Design of bifunctional chiral phenanthroline ligand with Lewis basic site for palladium-catalyzed asymmetric allylic substitution

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General Information.

Infrared (IR) spectra were recorded on a JASCO FT/IR-230 spectrometer. 1H NMR spectra were measured at 25 °C on a Varian Mercury 300 (300 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, ddd = double-double-doublet, dt = double-triplet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. 13C NMR spectra were measured at 25 °C on a Varian Mercury 300 (75 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed carried out on a JASCO GULLIVER 1500 series using 4.6 mm x 25 cm Daicel Chiral Columns. High-resolution mass spectra (HRMS) were performed on a double-focusing magnetic sector mass spectrometer JEOL JMS-700. For thin layer chromatography (TLC) analysis throughout this work, TLC Silica gel 60 F254 were used. The products were purified by flash column chromatography on silica gel 60 N (Kanto, 60-210 μm).

In experiments requiring dry solvent, CH2Cl2 and DMF were purchased from Wako Pure Chemical Industry as “Dehydrated”. CPME was purchased from Sigma-Aldrich as “Dehydrated”. Toluene and THF were purchased from Kanto Chemical as “Dehydrated” and further purified by passing through neutral alumina under nitrogen atmosphere. (S)-1 were prepared according to our previous reports.51 Allyl acetates 2 were synthesized according to the literature.52 Other commercially available chemicals were purchased and used as received.

A solution of (S)-1a (5.25 mg, 0.01 mmol), [Pd(π-allyl)Cl]₂ (2.48 mg, 0.004 mmol), allyl acetate 2 (0.1 mmol), dialkyl malonate 3 (0.15 mmol) and LiOAc (1.44 mg, 0.02 mmol) in CPME (1.0 mL) was stirred at 60 °C for 1 h. Then, BSA (50 μL, 0.15 mmol) was added to this solution. After stirring for the additional 6 h, the reaction mixture was evaporated and the residue was purified by silica gel column chromatography with hexane and EtOAc (10:1) to give 4.
Dimethyl \((R,E)\)-2-(1,3-diphenylallyl)malonate \(4a\).

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\hline
\text{C} & \quad \text{C} \\
\begin{array}{c}
\text{O} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{O} \\
\end{array}
\end{align*}
\]

Colorless oil: 22.7 mg, 70% yield


The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time: 17.0 min \((R)\) and 26.1 min \((S)\)). \([\text{e.e.} = 94\%]\)
Diethyl (R,E)-2-(1,3-diphenylallyl)malonate (4b).

![Chemical structure](image)

Colorless oil: 20.1 mg, 57% yield

The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* 2015, 71, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time: 15.0 min (R) and 22.3 min (S)). [e.r. = 98.2/1.8][e.e. = 96%]

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Diisopropyl (R,E)-2-(1,3-diphenylallyl)malonate (4c).

Colorless oil: 24.0 mg, 63% yield


The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 23.4 min (R) and 40.0 min (S)). [e.r. = 96.8/3.2][e.e. = 94%]
Di-tert-butyl (R,E)-2-(1,3-diphenylallyl)malonate (4d).

Colorless oil: 21.2 mg, 52% yield

The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, Tetrahedron 2015, 71, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 8.0 min (R) and 11.9 min (S)). [e.r. = 94.7/5.3] [e.e. = 89%]
Dibenzyl \((R,E)\)-2-(1,3-diphenylallyl)malonate (4e).

![Chemical Structure](image)

Colorless oil: 29.5 mg, 62% yield

The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, Tetrahedron 2015, 71, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 0.5 mL/min, retention time; 39.8 min \((R)\) and 51.8 min \((S)\)). [e.r. = 98.9/1.1][e.e. = 98%]
Diethyl (E)-2-(1,3-diphenylallyl)-2-methylmalonate (4f).

![Chemical Structure](image)

Colorless oil: 23.8 mg, 65% yield

The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* 2015, 71, 5985.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 99/1, flow rate = 0.5 mL/min, retention time; 23.6 min (minor) and 25.5 min (major)). [e.r. = 2.2/97.8] [e.e. = 96%]
Diethyl (E)-2-benzyl-2-(1,3-diphenylallyl)malonate (4g).

\[
\text{EtO}_2\text{C} \xrightarrow{\text{Bn}} \text{CO}_2\text{Et}
\]

Colorless oil: 26.1 mg, 59% yield

The detailed spectral data has been reported in the following literature: Z. Liu, H. Du, Org. Lett. 2010, 12, 3054.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 95/5, flow rate = 1.0 mL/min, retention time; 7.8 min (minor) and 10.0 min (major)). [e.r. = 7.8/92.9][e.e. = 86%]
Dimethyl (\(R,E\))-2-(1,3-di-\(p\)-tolylallyl)malonate (4h).

Colorless oil: 19.4 mg, 55% yield


The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 15.6 min (\(R\)) and 22.4 min (\(S\))). [\(\varepsilon = 93.6/6.4\)][\(\varepsilon = 87\%\)]

---

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Dimethyl (R,E)-2-(1,3-bis(4-chlorophenyl)allyl)malonate (4i).

\[
\text{MeO}_2\text{C=CCC}_\text{Cl}-\text{C}_\text{Cl}\text{MeO}_2\text{C}.
\]

Colorless oil: 24.8 mg, 63% yield


The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 24.9 min (R) and 40.1 min (S)). [e.r. = 94.0/6.0][e.e. = 88%]
Dimethyl (R,E)-2-(1,3-bis(4-bromophenyl)allyl)malonate (4j).

![Chemical Structure]

Colorless oil: 32.3 mg, 67% yield


The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPACK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 31.3 min (R) and 49.0 min (S)). [e.r. = 94.2/5.8][e.e. = 88%]

![HPLC Chromatogram]

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Dimethyl (R,E)-2-(1,3-bis(3-bromophenyl)allyl)malonate (4k).

Colorless oil: 13.0 mg, 27% yield
The detailed spectral data has been reported in the following literature: K. Balaraman, R. Vasanthan, V. Kesavan, *Tetrahedron* 2013, 69, 6162.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPACK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 12.9 min (major) and 19.2 min (minor)). [e.r. = 90.0/10.0][e.e. = 80%]
Dimethyl (E)-2-(1,3-bis(2-bromophenyl)allyl)malonate (4l).

[Chemical structure image]

Colorless oil: 3.9 mg, 8% yield
The detailed spectral data has been reported in the following literature: A.-P. Xing, Z.-B. Pang, H.-F. Li, L.-L. Wang, *Tetrahedron* 2014, 70, 8822.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 10.2 min (major) and 13.6 min (minor)). [e.r. = 62.7/37.4][e.e. = 25%]

<table>
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Dimethyl (R,E)-2-(1,3-di(naphthalen-2-yl)allyl)malonate (4m).

![Chemical Structure](image)

Colorless oil: 16.1 mg, 38% yield

The detailed spectral data has been reported in the following literature: K. Balaraman, R. Vasanthan, V. Kesavan, *Tetrahedron* **2013**, *69*, 6162.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time: 33.3 min (S) and 45.4 min (R)). [e.r. = 85.0/15.0][e.e. = 70%]
Dibenzyl (E)-2-(1,3-di-p-tolylallyl)malonate (4n).

Colorless oil: 30.2 mg, 60% yield

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 9/1, flow rate = 1.0 mL/min, retention time; 32.2 min (major) and 46.9 min (minor)). [e.r. = 98.6/1.4][e.e. = 97%]
Dibenzyl ($R,E$)-2-(1,3-bis(4-chlorophenyl)allyl)malonate (4o).

![Structure of Dibenzyl (R,E)-2-(1,3-bis(4-chlorophenyl)allyl)malonate (4o).]

Colorless oil: 31.6 mg, 58% yield
The detailed spectral data has been reported in the following literature: Y. Jin, D.-M. Du, *Tetrahedron* 2012, 68, 3633.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK IA, hexane/iPrOH = 8/2, flow rate = 1.0 mL/min, retention time: 48.8 min ($R$) and 93.9 min ($S$)). [e.r. = 97.8/2.2] [e.e. = 96%]
Dibenzyl \((R,E)-2-(1,3\text{-bis(4-bromophenyl)allyl})\text{malonate (4p).}

\[
\text{BnO}_2\text{C}-\text{CO}_2\text{Bn}
\]

\text{Br-}
\text{Br-}

Colorless oil: 40.0 mg, 63% yield
The detailed spectral data has been reported in the following literature: Y. Jin, D.-M. Du, \textit{Tetrahedron} 2012, 68, 3633.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/iPrOH = 8/2, flow rate = 1.0 mL/min, retention time; 58.1 min \((R)\) and 105.6 min \((S)\). [\(\epsilon_r = 98.0/2.0\)] [\(\epsilon.e. = 96\%\)]

\begin{tabular}{|c|c|c|c|c|}
\hline
\# & tR [min] & Area [\(\mu V\text{-sec}\)] & Height [\(\mu V\)] & Area/\(h\) & Height/\(h\) \\
\hline
1 & 58.063 & 6193059 & 53847 & 97.963 & 98.629 \\
2 & 105.612 & 127503 & 761 & 2.017 & 1.376 \\
\hline
\end{tabular}
·Supporting information about mechanistic studies.

1) Investigation of desilylation of aryl silyl ether by LiOAc in CPME

We carried out reproductive experiments of LiOAc-catalyzed desilylation of aryl silyl ether reported by Wang (Ref. 17 in the main manuscript). Several reactions of PhOTMS in various moisture solvents were tested at 60 °C and the result was summarized in the following Table S1. We obtained the same result as Wang’s report, namely LiOAc worked well only in a combination of DMF and H₂O (entry 2). No reaction proceeded in moisture THF and CPME even for the smallest trimethylsilyl ether (entries 3 and 4).

**Table S1.**

<table>
<thead>
<tr>
<th>entry</th>
<th>LiOAc (x mol%)</th>
<th>solvent/H₂O (50/1)</th>
<th>% yield</th>
</tr>
</thead>
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<tr>
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<td>0</td>
<td>DMF</td>
<td>no reaction</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>DMF</td>
<td>&gt;95</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>THF</td>
<td>no reaction</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>CPME</td>
<td>no reaction</td>
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In contrast to the aforementioned model reaction of PhOTMS, the desilylation of TMS-(S)-1a in moisture CPME proceeded at 60 °C for 30 min (Scheme S1). The conversion ratio of TMS-(S)-1a was ca. 50%.

**Scheme S1**

Compared to the model reaction, the presence of phenanthroline moiety in (S)-1a seems to contribute to the higher reactivity toward LiOAc-catalyzed desilylation. One possible explanation is that a lithium cation coordinated with phenanthroline moiety enables a Lewis acidic activation of oxygen atom of siloxy group and thus the desilylation by acetoxy anion undergoes more smoothly through the six-membered cyclic transition state as proposed in
Wang’s report.

More directly, we observed the complete conversion of TMS-(S)-1a to (S)-1a with $^1$H NMR analysis of crude reaction mixture (Scheme S2). Therefore, the desilylation step of the corresponding palladium complex of TMS-(S)-1a should be involved in the catalytic cycle.

Scheme S2

![Scheme S2 diagram](image-url)
2) Effect of hydrogen bonding provided from hydroxy group in ligand
To check the possibility of hydrogen bonding activation, we carried out the reaction with commercially available isolated ketene trimethylsilyl acetal in the absence of acetate salt, but no reaction proceeded (Scheme S3a). This result supports that the possibility of hydrogen bond activation can be omitted. Furthermore, the same reaction with LiOAc was also unsuccessful, and thus weaker Lewis basic LiOAc itself was found to be not the effective catalyst for the activation of silyl enolate in this system (Scheme S3b).

Scheme S3
3) Other control experiments
To check the deprotection of TMS-\((S)\)-\textbf{1a} with LiOAc promoted in CPME at 60 °C quickly, we tried other control reactions i) using \((S)\)-\textbf{1a}, BSA and LiOAc in moisture CPME and ii) using TMS-\((S)\)-\textbf{1a} and NaH in dry CPME. Unfortunately, the former reaction with ligand \textbf{1a}, BSA and LiOAc in CPME/H\textsubscript{2}O (20/1) resulted in no reaction probably due to the complete decomposition of BSA by H\textsubscript{2}O (Scheme S4a). Also, the later reaction with TMS-\((S)\)-\textbf{1a} and NaH in dry CPME led to the formation of complex mixture (Scheme S4b).

Scheme S4

\[
\begin{align*}
\text{a) } & \quad \text{Ph} - \overset{\text{OAc}}{\text{C}} - \overset{\text{MeO}_2\text{C}}{\text{CO}_2\text{Me}} + \text{Ph} - \overset{\text{OAc}}{\text{C}} - \overset{\text{MeO}_2\text{C}}{\text{CO}_2\text{Me}} \\
& \quad \text{[Pd(\pi-allyl)Cl\textsubscript{2} (4 mol\%) } \\
& \quad \text{ \((S)\)-\textbf{1a} (10 mol\%) } \\
& \quad \text{ \text{BSA (1.5 equiv) } } \\
& \quad \text{ \text{LiOAc (20 mol\%) } } \\
& \quad \text{CPME/H\textsubscript{2}O (20/1) } \\
& \quad \text{60 °C, 6 h } \\
& \quad \text{no reaction}
\end{align*}
\]

\[
\begin{align*}
\text{b) } & \quad \text{Ph} - \overset{\text{OAc}}{\text{C}} - \overset{\text{MeO}_2\text{C}}{\text{CO}_2\text{Me}} + \text{Ph} - \overset{\text{OAc}}{\text{C}} - \overset{\text{MeO}_2\text{C}}{\text{CO}_2\text{Me}} \\
& \quad \text{[Pd(\pi-allyl)Cl\textsubscript{2} (4 mol\%)} \\
& \quad \text{ \text{TMS-\((S)\)-\textbf{1a} (10 mol\%) } \\
& \quad \text{ \text{NaH (1.5 equiv) } } \\
& \quad \text{CPME } \\
& \quad \text{60 °C, 6 h } \\
& \quad \text{complex mixture}
\end{align*}
\]