Palladium-Catalyzed Asymmetric Addition of Diarylphosphines to α,β-Unsaturated N-Acylpyrroles

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Supporting Information

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General Methods

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or in a glove box under nitrogen. $^1$H, $^{13}$C and $^{31}$P NMR spectra were recorded on a Varian instrument (400 MHz, 100 MHz and 162 MHz, respectively). $^1$H, $^{13}$C NMR chemical shifts are reported vs tetramethylsilane signal or residual protio solvent signals.

Toluene, Et₂O, THF, and hexane were distilled over sodium benzophenone ketyl under nitrogen. Dichloromethane was distilled over CaH₂ under nitrogen.

The catalysts $^4$, $^1$, $^5$, $^2$ diarylphosphines and $\alpha,\beta$-unsaturated $N$-acylpyrroles were synthesized following the literature procedures. All other chemicals and solvents were purchased from commercial company and used as received.

Experimental Details and Characterization Data

Experimental Procedures for Table 1:

Diphenylphosphine (44.7 mg, 0.24 mmol) was added to a solution of $(S,S)$-4 (2.7 mg, 4 μmol Pd) in THF (3.0 mL) and the resulting solution was stirred for 2 min at room temperature, then $\alpha,\beta$-unsaturated $N$-acylpyrrole $1a$ (39.4 mg, 0.20 mmol) was added to it. The resulting solution was stirred for 2 h at room temperature, and then 30% H₂O₂ aqueous solution (0.1 mL) with EtOAc (2 mL) were added. After stirring for 1 h at room temperature, the mixture was concentrated under vacuum and the residue was purified by silica gel chromatography with CH₂Cl₂/MeOH = 100/1 to afford product as a white solid (75.9 mg, 0.190 mmol; 95% yield).
**Entry 1.** White solid. 95% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 17.7 min [(S)-enantiomer], 23.9 min [(R)-enantiomer]. 99% ee. $[\alpha]_{D}^{20} = -144$ (c 0.20, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): $\delta$ 8.00-7.96 (m, 2H), 7.59-7.10 (m, 15H), 6.21 (t, $J = 2.0$ Hz, 2H), 4.36 (ddd, $J_{HH} = 10.0$ and 2.0 Hz, $J_{HP} = 7.2$ Hz, 1H), 3.75 (ddd, $J_{HH} = 17.2$ and 10.8 Hz, $J_{HP} = 4.0$ Hz, 1H), 3.31 (ddd, $J_{HH} = 17.6$ and 2.4 Hz, $J_{HP} = 10.4$ Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$ 168.0 (d, $J_{CP} = 15.6$ Hz), 135.2 (d, $J_{CP} = 6.0$ Hz), 131.92 (d, $J_{CP} = 66.9$ Hz), 131.90 (d, $J_{CP} = 67.0$ Hz), 131.6 (d, $J_{CP} = 21.6$ Hz), 131.3 (d, $J_{CP} = 8.9$ Hz), 131.0 (d, $J_{CP} = 8.9$ Hz), 130.6 (d, $J_{CP} = 14.8$ Hz), 129.7 (d, $J_{CP} = 5.2$ Hz), 129.1 (d, $J_{CP} = 11.2$ Hz), 128.4 (d, $J_{CP} = 1.5$ Hz), 128.1 (d, $J_{CP} = 11.9$ Hz), 127.4 (d, $J_{CP} = 3.0$ Hz), 119.0, 113.4, 41.7 (d, $J_{CP} = 68.4$ Hz), 35.4. $^{31}$P{$^1$H} NMR (CDCl$_3$): $\delta$ 33.8 (s). HRMS (MALDI) calcd for C$_{25}$H$_{23}$NO$_2$P (M+H$^+$) 400.1454, found 400.1461.

The reaction was carried out as described above in entry 1. After stirred 2 h at room temperature, the solution was concentrated under vacuum without addition of H$_2$O$_2$. The residue was purified by silica gel chromatography with hexane/CH$_2$Cl$_2$ = 2/1 to afford product as a white solid (69.8 mg, 0.182 mmol, 91% yield).

**Entry 7.** The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): $\delta$ 7.71-7.65 (m, 2H), 7.43-7.40 (m, 3H), 7.23-7.09 (m, 12H), 6.18 (t, $J = 2.4$ Hz, 2H), 4.27 (ddd, $J_{HH} = 11.2$ and 3.2 Hz, $J_{HP} = 6.0$ Hz, 1H), 3.43 (ddd, $J_{HH} = 16.8$ and 10.8 Hz, $J_{HP} = 4.0$ Hz, 1H), 3.06 (ddd, $J_{HH} = 16.8$ and 3.2 Hz, $J_{HP} = 7.6$ Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$ 168.5 (d, $J_{CP} = 15.5$ Hz), 139.8 (d, $J_{CP} = 8.5$ Hz), 135.7 (d, $J_{CP} = 16.2$ Hz), 135.6 (d, $J_{CP} = 18.6$ Hz), 134.0 (d, $J_{CP} = 20.5$ Hz), 133.1 (d, $J_{CP} = 18.2$ Hz), 129.8 (d, $J_{CP} = 0.8$ Hz), 129.0 (d, $J_{CP} = 7.3$ Hz), 128.9 (d, $J_{CP} = 7.3$ Hz), 128.7, 128.4 (d, $J_{CP} = 0.7$ Hz), 128.0 (d, $J_{CP} = 7.0$ Hz), 126.7 (d, $J_{CP} = 2.4$ Hz),
118.9, 113.0, 40.2 (d, $J_{CP} = 11.6$ Hz), 38.6 (d, $J_{CP} = 24.3$ Hz). $^{31}$P{${}^1$H} NMR (CDCl$_3$): δ -0.1 (s). HRMS (EI) calcd for C$_{25}$H$_{22}$NOP (M$^+$) 383.1439, found 383.1436.

Diphenylphosphine (44.7 mg, 0.24 mmol) was added to a solution of (S,S)-4 (2.7 mg, 4 μmol Pd) in THF (3.0 mL) and the resulting solution was stirred for 2 min at room temperature, then α,β-unsaturated N-acylpyrrole 1a (39.4 mg, 0.20 mmol) was added to it. The resulting solution was stirred for 2 h at room temperature, then 2 eq Me$_2$S·BH$_3$ (2M solution in THF) was added. The mixture was stirred at room temperature for another 1 h and concentrated under vacuum. The residue was purified by silica gel chromatography with hexane/CH$_2$Cl$_2$ = 2/1 to afford product as a white solid (78.6 mg, 0.198 mmol, 99% yield).

**Entry 8.** White solid. 99% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 7.2 min [(S)-enantiomer], 10.0 min [(R)-enantiomer]. 99% ee. [α]$^{20}$D = -217 (c 1.00, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): δ 7.99 (t, $J_{HH} = 8.4$ Hz, 2H), 7.60-7.13 (m, 15H), 6.22 (s, 2H), 4.59 (ddd, $J_{HH} = 14.8$ and 0.8 Hz, $J_{HP} = 12.3$ Hz, 1H), 3.79 (ddd, $J_{HH} = 17.2$ and 11.6 Hz, $J_{HP} = 3.6$ Hz, 1H), 3.20 (ddd, $J_{HH} = 17.2$ and 1.2 Hz, $J_{HP} = 10.0$ Hz, 1H), 1.0 (br, 3H).

$^{13}$C NMR (CDCl$_3$): δ 167.7 (d, $J_{CP} = 16.2$ Hz), 134.8 (d, $J_{CP} = 1.2$ Hz), 132.8 (d, $J_{CP} = 8.4$ Hz), 132.7 (d, $J_{CP} = 8.8$ Hz), 131.56 (d, $J_{CP} = 67.0$ Hz), 131.53 (d, $J_{CP} = 67.4$ Hz), 129.6 (d, $J_{CP} = 4.4$ Hz), 129.2 (d, $J_{CP} = 9.3$ Hz), 128.2 (d, $J_{CP} = 10.1$ Hz), 128.1 (d, $J_{CP} = 2.0$ Hz), 127.6 (d, $J_{CP} = 2.4$ Hz), 127.3, 127.0, 126.8, 118.9, 113.4, 37.9 (d, $J_{CP} = 33.9$ Hz), 35.8 (d, $J_{CP} = 2.8$ Hz). $^{31}$P{${}^1$H} NMR (CDCl$_3$): δ 23.9 (brs). HRMS (MALDI) calcd for C$_{25}$H$_{24}$BNOP (M-H$^-$) 396.1688, found 396.1683.
Diphenylphosphine (44.7 mg, 0.24 mmol) was added to a solution of (S,S)-4 (2.7 mg, 4 μmol Pd) in THF (3.0 mL) and the resulting solution was stirred for 2 min at room temperature, then α,β-unsaturated N-acylpyrrole 1a (39.4 mg, 0.20 mmol) was added to it. The resulting solution was stirred for 2 h at room temperature, and then 1 eq S₈ was added. The mixture was stirred at room temperature for 1 h and concentrated under vacuum. The residue was purified by silica gel chromatography with hexane/CH₂Cl₂ = 2/1 to afford product as a pink solid (81.4 mg, 0.196 mmol, 98% yield).

**Entry 9.** The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 8.9 min [(S)-enantiomer], 10.6 min [(R)-enantiomer]. 98% ee. [α]²⁰⁺ = -209 (c 1.00, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4.

**1H NMR (CDCl₃):** δ 8.20-8.14 (m, 2H), 7.57-7.11 (m, 15H), 6.21 (t, J₁H = 2.0 Hz, 2H), 4.76 (td, J = 10.8 and 2.4 Hz, 1H), 3.83 (ddd, J₁H = 17.2 and 10.4 Hz, J₃H = 5.6 Hz, 1H), 3.27 (ddd, J₁H = 17.6 and 2.0 Hz, J₃H = 11.2 Hz, 1H). **13C NMR (CDCl₃):** δ 167.8 (d, J₃C = 18.1 Hz), 134.2 (d, J₃C = 4.4 Hz), 131.8 (d, J₃C = 9.3 Hz), 131.69 (d, J₃C = 71.0 Hz), 131.66 (d, J₃C = 71.4 Hz), 131.5 (d, J₃C = 9.7 Hz), 130.9 (d, J₃C = 40.3 Hz), 130.1 (d, J₃C = 34.7 Hz), 129.6 (d, J₃C = 5.3 Hz), 129.0 (d, J₃C = 11.7 Hz), 128.0 (d, J₃C = 3.7 Hz), 127.9 (d, J₃C = 5.6 Hz), 127.6 (d, J₃C = 3.2 Hz), 119.0, 113.4, 41.8 (d, J₃C = 52.9 Hz), 35.9 (d, J₃C = 5.2 Hz). **31P{1H} NMR (CDCl₃):** δ 50.8 (s). HRMS (MALDI) calcd for C₂₅H₂₂NOPSNa (M+Na⁺) 438.1063, found 438.1052.

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**General procedure for Table 2:** Diarylphosphine (0.24 mmol) was added to a solution of (S,S)-4 (2.7 mg, 4 μmol Pd) in THF (3.0 mL) and the resulting solution was stirred for 2 min at room temperature, then α,β-unsaturated N-acylpyrrole 1 (0.20 mmol) was added to it. The resulting solution was stirred for 2 h at room temperature, and then 30% H₂O₂ aqueous solution (0.1 mL) with EtOAc (2 mL) were added. After stirring for 1 h at room temperature, the mixture was concentrated under vacuum and the residue was purified by silica gel chromatography to afford 1,4-adduct 3.

**Entry 2.** White solid. 99% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 27.9 min [(S)-enantiomer], 48.5 min [(R)-enantiomer]. 99% ee. [α]₂⁰ D = -141 (c 1.00, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4.

**1H NMR** (CDCl₃): δ 7.98 (dd, J = 7.2 and 1.6 Hz, 2H), 7.59-7.26 (m, 10H), 7.20 (s, 2H), 6.71 (d, J = 8.8 Hz, 2H), 6.21 (t, J = 1.8 Hz, 2H), 4.31 (ddd, J_HH = 10.8 and 2.4 Hz, J_HP = 7.2 Hz, 1H), 3.70 (s, 3H), 3.69 (ddd, J_HH = 17.2 and 10.8 Hz, J_HP = 4.0 Hz, 1H), 3.27 (ddd, J_HH = 17.6 and 2.4 Hz, J_HP = 10.0 Hz, 1H). **13C NMR** (CDCl₃): δ 168.0 (d, J_CP = 16.2 Hz), 158.7 (d, J_CP = 2.4 Hz), 131.83 (d, J_CP = 62.4 Hz), 131.80 (d, J_CP = 62.4 Hz), 131.6 (d, J_CP = 20.1 Hz), 131.1 (d, J_CP = 8.3 Hz), 130.9 (d, J_CP = 8.7 Hz), 130.7 (d, J_CP = 5.6 Hz), 129.0 (d, J_CP = 11.1 Hz), 128.0 (d, J_CP = 11.9 Hz), 126.8 (d, J_CP = 5.5 Hz), 119.0, 113.9 (d, J_CP = 1.6 Hz), 113.3, 55.1, 40.7 (d, J_CP = 69.6 Hz), 35.4 (d, J_CP = 2.0 Hz). **31P{1H} NMR** (CDCl₃): δ 34.3 (s). MS (ESI): m/z (%) = 430 (M+H⁺). Anal. Calcd for C₂₆H₂₄NO₃P: C, 72.72; H, 5.63; N, 3.26. Found: C, 72.68; H, 5.72; N, 3.13.
Entry 3. White solid. 99% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 18.7 min [(S)-enantiomer], 32.8 min [(R)-enantiomer]. 99% ee. [α]$_D^{20}$ = -145 (c 1.00, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): δ 8.01-7.94 (m, 2H), 7.55-7.19 (m, 12H), 6.97 (d, $J_{HH} = 8.1$ Hz, 2H), 6.19 (t, $J_{HH} = 2.4$ Hz, 2H), 4.34 (ddd, $J_{HH} = 10.2$ and 2.4 Hz, $J_{HP} = 7.5$ Hz, 1H), 3.71 (ddd, $J_{HH} = 17.7$ and 10.8 Hz, $J_{HP} = 4.5$ Hz, 1H), 3.29 (ddd, $J_{HH} = 17.7$ and 2.4 Hz, $J_{HP} = 10.2$ Hz, 1H), 2.21 (s, 3H). $^{13}$C NMR (CDCl$_3$): δ 167.9 (d, $J_{CP} = 16.2$ Hz), 136.9 (d, $J_{CP} = 2.3$ Hz), 131.86 (d, $J_{CP} = 5.8$ Hz), 131.81 (d, $J_{CP} = 62.3$ Hz), 131.79 (d, $J_{CP} = 62.3$ Hz), 131.6 (d, $J_{CP} = 11.2$ Hz), 131.2 (d, $J_{CP} = 8.5$ Hz), 130.9 (d, $J_{CP} = 8.9$ Hz), 130.7 (d, $J_{CP} = 4.3$ Hz), 129.5 (d, $J_{CP} = 5.4$ Hz), 129.1 (d, $J_{CP} = 1.9$ Hz), 129.0 (d, $J_{CP} = 11.2$ Hz), 128.1 (d, $J_{CP} = 11.6$ Hz), 118.9, 113.3, 41.1 (d, $J_{CP} = 68.9$ Hz), 35.4 (d, $J_{CP} = 1.6$ Hz), 21.0 (d, $J_{CP} = 0.8$ Hz). $^{31}$P{$_1^H$} NMR (CDCl$_3$): δ 34.9 (s). MS (ESI): m/z (%) = 414 (M+H$^+$). Anal. Calcd for C$_{26}$H$_{24}$NO$_2$P: C, 75.53; H, 5.74; N, 3.39. Found: C, 75.19; H, 5.74; N, 3.26.

Entry 4. White solid. 98% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 17.7 min [(S)-enantiomer], 36.9 min [(R)-enantiomer]. >99% ee. [α]$_D^{20}$ = -165 (c 1.00, CH$_2$Cl$_2$). The absolute configurations of products were determined to be S by comparison of the specific optical rotation of the hydrolyzed product with the value reported in literature.

$^1$H NMR (CDCl$_3$): δ 7.99-7.95 (m, 2H), 7.62-7.19 (m, 12H), 7.14 (d, $J_{HH} = 8.8$ Hz, 2H), 6.22 (t, $J_{HH} = 2.4$ Hz, 2H), 4.33 (ddd, $J_{HH} = 9.6$ and 2.0 Hz, $J_{HP} = 6.8$ Hz, 1H), 3.68 (ddd, $J_{HH} = 17.6$ and 10.8 Hz, $J_{HP} = 4.4$ Hz, 1H), 3.29 (ddd, $J_{HH} = 17.6$ and 2.4 Hz, $J_{HP} = 10.0$ Hz, 1H). $^{13}$C NMR (CDCl$_3$): δ 167.7 (d, $J_{CP} = 16.2$ Hz), 133.8 (d, $J_{CP} = 15.4$ Hz), 133.4 (d, $J_{CP} = 3.1$ Hz), 132.15 (d, $J_{CP} = 57.7$ Hz), 132.07 (d, $J_{CP} = 57.7$ Hz), 132.07 (d, $J_{CP} = 57.7$ Hz),...
131.2 (d, $J_{CP} = 21.7$ Hz), 131.1 (d, $J_{CP} = 8.5$ Hz), 131.0 (d, $J_{CP} = 5.4$ Hz), 130.8 (d, $J_{CP} = 8.9$ Hz), 130.2 (d, $J_{CP} = 15.5$ Hz), 129.1 (d, $J_{CP} = 11.2$ Hz), 128.6 (d, $J_{CP} = 1.9$ Hz), 128.3 (d, $J_{CP} = 12.0$ Hz), 119.0, 113.5, 41.0 (d, $J_{CP} = 58.2$ Hz), 35.3 (d, $J_{CP} = 1.5$ Hz).

$^{31}$P{${}^1$H} NMR (CDCl$_3$): $\delta$ 33.3 (s). MS (ESI): m/z (%) = 434 (M+H$^+$). Anal. Caled for C$_{25}$H$_{21}$ClNO$_2$P: C, 69.21; H, 4.88; N, 3.23. Found: C, 68.94; H, 4.94; N, 3.02.

A solution of the obtained product (99.8 mg, 0.23 mmol) in entry 4 and NaOH (92 mg, 2.3 mmol) in MeOH (20 mL) and H$_2$O (20 mL) was stirred at 60 °C for 4 h. After cooling to room temperature, the solution was acidified to PH 1–2 with conc. hydrochloric acid and extracted with dichloromethane. The organic phase was concentrated under vacuum and the residue was purified by silica gel chromatography with CH$_2$Cl$_2$/MeOH = 50/1 to afford the hydrolyzed acid as a white solid (87.6 mg, 0.228 mmol; 99% yield).

The absolute configuration of the hydrolyzed product was determined to be $S$ by comparison of the optical rotation with the literature value ($[\alpha]_{20}^{20}$ = -35.2 (c 1.00, CHCl$_3$) for $S$-product.$^5$ This assignment leads to the determination of the absolute configuration of the phosphination product (Table 2, entry 4) as $S$. 

(CAS: 945743-40-8) 99% yield. >99% ee. $[\alpha]_{20}^{20}$ = -38 (c 0.040, CHCl$_3$). $^1$H NMR (CDCl$_3$): $\delta$ 7.89-7.52 (m, 5H), 7.43-7.28 (m, 5H), 7.15-7.08 (m, 4H), 4.21 (td, $J = 9.2$ and 3.6 Hz, 1H), 3.24 (dt, $J = 17.6$ and 9.2 Hz, 1H), 2.98 (ddd, $J_{HH} = 17.2$ and 4.0 Hz, $J_{HP} = 10.8$ Hz, 1H).

The absolute configuration of the hydrolyzed product was determined to be $S$ by comparison of the optical rotation with the literature value ($[\alpha]_{20}^{20}$ = -35.2 (c 1.00, CHCl$_3$) for $S$-product.$^5$ This assignment leads to the determination of the absolute configuration of the phosphination product (Table 2, entry 4) as $S$. 

S8
Entry 5. White solid. 97% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 13.1 min [(S)-enantiomer], 20.0 min [(R)-enantiomer]. 99% ee. \([\alpha]_{20}^D = -135\) (c 1.00, CH₂Cl₂). The absolute configuration was assigned by analogy with Table 2, entry 4.

\(^1\)H NMR (CDCl₃): \(\delta 7.99-7.95\) (m, 2H), 7.60-7.21 (m, 12H), 7.05 (d, \(J_{HH} = 8.4\) Hz, 2H), 6.23 (t, \(J_{HH} = 2.0\) Hz, 2H), 4.31 (ddd, \(J_{HH} = 10.0\) and 2.0 Hz, \(J_{HP} = 6.8\) Hz, 1H), 3.69 (ddd, \(J_{HH} = 18.0\) and 10.8 Hz, \(J_{HP} = 3.6\) Hz, 1H), 3.31 (ddd, \(J_{HH} = 17.6\) and 2.4 Hz, \(J_{HP} = 1.9\) Hz, 1H). \(^{13}\)C NMR (CDCl₃): \(\delta 167.6\) (d, \(J_{CP} = 16.3\) Hz), 137.5 (d, \(J_{CP} = 5.4\) Hz), 132.7 (d, \(J_{CP} = 5.4\) Hz), 132.13 (d, \(J_{CP} = 56.1\) Hz), 132.11 (d, \(J_{CP} = 56.1\) Hz), 131.2 (d, \(J_{CP} = 8.6\) Hz), 131.1 (d, \(J_{CP} = 22.1\) Hz), 130.8 (d, \(J_{CP} = 9.3\) Hz), 130.5 (d, \(J_{CP} = 1.9\) Hz), 130.1 (d, \(J_{CP} = 15.9\) Hz), 129.9 (d, \(J_{CP} = 1.9\) Hz), 129.1 (d, \(J_{CP} = 11.6\) Hz), 128.3 (d, \(J_{CP} = 12.0\) Hz), 128.1 (d, \(J_{CP} = 5.0\) Hz), 122.3 (d, \(J_{CP} = 2.3\) Hz), 119.0, 113.5, 41.4 (d, \(J_{CP} = 67.7\) Hz), 35.1. \(^{31}\)P\(^{1}\)H NMR (CDCl₃): \(\delta 38.3\) (s). HRMS (MALDI) calcd for C₂₅H₂₂BrNO₂P (M+H⁺) 478.0555, found 478.0566.

Entry 6. White solid. 95% yield. The ee was determined on a Daicel Chiralpak IC column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 9.2 min [(S)-enantiomer], 10.4 min [(R)-enantiomer]. 99% ee. \([\alpha]_{20}^D = -191\) (c 1.00, CH₂Cl₂). The absolute configuration was assigned by analogy with Table 2, entry 4.

\(^1\)H NMR (CDCl₃): \(\delta 8.04-7.99\) (m, 2H), 7.88 (s, 1H), 7.77-7.70 (m, 2H), 7.65 (d, \(J_{HH} = 8.4\) Hz, 1H), 7.58-7.16 (m, 9H), 7.21-7.15 (m, 4H), 6.18 (t, \(J_{HH} = 2.4\) Hz, 2H), 4.54 (ddd, \(J_{HH} = 10.4\) and 4.4 Hz, \(J_{HP} = 7.6\) Hz, 1H), 3.85 (ddd, \(J_{HH} = 17.2\) and 10.8 Hz, \(J_{HP} = 4.4\) Hz, 1H), 3.40 (ddd, \(J_{HH} = 17.6\) and 2.4 Hz, \(J_{HP} = 10.4\) Hz, 1H). \(^{13}\)C NMR (CDCl₃): \(\delta 167.9\) (d, \(J_{CP} = 16.3\) Hz), 133.1 (d, \(J_{CP} = 1.9\) Hz), 132.8 (d, \(J_{CP} = 5.8\) Hz), 132.4 (d, \(J_{CP} = 1.9\) Hz), 131.94 (d, \(J_{CP} = 64.6\) Hz), 131.91 (d, \(J_{CP} = 64.7\) Hz), 131.5,
131.2 (d, $J_{CP} = 8.5$ Hz), 130.9 (d, $J_{CP} = 9.2$ Hz), 130.5 (d, $J_{CP} = 8.4$ Hz), 129.1 (d, $J_{CP} = 11.2$ Hz), 128.8 (d, $J_{CP} = 6.9$ Hz), 128.1 (d, $J_{CP} = 11.6$ Hz), 128.07 (d, $J_{CP} = 1.5$ Hz), 127.9 (d, $J_{CP} = 0.8$ Hz), 127.6 (d, $J_{CP} = 5.1$ Hz), 127.5 (d, $J_{CP} = 1.2$ Hz), 126.0 (d, $J_{CP} = 0.8$ Hz), 125.9 (d, $J_{CP} = 0.8$ Hz), 119.0, 113.4, 41.7 (d, $J_{CP} = 68.5$ Hz), 35.6 (d, $J_{CP} = 1.2$ Hz). $^{31}$P{$^1$H}$^3$ NMR (CDCl$_3$): $\delta$ 33.6 (s). HRMS (MALDI) calcd for C$_{29}$H$_{25}$NO$_2$P (M+H$^+$) 450.1611, found 450.1617.

Entry 7. White solid. 94% yield. The ee was determined on a Daicel Chiralpak IC column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 14.0 min [(S)-enantiomer], 16.8 min [(R)-enantiomer]. 97% ee. [α]$^{20}$D = -101 (c 1.00, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): $\delta$ 7.92-7.87 (m, 2H), 7.59-7.19 (m, 11H), 6.25 (t, $J_{HH} = 2.0$ Hz, 2H), 6.19 (dd, $J_{HH} = 4.8$ and 2.0 Hz, 1H), 6.10 (t, $J_{HH} = 3.2$ Hz, 1H), 4.62 (ddd, $J_{HH} = 10.8$ and 2.8 Hz, $J_{HP} = 10.8$ Hz, 1H), 3.68 (ddd, $J_{HH} = 17.6$ and 10.8 Hz, $J_{HP} = 4.4$ Hz, 1H), 3.35 (ddd, $J_{HH} = 17.6$ and 2.8 Hz, $J_{HP} = 9.2$ Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$ 167.8 (d, $J_{CP} = 15.1$ Hz), 148.1 (d, $J_{CP} = 7.0$ Hz), 142.1 (d, $J_{CP} = 2.7$ Hz), 132.20 (d, $J_{CP} = 37.2$ Hz), 132.17 (d, $J_{CP} = 36.8$ Hz), 131.23 (d, $J_{CP} = 8.9$ Hz), 131.18 (d, $J_{CP} = 9.3$ Hz), 130.9 (d, $J_{CP} = 23.2$ Hz), 129.9 (d, $J_{CP} = 28.6$ Hz), 129.0 (d, $J_{CP} = 11.6$ Hz), 128.3 (d, $J_{CP} = 12.0$ Hz), 119.0, 113.4, 110.8 (d, $J_{CP} = 2.7$ Hz), 109.1 (d, $J_{CP} = 6.2$ Hz), 36.5 (d, $J_{CP} = 70.0$ Hz), 32.8 (d, $J_{CP} = 1.5$ Hz). $^{31}$P{$^1$H}$^3$ NMR (CDCl$_3$): $\delta$ 32.2 (s). HRMS (MALDI) calcd for C$_{25}$H$_{21}$NO$_3$P (M+H$^+$) 390.1243, found 390.1254.

Entry 8. White solid. 83% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 23.5
min [(S)-enantiomer], 31.5 min [(R)-enantiomer]. 98% ee. [α]_{20}^{D} = -113 (c 1.00, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4.

^1^H NMR (CDCl₃): δ 7.91 (t, J_Y = 8.8 Hz, 2H), 7.79 (dd, J = 10.0 and 8.0 Hz, 2H), 7.57-7.16 (m, 13H), 6.45 (dd, J = 15.6 and 3.6 Hz, 1H), 6.25 (s, 2H), 6.13 (ddd, J = 15.6, 8.8 and 2.4 Hz, 1H), 4.06 (q, J = 8.8 Hz, 1H), 3.41 (ddd, J_{HH} = 17.2 and 10.0 Hz, J_{HP} = 4.4 Hz, 1H), 3.21 (ddd, J_{HH} = 16.8 and 2.0 Hz, J_{HP} = 10.8 Hz, 1H). ^1^C NMR (CDCl₃): δ 167.9 (d, J_{CP} = 15.6 Hz), 136.3 (d, J_{CP} = 2.6 Hz), 135.9 (d, J_{CP} = 11.2 Hz), 132.10 (d, J_{CP} = 26.3 Hz), 132.07 (d, J_{CP} = 26.7 Hz), 131.4 (d, J_{CP} = 1.3 Hz), 131.3 (d, J_{CP} = 8.6 Hz), 131.1 (d, J_{CP} = 9.1 Hz), 130.4 (d, J_{CP} = 3.4 Hz), 129.0 (d, J_{CP} = 11.6 Hz), 128.5 (d, J_{CP} = 11.6 Hz), 128.4, 127.7, 126.3 (d, J_{CP} = 1.3 Hz), 122.3 (d, J_{CP} = 7.3 Hz), 119.0, 113.4, 39.6 (d, J_{CP} = 69.8 Hz), 33.6. ^3^P_{1}^¹^H NMR (CDCl₃): δ 33.7 (s). HRMS (MALDI) calecd for C_{27}H_{25}NO_{2}P (M+H⁺) 426.1621, found 426.1617.

**Entry 9.** White solid. 95% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 12.5 min [(S)-enantiomer], 16.3 min [(R)-enantiomer]. 91% ee. [α]_{20}^{D} = +2.2 (c 1.70, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4.

^1^H NMR (CDCl₃): δ 7.87-7.45 (m, 10H), 7.25 (s, 2H), 6.26 (t, J_{HH} = 2.8 Hz, 1H), 3.24-3.22 (m, 1H), 3.12-2.98 (m, 2H), 1.25 (dd, J = 16.0 and 6.4 Hz, 3H). ^1^C NMR (CDCl₃): δ 168.3 (d, J_{CP} = 16.4 Hz), 131.8 (d, J_{CP} = 3.0 Hz), 131.7 (d, J_{CP} = 3.0 Hz), 131.0 (d, J_{CP} = 95.2 Hz), 130.9 (d, J_{CP} = 97.4 Hz), 130.6 (d, J_{CP} = 8.9 Hz), 130.5 (d, J_{CP} = 8.9 Hz), 128.7 (d, J_{CP} = 11.2 Hz), 128.5 (d, J_{CP} = 11.8 Hz), 118.8, 113.2, 34.1, 28.1 (d, J_{CP} = 72.9 Hz), 12.7 (d, J_{CP} = 3.0 Hz). ^3^P_{1}^¹^H NMR (CDCl₃): δ 37.4 (s). HRMS (ESI) calecd for C_{20}H_{20}NO_{2}P (M) 337.1232, found 337.1232.
**Entry 10.** White solid. 92% yield. The ee was determined on a Daicel Chiralpak IC column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 8.1 min [(S)-enantiomer], 9.2 min [(R)-enantiomer]. 94% ee. \([\alpha]^{20}_{D} = -9.6\) (c 0.80, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): \(\delta 7.93-7.80\) (m, 4H), \(7.53-7.22\) (m, 8H), \(6.23\) (t, \(J_{HH} = 2.4\) Hz, 1H), \(3.42-3.36\) (m, 1H), \(3.13-3.09\) (m, 2H), \(2.25-2.14\) (m, 1H), \(1.09\) (d, \(J_{HH} = 6.8\) Hz, 3H), \(0.93\) (d, \(J_{HH} = 7.2\) Hz, 3H). $^{13}$C NMR (CDCl$_3$): \(\delta 169.2\) (d, \(J_{CP} = 10.5\) Hz), \(132.2\) (d, \(J_{CP} = 96.1\) Hz), \(132.1\) (d, \(J_{CP} = 96.1\) Hz), \(131.64\) (d, \(J_{CP} = 2.8\) Hz), \(131.61\) (d, \(J_{CP} = 2.8\) Hz), \(130.8\) (d, \(J_{CP} = 8.9\) Hz), \(130.7\) (d, \(J_{CP} = 8.4\) Hz), \(128.7\) (d, \(J_{CP} = 11.5\) Hz), \(128.6\) (d, \(J_{CP} = 11.5\) Hz), \(118.9\), \(113.2\), \(37.6\) (d, \(J_{CP} = 71.4\) Hz), \(28.0\), \(27.2\) (d, \(J_{CP} = 1.2\) Hz), \(22.6\) (d, \(J_{CP} = 13.7\) Hz), \(18.6\) (d, \(J_{CP} = 2.0\) Hz). $^{31}$P\{$^1$H\} NMR (CDCl$_3$): \(\delta 38.5\) (s). HRMS (MALDI) calcd for C$_{22}$H$_{25}$NO$_2$P (M+H$^+$) 366.1613, found 366.1617.

**Entry 11.** White solid. 93% yield. The ee was determined on a Daicel Chiralpak IC column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 7.6 min [(R)-enantiomer], 9.3 min [(S)-enantiomer]. 96% ee. \([\alpha]^{20}_{D} = -24.6\) (c 1.00, CH$_2$Cl$_2$). The absolute configuration was assigned by analogy with Table 2, entry 4.

$^1$H NMR (CDCl$_3$): \(\delta 7.90-7.80\) (m, 4H), \(7.53-7.38\) (m, 6H), \(7.19\) (s, 2H), \(6.95\) (t, \(J_{HH} = 2.4\) Hz, 2H), \(3.46-3.39\) (m, 1H), \(3.23\) (ddd, \(J_{HH} = 17.6\) and \(16.4\) Hz, \(J_{HP} = 4.4\) Hz, 1H), \(2.95\) (ddd, \(J_{HH} = 18.0\) and \(6.4\) Hz, \(J_{HP} = 9.2\) Hz, 1H), \(1.68-1.42\) (m, 3H), \(0.83\) (t, \(J_{HH} = 6.4\) Hz, 6H). $^{13}$C NMR (CDCl$_3$): \(\delta 169.2\) (d, \(J_{CP} = 10.5\) Hz), \(132.15\) (d, \(J_{CP} = 2.7\) Hz), \(132.12\) (d, \(J_{CP} = 2.7\) Hz), \(132.0\) (d, \(J_{CP} = 96.8\) Hz), \(131.9\) (d, \(J_{CP} = 94.8\) Hz), \(131.2\) (d, \(J_{CP} = 8.9\) Hz), \(131.15\) (d, \(J_{CP} = 8.9\) Hz), \(129.03\) (d, \(J_{CP} = 11.8\) Hz), \(128.98\) (d, \(J_{CP} = 11.3\) Hz), \(119.3\), \(113.6\), \(38.2\) (d, \(J_{CP} = 2.3\) Hz), \(34.0\), \(30.8\) (d, \(J_{CP} = 72.3\) Hz), \(26.0\) (d, #S12
Entry 12. White solid. 99% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 23.1 min [(S)-enantiomer], 29.0 min [(R)-enantiomer]. 96% ee. [α]_{20}^{D} = -26.9 (c 1.00, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4. 

$^{1}$H NMR (CDCl₃): δ 7.95-7.90 (m, 4H), 7.60-7.35 (m, 6H), 7.23 (s, 2H), 6.24 (t, $J_{HH}$ = 2.4 Hz, 2H), 3.38-3.30 (m, 1H), 3.26-3.00 (m, 2H), 2.20-2.12 (m, 1H), 1.85-1.45 (m, 5H), 1.18-0.94 (m, 5H). 

$^{13}$C NMR (CDCl₃): δ 169.3 (d, $J_{CP}$ = 11.2 Hz), 132.3 (d, $J_{CP}$ = 96.0 Hz), 132.2 (d, $J_{CP}$ = 94.1 Hz), 131.68 (d, $J_{CP}$ = 2.7 Hz), 131.66 (d, $J_{CP}$ = 2.7 Hz), 130.80 (d, $J_{CP}$ = 8.9 Hz), 130.79 (d, $J_{CP}$ = 8.1 Hz), 128.7 (d, $J_{CP}$ = 11.6 Hz), 128.6 (d, $J_{CP}$ = 11.2 Hz), 119.0, 113.3, 37.8 (d, $J_{CP}$ = 1.5 Hz), 37.6 (d, $J_{CP}$ = 71.2 Hz), 32.8 (d, $J_{CP}$ = 12.0 Hz), 29.4 (d, $J_{CP}$ = 2.3 Hz), 29.2 (d, $J_{CP}$ = 0.8 Hz), 26.6 (d, $J_{CP}$ = 1.2 Hz), 26.3, 25.8. 

$^{31}$P{¹H} NMR (CDCl₃): δ 37.9 (s). HRMS (MALDI) calcd for C₂₅H₂₉NO₂P (M+H⁺) 406.1929, found 406.1930.

Entry 13. White solid. 98% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 19.6 min [(S)-enantiomer], 40.5 min [(R)-enantiomer]. 97% ee. [α]_{20}^{D} = -139 (c 1.00, CH₂Cl₂), The absolute configuration was assigned by analogy with Table 2, entry 4. 

$^{1}$H NMR (CDCl₃): δ 7.87 (dd, $J$ = 10.0 and 8.8 Hz, 2H), 7.38-7.13 (m, 9H), 7.03 (dd, $J$ = 8.8 and 2.0 Hz, 2H), 6.73 (dd, $J$ = 9.2 and 2.4 Hz, 2H), 6.20 (t, $J$ = 2.4 Hz,
2H), 4.26 (ddd, \(J_{HH} = 10.4\) and 2.4 Hz, \(J_{HP} = 7.6\) Hz, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 3.70 (ddd, \(J_{HH} = 17.6\) and 10.8 Hz, \(J_{HP} = 4.8\) Hz, 1H), 3.32 (ddd, \(J_{HH} = 17.6\) and 2.4 Hz, \(J_{HP} = 10.4\) Hz, 1H). \(^{13}\)C NMR (CDCl\(_3\)): \(\delta 168.1\) (d, \(J_{CP} = 15.9\) Hz), 162.27 (d, \(J_{CP} = 57.7\) Hz), 162.25 (d, \(J_{CP} = 58.1\) Hz), 135.5 (d, \(J_{CP} = 5.4\) Hz), 133.0 (d, \(J_{CP} = 10.1\) Hz), 132.8 (d, \(J_{CP} = 10.1\) Hz), 129.7 (d, \(J_{CP} = 5.4\) Hz), 128.4 (d, \(J_{CP} = 1.9\) Hz), 127.2 (d, \(J_{CP} = 2.7\) Hz), 122.8 (d, \(J_{CP} = 70.5\) Hz), 121.7 (d, \(J_{CP} = 63.9\) Hz), 119.0, 114.6 (d, \(J_{CP} = 12.4\) Hz), 113.6 (d, \(J_{CP} = 12.8\) Hz), 113.2, 55.3, 55.1, 42.1 (d, \(J_{CP} = 68.9\) Hz), 35.4. \(^{31}\)P\(^{1}{\text{H}}\) NMR (CDCl\(_3\)): \(\delta 34.1\) (s). HRMS (MALDI) calcd for C\(_{27}\)H\(_{27}\)NO\(_4\)P (M+H\(^{+}\)) 460.1674, found 460.1672.

![Structural diagram](image_url)

**Entry 14.** White solid. 97% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 80/20, flow = 1.0 mL/min. Retention times: 17.3 min [(S)-enantiomer], 21.3 min [(R)-enantiomer]. 98% ee. [\(\alpha\)]\(^{20}\)\(_{D} = -137\) (c 1.00, CH\(_2\)Cl\(_2\)), The absolute configuration was assigned by analogy with Table 2, entry 4. \(^{1}\)H NMR (CDCl\(_3\)): \(\delta 7.90\) (ddd, \(J = 10.0\) and 8.0 Hz, 2H), 7.52 (d, \(J = 8.0\) and 2.0 Hz, 2H), 7.40-7.34 (m, 4H), 7.25-7.14 (m, 7H), 6.20 (t, \(J = 2.4\) Hz, 2H), 4.35 (ddd, \(J_{HH} = 10.0\) and 2.8 Hz, \(J_{HP} = 7.2\) Hz, 1H), 3.70 (ddd, \(J_{HH} = 17.6\) and 10.0 Hz, \(J_{HP} = 5.2\) Hz, 1H), 3.38 (ddd, \(J_{HH} = 16.8\) and 1.6 Hz, \(J_{HP} = 11.2\) Hz, 1H). \(^{13}\)C NMR (CDCl\(_3\)): \(\delta 167.6\) (d, \(J_{CP} = 15.5\) Hz), 138.76 (d, \(J_{CP} = 79.3\) Hz), 138.72 (d, \(J_{CP} = 78.9\) Hz), 134.6 (d, \(J_{CP} = 5.8\) Hz), 132.5 (d, \(J_{CP} = 9.3\) Hz), 132.2 (d, \(J_{CP} = 9.7\) Hz), 129.7 (d, \(J_{CP} = 33.3\) Hz), 129.6 (d, \(J_{CP} = 5.8\) Hz), 129.5 (d, \(J_{CP} = 11.6\) Hz), 128.7 (d, \(J_{CP} = 25.9\) Hz), 128.6, 128.5 (d, \(J_{CP} = 10.4\) Hz), 127.6 (d, \(J_{CP} = 2.4\) Hz), 118.9, 113.5, 41.5 (d, \(J_{CP} = 69.7\) Hz), 35.3. \(^{31}\)P\(^{1}{\text{H}}\) NMR (CDCl\(_3\)): \(\delta 34.1\) (s). HRMS (MALDI) calcd for C\(_{25}\)H\(_{21}\)Cl\(_2\)NO\(_2\)P (M+H\(^{+}\)) 468.0682, found 468.0688.
Synthesis of Phosphine-Oxazoline Ligand 6 (Scheme 1)

NaOH (480 mg, 12 mmol) was added to a solution of 3b (1.246 g, 3 mmol; 98% ee) in MeOH/H₂O (20 mL/20 mL), and the resulting mixture was refluxed for 2 h. After cooled to room temperature, the solution was acidified to pH 1–2 with conc. hydrochloric acid and extracted with dichloromethane. The organic phase was concentrated under vacuum and the residue was purified by silica gel chromatography with CH₂Cl₂/MeOH = 50/1 to afford S1 (CAS: 354816-38-9) as a white solid (1.090 g, 2.97 mmol; 99% yield). [α]₂⁰₀° = -167 (c 1.00, CH₂Cl₂).

¹H NMR (CDCl₃): δ 8.14-8.08 (m, 2H), 7.54-7.52 (m, 3H), 7.44 (dd, J_HH = 8.4 and 7.2 Hz, 2H), 7.36-7.11 (m, 8H), 4.38 (td, J = 11.2 and 3.2 Hz, 1H), 3.22 (ddd, J_HH = 17.6 and 11.2 Hz, J_HP = 6.8 Hz, 1H), 2.86 (ddd, J_HH = 17.2 and 3.2 Hz, J_HP = 10.4 Hz, 1H).

¹³C NMR (CDCl₃): δ 176.9 (d, J_CP = 19.3 Hz), 133.8 (d, J_CP = 5.4 Hz), 131.94, 131.9 (d, J_CP = 12.7 Hz), 131.5 (d, J_CP = 9.7 Hz), 131.3 (d, J_CP = 3.0 Hz), 130.8 (d, J_CP = 45.3 Hz), 130.0 (d, J_CP = 39.4 Hz), 129.6 (d, J_CP = 5.2 Hz), 128.9 (d, J_CP = 11.2 Hz), 127.9 (d, J_CP = 14.1 Hz), 127.85, 127.7 (d, J_CP = 3.0 Hz), 42.7 (d, J_CP = 51.9 Hz), 35.2 (d, J_CP = 3.7 Hz). ³¹P{¹H} NMR (CDCl₃): δ 50.4 (s).
(R)-Valine (370 mg, 2.82 mmol) was added to a mixture of S1 (860 mg, 2.35 mmol), HOBT (381 mg, 2.82 mmol) and EDC·HCl (540 mg, 2.82 mmol) in dichloromethane (20 mL) and acetonitrile (20 mL). The mixture was stirred at room temperature for 6 h until the starting materials disappeared (monitored by TLC). The solvent was removed under vacuum and the residue was purified by silica gel chromatography with CH₂Cl₂/MeOH = 100/1 to afford S2 (CAS: 216862-91-8) as a white solid (1.014 g, 2.11 mmol; 90% yield). \([\alpha]_{D}^{20} = -94.7 \text{ (c 1.00, CH}_2\text{Cl}_2)\).

\[^1\text{H}\] NMR (CDCl₃): \(\delta 8.20-8.15\) (m, 2H), \(7.56-7.45\) (m, 5H), \(7.32-7.10\) (m, 8H), \(5.92\) (d, \(J = 8.8\) Hz, 1H), \(4.54\) (ddd, \(J_{HH} = 14.8\) and 11.6 Hz, \(J_{HP} = 3.2\) Hz, 1H), \(4.33\) (dd, \(J_{HH} = 9.2\) and 4.8 Hz, 1H), \(3.67\) (s, 3H), \(3.06\) (ddd, \(J_{HH} = 18.8\) and 11.6 Hz, \(J_{HP} = 7.2\) Hz, 1H), \(2.86\) (ddd, \(J_{HH} = 14.4\) and 3.2 Hz, \(J_{HP} = 8.8\) Hz, 1H), \(1.89-1.78\) (m, 1H), \(0.49\) (d, \(J_{HH} = 6.8\) Hz, 3H), \(0.41\) (d, \(J_{HH} = 6.8\) Hz, 3H). \(^{31}\text{P}\{^1\text{H}\} \text{ NMR (CDCl}_3\): \(\delta 45.4\) (s).

A mixture of S2 (840 mg, 1.75 mmol) and LiBH₄ (76 mg, 3.50 mmol) in THF (40 mL) was stirred at room temperature for 6 h. The reaction was quenched by H₂O (1 mL) and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography with CH₂Cl₂/MeOH = 100/1 to afford S3 (CAS: 216863-12-6) as a white solid (771 mg, 1.71 mmol; 98% yield). \([\alpha]_{D}^{20} = -138 \text{ (c 1.00, CH}_2\text{Cl}_2)\).

\[^1\text{H}\] NMR (CDCl₃): \(\delta 8.21-8.15\) (m, 2H), \(7.56-7.42\) (m, 5H), \(7.32-7.08\) (m, 8H), \(5.66\) (d, \(J = 7.6\) Hz, 1H), \(4.57\) (td, \(J = 10.4\) and 3.6 Hz, 1H), \(3.50-3.38\) (m, 3H), \(3.00\) (ddd, \(J_{HH} = 14.4\) and 10.4 Hz, \(J_{HP} = 9.6\) Hz, 1H), \(2.82\) (ddd, \(J_{HH} = 13.6\) and 4.0 Hz, \(J_{HP} = 9.6\) Hz, 1H), \(2.32\) (bs, 1H), \(1.62-1.53\) (m, 1H), \(0.61\) (d, \(J_{HH} = 7.2\) Hz, 3H), \(0.47\) (d, \(J_{HH} = 6.8\) Hz, 3H). \(^{31}\text{P}\{^1\text{H}\} \text{ NMR (CDCl}_3\): \(\delta 45.4\) (s).
MsCl (4.24 g, 37 mmol) was added to a solution of S3 (667 mg, 1.48 mmol) in dichloromethane (30 mL) and Et₃N (10 ml) and the mixture was stirred at room temperature overnight. The mixture was filtered and washed with dichloromethane. The filtrate was concentrated under vacuum and the residue was purified by neutral alumina chromatography with dichloromethane to afford S4 (CAS: 192371-97-4) as a white solid (457 mg, 1.05 mmol; 71% yield). [α]²⁰_D = -146 (c 1.00, CH₂Cl₂).

1H NMR (CDCl₃): δ 8.19-8.14 (m, 2H), 7.57-7.43 (m, 5H), 7.33-7.07 (m, 8H), 5.66 (d, J = 7.6 Hz, 1H), 4.48 (ddd, J_HH = 13.2 and 3.2 Hz, J_HP = 10.0 Hz, 1H), 3.94 (dd, J_HH = 9.2 and 8.0 Hz, 1H), 3.76-3.67 (m, 2H), 3.21 (ddd, J_HH = 19.6 and 12.0 Hz, J_HP = 7.6 Hz, 1H), 2.75 (ddddd, J_HH = 16.4, 8.4, 2.8 and 4.0 Hz, 1H), 1.45-1.37 (m, 1H), 0.59 (d, J_HH = 6.4 Hz, 3H), 0.47 (d, J_HH = 7.2 Hz, 3H). 31P{¹H} NMR (CDCl₃): δ 50.3 (s).

Raney Ni (100 eq) in degassed H₂O (10 mL) was washed with degassed methanol (30 mL) for three times, then a solution of S4 (320 mg, 0.74 mmol) in acetonitrile (30 mL) was added to it. The mixture was stirred at room temperature for two days. Raney nickel was filtered under nitrogen with dichloromethane. The solvent was removed under vacuum to afford (5'R,2'S)-6 (CAS: 192372-08-0) as a white solid (225 mg, 0.56 mmol; 76% yield). [α]²⁰_D = -97.2 (c 1.00, CH₂Cl₂).

1H NMR (CDCl₃): δ 7.68-7.65 (m, 2H), 7.44-7.38 (m, 3H), 7.18-7.06 (m, 10H), 4.04-3.96 (m, 1H), 3.94 (dd, J_HH = 9.2 and 8.0 Hz, 1H), 3.72 (t, J_HH = 7.2 Hz, 1H), 3.70-3.62 (m, 1H), 2.80 (dd, J_HH = 15.6 and 12.0 Hz, J_HP = 6.4 Hz, 1H), 2.64 (dt, J_HH = 16.8 and 5.2 Hz, 1H), 1.51-1.41 (m, 1H), 0.70 (d, J_HH = 6.8 Hz, 3H), 0.63 (d, J_HH = 6.8 Hz, 3H). 31P{¹H} NMR (CDCl₃): δ 0.5 (s).
References:

### Shimadzu LCsolution Analysis Report

**Sample Name:** \( \text{Sample 175-5} \)  
**Date:**  
**Column:**  
**Mobile Phase:**  
**Velocity:**  
**Detection Wavelength:**

### Chromatogram

![Chromatogram](image)

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### Shimadzu LCsolution Analysis Report

**Sample Name:** \( \text{Sample 175-2} \)  
**Date:**  
**Column:**  
**Mobile Phase:**  
**Velocity:**  
**Detection Wavelength:**

### Chromatogram

![Chromatogram](image)

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
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<tbody>
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<td>99.72</td>
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SS2
**** Shimadzu LCsolution Analysis Report ****

Sample Name: 06-74-11  Date:

Column:  The mobile phase:

Velocity:  The detection wavelength:

<Chromatogram>

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<td>2</td>
<td>32.902</td>
<td>1109</td>
<td>92.16</td>
<td>0.133</td>
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<td>Total</td>
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**** Shimadzu LCsolution Analysis Report ****

Sample Name: 06-74-1  Date:

Column:  The mobile phase:

Velocity:  The detection wavelength:

<Chromatogram>

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<td>Total</td>
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<td>69501.7</td>
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<td>100.00</td>
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== Shimadzu LCsolution Analysis Report ==

Sample Name: 06051-214
Date:
Column: The mobile phase:
Velocity: The detection wavelength:

<Chromatogram>

Detector & Calc. 24/7

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Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2011

== Shimadzu LCsolution Analysis Report ==

Sample Name: 06051-214
Date:
Column: The mobile phase:
Velocity: The detection wavelength:

<Chromatogram>

Detector & Calc. 24/7

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==== Shimadzu LCsolution Analysis Report ====  

**Sample Name:** 666-227x-4 AD  
**Date:**

**Column:** The mobile phase: 
**Velocity:** The detection wavelength:

![Chromatogram](image)

<table>
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<th>Ret. Time</th>
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</tbody>
</table>

==== Shimadzu LCsolution Analysis Report ====  

**Sample Name:** 666-227x-4 AD  
**Date:**

**Column:** The mobile phase: 
**Velocity:** The detection wavelength:

![Chromatogram](image)

<table>
<thead>
<tr>
<th>Ret. Time</th>
<th>Area</th>
<th>Weight</th>
<th>Area %</th>
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<tbody>
<tr>
<td>1</td>
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<td>100.00</td>
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