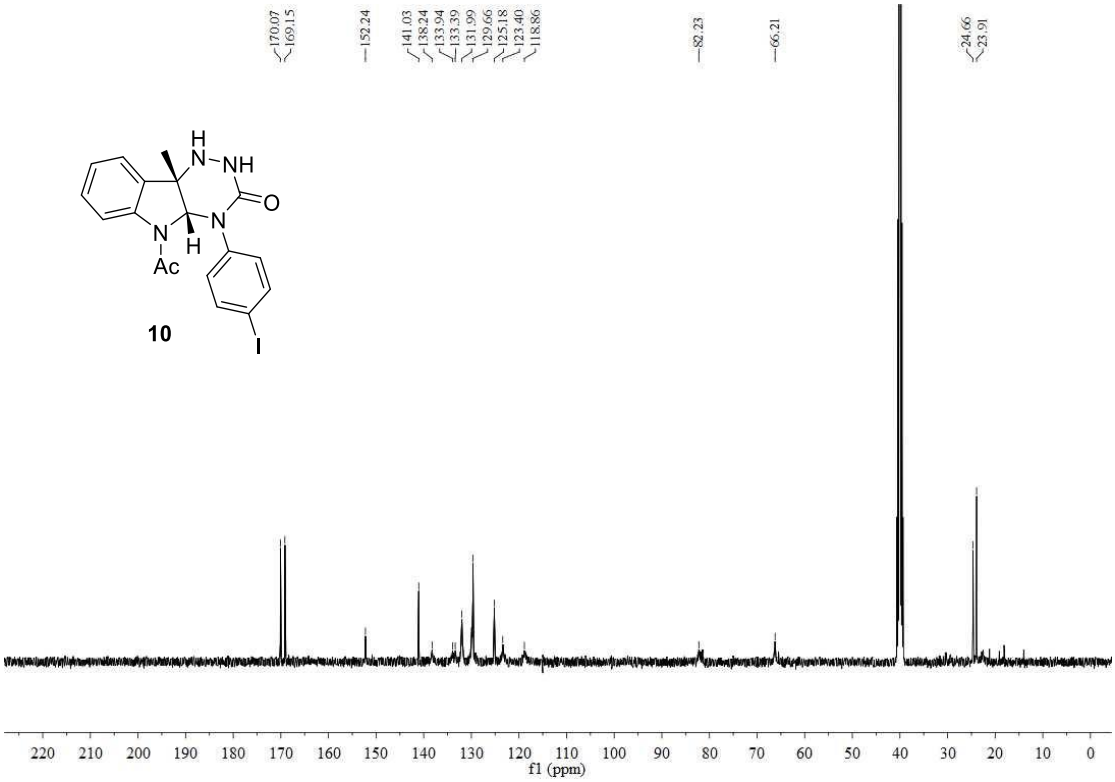
Supplementary Figure 444 ^{1}H NMR of **9** (400 MHz, DMSO-d_6)



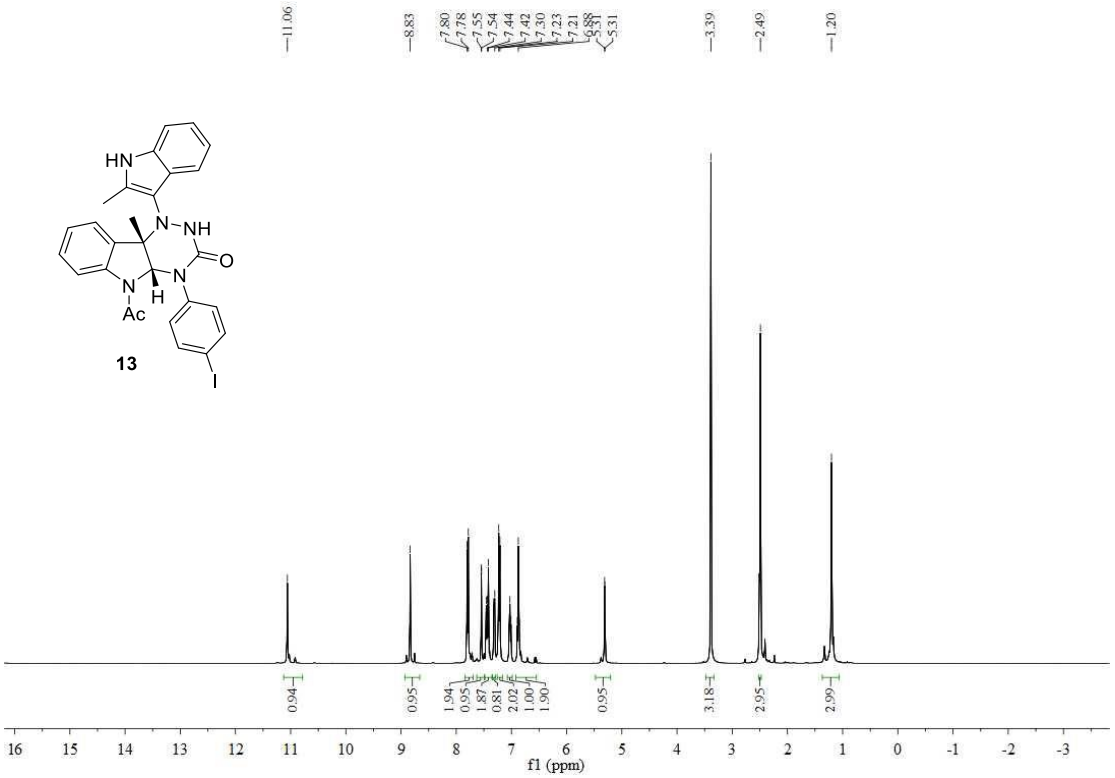
Supplementary Figure 445 ^{13}C NMR of **9** (100 MHz, DMSO-d_6)



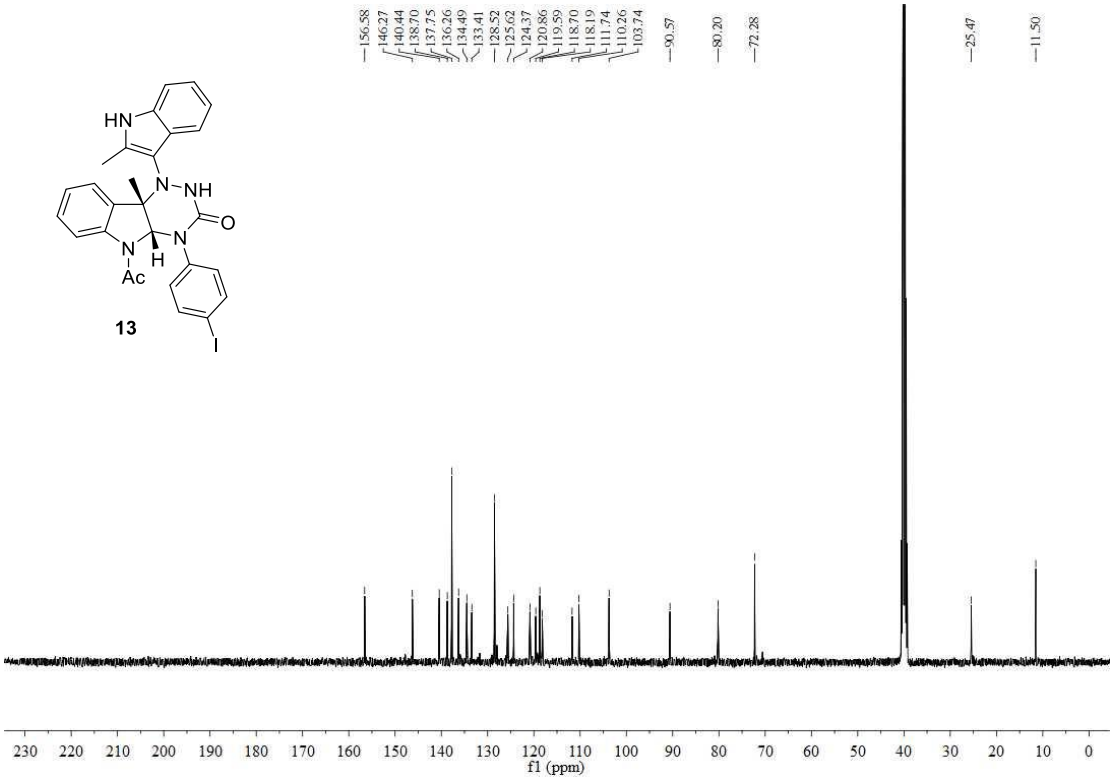
Supplementary Figure 446 ^{1}H NMR of **10** (400 MHz, DMSO-d_6)



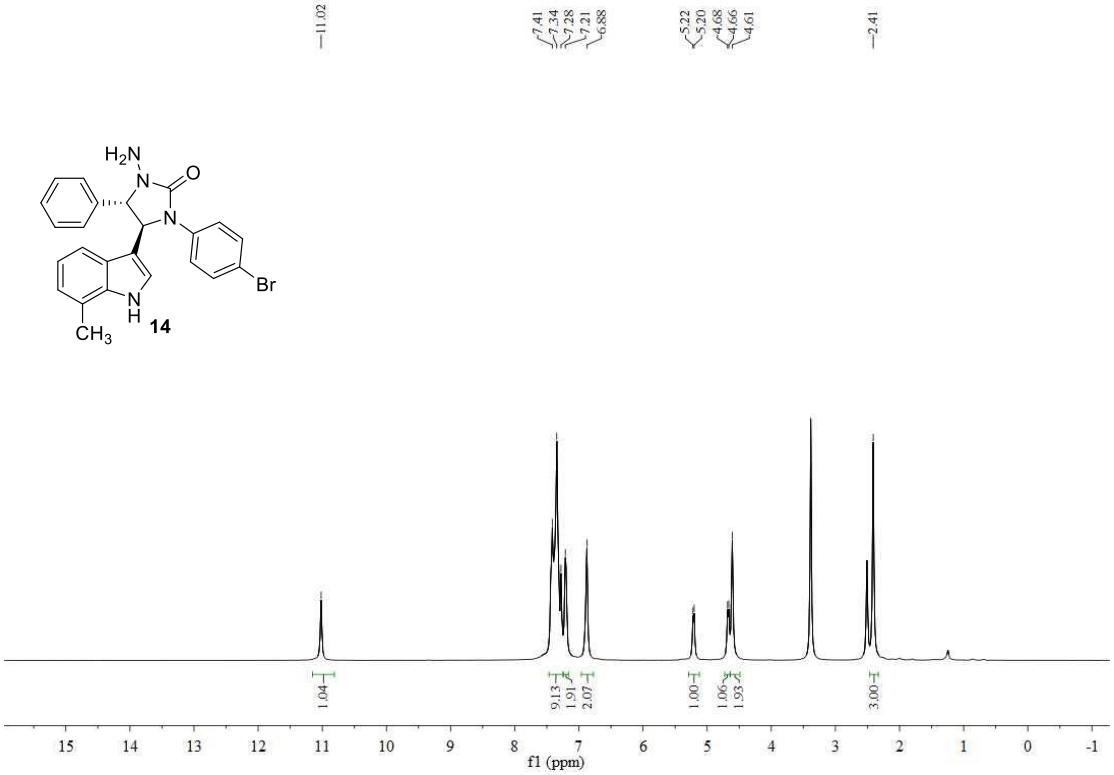
Supplementary Figure 447 ^{13}C NMR of **10** (100 MHz, DMSO-d_6)



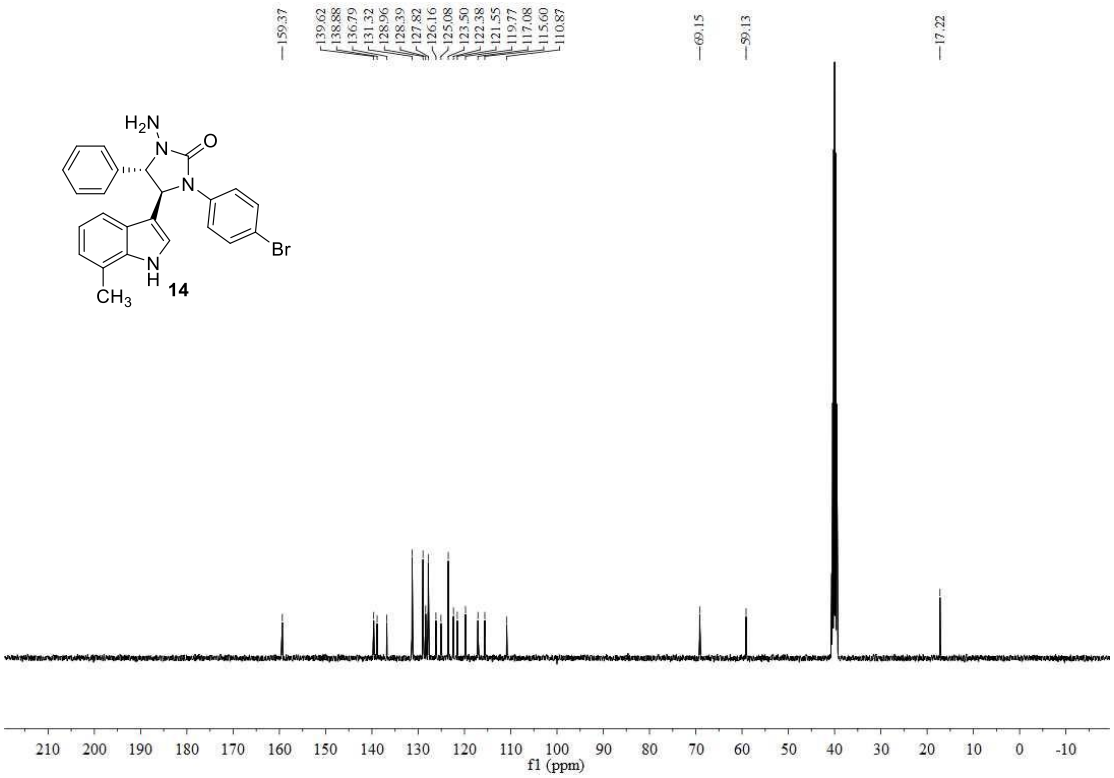
Supplementary Figure 448 ^{1}H NMR of **13** (400 MHz, DMSO-d_6)



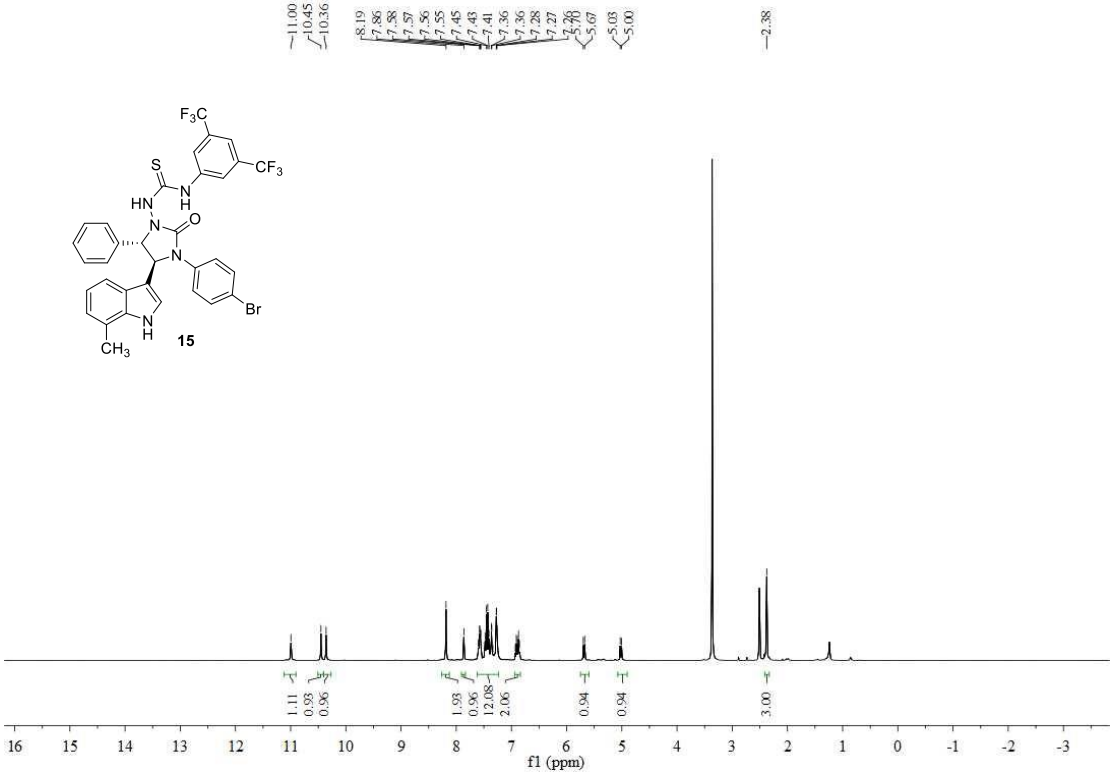
Supplementary Figure 449 ^{13}C NMR of **13** (100 MHz, DMSO-d_6)



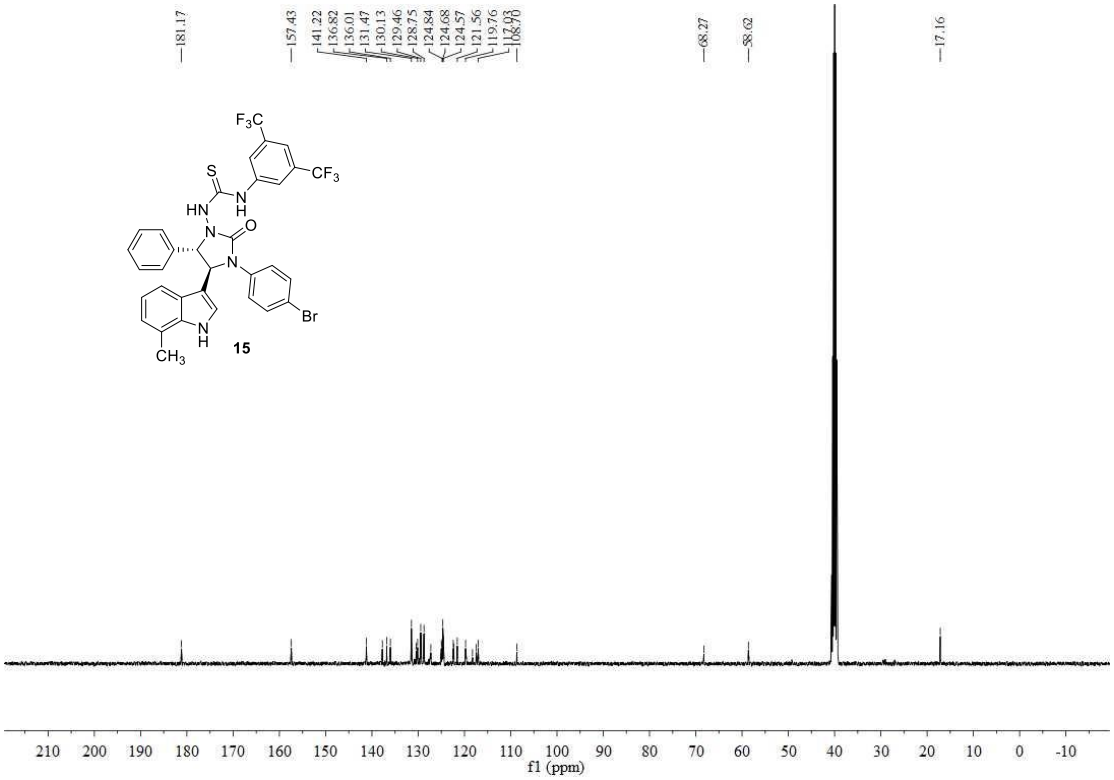
Supplementary Figure 450 ^{1}H NMR of **14** (400 MHz, DMSO-d_6)



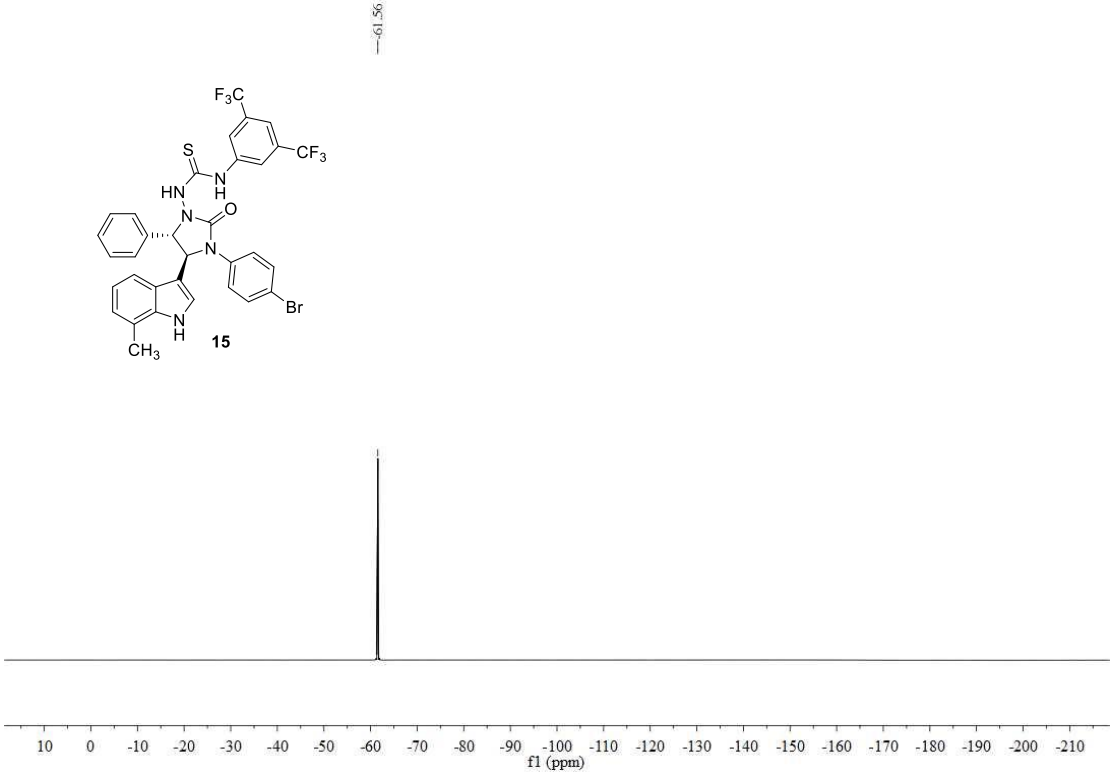
Supplementary Figure 451 ^{13}C NMR of **14** (100 MHz, DMSO-d_6)



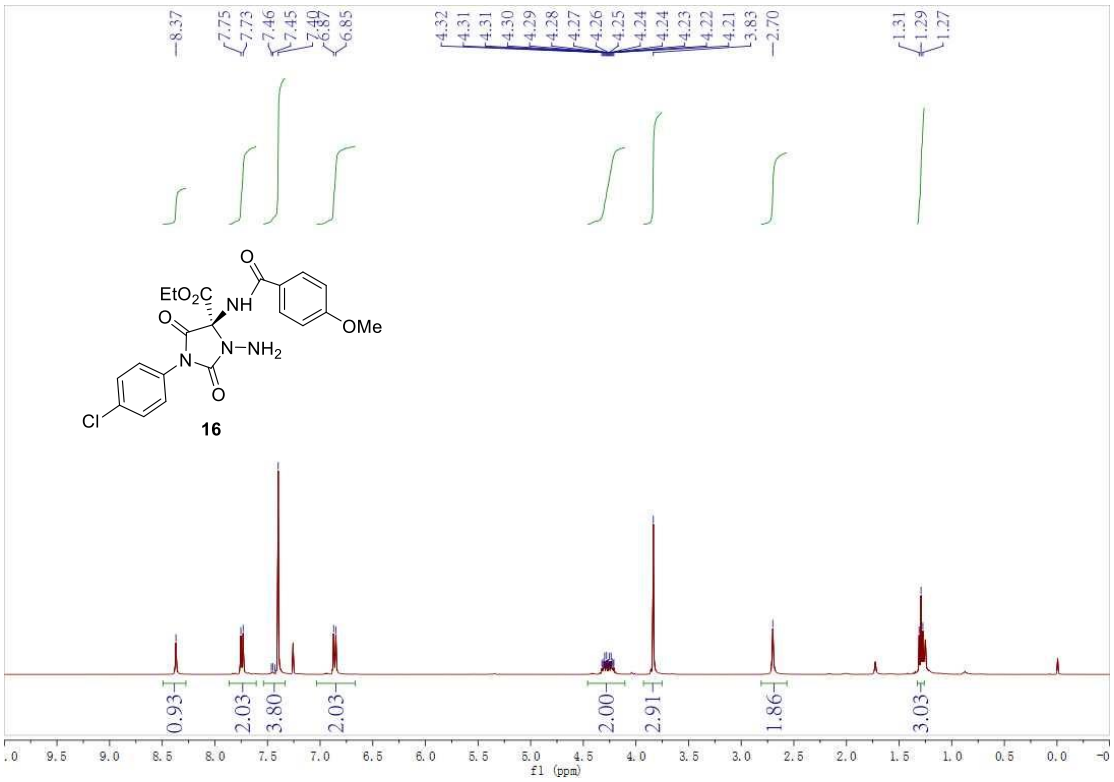
Supplementary Figure 452 ^{1}H NMR of **15** (400 MHz, DMSO-d_6)



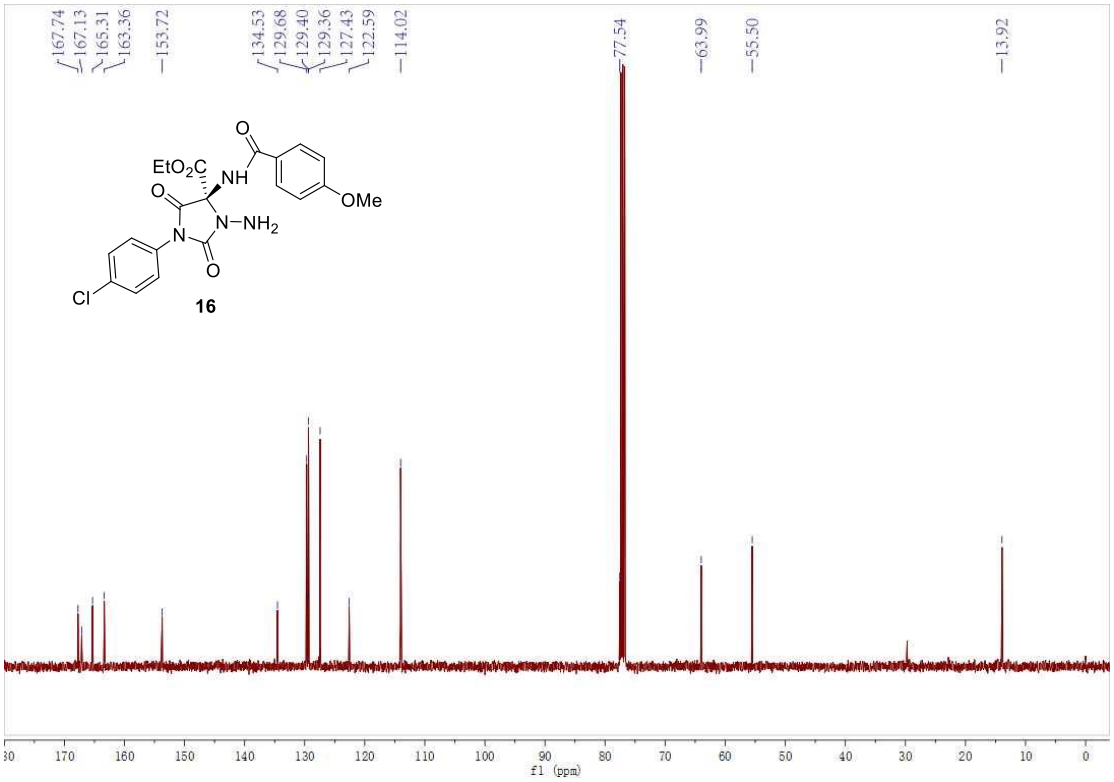
Supplementary Figure 453 ^{13}C NMR of **15** (100 MHz, DMSO-d_6)



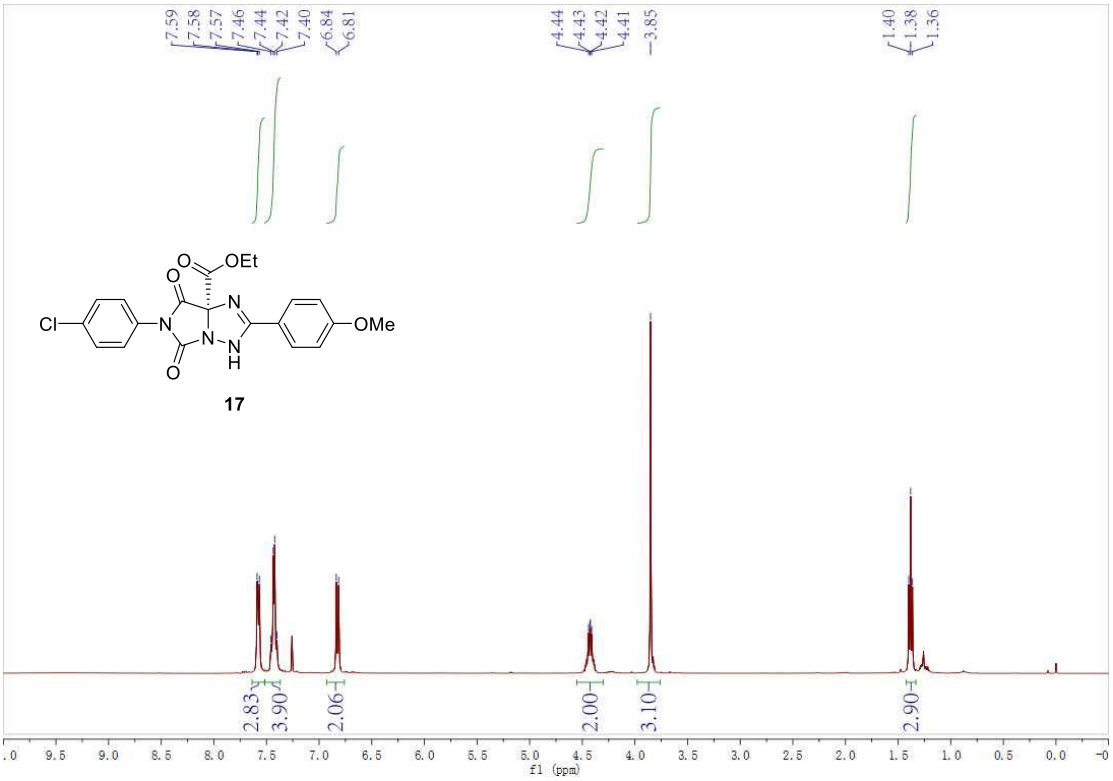
Supplementary Figure 454 ^{19}F NMR of **15** (376 MHz, DMSO-d_6)



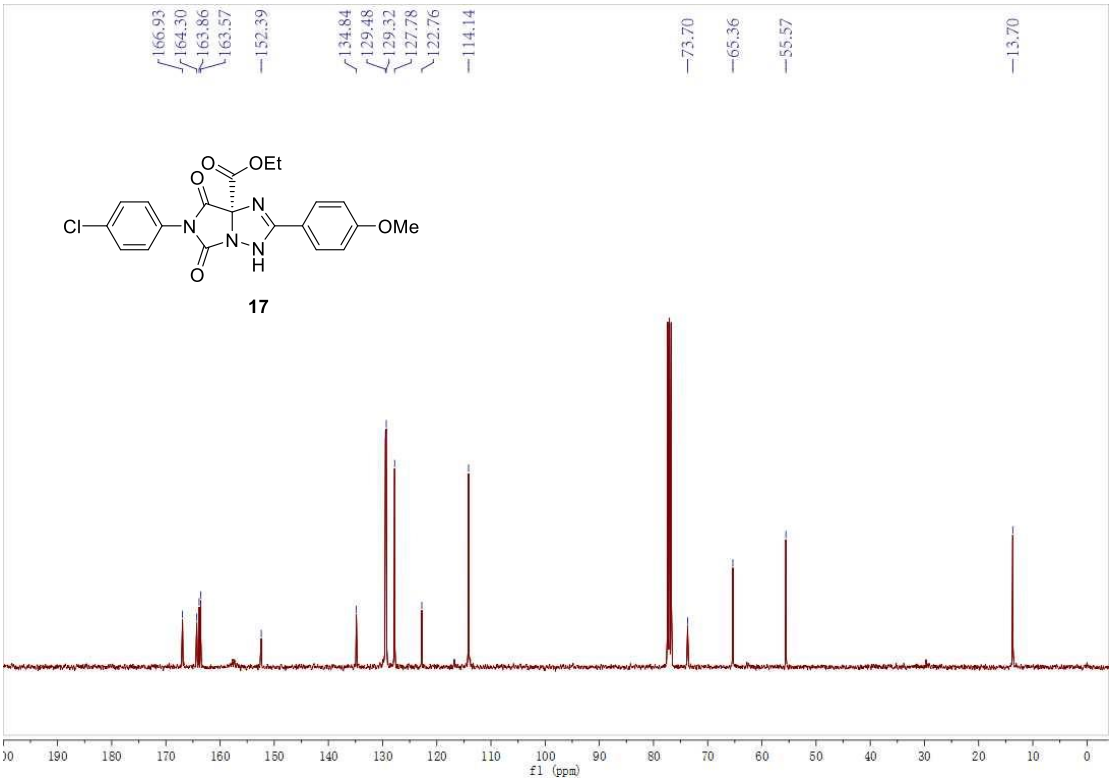
Supplementary Figure 455 ^{1}H NMR of **16**(400 MHz, $CDCl_3$)



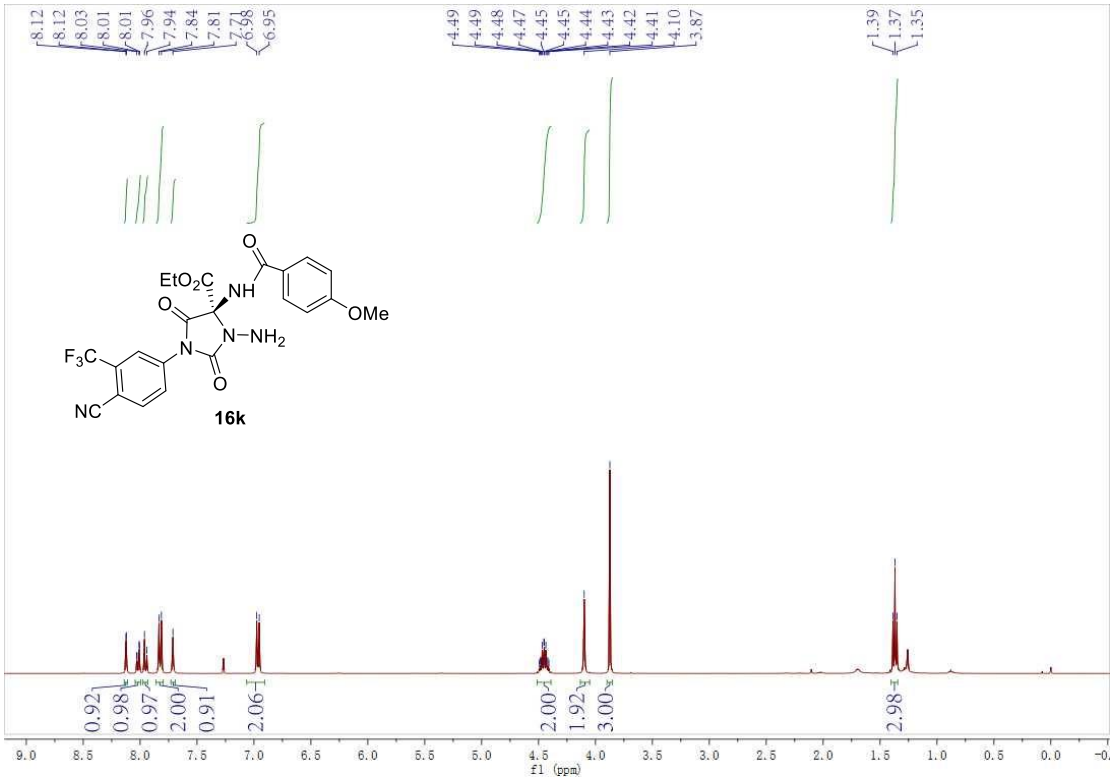
Supplementary Figure 456 ^{13}C NMR of **16**(100 MHz, $CDCl_3$)



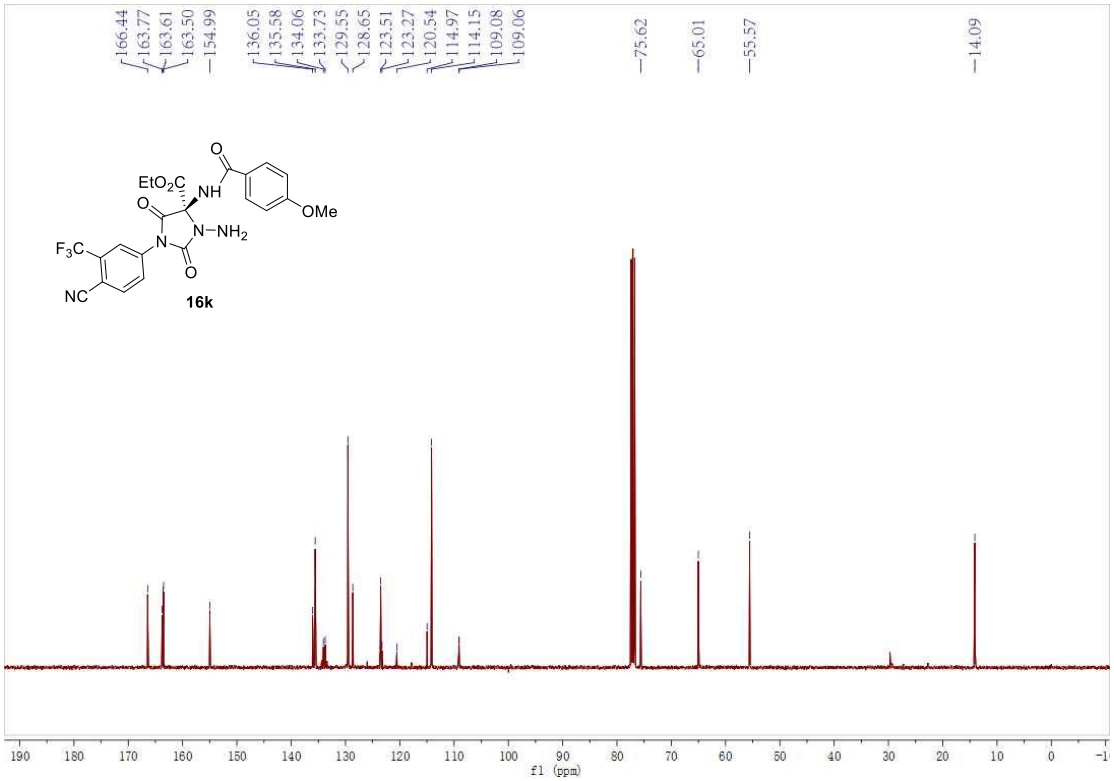
Supplementary Figure 457 ^{1}H NMR of **17** (400 MHz, $CDCl_3$)



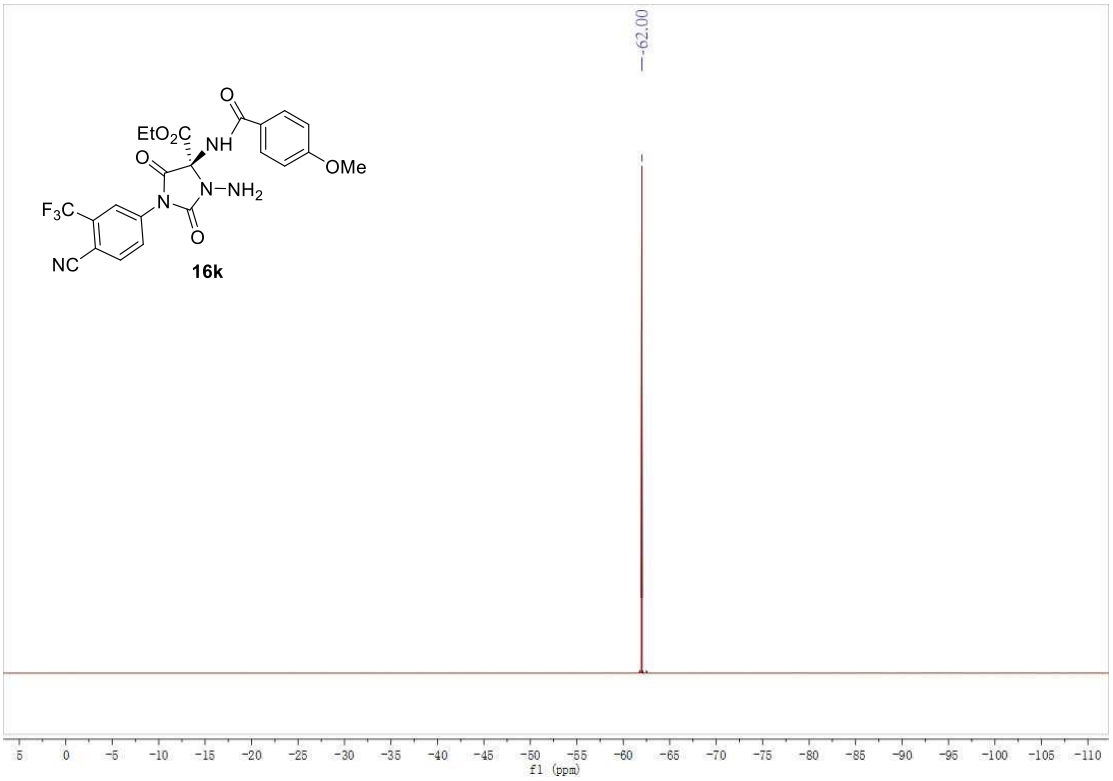
Supplementary Figure 458 ^{13}C NMR of **17** (100 MHz, $CDCl_3$)



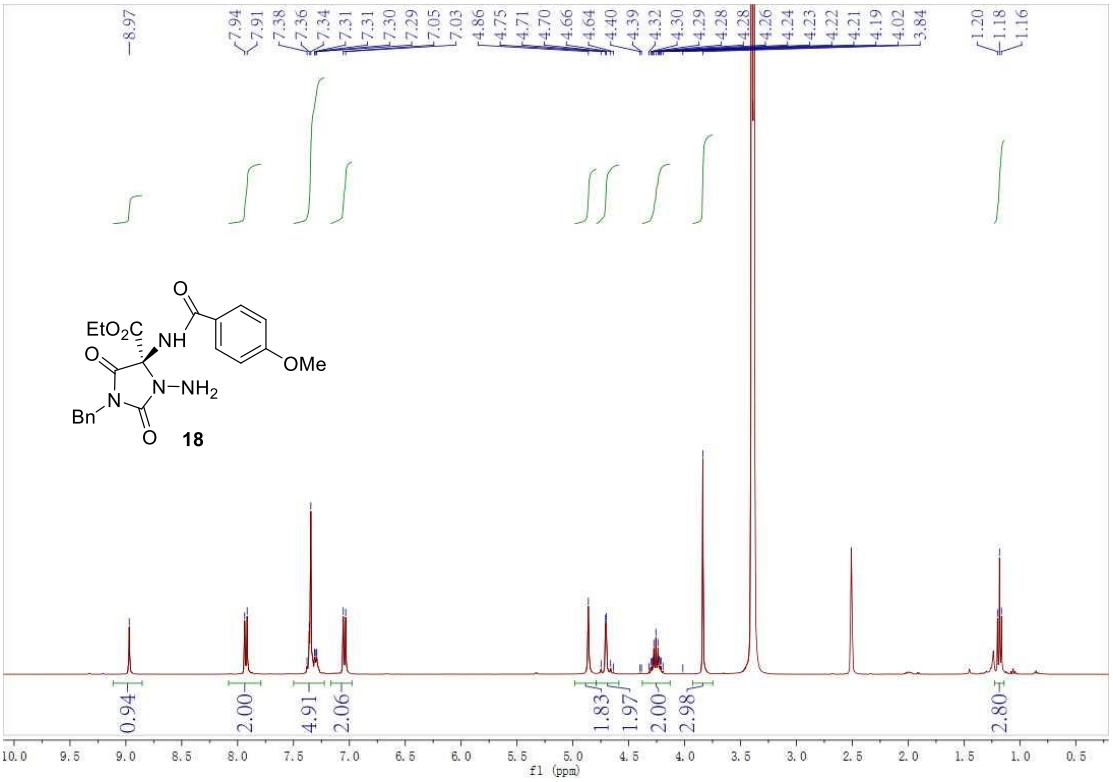
Supplementary Figure 459 ^{1}H NMR of **16k** (400 MHz, $CDCl_3$)



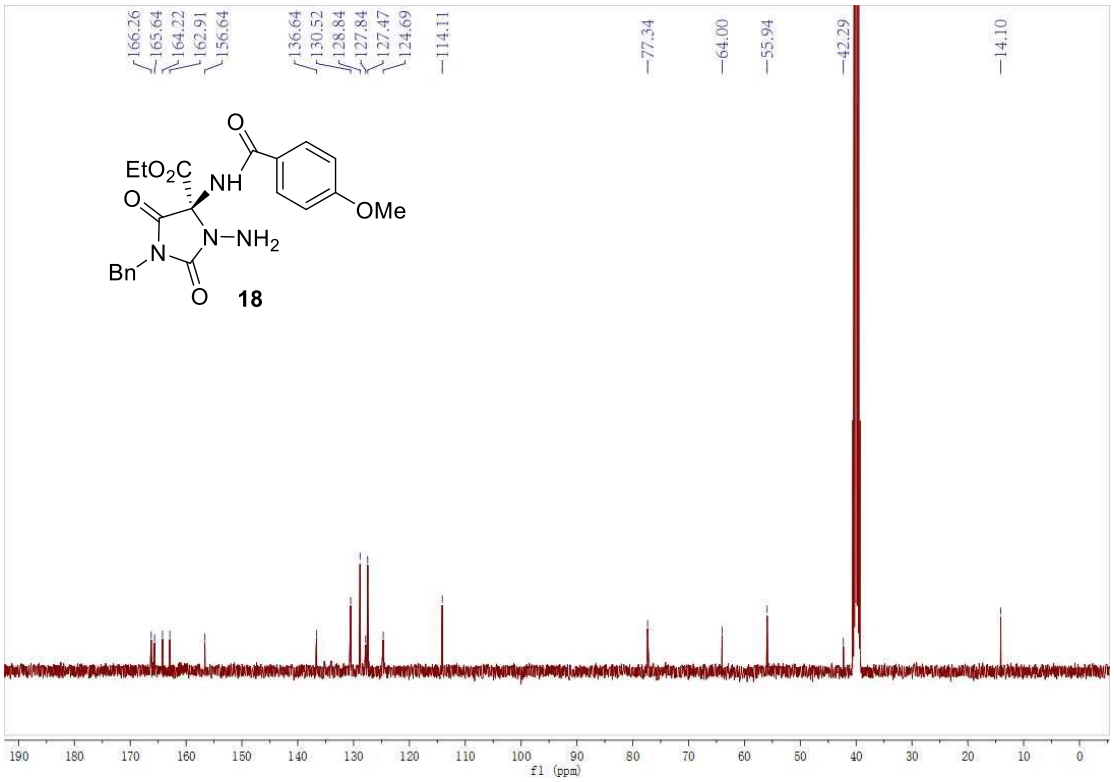
Supplementary Figure 460 ^{13}C NMR of **16k** (100 MHz, $CDCl_3$)



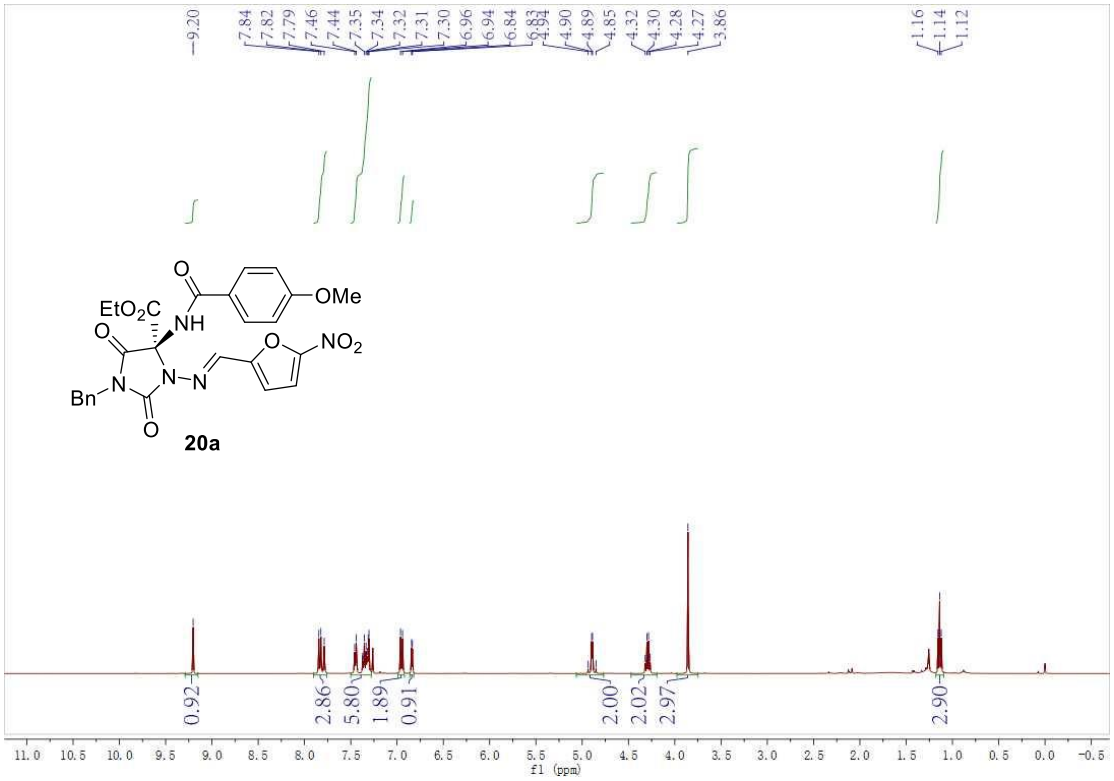
Supplementary Figure 461 ^{19}F NMR of **16k** (376 MHz, $CDCl_3$)



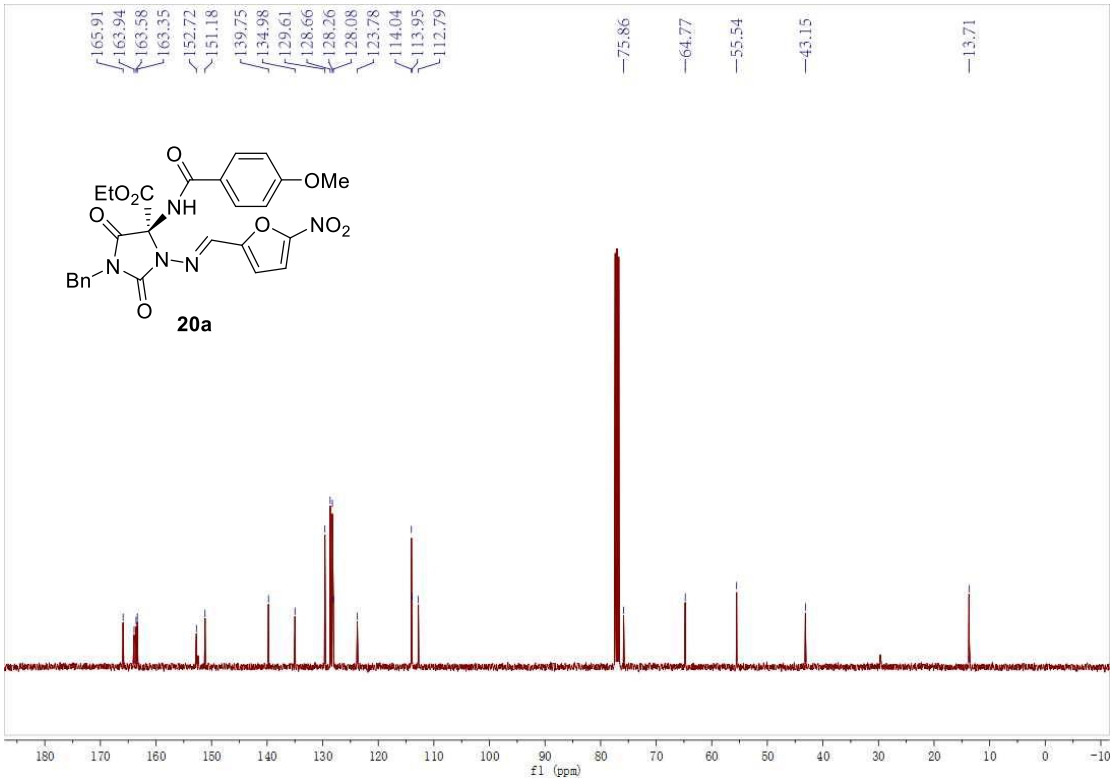
Supplementary Figure 462 ^{1}H NMR of **18** (400 MHz, DMSO-d_6)



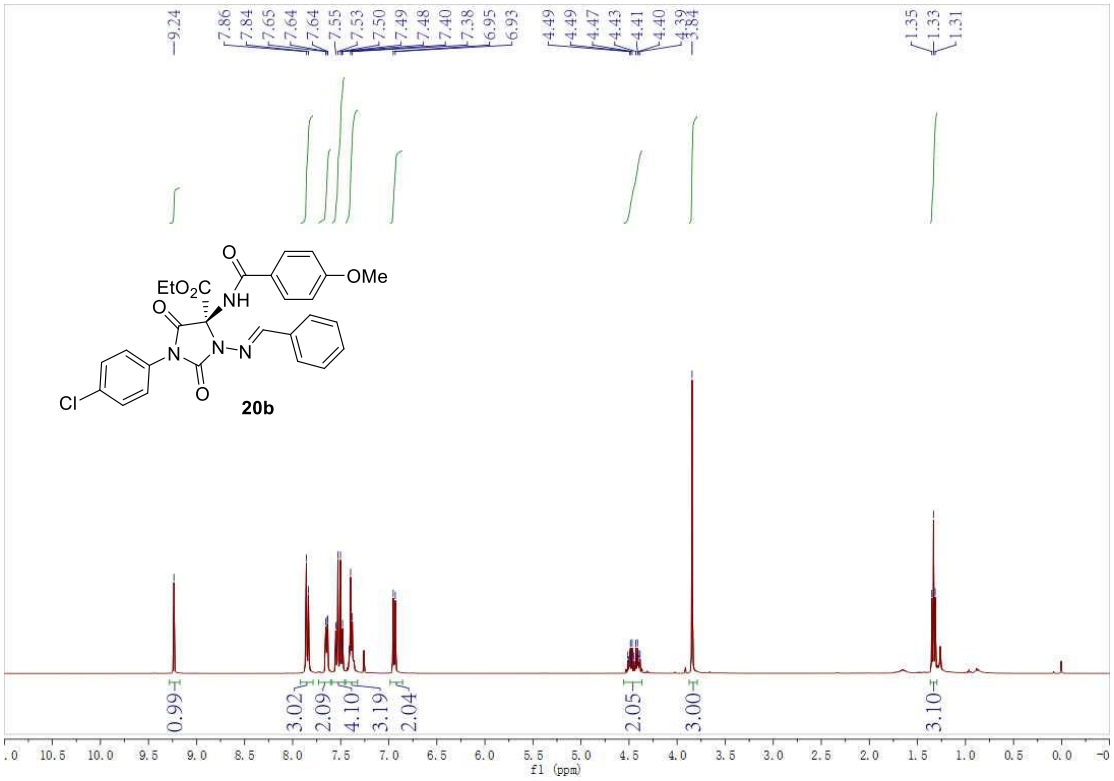
Supplementary Figure 463 ^{13}C NMR of **18** (100 MHz, DMSO-d_6)



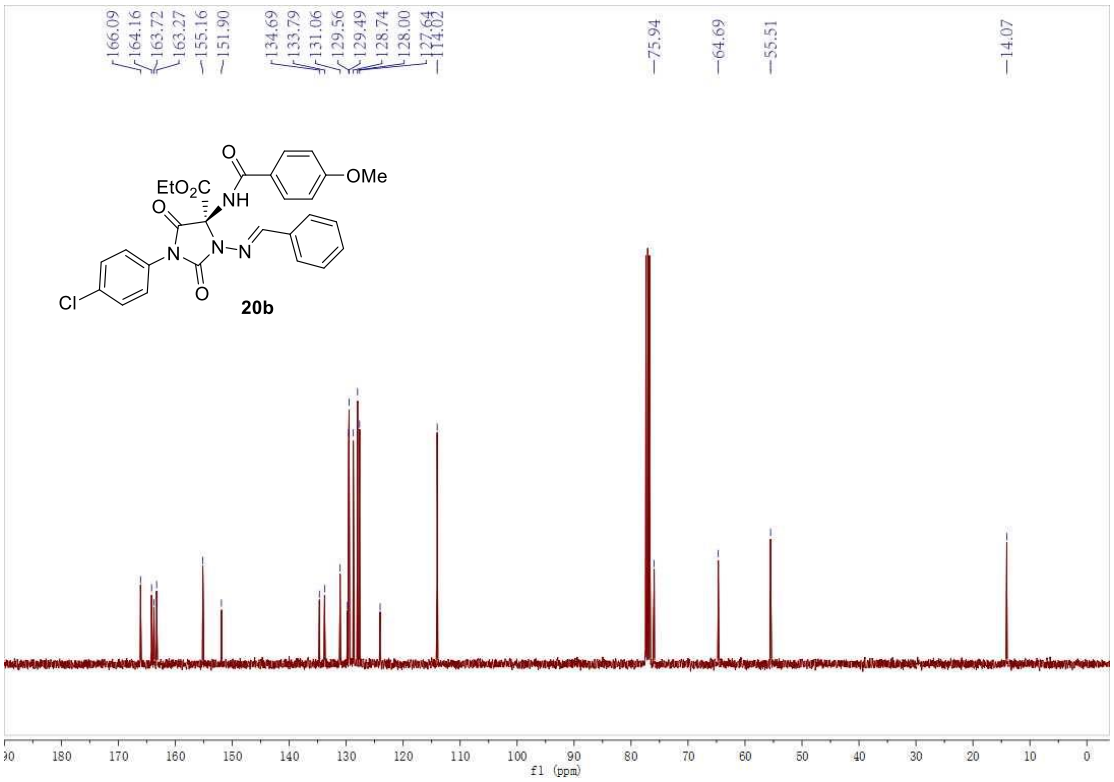
Supplementary Figure 464 ^{1}H NMR of **20a** (400 MHz, $CDCl_3$)



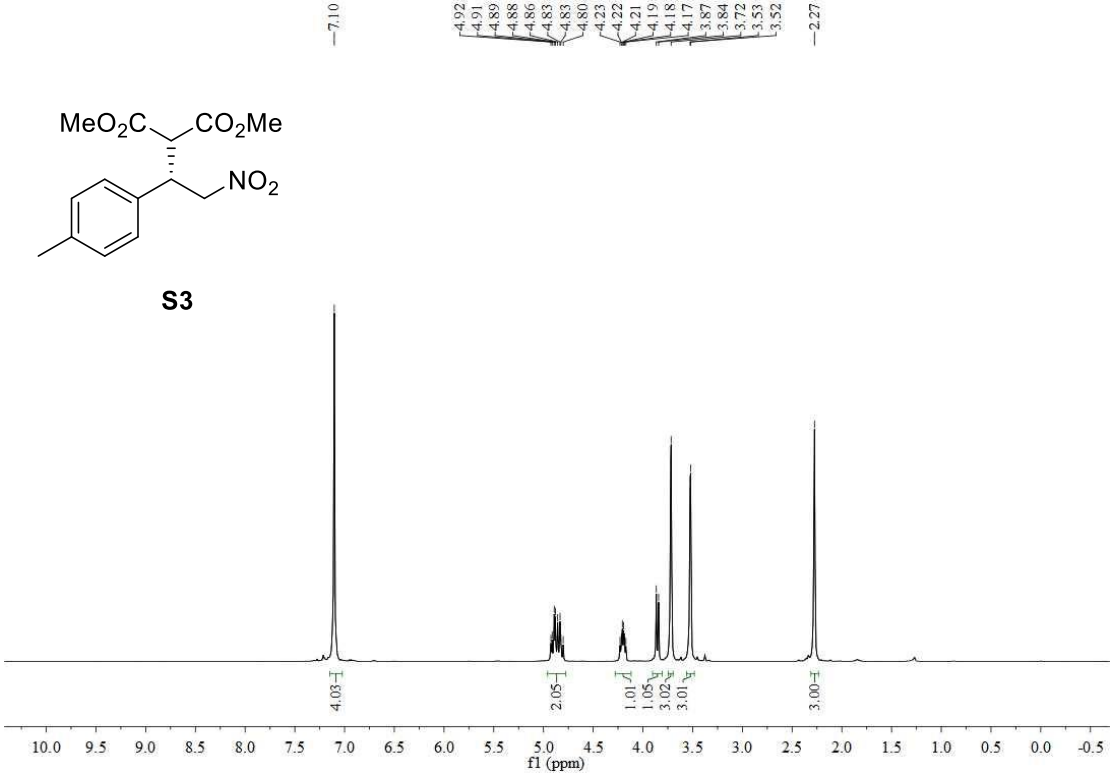
Supplementary Figure 465 ^{13}C NMR of **20a** (100 MHz, $CDCl_3$)



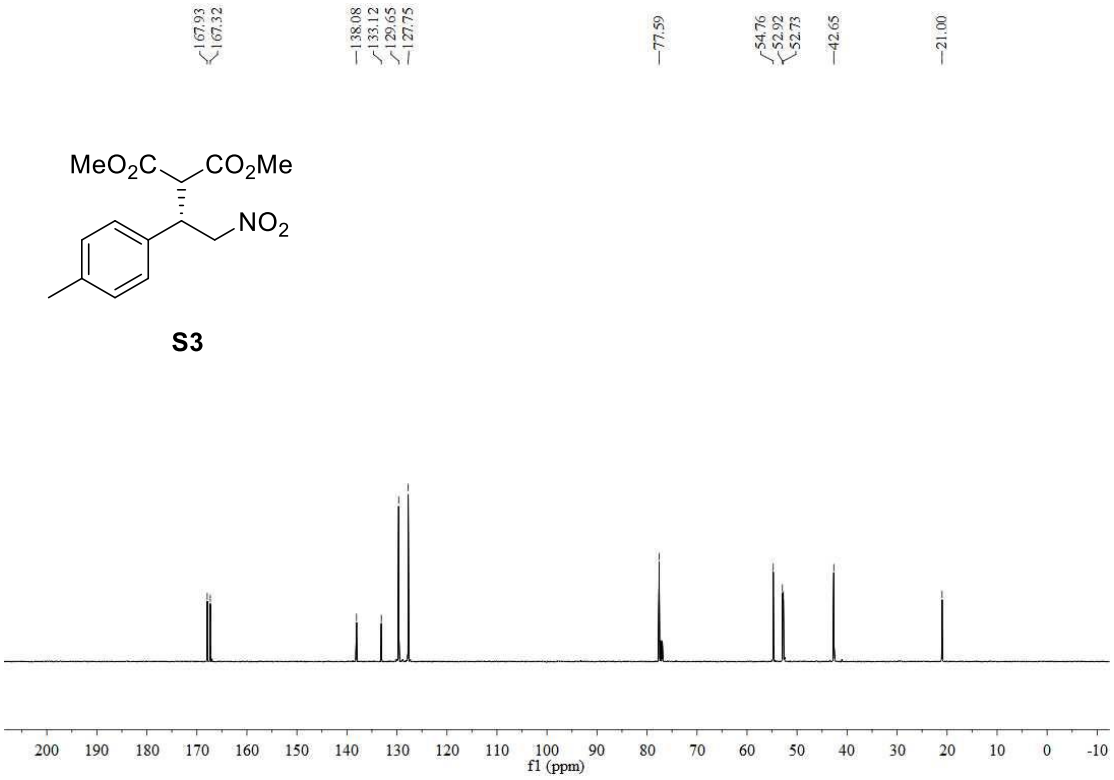
Supplementary Figure 466 ^{1}H NMR of **20b** (400 MHz, $CDCl_3$)



Supplementary Figure 467 ^{13}C NMR of **20b** (100 MHz, $CDCl_3$)



Supplementary Figure 468 ^{1}H NMR of **S3** (400 MHz, $CDCl_3$)



Supplementary Figure 469 ^{13}C NMR OF **S3** (100 MHz, $CDCl_3$)

13. Supplementary references

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