Chiral P,N-ligands Based on Ketopinic Acid in the Asymmetric Heck Reaction

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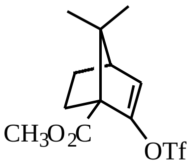
General information. ^{1}H NMR spectra were recorded on Varian Mercury 300 and Varian Unity 300 spectrometers. The spectra are of $CHCl_3$ solutions, unless indicated otherwise. The chemical shifts are referenced to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity, coupling constants, integration. ^{13}C NMR spectra were recorded on a Varian Mercury 300 (75 MHz) spectrometer with complete proton decoupling. The chemical shifts are referenced to tetramethylsilane. ^{31}P NMR spectra were recorded on a Varian Mercury 300 (125MHz) spectrometer and the chemical shifts are referenced to 85% H_3PO_4. IR spectra of films of chloroform solutions of the compounds were recorded on a Perkin Elmer Spectrum BX spectrometer. TLC was performed on Whatman 250μm silica gel plates. Column chromatography was performed on ICN silica gel 60. All reactions were carried out under a N_2 atmosphere. Dichloromethane, toluene and xylene were distilled from CaH_2 under N_2, THF was distilled from Na/benzophenon ketyl, C_6H_6 was dried over Na, anhydrous DMF was purchased from Aldrich and used without further purification. Melting points are uncorrected.

Experimental Section

Synthesis of phosphine Ligands

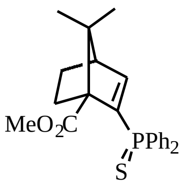
Synthesis of triflate **8**



8

(**A**) Synthesis of (1S)-(+)-ketopinic acid methyl ester: (1S)-(+)-ketopinic acid (**1**) was slowly added to a solution of thionyl chloride (10 mL, 137.2 mmol) in 28 mL of methanol. The resulting mixture was allowed to stir overnight while warming to room temperature. Upon completion, the solvent was removed *in vacuo* . The residue was dissolved in 100 mL of ethyl acetate and washed with 20 mL of water. After separation, the aqueous layer was extracted with ethyl acetate (30 mL x 2). The combined organic layers were subsequently washed with an aqueous saturated sodium bicarbonate solution, brine and water, then dried over anhydrous sodium sulfate. Removal of the solvent gave the crude product which was purified by column chromatography, using a 4 : 1 mixture of hexane-EtOAc as the eluent to give 5.1 g (95%) of the methyl ester. (**B**) Synthesis of triflate **8**: LDA was generated by drop wise addition of a 2.5M solution of *n*-butyllithium (3.21 mL, 22.94 mmol) in hexane to a -78°C solution of diisopropylamine (9.17 mL 22.9 mmol) in 46 mL of THF. After addition, this solution was stirred for additional 20 minutes before a solution of (1S)-(+)-ketopinic acid methyl ester (3.00 g, 15.3 mmol) in 30 mL of THF was slowly added at -78°C. The resulting mixture was stirred at -78°C for additional 1 hour, after which a solution of N-phenyltrifluoromethanesulfonimide (8.2 g, 22.93 mmol) in 76 mL of THF was slowly added at -78°C. This mixture was then warmed to room temperature while stirred overnight. Upon completion, 20 mL of ice water was added to quench the reaction and the organic solvent was removed *in vacuo*. Ethyl acetate (50 mL) was added to the residue. After separation, the aqueous layer was extracted with ethyl acetate (30 mL x 3). The combined organic layers were washed with water (20 mL x 2) and brine then dried over sodium sulfate. Removal of the solvent provided the crude product, which was purified by chromatography on a silica gel column [hexane/EtOAc (5: 95)] to give 4.7 g (93%) of the triflate **8**. ^{1}H NMR (300MHz, $CDCl_3$) δ 5.81(d, *J*=3.6 Hz, 1H), 3.78 (s, 3H), 2.51 (dd, *J*=3.6, 3.6 Hz, 1H), 2.39 (ddd, *J*=12.3, 8.7, 3.9 Hz, 1H), 2.04-2.14 (m, 1H), 1.65 (ddd, *J*=12.9, 9.3, 3.9 Hz, 1H), 1.24 (ddd, *J*=12.3, 9.0, 3.9 Hz, 1H), 1.12 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 150.8, 120.7, 63.1, 60.9, 51.7, 50.5, 27.6, 25.4, 20.7, 19.8. ^{19}F NMR (282.2M Hz, $CDCl_3$) δ -74.7. LR-FABMS m/z 351 $(M+Na)^+$. HR-FABMS m/z 351.0481 (calcd. for $C_{12}H_{15}F_3O_5SNa$ m/z 351.049).

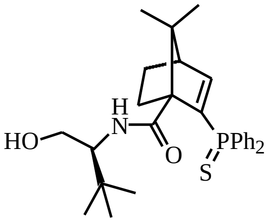
Synthesis of phosphine sulfide **9**



9

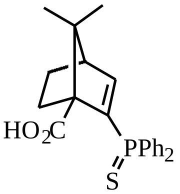
A mixture of triflate **8** (1.09g, 3.31mmol), palladium (II) acetate (37 mg, 0.165 mmol), 1,4-bis(phenylphosphino)butane (71 mg, 0.165 mmol) and triethylethylamine (1.73 mL, 9.93 mmol) in 7 mL of benzene was degassed before diphenylphosphine (0.576 mL, 3.31 mmol) was added. The resulting mixture was stirred at 90°C for 24 hours. Upon completion, the mixture was cooled to room temperature. Ethyl acetate (150 mL) was added. The organic layers were washed with 20 mL of 2N HCl, water and brine, then dried over anhydrous sodium sulfate. After evaproation of the solvent, the crude product was purified by chromatography on silica gel column using a mixture of hexane/EtOAc (5 : 95) as the eluent to give 1.20 g (91%) of the phosphine sulfide **9**. ^{1}H NMR (300M Hz, $CDCl_3$) δ 7.97-8.05 (m, 2H), 7.50 –7.63 (m, 5H), 7.34-7.46 (m, 3H), 6.15 (dd, *J*=11.4, 3.3 Hz, 1H), 3.18 (s, 3H), 2.58(ddd, *J*=4.2, 1.8, 1.8 Hz, 1H), 2.50 (ddd, *J*=12.6, 9.0, 3.6 Hz, 1H), 2.04-2.17 (m, 1H), 1.92 (ddd, *J*=12.6, 9.0, 3.6 Hz, 1H), 1.14 (ddd, *J*=12.6, 9.0, 3.3 Hz, 1H), 1.02 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 151.5, 151.4, 138.8, 138.7, 134.6, 133.4, 132.0, 131.8, 131.6, 131.1, 131.1, (two peaks are very close), 131.0, 130.8, 128.3, 128.1, 127.9, 66.1 (d, $J_{P\text{-}C}$=8.5 Hz), 60.0 (d, $J_{P\text{-}C}$=4.0 Hz), 55.3 (d, $J_{P\text{-}C}$=11.5 Hz), 50.6 (d, $J_{P\text{-}C}$=9.0 Hz), 29.4, 25.3, 20.7 (d, $J_{P\text{-}C}$=5.0 Hz), 20.1 (d, $J_{P\text{-}C}$=4.5 Hz); ^{31}P NMR (120 MHz, $CDCl_3$) δ35.4. LR-FABMS m/z 419 $(M+Na)^+$. HR-FABMS m/e 419.1229 $(M+Na)^+$ (calcd. for $C_{23}H_{25}O_2PSNa$ m/e 419.1211).

Synthesis of alcohol **10**



10

(**A**) Cleavage of methyl ester **8**: A mixture of methyl ester **8** (800 mg, 2.08 mmol) and lithium iodide (2.7 g, 20.8 mmol) in 11 mL of pyridine was refluxed for 24 hours. Upon completion, the solvent was removed in vacuo and 20 mL of a 2N HCl was added. This mixture was then extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with 2N HCl, water and brine then dried over sodium sulfate. After removal of the solvent by evaporation the crude product was purified by column chromatography [hexane /EtOAc (20 : 80)] to give 760 mg (98%) of the corresponding acid **9a**.

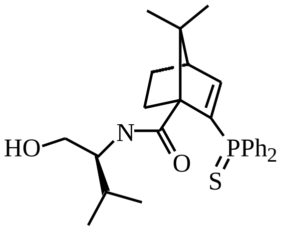


9a

9a: ^{1}H NMR (300MHz, $CDCl_3$) δ 7.91-7.99 (m, 2h), 7.35-7.64 (m, 8H), 6.20 (dd, *J*=11.4, 3.3 Hz, 1H), 2.58 (m, 1H), 2.45 (ddd, *J*=12.3, 8.7, 3.3 Hz, 1H), 2.0 5-2.16 (m, 1H), 1.94 (ddd, J=12.6, 9.3, 3.6 Hz, 1H), 1.15 (ddd, J=12.6, 9.3, 3.9 Hz, 1H), 1.08 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz,

$CDCl_3$)δ 176.1, 151.7 (d, $J_{P\text{-}C}$=5.4 Hz), 138.3, 137.2, 134.2, 133.1, 131.8, 131.7, 131.6, 131.5, 131.2, 131.1, 131.0, 130.9, 130.1, 128.1, 128.0, 127.9, 127.7, 66.1 (d, $J_{P\text{-}C}$=8.0 Hz), 60.4 (d, $J_{P\text{-}C}$=4.3 Hz), 55.3 (d, $J_{P\text{-}C}$=11.4 Hz), 29.3, 25.3, 20.6, 20.2; ^{31}P NMR (120 MHz, $CDCl_3$) δ 35.0. LR-FABMS m/z 383 $(M+H)^+$. HR-FABMS m/e 383.1221 $(M+H)^+$ (calcd. for $C_{22}H_{23}O_2PSH$ m/e 383.1235). (**B**) Synthesis of alcohol **10**: Method (1): A mixture of above acid **9a** (200 mg, 0.523 mmol), EDC (226 mg, 0.784 mmol), HOBT (159 mg, 0.784 mmol) and triethylamine (273 μL, 1.96 mmol) in 6 mL of methylene was stirred overnight at room temperature. After removal of the solvent, the residue was dissolved in 100 mL of ethyl acetate and washed with a saturated sodium bicarbonate, water and brine, then dried over sodium sulfate. After the solvent was removed, the residue was redissolved in 1.5 mL of DMF and 0.145 mL of triethylamine and 92 mg (0.784 mmol) of *tert*-leucinaol were added. The resulting mixture was stirred overnight. Upon completion, 10 mL of a 2N HCl solution was added and the mixture was extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with water, saturated sodium bicarbonate solution and brine, dried over sodium sulfate and the solvent was removed *in vacuo*. The crude product was purified by chromatography on silica gel[hexane/EtOAc (2 : 1)] to give 226 mg (90%) of alcohol **10**. Method (2): A mixture of acid **9a** (200 mg, 0.523 mmol), triethylamine (273 μL, 1.96 mmol), EDC (226 mg, 0.784 mmol), HOBT (159 mg, 0.784 mmol) and *tert*-leucinaol (92 mg, 0.784 mmol) in 5 mL of DMF was stirred at 70°C overnight. To the cooled mixture 15 mL of 2N HCl was added, and the resulting mixture was then extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with water (20 x 2) and brine, dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography [hexane/EtOAc (2 : 1)] to give 224 mg (88%) of alcohol **10**. ^{1}H NMR (300MHz, CDCl$_3$) δ 7.87-7.95 (m, 2H), 7.62-7.69 (m, 2H), 7.39-7.57 (m, 6H), 6.95 (d, *J*=9.6 Hz, 1H), 6.11 (dd, *J*=12.3, 3.3 Hz, 1H), 3.46-3.52 (m, 1H), 3.16 (dd, *J*=12.0, 5.4 Hz,1H), 2.91 (dd, *J*=11.7, 2.4 Hz, 1H), 2.77 (m, 1H), 2.48 (dd, *J*=3.3, 3.3 Hz, 1H), 2.01-2.29 (m, 3H), 1.38 (s, 3H), 1.15 (ddd, *J*=12.6, 8.7, 3.9 Hz, 1H), 1.06 (s, 3H), 0.90 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 170.9, 154.5 (d, $J_{P\text{-}C}$=6.5 Hz), 137.0, 135.9, 132.2, 132.2, (2 peaks very close), 132.1, 132.1 (2 peaks very close), 131.9, 131.6, 131.5, 131.5(2 peaks very close), 131.5, 130.9, 130.8, 128.7, 128.6, 128.4, 128.2, 65.7 (d, $J_{P\text{-}C}$=8.4 Hz), 62.2, 59.5 (d, $J_{P\text{-}C}$=7.5 Hz), 59.1, 55.0 (d, $J_{P\text{-}C}$=11.5 Hz), 33.7, 31.7, 27.1, 24.5, 21.1, 19.9. ^{31}P NMR (120 MHz, CDCl$_3$) δ 35.5. LR-FABMS m/z 482 (M+H)$^+$. HR-FABMS m/z 482.2293 (M+H)$^+$ (calcd. for $C_{28}H_{37}NO_2PS$ m/z 482.2283).

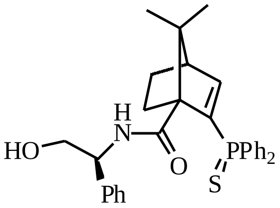
Synthesis of alcohol **11**



11

A mixture of acid **9a** (400 mg, 1.05 mmol), EDC (403 mg, 2.10 mmol), HOBT (284 mg, 2.10 mmol) and L-valinol (217 mg, 2.10 mmol) in 5 mL of DMF was stirred at 70°C overnight. Aqueous HCl (2N, 15 mL) was added to the cooled mixture and the resulting mixture was then extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with water (20 x 2) and brine, dried over sodium sulfate. After removal of solvent, the residue was purified by column chromatography [hexane/EtOAc (2 : 1)] to give 392 mg (80%) of the expected alcohol **11**. ^{1}H NMR (300MHz, CDCl$_3$) δ 7.86-7.94 (m, 2H), 7.62-7,69 (m, 2H), 7.38-7.60 (m, 6H), 7.0 (br d, *J*=9.0 Hz, 1H), 6.11 (dd, *J*=12.3, 3.6 Hz, 1H), 3.35-3.43 (m, 1H), 3.10 (dd, *J*=12.3, 4.5 Hz, 1H), 2.67 (dd, *J*=12.3, 3.0 Hz, 1H), 2.40-2.51 (m, 2H), 2.25 (ddd, *J*=12.3, 9.0, 3.9 Hz, 1H), 2.00-2.16 (m, 2H), 1.74-1.86 (m, 1H), 1.37 (s, 3H), 1.13 (ddd, *J*=12.6, 9.0, 3.6 Hz, 1H), 1.07 (s, 3H), 0.89 (d, *J*=6.6 Hz, 3H), 0.87 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 154.7(d, $J_{P\text{-}C}$=6.5 Hz), 136.9, 135.8, 132.4, 132.2, 132.1, 131.9, 131.8, 131.6, 131.4, 131.3, 130.7, 128.7, 128.6, 128.4, 128.2, 65.5 (d, $J_{P\text{-}C}$=8.0 Hz), 62.9, 59.4(d, $J_{P\text{-}C}$=5.0 Hz), 56.9, 55.0(d, $J_{P\text{-}C}$=11.5 Hz), 31.8, 28.9, 24.3, 21.1, 19.9, 19.5, 19.2. ^{31}P NMR (120 MHz, $CDCl_3$) δ 35.7. LR-FABMS m/z 468 $(M+H)^+$. HR-FABMS m/e 468.2143 $(M+H)^+$ (calcd. for $C_{27}H_{35}NO_2PS$ m/z 468.2126).

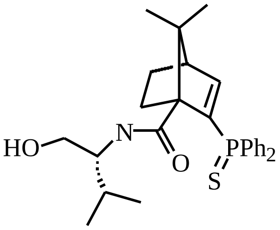
Synthesis of alcohol **12**



12

A mixture of acid **9a** (200 mg, 0.523 mmol), EDC (150 mg, 0.784 mmol), HOBT (106 mg, 0.784 mmol) and L-valinol (108 mg, 0.784 mmol) in 5 mL of dichloromethane was stirred at room temperature for 24 hours. After the solvent was removed *in vacuo*, 120 mL of ethyl acetate was added to dissolve the residue. This solution was then washed with water (20 mL x 2) and brine, dried over sodium sulfate and the solvent was removed by evaproation. The crude product was purified by chromatography [hexane/ethyl acetate (2:1)] to give 228 mg (87%) of alcohol **12**. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.90-7.97 (m, 2H), 7.41-7.74 (m, 6H), 7.21-7.32 (m, 2H), 6.14 (br d, *J*=11.7 Hz, 1H), 4.67 (br s, 1H), 3.35 (br dd, *J*=12.0, 5.7 Hz, 1H), 3.08 (br d, *J*=12.3 Hz, 1H), 2.48 (br s, 1H), 1.99-2.42 (m, 4H), 1.37 (s, 3H), 1.14 (m, 1H), 1.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 154.0(Jp-c=10.4 Hz), 139.6, 136.9, 135.8, 132.4, 132.1, 132.0, 131.9, 131.9, 131.7, 131.6, 131.6, 131.5, 131.4, 131.3, 130.5, 128.8, 128.6, 128.3, 128.3, 128.2, 127.1, 126.7, 65.5, 65.4 (d, $J_{P\text{-}C}$=8.0 Hz), 59.4 (Jpc=7.2 Hz), 55.6, 55.0(d, $J_{P\text{-}C}$=4.5 Hz), 31.8, 24.2, 24.2, 20.9, 19.5. ^{31}P NMR (120 MHz, $CDCl_3$) δ 35.9. LR-FABMS m/z 502 $(M+H)^+$. HR-FABMS m/z 502.1949 $(M+H)^+$ (calcd. for $C_{30}H_{32}NO_2PS$ m/z 502.1970).

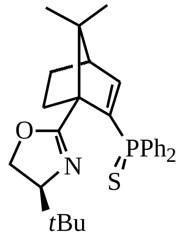
Synthesis of hydroxyl amide **13**



13

A mixture of acid **9a** (300 mg, 0.784 mmol), EDC (226 mg, 1.17 mmol), HOBT (159 mg, 1.17 mmol) and L-valinol (121 mg, 1.17 mmol) in 7 mL of DMF was stirred at 50°C for 24 hours. HCL (15mL, 2N) was added to the cooled mixture. The resulting mixture was then extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with water (20 x 2) and brine then dried over sodium sulfate. After removal of solvent, the residue was purified by column chromatography [hexane/EtOAc (2 : 1)] to give 311 mg (85%) of the expected alcohol **13**. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.95-8.06 (m, 2H), 7.54-7.64 (m, 5H), 7.37-7.50 (m, 3H), 6.26 (br d, *J*=7.8 Hz, 1H), 6.20 (dd, *J*=12.0, 3.3 Hz, 1H), 3.33 (dd, *J*=11.7, 2.1 Hz, 1H), 3.25 (m, 1H), 3.10 (dd, *J*=11.7, 6.3 Hz, 1H), 2.73 (br s, 1H), 2.54-2.66 (m, 2H), 2.10(m, 1H), 1.96 (ddd, *J*=12.9, 9.3, 3.9 Hz, 1H), 1.45 (m, 1H), 1.19 (s, 3H), 1.09 (ddd, *J*=12.3, 9.3, 3.9 Hz, 1H), 1.03 (s, 3H), 0.75 (d, *J*=6.9 Hz, 3H), 0.64 (d, J=6.9 Hz, 3H); ^{13}C NMR (75 M Hz, $CDCl_3$) δ 170.6, 155.1(d, $J_{P\text{-}C}$=6.0 Hz), 136.7, 136.6, 133.1, 132.2, 132.1, 131.9, 131.6, 131.5, 131.4, 131.3, 130.2, 128.9, 128.8, 128.4, 128.3, 67.5 (d, $J_{P\text{-}C}$=8.5 Hz), 62.4, 59.5(d, $J_{P\text{-}C}$=4.5 Hz), 58.2, 55.3 (d, $J_{P\text{-}C}$=11.5 Hz), 30.3, 28.2, 24.6, 20.9, 19.9, 18.9, 18.6. ^{31}P NMR (120 MHz, $CDCl_3$) δ 35.7. LR-FABMS m/z 468 $(M+H)^+$. HR-FABMS m/z 468.2140 $(M+H)^+$ (calcd. for $C_{27}H_{35}NO_2PS$ m/z 468.2126).

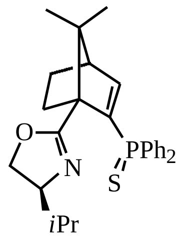
Synthesis of oxazoline phosphine sulfide **14**



14

To a mixture of alcohol **10** (130 mg, 0.27 mmol), diisopropylethylamine (188 μL, 1.08 mmol) and triethylamine (1.8 mL) in 5.5 mL of methylene chloride was added 41 μL (0.54mmol) of methanesulfonylchloride dropwise at 0°C. After addition, the resulting mixture was stirred overnight while warming to room temperature. The reaction was monitored by TCL. Upon completion, the solvent was removed, and the residue was redissolved in 100 mL of ethyl acetate and washed with water (15 mL x 2) and brine, then dried. The crude product was purified by chromatography [Et3N/hexane/EtOAc (1:20:80)] to give 104 mg (80%) of phosphino-oxazoline sulfide **14**. ^{1}H NMR (300MHz, CDCl$_3$) δ 7.92-7.99 (m, 2H), 7.71-7.79 (m, 2H), 7.35-7.49 (m, 6H), 6.23 (dd, J=11.7, 3.0 Hz, 1H), 3.60 (m, 1H), 3.42 (m, 1H), 2.54 (m, 1H), 2.17-2.28 (m, 1H), 1.89-2.07 (m, 2H), 1.08-1.17 (m, 1H), 1.19 (s, 3H), 0.98 (s, 3H), 0.73 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 163.7, 152.2(d, $J_{P\text{-}C}$=6.1 Hz), 139.1, 138.0, 134.0, 132.9, 132.7, 132.0, 131.9, 131.8, 131.6, 130.9, 130.9 (2 peaks very close), 130.8,128.1, 127.9, 127.9, 127.7, 75.7, 67.1, 60.4(d, $J_{P\text{-}C}$=7.6 Hz), 59.7 (d, $J_{P\text{-}C}$=4.0 Hz), 54.9 (d, $J_{P\text{-}C}$=11.6 Hz), 60.4, 60.3, 59.7, 59.6, 54.9, 54.8, 33.3, 30.0, 25.9, 24.3 (d, $J_{P\text{-}C}$=3.0 Hz), 20.6, 20.0. ^{31}P NMR (120 M Hz, CDCl$_3$) δ 34.9. LR-FABMS m/z 464 (M+H)$^+$. HR-FABMS m/z 464.2178 (M+H)$^+$ (calcd. for C$_{28}$H$_{35}$NOPS m/z 464.2177).

Synthesis of oxazoline phosphine sulfide **15**

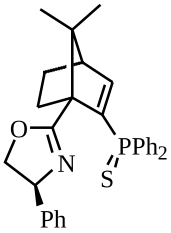


15

To a mixture of alcohol **11** (200 mg, 0.428 mmol), diisopropylethylamine (149 μL, 0.856 mmol) and triethylamine

(1.4 mL) in 4.3 mL of methylene chloride at 0°C was added 67 μL (0.856mmol) of methanesulfonylchloride. After addition, the resulting mixture was allowed to stir overnight while warmed to room temperature. The reaction was monitored by TCL. Upon completion, the solvent was removed, and the residue was redissolved in 120 mL of ethyl acetate and washed with water (15 mL x 2) and brine then dried over sodium sulfate. After removal of the solvent the crude product was purified by chromatography [Et_3N/hexane/EtOAc (1:20:80)] to give 173 mg (90%) of phosphino-oxazoline sulfide **15**. ^{1}H NMR (300MHz, $CDCl_3$) δ 794-8.01 (m, 2H), 7.66-7.74 (m, 2H), 7.34-7.51 (m, 6H), 6.23 (dd, *J*=11.4, 30.Hz, 1H), 3.40-3.58 (m, 3H), 2.54 (m, 1H), 2.33 (ddd, *J*=12.0, 8.4, 3.3 Hz, 1H), 1.89-2.08 (m, 2H), 1.61-1.72 (m, 1H), 1.1 (s, 3H), 1.03-1.16 (m, 1H), 0.97 (s, 3H), 0.85 (d, *J*=6.9 Hz, 3H), 0.76 (d, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 152.0 (d, $J_{P\text{-}C}$=5.7 Hz), 138.7, 137.7, 134.1, 133.0, 132.2, 131.9, 131.8, 137.7, 137.6, 131.0, 130.8, 130.8, 130.8 (3 peaks close), 128.1, 127.9, 127.8, 127.6, 72.1, 68.8, 60.6(d, $J_{P\text{-}C}$=7.4 Hz), 59.8(d, $J_{P\text{-}C}$=4.3 Hz), 55.0 (d, $J_{P\text{-}C}$=11.7 Hz), 32.4, 30.3, 24.5, 20.9, 20.1, 19.3, 18.9. ^{31}P NMR (120 MHz, $CDCl_3$) δ 34.8. LR-FABMS m/z 450 $(M+H)^+$. HR-FABMS m/z 450.1990 (M+H) (calcd. for $C_{27}H_{33}NOPS$ m/z 450.202).

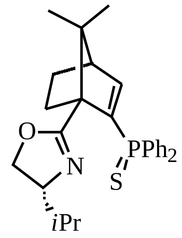
Synthesis of oxazoline phosphine sulfide **16**



16

To a mixture of alcohol **12** (165 mg, 0.328 mmol), diisopropylethylamine (172 μL, 0.98 mmol) and triethylamine (1.1 mL) in 3.3 mL of methylene chloride was added 64 μL (0.82mmol) of methanesulfonylchloride at 0°C. After addition, the resulting mixture was stirred overnight while warmed to room temperature. The reaction was monitored by TCL. Upon completion, the solvent was removed, and the residue was redissolved in 100 mL of ethyl acetate and washed with water (15 mL x 2) and brine, dried over sodium sulfate and then the solvent was removed by evaporated. The crude product was purified by chromatography[Et3N/hexane/EtOAc (1:20:80)] to give 158 mg (80%) of phosphino-oxazoline sulfide **16**. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.89-8.06 (m, 2H), 7.64-7.71 (m, 2H), 7.20-7.52 (m, 6H), 6.24 (dd, *J*=11.9, 3.0 Hz, 1H), 4.94 (dd, *J*=9.9, 9.9 Hz, 1H), 4.03 (dd, *J*=10.2, 8.1 Hz, 1H), 3.57 (dd, *J*=10.2, 8.1 Hz, 1H), 2.51-2.63 (m,2H), 2.03-3.16 (m, 2H), 1.18 (ddd, *J*=13.8, 9.0, 2.4 Hz, 1H), 1.10 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 151.6 (d, $J_{P\text{-}C}$=5.4 Hz), 142.1, 138.5, 137.4, 134.3, 133.2, 131.8, 131.7, 131.6, 131.5, 130.9, 130.8, 130.8 (2 peaks are very close.) 130.5, 128.3, 128.1, 127.9, 127.8, 127.6, 127.2, 127.0, 73.8, 69.8, 60.8(d, $J_{P\text{-}C}$=7.6 Hz), 59.9 (d, $J_{P\text{-}C}$=4.3 Hz), 55.1 (d, $J_{P\text{-}C}$=11.7 Hz), 30.4, 24.9 (d, $J_{P\text{-}C}$=2.9 Hz), 20.9, 19.9. ^{31}P NMR (120 MHz, $CDCl_3$) δ34.6. LR-FABMS m/z 484 $(M+H)^+$. HR-FABMS m/z 484.1850 $(M+H)^+$ (calcd. for $C_{30}H_{30}NOPS$ m/z 484.1684).

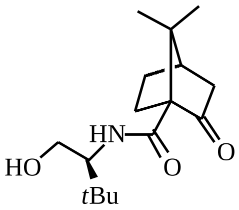
Synthesis of oxazoline phosphine sulfide **17**



17

To a mixture of alcohol **13** (260 mg, 0.556 mmol), diisopropylethylamine (242 μL, 1.39 mmol) and triethylamine (1.85 mL) in 5.56 mL of methylene chloride was added 86 μL (1.11mmol) of methanesulfonylchloride dropwise at 0°C. After addition, the resulting mixture was stirred overnight while warmed to room temperature. The reaction was monitored by TCL. Upon completion, the solvent was removed, and the residue was redissolved in 150 mL of ethyl acetate and washed with water (20 mL x 2) and brine, then dried over sodium sulfate. After evaporation of the solvent the crude product was purified by chromatography [Et_3N/hexane/EtOAc (1:20:80)] to give 232 mg (92%) of phosphino-oxazoline sulfide **17**. ^1H NMR (300MHz, $CDCl_3$) δ 7.96-8.04 (m, 2H), 7.31-7.63 (m, 8H), 6.22 (dd, *J*=11.1, 3.0 Hz, 1H), 3.84 (ddd, *J*=9.9, 6.6, 6.6 Hz, 1H), 3.66 (dd, *J*=9.9, 5.7 Hz, 1H), 3.48 (dd, *J*=8.1, 6.9 Hz, 1H), 2.49-2.58 (m, 2H), 2.03-2.13 (m, 1H), 1.95 (ddd, *J*=12.6, 9.3, 3.6 Hz, 1H), 1.63 (m, 1H), 1.13 (ddd, *J*=12.3, 9.0, 3.6 Hz, 1H), 1.00 (s, 3H), 0.96(s, 3H), 0.82 (d, *J*=6.9 Hz, 3H), 0.76 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 151.6(d, $J_{P\text{-}C}$=5.5 Hz), 138.8, 137.7, 135.0, 133.9, 132.0, 131.9, 131.7, 131.6, 130.9, 130.9, 130.9 (3 peaks very close), 128.1, 127.9, 127.8, 127.7, 71.7, 68.4, 61.0 (d, $J_{P\text{-}C}$=7.5 Hz), 59.7 (d, $J_{P\text{-}C}$=4.0 Hz), 55.1 (d, $J_{P\text{-}C}$=11.6 Hz), 31.8, 29.9, 24.9 (d, $J_{P\text{-}C}$=3.0 Hz), 20.9, 20.0, 18.9, 17.7. ^{31}P NMR (120 MHz, $CDCl_3$) δ34.9. LR-FABMS m/z 450 $(M+H)^+$. HR-FABMS m/z 450.2012 (M+H) (calcd. for $C_{27}H_{33}NOPS$ m/z 450.202).

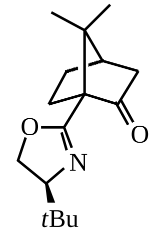
<u>Synthesis of amide **18**</u>:



18

A mixture of keto-acid (**1**) (1.29 g, 7.1 mmol), EDC (1.64 g, 8.53 mmol), HOBT (1.15 g, 8.53 mmol), *tert*-leucinol (1.0 mg, 8.53 mmol) and triethylamine (1.98 mL, 14.2 mmol) in 35 mL of methylene chloride was allowed to stir for 24 hours at room temperature. Reaction was monitored by TLC. Upon completion, 10 mL of a 2N HCl solution was added and the mixture was extracted with ethyl acetate (30 mL x 4). The combined extracts were washed with water, saturated sodium bicarbonate solution and brine, then dried over sodium sulfate. After evaporation of the solvent the crude product was purified by chromatography on a silica gel column [hexane/EtOAc (1:2)] to give 1.16 g (58%) of amide **18**. ^{1}H NMR (300MHz, CDCl$_3$) δ 7.90 (d, *J*=5.4 Hz, 1H), 3.80-3.91 (m, 2H), 3.46 (m, 1H), 3.06 (dd, *J*=5.1, 5.1 Hz, 1H), 2.48-2.58 (m, 2H), 2.08-2.22 (m, 2H), 1.61 (m, 1H), 1.44 (m, 1H), 1.25 (s, 3H), 1.00 (s, 3H), .098 (s, 9H); ^{13}C NMR (75MHz, CDCl$_3$) δ 217.6, 170.8, 64.6, 64.3, 60.5, 50.2, 43.8, 43.1, 33.2, 28.3, 27.8, 26.9, 21.0, 20.4. LR-FABMS m/z: 282 (M+H)$^+$. HR-FABMS m/z: 282.2065 (calcd. for $C_{16}H_{27}NO_3H$ m/z: 282.2069).

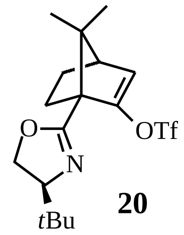
<u>Synthesis of keto-oxazoline **19**</u>:



19

To a mixture of amide **18** (1.0 g, 3.55 mmol), diisopropylethylamine (1.24 mL, 7.1 mmol) and triethylamine (6 mL) in 18 mL of methylene chloride was added 550 μL (7.1 mmol) of methanesulfonylchloride dropwise at 0°C. After addition, the resulting mixture was stirred overnight while warmed to room temperature. The reaction was monitored by TCL. Upon completion, the solvent was removed, and the residue was redissolved in 200 mL of ethyl acetate and washed with water (15 mL x 2) and brine, then dried over sodium sulfate. After evaporation of the solvent the crude product was purified by chromatography [Et$_3$N/hexane/EtOAc (1:50:100)] to give 856 mg (91%) of keto-oxazoline **19**. ^{1}H NMR (300MHz, CDCl$_3$) δ 4.04-4.17 (m, 2H), 3.88 (dd, *J*=10.2, 7.2 Hz, 1H), 2.52 (ddd, *J*=18.6, 4.8, 4.8 Hz, 1H), 2.36 (m, 1H), 2.11 (dd, *J*=4.2, 4.2 Hz, 1H), 1.94-2.08 (m, 2H), 1.78 (m, 1H), 1.40 (m, 1H), 1.16 (s, 3H), 1.07 (s, 3H), .089 (s, 9H); ^{13}C NMR (75MHz, CDCl$_3$) δ 211.9, 163.0, 75.6, 62.8, 49.2, 44.3, 43.9, 33.6, 27.3, 26.6, 25.8, 21.4, 19.9. LR-FABMS m/z: 264 (M+H)$^+$. HR-FABMS m/z: 264.1971 (calcd. for $C_{16}H_{25}NO_2H$ m/z: 264.1964).

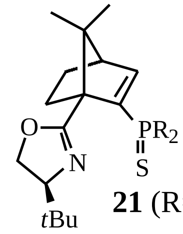
Synthesis of vinyl triflate **20**



20

LDA as generated by addition of 1.93 mL (4.83 mmol) of a 2.5M solution of *n*-butyllithium in hexane to a solution of diisopropylamine (678 μL, 4.83 mmol) in 8 mL of THF at -78°C. After addition, this solution was stirred for additional 20 minutes before a solution of keto-oxazoline **19** (850 mg, 3.22 mmol) in 8 mL of THF was slowly added at -78°C. The resulting mixture was stirred at -78°C for an additional 1 hour, after which a solution of N-phenyltrifluoromethane-sulfonimide (8.2 g, 22.93 mmol) in 10 mL of THF was slowly added at -78°C. This mixture was then allowed to warm to room temperature while stirring overnight. Upon completion, 20 mL of ice water was added to quench the reaction. After separation of the organic and aqueous layers the organic solvent was removed *in vacuo*. To the residue was added 50 mL of ethyl acetate. After separation, the aqueous layer was extracted with ethyl acetate (30 mL x 3). The combined organic layers were washed with water (20 mL x 2) and brine, then dried over sodium sulfate. After removal of the solvent the crude product was purified by chromatography on a silica gel [Et_3N/hexane/EtOAc (1:5: 95)] to give 1.16 g (91%) of vinyl triflate **20**. ^1H NMR (300MHz, $CDCl_3$) δ 5.78 (d, *J*=3.9 Hz, 1H), 4.04-4.18 (m, 2H), 3.88 (dd, *J*=10.2, 7.5 Hz, 1H), 2.50 (dd, *J*=3.6, 3..6 Hz, 1H), 2.35 (ddd, *J*=12.6, 8.7, 3.9 Hz, 1H), 2.04 (m, 1H), 1.64 (ddd, *J*=12.9, 9.3, 3.9 Hz, 1H), 1.21 (m, 1H), 1.14 (s, 3H), 0.94 (s, 3H), 0.89 (s, 9H); ^{13}C NMR (75MHz, $CDCl_3$) δ 162.1, 151.5, 119.5, 75.7, 60.1, 58.1, 50.8, 33.6, 28.2, 25.8, 25.2, 20.9, 20.3. ^{19}F NMR (282.2MHz, $CDCl_3$) δ -74.7. LR-EI m/z: 395 (M^+); HR-EI m/z: 395.1384 (calcd. for $C_{17}H_{24}F_3NO_4SH$ m/z: 395.1378).

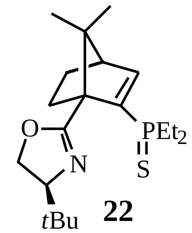
Synthesis of dicyclohexylphosphine sulfide oxazolinbe **21**



21 (R=C_6H_{11})

A mixture of 1,4-bis(phenylphosphino)butane (22 mg, 0.051 mmol) and $Pd(OAc)_2$ (11 mg, 0.051 mmol) in degassed 1 mL of benzene was stirred for 30 minutes at room temperature before a mixture of triflate **20** (200 mg, 0.51 mmol) and diisopropylethylamine (264 μL, 1.53 mmol) in 1.5 mL of benzene was added. The resulting mixture was degassed before diphenylphosphine (102 μL, 0.51 mmol) was added. This mixture was allowed stirred at 160°C for 36 hours. The reaction was monitored by TLC and ^{19}F NMR. Upon completion, the mixture was cooled to room temperature and sulfur (32 mg, 1.0 mmol) was added. After being stirred at room temperature for three hours, the mixture was diluted with 150 mL of additional ethyl acetate and washed with 20 mL of water and brine, then dried over anhydrous sodium sulfate. After evaporation of the crude product was purified by chromatography on a silica gel column [Et_3N/hexane/EtOAc (1:10 : 90)] to give 243 mg (95%) of the phosphine sulfide **21**. ^1H NMR (300MHz, $CDCl_3$) δ 6.77 (dd, *J*=9.9, 3.0 Hz, 1H), 4.18 (dd, *J*=9.0, 3.9 Hz, 1H), 3.85-3.96 (m, 2H), 2.54 (dd, *J*=3.3, 3.3 Hz, 1H), 2.25-2.43 (m, 2H), 1.41-2.37 (m, 15H0, 1.10-1.34 (m, 8H), 1.03 (s, 3H), 1.01 (obscured m, 1H), 0.891 (s, 12H); ^{13}C NMR (75MHz, $CDCl_3$) δ 164.4, 151.2, 135.4 (d, $J_{P\text{-}C}$=64.2 Hz), 76.3, 67.5, 60.7 (d, $J_{P\text{-}C}$=3.4 Hz), 60.3 (d, $J_{P\text{-}C}$=5.7 Hz), 5.39 (d, $J_{P\text{-}C}$=10.3 Hz), 39.2, 38.5, 36.1, 35.5, 33.3, 28.2, 27.1(d, $J_{P\text{-}C}$=2.8 Hz), 26.9 (d, $J_{P\text{-}C}$=2.8 Hz), 26.5, 26.3, 26.2, 26.0, 25.9, 25.8, 25.7, 25.6, 23.9, 23.9, 20.8, 20.3. ^{31}P NMR (125MH z, $CDCl_3$) δ 3.9. LR-FABMS m/z: 476 $(M+H)^+$. HR-FABMS m/z: 476.3118 (calcd. for $C_{28}H_{47}NOPS$ m/z: 476.3116).

Synthesis of phosphine sulfide oxazoline **22**


22

A mixture of 1,4-bis(phenylphosphino)butane (22 mg, 0.051 mmol) and Pd(OAc)$_2$ (11 mg, 0.051 mmol) in degassed 1 mL of benzene was stirred for 30 minutes at room temperature before a mixture of triflate **20** (200 mg, 0.51 mmol) and diisopropylethylamine (264 μL, 1.53 mmol) in 1.5 mL of benzene was added. The resulting mixture was degassed before diethylphosphine (64 μL, 0.55 mmol) was added. This mixture was stirred at 120°C for 36 hours. The reaction was monitored by TLC and ^{19}F NMR. Upon completion, the mixture was cooled to room temperature and sulfur (32 mg, 1.0 mmol) was added. After being stirred at room temperature for three hours, the mixture was diluted with 150 mL of ethyl acetate and washed with 20 mL of water and brine respectively, then dried over anhydrous sodium sulfate. After the solvent was removed the crude product was purified by chromatography on a silica gel [Et$_3$N/hexane/EtOAc (1:10 : 90)] to give 156 mg (84%) of the phosphine sulfide **22**. ^{1}H NMR (300MHz, CDCl$_3$) δ 7.08 (dd, *J*=12.0, 3.3 Hz, 1H), 4.19 (m, 1H), 3.86-3.97 (m, 2H), 2.55 (dd, *J*=3.3, 3.3 Hz, 1H), 2.29 (ddd, *J*=12.6, 8.7, 3.6 Hz, 1H), 1.81-2.21 (m, 5H), 1.40 (ddd, *J*=12.6, 9.3, 3.6 Hz, 1H), 1.01-1.24 (m, 7H), 1.03 (s, 3H), 0.93 (s, 3H), .0895 (s, 9H); ^{13}C NMR (75MHz, CDCl$_3$) δ 164.5, 154.1 (d, $J_{P\text{-}C}$=5.7 Hz), 136.8 (d, $J_{P\text{-}C}$=67.9 Hz), 76.1, 67.7, 61.2 (d, $J_{P\text{-}C}$=3.5 Hz), 60.2 (d, $J_{P\text{-}C}$=5.4 Hz), 53.8 (d, $J_{P\text{-}C}$=11.1 Hz), 33.4, 29.1, 26.1, 24.9, 24.2, 24.0, 23.8(d, $J_{P\text{-}C}$=2.8 Hz), 23.3, 20.7, 20.5, 6.7, (d, $J_{P\text{-}C}$=4.8 Hz), 6.23 (d, $J_{P\text{-}C}$=4.5 Hz); ^{31}P NMR (125MHz, CDCl$_3$) δ 44.4. LR-FABMS m/z: 368.2 (M+H)$^+$. HR-FABMS m/z: 368.2128 (calcd. for $C_{23}H_{37}NO_2PSH$ m/z: 368.2179).

Spectral data for phosphine sulfide of ligand **7**

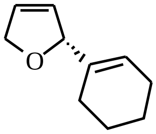
^{1}H NMR (300MHz, CDCl$_3$) δ 7.76-7.88 (m, 4H), 7.39-7.51 (m, 6H), 6.05 (d, *J*=44.1 Hz, 1H), 5.32 (d, *J*=21.3 Hz, 1H), 4.21 (dd, *J*=9.6, 8.1 Hz, 1H), 3.96 (dd, *J*=15.6, 8.1 Hz, 1H), 3.90 (m, 1H), 1.82 (m, 1H), 1.57 (s, 3H), 1.55 (s, 3H), 0.94 (d, *J*=6.9 Hz, 3H), 0.85 (d, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 170.8 (d, $J_{P\text{-}C}$=5.0 Hz), 147.4, 146.5, 133.6, 133.3, 132.5, 132.1, 132.1, 132.0, 131.9, 131.3, 130.4, 130.3, 128.3, 128.1, 71.8, 69.8, 43.1 (d, $J_{P\text{-}C}$=11.6 Hz), 32.1, 27.5, 19.0, 17.8. ^{31}P NMR (120 MHz, CDCl$_3$) δ 45.2. LR-FABMS m/z: 398 $(M+H)^+$. HR-FAB m/z 398.1717 $(M+H)^+$ (calcd. for $C_{23}H_{28}NOPSH$ m/z 398.1718)

Asymmetric Heck Reactions

General procedure for the Heck reaction: A mixture of ligand and $Pd_2(dba)_3$ in degassed benzene was stirred at the reaction temperature for 20 minutes before a degassed mixture of alkene, triflate and disopropylethylamine in benzene was added. The mixture was then degassed. This mixture was allowed to stir at reaction temperature until all starting material was consumed completely. The reaction was monitored by GC and TCL. Enantioselectivity was detected by chiral GC. Upon completion, the mixture was diluted with diethyl ether and washed with water and brine, dried and evaporated. The crude product was purified by column chromatography using a mixture of hexane and ethyl acetate or pentane and ether as the eluent to give the coupling product.

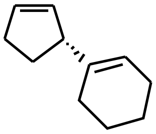
These products have all been reported previously and so only minimal spectral data is reported here.

2-cyclohexenyl-2,5-dihyrofuran (**25**)[1,2]



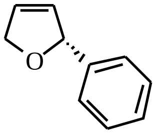
^{1}H NMR (300 MHz, CDCl$_3$) δ 5.92-5.96 (m, 1H), 5.68-5.71 (m, 2H), 5.13 (m, 1H), 4.64-4.69 (m, 2H), 1.76-2.03 (m, 4H), 1.44-1.73 (m, 4H); 13C NMR (75MHz, CDCl3) d 137.957, 128.724, 127.821, 124.210, 90.547, 75.625, 25.003, 23.273, 22.459. GC (CHIRALDEX G-TA, 30m, 70°C, 2.0Kg/cm^2): 24,6 min(S); 28.7 min (R).

3-Cyclohexenyl-cyclopentene (**28**)[1,2]



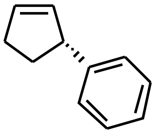
^{1}H NMR (300 MHz, CDC$_{l3}$) δ 5.78(m, 1H), 5.61(m, 1H), 5.42(m, 1H), 3.21(m, 1H), 2.20-2.50(m, 2H), 1.86-2.13(m, 5H), 1.48-1.73(m, 5H); GC (CHIRALDEX G-TA, 30m, 50°C, 2.0Kg/cm^2): 28.6 min(+); 30.9 min (-). 27.8 min (**29**)

2-Phenyl-2,5-dihyrofuran (**31**)[1-3]



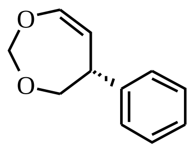
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.26-7.38 (m, 5H), 6.05 (m, 1H), 5.87 (m, 1H), 5.79 (m, 1H), 4.85-4.92 (m, 1H), 4.74-4.81 (m, 1H); ^{13}C NMR (75M Hz, CDCl3) δ 142.0, 129.9, 128.5, 127.8, 126.6, 126.4, 87.9, 75.8. GC (CHIRALDEX G-TA, 30m, 80°C, 2.0Kg/cm^2): 24.8 min(S); 29.2 min (R).

3-Phenyl-cyclopentene (**32**)[1,2]



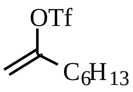
^{1}H NMR (300 MHz, CDC$_{l3}$) δ 7.25-7.32 (m, 2H), 7.16-7.20 (m, 3H), 5.97 (m, 1H), 5.80 (m, 1H), 3.91 (m, 1H), 2.33-2.58 (m, 3H), 1.75 (m 1H); GC (CHIRALDEX G-TA, 30m, 70°C, 2.0Kg/cm^2): 26.1 min(R); 28.7 min (S); 21.2 min (**33**).

4,5-dihydro-5-phenyl-1,3-dioxepin (**35**)[1,2]



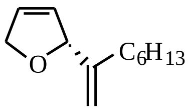
^{1}H NMR (300 MHz, CDC$_{l3}$) δ 7.25-7.35 (m, 5H), 6.47 (dd, *J*=7.2, 2.1 Hz, 1H), 5.19 (d, *J*=6.9 Hz, 1H), 4.95 (m, 1H), 4.85 (d, *J*=7.2 Hz, 1H), 3.98 (dd, *J*=11.7, 4.5 Hz, 1H), 3.81 (m, 1H), 3.46 (dd, *J*=11.4, 8.4 Hz, 1H); GC (CHIRALDEX G-TA, 30m, 85°C, 2.0Kg/cm^2): 60.9 min(R); 63.9 min (S)

1-Octaten-2-yl-triflate (**36**)



^{1}H NMR (300 MHz, CDC$_{l3}$) δ 5.08 (d, *J*=3.6 Hz, 1H), 4.92(ddd, *J*=3.3, 0.6, 0.6 Hz, 1H), 2.330 (dd, *J*=7.3, 7.3 Hz, 1H), 1.54 (m, 1H), 1.26-1.39 (m, 8H), 0.89 (t, *J*=6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDC$_{l3}$) δ 156.93, 103.953, 33.897, 31.443, 28.366, 25.988, 22.558, 14.103.

Synthesis of 2-Octat-1'-en-2'-yl-2,5-dihydrofuran (**37**)



A mixture of ligand **2** (12 mg, 0.027 mmol) and Pd$_2$(dba)$_3$ (9 mg, 0.0099 mmol) in 2 mL of degassed benzene was stirred at room temperature for 30 minutres before a degassed mixture of 1-Octaten-2-yl-triflate (**36**) (97 mg, 0.398 mmol), diisopropylethylamine (208 μL, 1.19 mmol) and 2,3-dihydrofuran (150 μL, 1.99 mmol) in 2 mL of benzene was added. The resulting mixture was degassed again and was then allowed to stir at 95°C for 30 hours. The reaction was monitored by GC. Upon completion, the mixture was cooled to room temperature and diluted with additional 150 mL of ethyl acetate. The mixture was washed with water, brine, dried and the solvent removed. The crude product was purified by chromatography on a silica gel column using a mixture of hexane/EtOAc (5/95) as eluent to give 59 mg

(83%) of the product. **37**: ^{1}H NMR (300 MHz, CDC$_{l3}$) δ 5.95 (m, 1H), 5.76 (m, 1H), 5.03 (m, 1H), 5.83 (dd, *J*=3.0, 1.5 Hz, 1H), 4.62-4.76 (m, 2H), 1.88-2.06 (m, 2H), 1.38-1.50 (m, 2H), 1.20(m, 6H), 0.88 (t, *J*=6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDC$_{l3}$) δ 149.78, 128.89, 126.97, 110.24, 89.74, 75.62, 31.74, 30.80, 29.29, 27.86, 22.60, 14.06; GC (CHIRALDEX G-TA, 30m, 85°C, 2.0Kg/cm^2): 24.3 min(S); 27.4 min (R).

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3)Ogasawara, M.; Yoshida, K.; Hayashi, T. *Heterocycles* **2000**, *52*, 195-201.