

## Supporting Information

### The asymmetric vinylogous Mannich reaction of noncyclic dicyanoolefins catalyzed by a bifunctional thiourea-ammonium salt phase transfer catalyst

Yanhong Fang, Zhonglin Wei, Ying Wang<sup>b</sup>, Shuo Liu, Jungang Cao, Dapeng Liang, Yingjie Lin, and Haifeng Duan

<sup>a</sup>*Department of Organic Chemistry, College of Chemistry, Jilin University, 2699 Qianjin Street, Changchun 130012, China.*

<sup>b</sup>*Department of Ophthalmology, the second Hospital of Jilin University, Changchun, 130041, China*

E-mail: linyj@jlu.edu.cn; duanhf@jlu.edu.cn; Tel: 0431-85168398;

#### Table of Contents

<b>1. General Information</b> .....	1
<b>2. Starting materials</b> .....	1
<b>3. General procedure for preparation of catalyst 1g-1i.</b> .....	2
<b>3.1 Preparation of catalyst 1g-1i.</b> .....	2
<b>3.2 Characterization of catalysts 1g.</b> .....	3
<b>4. General procedure for vinylogous Mannich reaction of dicyanoalkylidenes with <math>\alpha</math>-amido sulfones and characterization of products 4a-4t, derivative 5a</b> .....	5
<b>5. NMR spectra of addition products 4a-4t and derivative 5a</b> .....	16
<b>6. HPLC traces of all compounds 4a-4t and derivative 5a</b> .....	37
<b>7. Reference</b> .....	58

## 1. General Information

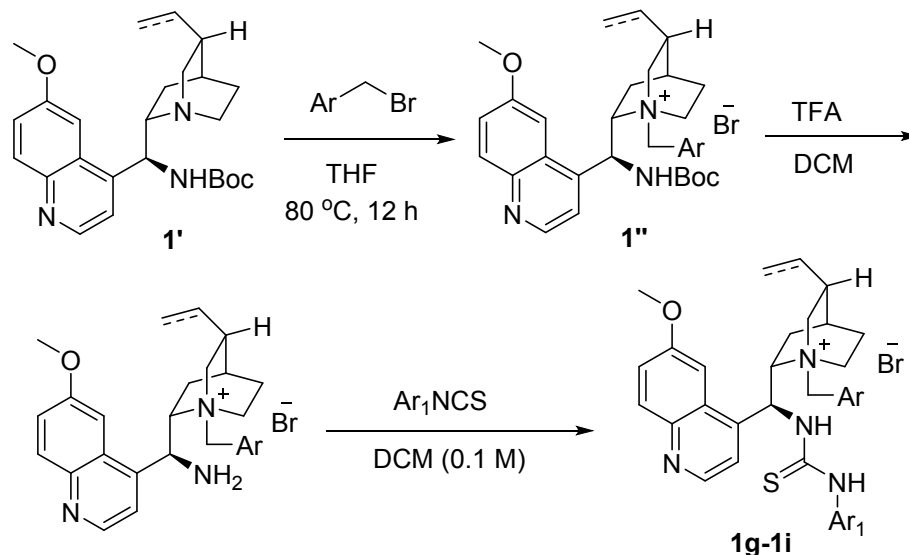
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All solvents were obtained from commercial sources and were purified according to standard procedures. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light. Purification of reaction products was carried out by flash column chromatography using silica gel (200-300 mesh).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian Mercury-300BB (300 MHz), a Bruker NMR Spectrometer (400 MHz) or a Bruker NMR Spectrometer (500 MHz). All chemical shifts ( $\delta$ ) were given in ppm. Chemical shifts ( $\delta$  ppm) are relative to the resonance of the deuterated solvent as the internal standard ( $\text{CDCl}_3$ ,  $\delta$  7.26 ppm for proton NMR,  $\delta$  77.16 ppm for carbon NMR;  $\text{CD}_3\text{OD-d}_4$ ,  $\delta$  3.31 ppm for proton NMR,  $\delta$  49.00 ppm for carbon NMR). Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass spectra were recorded on the Bruker Agilent 1290 MicroTOF Q II. Melting points were measured on a melting point apparatus and were uncorrected. The ee values determination was carried out using chiral HPLC (Waters) with Chiracel AD-H column, Chiracel OD-H column and Chiracel AS-H column. Optical rotations were measured on a Shanghai ShenGuang SGW-2 Polarimeter at  $\lambda = 589$  nm. Optical rotations are reported as follows:  $[\alpha]_{\text{D}}^{25}$  (c=g/100 mL, solvent).

## 2. Starting materials

Urea **1o** and compound **1i'** were prepared according to reported procedure.<sup>1, 2</sup> All  $\alpha,\alpha$ -dicyanoolefins were prepared according to literature procedure.<sup>3</sup> Differently substituted dicyanoolefins were also in accordance with similar synthetic method. All amidosulfones were prepared using reported procedures from corresponding aldehydes.<sup>4-6</sup> All phase-transfer catalysts **1a**<sup>7</sup>, **1b-1e**<sup>8, 9</sup> were synthesized according to procedures reported previously. *m*-xylene was dried over 4Å M.S.

### 3. General procedure for preparation of catalyst **1g-1i**.

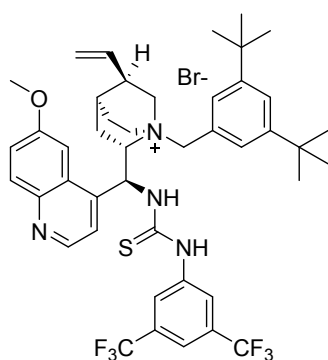
#### 3.1 Preparation of catalyst **1g-1i**.



Under argon protection, **1i''** (500 mg, 1.18 mmol, 1 eq.) was dissolved in 8 mL anhydrous THF, benzyl bromide ( 1.3 mmol, 1.1 eq.) was added, the mixture was heated to reflux, after 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (Et<sub>2</sub>O/MeOH = 10:1 to 8:1) to afford the desired product **1i''**.

Under argon protection, TFA (2.4 mL) was added to a solution of **1i''** (0.24 mmol) in 2.4 mL anhydrous CH<sub>2</sub>Cl<sub>2</sub> while stirring, the mixture was stirred overnight and concentrated to dryness under reduced pressure. The residue was redissolved in 10 mL CH<sub>2</sub>Cl<sub>2</sub>, the mixture was adjusted to pH 7-8 by aqueous ammonia and extracted by CH<sub>2</sub>Cl<sub>2</sub> (2×5 mL). The organic phases were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, evaporated under reduced pressure. The crude free amine was dried under vacuum and dissolved in 2.4 mL anhydrous CH<sub>2</sub>Cl<sub>2</sub>, Aryl isothiocyanate (0.26 mmol, 1.1 eq.) was added and the resulting mixture was stirred at rt overnight. After evaporation of the volatiles, the crude reaction mixture was purified by flash column chromatography (DCM/MeOH = 50:1 to 30:1) to give catalyst **1g-1i**.

### 3.2 Characterization of catalysts 1g.



Light yellow solid, 130 mg, 62 % yield for two steps.

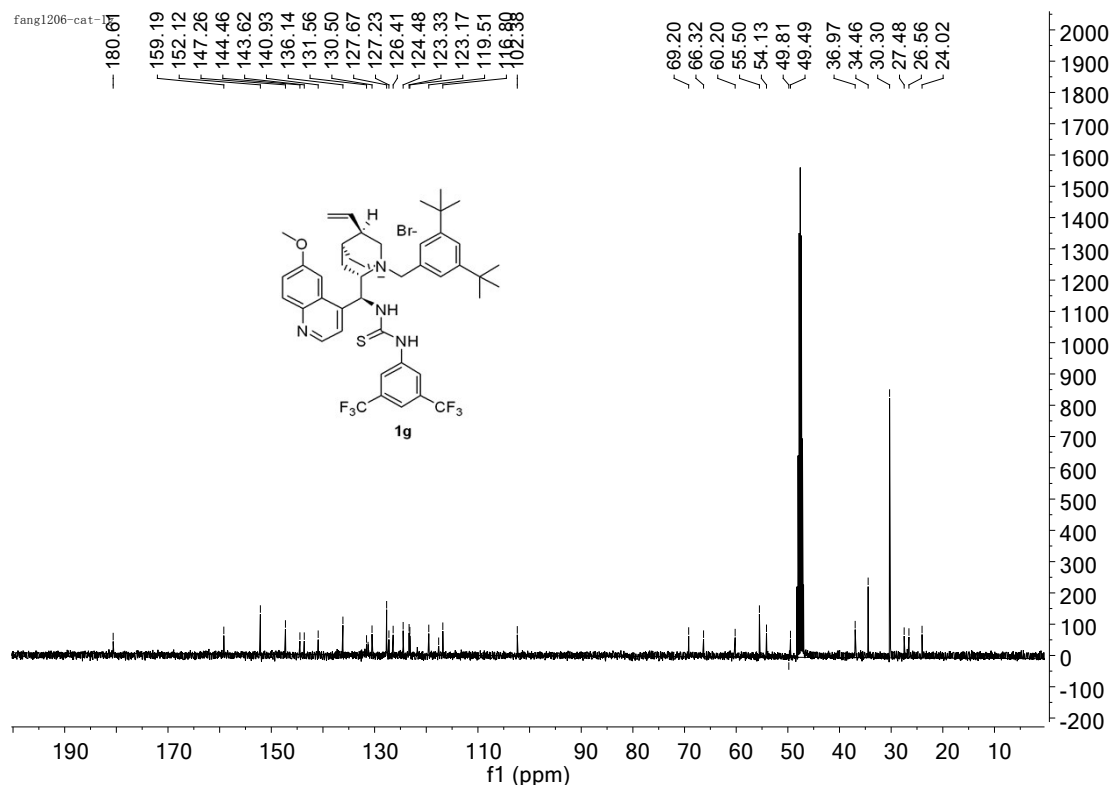
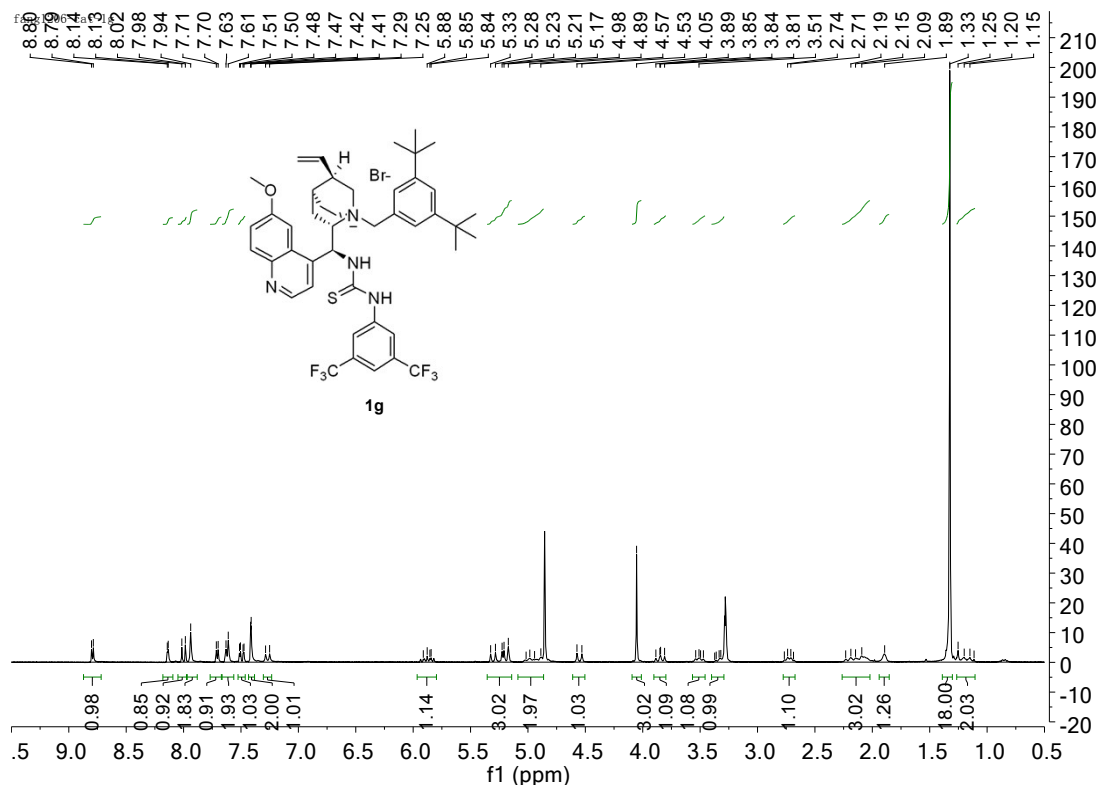
**m.p.** = 144-145°C,  $[\alpha]_D^{25} = -48.5$  (c = 0.5, CHCl<sub>3</sub>).

**<sup>1</sup>H NMR** (300 MHz, cd<sub>3</sub>od) δ 8.79 (d, J = 4.7 Hz, 1H), 8.14 (d, J = 2.5 Hz, 1H), 8.00 (d, J = 9.2 Hz, 1H), 7.94 (s, 2H), 7.71 (d, J = 4.8 Hz, 1H), 7.62 (d, J = 5.9 Hz, 2H), 7.49 (dd, J = 9.3, 2.5 Hz, 1H), 7.41 (d, J = 1.5 Hz, 2H),

7.27 (d, J = 10.6 Hz, 1H), 5.97 – 5.80 (m, 1H), 5.36 – 5.14 (m, 3H), 5.09 – 4.86 (m, 2H), 4.55 (d, J = 12.9 Hz, 1H), 4.05 (s, 3H), 3.90 – 3.80 (m, 1H), 3.57 – 3.46 (m, 1H), 3.40 – 3.29 (m, 1H), 2.73 (q, J = 16.2, 7.8 Hz, 1H), 2.26 – 2.02 (m, 3H), 1.89 (s, 1H), 1.33 (s, 18H), 1.26 – 1.11 (m, 2H).

**<sup>13</sup>C NMR** (101 MHz, MeOD) δ 180.61, 159.19, 152.12, 147.26, 144.46, 143.62, 140.93, 136.14, 131.56, 131.27, 130.50, 127.67, 127.23, 126.41, 124.48, 123.33, 123.17, 119.51, 117.60, 116.80, 102.38, 69.20, 66.32, 60.20, 55.50, 54.13, 49.81, 49.49, 36.97, 34.46, 30.30, 27.48, 26.56, 24.02.

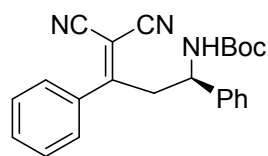
**HRMS** (ESI): calculated for C<sub>44</sub>H<sub>51</sub>F<sub>6</sub>N<sub>4</sub>OS [M-Br]<sup>+</sup>: 797.3682, found 797.3690.



#### 4. General procedure for vinylogous Mannich reaction of dicyanoalkylidenes with $\alpha$ -amido sulfones and characterization of products 4a-4t, derivative 5a

Dicyanoalkylidenes **2** (0.1 mmol),  $\alpha$ -amido sulfones **3** (0.11 mmol) and catalyst **1g** (8.8 mg, 0.01 mmol, 10 mol%) were dissolved in dry *m*-xylene (1 mL), the mixture was cooled to  $-30^{\circ}\text{C}$ , freshly grounded  $\text{K}_3\text{PO}_4$  (106 mg, 0.5 mmol, 5 eq.) was added in one portion, the resulting suspension was vigorously stirred for 48h, 1 mL sat. aq.  $\text{NH}_4\text{Cl}$  was added and the solution was allowed to warm to room temperature, the aqueous was extracted with EA (3 $\times$ 5 mL), then the organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA = 5:1).

##### tert-butyl (R)-(4,4-dicyano-1,3-diphenylbut-3-en-1-yl)carbamate (**4a**)



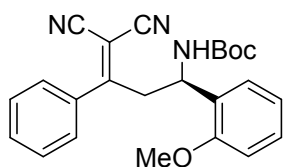
Colorless solid, 37.0 mg, 99% yield, **m.p.** =  $41\text{--}42^{\circ}\text{C}$ ,  $[\alpha]_{\text{D}}^{25} = +41.6$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ). The ee value was 91% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 6.414$  min.,  $t_{\text{minor}} = 5.264$  min).

**$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 – 7.31 (m, 5H), 7.30 – 7.17 (m, 3H), 7.16 – 6.92 (m, 2H), 4.77 (d,  $J = 4.9$  Hz, 1H), 4.53 (q,  $J = 7.5, 5.1$  Hz, 1H), 3.76 – 3.53 (m, 1H), 3.30 (dd,  $J = 13.5, 6.5$  Hz, 1H), 1.36 (s, 9H).

**$^{13}\text{C NMR}$**  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  176.13, 154.80, 139.05, 134.13, 132.29, 129.21, 129.17, 128.65, 128.00, 126.46, 112.51, 86.31, 80.26, 54.10, 44.29, 28.32.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{23}\text{N}_3\text{NaO}_2)^+$ : 396.1682, found 396.1681.

##### tert-butyl (R)-(4,4-dicyano-1-(2-methoxyphenyl)-3-phenylbut-3-en-1-yl)carbamate (**4b**)



Colorless solid, 39.9 mg, 99% yield, **m.p.** =  $40\text{--}41^{\circ}\text{C}$ ,  $[\alpha]_{\text{D}}^{25} = +55.3$  ( $c = 0.38$ ,  $\text{CHCl}_3$ ). The ee value was 88% (Chiralpak AS,

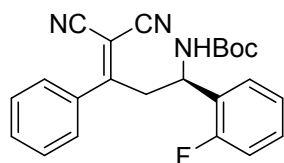
hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min, *t*<sub>major</sub> = 8.249 min., *t*<sub>minor</sub> = 10.802 min).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.73 – 7.37 (m, 5H), 7.35 – 7.26 (m, 1H), 7.06 – 6.80 (m, 2H), 6.799 – 6.713 (m, 1H), 5.70 (d, *J* = 9.7 Hz, 1H), 4.72 (q, *J* = 16.6, 8.0 Hz, 1H), 3.91 (s, 3H), 3.75 – 3.58 (m, 1H), 3.51 (dd, *J* = 13.1, 7.3 Hz, 1H), 1.44 (s, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 176.37, 157.08, 154.97, 144.31, 134.28, 132.22, 129.76, 129.08, 128.17, 126.46, 120.69, 112.88, 111.10, 85.90, 79.85, 55.33, 53.05, 42.81, 28.40.

HRMS (ESI): calculated for (C<sub>24</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>3</sub>)<sup>+</sup>: 426.1788, found 426.1789.

tert-butyl (R)-(4,4-dicyano-1-(2-fluorophenyl)-3-phenylbut-3-en-1-yl)carbamate (**4c**)



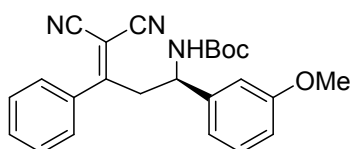
Colorless oil, 37.6 mg, 96% yield, [*a*]<sub>D</sub><sup>25</sup> = +13.9 (*c* = 0.49, CHCl<sub>3</sub>). The ee value was 95% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min, *t*<sub>major</sub> = 7.360 min., *t*<sub>minor</sub> = 6.236 min).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.65 – 7.41 (m, 5H), 7.36 – 7.27 (m, 1H), 7.17 – 6.98 (m, 3H), 5.14 (d, *J* = 9.0 Hz, 1H), 4.86 (q, *J* = 15.2, 8.1 Hz, 1H), 3.71 – 3.54 (m, 1H), 3.42 (dd, *J* = 13.6, 6.5 Hz, 1H), 1.43 (s, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 175.51, 161.78, 154.69, 134.04, 132.39, 130.27 (d, *J* = 8.5 Hz), 129.24, 128.55, 128.01, 124.70 (d, *J* = 3.4 Hz), 116.32 (d, *J* = 21.2 Hz), 112.53, 104.21, 80.40, 77.24, 50.35, 43.51, 28.29.

HRMS (ESI): calculated for (C<sub>23</sub>H<sub>22</sub>FN<sub>3</sub>NaO<sub>2</sub>)<sup>+</sup>: 414.1588, found 414.1583.

tert-butyl (R)-(4,4-dicyano-1-(3-methoxyphenyl)-3-phenylbut-3-en-1-yl)carbamate (**4d**)



Colorless solid, 39.1 mg, 97% yield, *m.p.* = 42-43 °C, [*a*]<sub>D</sub><sup>25</sup> = +46.8 (*c* = 0.53, CHCl<sub>3</sub>). The ee value was

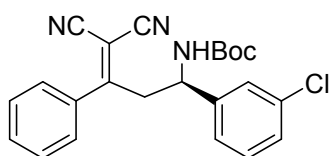
87% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 7.689$  min.,  $t_{\text{minor}} = 6.252$  min).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 – 7.38 (m, 5H), 7.357 – 7.212 (m, 1H), 6.946 – 6.883 (m, 1H), 6.72 (d,  $J = 7.0$  Hz, 1H), 6.67 (s, 1H), 4.90 (d,  $J = 6.3$  Hz, 1H), 4.59 (d,  $J = 5.7$  Hz, 1H), 3.81 (s, 3H), 3.78 – 3.59 (m, 1H), 3.41 (dd,  $J = 13.3, 7.0$  Hz, 1H), 1.47 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  176.05, 160.04, 154.83, 140.51, 134.10, 132.31, 130.28, 129.21, 128.04, 118.56, 114.21, 112.55, 112.06, 86.32, 80.27, 55.31, 54.10, 44.18, 28.32.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{25}\text{N}_3\text{NaO}_3)^+$ : 426.1788, found 426.1786.

tert-butyl (R)-(1-(3-chlorophenyl)-4,4-dicyano-3-phenylbut-3-en-1-yl)carbamate (**4e**)



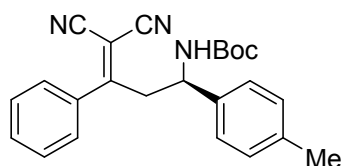
Colorless solid, 39.2 mg, 96% yield, **m.p.** = 40-41 °C,  $[\alpha]_{\text{D}}^{25} = +28.8$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ). The ee value was 93% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 6.443$  min.,  $t_{\text{minor}} = 5.542$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{cdCl}_3$ )  $\delta$  7.65 – 7.50 (m, 2H), 7.480 – 7.428 (m, 2H), 7.338 – 7.272 (m, 3H), 7.115 – 6.982 (m, 2H), 4.82 (d,  $J = 6.2$  Hz, 1H), 4.61 (q,  $J = 11.8, 4.3$  Hz, 1H), 3.92 – 3.44 (m, 1H), 3.35 (dd,  $J = 13.5, 6.6$  Hz, 1H), 1.44 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  178.48, 154.68, 141.35, 134.95, 134.00, 132.44, 130.48, 129.32, 128.74, 127.94, 126.78, 124.46, 112.37, 86.87, 80.54, 53.52, 44.19, 28.28.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{22}\text{ClN}_3\text{NaO}_2)^+$ : 430.1293, found 430.1293.

tert-butyl (R)-(4,4-dicyano-3-phenyl-1-(*p*-tolyl)but-3-en-1-yl)carbamate (**4f**)



Colorless solid, 36.4 mg, 94% yield, **m.p.** = 41-42 °C,  $[\alpha]_{\text{D}}^{25} = +59.2$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ). The ee value was 93%



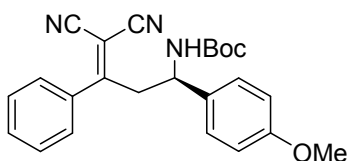
(Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 6.542$  min.,  $t_{\text{minor}} = 5.675$  min).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 – 7.52 (m, 3H), 7.503 – 7.452 (m, 2H), 7.17 (d,  $J = 7.9$  Hz, 2H), 7.02 (d,  $J = 7.9$  Hz, 2H), 4.84 (d,  $J = 6.5$  Hz, 1H), 4.57 (q,  $J = 14.4, 7.1$  Hz, 1H), 3.80 – 3.67 (m, 1H), 3.40 (dd,  $J = 13.6, 7.3$  Hz, 1H), 2.38 (s, 3H), 1.46 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  175.89, 154.79, 138.52, 136.01, 134.70, 134.11, 132.24, 129.80, 129.18, 128.01, 126.38, 86.21, 80.15, 53.83, 44.24, 28.32, 21.14.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{25}\text{N}_3\text{NaO}_2)^+$ : 410.1839, found 410.1838.

tert-butyl (R)-(4,4-dicyano-1-(4-methoxyphenyl)-3-phenylbut-3-en-1-yl)carbamate(**4g**)



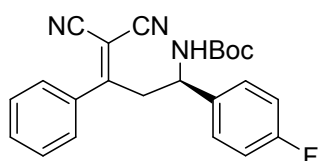
Colorless solid, 39.1 mg, 97% yield, **m.p.** = 43–44 °C,  
 $[\alpha]_{\text{D}}^{25} = +30.6$  ( $c = 0.51$ ,  $\text{CHCl}_3$ ). The ee value was 88%  
(Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 7.155$  min.,  $t_{\text{minor}} = 6.577$  min).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63 – 7.45 (m, 4H), 7.32 – 7.24 (m, 1H), 6.93 – 6.84 (m, 1H), 6.72 (d,  $J = 7.6$  Hz, 1H), 6.68 – 6.63 (m, 1H), 4.90 (d,  $J = 7.4$  Hz, 1H), 4.59 (q, 1H), 3.81 (s, 3H), 3.78 – 3.60 (m, 1H), 3.41 (dd,  $J = 13.6, 7.2$  Hz, 1H), 1.46 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  176.16, 160.04, 140.52, 134.10, 132.31, 130.28, 129.21, 128.04, 118.56, 114.21, 112.05, 86.34, 80.24, 55.31, 54.13, 44.18, 28.32.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{25}\text{N}_3\text{NaO}_3)^+$ : 426.1788, found 426.1788.

tert-butyl (R)-(4,4-dicyano-1-(4-fluorophenyl)-3-phenylbut-3-en-1-yl)carbamate(**4h**)



Colorless solid, 36 mg, 92% yield, **m.p.** = 42–43 °C,  
 $[\alpha]_{\text{D}}^{25} = +31.8$  ( $c = 0.44$ ,  $\text{CHCl}_3$ ). The ee value was 93%  
(Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1

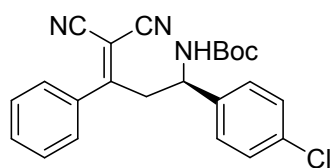
mL/min,  $t_{\text{major}} = 10.542$  min.,  $t_{\text{minor}} = 7.176$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63 – 7.49 (m, 3H), 7.486 – 7.384 (m, 2H), 7.19 – 7.08 (m, 2H), 7.07 – 6.95 (m, 2H), 4.79 (d,  $J = 7.5$  Hz, 1H), 4.59 (q,  $J = 13.8, 6.8$  Hz, 1H), 3.76 – 3.62 (m, 1H), 3.36 (dd,  $J = 13.6, 7.2$  Hz, 1H), 1.43 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  175.76, 163.79, 161.32, 155.49 (d,  $J = 17.7$  Hz), 134.00, 132.40, 129.30, 128.26 (d,  $J = 8.5$  Hz), 127.94, 116.10 (d,  $J = 21.6$  Hz), 112.40, 86.56, 80.43, 53.41, 44.15, 28.29.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{22}\text{FN}_3\text{NaO}_2)^+$ : 414.1588, found 414.1588.

tert-butyl (R)-(1-(4-chlorophenyl)-4,4-dicyano-3-phenylbut-3-en-1-yl)carbamate (**4i**)



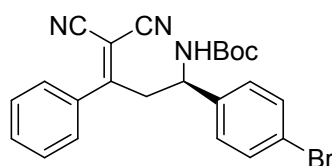
Colorless solid, 40.4 mg, 99% yield, **m.p.** = 45-46 °C,  $[\alpha]_{\text{D}}^{25} = +37.1$  ( $c = 0.48$ ,  $\text{CHCl}_3$ ). The ee value was 97% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 8.245$  min.,  $t_{\text{minor}} = 5.700$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.65 – 7.50 (m, 3H), 7.50 – 7.40 (m, 2H), 7.38 – 7.28 (m, 2H), 7.13 – 7.01 (m, 2H), 4.80 (d,  $J = 7.1$  Hz, 1H), 4.60 (q, 1H), 3.77 – 3.59 (m, 1H), 3.36 (dd,  $J = 13.7, 7.0$  Hz, 1H), 1.44 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  175.59, 154.68, 137.68, 134.50, 133.96, 132.44, 129.35, 129.33, 127.93, 127.85, 112.36, 86.51, 80.51, 53.42, 44.03, 28.29.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{22}\text{ClN}_3\text{NaO}_2)^+$ : 430.1293, found 430.1293.

tert-butyl (R)-(1-(4-bromophenyl)-4,4-dicyano-3-phenylbut-3-en-1-yl)carbamate (**4j**)



Colorless solid, 39.8 mg, 88% yield, **m.p.** = 42-43°C,  $[\alpha]_{\text{D}}^{25} = +36.3$  ( $c = 0.49$ ,  $\text{CHCl}_3$ ). The ee value was 95% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1

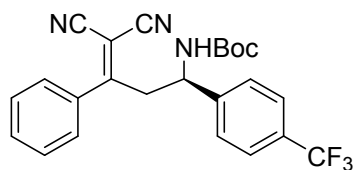
mL/min,  $t_{\text{major}} = 9.731$  min.,  $t_{\text{minor}} = 6.549$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 – 7.50 (m, 3H), 7.50 – 7.35 (m, 4H), 6.99 (d,  $J = 8.3$  Hz, 2H), 4.80 (d,  $J = 21.4$  Hz, 1H), 4.55 (q, 1H), 3.75 – 3.53 (m, 1H), 3.34 (dd,  $J = 13.6$ , 7.0 Hz, 1H), 1.42 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  175.61, 154.68, 138.24, 133.97, 132.44, 132.29, 129.33, 128.16, 127.93, 122.57, 112.36, 86.56, 80.50, 53.49, 43.99, 28.29.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{22}\text{BrN}_3\text{NaO}_2)^+$ : 474.0788, found 474.0787.

tert-butyl(R)-(4,4-dicyano-3-phenyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)carbamate (**4k**)



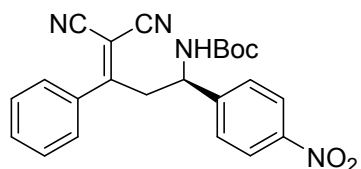
Colorless solid, 43.3 mg, 98% yield, **m.p.** = 58-59°C,  $[\alpha]_{\text{D}}^{25} = +22.9$  ( $c = 0.48$ ,  $\text{CHCl}_3$ ). The ee value was 97% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 9.000$  min.,  $t_{\text{minor}} = 6.567$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 – 7.50 (m, 5H), 7.50 – 7.43 (m, 2H), 7.31 – 7.26 (m, 2H), 4.84 (d,  $J = 6.8$  Hz, 1H), 4.72 (q,  $J = 13.4$ , 6.4 Hz, 1H), 3.72 – 3.58 (m, 1H), 3.38 (dd,  $J = 13.7$ , 6.4 Hz, 1H), 1.43 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  182.46, 154.66, 143.41, 136.83, 133.95, 132.50, 129.39, 127.87, 126.84, 126.15 (q,  $J = 7.2$ , 3.9 Hz), 112.30, 86.86, 80.84, 53.56, 44.05, 28.26.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{22}\text{F}_3\text{N}_3\text{NaO}_2)^+$ : 464.1556, found 464.1557.

tert-butyl (R)-(4,4-dicyano-1-(4-nitrophenyl)-3-phenylbut-3-en-1-yl)carbamate (**4l**)



Colorless solid, 38.5 mg, 92% yield, **m.p.** = 46-47°C,  $[\alpha]_{\text{D}}^{25} = +12.3$  ( $c = 0.57$ ,  $\text{CHCl}_3$ ). The ee value was 98%

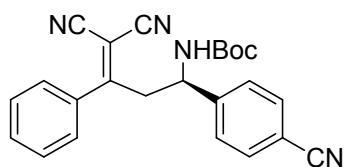
(Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 18.407$  min.,  $t_{\text{minor}} = 9.091$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (d,  $J = 8.3$  Hz, 2H), 7.72 – 7.52 (m, 3H), 7.515 – 7.415 (m, 2H), 7.36 (d,  $J = 8.2$  Hz, 2H), 4.83 (d,  $J = 19.6$  Hz, 2H), 3.72 – 3.54 (m, 1H), 3.40 (dd,  $J = 13.4, 6.1$  Hz, 1H), 1.44 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  177.82, 154.56, 147.83, 146.53, 133.80, 132.66, 129.51, 127.82, 127.38, 124.35, 112.09, 82.74, 80.96, 53.44, 43.88, 28.23.

**HRMS** (ESI): calculated for  $(\text{C}_{23}\text{H}_{23}\text{N}_3\text{NaO}_2)^+$ : 396.1682, found 396.1680.

tert-butyl (R)-(4,4-dicyano-1-(4-cyanophenyl)-3-phenylbut-3-en-1-yl)carbamate (**4m**)



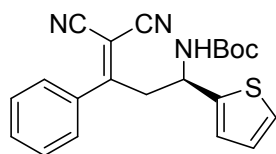
Colorless solid, 37.5 mg, 94% yield, **m.p.** = 52-53°C,  $[\alpha]_{\text{D}}^{25} = +14.1$  ( $c = 0.57$ ,  $\text{CHCl}_3$ ). The ee value was 97% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 21.024$  min.,  $t_{\text{minor}} = 9.052$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.73 – 7.60 (m, 2H), 7.60 – 7.48 (m, 3H), 7.48 – 7.34 (m, 2H), 7.29 – 7.23 (m, 2H), 4.82 (d,  $J = 7.4$  Hz, 1H), 4.69 (q,  $J = 15.0, 8.2$  Hz, 1H), 3.73 – 3.45 (m, 1H), 3.34 (dd,  $J = 13.7, 6.2$  Hz, 1H), 1.40 (s, 9H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  174.92, 154.70, 133.86, 132.91, 132.60, 129.46, 127.82, 127.20, 118.14, 112.53, 112.13, 81.12, 77.25, 53.60, 43.89, 28.24.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{22}\text{N}_4\text{NaO}_2)^+$ : 421.1635, found 421.1637.

tert-butyl (R)-(4,4-dicyano-3-phenyl-1-(thiophen-2-yl)but-3-en-1-yl)carbamate (**4n**)



Colorless oil, 37.6 mg, 99% yield,  $[\alpha]_{\text{D}}^{25} = +26.4$  ( $c = 0.56$ ,  $\text{CHCl}_3$ ). The ee value was 82% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 7.446$  min.,  $t_{\text{minor}} =$

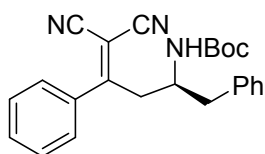
6.588 min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.74 – 7.35 (m, 5H), 7.24 – 7.22 (m, 1H), 7.10 – 6.90 (m, 1H), 6.896 – 6.652 (m, 1H), 5.04 – 4.61 (m, 2H), 3.80 – 3.63 (m, 1H), 3.45 (dd,  $J = 13.8$ , 6.8 Hz, 1H), 1.43 (s, 9H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  177.73, 162.29, 142.37, 133.89, 132.29, 129.22, 127.95, 127.17, 125.43, 125.06, 112.31, 80.55, 78.59, 49.35, 44.61, 28.29.

**HRMS** (ESI): calculated for  $(\text{C}_{21}\text{H}_{21}\text{N}_3\text{NaO}_2\text{S})^+$ : 402.1247, found 402.1248.

tert-butyl (S)-(5,5-dicyano-1,4-diphenylpent-4-en-2-yl)carbamate (**4o**)



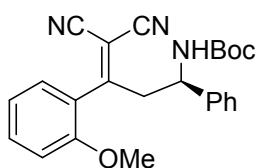
Colorless solid, 35.3 mg, 91% yield, **m.p.** = 125-126 °C,  $[\alpha]_D^{25} = +51.2$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ). The ee value was 76% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 6.309$  min.,  $t_{\text{minor}} = 5.397$  min).

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47 – 7.35 (m, 5H), 7.35 – 7.29 (m, 3H), 7.29 – 7.25 (m, 2H), 5.06 – 5.00 (m, 1H), 4.85 (d,  $J = 9.0$  Hz, 1H), 3.38 – 3.33 (m, 1H), 3.05 (t, 2H), 2.16 – 2.11 (m, 1H), 1.42 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  183.24, 153.55, 145.69, 136.78, 134.75, 129.17, 128.68, 128.08, 127.44, 122.66, 115.80, 80.75, 71.22, 49.42, 48.02, 32.53, 27.85.

**HRMS** (ESI): calculated for  $(\text{C}_{24}\text{H}_{25}\text{N}_3\text{NaO}_2)^+$ : 410.1839, found 410.1834.

tert-butyl (R)-(4,4-dicyano-3-(2-methoxyphenyl)-1-phenylbut-3-en-1-yl)carbamate (**4p**)



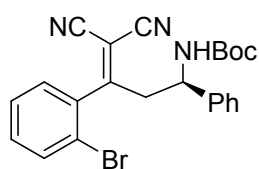
Colorless solid, 34.7 mg, 86% yield, **m.p.** = 39-40 °C,  $[\alpha]_D^{25} = +22.0$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ). The ee value was 77% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 9.429$  min.,  $t_{\text{minor}} = 6.331$  min).

**<sup>1</sup>H NMR** (300 MHz, cdcl<sub>3</sub>) δ 7.50 – 7.34 (m, 1H), 7.33 – 7.24 (m, 2H), 7.18 – 7.00 (m, 4H), 6.98 – 6.75 (m, 2H), 4.73 (d, 1H), 4.63 (q, 1H), 3.81 (s, 3H), 3.65 – 3.46 (m, 1H), 3.41 (dd, *J* = 14.2, 6.5 Hz, 1H), 1.39 (s, 9H).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 171.56, 155.89, 146.79, 133.01, 130.20, 129.86, 128.94, 128.75, 126.83, 126.35, 121.01, 120.56, 110.78, 82.75, 78.67, 63.78, 55.47, 43.61, 27.88.

**HRMS** (ESI): calculated for (C<sub>24</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>3</sub>)<sup>+</sup>: 426.1788, found 426.1788.

tert-butyl (R)-(3-(2-bromophenyl)-4,4-dicyano-1-phenylbut-3-en-1-yl)carbamate (**4q**)



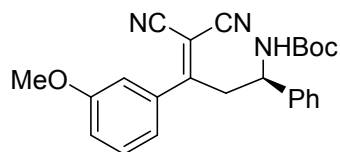
Colorless oil, 40.3 mg, 89% yield, [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +20.0 (*c* = 0.57, CHCl<sub>3</sub>). The ee value was 70% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 230 nm, 1 mL/min, *t*<sub>major</sub> = 18.702 min., *t*<sub>minor</sub> = 13.024 min).

**<sup>1</sup>H NMR** (300 MHz, cdcl<sub>3</sub>) δ 7.72 – 7.64 (m, 1H), 7.64 – 7.42 (m, 1H), 7.42 – 7.26 (m, 4H), 7.26 – 7.14 (m, 3H), 5.12 – 4.57 (m, 2H), 3.66 – 3.39 (m, 1H), 3.29 (dd, 1H), 1.46 (s, 9H).

**<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 176.82, 155.17, 136.01, 133.76, 132.04, 131.81, 129.18, 128.40, 128.14, 127.76, 126.14, 119.64, 111.10, 91.11, 80.57, 52.67, 44.74, 28.30.

**HRMS** (ESI): calculated for (C<sub>23</sub>H<sub>22</sub>BrN<sub>3</sub>NaO<sub>2</sub>)<sup>+</sup>: 474.0788, found 474.0786.

tert-butyl (R)-(4,4-dicyano-3-(3-methoxyphenyl)-1-phenylbut-3-en-1-yl)carbamate (**4r**)



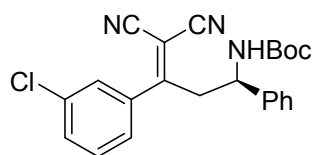
Colorless solid, 33.1 mg, 82% yield, **m.p.** = 38-39 °C, [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +35.1 (*c* = 0.65, CHCl<sub>3</sub>). The ee value was 86% (Chiralpak OD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min, *t*<sub>major</sub> = 6.648 min, *t*<sub>minor</sub> = 6.092 min).

<sup>1</sup>H NMR (300 MHz, cdcl<sub>3</sub>) δ 7.46 – 7.39 (m, 1H), 7.39 – 7.30 (m, 3H), 7.21 – 7.12 (m, 2H), 7.11 – 6.92 (m, 3H), 4.84 (d, *J* = 8.0 Hz, 1H), 4.64 (q, *J* = 14.1, 6.3 Hz, 1H), 3.85 (s, 3H), 3.77 – 3.55 (m, 1H), 3.36 (dd, *J* = 13.5, 6.9 Hz, 1H), 1.44 (s, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 175.91, 159.78, 154.81, 139.16, 135.28, 130.35, 129.14, 128.62, 126.48, 120.07, 118.35, 113.26, 112.49, 83.80, 80.23, 55.49, 54.12, 44.35, 28.30.

HRMS (ESI): calculated for (C<sub>24</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>3</sub>)<sup>+</sup>: 426.1788, found 426.1788.

tert-butyl (R)-(3-(3-chlorophenyl)-4,4-dicyano-1-phenylbut-3-en-1-yl)carbamate (**4s**)



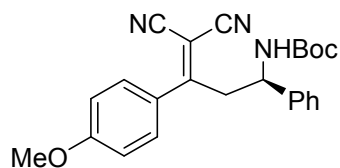
Colorless solid, 32.6 mg, 80% yield, **m.p.** = 39-40 °C, **[α]<sub>D</sub><sup>25</sup>** = +39.6 (*c* = 0.5, CHCl<sub>3</sub>). The ee value was 71% (Chiralpak AS-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min, *t*<sub>major</sub> = 6.126 min, *t*<sub>minor</sub> = 5.261 min).

<sup>1</sup>H NMR (300 MHz, cdcl<sub>3</sub>) δ 7.56 – 7.46 (m, 2H), 7.43 – 7.32 (m, 5H), 7.22 – 7.08 (m, 2H), 4.85 (d, *J* = 7.8 Hz, 1H), 4.64 (q, *J* = 14.2, 6.9 Hz, 1H), 3.82 – 3.57 (m, 1H), 3.34 (dd, *J* = 13.5, 6.5 Hz, 1H), 1.45 (s, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 174.48, 154.86, 138.99, 135.95, 135.69, 135.29, 132.08, 130.55, 129.76, 129.26, 128.77, 126.40, 112.62, 87.91, 80.16, 53.92, 44.57, 28.30.

HRMS (ESI): calculated for (C<sub>23</sub>H<sub>22</sub>ClN<sub>3</sub>NaO<sub>2</sub>)<sup>+</sup>: 430.1293, found 430.1291.

tert-butyl (R)-(4,4-dicyano-3-(4-methoxyphenyl)-1-phenylbut-3-en-1-yl)carbamate (**4t**)



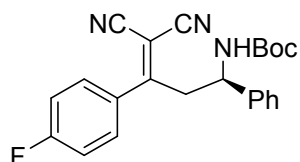
Colorless solid, 36.7 mg, 91% yield, **m.p.** = 44-45 °C, **[α]<sub>D</sub><sup>25</sup>** = +68.6 (*c* = 0.51, CHCl<sub>3</sub>). The ee value was 89% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min, *t*<sub>major</sub> = 7.359 min, *t*<sub>minor</sub> = 6.597 min).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.54 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.30 (m, 3H), 7.19 – 7.09 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 4.89 (d, *J* = 6.1 Hz, 1H), 4.63 (q, *J* = 14.5, 7.2 Hz, 1H), 3.91 (s, 3H), 3.79 – 3.63 (m, 1H), 3.39 (dd, *J* = 13.7, 7.3 Hz, 1H), 1.47 (s, 9H).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 175.18, 163.09, 154.97, 139.02, 130.33, 129.14, 128.62, 126.48, 126.04, 114.66, 113.30, 83.80, 80.20, 55.57, 54.52, 43.83, 28.32.

**HRMS** (ESI): calculated for (C<sub>24</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>3</sub>)<sup>+</sup>: 426.1788, found 426.1786.

tert-butyl (R)-(4,4-dicyano-3-(4-fluorophenyl)-1-phenylbut-3-en-1-yl)carbamate (**4u**)



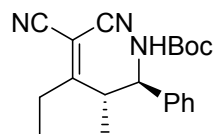
Colorless solid, 33.3 mg, 85% yield, **m.p.** = 35-36°C, [**a**]<sub>D</sub><sup>25</sup> = +89.2 (c = 0.37, CHCl<sub>3</sub>). The ee value was 91% (Chiralpak AS, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, *t*<sub>major</sub> = 8.751 min., *t*<sub>minor</sub> = 6.548 min).

**<sup>1</sup>H NMR** (300 MHz, cdcl<sub>3</sub>) δ 7.56 – 7.43 (m, 2H), 7.41 – 7.27 (m, 3H), 7.24 – 7.16 (m, 2H), 7.15 – 7.06 (m, 2H), 4.84 (d, *J* = 7.8 Hz, 1H), 4.56 (q, *J* = 15.2, 8.0 Hz, 1H), 3.78 – 3.60 (m, 1H), 3.36 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.43 (s, 9H).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 174.71, 163.81 (d, *J* = 32.9 Hz), 155.06, 138.80, 130.57 (d, *J* = 9.2 Hz), 130.12, 129.26, 128.78, 126.46, 116.60 (d, *J* = 22.2 Hz), 112.43, 86.18, 80.38, 54.20, 44.33, 28.30.

**HRMS** (ESI): calculated for (C<sub>23</sub>H<sub>22</sub>FN<sub>3</sub>NaO<sub>2</sub>)<sup>+</sup>: 414.1588, found 414.1588.

tert-butyl ((1R,2R)-3-(dicyanomethylene)-2-methyl-1-phenylpentyl)carbamate (**4v**)



Colorless oil, 26.1 mg, 77% yield, [**a**]<sub>D</sub><sup>25</sup> = +80.8 (c = 0.5, CHCl<sub>3</sub>). The ee value was 83% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 230 nm, 1 mL/min, major-*t*<sub>major</sub> = 11.793 min, *t*<sub>minor</sub> = 11.128 min, minor-*t*<sub>major</sub> = 6.704 min. *t*<sub>minor</sub> = 9.385min).

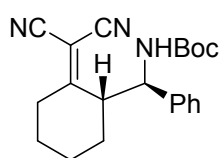


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 – 7.38 (m, 3H), 7.33 – 7.26 (m, 2H), 4.98 (d,  $J = 8.2$  Hz, 1H), 4.89 (t,  $J = 8.9$  Hz, 1H), 3.78 – 3.26 (m, 1H), 2.71 – 2.26 (m, 2H), 1.50 (s, 9H), 1.43 (d,  $J = 6.8$  Hz, 3H), 1.24 (t,  $J = 7.7$  Hz, 3H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  188.21, 155.24, 139.19, 129.26, 128.64, 126.43, 111.79, 111.45, 87.25, 80.40, 57.79, 48.46, 29.70, 28.30, 14.12, 13.70.

**HRMS** (ESI): calculated for  $(\text{C}_{20}\text{H}_{26}\text{N}_3\text{O}_2)^+$ : 340.2020, found 340.2027.

tert-butyl ((R)-((R)-2-(dicyanomethylene)cyclohexyl)(phenyl)methyl)carbamate (**4w**)



white solid, 25 mg, 71% yield, **m.p.** = 178-179 °C,  $[\alpha]_{\text{D}}^{25} = +79.6$  ( $c = 0.3$ ,  $\text{CHCl}_3$ ). The ee value was 93% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 230 nm, 1 mL/min, major- $t_{\text{major}} = 17.708$  min,  $t_{\text{minor}} =$

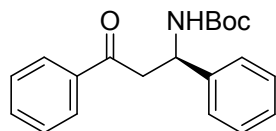
16.507 min, minor- $t_{\text{major}} = 11.235$  min.  $t_{\text{minor}} = 13.904$  min).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.39 (m, 3H), 7.34 – 7.29 (m, 2H), 5.20 (t, 1H), 4.86 (d, 1H), 3.59 – 3.54 (m, 1H), 3.53 – 3.06 (m, 2H), 2.43 (d,  $J = 12.8$  Hz, 1H), 1.66 – 1.63 (m, 1H), 1.41 – 1.35 (m, 4H), 1.32 (s, 9H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  183.62, 154.80, 139.40, 128.84, 127.31, 126.41, 112.62, 111.26, 89.25, 80.05, 55.54, 48.41, 31.58, 28.33, 28.20, 22.65, 16.55.

**HRMS** (ESI): calculated for  $(\text{C}_{21}\text{H}_{25}\text{N}_3\text{NaO}_2)^+$ : 374.1839, found 374.1837.

tert-butyl (R)-((R)-3-oxo-1,3-diphenylpropyl)carbamate (**5a**)



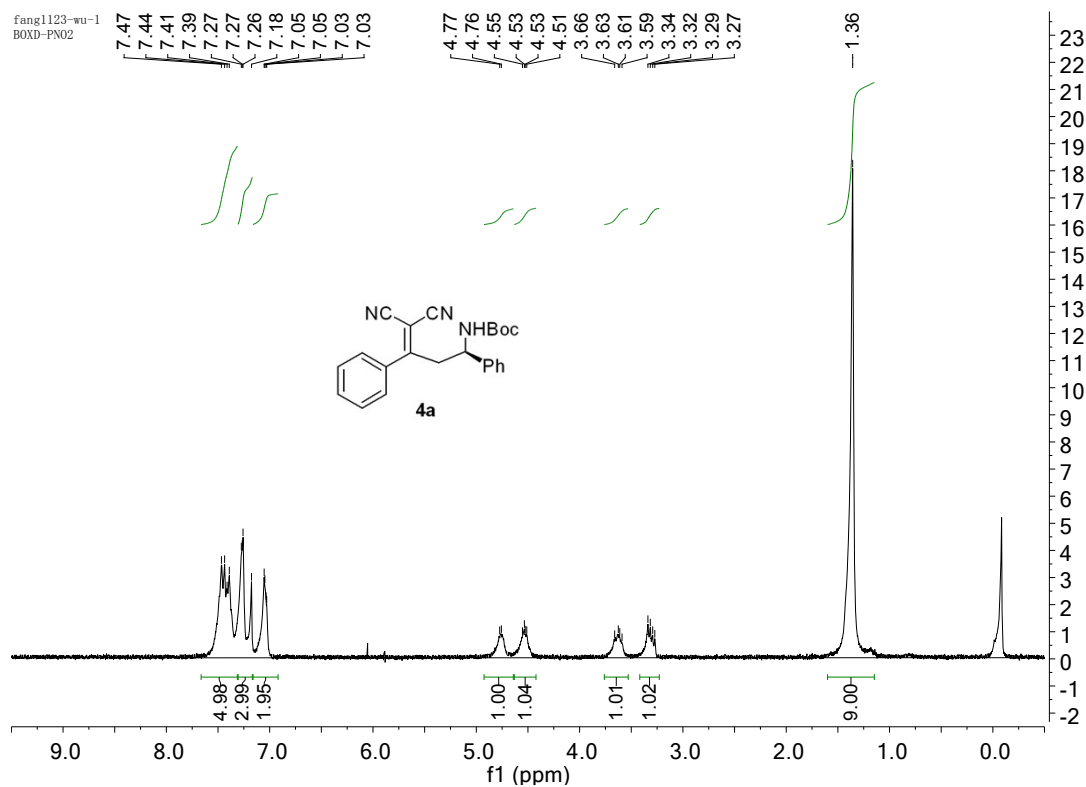
Colorless solid, 24.7 mg, 76% yield, **m.p.** = 39-40 °C,  $[\alpha]_{\text{D}}^{25} = +21.9$  ( $c = 0.53$ ,  $\text{CHCl}_3$ ). The ee value was 91% (Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 230 nm, 1 mL/min,  $t_{\text{major}} = 11.479$  min.,  $t_{\text{minor}} = 10.026$  min).

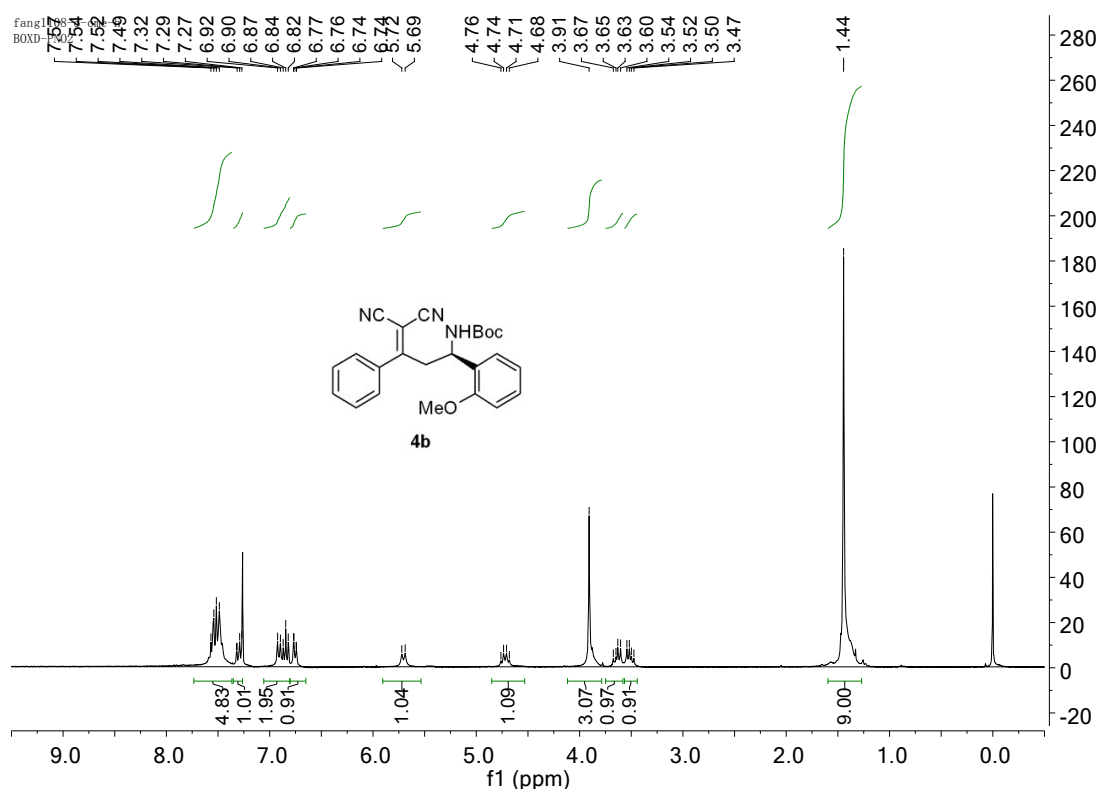
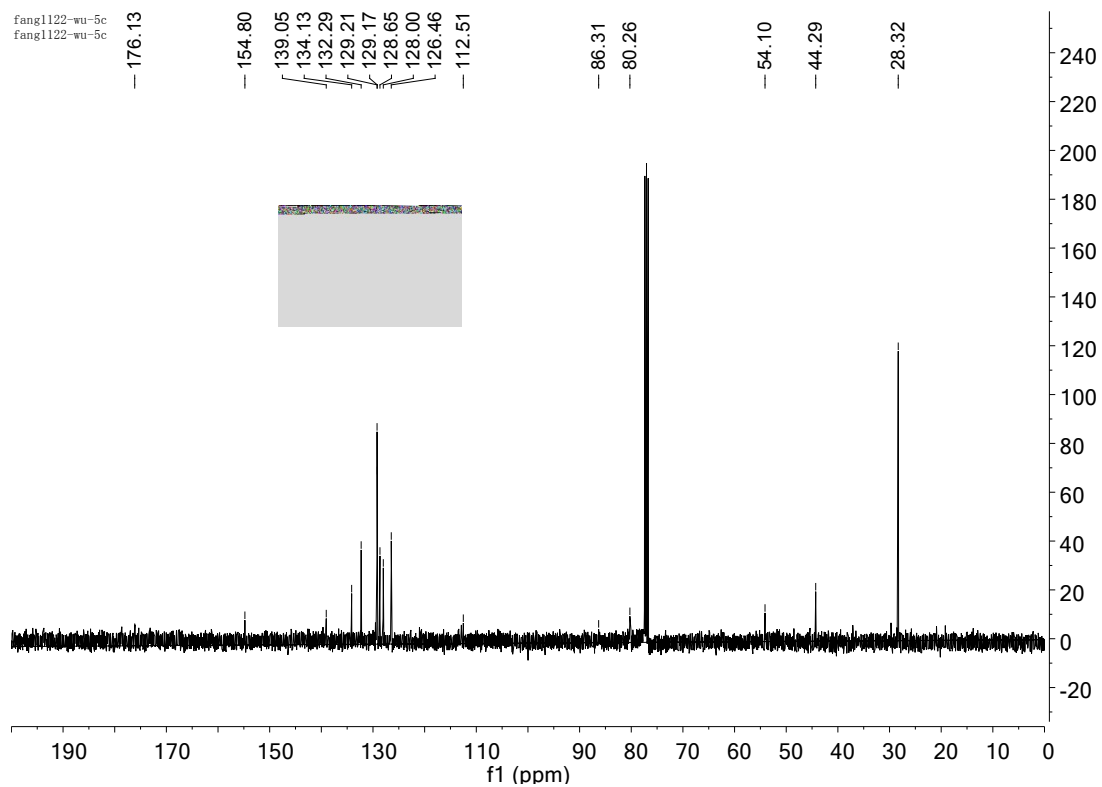
**<sup>1</sup>H NMR** (300 MHz, cdcl<sub>3</sub>) δ 7.98 – 7.79 (m, 2H), 7.60 – 7.51 (m, 1H), 7.49 – 7.38 (m, 2H), 7.38 – 7.18 (m, 5H), 5.55 (d, *J* = 5.0 Hz, 1H), 5.25 (q, *J* = 12.3, 5.8 Hz, 1H), 3.81 – 3.55 (m, 1H), 3.44 (dd, *J* = 16.7, 6.1 Hz, 1H), 1.41 (s, 9H).

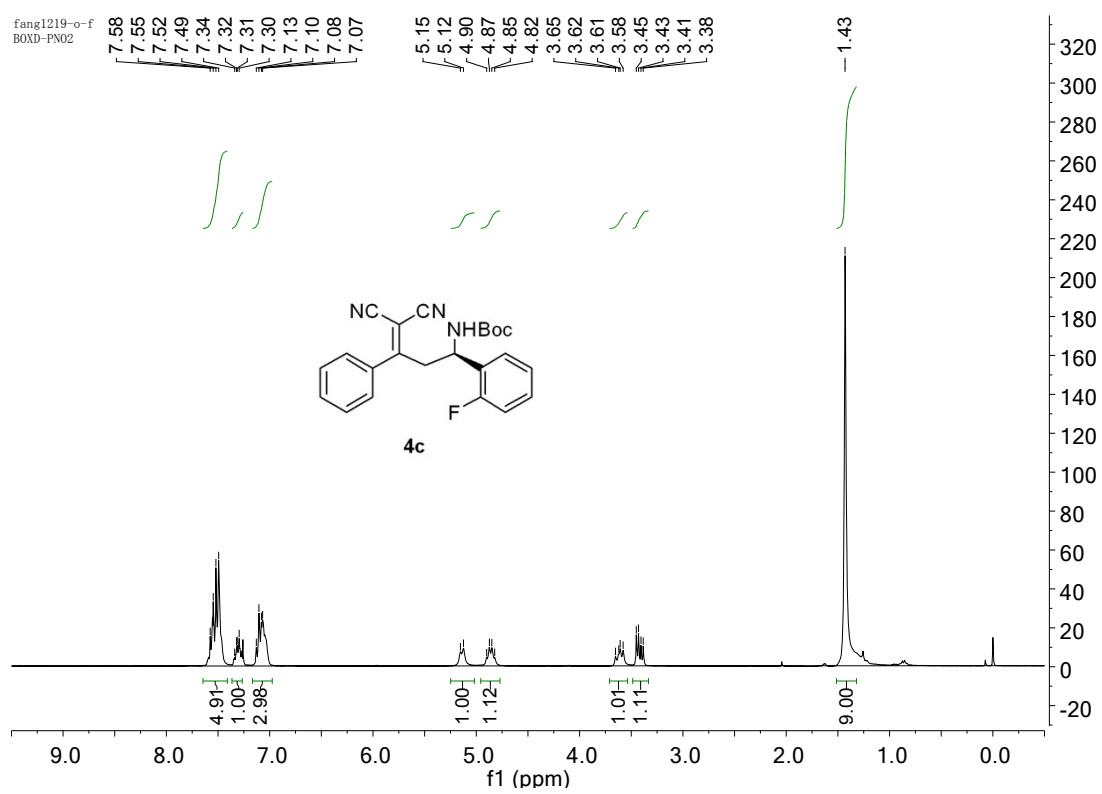
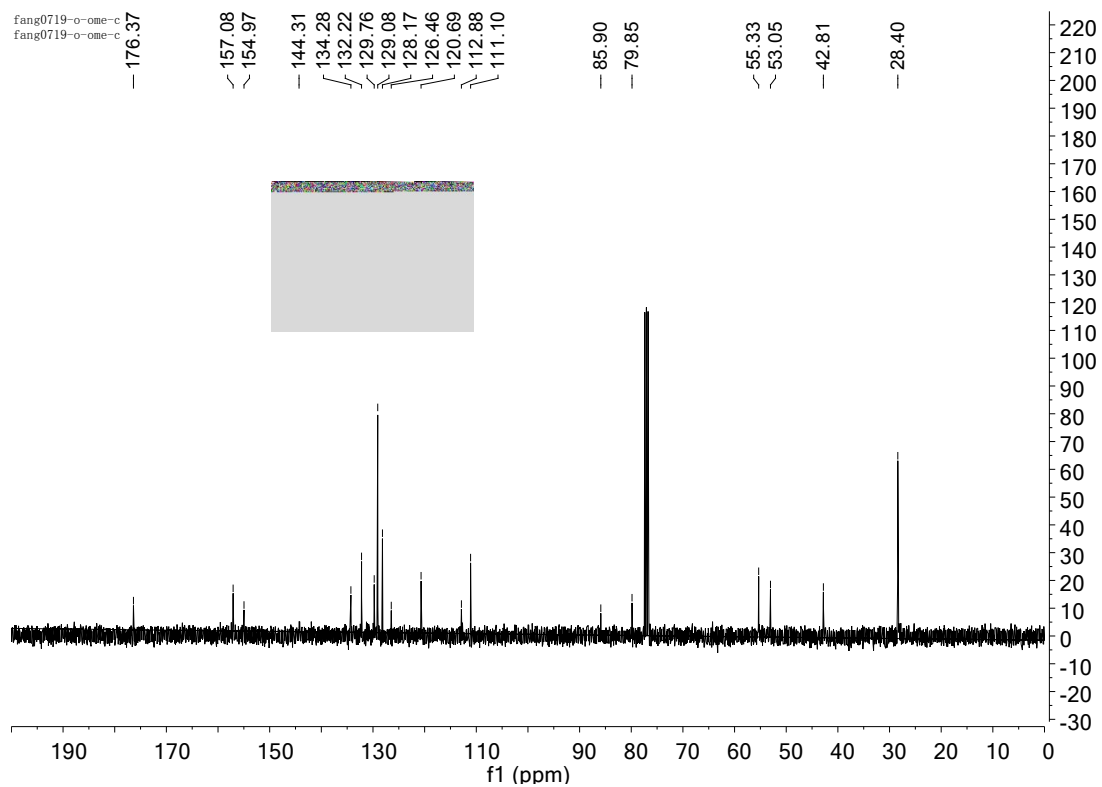
**<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 184.50, 155.17, 146.54, 136.75, 133.33, 128.64, 128.59, 128.11, 127.31, 126.33, 79.73, 77.22, 44.30, 28.36.

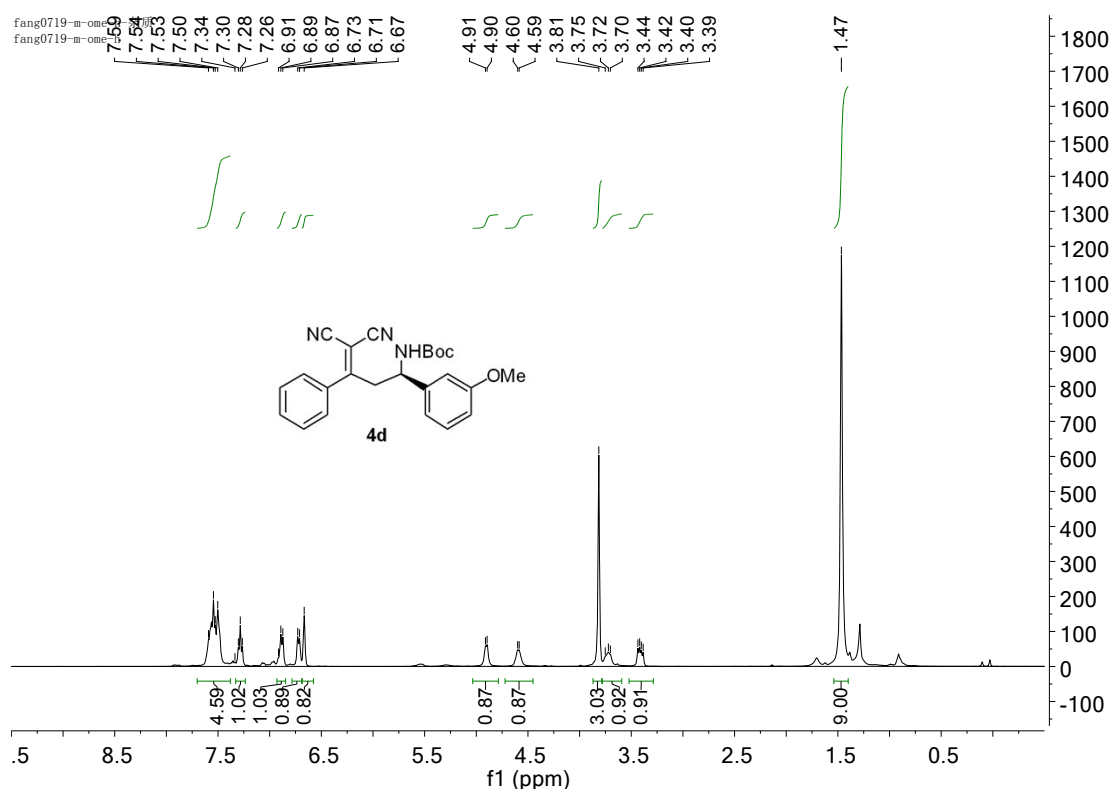
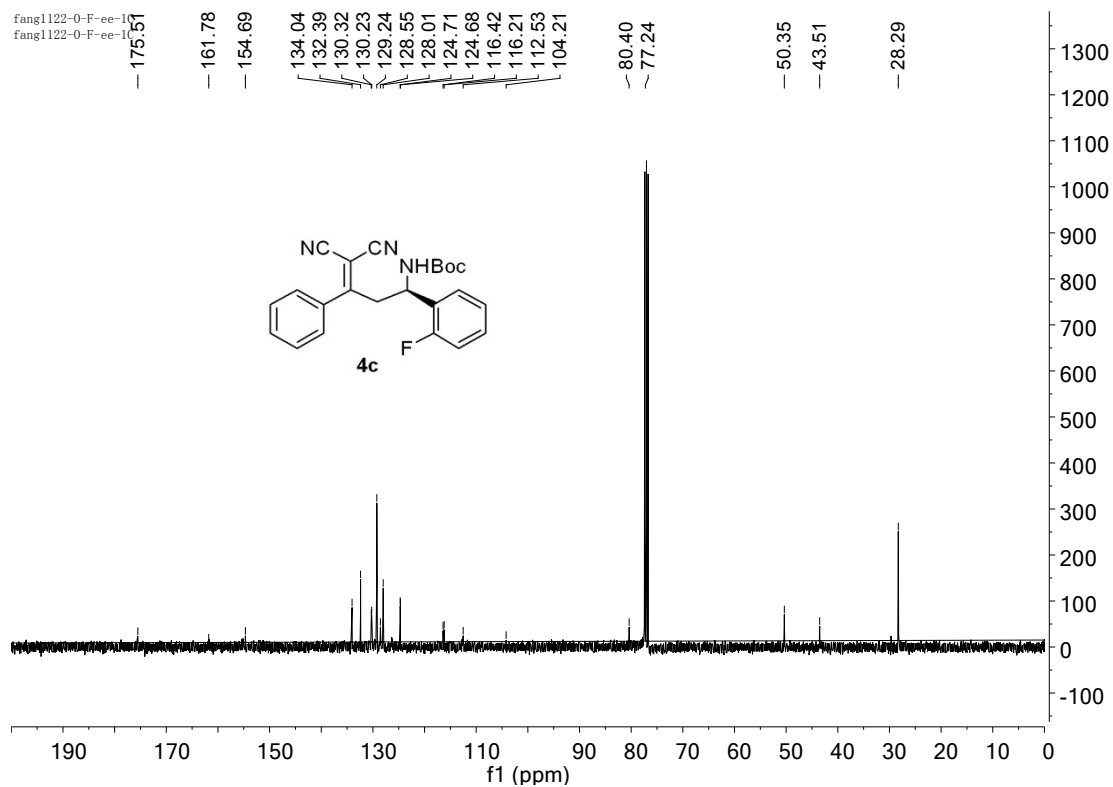
**HRMS** (ESI): calculated for (C<sub>20</sub>H<sub>23</sub>NNaO<sub>3</sub>)<sup>+</sup>: 348.1570, found 348.1568.

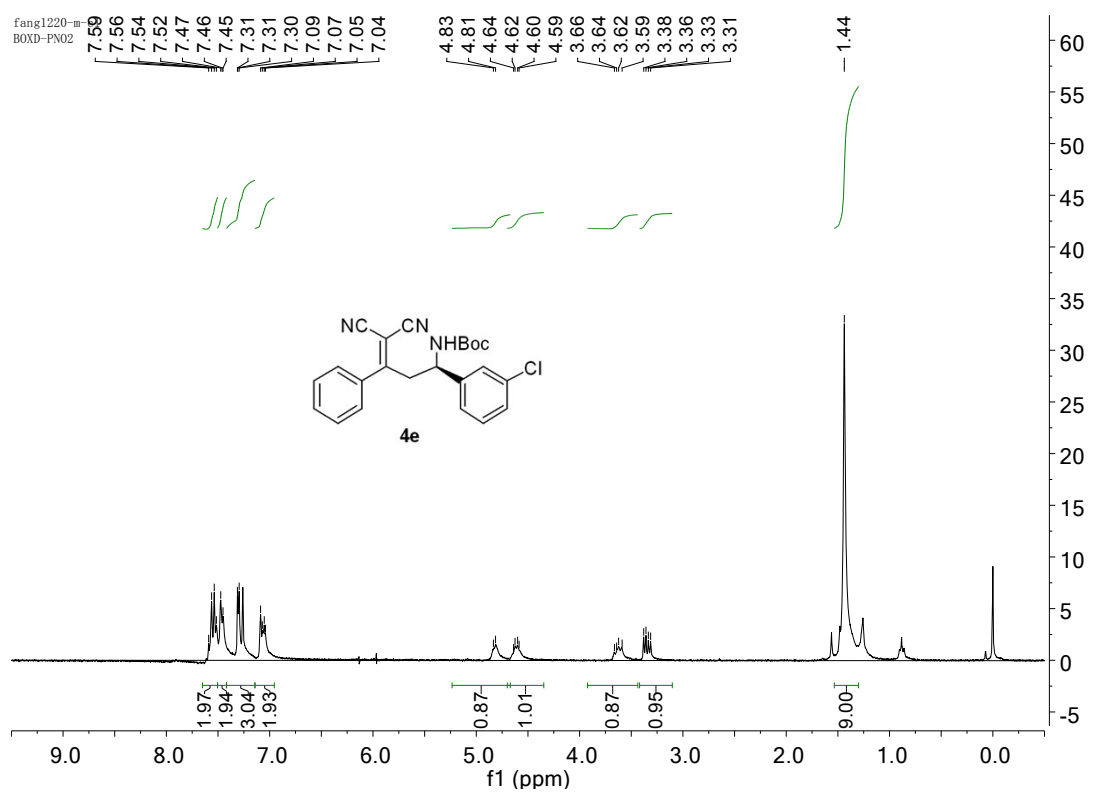
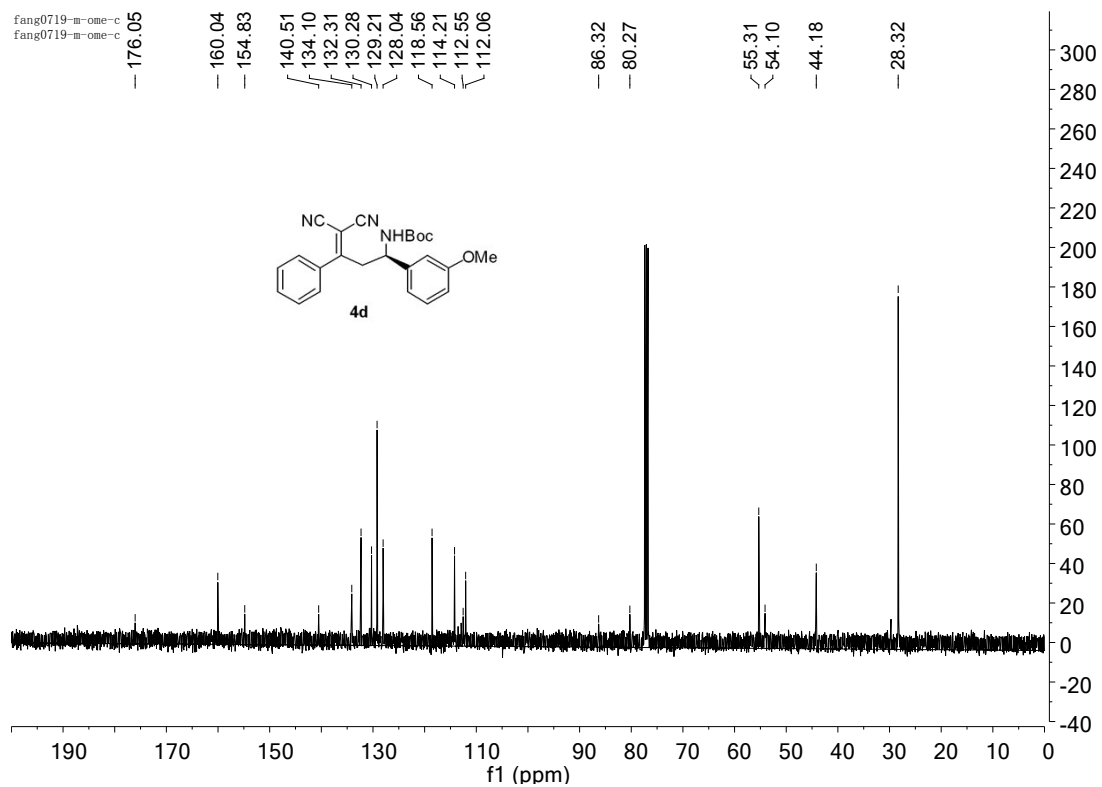
### 5. NMR spectra of addition products 4a-4t and derivative 5a

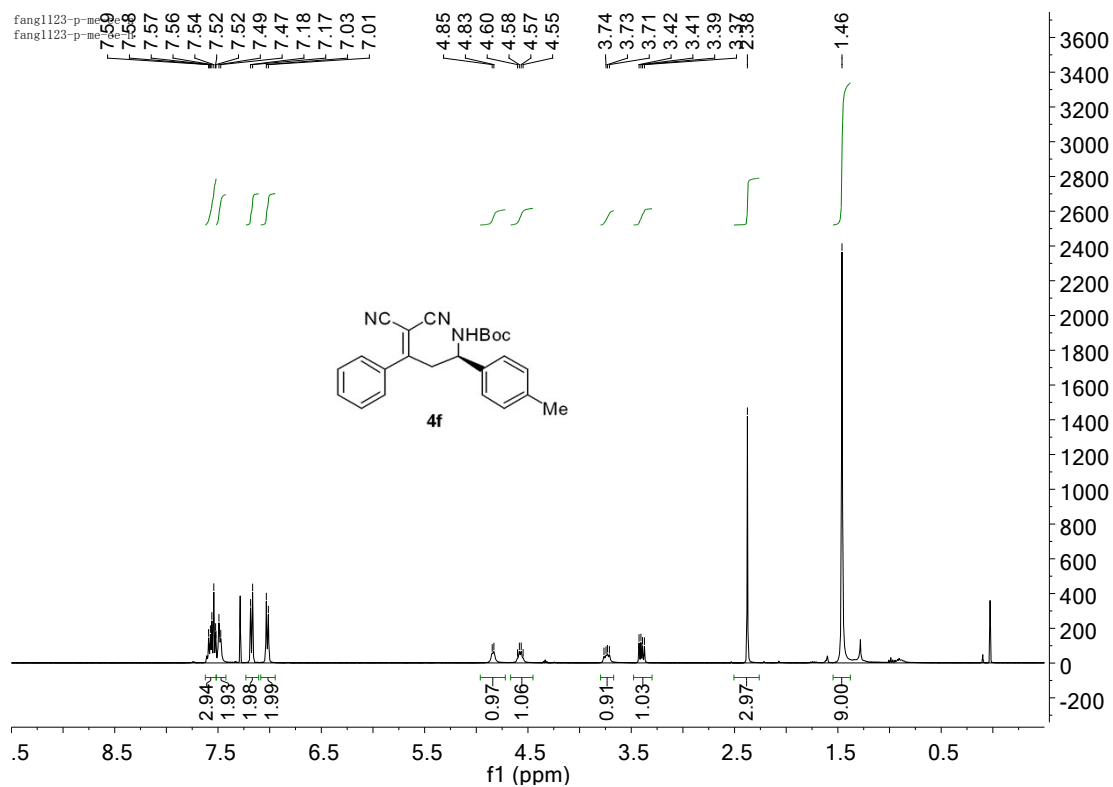
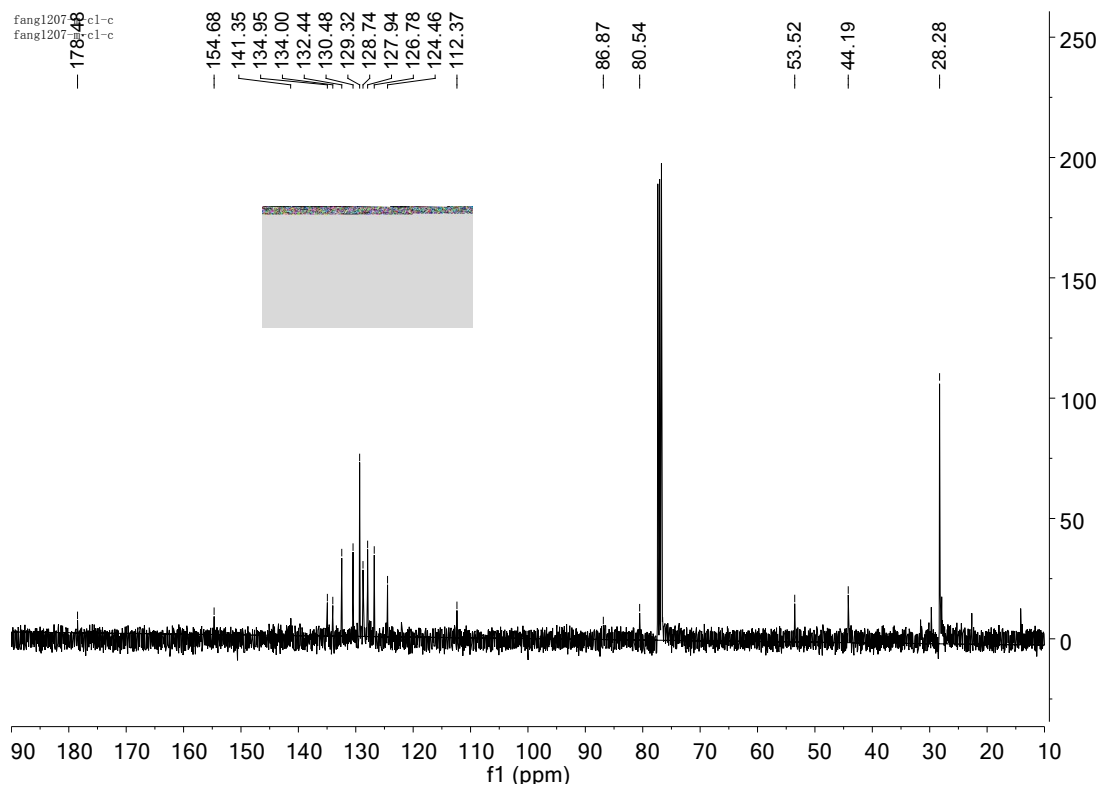


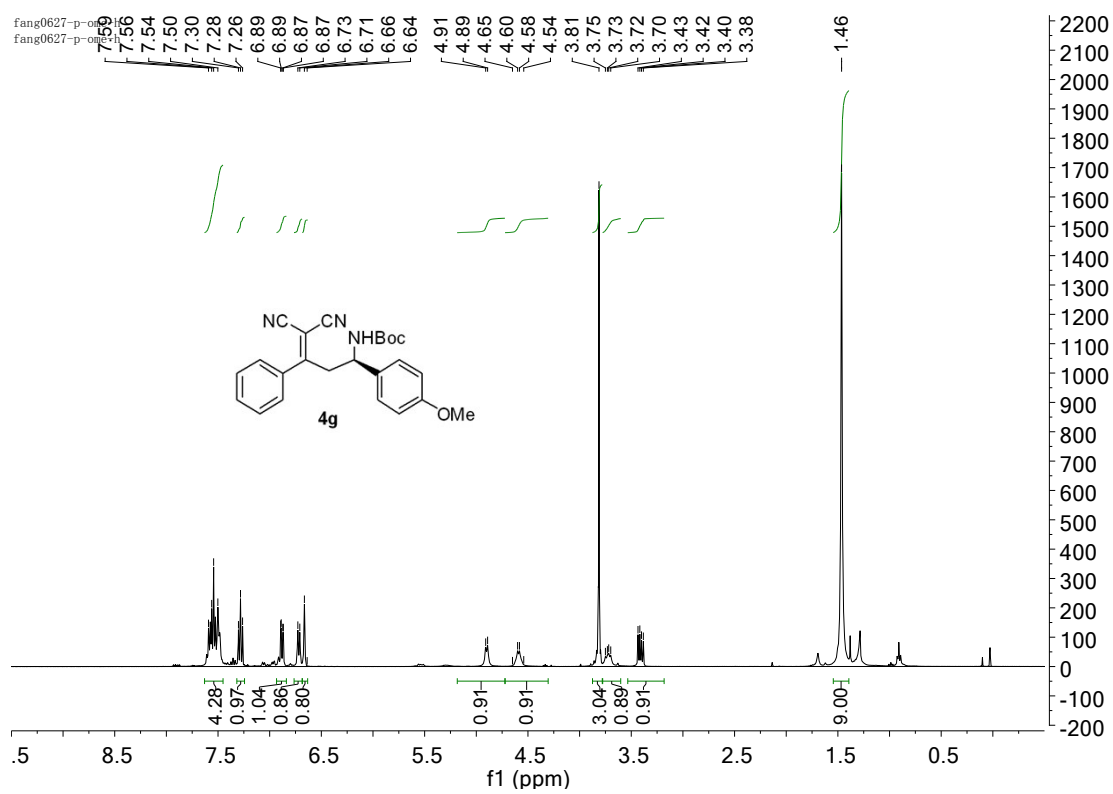
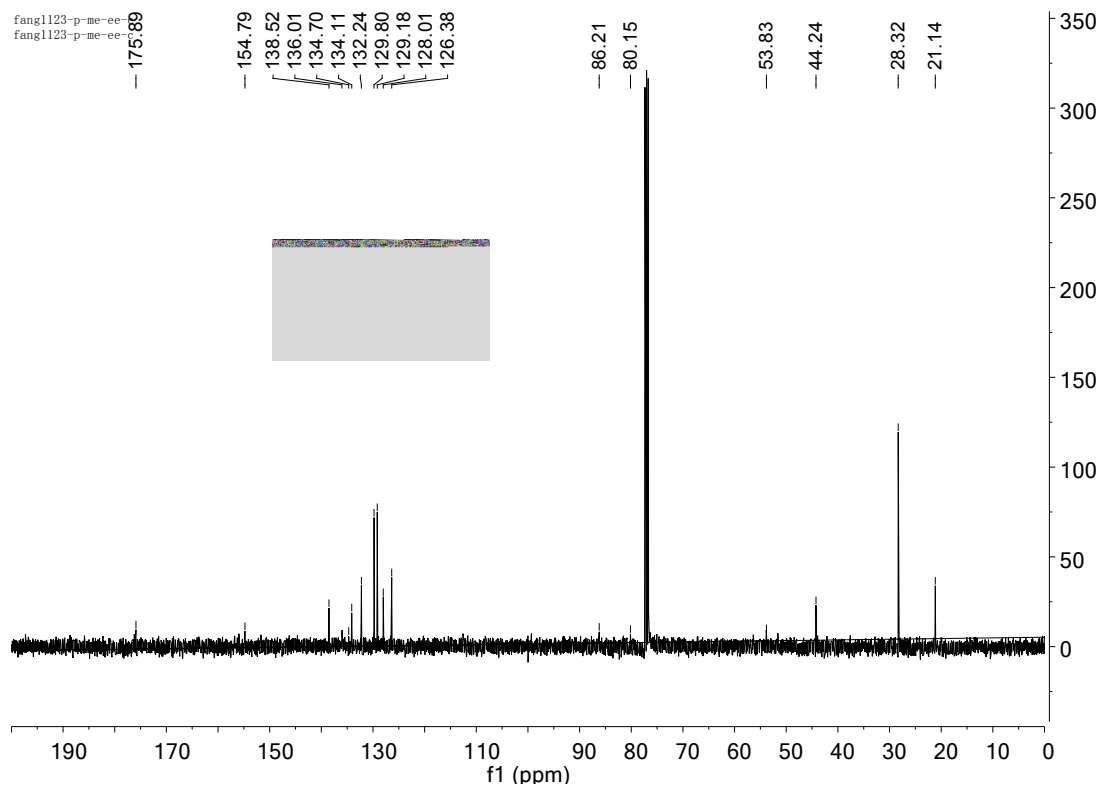




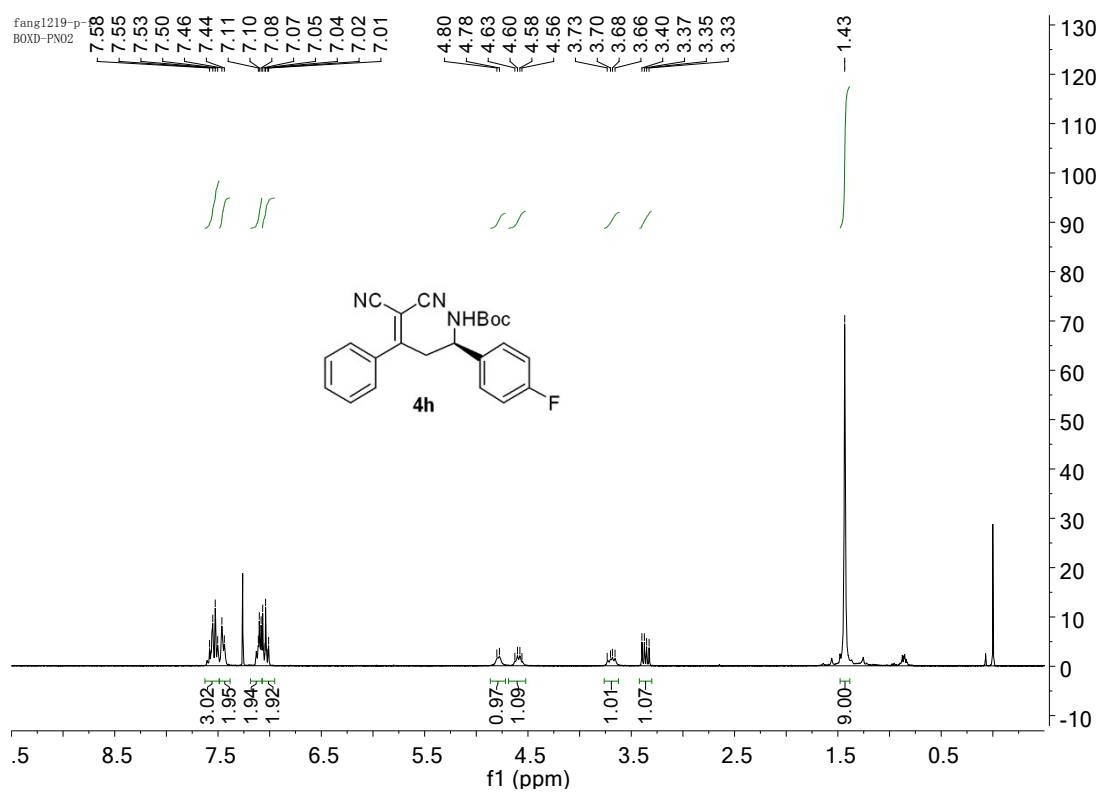
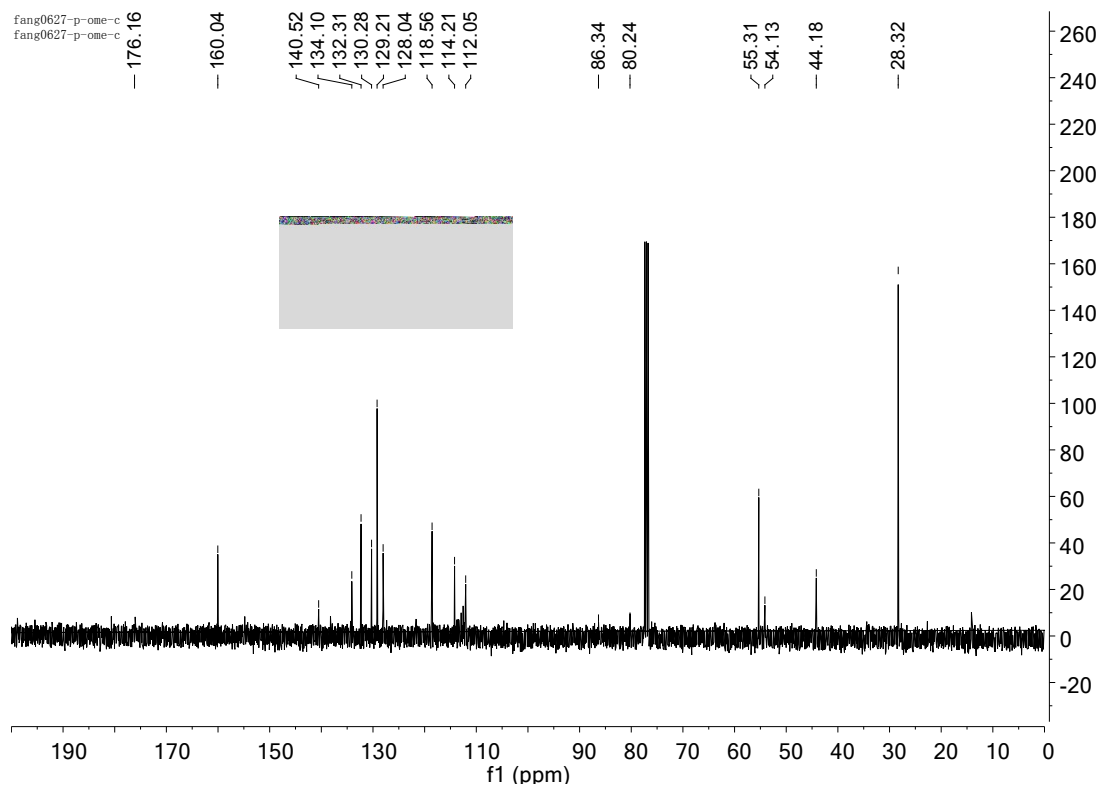


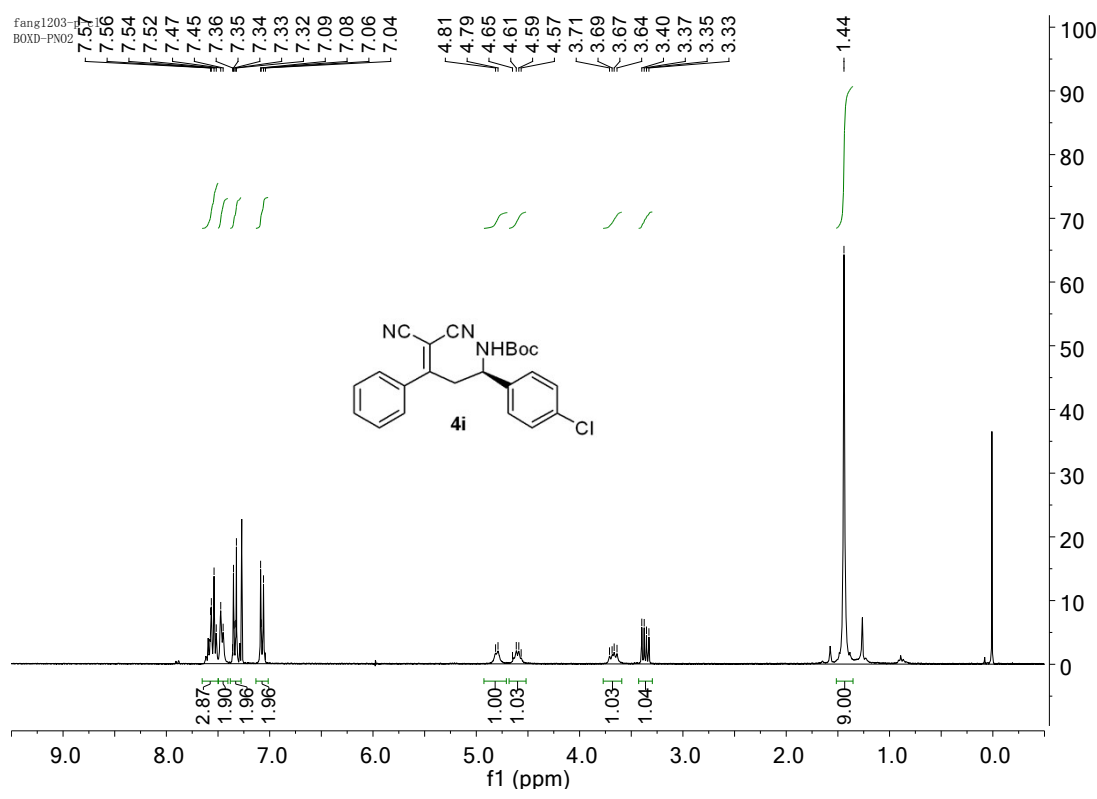
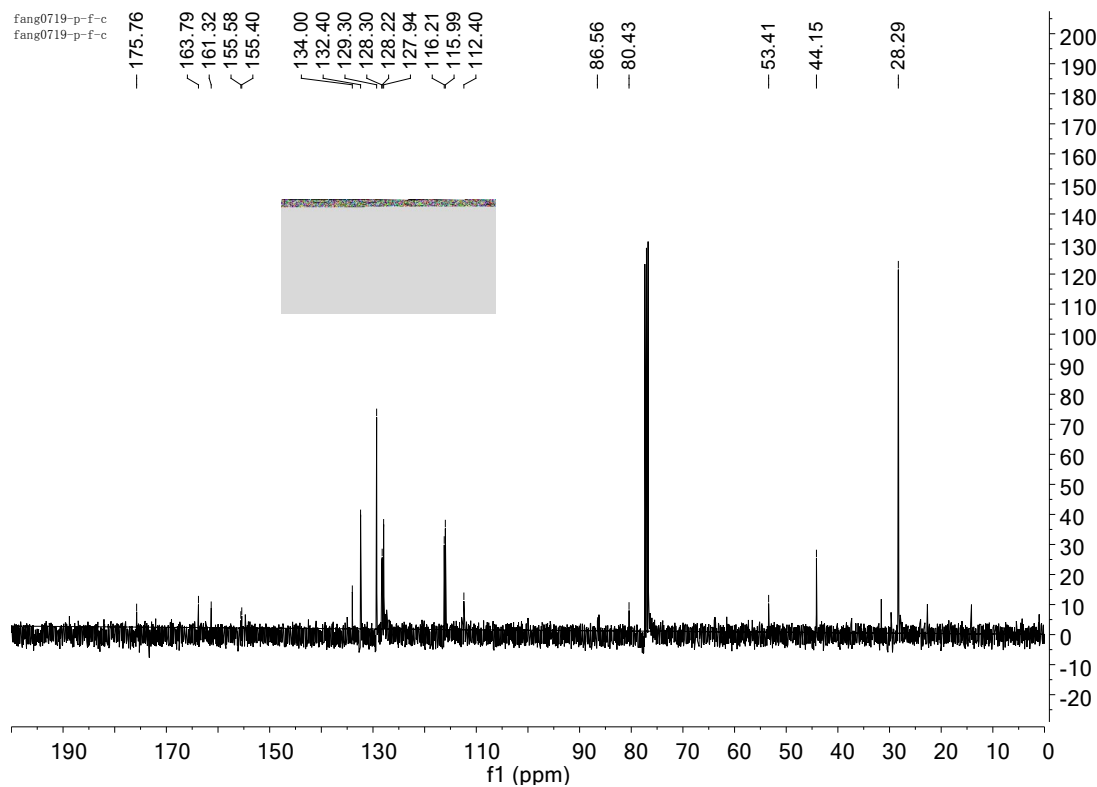


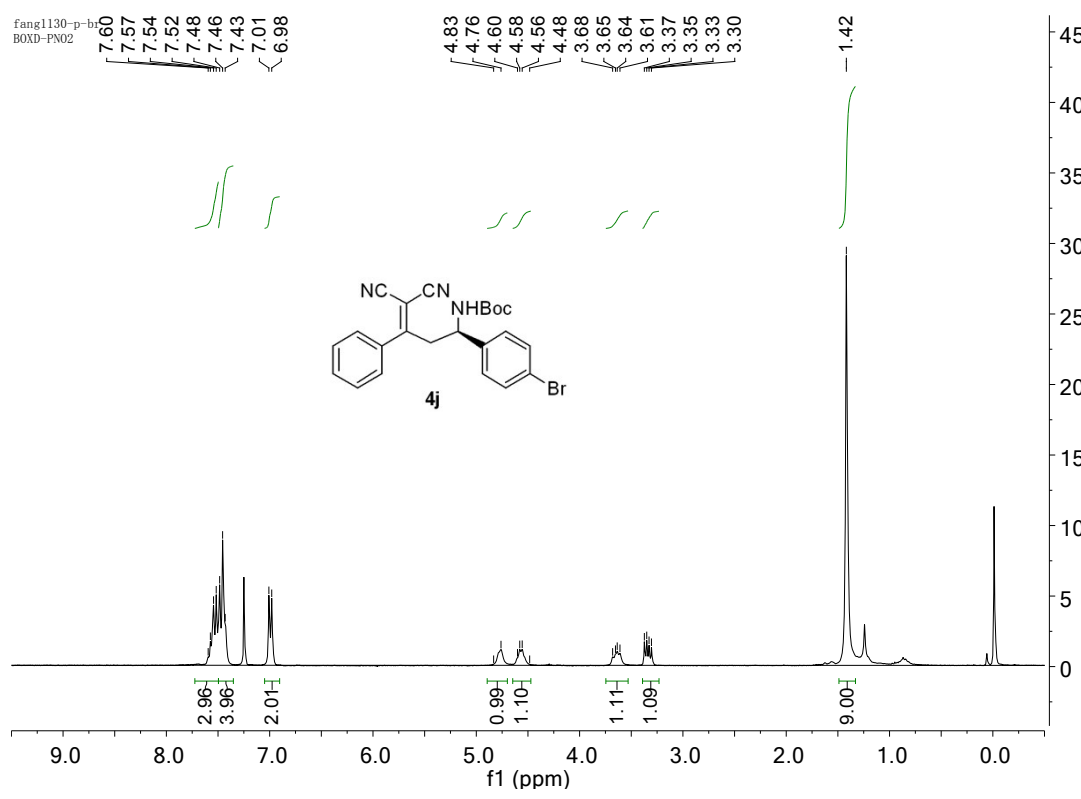
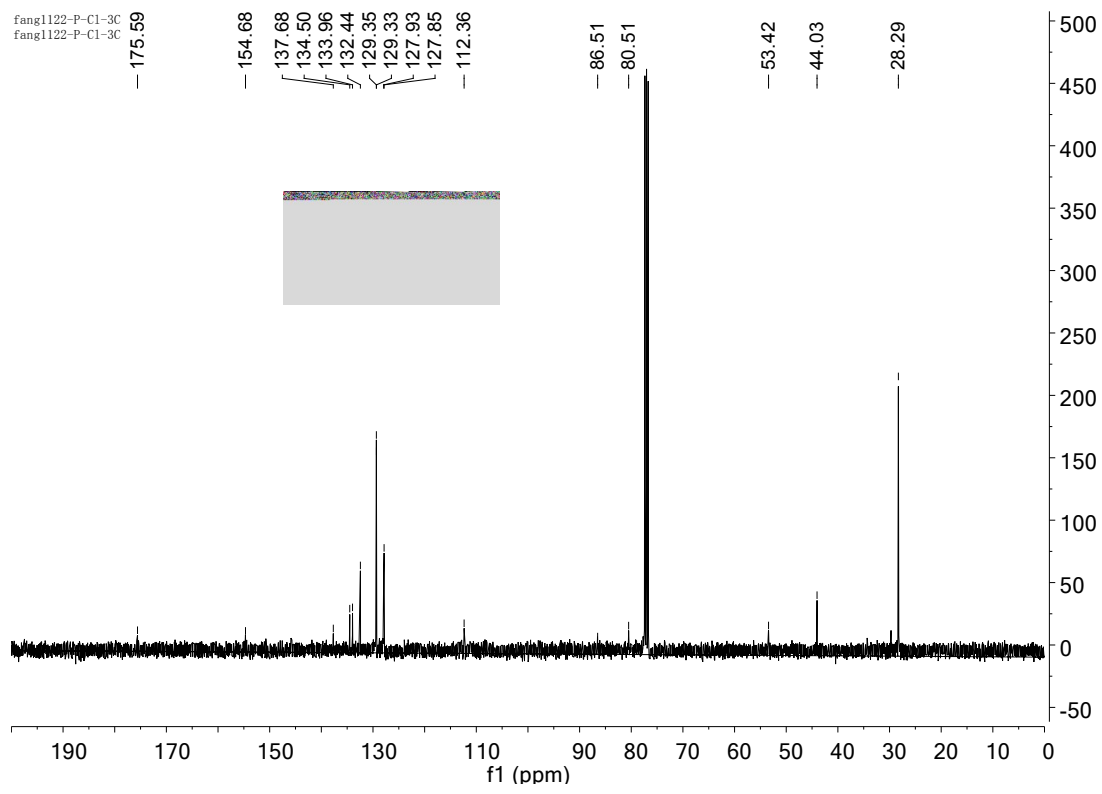


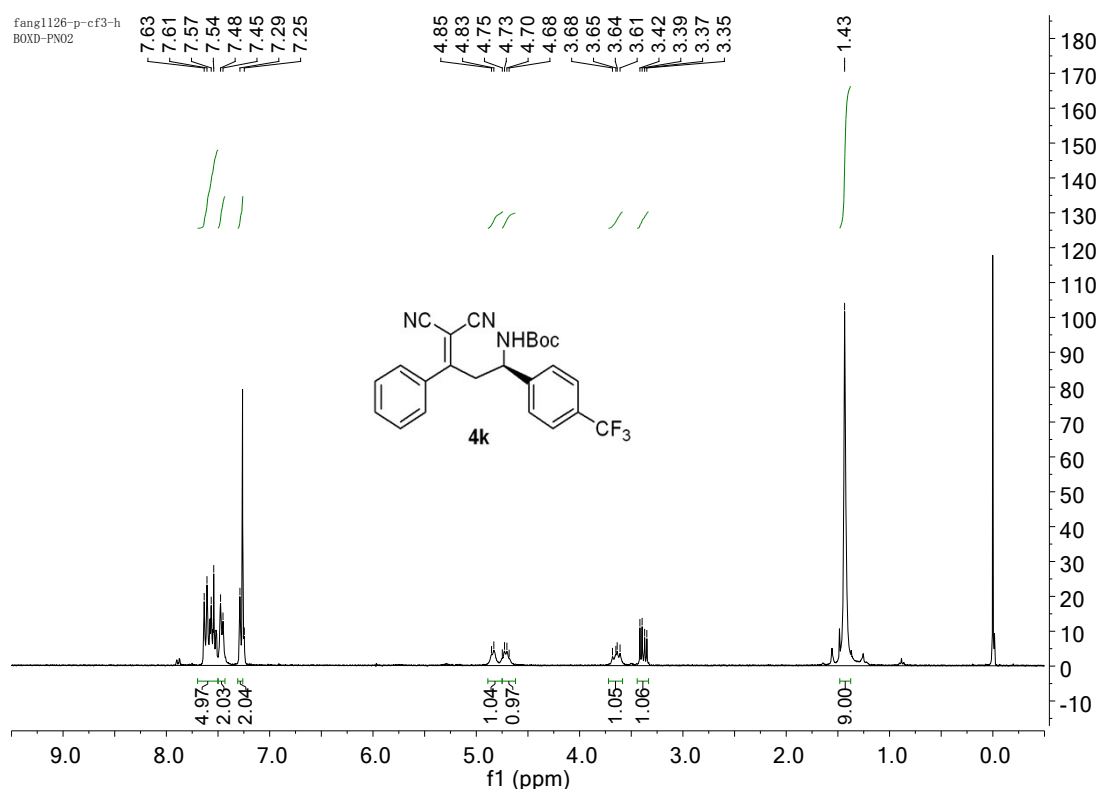
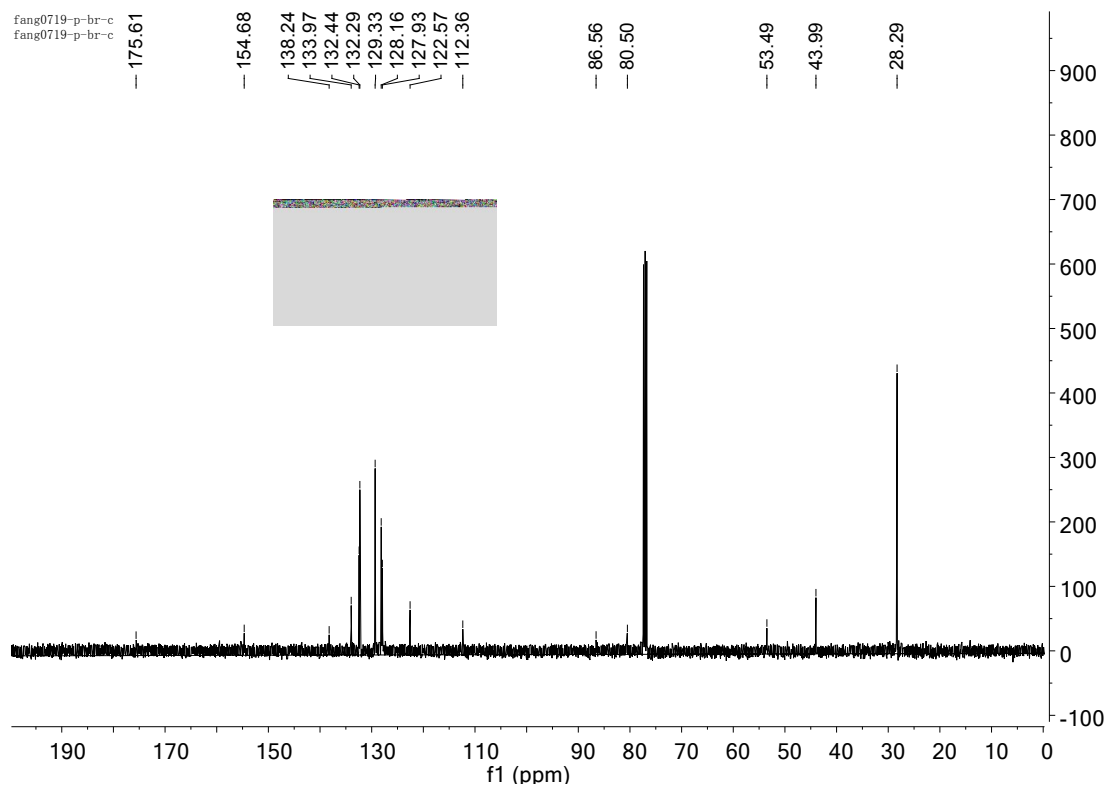


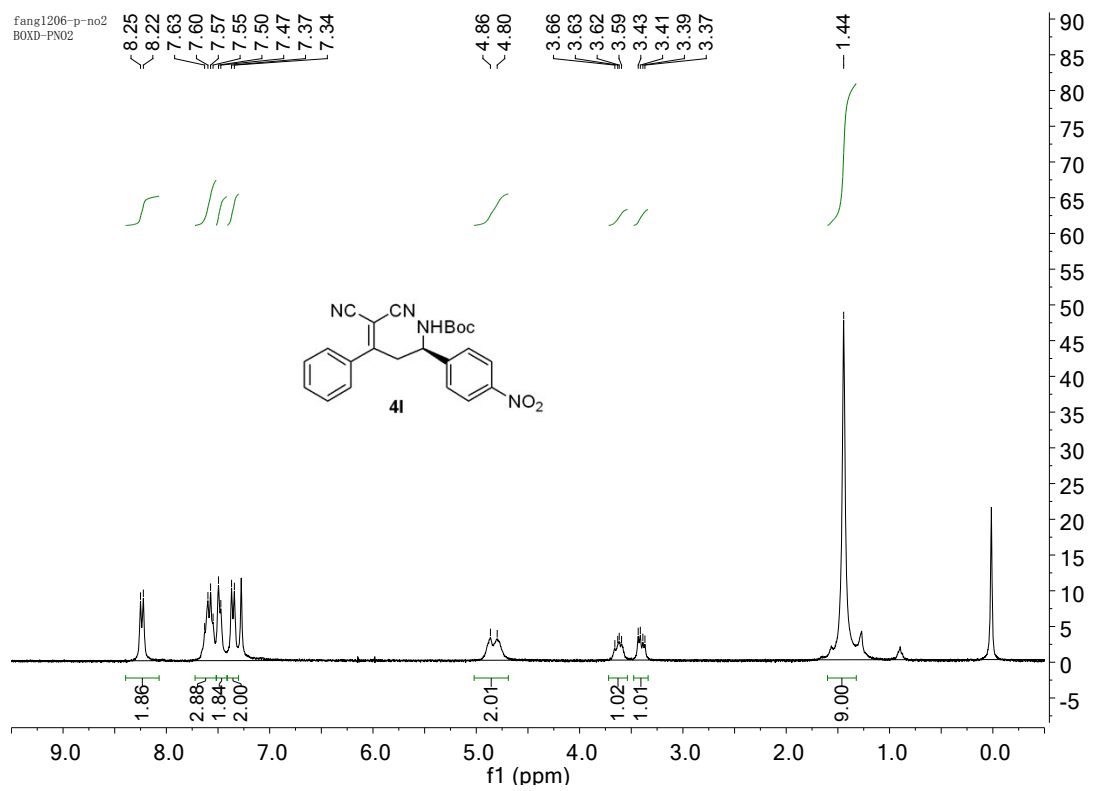
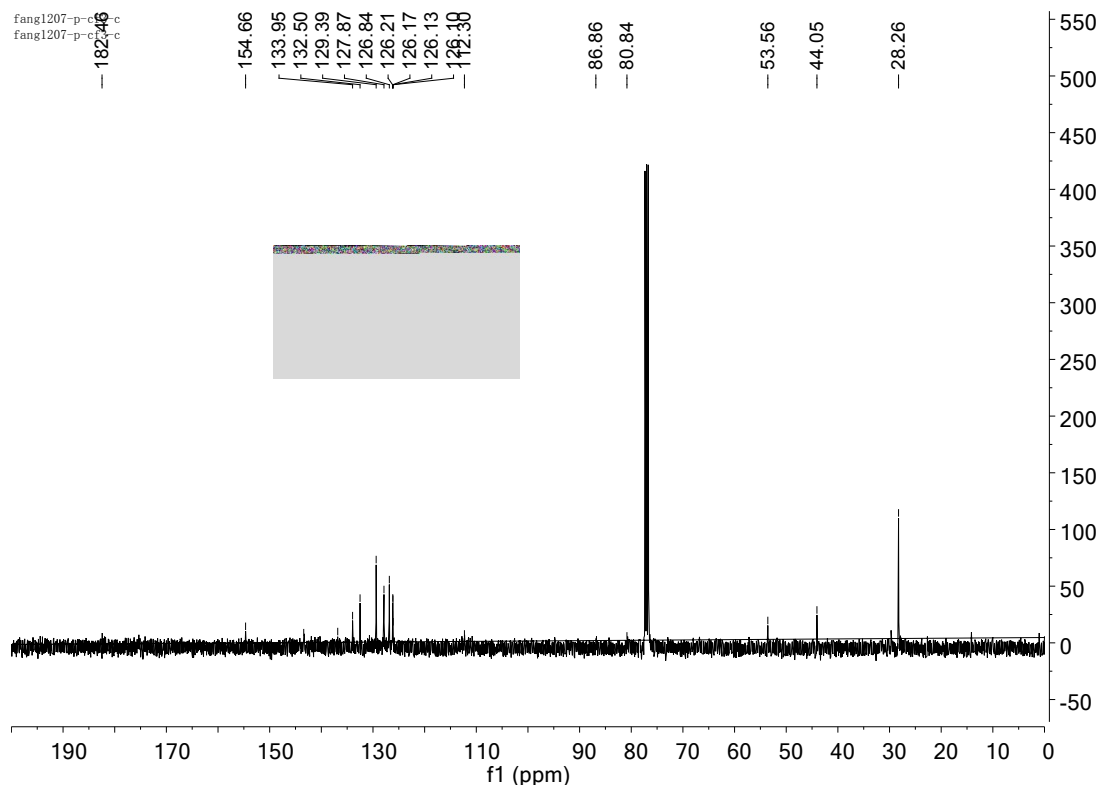


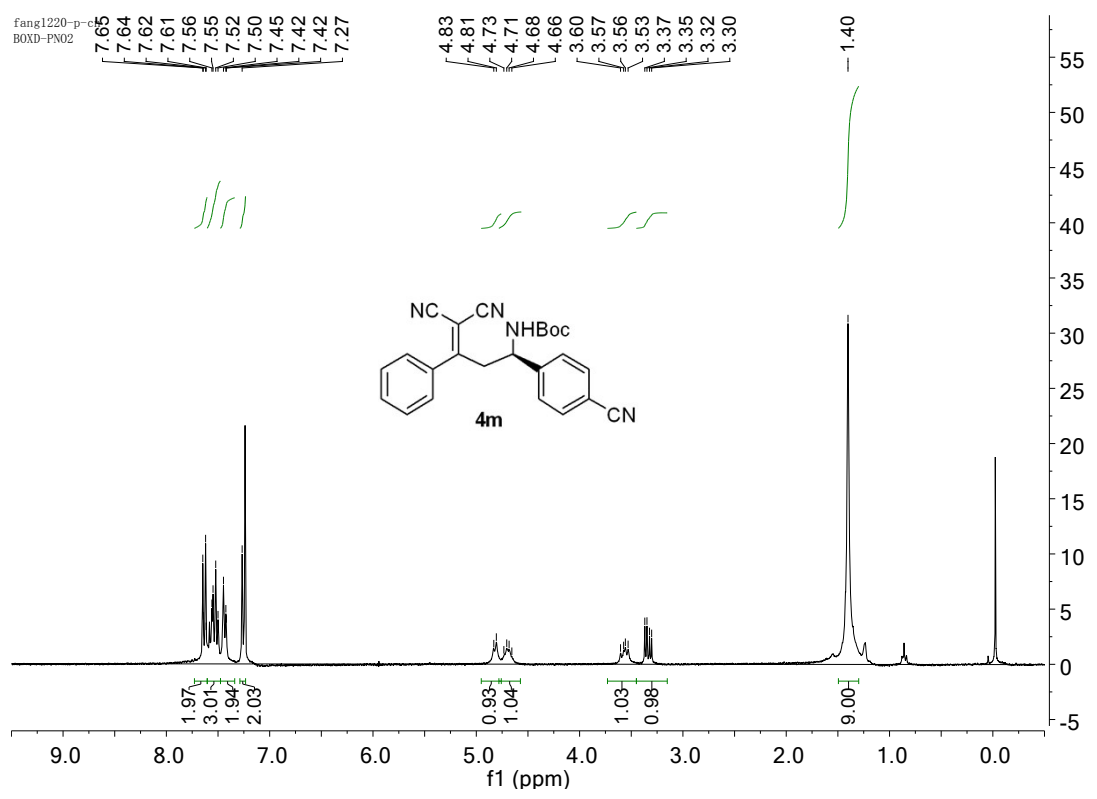
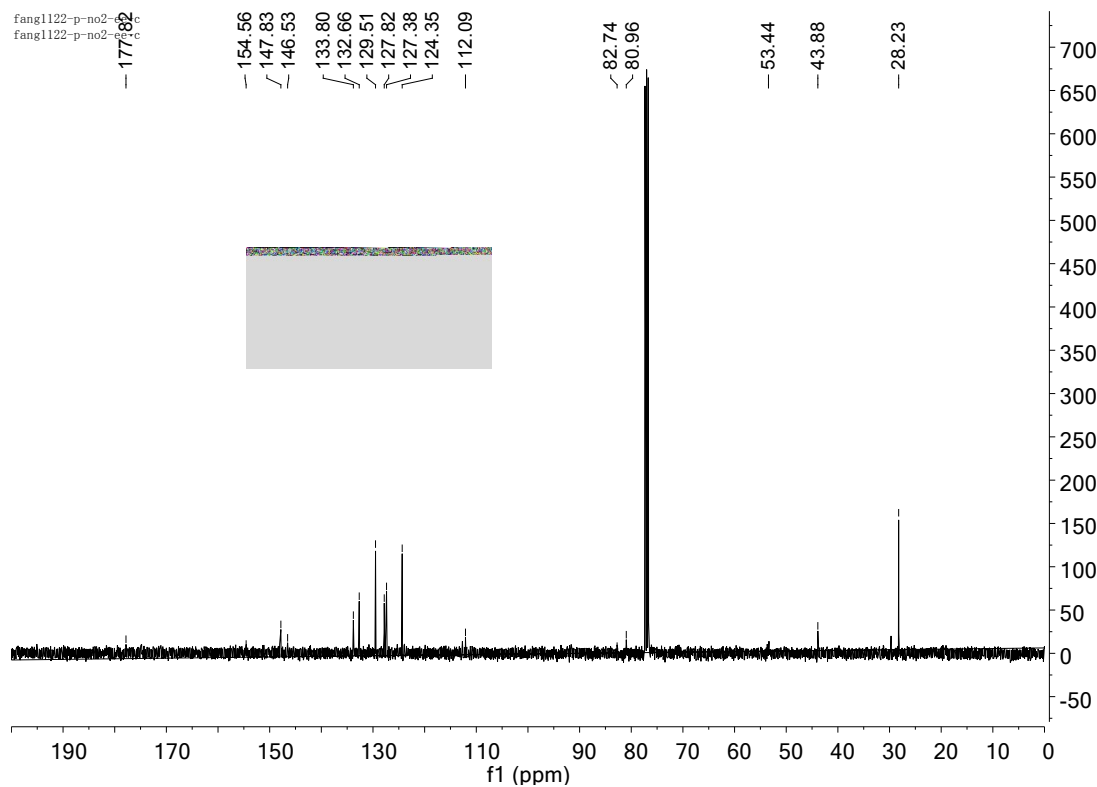


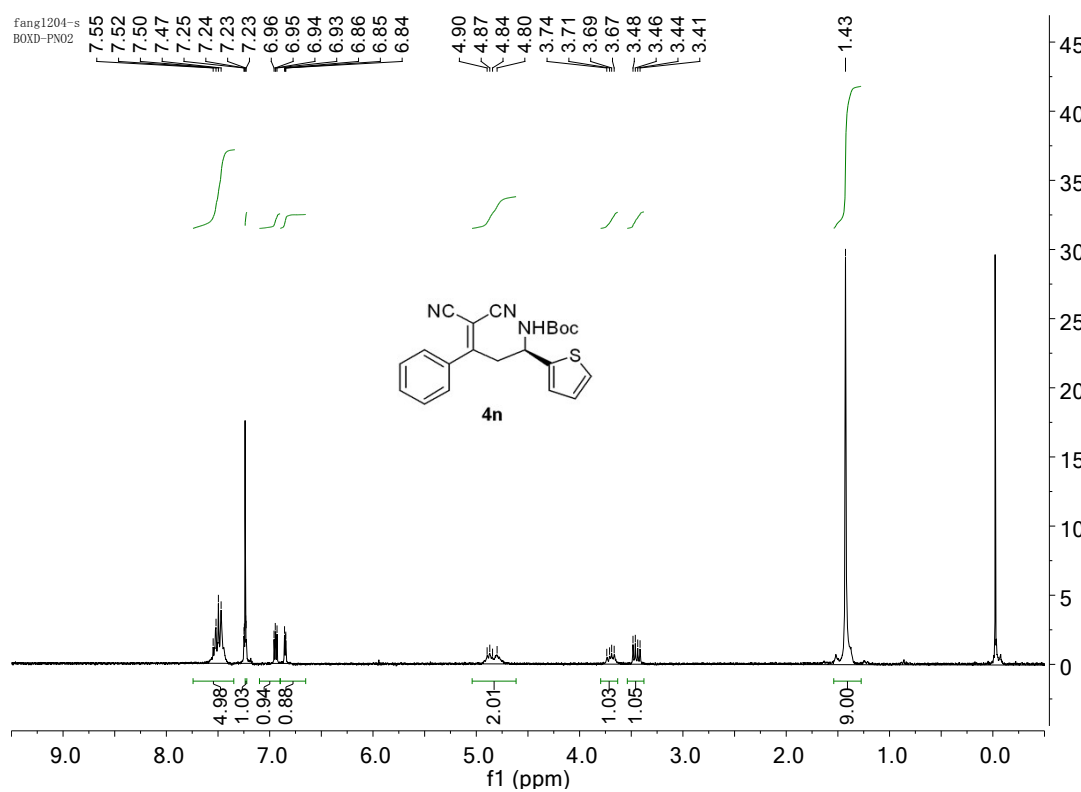
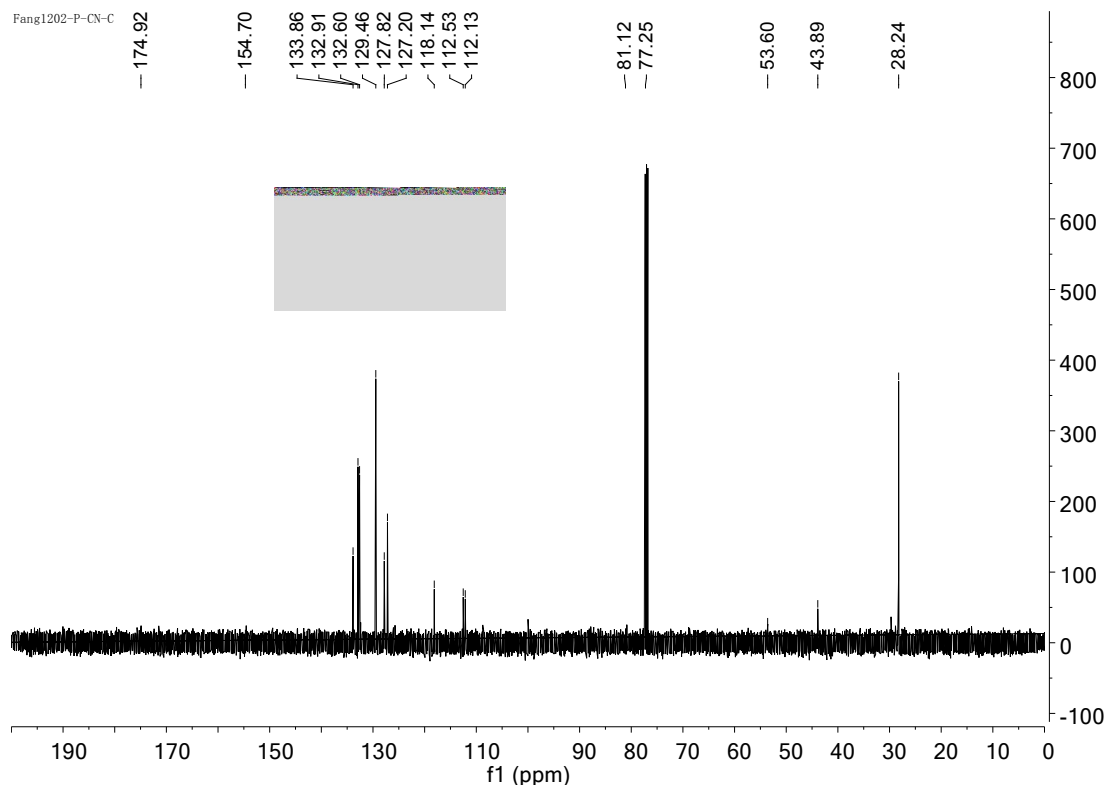


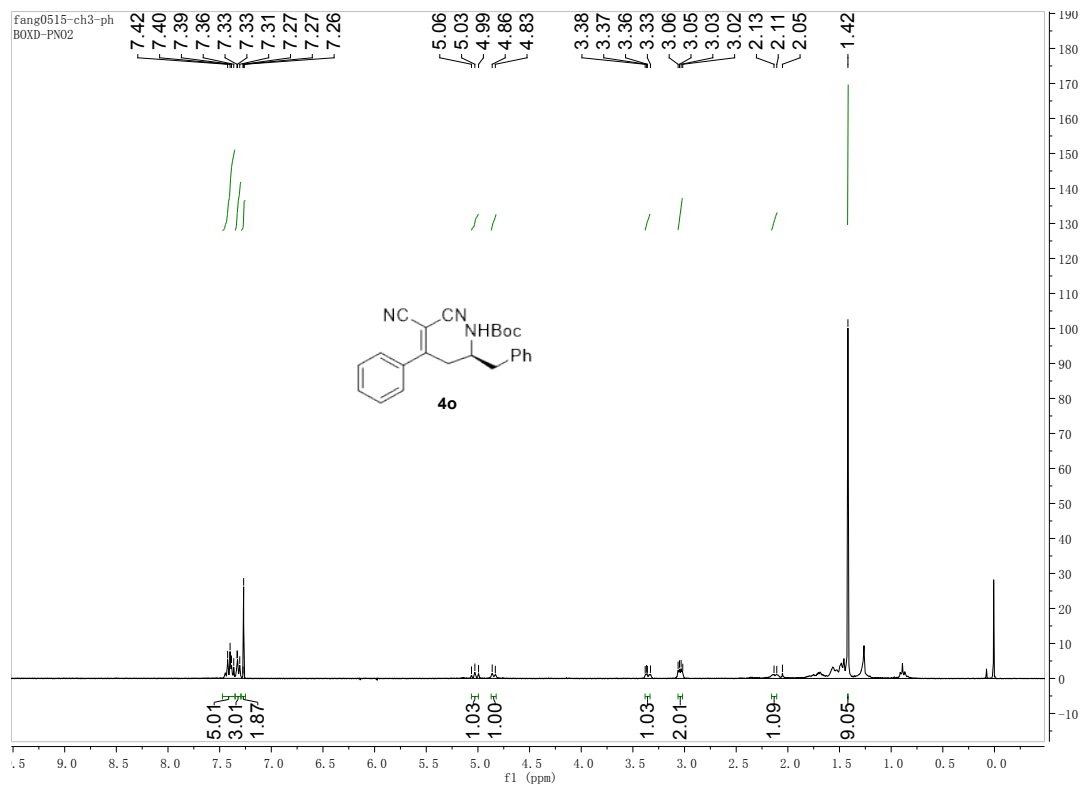
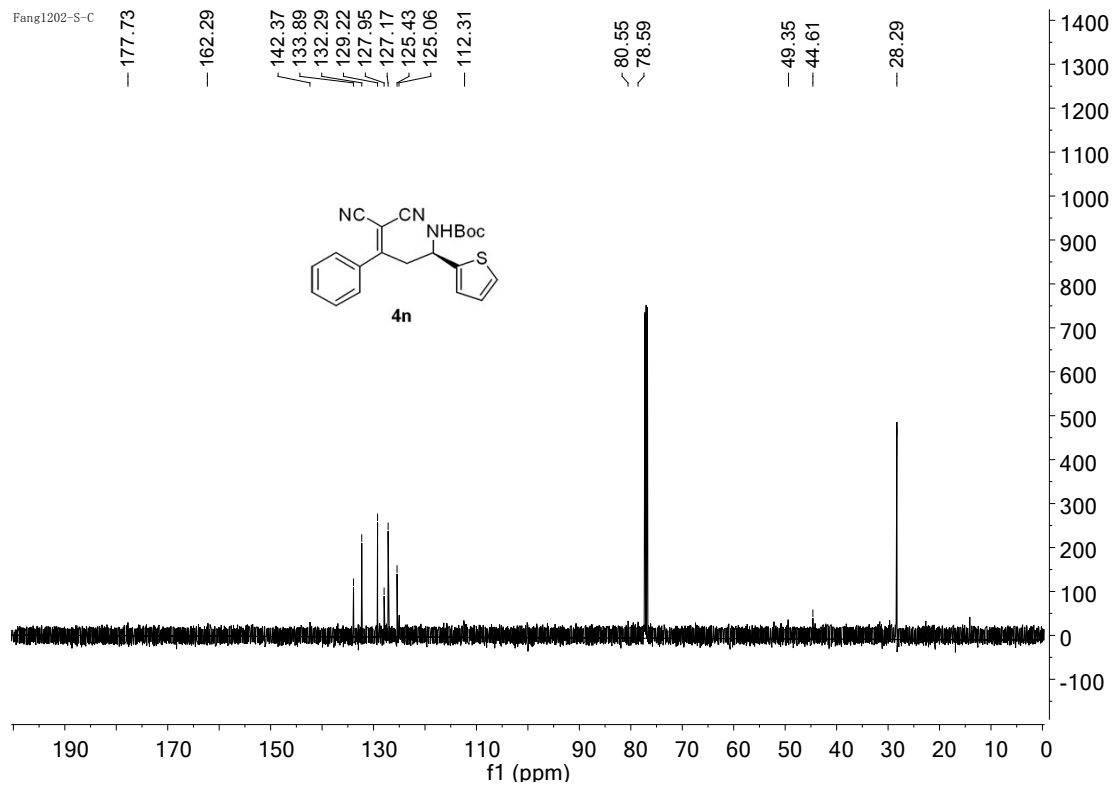




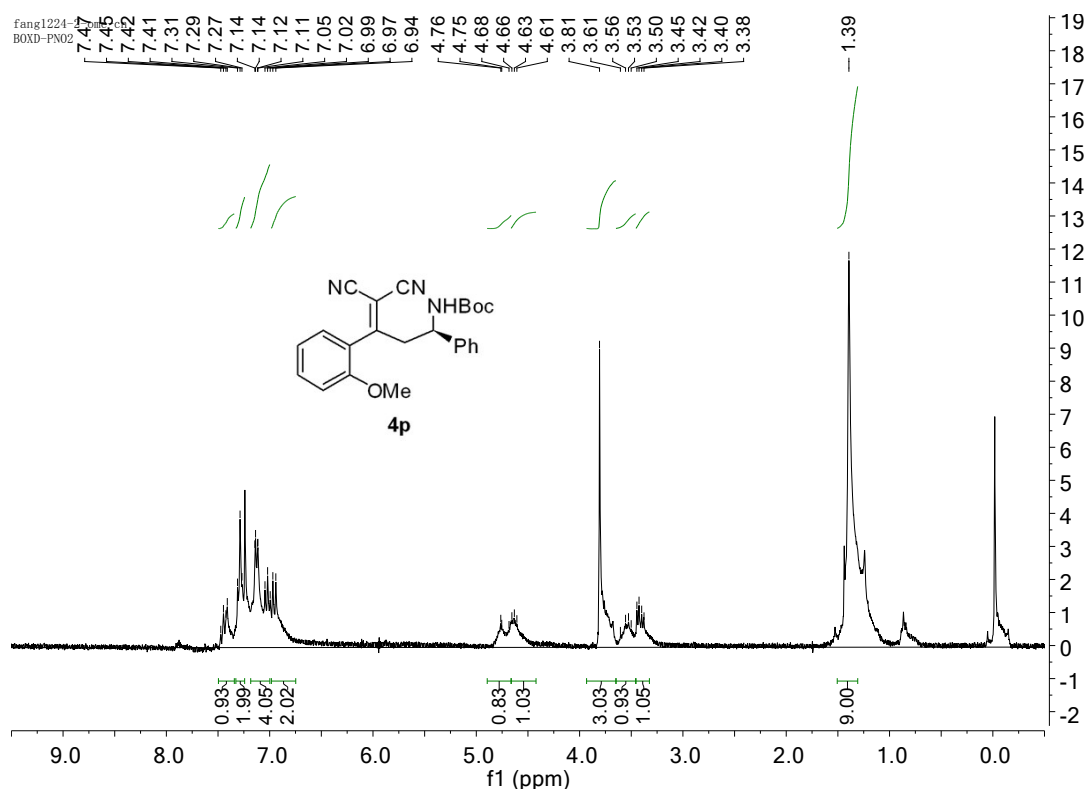
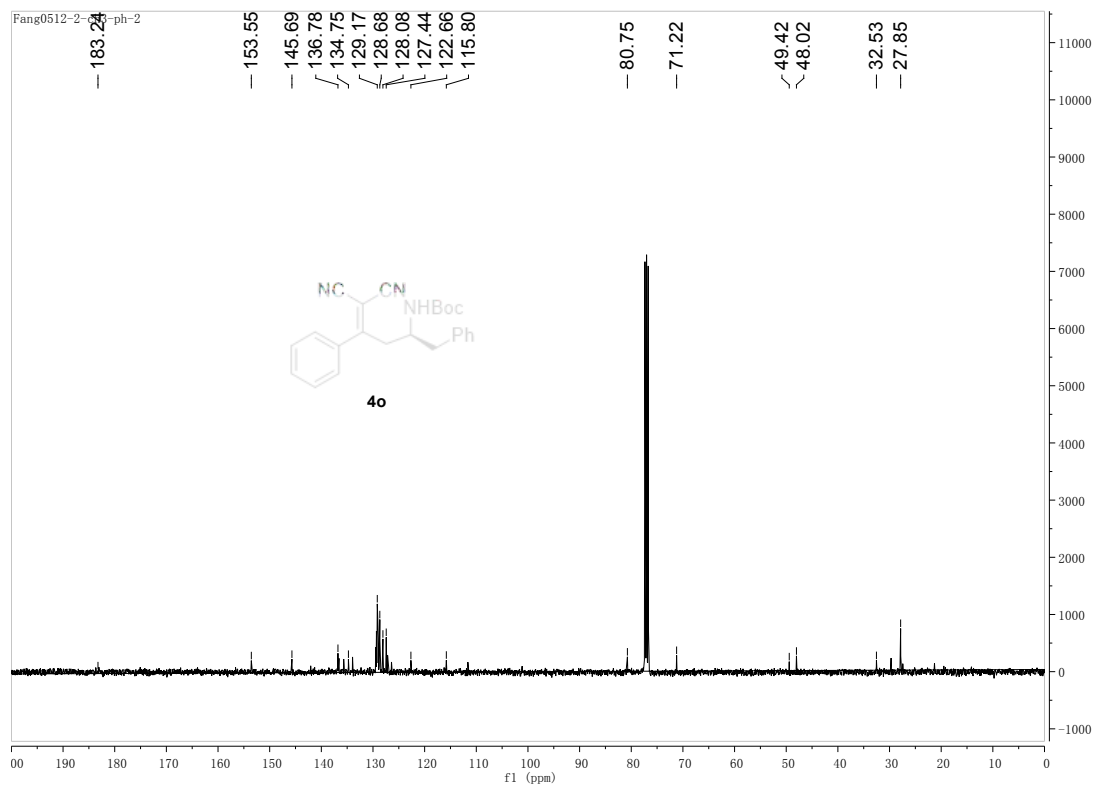


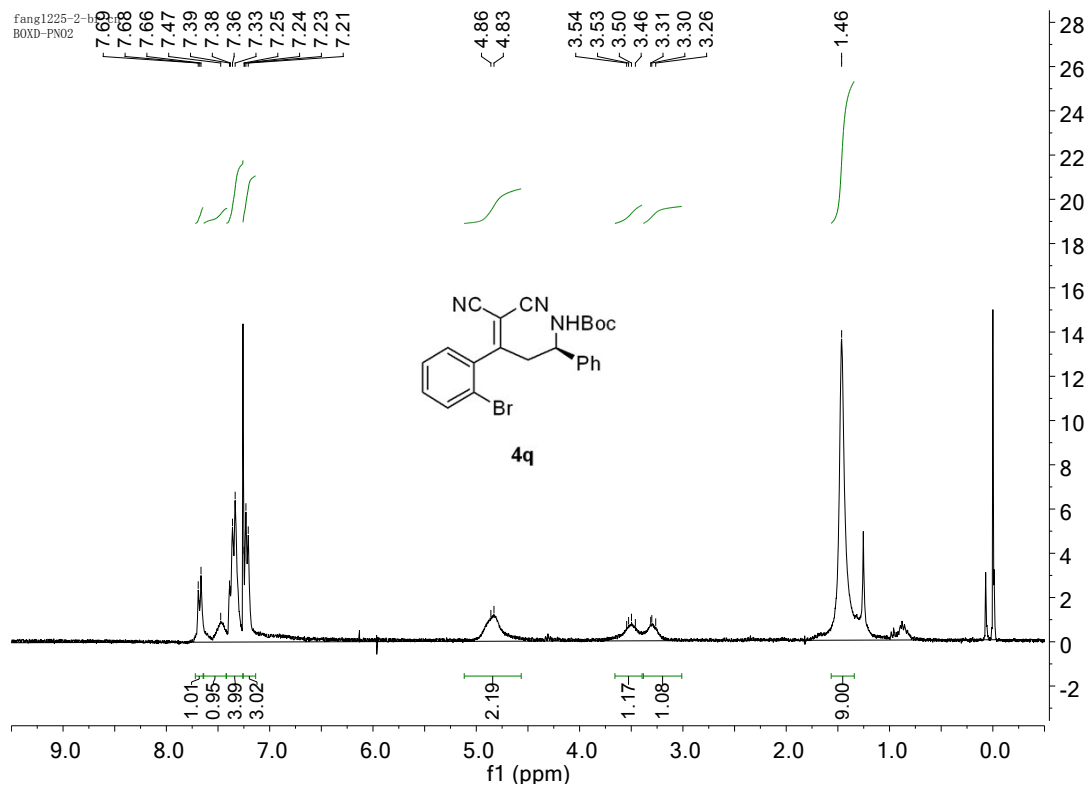
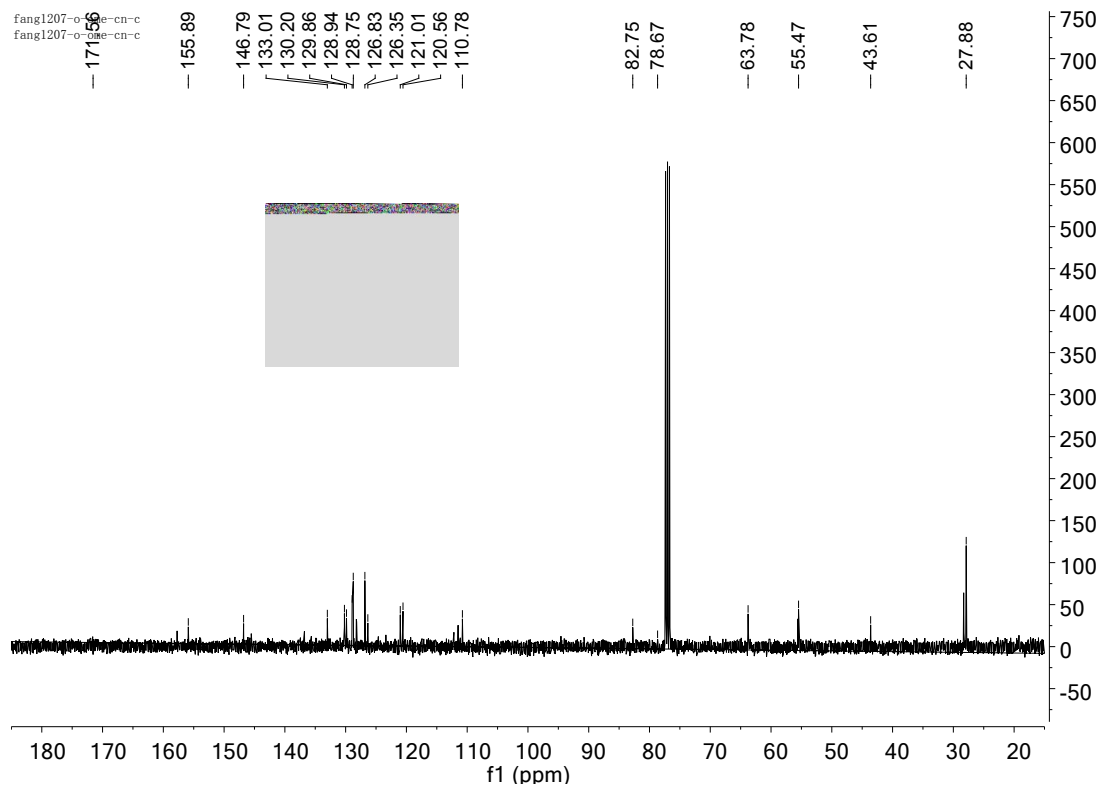


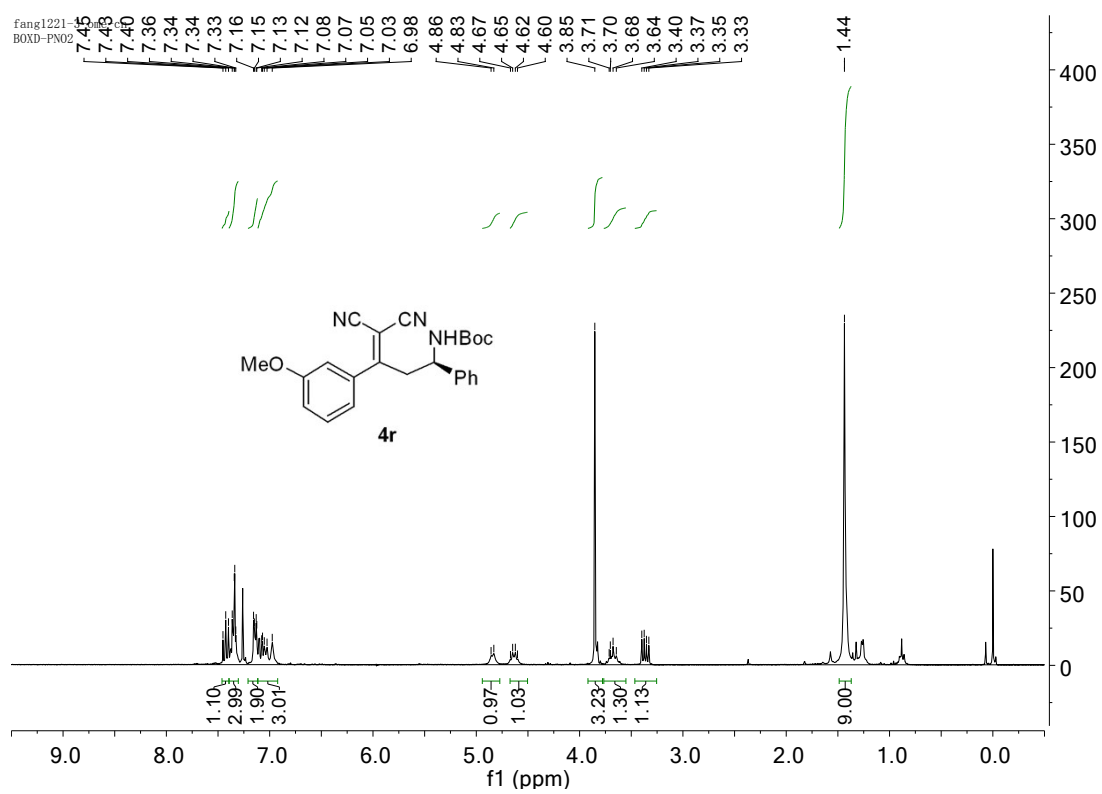
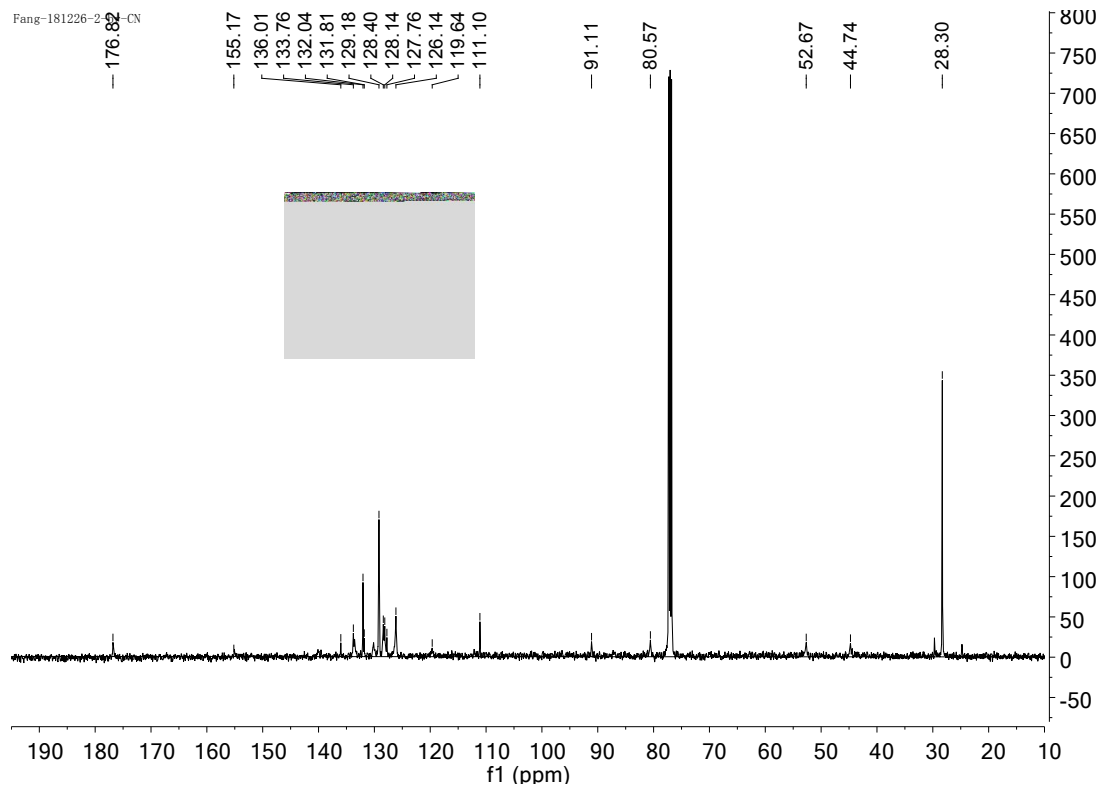


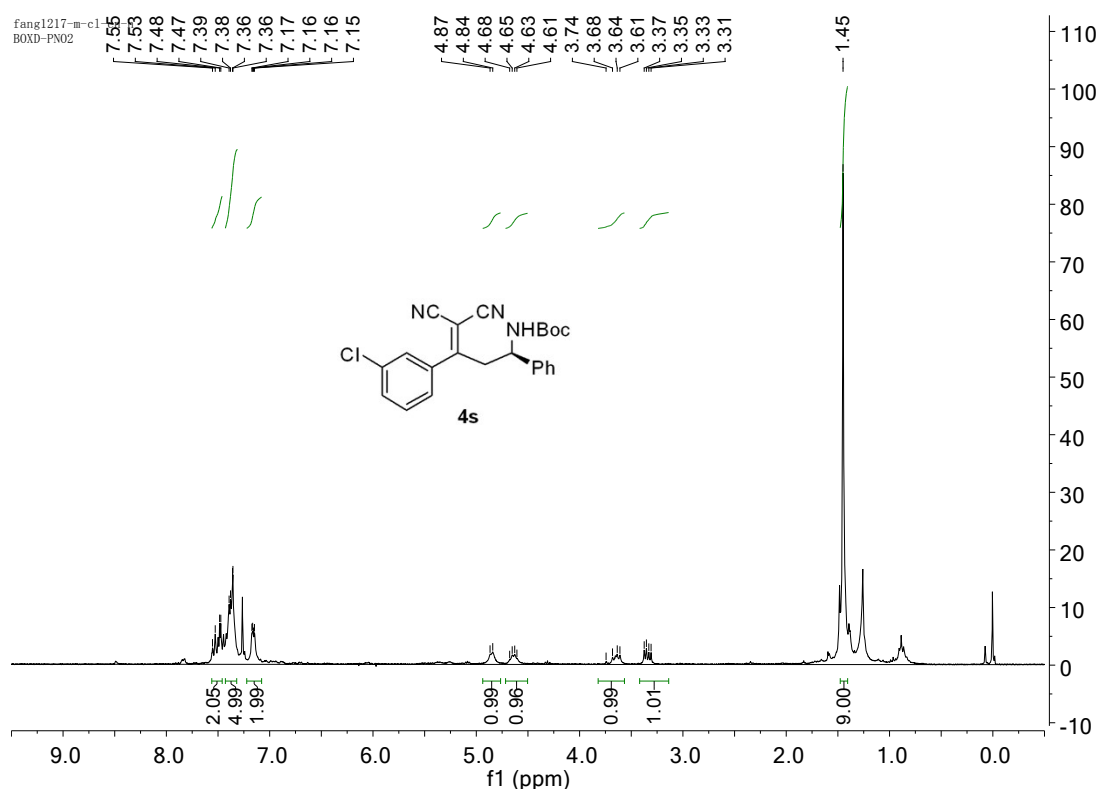
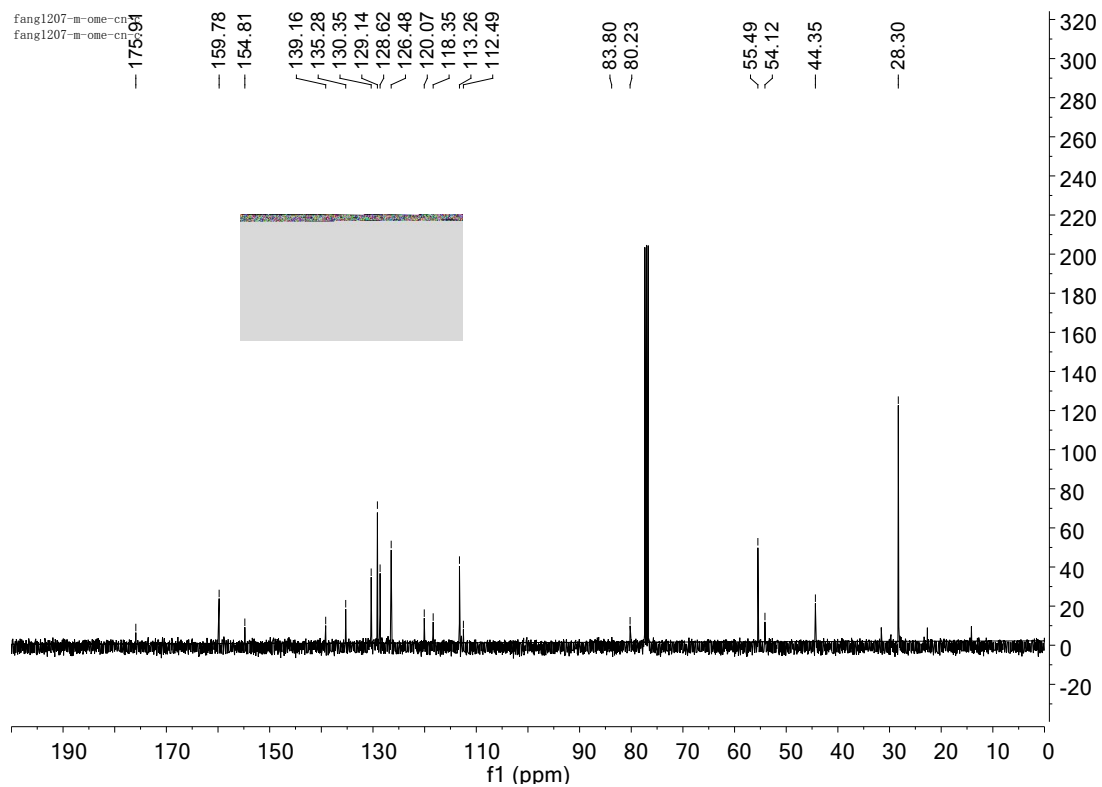


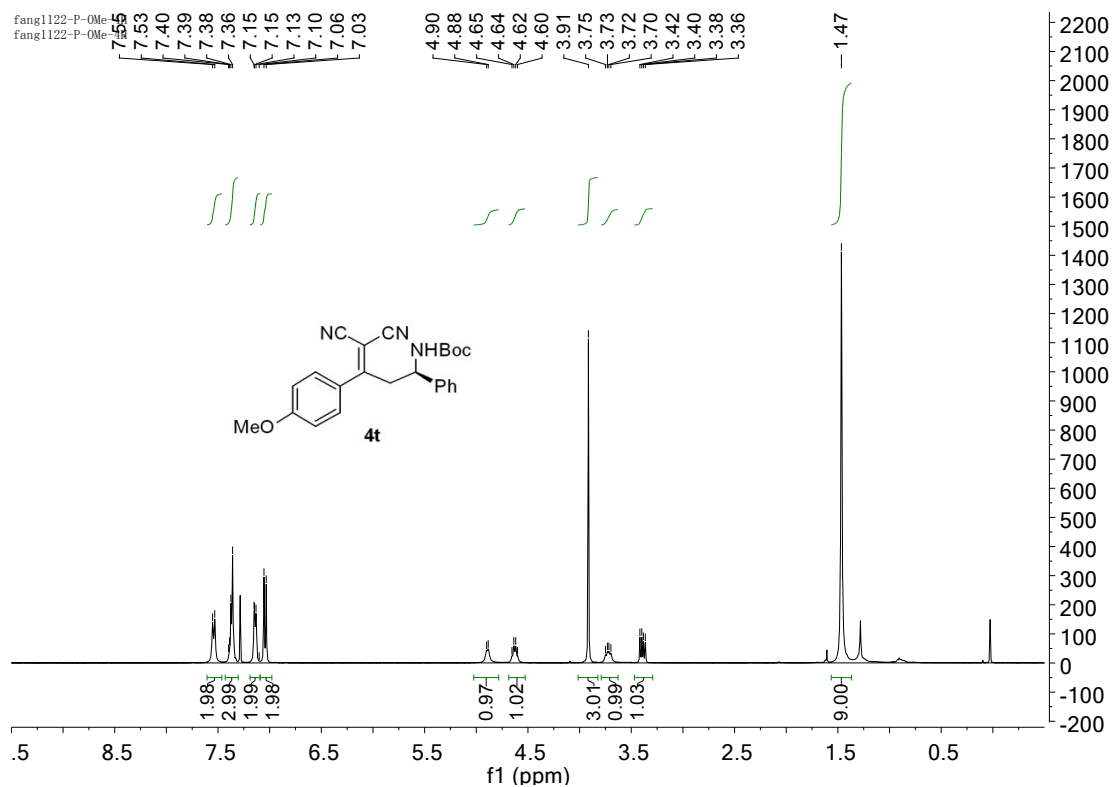
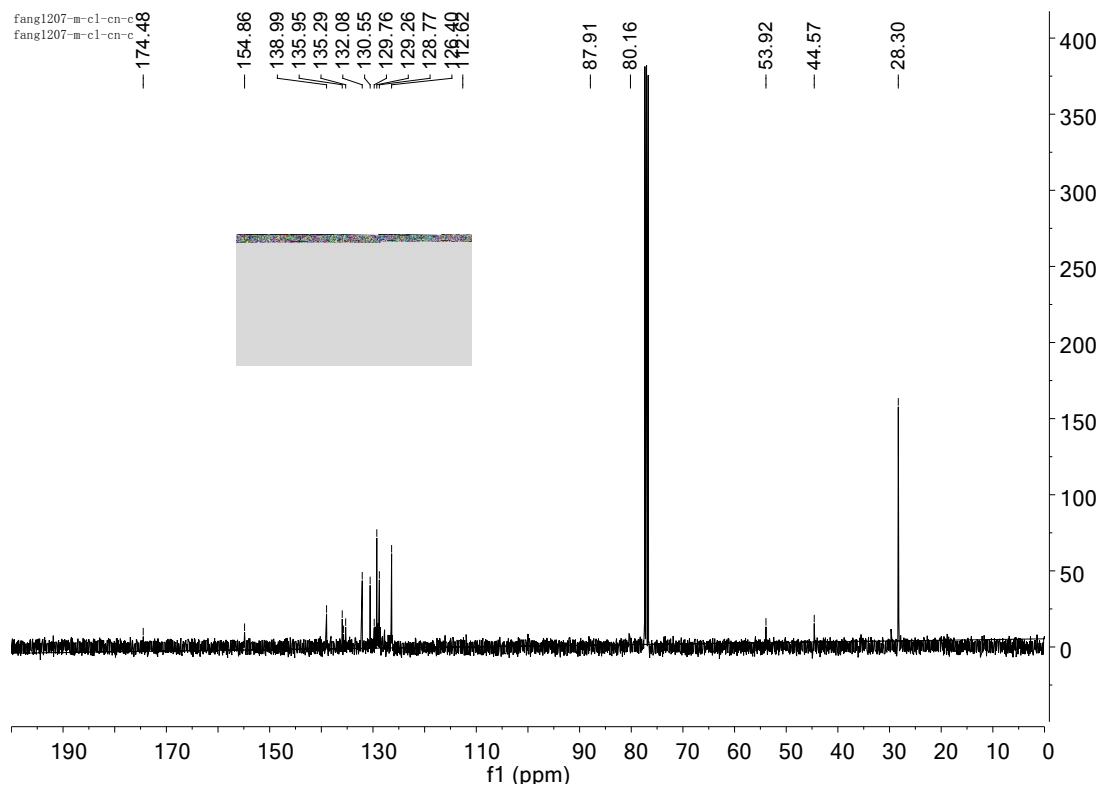


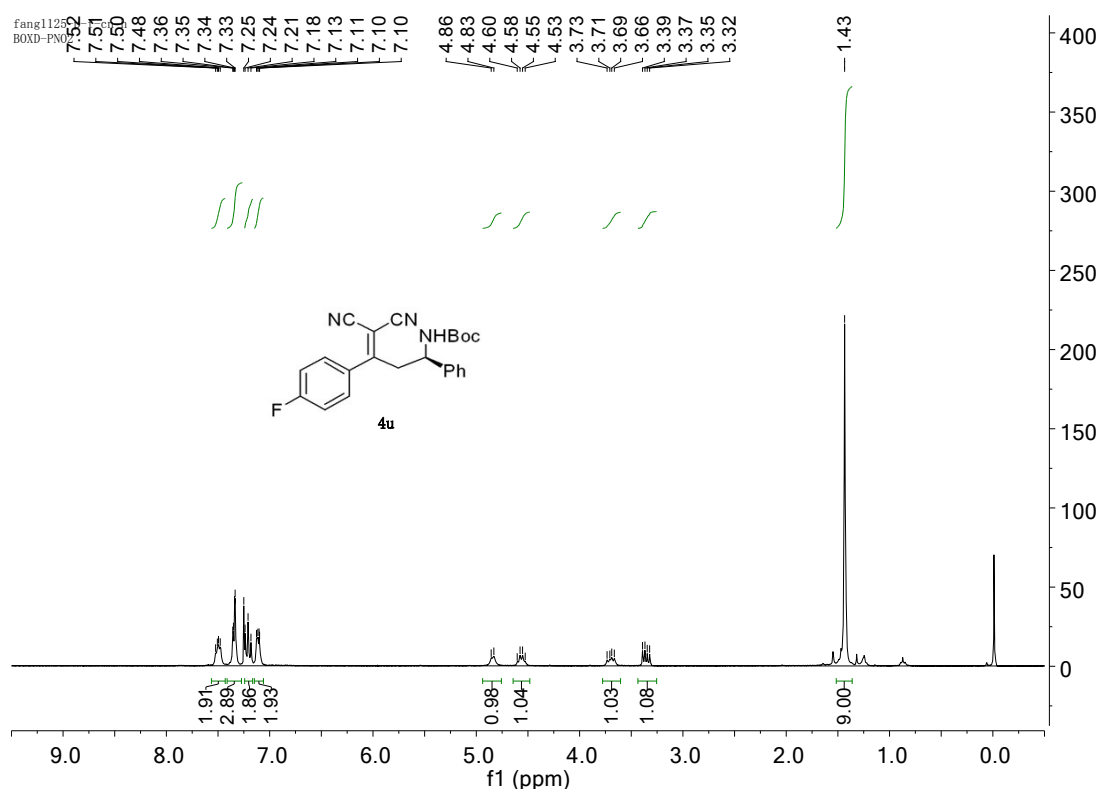
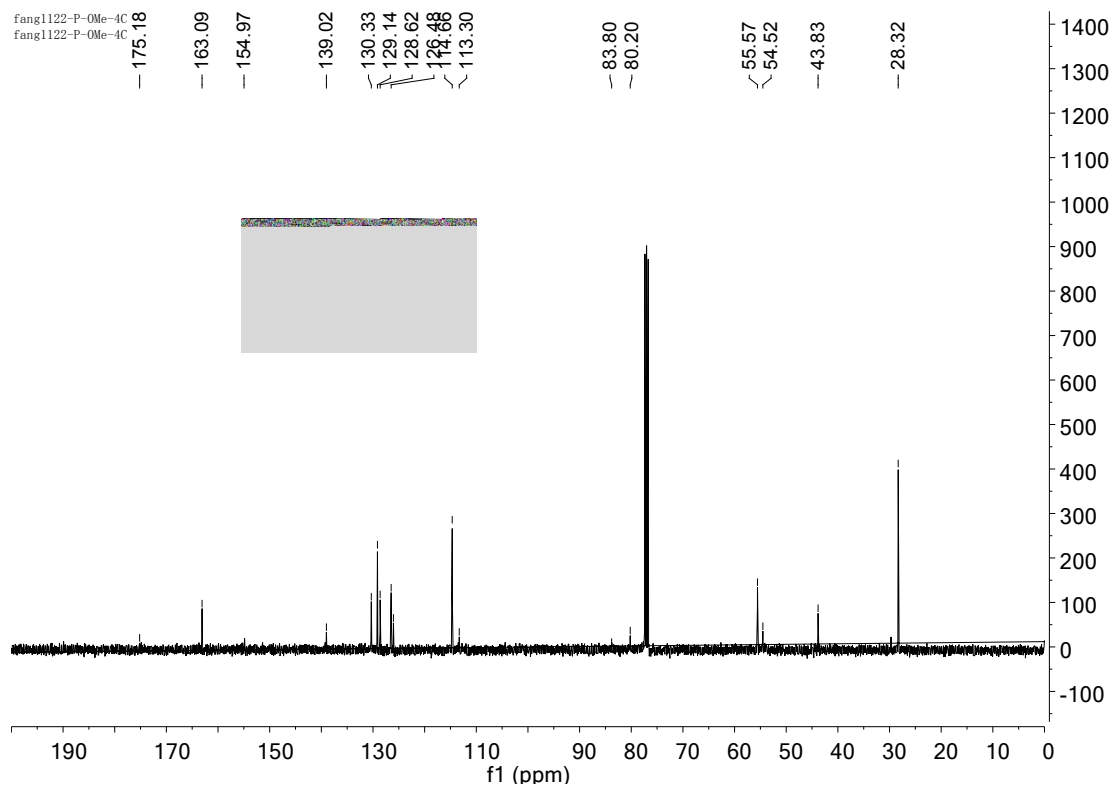


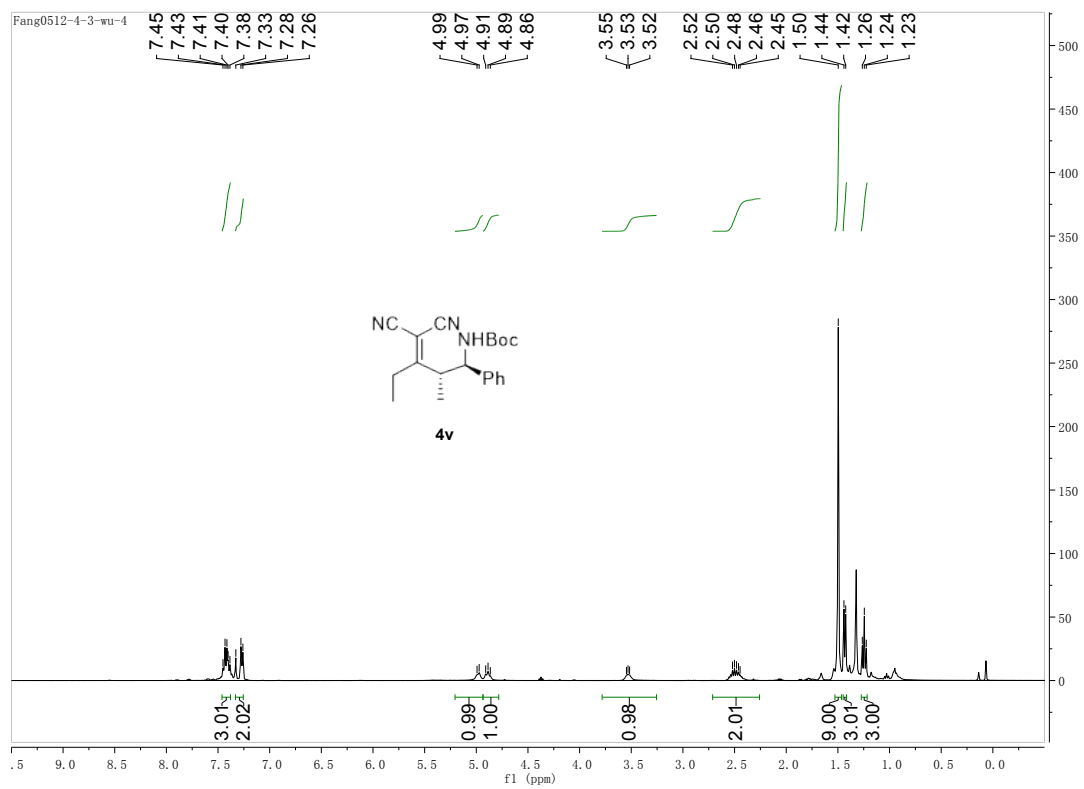
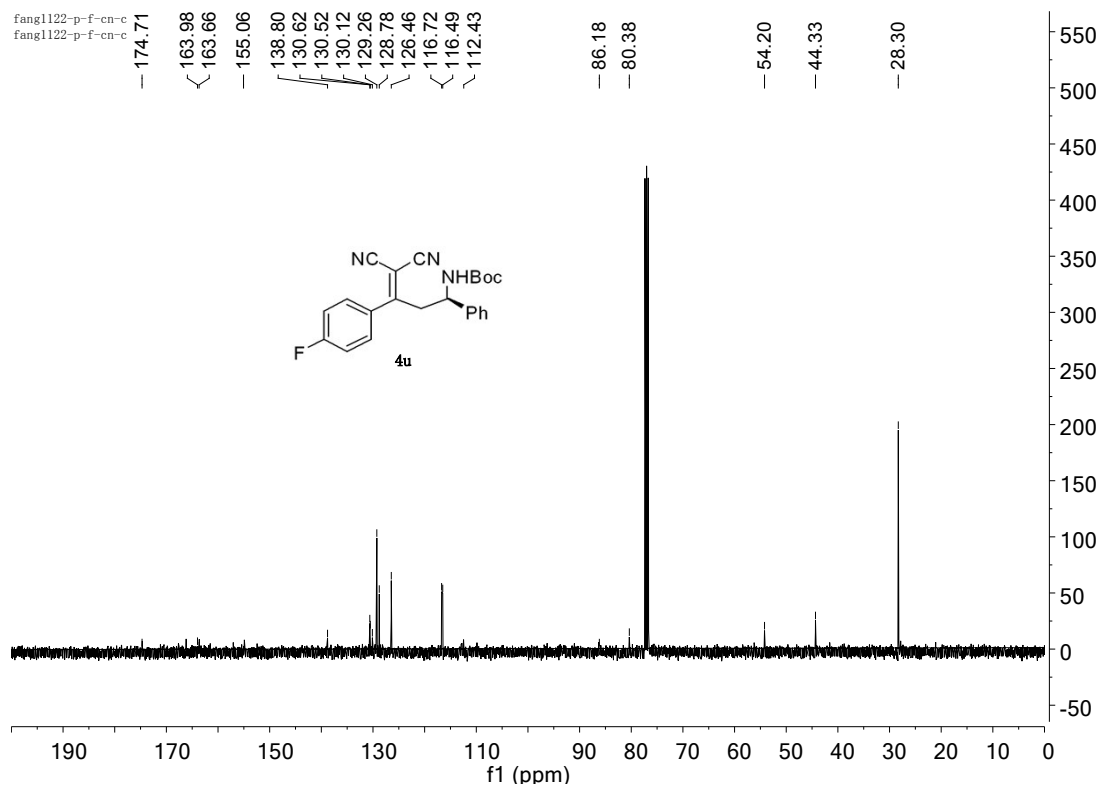


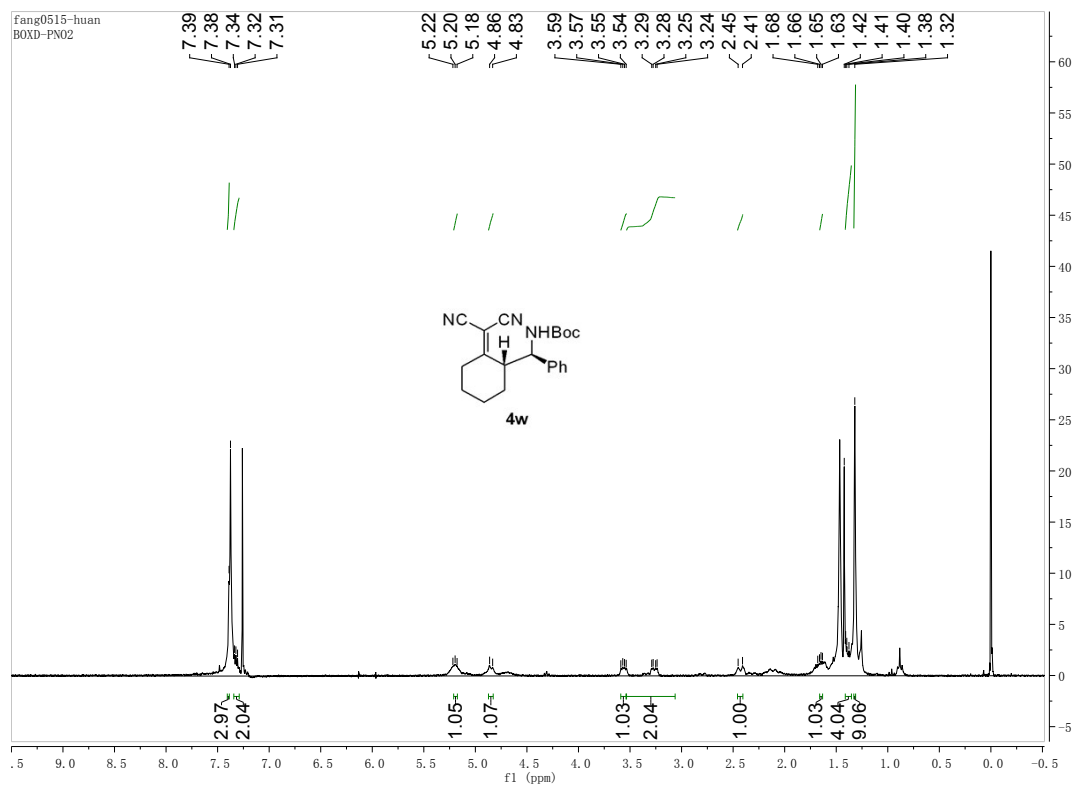
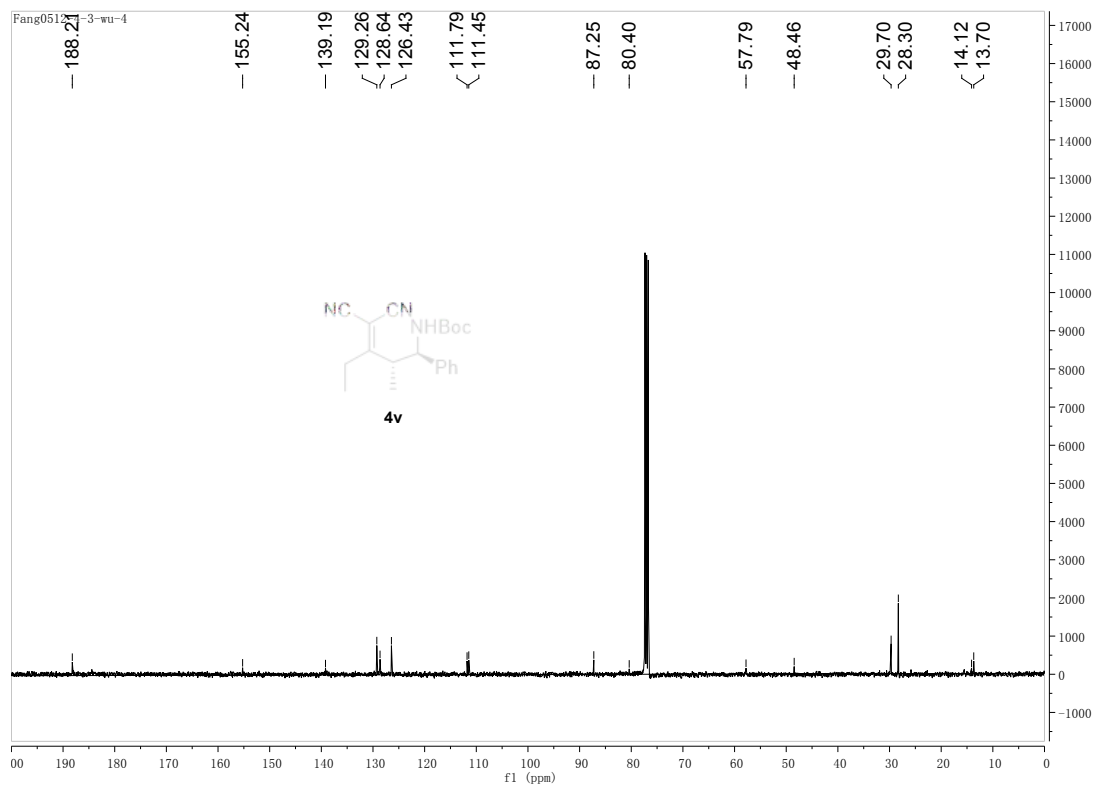




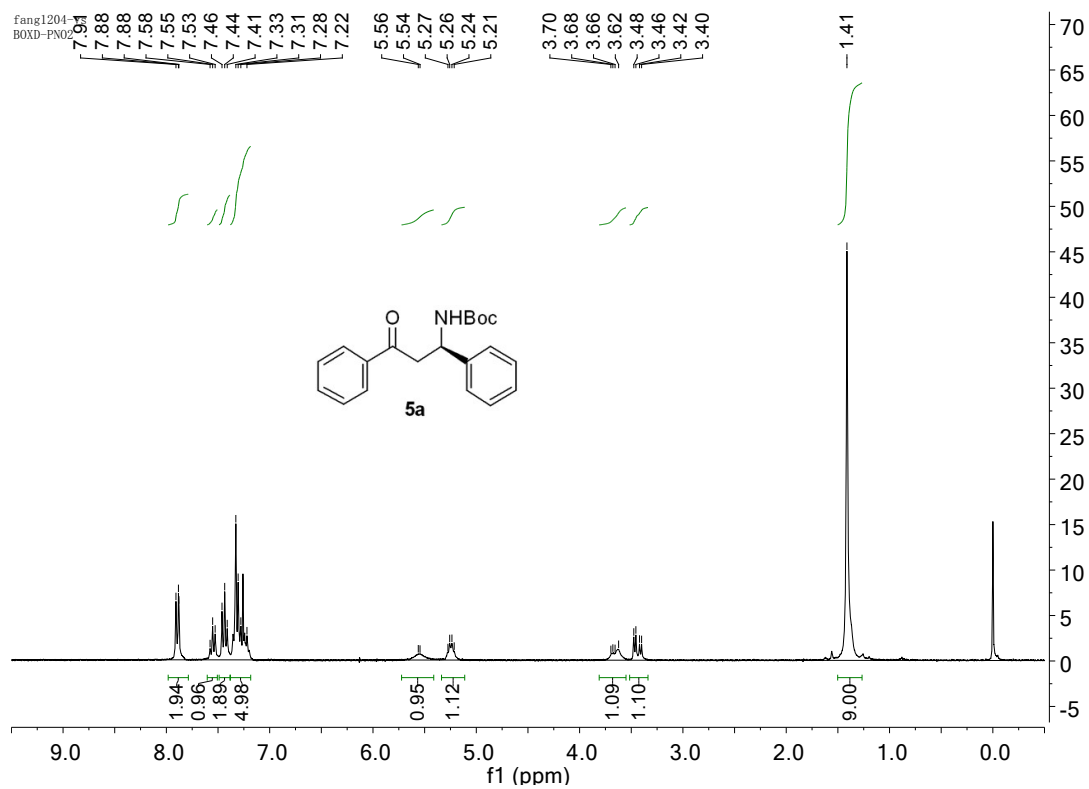
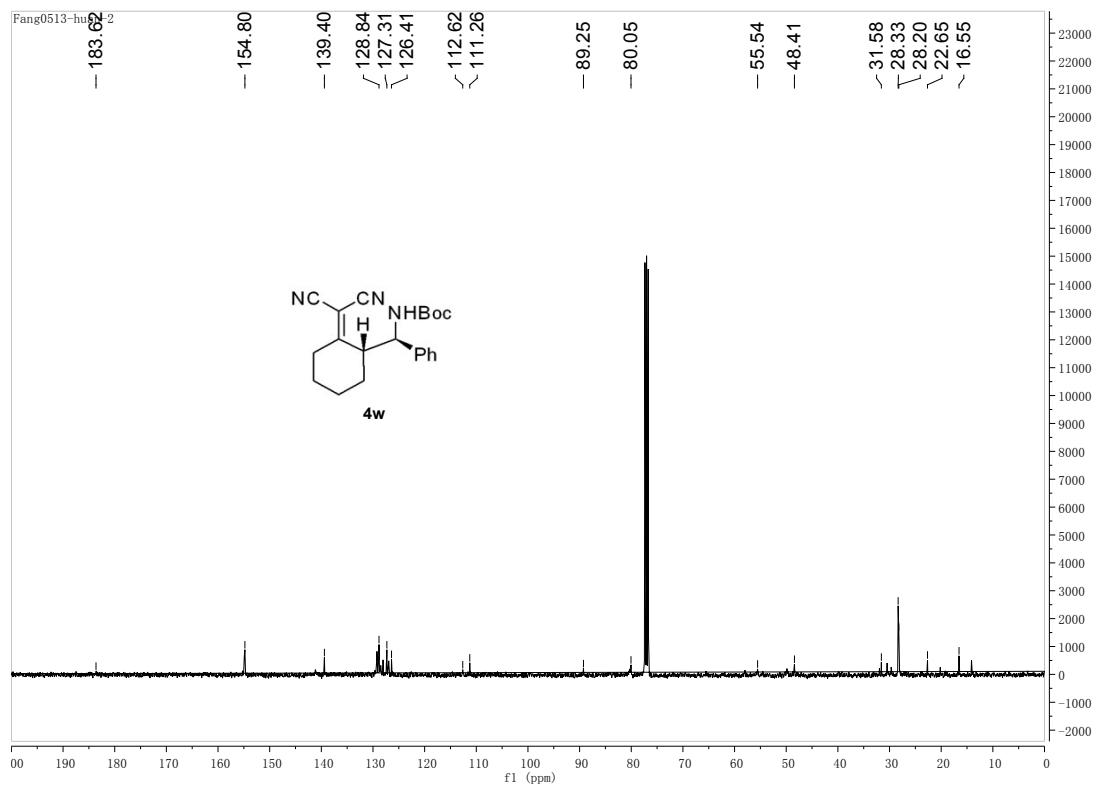


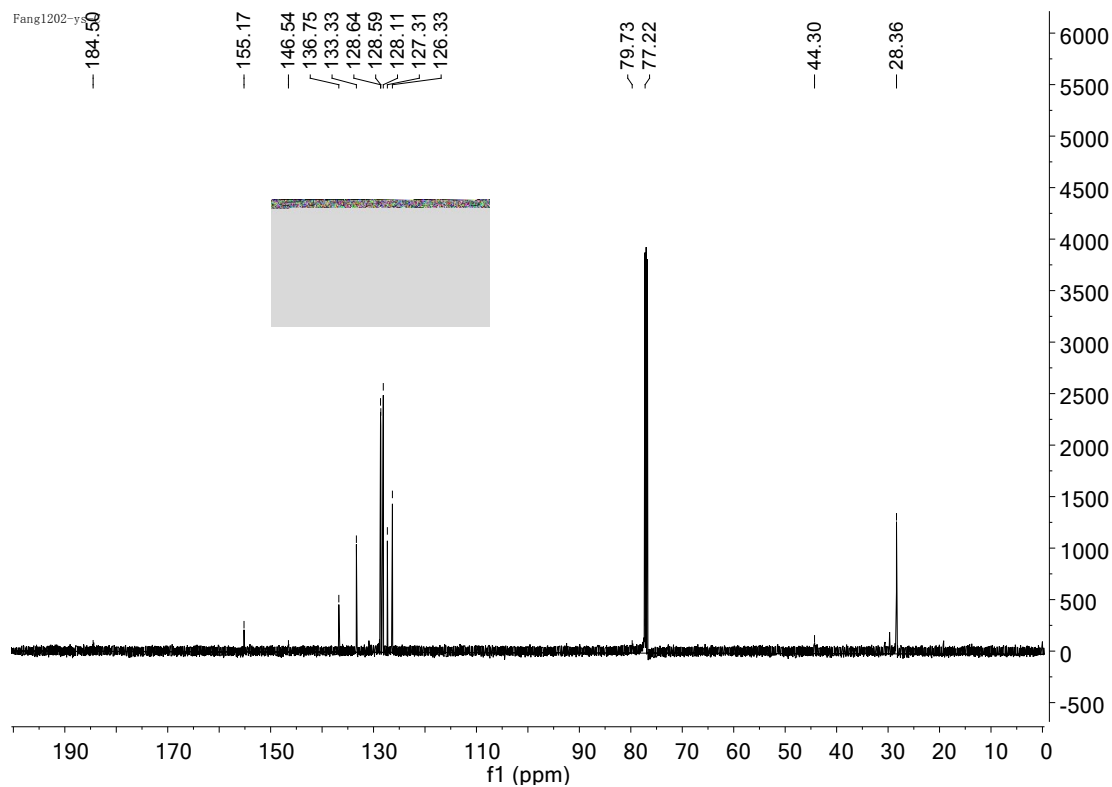




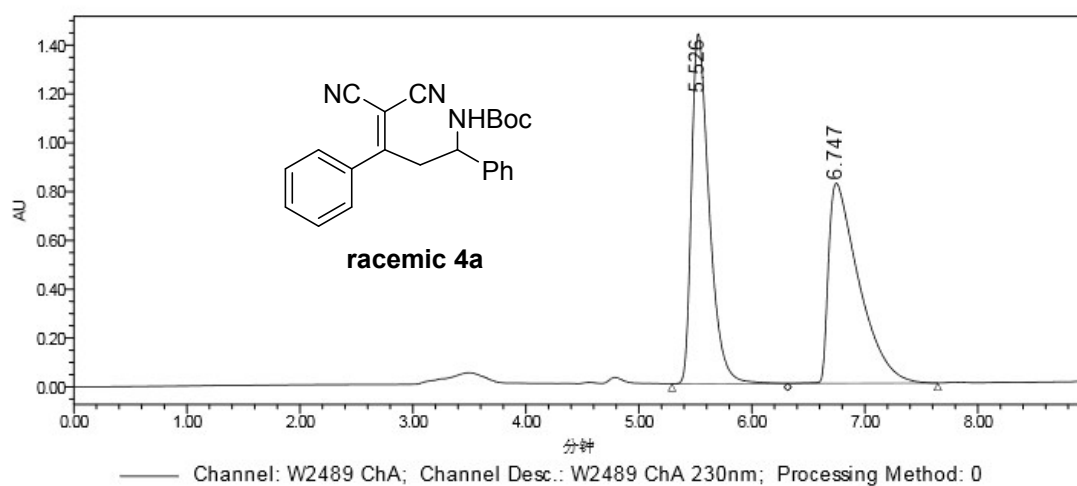




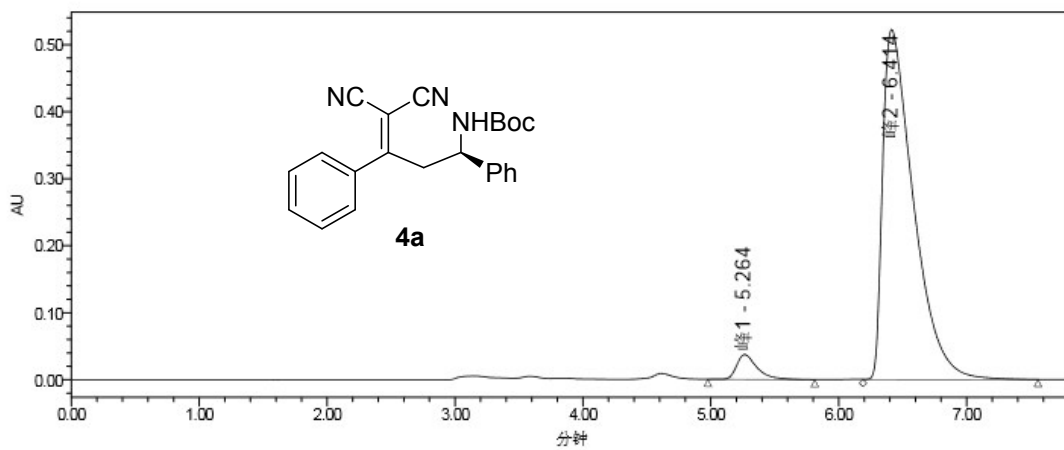




## 6. HPLC traces of all compounds 4a-4t and derivative 5a

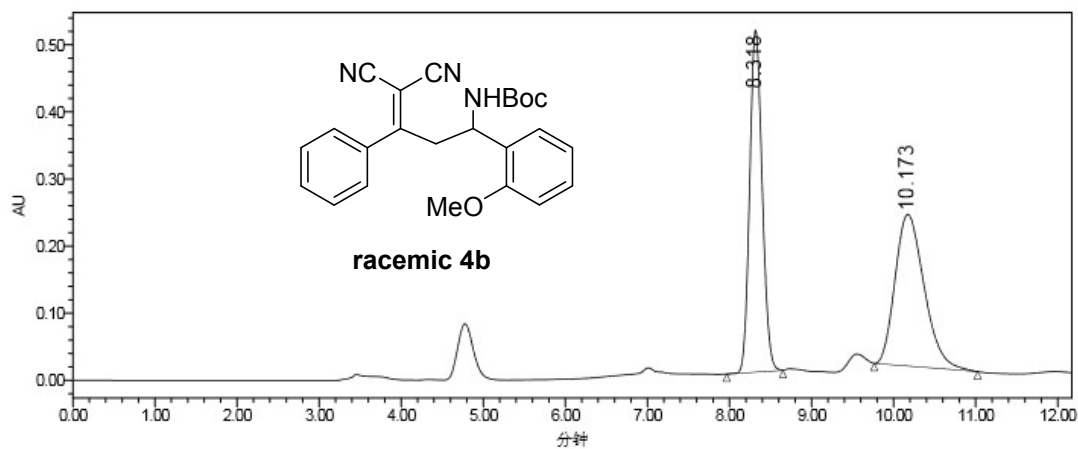


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	5.526	15621031	50.50	1432829
2	W2489 ChA 230nm	6.747	15312509	49.50	819484



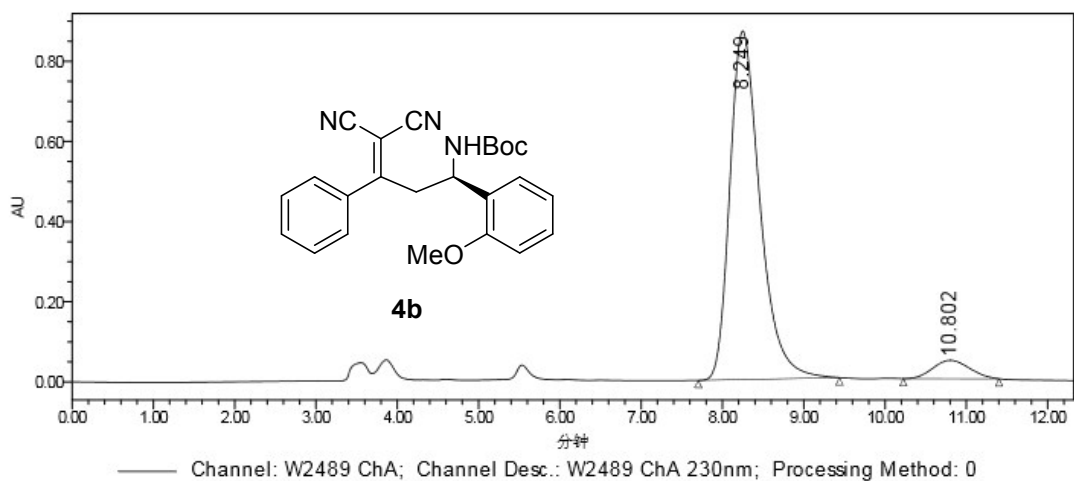
Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	5.264	406708	4.44	36906
2	W2489 ChA 230nm	峰2	6.414	8747568	95.56	522093

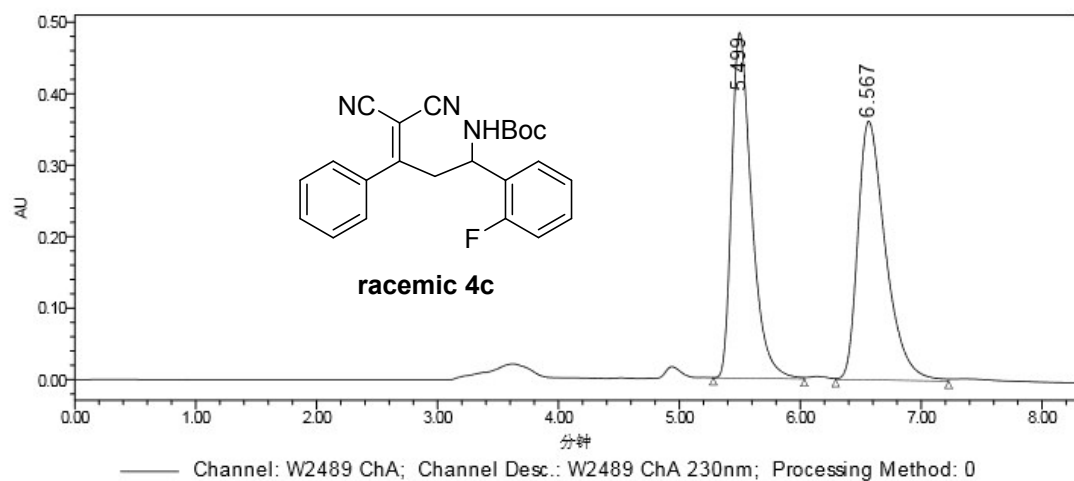


Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

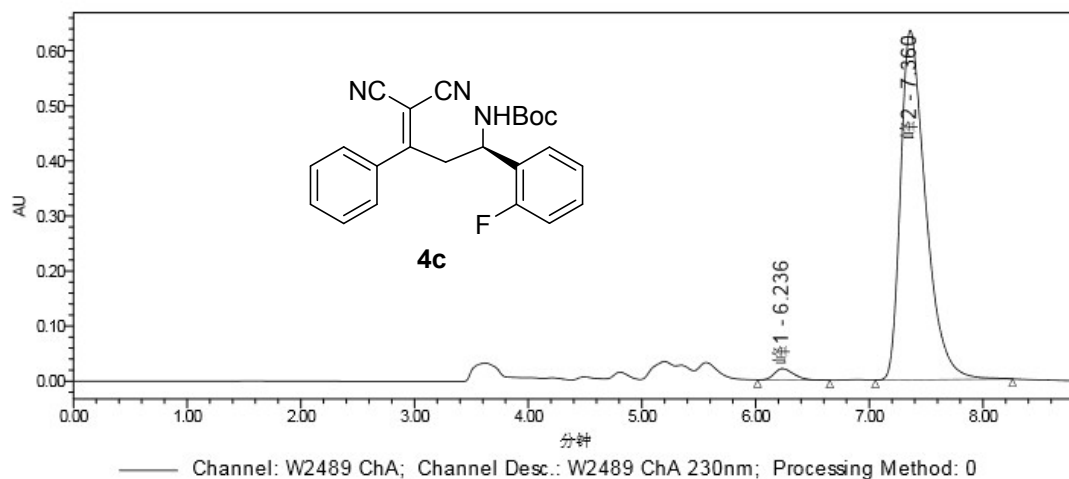
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	8.318	5376731	49.14	509657
2	W2489 ChA 230nm	10.173	5564872	50.86	225966



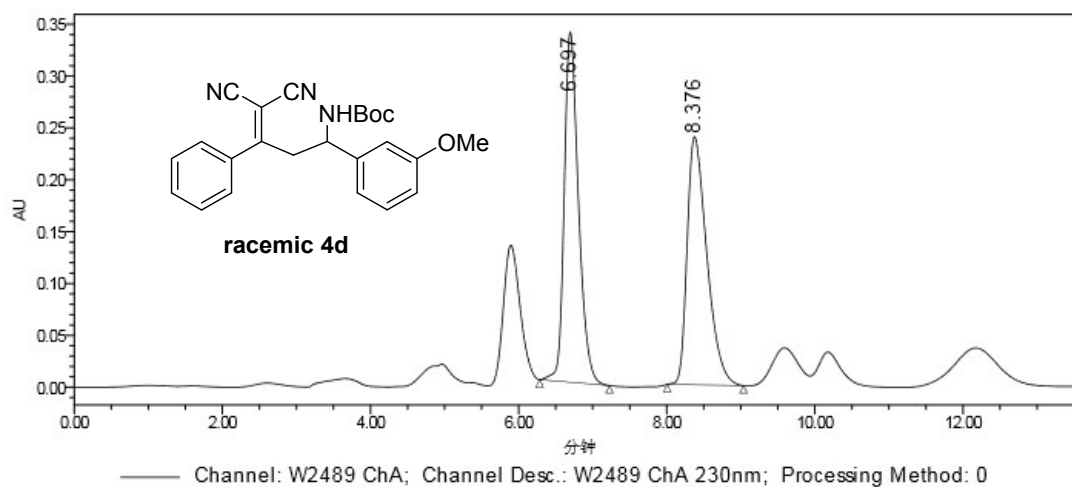
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	8.249	22424838	93.99	869221
2	W2489 ChA 230nm	10.802	1432841	6.01	45841



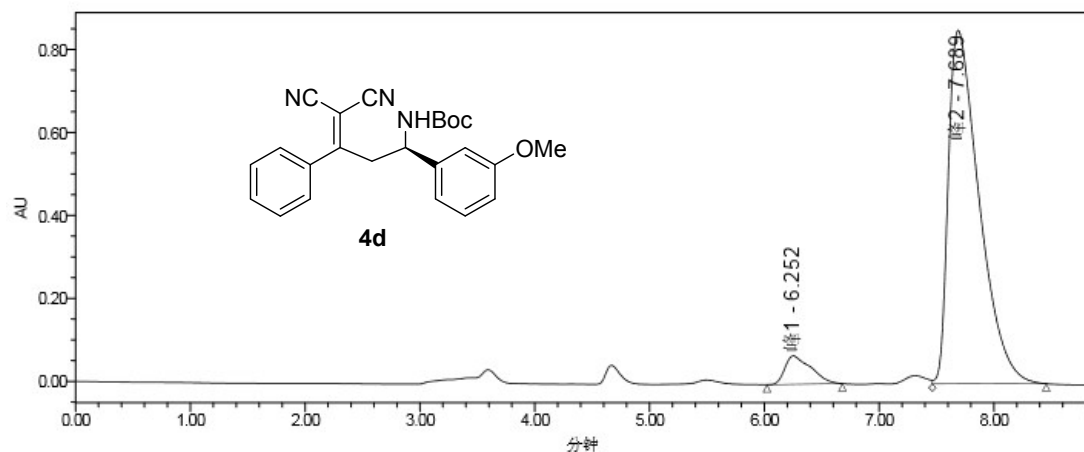
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	5.499	5541822	49.05	483303
2	W2489 ChA 230nm	6.567	5756794	50.95	361808



	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	6.236	244260	2.44	20565
2	W2489 ChA 230nm	峰2	7.360	9753718	97.56	634779

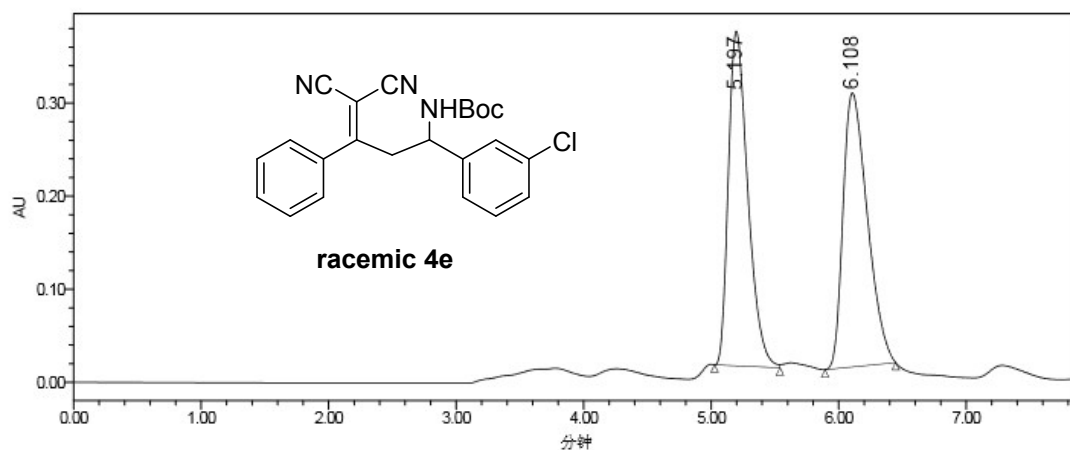


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	6.697	4508939	50.50	337567
2	W2489 ChA 230nm	8.376	4419809	49.50	239033



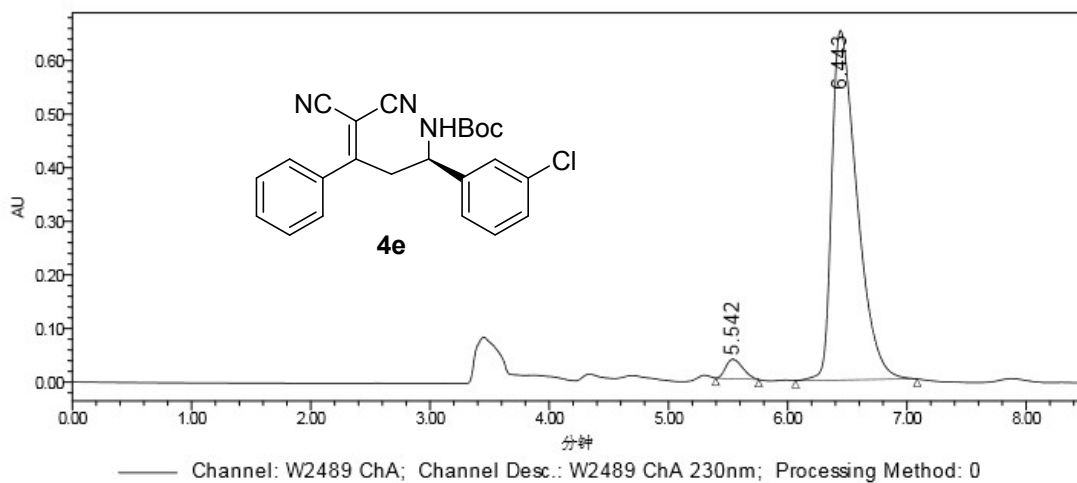
Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	6.252	1074575	6.32	68377
2	W2489 ChA 230nm	峰2	7.689	15922986	93.68	851939

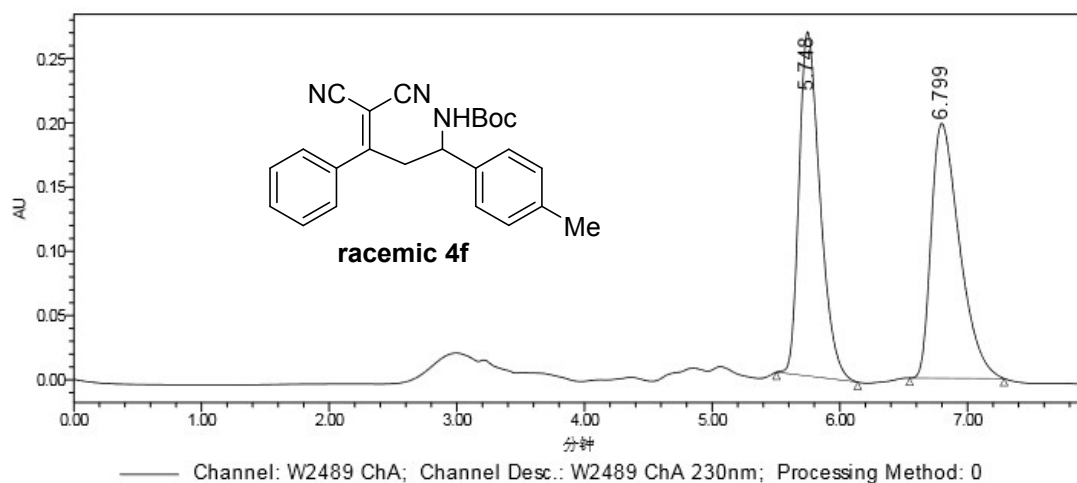


Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

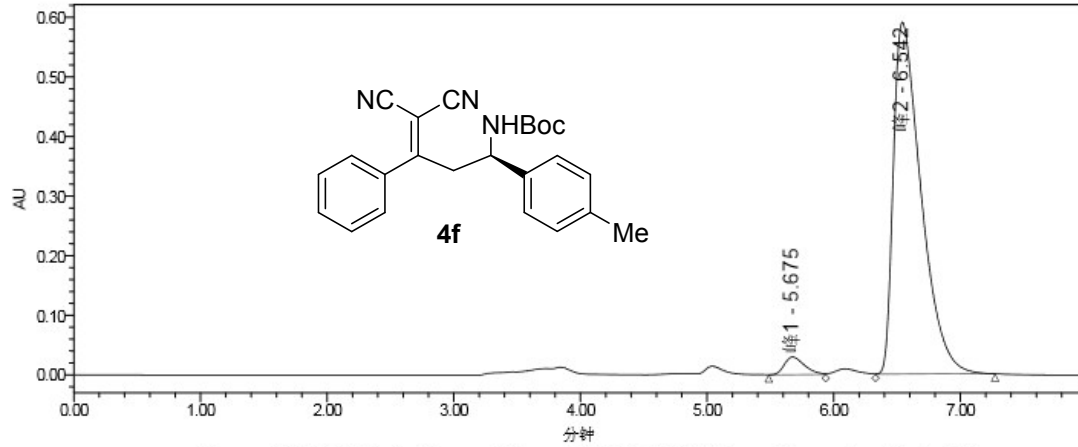
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	5.197	3806297	49.38	359396
2	W2489 ChA 230nm	6.108	3901400	50.62	294223



	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	5.542	357365	3.59	36161
2	W2489 ChA 230nm	6.443	9600649	96.41	651842

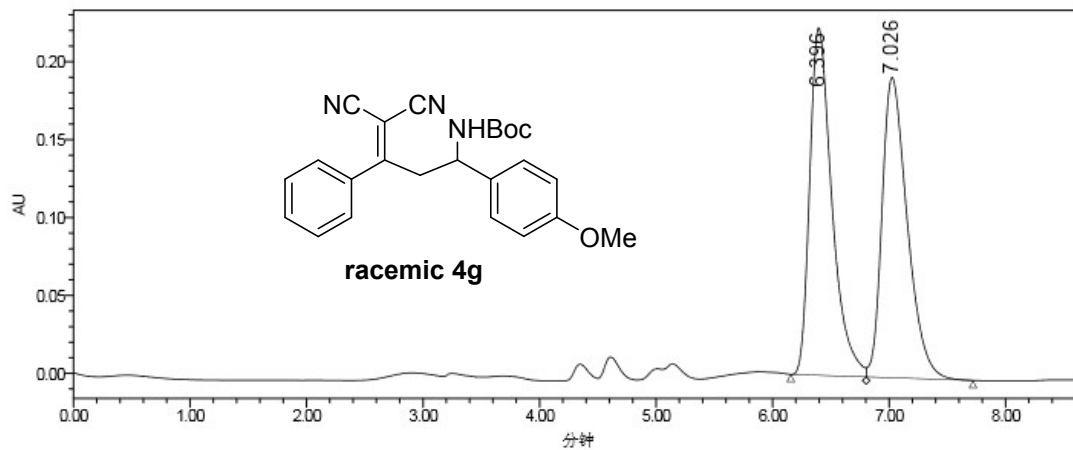


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	5.748	3065494	50.04	267677
2	W2489 ChA 230nm	6.799	3060306	49.96	198189



Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

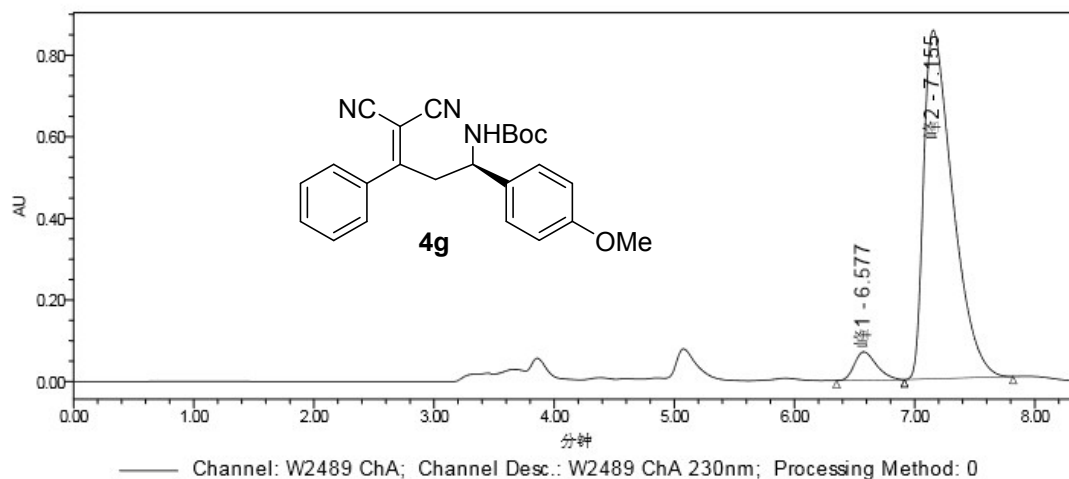
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	5.675	325879	3.50	29556
2	W2489 ChA 230nm	峰2	6.542	8973194	96.50	590411



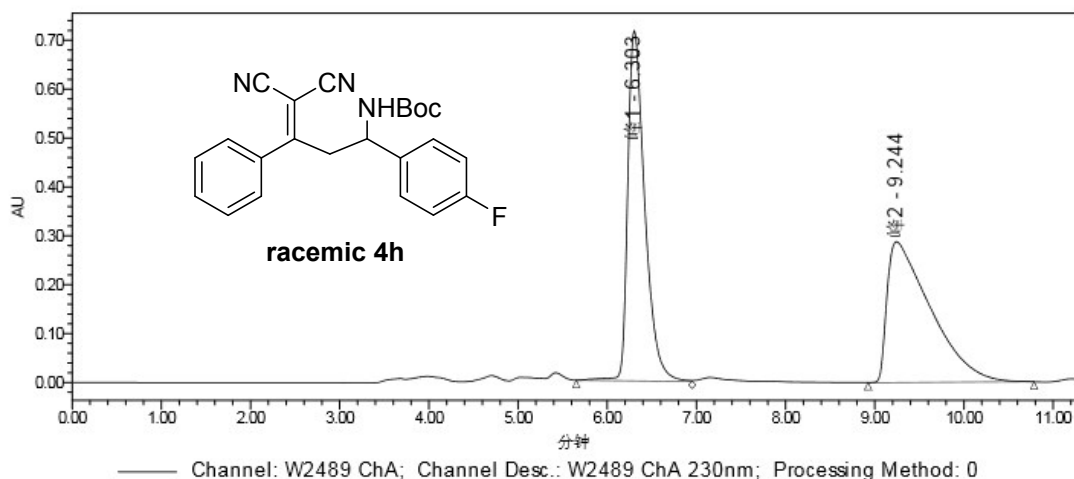
Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	6.396	2957632	50.47	222868
2	W2489 ChA 230nm	7.026	2902422	49.53	192630

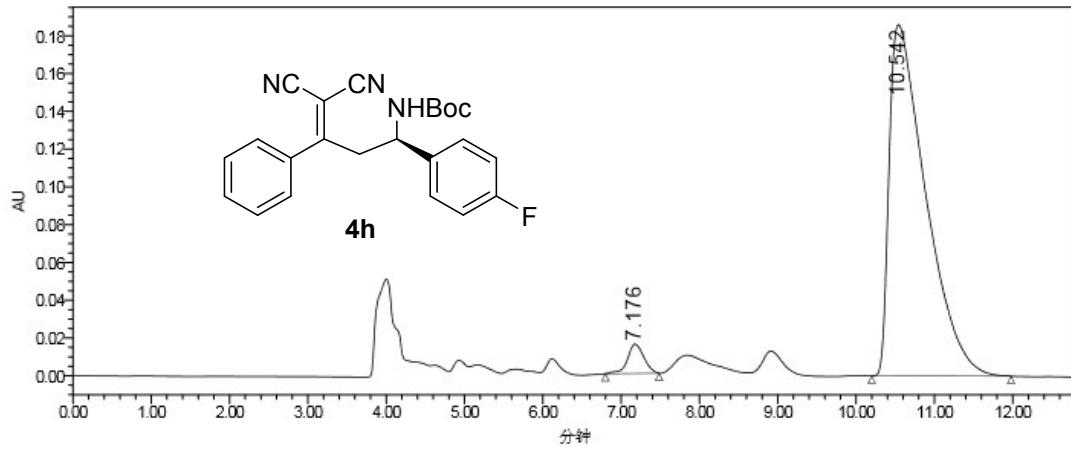




	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	峰1	6.577	886482	5.82	69329
2	W2489 ChA 230nm	峰2	7.155	14345980	94.18	854693

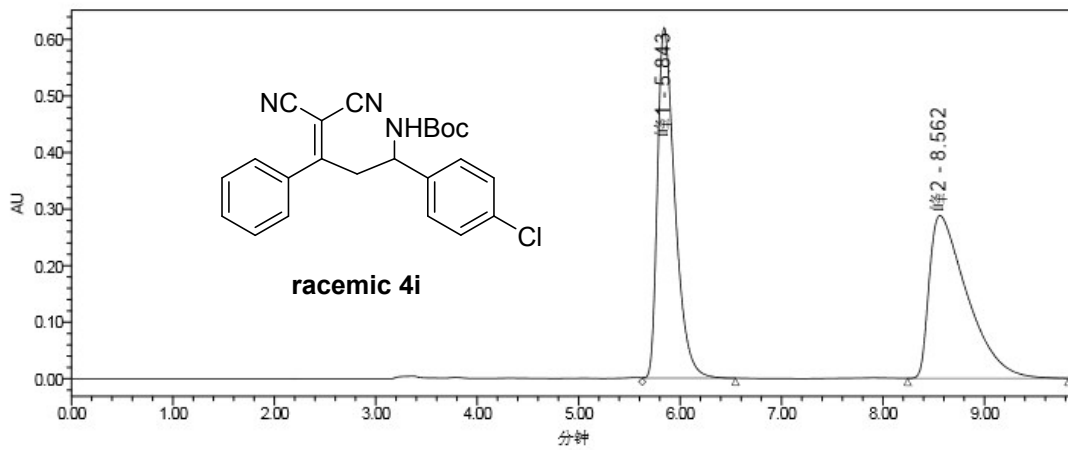


	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	峰1	6.303	9473002	49.29	715829
2	W2489 ChA 230nm	峰2	9.244	9743971	50.71	287685



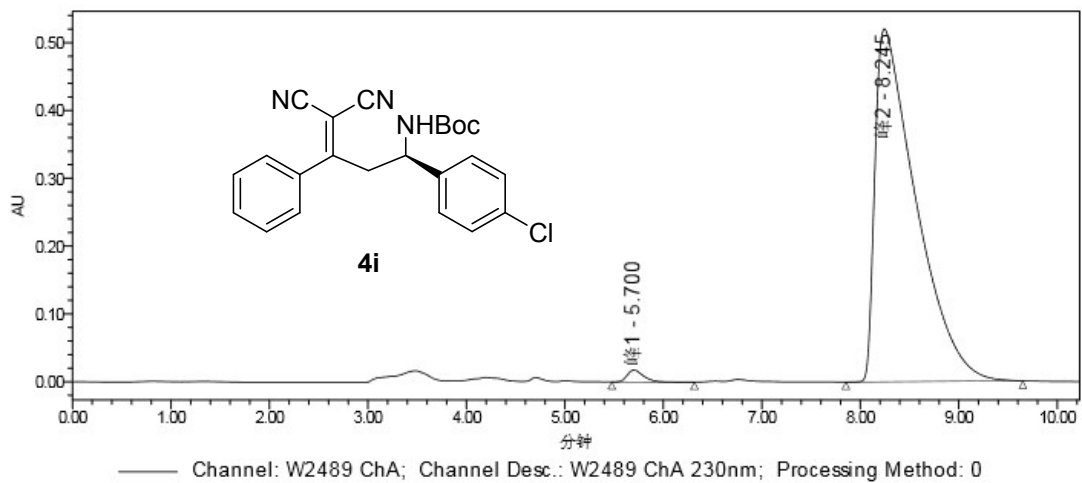
Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	7.176	225028	3.60	15463
2	W2489 ChA 230nm	10.542	6023730	96.40	185951

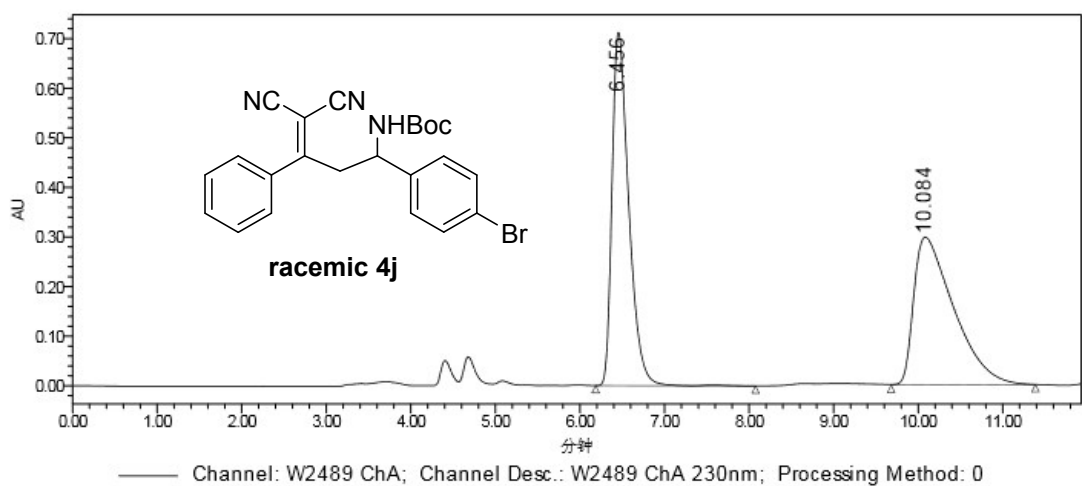


Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

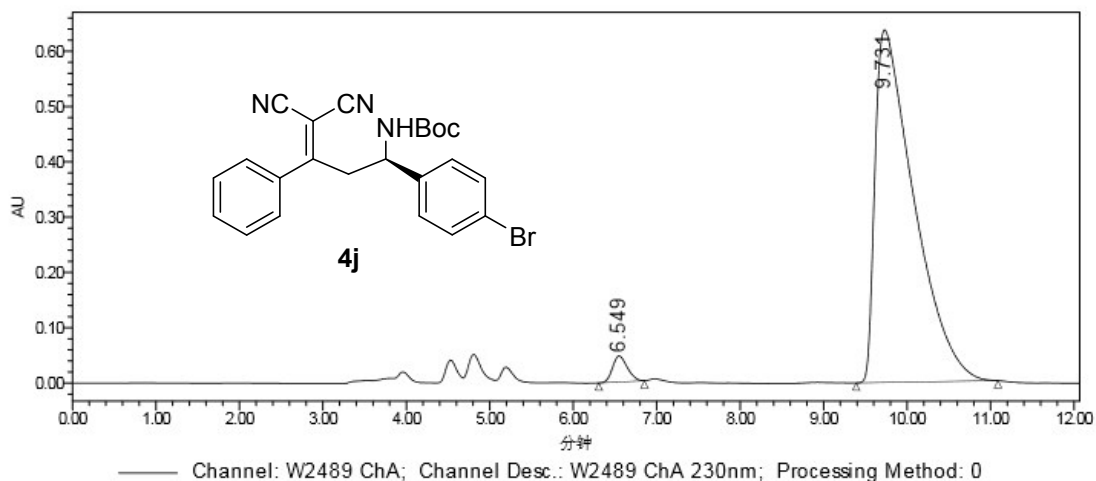
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	5.843	7410726	49.80	619642
2	W2489 ChA 230nm	峰2	8.562	7471520	50.20	287795



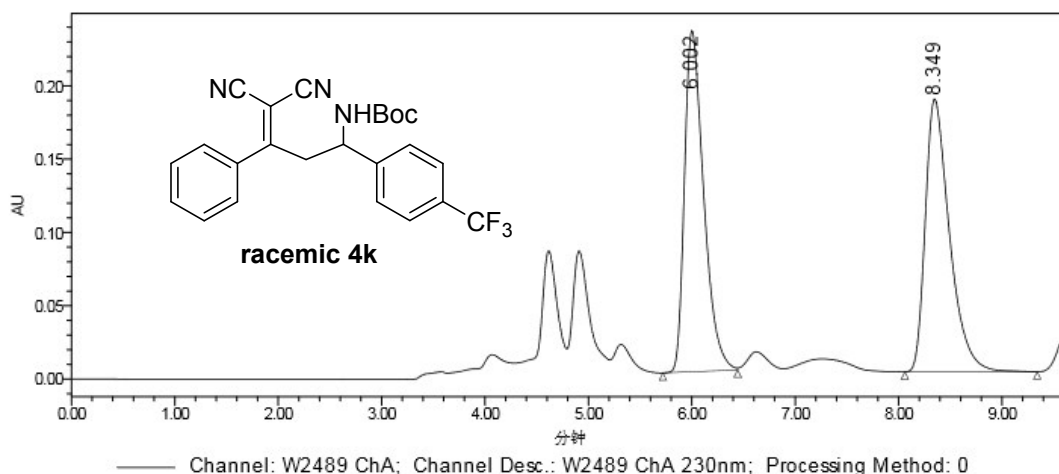
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	5.700	200784	1.32	17520
2	W2489 ChA 230nm	峰2	8.245	15014281	98.68	520221



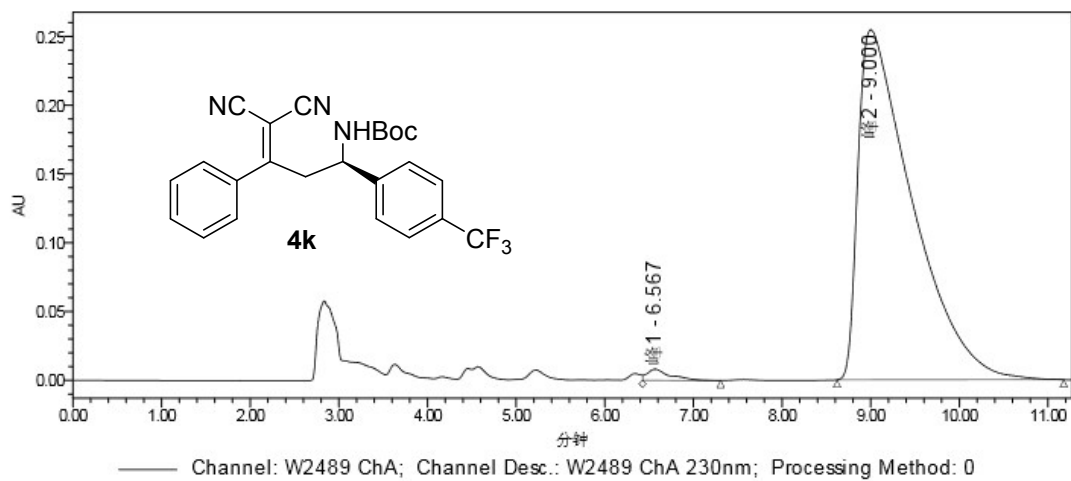
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	6.456	9788873	49.99	712311
2	W2489 ChA 230nm	10.084	9793105	50.01	298027



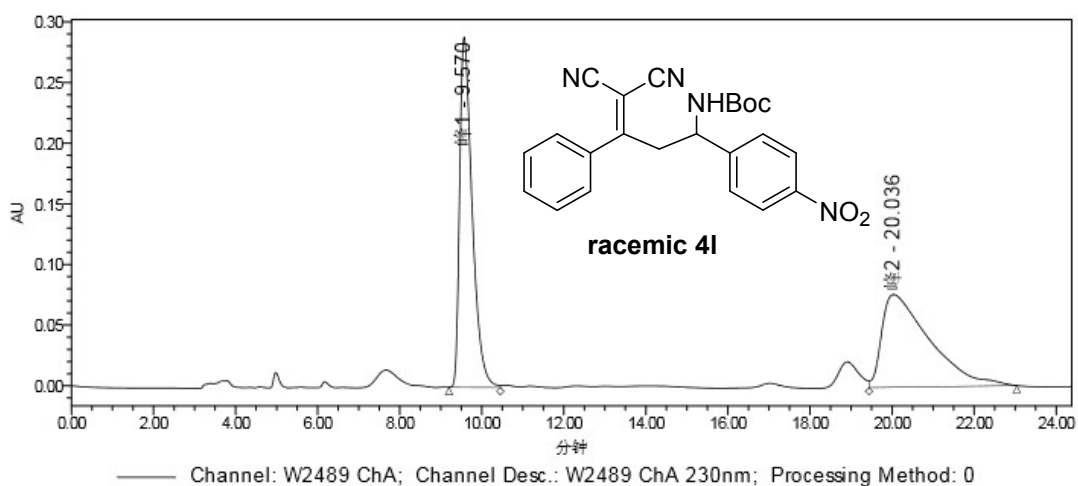
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	6.549	575253	2.71	46749
2	W2489 ChA 230nm	9.731	20631796	97.29	637038



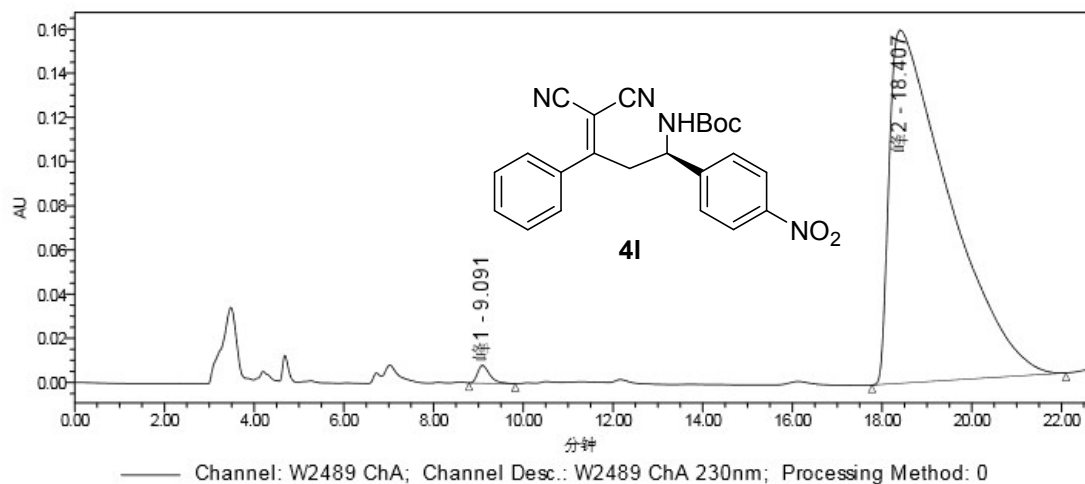
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	6.002	3007666	49.78	232639
2	W2489 ChA 230nm	8.349	3034043	50.22	186117



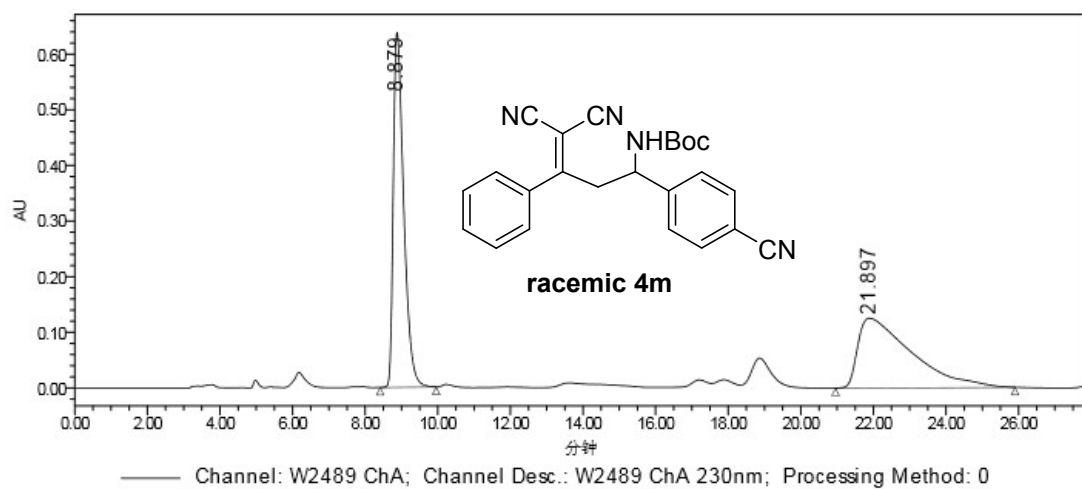
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	6.567	143714	1.31	8046
2	W2489 ChA 230nm	峰2	9.000	10807292	98.69	254465



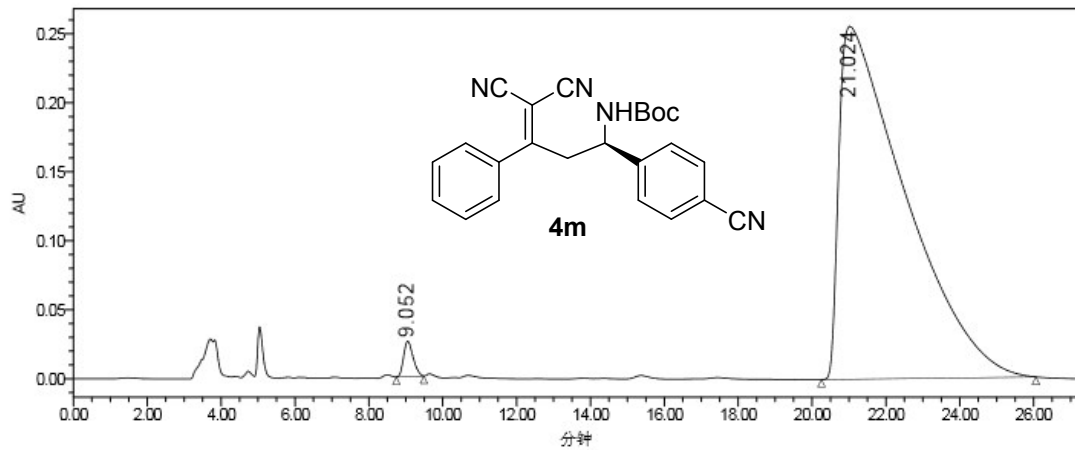
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	9.570	6108227	49.74	288635
2	W2489 ChA 230nm	峰2	20.036	6173151	50.26	76452



	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 230nm	峰1	9.091	150560	1.01	8035
2	W2489 ChA 230nm	峰2	18.407	14783321	98.99	159820

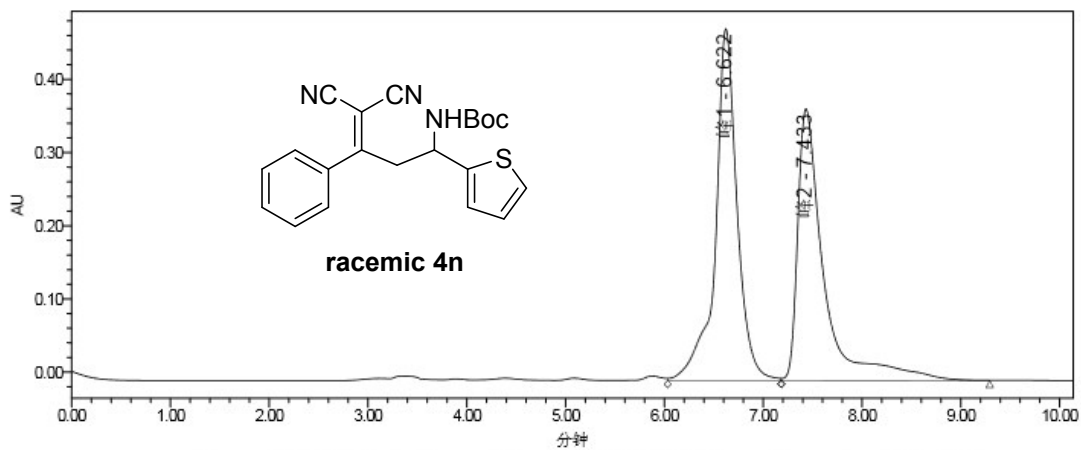


	Channel Description	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 230nm	8.879	12679704	49.77	638348
2	W2489 ChA 230nm	21.897	12795476	50.23	125310



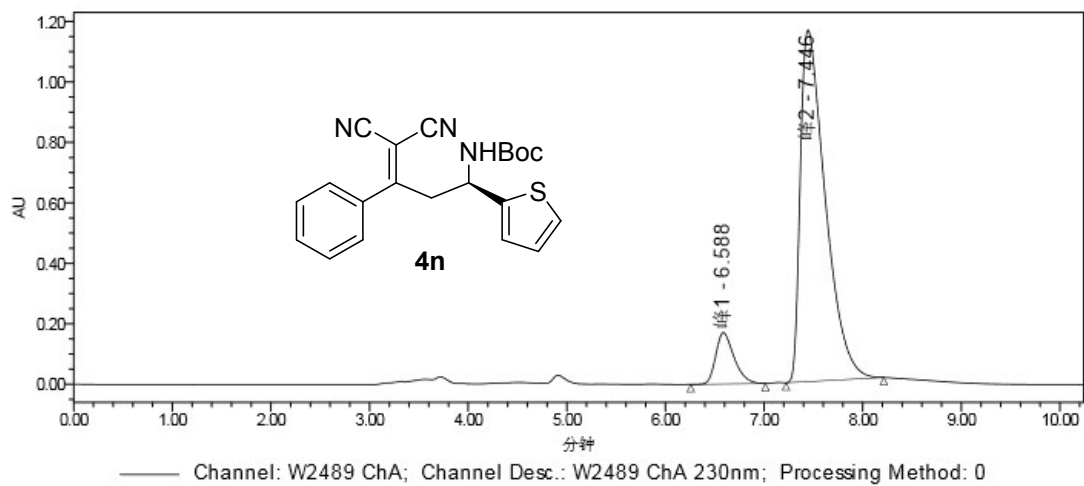
Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	9.052	459948	1.42	25723
2	W2489 ChA 230nm	21.024	31920405	98.58	255735

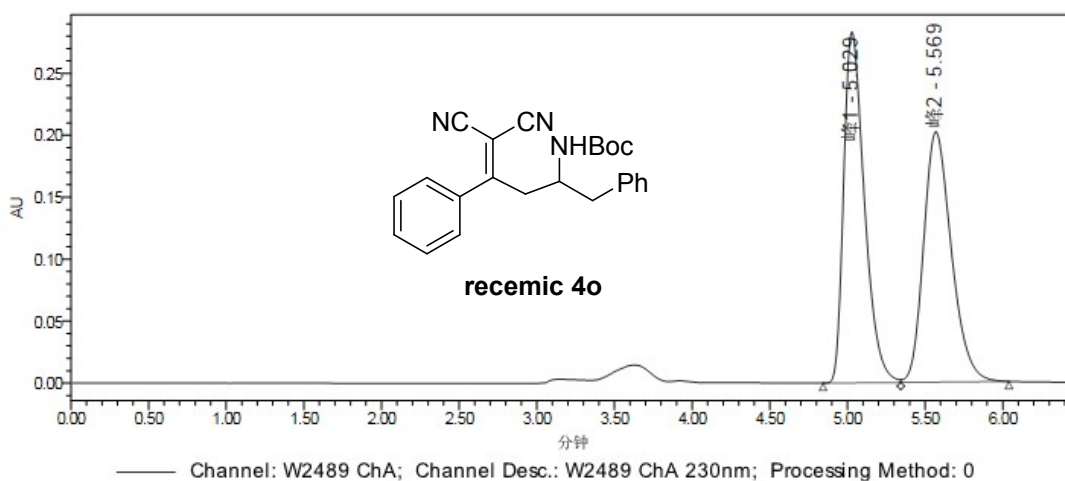


Channel: W2489 ChA; Channel Desc.: W2489 ChA 230nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	峰1	6.622	7353939	51.82	480284
2	W2489 ChA 230nm	峰2	7.433	6836650	48.18	370782

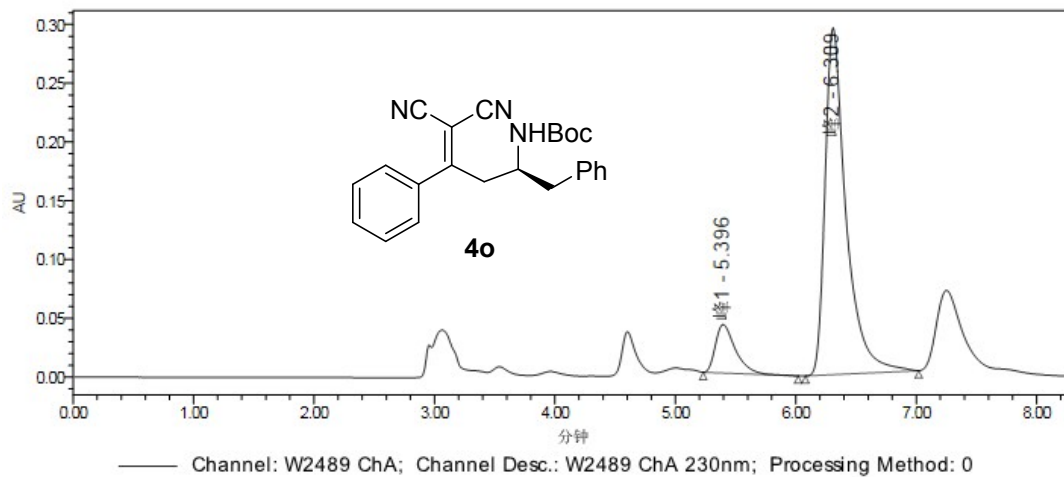


	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	峰1	6.588	2193944	9.71	169514
2	W2489 ChA 230nm	峰2	7.446	20395393	90.29	1162082

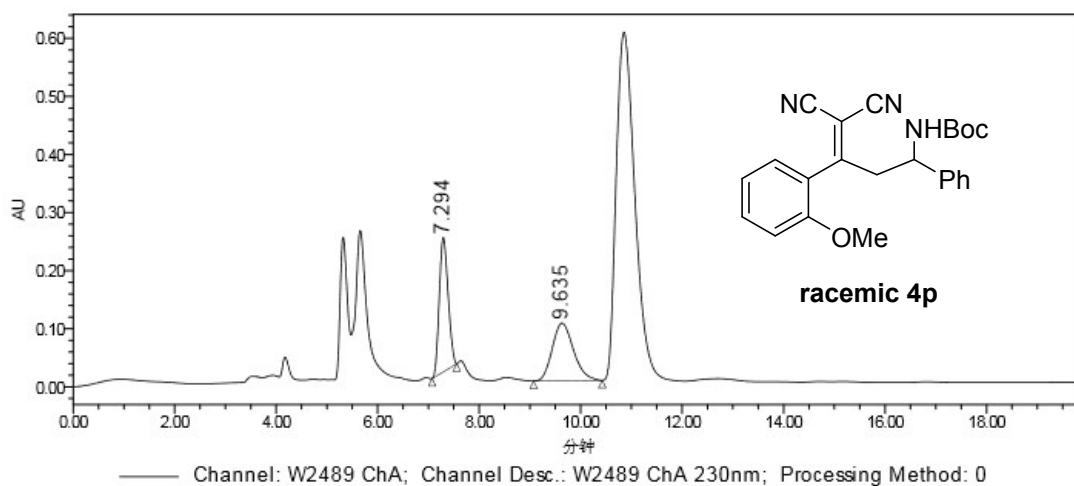


	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 230nm	峰1	5.029	2620125	51.09	282847
2	W2489 ChA 230nm	峰2	5.569	2508190	48.91	201942

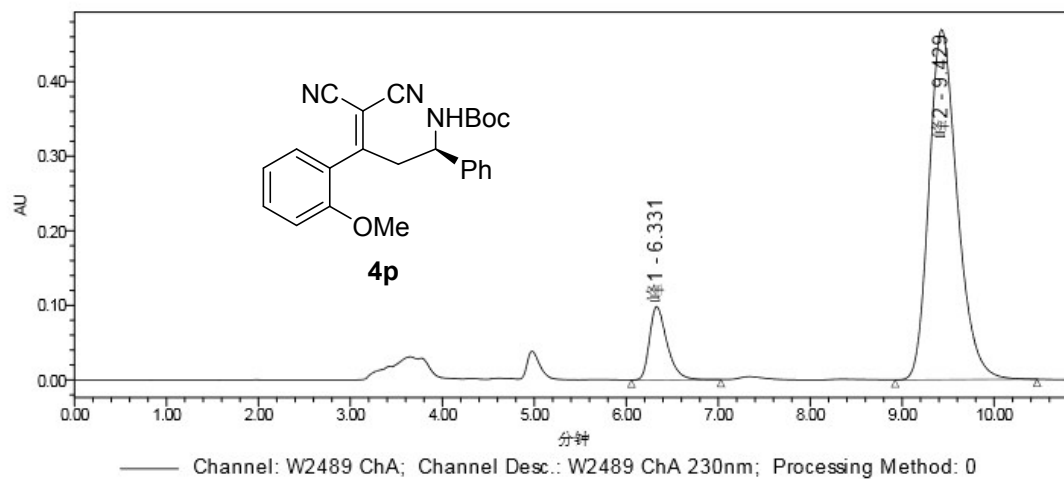




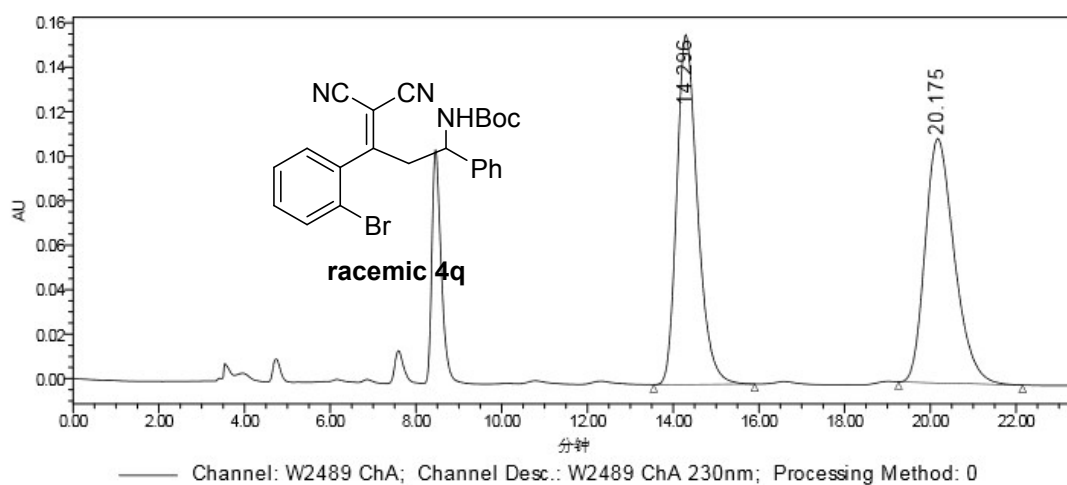
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	5.396	479027	11.81	41289
2	W2489 ChA 230nm	峰2	6.309	3576281	88.19	294786



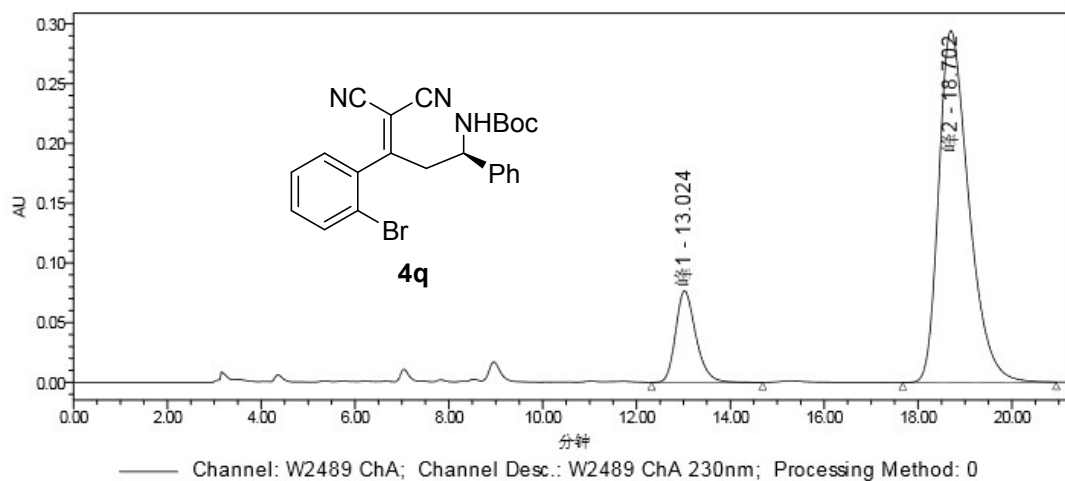
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	7.294	2794210	49.19	231045
2	W2489 ChA 230nm	9.635	2886330	50.81	99213



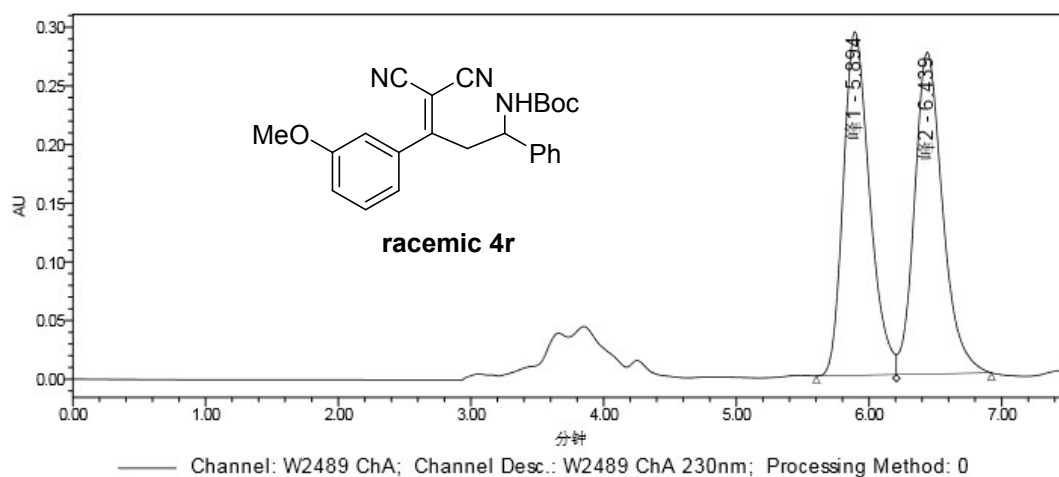
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	6.331	1296806	11.44	98208
2	W2489 ChA 230nm	峰2	9.429	10040423	88.56	469272



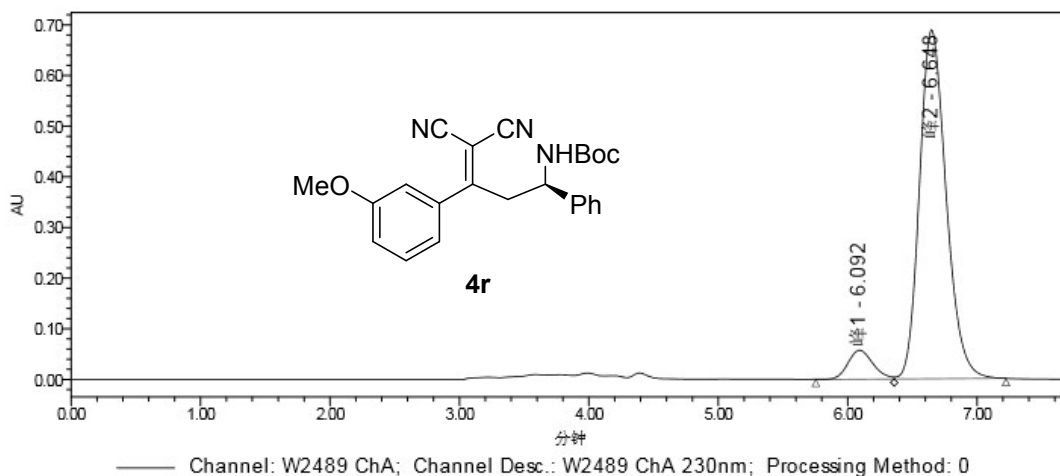
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	14.296	5288355	50.36	157215
2	W2489 ChA 230nm	20.175	5213429	49.64	109810



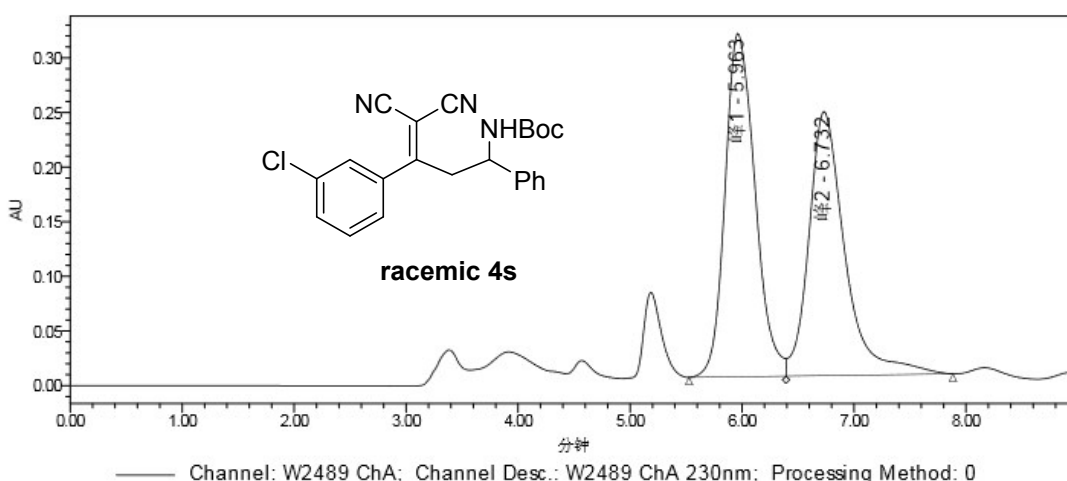
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	13.024	2296810	14.91	76691
2	W2489 ChA 230nm	峰2	18.702	13110814	85.09	294217



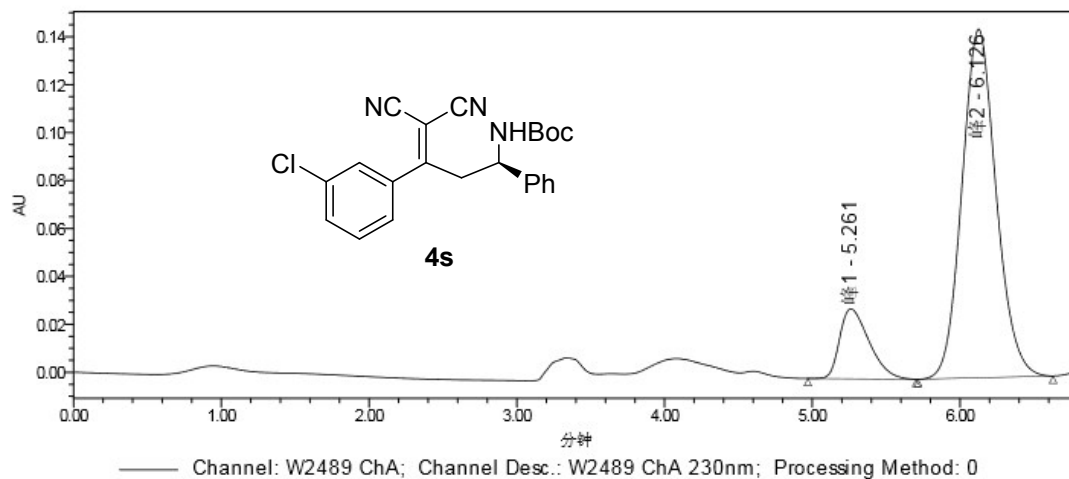
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	5.894	4041531	50.02	292668
2	W2489 ChA 230nm	峰2	6.439	4037886	49.98	274196



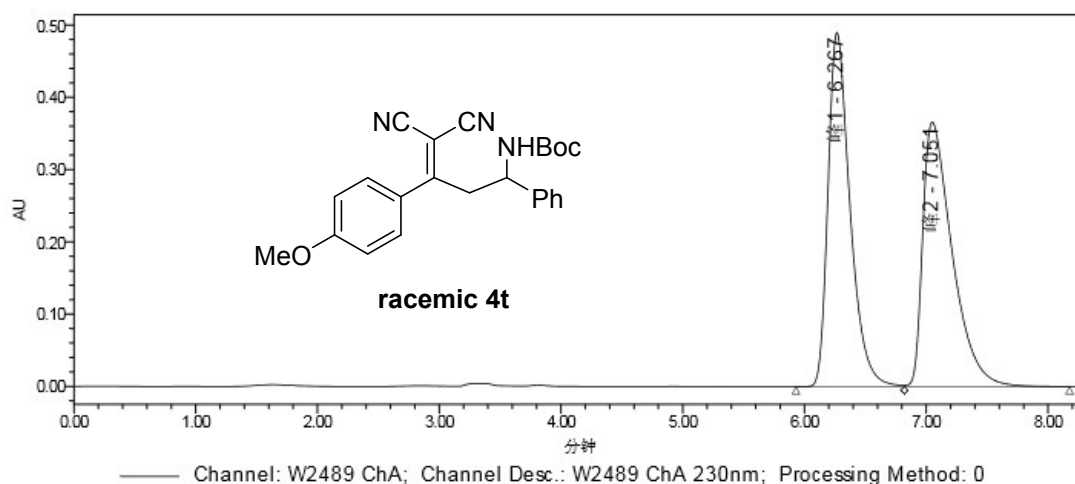
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.092	755993	7.14	56883
2	W2489 ChA 230nm	峰2	6.648	9839179	92.86	688401



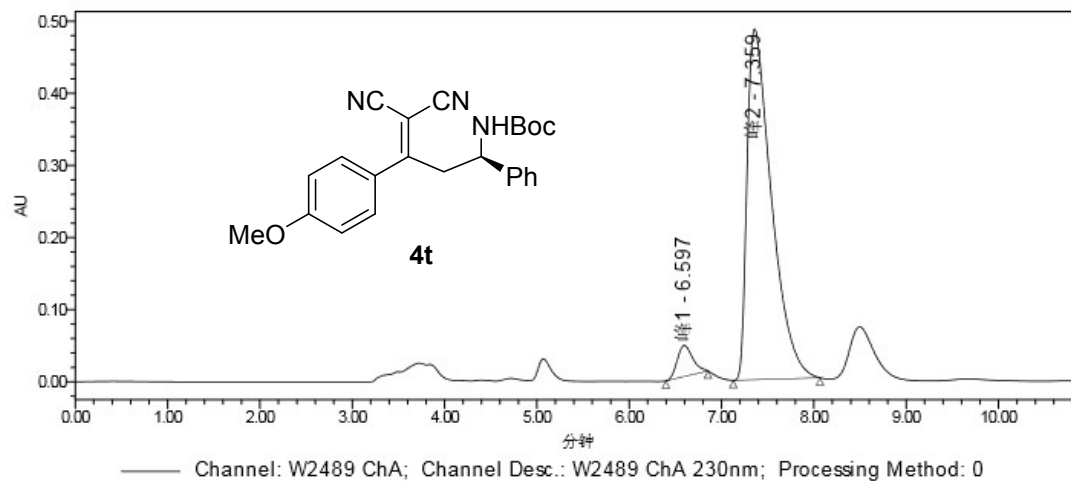
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	5.963	5842232	51.94	313969
2	W2489 ChA 230nm	峰2	6.732	5405224	48.06	241578



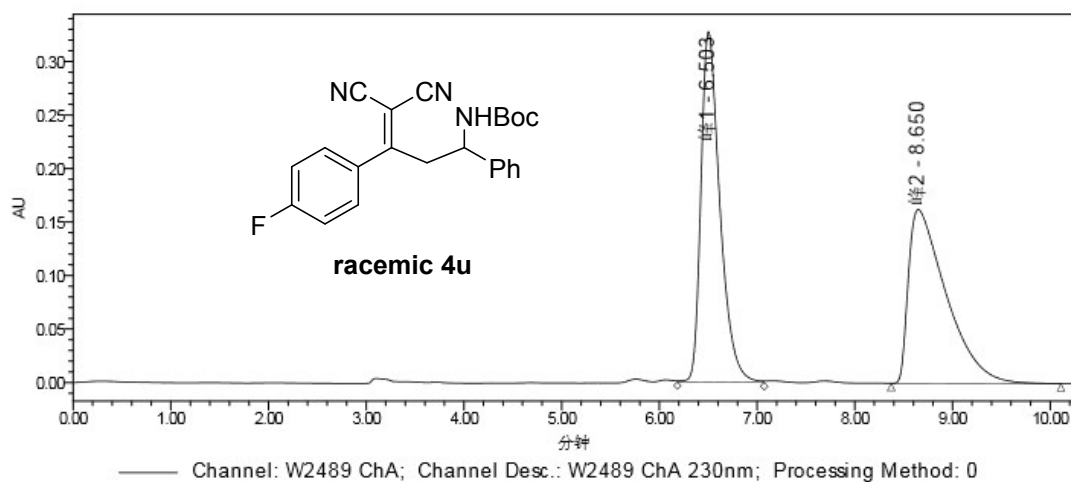
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	5.261	404013	14.74	29188
2	W2489 ChA 230nm	峰2	6.126	2337644	85.26	145388



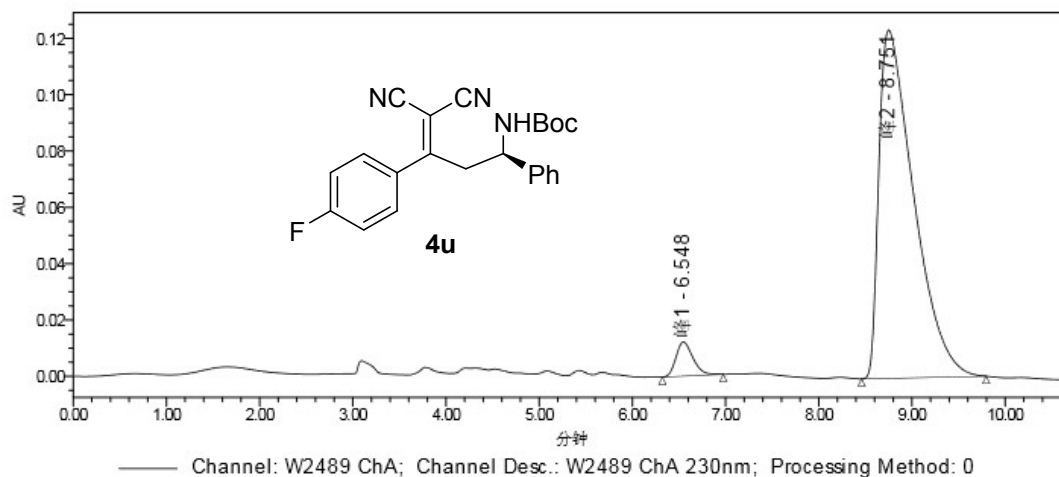
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.267	6138956	50.00	489935
2	W2489 ChA 230nm	峰2	7.051	6138059	50.00	365870



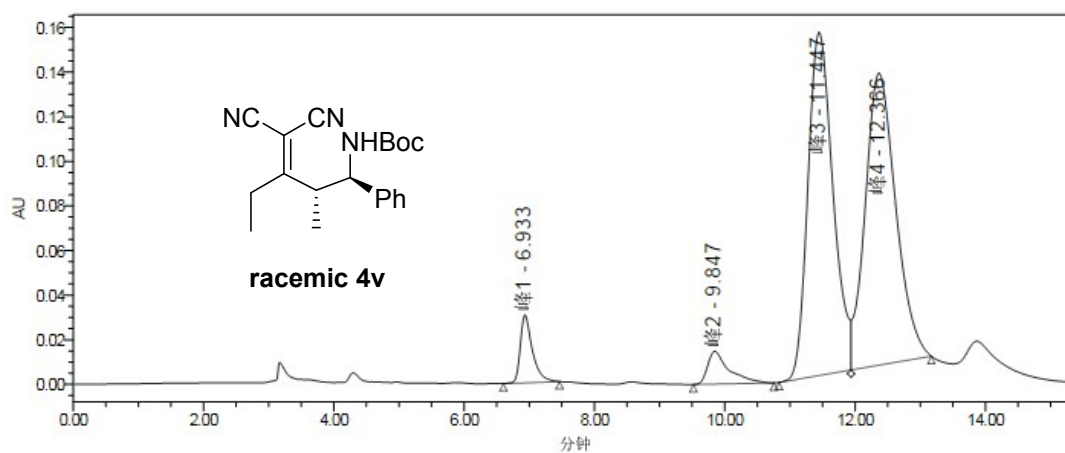
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.597	501983	5.32	42939
2	W2489 ChA 230nm	峰2	7.359	8938872	94.68	485997



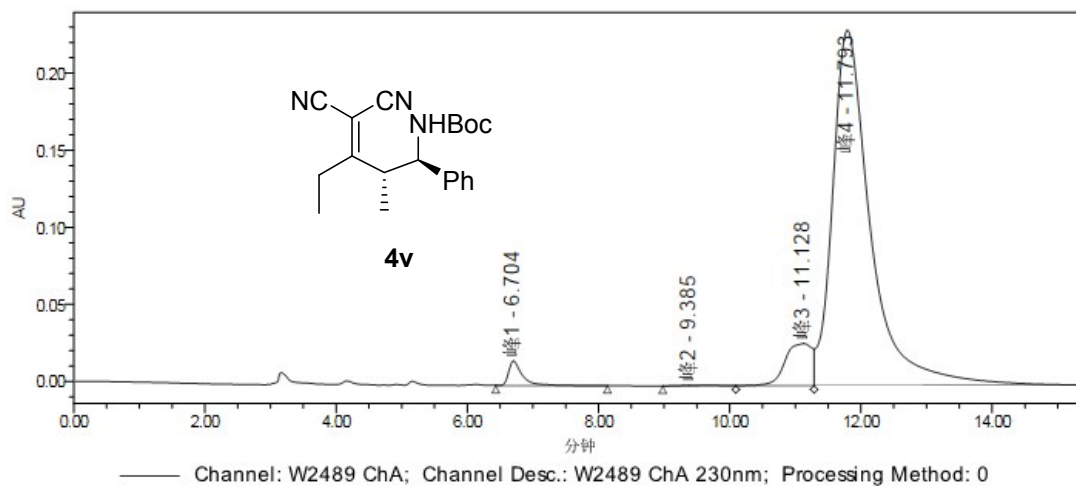
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.503	4416492	50.32	327353
2	W2489 ChA 230nm	峰2	8.650	4361053	49.68	162449



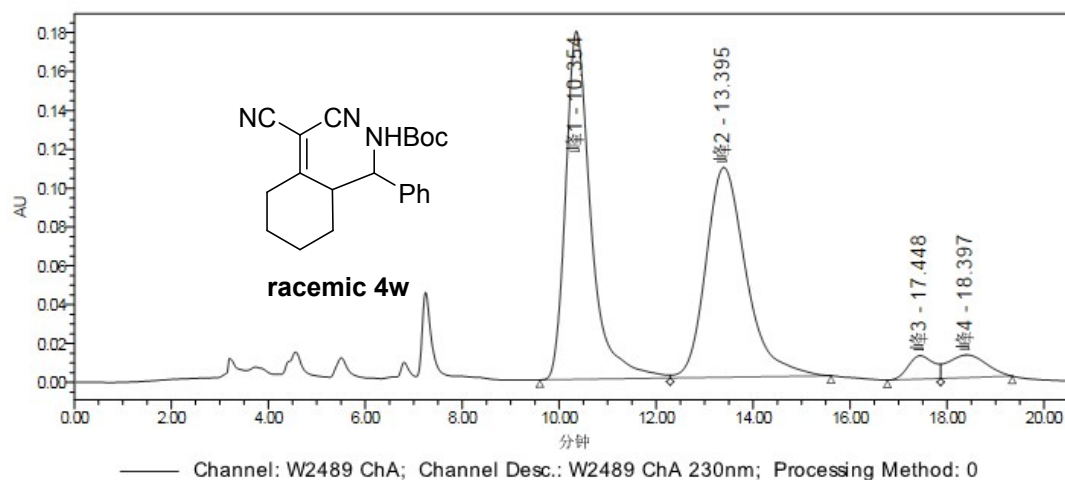
	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.548	153144	4.57	12126
2	W2489 ChA 230nm	峰2	8.751	3201026	95.43	123621



	Channel Description	Peak Name	RT (min)	Area (礦*sec)	% Area	Height (礦)
1	W2489 ChA 230nm	峰1	6.933	394554	4.33	30375
2	W2489 ChA 230nm	峰2	9.847	334354	3.67	14638
3	W2489 ChA 230nm	峰3	11.447	4104366	45.02	153824
4	W2489 ChA 230nm	峰4	12.366	4283365	46.98	130900

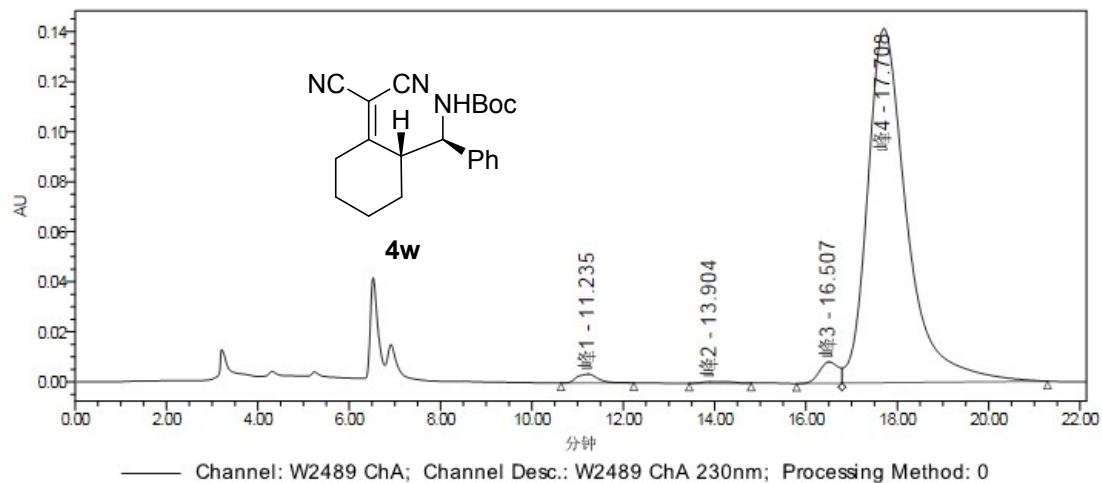


	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 230nm	峰1	6.704	231652	2.24	15946
2	W2489 ChA 230nm	峰2	9.385	10733	0.10	302
3	W2489 ChA 230nm	峰3	11.128	772061	7.48	27257
4	W2489 ChA 230nm	峰4	11.793	9307646	90.17	230463

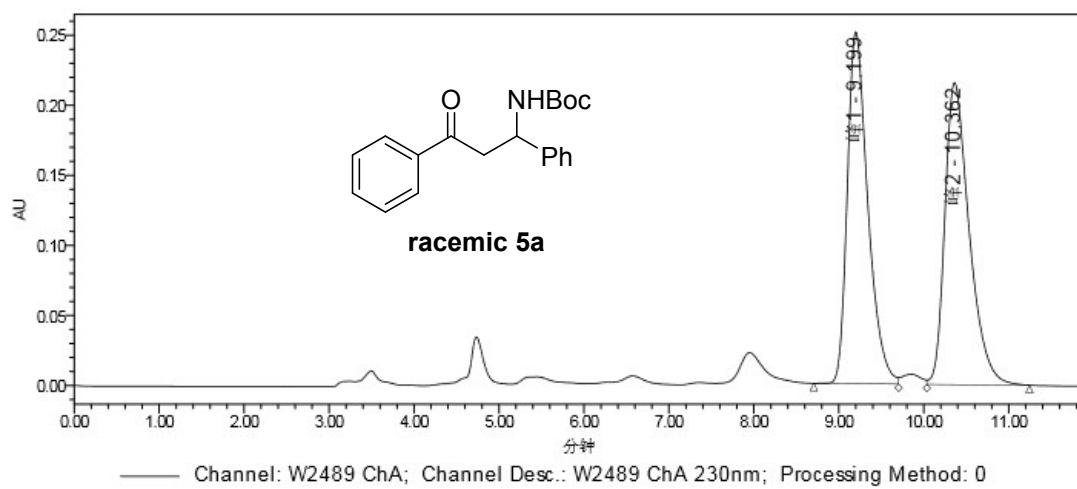


	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 230nm	峰1	10.354	6506488	47.15	179113
2	W2489 ChA 230nm	峰2	13.395	6213052	45.02	107990
3	W2489 ChA 230nm	峰3	17.448	441282	3.20	12024
4	W2489 ChA 230nm	峰4	18.397	639113	4.63	11636

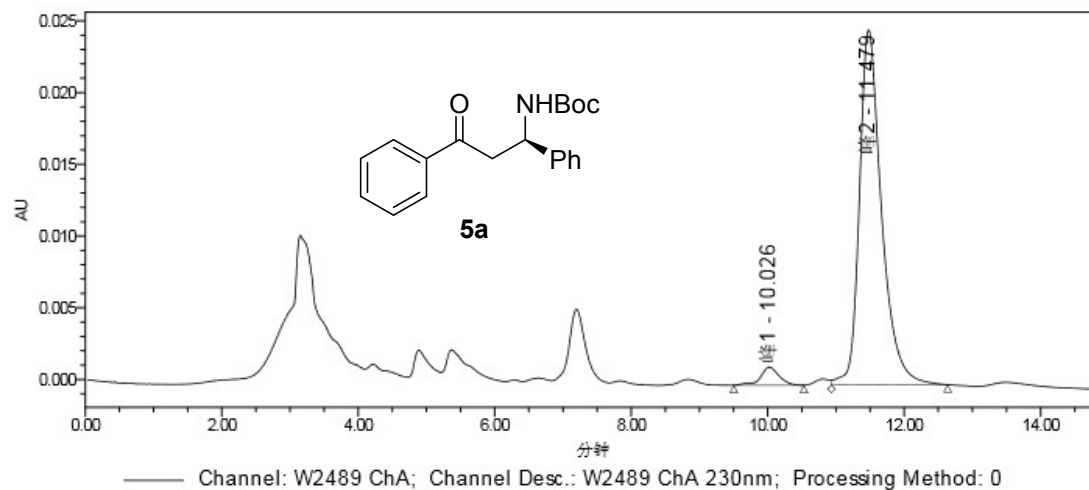




	Channel Description	Peak Name	RT (min)	Area (面积*sec)	% Area	Height (面积)
1	W2489 ChA 230nm	峰1	11.235	111460	1.26	3499
2	W2489 ChA 230nm	峰2	13.904	27641	0.31	639
3	W2489 ChA 230nm	峰3	16.507	247537	2.80	8534
4	W2489 ChA 230nm	峰4	17.708	8468310	95.63	141506



	Channel Description	Peak Name	RT (min)	Area (面积*sec)	% Area	Height (面积)
1	W2489 ChA 230nm	峰1	9.199	4210769	49.53	250995
2	W2489 ChA 230nm	峰2	10.362	4290116	50.47	215404



	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 230nm	峰1	10.026	24126	4.14	1264
2	W2489 ChA 230nm	峰2	11.479	559139	95.86	24739

## 7. Reference

1. A. F. Kyle, P. Jakubec, D. M. Cockfield, E. Cleator, J. Skidmore and D. J. Dixon, *Chem. Commun.*, 2011, **47**, 10037-10039.
2. W. Peng, J. Wan, B. Xie and X. Ma, *Org. Biomol. Chem.*, 2014, **12**, 8336-8345.
3. D. Villemin, Z. Belhadj, N. Cheikh, N. Choukchou-Braham, N. Bar and J.-F. Lohier, *Tetrahedron Letters*, 2013, **54**, 1664-1668.
4. A. G. Wenzel and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 12964-12965.
5. L. Huang and W. D. Wulff, *J. Am. Chem. Soc.*, 2011, **133**, 8892-8895.
6. T. Mecozzi and M. Petrini, *J. Org. Chem.*, 1999, **64**, 8970-8972.
7. N. Lu, R. Li, Z. Wei, J. Cao, D. Liang, Y. Lin and H. Duan, *J. Org. Chem.*, 2017, **82**, 4668-4676.
8. K. M. Johnson, M. S. Rattley, F. Sladojevich, D. M. Barber, M. G. Nuñez, A. M. Goldys and D. J. Dixon, *Org. Lett.*, 2012, **14**, 2492-2495.
9. B. Wang, T. Xu, L. Zhu, Y. Lan, J. Wang, N. Lu, Z. Wei, Y. Lin and H. Duan, *Org. Chem. Front.*, 2017, **4**, 1266-1271.