Asymmetric C(sp³)–H Functionalization of Unactivated Alkylarenes such as Toluene Enabled by Chiral Brønsted Base Catalysts

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Supplementary Information

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1. Supplementary Methods

1-1. Initial investigation of the ligand structures

Initial investigation of chiral ligand structures was conducted (Supplementary Table 1). A chiral macrocyclic crown ether (L0, 34-crown-10 ether) was not effective for the desired reaction (entry 1). On the other hand, chiral amines were found to be promising, and tetradeutate ligand L2 gave some level of ee in tert-butyl methyl ether (TBME) solvent (entry 2). In toluene solvent, the reaction with L2 gave the product in higher yield but almost the same ee (entry 3). Finally, chiral diamine L1 showed the most promising ee among them (entry 4).

Supplementary Table 1 Initial investigation of the ligand structures

| entry | base-cat. | ligand | solvent   | yield (%) | ee (%) |
|-------|-----------|--------|-----------|-----------|--------|
| 1     | KO\textsuperscript{b}Bu-LiTMP | L0     | TBME      | 43        | 0      |
| 2     | KO\textsuperscript{b}Bu-LiTMP | L2     | TBME      | 46        | 12\textsuperscript{a} |
| 3     | KCH\textsubscript{2}SiMe\textsubscript{3} | L2     | toluene   | 85        | 11\textsuperscript{a} |
| 4     | KCH\textsubscript{2}SiMe\textsubscript{3} | L1     | toluene   | 25        | 21     |

\textsuperscript{a} (R)-3aa was obtained as a major enantiomer.

1-2. Optimization of the catalyst preparation conditions

It is known that catalyst preparation conditions of chiral catalysts sometimes affect results of the asymmetric reactions dramatically. Here, catalyst preparation temperature and time were optimized (Supplementary Table 2). It was found that the preparation at –40 °C for 30 min gave the best result, and the ee was improved to 56% (entry 5).
Supplementary Table 2 Optimization of the catalyst preparation conditions

| entry | conditions of pre-mixing | yield (%) | ee (%) |
|-------|--------------------------|-----------|--------|
| 1     | −78 ℃, 30 min            | 25        | 21     |
| 2     | −60 ℃, 60 min            | 80        | 41     |
| 3     | −40 ℃, 60 min            | 88        | 50     |
| 4     | −20 ℃, 60 min            | 11        | 7      |
| 5     | −40 ℃, 30 min            | 85        | 56     |
| 6     | −40 ℃, 15 min            | 46        | 18     |

1-3. Optimization of the diamine ligand structures

In our initial investigation, ligand L1 showed the most promising enantioselectivity. Therefore, we investigated effect of chiral diamine ligands with related structures (Supplementary Table 3). Firstly, diamines derived from other chiral amino acids were examined (L7-L10); however, the selectivity was not improved. Next, structures of the N-alkyl substituents were examined. It was found that longer alkyl groups were all not effective, and methyl group showed the highest ee (L11-L13). The piperidine part was then modified. A noncyclic structure, smaller and larger ring systems, dimethyl substitution and oxygen introduction at the 4-position were investigated; however, further improvement of the enantioselectivity was not observed (L14-L18).
Supplementary Table 3 Optimization of the diamine ligand structures

![Chemical structure images and reactions]

* (R)-3aa was obtained as a major enantiomer.

### 1-4. Limitation of Substrates

The reactions of the following alkylarenes that were not shown in the main text were conducted (Supplementary Table 4).
**Supplementary Table 4** Reactions of other alkylarenes

| Reaction conditions: | Product | Notes |
|----------------------|---------|-------|
| 1 (0.5 mmol), 2 (1.0 mL), KCH$_2$SiMe$_3$ (0.10 mmol), KHMDS (0.10 mmol), L6 (0.11 mmol), –60 °C, 18 h. | ![Product Image] | ![Notes Image] |
| 1 (0.50 mmol), 2 (2.5 mmol), KCH$_2$SiMe$_3$ (0.10 mmol), KHMDS (0.10 mmol), L6 (0.11 mmol), Cumene (1.0 mL), –60 °C, 18 h. | ![Product Image] | ![Notes Image] |

When cumene (2g) was employed as a pronucleophile, the desired adduct was not obtained probably because of its low acidity or bulkiness at the reaction site. Next, p-cymene (2h) was used as a pronucleophile. However, the reaction proceeded with low enantioselectivity. p-Methoxytoluene (2i), whose freezing point is −50 °C, is a challenging substrate because it is frozen under the optimized conditions. To overcome this problem, cumene was used as a solvent, but the reaction did not proceed presumably because of its low acidity.

**1-5. Nonlinear effect**

Relationship between optical purity of L6 and that of the product obtained in the presence or absence of KHMDS was examined. When KHMDS was not used, almost linear relationship was observed (Supplementary Figure 1). On the other hand, when KHMDS was used, negative non-linear effect was observed but the level was not significant (Supplementary Figure 2). Those results could support that more reactive heterooligomer species of the catalyst (racemic) formed in the presence of KHMDS, but they did not deny formation of homooligomer species of the active catalyst in the reaction system.
**Supplementary Figure 1** Nonlinear effect between optical purity of L6 and that of the product (without KHMDS)

\[
\text{Product ee} \times \text{Ligand ee (w/o KHMDS)}
\]

**Supplementary Figure 2** Nonlinear effect between optical purity of L6 and that of the product (with KHMDS)
1-6. NMR experiments

NMR experiments were conducted to obtain information of the base catalyst system. Firstly, KCH$_2$SiMe$_3$, KHMDS, and L$\textbf{6}$ were mixed in 1:1:1 ratio in toluene-$_d_8$ to form an active chiral benzyl potassium species, and a spectrum was collected at –78 °C (Supplementary Figure 3). On the spectrum, remained free L$\textbf{6}$, a new set of peaks derived from L$\textbf{6}$, free KHMDS, and other new KHMDS species were observed. The ratio of the new KHMDS species (Me$_3$Si protons, 18 H), which might coordinate to the active catalyst, and a newly appeared species derived from L$\textbf{6}$ looks almost 1:1 ratio. This result might support that the active chiral benzyl potassium complex is consisting of benzyl potassium, L$\textbf{6}$ and KHMDS in 1:1:1 ratio; however, the spectrum was a little messy, therefore we also investigated the complex prepared from L$\textbf{1}$. 

![Graph showing Product ee - Ligand ee (w/ KHMDS)](image-url)
Supplementary Figure 3

KCH$_2$SiMe$_3$ : KHMDS : L6 = 1 : 1 : 1

Newly appeared peek of KHMDS

Newly appeared peaks derived from L6
The spectrum of the NMR experiment using \textbf{L1} was shown in Figure S4. KCH$_2$SiMe$_3$ KHMDS, and \textbf{L1} were mixed in 1:1:1 ratio in toluene-$d_8$, and a spectrum was collected at $-78^\circ$C. Compared to the spectrum of the \textbf{L6} complex, a cleaner spectrum was obtained, and the ratio of the new KHMDS species (Me$_3$Si protons, 2 peaks) and a newly appeared peak derived from \textbf{L1} was almost 1:1. Furthermore, when KCH$_2$SiMe$_3$ KHMDS, and \textbf{L1} were mixed in 1:0.5:1 ratio in toluene-$d_8$, almost the same spectrum was observed, and the ratio of the new KHMDS species and the newly appeared peak from \textbf{L1} was the same (Supplementary Figure 5). Those results might support that the active complex is consisting of benzyl potassium, \textbf{L1} and KHMDS in 1:1:1.

However, the amount of the newly appeared species was small, and much amount of the free ligand was observed. This observation indicated the complex formation was not perfect, and the amount of the active species should be small in the reaction system.
Supplementary Figure 4

KCH₂SiMe₃ + KHMDS = L1

KCH₂SiMe₃ : KHMDS : L1 = 1 : 1 : 1

Spectrum of Figure S4

(1 : 1 : 1)
toluene-d₈
-40 °C
30 min

Free KHMDS → Newly appeared peak of KHMDS

Newly appeared peaks derived from L1
Supplementary Figure 5

KCH₂SiMe₃ + KHMDS → \(\text{L1}^{\text{Ph}}\) \(\text{HN}\) \(\text{HN}\) \(\text{L1}\) → Spectrum of Figure S5

toluene-d₈

\(\text{−78 °C}\)

\(\text{−40 °C}\)

30 min

\(\text{1 : 0.5 : 1}\)

L1

KCH₂SiMe₃ : KHMDS : L1 = 2 : 1 : 2

Free KHMDS ↓

Newly appeared peek of KHMDS ↑

Newly appeared peeks derived from L1 ↓ ↓
1-7. Effect of the ligand structure (the piperazine part)

Detailed investigation of the ligand structure about the piperazine part of L6 was performed (Supplementary Table 5). When the methyl group on the piperazine part was changed into sterically larger alkyl groups, the enantioselectivity was not improved. However, enantioselectivities using the ligands bearing the piperazine parts was higher than that of L1. The ligand L22, which has 4-methyl group on the piperidine part of L1, gave almost the same result to the reaction using L1. Those results suggested that the nitrogen atom of the piperazine ring played an important role in the asymmetric environment.
1-8. Investigation of backward reaction

Possibility of backward reaction was investigated (Supplementary Figure 6). When product 3aa with 99% ee was treated by the chiral base catalyst for 18 h at –78 °C, the product was recovered in high yield with the same ee. This result indicated that the backward reaction in the process under the reaction conditions could be ignored.
2. Experimental Section

2-1. General

Melting points were measured with Büchi Melting Point D-545. \(^1\)H and \(^{13}\)C NMR spectra were recorded on JEOL JNM-ECA500 and JNM-ECX600 spectrometers in CDCl\(_3\) unless otherwise noted. Tetramethylsilane (TMS) served as internal standard (\(\delta = 0\)) for \(^1\)H NMR, and CDCl\(_3\) served as internal standard (\(\delta = 77.0\)) for \(^{13}\)C NMR. IR spectra were measured on JASCO FT/IR-610 spectrometer. WILMAD screw-cap NMR tube (Aldrich Co., Ltd.) was used for NMR experiments. HPLC analysis was performed on Shimadzu LC-20AB, SPD-20A, and DGU-20A3. DART mass spectra were recorded on JEOL JMS-T100TD mass spectrometer. Preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F. Potassium tert-butoxide (KO\(\text{Bu}\)) was purchased from Kanto Chemical Co., Inc. Lithium 2,2,6,6-tetramethylpiperizide (LiTMP), potassium bis(trimethylsilyl)amide (KHMDMS), sodium bis(trimethylsilyl)amide (NaHMDS), and lithium bis(trimethylsilyl)amide (LiHMDS) were purchased from Aldrich Co., Ltd. Trimethylsilylmethylpotassium (KCH\(_2\)SiMe\(_3\)) was prepared according to literature. Potassium 2,2,6,6-tetramethylpiperidide (KTMP) was prepared by deprotonation of 2,2,6,6-tetramethylpiperididine with KCH\(_2\)SiMe\(_3\). Potassium bis(trialkylsilyl)amides were also prepared by deprotonation of the corresponding bis(trialkylsilyl)amine. Ethylbenzene was purchased from Tokyo Chemical Industry Co., Ltd. and was distilled and stored in an ampule. Toluene was purchased from Kanto Chemical Co., Inc. and purified further by Glass Contour NIKKO HANSEN & Co., LTD. TBME was distilled in the presence of benzophenone and sodium. L\(_0\), \(^2\)L\(_1\), \(^3\) and L\(_2\)\(^4\) were prepared according to the literatures.
2-2. Preparation of imines

The imines were prepared according to the literature.\textsuperscript{5} \textit{p}-Methoxycumylamine S1 (10.0 mmol) was added to a solution of aldehyde (1.0 eq.) and MS 4 Å (5 g) in DCM (10 mL). The whole mixture was stirred for 12 h or more at room temperature, and then filtered through a Celite pad. The filtrate was concentrated under reduced pressure, and the crude product obtained was purified by distillation or recrystallization to afford the corresponding imine 1. Structures of 1a-1c, 1g-1j and 1l were confirmed by comparison with data shown in the literature which our group have reported\textsuperscript{17}.

\textbf{(E)-1-(4-ethylphenyl)-N-((2-(4-methoxyphenyl)propan-2-yl)methanimine} (1d);

Colorless oil; \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) \(\delta\): 8.13 (1H, s), 7.68 (2H, d, \(J = 8.50\) Hz), 7.34 (2H, d, \(J = 9.07\) Hz), 7.23 (2H, d, \(J = 8.50\) Hz), 6.86 (2H, d, \(J = 9.07\) Hz), 3.80 (3H, s), 2.67 (2H, q, \(J = 7.56\) Hz), 1.62 (6H, s), 1.24 (3H, t, \(J = 7.65\) Hz); \textit{\textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}): \(\delta = 157.9, 157.0, 146.9, 140.3, 134.6, 128.1, 128.0, 127.3, 113.4, 62.1, 55.2, 29.9, 28.8, 15.5; IR (neat, cm\textsuperscript{-1})}; 798, 827, 977, 1034, 1180, 1244, 1298, 1509, 1609, 1644, 2966; HRMS (DART) calcd for C\textsubscript{19}H\textsubscript{24}NO [M + H]\textsuperscript{+} 282.18579. found: 282.18523.

\textbf{(E)-1-([1,1'-biphenyl]-4-y1)-N-((2-(4-methoxyphenyl)propan-2-yl)methanimine} (1e);

Colorless solid; Mp: 88-89 °C; \textit{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz) \(\delta\): 8.19 (1H, s), 7.84 (2H, d, \(J = 8.25\) Hz), 7.63-7.61 (4H, m), 7.43 (2H, t, \(J = 7.56\) Hz), 7.36-7.33 (3H, m), 6.88 (2H, d, \(J = 8.94\) Hz), 3.79 (3H, s), 1.65 (6H, s); \textit{\textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}): \(\delta = 158.0, 156.7, 143.1, 140.6, 140.2, 135.9, 128.8, 128.5, 127.6, 127.4, 127.2, 127.1, 113.5, 62.3, 55.2, 29.9; IR (neat, cm\textsuperscript{-1})}; 418, 558, 769, 811, 832, 1035, 1246, 1508, 1559; HRMS (DART) calcd for C\textsubscript{23}H\textsubscript{24}NO [M + H]\textsuperscript{+} 330.18524. found: 330.18627.

\textbf{(E)-N-((2-(4-methoxyphenyl)propan-2-yl)-1-(naphthalen-1-yl)methanimine} (1f);

Colorless oil; \textit{\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\): 8.80-8.78 (2H, m), 7.90-7.88 (3H, m), 7.55-7.51 (3H, m), 7.42 (2H, d, \(J = 9.07\) Hz), 6.91 (2H, d, \(J = 8.50\) Hz), 3.82 (3H, s), 1.74 (6H, s); \textit{\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta = 158.1, 157.1, 140.0, 133.8, 132.4, 131.4, 130.6, 128.6, 128.1, 127.5, 126.9, 125.9, 125.3, 124.2, 113.5, 63.1, 55.3, 30.1; IR (neat, cm\textsuperscript{-1})}; 2970, 1637, 1611, 1508, 1242, 1177, 1034, 828, 800, 774, 565; HRMS (DART) calcd for C\textsubscript{21}H\textsubscript{22}NO [M + H]\textsuperscript{+} 304.17014, found 304.16882.
(E)-N-(2-(4-methoxyphenyl)propan-2-yl)-1-(4-(methylthio)phenyl)methanimine

(1k); Colorless solid; Mp: 55-57 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta:\) 8.09 (1H, s), 7.67 (2H, d, \(J = 8.50\) Hz), 7.33 (2H, d, \(J = 9.07\) Hz), 7.25 (2H, m), 6.87 (2H, d, \(J = 8.50\) Hz), 3.81 (3H, s), 2.50 (3H, s), 1.62 (6, s); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta:\) 157.9, 156.4, 141.5, 140.2, 133.7, 128.4, 127.3, 125.8, 113.4, 62.2, 55.2, 29.9, 15.3; IR (neat, cm\(^{-1}\)) 1634, 1511, 1300, 1240, 1177, 1085, 1034, 825, 557, 494; HRMS (DART) calcd for C\(_{18}\)H\(_{22}\)NOS [M + H]\(^+\) 300.14221, found 300.14115.
2-3. Preparation of chiral ligands

Preparation of chiral ligand L4

\[
\begin{align*}
\text{L1} \cdot 2\text{HCl} (10 \text{ eq.}) & \xrightarrow{\text{(COCl)}_2 (1.0 \text{ eq.})} \text{S2} \quad \text{DCM} \\
& \xrightarrow{\text{LiAlH}_4 (6.0 \text{ eq.})} \text{THF} \quad \text{reflux} \\
& \rightarrow \text{L4}
\end{align*}
\]

Ammonium chloride salt L1·2HCl was prepared by acidic treatment of L1 with 4N HCl (in ethyl acetate) and was recrystallized in EtOH. Then, Ammonium chloride salt L1·2HCl was converted to ligand L4 by the following procedure. Triethylamine (4.88 mL, 35.0 mmol) was added to dispersion of S2 (2.91 g, 10.0 mmol) in dichloromethane (DCM, 50 mL). After the mixture was cooled to 0 °C, oxalyl chloride (0.43 mL, 5.0 mmol) was added. Subsequently, the reaction mixture was stirred overnight at room temperature. After the reaction was quenched by adding saturated aq. NaHCO₃, the mixture was extracted with DCM (30 mL x 3). The combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the obtained crude product was purified by column chromatography (hexane-ethyl acetate) and recrystallization (in hexane-ethyl acetate) to afford the desired amide S1 (0.930 mg, 38% yield). The obtained product was used without further purification in the next step.

Solution of the obtained amide S1 (0.900 mg, 1.83 mmol) in THF (20 mL) was added to dispersion of LiAlH₄ (417.5 mg, 10.98 mmol) in THF (15 mL) at 0 °C. Subsequently, the reaction mixture was refluxed overnight and quenched with 3% aq. NaOH (5 mL). After filtration through a Celite pad and concentration under reduced pressure, the crude product was distilled to afford the desired tetraamine L4 (296.5 mg, 35% yield).

\textit{N}_1^1,\textit{N}_2^2\text{dimethyl-\textit{N}_1^1,\textit{N}_2^2\text{bis((R)-1-phenyl-2-(piperidin-1-yl)ethyl)ethane-1,2-diamine}} (L4): Colorless oil; \(^1\)H NMR (600 MHz, CDCl₃) δ: 7.21-7.20 (4H, m), 7.15-7.13 (6H, m), 3.62 (2H, dd, \(J = 7.33, 3.67 \) Hz), 2.75 (2H, dd, \(J = 6.42, 3.21 \) Hz), 2.52 (2H, dd, \(J = 6.42, 3.21 \) Hz), 2.46-2.38 (4H, m), 2.28 (8H, s), 2.08 (6H, s), 1.43-1.39 (8H, m), 1.29 (4H, d, \(J = 4.81 \) Hz); \(^{13}\)C NMR (150 MHz, CDCl₃) δ: 140.1, 128.6, 127.7, 126.6, 65.8, 61.7, 55.1, 52.5, 39.0, 25.9, 24.3; IR (neat, cm\(^{-1}\)) 2932, 2783, 1451, 1305, 1154, 1111, 1040, 994, 867, 781, 740, 698, 591, 530; HRMS (DART) calcd for C\(_{30}\)H\(_{47}\)N\(_4\) [M + H]\(^+\) 463.38007, found 463.37806; \([\alpha]_D^{20} = -13.69 \) (c = 0.93, CHCl₃).
Preparation of chiral ligand L5

Carbonyl chloride S5 was synthesized from tartrate S3 according to the literatures. Ester mixture S4 was used instead of pure methyl ester, which was employed in the literature. Then, carbonyl chloride S5 was converted to ligand L5 by the following procedure.

Carbonyl chloride S5 (2.10 g, 9.25 mmol) dissolved in THF (10 mL) was added to a solution of piperidine (4.57 mL, 46.3 mmol) in THF (8.5 mL) at 0 °C. Then, the reaction mixture was stirred overnight at room temperature, and quenched with water. The mixture was extracted with DCM (20 mL x 3). Then, the combined organic layer was washed with saturated NaHCO₃ and was dried over Na₂SO₄. After filtration and concentration under reduced pressure, the crude product obtained was recrystallized (in hexane) to afford the desired amide S6 (2.22 g, 6.86 mmol, 74% yield). In the next step, hydride reduction similar to ligand L4 was performed to afford ligand L5 (70% yield).

1,1’-(((4S,5S)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene))dipiperidine (L5);
Colorless solid; Mp 37–39 ºC; ¹H NMR (500 MHz, CDCl₃) δ: 3.83 (2H, dd, J = 12.47, 10.20 Hz), 2.51-2.45 (12H, m), 1.60-1.56 (4H, m), 1.43-1.39 (10H, m); ¹³C NMR (125 MHz, CDCl₃) δ: 109.0, 77.9, 62.1, 55.3, 27.2, 25.8, 24.2; IR (neat, cm⁻¹) 2932, 2853, 1442, 1368, 1301, 1157, 1124, 1077, 1058, 995, 863, 845, 805, 780, 513; HRMS (Dart) calcd for C₁₇H₃₃N₂O₂ [M + H⁺]²⁺ 297.25358, found 297.25420; [α]D²⁰ = −23.73 (c 1.22, CHCl₃).

Preparation of chiral ligands L6-L10 and L14-L22
Title ligands were synthesized from Cbz-protected amino acids according to the reported procedure for synthesis of L1.

Isobutyl chloroformate (6.57 mL, 50.0 mmol) was added to a solution of N-Cbz-
protected amino acid S7 (50.0 mmol) and 4-methylmorpholine (5.50 mL, 50.0 mmol) in 125 mL of THF at −15 °C with stirring, and the corresponding secondary amine (50.0 mmol) was subsequently added to the reaction mixture. The reaction mixture was stirred for 1 h at the same temperature, and then stirring was continued at room temperature overnight. The reaction mixture was concentrated and dissolved in 200 mL of ethyl acetate. The obtained mixture was washed with 1 N HCl (100 mL x 2), water (100 mL), saturated NaHCO₃ aqueous solution (100 mL x 2), and water (100 mL). The ethyl acetate layer was dried over anhydrous Na₂SO₄. After filtration, the corrected organic layer was concentrated under vacuumed condition to afford crude S8, and the obtained product S8 was used in the next step without further purification.

The crude product obtained above was dissolved in THF (100 mL) and was added dropwise to a dispersion of LiAlH₄ (15.2 g, 400 mmol) in THF (150 mL) at 0 °C under argon atmosphere. Subsequently, the dispersion was refluxed overnight. The dispersion was cooled to 0 °C and quenched with 15 mL of water followed sequentially by 15 mL of 15% NaOH aq. and 10 ml of water. After filtration to remove white solid, the filtrate was concentrated to afford an oily residue. The oily residue was dissolved in 200 mL of Et₂O, and 50 mL of 4N HCl in EtOAc was added to this solution to afford an ammonium salt derived from the desired amine. The salt was collected by filtration and dried under reduced pressure. Subsequently, the obtained salt was recrystallized in EtOH to enhance the enantiopurity. The purified salt was dissolved in 100 mL water and was basified with 15% aq. NaOH. The mixture was extracted with DCM (50 mL x 3), and the combined organic layer was dried over anhydrous Na₂CO₃. After filtration and concentration, the obtained crude product was distilled under vacuumed condition to afford the desired amine. Structures of L7-L9, L14-L16, and L18 were confirmed by comparison with data shown in the literature²⁸.

(R)-N-methyl-2-(4-methylpiperazin-1-yl)-1-phenylethan-1-amine (L6); Colorless solid; Mp 31–33 °C; ¹H NMR (600 MHz, CDCl₃) δ: 7.35-7.32 (4H, m), 7.26-7.24 (1H, m), 3.62 (1H, dd, J = 11.00, 3.44 Hz), 2.66-2.29 (17H, m); ¹³C NMR (150 MHz, CDCl₃) δ: 142.3, 128.3, 127.4, 127.2, 65.7, 62.2, 55.3, 53.3 (broaden), 46.1, 34.7; IR (neat, cm⁻¹) 2930, 2789, 1454, 1357, 1282, 1164, 1132, 1117, 1033, 1011, 910, 837, 763, 703, 608, 566; HRMS (DART) caleed for C₁₄H₂₄N₃ [M + H]⁺ 234.29702, found 234.19794; [α]D²⁰ = −93.04 (c 1.86, CHCl₃).

(S)-N,4-dimethyl-1-(piperidin-1-yl)pentan-2-amine (L10); Colorless oix; ¹H NMR (600 MHz, CDCl₃) δ: 2.56-2.35 (6H, m), 2.28-2.15 (4H, m), 2.00 (1H, s), 1.69-1.61 (1H, m), 1.59-1.50 (4H, m), 1.42-1.33 (3H, m), 1.10-1.03 (1H, m), 0.93-0.87 (6H, m); ¹³C NMR (150 MHz, CDCl₃) δ:63.8, 54.9, 54.2, 42.1, 34.1, 26.1, 24.9, 24.5, 23.5, 22.6; IR (neat, cm⁻¹) 2933, 2785, 1468, 1442, 1365, 1302, 1155, 1121, 1105, 1040, 992, 780, 418; HRMS (DART) caleed for C₁₂H₂₇N₂ [M + H]⁺ 199.21742, found 199.21766; [α]D²⁰ = +96.98 (c 1.33, CHCl₃).
(R)-2-(meso-3,5-dimethylpiperidin-1-yl)-N-methyl-1-phenylethan-1-amine  (L17); Colorless oil; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.35-7.32 (4H, m), 7.25-7.23 (1H, m), 3.63 (1H, dd, $J = 11.34$, 3.40 Hz), 2.97 (1H, dt, $J = 10.77$, 1.70 Hz), 2.71 (1H, dt, $J = 10.58$, 1.56 Hz), 2.47 (1H, dd, $J = 12.47$, 10.77 Hz), 2.34-2.30 (4H, m), 2.24 (1H, dd, $J = 12.75$, 3.12 Hz), 1.76-1.58 (4H, m), 1.37 (1H, t, $J = 11.05$ Hz), 0.88 (3H, d, $J = 6.24$ Hz), 0.82 (3H, d, $J = 6.24$ Hz), 0.51 (1H, q, $J = 12.28$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 142.8, 128.3, 127.3, 127.0, 66.2, 63.7, 62.5, 60.2, 42.3, 34.7, 31.3, 31.2, 19.7, 19.5; IR (neat, cm$^{-1}$) 2949, 2785, 1454, 1354, 1312, 1191, 1137, 1080, 1023, 881, 755, 700, 635, 576, 501; HRMS (DART) calcd for C$_{16}$H$_{20}$N$_2$ [M + H]$^+$ 247.21742, found 247.21673; $[\alpha]_D^{20} = -83.14$ (c 1.33, CHCl$_3$).

(R)-2-(4-ethylpiperazin-1-yl)-N-methyl-1-phenylethan-1-amine  (L19); Colorless solid; Mp 51–55 ºC; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.34-7.32 (4H, m), 7.26-7.23 (1H, m), 3.62 (1H, dd, $J = 11.00$, 3.44 Hz), 2.67-2.26 (16H, m), 1.09 (3H, t, $J = 7.22$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 142.4, 128.3, 127.4, 127.1, 65.8, 62.1, 53.3 (broaden), 52.9, 52.3, 34.7, 12.0; IR (neat, cm$^{-1}$) 2942, 2809, 1448, 1350, 1290, 1162, 1121, 1011, 837, 757, 701, 640, 606, 563, 514; HRMS (DART) calcd for C$_{15}$H$_{26}$N$_3$ [M + H]$^+$ 248.21267, found 248.21301; $[\alpha]_D^{20} = -73.42$ (c 2.19, CHCl$_3$).

(R)-2-(4-cyclohexyl-1-yl)-N-methyl-1-phenylethan-1-amine  (L20); Colorless solid; Mp 56–60 ºC; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.34-7.32 (4H, m), 7.26-7.21 (2H, m), 3.61 (1H, dd, $J = 11.00$, 2.75 Hz), 2.62-2.17 (14H, m), 1.90-1.62 (6H, m), 1.24-1.20 (4H, m), 1.14-1.03 (1H, m); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 142.5, 128.3, 127.4, 127.1, 65.9, 63.5, 62.2, 49.1, 34.7, 29.1, 29.0, 26.3, 25.9; IR (neat, cm$^{-1}$) 2926, 2853, 2809, 1452, 1345, 1292, 1157, 1122, 1052, 1008, 979, 754, 701; HRMS (DART) calcd for C$_{19}$H$_{25}$N$_3$ [M + H]$^+$ 302.25962, found 302.25934; $[\alpha]_D^{20} = -54.82$ (c 1.05, CHCl$_3$).

(R)-2-(4-(tert-butyl)piperazin-1-yl)-N-methyl-1-phenylethan-1-amine  (L21); Colorless solid; Mp 58–64 ºC; $[\alpha]_D^{20} = -66.02$ (c 1.20, CHCl$_3$); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.34-7.32 (4H, m), 7.26-7.24 (1H, m), 3.61 (1H, dd, $J = 11.00$, 3.44 Hz), 2.65-2.26 (14H, m), 1.09 (9H, s.); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 142.5, 128.3, 127.4, 127.1, 65.8, 62.2, 53.9 (broaden), 45.8, 34.7, 25.8; IR (neat, cm$^{-1}$) 2966, 2938, 2803, 1438, 1357, 1297, 1207, 1128, 1010, 967, 907, 838, 753, 728, 700, 601, 494; HRMS (DART) calcd for C$_{17}$H$_{30}$N$_3$ [M + H]$^+$ 276.24397, found 276.24364.
(R)-N-methyl-2-(4-methylpiperidin-1-yl)-1-phenylethan-1-amine (L22): Colorless oil; 1H NMR (500 MHz, CDCl3) δ: 7.36-7.30 (4H, m), 7.25-7.23 (1H, m), 3.61 (1H, dd, J = 10.77, 3.40 Hz), 3.03 (1H, d, J = 11.34 Hz), 2.47 (1H, dd, J = 12.47, 11.34 Hz), 2.29-2.25 (5H, m), 2.10 (1H, td, J = 11.34, 2.46 Hz), 1.85 (1H, td, J = 11.48, 2.65 Hz), 1.66-1.56 (2H, m), 1.36-1.17 (3H, m), 0.92 (3H, d, J = 6.24 Hz); 13C NMR (125 MHz, CDCl3) δ: 142.8, 128.3, 127.4, 127.0, 66.3, 62.5, 55.9, 52.5, 34.8, 34.6, 34.5, 30.9, 21.9; IR (neat, cm⁻¹) 2922, 2788, 1442, 1351, 1288, 1142, 1083, 1025, 977, 911, 837, 754, 700, 637, 603; HRMS (DART) calcd for C₁₅H₂₅N₂ [M + H]+ 233.20177, found 233.20201; [α]D²⁰ = -90.42 (c 1.12, CHCl₃).

Preparation of chiral ligands L11-L13

Diamine S9 was synthesized according to the literature and was converted to the desired ligands L11-L13. To a mixture of diamine S9 (5.0 mmol), triethylamine (25 mmol), and DCM (25 mL), the corresponding alkanoyl chloride (6.0 mmol) was added. Then, the reaction mixture was stirred overnight at room temperature and quenched with saturated NaHCO₃. Subsequently, the mixture was extracted with DCM (20 mL x 3), and the combined organic layer was dried over Na₂SO₄. After filtration and concentration under reduced pressure, the crude product S10 was obtained and used without further purification in the next step.

The crude product S10 dissolved in THF (5.0 mL) was added to dispersion of LiAlH₄ (20 mmol) in THF (5.0 mL) at 0 °C. Then, the reaction mixture was refluxed overnight and quenched with saturated Na₂SO₄. After filtration through a Celite pad, the crude product obtained was distilled to afford the desired amine. Structure of L13 was confirmed by comparison with data shown in the literature.

(R)-N-ethyl-1-phenyl-2-(piperidin-1-yl)ethan-1-amine (L11): The title compound is known as its racemic form. The structure was confirmed by comparison with data shown in the literature. [α]D²⁰ = -97.62 (c 1.07, CHCl₃).

(R)-N-propyl-1-phenyl-2-(piperidin-1-yl)ethan-1-amine (L12): Colorless oil; 1H NMR (500 MHz, CDCl3) δ: 7.37 (2H, d, J = 7.37 Hz), 7.31 (2H, t, J = 7.37 Hz), 7.24 (1H, q, J = 6.99 Hz), 3.75 (1H, dd, J = 11.34, 3.40 Hz), 2.55-2.24 (9H, m), 1.65-1.43 (8H, m), 0.89 (3H, t, J = 7.37 Hz); 13C NMR (125 MHz, CDCl3) δ: 143.4, 128.2, 127.3, 126.8, 66.6, 60.0, 54.6, 49.8, 26.2, 24.5, 23.1, 11.8; IR (neat, cm⁻¹) 2933, 2799, 1452, 1357, 1301,
1154, 1110, 994, 865, 753, 700, 627, 583, 528; HRMS (DART) calcd for C_{16}H_{27}N_{2} [M + H]^{+} 247.21742, found 247.21691; \([\alpha]^{20}_{D} = -94.91\) (c 1.13, CHCl_{3}).
2-4. Optimization

**General procedure of initial investigations (Supplementary Table 1)**

A mixed base (KO'Bu 5.6 mg, 5.0 x 10^{-2} mmol; LiTMP 7.4 mg, 5.0 x 10^{-2} mmol) or KCH₂SiMe₃ (6.3 mg, 5.0 x 10^{-2} mmol) was placed in a flame-dried 10 mL flask inside a glove box filled with argon. The flask was cooled to −78 °C, then the corresponding ligand (5.5 x 10^{-2} mmol) dissolved in the employed solvent (0.40 mL) was added. When TBME was employed as a solvent, toluene (63.8 μL, 0.60 mmol) was also introduced into the flask. After the mixture was stirred for 30 min at the same temperature, p-methoxycumylimine 1a (126.7 mg, 0.50 mmol) dissolved in the solvent (0.60 mL) was successively introduced into the flask via a well-dried cannula, and the whole mixture was stirred for 18 h at the same temperature. The reaction was quenched by adding a few drops of MeOH, and the obtained mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the obtained crude product was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa. The enantioselectivity was determined by HPLC.

**General procedure of catalyst preparation conditions (Supplementary Table 2)**

A mixed base (KO'Bu 5.6 mg, 5.0 x 10^{-2} mmol; LiTMP 7.4 mg, 5.0 x 10^{-2} mmol) or KCH₂SiMe₃ (6.3 mg, 5.0 x 10^{-2} mmol) was placed in a flame-dried 10 mL flask inside a glove box filled with argon. After the flask was cooled to −40 °C, the corresponding amine ligand L (5.5 x 10^{-2} mmol) in toluene (0.40 mL) was added, and the mixture was stirred at the same temperature for 30 minutes. Subsequently, the flask was cooled to −78 °C, and imine 1a (126.7 mg, 0.500 mmol) dissolved in toluene (0.60 mL) was...
successively introduced into the flask via a well-dried cannula. After the whole mixture was stirred for 18 h at the same temperature, the reaction was quenched by adding a few drops of MeOH, and the obtained mixture was extracted with DCM (10 mL x 3), then combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the obtained crude product was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa. The enantioselectivities were determined by HPLC.

**General procedure for investigation of additives (Table 2)**

KCH₂SiMe₃ (6.3 mg, 5.0 x 10⁻² mmol) and the employed additive (5.0 x 10⁻² mmol) were placed in a flame-dried 10 mL flask inside a glove box filled with argon. After the flask was cooled to the corresponding temperature, the corresponding amine ligand L₆ (12.8 mg, 5.5 x 10⁻² mmol) in toluene (0.40 mL) was added, and the mixture was stirred at –40 ℃ for 30 minutes. Subsequently, the flask was cooled to –78 ℃, and imine 1a (126.7 mg, 0.500 mmol) dissolved in toluene (0.60 mL) was successively introduced into the flask via a well-dried cannula. After the whole mixture was stirred for 18 h at the same temperature, the reaction was quenched by adding a few drops of MeOH, and the obtained mixture was extracted with DCM (10 mL x 3), then combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the obtained crude product was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa. The enantioselectivities were determined by HPLC.
2-5. Substrate scope

Experimental procedure of the catalytic asymmetric addition reaction (Figure 1)

KCH$_2$SiMe$_3$ (9.6 mg, 7.5 x 10$^{-2}$ mmol) and KHMDS (15.0 mg, 7.5 x 10$^{-2}$ mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to –40 ºC, then diamine ligand L6 (19.4 mg, 8.3 x 10$^{-2}$ mmol) in toluene (0.80 mL) was added, and the chiral base mixture was stirred for 30 min at the same temperature. After the flask was cooled at –78 ºC, p-methoxycumylimine 1a (253.4 mg, 1.00 mmol) dissolved in toluene (1.20 mL) was successively introduced via a well-dried cannula, and the whole mixture was stirred for 18 h at the same temperature. After the reaction was quenched by adding water, the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired adduct 3. As for 3aa, 3ea, 3fa, and 3ga, the enantiopurities could be enhanced by recrystallization. After a tiny amount of the obtained products was used for characterization, the remaining parts were employed for the recrystallization. The recovery yields were calculated based on the remaining parts.

In order to determine the absolute configuration of 3aa, it was derivatized to the corresponding amide via removal of PMC group and typical amidation as shown below. Those of the other adducts were determined as analogies.

![Diagram](Image)

Experimental procedure of the catalytic asymmetric addition reaction in cumene solvent (Figure 1, for 3ad, 3ae, 3af)

KCH$_2$SiMe$_3$ (12.3 mg, 0.100 mmol) and KHMDS (20.0 mg, 0.100 mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to –40 ºC, and cumene (0.20 mL) was added. Then alkylarene (2.5 mmol) was introduced into the flask, and diamine ligand L6 (25.7 mg, 0.110 mmol) in cumene (0.20 mL) was added, and the chiral base mixture was stirred for 30 min at the same temperature. After the flask was cooled at –60 ºC, p-methoxycumylimine 1a (126.7 mg, 0.5000 mmol) dissolved in cumene (0.60 mL) was successively introduced via a well-dried cannula, and the whole mixture was stirred for 18 h at the same temperature. After the reaction was quenched by adding water, the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired adduct 3.
(S)-N-(1,2-diphenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3aa); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.\(^5\) The product obtained in the gram-scale reaction was used for the recrystallization to enhance the enantiopurity (the result is shown in its procedure). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.25-7.15 (8H, m), 6.94 (2H, td, $J = 7.37$, 1.70 Hz), 6.69 (2H, td, $J = 6.09$, 3.59 Hz), 3.79 (3H, s), 3.55 (1H, dd, $J = 9.15$, 5.15 Hz), 2.78 (1H, dd, $J = 13.60$, 5.10 Hz), 2.67 (1H, dd, $J = 13.60$, 9.07 Hz), 1.75 (1H, s), 1.21 (3H, s), 1.07 (3H, s); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 157.7, 147.3, 140.1, 138.9, 129.5, 128.3, 128.0, 127.1, 126.9, 126.4, 126.3, 113.1, 59.8, 56.0, 55.2, 46.9, 32.4, 27.9; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-PhCD column (20 mM KH$_2$PO$_4$:MeCN = 75:25, 1.0 mL/min, 210 nm, tR = 42.4 min ($R$), 47.6 min ($S$)); $[\alpha]_D^{20} = -47.12$ (99% ee, c 0.63, CHCl$_3$).

(S)-N-(1-((tert-butyl)phenyl)-2-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3ba); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.\(^5\) $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.24-7.22 (5H, m), 7.16 (2H, d, $J = 7.94$ Hz), 7.01 (2H, dd, $J = 7.65$, 1.42 Hz), 6.91 (2H, d, $J = 8.50$ Hz), 6.67 (2H, d, $J = 8.50$ Hz), 3.79 (3H, s), 3.53 (1H, dd, $J = 4.72$, 2.36 Hz), 2.79 (1H, dd, $J = 13.60$, 5.10 Hz), 2.65 (1H, dd, $J = 13.60$, 9.07 Hz), 1.74 (1H, s), 1.31 (9H, s), 1.12 (3H, s), 1.06 (3H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 157.6, 149.2, 144.1, 140.1, 139.2, 129.5, 128.2, 127.0, 126.7, 126.2, 124.8, 113.0, 59.4, 55.9, 55.1, 46.8, 34.4, 32.2, 31.5, 28.1; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-OVM column (20 mM KH$_2$PO$_4$:MeCN = 85:15, 1.0 mL/min, 210 nm, tR = 5.8 min ($R$), 7.7 min ($S$)); $[\alpha]_D^{20} = -45.86$ (89% ee, c 1.47, CHCl$_3$).

(S)-N-(1-(4-isopropylphenyl)-2-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3ca); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.\(^5\) $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.23-7.21 (3H, m), 7.16 (2H, d, $J = 8.50$ Hz), 7.09 (2H, d, $J = 7.94$ Hz), 7.00 (2H, d, $J = 6.24$ Hz), 6.91 (2H, d, $J = 9.07$ Hz), 6.67 (2H, d, $J = 8.50$ Hz), 3.79 (3H, s), 3.53 (1H, dd, $J = 4.72$, 2.36 Hz), 2.91-2.83 (1H, m), 2.78 (1H, dd, $J = 13.32$, 4.82 Hz), 2.65 (1H, dd, $J = 13.32$, 9.35 Hz), 1.58 (1H, s), 1.23-1.21 (9H, m), 1.06 (3H, s); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 157.6, 146.9, 144.5, 140.1, 139.2, 129.5, 128.3, 127.0, 126.9, 126.2, 126.0, 113.0, 59.5, 56.0, 55.2, 46.8, 33.7, 32.3, 28.0, 24.08, 24.06; The ee value was evaluated after derivatization to 4ca.
(S)-N-(1-(4-ethylphenyl)-2-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3da): Colorless solid; Mp: 65-67 °C; 1H NMR (500 MHz, CDCl3) δ: 7.24-20 (3H, m), 7.16 (2H, d, J = 7.94 Hz), 7.07 (2H, td, J = 7.94 Hz), 6.99 (2H, d, J = 6.24 Hz), 6.92 (2H, d, J = 8.50 Hz), 6.68 (2H, d, J = 9.07 Hz), 3.79 (3H, s), 3.53 (1H, dd, J = 4.72, 2.36 Hz), 2.78 (1H, dd, J = 13.32, 4.82 Hz), 2.65-2.62 (3H, m), 1.73 (1H, s), 1.23-1.22 (6H, m), 1.07 (3H, s); 13C NMR (150 MHz, CDCl3) δ: 157.6, 144.5, 142.3, 140.2, 130.1, 129.5, 128.3, 127.5, 127.5, 127.00, 126.95, 126.2, 113.0, 59.5, 56.0, 55.2, 46.9, 32.4, 28.4, 28.0, 15.5; IR (neat, cm⁻¹) 2970, 1608, 1579, 1508, 1457, 1300, 1251, 1180, 1031, 825, 737, 697, 548; HRMS (DART)caled for C26H32NO [M + H]+ 374.24839, found 374.24985; The ee value was evaluated after derivatization to 4da.

(5)-N-(1-[[1,1’-biphenyl]-4-yl]-2-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3ea): The enantiopurity was enhanced by recrystallization (99% ee, 59% recovery). Colorless solid, Mp: 78-81 °C; 1H NMR (500 MHz, CDCl3) δ: 7.60 (2H, d, J = 8.50 Hz), 7.49 (2H, d, J = 7.94 Hz), 7.43 (2H, t, J = 7.65 Hz), 7.32-7.22 (6H, m), 7.02 (2H, d, J = 7.94 Hz), 6.95 (2H, d, J = 8.50 Hz), 6.69 (2H, d, J = 8.50 Hz), 3.79 (3H, s), 3.61 (1H, dd, J = 4.72, 2.36 Hz), 2.83 (1H, dd, J = 13.32, 5.38 Hz), 2.70 (1H, dd, J = 13.60, 9.07 Hz), 1.80 (1H, s), 1.24 (3H, s), 1.11 (3H, s); 13C NMR (125 MHz, CDCl3) δ: 157.7, 146.5, 141.1, 140.0, 139.2, 138.9, 138.9, 129.5, 128.7, 128.3, 128.0, 127.8, 127.6, 127.5, 126.9, 126.7, 126.3, 113.1, 59.5, 56.1, 55.2, 46.8, 32.3, 28.1; IR (neat, cm⁻¹) 3022, 1602, 1508, 1482, 1105, 1248, 1180, 1028, 825, 763, 725, 691, 614, 586, 554, 526, 491; HRMS (DART)caled for C30H32NO [M + H]+ 422.24839, found 422.24712; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-OVM column (20 mM K2HPO4;MeCN = 85:15, 1.0 mL/min, 210 nm, tR = 16.0 min (S), 70.0 min (R)); [α]D20 = -71.73 (99% ee, c 0.46, CHCl3).

(S)-2-(4-methoxyphenyl)-N-(1-(naphthalen-1-yl)-2-phenylethyl)propan-2-amine (3fa): The enantiopurity was enhanced by recrystallization (>99% ee, 71% recovery). Colorless solid, Mp: 104-108 °C; 1H NMR (500 MHz, CDCl3) δ: 7.95-7.89 (2H, m, broaden), 7.72 (1H, d, J = 7.94 Hz), 7.46-7.43 (3H, m, broaden), 7.27-7.21 (4H, overlapped with CHCl3), 7.05 (2H, d, J = 5.67 Hz), 6.91 (2H, d, J = 9.07 Hz), 6.65 (2H, d, J = 8.50 Hz), 4.47 (1H, s, broaden), 3.79 (3H, s), 2.97 (1H, d, J = 11.34), 2.65 (1H, s, broaden), 1.90 (1H, s), 1.22 (3H, s), 0.99 (3H, s); 13C NMR (150 MHz, CDCl3) δ: 157.6, 143.3, 140.1, 139.1, 133.9, 130.5, 129.4, 128.9, 128.4, 126.9, 126.7, 126.3, 125.54, 125.48, 125.0, 124.9, 122.0, 113.1, 56.1, 55.2, 53.4, 45.8, 32.1, 27.4; IR (neat, cm⁻¹) 1608, 1508, 1462, 1374, 1302, 1251, 1180, 1034, 831, 803, 785, 743, 697, 622, 517, 500, 431; HRMS (DART)caled for C28H32NO [M + H]+ 396.23274, found 396.23452; HPLC analysis using Shinwa Chemical Industries Ltd.
ULTRON ES-OVM column (20 mM KH₂PO₄:MeCN = 80:20, 1.0 mL/min, 210 nm, tR = 4.6 min (R), 5.7 min (S)); [α]D²⁰ = -37.61 (>99% ee, c 0.60, CHCl₃).

**S)-2-(4-methoxyphenyl)-N-(1-(naphthalen-2-yl)-2-phenylethyl)propan-2-amine (3ga)**: The structure was confirmed by comparison with data of ¹H and ¹³C NMR shown in literature which our group reported.⁵ The enantiopurity was enhanced by recrystallization (99% ee, 24% recovery). ¹H NMR (500 MHz, CDCl₃) δ: 7.80-7.75 (3H, m), 7.59 (1H, s), 7.52 (1H, d, J = 8.50 Hz), 7.43-7.42 (2H, m), 7.29-7.20 (3H, m), 7.02 (2H, d, J = 7.37 Hz), 6.93 (2H, d, J = 9.07 Hz), 6.68 (2H, d, J = 8.50 Hz), 3.77 (3H, s), 3.73 (1H, dd, J = 8.79, 5.38 Hz), 2.86 (1H, dd, J = 13.60, 5.10 Hz), 2.75 (1H, dd, J = 13.60, 9.07 Hz), 1.87 (1H, s), 1.23 (3H, s), 1.07 (3H, s); ¹³C NMR (125 MHz, CDCl₃) δ: 157.7, 144.9, 140.0, 138.9, 133.4, 132.6, 129.5, 128.3, 127.67, 127.65, 127.58, 126.9, 126.3, 125.8, 125.6, 125.2, 113.1, 59.9, 56.1, 55.2, 46.7, 32.3, 28.0; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-OVM column (20 mM KH₂PO₄:MeCN = 85:15, 1.0 mL/min, 210 nm, tR = 51.4 min (S), 47.1 min (R)); [α]D²⁰ = -81.11 (99% ee, c 0.51, CHCl₃).

**S)-2-(4-methoxyphenyl)-N-(1-(4-methoxyphenyl)-2-phenylethyl)propan-2-amine (3ha)**: The structure was confirmed by comparison with data of ¹H and ¹³C NMR shown in literature which our group reported.⁵ ¹H NMR (500 MHz, CDCl₃) δ: 7.24-7.16 (3H, m), 7.14 (2H, d, J = 8.25 Hz), 6.97 (2H, d, J = 6.19 Hz), 6.93 (2H, d, J = 8.94 Hz), 6.78 (2H, d, J = 8.25 Hz), 6.70 (2H, d, J = 8.94 Hz), 3.79 (6H, m), 3.50 (1H, dd, J = 8.25, 5.50 Hz), 2.76 (1H, dd, J = 6.19, 3.09 Hz), 2.66 (1H, dd, J = 13.75, 8.94 Hz), 1.56 (1H, s), 1.21 (3H, s), 1.07 (3H, s); ¹³C NMR (150 MHz, CDCl₃) δ: 158.2, 157.7, 140.1, 139.3, 139.1, 129.5, 128.2, 128.1, 126.9, 126.2, 113.4, 113.1, 59.1, 56.0, 55.21, 55.19, 46.9, 32.4, 28.0; The ee value was evaluated after derivatization to 4ha.

**S)-2-(4-methoxyphenyl)-N-(1-(3-methoxyphenyl)-2-phenylethyl)propan-2-amine (3ia)**: The structure was confirmed by comparison with data of ¹H and ¹³C NMR shown in literature which our group reported.⁵ ¹H NMR (500 MHz, CDCl₃) δ: 7.24-7.22 (3H, m), 6.99 (2H, dd, J = 7.37, 1.70 Hz), 6.93 (2H, d, J = 9.07 Hz), 6.84-6.82 (2H, m), 6.72-6.69 (3H, m), 3.79 (6H, m), 3.53 (1H, dd, J = 4.72, 2.36 Hz), 2.79 (1H, dd, J = 13.60, 5.10 Hz), 2.66 (1H, dd, J = 11.34, 5.67 Hz), 1.62 (1H, s), 1.21 (3H, s), 1.09 (3H, s); ¹³C NMR (150 MHz, CDCl₃) δ: 159.4, 157.7, 149.2, 140.0, 138.9, 129.5, 128.9, 128.3, 126.9, 126.3, 119.6, 113.1, 112.6, 111.9, 59.8, 56.0, 55.2, 46.8, 32.3, 27.9; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-OVM column (20 mM KH₂PO₄:MeCN = 80:20, 1.0 mL/min, 210 nm, tR = 2.6 min (R), 2.9 min (S)); [α]D²⁰ = -34.12 (73% ee, c 1.33, CHCl₃).
(S)-2-(4-methoxyphenyl)-N-(1-(2-methoxyphenyl)-2-phenylethyl)propan-2-amine (3ja); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported. $^5$ $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.38 (1H, s), 7.20-7.12 (4H, m), 7.09 (2H, d, J = 9.07 Hz), 6.98 (2H, d, J = 6.80 Hz), 6.86 (1H, t, J = 7.37 Hz), 6.77 (1H, d, J = 7.94 Hz), 6.68 (2H, d, J = 9.07 Hz), 4.06 (1H, s), 3.77 (3H, s), 2.86 (1H, dd, J = 13.32, 5.38 Hz), 2.61 (1H, dd, J = 10.20, 5.10 Hz), 1.75 (1H, s), 1.18 (3H, s), 1.09 (3H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) δ: 165.3, 156.3, 140.8, 139.8, 135.5, 129.5, 128.5 (broaden), 128.0, 126.98, 126.95, 125.9, 120.3, 112.9, 110.3, 55.9, 55.24, 55.18, 45.0, 31.7, 27.9; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-0V column (20 mM KH$_2$PO$_4$:MeCN = 80:20, 1.0 mL/min, 210 nm, tR = 2.9 min (S), 4.7 min (R)); [α]$^D_{20}$ = −24.8 (84% ee, c 1.71, CHCl$_3$).

(S)-2-(4-methoxyphenyl)-N-(1-(4-(methylthio)phenyl)-2-phenylethyl)propan-2-amine (3ka); Slightly yellow solid, Mp = 86-88 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.24-7.19 (3H, m), 7.17-7.14 (4H, m), 6.97 (2H, dd, J = 7.37, 1.70 Hz), 6.92 (2H, d, J = 8.50 Hz), 6.69 (2H, d, J = 9.07 Hz), 3.79 (3H, s), 3.52 (1H, dd, J = 8.79, 5.38 Hz), 2.75 (1H, dd, J = 13.60, 5.10 Hz), 2.65 (1H, dd, J = 13.60, 9.07 Hz), 2.47 (3H, s), 1.75 (1H, s), 1.21 (3H, s), 1.07 (3H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) δ: 157.7, 144.5, 140.0, 138.8, 135.8, 129.4, 128.3, 127.7, 126.9, 126.5, 126.3, 113.1, 59.3, 56.0, 55.2, 46.8, 32.3, 28.1, 16.1; IR (neat, cm$^{-1}$) 2976, 1605, 1508, 1494, 1434, 1297, 1248, 1180, 1094, 1028, 825, 700, 646, 543; HRMS (DART) calcd for C$_{25}$H$_{30}$NOS [M + H]$^+$ 392.20481, found 392.20409; The ee value was evaluated after derivatization to 4ka.

(S)-4-(1-((2-(4-methoxyphenyl)propan-2-yl)amino)-2-phenylethyl)-N,N-dimethylaniline (3la); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported. $^5$ $^1$H NMR (600 MHz, CDCl$_3$) δ: 7.23-7.20 (3H, m), 7.10 (2H, d, J = 8.94 Hz), 6.99 (2H, d, J = 6.19 Hz), 6.93 (2H, d, J = 8.94 Hz), 6.70 (2H, d, J = 8.94 Hz), 6.65 (2H, d, J = 8.94 Hz), 3.80 (3H, s), 3.46 (1H, d, J = 4.81 Hz), 2.92 (6H, s), 2.78 (1H, dd, J = 13.75, 5.50 Hz), 2.67 (1H, dd, J = 13.06, 8.94 Hz), 1.73 (1H, s), 1.22 (3H, s), 1.09 (3H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) δ: 157.6, 149.4, 140.2, 139.4, 129.5, 128.2, 127.8, 127.0, 126.1, 113.0, 112.4, 59.1, 56.0, 55.2, 46.9, 40.8, 32.5, 27.9; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-0V column (20 mM KH$_2$PO$_4$:MeCN = 85:15, 1.0 mL/min, 210 nm, tR = 3.1 min (R), 4.9 min (S)); [α]$^D_{20}$ = −36.33 (99% ee, c 0.51, CHCl$_3$).
(S)-N-(2-(4-ethylphenyl)-1-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine (3ab); The structure was confirmed by comparison with data of \(^1\)H and \(^13\)C NMR shown in literature which our group reported.\(^5\) \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\): 7.26-7.23 (4H, m), 7.18-7.16 (1H, m), 7.07 (2H, d, \(J = 7.56\) Hz), 6.92-6.90 (4H, m), 6.67 (2H, d, \(J = 8.25\) Hz), 3.79 (3H, s), 3.54 (1H, dd, \(J = 4.58, 2.29\) Hz), 2.75 (1H, dd, \(J = 13.40, 5.15\) Hz), 2.64-2.62 (3H, m), 1.71 (1H, s), 1.24 (3H, t, \(J = 7.56\) Hz), 1.20 (3H, s), 1.06 (3H, s); \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\): 157.6, 147.5, 142.2, 140.1, 136.0, 129.4, 128.0, 127.8, 127.1, 126.9, 126.3, 113.0, 59.8, 56.0, 55.2, 46.4, 32.5, 28.5, 27.9, 15.8; The ee value was evaluated after derivatization to 4ab.

(ISR,2RS)-N-(2-(4-methoxyphenyl)propan-2-yl)-1,2-diphenylpropan-1-amine (3ac); The structure was confirmed by comparison with data of \(^1\)H and \(^13\)C NMR shown in literature which our group reported.\(^5\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 7.26-7.11 (8H, m), 7.05 (2H, d, \(J = 6.87\) Hz), 6.72 (2H, d, \(J = 8.94\) Hz), 6.63 (2H, d, \(J = 8.25\) Hz), 3.74 (3H, s), 3.21 (1H, d, \(J = 8.94\) Hz), 2.64 (1H, dt, \(J = 16.50, 6.87\) Hz), 1.64 (1H, s), 1.00 (3H, s), 0.85 (3H, s), 0.73 (3H, d, \(J = 6.87\) Hz); \(^13\)C NMR (CDCl\(_3\), 150 MHz) \(\delta\): 157.6, 145.8, 144.7, 139.7, 128.4, 128.3, 128.1, 127.8, 127.1, 126.1, 126.5, 112.9, 64.5, 55.7, 55.2, 47.8, 32.4, 27.6, 19.3; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-PhCD column (20 mM KH\(_2\)PO\(_4\):MeCN = 60:40, 2.0 mL/min, 210 nm, tR = 12.4 min (IR,2S), 31.3 min (IR,3S)).

(S)-2-(4-methoxyphenyl)-N-(1-phenyl-2-(p-tolyl)ethyl)propan-2-amine (3ad); The structure was confirmed by comparison with data of \(^1\)H and \(^13\)C NMR shown in literature which our group reported.\(^5\) \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\): 7.25-7.21 (4H, m), 7.17-7.15 (1H, m), 7.02 (2H, d, \(J = 7.56\) Hz), 6.92 (2H, d, \(J = 8.25\) Hz), 6.86 (2H, d, \(J = 7.56\) Hz), 6.67 (2H, d, \(J = 8.94\) Hz), 3.78 (3H, s), 3.52 (1H, dd, \(J = 4.81, 2.41\) Hz), 2.74 (1H, dd, \(J = 13.40, 5.15\) Hz), 2.61 (1H, dd, \(J = 13.75, 8.94\) Hz), 2.32 (3H, s), 1.75 (1H, s), 1.19 (3H, s), 1.05 (3H, s); \(^13\)C NMR (CDCl\(_3\), 150 MHz) \(\delta\): 157.6, 147.4, 140.1, 135.72, 135.67, 129.3, 128.9, 128.0, 127.1, 126.9, 126.3, 113.0, 59.7, 56.0, 55.1, 46.4, 32.4, 27.9, 21.0; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-PhCD column (20 mM KH\(_2\)PO\(_4\):MeCN = 75:25, 1.0 mL/min, 210 nm, tR = 48.1 min (R), 68.7 min (S)); \([\alpha]_{D}^{20} = -10.57\) (68% ee, c 1.01, CHCl\(_3\)).
(S)-2-(4-methoxyphenyl)-N-(1-phenyl-2-(m-tolyl)ethyl)propan-2-amine (3ae): The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.$^5$ $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.21-7.13 (4H, m), 7.11-7.04 (2H, m), 6.95 (1H, d, $J = 7.37$ Hz), 6.80 (2H, d, $J = 8.50$ Hz), 6.74 (1H, d, $J = 7.37$ Hz), 6.71 (1H, s), 6.59 (2H, d, $J = 9.07$ Hz), 3.70 (3H, s), 3.45 (1H, dd, $J = 4.72$, 2.36 Hz), 2.67 (1H, dd, $J = 13.32$, 9.35 Hz), 2.21 (3H, s), 1.71 (1H, s), 1.12 (3H, s), 0.97 (3H, s); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$: 157.6, 147.5, 140.0 138.7, 137.8, 130.2, 128.1, 128.0, 127.1, 127.0, 126.9, 126.5, 126.3, 113.0, 59.7, 56.0, 55.1, 46.8, 32.5, 27.8, 21.3; The ee value was evaluated after derivatization to 4ae.

(5)-2-(4-methoxyphenyl)-N-(1-phenyl-2-(o-tolyl)ethyl)propan-2-amine (3af): The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.$^5$ $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.18-7.14 (4H, m), 7.09 (1H, t, $J = 6.87$ Hz), 7.05 (1H, t, $J = 7.22$ Hz), 6.99 (2H, d, $J = 6.53$ Hz), 6.85 (1H, d, $J = 6.87$ Hz), 6.78 (2H, d, $J = 8.94$ Hz), 6.59 (2H, t, $J = 5.84$ Hz), 3.70 (3H, s), 3.44 (1H, dd, $J = 4.81$, 2.41 Hz), 2.70 (1H, dd, $J = 13.40$, 5.15 Hz), 2.59 (1H, dd, $J = 13.75$, 9.62 Hz), 1.95 (3H, s), 1.75 (1H, s), 1.13 (3H, s), 0.96 (3H, s); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$: 157.63, 147.7, 140.1, 135.72, 135.67, 129.3, 128.9, 128.0, 127.1, 126.9, 126.8, 126.5, 126.3, 125.6, 113.1; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-OVM column (20 mM KH$_2$PO$_4$:MeCN = 85:15, 1.0 mL/min, 210 nm, tR = 4.4 min (S), 6.3 min (R)); $[\alpha]_D^{20} = -57.45$ (75% ee, c 1.22, CHCl$_3$).

(S)-N-(2-(4-isopropylphenyl)-1-phenylethyl)-2-(4-methoxyphenyl)propan-2-amine  (3ah); The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in literature which our group reported.$^5$ $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.27-7.23 (4H, m), 7.17 (1H, t, $J = 7.22$ Hz), 7.11 (2H, d, $J = 8.25$ Hz), 6.94 (2H, d, $J = 8.25$ Hz), 6.86 (2H, d, $J = 8.25$ Hz), 6.66 (2H, d, $J = 8.25$ Hz), 3.78 (3H, s), 3.52 (1H, dd, $J = 4.81$, 2.41 Hz), 2.90 (1H, dd, $J = 27.49$, 13.75 Hz), 2.77-2.74 (1H, m), 2.62 (1H, dd, $J = 13.40$, 9.28 Hz), 1.81 (1H, s), 1.26 (6H, dd, $J = 3.44$, 1.72 Hz), 1.19 (3H, s), 1.05 (3H, s); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$: 157.6, 147.4, 140.1, 135.72, 135.67, 129.3, 128.9, 128.0, 127.1, 126.9, 126.3, 59.7, 56.0, 55.1, 46.4, 32.4, 27.9, 21.0; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-PhCD column (20 mM KH$_2$PO$_4$:MeCN = 70:30, 1.0 mL/min, 210 nm, tR = 53.8 min (R), 94.3 min (S)); $[\alpha]_D^{20} = +2.39$ (18% ee, c 1.39, CHCl$_3$).
2-6. Synthetic utility

2-6-1. Gram-scale reaction (Figure 2-a)

KCH$_2$TMS (94.7 mg, 0.750 mmol) and KHMDS (149.6 mg, 0.750 mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to −40 °C, and toluene (3.0 mL) was added followed by diamine ligand L$_6$ (193.7 mg, 0.830 mmol) dissolved in toluene (3.0 mL) was added. Subsequently, the mixture was stirred for 30 min at the same temperature. After the flask was cooled at −78 °C, toluene (4.0 mL) was added to the reaction mixture. Then, p-methoxycumylimine 1a (2.53 g, 0.500 mmol) dissolved in toluene (10.0 mL) was successively introduced via a well-dried cannula, and the whole mixture was stirred for 18 h at the same temperature. After the reaction was quenched by adding MeOH, the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the crude product obtained was purified by column chromatography (hexane-ethyl acetate) to afford the desired amine 3aa (3.09 g, 89% yield). The enantioselectivity was determined by HPLC (86% ee). The obtained product (3.09 g) was recrystallized in hexane-chloroform to enhance its enantiopurity (99% ee, 2.14 g, 69% recovery).

2-6-2. In situ preparation of imine (Figure 2-b)

p-Methoxycumylamine S1 (337.1 mg, 2.04 mmol), aldehyde (212.2 mg, 2.00 mmol), and pellet-type MS 4 Å (1.00 g) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. Toluene (1.0 mL) was introduced to the flask, and the reaction mixture was gently stirred for 18 h at room temperature with preventing the pellets of MS 4 Å from being broken. The obtained solution was directly used in the next step.

KCH$_2$TMS (18.9 mg, 0.150 mmol) and KHMDS (29.9 mg, 0.150 mmol) were placed in another flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to −40 °C, then diamine ligand L$_6$ (38.7 mg, 0.166 mmol) dissolved in toluene (1.20 mL) was added, and the chiral base mixture was stirred for 30 min at the same temperature. After the flask was cooled at −78 °C, toluene (0.80 mL) was added, and the imine solution prepared above was successively introduced via a well-dried cannula. The flask for imine preparation was rinsed with toluene (1.0 mL), and the solution was also added in the reaction mixture. The whole mixture was stirred for 18 h at the same temperature. After the reaction was quenched by adding MeOH, the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa (559.7 mg, 81% yield). The enantioselectivity was determined by HPLC (84% ee).
2-6-3. Removal of $p$-methoxy group (Figure 2-c)

$p$-Methoxycumylamine 3 was placed in a 10 mL flask, and TFA (2.0 mL per mmol of 3) was subsequently added to the flask. The mixture was heated to 50 °C and stirred for 12 h at the same temperature. Subsequently, water (1.0 mL per mmol of 3) was added to the flask, and the mixture was stirred for 15 min at the same temperature. After cooling to room temperature, the reaction was basified with 15% NaOH aq. and extracted with DCM (20 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and evaporation, the obtained crude was diluted with Et$_2$O, and was extracted with 1N HCl aq. (20 mL x 2). The combined aqueous layer was washed with Et$_2$O (10 mL x 2) and then was basified with 15% NaOH aq.. The basified aqueous layer was extracted with DCM (20 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, and concentrated under reduced vacuum after filtration to afford the desired almost pure primary amine 4. If the purity was not enough, the product was further purified by PTLC (Et$_2$O-Hexane-Et$_2$NH).

As for 4ba, 4ca, 4ia, and 4ja, the enantiopurities could be enhanced by recrystallization (in CPME-Acetone-EtOH) of the corresponding ammonium chloride salt formed with 1N HCl in Et$_2$O. After a tiny amount of the obtained products was used for characterization, the remaining parts were employed for the recrystallization. The recovery yields were calculated based on the remaining parts.

(S)-N-(1,2-diphenylethyl)-2-(4-methoxyphenyl)propan-2-amine (4aa); (S)-3aa (345.5 mg, 1.00 mmol, 99% ee) was used, and 4aa (179.2 mg, 91% yield, 99% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature which our group reported.$^5$ $^1$H NMR (600 MHz, CDCl$_3$) δ: 7.36-7.17 (10H, m), 4.19 (1H, dd, $J = 4.58, 2.29$ Hz), 3.01 (1H, dd, $J = 13.06, 4.81$ Hz), 2.82 (1H, dd, $J = 13.75, 8.94$ Hz), 1.50 (2H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) δ: 145.6, 139.1, 129.3, 128.4, 127.0, 126.4, 124.3, 57.5, 46.5; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:PrOH:Et$_2$NH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 7.6 min ($R$), 11.4 min ($S$)); [α]$^D_{20}$ = −0.27 (99% ee, c 1.36, CHCl$_3$).

(S)-1-(4-(tert-butyl)phenyl)-2-phenylethan-1-amine (4ba); 3ba (324.3 mg, 0.808 mmol, 89% ee) was used, and 4ba (132.8 mg, 65% yield, 89% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature.$^10$ The enantiopurity was enhanced by recrystallization of the corresponding ammonium chloride salt (>99% ee, 31% recovery). $^1$H NMR (600 MHz, CDCl$_3$) δ: 7.30-7.28 (2H, m), 7.25-7.21 (4H, m), 7.16-7.13 (3H, m), 4.10 (1H, dd, $J = 4.58, 2.29$ Hz), 2.96 (1H, dd,
(S)-1-(4-isopropylphenyl)-2-phenylethan-1-amine (4ca); 3ca (277.2 mg, 0.715 mmol) was used, and 4ca (135.5 mg, 79% yield, 89% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature. The enantiopurity was enhanced by recrystallization of the corresponding ammonium chloride salt (>99% ee, 15% recovery). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.30-7.28 (4H, m), 7.23-7.19 (5H, m), 4.17 (1H, dd, $J = 4.58, 2.29$ Hz), 3.02 (1H, dd, $J = 13.40, 8.59$ Hz), 1.63 (2H, s), 2.62 (2H, q, $J = 7.56$ Hz), 1.22 (3H, t, $J = 7.56$ Hz), 1.25 (6H, d, $J = 6.87$ Hz); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 147.7, 142.8, 139.2, 129.3, 128.4, 126.4, 126.3, 57.2, 46.3, 33.7, 24.0; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:PrOH:Et$_3$NH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 6.4 min (R), 6.7 min (S), using Daicel Chiralcel OD-RH column (for 4ba-HCl, 20 mM NaB(OH)$_2$/ MeCN = 60/40, 0.5 mL/min, 210 nm, tR = 79.3 min (R), 82.7 min (S)); [\(\alpha\)]$_D^{20} = +105.62$ (as 4ba-HCl, >99% ee, c 0.14, EtOH).

(S)-1-(4-ethylphenyl)-2-phenylethan-1-amine (4da); 3da (134.5 mg, 0.360 mmol) was used, and 4da (72.8 mg, 90% yield, 81% ee) was obtained. Colorless oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.32-7.15 (9H, m), 4.20 (1H, dd, $J = 8.25, 5.50$ Hz), 3.04 (1H, dd, $J = 13.75, 5.50$ Hz), 2.91 (1H, dd, $J = 13.40, 7.90$ Hz), 2.62 (2H, q, $J = 7.56$ Hz), 1.22 (3H, t, $J = 7.56$ Hz); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 143.2, 142.4, 139.1, 129.3, 128.4, 126.4, 126.3, 57.2, 46.3, 28.5, 15.5; IR (neat, cm$^{-1}$) 2965, 1602, 1511, 1494, 1077, 1031, 828, 700, 543; HRMS (Dart) calcd for C$_{16}$H$_{20}$N [M + H]$^+$ 226.15957, found 226.15966; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:PrOH:Et$_3$NH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 6.4 min (R), 7.5 min (S)); [\(\alpha\)]$_D^{20} = +16.38$ (84% ee, c 0.24, CHCl$_3$).

(S)-1-(4-methoxyphenyl)-2-phenylethan-1-amine (4ha); 3ha (256.7 mg, 0.684 mmol) was used, and 4ca (134.2 mg, 86% yield, 90% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.29-7.26 (4H, m), 7.21 (1H, t, $J = 7.56$ Hz), 7.16 (2H, d, $J = 7.56$ Hz), 6.86 (2H, d, $J = 8.25$ Hz), 4.15 (1H, dd, $J = 4.58, 2.29$ Hz), 3.80 (3H, s), 2.98 (1H, dd, $J = 13.06, 4.81$ Hz), 2.81 (1H, dd, $J = 13.40, 8.59$ Hz), 1.63 (2H, s); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 158.6, 139.1, 137.6, 129.3, 128.4, 127.5, 126.3, 113.7, 56.9, 55.3, 46.5; HPLC analysis using
(S)-1-(3-methoxyphenyl)-2-phenylethan-1-amine (4ia): 3ia (256.7 mg, 0.684 mmol, 76% ee) was used, and 4ia (76.8 mg, quant., 76% ee) was obtained. The enantiopurity was enhanced by recrystallization of the corresponding ammonium chloride salt (97% ee, 11% recovery). Colorless oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.30-7.17 (6H, m), 6.94-6.93 (2H, m), 6.80 (1H, dd, $J = 8.25, 2.06$ Hz), 4.18 (1H, dd, $J = 4.58, 2.29$ Hz), 3.79 (3H, s), 3.02 (1H, dd, $J = 13.40, 5.15$ Hz), 2.84 (1H, dd, $J = 13.40, 8.59$ Hz), 1.86 (2H, s); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 159.7, 146.9, 138.9, 129.4, 129.3, 128.4, 126.4, 118.8, 112.7, 111.9, 57.5, 55.2, 46.2; IR (neat, cm$^{-1}$) 3002, 1599, 1454, 1434, 1254, 1074, 1043, 871, 780, 697, 511, 468; HRMS (Dart) calcd for C$_{15}$H$_{18}$NO $[M + H]^+$ 228.13884, found 228.13884; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:$^3$PrOH:EtOH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 10.2 min (R), 13.0 min (S)); $[\alpha]_D^{20}$ = +110.66 (as 4ia-HCl, 97% ee, c 0.10, EtOH).

(S)-1-(2-methoxyphenyl)-2-phenylethan-1-amine (4ja): 3ja (335.3 mg, 0.893 mmol, 84% ee) was used, and 4ja (163.2 mg, 80% yield, 84% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature.$^{10}$ The enantiopurity was enhanced by recrystallization of the corresponding ammonium chloride salt (>99% ee, 37% recovery). $^1$H NMR (600 MHz, CDCl$_3$) $\delta$: 7.26 (1H, dd, $J = 7.56, 1.37$ Hz), 7.22-7.12 (6H, m), 6.86 (1H, t, $J = 7.90$ Hz), 6.81 (1H, d, $J = 8.25$ Hz), 4.40 (1H, dd, $J = 4.35, 2.18$ Hz), 3.77 (3H, s), 3.05 (1H, dd, $J = 13.75, 4.81$ Hz), 2.71 (1H, dd, $J = 13.06, 8.94$ Hz), 1.68 (2H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 156.7, 139.8, 133.5, 129.4, 128.3, 127.8, 126.7, 126.1, 120.6, 110.4, 55.3, 52.2, 44.2; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:$^3$PrOH:EtOH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 7.7 min (R), 8.1 min (S)); $[\alpha]_D^{20}$ = +90.76 (as 4ja-HCl, >99% ee, c 0.11, EtOH).

(S)-1-(4-(methylthio)phenyl)-2-phenylethan-1-amine (4ka): 3ka (308.9 mg, 0.789 mmol) was used, and 4ka (117.9 mg, 61% yield, 80% ee) was obtained. The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature.$^{10}$ $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 7.27-7.25 (5H, m), 7.21-7.19 (3H, m), 7.14 (2H, d, $J = 6.80$ Hz), 4.14 (1H, dd, $J = 4.53, 2.27$ Hz), 2.96 (1H, dd, $J = 13.32, 4.82$ Hz), 2.78 (1H, dd, $J = 13.32, 8.79$ Hz), 2.46 (3H, s), 1.52 (2H, s); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$: 142.7, 138.9, 136.8, 129.3, 128.4, 127.0, 126.8, 126.4, 57.1, 46.4, 16.1; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:$^3$PrOH:EtOH = 90:10:0.1, 1.0 mL/min, 254 nm, tR = 10.7 min (R), 11.8 min (S)); $[\alpha]_D^{20}$ = +106.44 (as 4ka-HCl, 84% ee, c 0.12, EtOH).
(S)-2-(4-ethylphenyl)-1-phenylethan-1-amine (4ab); 3ab (167.8 mg, 0.449 mmol) was used, and 4ab (63.4 mg, 65% yield, 62% ee) was obtained. Colorless oil; \(^{1}H\) NMR (500 MHz, CDCl\(_3\)) \(\delta: 7.38-7.07 (9H, m), 4.19 (1H, dd, J = 4.53, 2.27 Hz), 3.01 (1H, dd, \(J = 13.60, 5.10\) Hz), 2.86 (1H, dd, \(J = 13.32, 8.79\) Hz), 2.64-2.42 (4H, m), 1.24-1.19 (3H, m); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)) \(\delta: 145.6, 142.2, 136.2, 129.2, 128.4, 127.9, 126.4, 57.5, 46.0, 28.4, 15.6\); IR (neat, cm\(^{-1}\)) 3025, 2963, 2929, 1602, 1514, 1492, 1452, 813, 760, 698, 554, 537; HRMS (Dart) calcd for C\(_{15}\)H\(_{18}\)NO [M + H]\(^+\) 226.15957, found 226.15912; HPLC analysis using Daicel Chiralcel OD-H column (Hexane:iPrOH:Et\(_2\)NH = 90:10:0.1, 1.0 mL/min, 254 nm, \(t_R = 6.6\) min (\(R\)), 11.1 min (\(S\)); [\(\alpha\)]\(_D\)^{20} = +9.92 (62% ee, c 0.94, CHCl\(_3\)).

(S)-1-phenyl-2-(m-tolyl)ethan-1-amine (4ae); 3ae (167.6 mg, 0.459 mmol) was used, and 4ae (65.7 mg, 64% yield, 71% ee) was obtained. The structure was confirmed by comparison with data of \(^{1}H\) and \(^{13}C\) NMR shown in the literature.\(^{10}\) \(^{1}H\) NMR (500 MHz, CDCl\(_3\)) \(\delta: 7.38-7.31 (4H, m), 7.27-7.24 (2H, m), 7.17 (1H, t, \(J = 7.37\) Hz), 7.04-6.95 (3H, m), 4.20 (1H, dd, \(J = 4.53, 2.27\) Hz), 3.00 (1H, dd, \(J = 13.04, 5.10\) Hz), 2.84 (1H, dd, \(J = 6.52, 3.26\) Hz), 2.33-2.31 (5H, m); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)) \(\delta: 145.6, 139.0, 138.0, 130.1, 128.4, 128.3, 127.1, 127.0, 126.4, 126.3, 57.5, 46.4, 21.4\); HPLC analysis using Daicel Chiralcel OD-H column (Hexane:iPrOH:Et\(_2\)NH = 90:10:0.1, 1.0 mL/min, 254 nm, \(t_R = 6.7\) min (\(R\)), 12.2 min (\(S\)); [\(\alpha\)]\(_D\)^{20} = +16.50 (71% ee, c 0.61, CHCl\(_3\)).

2-6-4 N-alkylation (Figure 2-c)

\(p\)-Methoxycumylamine (S)-3aa (197.3 mg, 1.00 mmol), benzaldehyde (106.1 mg, 1.00 mmol), MS 4 Å (1 g) were placed in a 10 mL flask, and DCM was added to the flask. The mixture was stirred for 18 h at room temperature. After MS 4 Å was removed by filtration through a Celite pad, the filtrate was concentrated and dried to afford the corresponding imine. The obtained imine was placed in 30 mL flask and was dissolved in DCM. The reaction mixture was stirred for 24 h at room temperature. The mixture was concentrated under vacuum condition, and the obtained solid was dissolved in DCM and water. The two layers solution was extracted with DCM (20 mL x 3). The combined organic layer was dried over anhydrous Na\(_2\)SO\(_4\). After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired amine (239.9 mg, 83% yield).

Furthermore, amine 5 was derivatized to tertiary amine 6. Amine 5 (71.9 mg, 0.25 mmol) was placed in a 8 mL tube, and 37% HCHO aq. (162 \(\mu\)L, 2.0 mmol) and formic acid were added.
acid (38 μL, 4.0 mmol) added to the flask. The mixture was stirred for 12 h at 70 °C. The reaction was quenched with 15% NaOH aq., and the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 6 (67.6 mg, 90% yield).

(S)-N-Benzyl-1,2-diphenylethan-1-amine (5): The structure was confirmed by comparison with data of ¹H and ¹³C NMR shown in the literature.¹¹ ¹H NMR (500 MHz, CDCl₃) δ: 7.35-7.33 (4H, m), 7.28-7.23 (5H, m), 7.21-7.19 (2H, m), 7.10 (4H, d, J = 7.37 Hz), 3.88 (1H, dd, J = 8.50, 5.67 Hz), 3.65 (1H, d, J = 13.60 Hz), 3.46 (1H, d, J = 13.60 Hz), 2.92 (2H, m), 1.60 (s, 1H); ¹³C NMR (150 MHz, CDCl₃) δ: 143.7, 140.4, 138.8, 129.2, 128.35, 128.33, 128.2, 127.9, 127.4, 127.1, 126.7, 126.3, 63.6, 51.3, 45.3; [α]D²⁰ = −31.82 (c 0.55, CHCl₃).

(S)-N-benzyl-N-methyl-1,2-diphenylethan-1-amine (6): The structure was confirmed by comparison with data of ¹H and ¹³C NMR shown in the literature.¹² ¹H NMR (600 MHz, CDCl₃) δ: 7.27-7.21 (12H, m), 7.13 (1H, dd, J = 8.59, 5.84 Hz), 7.06 (2H, d, J = 6.87 Hz), 3.82 (1H, dd, J = 7.56, 3.78 Hz), 3.63 (1H, d, J = 13.75 Hz), 3.37 (1H, dd, J = 6.87, 3.44 Hz), 3.30 (1H, d, J = 13.06 Hz), 3.02 (1H, dd, J = 13.75, 8.25 Hz), 2.19 (3H, s); ¹³C NMR (150 MHz, CDCl₃) δ: 139.9, 139.8, 139.4, 129.4, 128.8, 128.7, 128.1, 127.9, 127.8, 127.0, 126.7, 125.7, 69.5, 58.8, 38.9, 38.0; HPLC analysis using Shinwa Chemical Industries Ltd. ULTRON ES-PhCD column (20 mM KH₂PO₄:MeCN = 75:25, 1.0 mL/min, 210 nm, tR = 74.3 min (R), 96.9 min (S)); [α]D²⁰ = +22.50 (c 0.51, CHCl₃).

2-6-5. Transformation to 1,2,3,4-tetrahydroisoquinoline (Figure 2-d)

p-Methoxycumylamine (S)-3aa (98.6 mg, 0.500 mmol) and paraformaldehyde (18.0 mg, 0.600 mmol as HCHO) were placed in a 10 mL flask, and 4 N HCl in dioxane was subsequently added. The reaction mixture was stirred for 10 h at 100 °C. After cooling, the mixture was basified with 15% NaOH aq., and was extracted with DCM (20 mL x 3). The combined organic layer was dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired tetrahydroisoquinoline (36.1 mg, 36% yield).
(S)-3-phenyl-1,2,3,4-tetrahydroisoquinoline (7): The structure was confirmed by comparison with data of $^1$H and $^{13}$C NMR shown in the literature. $^1$H NMR (600 MHz, CDCl$_3$) δ: 7.44 (2H, d, J = 7.56 Hz), 7.37 (2H, m), 7.29 (1H, t, J = 7.56 Hz), 7.16-7.15 (m, 2H), 7.10-7.08 (m, 2H), 4.27 (1H, d, J = 15.81 Hz), 4.17 (1H, d, J = 15.81 Hz), 4.02 (dd, 1H, J = 8.25, 6.87 Hz), 2.99 (2H, d, J = 7.56 Hz), 2.04 (s, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 144.3, 135.0, 134.9, 129.1, 128.6, 127.4, 126.5, 126.2, 126.1, 125.9, 58.6, 49.2, 37.7; HPLC analysis using Daicel Chiralcel OJ-3 column (Hexane:iPrOH = 98:2, 1.0 mL/min, 254 nm, tR = 34.5 min (S), 44.7 min (R)); [α]$_D^{20}$ = −123.02 (98% ee, c 0.35, CHCl$_3$).
2-7. Mechanistic studies
2-7-1. General procedure of nonlinear effect

Experimental procedure (Supplementary Figures 1, 2)

KCH$_2$TMS (6.3 mg, 5.0 x 10$^{-2}$ mmol) and KHMDS (10.0 mg, 5.0 x 10$^{-2}$ mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to –40 ºC, then diamine ligand L6 (19.4 mg, 8.3 x 10$^{-2}$ mmol) in toluene (0.20 mL) was added, and the chiral base mixture was stirred for 30 min at the same temperature. After the flask was cooled at –78 ºC, p-methoxycumylimine 1a (2.53 g, 10.0 mmol) dissolved in toluene (0.80 mL) was successively introduced via a well-dried cannula, and the whole mixture was stirred for 18 h at the same temperature. After the reaction was quenched by adding water, the mixture was extracted with DCM (10 mL x 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the crude product obtained was purified by PTLC (hexane-ethyl acetate) to afford the desired adduct 3.

2-7-2. NMR experiments

Preparation of samples (Supplementary Figures 3-5)

KCH$_2$TMS (6.3 mg, 5.0 x 10$^{-2}$ mmol) KHMDS (10.0 mg, 5.0 x 10$^{-2}$ mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. The flask was cooled to –40 ºC, then diamine ligand L2 (12.8 mg, 5.5 x 10$^{-2}$ mmol) in toluene-d$_8$ (0.20 mL) was added, and the mixture was stirred for 30 min at the same temperature. After the flask was cooled to –78 ºC, the mixture was diluted with toluene-d$_8$ (0.80 mL) and was successively transferred into a screw-cap NMR tube via a well-dried cannula. Subsequently, NMR measurement was conducted with keeping –78 ºC.

2-7-3. Effect of the piperazine part

General procedure for ligand structure activity (Supplementary Table 4)

KCH$_2$SiMe$_3$ (6.3 mg, 5.0 x 10$^{-2}$ mmol) and KHMDS (10.0 mg, 5.0 x 10$^{-2}$ mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. After the flask was cooled to the corresponding temperature, the corresponding amine ligand L (5.5 x 10$^{-2}$ mmol) in toluene (0.40 mL) was added, and the mixture was stirred at –40 ºC for 30 minutes. Subsequently, the flask was cooled to –78 ºC, and the corresponding imine 1a (126.7 mg, 0.50 mmol) dissolved in toluene (0.60 mL) was successively introduced into the flask via a well-dried cannula. After the whole mixture was stirred for 18 h at the same temperature, the reaction was quenched by adding a few drops of MeOH, and the obtained mixture was extracted with DCM (10 mL x 3), then combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the obtained crude product was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa. The enantioselectivities were determined by HPLC.
2-7-4. Investigation of backward reaction

Experimental procedure (Supplementary Figure 6)

KCH$_2$SiMe$_3$ (6.3 mg, 5.0 x 10$^{-2}$ mmol) and KHMD$S$ (10.0 mg, 5.0 x 10$^{-2}$ mmol) were placed in a flame-dried 10 mL flask inside a glove box fulfilled with argon. After the flask was cooled to the corresponding temperature, the corresponding amine ligand L (5.5 x 10$^{-2}$ mmol) in toluene (0.40 mL) was added, and the mixture was stirred at –40 ℃ for 30 minutes. Subsequently, the flask was cooled to –78 ℃, and the corresponding imine 3aa (126.7 mg, 0.50 mmol, 99% ee) dissolved in toluene (0.60 mL) was successively introduced into the flask via a well-dried cannula. After the whole mixture was stirred for 18 h at the same temperature, the reaction was quenched by adding a few drops of MeOH, and the obtained mixture was extracted with DCM (10 mL x 3), then combined organic layer was dried over anhydrous Na$_2$SO$_4$. After filtration and concentration under reduced pressure, the obtained crude product was purified by PTLC (hexane-ethyl acetate) to afford the desired amine 3aa (93% yield). The enantiopurity was determined by HPLC as 99% ee.
3. References

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4. NMR and HPLC charts

Supplementary Figure 7 $^1$H NMR of 1d
Supplementary Figure 8 $^{13}$C NMR of 1d
Supplementary Figure 9 $^1$H NMR of 1e
Supplementary Figure 10 $^{13}$C NMR of 1e
Supplementary Figure 11 $^1$H NMR of 1f
Supplementary Figure 12 $^{13}$C NMR of 1f
Supplementary Figure 13 $^1$H NMR of 1k
Supplementary Figure 14 $^{13}$C NMR of 1k
Supplementary Figure 15 $^1$H NMR of L4
Supplementary Figure 16 $^{13}$C NMR of L4
Supplementary Figure 17 $^1$H NMR of L5
Supplementary Figure 18 $^{13}$C NMR of L5
Supplementary Figure 19 \( ^1\)H NMR of L6
Supplementary Figure 20 $^{13}$C NMR of L6
Supplementary Figure 21 $^1$H NMR of L10
Supplementary Figure 22 $^{13}$C NMR of L10
Supplementary Figure 23 $^1$H NMR of L12
Supplementary Figure 24 $^{13}$C NMR of L12
Supplementary Figure 25 $^1$H NMR of L17
Supplementary Figure 26 $^{13}$C NMR of L17
Supplementary Figure 26 $^1$H NMR of L19
Supplementary Figure 27 $^{13}$C NMR of L19
Supplementary Figure 28 $^1$H NMR of L20
Supplementary Figure 29 $^{13}$C NMR of L20
Supplementary Figure 30 $^1$H NMR of L21
Supplementary Figure 31 $^{13}$C NMR of L21
Supplementary Figure 32 \textsuperscript{1}H NMR of L22
Supplementary Figure 33 $^{13}$C NMR of L22
Supplementary Figure 34 $^1$H NMR of 3aa
Supplementary Figure 35: $^{13}$C NMR of 3aa
Supplementary Figure 36 HPLC analysis of 3aa

Supplementary Figure 37 HPLC analysis of 3aa (after recrystallization)
Supplementary Figure 38 HPLC analysis of 3aa (racemic)
Supplementary Figure 39 $^1$H NMR of 3ba
Supplementary Figure 40 $^{13}$C NMR of 3ba
**Supplementary Figure 41** HPLC analysis of 3ba

![Graph 1 showing HPLC analysis of 3ba with a peak table below.]

**Supplementary Figure 42** HPLC analysis of 3ba (racemic)

![Graph 2 showing HPLC analysis of 3ba (racemic) with a peak table below.]
Supplementary Figure 43 $^1$H NMR of 3ca
Supplementary Figure 44 $^{13}$C NMR of 3ca
Supplementary Figure 45 $^1$H NMR of 3da
Supplementary Figure 46 $^{13}$C NMR of 3da
Supplementary Figure 47 $^1$H NMR of 3ea
Supplementary Figure 48 $^{13}$C NMR of 3ea
**Supplementary Figure 49** HPLC analysis of 3ea

Supplementary Figure 50 HPLC analysis of 3ea (after recrystallization)
Supplementary Figure 51 HPLC analysis of 3ea (racemic)
Supplementary Figure 52 $^1$H NMR of 3fa
Supplementary Figure 53 $^{13}$C NMR of 3fa
Supplementary Figure 54 HPLC analysis of 3fa

Supplementary Figure 55 HPLC analysis of 3fa (after recrystallization)
**Supplementary Figure 56** HPLC analysis of 3fa (racemic)

**Table:**

| Peak | Ret. Time | Area   | Height | Area% |
|------|-----------|--------|--------|-------|
| 1    | 4.94      | 778200 | 49242  | 97.64 |
| 2    | 5.87      | 644175 | 73413  | 22.71 |
| Tot. | 1113184   | 970003 | 100.00 | 100.00 |

mAU

PDA Multi 1 210nm 440nm

min
Supplementary Figure 57 $^1$H NMR of 3ga
Supplementary Figure 58 $^{13}$C NMR of 3ga
Supplementary Figure 59 HPLC analysis of 3ga

Supplementary Figure 60 HPLC analysis of 3ga (after recrystallization)
Supplementary Figure 61 HPLC analysis of 3ga (racemic)
Supplementary Figure 62 $^1$H NMR of 3ha
Supplementary Figure 63 $^{13}$C NMR of 3ha
Supplementary Figure 64 $^1$H NMR of 3ia
Supplementary Figure 65 $^{13}$C NMR of 3ia
Supplementary Figure 66 HPLC analysis of 3ia

Supplementary Figure 67 HPLC analysis of 3ia (racemic)
Supplementary Figure 68 $^1$H NMR of 3ja
Supplementary Figure 69 $^{13}$C NMR of 3ja
Supplementary Figure 70 HPLC analysis of 3ja

Supplementary Figure 71 HPLC analysis of 3ja (racemic)
Supplementary Figure 72 $^1$H NMR of 3ka
Supplementary Figure 73 $^{13}$C NMR of 3ka
Supplementary Figure 74 \textsuperscript{1}H NMR of 3la
Supplementary Figure 75 $^{13}$C NMR of 3la
**Supplementary Figure 76** HPLC analysis of 3la

**Supplementary Figure 77** HPLC analysis of 3la (racemic)
Supplementary Figure 78 $^1$H NMR of 3ab
Supplementary Figure 79 $^{13}$C NMR of 3ab
Supplementary Figure 80
$^1$H NMR of 3ac (crude)
Supplementary Figure 81 $^1$H NMR of 3ac
Supplementary Figure 83 HPLC analysis of 3ac

Supplementary Figure 84 HPLC analysis of 3ac (racemic)
Supplementary Figure 85 $^1$H NMR of 3ad
Supplementary Figure 86 $^{13}$C NMR of 3ad
Supplementary Figure 87 HPLC analysis of 3ad

Supplementary Figure 88 HPLC analysis of 3ad (racemic)
Supplementary Figure 89 $^1$H NMR of 3ae
Supplementary Figure 90 $^{13}$C NMR of 3ae
Supplementary Figure 91 $^1$H NMR of 3af
Supplementary Figure 92  $^{13}$C NMR of 3af
Supplementary Figure 93 HPLC analysis of 3af

Supplementary Figure 94 HPLC analysis of 3af (racemic)
Supplementary Figure 95 $^1$H NMR of 3ah
Supplementary Figure 96 $^{13}$C NMR of 3ah
Supplementary Figure 97 HPLC analysis of 3ah

Supplementary Figure 98 HPLC analysis of 3ah (racemic)
Supplementary Figure 99 $^1$H NMR of 4aa
Supplementary Figure 100 $^{13}$C NMR of 4aa
**Supplementary Figure 101** HPLC analysis of 4aa

**Supplementary Figure 102** HPLC analysis of 4aa (racemic)
Supplementary Figure 103 $^1$H NMR of 4ba
Supplementary Figure 104 $^{13}$C NMR of 4ba
Supplementary Figure 105 HPLC analysis of 4ba (Daicel Chiralpak OD-H column)

Supplementary Figure 106 HPLC analysis of 4ba (racemic, Daicel Chiralpak OD-H column)
**Supplementary Figure 107** HPLC analysis of 4ba·HCl (after recrystallization, Daicel Chiralpak OD-RH column)

**Supplementary Figure 108** HPLC analysis of 4ba (racemic, Daicel Chiralpak OD-RH column)
Supplementary Figure 109 \( ^{1}H \) NMR of 4ca
Supplementary Figure 110 $^{13}$C NMR of 4ca
Supplementary Figure 111 HPLC analysis of 4ca (Daicel Chiralpak OD-H column)

Supplementary Figure 112 HPLC analysis of 4ca (racemic, Daicel Chiralpak OD-H column)
Supplementary Figure 113 HPLC analysis of 4ca·HCl (after recrystallization, Daicel Chiralpak OD-RH column)

Supplementary Figure 114 HPLC analysis of 4ca·HCl (racemic, Daicel Chiralpak OD-RH column)
Supplementary Figure 115 $^1$H NMR of 4da
Supplementary Figure 116 $^{13}$C NMR of 4da
Supplementary Figure 117 HPLC analysis of 4da

Supplementary Figure 118 HPLC analysis of 4da (racemic)
Supplementary Figure 119 $^1$H NMR of 4ha
Supplementary Figure 120 $^{13}$C NMR of 4ha
Supplementary Figure 122 HPLC analysis of 4ha

Supplementary Figure 123 HPLC analysis of 4ha (racemic)
Supplementary Figure 124 ¹H NMR of 4ia
Supplementary Figure 125 $^{13}$C NMR of 4ia
Supplementary Figure 126 HPLC analysis of 4ia

Supplementary Figure 127 HPLC analysis of 4ia (racemic)
Supplementary Figure 128 HPLC analysis of 4ia (after recrystallization)

Supplementary Figure 129 HPLC analysis of 4ia (racemic)
Supplementary Figure 130 $^1$H NMR of 4ja
Supplementary Figure 131 $^{13}\text{C}$ NMR of 4ja
Supplementary Figure 132 HPLC analysis of 4ja

Supplementary Figure 133 HPLC analysis of 4ja (after recrystallization)
Supplementary Figure 134 HPLC analysis of 4ja (racemic)
Supplementary Figure 135 $^1$H NMR of 4ka
Supplementary Figure 136 $^{13}$C NMR of 4ka
Supplementary Figure 137 HPLC analysis of 4ka

Supplementary Figure 138 HPLC analysis of 4ka (racemic)
Supplementary Figure 139 $^1$H NMR of 4ab
Supplementary Figure 140 $^{13}$C NMR of 4ab
**Supplementary Figure 141** HPLC analysis of 4ab

**Supplementary Figure 142** HPLC analysis of 4ab (racemic)
Supplementary Figure 143 $^1$H NMR of 4ae
Supplementary Figure 144 $^{13}$C NMR of 4ae
Supplementary Figure 145 HPLC analysis of 4ae

Supplementary Figure 146 HPLC analysis of 4ae (racemic)
Supplementary Figure 147 $^1$H NMR of 5
Supplementary Figure 148 $^{13}$C NMR of 5
Supplementary Figure 149 $^1$H NMR of 6
Supplementary Figure 150 $^{13}$C NMR of 6
Supplementary Figure 151 HPLC analysis of 6

Supplementary Figure 152 HPLC analysis of 6 (racemic)
Supplementary Figure 153 $^1$H NMR of 7
Supplementary Figure 154  $^{13}$C NMR of 7
Supplementary Figure 155 HPLC analysis of 7

Supplementary Figure 156 HPLC analysis of 7 (racemic)