

# Enantioselective N-Alkylation of Isatins and Synthesis of Chiral N- Alkylated Indoles

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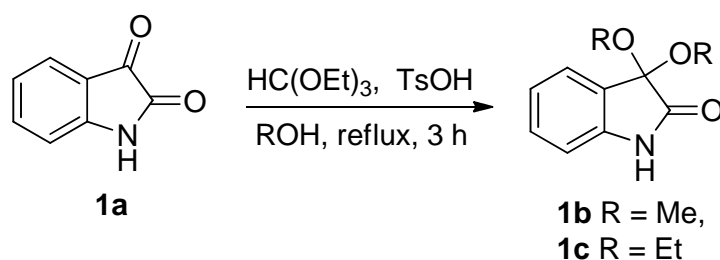
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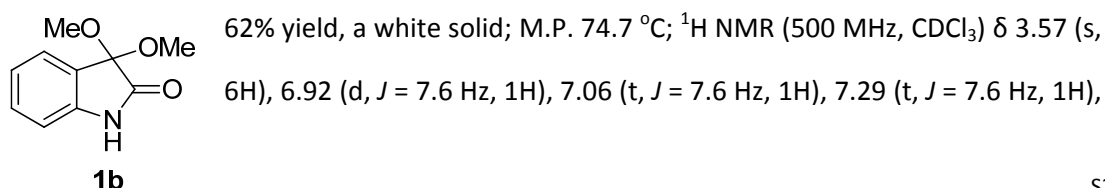
## A. General Information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker ACF300 or AMX500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform  $\delta$  7.26), carbon (chloroform  $\delta$  77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. Melting point (M.P.) was measured using BÜCHI Melting Point B-540. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or ceric ammonium molybdate followed by heating on a hot plate. Flash chromatographic separations were performed on Merck 60 (0.040-0.063 mm) mesh silica gel.

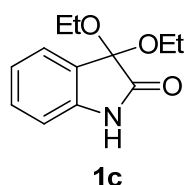
## B. Preparation of Isatin Ketals.



Isatin **1a** (441.3 mg, 3 mmol) was suspended in alcohol (ROH, 15.0 mL) at room temperature under an atmosphere of argon. Triethyl orthoformate (0.5 mL, 3 mmol) and *p*-toluenesulfonic acid monohydrate (28.5 mg, 0.15 mmol) were added and the reaction mixture was brought to reflux for 3 h. At the end of the reaction, excess solvent was removed and the residue was purified by flash chromatography (hexane/ethyl acetate 2:1) to provide ketals **1b** or **1c** as a white solid.

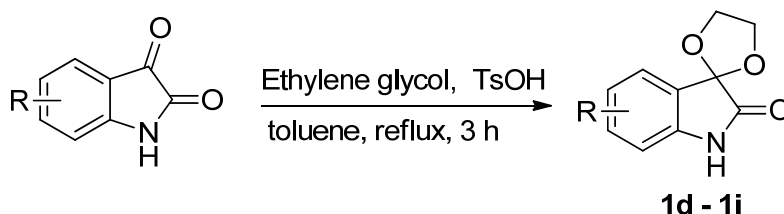


7.39 (d,  $J = 6.9$  Hz, 1H), 9.24 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  50.81, 97.45, 111.06, 122.63, 124.98, 125.02, 130.70, 140.62, 173.39; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{10}\text{H}_{10}\text{NO}_3$   $[\text{M}-\text{H}]^-$  = 192.0666, found = 192.0659.

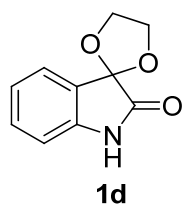


56% yield, a white solid; M.P. 92.4 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.24 (t,  $J = 7.0$  Hz, 6H), 3.72-3.83 (m, 2H), 3.90-3.96 (m, 2H), 6.91 (d,  $J = 7.6$  Hz, 1H), 7.04 (t,  $J = 7.6$  Hz, 1H), 7.28 (t,  $J = 6.3$  Hz, 1H), 7.39 (d,  $J = 7.6$  Hz, 1H), 9.11 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  15.24, 58.89, 97.36, 110.93,

122.62, 125.03, 125.87, 130.47, 140.53, 173.90; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{14}\text{NO}_3$   $[\text{M}-\text{H}]^-$  = 220.0979, found = 220.0975.

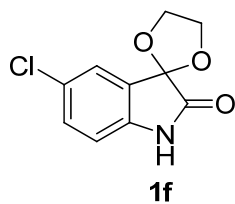


Isatin (3 mmol) was suspended in toluene (15.0 mL) at room temperature under an atmosphere of argon. Ethylene glycol (0.2 mL, 3.6 mmol) and *p*-toluenesulfonic acid monohydrate (28.5 mg, 0.15 mmol) were added and the reaction mixture was brought to reflux for 3 h. At the end of the reaction, excess solvent was removed and the residue was purified by flash chromatography (hexane/ethyl acetate 2:1) to provide ketals.

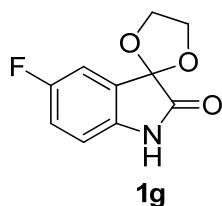


82% yield, a white solid; M.P. 133.4 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.29-4.36 (m, 2H), 4.53-4.60 (m, 2H), 6.82 (d,  $J = 7.6$  Hz, 1H), 7.05 (t,  $J = 7.6$  Hz, 1H), 7.27-7.30 (m, 1H), 7.35 (d,  $J = 7.6$  Hz, 1H), 8.76 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  65.82, 102.40, 110.80, 123.28, 124.38, 125.05,

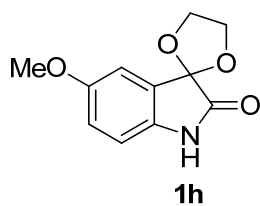
131.61, 141.87, 175.84; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{10}\text{H}_8\text{NO}_3$   $[\text{M}-\text{H}]^-$  = 190.0510, found = 190.0501.



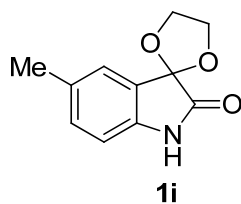
80% yield, a white solid; M.P. 179.3 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.29-4.35 (m, 2H), 4.51-4.58 (m, 2H), 6.77 (d,  $J$  = 8.2 Hz, 1H), 7.26-7.28 (m, 1H), 7.32 (d,  $J$  = 2.6 Hz, 1H), 8.61 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  65.98, 102.04, 111.81, 125.65, 126.07, 128.69, 131.48, 140.21, 175.40; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{10}\text{H}_7\text{ClNO}_3$   $[\text{M}-\text{H}]^-$  = 224.0120, found = 224.0122.



86% yield, a white solid; M.P. 174.5 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.29-4.36 (m, 2H), 4.53-4.59 (m, 2H), 6.77 (dd,  $J$  = 4.4 Hz, 6.3 Hz, 1H), 7.00-7.04 (m, 1H), 7.09 (dd,  $J$  = 2.6 Hz, 7.6 Hz, 1H), 8.11 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  65.96, 102.12, 111.36, 111.42, 113.04, 113.24, 117.97, 118.16, 125.92, 125.99, 137.57, 158.38, 160.31, 175.40; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{10}\text{H}_7\text{FNO}_3$   $[\text{M}-\text{H}]^-$  = 208.0415, found = 208.0414.



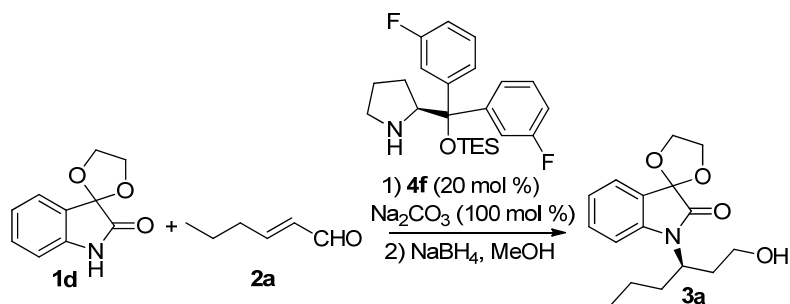
82% yield, a white solid; M.P. 160.5 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  3.76 (s, 3H), 4.29-4.35 (m, 2H), 4.53-4.60 (m, 2H), 6.73 (d,  $J$  = 8.3 Hz, 1H), 6.82-6.84 (m, 1H), 6.94 (d,  $J$  = 2.6 Hz, 1H), 8.53 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  55.84, 65.89, 102.70, 111.21, 111.47, 117.12, 125.38, 135.08, 156.34, 175.85; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{10}\text{NO}_4$   $[\text{M}-\text{H}]^-$  = 220.0615, found = 220.0613.



85% yield, a white solid; M.P. 143.1 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.30 (s, 3H), 4.29-4.35 (m, 2H), 4.53-4.60 (m, 2H), 6.71 (d,  $J$  = 7.6 Hz, 1H), 7.09 (d,  $J$  = 8.2 Hz, 1H), 7.18 (s, 1H), 8.25 (br s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  20.91, 65.82, 102.50, 110.46, 124.31, 125.75, 131.92, 132.98, 139.31, 175.53; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{10}\text{NO}_3$   $[\text{M}-\text{H}]^-$  = 204.0666, found = 204.0665.

### **C. Representative Procedure.**

#### **4f-Catalyzed addition of 1d to enal 2a.**



Isatin ketal **1d** (38.2 mg, 0.2 mmol),  $\text{Na}_2\text{CO}_3$  (21.2 mg, 0.2 mmol) and **4f** (16.1 mg, 0.04 mmol) were suspended in  $\text{CHCl}_3$  (1.0 mL) under an atmosphere of argon. Enal **2a** (46.4  $\mu\text{L}$ , 0.4 mmol) was added and the reaction mixture was stirred at room temperature for 3 d. At the end of the reaction, the mixture was directly subject to a short pad of silica gel with dichloromethane as eluent to get crude product, which was then dissolved in MeOH (2 mL) and cooled to 0 °C.  $\text{NaBH}_4$  (22.8 mg, 0.6 mmol) was added and the reaction was stirred at 0 °C for 15 min. The reaction solution was quenched by addition of 0.5 N HCl. The resulting mixture was extracted with EtOAc several times (5 mL $\times$ 3) and combined. Removal of the organic phase and purification of the residue by flash chromatography (hexane/ethyl acetate 2:1) afforded **3a** as a colorless oil (42.5 mg, 73% yield).

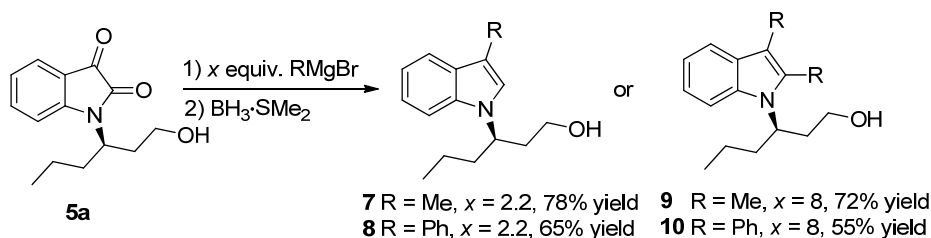
#### Conversion of chiral isatin ketal **3** to indole **6**.



Isatin ketal **3** (0.1 mmol) was dissolved in MeOH (1.0 mL) and cooled to 0 °C, 8N HCl (1.0 mL) was then added and the resulting solution was stirred at room temperature for 16 h. The reaction was then extracted with EtOAc (5 mL $\times$ 3). The combined organic phases were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and then concentrated under reduced pressure. The red residue was then dissolved in THF (1.0 mL) under an atmosphere of argon and cooled to 0 °C,  $\text{BH}_3 \cdot \text{SMe}_2$  (0.3 mL, 2 M solution in THF) was then added and the resulting solution was

stirred at room temperature for 12 h. MeOH (0.5 mL) and 1N HCl (2 mL) was added at 0 °C to quench the reaction and the mixture was extracted with EtOAc (5 mL×3). Removal of the organic phase and purification of the residue by flash chromatography (hexane/ethyl acetate 2:1) afforded indole **6** as a colorless oil.

### Diverse indole synthesis.



Preparation of **7, 8**: **5a** (49.5 mg, 0.2 mmol) in THF (2.0 mL) was cooled to 0 °C under an atmosphere of argon. Grignard reagent (0.44 mmol) was added in a dropwise manner. After stirring at 0 °C for 1 h. The reaction was quenched by addition of 1N HCl and the mixture was extracted with EtOAc (5 mL×3). The combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give the crude 3-hydroxy oxindole intermediate, which was then dissolved THF (1.0 mL) and cooled to 0 °C. BH<sub>3</sub>·SMe<sub>2</sub> (0.5 mL, 2 M solution in THF) was added to the reaction solution, and the resulting reaction solution was stirred at 0 °C to room temperature for 12 h. MeOH (0.5 mL) and 1N HCl (3 mL) were added at 0 °C to quench the reaction and the mixture was extracted with EtOAc (6 mL×3). Removal of the combined organic phase and purification of the residue by flash chromatography (hexane/ethyl acetate 2:1) afforded indole **7** or **8** as a colorless oil.

**7**: A colorless oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.87 (t, *J* = 7.3 Hz, 3H), 1.08-1.28 (m, 2H), 1.73-1.99 (m, 2H), 2.00-2.12 (m, 2H), 2.35 (d, *J* = 1.0 Hz, 3H), 3.21-3.29 (m, 1H), 3.46-3.53 (m, 1H), 4.49-4.58 (m, 1H), 6.91 (s, 1H), 7.07-7.12 (m, 1H), 7.16-7.21 (m, 1H), 7.37 (d, *J* = 13.7 Hz, 1H), 7.55-7.58 (m, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 9.76, 13.80, 19.52, 38.11, 38.40, 52.07, 59.37, 109.21, 111.03, 118.45, 118.95, 121.27, 121.67, 128.32, 137.04; HRMS (ESI) *m/z* calcd for C<sub>15</sub>H<sub>22</sub>NO [M+H]<sup>+</sup> = 232.1696, found = 232.1699.

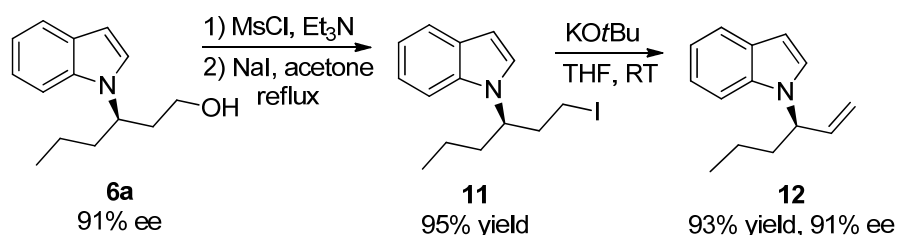
**8:** A colorless oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.89 (t,  $J = 7.1$  Hz, 3H), 1.14-1.31 (m, 2H), 1.83-2.04 (m, 2H), 2.08-2.16 (m, 2H), 3.28-3.36 (m, 1H), 3.52-3.59 (m, 1H), 4.61-4.71 (m, 1H), 7.16-7.33 (m, 4H), 7.43-7.50 (m, 3H), 7.70 (dd,  $J = 1.2$  Hz, 8.3 Hz, 2H), 7.97 (dd,  $J = 1.2$  Hz, 7.6 Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  13.80, 19.52, 38.05, 38.35, 52.40, 59.18, 109.81, 117.56, 119.86, 119.96, 121.83, 121.97, 125.73, 125.85, 127.28, 128.72, 135.68, 137.61; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{24}\text{NO}$   $[\text{M}+\text{H}]^+ = 294.1852$ , found =294.1855.

Preparation of **9**, **10**: **5a** (49.5 mg, 0.2 mmol) in THF (1.0 mL) was cooled to 0 °C under an atmosphere of argon. Grignard reagent (1.60 mmol) was then added in a dropwise manner. After stirring at 0 °C for 2 h.  $\text{BH}_3\text{-SMe}_2$  (0.5 mL, 2 M solution in THF) was added to the reaction solution, and the resulting reaction solution was stirred at 0 °C to room temperature (1h for MeMgBr, 6h for PhMgBr). MeOH (0.5 mL) and 1N HCl (3 mL) were added at 0 °C to quench the reaction and the mixture was extracted with EtOAc (6 mL $\times$ 3). Removal of the combined organic phase and purification of the residue by flash chromatography (hexane/ethyl acetate 2:1) afforded indole **9** or **10** as a colorless oil.

**9:** A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7.3$  Hz, 3H), 1.05-1.11 (m, 1H), 1.22-1.28 (m, 1H), 1.52 (br s, 1H), 1.77-1.84 (m, 1H), 2.00-2.07 (m, 1H), 2.27-2.29 (m, 4H), 2.38 (s, 3H), 2.46-2.51 (m, 1H), 3.19-3.24 (m, 1H), 3.46-3.50 (m, 1H), 4.45-4.51 (m, 1H), 7.07-7.11 (m, 2H), 7.41 (t,  $J = 4.4$  Hz, 1H), 7.52 (t,  $J = 4.4$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  9.09, 10.85, 13.98, 20.09, 36.25, 36.34, 52.54, 59.61, 105.89, 111.21, 118.23, 118.27, 119.90, 129.79, 133.78, 133.87; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{24}\text{NO}$   $[\text{M}+\text{H}]^+ = 246.1852$ , found =246.1859.

**10:** A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (t,  $J = 7.3$  Hz, 3H), 1.11-1.19 (m, 1H), 1.23-1.32 (m, 2H), 1.86-1.93 (m, 1H), 2.03-2.09 (m, 1H), 2.26-2.34 (m, 1H), 2.50-2.57 (m, 1H), 3.35-3.40 (m, 1H), 3.43-3.48 (m, 1H), 4.33-4.39 (m, 1H), 7.15-7.20 (m, 2H), 7.24-7.29 (m, 5H), 7.33-7.40 (m, 5H), 7.61 (d,  $J = 8.1$  Hz, 1H), 7.82 (d,  $J = 7.6$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  13.91, 19.97, 29.65, 36.53, 53.43, 59.74, 112.27, 115.15, 119.87,

119.96, 121.58, 121.97, 125.39, 127.97, 128.21, 128.38, 129.85, 131.63, 132.48, 134.51, 135.04, 138.94; HRMS (ESI)  $m/z$  calcd for  $C_{26}H_{28}NO$   $[M+H]^+ = 370.2165$ , found = 370.2168.



Preparation of **11**: Indole **6a** (20.3 mg, 0.1 mmol) was stirred in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) at 0 °C under an atmosphere of argon. Et<sub>3</sub>N (35  $\mu$ L, 0.25 mmol) and MsCl (12  $\mu$ L, 0.15 mmol) was added and the reaction solution was stirred at 0 °C for 15 min. The reaction was directly subject to a short pad of silica gel with dichloromethane as eluent. Removal of the solvent afforded the crude mesylated product, which was used for next step without further purification. The crude product was then dissolved in acetone (3.0 mL), followed by addition of NaI (74.5 mg, 0.5 mmol). The resulting reaction mixture was brought to reflux for 3 h. At the end of the reaction, the reaction solution was concentrated and purified by flash chromatography (hexane/CH<sub>2</sub>Cl<sub>2</sub> 10:1) to provide indole **11** as a colorless oil (29.7 mg, 95% yield for two steps).

**11**: A colorless oil; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  0.86 (t,  $J = 7.6$  Hz, 3H), 1.10-1.14 (m, 1H), 1.20-1.26 (m, 1H), 1.78-1.85 (m, 1H), 1.92-1.99 (m, 1H), 2.29-2.36 (m, 1H), 2.41-2.48 (m, 1H), 2.78-2.83 (m, 1H), 3.00-3.04 (m, 1H), 4.49-4.55 (m, 1H), 6.57 (d,  $J = 3.2$  Hz, 1H), 7.10-7.13 (m, 2H), 7.20-7.24 (m, 1H), 7.48 (d,  $J = 8.2$  Hz, 1H), 7.64 (d,  $J = 8.2$  Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  2.37, 13.71, 19.43, 37.46, 39.66, 56.37, 102.33, 109.83, 119.43, 120.98, 121.48, 124.17, 128.41, 136.52;  $[\alpha]_D^{25} = -29.60$  ( $c = 0.75$ , CHCl<sub>3</sub>).

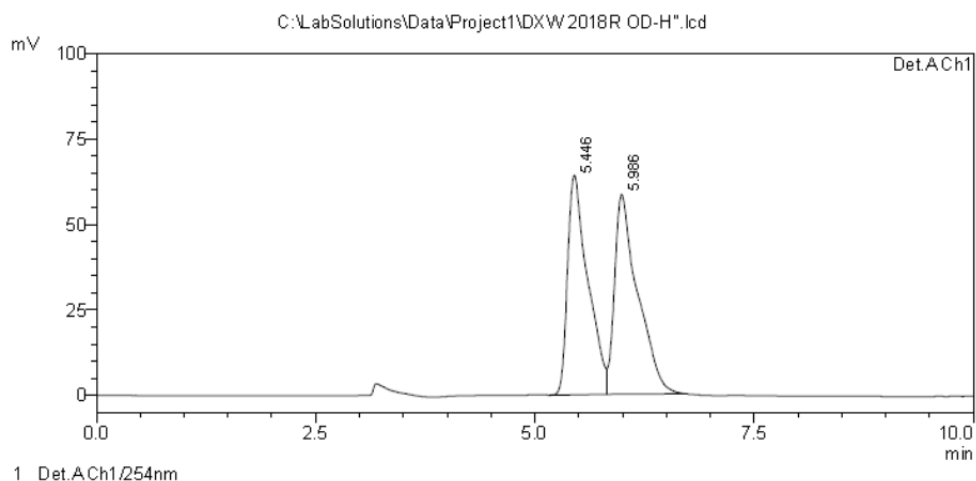
Preparation of **12**: Indole **11** (18.8 mg, 0.06 mmol) was stirred in THF (1.2 mL) at room temperature under an atmosphere of argon. KO<sup>t</sup>Bu (33.6 mg, 0.3 mmol) was added and the reaction mixture was stirred for 5 min before quenching with 1N HCl. The resulting mixture was extracted with EtOAc (5 mL $\times$ 3). Removal of the combined organic phases and



purification of the residue by flash chromatography (hexane/CH<sub>2</sub>Cl<sub>2</sub> 10:1) yielded indole **12** as a colorless oil (11.1 mg, 93% yield).

**12**: A colorless oil; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 0.93 (t, *J* = 7.6 Hz, 3H), 1.21-1.37 (m, 2H), 1.93-2.07 (m, 2H), 4.90 (dd, *J* = 6.3 Hz, 14.5Hz, 1H), 5.05 (dd, *J* = 1.3 Hz, 17.0Hz, 1H), 5.14-5.17 (m, 1H), 6.00-6.07 (m, 1H), 6.56 (d, *J* = 3.2 Hz, 1H), 7.10-7.13 (m, 1H), 7.17-7.22 (m, 2H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 13.78, 19.50, 36.40, 57.91, 101.54, 109.77, 115.91, 119.34, 120.94, 121.27, 125.00, 128.59, 136.14, 137.98; The ee value was 91%, *t*<sub>R</sub> (minor) = 5.55 min, *t*<sub>R</sub> (major) = 6.13 (Chiralcel OD-H, λ = 254 nm, 1% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (EI) *m/z* calcd for C<sub>14</sub>H<sub>17</sub>N (M<sup>+</sup>) = 199.1361, found = 199.1362; [α]<sub>D</sub><sup>25</sup> = -7.38 (c = 1.00, CHCl<sub>3</sub>).

<Chromatogram>

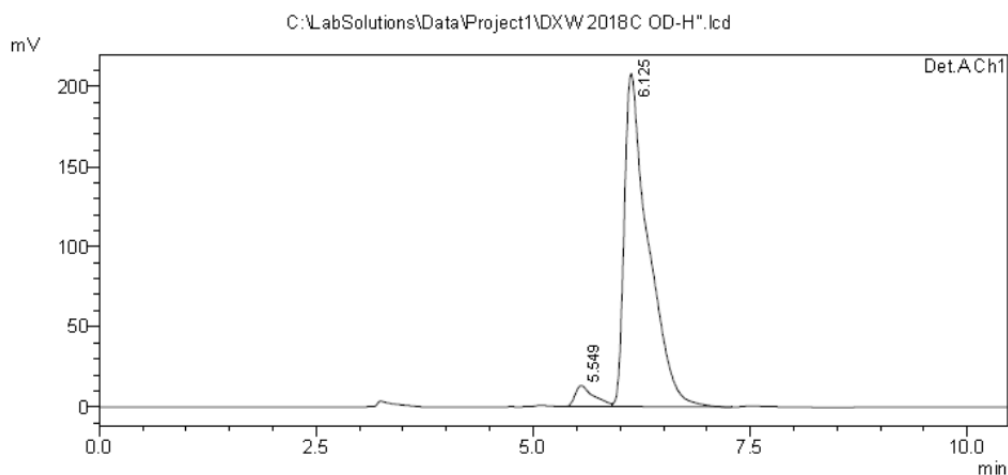


PeakTable

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(racemic **12**)

<Chromatogram>



PeakTable

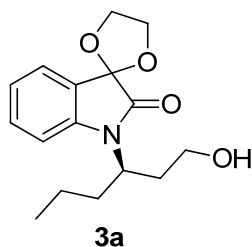
Peak#	Ret. Time	Area	Height	Area %	Height %
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2	6.125	3981947	207726	95.349	94.162
Total		4176202	220606	100.000	100.000

(enantiomerically enriched **12**)

The absolute configuration of **12** was determined to be *R* by comparison with the reported compound<sup>[1]</sup>. The absolute configurations of other chiral indoles and isatin ketal products were assigned by analogy.

**D. Analytical Data of the Products.**

***(R)*-1'-(1-Hydroxyhexan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3a****

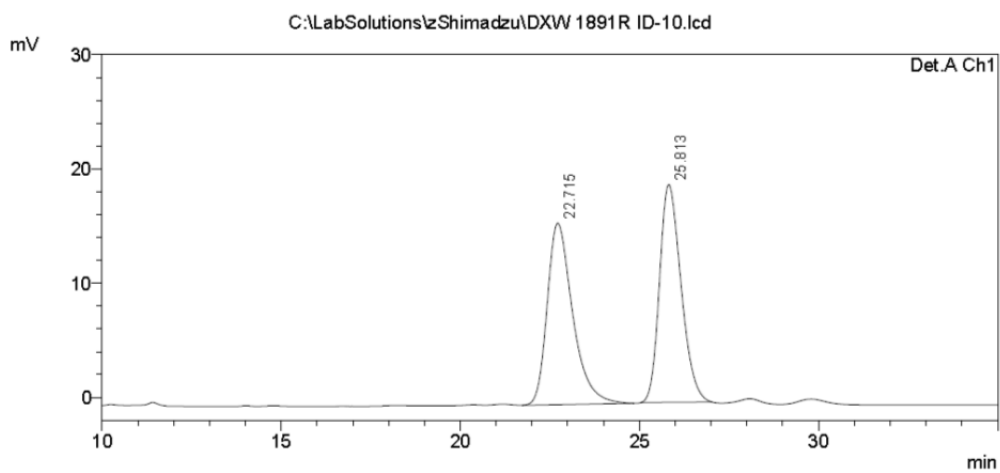


A colorless oil; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 0.89 (t, *J* = 7.6 Hz, 3H), 1.27-1.35 (m, 2H), 1.64-1.71 (m, 1H), 1.88-2.03 (m, 4H), 3.46-3.51 (m, 1H), 3.61 (t, *J* = 5.4 Hz, 1H), 4.28-4.33 (m, 2H), 4.52-4.60 (m, 2H), 6.95 (d, *J* = 8.2 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.30-7.33 (m, 1H), 7.36 (d, *J* = 7.6 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 13.68, 19.75,

33.79, 34.11, 59.03, 65.80, 65.88, 101.76, 123.05, 124.37, 125.03, 131.51, 174.51; The ee value was 91%, *t<sub>R</sub>* (minor) = 25.08 min, *t<sub>R</sub>* (major) = 21.74 (Chiralcel ID, λ = 254 nm, 10%

iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $C_{16}H_{21}NNaO_4 [M+Na]^+$  = 314.1361, found = 314.1371;  $[\alpha]_D^{25} = 1.48$  ( $c = 1.03$ ,  $CHCl_3$ ).

<Chromatogram>

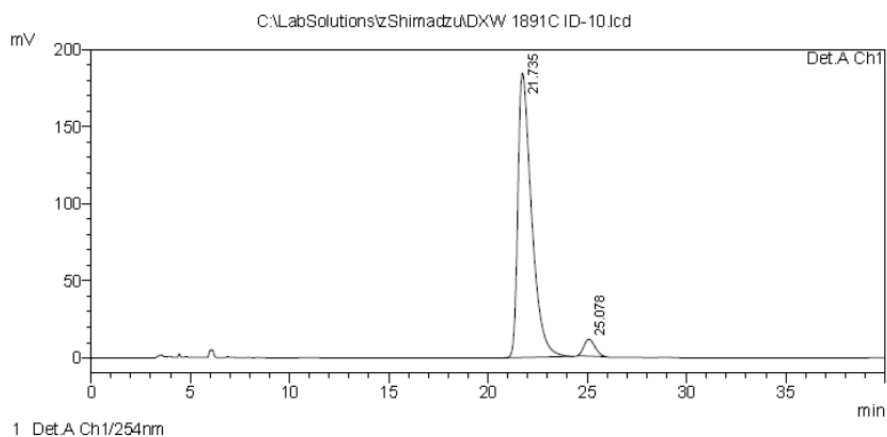


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.715	785968	15890	49.672	45.462
2	25.813	796351	19062	50.328	54.538
Total		1582319	34952	100.000	100.000

(racemic **3a**)

<Chromatogram>

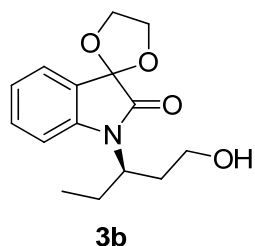


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.735	8846626	184225	95.383	94.401
2	25.078	428187	10926	4.617	5.599
Total		9274812	195151	100.000	100.000

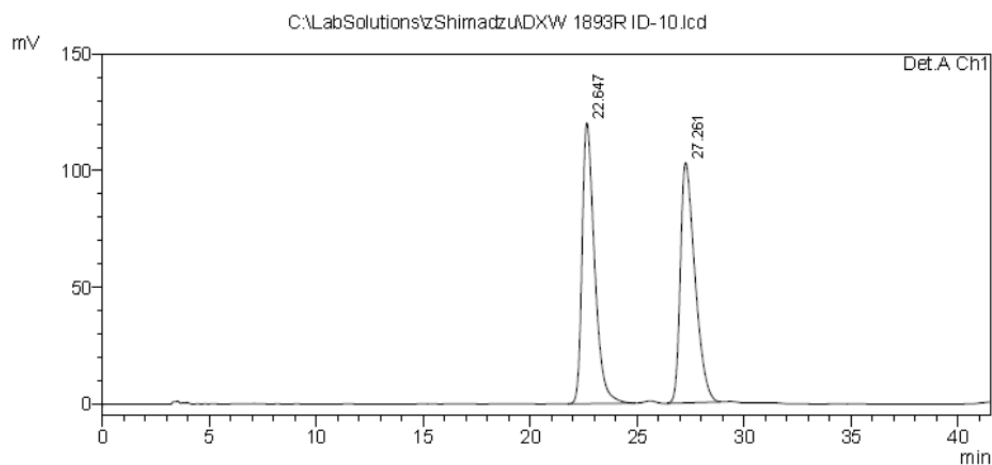
(enantiomerically enriched **3a**)

(R)-1'-(1-Hydroxypentan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3b**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.89 (t,  $J = 7.6$  Hz, 3H), 1.72-1.81 (m, 1H), 1.90-1.96 (m, 1H), 2.03-2.30 (m, 3H), 3.46-3.51 (m, 1H), 3.58-3.63 (m, 1H), 4.27-4.32 (m, 2H), 4.51-4.59 (m, 2H), 6.94 (d,  $J = 7.6$  Hz, 1H), 7.06 (t,  $J = 7.6$  Hz, 1H), 7.29-7.32 (m, 1H), 7.36 (d,  $J = 7.6$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  11.02, 24.83, 33.91, 51.02, 59.04, 65.78, 65.85, 101.76, 110.39, 123.02, 124.34, 125.01, 131.48, 174.55; The ee value was 91%,  $t_R$  (minor) = 27.60 min,  $t_R$  (major) = 22.52 min (Chiralcel ID,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{19}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+ = 300.1206$ , found = 300.1209;  $[\alpha]_D^{25} = 29.73$  ( $c = 1.20$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

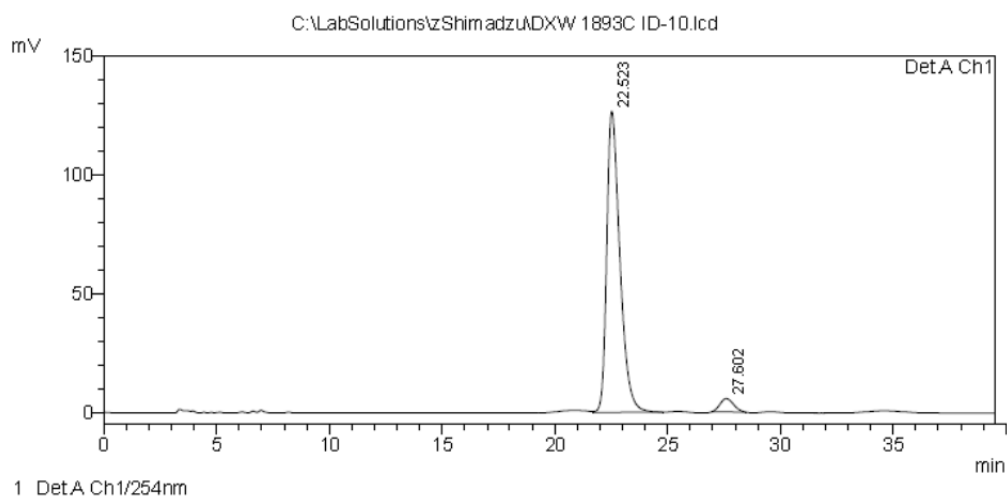


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.647	4869693	120236	49.945	53.894
2	27.261	4880441	102860	50.055	46.106
Total		9750134	223097	100.000	100.000

(racemic **3b**)

<Chromatogram>

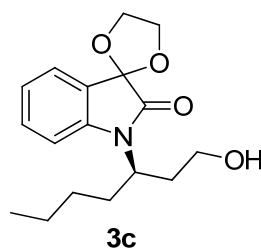


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.523	5139413	126841	95.624	95.757
2	27.602	235214	5621	4.376	4.243
Total		5374627	132462	100.000	100.000

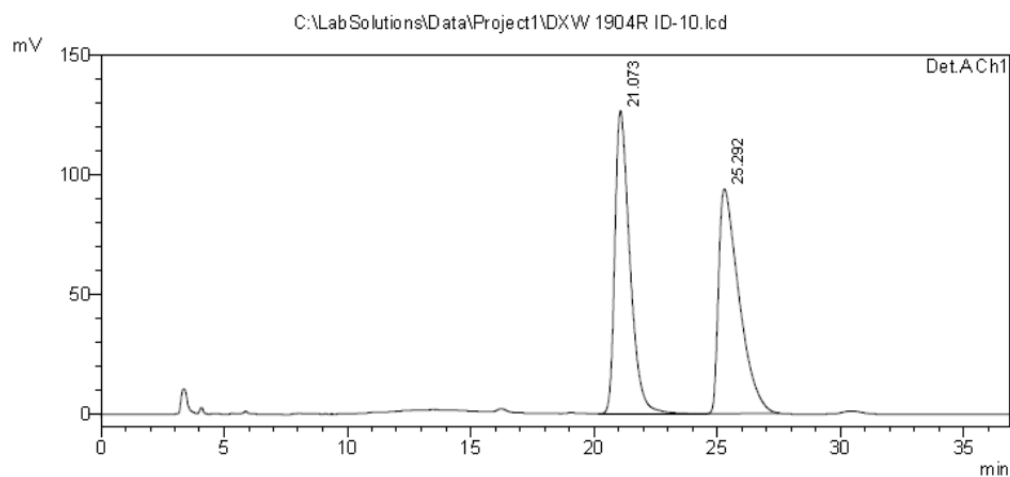
(enantiomerically enriched **3b**)

(R)-1'-(1-Hydroxyheptan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3c**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (t,  $J = 6.9$  Hz, 3H), 0.91 (t,  $J = 7.3$  Hz, 2H), 1.25-1.40 (m, 5H), 1.53-1.59 (m, 1H), 1.67-1.74 (m, 1H), 1.88-2.05 (m, 3H), 3.45-3.52 (m, 3H), 3.59-3.62 (m, 1H), 3.70 (t,  $J = 4.5$  Hz, 1H), 4.27-4.32 (m, 2H), 4.53-4.58 (m, 2H), 6.94 (d,  $J = 7.6$  Hz, 1H), 7.06 (t,  $J = 7.6$  Hz, 1H), 7.31 (t,  $J = 7.6$  Hz, 1H), 7.36 (d,  $J = 6.9$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.81, 13.84, 19.22, 22.25, 28.59, 31.40, 31.65, 34.14, 59.00, 61.78, 65.78, 65.86, 71.05, 71.68, 101.76, 110.41, 123.02, 124.38, 125.01, 131.48, 174.47; The ee value was 91%,  $t_{\text{R}}$  (minor) = 26.13 min,  $t_{\text{R}}$  (major) = 21.06 min (Chiralcel ID,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{23}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+ = 328.1519$ , found = 328.1532;  $[\alpha]_{\text{D}}^{25} = 2.70$  ( $c = 1.02$ ,  $\text{CHCl}_3$ ).

<Chromatogram>



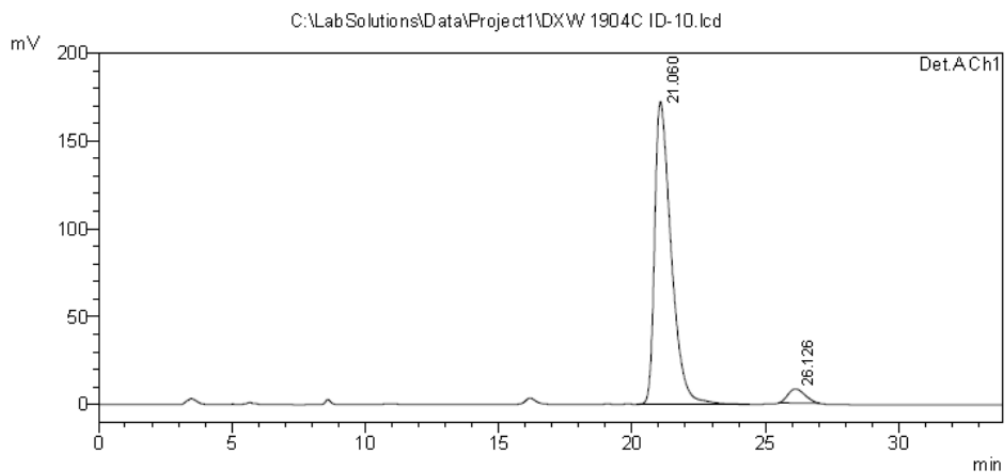
1 Det.A.Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.073	5372212	126578	49.773	57.416
2	25.292	5421216	93878	50.227	42.584
Total		10793428	220457	100.000	100.000

(racemic **3c**)

<Chromatogram>



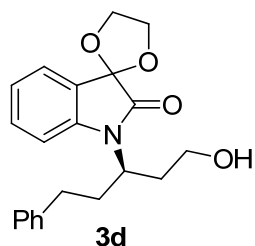
1 Det.A.Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.060	7420483	172359	95.391	95.520
2	26.126	358553	8084	4.609	4.480
Total		7779036	180442	100.000	100.000

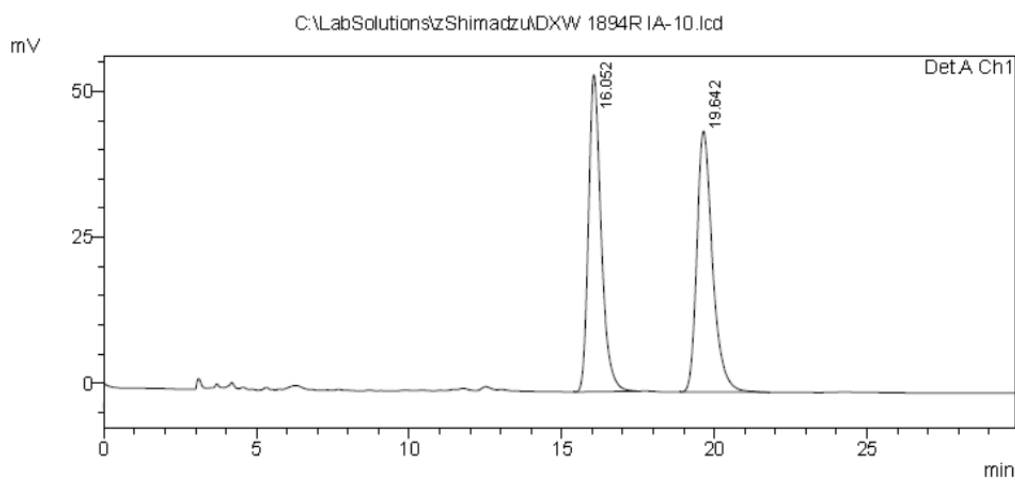
(enantiomerically enriched **3c**)

**(R)-1'-(1-Hydroxy-5-phenylpentan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one 3d**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.91-1.98 (m, 1H), 2.01-2.08 (m, 1H), 2.45 (br s, 1H), 2.55-2.64 (m, 2H), 3.47-3.52 (m, 1H), 3.62-3.64 (m, 1H), 4.30-4.36 (m, 2H), 4.55-4.63 (m, 2H), 6.91 (br s, 1H), 7.08-7.11 (m, 3H), 7.16 (t,  $J = 7.3$  Hz, 1H), 7.22-7.26 (m, 2H), 7.32 (t,  $J = 7.9$  Hz, 1H), 7.40 (d,  $J = 7.0$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  32.75, 33.60, 34.21, 58.99, 65.87, 65.94, 101.84, 123.21, 124.41, 125.16, 126.05, 128.42, 131.60, 140.98, 174.64; The ee value was 92%,  $t_{\text{R}}$  (minor) = 19.64 min,  $t_{\text{R}}$  (major) = 16.07 min (Chiralcel IA,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{23}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+ = 376.1519$ , found = 376.1531;  $[\alpha]_{\text{D}}^{25} = -4.10$  ( $c = 1.53$ ,  $\text{CHCl}_3$ ).

**<Chromatogram>**

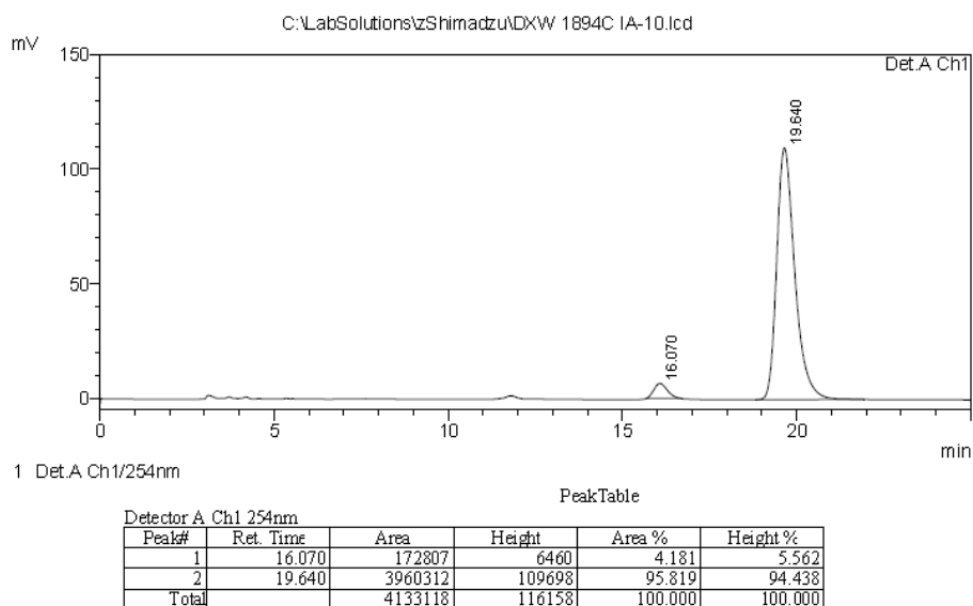


PeakTable

Peak#	Ret. Time	Area	Height	Area%	Height%
1	16.052	1563898	54170	49.543	54.851
2	19.642	1592767	44588	50.457	45.149
Total		3156666	98758	100.000	100.000

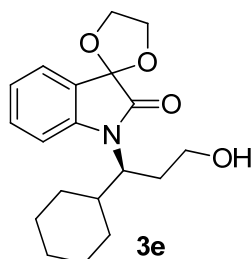
(racemic **3d**)

<Chromatogram>



(enantiomerically enriched **3d**)

(S)-1'-(1-Cyclohexyl-3-hydroxypropyl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3e**

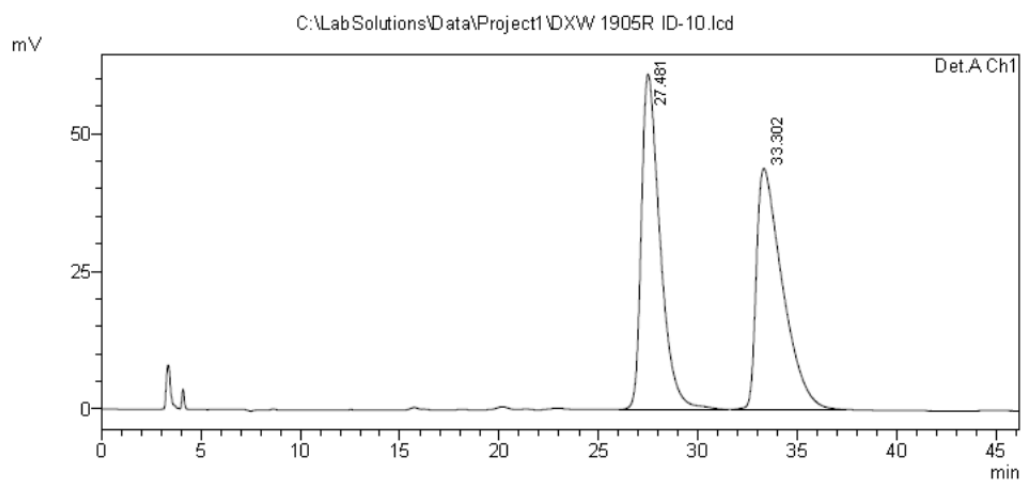


A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85-1.14 (m, 4H), 1.22-1.28 (m, 2H), 1.58-1.64 (m, 3H), 1.93 (s, 1H), 1.95-2.07 (m, 5H), 3.44-3.56 (m, 2H), 4.27-4.31 (m, 2H), 4.54-4.59 (m, 2H), 6.95 (br s, 1H), 7.07 (br s, 1H), 7.30-7.36 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.90, 19.28, 25.70, 25.89, 26.15, 29.69, 30.82, 30.87, 31.72, 38.36,

53.70, 59.25, 61.84, 65.84, 65.95, 71.10, 71.73, 101.79, 111.23, 123.20, 124.42, 125.08, 131.54, 142.65, 174.84; The ee value was 95%,  $t_R$  (minor) = 34.48 min,  $t_R$  (major) = 27.24 min (Chiralcel ID,  $\lambda$  = 254 nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI) m/z calcd for  $\text{C}_{19}\text{H}_{25}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+$  = 354.1676, found = 354.1687;  $[\alpha]_D^{25}$  = -3.51 (c = 1.13,  $\text{CHCl}_3$ ).



<Chromatogram>

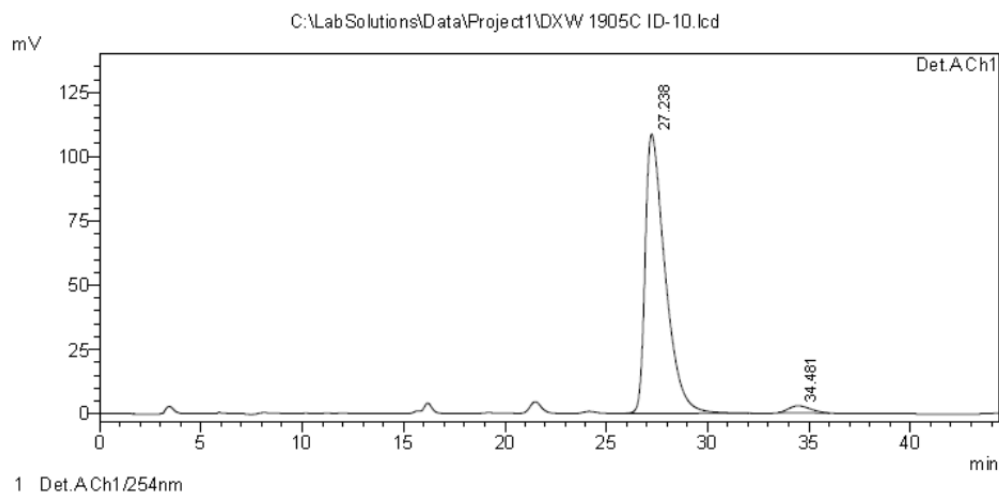


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.481	3996137	60874	50.079	58.187
2	33.302	3983505	43744	49.921	41.813
Total		7979641	104619	100.000	100.000

(racemic **3e**)

<Chromatogram>

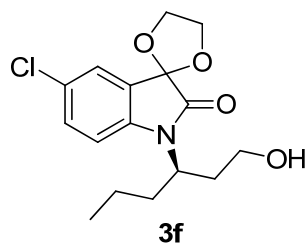


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.238	7444564	108671	97.337	97.559
2	34.481	203688	2719	2.663	2.441
Total		7648252	111390	100.000	100.000

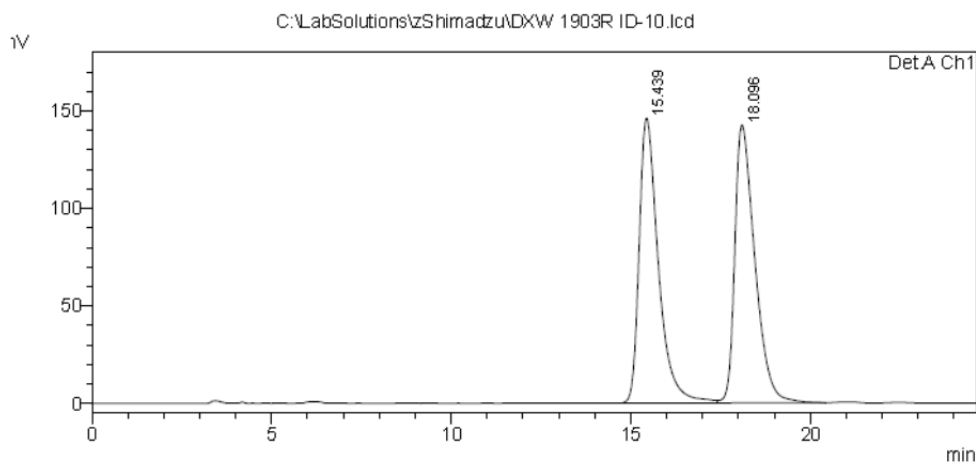
(enantiomerically enriched **3e**)

(R)-5'-Chloro-1'-(1-hydroxyhexan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3f**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (t,  $J = 7.3$  Hz, 3H), 1.25-1.32 (m, 2H), 1.62-1.70 (m, 1H), 1.87-1.94 (m, 1H), 2.03 (br s, 2H), 3.46-3.50 (m, 1H), 3.62 (t,  $J = 5.8$  Hz, 1H), 4.27-4.32 (m, 2H), 4.52-4.57 (m, 2H), 6.88 (d,  $J = 8.2$  Hz, 1H), 7.26-7.29 (m, 1H), 7.33 (d,  $J = 1.9$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.65, 19.71, 33.72, 34.04, 58.97, 65.96, 66.03, 101.34, 125.58, 126.18, 128.57, 131.29, 174.04; The ee value was 89%,  $t_R$  (minor) = 18.33 min,  $t_R$  (major) = 15.31 min (Chiralcel ID,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{20}\text{ClNNaO}_4$   $[\text{M}+\text{Na}]^+ = 348.0973$ , found = 348.0980;  $[\alpha]_D^{25} = 0.22$  ( $c = 1.30$ ,  $\text{CHCl}_3$ ).

<Chromatogram>



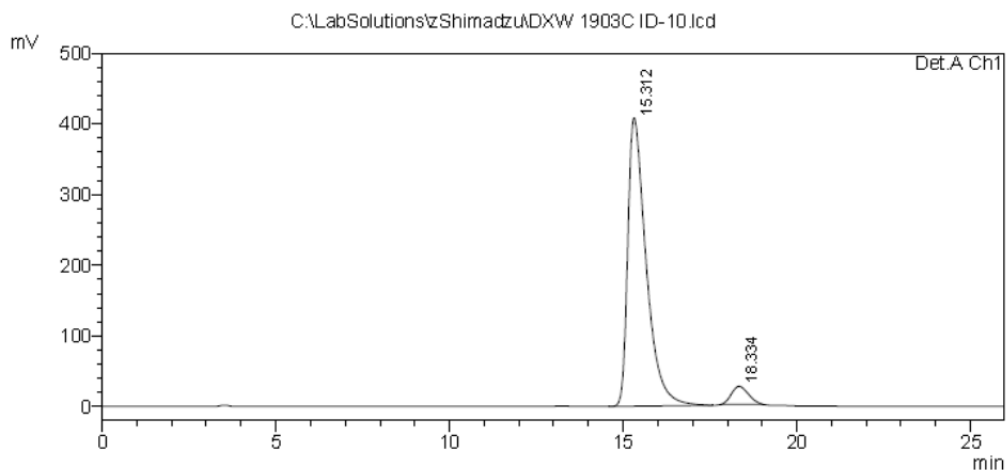
Det.A Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.439	5450106	146219	49.636	50.634
2	18.096	5530027	142557	50.364	49.366
Total		10980134	288776	100.000	100.000

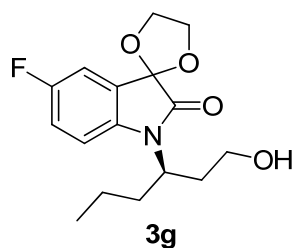
(racemic **3f**)

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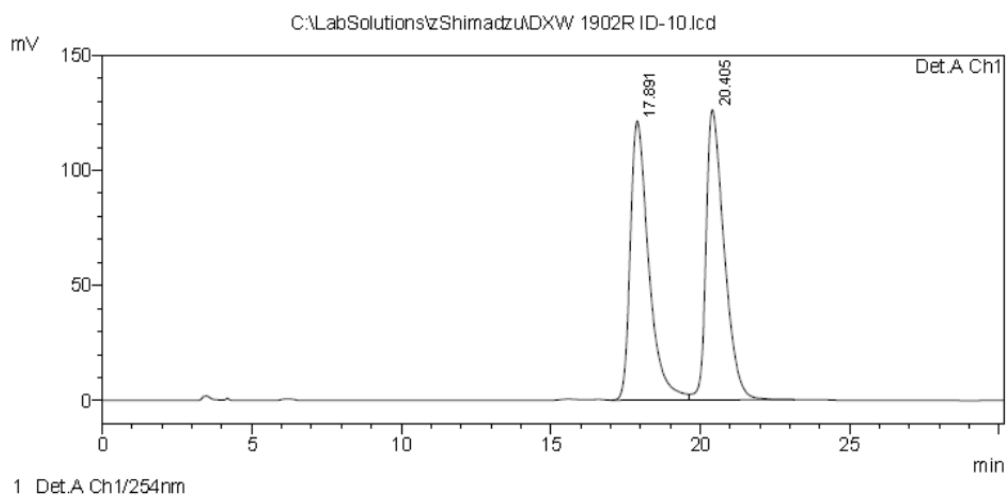
(enantiomerically enriched **3f**)

(R)-5'-Fluoro-1'-(1-hydroxyhexan-3-yl)spiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3g**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (t,  $J = 7.3$  Hz, 3H), 1.24-1.33 (m, 2H), 1.62-1.69 (m, 1H), 1.87-1.94 (m, 1H), 2.03 (br s, 2H), 3.45-3.50 (m, 1H), 3.61 (t,  $J = 5.7$  Hz, 1H), 4.27-4.31 (m, 2H), 4.52-4.57 (m, 2H), 6.88 (dd,  $J = 3.8$  Hz, 8.8 Hz, 1H), 6.99-7.03 (m, 1H), 7.09 (dd,  $J = 2.9$  Hz, 7.3 Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.65, 19.70, 33.72, 34.05, 58.97, 65.92, 65.99, 101.40, 111.23, 112.98, 113.18, 117.61, 117.80, 126.16, 158.21, 160.15, 174.34; The ee value was 91%,  $t_{\text{R}}$  (minor) = 20.62 min,  $t_{\text{R}}$  (major) = 17.77 min (Chiralcel ID,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{20}\text{FNNaO}_4$   $[\text{M}+\text{Na}]^+$  = 332.1269, found = 332.1274;  $[\alpha]_{\text{D}}^{25} = 0.97$  ( $c = 1.17$ ,  $\text{CHCl}_3$ ).

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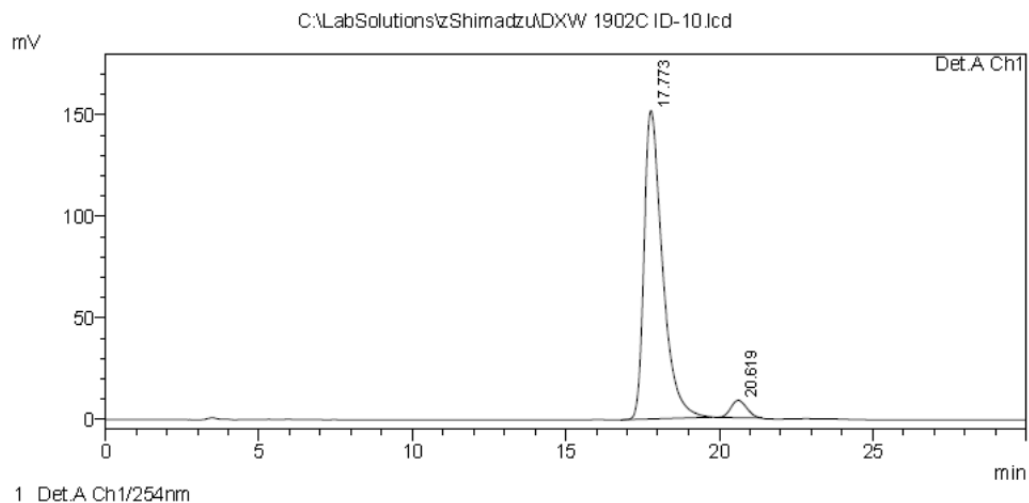


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.891	5208066	121297	49.466	49.015
2	20.405	5320617	126173	50.534	50.985
Total		10528683	247471	100.000	100.000

(racemic **3g**)

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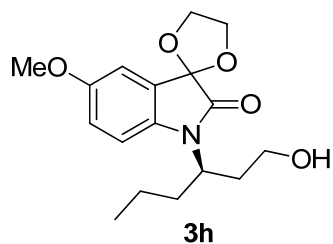


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.773	6334024	151709	95.342	94.676
2	20.619	309426	8532	4.658	5.324
Total		6643450	160241	100.000	100.000

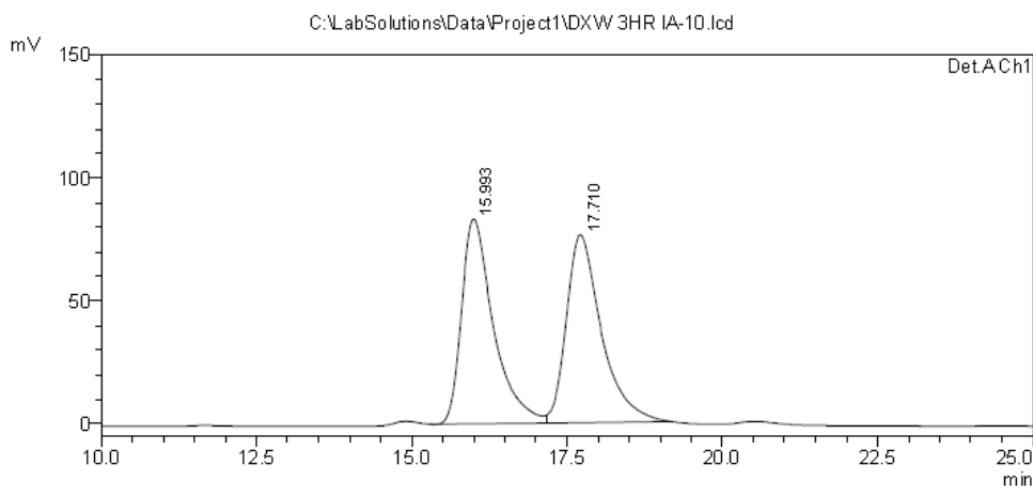
(enantiomerically enriched **3g**)

(R)-1'-(1-Hydroxyhexan-3-yl)-5'-methoxyspiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3h**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (t,  $J = 7.3$  Hz, 3H), 1.28-1.33 (m, 2H), 1.62-1.69 (m, 1H), 1.88-1.93 (m, 1H), 2.03 (br s, 2H), 3.46-3.50 (m, 1H), 3.58-3.62 (m, 1H), 3.78 (s, 3H), 4.28-4.31 (m, 2H), 4.54-4.59 (m, 2H), 6.85 (dd,  $J = 8.8$  Hz, 16.4 Hz, 2H), 6.97 (s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.69, 19.74, 33.83, 34.18, 55.79, 59.02, 65.85, 65.93, 101.96, 111.44, 116.59, 125.60, 156.19, 174.44; The ee value was 92%,  $t_R$  (minor) = 16.10 min,  $t_R$  (major) = 17.75 min (Chiralcel IA,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{23}\text{NNaO}_5$   $[\text{M}+\text{Na}]^+ = 344.1468$ , found = 344.1477;  $[\alpha]_D^{25} = 4.16$  ( $c = 1.13$ ,  $\text{CHCl}_3$ ).

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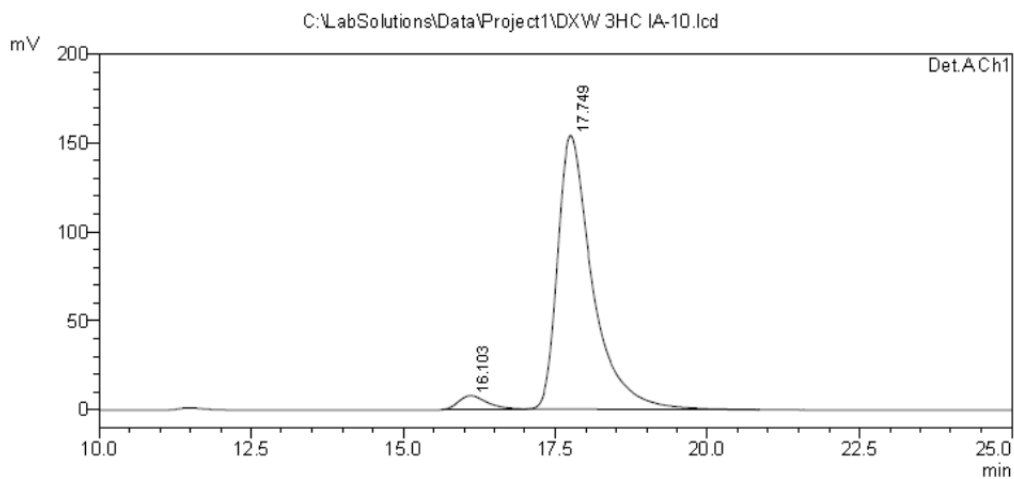


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.993	2973796	83351	49.822	52.153
2	17.710	2995023	76470	50.178	47.847
Total		5968819	159821	100.000	100.000

(racemic **3h**)

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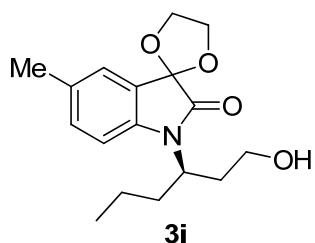


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.103	253763	7713	3.976	4.775
2	17.749	6127811	153803	96.024	95.225
Total		6381574	161516	100.000	100.000

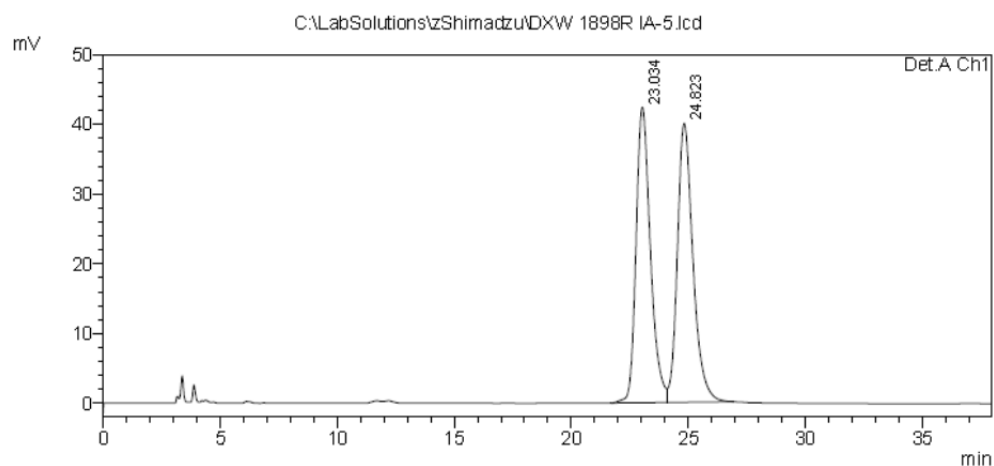
(enantiomerically enriched **3h**)

(R)-1'-(1-Hydroxyhexan-3-yl)-5'-methylspiro[[1,3]dioxolane-2,3'-indolin]-2'-one **3i**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (t,  $J = 7.3$  Hz, 3H), 1.29-1.33 (m, 2H), 1.63-1.70 (m, 1H), 1.88-1.94 (m, 1H), 2.06 (br s, 2H), 2.30 (s, 3H), 3.46-3.51 (m, 1H), 3.59-3.62 (m, 1H), 3.78 (s, 3H), 4.28-4.31 (m, 2H), 4.54-4.59 (m, 2H), 6.84 (d,  $J = 7.6$  Hz, 1H), 7.11 (d,  $J = 7.6$  Hz, 1H), 7.20 (s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.69, 19.76, 20.77, 33.82, 34.17, 59.05, 65.82, 65.91, 101.96, 124.37, 125.77, 131.76, 132.82, 174.55; The ee value was 92%,  $t_R$  (minor) = 23.09 min,  $t_R$  (major) = 24.81 min (Chiralcel IA,  $\lambda = 254$  nm, 5% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{23}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+ = 328.1519$ , found = 328.1527;  $[\alpha]_D^{25} = 4.51$  ( $c = 1.13$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

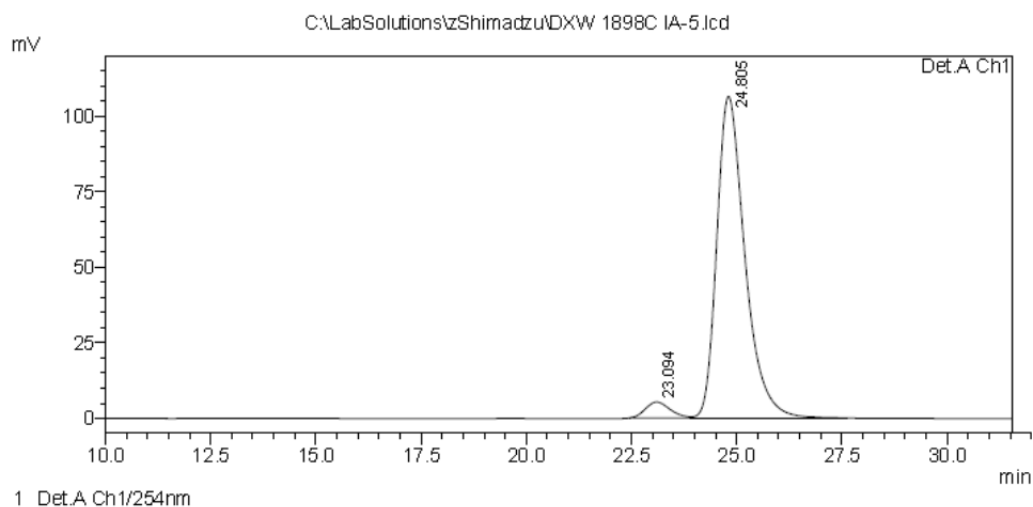


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.034	1809938	42357	49.377	51.458
2	24.823	1855598	39957	50.623	48.542
Total		3665535	82314	100.000	100.000

(racemic **3i**)

<Chromatogram>

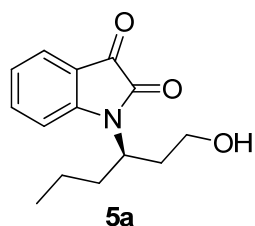


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.094	212580	5241	4.112	4.695
2	24.805	4957434	106384	95.888	95.305
Total		5170014	111626	100.000	100.000

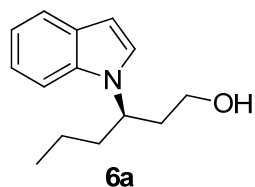
(enantiomerically enriched **3i**)

(R)-1-(1-Hydroxyhexan-3-yl)indoline-2,3-dione 5a



A red oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.86 (t,  $J = 7.6$  Hz, 3H), 1.24-1.32 (m, 2H), 1.65-1.72 (m, 1H), 1.91-1.98 (m, 1H), 2.04 (br s, 1H), 2.19 (br s, 1H), 2.53 (br s, 1H), 3.51-3.55 (m, 1H), 3.62-3.65 (m, 1H), 4.38 (br s, 1H), 7.04 (t,  $J = 8.5$  Hz, 1H), 7.50-7.54 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.54, 19.68, 33.71, 34.10, 50.46, 59.00, 111.47, 117.59, 123.31, 125.36, 138.28, 158.57, 183.44; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{16}\text{NO}_3$   $[\text{M}-\text{H}]^- = 246.1136$ , found = 246.1138.

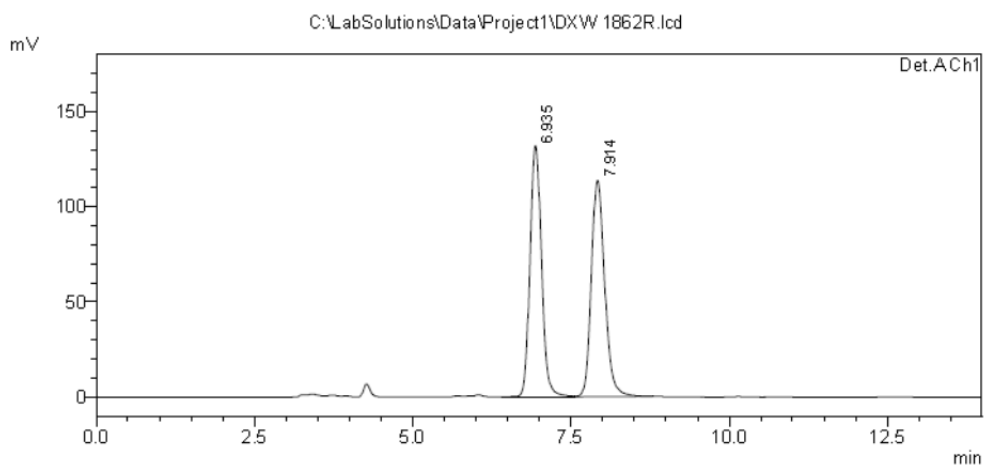
(R)-3-(1H-Indol-1-yl)hexan-1-ol 6a



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7.6$  Hz, 3H), 1.09-1.16 (m, 1H), 1.19-1.26 (m, 1H), 1.79-1.86 (m, 1H), 1.90-1.98 (m, 1H), 2.01-2.13 (m, 2H), 3.22-3.25 (m, 1H), 3.47-3.51 (m, 1H), 4.57-4.63 (m, 1H), 6.57 (d,  $J = 3.2$  Hz, 1H), 7.09-7.15 (m, 2H), 7.20 (t,  $J = 7.6$  Hz, 1H), 7.43 (d,  $J = 8.2$  Hz, 1H), 7.63 (d,  $J = 8.2$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.84, 19.55, 38.11, 38.42, 52.47, 59.28, 101.95, 109.56, 119.28, 120.99, 121.39, 124.30, 128.28, 136.74; The ee value was 91%,  $t_{\text{R}}$  (minor) = 6.87 min,  $t_{\text{R}}$  (major) = 7.82 min (Chiralcel ID,  $\lambda = 254$  nm, 5% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{NO}$   $[\text{M}+\text{H}]^+ = 218.1539$ , found = 218.1536;  $[\alpha]_{\text{D}}^{25} = -10.93$  ( $c = 1.00$ ,  $\text{CHCl}_3$ ).



<Chromatogram>

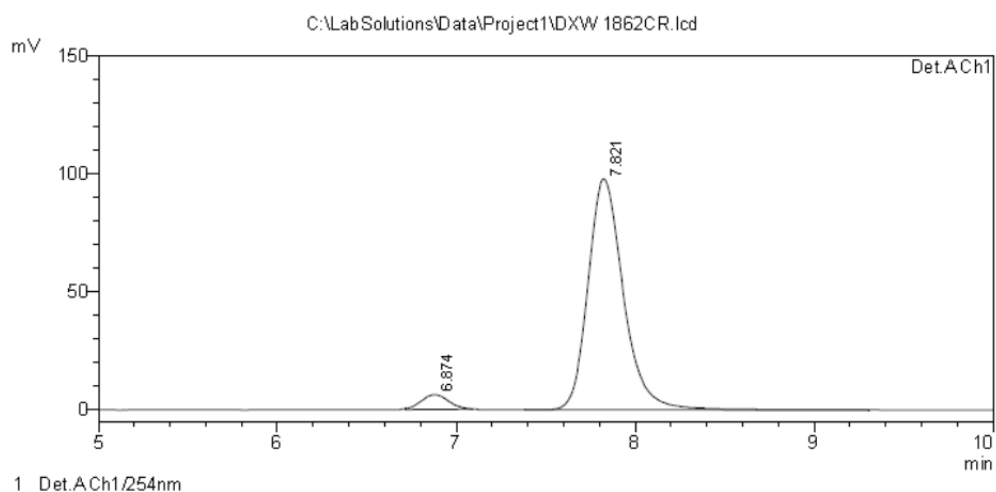


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.935	1677794	131796	49.967	53.700
2	7.914	1680017	113635	50.033	46.300
Total		3357811	245431	100.000	100.000

(racemic **6a**)

<Chromatogram>

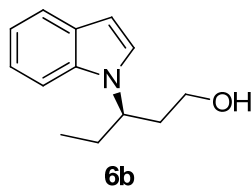


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.874	65464	6202	4.624	5.949
2	7.821	1350414	98053	95.376	94.051
Total		1415878	104255	100.000	100.000

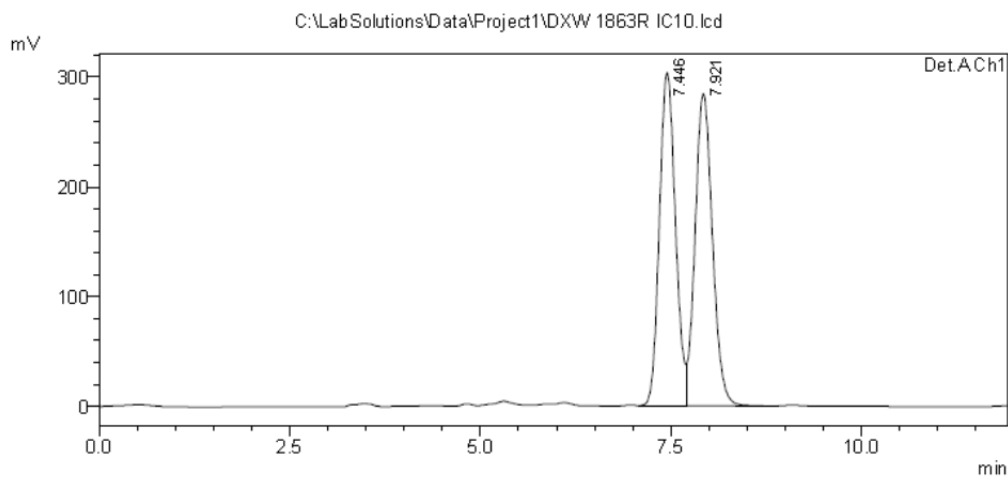
(enantiomerically enriched **6a**)

(R)-3-(1H-Indol-1-yl)pentan-1-ol **6b**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.79 (t,  $J = 7.3$  Hz, 3H), 1.90-1.97 (m, 2H), 2.02-2.16 (m, 2H), 3.24-3.29 (m, 1H), 3.49-3.54 (m, 1H), 4.47-4.53 (m, 1H), 6.57 (d,  $J = 3.2$  Hz, 1H), 7.10 (t,  $J = 6.9$  Hz, 1H), 7.14-7.21 (m, 2H), 7.43 (d,  $J = 8.2$  Hz, 1H), 7.63 (d,  $J = 8.2$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  10.94, 29.01, 38.08, 54.39, 59.33, 101.95, 109.57, 119.28, 120.98, 121.37, 124.28, 128.32, 136.82; The ee value was 91%,  $t_R$  (minor) = 7.83 min,  $t_R$  (major) = 7.35 min (Chiralcel IC,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{18}\text{NO}$   $[\text{M}+\text{H}]^+ = 204.1383$ , found = 204.1373;  $[\alpha]_D^{25} = -0.37$  ( $c = 1.30$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

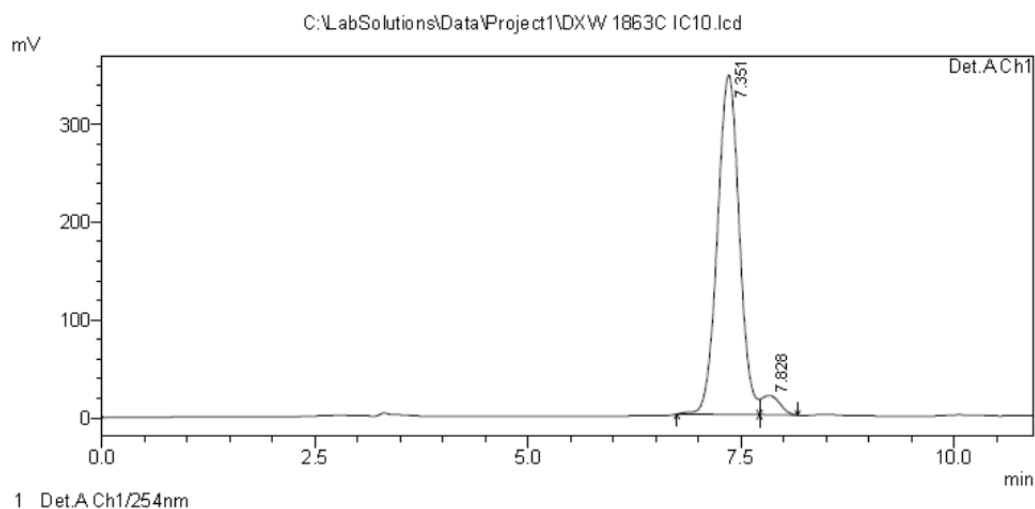


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.446	4439947	303422	49.609	51.627
2	7.921	4510023	284295	50.391	48.373
Total		8949970	587717	100.000	100.000

(racemic **6b**)

<Chromatogram>

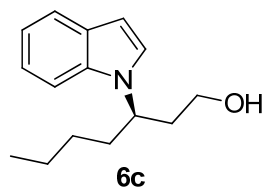


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.351	6234808	347606	95.444	94.546
2	7.828	297640	20054	4.556	5.454
Total		6532449	367659	100.000	100.000

(enantiomerically enriched **6b**)

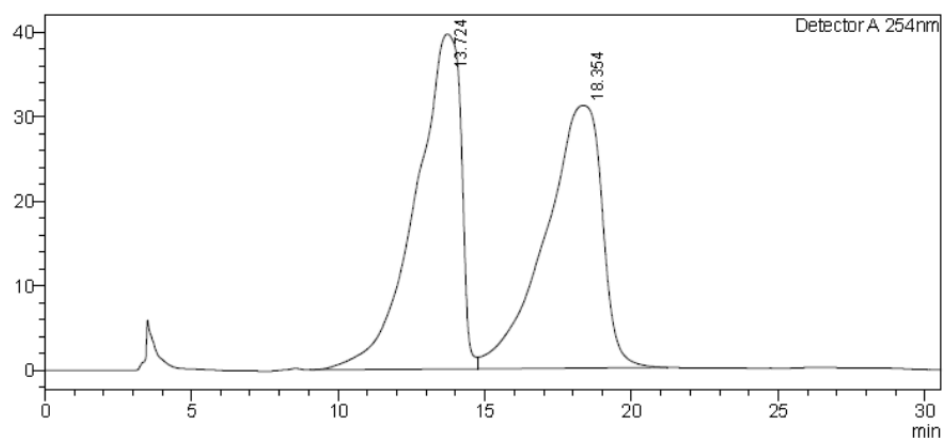
(R)-3-(1H-Indol-1-yl)heptan-1-ol **6c**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (t,  $J = 7.3$  Hz, 3H), 1.03-1.11 (m, 1H), 1.18-1.35 (m, 4H), 1.83-1.98 (m, 2H), 2.01-2.14 (m, 2H), 3.22-3.27 (m, 1H), 3.47-3.52 (m, 1H), 4.55-4.61 (m, 1H), 6.56 (d,  $J = 3.2$  Hz, 1H), 7.10 (t,  $J = 7.6$  Hz, 1H), 7.15 (d,  $J = 8.2$  Hz, 1H), 7.20 (t,  $J = 7.6$  Hz, 1H), 7.42 (d,  $J = 8.2$  Hz, 1H), 7.64 (d,  $J = 7.6$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.84, 22.39, 28.40, 35.59, 38.41, 52.75, 59.26, 101.90, 109.50, 119.22, 120.92, 121.34, 124.23, 128.25, 136.67; The ee value was 91%,  $t_R$  (minor) = 13.91 min,  $t_R$  (major) = 18.25 min (Chiralcel ID,  $\lambda = 254$  nm, 1% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{NO}$   $[\text{M}+\text{H}]^+ = 232.1696$ , found = 232.1703;  $[\alpha]_D^{25} = -9.91$  ( $c = 1.10$ ,  $\text{CHCl}_3$ ).

**<Chromatogram>**

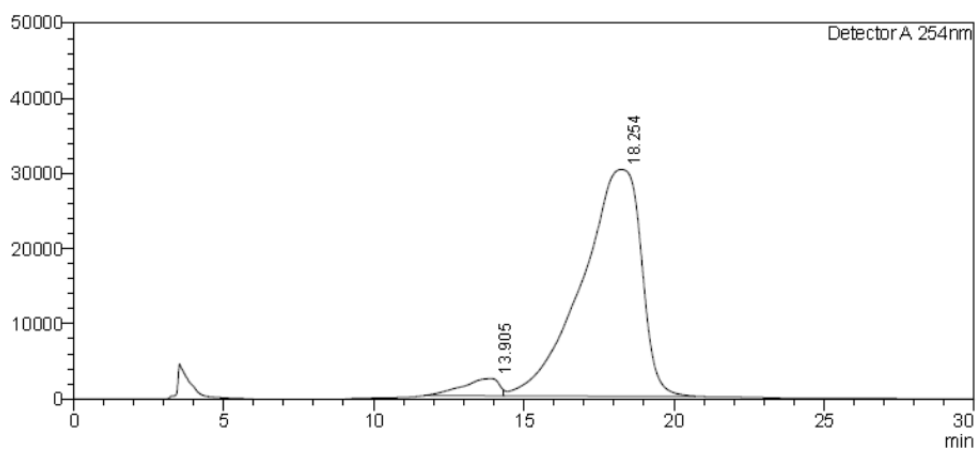
mV

**<Peak Table>**

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.724	4262365	39586	50.421			
2	18.354	4191183	31060	49.579		V	
Total		8453548	70646				

(racemic **6c**)**<Chromatogram>**

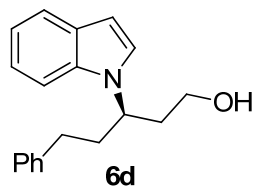
uV

**<Peak Table>**

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.905	192898	2287	4.439		M	
2	18.254	4152642	30150	95.581		V M	
Total		4345540	32438				

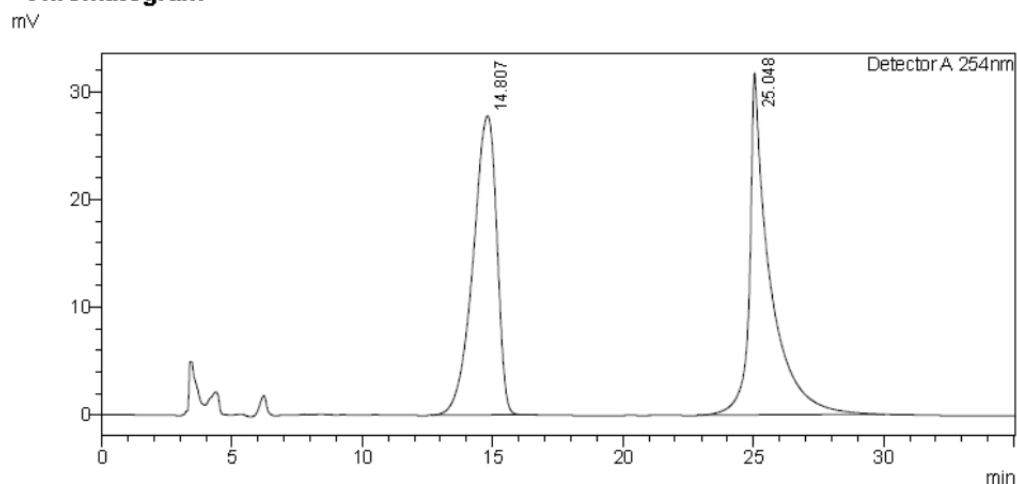
(enantiomerically enriched **6c**)

(R)-3-(1H-Indol-1-yl)-5-phenylpentan-1-ol **6d**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.05-2.11 (m, 2H), 2.17-2.24 (m, 1H), 2.28-2.35 (m, 1H), 2.41-2.52 (m, 1H), 3.19-3.24 (m, 1H), 3.45-3.49 (m, 1H), 4.57-4.63 (m, 1H), 6.63 (d,  $J = 3.2$  Hz, 1H), 7.07 (d,  $J = 6.9$  Hz, 2H), 7.13-7.29 (m, 6H), 7.37 (d,  $J = 8.2$  Hz, 1H), 7.68 (d,  $J = 7.6$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  32.38, 37.51, 38.40, 52.09, 59.08, 102.26, 109.66, 119.35, 120.97, 121.41, 124.13, 125.96, 128.35, 128.37, 136.64, 141.10; The ee value was 91%,  $t_R$  (minor) = 14.79 min,  $t_R$  (major) = 23.89 min (Chiralcel ID,  $\lambda = 254$  nm, 2% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{22}\text{NO}$   $[\text{M}+\text{H}]^+$  = 280.1696, found = 280.1700;  $[\alpha]_D^{25} = -22.60$  ( $c = 1.00$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

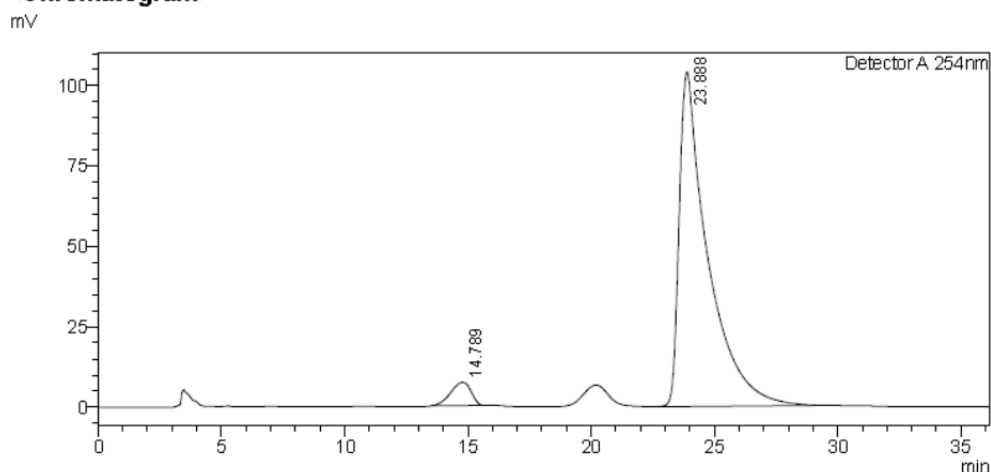


<Peak Table>

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.807	1761261	27754	50.764			
2	25.048	1708217	31735	49.236			
Total		3469478	59489				

(racemic **6d**)

<Chromatogram>

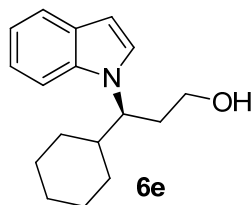


<Peak Table>

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.789	415861	7234	4.730		M	
2	23.888	8376827	104037	95.270			
Total		8792688	111271				

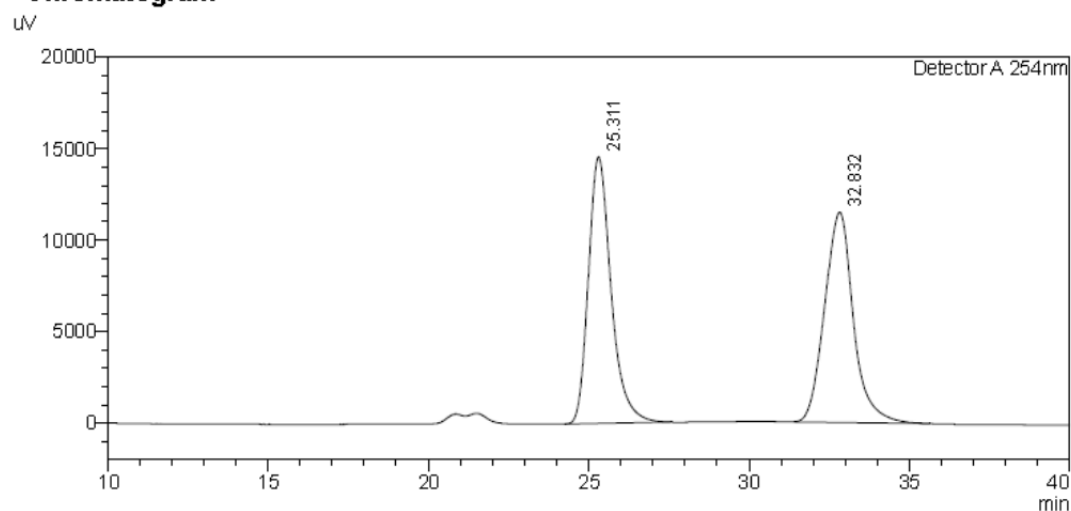
(enantiomerically enriched **6d**)

(S)-3-Cyclohexyl-3-(1H-indol-1-yl)propan-1-ol **6e**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84-0.91 (m, 1H), 1.02-1.13 (m, 3H), 1.21-1.31 (m, 3H), 1.59-1.62 (m, 2H), 1.78-1.80 (m, 2H), 1.95-2.04 (m, 2H), 2.24-2.30 (m, 2H), 3.13-3.18 (m, 1H), 3.43-3.47 (m, 1H), 4.26-4.31 (m, 1H), 6.56 (d,  $J = 3.2$  Hz, 1H), 7.08-7.11 (m, 2H), 7.19 (t,  $J = 7.6$  Hz, 1H), 7.40 (d,  $J = 8.2$  Hz, 1H), 7.63 (d,  $J = 8.2$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  25.96, 26.11, 26.27, 29.79, 30.74, 34.76, 43.38, 59.46, 101.78, 109.74, 119.24, 120.94, 121.38, 124.74, 128.11, 137.09; The ee value was 94%,  $t_{\text{R}}$  (minor) = 24.67 min,  $t_{\text{R}}$  (major) = 31.33 min (Chiralcel IA,  $\lambda = 254$  nm, 1.2% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{24}\text{NO}$   $[\text{M}+\text{H}]^+$  = 258.1852, found = 258.1863;  $[\alpha]_{\text{D}}^{25} = -30.90$  ( $c = 1.00$ ,  $\text{CHCl}_3$ ).

### <Chromatogram>



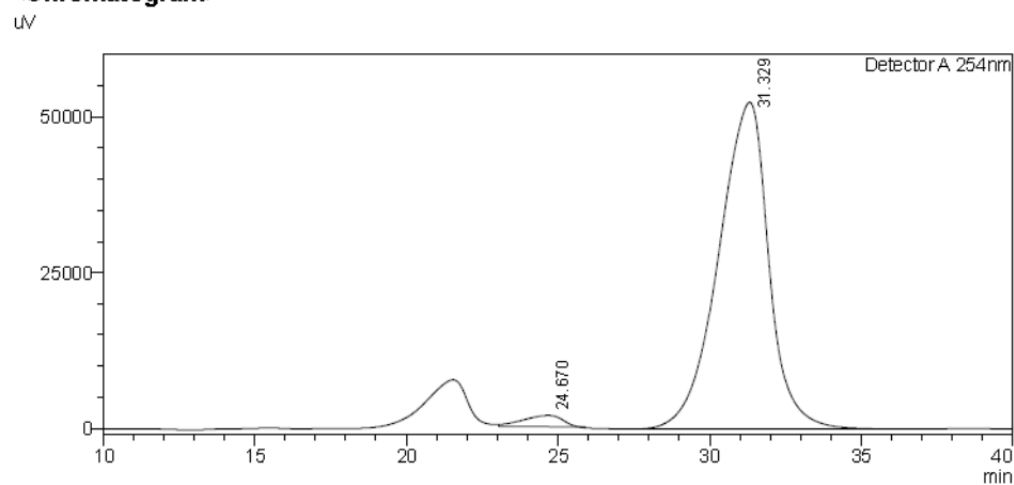
### <Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	25.311	718394	14584	50.036			
2	32.832	717369	11498	49.964			
Total		1435763	26082				

(racemic **6e**)

### <Chromatogram>



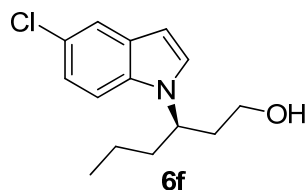
### <Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	24.670	164346	1814	2.644		M	
2	31.329	6052072	52405	97.356			
Total		6216419	54219				

(enantiomerically enriched **6e**)

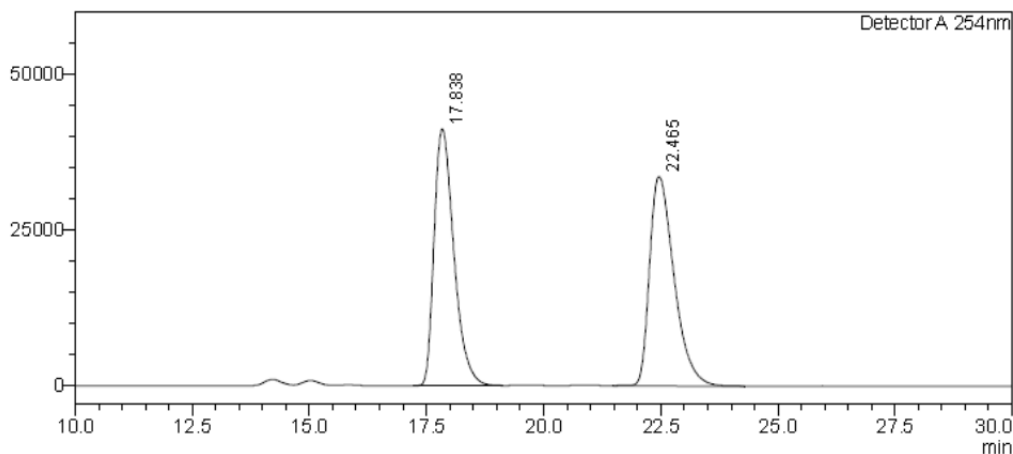
(R)-3-(5-Chloro-1H-indol-1-yl)hexan-1-ol 6f



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85 (t,  $J = 7.6$  Hz, 3H), 1.05-1.09 (m, 1H), 1.10-1.23 (m, 1H), 1.53 (br s, 1H), 1.78-1.85 (m, 1H), 1.87-1.95 (m, 1H), 1.98-2.12 (m, 2H), 3.19-3.24 (m, 1H), 3.49-3.53 (m, 1H), 4.53-4.59 (m, 1H), 6.49 (d,  $J = 3.2$  Hz, 1H), 7.12-7.15 (m, 2H), 7.33 (d,  $J = 8.1$  Hz, 1H), 7.58 (d,  $J = 1.9$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.72, 19.45, 37.97, 38.31, 52.71, 59.05, 101.61, 110.52, 120.23, 121.65, 124.86, 125.54, 129.12, 135.12; The ee value was 89%,  $t_r$  (minor) = 16.73 min,  $t_r$  (major) = 21.15 min (Chiralcel IB,  $\lambda = 254$  nm, 2% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{ClNO}$   $[\text{M}+\text{H}]^+ = 252.1150$ , found = 252.1156;  $[\alpha]_D^{25} = -20.11$  ( $c = 0.55$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

uV



<Peak Table>

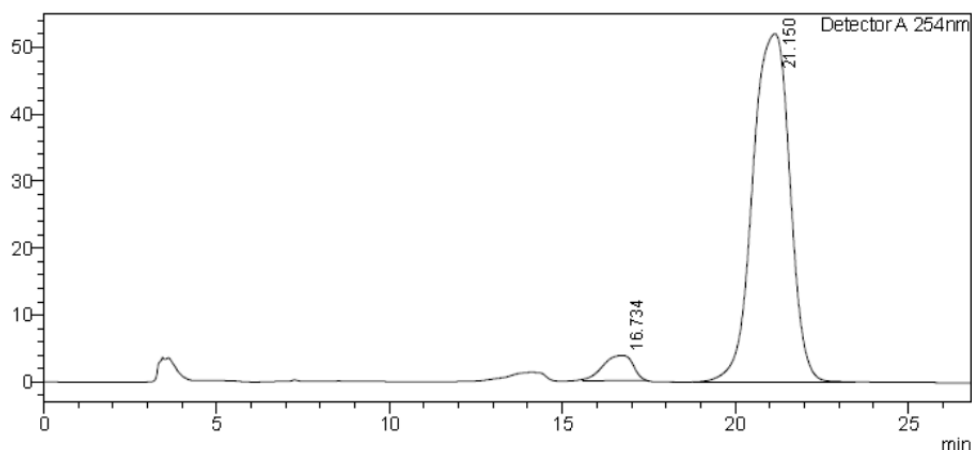
Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	17.838	1215433	41268	49.827			
2	22.465	1223889	33663	50.173			
Total		2439322	74931				

(racemic 6f)

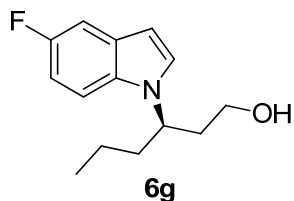


**<Chromatogram>**

mV

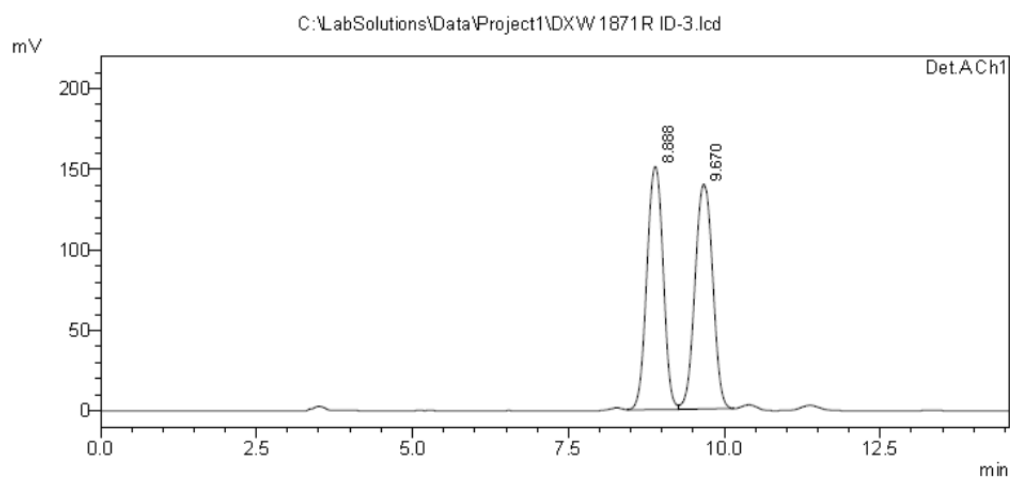
**<Peak Table>**

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.734	225664	3752	5.487		M	
2	21.150	3887223	52085	94.513			
Total		4112887	55837				

(enantiomerically enriched **6f**)**(R)-3-(5-Fluoro-1H-indol-1-yl)hexan-1-ol 6g**

A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.86 (t,  $J = 7.3$  Hz, 3H), 1.06-1.13 (m, 1H), 1.15-1.24 (m, 1H), 1.78-1.85 (m, 1H), 1.87-1.95 (m, 1H), 1.99-2.13 (m, 2H), 3.22-3.27 (m, 1H), 3.51-3.55 (m, 1H), 4.53-4.59 (m, 1H), 6.50 (d,  $J = 3.2$  Hz, 1H), 6.91-6.95 (m, 1H), 7.17 (d,  $J = 3.2$  Hz, 1H), 7.25 (dd,  $J = 2.6$  Hz, 9.5 Hz, 1H), 7.33 (dd,  $J = 4.4$  Hz, 8.9 Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.75, 19.48, 38.02, 38.37, 52.76, 59.16, 101.82, 101.85, 105.40, 105.58, 109.65, 109.86, 110.00, 110.08, 125.81, 128.26, 128.34, 133.34, 156.71, 158.57; The ee value was 90%,  $t_R$  (minor) = 8.77 min,  $t_R$  (major) = 9.54 min (Chiralcel IC,  $\lambda = 254$  nm, 10% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{FNO}$   $[\text{M}+\text{H}]^+ = 236.1445$ , found = 236.1453;  $[\alpha]_D^{25} = -4.29$  ( $c = 0.70$ ,  $\text{CHCl}_3$ ).

<Chromatogram>



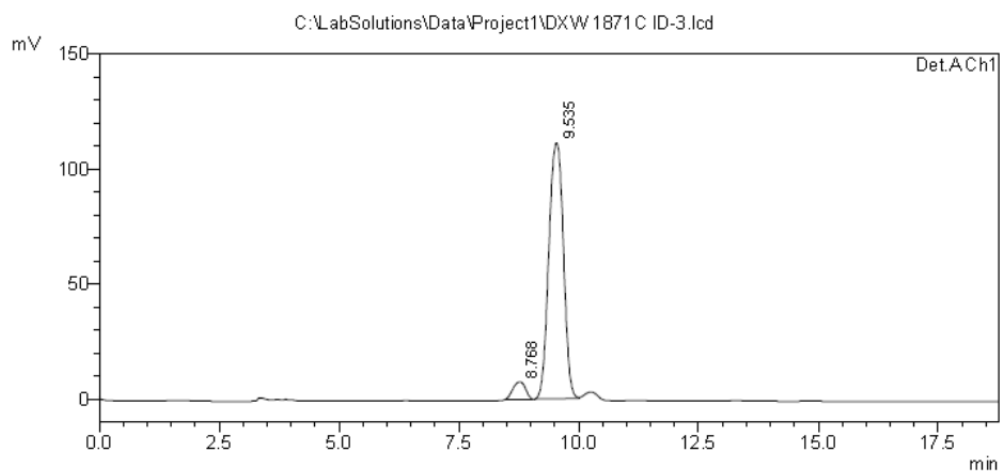
1 Det.ACh1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.888	2750285	150713	50.337	51.959
2	9.670	2713477	139346	49.663	48.041
Total		5463762	290059	100.000	100.000

(racemic **6g**)

<Chromatogram>



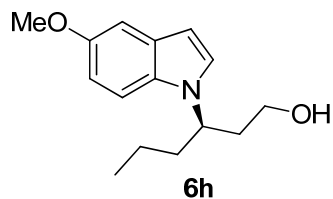
1 Det.ACh1/254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.768	132378	7416	5.321	6.243
2	9.535	2355425	111383	94.679	93.757
Total		2487803	118799	100.000	100.000

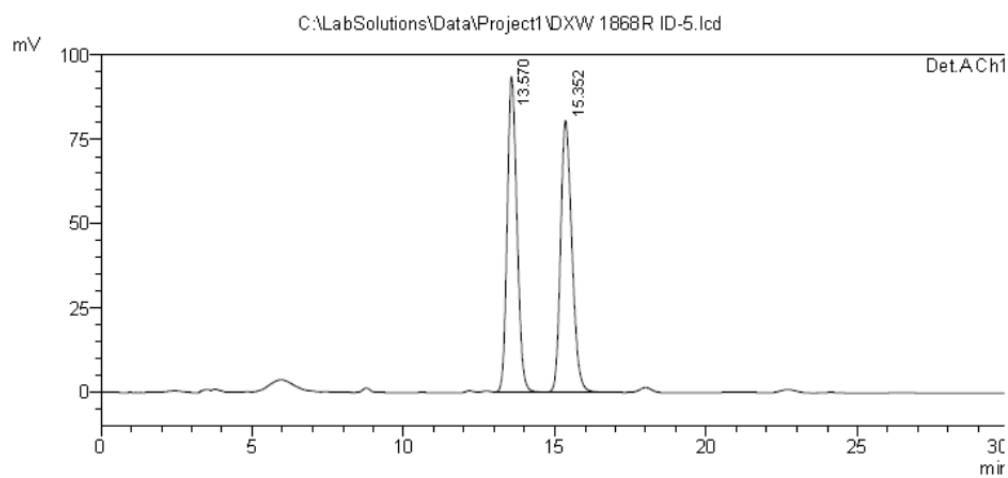
(enantiomerically enriched **6g**)

(R)-3-(5-Methoxy-1H-indol-1-yl)hexan-1-ol 6h



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85 (t,  $J = 7.3$  Hz, 3H), 1.05-1.17 (m, 1H), 1.18-1.26 (m, 1H), 1.77-1.83 (m, 1H), 1.88-1.96 (m, 1H), 2.01-2.12 (m, 2H), 3.23-3.28 (m, 1H), 3.49-3.54 (m, 1H), 3.85 (s, 3H), 4.50-4.56 (m, 1H), 6.47 (d,  $J = 3.2$  Hz, 1H), 6.85 (dd,  $J = 2.2$  Hz, 9.1 Hz, 1H), 7.09 (dd,  $J = 2.8$  Hz, 11.0 Hz, 1H), 7.31 (d,  $J = 8.0$  Hz, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.79, 19.50, 38.05, 38.39, 52.71, 55.79, 59.30, 101.37, 102.41, 110.24, 111.74, 124.87, 131.97, 153.81; The ee value was 92%,  $t_R$  (minor) = 13.66 min,  $t_R$  (major) = 15.27 min (Chiralcel ID,  $\lambda = 254$  nm, 5% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{NO}_2$   $[\text{M}+\text{H}]^+$  = 248.1645, found = 248.1653;  $[\alpha]_D^{25} = -5.66$  ( $c = 0.50$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

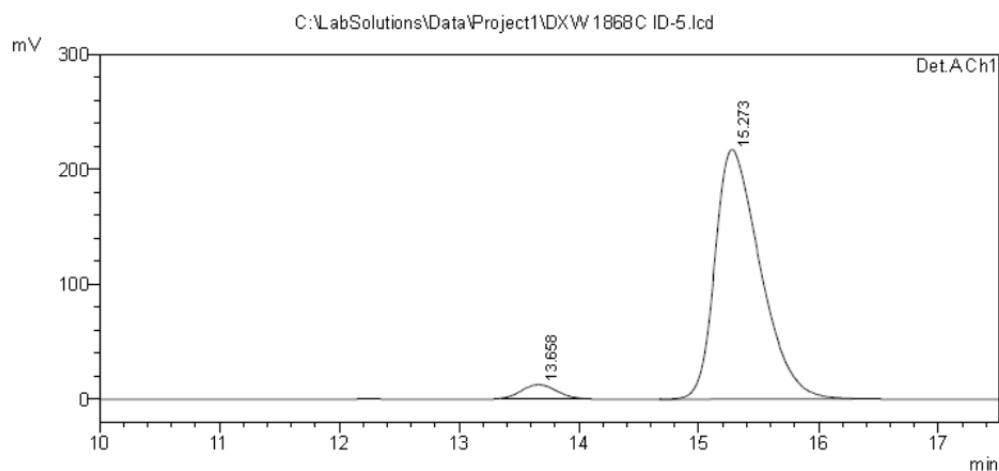


PeakTable

Peak#	Ret. Time	Area	Height	Area%	Height%
1	13.570	2101636	93630	49.988	53.701
2	15.352	2102667	80724	50.012	46.299
Total		4204302	174354	100.000	100.000

(racemic 6h)

<Chromatogram>

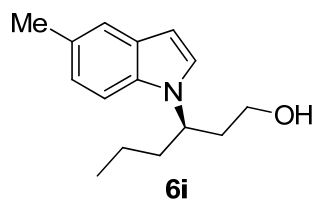


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.658	236023	11985	3.964	5.221
2	15.273	5717447	217574	96.036	94.779
Total		5953470	229559	100.000	100.000

(enantiomerically enriched **6h**)

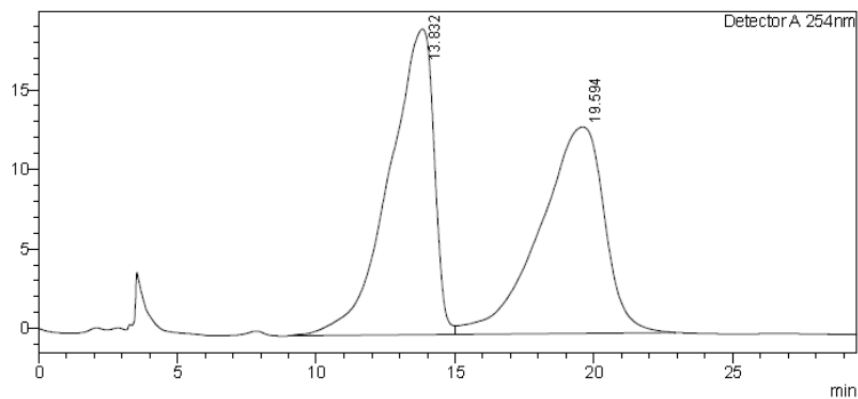
(R)-3-(5-Methyl-1H-indol-1-yl)hexan-1-ol **6i**



A colorless oil;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.86 (t,  $J = 7.3$  Hz, 3H), 1.08-1.16 (m, 1H), 1.18-1.25 (m, 1H), 1.77-1.84 (m, 1H), 1.89-1.97 (m, 1H), 2.01-2.13 (m, 2H), 2.45 (s, 3H), 3.23-3.28 (m, 1H), 3.49-3.53 (m, 1H), 4.53-4.59 (m, 1H), 6.47 (d,  $J = 2.6$  Hz, 1H), 7.02 (t,  $J = 5.1$  Hz, 1H), 7.10 (d,  $J = 8.2$  Hz, 1H), 7.32 (d,  $J = 8.8$  Hz, 1H), 7.42 (s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  13.76, 19.48, 21.28, 38.05, 38.37, 52.55, 59.32, 101.31, 109.17, 120.59, 122.97, 124.36, 128.41, 128.51, 135.06; The ee value was 92%,  $t_{\text{R}}$  (minor) = 13.69 min,  $t_{\text{R}}$  (major) = 19.44 min (Chiralcel ID,  $\lambda = 254$  nm, 1% iPrOH/hexanes, flow rate = 1.0 mL/min); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{NO}$   $[\text{M}+\text{H}]^+$  = 232.1696, found = 232.1702;  $[\alpha]_{\text{D}}^{25} = -4.08$  ( $c = 0.60$ ,  $\text{CHCl}_3$ ).

<Chromatogram>

mV



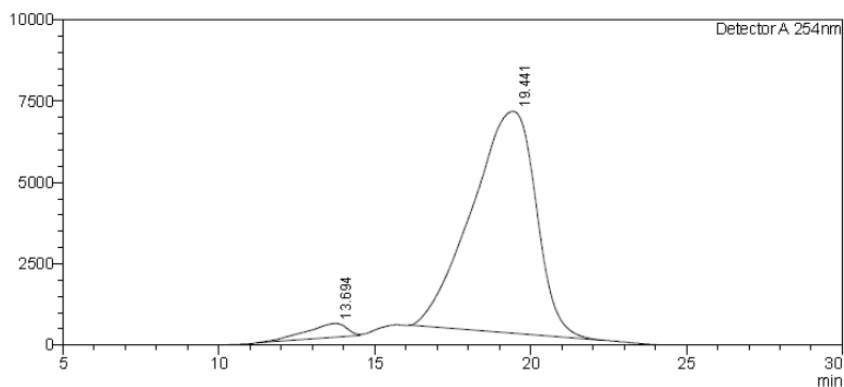
<Peak Table>

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.832	2155388	19204	50.666			
2	19.594	2088744	12964	49.334		V	
Total		4254132	32168				

(racemic **6i**)

<Chromatogram>

uV



<Peak Table>

Detector A 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.694	39167	421	3.847		M	
2	19.441	978913	6831	96.153			
Total		1018080	7251				

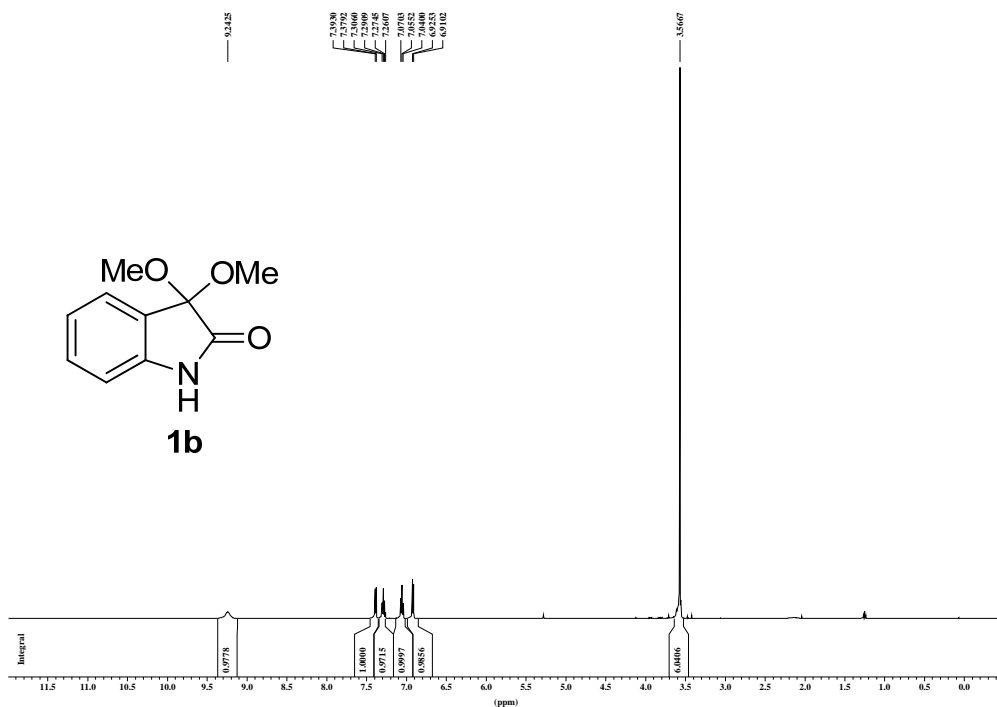
(enantiomerically enriched **6i**)

Reference

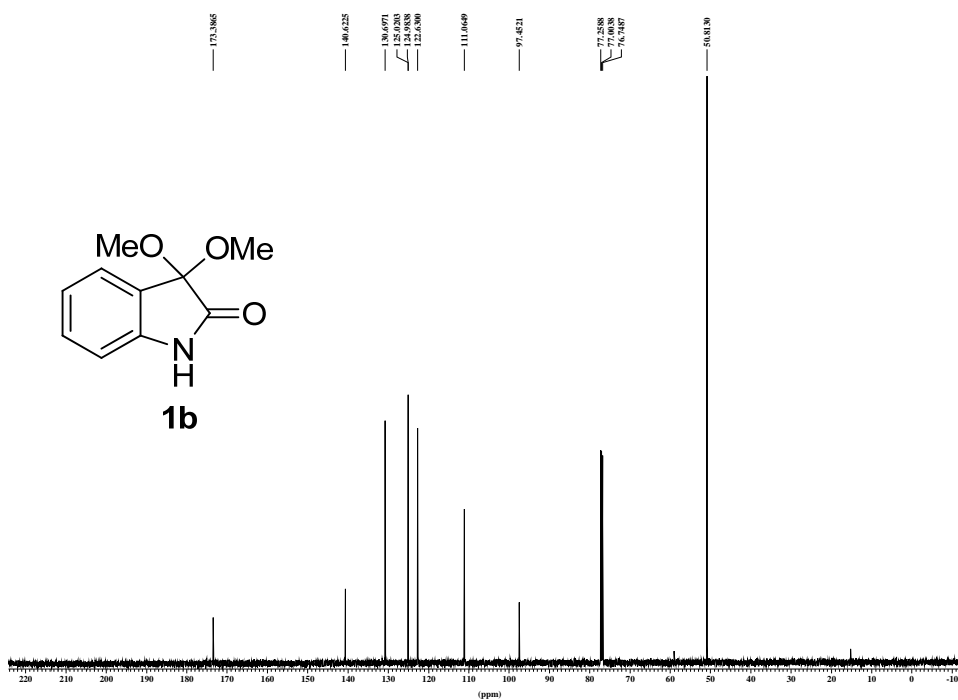
[1] W.-B. Liu, X. Zhang, L.-X. Dai, S.-L. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 5183.

## E. NMR Spectra of the Substrates and Products.

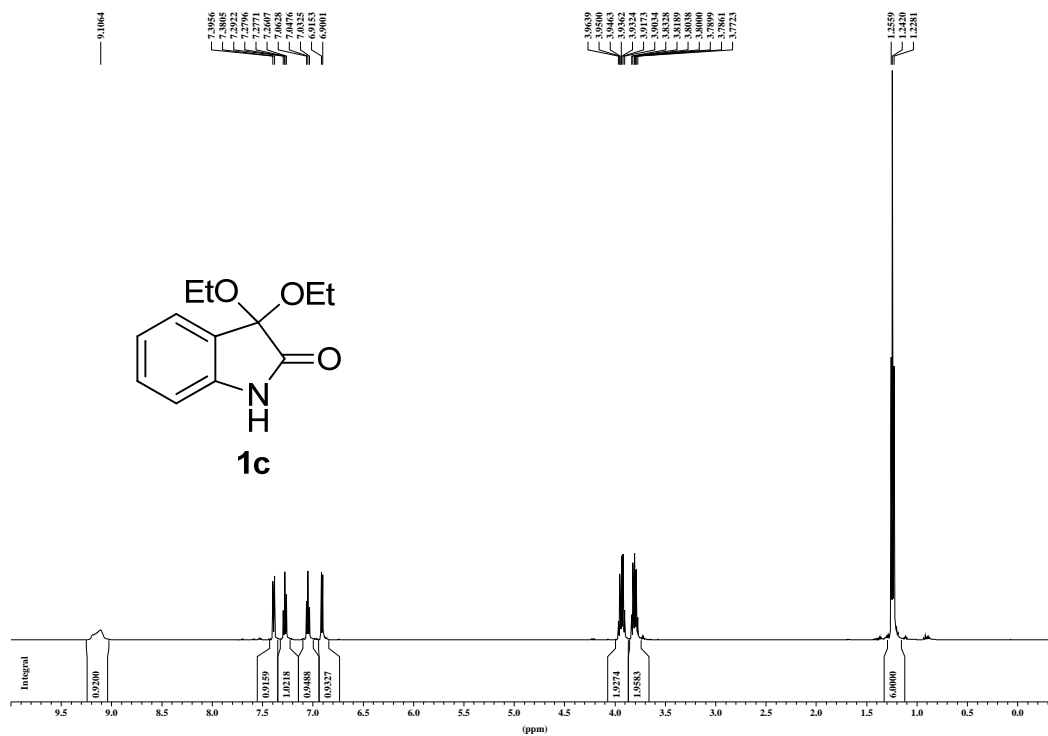
<sup>1</sup>H AMX500 dxw0311-1 1796H



<sup>13</sup>C AMX500 dxw0311-2 1796C

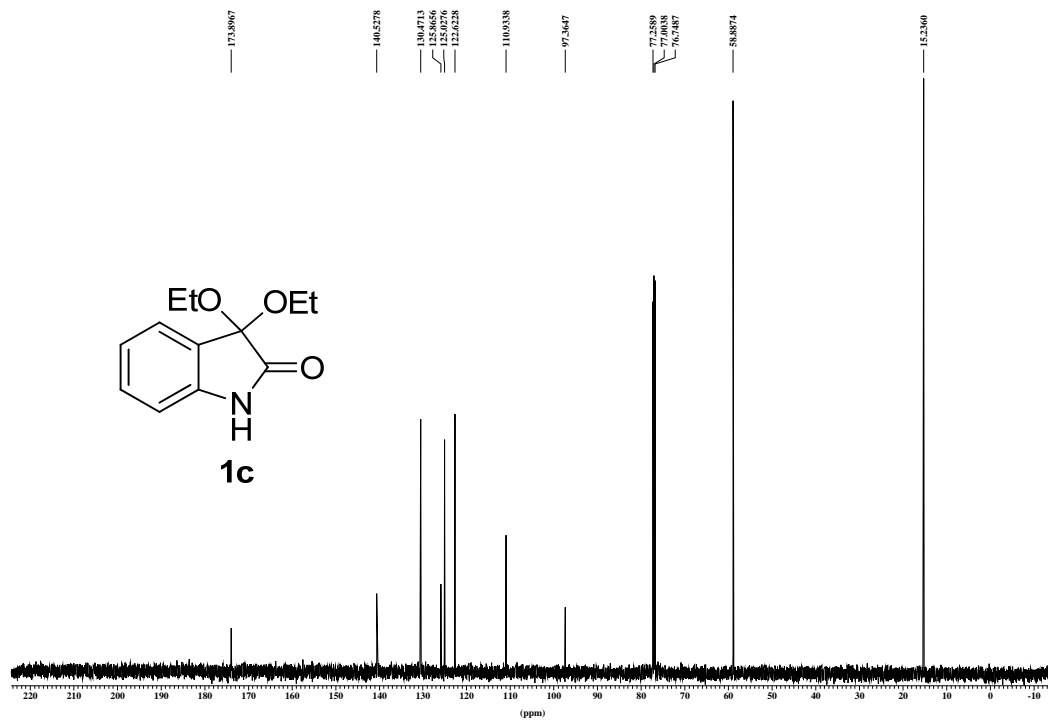


1H AMX500 dxw0324-1 1b

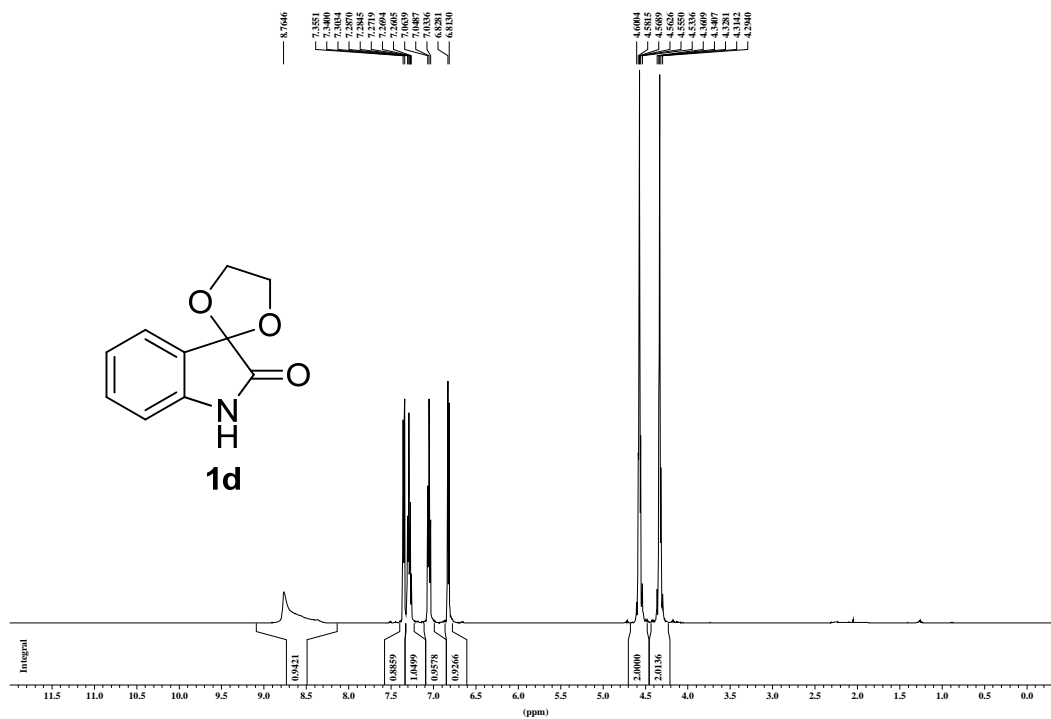


13C AMX500 dxw0324-2 1b

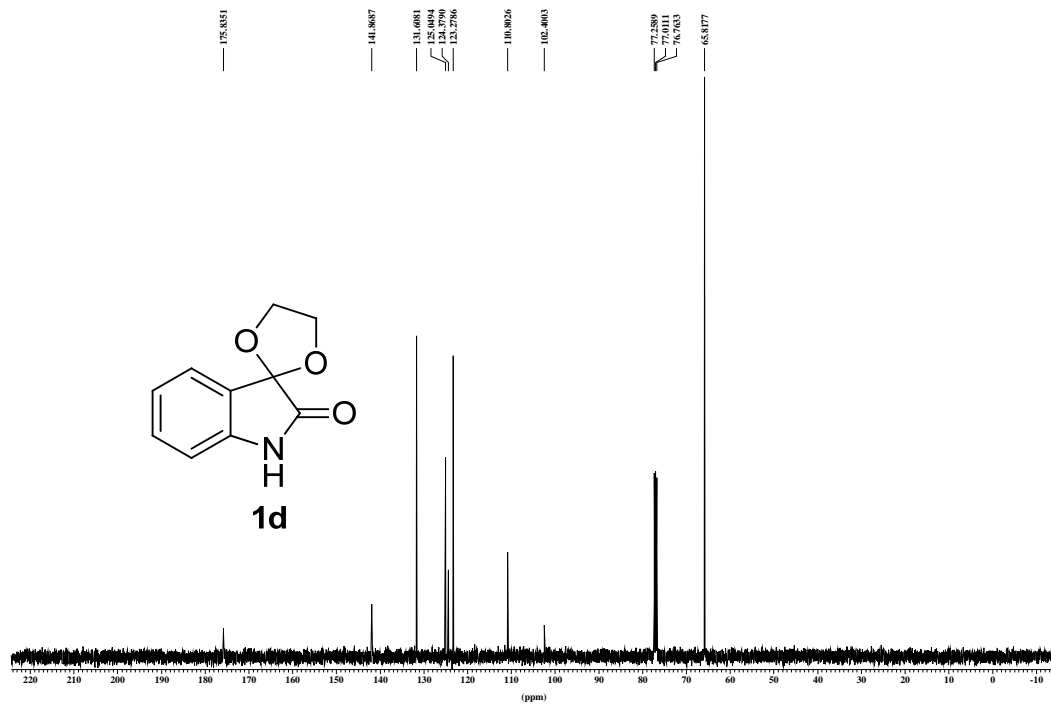
A1 hydr



1H AMX500 dxw0324-3 1d

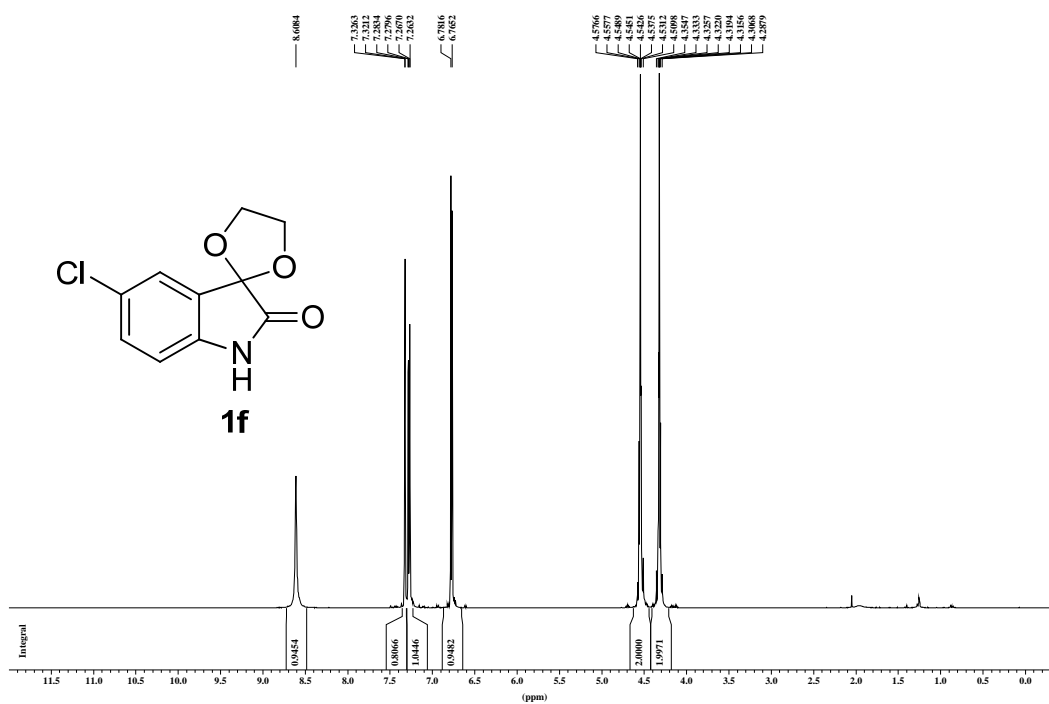


13C AMX500 dxw0324-4 1d  
A1 hydr



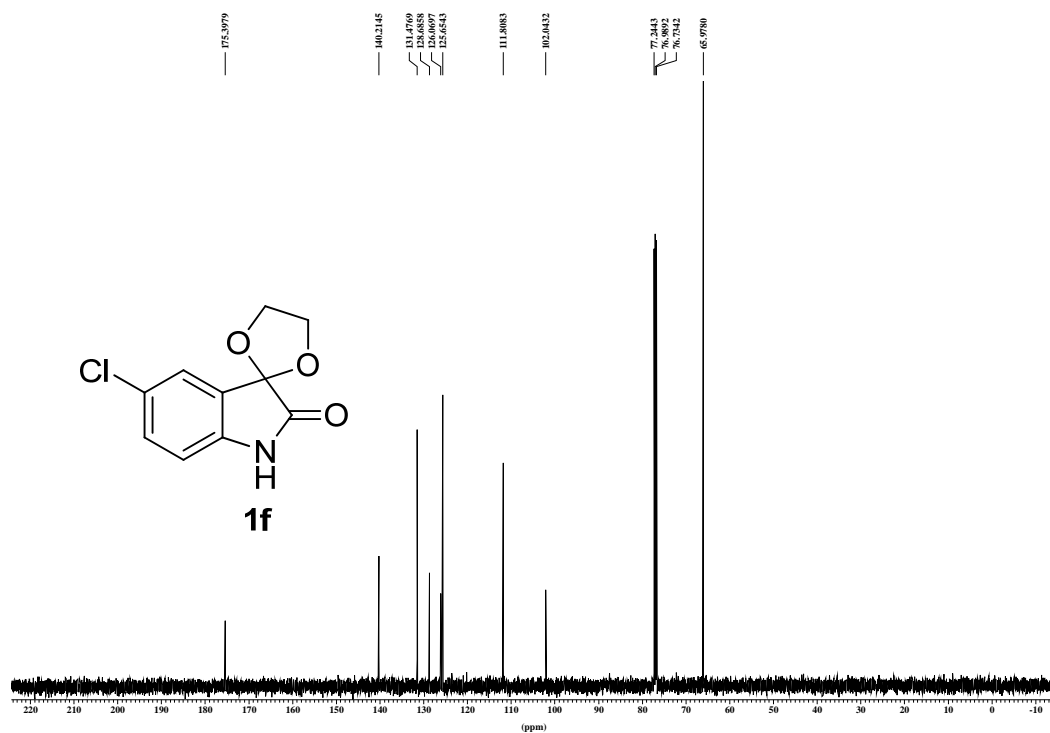


1H AMX500 dsw0324-5 1f

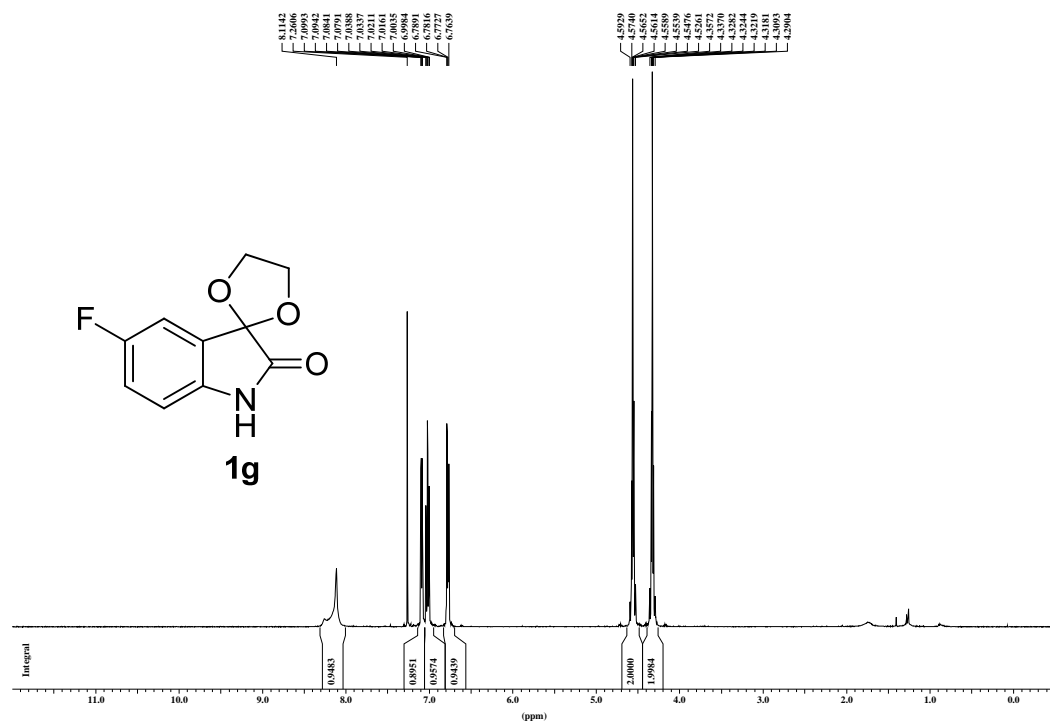


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A1 hydr

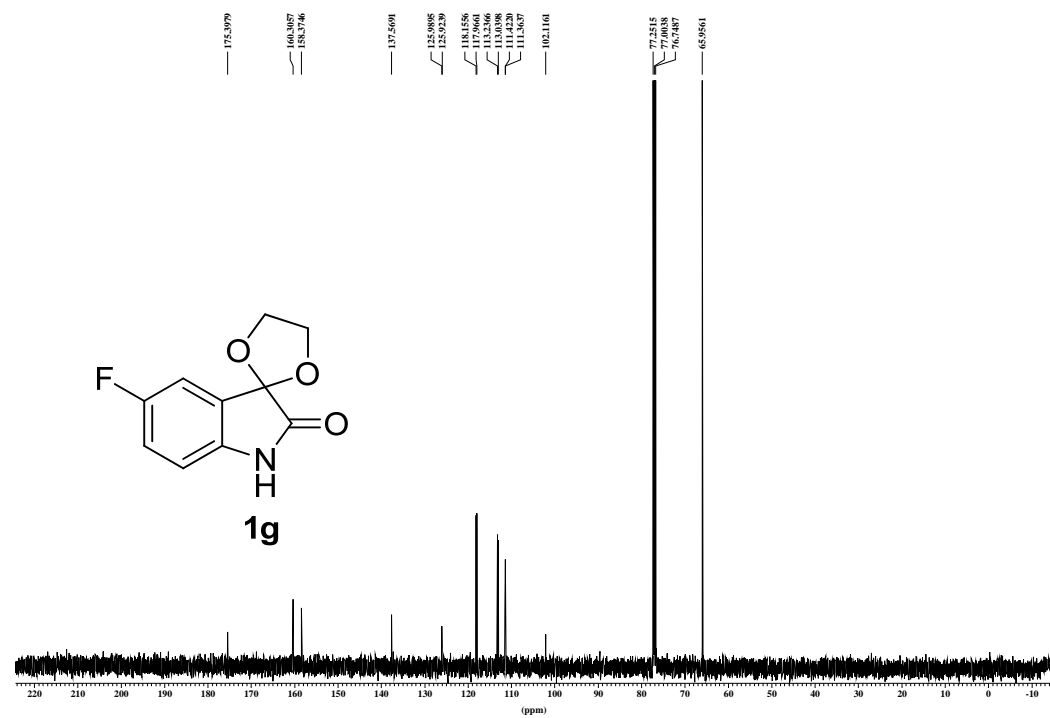


1H AMX500 dxw0324-2-1 1g

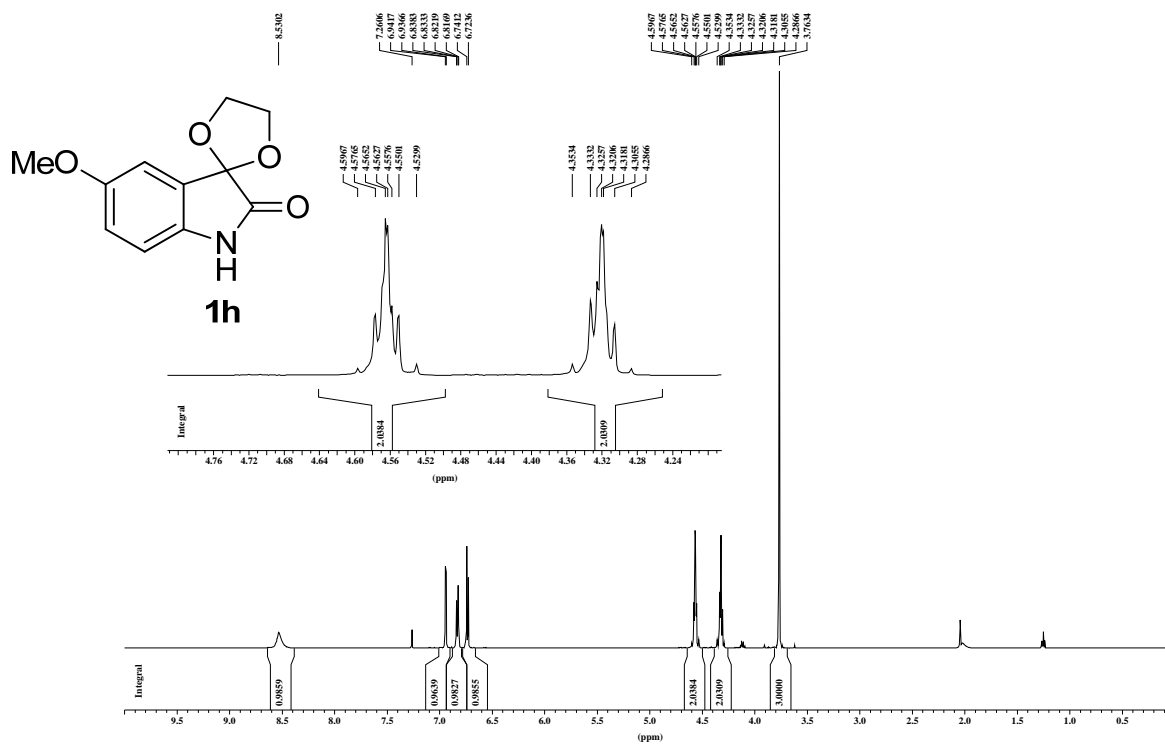


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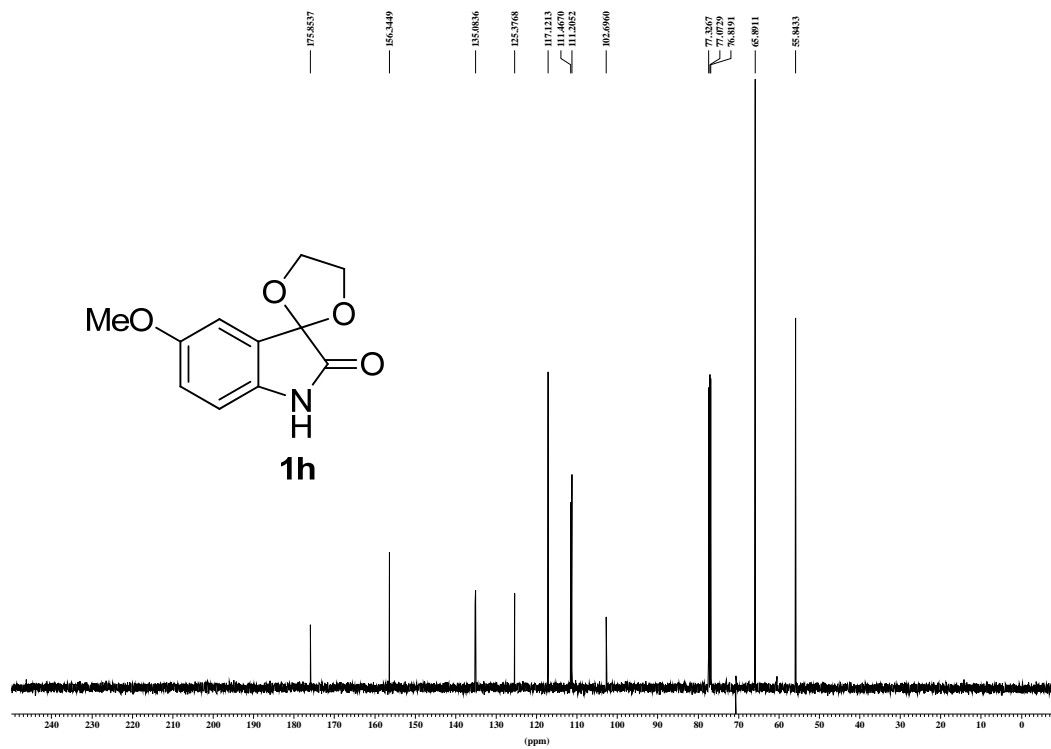
A1 hydr



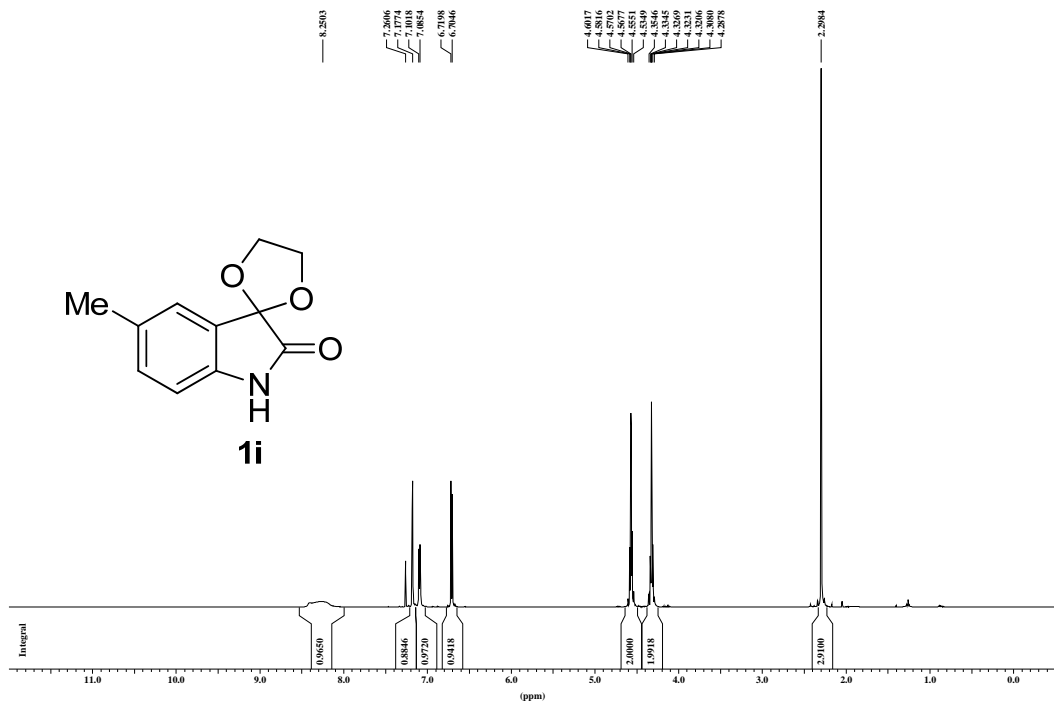
1H AMX500 dxw0721-3-5-OMe substrate



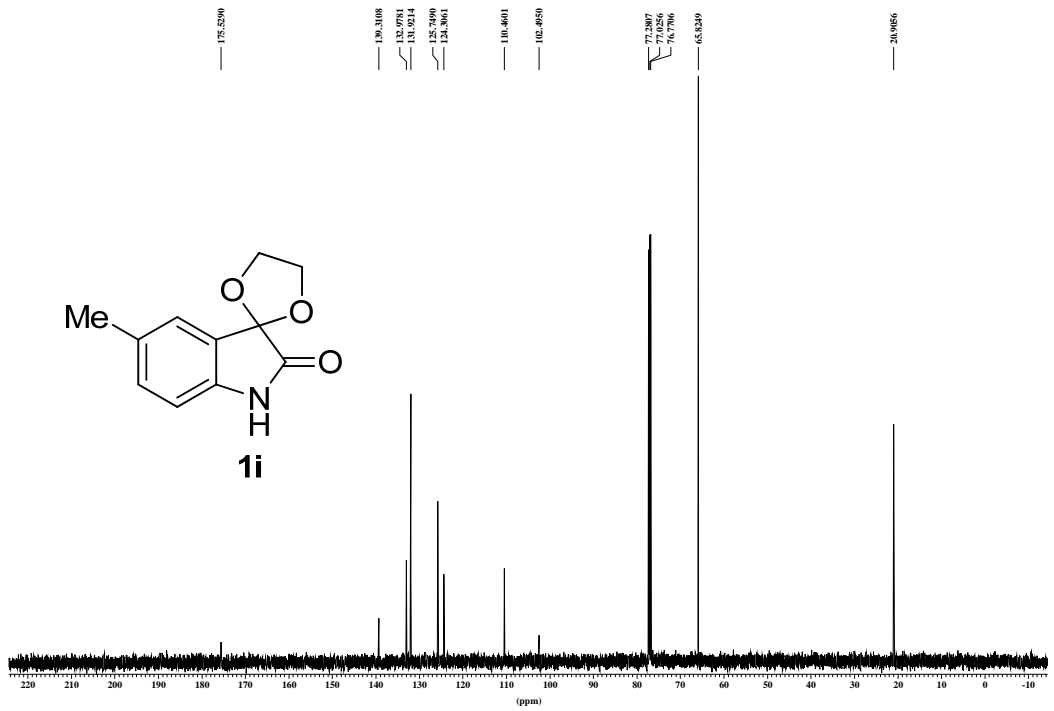
13C AMX500 dxw0721-4 5-OMe-substrate



1H AMX500 dsw0324-2-5 li

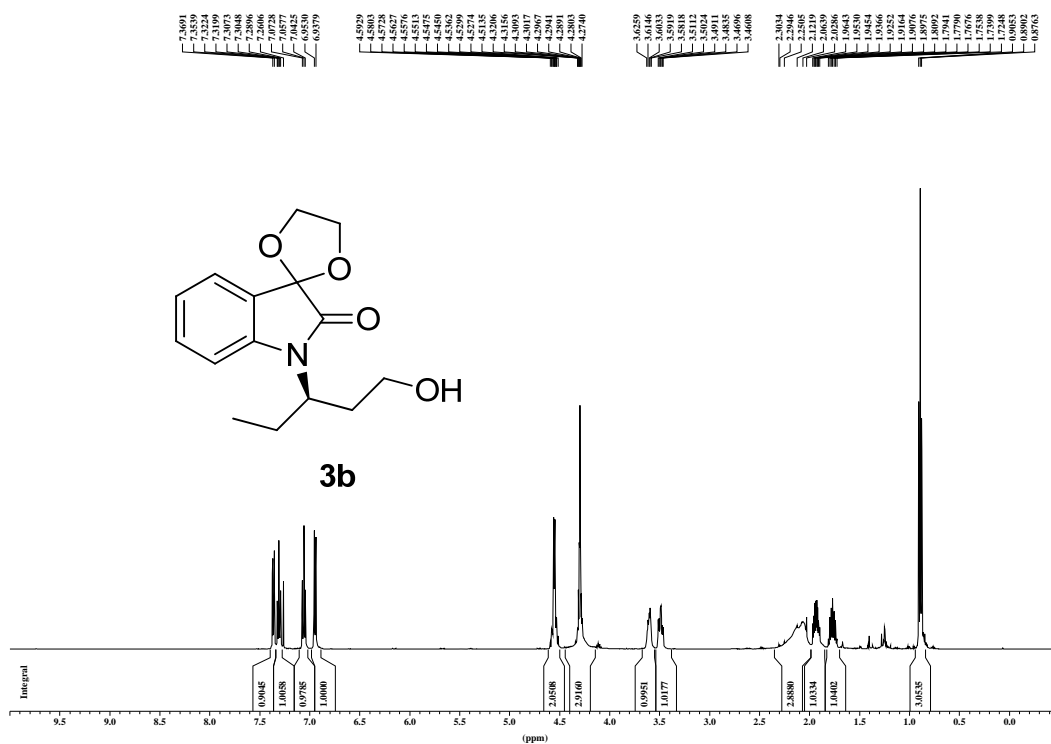


13C AMX500 dsw0324-2-6 li  
A1 hydr

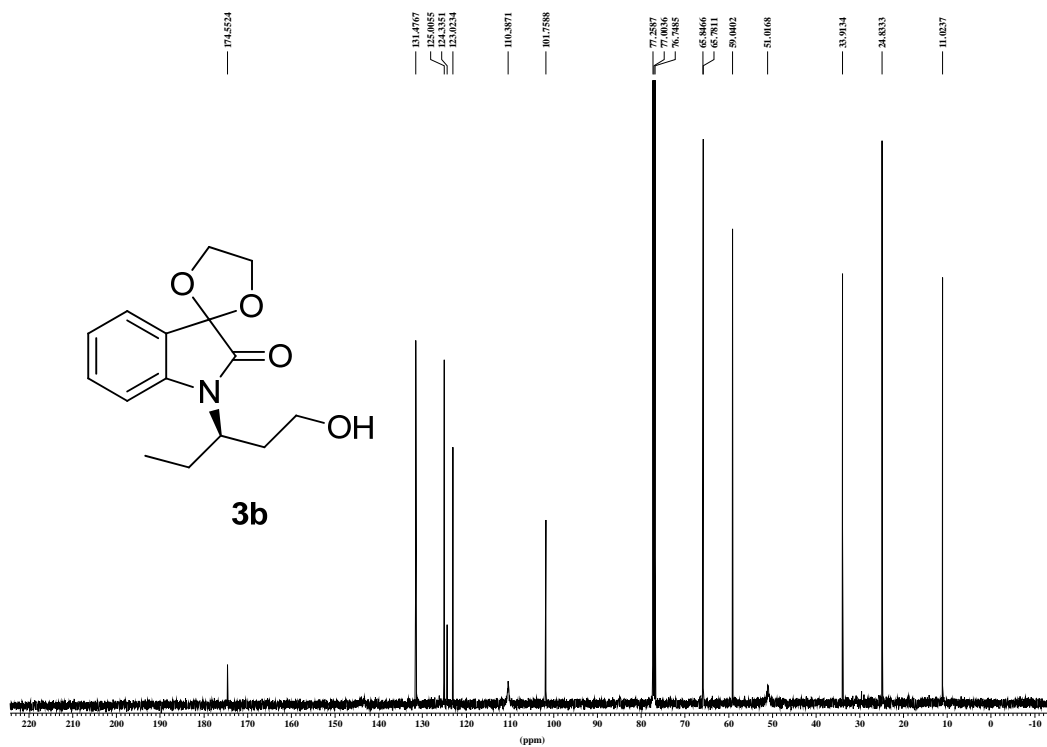




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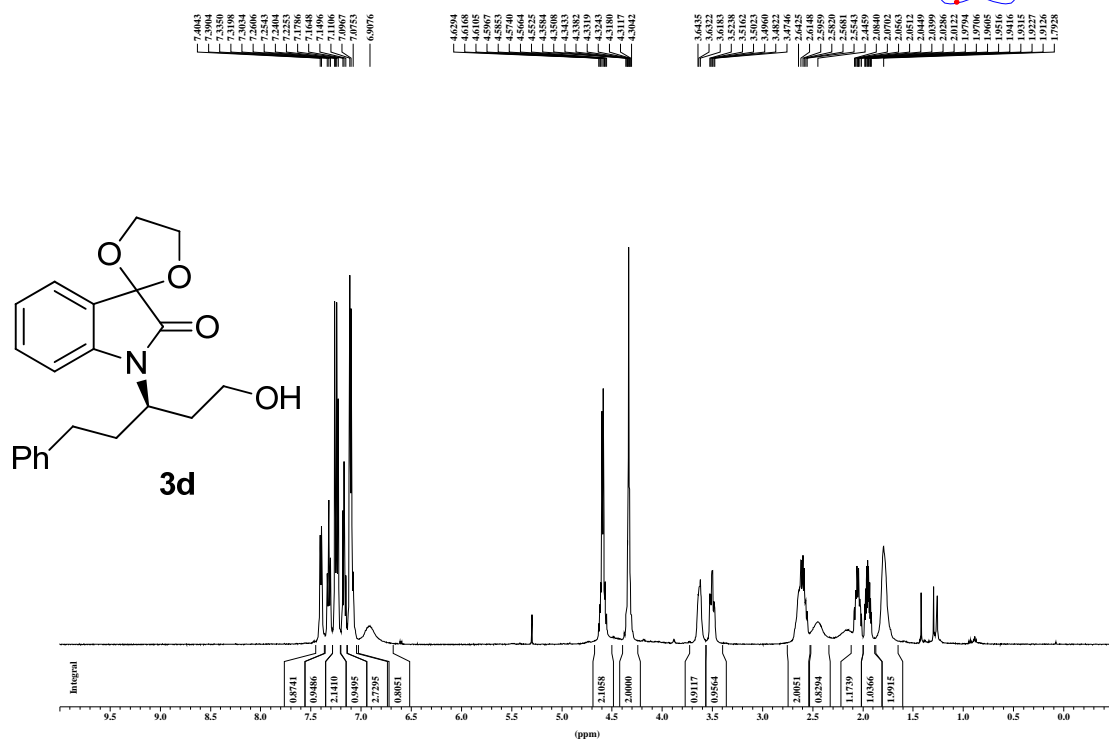


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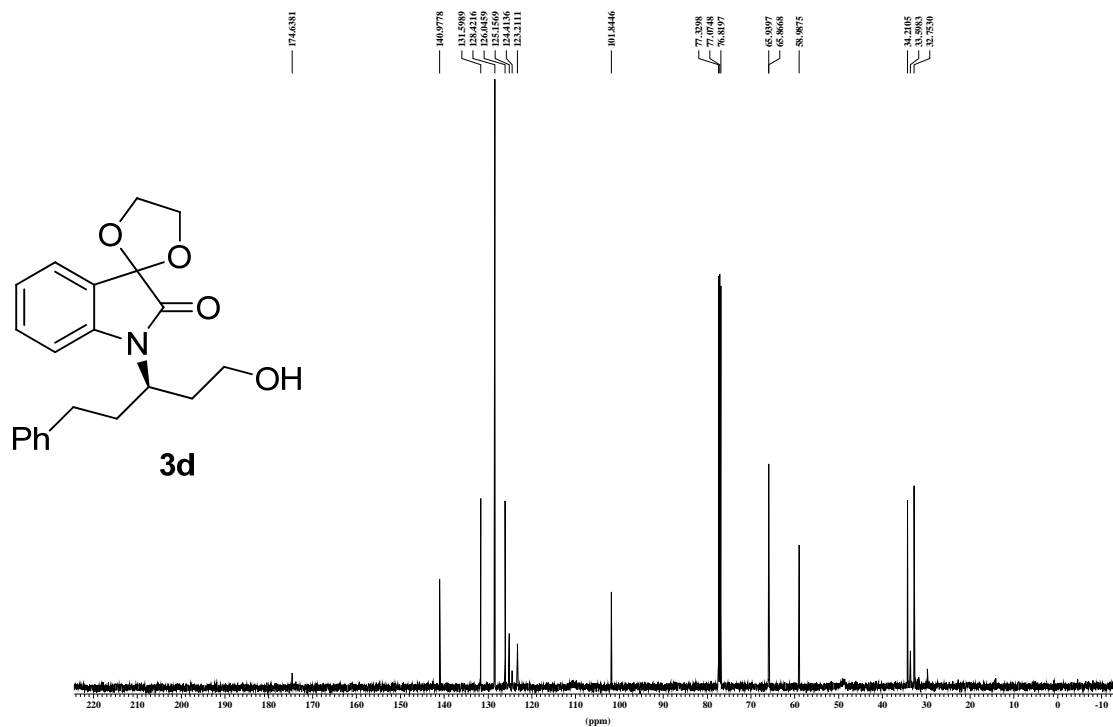




1H AMX500 dxw0218-1 1894H

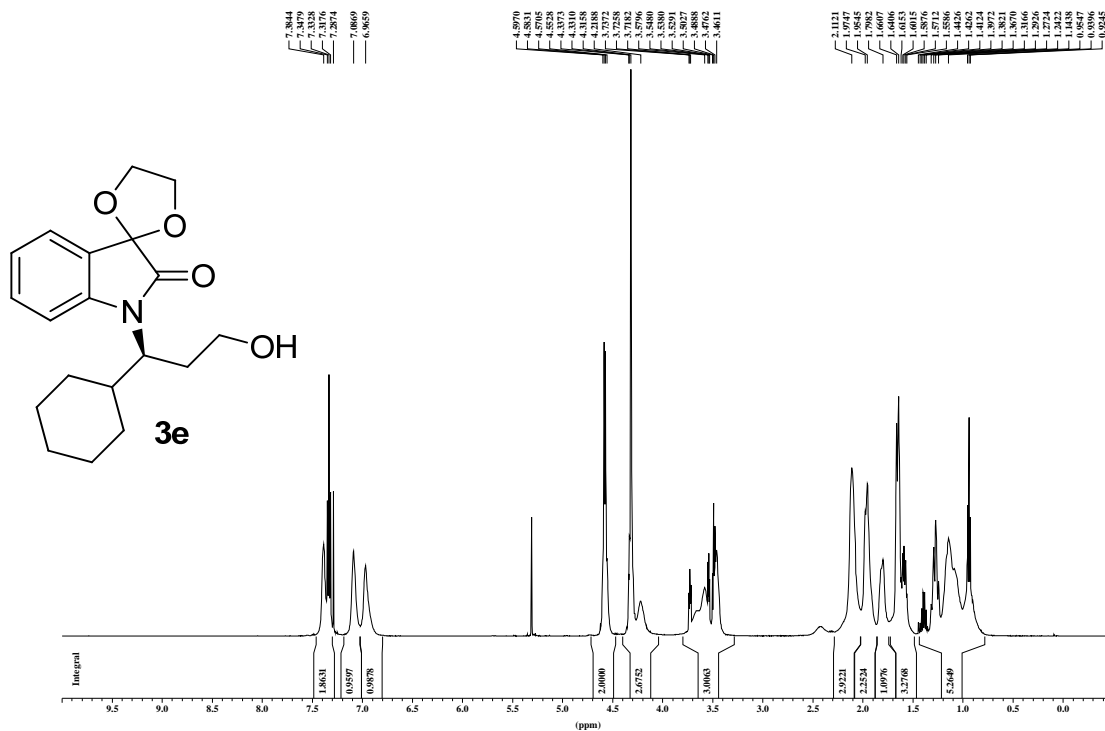


13C AMX500 dxw0312-4 1894C  
A1 hydr

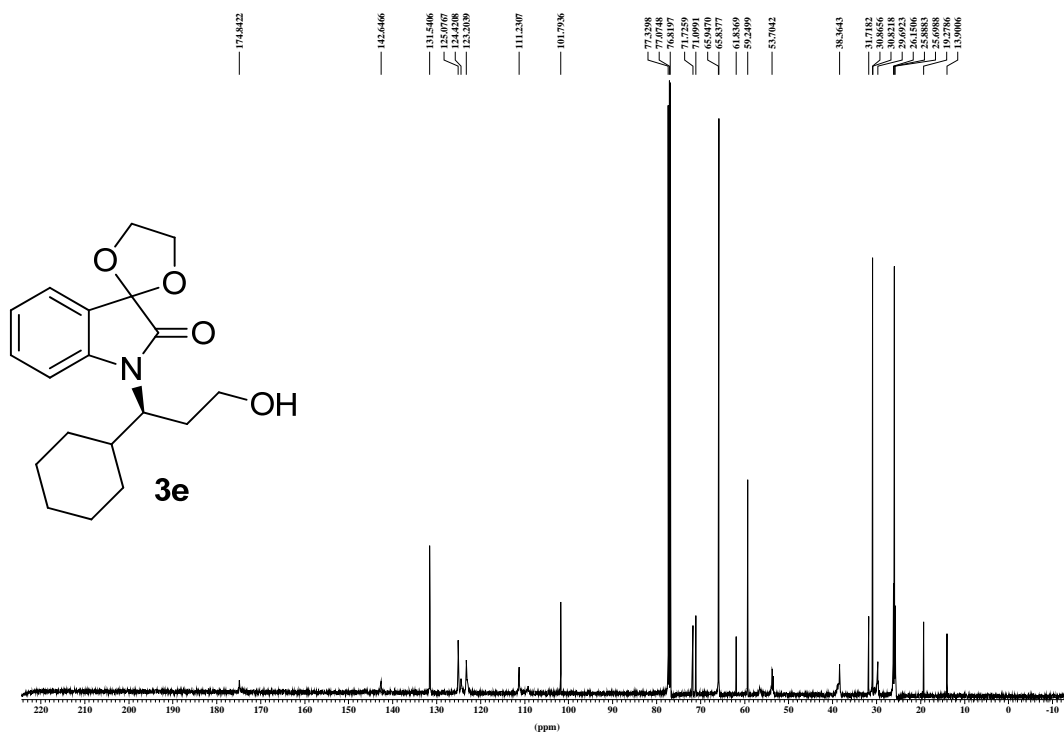




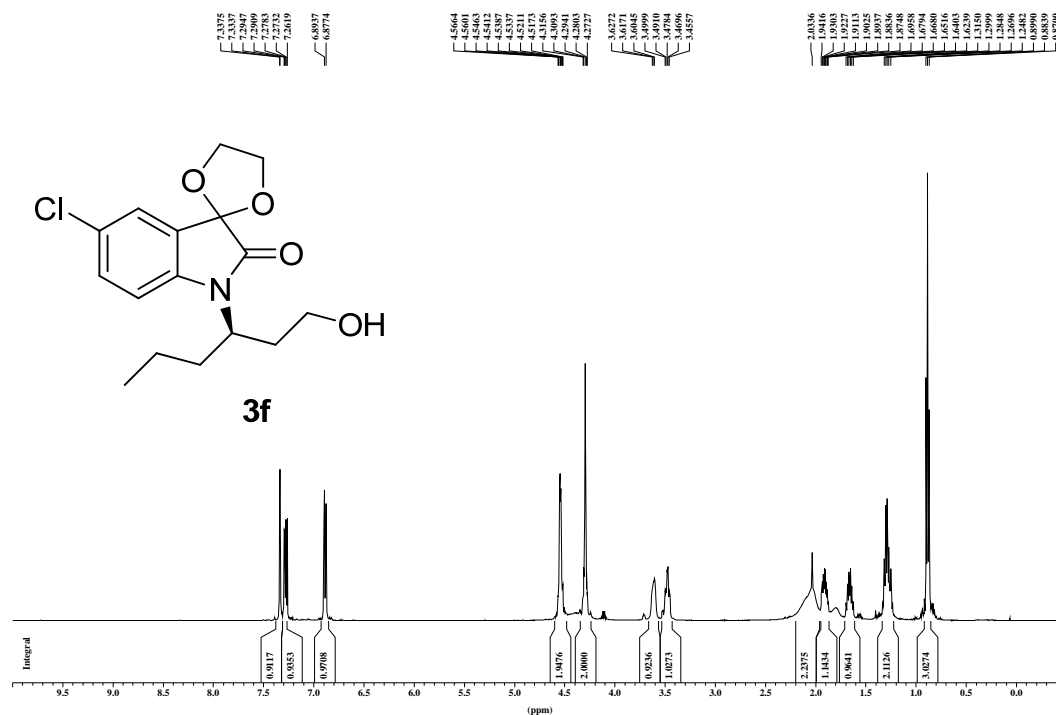
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dxw



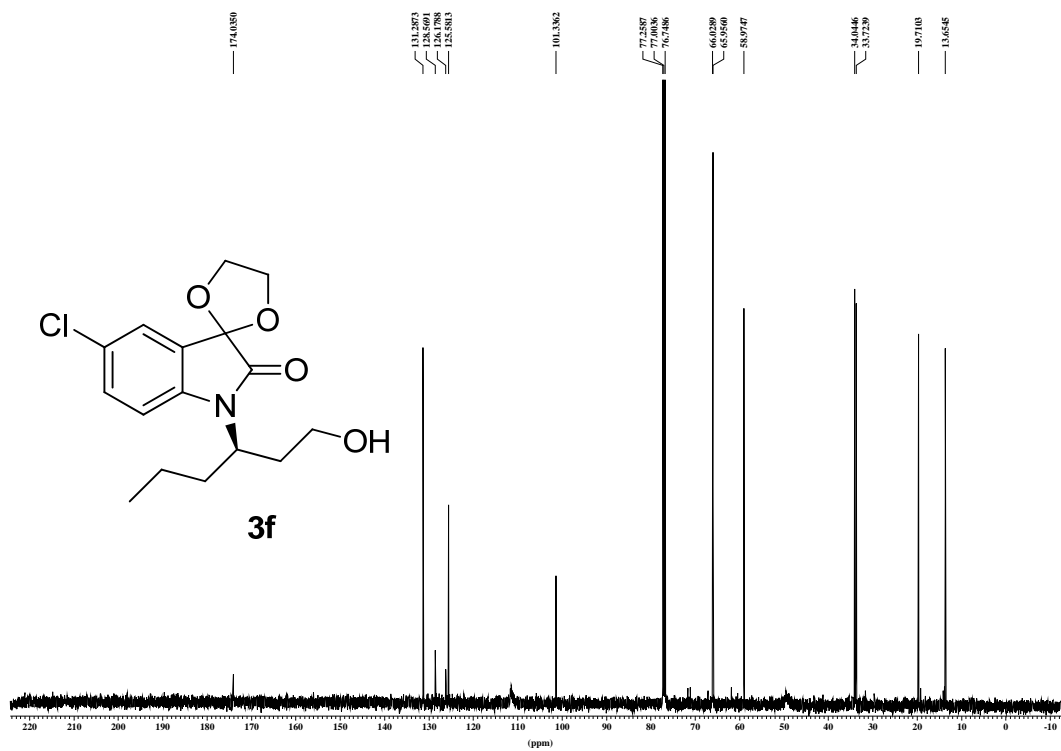
13C AMX500  
dxw



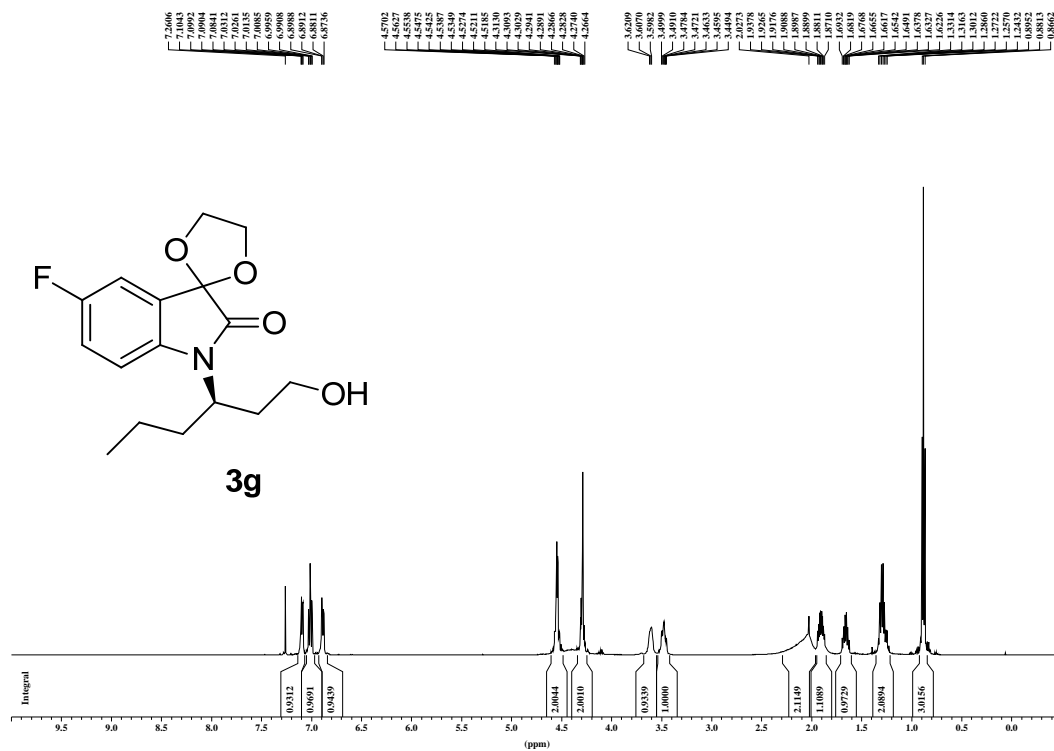
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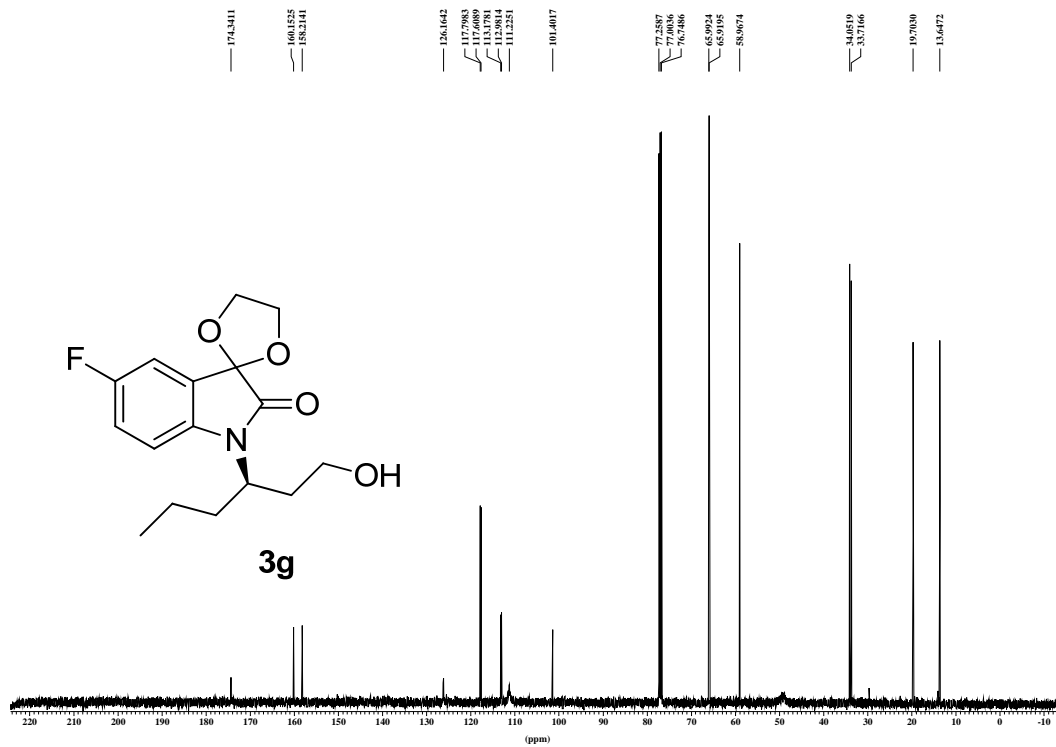
13C AMX500 dxw0904-4 1903C



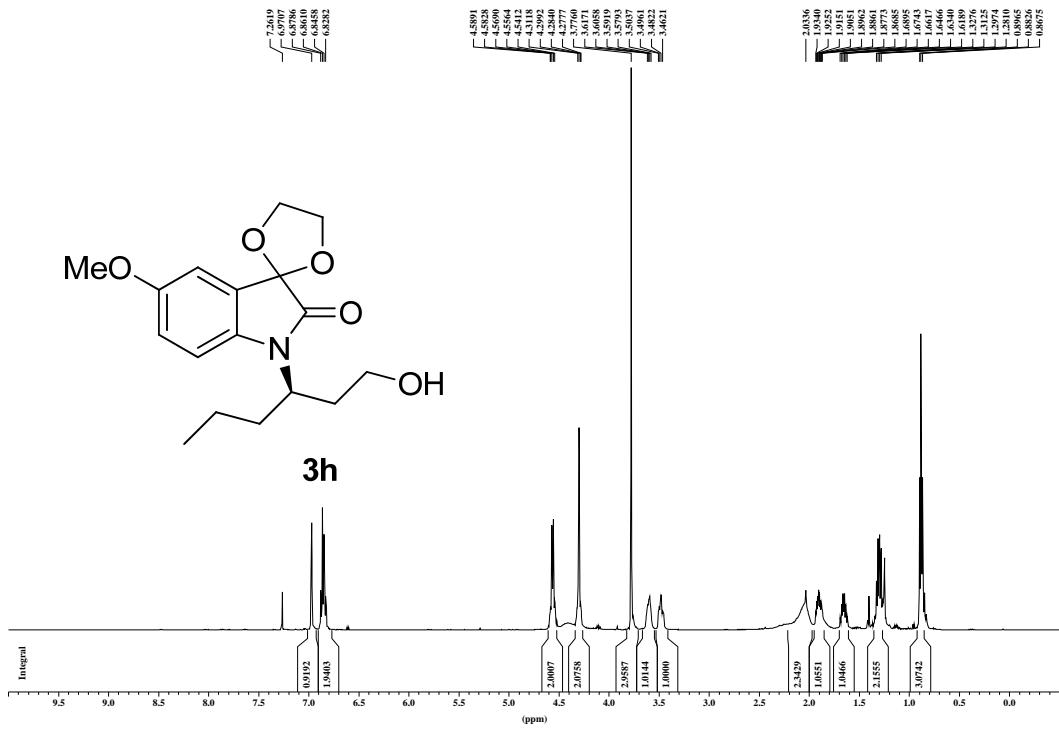
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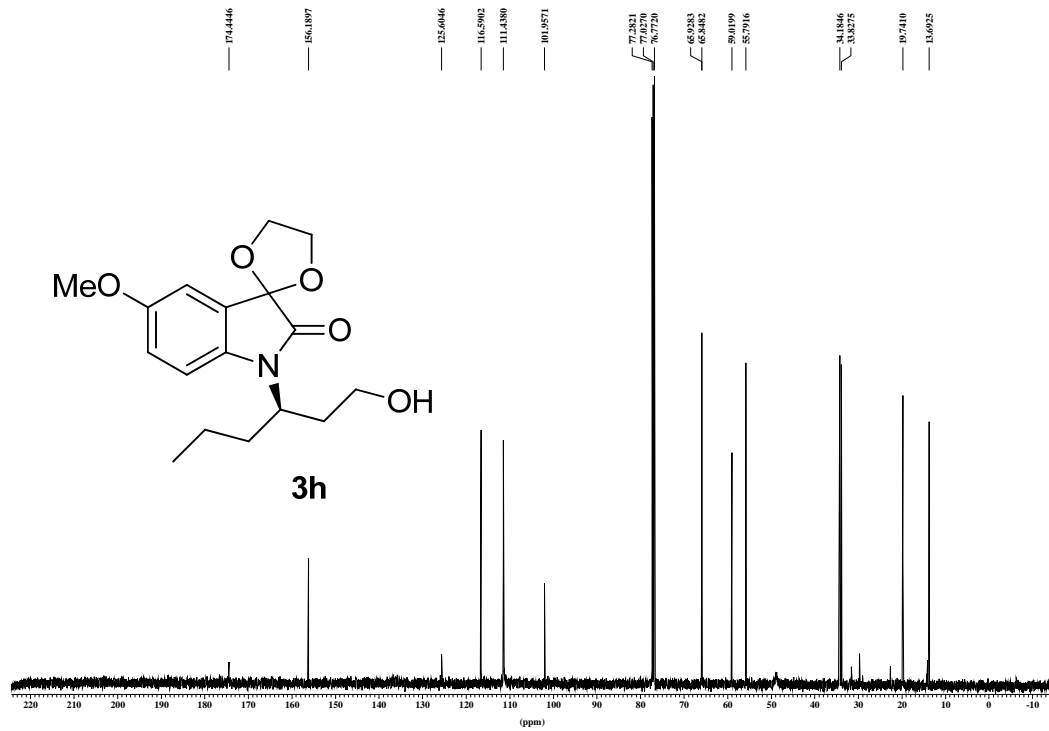
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1H AMX500 dxw0829-3 1899H



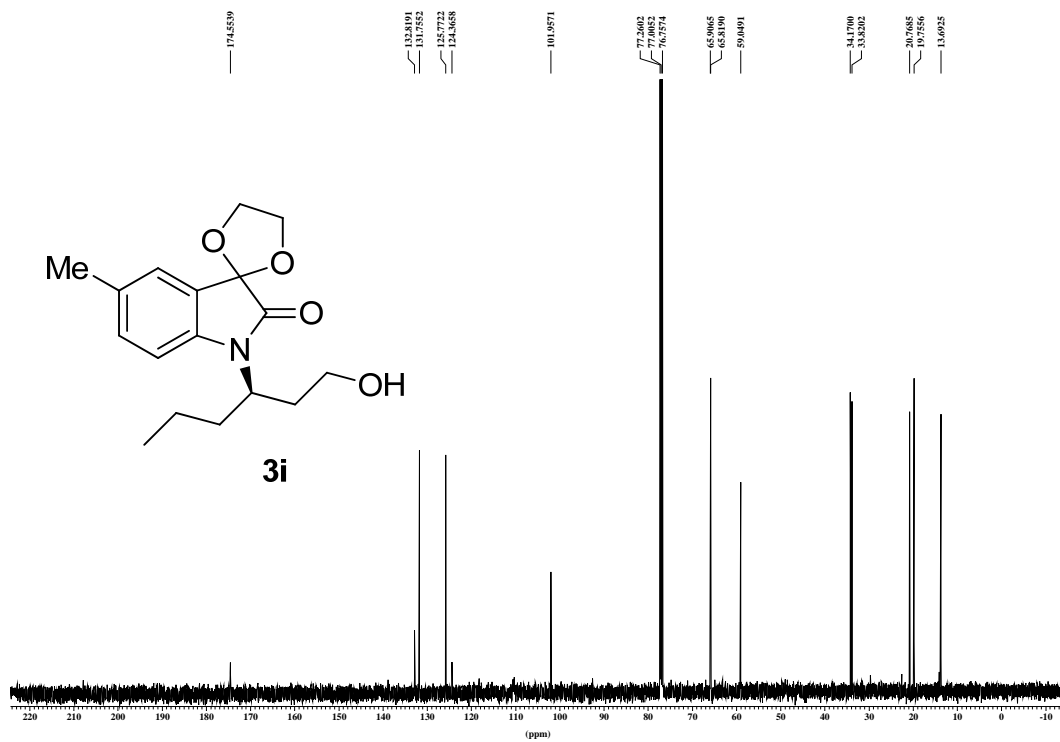
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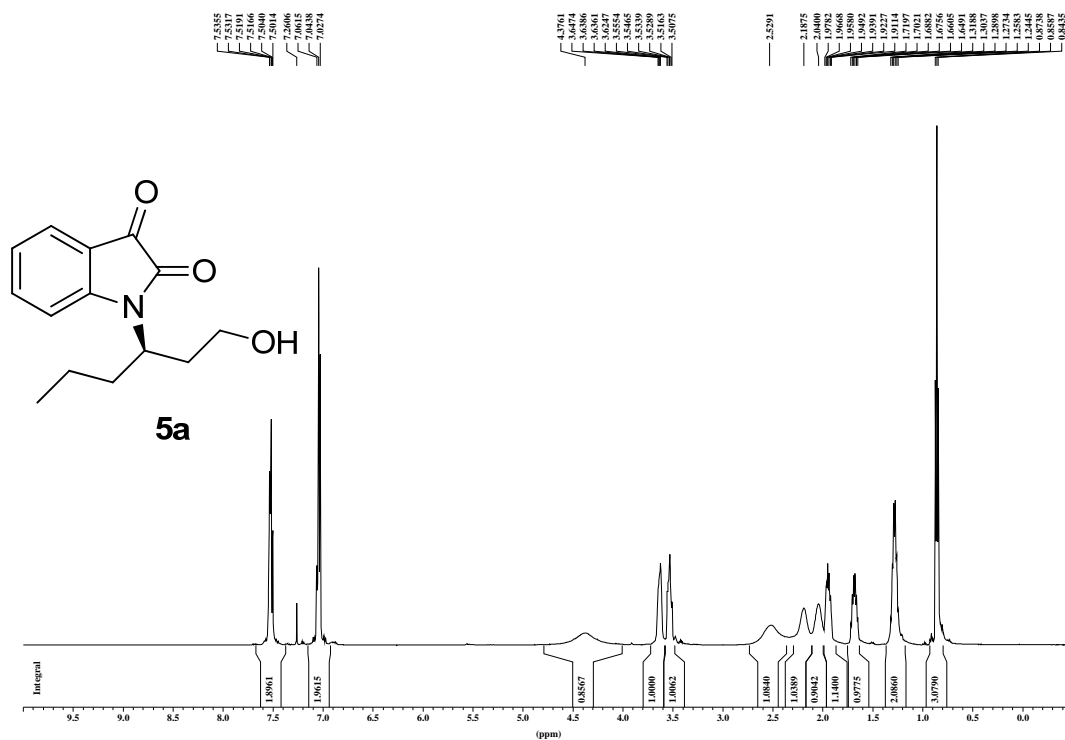
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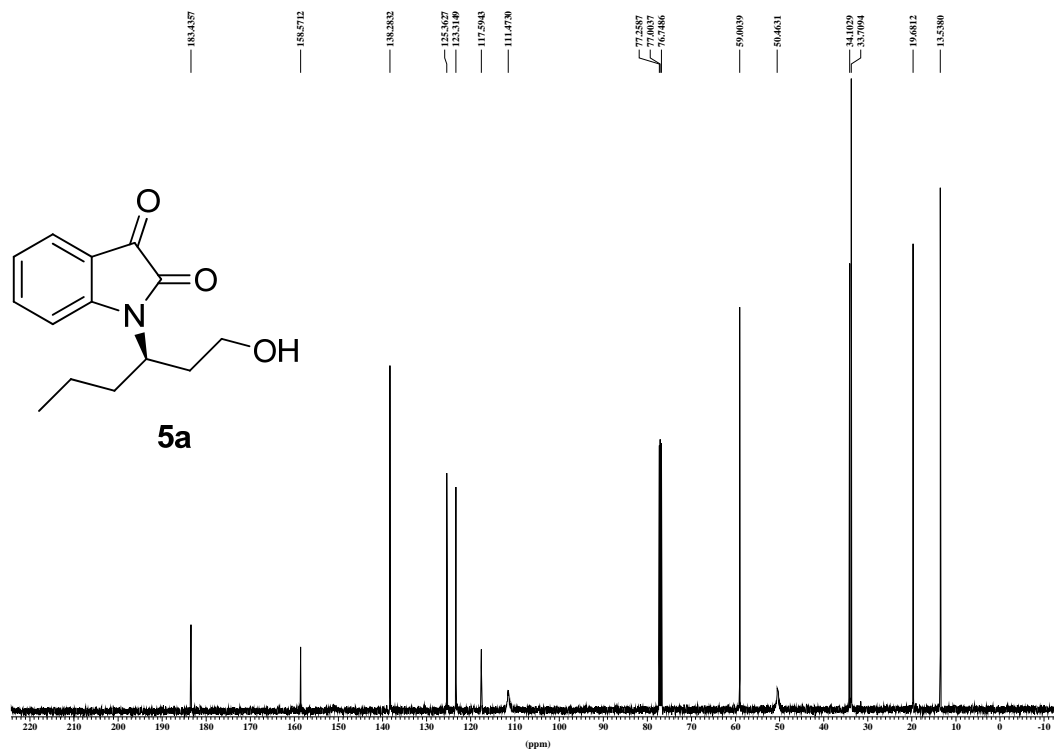
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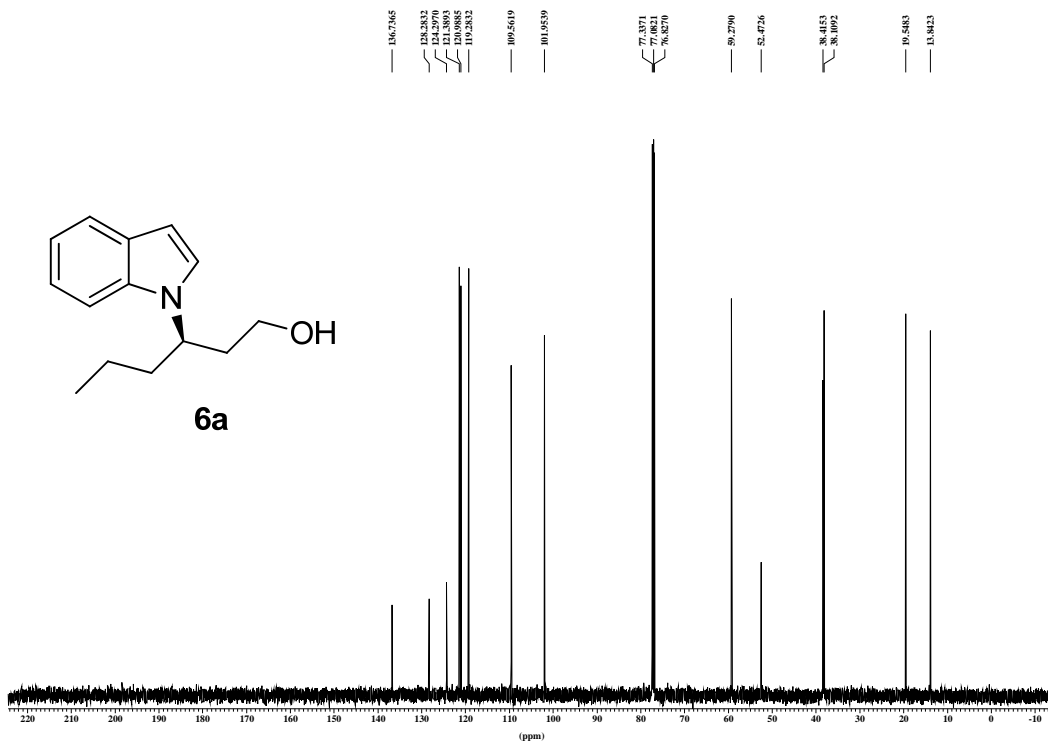
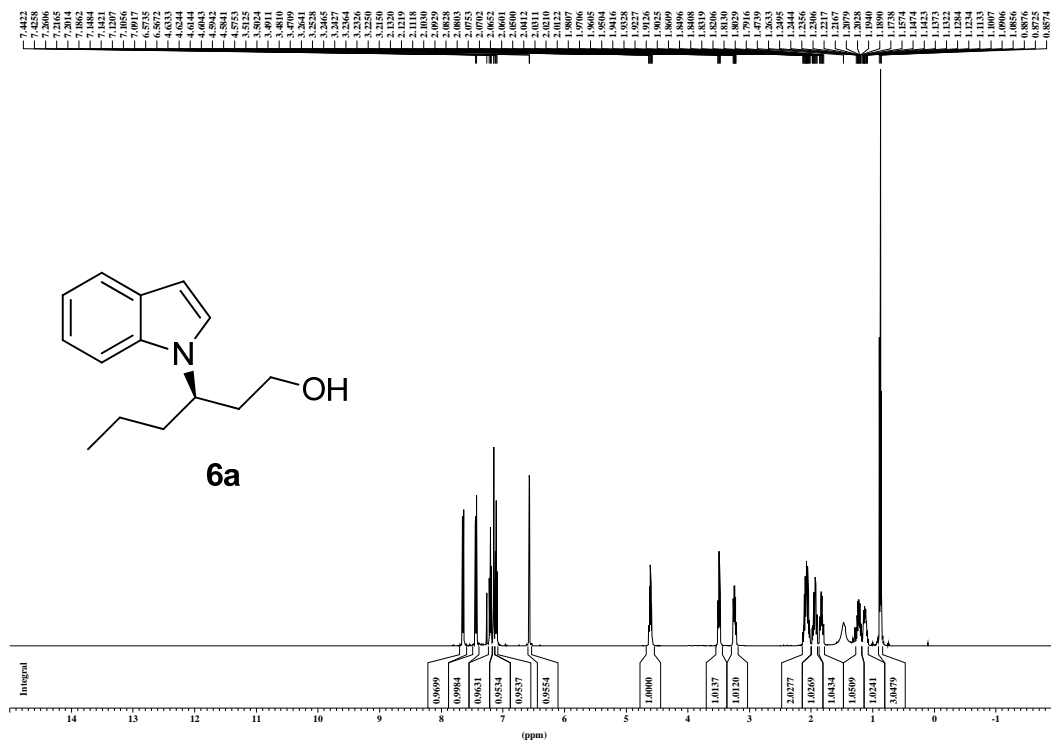


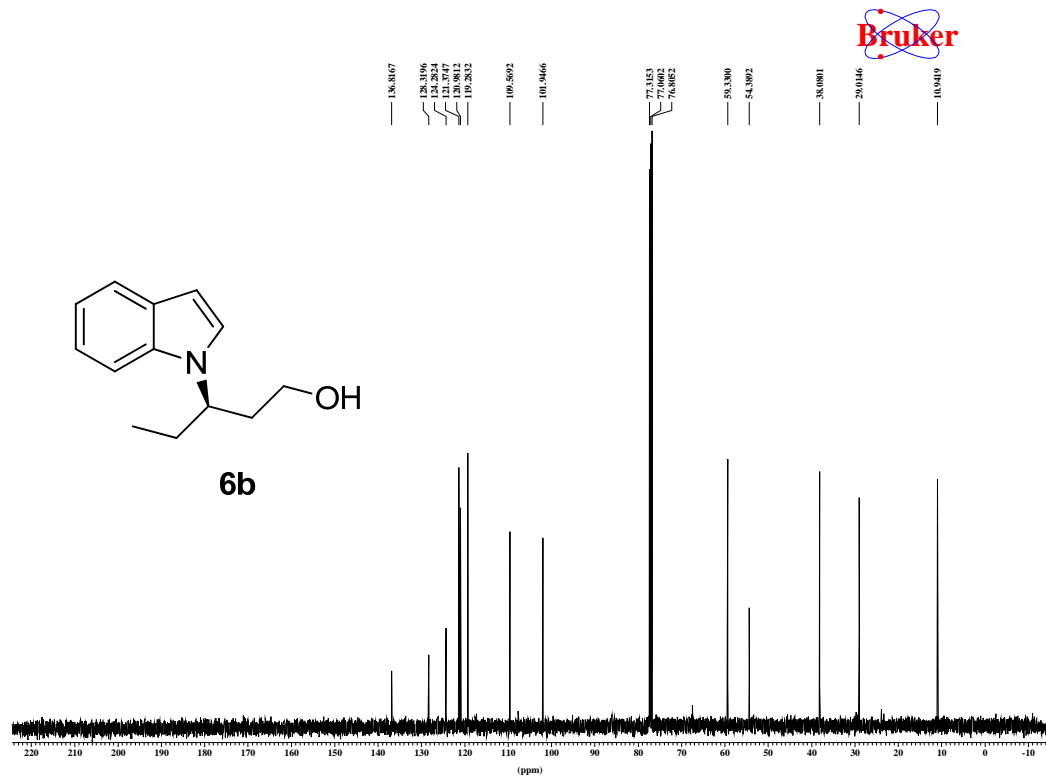
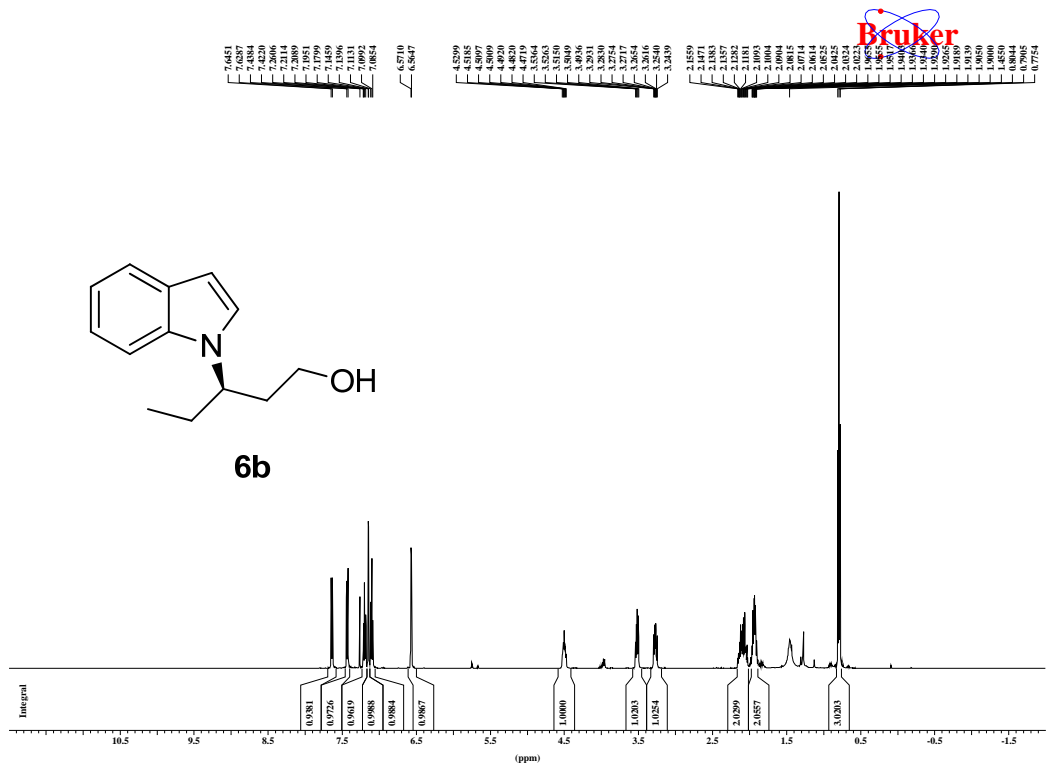
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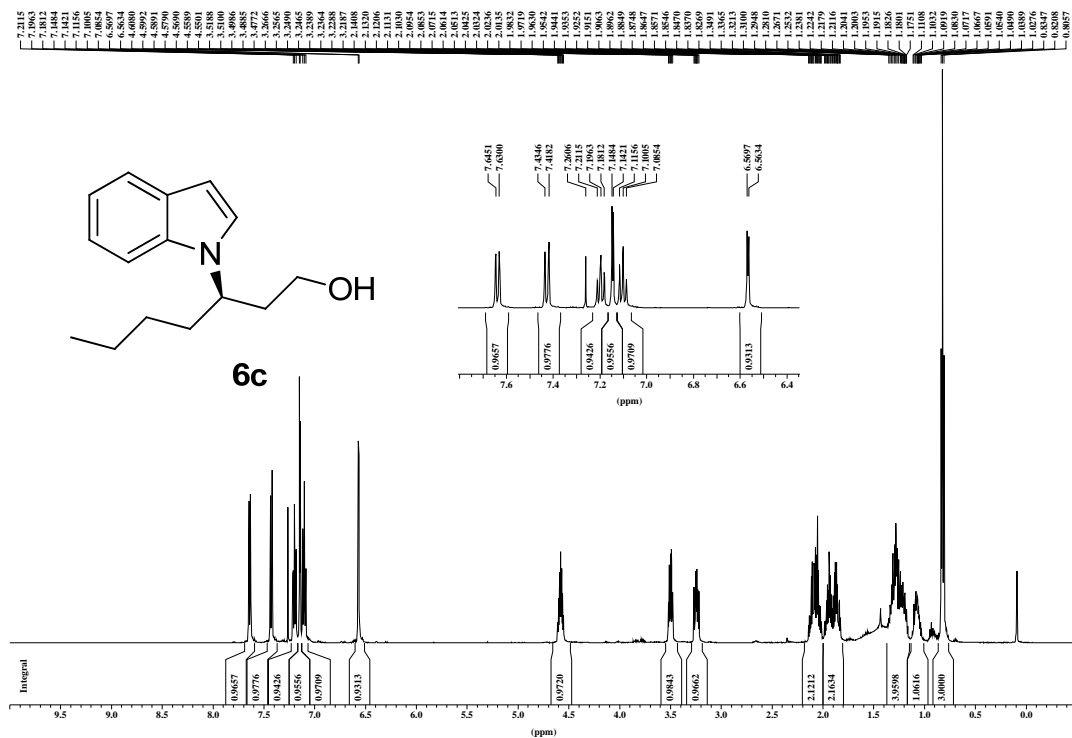




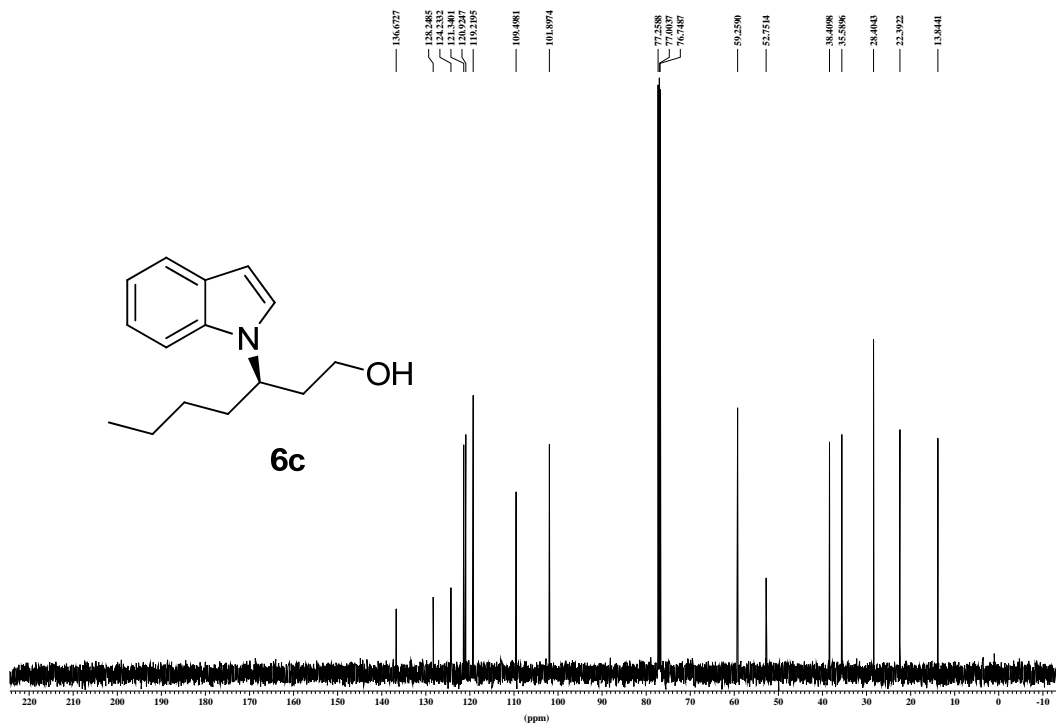




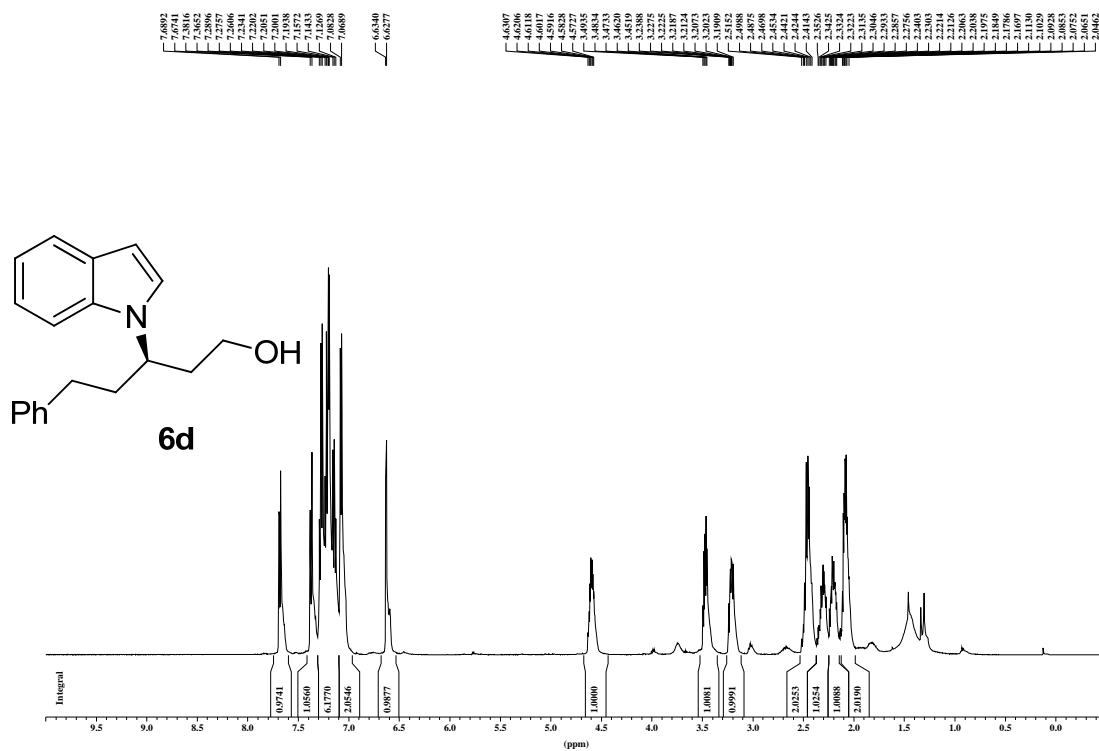
<sup>1</sup>H AMX500 dxw0318-1 indole 6c



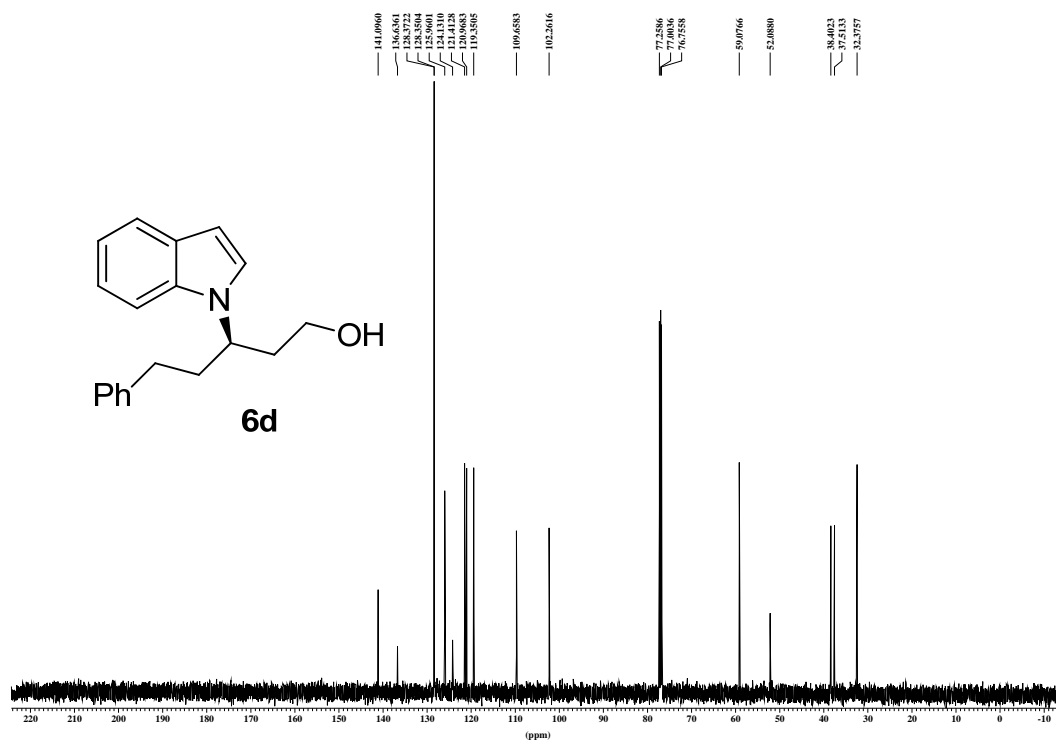
<sup>13</sup>C AMX500 dxw0318-2 indole 6c  
A1 hydr

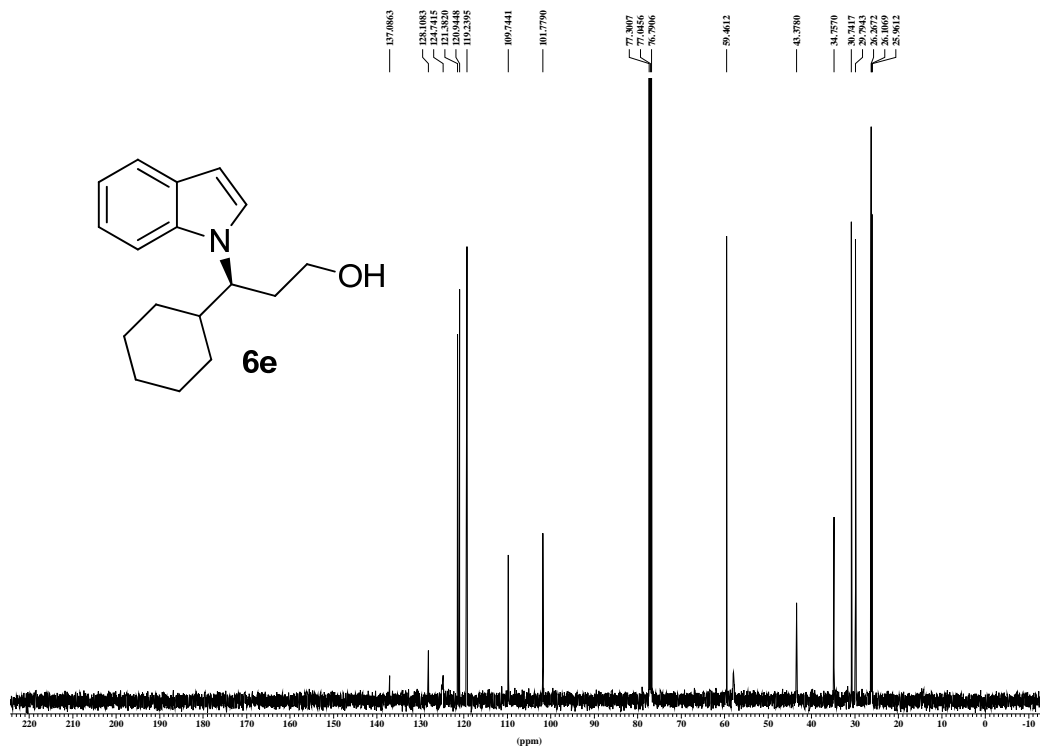
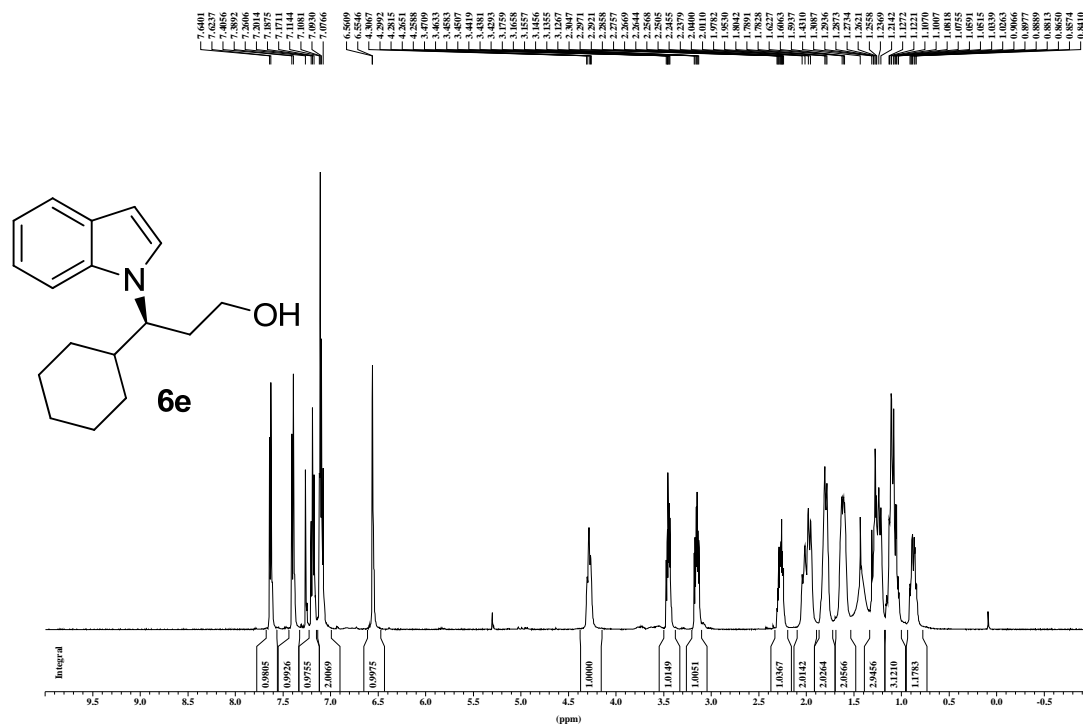


1H AMX500 dxw0704-1 1877H

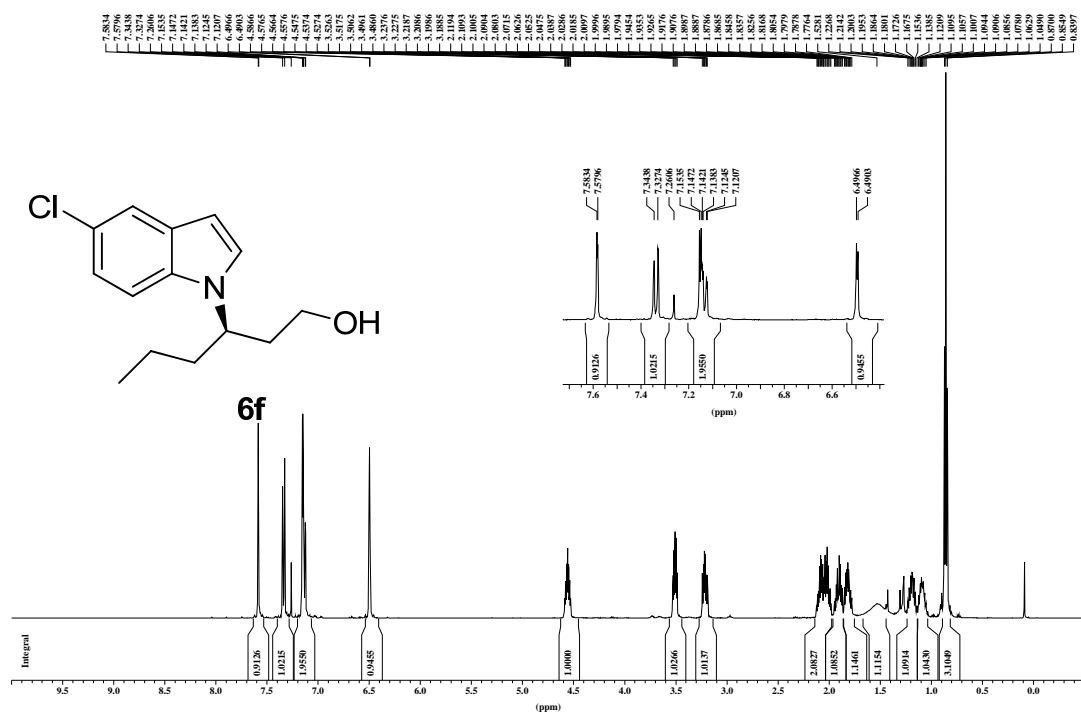


13C AMX500 dxw0704-2 1877C

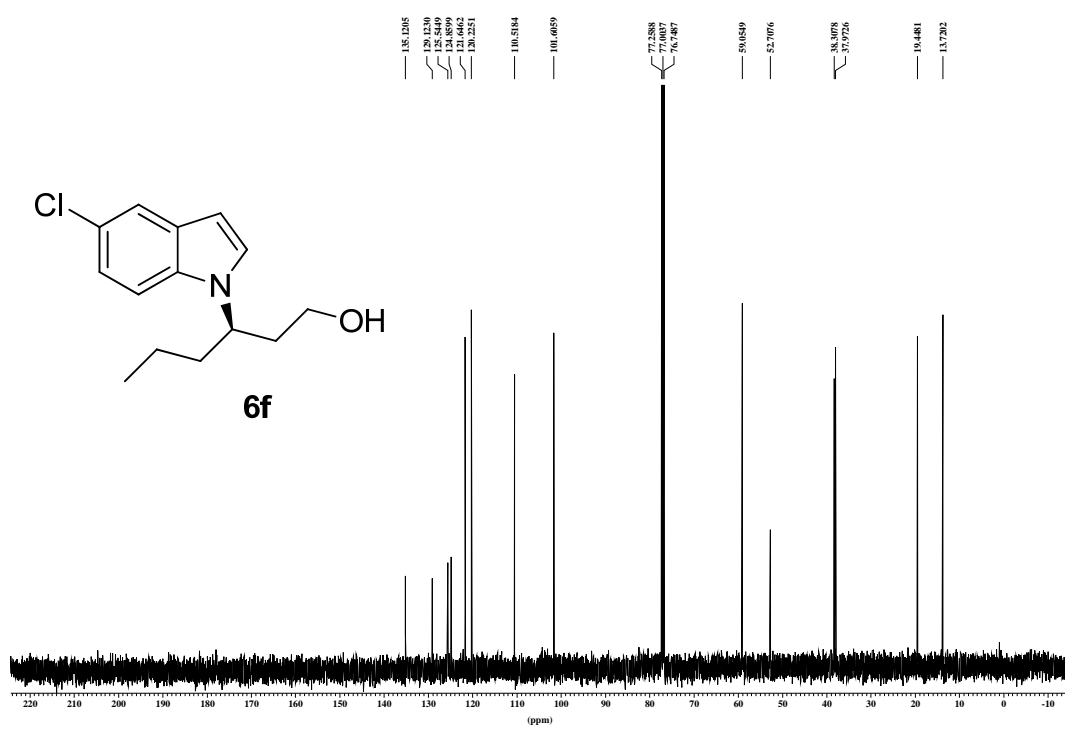


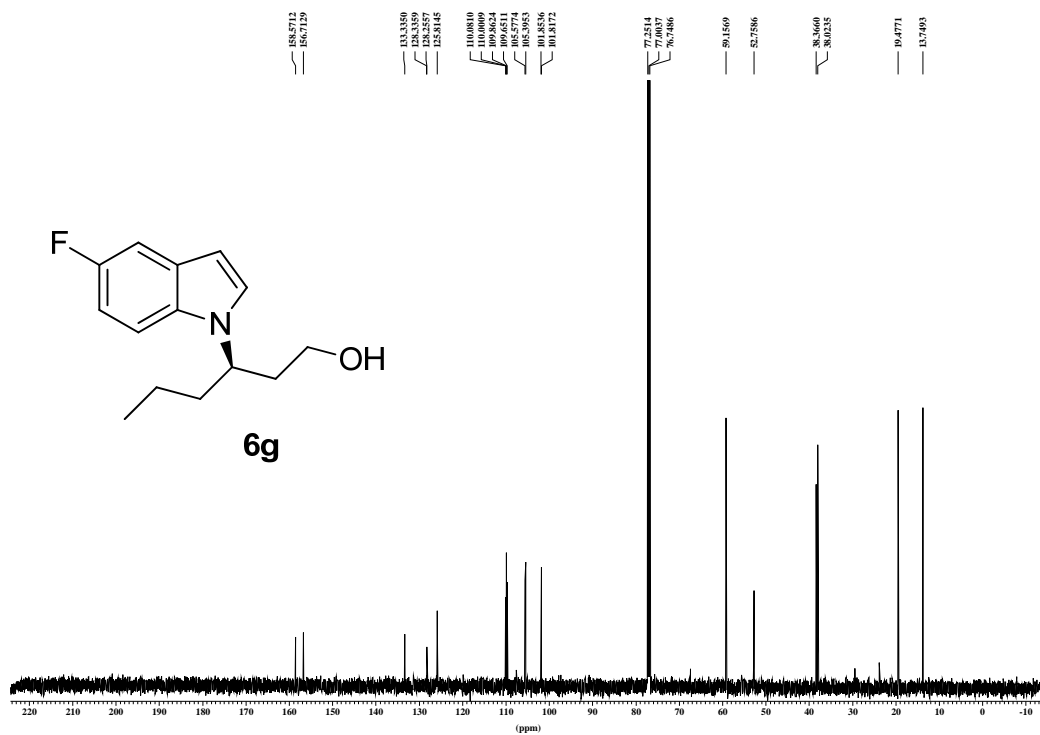
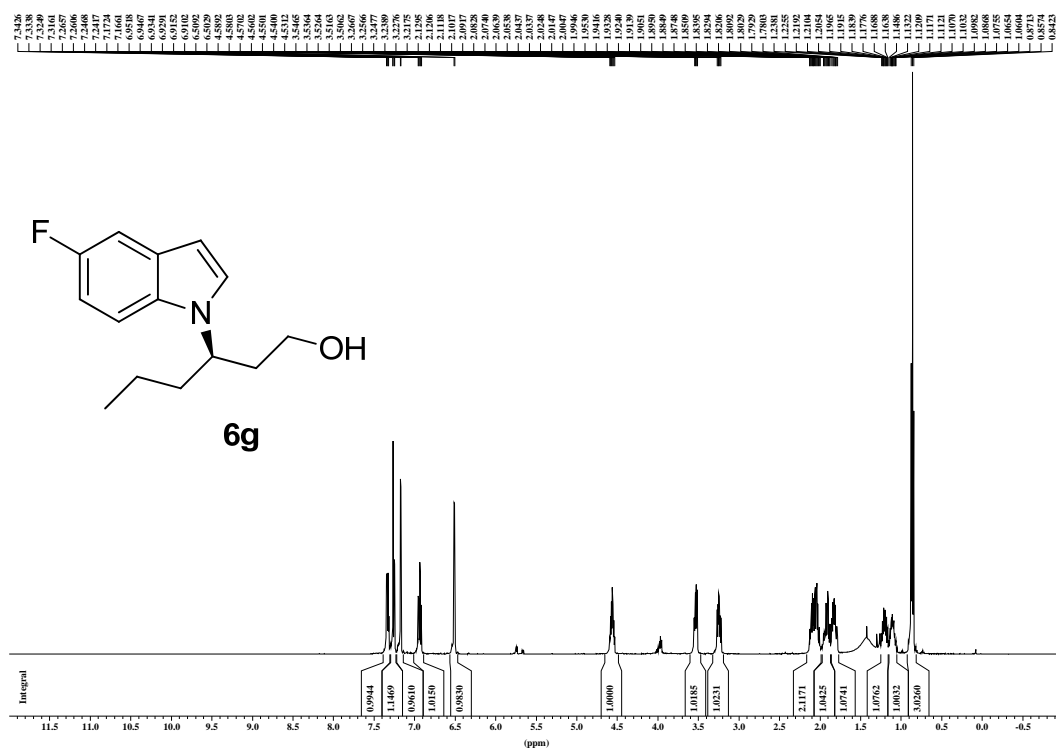


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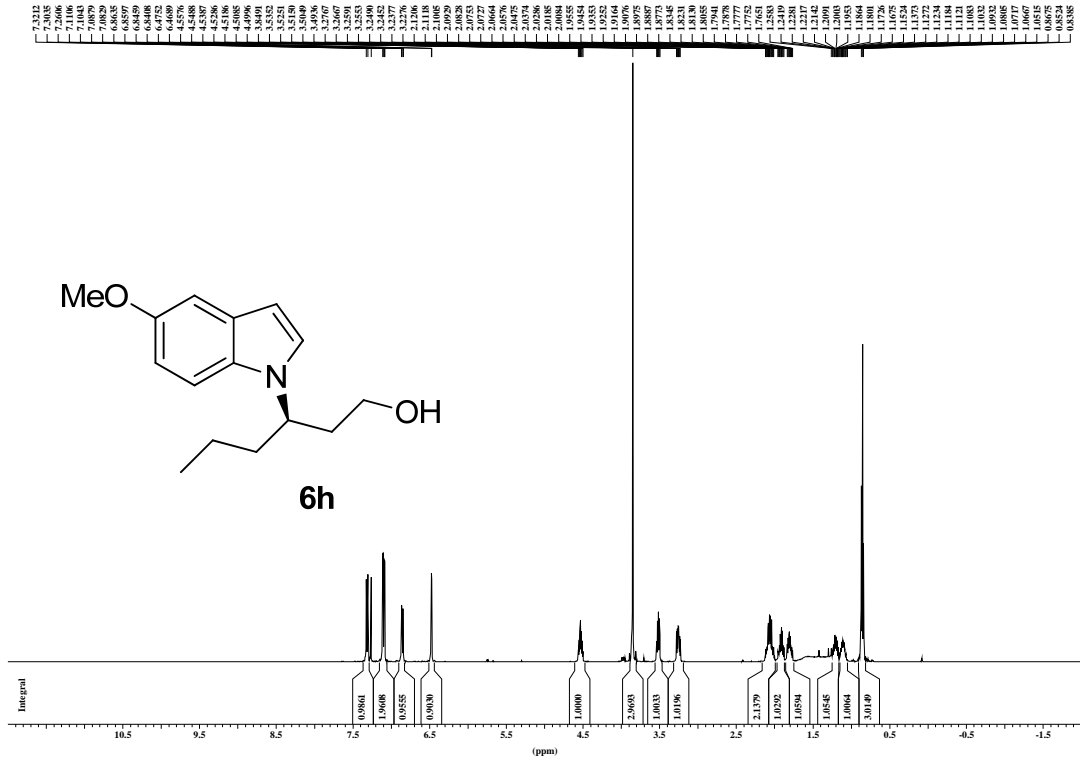


13C AMX500 dxw0318-4 indole 6f  
A1 hydr

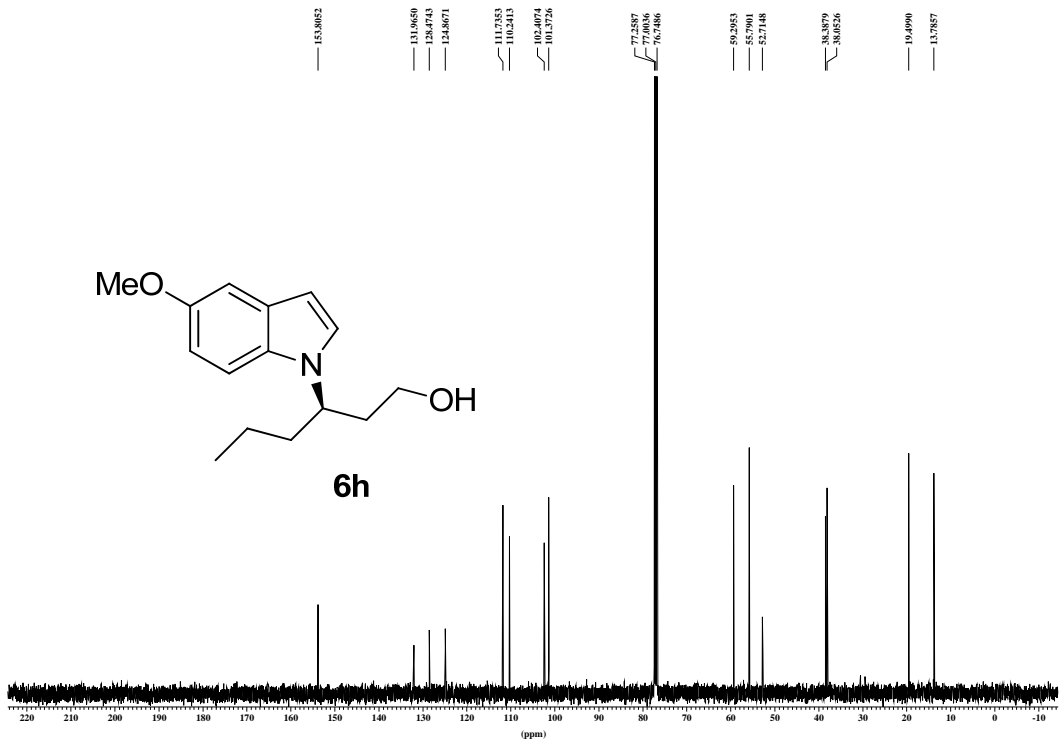




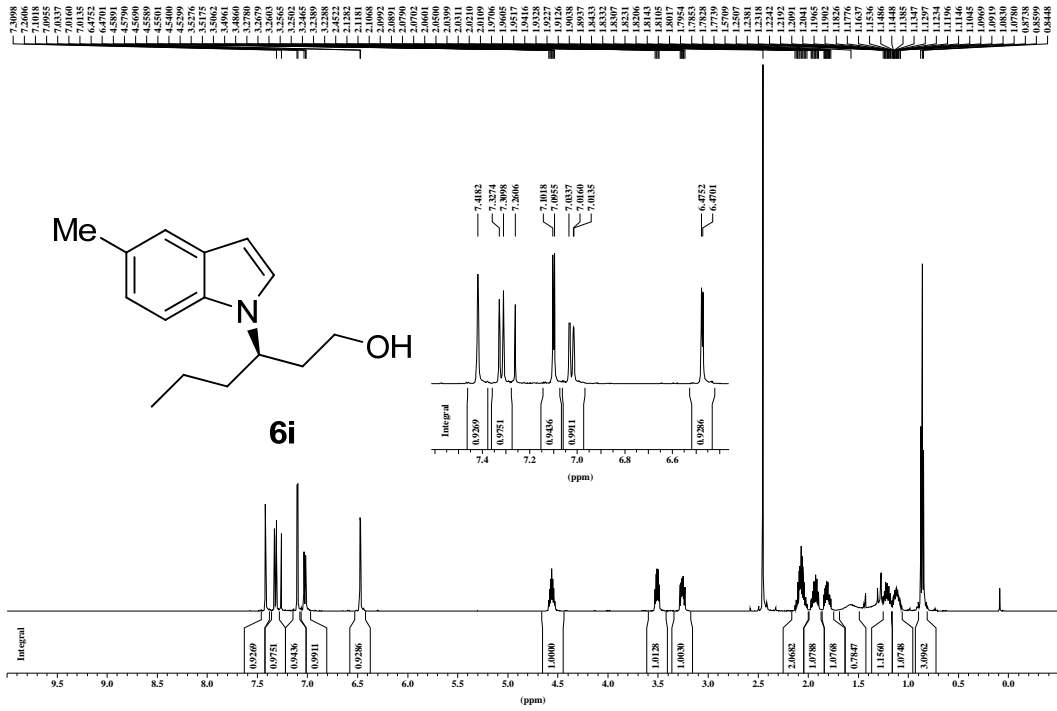
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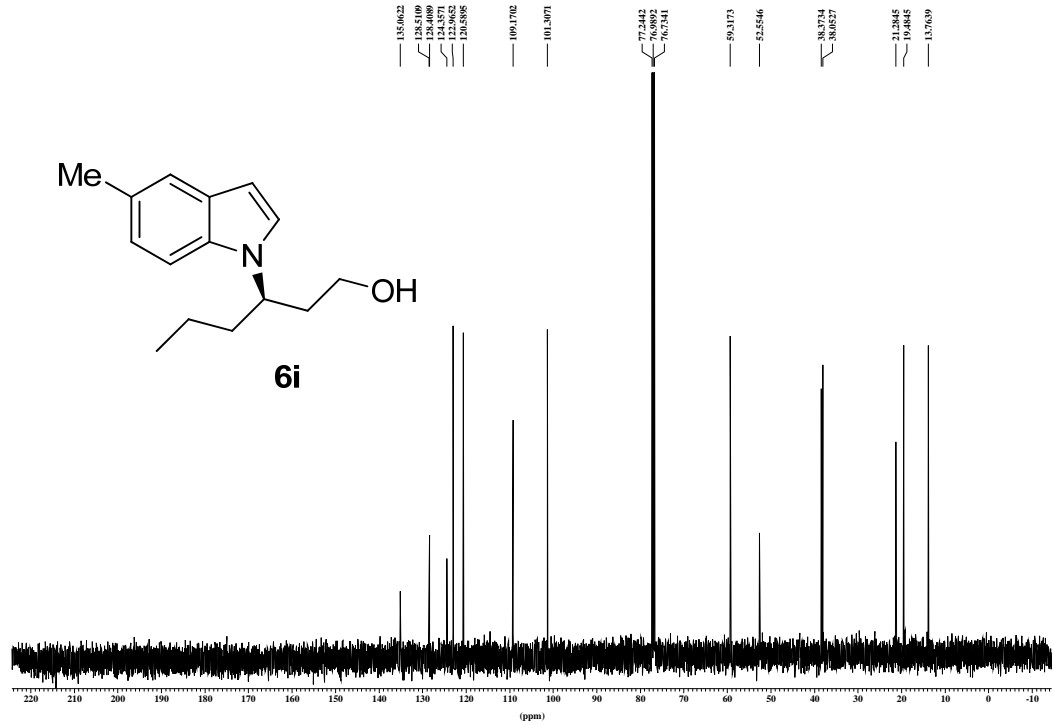
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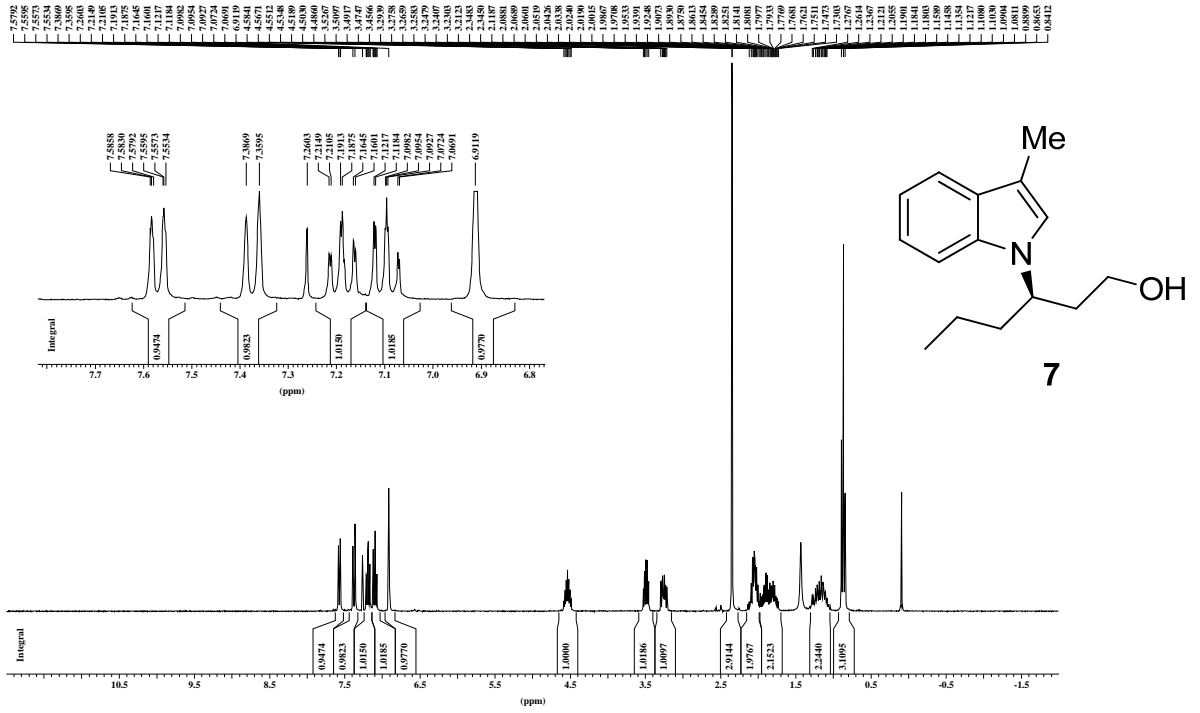
1H AMX500 dxw0318-5 indole 6i



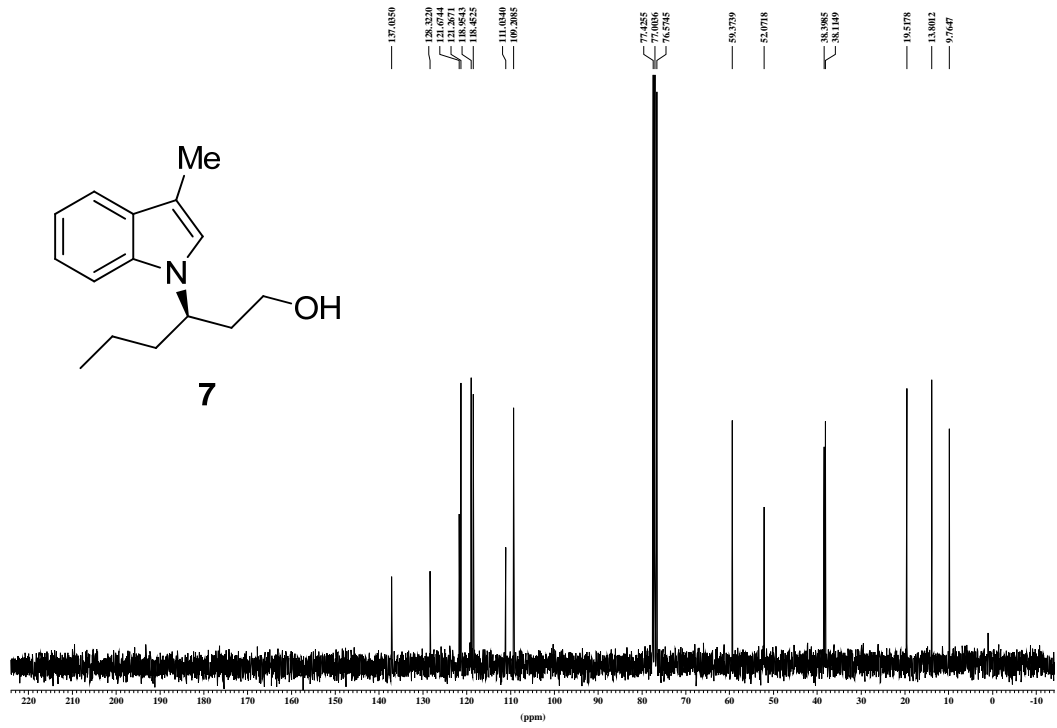
13C AMX500 dxw0318-6 indole 6i  
A1 hydr



<sup>1</sup>H normal range AC300 ma05dxw-3 2020H



<sup>13</sup>C Standard AC300 ma05dxw-4 2020C

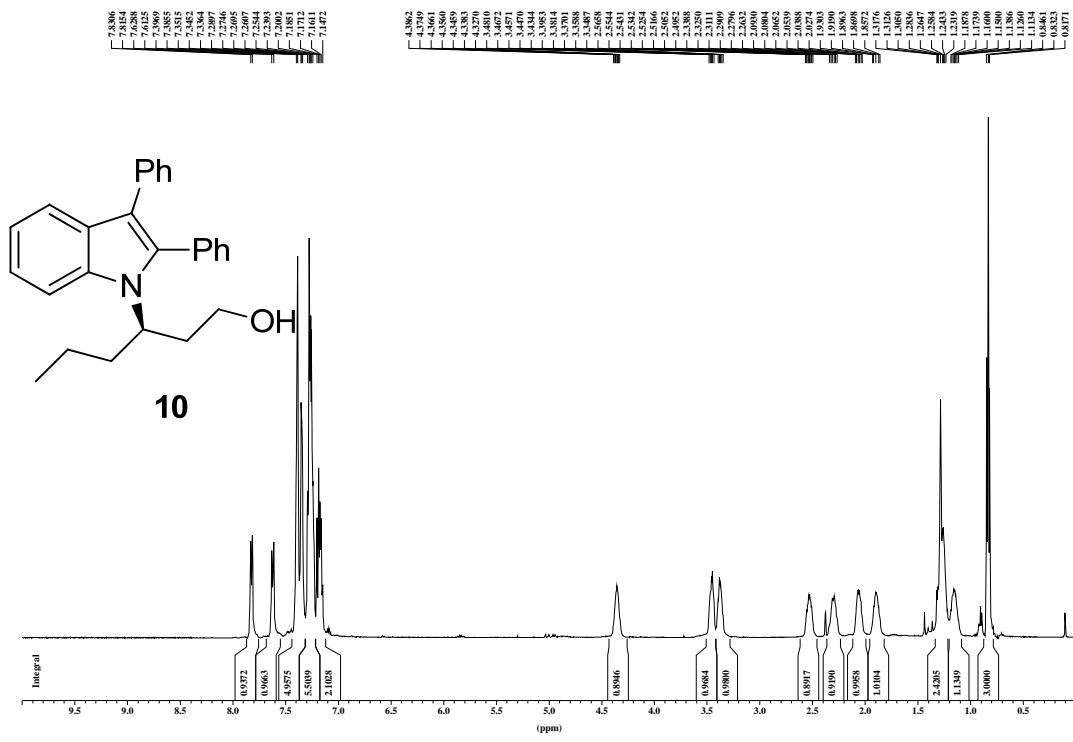




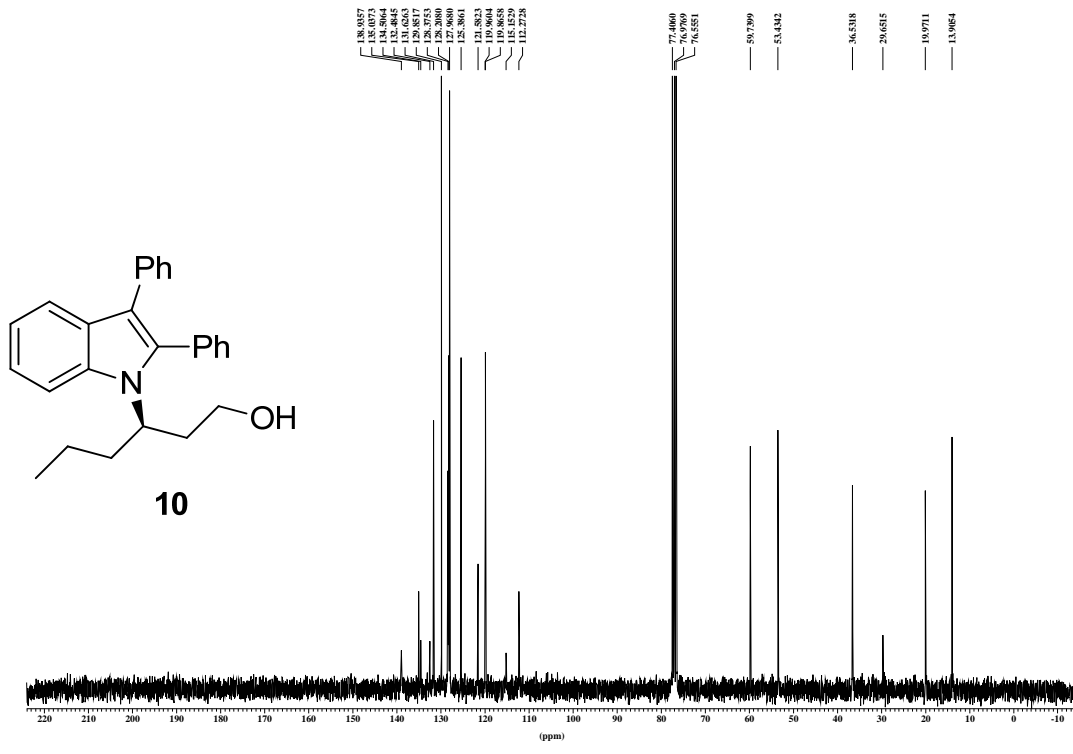


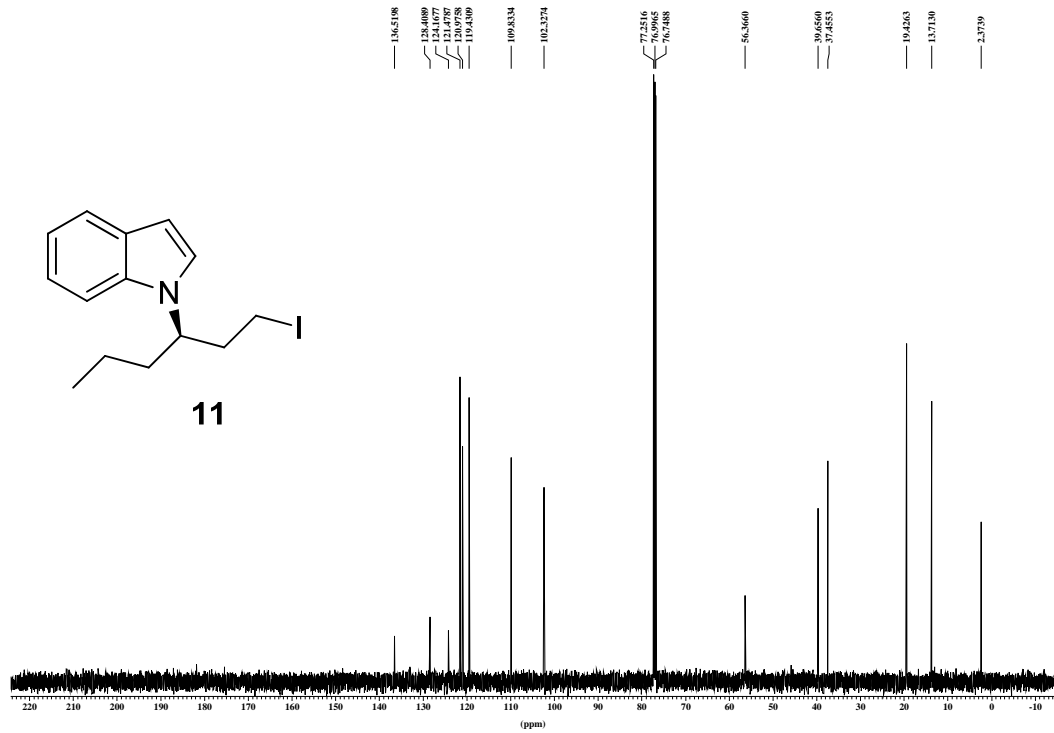
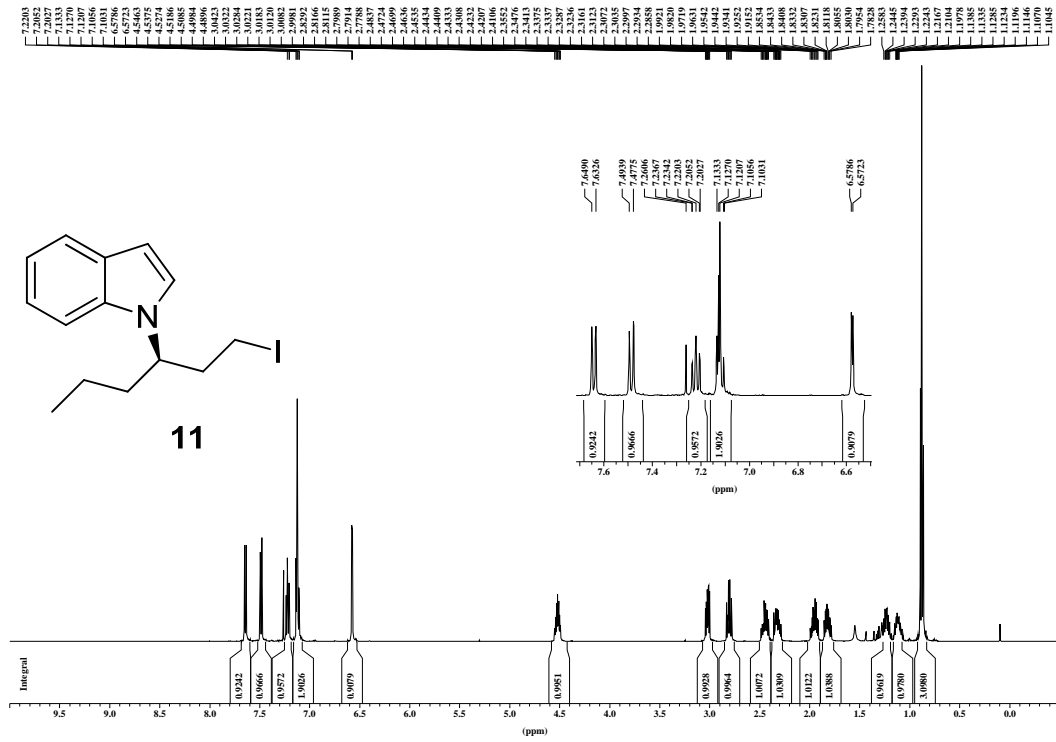


<sup>1</sup>H AMX500 indole 10

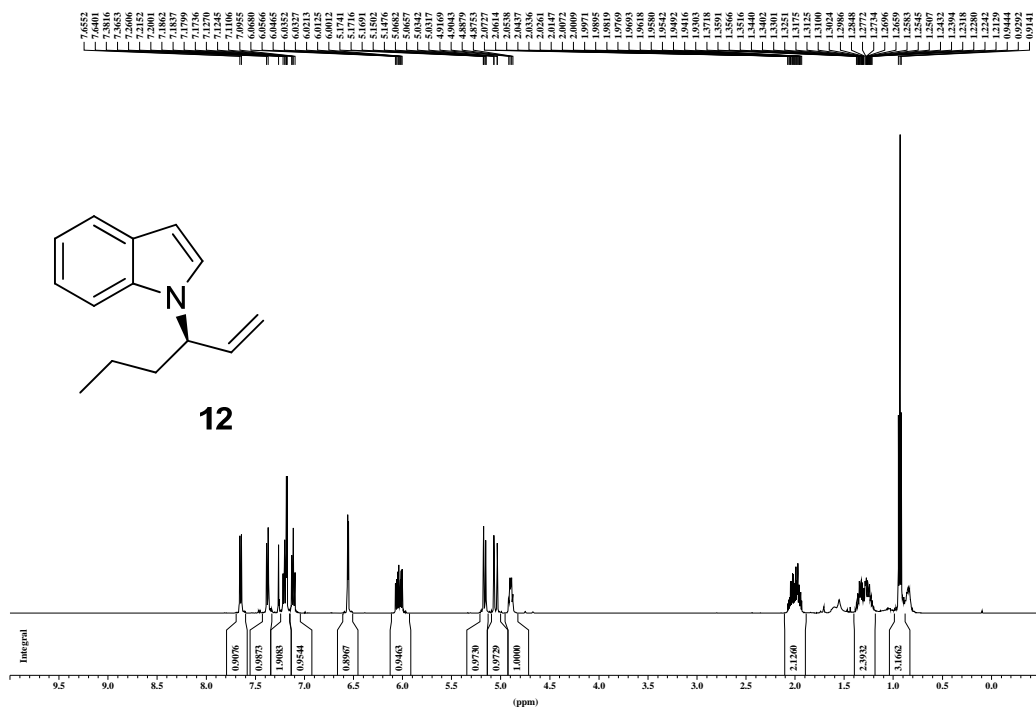


<sup>13</sup>C Standard AC300 j123dxw-2 10indole





1H AMX500 dxw0319-3 2018H



13C AMX500 dxw0319-4 2018C  
A1 hydr

