Supporting Information For:

Hammett Studies of Enantiocontrol by PHOX Ligands in Pd-Catalyzed Allylic Substitution Reactions

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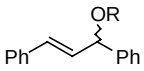
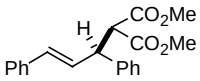
General Experimental Procedures.

Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone ketyl. Methylene chloride was distilled from calcium hydride. Anhydrous hexane and other reagents were purchased from Aldrich or Acros and used as received unless otherwise noted. Reactions were carried out under nitrogen using oven-dried glassware and monitored by TLC: silica gel 60 EM Science, 0.25mm, F254, visualizing with uv-light, potassium permanganate or *p*-anisaldehyde stains. Flash column chromatography was performed on silica gel, 0.035-0.07 mm, purchased from Acros. ^{1}H, ^{13}C and ^{31}P NMR, were taken on a Bruker 400 MHz instrument at the frequencies indicated. ^{1}H and ^{13}C spectra and referenced to the residual solvent peak (relative to tetramethylsilane at 0.00 ppm). For ^{31}P spectra 100% phosphoric acid (0.00 ppm) was used as an external reference.



1a R = Ac
1b R = CO_2Et

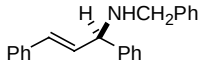
Substrates **1a**[1] and **1b**[2] were prepared from the corresponding allylic alcohol by literature methods and gave satisfactory spectral data. **1a**: ^{1}H NMR (400 MHz, $CDCl_3$): • 7.3-7.5 (m, 10H), 6.7 (d, *J* = 15.7 Hz, 1H), 6.5 (d, *J* = 6.9 Hz, 1H), 6.4 (dd, *J* = 15.7, 6.9 Hz, 1H), 2.2 (s, 3H). **1b**: ^{1}H NMR (400 MHz, $CDCl_3$): • 7.3-7.5 (m, 10H), 6.7 (d, *J* = 15.8 Hz, 1H), 6.4 (dd, *J* = 15.8, 7.0 Hz, 1H), 6.3 (d, *J* = 7.0 Hz), 4.2 (m, 2 H), 1.3 (t, *J* = 7.1 Hz, 3H).



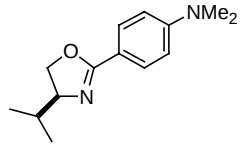
Typical Procedure for palladium-catalyzed dimethyl malonate alkylations (**2a**). To an 8 mL disposable test-tube was added 0.016 g of sodium hydride as a 60% dispersion in mineral oil (0.40 mmol; 2.0 equivalents), 1.0 mL of tetrahydrofuran, and 0.059 g of dimethyl malonate (0.45 mmol, 2.25 equivalents). After stirring for 10 min the dimethyl sodiomalonate solution was added to a second 8 mL disposable test tube containing 0.0018 g of η^3-allylpalladium chloride dimer (0.005 mmol, 0.025 equivalents), 5-7 mg of the appropriate chiral ligand (0.015 mmol, 0.075 equivalents), and 1.0 mL of tetrahydrofuran. Then, 0.050 g of 1,3-diphenylprop-2-enyl acetate (0.20 mmol, 1 equivalent) was added. The reaction was stirred at room temperature and monitored by TLC for the complete disappearance of starting material (typically 16-24 hours). Upon completion, the reaction was diluted with 5 mL of water and extracted with diethyl ether (3 × 10 mL). The combined organic phases were dried over sodium sulfate. The product was purified by flash column chromatography (1.5 cm × 15 cm, 10% ethyl acetate in hexanes) to give

[1] Trost, B.M.; Murphy, D.J. *Organometallics* **1985**, *4*, 1143.
[2] Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301.

the product as a white solid (typically 85-95% yield) which was analyzed by HPLC (Chiralpak AD, 90:10 hexane:2-propanol, 1.0 mL/min, detection at 254 nm) to determine the ee. HPLC analysis of several crude product mixtures confirmed that the ee did not change upon chromatographic purification. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.2-7.3 (m, 10H), 6.5 (d, *J* = 16.0 Hz, 1H), 6.3 (dd, *J* = 16.0, 8.5 Hz, 1H), 4.3 (dd, *J* = 10.8, 8.5 Hz, 1H), 3.9 (d, *J* = 10.8 Hz, 1H), 3.7 (s, 3H), 3.5 (s, 3H). Lit.[1]



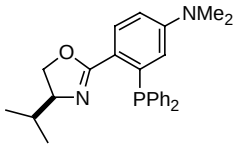
Typical Procedure for palladium-catalyzed benzylamine aminations (**2b**). To a 20 mL 14/20 reaction tube was added 0.0565 g of 1,3-diphenylprop-2-enyl ethyl carbonate (0.20 mmol, 1 equivalent) and 1.0 mL of a tetrahydrofuran solution containing 0.0037 g of η^3-allylpalladium chloride dimer (0.001 mmol, 0.05 equivalents (= 0.10 equivalents of palladium)) and the appropriate amount (8-10 mg) of chiral ligand (0.022 mmol, 0.11 equivalents). The tube was fitted with a stopcock adapator and then evacuated and backfilled with nitrogen via three freeze-pump-thaw cycles in liquid nitrogen. The stopcock adaptor was fitted with a septum, 0.0429 g of benzylamine (0.4 mmol, 2 equivalents) were added via syringe, and the stopcock was closed. The sealed reaction vessel was heated at 40 °C and monitored by TLC for the complete disappearance of starting material (typically 12-18 hours). The color change from yellow to orange to a final wine-red could also be used to guage the reaction progress and avoid excessive TLC analysis. Upon completion, the reaction mixture was filtered through a short plug of silica gel (~ 2 cm) washing with 10% ethyl acetate in hexanes, concentrated *in vacuo* and analyzed by HPLC (Chiralcel OJ, 85:15 hexane:2-propanol, 0.5 mL/min, detection at 254 nm) to determine the ee of the crude reaction mixture. The product was purified by flash column chromatography (1.5 cm × 18 cm, 10% ethyl acetate in hexanes) to give the product as an oil (typically 85-95% yield). HPLC analysis of several purified products confirmed that the ee did not change upon chromatographic purification. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.2-7.5 (m, 10H), 6.6 (d, *J* = 15.8 Hz, 1H), 6.3 (dd, *J* = 15.8, 7.5 Hz, 1H), 4.5 (d, *J* = 7.5 Hz, 1H), 3.8 (m, *2*H), 2.6 (bs, 1H). Lit.[2]



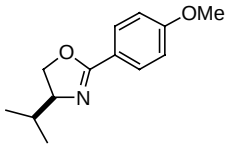
(–)-(4*S*)-4,5-dihydro-2-(4'-dimethylaminophenyl)-4-isopropyloxazole (7a). To a 100 mL round bottom flask was added 1.82 g of 4-dimethylaminobenzoic acid (11.0 mmol, 1.1 equivalents), 1.62 g of 1-hydroxybenzotriazole (12.0 mmol, 1.2 equivalents), 30 mL of methylene chloride, 1.03 g of (*S*)-2-amino-3-metyl-1-butanol (10.0 mmol, 1.0 equivalents), and, after cooling to 0 ºC, 2.48 g of dicyclohexylcarbodiimide (12.0 mmol, 1.2 equivalents). The reaction was allowed to warm to room temperature overnight (16 h). The reaction mixture was filtered through celite which was then washed with additional methylene chloride (2 × 20 mL). The combined organic phases were concentrated *in vacuo*. The product was separated by flash column chromatography (3 cm × 16 cm, 50-100% ethyl acetate in hexanes) yielding 2.35 g of yellow/white solid that was used without further purification in the following step. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.60 (d, *J* = 8.9 Hz, 2H), 6.53 (d, *J* = 8.9 Hz, 2H), 6.45 (d, *J* = 8.2 Hz, 1H), 3.83 (m, 1H), 3.71 (m, 2H), 2.93 (s, 6H), 1.97 (m, 1H), 0.93 (m, 6H).

To a 100 mL round bottom flask containing 2.35 g (~9.4 mmol) of the above yellow solid was added 1.93 g of *p*-toluenesufonyl chloride (10.1 mmol, 1.08 equivalents), 28.5 mL of

methylene chloride and 4.76g of triethylamine (47.0 mmol, 5.0 equivalents). The reaction was heated at reflux under nitrogen for 24 h. Then 0.75 mL of water was added and heating continued for an additional 1 h. The organic layer was washed with water (3 × 10 mL) and dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (3 cm × 15 cm, 15% ethyl acetate in hexanes) to give 1.48 g (6.4 mmol) of a yellow solid (64% from the aminoalcohol). m.p. = 51-54 °C. $[\alpha]_D$ = –45.9° (c 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): • 7.8 (d, *J* = 9.0 Hz, 2H), 6.7 (d, *J* = 9.0 Hz, 2H), 4.3 (m, 1H), 4.1 (m, 2H), 3.0 (s, 6H), 1.85 (m, 1H), 1.0 (d, *J* = 6.8 Hz, 3H), 0.9 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 163.6, 152.1, 129.4, 115.0, 111.0, 72.2, 69.5, 40.0, 32.8, 18.9, 17.8. IR (thin film) 2956, 2890, 1643, 1611, 1527, 1357, 1188, 1075, 946, 822 cm^{-1}. Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.38; H, 8.68; N, 12.06. Found: C, 72.14; H, 8.48; N, 12.14.



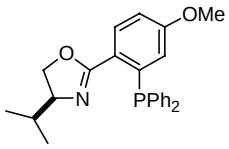
(–)-(4*S*)-4,5-dihydro -2-(4'-dimethylamino-2'-diphenylphosphinophenyl)-4-isopropyloxazole (3a). To a 100 mL round bottom flask was added 12.0 mL of anhydrous hexanes and 4.0 mL of 1.3 M *sec*-butyllithium in cyclohexane (5.2 mmol, 1.2 equivalents). The solution was cooled to –78 ºC and 0.55 g of N,N,N',N'-tetramethylethylenediamine (4.7 mmol, 1.1 equivalents) was added dropwise over 1-2 minutes resulting in a faint yellow color. After 10 minutes a solution of 1.00 g of **7a** (4.3 mmol) in 2.2 mL of hexanes was added dropwise via cannula over 5 minutes resulting in a deep orange to dark red color. After stirring at –78 ºC for 2 hours a solution of hexanes (4.3 mL) and 1.90 g of chlorodiphenylphosphine (8.6 mmol, 2.0 equivalents) was added dropwise via cannula over 1-2 minutes. The reaction was stirred at –78 ºC for 3 hours and was then allowed to warm to room temperature overnight. The reaction was quenched by adding 10.0 g of dry silica gel via syringe and evaporation of the solvent *in vacuo*. The product was purified by flash column chromatography (3 cm × 14 cm, 10% ethyl acetate in hexanes) yielding 1.79 g (4.3 mmol) of clear oil (99%). $[\alpha]_D$ –29.9 (c 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): • 7.88 (dd, *J* = 8.7, 4.1 Hz, 1H), 7.33 (m, 10H), 6.62 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.10 (dd, *J* = 5.0, 2.7 Hz, 1H), 4.11 (m, 1H), 3.88 (m, 1H), 3.80 (m, 1H), 2.71 (s, 6H), 1.47 (m, 1H), 0.78 (d, *J* = 6.7 Hz, 3H), 0.67 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 163.4 (d, *J* = 3.6 Hz), 151.4, 140.3 (d, *J* = 26.0 Hz), 139.6 (d, *J* = 13.2 Hz), 139.1 (d, *J* = 9.9 Hz), 135.0 (d, *J* = 20.7 Hz), 134.1 (d, *J* = 20.2 Hz), 131.7 (d, *J* = 2.6 Hz), 128.9, 128.7, 128.63, 128.57, 128.5, 119.0 (d, *J* = 17.4 Hz), 118.1 (d, *J* = 2.2 Hz), 77.8, 73.2, 69.9, 40.0, 33.2, 19.3, 18.7. ^{31}P NMR (162 MHz, $CDCl_3$): • –3.0. IR (thin film) 3068, 2955, 1649, 1593, 1359, 1175, 1093, 746, 697 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_2OP$: C, 74.98; H, 7.02; N, 6.73. Found: C, 75.13; H, 7.12; N, 6.71.



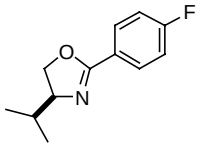
(–)-(4*S*)-4,5-dihydro-4-isopropyl-2-(4'-methoxyphenyl)oxazole (7b). To a 100 mL round bottom flask was added 0.52 g of (*S*)-2-amino-3-methyl-1-butanol (5.0 mmol, 1.0 equivalents), 1.01 g of triethylamine (10.0 mmol, 2.0 equivalents), 0.030 g of 4-dimethylaminopyridine (0.25 mmol, 0.05 equivalents), and 10.0 mL of tetrahydrofuran. The solution was cooled to 0 ºC and

0.94 g of 4-methoxybenzoyl chloride (5.5 mmol, 1.1 equivalents) was added, which formed a cloudy white solution. The reaction was allowed to warm to room temperature overnight (16 h). The reaction mixture was quenched with 10 mL of saturated aqueous sodium bicarbonate, extracted with methylene chloride (4 × 10 mL), and the combined organic phases dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (4.5 cm × 14 cm, 50-70% ethyl acetate in hexanes) yielding 1.02 g of white solid that was used without further purification in the following step. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.68 (m, 2H), 6.83 (m, 2H), 6.47 (d, *J* = 8.0 Hz, 1H), 3.85 (m, 1H), 3.78 (s, 3H), 3.70 (d, *J* = 6.2 Hz, 2H), 3.36 (s, 1H), 1.95 (m, 1H), 0.95 (t, *J* = 6.8 Hz, 6H).

To a 100 mL round bottom flask containing 0.50 g of the above white solid (~2.1 mmol) was added 0.44 g of *p*-toluenesufonyl chloride (2.3 mmol. 1.08 equivalents), 6.3 mL of methylene chloride and 1.07 g of triethylamine (10.5 mmol, 5.0 equivalents). The reaction was heated at reflux under nitrogen 24 hours. Then 0.50 mL of water was added and heating continued for an additional 1 h. The organic layer was washed with water (3 × 10 mL) and dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (3 cm × 14 cm, 20% ethyl acetate in hexanes) yielding 0.41 g (1.9 mmol) of clear oil (76% from the aminoalcohol). $[\alpha]_D$ = –66.5° (c 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): • 7.8 (m, 2H), 6.78 (m, 2H), 4.26 (m, 1H), 3.96 (m, 2H), 3.68 (s, 3H), 1.73 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 163.5, 162.4, 130.3, 120.8, 114.0, 72.9, 70.4, 55.7, 33.2, 19.4, 18.4. IR (thin film) 2959, 2888, 1651, 1611, 1514, 1356, 1309, 1257, 1170, 1076, 1031, 968, 841 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N,6.39. Found: C, 71.24; H, 7.89; N, 6.52.

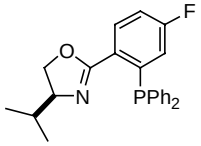


(–)-(4*S*)-4,5-dihydro -2-[2'-(diphenylphosphino)-4'-(methoxy)phenyl]-4-isopropyloxazole (3b). To a 100 mL round bottom flask was added 17.7 mL of anhydrous hexanes and 4.3 mL of 1.3 M *sec*-butyllithium in cyclohexane (5.6 mmol, 1.2 equivalents). The solution was cooled to -78 ºC and 0.59 g of N,N,N',N'-tetramethylethylenediamine (5.1 mmol, 1.1 equivalents) was added dropwise over 1-2 minutes resulting in a faint yellow color. After 10 minutes a solution of 1.00 g of **7b** (4.6 mmol) in 2.3 mL of hexanes was added dropwise via cannula over 5 minutes resulting in a deep orange to dark red color. After stirring at –78 ºC for 2 hours a solution of hexanes (4.6 mL) and 2.03 g of chlorodiphenylphosphine (9.2 mmol, 2.0 equivalents) was added dropwise via cannula over 1-2 minutes. The reaction was stirred at –78 ºC for 3 hours and was then allowed to warm to room temperature overnight. The reaction was quenched by adding 10.0 g of dry silica gel via syringe and evaporation of the solvent *in vacuo*. The product was purified by flash column chromatography (3 cm × 14 cm, 10% ethyl acetate in hexanes) yielding 1.71 g (4.2 mmol) of clear oil (92%). $[\alpha]_D$ –29.9 (c 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): • 7.95 (m, 1H), 7.32 (m, 10H), 6.87 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.38 (dd, *J* = 4.2, 2.7 Hz, 1H), 4.14 (m, 1H), 3.86 (m, 2H), 3.61 (s, 3H), 1.51 (m, 1H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.70 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 163.0 (d, *J* = 2.3 Hz), 161.2, 141.6 (d, *J* = 27.7 Hz), 138.8 (d, *J* = 12.8 Hz), 138.4 (d, *J* = 10.1 Hz), 134.8 (d, *J* = 20.8 Hz), 134.1 (d, *J* = 4.0 Hz), 132.1, 131.8 (d, *J* = 9.6 Hz), 128.95 (d, *J* = 26.4 Hz), 128.87, 128.79, 128.74, 128.6, 120.3 (d, *J* = 2.2 Hz), 113.2, 77.7, 73.3, 70.3, 55.4, 33.2, 19.3, 18.7. ^{31}P NMR (162 MHz, $CDCl_3$): • –4.2. IR (thin film) 2957, 1650, 1592, 1561, 1434, 1350, 1243, 1087, 1029, 745, 696 cm^{-1}. Anal. Calcd for $C_{25}H_{26}NO_2P$: C, 74.42; H, 6.50; N, 3.47. Found: C, 74.57; H, 6.58; N, 3.44.



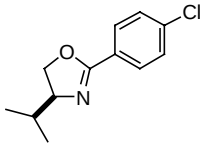
(–)-(4*S*)-4,5-dihydro-2-(4'-fluorophenyl)-4-isopropyloxazole (7d). To a 100 mL round bottom flask was added 1.03 g of (*S*)-(+)-2-amino-3-methyl-1-butanol (10.0 mmol, 1.0 equivalents), 2.02 g of triethylamine (20.0 mmol, 2 equivalents), 0.060 g of 4-dimethylaminopyridine (0.49 mmol, 0.05 equivalents), and 20.0 mL of methylene chloride. The solution was cooled to 0 ºC and 1.74 g of 4-fluorobenzoyl chloride (11.0 mmol, 1.1 equivalents) was added, which formed a cloudy white solution. The reaction was allowed to warm to room temperature overnight (16 h). The reaction mixture was quenched with 20 mL of saturated aqueous sodium bicarbonate, extracted with methylene chloride (3 × 20 mL), and the combined organic phases dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (3 cm × 15 cm, 50-75% ethyl acetate in hexanes) yielding 2.71 g of white solid that was used without further purification in the following step. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.62 (m, 2H), 6.97 (d, J = 8 Hz, 1H), 6.88 (m, 2H), 4.11 (s, 1H), 3.76 (m,1H), 3.62 (m, 2H), 1.90 (m, 1H), 0.87 (m, 6H).

To a 100 mL round bottom flask containing 2.71 g (≤10.0 mmol) of the above white solid was added 2.06 g of *p*-toluenesufonyl chloride (10.8 mmol. 1.1 equivalents), 30.0 mL of methylene chloride and 5.06 g of triethylamine (50.0 mmol, 5.0 equivalents). The reaction was heated at reflux under nitrogen 24 hours. Then 0.75 mL of water was added and heating continued for an additional 1 h. The an additional 20 mL of methylene chloride was added and the organic layer was washed with water (3 × 20 mL) and dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (3 cm × 14 cm, 15% ethyl acetate in hexanes) yielding 1.83 g (8.8 mmol) of clear oil (88% from the aminoalcohol). $[\alpha]_D$ = – 63.7° (c 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): • 7.95 (m, 2H), 7.07 (m, 2H), 4.40 (m, 1H), 4.11 (m, 2H), 1.85 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 164.6 (d, J = 341 Hz), 163.8, 130.9, 124.5, 115.7 (d, J = 22 Hz), 72.5, 70.1, 32.7, 18.8, 18.0. IR (thin film) 2960, 1654, 1606, 1509, 1353, 1222, 1154, 1073, 967, 846 cm^{-1}. Anal. Calcd for $C_{12}H_{14}FNO$: C, 69.55; H, 6.81; N, 6.76. Found: C, 69.28; H, 6.72; N, 6.78.



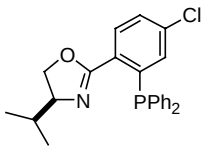
(–)-(4*S*)-4,5-dihydro-2-[2'-(diphenylphosphino)-4'-(fluoro)phenyl]-4-isopropyloxazole (3d). To a 100 mL round bottom flask was added 13.0 mL of anhydrous hexanes and 3.1 mL of 1.3 M *sec*-butyllithium in cyclohexane (4.1 mmol, 1.2 equivalents). The solution was cooled to –78 ºC and 0.43 g of N,N,N',N'-tetramethylethylenediamine (3.7 mmol, 1.1 equivalents) was added dropwise over 1-2 minutes resulting in a faint yellow color. After 10 minutes a solution of 0.70 g of **7d** (3.4 mmol) in 1.70 mL of hexanes was added dropwise via cannula over 5 minutes resulting in dark red color. After stirring at –78 ºC for 2 hours a solution of hexanes (3.4 mL) and 1.49 g of chlorodiphenylphosphine (6.8 mmol, 2.0 equivalents) was added dropwise via cannula over 1-2 minutes. The reaction was stirred at –78 ºC for 3 hours and was then allowed to warm to room temperature overnight. The reaction was quenched by adding 7.0 g of dry silica gel via syringe and evaporation of the solvent *in vacuo*. The product was purified by flash column chromatography (3 cm × 15 cm, 5% ethyl acetate in hexanes) yielding 1.05 g (2.7 mmol) of a

clear oil (79%). $[\alpha]_D$ –41.0 (c 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): • 7.95 (m, 1H), 7.33 (m, 10H), 7.04 (td, *J* = 8.3, 2.7 Hz, 1H), 6.50 (dt, *J* = 9.9, 3.0 Hz, 1H), 4.15 (m, 1H), 3.87 (m, 2H), 1.49 (m, 1H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.72 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 164.1 (d, *J* = 253 Hz), 162.5 (d, *J* = 3.0 Hz), 143.4 (dd, *J* = 29.5, 5.5 Hz), 138.1 (d, *J* = 12.2 Hz), 137.8 (d, *J* = 9.9 Hz), 134.7 (d, *J* = 20.9 Hz), 134.1 (d, *J* = 20.7 Hz), 132.5 (dd, *J* = 8.2, 2.6 Hz), 129.3, 129.05, 129.03 (d, *J* = 11.1 Hz), 128.9, 128.8, 121.1 (dd, *J* = 23.0, 2.2 Hz), 115.3 (d, *J* = 22.0 Hz), 77.7, 73.5, 70.5, 33.2, 19.3, 18.8. ^{31}P NMR (162 MHz, $CDCl_3$): • –4.5. IR (thin film) 3070, 2959, 1654, 1573, 1484, 1434, 1350, 1258, 1209, 1082, 745, 696 cm^{-1}. Anal. Calcd for $C_{24}H_{23}FNOP$: C, 73.64; H, 5.92; N, 3.58. Found: C, 73.92; H, 6.13; N, 3.55.



(–)-(4*S*)-2-(4'-chlorophenyl)-4,5-dihydro-4-isopropyloxazole (7e). To a 100 mL round bottom flask was added 1.03 g of (*S*)-(+)-2-amino-3-methyl-1-butanol (10.0 mmol, 1.0 equivalents), 2.02 g of triethylamine (20.0 mmol, 2.0 equivalents), 0.060 g of 4-dimethylaminopyridine (0.5 mmol, 0.05 equivalents), and 20.0 mL of methylene chloride. The solution was cooled to 0 ºC and 1.93 g of 4-chlorobenzoyl chloride (11.0 mmol, 1.1 equivalents) was added, which formed a cloudy white solution. The reaction was allowed to warm to room temperature overnight (16 h). The reaction mixture was quenched with 20 mL of saturated aqueous sodium bicarbonate, extracted with methylene chloride (3 × 20 mL), and the combined organic phases dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (3 cm × 15 cm, 50-75% ethyl acetate in hexanes) yielding 2.52 g of white solid that was used without further purification in the following step. ^{1}H NMR (400 MHz, $CDCl_3$): • 7.55 (m, 2H), 7.15 (m, 2H), 6.85 (d, *J* = 8 Hz, 1H), 3.91 (m, 1H), 3.77 (m, 1H), 3.65 (m, 2H), 1.86 (m, 1H), 0.85 (m, 6H).

To a 100 mL round bottom flask containing 2.52 g (≤10.0 mmol) of the above white solid was added 2.06 g of *p*-toluenesufonyl chloride (10.8 mmol. 1.1 equivalents), 30.0 mL of methylene chloride and 5.06 g of triethylamine (50.0 mmol, 5.0 equivalents). The reaction was heated at reflux under nitrogen 24 hours. Then 0.75 mL of water was added and heating continued for an additional 1 h. The an additional 20 mL of methylene chloride was added and the organic layer was washed with water (3 × 20 mL) and dried over anhydrous sodium sulfate. The product was purified by flash column chromatography (4 cm × 13 cm, 10% ethyl acetate in hexanes) yielding 1.94 g (8.6 mmol) of clear oil (87% from the aminoalcohol). $[\alpha]_D$ = – 61.3° (c 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): • 7.90 (m, 2H), 7.38 (m, 2H), 4.42 (m, 1H), 4.11 (m, 2H), 1.86 (m, 1H), (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 162.3, 137.2, 129.5, 128.4, 126.3, 72.6, 70.2, 32.7, 18.8, 18.0. IR (thin film) 2959, 2901, 1654, 1599, 1490, 1403, 1352, 1090, 1072, 1015, 966, 839, 730 cm^{-1}. Anal. Calcd for $C_{12}H_{14}ClNO$: C, 64.43; H, 6.31; Cl, 15.85; N, 6.26. Found: C, 64.55; H, 6.41; Cl, 15.64; N, 6.17.



(–)-(4*S*)-2-[4'-(chloro)-2'-(diphenylphosphino)phenyl)]-4,5-dihydro-4-isopropyloxazole (3e). To a 100 mL round bottom flask was added 12.0 mL of anhydrous hexanes and 2.9 mL of 1.3 M *sec*-butyllithium in cyclohexane (3.8 mmol, 1.2 equivalents). The solution was cooled to –78 ºC

and 0.40 g of N,N,N',N'-tetramethylethylenediamine (3.4 mmol, 1.1 equivalents) was added dropwise over 1-2 minutes resulting in a faint yellow color. After 10 minutes a solution of 0.70 g of **7e** (3.1 mmol) in 1.6 mL of hexanes was added dropwise via cannula over 5 minutes resulting in dark red color. After stirring at –78 ºC for 2 hours a solution of hexanes (3.1 mL) and 1.38 g of chlorodiphenylphosphine (6.3 mmol, 2.0 equivalents) was added dropwise via cannula over 1-2 minutes. The reaction was stirred at –78 ºC for 3 hours and was then allowed to warm to room temperature overnight. The reaction was quenched by adding 7.0 g of dry silica gel via syringe and evaporation of the solvent *in vacuo*. The product was purified by flash column chromatography (3 cm × 15 cm, 5% ethyl acetate in hexanes) yielding 1.02 g (2.5 mmol) of a clear oil (80%). $[\alpha]_D$ –29.0 (c 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): • 7.87 (m, 1H), 7.32 (m, 11H), 6.82 (m, 1H), 4.15 (m, 1H), 3.86 (m, 2H), 1.49 (m, 1H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.71 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): • 162.6 (d, *J* = 2.8 Hz), 142.2 (d, *J* = 30.0 Hz), 137.9 (d, *J* = 12.3 Hz), 137.7 (d, *J* = 9.5 Hz), 137.3, 134.7 (d, *J* = 21.4 Hz), 134.1 (d, *J* = 20.8 Hz), 133.9 (d, *J* = 1.7 Hz), 131.6 (d, *J* = 2.6 Hz), 129.4, 129.06, 129.05 (d, *J* = 13.2 Hz), 128.9, 128.8, 128.5, 77.7, 73.5, 70.6, 33.1, 19.3, 18.8. ^{31}P NMR (162 MHz, $CDCl_3$): • –4.7. IR (thin film) 3069, 2959, 1653, 1469, 1434, 1350, 1105, 1089, 1043, 745, 696 cm^{-1}. Anal. Calcd for $C_{24}H_{23}ClNOP$: C, 70.67; H, 5.68; N, 3.43. Found: C, 70.27; H, 5.81; N, 3.51.

Table 2. Data for Hammett Analysis of Enantioselectivity with Ligand **3**

ligand	product	ee	er	log (er)	σ_M [a]	σ_p
3a	**2a**	89.3	17.7	1.248	-0.16	-0.83
3b	**2a**	89.7	18.4	1.265	0.12	-0.27
3c	**2a**	89.9	18.8	1.274	0	0
3d	**2a**	93.0	27.6	1.440	0.34	0.06
3e	**2a**	93.4	29.3	1.467	0.37	0.23
3a	**2b**	16.4	1.39	0.144	-0.16	-0.83
3b	**2b**	22.7	1.59	0.201	0.12	-0.27
3c	**2b**	28.4	1.79	0.254	0	0
3d	**2b**	44.9	2.63	0.420	0.34	0.06
3e	**2b**	66.6	4.99	0.698	0.37	0.23

(a) All sigma values taken from: Hansch, C.; Leo, A.; Taft, R.W. *Chem. Rev.* **1991**, *91*, 165.

Table 3. Data for Hammett Analysis of Enantioselectivity with Ligand **6**.

substituent	product	ee[a]	er	log (er)	σ_M	σ_p
$-NMe_2$	**2a**	92.0	24.0	1.380	-0.16	-0.83
-OMe	**2a**	85.0	12.3	1.091	0.12	-0.27
-Me	**2a**	74.0	6.69	0.826	-0.07	-0.17
-H	**2a**	52.0	3.17	0.501	0	0
$-CF_3$	**2a**	38.0	2.23	0.347	0.43	0.54
$-CO_2Me$	**2a**	19.0	1.47	0.167	0.37	0.45

(a) Data taken from: Saitoh, A.; Achiwa, K.; Tanaka, K.; Morimoto, T. *J. Org. Chem.* **2000**, *65*, 4227.