

**Asymmetric Palladium-Catalyzed Decarboxylative [3+2]  
Cycloaddition: Straightforward Construction of Chiral *Spiro*-  
heterocyclic Scaffolds**

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## 1. General information

General Procedures. All commercial solvents and chemicals were purchased from Bidepharm, Leyan, Energy Chemical, and Adamas and used as received. Toluene was distilled and stored over 4Å molecular sieves. All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Column chromatography was performed over silica gel (200-300 mesh). TLC plates were visualized by exposure to UV light (254 nm).

Instrumentation. <sup>1</sup>H NMR spectra was recorded with a Bruker AM 400 (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) units on the delta ( $\delta$ ) scale, and are referenced from the residual protium in the CDCl<sub>3</sub> (7.26 ppm). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qd = quartet of doublet, m = multiplet), coupling constant (s) in Hertz, integration]. <sup>13</sup>C NMR spectra was recorded with a Bruker AM 400 (100 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) units on the delta ( $\delta$ ) scale, and are referenced from the carbon resonances of CDCl<sub>3</sub> (77.0 ppm). High-resolution mass spectra (HRMS) were recorded on on a Bruker microTOF Q III spectrometer using an electrospray ionization source (ESI). Melting point (MP) was obtained with Hanon MP-430. Optical rotations were measured on a Autopol I polarimeter. All HPLC analyses were performed on an Agilent 1220 Series HPLC system with n-hexane, isopropanol. IR datas of all compounds were determined by Thermo Fisher Scientific FT-IR (nicolet iS10).

## 2. Supporting figures

Figure S1. HRMS analysis of  $[\text{L1-Pd-dba-H}]^+$

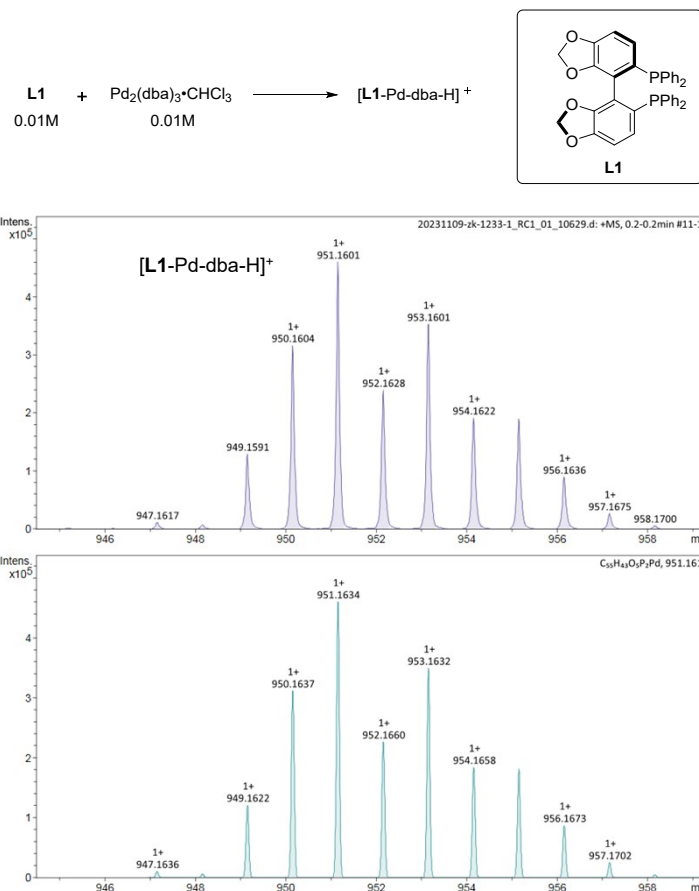


Figure S2. The binding interaction of  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  and **L1**

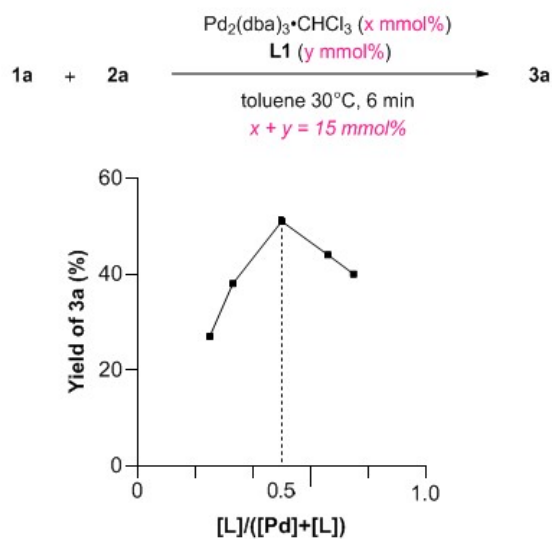
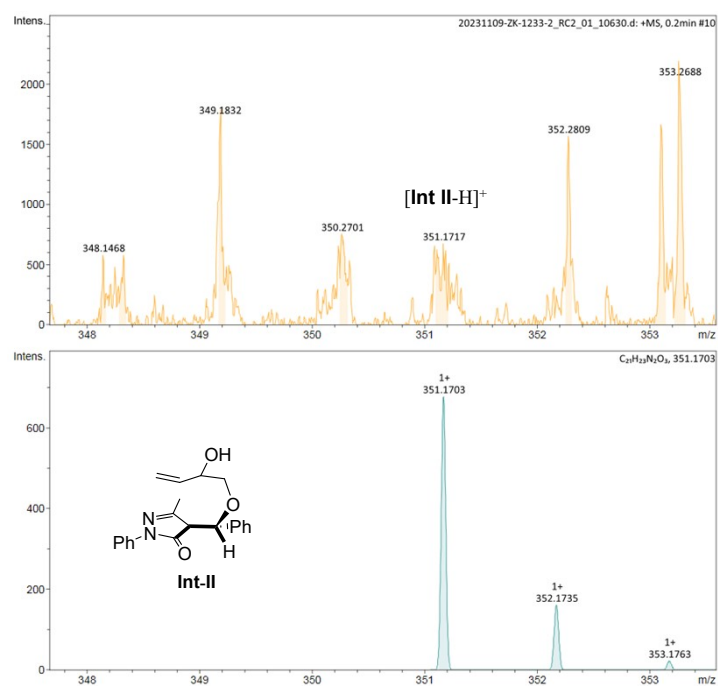
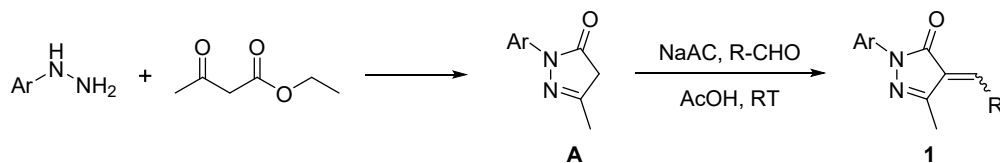


Figure S3. HRMS analysis of intermediate **Int-II**



### 3. General procedure for the synthesis of unsaturated pyrazolones



Phenylhydrazine (5.00 g, 46.24 mmol) was slowly added to the solution of ethyl acetoacetate (6.62 g, 50.86 mmol) at 0 °C. The resulting mixture was stirred for 1 h at 80 °C and for 1 h at 90 °C. Finally, the crude product was concentrated under reduced pressure to dryness and the residue was washed with diethyl ether (20 × 2 mL) giving pale yellow solids.<sup>1</sup>

To a solution of above product A (2.00 g, 11.50 mmol, 1.1 equiv) in acetic acid (26 mL) was added corresponding benzaldehyde (10.45 mmol, 1.0 equiv) and sodium acetic (0.94 g, 11.50 mmol, 1.1 equiv). The mixture was stirred at room temperature for 1-12 h. After the reaction was completed, H<sub>2</sub>O (26 mL) was added to reaction mixture. The aqueous layer extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> then concentrated in vacuo. The product was obtained after quickly purified by flash column chromatography on silica gel (Petroleum / EtOAc). compounds **1a-1q** and **1t-1ae** were obtained exclusively in *Z*-form, and the compounds **1r** and **1s** were obtained in *Z/E*-isomers with 3:1 and 10:1 *Z/E*-ratios, respectively.<sup>2</sup>

### 4. General procedure for preparation of racemic [3+2] cycloadducts

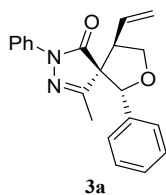
Under argon atmosphere, to an oven dried Schlenk tube equipped with a magnetic stir bar, Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (5.2 mg, 0.005 mmol, 5 mol%), dppe (1,2-bis(diphenylphosphino)ethane) (4.0 mg, 0.01 mmol, 10 mol%), **1a** (0.15 mmol) and **2a** (0.1 mmol) were added. Anhydrous 1 mL of toluene was added at 30 °C. The resulting mixture was stirred until the starting material was completely consumed (monitored by TLC) and then was concentrated to dryness. The residue was purified through flash column chromatography (Petroleum / EtOAc) to afford the corresponding cycloaddition products .

### 5. General procedure for asymmetric [3+2] cycloaddition

Under argon atmosphere, to an oven dried Schlenk tube equipped with a magnetic stir bar, Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (5.2 mg, 0.005 mmol, 5 mol%), (*R*)-Segphos (6.1 mg, 0.01 mmol, 10 mol%), **1a**

(0.15 mmol) and **2a** (0.1 mmol) were added. Anhydrous 1 mL of toluene was added at 30 °C. The resulting mixture was stirred until the starting material was completely consumed (monitored by TLC) and then was concentrated to dryness. The residue was purified through flash column chromatography (Petroleum / EtOAc) to afford the corresponding cycloaddition products **3**.

## 6. Characterization data of the products 3



### (5*R*,6*R*,9*R*)-4-methyl-2,6-diphenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3a)

White solid, 28.0 mg, 85% yield, 3.5:1 *dr*, 98/66% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.91 (d,  $J = 7.7$  Hz, 2H), 7.44 (t,  $J = 8.0$  Hz, 2H), 7.36 – 7.27 (m, 3H), 7.26 – 7.18 (m, 3H), 6.07 – 5.88 (m, 1H), 5.46 (s, 1H), 5.16 (dd,  $J = 13.8, 6.0$  Hz, 2H), 4.55 – 4.36 (m, 1H), 4.15 (dd,  $J = 10.0, 8.9$  Hz, 1H), 3.31 (dd,  $J = 17.1, 9.5$  Hz, 1H), 1.58 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.9, 160.7, 137.9, 137.0, 131.7, 128.9, 128.6, 128.1, 125.2, 124.7, 120.0, 118.9, 87.1, 72.3, 68.6, 52.2, 14.7.

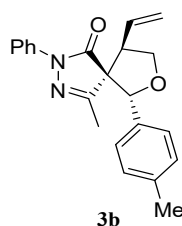
**IR:** 3078, 2856, 1698, 1591, 1488, 1324, 751, 708  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 355.1417, found: 355.1411.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 6.8$  min (minor), 10.6 min (major), minor diastereomer:  $t_R = 8.5$  min (major), 13.5 min (minor).

$[\alpha]_D^{25} = 77.56$  ( $c = 0.26$  in  $\text{CHCl}_3$ ).

**Mp:** 154.6-155.4 °C.



### (5*R*,6*R*,9*R*)-4-methyl-2-phenyl-6-(*p*-tolyl)-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one

#### (3b)

White solid, 29.4 mg, 85% yield, 3.5:1 *dr*, 98/14% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  8.01 – 7.84 (m, 2H), 7.52 – 7.36 (m, 2H), 7.27 – 7.18 (m, 1H), 7.12 (s, 4H), 5.99 (ddd,  $J = 16.9, 10.2, 9.2$  Hz, 1H), 5.43 (s, 1H), 5.23 – 5.05 (m, 2H), 4.45 (dd,  $J = 8.5, 7.6$  Hz, 1H), 4.13 (dd,  $J = 10.0, 8.8$  Hz, 1H), 3.31 (dd,  $J = 17.0, 9.6$  Hz, 1H), 2.34 (s, 3H), 1.61 (s, 3H).



$^{13}\text{C}$  NMR (100 MHz, Chloroform-*d*)  $\delta$  172.9, 160.9, 137.9, 137.8, 133.9, 131.8, 129.2, 128.9, 125.2, 124.6, 119.9, 118.9, 87.2, 72.3, 68.7, 52.2, 21.2, 14.8.

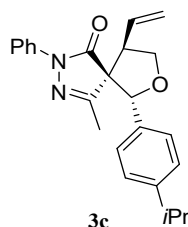
IR: 3075, 2853, 1698, 1593, 1490, 1365, 755, 690  $\text{cm}^{-1}$ ;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 369.1573, found: 369.1570.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}}$  = 7.1 min (minor), 9.3 min (major), minor diastereomer:  $t_{\text{R}}$  = 8.6 min (minor), 10.9 min (major).

$[\alpha]_{\text{D}}^{25} = +117.87$  ( $c = 0.44$  in  $\text{CHCl}_3$ ).

Mp: 115.4-116.8  $^{\circ}\text{C}$ .



**(5R,6R,9R)-6-(4-isopropylphenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3c)**

Colorless oil, 29.9 mg, 80% yield, 3.8:1 *dr*, 98/71% *ee*.

$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.91 (d,  $J = 8.1$  Hz, 2H), 7.43 (t,  $J = 7.5$  Hz, 2H), 7.26 – 7.11 (m, 5H), 6.10 – 5.80 (m, 1H), 5.43 (s, 1H), 5.22 – 5.06 (m, 2H), 4.44 (t,  $J = 8.0$  Hz, 1H), 4.14 (t,  $J = 9.4$  Hz, 1H), 3.30 (q,  $J = 8.8$  Hz, 1H), 2.95 – 2.80 (m, 1H), 1.57 (s, 3H), 1.24 (d,  $J = 6.8$  Hz, 6H).

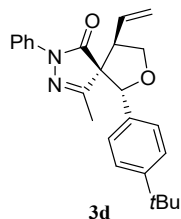
$^{13}\text{C}$  NMR (100 MHz, Chloroform-*d*)  $\delta$  173.0, 160.9, 148.9, 137.9, 134.3, 131.7, 128.9, 126.6, 125.2, 124.6, 120.0, 119.0, 87.1, 72.2, 68.7, 52.3, 33.8, 24.0, 14.7.

IR: 2959, 2868, 1705, 1596, 1500, 1367, 1071, 765, 691  $\text{cm}^{-1}$ ;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 397.1886, found: 397.1907.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 98/2, flow rate 0.6 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}}$  = 9.4 min (minor), 14.1 min (major), minor diastereomer:  $t_{\text{R}}$  = 12.8 min (major), 16.7 min (minor).

$[\alpha]_{\text{D}}^{25} = +132.49$  ( $c = 0.40$ ,  $\text{CHCl}_3$ ).



**(5R,6R,9R)-6-(4-(tert-butyl)phenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3d)**

White solid, 27.5 mg, 71% yield, 4:1 *dr*, 98/50% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.94 – 7.88 (m, 2H), 7.47 – 7.39 (m, 2H), 7.35 – 7.31 (m, 2H), 7.26 – 7.19 (m, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.02 – 5.88 (m, 1H), 5.43 (s, 1H), 5.14 (dd, *J* = 9.5, 8.3 Hz, 2H), 4.44 (dd, *J* = 8.5, 7.5 Hz, 1H), 4.13 (dd, *J* = 10.1, 8.8 Hz, 1H), 3.30 (dd, *J* = 17.0, 9.6 Hz, 1H), 1.56 (s, 3H), 1.30 (s, 9H).

<sup>13</sup>C NMR (100 MHz, Chloroform-*d*)  $\delta$  173.0, 160.9, 151.1, 137.9, 134.0, 131.7, 128.9, 125.4, 125.2, 124.4, 120.0, 119.0, 87.1, 72.2, 68.6, 52.3, 34.6, 31.3, 14.7.

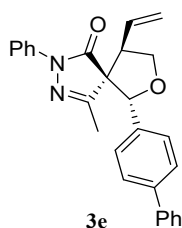
IR: 2962, 2866, 1705, 1596, 1500, 1367, 1071, 765, 691 cm<sup>-1</sup>;

HRMS (ESI) *m/z* calcd for C<sub>25</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 411.2043, found: 411.2040.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 98/2, flow rate 0.6 mL/min, detection at 254 nm, major diastereomer: *t*<sub>R</sub> = 8.5 min (minor), 9.0 min (major), minor diastereomer: *t*<sub>R</sub> = 10.8 min (minor), 11.9 min (major).

$[\alpha]_{\text{D}}^{25} = 125.91$  (*c* = 0.40, CHCl<sub>3</sub>).

Mp: 95.6-96.2 °C.



**(5R,6R,9R)-6-([1,1'-biphenyl]-4-yl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3e)**

White solid, 33.0 mg, 81% yield, 4:1 *dr*, 98/74% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.96 – 7.91 (m, 2H), 7.62 – 7.55 (m, 4H), 7.49 – 7.42 (m, 4H), 7.40 – 7.34 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.21 (m, 1H), 6.14 – 5.91 (m, 1H), 5.50

(s, 1H), 5.26 – 5.08 (m, 2H), 4.49 (dd,  $J = 8.6, 7.6$  Hz, 1H), 4.17 (dd,  $J = 10.0, 8.8$  Hz, 1H), 3.35 (dd,  $J = 17.0, 9.6$  Hz, 1H), 1.66 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz, Chloroform- $d$ )  $\delta$  172.8, 160.7, 140.9, 140.4, 137.9, 136.0, 131.7, 128.9, 128.8, 127.5, 127.2, 127.0, 125.3, 125.1, 120.0, 119.0, 87.1, 72.4, 68.7, 52.3, 14.9.

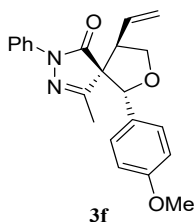
**IR:** 3028, 2856, 1687, 1595, 1499, 1368, 740, 689  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{24}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 431.1730, found: 431.1714.

**HPLC** (CHIRALPAK IA-H),  $n$ -hexane/isopropanol = 98/2, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}} = 12.1$  min (major), 13.4 min (minor), minor diastereomer:  $t_{\text{R}} = 15.2$  min (minor), 26.3 min (major).

$[\alpha]_{\text{D}}^{25} = +224.60$  ( $c = 0.46$ ,  $\text{CHCl}_3$ ).

**Mp:** 110.7-111.9  $^{\circ}\text{C}$ .



**(5R,6R,9R)-6-(4-methoxyphenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3f)**

White solid, 27.9 mg, 77% yield, 3:1 *dr*, 95/86% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform- $d$ )  $\delta$  7.96 – 7.88 (m, 2H), 7.47 – 7.39 (m, 2H), 7.25 – 7.19 (m, 1H), 7.16 (d,  $J = 8.4$  Hz, 2H), 6.91 – 6.82 (m, 2H), 6.14 – 5.91 (m, 1H), 5.40 (s, 1H), 5.23 – 5.08 (m, 2H), 4.45 (dd,  $J = 8.6, 7.6$  Hz, 1H), 4.13 (dd,  $J = 10.0, 8.8$  Hz, 1H), 3.80 (s, 3H), 3.31 (dd,  $J = 17.0, 9.5$  Hz, 1H), 1.63 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz, Chloroform- $d$ )  $\delta$  172.9, 160.9, 159.3, 137.9, 131.8, 129.0, 128.9, 125.9, 125.2, 119.9, 118.9, 113.9, 87.1, 72.3, 68.7, 55.2, 52.1, 14.9.

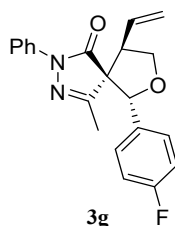
**IR:** 3021, 2858, 1694, 1505, 1330, 1224, 1066, 838, 717  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_3$   $[\text{M}+\text{Na}]^+$ : 385.1522, found: 385.1524.

**HPLC** (CHIRALPAK AD-H),  $n$ -hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}} = 10.2$  min (minor), 11.3 min (major), minor diastereomer:  $t_{\text{R}} = 13.1$  min (minor), 14.4 min (major).

$[\alpha]_D^{25} = +62.07$  ( $c = 0.34$ ,  $\text{CHCl}_3$ ).

**Mp:** 129.1-130.3 °C.



**(5R,6R,9R)-6-(4-fluorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3g)**

White solid, 31.5 mg, 90% yield, 3.8:1 *dr*, 97/20% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.94 – 7.87 (m, 2H), 7.48 – 7.39 (m, 2H), 7.27 – 7.19 (m, 3H), 7.07 – 6.98 (m, 2H), 5.99 (ddd,  $J = 16.9, 10.2, 9.2$  Hz, 1H), 5.41 (s, 1H), 5.16 (ddd,  $J = 12.8, 8.4, 0.9$  Hz, 2H), 4.46 (dd,  $J = 8.6, 7.5$  Hz, 1H), 4.12 (dd,  $J = 10.0, 8.9$  Hz, 1H), 3.31 (dd,  $J = 17.0, 9.5$  Hz, 1H), 1.63 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz, Chloroform-*d*)  $\delta$  172.6, 162.4 (d,  $J = 246.8$  Hz), 160.5, 137.8, 132.7 (d,  $J = 3.2$  Hz), 131.6, 128.9, 126.4 (d,  $J = 8.1$  Hz), 125.3, 120.1, 118.9, 115.6 (d,  $J = 21.6$  Hz), 86.7, 72.4, 68.6, 52.2, 14.8.

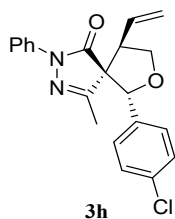
**IR:** 3075, 2854, 1699, 1592, 1489, 1351, 1229, 755, 691  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{19}\text{FN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 373.1323, found: 373.1325.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 6.9$  min (minor), 7.6 min (major), minor diastereomer:  $t_R = 8.9$  min (minor), 10.8 min (major).

$[\alpha]_D^{25} = +79.44$  ( $c = 0.42$ ,  $\text{CHCl}_3$ ).

**Mp:** 134.4-135.3 °C.



**(5R,6R,9R)-6-(4-chlorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3h)**

White solid, 29.3 mg, 80% yield, 3.7:1 *dr*, 97/78% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.95 – 7.87 (m, 2H), 7.46 – 7.39 (m, 2H), 7.27 – 7.19 (m, 2H), 6.98 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.83 (dt, *J* = 3.6, 1.1 Hz, 1H), 6.05 – 5.87 (m, 1H), 5.62 (d, *J* = 0.6 Hz, 1H), 5.23 – 4.96 (m, 2H), 4.45 (dd, *J* = 8.7, 7.6 Hz, 1H), 4.16 (dd, *J* = 9.8, 8.9 Hz, 1H), 3.49 – 3.29 (m, 1H), 1.72 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.5, 160.4, 137.7, 135.4, 133.9, 131.6, 128.9, 128.8, 126.1, 125.3, 120.1, 118.9, 86.6, 72.4, 68.5, 52.2, 14.9.

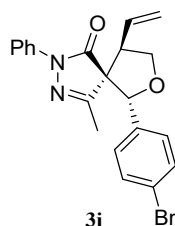
**IR:** 3083, 2851, 1701, 1593, 1488, 1367, 1082, 762, 693 cm<sup>-1</sup>;

**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>19</sub>ClN<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 389.1027, found: 389.1007.

**HPLC** (CHIRALPAK IA-H), *n*-hexane/isopropanol = 98/2, flow rate 1 mL/min, detection at 254 nm, major diastereomer: *t<sub>R</sub>* = 8.6 min (minor), 9.4 min (major), minor diastereomer: *t<sub>R</sub>* = 11.0 min (minor), 11.9 min (major).

**$[\alpha]_D^{25}$**  = + 139.01 (*c* = 0.40, CHCl<sub>3</sub>).

**Mp:** 160.0-161.4 °C.



**(5*R*,6*R*,9*R*)-6-(4-bromophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3i)**

White solid, 28.7 mg, 70% yield, 3.8:1 *dr*, 98/73% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.90 (d, *J* = 8.1 Hz, 2H), 7.44 (dd, *J* = 13.4, 7.6 Hz, 4H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.11 – 5.88 (m, 1H), 5.37 (s, 1H), 5.23 – 5.09 (m, 2H), 4.45 (t, *J* = 8.1 Hz, 1H), 4.10 (t, *J* = 9.4 Hz, 1H), 3.29 (q, *J* = 8.9 Hz, 1H), 1.64 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.5, 160.4, 137.7, 135.9, 131.7, 131.6, 128.9, 126.4, 125.3, 122.0, 120.1, 118.9, 86.6, 72.4, 68.5, 52.2, 14.9.

**IR:** 3083, 2860, 1691, 1595, 1489, 1364, 780, 754, 693 cm<sup>-1</sup>;

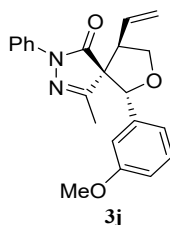
**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>19</sub>BrN<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 433.0522, found: 433.0521.

**HPLC** (CHIRALPAK IA-H), *n*-hexane/isopropanol = 98/2, flow rate 1 mL/min, detection at 254

nm, major diastereomer:  $t_R = 9.9$  min (minor), 10.8 min (major), minor diastereomer:  $t_R = 12.8$  min (minor), 14.1 min (major).

$[\alpha]_D^{25} = 164.30$  ( $c = 0.40$ ,  $\text{CHCl}_3$ ).

**Mp:** 156.2-156.8 °C.



**(5R,6R,9R)-6-(3-methoxyphenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3j)**

Colorless oil, 24.2 mg, 67% yield, 2.5:1 *dr*, 94/80% *ee*.

**$^1\text{H NMR}$**  (400 MHz, Chloroform-*d*)  $\delta$  7.91 (dd,  $J = 8.7, 1.1$  Hz, 2H), 7.47 – 7.36 (m, 2H), 7.26 – 7.16 (m, 2H), 6.85 – 6.74 (m, 3H), 6.09 – 5.89 (m, 1H), 5.42 (s, 1H), 5.23 – 5.07 (m, 2H), 4.45 (dd,  $J = 8.6, 7.6$  Hz, 1H), 4.13 (dd,  $J = 10.1, 8.8$  Hz, 1H), 3.72 (s, 3H), 3.30 (dd,  $J = 17.0, 9.5$  Hz, 1H), 1.62 (s, 3H).

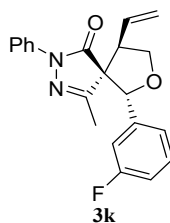
**$^{13}\text{C NMR}$**  (100 MHz, Chloroform-*d*)  $\delta$  172.8, 160.7, 159.7, 138.6, 137.8, 131.7, 129.7, 128.9, 125.2, 120.0, 118.9, 116.9, 113.9, 109.9, 87.0, 72.3, 68.6, 55.2, 52.1, 14.8.

**IR:** 2926, 2859, 1689, 1595, 1489, 1366, 1278, 1067, 995, 758, 692  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_3$   $[\text{M}+\text{Na}]^+$ : 385.1523, found: 385.1520.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 7.7$  min (minor), 17.2 min (major), minor diastereomer:  $t_R = 10.7$  min (major), 20.3 min (minor).

$[\alpha]_D^{25} = +113.72$  ( $c = 0.20$ ,  $\text{CHCl}_3$ ).



**(5R,6R,9R)-6-(3-fluorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3k)**

White solid, 26.6 mg, 76% yield, 2.5:1 *dr*, 94/71% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.90 (dd,  $J = 8.7, 1.0$  Hz, 2H), 7.48 – 7.38 (m, 2H), 7.31 – 7.19 (m, 2H), 7.07 (d,  $J = 9.7$  Hz, 1H), 6.99 (td,  $J = 8.4, 2.5$  Hz, 1H), 6.91 (d,  $J = 7.7$  Hz, 1H), 6.05 – 5.88 (m, 1H), 5.42 (s, 1H), 5.25 – 5.05 (m, 2H), 4.45 (dd,  $J = 8.6, 7.5$  Hz, 1H), 4.13 (dd,  $J = 10.0, 8.9$  Hz, 1H), 3.30 (dd,  $J = 17.0, 9.5$  Hz, 1H), 1.62 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.6, 162.9 (d,  $J = 247.0$  Hz), 160.3, 139.6 (d,  $J = 7.3$  Hz), 137.7, 131.4, 130.3 (d,  $J = 8.2$  Hz), 128.9, 125.3, 120.3 (d,  $J = 3.0$  Hz), 120.2, 119.0, 115.0 (d,  $J = 21.2$  Hz), 112.1 (d,  $J = 23.0$  Hz), 86.3, 86.3, 72.3, 68.5, 52.2, 14.7.

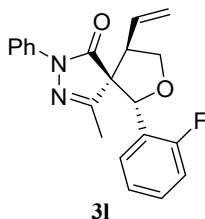
**IR:** 2922, 2859, 1697, 1590, 1486, 1367, 1271, 787, 736  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{19}\text{FN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 373.1323, found: 373.1310.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 90/10, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 5.4$  min (minor), 7.9 min (major), minor diastereomer:  $t_R = 6.6$  min (major), 9.5 min (minor).

$[\alpha]_D^{25} = +78.94$  ( $c = 0.34$ ,  $\text{CHCl}_3$ ).

**Mp:** 114.3-114.9 °C.



**(5R,6S,9R)-6-(2-fluorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (31)**

Light yellow solid, 21.0 mg, 60% yield, 2.4:1 *dr*, 93/78% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.90 (dd,  $J = 8.7, 1.0$  Hz, 2H), 7.49 – 7.37 (m, 2H), 7.32 – 7.20 (m, 2H), 7.11 – 6.85 (m, 3H), 5.97 (ddd,  $J = 16.9, 10.2, 9.2$  Hz, 1H), 5.42 (s, 1H), 5.28 – 5.05 (m, 2H), 4.46 (dd,  $J = 8.6, 7.6$  Hz, 1H), 4.13 (dd,  $J = 10.0, 8.9$  Hz, 1H), 3.30 (dd,  $J = 17.0, 9.5$  Hz, 1H), 1.62 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.6, 162.9 (d,  $J = 247.0$  Hz), 160.3, 139.7 (d,  $J = 7.3$  Hz), 137.7, 131.4, 130.3 (d,  $J = 8.2$  Hz), 128.9, 125.3, 120.3 (d,  $J = 3.0$  Hz), 120.2, 119.0, 115.0 (d,  $J = 21.1$  Hz), 112.1 (d,  $J = 23.0$  Hz), 86.3, 86.3, 72.3, 68.5, 52.3, 14.7.

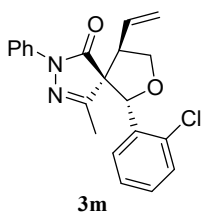
**IR:** 3081, 2987, 2855, 1698, 1593, 1490, 1368, 1250, 759, 652 cm<sup>-1</sup>;

**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>19</sub>FN<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 373.1323, found: 373.1320.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer: *t<sub>R</sub>* = 6.3 min (minor), 9.6 min (major), minor diastereomer: *t<sub>R</sub>* = 7.9 min (major), 12.1 min (minor).

$[\alpha]_{\text{D}}^{25} = 77.89$  (*c* = 0.28, CHCl<sub>3</sub>).

**Mp:** 109.9-110.9 °C.



**(5R,6S,9R)-6-(2-chlorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3m)**

White solid, 24.2 mg, 66% yield, 2:1 *dr*, 96/90% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 7.8 Hz, 2H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.40 – 7.30 (m, 3H), 7.22 (t, *J* = 7.0 Hz, 1H), 5.87 – 5.59 (m, 2H), 5.18 (d, *J* = 12.3 Hz, 2H), 4.35 (dd, *J* = 18.9, 8.0 Hz, 2H), 3.24 (dd, *J* = 17.2, 8.9 Hz, 1H), 1.38 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*) δ 173.8, 158.5, 137.8, 136.1, 131.6, 129.6, 129.5, 129.3, 128.9, 127.7, 126.8, 125.2, 121.1, 119.1, 83.5, 71.0, 67.7, 53.9, 14.3.

**IR:** 2918, 2872, 1699, 1590, 1498, 1329, 1270, 1080, 761, 688 cm<sup>-1</sup>;

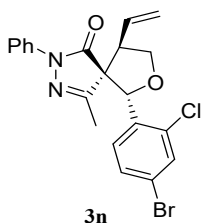
**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>19</sub>ClN<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 389.1024, found: 389.1027.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer: *t<sub>R</sub>* = 7.0 min (minor), 8.1 min (major), minor diastereomer: *t<sub>R</sub>* = 8.8 min (major), 10.6 min (minor).

$[\alpha]_{\text{D}}^{25} = 63.50$  (*c* = 0.20, CHCl<sub>3</sub>).

**Mp:** 124.1-124.9 °C.





**(5R,6S,9R)-6-(4-bromo-2-chlorophenyl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3n)**

Colorless oil, 29.7 mg, 67% yield, 3:1 *dr*, 96/20% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.90 – 7.82 (m, 2H), 7.67 (dd,  $J = 8.6, 0.8$  Hz, 1H), 7.52 – 7.48 (m, 2H), 7.46 – 7.38 (m, 2H), 7.25 – 7.19 (m, 1H), 5.84 – 5.67 (m, 1H), 5.61 (s, 1H), 5.27 – 5.06 (m, 2H), 4.42 – 4.18 (m, 2H), 3.31 – 3.12 (m, 1H), 1.45 (s, 3H).

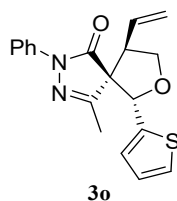
$^{13}\text{C NMR}$  (100 MHz, Chloroform-*d*)  $\delta$  173.6, 158.1, 137.7, 135.3, 132.4, 132.1, 130.1, 129.4, 129.0, 128.9, 125.3, 122.3, 121.3, 119.1, 83.2, 71.0, 67.6, 53.9, 14.6.

**IR:** 3081, 2872, 1706, 1596, 1500, 1368, 1272, 1078, 757, 690  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{18}\text{BrClN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 467.0132, found: 467.0154.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 6.6$  min (minor), 7.6 min (major), minor diastereomer:  $t_R = 8.4$  min (minor), 9.5 min (major).

$[\alpha]_D^{25} = +53.49$  ( $c = 0.34$ ,  $\text{CHCl}_3$ ).



**(5R,6S,9R)-4-methyl-2-phenyl-6-(thiophen-2-yl)-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3o)**

White solid, 21.3 mg, 63% yield, 3:1 *dr*, 95/70% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.96 – 7.86 (m, 2H), 7.46 – 7.39 (m, 2H), 7.28 – 7.20 (m, 2H), 6.98 (dd,  $J = 5.0, 3.6$  Hz, 1H), 6.83 (dt,  $J = 3.6, 1.1$  Hz, 1H), 6.03 – 5.87 (m, 1H), 5.62 (d,  $J = 0.6$  Hz, 1H), 5.25 – 5.09 (m, 2H), 4.45 (dd,  $J = 8.7, 7.6$  Hz, 1H), 4.16 (dd,  $J = 9.8, 8.9$  Hz, 1H), 3.39 (dd,  $J = 17.0, 9.4$  Hz, 1H), 1.72 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz, Chloroform-*d*)  $\delta$  172.2, 160.2, 140.0, 137.8, 131.4, 128.9, 127.3, 125.3, 124.7,

123.3, 120.1, 118.9, 84.2, 72.4, 68.6, 51.9, 14.7.

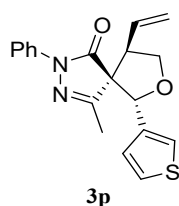
**IR:** 3080, 2858, 1698, 1591, 1488, 1366, 1325, 1269, 1060, 731, 709, 690  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{18}\text{N}_2\text{NaO}_2\text{S}$   $[\text{M}+\text{Na}]^+$ : 361.0981, found: 361.0986.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R$  = 7.8 min (minor), 12.9 min (major), minor diastereomer:  $t_R$  = 11.0 min (major), 15.7 min (minor).

$[\alpha]_D^{25} = +110.38$  ( $c = 0.26$ ,  $\text{CHCl}_3$ ).

**Mp:** 145.0-145.5  $^\circ\text{C}$ .



**(5R,6S,9R)-4-methyl-2-phenyl-6-(thiophen-3-yl)-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3p)**

White solid, 25.3 mg, 75% yield, 3:1 *dr*, 95/75% *ee*.

**$^1\text{H}$  NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.91 (d,  $J = 8.1$  Hz, 2H), 7.43 (t,  $J = 7.6$  Hz, 2H), 7.33 – 7.19 (m, 3H), 6.78 (d,  $J = 4.8$  Hz, 1H), 6.08 – 5.90 (m, 1H), 5.43 (s, 1H), 5.15 (dd,  $J = 14.0, 7.0$  Hz, 2H), 4.43 (t,  $J = 8.1$  Hz, 1H), 4.09 (t,  $J = 9.3$  Hz, 1H), 3.32 (q,  $J = 8.8$  Hz, 1H), 1.69 (s, 3H).

**$^{13}\text{C}$  NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.4, 160.9, 137.9, 137.8, 131.8, 128.9, 126.8, 125.2, 124.3, 120.7, 119.9, 118.9, 85.0, 72.4, 68.1, 52.1, 14.6.

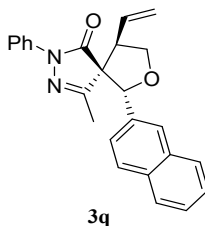
**IR:** 3080, 2855, 1698, 1592, 1489, 1366, 1325, 1270, 1068, 769, 733, 691  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{18}\text{N}_2\text{NaO}_2\text{S}$   $[\text{M}+\text{Na}]^+$ : 361.0981, found: 361.0985.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R$  = 7.7 min (minor), 13.1 min (major), minor diastereomer:  $t_R$  = 9.8 min (major), 15.2 min (minor).

$[\alpha]_D^{25} = +76.36$  ( $c = 0.38$ ,  $\text{CHCl}_3$ ).

**Mp:** 126.8-127.9  $^\circ\text{C}$ .



**(5R,6R,9R)-4-methyl-6-(naphthalen-2-yl)-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3q)**

White solid, 26.7 mg, 70% yield, 2.5:1 *dr*, 98/71% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.93 (d, *J* = 8.0 Hz, 2H), 7.88 – 7.76 (m, 4H), 7.54 – 7.42 (m, 4H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.14 – 5.92 (m, 1H), 5.62 (s, 1H), 5.26 – 5.09 (m, 2H), 4.53 (t, *J* = 8.1 Hz, 1H), 4.21 (t, *J* = 9.4 Hz, 1H), 3.37 (q, *J* = 8.7 Hz, 1H), 1.55 (s, 3H).

<sup>13</sup>C NMR (100 MHz, Chloroform-*d*)  $\delta$  172.9, 160.7, 137.9, 134.4, 133.0, 133.0, 131.6, 128.9, 128.5, 128.1, 127.8, 126.5, 126.2, 125.3, 123.7, 122.5, 120.1, 119.0, 87.3, 72.4, 68.6, 52.4, 14.9.

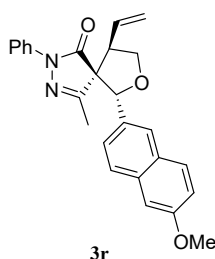
IR: 3056, 2852, 1694, 1594, 1493, 1382, 1325, 756, 692 cm<sup>-1</sup>;

HRMS (ESI) *m/z* calcd for C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 405.1573, found: 405.1559.

HPLC (CHIRALPAK IC-H), *n*-hexane/isopropanol = 95/5, flow rate 1 mL/min, detection at 254 nm, major diastereomer: *t<sub>R</sub>* = 12.3 min (major), 16.9 min (minor), minor diastereomer: *t<sub>R</sub>* = 12.8 min (major), 16.7 min (minor).

$[\alpha]_{\text{D}}^{25} = + 213.41$  (*c* = 0.32, CHCl<sub>3</sub>).

Mp: 135.9-137.1 °C.



**(5R,6R,9R)-6-(6-methoxynaphthalen-2-yl)-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3r)**

White solid, 30.5 mg, 74% yield, 2.5:1 *dr*, 96/31% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.97 – 7.89 (m, 2H), 7.78 (s, 1H), 7.69 (dd, *J* = 15.0, 8.8 Hz, 2H), 7.49 – 7.41 (m, 2H), 7.27 – 7.22 (m, 1H), 7.20 – 7.11 (m, 3H), 6.10 – 5.92 (m, 1H), 5.59 (s, 1H), 5.24 – 5.11 (m, 2H), 4.52 (dd, *J* = 8.6, 7.5 Hz, 1H), 4.21 (dd, *J* = 10.1, 8.8 Hz, 1H), 3.93 (s,

3H), 3.37 (dd,  $J = 17.0, 9.6$  Hz, 1H), 1.58 (d,  $J = 16.3$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz, Chloroform- $d$ )  $\delta$  173.0, 160.8, 157.9, 137.9, 134.2, 132.1, 131.7, 129.6, 128.9, 128.5, 127.3, 125.2, 123.5, 123.1, 120.0, 119.3, 119.0, 105.7, 87.3, 72.4, 68.7, 55.3, 52.3, 14.9.

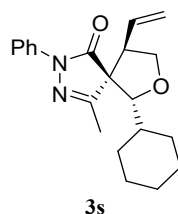
IR: 3055, 2857, 1688, 1596, 1488, 1369, 1268, 1175, 779, 690  $\text{cm}^{-1}$ ;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{NaO}_3$   $[\text{M}+\text{Na}]^+$ : 435.1679, found: 435.1678.

HPLC (CHIRALPAK IC-H),  $n$ -hexane/isopropanol = 95/5, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}} = 12.3$  min (major), 16.9 min (minor), minor diastereomer:  $t_{\text{R}} = 14.3$  min (major), 22.4 min (minor).

$[\alpha]_{\text{D}}^{25} = +241.65$  ( $c = 0.38$ ,  $\text{CHCl}_3$ ).

Mp: 102.4-102.9  $^{\circ}\text{C}$ .



**(5R,6R,9R)-6-cyclohexyl-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one**  
**(3s)**

Colorless oil, 16.9 mg, 50% yield, 4:1  $dr$ , 90/74%  $ee$ .

$^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  7.86 (dd,  $J = 8.7, 1.1$  Hz, 2H), 7.45 – 7.35 (m, 2H), 7.23 – 7.15 (m, 1H), 6.05 – 5.88 (m, 1H), 5.15 – 4.99 (m, 2H), 4.24 (dd,  $J = 8.7, 7.8$  Hz, 1H), 3.89 (d,  $J = 10.5$  Hz, 1H), 3.72 (t,  $J = 9.2$  Hz, 1H), 3.11 (dd,  $J = 17.1, 9.3$  Hz, 1H), 2.27 (s, 3H), 2.09 (d,  $J = 13.2$  Hz, 1H), 1.79 – 1.72 (m, 1H), 1.68 – 1.56 (m, 4H), 1.30 – 0.94 (m, 2H), 0.93 – 0.76 (m, 1H).

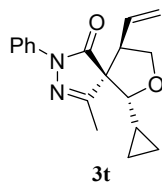
$^{13}\text{C}$  NMR (100 MHz, Chloroform- $d$ )  $\delta$  172.4, 161.4, 138.0, 132.8, 128.9, 125.1, 119.3, 119.0, 91.7, 72.0, 66.1, 52.9, 39.5, 31.2, 27.8, 26.1, 25.6, 25.4, 15.6.

IR: 2926, 2852, 1708, 1597, 1500, 1370, 1122, 1062, 757, 651  $\text{cm}^{-1}$ ;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 361.1886, found: 361.1882.

HPLC (CHIRALPAK AD-H),  $n$ -hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_{\text{R}} = 5.5$  min (minor), 7.0 min (major), minor diastereomer:  $t_{\text{R}} = 6.6$  min (minor), 9.9 min (major).

$[\alpha]_{\text{D}}^{25} = -54.56$  ( $c = 0.20$ ,  $\text{CHCl}_3$ ).



**(5R,6R,9R)-6-cyclopropyl-4-methyl-2-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3t)**

Colorless oil, 23.2 mg, 77% yield, 5.1:1 *dr*, 97% *ee*.

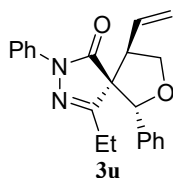
<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.96 – 7.82 (m, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.15 – 5.88 (m, 1H), 5.21 – 5.01 (m, 2H), 4.30 (t, *J* = 8.2 Hz, 1H), 3.84 (t, *J* = 9.1 Hz, 1H), 3.47 (d, *J* = 9.4 Hz, 1H), 3.24 (q, *J* = 8.9 Hz, 1H), 2.31 (d, *J* = 1.5 Hz, 3H), 1.07 – 0.85 (m, 1H), 0.78 – 0.62 (m, 1H), 0.55 – 0.33 (m, 2H), 0.22 – 0.07 (m, 1H).

<sup>13</sup>C NMR (100 MHz, Chloroform-*d*)  $\delta$  172.4, 161.1, 137.9, 132.7, 128.9, 125.1, 119.1, 118.9, 92.4, 72.5, 67.3, 51.5, 15.7, 10.8, 4.5, 0.9. IR: 3081, 2861, 1706, 1596, 1500, 1368, 1126, 1072, 760, 692 cm<sup>-1</sup>;

HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 319.1418, found: 319.1417.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, *t*<sub>R</sub> = 6.1 min (minor), 9.0 min (major).

[ $\alpha$ ]<sub>D</sub><sup>25</sup> = - 3.68 (*c* = 0.38, CHCl<sub>3</sub>).



**(5R,6R,9R)-4-ethyl-2,6-diphenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3u)**

Colorless oil, 21.8 mg, 63% yield, 2.2:1 *dr*, 95/78% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.97 – 7.91 (m, 2H), 7.47 – 7.40 (m, 2H), 7.36 – 7.27 (m, 3H), 7.25 – 7.17 (m, 3H), 6.07 – 5.91 (m, 1H), 5.43 (s, 1H), 5.26 – 5.07 (m, 2H), 4.44 (dd, *J* = 8.5, 7.5 Hz, 1H), 4.11 (dd, *J* = 10.2, 8.8 Hz, 1H), 3.30 (dd, *J* = 17.1, 9.6 Hz, 1H), 2.11 (dq, *J* = 17.3, 7.3 Hz, 1H), 1.62 (dq, *J* = 17.3, 7.4 Hz, 1H), 0.86 (t, *J* = 7.3 Hz, 3H).

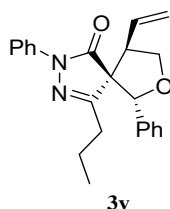
<sup>13</sup>C NMR (100 MHz, Chloroform-*d*)  $\delta$  172.9, 164.7, 138.1, 137.0, 131.8, 128.9, 128.5, 128.0, 125.1, 124.6, 119.9, 119.0, 87.42, 72.4, 68.9, 52.2, 22.0, 9.4.

IR: 3064, 2978, 1705, 1597, 1499, 1351, 1067, 757, 726 cm<sup>-1</sup>;

**HRMS** (ESI)  $m/z$  calcd for  $C_{22}H_{22}N_2NaO_2$   $[M+Na]^+$ : 369.1573, found: 369.1565.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R$  = 5.9 min (minor), 10.8 min (major), minor diastereomer:  $t_R$  = 7.2 min (major), 13.5 min (minor).

$[\alpha]_D^{25} = +89.64$  ( $c = 0.20$ ,  $CHCl_3$ ).



**(5R,6R,9R)-2,6-diphenyl-4-propyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3v)**

Colorless oil, 20.5 mg, 57% yield, 2.3:1 *dr*, 95/75% *ee*.

**$^1H$  NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.96 – 7.91 (m, 2H), 7.46 – 7.40 (m, 2H), 7.34 – 7.29 (m, 3H), 7.25 – 7.19 (m, 3H), 6.09 – 5.91 (m, 1H), 5.44 (s, 1H), 5.21 – 5.07 (m, 2H), 4.44 (dd,  $J = 8.5$ , 7.6 Hz, 1H), 4.11 (dd,  $J = 10.2$ , 8.8 Hz, 1H), 3.31 (dd,  $J = 17.1$ , 9.6 Hz, 1H), 2.13 – 1.97 (m, 1H), 1.59 – 1.44 (m, 2H), 1.28 – 1.06 (m, 1H), 0.75 (dd,  $J = 8.9$ , 5.5 Hz, 3H).

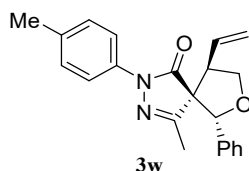
**$^{13}C$  NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.8, 163.7, 138.1, 136.9, 131.8, 128.9, 128.5, 128.0, 125.1, 124.7, 119.9, 118.9, 87.5, 72.4, 68.8, 52.2, 30.5, 18.4, 13.7.

**IR**: 3064, 2962, 1706, 1597, 1500, 1359, 1068, 756, 692  $cm^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $C_{23}H_{25}N_2NaO_2$   $[M+Na]^+$ : 383.1730, found: 383.1738.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R$  = 5.6 min (minor), 8.4 min (major), minor diastereomer:  $t_R$  = 6.5 min (major), 10.8 min (minor).

$[\alpha]_D^{25} = +92.78$  ( $c = 0.26$ ,  $CHCl_3$ ).



**(5R,6R,9R)-4-methyl-6-phenyl-2-(*p*-tolyl)-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3w)**

White solid, 22.5 mg, 65% yield, 4:1 *dr*, 96/75% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.79 – 7.74 (m, 2H), 7.34 – 7.29 (m, 3H), 7.25 – 7.19 (m, 4H), 6.07 – 5.90 (m, 1H), 5.44 (s, 1H), 5.20 – 5.10 (m, 2H), 4.45 (dd,  $J = 8.6, 7.5$  Hz, 1H), 4.13 (dd,  $J = 10.1, 8.8$  Hz, 1H), 3.30 (dd,  $J = 17.0, 9.6$  Hz, 1H), 2.38 (s, 3H), 1.57 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.6, 160.5, 137.0, 135.4, 135.0, 131.7, 129.4, 128.6, 128.1, 124.7, 119.9, 119.0, 87.1, 72.3, 68.5, 52.2, 21.0, 14.7.

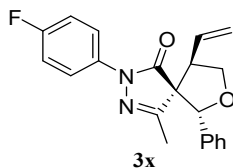
**IR:** 3022, 2855, 1694, 1508, 1367, 1330, 1064, 823, 751  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 369.1573, found: 369.1585.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 90/10, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 6.5$  min (minor), 14.9 min (major), minor diastereomer:  $t_R = 7.7$  min (major), 20.1 min (minor).

$[\alpha]_D^{25} = +98.58$  ( $c = 0.28$ ,  $\text{CHCl}_3$ ).

**Mp:** 119.8-120.7 °C.



**(5R,6R,9R)-2-(4-fluorophenyl)-4-methyl-6-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3x)**

Colorless oil, 24.1 mg, 69% yield, 2:1 *dr*, 94/74% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.92 – 7.83 (m, 2H), 7.37 – 7.29 (m, 3H), 7.26 – 7.21 (m, 2H), 7.14 – 7.04 (m, 2H), 6.10 – 5.87 (m, 1H), 5.44 (s, 1H), 5.24 – 5.08 (m, 2H), 4.46 (dd,  $J = 8.6, 7.5$  Hz, 1H), 4.14 (dd,  $J = 10.1, 8.8$  Hz, 1H), 3.31 (dd,  $J = 17.0, 9.6$  Hz, 1H), 1.58 (s, 3H).

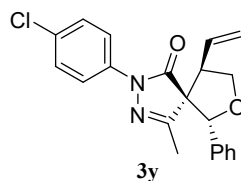
**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  172.7, 160.9, 160.0(d,  $J = 244.7$  Hz), 136.9, 134.0(d,  $J = 2.8$  Hz), 131.6, 128.6, 128.2, 124.7, 120.7(d,  $J = 8.0$  Hz), 120.1, 115.6(d,  $J = 22.6$  Hz), 87.1, 72.3, 68.6, 52.2, 14.7.

**IR:** 3077, 2921, 2853, 1705, 1596, 1515, 1368, 1251, 1072, 762  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{19}\text{FN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 373.1323, found: 373.1319.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 7.4$  min (minor), 10.4 min (major), minor diastereomer:  $t_R = 9.3$  min (major), 14.3 min (minor).

$[\alpha]_D^{25} = +133.82$  ( $c = 0.22$ ,  $\text{CHCl}_3$ ).



**(5R,6R,9R)-2-(4-chlorophenyl)-4-methyl-6-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3y)**

White solid, 22.3 mg, 62% yield, 2:1 *dr*, 85/75% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.89 (d,  $J = 7.9$  Hz, 2H), 7.38 (d,  $J = 7.9$  Hz, 2H), 7.31 (d,  $J = 7.3$  Hz, 3H), 7.21 (d,  $J = 7.0$  Hz, 2H), 6.09 – 5.85 (m, 1H), 5.43 (s, 1H), 5.16 (dd,  $J = 13.6, 8.6$  Hz, 2H), 4.46 (t,  $J = 8.0$  Hz, 1H), 4.13 (t,  $J = 9.4$  Hz, 1H), 3.31 (q,  $J = 8.8$  Hz, 1H), 1.58 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz, Chloroform-*d*)  $\delta$  172.8, 161.0, 136.8, 136.4, 131.5, 130.2, 128.9, 128.6, 128.2, 124.6, 120.1, 119.9, 87.1, 72.3, 68.7, 52.2, 14.7.

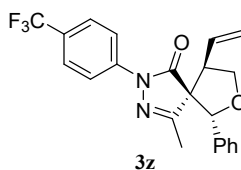
**IR:** 3021, 2856, 1698, 1488, 1328, 1065, 833, 726  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{19}\text{ClN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 389.1027, found: 389.1031.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 85/15, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 5.2$  min (minor), 8.8 min (major), minor diastereomer:  $t_R = 6.6$  min (major), 12.8 min (minor).

$[\alpha]_D^{25} = +101.16$  ( $c = 0.26$ ,  $\text{CHCl}_3$ ).

**Mp:** 98.8-100.6 °C.



**(5R,6R,9R)-4-methyl-6-phenyl-2-(4-(trifluoromethyl)phenyl)-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3z)**

Colorless oil, 24.4 mg, 61% yield, 2.9:1 *dr*, 93/72% *ee*.

$^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  8.09 (d,  $J = 8.5$  Hz, 2H), 7.68 (d,  $J = 8.6$  Hz, 2H), 7.36 – 7.29 (m, 3H), 7.24 – 7.18 (m, 2H), 6.02 – 5.87 (m, 1H), 5.44 (s, 1H), 5.23 – 5.08 (m, 2H), 4.47 (dd,  $J = 8.7, 7.5$  Hz, 1H), 4.14 (dd,  $J = 10.1, 8.9$  Hz, 1H), 3.32 (dd,  $J = 17.0, 9.6$  Hz, 1H), 1.60 (s, 3H).



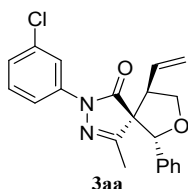
$^{13}\text{C}$  NMR (100 MHz, Chloroform-*d*)  $\delta$  173.2, 161.4, 140.2, 136.7, 131.4, 128.6, 128.3, 126.7 (q,  $J = 32.8$  Hz), 126.1 (q,  $J = 3.8$  Hz), 124.6, 124.1 (q,  $J = 271.7$  Hz), 120.27, 118.22, 87.19, 72.31, 68.87, 52.33, 14.76.

**IR:** 3065, 2863, 1713, 1614, 1520, 1325, 1165, 1125, 1068, 843, 718  $\text{cm}^{-1}$ ;

**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{19}\text{F}_3\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 423.1291, found: 423.1299.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 85/15, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 4.3$  min (minor), 7.0 min (major), minor diastereomer:  $t_R = 5.1$  min (major), 8.6 min (minor).

$[\alpha]_{\text{D}}^{25} = 106.84$  ( $c = 0.26$ ,  $\text{CHCl}_3$ ).



**(5*R*,6*R*,9*R*)-2-(3-chlorophenyl)-4-methyl-6-phenyl-9-vinyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (3aa)**

Colorless oil, 20.1 mg, 55% yield, 3:1 *dr*, 91/77% *ee*.

$^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.98 (t,  $J = 2.0$  Hz, 1H), 7.88 (ddd,  $J = 8.3, 2.0, 0.9$  Hz, 1H), 7.38 – 7.30 (m, 4H), 7.26 – 7.16 (m, 3H), 6.08 – 5.83 (m, 1H), 5.44 (s, 1H), 5.28 – 5.01 (m, 2H), 4.47 (dd,  $J = 8.7, 7.5$  Hz, 1H), 4.13 (dd,  $J = 10.1, 8.8$  Hz, 1H), 3.53 – 3.16 (m, 1H), 1.58 (s, 3H).

$^{13}\text{C}$  NMR (100 MHz, Chloroform-*d*)  $\delta$  172.9, 161.1, 138.8, 136.8, 134.7, 131.4, 130.0, 128.6, 128.2, 125.1, 124.6, 120.2, 118.7, 116.5, 87.1, 72.3, 68.8, 52.3, 14.7.

**IR:** 3076, 2863, 1709, 1593, 1483, 1366, 1088, 780, 715  $\text{cm}^{-1}$ ;

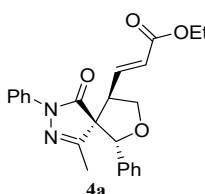
**HRMS** (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{19}\text{ClN}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 389.1027, found: 389.1031.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 94/6, flow rate 1 mL/min, detection at 254 nm, major diastereomer:  $t_R = 5.0$  min (minor), 5.8 min (major), minor diastereomer:  $t_R = 6.5$  min (major), 7.0 min (minor).

$[\alpha]_{\text{D}}^{25} = + 53.49$  ( $c = 0.34$ ,  $\text{CHCl}_3$ ).

## 7. Synthetic transforms of the enantioenriched **3a**

To a stirred solution of Hoveyda-Grubbs 2<sup>nd</sup> generation catalyst (0.009 mmol, 5.6 mg, 6 mol%) in toluene (1.0 mL) under an N<sub>2</sub> atmosphere, optically active substrate **3a** (49.8 mg, 0.15 mmol, 1.0 equiv., 98% ee) in toluene (2.0 mL) and ethyl acrylate (164 μL, 1.5 mmol, 10 equiv.) were added in this order. Then the reaction mixture was heated at 90 °C. After being stirred at the same temperature for 2 h, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with Petroleum / EtOAc (85:15) to afford (**4a**) (49.6 mg, 82%) as a colorless oil.<sup>3</sup>



**Ethyl (E)-3-((5R,6R,9R)-1-methyl-4-oxo-3,6-diphenyl-7-oxa-2,3-diazaspiro[4.4]non-1-en-9-yl)acrylate (**4a**)**

Colorless oil, 49.6 mg, 82% yield, 20:1 *dr*, 97% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.83 (m, 2H), 7.46 – 7.39 (m, 2H), 7.36 – 7.29 (m, 3H), 7.26 – 7.19 (m, 3H), 7.07 (dd, *J* = 15.6, 9.3 Hz, 1H), 5.87 (dd, *J* = 15.6, 0.8 Hz, 1H), 5.47 (s, 1H), 4.51 (dd, *J* = 8.7, 7.5 Hz, 1H), 4.29 – 4.10 (m, 3H), 3.42 (td, *J* = 9.1, 7.6 Hz, 1H), 1.61 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, Chloroform-*d*) δ 172.0, 165.1, 160.1, 140.8, 137.6, 136.3, 128.9, 128.6, 128.3, 125.6, 125.4, 124.6, 119.2, 87.6, 71.9, 68.2, 60.7, 49.7, 14.8, 14.2.

IR: 2981, 2868, 1709, 1596, 1500, 1369, 1254, 1183, 1069, 985, 758, 720 cm<sup>-1</sup>;

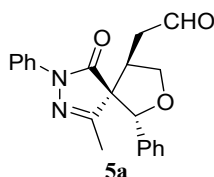
HRMS (ESI) *m/z* calcd for C<sub>24</sub>H<sub>24</sub>N<sub>2</sub>NaO<sub>4</sub> [M+Na]<sup>+</sup>: 427.1628, found: 427.1620.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 92/8, flow rate 1 mL/min, detection at 254 nm, *t<sub>R</sub>* = 14.0 min (major), 16.1 min (minor).

[α]<sub>D</sub><sup>25</sup> = + 147.72 (*c* = 0.92, CHCl<sub>3</sub>).

To a stirred solution of optically active substrate **3a** (66.4 mg, 0.2 mmol, 1.0 equiv., 98% ee) in THF (2 mL) and H<sub>2</sub>O (2 mL), PdCl<sub>2</sub> (7.1 mg, 0.04 mmol, 0.2 equiv.), CuCl (39.6 mg, 0.4 mmol, 2.0

equiv.) were added at room temperature under an O<sub>2</sub> atmosphere. After being stirred at room temperature for 24 h under an O<sub>2</sub> atmosphere, the reaction mixture was diluted with EtOAc and poured into water. The aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with Petroleum / EtOAc (80 : 20) to afford (**5a**) (35.3 mg, 51%) as a colorless oil.<sup>3</sup>



**2-((5R,6R,9R)-1-methyl-4-oxo-3,6-diphenyl-7-oxa-2,3-diazaspiro[4.4]non-1-en-9-yl)acetaldehyde (**5a**)**

Colorless oil, 35.3 mg, 51% yield, 20:1 *dr*, 97% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  9.73 (s, 1H), 7.97 – 7.67 (m, 2H), 7.47 – 7.37 (m, 2H), 7.30 (dd, *J* = 4.9, 1.9 Hz, 2H), 7.28 – 7.26 (m, 1H), 7.25 – 7.19 (m, 3H), 5.20 (s, 1H), 4.65 (dd, *J* = 8.7, 7.6 Hz, 1H), 3.81 (t, *J* = 8.9 Hz, 1H), 3.36 – 3.08 (m, 2H), 2.87 (dd, *J* = 18.7, 5.6 Hz, 1H), 1.82 (s, 3H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  199.6, 172.6, 161.8, 137.7, 135.7, 128.9, 128.5, 128.3, 125.5, 124.4, 119.4, 88.0, 73.1, 66.3, 42.8, 39.7, 15.0.

**IR**: 3064, 2857, 2729, 1720, 1702, 1670, 1596, 1500, 1369, 1095, 761, 718 cm<sup>-1</sup>;

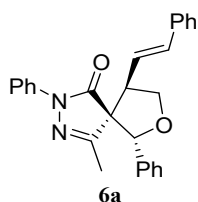
**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>NaO<sub>3</sub> [M+Na]<sup>+</sup>: 371.1366, found: 371.1365.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 98/2, flow rate 1 mL/min, detection at 254 nm, *t<sub>R</sub>* = 8.7 min (minor), 14.0 min (major).

**$[\alpha]_D^{25}$**  = + 218.64 (*c* = 0.40, CHCl<sub>3</sub>).

To a mixture of optically active substrate **3a** (66.4 mg, 0.2 mmol, 1.0 equiv., 98% *ee*), iodobenzene (81.6 mg, 0.4 mmol, 2 equiv.), K<sub>2</sub>CO<sub>3</sub> (55.2 mg, 0.4 mmol, 2 equiv.), Pd(OAc)<sub>2</sub> (4.6 mg, 0.02 mmol, 0.1 equiv.) in a sealed vial, DMF (3.0 mL) was added at room temperature under an argon atmosphere. After being stirred at 100 °C for 12 h, the reaction mixture was passed through a pad of celite, and concentrated under reduced pressure. The residue was purified by silica gel column

chromatography with Petroleum / EtOAc (95 : 5) to afford (**6a**) (64.1 mg, 81% ) as a white solid.<sup>3</sup>



**(5R,6R,9R)-4-methyl-2,6-diphenyl-9-((E)-styryl)-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one**  
**(6a)**

White solid, 64.1 mg, 81% yield, 20:1 *dr*, 97% *ee*.

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.97 – 7.76 (m, 2H), 7.43 – 7.37 (m, 2H), 7.32 (dd, *J* = 9.7, 4.4 Hz, 5H), 7.30 (d, *J* = 4.0 Hz, 2H), 7.28 – 7.23 (m, 3H), 7.22 – 7.17 (m, 1H), 6.54 – 6.33 (m, 2H), 5.51 (s, 1H), 4.52 (dd, *J* = 8.6, 7.6 Hz, 1H), 4.21 (dd, *J* = 10.0, 8.9 Hz, 1H), 3.50 (ddd, *J* = 10.0, 8.8, 7.5 Hz, 1H), 1.65 (s, 3H).

<sup>13</sup>C NMR (100 MHz, Chloroform-*d*)  $\delta$  172.8, 160.8, 137.8, 136.9, 136.2, 134.7, 128.9, 128.6, 128.6, 128.2, 128.0, 126.6, 125.3, 124.7, 122.9, 119.1, 87.4, 72.7, 68.8, 51.7, 14.8.

IR: 3028, 2863, 1704, 1596, 1499, 1368, 1068, 971, 756, 692 cm<sup>-1</sup>;

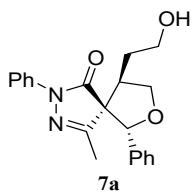
HRMS (ESI) *m/z* calcd for C<sub>27</sub>H<sub>24</sub>N<sub>2</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 431.1730, found: 431.1731.

HPLC (CHIRALPAK AD-H), *n*-hexane/isopropanol = 90/10, flow rate 1 mL/min, detection at 254 nm, *t*<sub>R</sub> = 8.5 min (minor), 10.0 min (major).

$[\alpha]_D^{25} = +250.85$  (*c* = 0.82, CHCl<sub>3</sub>).

Mp: 88.5-89.4 °C.

A solution of **3a** (49.8 mg, 0.15 mmol, 1.0 equiv., 98% *ee*) in dry THF (2 mL) at room temperature was added dropwise 9-BBN (0.5 M in THF, 4.5 mL, 15 equiv.). The mixture was stirred at 25 °C for 2 h, and this mixture was added dropwise water (0.5 mL), aq NaOH (3 M, 2 mL), then 30% aq H<sub>2</sub>O<sub>2</sub> (2 mL). After being stirred at 40 °C for 2 h, the mixture was extracted with ether (3×20 mL). The organic layer was combined and dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvents under reduced pressure, The residue was purified by silica gel column chromatography with Petroleum / EtOAc (50:50) to afford (**7a**) (26.3 mg, 49%) as a colorless oil.<sup>4</sup>



**(5R,6R,9R)-9-(2-hydroxyethyl)-4-methyl-2,6-diphenyl-7-oxa-2,3-diazaspiro[4.4]non-3-en-1-one (7a)**

Colorless oil, 26.7 mg, 49% yield, 20:1 *dr*, 98% *ee*.

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.94 – 7.88 (m, 2H), 7.48 – 7.41 (m, 2H), 7.33 – 7.28 (m, 3H), 7.26 – 7.19 (m, 3H), 5.33 (s, 1H), 4.62 – 4.47 (m, 1H), 3.95 (dd, *J* = 10.3, 8.7 Hz, 1H), 3.58 (m, 2H), 2.97 (dq, *J* = 10.3, 7.3 Hz, 1H), 1.91 (ddd, *J* = 13.3, 6.6, 2.8 Hz, 2H), 1.64 (s, 3H), 1.40 (s, 1H).

**<sup>13</sup>C NMR** (100 MHz, Chloroform-*d*)  $\delta$  173.4, 162.3, 137.9, 136.7, 128.9, 128.5, 128.1, 125.3, 124.6, 119.0, 87.9, 73.5, 67.3, 60.9, 44.339, 30.0, 14.8.

**IR:** 3413, 2923, 2869, 1709, 1596, 1500, 1368, 1066, 758, 715 cm<sup>-1</sup>;

**HRMS** (ESI) *m/z* calcd for C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>NaO<sub>3</sub> [M+Na]<sup>+</sup>: 373.1523, found: 373.1518.

**HPLC** (CHIRALPAK AD-H), *n*-hexane/isopropanol = 85/15, flow rate 1 mL/min, detection at 254 nm, *t<sub>R</sub>* = 7.2 min (minor), 8.0 min (major).

**$[\alpha]_D^{25}$**  = + 173.54 (*c* = 0.52, CHCl<sub>3</sub>).

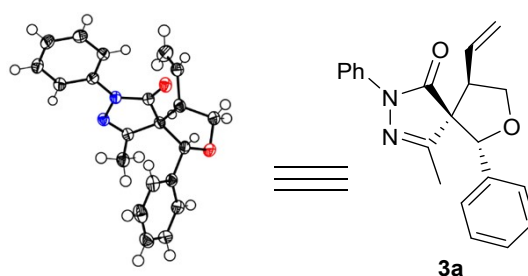
## 8. Crystal data for enantiopure products 3a

**Preparations:** Compound **3a** (20.0 mg) was dissolved in *n*-hexane (3 mL) in a vial.

The vial was properly sealed with parafilm and kept at 20°C to allow the slow evaporation of the solvent until a single crystal was obtained. The crystals were subjected for single crystal XRD to determine the absolute configuration of **3a**.

**Methods:** The data set was collected by a Bruker D8 VENTURE with MetalJet source at 173 K equipped with micro-focus Ga radiation source ( $K\alpha = 1.34138 \text{ \AA}$ ). Applied with face-indexed numerical absorption correction, the structure solution and refinement were processed by SHELXTL program package.

**Date of 3a:** CCDC 2301125 contains the supplementary crystallographic data, and can be obtained via <https://www.ccdc.cam.ac.uk/>



**Figure S4.** Single crystal structure **3a** (ellipsoid contour probability 50%).

**Table 1.** Crystal data and structure refinement for **3a**.

Identification code	<b>3a</b>
Empirical formula	$C_{21}H_{20}N_2O_2$
Formula weight	332.39
Temperature	173(2) K
Wavelength	1.34139 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	$a = 7.7270(4) \text{ \AA}$ $a = 90^\circ$ $b = 11.6009(6) \text{ \AA}$ $b = 90^\circ$ $c = 19.1442(10) \text{ \AA}$ $g = 90^\circ$
Volume	$1716.09(15) \text{ \AA}^3$
Z	4
Density (calculated)	$1.287 \text{ Mg/m}^3$

Absorption coefficient	0.424 mm <sup>-1</sup>
F(000)	704
Crystal size	0.310 x 0.240 x 0.070 mm <sup>3</sup>
Theta range for data collection	3.876 to 57.106°.
Index ranges	-9<=h<=9, -14<=k<=14, -23<=l<=23
Reflections collected	32396
Independent reflections	3507 [R(int) = 0.0473]
Completeness to theta = 53.594°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.751 and 0.592
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	3507 / 0 / 228
Goodness-of-fit on F <sup>2</sup>	1.054
Final R indices [I>2sigma(I)]	R <sub>1</sub> = 0.0284, wR <sub>2</sub> = 0.0748
R indices (all data)	R <sub>1</sub> = 0.0292, wR <sub>2</sub> = 0.0756
Absolute structure parameter	0.00(7)
Extinction coefficient	0.0087(13)
Largest diff. peak and hole	0.186 and -0.151 e.Å <sup>-3</sup>

**Table 2.** Atomic coordinates (x 10<sup>4</sup>) and equivalent isotropic displacement parameters (Å<sup>2</sup> x 10<sup>3</sup>). for **3a** U(eq) is defined as one third of the trace of the orthogonalized U<sup>ij</sup> tensor.

	x	y	z	U(eq)
O(1)	8478(1)	2126(1)	8351(1)	32(1)
O(2)	9762(2)	3513(1)	6523(1)	36(1)
N(1)	5566(2)	2526(1)	8164(1)	24(1)
N(2)	4554(2)	3025(1)	7627(1)	25(1)
C(1)	7302(2)	2560(1)	8017(1)	23(1)
C(2)	5590(2)	3398(1)	7153(1)	24(1)
C(3)	7465(2)	3242(1)	7340(1)	23(1)
C(4)	8369(2)	4449(1)	7451(1)	27(1)
C(5)	10118(2)	4272(2)	7092(1)	36(1)
C(6)	8708(2)	2625(1)	6813(1)	27(1)
C(7)	4689(2)	2037(1)	8744(1)	23(1)

C(8)	2885(2)	1966(1)	8730(1)	27(1)
C(9)	2017(2)	1482(2)	9291(1)	33(1)
C(10)	2922(2)	1065(2)	9863(1)	36(1)
C(11)	4706(2)	1142(2)	9873(1)	35(1)
C(12)	5610(2)	1630(1)	9320(1)	29(1)
C(13)	4915(2)	3956(2)	6510(1)	33(1)
C(14)	8502(2)	4852(1)	8194(1)	30(1)
C(15)	7757(3)	5796(2)	8430(1)	44(1)
C(16)	7868(2)	1928(1)	6244(1)	26(1)
C(17)	7129(2)	873(1)	6407(1)	35(1)
C(18)	6331(3)	216(2)	5891(1)	44(1)
C(19)	6281(2)	611(2)	5211(1)	44(1)
C(20)	7020(2)	1660(2)	5044(1)	41(1)
C(21)	7808(2)	2317(2)	5559(1)	34(1)

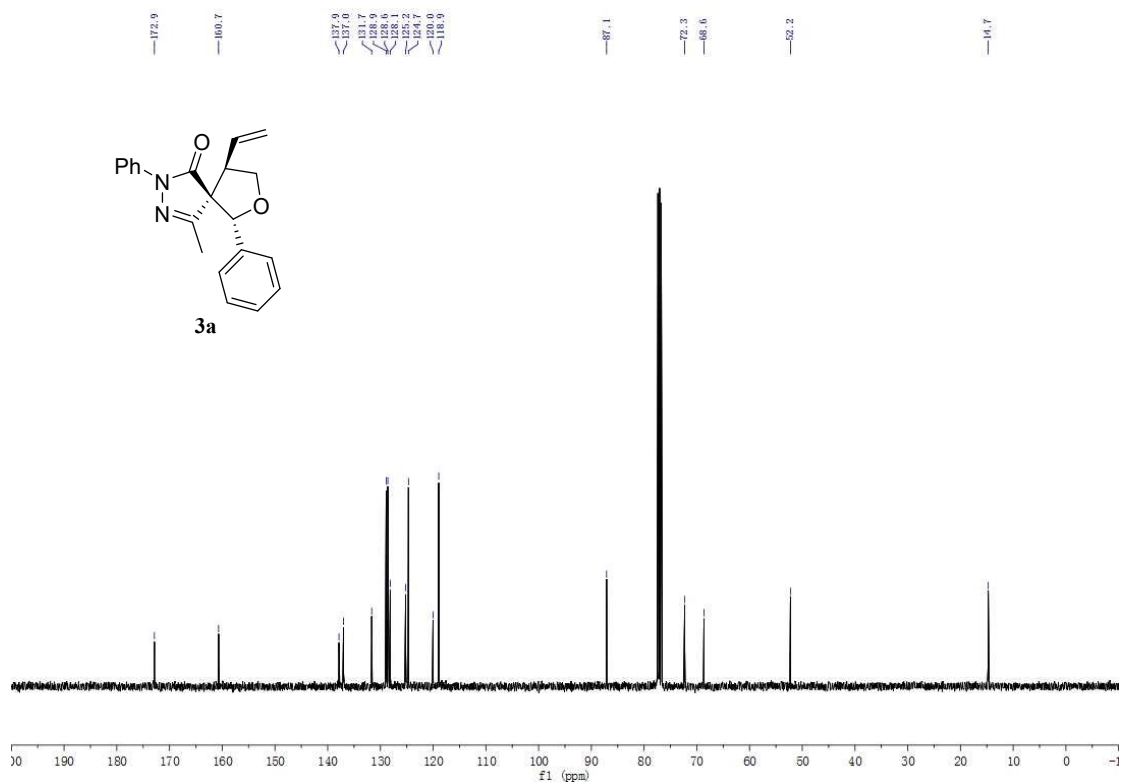
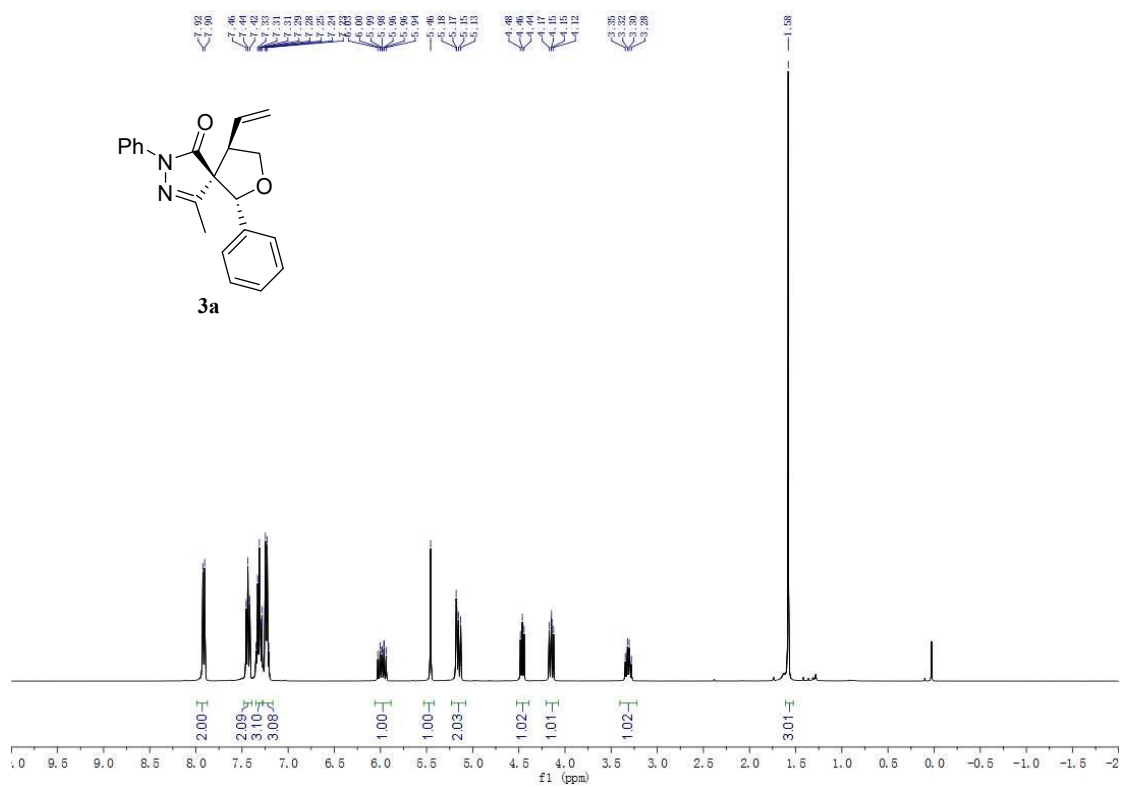
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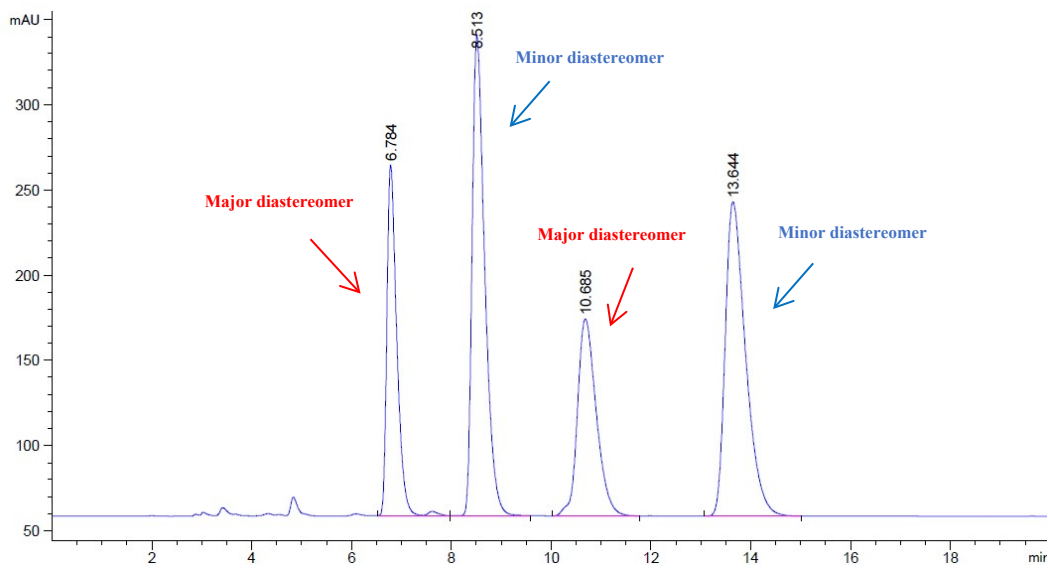


## 9. Reference

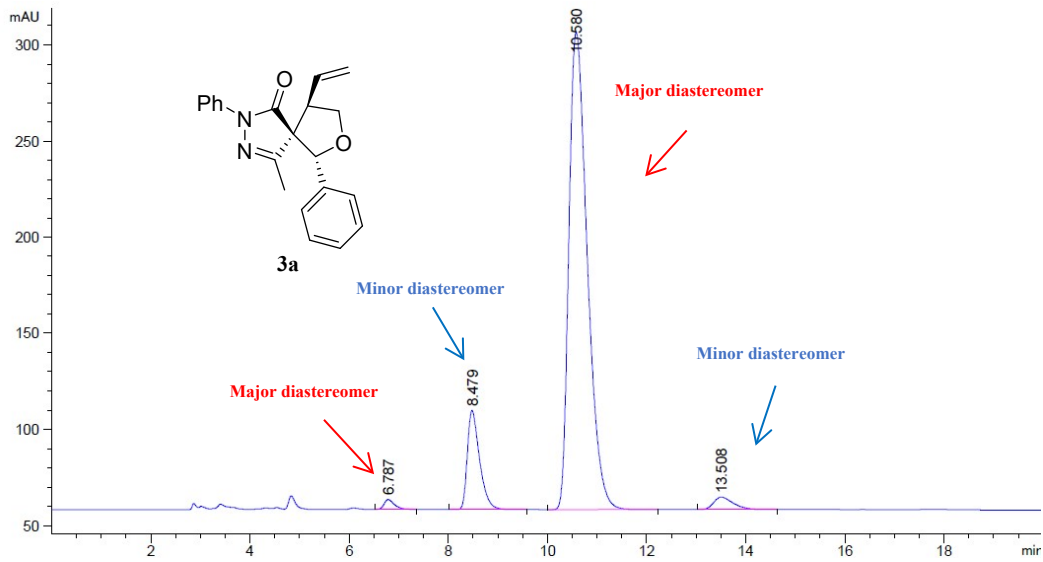
- (1) H. Fakhraian, Y. Nafari, *J. Chem. Sci.* **2021**, 133, 40, 2-11.
- (2) S. Meninno, A. Roselli, A. Capobianco, J. Overgaard, A. Lattanzi, *Org. Lett.* **2017**, 19, 5030-5033
- (3) T. Morita, H. Murakami, Y. Asawa, H. Nakamura, *Angew. Chem. Int. Ed.* **2021**, e202113558 (1 of 5).
- (4) X.B. Huang, X.J. Li, T.T. Li, B. Chen, W.D. Chu, L. He, Q.Z. Liu, *Org. Lett.* **2019**, 21, 1713-1716.

## 10. The NMR spectra and HPLC chromatograms of compounds

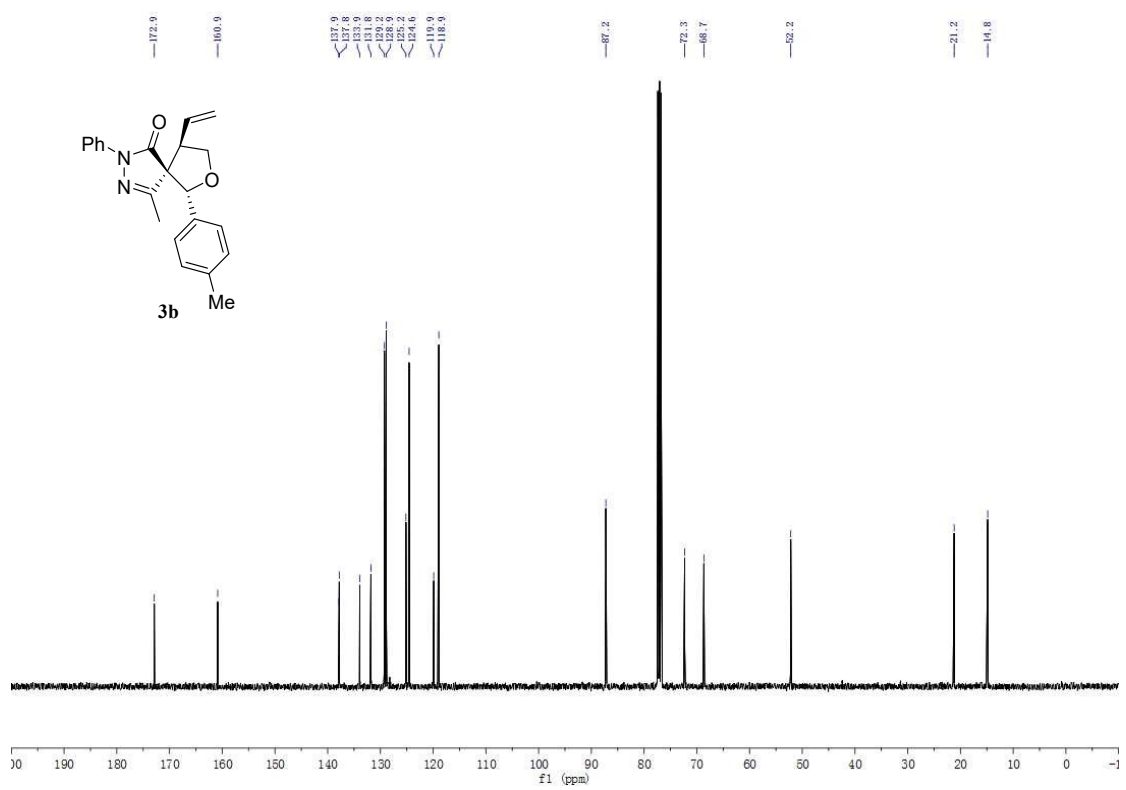
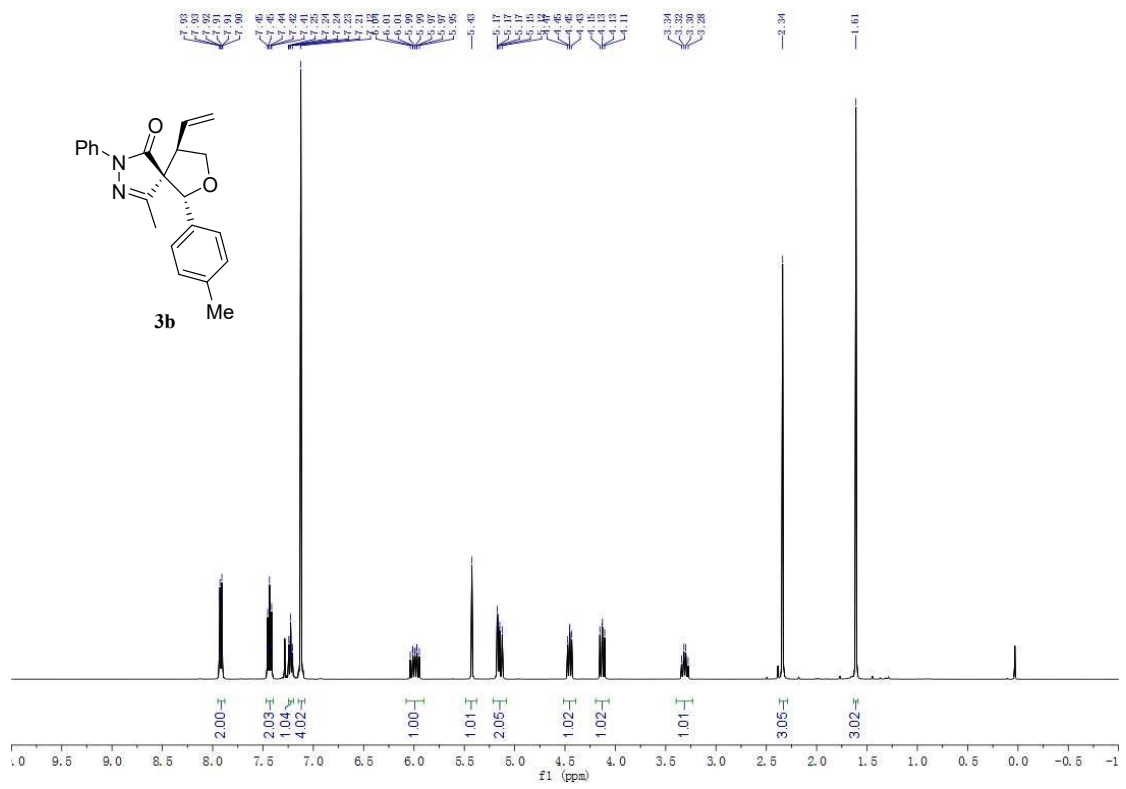


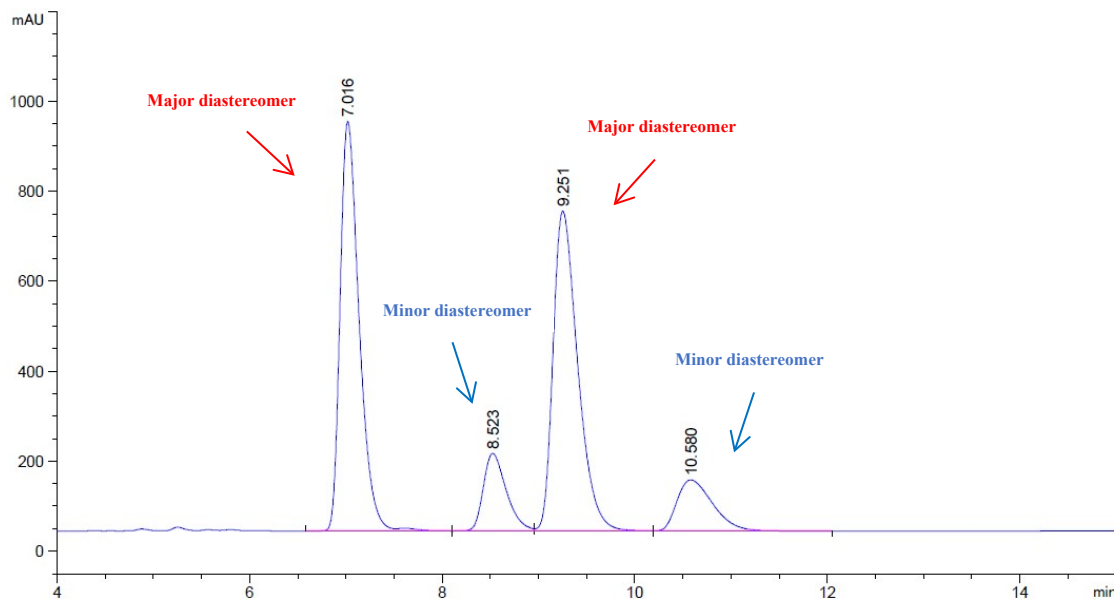


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1	6.784	BV R	0.2054	2844.04980	205.78218	17.7197
2	8.513	BB	0.2661	4953.42578	281.72397	30.8621
3	10.685	BB	0.4006	3027.42920	115.56310	18.8623
4	13.644	BB	0.4286	5225.27051	184.41006	32.5558

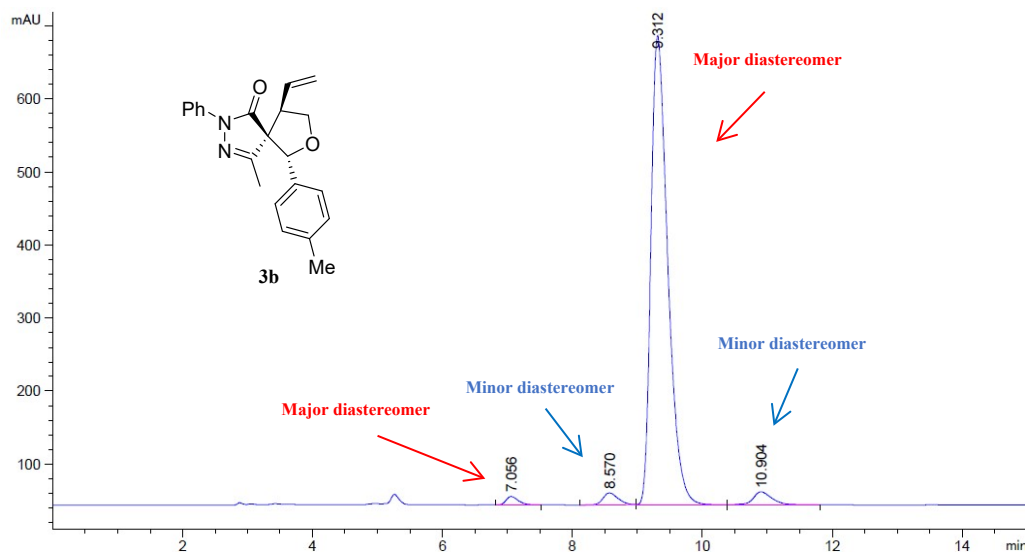


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1	6.787	BB	0.2155	72.13745	5.05490	0.9604
2	8.479	BB	0.2569	877.63507	51.48354	11.6840
3	10.580	BB	0.3971	6383.95410	248.21346	84.9902
4	13.508	BB	0.4094	177.67122	6.48986	2.3654

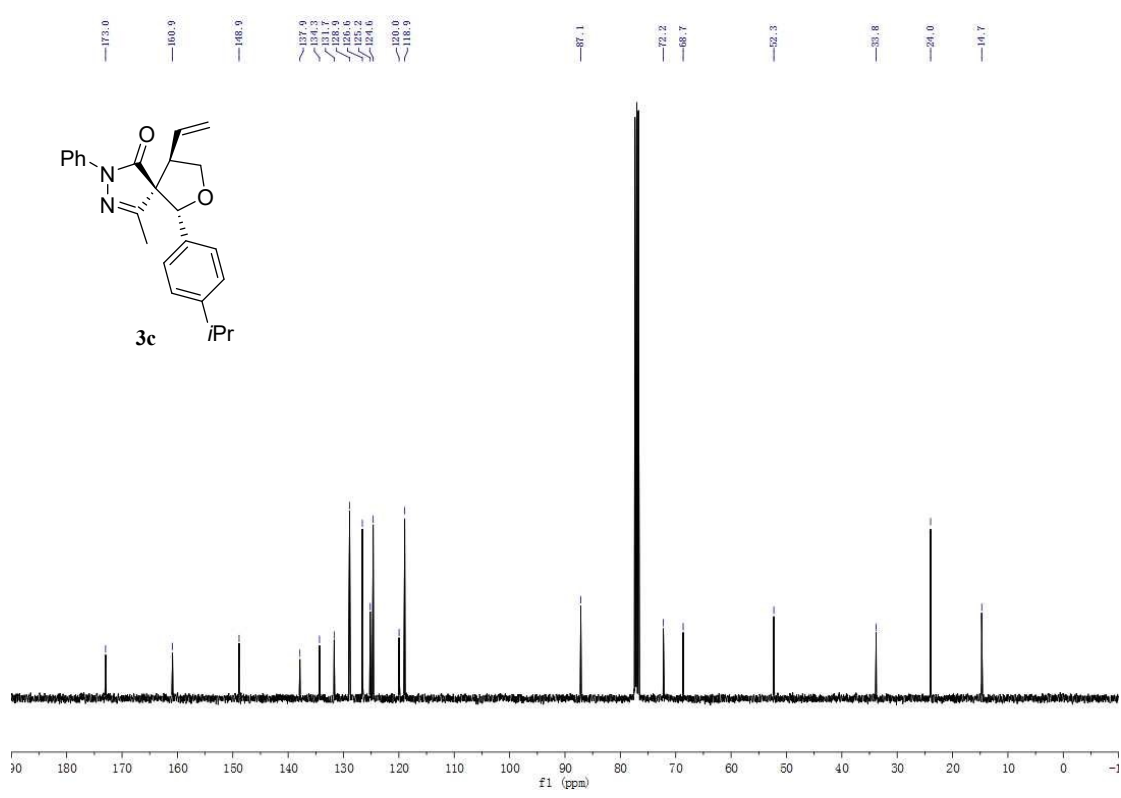
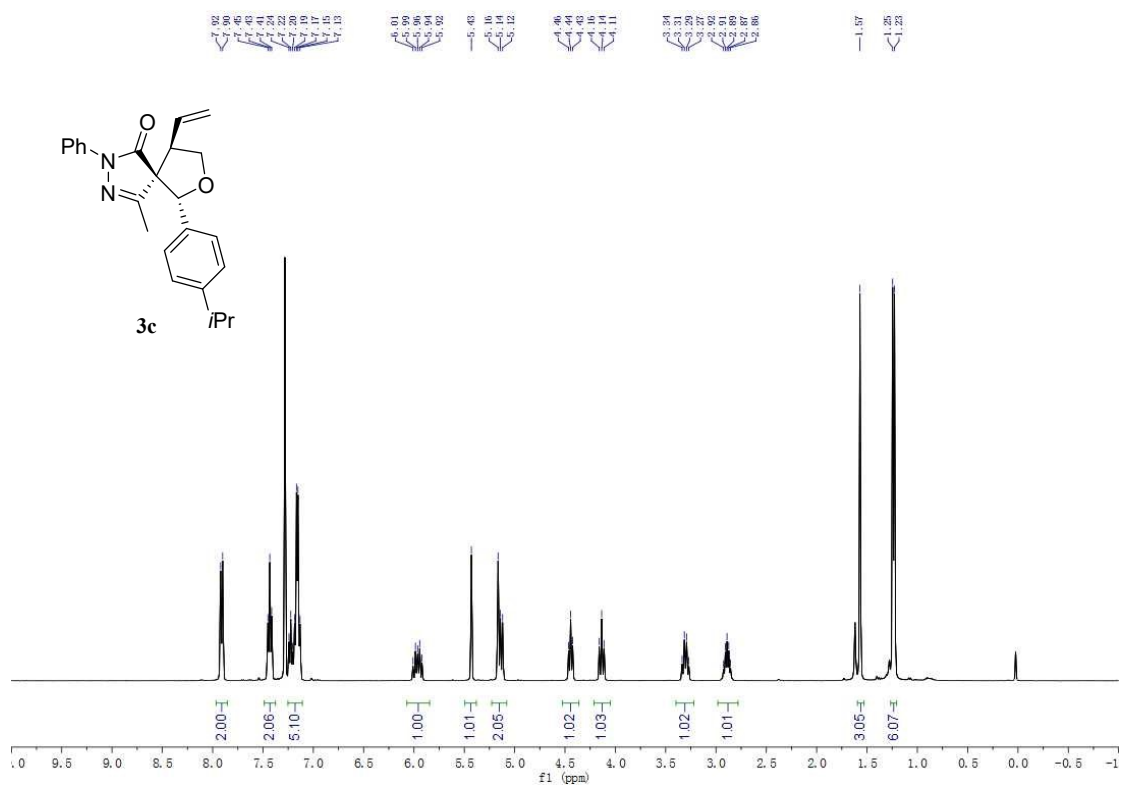


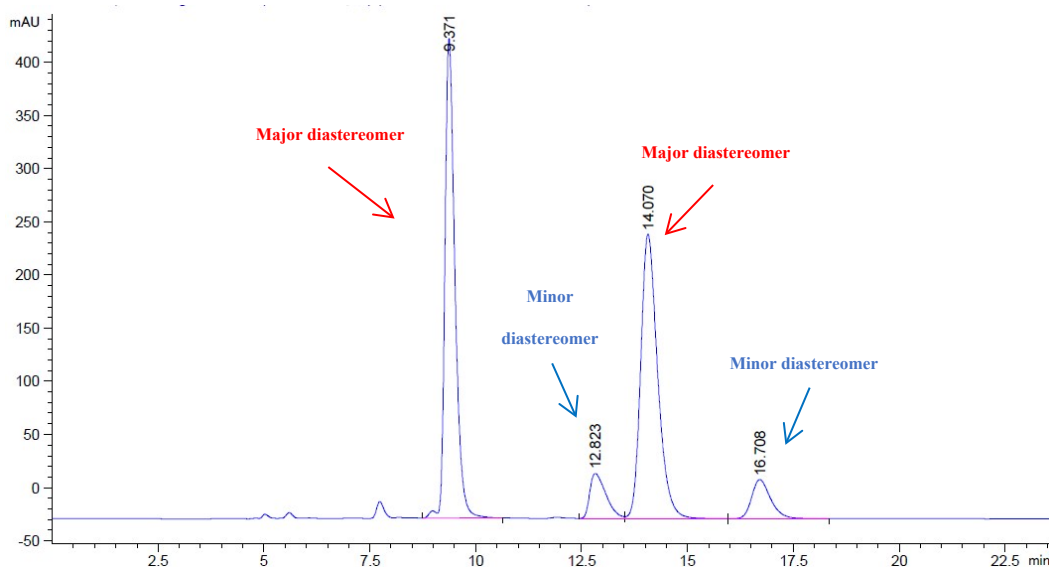


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1	7.016	BV R	0.2099	1.25577e4	910.45563	40.5590
2	8.523	BV	0.2530	2852.03906	172.37343	9.2115
3	9.251	VV	0.2722	1.26334e4	711.49420	40.8035
4	10.580	VB	0.4030	2918.43774	113.48211	9.4260

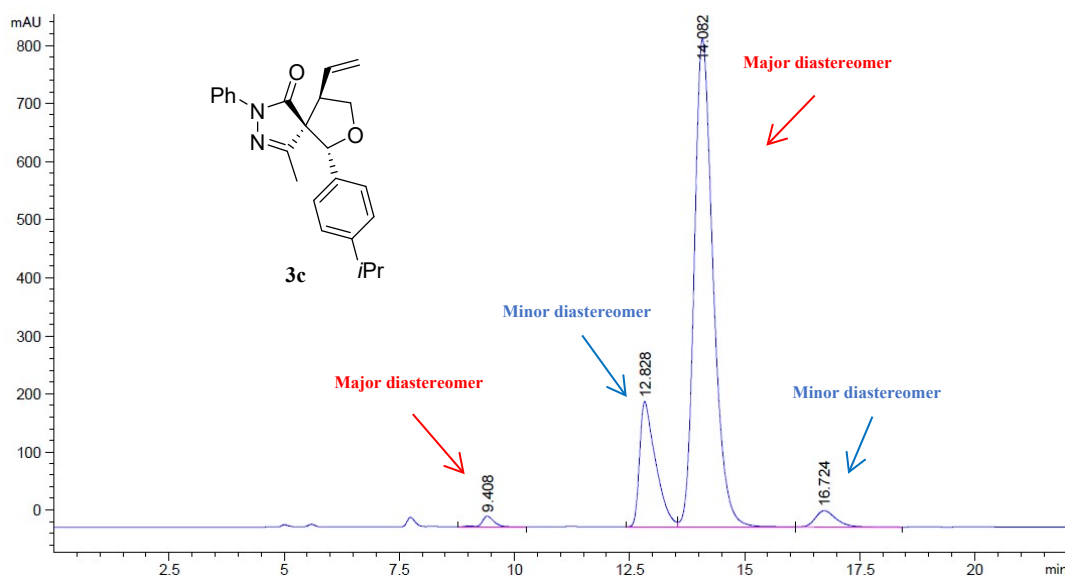


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.056	BB	0.1997	151.15945	11.54569	1.2271
2	8.570	BV	0.2521	274.53577	16.50154	2.2287
3	9.312	VB	0.2745	1.15288e4	642.08301	93.5902
4	10.904	BB	0.3030	363.88870	17.91195	2.9540

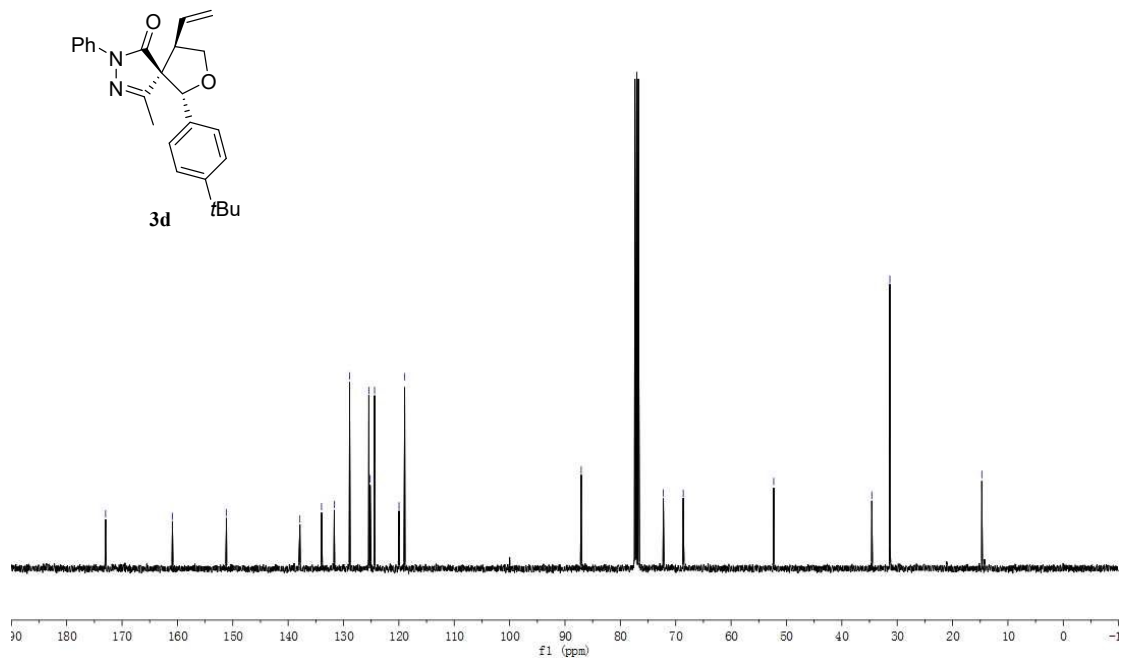
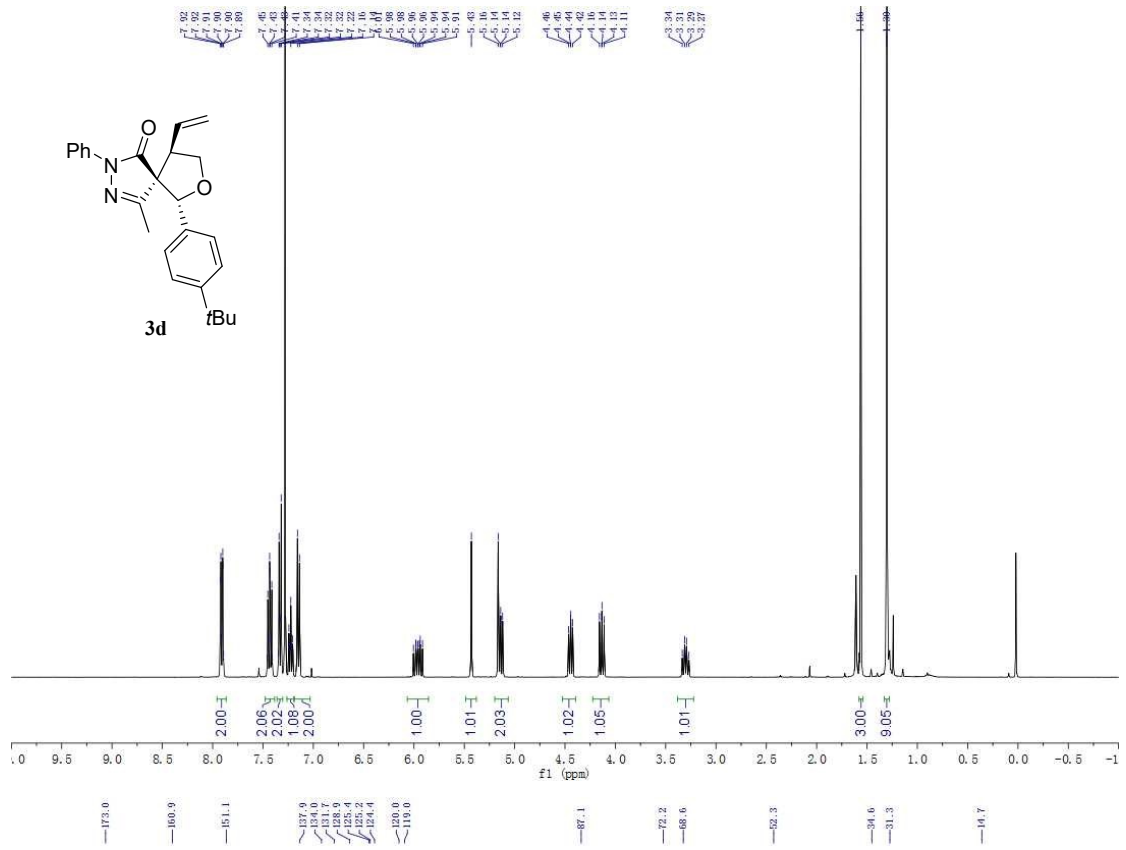




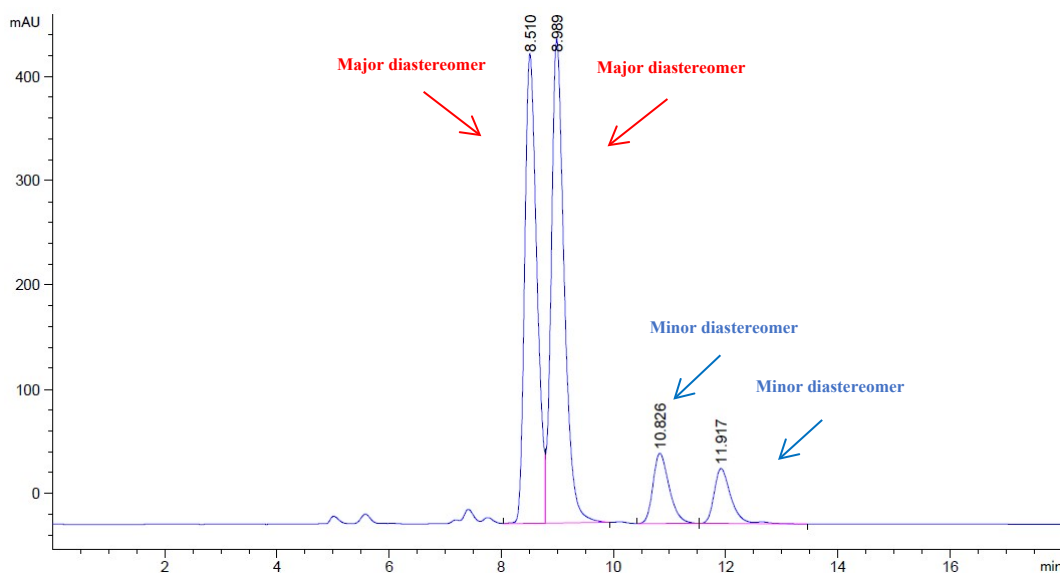
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.371	VB R	0.2469	7426.61523	451.44104	43.3835
2	12.823	BV	0.4165	1118.96069	42.45557	6.5366
3	14.070	VB	0.4209	7428.18115	267.59888	43.3927
4	16.708	BB	0.4758	1144.76147	36.81086	6.6873



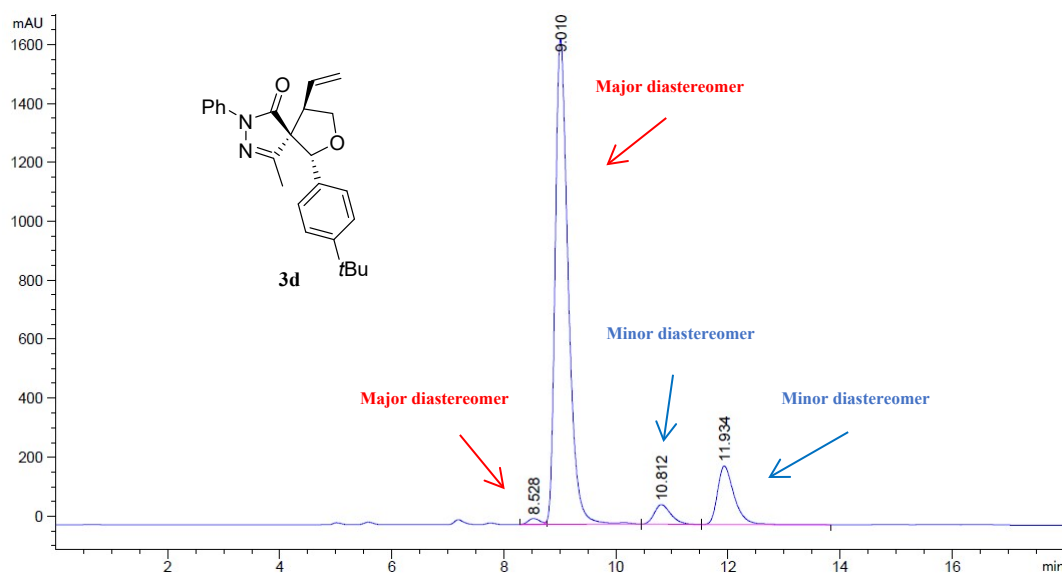
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1	9.408	VB R	0.2574	335.31424	18.48689	1.1073
2	12.828	BV	0.3460	5225.16064	215.43951	17.2552
3	14.082	VB	0.4330	2.38420e4	840.40344	78.7343
4	16.724	BB	0.4704	879.12665	28.07169	2.9032



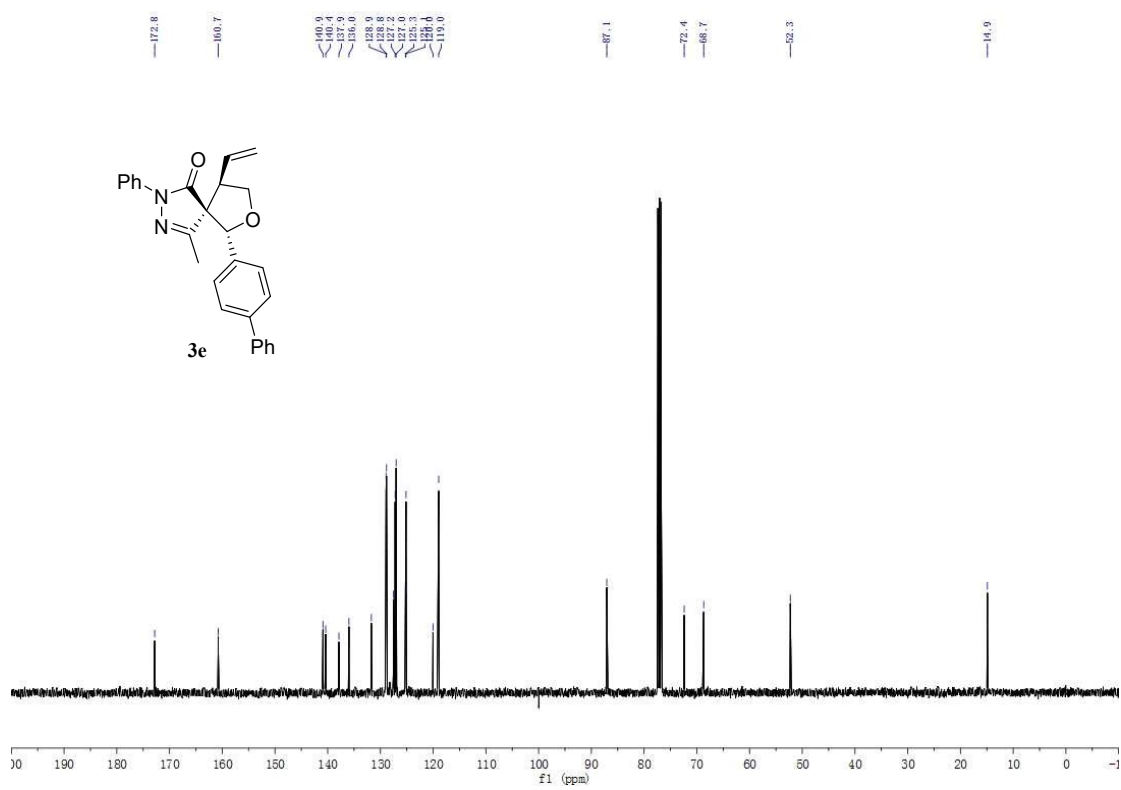
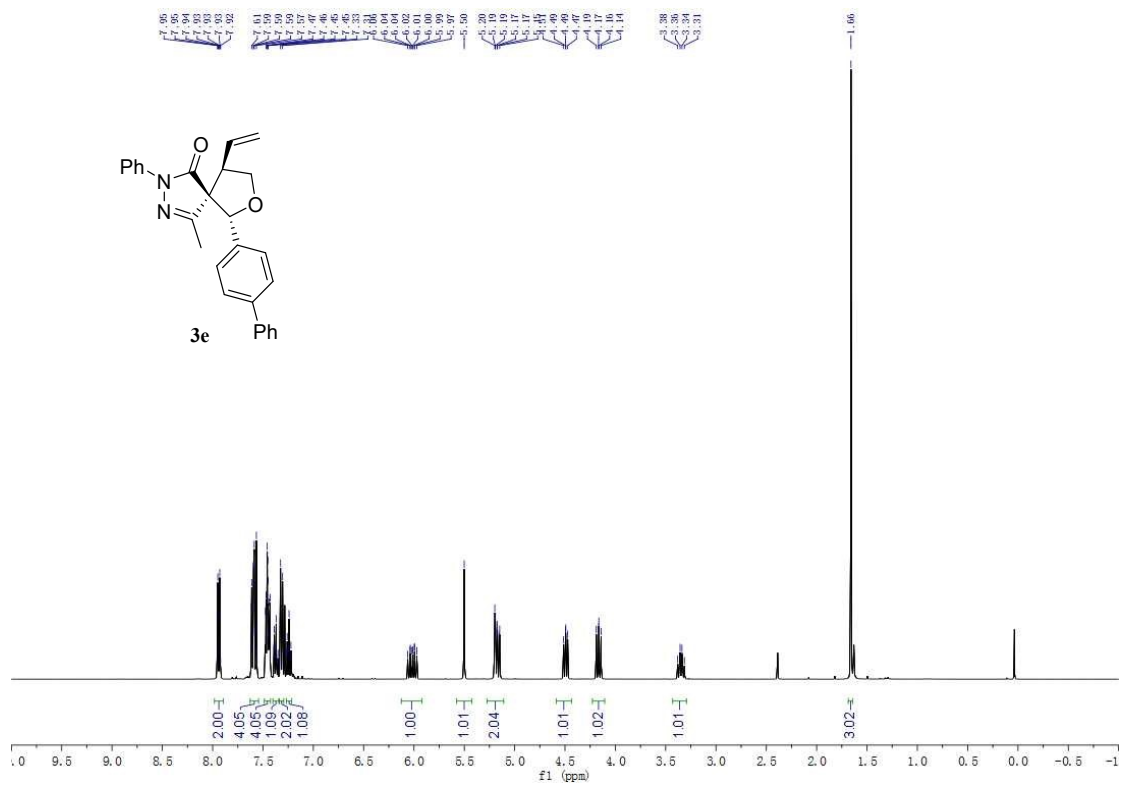


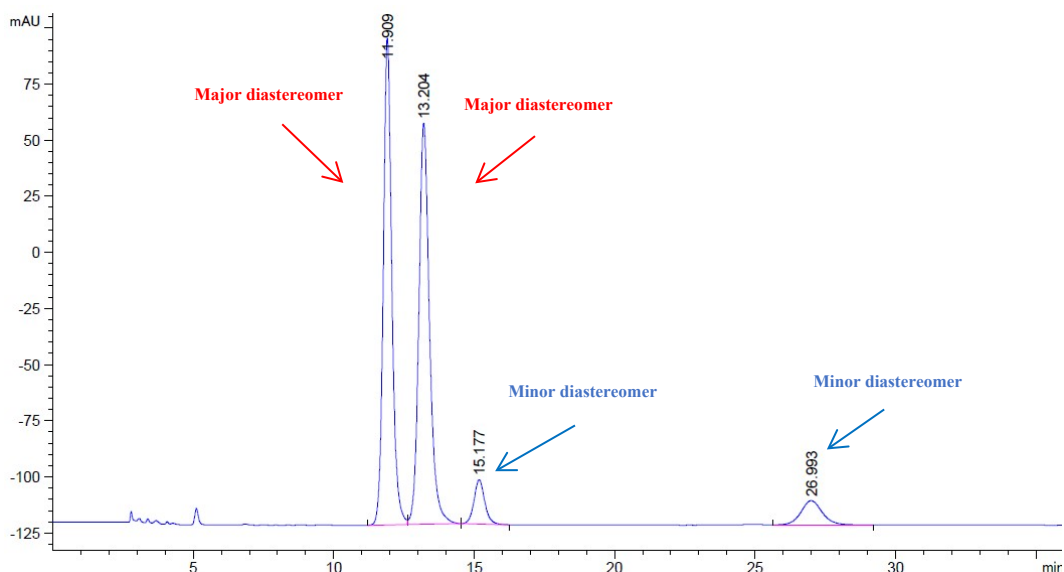


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.510	BV	0.2305	6775.79785	450.34171	40.6544
2	8.989	VB	0.2420	7445.92285	464.53021	44.6751
3	10.826	BB	0.3042	1345.72620	67.32690	8.0743
4	11.917	BV R	0.3143	1099.39868	52.71207	6.5963

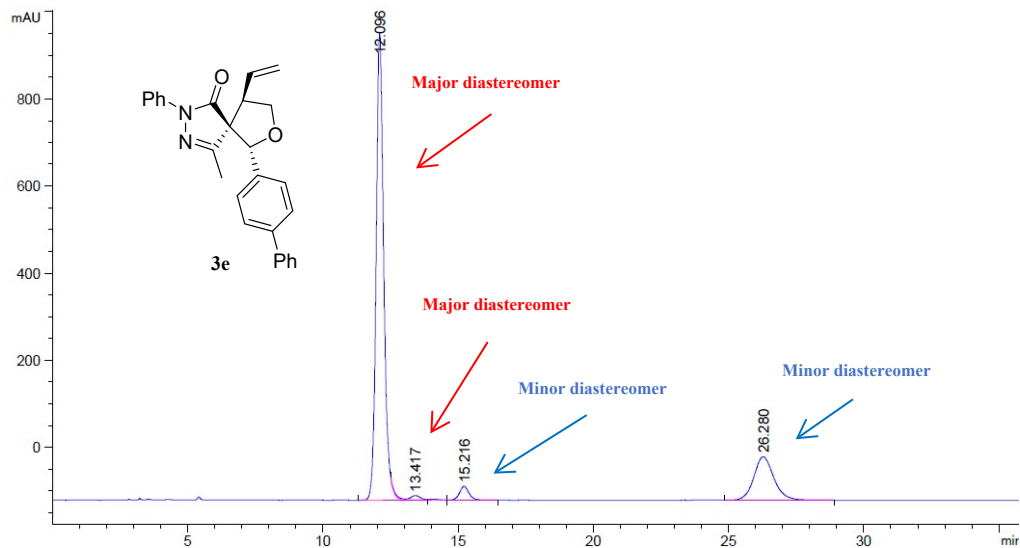


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1	8.528	BV E	0.2180	277.98630	20.01963	0.8629
2	9.010	VV R	0.2452	2.64822e4	1647.21118	82.2009
3	10.812	BB	0.3112	1366.97607	66.68384	4.2431
4	11.934	BB	0.3115	4089.26318	198.40981	12.6931

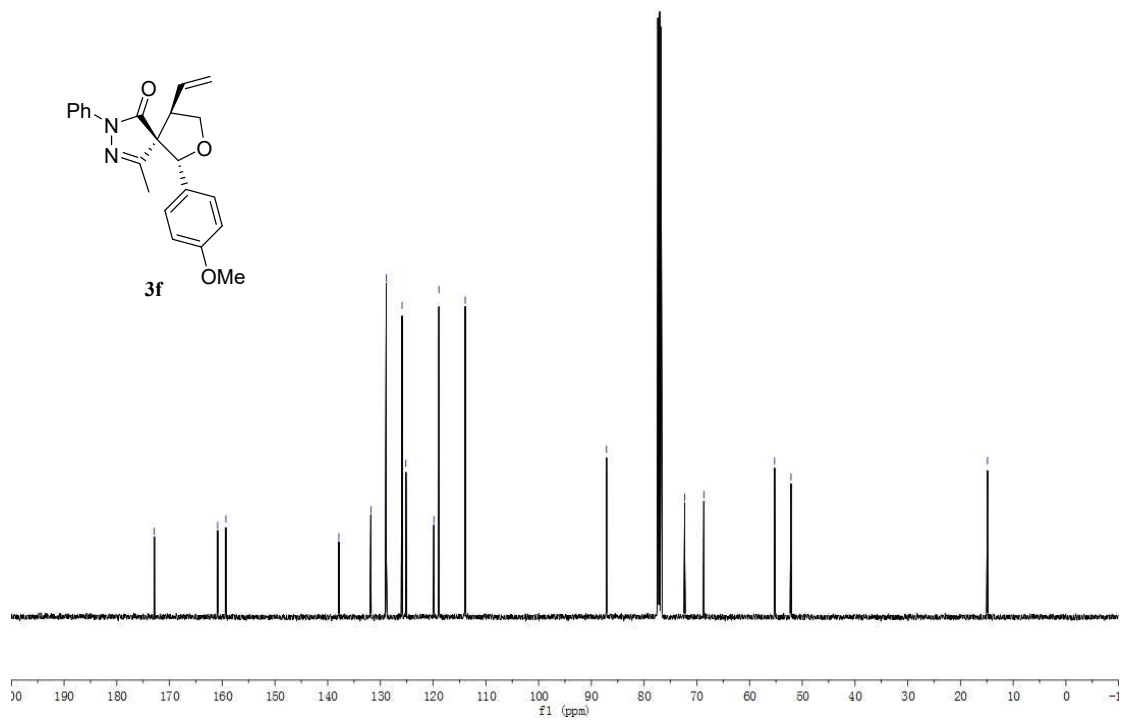
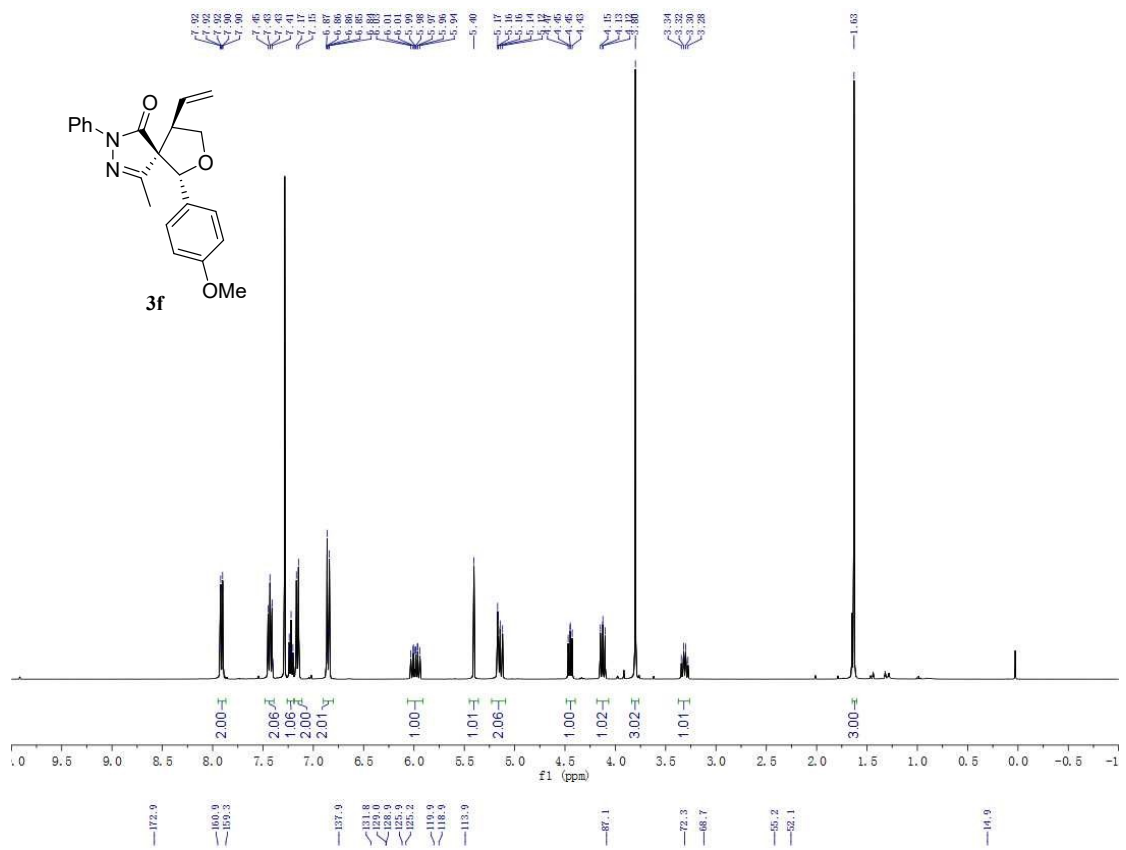


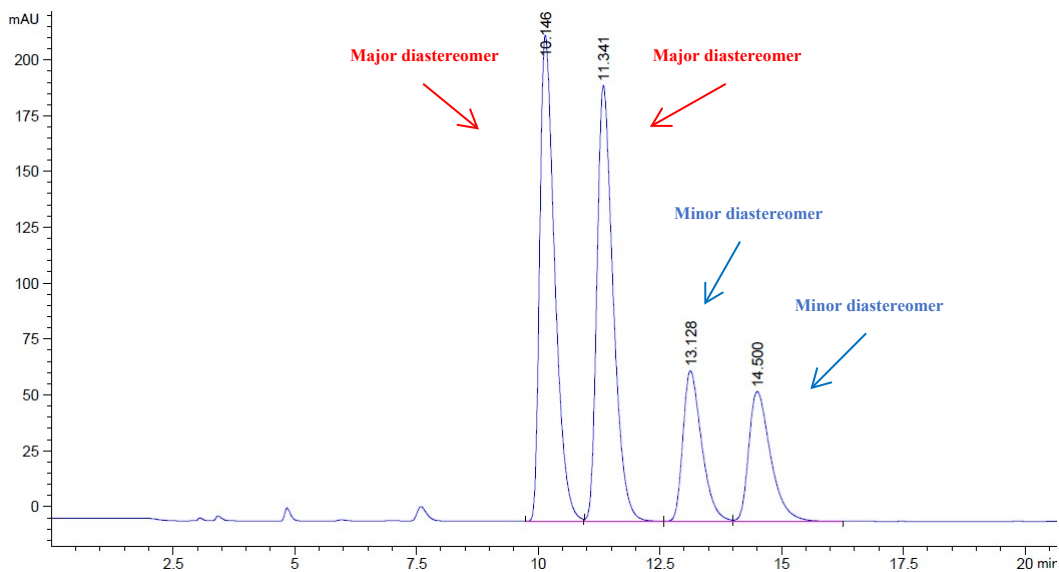


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1	11.909	BV	0.3188	4573.96924	217.08252	44.0840
2	13.204	VB	0.3961	4706.44043	178.79344	45.3608
3	15.177	BB	0.4033	522.03986	19.68804	5.0314
4	26.993	BB	0.7825	573.11578	10.84538	5.5237

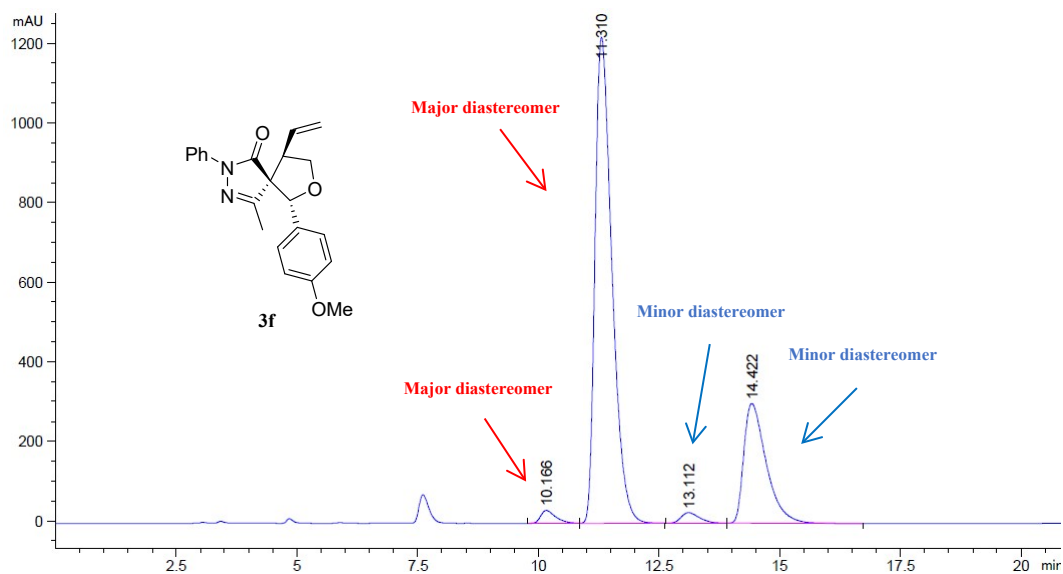


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.096	BV R	0.2948	2.09774e4	1071.42883	76.9236
2	13.417	VV E	0.4584	346.37708	10.76420	1.2702
3	15.216	BB	0.3731	780.98303	31.62971	2.8638
4	26.280	BB	0.7876	5165.70215	99.68423	18.9424

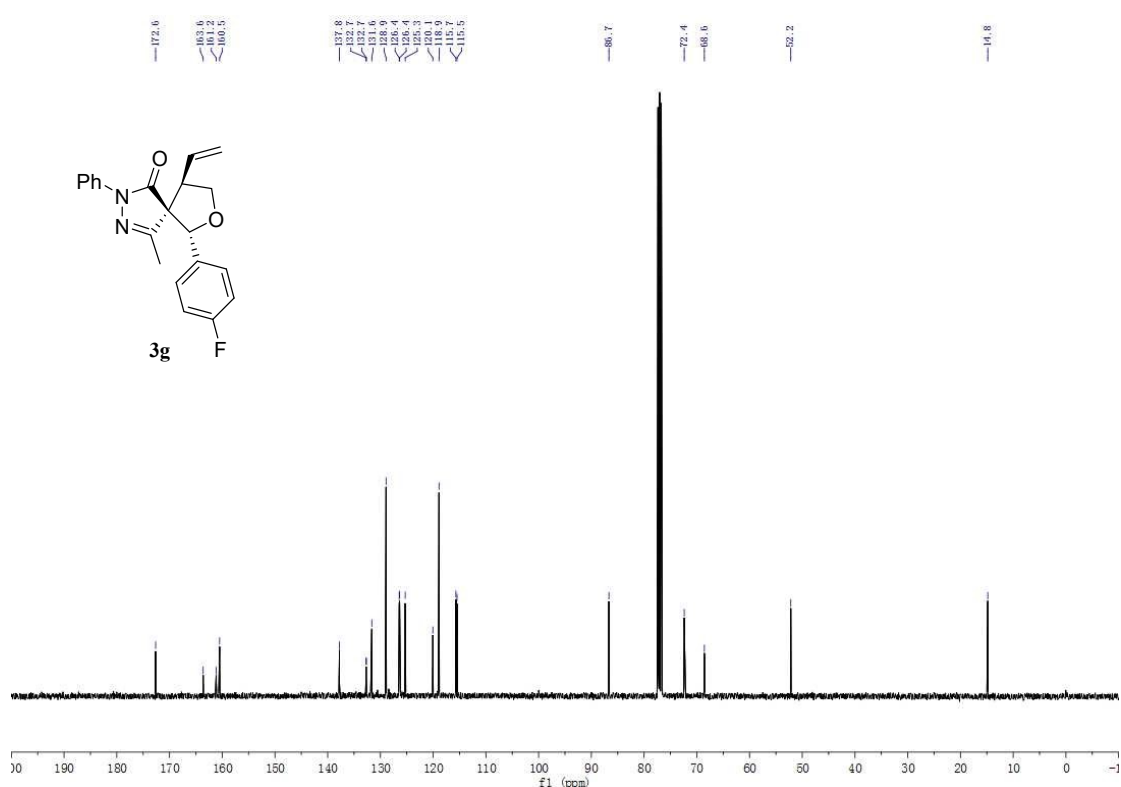
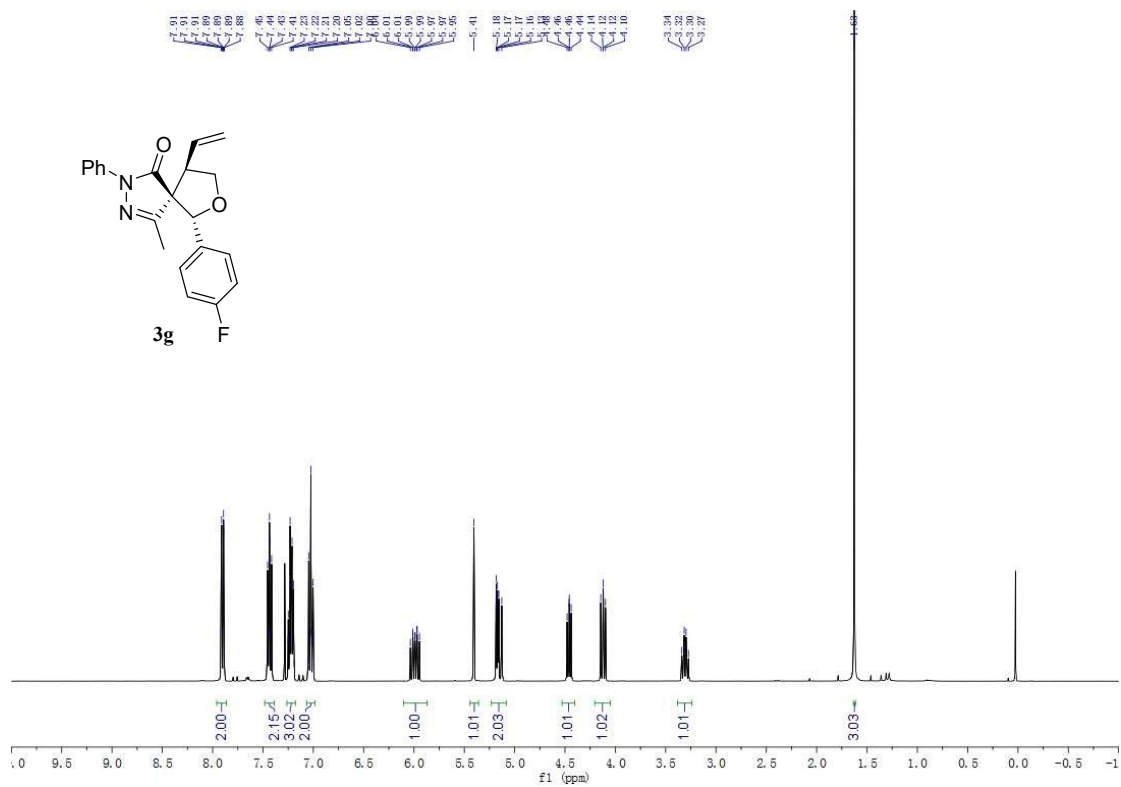


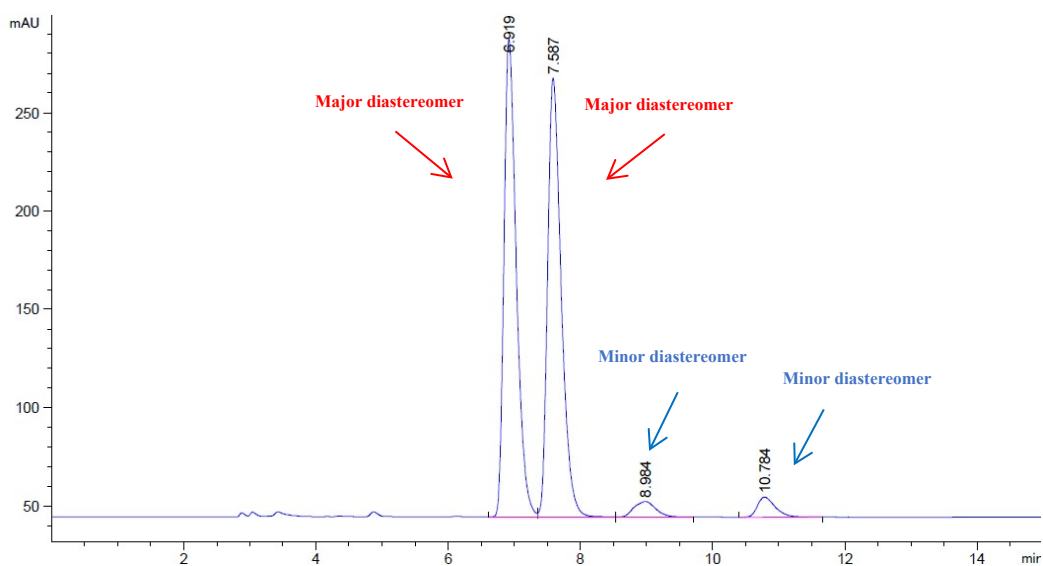


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.146	BV	0.3280	4660.49219	217.47002	36.4319
2	11.341	VB	0.3526	4521.51270	194.96413	35.3455
3	13.128	BV	0.4056	1799.64294	67.37967	14.0681
4	14.500	VB	0.4760	1810.68896	58.02831	14.1545

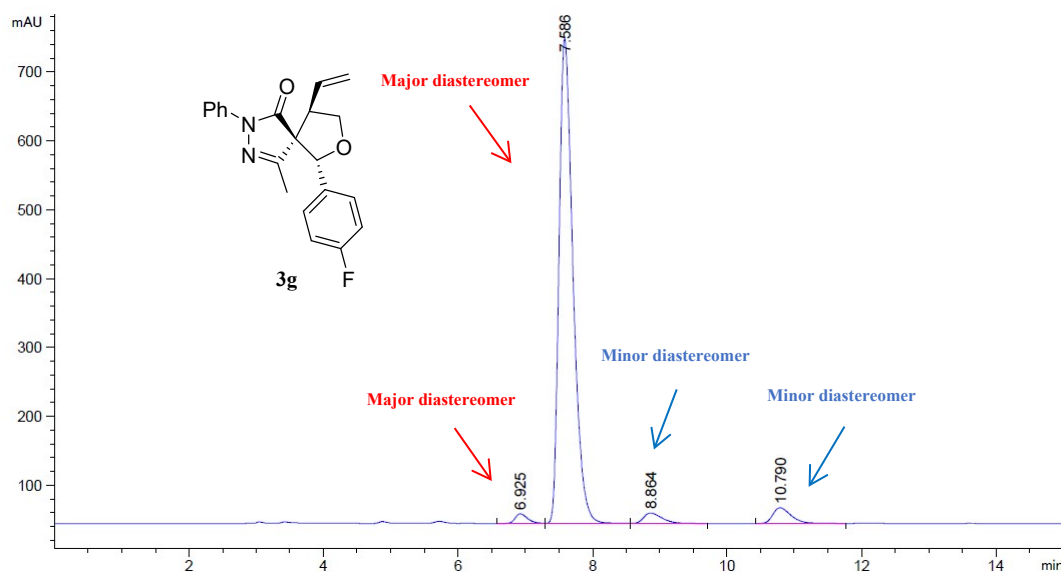


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.166	BV	0.3258	712.32294	32.74480	1.7411
2	11.310	VB	0.3743	2.97545e4	1220.88098	72.7280
3	13.112	BV	0.4019	709.52179	26.80070	1.7343
4	14.422	VB	0.4923	9735.71191	301.07224	23.7967

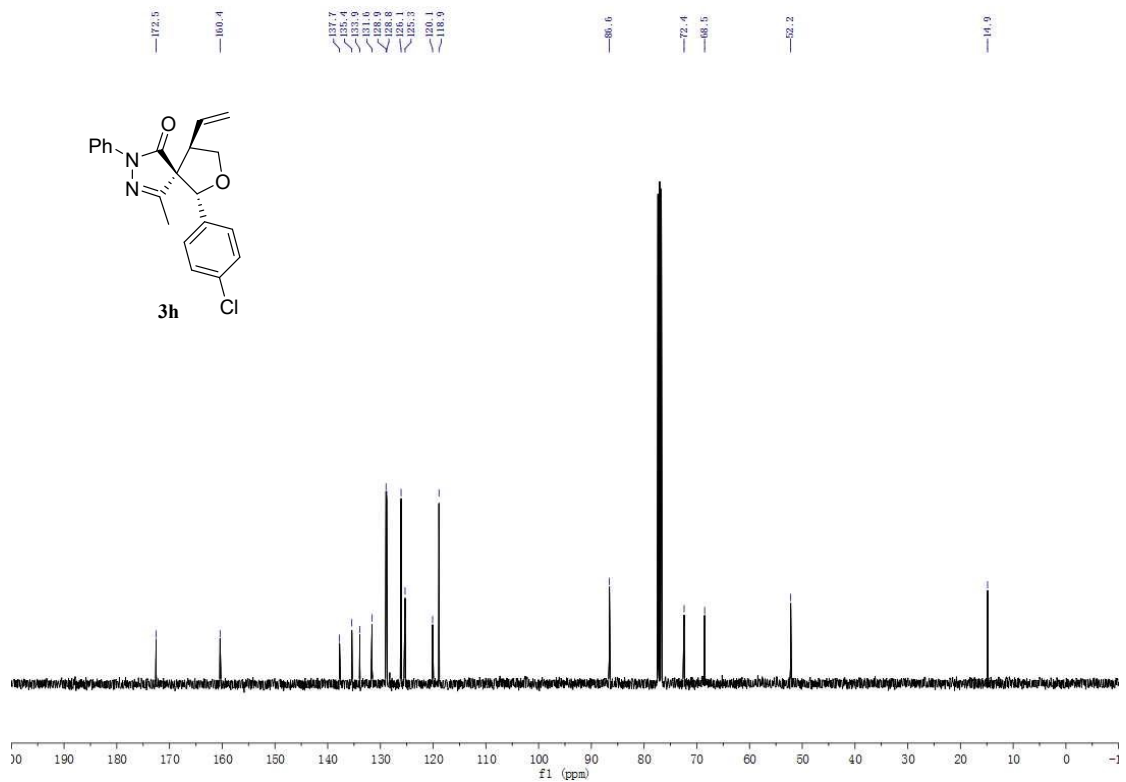
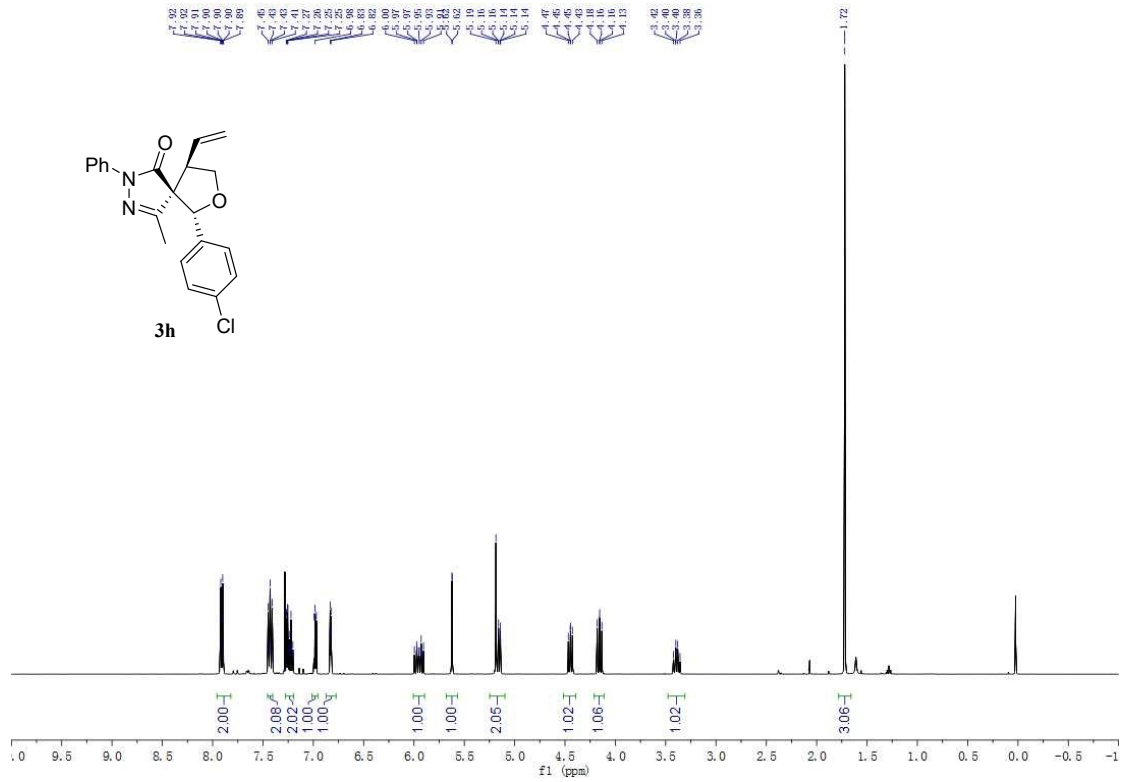




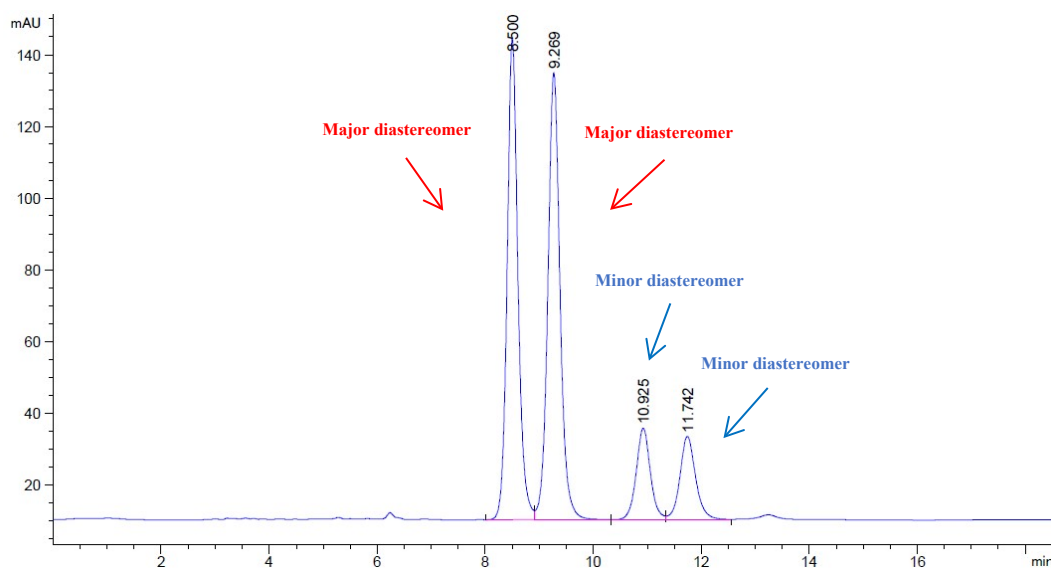
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.919	BV	0.1975	3153.67773	242.83080	47.0298
2	7.587	VB	0.2175	3183.11646	223.03360	47.4688
3	8.984	BB	0.3649	177.85356	7.86339	2.6523
4	10.784	BB	0.2852	191.06012	10.16808	2.8492



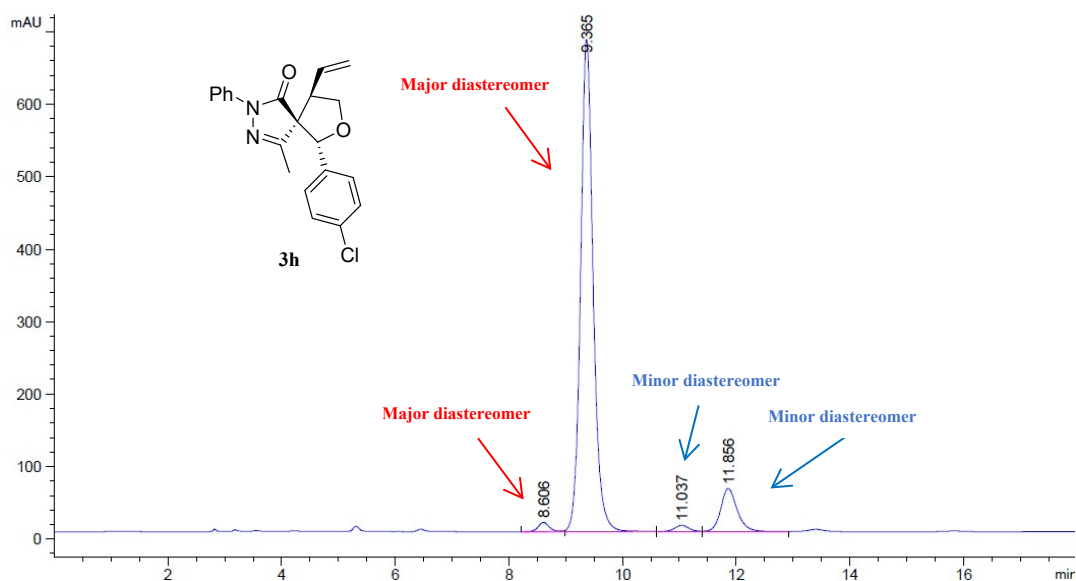
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.925	BV	0.1974	183.34439	14.12690	1.6611
2	7.586	VV	0.2199	1.01282e4	703.84113	91.7630
3	8.864	VB	0.2920	291.23074	15.30802	2.6386
4	10.790	BB	0.2880	434.57275	22.93739	3.9373



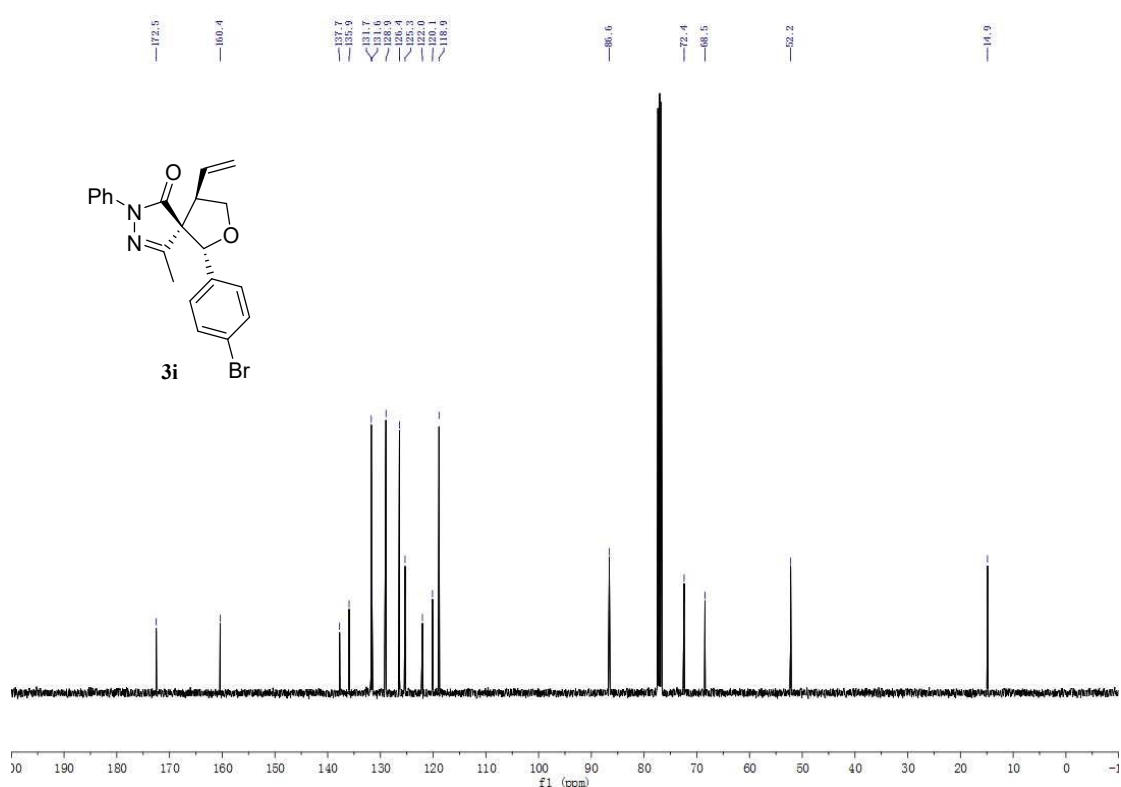
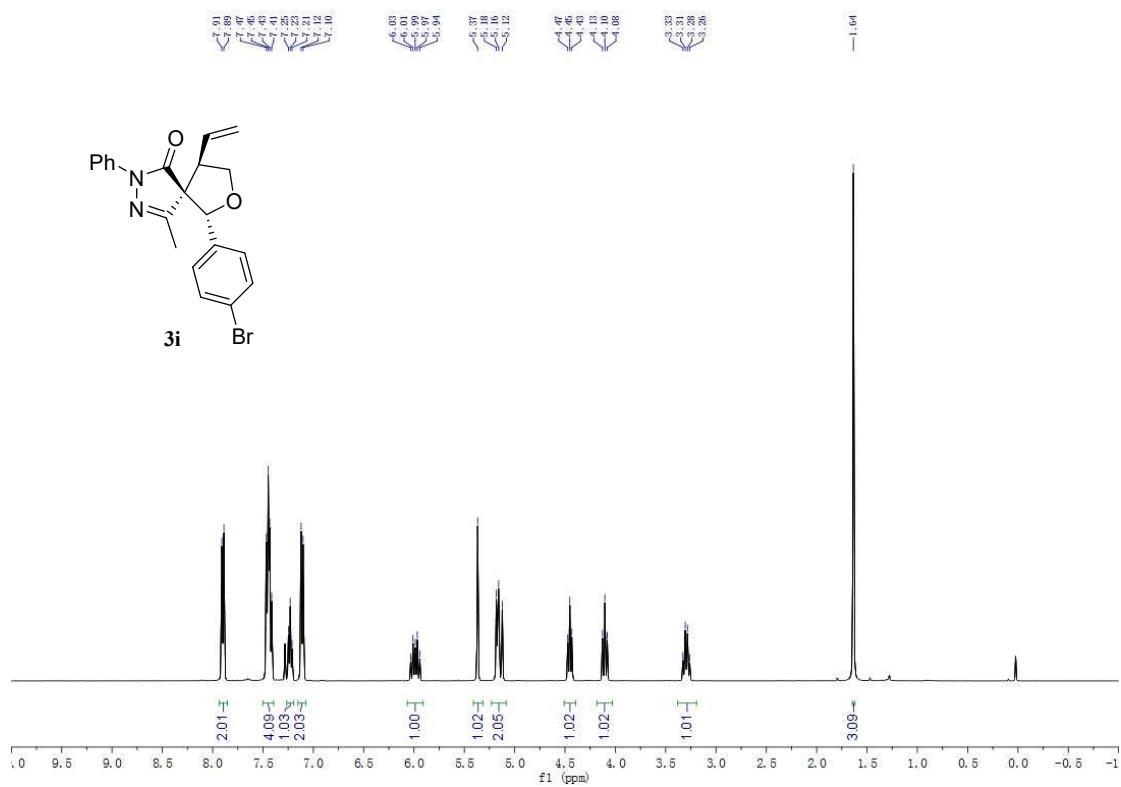


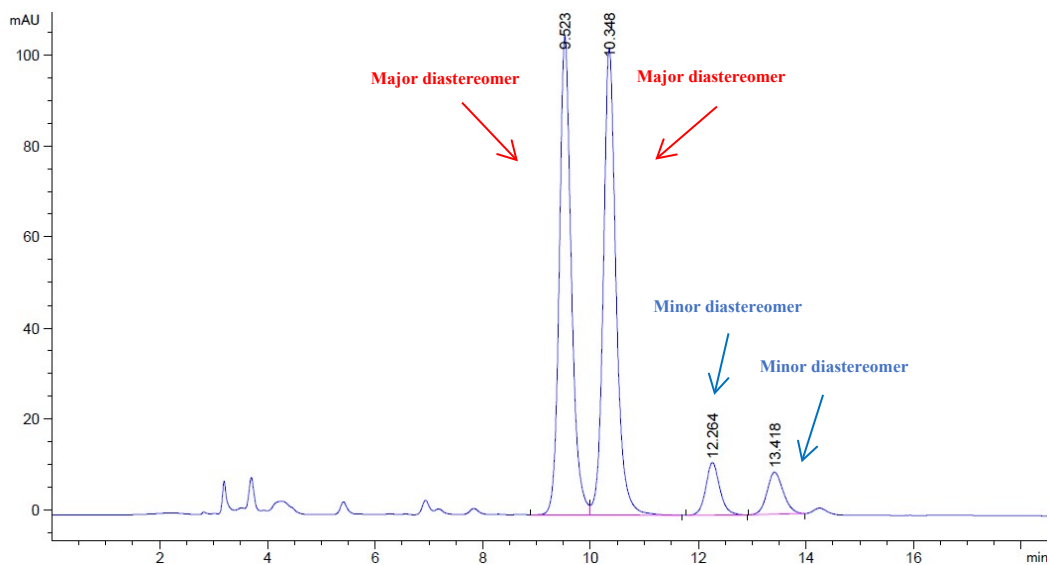


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.500	BV	0.2108	1872.77112	134.23164	39.4157
2	9.269	VB	0.2365	1951.36304	124.74901	41.0698
3	10.925	BV	0.2751	462.81790	25.45723	9.7408
4	11.742	VB	0.3038	464.38257	23.17167	9.7737

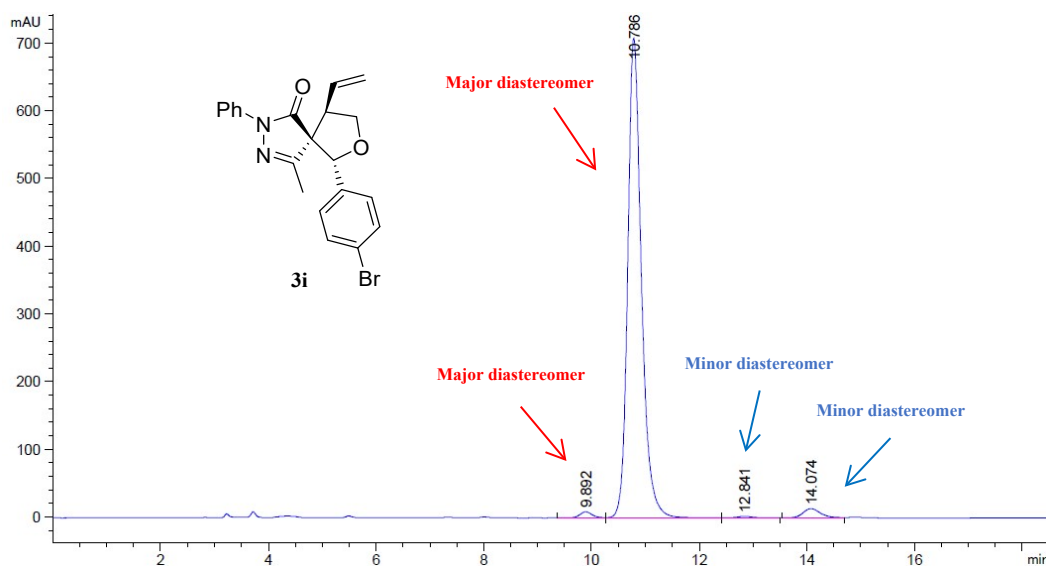


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.606	BV E	0.2062	175.59338	12.87129	1.4720
2	9.365	VB R	0.2316	1.04057e4	679.89783	87.2295
3	11.037	BV	0.2674	148.79044	8.49326	1.2473
4	11.856	VB	0.3045	1199.02478	59.39119	10.0513

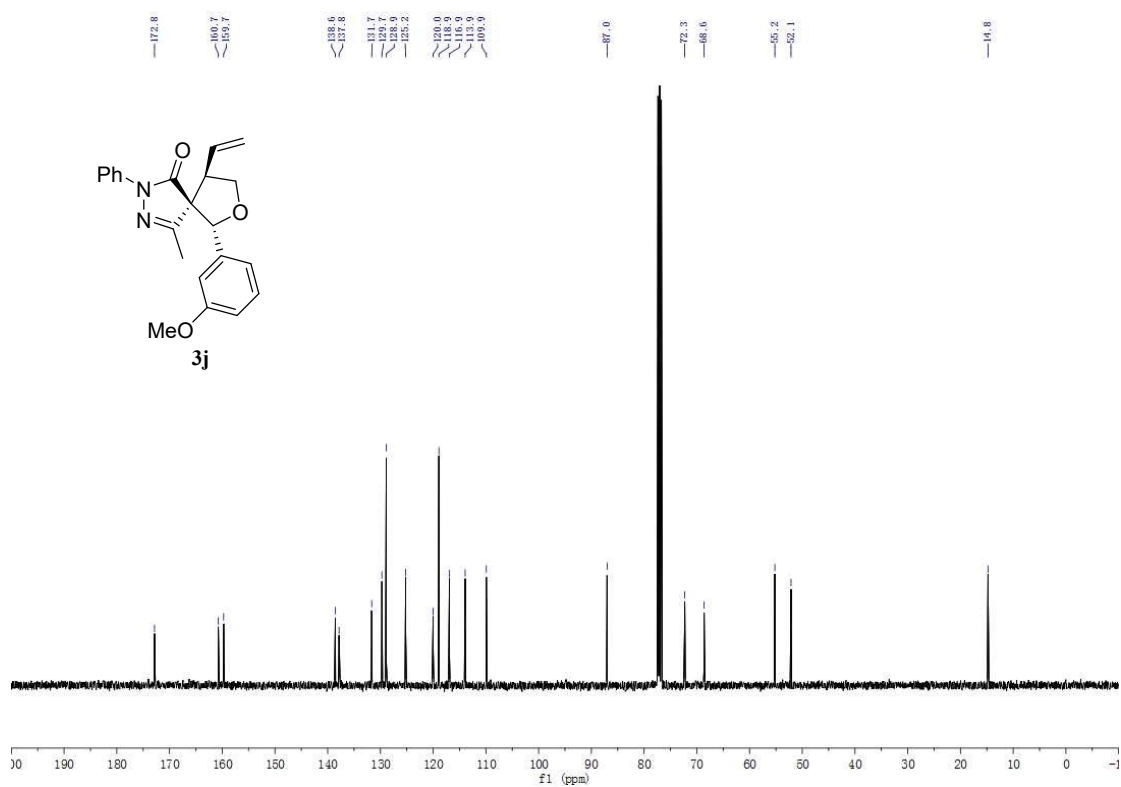
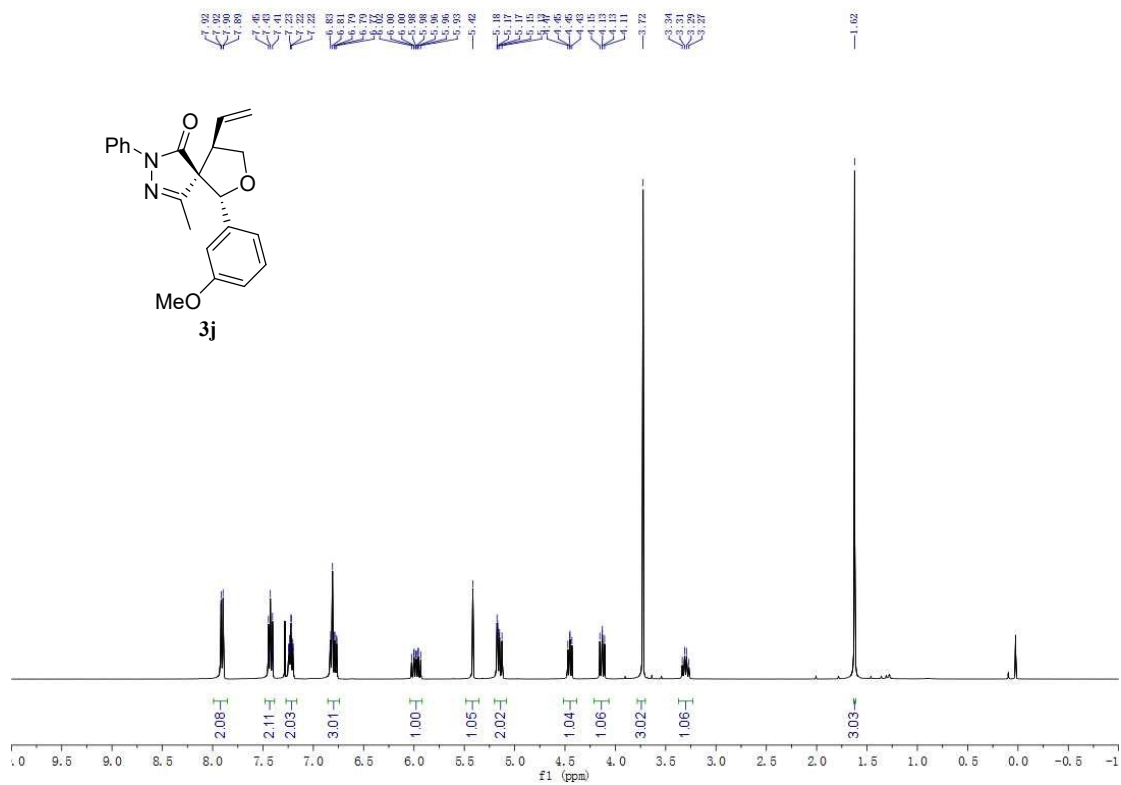


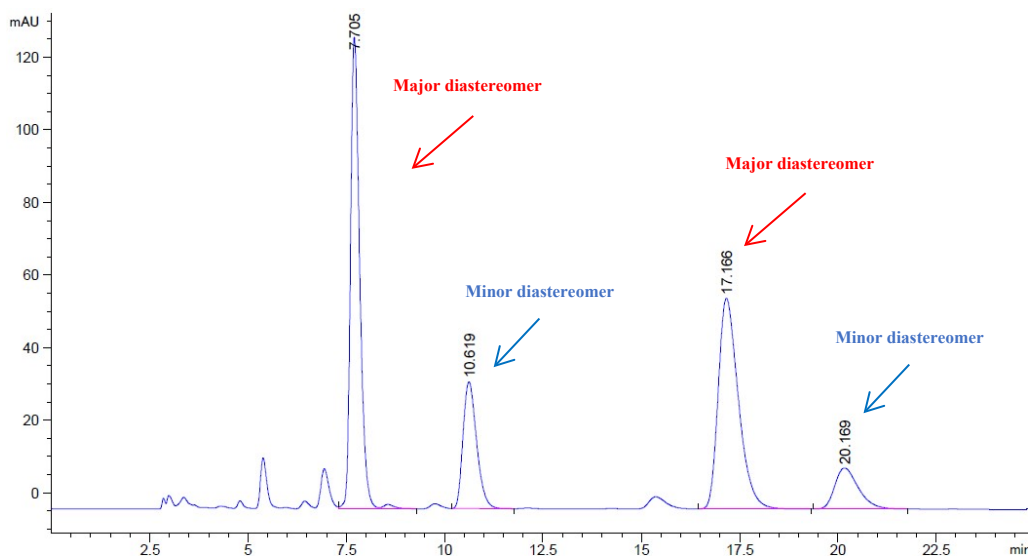


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.523	BV	0.2357	1637.89612	105.19537	43.9295
2	10.348	VB	0.2467	1687.25098	102.67364	45.2532
3	12.264	BB	0.2738	209.72852	11.55351	5.6251
4	13.418	BB	0.3188	193.59175	9.26301	5.1923

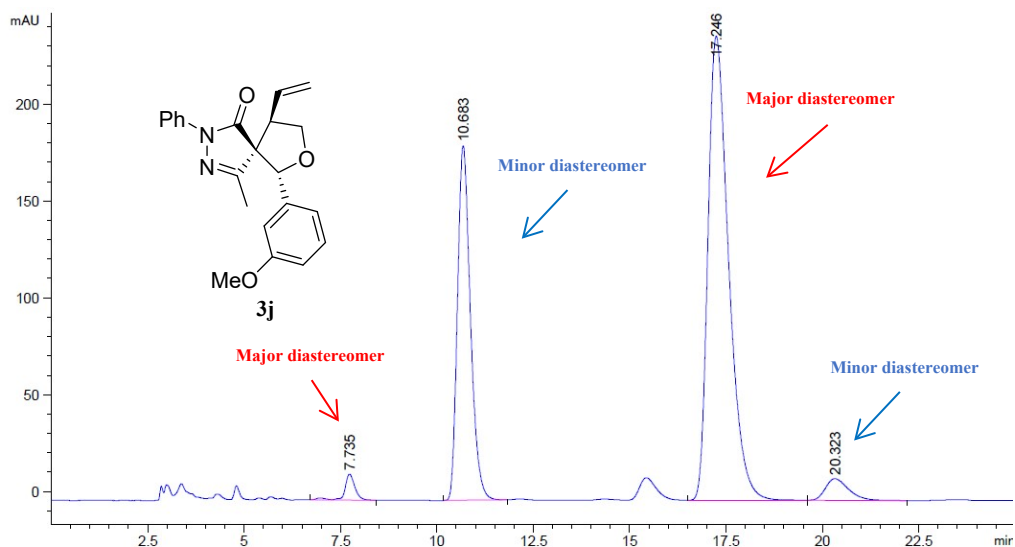


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.892	BV	0.2443	146.01419	9.04813	1.1213
2	10.786	VB	0.2663	1.25274e4	708.54755	96.2019
3	12.841	BB	0.2887	47.81048	2.50442	0.3672
4	14.074	BB	0.3400	300.76077	13.49817	2.3096

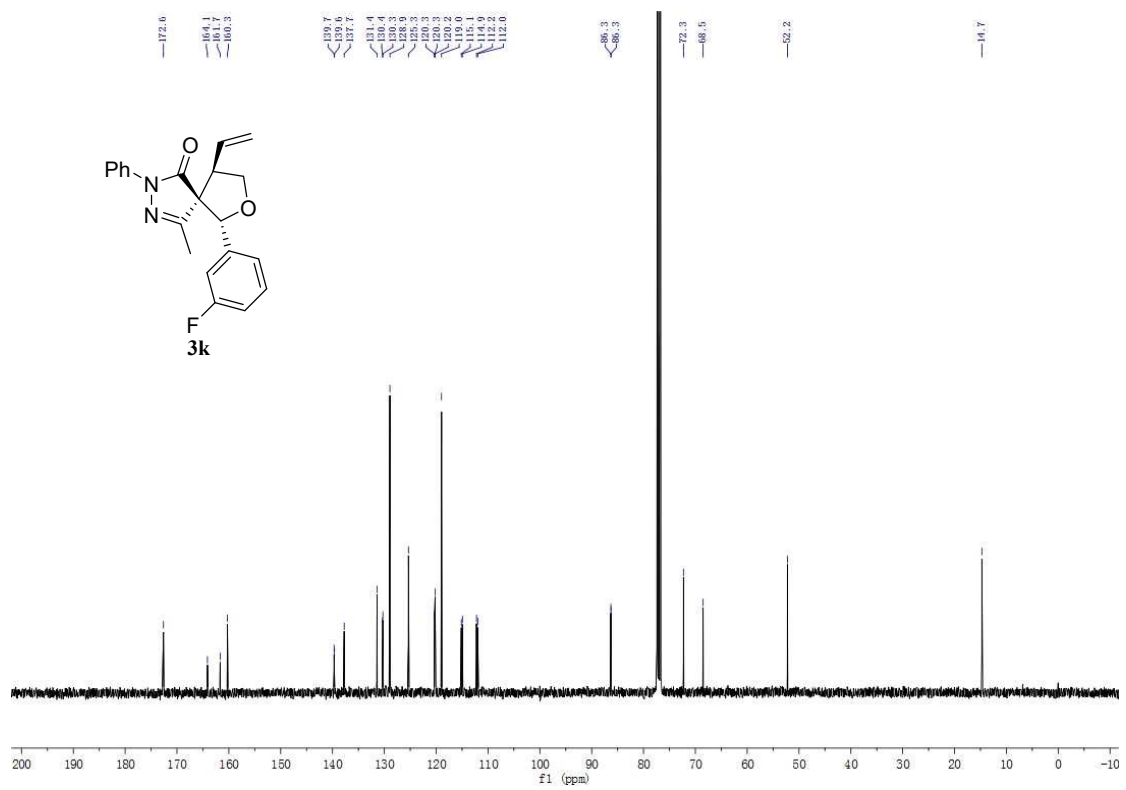
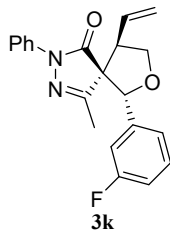
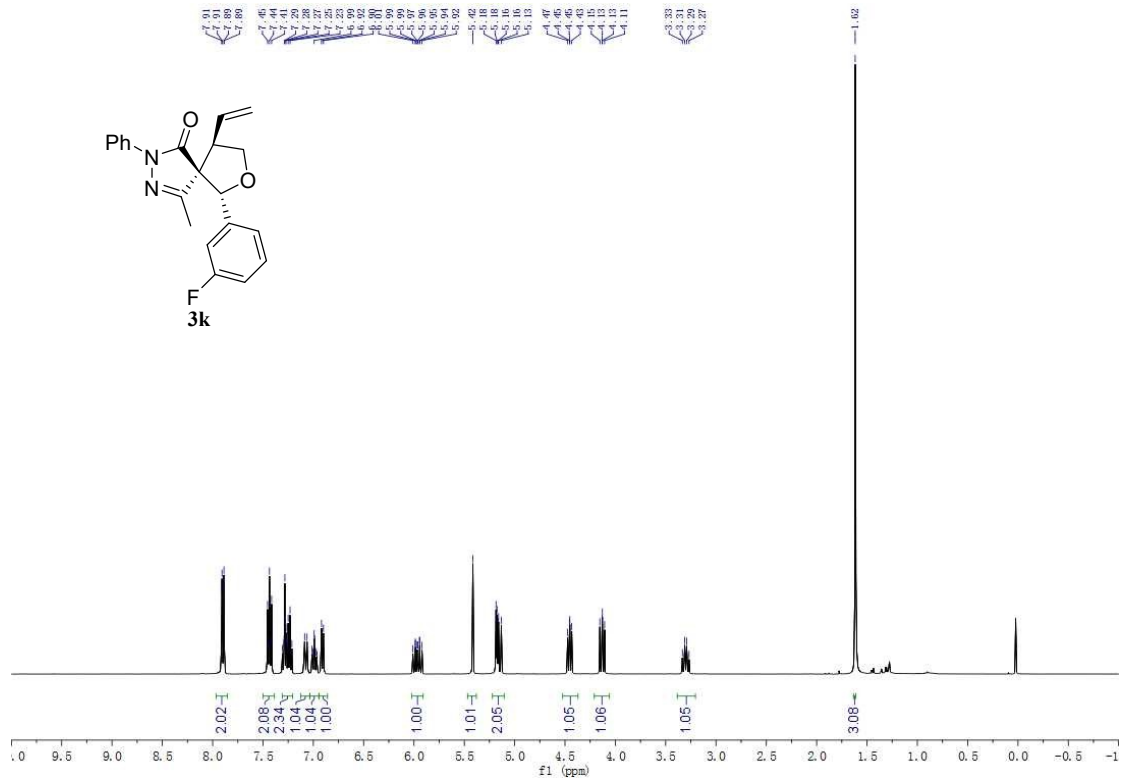
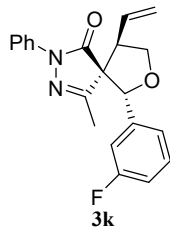


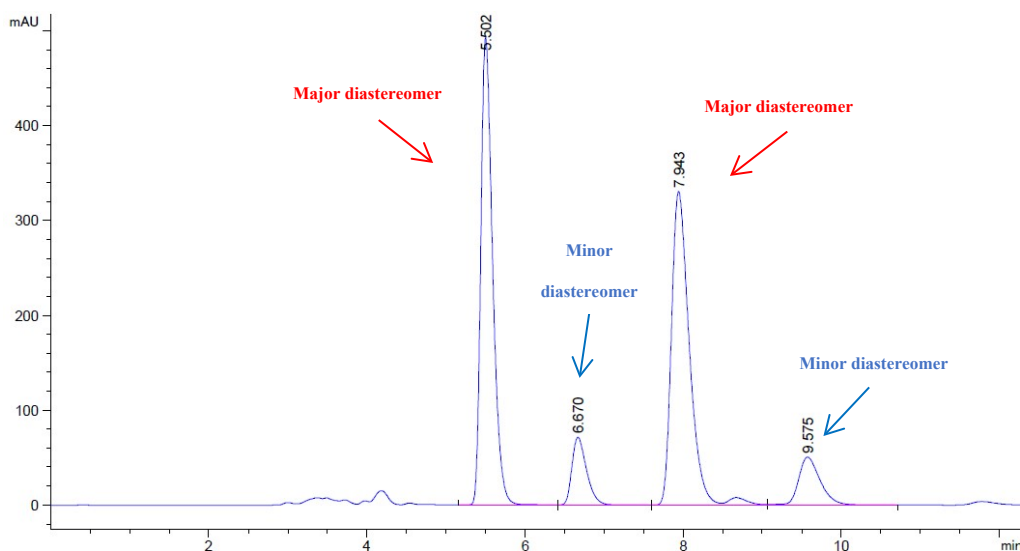


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.705	VV R	0.2475	2110.91895	129.95506	38.4674
2	10.619	BB	0.3736	836.72284	34.91285	15.2477
3	17.166	BB	0.5499	2069.24414	58.04562	37.7080
4	20.169	BB	0.6230	470.66351	11.29900	8.5769

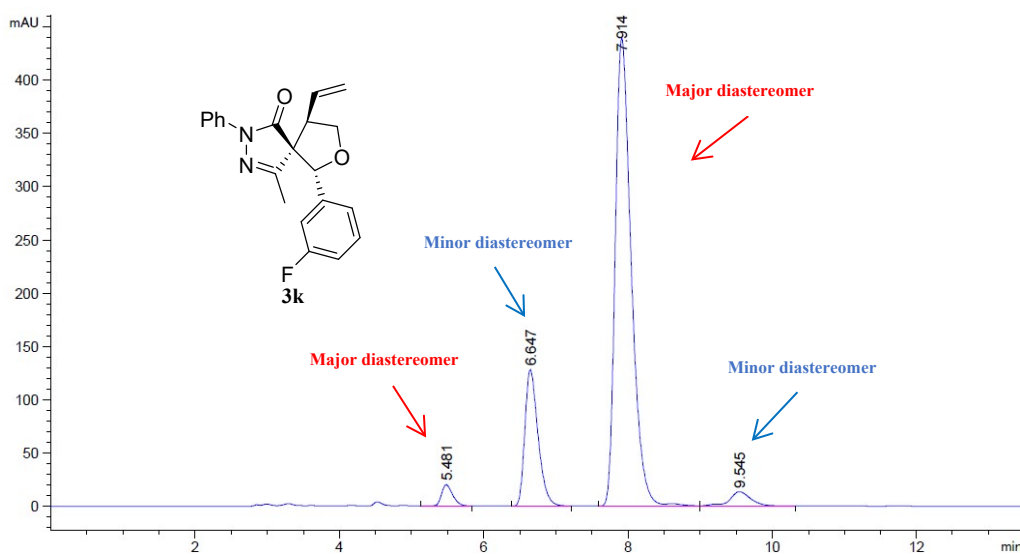


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.735	VB R	0.2734	247.93848	13.42982	1.7855
2	10.683	BB	0.3567	4265.29932	183.13150	30.7152
3	17.246	BB	0.5687	8907.58008	239.59225	64.1452
4	20.323	BB	0.6297	465.76721	11.11990	3.3541

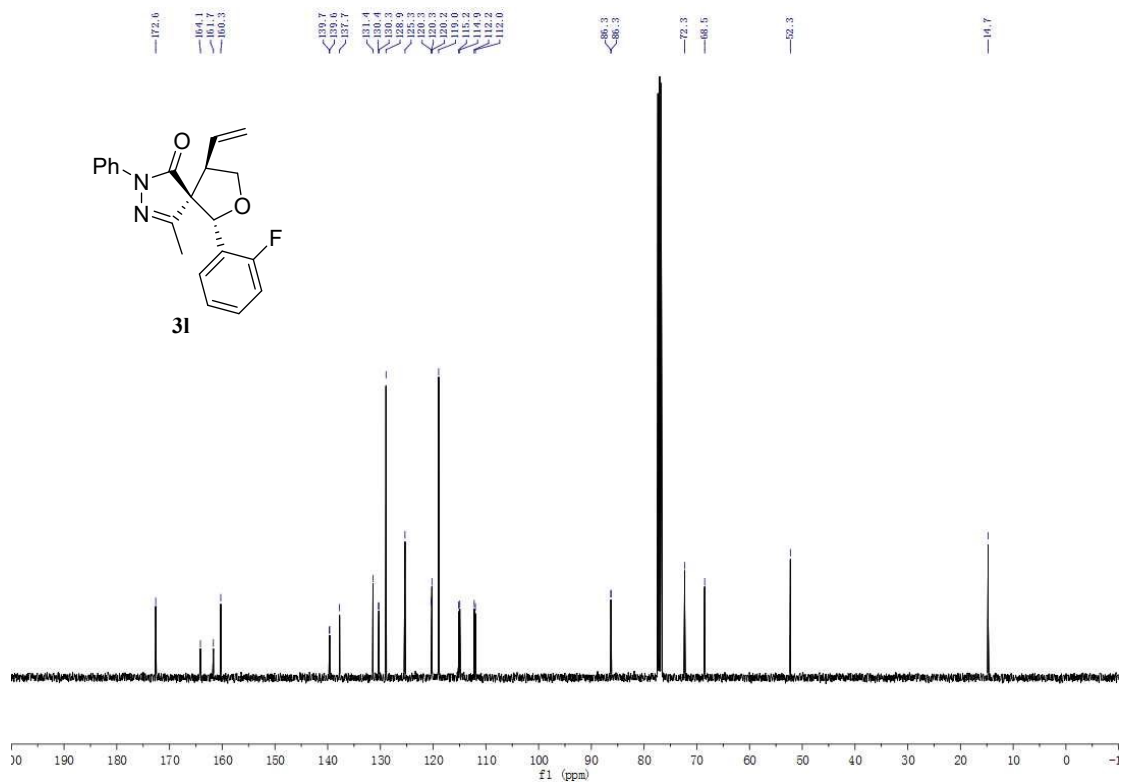
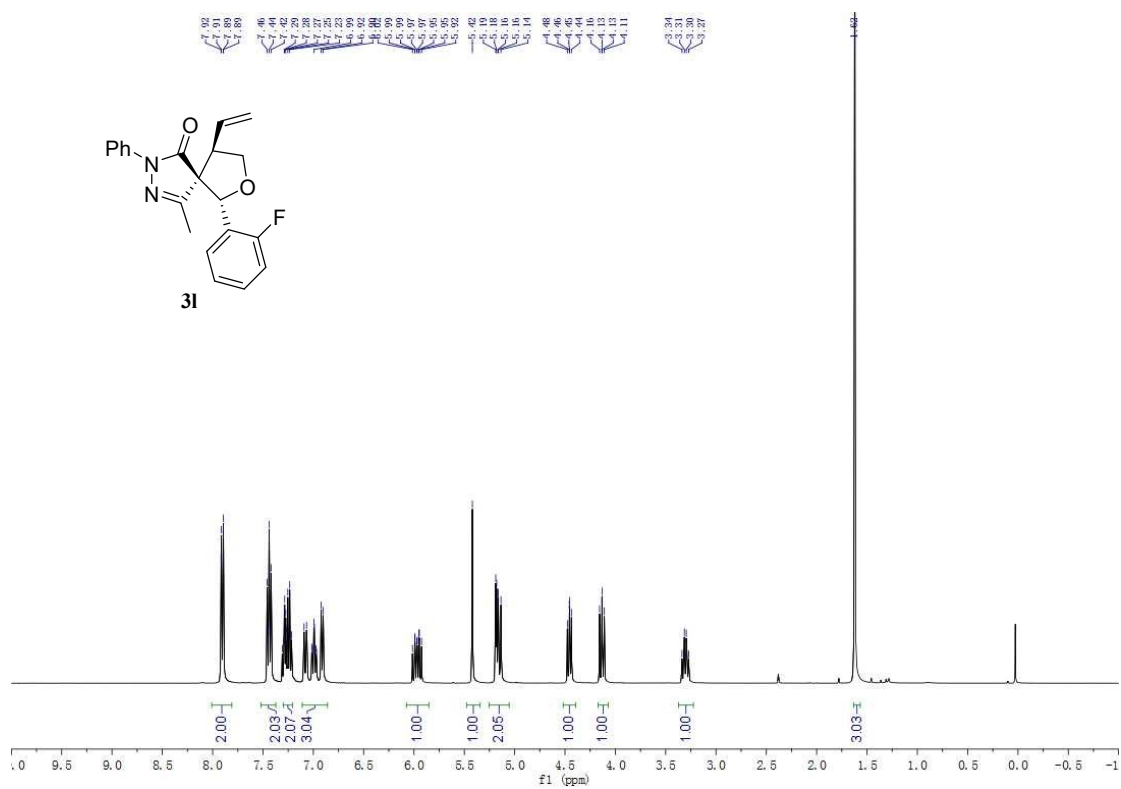




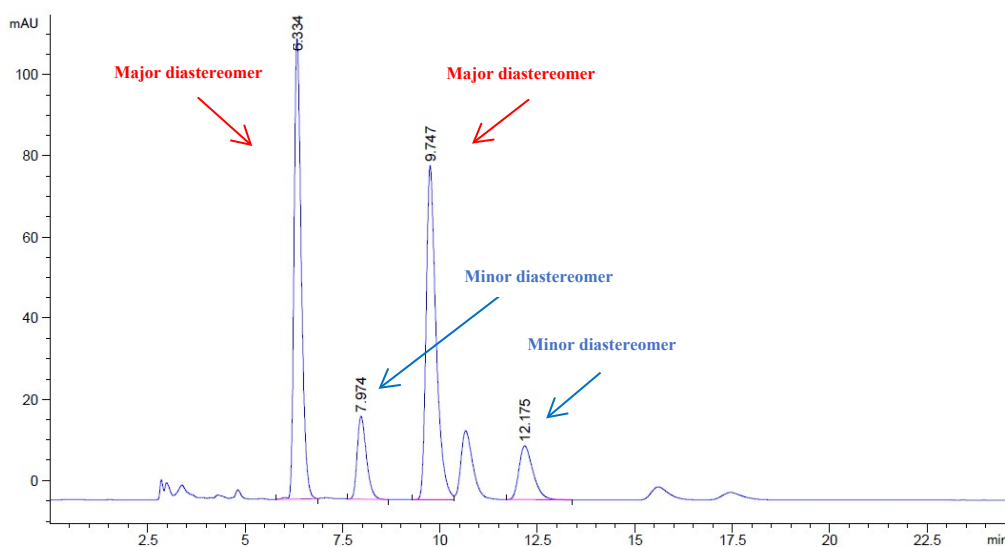
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.502	BV	0.1592	5123.36963	493.13336	41.8348
2	6.670	VB	0.1962	921.89142	71.58896	7.5277
3	7.943	BV R	0.2353	5239.55469	330.75372	42.7835
4	9.575	VB	0.2884	961.85419	50.67498	7.8540



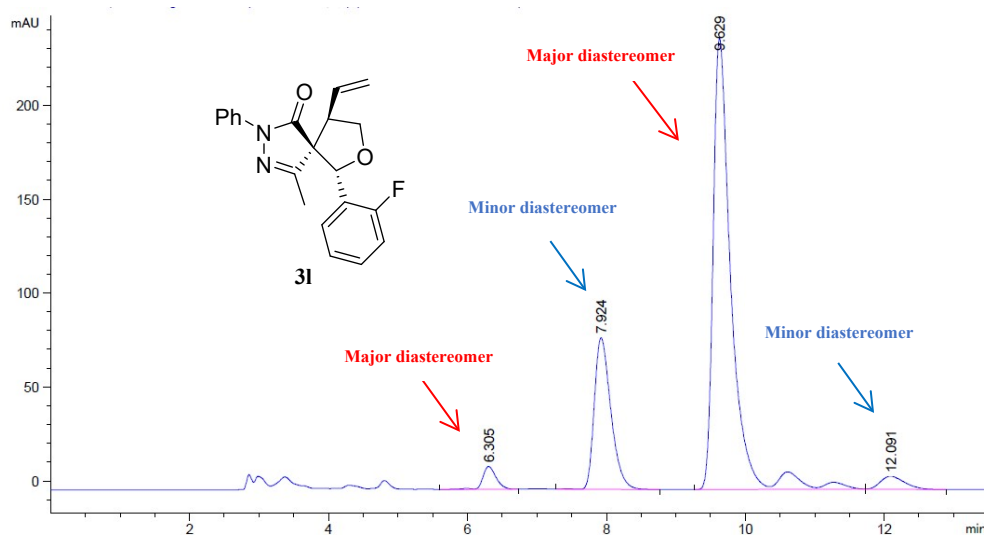
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.481	BB	0.1653	213.80617	19.91077	2.4063
2	6.647	BB	0.1940	1627.87146	128.28235	18.3212
3	7.914	BV R	0.2338	6771.42383	439.91031	76.2103
4	9.545	VB R	0.3039	272.08014	13.40038	3.0622



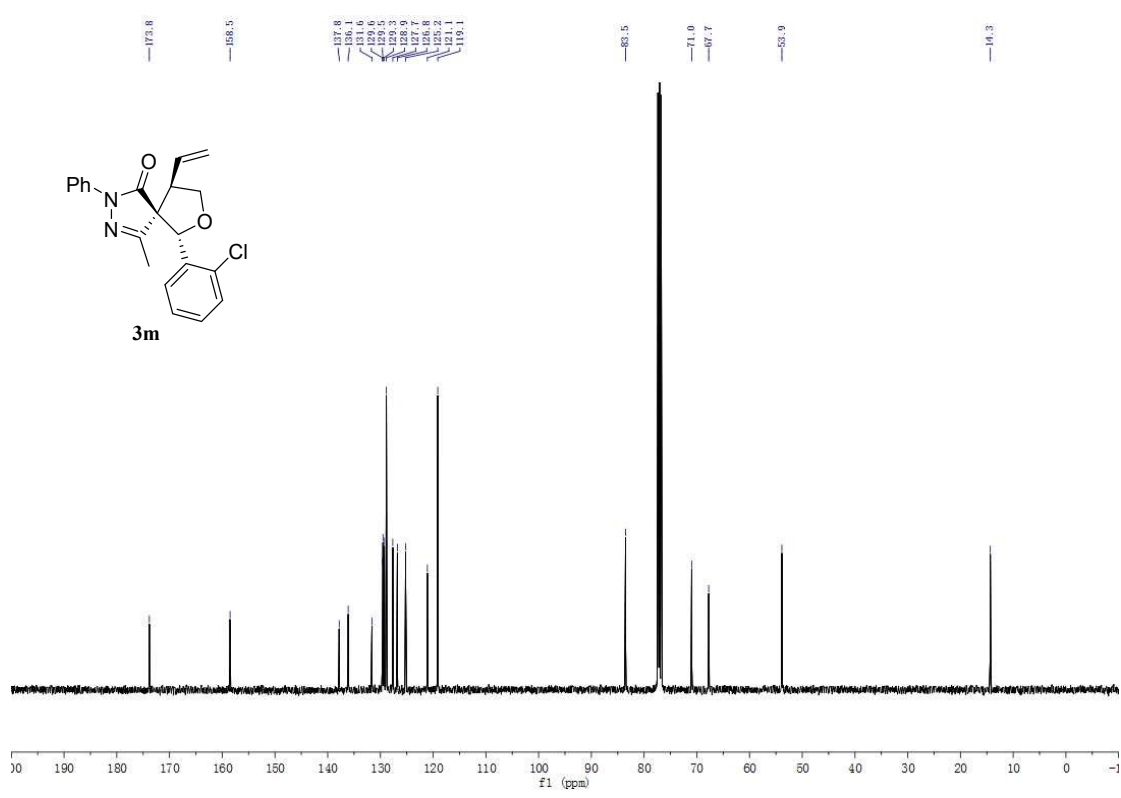
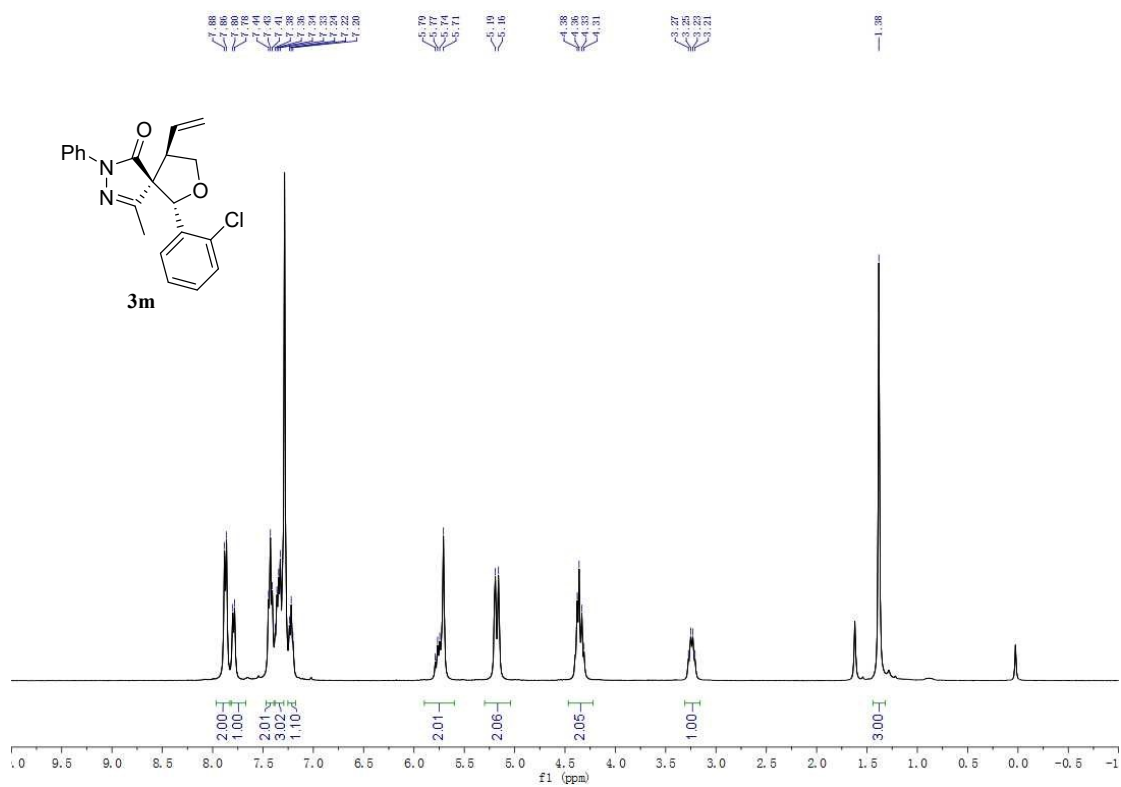


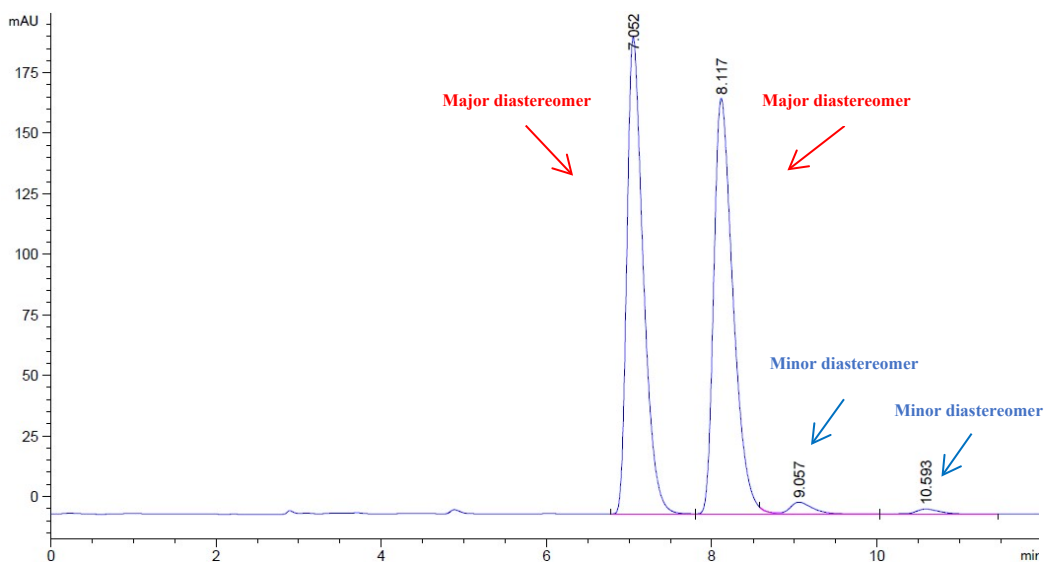


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.334	VB R	0.1969	1457.74060	113.43548	40.6318
2	7.974	BB	0.2516	335.49155	20.42393	9.3512
3	9.747	BV	0.2664	1460.72522	82.16869	40.7150
4	12.175	BB	0.3825	333.72293	13.26767	9.3019

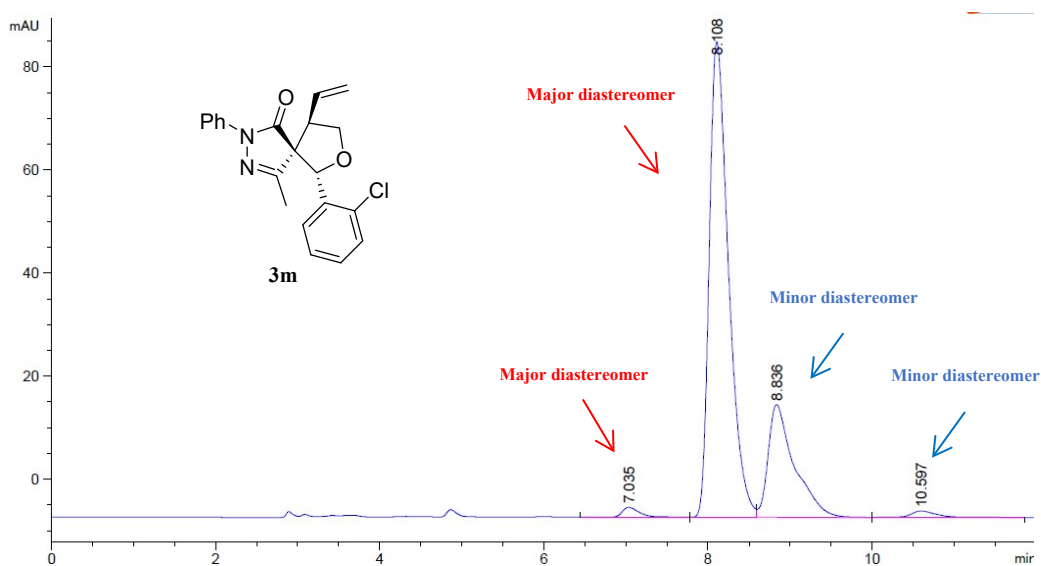


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.305	VB R	0.2047	163.67920	12.18581	2.6903
2	7.924	VB R	0.2548	1340.79492	80.70387	22.0380
3	9.629	BV R	0.2555	4411.87744	240.35065	72.5160
4	12.091	BB	0.3734	167.65053	6.92540	2.7556

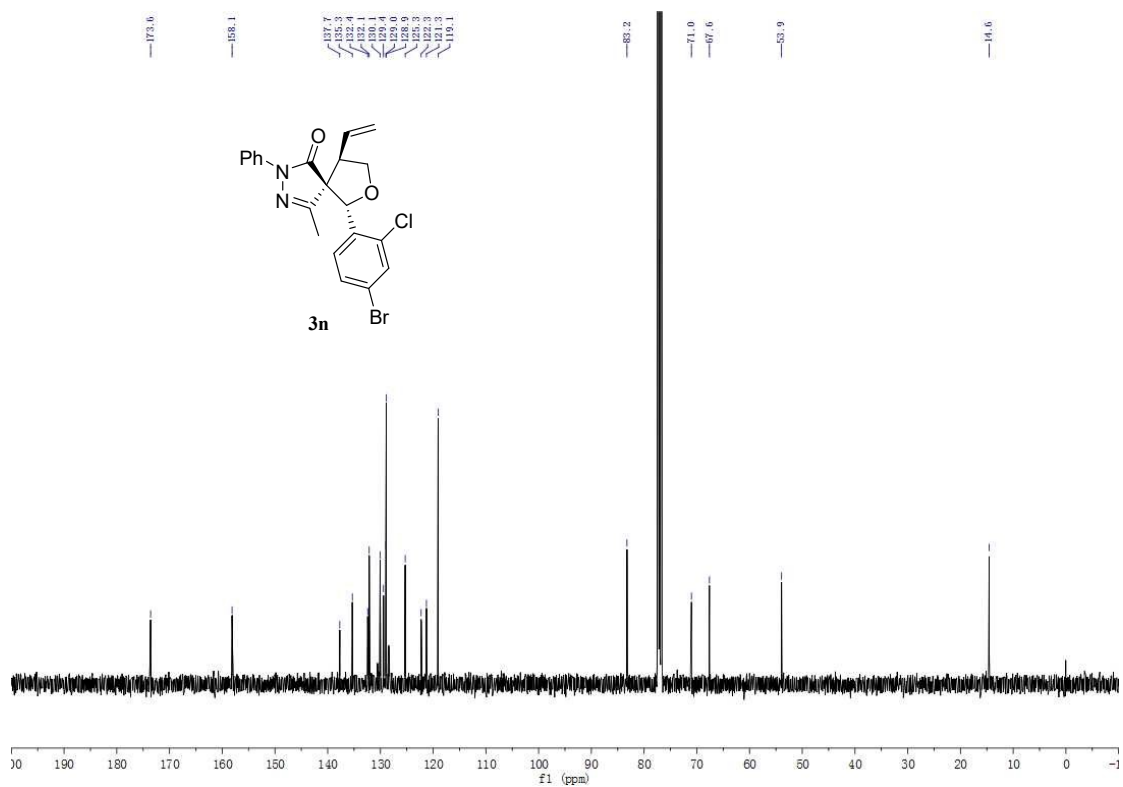
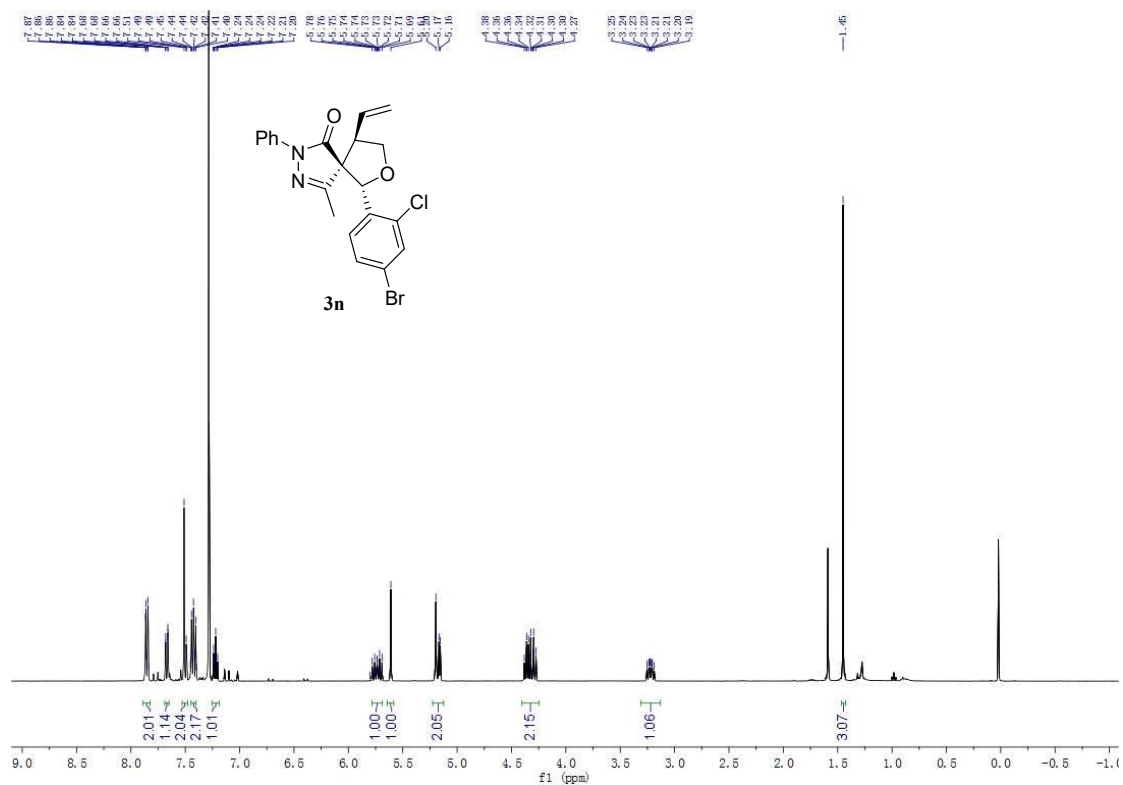


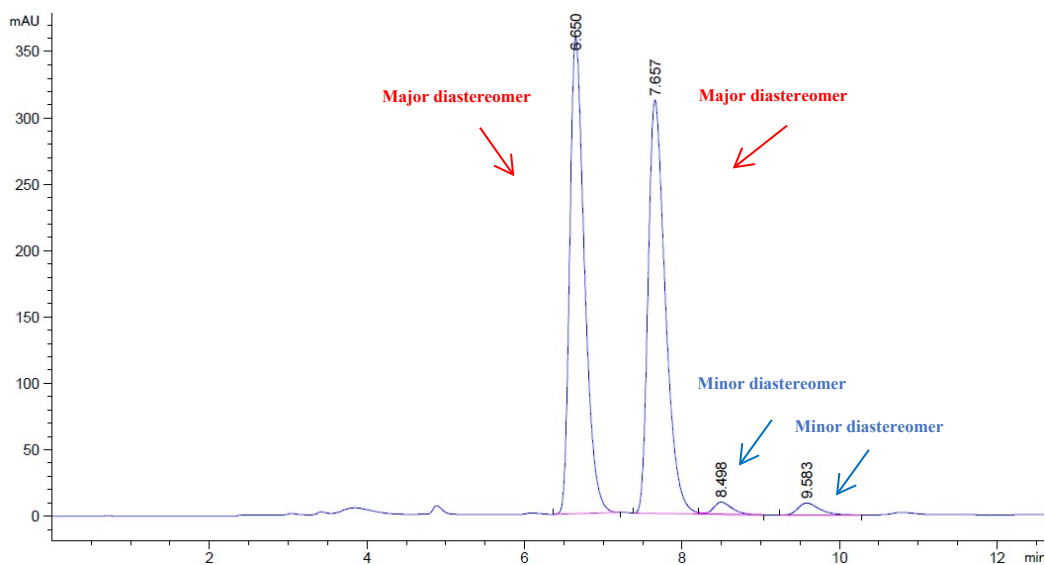


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.052	BB	0.2085	2711.14453	197.06419	48.1505
2	8.117	BV R	0.2461	2784.05420	171.74294	49.4454
3	9.057	VB E	0.2856	92.78759	4.86241	1.6479
4	10.593	BB	0.2999	42.57981	2.09712	0.7562

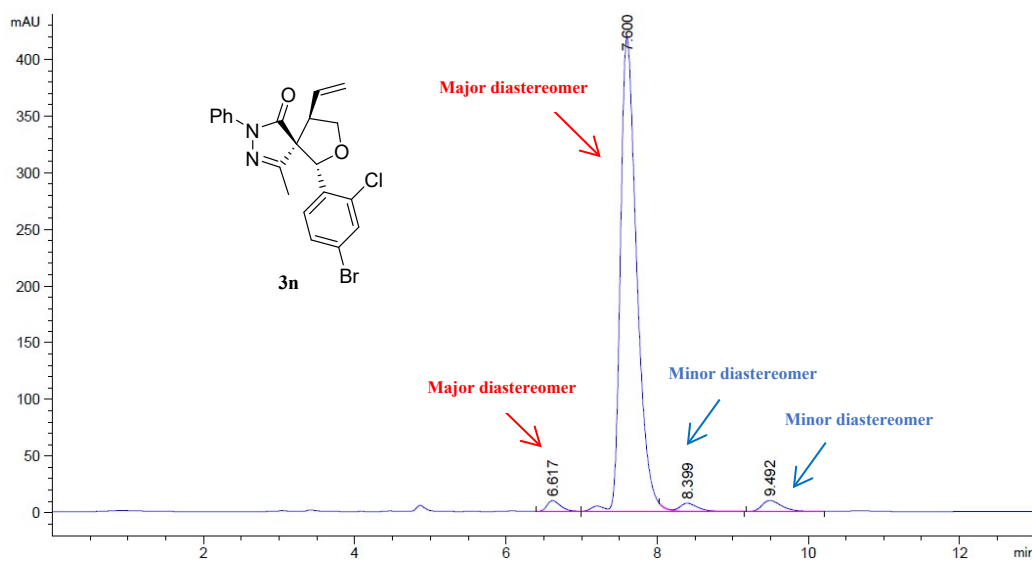


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.035	VB R	0.2191	28.80957	1.93619	1.4083
2	8.108	BV	0.2464	1503.82275	92.12729	73.5126
3	8.836	VB	0.3196	486.36945	21.85480	23.7756
4	10.597	BB	0.3194	26.66484	1.23723	1.3035

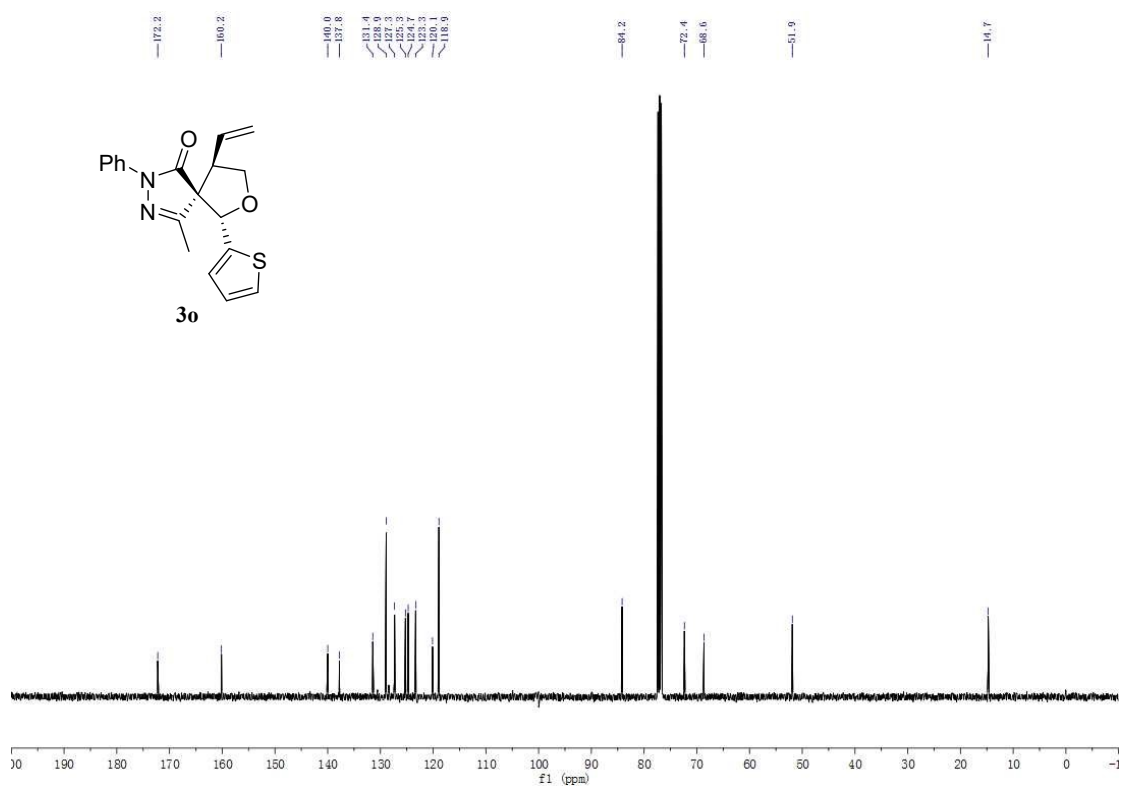
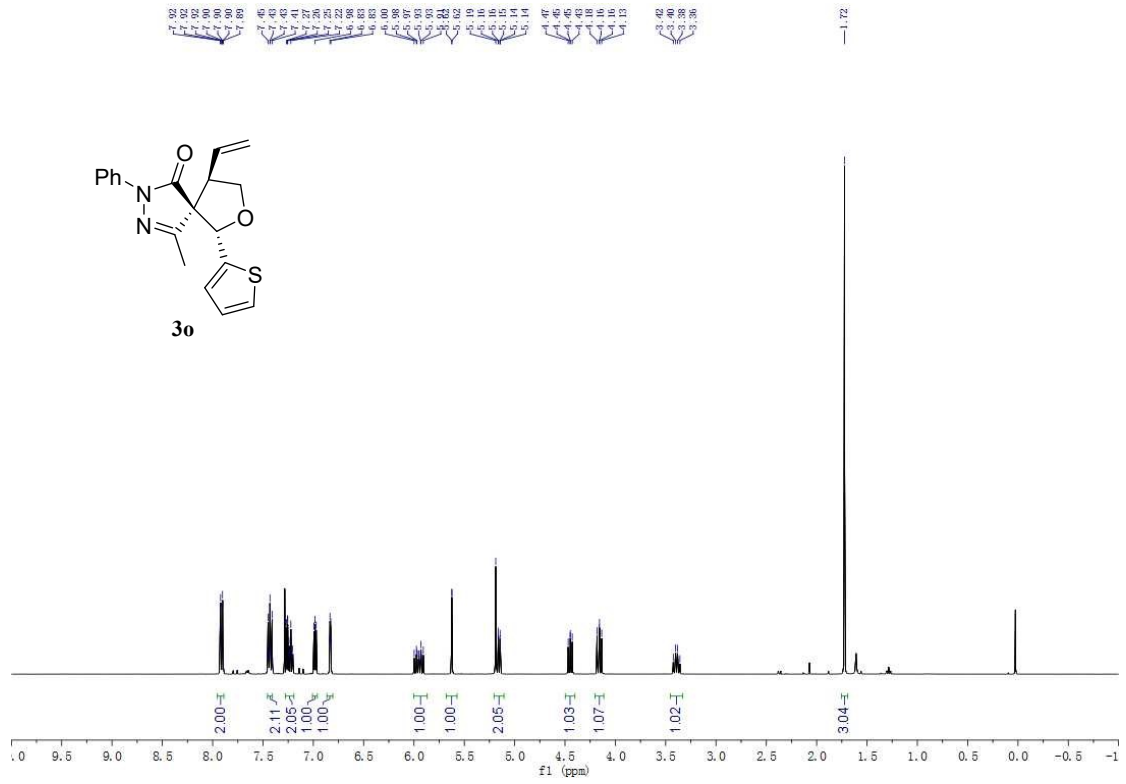


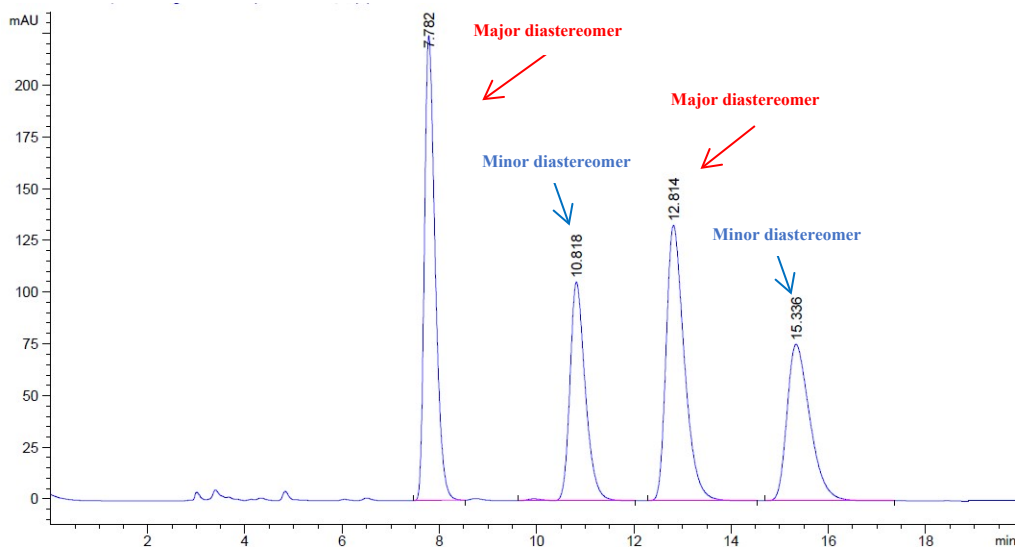


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.650	BB	0.1978	4674.19238	359.20905	48.1785
2	7.657	BV R	0.2316	4719.32959	311.72672	48.6438
3	8.498	VB E	0.2402	143.49341	9.13688	1.4790
4	9.583	BB	0.2788	164.79727	8.95108	1.6986

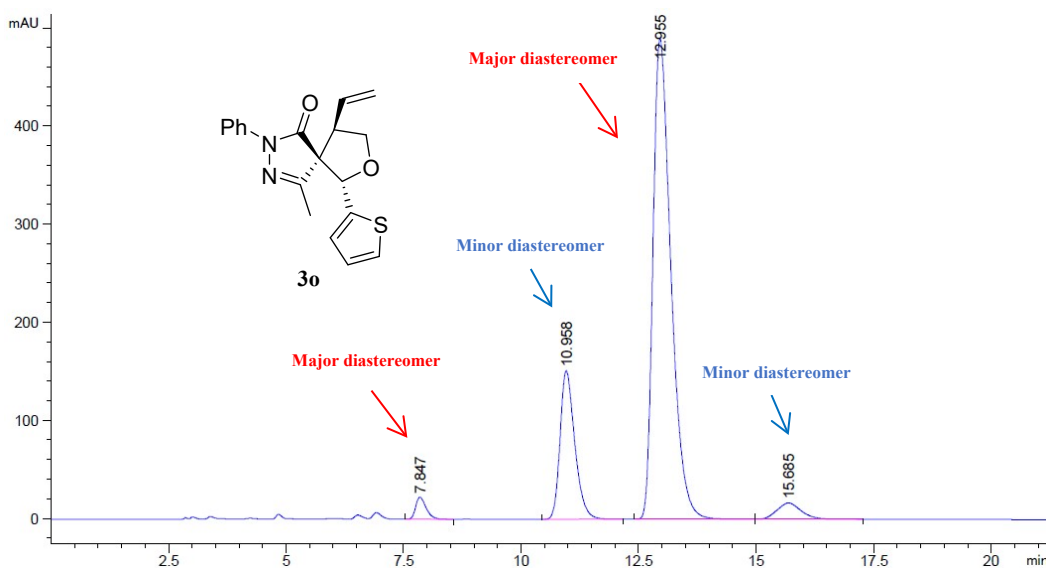


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.617	BB	0.1884	116.07354	9.44260	1.7336
2	7.600	VV R	0.2280	6287.54492	417.85553	93.9050
3	8.399	VB E	0.2476	117.47029	7.15135	1.7544
4	9.492	BB	0.2741	174.55421	9.69430	2.6070

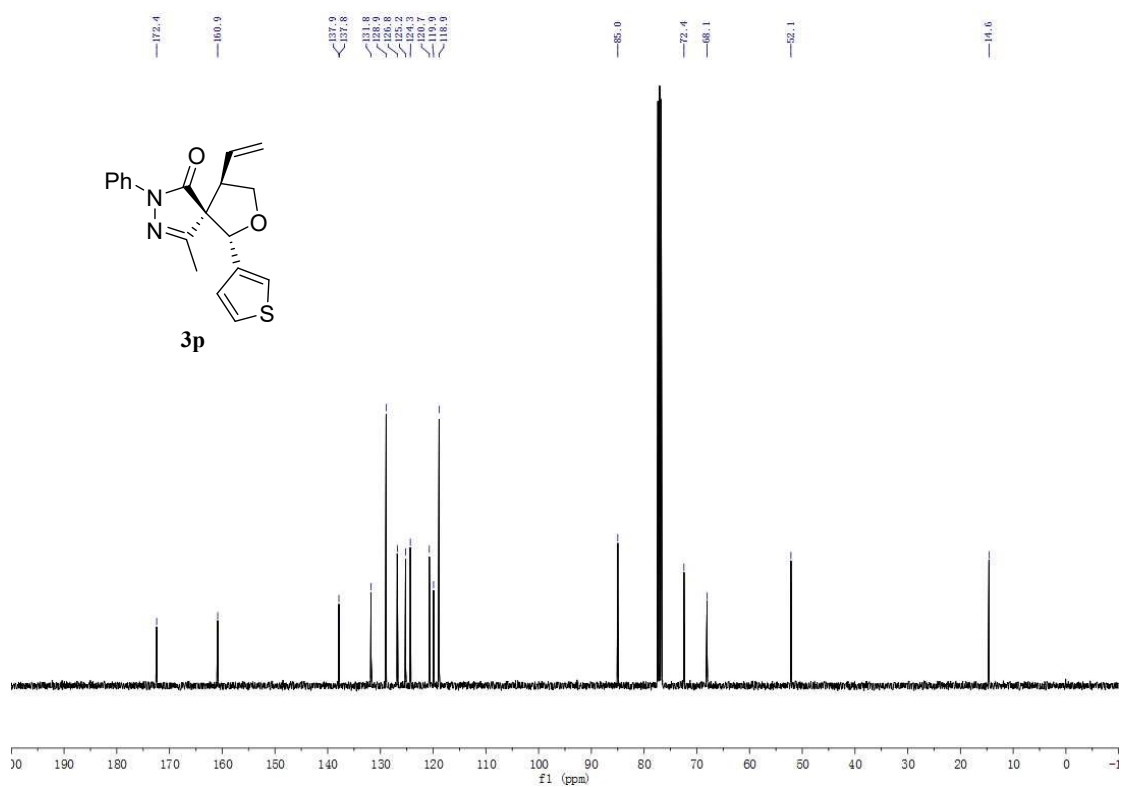
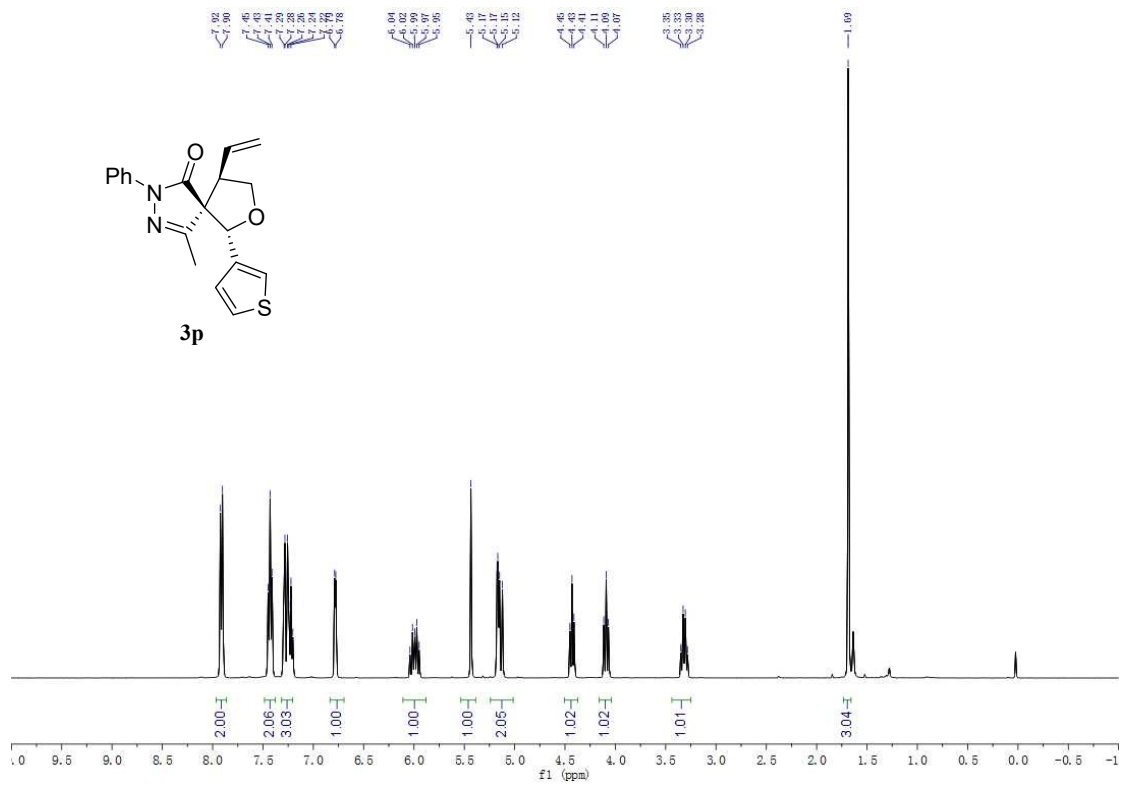




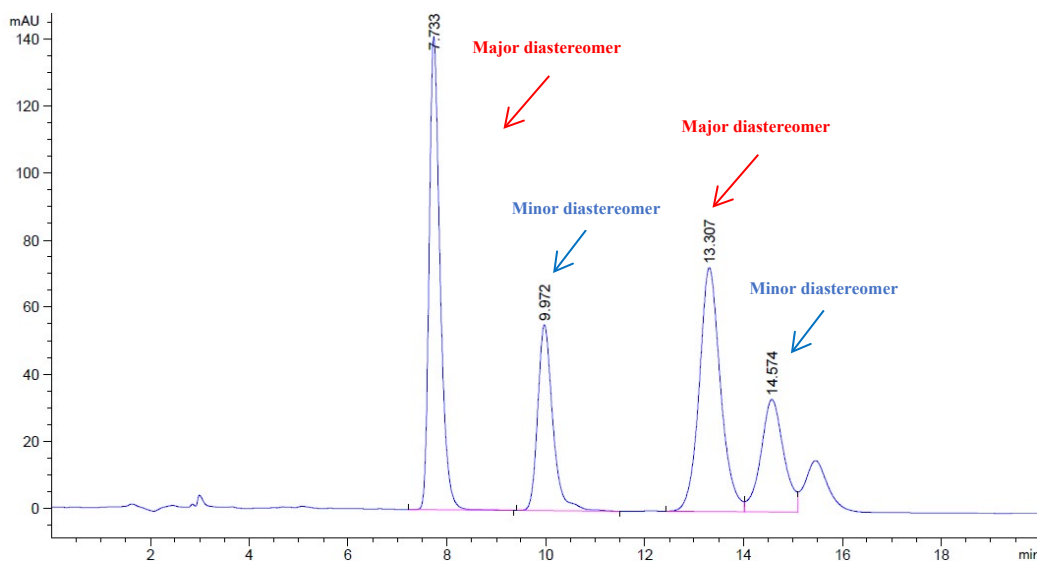
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.782	BB	0.2337	3440.80298	224.68813	29.4824
2	10.818	VB R	0.3325	2320.58179	105.56754	19.8838
3	12.814	BB	0.3951	3443.92358	133.00270	29.5091
4	15.336	BB	0.5017	2465.41040	75.54914	21.1248



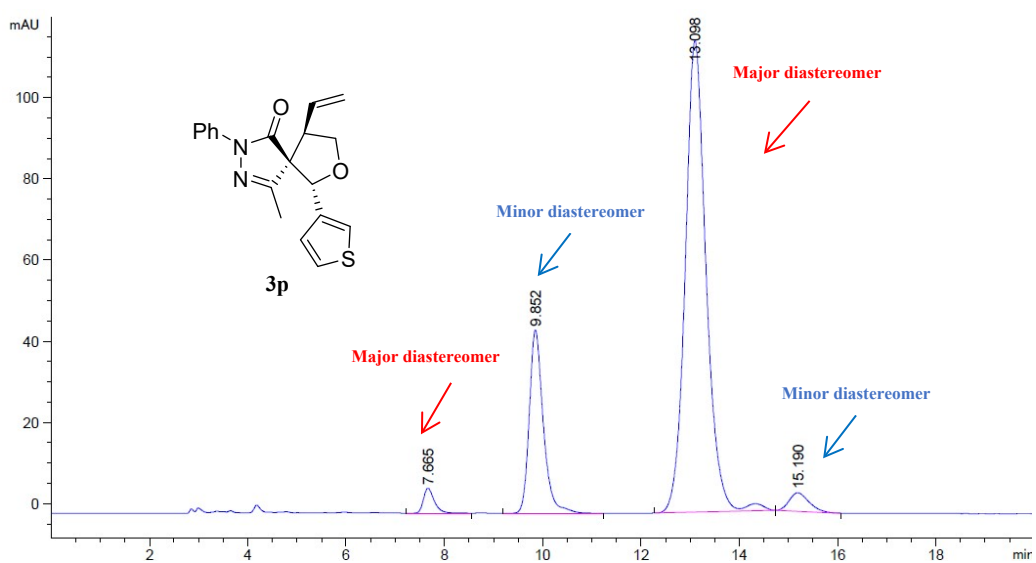
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.847	BB	0.2345	345.95560	22.48843	2.0130
2	10.958	BB	0.3298	3292.31421	151.33138	19.1565
3	12.955	BB	0.4038	1.29642e4	489.83395	75.4329
4	15.685	BB	0.5350	583.94543	16.45460	3.3977



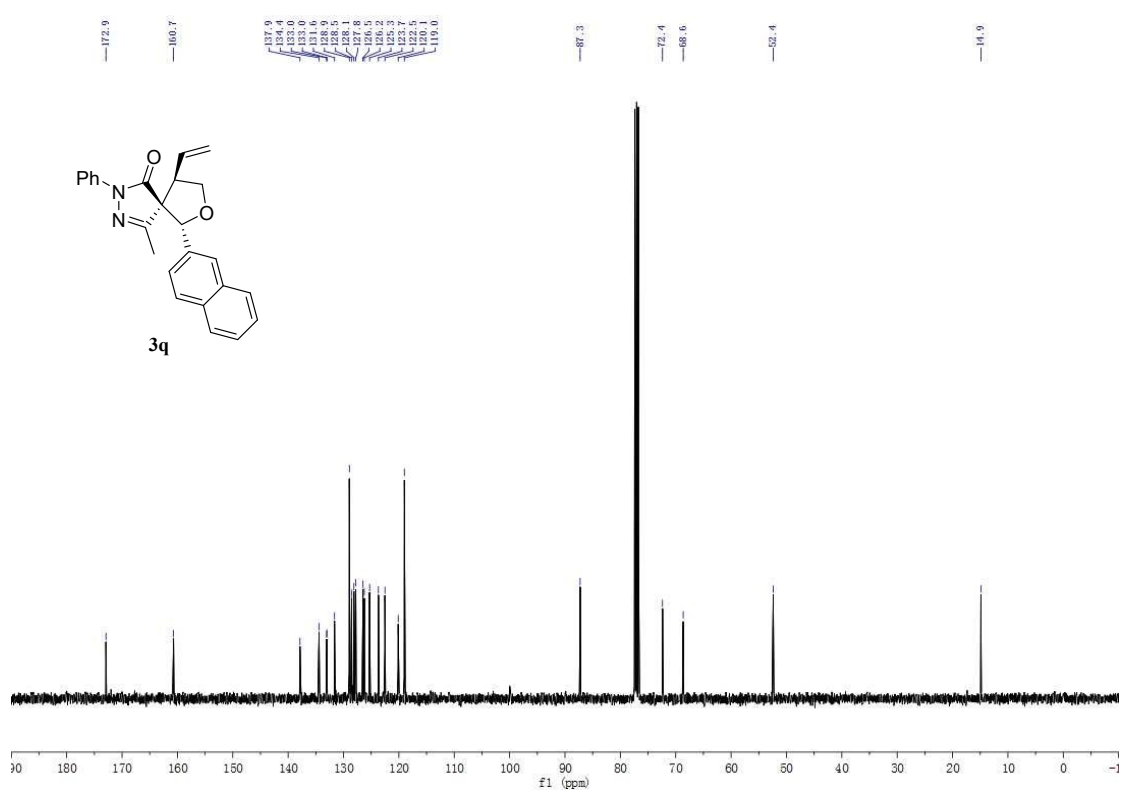
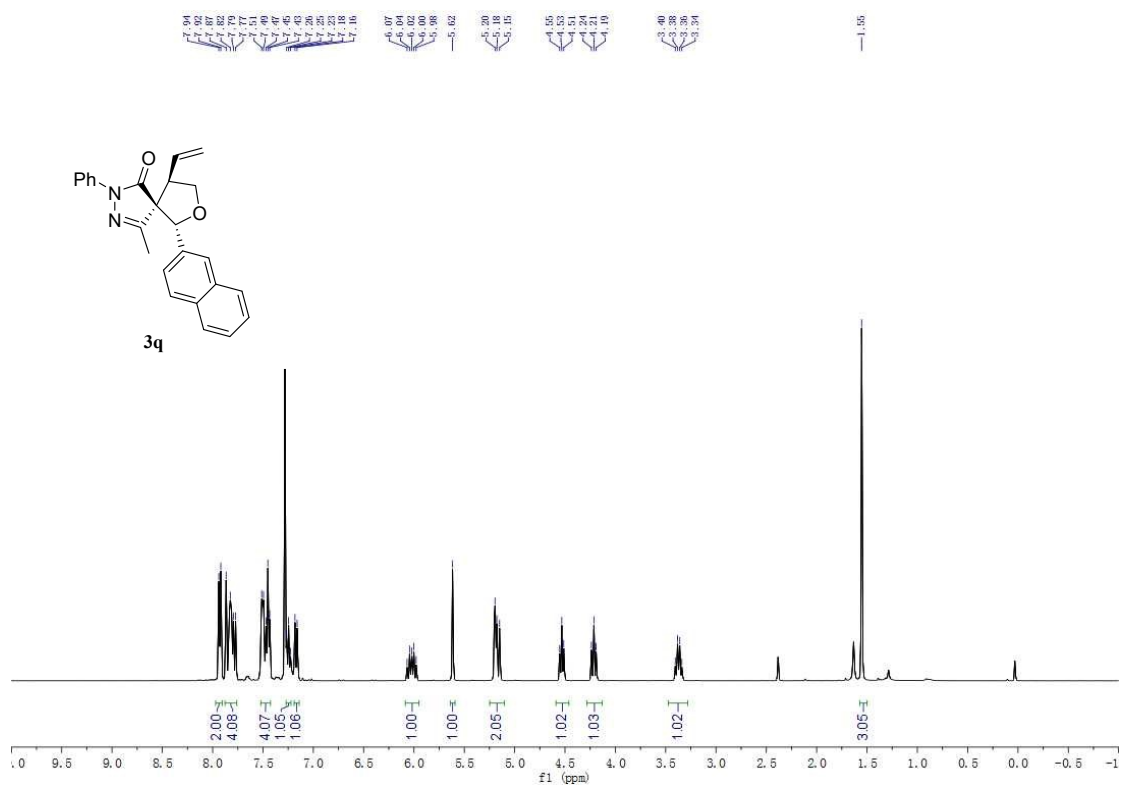


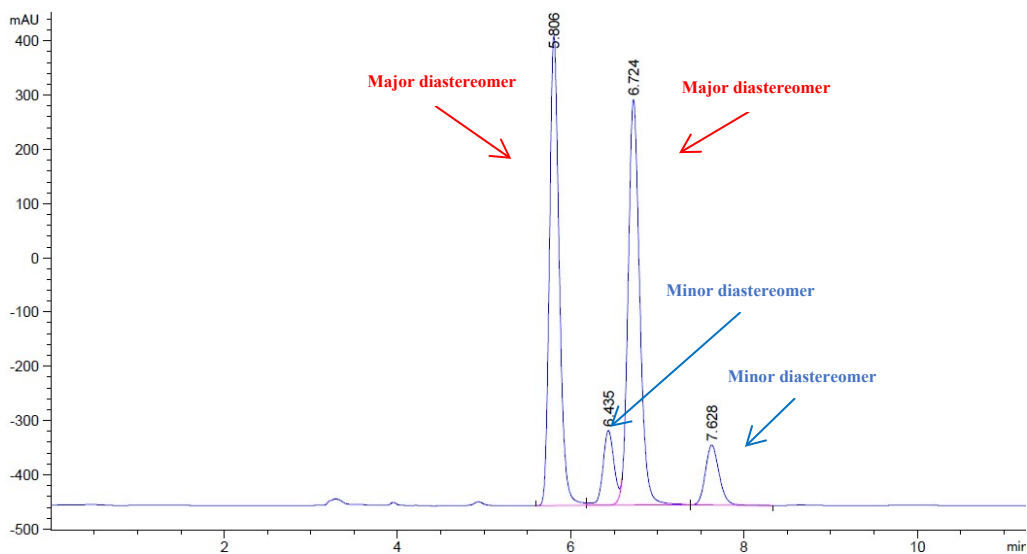


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.733	BB	0.2325	2169.93628	141.02448	32.9265
2	9.972	BB	0.3198	1172.89709	55.43604	17.7975
3	13.307	BV	0.4476	2172.80225	72.71928	32.9700
4	14.574	VV	0.4798	1074.60742	33.53859	16.3060

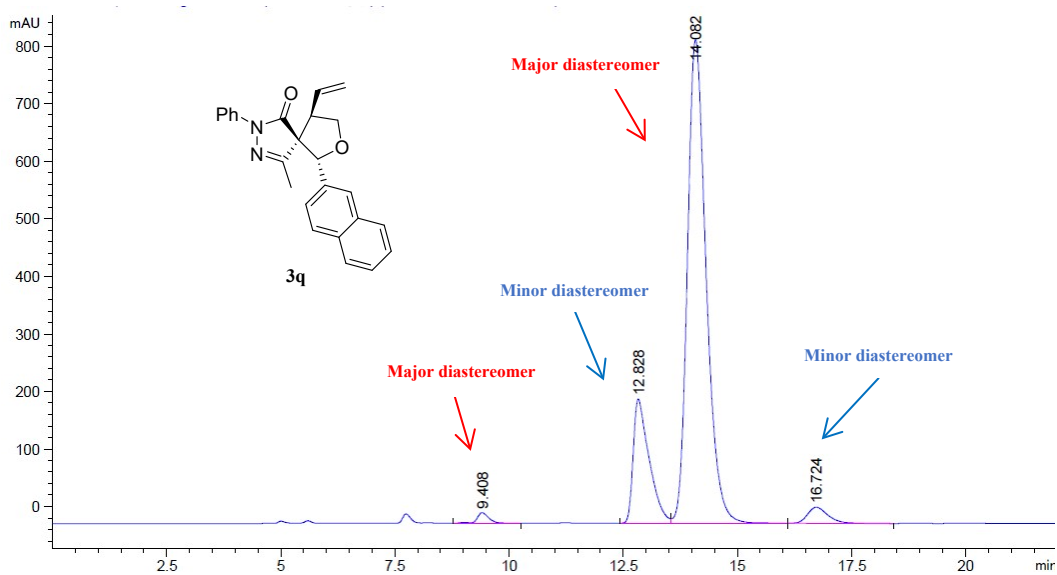


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.665	BB	0.2321	96.15626	6.19369	2.1098
2	9.852	BB	0.2987	900.67169	45.16088	19.7621
3	13.098	BV R	0.4406	3432.49585	116.15692	75.3141
4	15.190	BB	0.4173	128.25304	4.58601	2.8141

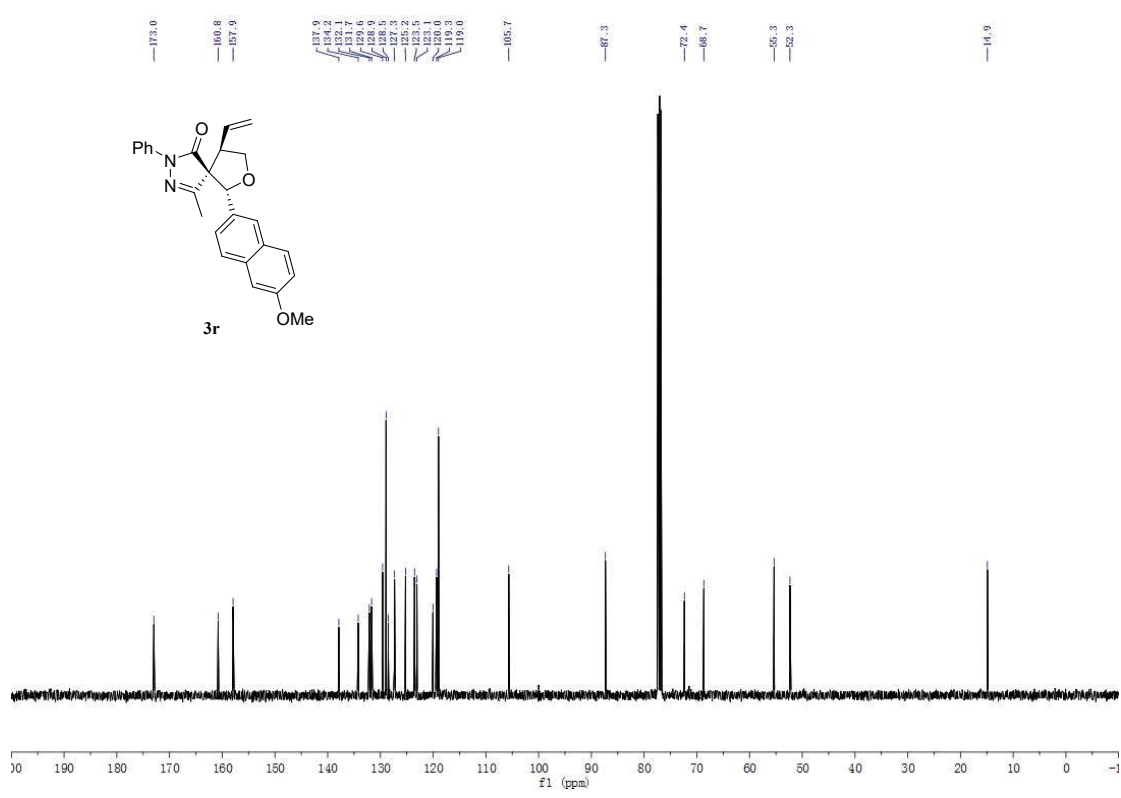
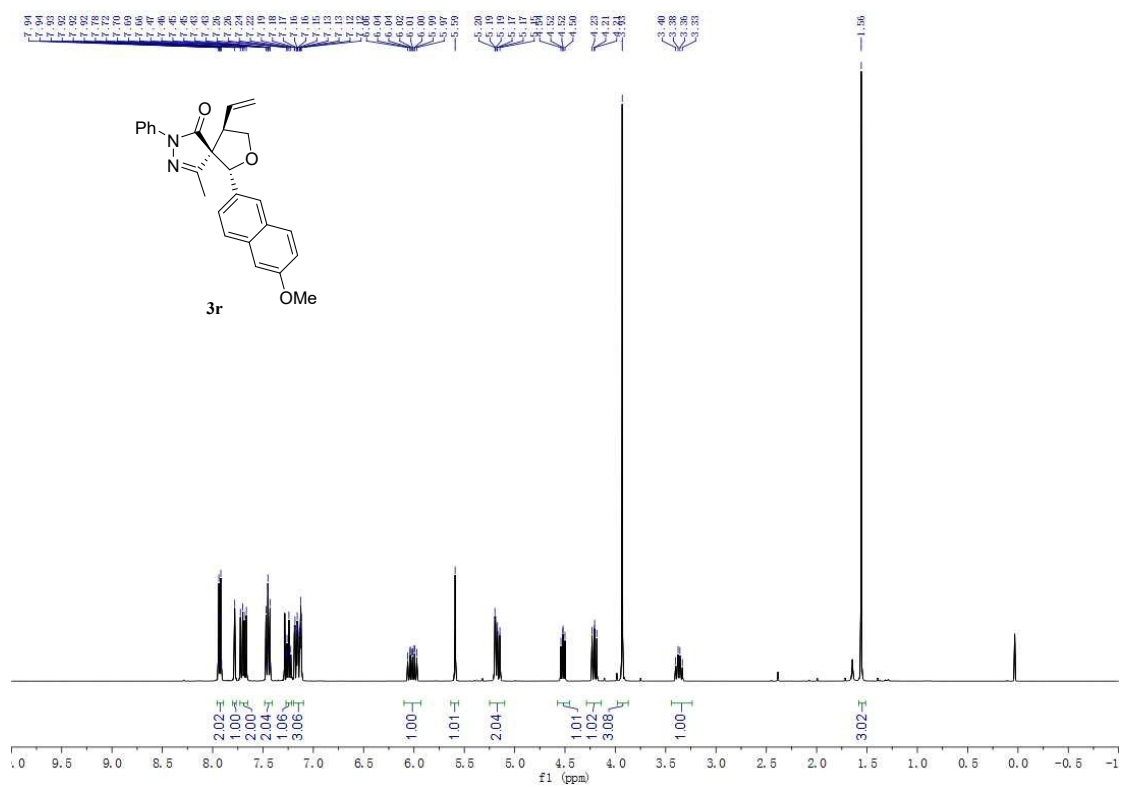


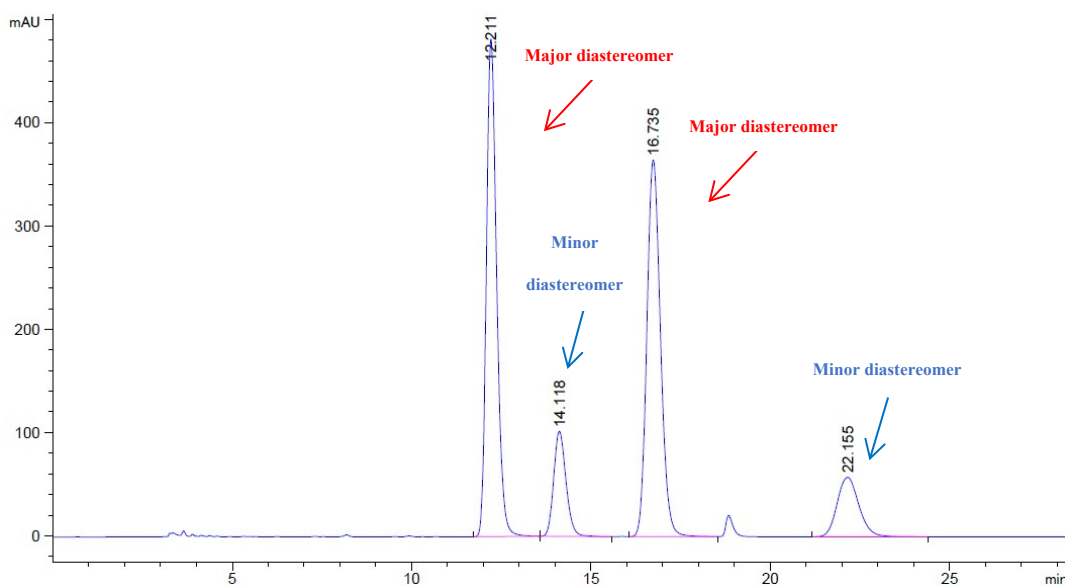


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.806	BV	0.1207	6808.12158	866.34723	41.9060
2	6.435	VV E	0.1351	1206.46399	137.90697	7.4261
3	6.724	VB R	0.1435	7016.41699	747.70532	43.1882
4	7.628	BB	0.1705	1215.15698	110.34270	7.4797

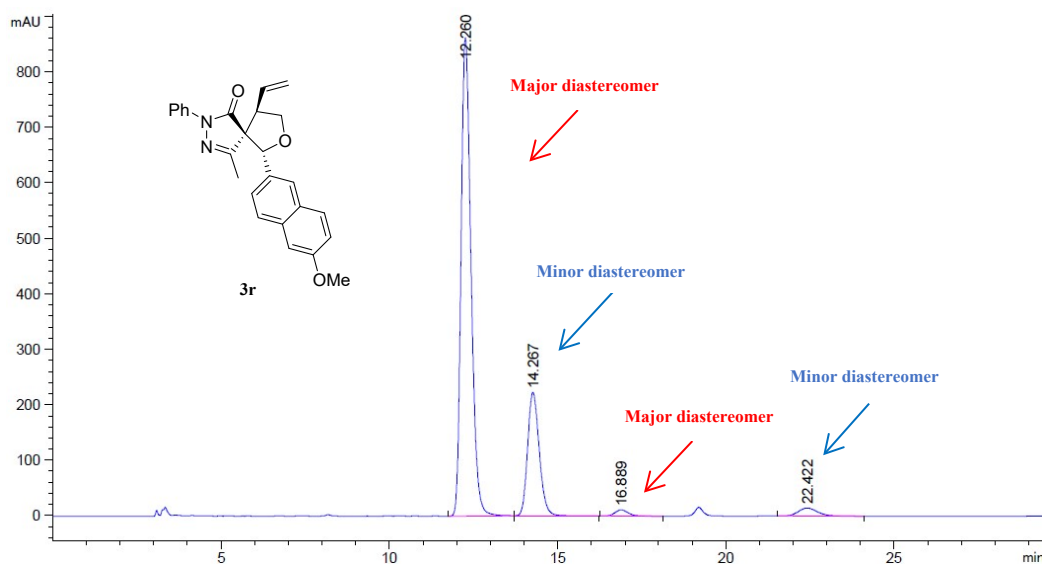


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.408	VB R	0.2574	335.31424	18.48689	1.1073
2	12.828	BV	0.3460	5225.16064	215.43951	17.2552
3	14.082	VB	0.4330	2.38420e4	840.40344	78.7343
4	16.724	BB	0.4704	879.12665	28.07169	2.9032

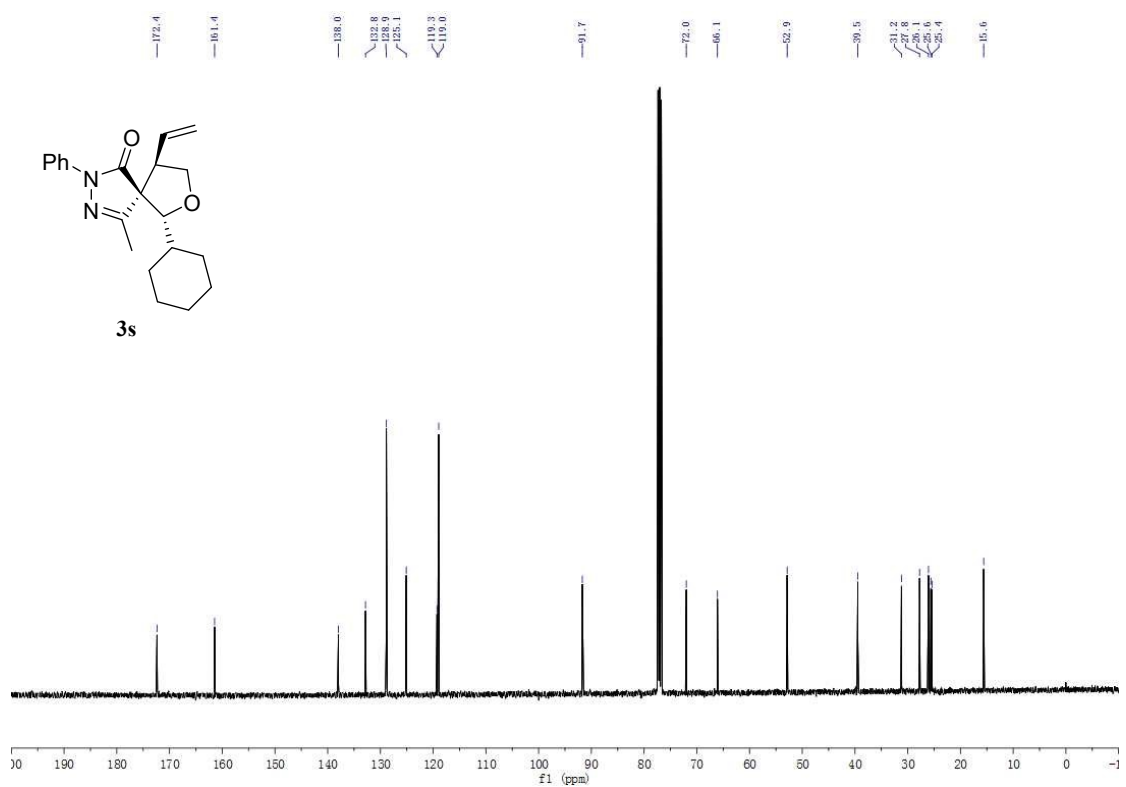
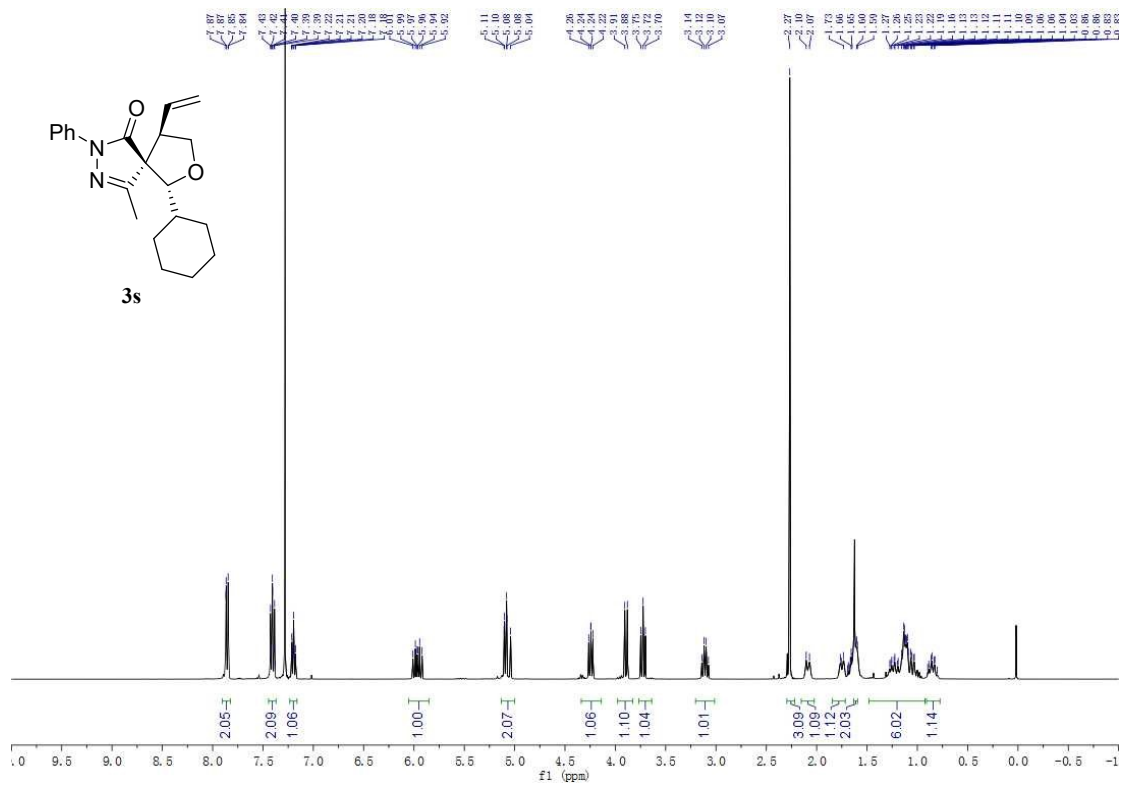


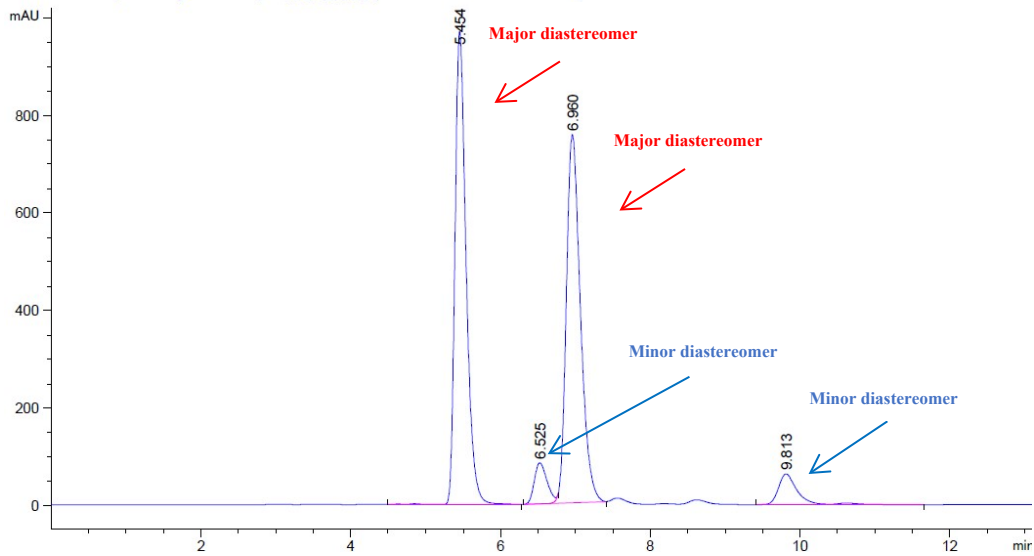


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.211	BB	0.3055	9558.79199	481.74152	39.7659
2	14.118	BB	0.3691	2433.08545	101.70821	10.1220
3	16.735	BB	0.4083	9613.46680	364.96213	39.9934
4	22.155	BB	0.6584	2432.28662	57.63498	10.1187

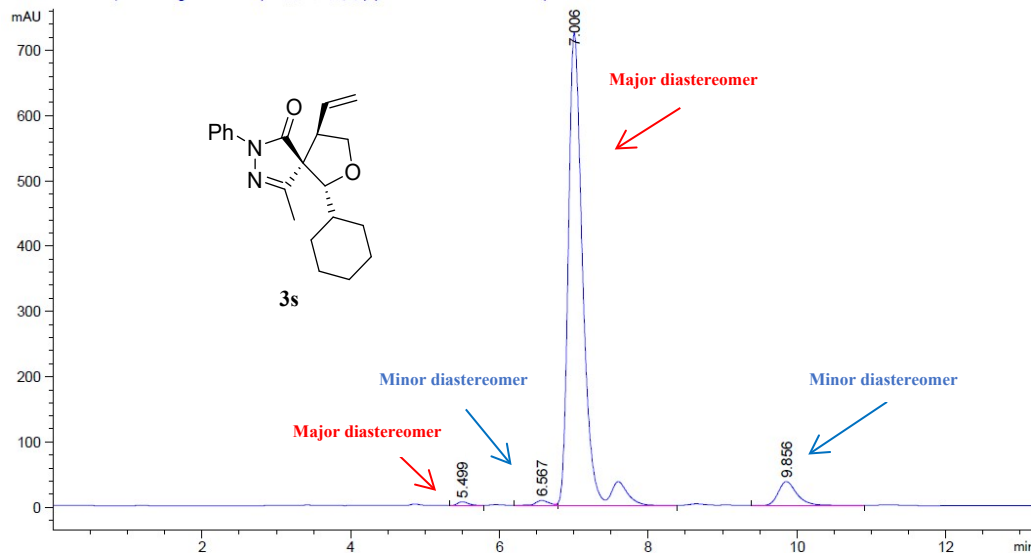


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.260	BB	0.3162	1.76638e4	861.63062	73.9421
2	14.267	BB	0.3695	5335.29248	222.67987	22.3339
3	16.889	BB	0.4204	305.70959	11.16817	1.2797
4	22.422	BB	0.6141	583.89417	14.49125	2.4442

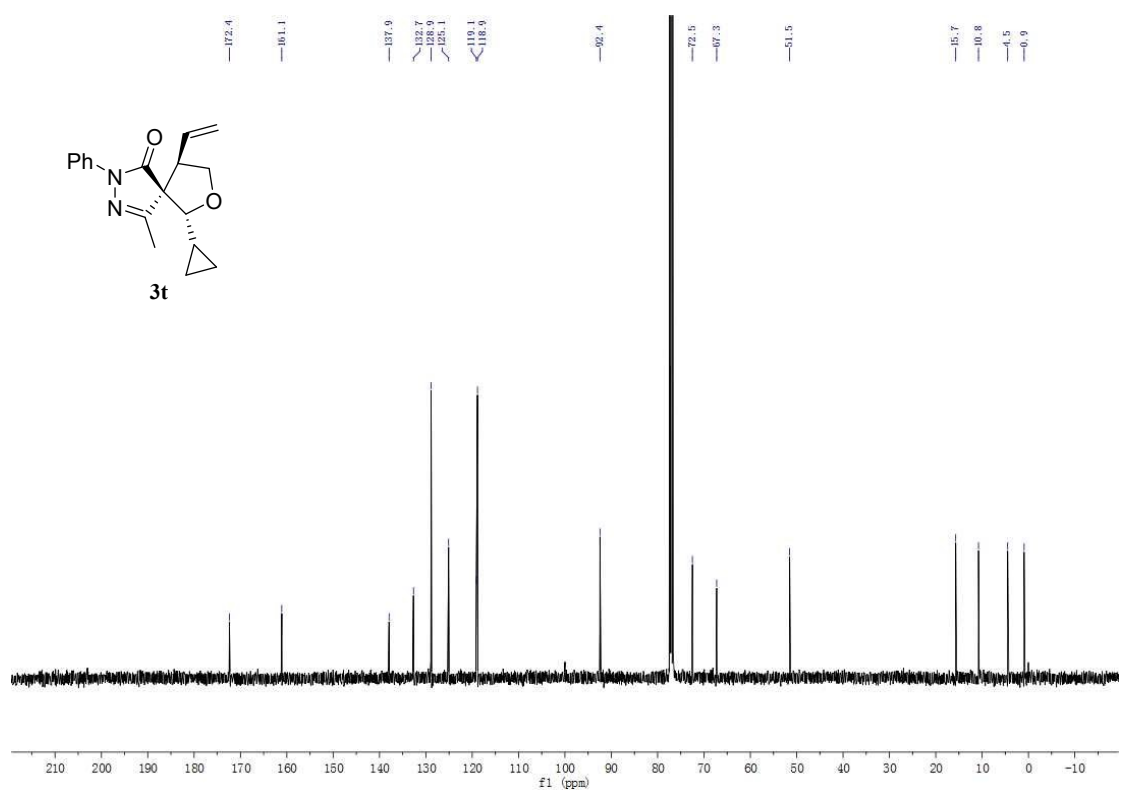
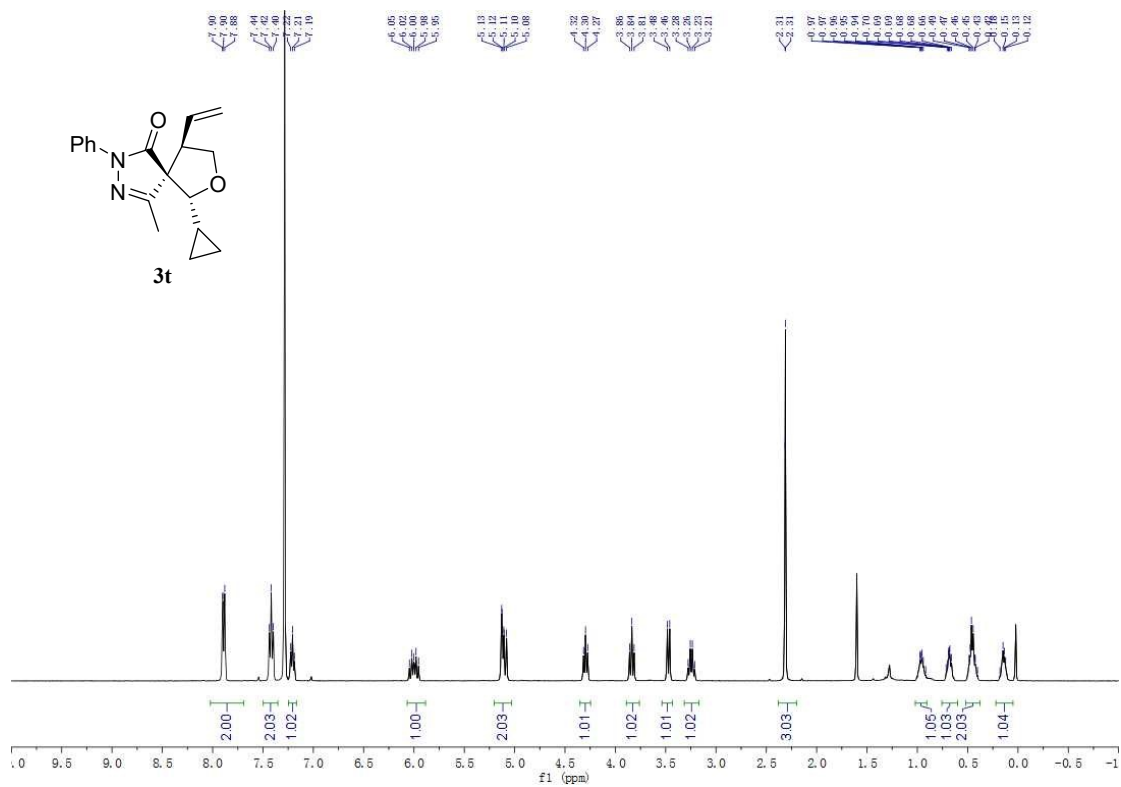




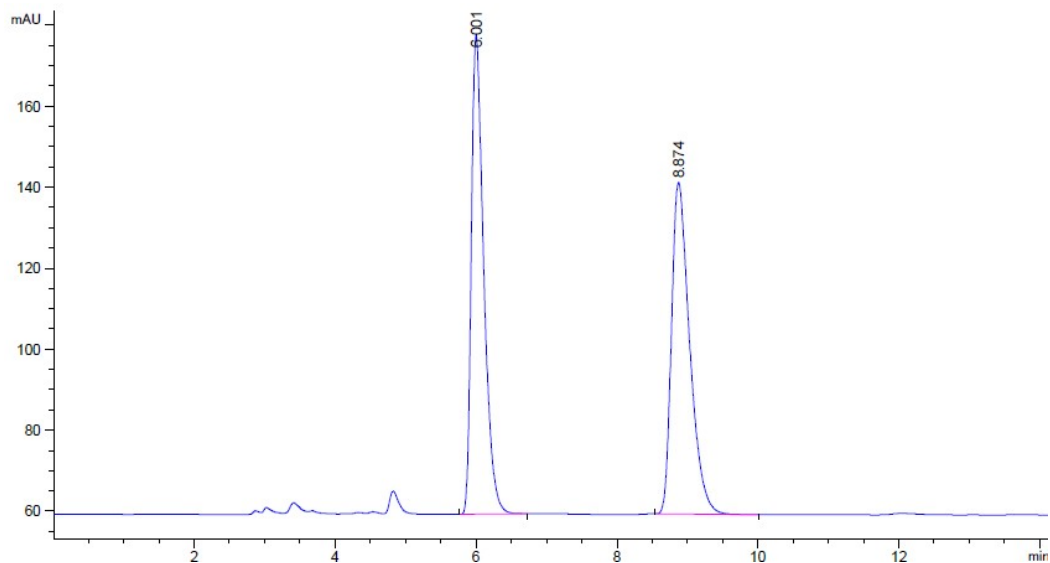
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.454	VB R	0.1575	1.00008e4	968.51599	45.4605
2	6.525	BV E	0.1803	982.32611	84.07376	4.4653
3	6.960	VB R	0.2009	9884.17383	754.42230	44.9303
4	9.813	BV R	0.2526	1131.60608	62.97055	5.1439



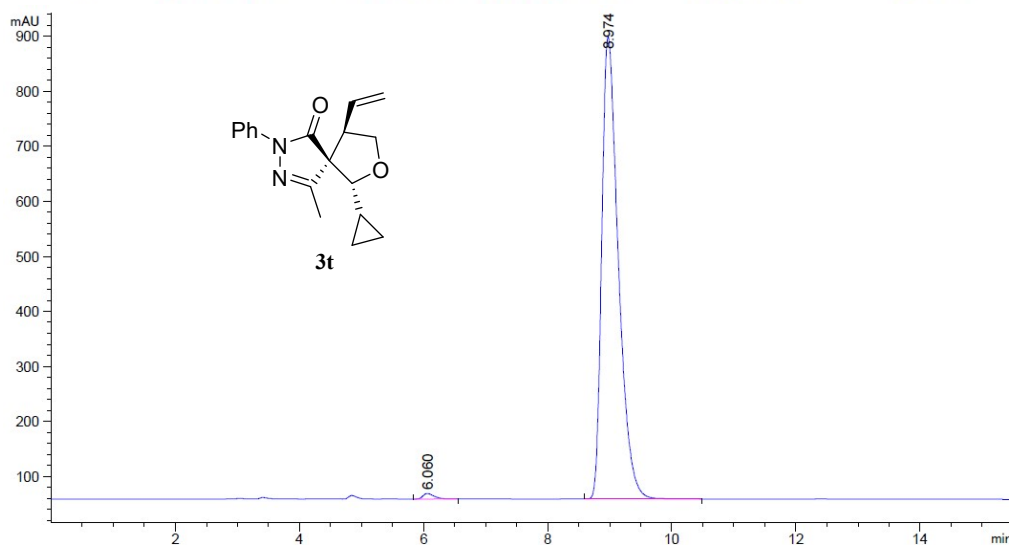
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.499	BV	0.1537	59.34518	5.93371	0.5474
2	6.567	BV E	0.1870	95.41780	7.78400	0.8801
3	7.006	VV R	0.2000	1.00379e4	724.26819	92.5849
4	9.856	BB	0.2648	649.16400	36.79922	5.9876



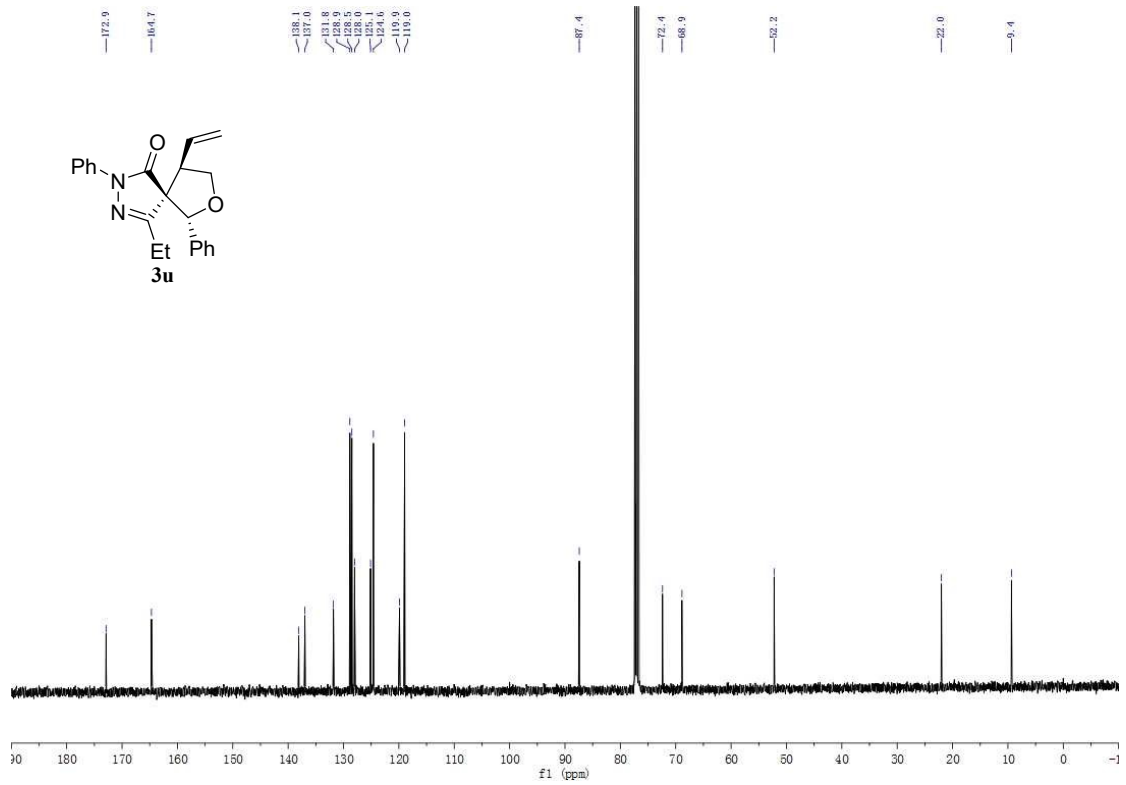
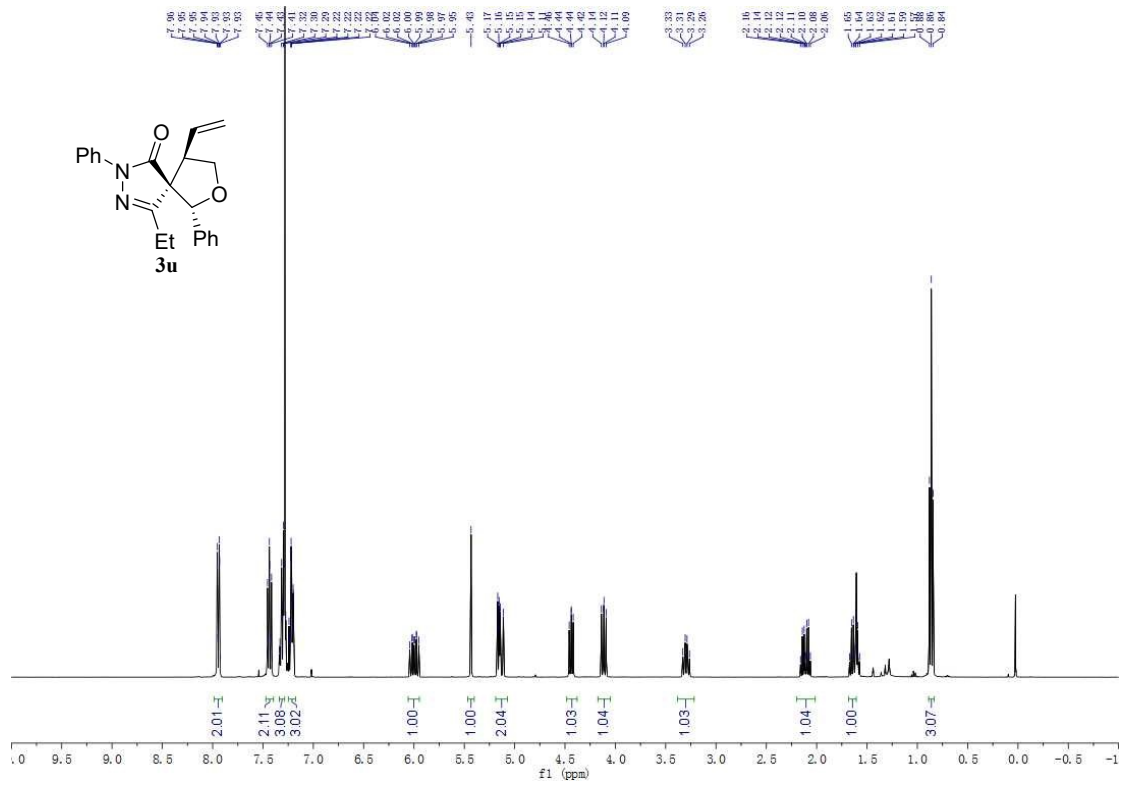


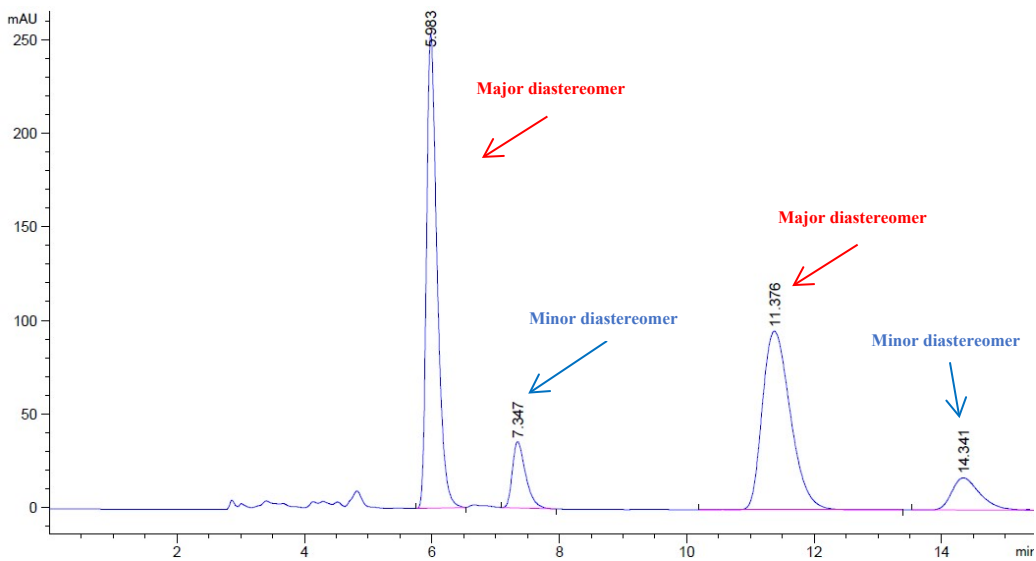


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.001	BB	0.1837	1447.63599	118.35202	49.7124
2	8.874	BB	0.2696	1464.38867	81.90359	50.2876

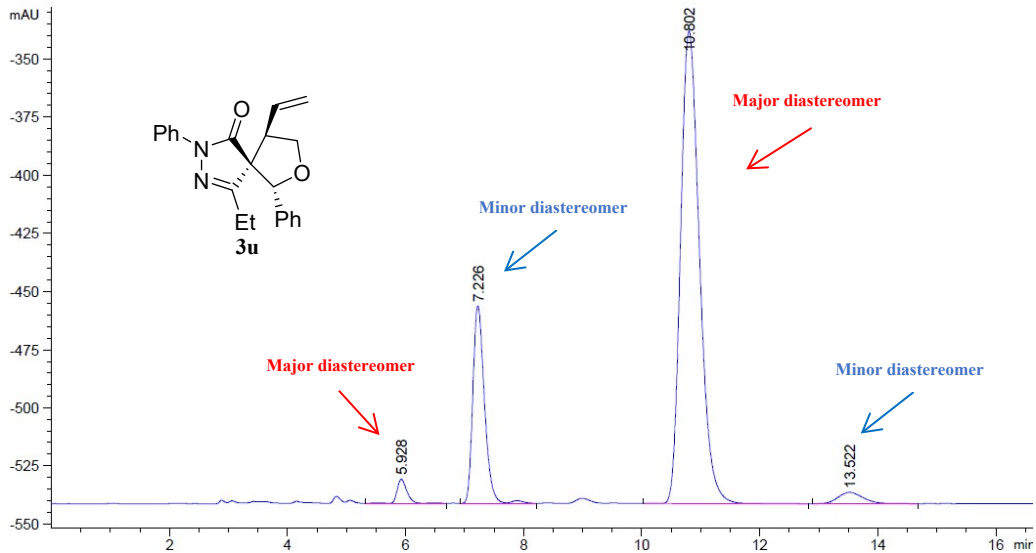


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.060	BB	0.1899	125.26244	10.01338	0.8006
2	8.974	BB	0.2794	1.55214e4	840.50482	99.1994

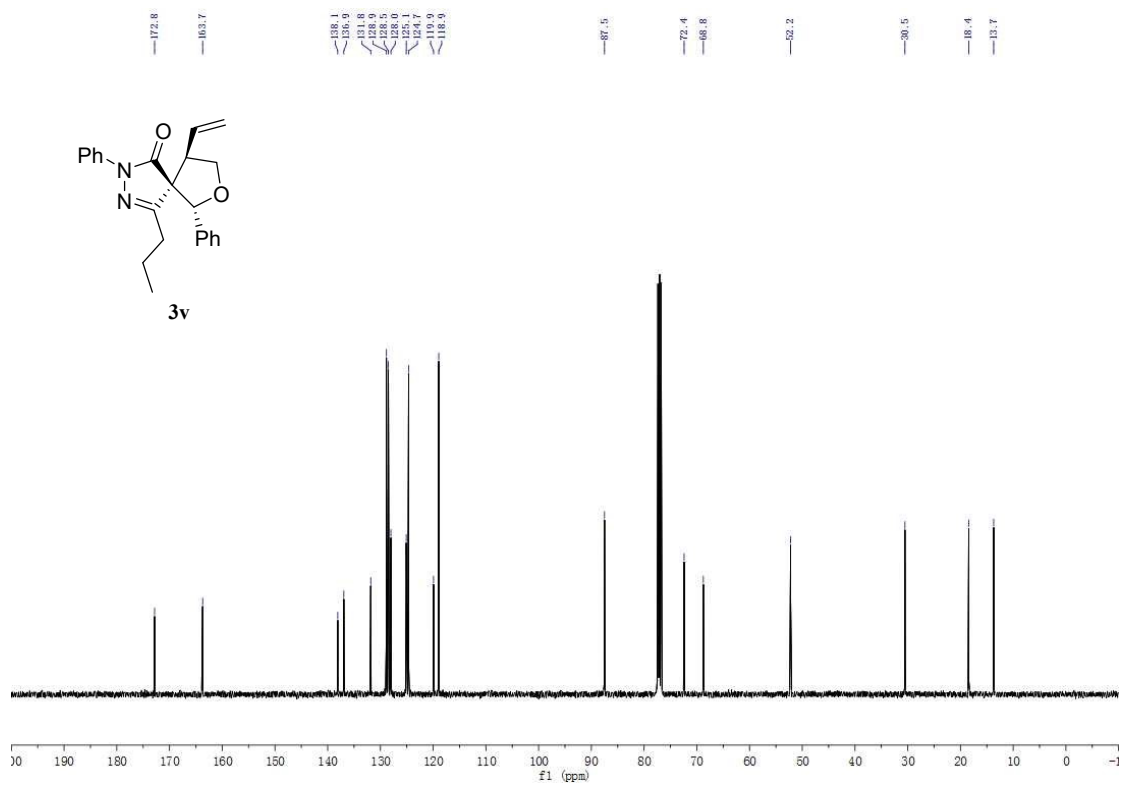
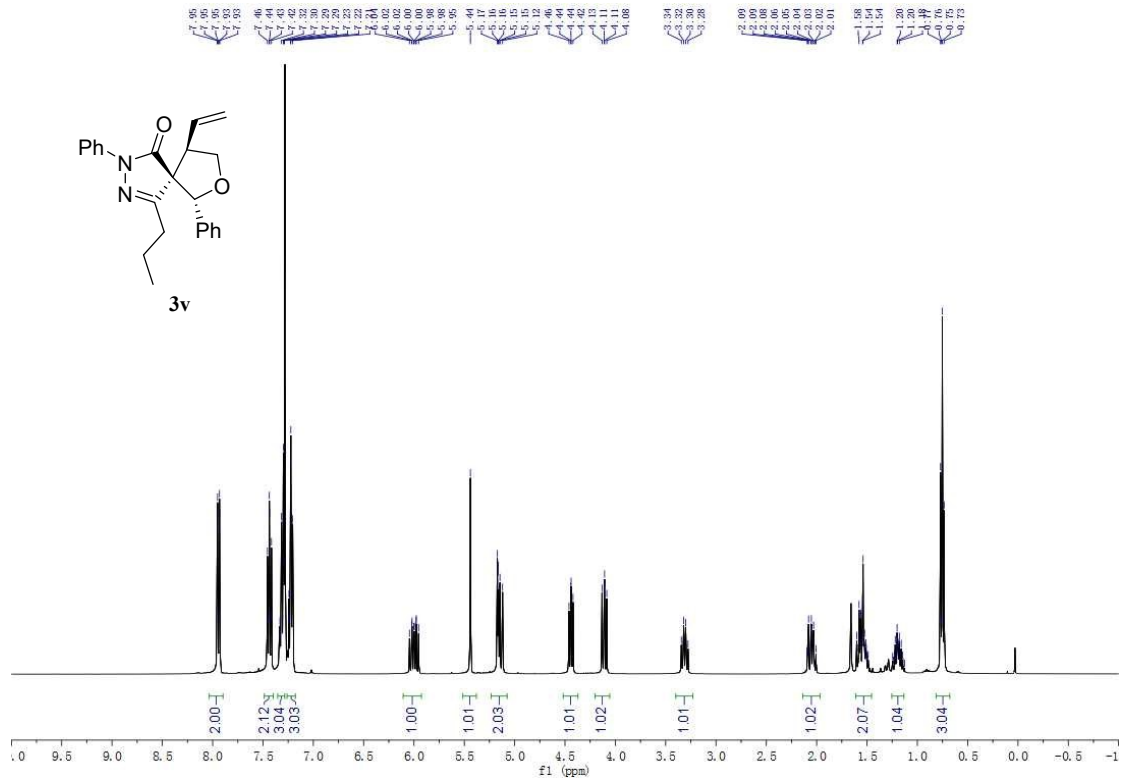


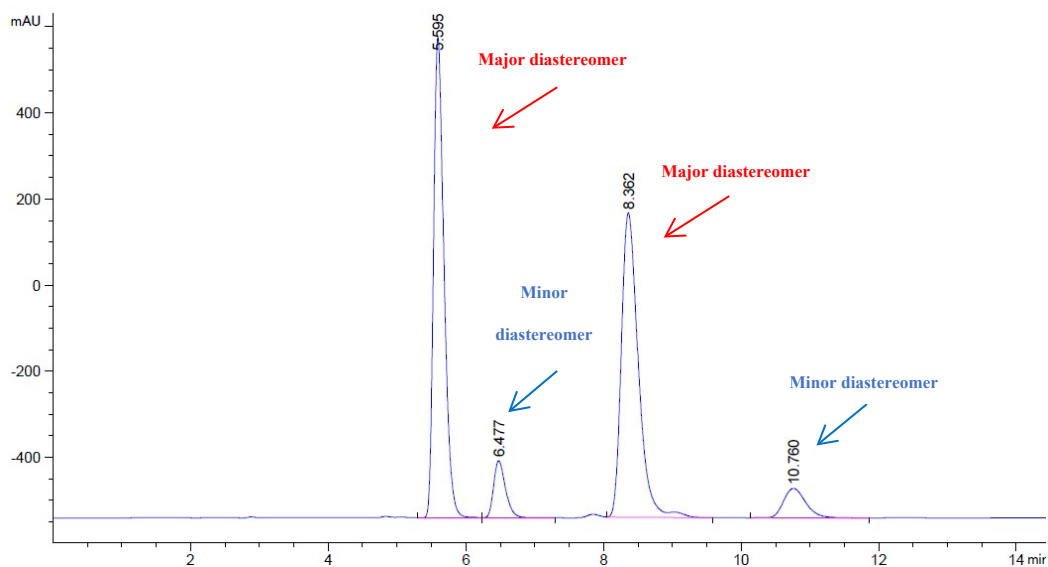


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.983	BB	0.1754	2934.96265	252.81757	42.5867
2	7.347	BB	0.2165	510.68759	35.36918	7.4101
3	11.376	VB R	0.4804	2916.62012	95.43499	42.3205
4	14.341	BBA	0.4664	529.46680	17.23672	7.6826

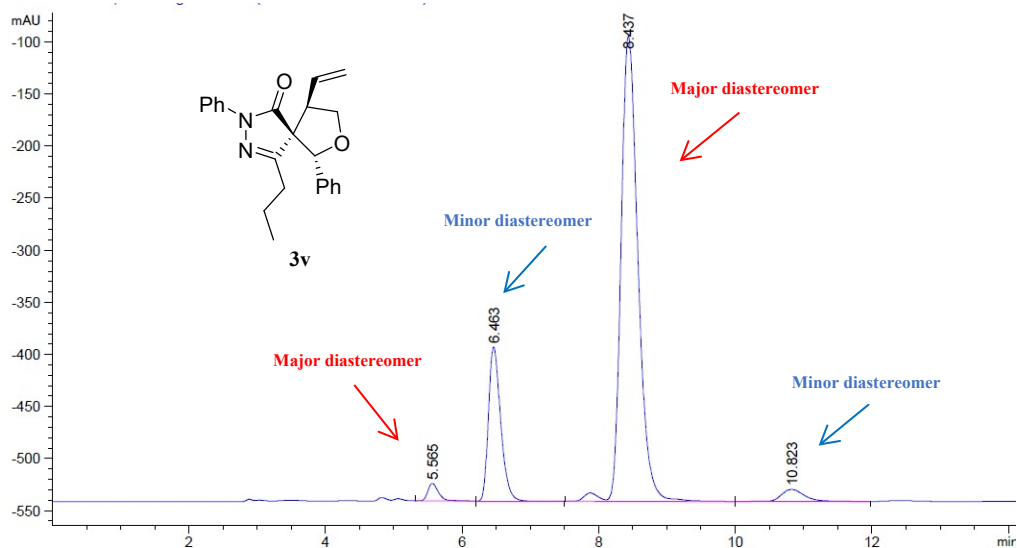


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.928	VV R	0.1746	119.88450	10.34484	2.0192
2	7.226	BV R	0.2058	1163.86255	84.82523	19.6031
3	10.802	BV R	0.3467	4509.91992	203.19647	75.9611
4	13.522	BB	0.4568	143.47853	4.85515	2.4166

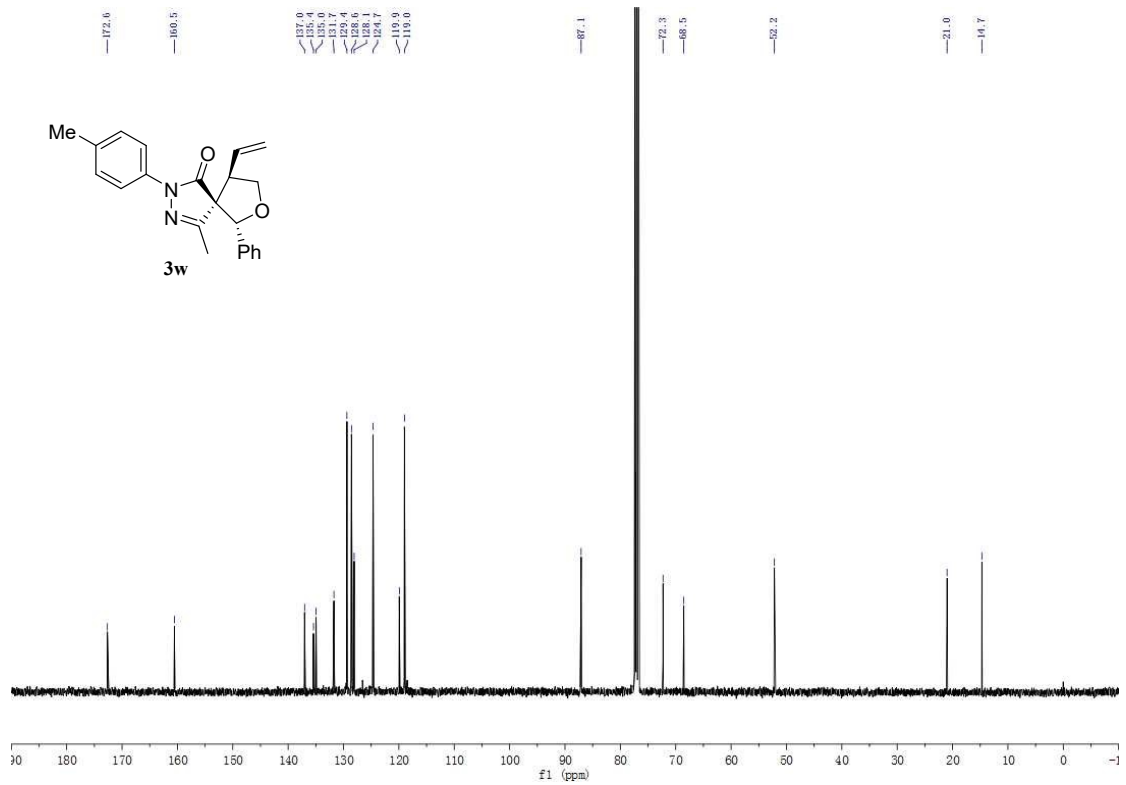
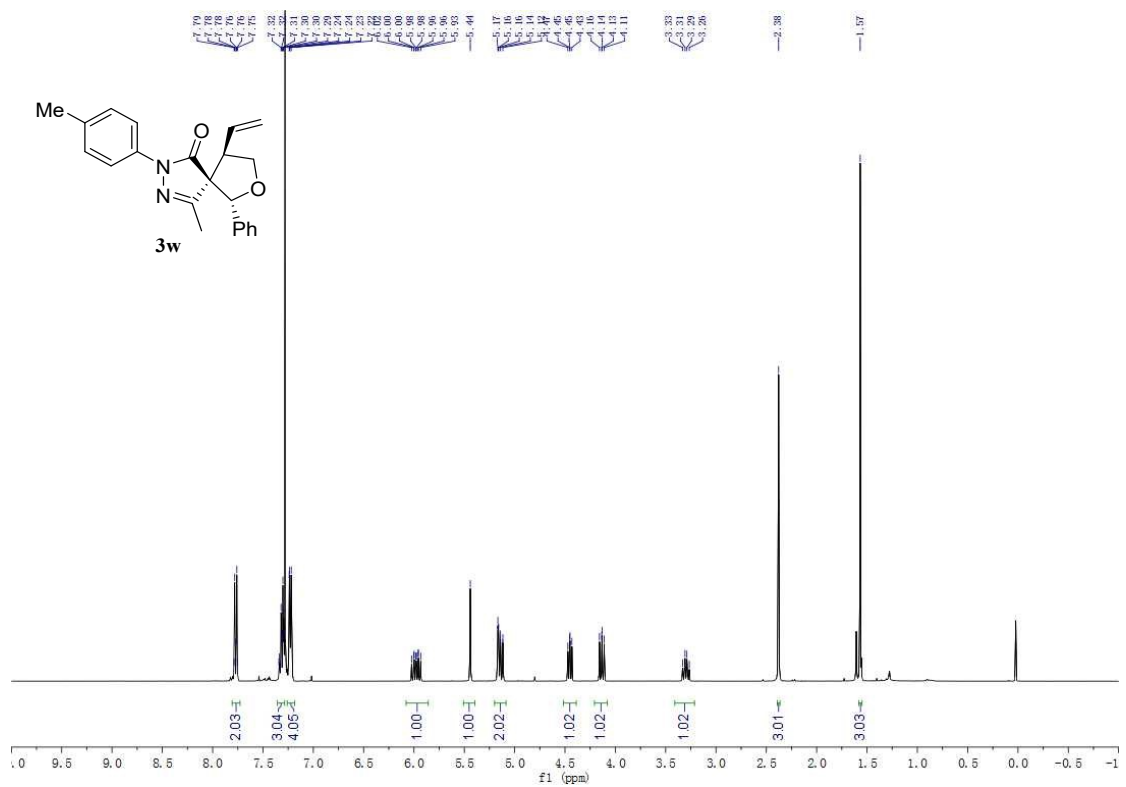


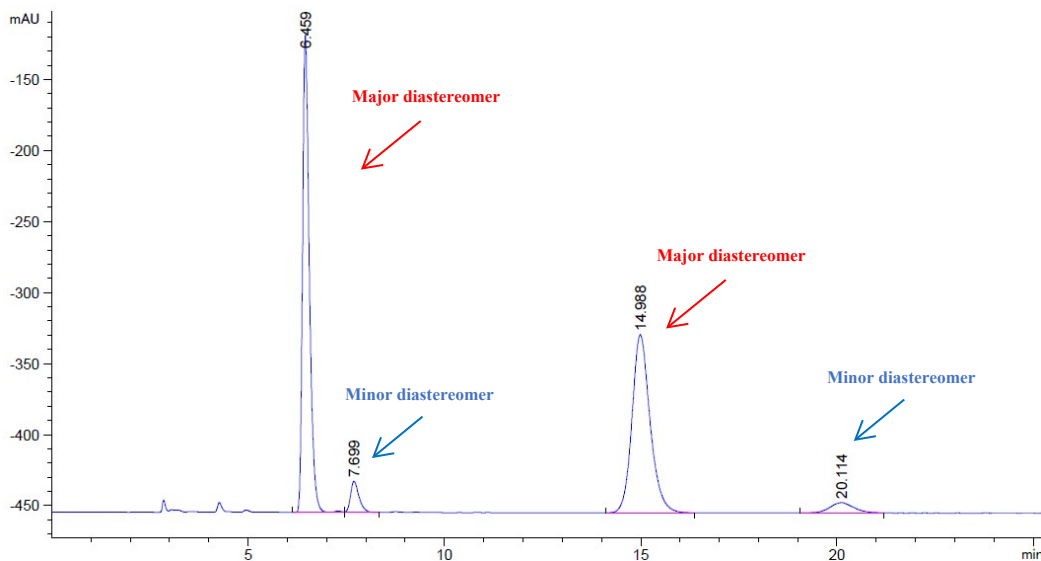


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.595	BV	0.1630	1.17630e4	1115.97266	43.5022
2	6.477	VB	0.1869	1601.42151	132.58990	5.9224
3	8.362	BV R	0.2618	1.21348e4	706.35474	44.8769
4	10.760	BV	0.3498	1540.89233	68.67101	5.6985

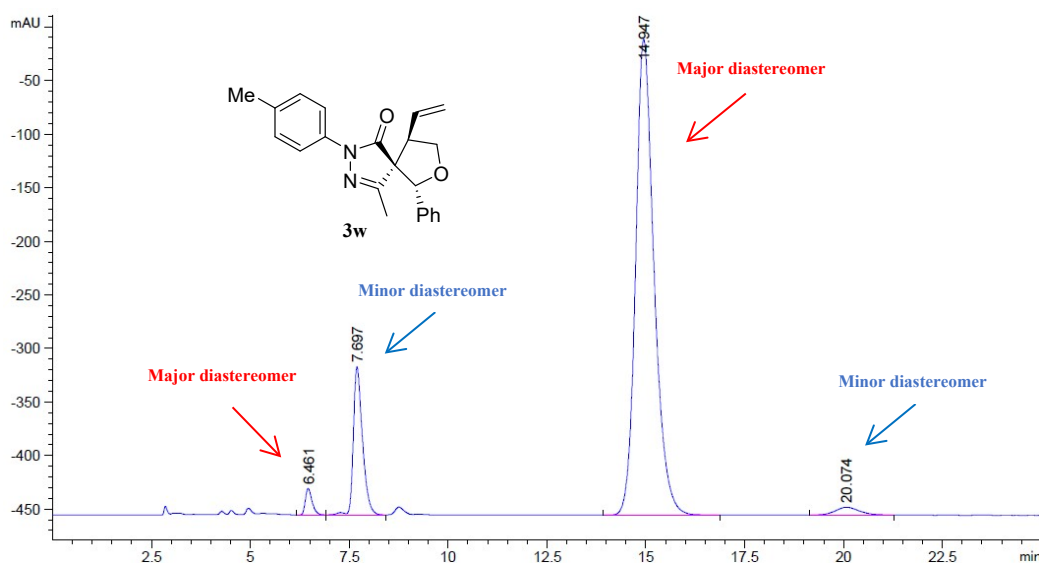


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.565	BB	0.1674	187.67735	16.91838	1.8630
2	6.463	BV R	0.1912	1845.10120	148.03413	18.3157
3	8.437	VB R	0.2661	7772.38965	446.45950	77.1538
4	10.823	BV	0.3541	268.71832	11.60821	2.6675

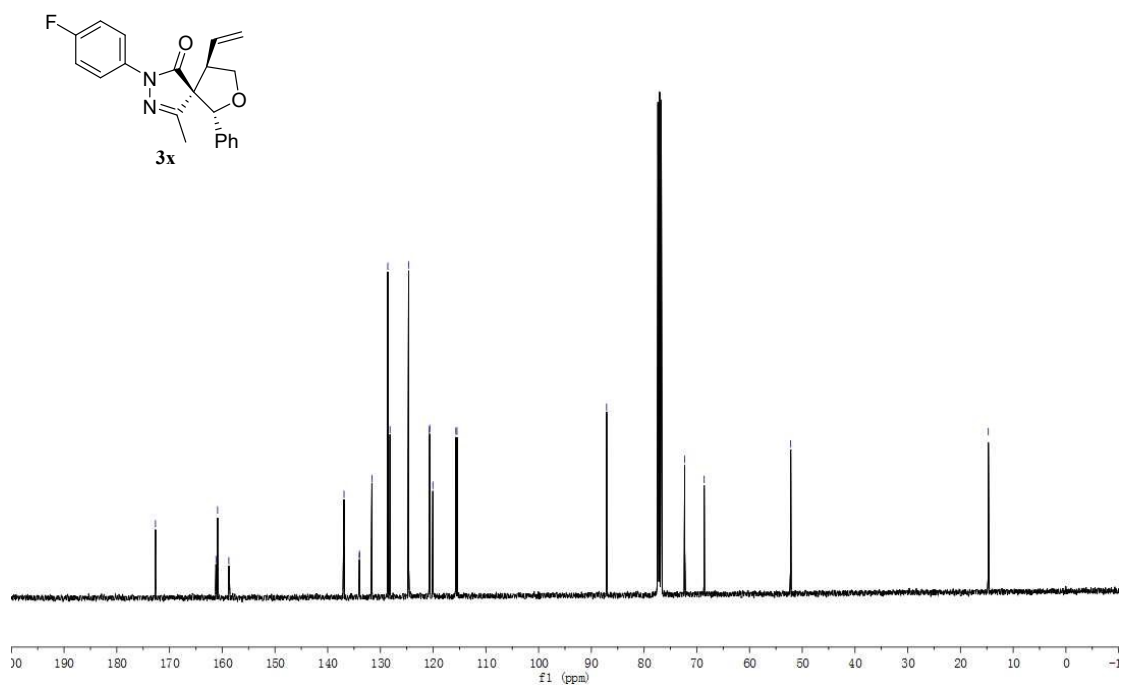
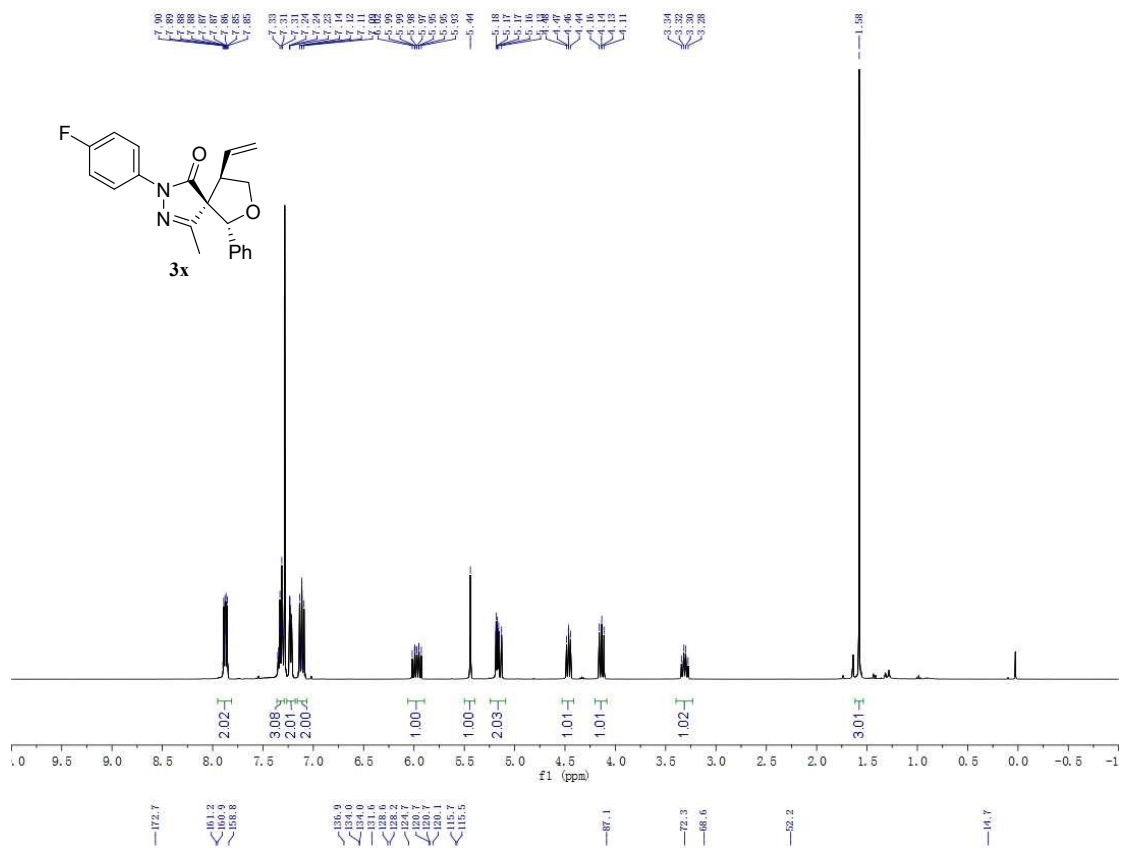




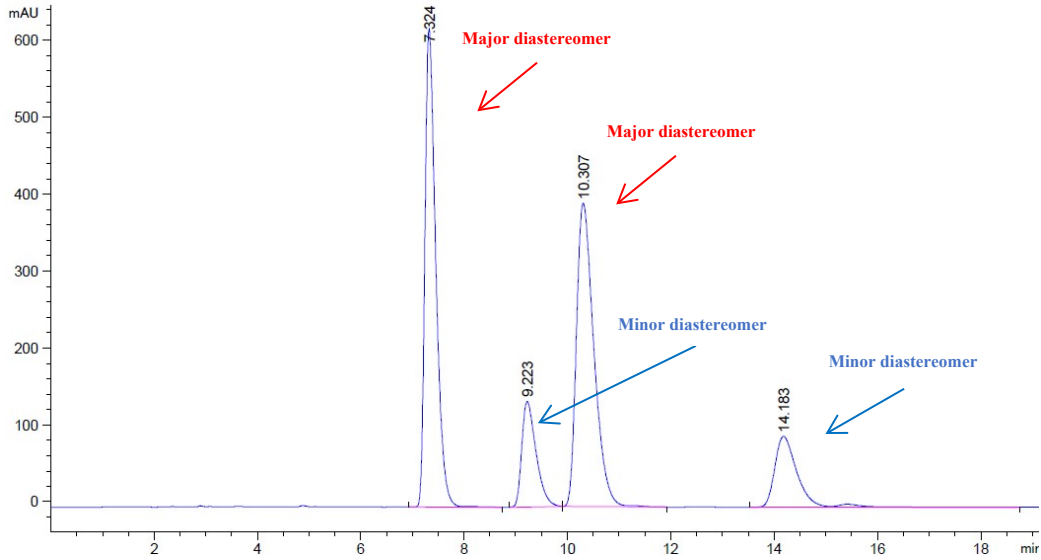
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.459	BV R	0.1813	4046.92871	336.46686	46.3834
2	7.699	VB	0.2248	331.65207	22.14004	3.8012
3	14.988	BB	0.4858	4032.69336	125.52077	46.2202
4	20.114	BB	0.6370	313.67917	7.30413	3.5952



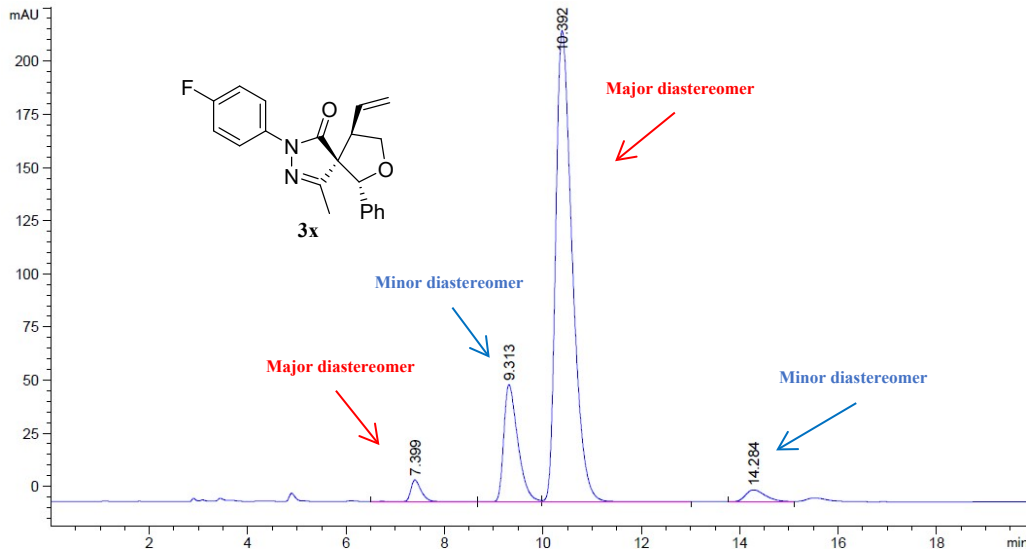
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.461	BB	0.1795	294.70245	24.82700	1.7092
2	7.697	VB R	0.2354	2218.00024	138.29692	12.8636
3	14.947	BB	0.4873	1.44102e4	444.45917	83.5739
4	20.074	BB	0.6302	319.56622	7.45342	1.8534



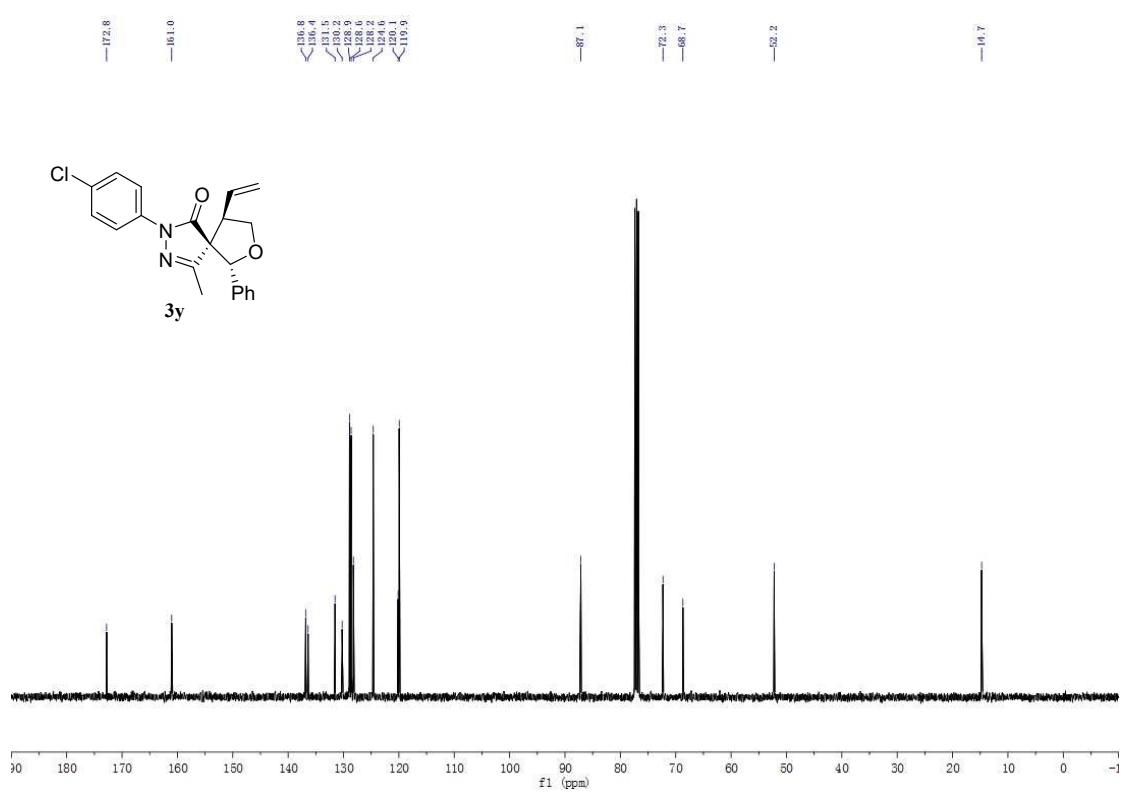
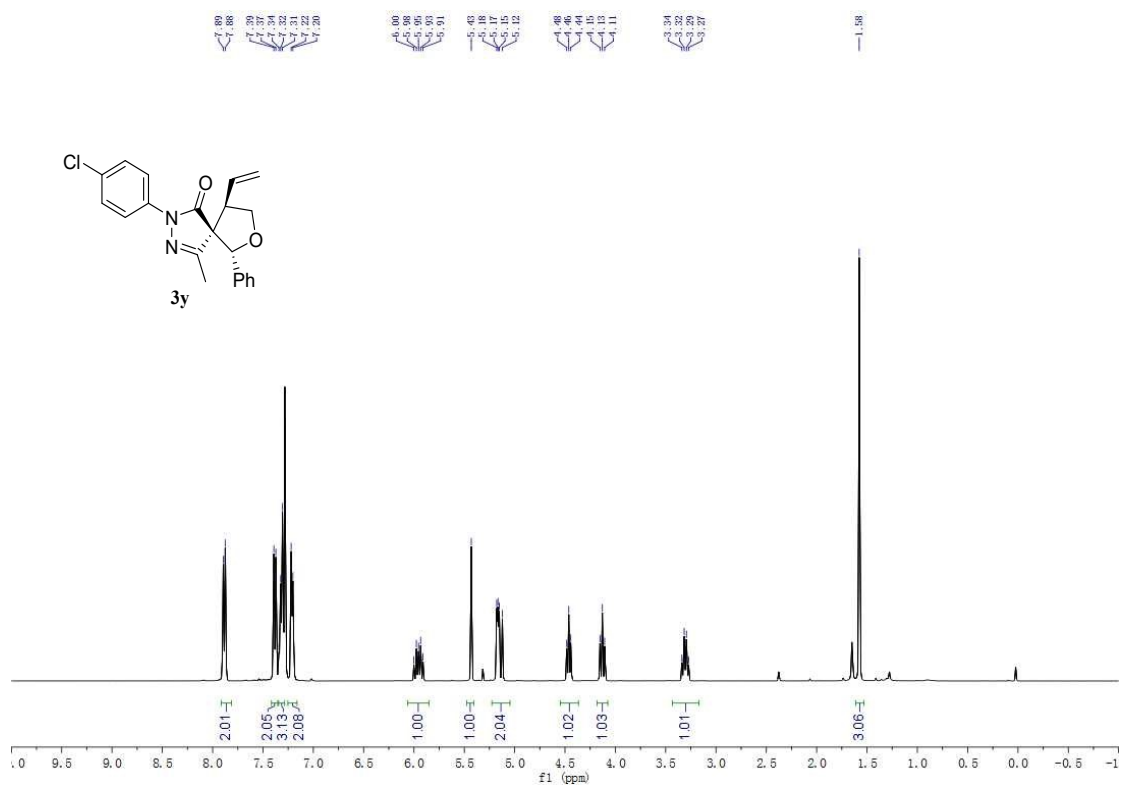


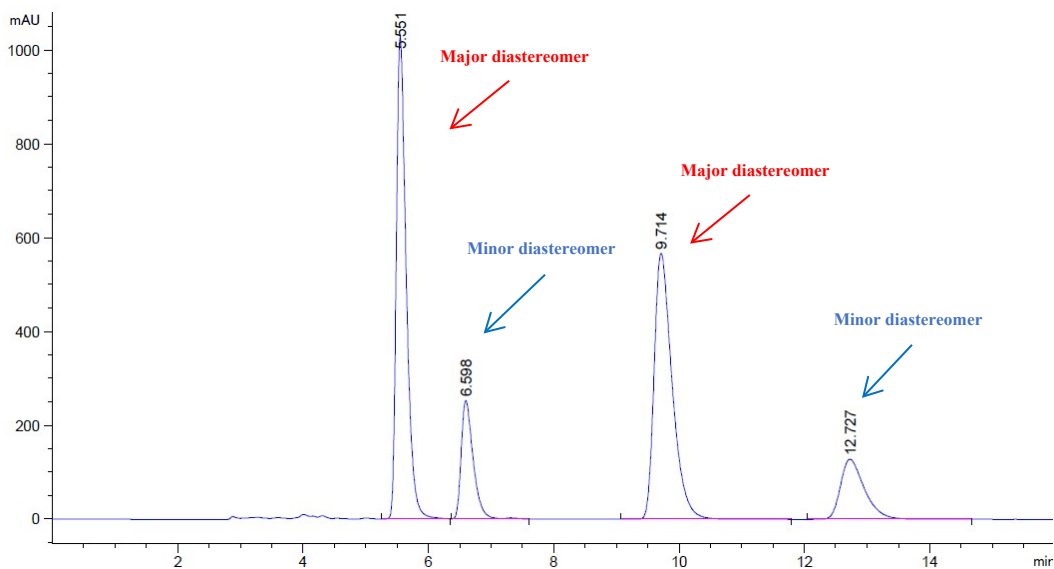


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.324	BV R	0.2220	9063.75195	620.75916	38.1754
2	9.223	BB	0.2912	2622.20996	137.07372	11.0444
3	10.307	BV R	0.3568	9252.33887	394.23352	38.9697
4	14.183	BV R	0.4429	2804.11353	92.12141	11.8106

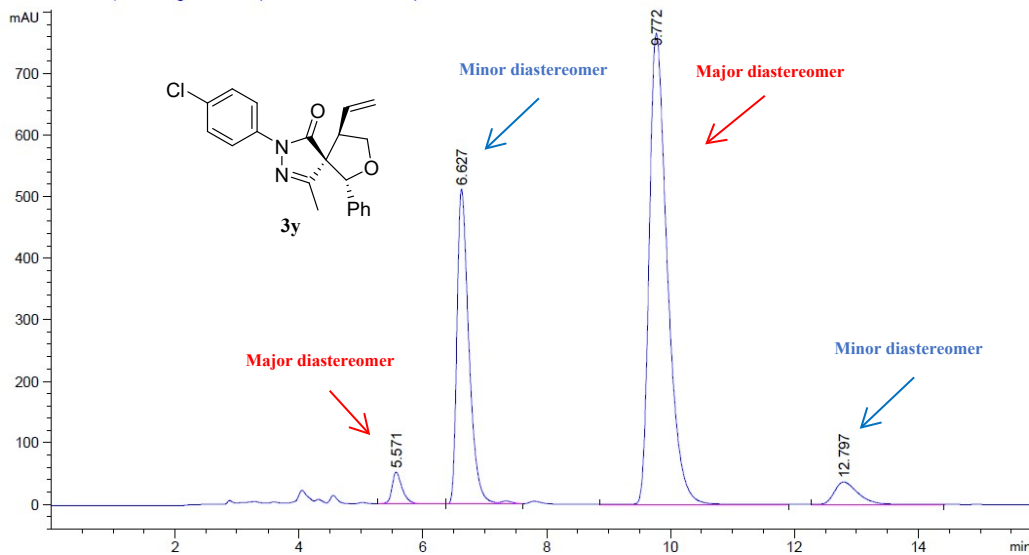


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.399	VV R	0.2173	152.11389	10.24701	2.3147
2	9.313	BV	0.2991	1091.17554	55.07583	16.6044
3	10.392	VB	0.3562	5169.67822	221.54630	78.6670
4	14.284	BV	0.4297	158.62973	5.61250	2.4139

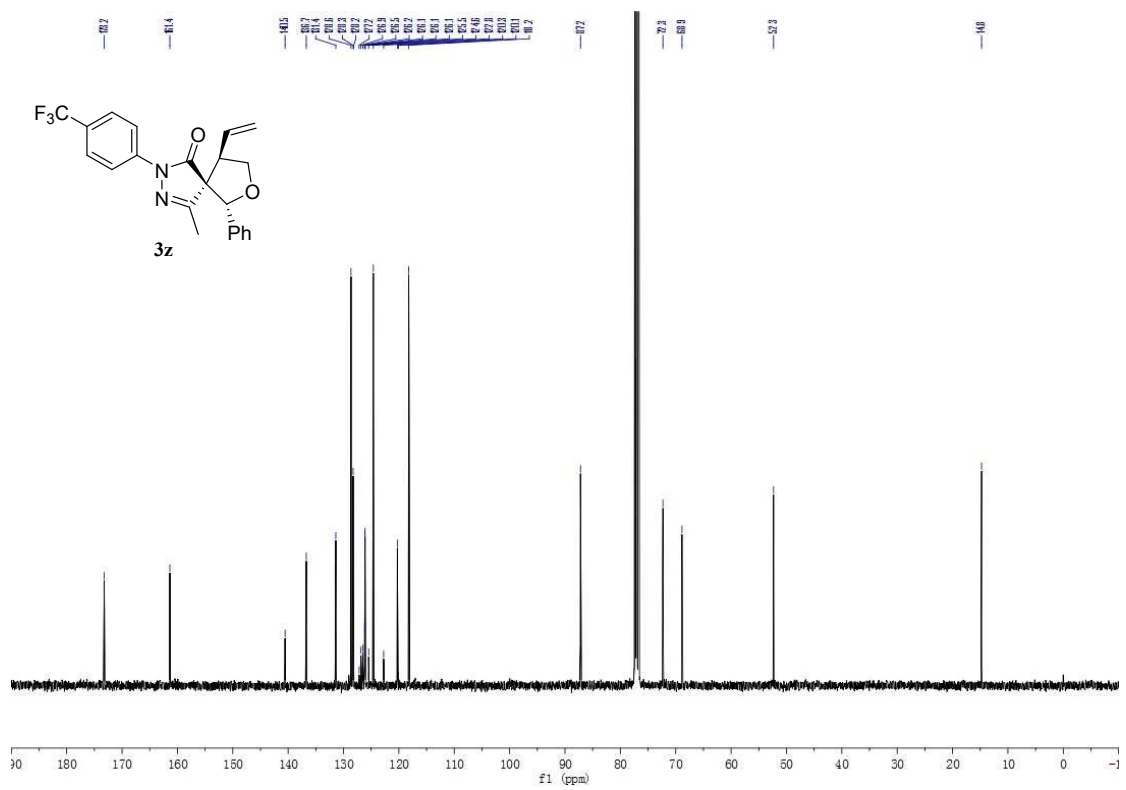
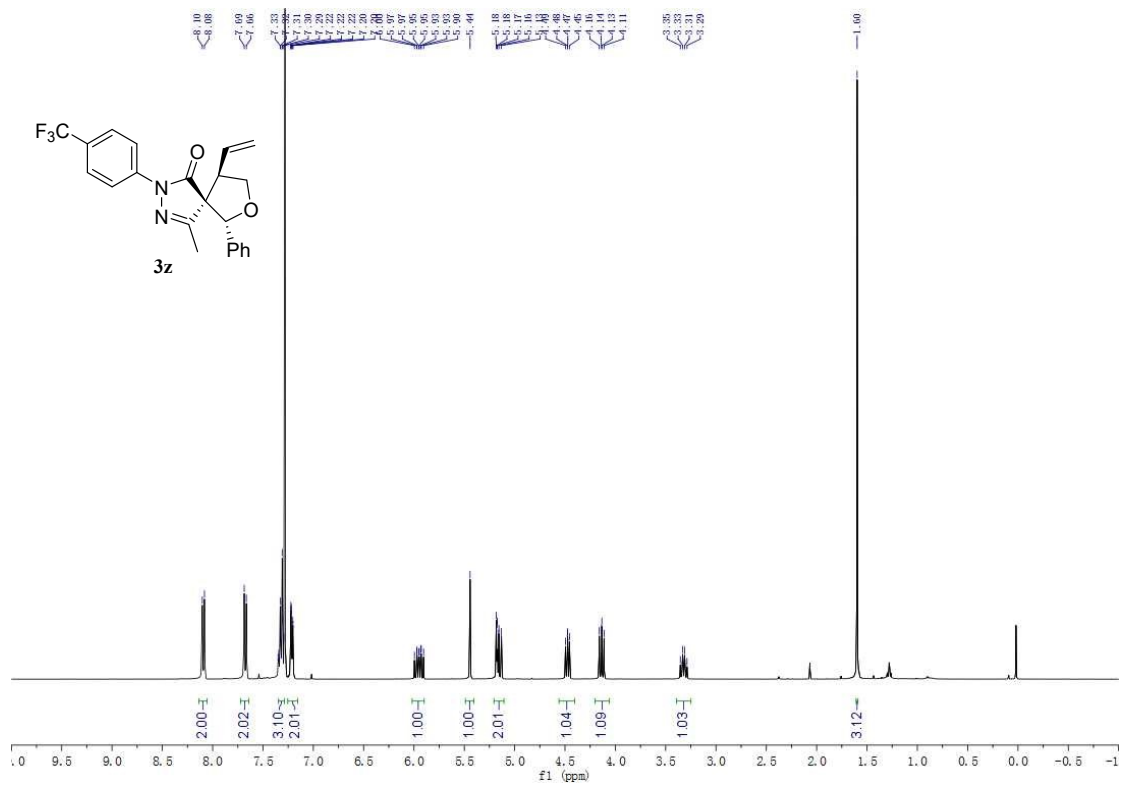


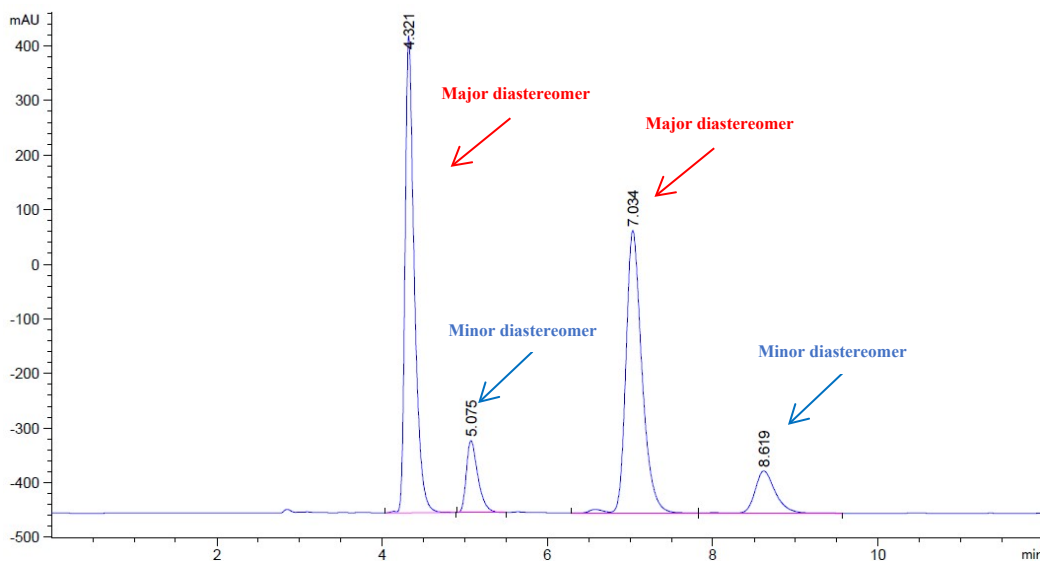


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.551	BB	0.1659	1.12888e4	1030.03174	38.4384
2	6.598	BV R	0.1977	3359.40308	252.82301	11.4388
3	9.714	BV R	0.3028	1.13226e4	567.31915	38.5536
4	12.727	BV R	0.4032	3397.67334	128.12959	11.5692

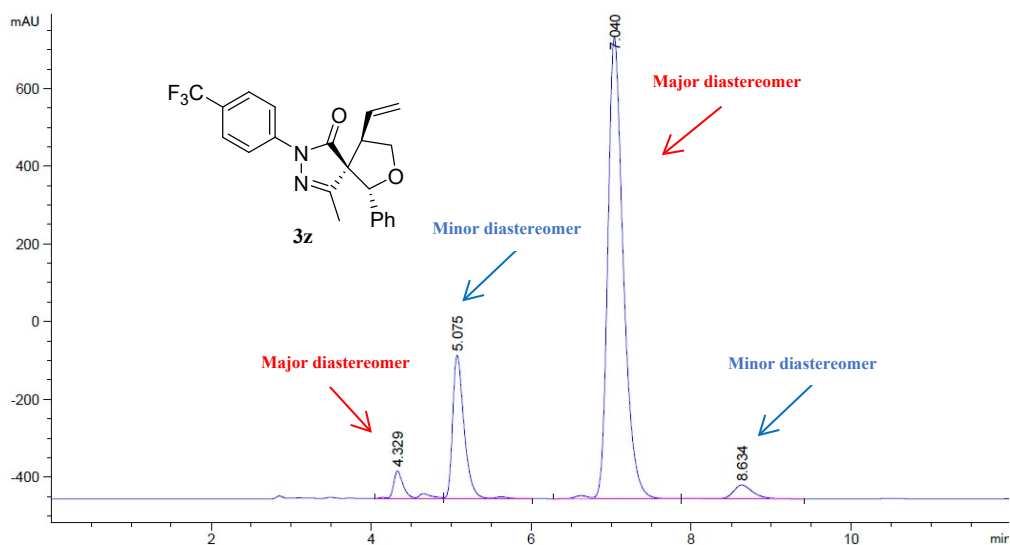


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.571	BV R	0.1711	596.71613	51.79629	2.4971
2	6.627	BV R	0.2018	6879.79932	511.78470	28.7907
3	9.772	BV R	0.3073	1.54481e4	766.03033	64.6476
4	12.797	BV R	0.4065	971.27191	36.47309	4.0646

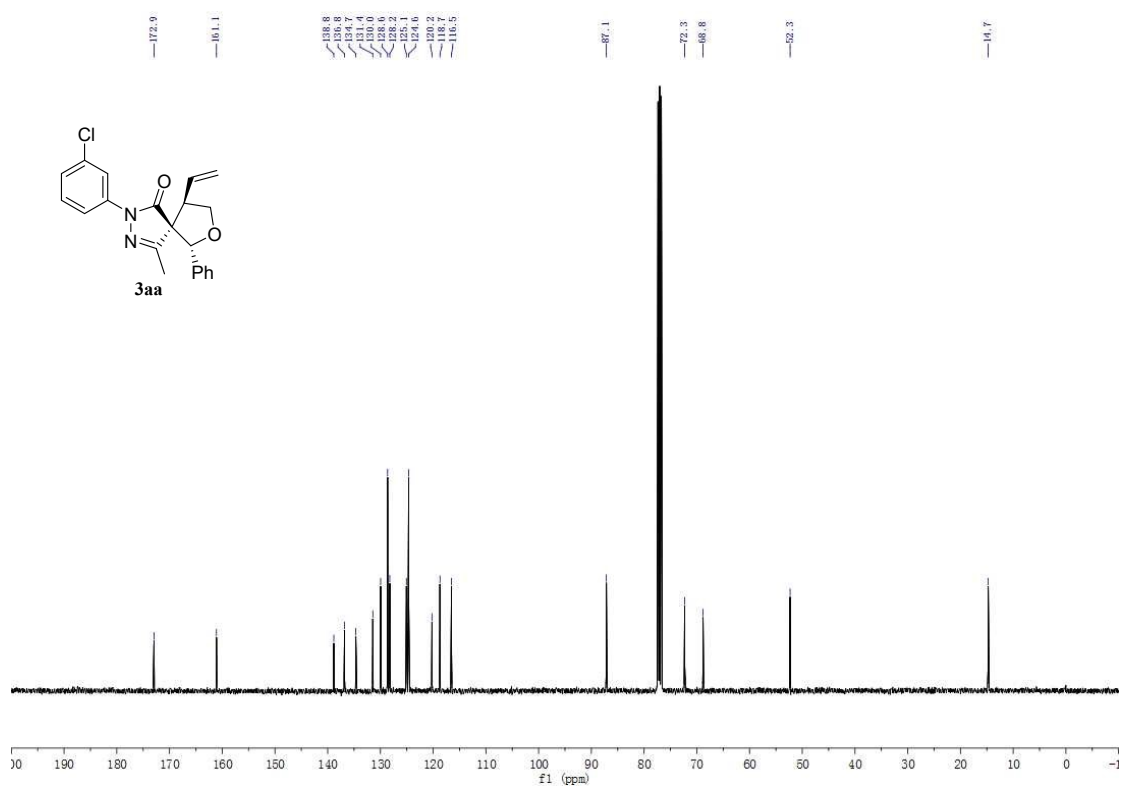
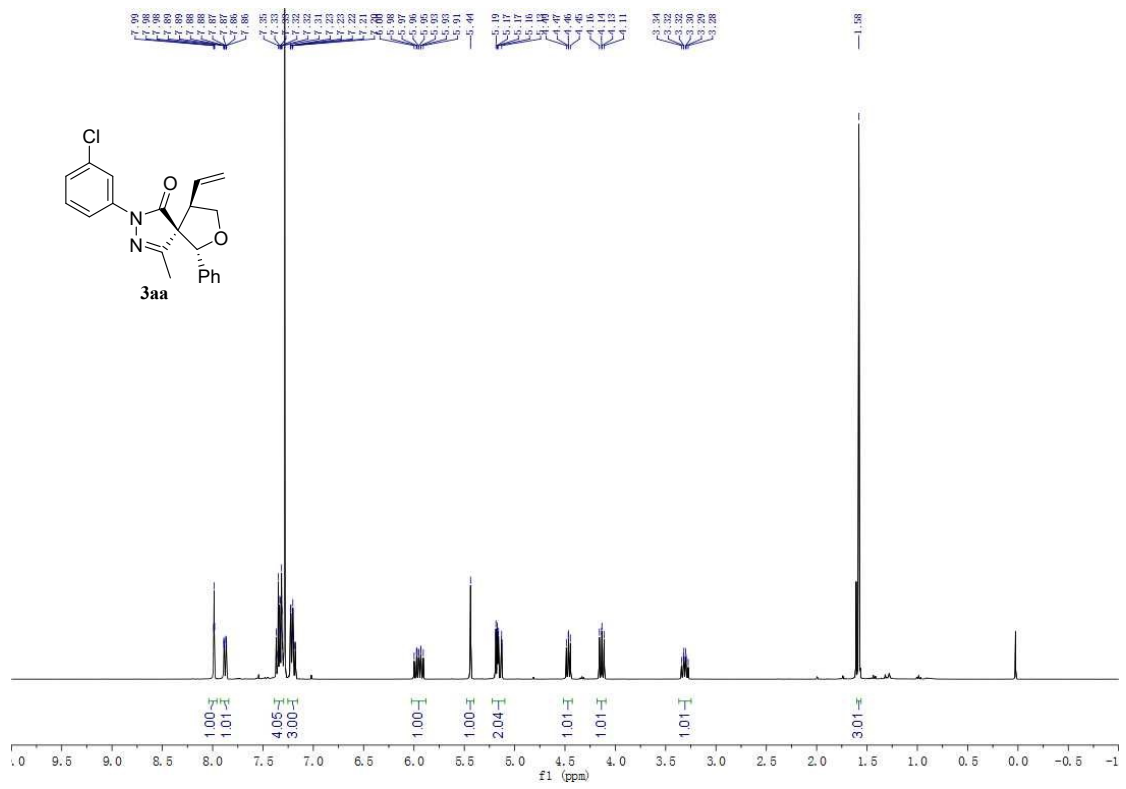


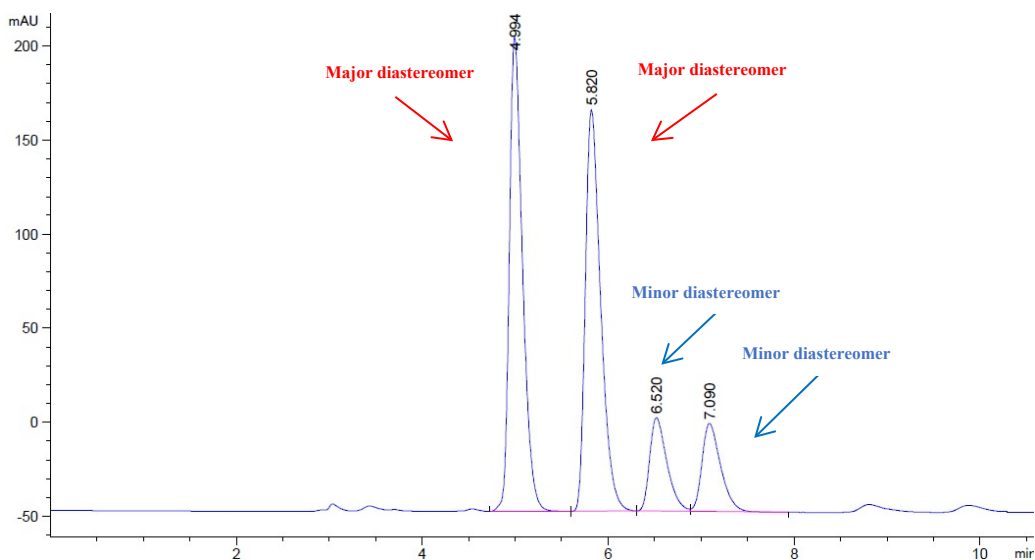


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.321	VB R	0.1162	6842.07178	874.00989	41.6687
2	5.075	BB	0.1474	1284.56775	132.16942	7.8231
3	7.034	VB R	0.2018	6988.04590	517.52673	42.5577
4	8.619	VB R	0.2548	1305.50085	77.37661	7.9506

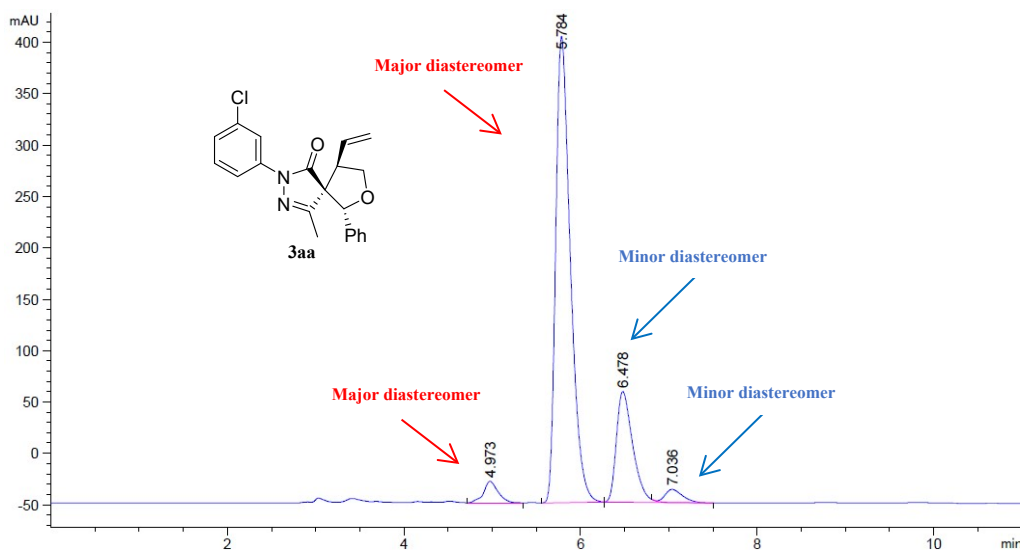


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.329	VV R	0.1203	727.81238	71.08894	3.4533
2	5.075	VV R	0.1489	3694.73047	369.75967	17.5308
3	7.040	VB R	0.2037	1.60572e4	1188.69604	76.1882
4	8.634	VB R	0.2541	595.96979	35.26865	2.8278

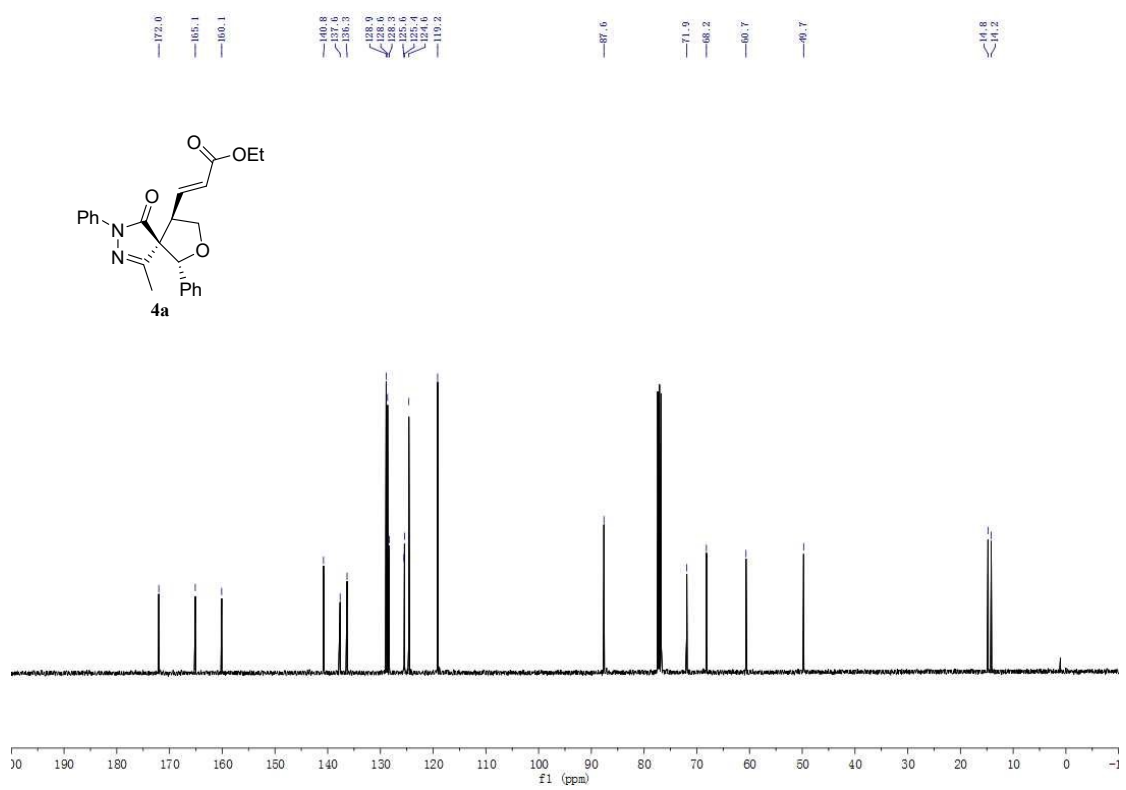
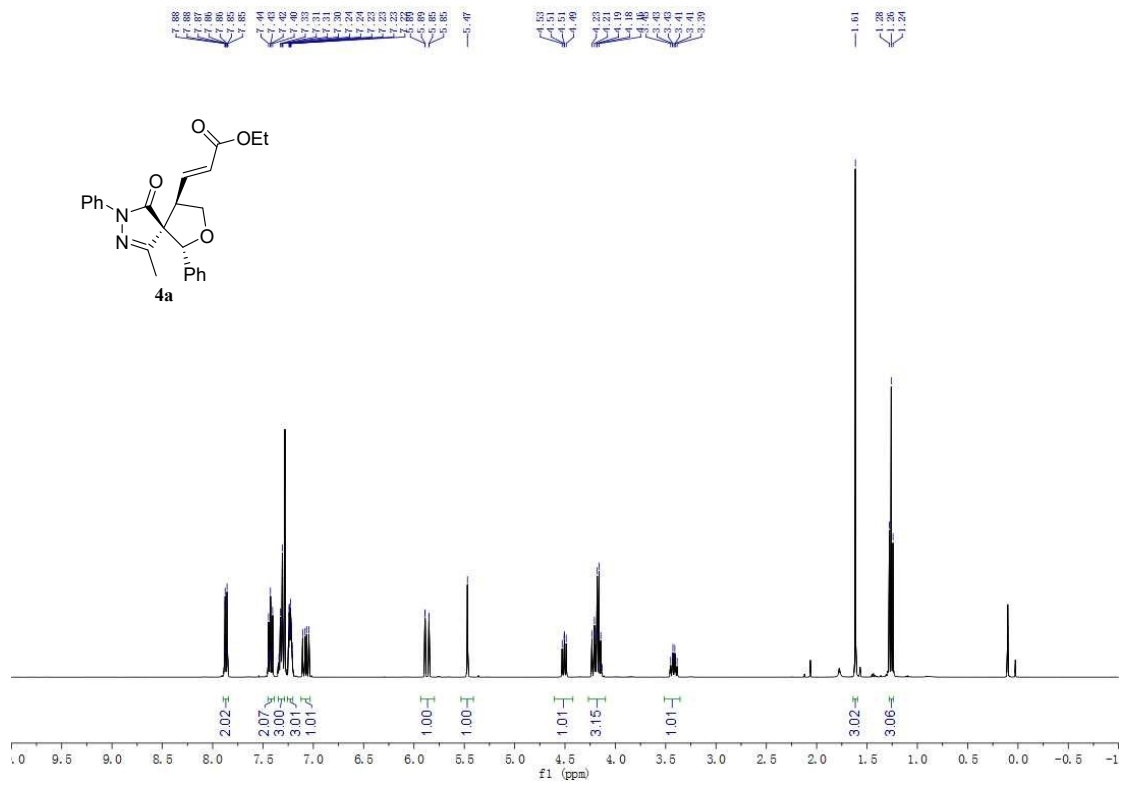




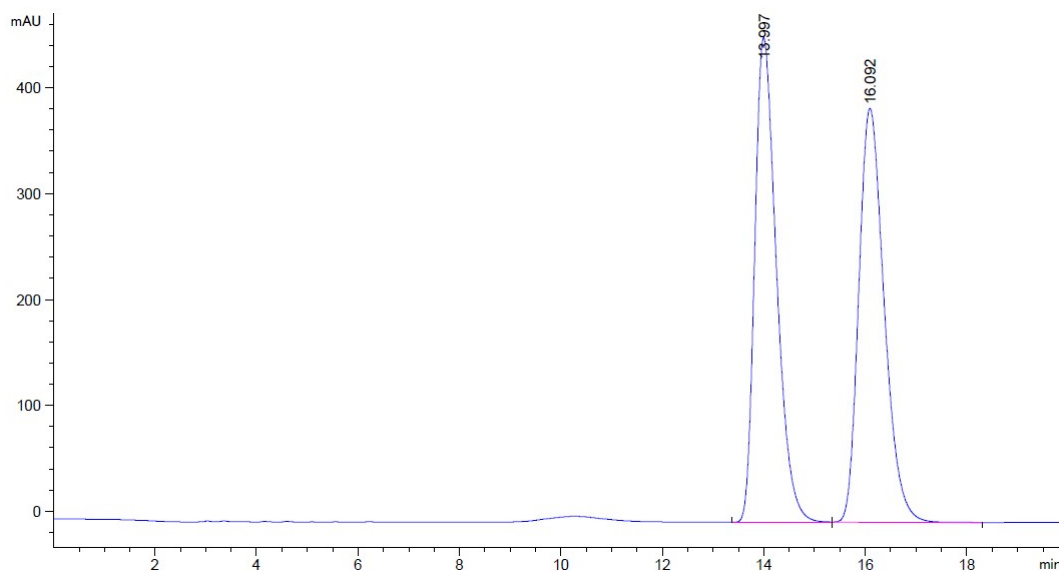
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.994	VB	0.1488	2481.94971	252.20412	39.8237
2	5.820	BB	0.1751	2452.52588	213.43100	39.3516
3	6.520	BV	0.1959	642.70502	49.68326	10.3124
4	7.090	VB	0.2108	655.15601	46.94535	10.5122



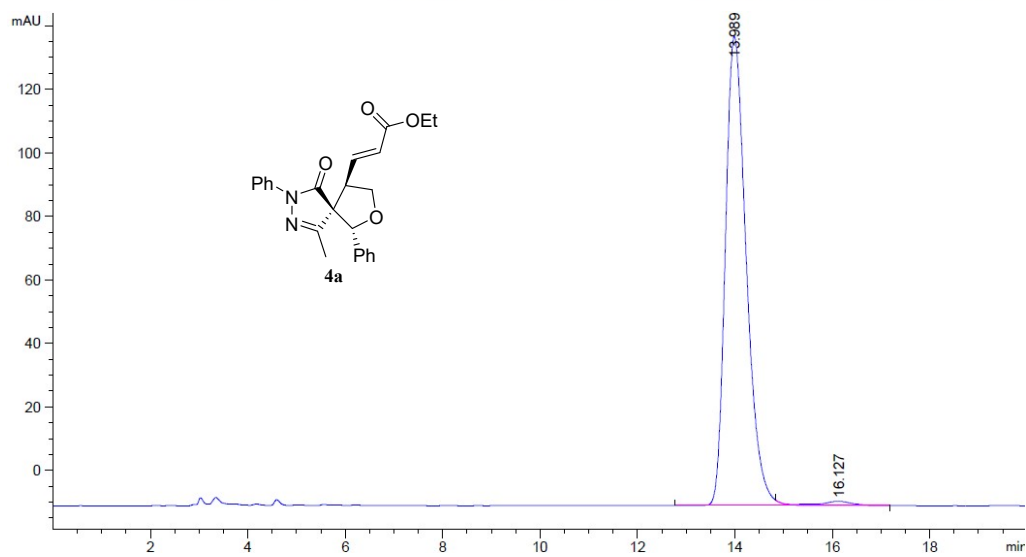
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.973	BB	0.1673	239.26764	20.94613	3.4041
2	5.784	BB	0.1746	5231.60205	453.61728	74.4299
3	6.478	BV R	0.1947	1382.15759	107.69213	19.6639
4	7.036	VB E	0.2088	175.87035	12.75713	2.5021



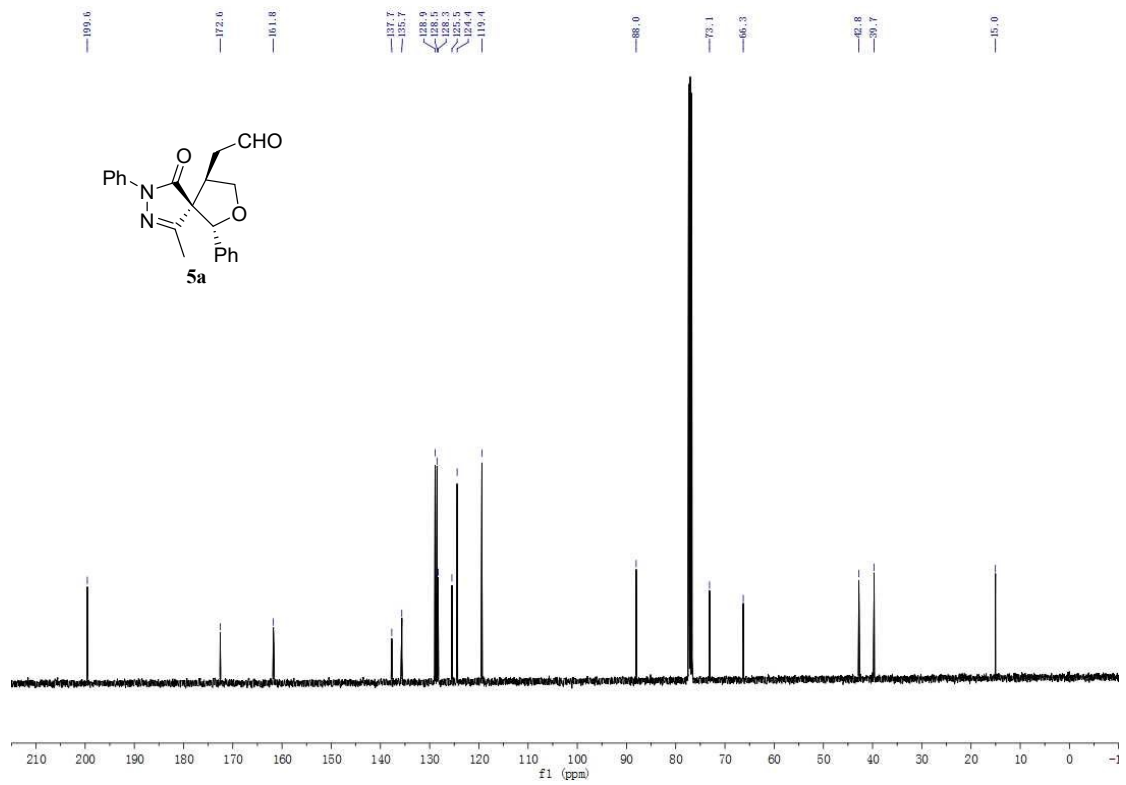
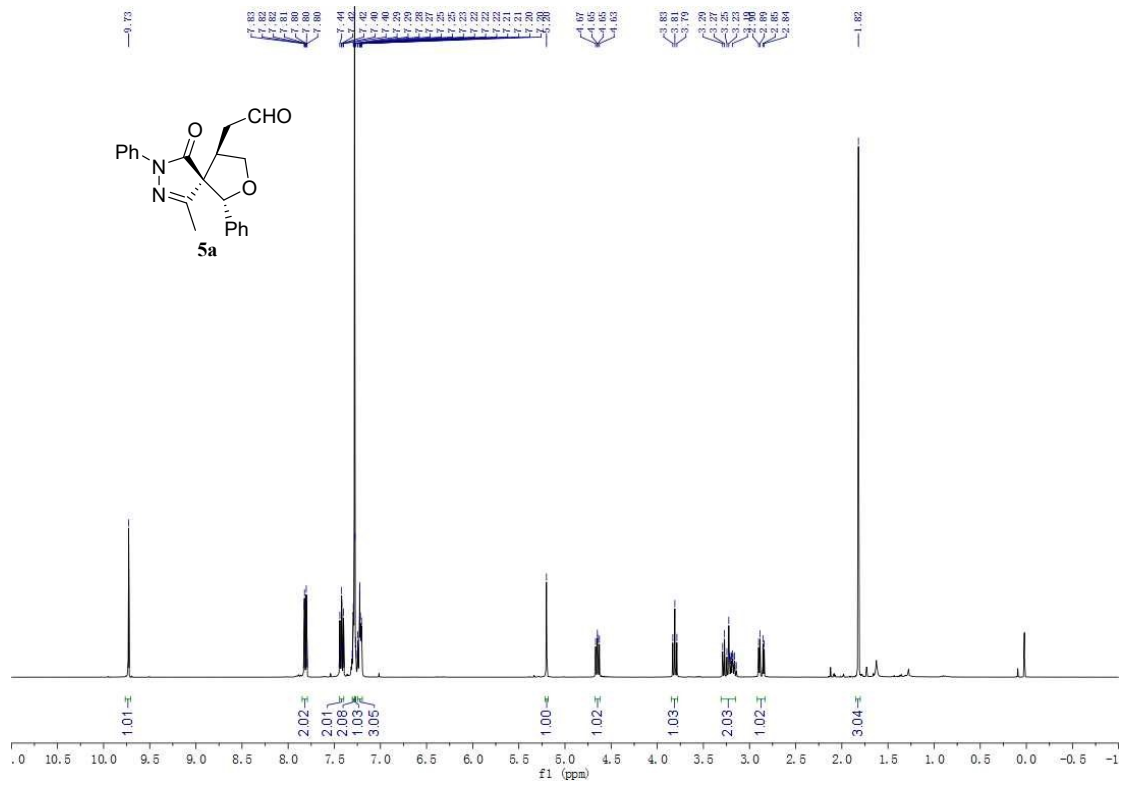


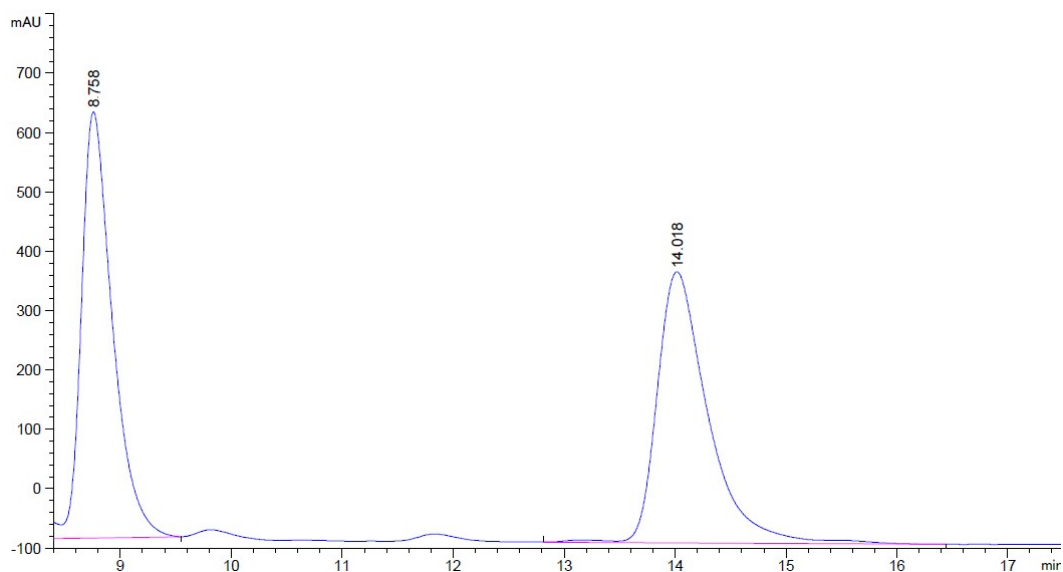


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.997	BB	0.4573	1.35937e4	457.98962	50.0463
2	16.092	BB	0.5369	1.35685e4	390.96564	49.9537

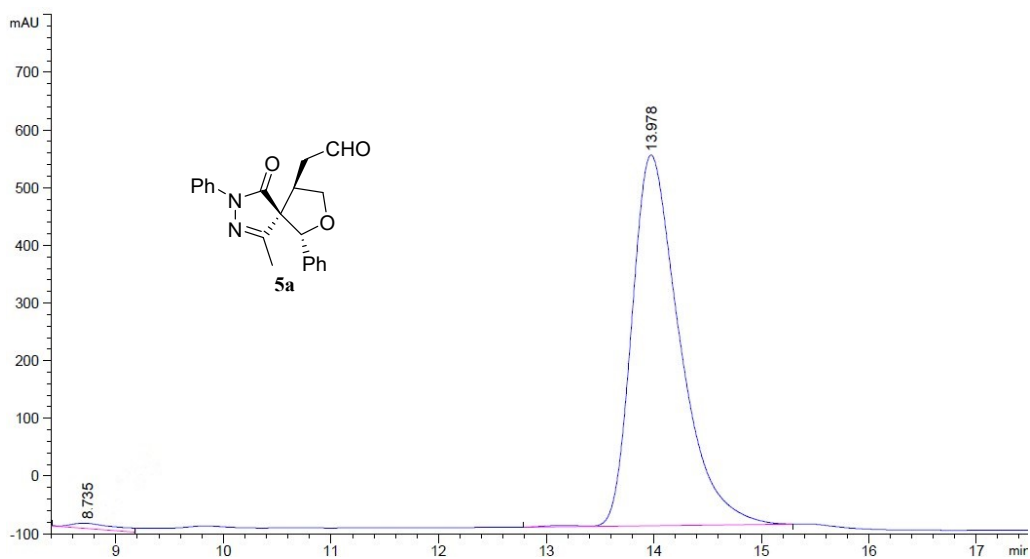


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.989	BV R	0.4589	4391.33350	147.68993	98.5639
2	16.127	VB E	0.6857	63.98387	1.33856	1.4361

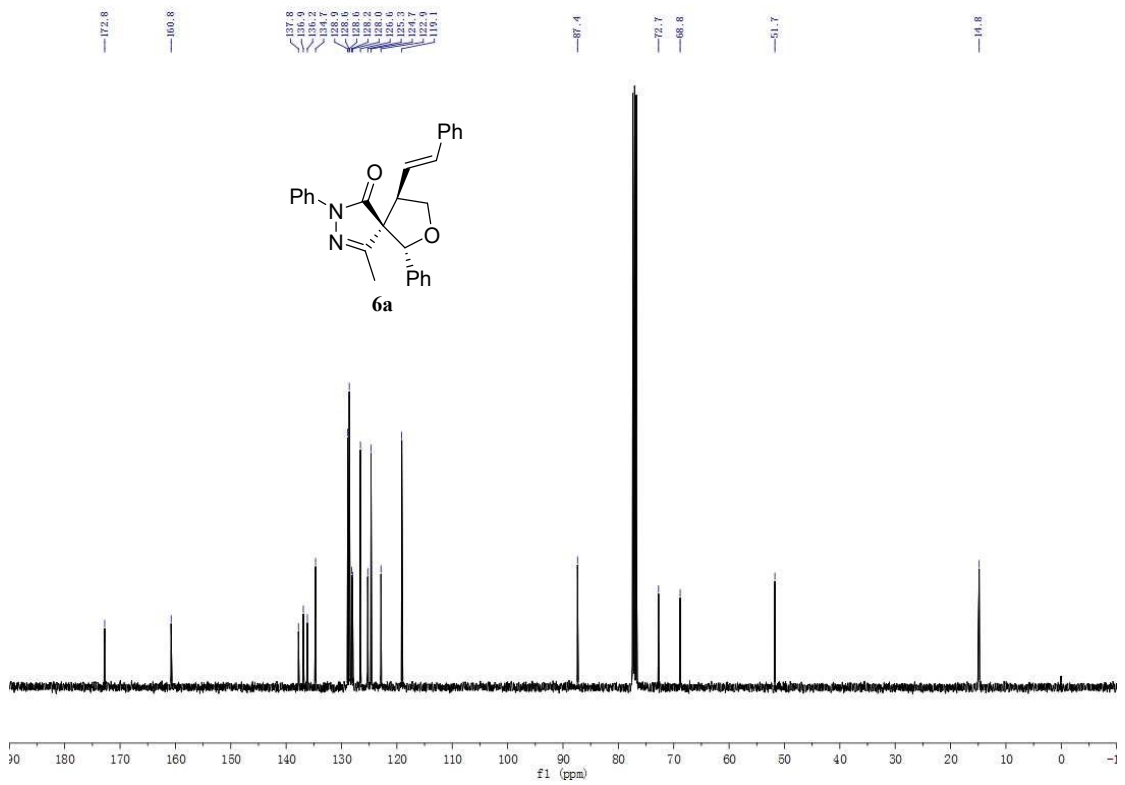
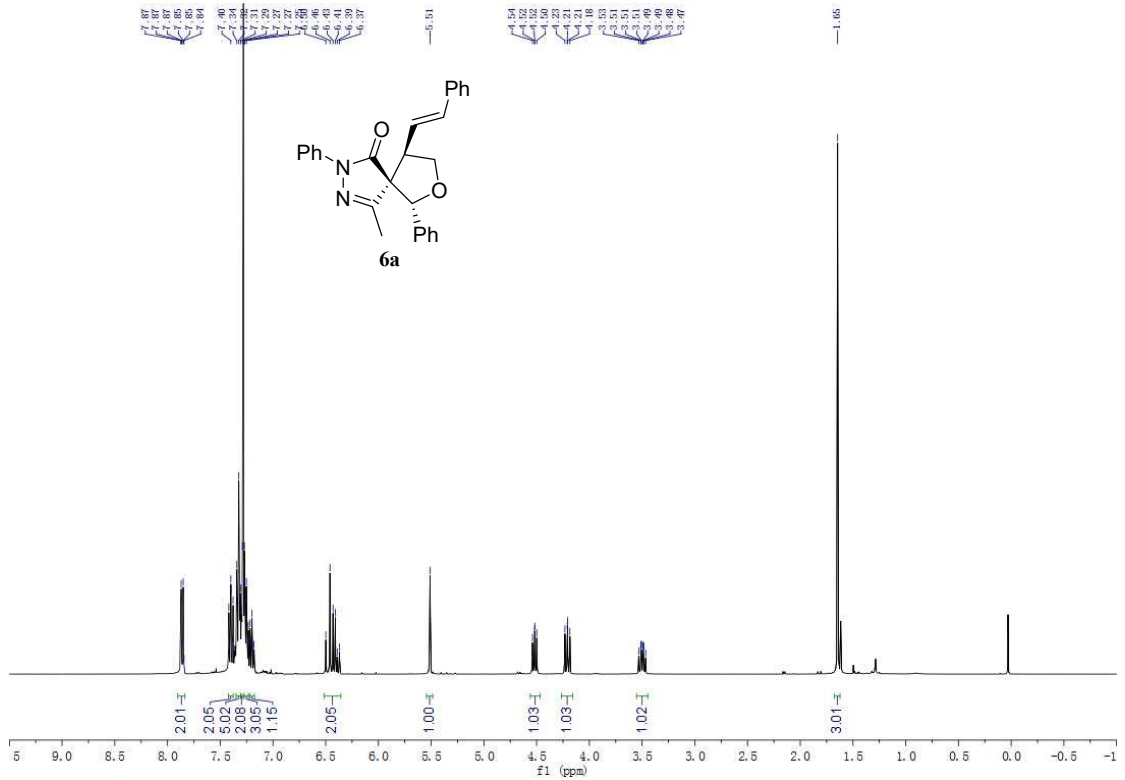


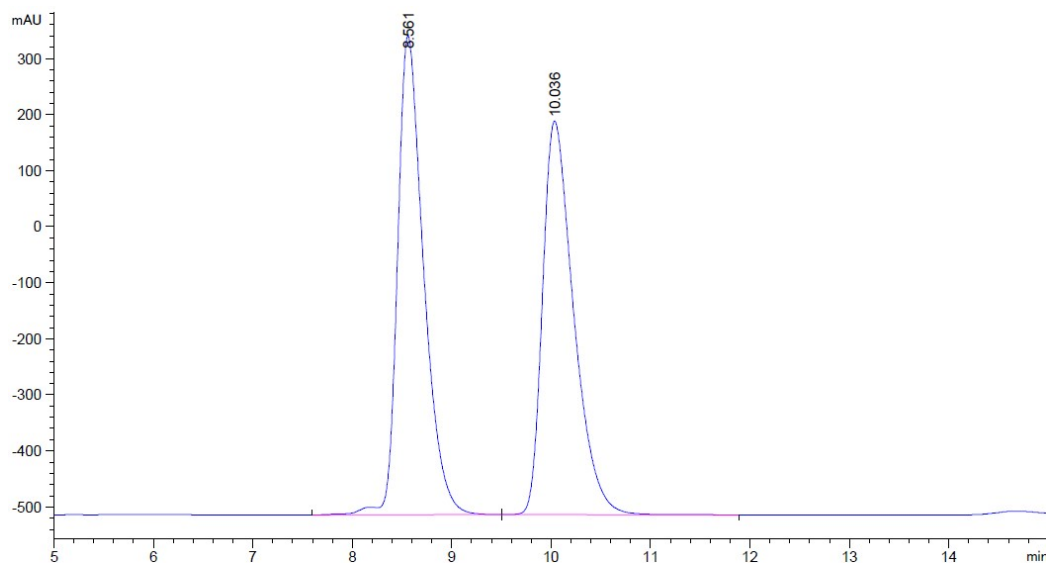


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.758	FM	0.3275	1.41071e4	717.99670	49.1596
2	14.018	VB R	0.4719	1.45894e4	456.79312	50.8404

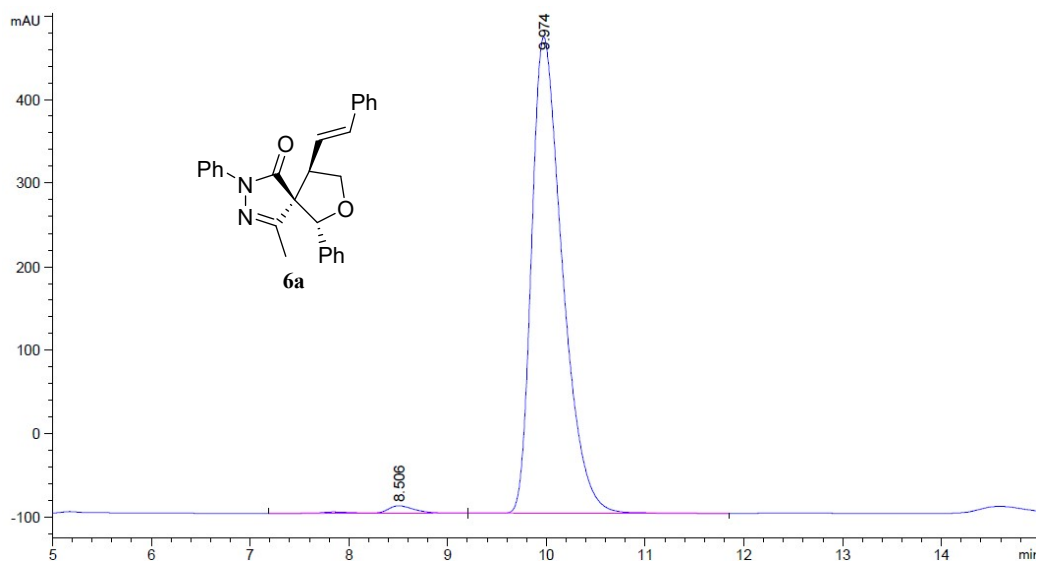


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.735	MM	0.5262	296.32031	9.38614	1.4737
2	13.978	VB R	0.4588	1.98114e4	642.40222	98.5263

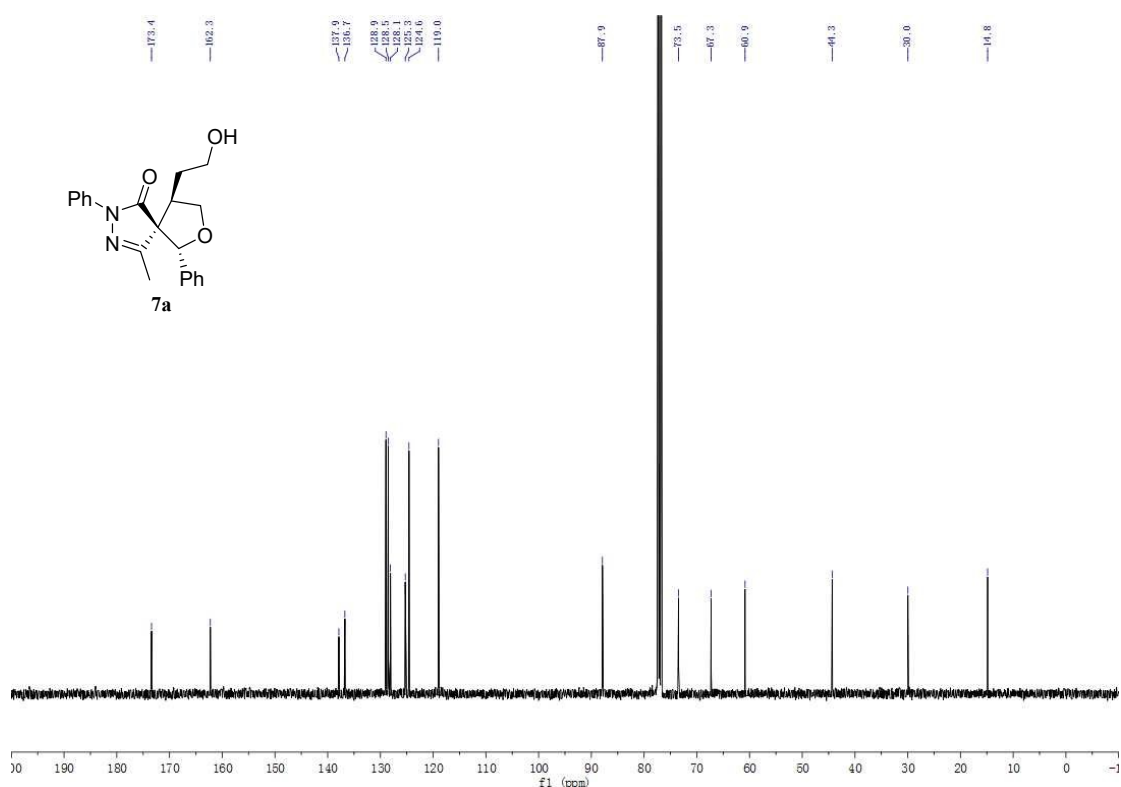
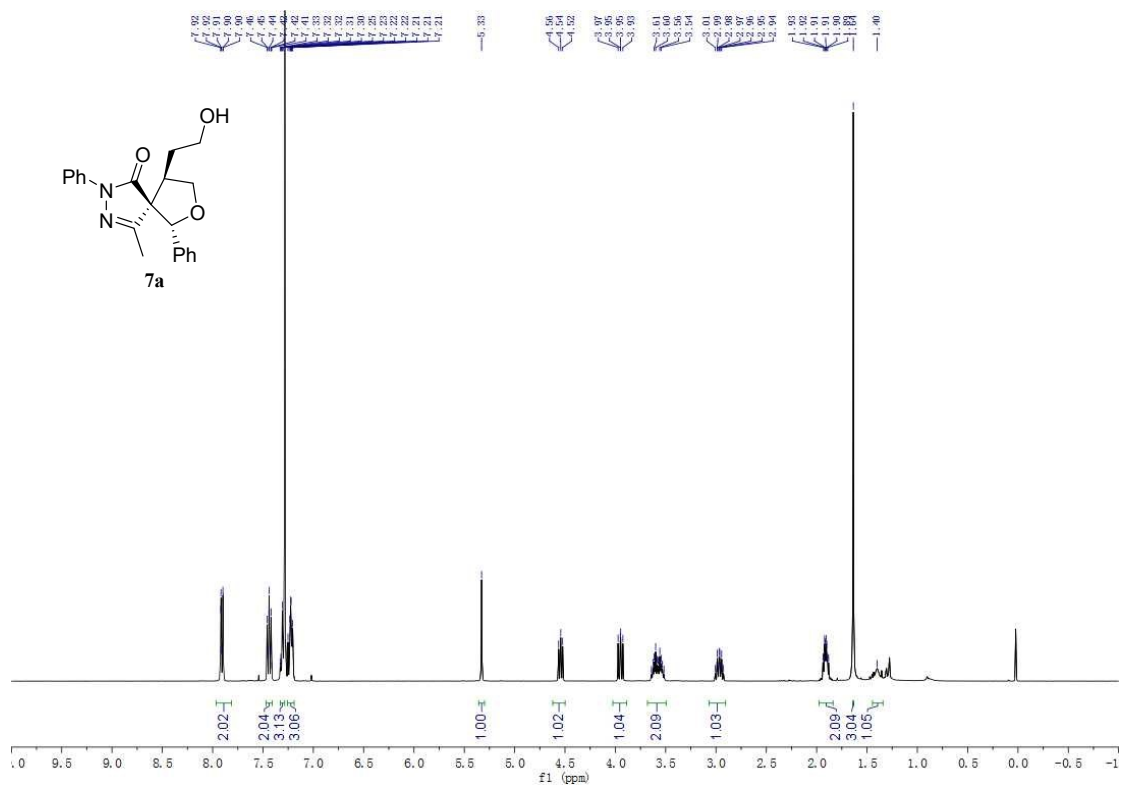


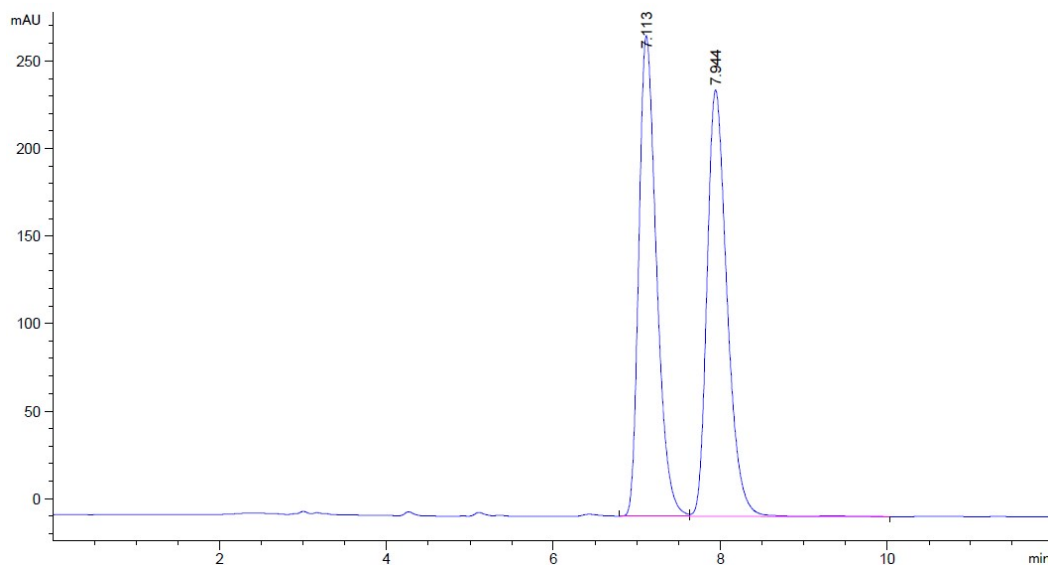


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.561	VB R	0.2746	1.56064e4	853.96558	50.6157
2	10.036	BB	0.3291	1.52267e4	701.83221	49.3843

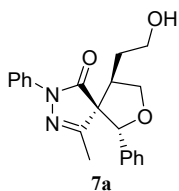
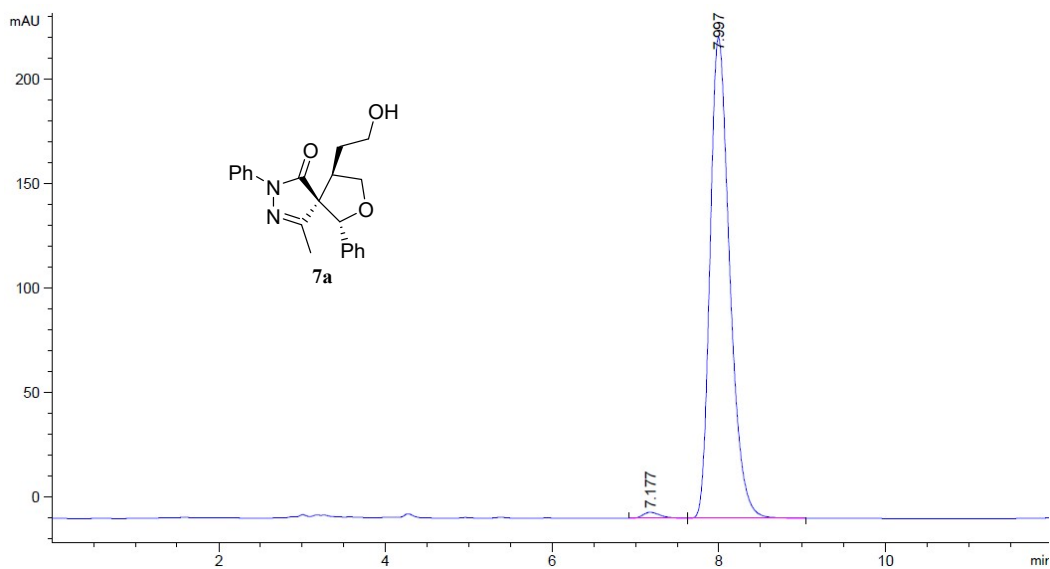


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.506	VB R	0.2768	198.36057	9.07093	1.5819
2	9.974	BB	0.3288	1.23412e4	569.57239	98.4181





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.113	BV	0.2237	4033.87573	274.01920	49.9269
2	7.944	VV R	0.2535	4045.69189	243.37596	50.0731



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.177	BV	0.2225	42.35038	2.89731	1.1115
2	7.997	VB	0.2508	3767.88745	230.35110	98.8885