Supporting Information

Enantiodivergent Synthesis of 1,2-Bis(diphenylphosphino)ethanes via Asymmetric [3+2]-cycloaddition

Bing Liu, Wenbo Li, Haihong Wu, and Junliang Zhang*
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1. General Information

All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. $^1$H NMR spectra, $^{19}$F NMR spectra, $^{13}$C NMR spectra were recorded on a Bruker 300, 400 and 500 MHz spectrometer in CDCl$_3$. All signals are reported in ppm with the internal TMS signal at 0 ppm as a standard. Data for $^1$H NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, coupling constant(s) in Hz, integration), coupling constant (Hz), and integration. Data for $^{13}$C NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak (CDCl$_3$: 77.0 ppm). Reactions were monitored by thin layer chromatography (TLC) using silica gel plates. Flash column chromatography was performed over silica gel (300-400 mesh). THF, Et$_2$O and MTBE were freshly distilled from sodium metal prior to use. The ligands L$_2$-L$_{13}$ were synthesized according to the procedure of reference.$^1$ Other known ligands were commercially available. The substrate 1a were synthesized according to the procedure of references.$^2$ 2a-2o were synthesized according to the procedure of references.$^3$
2. Table S1. Screening the Known Ligands\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Yield (%)\textsuperscript{[b]}</th>
<th>Ee (%)(X/(-X) 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L6</td>
<td>100% conv.</td>
<td>-/42</td>
</tr>
<tr>
<td>2</td>
<td>L7</td>
<td>100% conv.</td>
<td>51/27</td>
</tr>
<tr>
<td>3</td>
<td>L8</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>L9</td>
<td>80% conv.</td>
<td>42/15</td>
</tr>
<tr>
<td>5</td>
<td>L10</td>
<td>100% conv.</td>
<td>25/31</td>
</tr>
<tr>
<td>6</td>
<td>L11</td>
<td>100% conv.</td>
<td>30/18</td>
</tr>
<tr>
<td>7</td>
<td>L12</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>L13</td>
<td>23% conv.</td>
<td>-/16</td>
</tr>
</tbody>
</table>

\begin{itemize}
\item \textbf{L5}, (R,S,S) 100% Conv., 42% ee
\item \textbf{L6}, (S,R,S) 100% Conv., 51/27% ee
\item \textbf{L7}, (R,S,R), trace
\item \textbf{L8}, (S,R,R) 80% Conv., 42/15% ee
\item \textbf{L9}, (R) 100% Conv., 25/31% ee
\item \textbf{L10}, (R) 100% Conv., 30/18% ee
\item \textbf{L11}, (R), trace
\item \textbf{L12}, (R,S,S) 23% Conv., 42/15% ee
\end{itemize}

\textsuperscript{[a]} All reactions were carried out with 0.025 mmol of 1a, 0.2 mmol of 2a, 20 mol% of catalyst ([Cu] to Ligand = 1:0.05), 50 mol% Cs\textsubscript{2}CO\textsubscript{3} in 1.5 ml Solvent (CHCl\textsubscript{3}/Et\textsubscript{2}O = 1) at rt for 24 h. \textsuperscript{[b]} NMR yield with CH\textsubscript{2}Br\textsubscript{2} as an internal standard. \textsuperscript{[c]} Determined by chiral HPLC.
3. Table S2. Optimization of Reaction Conditions for (−)-3a \[a\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Cu]</th>
<th>Solvent</th>
<th>Dr(^{[b]})(X:(−))</th>
<th>Yield (%)[^{[c]}]</th>
<th>Ee (%)[^{[d]}]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(CH(_3)CN)(_4)BF(_4)</td>
<td>CHCl(_3)/Et(_2)O = 1</td>
<td>30% conv.</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Cu(CH(_3)CN)(_4)NTf(_2)</td>
<td>CHCl(_3)/Et(_2)O = 1</td>
<td>50% conv.</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cu(CH(_3)CN)(_4)ClO(_4)</td>
<td>CHCl(_3)/Et(_2)O = 1</td>
<td>60% conv.</td>
<td>99%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Cu(CH(_3)CN)(_4)PF(_6)</td>
<td>CHCl(_3)/Et(_2)O = 1</td>
<td>1:13</td>
<td>100% conv.</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>5</td>
<td>Cu(CH(_3)CN)(_4)PF(_6)</td>
<td>CHCl(_3)/THF = 1</td>
<td>Trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cu(CH(_3)CN)(_4)PF(_6)</td>
<td>CHCl(_3)/MTBE = 1</td>
<td>40% conv.</td>
<td>97%</td>
<td></td>
</tr>
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</table>

[a] All reactions were carried out with 0.025 mmol of 1a, 0.2 mmol of 2a, 20 mol% of catalyst ([Cu] to Ligand = 1:1.05), 50% Cs\(_2\)CO\(_3\) in 1.5 ml Solvent at -10 °C for 24 h. \[b\] The diastereomeric ratios were determined by \(^1\)H, \(^{31}\)P NMR analysis of the crude products. \[c\] NMR yield with CH\(_2\)Br\(_2\) as an internal standard. \[d\] Determined by chiral HPLC.

4. General Procedure for the Synthesis of products 3-13

Typical procedure for asymmetric copper-catalyzed cycloaddition of alkene with glycine ketoimino ester.

The solution of Ligand (21.0 mol%) and Cu(CH\(_3\)CN)\(_4\)PF\(_6\) (20 mol%) in CHCl\(_3\)/Et\(_2\)O = 1:1 (6 mL) was stirred at room temperature for 1 h. After the reaction temperature was dropped to -10 °C, azomethine ylides 2 (0.2 mmol), Cs\(_2\)CO\(_3\) (0.05 mmol) and alkene 1 (0.1 mmol) were added sequentially. After the alkene 1 was consumed completely, remove the solvent under reduced pressure. The crude product was analyzed with \(^1\)H NMR and \(^{31}\)P NMR to determine the diastereomeric ratio. Then the crude product was purified by flash column chromatography on silica gel to afford the desired product. The enantionmeric excesses of the products were determined by chiral stationary phase HPLC.

**Conditions A:** using (S, R, R)-L\(_4\) as the ligand.  
**Conditions B:** using (R, R, R)-L\(_4\) as the ligand.
1. Synthesis of (-)-3a and (+)-3a.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2a (51.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3a as a white solid (58.7 mg, 86% yield) with 14:1 dr and 99% ee. mp: 220-221 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.74 (t, $J$ = 8.7 Hz, 2H), 7.44-7.36 (m, 8H), 7.33-7.26 (m, 6H), 7.23-7.12 (m, 8H), 4.45-4.34 (m, 2H), 3.76 (d, $J$ = 10.2 Hz, 1H), 3.49-3.43 (m, 1H), 3.27 (s, 1H), 2.88 (s, 3H). $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ 33.37 (d, $J$ = 30.4 Hz), 33.13 (d, $J$ = 30.5 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.47 (d, $J$ = 3.6 Hz), 139.70 (d, $J$ = 2.2 Hz), 131.86, 131.41, 131.30, 131.28, 131.19, 130.51 (d, $J$ = 8.1 Hz), 130.32 (d, $J$ = 8.3 Hz), 129.99, 128.69 (t, $J$ = 9.0 Hz), 128.27 (t, $J$ = 11.2 Hz), 121.64, 65.15, 63.04, 51.09, 46.71 (dt, $J$ = 31.2, 17.5 Hz), 42.04 (dt, $J$ = 63.7, 16.1 Hz). ESI-MS calculated for C$_{36}$H$_{33}$BrNO$_4$P$_2$: m/z (%): 684.1063 (M+H$^+$), found: 684.1066. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 18.0 min, minor enantiomer tr = 42.6 min. $[\alpha]_D^{25}$ = -16.4 ($c$ = 0.25, CHCl$_3$).

![Chemical Structure](image)

Under conditions B: the product (+)-3a was obtained as a white solid (54.6 mg, 80% yield) with 11:1 dr and 99% ee. mp: 191-192 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 41.5 min, minor enantiomer tr = 17.6 min. $[\alpha]_D^{25}$ = +21.2 ($c$ = 0.25, CHCl$_3$).
2. Synthesis of (-)-3b and (+)-3b.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2b (51.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3b as a white solid (60.1 mg, 88% yield) with >20:1 dr and 96% ee. mp: 231-232 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.61-8.59 (m, 1H), 7.75 (t, $J$ = 9.0 Hz, 2H), 7.53-7.38 (m, 10H), 7.33-7.23 (m, 4H), 7.19-7.05 (m, 7H), 5.04 (s, 1H), 4.44 (d, $J$ = 23.4 Hz, 1H), 3.89-3.81 (m, 2H), 3.13 (s, 1H), 2.90 (s, 3H). $^{31}$P NMR (202 MHz, CDCl$_3$) $\delta$ 33.67. $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.48, 139.62, 132.22, 131.73, 131.50 (dd, $J$ = 6.1, 3.0 Hz), 131.28, 130.99 (dd, $J$ = 6.3, 2.9 Hz), 130.47 (dd, $J$ = 5.9, 2.6 Hz), 130.32 (dd, $J$ = 6.2, 2.7 Hz), 129.66, 129.12, 128.73-128.40 (m), 128.28, 128.21-127.87 (m), 125.85, 65.23, 61.14, 51.09, 46.12 (dt, $J$ = 39.4, 13.4 Hz), 41.90 (dt, $J$ = 34.2, 12.6 Hz). ESI-MS calculated for C$_{36}$H$_{55}$BrNO$_4$P$_2$: m/z (%): 684.1063 (M+H$^+$), found: 684.1065. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 65:45 to 45:65, 0.8 mL/min, 230 nm); major enantiomer tr = 13.1 min, minor enantiomer tr = 76.0 min. $[\alpha]_D^{25}$ = -5.6 (c = 0.25, CHCl$_3$).
Under conditions B: the product (+)-3b was obtained as a white solid (60.7 mg, 89% yield) with >20:1 dr and 99% ee. mp: 236-237 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 65:45 to 45:65, 0.8 mL/min, 230 nm); major enantiomer tr = 75.2 min, minor enantiomer tr = 14.0 min. [α]D²⁵ = +5.2 (c = 0.25, CHCl₃).

3. Synthesis of (-)-3c and (+)-3c.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2c (51.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3c as a white solid (60.1 mg, 88% yield) with 14:1 dr and 98% ee. mp: 115-116 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (s, 2H), 7.51 (d, J = 6.6 Hz, 1H), 7.36-7.26 (m, 11H), 7.24-7.19 (m, 4H), 7.11-7.05 (m, 5H), 6.98 (s, 1H), 4.38 (d, J = 23.0 Hz, 1H), 4.26 (d, J = 9.1 Hz, 1H), 3.72 (d, J = 13.5 Hz, 1H), 3.39 (d, J = 14.8 Hz, 1H), 3.26 (s, 1H), 2.85 (s, 3H). ³¹P NMR (162 MHz, CDCl₃) δ 33.15 (q, J = 30.7 Hz). ¹³C NMR (126 MHz, CDCl₃) δ 168.61 (d, J = 4.1 Hz), 142.97 (d, J = 2.7 Hz), 132.34 (d, J = 2.1 Hz), 131.97 (d, J = 2.0 Hz), 131.66 (d, J = 2.1 Hz), 131.58, 131.55, 131.36 (t, J = 7.9 Hz), 130.88, 130.67 (d, J = 8.2 Hz), 130.50 (d, J = 8.3 Hz), 130.26, 128.86 (t, J = 10.9 Hz), 128.39 (t, J = 10.4 Hz), 126.58, 122.11, 63.18, 51.22, 47.13 (dd, J = 59.4, 5.1 Hz), 42.10 (dd, J = 58.2, 7.2 Hz). ESI-MS calculated for C₃₆H₃₃BrNO₄P₂: m/z (%): 684.1063 (M+H⁺), found: 684.1057. Enantiomeric excess was determined by
HPLC with a Chiralpak IA column (hexanes: 2-propanol = 70:30, 0.8 mL/min, 230 nm); major enantiomer tr = 23.2 min, minor enantiomer tr = 32.0 min. $[\alpha]_D^{25} = -14.4$ (c = 0.25, CHCl$_3$).

Under conditions B: the product (+)-3c was obtained as a white solid (64.8 mg, 95% yield) with >20:1 dr and >99% ee. mp: 121-122 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 70:30, 0.8 mL/min, 230 nm); major enantiomer tr = 29.2 min, minor enantiomer tr = 23.1 min. $[\alpha]_D^{25} = +13.2$ (c = 0.25, CHCl$_3$).

4. Synthesis of (-)-3d and (+)-3d.
Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2d (39.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3d as a white solid (56.7 mg, 91% yield) with 19:1 dr and >99% ee. mp: 212-213 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79-7.74 (m, 2H), 7.50-7.35 (m, 10H), 7.34-7.28 (m, 4H), 7.23 (t, $J = 6.9$ Hz, 2H), 7.15 (t, $J = 7.7$ Hz, 4H), 6.85 (t, $J = 8.7$ Hz, 2H), 4.43 (d, $J = 21.3$ Hz, 2H), 3.83-3.76 (m, 1H), 3.57-3.50 (m,
1H), 3.26 (s, 1H), 2.91 (s, 3H). \(^{19}\text{F NMR} (282 \text{ MHz, } \text{CDCl}_3) \delta -114.53. \(^{31}\text{P NMR} (162 \text{ MHz, } \text{CDCl}_3) \delta 33.39 (d, J = 2.7 \text{ Hz}). \(^{13}\text{C NMR} (126 \text{ MHz, } \text{CDCl}_3) \delta 168.65, 162.30 (d, J = 246.3 \text{ Hz}), 136.55, 131.96, 131.51, 131.44-131.25 (m), 130.76-130.59 (m), 130.59-130.34 (m), 130.10 (d, J = 8.1 \text{ Hz}), 129.05-128.63 (m), 128.38 (dd, J = 11.8, 7.4 Hz), 115.38, 115.21, 65.24, 63.11, 51.24, 46.82 (dt, J = 38.6, 13.9 Hz), 42.16 (dt, J = 41.0, 12.6 Hz). ESI-MS calculated for C\text{36}H\text{32}FNNaO\text{4}P\text{2}: m/z (%): 646.1683 (M+Na\text{+}), found: 646.1680. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 8.1 min, minor enantiomer tr = 65.9 min. \([\alpha]_D^{25} = -14.4 \text{ (c = 0.25, CHCl}_3\text{)}.\]

**Under conditions B:** the product (+)-3d was obtained as a white solid (54.2 mg, 87% yield) with >20:1 dr and 99% ee. mp: 203-204 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 62.8 min, minor enantiomer tr = 8.2 min. \([\alpha]_D^{25} = +14.4 \text{ (c = 0.25, CHCl}_3\text{)}.\]

5. Synthesis of (-)-3e and (+)-3e.
**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2e (42.2 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3e as a white solid (46.6 mg, 73% yield) with 15:1 dr and 99% ee. mp: 111-112 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.77-7.34 (m, 2H), 7.48-7.38 (m, 8H), 7.37-7.29 (m, 4H), 7.26-7.21 (m, 4H), 7.17-7.12 (m, 6H), 4.46-4.34 (m, 2H), 3.81-3.77 (m, 1H), 3.52-3.48 (m, 1H), 3.29 (s, 1H), 2.90 (s, 3H). $^{31}$P NMR (202 MHz, CDCl$_3$) δ 33.37, 33.34. $^{13}$C NMR (126 MHz, CDCl$_3$) δ 168.62 (d, $J$ = 3.6 Hz), 139.30, 133.56, 132.00 (d, $J$ = 2.7 Hz), 131.54, 131.50, 131.39 (d, $J$ = 8.7 Hz), 130.68 (d, $J$ = 8.4 Hz), 130.48 (d, $J$ = 8.7 Hz), 129.79, 128.82 (dd, $J$ = 11.4, 9.1 Hz), 128.61, 128.55-128.18 (m), 65.29, 63.12, 51.25, 46.85 (dt, $J$ = 67.6, 16.2 Hz), 42.19 (dt, $J$ = 34.0, 14.3 Hz). ESI-MS calculated for C$_{36}$H$_{32}$ClNNaO$_4$P$_2$: m/z (%): 662.1387 (M+Na$^+$), found: 662.1385. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 16.9 min, minor enantiomer tr = 49.1 min. [α]$_D^{25}$ = -22.0 (c = 0.25, CHCl$_3$).

**Under conditions B:** the product (+)-3e was obtained as a white solid (55.0 mg, 86% yield) with >20:1 dr and 98% ee. mp: 97-98 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 48.5 min, minor enantiomer tr = 17.3 min. [α]$_D^{25}$ = +20.0 (c = 0.25, CHCl$_3$).
6. **Synthesis of (-)-3f and (+)-3f.**

**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2f (49.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3f as a white solid (61.9 mg, 92% yield) with 13:1 dr and >99% ee. mp: 224-225 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.72-7.67 (m, 2H), 7.43-7.25 (m, 16H), 7.16-7.08 (m, 6H), 4.43-4.36 (m, 2H), 3.75-3.70 (m, 1H), 3.57-3.50 (m, 1H), 3.23 (s, 1H), 2.86 (s, 3H). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -62.55. $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ 33.14 (dd, $J = 81.0, 30.1$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.54 (d, $J = 4.5$ Hz), 144.77, 131.99 (dd, $J = 5.3, 2.5$ Hz), 131.66 (q, $J_{C-P} = 281.4$ Hz), 131.65, 131.56, 131.51, 131.31 (d, $J = 8.7$ Hz), 130.67 (d, $J = 8.6$ Hz), 130.48 (d, $J = 8.8$ Hz), 128.87, 128.76 (t, $J = 5.6$ Hz), 128.35 (t, $J = 11.0$ Hz), 125.31 (d, $J = 3.8$ Hz), 65.32, 63.08, 51.25, 46.76 (d, $J = 64.4$ Hz), 42.22 (d, $J = 62.2$ Hz). ESI-MS calculated for C$_{37}$H$_{32}$F$_3$NaO$_4$P$_2$: m/z (%): 696.1651 (M+Na$^+$), found: 696.1651. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 210 nm); major enantiomer tr = 7.5 min, minor enantiomer tr = 68.8 min. $[\alpha]_D^{25} = -28.0$ (c = 0.25, CHCl$_3$).
Under conditions B: the product (+)-3f was obtained as a white solid (57.2 mg, 85% yield) with 18:1 dr and 96% ee. mp: 197-198 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 65.5 min, minor enantiomer tr = 7.7 min. [α]D^25 = +31.6 (c = 0.25, CHCl3).

7. Synthesis of (-)-3g and (+)-3g.
Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2g (40.4 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3g as a white solid (59.2 mg, 94% yield) with >20:1 dr and >99% ee. mp: 86-87 °C. ^1H NMR (500 MHz, CDCl3) δ 7.75-7.71 (m, 2H), 7.50-7.31 (m, 16H), 7.24-7.14 (m, 6H), 4.46 (d, J = 20.1 Hz, 2H), 3.77-3.72 (m, 1H), 3.61-3.55 (m, 1H), 3.27 (s, 1H), 2.91 (s, 3H). ^31P NMR (202 MHz, CDCl3) δ 33.16 (dd, J = 158.7, 30.1 Hz). ^13C NMR (126 MHz, CDCl3) δ 168.45 (d, J = 4.6 Hz), 146.19 (d, J = 3.0 Hz), 131.29 (d, J = 9.0 Hz), 131.47 (dd, J = 44.4, 9.1 Hz), 130.57 (dd, J = 21.5, 8.9 Hz), 129.21, 128.89 (dd, J = 11.5, 6.9 Hz), 128.45 (dd, J = 23.2, 11.6 Hz), 118.80, 115.66, 111.51, 65.27 (d, J = 3.0 Hz), 62.92, 51.32, 46.74 (d, J = 66.7 Hz), 42.21 (d, J = 65.3 Hz). ESI-MS calculated
for \( \text{C}_{37}\text{H}_{32}\text{NaO}_{4}\text{P}_{2} \): m/z (%): 653.1730 (M+Na\(^{+}\)), found: 653.1737. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 210 nm); major enantiomer tr = 11.3 min, minor enantiomer tr = 76.9 min. \([\alpha]_{D}^{25} = -20.8\) (c = 0.25, CHCl\(_3\)).

**Under conditions B:** the product (+)-3g was obtained as a white solid (60.5 mg, 96% yield) with >20:1 dr and >99% ee. mp: 93-94 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 53.9 min, minor enantiomer tr = 11.3 min. \([\alpha]_{D}^{25} = +24.8\) (c = 0.25, CHCl\(_3\)).

8. **Synthesis of (-)-3h and (+)-3h.**

**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2h (44.4 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3h as a white solid (63.7 mg, 98% yield) with >20:1 dr and >99% ee. mp: 87-88 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.01 (d, \(J = 8.7\) Hz, 2H), 7.78-7.74(m, 2H), 7.53-7.34 (m, 14H), 7.26-7.18 (m, 6H), 4.57-4.48 (m, 2H), 3.82-3.76
(m, 1H), 3.67-3.60 (m, 1H), 3.33 (s, 1H), 2.94 (s, 3H). $^3$P NMR (202 MHz, CDCl$_3$) $\delta$ 33.33 (dd, $J = 157.7$, 30.0 Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.44 (d, $J = 4.7$ Hz), 147.40, 132.21 (d, $J = 21.8$ Hz), 131.70 (d, $J = 9.3$ Hz), 131.31 (d, $J = 9.0$ Hz), 130.69 (d, $J = 8.8$ Hz), 130.51 (d, $J = 9.0$ Hz), 128.92 (dd, $J = 11.6$, 6.8 Hz), 128.62 (d, $J = 11.5$ Hz), 128.39 (d, $J = 11.8$ Hz), 129.41, 123.57, 115.65, 65.28, 62.55, 51.37, 46.84 (d, $J = 66.4$ Hz), 42.28 (d, $J = 65.2$ Hz). ESI-MS calculated for C$_{36}$H$_{33}$N$_2$O$_6$P$_2$: m/z (%): 651.1808 (M+H$^+$), found: 651.1812. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 50:50, 0.8 mL/min, 230 nm); major enantiomer $t_r = 11.7$ min, minor enantiomer $t_r = 68.0$ min. $[\alpha]_D^{25} = -10.4$ ($c = 0.25$, CHCl$_3$).

Under conditions B: the product (+)-3h was obtained as a white solid (59.2 mg, 91% yield) with $>20:1$ dr and 99% ee. mp: 116-117 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35, 0.8 mL/min, 230 nm); major enantiomer $t_r = 68.2$ min, minor enantiomer $t_r = 12.3$ min. $[\alpha]_D^{25} = +8.0$ ($c = 0.25$, CHCl$_3$).
9. Synthesis of (-)-3i and (+)-3i.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2i (47.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3i as a white solid (61.7 mg, 93% yield) with >20:1 dr and >99% ee. mp: 120-121 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82 (d, $J = 8.3$ Hz, 2H), 7.77-7.73 (m, 2H), 7.49-7.29 (m, 14H), 7.20-7.12 (m, 6H), 4.48-4.41 (m, 2H), 3.89 (s, 3H), 3.82-3.77 (m, 1H), 3.55-3.49 (m, 1H), 3.35 (s, 1H), 2.90 (s, 3H). $^{31}$P NMR (202 MHz, CDCl$_3$) δ 33.36 (q, $J = 30.3$ Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 168.60 (d, $J = 4.1$ Hz), 166.96, 145.75, 132.06 (d, $J = 13.8$ Hz), 131.53, 131.34 (d, $J = 8.3$ Hz), 130.71 (d, $J = 8.0$ Hz), 130.50 (d, $J = 8.3$ Hz), 129.77, 129.51, 128.84 (t, $J = 10.6$ Hz), 128.43 (dd, $J = 15.3, 10.1$ Hz), 128.40, 115.68, 65.39, 63.42, 52.14, 51.27, 46.93 (d, $J = 64.5$ Hz), 42.27 (d, $J = 65.6$ Hz). ESI-MS calculated for C$_{38}$H$_{35}$NNaO$_6$P$_2$: m/z (%): 686.1832 (M+Na$^+$), found: 686.1839. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 45:55, 0.8 mL/min, 230 nm); major enantiomer tr = 10.0 min, minor enantiomer tr = 51.8 min. $[\alpha]_D^{25} = -20.4$ (c = 0.25, CHCl$_3$).

Under conditions B: the product (+)-3i was obtained as a white solid (61.0 mg, 92% yield) with >20:1 dr and 98% ee. mp: 111-112 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 45:55, 0.8 mL/min, 230 nm); major enantiomer tr = 50.8 min, minor enantiomer tr = 10.9 min. $[\alpha]_D^{25} = +24.4$ (c = 0.25, CHCl$_3$).
10. Synthesis of \((-\)-3j and \((+)-3j\).

**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2j (51.0 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product \((-\)-3j) as a white solid (54.0 mg, 79% yield) with 7:1 dr and >99% ee. mp: 101-102 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.76-7.72 (m, 4H), 7.52 (d, \(J = 8.4\) Hz, 2H), 7.49-7.33 (m, 12H), 7.23-7.14 (m, 4H), 4.51-4.44 (m, 2H), 3.79-3.73 (m, 1H), 3.55-3.49 (m, 1H), 3.33 (s, 1H), 3.01 (s, 3H), 2.90 (s, 3H). \(^{31}\)P NMR (202 MHz, CDCl\(_3\)) \(\delta\) 33.98 (dd, \(J = 223.2, 33.7\) Hz), 32.31 (dd, \(J = 178.8, 33.7\) Hz). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 168.47 (d, \(J = 4.6\) Hz), 147.12 (d, \(J = 3.1\) Hz), 139.77, 132.19 (d, \(J = 21.6\) Hz), 131.71, 131.55 (d, \(J = 9.0\) Hz), 131.31 (d, \(J = 8.8\) Hz), 130.56 (dd, \(J = 16.0, 8.9\) Hz), 129.48, 128.94 (dd, \(J = 11.6, 4.4\) Hz), 128.58 (d, \(J = 11.4\) Hz), 128.40 (d, \(J = 11.6\) Hz), 127.52, 65.35, 62.99, 51.30, 46.95 (d, \(J = 65.8\) Hz), 44.49, 42.22 (d, \(J = 65.4\) Hz). ESI-MS calculated for C\(_{37}\)H\(_{35}\)NNaO\(_6\)P\(_2\)S: m/z (%): 706.1553 (M+Na\(^+\)), found: 706.1551. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 45:55, 0.8 mL/min, 230 nm); major enantiomer \(\text{tr} = 18.0\) min, minor enantiomer \(\text{tr} = 80.2\) min. \([\alpha]_D^{25} = -24.4\) (\(c = 0.25, \text{CHCl}_3\)).
Under conditions B: the product (+)-3j was obtained as a white solid (54.6 mg, 80% yield) with 10:1 dr and 94% ee. mp: 96-97 ºC. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 45:55, 0.8 mL/min, 230 nm); major enantiomer tr = 80.0 min, minor enantiomer tr = 18.3 min. $\left[\alpha\right]_D^{25} = +22.8$ (c = 0.25, CHCl$_3$).

11. Synthesis of (-)-3k and (+)-3k.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2k (50.6 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3k as a white solid (55.2 mg, 81% yield) with 10:1 dr and 94% ee. mp: 95-96 ºC. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82-7.78 (m, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.50-7.29 (m, 8H), 7.22-7.15 (m, 3H), 4.74-4.32 (m, 2H), 4.09-3.80 (m, 1H), 3.62 (dd, J = 18.8, 5.2 Hz, 1H), 3.36 (s, 1H), 2.92 (s, 3H). $^{31}$P NMR (202 MHz, CDCl$_3$) δ 33.59 (q, J = 30.2 Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 168.60, 140.71, 140.38, 131.81, 131.48, 131.40, 131.36, 131.34, 130.66 (d, J = 8.3 Hz), 130.42 (d, J = 8.5 Hz), 128.69, 128.67 (dd, J = 14.2, 6.4 Hz), 128.26 (dd, J = 11.1, 6.0 Hz), 127.22, 127.06, 126.92, 65.28, 63.51, 51.12, 46.76 (d, J = 64.5 Hz), 42.18 (d, J = 64.9 Hz). ESI-MS calculated for C$_{42}$H$_{38}$NO$_4$P$_2$: m/z (%): 682.2271 (M+Na$^+$), found: 682.2254.
Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 20.9 min, minor
enantiomer tr = 45.5 min. \([\alpha]_D^{25} = -30.0\) (c = 0.25, CHCl₃).

**Under conditions B:** the product (+)-3k was obtained as a white solid (42.2 mg, 62% yield) with 16:1 dr and 97% ee. mp: 110-111 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 42.3 min, minor enantiomer tr = 21.9 min. \([\alpha]_D^{25} = +32.8\) (c = 0.25, CHCl₃).

12. **Synthesis of (-)-3l and (+)-3l.**

**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2l (44.6 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3l as a white solid (44.3 mg, 68% yield) with 10:1 dr and >99% ee. mp: 95-96 °C. \(^1\)H NMR (300 MHz, CDCl₃) δ 7.82-7.76 (m, 2H), 7.51-7.34 (m, 12H), 7.29-7.19 (m, 8H), 7.09 (d, \(J = 8.0\) Hz, 2H), 5.35 (s, 1H), 4.74-4.32 (m, 1H), 3.91 (d, \(J = 16.2\) Hz, 1H), 3.49 (m, 1H), 2.93 (s, 3H), 2.47 (s, 3H). \(^{31}\)P NMR (122 MHz, CDCl₃) δ 33.69 (d, \(J = 109.2\) Hz). \(^{13}\)C NMR (126 MHz, CDCl₃) δ 167.12, 138.94, 132.12, 131.69, 131.33 (d, \(J = 9.1\) Hz), 131.20 (d, \(J = 9.0\) Hz), 130.43 (dd, \(J = 8.8, 6.2\) Hz), 128.93, 128.82, 128.79, 128.48, 128.39, 126.45, 64.21, 62.68, 51.56, 15.56, 15.56, 45.67
(d, J = 62.3 Hz), 40.97 (d, J = 66.8 Hz). ESI-MS calculated for C$_{37}$H$_{36}$NO$_4$P$_2$S: m/z (%): 652.1835 (M+H$^+$), found: 652.1818. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:45 to 45:65, 0.8 mL/min, 210 nm); major enantiomer tr = 9.9 min, minor enantiomer tr = 56.1 min. [α]$_D^{25}$ = -77.1 (c = 0.25, CHCl$_3$).

Under conditions B: the product (+)-3l was obtained as a white solid (52.7 mg, 81% yield) with 10:1 dr and 99% ee. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:45 to 45:65, 0.8 mL/min, 210 nm); major enantiomer tr = 49.0 min, minor enantiomer tr = 10.8 min. [α]$_D^{25}$ = +63.4 (c = 0.25, CHCl$_3$).

13. Synthesis of (-)-3m and (+)-3m.

Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2m (45.4 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3m as a white solid (49.8 mg, 76% yield) with 6:1 dr and
99% ee. mp: 133-134 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.89-7.79 (m, 5H), 7.57-7.28 (m, 17H), 7.15-7.11 (m, 5H), 4.59-4.50 (m, 2H), 3.91 (d, $J$ = 15.7 Hz, 1H), 3.61-3.56 (m, 1H), 3.40 (s, 1H), 2.93 (s, 3H). $^{31}$P NMR (202 MHz, CDCl$_3$) $\delta$ 33.63 (q, $J$ = 30.4 Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.67, 137.67, 132.87 (d, $J$ = 4.3 Hz), 131.85, 131.40, 131.37, 130.48 (dd, $J$ = 34.7, 8.3 Hz), 128.75, 128.67, 128.58, 128.49, 128.30, 128.21, 128.08, 127.80, 127.38, 125.83, 125.70, 125.32, 65.30, 64.00, 51.09, 46.68 (d, $J$ = 58.1 Hz), 42.22 (d, $J$ = 65.6 Hz). ESI-MS calculated for C$_{40}$H$_{35}$NNaO$_4$P$_2$: m/z (%): 678.1934 (M+Na$^+$), found: 678.1943. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 10.3 min, minor enantiomer tr = 61.8 min. $[\alpha]_D^{25}$ = -35.6 (c = 0.25, CHCl$_3$).

Under conditions B: the product (+)-3m was obtained as a white solid (41.3 mg, 63% yield) with 11:1 dr and 98% ee. mp: 128-129 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 58.6 min, minor enantiomer tr = 10.2 min. $[\alpha]_D^{25}$ = +31.6 (c = 0.25, CHCl$_3$).
14. Synthesis of (-)-3n and (+)-3n.

**Under conditions A:** The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2n (66.2 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3n as a white solid (67.6 mg, 89% yield) with 15:1 dr and 95% ee. mp: 219-220 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.81-7.77 (m, 2H), 7.51-7.38 (m, 10H), 7.33-7.25 (m, 7H), 7.25-7.21 (m, 4H), 7.19-7.11 (m, 6H), 4.53-3.87 (m, 2H), 4.45-4.35 (m, 1H), 3.83-3.77 (m, 1H), 3.68-3.61 (m, 1H). $^{31}$P NMR (162 MHz, CDCl$_3$) δ 33.24 (q, $J = 29.7$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.08 (d, $J = 4.3$ Hz), 139.81 (d, $J = 2.7$ Hz), 134.81, 131.86, 131.71 (d, $J = 8.6$ Hz), 131.46, 131.40, 131.25 (d, $J = 8.5$ Hz), 130.65 (d, $J = 8.1$ Hz), 130.34 (d, $J = 8.3$ Hz), 130.08, 128.85-128.46 (m), 128.45-128.17 (m), 128.32, 128.10, 128.04, 121.68, 66.14, 65.24, 62.87, 46.48 (d, $J = 64.7$ Hz), 42.25 (d, $J = 65.9$ Hz). ESI-MS calculated for C$_{42}$H$_{37}$BrNO$_4$P$_2$: m/z (%) 760.1376 (M+H$^+$), found: 760.1373. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 7.0 min, minor enantiomer tr = 9.3 min. [$\alpha$]$_D^{25}$ = -18.4 (c = 0.25, CHCl$_3$).
Under conditions B: the product (+)-3n was obtained as a white solid (63.0 mg, 83% yield) with 14:1 dr and 97% ee. mp: 205-206 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 9.2 min, minor enantiomer tr = 6.8 min. \([\alpha]_D^{25} = +18.4\) (c = 0.25, CHCl3).

15. Synthesis of (-)-3o and (+)-3o.
Under conditions A: The reaction of alkene 1a (42.8 mg, 0.1 mmol) and glycine imino ester 2o (55.2 mg, 0.2 mmol), after a flash column chromatography (DCM: MeOH = 10:1) afforded the product (-)-3o as a white solid (53.2 mg, 84% yield) with 18:1 dr and 98% ee. mp: 95-96 °C. \(^1^H\) NMR (300 MHz, CDCl3) \(\delta\) 9.96 (s, 1H), 7.75-7.66 (m, 4H), 7.49-7.31 (m, 14H), 7.22-7.16 (m, 6H), 4.51-4.44 (m, 2H), 3.83-3.77 (m, 1H), 3.65-3.56 (m, 1H), 3.33 (t, \(J = 10.5\) Hz, 1H), 2.92 (s, 3H). \(^{31}\)P NMR (202 MHz, CDCl3) \(\delta\) 33.38 (dd, \(J = 93.8, 30.0\) Hz). \(^{13}\)C NMR (126 MHz, CDCl3) \(\delta\) 192.09, 168.53 (d, \(J = 4.6\) Hz), 147.57, 135.76, 132.11 (d, \(J = 11.1\) Hz), 131.62 (d, \(J = 9.1\) Hz), 131.34 (d, \(J = 8.8\) Hz), 130.62 (dd, \(J = 26.6, 8.8\) Hz), 129.91, 129.09, 128.86 (dd, \(J = 11.4, 8.8\) Hz), 128.45 (dd, \(J = 18.6, 11.4\) Hz), 119.51, 115.66, 65.38, 63.25, 51.31, 46.83 (d, \(J = 64.9\) Hz), 42.31 (d, \(J = 64.7\) Hz). ESI-MS calculated for C37H33NNaO5P2: m/z (%): 656.1726 (M+Na\(^+\)), found: 656.1733. Enantiomeric excess was determined by HPLC with a
Chiralpak IB column (hexanes: 2-propanol = 65:35 to 50:50, 0.8 mL/min, 230 nm); major enantiomer $t_r = 12.9$ min, minor enantiomer $t_r = 58.9$ min. $[\alpha]_D^{25} = -12.4$ ($c = 0.25$, CHCl$_3$).

Under conditions B: the product (+)-3o was obtained as a white solid (57.6 mg, 91% yield) with 24:1 dr and 97% ee. mp: 105-106 $^\circ$C. Enantiomeric excess was determined by HPLC with a Chiralpak IB column (hexanes: 2-propanol = 65:35 to 50:50, 0.8 mL/min, 230 nm); major enantiomer $t_r = 57.1$ min, minor enantiomer $t_r = 10.6$ min. $[\alpha]_D^{25} = +21.6$ ($c = 0.25$, CHCl$_3$).


The solution of compound (-)-3a (68.3 mg, 0.1 mmol) in THF (2 mL) was stirred at -50 $^\circ$C in a sealed tube. Subsequently, DIBAL-H (0.5 mmol) was added to the above solution. Then the reaction was determined by TLC analysis. After the (-)-3a was consumed completely, the reaction mixture was quenched by the addition of NH$_4$Cl aq. and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na$_2$SO$_4$, filtered, concentrated. Then the crude product was then purified by flash column
chromatography on silica gel (DCM: MeOH = 10:1) afforded the product (-)4 as a white solid (44.6 mg, 68% yield) with 98% ee. mp: 266-267 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.85-7.80 (m, 2H), 7.56-7.52 (m, 3H), 7.46-7.19 (m, 15H), 7.14-7.09 (m, 4H), 4.35-4.29 (m, 1H), 3.95-3.88 (m, 1H), 3.73-3.65 (m, 2H), 3.48-3.43 (m, 2H), 3.24-3.13 (m, 1H). $^{31}$P NMR (162 MHz, CDCl$_3$) δ 35.57 (d, $J = 29.8$ Hz), 33.28 (d, $J = 29.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 140.35, 131.81, 131.41 (d, $J = 20.2$ Hz), 130.50 (d, $J = 8.7$ Hz), 130.35-130.08 (m), 129.69, 128.93, 128.81, 128.78-128.58 (m), 128.32 (d, $J = 11.6$ Hz), 125.15, 121.50, 67.44, 64.12, 61.58, 48.35 (d, $J = 65.0$ Hz), 41.73 (d, $J = 66.5$ Hz). ESI-MS calculated for C$_{37}$H$_{33}$NNaO$_5$P$_2$: m/z (%): 656.1726 (M+Na$^+$), found: 656.1733. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 9.6 min, minor enantiomer tr = 17.0 min. $[\alpha]_D^{25} = -52.8$ (c = 0.25, CHCl$_3$).

The product (+)-4 was obtained as a white solid (49.9 mg, 76% yield) with 97% ee. mp: 245-246 °C. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 16.7 min, minor enantiomer tr = 10.0 min. $[\alpha]_D^{25} = +48.8$ (c = 0.25, CHCl$_3$).
17. Synthesis of (-)-5 and (+)-5.
The solution of compound (-)-3a (68.3 mg, 0.1 mmol) and K$_2$CO$_3$ (6.0 eq) in DMF (2 mL) was stirred at rt in a sealed tube. Subsequently, MeI (2.0 eq) was added to the above solution. Then the reaction was determined by TLC analysis. After the (-)-3a was consumed completely, the reaction mixture was quenched by the addition of NaCl aq. and the aqueous layer was extracted three or more times with EtOAc. The combined organic layers were dried over Na$_2$SO$_4$, filtered, concentrated. Then the crude product was then purified by flash column chromatography on silica gel (DCM: MeOH = 10:1) afforded the product (-)-5 as a white solid (66.9 mg, 96% yield) with 98% ee. mp: 65-66 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.66-7.61 (m, 2H), 7.48-7.39 (m, 7H), 7.35-7.26 (m, 5H), 7.21-7.13 (m, 6H), 7.04-6.97 (m, 4H), 3.88-3.77 (m, 2H), 3.69-3.62 (m, 1H), 3.54-3.47 (m, 1H), 2.90 (s, 3H), 2.13 (s, 3H). $^{31}$P NMR (162 MHz, CDCl$_3$) δ 34.52 (dd, $J = 416.8$, 34.6 Hz), 30.27 (dd, $J = 673.2$, 34.7 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.54 (d, $J = 5.0$ Hz), 140.02 (d, $J = 3.1$ Hz), 132.76 (d, $J = 9.7$ Hz), 131.88, 131.60, 131.43, 131.32 (d, $J = 3.2$ Hz), 131.22, 130.94, 130.80 (d, $J = 8.9$ Hz), 128.46 (dd, $J = 17.0$, 5.7 Hz), 128.00 (d, $J = 11.9$ Hz), 121.54, 77.30 (d, $J = 3.1$ Hz), 70.07, 69.66, 51.02 (d, $J = 3.1$ Hz), 42.35 (dd, $J = 148.2$, 66.0 Hz), 38.83 (d, $J = 3.6$ Hz). ESI-MS calculated for C$_{37}$H$_{34}$BrNNaO$_4$P$_2$: m/z (%): 720.1039 (M+Na$^+$), found: 720.1031. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 13.7 min, minor enantiomer tr = 48.7 min. [α]$_D^{25}$ = -14.9 (c = 0.25, CHCl$_3$).
The product (+)-5 was obtained as a white solid (64.8 mg, 93% yield) with 99% ee. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer $\text{tr} = 49.4$ min, minor enantiomer $\text{tr} = 13.9$ min. $[\alpha]_D^{25} = +15.6$ ($c = 0.25$, CHCl$_3$).


The solution of compound (-)-3a (68.3 mg, 0.1 mmol) in PhMe (2 mL) was stirred at 0°C in a sealed tube. Subsequently, BH$_3$·THF (0.5 mmol) was added to the above solution. Then the reaction was determined by TLC analysis. After the (-)-3a was consumed completely, the reaction mixture was quenched by the addition of NaCl aq. and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na$_2$SO$_4$, filtered, concentrated. Then the crude product was then purified by flash column chromatography on silica gel (DCM: MeOH = 10:1) afforded the product (-)-6 as a white solid (68.3 mg, 98% yield) with 94% ee. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78-7.74 (m, 2H), 7.54-7.30 (m, 16H), 7.26-7.10 (m, 6H), 5.87 (t, $J = 10.0$ Hz, 1H), 4.51-4.54 (m, 1H), 3.88-3.94 (m, 1H), 3.22-3.27 (m, 1H), 2.53-2.58 (m, 1H), 2.01-2.08 (m, 1H), 1.94-1.99 (m, 1H), 1.77-1.82 (m, 1H).
Hz, 1H), 4.53-4.41 (m, 1H), 4.32-4.23 (m, 1H), 3.91-3.82 (m, 1H), 3.44-3.38 (m, 1H), 2.91 (s, 3H). $^{31}$P NMR (162 MHz, CDCl$_3$) δ 33.06 (dd, $J = 349.2, 27.7$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 164.84 (d, $J = 4.6$ Hz), 135.25 (d, $J = 3.2$ Hz), 132.48 (d, $J = 9.4$ Hz), 132.04 (s), 131.83, 131.46 (d, $J = 9.1$ Hz), 130.81, 130.52 (d, $J = 7.7$ Hz), 130.27 (s), 129.04 (t, $J = 9.9$ Hz), 128.83 (d, $J = 2.9$ Hz), 128.71 (d, $J = 2.9$ Hz), 123.19, 77.20, 69.71 (d, $J = 17.0$ Hz), 51.70, 44.73 (d, $J = 64.7$ Hz), 38.74 (d, $J = 65.7$ Hz). ESI-MS calculated for C$_{36}$H$_{35}$BBrNNaO$_4$P$_2$: m/z (%): 720.1210 (M+Na$^+$), found: 720.1207.

Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 60:40, 0.8 mL/min, 230 nm); major enantiomer tr = 28.1 min, minor enantiomer tr = 13.3 min. [α]$_D^{25}$ = -32.2 (c = 0.25, CHCl$_3$).


The reaction of (-)-4a (0.29 mmol, 200 mg) in THF (5.3 ml) was stirred at rt. Subsequently, (Me$_2$HSi)$_2$O (0.33 ml, 6.0 equiv) and Ti(O'Pr)$_4$ (0.37 ml, 4.6 equiv) were added to the above solution. The solution was reacted at 65 °C for 12 h. Then the reaction was determined by TLC analysis. After the substrate was consumed
completely, the reaction mixture was then purified by flash column chromatography on silica gel (PE: EA = 4:1 to 1:1) afforded the product 7 as white solid (138 mg, 70% yield) with 97% ee.Mp = 88-89 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.78-7.74 (m, 2H), 7.50-7.38 (m, 5H), 7.33-7.24 (m, 7H), 7.22-7.15 (m, 5H), 7.14-7.06 (m, 5H), 3.77 (m, 1H), 3.46-3.34 (m, 1H), 3.27 (m, 1H), 3.17 (m, 1H), 2.95 (s, 3H), 2.15 (s, 3H). ³¹P NMR (202 MHz, CDCl₃) δ 30.29 (d, J = 24.9 Hz), -1.04 (d, J = 24.8 Hz). ¹³C NMR (126 MHz, CDCl₃) δ 169.30 (d, J = 5.0 Hz), 140.67 (d, J = 5.5 Hz), 135.07 (d, J = 21.2 Hz), 133.56 (d, J = 20.2 Hz), 131.84 (d, J = 8.8 Hz), 131.27 (d, J = 8.7 Hz), 130.97 (d, J = 10.0 Hz), 129.84, 128.95, 128.33 (dd, J = 6.6, 3.5 Hz), 128.14 (d, J = 11.5 Hz), 128.42, 121.16, 74.90 (d, J = 20.8 Hz), 69.09 (d, J = 2.1 Hz), 51.09, 44.37 (dd, J = 66.8, 20.5 Hz), 41.35 (d, J = 16.0 Hz), 39.38. ESI-MS calculated for C₃₇H₃₄BrNNaO₃P₂: m/z (%): 704.1090 (M+Na⁺), found: 704.1082. Enantiomeric excess was determined by HPLC with a Chiralpak IA column (hexanes: 2-propanol = 65:35-45:55-65:35, 0.8 mL/min, 230 nm); major enantiomer tr = 15.1 min, minor enantiomer tr = 57.2 min. [α]D²⁵ = -74.7 (c = 0.25, CHCl₃).
"$^1$H 谱对照：

二维谱 HMBC：（C-H 间接相关）

The reaction of ligand (−)-3a (10 mol%, 19.5 mg) and DIPEA (10.0 eq.) in iPrCN (2 ml) was stirred at 0 °C. Subsequently, (2,2,2-trifluoroethyl)-S-2-phenylethanthioate (140.4 mg, 0.6 mmol) and SiCl₄ (1.5 eq.) were added to the above solution. After 15 min, PhCHO (0.3 mmol) was added to the above solution. Stirred for overnight, SiCl₄ (1.5 eq.) was added to the above solution. Then the reaction was determined by TLC analysis. After the substrate was consumed completely, the reaction mixture was quenched by the addition of NaHCO₃ aq. and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na₂SO₄, filtered, concentrated. Then the crude product
was then purified by flash column chromatography on silica gel (PE: EA = 10:1) afforded the product 10 as liquid (66.3 mg, 65% yield) with 91:9 dr and 36% ee. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36-7.32 (m, 5H), 7.29-7.25 (m, 5H), 5.34 (d, $J$ = 7.6 Hz, 1H), 4.06 (d, $J$ = 7.6 Hz, 1H), 3.44-3.34 (m, 2H), 2.34 (s, 1H). $^{19}$F NMR (282 MHz, CDCl$_3$) δ -66.36. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 195.38, 140.26, 133.59, 129.38, 128.84, 128.46, 128.34, 128.19, 126.61, 124.37 ($J$$_{C-F}$ = 277.1 Hz), 74.95, 68.15, 30.63 (q, $J$ = 34.3 Hz). ESI-MS calculated for C$_{17}$H$_{15}$F$_{3}$NaO$_{2}$S: m/z (%): 363.0637 (M+Na$^+$), found: 363.0637. Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexanes: 2-propanol = 90:10, 0.8 mL/min, 230 nm); major enantiomer tr = 11.8 min, minor enantiomer tr = 22.0 min. [$\alpha$]$_D$$^{25}$ = +2.8 (c = 0.25, CHCl$_3$).

21. Synthesis of (1S,4R)-5-butyl-7-methyl-1,3-diphenyl-4-(3,4,5-trimethoxyphenyl)-3,4-dihydro-1H-furo[3,4-d][1,2]oxazine (13).

![Integration Results](image)

The reaction of AuCl(Me$_2$S) (5 mol%) and ligand (-)-3a (5.5 mol%) in DCM (2 ml) was stirred at rt. After stirred for 1h, AgSbF$_6$ (5 mol%) was added above solution and continue stirred for 10 min in -50 °C. Subsequently, 2-(1-alkynl)-alk-2-en-1-one 11 (0.1 mol) and nitrone 12 (2.0 equiv) were added to the above solution. After 48 h, then the reaction was determined by TLC analysis. After the substrate was consumed completely, the crude product was then purified by flash column chromatography on
silica gel (PE: EA = 10:1) afforded the product 13 as liquid (37.4 mg, 73% yield) with >20:1 dr and 77% ee. Mp = 38-39 °C. $^1$H NMR (300 MHz, CDCl$_3$) δ 7.56-7.53 (m, 2H), 7.41-7.39 (m, 3H), 7.24-7.19 (m, 2H), 7.06 (d, $J = 7.6$ Hz, 2H), 6.92 (t, $J = 7.3$ Hz, 1H), 6.49 (s, 2H), 5.97 (d, $J = 0.8$ Hz, 1H), 5.63 (s, 1H), 3.79 (s, 3H), 3.69 (s, 6H), 2.50-2.45 (m, 2H), 1.82 (s, 3H), 1.53-1.45 (m, 2H), 1.32-1.22 (m, 2H), 0.84 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 152.21, 148.45, 148.07, 143.26, 137.80, 137.17, 134.52, 129.14, 128.90, 128.39, 128.36, 122.12, 117.83, 116.85, 116.79, 106.45, 78.57, 62.50, 60.61, 55.82, 29.91, 26.24, 22.19, 13.62, 12.38. ESI-MS calculated for C$_{32}$H$_{35}$NNaO$_5$: m/z (%): 536.2407 (M+Na$^+$), found: 536.2410.

Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (hexanes: 2-propanol = 90:10, 0.8 mL/min, 254 nm); major enantiomer tr = 7.8 min, minor enantiomer tr = 9.5 min. [$\alpha$]$_D^{25}$ = +88.6 (c = 0.25, CHCl$_3$).
5. References


6. $^1$H, $^{31}$P, $^{13}$C NMR and HPLC Spectra

$^1$H NMR (400 MHz, CDCl$_3$), $^{31}$P NMR (162 MHz, CDCl$_3$) and $^{13}$C NMR (101 MHz, CDCl$_3$) of 3a
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3b
$^1$H NMR (400 MHz, CDCl$_3$), $^{31}$P NMR (162 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3c
$^1$H NMR (400 MHz, CDCl$_3$), $^{19}$F NMR (282 MHz, CDCl$_3$), $^{31}$P NMR (162 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3d
$^{1}H$ NMR (400 MHz, CDCl$_3$), $^{31}P$ NMR (162 MHz, CDCl$_3$) and $^{13}C$ NMR (126 MHz, CDCl$_3$) of 3e
$^1\text{H NMR}$ (400 MHz, CDCl$_3$), $^{19}\text{F NMR}$ (282 MHz, CDCl$_3$), $^{31}\text{P NMR}$ (101 MHz, CDCl$_3$) and $^{13}\text{C NMR}$ (126 MHz, CDCl$_3$) of 3f
$^1\text{H NMR}$ (400 MHz, CDCl$_3$), $^{31}\text{P NMR}$ (202 MHz, CDCl$_3$) and $^{13}\text{C NMR}$ (126 MHz, CDCl$_3$) of 3g
$^{1}H$ NMR (500 MHz, CDCl$_3$), $^{31}P$ NMR (202 MHz, CDCl$_3$) and $^{13}C$ NMR (126 MHz, CDCl$_3$) of 3h
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3i
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3j
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3k
$^1$H NMR (300 MHz, CDCl$_3$), $^{31}$P NMR (122 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3l
**3I**

**Chemical Structure:**

- Ph$_2$OP
- PPOPh$_2$
- MeS
- CO$_2$Me

**S$^{14}$C NMR Spectra:**

The spectra show resonances at various ppm values, indicating the presence of different chemical shifts.

- **1st Spectrum:**
  - Resonance at 140 ppm
  - Resonance at 110 ppm
  - Other resonances at 90, 80, 70, 60, 50, 40, 30, 20, and 0 ppm

- **2nd Spectrum:**
  - Resonance at 190 ppm
  - Resonance at 150 ppm
  - Other resonances at 130, 110, 90, 80, 70, 60, 50, 40, 30, 20, and 0 ppm

**Label:**

- 3I

**Additional Notes:**

- The spectra are labeled with chemical shifts in ppm.
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3m
H NMR (400 MHz, CDCl₃), ³¹P NMR (162 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) of 3n
$^1$H NMR (300 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 3o
$^1$H NMR (400 MHz, CDCl$_3$), $^{31}$P NMR (162 MHz, CDCl$_3$) and $^{13}$C NMR (101 MHz, CDCl$_3$) of 4
$^1$H NMR (400 MHz, CDCl$_3$), $^{31}$P NMR (162 MHz, CDCl$_3$) and $^{13}$C NMR (101 MHz, CDCl$_3$) of 5
$^{1}H$ NMR (400 MHz, CDCl$_3$), $^{31}P$ NMR (162 MHz, CDCl$_3$) and $^{13}C$ NMR (101 MHz, CDCl$_3$) of 6.
$^1$H NMR (500 MHz, CDCl$_3$), $^{31}$P NMR (202 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 7
$^1$H NMR (400 MHz, CDCl$_3$), $^{19}$F NMR (282 MHz, CDCl$_3$) and $^{13}$C NMR (101 MHz, CDCl$_3$) of 10
$^1$H NMR (300 MHz, CDCl$_3$) and $^{13}$C NMR (126 MHz, CDCl$_3$) of 13