Enantioselective Reduction of Imines Catalyzed by a Rhenium(V)-Oxo Complex

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General Information. Unless otherwise noted all commercial materials were purchased from Aldrich and used without purification. Small scale reactions (< 4 mL) were carried out in Fisher Scientific disposable scintillation vials. ACS grade acetone, ethyl acetate, hexane, and dichloromethane were obtained from EM Science. Dry solvents were passed through an alumina column unless otherwise noted. N,N,N',N' Tetramethylethylenediamine (TMEDA) was distilled from CaH prior to use. All reaction mixtures were stirred with a magnetic stir bar. TLC analysis of reaction mixtures was performed on Merck silica gel 60 F₂₅₄ TLC plates. Chromatography was carried out on Merck 60 silica gel (32-63 μ m) and Aldrich neutral activated aluminum oxide (~150 mesh, 58Å). ¹H and ¹³C NMR spectra were recorded with Bruker AV-300, AVQ-400, AVB-400, and DRX-500 spectrometers and referenced to CDCl₃ unless otherwise noted. Enantiomeric excess was determined using an Agilent 1100 Series Chiral HPLC or Shimatzu 10A VP Series Chiral HPLC with detection at 254 nm. Mass spectral and analytical data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley. Crystal structures were solved by the Crystallographic Facilities at the University of California, Berkeley.

Experimental:

2,2'-Methylenebis[(4R)-4-(*p*-*tert*-butylphenyl)-2-oxazoline].¹ Diethyl malonimidate dihydrochloride (0.962 mg, 4 mmol) in dry CH₂Cl₂ (44 mL) was cooled to 0 °C in an oven-dried round-bottom flask equipped with a magnetic stir bar under N₂ atmosphere.

(*R* or *S*)-2-Amino-2-(*p*-*tert*-butylphenyl)ethanol² (1.9322 g, 10 mmol) was added to the reaction mixture and the ice bath was removed. The solution was stirred at room temperature for 3 days. Upon completion, the reaction was quenched with ice water and extracted three times with CH₂Cl₂. The organic phases were combined, dried with Na₂SO₄, filtered and the solvents were evaporated. The residue was chromatographed yielding a white solid. (silica gel chromatography, eluent 2.5-10% MeOH in CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 7.37 (d, *J* = 8.4 Hz, 4H), 7.24 (d, *J* = 8.3 Hz, 4H), 5.24 (t, *J* = 9.1 Hz, 2H), 4.68 (dd, *J* = 10.2, 8 Hz, 2H), 4.22 (t, *J* = 8.1 Hz, 2H), 3.57 (s, 2H), 1.31 (s, 18H); ¹³C{¹H} NMR (100 MHz,

□□□□□□□□□□□□HRMS (EI) calcd for $[C_{27}H_{34}N_2O_2]^+$ 418.2620, Found 418.2622. Yield: 1.3 g, 78%

added slowly to the reaction solution. Immediately following, TMEDA (0.55 mL, 3.64 mmol) was added to the reaction solution and the solution was stirred at -78°C for 1 h then 0°C for 30 min. The reaction solution was cooled to -78°C and 1.12 equiv of *p*-toluenesulfonyl cyanide was added. The reaction solution was allowed to warm slowly to room temperature and stirred overnight. After 12 h, the reaction was quenched with sat. NH_4Cl and was stirred at room temperature for 5 min then triturated with Et_2O and filtered. The reaction solution was extracted 3 times with Et_2O and 2 times with CH_2Cl_2 . The organic layers were combined, dried, filtered, and the solvents were evaporated. The residue was then chromatographed yielding a white solid, the pure cyanobis(oxazoline), 925 mg, 67% (neutral activated aluminum oxide chromatography, eluent 20% EtOAc in hexanes); ^1H NMR (400MHz, CDCl_3) δ 7.38 (d, J = 8.3 Hz, 4H), 7.17 (d, J = 8.3 Hz, 4H), 5.14-5.10 (m, 2H), 4.83-4.78 (m, 2H), 4.33-4.29 (m, 2H), 1.30 (s, 18H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100MHz, CDCl_3) δ 167.6, 151.6, 137.6, 126.2, 126.0, 76.0, 64.2, 34.6, 31.3; Anal. Calcd. for $\text{C}_{28}\text{H}_{33}\text{N}_3\text{O}_5$: C 75.81, H 7.50, N 9.47; Found C 75.64, H 7.61, N 9.20.

General Procedure for Synthesis of *Catalyst 3*. Re(V)dimethylsulfide complex **1**⁴ (1 equiv) was added to a round-bottom flask charged with a magnetic stir bar. CH₂Cl₂ was added to a reaction flask to a concentration of 5 mM. In a scintillation vial, 1.1 equiv of cyanobis(oxazoline) ligand was diluted in CH₂Cl₂ (5 mM). Ligand solution was added slowly to Re suspension. Reaction solution quickly changes from light green to very dark green. Reaction stirred at rt for ~5 h at which time the solution is a bright emerald green. (Note: This reaction time can be reduced to 30 minutes by adding 1 drop of DMSO; however, isolation of the product becomes more difficult.) Solvent was evaporated and the dark green film was diluted with a small amount of CH₂Cl₂, then triturated with Et₂O. Filtration with a Buchner funnel

yields Re complex **3**, a bright green solid. The trituration was repeated 4 times or until no significant material was isolated. The resultant solid was dried *in vacuo*.

Re(V) complex 3: Yield: 74%; ^1H NMR (400 MHz, CD_2Cl_2) δ 7.65 (t, J = 7.6 Hz, 3H), 7.52-7.47 (m, 6H), 7.28-7.15 (m, 8H), 6.95 (dd, J = 7.6, 2.1 Hz, 4H), 6.62 (bs, 2H), 6.06 (d, J = 6.4 Hz, 1H), 5.19 (bs, 1H), 4.81 (t, J = 8.4 Hz, 1H), 4.64 (d, J = 8.4 Hz, 1H), 4.46 (d, J = 6.4 Hz, 1H), 4.19 (bs, 1H), 1.24 (s, 9H), 0.94 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR Dept 135 (100 MHz, CD_2Cl_2) δ 135.4, 130.7, 130.5, 128.9; $^{31}\text{P}\{^1\text{H}\}$ (162 MHz, CD_2Cl_2) 43.2 (very broad, s); IR 2950, 2215, 1600, 1493, 1135, 1086, 996 ν max cm^{-1} ; Anal. Calcd. for $\text{C}_{46}\text{H}_{47}\text{Cl}_2\text{N}_3\text{O}_4\text{PRe}$: C 55.58, H 4.77, N 4.23; Found C 55.31, H 5.09, N 3.98.

Imine **4** was synthesized by modification literature procedure.⁵ This procedure was followed for the synthesis of imines **6a-j** and **10a-f**. Oxime (12.6 mmol) was added to an oven-dried round-bottom flask charged with a magnetic stir bar under N_2 . Dry CH_2Cl_2 (150 mL) and hexanes (150 mL) were added to a reaction flask. Dry triethylamine (2.00 mL, 14.2 mmol) was added to the reaction solution, which was then cooled to -45°C and stirred for 5 minutes. Chlorodiphenylphosphine (2.54 mL, 14.1 mmol) was diluted with 10 mL of dry CH_2Cl_2 and then was added dropwise to reaction solution over a period of 45 minutes. The reaction solution was stirred at -45°C for 1 hour, slowly warmed to room temperature, and then stirred for 1 hour at room temperature. The solvents were evaporated under 20°C . The residue was diluted CH_2Cl_2 and washed twice with water and once with brine. The organic phase was dried with Na_2SO_4 , filtered, and solvents evaporated. The residue was chromatographed yielding the phosphinyl imine (silica gel chromatography, eluent 10-50% acetone in CH_2Cl_2). (On occasion, recrystallization was needed for isolation of pure imine.) Yield: 61%; ^1H NMR (400 MHz, CDCl_3) δ 8.03-7.98 (m, 4H), 7.62 (d, J = 3.6 Hz, 1H), 7.58 (d, J = 4.8 Hz, 1H), 7.45-7.41 (m, 6H), 7.10 (t, J = 4.4 Hz, 1H), 2.90 (d, J = 1.6 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 174.7 (d, J = 5.8 Hz), 147.6 (d, J = 27.4 Hz), 135.6, 134.3, 133.5, 131.6 (d, J = 9.0 Hz), 131.4 (d, J = 2.4 Hz), 128.5 (d, J = 12.4 Hz), 128.5, 22.9 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, CDCl_3) δ 18.3. HRMS (EI) calcd for $[\text{C}_{18}\text{H}_{16}\text{NOPS}]^+$

325.0690, Found 325.0688; Anal. Calcd. for C₁₈H₁₆NOPS: C 66.45, H 4.96, N 4.30, S 9.86; Found C 66.29, H 5.14, N 4.20, S 9.72.

α -Imino ester **8a** was synthesized by literature procedure.⁶ This procedure was followed for the synthesis of imines **8 b-c**. Imine was purified by column chromatography (silica gel chromatography, eluent 10-50% acetone in CH₂Cl₂). Yield: 61%; ¹H NMR (400 MHz, CDCl₃) δ 7.99-7.90 (m, 6H), 7.59-7.55 (m, 1H), 7.49-7.41 (m, 8H), 4.55 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 170.5 (d, *J* = 8.0 Hz), 165.6 (d, *J* = 16 Hz), 133.8, 133.6, 133.3, 132.0-131.6 (m), 129.9 (d, *J* = 13.0 Hz), 128.5 (d, *J* = 13 Hz), 62.6, 14.0; ³¹P NMR (162 MHz, CDCl₃) δ 21.7. HRMS (EI) calcd for [C₂₂H₂₁NO₃P]⁺ 378.1259, Found 378.1259; Anal. Calcd. for C₁₈H₁₆NOPS: C 70.02, H 5.34, N 3.71; Found C 69.81, H 5.18, N 3.55.

General Procedure for Asymmetric Reduction of Phosphinyl Imines with Asymmetric Catalyst. To a 7.4 mL Fischer vial charged with a solution of imine (50 mg, 1 equiv) in CH₂Cl₂ (1 M), was added silane (2 equiv) followed by catalyst **1** (3 mol%). The reaction was monitored by TLC. Upon completion or 72 hours, the reaction was chromatographed. The reaction mixture was loaded directly on to a silica gel column and chromatographed with the 10-50% acetone in CH₂Cl₂ to give the amine. Absolute configurations were assigned by comparison of the HPLC retention times to literature values.⁷

(**5**) Yield: 75%; ¹H NMR (400 MHz, CDCl₃) δ 8.05-7.90 (m, 4H), 7.52-7.40 (m, 6H), 7.22-7.20 (m, 1H), 6.94-6.92 (m, 2H), 4.62-4.53 (m, 1H), 3.36-3.32 (m, 1H), 1.70 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 149.7 (d, *J* = 9.0 Hz), 133.5, 132.5, 132.5 (d, *J* = 9.5 Hz), 132.3, 132.2, 131.9, 131.8, 131.0, 128.5 (d, *J* = 12.5 Hz), 126.9, 124.1, 123.6, 47.2, 26.0; ³¹P NMR (162 MHz, CDCl₃) δ 22.1; HRMS (EI) calcd for [C₁₈H₁₉NOPS]⁺ 328.0925, Found 328.0929; Anal. Calcd. for C₁₈H₁₈NOPS: C 66.04, H 5.54, N 4.28, S 9.79; Found C 65.74, H 5.70, N 4.32, S 9.42; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 8.3 min, major isomer 10.2min): 99% ee.

(7a) Yield: 51%;⁷ %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 7.9 min, major isomer 10.5 min): 99% ee.

(7b) Yield: 61%; ¹H NMR (500 MHz, CDCl₃) δ 7.92-7.81 (m, 4H), 7.50-7.36 (m, 6H), 7.21 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 4.40-4.30 (m, 1H), 3.79 (s, 3H), 3.23-3.13 (m, 1H), 1.55 (d, *J* = 6.5 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 158.6, 133.6, 132.4-131.6 (m), 128.5-128.3 (m), 127.1, 113.8, 55.2, 50.4, 25.8; ³¹P NMR (162 MHz, CDCl₃) δ 21.3; HRMS (EI) calcd for [C₂₁H₂₃NO₂P]⁺ 352.1466, Found 352.1468; %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 10.3 min, major isomer 11.5 min): 98% ee.

(7c) Yield: 78%; ¹H NMR (400 MHz, CDCl₃) δ 7.92-7.87 (m, 2H), 7.80-7.75 (m, 2H), 7.55-7.33 (m, 10H), 4.49-4.38 (m, 1H), 3.38-3.34 (m, 1H), 1.58 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 149.0 (d, *J* = 9 Hz), 132.4-131.9 (m), 128.7-128.4 (m), 126.4, 125.5 (bq, *J* = 4 Hz), 50.7, 25.8 (d, *J* = 4 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -61.63; ³¹P NMR (162 MHz, CDCl₃) δ 22.9; HRMS (EI) calcd for [C₂₁H₂₀F₃NOP]⁺ 390.1235, Found 390.1233; Anal. Calcd. for C₁₈H₁₈NOPS: C 64.78, H 4.92, N 3.60; Found C 64.55, H 5.13, N 3.43; %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 7.7 min, major isomer 9.1 min): 98% ee.

(7d) Yield: 71%; ¹H NMR (400 MHz, CDCl₃) δ 7.92-7.89 (m, 2H), 7.84-7.79 (m, 2H), 7.59 (d, *J* = 7.6, 2H), 7.52-7.44 (m, 4H), 7.41-7.37 (m, 2H), 7.07 (d, *J* = 8.4, 2H), 4.40-4.30 (m, 1H), 3.37-3.33 (m, 1H), 1.57 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 144.8 (d, *J* = 6 Hz), 137.6, 132.7-131.9 (m), 128.6-128.4 (m), 128.2, 92.4, 50.6, 25.8 (d, *J* = 3 Hz); ³¹P NMR (162 MHz, CDCl₃) δ 22.9; HRMS (EI) calcd for [C₂₀H₂₀INOP]⁺ 448.0327, Found 448.0336; %ee by HPLC (Chiralcel OD Column , ethanol:hexanes = 2:98 (1.5 mL/min), minor isomer 12.5 min, major isomer, 14.3 min): 99% ee.

(7e) Yield: 81%; ^1H NMR (400 MHz, CDCl_3) δ 8.00-7.78 (m, 7H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.56-7.47 (m, 5H), 7.39-7.23 (m, 6H), 4.74-4.62 (m, 1H), 3.35-3.26 (m, 1H), 2.38 (s, 3H), 1.68 (d, $J = 6.4$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 145.0, 135.4 (d, $J = 22$ Hz), 132.2-131.9 (m), 130.0, 128.7-128.4 (m), 126.9, 124.9, 123.2, 122.6, 120.4, 113.7, 43.9, 24.6, 21.6; ^{31}P NMR (162 MHz, CDCl_3) δ 23.08; HRMS (EI) calcd for $[\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_3\text{PS}]^+$ 515.1558, Found 515.1556; Anal. Calcd. for $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_3\text{PS}$: C 67.69, H 5.27, N 5.44, S 6.23; Found C 67.30, H 5.27, N 5.32, S 6.40; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 29.0 min, major isomer 40.7 min): 99% ee.

(7f) Yield: 68%; ^1H NMR (400 MHz, CDCl_3) δ 7.92-7.75 (m, 4H), 7.51-7.16 (m, 11 H), 4.25-4.11 (m, 1H), 3.38-3.23 (m, 1H), 2.00-1.94 (m, 1H), 1.86-1.77 (m, 1H), 1.39-1.12 (m, 2H), 0.85 (t, $J = 8.0$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 143.9 (d, $J = 5$ Hz), 133.9-131.6 (m), 128.5-128.2 (m), 127.0, 126.4, 55.6, 42.0, 19.4, 13.8; ^{31}P NMR (162 MHz, CDCl_3) δ 22.6; HRMS (EI) calcd for $[\text{C}_{22}\text{H}_{25}\text{NOP}]^+$ 350.1674, Found 350.1666; Anal. Calcd. for $\text{C}_{22}\text{H}_{24}\text{NOP}$: C 75.62, H 6.92, N 4.01; Found C 75.46, H 7.09, N 3.87; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 6.3 min, major isomer 10.2 min): 99% ee.

(7g) Yield: 76%; ^1H NMR (400 MHz, CDCl_3) δ 7.95-7.85 (m, 4H), 7.80-7.75 (m, 7H), 6.26 (s, 1H), 6.12 (d, $J = 2.8$ Hz, 1H), 4.41-4.35 (m, 1H), 3.31-3.27 (m, 1H), 1.58 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 157.0 (d, $J = 8$ Hz), 141.7, 133.6-131.2 (m), 128.5, 128.4, 110.1, 105.2, 45.1, 23.1; ^{31}P NMR (162 MHz, CDCl_3) δ 22.5; HRMS (EI) calcd for $[\text{C}_{18}\text{H}_{18}\text{NO}_2\text{P}]^+$ 311.1075, Found 311.1072; Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}_2\text{P}$: C 69.45, H 5.83, N 4.50; Found C 69.22, H 5.81, N 4.67; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 5:95 (1.0 mL/min), major isomer 12.2 min, minor isomer 13.7 min): 99% ee.

(7h) Yield: 71%; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 7.13 min, minor isomer 12.6 min): 96% ee.

(7i) Yield: 89%;⁷ %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 5:95 (1.0 mL/min), minor isomer 12.2 min, major isomer 13.7 min): 95% ee.

(7j) Yield: 69%; ¹H NMR (400 MHz, CDCl₃) δ 8.04-8.00 (m, 4H), 7.54-7.50 (m, 6H), 7.37 (d, *J* = 7.6 Hz, 1H) 7.24 (t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.0 Hz), 4.40-4.31 (m, 1H), 3.83 (s, 3H), 3.30-3.22 (m, 1H), 2.69-2.55 (m, 2H), 2.14-2.05 (m, 1H), 2.00-1.83 (m, 2H), 1.81-1.70 (m, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.0, 139.8, 132.4-131.9 (m), 128.7-128.5 (m), 126.5, 121.0, 108.2, 55.37, 49.8, 32.7, 22.91, 19.1; ³¹P NMR (162 MHz, CDCl₃) δ 22.1; HRMS (EI) calcd for [C₂₃H₂₅NO₂P]⁺ 378.1623, Found 378.1630; %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 10:90 (1.0 mL/min), major isomer 10.7 min, minor isomer 12.2 min): 99% ee.

(7k) Yield: 76%; ¹H NMR (400 MHz, CDCl₃) δ 7.14 (t, *J* = 8 Hz, 1H), 7.04 (d, *J* = 8 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8 Hz, 1H), 6.63 (d, *J* = 8 Hz, 2H), 4.25 (t, *J* = 4.0 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.60(bs, 1H), 2.81-2.74 (m, 1H), 2.59-2.51 (m, 1H), 1.97-1.71 (m, 4H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.0, 151.8, 141.8, 139.6, 126.6, 126.2, 121.2, 115.0, 114.2, 108.0, 55.8, 55.3, 52.0, 28.1, 23.0, 18.6; HRMS (EI) calcd for [C₁₈H₂₁NO₂]⁺ 283.1572, Found 283.1574; %ee by HPLC (Chiralcel OD Column , 2-propanol:hexanes = 1:99 (1.0 mL/min), major isomer 18.1 min, minor isomer 20.3 min): 92% ee.

(7l) Yield: 69%; ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.86 (m, 4H), 7.48-7.38 (m, 6H), 3.06-2.94 (m, 1H), 2.78-2.75 (m, 1H), 1.78-1.68 (m, 3H), 1.67-1.58 (m, 2H), 1.41-1.31 (m, 1H), 1.26-0.87 (m, 5H), 1.16 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 134.1, 133.6, 132.8, 132.3-132.1 (m), 131.9-131.7 (m), 128.5-128.3 (m), 52.0 (d, *J* = 2.0 Hz), 45.0 (d, *J* = 6 Hz), 29.4, 28.3, 26.5, 26.4, 26.3, 20.6 (d, *J* = 4 Hz); ³¹P NMR (162 MHz, CDCl₃) δ 22.1; HRMS (EI) calcd for [C₂₀H₂₇NOP]⁺ 328.1830, Found 328.1829; Anal. Calcd. for C₂₀H₂₆NOP: C 73.37, H 8.00, N 4.28; Found C 72.37, H 7.90, N 4.15. %ee by HPLC (Chiralcel OD Column , ethanol:hexanes = 1:99 (1.0 mL/min), major isomer 10.2 min, minor isomer 13.0 min): 32% ee.

(9a) Yield: 83%; ^1H NMR (400 MHz, CDCl_3) δ 7.89-7.86 (m, 2H), 7.76-7.62 (m, 3H), 7.53-7.38 (m, 5H), 7.35-7.22 (m, 5H), 4.91 (t, J = 9.9 Hz, 1H), 4.35-4.30 (m, 1H), 4.23-4.02 (m, 2H), 1.14 (t, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 172.4, 138.6 (d, J = 8 Hz), 133.2, 132.7-132.1 (m), 131.5, 130.85, 129.0-128.4 (m), 127.3, 62.3, 57.2, 14.22; ^{31}P NMR (162 MHz, CDCl_3) δ 23.9; HRMS (EI) calcd for $[\text{C}_{19}\text{H}_{17}\text{NOP}]^+$ (M- $\bullet\text{C}(\text{O})\text{OEt}$) 306.1049, Found 306.1052; Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{P}$: C 69.65, H 5.84, N 3.69; Found C 69.44, H 5.84, N 3.47; %ee by HPLC (Chiralcel OJ Column, 2-propanol:hexanes = 5:95 (1.0 mL/min), major isomer 12.1 min, minor isomer 22.5 min): 99% ee.

(9b) Yield: 47%; ^1H NMR (400 MHz, CDCl_3) δ 7.88-7.83 (m, 2H), 7.77-7.72 (m, 2H), 7.54-7.42 (m, 4H), 7.35-7.31 (m, 2H), 7.17 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 4.90 (t, J = 10.0 Hz, 1H), 4.29-4.25 (m, 1H), 3.78 (s, 3H), 3.67 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 172.8 (d, J = 7 Hz), 159.4, 132.8, 132.4-131.8 (m), 131.6, 131.0, 130.4 (d, J = 5 Hz), 128.6-128.2 (m), 114.1, 56.2, 55.3, 52.8; ^{31}P NMR (162 MHz, CDCl_3) δ 23.5; HRMS (EI) calcd for $[\text{C}_{22}\text{H}_{23}\text{NO}_4\text{P}]^+$ 396.1365, Found 396.1371; Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{NO}_4\text{P}$: C 66.83, H 5.61, N 3.54; Found C 66.89, H 5.81, N 3.63; %ee by HPLC (Chiralcel OJ Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), major isomer 12.0 min, minor isomer 18.2 min): 95% ee.

(9c) Yield: 69%; ^1H NMR (400 MHz, CDCl_3) δ 7.90-7.85 (m, 2H), 7.69-7.64 (m, 2H), 7.54-7.37 (m, 4H), 7.30-7.22 (m, 3H), 7.20-7.12 (m, 2H), 7.02-7.00 (m, 1H), 4.173 (dd, J = 11.6, 8.4 Hz, 1H), 4.39 (dd, J = 8.4, 8.0 Hz, 1H), 3.64 (s, 3H), 2.05 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 173.0 (d, J = 6 Hz), 159.6, 137.1 (d, J = 3 Hz), 132.9, 132.5-131.7 (m), 130.7, 130.5, 128.6-128.0 (m), 126.6, 126.4, 52.9, 52.8, 19.0; ^{31}P NMR (162 MHz, CDCl_3) δ 23.3; HRMS (EI) calcd for $[\text{C}_{22}\text{H}_{23}\text{NO}_3\text{P}]^+$ 380.1416, Found 380.1420; %ee by HPLC (Chiralcel OJ Column, 2-propanol:hexanes = 5:95 (1.0 mL/min), major isomer 9.9 min, minor isomer 17.9 min): 99% ee.

(11a) Yield: 71%; ^1H NMR (400 MHz, CDCl_3) δ 7.95-7.85 (m, 4H), 7.69-7.62 (m, 1H), 7.56-7.37 (m, 5H), 7.32-7.25 (m, 2H), 7.21-7.11 (m, 3H), 6.08 (s, 1H), 3.70-3.59 (m, 1H), 3.04-3.00 (m, 1H), 1.87-1.59 (m, 5H), 0.88 (t, $J = 7.5$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 138.3, 137.9, 133.0-132.0 (m), 129.2-128.3 (m), 127.5, 126.6, 61.0, 29.3 (d, $J = 4.5$ Hz), 13.3, 10.9; ^{31}P NMR (162 MHz, CDCl_3) δ 22.5; HRMS (EI) calcd for $[\text{C}_{24}\text{H}_{27}\text{NOP}]^+$ 375.1830, Found 376.1833; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 15:85 (1.0 mL/min), minor isomer 5.3 min, major isomer 10.9 min): 99% ee.

(11b) Yield: 61%; ^1H NMR (400 MHz, CDCl_3) δ 7.94-7.87 (m, 4H), 7.51-7.39 (m, 6H), 7.08 (d, $J = 8.4$ Hz, 2H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.02 (s, 1H), 3.82 (s, 3H), 3.68-3.60 (m, 1H), 3.02-2.98 (m, 1H), 1.80 (s, 3H), 2.75-1.48 (m, 2H), 0.89 (t, $J = 7.6$ Hz, 3H); ^{31}P NMR (162 MHz, CDCl_3) δ 22.4; HRMS (EI) calcd for $[\text{C}_{25}\text{H}_{28}\text{NO}_2\text{P}]^+$ 405.1858, Found 405.1855; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 5:95 (1.0 mL/min), minor isomer 15.0 min, major isomer 18.1 min): 92% ee.

(11c) Yield: 67%; ^1H NMR (400 MHz, CDCl_3) δ 7.93-7.86 (m, 4H), 7.52-7.38 (m, 6H), 7.26 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 6.02 (s, 1H), 3.69-3.61 (m, 1H), 3.03-2.99 (m, 1H), 1.77 (d, $J = 1.2$ Hz, 3H), 1.83-1.75 (m, 1H), 1.72-1.63 (m, 1H), 0.90 (t, $J = 7.6$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 138.7 (d, $J = 4.0$ Hz), 135.9, 132.6, 132.0-131.7 (m), 130.1, 128.5-128.1 (m), 126.1, 60.6, 28.8, 12.9, 10.6; ^{31}P NMR (162 MHz, CDCl_3) δ 22.2; HRMS (EI) calcd for $[\text{C}_{24}\text{H}_{25}\text{ClNOP}]^+$ 409.1362, Found 409.1363; %ee by HPLC (Chiralpak AD Column, ethanol:hexanes = 5:95 (1.3 mL/min), minor isomer 12.2 min, major isomer 13.5 min): 97% ee.

(11d) Yield: 63%; ^1H NMR (300 MHz, CDCl_3) δ 7.98-7.86 (m, 4H), 7.48-7.39 (m, 6H), 7.17-7.11 (m, 3H), 7.06-7.02 (m, 1H), 6.16 (s, 1H), 3.75-3.64 (m, 1H), 3.06-3.01 (m, 1H), 2.15 (s, 3H), 1.92-1.78 (m, 1H), 1.77-1.60 (m, 1H), 1.65 (d, $J = 1.2$ Hz, 3H), 0.91 (t, $J = 9.6$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 138.4 (d, $J = 5.3$ Hz), 137.1, 136.7, 132.9-128.6 (m), 127.0, 126.4, 125.5, 60.5, 29.4 (d, $J = 4.5$ Hz), 20.2, 13.1, 10.9; ^{31}P NMR (122 MHz, CDCl_3) δ 22.3; HRMS (EI) calcd for

[C₂₅H₂₈NOP]⁺ 389.1909, Found 389.1900; %ee by HPLC (Chiralpak AD Column, 2-propanol:hexanes = 10:90 (1.0 mL/min), minor isomer 10.1 min, major isomer 13.6 min): 74% ee.

(11e) Yield: 72%; ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.85 (m, 4H), 7.52-7.40 (m, 6H), 7.36-7.12 (m, 5H), 6.44 (d, *J* = 16.0 Hz, 1H), 6.25 (dd, *J* = 16.0, 5.6 Hz, 1H), 4.04-3.93 (m, 1H), 2.99-2.95 (m, 1H), 1.44 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 136.7, 133.7-131.8, 128.9, 128.6-128.3 (m), 127.5, 126.4, 49.0, 24.1 (d, *J* = 4.0 Hz); ³¹P NMR (122 MHz, CDCl₃) δ 22.5; HRMS (EI) calcd for [C₂₂H₂₂NOP]⁺ 347.1439, Found 347.1444; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 15:85 (1.0 mL/min), minor isomer 7.3 min, major isomer 8.5 min): 75% ee.

(11f) Yield: 48%; ¹H NMR (400 MHz, CDCl₃) δ 7.90-7.84 (m, 4H), 7.49-7.40 (m, 6H), 7.29-7.25 (m, 2H), 7.20-7.16 (m, 3H), 5.10 (t, *J* = 6.8 Hz, 1H), 3.51-3.3.42 (m, 1H), 2.89-2.83 (m, 1H), 2.59-2.53 (m, 2H), 2.28-2.22 (m, 2H), 1.72-1.64 (m, 1H), 1.57-1.49 (m, 1H), 1.52 (s, 3H), 0.75 (t, *J* = 7.6 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 132.6-131.7 (m), 128.5-128.1 (m), 126.4, 125.7, 60.2, 35.6, 29.4, 28.7 (d, *J* = 4.0 Hz), 11.4, 10.4; ³¹P NMR (122 MHz, CDCl₃) δ 22.0; HRMS (EI) calcd for [C₂₆H₃₀NOP]⁺ 403.2065, Found 403.2068; %ee by HPLC (Chiralcel OD Column, 2-propanol:hexanes = 5:95 (1.0 mL/min), minor isomer 12.7 min, major isomer 14.7 min): 83% ee.

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