Supporting Information

Catalytic enantioselective synthesis of 2-(2-hydroxyethyl)indole scaffolds via consecutive intramolecular amido-cupration of allenes and asymmetric addition of carbonyl compounds

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1. General:

Unless otherwise noted, all the reactions were performed in a flame-dried 20 mL test tube with a Teflon-coated magnetic stirring bar fitted with a 3-way glass stopcock. Air- and moisture-sensitive liquids were transferred via a gas-tight syringe and stainless-steel needle and reactions were run under argon atmosphere. All reaction work-up and purification procedures were carried out with reagent-grade solvents in air at ambient temperature. Column chromatographic purifications were performed with silica gel Merck 60 (230-400 mesh ASTM). The absolute configuration of product 3aa was determined (see S48). For other products, the absolute configuration was tentatively assigned from the analogy to 3aa.

Instrumentation:

$^1$H and $^{13}$C NMR spectra were recorded on JEOL ECX500 (500 MHz for $^1$H NMR and 125 MHz for $^{13}$C NMR) and JEOL ECS400 (400 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR) spectrometers. Chemical shifts were reported in ppm in the scale relative to the solvent used as an internal reference for $^1$H ($\delta = 7.26$ ppm for CDCl$_3$, 2.05 ppm for acetone-$d_6$, and 3.31 for CD$_2$OD) and $^{13}$C NMR ($\delta = 77.00$ ppm for CDCl$_3$, 206.26 ppm for acetone-$d_6$, and 49.0 ppm for CD$_2$OD). Data are reported as follows: chemical shift, multiplicity ($s =$ singlet, $d =$ doublet, $dd =$ doublet of doublet, $td =$ triplet of doublet, $m =$ multiplet), coupling constants (Hz) and integration. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI-mass spectra were measured on JEOL JMS-T100LC AccuTOF spectrometer (for High resolution mass spectra). The enantiomeric excesses ($ee$’s) were determined by high-performance liquid chromatography analysis conducted by JASCO HPLC systems (pump: PU-2080; detector: UV-2075, measured at 254 nm; chiral column; mobile phase: 2-propanol/hexane, ethanol/hexane).

Materials:

All non-commercially available compounds were prepared and characterized as described below. Other reagents were purchased from Aldrich chemical company, Tokyo Chemical Industry Co., Ltd. (TCI), Kanto Chemical Co., Inc., and Wako Pure Chemical Industries, Ltd. and used without further purification.

($S, S$)-Ph-BPE was purchased from Aldrich chemical company.

Mesitylcopper was prepared by following the reported procedure.¹

1, 3- Bis(diphenylphosphino)propane (dppp) was purchased from Wako Pure chemical industries.

All aliphatic and aromatic aldehydes and ketones were purchased from commercial sources and further purified by distillation/crystallization.

2-Iodo-5-methoxyaniline was prepared from 4-methoxy-2-nitroaniline in 69% yield.² ³

2-Iodo-3-methylaniline was prepared from 2-iodo-3-nitroaniline in 99% yield.⁴

N-(2-iodophenyl)acetamide and tert-butyl 2-iodophenylcarbamate were synthesized by using the reported procedure.4,5

2. N-Protection of o-Iodoanilines to carbamates and characterization:

**General procedure for the synthesis of N-methylcarbamate:**
To a stirred solution of o-iodoaniline (5g, 22.82 mmol) in pyridine (40 mL) at 0 °C was added methyl chloroformate (2.65 mL, 34.2 mmol) dropwise via syringe over 10 min. The solution was slowly warmed to room temperature and stirred for 12 h. The mixture was recooled to 0 °C, and a second portion of methyl chloroformate (2.65 mL, 34.2 mmol) was added in the same manner. The mixture was stirred at room temperature for further 12 h. The reaction completion was confirmed by TLC analysis, and the reaction was quenched with water. The mixture was extracted with EtOAc (100 mL×3), and the combined organic layers were washed sequentially with water, sat. CuSO4 solution, 0.3 N HCl and brine. After dried over Na2SO4, solvents were evaporated under vacuum. The crude residue was purified by silica gel column chromatography.

**Methyl 2-iodophenylcarbamate (17):**

Yield: 94%; White solid; Rf = 0.33 (Ethyl acetate: Hexane (1.5:8.5)); IR (thin film): 3387, 2947, 1715, 1520, 1437 cm⁻¹; ¹H NMR (CDCl3, 500 MHz): δ 8.03 (d, J = 8 Hz, 1H), 7.73 (dd, J = 8 Hz, 1.7 Hz, 1H), 7.33 - 7.29 (m, 1H), 6.97 (brs, 1H), 6.79 - 6.76 (m, 1H), 3.7 (s, 3H); ¹³C NMR (CDCl3, 125 MHz): δ 153.6, 138.7, 138.1, 129.1 124.9, 120.2, 88.8, 52.4; HRMS (ESI): calcd for C₈H₈INO₂ m/z 299.9497 [M+Na]+, Found 299.9505.

**Methyl 2-iodo-5-methoxyphenyl carbamate (18):**

Yield: 88.6%; White solid; Rf = 0.45 (Ethyl acetate: Hexane (2:8)); IR (thin film): 3385, 2948, 1710, 1521, 1217 cm⁻¹; ¹H NMR (CDCl3, 500 MHz): δ 7.75 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 6.41 (dd, J = 8.59 Hz, 2.86 Hz, 1H), 3.78 (s, 6H); ¹³C NMR (CDCl3, 125 MHz): δ153.6, 138.7, 138.1, 129.1 124.9, 120.2, 88.8, 52.4; HRMS (ESI): calcd for C₉H₁₀INO₃ m/z 329.96031 [M+Na]+, Found 329.9591.

**Methyl 5-chloro-2-iodophenyl carbamate (19):**

Yield: 94%; White fluffy solid; Rf = 0.26 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): 3282, 2965, 1698, 1540, 1091 cm⁻¹; ¹H NMR (CDCl3, 500 MHz): δ8.15 (brs, 1H), 7.66-7.63 (m, 1H), 6.97 (brs, 1H), 6.82-6.80 (m, 1H), 3.81 (s, 3H); ¹³C NMR (CDCl3, 125 MHz): δ153.4, 139.33, 139.31, 135.5, 125.0, 119.91, 85.2, 52.7; HRMS (ESI): calcd for C₈H₇ClNO₂ m/z 333.9108 [M+Na]+, Found 333.9115.

**Methyl 2-iodo-4-(trifluromethyl)phenylcarbamate (20):**

Yield: 93%; White fluffy solid; Rf = 0.25 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): 3391, 2961, 2369, 1700, 1540, 1215 cm⁻¹; ¹H NMR (CDCl3, 500 MHz): δ 8.23 (d, J = 8.59 Hz, 1H), 7.99 (d, 1H, J = 1.14 Hz, 1H), 7.59 (dd, J= 1.14 Hz, 1H), 7.19 (d, J = 8.59 Hz, 1H), 6.30 (t, J = 1.14 Hz, 4H); ¹³C NMR (CDCl3, 125 MHz): δ 153.4, 139.33, 139.31, 135.5, 125.0, 119.91, 85.2, 52.7; HRMS (ESI): calcd for C₂₃H₁₈F₃INO₂ m/z 505.9693 [M+Na]+, Found 505.9692.

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8.59 Hz, 1.7 Hz, 1H), 7.15 (brs, 1H), 3.89 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 153.4, 141.0, 135.8 (q, $^3$J$_{CF}$ 3.6 Hz), 126.8 (q, $^2$J$_{CF}$ 33.5 Hz), 126.4 (q, $^3$J$_{CF}$ 3.6 Hz), 121.8 (q, $^2$J$_{CF}$ 272 Hz), 118.9, 87.1, 52.8; HRMS (ESI): calecd for C$_9$H$_7$F$_3$I NO$_2$m/z 367.9371 [M+Na$^+$], Found 367.9371.

Methyl 2-iodo-3-methylphenylcarbamate (21):

Yield: 93.5%; White solid; $R_f$ = 0.25 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): $\nu$ 3396, 2930, 2369, 1705, 1213, 756 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.89 (d, $J$ = 8 Hz, 1H), 7.27-7.24 (m, 1H), 7.19 (brs, 1H), 7.02 (d, $J$ = 7.4 Hz, 1H), 3.85 (s, 3H), 2.48 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 153.8, 142.1, 138.3, 128.43, 124.8, 117.5, 96.63, 52.38, 29.59; HRMS (ESI): calecd for C$_9$H$_{10}$INO$_2$m/z 313.9654 [M+Na$^+$], Found 313.9652.

3. Palladium(0)-catalyzed coupling reaction of iodoanilides with allenylstannane.$^6$

General procedure for the preparation of 2-allenylanilides:
The solution of N-Boc iodoanilide (1.5 g, 4.7 mmol) and allenylstannane (2.32 g, 7.05 mmol) in anhydrous DMF (40 mL) was degassed and purged with argon gas. Tris(2-furyl)phosphine (0.218 g, 0.94 mmol), Pd$_2$(dba)$_3$ (0.145 g, 0.141 mmol) and CuI (0.09 g, 0.47 mmol) were added to the reaction mixture at rt under argon atmosphere. The reaction mixture was stirred at rt for allotted time, quenched by addition of 10% aqueous NH$_3$ solution and extracted with diethyl ether. The combined extracts were washed with water, brine, dried over sodium sulfate and concentrated under vacuum.

tert-butyl 2-(propa-1,2-dienyl)phenylcarbamate (22):

Reaction carried out in 4.7 mmol scale;

Time required for completion of reaction: 3 h

Purified by silica gel column chromatography (Et$_2$O:Hexane (0.5:9.5))

Isolated yield: 2.759 g, (81%); colorless liquid; $R_f$ = 0.37 (EtOAc: Hexane (1:9)); IR (thin film): $\nu$ 3387, 2977, 1943, 1710, 1520, 1156, 754 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.83 (brs, 1H), 7.23-7.20 (m, 2H), 7.10 (brs, 1H), 7.04 (td, $J$ = 7.45 Hz, 1.15 Hz, 1H), 6.28 (t, $J$ = 6.87 Hz, 1H), 5.19 (d, $J$ = 6.87 Hz, 2H), 1.52 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 209.9, 152.9, 135.5, 128.6, 127.7, 123.7, 122.9, 121.8, 90.5, 80.2, 78.4, 28.2; HRMS (ESI): calecd for C$_{14}$H$_{17}$NO$_2$m/z 254.1157 [M+Na$^+$], Found 254.1150.

Methyl 2-(propa-1,2-dienyl)phenylcarbamate (1a):

Reaction carried out in 5.41 mmol scale;

Time required for completion of reaction: 3 h

Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 0.921 g (90%); white solid; $R_f$ = 0.34 (Ethyl acetate: Hexane (2:8)); IR (thin film): $\nu$ 3313, 2947, 1941, 1716, 1523, 1225, 1060, 757 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.82 (brs, 1H), 7.31 (brs, 1H), 7.24-7.21 (m, 2H), 7.07 (t, $J$ = 7.45 Hz, 1H), 6.28 (t, $J$ = 6.87 Hz, 1H), 5.2 (d, $J$ = 6.87 Hz, 2H), 3.76 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 209.8, 154.3, 135.1, 128.7, 127.8, 124.1, 90.5, 80.2, 78.4, 28.2; HRMS (ESI): calecd for C$_{14}$H$_{17}$NO$_2$m/z 254.1157 [M+Na$^+$], Found 254.1150.

Methyl 5-chloro-2-(propa-1,2-diencyl)phenylcarbamate (1b):

Reaction carried out in 6.42 mmol scale; Time required for completion of reaction: 3.5 h
Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 1.249 g (87%); yellow solid; Rf = 0.17 (Ethyl acetate: Hexane (1:9)); IR (thin film): \( \nu \) 3383, 2961, 2321, 1941, 1709, 1521, 1224, 1058, 868 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 7.96 (brs, 1H), 7.41-7.4 (m, 1H), 7.1-7.07 (m, 1H), 7.01 (dd, \( J = 8 \) Hz, 1.72 Hz, 1H), 6.22 (t, \( J = 6.87 \) Hz, 1H), 5.23 (d, \( J = 6.87 \) Hz, 1H), 3.77 (s, 3H); \(^1^3\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 209.8, 153.8, 136.4, 133.5, 129.8, 123.9, 121.1, 99.8, 90.2, 79.3, 52.55; HRMS (ESI): calcd for C\(_{11}\)H\(_{11}\)ClNO \( m/z \) 246.0298 [M+Na]\(^+\), Found 246.0286.

Methyl 3-methyl-2-(propa-1,2-diencyl)phenylcarbamate (1c):

Reaction carried out in 4.8 mmol scale; Duration of reaction: 2 days at rt
Purified by silica gel column chromatography (Et\(_2\)O: Hexane (1:9))

Isolated yield: 0.53 g (37%) 63% (brsm); liquid; Rf = 0.45 (Ethyl acetate: Hexane (2:8)); IR (thin film): \( \nu \) 3380, 2369, 1915, 1716, 1540, 1228, 1059, 765; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 7.8 (brs, 1H), 7.32-7.34 (m, 1H), 7.15 (t, \( J = 8.0 \) Hz, 1H), 6.94 (d, \( J = 7.45 \) Hz, 1H), 6.25 (t, \( J = 7.45 \) Hz, 1H), 5.09 (d, \( J = 6.87 \) Hz, 2H), 3.77 (s, 3H); \(^1^3\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 209.4, 154.1, 136.6, 135.8, 127.6, 125.6, 124.7, 118.6, 87.2, 76.7, 52.2, 20.8; HRMS (ESI): calcd for C\(_{12}\)H\(_{13}\)NO \( m/z \) 226.0844 [M+Na]\(^+\), Found 226.0844.

Methyl 5-methoxy-2-(propa-1,2-diencyl)phenylcarbamate (1e):

Reaction carried out in 8.14 mmol scale; Duration of the reaction: 12 h
Purified by silica gel column chromatography (EtOAc: Hexane (1:5:8.5))

Isolated yield: 0.95 g (53%) (76%, brsm); white solid; Rf = 0.3 (Ethyl acetate: Hexane (2:8); IR (thin film): \( \nu \) 3382, 3008, 2953, 1941, 1710, 1531, 1228, 1059, 765; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 7.6 (brs, 1H), 7.51 (brs, 1H), 7.06 (d, \( J = 8.59 \) Hz, 1H), 6.61 (dd, \( J = 8.59 \) Hz, 2.29 Hz, 1H), 6.23 (t, \( J = 6.87 \) Hz, 1H), 5.2 (d, \( J = 6.87 \) Hz, 2H), 3.8 (s, 3H), 3.77 (s, 3H); \(^1^3\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 209.2, 159.5, 154.0, 136.8, 129.9, 113.9, 110.3, 105.8, 79.0, 55.3, 52.3; HRMS (ESI): calcd for C\(_{12}\)H\(_{13}\)NO\(_3\) \( m/z \) 242.0793 [M+Na]\(^+\), Found 242.0787.

Methyl 2-(propa-1,2-diencyl)-4(trifluoromethyl)phenylcarbamate (1d):

Reaction carried out in 5.79 mmol scale; Time required for completion of reaction: 3.5 h
Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 1.2 g (81%); white fluffy solid; Rf = 0.36 (Ethyl acetate: Hexane (2:8); IR (thin film): \( \nu \) 3273, 2961, 2365, 1960, 1700, 1540, 1213, 769 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 8.1 (d, \( J = 8.59 \) Hz, 1H), 7.56 (brs, 1H), 7.42-7.47(m, 2H), 6.28 (t, \( J = 6.87 \) Hz, 1H), 5.29 (d, \( J = 7.45 \) Hz, 2H), 3.79 (s,
3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 209.9, 153.8, 138.5, [(127.2, 125.0, 122.9, 120.7) (q, $^1J_{CF}$ 272 Hz)], 125.97 (q, $^1J_{CF}$ 3.6 Hz), [(125.9, 125.7, 125.4, 125.2) (q, $^2J_{CF}$ 32 Hz)], 124.8 (q, $^2J_{CF}$ 3.6 Hz), 122.0, 120.5, 90.1, 79.7, 52.6; HRMS (ESI): calcd for C$_{12}$H$_{10}$F$_3$NO$_2$m/z 280.0561 [M+Na]$^+$, Found 280.0563.

Preparation of N-(2-(propa-1,2-dienyl)phenyl)acetamide (23):$^7$

**Procedure:** N-(2-iodophenyl)acetamide (2 g, 7.66 mmol) was added to a suspension of [Pd(PPh$_3$)$_4$] (0.354g, 0.3 mmol) and lithium iodide (3 g, 22.9 mmol) in DMF (45 mL) under argon atmosphere. After 10 min, the allenylindium reagent, which was generated from propargyl bromide (0.86 mL, 11.49 mmol) and indium (1.93 g, 16.8 mmol) in DMF (25 mL) was added, and the reaction mixture was stirred at 90 to 100 °C for 1 h 15 min. The reaction mixture was cooled to room temperature and quenched slowly with sat. NaHCO$_3$ solution. The reaction mixture was extracted with diethyl ether. Combined organic layers were washed with water, brine, dried over sodium sulfate and concentrated under vacuum. Purification by silica gel column chromatography (EtOAc: hexane 4:6) afforded white fluffy solid (0.748 g, 56.6%). $R_f$ = 0.27 (Ethyl acetate: Hexane (1:1); IR (thin film): $\nu$ 3221, 3025, 2369, 1646, 1541, 858 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.97 (brs, 1H), 7.85 (d, $J$ = 6.3 Hz, 1H), 7.23-7.19 (m, 2H), 7.09 (t, $J$ = 7.45 Hz, 1H), 6.29 (t, $J$ = 6.87 Hz, 1H), 5.19 (d, $J$ = 6.87 Hz, 2H), 2.12 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 210.1, 168.4, 135.0, 128.7, 78.4, 24.0; HRMS (ESI): calcd for C$_{11}$H$_{11}$NO/m/z 196.0738 [M+Na]$^+$, Found 196.0732.

4. Catalytic tandem amidocupration of allene and asymmetric allylation: Optimization of reaction conditions:

4-1. Ligand screening:

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<th>Entry</th>
<th>Ligand</th>
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<th>ee (24/25) (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>1</td>
<td>(R)-DTBM-SEGPHOS</td>
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<td>(S)-Josiphos</td>
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<td>4</td>
<td>(S, S)-Ph-BPE</td>
<td>52/28</td>
<td>82/ &gt;99</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield determined by <sup>1</sup>H NMR spectrum of the crude products using tert-butyl methyl ether as an internal standard. <sup>b</sup>Enantiomeric excess was determined by chiral HPLC analysis.

**Experimental procedure:**
To a flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (3.64 mg, 0.02 mmol, 10 mol%), and ligand (0.022 mmol, 11 mol%) under nitrogen atmosphere in a glove box. Anhydrous THF (418 µL) and HMPA (33 µL) were added, and the mixture was stirred at ambient temperature for 10 minutes. To the stirred solution, benzaldehyde (40 µL, 0.4 mmol) and 1 M solution of allenylanilide (22) (46.22 mg, 200 µL, 0.2 mmol) were added sequentially. The resulting solution was stirred at the same temperature for 44 h. Quenched with sat. NH₄Cl solution, products were extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. The racemic sample was prepared by performing reaction with achiral ligand 1,3-bis(diphenylphosphino)propane (dppp).

Ligand screening revealed that (S,S)-Ph-BPE was the best ligand for this asymmetric transformation.

**3-Phenyl-3,4-dihydro-1H-[1,3]oxazino[3,4-a]indol-1-one (24):**

![3-Phenyl-3,4-dihydro-1H-[1,3]oxazino[3,4-a]indol-1-one (24)](image)

Purified by silica gel column chromatography (EtOAc: Hexane (1:9); white solid; Rₖ = 0.35 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3021, 2369, 1739, 1535, 1213, 1104, 769 cm⁻¹; <sup>1</sup>H NMR (CDCl₃, 500 MHz): δ 8.31 (d, J = 8.59 Hz, 1H), 7.54 (d, J = 8.02 Hz, 1H), 7.43-7.39 (m, 5H), 7.34 (t, J = 7.45 Hz, 1H), 7.29 (t, J = 7.45 Hz, 1H), 6.42 (s, 1H), 5.59 (dd, J = 10.8 Hz, 3.4 Hz, 1H), 3.43-3.31 (m, 2H); <sup>13</sup>C NMR (CDCl₃, 125 MHz): δ 147.8, 137.0, 135.1, 132.7, 129.4, 129.0, 128.8, 125.9, 124.4, 123.8, 120.3, 115.3, 104.5, 79.8, 30.3; HRMS (ESI) calcd for C₁₁H₁₃NO₂ m/z 286.08440 [M+Na]<sup>+</sup>, Found 286.0850. Specific optical rotation [α]<sub>D</sub><sup>24</sup> = -108.8 (c = 1.21, CHCl₃) for an enantiomerically enriched sample of 82% ee. Enantiomeric excess was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H; Mobile phase: Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm, tᵣ = 12.7 min (major), 19.3 min (minor).
(S)-tert-butyl-2-(2-hydroxy-2-phenylethyl)-1H-indole-1-carboxylate (25):

Purified by silica gel column chromatography (EtOAc: Hexane (1:9); colorless liquid; Ret = 0.33 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3403, 2978, 2369, 1734, 1456, 1155, 751 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 8.03 (d, J = 8.98 Hz, 1H), 7.48-7.45 (m, 3H), 7.39-7.19 (m, 5H), 6.43 (s, 1H), 5.09-5.05 (m, 1H), 3.62 (dd, J = 14.8 Hz, 4.04 Hz, 1H), 3.33 (dd, J = 14.8 Hz, 8.98 Hz, 1H), 2.67-2.65 (m, 1H), 1.72 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz): δ 151.0, 143.9, 138.0, 136.4, 129.0, 128.3, 127.4, 125.7, 123.6, 122.7, 120.0, 115.6, 110.0, 84.3, 73.15, 39.8, 28.2; HRMS (ESI): calcd for C₂₅H₂₃NO₃ m/z 360.15756 [M+Na]⁺, Found 360.1562. Specific optical rotation [α]D²⁴ = -14.2 (c = 0.77, CHCl₃) (>99% ee); HPLC analysis: (column - ChiralpakIA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), tₘ = 6.9 min (minor), tᵣ = 10.2 min (major).
4.2. Tuning of enantiomeric excess and yield by switching different protecting groups in allenylanilide:

The reactions were performed using (S, S)-PhBPE (11 mol%) and MesCu (10 mol%) in a HMPA:THF (1:19) solvent system (0.3 M concentration) (0.2 mmol scale).

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<th>#</th>
<th>PG-Yield (%)a</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A/B/C</td>
<td>No reaction (SM recovered)</td>
</tr>
<tr>
<td>2</td>
<td>A/B/C</td>
<td>No reaction (SM recovered)</td>
</tr>
<tr>
<td></td>
<td>Yield</td>
<td>Enantiomeric excess</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>---------------------</td>
</tr>
<tr>
<td>N-acyl migration</td>
<td>52/28</td>
<td>80/82/99/nd</td>
</tr>
<tr>
<td></td>
<td>70/14</td>
<td>11/95/86/85/nd</td>
</tr>
</tbody>
</table>

\(^a\)Yield determined by \(^1\)H NMR spectrum of the crude products using t-butyl methyl ether as an internal standard. \(^b\)Enantiomeric excess was determined by chiral HPLC analysis.

The racemic sample was prepared by performing the reaction with achiral ligand 1,3-bis(diphenylphosphino)propane (dppp).

\(N\)-COOME (-PG) substrate showed the best result in terms of yield and enantioselectivity {Further, the ligand screening with this substrate was carried out and found the optimum result in case of \((S, S)\)-Ph-BPE \).

**\((S)\)-2-\((1H\)-indol-2-yl\)-1-phenylethyl acetate (26):**

Purified by silica gel column chromatography (EtOAc: Hexane (1:9); liquid; \(R_f = 0.25\) (Ethyl acetate: Hexane (2:8); IR (thin film): \(\nu = 3395, 1717, 2943, 1238, 1024, 750\) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 7.87\) (brs, 1H), 7.52 (d, \(J = 6.87\) Hz, 1H), 7.36-7.30 (m, 5H), 7.27-7.25 (m, 1H), 7.14-7.11 (m, 1H), 7.08-7.05 (m, 1H), 6.24-6.23 (m, 1H), 6.03 (t, \(J = 6.87\) Hz, 1H), 3.36 (dd, \(J = 15.4\) Hz, 6.3 Hz, 1H), 3.25 (dd, \(J = 15.4\) Hz, 6.3 Hz, 1H), 2.09 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 170.1, 139.6, 136.0, 134.1, 128.6, 128.4, 128.3, 126.4, 121.4, 120.0, 119.6, 110.4, 101.9, 75.3, 35.7, 21.2\); HRMS (ESI): calcd for C\(_{18}\)H\(_{17}\)NO\(_2\) m/z 302.1157 [M+Na]\(^+\), Found 302.1153. Specific optical rotation [\(\alpha\)]\(_D\)\(^{24}\) = 17.0 (c = 0.56, CHCl\(_3\)) (68% ee); HPLC analysis: (column - Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_r = 8.9\) min (major), 9.3 min (minor)
(S)-Methyl 2-(2-hydroxy-2-phenylethyl)-1H-indole-1-carboxylate (27):

Purified by silica gel column chromatography (EtOAc: Hexane (1:9); R_f = 0.25 (Ethyl acetate: Hexane (2:8)); IR (thin film): \( \nu \) 3397, 2961, 2369, 1748, 1268 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 8.0 (brs, 1H), 7.52 (d, \( J = 7.18 \) Hz, 1H), 7.36-7.28 (m, 6H), 7.13 (td, \( J = 7.18 \) Hz, 1.35 Hz, 1H), 7.07 (td, \( J = 8.07 \) Hz, 1.35 Hz, 1H), 6.27 (s, 1H), 5.82 (dd, \( J = 7.63 \) Hz, 5.38 Hz, 1H), 3.74 (s, 3H), 3.39 (dd, \( J = 15.2 \) Hz, 7.6 Hz, 1H), 3.25 (dd, \( J = 14.8 \) Hz, 5.38 Hz, 1H); \(^13\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 154.8, 139.1, 136.1, 134.0, 128.6, 128.5, 128.3, 126.3, 121.4, 120.1, 119.6, 110.5, 102.0, 79.6, 54.9, 35.7; HRMS (ESI): calcd for C\(_{18}\)H\(_{17}\)NO\(_3\) m/z 318.11061 \([M+Na]^+\), Found 318.1113. Specific optical rotation \([\alpha]_D^{24} = -5.2 \) (c = 0.15, CHCl\(_3\)) (85% ee); HPLC analysis: (column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), \( t_r \) = 15.4 min (major), 18.5 min (minor).
4-3. Ligand screening with the –N-COOOMe allenylanilide substrate (1a):

I. MesCu (10 mol%)
Ligand (11 mol%)
THF:HMPA (19:1)
rt, 10 h

II. 2N NaOH, 6 h, rt
one pot reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ee (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(S, S)-Ph-BPE</td>
<td>85</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>(R)-DTBM-SEGPHOS</td>
<td>51</td>
<td>67</td>
</tr>
<tr>
<td>3</td>
<td>(S,S),iPr-Duphos</td>
<td>90</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>(S)-BINAP</td>
<td>94</td>
<td>42</td>
</tr>
<tr>
<td>5</td>
<td>Taniaphos</td>
<td>86</td>
<td>29</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield determined by <sup>1</sup>H NMR spectrum of the crude products using t-butyl methyl ether as an internal standard. <sup>b</sup>Enantiomeric excess was determined by chiral HPLC analysis.
4-4. Solvent screening:

\[
\text{Entry} \quad \text{Solvent} \quad \text{Yield} \quad \text{ee} \quad \text{Entry} \quad \text{Solvent} \quad \text{Yield} \quad \text{ee} \\
1 \quad \text{DMF} \quad 92 \quad 82 \quad 7 \quad \text{TBME} \quad 74 \quad 86 \\
2 \quad \text{DME} \quad 82 \quad 85 \quad 8 \quad \text{THF} \quad 89 \quad 87 \\
3 \quad \text{CH}_2\text{Cl}_2 \quad 60 \quad 80 \quad 9 \quad \text{THF}:\text{HMPA} (19:1) \quad 90 \quad 87 \\
4 \quad \text{iPr}_2\text{O} \quad 50 \quad 84 \quad 10 \quad \text{Dioxane}:\text{HMPA} (2:1) \quad 92 \quad 89 \\
5 \quad \text{Dioxane} \quad 93 \quad 88 \quad 11^{c} \quad \text{DMPU} \quad 50 \quad 91 \\
6 \quad \text{Toluene} \quad 50 \quad 88 \quad 12^{c} \quad \text{Dioxane} \quad 92 \quad 91
\]

\( ^a \)Yield determined by \(^1\)H NMR spectrum of the crude products using \(t\)-butyl methyl ether as an internal standard. \( ^b \)Enantiomeric excess was determined by chiral HPLC analysis. \( ^c \)Reaction carried out at 15 °C.

Inference: Dioxane showed the best result in this asymmetric transformation.

Experimental procedure:
A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (3.64 mg, 0.02 mmol, 10 mol%) and (S, S)-Ph-BPE (11.14 mg, 0.022 mmol, 11 mol%) under argon atmosphere. The anhydrous solvent (470 µL) was added, and the mixture was stirred at ambient temperature for 15 minutes. To the stirred solution, benzaldehyde (40 µL, 0.4 mmol) and 1.04 M solution of allenylanilide (1a) (37.8 mg, 192 µL, 0.2 mmol) were added sequentially. After stirring for 10 h at room temperature, the reaction was diluted with THF/dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 6 h, extracted the suspension with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum.

4-5. Effect of additives:
The effect of molecular sieves, alcohol and water on yield and enantioselectivity were examined, and results are illustrated below.
Entry | Additive | \(^a\)Yield (%) | \(^b\)ee (%) |
---|---|---|---|
1 | - | 93 | 88 |
2 | MS 3A (50 mg) | 91 | 88 |
3 | MS 4A (50 mg) | 95 | 88 |
4 | MS 5A (50 mg) | 97 | 88 |
5 | MS 13X (50 mg) | 97 | 88 |
6 | EtOH (100 mol%) | 86 | 87 |
7 | H₂O (40 mol%) | 75 | 89 |

\(^a\)Yield determined by \(^1\)H NMR spectrum of the crude products using \(t\)-butyl methyl ether as an internal standard. \(^b\)Enantiomeric excess was determined by chiral HPLC analysis.

### 4-6. Effect of copper source and base:
Several copper sources and bases were screened, and the results obtained are shown below.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cu(I)</th>
<th>Base</th>
<th>(^a)Yield (%)</th>
<th>(^b)ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MesCu</td>
<td>-</td>
<td>93</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>Cu(CH₃CN)₄BF₄</td>
<td>LiO’Bu</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>Cu(CH₃CN)₄PF₆</td>
<td>LiO’Bu</td>
<td>77</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>CuOAc</td>
<td>LiO’Bu</td>
<td>75</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>LiO’Bu</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>CuOTf.1/2Toluene</td>
<td>LiO’Bu</td>
<td>72</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>Cu(I)-3-methylsalicylate</td>
<td>LiO’Bu</td>
<td>88</td>
<td>87</td>
</tr>
</tbody>
</table>

\(^a\)Yield determined by \(^1\)H NMR spectrum of the crude products using \(t\)-butyl methyl ether as an internal standard. \(^b\)Enantiomeric excess was determined by chiral HPLC analysis.
Effect of concentration on chemical yield and enantioselectivity:

The reactions were conducted at different concentrations. The chemical yield and enantioselectivity are shown below.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Concentration (M)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ee (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1</td>
<td>92</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>91</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>0.6</td>
<td>86</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>0.9</td>
<td>85</td>
<td>90</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield determined by <sup>1</sup>H NMR spectrum of the crude products using t-butyl methyl ether as an internal standard. <sup>b</sup>Enantiomeric excess was determined by chiral HPLC analysis.

Catalyst loading:

The amount of catalyst required to procure optimum result in the desired transformation was measured and shown below.

<table>
<thead>
<tr>
<th>Entry</th>
<th>MesCu (mol%)</th>
<th>(S, S)-Ph-BPE (mol%)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>ee (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>-</td>
<td>No reaction</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>3</td>
<td>81</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>5</td>
<td>96</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>7</td>
<td>97</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>10</td>
<td>93</td>
<td>88</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield determined by <sup>1</sup>H NMR spectrum of the crude products using t-butyl methyl ether as an internal standard. <sup>b</sup>Enantiomeric excess was determined by chiral HPLC analysis.

General Procedure for constructing 2-(2-hydroxyethyl)indoles: Reaction of allenyl anilides with aromatic aldehydes:

General procedure for constructing 2-(2-hydroxyethyl)indoles: (Condition A)
A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (1.82 mg, 0.01 mmol, 5 mol%) and (S, S)-PhBPE (5.06 mg, 0.01 mmol, 5 mol%) under argon atmosphere. Anhydrous dioxane (480 µL) was added, and the mixture was stirred at ambient temperature for 15 minutes. To the stirred solution, aromatic aldehyde (0.4 mmol) and 1.1 M solution of allenylanilide (1a) (37.8 mg, 181 µL, 0.2 mmol) were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compounds.

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (S, S)-Ph-BPE.

The absolute configuration for all the compounds were assigned based on analogy of 3aa (see page S48-S51)

(S)-2-(1H-indol-2-yl)-1-phenylethanol (3aa):

Purified by silica gel column chromatography (EtOAc: Hexane (2:8);

white solid;

(Yield, ee) (%): 96%, 89% (reaction conducted at rt)

: 92%, 91% (reaction conducted at 15 °C)

Rf = 0.33 (Ethyl acetate: Hexane (3:7)); IR (thin film): ν 3410, 3021, 2369, 1215, 756 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 8.49 (brs, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.41-7.31 (m, 6H), 7.16 (t, J = 8.0 Hz, 1H), 7.10 (t, J = 7.45 Hz, 1H), 6.3 (s, 1H), 5.0-4.98 (m, 1H), 3.17 (d, J = 6.3 Hz, 2H), 2.28 (brs, 1H); ¹³C NMR (CDCl₃, 125 MHz): δ 143.5, 136.17, 136.13, 128.6, 128.3, 127.9, 125.6, 121.3, 119.9, 119.5, 110.5, 101.0, 74.3, 37.8; HRMS (ESI): calcd for C₂₀H₁₅NO m/z 260.1051 [M+Na]⁺, Found 260.1040.

Specific optical rotation [α]D⁰ = -48.0 (c = 0.5, CHCl₃) (91% ee); HPLC analysis: (91% ee);

(Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), tᵣ = 10.2 min (major), 14.6 min (minor).
(S)-1-(4-tert-butyphenyl)-2-(1H-indol-2-yl)ethanol (3ab):

Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; Yield: 89%);

$R_f = 0.23$ (Ethyl acetate: Hexane (2:8); IR (thin film): $\nu$ 3504, 3278, 2956 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.5 (brs, 1H), 7.56 (d, $J = 7.4$ Hz, 1H), 7.42-7.40 (m, 2H), 7.34-7.31 (m, 3H), 7.14 (t, $J = 6.87$ Hz, 1H), 7.08 (t, $J = 6.87$ Hz, 1H), 6.30 (s, 1H), 4.99 (dd, $J = 8.59$ Hz, 4.0 Hz, 1H), 3.22-3.13 (m, 2H), 2.2 (brs, 1H), 1.34 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 151.0, 140.6, 136.5, 136.1, 128.3, 125.5, 125.4, 121.2, 119.9, 119.5, 111.5, 100.9, 74.2, 37.6, 34.5, 31.3; HRMS (ESI): calcd for C$_{20}$H$_{23}$NO $m/z$ 316.1677 [M+Na]$^+$, Found 316.1678. Specific optical rotation $[\alpha]_D^{24} = -26.9 (c = 0.57, CHCl$_3$) (94% ee); HPLC analysis: (94% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r = 8.6$ min (major), 10.5 min (minor).
(S)-2-(1H-indol-2-yl)-1-(4-methoxyphenyl)ethanol (3ac):

Purified by silica gel column chromatography (EtOAc: Hexane (3:7); white solid; Yield: 80%);

$R_f = 0.23$ (Ethyl acetate: Hexane 3:7); IR (thin film): $\nu 3252, 2930, 2369, 1034, 749$ cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.52 (brs, 1H), 7.57 (d, $J = 7.4$ Hz, 1H), 7.33-7.27 (m, 3H), 7.16 (t, $J = 8.02$ Hz, 1H), 6.92-6.89 (m, 2H), 6.29 (s, 1H), 4.93 (dd, $J = 8.0$ Hz, 4.58 Hz, 1H), 3.82 (s, 1H), 3.18-3.11 (m, 2H), 2.29 (brs, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 159.2, 136.3, 136.0, 135.7, 128.3, 121.2, 119.8, 119.5, 113.9, 110.5, 100.9, 73.9, 55.2, 37.7; HRMS (ESI): calcd for C$_{17}$H$_{17}$NO$_2$ m/z 290.1157 [M+Na]$^+$, Found 290.1153. Specific optical rotation $[\alpha]_D^{24} = -34.6$ (c = 1.09, CHCl$_3$) (91% ee); HPLC analysis: (91.4% ee); (Column – Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r = 13.3$ min (major), 17.0 min (minor).
(S)-2-(1H-indol-2-yl)-1-(thiophene-2-yl)ethanol (3ad):

Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; Yield: 98%);

R_f = 0.16 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3393, 3100, 2369, 1540, 1032, 705 cm⁻¹; ^1H NMR (CDCl₃, 500 MHz): δ 8.5 (brs, 1H), 7.56 (d, J = 7.45 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.29 (dd, J = 5.16 Hz, 1.15 Hz, 1H), 7.15 (td, J = 8.0 Hz, 1.15 Hz, 1H), 3.33-3.25 (m, 2H), 2.43 (d, J = 3.4 Hz, 1H); ^13C NMR (CDCl₃, 125 MHz): δ 147.1, 136.1, 135.4, 128.2, 126.8, 125.0, 124.0, 121.4, 119.9, 119.6, 110.6, 101.4, 70.1, 37.9; HRMS (ESI): calcd for C_{14}H_{13}NOS m/z 266.0616 [M+Na]^+; Found 266.0613. Specific optical rotation [α]D²⁴ = -25.1 (c = 0.73, CHCl₃) (96% ee); HPLC analysis: (96% ee); (Column -Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.0 min (major), 12.8 min (minor).
(S)-1-(furan-2-yl)-2-(1H-indol-2-yl)ethanol (3ae):

Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 94 %;

$R_f = 0.38$ (Ethyl acetate: Hexane 4:6); IR (thin film): $\nu$ 3408, 2926, 2360, 1507, 1022 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.46 (brs, 1H), 7.56 (d, $J = 8.0$ Hz, 1H), 7.43 (d, $J = 1.72$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.16-7.13 (m, 1H), 6.36 (m, 1H), 6.32 (d, $J = 1.1$ Hz, 1H), 6.27 (d, $J = 4.0$ Hz, 1H), 5.03-5.0 (m, 1H), 3.31 (d, $J = 5.7$ Hz, 2H), 2.38 (s, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 155.4, 142.1, 136.1, 135.3, 128.2, 121.3, 119.9, 119.6, 110.6, 106.4, 101.2, 67.6, 34.2; HRMS (ESI): calcd for C$_{14}$H$_{13}$NO$_2$ $m/z$ 250.0844 [M+Na]$^+$, Found 250.833. Specific optical rotation $[\alpha]_D^{24} = -16.96$ (c = 0.88, CHCl$_3$) (95.77% ee); HPLC analysis: (96% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r =$ 10.9 min (major), 11.9 min (minor).
(S)-2-((1H-indol-2-yl)-1-(napthalen-1-yl)ethanol (3af):

Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 85%;

\[ R_f = 0.3 \] (Ethyl acetate: Hexane 3:7); IR (thin film): v 3440, 3017, 2361, 1540, 1214, 757 cm\(^{-1}\); \(^1\)H NMR (CD\(_3\)COCD\(_3\), 500 MHz): \( \delta \) 10.04 (brs, 1H), 7.91 (s, 1H), 7.86 (m, 3H), 7.59 (dd, \( J = 8.59 \) Hz, 1.72 Hz, 1H), 7.49-7.44 (m, 2H), 7.43 (d, \( J = 8.0 \) Hz, 1H), 7.35 (d, \( J = 7.45 \) Hz, 1H), 7.03-7.00 (m, 1H), 6.96-6.93 (m, 1H), 6.22 (s, 1H), 5.27-5.23 (m, 1H), 3.3-3.2 (m, 2H); \(^{13}\)C NMR (CD\(_3\)COCD\(_3\), 125 MHz): \( \delta \) 143.8, 138.0, 134.3, 133.9, 129.8, 128.8, 128.6, 128.5, 126.8, 126.5, 125.3, 125.2, 121.3, 120.3, 119.7, 111.5, 101.2, 74.3, 39.3; HRMS (ESI): calcd for C\(_{20}\)H\(_{17}\)NO m/z 310.1207 [M+Na]\(^+\), Found 310.1208. Specific optical rotation \( [\alpha]_D^{24} = -5.9 \) (c = 0.39, CH\(_3\)CN) (91% ee); HPLC analysis: (91% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \( t_r \) = 16.1 min (major), 19.5 min (minor).
(S)-1-(4-Fluorophenyl)-2-(1H-indol-2-yl)ethanol (3ag):

Purified by silica gel column chromatography (EtOAc: Hexane 2:8);
Solid; Yield: 97 %;

$R_f = 0.29$ (Ethyl acetate: Hexane 3:7); IR (thin film): $\nu$ 3399, 3021, 2365, 1540, 1215 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.47 (brs, 1H), 7.56 (d, $J = 7.4$ Hz, 1H), 7.36-7.32 (m, 3H), 7.18-7.14 (m, 1H), 7.11-7.03 (m, 3H), 6.28 (s, 1H), 4.98 (t, $J = 6.3$ Hz, 1H), 3.14-3.13 (m, 2H), 2.25 (brs, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 163.3, 161.3, ($^1$J$_{CF}$ 243.5 Hz), 139.33, 139.31 ($^2$J$_{CF}$, 3.59 Hz), 136.1, 135.8, 128.3, 127.38, 127.32 ($^3$J$_{CF}$, 8.4), 121.4, 119.9, 119.6, 115.55 ($^4$J$_{CF}$ 21.5), 110.5, 101.2, 73.6, 37.9; HRMS (ESI): calcd for C$_{16}$H$_{14}$NOF m/z 278.0957 [M+Na]$^+$, Found 278.0960. Specific optical rotation $[\alpha]_D^{24} = -43.4$ (c = 0.8, CHCl$_3$) (89% ee); HPLC analysis: (89% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t$_r$ = 9.1 min (major), 10.8 min (minor).
**Purification and Characterization:**

- **Purified by** silica gel column chromatography (EtOAc: Hexane 2:8);
- **Yield:** 97 %;
- **Rf** = 0.3 (Ethyl acetate: Hexane 3:7);
- **IR** (thin film): ν 3412, 3021, 2369, 1716, 1455, 970, 750 cm⁻¹;
- **1H NMR** (CDCl₃, 500 MHz):
  - δ 8.59 (brs, 1H), 7.58 (d, J = 8.0 Hz, 1H),
  - 7.39 - 7.26 (m, 6H),
  - 7.16 (t, J = 7.4 Hz, 1H),
  - 7.10 (t, J = 8.0 Hz, 1H),
  - 6.65 (d, J = 16 Hz, 1H),
  - 6.33 (m, 1H),
  - 6.30 (dd, J = 16 Hz, 6.87 Hz, 1H),
  - 4.61 - 4.64 (m, 1H),
  - 3.15 (dd, J = 14.9, 3.4 Hz, 1H),
  - 3.04 (dd, J = 14.9 Hz, 8.0 Hz, 1H),
  - 2.05 (brs, 1H);
- **13C NMR** (CDCl₃, 125 MHz): δ 136.2, 136.1, 135.8, 131.2, 130.8, 128.6, 128.3, 127.9, 126.5, 121.3, 119.9, 119.6, 110.6, 101.19, 72.8, 35.9;
- **HRMS (ESI)**: calcd for C₁₈H₁₇NO m/z 286.1207 [M+Na]⁺, Found 286.1209.
- **Specific optical rotation**: [α]D²⁴ = -31.3 (c = 0.36, CHCl₃) (87% ee);
- **HPLC analysis**: (87% ee); (Column –Chiralpak IB; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t₁ = 19.3 min (major), 26.4 min (minor).
(S)-1-(4-(2-hydroxyethoxy)phenyl)-2-(1H-indol-2-yl)ethanol (3ai):

The procedure for the synthesis of this molecule is as same as the general procedure mentioned above (Condition A), but the solvent used for the reaction is (Dioxane: HMPA (10:1)) and stirred the reaction for 5h at rt.

Purified by silica gel column chromatography (Acetone: Hexane 3:7); white solid; Yield: 85 %; Rf = 0.21 (Acetone: Hexane 1:1);

IR (thin film): ν 3410, 3017, 2369, 1540, 1215, 757 cm⁻¹; ¹H NMR (CD₃OD, 400 MHz): δ 7.36 (d, J = 8.0 Hz, 1H), 7.25-7.22 (m, 3H), 6.97 (td, J = 7.2 Hz, 1.4 Hz, 1H), 6.92-6.83 (m, 3H), 6.07 (s, 1H), 4.93 (t, J = 6.3 Hz, 1H), 3.97 (t, J = 4.5 Hz, 2H), 3.19-3.13 (m, 1H), 3.08-3.03 (m, 1H); ¹³C NMR (CD₃OD, 100 MHz): δ 159.8, 138.2, 137.9, 137.7, 130.2, 128.4, 121.5, 120.5, 119.9, 115.4, 111.6, 101.3, 74.7, 70.6, 61.8, 39.4; HRMS (ESI): calcd for C₁₈H₁₉NO₃ m/z 320.1263 [M+Na]⁺. Found 320.1263. Specific optical rotation [α]D²⁴ = -29.9 (c = 0.88, CHCl₃) (93% ee); HPLC analysis: (93%
(S)-2-(1H-indol-2-yl)-1-(4-iodophenyl)ethanol (3ah):

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); White solid; Yield: 79%; $R_f = 0.25$ (EtOAc: Hexane 3:7); IR (thin film): ν 3440, 3019, 2359, 1621, 1215, 756; $^1$H NMR (CD$_3$COCD$_3$, 500 MHz): δ 9.95 (brs, 1H), 7.67 (d, $J = 8$ Hz, 2H), 7.43 (d, $J = 7.5$ Hz, 1H), 7.34 (d, $J = 7.5$ Hz, 1H), 7.23 (d, $J = 7.5$ Hz, 2H), 7.02 (t, $J = 7.5$ Hz, 1H), 6.95 (t, $J = 7.5$ Hz, 1H), 6.18 (s, 1H), 5.07-5.04 (m, 1H), 4.68 (s, 1H), 3.17-3.10 (m, 2H); $^{13}$C NMR (CD$_3$COCD$_3$, 125 MHz): δ 146.2, 138, 137.59, 137.54, 129.7, 129.1, 121.1, 121.3, 120.3, 119.7, 111.6, 101.4, 92.7, 73.7, 39.3; HRMS (ESI): calcd for C$_{16}$H$_{14}$IN$_{1}$O$_{1}$ m/z 386.0018 [M+Na]$^+$, Found 386.0040; Specific optical rotation $[\alpha]_{D}^{20} = -18$ (c = 1.08, CHCl$_3$) (for 85% ee); HPLC analysis: (85% ee): (Column –Chiralcel OD-H; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r$ = 17.8 min (minor), 19.5 min (major).
Reactions of allenyl anilides with aliphatic aldehydes: Screening of additives

Due to the lower electrophilicity (low reactivity) of aliphatic aldehydes, allylation proceeded to procure desired product only in low to moderate yield. To improve the yield, we envisioned that adding additional Lewis acids could enhance the electrophilicity of the aliphatic aldehyde and could accelerate the rate of the reaction. We also speculated that these additives could improve the turnover of the Cu-catalyst. Considering these aspects, we examined additive effect in the reaction of an aliphatic aldehyde (hexanal)(2k) and allenylanilide (1a). It was found that magnesium isopropoxide profoundly accelerated the rate of the reaction, resulting the desired product in good yield.

Screening of Additives:

I. MesCu (5 mol%)
(S, S) - Ph-BPE (5 mol%)

Experimental procedure: A flame-dried 20 mL test tube equipped with magnetic stirring bar and a
A 3-way glass stopcock was charged with mesitylcopper (1.8 mg, 0.01 mmol, 5 mol%), additive (5-10 mol%) and (S, S)-PhBPE (5.1 mg, 0.01 mmol, 5 mol%) under argon atmosphere. Anhydrous dioxane (480 µL) was added, and the mixture was stirred at ambient temperature for 20 minutes. To the stirred solution, hexanal (2k) (0.3 mmol) and 1.1 M solution of allenylanilide (1a) (38 mg, 181 µL, 0.2 mmol) in dioxane were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compound (3ak).

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (S, S)-Ph-BPE.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive (X mol%)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
<th>Yield (bb)(%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>9</td>
<td>94</td>
<td>83</td>
</tr>
<tr>
<td>1</td>
<td>Al(O'Bu)3 (5 mol%)</td>
<td>30</td>
<td>94</td>
<td>60</td>
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<tr>
<td>2</td>
<td>Zr(O'Pr)4 (5 mol%)</td>
<td>46</td>
<td>94</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>Ba(O'Pr)2 (5 mol%)</td>
<td>14</td>
<td>94</td>
<td>75</td>
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<tr>
<td>4</td>
<td>Y(O'Pr)2 (5 mol%)</td>
<td>27</td>
<td>95</td>
<td>62</td>
</tr>
<tr>
<td>5</td>
<td>La(O'Pr)3 (5 mol%)</td>
<td>50</td>
<td>95</td>
<td>42</td>
</tr>
<tr>
<td>6</td>
<td>Yb(O'Pr)3 (5 mol%)</td>
<td>53</td>
<td>94</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>Sm(O'Pr)3 (5 mol%)</td>
<td>45</td>
<td>94</td>
<td>51</td>
</tr>
<tr>
<td>8</td>
<td>Mg(O'Pr)2 (5 mol%)</td>
<td>58</td>
<td>94</td>
<td>34</td>
</tr>
<tr>
<td>9</td>
<td>Mg(O'Pr)2 (10 mol%)</td>
<td>75</td>
<td>92</td>
<td>22</td>
</tr>
<tr>
<td>10</td>
<td>Mg(O'Pr)2 (20 mol%)</td>
<td>78</td>
<td>92</td>
<td>20</td>
</tr>
<tr>
<td>11</td>
<td>Mg(O'Pr)2 (10 mol%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>Mg(OEt)2 (5 mol%)</td>
<td>60</td>
<td>91</td>
<td>33</td>
</tr>
</tbody>
</table>

aYield determined by 1H NMR spectrum of the crude products using t-butyl methyl ether as an internal standard. bEnantiomeric excess was determined by chiral HPLC analysis. cThe reaction was performed without MesCu and observed no reaction.
7. General procedure for the reaction of allenyl anilides with aliphatic aldehydes:

I. MesCu (5 mol%)

\[
\text{MesCu} + \text{Ph-BPE (5 mol%)} \rightarrow \text{3(k-p)}
\]

Dioxane

rt, 3.5 h

(0.3 M)

II. 2N NaOH, 12 h, rt

General procedure (Condition B):

A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (1.8 mg, 0.01 mmol, 5 mol%), magnesium isopropoxide (2.8 mg, 0.02 mmol, 10 mol%) and (S, S)-PhBPE (5.1 mg, 0.01 mmol, 5 mol%) under an argon atmosphere. Anhydrous dioxane (480 µL) was added, and the mixture was stirred at ambient temperature for 20 minutes. To the stirred solution, aliphatic aldehyde (0.3 mmol) and 1.1 M solution of allenylanilide (1a) (37.8 mg, 181 µL, 0.2 mmol) in dioxane were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compound.

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (S, S)-Ph-BPE.

The absolute configuration of all the secondary alcohols (3ak-3ap) were assigned based on analogy of 3aa (see page S48-S51)

(S)-1-(1H-indol-2-yl)heptan-2-ol (3ak):

Purified by silica gel column chromatography (EtOAc: Hexane 2:8); yellow liquid; Yield: 73%; Rf = 0.2 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3456, 3408, 3019, 2399, 1214 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 8.55 (brs, 1H), 7.55 (d, J = 8.02 Hz, 1H), 7.32 (d, J = 8.02 Hz, 1H), 7.15-7.12 (m, 1H), 7.10-7.06 (m, 1H), 6.28 (s, 1H), 3.97-3.92 (m, 1H), 3.02-2.98 (dd, J = 14.89 Hz, 2.86 Hz, 1H), 2.81 (dd, J = 15.47 Hz, 8.02 Hz, 1H), 1.81 (brs, 1H), 1.55-1.26 (m, 8H), 0.9 (t, J = 6.87 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ136.6, 136.1, 128.4, 121.1, 119.8, 119.5, 110.5, 100.8, 71.8, 37.0, 35.5, 31.7, 25.3, 22.5, 14.0; HRMS (ESI): calcd for C₁₅H₂₁NO m/z 254.1521 [M+Na]⁺, Found 254.1509. Specific optical rotation [α]D⁺²⁴ = -15.0 (c = 0.48, CHCl₃) (92% ee); HPLC analysis: (92% ee); (Column – Chiralpak IA; Hexane/2-propanol = 20/1, flow rate 1.0 mL/min, detection at 254 nm), tᵣ = 16.0 min (major), 17.4 min (minor).
(S)-1-(1H-indol-2-yl)-3,3-dimethylbutan-2-ol (3al):

\[
\text{\begin{tikzpicture}[baseline]
  
  \node (h) at (0,0) {
    \text{CH}_3 \hspace{1cm} \text{CH}_3 \hspace{1cm} \text{OH}\hspace{1cm} \text{N}
  \};

  \node (a) at (1.5,0) {
    \text{\(1\)}
  };

  \node (b) at (3,0) {
    \text{\(2\)}
  };

  \node (c) at (4.5,0) {
    \text{\(3\)}
  };

  \node (d) at (6,0) {
    \text{\(4\)}
  };

  \node (e) at (7.5,0) {
    \text{\(5\)}
  };

  \draw (a) -- (b) -- (c) -- (d) -- (e);
\end{tikzpicture}}
\]

Purified by silica gel column chromatography (EtOAc: Hexane 1:9); white solid;

(Yield, ee): (75%, 99%) [Reaction carried out without additive]

(Yield, ee): (95%, 96%) [Reaction carried out with additive Mg(O\text{Pr})\_2 (10 mol\%)]

\(R_f = 0.35\) (Ethyl acetate: Hexane 2:8); IR (thin film): \(\nu\) 3417, 2960, 2369 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): 8.61 (brs, 1H), 7.55 (d, \(J = 8.0\) Hz, 1H), 7.15-7.12 (m, 1H), 7.10-7.07 (m, 1H), 6.29 (s, 1H), 3.56-3.53 (m, 1H), 3.01 (d, \(J = 14.9\) Hz, 1H), 2.72 (dd, \(J = 14.9\) Hz, 10.3 Hz, 1H), 1.89 (d, \(J = 4\) Hz, 1H), 1.0 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 137.9, 136.0, 128.4, 121.1, 119.7, 119.5, 110.4, 100.2, 79.8, 34.9, 30.4, 25.5; HRMS (ESI): calculated for C\(_{14}\)H\(_{20}\)NO m/z 240.1364 [M+Na]\(^+\), Found 240.1352. Specific optical rotation \([\alpha]_D^{24} = -32.6\) (c = 0.63, CHCl\(_3\)) (99% ee); HPLC analysis: (99% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_r = 6.7\) min (major), 7.1 min (minor).
(S)-3-ethyl-1-(1H-indol-2-yl)pentan-2-ol (3am):

Purified by silica gel column chromatography (EtOAc: Hexane 1:9); yellow liquid; Yield: 89 %; $R_t = 0.28$ (Ethyl acetate: Hexane 2:8); IR (thin film): $\nu$ 3403, 2962, 2874, 2365, 1685, 1457, 1289, 1014 cm$^{-1}$; $^1$H NMR
(CDCl₃, 500 MHz): δ 8.61 (brs, 1H), 7.14 (td, J = 8.0 Hz, 1.2 Hz, 1H), 7.08 (td, J = 8.0 Hz, 1.2 Hz, 1H), 6.29 (s, 1H), 3.95-3.92 (m, 1H), 2.95 (dd, J = 15.1 Hz, 2.2 Hz, 1H), 2.86 (dd, J = 15.1Hz, 9 Hz, 1H), 1.7 (brs, 1H), 1.55-1.49(m, 2H), 1.46-1.31(m, 3H), 0.96-0.93(m, 6H); ¹³C NMR (CDCl₃, 125 MHz): δ 137.4, 136.0, 128.4, 121.1, 119.7, 119.5, 110.5, 100.5, 73.3, 46.3, 32.6, 21.7, 11.4; HRMS (ESI): calcd for C₁₄H₁₉NO m/z 254.1521 [M+Na]^+, Found 240.1508. Specific optical rotation [α]D²⁴ = - 40.5 (c = 1.76, CHCl₃) (94% ee); HPLC analysis: (94% ee); (Column –Chiralpak IA; Hexane/Ethanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t₁ = 10.7 min (major), 12.2 min (minor).

(3S)-1-cyclopropyl-2-(1H-indol-2-yl)ethanol (3an):

Purified by silica gel column chromatography (EtOAc: Hexene 2:8); colorless liquid; Yield: 95 %; Rf = 0.34 (Etihl acetate: Hexane 4:6); IR (thin film): ν 3408, 3006, 2900, 2369, 1456, 1027, 752 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 8.69 (brs, 1H), 8.56 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H), 6.30 (s, 1H), 3.19-3.12 (m, 2H), 3.02-2.97 (dd, J = 14.8, 7.5 Hz, 1H), 1.98 (brs, 1H), 1.02-0.96 (m, 1H), 0.62-0.52 (m, 2H), 0.37-0.32 (m, 1H), 0.3-0.25 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz): δ 136.8, 136.0, 128.3, 121.0, 119.7, 119.4, 110.5, 100.6, 35.0, 17.4, 3.1, 2.7; HRMS (ESI): calcd for C₁₃H₁₅NO m/z 224.1051 [M+Na]^+, Found 224.1040. Specific optical rotation
\([\alpha]_D^{21} = +3.1\ (c = 1.45, \text{CHCl}_3)\) (90% ee); HPLC analysis: (90% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_r = 8.0\) min (major), 8.9 min (minor).

\((S)\)-1-cyclopentyl-2-(1H-indol-2-yl)ethanol (3ap):

Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 82%; \(R_f = 0.21\) (Ethyl acetate: Hexane 2:8); IR (thin film): 
\(\nu\)3400, 2369, 1540, 1215, 760 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 8.64 (brs, 1H), 7.56 (d, \(J = 8.0\) Hz, 1H), 7.33 (d, \(J = 8.0\) Hz, 1H), 7.14 (td, \(J = 8.0, 1.2\) Hz, 1H), 7.08 (td, \(J = 8.0, 1.2\) Hz, 1H), 6.28 (s, 1H), 3.73-3.70 (m, 1H), 3.05 (dd, \(J = 15.1, 8.0\) Hz, 1H), 2.83 (dd, \(J = 15.3, 8.0\) Hz, 1H), 1.94-1.76 (m, 4H), 1.69-1.53 (m, 4H), 1.41-1.35 (m, 1H), 1.29-1.23 (m, 1H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 136.9, 136.0, 128.3, 121.0, 119.7, 119.4, 110.5, 100.7, 76.3, 45.6, 34.4, 29.1, 25.5; HRMS (ESI): calcd for C\(_{15}\)H\(_{19}\)NO \(m/z\) 252.1364 [M+Na]\(^+\), Found 252.1354; Specific optical rotation \([\alpha]_D^{24} = -13.0\ (c = 0.52, \text{CHCl}_3)\) (92% ee); HPLC analysis: (92% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_r = 7.7\) min (major), 8.6 min (minor).
Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 89%; \( R_f = 0.24 \) (Ethyl acetate: Hexane 2:8); IR (thin film): \( \nu \) 3300, 2921, 2369, 1540, 1025 cm\(^{-1}\); \( ^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 8.62 (brs, 1H), 7.56 (d, \( J = 7.4 \) Hz, 1H), 7.32 (d, \( J = 8.0 \) Hz, 1H), 7.14 (td, \( J = 7.4 \) Hz, 1.2 Hz, 1H), 7.09 (td, \( J = 7.4 \) Hz, 1.2 Hz, 1H), 6.28 (s, 1H), 3.66 (m, 1H), 3.00 (m, 1H), 2.98 (m, 1H), 2.85 (dd, \( J = 15.2 \) Hz, 8.6 Hz, 1H), 1.92-1.86 (m, 2H), 1.82-1.76 (m, 3H), 1.71-1.68 (m, 1H), 1.44-1.37 (m, 1H), 1.30-1.14 (m, 3H), 1.13-1.02 (m, 2H); \( ^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 137.2, 136.0, 128.4, 121.0, 119.7, 119.4, 110.5, 100.6, 76.17, 43.0, 32.6, 29.0, 26.3, 25.9; HRMS (ESI): calcd for C\(_{16}\)H\(_{21}\)NO \( m/z \) 266.1521 [M+Na]\(^+\), Found 266.1515; Specific optical rotation \([\alpha]_D^{21} = -18.6 (c = 0.79, \text{CHCl}_3)(90% \text{ ee})\); HPLC analysis: (90% ee): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \( t_R = 7.9 \) min (major), 9.2 min (minor)
8. Allenyl anilide substrate scope: Reactions of various allenyl anilides with aromatic aldehydes

The reaction of aromatic aldehyde and allenylanilides having different electron donating or electron withdrawing substituents on the aromatic ring were examined under conditions A and B. The results obtained are shown below.

The absolute configuration of all the secondary alcohols were assigned based on analogy of 3aa (see page S48-S51)
(S)-2-(6-chloro-1H-indol-2-yl)-1-phenylethanol (3ba):

(Reaction condition: B) Purified by silica gel column chromatography (EtOAc: Hexane 1.5:8.5); white solid; Yield: 84%; $R_f = 0.23$ (Ethyl acetate: Hexane 2:8); IR (thin film): $\nu$ 3252, 3021, 2369, 1215 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.59 (brs, 1H), 7.43 (d, $J = 8.6$ Hz, 1H), 7.40-7.29 (m, 6H), 7.05 (dd, $J = 8.6$ Hz, 1.7 Hz, 1H), 6.24 (s, 1H), 5.02-4.99 (m, 1H), 3.19-3.12 (m, 2H), 2.28 (brs, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 143.4, 137.1, 136.4, 128.7, 128.1, 127.0, 126.8, 125.6, 120.6, 120.2, 110.5, 101.0, 74.4, 37.6; HRMS (ESI): calcd for C$_{16}$H$_{14}$ClNO $m/z$ 294.0662 [M+Na]$^+$, Found 294.0674; Specific optical rotation $[\alpha]_D^{21} = -40.8$ (c = 0.54, CHCl$_3$) (90% ee); HPLC analysis: (90% ee): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r = 10.5$ min (major), 14.4 min (minor)

![Graph of PK-23(1) - CH1](image1)

![Graph of PK-23(2) - CH1](image2)

(S)-2-(4-methyl-1H-indol-2-yl)-1-phenylethanol (3ca):

(Reaction condition: B) Purified by silica gel column chromatography (EtOAc: Hexane 1.5:8.5); Yellow liquid; Yield: 91%; $R_f = 0.26$ (Ethyl acetate: Hexane 2:8); IR (thin film): $\nu$ 3404, 2917, 2369, 1540, 1039, 766 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.47 (brs, 1H), 7.42-7.34 (m,
5H), 7.18 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7.5 Hz, 1H), 6.3 (s, 1H), 4.97 (t-like, J = 6.3 Hz, 1H), 3.17 (brd, J = 5.7 Hz, 2H), 2.55 Hz, (s, 1H), 2.33 (brs, 1H), \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 143.6, 135.7, 135.5, 129.4, 128.6, 128.1, 127.9, 125.6, 121.4, 119.7, 108.2, 99.6, 74.3, 37.9, 18.7; HRMS (ESI): calcd for C\(_{17}\)H\(_{17}\)NO \(m/z\) 274.1207 [M+Na]\(^+\), Found 274.1204; Specific optical rotation \([\alpha]_D^{21}\) = -31.3 \((c = 1.62, \text{CHCl}_3)\) (83% ee); HPLC analysis: (83% ee): (Column – Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_r\) = 7.7 min (major), 8.5 min (minor).

(5)-1-phenyl-2-(5-trifluoromethyl)-1H-indol-2-yl)ethanol (3da):

(Reaction condition: B); Purified by silica gel column chromatography (EtOAc: Hexane 1:9); White solid; Yield: 83%; \(R_f\) = 0.21 (Ethyl acetate: Hexane 2:8); IR (thin film): \(\nu\) 3350, 2365, 1540, 1039, 766 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 8.85 (brs, 1H), 7.84 (s, 1H), 7.14-7.33 (m, 7H), 6.34 (s, 1H), 5.04-5.02 (m, 2H), 2.31(brs, 1H), \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 143.3, 138.2, 137.4, 128.7, 128.2, 128.1, 128.6, 125.6, 124.3, 122.2 \(^1\)J\(_{CF}\) 271 Hz), (122.0, 121.7, 121.5 \(^2\)J\(_{CF}\) 32 Hz), 118.0(q, \(^3\)J\(_{CF}\) 3.6 Hz), 117.6 (q, \(^4\)J\(_{CF}\) 3.6 Hz), 110.7, 101.7, 74.4, 37.5; HRMS (ESI): calcd for C\(_{17}\)H\(_{14}\)F\(_3\)NO \(m/z\) 328.0925 [M+Na]\(^+\), Found -328.0931; Specific optical rotation \([\alpha]_D^{21}\) = -37.3 \((c = 0.53, \text{CHCl}_3)\) (84%ee); HPLC analysis: (84% ee): (Column –
Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r = 8.0$ min (major), 8.9 min (minor).

(S)-2-(6-methoxy-1H-indol-2-yl)-1-phenylethanol (3ea):

(Reaction condition: A); Purified by silica gel column chromatography (Et₂O: Hexane 4:6); Liquid; Yield: 70%; $R_f = 0.27$

(Diethyl ether: Hexane 6:4); IR (thin film): $\nu$ 3448, 3021, 2369, 1215, 755 cm⁻¹; $^1$H NMR (CDCl₃, 400 MHz): $\delta$ 8.39 (brs, 1H), 7.42-7.31(m, 5H), 6.82 (d, $J = 2.2$ Hz, 1H), 6.76 (dd, $J = 8.5$ Hz, 2.2 Hz, 1H), 6.21 (s, 1H), 4.97 (t, $J = 5.8$ Hz, 1H), 3.84 (s, 3H), 3.13 (d, $J = 5.8$ Hz, 2H), 2.33 (brs, 1H); $^{13}$C NMR (CDCl₃, 100 MHz): $\delta$ 155.9, 143.6, 136.8, 134.9, 128.6, 127.9, 125.6, 122.5, 120.4, 109.2, 100.8, 94.4, 74.3, 55.6, 37.9; HRMS (ESI): calcd for C₁₇H₁₄NO₂ m/z 290.1157 [M+Na]⁺, Found 290.1167; Specific optical rotation $[\alpha]_D^{24} = -23.5$ ($c = 1.19$, CHCl₃) (85% ee); HPLC analysis: (85% ee): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), $t_r = 15.2$ min (major), 17.3 min (minor).
9. Reaction of allenyl anilide with ketones-Additive effect and general procedure

Additive effect: In the reaction between allenyl anilide and ketones, protonation of the \textit{in situ}-generated allylcopper species was predominant over nucleophilic addition to carbonyl group due to the lower electrophilicity of ketones. Thus, the additive effect in this key transformation was examined and the results are summarized in the table below. Here again, the magnesium isopropoxide was proved to be the best among other additives.

![HPLC chromatogram](image)

<table>
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<tr>
<th>Entry</th>
<th>Additive (30 mol%)</th>
<th>Yield (%)$^a$</th>
<th>ee (%)$^b$</th>
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<td>40</td>
<td>73</td>
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<tr>
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<tr>
<td>5</td>
<td>MgBr$_2$</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>
Yield determined by $^1$H NMR spectrum of the crude products using $t$-Butyl methyl ether as an internal standard. Enantiomeric excess was determined by chiral HPLC analysis.

**9-1. General procedure for reaction between allenyl anilide and ketones:**

A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesityl copper (1.8 mg, 0.01 mmol, 5 mol%), (S, S)-Ph-BPE (5.0 mg, 0.01 mmol, 5 mol%) and Mg(O’Pr)$_2$ (8.5 mg, 0.06 mmol, 30 mol%) under argon atmosphere. Anhydrous dioxane (480 µL) was added, and the mixture was stirred at ambient temperature for 45 minutes. To the stirred solution, ketone (0.3 mmol) and 1.1 M solution of allenyl anilide (1a) (37.8 mg, 181 µL, 0.2 mmol) were added sequentially. After stirring for 5 h at room temperature, the reaction was diluted with THF (3 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 48 h, and products were extracted with ethyl acetate (20 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compounds.

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (S, S)-Ph-BPE.

The absolute configuration of the major enantiomer of obtained tertiary alcohols can be assigned by analogy of 3aa (See page S48-S51)

**Condition A: Without additive**

**Condition B: With additive (Mg(O’Pr)$_2$(30 mol%)**

Reaction condition- A (Without additive): 53% yield, 83% ee

Reaction condition- B: 64% yield, 73% ee

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; $R_f=0.23$ (EtOAc: Hexane 2:8); IR (thin film): ν 3410, 3072, 2342, 1455, 1288 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500
(S)-1-((1H-indol-2-yl)methyl)-6-(trifluoromethyl)-2,3-dihydro-1H-inden-1-ol (3av):

Reaction condition: B; Purified by silica gel column chromatography (Ethyl acetate: Hexane 15:85); Yellow liquid; Yield: 83%; Rf = 0.23 (EtOAc: Hexane 2:8); IR (thin film): ν 3448, 3019, 2921, 2359, 1621, 1215, 1123, 756 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 8.66 (brs, 1H), 7.57 (d, J = 8 Hz, 2H), 7.52 (s, 1H), 7.36-7.34 (m, 2H), 7.17 (t, J = 7.5 Hz, 1H), 6.26 (s, 1H), 3.31 (d, J = 14.9 Hz, 1H), 3.06-2.99 (m, 2H), 2.89-2.83 (m, 1H), 2.45-2.40 (m, 1H), 2.19 (s, 1H), 2.04-1.98 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz): δ 147.8, 146.7, 136.2, 135.1, (129.9, 129.6, 129.4, 129.1) (²JCF 32 Hz), 128.1, (127.5, 125.3, 123.1, 121.0) (¹JCF 272 Hz), 125.7 (q, ³JCF 3.6 Hz), 125.4, 121.4, 119.96 (q, ³JCF 3.6 Hz), 119.9, 119.6, 110.6, 102.3, 83.4, 39.8, 38.6, 29.2; HRMS (ESI): calcd for C₁₇H₁₇NO m/z 274.1208 [M+Na]⁺, Found 274.1200; Specific optical rotation [α]D = -42.6 (c = 0.8, CHCl₃) (83% ee): HPLC analysis: (83% ee): (Column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t₁ = 15.6 min (minor), 18.0 min (major).
C_{13}H_{16}F_{3}N_{1}O_{1} m/z 354.1082 [M+Na]^+; Found 354.1082; Specific optical rotation [α]_{D}^{24} = -13.8 (c = 1.76, CHCl_{3}) (for 77% ee); HPLC analysis: (77% ee): (Column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_{r} = 10 min (minor), 11.7 min (major).

(S)-1-(1H-indol-2-yl)-2-o-tolylpropan-2-ol (3ar):

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 57%; R_{f} = 0.26 (EtOAc: Hexane 2:8); IR (thin film): ν 3446, 3019, 2399, 1652, 1215, 1094, 756 cm\(^{-1}\); \(^1\)H NMR (CDCl_{3}, 500 MHz): δ 8.26 (brs, 1H), 7.54 (d, J = 7.5 Hz, 1H), 7.48 (d, J = 7.5 Hz, 1H), 7.48 (d, J = 7.5 Hz, 1H), 7.12 (t, J = 8 Hz, 1H), 7.06 (t, J = 8 Hz, 1H), 6.28 (s, 1H), 3.5 (d, J = 14.9 Hz, 1H), 3.2 (d, J = 14.9 Hz, 1H), 2.65 (s, 3H), 2.10 (s, 1H), 1.66 (s, 3H); \(^13\)C NMR (CDCl_{3}, 125 MHz): δ 144.5, 136.2, 135.3, 135.2, 132.9, 128.1, 127.4, 126.0, 125.8, 121.2, 119.8, 119.4, 110.5, 102.5, 75.9, 40.7, 28.7, 22.5; HRMS (ESI): calcd for C_{13}H_{16}F_{3}N_{1}O_{1} m/z 288.1364 [M+Na]^+, Found 288.1362; Specific optical rotation [α]_{D}^{24} = -23.8 (c = 0.65, CHCl_{3}) (for 83% ee); HPLC analysis: (83% ee): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_{r} = 8.1 min (major), 11.2 min (minor).
(S)-2-(2-chlorophenyl)-1-\(\text{1H-indol-2-yl}\)propan-2-ol (3as):

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 67%; \(R_t = 0.25\) (EtOAc: Hexane 2:8); IR (thin film): \(\nu\) 3462, 3019, 2399, 1215, 1034 cm\(^{-1}\); \(\text{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz)}\): \(\delta\) 8.24 (brs, 1H), 7.66-7.64 (m, 1H), 7.52 (d, \(J = 8.0\) Hz, 1H), 7.42-7.40 (m, 3H), 7.10 (t, \(J = 7.5\) Hz, 1H), 7.05 (t, \(J = 7.5\) Hz, 1H), 6.28 (s, 1H), 6.28 (s, 1H), 3.8 (d, \(J = 14.9\) Hz, 1H), 3.4 (d, \(J = 14.9\) Hz, 1H), 2.76 (s, 1H), 1.77 (s, 3H); \(\text{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz)}\): \(\delta\) 143.2, 136.2, 134.9, 131.4, 130.6, 128.6, 128.2, 127.6, 127.2, 121.2, 119.8, 119.4, 110.5, 102.5, 75.2, 39.2, 27.6; HRMS (ESI): calcd for C\(_17\)H\(_{16}\)ClN\(_1\)O\(_1\) m/z 308.0818 [M+Na\(^+\)], Found 308.0813; Specific optical rotation \(\left[\alpha\right]_D^{24} = -62.8\ (c = 0.85, \text{CHCl}_3\) (85% ee\); HPLC analysis: (85% ee): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), \(t_1 = 8.9\) min (major), 15.2 min (minor).
(S)-2-(4-Fluoro-2-methyl phenyl)-1-(1H-indol-2-yl)propan-2-ol (3au):

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 62%; Rf = 0.23 (EtOAc: Hexane 2:8); IR (thin film): ν 3455, 3019, 2399, 1215, 1094, 756 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 8.30 (brs, 1H), 7.53 (d, J = 8 Hz, 1H), 7.45-7.42 (m, 1H), 7.28 (d, J = 8 Hz, 1H), 7.14-7.05 (m, 2H), 6.92-6.82 (m, 2H), 6.26 (s, 1H), 3.46 (d, J = 14.9 Hz, 1H), 3.17 (d, J = 14.9 Hz, 1H), 2.63 (s, 1H), 1.64 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ (162.5, 160.6 ¹JCF, 245.9 Hz), 140.3, 137.9, 137.8 (¹JCF, 7.2 Hz), 136.2, 135.1, 128.1, (127.6, 127.5 ³JCF, 8.4 Hz), 121.3, 119.8, 119.5, (119.2, 119.1 ²JCF, 20.4 Hz), (112.3, 112.2 ²JCF, 20.4 Hz), 110.5, 102.5, 75.6, 40.8, 29.0, 22.5; HRMS (ESI): calcd for C₁₈H₁₈FN₁O₁ m/z 306.127 [M+Na]⁺, Found 306.1289; Specific optical rotation [α]D²⁴ = -22.2 (c = 0.75, CHCl₃) (95% ee); HPLC analysis: (95% ee): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), tₗ = 8.5 min (major), 10.4 min (minor).
(S)-1-(1H-indol-2-yl)-2-(2-(trifluoromethyl) phenyl) propan-2-ol (3at):

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 66%; $R_f = 0.26$ (EtOAc: Hexane 2:8); IR (thin film): ν 3447, 3019, 2358, 1551, 1215, 1122 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz): δ 8.52 (brs, 1H), 7.79 (d, $J = 7.5$ Hz, 1H), 7.62 (d, $J = 8$ Hz, 1H), 7.53-7.48 (m, 2H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.29 (d, $J = 8$ Hz, 1H), 7.12 (t, $J = 7.5$ Hz, 1H), 7.05 (t, $J = 7$ Hz, 1H), 6.27 (s, 1H), 3.51 (d, $J = 14.9$ Hz, 1H), 3.22 (d, $J = 14.9$ Hz, 1H), 2.39 (s, 1H), 1.7 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 146.4, 136.2, 134.8, 131.6, 128.3, 128.2, 128.1, 127.8, 127.2, 127.0, 126.7 ($^2J_{CF}$ 31 Hz), (128.1, 126.0, 123.8, 121.6) ($^1J_{CF}$ 272 Hz), 121.3, 119.8, 119.4, 110.5, 102.5, 75.9, 42.4, 30.5; HRMS (ESI): calcd for C$_{18}$H$_{16}$F$_3$N$_1$O$_1$ m/z 342.1082 [M+Na$^+$]. Found 342.1070; Specific optical rotation $[\alpha]_D^{24} = -25.9$ (c = 0.67, CHCl$_3$) (91% ee); HPLC analysis: (91% ee): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t$_r$ = 7.2 min (major), 9 min (minor).
10. Applications: Towards the syntheses of tetrahydropyranoindoles and spiroxindole:-

10-1. Synthesis of (S)-1, 1-dimethyl-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole (9):

To a stirred solution of (S)-2-(1H-indol-2-yl)-1-phenylethanol (3aa) (60 mg, 0.252 mmol) in anhydrous 1,2-dichloroethane (3 mL) was added 2, 2-dimethoxypropane (39 µL, 0.316 mmol) followed by boron trifluoride-etherate complex (16.8 µL, 0.136 mmol) at ambient temperature under argon atmosphere. The resulting reaction mixture was stirred at room temperature for 4 h and the mixture was slowly quenched with sat. aq. NaHCO₃ solution (5 mL). The reaction mixture was extracted with ethylacetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / n-hexane 1/9) afforded colorless sticky liquid (69.2 mg, 99%); $R_f =$
0.36 (EtOAc: Hexane 2:8); IR (thin film): ν 3405, 3018, 2977, 2360, 1457, 1216, 754 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 7.57 (brs, 1H), 7.4-7.37 (m, 3H), 7.27-7.25 (m, 2H), 7.2-7.14 (m, 2H), 7.07-6.98 (m, 2H), 4.83-4.81 (m, 1H), 2.81 (dd, J = 10.3 Hz, 15.5 Hz, 1H), 2.66 (dd, J = 3.4 Hz, 15.5 Hz, 1H), 1.61 (s, 3H), 1.57 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ 142.3, 135.8, 130.5, 128.4, 127.6, 126.3, 124.5, 121.1, 119.4, 118.7, 116.5, 110.9, 74.7, 70.7, 31.6, 29.9, 26.5; HRMS (ESI): calced for C₁₉H₁₉NO m/z 300.13643 [M+Na]⁺, Found 300.1364; Specific optical rotation [α]D²⁴ = - 66.1 (c = 1.04, CHCl₃) (91% ee).

10-2. 2,2-dimethyl-5-phenyl-4,5-dihydro-2H-spiro[furan-3,2'-indolin]-3-one (10)

To a stirred solution of 9 (80.7 mg, 0.29 mmol) in tetrahydrofuran (8 mL) was added m-CPBA (66 mg, 0.37 mmol) at room temperature and stirred for 15 h. The reaction mixture was quenched with saturated sodium thiosulfite solution, extracted with ethyl acetate (20 mL x 3) and washed the organic layer with water, brine and dried over sodium sulfate and concentrated. The crude residue was dissolved in 1M MeONa/MeOH (15 mL) solution, refluxed for 2 h and cooled to room temperature, quenched the reaction with 3N HCl. Products were extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / n-hexane 2/8) afforded 10 as liquid (58 mg, 68%); dr : 6:4; Rf = 0.38 and 0.34 (diastereomeric mixture) (EtOAc: Hexane 2:8); IR (thin film): ν 3355, 3011, 2358, 1683, 1617, 1216, 754 cm⁻¹; ¹H NMR (CDCl₃, 125 MHz) (diastereomeric mixture): δ 7.6 (d, J = 7.45 Hz, 1H), 7.48-7.35 (m, 5H), 7.31-7.26 (m, 1H), 6.91-6.79 (m, 2H), 5.48-5.45 (m, 0.6H), 5.27-5.23 (m, 0.4 H), 5.1 (brs, 0.4 H), 4.79 (brs, 0.6H), 3.03 (dd, J = 13.1 Hz, 8.6 Hz, 0.6 H), 2.72 (dd, J = 13.1 Hz, 10.3 Hz, 0.4 H), 2.43 (dd, J = 13.1 Hz, 6.87 Hz, 0.4H), 2.2 (dd, J = 13.1 Hz, 6.3 Hz, 0.6 H), 1.64 (brs, 1H), 1.43 (s, 3H), (1.33, 1.30) (2s, 3H); ¹³C NMR (CDCl₃, 125 MHz) (diastereomeric mixture): δ 200.1 (199.5), 159.4, 142.8 (142.1), 137.19 (137.15), 128.5 (128.3), 127.4 (127.3), 125.8 (125.3), 124.5 (124.4), 120.9 (120.6), 118.8 (118.7), 111.68 (111.64), 84.89 (84.7), 78.1 (77.0), 76.5 (76.1), 44.9 (44.0), 25.7 (24.0), 23.3 (22.7); HRMS (ESI): calced for C₁₉H₁₉NO₂ m/z 316.1314 [M+Na]⁺, Found 316.1309.

10-3. Synthesis of 1-(4-methoxyphenyl)-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole (28):
To a stirred solution of 2-(1H-indol-2-yl)-1-phenylethanol (3aa) (30 mg, 0.13 mmol) in anhydrous CH₂Cl₂ (3 mL) at 0 °C under argon atmosphere was added p-anisaldehyde dimethylacetal (27 µL, 0.16 mmol) followed by boron trifluoride-etherate complex (8.4 µL, 0.068 mmol). The resulting reaction mixture was warmed to room temperature and stirred for 5 h. The reaction mixture was slowly quenched with sat. aq. NaHCO₃ solution (5 mL). Products were extracted with dichloromethane (5 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / n-hexane 2/8) afforded yellow liquid (39 mg, 87%); Rf = 0.26 (EtOAc: Hexane 2:8); IR (thin film): ν 3396, 2921, 2360, 1508, 1247 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) (diastereomeric mixture in the ratio 6: 4): δ 8.0 (7.94) (brs, 1H), 7.5 (d, J = 7.4 Hz, 1H), 7.42-7.27 (m, 7H), 7.19-7.16 (m, 1H), 7.11-7.03 (m, 1H), 6.91-6.77 (m, 3H), 6.18 (6.0) (s, 1H), 5.02 (dd, J = 10.8 Hz, 3.4 Hz, 0.6 H), 4.85 (dd, J = 10.3 Hz, 4.0 Hz, 0.4 H), 3.81 (3.79) (s, 3H), 3.23-3.12 (m, 1H), 3.05-3.0 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz) (diastereomeric mixture): δ 159.5 (159.8), 142.0 (141.7), 135.8 (135.7), 133.3 (133.2), 132.7 (132.3), 130.08 (130.04), 128.4 (128.3), 127.68 (127.63), 126.3 (126.1), 125.9 (125.1), 121.5 (121.3), 119.7 (119.5), 119.0 (118.8), 113.7 (113.4), 111.7 (110.7), 110.6 (110.1), 78.1 (77.2), 74.0 (69.4), 55.22 (55.20), 31.9 (30.6); HRMS (ESI): calcd for C₂₄H₂₁NO₂ m/z 378.147 [M+Na]+, Found 378.1460.

10-4. Methyl 2-(1-methyl-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indol-1-yl)acetate (29):

To a stirred solution of 2-(1H-indol-2-yl)-1-phenylethanol (3aa) (30 mg, 0.126 mmol) in anhydrous THF (5 mL) at rt under argon atmosphere was added methyl acetoacetate (20.4 µL, 0.189 mmol) followed by boron trifluoride-etherate complex (187 µL, 1.51 mmol). After stirring for 12 h at room temperature, the reaction was cautiously quenched with sat. aq. NaHCO₃ solution (5 mL), and products were extracted with dichloromethane (5 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, passed through a pad of celite, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / n-hexane 2/8) afforded 29 as colorless liquid (39 mg, 92%); Rf = 0.18 (EtOAc: Hexane 2:8); IR (thin film): ν 3397, 2947, 2365, 1732, 1456, 1326, 1219, 746 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) (diastereomeric mixture in the ratio 6: 4): δ 7.96 (7.91) (brs, 1H), 7.54-7.48 (m, 3H), 7.42-7.39 (m, 2H), 7.35-7.32 (m, 2H), 7.18-7.12 (m, 2H), 5.11 (4.96) (dd, J = 10.8 Hz, 3.4 Hz, 1H), 3.6 (s, 3H), 3.17-3.12 (m, 1H), 3.09-2.84 (m, 3H), 1.89 (1.83) (s, 2H); ¹³C NMR (CDCl₃, 125 MHz) (diastereomeric mixture): δ 170.9 (170.8), 142.3 (141.5), 135.8, 131.3 (130.87), 128.4 (128.3), 127.6 (127.5), 126.3 (125.9), 124.3 (124.0), 121.4 (121.3), 119.7 (119.6), 118.6 (118.3), 115.5 (114.1), 111.07 (111.01), 75.4 (75.3), 70.9 (70.7), 51.5 (51.2), 46.72 (43.83), 32.07 (30.54), 27.18 (25.37); HRMS (ESI): calcd for C₂₁H₂₁NO₃ m/z 358.1419 [M+Na]⁺, Found 358.1401.

S47
11. Confirmation of the absolute configuration of 3aa:
The reaction of allenyl anilide (1a) (0.2 mmol scale) with benzaldehyde (2a) (2 eq) in presence of 5 mol% of copper catalyst [MesCu (5 mol%) and (S, S)-Ph-BPE (5 mol%) as chiral ligand] in dioxane (0.3 molar concentration) at room temperature afforded 3aa as a white solid (92%, 91% ee).

The absolute configuration of the obtained product (3aa) was confirmed by comparing the HPLC data and specific optical rotation of the product obtained using two step synthetic protocol\(^8\) as shown below.

Experimental procedure:
(S)-1-phenyl-2-(1-(phenylsulfonyl)-1H-indol-2-yl)ethanol (30):
To a solution of 1-phenylsulfonylindole (1 g, 3.88 mmol) in dry THF (15 mL) was added dropwise n-butyllithium (2.9 mL, 1.6 M in hexane, 4.66 mmol) over 10 min under argon at –78 °C. The mixture was stirred for 1.5 h at -78 °C and then allowed to warm slowly to 0 °C over 1 h. The solution was again cooled to -78 °C and (R)- (+)- styrene oxide (0.44 mL, 3.88 mmol) was added drop by drop. The reaction mixture was allowed slowly to warm up to room temperature overnight and quenched with saturated aqueous solution of ammonium chloride (10 mL). Products were extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under high vacuum. The crude mixture was purified by silica gel column chromatography (Ethyl acetate / n-hexane 2/8) afforded the desired compound as a liquid (501 mg, 34%); IR (thin film): ν 3584, 3063, 1592, 1449, 1366, 750 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): δ 8.20 (d, \(J = 8.0\) Hz, 1H), 7.73-7.71 (m, 2H), 7.51-7.48 (m, 3H), 7.44-7.36 (m, 5H), 7.32-7.29 (m, 2H), 7.25-7.22 (m, 1H), 8.51 (s, 1H), 5.23 (dd, \(J = 9.1\)Hz, 3.4 Hz, 1H), 3.55 (dd, \(J = 14.5\) Hz, 2.9 Hz, 1H), 3.25 (dd, \(J = 14.5\) Hz, 8.6 Hz, 1H), 2.25 (brs, 1H); \(^13\)C NMR (CDCl\(_3\), 125 MHz): δ 143.7, 138.6, 137.8, 137.4, 133.7, 129.6, 129.2, 128.4, 127.6, 126.1, 125.7, 124.4, 123.8, 120.4, 115.0, 112.2, 73.0, 39.8; HRMS (ESI): calcd for C\(_{22}\)H\(_{19}\)NO\(_3\)S m/z 400.0983 [M+Na]\(^+\), Found 400.0989.

\(^8\) Wang, J-C.; Just, G. J. Org. Chem. 1999, 64, 8090-8097
(S)-2-(1H-indol-2-yl)-1-phenylethanol:

To a solution of (S)-1-phenyl-2-(1-phenylsulfonyl)-1H-indol-2-yl)ethanol (30) (0.45 g, 1.192 mmol) in 6 mL of methanol/water (3:1) containing KOH (335 mg, 5.96 mmol) was refluxed for 7 h and the reaction was quenched with sat. aq. ammonium chloride solution. The reaction mixture was extracted with ethylacetate and the combined extracts were washed with water and brine, dried over anhydrous sodium sulfate, concentrated under high vacuum. Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; (212 mg, 75%)

All the spectroscopic data were in good agreement with the sample (3aa) obtained via key transformation. Specific optical rotation [α]_{D}^{20} = -52 (c = 0.5, CHCl₃) (98% ee); HPLC analysis: (98% ee); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), tᵣ = 9.37 min (major), 12.47 min (minor).

The specific optical rotation and HPLC chromatograms comparison of 3aa obtained by amido-cupration-asymmetric allylation {[(S, S)-Ph-BPE]} method and derivatization of (R)(+)-styrene oxide unambiguously revealed that the obtained compound (3aa) has (S)-configuration.
12. NMR spectra of new compounds:
Chemical Shift (ppm)

I

NHCOOMe

17
Chemical Shift (ppm)

52.44  55.32
76.75  77.00  77.26
105.38
111.87
138.65  139.01
153.63  160.60

NHCOOMe

I

O

18
PKC-146-o-methyl-6-13-1-1.als

Chemical Shift (ppm)

Me
NH
COOMe

1c
Chemical Shift (ppm):

- 192.0
- 153.80
- 138.54
- 127.23
- 126.01
- 125.98
- 125.72
- 125.47
- 125.06
- 124.85
- 122.91
- 120.74
- 90.18
- 79.71
- 77.26
- 77.00
- 76.74
- 52.60

Chemical structure:

\[
\begin{array}{c}
\text{F}_3\text{C} \\
\text{NH} \\
1d \\
\text{COOMe}
\end{array}
\]
Chemical Shift (ppm)

209.88
154.32
135.18
128.73
127.85
124.17
90.52
78.70
77.50
76.74
52.30

NH
COOMe

1a
PK---14(3)-1-1.als

Chemical Shift (ppm)

N

OH

3an

S89
<table>
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<th>Chemical Shift (ppm)</th>
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<tr>
<td>136.95</td>
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</table>

The diagram shows a chemical structure with labels indicating positions 3ap.
Chemical Shift (ppm)

- 1.00
- 1.01
- 2.03
- 1.06
- 2.02

Structure:

- NH
- O
- HO
- 3ai
3ai

Chemical Shift (ppm)

39.42 48.72 48.94 49.15 49.37 49.59 49.80 61.86 70.61 74.71 101.36 111.65 115.40 119.91 120.51 121.55 128.44 130.26 137.77 137.92 138.21 159.88
Chemical Shift (ppm)
Chemical Shift (ppm)

147.17  136.15  135.43  128.26  126.80  125.05  124.05  121.41  119.98  119.64  110.63  101.45

77.00  70.19  37.97

N  H

$\text{HO}$

S

3ad
PK---16(2)-C13-1-1.als

Chemical Shift (ppm)

159.26
136.32
136.08
135.77
128.31
126.94
121.21
119.89
119.52
113.95
110.58
100.97
77.00
73.91
55.27
37.75

N
H
OH
3ac

[Chemical structure diagram]
\[
\begin{align*}
\text{Chemical Shift (ppm)} & \quad 143.46 \\
& \quad 137.12 \\
& \quad 136.44 \\
& \quad 128.71 \\
& \quad 128.12 \\
& \quad 127.01 \\
& \quad 126.83 \\
& \quad 125.62 \\
& \quad 120.69 \\
& \quad 120.20 \\
& \quad 110.53 \\
& \quad 101.07 \\
& \quad 77.00 \\
& \quad 74.40 \\
& \quad 37.63 \\
& \quad \text{N} \\
& \quad \text{NH} \\
& \quad \text{OH} \\
& \quad \text{Cl} \\
& \quad 3\text{ba}
\end{align*}
\]
PK-50(6)-C13-1-1.als

![NMR Spectrogram](image)

- **Chemical Shifts (ppm)**:
  - 143.26
  - 136.22
  - 134.93
  - 131.46
  - 130.62
  - 128.68
  - 128.20
  - 127.69
  - 127.21
  - 121.28
  - 119.87
  - 119.47
  - 110.51
  - 102.54
  - 39.28
  - 27.60

- **Structural Formula**:
  - ![Structure Image]
Chemical Shift (ppm)

8.30 7.54 7.45 7.43 7.48 7.47 7.13 7.28 7.27 7.26 7.13 7.08 7.07 6.91 6.89 6.26 5.30 3.48 3.15 2.63 2.08 1.66
Chemical Shift (ppm)

1.18 1.70 3.00 0.98 2.91 0.40 0.60 2.09 2.07 2.08 3.15 0.41 0.59

7.96 7.54 7.52 7.48 7.48 7.40 7.40 7.39 7.34 7.33 7.26 7.14

5.12 5.11 5.10 5.09 4.97 4.97 4.95 3.61 3.60 3.17 3.14 3.12 3.07 3.04 3.03

2.96 2.93 2.85 1.89 1.88 1.83 1.82 1.60

N

H

\(\text{O}^{\#}\)

H3C

COOMe