

**Supporting Information**  
**for**  
**Organocatalytic cascade aza-Michael/hemiacetal reaction between disubstituted hydrazines and  $\alpha,\beta$ -unsaturated aldehydes: Highly diastereo- and enantioselective synthesis of pyrazolidine derivatives**

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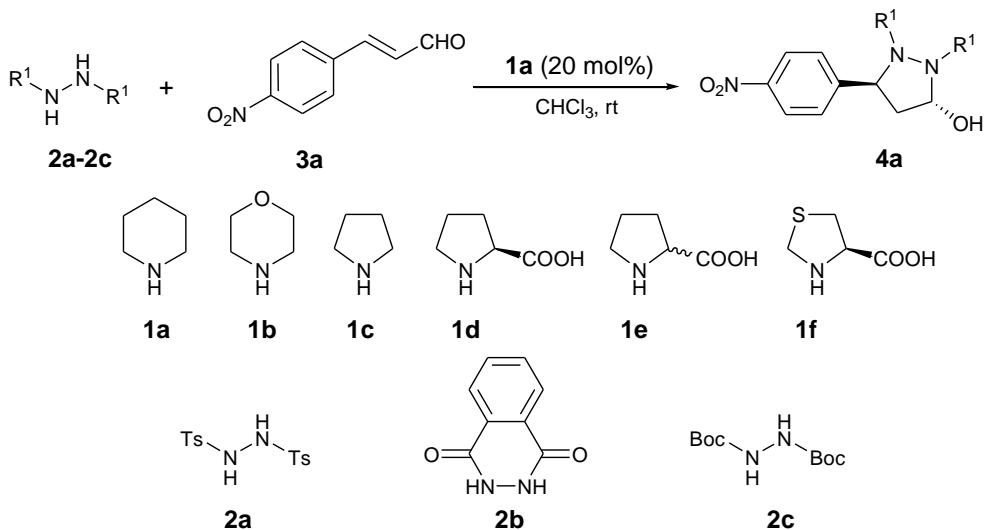
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## 1. General methods

All commercially available solvents and reagents were used as received. Purification of reaction products was carried out by flash chromatography using silica gel (0.03–0.04 mm). Analytical thin-layer chromatography was performed on silica-gel precoated glass plates (0.2 ± 0.03 mm thickness, GF-254, particle size 0.01–0.04 mm).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  or  $\text{DMSO}-d_6$  on a Varian Inova (400 MHz or 300 MHz and 100 MHz or 75 MHz, respectively) spectrometer. Chemical shifts ( $\delta$  ppm) are relative to the resonance of the deuterated solvent as the internal standard ( $\text{CDCl}_3$ ,  $\delta$  7.27 ppm,  $\text{DMSO}-d_6$ ,  $\delta$  2.50 ppm for proton NMR;  $\text{CDCl}_3$ ,  $\delta$  77.23 ppm,  $\text{DMSO}-d_6$ ,  $\delta$  39.51 ppm for carbon NMR).

## 2. Reaction optimization

**Table S1:** Effect of catalysts and solvents.



| Entry <sup>a</sup> | Catalyst  | Donor     | Additive | Solvent                 | dr <sup>b</sup> | Yield(%) <sup>c</sup> |
|--------------------|-----------|-----------|----------|-------------------------|-----------------|-----------------------|
| 1                  | <b>1a</b> | <b>2a</b> | —        | CHCl <sub>3</sub>       | —               | —                     |
| 2                  | <b>1a</b> | <b>2b</b> | —        | <b>CHCl<sub>3</sub></b> | —               | —                     |
| 3                  | <b>1a</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | >20:1           | 40                    |
| 4                  | —         | <b>2c</b> | —        | CHCl <sub>3</sub>       | —               | —                     |
| 5                  | <b>1b</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | —               | <20                   |
| 6                  | <b>1c</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | >20:1           | 68                    |
| 7                  | <b>1d</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | —               | <20                   |
| 8                  | <b>1e</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | —               | <20                   |
| 9                  | <b>1f</b> | <b>2c</b> | —        | CHCl <sub>3</sub>       | —               | <20                   |

<sup>a</sup>Reaction was conducted on 0.25 mmol scale in solvents (0.5 mL) at room temperature for 5 d, and the ratio of **2/3** is 1.2:1. <sup>b</sup>Determined by <sup>1</sup>H NMR. <sup>c</sup>Isolated yield.

### 3. Typical experimental procedure

Representative experimental procedure for the cascade aza-Michael/hemiacetal reaction of disubstituted hydrazines with  $\alpha,\beta$ -unsaturated aldehydes: To a stirred solution of catalyst **1c** or **1m** (20 mol %) in CH<sub>2</sub>Cl<sub>2</sub> or toluene (0.5 mL) was added  $\alpha,\beta$ -unsaturated aldehyde **3** (1.0 equiv 0.25 mmol) and disubstituted hydrazine **2** (1.2 equiv or 2.0 or 5.0 equiv and 0.3 mmol or 0.5 mmol or 1.25 mmol) at rt. The reaction mixture was vigorously stirred for 2–5 days. Then, the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate) to afford the corresponding products **4**. Yields and spectral and analytical data for compounds **4a–x** are as follows:

#### (–)-Di-*tert*-butyl 3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1,2-dicarboxylate (**4a**):

80% yield, >20/1 dr, 92% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min), *t*<sub>major</sub> = 7.219 min,

$t_{\text{minor}} = 6.013$  min;  $[\alpha]_D^{26} = -11.8$  ( $c$  0.38, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.6$  Hz, 2H), 7.55 (d,  $J = 8.6$  Hz, 2H), 5.92 (d,  $J = 4.7$  Hz, 1H), 5.52–5.39 (m, 1H), 3.40 (s, 1H), 2.71 (dd,  $J = 13.2, 8.4$  Hz, 1H), 2.13–2.03 (m, 1H), 1.53 (s, 9H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.27, 149.72, 147.21, 126.75, 124.01, 82.62, 82.56, 82.19, 61.66, 43.43, 28.33, 28.19; IR (KBr)  $\nu_{\text{max}}$ : 3354.8, 2980.4, 2934.2, 2854.2, 1728.7, 1705.9, 1600.2, 1518.9, 1456.0, 1367.7, 1345.9, 1311.6, 1243.1, 1145.0, 990.9, 853.5, 758.4  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z = 432.1724$  (calcd for  $\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_7+\text{Na}^+ = 432.1741$ ).

**(–)-Di-*tert*-butyl 3-hydroxy-5-(3-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4b):**  
 83% yield, >20/1 dr, 91% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 8.652$  min,  $t_{\text{minor}} = 5.858$  min;  $[\alpha]_D^{26} = -0.3$  ( $c$  0.61, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31 (s, 1H), 8.13 (d,  $J = 7.9$  Hz, 1H), 7.66 (d,  $J = 7.7$  Hz, 1H), 7.52 (t,  $J = 7.9$  Hz, 1H), 5.94 (d,  $J = 5.1$  Hz, 1H), 5.53–5.44 (m, 1H), 3.00 (s, 1H), 2.72 (dd,  $J = 13.3, 8.4$  Hz, 1H), 2.19–2.09 (m, 1H), 1.56 (s, 9H), 1.45 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.45, 148.70, 144.65, 132.31, 129.62, 122.36, 120.66, 82.79, 82.48, 82.09, 61.57, 43.62, 28.17; IR (KBr)  $\nu_{\text{max}}$ : 3432.4, 3077.2, 2979.6, 2934.8, 2873.1, 1711.0, 1681.4, 1535.4, 1479.5, 1455.1, 1392.7, 1367.5, 1252.3, 1170.0, 1303.9, 1278.7, 1144.2, 870.0, 807.8, 736.2  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z = 432.1742$  (calcd for  $\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_7+\text{Na}^+ = 432.1741$ ).

**(–)-Di-*tert*-butyl 3-(4-cyanophenyl)-5-hydroxypyrazolidine-1,2-dicarboxylate (4c):** 86% yield, >20/1 dr, 89% ee. The enantiomeric ratio was determined by HPLC

on Chiralpak OD-H column (5% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 12.326$  min,  $t_{\text{minor}} = 9.171$  min;  $[\alpha]_D^{26} = -8.3$  ( $c$  0.36, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63 (d,  $J = 8.0$  Hz, 2H), 7.49 (d,  $J = 8.0$  Hz, 2H), 5.90 (d,  $J = 4.4$  Hz, 1H), 5.50–5.33 (m, 1H), 3.23 (s, 1H), 2.68 (dd,  $J = 13.0, 8.6$  Hz, 1H), 2.20–1.95 (m, 1H), 1.51 (s, 9H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.37, 147.73, 132.56, 126.70, 118.87, 111.15, 82.66, 82.48, 82.08, 61.85, 43.41, 28.35, 28.22; IR (KBr)  $\nu_{\text{max}}$ : 3436.0, 2978.7, 2934.1, 2228.7, 1706.9, 1610.0, 1506.1, 1457.6, 1392.8, 1368.6, 1251.8, 1156.0, 1091.5, 850.2, 806.0, 760.4  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z = 422.1255$  (calcd for  $\text{C}_{20}\text{H}_{27}\text{N}_3\text{O}_5+\text{Na}^+ = 422.1242$ ).

**(–)-Di-*tert*-butyl 3-(4-chlorophenyl)-5-hydroxypyrazolidine-1,2-dicarboxylate (4d):** 61% yield, >20/1 dr, 74% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 5.676$  min,  $t_{\text{minor}} = 4.273$  min;  $[\alpha]_D^{26} = -7.1$  ( $c$  0.56, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32–7.28 (m, 4H), 5.89 (d,  $J = 5.2$  Hz, 1H), 5.41–5.29 (m, 1H), 3.24 (s, 1H), 2.62 (dd,  $J = 13.2, 8.3$  Hz, 1H), 2.19–2.07 (m, 1H), 1.50 (s, 9H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.47, 140.62, 132.80, 128.59, 127.28, 82.59, 82.05, 81.64, 61.46, 43.43, 28.23, 28.15; IR (KBr)  $\nu_{\text{max}}$ : 3406.6, 2980.1, 2935.6, 1720.5, 1591.3, 1494.0, 1454.8, 1367.3, 1332.9, 1245.4, 1184.6, 1088.6, 855.5, 823.7  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 421.1500$  (calcd for  $\text{C}_{19}\text{H}_{27}\text{ClN}_2\text{O}_5+\text{Na}^+ = 421.1501$ ).

**(–)-Di-*tert*-butyl 3-(4-bromophenyl)-5-hydroxypyrazolidine-1,2-dicarboxylate (4e):** 62% yield, >20/1 dr, 77% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 5.605$  min,

$t_{\text{minor}} = 4.373 \text{ min}$ ;  $[\alpha]_D^{26} = -5.0$  ( $c$  0.54, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (d,  $J = 8.2$  Hz, 2H), 7.24 (d,  $J = 8.1$  Hz, 2H), 5.89 (d,  $J = 4.7$  Hz, 1H), 5.39–5.27 (m, 1H), 3.33 (s, 1H), 2.62 (dd,  $J = 13.2, 8.3$  Hz, 1H), 2.19–2.04 (m, 1H), 1.50 (s, 9H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.41, 141.13, 131.64, 127.69, 121.01, 82.68, 82.16, 81.75, 61.57, 43.36, 28.32, 28.24; IR (KBr)  $\nu_{\text{max}}$ : 3406.4, 2978.9, 2933.1, 1720.2, 1590.6, 1491.0, 1454.0, 1244.2, 1141.9, 1010.3, 855.3  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 465.0994$  (calcd for  $\text{C}_{19}\text{H}_{27}\text{BrN}_2\text{O}_5 + \text{Na}^+ = 465.0996$ ).

**(–)-Diisopropyl 3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4h):**  
 60% yield, >20/1 dr, 72% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 8.499$  min,  $t_{\text{minor}} = 9.345$  min;  $[\alpha]_D^{26} = -10.0$  ( $c$  0.36, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.6$  Hz, 2H), 7.55 (d,  $J = 8.6$  Hz, 2H), 5.98 (d,  $J = 4.6$  Hz, 1H), 5.56–5.48 (m, 1H), 5.10–4.93 (m, 2H), 3.33 (s, 1H), 2.75 (dd,  $J = 13.2, 8.5$  Hz, 1H), 2.18–2.07 (m, 1H), 1.32 (d,  $J = 6.2$  Hz, 6H), 1.27 (d,  $J = 6.2$  Hz, 3H), 1.21 (d,  $J = 6.0$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.93, 149.16, 147.22, 126.76, 123.92, 82.83, 70.88, 70.82, 61.80, 43.25, 22.06, 21.98, 21.96, 21.87; IR (KBr)  $\nu_{\text{max}}$ : 3364.8, 2990.1, 2930.4, 1745.6, 1699.4, 1597.9, 1518.8, 1345.9, 1170.1, 1000.2, 853.5  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 404.1428$  (calcd for  $\text{C}_{19}\text{H}_{27}\text{BrN}_2\text{O}_5 + \text{Na}^+ = 404.1428$ ).

**(±)-Diisopropyl 3-hydroxy-5-(3-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4i):**  
 82% yield, >20/1 dr.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.27 (s, 1H), 8.14 (d,  $J = 8.1$  Hz, 1H), 7.69 (d,  $J = 7.7$  Hz, 1H), 7.52 (t,  $J = 7.9$  Hz, 1H), 5.99 (d,  $J = 4.4$  Hz, 1H), 5.59–5.48 (m, 1H), 5.09–4.94 (m, 2H), 3.52 (s, 1H), 2.76 (dd,  $J = 13.2, 8.4$  Hz, 1H),

2.22–2.11 (m, 1H), 1.37–1.31 (m, 6H), 1.28 (d,  $J$  = 6.2 Hz, 3H), 1.22 (d,  $J$  = 5.8 Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.56, 155.14, 148.68, 144.08, 132.32, 129.74, 122.54, 120.89, 82.91, 71.19, 70.96, 61.77, 43.37, 22.01; IR (KBr)  $\nu_{\text{max}}$ : 3511.5, 3265.9, 3106.8, 2929.3, 1587.9, 1479.3, 1383.5, 1332.8, 1222.8, 1146.8, 994.3, 918.2, 815.5, 744.9, 699.3, 635.6  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z$  = 404.1427 (calcd for  $\text{C}_{17}\text{H}_{23}\text{N}_3\text{O}_7+\text{Na}^+$  = 404.1428).

**( $\pm$ )-Dibenzyl 3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4j):**  
 90% yield, >20/1 dr.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J$  = 8.8 Hz, 2H), 7.46–7.18 (m, 12H), 6.00 (d,  $J$  = 4.8 Hz, 1H), 5.52 (t,  $J$  = 7.8 Hz, 1H), 5.32 (d,  $J$  = 12.0 Hz, 1H), 5.18 (s, 2H), 5.10 (d,  $J$  = 12.0 Hz, 1H), 3.51 (s, 1H), 2.72 (dd,  $J$  = 13.0, 9.0 Hz, 1H), 2.20–2.04 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) 157.64, 155.22, 148.40, 147.24, 135.61, 135.34, 128.76, 128.56, 128.44, 128.29, 127.60, 126.81, 124.00, 83.16, 68.62, 68.50, 62.12, 43.15. IR (film)  $\nu_{\text{max}}$ : 3437.2, 3112.6, 3066.6, 3033.5, 2954.1, 1712.2, 1601.7, 1521.9, 1455.8, 1395.9, 1306.4, 1215.2, 1156.6, 1079.7, 851.7  $\text{cm}^{-1}$ , HRMS (EI):  $m/z$  = 478.1609 (calcd for  $\text{C}_{25}\text{H}_{24}\text{N}_3\text{O}_7+\text{Na}^+$  = 478.1609).

**( $\pm$ )-Dibenzyl 3-hydroxy-5-(3-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4k):**  
 76% yield, >20/1 dr.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (s, 1H), 8.09 (d,  $J$  = 8.1 Hz, 1H), 7.61 (d,  $J$  = 7.5 Hz, 1H), 7.39 (t,  $J$  = 8.0 Hz, 1H), 7.36–7.19 (m, 10H), 6.01 (d,  $J$  = 4.2 Hz, 1H), 5.55 (t,  $J$  = 7.6 Hz, 1H), 5.29–5.11 (m, 4H), 3.20 (s, 1H), 2.74 (dd,  $J$  = 13.2, 8.3 Hz, 1H), 2.22–2.12 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.76, 155.31, 148.59, 143.36, 135.63, 135.45, 132.19, 129.88, 128.73, 128.62, 128.60, 128.37, 128.33, 127.69, 122.64, 121.17, 83.24, 68.72, 68.61, 62.09, 43.21.; IR (film)

$\nu_{\text{max}}$ : 3436.9, 2989.7, 2949.3, 1693.4, 1584.5, 1529.2, 1455.7, 1343.8, 1303.8, 1097.0, 865.0, 696.0  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 478.1611$  (calcd for  $\text{C}_{25}\text{H}_{24}\text{N}_3\text{O}_7+\text{Na}^+ = 478.1609$ ).

**( $\pm$ )-Dibenzyl 3-hydroxy-5-(4-methoxyphenyl)pyrazolidine-1,2-dicarboxylate**

**(4l):** 52% yield,  $>20/1$  dr.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36–7.20 (m, 10H), 7.16 (d,  $J = 8.5$  Hz, 2H), 6.75 (d,  $J = 8.5$  Hz, 2H), 6.01–5.93 (m, 1H), 5.43(t,  $J = 7.2$  Hz, 1H), 5.26 (d,  $J = 12.3$  Hz, 1H), 5.17 (s, 2H), 5.09 (d,  $J = 12.2$  Hz, 1H), 3.76 (s, 3H), 3.66 (s, 1H), 2.57 (dd,  $J = 13.1, 8.3$  Hz, 1H), 2.28–2.17 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  158.96, 157.88, 155.44, 136.04, 135.75, 132.88, 128.64, 128.51, 128.37, 128.23, 128.07, 127.56, 127.28, 114.08, 83.33, 68.26, 68.15, 62.21, 55.38, 43.08; IR (film)  $\nu_{\text{max}}$ : 3440.6, 3033.0, 2955.6, 2836.8, 1711.9, 1612.2, 1514.2, 1455.6, 1396.2, 1304.3, 1247.6, 1029.2, 829.4  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 485.1683$  (calcd for  $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_6+\text{Na}^+ = 485.1683$ ).

**( $\pm$ )-Diethyl 3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1,2-dicarboxylate (4m):**

77% yield,  $>20/1$  dr.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (d,  $J = 8.7$  Hz, 2H), 7.55 (d,  $J = 8.6$  Hz, 2H), 5.98 (d,  $J = 5.2$  Hz, 1H), 5.53 (t,  $J = 7.9$  Hz, 1H), 4.34–4.16 (m, 4H), 3.01 (s, 1H), 2.76 (ddd,  $J = 13.3, 8.4, 1.1$  Hz, 1H), 2.20–2.10 (m, 1H), 1.33 (t,  $J = 7.1$  Hz, 3H), 1.25 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.94, 155.30, 148.93, 147.37, 126.84, 124.13, 82.97, 63.24, 63.12, 62.08, 43.39, 14.63, 14.49; IR (film)  $\nu_{\text{max}}$ : 3434.7, 2983.1, 2937.4, 1712.1, 1601.6, 1522.1, 1468.1, 1347.4, 1224.9, 1173.4, 1013.1, 853.4  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 376.1116$  (calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_7+\text{Na}^+ = 376.1115$ ).

**(+)-*tert*-Butyl 3-hydroxy-5-(4-nitrophenyl)-2-phenylpyrazolidine-1-carboxylate**

**(4n):** 58% yield, >20/1 dr, 88% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 6.570$  min,  $t_{\text{minor}} = 5.722$  min;  $[\alpha]_D^{26} = +40.6$  ( $c$  0.48, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (d,  $J = 8.4$  Hz, 2H), 7.49 (d,  $J = 8.4$  Hz, 2H), 7.31 (t,  $J = 7.8$  Hz, 2H), 6.98–7.07 (m, 3H), 5.69 (d,  $J = 3.6$  Hz, 1H), 5.35 (dd,  $J = 10.0, 7.6$  Hz, 1H), 3.51 (s, 1H), 2.68 (dd,  $J = 13.0, 7.4$  Hz, 1H), 1.97–2.12 (m, 1H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  156.24, 150.23, 147.77, 146.54, 128.84, 128.07, 123.49, 120.63, 114.99, 87.81, 80.44, 61.38, 41.98, 27.78; IR (KBr)  $\nu_{\text{max}}$ : 3402.3, 2976.6, 1703.1, 1598.6, 1524.9, 1489.7, 1428.4, 1347.0, 1228.2, 1142.2, 989.4, 848.1, 752.1, 695.5  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 408.1543$  (calcd for  $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_5+\text{Na}^+ = 408.1530$ ).

**(−)-*tert*-Butyl 5-hydroxy-3-(4-nitrophenyl)-2-phenylpyrazolidine-1-carboxylate**

**(4n'): 32% yield, >20/1 dr, 55% ee.** The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 7.745$  min,  $t_{\text{minor}} = 8.266$  min;  $[\alpha]_D^{26} = -3.7$  ( $c$  0.41, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J = 8.8$  Hz, 2H), 7.71 (d,  $J = 8.4$  Hz, 2H), 7.25–7.20 (m, 2H), 6.95 (t,  $J = 7.6$  Hz, 1H), 6.89 (d,  $J = 8.0$  Hz, 2H), 5.92 (m, 1H), 5.07 (t,  $J = 7.0$  Hz, 1H), 2.86 (s, 1H), 2.74 (m, 1H), 2.28 (m, 1H), 1.49 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  160.29, 151.24, 151.00, 146.75, 128.46, 127.08, 123.96, 119.75, 113.50, 82.23, 80.71, 66.49, 44.13, 27.91; IR (KBr)  $\nu_{\text{max}}$ : 3416.4, 3070.8, 2979.1, 2941.0, 1686.2, 1595.9, 1520.7, 1490.9, 1454.3, 1435.7, 1370.0, 1261.3, 1147.5, 1079.9, 1011.7, 826.2, 763.6, 715.7  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 386.1718$  (calcd for  $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_5+\text{H}^+ = 386.1710$ ).

**(+)-*tert*-Butyl 2-(4-chlorophenyl)-3-hydroxy-5-(3-nitrophenyl)pyrazolidine-1-carboxylate (4o):** 60% yield, >20/1 dr, 88% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (5% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 11.474$  min,  $t_{\text{minor}} = 18.868$  min;  $[\alpha]_D^{26} = +4.1$  ( $c$  0.27, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (s, 1H), 8.15 (d,  $J = 8.0$  Hz, 2H), 7.63 (d,  $J = 7.6$  Hz, 1H), 7.51 (t,  $J = 8.0$  Hz, 2H), 7.24 (d,  $J = 8.8$  Hz, 2H), 6.98 (d,  $J = 8.8$ , 1H), 5.65 (d,  $J = 7.6$ , 1H), 5.36 (dd,  $J = 9.8$ , 7.8 Hz, 1H), 4.19 (s, 1H), 2.68 (dd,  $J = 12.8$ , 7.6 Hz, 1H), 2.16–1.99 (m, 1H), 1.45 (s, 9H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  157.98, 149.29, 148.50, 145.90, 143.89, 133.36, 129.70, 129.42, 127.53, 122.77, 117.26, 89.13, 82.84, 62.41, 41.83, 28.43; IR (KBr)  $\nu_{\text{max}}$ : 3415.4, 2980.4, 1698.2, 1646.7, 1527.7, 1489.2, 1448.3, 1348.1, 1259.7, 1147.6, 1014.9, 904.1, 826.7, 781.6  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z = 442.1148$  (calcd for  $\text{C}_{20}\text{H}_{22}\text{ClN}_3\text{O}_5+\text{Na}^+ = 442.1140$ ).

**(+)-*tert*-Butyl 2-(4-chlorophenyl)-3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1-carboxylate (4p):** 72% yield, >20/1 dr, 99% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (5% 2-propanol/hexane, 0.8 mL/min),  $t_{\text{major}} = 13.126$  min,  $t_{\text{minor}} = 15.819$  min;  $[\alpha]_D^{26} = +21.1$  ( $c$  0.18, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.19 (d,  $J = 7.6$  Hz, 2H), 7.60 (d,  $J = 7.6$  Hz, 2H), 7.31 (d,  $J = 7.6$  Hz, 2H), 7.01 (d,  $J = 8.0$  Hz, 2H), 6.53 (s, 1H), 5.58 (s, 1H), 5.30 (t,  $J = 8.0$  Hz, 1H), 3.30–3.23 (m, 1H), 2.08–1.84 (m, 1H), 1.30 (s, 9H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ )  $\delta$  156.05, 149.99, 146.65, 128.64, 128.13, 124.17, 123.57, 116.50, 113.16, 87.75, 80.71, 61.42, 41.99, 27.77; IR (KBr)  $\nu_{\text{max}}$ : 3405.9, 2983.5, 2938.5, 1698.3, 1598.2, 1523.9, 1487.8, 1428.1, 1350.3, 1367.5, 1235.6, 1147.8,

1090.9, 999.4, 832.8 cm<sup>-1</sup>; HRMS (EI): *m/z* = 442.1150 (calcd for C<sub>20</sub>H<sub>22</sub>ClN<sub>3</sub>O<sub>5</sub>+Na<sup>+</sup> = 442.1140).

**(+)-*tert*-Butyl 2-(4-chlorophenyl)-5-(4-cyanophenyl)-3-hydroxypyrazolidine-1-carboxylate (4q):** 65% yield, >20/1 dr, 93% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AS-H column (5% 2-propanol/hexane, 1 mL/min), *t*<sub>major</sub> = 13.462 min, *t*<sub>minor</sub> = 16.982 min; [α]<sub>D</sub><sup>26</sup> = +23.3 (*c* 0.18, acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.62 (d, *J* = 6.8 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.26–7.17 (m, 2H), 6.81 (d, *J* = 7.6 Hz, 2H), 5.63 (s, 1H), 5.29 (t, *J* = 8.8, 1H), 3.72 (s, 1H), 2.64 (dd, *J* = 12.6, 7.4 Hz, 1H), 2.15–1.89 (m, 1H) 1.41 (s, 9H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 156.25, 147.85, 146.65, 132.33, 128.59, 127.80, 124.12, 118.75, 116.44, 109.92, 89.13, 82.84, 62.41, 41.83, 28.43; IR (KBr)  $\nu_{\text{max}}$ : 3372.8, 2980.5, 2229.4, 1693.5, 1609.9, 1487.9, 1445.5, 1376.8., 1350.9, 1146.0, 1090.2, 824.2 cm<sup>-1</sup>; HRMS (EI): *m/z* = 422.1255 (calcd for C<sub>21</sub>H<sub>22</sub>ClN<sub>3</sub>O<sub>3</sub>+Na<sup>+</sup> = 422.1242).

**(-)-*tert*-Butyl 2-(4-chlorophenyl)-3-hydroxy-5-(3-(trifluoromethyl)phenyl)pyrazolidine-1-carboxylate (4r):** 53% yield, >20/1 dr, 81% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (10% 2-propanol/hexane, 1 mL/min), *t*<sub>major</sub> = 4.422 min, *t*<sub>minor</sub> = 5.016 min; [α]<sub>D</sub><sup>26</sup> = -42.9 (*c* 0.07, acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.60 (s, 1H), 7.54 (d, *J* = 6.8 Hz, 1H), 7.50–7.39 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 5.72–5.56 (m, 1H), 5.39–5.25 (m, 1H), 4.05 (s, 1H), 2.65 (dd, *J* = 12.8, 7.6 Hz, 1H), 2.15–1.99 (m, 1H), 1.42 (s, 9H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 155.96, 146.76, 143.61, 130.79, 129.38, 129.01, 128.53, 125.51, 124.30, 123.89, 122.81, 116.52, 87.86, 80.49, 61.59, 42.20,

27.69; IR (KBr)  $\nu_{\text{max}}$ : 3421.5, 2999.8, 1697.8, 1639.5, 1486.4, 1446.5, 1327.5, 1212.0, 1158.3, 1117.6, 991.4, 902.5, 823.3, 798.3, 780.4, 700.0  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z$  = 465.1172 (calcd for  $\text{C}_{21}\text{H}_{22}\text{ClF}_3\text{N}_2\text{O}_3+\text{Na}^+$  = 465.1183).

**(+)-*tert*-Butyl 2-(4-bromophenyl)-3-hydroxy-5-(4-nitrophenyl)pyrazolidine-1-carboxylate (4s):** 74% yield, >20/1 dr, 99% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (5% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}}$  = 12.291 min,  $t_{\text{minor}}$  = 14.194 min;  $[\alpha]_D^{26}$  = +29.2 ( $c$  0.24, acetone);  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.19 (d,  $J$  = 8.0 Hz, 2H), 7.60 (d,  $J$  = 8.4 Hz, 2H), 7.43 (d,  $J$  = 8.0 Hz, 2H), 6.96 (d,  $J$  = 8.0 Hz, 2H), 6.54 (s, 1H), 5.58 (s, 1H), 5.30 (t,  $J$  = 8.6 Hz, 1H), 3.30–3.23 (m, 1H), 2.06–1.79 (m, 1H), 1.30 (s, 9H);  $^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ )  $\delta$  149.97, 147.04, 146.60, 131.50, 128.13, 123.58, 116.96, 111.92, 87.70, 80.73, 61.39, 42.01, 27.77; IR (KBr)  $\nu_{\text{max}}$ : 3408.1, 2982.4, 2936.0, 1697.3, 1598.3, 1523.6, 1485.2, 1426.7, 1349.3, 1236.9, 1146.7, 1092.0, 1000.8, 847.5  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z$  = 486.0643 (calcd for  $\text{C}_{20}\text{H}_{22}\text{BrN}_3\text{O}_5+\text{Na}^+$  = 486.0635).

**(+)-*tert*-Butyl 2-(4-bromophenyl)-5-(4-cyanophenyl)-3-hydroxypyrazolidine-1-carboxylate (4t):** 72% yield, >20/1 dr, 90% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (5% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}}$  = 13.878 min,  $t_{\text{minor}}$  = 19.994 min;  $[\alpha]_D^{26}$  = +12.2 ( $c$  0.41, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 (d,  $J$  = 7.6 Hz, 2H), 7.42 (d,  $J$  = 8.4 Hz, 2H), 7.38 (d,  $J$  = 8.4 Hz, 2H), 6.91 (d,  $J$  = 8.4 Hz, 2H), 5.68–5.57 (m, 1H), 5.40–5.19 (m, 1H), 3.69 (s, 1H), 2.64 (dd,  $J$  = 13.0, 7.4 Hz, 1H), 2.10–1.93 (m, 1H) 1.41 (s, 9H);

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 156.16, 147.87, 147.03, 132.35, 131.46, 127.81, 118.77, 116.90, 111.84, 109.90, 87.58, 80.63, 61.62, 42.00, 27.76; IR (KBr) ν<sub>max</sub>: 3416.6, 2982.0, 2228.1, 1693.8, 1609.0, 1586.1, 1485.2, 1420.0, 1381.1, 1353.4, 1145.3, 1094.8, 823.5 cm<sup>-1</sup>; HRMS (EI): *m/z* = 466.0745 (calcd for C<sub>21</sub>H<sub>22</sub>BrN<sub>3</sub>O<sub>3</sub>+Na<sup>+</sup> = 466.0737).

**(-)-*tert*-Butyl 5-hydroxy-2-(4-methoxyphenyl)-3-(4-nitrophenyl)pyrazolidine-1-carboxylate (4u')**: 75% yield, >20/1 dr, 11% ee. The enantiomeric ratio was determined by HPLC on Chiralpak OD-H column (10% 2-propanol/hexane, 1 mL/min), *t*<sub>major</sub> = 9.927 min, *t*<sub>minor</sub> = 10.830 min; [α]<sub>D</sub><sup>26</sup> = -6.8 (*c* 0.37, acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.23 (d, *J* = 10.0 Hz, 2H), 7.70 (d, *J* = 9.6 Hz, 2H), 6.94 (d, *J* = 9.6 Hz, 2H), 6.81 (d, *J* = 9.2 Hz, 2H), 5.83 (s, 1H), 4.91 (s, 1H), 3.77 (s, 1H), 3.01 (s, 1H), 2.70 (m, 1H), 2.35 (m, 1H), 1.46 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 155.17, 155.06, 149.87, 147.45, 145.08, 127.18, 124.15, 117.58, 114.28, 82.73, 82.04, 69.22, 55.65, 42.49, 28.43; IR (KBr) ν<sub>max</sub>: 3419.3, 3109.9, 2975.7, 2944.2, 1677.4, 1598.1, 1508.4, 1474.4, 1390.5, 1345.4, 1239.1, 1174.2, 1091.2, 998.8, 842.5 cm<sup>-1</sup>; HRMS (EI): *m/z* = 416.1832 (calcd for C<sub>21</sub>H<sub>25</sub>N<sub>3</sub>O<sub>6</sub>+H<sup>+</sup> = 416.1816).

**(+)-*tert*-Butyl 2-(4-chlorophenyl)-3-hydroxy-5-methylpyrazolidine-1-carboxylate (4v)**: 78% yield, >20/1 dr, 72% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (8% 2-propanol/hexane, 1 mL/min), *t*<sub>major</sub> = 7.352 min, *t*<sub>minor</sub> = 5.753 min; [α]<sub>D</sub><sup>26</sup> = +27.8 (*c* 1.07, acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.20 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 5.92 (dd, *J* = 8.0, 5.6 Hz, 1H),

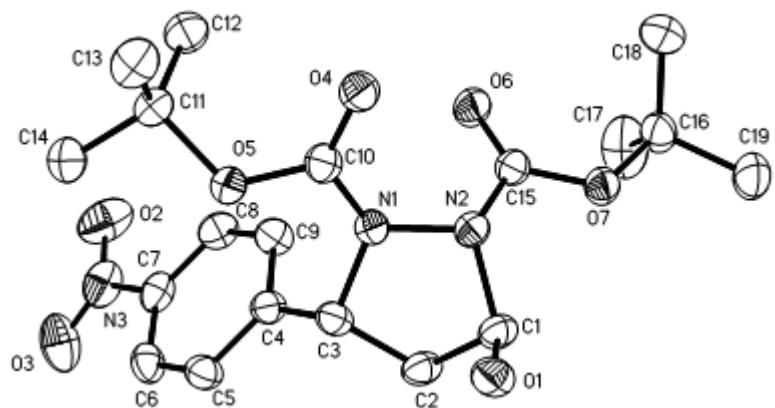
4.02–3.82 (m, 1H), 3.15 (s, 1H), 2.25–2.12 (m, 1H), 2.12–1.94 (m, 1H), 1.44 (s, 9H), 1.28 (d,  $J = 6.4$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.26, 150.22, 128.78, 126.78, 118.20, 83.09, 81.74, 62.44, 40.18, 28.44, 20.65. IR (KBr)  $\nu_{\text{max}}$ : 3453.5, 2975.7, 1679.4, 1480, 1402.2, 1087.3, 952.2, 841.5  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z$  = 335.1134 (calcd for  $\text{C}_{15}\text{H}_{21}\text{ClN}_2\text{O}_3+\text{Na}^+ = 335.1133$ ).

**(+)-*tert*-Butyl 2-(4-bromophenyl)-3-hydroxy-5-methylpyrazolidine-1-carboxylate (4w):** 83% yield, >20/1 dr, 74% ee. The enantiomeric ratio was determined by HPLC on Chiralpak AD-H column (8% 2-propanol/hexane, 1 mL/min),  $t_{\text{major}} = 8.184$  min,  $t_{\text{minor}} = 6.063$  min;  $[\alpha]_D^{26} = +32.9$  ( $c$  1.19, acetone);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (d,  $J = 8.8$  Hz, 2H), 6.92 (d,  $J = 8.8$  Hz, 2H), 6.00–5.84 (m, 1H), 4.10–3.81 (m, 1H), 3.13 (s, 1H), 2.30–2.10 (m, 1H), 2.10–1.95 (m, 1H), 1.44 (s, 9H), 1.28 (d,  $J = 6.8$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.35, 150.68, 131.61, 118.35, 113.99, 82.97, 81.69, 62.19, 40.35, 28.38, 20.69. IR (KBr)  $\nu_{\text{max}}$ : 3336.8, 2974.5, 1692.1, 1482.1, 1356.5, 1145.3, 1066.6, 828.8  $\text{cm}^{-1}$ ; HRMS (EI):  $m/z$  = 357.0810 (calcd for  $\text{C}_{15}\text{H}_{21}\text{BrN}_2\text{O}_3+\text{H}^+ = 357.0808$ ).

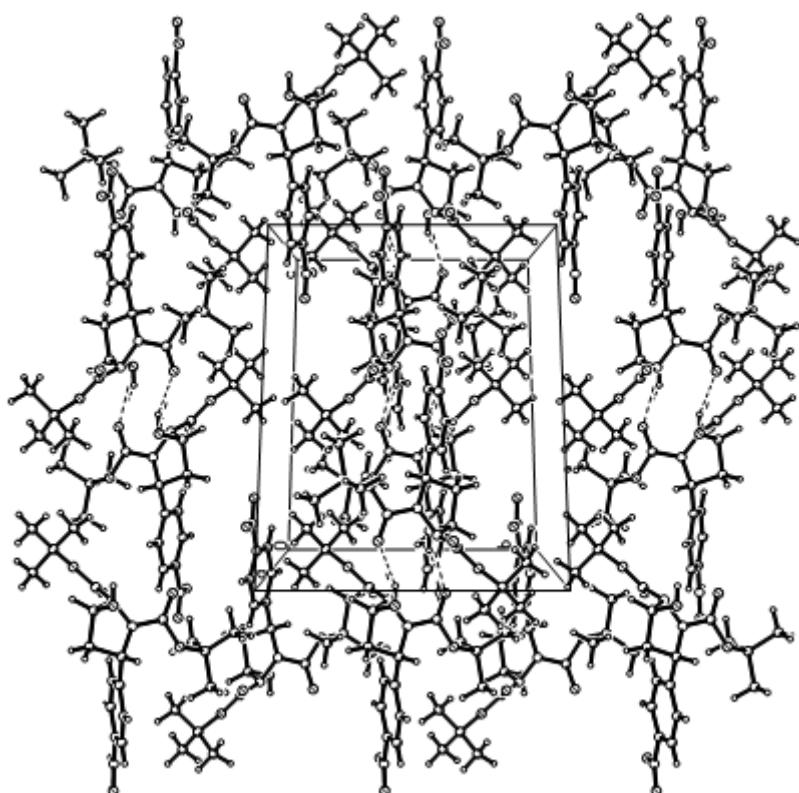
#### 4. X-ray crystal structure of 4a, 4n, 4s

##### 4a

|                                   |  |                           |
|-----------------------------------|--|---------------------------|
| Identification code               | shelxl   |                           |
| Empirical formula                 | $C_{19}H_{27}N_3O_7$   |                           |
| Formula weight                    | 409.44   |                           |
| Temperature                       | 223(2) K   |                           |
| Wavelength                        | 0.71075 Å  |                           |
| Crystal system, space group       | Monoclinic, C 2/c  |                           |
| Unit cell dimensions              | $a = 27.633(9)$ Å  | $\alpha = 90$ deg.        |
|                                   | $b = 11.435(3)$ Å  | $\beta = 124.665(7)$ deg. |
|                                   | $c = 16.853(6)$ Å  | $\gamma = 90$ deg.        |
| Volume                            | 4380(2) Å <sup>3</sup>                                       |                           |
| Z, Calculated density             | 8,1.242 Mg/m <sup>3</sup>                                    |                           |
| Absorption coefficient            | 0.095 mm <sup>-1</sup>                                       |                           |
| F(000)                            | 1744   |                           |
| Crystal size                      | 0.76 x 0.75 x 0.42 mm  |                           |
| Theta range for data collection   | 3.08 to 25.50 deg.   |                           |
| Limiting indices                  | $-27 \leq h \leq 33, -13 \leq k \leq 13, -20 \leq l \leq 17$ |                           |
| Reflections collected / unique    | 10678 / 4039 [R(int) = 0.0391]                               |                           |
| Completeness to theta = 25.50     | 99.0%  |                           |
| Absorption correction             | Semi-empirical from equivalents                              |                           |
| Max. and min. transmission        | 0.962 and 0.485  |                           |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>                  |                           |
| Data / restraints / parameters    | 4039 / 15 / 270  |                           |
| Goodness-of-fit on F <sup>2</sup> | 1.020  |                           |
| Final R indices [I>2sigma(I)]     | R1 = 0.0606, wR2 = 0.1585                                    |                           |
| R indices (all data)              | R1 = 0.0997, wR2 = 0.1867                                    |                           |
| Largest diff. peak and hole       | 0.208 and -0.267 e.Å <sup>-3</sup>                           |                           |



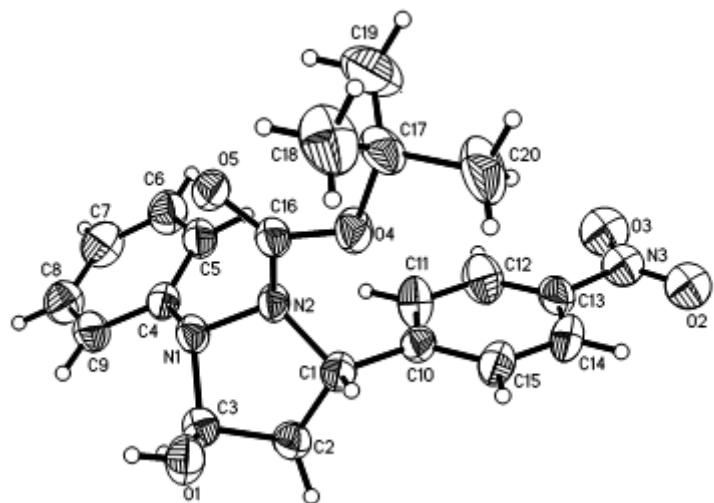
**Figure S1.** ORTEP drawing of racemic 4a (25% thermal ellipsoids).



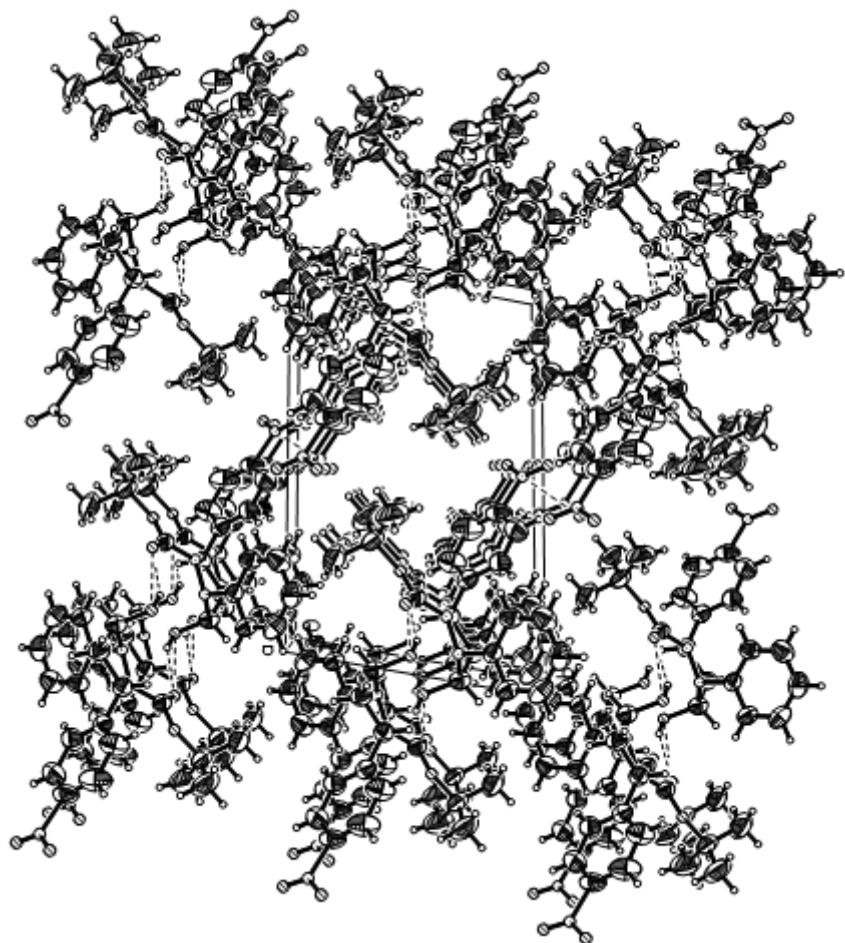
**Figure S2.** Packing of molecules in a unit cell for racemic 4a.

**4n**

|                                   |   |
|-----------------------------------|---|
| Identification code               | shelxl  |
| Empirical formula                 | C <sub>20</sub> H <sub>23</sub> N <sub>3</sub> O <sub>5</sub>   |
| Formula weight                    | 385.41  |
| Temperature                       | 293(2) K  |
| Wavelength                        | 0.71070 Å   |
| Crystal system, space group       | Triclinic, P -1   |
| Unit cell dimensions              | a = 7.7399(14) Å      alpha = 98.408(4) deg.<br>b = 9.2877(17) Å      beta = 103.948(4) deg.<br>c = 14.911(3) Å      gamma = 97.043(4) deg. |
| Volume                            | 1015.1(3) Å <sup>3</sup>  |
| Z, Calculated density             | 2, 1.261 Mg/m <sup>3</sup>  |
| Absorption coefficient            | 0.092 mm <sup>-1</sup>  |
| F(000)                            | 408   |
| Crystal size                      | 0.80 x 0.60 x 0.20 mm   |
| Theta range for data collection   | 3.25 to 25.35 deg.  |
| Limiting indices                  | -9<=h<=7, -11<=k<=11, -17<=l<=17  |
| Reflections collected / unique    | 9794 / 3688 [R(int) = 0.0221]   |
| Completeness to theta = 25.35     | 99.1 %  |
| Absorption correction             | Semi-empirical from equivalents   |
| Max. and min. transmission        | 0.995 and 0.809   |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>   |
| Data / restraints / parameters    | 3688 / 0 / 255  |
| Goodness-of-fit on F <sup>2</sup> | 1.080   |
| Final R indices [I>2sigma(I)]     | R1 = 0.0758, wR2 = 0.1919   |
| R indices (all data)              | R1 = 0.0899, wR2 = 0.2037   |
| Largest diff. peak and hole       | 0.492 and -0.574 e.Å <sup>-3</sup>  |



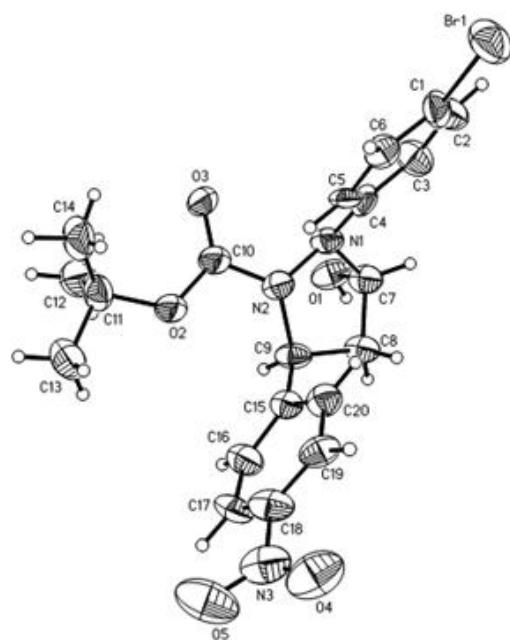
**Figure S3.** ORTEP drawing of racemic **4n** (25% thermal ellipsoids).



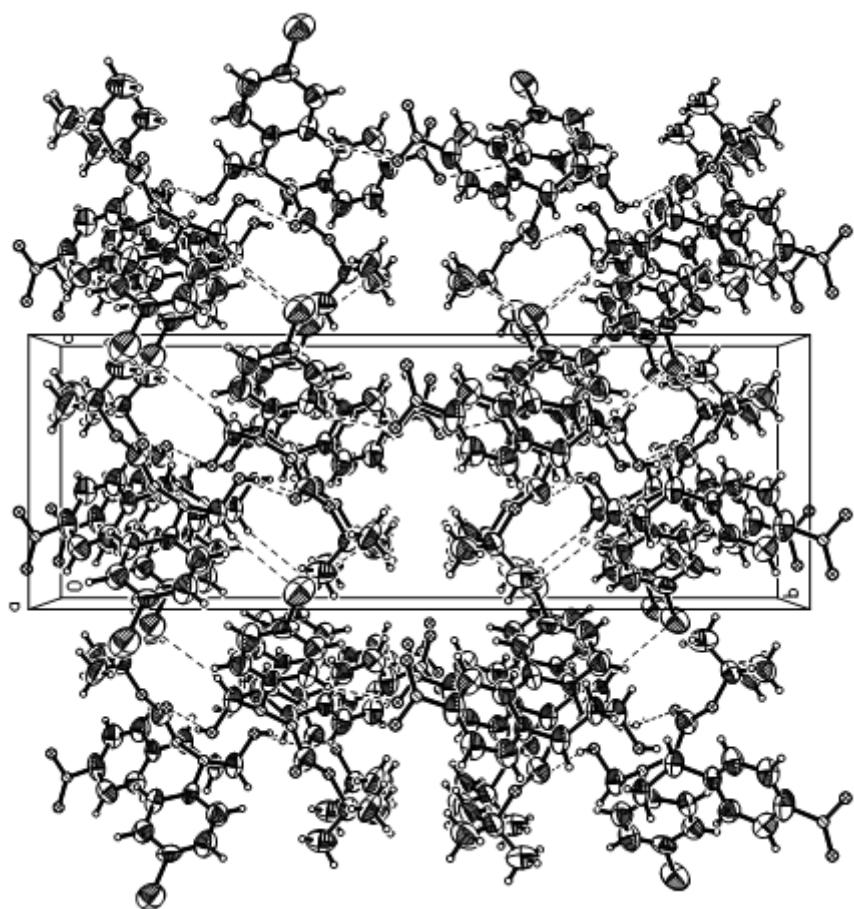
**Figure S4.** Packing of molecules in a unit cell for racemic **4n**.

**4s**

|                                   |  |                    |
|-----------------------------------|--|--------------------|
| Identification code               | shelxl   |                    |
| Empirical formula                 | $C_{20}H_{22}BrN_3O_5$                                     |                    |
| Formula weight                    | 464.32   |                    |
| Temperature                       | 293(2) K   |                    |
| Wavelength                        | 0.71070 Å  |                    |
| Crystal system, space group       | Monoclinic, P 21   |                    |
| Unit cell dimensions              | $a = 8.140(3)$ Å   | $\alpha = 90$ deg. |
|                                   | $b = 27.227(10)$ Å   | $\beta = 90$ deg.  |
|                                   | $c = 9.566(5)$ Å   | $\gamma = 90$ deg. |
| Volume                            | 2120.1(16) Å <sup>3</sup>                                  |                    |
| Z, Calculated density             | 4, 1.455 Mg/m <sup>3</sup>                                 |                    |
| Absorption coefficient            | 1.974 mm <sup>-1</sup>                                     |                    |
| F(000)                            | 952  |                    |
| Crystal size                      | 0.50 x 0.27 x 0.20 mm                                      |                    |
| Theta range for data collection   | 3.09 to 25.49 deg.   |                    |
| Limiting indices                  | $-9 \leq h \leq 9, -32 \leq k \leq 32, -11 \leq l \leq 11$ |                    |
| Reflections collected / unique    | 15685 / 3740 [R(int) = 0.1609]                             |                    |
| Completeness to theta = 25.49     | 97.6 %   |                    |
| Absorption correction             | Semi-empirical from equivalents                            |                    |
| Max. and min. transmission        | 0.673 and 0.331  |                    |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>                |                    |
| Data / restraints / parameters    | 3740 / 77 / 261  |                    |
| Goodness-of-fit on F <sup>2</sup> | 1.115  |                    |
| Final R indices [I>2sigma(I)]     | R1 = 0.1185, wR2 = 0.2012                                  |                    |
| R indices (all data)              | R1 = 0.2120, wR2 = 0.2443                                  |                    |
| Absolute structure parameter      | 0.02(3)  |                    |
| Largest diff. peak and hole       | 0.428 and -0.293 e.Å <sup>-3</sup>                         |                    |



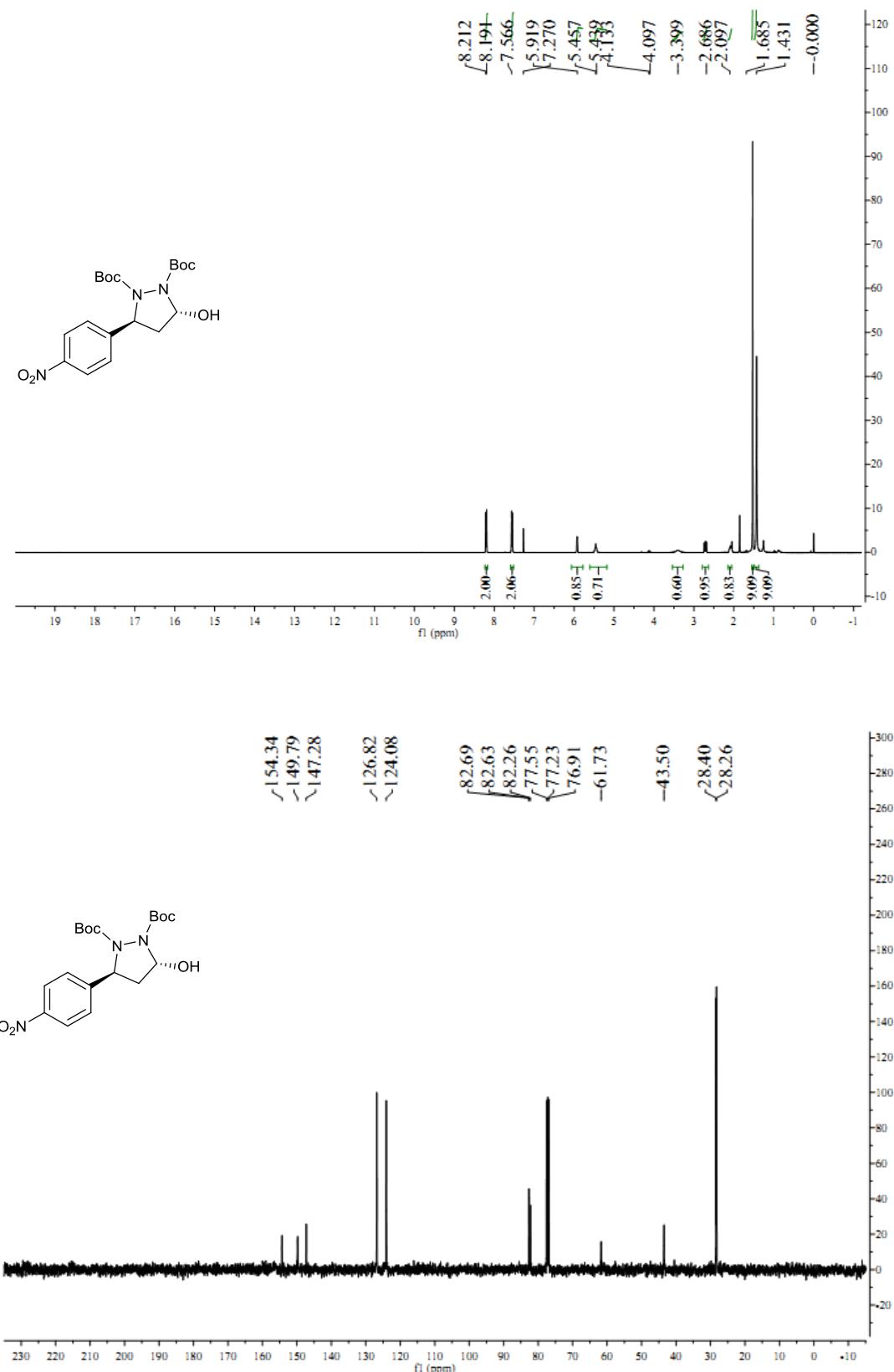
**Figure S5.** ORTEP drawing of chiral **4s** (40% thermal ellipsoids).



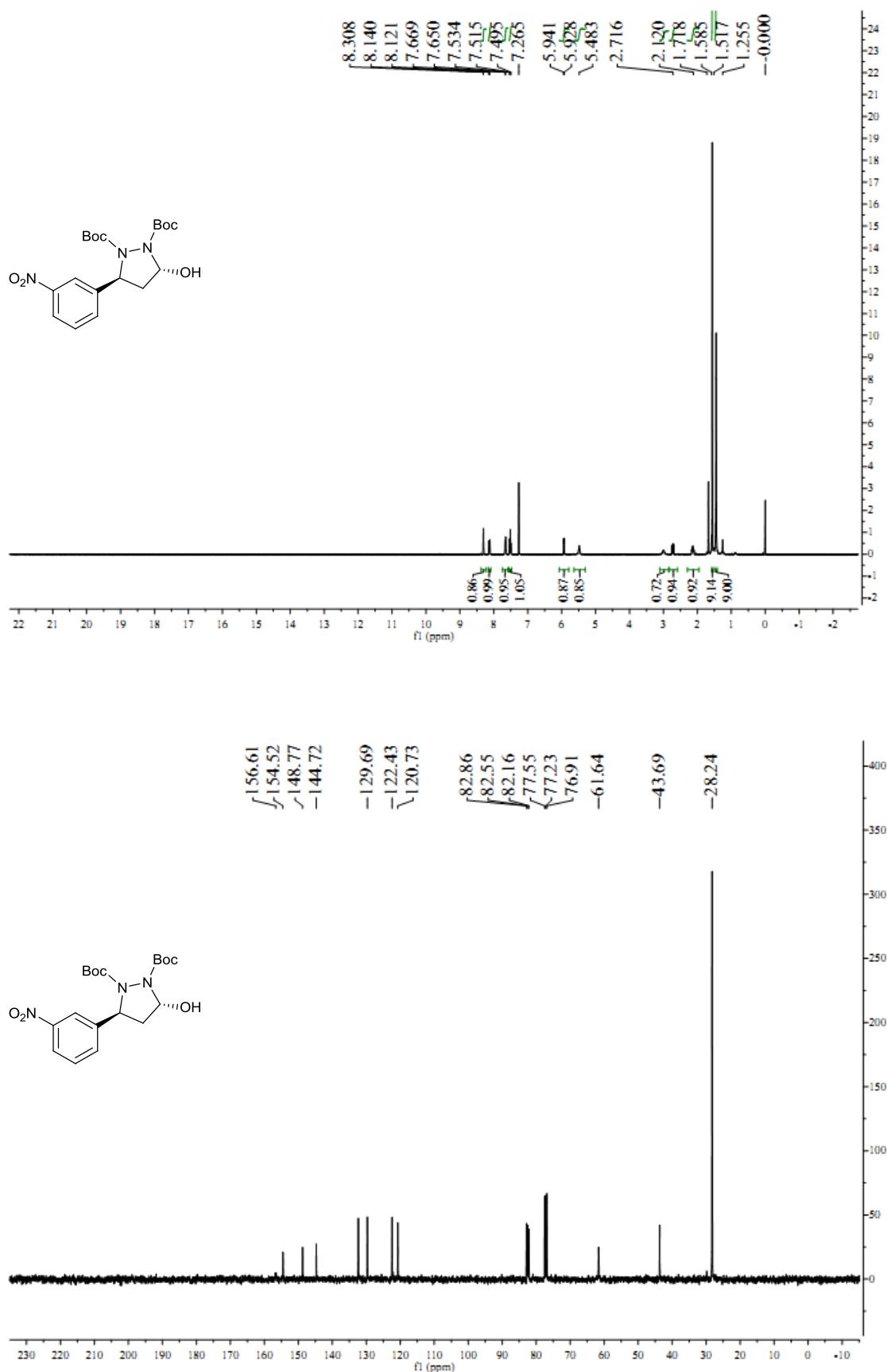
**Figure S6.** Packing of molecules in a unit cell for chiral **4s**.

**5.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra**

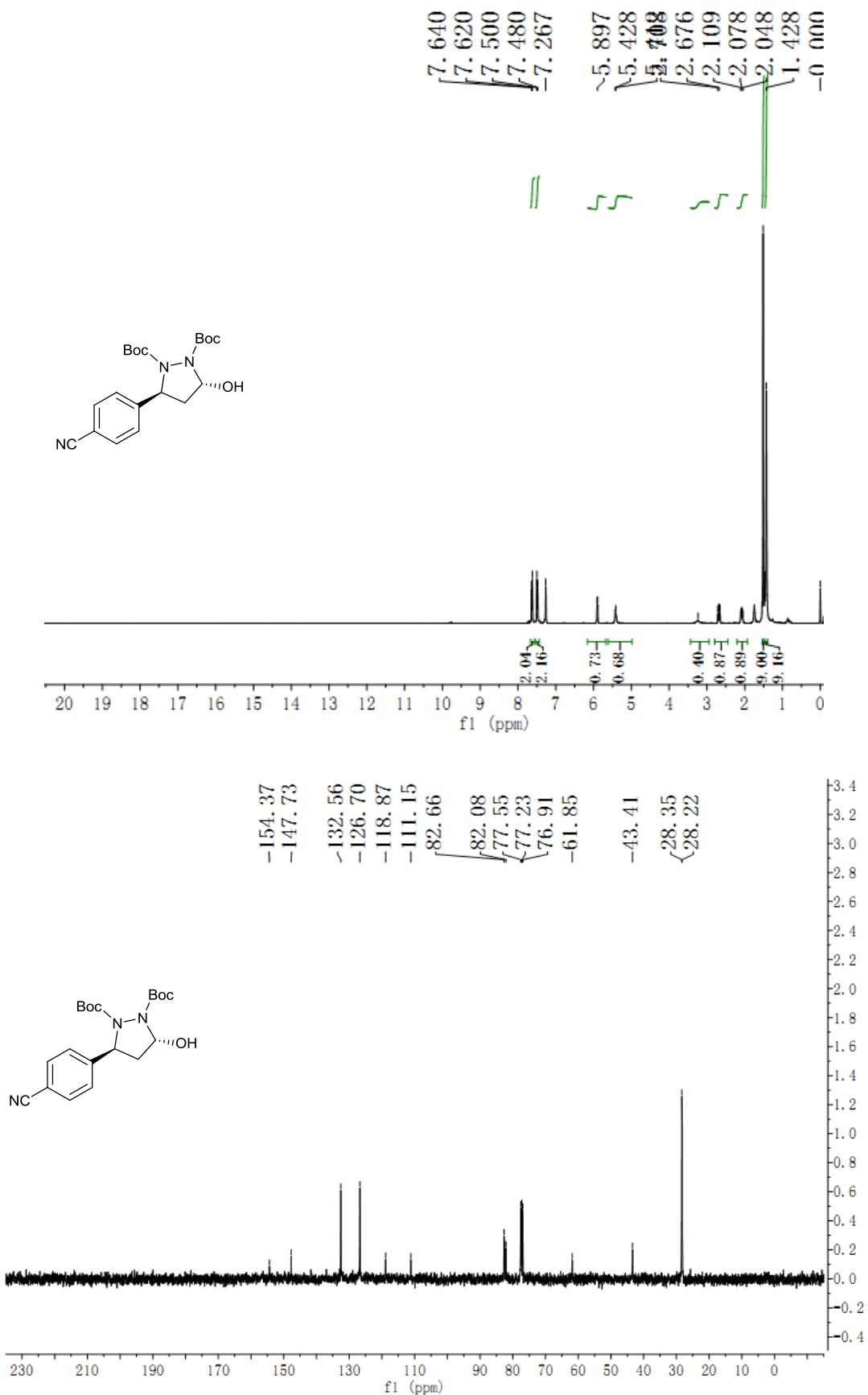
**4a**



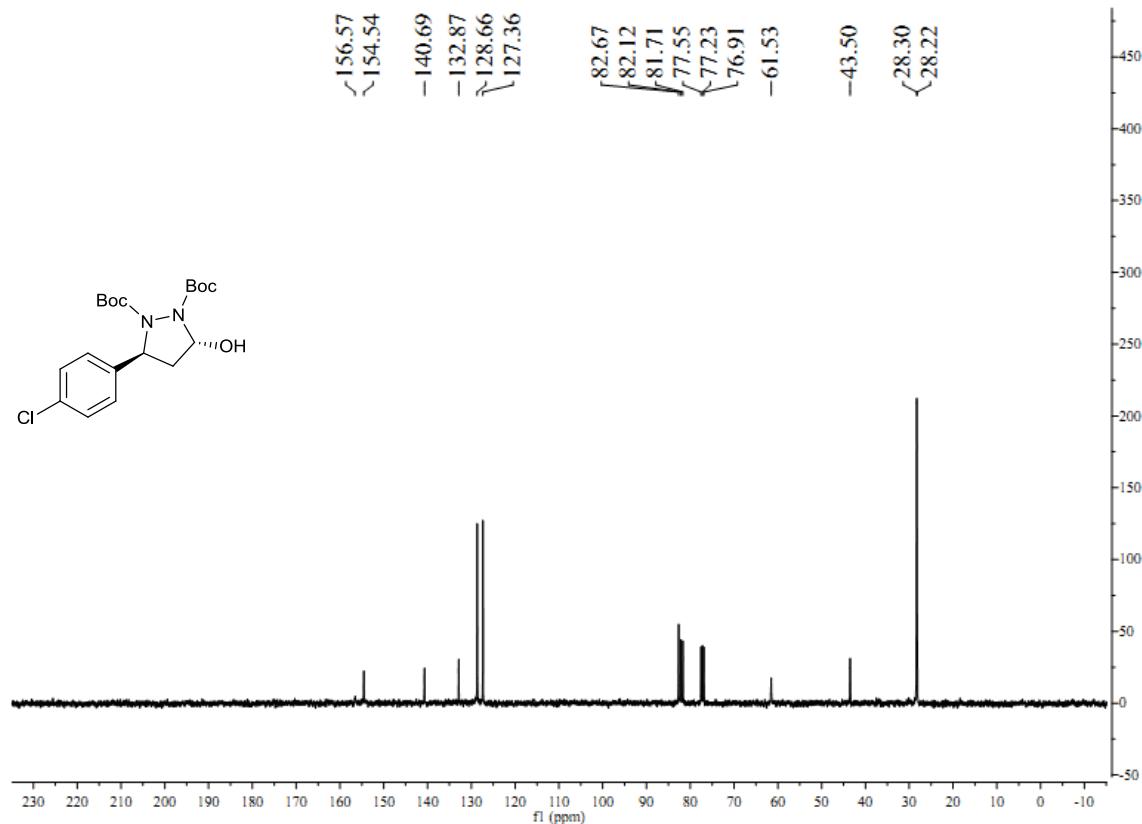
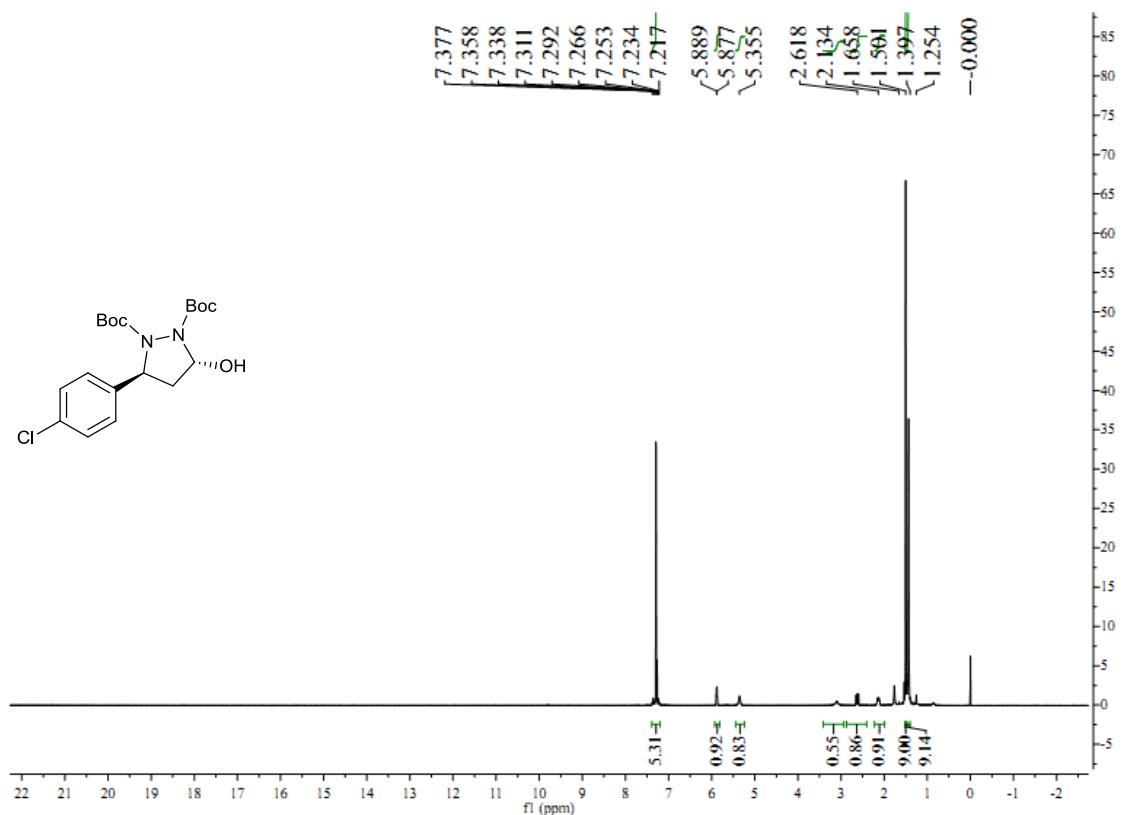
**4b**



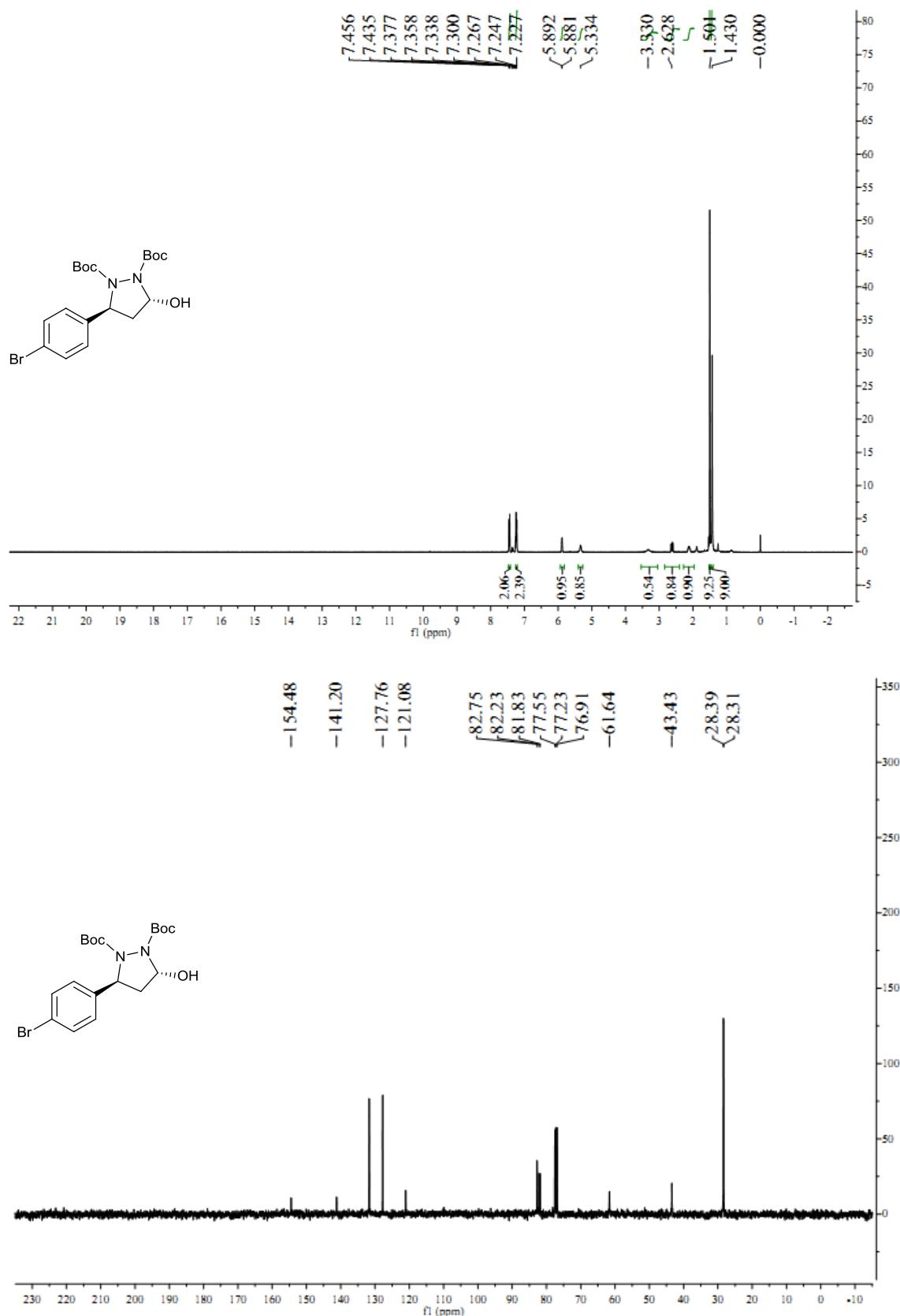
**4c**



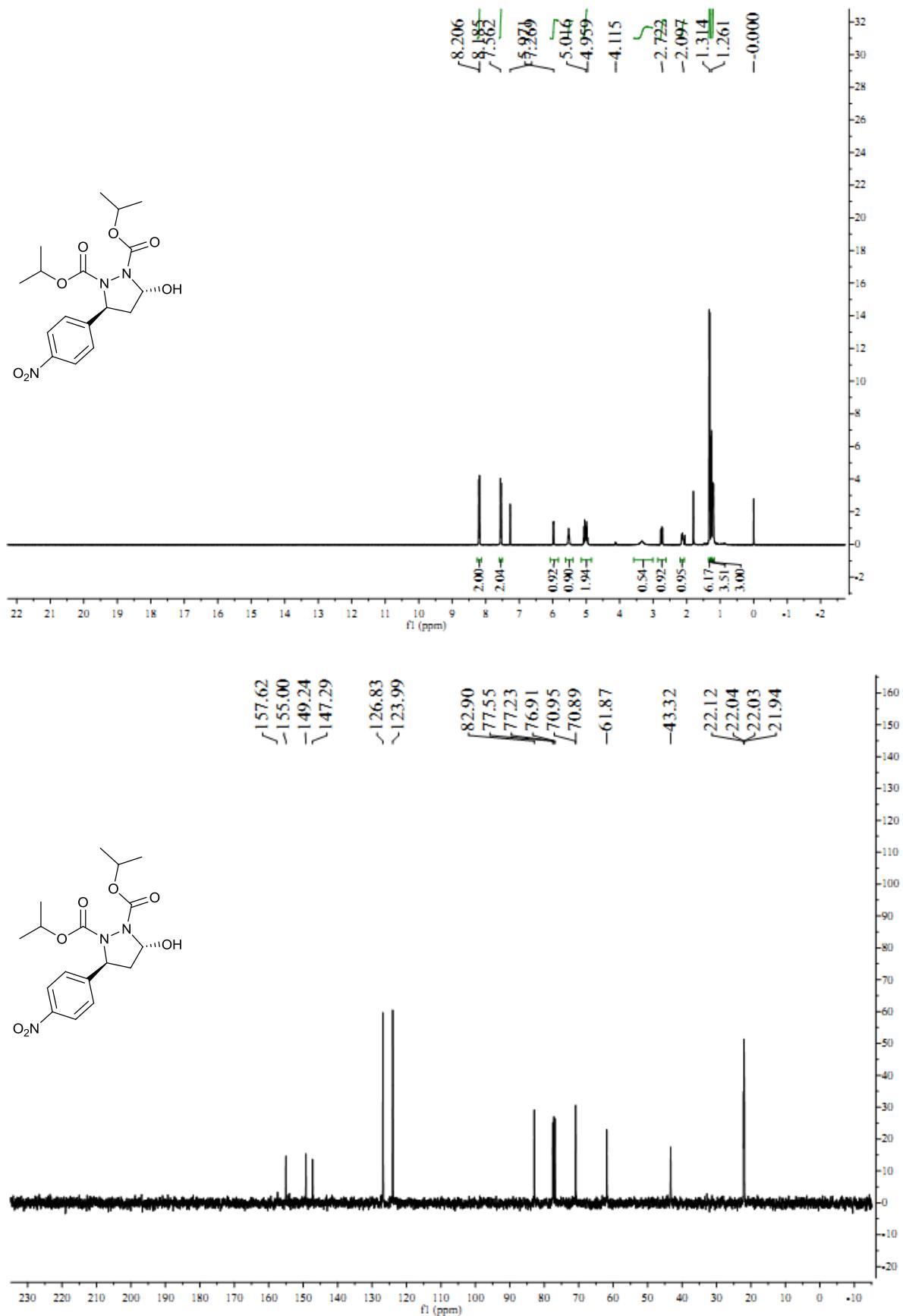
**4d**



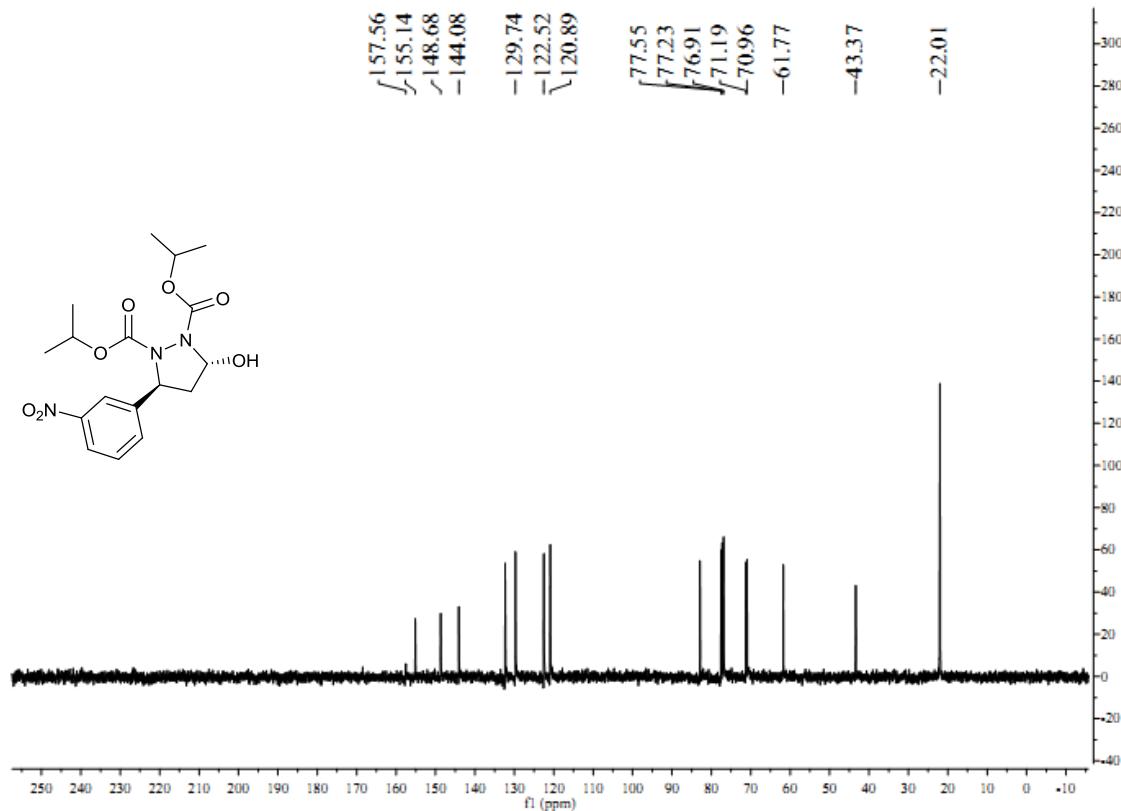
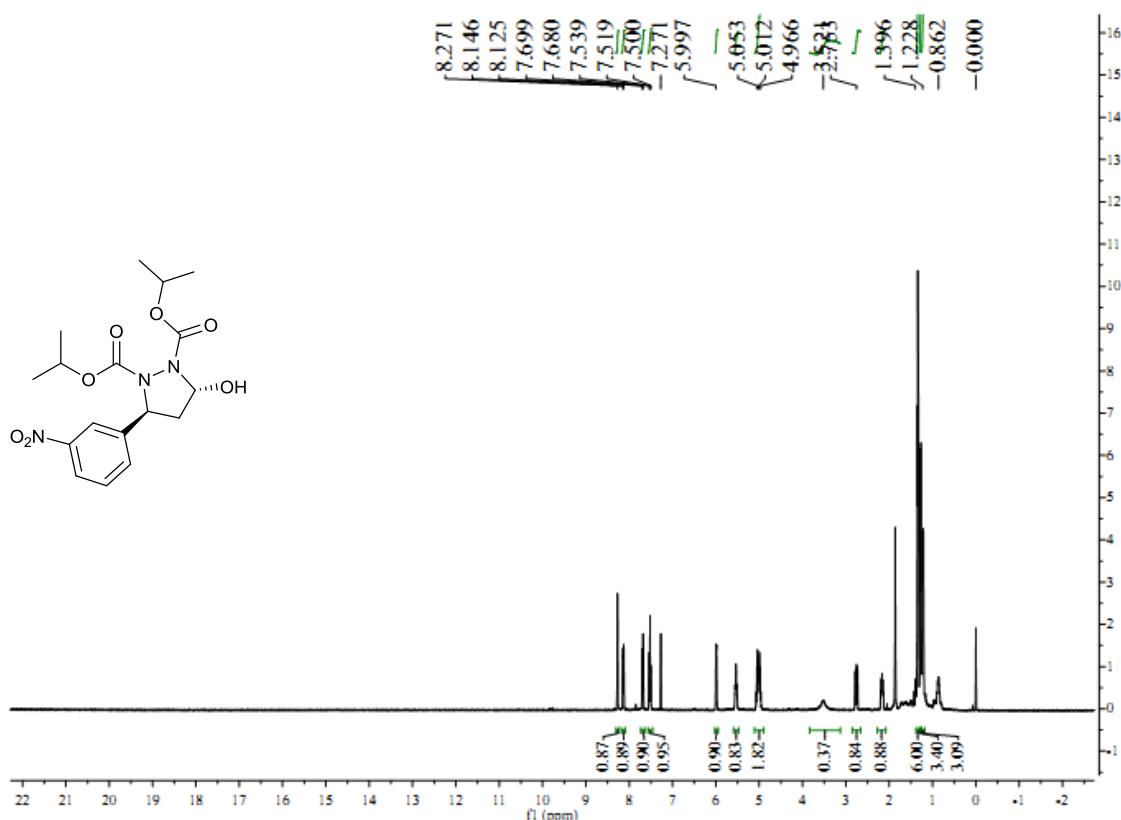
**4e**



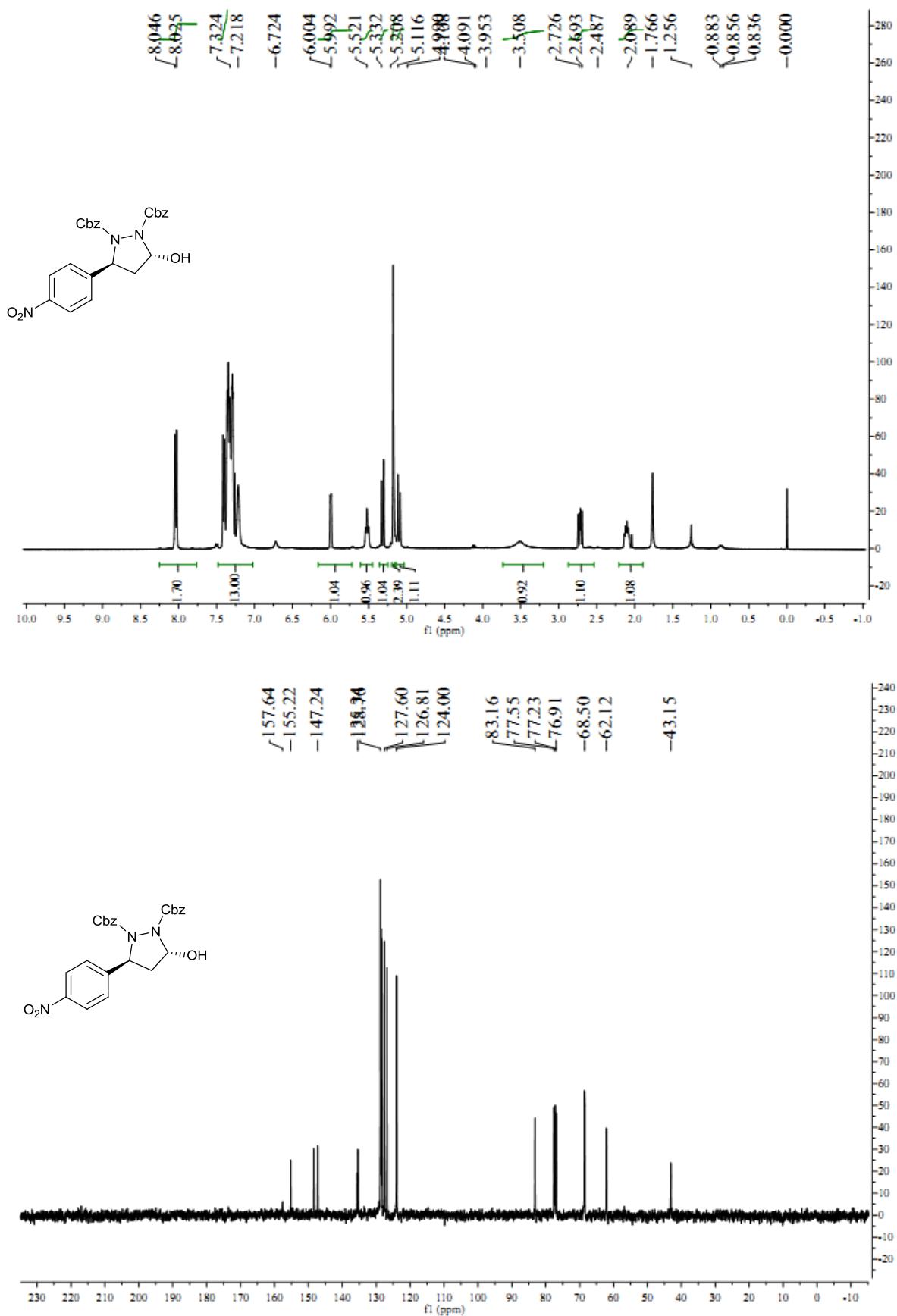
**4h**



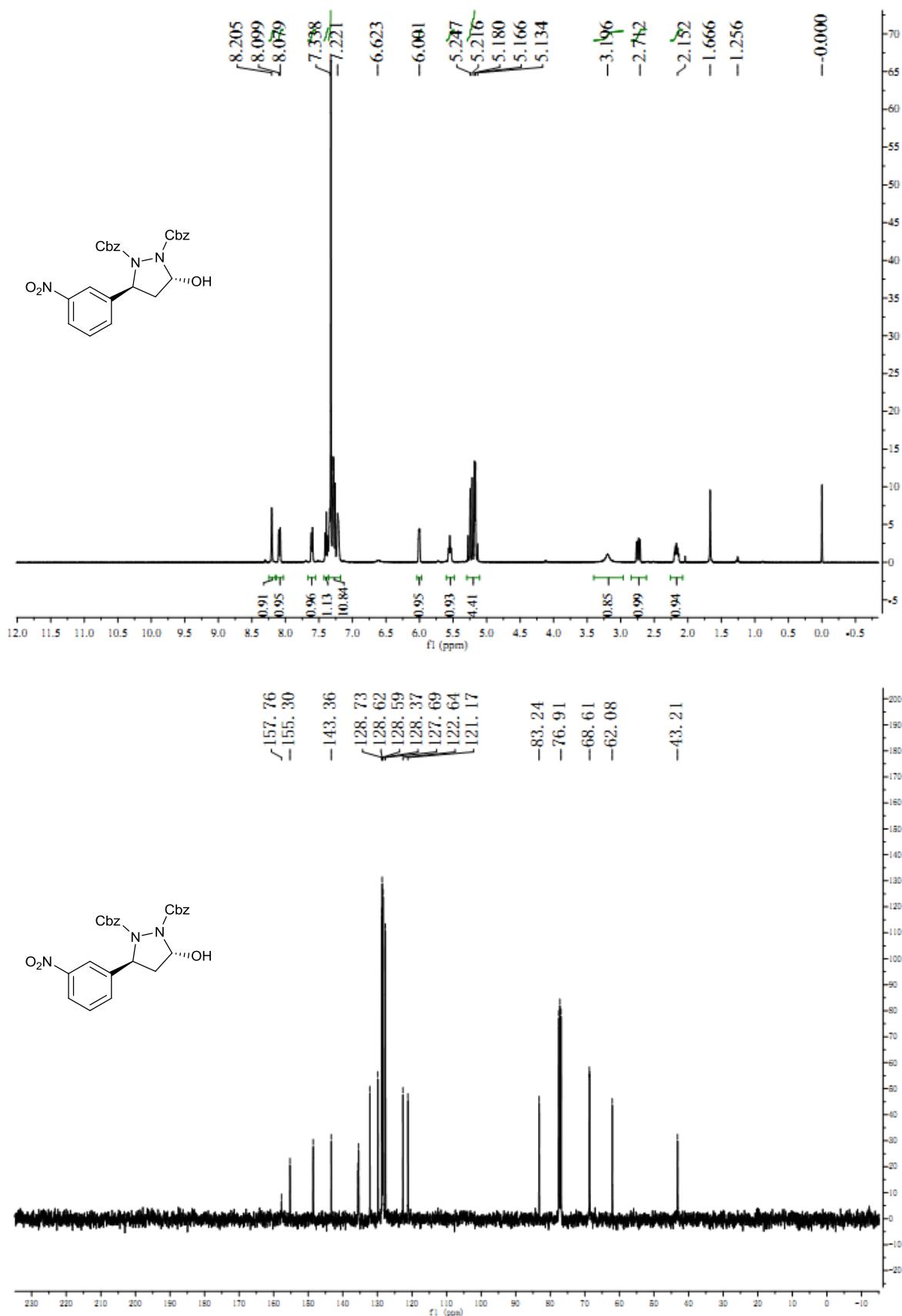
**4i**

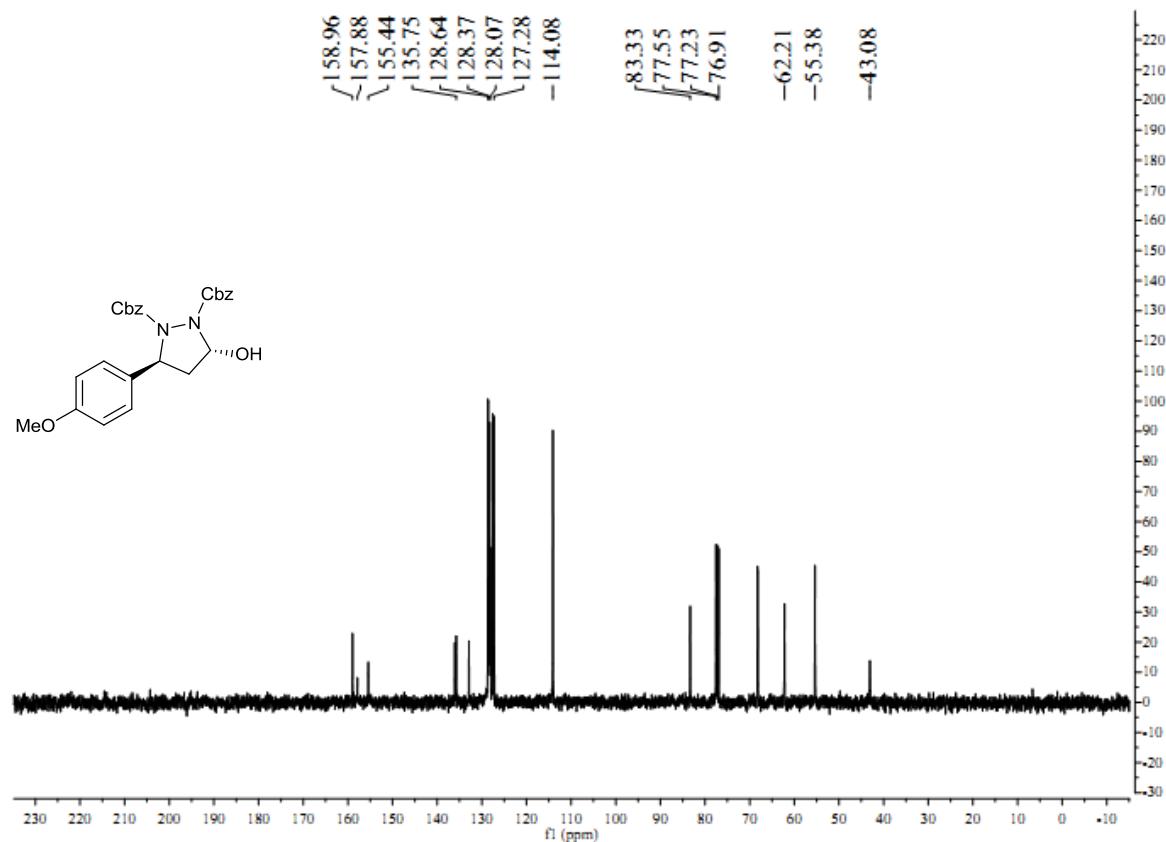
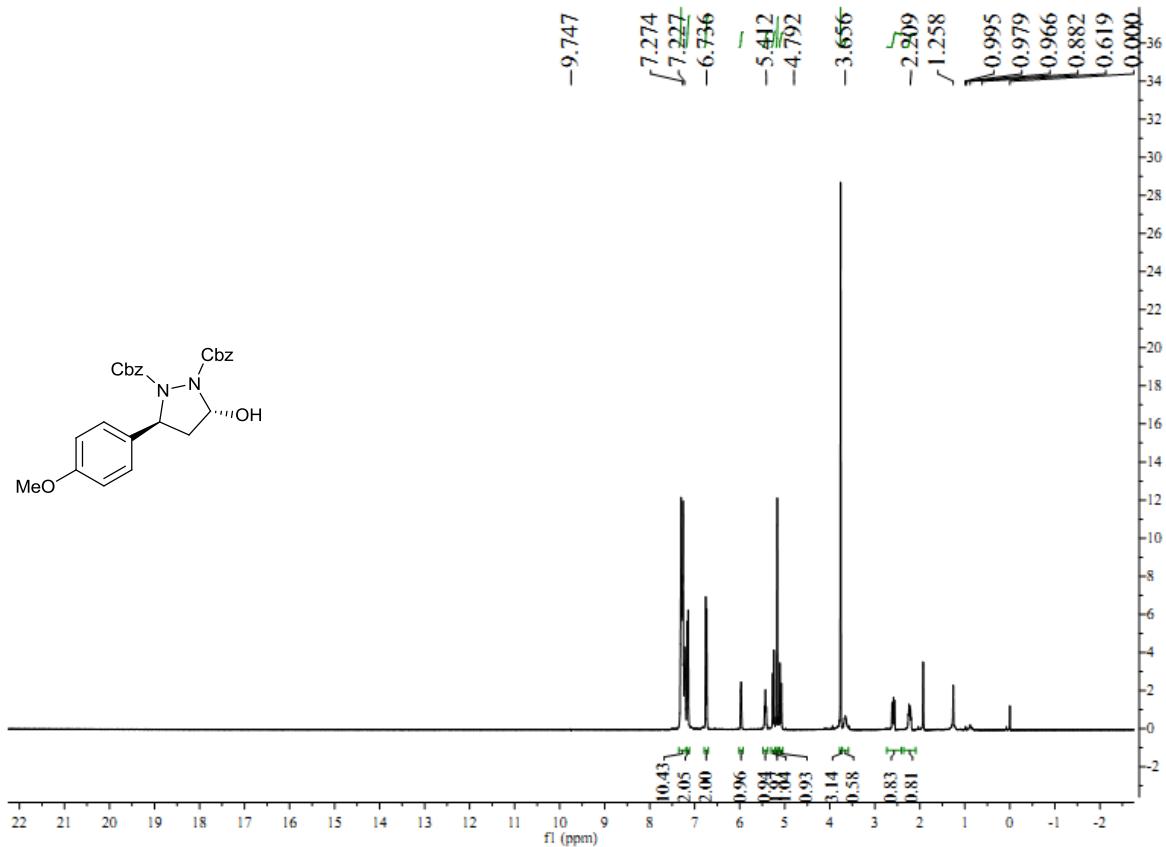


4j

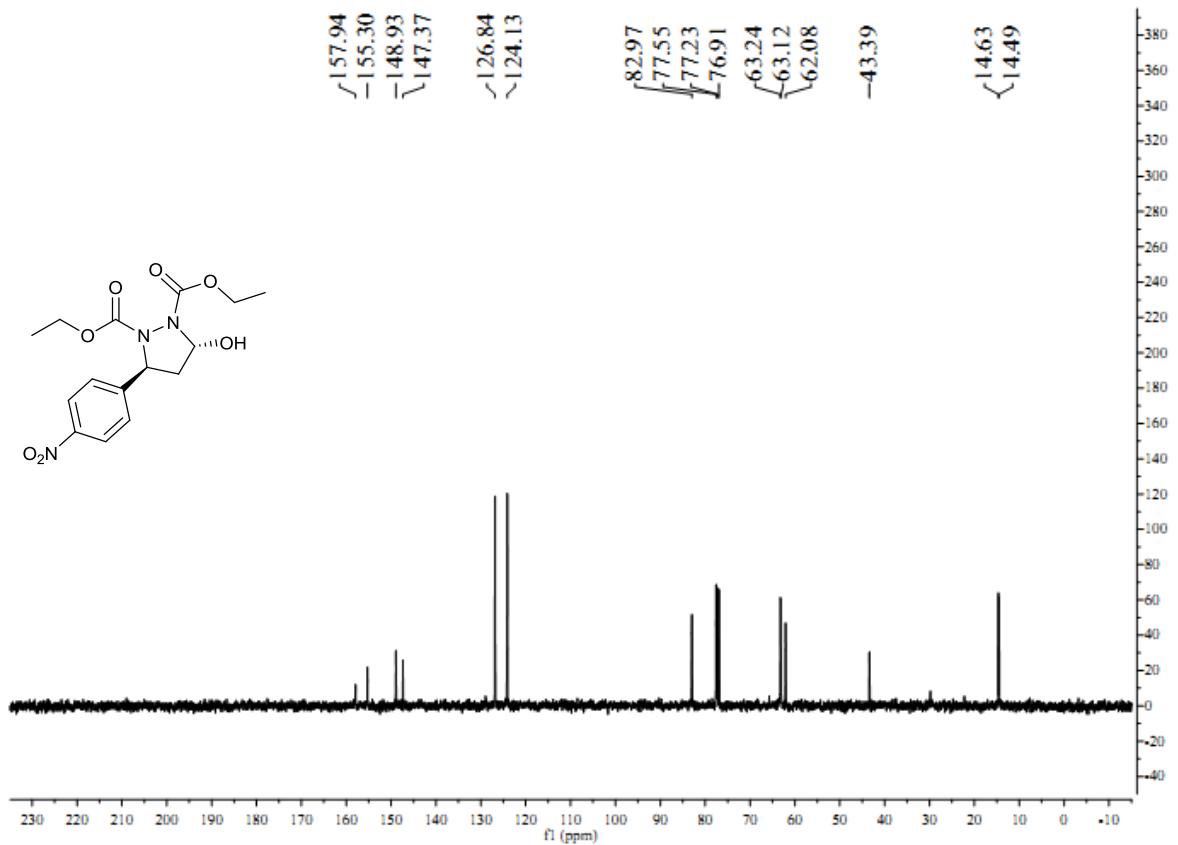
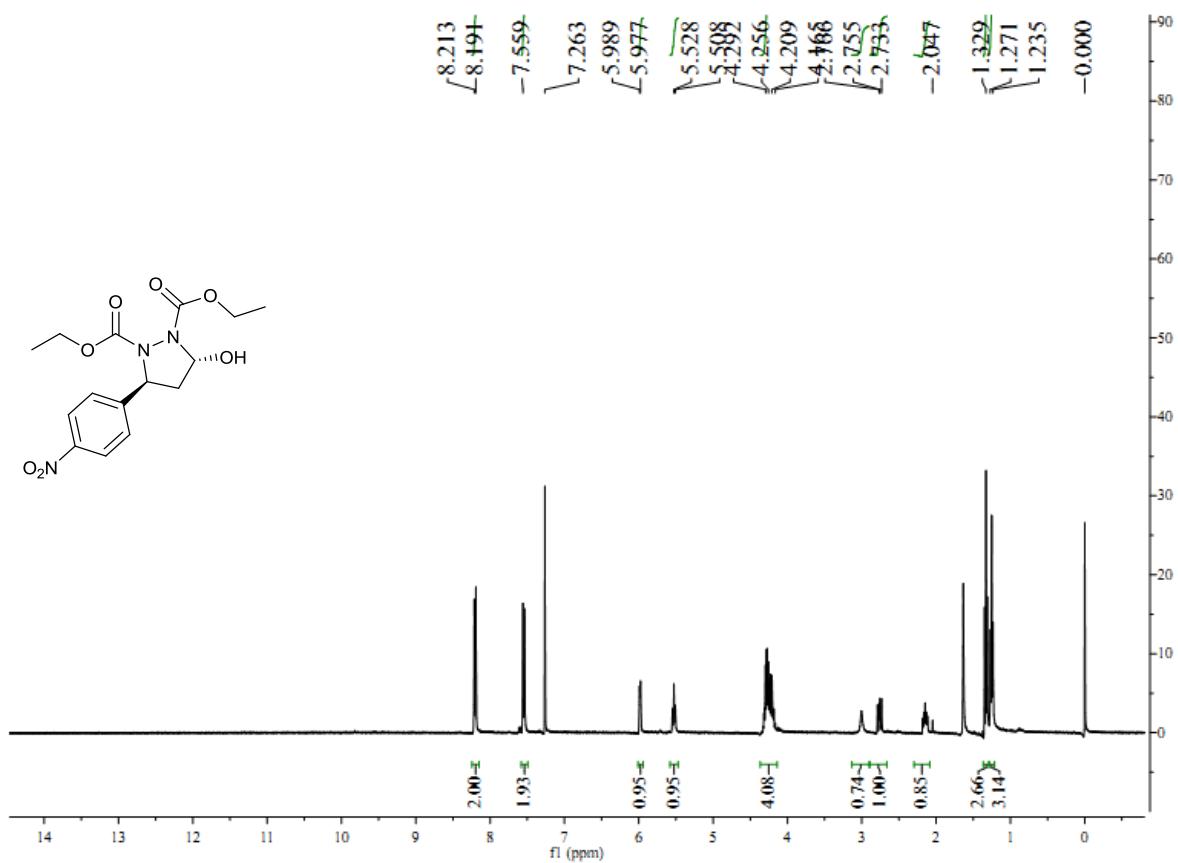


**4k**

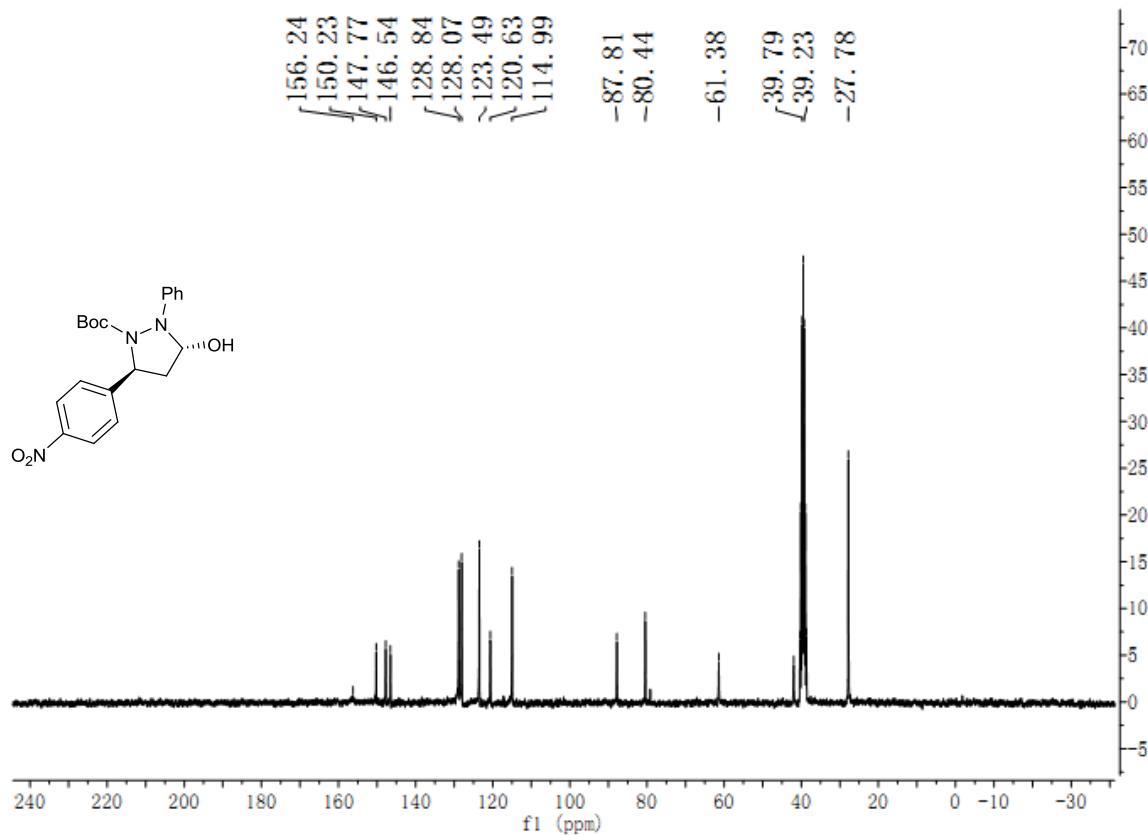
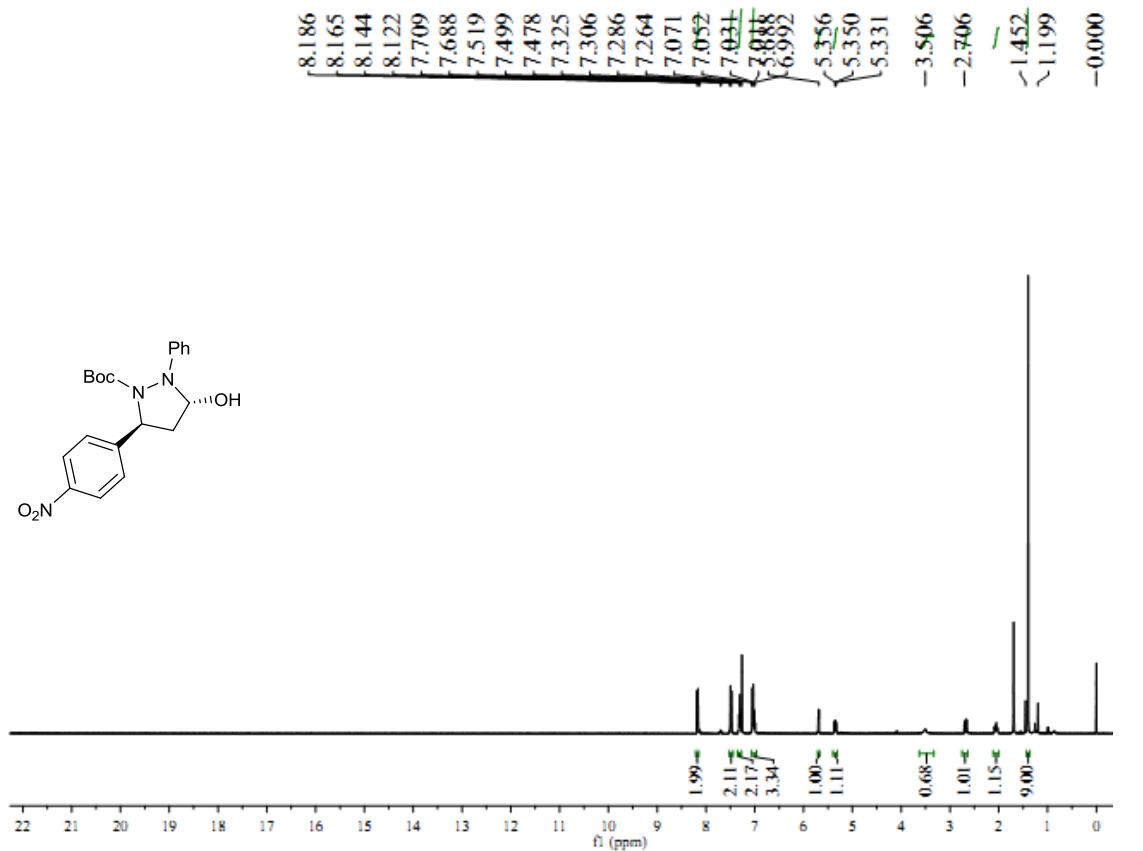




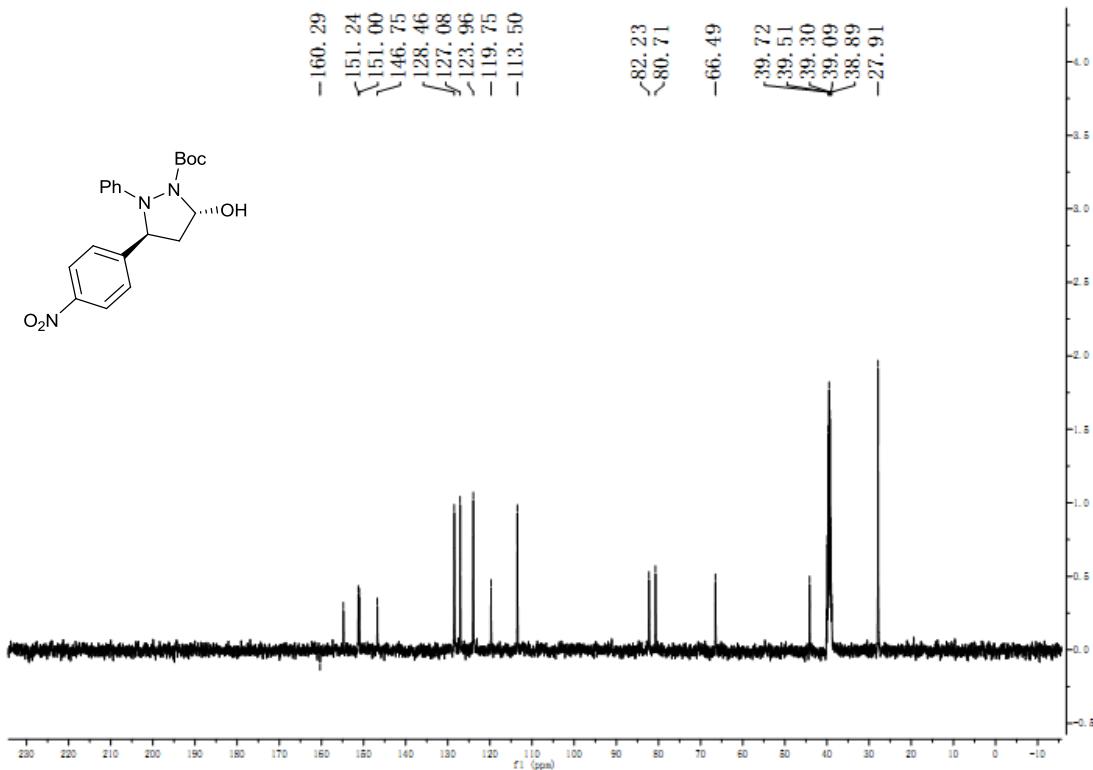
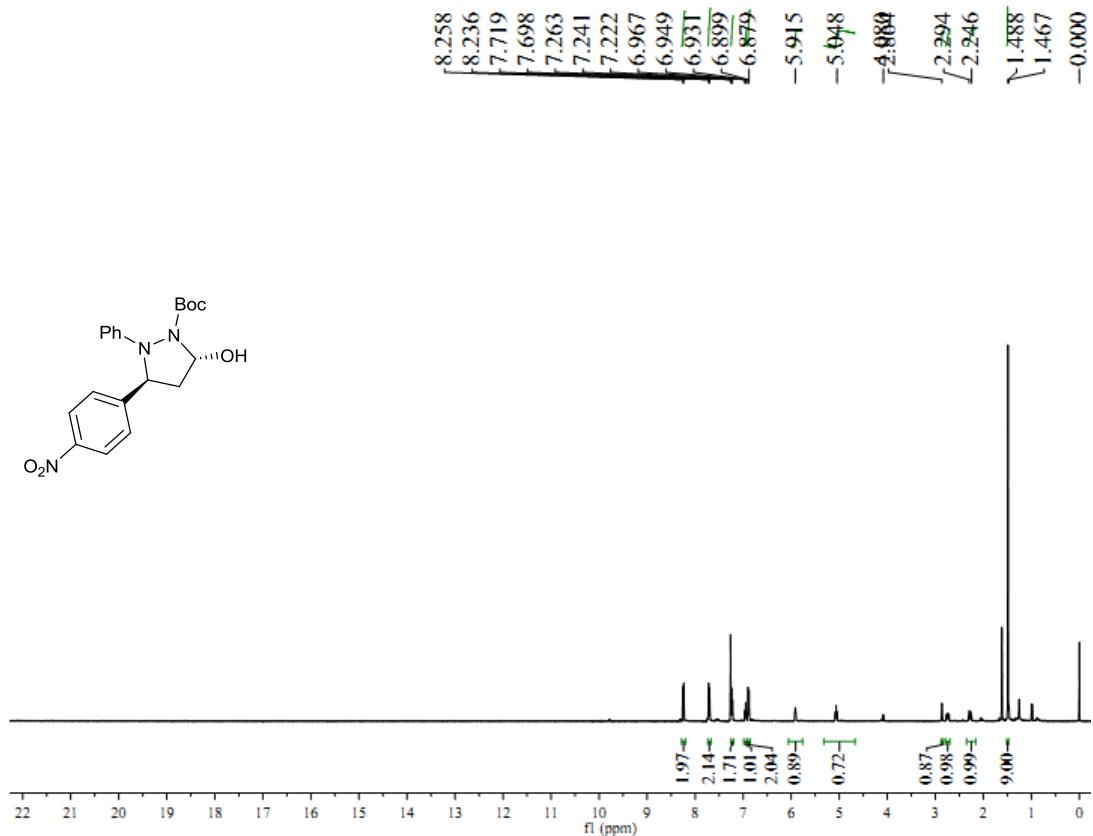
**4m**



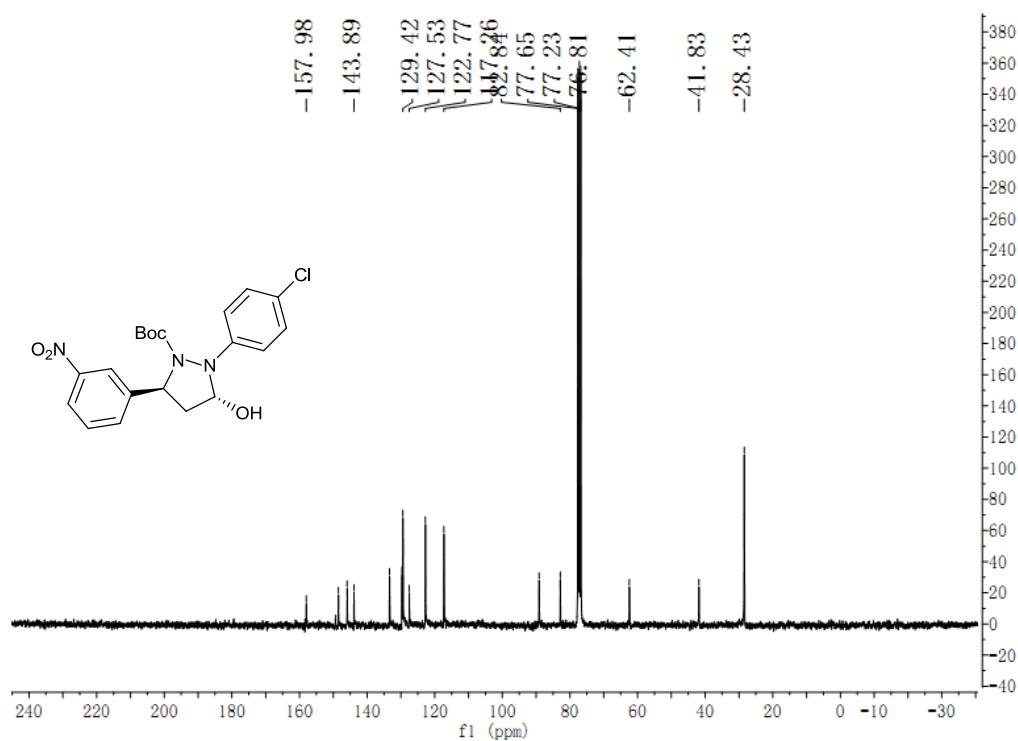
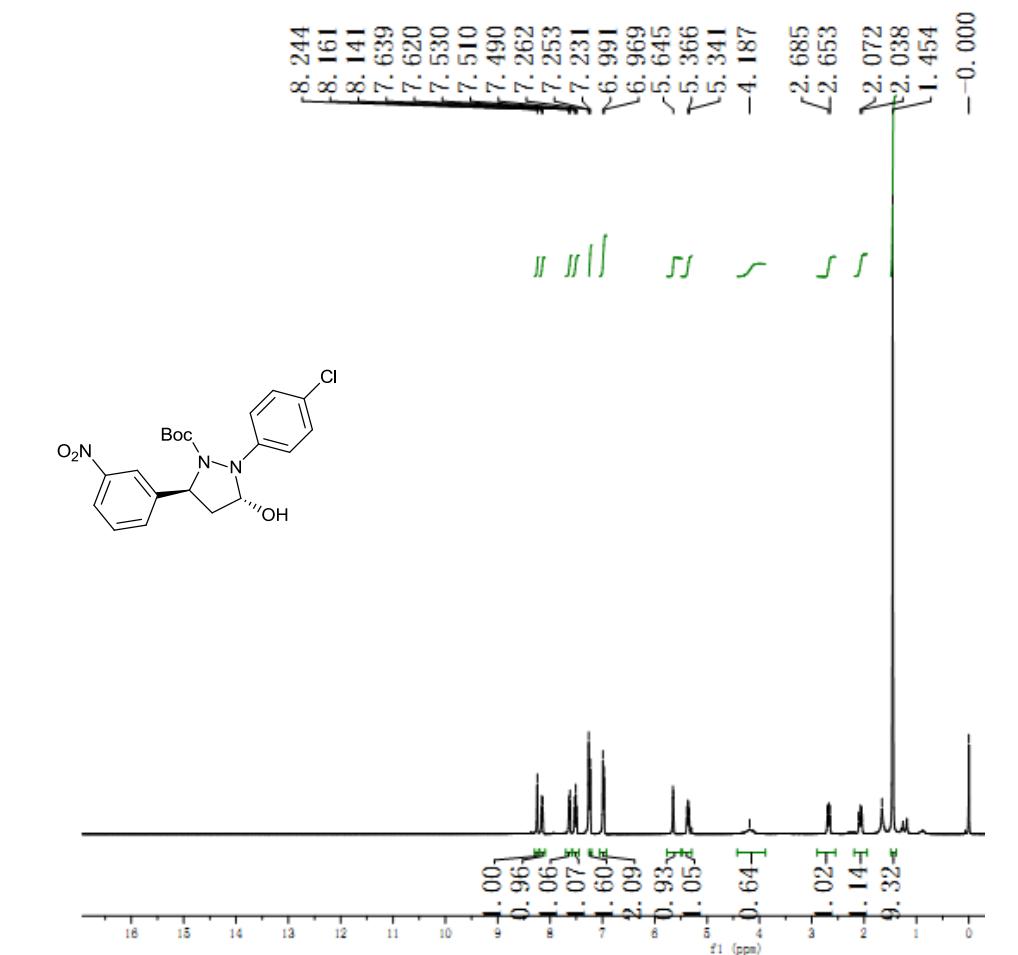
**4n**



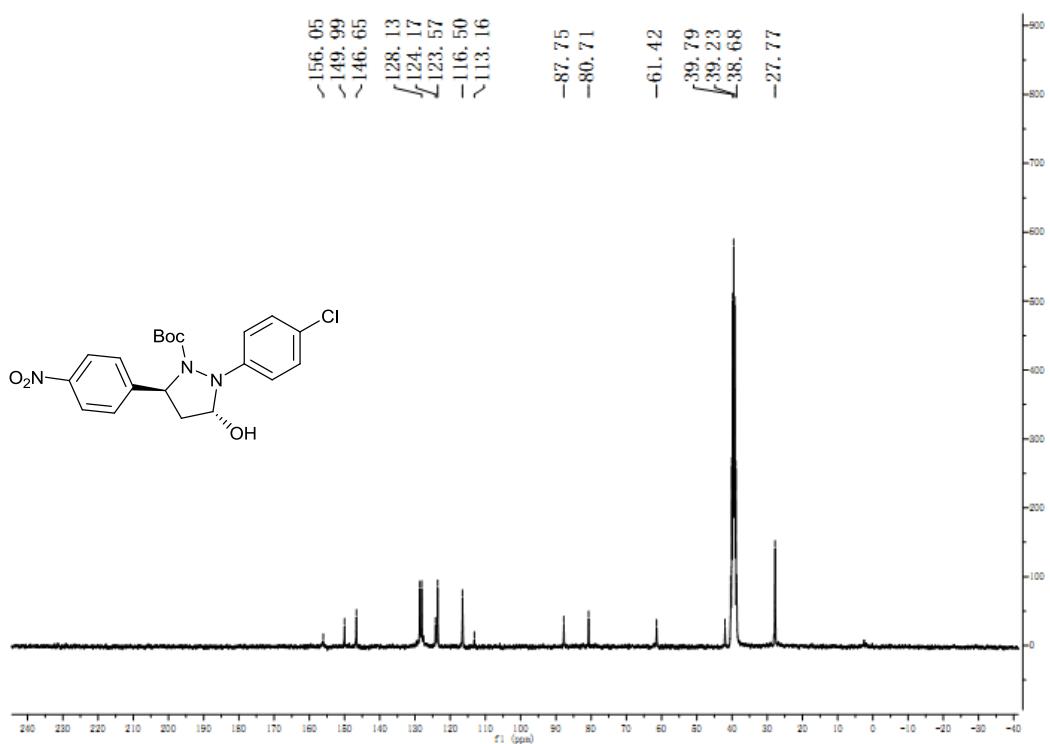
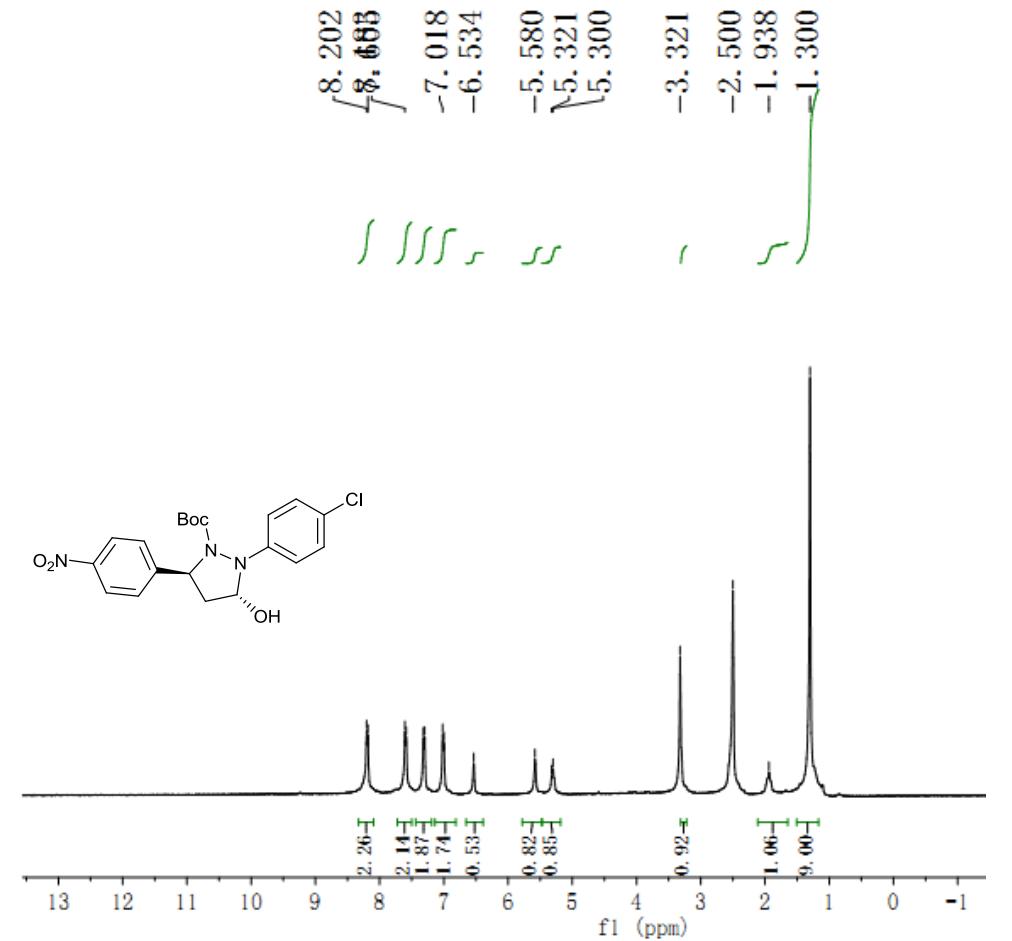
**4n'**



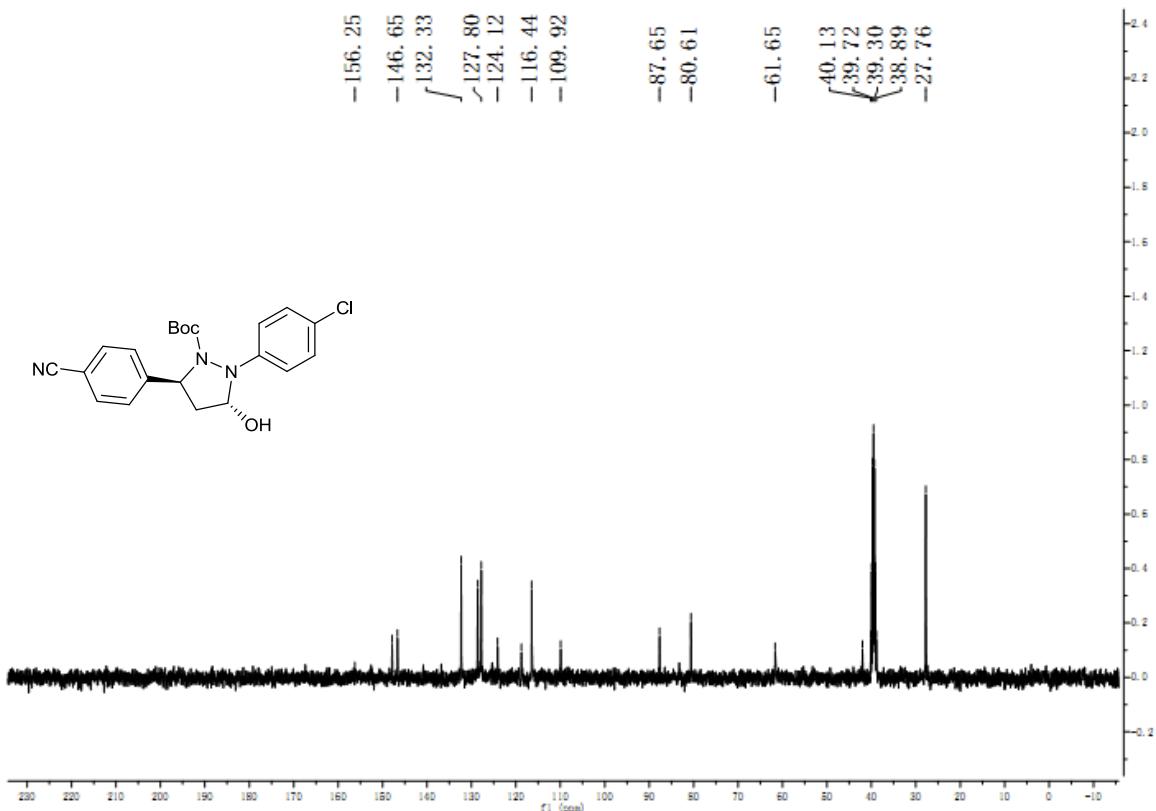
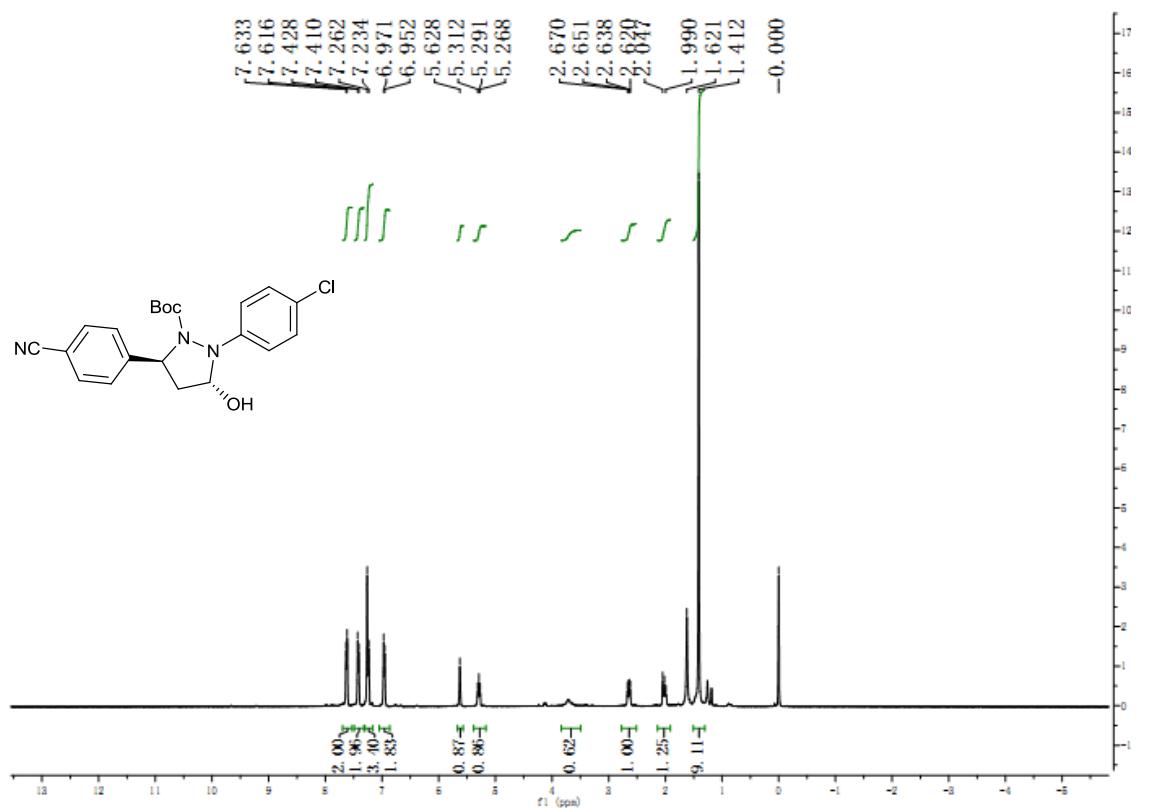
**4o**



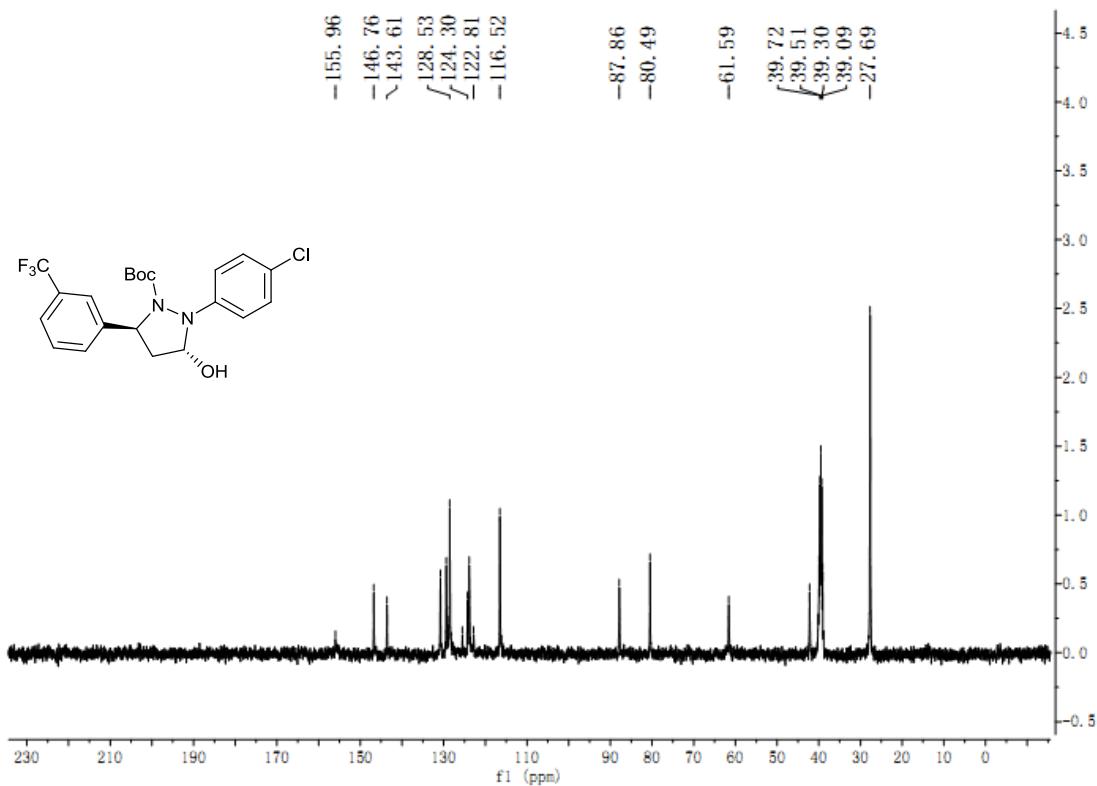
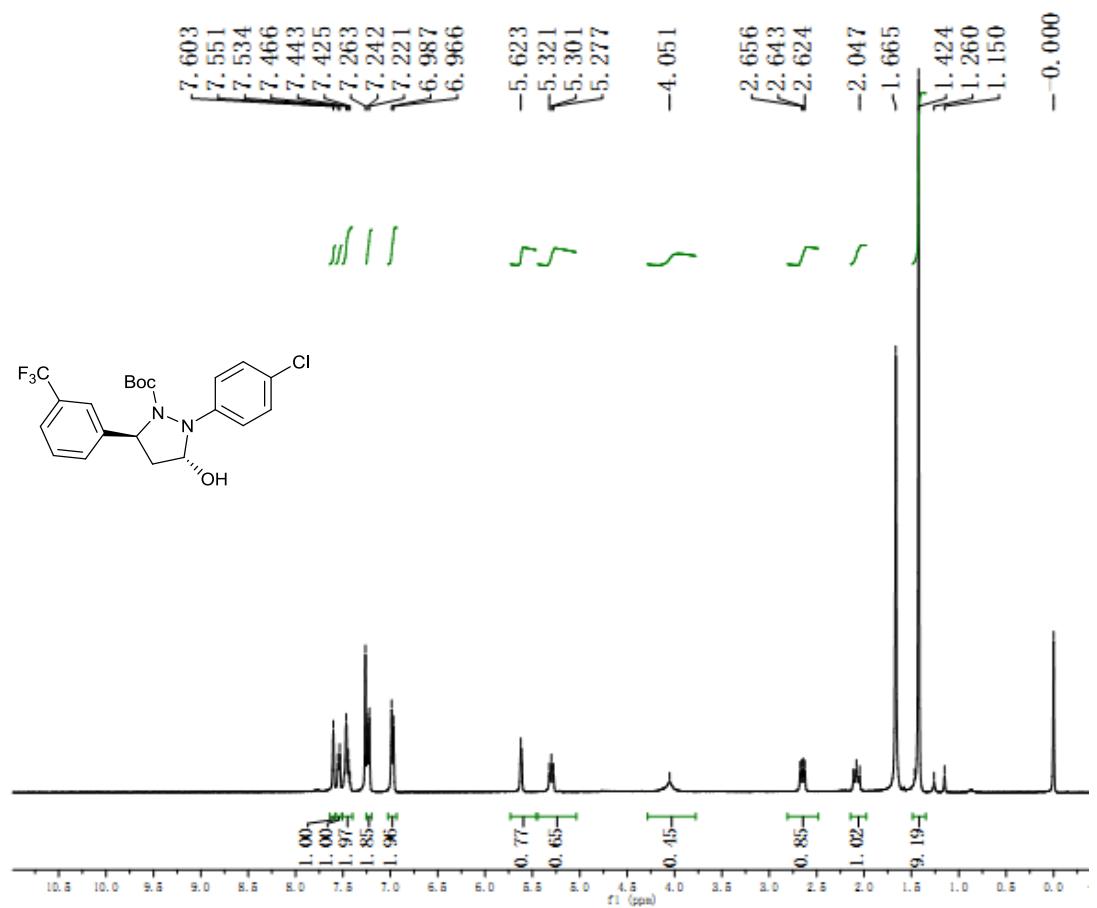
4p



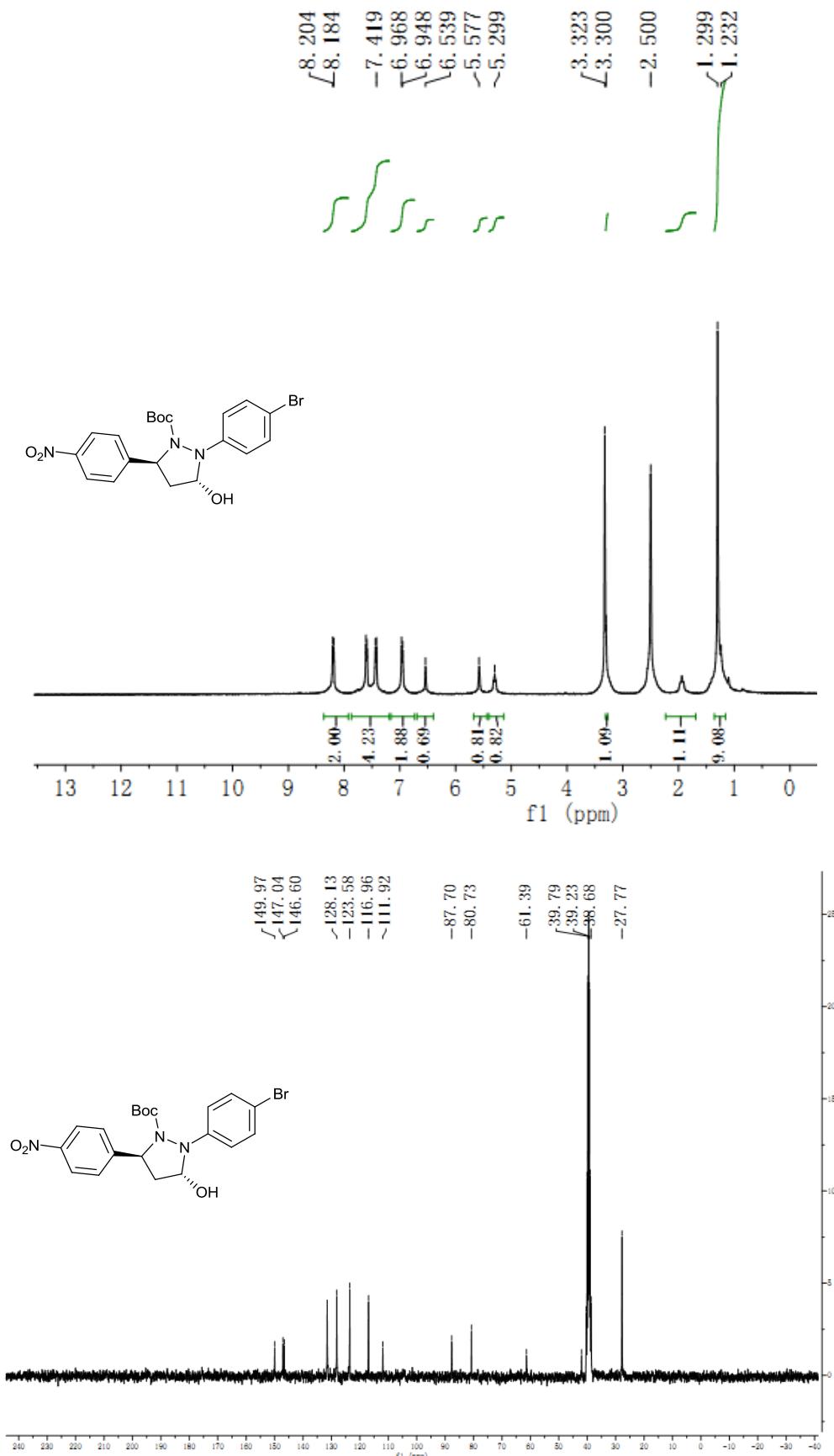
**4q**



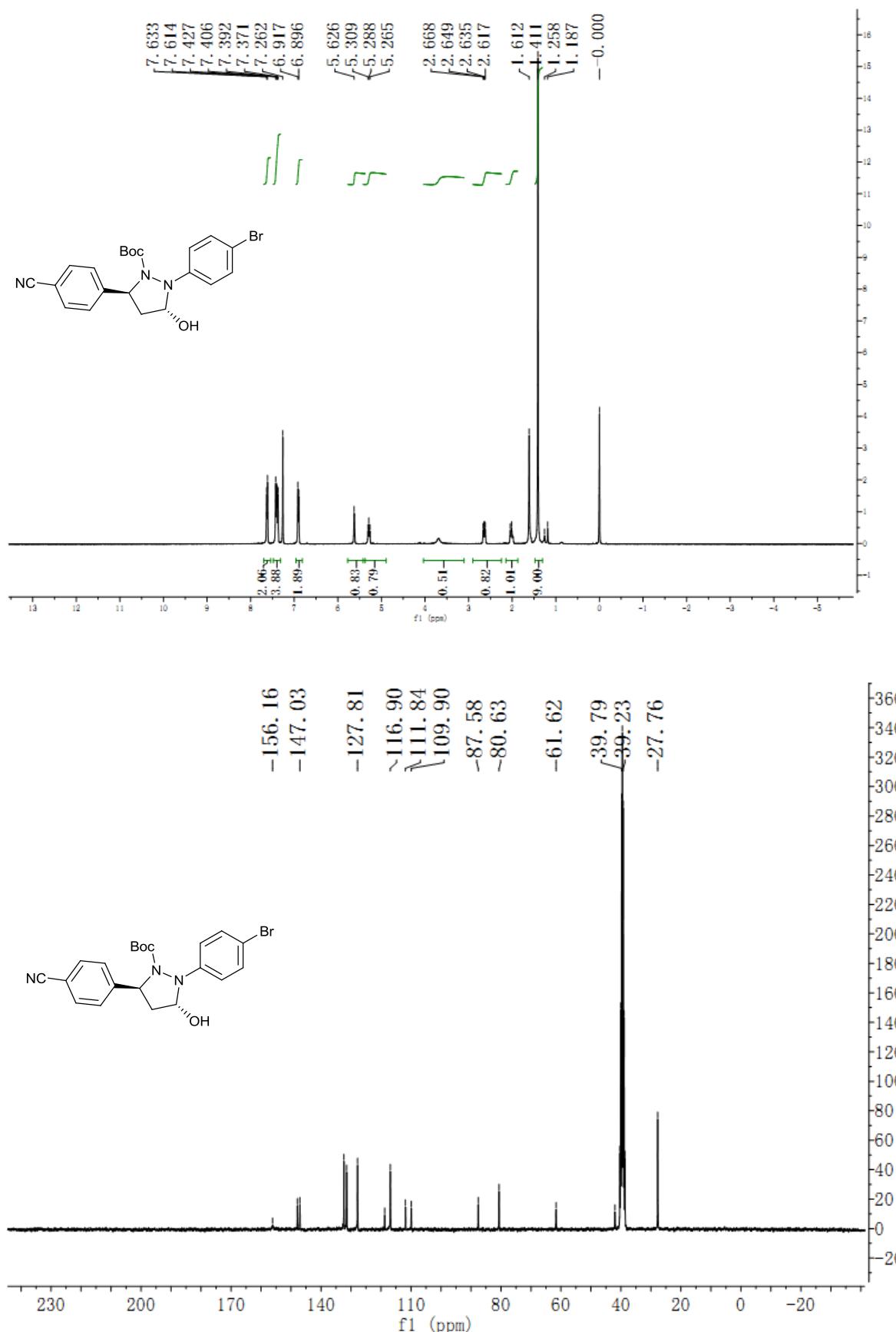
**4r**



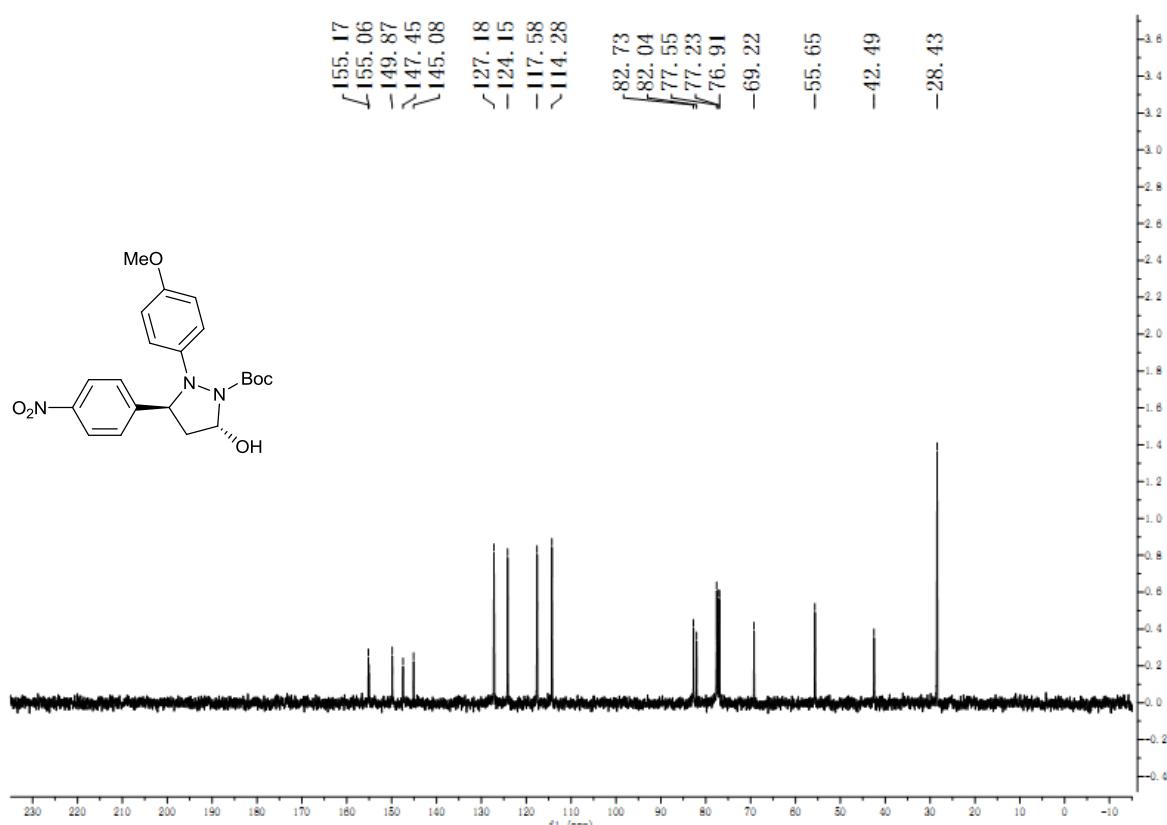
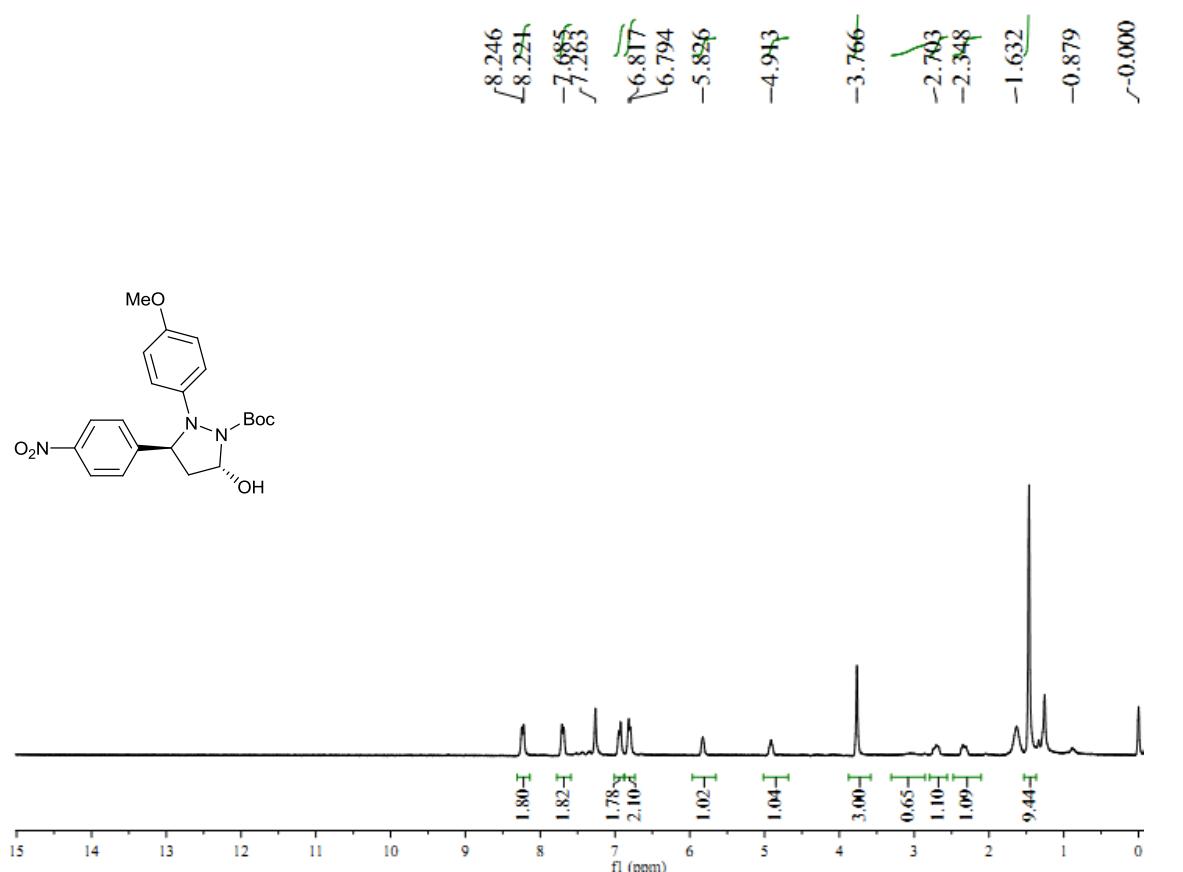
**4s**



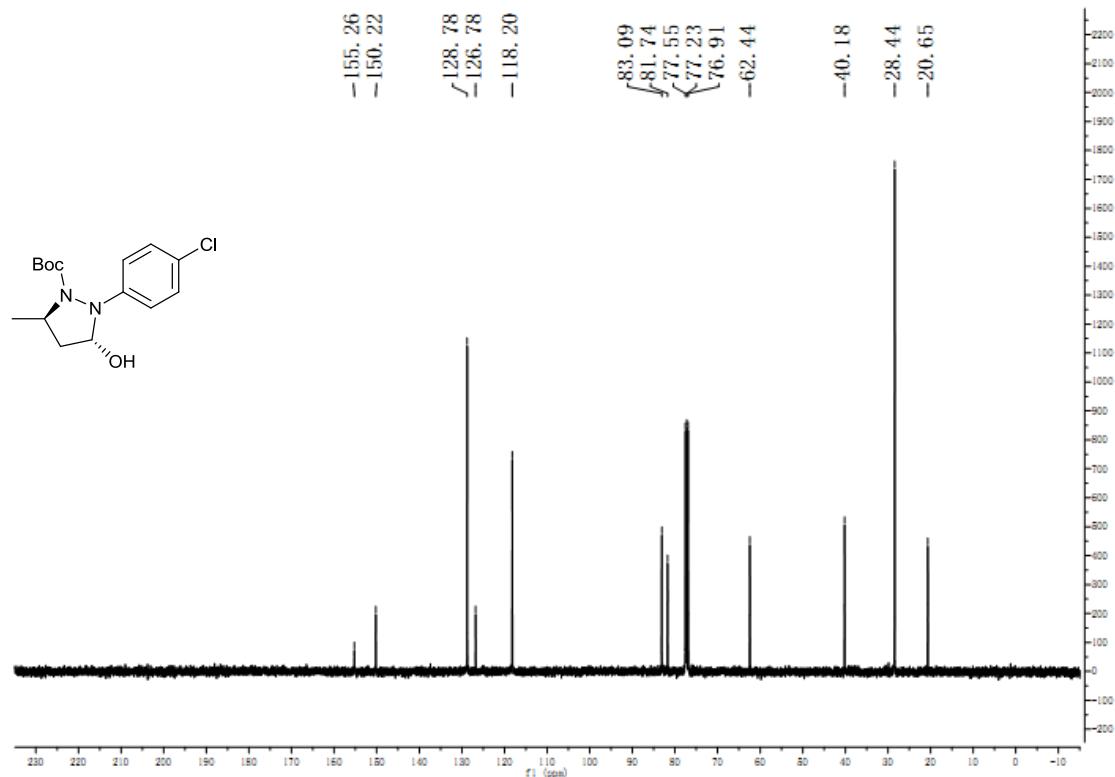
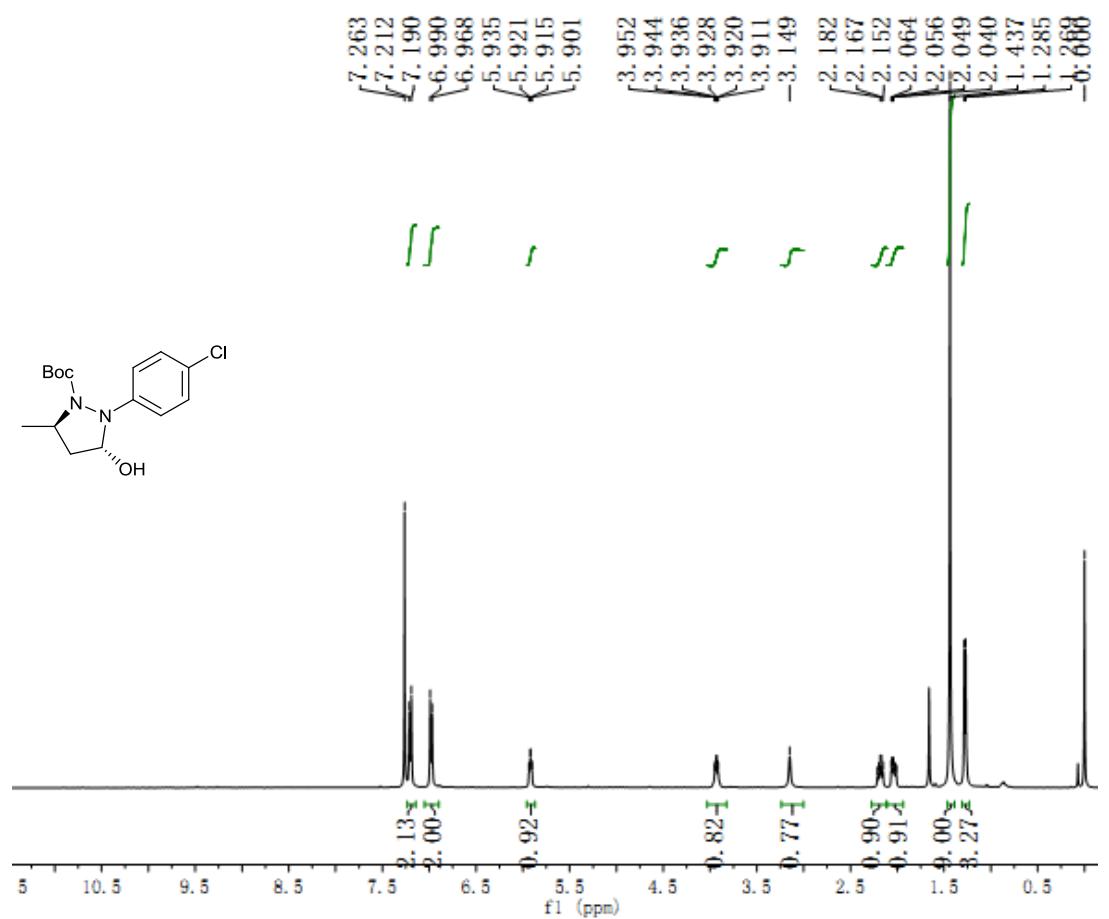
**4t**



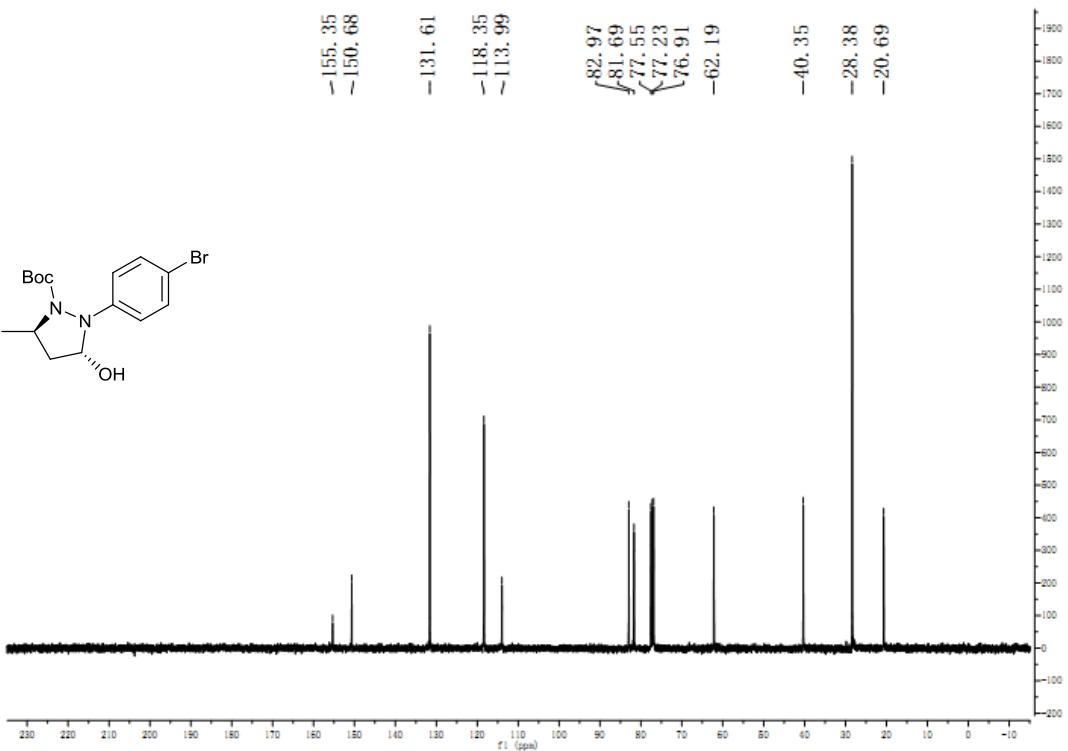
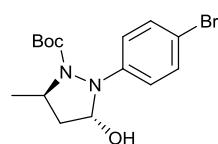
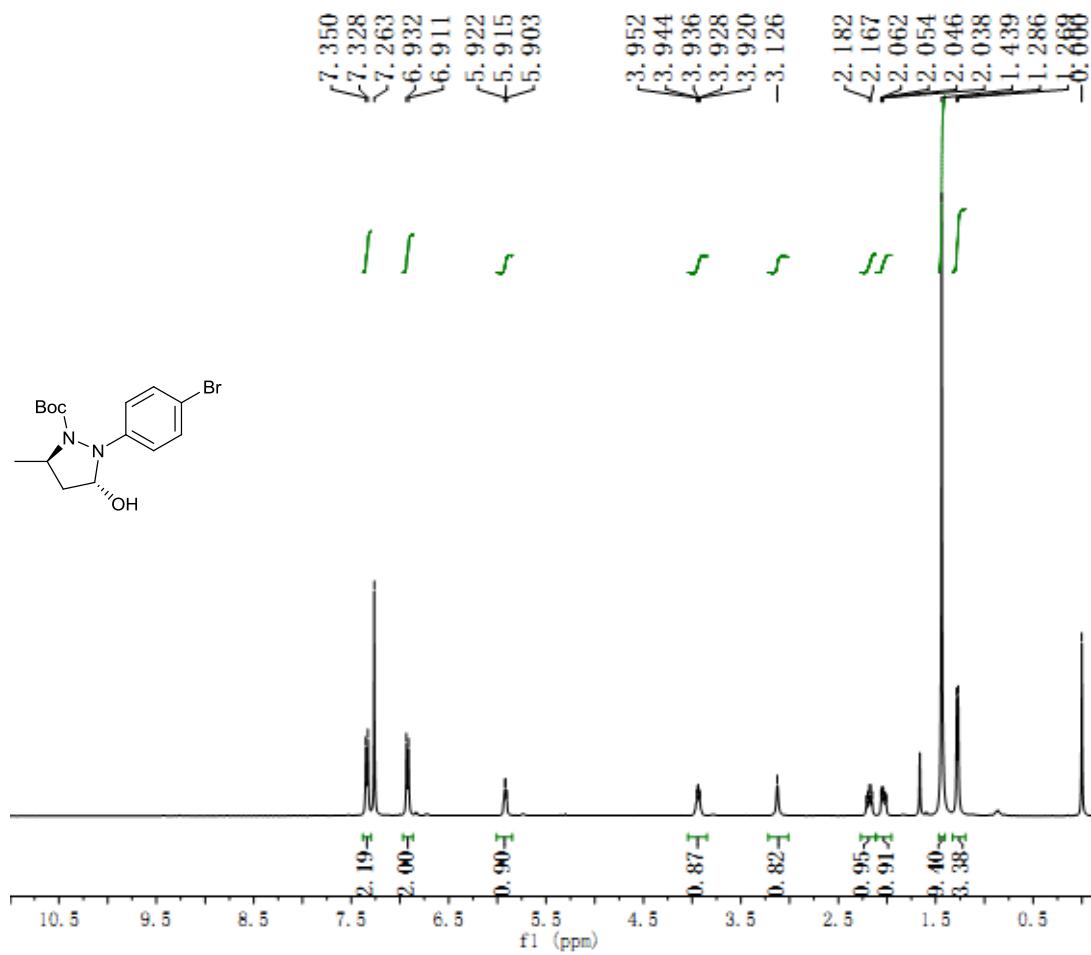
**4u'**



**4v**

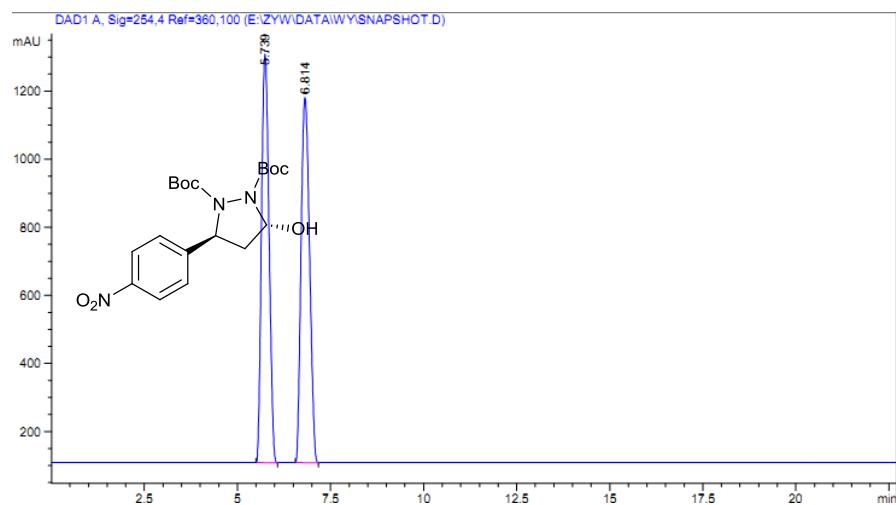


4w

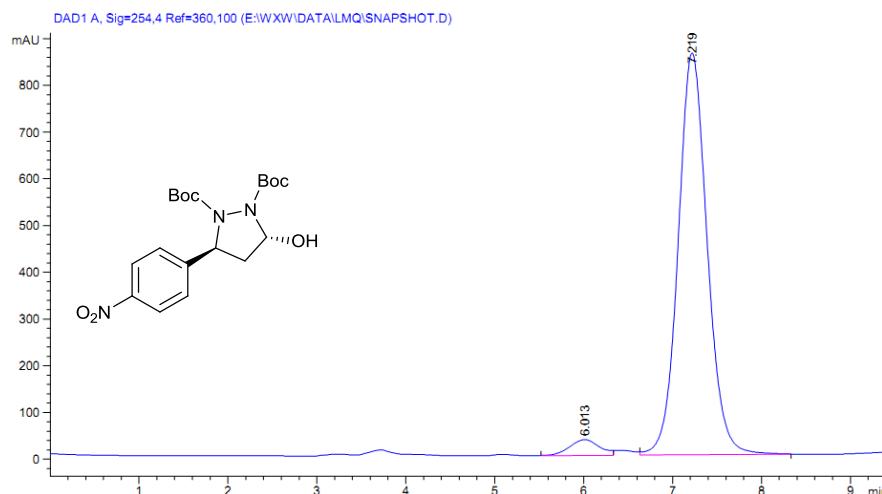


## 6. HPLC spectra

**4a**

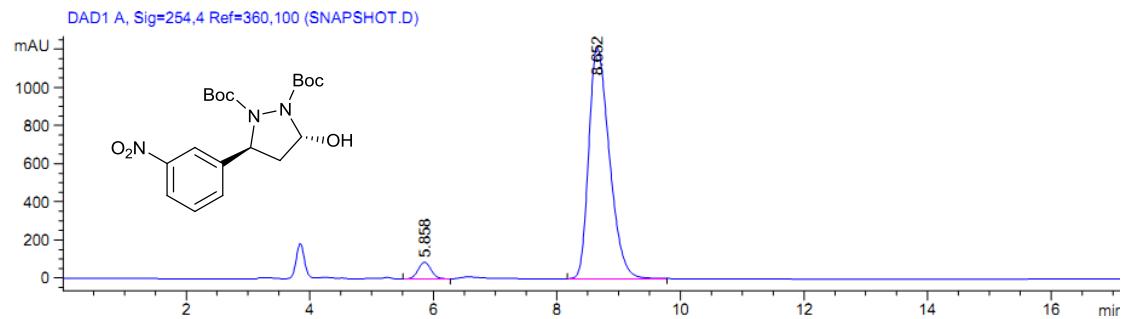
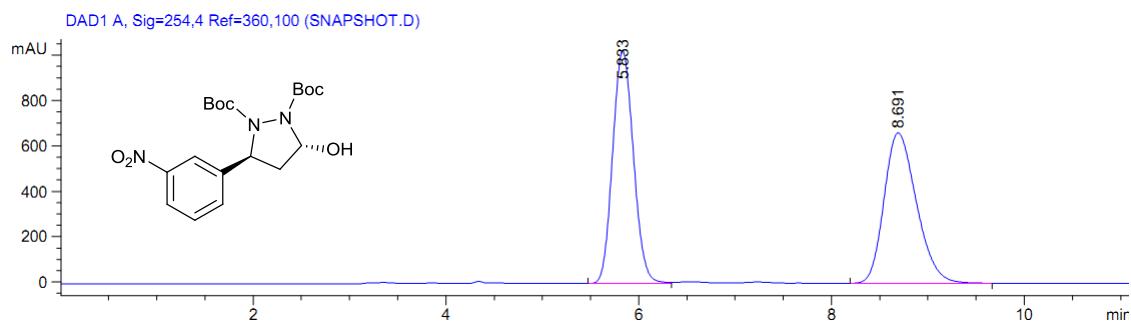


Totals : 3.37339e4 2272.73108

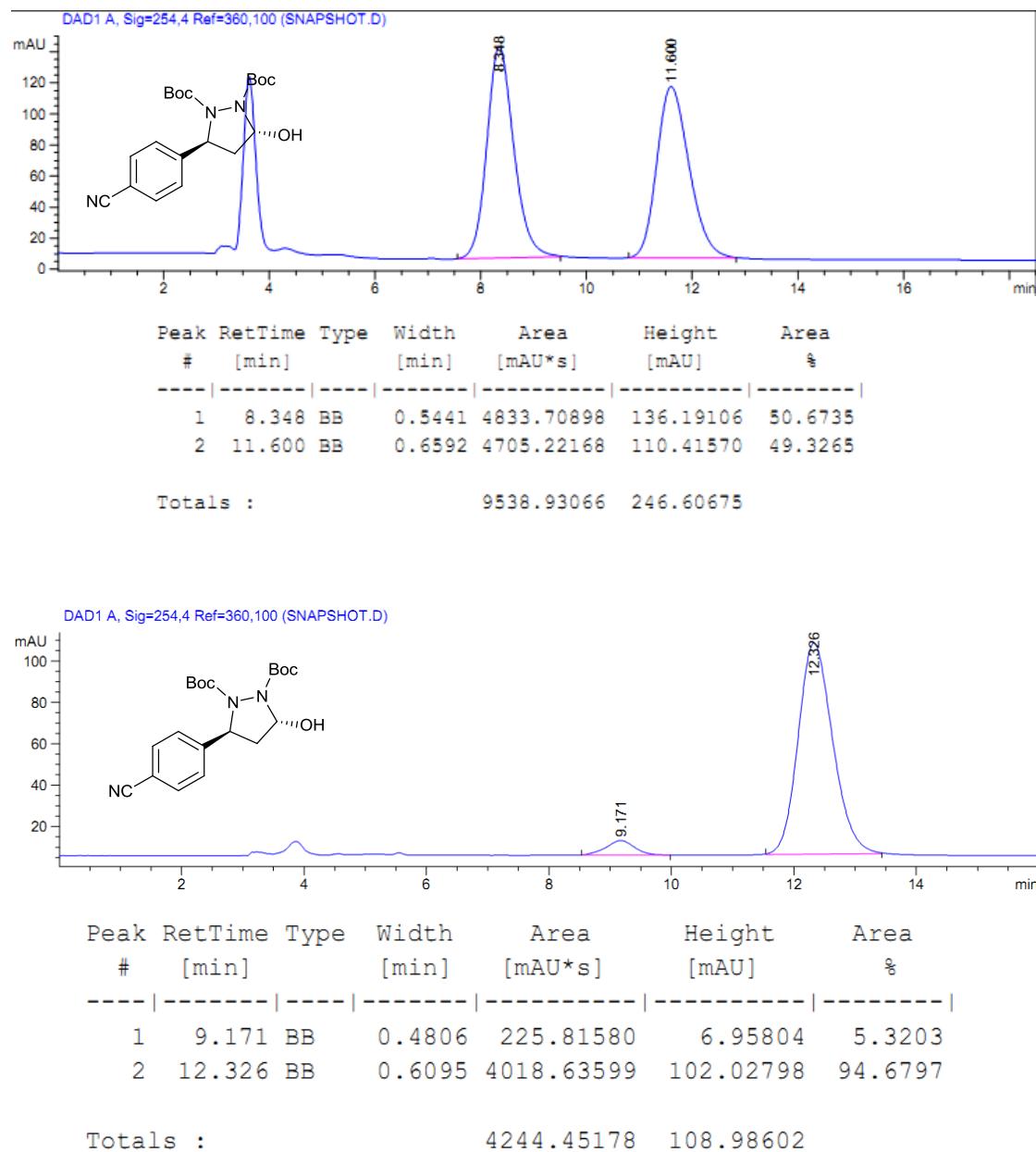


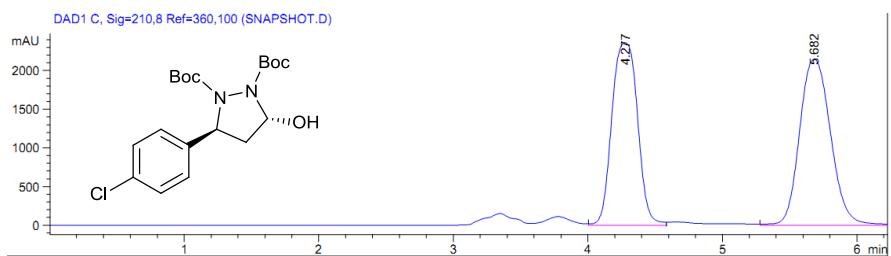
| Peak RetTime | Type | Width  | Area      | Height    | Area %  |
|--------------|------|--------|-----------|-----------|---------|
| # [min]      |      | [min]  | [mAU*s]   | [mAU]     |         |
| 1 6.013      | BV   | 0.3515 | 777.24738 | 33.64997  | 3.8339  |
| 2 7.219      | VB   | 0.3465 | 1.94957e4 | 859.92670 | 96.1661 |

Totals : 2.02730e4 893.57666

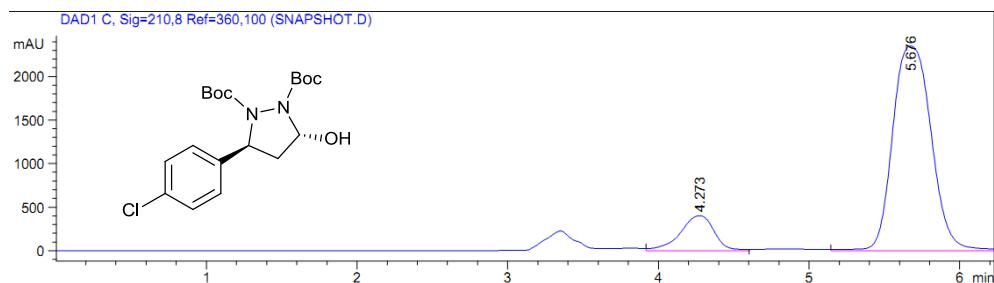
**4b**

Totals : 2.93308e4 1297.73032

**4c**

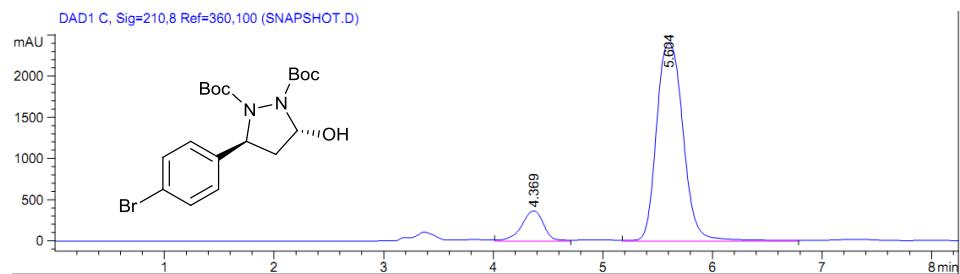
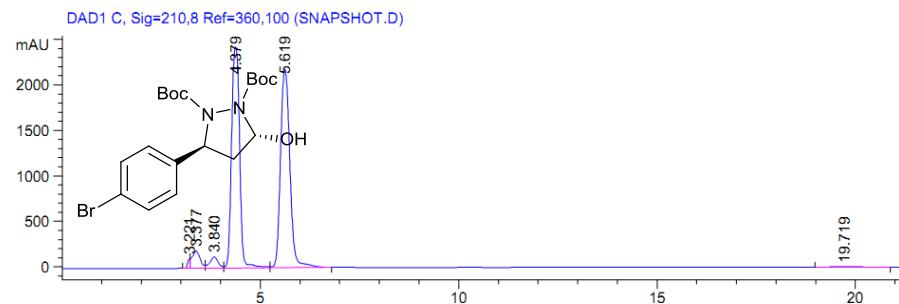
**4d**

| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %               |
|----------|---------------|------|-------------|--------------|--------------|----------------------|
| 1        | 4.277         | VV   | 0.2146      | 3.13104e4    | 2362.74780   | 47.6812              |
| 2        | 5.682         | VBA  | 0.2527      | 3.43558e4    | 2146.62744   | 52.3188              |
| Totals : |               |      |             |              |              | 6.56663e4 4509.37524 |



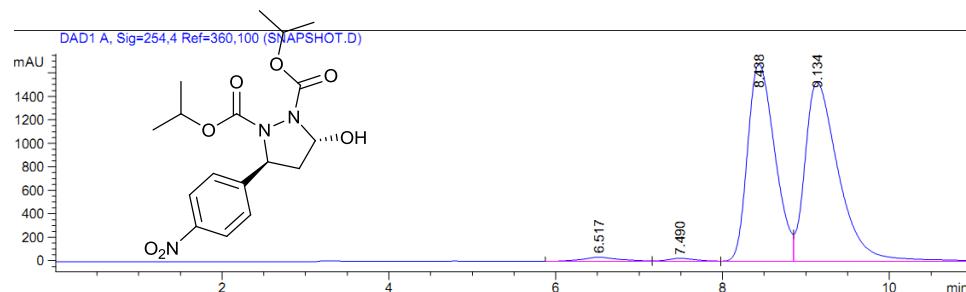
| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %               |
|----------|---------------|------|-------------|--------------|--------------|----------------------|
| 1        | 4.273         | VV   | 0.2430      | 6286.99902   | 400.71469    | 13.0882              |
| 2        | 5.676         | VBA  | 0.2831      | 4.17485e4    | 2351.78198   | 86.9118              |
| Totals : |               |      |             |              |              | 4.80355e4 2752.49667 |

**4e**



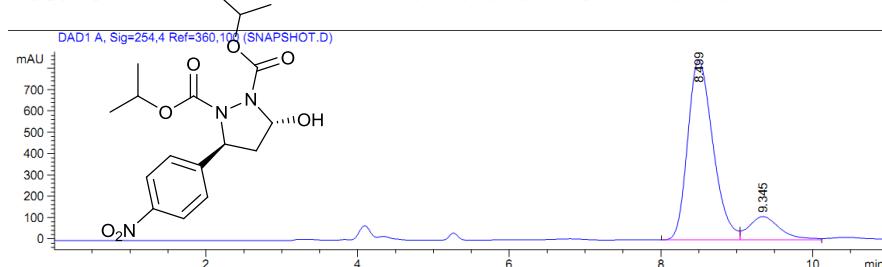
| Peak | RetTime | Type | Width  | Area       | Height     | Area %  |
|------|---------|------|--------|------------|------------|---------|
| #    | [min]   |      | [min]  | [mAU*s]    | [mAU]      | %       |
| 1    | 4.369   | VV   | 0.2187 | 5168.65137 | 366.23688  | 11.3073 |
| 2    | 5.604   | VB   | 0.2674 | 4.05419e4  | 2395.49609 | 88.6927 |

Totals : 4.57105e4 2761.73297

**4h**

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 6.517         | BV   | 0.4349      | 1180.11609   | 37.52028     | 1.4272  |
| 2      | 7.490         | VV   | 0.3694      | 646.00006    | 26.22237     | 0.7812  |
| 3      | 8.438         | VV   | 0.3516      | 3.80539e4    | 1684.24658   | 46.0201 |
| 4      | 9.134         | VBA  | 0.4230      | 4.28097e4    | 1527.50183   | 51.7715 |

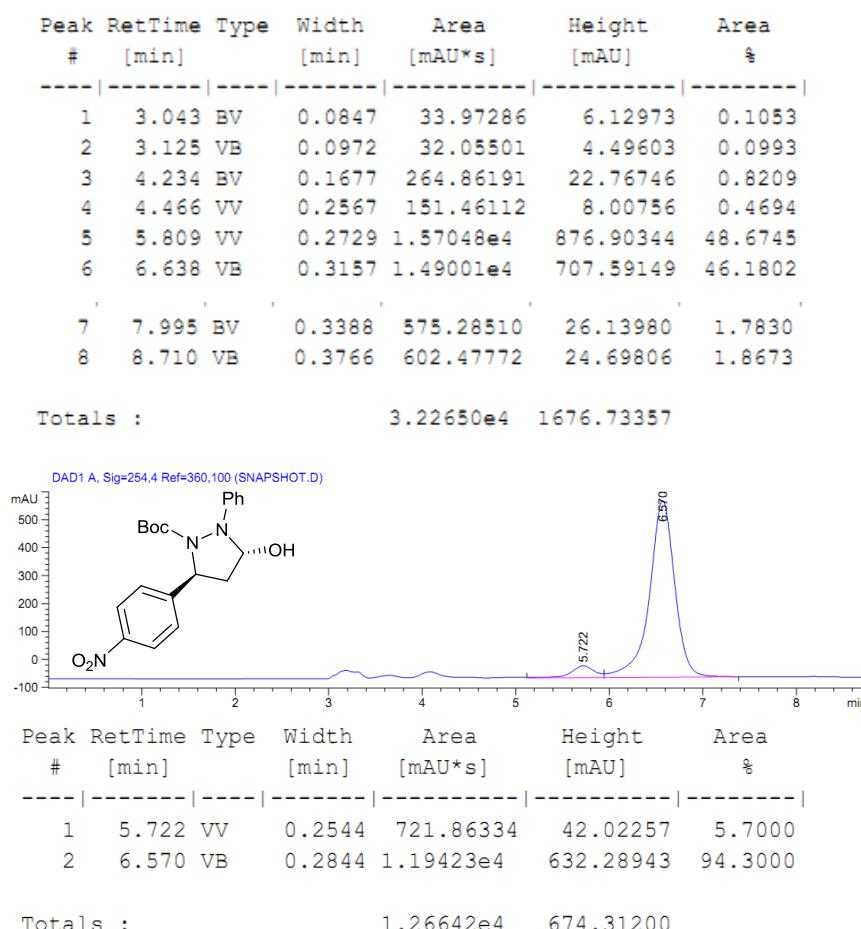
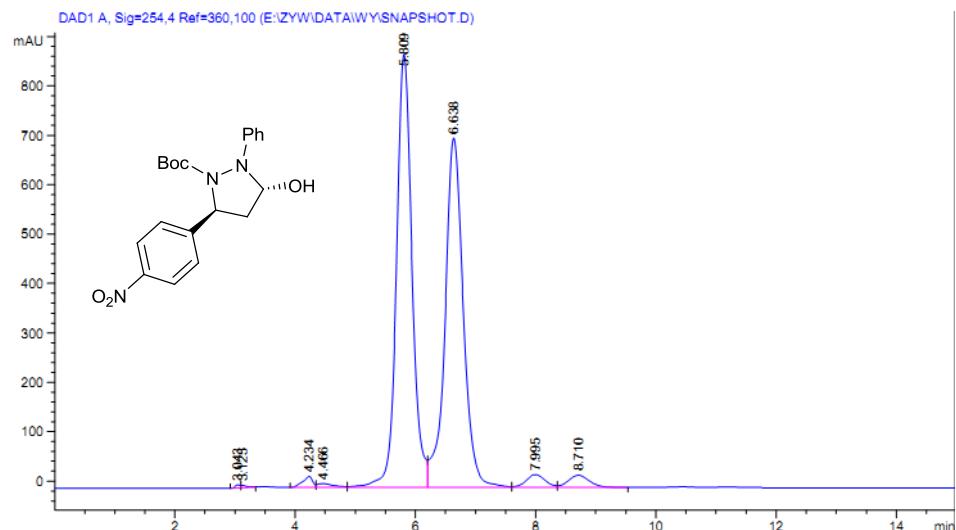
Totals : 8.26897e4 3275.49106



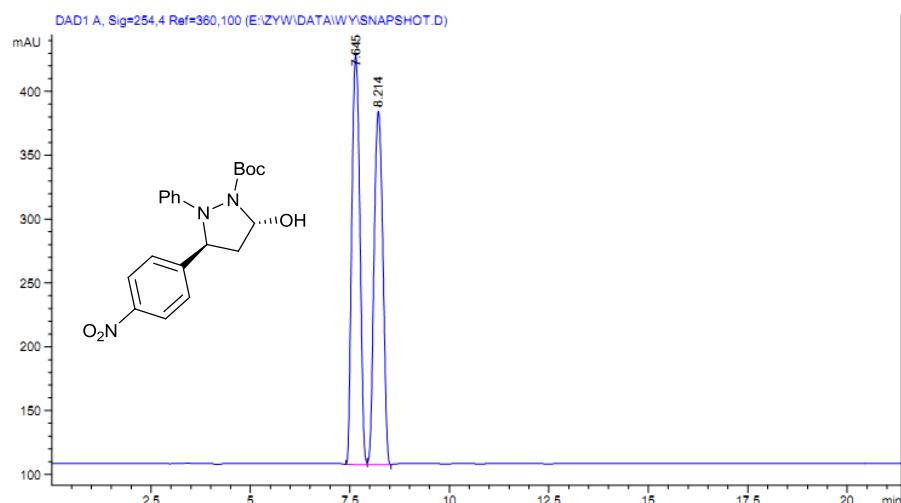
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 8.499         | BV   | 0.3601      | 1.94746e4    | 841.03552    | 86.0585 |
| 2      | 9.345         | VV   | 0.4301      | 3154.87695   | 109.49943    | 13.9415 |

Totals : 2.26295e4 950.53495

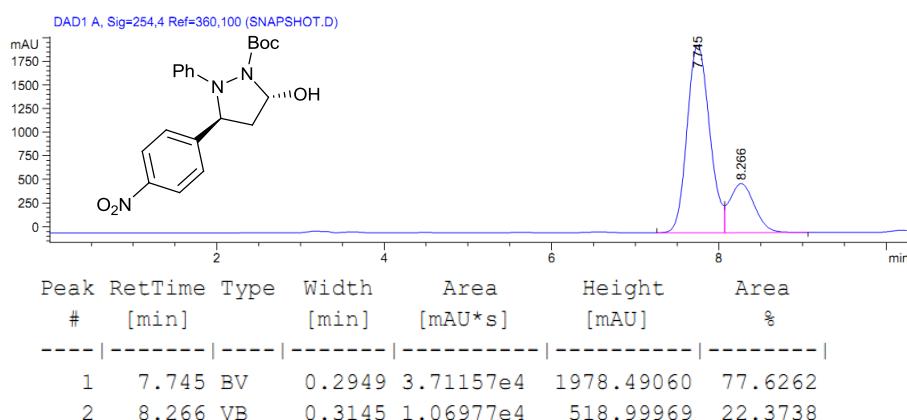
**4n**



**4n'**

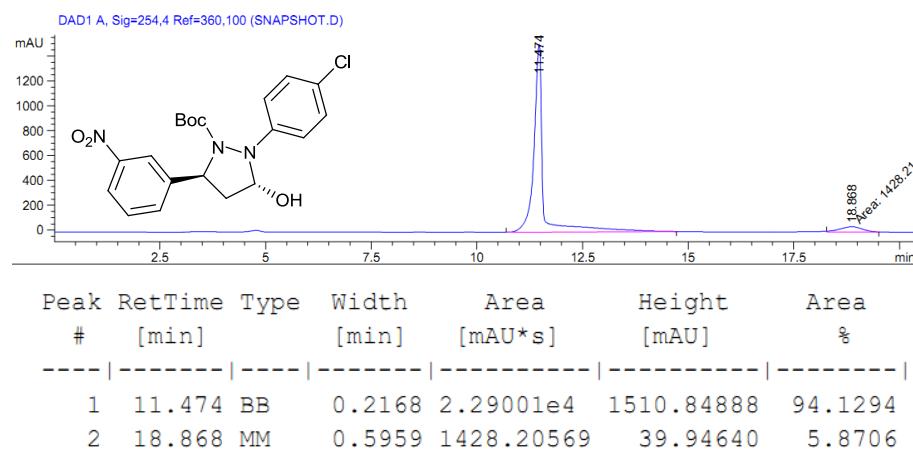
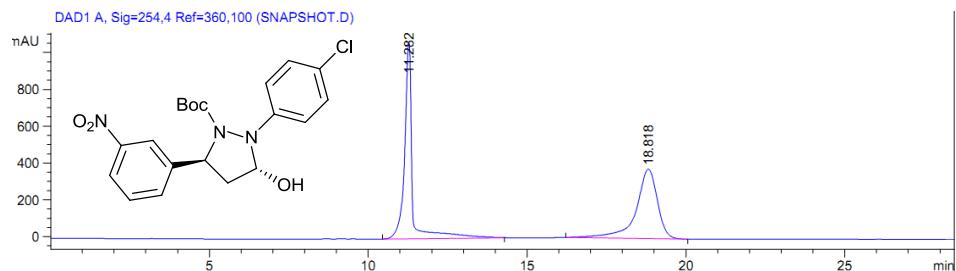


Totals : 8761.02197 597.79047

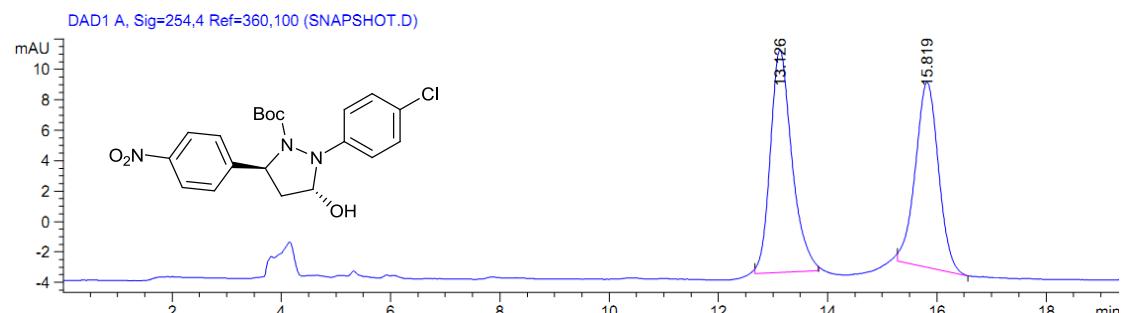


Totals : 4.78134e4 2497.49030

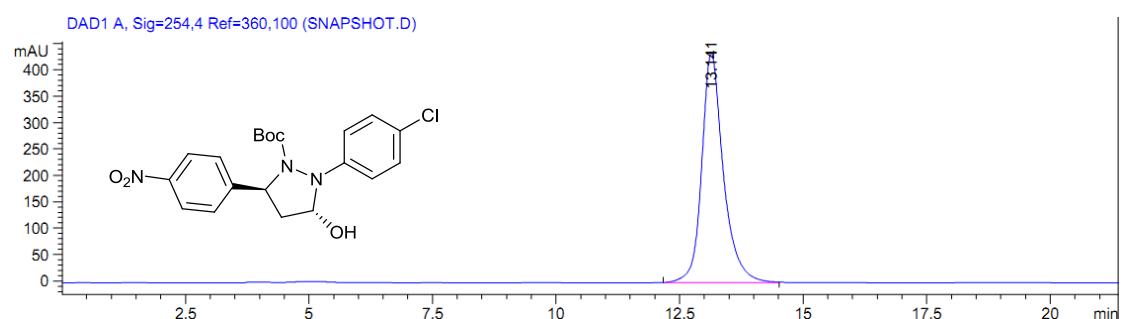
**4o**



**4p**

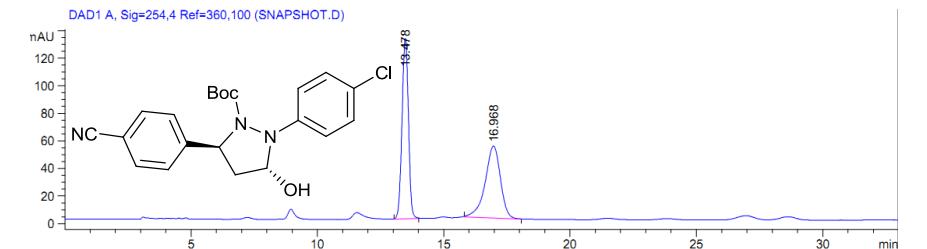


| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %   |
|----------|---------------|------|-------------|--------------|--------------|----------|
| 1        | 13.126        | BB   | 0.4110      | 402.69333    | 14.63496     | 53.0819  |
| 2        | 15.819        | BB   | 0.4515      | 355.93338    | 12.15998     | 46.9181  |
| Totals : |               |      |             |              | 758.62671    | 26.79494 |



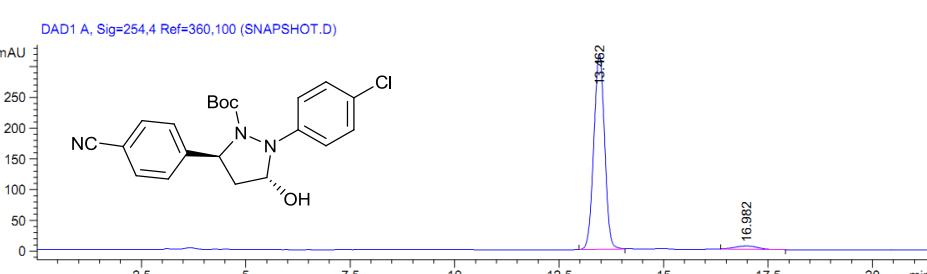
| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %    |
|----------|---------------|------|-------------|--------------|--------------|-----------|
| 1        | 13.141        | BB   | 0.4503      | 1.32145e4    | 435.12561    | 100.0000  |
| Totals : |               |      |             |              | 1.32145e4    | 435.12561 |

**4q**



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 13.478        | BB   | 0.2803      | 2312.92480   | 130.79883    | 51.2717 |
| 2      | 16.968        | BB   | 0.6386      | 2198.19312   | 52.27586     | 48.7283 |

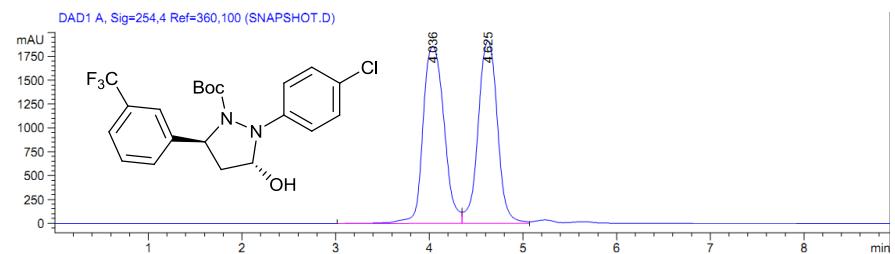
Totals : 4511.11792 183.07469



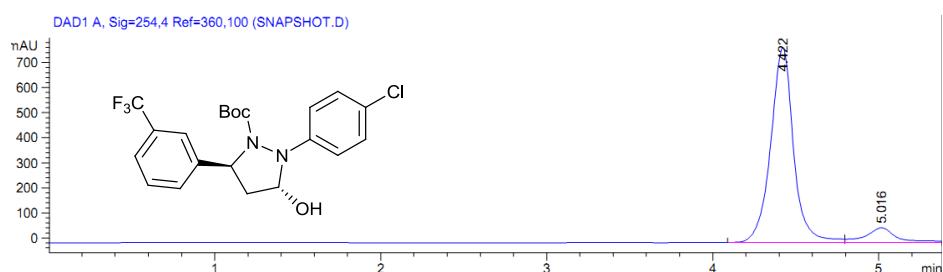
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 13.462        | BB   | 0.2832      | 5680.49854   | 316.81180    | 96.6309 |
| 2      | 16.982        | BB   | 0.5374      | 198.05397    | 5.45727      | 3.3691  |

Totals : 5878.55251 322.26907

**4r**



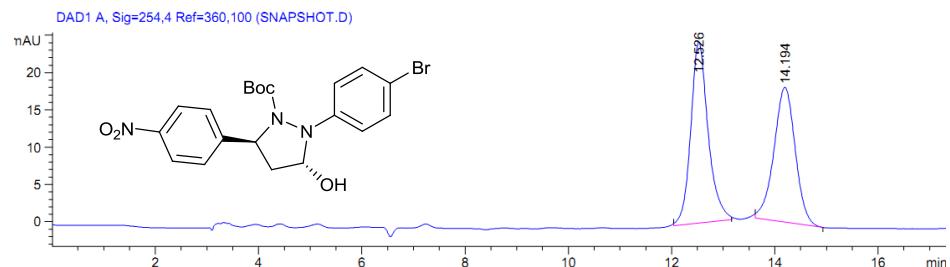
| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %     |
|----------|---------------|------|-------------|--------------|--------------|------------|
| 1        | 4.036         | BV   | 0.2557      | 2.89939e4    | 1861.48999   | 51.4682    |
| 2        | 4.625         | VV   | 0.2268      | 2.73398e4    | 1911.89856   | 48.5318    |
| Totals : |               |      |             |              | 5.63337e4    | 3773.38855 |



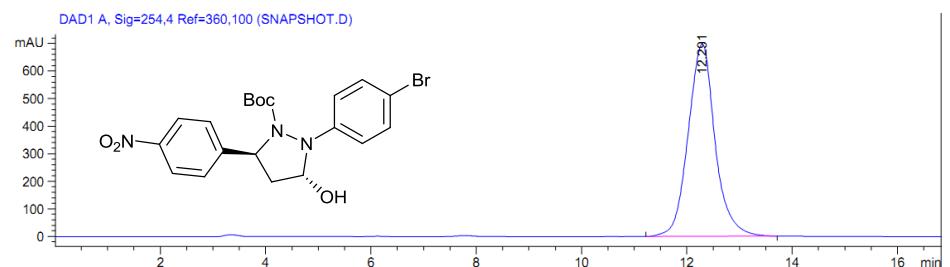
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 4.422         | BV   | 0.1442      | 7497.35645   | 779.29291    | 90.5720 |
| 2      | 5.016         | VBA  | 0.1852      | 780.42657    | 59.45105     | 9.4280  |

Totals : 8277.78302 838.74395

**4s**

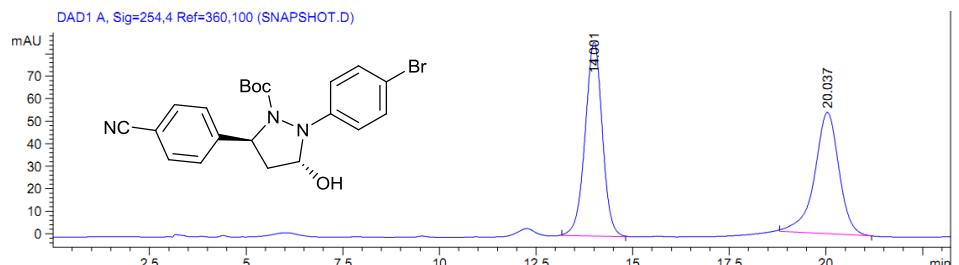


| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %   |
|----------|---------------|------|-------------|--------------|--------------|----------|
| 1        | 12.526        | BB   | 0.3511      | 567.27557    | 24.23341     | 52.2384  |
| 2        | 14.194        | BB   | 0.4404      | 518.66034    | 18.09674     | 47.7616  |
| Totals : |               |      |             |              | 1085.93591   | 42.33016 |



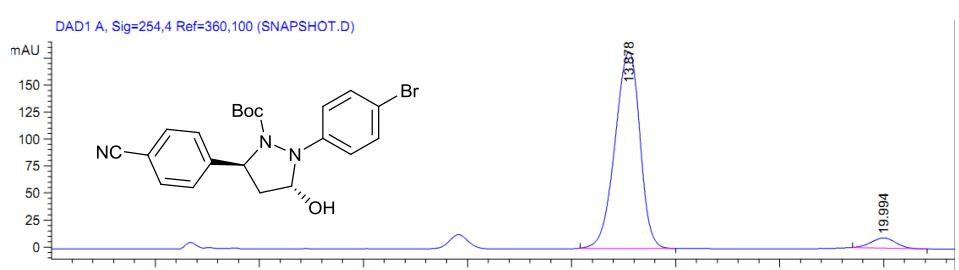
| Peak #   | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %    |
|----------|---------------|------|-------------|--------------|--------------|-----------|
| 1        | 12.291        | BB   | 0.5421      | 2.47936e4    | 698.52704    | 100.0000  |
| Totals : |               |      |             |              | 2.47936e4    | 698.52704 |

**4t**



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 14.001        | BB   | 0.4759      | 2673.70679   | 86.19019     | 52.9521 |
| 2      | 20.037        | BB   | 0.6606      | 2375.58862   | 54.06293     | 47.0479 |

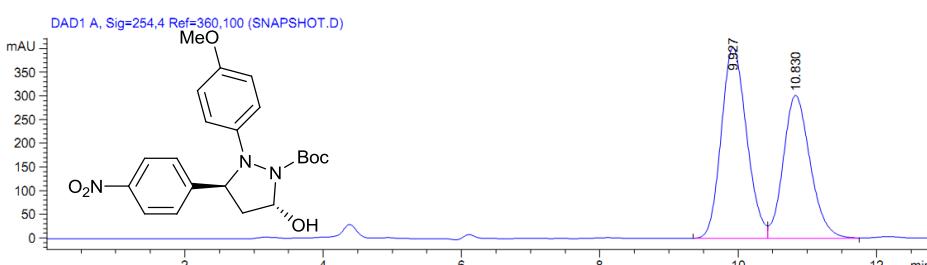
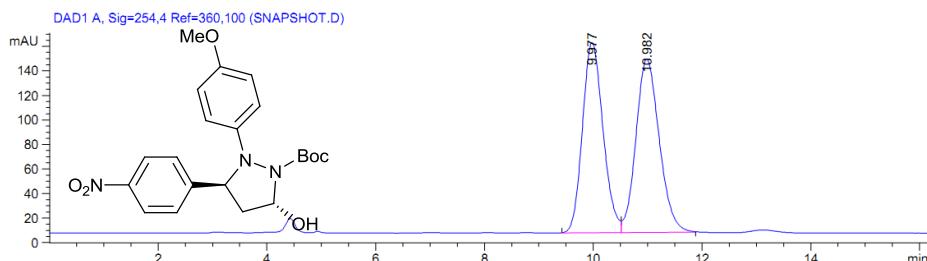
Totals : 5049.29541 140.25311



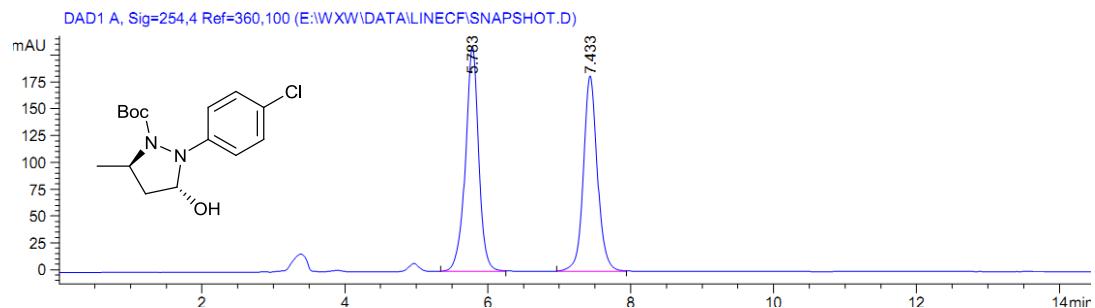
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 13.878        | BB   | 0.6524      | 7573.98975   | 182.40045    | 95.1768 |
| 2      | 19.994        | BB   | 0.6235      | 383.82449    | 9.37711      | 4.8232  |

Totals : 7957.81424 191.77756

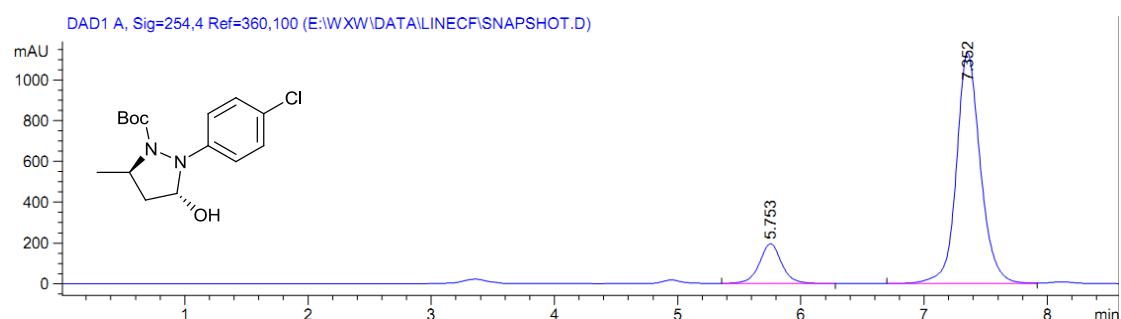
**4u'**



**4v**

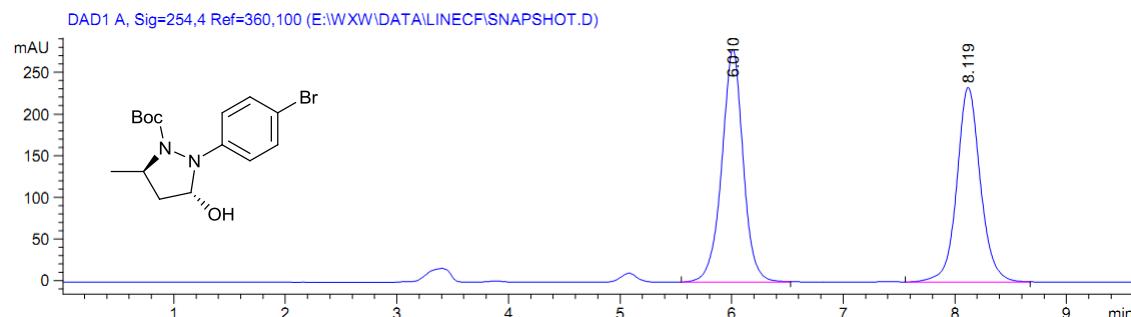


| Peak #          | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU]      | Area %           |
|-----------------|---------------|------|-------------|--------------|-------------------|------------------|
| 1               | 5.783         | BB   | 0.1927      | 2700.02515   | 209.00623         | 52.2106          |
| 2               | 7.433         | BB   | 0.2064      | 2471.38770   | 181.97112         | 47.7894          |
| <b>Totals :</b> |               |      |             |              | <b>5171.41284</b> | <b>390.97734</b> |



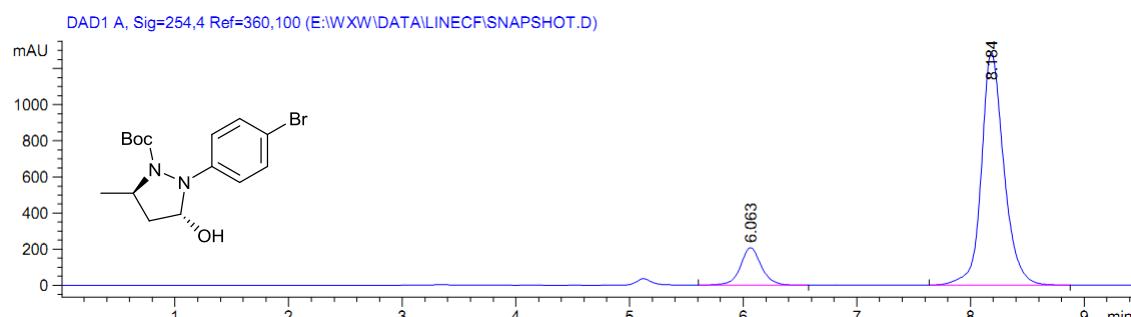
| Peak #          | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU]     | Area %            |
|-----------------|---------------|------|-------------|--------------|------------------|-------------------|
| 1               | 5.753         | BB   | 0.1898      | 2479.35278   | 195.70689        | 13.9110           |
| 2               | 7.352         | BV   | 0.2062      | 1.53436e4    | 1131.24634       | 86.0890           |
| <b>Totals :</b> |               |      |             |              | <b>1.78229e4</b> | <b>1326.95323</b> |

**4w**



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 6.010         | BB   | 0.1994      | 3720.07837   | 279.23526    | 52.0093 |
| 2      | 8.119         | VB   | 0.2236      | 3432.63477   | 233.32574    | 47.9907 |

Totals : 7152.71313 512.56100



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %  |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1      | 6.063         | BB   | 0.1944      | 2685.58301   | 208.35497    | 13.1815 |
| 2      | 8.184         | BB   | 0.2062      | 1.76884e4    | 1287.95874   | 86.8185 |

Totals : 2.03739e4 1496.31371