

## **Supplemental information**

### **Four-step Continuous-Flow Total Synthesis of (-)- Debromoflustramine B using Chiral Heterogeneous Pd NPs Catalyst**

**Junwen Wang<sup>†</sup>, Feng Liang<sup>†</sup>, Zhen Dong, Junrong Huang, Yuxiang Zhu\*,  
Hengzhi You\*, Fen-Er Chen\***

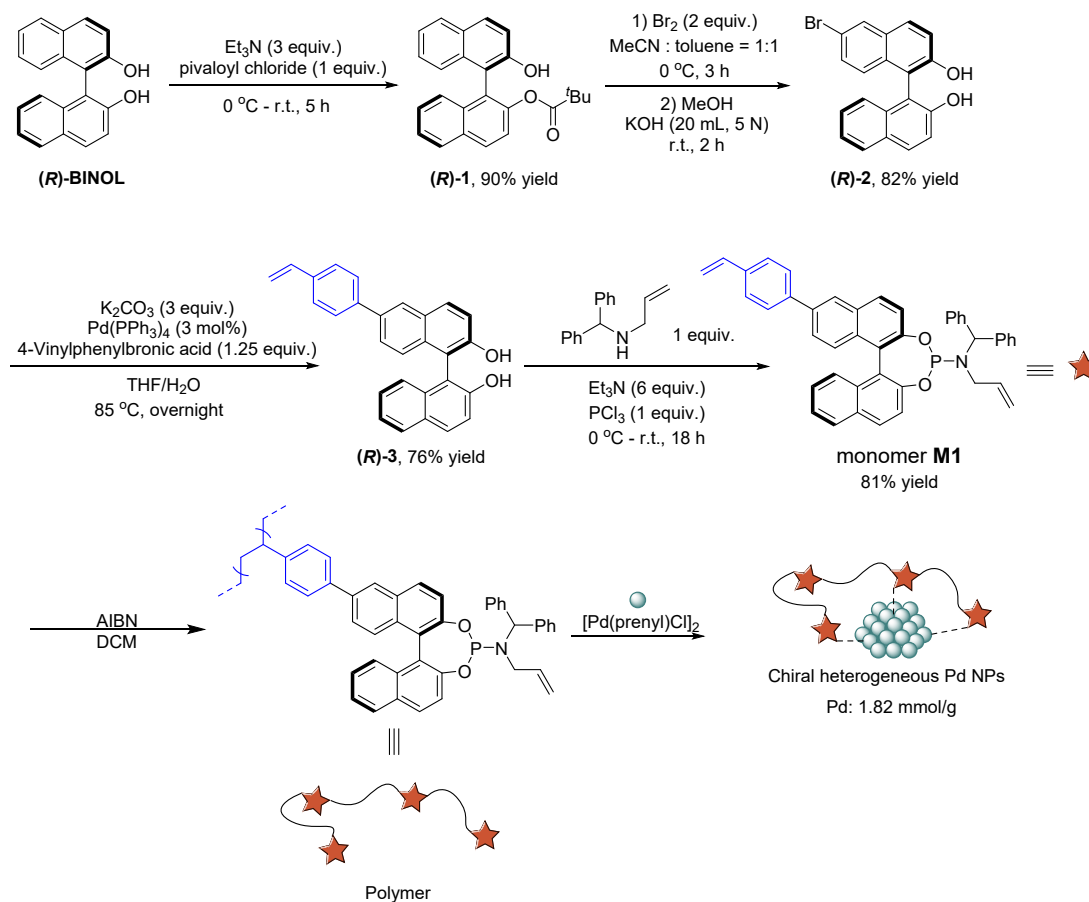
# Table of contents

General experimental details.....	3
Preparation of the Pd NPs catalyst.....	4
Characterization of M1, polymer, and Pd NPs .....	6
Optimization table.....	12
General experimental procedure for the enantioselective dearomative prenylation of indole derivatives.....	13
General experimental procedure for recycling experiments .....	14
General experimental procedure for the enantioselective dearomative prenylation of indole derivatives under flow .....	16
General experimental procedure for the four-step continuous-flow total synthesis of (-)-debromoflustramine B.....	17
Evaluation of the catalyst performance after flow .....	19
Characterization of compounds.....	20
NMR spectra .....	28
HPLC spectra .....	46

## General experimental details

$^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR spectrum were recorded using Q.One Instruments Quantum-I 400M spectrometer.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane. Coupling constants ( $J$ ) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference:  $^1\text{H}$  NMR (chloroform  $\delta$  7.26) and  $^{13}\text{C}$  NMR (chloroform  $\delta$  77.0). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. HRMS were obtained on Waters Xevo G2-XS QToF. All substrate compounds and complex molecules were prepared according to the published procedures. Other reagents were received from commercial sources. Solvents were freshly dried and degassed according to the published procedures prior to use. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60 or performed by flash chromatography using SepaBean<sup>®</sup> machine and SepaBean<sup>®</sup> machine U100. Enantioselectivities were measured by HPLC (Thermo Ultimate 3000). Transmission electron microscopic (TEM) images were performed using a JEOL-JEM-3200FS. The X-ray photoelectron spectroscopy (XPS) was conducted using a Thermo Scientific ESCALAB Xi+ with the Al K $\alpha$  irradiation.

## Preparation of the Pd NPs catalyst



**Scheme S1.** Preparation of the polymer-supported Pd NPs catalyst

To a solution of **(R)-1,1'-bi(2-naphthol)** (2.86 g, 10 mmol) and  $\text{Et}_3\text{N}$  (3.03 g, 30 mmol) in acetonitrile (50 mL) was added pivaloyl chloride (1.22 g, 10.1 mmol) dropwise at 0 °C. The mixture was then allowed to warm to r.t. and stirred for 5 h. The reaction mixture was diluted with ether and washed with aqueous HCl (1 N, 30 mL), saturated  $\text{NaHCO}_3$  (50 mL) and brine (50 mL). The organic layer was dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was purified by flash column chromatography over silica gel to give the **(R)-1** product as a white solid in 90% yield.

Bromine (3.2 g, 20 mmol) was slowly added to a solution of **(R)-1** (3.7 g, 10 mmol) in acetonitrile (30 mL) and toluene (30 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h and quenched with aqueous  $\text{NaHSO}_3$  (3 N, 10 mL). After addition of 100 mL of ether, the organic phase was separated and concentrated. To this residue

were added MeOH (20 mL) and KOH (5 N, 20 mL). The resulting mixture was stirred at r.t. for 2 h and was then acidified with 3 N HCl to a pH of 1. After addition of EtOAc (100 mL), the organic phase was washed with saturated NaHCO<sub>3</sub>, brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The crude product was purified by flash column chromatography over silica gel to give the product (**R**)-**2** as a white solid in 82% yield.

The mixture of (4-vinylphenyl)boronic acid (1.22g, 1.25 equiv.), Pd(PPh<sub>3</sub>)<sub>4</sub> (227 mg, 3 mmol %), (**R**)-**2** (2.4 g, 6.57 mmol), K<sub>2</sub>CO<sub>3</sub> (1 M, 20 mL) in THF (96 mL) was reflux overnight under N<sub>2</sub>. After cooling to r.t., the mixture was extracted with DCM (3 × 40 mL). The combined organic phase was washed with brine, dried over MgSO<sub>4</sub>, and concentrated. The residue was purified by column chromatography over silica gel to give product (**R**)-**3** as a white solid in 76% yield.

To a stirred mixture of Et<sub>3</sub>N (6 equiv.) and PCl<sub>3</sub> (1 equiv.) in THF (37 mL) at 0 °C was added dropwise a solution of amine (3.73 mmol, 1 equiv.), and the mixture was stirred for 4 h at r.t. (**R**)-**3** (3.73 mmol) was slowly added to the reaction mixture at 0 °C and then the suspension was stirred at r.t. for 18 h. The suspension was diluted in DCM (8 mL) and filtered on neutral alumina, the filtrate was concentrated and purified by flash chromatography through silica gel to give the pure monomer **1** as a white solid in 81% yield.

To a solution of monomer **1** (186 mg) in DCM (2 mL) was added 2,2'-azobis(2-methylpropionitrile) (AIBN, 12.5 mg). The mixture was transferred into an autoclave at 80 °C for 72 h. [Pd(prenyl)Cl]<sub>2</sub> (1 equiv.) was added under Ar after the mixture cool to r.t. After stirring at r.t. for 3 h. Evaporation of DCM under vacuum afforded a white solid which denoted as Pd NPs. ICP-OES: Pd 19.3% (cal. 1.82 mmol/g); P 3.09% (cal. 1 mmol/g)

## Characterization of M1, polymer, and Pd NPs

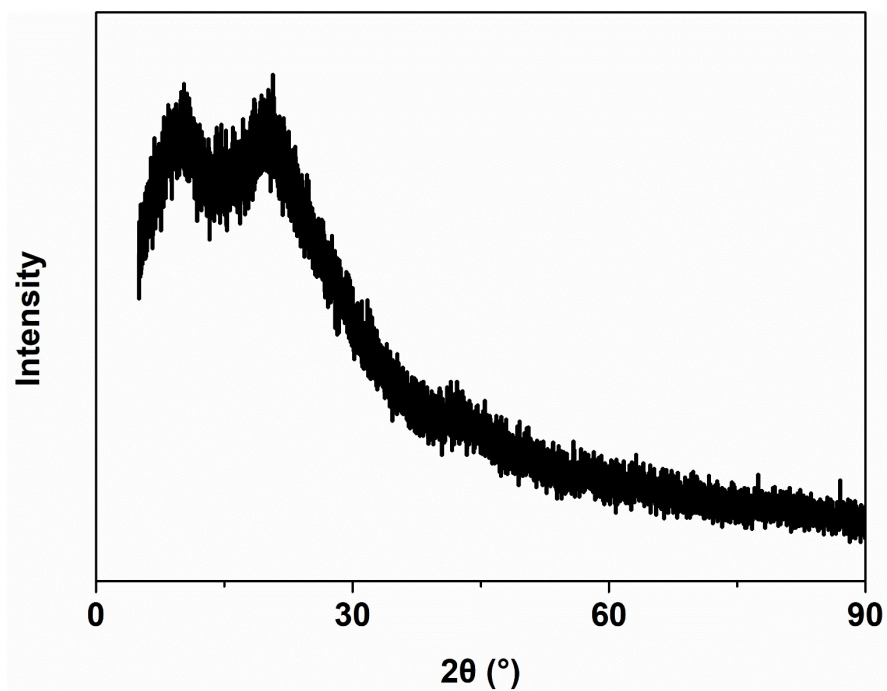


Figure S1. XRD of polymer.

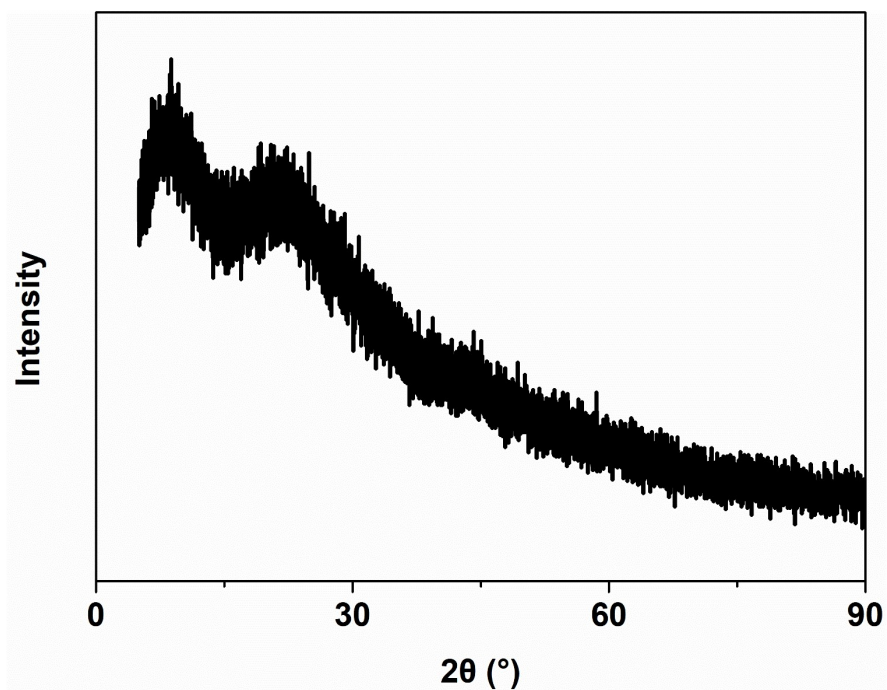


Figure S2. XRD of Pd NPs catalyst.

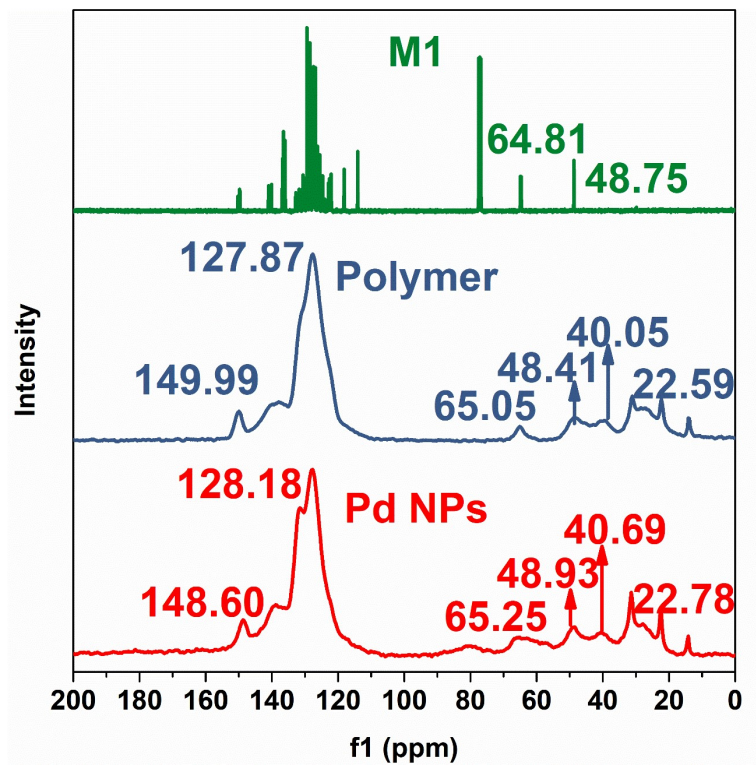


Figure S3. Solid-state  $^{13}\text{C}$  NMR of M1 and polymer.

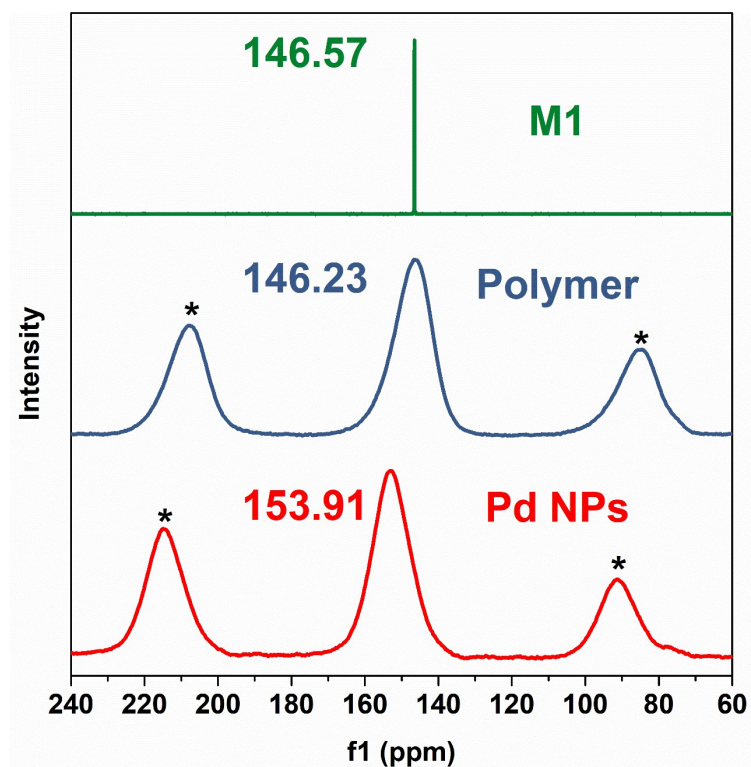


Figure S4. Solid-state  $^{31}\text{P}$  NMR of M1 and polymer

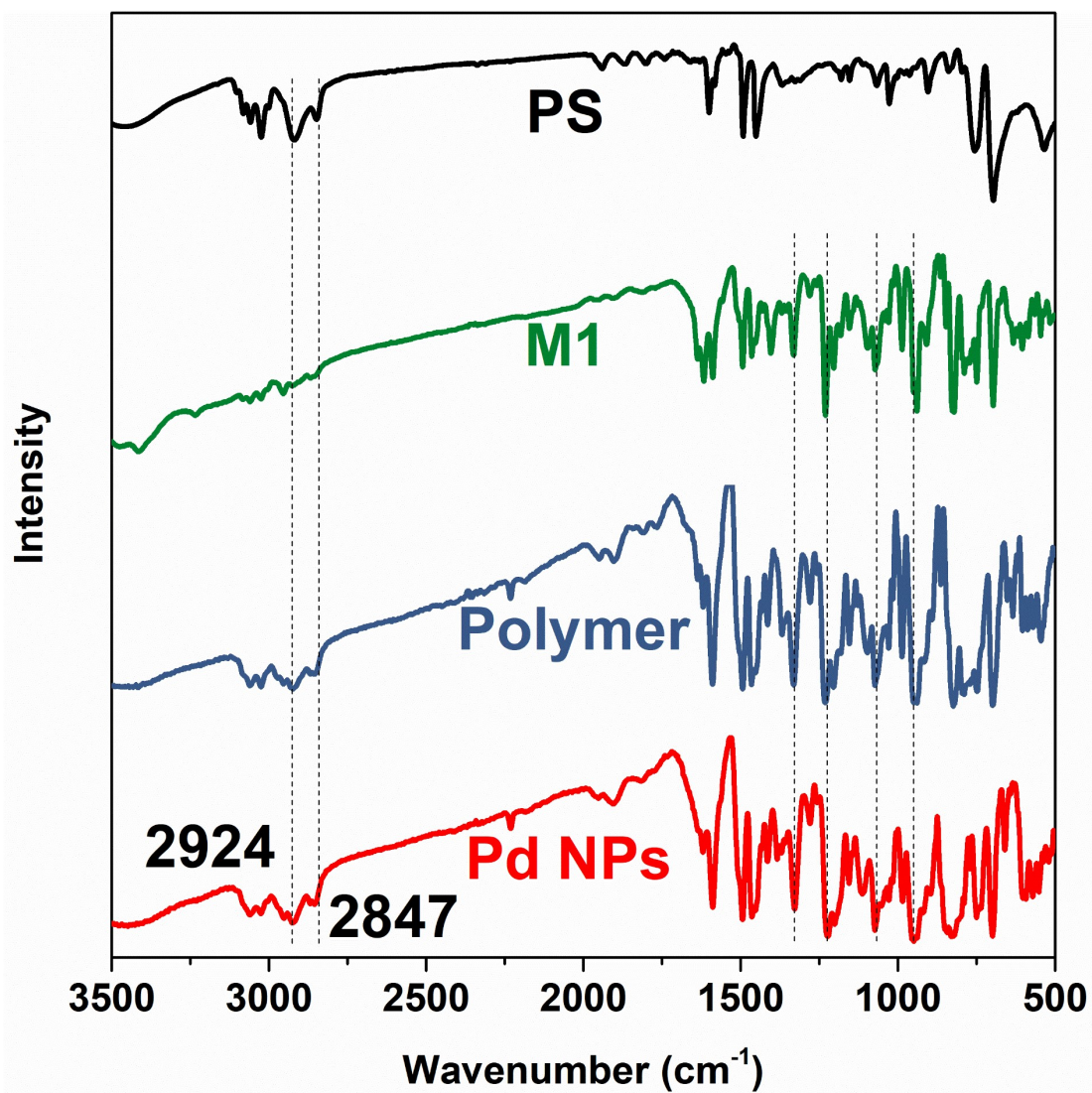


Figure S5. FT-IR of PS, M1, polymer, and Pd NPs



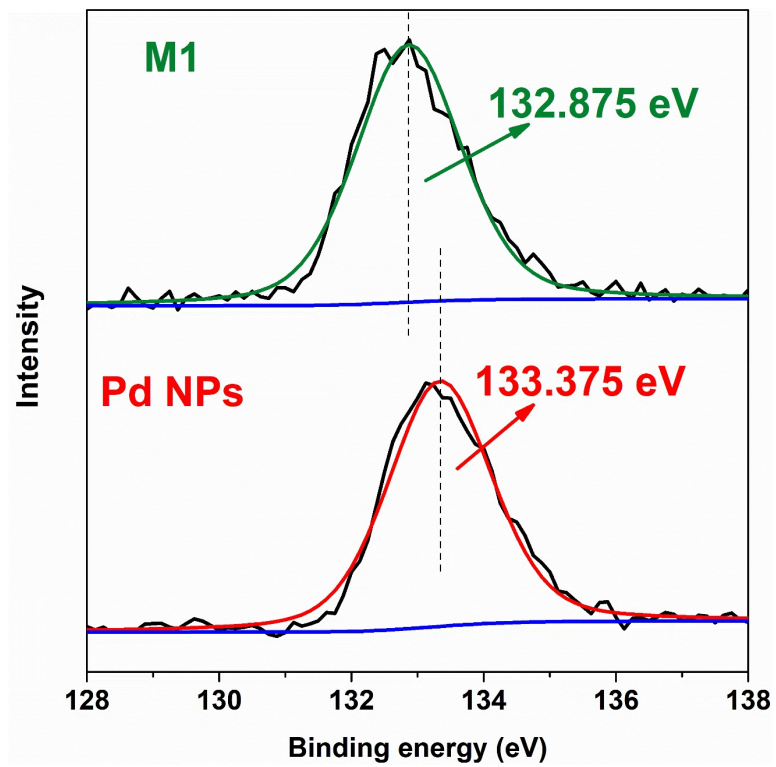


Figure S6. XPS P 2p of **M1**, and Pd NPs

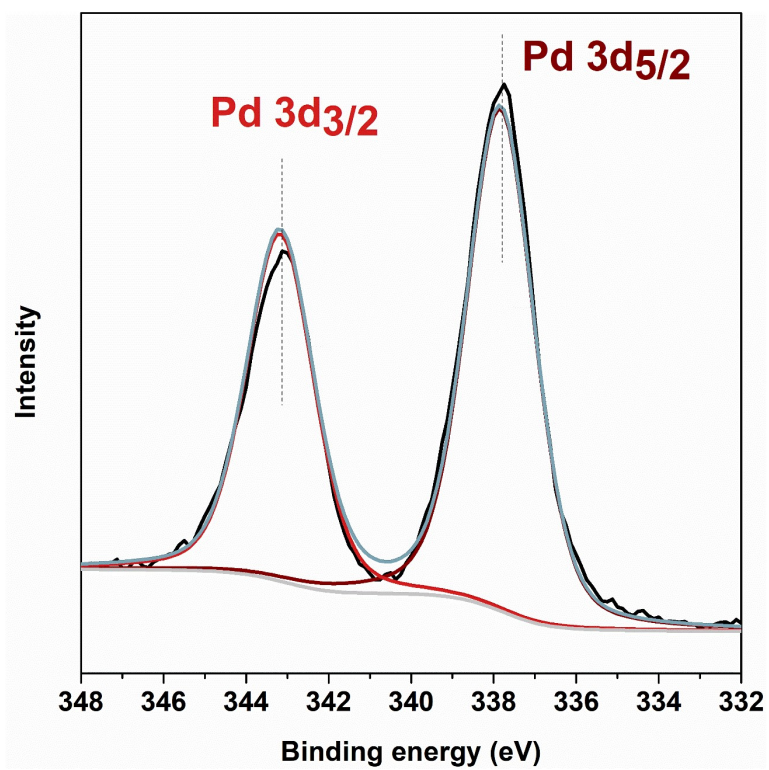


Figure S7. XPS Pd 3d of Pd NPs

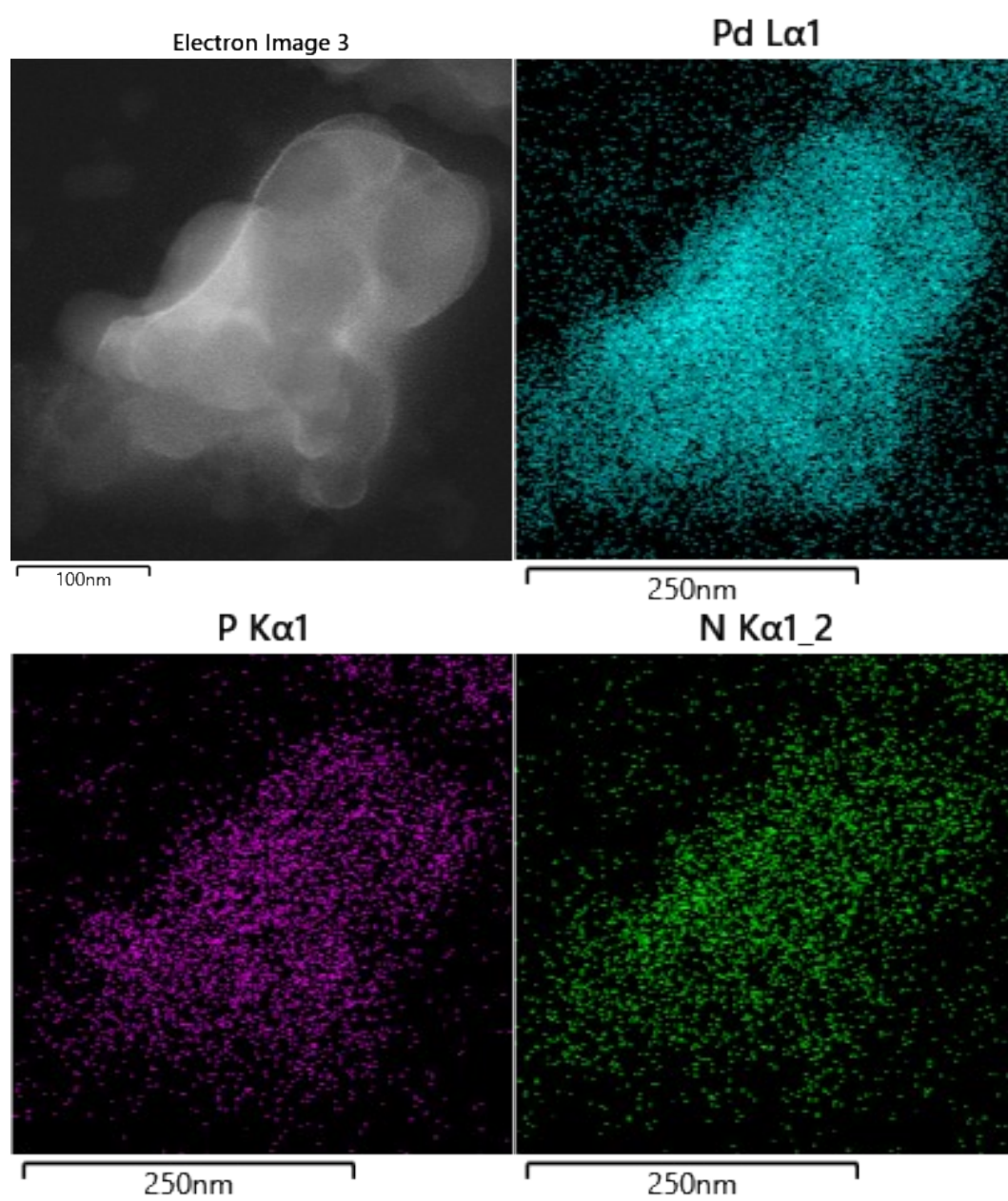


Figure S8. EDS of Pd NPs catalyst.

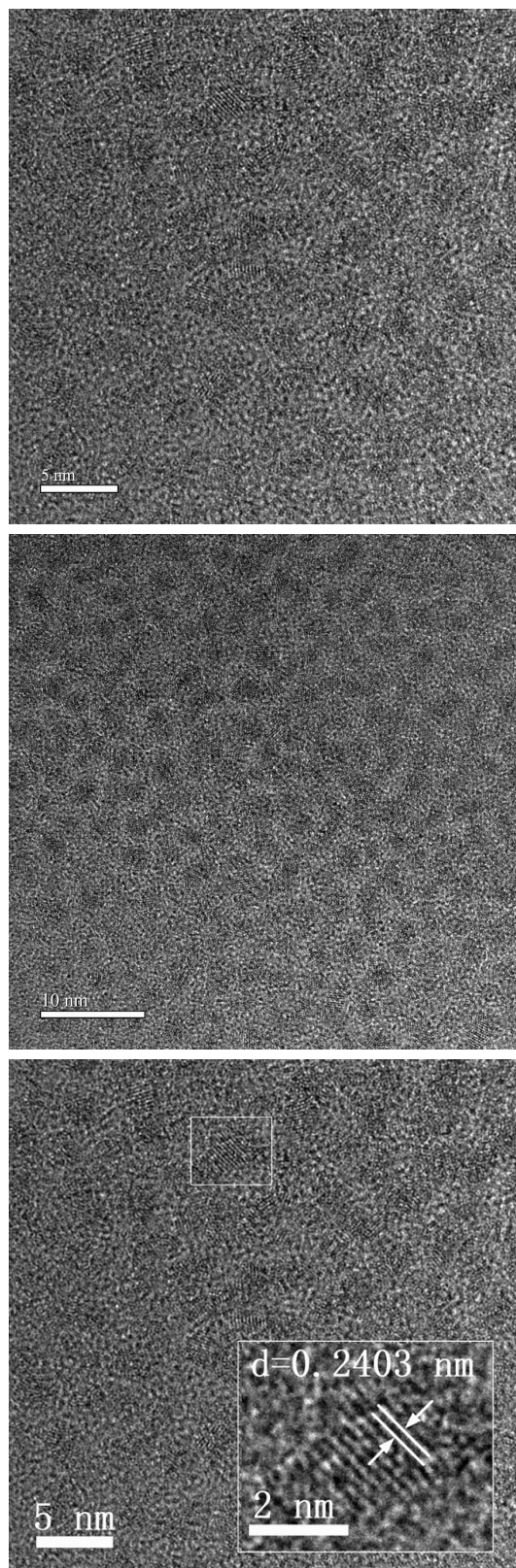
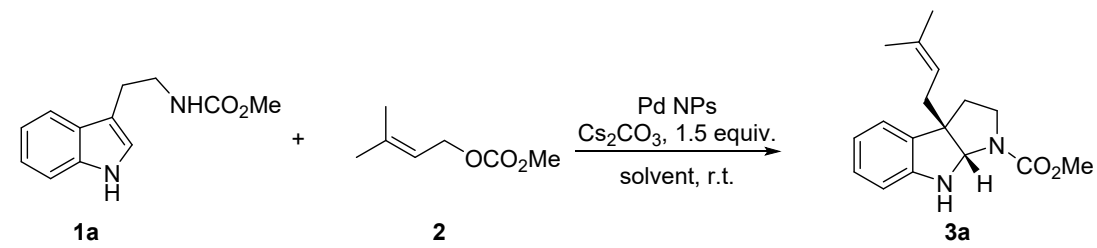


Figure S9. TEM of Pd NPs catalyst.

## Optimization table

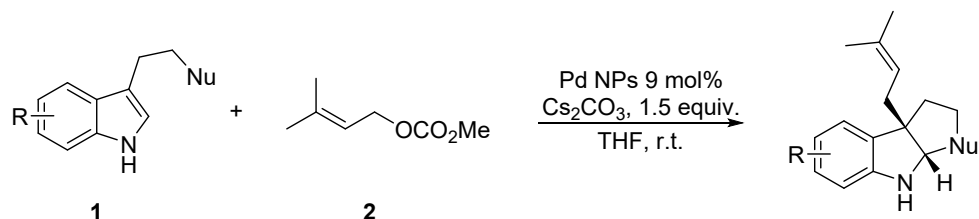
**Table S1.** Optimization of the enantioselective dearomative prenylation<sup>a</sup>



Entry	Solvent	Base	Pd NPs (mol%)	Time (h)	Yield (%)	e.e. (%)
1	THF	Cs <sub>2</sub> CO <sub>3</sub>	18	24	98	91
2	Dioxane	Cs <sub>2</sub> CO <sub>3</sub>	18	24	96	86
3	Toluene	Cs <sub>2</sub> CO <sub>3</sub>	18	24	92	91
4	hexane	Cs <sub>2</sub> CO <sub>3</sub>	18	24	>99	60
5	Et <sub>2</sub> O	Cs <sub>2</sub> CO <sub>3</sub>	18	24	>99	85
6	THF	Cs <sub>2</sub> CO <sub>3</sub>	15	24	92	91
7	THF	Cs <sub>2</sub> CO <sub>3</sub>	9	24	96	91
8	THF	Cs <sub>2</sub> CO <sub>3</sub>	9	16	95	91
9	THF	Cs <sub>2</sub> CO <sub>3</sub>	9	12	95	91
10	THF	Cs <sub>2</sub> CO <sub>3</sub>	9	9	86	91
11	THF	Et <sub>3</sub> N	9	9	29	67
12	THF	DMAP	9	9	11	53
13	THF	DBU	9	9	13	60
14	THF	PhNH <sub>2</sub>	9	9	N.D.	N.D.
15	Et <sub>2</sub> O	Et <sub>3</sub> N	9	9	27	58

<sup>a</sup>Condition: **2** (2.0 equiv.) was added to a solution of **1a** (0.1 mmol), Pd NPs (x mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 equiv.) in dry solvent (1 mL) under Argon. The reaction mixture was stirred at room temperature for 12 hours. Yields were isolated yield. Enantiomeric excess (e.e.) were determined by chiral HPLC.

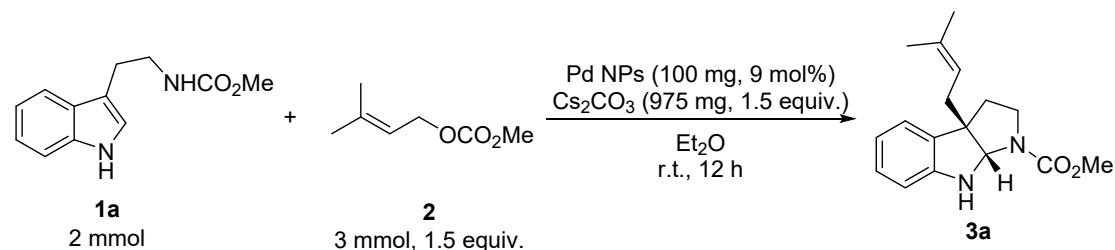
## General experimental procedure for the enantioselective dearomative prenylation of indole derivatives



To a flame-dried Schlenk tube was added Pd NPs (10 mg, 9 mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 equiv.), **1** (0.2 mmol, 1 equiv.). After the flask was evacuated and refilled with argon, freshly distilled THF (2 mL) and **2** (1.5 equiv.) were added. The reaction mixture was stirred at r.t. for 12 h. The crude reaction mixture was filtered and concentrated by rotary evaporation. Then the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the desired products.

## General experimental procedure for recycling experiments

Table S2. Recycling experiment of the Pd NPs catalyst



Entry	Pd NPs (mg)	Scale (mmol)	Yield (%)	e.e. (%)
Run 1	100	2	95	86
Run 2	75	1.4	51	74
Run 3	53	1.1	36	51

To a flame-dried Schlenk tube was added Pd NPs (100 mg, 9 mol%), Cs<sub>2</sub>CO<sub>3</sub> (975 mg, 1.5 equiv.), **1a** (2 mmol, 1 equiv.). After the flask was evacuated and refilled with argon, freshly distilled Et<sub>2</sub>O (20 mL) and **2** (3 mmol, 1.5 equiv.) were added. After each run, the reaction mixture was firstly centrifuged, and the supernatant was separated. The remaining solid was re-dissolved in Et<sub>2</sub>O and this process was repeated until no fluorescence signal was detected in the supernatant. Centrifugation after addition of water failed to isolate the Pd catalyst, as a layer of the Pd catalyst formed on the top of the supernatant. Consequently, a simple filtration was performed. The solid residue was then washed with saturated NH<sub>4</sub>Cl solution until the pH of the filtrate reached 7-8, ensuring complete removal of Cs<sub>2</sub>CO<sub>3</sub>. The collected solid catalyst was washed with water, ethanol, and Et<sub>2</sub>O, then dried under vacuum for 12 hours before being reused in the subsequent run. It should be noted that part of the Pd catalyst remained on the filter paper and could not be recovered. Therefore, the stoichiometry for the subsequent run was recalculated based on the amount of Pd catalyst recovered.

**Table S3. ICP-OES analysis**

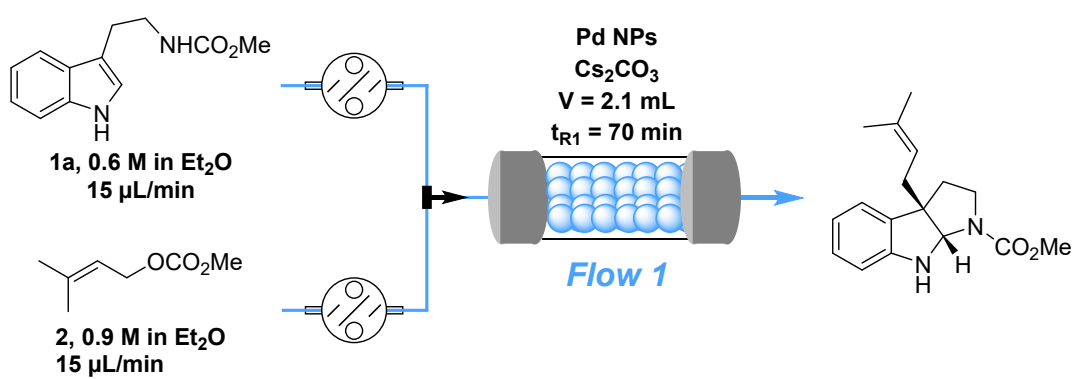
ICP-OES of Pd	Pd (%)
Fresh Pd NPs	19.3
Used Pd NPs after 3 <sup>rd</sup> run	8.4
Dry residue of the filtrate after 1 <sup>st</sup> run	0.213

The yield and enantiomeric excess dramatically dropped after each run. ICP-OES analysis indicated that only 44% of Pd remained in the catalyst after the third run. This could be attributed to two reasons: (1) complexation of  $\text{NH}_4\text{Cl}$  with Pd, which was confirmed by the ICP-OES analysis of the dried filtrates (2.3564 g of dried filtrate contained 5.02 mg of Pd, indicating 26% of the Pd was leached). (2) part of the catalyst stuck on the filter paper.

## General experimental procedure for the enantioselective dearomative prenylation of indole derivatives under flow

The system was firstly purged with argon to remove any residual air, ensuring an inert atmosphere throughout the whole process. Tryptophan derivatives **1a** (0.6 M in Et<sub>2</sub>O, 1 equiv.) and methyl prenyl carbonate **2a** (0.9 M in Et<sub>2</sub>O, 1.5 equiv.) were pumped into a column packed-bed reactor with chiral heterogeneous Pd NPs catalyst (100 mg) and Cs<sub>2</sub>CO<sub>3</sub> (600 mg) at the same velocity (15 μL/min). it was tested every two hours, when effluent was present.

**Table S4. Enantioselective dearomative prenylation of indole derivatives under flow**

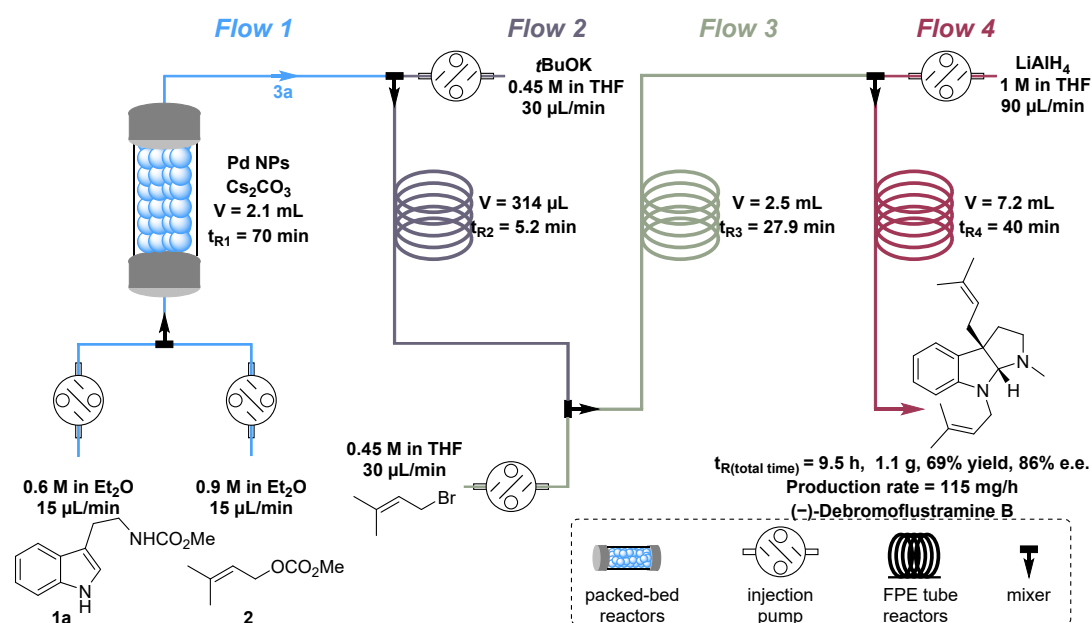


Reaction scheme showing the enantioselective dearomative prenylation of indole derivative **1a** (0.6 M in Et<sub>2</sub>O, 15 μL/min) and methyl prenyl carbonate **2** (0.9 M in Et<sub>2</sub>O, 15 μL/min) using Pd NPs and Cs<sub>2</sub>CO<sub>3</sub> catalyst in a flow reactor (V = 2.1 mL, t<sub>R1</sub> = 70 min). The product is a prenylated indole derivative.

Time (h)	2	4	6	8	10
Yield (%)	91	93	94	90	85
e.e. (%)	86	86	86	86	86



## General experimental procedure for the four-step continuous-flow total synthesis of (–)-debromoflustramine B



The continuous flow apparatus was assembled following the Fig. S10 provided. The system was firstly purged with argon to remove any residual air, ensuring an inert atmosphere throughout the whole process. Tryptophan derivatives **1a** (0.6 M in Et<sub>2</sub>O, 1 equiv.) and methyl prenyl carbonate **2a** (0.9 M in Et<sub>2</sub>O, 1.5 equiv.) were pumped into a column packed-bed reactor with chiral heterogeneous Pd NPs catalyst (100 mg) and Cs<sub>2</sub>CO<sub>3</sub> (600 mg) at the same velocity (15 μL/min) in **flow 1**. Upon generation of **3a**, it was premixed with *t*BuOK (0.45 M in THF, 1.5 equiv., 30 μL/min) in FEP tube for 5 min in **flow 2** before being mixed in **flow 3** with prenyl bromide (0.45 M in THF, 1.5 equiv., 30 μL/min) to afford precursor of (–)-debromoflustramine B. Subsequent reduction with LiAlH<sub>4</sub> (1 M in THF, 10 equiv., 90 μL/min) in **flow 4** delivered the desired natural product (–)-debromoflustramine B. A FPE tube with a large inner diameter was conducive to the process, and ultrasonic treatment was performed on the flow path to further prevent clogging in the flow paths. Upon completion, the combined fluid was quenched by dropwise addition to the water. The organic layer was separated, and the aqueous layer was extracted with EtOAc three times. The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and then filtered. The crude reaction

mixture was concentrated by rotary evaporation and purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the desired products with an overall yield of 69% (1.1 g) and complete retention of the enantiomeric purity (86% e.e.).

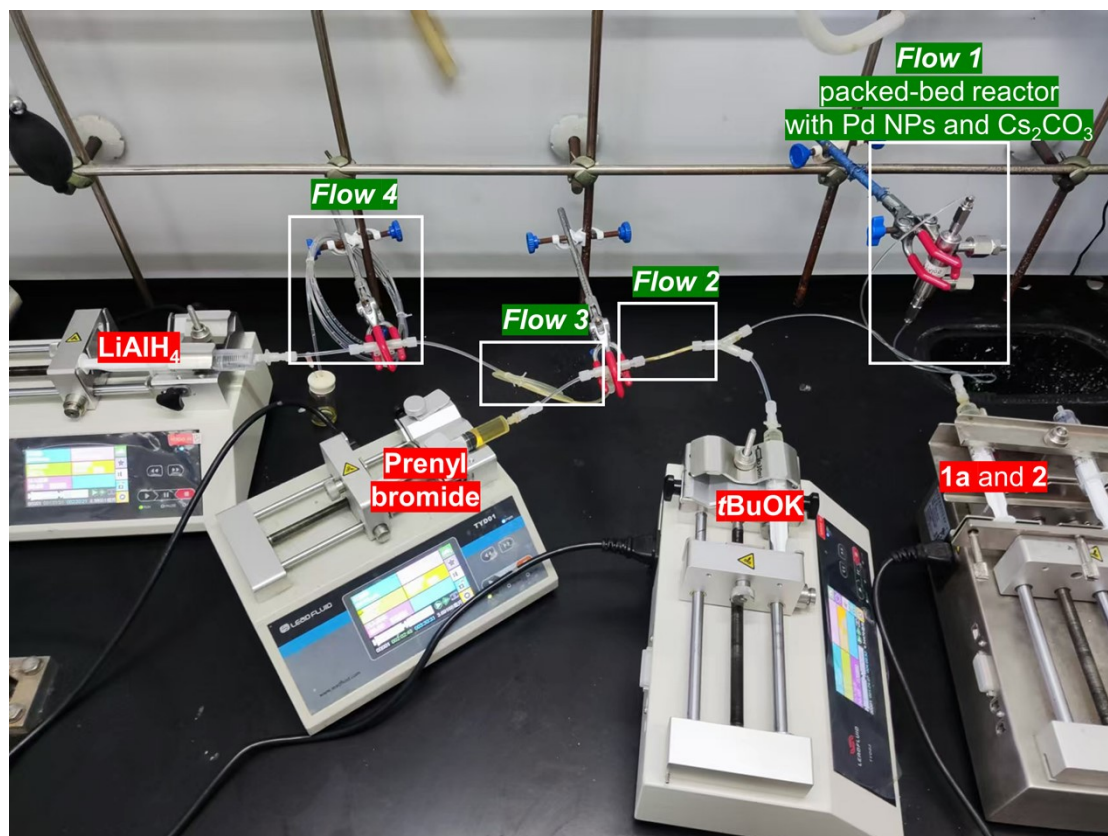
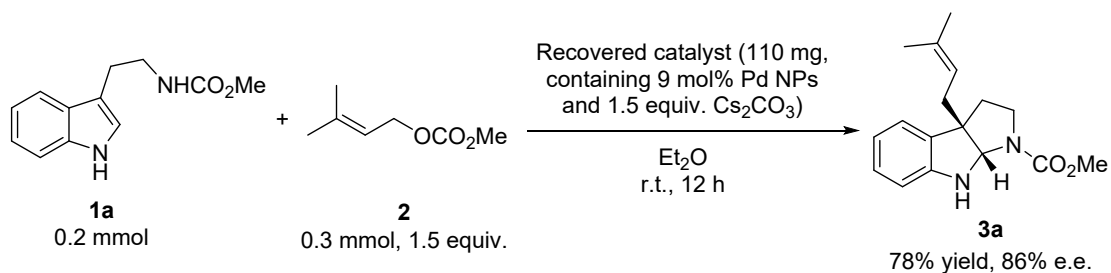


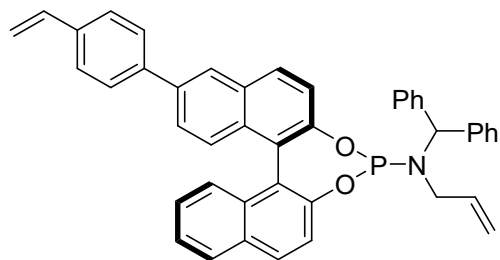
Figure S10. Photographic representation of the flow system.

## Evaluation of the catalyst performance after flow

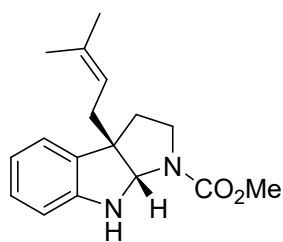
To determine the residual activity of the Pd NPs catalyst after flow, the mixture of Pd NPs catalyst and  $\text{Cs}_2\text{CO}_3$  was subjected to a cleaning process by pumping diethyl ether through the system. Subsequently, the mixture was dried by purging with argon. Following the drying procedure, the mixture was carefully removed, and a 110 mg aliquot was taken for the model reaction to evaluate the catalyst performance. To a flame-dried Schlenk tube was added the above catalyst mixture (110 mg, containing 9 mol% Pd NPs and 1.5 equiv.  $\text{Cs}_2\text{CO}_3$ ) and **1a** (0.2 mmol, 1 equiv.). After the flask was evacuated and refilled with argon, freshly distilled  $\text{Et}_2\text{O}$  (2 mL) and **2** (1.5 equiv.) were added. The reaction mixture was stirred at r.t. for 12 h before being filtered and concentrated by rotary evaporation. Then the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the desired product **3a** in 78% yield with 86% e.e.



## Characterization of compounds

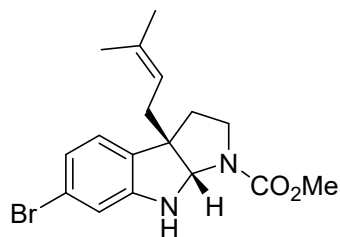


Monomer **M1**, white solid in 81% yield. Mp: 87-90 °C.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  8.17 (d,  $J = 3.92$  Hz, 1H), 8.03 (dd,  $J = 13.52, 8.77$  Hz, 1H), 7.95 (dt,  $J = 17.97, 7.08$  Hz, 2H), 7.74 (dd,  $J = 8.10, 4.20$  Hz, 2H), 7.57 (dt,  $J = 18.40, 6.86$  Hz, 9H), 7.51 – 7.43 (m, 7H), 7.42 – 7.27 (m, 3H), 6.85 (dd,  $J = 17.58, 10.85$  Hz, 1H), 5.89 (d,  $J = 17.61$  Hz, 1H), 5.76 (t,  $J = 14.71$  Hz, 2H), 5.36 (d,  $J = 10.79$  Hz, 1H), 5.12 (d,  $J = 10.06$  Hz, 1H), 5.00 (dd,  $J = 17.15, 4.98$  Hz, 1H), 3.52 (ddt,  $J = 15.89, 10.42, 4.85$  Hz, 1H), 3.28 (dddd,  $J = 14.50, 10.32, 7.29, 2.83$  Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  150.3 – 150.0 (m), 149.7 (d,  $J = 7.5$  Hz), 141.0 (d,  $J = 4.3$  Hz), 140.8 (d,  $J = 5.9$  Hz), 140.1 (d,  $J = 2.7$  Hz), 136.9, 136.7, 136.5, 136.0, 132.8, 132.7, 132.1, 132.0, 131.8, 131.5, 131.0, 130.7, 130.6, 130.4, 130.2, 130.1, 129.4 (t,  $J = 3.1$  Hz), 128.6 (d,  $J = 10.7$  Hz), 128.4 (d,  $J = 5.7$  Hz), 127.7 (d,  $J = 8.6$  Hz), 127.5 (d,  $J = 10.5$  Hz), 127.1, 126.9, 126.2, 125.9 (d,  $J = 3.2$  Hz), 125.5, 124.9, 124.7, 124.1 (d,  $J = 6.6$  Hz), 122.9, 122.6, 122.4, 122.3 (d,  $J = 7.5$  Hz), 122.1, 118.2 (d,  $J = 4.4$  Hz), 114.1, 64.8 (d,  $J = 26.9$  Hz), 48.7.  $^{31}\text{P}$  NMR (162 MHz, Chloroform-*d*)  $\delta$  146.57. HRMS (ESI) calcd for  $\text{C}_{44}\text{H}_{35}\text{NO}_2\text{P}$   $[\text{M}+\text{H}]^+$ : found 640.2400, found 640.2402.

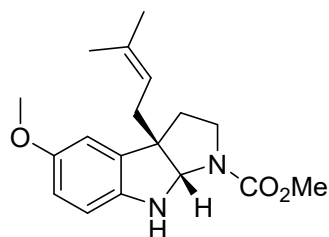


**3a**. Yellow oil. 54.9 mg, 96% yield. 91% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0$  mL $\cdot$ min $^{-1}$ ,  $\lambda = 254$  nm,  $t$  (minor) = 10.167 min,  $t$  (major) = 6.837 min];  $[\alpha]_{\text{D}}^{25} = -240.6$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.13 – 6.99 (m, 2H), 6.80 – 6.70 (m, 1H), 6.59 (dd,  $J = 7.74, 3.42$  Hz, 1H), 5.43 – 4.52 (m, 3H), 3.95 – 3.44 (m, 4H), 3.14 – 2.79 (m, 1H), 2.38 (q,  $J = 12.15, 9.54$  Hz, 2H), 2.13 (td,  $J = 11.02, 10.19, 6.47$  Hz, 2H), 1.70 (s, 3H), 1.53 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  155.6, 154.8, 149.2, 148.8, 135.2, 135.1, 132.4, 132.3, 128.3, 128.3,

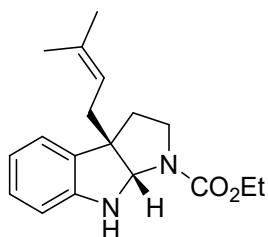
123.2, 123.2, 119.2, 119.1, 118.8, 109.5, 109.3, 80.1, 79.6, 58.1, 57.1, 52.6, 52.3, 46.0, 45.7, 35.9, 35.6, 34.4, 34.4, 26.1, 18.0, 18.0. HRMS (ESI) calcd for C<sub>17</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 287.1754. Found: 287.1757.



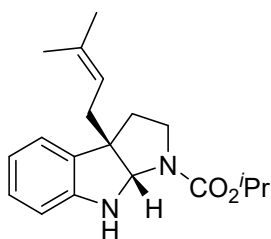
**3b.** Yellow oil. 54.6 mg, 75% yield. 90% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $\nu$  = 1.0 mL·min<sup>-1</sup>,  $\lambda$  = 254 nm, t (minor) = 8.043 min, t (major) = 10.657 min]; [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -173.4 (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  6.97 – 6.76 (m, 2H), 6.68 (d, *J* = 1.97 Hz, 1H), 5.56 – 4.74 (m, 3H), 3.90 – 3.44 (m, 4H), 3.00 (q, *J* = 9.26 Hz, 1H), 2.58 – 2.20 (m, 2H), 2.09 (dt, *J* = 8.84, 5.36 Hz, 2H), 1.68 (s, 3H), 1.49 (s, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  155.5, 154.6, 150.7, 150.4, 135.4 (d, *J* = 2.53 Hz), 131.5, 131.3, 124.4, 124.4, 121.8, 121.6, 121.3, 118.8, 112.3, 112.1, 80.3, 79.8, 57.7, 56.6, 52.7, 52.4, 46.0, 45.6, 35.9, 35.6, 34.5, 26.0, 18.0, 18.0. HRMS (ESI) calcd for C<sub>17</sub>H<sub>22</sub>BrN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 365.0859. Found: 365.0856.



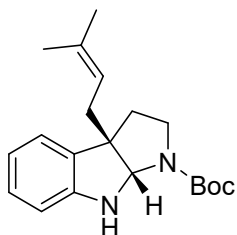
**3c.** Yellow oil. 61.3 mg, 97% yield. 89% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $\nu$  = 1.0 mL·min<sup>-1</sup>,  $\lambda$  = 254 nm, t (minor) = 10.597 min, t (major) = 12.267 min]; [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -210.1 (c = 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  6.69 – 6.58 (m, 2H), 6.49 (dd, *J* = 8.32, 5.01 Hz, 1H), 5.20 – 4.78 (m, 3H), 3.72 – 3.51 (m, 2H), 3.71 (s, 3H), 3.64 (s, 2H), 3.10 – 2.97 (m, 1H), 2.45 – 2.24 (m, 2H), 2.10 – 2.03 (m, 2H), 1.68 (s, 3H), 1.50 (s, 3H). <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  155.5, 154.8, 153.7, 153.5, 143.1, 142.8, 135.1, 135.1, 134.0, 133.9, 119.2, 113.0, 112.9, 110.2, 110.1, 110.0, 109.8, 80.8, 80.3, 58.4, 57.4, 56.0, 55.9, 52.6, 52.2, 46.0, 45.6, 35.7, 35.4, 34.3, 34.3, 26.0, 18.0, 18.0. HRMS (ESI) calcd for C<sub>18</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub> [M+H]<sup>+</sup>: 317.1860. Found: 317.1864.



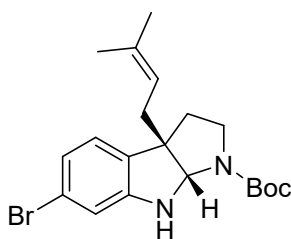
**3d.** Yellow oil. 52.8 mg, 88% yield. 92% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 8.557 min,  $t$  (major) = 7.717 min];  $[\alpha]_{\text{D}}^{25} = -296.8$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.04 (t,  $J = 6.89 \text{ Hz}$ , 2H), 6.72 (q,  $J = 7.15$ , 6.73 Hz, 1H), 6.58 (d,  $J = 7.76 \text{ Hz}$ , 1H), 5.42 – 4.64 (m, 3H), 4.43 – 3.90 (m, 2H), 3.79 – 3.50 (m, 1H), 3.03 (tt,  $J = 10.33$ , 7.74 Hz, 1H), 2.37 (dhept,  $J = 21.38$ , 7.00, 6.46 Hz, 2H), 2.13 (dd,  $J = 9.85$ , 5.66 Hz, 2H), 1.70 (s, 3H), 1.52 (s, 3H), 1.32 and 1.22 (t, 7.10 Hz, 3H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  155.2, 154.4, 149.3, 149.0, 134.9, 132.4, 132.3, 128.3, 128.3, 123.2, 123.1, 119.3, 119.0, 118.7, 109.4, 109.2, 80.1, 79.7, 61.3, 61.0, 58.1, 57.0, 45.9, 45.6, 36.0, 35.7, 34.5, 34.4, 26.1, 18.0, 18.0, 15.0, 14.8. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{25}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 301.1911. Found: 301.1910.



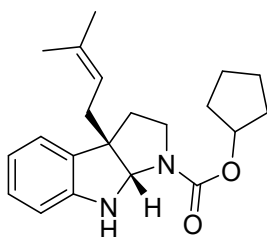
**3e.** Yellow oil. 62.2 mg, 99% yield. 92% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 4.377 min,  $t$  (major) = 5.337 min];  $[\alpha]_{\text{D}}^{25} = -215.9$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.06 (t,  $J = 7.97 \text{ Hz}$ , 2H), 6.73 (q,  $J = 6.87 \text{ Hz}$ , 1H), 6.59 (dd,  $J = 7.70$ , 2.83 Hz, 1H), 5.24 – 5.04 and 4.66 (m, 3H), 5.00 and 4.92 (p,  $J = 6.26 \text{ Hz}$ , 1H), 3.95 – 3.38 (m, 1H), 3.16 – 2.87 (m, 1H), 2.57 – 2.26 (m, 2H), 2.24 – 2.00 (m, 2H), 1.71 (s, 3H), 1.53 (s, 3H), 1.37 – 1.17 (m, 6H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  154.9, 154.0, 149.3, 149.0, 134.9, 132.5, 132.2, 128.3, 128.2, 123.2, 123.1, 119.3, 119.0, 118.6, 109.4, 109.2, 80.0, 79.7, 68.6, 68.3, 58.0, 57.0, 45.8, 45.6, 35.9, 35.7, 34.5, 34.4, 26.0, 22.5, 22.4, 22.3, 18.0. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 315.2067. Found: 315.2068.



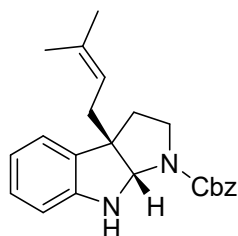
**3f.** Yellow oil. 65.0 mg, 99% yield. 92% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 10.843 min,  $t$  (major) = 7.670 min];  $[\alpha]_{\text{D}}^{25} = -282.6$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform- $d$ )  $\delta$  7.05 (t,  $J = 8.39 \text{ Hz}$ , 2H), 6.73 (d,  $J = 7.40 \text{ Hz}$ , 1H), 6.60 (d,  $J = 7.74 \text{ Hz}$ , 1H), 5.45 – 4.58 (m, 3H), 3.89 – 3.39 (m, 1H), 3.01 (q,  $J = 9.89, 9.34 \text{ Hz}$ , 1H), 2.37 (tp,  $J = 14.33, 6.93, 6.17 \text{ Hz}$ , 2H), 2.19 – 1.85 (m, 2H), 1.71 (s, 3H), 1.61 – 1.32 (m, 12H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform- $d$ )  $\delta$  154.6, 153.6, 149.3, 148.9, 134.8, 132.5, 132.3, 128.2, 128.1, 123.2, 123.1, 119.3, 119.3, 118.9, 118.5, 109.2, 109.1, 80.0, 79.9, 79.8, 79.6, 57.9, 56.9, 45.8, 45.4, 35.8, 35.6, 34.3, 28.7, 28.5, 26.0, 17.9. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 329.2224. Found: 329.2224.



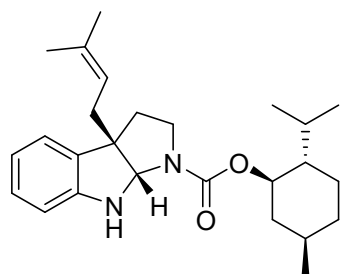
**3g.** Yellow oil. 77.2 mg, 95% yield. 93% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 3.880 min,  $t$  (major) = 5.097 min];  $[\alpha]_{\text{D}}^{25} = -272.8$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform- $d$ )  $\delta$  6.86 – 6.73 (m, 2H), 6.72 – 6.65 (m, 1H), 5.42 – 4.69 (m, 3H), 3.78 – 3.21 (m, 1H), 3.12 – 2.79 (m, 1H), 2.31 (qt,  $J = 14.59, 6.90 \text{ Hz}$ , 2H), 2.11 – 2.00 (m, 2H), 1.66 (s, 3H), 1.48 (d,  $J = 9.17 \text{ Hz}$ , 6H), 1.42 (s, 6H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform- $d$ )  $\delta$  154.5, 153.4, 150.9, 150.5, 135.2, 135.1, 131.6, 131.4, 124.5, 124.4, 121.7, 121.5, 121.1, 119.0, 119.0, 112.2, 112.1, 80.2, 80.2, 80.0, 79.9, 57.6, 56.5, 45.8, 45.4, 35.9, 35.8, 34.5, 34.5, 28.7, 28.5, 26.0, 18.0. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{28}\text{BrN}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 407.1329. Found: 407.1334.



**3h.** Yellow oil. 67.4 mg, 99% yield. 90% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t(\text{minor}) = 4.787 \text{ min}$ ,  $t(\text{major}) = 6.417 \text{ min}$ ];  $[\alpha]_{\text{D}}^{25} = -326.4$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.05 (t,  $J = 7.70 \text{ Hz}$ , 2H), 6.73 (q,  $J = 7.12 \text{ Hz}$ , 1H), 6.59 (dd,  $J = 7.72, 2.92 \text{ Hz}$ , 1H), 5.39 – 4.51 (m, 4H), 3.80 – 3.44 (m, 1H), 3.23 – 2.87 (m, 1H), 2.36 (dq,  $J = 18.17, 7.55, 6.32 \text{ Hz}$ , 2H), 2.23 – 2.00 (m, 2H), 1.96 – 1.75 (m, 4H), 1.74 – 1.61 (m, 6H), 1.59 – 1.52 (m, 4H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  155.1, 154.2, 149.3, 148.9, 135.0, 132.5, 132.3, 128.3, 128.2, 123.3, 123.2, 119.3, 119.0, 118.6, 109.4, 109.3, 80.0, 79.8, 77.6, 58.1, 57.0, 45.8, 45.6, 35.9, 35.7, 34.4, 34.3, 33.1, 33.1, 33.0, 32.8, 26.1, 23.8, 23.8, 18.0. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 341.2224. Found: 341.2228.



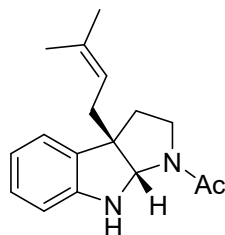
**3i.** Yellow oil. 53.6 mg, 74% yield. 91% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t(\text{minor}) = 10.617 \text{ min}$ ,  $t(\text{major}) = 12.773 \text{ min}$ ];  $[\alpha]_{\text{D}}^{25} = -293.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.46 – 7.29 (m, 5H), 7.16 – 7.04 (m, 2H), 6.77 (t,  $J = 7.38 \text{ Hz}$ , 1H), 6.59 (dd,  $J = 30.47, 7.79 \text{ Hz}$ , 1H), 5.34 – 4.52 (m, 5H), 3.93 – 3.58 (m, 1H), 3.11 (tt,  $J = 11.27, 6.55 \text{ Hz}$ , 1H), 2.48 – 2.32 (m, 2H), 2.22 – 2.11 (m, 2H), 1.73 (s, 3H), 1.55 (d,  $J = 4.55 \text{ Hz}$ , 3H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  155.0, 154.2, 149.2, 148.9, 136.7, 136.7, 135.2, 135.1, 132.4, 132.2, 128.8, 128.6, 128.3, 128.2, 128.1, 128.0, 123.3, 123.2, 119.3, 119.1, 118.8, 109.5, 109.3, 80.2, 79.8, 67.1, 66.8, 58.2, 57.1, 46.1, 45.8, 35.9, 35.7, 34.4, 26.1, 18.0. HRMS (ESI) calcd for  $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 363.2067. Found: 363.2062.



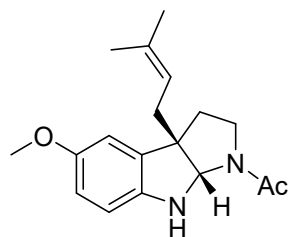
**3j.** Yellow oil. 68.9 mg, 84% yield. 96% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t(\text{minor}) = 3.620 \text{ min}$ ,  $t(\text{major}) = 4.200 \text{ min}$ ];  $[\alpha]_{\text{D}}^{25} = -192.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.09 – 7.01 (m, 2H), 6.74 (q,  $J = 7.23$



Hz, 1H), 6.66 – 6.47 (m, 1H), 5.49 – 4.33 (m, 4H), 3.85 – 3.40 (m, 1H), 3.23 – 2.87 (m, 1H), 2.39 (hept,  $J = 7.67$  Hz, 2H), 2.20 – 2.06 (m, 3H), 1.96 (ttt,  $J = 13.90, 7.63, 6.87, 3.23$  Hz, 1H), 1.77 – 1.59 (m, 5H), 1.58 – 1.21 (m, 5H), 1.16 – 0.98 (m, 2H), 0.98 – 0.74 (m, 10H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  155.2, 155.1, 154.2, 154.1, 149.3, 148.9, 135.0, 132.5, 128.3, 128.2, 123.3, 123.2, 123.1, 119.3, 119.1, 119.0, 118.6, 118.6, 109.4, 109.3, 109.2, 80.3, 80.1, 79.8, 79.6, 75.1, 74.9, 74.9, 58.1, 57.0 (d,  $J = 2.92$  Hz), 47.6, 47.6, 47.4, 47.3, 46.0, 45.8, 45.6, 45.5, 41.8, 41.8, 41.7, 35.8, 34.6, 34.5, 34.4, 34.3, 31.5, 26.8, 26.5, 26.4, 26.2, 26.1, 23.6, 23.6, 23.3, 22.2, 22.1, 21.2, 21.0, 20.8, 18.0, 16.7, 16.6, 16.5, 16.4. HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{39}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 411.3006. Found: 411.3009.

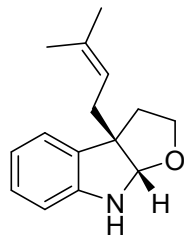


**3k.** Yellow oil. 47.6 mg, 88% yield. 89% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0$  mL $\cdot$ min $^{-1}$ ,  $\lambda = 254$  nm,  $t$  (minor) = 7.787 min,  $t$  (major) = 13.740 min];  $[\alpha]_{\text{D}}^{25} = -361.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.06 (t,  $J = 7.48$  Hz, 2H), 6.73 (td,  $J = 7.44, 1.01$  Hz, 1H), 6.58 (d,  $J = 7.75$  Hz, 1H), 5.32 – 4.52 (m, 3H), 3.56 (ddd,  $J = 9.80, 6.16, 3.36$  Hz, 1H), 3.18 (td,  $J = 10.01, 7.76$  Hz, 1H), 2.37 (qt,  $J = 14.48, 6.29$  Hz, 2H), 2.27 – 2.13 (m, 2H), 1.99 (s, 3H), 1.70 (s, 3H), 1.52 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  170.3, 149.3, 135.3, 132.0, 128.4, 123.1, 119.1, 118.7, 109.4, 79.7, 56.5, 47.3, 35.5, 34.4, 26.1, 22.8, 18.0. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ : 271.1805. Found: 271.1803.

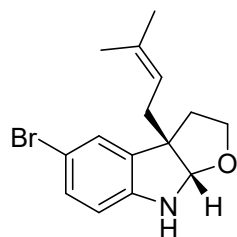


**3l.** Yellow oil. 52.8 mg, 88% yield. 90% e.e. [Daicel Chiralcel OD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0$  mL $\cdot$ min $^{-1}$ ,  $\lambda = 254$  nm,  $t$  (minor) = 10.583 min,  $t$  (major) = 20.747 min];  $[\alpha]_{\text{D}}^{25} = -330.4$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  6.70 – 6.60 (m, 2H), 6.51 (d,  $J = 8.32$  Hz, 1H), 5.24 – 4.89 (m, 3H), 3.74 (s, 3H), 3.60 – 3.51 (m, 1H), 3.22 – 3.14 (m, 1H), 2.47 – 2.25 (m, 2H), 2.21 – 2.12 (m, 2H), 1.99 (s, 3H), 1.70 (s, 3H), 1.52 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$

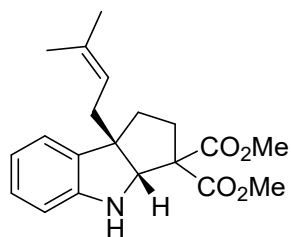
170.2, 153.4, 143.3, 135.4, 133.7, 119.0, 112.9, 110.3, 109.9, 80.4, 56.8, 56.0, 47.3, 35.3, 34.2, 26.1, 22.8, 18.0. HRMS (ESI) calcd for  $C_{18}H_{25}N_2O_2$   $[M+H]^+$ : 301.1911. Found: 301.1912.



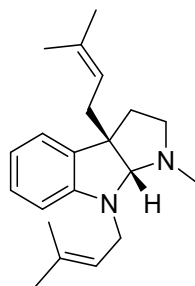
**3m.** Yellow oil. 37.1 mg, 81% yield. 83% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 6.497 min,  $t$  (major) = 11.213 min];  $[\alpha]_D^{25} = -127.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.07 (td,  $J = 7.55, 5.63 \text{ Hz}$ , 2H), 6.75 (t,  $J = 7.40 \text{ Hz}$ , 1H), 6.58 (d,  $J = 7.73 \text{ Hz}$ , 1H), 5.34 (s, 1H), 5.14 (ddt,  $J = 8.18, 6.67, 1.63 \text{ Hz}$ , 1H), 4.68 (s, 1H), 3.96 (ddd,  $J = 8.61, 7.09, 1.49 \text{ Hz}$ , 1H), 3.56 (ddd,  $J = 11.07, 8.53, 5.17 \text{ Hz}$ , 1H), 2.58 – 2.42 (m, 2H), 2.24 – 2.06 (m, 2H), 1.71 (s, 3H), 1.59 (s, 3H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  149.6, 134.5, 132.9, 128.1, 123.6, 119.8, 118.8, 108.3, 97.6, 67.3, 58.1, 39.3, 36.2, 26.1, 18.2. HRMS (ESI) calcd for  $C_{15}H_{20}NO$   $[M+H]^+$ : 230.1539. Found: 230.1542.



**3n.** Yellow oil. 53.4 mg, 87% yield. 82% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 6.230 min,  $t$  (major) = 10.550 min];  $[\alpha]_D^{25} = -99.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.19 – 7.08 (m, 2H), 6.42 (d,  $J = 8.15 \text{ Hz}$ , 1H), 5.30 (s, 1H), 5.15 – 5.03 (m, 1H), 4.64 (s, 1H), 4.05 – 3.79 (m, 1H), 3.52 (ddd,  $J = 11.15, 8.61, 5.10 \text{ Hz}$ , 1H), 2.52 – 2.34 (m, 2H), 2.21 – 2.02 (m, 2H), 1.69 (s, 3H), 1.55 (s, 3H).  $^{13}\text{C NMR}$  (101 MHz, )  $\delta$  148.6 (s), 135.2 (s), 135.1 (s), 130.7 (s), 126.7 (s), 119.1 (s), 110.2 (s), 109.5 (s), 97.7 (s), 67.2 (s), 58.2 (s), 39.2 (s), 36.0 (s), 26.0 (s), 18.1 (s). HRMS (ESI) calcd for  $C_{15}H_{19}BrNO$   $[M+H]^+$ : 308.0645. Found: 308.0641.



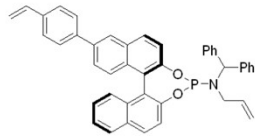
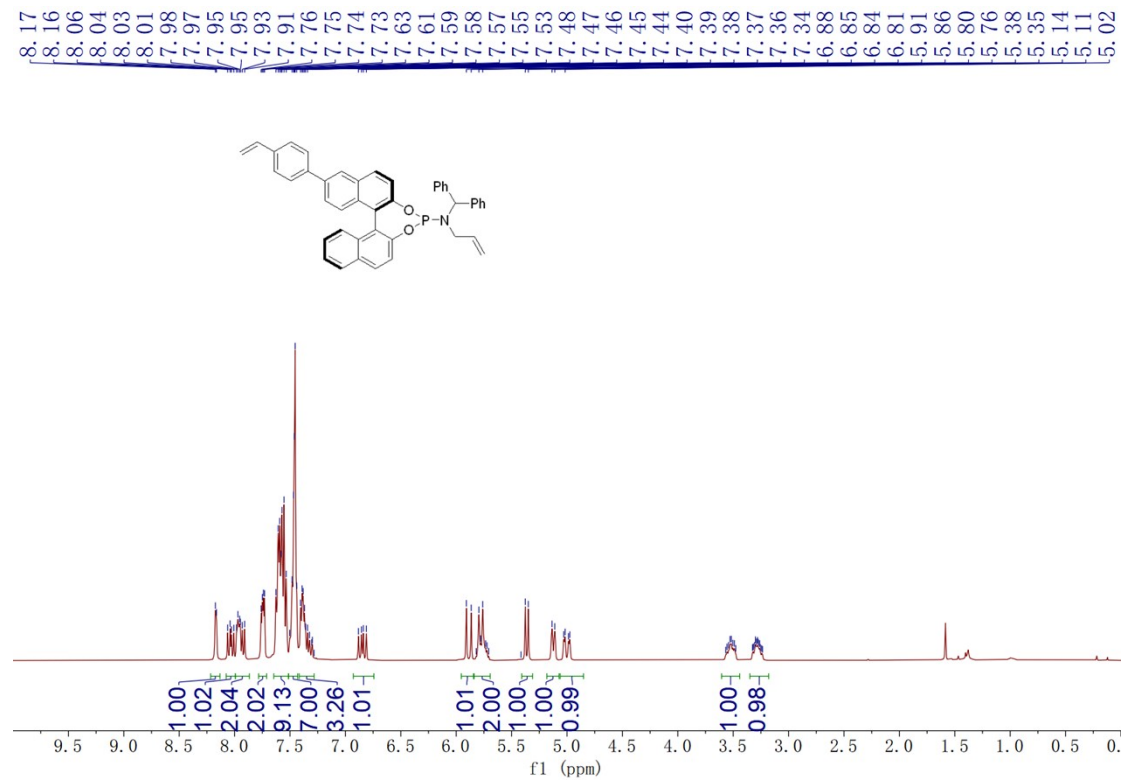
**30.** Yellow oil. 61.8 mg, 90% yield. 91% e.e. [Daicel Chiralcel AD-H (0.46 cm x 25 cm), n-hexane/2-propanol = 90/10,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 6.813 min,  $t$  (major) = 5.613 min];  $[\alpha]_{\text{D}}^{25} = -43.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.02 – 6.94 (m, 2H), 6.70 (td,  $J = 7.43$ , 1.05 Hz, 1H), 6.50 (dd,  $J = 8.09$ , 0.99 Hz, 1H), 4.91 (dddd,  $J = 7.28$ , 5.88, 2.93, 1.39 Hz, 1H), 4.58 (d,  $J = 4.55$  Hz, 1H), 3.94 (d,  $J = 4.81$  Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 2.61 – 2.40 (m, 2H), 2.27 – 2.10 (m, 2H), 2.00 (ddd,  $J = 12.75$ , 6.33, 1.63 Hz, 1H), 1.78 (td,  $J = 13.13$ , 6.43 Hz, 1H), 1.63 (d,  $J = 1.83$  Hz, 6H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  171.5, 169.9, 150.5, 135.0, 133.8, 127.7, 123.2, 120.7, 118.9, 109.1, 70.6, 68.0, 58.7, 52.7, 52.4, 38.8, 38.4, 31.6, 26.0, 18.2. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{26}\text{NO}_4$   $[\text{M}+\text{H}]^+$ : 344.1856. Found: 344.1855.



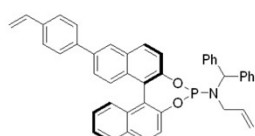
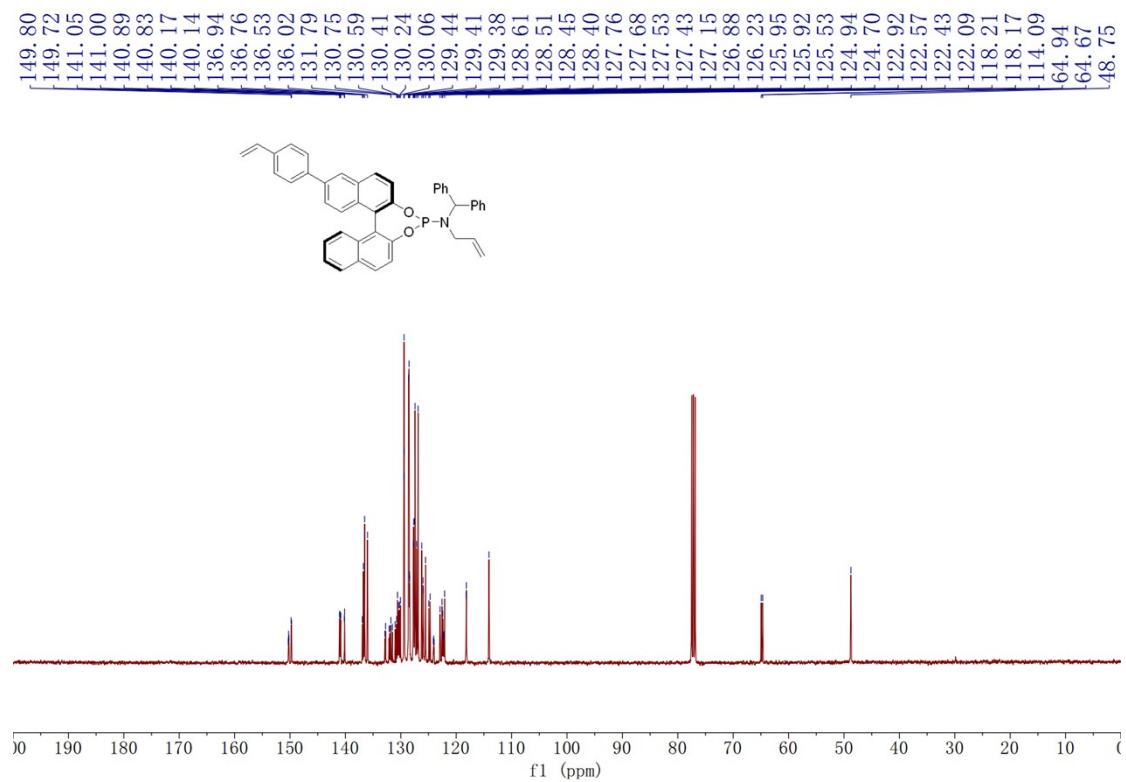
(-)-Debromoflustramine **B**. Yellow oil. 1.1 g, 69% yield. 86% e.e. [Daicel Chiralcel IC (0.46 cm x 25 cm), n-hexane/2-propanol = 98/2, 0.2%  $\text{Et}_2\text{NH}$ ,  $v = 1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 254 \text{ nm}$ ,  $t$  (minor) = 4.080 min,  $t$  (major) = 4.517 min];  $[\alpha]_{\text{D}}^{25} = -52.6$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.04 (td,  $J = 7.63$ , 1.26 Hz, 1H), 6.97 (dd,  $J = 7.32$ , 1.35 Hz, 1H), 6.69 – 6.59 (m, 1H), 6.42 (d,  $J = 7.94$  Hz, 1H), 5.17 (ddq,  $J = 7.24$ , 4.39, 1.61 Hz, 1H), 5.01 – 4.92 (m, 1H), 4.26 (s, 1H), 3.93 (dd,  $J = 16.19$ , 5.73 Hz, 1H), 3.80 (dd,  $J = 16.11$ , 7.28 Hz, 1H), 2.67 (ddd,  $J = 9.75$ , 6.64, 3.38 Hz, 1H), 2.56 (td,  $J = 9.16$ , 5.82 Hz, 1H), 2.49 (s, 3H), 2.42 (d,  $J = 7.41$  Hz, 2H), 2.05 (ddd,  $J = 11.88$ , 9.18, 6.62 Hz, 1H), 1.91 (ddd,  $J = 11.88$ , 5.83, 3.38 Hz, 1H), 1.74 – 1.66 (m, 6H), 1.65 (d,  $J = 1.61$  Hz, 3H), 1.58 (s, 3H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  150.9, 134.7, 133.1, 132.5, 126.5, 121.8, 120.4, 119.8, 116.4, 106.3, 90.3, 56.0, 51.7, 45.8, 38.1, 37.5, 36.9, 28.7, 24.9, 24.7, 17.1. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{31}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 311.2482. Found: 311.2481.

# NMR spectra

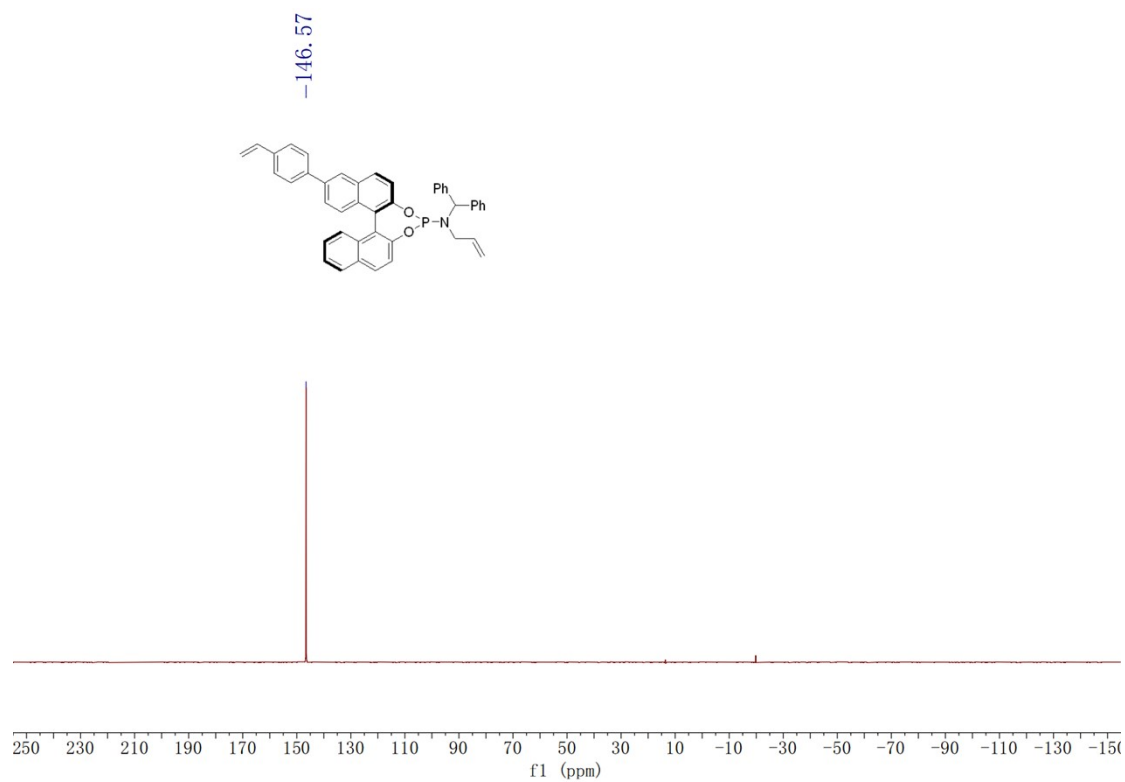
## <sup>1</sup>H NMR Spectrum of M1



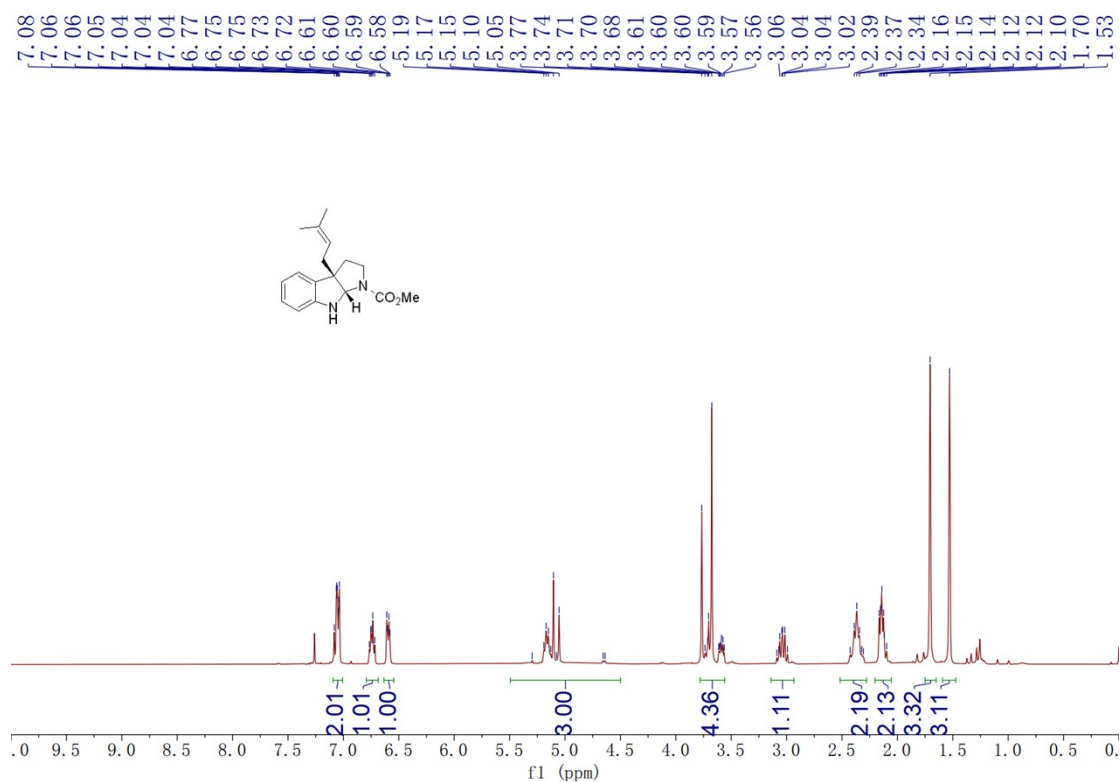
## <sup>13</sup>C NMR Spectrum of M1



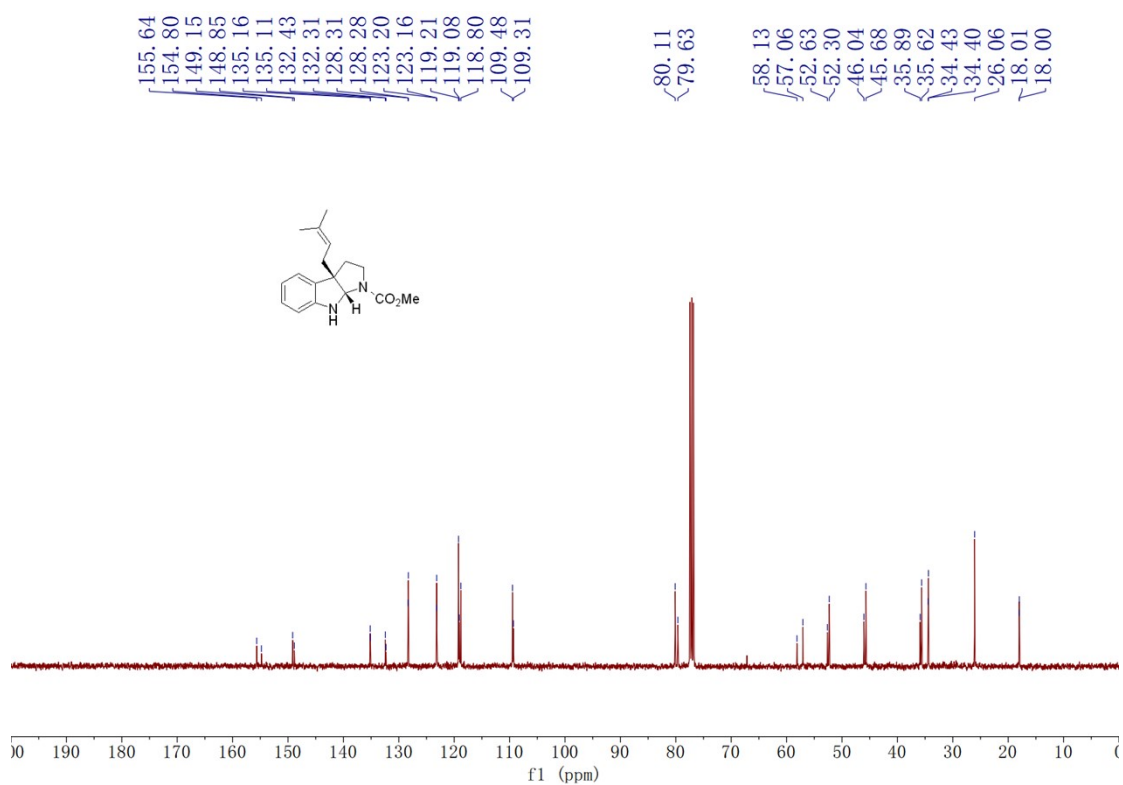
# $^{31}\text{P}$ NMR Spectrum of **M1**



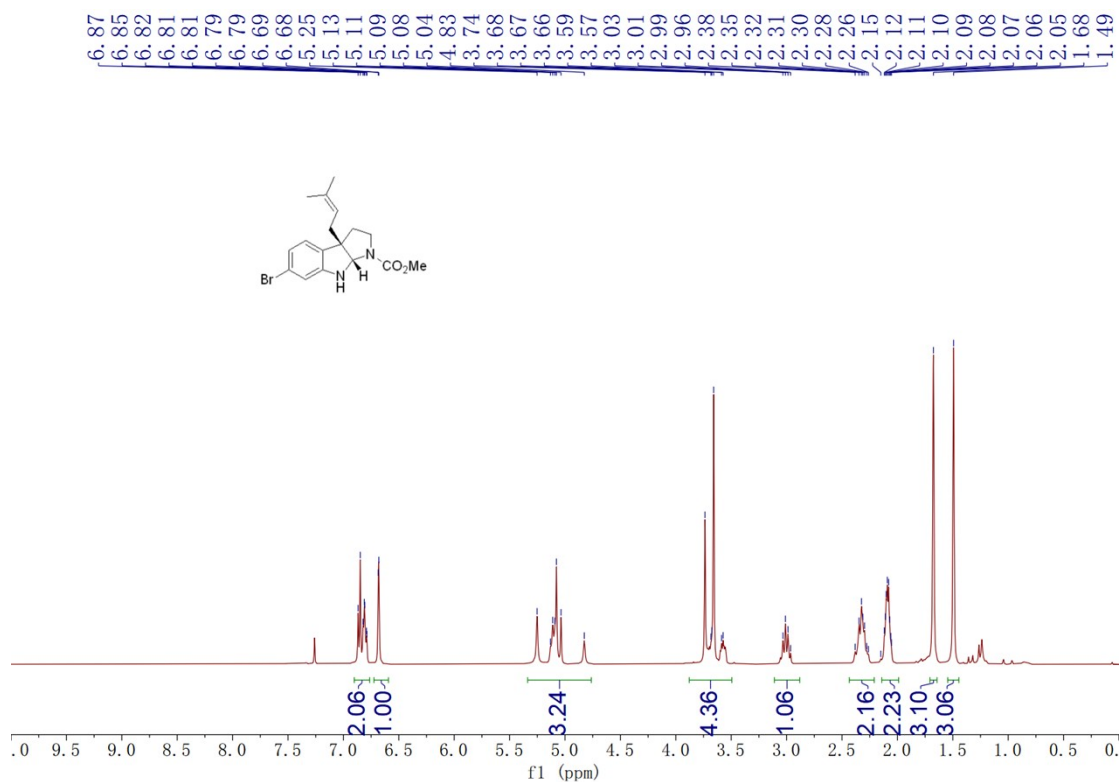
### <sup>1</sup>H NMR Spectrum of 3a



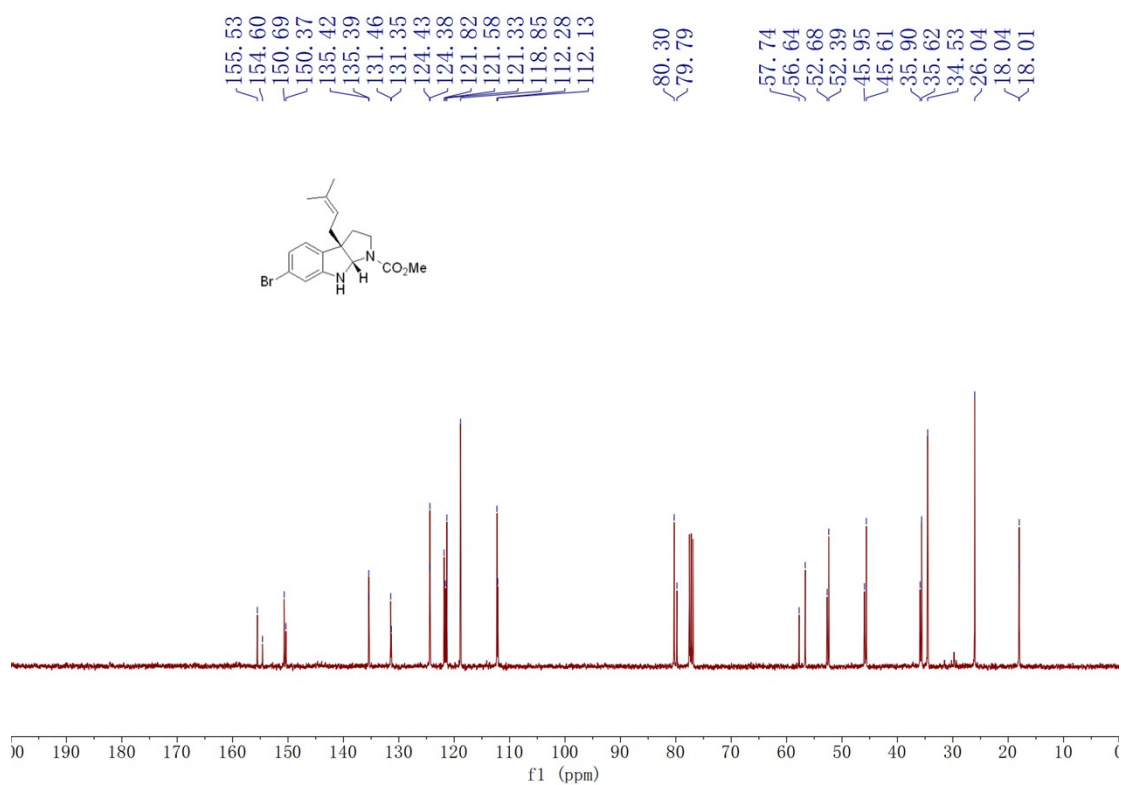
### <sup>13</sup>C NMR Spectrum of 3a



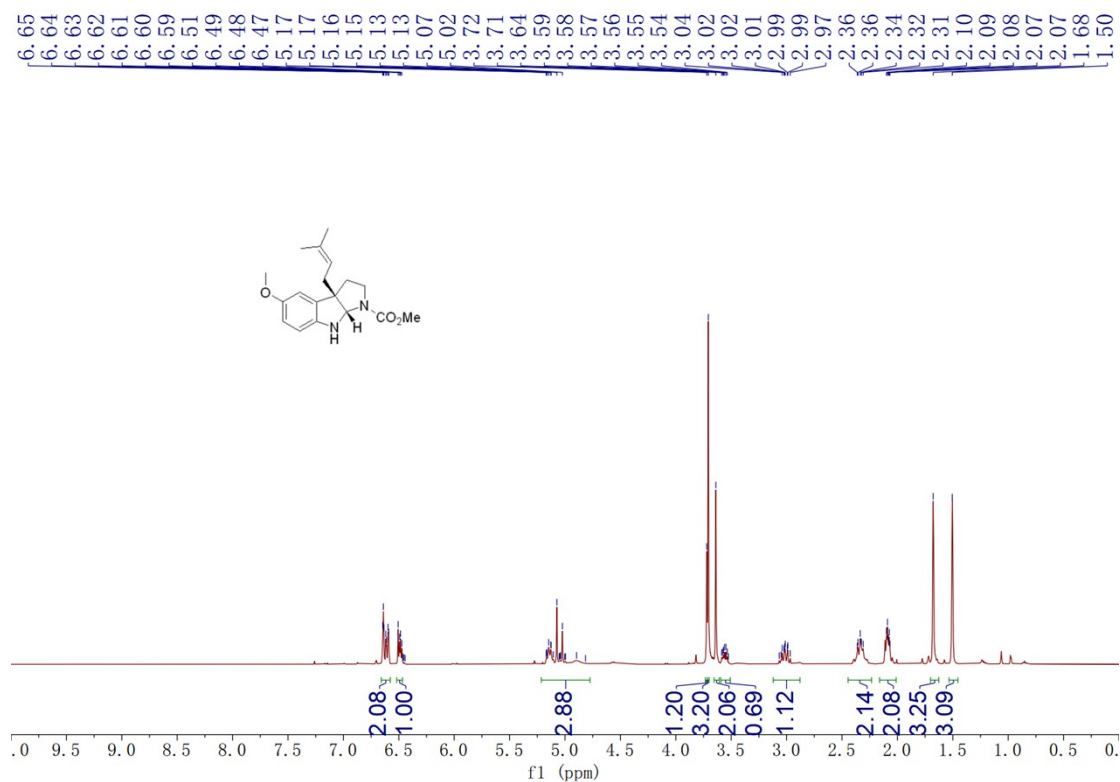
### <sup>1</sup>H NMR Spectrum of **3b**



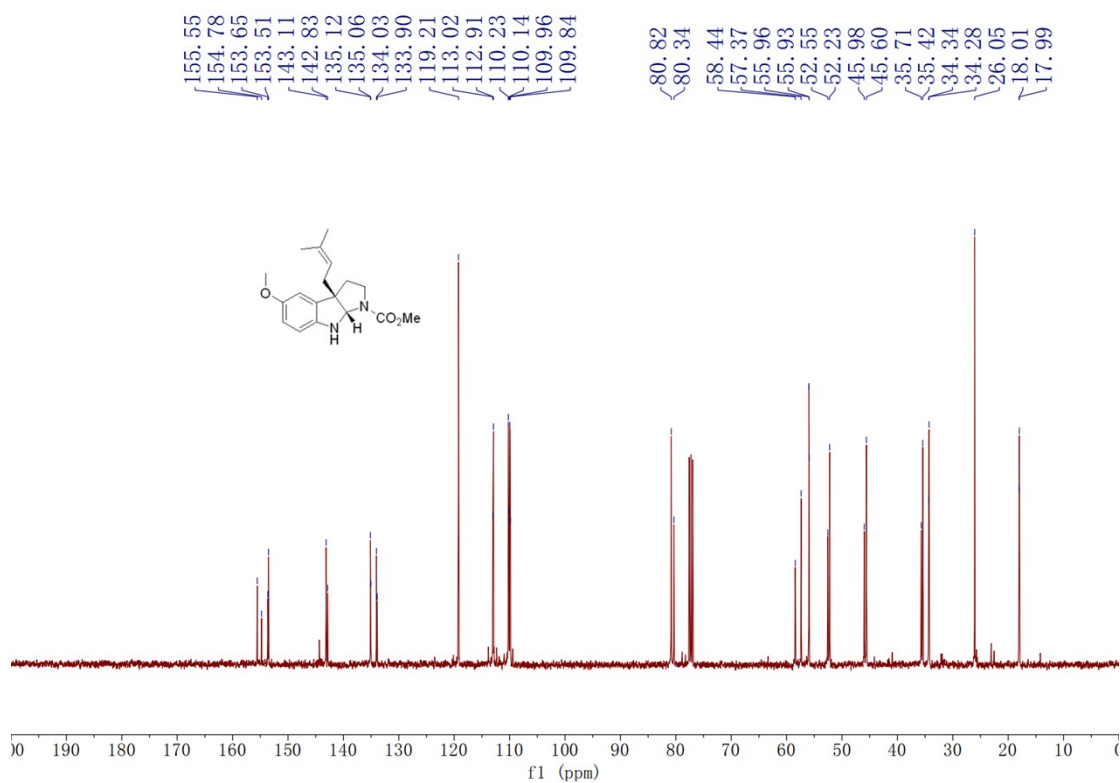
### <sup>13</sup>C NMR Spectrum of **3b**



### <sup>1</sup>H NMR Spectrum of **3c**

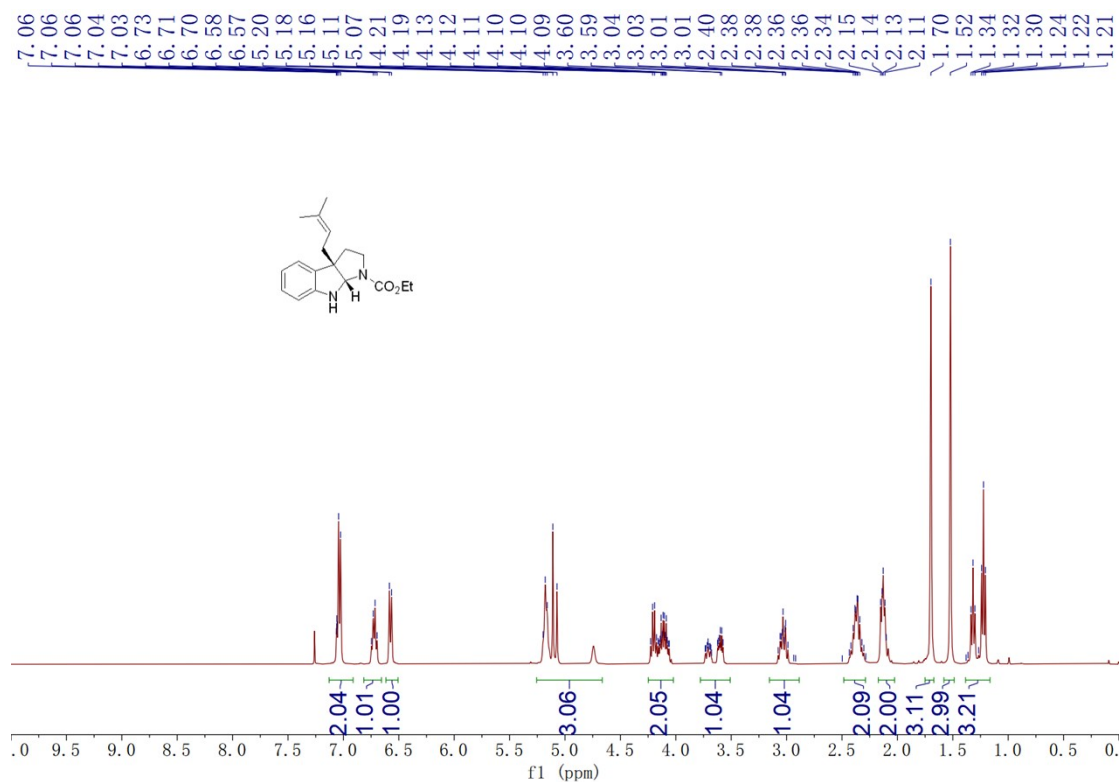


### <sup>13</sup>C NMR Spectrum of **3c**

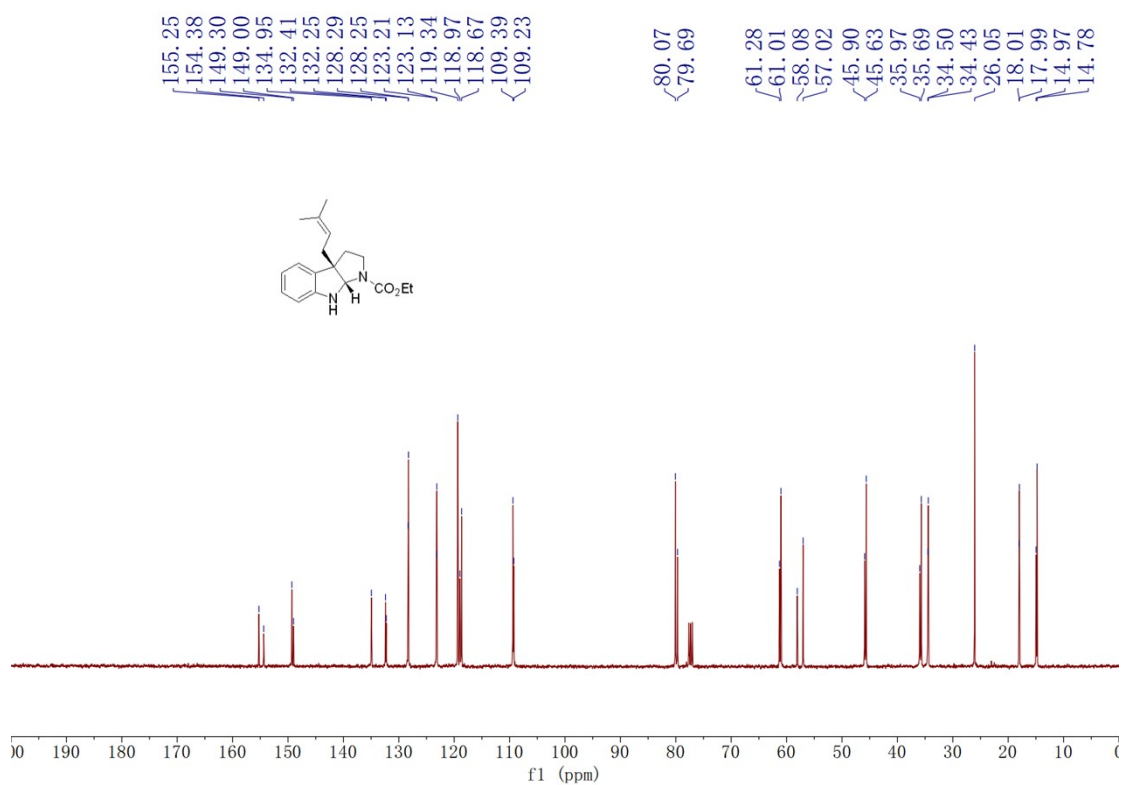




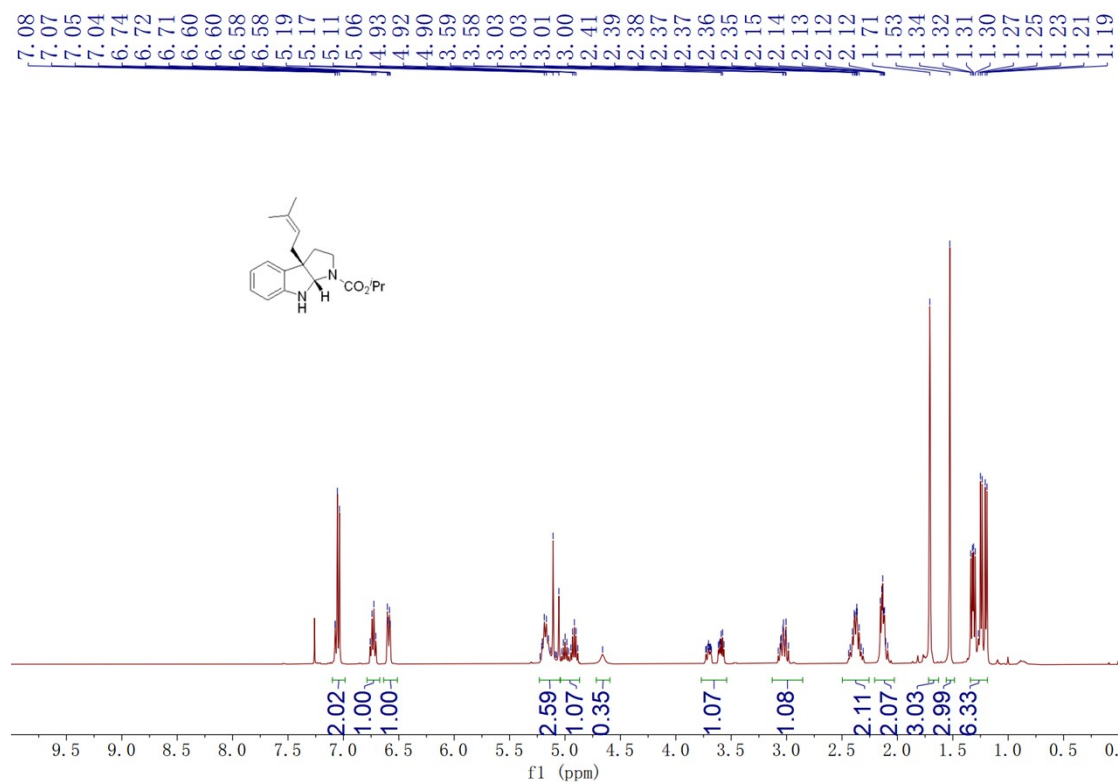
### <sup>1</sup>H NMR Spectrum of **3d**



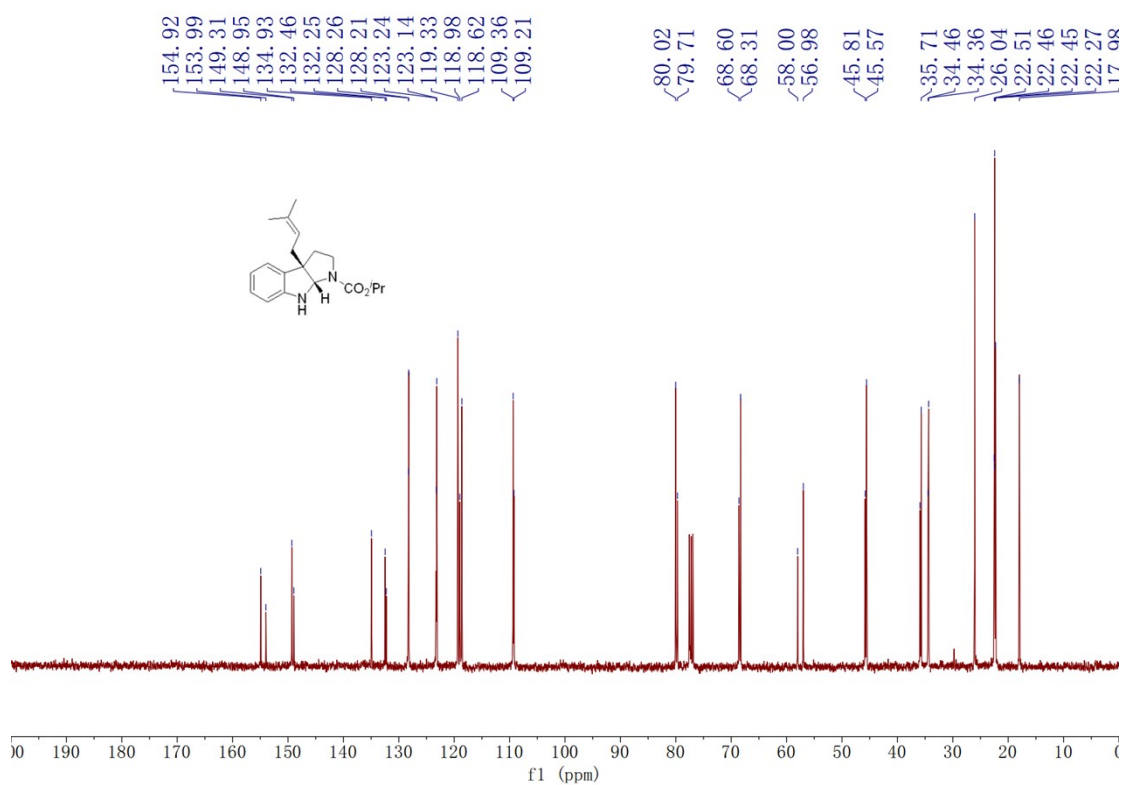
### <sup>13</sup>C NMR Spectrum of **3d**



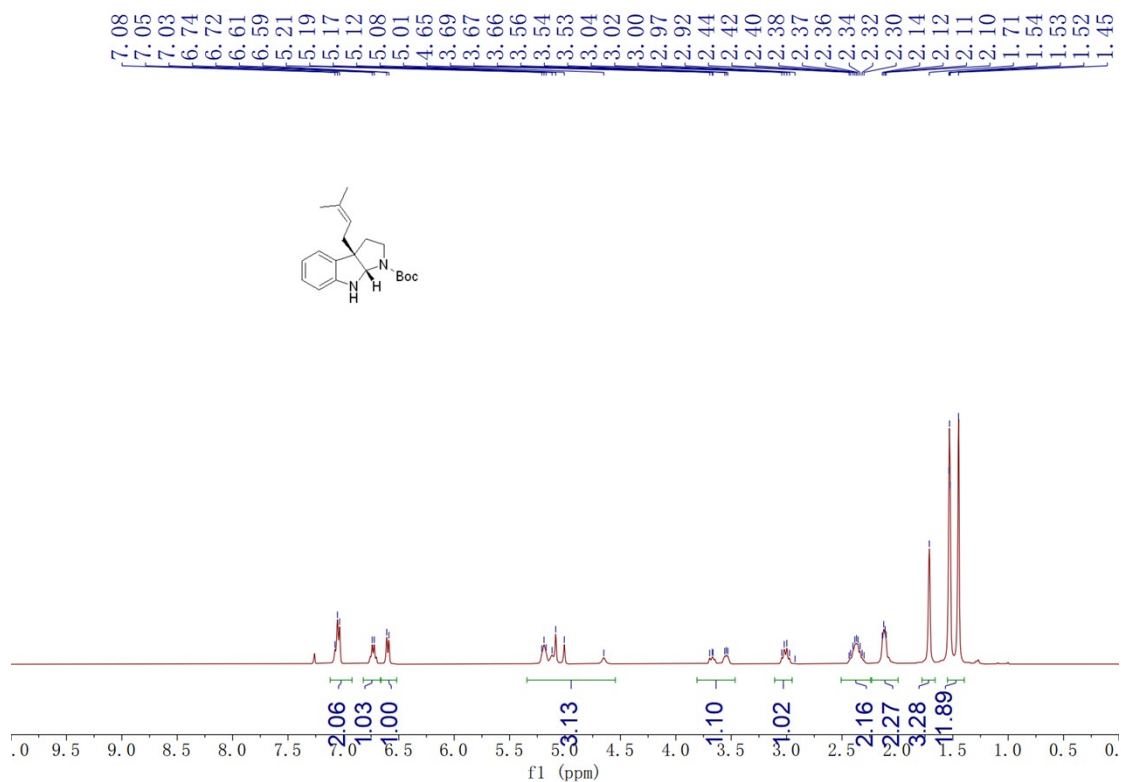
### <sup>1</sup>H NMR Spectrum of 3e



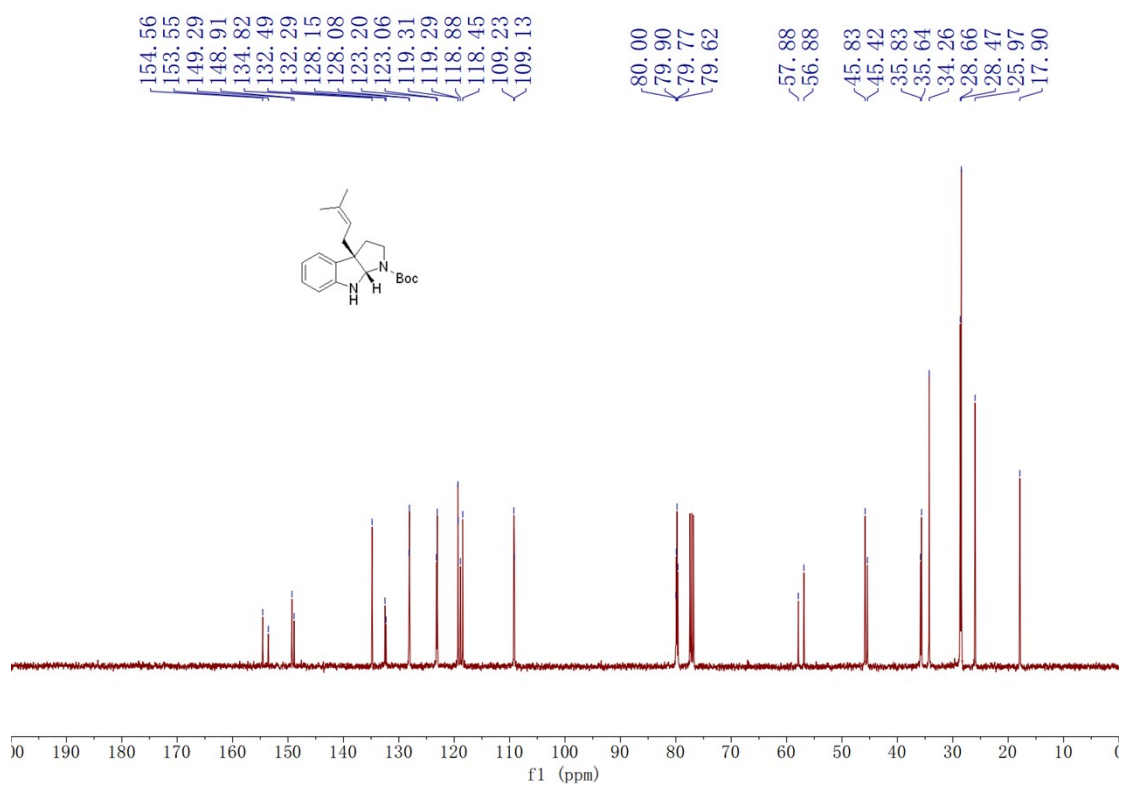
### <sup>13</sup>C NMR Spectrum of 3e



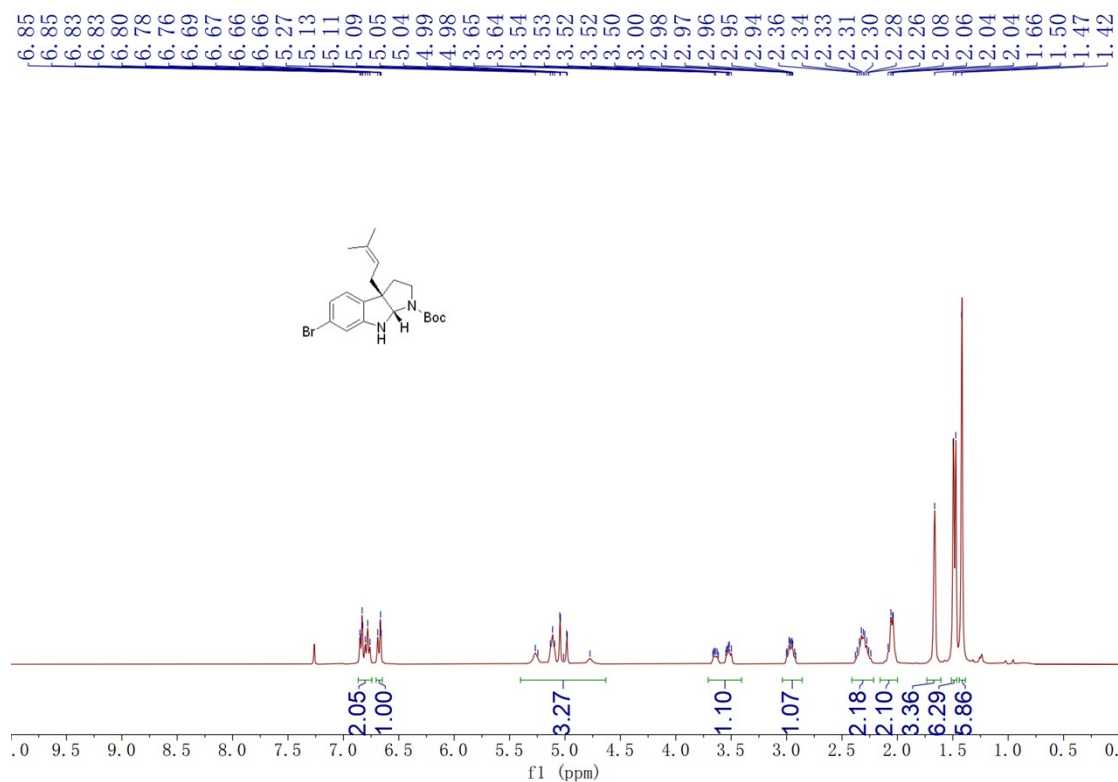
### <sup>1</sup>H NMR Spectrum of **3f**



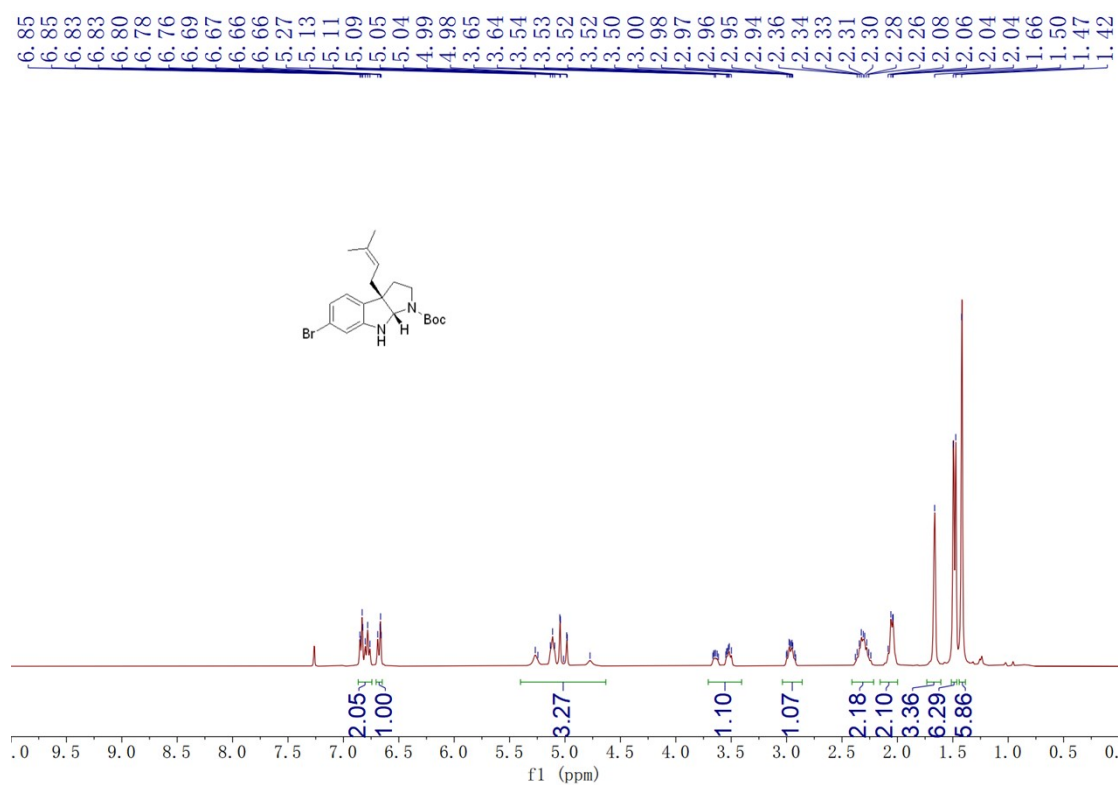
### <sup>13</sup>C NMR Spectrum of **3f**



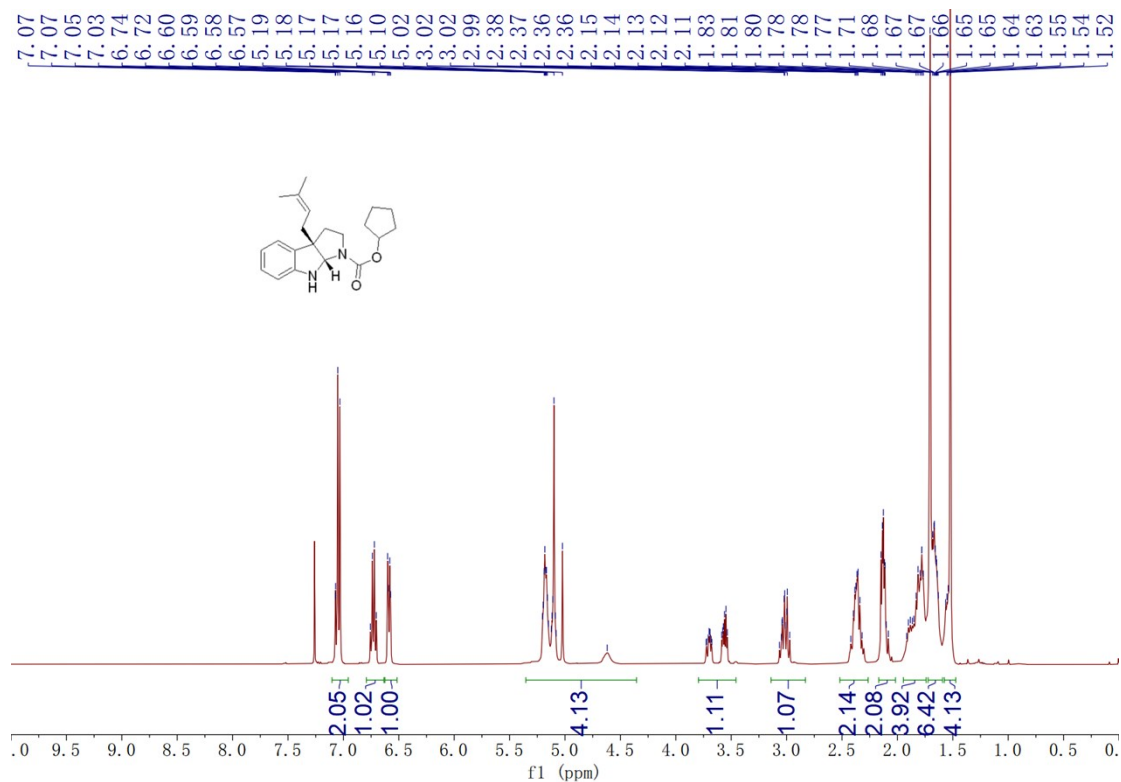
### <sup>1</sup>H NMR Spectrum of **3g**



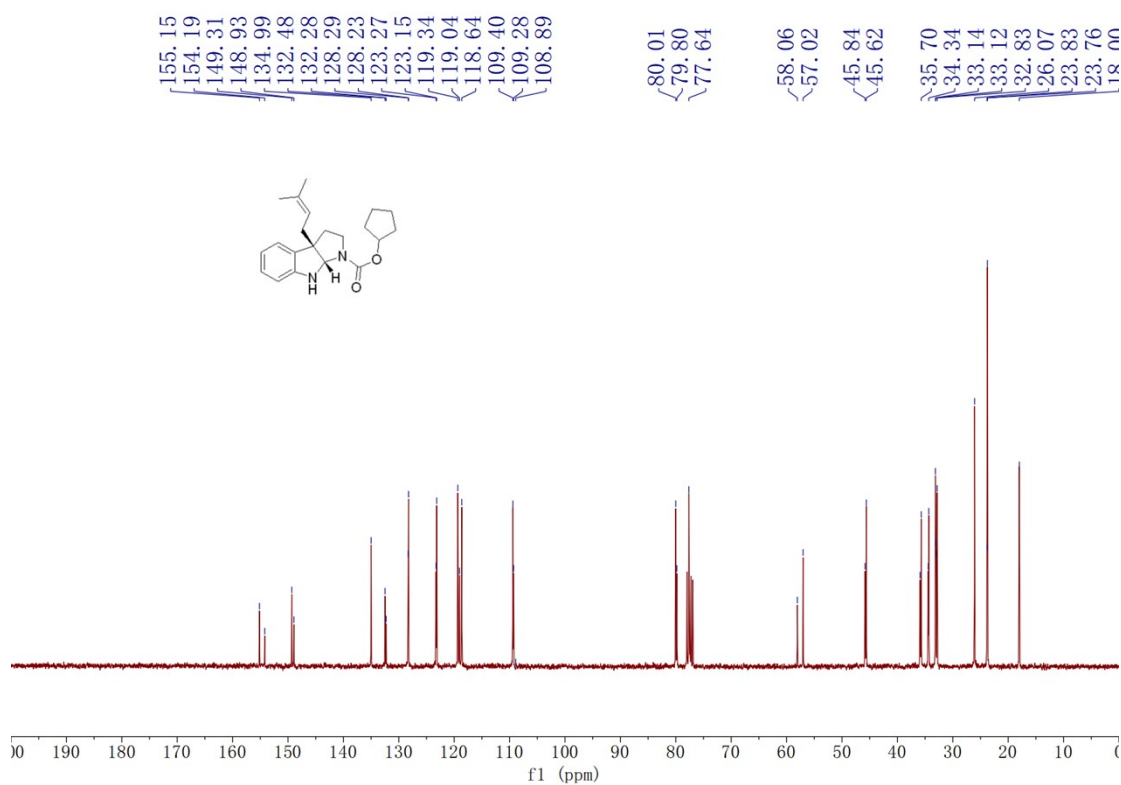
### <sup>13</sup>C NMR Spectrum of **3g**



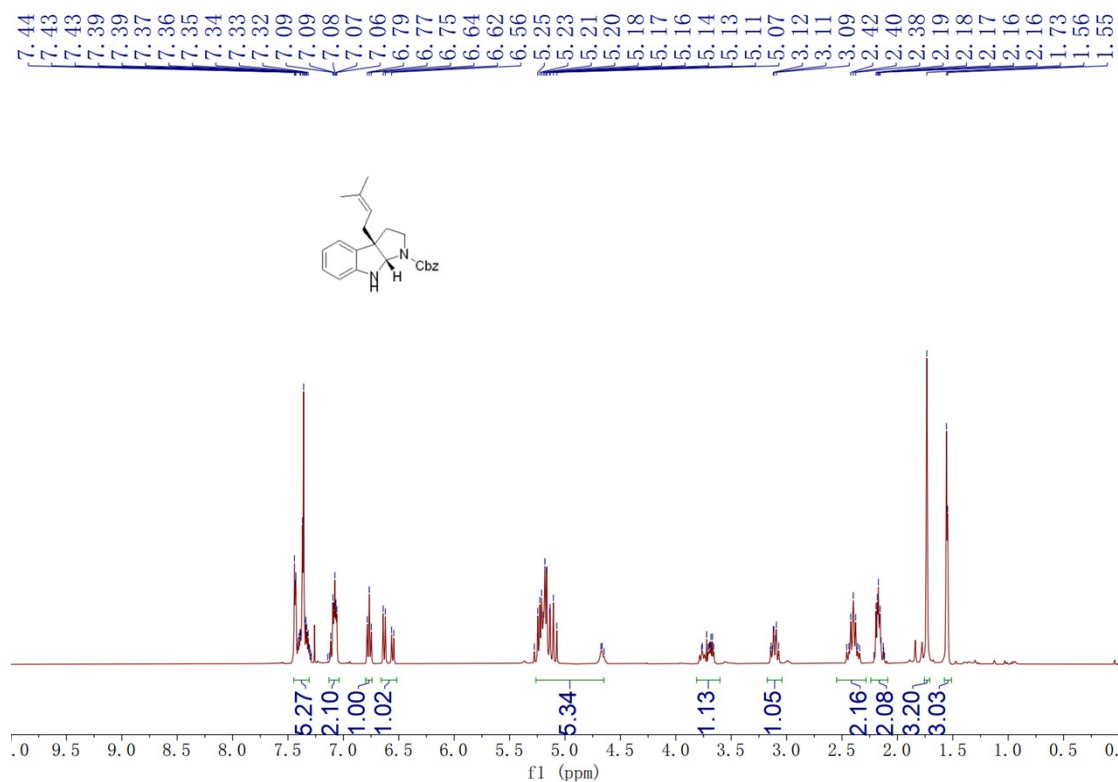
### <sup>1</sup>H NMR Spectrum of **3h**



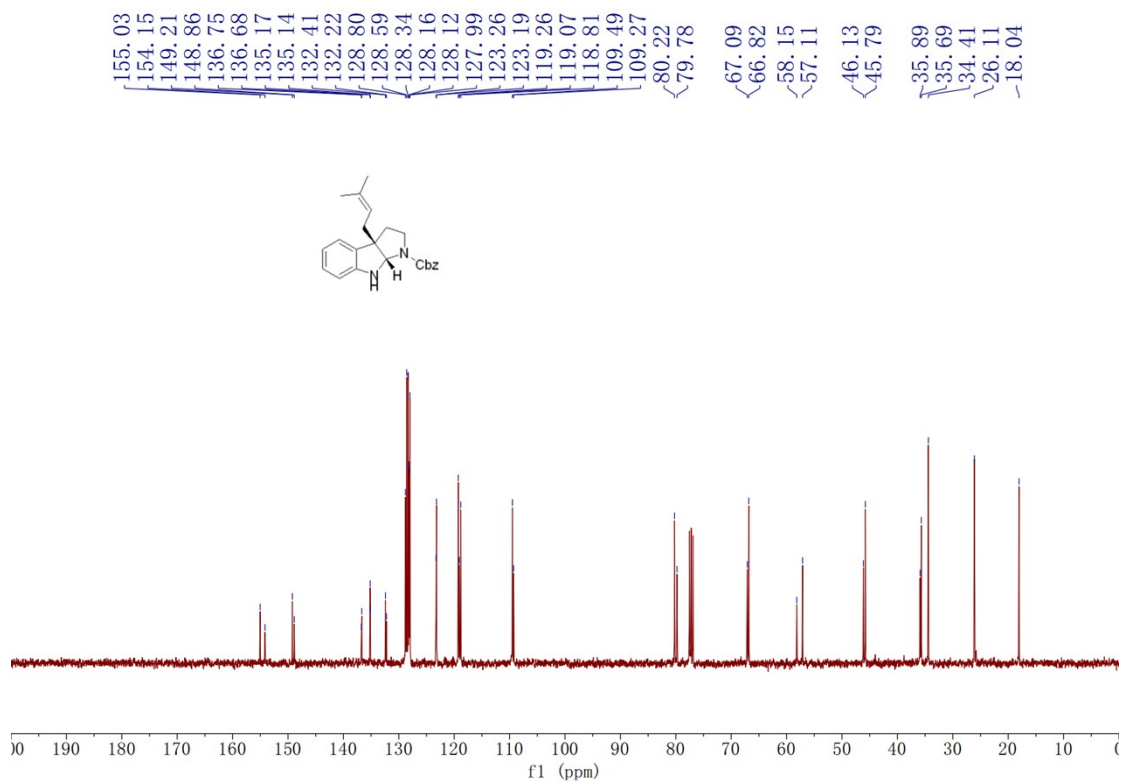
### <sup>13</sup>C NMR Spectrum of **3h**



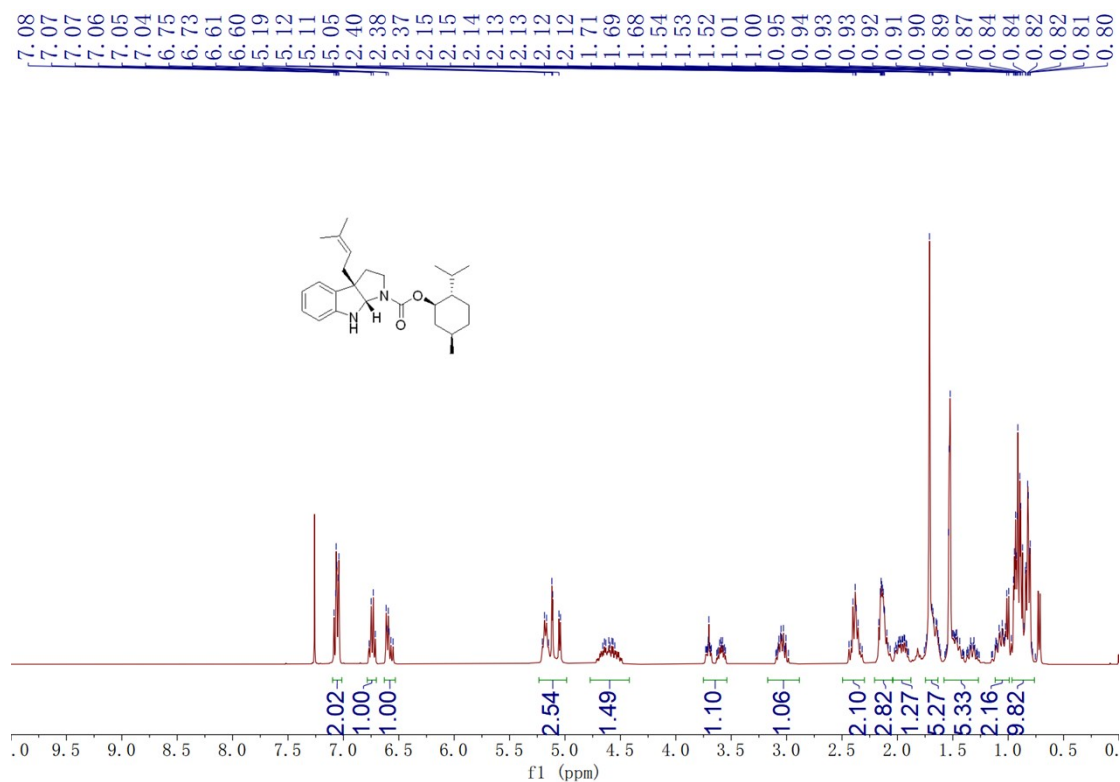
### <sup>1</sup>H NMR Spectrum of **3i**



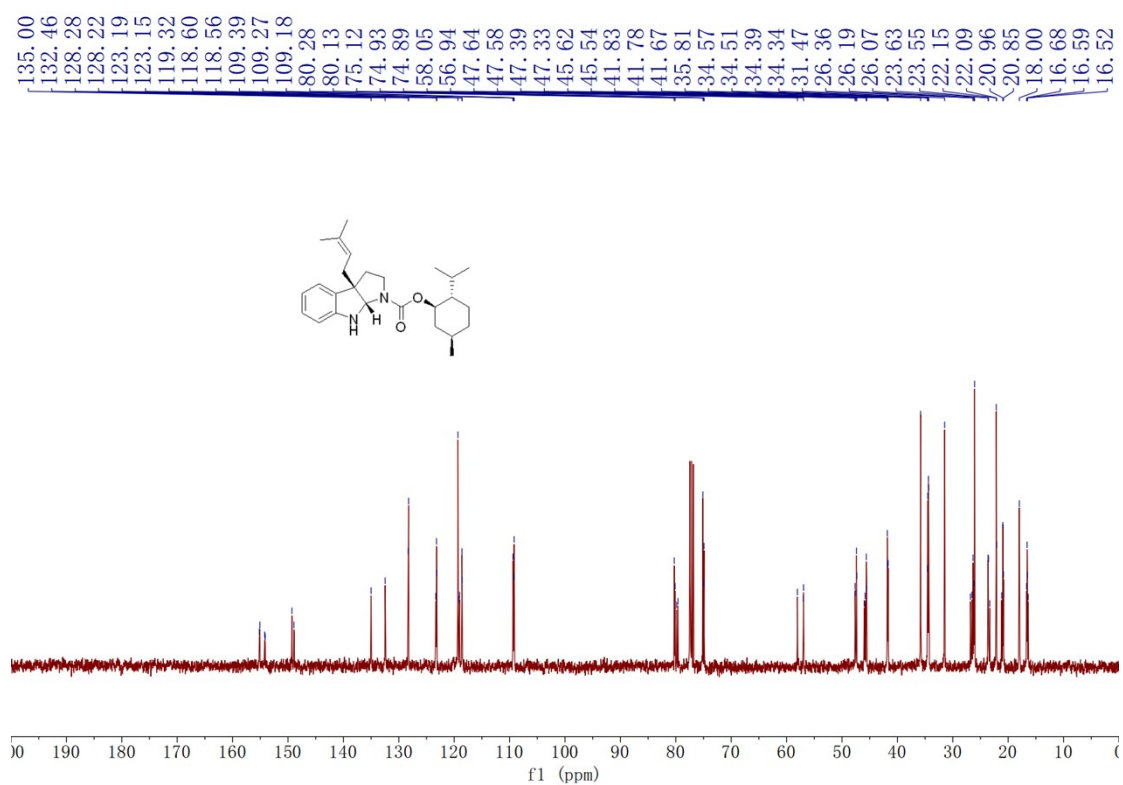
### <sup>13</sup>C NMR Spectrum of **3i**



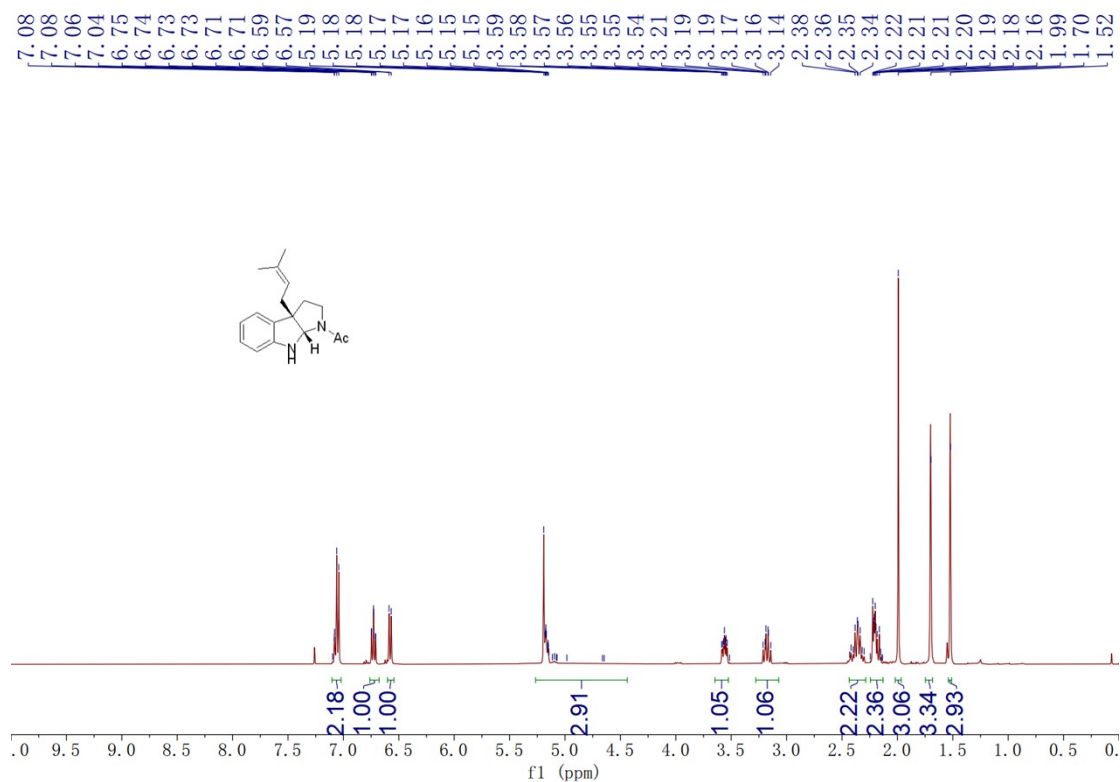
### <sup>1</sup>H NMR Spectrum of **3j**



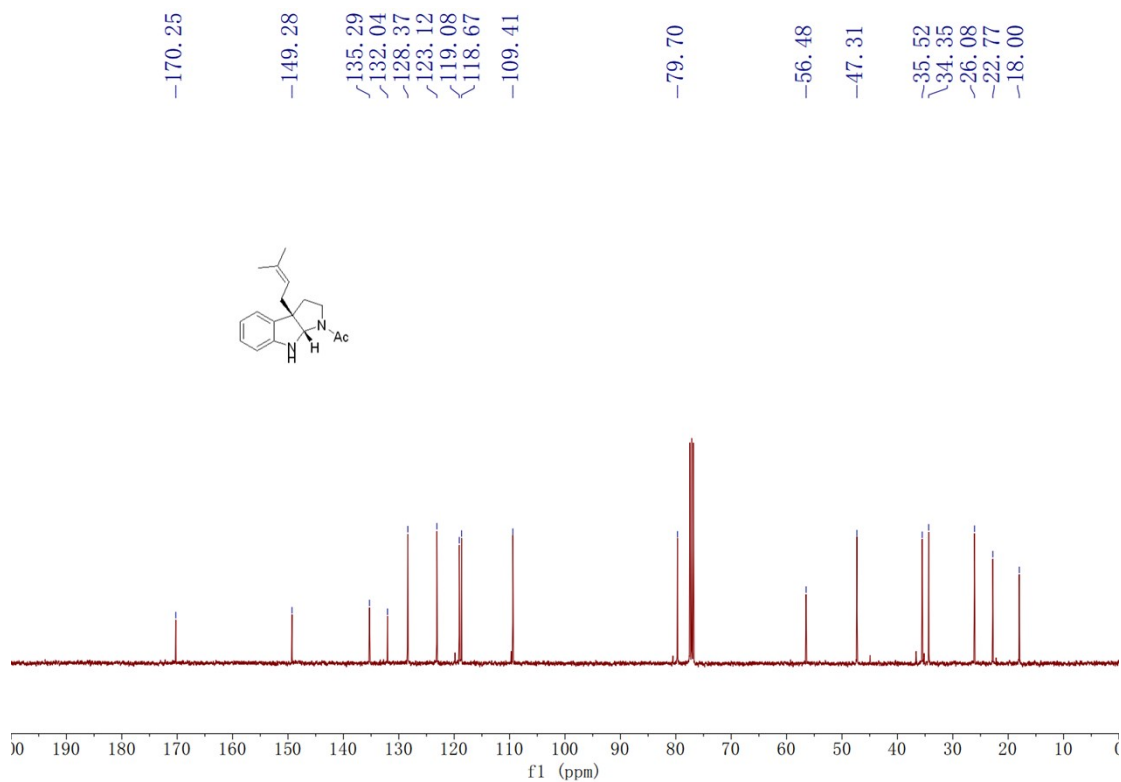
### <sup>13</sup>C NMR Spectrum of **3j**



### <sup>1</sup>H NMR Spectrum of **3k**

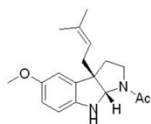
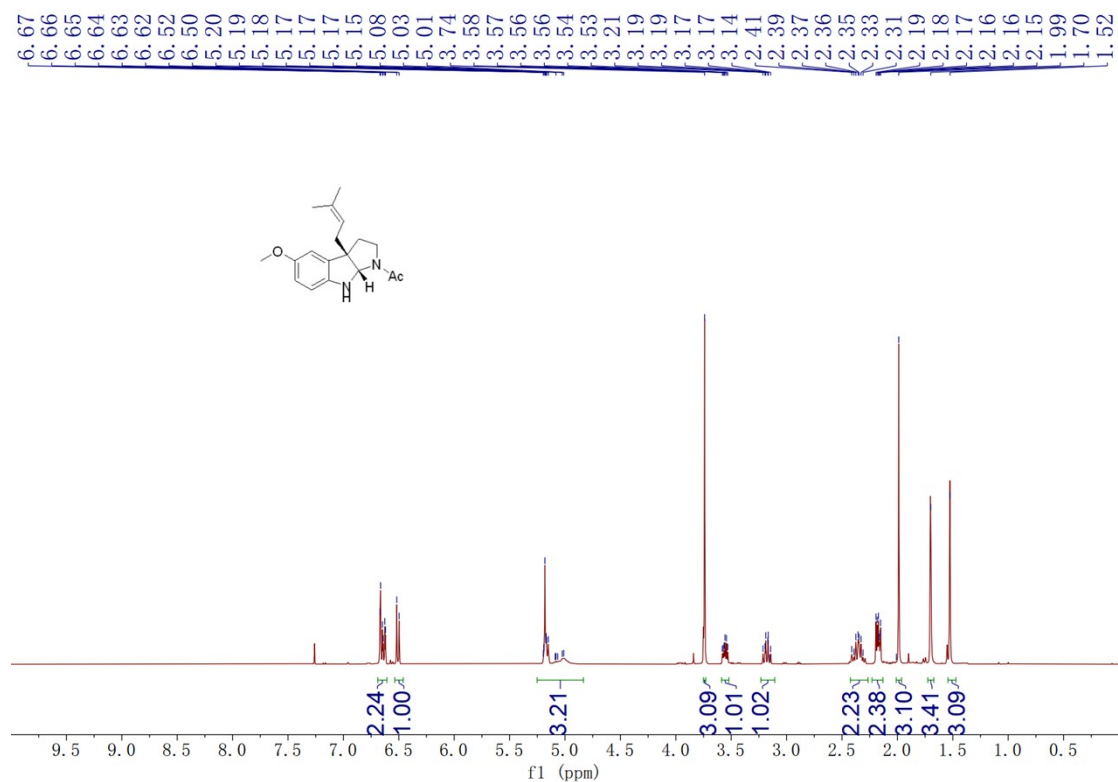


### <sup>13</sup>C NMR Spectrum of **3k**

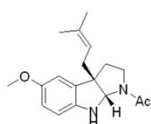
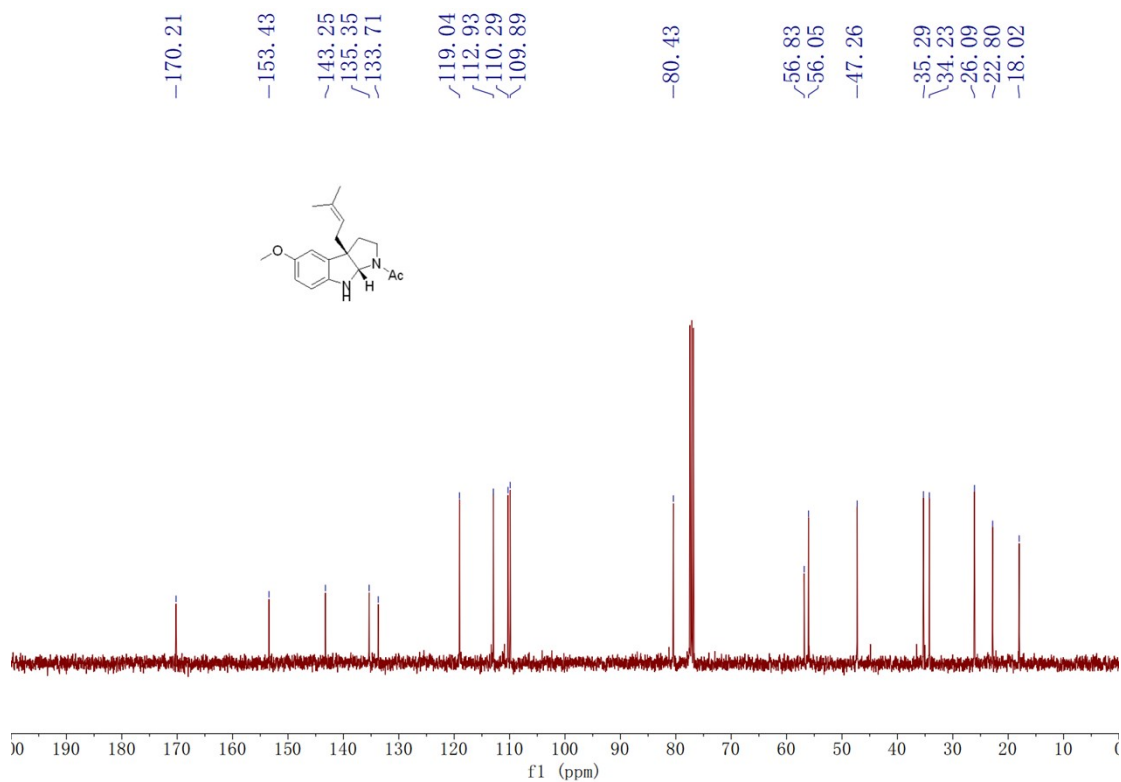




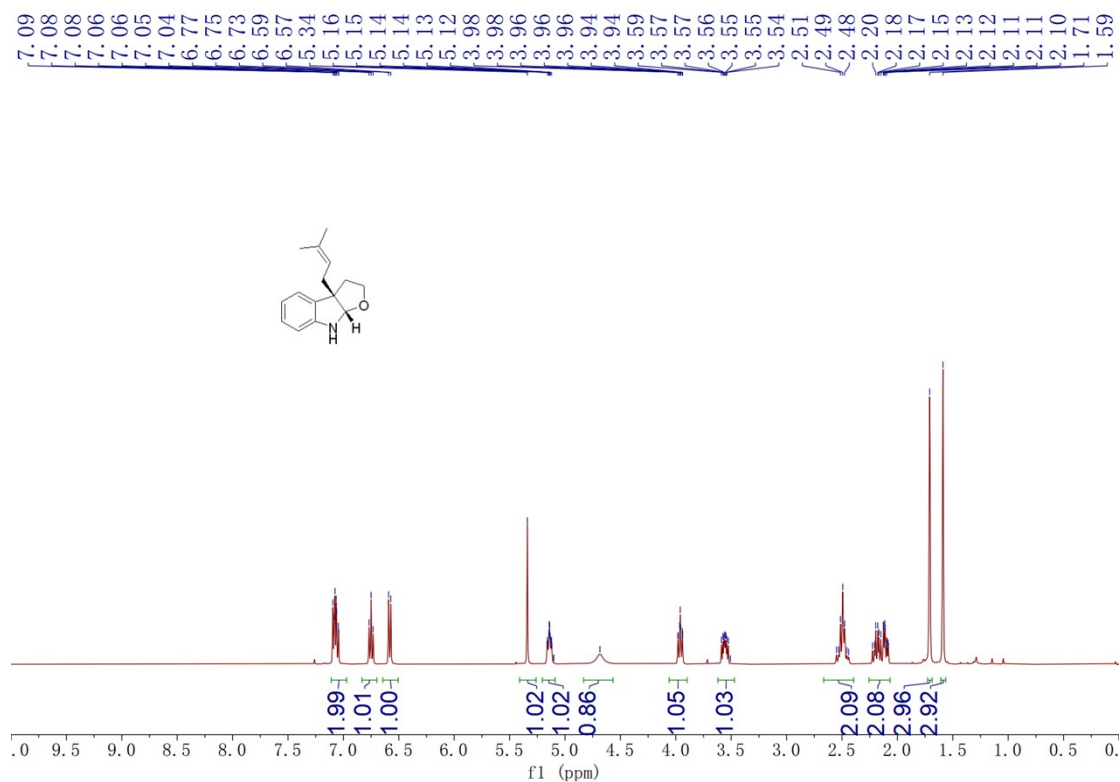
### <sup>1</sup>H NMR Spectrum of **31**



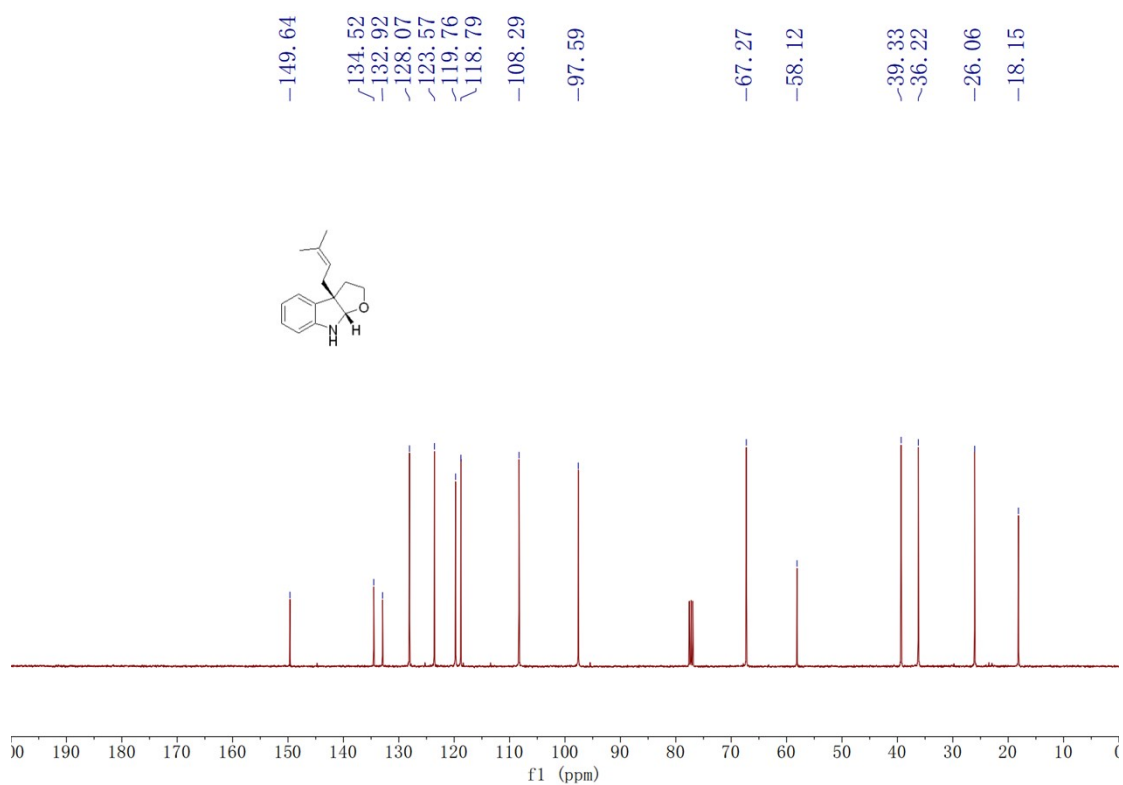
### <sup>13</sup>C NMR Spectrum of **31**



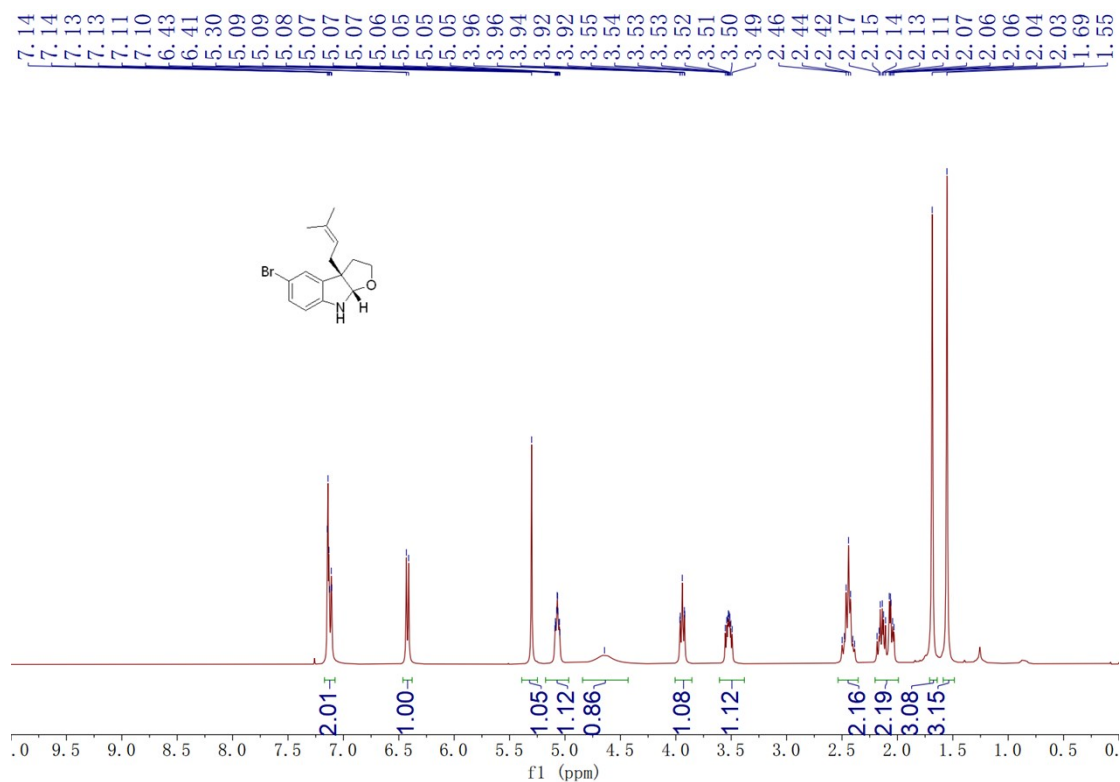
### <sup>1</sup>H NMR Spectrum of **3m**



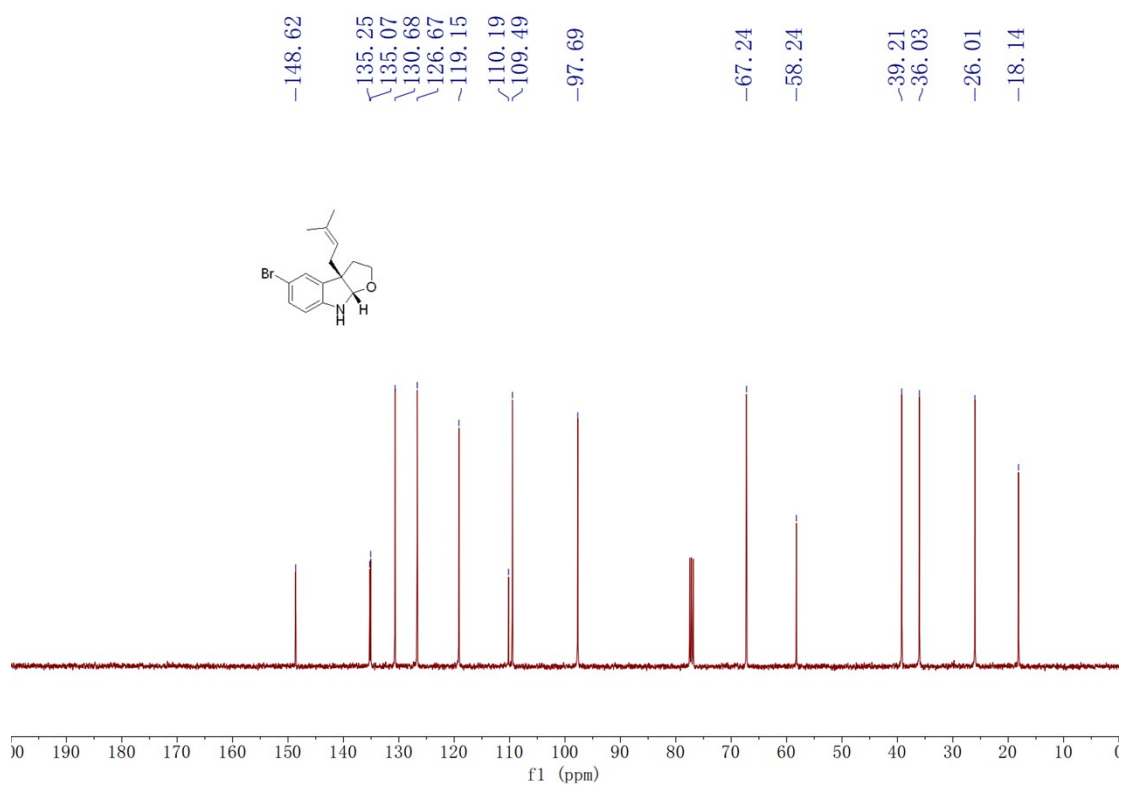
### <sup>13</sup>C NMR Spectrum of **3m**



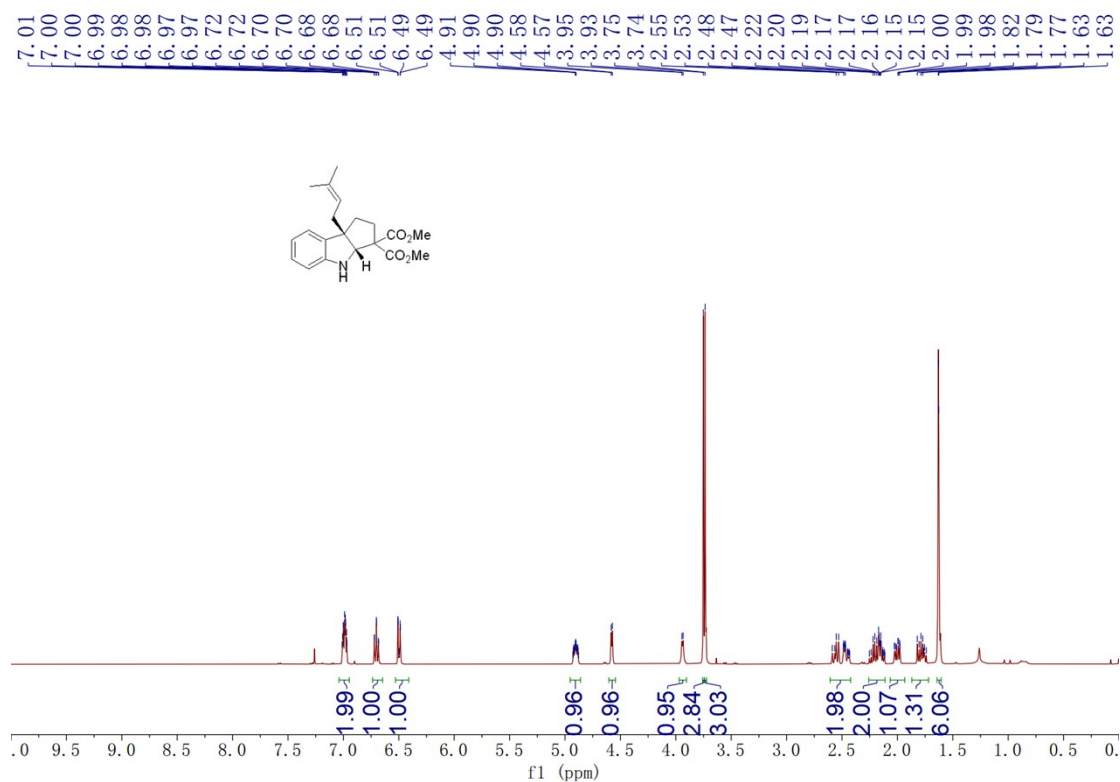
### <sup>1</sup>H NMR Spectrum of **3n**



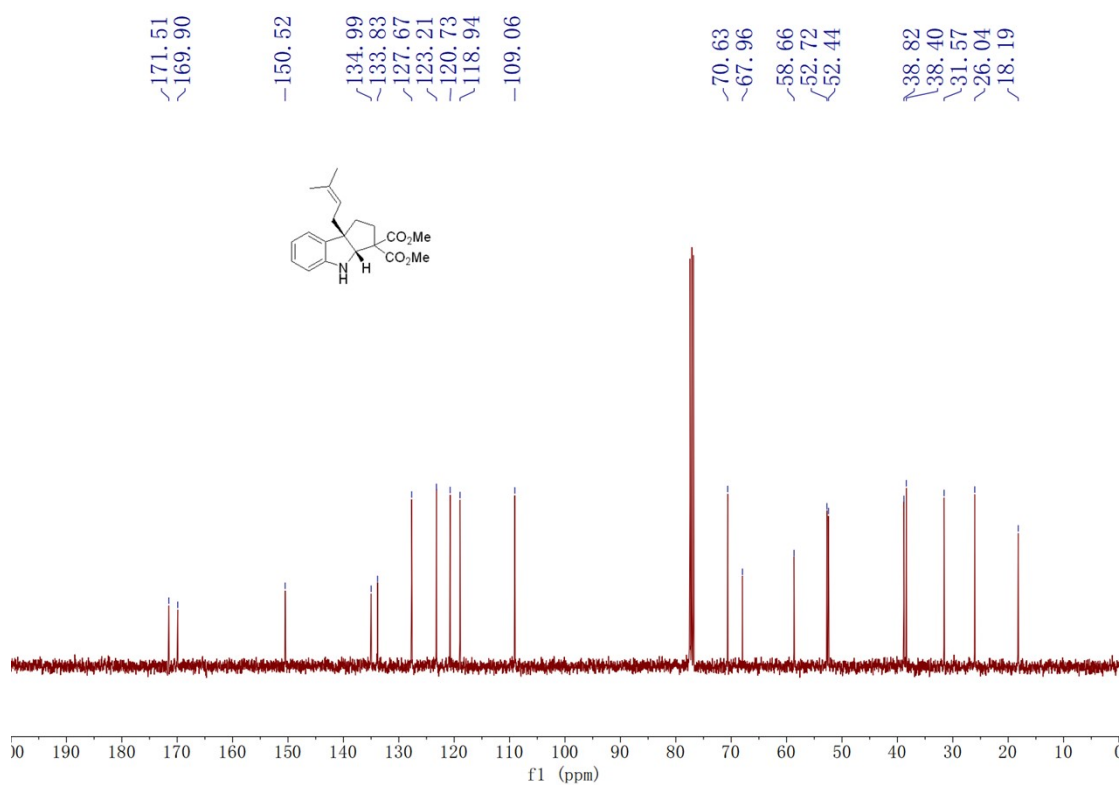
### <sup>13</sup>C NMR Spectrum of **3n**



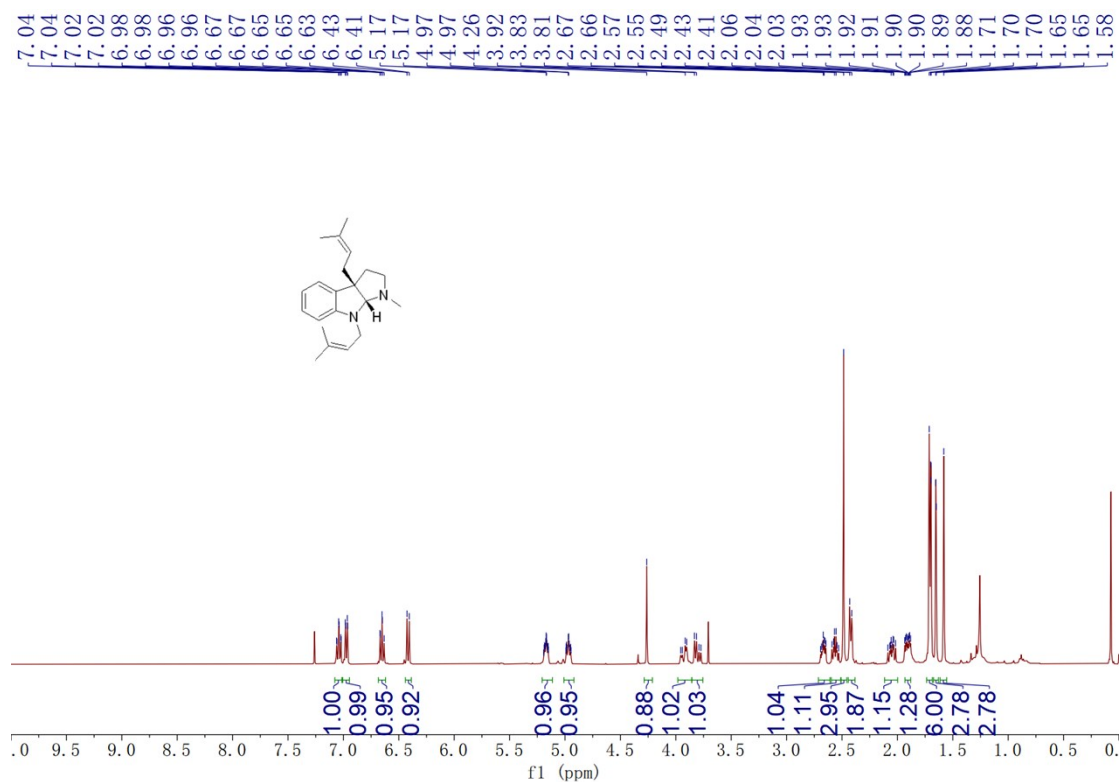
### <sup>1</sup>H NMR Spectrum of **30**



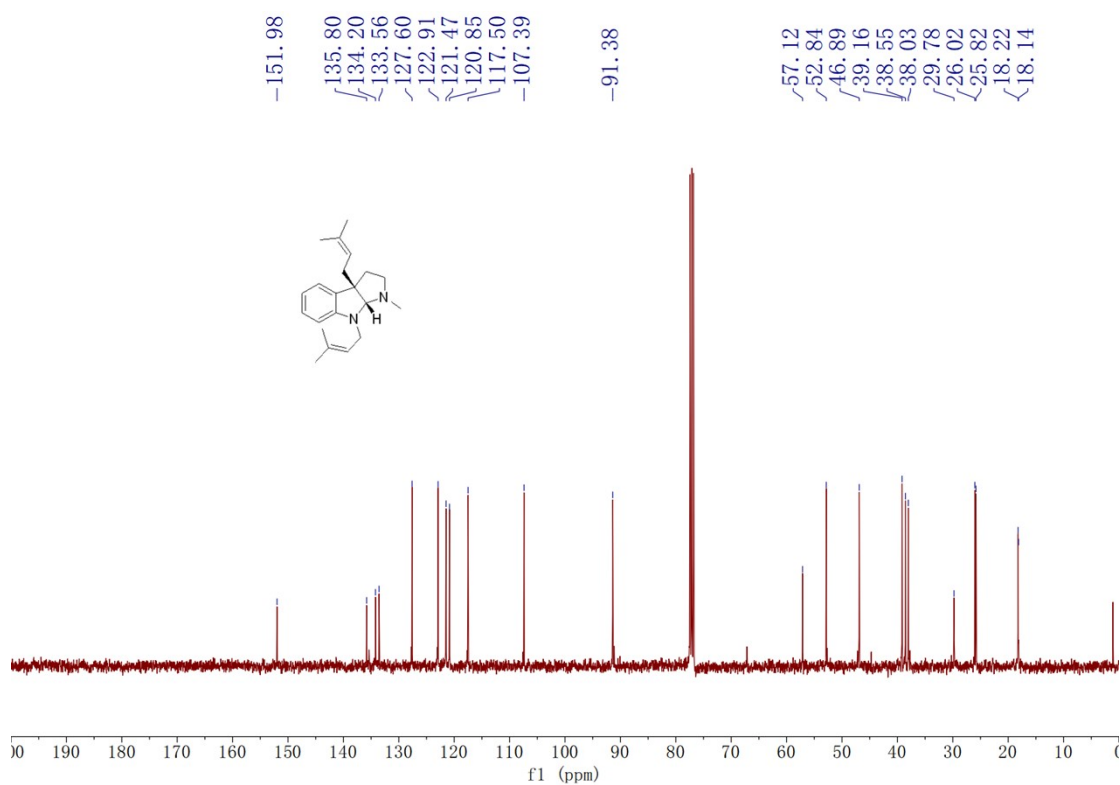
### <sup>13</sup>C NMR Spectrum of **30**



<sup>1</sup>H NMR Spectrum of (-)-debromoflustramine **B**

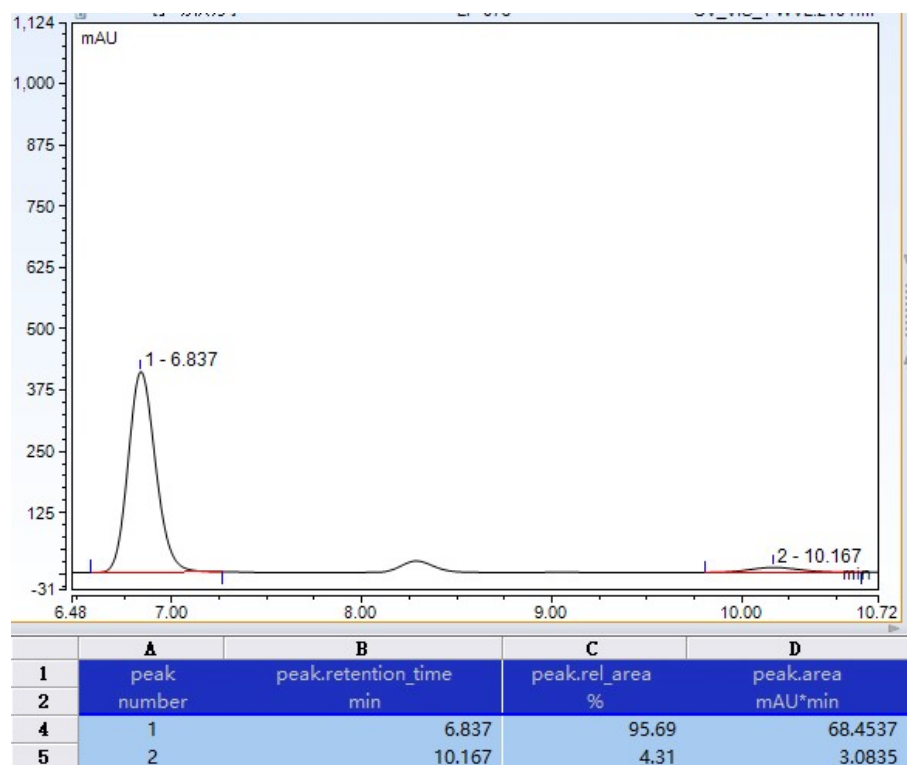
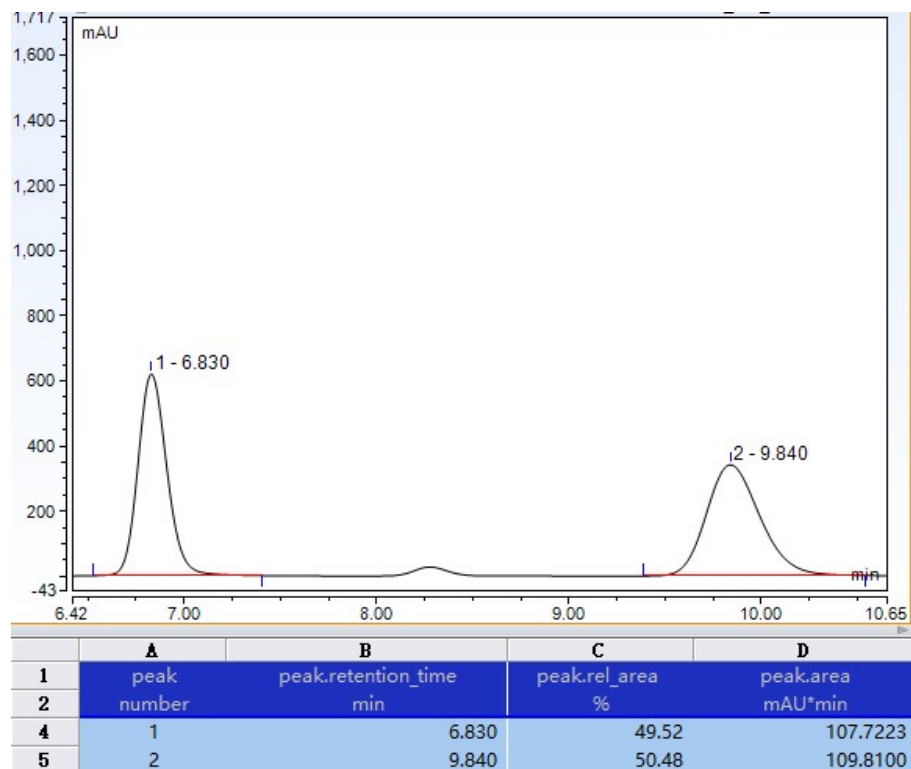


<sup>13</sup>C NMR Spectrum of (-)-debromoflustramine **B**

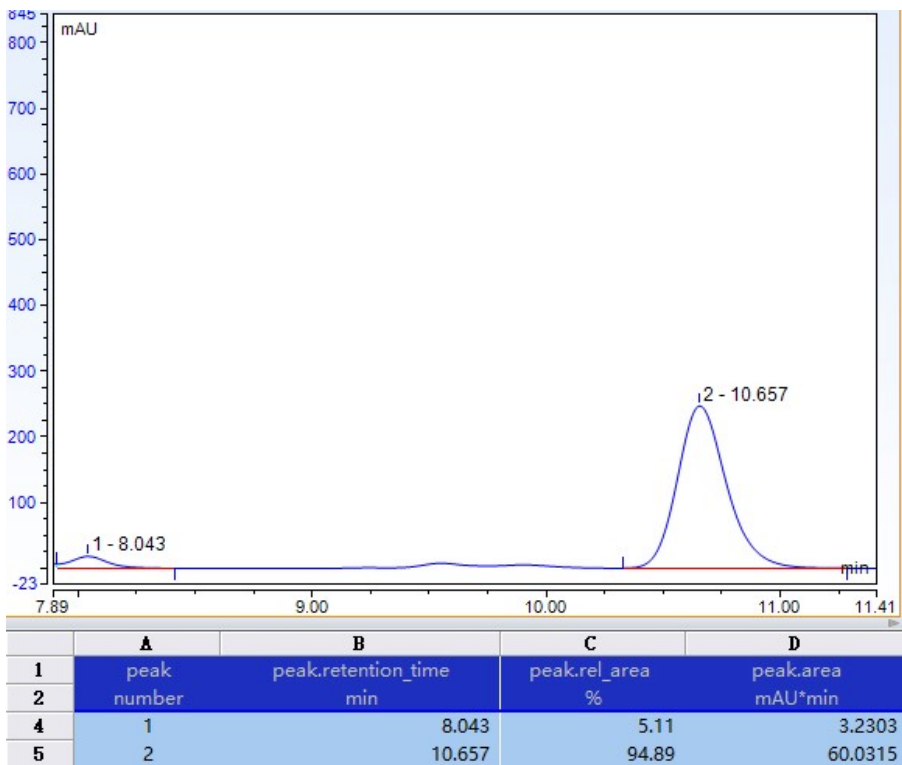
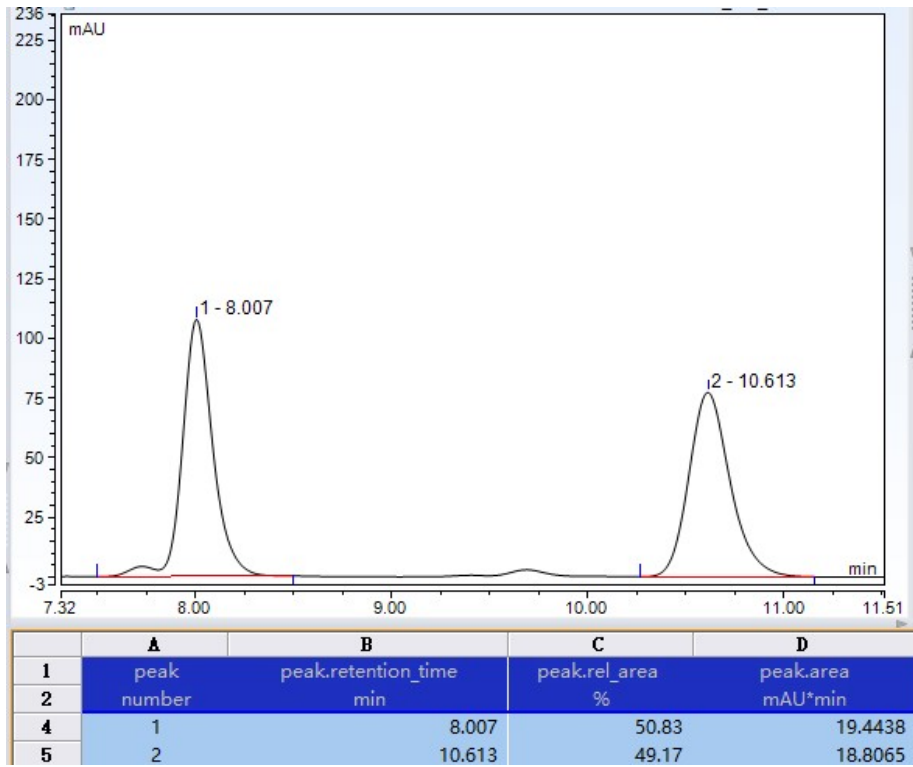


# HPLC spectra

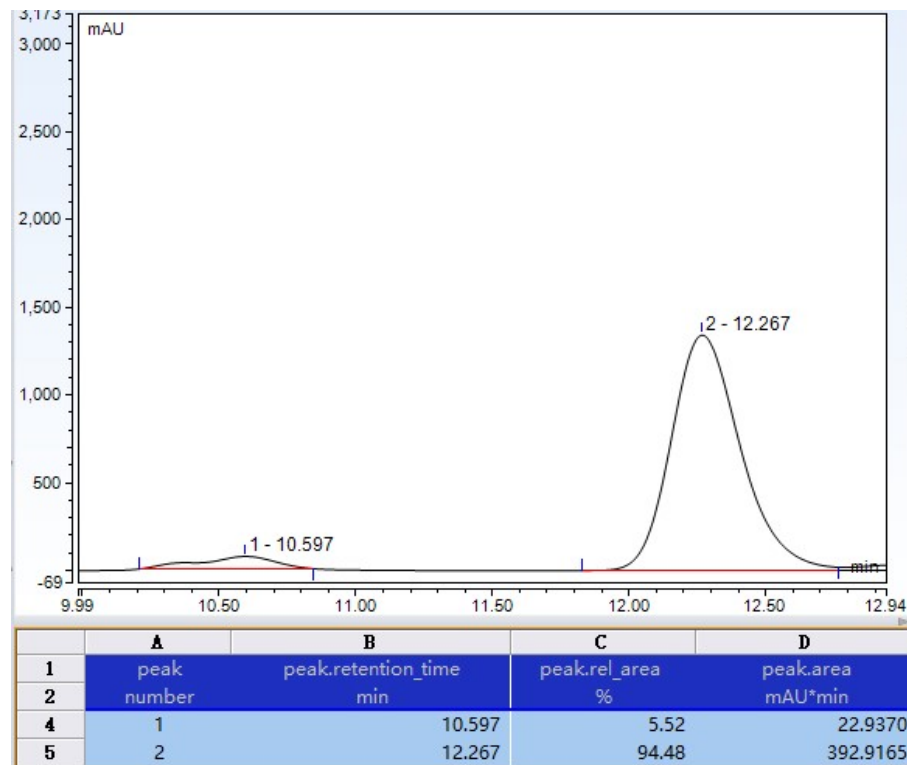
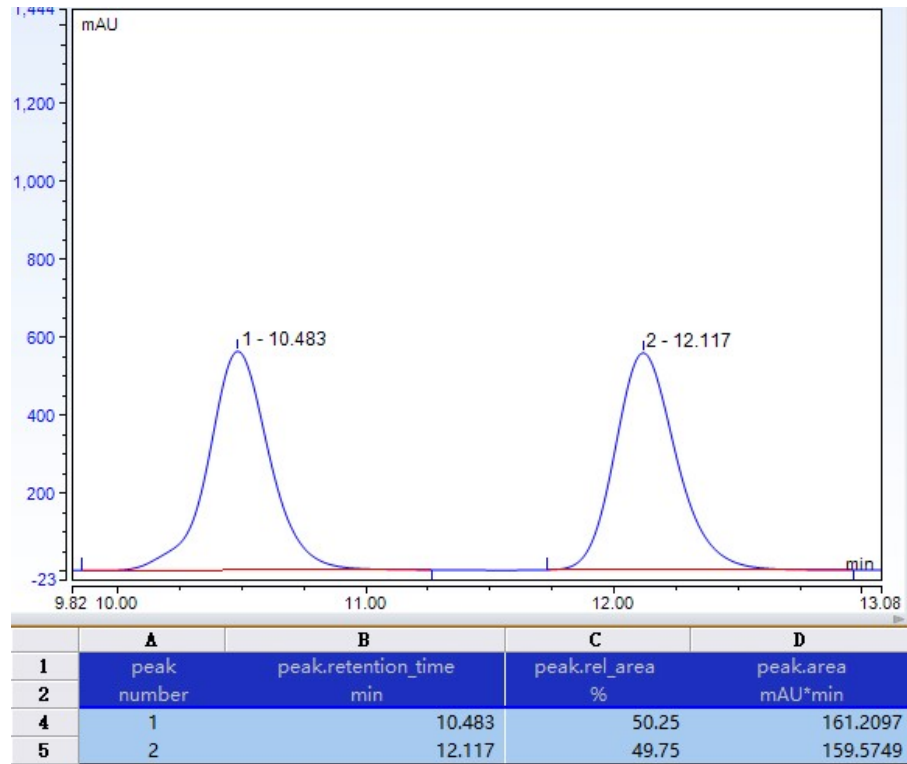
## HPLC analysis of 3a



### HPLC analysis of 3b

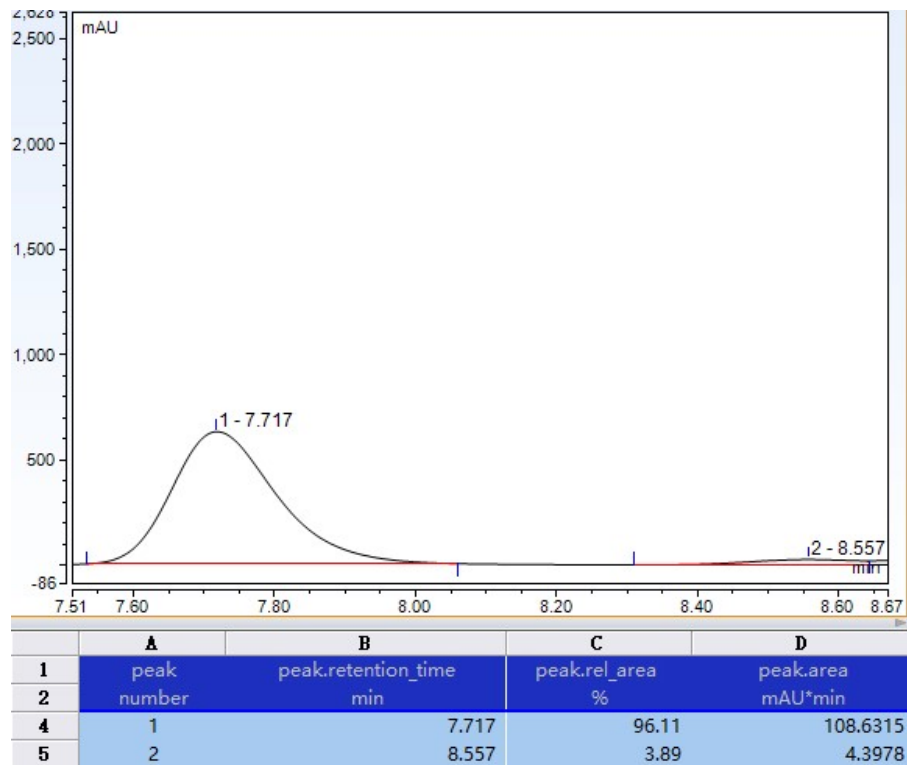
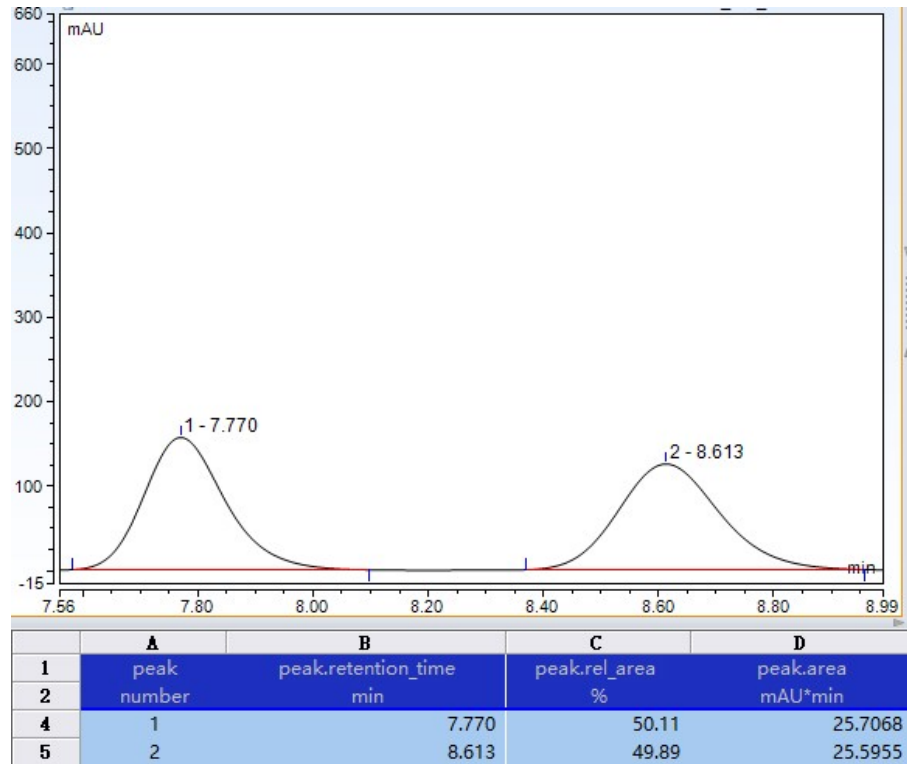


### HPLC analysis of 3c

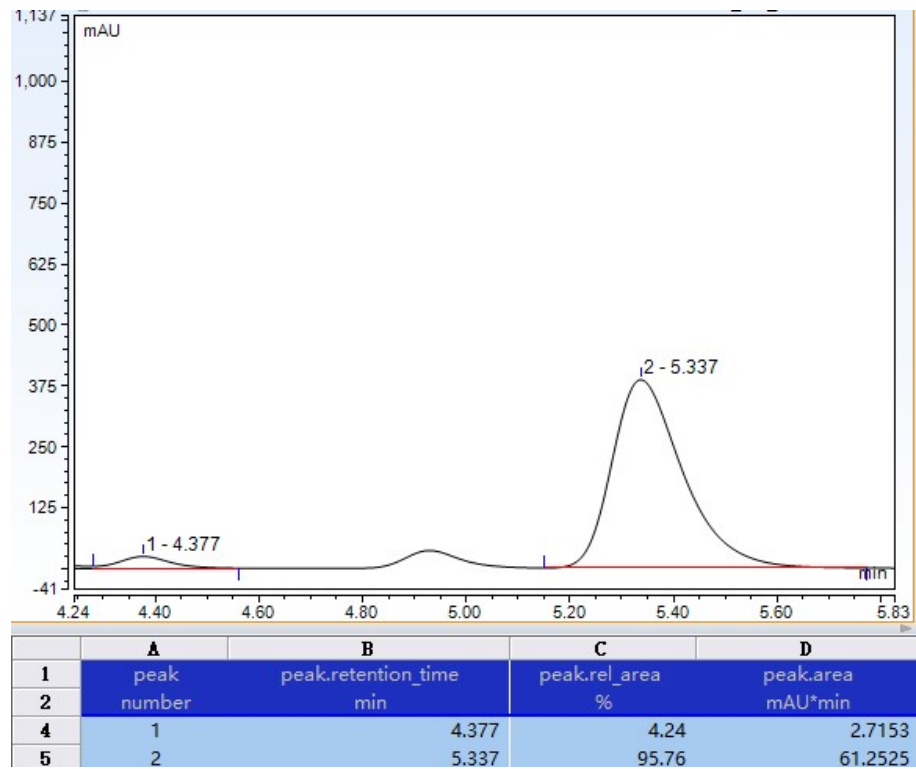
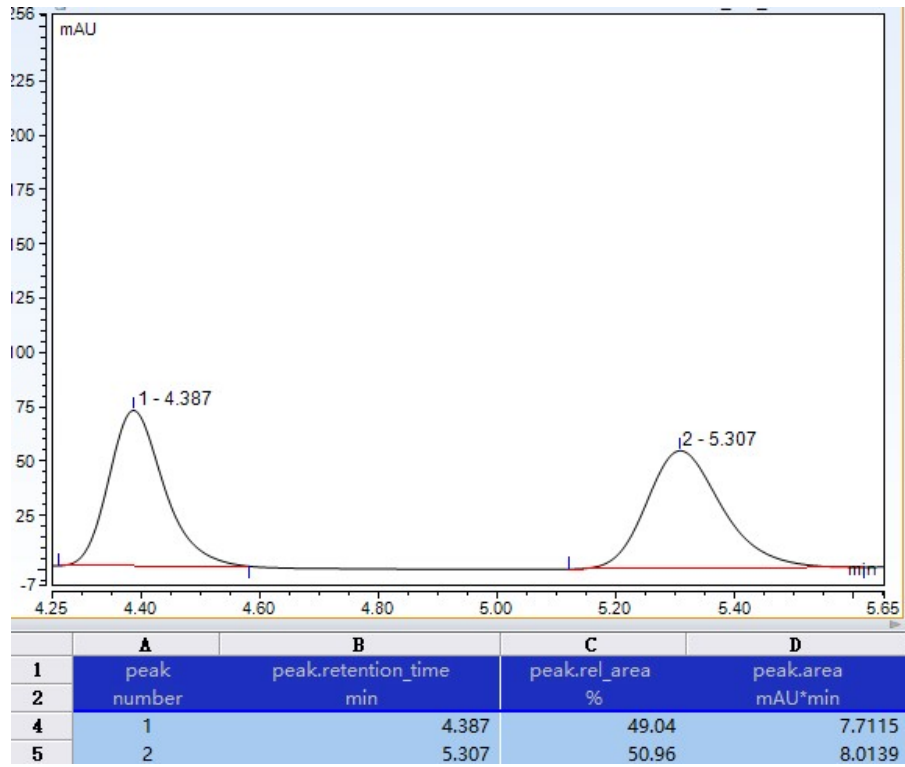




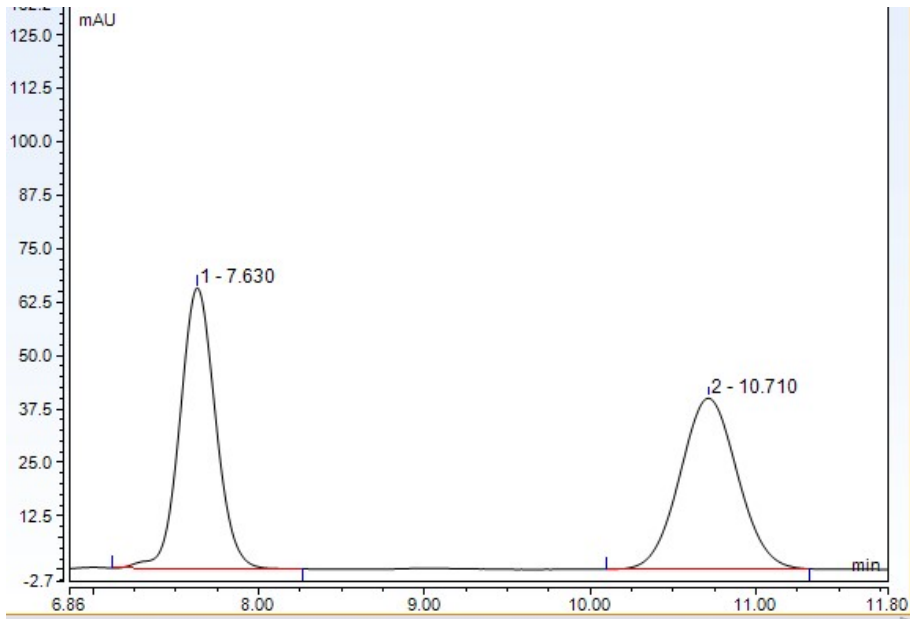
### HPLC analysis of 3d



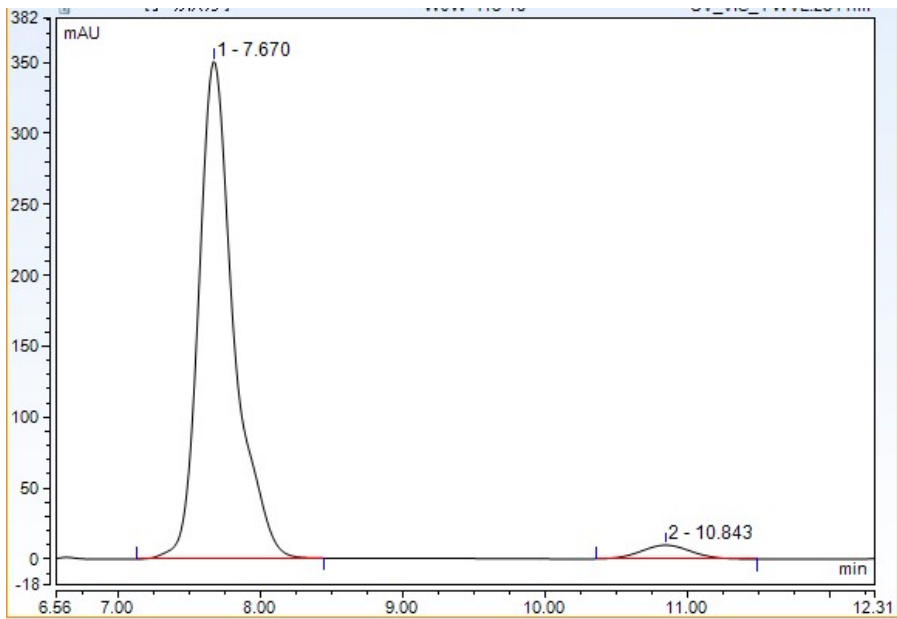
### HPLC analysis of 3e



### HPLC analysis of 3f

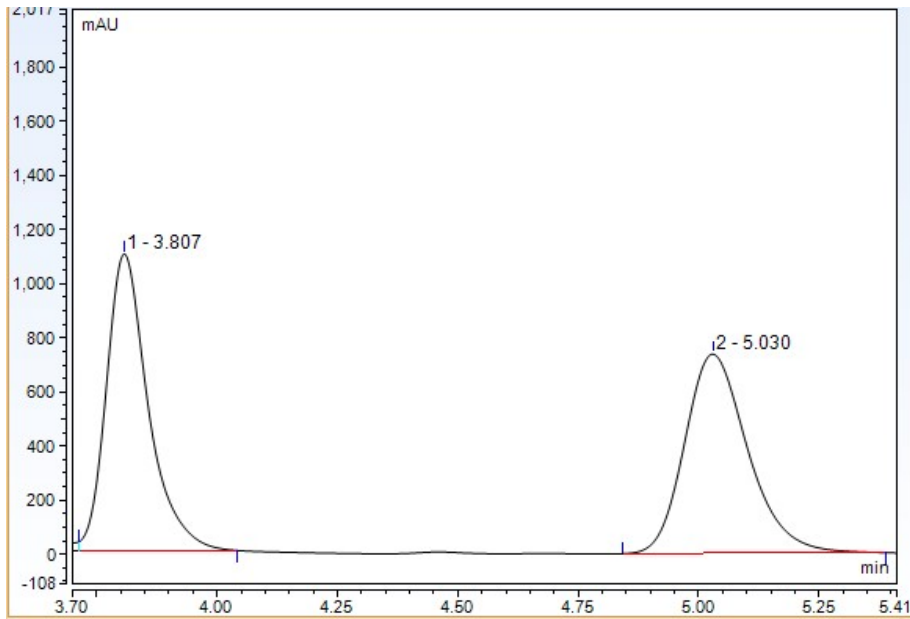


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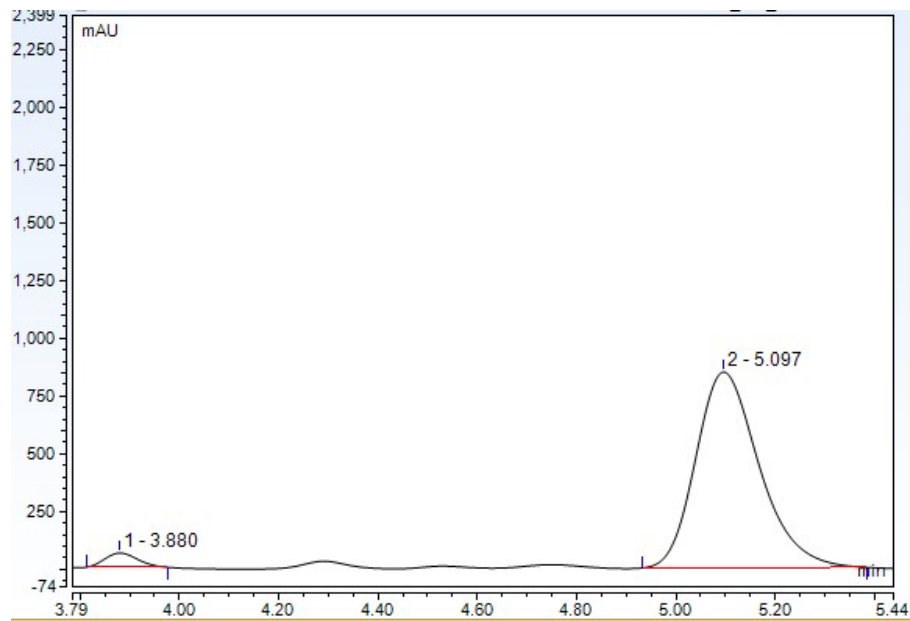


	A	B	C	D
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### HPLC analysis of 3g

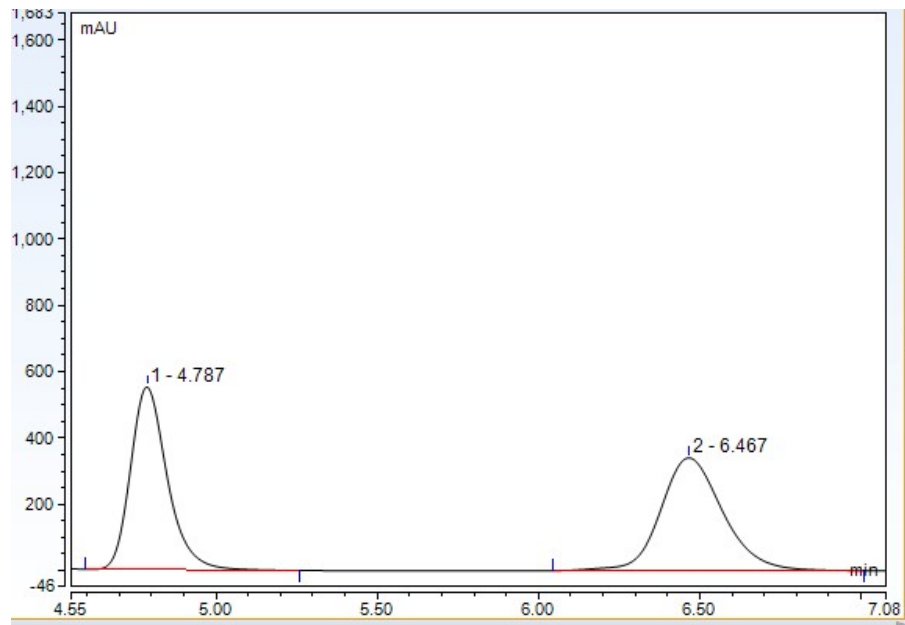


	A	B	C	D
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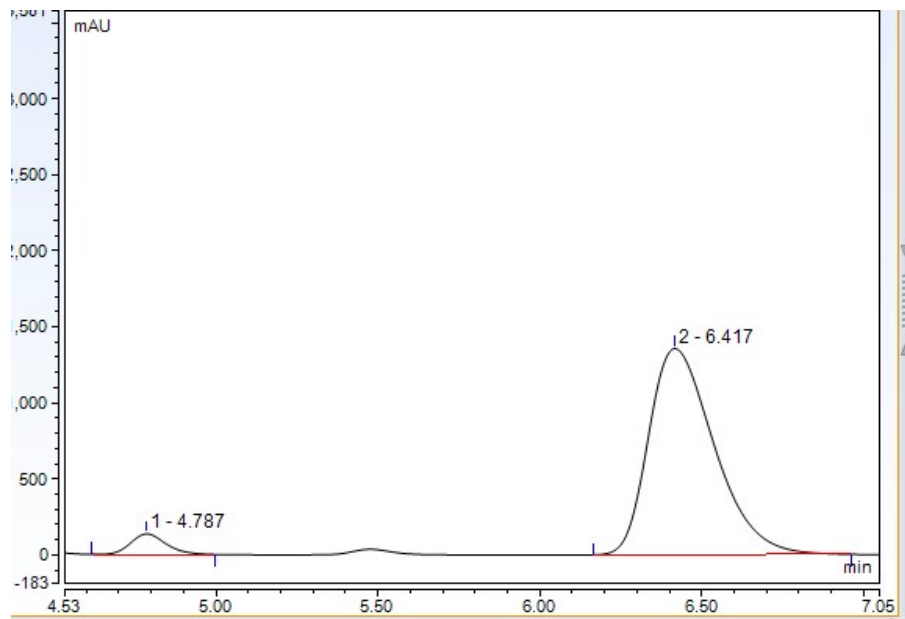


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### HPLC analysis of 3h

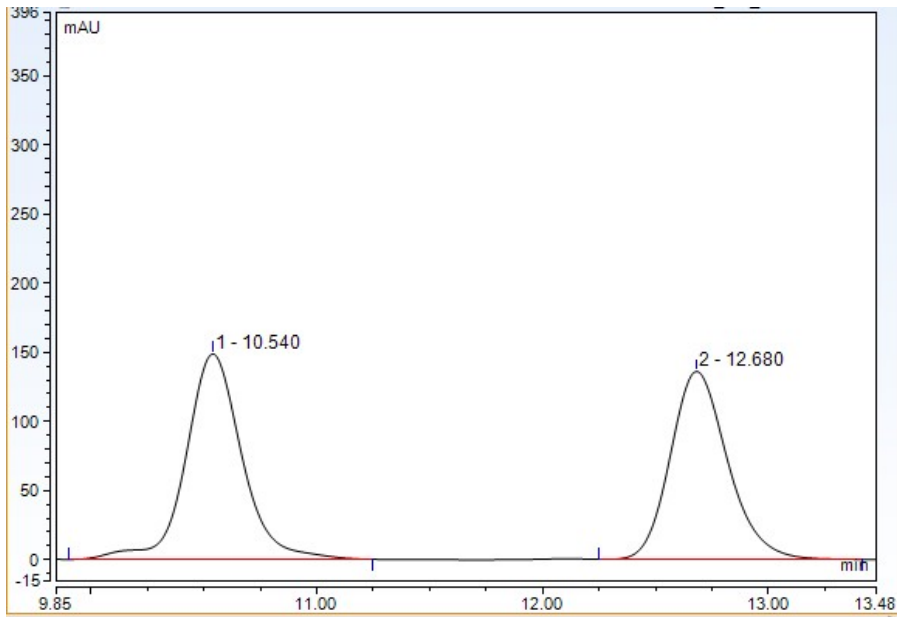


	A	B	C	D
1	peak number	peak.retention_time min	peak.rel_area %	peak.area mAU*min
4	1	4.787	48.75	72.7382
5	2	6.467	51.25	76.4693

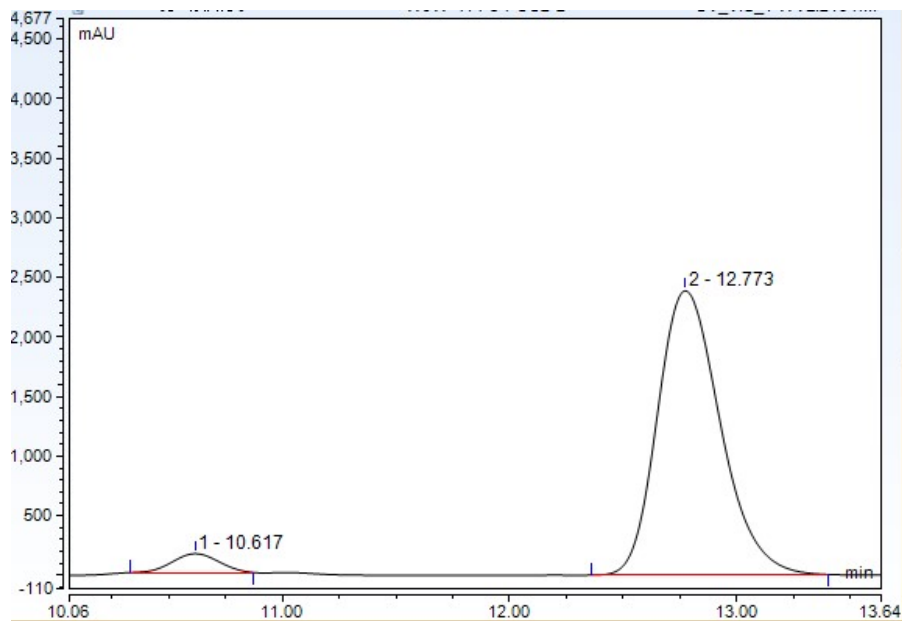


	A	B	C	D
1	peak number	peak.retention_time min	peak.rel_area %	peak.area mAU*min
4	1	4.787	5.08	17.0215
5	2	6.417	94.92	318.3660

### HPLC analysis of 3i

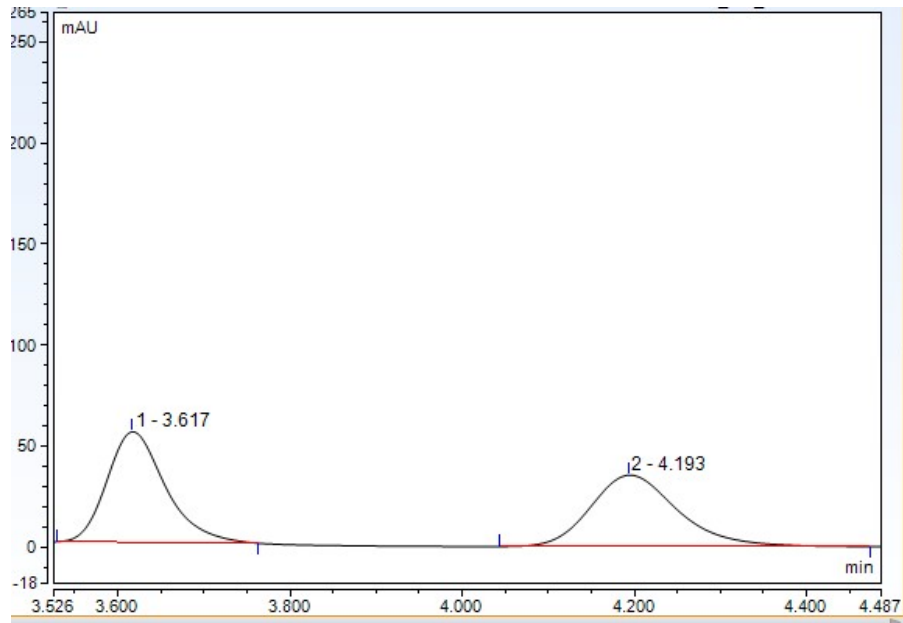


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	10.540	51.72	42.7486
5	2	12.680	48.28	39.8994

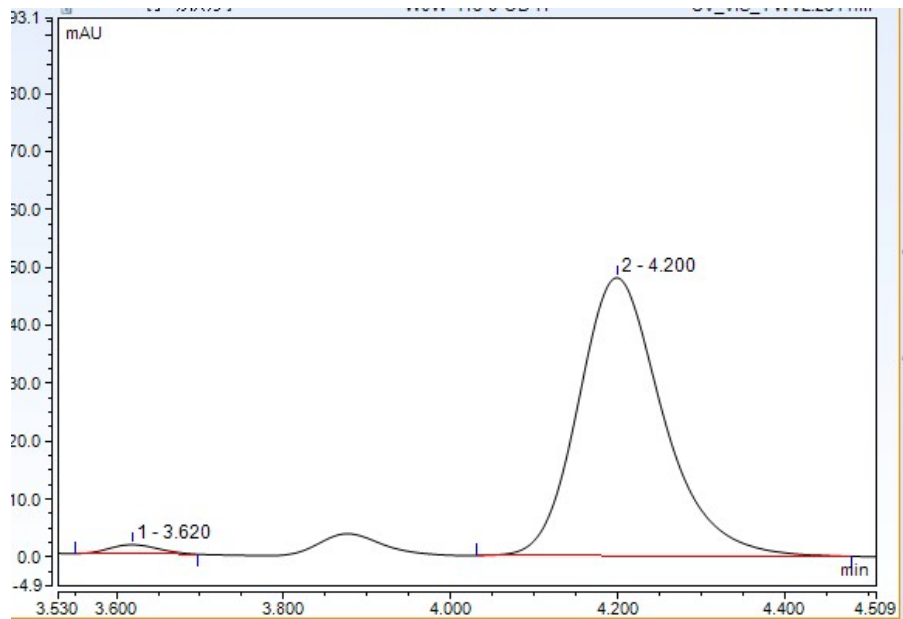


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	10.617	4.66	37.3002
5	2	12.773	95.34	762.6490

### HPLC analysis of 3j

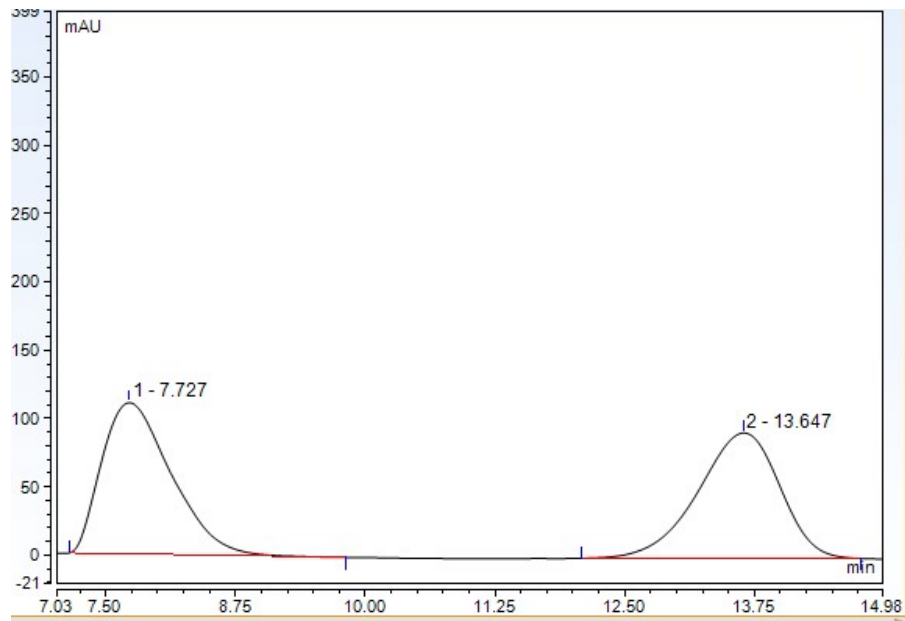


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	3.617	50.92	4.3017
5	2	4.193	49.08	4.1469

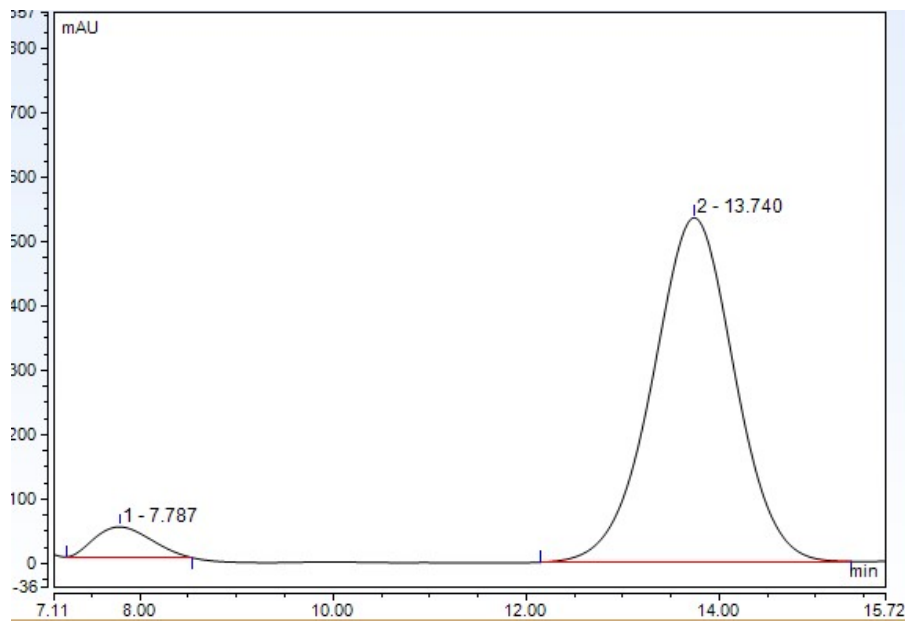


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	3.620	1.89	0.1082
5	2	4.200	98.11	5.6233

### HPLC analysis of 3k



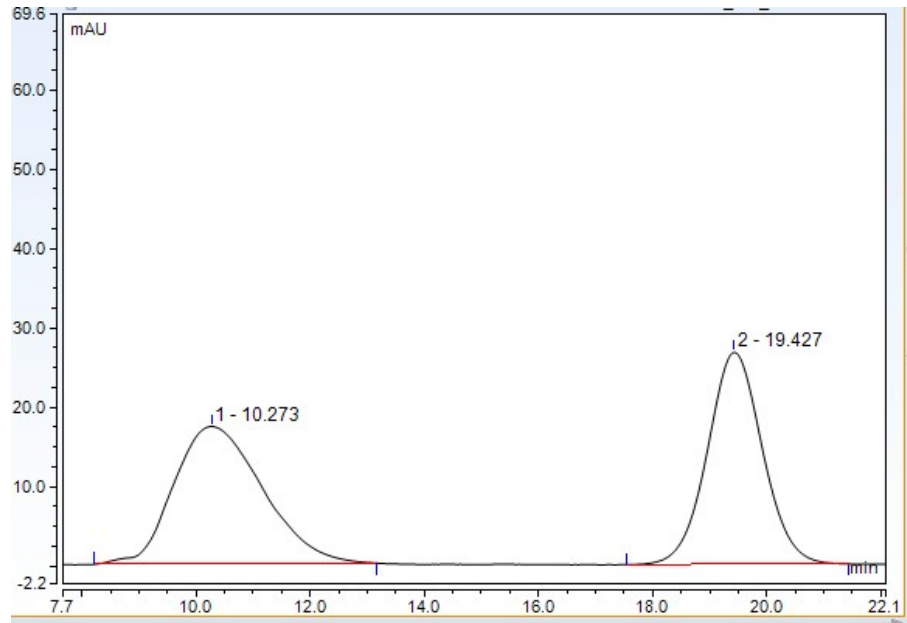
	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	7.727	50.54	85.9312
5	2	13.647	49.46	84.0859



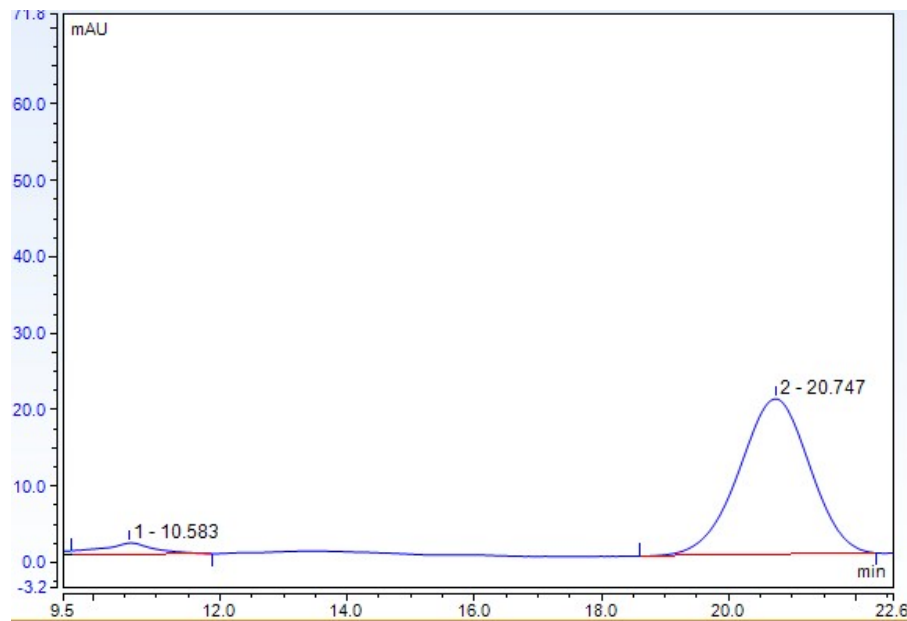
	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	7.787	5.70	31.8529
5	2	13.740	94.30	526.7954



### HPLC analysis of 31

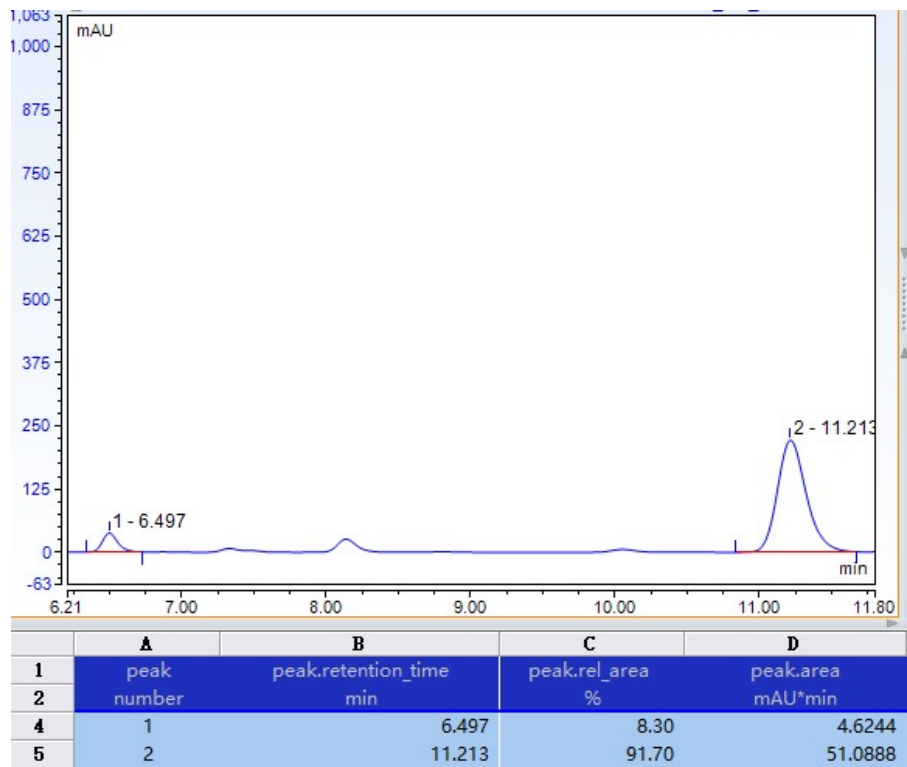
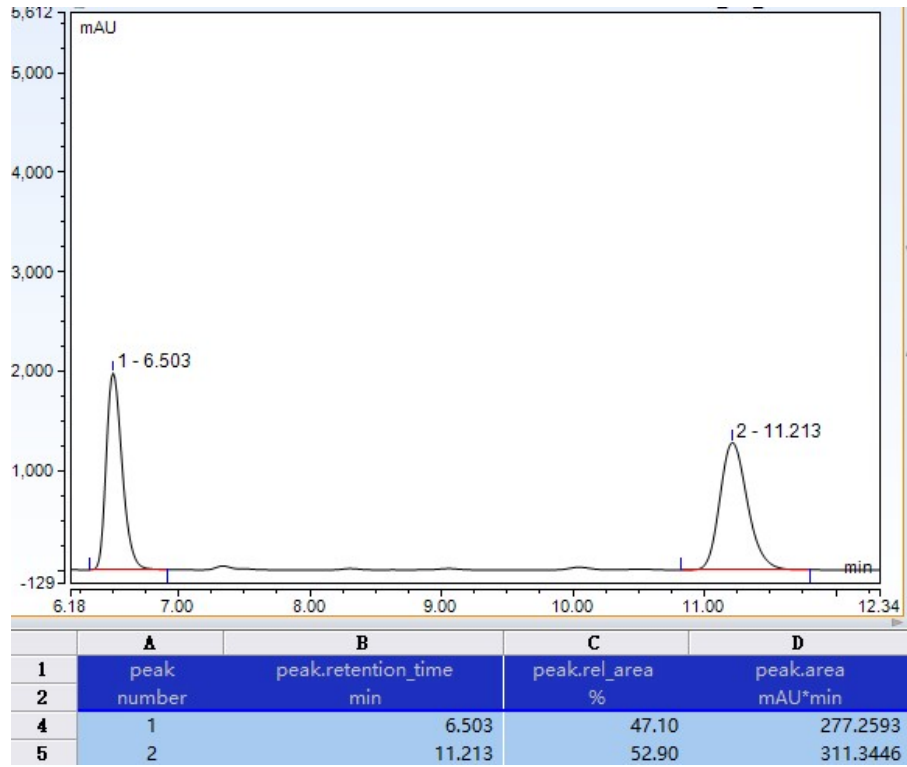


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	10.273	51.11	31.2117
5	2	19.427	48.89	29.8564

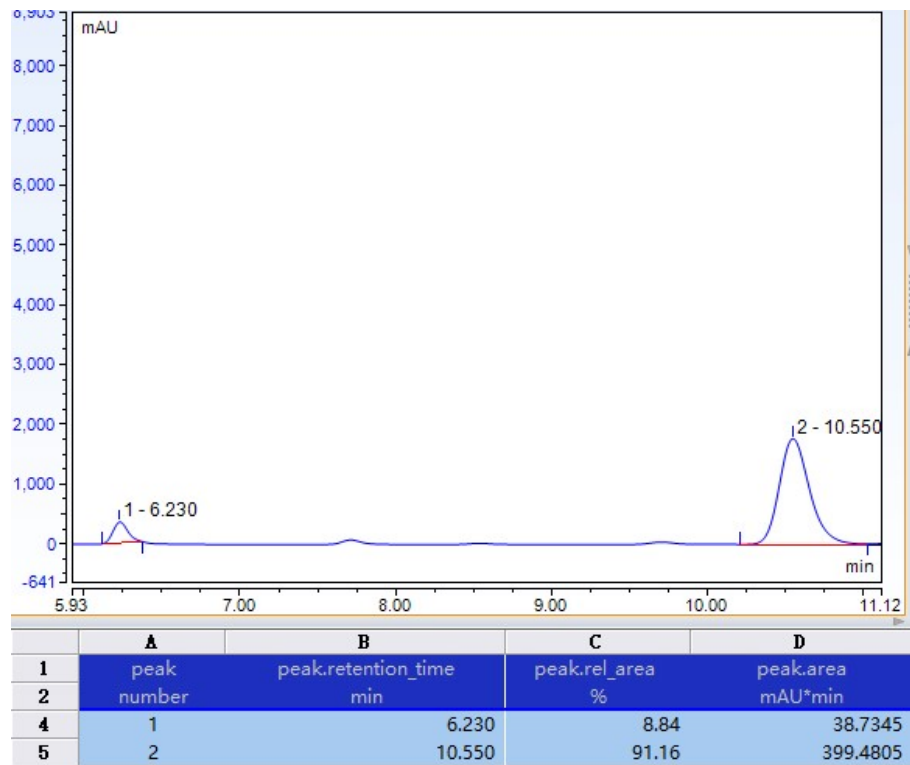
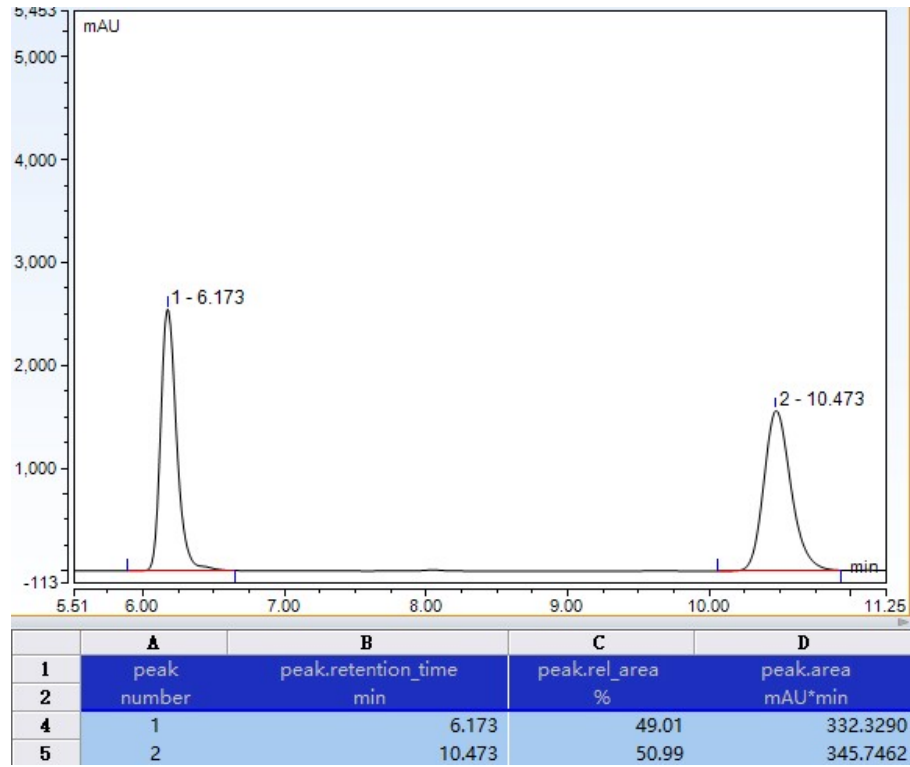


	A	B	C	D
1	peak	peak.retention_time	peak.rel_area	peak.area
2	number	min	%	mAU*min
4	1	10.583	5.16	1.4274
5	2	20.747	94.84	26.2333

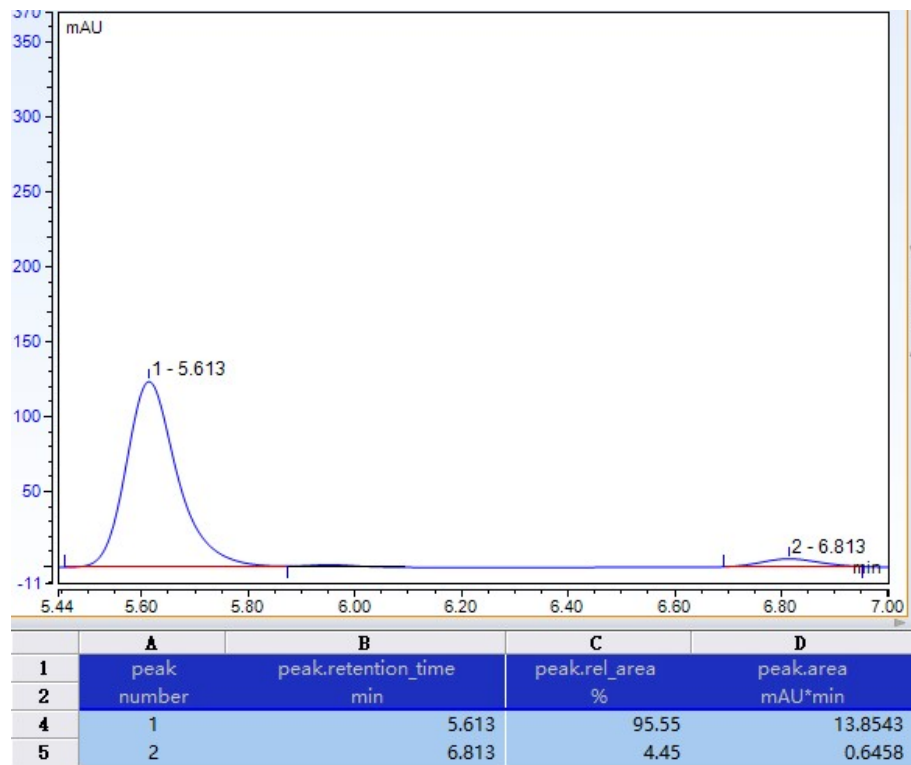
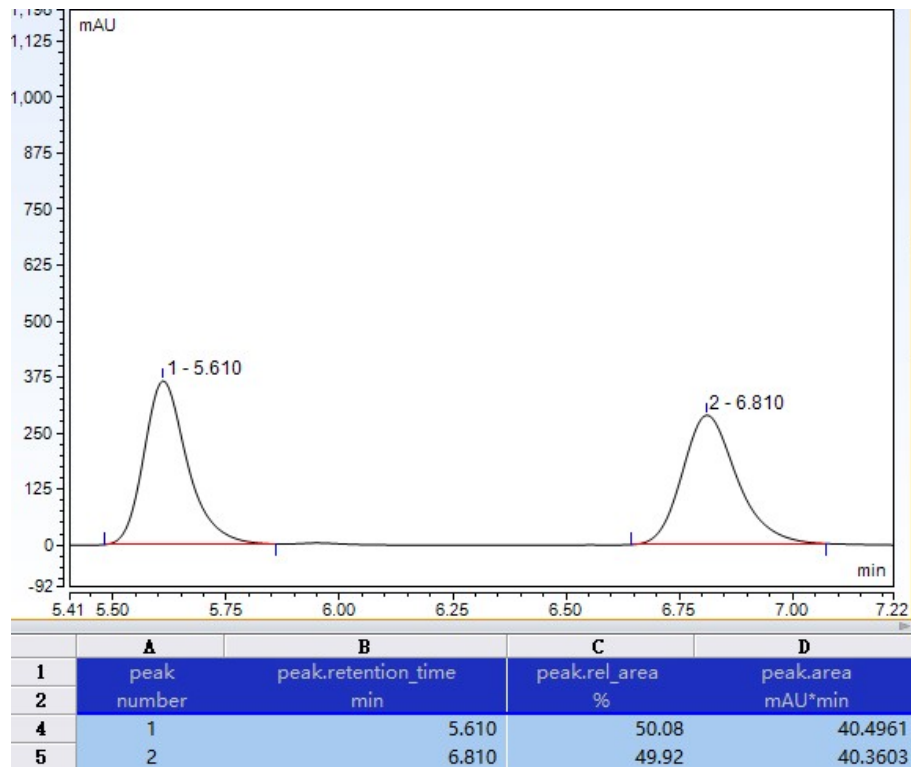
### HPLC analysis of 3m



### HPLC analysis of 3n



### HPLC analysis of **3o**



### HPLC analysis of (-)-debromoflustramine B

