Ni-Catalyzed Enantioselective Reductive Aryl-Alkenylation of Alkenes: Application to the Synthesis of (+)-Physovenine and (+)-Physostigmine

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1. General Information

$^1$H and $^{13}$C NMR data were recorded with Bruker ADVANCE III (400 MHz) or JNM-ECZ400S/L1 (400 MHz) spectrometers. Chemical shifts are given in ppm. The spectra are calibrated to the residual $^1$H and $^{13}$C signals of the solvents. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet-doublet (dd), quintet (quint), septet (sept), multiplet (m), and broad (b). $^{19}$F NMR spectra were recorded using CFCl$_3$ as internal standard. Gas chromatography were determined with a Varian GC 2000 gas chromatography instrument with a FID detector. High-resolution mass spectra (HRMS) were recorded on DIONEX UltiMate 3000 & Bruker Compact TOF mass spectrometer. Enantiomeric excesses were determined with a SHIMADZU LC-20ADXR system using chiral stationary phase columns (DAICEL) by comparing the samples with the corresponding racemic samples. Column and elution details were specified in each entry.

**Materials and Methods:** Unless otherwise stated, starting materials were purchased from commercial suppliers (Adamas-beta®, Alfa, Aldrich and so on). All reactions dealing with air- or moisture-sensitive compounds were performed in the argon-filled glove box or by standard Schlenk techniques in oven-dried reaction vessels under argon atmosphere. Solvents were purchased in HPLC quality, degassed by purging thoroughly with nitrogen and dried over activated molecular sieves of appropriate size. More sensitive compounds were stored in a desiccator or in a glove-box if required. Reactions were monitored by thin layer chromatography (TLC) using glass 0.25 mm silica gel plates. Compounds were visualized by UV-light at 254 nm and by dipping the plates in an aqueous potassium permanganate solution followed by heating. Flash column chromatography was performed over silica gel (200-400 mesh).
2. General Procedures

2.1 General Procedure for Racemic Aryl-Alkenylation Reaction:

To a mixture of 1 (0.1 mmol), NiBr$_2$ (10 mol%), L1 (20 mol%), Mn (3 equiv), MgCl$_2$ (4 equiv) and dry DMSO (2 mL) in a sealed tube was added alkenyl bromide 2 (0.3 mmol) under Argon. The reaction mixture was heated at 60 °C until the reaction was complete (monitored by TLC). The resulting mixture was quenched with sat. NH$_4$Cl solution (5 mL) and further diluted with water (10 mL). The aqueous layer was extracted with EtOAc (3 x 15 mL) and the combined organic layers were washed with brine (2 x 20 mL), dried with MgSO$_4$, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel, eluting with ethyl acetate/petroleum ether 1:40~1:5 (v/v) to afford the desired product 3.

2.2 General Procedure for Asymmetric Aryl-Alkenylation Reaction:

To a mixture of 1 (0.1 mmol), Ni(COD)$_2$ (10 mol%), L15 (20 mol%), Zn (3 equiv) and dry DMA (2 mL) in a sealed tube was added alkenyl bromide 2 (0.3 mmol) under Argon. The reaction mixture was heated at room temperature until the reaction was complete (monitored by TLC). The resulting mixture was quenched with sat. NH$_4$Cl solution (5 mL) and further diluted with water (10 mL). The aqueous layer was extracted with
EtOAc (3 x 15 mL) and the combined organic layers were washed with brine (2 x 20 mL), dried with MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel, eluting with ethyl acetate/petroleum ether 1:40~1:5 (v/v) to afford the desired product 3.
3. Additional experiments

Table S1. Optimization of reaction conditions

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<sup>a</sup>Reactions were carried out with 1a (0.1 mmol), 2a (0.3 mmol), NiBr<sub>2</sub> (10 mol%), ligand (20 mol%), Mn (0.3 mmol), MgC<sub>2</sub> (0.4 mmol) in 2 mL solvent at 60 °C for 12 h, unless noted otherwise. <sup>b</sup>Isolated yields. <sup>c</sup>Without NiBr<sub>2</sub>. 

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![Chemical structures](image-url)

*Note: The image contains chemical structures and reaction conditions.*
4. Characterization data of products

\((E)-3-(3-(4\text{-}\text{Methoxyphenyl})\text{-}\text{allyl})\text{-}1,3\text{-}\text{dimethylindolin}-2\text{-}\text{one (3aa)}\)

\[
\begin{align*}
\text{Chemical Formula} & \quad \text{C}_{20}\text{H}_{26}\text{NO}_2 \\
\text{Exact Mass} & \quad 307.1572
\end{align*}
\]

3aa was prepared according to general procedure 2.1 using 1a and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3aa as yellow oil (90% yield). The \(^1\)H NMR data matched those reported in the literature:\(^1\) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.29-7.24 (m, 1H), 7.22 (dd, \(J = 7.3, 0.7\) Hz, 1H), 7.16-7.10 (m, 2H), 7.07 (td, \(J = 7.5, 0.9\) Hz, 1H), 6.82 (d, \(J = 7.7\) Hz, 1H), 6.80-6.75 (m, 2H), 6.29 (d, \(J = 15.7\) Hz, 1H), 5.74 (ddd, \(J = 15.5, 8.0, 7.1\) Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H), 2.70-2.52 (m, 2H), 1.41 (s, 3H); \(^1\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 180.3, 158.8, 143.1, 133.6, 133.0, 130.0, 127.7, 127.2, 122.9, 122.3, 121.8, 113.7, 107.9, 55.2, 48.7, 41.6, 26.1, 22.4.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. \(t_R = 6.7\) min (minor), 8.0 min (major).

Optical Rotation: \(\text{[\alpha]}_{D}^{33} +4.6\) (c 0.2, iPrOH) for 82% ee.
### 色谱图

![色谱图](image1.png)

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### 色谱图

![色谱图](image2.png)

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height       高度  height
(E)-3-(3-(4-Methoxyphenyl)allyl)-1,3,5-trimethylindolin-2-one (3ba)

Chemical Formula: \( \text{C}_{21}\text{H}_{23}\text{NO}_2 \)
Exact Mass: 321.1729

3ba was prepared according to general procedure 2.2 using 1b and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ba as yellow oil (81% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.16-7.09 (m, 2H), 7.08-7.02 (m, 2H), 6.81-6.74 (m, 2H), 6.70 (d, \( J = 7.8 \) Hz, 1H), 6.29 (d, \( J = 15.7 \) Hz, 1H), 5.77-5.66 (m, 1H), 3.77 (s, 3H), 3.15 (s, 3H), 2.61 (dd, \( J = 7.6, 1.0 \) Hz, 2H), 2.35 (s, 3H), 1.39 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 180.2, 158.8, 140.8, 133.7, 132.9, 131.8, 130.2, 127.9, 127.2, 123.8, 122.1, 113.8, 107.6, 55.2, 48.7, 41.7, 26.1, 22.5, 21.2; HRMS: (ESI) calcd for \( \text{C}_{21}\text{H}_{24}\text{NO}_2 \)[M+H]\(^+\) 322.1802; found 322.1795.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, \( n\)-Hexane/\( i\)-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. t\( R \) = 6.3 min (minor), 7.2 min (major).

Optical Rotation: \([\alpha]_{D}^{32} +38.0\) (c 0.5, \( \text{iPrOH} \)) for 90% ee.
(E)-5-Methoxy-3-(3-(4-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (3ca)

3ca was prepared according to general procedure 2.1 using 1c and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ca as yellow oil (67% yield). 1H NMR (400 MHz, CDCl3): δ 7.17-7.09 (m, 2H), 6.85 (d, J = 2.4 Hz, 1H), 6.81-6.75 (m, 3H), 6.72 (d, J = 8.4 Hz, 1H), 6.30 (d, J = 15.7 Hz, 1H), 5.73 (dt, J = 15.5, 7.5 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.15 (s, 3H), 2.62 (dd, J = 7.5, 1.0 Hz, 2H), 1.40 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 179.9, 158.8, 155.8, 136.7, 135.0, 133.0, 130.0, 127.2, 121.8, 113.7, 111.6, 110.6, 108.1, 55.8, 55.2, 49.1, 41.6, 26.2, 22.6; HRMS: (ESI) calcd for C21H24NO3 [M+H]+ 338.1751; found 338.1743.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 8.4 min (minor), 10.4 min (major).

Optical Rotation: [α]D33° +51.6 (c 0.2, iPrOH) for 80% ee.
(E)-5-Fluoro-3-(3-(4-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (3da)

3da was prepared according to general procedure 2.2 using 1d and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3da as yellow oil (74% yield). 1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.17-7.11 (m, 2H), 7.00-6.92 (m, 2H), 6.82-6.75 (m, 2H), 6.73 (dt, $J = 8.3$, 3.3 Hz, 1H), 6.30 (t, $J = 13.5$ Hz, 1H), 5.70 (dt, $J = 15.5$, 7.6 Hz, 1H), 3.78 (s, 3H), 3.17 (s, 3H), 2.70-2.53 (m, 2H), 1.39 (d, $J = 11.8$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 179.9, 159.2 (d, $J = 240.3$ Hz), 158.9, 139.0, 135.3 (d, $J = 7.8$ Hz), 133.3, 129.8, 127.3, 121.3, 113.9 (d, $J = 21.8$ Hz), 113.8, 111.1 (d, $J = 24.6$ Hz), 108.3 (d, $J = 8.1$ Hz), 55.2, 49.2, 41.6, 26.3, 22.5; $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -120.83; HRMS: (ESI) calcd for C$_{20}$H$_{21}$FNO$_2$ $^{\text{[M+H]}^+}$ 326.1551; found 326.1550.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 7.0 min (minor), 8.2 min (major).

Optical Rotation: [$\alpha$]$_D^{32}$ +3.7 (c 0.5, iPrOH) for 89% ee.
(E)-3-(3-(4-Methoxyphenyl)allyl)-1,3-dimethyl-5-(trifluoromethyl)indolin-2-one (3ea)

3ea was prepared according to general procedure 2.1 using 1e and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ea as yellow oil (67% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.55 (dd, J = 8.1, 0.9 Hz, 1H), 7.45 (d, J = 1.1 Hz, 1H), 7.15-7.08 (m, 2H), 6.88 (d, J = 8.2 Hz, 1H), 6.82-6.74 (m, 2H), 6.28 (d, J = 15.7 Hz, 1H), 5.67 (dt, J = 15.5, 7.6 Hz, 1H), 3.77 (s, 3H), 3.20 (s, 3H), 2.65 (dd, J = 7.6, 1.0 Hz, 2H), 1.44 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 180.2, 159.0, 146.2, 134.2, 133.8, 129.8, 127.3, 126.1 (d, J = 58.0 Hz), 125.7 (q, J = 4.1 Hz), 124.6 (d, J = 32.6 Hz), 120.9, 119.9 (q, J = 3.6 Hz), 113.9, 107.7, 55.3, 48.8, 41.6, 26.4, 22.4; ¹⁹F NMR (377 MHz, CDCl₃) δ -61.27; HRMS: (ESI) calcd for C₂₁H₂₁F₃NO₂[M+H]⁺ 376.1519; found 376.1525.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 5.3 min (minor), 5.8 min (major).

Optical Rotation: [α]D³⁴ +17.6 (c 0.5, iPrOH) for 82% ee.
(E)-3-(3-(4-Methoxyphenyl)allyl)-1,3,6-trimethylindolin-2-one (3fa)

Chemical Formula: C_{21}H_{24}NO_2
Exact Mass: 321.1729

3fa was prepared according to general procedure 2.1 using 1f and 2a and was purified by silica gel column chromatography (PE/EA = 40/1 to 5/1) to obtain 3fa as yellow oil (64% yield). £H NMR (400 MHz, CDCl_3): δ 7.15 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 7.5 Hz, 1H), 6.87 (d, J = 7.4 Hz, 1H), 6.78 (t, J = 5.8 Hz, 2H), 6.65 (s, 1H), 6.29 (d, J = 15.7 Hz, 1H), 5.76 (ddd, J = 15.5, 8.0, 7.1 Hz, 1H), 3.78 (s, 3H), 3.16 (s, 3H), 2.70-2.48 (m, 2H), 2.38 (s, 3H), 1.39 (s, 3H); £C NMR (101 MHz, CDCl_3) δ 180.6, 158.8, 143.1, 137.8, 132.9, 130.7, 130.1, 127.2, 122.8, 122.7, 122.1, 113.7, 108.9, 55.2, 48.4, 41.6, 26.1, 22.6, 21.8; HRMS: (ESI) calcd for C_{21}H_{24}NO_2+ [M+H]^+ 322.1802; found 322.1804.
(E)-6-chloro-3-(3-(4-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (3ga)

3ga was prepared according to general procedure 2.2 using 1g and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ga as yellow oil (44% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.17-7.10 (m, 3H), 7.03 (dd, $J$ = 7.9, 1.8 Hz, 1H), 6.81 (d, $J$ = 1.8 Hz, 1H), 6.80-6.76 (m, 2H), 6.28 (d, $J$ = 15.7 Hz, 1H), 5.70 (dt, $J$ = 15.4, 7.6 Hz, 1H), 3.78 (s, 3H), 3.16 (s, 3H), 2.68-2.49 (m, 2H), 1.39 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 180.1, 159.0, 144.3, 133.5, 133.4, 131.9, 129.8, 127.3, 123.8, 122.1, 121.3, 113.8, 108.7, 55.3, 48.5, 41.5, 26.2, 22.5; HRMS: (ESI) calcd for C$_{20}$H$_{21}$ClNO$_2$ [M+H]$^+$ 342.1255; found 342.1253.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. $t_R$ = 6.6 min (minor), 6.9 min (major).

Optical Rotation: $[\alpha]_D^{33}$ +7.9 (c 0.2, iPrOH) for 85% ee.
(E)-6-Methoxy-3-(3-(4-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (3ha)

3ha was prepared according to general procedure 2.1 using 1h and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ha as yellow oil (74% yield). 1H NMR (400 MHz, CDCl3) δ 7.18-7.12 (m, 2H), 7.10 (d, J = 8.1 Hz, 1H), 6.82-6.75 (m, 2H), 6.56 (dd, J = 8.1, 2.3 Hz, 1H), 6.41 (d, J = 2.3 Hz, 1H), 6.29 (d, J = 15.8 Hz, 1H), 5.80-5.68 (m, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.15 (s, 3H), 2.67-2.50 (m, 2H), 1.38 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 180.8, 159.8, 158.8, 144.3, 132.9, 130.1, 127.2, 125.6, 123.4, 122.1, 113.7, 106.0, 96.0, 55.5, 55.2, 48.2, 41.8, 26.1, 22.6; HRMS: (ESI) calcd for C21H24NO3 [M+H]+ 338.1751; found 338.1747.

(E)-3-(3-(4-Methoxyphenyl)allyl)-1,3,7-trimethylindolin-2-one (3ia)

3ha was prepared according to general procedure 2.1 using 1h and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ha as yellow oil (63% yield). 1H NMR (400 MHz, CDCl3) δ 7.19-7.10 (m, 2H), 7.06 (dd, J = 6.9, 1.4 Hz, 1H), 7.01-6.90 (m, 2H), 6.82-6.75 (m, 2H), 6.28 (d, J = 15.7 Hz, 1H), 5.73 (dt, J = 15.5, 7.5 Hz, 1H), 3.78 (s, 3H), 3.46 (s, 3H), 2.63-2.58 (m, 2H), 2.56 (s, 3H), 1.38 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 181.0, 158.8, 140.84 134.3, 132.9, 131.5, 130.1, 127.3, 122.2, 122.1, 120.8, 119.5, 113.8, 55.2, 47.9, 41.9, 29.5, 22.9, 19.1; HRMS: (ESI) calcd for C21H24NO2 [M+H]+ 322.1802; found 322.1809.

(E)-1-(3-(4-Methoxyphenyl)allyl)-1,8-dimethyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one (3ja)
3ja was prepared according to general procedure 2.1 using 1j and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ja as yellow oil (74% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.14 (t, \(J = 5.7\) Hz, 2H), 6.85 (d, \(J = 16.4\) Hz, 2H), 6.81-6.75 (m, 2H), 6.30 (d, \(J = 15.8\) Hz, 1H), 5.78 (dt, \(J = 15.4, 7.5\) Hz, 1H), 3.77 (s, 3H), 3.65 (td, \(J = 6.8, 4.7\) Hz, 2H), 2.70 (t, \(J = 6.0\) Hz, 2H), 2.65-2.50 (m, 2H), 2.32 (s, 3H), 2.03-1.80 (m, 2H), 1.39 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 179.0, 158.8, 156.6, 146.7, 133.7, 130.4, 128.7, 128.0, 127.3, 120.9, 117.9, 113.9, 55.3, 48.3, 41.1, 25.3, 21.9; HRMS: (ESI) calcd for C\(_{23}\)H\(_{26}\)NO\(_2\)\([\text{M+H}]^+\) 348.1958; found 348.1953.

\((E)-3-(3-(4-Methoxyphenyl)allyl)-1,3-dimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one\) (3ka)

3ka was prepared according to general procedure 2.1 using 1k and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ka as yellow oil (89% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.17 (dd, \(J = 5.3, 1.5\) Hz, 1H), 7.43 (dd, \(J = 7.2, 1.5\) Hz, 1H), 7.15 (t, \(J = 5.7\) Hz, 2H), 6.95 (dd, \(J = 7.2, 5.3\) Hz, 1H), 6.82-6.76 (m, 2H), 6.30 (d, \(J = 15.7\) Hz, 1H), 5.77 (dt, \(J = 15.5, 7.6\) Hz, 1H), 3.78 (s, 3H), 3.28 (s, 3H), 2.73-2.52 (m, 2H), 1.43 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 179.9, 159.0, 156.6, 146.7, 133.7, 130.4, 128.7, 128.0, 127.3, 120.9, 117.9, 113.9, 55.3, 48.3, 41.1, 25.3, 21.9; HRMS: (ESI) calcd for C\(_{19}\)H\(_{21}\)N\(_2\)O\(_2\)\([\text{M+H}]^+\) 305.1598; found 309.1593.
(E)-3-Hexyl-3-(3-(4-methoxyphenyl)allyl)-1-methylindolin-2-one (3la)

3la was prepared according to general procedure 2.1 using 1l and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3la as yellow oil (82% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.29-7.22 (m, 1H), 7.19 (d, $J = 7.3$ Hz, 1H), 7.15-7.03 (m, 3H), 6.79 (dd, $J = 15.0$, 8.2 Hz, 3H), 6.26 (d, $J = 15.7$ Hz, 1H), 5.70 (dt, $J = 15.5$, 7.5 Hz, 1H), 3.77 (s, 3H), 3.17 (s, 3H), 2.71-2.53 (m, 2H), 1.95 (td, $J = 12.8$, 4.6 Hz, 1H), 1.81 (td, $J = 12.8$, 4.4 Hz, 1H), 1.32-1.06 (m, 7H), 1.03-0.89 (m, 1H), 0.80 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 179.7, 158.8, 143.8, 132.8, 132.0, 130.1, 127.6, 127.2, 123.0, 122.3, 121.9, 113.7, 107.8, 55.2, 53.4, 41.4, 36.8, 31.5, 29.4, 26.0, 24.2, 22.5, 14.0; HRMS: (ESI) calcd for C$_{25}$H$_{32}$NO$_2$ [M+H]+ 378.2428; found 378.2427.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 6.2 min (minor), 7.0 min (major).

Optical Rotation: $[\alpha]_D^{35} +3.8$ (c 0.5, iPrOH) for 80% ee.
(E)-3-Isopropyl-3-(3-(4-methoxyphenyl)allyl)-1-methylindolin-2-one (3ma)

3ma was prepared according to general procedure 2.1 using 1m and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ma as yellow oil (55% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.29-7.21 (m, 2H), 7.06 (ddd, \(J = 7.6, 4.6, 1.6\) Hz, 3H), 6.78 (d, \(J = 7.6\) Hz, 1H), 6.76-6.70 (m, 2H), 6.24 (d, \(J = 15.7\) Hz, 1H), 5.66-5.53 (m, 1H), 3.75 (s, 3H), 3.14 (s, 3H), 2.73 (dddd, \(J = 13.5, 9.1, 7.5, 1.0\) Hz, 2H), 2.25 (hept, \(J = 6.8\) Hz, 1H), 0.99 (d, \(J = 6.9\) Hz, 3H), 0.77 (d, \(J = 6.8\) Hz, 3H);

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 179.4, 158.7, 144.1, 132.5, 130.9, 130.2, 127.6, 127.1, 123.7, 122.2, 122.0, 113.7, 107.6, 56.6, 55.2, 38.7, 34.6, 25.8, 17.4, 17.3; HRMS: (ESI) calcd for C\(_{22}\)H\(_{26}\)NO\(_2\)\([M+H]\)^+ 336.1958; found 336.1956.
(E)-3-Benzyl-3-(3-(4-methoxyphenyl)allyl)-1-methylindolin-2-one (3na)

3na was prepared according to general procedure 2.1 using 1n and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3na as yellow oil (82% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.22 (dd, $J = 7.3$, 0.7 Hz, 1H), 7.19-7.14 (m, 1H), 7.14-7.10 (m, 2H), 7.08-6.98 (m, 4H), 6.85 (dd, $J = 7.2$, 2.2 Hz, 2H), 6.81-6.72 (m, 2H), 6.56 (d, $J = 7.7$ Hz, 1H), 6.33 (d, $J = 15.7$ Hz, 1H), 5.80-5.66 (m, 1H), 3.76 (s, 3H), 3.20 (d, $J = 13.0$ Hz, 1H), 3.09 (d, $J = 13.0$ Hz, 1H), 2.93 (s, 3H), 2.86-2.74 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 178.7, 158.8, 143.6, 135.9, 133.1, 130.7, 130.0, 129.8, 127.8, 127.5, 127.3, 126.3, 123.8, 121.9, 121.7, 113.7, 107.7, 55.2, 54.8, 43.1, 40.5, 25.8; HRMS: (ESI) calcd for C$_{26}$H$_{26}$NO$_2$ [M+H]$^+$ 384.1958; found 384.1962.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 9.9 min (major), 10.4 min (minor).

Optical Rotation: $[\alpha]_D^{32}$ -9.8 (c 0.5, iPrOH) for 76% ee.
(E)-3-(Methoxymethyl)-3-(3-(4-methoxyphenyl)allyl)-1-methylindolin-2-one (3oa)

3oa was prepared according to general procedure 2.1 using 1o and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3oa as yellow oil (63% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.32 (dd, $J = 7.3$, 0.7 Hz, 1H), 7.30-7.26 (m, 2H), 7.16-7.04 (m, 3H), 6.86-6.72 (m, 3H), 6.29 (d, $J = 15.7$ Hz, 1H), 5.69 (ddd, $J = 15.5$, 8.2, 7.0 Hz, 1H), 3.77 (s, 3H), 3.72 (q, $J = 9.0$ Hz, 2H), 3.25 (d, $J = 4.8$ Hz, 3H), 3.22 (d, $J = 3.4$ Hz, 1H), 3.18 (s, 3H), 2.72 (ddd, $J = 13.5$, 6.9, 1.2 Hz, 1H), 2.61 (ddd, $J = 13.6$, 8.2, 0.8 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 177.9, 158.8, 143.9, 133.1, 130.6, 129.9, 128.1, 127.2, 123.4, 122.3, 121.0, 113.7, 107.9, 76.1, 59.5, 55.2, 54.0, 37.5, 26.2; HRMS: (ESI) calcd for C$_{21}$H$_{24}$NO$_3$[M+H]$^+$ 338.1751; found 338.1752.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 9.9 min (major), 10.7 min (minor).

Optical Rotation: $[\alpha]_D^{34} +5.6$ (c 0.5, iPrOH) for 89% ee.
(E)-1-Benzyl-3-(3-(4-methoxyphenyl)allyl)-3-methylindolin-2-one (3pa)

3pa was prepared according to general procedure 2.1 using 1p and 2a and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3pa as yellow oil (84% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.28-7.22 (m, 1H), 7.12 (ddd, J = 18.0, 11.9, 5.0 Hz, 6H), 7.04 (td, J = 7.6, 1.0 Hz, 1H), 6.99 (t, J = 7.6 Hz, 2H), 6.82-6.74 (m, 2H), 6.35 (d, J = 15.8 Hz, 1H), 5.74-5.54 (m, 1H), 5.17 (d, J = 15.8 Hz, 1H), 4.60 (d, J = 15.8 Hz, 1H), 3.79 (s, 3H), 2.85-2.59 (m, 2H), 1.48 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 180.3, 158.9, 142.3, 135.7, 133.5, 133.2, 130.0, 128.7, 127.8, 127.4, 127.3, 127.0, 122.9, 122.5, 121.9, 113.8, 109.2, 55.3, 49.0, 43.7, 42.0, 23.4; HRMS: (ESI) calcd for C₂₆H₂₅NO₂ [M+H]⁺ 384.1958; found 384.1959.
(E)-3-Cinnamyl-1,3-dimethylindolin-2-one (3ab)

3ab was prepared according to general procedure 2.1 using 1a and 2b and was purified by silica gel column chromatography (PE/EA = 40/1–5/1) to obtain 3ab as yellow oil (60% yield). The 1H NMR data matched those reported in the literature: 1H NMR (400 MHz, CDCl3): δ 7.31-7.14 (m, 7H), 7.11-7.03 (m, 1H), 6.82 (d, J = 7.7 Hz, 1H), 6.35 (d, J = 15.8 Hz, 1H), 5.95-5.82 (m, 1H), 3.18 (s, 3H), 2.72-2.58 (m, 2H), 1.42 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 180.2, 143.1, 137.2, 133.6, 133.5, 128.4, 127.8, 127.2, 126.1, 124.2, 122.9, 122.4, 108.0, 77.3, 77.0, 76.7, 48.6, 41.6, 26.1, 22.5.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 8.5 min (minor), 10.2 min (major).

Optical Rotation: [α]D33 +4.6 (c 0.2, iPrOH) for 83% ee.
(E)-1,3-Dimethyl-3-(3-(p-tolyl)allyl)indolin-2-one (3ac)

![Chemical Structure: C_{20}H_{22}NO]

Chemical Formula: C_{20}H_{22}NO
Exact Mass: 291.1623

3ac was prepared according to general procedure 2.1 using 1a and 2c and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ac as yellow oil (75% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25 (td, $J$ = 7.6, 1.3 Hz, 1H), 7.23-7.20 (m, 1H), 7.11-7.02 (m, 5H), 6.81 (d, $J$ = 7.7 Hz, 1H), 6.31 (d, $J$ = 15.6 Hz, 1H), 5.90-5.75 (m, 1H), 3.17 (s, 3H), 2.69-2.57 (m, 2H), 2.29 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.2, 143.1, 136.9, 134.5, 133.5, 129.1, 127.8, 126.0, 123.1, 122.9, 122.3, 107.9, 48.6, 41.6, 26.1, 22.5, 21.1; HRMS: (ESI) calcd for C$_{20}$H$_{22}$NO$^+ [M+H]^+$ 292.1696; found 292.1703.

(E)-3-(3-(4-Chlorophenyl)allyl)-1,3-dimethylindolin-2-one (3ad)

![Chemical Structure: C_{20}H_{19}ClNO]

Chemical Formula: C_{19}H_{19}ClNO
Exact Mass: 311.1077

3ad was prepared according to general procedure 2.1 using 1a and 2d and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ad as yellow oil (75% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.27 (td, $J$ = 7.7, 1.3 Hz, 1H), 7.24-7.17 (m, 3H), 7.13-7.03 (m, 3H), 6.82 (m, 1H), 6.29 (d, $J$ = 15.8 Hz, 1H), 5.90-5.79 (m, 1H), 3.18 (s, 3H), 2.64 (dd, $J$ = 7.6, 1.1 Hz, 2H), 1.42 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.1, 143.1, 135.7, 133.5, 132.8, 132.5, 128.6, 127.9, 127.3, 125.0, 122.9, 122.5, 108.1, 48.6, 41.6, 26.2, 22.6; HRMS: (ESI) calcd for C$_{19}$H$_{19}$ClNO$^+ [M+H]^+$ 312.1150; found 312.1149.

(E)-3-(3-(4-Fluorophenyl)allyl)-1,3-dimethylindolin-2-one (3ae)
3ae was prepared according to general procedure 2.1 using 1a and 2e and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ae as yellow oil (70% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.30-7.25 (m, 1H), 7.24-7.20 (m, 1H), 7.18-7.11 (m, 2H), 7.08 (td, $J = 7.5$, 0.9 Hz, 1H), 6.97-6.88 (m, 2H), 6.80 (d, $J = 7.8$ Hz, 1H), 6.30 (d, $J = 15.8$ Hz, 1H), 5.78 (dt, $J = 15.4$, 7.5 Hz, 1H), 3.18 (s, 3H), 2.70-2.58 (m, 2H), 1.42 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.2, 163.3, 143.1, $^1$H NMR (377 MHz, CDCl$_3$) $\delta$ -115.06; HRMS: (ESI) calcd for C$_{19}$H$_{19}$FNO$^+$ [M+H]$^+$ 296.1145; found 296.1439.

(E)-1,3-Dimethyl-3-(3-(4-(trifluoromethyl)phenyl)allyl)indolin-2-one (3af)

3af was prepared according to general procedure 2.1 using 1a and 2f and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3af as yellow oil (43% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.48 (d, $J = 8.2$ Hz, 2H), 7.30-7.26 (m, 2H), 7.25 (d, $J = 2.4$ Hz, 1H), 7.24-7.21 (m, 1H), 7.08 (td, $J = 7.5$, 1.0 Hz, 1H), 6.83 (d, $J = 7.7$ Hz, 1H), 6.36 (d, $J = 14.8$ Hz, 1H), 5.95 (dq, $J = 15.9$, 7.9 Hz, 1H), 3.18 (s, 3H), 2.72-2.65 (m, 2H), 1.43 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.1, 173.8, 158.3, 143.2, 133.4, 132.5, 128.1, 126.3, 125.5 (q, $J = 3.8$ Hz), 123.2, 122.9, 122.6, 108.2, 48.7, 41.7, 26.3, 22.7; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -62.4; HRMS: (ESI) calcd for C$_{20}$H$_{19}$F$_3$NO$^+$ [M+H]$^+$ 346.1413; found 346.1419.
(E)-1,3-Dimethyl-3-(3-(4-(methylsulfonyl)phenyl)allyl)indolin-2-one (3ag)

3ag was prepared according to general procedure 2.1 using 1a and 2g and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ag as yellow oil (41% yield). $^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82-7.76 (m, 2H), 7.36-7.32 (m, 2H), 7.31-7.27 (m, 1H), 7.23 (ddd, $J = 7.4, 1.3, 0.5$ Hz, 1H), 7.09 (td, $J = 7.5, 1.0$ Hz, 1H), 6.84 (d, $J = 7.6$ Hz, 1H), 6.39 (d, $J = 15.8$ Hz, 1H), 6.04 (ddd, $J = 15.7, 8.0, 7.1$ Hz, 1H), 3.18 (s, 3H), 3.02 (s, 3H), 2.75-2.65 (m, 2H), 1.44 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 179.8, 143.0, 142.6, 138.7, 133.2, 131.9, 128.9, 128.1, 127.6, 126.8, 122.8, 122.6, 108.1, 48.5, 44.5, 41.6, 26.2, 22.7; HRMS: (ESI) calcd for C$_{20}$H$_{22}$NO$_3$S$^{+}$[M+H]$^+$ 378.1134; found 378.1126.

(E)-1,3-Dimethyl-3-(3-(m-tolyl)allyl)indolin-2-one (3ah)

3ah was prepared according to general procedure 2.1 using 1a and 2h and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ah as yellow oil (70% yield). $^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27 (td, $J = 7.7, 1.2$ Hz, 2H), 7.24-7.21 (m, 1H), 7.13 (t, $J = 7.5$ Hz, 1H), 7.07 (td, $J = 7.5, 0.9$ Hz, 1H), 7.04-6.97 (m, 3H), 6.82 (d, $J = 7.7$ Hz, 1H), 6.31 (d, $J = 15.7$ Hz, 1H), 5.95-5.83 (m, 1H), 3.19 (s, 3H), 2.71-2.55 (m, 2H), 2.29 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.2, 143.1, 137.9, 137.2, 133.8, 133.6, 128.3, 128.0, 127.8, 126.9, 123.9, 123.2, 122.9, 122.4, 108.0, 77.3, 77.0, 76.7, 48.6, 41.6, 26.2, 22.5, 21.3; HRMS: (ESI) calcd for C$_{20}$H$_{22}$NO$^+$[M+H]$^+$ 292.1696; found 292.1698.
(E)-1,3-Dimethyl-3-(3-(o-tolyl)allyl)indolin-2-one (3ai)

Chemical Formula: C_{20}H_{21}NO

Exact Mass: 291.1623

3ai was prepared according to general procedure 2.1 using 1a and 2i and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ai as yellow oil (70% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.29-7.22 (m, 3H), 7.14 (dd, \(J = 7.3, 2.3\) Hz, 1H), 7.10-7.04 (m, 4H), 6.82 (d, \(J = 7.7\) Hz, 1H), 6.49 (d, \(J = 15.6\) Hz, 1H), 5.70 (dt, \(J = 15.4, 7.6\) Hz, 1H), 3.18 (s, 3H), 2.68 (d, \(J = 7.8\) Hz, 2H), 2.17 (s, 3H), 1.43 (s, 3H);

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 180.2, 143.1, 136.6, 135.2, 133.5, 132.0, 130.0, 127.8, 127.1, 125.9, 125.8, 125.7, 122.9, 122.3, 108.0, 48.8, 41.9, 26.1, 22.7, 19.7; HRMS: (ESI) calcd for C\(_{20}\)H\(_{21}\)NONa\(^+\)[M+Na]\(^+\) 314.1515; found 314.1511.
(E)-1,3-Dimethyl-3-(3-(naphthalen-1-yl)allyl)indolin-2-one (3aj)

3aj was prepared according to general procedure 2.2 using 1a and 2j and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3aj as yellow oil (72% yield). 1H NMR (400 MHz, CDCl3): δ 7.79 (dt, J = 3.9, 2.8 Hz, 2H), 7.70 (d, J = 8.1 Hz, 1H), 7.47-7.39 (m, 2H), 7.38-7.23 (m, 5H), 7.14-7.07 (m, 1H), 7.00 (d, J = 15.5 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 5.81 (dt, J = 15.3, 7.6 Hz, 1H), 3.17 (s, 3H), 2.88-2.66 (m, 2H), 1.48 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 180.1, 143.2, 135.3, 133.5, 133.3, 131.6, 131.0, 128.3, 127.8, 127.6, 127.5, 125.8, 125.7, 125.5, 124.1, 123.8, 122.9, 122.4, 108.0, 77.3, 77.0, 76.7, 48.9, 42.0, 26.1, 22.7; HRMS: (ESI) calcd for C23H22NO+ [M+H]+ 328.1696; found 328.1696.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 5.7 min (minor), 6.5 min (major).

Optical Rotation: [α]D33 +47.7 (c 0.2, iPrOH) for 84% ee.
(E)-3-(3-(Benzo[d][1,3]dioxol-5-yl)allyl)-1,3-dimethylindo1-2-one (3ak)

3ak was prepared according to general procedure 2.1 using 1a and 2k and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3ak as yellow oil (73% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29-7.23 (m, 1H), 7.21 (dd, $J = 7.4$, 1.2 Hz, 1H), 7.07 (td, $J = 7.5$, 1.0 Hz, 1H), 6.82 (d, $J = 7.7$ Hz, 1H), 6.71 (d, $J = 1.7$ Hz, 1H), 6.68 (d, $J = 8.0$ Hz, 1H), 6.63 (dd, $J = 8.0$, 1.7 Hz, 1H), 6.25 (d, $J = 15.7$ Hz, 1H), 5.90 (s, 2H), 5.69 (dt, $J = 15.4$, 7.5 Hz, 1H), 3.18 (s, 3H), 2.68-2.55 (m, 2H), 1.40 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.3, 147.9, 146.9, 143.2, 133.7, 133.3, 131.8, 127.9, 123.0, 122.5, 120.8, 108.2, 108.1, 105.5, 101.0, 48.8, 41.7, 26.2, 22.6; HRMS: (ESI) calcd for C$_{20}$H$_{20}$NO$_3^+$ [M+H]$^+$ 322.1438; found 322.1443.

(E)-3-(3-(9-Ethyl-9H-carbazol-2-yl)allyl)-1,3-dimethylindo1-2-one (3al)

3al was prepared according to general procedure 2.1 using 1a and 2l and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3al as yellow oil (64% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (dd, $J = 6.8$, 0.8 Hz, 1H), 7.91 (d, $J = 1.5$ Hz, 1H), 7.44 (ddd, $J = 8.2$, 7.1, 1.2 Hz, 1H), 7.38-7.33 (m, 2H), 7.29-7.24 (m, 3H), 7.20 (ddd, $J = 8.0$, 7.2, 1.0 Hz, 1H), 7.12-7.05 (m, 1H), 6.84-6.79 (m, 1H), 6.52 (d, $J = 15.7$ Hz, 1H), 5.91 (ddd, $J = 15.5$, 8.0, 7.1 Hz, 1H), 4.32 (q, $J = 7.2$ Hz, 2H), 3.19 (s, 3H), 2.78-2.56 (m, 2H), 1.45 (s, 3H), 1.39 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 211.8, 174.6, 171.6, 170.8, 165.8, 165.2, 159.9, 159.1, 157.1, 155.5, 154.4, 154.4, 154.3, 153.7, 152.6, 151.8, 150.2, 149.6, 139.9, 139.7, 139.4, 80.2, 73.2, 68.9, 57.6, 53.8, 45.2; HRMS: (ESI) calcd for C$_{27}$H$_{26}$N$_2$O$_2$Na$^+^+$[M+Na]$^+$ 417.1937; found 417.1929.
3-(2-(1H-Inden-2-yl)ethyl)-1,3-dimethylindolin-2-one (3am)

3am was prepared according to general procedure 2.1 using 1a and 2m and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3am as yellow oil (70% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.28-7.18 (m, 3H), 7.18-7.11 (m, 2H), 7.08 (td, $J = 7.7$, 0.9 Hz, 1H), 7.05-7.00 (m, 1H), 6.73 (d, $J = 7.7$ Hz, 1H), 6.32 (d, $J = 0.7$ Hz, 1H), 3.15 (d, $J = 13.9$ Hz, 1H), 3.11 (s, 3H), 2.95 (dd, $J = 18.1$, 15.1 Hz, 2H), 2.74 (d, $J = 22.8$ Hz, 1H), 1.47 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.1, 144.8, 144.4, 143.3, 143.1, 133.6, 129.8, 127.9, 125.9, 123.8, 123.2, 122.7, 122.4, 120.2, 108.1, 49.3, 42.0, 39.5, 26.1, 24.2; HRMS: (ESI) calcd for C$_{20}$H$_{20}$NO$^+$/[M+H]$^+$ 290.1539; found 290.1546.

1,3-Dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)indolin-2-one (3an)

3an was prepared according to general procedure 2.1 using 1a and 2n and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3an as yellow oil (90% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.34-7.30 (m, 2H), 7.30-7.24 (m, 3H), 7.23-7.15 (m, 2H), 7.07 (td, $J = 7.5$, 1.0 Hz, 1H), 6.83 (d, $J = 7.8$ Hz, 1H), 6.64-6.52 (m, 1H), 6.39 (d, $J = 15.7$ Hz, 1H), 6.16 (ddd, $J = 15.0$, 10.4, 0.5 Hz, 1H), 5.46 (dt, $J = 15.2$, 7.6 Hz, 1H), 3.19 (s, 3H), 2.59 (d, $J = 7.7$ Hz, 2H), 1.39 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 180.3, 143.2, 137.4, 134.3, 133.7, 131.4, 128.7, 128.6, 128.6, 127.9, 127.4, 126.3, 123.0, 122.5, 108.1, 48.7, 41.6, 26.3, 22.7; HRMS: (ESI) calcd for C$_{21}$H$_{22}$NO$^+$/[M+H]$^+$ 304.1696; found 304.1689.
(E)-3-(3-(4-chlorophenyl)allyl)-1,3,5-trimethylindolin-2-one (3bd)

![Chemical structure of 3bd]

Chemical Formula: C$_{20}$H$_{20}$ClONa
Exact Mass: 325.1233

3bd was prepared according to general procedure 2.2 using 1b and 2d and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3bd as yellow oil (66% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.24-7.16 (m, 2H), 7.13-7.08 (m, 2H), 7.08-7.04 (m, 1H), 7.04-7.00 (m, 1H), 6.71 (d, $J = 7.8$ Hz, 1H), 6.30 (d, $J = 15.7$ Hz, 1H), 5.97-5.74 (m, 1H), 3.15 (s, 3H), 2.63 (dt, $J = 7.1$, 1.2 Hz, 2H), 2.35 (s, 3H), 1.39 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 180.0, 140.7, 135.7, 133.5, 132.7, 132.3, 131.9, 128.5, 128.1, 127.3, 125.1, 123.7, 107.7, 48.7, 41.7, 26.2, 22.6, 21.2; HRMS: (ESI) calcd for C$_{20}$H$_{20}$ClONa$^+$(M+Na)$^+$ 348.1126; found 348.1116.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. tR = 5.1 min (minor), 5.6 min (major).

Optical Rotation: [α]$_D^{33}$ +51.4 (c 0.5, 1PrOH) for 77% ee.
### 色谱图

- **Peak number**: 留时间
- **Area**: 面积
- **Height**: 高度

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\((E)-3-(3-(benzo[d][1,3]dioxol-5-yl)allyl)-1,3,5-trimethylindolin-2-one (3bk)\)

\[
\begin{align*}
\text{Chemical Formula: } & C_{21}H_{21}NO_3 \\
\text{Exact Mass: } & 335.1521
\end{align*}
\]

3bk was prepared according to general procedure 2.2 using 1b and 2k and was purified by silica gel column chromatography (PE/EA = 40/1~5/1) to obtain 3bk as yellow oil (75% yield). \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.09-7.02 (m, 2H), 6.73-6.66 (m, 3H), 6.66-6.60 (m, 1H), 6.26 (d, \(J = 15.5\) Hz, 1H), 5.90 (s, 2H), 5.74-5.62 (m, 1H), 3.15 (s, 3H), 2.60 (d, \(J = 7.5\) Hz, 2H), 2.36 (s, 3H), 1.39 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 180.2, 147.8, 146.8, 140.8, 133.7, 133.1, 131.9, 128.0, 123.7, 122.6, 120.7, 108.1, 107.7, 105.5, 100.9, 48.7, 41.6, 26.2, 22.6, 21.2; HRMS: (ESI) calcd for \(C_{21}H_{21}NO_3Na^+\) [M+Na\(^+\)] 358.1414; found 358.1390.

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-Propanol = 80/20 as eluent, 254 nm, 1 mL/min. \(t_R = 5.1\) min (minor), 5.9 min (major).

Optical Rotation: \([\alpha]_D^{31} +11.4\) (c 0.1, \(\text{PrOH}\)) for 81% ee.
3-((1H-inden-2-yl)methyl)-1,3,5_trimethylindolin-2-one (2bm)

\[
\begin{align*}
\text{Chemical Formula: } & C_{21}H_{22}NO \\
\text{Exact Mass: } & 303.1623
\end{align*}
\]

3bm was prepared according to general procedure 2.2 using 1b and 2m and was purified by silica gel column chromatography (PE/EA = 40/1–5/1) to obtain 3bm as yellow oil (62% yield). 

\( ^1 \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.24-7.20 \text{ (m, 1H), 7.19-7.11 (m, 2H), 7.08-7.06 (m, 1H), 7.06-7.00 (m, 2H), 6.62 (d, } J = 7.9 \text{ Hz, 1H), 6.31 (s, 1H), 3.14 (d, } J = 13.1 \text{ Hz, 1H), 3.09 (s, 3H), 2.97 (d, } J = 22.1 \text{ Hz, 1H), 2.90 (d, } J = 14.5 \text{ Hz, 1H), 2.76 (d, } J = 22.1 \text{ Hz, 1H), 2.37 (s, 3H), 1.45 (s, 3H); } ^{13} \text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 180.1, 144.9, 144.6, 143.4, 140.8, 133.7, 131.9, 129.6, 128.2, 125.0, 123.8, 123.5, 123.2, 120.2, 107.8, 49.3, 42.0, 39.6, 26.2, 24.4, 21.2; \text{ HRMS: (ESI) calcd for } C_{21}H_{22}NO\cdot[M+H]^+ 304.1696; \text{ found 304.1688.}
\]

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, n-Hexane/i-PrOH = 90/10 as eluent, 254 nm, 1 mL/min. tR = 4.9 min (minor), 5.6 min (major).

Optical Rotation: \([\alpha]_D^{33} +56.2 \text{ (c 0.2, } i\text{PrOH) for 73% ee.}\)
(E)-3-(3-(4-methoxyphenyl)allyl)-1,3,4-trimethylindolin-2-one (3qa)

\[
\text{Chemical Formula: } C_{21}H_{23}NO_2 \\
\text{Exact Mass: } 321.1729
\]

\[
\begin{align*}
^1H \text{ NMR (400 MHz, CDCl}_3\text{)} & \delta 7.15 (t, J = 7.8 \text{ Hz, 1H}), 7.06-6.98 (m, 2H), 6.84 (d, J = 7.7 \text{ Hz, 1H}), 6.76-6.69 (m, 2H), 6.67-6.61 (m, 1H), 6.26 (d, J = 15.6 \text{ Hz, 1H}), 5.53-5.40 (m, 1H), 3.74 (s, 3H), 3.14 (s, 3H), 2.90-2.74 (m, 2H), 2.44 (s, 3H), 1.50 (s, 3H); \\
^{13}C \text{ NMR (101 MHz, CDCl}_3\text{)} & \delta 180.1, 158.8, 143.5, 134.0, 132.1, 130.2, 130.1, 127.6, 127.2, 125.0, 122.3, 113.7, 105.7, 55.2, 50.0, 39.7, 26.2, 21.5, 18.4; \\
\text{HRMS: (ESI) calcd for } C_{21}H_{23}NO_2\text{H}^+ [M+H]^+ & 322.1802; \text{ found: } 322.1797.
\end{align*}
\]

The enantiomeric purity was established by HPLC analysis using a chiral column: AD-H column, 30 °C, \(\text{n-Hexane/i-Propanol = 90/10 as eluent, 254 nm, 1 mL/min. } t_R = 8.2 \text{ min (minor), 9.2 min (major).} \)
5. Synthetic Applications

Scheme S1. Formal total synthesis of (+)-physovenine and (+)-physostigmine.

Procedure for the synthesis of the aldehyde intermediate 4: To a solution of 3ca (100 mg, 0.3 mmol) in CH\(_2\)Cl\(_2\)/MeOH (3 mL/3 mL), O\(_3\) was bubbled at -78 °C until the reaction was complete (monitored by TLC). Argon was bubbled into the solution for 5 min to remove the excess O\(_3\). PPh\(_3\) was added at -78 °C and the mixture was kept stirring for another hour. The reaction mixture was passed through a short pad of silica gel, and eluted with EtOAc. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (PE/ethyl acetate = 5/1 to 2/1) to afford the aldehyde intermediate 4 as a white solid (42.1 mg, 60% yield).

Procedure for the synthesis of 5: To a solution of LiAlH\(_4\) (260 μL, 0.65 mmol, 2.5 mol/L in THF) in dry THF (3 mL), the aldehyde intermediate 4 (15.1 mg, 0.065 mmol) was added under Ar, the mixture was stirred at room temperature for 40 min. The reaction was quenched by EtOAc and saturated aqueous NaHCO\(_3\) successively. The phases were separated, the aqueous layer was extracted with EtOAc, and the combined organic extracts were dried with Na\(_2\)SO\(_4\) and concentrated. The residue was
purified by silica gel column chromatography (PE/acetone/NEt$_3$ = 10/1/0.1) to afford 5 as a pale yellow oil (13.0 mg, 91%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.74-6.62 (m, 2H), 6.29 (d, $J = 8.3$ Hz, 1H), 5.03 (s, 1H), 4.03-3.86 (m, 1H), 3.75 (s, 3H), 3.47 (ddd, $J = 10.9, 8.6, 5.4$ Hz, 1H), 2.88 (s, 3H), 2.13 (ddd, $J = 11.8, 5.3, 1.5$ Hz, 1H), 2.09-1.99 (m, 1H), 1.45 (s, 3H); $[\alpha]_{D}^{20} +24$ (c 0.25, EtOH), literature value $[\alpha]_{D}^{22} -81.2$ (c 0.6, EtOH) for the opposite enantiomer.\(^3\)

Procedure for the synthesis of 6: To a solution of the aldehyde intermediate 4 (15.1 mg, 0.065 mmol) and TEA (90 μL, 0.65 mmol) in anhydrous THF (3 mL), MeNH$_2$·HCl (43.9 mg, 0.65 mmol) and MgSO$_4$ (50 mg) was added under Ar, the mixture was stirred at room temperature for 16 h. Then LiAlH$_4$ (260 μL, 0.65 mmol, 2.5 mol/L in THF) was added and the mixture was refluxed at 80 °C for 1.5 h. The reaction was quenched by EtOAc and saturated aqueous NaHCO$_3$ successively. The phases were separated, the aqueous layer was extracted with EtOAc, and the combined organic extracts were dried with Na$_2$SO$_4$ and concentrated. The residue was purified by silica gel column chromatography (PE/acetone/NEt$_3$ = 8/1/0.1) to afford 6 as a pale yellow oil (12.8 mg, 86%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.65 (dt, $J = 4.0, 2.4$ Hz, 2H), 6.36 (d, $J = 8.2$ Hz, 1H), 4.05 (s, 1H), 3.75 (s, 3H), 2.89 (s, 3H), 2.73 (dt, $J = 9.5, 5.4$ Hz, 1H), 2.68-2.60 (m, 1H), 2.54 (s, 3H), 1.95 (dd, $J = 7.4, 5.4$ Hz, 2H), 1.43 (s, 3H); $[\alpha]_{D}^{30} +62$ (c 0.2, MeOH), literature value $[\alpha]_{D}^{22} -98$ (c 1.0, MeOH) for the opposite enantiomer.\(^3\)
6. Copies of the $^1$H, $^{19}$F and $^{13}$C NMR spectra

3aa
3fa

Chemical Formula: C₂₇H₂₉NO₃
Exact Mass: 321.1725

Chemical Formula: C₂₇H₂₉NO₃
Exact Mass: 321.1725
3ma

Chemical Formula: C₆H₁₂NO₃
Exact Mass: 335.1685
3ac

Chemical Formula: C₂₀H₂₂NO
Exact Mass: 291.1623

Chemical Formula: C₂₀H₂₂NO
Exact Mass: 291.1623
3ad

Chemical Formula: C₈H₇NO
Exact Mass: 311.1077

by 6-156-3 & 4-Cl

Chemical Formula: C₈H₇NO
Exact Mass: 311.1077

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2.04 3.04

9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0

1H ppm

100
3ag

Chemical Formula: C_{12}H_{18}N_{OS}
Exact Mass: 355.1242

Chemical Formula: C_{12}H_{18}N_{OS}
Exact Mass: 355.1242

S73
3am
7. References

