Supporting Information

Highly asymmetric aldol reaction of isatins and ketones catalyzed by chiral bifunctional primary-amine organocatalyst on water

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1. General Experimental Details

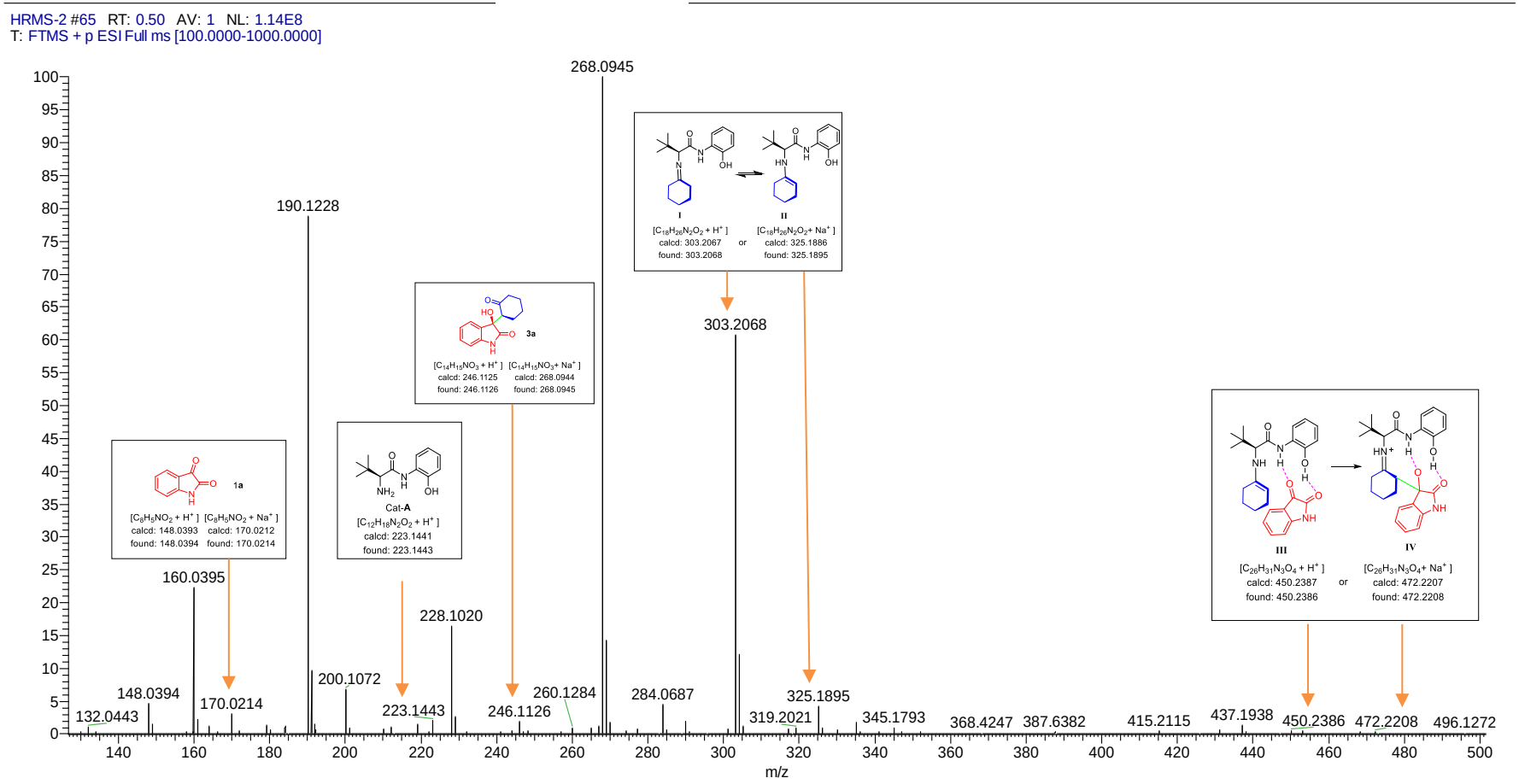
The reactions were carried out in vials and stirred with a magnetic bar without inert atmosphere unless specified. All commercial reagents were purchased with the analysis purity grade. They were used without further purification unless specified.

The reactions were monitored by TLC (thin layer chromatography) method; column and preparative TLC purifications were carried out using silica gel. Melting points were uncorrected and recorded on XT-5 melting point apparatus.

NMR spectra were acquired on a Bruker 400/600 spectrometer, running at 400/600 MHz and 100/151 MHz for ^{1}H and ^{13}C, respectively. NMR in $CDCl_3$, DMSO-d_6 with TMS as an internal standard, chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$, 7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C NMR; DMSO-d_6, 2.50 ppm for ^{1}H NMR, 40.00 ppm for ^{13}C NMR). The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septuplet), m (multiplet), br (broad). High resolution mass spectra (HR-MS) were measured with ESI-Orbitrap mass spectrometer.

Enantiomeric excess (ee) were determined by chiral HPLC, Waters 1525 Binary HPLC.

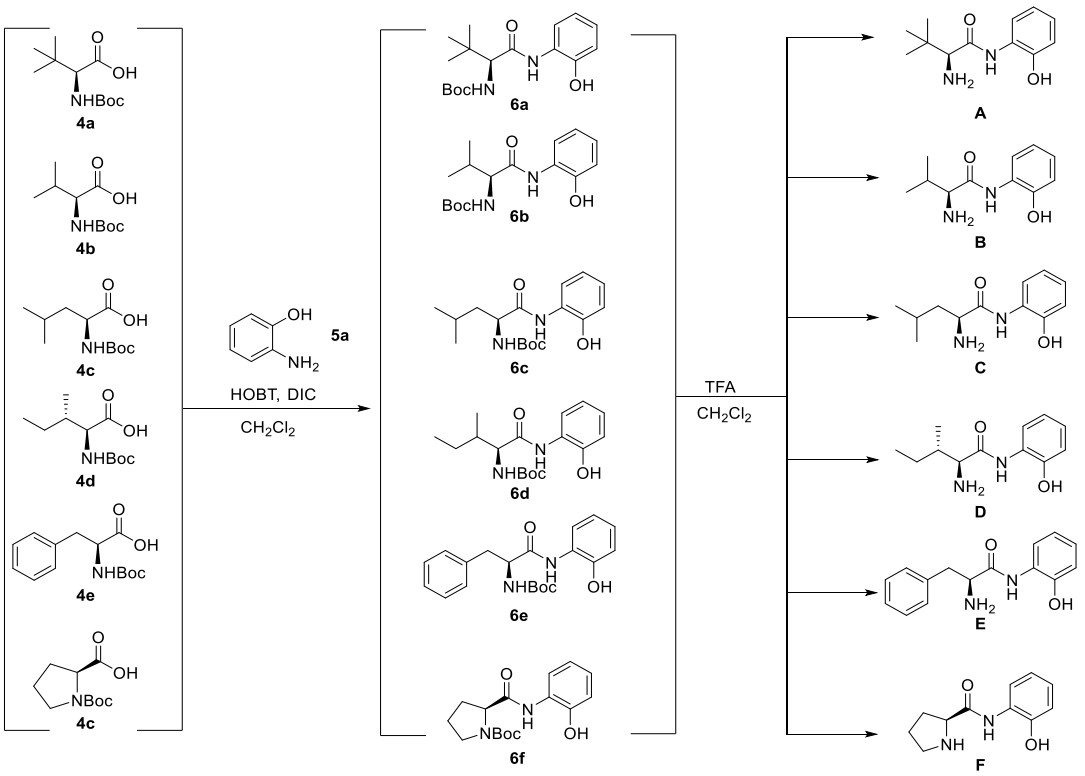
2. HR-MS information of reaction intermediates Reaction mechanism



3. Preparation and characterization of catalysts

The catalyst **C-H** were reported in our previous work [1]

3.1 General procedure for the synthesis of catalyst A-F.

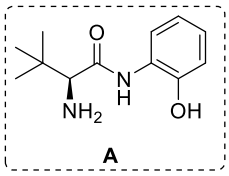


1-hydroxyben-zotriazole (HOBt, 2.97 g, 22 mmol) and Boc-AA-OH **4** (20 mmol) were added to 50 mL dry CH_2Cl_2 in a 100 mL round bottom flask under argon. The reaction mixture was cooled to 0 °C, and DIC (*N*, *N*-diisopropylcarbodiimide) (3.4 mL, 22 mmol) was slowly added dropwise. After 30 min, 2-aminophenol **5a** (20 mmol, 2.18 g) was added and the stirring was continued at this temperature for another 30 min. Then the reaction was warmed to room temperature and the stirring was continued for 48 h. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate again and washed successively with 1.0 M NaOH solution, water, 1.0 M hydrochloric acid solution, saturated brine, dried with anhydrous Na_2SO_4, concentrated under reduced pressure and quickly prepared by column chromatography (petroleum ether: ethyl acetate = 8:1) to give the intermediate amides **6a-6f** (80~95% yield).

The amide **6a-6f** was dissolved in 20 mL CH_2Cl_2. The reaction mixture was cooled to 0 °C, and trifluoroacetic acid (TFA, 20 mL) was slowly added dropwise. After stirring at room temperature for 6 h, the mixture was concentrated under reduced pressure to remove off TFA.

The residue was dissolved in dichloromethane, and added 1.0 M aqueous NaOH at 0 °C to the solution, adjust pH to 9.0, then the organic solution was extracted with dichloromethane (20 mL×3), and then washed with a small amount of saturated brine, dried with $MgSO_4$ and concentrated under reduced pressure to give target catalyst. The catalyst was directly obtained by recrystallization from petroleum ether and ethyl acetate.

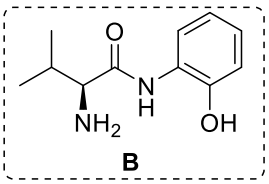
(*S*)-2-Amino-N-(2-hydroxyphenyl)-3,3-dimethylbutanamide (A) [1]



A

Yield 4.0 g, 90% (for 2 steps); White solid; M.p: 152-154 ºC; $[\alpha]_D^{25}$= -32.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.13 – 7.09 (m, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.87 – 6.82 (m, 1H), 3.35 (s, 1H), 1.08 (s, 9H).

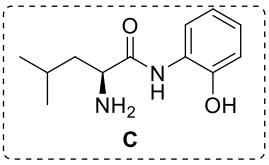
(*S*)-2-amino-N-(2-hydroxyphenyl)-3-methylbutanamide (B) [1]



B

Yield 3.66 g, 88% (for 2 steps); White solid; M.p:147.8-149.0 ºC; $[\alpha]_D^{25}$= - 39.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.83 (s, 2H), 7.15 – 7.08 (m, 1H), 7.02 (dd, J = 8.1, 1.1 Hz, 1H), 6.94 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.86 – 6.82 (m, 1H), 3.47 (d, *J* = 3.6 Hz, 1H), 2.44 – 2.50 (m, 1H), 1.57 (s, 2H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H).

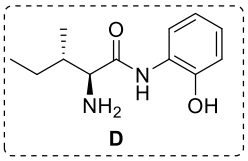
(*S*)-2-Amino-N-(2-hydroxyphenyl)-4-methylpentanamide (C) [1]



C

Yield 3.33 g, 75% (for 2 steps); White solid; M.p:143.4-144.5 ºC; $[\alpha]_D^{25}$= - 17.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.04 – 6.91, 6.84 (t, *J* = 7.2 Hz, 1H), 3.57 (d, *J* = 9.0 Hz, 1H), 1.87 – 1.74 (m, 2H), 1.49 – 1.41 (m, 1H), 0.99 (dd, *J* = 15.6, 6.0 Hz, 6H).

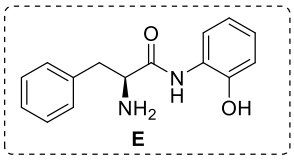
(2*S*)-2-amino-N-(2-hydroxyphenyl)-3-methylpentanamide (D) [1]



D

Yield 3.1 g, 70% (for 2 steps); White solid; M.p:115 -117 °C; $[\alpha]_D^{25}$= - 22.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 2H), 7.13 – 7.07 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.98 – 6.93 (m, 1H), 6.87 – 6.80 (m, 1H), 3.49 (d, *J* = 3.6 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.59 (s, 2H), 1.45 – 1.38 (m, 1H), 1.19 – 1.12 (m, 1H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H).

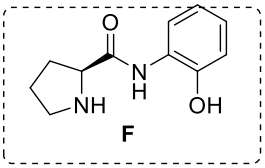
(*S*)-2-amino-N-(2-hydroxyphenyl)-3-phenylpropanamide (E) [1]



E

Yield 4.25 g, 83% (for 2 steps); White solid; M.p:133.8-135.2 °C; $[\alpha]_D^{25}$= - 83 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 – 9.49 (m, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.31 – 7.23 (m, 3H), 7.15 – 7.10 (m, 2H), 7.06 – 7.00 (m, 1H), 6.92 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.86 – 6.82 (m, 1H), 3.82 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.36 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.85 (dd, *J* = 13.8, 9.0 Hz, 1H), 1.59 (s, 2H).

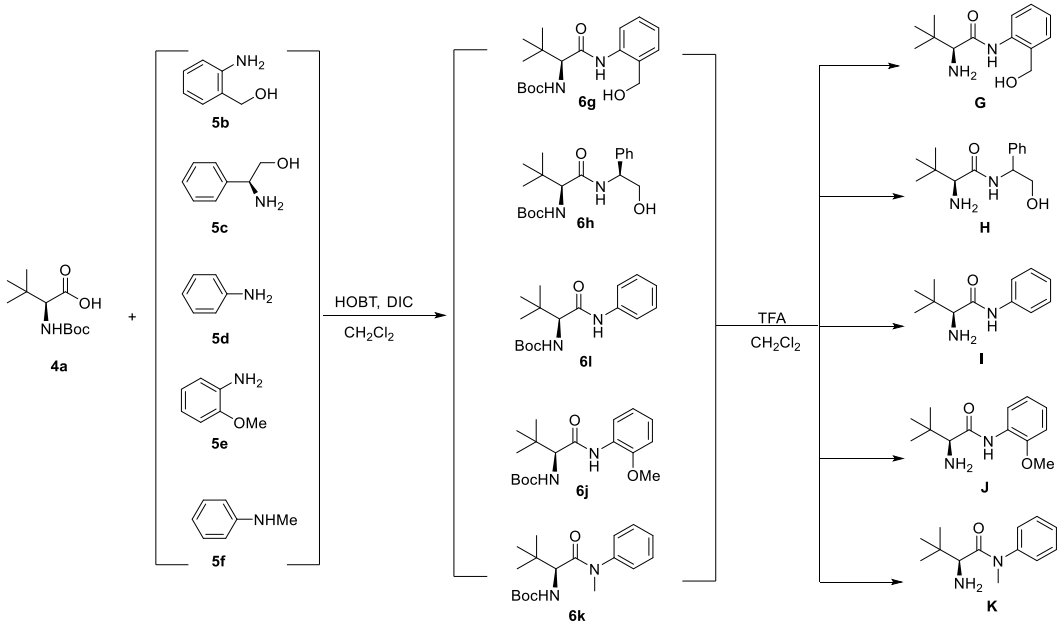
(*S*)-N-(2-hydroxyphenyl) pyrrolidine-2-carboxamide (F) [1]



F

Yield 3.13 g, 76% (for 2 steps); White solid; M.p:169.5-170.8 °C; $[\alpha]_D^{25}$= - 24.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.98 (s, 2H), 7.13 – 7.08 (m, 1H), 7.00 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.91 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.86 – 6.81 (m, 1H), 3.93 (dd, *J* = 9.6, 4.8 Hz, 1H), 3.14 – 3.08 (m, 1H), 3.04 – 3.99 (m, 1H), 2.36 – 2.16 (m, 2H), 2.08 – 2.02 (m, 1H), 1.86 – 1.72 (m, 2H), 1.59 – 1.63 (m, 1H)

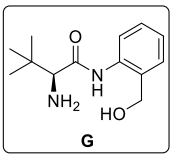
3.2 The procedure for the synthesis of catalyst G-K



1-hydroxyben-zotriazole (HOBt, 2.97 g, 22 mmol) and Boc-Tle-OH **4a** (20 mmol, 4.620 g) were added to 50 mL dry CH_2Cl_2 in a 100 mL round bottom flask under argon. The reaction mixture was cooled to 0 °C, and DIC (*N*, *N*-diisopropylcarbodiimide) (3.4 mL, 22 mmol) was slowly added dropwise. After 0.5 h, the amine **5** (20 mmol) was added and the stirring was continued at this temperature for another 0.5 h. Then the reaction was warmed to room temperature and the stirring was continued for 48 h. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate again and washed successively with 1.0 M NaOH solution, water, 1.0 M hydrochloric acid solution, saturated brine, dried with anhydrous Na_2SO_4, concentrated under reduced pressure and quickly prepared by column chromatography (petroleum ether: ethyl acetate = 8:1) to give the intermediate amides **6g-6k**.

The amide **6g-6k** were dissolved in 20 mL CH_2Cl_2. The reaction mixture was cooled to 0 °C, and trifluoroacetic acid (TFA, 20 mL) was slowly added dropwise. After stirring at room temperature for 6 h, the mixture was concentrated under reduced pressure to remove off TFA. The residue was dissolved in dichloromethane, and added 1.0 M aqueous NaOH at 0 °C to the solution, adjust pH to 9.0, then the organic solution was extracted with dichloromethane (20 mL×3), and then washed with a small amount of saturated brine, dried with $MgSO_4$ and concentrated under reduced pressure to give target catalyst. The catalyst was directly obtained by recrystallization from petroleum ether and ethyl acetate.

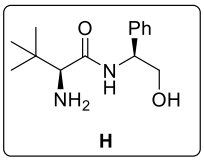
(*S*)-2-amino-N-(2-(hydroxymethyl)phenyl)-3,3-dimethylbutanamide (G)



G

Yield 4.01 g, 85% (for 2 steps); White solid; M.p:134.6-135.4 °C; $[\alpha]_D^{25}$= + 62.08 (*c* = 0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.14 (s, 1H), 8.38 (s, 3H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.30 - 7.15 (m, 2H), 4.54 (s, 2H), 4.02 (d, *J* = 5.2 Hz, 1H), 3.60 (t, *J* = 6 Hz, 1H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ 167.0, 136.4, 134.4, 128.2, 127.4, 126.0, 125.1, 67.5, 60.9, 60.0, 40.6, 40.4, 40.2, 40.0, 39.8, 39.6, 33.6, 26.9, 25.6; HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{20}N_2O_2Na$ 259.1422, found: 259.1415.

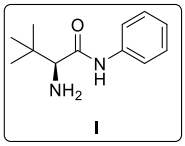
(*S*)-2-amino-N-((S)-2-hydroxy-1-phenylethyl)-3,3-dimethylbutanamide(H)



H

Yield 3.90 g, 78% (for 2 steps); White solid; M.p: 114.6-115.9 °C; $[\alpha]_D^{25}$= 124.48 (*c* = 0.25, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 6.8 Hz, 1H), 7.40 – 7.22 (m, 5H), 5.10 – 5.00 (m, 1H), 3.91 – 3.78 (m, 2H), 3.13 (s, 1H), 2.25 (s, 2H), 0.97 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 139.2, 128.8, 127.8, 126.8, 66.7, 64.3, 55.8, 34.26, 26.8; HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{22}N_2O_2Na$ 273.1579, found:273.1577.

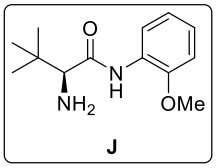
(*S*)-2-amino-3,3-dimethyl-N-phenylbutanamide (I) [1]



I

Yield 3.3 g, 80% (for 2 steps); White solid; M.p: 222 - 224 °C; $[\alpha]_D^{25}$= +38 (*c* = 1.0, MeOH); ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 10.97 (s, 1H), 8.38 (s, 2H), 7.68 – 7.62 (m, 2H), 7.33 – 7.28 (m, 2H), 7.07 (dd, *J* = 8.8, 4.9 Hz, 1H), 3.92 (s, 1H), 3.34 (s, 1H), 1.04 (s, 9H).

(*S*)-2-amino-N-(2-methoxyphenyl)-3,3-dimethylbutanamide (J)

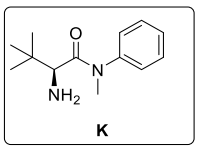


J

Yield 4.48 g, 95% (for 2 steps); White solid; M.p: 168-170 °C; $[\alpha]_D^{25}$= 16.40 (*c* = 0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.69 (s, 1H), 8.16 (d, *J* = 8 Hz, 1H), 7.04 (d, *J* = 4 Hz, 2H),

6.94 – 6.87 (m, 1H), 3.84 (s, 3H), 3.19 (s, 1H), 2.64 (s, 2H), 0.97 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 149.2, 127.7, 124.1, 120.9, 120.3, 111.4, 64.2, 56.3, 39.38, 34.5, 27.2; HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{20}N_2O_2Na$ 259.1422, found:259.1420.

(S)-2-amino-N-(2-hydroxyphenyl)-N,3,3-trimethylbutanamide (K)



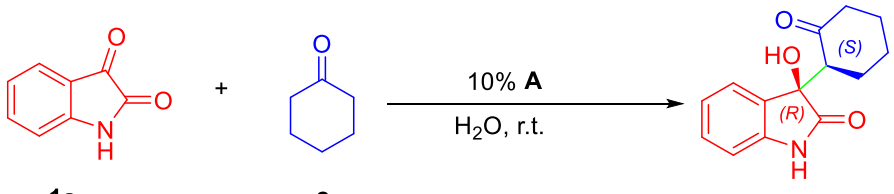
K

Yield 3.61 g, 82% (for 2 steps); White solid; M.p: 188.2-190.1 °C; $[\alpha]_D^{25}$ = -273.36 (*c* = 0.25, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 3H), 7.70 – 7.30 (m, 5H), 3.94 (d, *J* = 5.6 Hz, 1H), 3.34 (s, 3H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 142.7, 130.2, 128.3, 128.0, 57.6, 38.5, 34.6, 26.8; HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{22}N_2ONa$ 243.1473, found:243.1469.

4. General procedure for the Aldol reaction

4.1 The effect of the amount of water on the stereoselectivity and yield of the reaction

S-Table 1 Optimization of the amount of water.

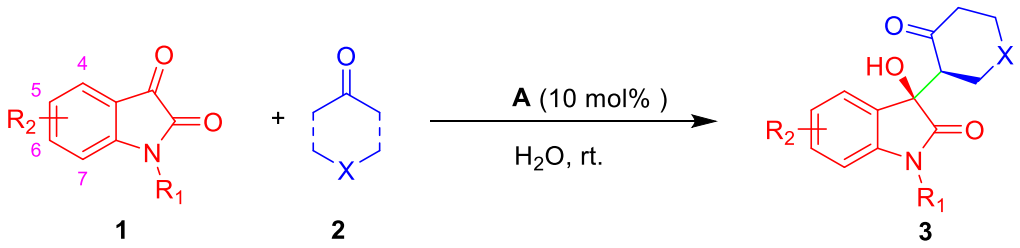


1a **2a** *syn*-**3a**

entry	H_2O (mL)	Time (h)	Yield (%)[b]	dr [c] (*syn*: *anti*)	*ee* (%)[d]
1	0.5	48	95	97:3	97
2	1.0	48	98	98:2	98
3	2.0	48	98	98:2	97
4	3.0	48	96	98:2	98
5	4.0	48	97	97:3	97
6	5.0	48	96	97:3	96

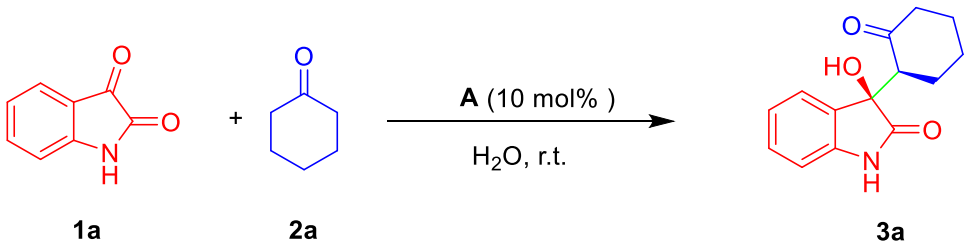
[a] **1a** (0.5 mmol), **2a** (1.0 mmol) were used; [b] isolated yields are reported; [c] dr (*syn*: *anti*) was determined by chiral HPLC; [d] the ee of *syn*-**3a** was determined by chiral HPLC (absolute configuration is inferred from the single-crystal structure of **3d**).

4.2. General procedure for synthesis of product **3**



In a 5 mL reaction flask equipped with a magnetic stirrer, catalyst **A** (11 mg, 0.05 mmol, 10%) and isatins **1** (0.5 mmol) were added, then 1.0 mL water and ketone (1.0 mmol) was added dropwise then. The reaction mixture was stirred at room temperature and detected by TLC. After the reaction was completed, the reaction mixture was purified by column chromatography on silica gel (CH_2Cl_2: MeOH = 100:1~50:1) to give **3a – 3s**.

4.3. Scale-up reaction and reuse of catalyst



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

In a 50 mL round bottomed flask equipped with a magnetic stirrer, catalyst **A** (222 mg, 1.0 mmol, 10%) and isatins **1a** (1.47g, 10 mmol) were added, then 20 mL water and cyclohexanone (2 mL, 20 mmol) was added dropwise then. The reaction mixture was stirred at room temperature until completed. After the reaction was completed, the mixture was filtered directly to give product **3a**, and the solution is directly used in the next cycle.

(a) Reaction in progress

（b）The reaction was completed

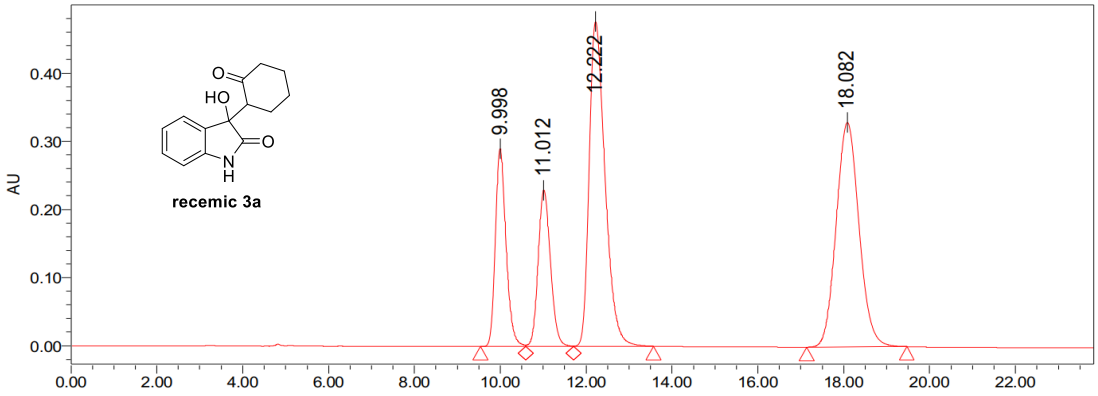
S-Table 1 Recovery and Reuse of Catalyst **A**

Run	time （h）	yield %	dr	ee %
1	48	98	99:1	96
2	48	96	99:1	93
3	72	85	99:1	93

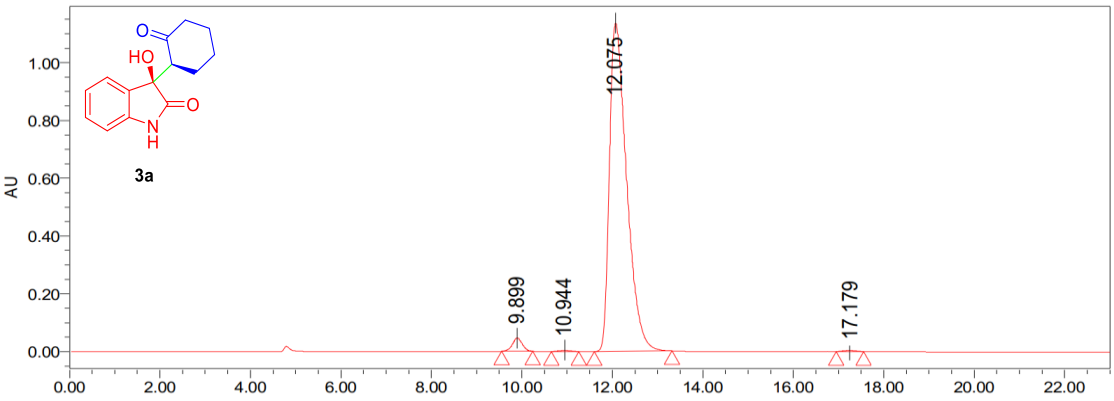
5. Characterization of Aldol reaction products

(*R*)-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3a) [2]

3a: white solid, 120 mg, 98% yield, 98:2dr, 99% ee, $[\alpha]_D^{25}$ = 44.64 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.16 – 7.12 (m, 1H), 6.85 – 6.81 (m, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 5.78 (s, 1H), 3.08 – 3.03 (m, 1H), 2.61 – 2.55 (m, 1H), 2.33 – 2.24 (m, 1H), 2.04 – 1.87 (m, 3H), 1.85 – 1.76 (m, 1H), 1.70 – 1.59 (m, 1H), 1.49 – 1.38 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=80:20; flow rate 1.0 mL/min; 254 nm; retention time: 17.2 min (minor) and 12.1 min (major).



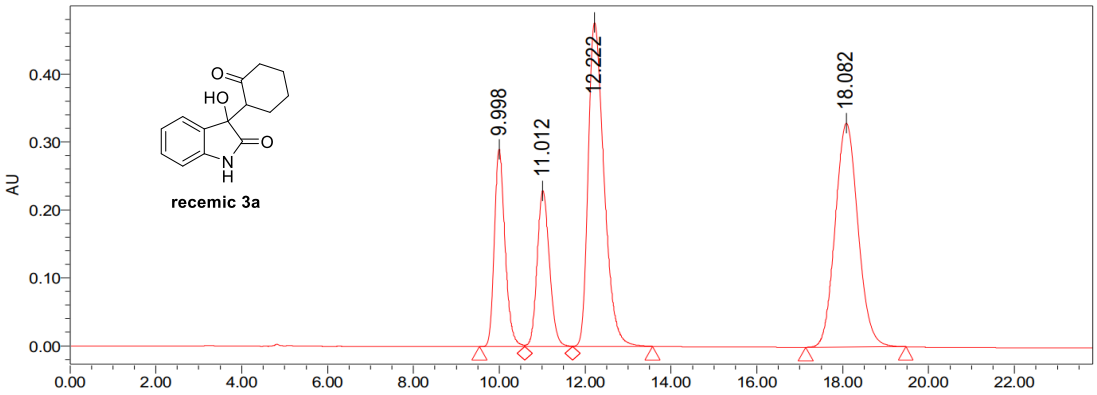
	name	Retention	Area(μV*s)	Height	% Area
1		9.998	4992029	290132	14.71
2		11.012	4560492	229170	13.43
3		12.222	12206981	476518	35.96
4		18.082	12187889	329200	35.90



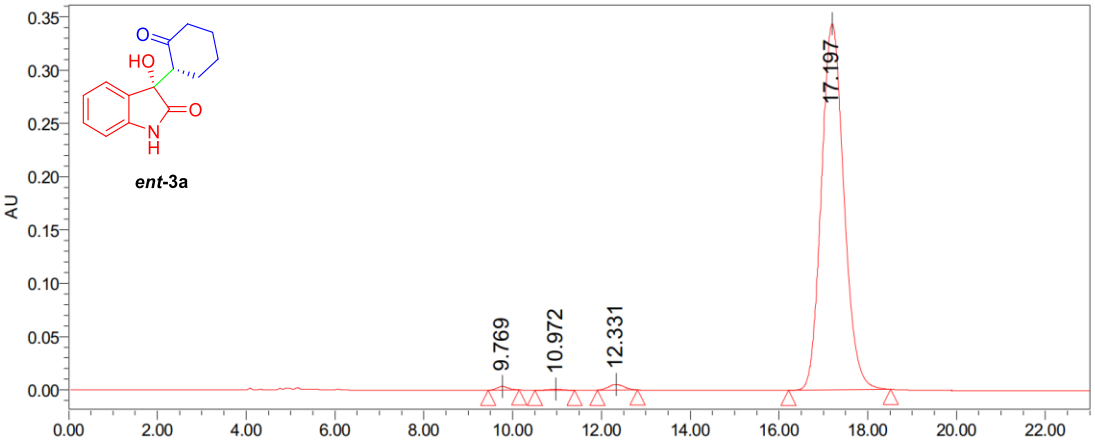
	name	Retention	Area(μV*s)	Height	% Area
1		9.899	697998	46149	1.98
2		10.944	78604	4428	0.22
3		12.075	29746330	1136296	97.57
4		17.179	4753908	4475	0.23

(*S*)-3-hydroxy-3-((*R*)-2-oxocyclohexyl) indolin-2-one (*ent*-3a) [2]

***ent*-3a**: white solid, 120 mg, 98% yield, 99:1 dr, 99% ee, $[\alpha]_D^{25}$ = -44.72 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.16 – 7.12 (m, 1H), 6.85 – 6.81 (m, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 5.78 (s, 1H), 3.08 – 3.03 (m, 1H), 2.61 – 2.55 (m, 1H), 2.33 – 2.24 (m, 1H), 2.04 – 1.87 (m, 3H), 1.85 – 1.76 (m, 1H), 1.70 – 1.59 (m, 1H), 1.49 – 1.38 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=80:20; flow rate 1.0 mL/min; 254 nm; retention time: 12.3 min (minor) and 17.2 min (major).



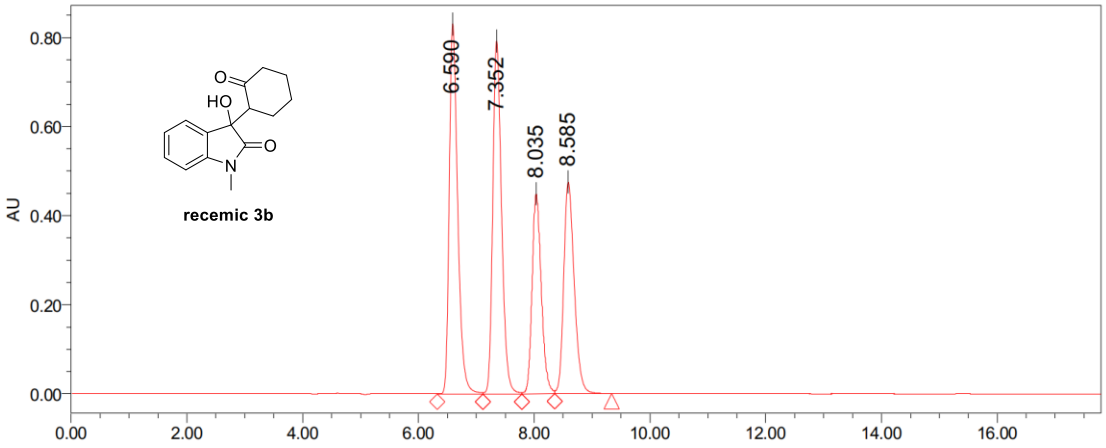
	name	Retention	Area(μV*s)	Height	% Area
1		9.998	4992029	290132	14.71
2		11.012	4560492	229170	13.43
3		12.222	12206981	476518	35.96
4		18.082	12187889	329200	35.90



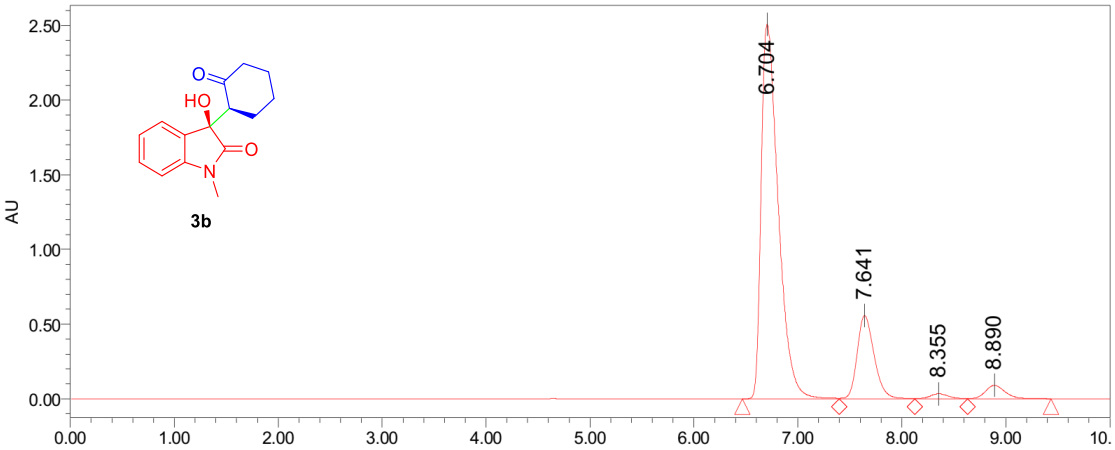
	name	Retention	Area(μV*s)	Height	% Area
1		9.769	57933	3369	0.47
2		10.972	19688	979	0.16
3		12.331	126329	5256	1.03
4		17.197	12046194	343594	98.34

(*R*)-3-hydroxy-1-methyl-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3b) [2]

3b: white solid, 117 mg, 90% yield, 96:4 dr, 64% ee, $[\alpha]_D^{25}$ = 59.84 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.37 – 7.20 (m, 2H), 7.02 – 6.87 (m, 2H), 5.89 (s, 1H), 3.20 – 3.02 (m, 3H), 2.68 – 2.56 (m, 1H), 2.35 – 2.25 (m, 1H), 2.08 – 1.75 (m, 4H), 1.75 – 1.60 (m, 1H), 1.51 – 1.36 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=80:20; flow rate 1.0 mL/min; 254 nm; retention time: 6.6 min (major) and 7.4 min (minor).



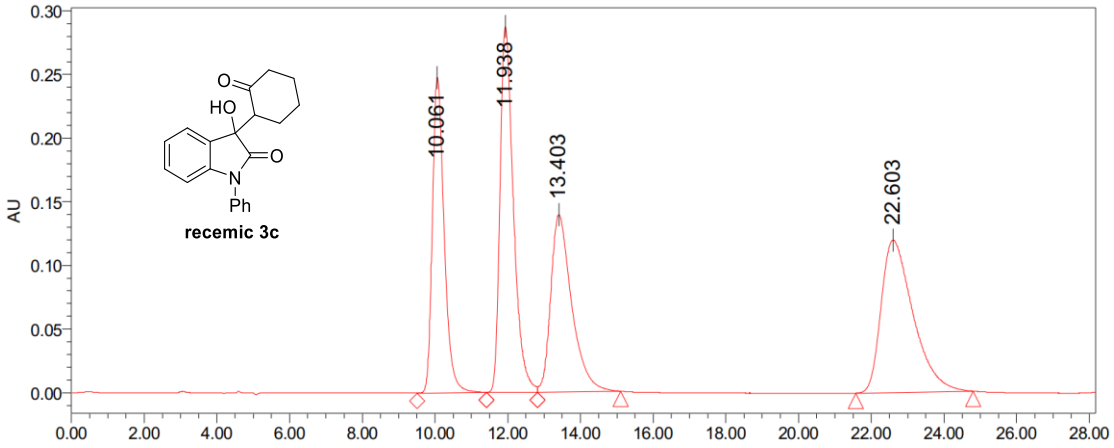
	name	Retention	Area(μV*s)	Height	% Area
1		6.590	8460930	830586	30.40
2		7.352	8363231	792101	30.05
3		8.035	5011171	448856	18.01
4		8.585	5994470	475117	21.54



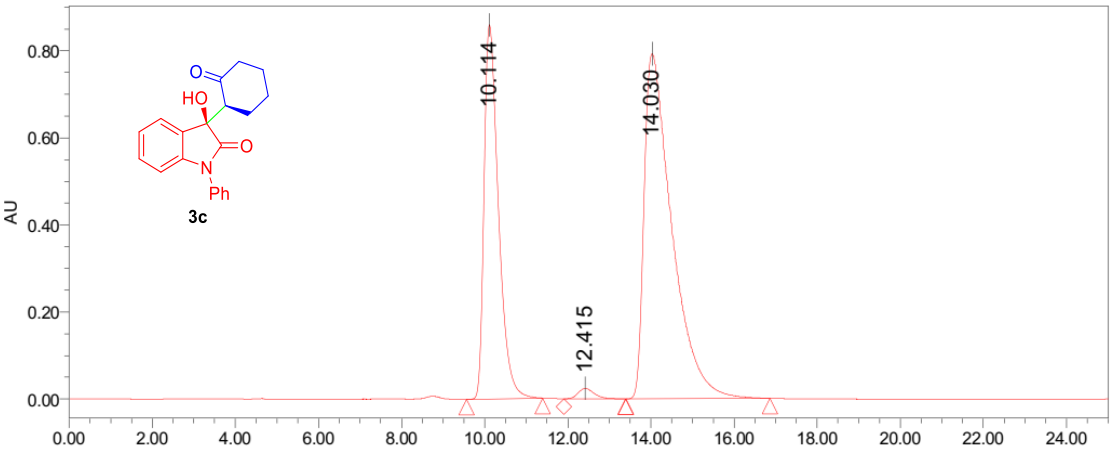
	name	Retention	Area(μV*s)	Height	% Area
1		6.704	28432366	2506587	78.24
2		7.641	6333456	557202	17.43
3		8.355	404646	33097	1.11
4		8.890	1170586	89103	3.22

(*R*)-3-hydroxy-3-((R)-2-oxocyclohexyl)-1-phenylindolin-2-one (3c) [2]

3c: white solid, 138 mg, 86% yield, 99:1 dr, 28% ee, $[\alpha]_D^{25}$ = –53.28 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (t, *J* = 7.6 Hz, 2H), 7.50 – 7.35 (m, 3H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 6.16 (s, 1H), 3.28 – 3.18 (m, 1H), 2.77 – 2.21 (m, 3H), 2.11 – 1.84 (m, 3H), 1.80 – 1.65 (m, 1H), 1.55– 1.40 (m, 1H). The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=80:20; flow rate 1.0 mL/min; 254 nm; retention time: 10.1 min (major) and 13.4 min (minor).



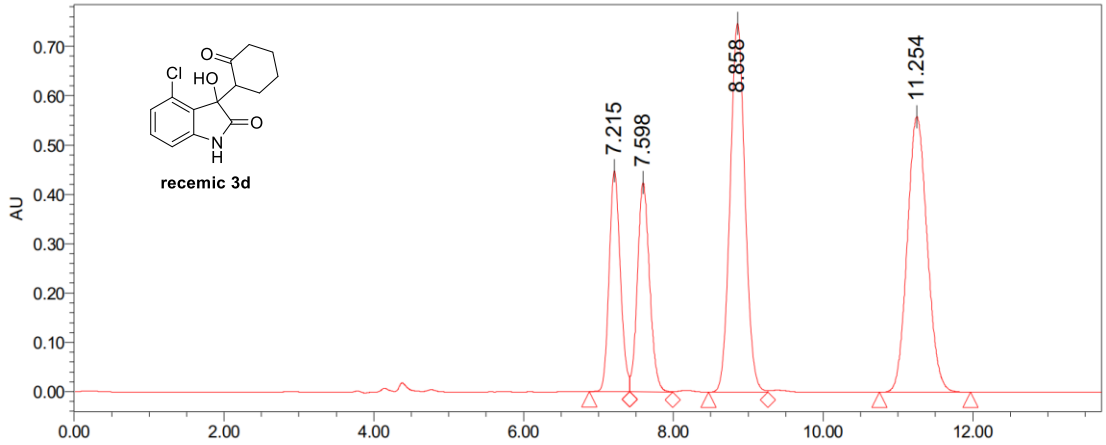
	name	Retention	Area(μV*s)	Height	% Area
1		10.061	5580182	247905	21.63
2		11.938	7358284	287335	28.53
3		13.403	5557665	139106	21.55
4		22.603	7297073	119622	28.29



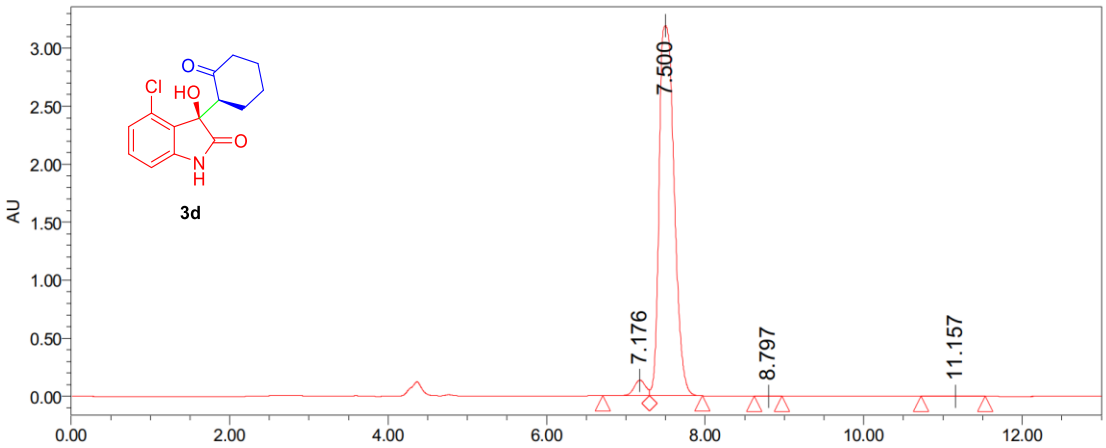
	name	Retention	Area(μV*s)	Height	% Area
1		10.114	20646687	859139	35.62
2		12.415	678537	24318	1.17
3		14.030	36644049	792727	63.21

(*R*)-4-chloro-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3d) [3]

3d: white solid, 133 mg, 95% yield, 99:1 dr, 94% ee, $[\alpha]_D^{25}$ = –36.80 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.35 (s, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.04 (s, 1H), 3.79 (dd, *J* = 12.8, 5.2 Hz, 1H), 2.40 – 2.11 (m, 2H), 2.10 – 1.79 (m, 3H), 1.71 – 1.39 (m, 2H)； The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 7.2 min (minor) and 7.5 min (major).



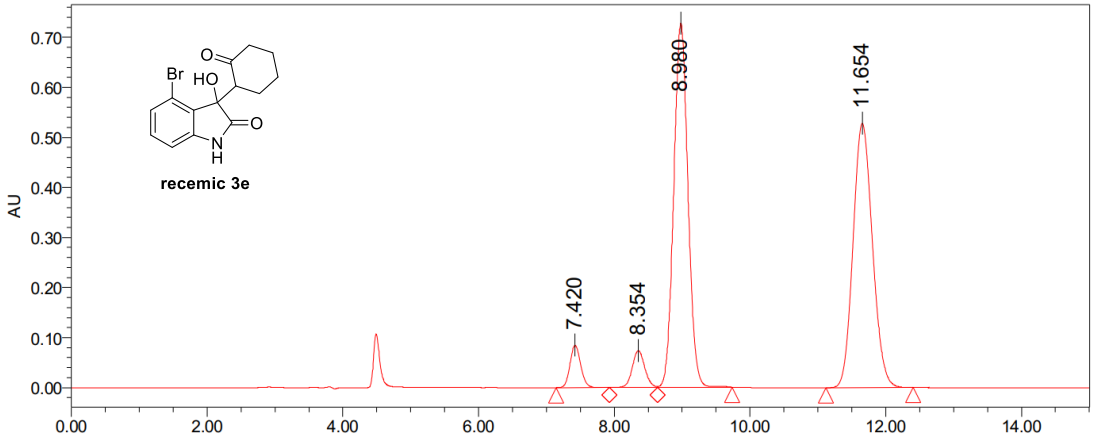
	name	Retention	Area(μV*s)	Height	% Area
1		7.215	4663961	447308	15.48
2		7.598	4764564	423967	15.81
3		8.858	10376137	747293	34.43
4		11.254	10333971	558639	34.29



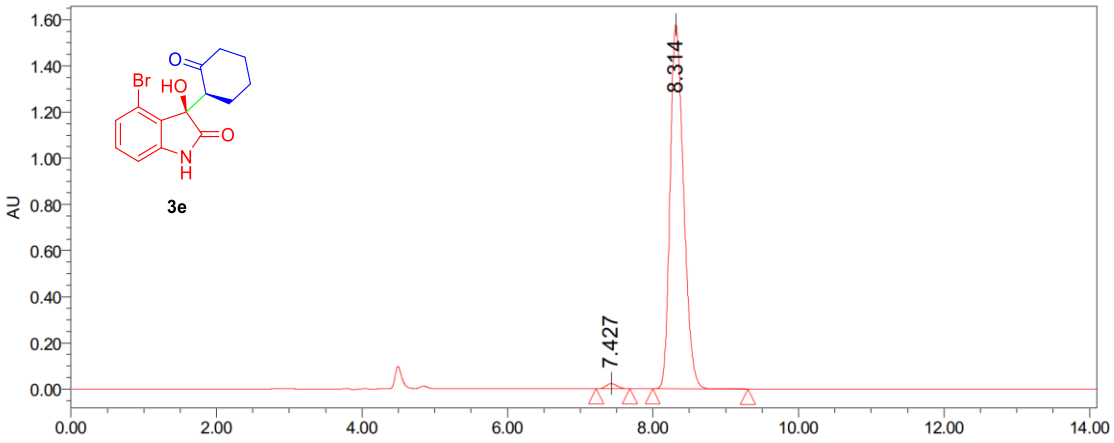
	name	Retention	Area(μV*s)	Height	% Area
1		7.176	1393340	134528	3.20
2		7.500	42112208	3189035	96.70
3		8.797	12966	1157	0.03
4		11.157	29898	1484	0.07

(*R*)-4-bromo-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3e) [3]

3e: white solid, 153 mg, 95% yield, 99:1 dr, 98% ee, $[\alpha]_D^{25}$ = –54.08 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 7.21 – 7.09 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.18 (s, 1H), 2.44 – 2.26 (m, 2H), 1.96 – 1.69 (m, 3H), 1.64 – 1.41 (m, 3H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 7.4 min (minor) and 8.3 min (major).



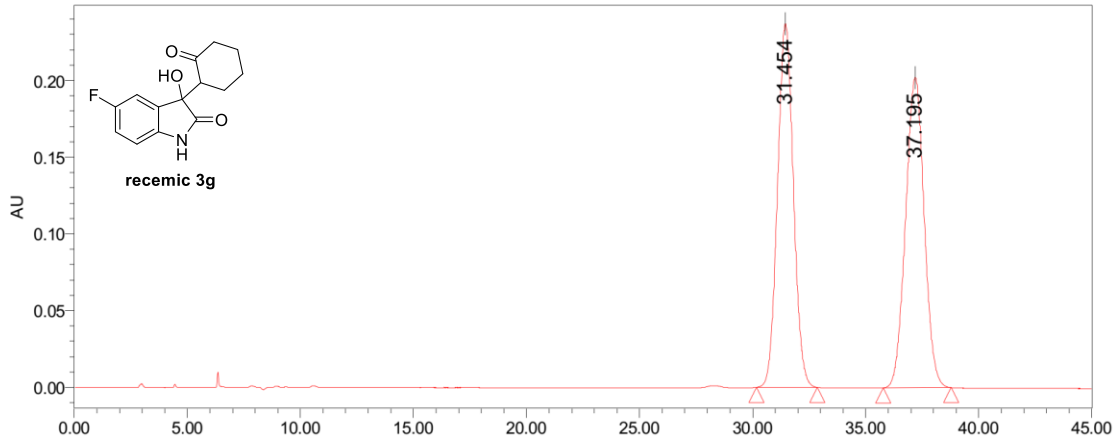
	name	Retention	Area(μV*s)	Height	% Area
1		7.420	924451	84560	4.04
2		8.354	931122	73594	4.07
3		8.980	10524095	727335	46.01
4		11.654	10494960	527942	45.88



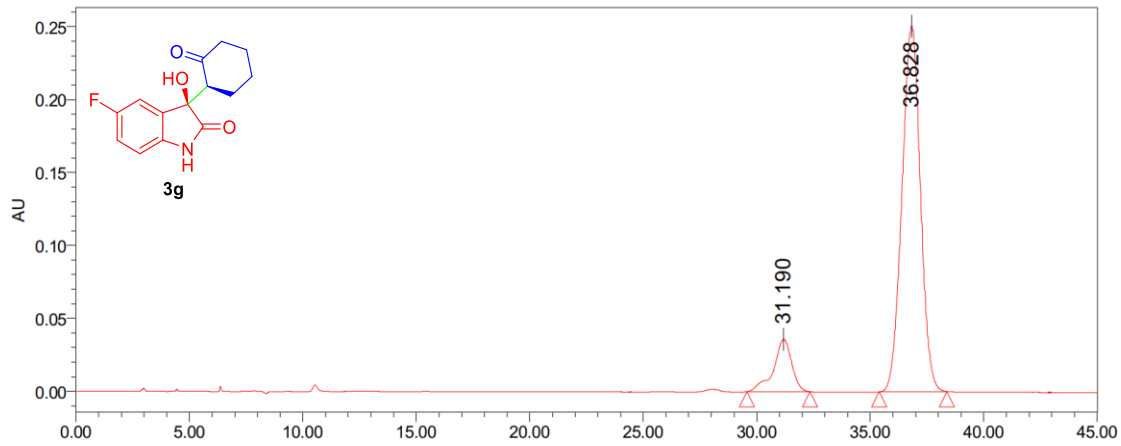
	name	Retention	Area(μV*s)	Height	% Area
1		7.427	240468	22763	1.17
2		8.314	20303376	1577429	98.83

(*R*)-5--fluoro-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3f) [3]

3f: white solid, 125 mg, 95% yield, 99:1 dr, 75% ee, $[\alpha]_D^{25}$ = 57.92 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.56 (t, *J* = 7.8 Hz, 2H), 7.39 (m, 4H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 6.14 (d, *J* = 4.2 Hz, 1H), 3.21 (dd, *J* =4.8, 13.2Hz, 1H), 2.70 – 2.61 (m, 1H), 2.33 (m, 1H), 2.10 – 2.00 (m, 1H), 1.91 (m, 3H), 1.70 (m, 1H), 1.52 – 1.41 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol= 90:10; flow rate 1.0 mL/min; 254 nm; retention time: 31.2 min (minor) and 36.8 min (major).



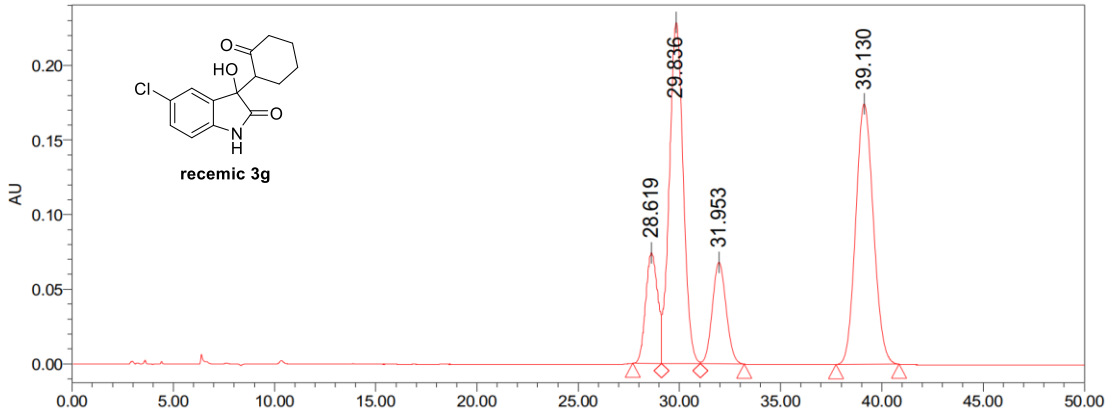
	name	Retention	Area(μV*s)	Height	% Area
1		31.454	11578994	50.10	236994
2		37.195	11534632	49.90	202277



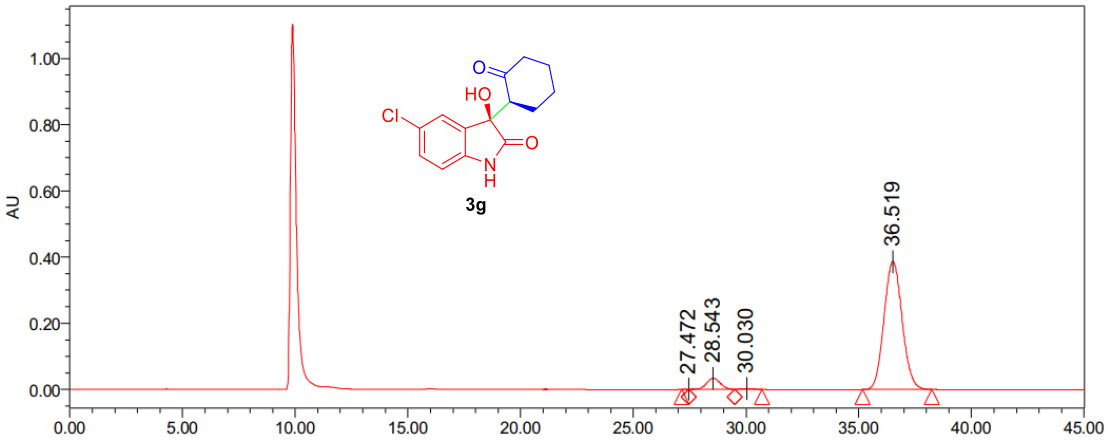
	name	Retention	Area(μV*s)	Height	% Area
1		31.190	2008322	12.46	35933
2		36.828	14115499	87.54	250592

(*R*)-5-chloro-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3g) [3]

3g: white solid, 134 mg, 96% yield, 99:1 dr, 87% ee, $[\alpha]_D^{25}$ = 36.16 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.35 (s, 1H), 7.25 – 7.17 (m, 2H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.00 (s, 1H), 3.13 – 3.07 (m, 1H), 2.62 – 2.55 (m, 1H), 2.37 – 2.28 (m, 1H), 2.07 – 2.01 (m, 1H), 1.98 – 1.88 (m, 2H),1.83 – 1.74 (m, 1H), 1.73 – 1.62 (m, 1H), 1.56 – 1.45 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=90:10; flow rate 1.0 mL/min; 254 nm; retention time: 29.8 min (minor) and 39.0 min (major).



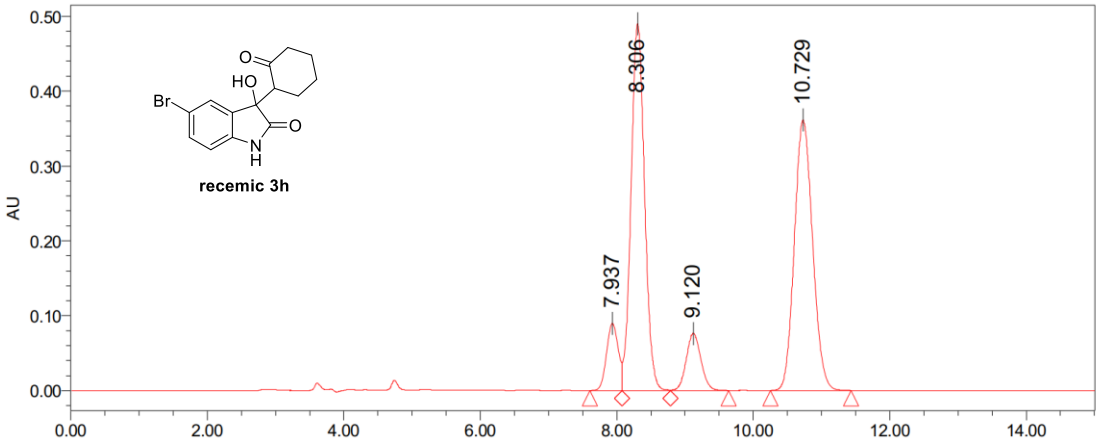
	name	Retention	Area(μV*s)	Height	% Area
1		28.619	3065513	74079	11.05
2		29.836	10817908	228591	38.98
3		31.953	3241017	68060	11.68
4		39.130	10629418	174587	38.30



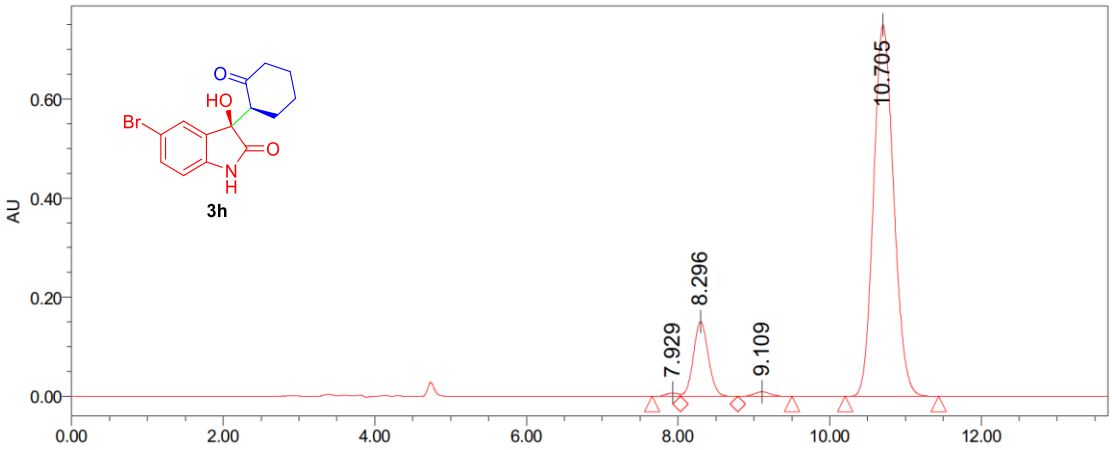
	name	Retention	Area(μV*s)	Height	% Area
1		27.472	10353	1012	0.04
2		28.543	1474897	33858	6.37
3		30.030	120363	2997	0.52
4		36.519	21547280	386378	93.07

(*R*)-5-bromo-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3h) [3]

3h: white solid, 149 mg, 92% yield, 99:1 dr, 74% ee, $[\alpha]_D^{25}$ = 22.24 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.36 (s, 1H), 7.36 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.30 (d, *J* = 1.8 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.01 (s, 1H), 3.10 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.33 (td, *J* = 13.8, 6.0 Hz, 1H), 2.07 – 1.45 (m, 6H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 8.3 min (minor) and 10.7 min (major).



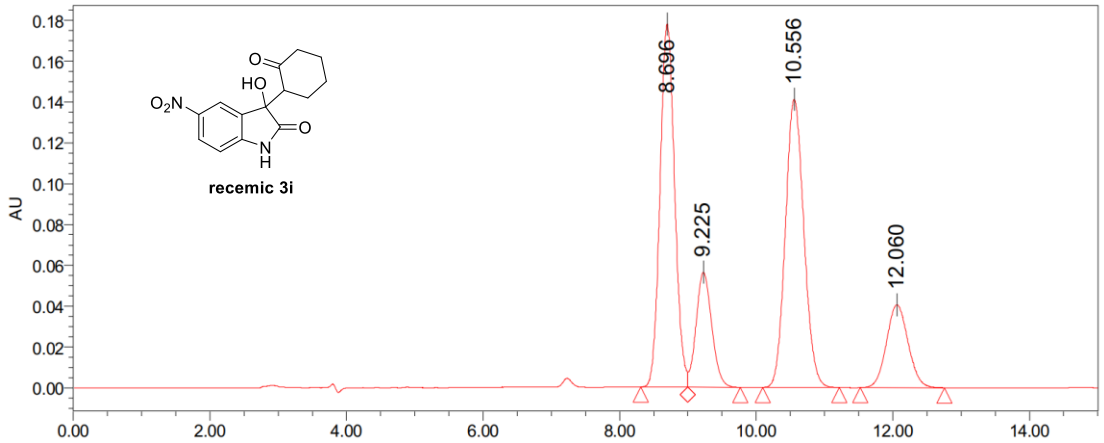
	name	Retention	Area(μV*s)	Height	% Area
1		7.937	1072869	89586	6.88
2		8.306	6727772	489574	43.11
3		9.120	1131061	76153	7.25
4		10.729	6673305	361228	42.76



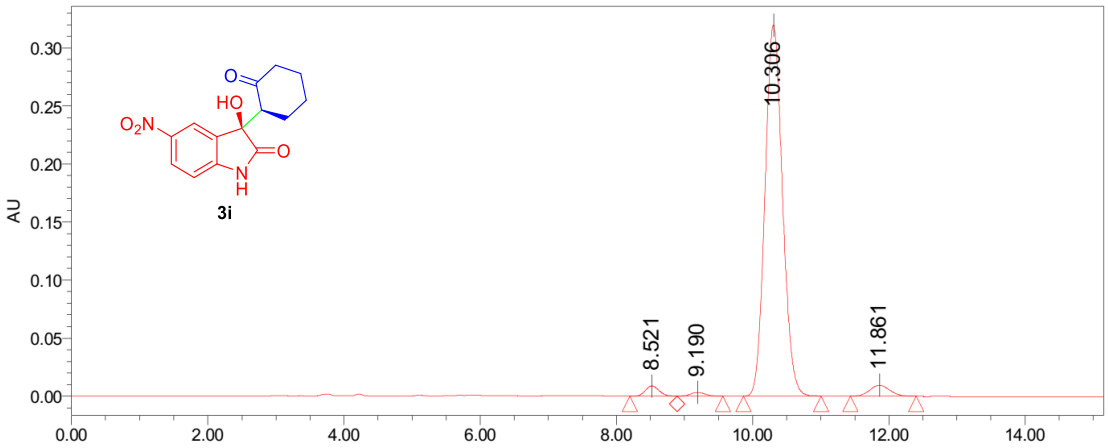
	name	Retention	Area(μV*s)	Height	% Area
1		7.929	78466	7026	0.49
2		8.296	2061410	151004	12.77
3		9.109	135856	9151	0.84
4		10.705	13860892	749816	85.90

(*R*)-3-hydroxy-5-nitro-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3i) [2]

3i: white solid, 131 mg, 91% yield, 96:4 dr, 96% ee, $[\alpha]_D^{25}$ = 71.92 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 7.41 – 7.23 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 1H), 3.09 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.57 (d, *J* = 12.0 Hz, 1H), 2.41 – 2.23 (m, 1H), 2.11 – 1.39 (m, 6H)； The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 8.5 min (minor). and 10.3 min (major).



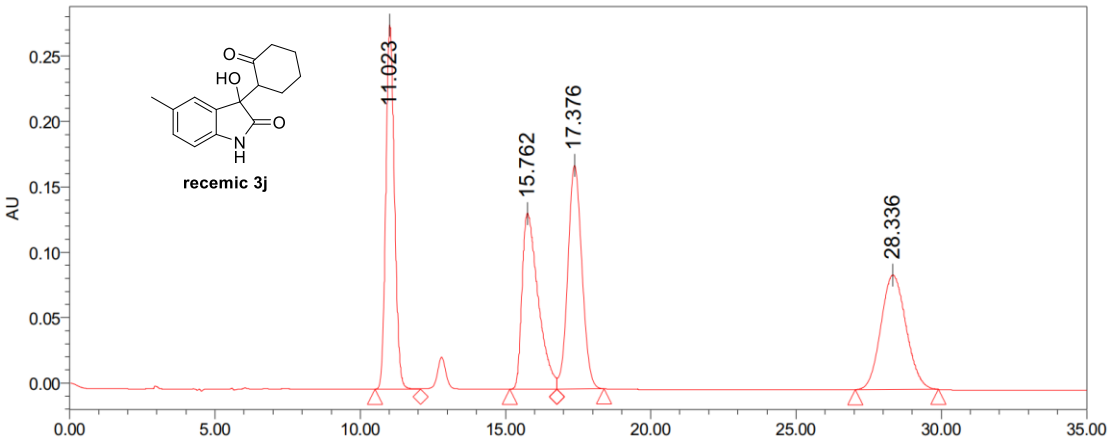
	name	Retention	Area(μV*s)	Height	% Area
1		8.696	2642045	177686	37.27
2		9.225	898860	56313	12.68
3		10.556	2655420	141070	37.45
4		12.060	893318	40563	12.60



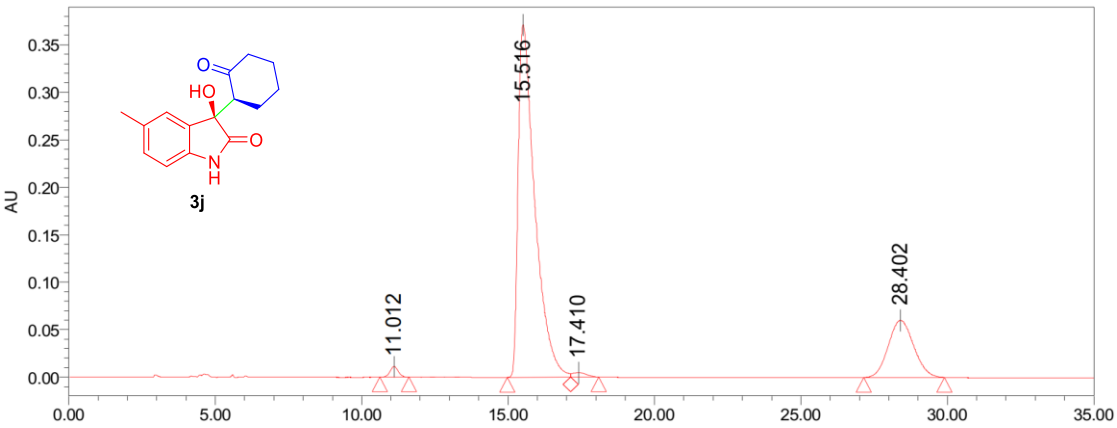
	name	Retention	Area(μV*s)	Height	% Area
1		8.521	126062	8916	2.08
2		9.190	51933	3349	0.86
3		10.306	5690559	319652	93.82
4		11.861	197040	9516	3.25

(*R*)-3-hydroxy-5-methyl-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3j) [3]

3j: white solid, 123 mg, 95% yield, 98:2 dr, 60% ee, $[\alpha]_D^{25}$ = 29.44 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.07 (s, 1H), 7.08 – 6.92 (m, 2H), 6.67 (d, *J* = 7.8 Hz, 1H), 5.75 (s, 1H), 3.06 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.58 (s, 1H), 2.31 (td, *J* = 13.8, 6.0 Hz, 1H), 2.22 (s, 3H), 2.08 – 1.78 (m, 4H), 1.73 – 1.61 (m, 1H), 1.57 – 1.41 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 15.5 min (major) and 28.4 min (minor).



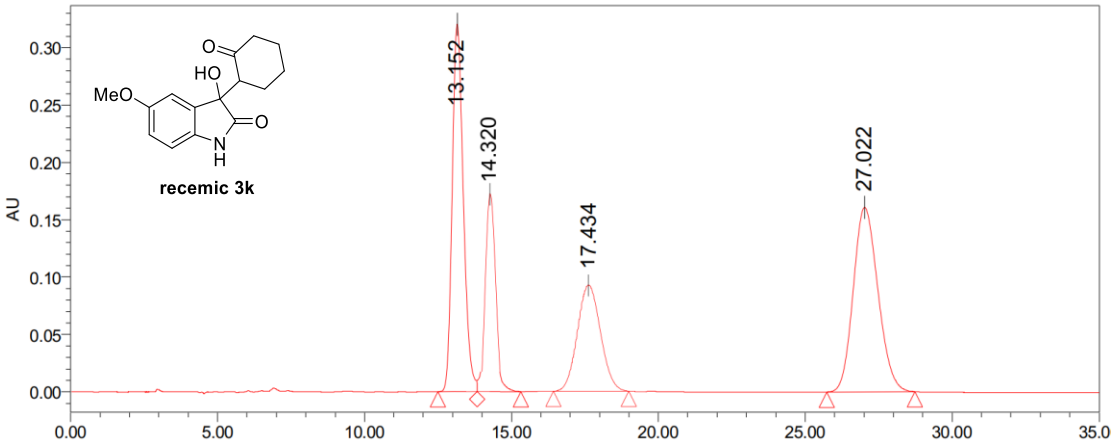
	name	Retention	Area(μV*s)	Height	% Area
1		11.023	5689167	278233	25.95
2		15.762	5189404	134418	23.67
3		17.376	5782433	171005	26.37
4		28.336	5266261	87504	24.02



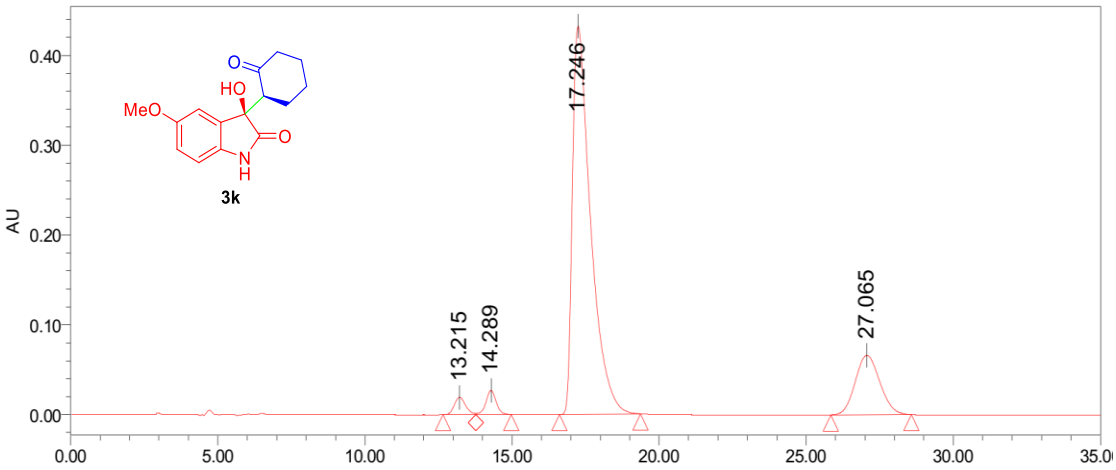
	name	Retention	Area(μV*s)	Height	% Area
1		11.012	223670	11320	1.20
.		15.516	14623276	370916	78.54
3		17.410	155526	4636	0.84
4		28.402	3615984	60111	19.42

(*R*)-3-hydroxy-5-methyl-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3k) [2]

3k: white solid, 129 mg, 94% yield, 97:3 dr, 70% ee, $[\alpha]_D^{25}$ = 38.0 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.02 (s, 1H), 6.87 – 6.61 (m, 3H), 5.82 (s, 1H), 3.68 (s, 3H), 3.06 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.60 – 2.53 (m, 1H), 2.31 (td, *J* = 13.6, 6.0 Hz, 1H), 2.07 – 1.45 (m, 6H).; The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 15.5 min (major) and 28.4 min (minor).



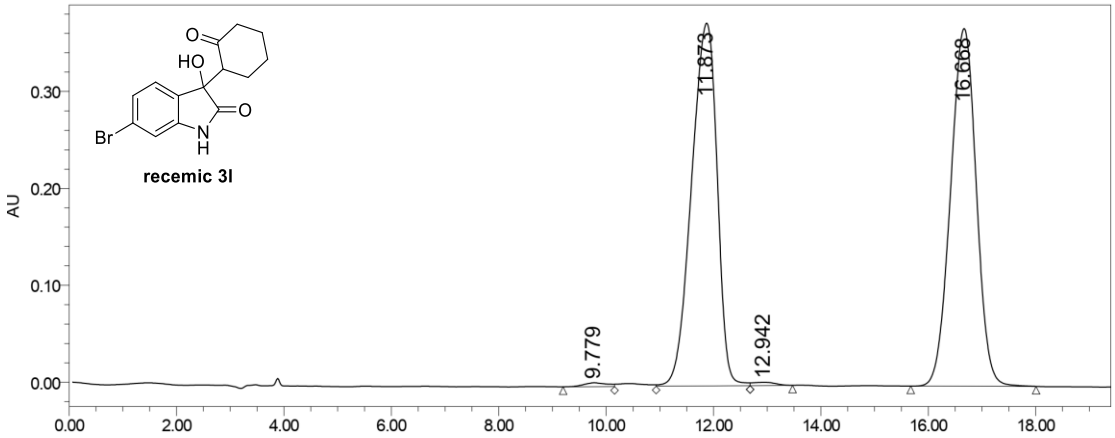
	name	Retention	Area(μV*s)	Height	% Area
1		13.152	13895059	1131106	30.67
2		14.320	6818994	625324	18.51
3		17.434	7095719	339332	19.18
4		27.022	13907610	565558	30.64



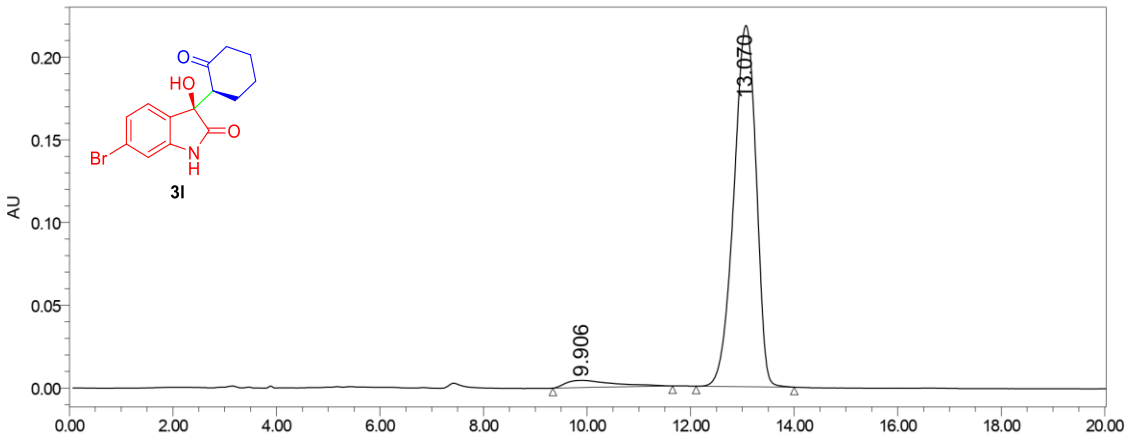
	name	Retention	Area(μV*s)	Height	% Area
1		13.215	521317	2.20	19355
.		14.289	648526	2.74	26769
3		17.246	18638890	78.74	432090
4		27.065	3863815	16.32	66216

(*R*)-6-bromo-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3l) [4]

3l: white solid, 147 mg, 91% yield, 99:1 dr, 92% ee, $[\alpha]_D^{25}$ = 57.04 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.35 (s, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.94 – 6.92 (m, 1H), 5.94 (s, 1H), 3.13 – 3.04 (m, 1H), 2.62 – 2.55 (m, 1H), 2.36 – 2.28 (m, 1H), 2.06 – 1.41 (m, 6H); The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 9.6 min (minor) and 13.1 min (major).



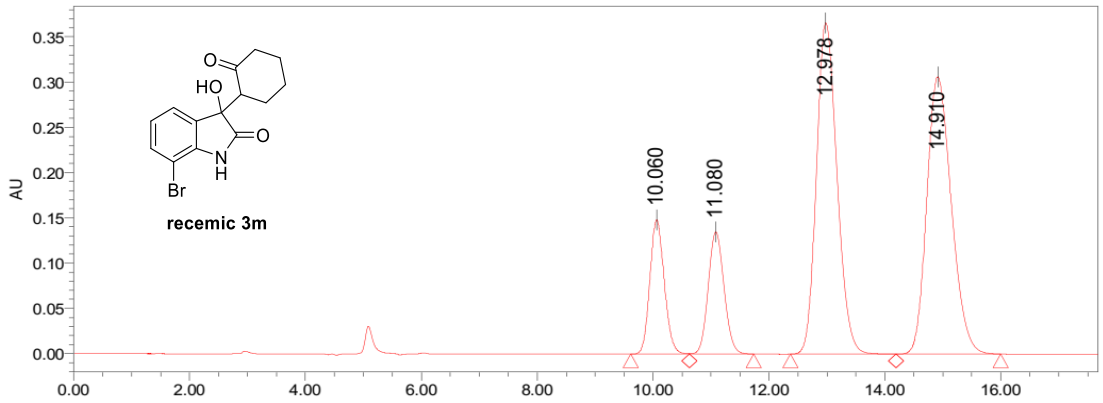
	name	Retention	Area(μV*s)	Height	% Area
1		9.779	120307	3935	0.48
2		11.873	12395188	374293	49.81
3		12.942	96078	3321	0.39
4		16.668	12271286	369089	49.32



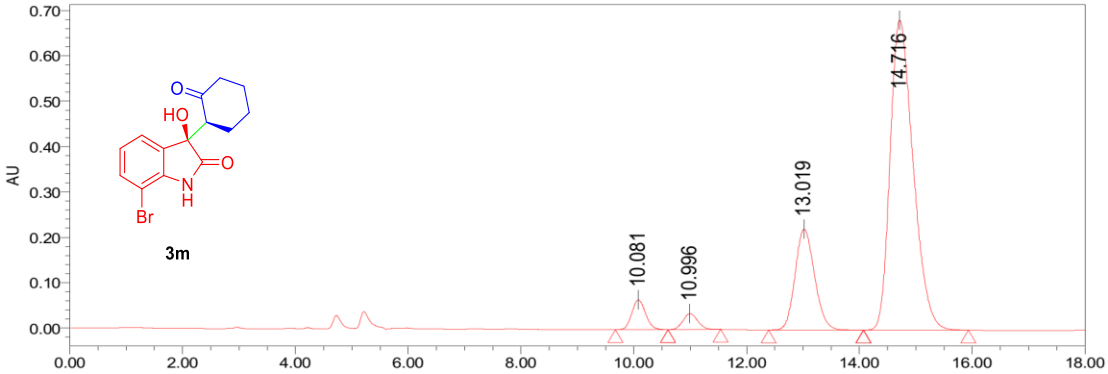
	name	Retention	Area(μV*s)	Height	% Area
1		9.906	279374	4375	4.11
2		13.070	6523136	218319	95.89

(*R*)-7-bromo-3-hydroxy-3-((*S*)-2-oxocyclohexyl) indolin-2-one (3m)

3m: white solid, 155 mg, 96% yield, 93:7 dr, 57% ee, $[\alpha]_D^{25}$ = 44.08 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.02 (s, 1H), 3.11 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.58 (d, *J* = 12.0 Hz, 1H), 2.41 – 2.26 (m, 1H), 2.11 – 1.36 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 209.7, 179.0, 143.2, 133.4, 131.99, 124.3, 123.1, 102.5, 75.1, 58.0, 41.9, 27.1, 24.9； The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 13.0 min (minor) and 14.9 min (major). HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{14}NO_3NaBr$, 346.0055, found: 346.0049.



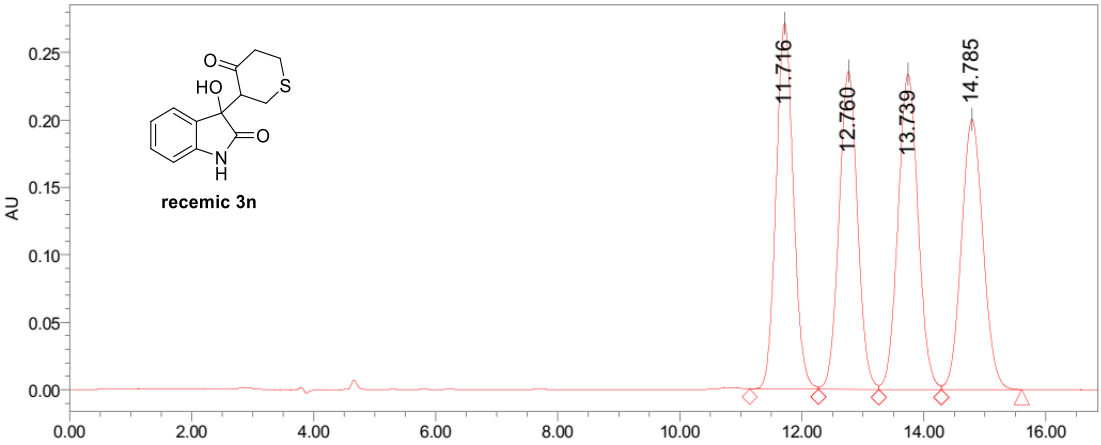
	name	Retention	Area(μV*s)	Height	% Area
1		10.060	2564597	148184	11.08
2		11.080	2564605	134889	11.08
3		12.978	9027078	365855	38.99
4		14.910	8996628	306469	38.86



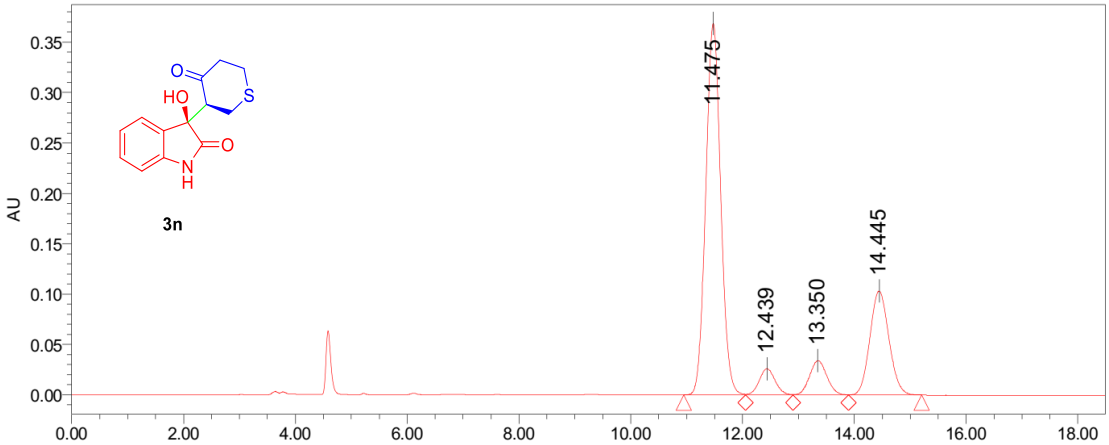
	name	Retention	Area(μV*s)	Height	% Area
1		10.081	1101602	65610	4.17
2		10.996	630157	34930	2.38
3		13.019	5318204	222414	20.12
4		14.716	19381005	682971	73.33

(*R*)-3-hydroxy-3-((*S*)-4-oxotetrahydro-2H-thiopyran-3-yl) indolin-2-one (3n) [2]

3n: white solid, 124 mg, 94% yield, 72:28 dr, 80% ee, $[\alpha]_D^{25}$ = 57.04 (*c* =0.25, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.26 (s, 1H), 7.26 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.17 (td, *J* = 7.8, 1.2 Hz, 1H), 6.89 - 6.84 (m, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.04 (s, 1H), 3.50 – 3.45 (m, 1H), 3.23 (t, *J* = 12.6 Hz, 1H), 2.94 – 2.85 (m, 2H), 2.60 – 2.53 (m, 1H), 2.44 – 2.38 (m, 1H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 11.7 min (major) and 13.7min (minor).



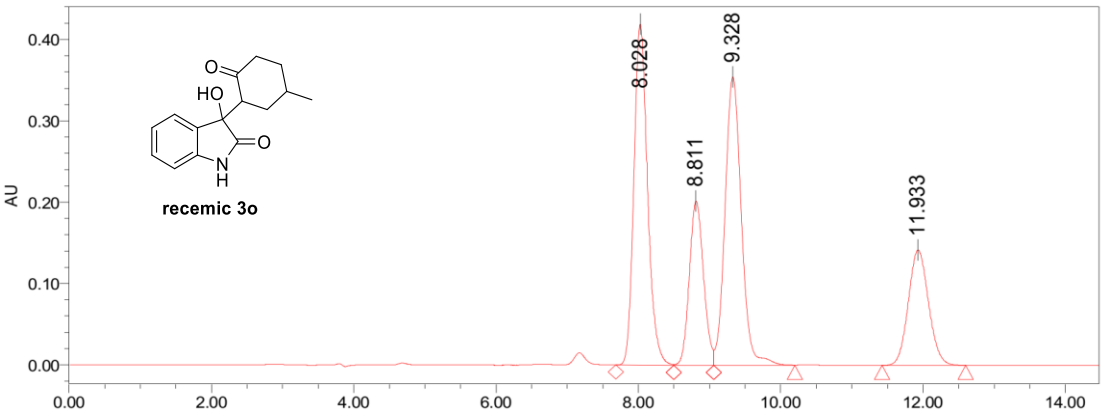
	name	Retention	Area(μV*s)	Height	% Area
1		11.716	5344912	271241	25.90
2		12.760	4987723	235880	24.17
3		13.739	5338445	233648	25.87
4		14.785	4964819	200248	24.06



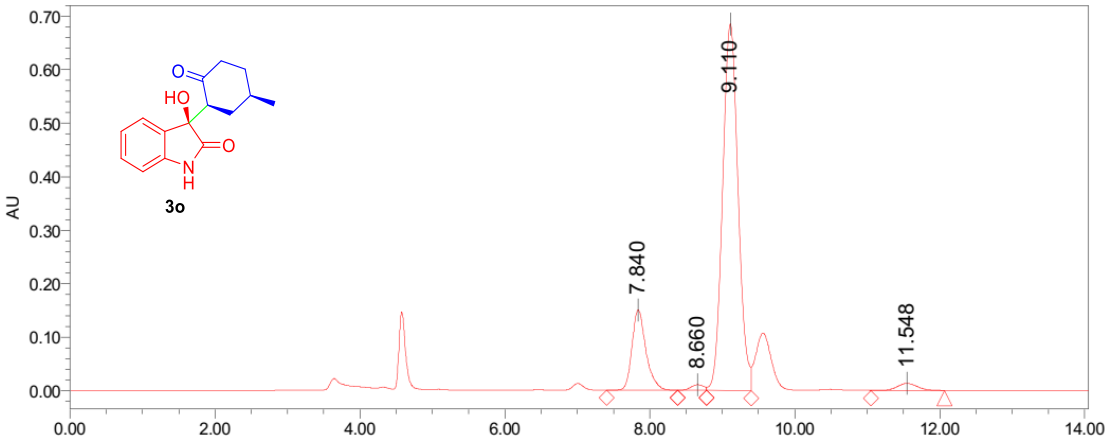
	name	Retention	Area(μV*s)	Height	% Area
1		11.475	6872671	368800	64.95
2		12.439	518562	25998	4.90
3		13.350	734886	34042	6.95
4		14.445	2454901	103312	23.20

(*R*)-3-hydroxy-3-((*1S*,*5R*)-5-methyl-2-oxocyclohexyl) indolin-2-one (3o) [2]

3o: white solid, 56 mg, 43% yield, 97:3 dr, 67% ee, $[\alpha]_D^{25}$ = 57.04 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (s, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.93 -8.82 (m, 1H), 6.74 (d, *J* = 7.7 Hz, 1H), 5.71 (s, 1H), 3.30 (d, *J* = 4.9 Hz, 1H), 2.42 (dd, *J* = 13.6, 5.6 Hz, 1H), 2.26 – 2.15 (m, 1H), 2.05 – 1.86 (m, 3H), 1.53 (q, *J* = 12.8 Hz, 1H), 1.27 – 1.12 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 7.8 min (minor) and 9.1 min (major).



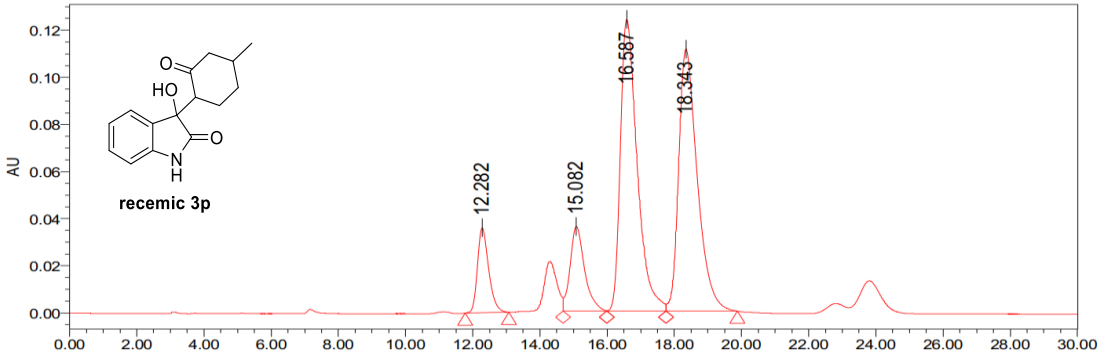
	name	Retention	Area(μV*s)	Height	% Area
1		8.028	5544941	419069	33.07
2		8.811	2785714	201548	16.62
3		9.328	5644301	354316	33.67
4		11.933	2790777	141603	16.65



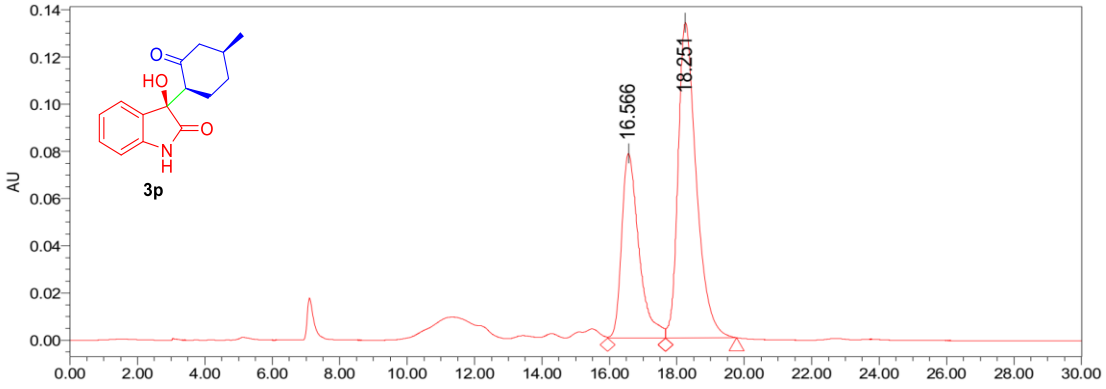
	name	Retention	Area(μV*s)	Height	% Area
1		7.840	2018990	150543	16.02
2		8.660	133971	10670	1.06
3		9.110	10197059	685297	80.92
4		11.548	251907	13119	2.00

(*R*)-3-hydroxy-3-((*1S,4R*)-4-methyl-2-oxocyclohexyl) indolin-2-one (3p)

Yellow solid, 123 mg, 95% yield, 99:1 dr, 29% ee, $[\alpha]_D^{25}$ = 15.84 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.23 – 7.11 (m, 2H), 6.88 – 6.76 (m, 2H), 5.81 (s, 1H), 3.03 (dd, *J* = 13.6, 5.2 Hz, 1H), 2.61 – 2.52 (m, 1H), 2.08 – 1.98 (m, 2H), 1.96 – 1.77 (m, 2H), 1.75 – 1.61 (m, 1H), 1.47 – 1.34 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 209.1, 179.2, 143.9, 131.3, 129.0, 125.3, 121.3, 109.9, 74.3, 57.1, 50.0, 34.7, 33.5, 26.1, 22.4. The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=90:10; flow rate 1.0 mL/min; 254 nm; retention time: 16.6 min (minor) and 18.3 min (major). HRMS (ESI-Orbitrap) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{17}NO_3Na$, 282.1106, found: 282.1099.



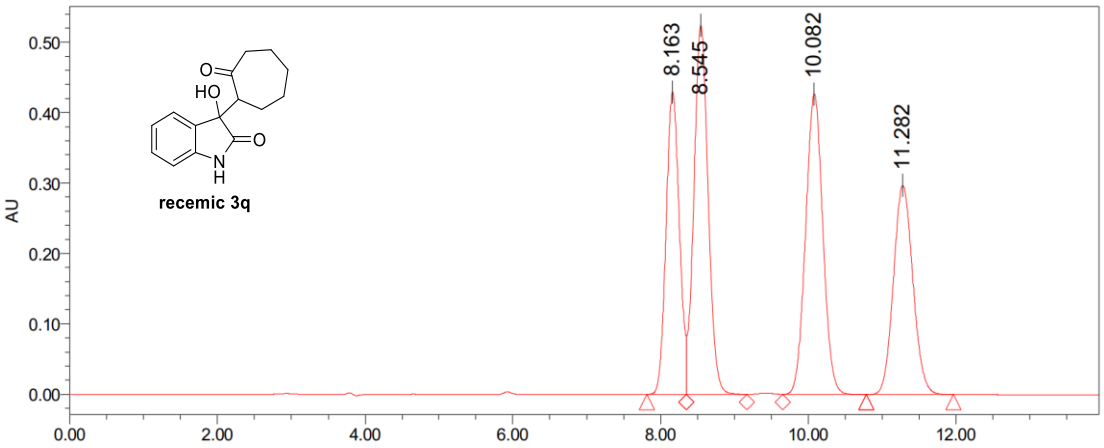
	name	Retention	Area(μV*s)	Height	% Area
1		12.282	837567	36013	7.97
2		15.082	1081496	35959	10.29
3		16.587	4298135	123899	40.90
4		18.343	4292375	111267	40.84



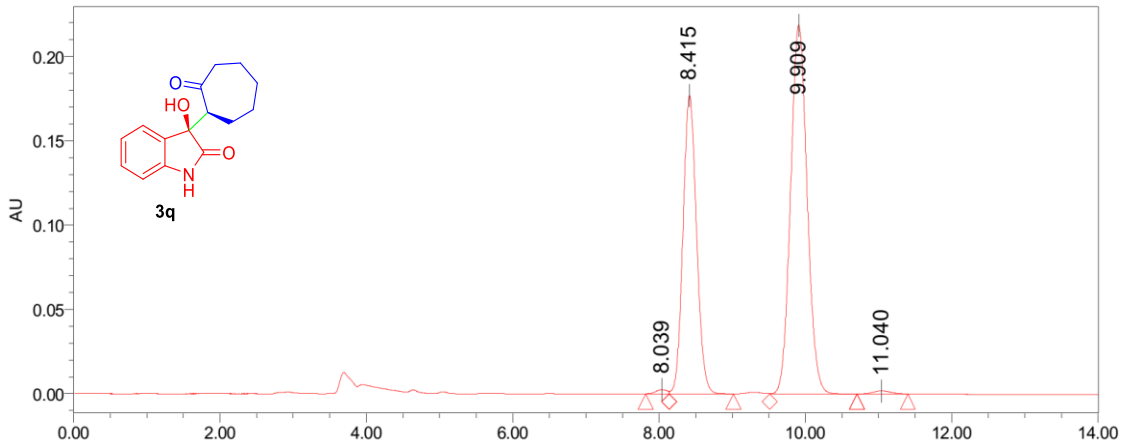
	name	Retention	Area(μV*s)	Height	% Area
1		16.566	2775336	78229	35.57
2		18.251	5027280	133494	64.43

(*R*)-3-hydroxy-3-((*S*)-2-oxocycloheptyl) indolin-2-one (3q) [2]

3p: white solid, 128 mg, 99% yield, 99:1 dr, 32% ee, $[\alpha]_D^{25}$ = -0.48 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.29 – 7.11 (m, 2H), 6.94 – 6.71 (m, 2H), 5.95 (s, 1H), 3.09 (dd, *J* = 11.3, 2.8 Hz, 1H), 2.48 – 2.36 (m, 1H), 2.29 – 2.11 (m, 2H), 2.08 – 1.80 (m, 2H), 1.79 – 1.58 (m, 2H), 1.53 – 1.21 (m, 3H); The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 8.4 min (minor) and 9.9 min (major).



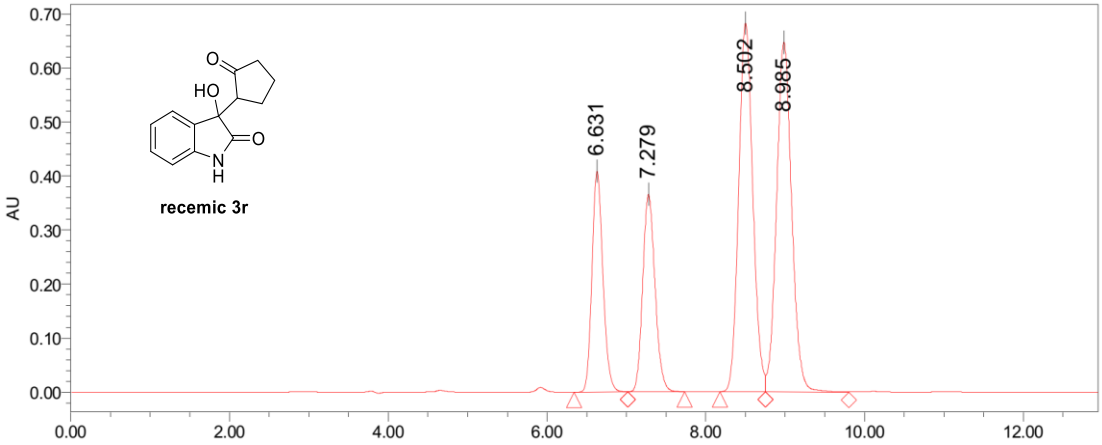
	name	Retention	Area(μV*s)	Height	% Area
1		8.163	5351264	429208	21.65
2		8.545	7024368	523941	28.42
3		10.082	6923294	426618	28.01
4		11.282	5420777	296805	21.93



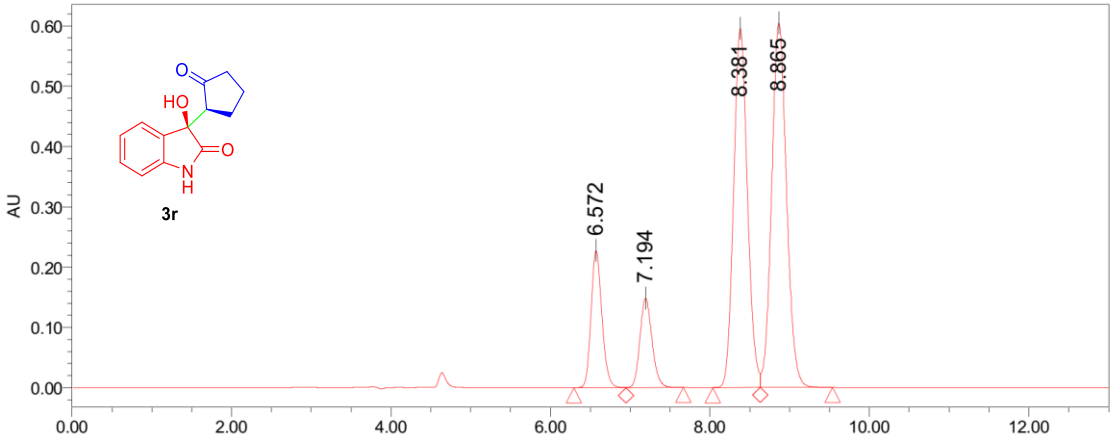
	name	Retention	Area(μV*s)	Height	% Area
1		8.039	26641	2518	0.46
2		8.415	2270146	177014	39.50
3		9.909	3420013	218507	59.50
4		11.040	30997	1847	0.54

(*R*)-3-hydroxy-3-((*S*)-2-oxocycloheptyl) indolin-2-one (3r) [2]

3q: white solid, 114 mg, 99% yield, 80:20 dr, 4% ee, $[\alpha]_D^{25}$ = 2.64 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (d, *J* = 6.8 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.22 – 7.10 (m, 1H), 6.95 – 6.85 (m, 1H), 6.81 -6.72 (m, 1H), 5.98 (d, *J* = 20.4 Hz, 1H), 2.93 – 2.78 (m, 1H), 2.29 – 1.54 (m, 6H).; The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 8.4 min (minor) and 8.7 min (major).



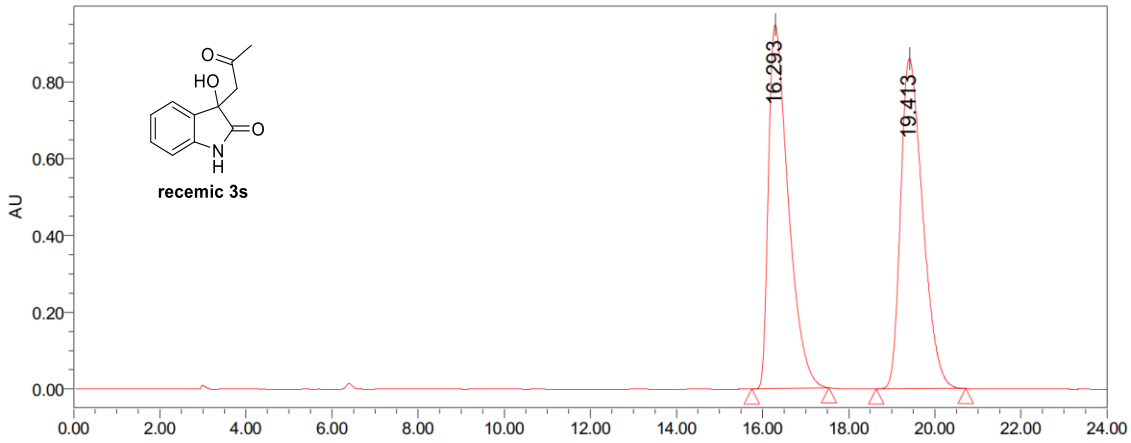
	name	Retention	Area(μV*s)	Height	% Area
1		6.631	3937221	409016	15.81
2		7.279	3921954	365875	15.75
3		8.502	8455868	682302	33.96
4		8.985	8582274	646911	34.47



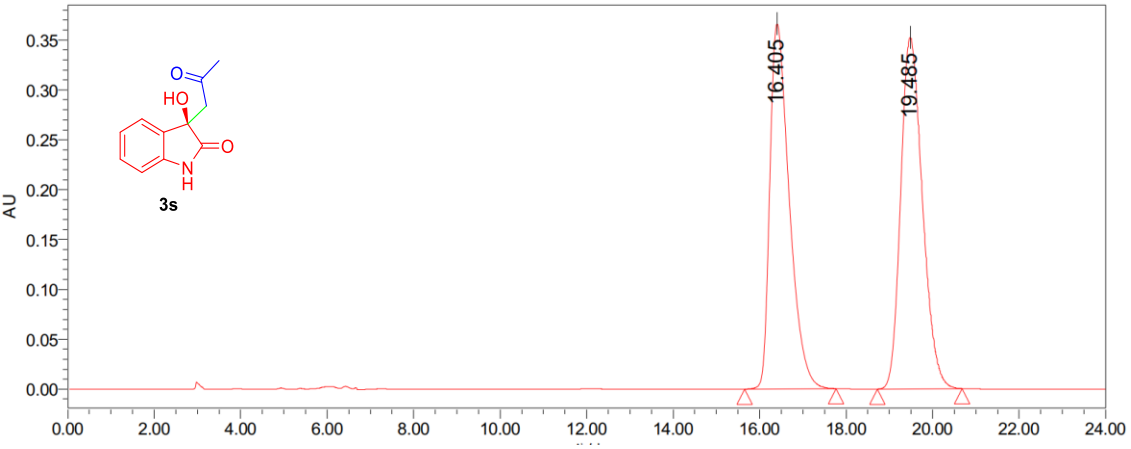
	name	Retention	Area(μV*s)	Height	% Area
1		6.572	2150562	227343	11.50
2		7.194	1558343	148141	8.33
3		8.381	7175133	595472	38.37
4		8.865	7814125	604698	41.79

(*R*)-3-hydroxy-3-(2-oxopropyl) indolin-2-one (3s) [5]

3r: white solid, 97 mg, 95% yield, 3% ee, $[\alpha]_D^{25}$ = 0.80 (*c* =0.25, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.20 (s, 1H), 7.30 – 7.11 (m, 2H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 5.97 (s, 1H), 3.35 – 3.23 (m, 1H), 3.00 (d, *J* = 16.4 Hz, 1H), 2.00 (s, 3H); The ee was determined by HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol=70:30; flow rate 1.0 mL/min; 254 nm; retention time: 16.4 min (minor) and 19.5 min (major).



	name	Retention	Area(μV*s)	Height	% Area
1		16.293	30481278	948609	49.82
2		19.413	30698713	860830	50.18



	name	Retention	Area(μV*s)	Height	% Area
1		16.405	11476051	366165	48.30
2		19.485	12283547	352285	51.70

6. Copies of NMR spectra

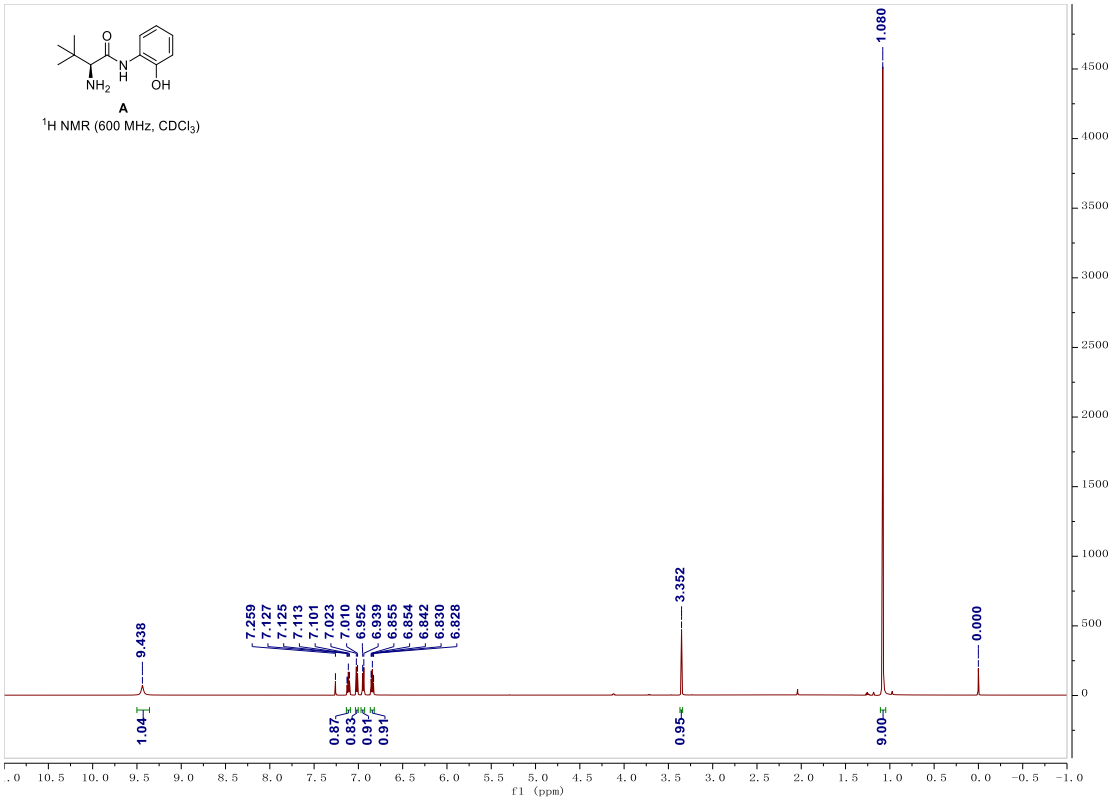


Figure S1. ^{1}H NMR (600 MHz, $CDCl_3$) of Catalyst **A**

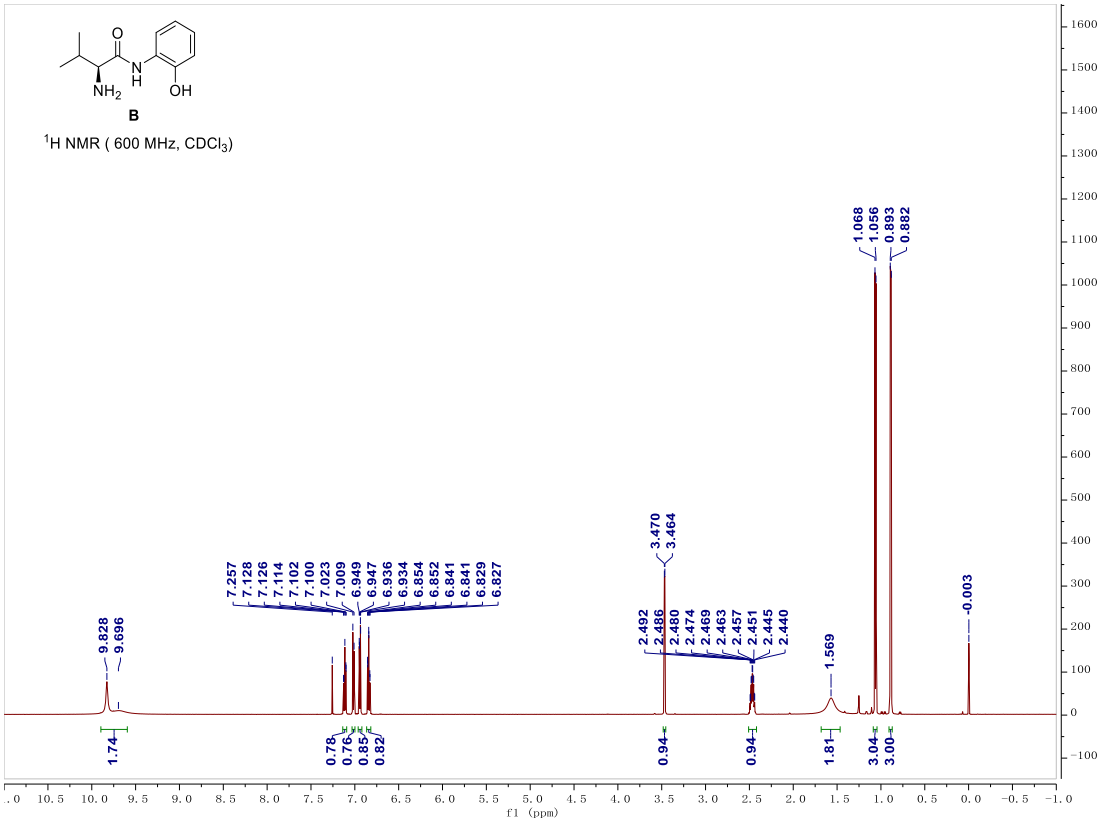


Figure S2. ^{1}H NMR (600 MHz, $CDCl_3$) of Catalyst **B**

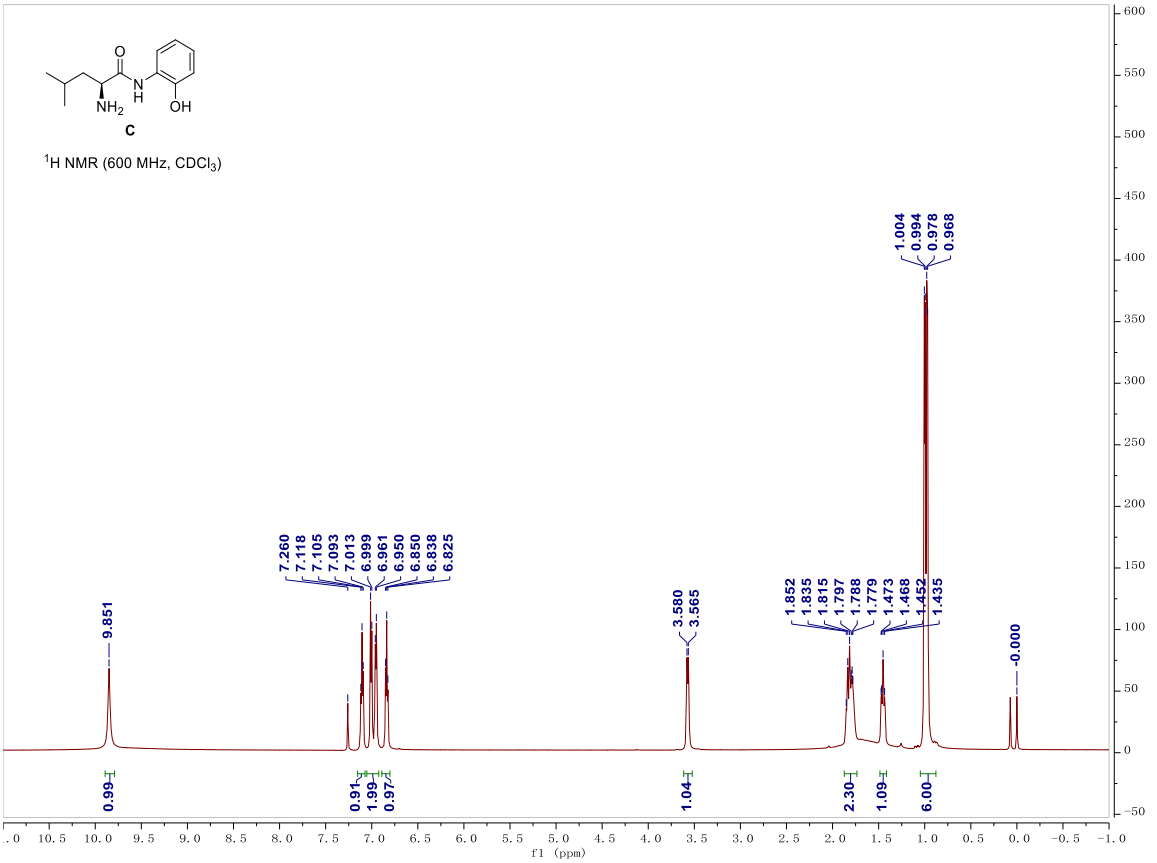


Figure S3. ^{1}H NMR (600 MHz, CDCl$_3$) of Catalyst **C**

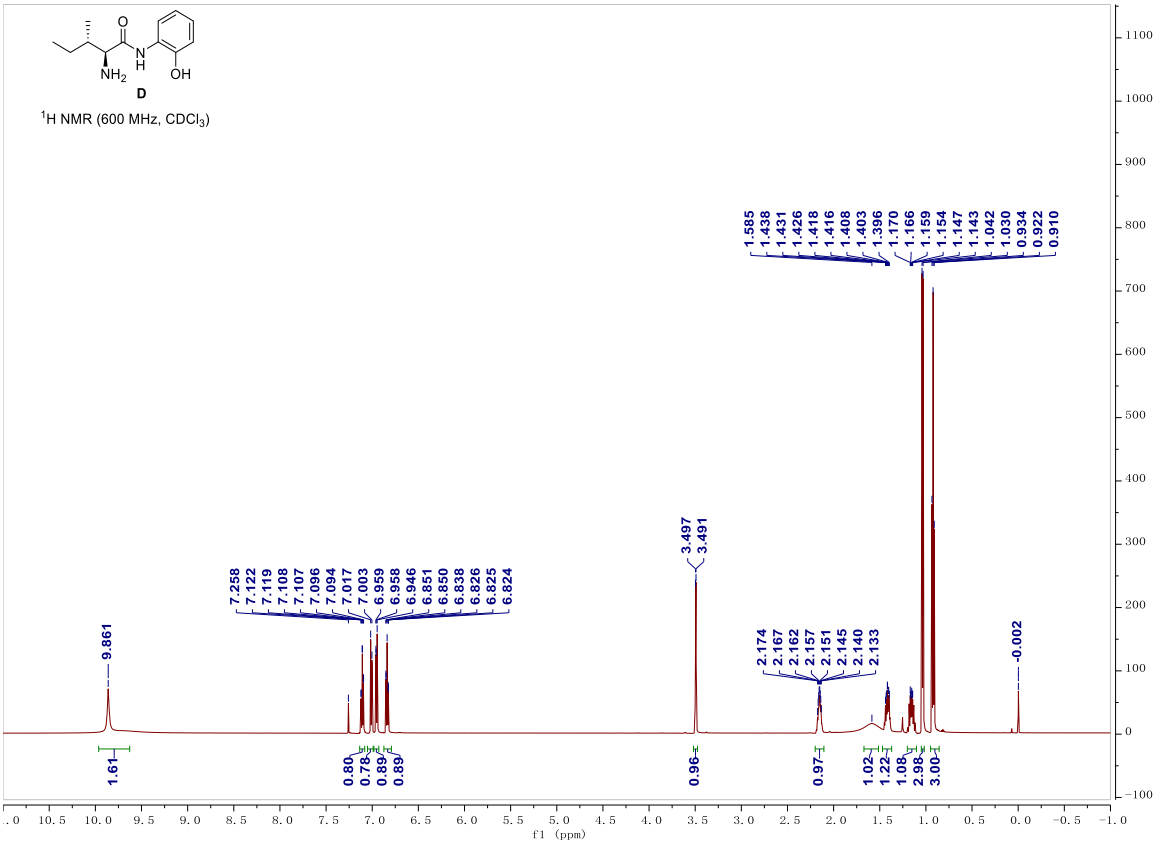


Figure S4. ^{1}H NMR (600 MHz, CDCl$_3$) of Catalyst **D**

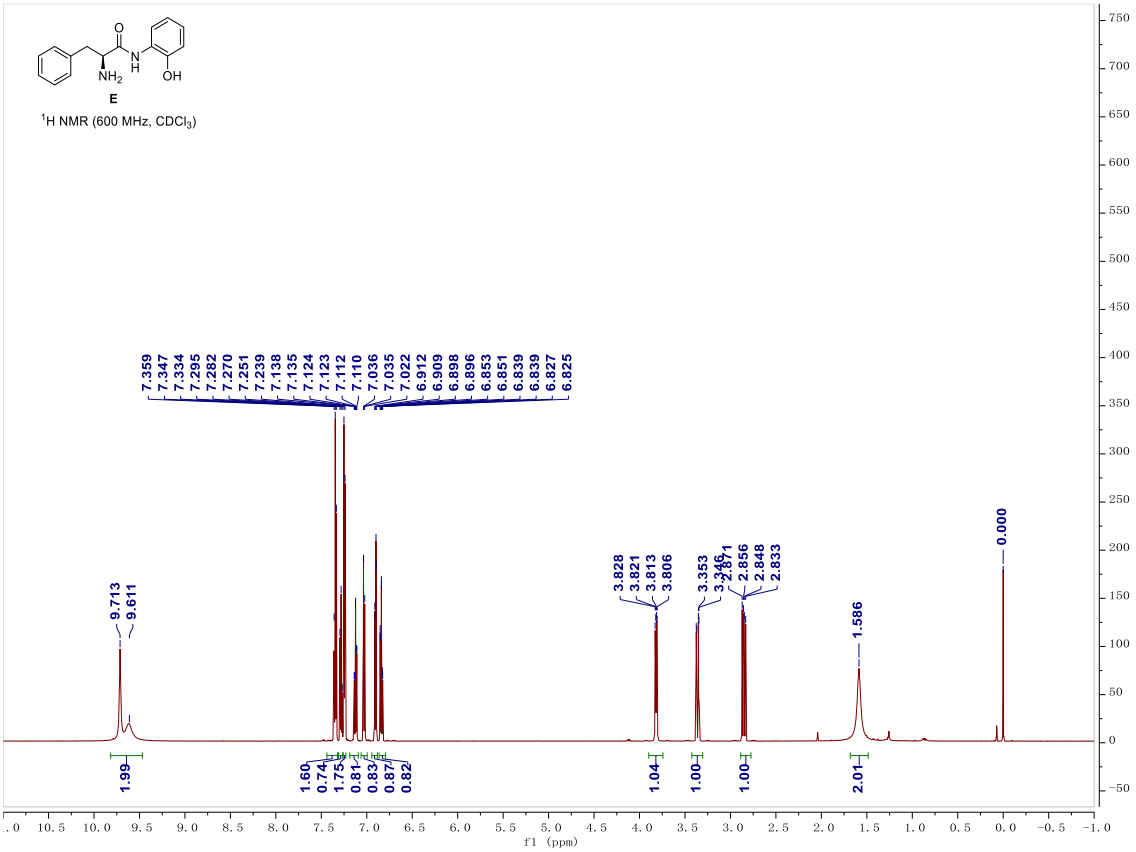


Figure S5. ^{1}H NMR (600 MHz, $CDCl_3$) of Catalyst **E**

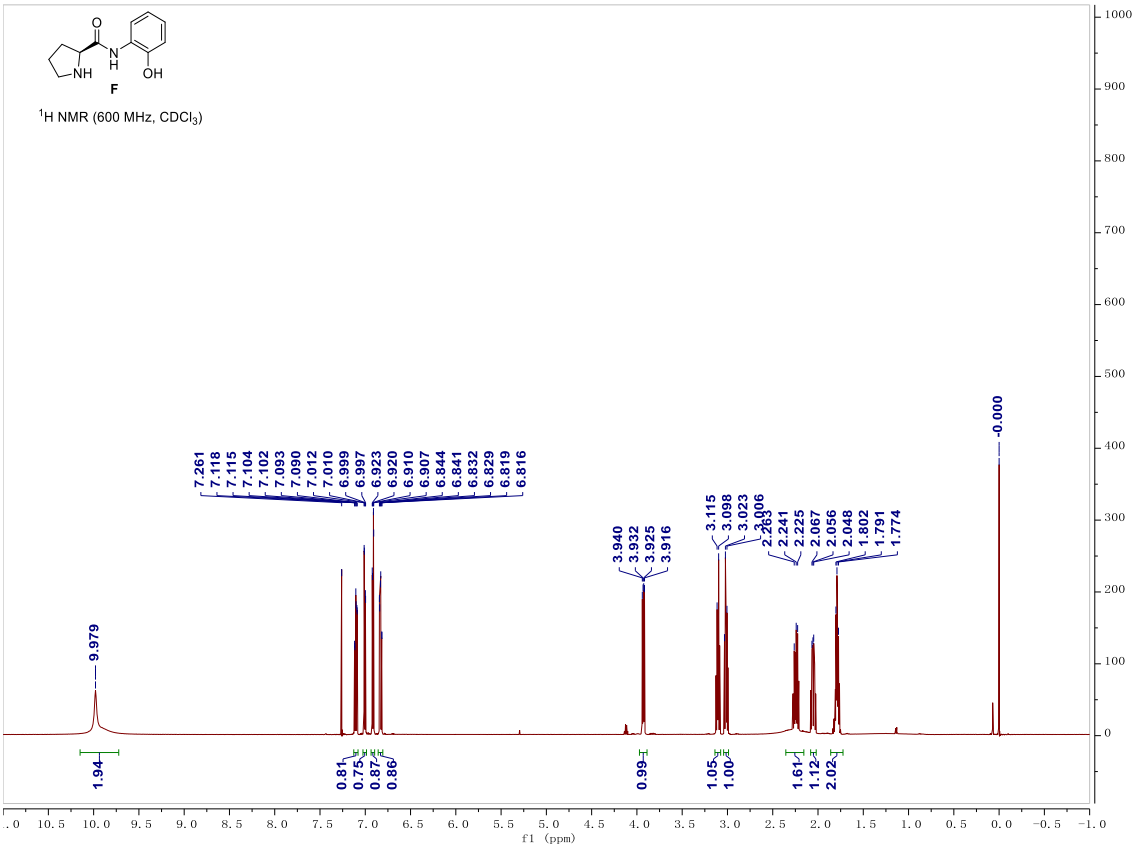


Figure S6. ^{1}H NMR (600 MHz, $CDCl_3$) of Catalyst **F**

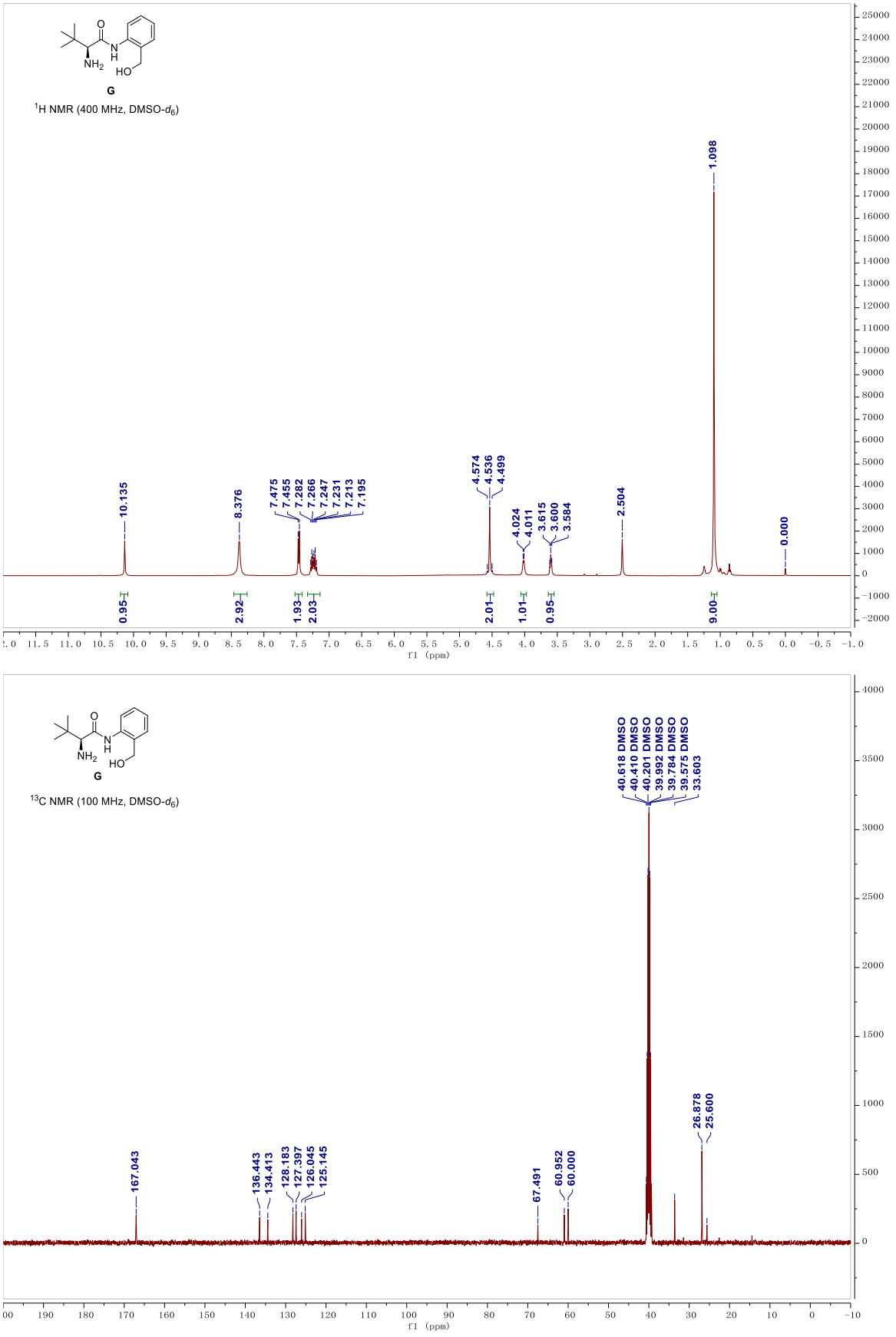
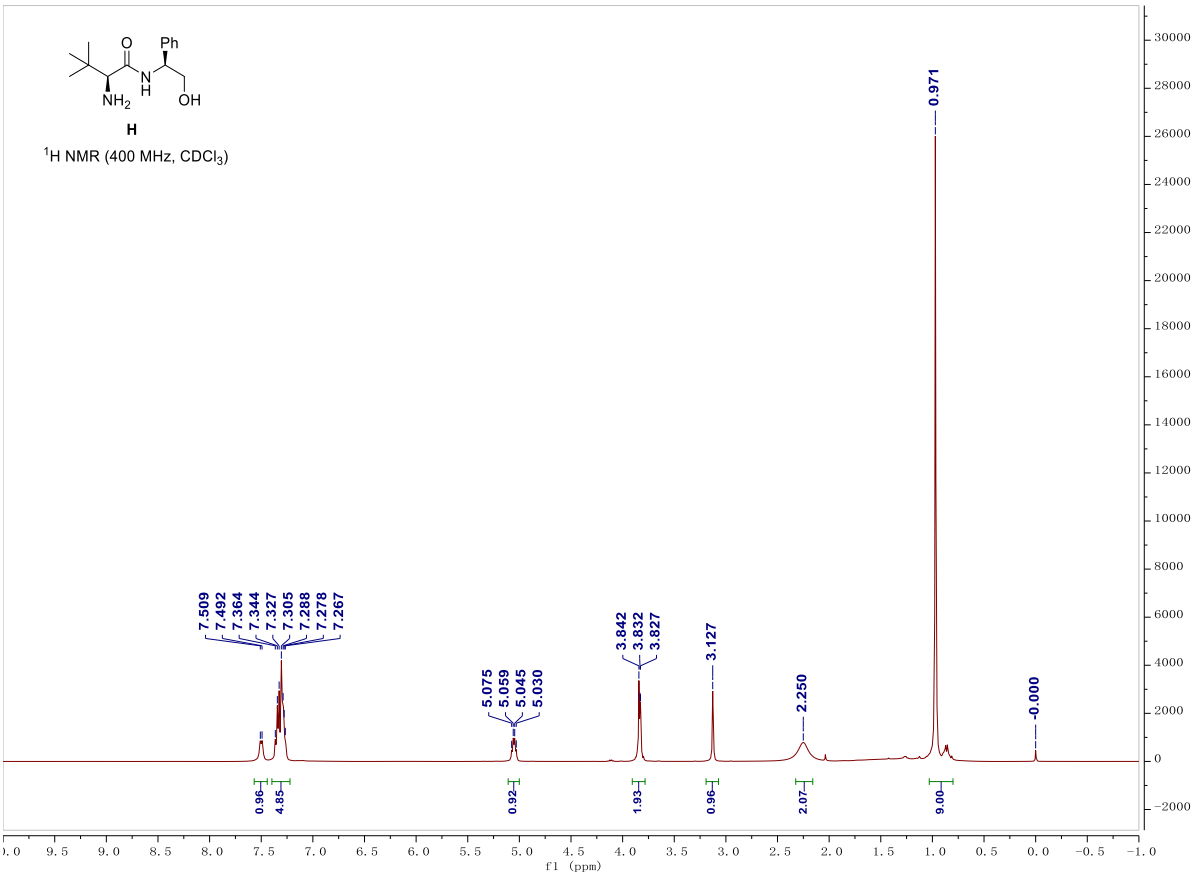


Figure S7. ^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) of Catalyst **G**



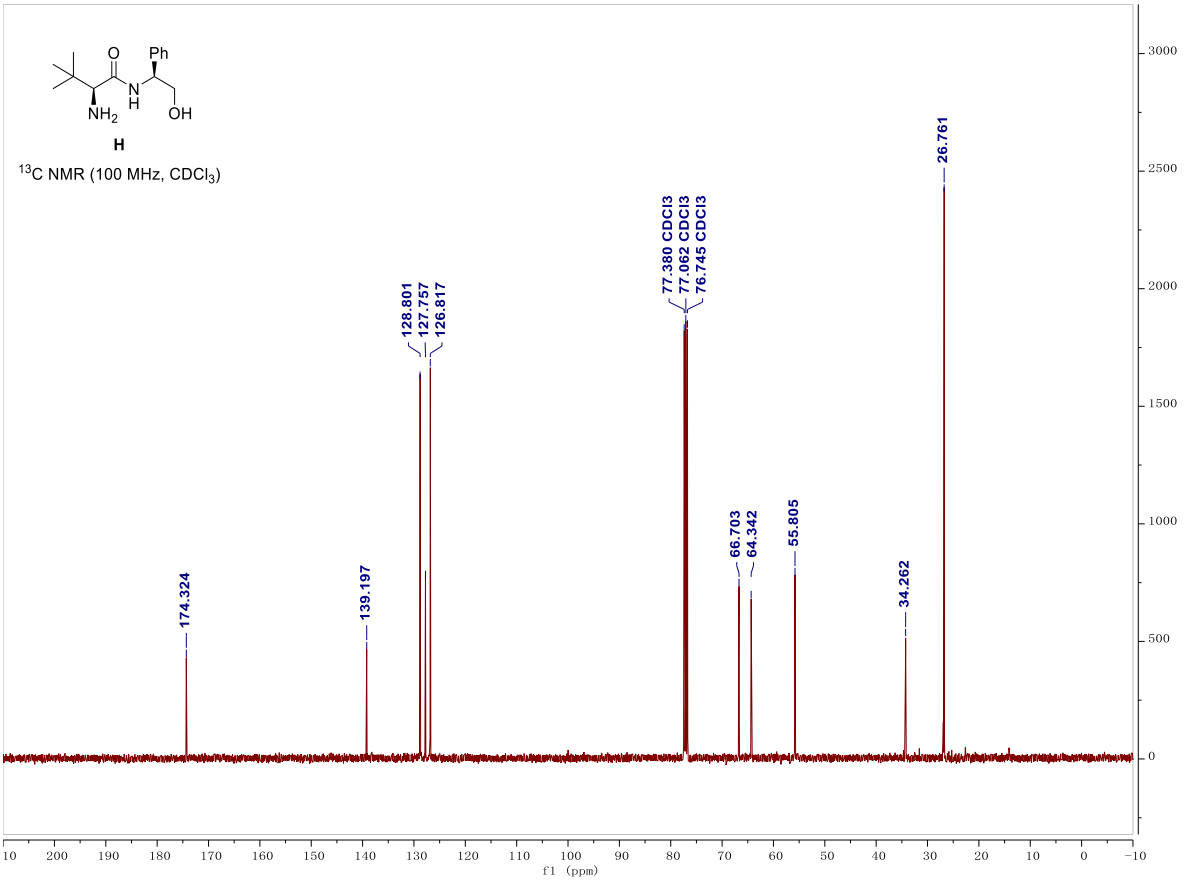


Figure S8. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of Catalyst **H**

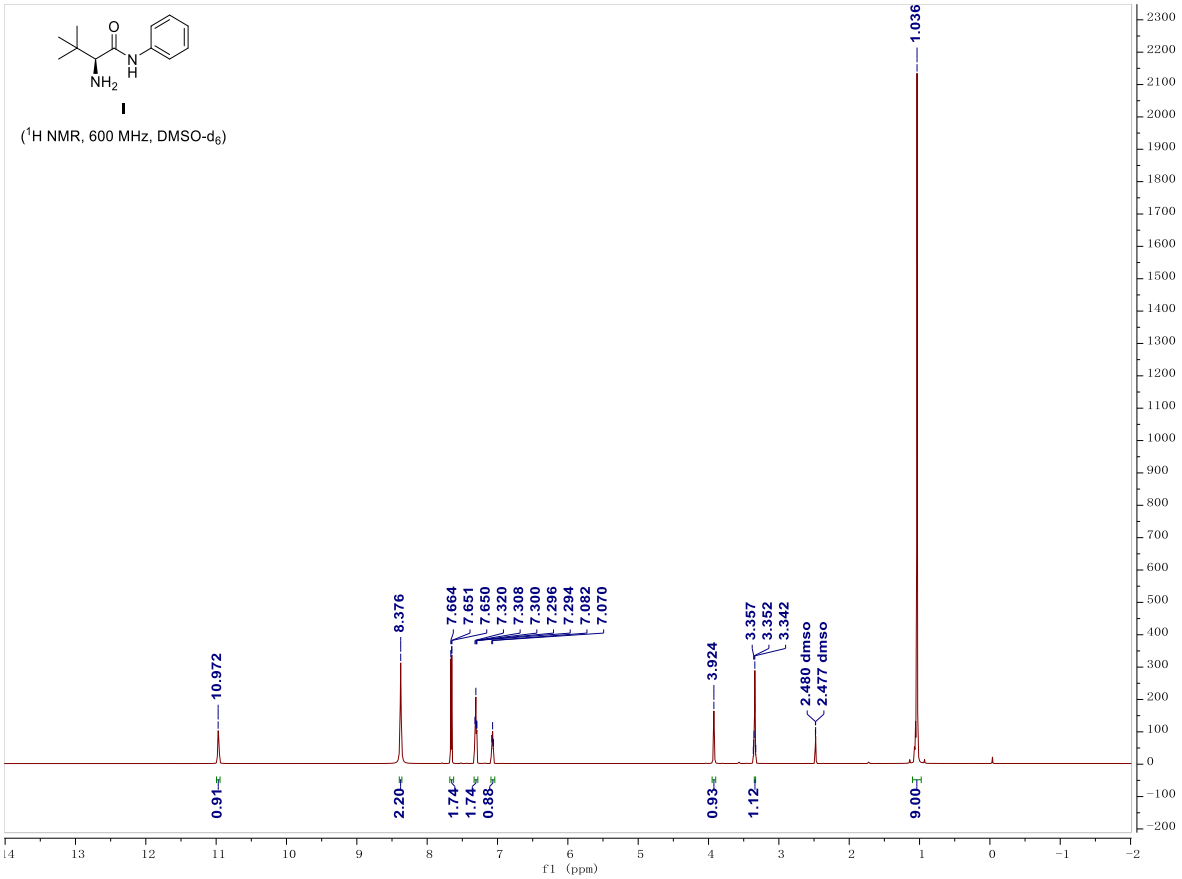


Figure S9. ^{1}H NMR (600 MHz，DMSO-d_6) of Catalyst **K**

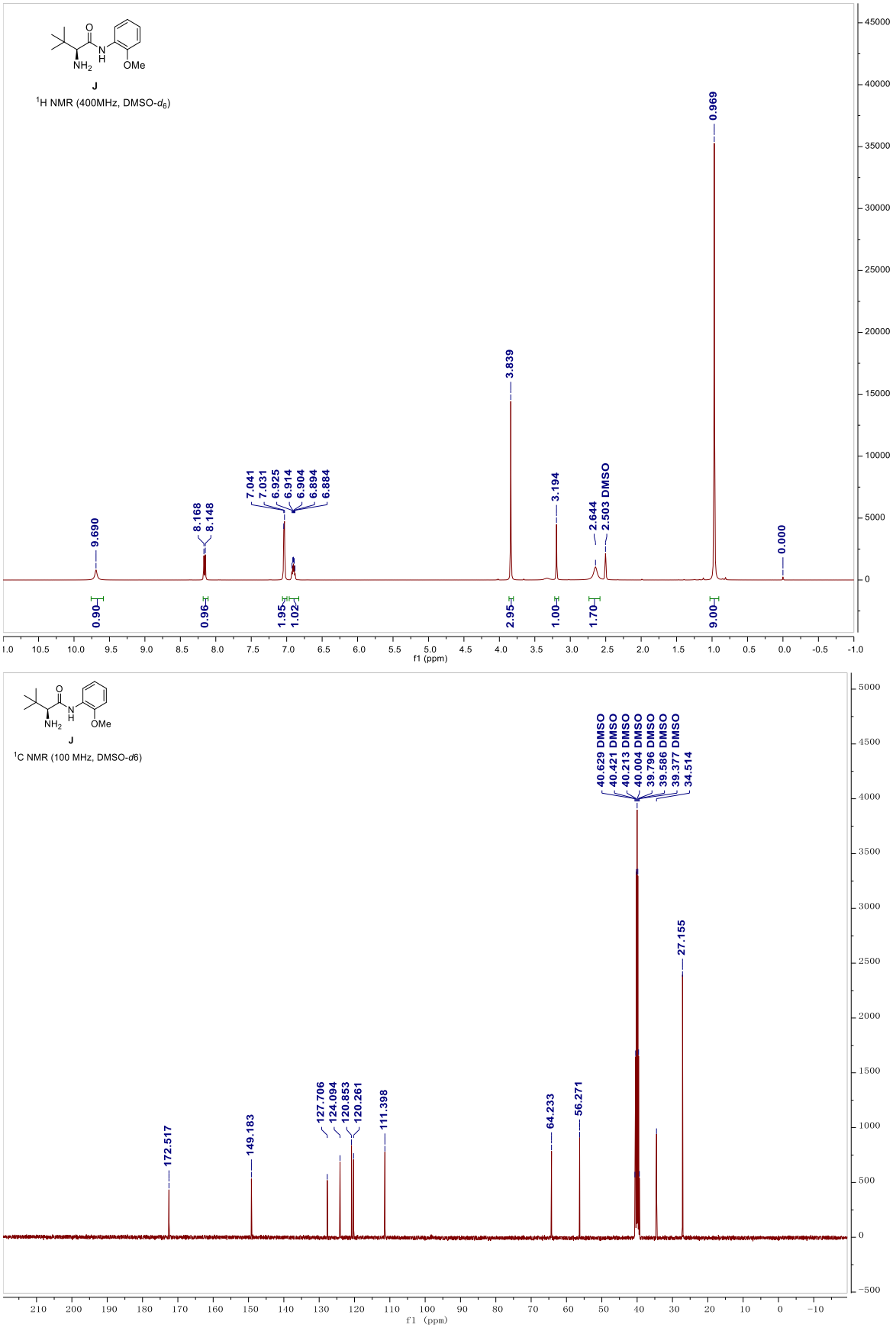


Figure S10. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (600 MHz, $CDCl_3$) of Catalyst **K**

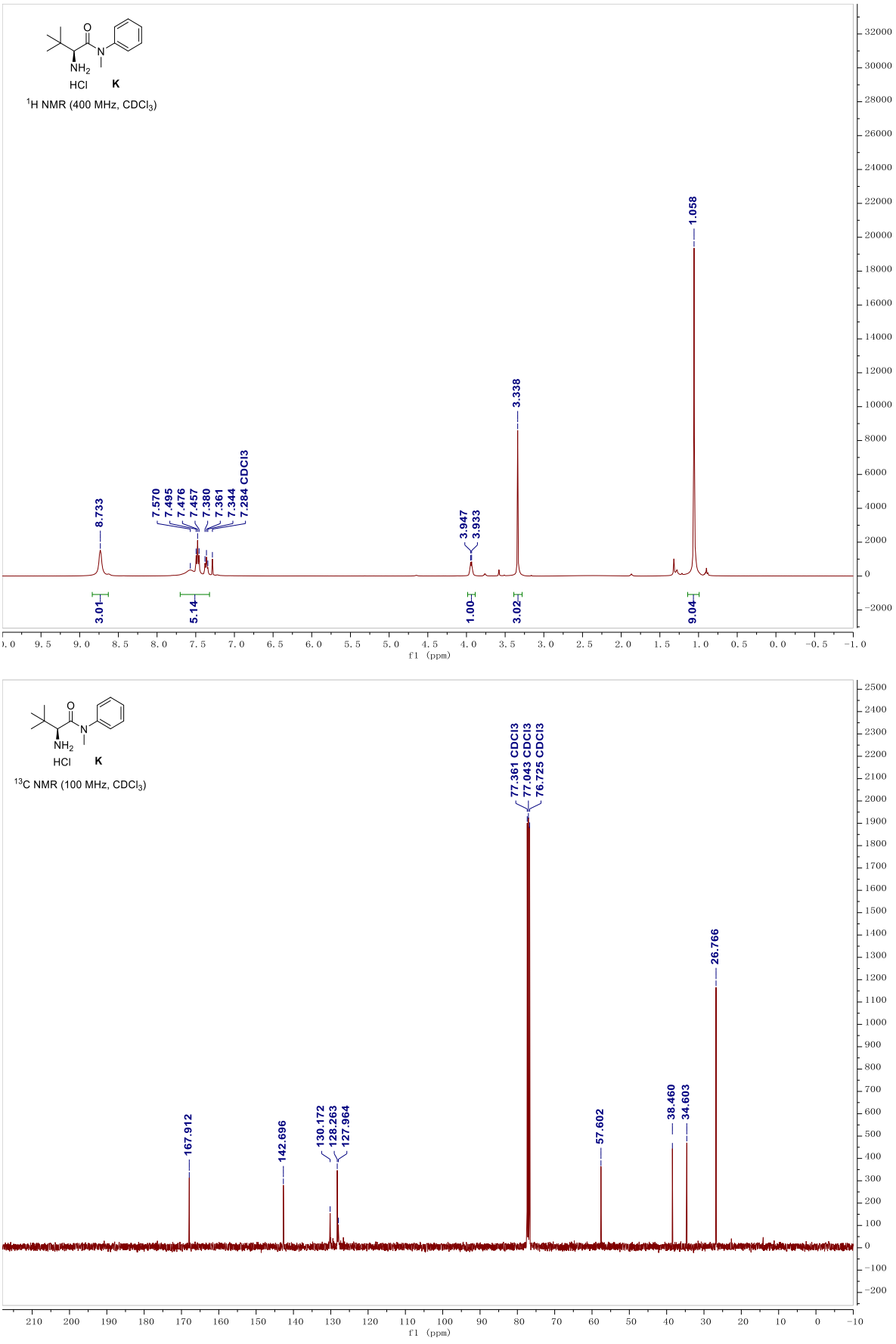


Figure S11. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of Catalyst **K**

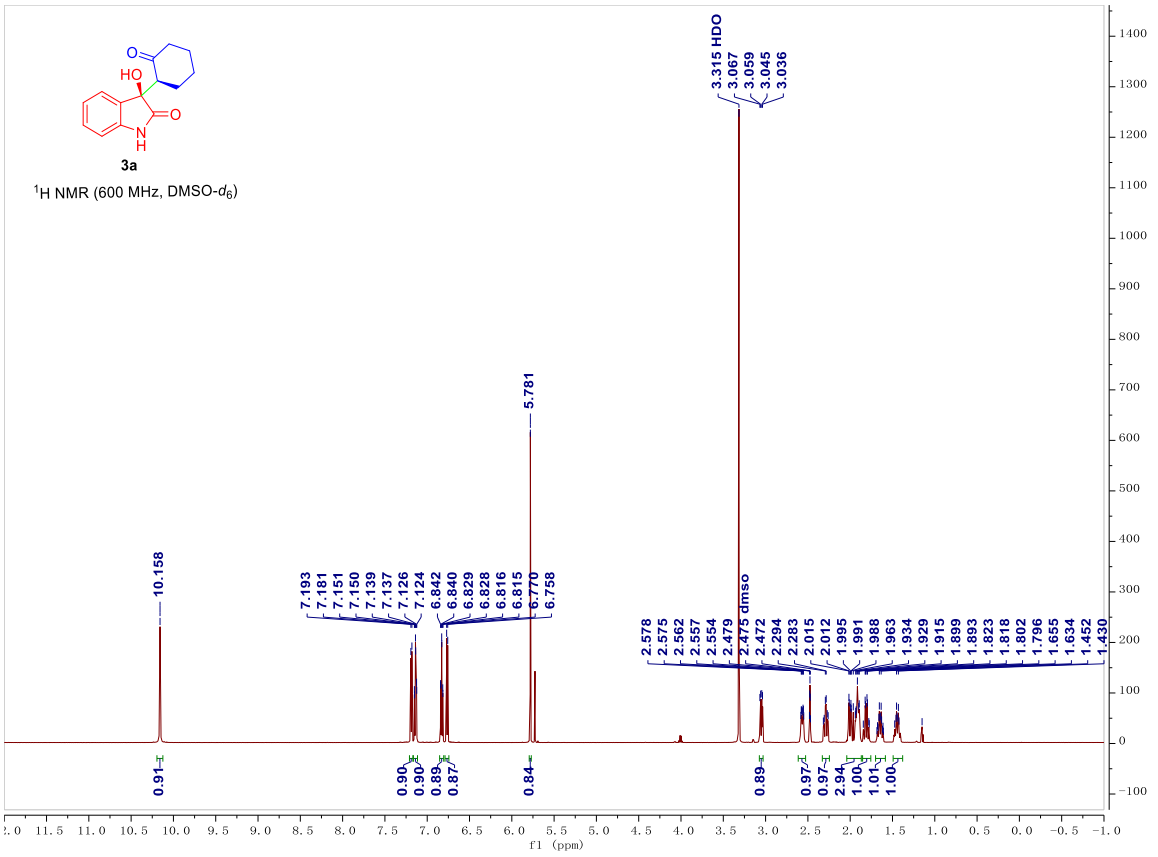


Figure S12. ^{1}H NMR (600 MHz, DMSO-d_6) of **3a**.

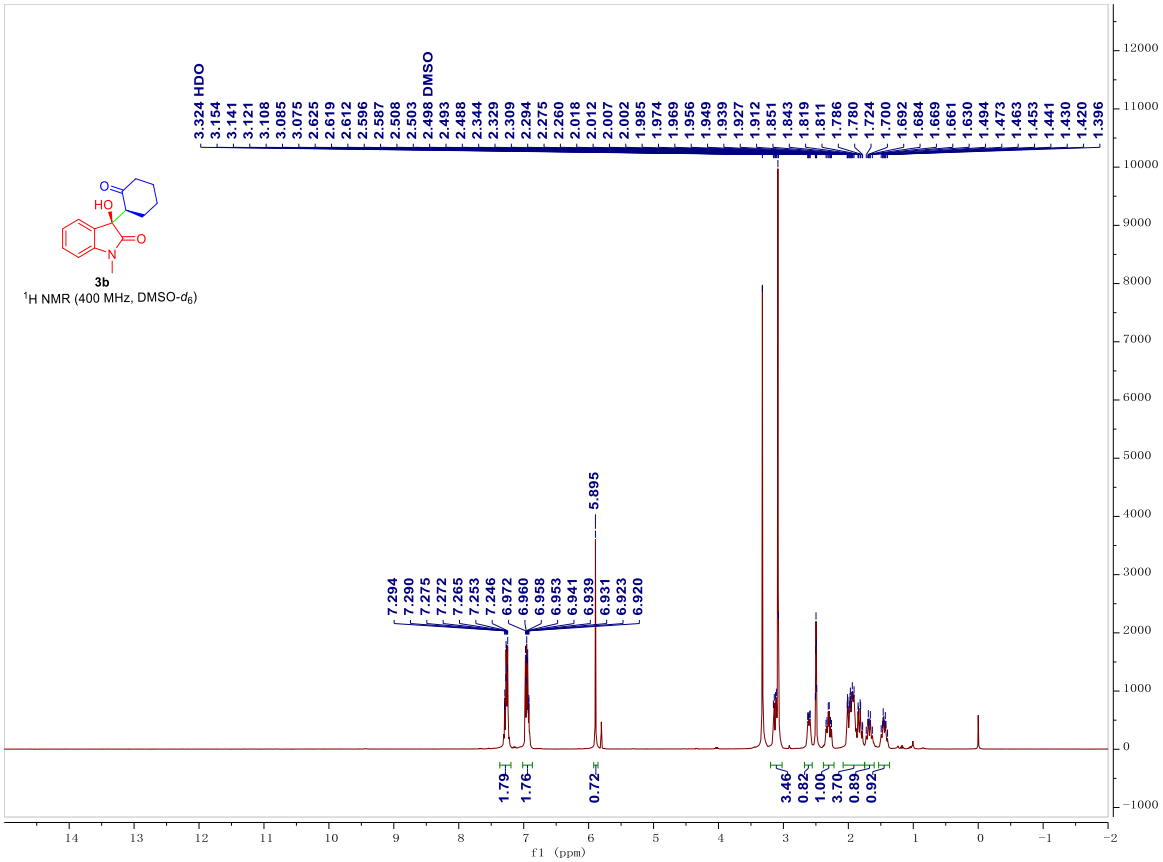


Figure S13. ^{1}H NMR (400 MHz, DMSO-d_6) of **3b**.

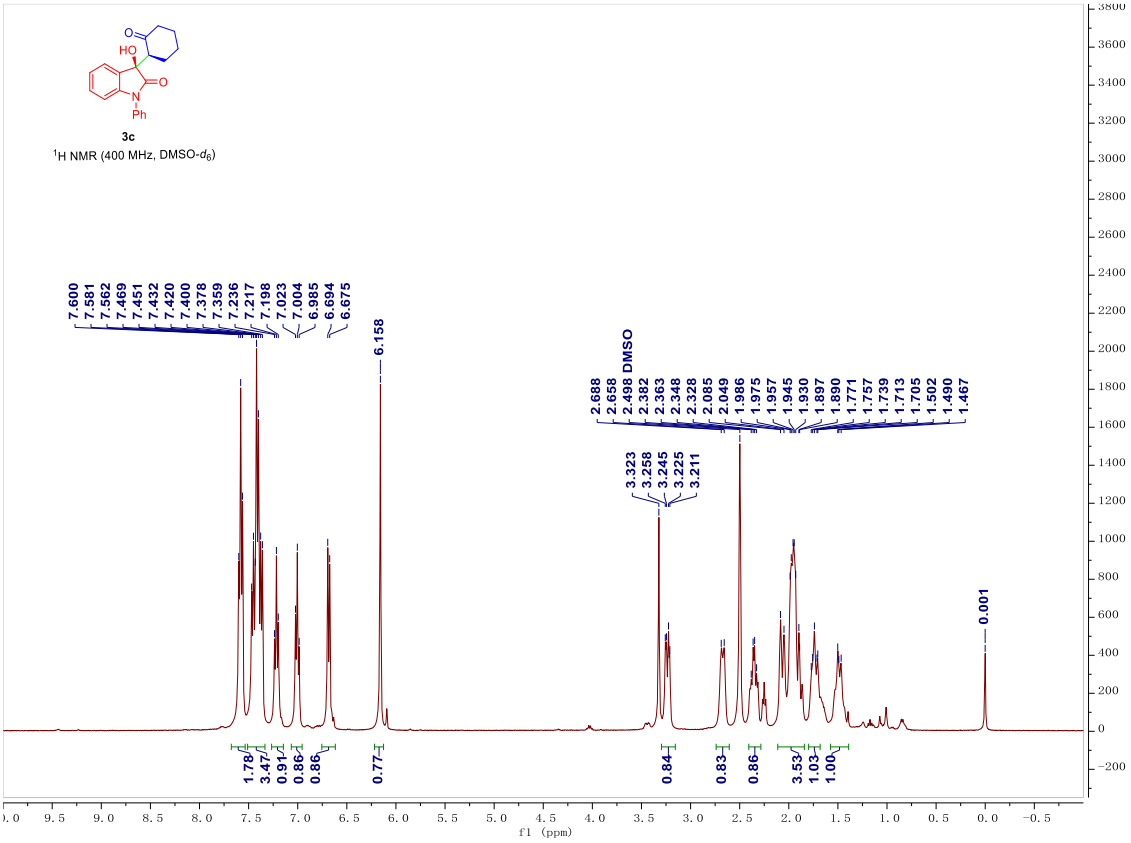


Figure S14. ^{1}H NMR (400 MHz, DMSO-d_6) of **3f**.

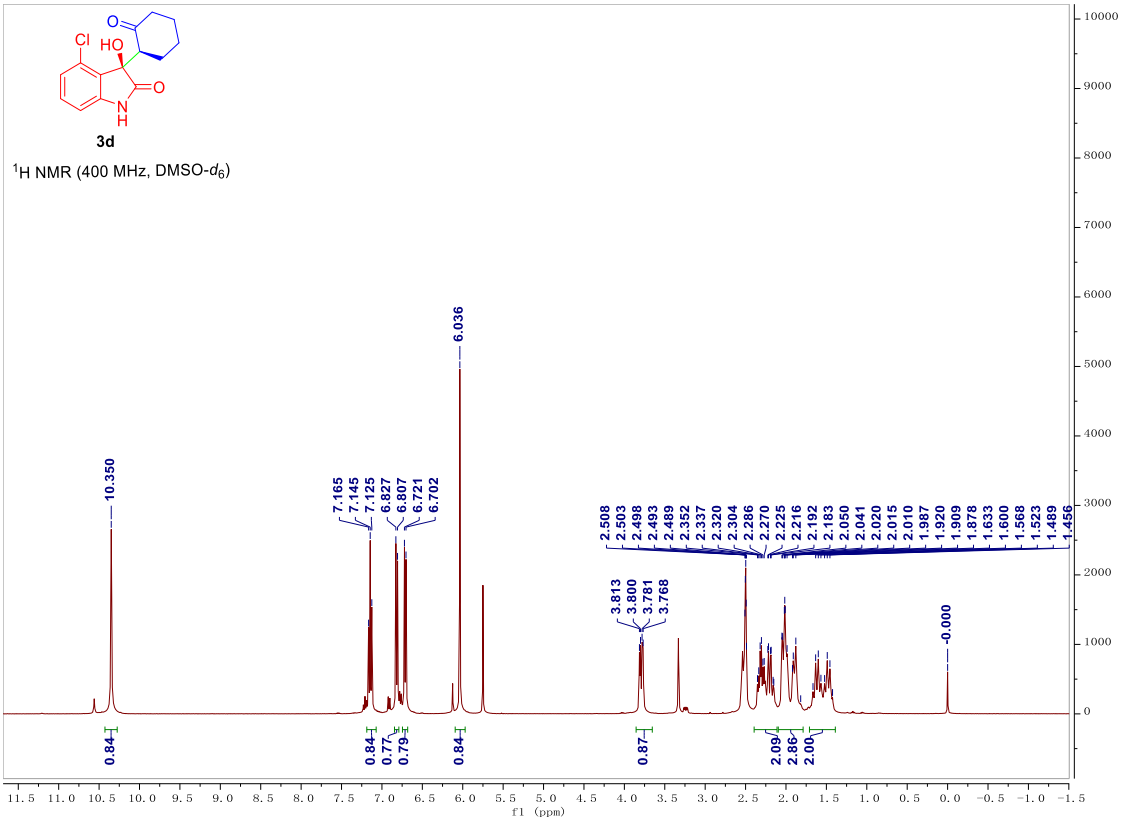


Figure S15. ^{1}H NMR (400 MHz, DMSO-d_6) of **3d**

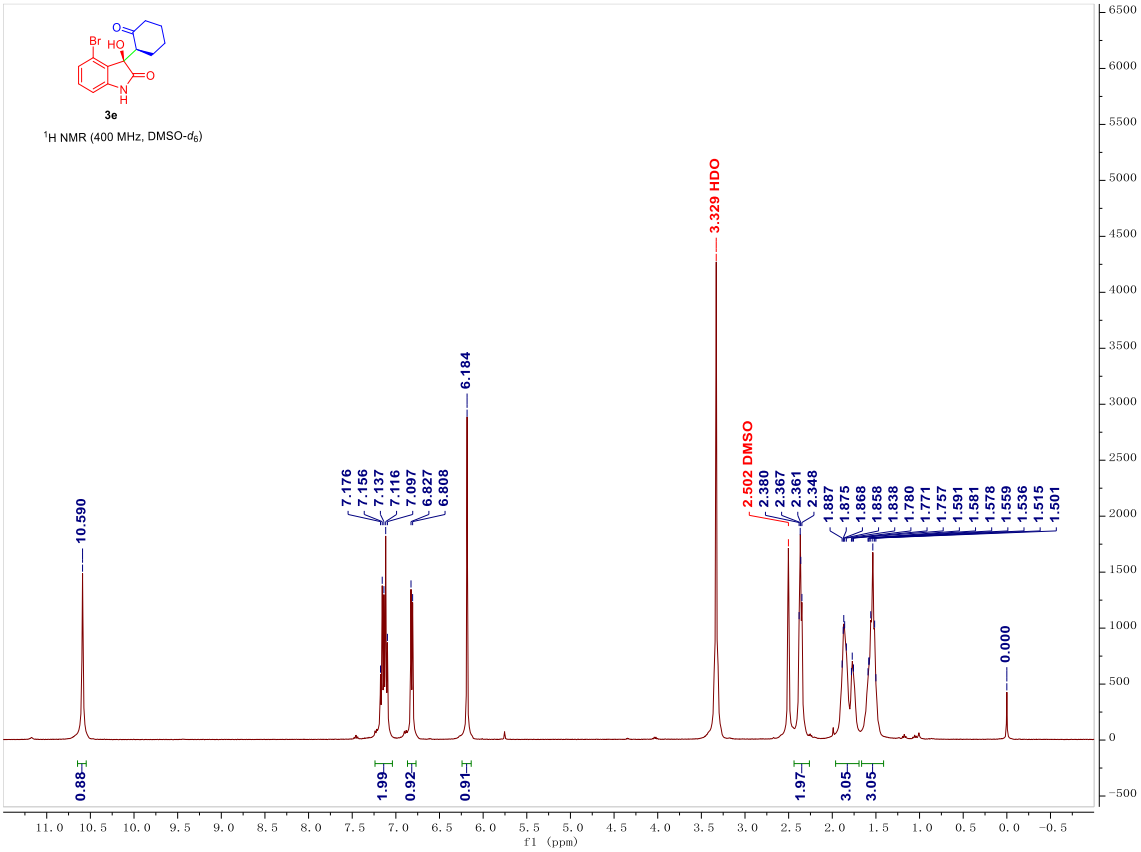


Figure S16. ^{1}H NMR (400 MHz, DMSO-d_6) of **3e**.

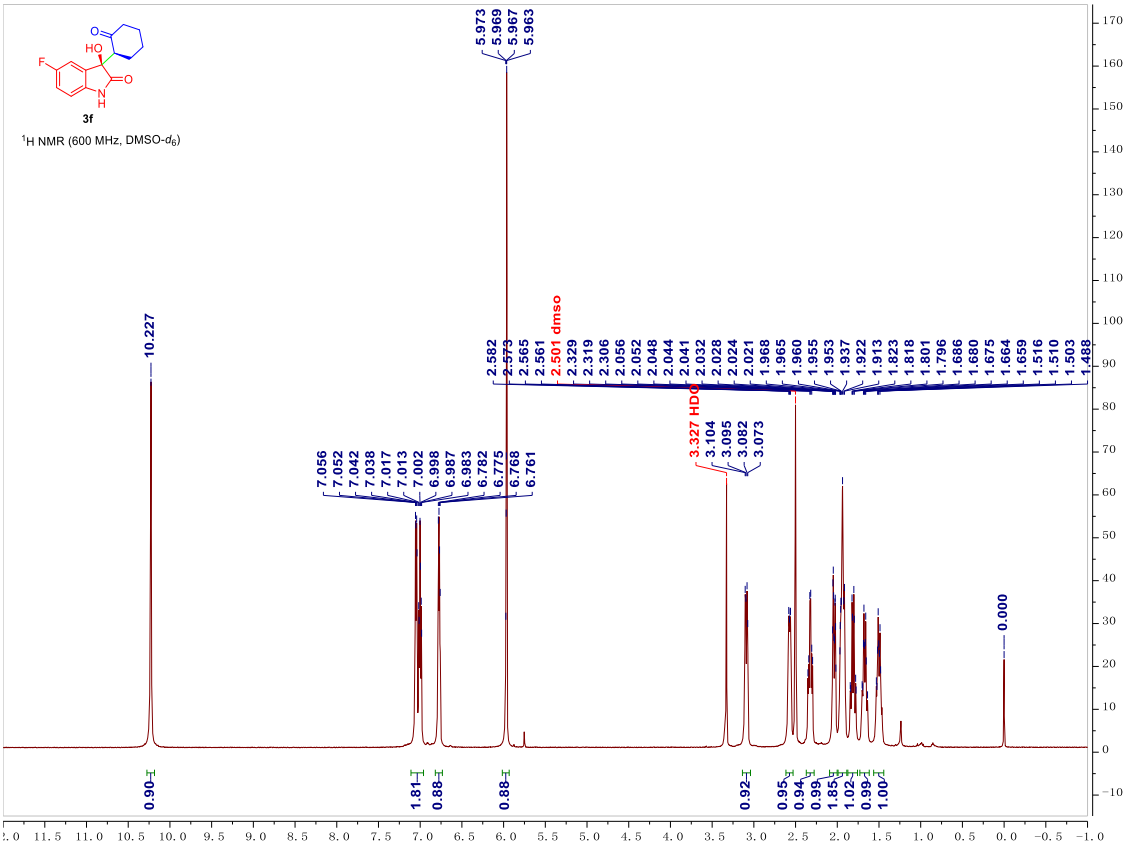


Figure S17. ^{1}H NMR (600 MHz, DMSO-d_6) of **3f**.

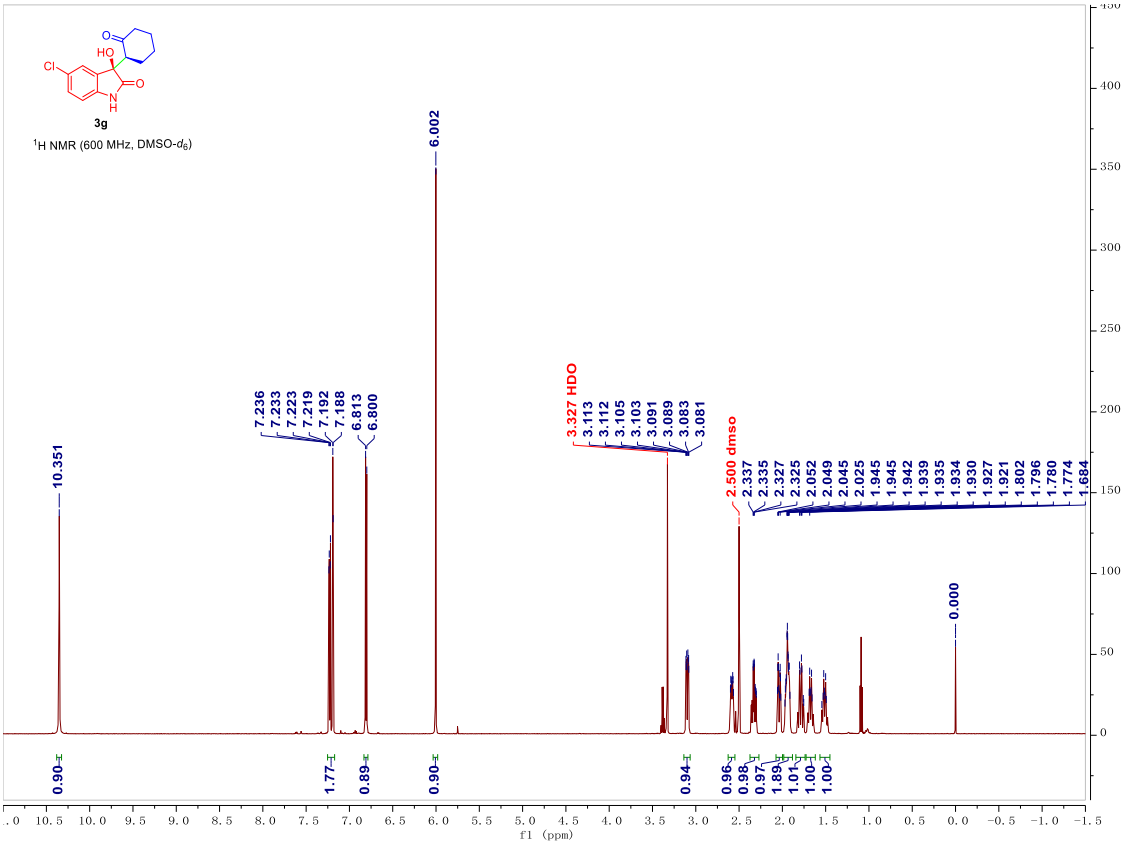


Figure S18. ^{1}H NMR (400 MHz, DMSO-d_6) of **3g**.

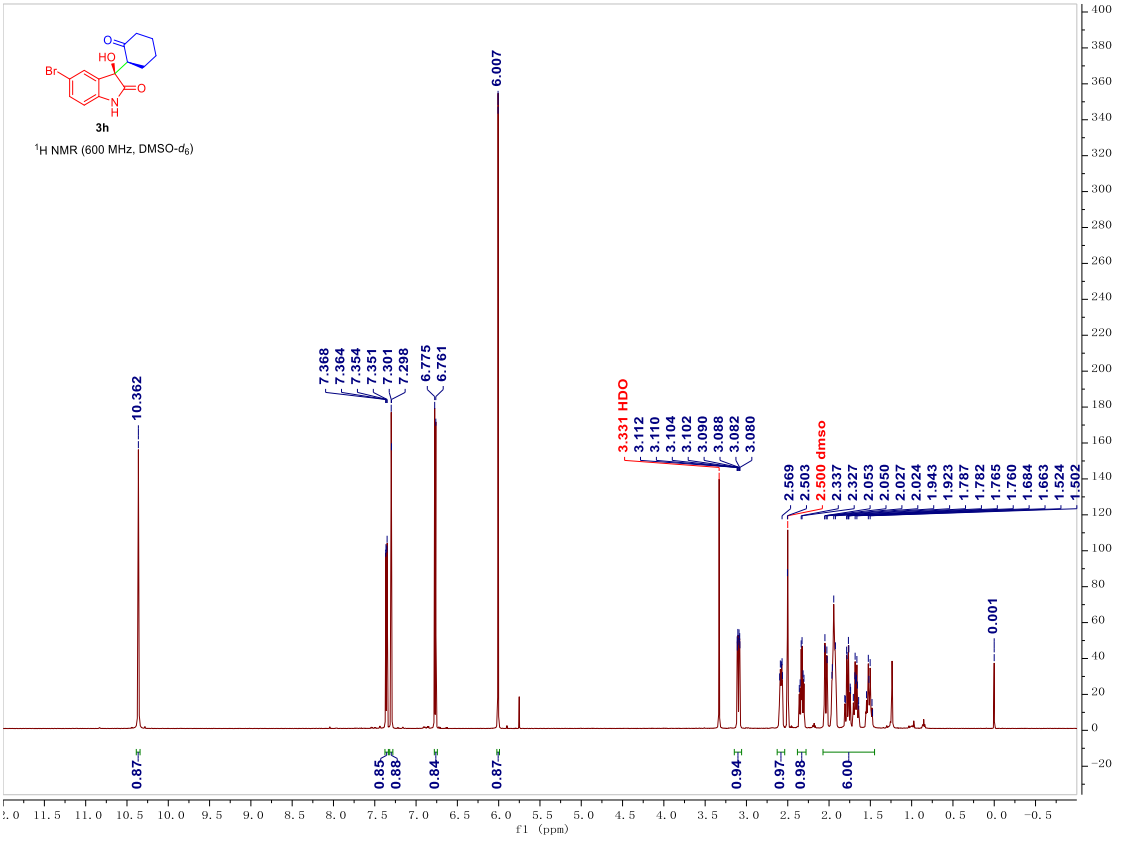


Figure S19. ^{1}H NMR (600 MHz, DMSO-d_6) of **3h**.

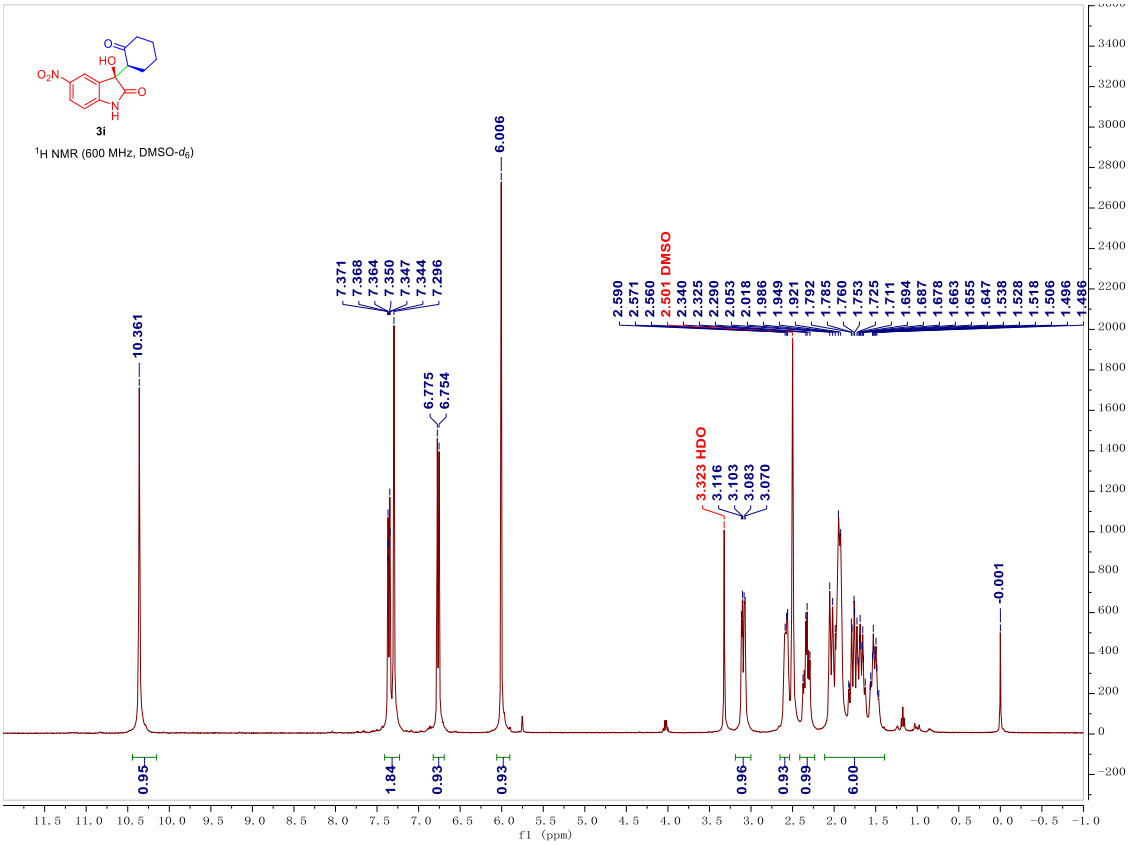


Figure S20. ^{1}H NMR (600 MHz, DMSO-d_6) of **3i**.

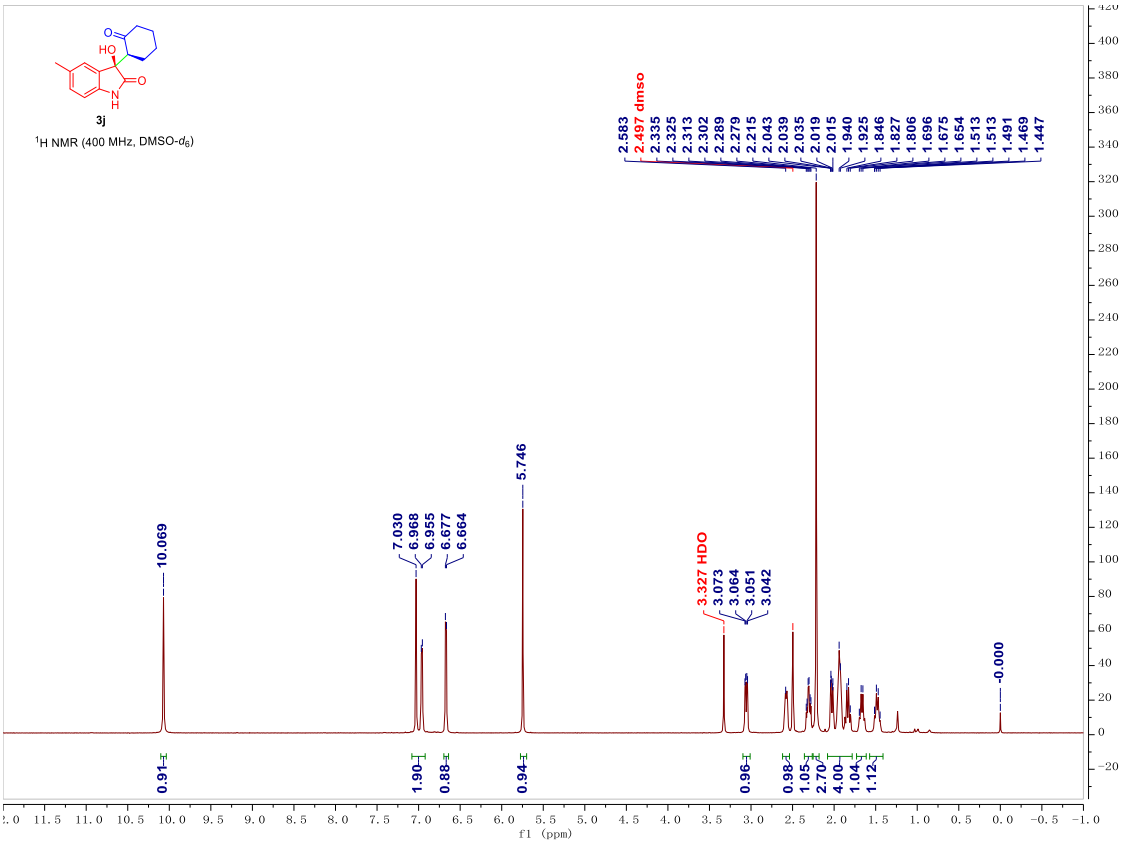


Figure S21. ^{1}H NMR (400 MHz, DMSO-d_6) of **3j**.

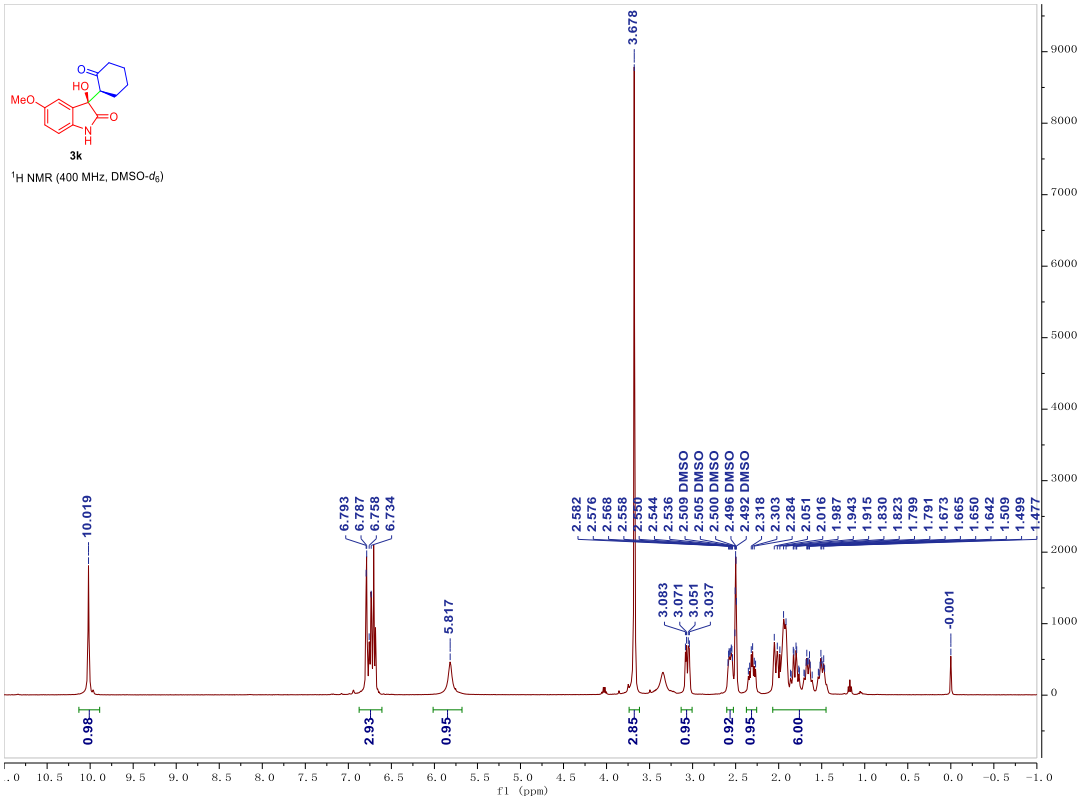


Figure S22. ^{1}H NMR (400 MHz, DMSO-d_6) of **3k**.

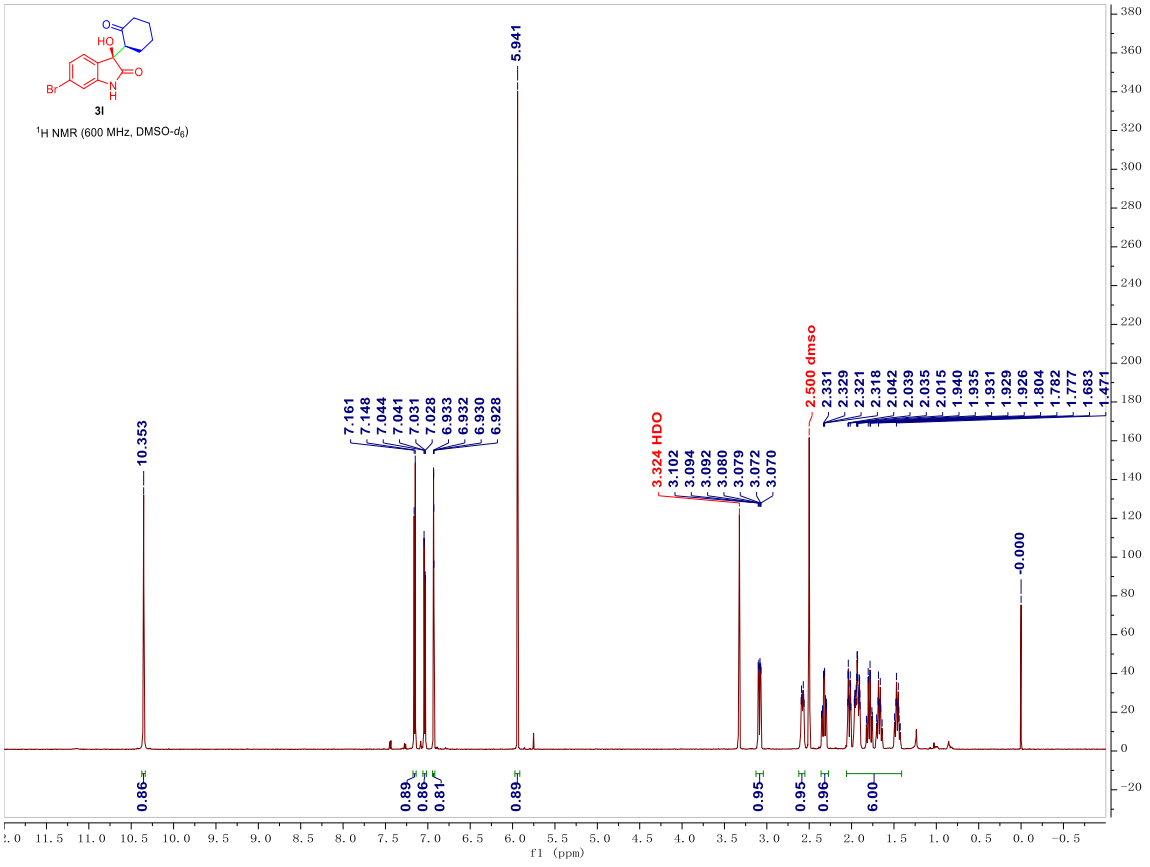


Figure S23. ^{1}H NMR (600 MHz, DMSO-d_6) of **3l**.

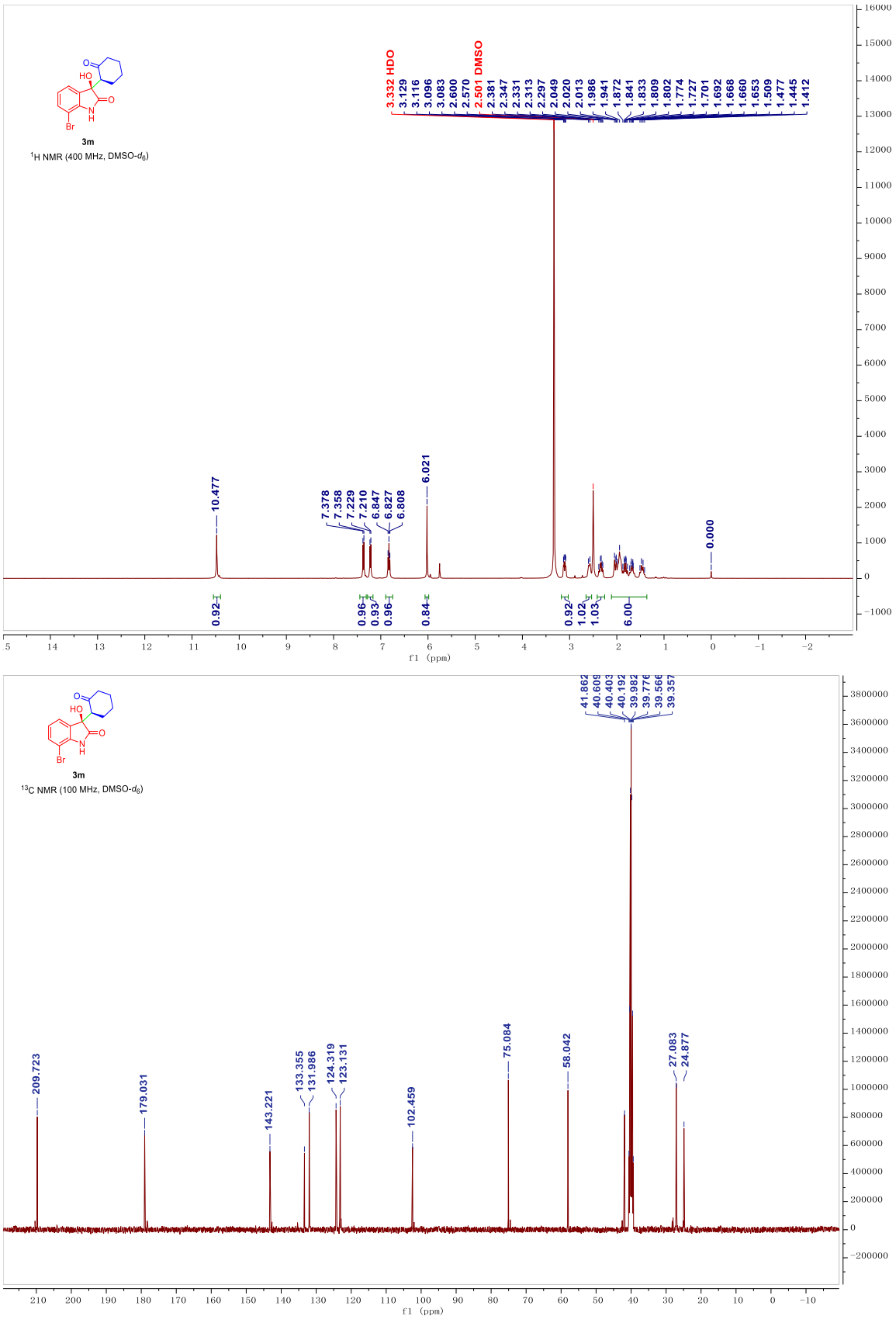


Figure S24. ^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) of **3m**.

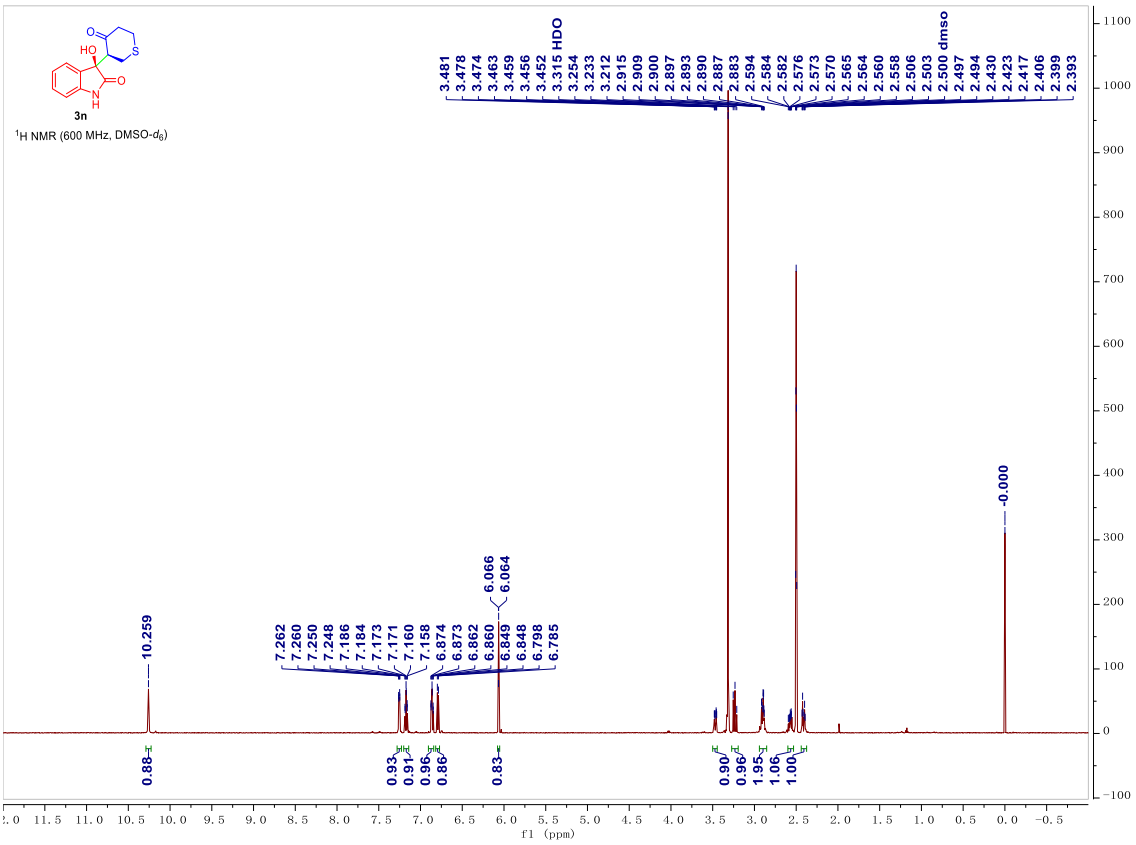


Figure S25. ^{1}H NMR (600 MHz, DMSO-d_6) of **3n**.

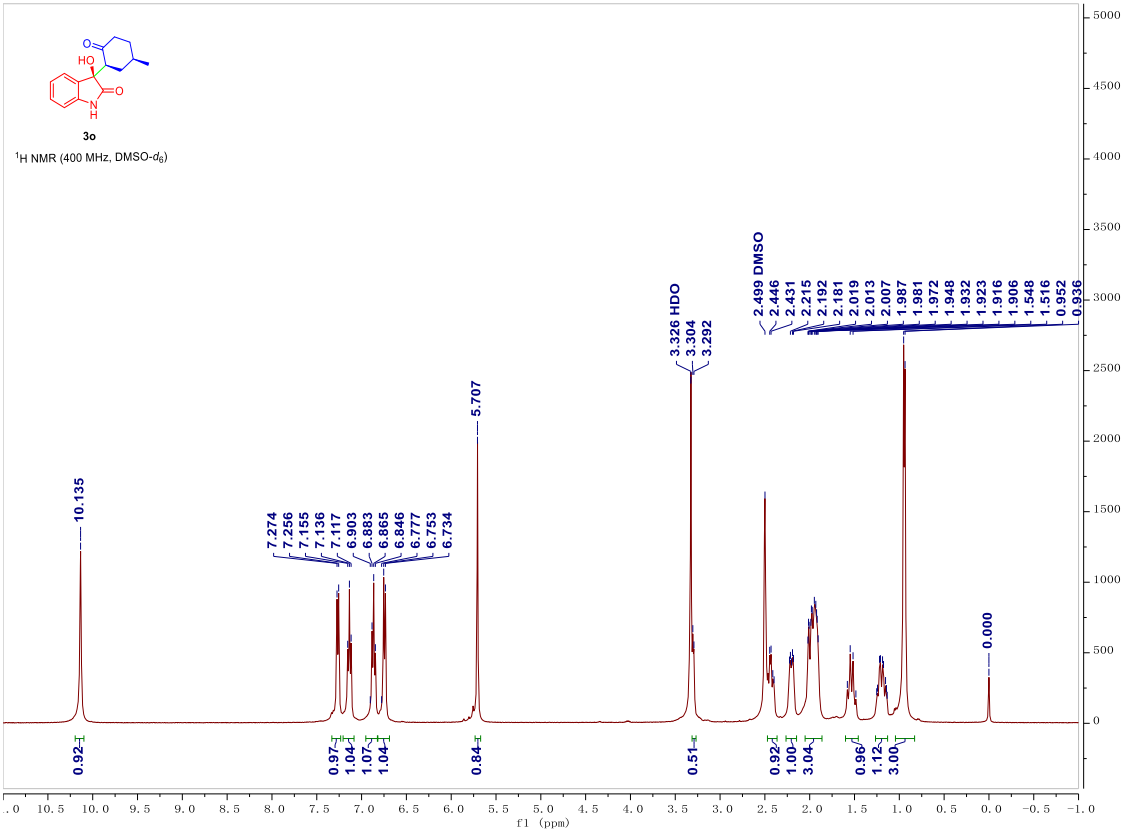


Figure S26. ^{1}H NMR (400 MHz, DMSO-d_6) of **3o**.

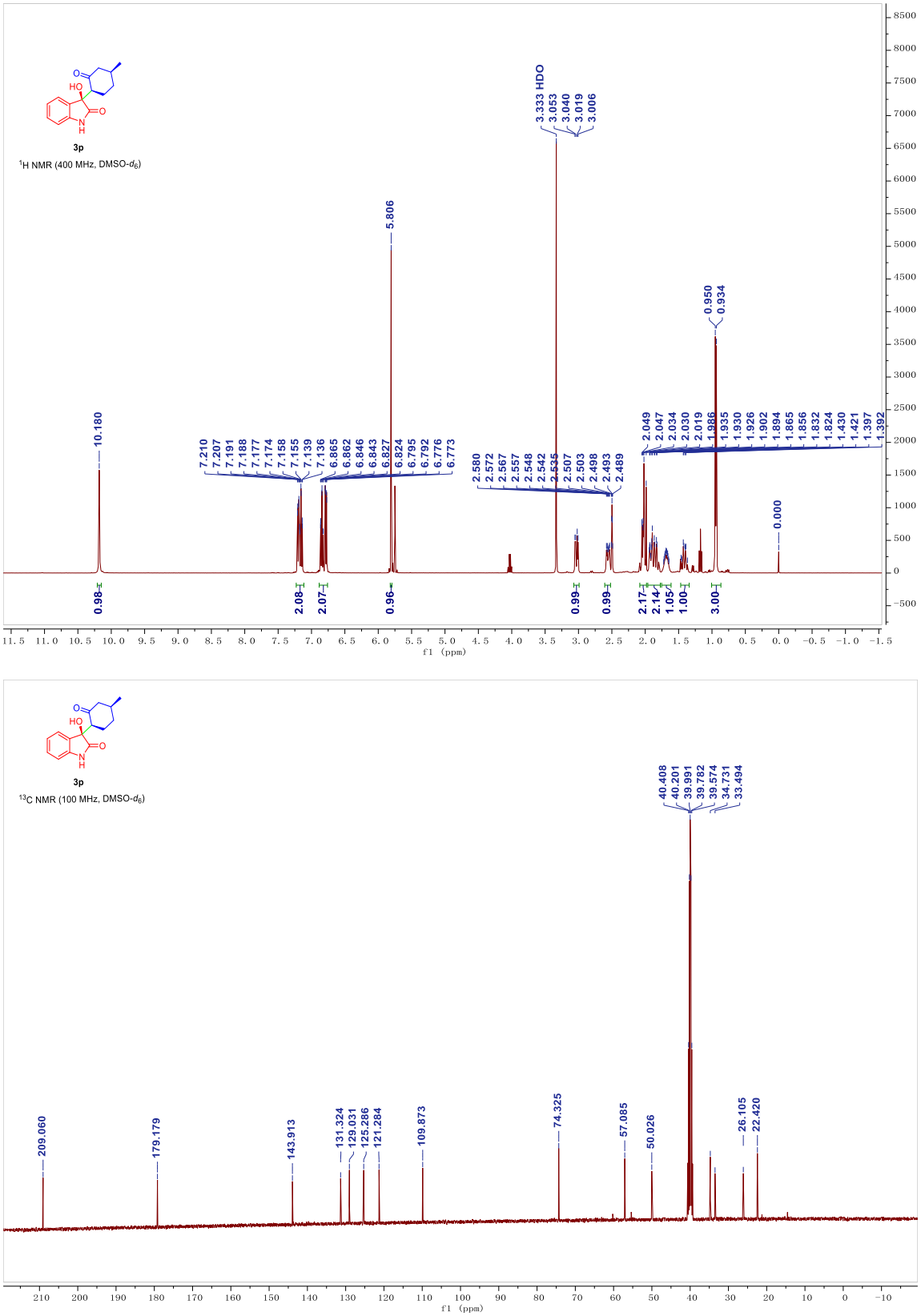


Figure S27. ^{1}H NMR (400 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) of **3p**.

Figure S28. ^{1}H NMR (400 MHz, DMSO-d_6) of **3q**.

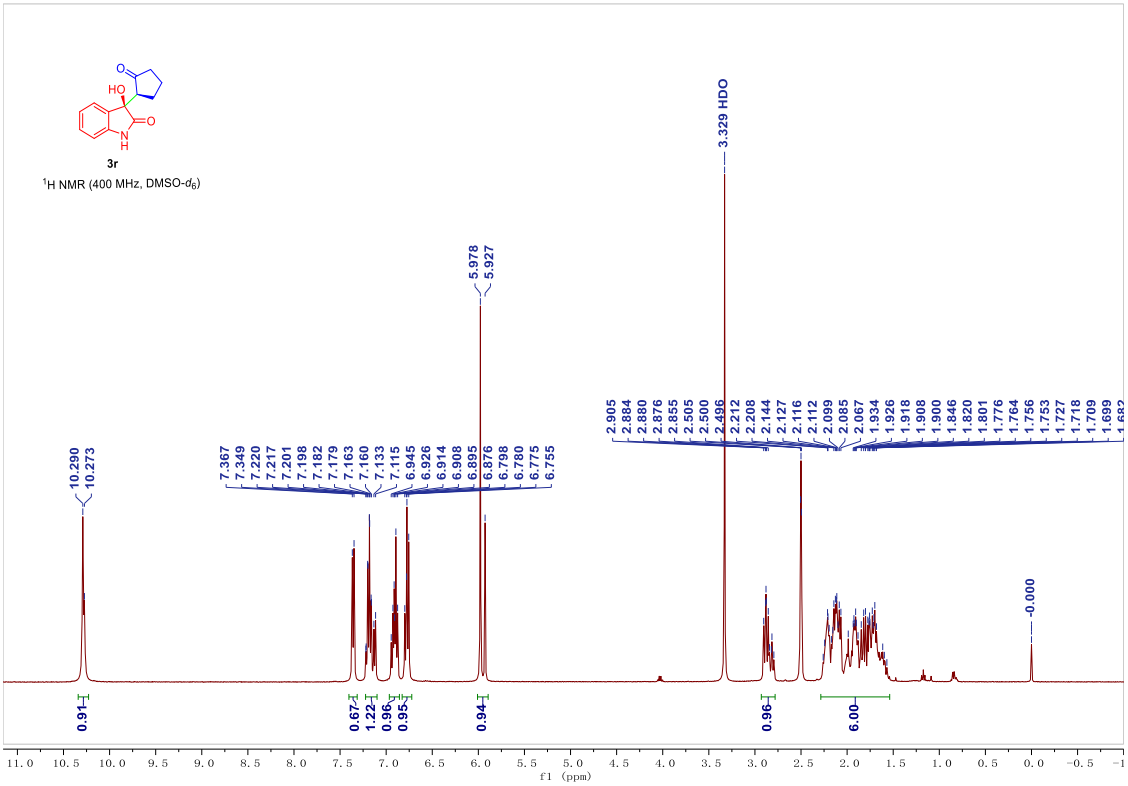


Figure S29. ^{1}H NMR (400 MHz, DMSO-d_6) of **3r**.

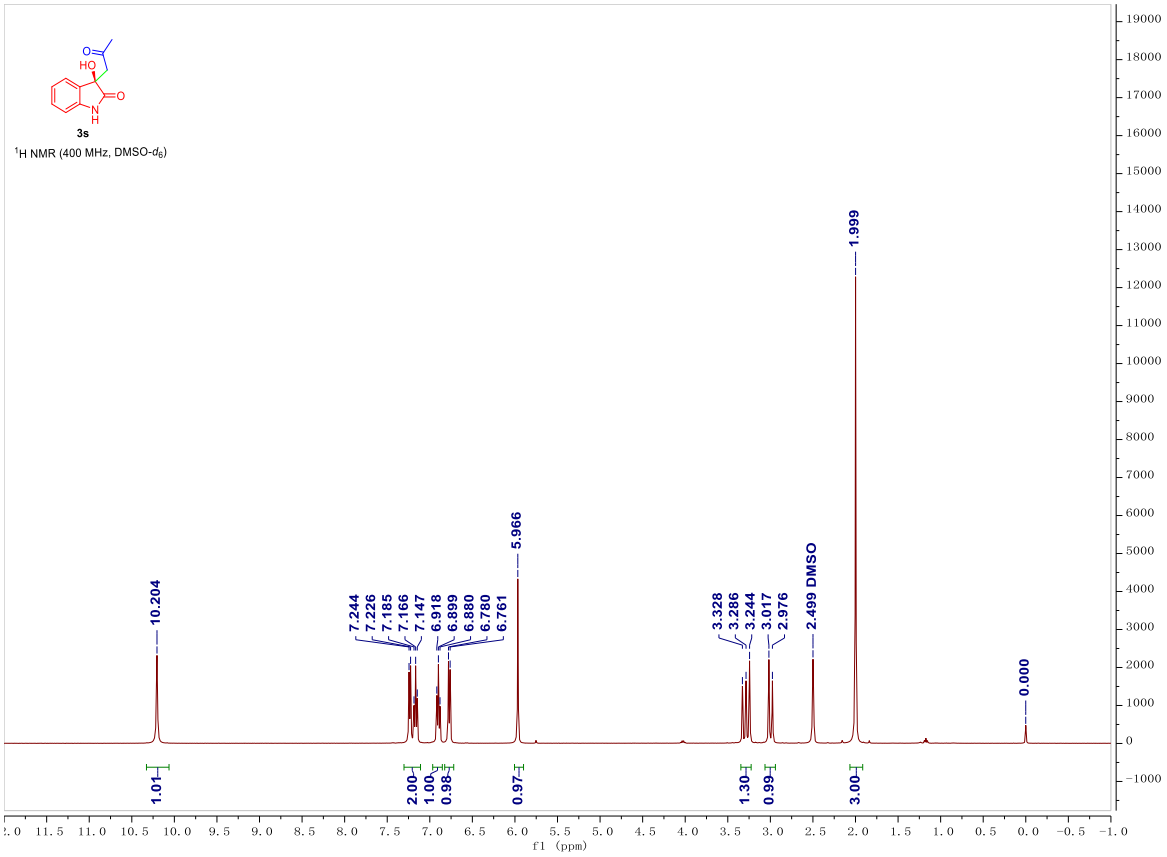
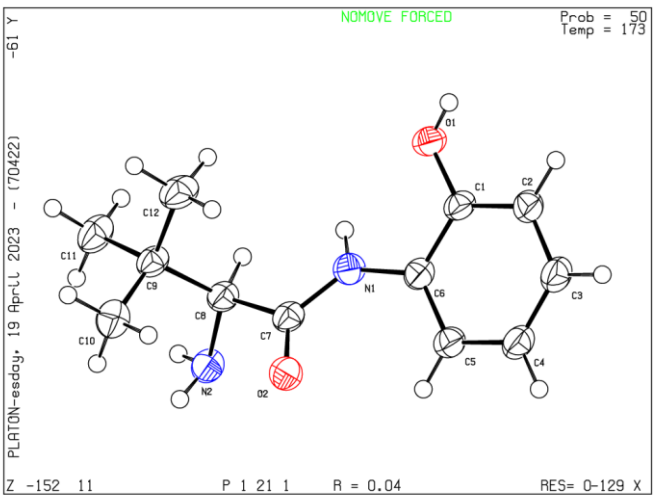
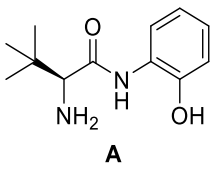


Figure S30. ^{1}H NMR (400 MHz, DMSO-d_6) of **3s**.

7. Single crystal X-ray crystallographic data

7.1. Single crystal data, structural refinement and measurement of catalyst A





A

(CCDC 2184491)

C: **Crystal Data** for $C_{12}H_{18}N_2O_2$ (M =222.28 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 6.0452(3) Å, b = 10.0440(5) Å, c = 9.6566(4) Å, β = 90.901(2)°, V = 586.26(5) Å^3, Z = 2, T =

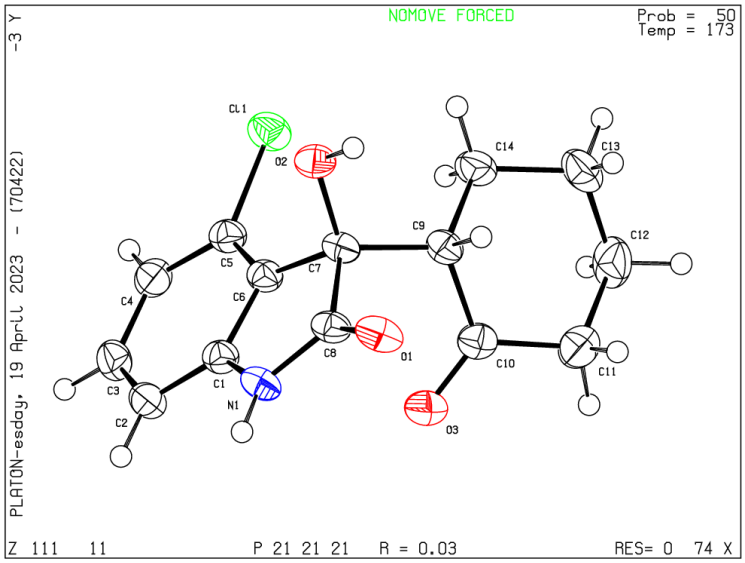
173.0 K, μ(CuKα) = 0.698 mm^{-1}, *Dcalc* = 1.259 g/cm^3, 12901 reflections measured (9.158° ≤ 2Θ ≤ 149.614°), 2372 unique (R_{int} = 0.0540, R_{sigma} = 0.0338) which were used in all calculations. The final R_1 was 0.0369 (I > 2σ(I)) and wR_2 was 0.0936 (all data). A suitable crystal was selected on a Bruker D8 Venture diffractometer. The crystal was kept at 173.00 K during data collection. Using Olex2 [1], the structure was solved with the olex2.solve [2] structure solution program using Charge Flipping and refined with the olex2.refine [3] refinement package using Gauss-Newton minimization.

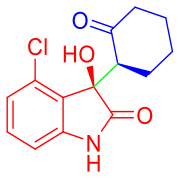
Table 1 Crystal data and structure refinement for A.

Identification code	A
Empirical formula	$C_{12}H_{18}N_2O_2$
Formula weight	222.28
Temperature/K	173.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	6.0452(3)
b/Å	10.0440(5)
c/Å	9.6566(4)
α/°	90
β/°	90.901(2)
γ/°	90
Volume/$Å^3$	586.26(5)
Z	2
$\rho_{calc}g/cm^3$	1.259
μ/mm^{-1}	0.698
F(000)	240.0
Crystal size/mm^3	0.25 × 0.22 × 0.19
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.158 to 149.614
Index ranges	-7 ≤ h ≤ 7, -12 ≤ k ≤ 12, -12 ≤ l ≤ 12
Reflections collected	12901
Independent reflections	2372 [R_{int} = 0.0540, R_{sigma} = 0.0338]
Data/restraints/parameters	2372/1/156
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0369, wR_2 = 0.0915
Final R indexes [all data]	R_1 = 0.0386, wR_2 = 0.0936
Largest diff. peak/hole / e $Å^{-3}$	0.22/-0.18

Flack parameter 0.06(9)

7.2 Single crystal data, structural refinement and measurement of 3d





3d

(CCDC: 2184490)

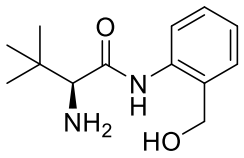
3d: Single crystals of $C_{14}H_{14}ClNO_3$ (M =279.725 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 7.2587(2) Å, b = 11.3133(3) Å, c = 15.3314(4) Å, V = 1259.01(6) Å^3, Z = 4, T = 173.00 K, μ(Cu Kα) = 2.730 mm^{-1}, *Dcalc* = 1.476 g/cm^3, 30428 reflections measured (9.72° ≤ 2Θ ≤ 144.08°), 2467 unique (R_{int} = 0.0533, R_{sigma} = 0.0207) which were used in all calculations. The final R_1 was 0.0298 (I>=2u(I)) and wR_2 was 0.0768 (all data). A suitable crystal was selected on a Bruker D8 Venture diffractometer. The crystal was kept at 173.00 K during data collection. Using Olex2 [1], the structure was solved with the olex2.solve [2] structure solution program using Charge Flipping and refined with the olex2.refine [3] refinement package using Gauss-Newton minimization.

Table 1 Crystal data and structure refinement for 3d.

Identification code	**3d**
Empirical formula	$C_{14}H_{14}ClNO_3$
Formula weight	279.725
Temperature/K	173.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.2587(2)
b/Å	11.3133(3)
c/Å	15.3314(4)
α/°	90

β/°	90
γ/°	90
Volume/Å^3	1259.01(6)
Z	4
ρ_{calc}g/cm^3	1.476
μ/mm^{-1}	2.730
F(000)	587.4
Crystal size/mm^3	0.19 × 0.17 × 0.16
Radiation	Cu Kα (λ = 1.54178)
2Θ range for data collection/°	9.72 to 144.08
Index ranges	-8 ≤ h ≤ 8, -13 ≤ k ≤ 13, -18 ≤ l ≤ 17
Reflections collected	30428
Independent reflections	2467 [R_{int} = 0.0533, R_{sigma} = 0.0207]
Data/restraints/parameters	2467/0/173
Goodness-of-fit on F^2	1.086
Final R indexes [I>=2σ (I)]	R_1 = 0.0298, wR_2 = 0.0761
Final R indexes [all data]	R_1 = 0.0307, wR_2 = 0.0768
Largest diff. peak/hole / e Å^{-3}	0.29/-0.18
Flack parameter	0.027(6)

8. Copies of HRMS spectra



G

Chemical Formula: $C_{13}H_{20}N_2O_2$

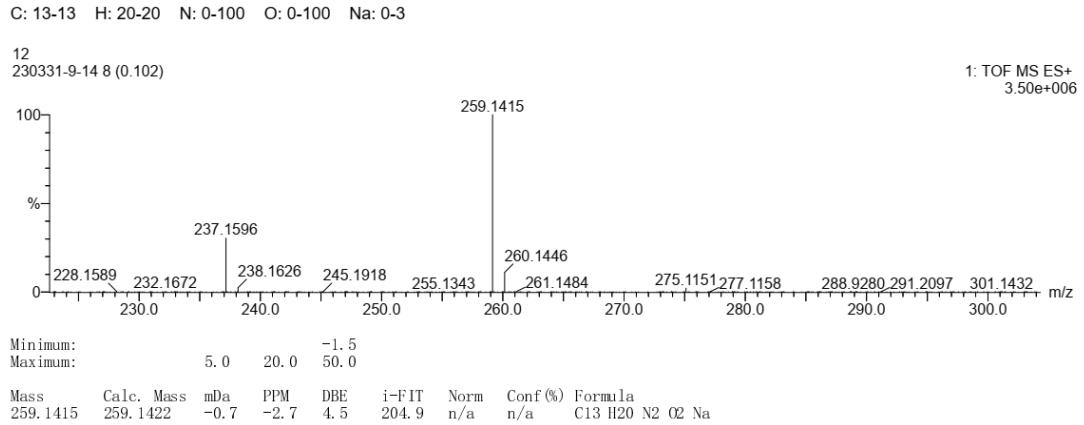
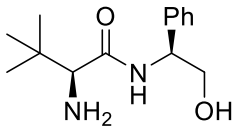


Figure S31. HRMS spectra of **G.**



H

Chemical Formula: $C_{14}H_{22}N_2O_2$

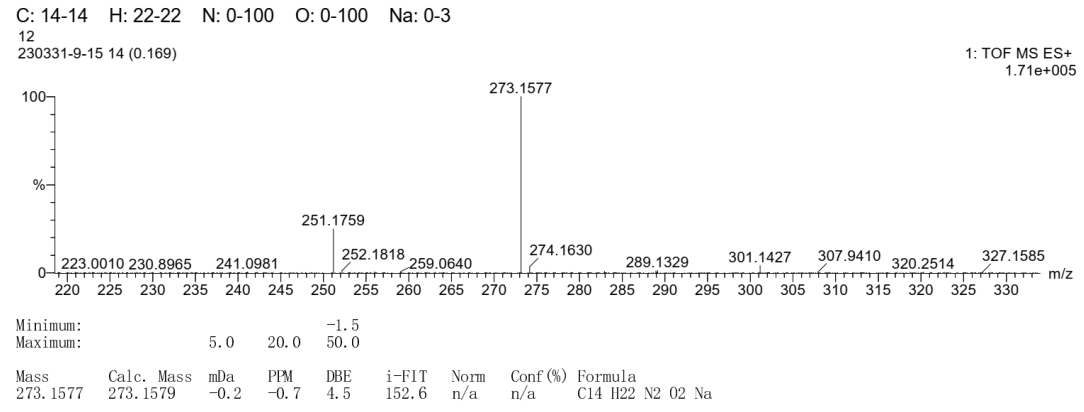
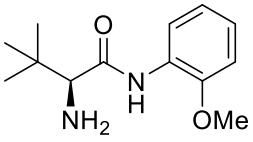


Figure S32. HRMS spectra of **H.**



J

Chemical Formula: $C_{13}H_{20}N_2O_2$

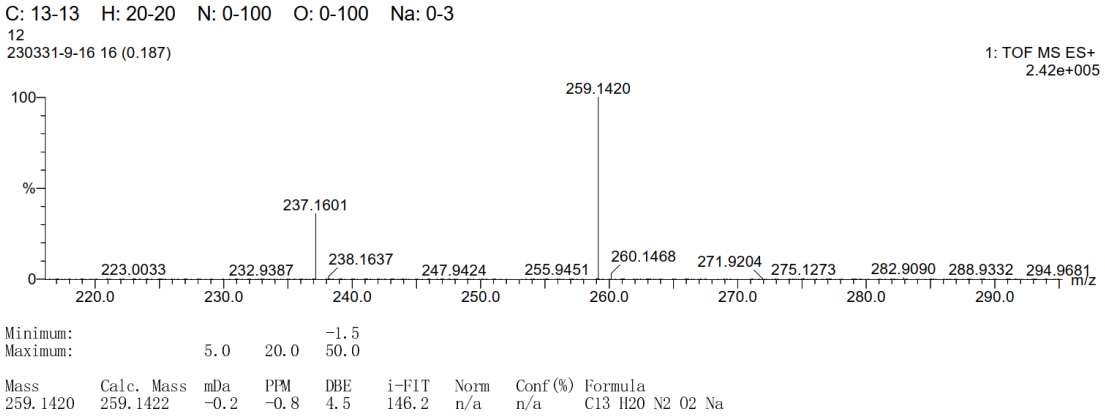
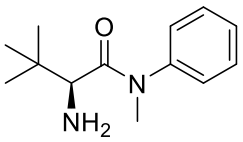


Figure S33. HRMS spectra of **J.**



K

Chemical Formula: $C_{13}H_{20}N_2O$

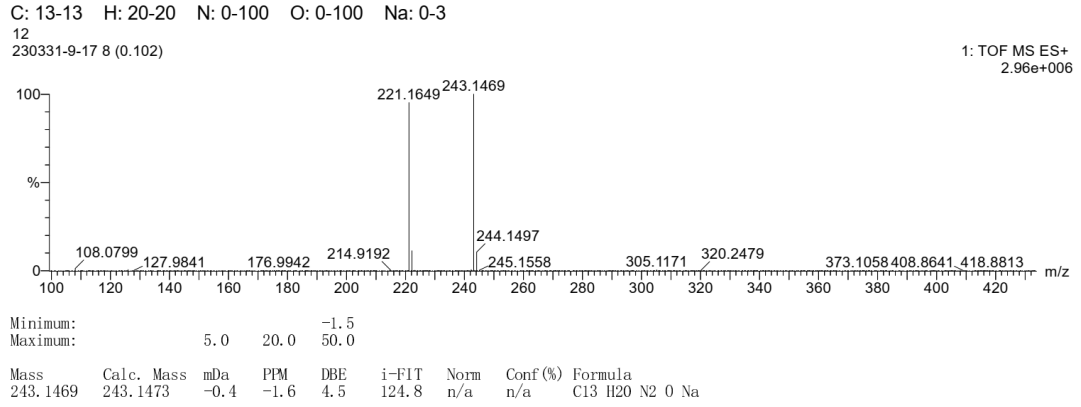
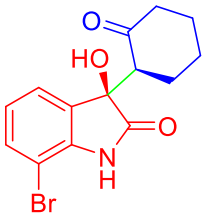


Figure S34. HRMS spectra of **K**



3m

Chemical Formula: $C_{14}H_{14}BrNO_3$

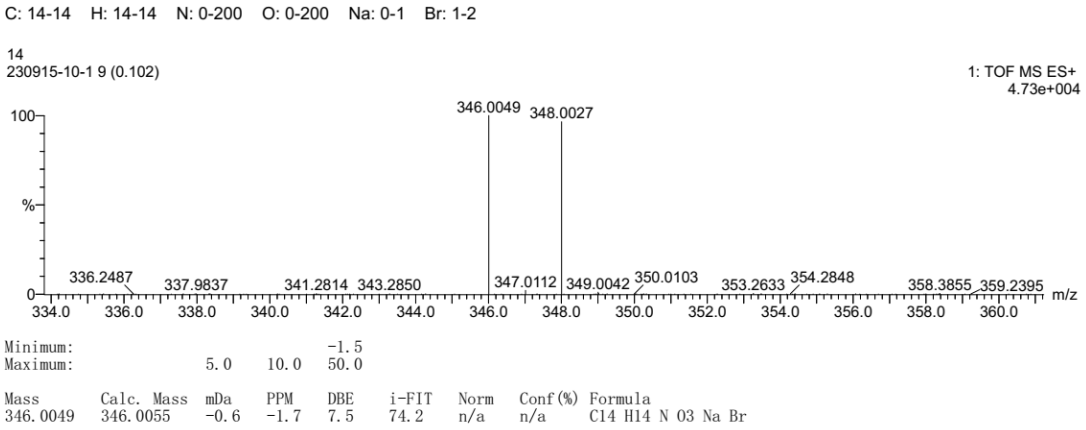
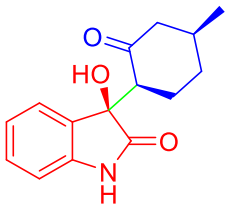


Figure S35. HRMS spectra of **3m**



3p

Chemical Formula: $C_{15}H_{17}NO_3$

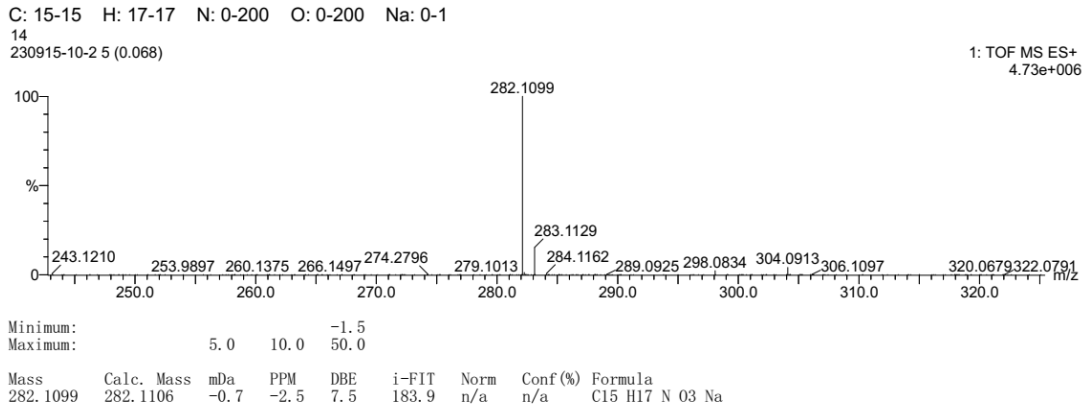


Figure S36. HRMS spectra of **3p**

9 References

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[2] S. Cañellas, P. Alonso, and M. Pericàs, A. *Org. Lett*. **2018**, *20*, 4806.

[3] Z. Mao, X. Zhu, A. Lin, W. Li, Y. Shi, H. Mao, C. Zhu, and Y. Cheng, *Adv. Synth. Catal*. **2013**, *355*, 2029.

[4] Y. Liu, P. Gao, J. Wang, Q. Sun, Z. Ge, R. Li, *Synlett* **2012**, *23*, 1031.

[5] C. Shen, F. Shen, H. Xia, P. Zhang, X. Chen, *Tetrahedron: Asymmetry* **2011**, *22*, 708.