Regio- and Stereoselective Ring-Opening Reaction of Spiro-
Epoxypindoles with Ammonia under Catalyst-Free Conditions

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1. General information

Unless stated otherwise, all reactions were carried out in flame dried glassware. All solvents were purified and dried according to standard methods prior to use. Spiro-Epoxyoxindoles 1 were prepared according to literature.\(^1\) \(^1\)H and \(^{13}\)C NMR spectra were recorded on a Varian instrument (300 MHz and 75 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for \(^1\)H NMR are recorded as follows: chemical shift (\(\delta\), ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for \(^{13}\)C NMR are reported in terms of chemical shift (\(\delta\), ppm). IR spectra were recorded on a FT-IR spectrometer and only major peaks were reported in cm\(^{-1}\). Optical rotations were reported as follows: \([\alpha]\)\(_{D}\) (c: g/100 mL, in solvent). High resolution mass spectra (HRMS) were obtained by the ESI ionization sources. The ee value determination was carried out using chiral HPLC with Daicel Chiracel column on Waters with a 996 UV-detector.

2. General procedure for preparation of 2

\[
\begin{align*}
\text{R}^2 \backslash \text{N} & \text{O} \\
\text{R}^1 \backslash \text{O} & \text{MeOH} \\
\text{NH}_3 (g) & \text{balloon} \\
\text{MeOH} & \text{rt} \\
\text{R}^2 \backslash \text{N} & \text{O} \\
\text{HO} & \text{NH}_2 \\
\end{align*}
\]

In an ordinary vial, spiro-epoxyoxindoles 1 (0.10 mmol) was added to MeOH (1.0 mL) in the ammonia atmosphere at room temperature. The mixture was stirred at this temperature for the requisite amount of time as monitored by TLC. The solvent was removed under vacuum and residue was chromatographed on silica gel (DCM:MeOH 20:1) and fractions were collected and concentrated in vacuo to provide the pure desired products 2.

3. Scale-up Experiment

\[
\begin{align*}
\text{R}^2 \backslash \text{N} & \text{O} \\
\text{R}^1 \backslash \text{O} & \text{MeOH} \\
\text{NH}_3 (g) & \text{balloon} \\
\text{MeOH} & \text{rt} \\
\text{R}^2 \backslash \text{N} & \text{O} \\
\text{HO} & \text{NH}_2 \\
\end{align*}
\]

In an ordinary vial, spiro-epoxyoxindoles 1’ (10.0 mmol) was added to MeOH (60.0 mL) in the ammonia atmosphere at room temperature. The mixture was stirred at this temperature for the requisite amount of time as monitored by TLC. The solvent was removed under vacuum and residue was chromatographed on silica gel (DCM:MeOH 20:1) and fractions were collected and concentrated in vacuo to provide the pure desired products 2a’.

4. Transformations of the Product of 2a’

\[
\begin{align*}
\text{HO} & \text{NH}_2 \\
\text{Bn} & 99\% \text{ ee} \\
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \text{NH}_2 \\
\text{Bn} & 99\% \text{ ee} \\
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \text{NH}_2 \\
\text{Bn} & 64\% \text{ yield, } 98\% \text{ ee} \\
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \text{NH}_2 \\
\text{Bn} & 51\% \text{ yield, } 96\% \text{ ee} \\
\end{align*}
\]
(a) To a solution of 2a* (80 mg, 0.3 mmol) in CH₂Cl₂ (1 mL) was added dry pyridine (48 µL) and CS₂ (14 µL) at 0 °C. After 4h, MeI (15 µL) was added and the mixture stirred at room temperature for 4h. Then the mixture was acidified with 1N HCl and extracted with EtOAc. The combined organic layers were washed with water, brine, dried over Na₂SO₄ and the solvent was removed under vacuum and residue was chromatographed on silica gel (petroleum ether/AcOEt 1:1) and fractions were collected and concentrated in vacuo to provide the pure desired products 3 (68.8 mg, 64% yield).

(b) To a solution of 3 (0.22 mmol) in CH₂Cl₂ (1 mL) was added dry pyridine (35 µL) and MsCl (58 µL) at room temperature for overnight. Then the mixture was neutralized with 1N HCl, and extracted with EtOAc. The combined organic layers were washed with water, brine, dried over Na₂SO₄ and the solvent was removed under vacuum and residue was chromatographed on silica gel and fractions were collected and concentrated in vacuo to provide the pure desired products 4 (38 mg, 51% yield).
5. Characterization of 2-4

3-(aminomethyl)-1-benzyl-3-hydroxyindolin-2-one (2a).

![Structure of 2a]

90% yield; 
White solid, m.p. 95 – 97 °C; 

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.46 – 7.14 (m, 7H), 7.05 (t, J = 7.3 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.96 (d, J = 15.7 Hz, 1H), 4.78 (d, J = 15.7 Hz, 1H), 3.08 (s, 2H), 2.87 (bs, 3H); 

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 178.1, 142.6, 135.4, 129.7, 129.2, 128.8, 127.7, 127.1, 123.8, 123.1, 109.5, 75.0, 48.6, 43.6; 
IR: 3370, 1716, 1614, 1468, 1358, 1266, 1177, 1081, 737 cm$^{-1}$; 
HRMS (ESI): C$_{16}$H$_{16}$N$_2$O$_2$+H, Calc: 269.1285, Found: 269.1289.

3-(aminomethyl)-1-benzyl-4-chloro-3-hydroxyindolin-2-one (2b).

![Structure of 2b]

86% yield; 
White solid, m.p. 60 – 62 °C; 

$^1$H NMR (300 MHz, DMSO) $\delta$ 7.43 – 7.28 (m, 4H), 7.23 (dd, J = 16.5, 7.8 Hz, 2H), 7.00 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.22 (bs, 1H), 4.88 (q, J = 16.1 Hz, 2H), 3.35 (bs, 1H), 3.34 (d, J = 12.4 Hz, 3H), 3.11 (d, J = 12.4 Hz, 1H); 

$^{13}$C NMR (75 MHz, DMSO) $\delta$ 177.16, 145.28, 135.94, 130.67, 130.18, 128.54, 127.32, 127.15, 126.66, 123.18, 107.91, 77.90, 45.58, 42.63; 
IR: 3435, 2252, 1657, 1027, 824, 761 cm$^{-1}$; 
HRMS (ESI): C$_{16}$H$_{16}$ClN$_2$O$_2$+H, Calc: 303.0895, Found: 303.0900.
3-aminomethyl)-1-benzyl-5-fluoro-3-hydroxyindolin-2-one (2c).

83% yield;
White solid, m.p. 154 – 156 ℃;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.36 – 7.19 (m, 5H), 7.11 (dd, $J = 7.5$, 2.5 Hz, 1H), 6.88 (td, $J = 8.9$, 2.6 Hz, 1H), 6.60 (dd, $J = 8.6$, 4.0 Hz, 1H), 4.93 (d, $J = 15.8$ Hz, 1H), 4.75 (d, $J = 15.8$ Hz, 1H), 3.18 (bs, 3H), 3.05 (q, $J = 13.3$ Hz, 2H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 177.91, 159.40 (d, $J = 240.75$ Hz), 138.31, 135.03, 130.96 (d, $J = 7.5$ Hz), 128.87, 127.78, 127.06, 115.88 (d, $J = 23.25$ Hz), 112.08 (d, $J = 24.75$ Hz), 110.19 (d, $J = 7.5$ Hz), 75.18, 48.40, 43.71;

IR: 3366, 1718, 1491, 1345, 1267, 1174, 1026, 736 cm$^{-1}$;
HRMS (ESI): C$_{16}$H$_{15}$FN$_2$O$_2$+H, Calc: 287.1190, Found: 287.1194.

3-aminomethyl)-1-benzyl-5-chloro-3-hydroxyindolin-2-one (2d).

85% yield;
White solid, m.p. 110 – 112 ℃;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.39 – 7.19 (m, 6H), 7.14 (dd, $J = 8.3$, 2.0 Hz, 1H), 6.59 (d, $J = 8.3$ Hz, 1H), 4.91 (d, $J = 15.8$ Hz, 1H), 4.73 (d, $J = 15.8$ Hz, 1H), 3.12 (bs, 3H), 3.06 – 2.90 (m, 2H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 177.73, 159.40 (d, $J = 240.75$ Hz), 138.31, 135.03, 130.96 (d, $J = 7.5$ Hz), 128.87, 127.78, 127.06, 115.88 (d, $J = 23.25$ Hz), 112.08 (d, $J = 24.75$ Hz), 110.19 (d, $J = 7.5$ Hz), 75.41, 48.50, 43.60;

IR: 3345, 1722, 1484, 1343, 1174, 813, 736 cm$^{-1}$;
HRMS (ESI): C$_{16}$H$_{15}$ClN$_2$O$_2$+H, Calc: 303.0895, Found: 303.0896.
3-(aminomethyl)-1-benzyl-5-bromo-3-hydroxyindolin-2-one (2e).

![Chemical structure of 2e](image)

81% yield;

White solid, m.p. 115 – 117 °C;

1H NMR (300 MHz, DMSO) δ 7.54 (d, J = 2.0 Hz, 1H), 7.47 – 7.19 (m, 6H), 6.76 (d, J = 8.3 Hz, 1H), 4.87 (q, J = 16.0 Hz, 2H), 3.39 (bs, 3H), 3.00 (d, J = 12.7 Hz, 1H), 2.89 (d, J = 12.7 Hz, 1H);

13C NMR (75 MHz, DMSO) δ 177.14, 142.05, 135.97, 133.36, 131.48, 128.60, 127.36, 127.13, 127.00, 114.25, 110.93, 76.49, 48.38, 42.48;

IR: 3436, 1716, 1614, 1468, 1358, 1266, 1177, 1054, 761 cm⁻¹;


3-(aminomethyl)-1-benzyl-3-hydroxy-5-methylindolin-2-one (2f).

![Chemical structure of 2f](image)

73% yield;

White solid, m.p. 98 – 101 °C;

1H NMR (300 MHz, DMSO) δ 7.45 – 7.19 (m, 6H), 7.00 (d, J = 7.9 Hz, 1H), 6.68 (d, J = 7.9 Hz, 1H), 4.84 (q, J = 15.9 Hz, 2H), 3.29 (bs, 3H), 2.91 (q, J = 12.9 Hz, 2H), 2.25 (s, 3H);

13C NMR (75 MHz, DMSO) δ 177.40, 140.24, 136.39, 131.25, 130.65, 129.04, 128.54, 127.26, 127.14, 124.72, 108.75, 76.07, 48.53, 42.44, 20.70;

IR: 3438, 2250, 1656, 1468, 1358, 1266, 1177, 1055, 761 cm⁻¹;

3-(aminomethyl)-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (2g).

![2g](image)

76% yield;
White solid, m.p. 90 – 92 °C;

\[1H\text{ NMR (300 MHz, CDCl}_3\] \(\delta\) 7.35 – 7.15 (m, 5H), 6.97 (d, \(J = 2.4\) Hz, 1H), 6.69 (dd, \(J = 8.5, 2.4\) Hz, 1H), 6.56 (d, \(J = 8.5\) Hz, 1H), 4.91 (d, \(J = 15.7\) Hz, 1H), 4.70 (d, \(J = 15.7\) Hz, 1H), 3.71 (s, 3H), 3.15 (bs, 3H), 2.99 (s, 2H);

\[13C\text{ NMR (75 MHz, CDCl}_3\] \(\delta\) 177.80, 156.18, 135.52, 135.41, 130.70, 128.70, 127.53, 127.02, 113.95, 110.76, 109.94, 75.67, 55.64, 48.74, 43.54;

IR: 3368, 1710, 1604, 1494, 1346, 1275, 1179, 1018, 734 cm\(^{-1}\);


3-(aminomethyl)-1-benzyl-6-chloro-3-hydroxyindolin-2-one (2h).

![2h](image)

89% yield;
White solid, m.p. 79 – 81 °C;

\[1H\text{ NMR (300 MHz, CDCl}_3\] \(\delta\) 7.38 – 7.17 (m, 6H), 7.01 (dd, \(J = 7.9, 1.6\) Hz, 1H), 6.68 (d, \(J = 1.6\) Hz, 1H), 4.92 (d, \(J = 15.8\) Hz, 1H), 4.71 (d, \(J = 15.8\) Hz, 1H), 3.02 (q, \(J = 13.1\) Hz, 2H), 3.01 (bs, 3H);

\[13C\text{ NMR (75 MHz, CDCl}_3\] \(\delta\) 178.08, 143.76, 135.36, 134.83, 128.92, 127.85, 127.74, 127.01, 124.78, 122.99, 110.04, 74.84, 48.43, 43.63;

IR: 3340, 1726, 1611, 1490, 1374, 1265, 1178, 1075, 738 cm\(^{-1}\);

3-(aminomethyl)-1-benzyl-6-bromo-3-hydroxyindolin-2-one (2i).

![Chemical structure of 3-(aminomethyl)-1-benzyl-6-bromo-3-hydroxyindolin-2-one (2i).](image)

83% yield;
White solid, m.p. 99 – 101 °C;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42 – 7.04 (m, 7H), 6.83 (s, 1H), 4.91 (d, $J = 15.8$ Hz, 1H), 4.70 (d, $J = 15.8$ Hz, 1H), 2.98 (d, $J = 13.7$ Hz, 2H), 2.88 (bs, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 177.96, 143.90, 134.83, 128.95, 128.26, 127.88, 127.02, 125.98, 125.15, 123.30, 112.78, 74.84, 48.36, 43.64;

IR: 3361, 1720, 1605, 1486, 1430, 1353, 1176, 1117, 1061, 734 cm$^{-1}$;

HRMS (ESI): C$_{16}$H$_{15}$BrN$_2$O$_2$+H, Calc: 347.0390, Found: 347.0389.

3-(aminomethyl)-1-benzyl-7-chloro-3-hydroxyindolin-2-one (2j).

![Chemical structure of 3-(aminomethyl)-1-benzyl-7-chloro-3-hydroxyindolin-2-one (2j).](image)

78% yield;
White solid, m.p. 83 -85 °C;

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.35 – 7.12 (m, 7H), 6.99 (t, $J = 7.8$ Hz, 1H), 5.28 (s, 2H), 3.05 (d, $J = 13.2$ Hz, 2H), 3.02 (bs, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 178.73, 143.90, 134.83, 128.95, 128.26, 127.88, 127.02, 125.98, 125.15, 123.30, 115.72, 74.39, 48.69, 44.59;

IR: 3332, 1721, 1608, 1452, 1353, 1267, 1134, 735 cm$^{-1}$;

HRMS (ESI): C$_{16}$H$_{15}$ClN$_2$O$_2$+H, Calc: 303.0895, Found: 303.0894.
3-(aminomethyl)-1-benzyl-3-hydroxy-7-methylindolin-2-one (2k).

![2k]

75% yield;
White solid, m.p. 82 – 84 °C;

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.35 – 7.18 (m, 4H), 7.14 (d, \(J = 7.0\) Hz, 2H), 6.96 (d, \(J = 4.6\) Hz, 2H), 5.16 (d, \(J = 16.9\) Hz, 1H), 5.06 (d, \(J = 16.9\) Hz, 1H), 3.03 (s, 5H), 2.21 (s, 3H);

\(^1^3\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 179.14, 140.43, 137.17, 133.53, 130.14, 128.81, 127.15, 125.50, 123.22, 121.66, 120.17, 74.44, 48.94, 44.71, 18.62;

IR: 3365, 1714, 1452, 1354, 1163, 733 cm\(^{-1}\);


3-(aminomethyl)-3-hydroxyindolin-2-one (2l).

![2l]

80% yield;
White solid, m.p. 214 – 216 °C;

\(^1\)H NMR (300 MHz, DMSO) \(\delta\) 10.37 (bs, 1H), 7.35 (d, \(J = 7.3\) Hz, 1H), 7.23 (dd, \(J = 13.5, 5.8\) Hz, 1H), 6.98 (t, \(J = 7.4\) Hz, 1H), 6.81 (dd, \(J = 14.2, 7.6\) Hz, 1H), 3.39 (bs, 3H), 2.92 (q, \(J = 13.2\) Hz, 2H);

\(^1^3\)C NMR (75 MHz, DMSO) \(\delta\) 178.24, 141.91, 130.29, 129.45, 124.37, 121.75, 109.82, 74.12, 46.61;

IR: 3432, 2251, 1656, 1027, 737 cm\(^{-1}\);

1-acetyl-3-(aminomethyl)-3-hydroxyindolin-2-one (2m).

88% yield; White solid, m.p. 136 – 138 °C;

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } & \delta 9.80 (bs, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.37 (t, J = 7.4 Hz, 2H), \\
& 7.13 (t, J = 7.5 Hz, 1H), 6.59 (bs, 1H), 6.30 (d, J = 24.3 Hz, 1H), 3.22 (d, J = 5.8 Hz, 1H), 2.93 (d, J = 5.8 Hz, 1H), 2.19 (s, 3H); \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) } & \delta 173.21, 168.85, 136.78, 129.51, 127.17, 126.72, 124.53, 124.25, 57.49, 54.15, 24.39; \\
\text{IR: } & 3275, 1668, 1522, 1451, 1299, 927, 735 \text{ cm}^{-1}; \\
\text{HRMS (ESI): } & \text{C}_{11}\text{H}_{12}\text{N}_{2}\text{O}_{3}^+ \text{Na, Calc: 243.0740, Found: 243.0745.}
\end{align*}
\]

3-(aminomethyl)-3-hydroxy-1-methylindolin-2-one (2n).

87% yield; White solid, m.p. 68 – 71 °C;

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } & \delta 7.42 – 7.23 (m, 2H), 7.07 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 3.15 (s, 3H), 3.15 (bs, 3H), 3.04 – 2.86 (m, 2H); \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) } & \delta 177.87, 143.28, 129.65, 129.36, 123.65, 123.05, 108.38, 75.12, 48.36, 26.06; \\
\text{IR: } & 2929, 1722, 1614, 1470, 1375, 1249, 1121, 839 \text{ cm}^{-1}; \\
\text{HRMS (ESI): } & \text{C}_{11}\text{H}_{12}\text{N}_{2}\text{O}_{3}^+ \text{H, Calc: 193.0972, Found: 193.0973.}
\end{align*}
\]
1-allyl-3-(aminomethyl)-3-hydroxyindolin-2-one (2o).

![Structure](image)

85% yield;  
White solid, m.p. 62 – 64°C;  

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.35 (d, $J = 7.2$ Hz, 1H), 7.28 (t, $J = 7.7$ Hz, 1H), 7.07 (t, $J = 7.4$ Hz, 1H), 6.81 (d, $J = 7.8$ Hz, 1H), 5.80 (ddd, $J = 22.1$, 10.2, 5.1 Hz, 1H), 5.22 (d, $J = 7.2$ Hz, 1H), 5.18 (s, 1H), 4.34 (dd, $J = 16.4$, 4.9 Hz, 1H), 4.20 (dd, $J = 16.4$, 5.0 Hz, 1H), 3.24 (s, 3H), 2.96 (s, 2H);  
$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 177.65, 142.41, 130.98, 129.51, 129.35, 123.71, 123.00, 117.58, 109.26, 75.12, 48.48, 42.07;  
IR: 3360, 1715, 1613, 1468, 1364, 1184, 1106, 929, 755 cm$^{-1}$;  

3-(aminomethyl)-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (2p).

![Structure](image)

89% yield;  
White solid, m.p. 66 – 68°C;  

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.34 (d, $J = 7.3$ Hz, 1H), 7.18 (dd, $J = 9.5$, 4.7 Hz, 3H), 7.02 (t, $J = 7.4$ Hz, 1H), 6.81 (d, $J = 8.4$ Hz, 2H), 6.71 (d, $J = 7.8$ Hz, 1H), 4.86 (d, $J = 15.4$ Hz, 1H), 4.69 (d, $J = 15.5$ Hz, 1H), 3.74 (d, $J = 4.6$ Hz, 3H), 3.24 (bs, 3H), 3.01 (s, 2H);  
$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 178.00, 158.93, 142.39, 129.52, 129.37, 128.45, 127.36, 123.72, 123.02, 114.08, 109.44, 75.25, 55.14, 48.53, 42.97;  
IR: 3357, 1716, 1613, 1513, 1356, 1248, 1178, 1109, 1032, 751 cm$^{-1}$;  
HRMS (ESI): C$_{17}$H$_{18}$N$_2$O$_3$+H, Calc: 299.1390, Found: 299.1394.
(R)-3-(aminomethyl)-1-benzyl-3-hydroxyindolin-2-one (2a').

![Chemical structure](image)

91% yield;

\[\alpha\]Drt = - 46° (c = 1.00, CHCl3);

**HPLC:** DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:

\[ t_{major} = 8.9, t_{minor} = 6.1, 99\% \text{ ee.} \]

(R)-3-(aminomethyl)-1-benzyl-3-hydroxy-5-methylindolin-2-one (2f').

![Chemical structure](image)

75% yield;

\[\alpha\]Drt = - 37° (c = 1.00, CHCl3);

**HPLC:** DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:

\[ t_{major} = 9.7, t_{minor} = 5.7, 97\% \text{ ee.} \]

(R)-3-(aminomethyl)-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (2g').

![Chemical structure](image)

74% yield;

\[\alpha\]Drt = - 106° (c = 1.00, CHCl3);

**HPLC:** DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:

\[ t_{major} = 12.1, t_{minor} = 7.1, 99\% \text{ ee.} \]
(\(R\))-3-(aminomethyl)-1-benzyl-6-chloro-3-hydroxyindolin-2-one (2h’).

\[
\text{HPLC: DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:}
\]
\[
t_{\text{major}} = 8.6, t_{\text{minor}} = 6.5, 98\% \text{ ee.}
\]

(\(R\))-3-(aminomethyl)-1-benzyl-6-bromo-3-hydroxyindolin-2-one (2i’).

\[
\text{HPLC: DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:}
\]
\[
t_{\text{major}} = 8.9, t_{\text{minor}} = 6.7, 96\% \text{ ee.}
\]

(\(R\))-3-(aminomethyl)-1-benzyl-7-chloro-3-hydroxyindolin-2-one (2j’).

\[
\text{HPLC: DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:}
\]
\[
t_{\text{major}} = 10.4, t_{\text{minor}} = 6.3, 96\% \text{ ee.}
\]
(R)-3-(aminomethyl)-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (2p').

![2p']

86% yield;

$[\alpha]_D^{19} = -51^\circ (c = 1.00, \text{CHCl}_3)$.

**HPLC:** DAICEL CHIRALCEL OD, Hexane/EtOH = 7/3, flow rate = 1.0 ml/min, retention time:

$t_{major} = 9.9$, $t_{minor} = 7.1$, 98% ee.

methyl (R)-((1-benzyl-3-hydroxy-2-oxoindolin-3-yl)methyl)carbamodithioate (3).

![3]

64% yield;

White solid, m.p. 67 – 68 ℃;

$^1H\text{ NMR (300 MHz, CDCl}_3\delta 8.30 (bs, 1H), 7.42 (d, J = 7.3 Hz, 1H), 7.36 – 7.16 (m, 6H), 7.05 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.87 (d, J = 15.8 Hz, 1H), 4.82 (bs, 1H), 4.71 (d, J = 15.7 Hz, 1H), 4.54 (dd, J = 14.3, 6.2 Hz, 1H), 3.96 (dd, J = 14.3, 4.0 Hz, 1H), 2.59 (s, 3H);

$^{13}C\text{ NMR (75 MHz, CDCl}_3\delta 200.96, 176.72, 141.70, 134.72, 130.20, 128.84, 128.15, 127.77, 127.08, 124.20, 123.68, 109.91, 74.68, 52.45, 43.84, 18.22;

IR: 3454, 1716, 1614, 1358, 1260, 1177, 1005, 730 cm$^{-1}$;

HRMS (ESI): $C_{18}H_{18}N_2O_2S_2$+H, Calc: 359.0882, Found: 359.0889.

**HPLC:** DAICEL CHIRALCEL AS, Hexane/EtOH =8/2, flow rate = 1.0 ml/min, retention time:

$t_{major} = 17.9$, $t_{minor} = 13.6$, 98% ee.
(R)-1-benzyl-2'-((methylthio)-4'H-spiro[indoline-3,5'-thiazol]-2-one (4).

\[
\begin{align*}
&\text{MeS} \\
&\text{S} \quad \text{N} \\
&\text{N} \quad \text{O} \\
&\text{Bn}
\end{align*}
\]

51% yield;

White solid, m.p. 43 – 45 °C;

\textbf{\textit{H NMR (300 MHz, CDCl}_3\textit{)}} \( \delta \) 7.46 – 7.24 (m, 6H), 7.20 (td, \( J = 7.8, 1.2 \) Hz, 1H), 7.06 (td, \( J = 7.6, 0.8 \) Hz, 1H), 6.73 (d, \( J = 7.8 \) Hz, 1H), 4.92 (d, \( J = 1.7 \) Hz, 2H), 4.71 (d, \( J = 15.1 \) Hz, 1H), 4.52 (d, \( J = 15.1 \) Hz, 1H), 2.63 (s, 3H);

\textbf{\textit{13C NMR (75 MHz, CDCl}_3\textit{)}} \( \delta \) 176.02, 164.03, 141.35, 135.15, 130.66, 129.54, 128.85, 127.82, 127.28, 124.11, 123.60, 109.46, 74.97, 64.23, 44.32, 15.66;

\textbf{IR}: 3378, 1745, 1614, 1490, 1358, 1249, 1177, 1081, 737 cm\(^{-1}\);

\textbf{HRMS (ESI)}: \( \text{C}_{18}\text{H}_{16}\text{N}_2\text{OS}_2+\text{H} \), Calc: 341.0777, Found: 341.0785;

\( [\alpha]_D^{\text{rt}} = -72^\circ \) (c = 1.00, CHCl\(_3\));

\textbf{HPLC}: DAICEL CHIRALCEL AD, Hexane/EtOH = 8/2, flow rate = 1.0 ml/min, retention time:

\( t_{\text{major}} = 17.8, t_{\text{minor}} = 21.2, 96\% \text{ ee.} \)
6. Copies of HPLC spectra for 2-4

*(R)*-3-(aminomethyl)-1-benzyl-3-hydroxyindolin-2-one (Table 3, entry 1)

Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min

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(R)-3-(aminomethyl)-1-benzyl-3-hydroxy-5-methylindolin-2-one (Table 3, entry 2)

\[
\begin{align*}
\text{Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min}
\end{align*}
\]

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(R)-3-(aminomethyl)-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (Table 3, entry 3)

![Chemical Structure](image)

Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min

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(R)-3-(aminomethyl)-1-benzyl-6-chloro-3-hydroxyindolin-2-one (Table 3, entry 4)

\[
\begin{align*}
\text{HO} & \quad \text{NH}_2 \\
\text{Cl} & \quad \text{Bn}
\end{align*}
\]

Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min

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<td>8.624</td>
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(R)-3-(aminomethyl)-1-benzyl-6-bromo-3-hydroxyindolin-2-one (Table 3, entry 5)

Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min

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<td>8.924</td>
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(R)-3-(aminomethyl)-1-benzyl-7-chloro-3-hydroxyindolin-2-one (Table 3, entry 6)

\[
\begin{align*}
\text{Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min}
\end{align*}
\]

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<td>10.443</td>
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</table>
(R)-3-(aminomethyl)-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (Table 3, entry 7)

![Chemical structure of the compound](image)

Chiralpak OD-H column, hexane/EtOH (7:3), flow rate 1.0 mL/min

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</table>
(R)-methyl ((1-benzyl-3-hydroxy-2-oxoindolin-3-yl)methyl)carbamothioate (Scheme 2, 3)

Chiralpak AS column, hexane/EtOH (8:2), flow rate 1.0 mL/min

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</table>
(R)-1-benzyl-2'-(methylthio)-4'H-spiro[indoline-3,5'-thiazol]-2-one (Scheme 2, 4)

Chiralpak AD column, hexane/EtOH (8:2), flow rate 1.0 mL/min

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