Development of an Asymmetric Trimethylenemethane Cycloaddition Reaction: Application in the Enantioselective Synthesis of Highly Substituted Carbocycles

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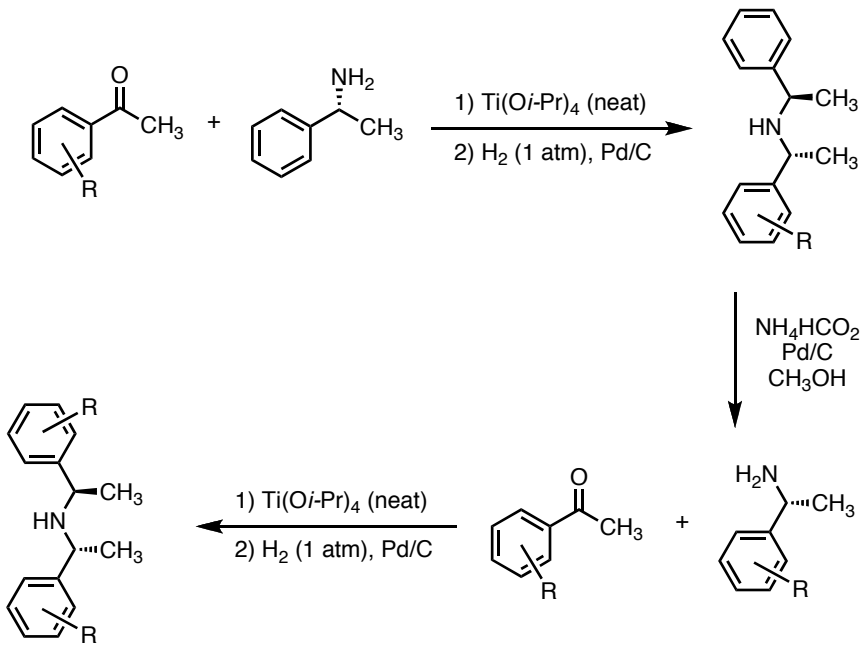
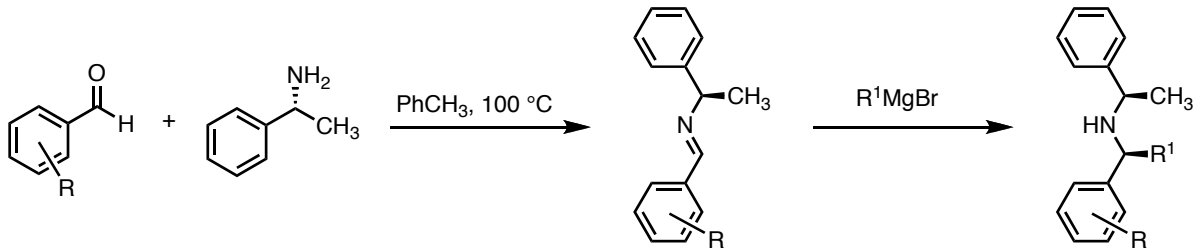
Supporting Information

General Methods. All reactions were performed under an argon atmosphere in flame- or oven-dried glassware with magnetic stirring. All solvents were freshly distilled or were dried by passing through an alumina column. Reactions conducted below room temperature were cooled using a Thermo-Fisher Scientific Neslab Cryocool or performed in a cold room. Reactions performed above room temperature utilized an oil bath preheated to the stated temperature. Thin-layer chromatography was performed on EMD silica gel 60 F_{254} plates (0.25 mm); visualization of the developed chromatogram was performed by fluorescence and staining with potassium permanganate. All reagents were purchased from commercial sources and used without further purification unless otherwise noted. The following compounds were prepared according to known literature procedures: $Pd(dba)_2$,[1] 3-acetoxy–2–trimethylsilylmethyl–1–propene (**1**),[2] **L1**,[3] **L21**,[4] **L25**,[5] **L26**,[6] **L27**,[7] and other phosphoramidites not characterized below.[8] Organic solutions were concentrated by rotary evaporation below 40 °C at *ca.* 25 mmHg. Flash chromatography was performed with Acros 0.035-0.07 μm silica gel unless otherwise noted. ^{1}H and ^{13}C-NMR spectroscopy was performed on a Varian Mercury NMR at 400 (^{1}H) or 100 (^{13}C) MHz, Unity NMR at 500 (^{1}H) or 125 (^{13}C) MHz, or Unity NMR at 600 (^{1}H) or 150 (^{13}C) MHz. Chemical shifts are reported in ppm relative to tetramethylsilane or residual protiated solvent. All ^{13}C-NMR spectra were proton decoupled. Data for ^{1}H are reported as chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sex = sextet, sept = septet, m = multiplet), coupling constant, integration; data for ^{13}C are reported in terms of chemical shift. Infrared spectroscopic data was recorded on sodium chloride plates as thin films on a Thermo Scientific Nicolet IR100 FT-IR spectrometer. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter using 5 cm glass cells with a sodium 589 nm filter. Mass spectrometry data were collected on a Micromass Q-Tof API-US mass spectrometer (Waters Corporation, Milford, MA). Chiral GC analysis was performed on an HP 6850 Series GC System using a CycloSil-B column. Chiral HPLC analysis was performed on a Thermo Separation Products Spectra Series P-100 or an Agilent 1200 Series HPLC using Chiralcel® and Chiralpak® columns.

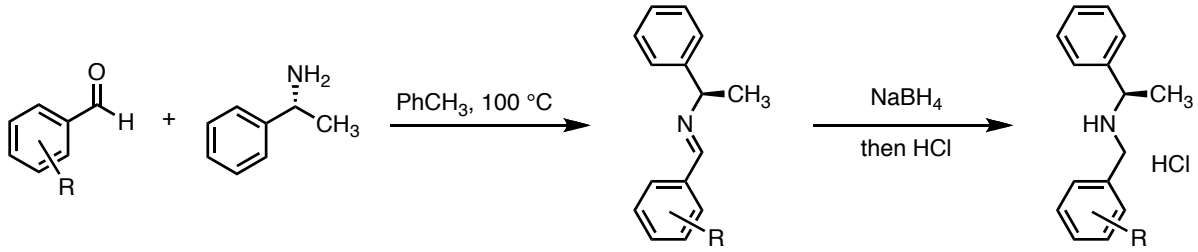


General procedure for the synthesis of C_2-symmetric and pseudo C_2-symmetric secondary amines (Procedure A).[8] A mixture of the appropriately substituted acetophenone (20 mmol, 1.0 eq) and (*R*)-α-methylbenzylamine (20 mmol, 1.0 eq) in Ti(O*i*-Pr)$_4$ (17.9 mL, 60 mmol, 3.0 eq) was stirred for 45 minutes. Pd/C (10%, 400 mg) was added and the mixture stirred under an atmosphere of hydrogen for 48 hours. Aqueous NaOH (1M, 40 mL) was added and the mixture stirred for 45 minutes. Water (100 mL) was added and the mixture extracted with ethyl acetate (5 x 50 mL). The organic extracts were dried over $MgSO_4$, filtered, and concentrated to give the amine. If necessary, flash chromatography on silica gel (diethyl ether in petroleum ether) could be used to separate diastereomers, though little, if any separation was observed by thin-layer chromatography so GC analysis was necessary.

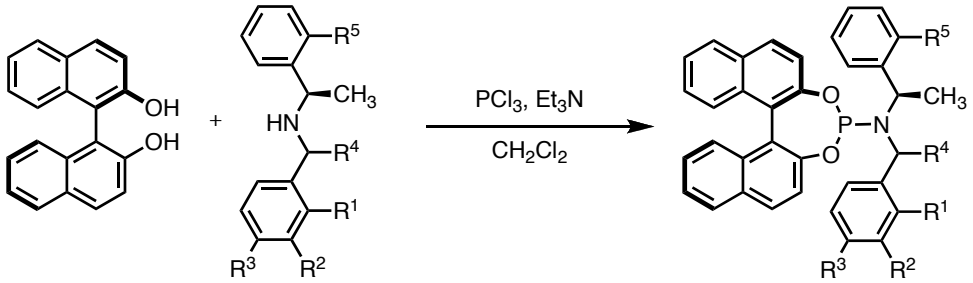


General procedure for the preparation of pseudo S_1-symmetric secondary imines (Procedure B). The appropriately substituted benzaldehyde (20 mmol, 1.0 eq) and (*R*)-α-methylbenzylamine (20

mmol, 1.0 eq) were combined in toluene and stirred at 100 °C for 2 hours. The mixture was cooled to room temperature, dried over $MgSO_4$, filtered, and concentrated to give pure imine in quantitative yield. A solution of imine (5.0 mmol, 1.0 eq) in diethyl ether (25 mL) was cooled to 0 °C and Grignard reagent (10.0 mmol, 2.0 eq) was added. The reaction was allowed to warm to room temperature and stirred for 3 hours, at which point additional Grignard reagent (1.0 eq) was added if starting material remained as determined by GC. If necessary, the reaction was allowed to stir until starting material was consumed. The mixture was cooled to 0 °C and quenched by slow addition of saturated aqueous ammonium chloride. Diethyl ether (25 mL) and water (25 mL) were added. The organic layer was washed with water (2 x 25 mL), dried over $MgSO_4$, and concentrated. The diastereomers could be separated by flash chromatography on silica gel (diethyl ether in petroleum ether with 1% triethylamine), though minimal separation was observed by TLC and analysis by GC was often necessary to determine the composition of the eluted fractions. Diastereomeric ratios generally ranged from 2:1 to 10:1 and were not optimized.

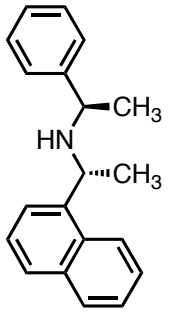


General procedure for the preparation of desmethyl secondary imines (Procedure C). The appropriately substituted benzaldehyde (20 mmol, 1.0 eq) and (*R*)-α-methylbenzylamine (20 mmol, 1.0 eq) were combined in toluene and stirred at 100 °C for 2 hours. The mixture was cooled to room temperature, dried over $MgSO_4$, filtered, and concentrated to give pure imine in quantitative yield. A solution of imine (10.0 mmol, 1.0 eq) in methanol (30 mL) was cooled to 0 °C and $NaBH_4$ (10.0 mmol, 1.0 eq) was added slowly. The reaction was allowed to warm to room temperature and stirred for 1 hour, at which point water (30 mL) and ethyl acetate (75 mL) were added. The aqueous layer was removed and the organic layer washed with brine, dried over $MgSO_4$, and filtered to give a yellow oil. Diethyl ether (25 mL) was added, followed by anhydrous 2.0M HCl in diethyl ether (10 mL, 2.0 eq). The mixture was stirred for 30 minutes and the white solid precipitate was isolated by filtration to give the pure amine hydrochloride.

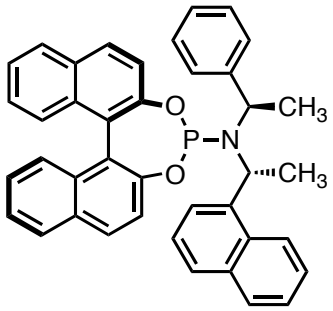


General procedure for preparation of acyclic amine phosphoramidites (Procedure D). Triethylamine (347 μL, 2.5 mmol, 5.0 eq) was added dropwise to a solution of phosphorus trichloride (44 μL, 0.5 mmol, 1.0 eq) in dichloromethane (2 mL) at 0 °C. The solution was warmed to room temperature and the amine (0.5 mmol, 1.0 eq) was added neat as either the free base or HCl salt. The mixture was stirred for 5 hours, at which time (*R*)-BINOL (143 mg, 0.5 mmol, 1.0 eq) was added neat and the mixture stirred overnight. The suspension was concentrated and the ligand purified by flash chromatography on silica gel (dichloromethane in petroleum ether with 1% triethylamine) to give the ligand as a white solid.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(1-Naphthyl)-ethyl)-phosphoramidite (L3):

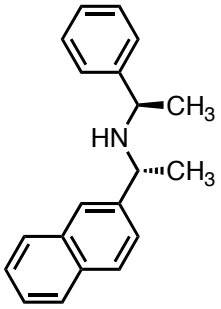


(*R*)-1-(naphthalen-1-yl)-*N*-((*R*)-1-phenylethyl)ethanamine[9]: The reaction was performed according to Procedure A with 2.34 mL (20 mmol) of acetophenone and 3.42 g (20 mmol) of (*R*)-(1-naphthyl)-ethylamine. Purified by crystallization from hot hexane to give the product as a tan solid (5.23 g, 95%). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.88 (t, *J* = 9.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 6.9 Hz, 1H), 7.54-7.23 (m, 6H), 7.18-7.14 (m, 2H), 4.39 (q, *J* = 6.6 Hz, 1H), 3.59 (q, *J* = 6.6 Hz, 1H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.34 (d, *J* = 6.9 Hz, 3H).



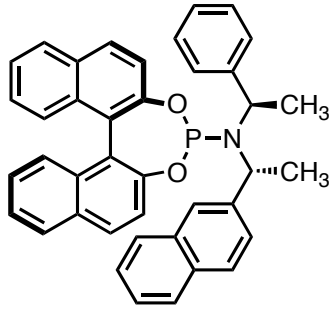
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(1-Naphthyl)-ethyl)-phosphoramidite (L3): The reaction was performed according to Procedure D with 138 mg (0.5 mmol) of (*R*)-1-(naphthalen-1-yl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether) to give the product as a white solid (60.0 mg, 20%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.01 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.77-7.74 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.59 (dd, *J* = 8.5, 0.5 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.46-7.39 (m, 2H), 7.37-7.33 (m, 3H), 7.28-7.20 (m, 5H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.91-6.84 (m, 3H), 5.26-5.19 (m, 1H), 4.62-4.57 (m, 1H), 1.81 (dd, *J* = 7.5, 1.0 Hz, 3H), 1.61 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.6, 149.8, 141.7, 140.8, 133.5, 133.0, 132.8, 131.5, 130.6, 130.5, 130.4, 129.6, 128.6, 128.4, 128.22, 128.18, 127.5, 127.4, 127.2, 126.4, 126.1, 125.9, 125.5, 125.2, 125.1, 124.9, 124.6, 124.40, 124.36, 124.3, 123.0, 122.5, 122.4, 121.4, 55.5, 51.7, 25.0; ^{31}P NMR (162 MHz, $CDCl_3$): 151.8; IR (neat): 3057, 2968, 2925, 2851, 1619, 1591, 1509, 1463, 1327, 1230, 1070, 947, 821, 751, 702; $[\alpha]_{25}^{D}$ = -89.5 (*c* 1.22, $CHCl_3$); HRMS (EI): calculated for $C_{40}H_{32}NO_2P$: 589.2171, found 589.2171.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(2-Naphthyl)-ethyl)-phosphoramidite (L4):



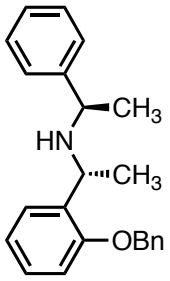
(*R*)-1-(naphthalen-2-yl)-*N*-((*R*)-1-phenylethyl)ethanamine: The reaction was performed according to Procedure A with 1.70 g (10 mmol) of 2-acetonaphthone and 1.28 mL (10 mmol) of (*R*)-α-

methylbenzylamine. Purified by flash chromatography on silica gel (30% diethyl ether in petroleum ether) to give the product as a clear oil (2.7 g, 98%). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.85-7.78 (m, 3H), 7.58 (s, 1H), 7.50-7.20 (m, 8H), 3.67 (q, *J* = 6.6 Hz, 1H), 3.52 (q, *J* = 6.6 Hz, 1H), 1.67-1.63 (m, 1H), 1.35 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 6.9 Hz, 3H).

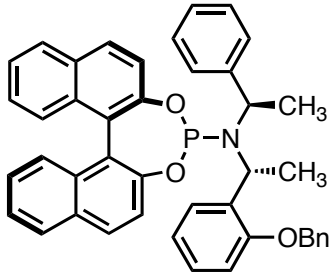


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(2-Naphthyl)-ethyl)-phosphoramidite (L4): The reaction was performed according to Procedure D with 138 mg (0.5 mmol) of (*R*)-1-(naphthalen-2-yl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (175 mg, 59%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.01 (d, *J* = 11.0 Hz, 1H), 7.93 (d, *J* = 10.5 Hz, 1H), 7.80-7.78 (m, 2H), 7.69-7,64 (m, 3H), 7.59 (dd, *J* = 11.0, 1.0 Hz, 1H), 7.49 (s, 1H), 7.45-7.32 (m, 7H), 7.28-7.12 (m, 8H), 4.61-4.52 (m, 1H), 4.48-4.40 (m, 1H), 1.78 (d, *J* = 8.5, 3H), 1.72 (d, *J* = 8.5 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.6, 149.8, 143.1, 140.6, 133.0, 132.9, 132.8, 132.4, 131.4, 130.5, 130.4, 129.7, 128.4, 128.19, 128.17, 128.1, 127.9, 127.5, 127.3, 127.2, 126.9, 126.8, 126.4, 126.1, 125.9, 125.8, 125.7, 124.9, 124.4, 124.2, 122.54, 122.46, 121.2, 54.7, 23.3, 23.0; ^{31}P NMR (162 MHz, $CDCl_3$): 150.9; IR (neat): 3057, 2970, 2929, 1619, 1591, 1506, 1463, 1374, 1327, 1230, 1203, 1128, 1113, 1070, 947, 926, 821, 750, 696; $[\alpha]_{25}^{D}$ = 139.0 (*c* 1.52, $CHCl_3$); HRMS (EI): calculated for $C_{40}H_{32}NO_2P$: 589.2171, found 589.2158.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(2-Benzyloxyphenyl)-ethyl)-phosphoramidite (L6):

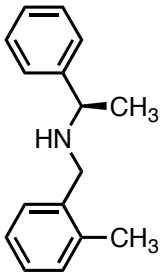


(*R*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine: A solution of 2-benzyloxybenzaldehyde (5.31 g, 25.0 mmol, 1.0 eq) and (*R*)-α-methylbenzylamine (3.03 g, 25.0 mmol, 1.0 eq) were combined in toluene and stirred at 100 °C for 2 hours. The mixture was cooled to room temperature, dried over $MgSO_4$, filtered, and concentrated to give pure imine (7.81 g, 99%). A solution of imine (1.58 g, 5.0 mmol, 1.0 eq) in diethyl ether (25 mL) was cooled to 0 °C and methylmagnesium bromide (10.0 mmol, 2.0 eq) was added. The reaction was allowed to warm to room temperature and stirred for 3 hours, at which point the reaction appeared incomplete by GC. Additional Grignard reagent (15.0 mmol, 3.0 eq) was added and the reaction was allowed to stir for 24 hours. The mixture was cooled to 0 °C and quenched by slow addition of saturated aqueous ammonium chloride. Diethyl ether (25 mL) and water (25 mL) were added. The organic layer was washed with water (2 x 25 mL), dried over $MgSO_4$, and concentrated. GC analysis of the crude mixture shows a 2:1 ratio of (*R,S*):(*R,R*) amines. The diastereomers could be separated by flash chromatography on silica gel (diethyl ether in petroleum ether with 1% triethylamine), to give 253 mg (15%) of the (*R,R*) amine as a clear oil, 446 mg (27%) of the (*R,S*) amine as a clear oil, and 364 mg (22%) of a mixture of both diastereomers (64% combined, isolated yield). (*R*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.26 (m, 7H), 7.24-7.15 (m, 5H), 6.97-6.93 (m, 2H), 5.02 (dd, *J* = 14.8, 11.6 Hz, 2H), 3.83 (q, *J* = 6.8 Hz, 1H), 3.54 (q, *J* = 6.8 Hz, 1H), 1.80 (br s, 1H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 156.7, 145.9, 137.1, 133.6, 128.6, 128.3, 128.3, 127.9, 127.6, 127.3, 126.9, 126.7, 121.0, 112.0, 70.0, 55.4, 51.8, 25.3, 23.0.

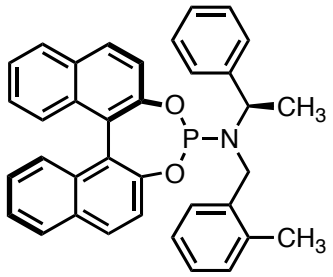


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*,*R*)-(1-Phenyl-ethyl)-[1-(2-Benzyloxyphenyl)-ethyl)-phosphoramidite (L6): The reaction was performed according to procedure D with 166 mg (0.5 mmol) of (*R*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (220 mg, 68%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.99 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.85 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.55 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.42-7.39 (m, 1H), 7.37-7.27 (m, 7H), 7.24-7.16 (m, 6H), 7.11-7.07 (m, 1H), 7.04-6.95 (m, 4H), 6.58 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.91-4.83 (m, 1H), 4.80 (d, *J* = 12.5 Hz, 1H), 4.60-4.55 (m, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 1.67 (dd, *J* = 7.2, 1.7 Hz, 3H), 1.52 (d, *J* = 6.5 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 154.7, 150.7, 149.8, 141.6, 137.5, 134.4, 133.0, 132.8, 131.4, 130.44, 130.37, 129.5, 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.6, 127.4, 127.3, 127.1, 126.9, 126.3, 126.1, 125.8, 124.8, 124.3, 122.61, 122.57, 121.3, 120.7, 111.1, 69.6, 54.8, 49.3, 25.1, 20.5; ^{31}P NMR (162 MHz, $CDCl_3$): 151.9; IR (neat): 3061, 2969, 2927, 1619, 1591, 1495, 1463, 1431, 1372, 1327, 1230, 1070, 948, 822, 749; $[\alpha]_{24}^{D}$ = -66.8 (*c* 1.53, $CHCl_3$); HRMS (EI): calculated for $C_{43}H_{36}NO_3P$: 645.2433, found 645.2450.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-(o-tolulyl-methyl)-phosphoramidite (L9):

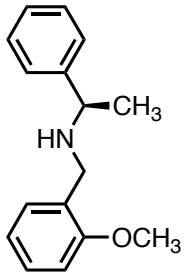


(*R*)-*N*-(2-methylbenzyl)-1-phenylethanamine hydrochloride: The amine was prepared from (*R*)-*N*-(2-methylbenzylidene)-1-phenylethanamine (670 mg, 3.0 mmol) and $NaBH_4$ (113 mg, 3.0 mmol) according to Procedure C. The product was obtained as a white solid (677 mg, 86%). ^{1}H-NMR (400 MHz, CD_3OD): 7.56-7.50 (m, 5H), 7.36-7.24 (m, 4H), 4.53 (q, *J* = 6.8 Hz, 1H), 4.13 (d, *J* = 13.2 Hz, 1H), 3.91 (d, *J* = 13.2 Hz, 1H), 2.14 (s, 3H), 1.74 (d, *J* = 7.2 Hz, 3H).



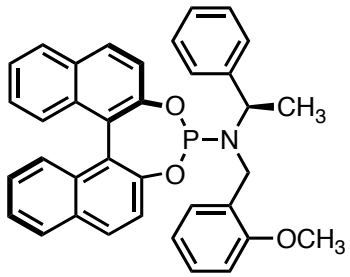
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-(o-tolulyl-methyl)-phosphoramidite (L9): The reaction was performed according to Procedure D with 131 mg (0.5 mmol) of (*R*)-*N*-(2-methylbenzyl)-1-phenylethanamine hydrochloride and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (133 mg, 49%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.97 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.59 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.51-7.45 (m, 4H), 7.41-7.37 (m, 3H), 7.34-7.29 (m, 3H), 7.24-7.16 (m, 3H), 7.05 (t, *J* = 7.0 Hz, 1H), 6.96 (d, *J* = 9.0 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 4.13-4.05 (m, 1H), 3.81 (d, *J* = 15.0 Hz, 1H), 3.24 (dd, *J* = 16.0, 1.5 Hz, 1H), 1.78 (dd, *J* = 7.5, 3.5 Hz, 3H), 1.70 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.4, 149.6, 143.7, 136.2, 136.0, 132.8, 132.5, 131.4, 130.6, 130.3, 130.0, 129.9, 128.6, 128.4, 128.1, 127.6, 127.5, 127.1, 127.05, 127.0, 126.5, 126.1, 126.0, 124.8, 124.6, 124.1, 122.6, 122.4, 121.7, 58.2, 45.7, 23.4, 18.8; ^{31}P NMR (162 MHz, $CDCl_3$): 145.4; IR (neat): 3060, 3026, 2972, 2927, 1619, 1590, 1508, 1493, 1463, 1328, 1231, 1205, 1071, 950, 897, 822, 791, 751; $[\alpha]_{24}^{D}$ = -204.5 (*c* 0.75, $CHCl_3$); HRMS (EI): calculated for $C_{36}H_{29}NO_2P$: 538.1936, found 538.1936.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-(2-Methoxyphenyl-methyl)-phosphoramidite (L10):



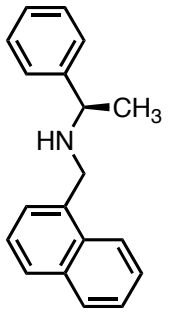
(*R*)-*N*-(2-methoxybenzyl)-1-phenylethanamine hydrochloride: The amine was prepared from (*R*)-*N*-(2-methoxybenzylidene)-1-phenylethanamine (2.39 g, 10.0 mmol) and $NaBH_4$ (378 mg, 10.0 mmol) according to Procedure C. The product was obtained as a white solid (2.59 g, 93%). ^{1}H-NMR (400 MHz, CD_3OD): 7.52-7.40 (m, 6H), 7.30-7.28 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H),

4.44 (q, *J* = 6.8 Hz, 1H), 4.04 (d, *J* = 12.8 Hz, 1H), 3.97 (d, *J* = 12.8 Hz, 1H), 3.83 (s, 3H), 1.71 (d, *J* = 6.8 Hz, 3H).

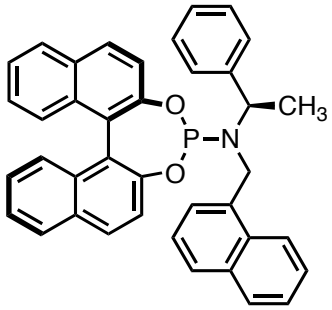


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-(2-Methoxyphenyl-methyl)-phosphoramidite (L10): The reaction was performed according to Procedure D with 556 mg (2.0 mmol) of (*R*)-*N*-(2-methoxybenzyl)-1-phenylethanamine hydrochloride, 174 μL (2.0 mmol) of PCl_3, 1.39 mL (5.0 mmol) of triethylamine and 573 mg (2.0 mmol) of (*R*)-BINOL in dichloromethane (8 mL). Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (947 mg, 85%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.97 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.80-7.78 (m, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 9.0, 0.5 Hz, 1H), 7.54-7.52 (m, 2H), 7.45-7.41 (m, 3H), 7.40-7.29 (m, 5H), 7.23-7.15 (m, 2H), 7.10 (td, *J* = 7.7, 1.8 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 1H), 6.90 (td, *J* = 7.5, 1.0 Hz, 1H), 4.16 (sext, *J* = 7.3 Hz, 1H), 3.68 (dd, *J* = 15.7, 3.2 Hz, 1H), 3.59 (dd, *J* = 15.7, 2.2 Hz, 1H), 3.51 (s, 3H), 1.71 (dd, *J* = 7.0, 3.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 157.4, 150.3, 149.7, 143.9, 132.8, 132.5, 131.4, 130.6, 130.2, 130.1, 129.3, 128.3, 128.2, 128.1, 127.7, 127.6, 127.3, 127.2, 127.1, 127.0, 126.0, 125.9, 124.8, 124.4, 124.2, 122.4, 122.3, 121.8, 120.5, 110.0, 57.9, 55.0, 41.8, 24.9, 23.1; ^{31}P NMR (162 MHz, $CDCl_3$): 145.2; IR (neat): 3061, 3008, 2971, 2836, 1619, 1589, 1492, 1463, 1329, 1231, 1205, 1145, 1071, 1033, 949, 896, 823, 753, 698; $[\alpha]_{22}^{D}$ = -201.2 (*c* 1.90, $CHCl_3$); HRMS (EI): calculated for $C_{36}H_{30}NO_3P$: 555.1963, found 555.1946.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-[(1-Naphthyl)-methyl]-phosphoramidite (L11):

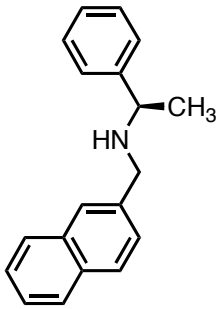


(*R*)-*N*-(naphthalen-1-ylmethyl)-1-phenylethanamine hydrochloride: The amine was prepared from (*R*)-*N*-(naphthalen-1-ylmethylene)-1-phenylethanamine (778 mg, 3.0 mmol) and $NaBH_4$ (113 mg, 3.0 mmol) according to Procedure C. The product was obtained as a white solid (762 mg, 85%). ^{1}H-NMR (400 MHz, CD_3OD): 8.00-7.94 (m, 2H), 7.63-7.51 (m, 10H), 4.65 (q, *J* = 6.8 Hz, 1H), 4.59 (d, *J* = 13.6 Hz, 1H), 4.38 (d, *J* = 13.2 Hz, 1H), 1.76 (d, *J* = 6.8 Hz, 3H).

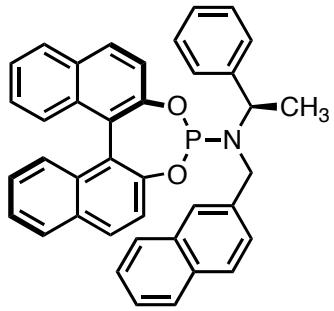


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-[(1-Naphthyl)-methyl]-phosphoramidite (L11): The reaction was performed according to Procedure D with 149 mg (0.5 mmol) of (*R*)-*N*-(naphthalen-1-ylmethyl)-1-phenylethanamine hydrochloride and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (255 mg, 89%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.98 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.49-7.20 (m, 14H), 7.16-7.12 (m, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 4.38 (d, *J* = 15.5 Hz, 1H), 4.16-4.08 (m, 1H), 3.75 (dd, *J* = 16.0, 1.5 Hz, 1H), 1.75 (dd, *J* = 7.5, 3.5 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.4, 149.6, 143.6, 133.7, 133.6, 132.8, 132.5, 131.7, 131.5, 130.6, 130.3, 130.1, 128.5, 128.4, 128.1, 127.7, 127.6, 127.1, 127.0, 126.1, 125.8, 125.5, 125.3, 124.9, 124.6, 124.2, 123.1, 122.6, 122.3, 121.7, 58.1, 45.8, 23.4; ^{31}P NMR (162 MHz, $CDCl_3$): 145.2; IR (neat): 3059, 2973, 2926, 1619, 1590, 1509, 1463, 1370, 1328, 1230, 1214, 1144, 1071, 949, 822, 799, 753, 697; $[\alpha]_{25}^{D}$ = -113.4 (*c* 1.43, $CHCl_3$); HRMS (EI): calculated for $C_{39}H_{30}NO_2P$: 575.2014, found 575.2014.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-[(2-Naphthyl)-methyl]-phosphoramidite (L12):



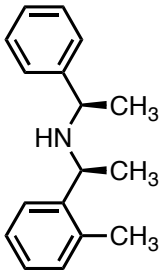
(*R*)-*N*-(naphthalen-2-ylmethyl)-1-phenylethanaminehydrochloride: The amine was prepared from (*R*)-*N*-(naphthalen-1-ylmethylene)-1-phenylethanamine (778 mg, 3.0 mmol) and $NaBH_4$ (113 mg, 3.0 mmol) according to Procedure C. The product was obtained as a white solid (846 mg, 95%). ^{1}H-NMR (400 MHz, CD_3OD): 7.94 (d, *J* = 8.4 Hz, 1H), 7.91-7.88 (m, 3H), 7.57-7.48 (m, 8H), 4.50 (q, *J* = 6.8 Hz, 1H), 4.30 (d, *J* = 13.2 Hz, 1H), 4.08 (d, *J* = 13.2 Hz, 1H), 1.75 (d, *J* = 6.8 Hz, 3H).



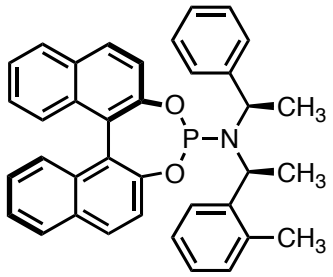
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R*)-(1-Phenyl-ethyl)-[(2-Naphthyl)-methyl]-phosphoramidite (L12): The reaction was performed according to Procedure D with 149 mg (0.5 mmol) of (*R*)-*N*-(naphthalen-2-ylmethyl)-1-phenylethanaminehydrochloride and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (154 mg, 54%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.02 (d, *J* = 9.0 Hz, 1H), 7.92 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.76-7.69 (m, 5H), 7.54-7.48 (m, 4H), 7.46 (s, 1H), 7.43-7.37 (m, 5H), 7.35-7.29 (m, 3H), 7.24-7.21 (m, 1H), 7.19-7.16 (m, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 4.19 (d, *J* = 15.0 Hz, 1H), 4.12-4.05 (m, 1H), 3.19 (dd, *J* = 14.7, 1.2 Hz, 1H), 1.68 (dd, *J* = 7.5, 4.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.2, 149.7, 143.8, 136.1, 133.1, 132.9, 132.7, 132.5, 131.5, 130.6, 130.4, 130.2, 128.7, 128.4, 128.2, 128.1, 127.7, 127.6, 127.5, 127.3, 127.1, 127.0, 126.6,

126.1, 126.0, 125.7, 124.9, 124.6, 124.2, 122.6, 122.4, 121.8, 57.5, 48.5, 23.5; ^{31}P NMR (162 MHz, $CDCl_3$): 142.3; IR (neat): 3057, 3026, 2972, 2926, 1619, 1590, 1508, 1463, 1328, 1231, 1206, 1141, 1071, 949, 912, 823, 752, 696; $[\alpha]_{24}^{D}$ = -207.8 (*c* 1.68, $CHCl_3$); HRMS (EI): calculated for $C_{39}H_{29}NO_2P$ (*m*-H^-): 574.1936, found 574.1936.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-(1-o-tolyl-ethyl)-phosphoramidite (L14):

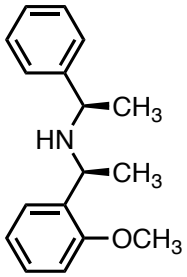


(*R*)-1-phenyl-*N*-((*S*)-1-*o*-tolylethyl)ethanamine: To a solution of 2-methylacetophenone (2.68g, 20.0 mmol, 1.0 eq), (*R)*-α-methylbenzylamine (2.42 g, 20.0 mmol, 1.0 eq) and triethylamine (6.12 mL, 44.0 mmol, 2.2 eq) in CH_2Cl_2 (100 mL) at 0 °C was added $TiCl_4$ (1.21 mL, 11.0 mmol, 0.55 eq) dropwise. The solution was warmed to room temperature and stirred overnight. Methanol (5 mL) was added and the mixture filtered through celite. The filtrate was concentrated to give the imine as a pale, yellow solid containing trace impurities by NMR. The mixture was dissolved in methanol (70 mL) and $NaBH_4$ (980 mg, 25.9 mmol, 1.5 eq) was added. The imine was completely consumed after 30 minutes. Diethyl ether (250 mL) and water (50 mL) were added. The aqueous layer was removed and the organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by column chromatography on silica gel (25% diethyl ether in petroleum ether) to give 873 mg (18% for two steps) of the (*R,S*) amine, 648 mg (14% for two steps) of the (*R,R*) amine, and additional mixed fractions for a total yield of 1.9 g (40% for two steps). (*R*)-1-phenyl-*N*-((*S*)-1-*o*-tolylethyl)ethanamine: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.41-7.08 (m, 9H), 4.00 (q, *J* = 6.4 Hz, 1H), 3.78 (q, *J* = 6.4 Hz, 1H), 2.17 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.31 (d, *J* = 6.4 Hz, 3H).



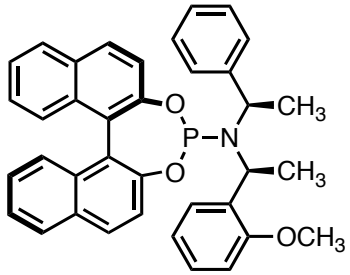
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-(1-o-tolyl-ethyl)-phosphoramidite (L14): The reaction was performed according to Procedure D with 120 mg (0.5 mmol) of (*R*)-1-phenyl-*N*-((*S*)-1-*o*-tolylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (263 mg, 95%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.03 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.78-7.76 (m, 1H), 7.65 (dd, *J* = 8.5, 0.5 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.54-7.52 (m, 2H), 7.47-7.40 (m, 3H), 7.36-7.30 (m, 4H), 7.25-7.18 (m, 4H), 7.13 (td, *J* = 7.5, 1.0 Hz, 1H), 7.01 (d, *J* = 7.0 Hz, 1H), 4.69-4.64 (m, 1H), 4.46-4.39 (m, 1H), 1.88 (s, 3H), 1.56-1.55 (m, 3H), 1.05 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.9, 149.9, 145.2, 143.2, 133.5, 132.9, 132.8, 131.4, 130.54, 130.50, 130.4, 129.6, 128.45, 128.42, 128.1, 127.4, 127.3, 126.9, 126.4, 126.1, 126.0, 125.9, 124.9, 124.4, 124.31, 124.27, 122.5, 122.1, 121.0, 54.4, 51.9, 24.1, 21.0, 18.7; ^{31}P NMR (162 MHz, $CDCl_3$): 146.7; IR (neat): 3059, 3010, 2976, 2928, 2870, 1953, 1903, 1619, 1591, 1507, 1494, 1463, 1372, 1327, 1231, 1215, 1154, 1131, 1070, 947, 821, 752; $[\alpha]_{22}^{D}$ = -66.0 (*c* 2.29, $CHCl_3$); HRMS (EI): calculated for $C_{37}H_{32}NO_2P$: 553.2171, found 553.2157.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-ethyl)-phosphoramidite (L15):



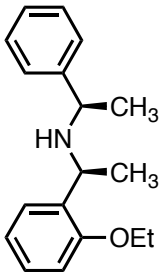
(*S*)-1-(2-methoxyphenyl)-*N*-((*R*)-1-phenylethyl)ethanamine hydrochloride: The amine was prepared according to Procedure B with 1.20 g (5.0 mmol) of (*R*)-*N*-(2-methoxybenzylidene)-1-phenylethanamine and methyl magnesium bromide (15.0 mmol). Purified by flash chromatography on silica gel (30% diethyl ether in petroleum ether) to give the product as a clear oil (1.05 g, 82%)

consisting of a 2:1 mixture of (*R,S*):(*R,R*) amines. This ratio was enhanced through additional chromatographies and pure (*R,S*) amine was obtained through recrystallization of the HCl salt. ^{1}H-NMR (400 MHz, CD_3OD): 7.49-7.37 (m, 7H), 7.09-7.05 (m, 2H), 4.52 (q, *J* = 6.8 Hz, 1H), 4.26 (q, *J* = 6.4 Hz, 1H), 3.81 (s, 3H), 1.66-1.63 (m, 6H); $[\alpha]_{22}^{D}$ = 12.7 (*c* 0.57, CH_3OH).

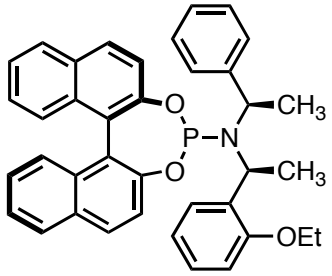


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-ethyl)-phosphoramidite (L15): The reaction was performed according to Procedure D with 146 mg (0.5 mmol) of (*S*)-1-(2-methoxyphenyl)-*N*-((*R*)-1-phenylethyl)ethanamine hydrochloride and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (20% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (79 mg, 28%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.01 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.78-7.76 (m, 1H), 7.61 (dd, *J* = 9.0, 0.5 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.51-7.49 (m, 2H), 7.46-7.39 (m, 3H), 7.36-7.28 (m, 4H), 7.25-7.18 (m, 3H), 7.10-7.07 (m, 2H), 6.77-6.76 (m, 1H), 4.73-4.63 (m, 2H), 3.58 (s, 3H), 1.60 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 155.4, 150.9, 149.9, 143.7, 135.6, 132.9, 132.7, 131.4, 130.4, 130.3, 129.4, 128.4, 128.3, 128.1, 127.6, 127.4, 127.3, 127.2, 126.7, 126.1, 125.8, 124.8, 124.4, 124.3, 122.5, 122.2, 120.9, 120.6, 110.4, 55.1, 54.4, 49.4, 23.7, 20.9; ^{31}P NMR (162 MHz, $CDCl_3$): 147.8; IR (neat): 3059, 3007, 2976, 2934, 2837, 1619, 1591, 1491, 1463, 1327, 1230, 1202, 1070, 948, 821, 751; $[\alpha]_{22}^{D}$ = -82.2 (*c* 2.00, $CHCl_3$); HRMS (EI): calculated for $C_{37}H_{32}NO_3P$: 569.2120, found 569.2101.

***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N,N′*-(*R,S*)-(1-Phenyl-ethyl)-(1-(2-Ethoxyphenyl)-ethyl)-phosphoramidite (L16):**



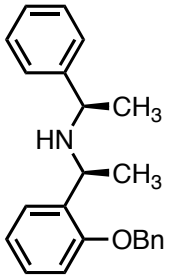
(*S*)-1-(2-ethoxyphenyl)-*N*-((*R*)-1-phenylethyl)ethanamine: The amine was prepared according to Procedure B with 1.27 g (5.0 mmol) of (*R*)-*N*-(2-ethoxybenzylidene)-1-phenylethanamine and methyl magnesium bromide (15.0 mmol). Purified by flash chromatography on silica gel (30% diethyl ether in petroleum ether) to give the product as a clear oil (966 mg, 72%) consisting of a 1.9:1 mixture of (*R,S*):(*R,R*) amines. Successive chromatographies, carefully monitoring the eluted fractions by GC gave the desired product as a clear oil (277 mg, 21%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.29-7.16 (m, 7H), 6.92 (dt, *J* = 7.2, 0.8 Hz, 1H), 6.84 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.14 (q, *J* = 6.4 Hz, 1H), 4.04-3.96 (m, 2H), 3.68 (q, *J* = 6.4 Hz, 1H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.35-1.31 (m, 6H).



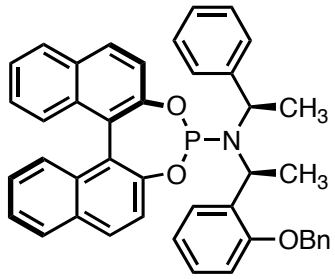
***O,O'*-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-*N,N'*-(*R,S*)-(1-Phenyl-ethyl)-(1-(2-Ethoxyphenyl)-ethyl)-phosphoramidite (L16):** The reaction was performed according to Procedure D with 135 mg (0.5 mmol) of (*S*)-1-(2-ethoxyphenyl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 0.5% triethylamine) to give the product as a white solid (232 mg, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.04 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.66-7.61 (m, 2H), 7.56-7.54 (m, 2H), 7.48-7.41 (m, 3H), 7.38-7.32 (m, 4H), 7.27-7.20 (m, 4H), 7.11 (td, *J* = 7.6, 0.8 Hz, 1H), 6.78 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.80-4.66 (m, 2H), 3.96-3.80 (m, 2H), 1.62 (dd, *J* = 7.4, 1.8 Hz, 3H), 1.18 (d, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 154.7, 150.8, 149.9, 143.5, 135.5, 132.9, 132.6, 131.3, 130.4, 130.3, 129.4, 128.3, 128.1, 128.0, 127.5, 127.4, 127.3, 127.2, 126.6, 126.0, 125.7, 124.7, 124.3, 124.2, 122.4, 122.1, 120.9, 120.4, 111.4, 63.4, 54.4, 49.5, 23.8, 20.6, 14.6; ^{31}P NMR (162 MHz, $CDCl_3$): 147.6; IR (neat): 3059, 2978, 2928, 1619, 1591, 1493, 1463, 1390, 1369, 1327,

1280, 1229, 1202, 1152, 1116, 1070, 947, 821, 750, 704; $[\alpha]_{25}^{D}$ = -44.6 (*c* 0.79, $CHCl_3$); HRMS (EI): calculated for $C_{38}H_{34}NO_3P$: 583.2276, found 583.2260.

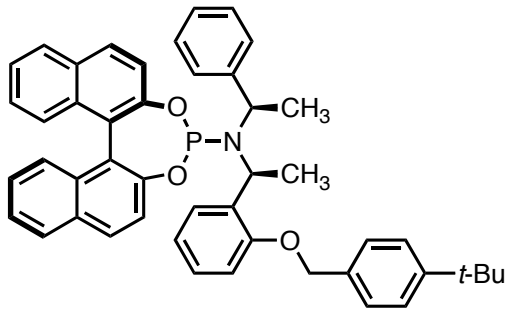
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-(1-(2-Benzyloxyphenyl)-ethyl)-phosphoramidite (L17):



(*S*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine: A solution of 2-benzyloxybenzaldehyde (5.31 g, 25.0 mmol, 1.0 eq) and (*R*)-α-methylbenzylamine (3.03 g, 25.0 mmol, 1.0 eq) were combined in toluene and stirred at 100 °C for 2 hours. The mixture was cooled to room temperature, dried over $MgSO_4$, filtered, and concentrated to give pure imine (7.81 g, 99%). A solution of imine (1.58 g, 5.0 mmol, 1.0 eq) in diethyl ether (25 mL) was cooled to 0 °C and methylmagnesium bromide (10.0 mmol, 2.0 eq) was added. The reaction was allowed to warm to room temperature and stirred for 3 hours, at which point the reaction appeared incomplete by GC. Additional Grignard reagent (15.0 mmol, 3.0 eq) was added and the reaction was allowed to stir for 24 hours. The mixture was cooled to 0 °C and quenched by slow addition of saturated aqueous ammonium chloride. Diethyl ether (25 mL) and water (25 mL) were added. The organic layer was washed with water (2 x 25 mL), dried over $MgSO_4$, and concentrated. GC analysis of the crude mixture shows a 2:1 ratio of (*R,S*):(*R,R*) amines. The diastereomers could be separated by flash chromatography on silica gel (30% diethyl ether in petroleum ether with 1% triethylamine), to give 253 mg (15%) of the (*R,R*) amine as a clear oil, 446 mg (27%) of the (*R,S*) amine as a clear oil, and 364 mg (22%) of a mixture (64% combined, isolated yield). (*S*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.27 (m, 6H), 7.24-7.17 (m, 6H), 6.97-6.90 (m, 2H), 5.03 (dd, *J* = 14.4, 11.6 Hz, 2H), 4.20 (q, *J* = 6.4 Hz, 1H), 3.72 (q, *J* = 6.8 Hz, 1H), 1.90 (br s, 1H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.31 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 156.3, 146.2, 137.1, 133.8, 128.6, 128.4, 127.9, 127.8, 127.7, 127.5, 126.8, 126.7, 121.1, 111.9, 70.0, 54.9, 50.4, 23.1, 21.8.



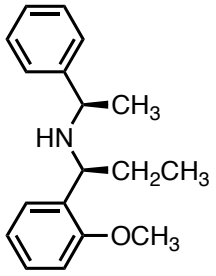
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-(1-(2-Benzyloxyphenyl)-ethyl)-phosphoramidite (L17): The reaction was performed according to Procedure D with 166 mg (0.5 mmol) of (*S*)-1-(2-(benzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (230 mg, 71%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.03 (d, *J* = 8.5 Hz, 1H), 7.94 – 7.92 (m, 2H), 7.77-7.75 (m, 1H), 7.63 (dd, *J* = 9.0, 0.7 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.51-7.49 (m, 2H), 7.44-7.40 (m, 3H), 7.37-7.30 (m, 4H), 7.25-7.16 (m, 8H), 7.13 (td, *J* = 7.5, 1.0 Hz, 1H), 7.06-7.04 (m, 2H), 6.84 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.91 (s, 2H), 4.89-4.82 (m, 1H), 4.68-4.63 (m, 1H), 1.64 (dd, *J* = 7.2, 1.7 Hz, 3H), 1.11 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 154.3, 150.9, 149.8, 143.1, 137.1, 136.1, 133.0, 132.7, 131.4, 130.5, 130.3, 129.5, 128.5, 128.4, 128.3, 128.1, 127.61, 127.56, 127.5, 127.4, 127.33, 127.30, 126.71, 126.66, 126.1, 125.8, 124.9, 124.4, 124.3, 122.5, 122.2, 121.1, 120.9, 111.9, 69.7, 54.4, 49.2, 24.3, 20.6; ^{31}P NMR (162 MHz, $CDCl_3$): 147.3; IR (neat): 3061, 3032, 2976, 2927, 2870, 1619, 1591, 1496, 1463, 1452, 1372, 1328, 1281, 1229, 1153, 1132, 1070, 1026, 947, 821, 750; $[\alpha]_{25}^{D}$ = –23.5 (*c* 1.93, $CHCl_3$).



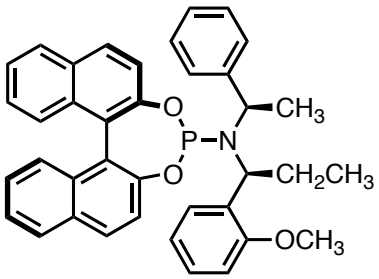
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N,N′*-(*R,S*)-(1-Phenyl-ethyl)-(1-(2-(4-tert-butylbenzyloxy)phenyl)-ethyl)-phosphoramidite (L18):** The reaction was performed according to Procedure D with 194 mg (0.5 mmol) of (*S*)-1-(2-(4-*tert*-butylbenzyloxy)phenyl)-*N*-((*R*)-1-phenylethyl)ethanamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 0.5% triethylamine) to give the product as a white solid (239 mg, 68%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.02 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.4 Hz,

2H), 7.75 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.43-7.38 (m, 3H), 7.36-7.29 (m, 4H), 7.24-7.12 (m, 7H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.85 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.91-4.81 (m, 3H), 4.69-4.63 (m, 1H), 1.64 (dd, *J* = 7.4, 1.8 Hz, 3H), 1.32 (s, 9H), 1.10 (d, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 154.3, 150.9, 150.4, 149.9, 143.0, 136.0, 134.0, 132.9, 132.6, 131.3, 130.4, 130.3, 129.4, 128.3, 128.2, 128.0, 127.5, 127.5, 127.4, 127.3, 127.2, 126.5, 126.5, 126.0, 125.7, 125.3, 124.8, 124.2, 122.4, 122.1, 120.9, 120.8, 111.9, 69.5, 54.3, 49.0, 34.5, 31.3, 24.2, 20.4; ^{31}P NMR (162 MHz, $CDCl_3$): 147.4; IR (neat): 3059, 2964, 2869, 1953, 1903, 1816, 1767, 1688, 1619, 1591, 1506, 1489, 1463, 1371, 1328, 1230, 1070, 947, 909, 820, 749, 704, 626.

O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-propyl)-phosphoramidite (L19):

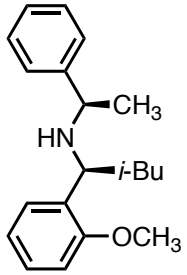


(*S*)-1-(2-methoxyphenyl)-*N*-((*R*)-1-phenylethyl)propan-1-amine: The amine was prepared according to Procedure B with 2.39 g (10.0 mmol) of (*R*)-*N*-(2-methoxybenzylidene)-1-phenylethanamine and ethylmagnesium bromide (20.0 mmol). Purified by flash chromatography on silica gel (25% diethyl ether in petroleum ether) to give the product as a clear oil (2.38 g, 88%) consisting of a 2.3:1 mixture of (*R,S*):(*R,R*) amines. Successive chromatographies, carefully monitoring the eluted fractions by GC gave the desired product as a clear oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.29-7.17 (m, 7H), 6.93 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.86 (dd, *J* = 8.8, 0.8 Hz, 1H), 3.96 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.76 (s, 3H), 3.62 (q, *J* = 6.4 Hz, 1H), 1.84-1.64 (m, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 0.79 (t, *J* = 7.2 Hz, 3H).

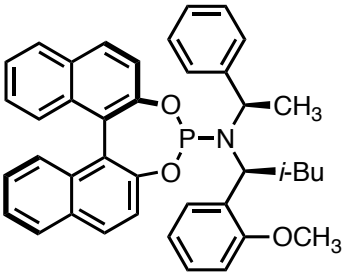


O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-propyl)-phosphoramidite (L19): The reaction was performed according to Procedure D with 67 mg (0.25 mmol) of (*S*)-1-(2-methoxyphenyl)-*N*-((*R*)-1-phenylethyl)propan-1-amine, 22 μL (0.25 mmol) of PCl_3, 174 μL (1.25 mmol) of triethylamine and 72 mg (0.25 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (55 mg, 38%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.02 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.79-7.77 (m, 2H), 7.64 (d, *J* = 9.0, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.53-7.52 (m, 2H), 7.45-7.39 (m, 3H), 7.35-7.29 (m, 5H), 7.25-7.17 (m, 3H), 7.10 (td, *J* = 7.5, 1.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.67-4.62 (m, 1H), 4.44-4.38 (m, 1H), 3.68 (s, 3H), 2.18-2.10 (m, 1H), 2.02-1.93 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.73 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): 156.3, 151.1, 150.0, 142.9, 134.4, 133.0, 132.8, 131.4, 130.5, 130.3, 129.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.3, 126.7, 126.1, 125.8, 124.8, 124.4, 124.3, 124.2, 122.5, 122.4, 120.8, 120.7, 110.5, 55.2, 54.1, 54.0, 30.8, 19.9, 11.6; ^{31}P NMR (162 MHz, $CDCl_3$): 147.2; IR (neat): 3059, 3007, 2966, 2933, 2874, 2837, 1619, 1591, 1492, 1463, 1328, 1230, 945, 821, 784, 750, 695, 626; $[\alpha]_{22}^{D}$ = –38.3 (*c* 1.14, $CHCl_3$); HRMS (EI): calculated for $C_{38}H_{34}NO_3P$: 583.2276, found 583.2248.

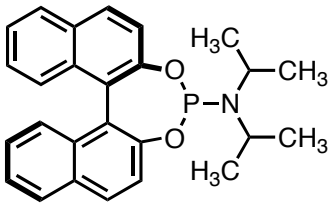
O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-isobutyl)-phosphoramidite (L20):



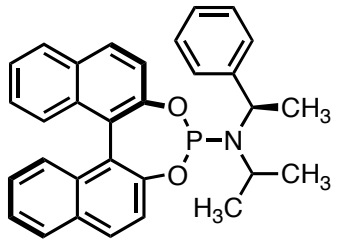
(*S*)-1-(2-methoxyphenyl)-3-methyl-*N*-((*R*)-1-phenylethyl)butan-1-amine: The amine was prepared according to Procedure B with 1.20 g (5.0 mmol) of (*R*)-*N*-(2-methoxybenzylidene)-1-phenylethanamine and isobutylmagnesium chloride (11.0 mmol). Purified by flash chromatography on silica gel (20% diethyl ether in hexanes) to give the product as a clear oil consisting of a 5:1 mixture of (*R,S*):(*R,R*) amines. Successive chromatographies, carefully monitoring the eluted fractions by GC gave the desired product as a clear oil, which was further purified by recrystallization of the HCl salt to give a yellow solid (400 mg, 24%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.28-7.16 (m, 7H), 6.92 (dt, *J* = 7.2, 1.2 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 4.14 (t, *J* = 7.2 Hz, 1H), 3.77 (s, 3H), 3.58 (q, *J* = 6.4 Hz, 1H), 1.61-1.42 (m, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 6H).



O,O′-(*R*)-1,1′-dinaphthyl-2,2′-diyl)-N,N′-(*R,S*)-(1-Phenyl-ethyl)-[1-(2-Methoxyphenyl)-isobutyl)-phosphoramidite (L20): The reaction was performed according to Procedure D with 167 mg (0.5 mmol) of (*S*)-1-(2-methoxyphenyl)-3-methyl-*N*-((*R*)-1-phenylethyl)butan-1-amine hydrochloride and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (244 mg, 80%). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.02 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.79-7.77 (m, 1H), 7.67 (d, *J* = 9.0, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.53-7.51 (m, 2H), 7.45-7.39 (m, 3H), 7.35-7.29 (m, 5H), 7.27-7.17 (m, 3H), 7.11 (t, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 4.65-4.57 (m, 2H), 3.73 (s, 3H), 1.97-1.91 (m, 2H), 1.34-1.27 (m, 1H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.63-0.61 (m, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$): 156.2, 151.1, 150.0, 142.5, 134.9, 133.0, 132.8, 131.4, 130.5, 130.3, 129.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 126.8, 126.1, 125.8, 124.8, 124.4, 124.3, 124.2, 122.5, 120.8, 110.4, 55.1, 54.1, 50.4, 48.0, 24.9, 23.3, 21.8, 19.4; ^{31}P NMR (162 MHz, $CDCl_3$): 147.3; IR (neat): 3059, 2954, 2867, 1619, 1591, 1491, 1463, 1367, 1327, 1230, 1052, 1030, 946, 821, 751, 695; $[\alpha]_{22}^{D}$ = –11.1 (*c* 2.04, $CHCl_3$); HRMS (EI): calculated for $C_{40}H_{38}NO_3P$: 611.2589, found 611.2567.

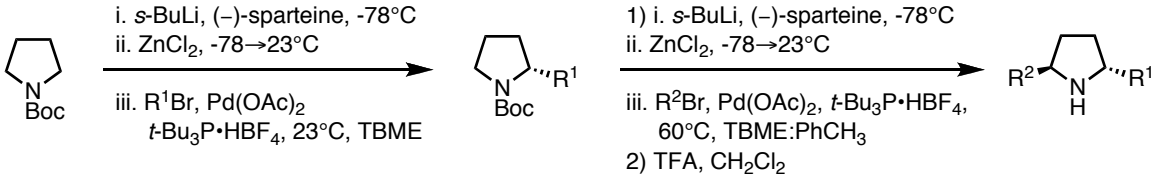


***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N,N′*-di-*iso*-propyl phosphoramidite (L23)[10]:** The reaction was performed with 0.7 mL (5.0 mmol) of diisopropylamine and 143 mg (0.5 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (115 mg, 55%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.95 (d, *J* = 8.8 Hz, 1H), 7.91-7.88 (m, 3H), 7.50 (dd, *J* = 8.8, 0.8 Hz, 1H), 7.44-7.37 (m, 4H), 7.31-7.16 (m, 3H), 3.44-3.32 (m, 2H), 1.22 (d, *J* = 6.8 Hz, 6H), 1.18 (d, *J* = 6.8 Hz, 6H); ^{31}P NMR (162 MHz, $CDCl_3$): 152.3.



***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N,N′*-(*R*)-(1-Phenyl-ethyl)-isopropyl-phosphoramidite (L24):** The reaction was performed according to Procedure D with 163 mg (1.0 mmol) of (*R*)-*N*-(1-phenylethyl)propan-2-amine and 286 mg (1.0 mmol) of (*R*)-BINOL. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (90 mg, 19%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.96 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.61-7.58 (m, 2H), 7.53 (dd, *J* = 8.8, 0.8 Hz, 1H), 7.41-7.19 (m, 10H), 4.55-4.46 (m, 1H), 3.37-3.29 (m, 1H), 1.71 (dd, *J* = 7.2, 1.2 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 150.4, 150.0, 145.7, 132.8, 132.6, 131.3, 130.4, 130.2, 130.1, 129.8, 129.4, 128.3, 128.2, 127.1, 127.0, 126.6, 125.9, 125.8, 124.7, 124.3, 124.0, 122.4, 122.2, 121.6, 53.0, 46.5, 24.7, 23.8, 23.1; ^{31}P NMR (162 MHz, $CDCl_3$): 151.4; IR (neat): 3059, 2973, 2931, 2870, 1953, 1902, 1819, 1769, 1619, 1591, 1506, 1463, 1369, 1329, 1233, 1207, 1156, 1071, 949, 908, 822, 733, 698, 626; HRMS (EI): calculated for $C_{31}H_{28}NO_2P$: 477.1828, found 477.1836.

General procedures for the synthesis of disubstituted pyrrolidines.[11]



General procedure for first arylation. A solution of *N*-Boc pyrrolidine (1.2 eq) and (–)-sparteine (1.2 eq) in *tert*-butyl methyl ether (~0.4M) was cooled to –78 °C and *s*-BuLi (1.2 eq of a solution in cyclohexane) was added dropwise over 15 minutes. The solution was stirred at this temperature for 3 hours, at which point $ZnCl_2$ (0.72 eq, 1.0M solution in diethyl ether) was added dropwise slowly over 15 minutes. The solution was stirred at –78 °C for 30 minutes and then allowed to warm to room temperature and stir for an additional 30 minutes. The appropriate aryl bromide (1.0 eq) was added followed by $Pd(OAc)_2$ (0.048 eq) and *t*-Bu_3P-HBF_4 (0.06 eq) and the solution stirred overnight at room temperature. After 12 hours aqueous ammonia (approximately 100 μl per mmol of aryl

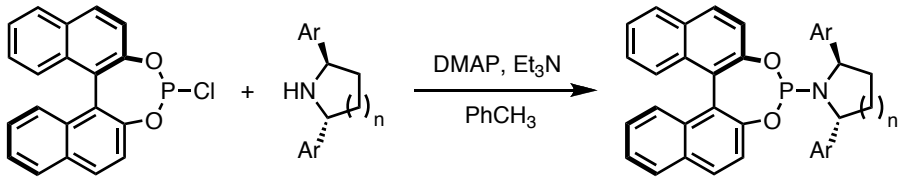
bromide) was added and the mixture stirred for one hour. At this time, the mixture was filtered through celite to remove salts and washed with *tert*-butyl methyl ether. The filtrate was washed with 1 N HCl and water, dried over $MgSO_4$, filtered, and concentrated. The product was purified by flash chromatography on silica gel (methylene chloride in petroleum ether or ethyl acetate in petroleum ether) to give the desired product. Enantiomeric excess was checked using chiral HPLC (AD column, 254 nm, 99:1 heptane: *i*-PrOH, 1.0 mL min^{-1}).

General procedure for second arylation. A solution of monosubstituted *N*-Boc pyrrolidine (1.2 eq) and (–)-sparteine (1.2 eq) in *tert*-butyl methyl ether (~0.4M) was cooled to –78 °C. Toluene (generally 10-30 vol%) was added to aid in solubility; no effect on rate or selectivity was observed. *s*-BuLi (1.2 eq of a solution in cyclohexane) was added dropwise over 15 minutes to give a strongly colored solution. The solution was stirred at this temperature for 3 hours, at which point $ZnCl_2$ (0.72 eq, 1.0M solution in diethyl ether) was added dropwise slowly over 15 minutes. The solution was stirred at –78 °C for 30 minutes and then allowed to warm to room temperature and stir for an additional 30 minutes. The appropriate aryl bromide (1.0 eq) was added followed by $Pd(OAc)_2$ (0.048 eq) and *t*-Bu_3P-HBF_4 (0.06 eq), and the solution stirred overnight at 60 °C. After 12 hours, the solution was cooled to room temperature and aqueous ammonia (approximately 100 μl per mmol of aryl bromide) was added and the mixture stirred for one hour. At this time, the mixture was filtered through celite to remove salts and washed with *tert*-butyl methyl ether. The filtrate was washed with 1 N HCl and water, dried over $MgSO_4$, filtered, and concentrated. The product was purified by flash chromatography on silica gel (ethyl acetate in petroleum ether) to give the desired product.

General procedure for TFA deprotection. A solution of *N*-Boc pyrrolidine (1.0 eq) in CH_2Cl_2 (0.1M) was cooled to 0 °C and TFA (20.0 eq) added. The mixture was stirred for 4-8 hours and then concentrated. Ethyl acetate was added, followed by 2N NaOH. If precipitate persisted, triethylamine (3-5 mL) was added. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated in vacuo to give the desired product. In cases where impurities were detected by ^{1}H-NMR, a short column (EtOAc:Pentane) was run to purify the product.

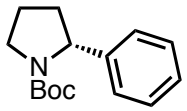
General Procedure for Ligand Synthesis. To a suspension of (*R*)-1,1'-binaphthyl-2,2'-diol (2.86 g, 10.0 mmol, 1.0 eq) in PCl_3 (14.0 mL, 160 mmol, 16 eq) was added *N*-methylpyrrolidone (3 drops). The mixture was stirred at 60 °C for 15 minutes, cooled, and carefully concentrated to give a yellow,

foamy solid. The residue was twice azeotroped with toluene (10 mL) and finally dissolved in toluene (20 mL) to make a 0.5M stock solution of chlorophosphite, which could be stored for several days at –15 °C. The intermediate was observed to be air sensitive, but the brief exposure during this procedure resulted in no more than 5% oxidation products (as judged by ^{31}P NMR), which did not effect the subsequent reaction. ^{31}P NMR (162 MHz, $CDCl_3$): 179.0.

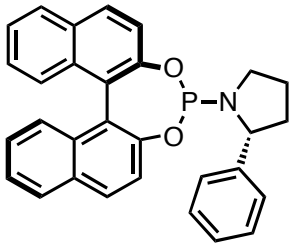


A solution of BINOL chlorophosphite (0.5 M in solution in toluene, 1.2 eq) was added dropwise to a mixture of azetidine or pyrrolidine (1.0 eq), triethylamine (5.0 eq), and DMAP (0.2 eq) in toluene (0.2M) at 0°C. The mixture was stirred overnight at room temperature and the ligand purified by column chromatography to give the product as a white solid. If the solid remained oily, it could be triturated from pentane.

***O,O'-(R)*-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R*)-2-phenylpyrrolidine) phosphoramidite (L34):**

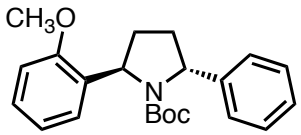


(*R*)-*tert*-butyl 2-phenylpyrrolidine-1-carboxylate (10a): The reaction was performed with 2.93 g (17.1 mmol) of *N*-Boc pyrrolidine, 3.93 mL (17.1 mmol) of (–)-sparteine, 17.1 mmol (16.3 mL of a 1.05M solution in cyclohexane) of *s*-BuLi, 10.3 mmol (10.3 mL of a 1.0M solution in diethyl ether) of $ZnCl_2$, 154 mg (0.684 mmol) of $Pd(OAc)_2$, 248 mg (0.855 mmol) of *t*-$Bu_3P{\cdot}HBF_4$, and 1.5 mL (14.25 mmol) of bromobenzene. Purified by flash chromatography on silica gel (80→90% dichloromethane in petroleum ether) to give the product as a white solid (2.70 g, 77%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.31-7.27 (m, 2H), 7.23-7.15 (m, 3H), 4.95 (s, 0.3H), 4.77-4.74 (m, 0.7H), 3.65-3.50 (m, 2H), 2.36-2.26 (m, 1H), 1.94-1.82 (m, 3H), 1.46 (s, 3H), 1.17 (s, 6H); Chiral HPLC: Chiralcel® AD column, 1% isopropanol in heptane, 1.0 mL/min, $\lambda = 230$ nm, $t_R = 7.49$ (minor), 8.88 (major).



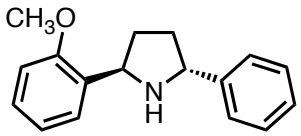
***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R*)-2-phenylpyrrolidine) phosphoramidite (L34):** The reaction was performed with 118 mg (0.8 mmol) of (*R*)-2-phenylpyrrolidine and 0.96 mmol (1.92 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (142 mg, 38%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.93 (d, *J* = 8.5 Hz, 1H), 7.90-7.88 (m, 2H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.48 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.42-7.20 (m, 12H), 4.98-4.94 (m, 1H), 3.23-3.18 (m, 1H), 2.78-2.72 (m, 1H), 2.33-2.26 (m, 1H), 1.86-1.80 (m, 1H), 1.68-1.63 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): 150.5 (d, *J* = 5.0 Hz), 149.8, 145.3, 132.7 (d, *J* = 13.0 Hz), 131.3, 130.6, 130.2, 129.7, 128.4, 128.2 (d, *J* = 9.5 Hz), 127.0, 126.8, 126.3, 126.0 (d, *J* = 4.0 Hz), 124.7, 124.5, 124.0 (d, *J* = 4.5 Hz), 122.5, 122.0, 121.9, 61.3 (d, *J* = 29.6 Hz), 46.4, 36.4 (d, *J* = 5.0 Hz), 24.4; ^{31}P NMR (162 MHz, $CDCl_3$): 152.0; IR (neat): 3059, 2969, 2872, 1953, 1742, 1619, 1590, 1506, 1463, 1431, 1327, 1232, 1067, 948, 825, 751, 699; $[\alpha]_{25}^{D}$ = –275.8 (*c* 0.5, $CHCl_3$); HRMS (EI): calculated for $C_{30}H_{24}NO_2P$: 461.1545, found 461.1556.

***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(2-methoxyphenyl)-5-phenylpyrrolidine) phosphoramidite (L35):**

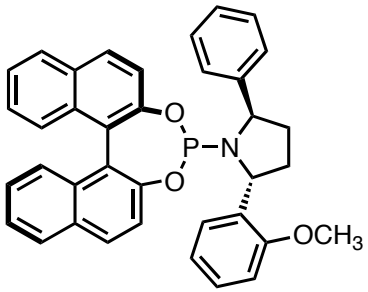


(2*R*,5*R*)-*tert*-butyl 2-(2-methoxyphenyl)-5-phenylpyrrolidine-1-carboxylate (11ab): The reaction was performed with 705 mg (2.85 mmol) of (*R*)-*tert*-butyl 2-phenylpyrrolidine-1-carboxylate, 655 μL (2.85 mmol) of (–)-sparteine, 2.85 mmol (3.35 mL of a 0.85M solution in cyclohexane) of *s*-BuLi, 1.71 mmol (1.71 mL of a 1.0M solution in diethyl ether) of $ZnCl_2$, 26 mg (0.114 mmol) of $Pd(OAc)_2$, 41 mg (0.142 mmol) of *t*-$Bu_3P{\cdot}HBF_4$, and 296 μL (2.37 mmol) of 2-bromoanisole. Purified by flash chromatography on silica gel (80/15/5 dichloromethane/petroleum ether/*tert*-butyl methyl ether) to give the product as a thick yellow oil (745 mg, 44%). Alternatively, the reaction could be performed with 84 μL (0.8 mmol) of bromobenzene and 266 mg (0.96 mmol) of (*R*)-*tert*-butyl 2-(2-methoxyphenyl)pyrrolidine-1-carboxylate to give the same product (93 mg, 33%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36-7.30 (m, 2H),

7.26-7.20 (m, 4H), 7.15-7.10 (m, 1H), 6.96-6.86 (m, 2H), 5.60 (d, *J* = 7.6 Hz, 0.5H), 5.47 (d, *J* = 7.6 Hz, 0.5H), 5.29 (d, *J* = 7.2 Hz, 0.5H), 5.12 (d, *J* = 8.0 Hz, 0.5H), 3.87 (s, 1.5H), 3.85 (s, 1.5H), 2.46-2.28 (m, 2H), 1.72-1.65 (m, 2H), 1.15-1.13 (m, 9H).



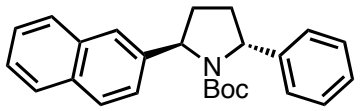
(2*R*,5*R*)-2-(2-methoxyphenyl)-5-phenylpyrrolidine (12ab): The reaction was performed with 217 mg (0.61 mmol) of (2*R*,5*R*)-*tert*-butyl 2-(2-methoxyphenyl)-5-phenylpyrrolidine-1-carboxylate. Obtained the product as a yellow oil that solidified on standing (146 mg, 94%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.49-7.46 (m, 1H), 7.44-7.41 (m, 2H), 7.37-7.32 (m, 2H), 7.26-7.20 (m, 2H), 6.98-6.94 (m, 1H), 6.88 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.83 (t, *J* = 6.8 Hz, 1H), 4.47 (t, *J* = 7.2 Hz, 1H), 3.85 (s, 3H), 2.42-2.33 (m, 2H), 1.94-1.83 (m, 2H).



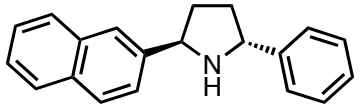
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(2-methoxyphenyl)-5-phenylpyrrolidine) phosphoramidite (L35):** The reaction was performed with 253 mg (1.0 mmol) of (2*R*,5*R*)-2-(2-methoxyphenyl)-5-phenylpyrrolidine and 1.2 mmol (2.4 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (461 mg, 81%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.84 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.60 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.46-7.39 (m, 4H), 7.36-7.29 (m, 5H), 7.24-7.22 (m, 1H), 7.18-7.16 (m, 2H), 7.15-7.10 (m, 4H), 6.78 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.92 (dd, *J* = 8.8, 0.8 Hz, 1H), 5.36 (d, *J* = 5.2 Hz, 1H), 5.15 (d, *J* = 7.2 Hz, 1H), 3.40 (s, 3H), 2.40-2.28 (m, 2H), 1.71-1.56 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 156.1, 149.5 (d, *J* = 9.8 Hz), 149.2, 146.4 (d, *J* = 6.9 Hz), 133.9, 133.9, 132.7, 132.7, 132.3 (d, *J* = 1.5 Hz), 131.2, 130.1, 129.9, 128.4, 128.2, 128.1, 127.9, 127.6, 127.6, 127.1 (d, *J* = 1.5 Hz), 127.0 (d, *J* = 2.3 Hz), 125.8, 125.3, 124.5, 124.1, 124.0, 122.0 (d, *J* = 1.5 Hz), 121.9, 121.1 (d, *J* = 3.1 Hz), 120.0, 110.3, 63.6 (d, *J* = 22.1 Hz), 55.8, 54.8, 33.1 (d, *J* = 2.3 Hz), 31.6; ^{31}P NMR (162 MHz, $CDCl_3$): 146.8; IR (neat): 3060, 3030, 2969, 2945, 2902,

2836, 1950, 1899, 1816, 1770, 1619, 1590, 1506, 1488, 1463, 1437, 1328, 1231, 1202, 1098, 1068, 947, 909, 823; $[\alpha]_{24}^{D}$ = –253.8 (*c* 0.78, $CHCl_3$); HRMS (EI): calculated for $C_{37}H_{30}NO_3P$: 567.1963, found 567.1945.

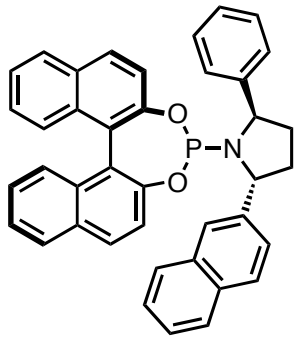
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(2-naphthyl)-5-phenylpyrrolidine) phosphoramidite (L36):**



(2*R*,5*R*)-*tert*-butyl 2-(naphthalen-2-yl)-5-phenylpyrrolidine-1-carboxylate (11ac): The reaction was performed with 492 mg (2.37 mmol) of 2-bromonaphthalene and 705 mg (2.85 mmol) of (*R*)-*tert*-butyl 2-phenylpyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (20% *tert*-butyl methyl ether in petroleum ether) to give the product as a white solid (402 mg, 45%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85-7.80 (m, 3H), 7.65 (d, *J* = 10.0 Hz, 1H), 7.50-7.33 (m, 5H), 7.29-7.23 (m, 3H), 5.47 (d, *J* = 7.6 Hz, 0.5H), 5.40 (d, *J* = 7.2 Hz, 0.5H), 5.31 (d, *J* = 7.2 Hz, 0.5H), 5.23 (d, *J* = 8.0 Hz, 0.5H), 2.56-2.44 (m, 2H), 1.82-1.74 (m, 2H), 1.15 (s, 4.5H), 1.10 (s, 4.5H).



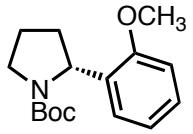
(2*R*,5*R*)-2-(naphthalen-2-yl)-5-phenylpyrrolidine (12ac): The reaction was performed with 280 mg (0.75 mmol) of (2*R*,5*R*)-*tert*-butyl 2-(naphthalen-2-yl)-5-phenylpyrrolidine-1-carboxylate. Obtained the product as a yellow oil that solidified on standing (205 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85-7.81 (m, 4H), 7.55 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.48-7.42 (m, 4H), 7.38-7.34 (m, 2H), 7.28-7.24 (m, 1H), 4.73 (t, *J* = 7.0 Hz, 1H), 4.62 (t, *J* = 7.2 Hz, 1H), 2.51-2.41 (m, 2H), 2.04-1.91 (m, 2H).



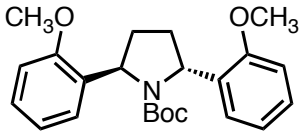
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(2-naphthyl)-5-phenylpyrrolidine) phosphoramidite**

(L36): The reaction was performed with 205 mg (0.75 mmol) of (2*R*,5*R*)-2-(naphthalen-2-yl)-5-phenylpyrrolidine and 0.9 mmol (1.8 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (363 mg, 82%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.93-7.91 (m, 1H), 7.88-7.81 (m, 5H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.58-7.51 (m, 2H), 7.45-7.28 (m, 9H), 7.22-7.16 (m, 2H), 7.13-7.12 (m, 2H), 6.87 (d, *J* = 8.4 Hz, 1H), 5.91 (dd, *J* = 8.8, 0.8 Hz, 1H), 5.28 (d, *J* = 7.2 Hz, 1H), 5.20 (d, *J* = 6.8 Hz, 1H), 2.53-2.39 (m, 2H), 1.80-1.69 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 149.5, 149.0, 145.8, 143.3, 133.4, 132.7, 132.7, 132.2, 131.2, 130.2, 129.9, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.1, 127.0, 126.9, 126.2, 125.8, 125.7, 125.4, 125.4, 125.2, 124.6, 124.0, 122.0, 120.9, 62.6, 62.5, 33.4, 33.1; ^{31}P NMR (162 MHz, $CDCl_3$): 145.8; IR (neat): 3182, 3058, 2973, 2946, 2875, 1951, 1916, 1822, 1769, 1621, 1592, 1505, 1463, 1369, 1327, 1230, 1108, 1069, 947, 908, 820, 732; $[\alpha]_{24}^{D}$ = –77.4 (*c* 0.96, $CHCl_3$); HRMS (EI): calculated for $C_{40}H_{30}NO_2P$: 587.2014, found 587.2014.

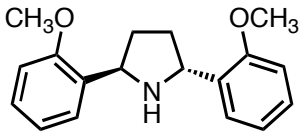
***O,O'-(R)*-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R,R*)-2,5-di(2-methoxyphenyl)pyrrolidine) phosphoramidite (L37):**



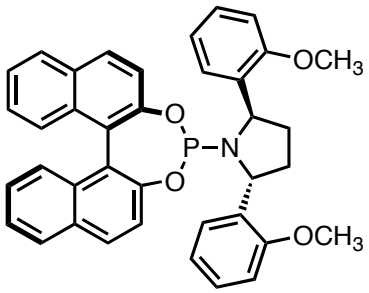
(*R*)-*tert*-butyl 2-(2-methoxyphenyl)pyrrolidine-1-carboxylate (10b): The reaction was performed with 976 mg (5.7 mmol) of *N*-Boc pyrrolidine, 1.31 mL (5.7 mmol) of (–)-sparteine, 5.7 mmol (6.7 mL of a 0.85M solution in cyclohexane) of *s*-BuLi, 3.4 mmol (3.4 mL of a 1.0M solution in diethyl ether) of $ZnCl_2$, 51 mg (0.23 mmol) of $Pd(OAc)_2$, 83 mg (0.285 mmol) of *t*-$Bu_3P{\cdot}HBF_4$, and 591 μL (4.75 mmol) of 2-bromoanisole. Purified by flash chromatography on silica gel (85/10/5 dichloromethane/petroleum ether/*tert*-butyl methyl ether) to give the product as a clear oil (1.02 g, 77%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.21-7.17 (m, 2H), 7.06-6.98 (m, 1H), 6.91-6.83 (m, 2H), 5.24 (d, *J* = 8.0 Hz, 0.3H), 5.11-5.07 (m, 0.7H), 3.83-3.81 (m, 3H), 3.66-3.54 (m, 1.5H), 3.51-3.43 (m, 0.5H), 2.31-2.18 (m, 1H), 1.86-1.75 (m, 3H), 1.46 (s, 3H), 1.18 (s, 6H); Chiral HPLC: Chiralcel® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 230 nm, t_R = 10.13 (minor), 11.97 (major).



(2*R*,5*R*)-*tert*-butyl 2,5-bis(2-methoxyphenyl)pyrrolidine-1-carboxylate (11ba): The reaction was performed with 249 μL (2.0 mmol) of 2-bromoanisole and 666 mg (2.4 mmol) of (*R*)-*tert*-butyl 2-(2-methoxyphenyl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (20% *tert*-butyl methyl ether in petroleum ether, then 85/10/5 dichloromethane/petroleum ether/*tert*-butyl methyl ether) to give the product as a white solid (280 mg, 37%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.24-7.11 (m, 4H), 6.95-6.86 (m, 4H), 5.58 (d, *J* = 7.6 Hz, 1H), 5.47 (d, *J* = 7.6 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2.36-2.24 (m, 2H), 1.68-1.62 (m, 2H), 1.15 (s, 9H).



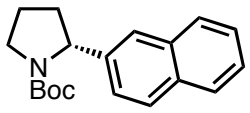
(2*R*,5*R*)-2,5-bis(2-methoxyphenyl)pyrrolidine (12ba): The reaction was performed with 230 mg (0.6 mmol) of (2*R*,5*R*)-*tert*-butyl 2,5-bis(2-methoxyphenyl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel 75% diethyl ether in petroleum ether) to give the product as a clear oil (120 mg, 71%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.50 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.22 (dt, *J* = 7.6, 1.6 Hz, 2H), 6.96 (dt, *J* = 7.6, 1.2 Hz, 2H), 6.87 (dd, *J* = 8.2, 1.0 Hz, 2H), 4.77 (t, *J* = 6.4 Hz, 2H), 3.85 (s, 6H), 2.39-2.25 (m, 3H), 1.90-1.79 (m, 2H).



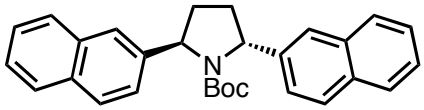
***O,O'*-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R,R*)-2,5-di(2-methoxyphenyl)pyrrolidine) phosphoramidite (L37):** The reaction was performed with 100 mg (0.35 mmol) of (2*R*,5*R*)-2,5-bis(2-methoxyphenyl)pyrrolidine and 0.42 mmol (0.84 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in petroleum ether with 1% triethylamine) to give the product as a white solid (86 mg, 41%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 3H), 7.36-7.26 (m, 5H), 7.18-7.10 (m, 7H), 6.83 (d, *J* = 8.0 Hz, 2H), 5.88 (d, *J* = 8.8 Hz, 1H), 5.47 (d, *J* = 6.8 Hz, 2H), 3.56 (s, 6H), 2.35-2.25 (m, 2H), 1.62-1.55 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): 156.2, 149.6, 149.5, 149.3, 134.4 (d, *J* = 4.5 Hz), 132.7, 132.3, 131.2, 130.0, 129.8, 128.2, 128.1, 127.9, 127.5, 127.2, 127.0, 125.8, 125.2, 124.5, 124.1, 122.1, 121.9,

121.2, 120.1, 110.3, 56.2, 55.0, 31.6; ^{31}P NMR (162 MHz, $CDCl_3$): 147.3; IR (neat): 3052, 3000, 2941, 2835, 1617, 1590, 1489, 1461, 1436, 1367, 1327, 1235, 1202, 1097, 1069, 946, 822, 795, 750; $[\alpha]_{25}^{D} = -262.1$ (c 0.29, CH_2Cl_2); HRMS (ESI): calculated for $C_{38}H_{32}NNaO_4P$ $[M+Na]^+$: 620.1967, found 620.1967.

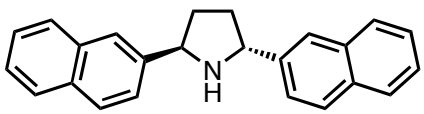
***O,O'-(R)*-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R,R*)-2,5-di(2-naphthyl)pyrrolidine) phosphoramidite (L38):**



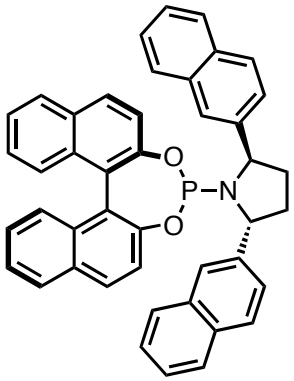
(*R*)-*tert*-butyl 2-(naphthalen-2-yl)pyrrolidine-1-carboxylate (10c): The reaction was performed with 4.9 g (28.5 mmol) of *N*-Boc pyrrolidine, 6.5 mL (28.5 mmol) of (–)-sparteine, 28.5 mmol (27.1 mL of a 1.05M solution in cyclohexane) of *s*-BuLi, 17.1 mmol (17.1 mL of a 1.0M solution in diethyl ether) of $ZnCl_2$, 256 mg (1.14 mmol) of $Pd(OAc)_2$, 413 mg (1.42 mmol) of *t*-$Bu_3P{\cdot}HBF_4$, and 4.92g (23.75 mmol) of 2-bromonaphthalene. Purified by flash chromatography on silica gel (90% dichloromethane in petroleum ether) to give the product as a white solid (5.3 g, 75%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.82-7.77 (m, 3H), 7.58 (s, 1H), 7.45 (br s, 2H), 7.31 (d, J = 8.4 Hz, 1H), 5.11 (s, 0.3H), 4.96 (s, 0.7H), 3.70-3.54 (m, 2H), 2.38 (br s, 1H), 1.99-1.87 (m, 3H), 1.50-1.43 (m, 3H), 1.14 (s, 6H); Chiral HPLC: Chiralcel® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 15.06 (major), 16.65 (minor).



(2*R*,5*R*)-*tert*-butyl 2,5-di(naphthalen-2-yl)pyrrolidine-1-carboxylate (11ca): The reaction was performed with 984 mg (4.75 mmol) of 2-bromonaphthalene and 1.70 g (5.7 mmol) of (*R*)-*tert*-butyl 2-(naphthalen-2-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in petroleum ether) to give the product as a white solid (1.01 g, 50%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.86-7.82 (m, 6H), 7.69 (d, J = 9.2 Hz, 2H), 7.52-7.38 (m, 6H), 5.56 (d, J = 7.2 Hz, 1H), 5.41 (d, J = 7.6 Hz, 1H), 2.62-2.51 (m, 2H), 1.88-1.79 (m, 2H), 1.11 (s, 9H).

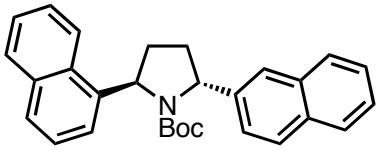


(2*R*,5*R*)-2,5-di(naphthalen-2-yl)pyrrolidine (12ca): The reaction was performed with 1.06 g (2.5 mmol) of (2*R*,5*R*)-*tert*-butyl 2,5-di(naphthalen-2-yl)pyrrolidine-1-carboxylate. Triethylamine (5 mL) was added during extraction to dissolve precipitate; this significantly increased the yield of isolated solid. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to give the product as a white solid (795 mg, 98%); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.88-7.82 (m, 8H), 7.58 (dd, *J* = 8.6, 1.6 Hz, 2H), 7.50-7.43 (m, 4H), 4.80 (t, *J* = 7.0 Hz, 2H), 2.58-2.47 (m, 2H), 2.10-2.00 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.2, 133.4, 132.6, 128.3, 127.8, 127.6, 126.0, 125.5, 125.0, 124.5, 62.5, 35.5.

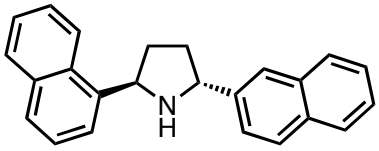


***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(2-naphthyl)pyrrolidine) phosphoramidite (L38):** The reaction was performed with 420 mg (1.30 mmol) of (2*R*,5*R*)-2,5-di(naphthalen-2-yl)pyrrolidine and 1.56 mmol (3.12 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in pentane with 1% triethylamine) to give the product as a white solid (694 mg, 84%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.94-7.80 (m, 9H), 7.57-7.52 (m, 5H), 7.43 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.32-7.28 (m, 3H), 7.23-7.09 (m, 5H), 6.59 (d, *J* = 8.8 Hz, 1H), 5.86 (dd, *J* = 8.8, 0.8 Hz, 1H), 5.38 (d, *J* = 7.2 Hz, 2H), 2.59-2.48 (m, 2H), 1.84-1.76 (m, 2H); ^{31}P NMR (162 MHz, $CDCl_3$): 145.5; ^{13}C-NMR (100 MHz, $CDCl_3$): 149.4 (d, *J* = 9.8 Hz), 149.0, 143.3 (d, *J* = 4.5 Hz), 133.4, 132.8, 132.7, 132.1, 131.2, 130.2, 129.9, 128.5, 128.2, 128.1, 128.0, 127.9, 127.7, 127.1, 126.9, 126.2, 125.8, 125.7, 125.4, 125.3, 125.2, 124.6, 124.0, 122.0, 121.9, 120.8 (d, *J* = 3.1 Hz), 62.7 (d, *J* = 12.9 Hz), 33.2; IR (neat): 3054, 3008, 2970, 2933, 2870, 1619, 1591, 1507, 1463, 1326, 1230, 1068, 946, 818, 748; $[\alpha]_{24}^{D}$ = –117.8 (c 0.34, $PhCH_3$), -1.3 (c 2.51, $CHCl_3$); HRMS (ESI): calculated for $C_{44}H_{32}NNaO_2P$ $[M+Na]^+$: 660.2068, found 660.2075.

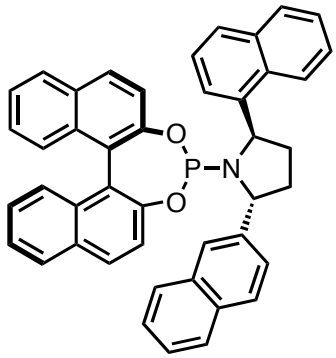
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(1-naphthyl)-5-(2-naphthyl)-pyrrolidine) phosphoramidite (L39):**



(2*R*,5*R*)-*tert*-butyl 2-(naphthalen-1-yl)-5-(naphthalen-2-yl)pyrrolidine-1-carboxylate (11cb): The reaction was performed with 661 μL (4.75 mmol) of 1-bromonaphthalene and 1.70 g (5.7 mmol) of (*R*)-*tert*-butyl 2-(naphthalen-2-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to give the product as a white solid (911 mg, 45%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.11 (d, *J* = 8.8 Hz, 1H), 7.92-7.72 (m, 6H), 7.58-7.35 (m, 7H), 6.19 (d, *J* = 8.4 Hz, 0.5H), 6.05 (d, *J* = 8.4 Hz, 0.5H), 5.56 (d, *J* = 8.4 Hz, 0.4H), 5.42 (d, *J* = 8.4 Hz, 0.6H), 2.68-2.62 (m, 1H), 2.51-2.44 (m, 1H), 1.89-1.80 (m, 2H), 1.12 (s, 5.5H), 1.07 (s, 3.5H).



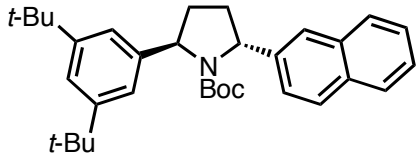
(2*R*,5*R*)-2-(naphthalen-1-yl)-5-(naphthalen-2-yl)pyrrolidine (12cb): The reaction was performed with 890 mg (2.1 mmol) of (2*R*,5*R*)-*tert*-butyl 2-(naphthalen-1-yl)-5-(naphthalen-2-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to give the product as a white solid (679 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.23 (d, *J* = 8.4 Hz, 1H), 7.91-7.83 (m, 5H), 7.78 (t, *J* = 7.6 Hz, 2H), 7.59 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.56-7.43 (m, 5H), 5.40 (t, *J* = 6.8 Hz, 1H), 4.78 (t, *J* = 7.2 Hz, 1H), 2.72-2.63 (m, 1H), 2.53-2.45 (m, 1H), 2.11-2.01 (m, 3H).



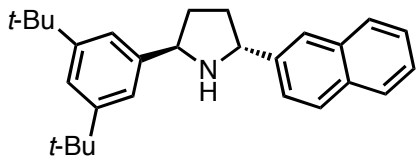
***O*,*O*′-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R*,*R*)-2-(1-naphthyl)-5-(2-naphthyl)-pyrrolidine) phosphoramidite (L39):** The reaction was performed with 404 mg (1.25 mmol) of (2*R*,5*R*)-2-(naphthalen-1-yl)-5-(naphthalen-2-yl)pyrrolidine and 1.50 mmol (3.0 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in

hexane with 1.5% triethylamine) to give the product as a white solid (616 mg, 77%). ^{1}H-NMR (400 MHz, C_6D_6): 8.01 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.82-7.75 (m, 3H), 7.62 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.55-7.37 (m, 7H), 7.30-7.24 (m, 3H), 7.13-7.11 (m, 1H), 7.07-7.01 (m, 2H), 6.97-6.88 (m, 2H), 6.81-6.77 (m, 1H), 6.35 (d, *J* = 8.8 Hz, 1H), 5.87 (d, *J* = 8.4 Hz, 1H), 5.78 (d, *J* = 7.2 Hz, 1H), 5.25 (d, *J* = 8.4 Hz, 1H), 2.35-2.25 (m, 1H), 2.16-2.06 (m, 1H), 1.43-1.34 (m, 2H); ^{13}C-NMR (100 MHz, C_6D_6): 149.9 (d, *J* = 10.4 Hz), 149.6, 144.4 (d, *J* = 8.2 Hz), 141.4, 134.4, 134.1, 133.5, 133.3, 132.7, 131.8, 131.2, 130.7, 130.4, 128.7, 128.6 (d, *J* = 2.2 Hz), 128.3, 128.1, 127.8, 127.4, 127.3, 126.6, 126.5, 126.3, 126.1, 125.9, 125.9, 125.6, 125.3, 124.8, 124.7 (d, *J* = 5.2 Hz), 124.3, 124.2, 123.6, 122.2 (d, *J* = 2.2 Hz), 122.1, 121.7, 64.7 (d, *J* = 25.3 Hz), 58.4, 33.3, 32.2; ^{31}P NMR (162 MHz, C_6D_6): 146.6; IR (neat): 3232, 3052, 2970, 2945, 2278, 1921, 1811, 1768, 1690, 1619, 1591, 1508, 1462, 1328, 1231, 1201, 1113, 1069, 946; $[\alpha]_{25}^{D}$ = –413.4 (c 1.06, $PhCH_3$); HRMS (ESI) *m*/*z* 638.2247 ($C_{44}H_{33}NO_2P$ [M+H$^+$] requires 638.2249).

***O,O'*-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R,R*)-2-(3,5-di-*tert*-butylphenyl)-5-(2-naphthyl)pyrrolidine) phosphoramidite (L40):**

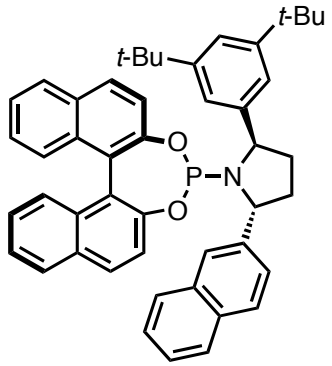


(2*R*,5*R*)-*tert*-butyl 2-(3,5-di-*tert*-butylphenyl)-5-(naphthalen-2-yl)pyrrolidine-1-carboxylate (11cc): The reaction was performed with 1.08 g (4.0 mmol) of 1-bromo-3,5-di-*tert*-butylbenzene and 1.43 g (4.8 mmol) of (*R*)-*tert*-butyl 2-(naphthalen-2-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (7% ethyl acetate in hexanes) to give the product as a white solid (1.18 g, 61%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.86-7.81 (m, 3H), 7.68-7.66 (m, 1H), 7.49-7.37 (m, 3H), 7.31-7.29 (m, 1H), 7.08-7.07 (m, 2H), 5.51-5.49 (m, 0.5H), 5.42-5.40 (m, 0.5H), 5.32-5.30 (m, 0.5H), 5.20-5.18 (m, 0.5H), 2.62-2.43 (m, 2H), 1.83-1.74 (m, 2H), 1.34 (s, 18H), 1.13 (s, 4H), 1.09 (s, 5H).



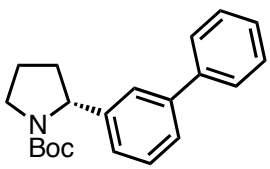
(2*R*,5*R*)-2-(3,5-di-*tert*-butylphenyl)-5-(naphthalen-2-yl)pyrrolidine (12cc): The reaction was performed with 656 mg (1.35 mmol) of (2*R*,5*R*)-*tert*-butyl 2-(3,5-di-*tert*-butylphenyl)-5-(naphthalen-2-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in

hexanes) to give the product as a white solid (450 mg, 86%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.86-7.81 (m, 4H), 7.56 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.49-7.41 (m, 2H), 7.34 (t, *J* = 2.0 Hz, 1H), 7.29-7.28 (m, 2H), 4.76 (t, *J* = 7.2 Hz, 1H), 4.61-4.58 (m, 1H), 2.53-2.40 (m, 2H), 2.04-1.94 (m, 2H), 1.35 (s, 18H).

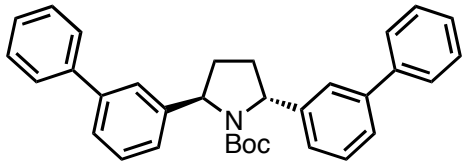


***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2-(3,5-di-*tert*-butylphenyl)-5-(2-naphthyl)pyrrolidine) phosphoramidite (L40):** The reaction was performed with 386 mg (1.0 mmol) of (2*R*,5*R*)-2-(3,5-di-*tert*-butylphenyl)-5-(naphthalen-2-yl)pyrrolidine and 1.2 mmol (2.4 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in hexanes with 1% triethylamine) to give the product as a white solid (477 mg, 68%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.92-7.90 (m, 1H), 7.85-7.80 (m, 4H), 7.57-7.52 (m, 3H), 7.42-7.38 (m, 2H), 7.33-7.23 (m, 4H), 7.19-7.15 (m, 4H), 7.11-7.10 (m, 2H), 6.78 (d, *J* = 8.8 Hz, 1H), 5.91 (dd, *J* = 8.8, 0.8 Hz, 1H), 5.30 (d, *J* = 7.6 Hz, 1H), 5.20 (d, *J* = 7.2 Hz, 1H), 2.52-2.39 (m, 2H), 1.75-1.67 (m, 2H), 1.43 (s, 18H); ^{13}C-NMR (100 MHz, $CDCl_3$): 150.6, 149.5, 149.4, 149.1, 144.7, 143.7, 137.9, 133.4, 132.7, 132.2, 131.2, 130.1, 129.8, 129.0, 128.2, 128.2, 128.1, 128.0, 127.9, 127.7, 127.1, 127.0, 126.2, 125.8, 125.6, 125.4, 125.3, 124.5, 124.1, 124.0, 122.0, 120.1, 120.8, 62.9 (d), 62.7 (d), 34,9, 33.5, 33.1, 31.7; ^{31}P NMR (162 MHz, $CDCl_3$): 146.0;
IR (neat): 3181, 3057, 2963, 2905, 2868, 1621, 1595, 1507, 1462, 1362, 1327, 1229, 1110, 1070, 966, 947, 862, 818, 750; $[\alpha]_{23}^{D}$ = –41.4 (*c* 0.90, $CHCl_3$); HRMS (ESI): calculated for $C_{48}H_{46}NNaO_2P$ $[M+Na]^+$: 722.3164, found 722.3165.

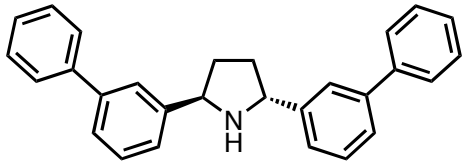
***O,O′*-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(3-biphenyl)pyrrolidine) phosphoramidite (L41):**



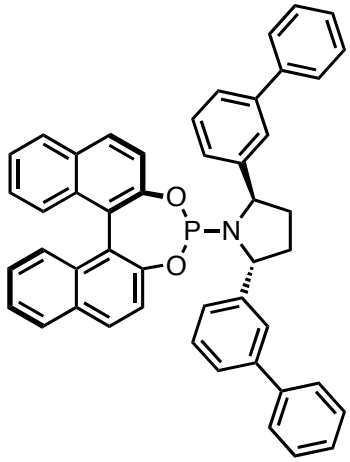
(*R*)-*tert*-butyl 2-(biphenyl-3-yl)pyrrolidine-1-carboxylate (10d): The reaction was performed with 3.33 mL (20 mmol) of 3-bromobiphenyl and 4.11 g (24 mmol) of *N*-Boc pyrrolidine. Purified by flash chromatography on silica gel (90% dichloromethane in hexanes) to give the product as a clear oil (5.59 g, 86%). ^{1}H-NMR (400 MHz, $CDCl_3$, 60 °C): 7.57-7.54 (m, 2H), 7.43-7.30 (m, 6H), 7.14 (d, J = 7.6 Hz, 1H), 4.88 (br s, 1H), 3.66-3.58 (m, 2H), 2.39-2.29 (m, 1H), 1.98-1.80 (m, 3H), 1.27 (br s, 9H).



(2*R*,5*R*)-*tert*-butyl 2,5-di(biphenyl-3-yl)pyrrolidine-1-carboxylate (11d): The reaction was performed with 792 μL (4.75 mmol) of 3-bromobiphenyl and 1.84 g (5.7 mmol) of (*R*)-*tert*-butyl 2-(biphenyl-3-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to give the product as a white solid (1.11 g, 49%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.61-7.58 (m, 4H), 7.49-7.34 (m, 12H), 7.26-7.21 (m, 2H), 5.42 (d, J = 7.0 Hz, 1H), 5.22 (d, J = 8.0 Hz, 1H), 2.58-2.48 (m, 2H), 1.82-1.79 (m, 2H), 1.17 (s, 9H).

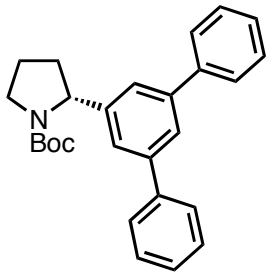


(2*R*,5*R*)-2,5-di(biphenyl-3-yl)pyrrolidine (12d): The reaction was performed with 951 mg (2.0 mmol) of (2*R*,5*R*)-*tert*-butyl 2,5-di(biphenyl-3-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (15→20% ethyl acetate in hexanes) to give the product as a yellow oil that solidified on standing (731 mg, 97%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.65-7.60 (m, 6H), 7.49-7.41 (m, 10H), 7.37-7.33 (m, 2H), 4.67-4.64 (m, 2H), 2.50-2.43 (m, 2H), 2.03-1.93 (m, 3H).



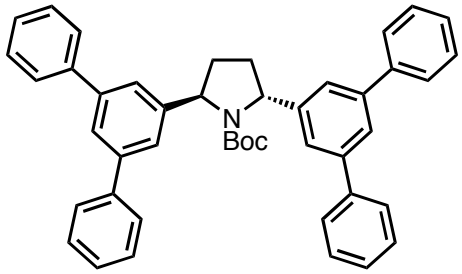
***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(3-biphenyl)pyrrolidine) phosphoramidite (L41):** The reaction was performed with 676 mg (1.8 mmol) of (2*R*,5*R*)-2,5-di(biphenyl-3-yl)pyrrolidine and 2.16 mmol (4.32 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in pentane with 1% triethylamine) to give the product as a white solid (500 mg, 40%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.81 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.65-7.60 (m, 7H), 7.52-7.46 (m, 8H), 7.40-7.37 (m, 4H), 7.34-7.30 (m, 3H), 7.21-7.18 (m, 1H), 7.13-7.05 (m, 4H), 6.01 (d, J = 9.0 Hz, 1H), 5.24 (d, J = 6.5 Hz, 2H), 2.50-2.47 (m, 2H), 1.76-1.72 (m, 2H); ^{31}P NMR (162 MHz, $CDCl_3$): 145.7; ^{13}C-NMR (125 MHz, $CDCl_3$): 149.4 (d, J = 10.1 Hz), 149.0, 146.6, 141.2 (d, J = 14.5 Hz), 132.6, 132.3, 131.2, 130.2, 129.9, 128.3, 128.2, 128.2, 127.9, 127.4, 127.2, 127.0, 125.8, 125.7, 125.4, 124.6, 124.1, 121.9, 121.9, 121.0, 62.6 (d, J = 13.0 Hz), 33.2; IR (neat): 3058, 2970, 1949, 1592, 1506, 1478, 1463, 1425, 1328, 1230, 1203, 1157, 1114, 1069, 1006, 947, 908, 822, 800; $[\alpha]_{24}^{D}$ = –118.1 (*c* 1.06, $CHCl_3$); HRMS (ESI) *m*/*z* 690.2548 ($C_{48}H_{37}NO_2P$ [M+H$^+$] requires 690.2562).

***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(5-phenylbiphenyl-3-yl)pyrrolidine) phosphoramidite (L42):**

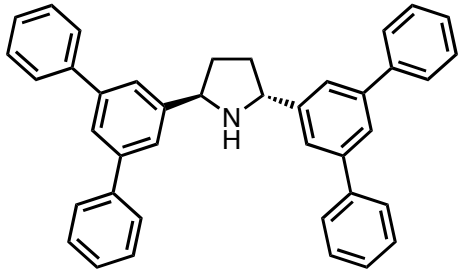


(*R*)-*tert*-butyl 2-(5-phenylbiphenyl-3-yl)pyrrolidine-1-carboxylate (10e): The reaction was performed with 4.95 g (16 mmol) of 1-bromo-3,5-diphenylbenzene and 3.29 g (19.2 mmol) of *N*-Boc

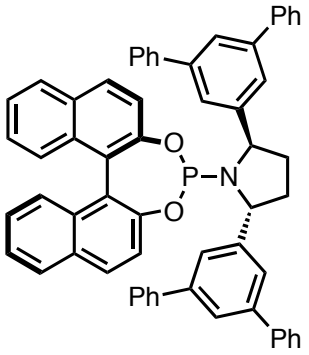
pyrrolidine. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) followed by trituration with hexanes to give the product as a white solid (4.48 g, 70%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.66-7.61 (m, 5H), 7.45 (t, *J* = 2.5 Hz, 4H), 7.38-7.36 (m, 4H), 5.14-5.08 (m, 0.3H), 4.92-4.85 (m, 0.7H), 3.73-3.52 (m, 2H), 2.45-2.31 (m, 1H), 2.01-1.86 (m, 3H), 1.50 (br s, 3H), 1.20 (br s, 6H).



(2*R*,5*R*)-*tert*-butyl 2,5-bis(5-phenylbiphenyl-3-yl)pyrrolidine-1-carboxylate (11e): The reaction was performed with 928 mg (3.0 mmol) of 1-bromo-3,5-diphenylbenzene and 1.44 g (3.6 mmol) of (*R*)-*tert*-butyl 2-(5-phenylbiphenyl-3-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) to give the product as a white solid (903 mg, 48%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (t, *J* = 1.6 Hz, 1H), 7.67-7.64 (m, 9H), 7.50-7.44 (m, 12H), 7.41-7.36 (m, 4H), 5.53 (d, *J* = 7.6 Hz, 1H), 5.31 (d, *J* = 7.6 Hz, 1H), 2.68-2.51 (m, 2H), 1.91-1.87 (m, 2H), 1.21 (s, 9H).

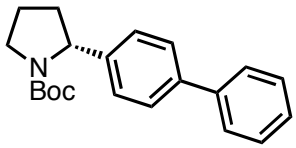


(2*R*,5*R*)-2,5-bis(5-phenylbiphenyl-3-yl)pyrrolidine (12e): The reaction was performed with 850 mg (1.35 mmol) of (2*R*,5*R*)-*tert*-butyl 2,5-bis(5-phenylbiphenyl-3-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) to give the product as a white solid (665 mg, 92%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.70-7.65 (m, 14H), 7.49-7.45 (m, 8H), 7.40-7.36 (m, 4H), 4.75 (t, *J* = 7.2 Hz, 2H), 2.56-2.51 (m, 2H), 2.07-2.03 (m, 2H).



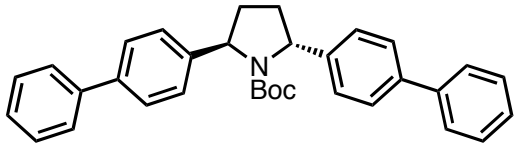
***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(5-phenylbiphenyl-3-yl)pyrrolidine) phosphoramidite (L42):** The reaction was performed with 132 mg (0.25 mmol) of (2*R*,5*R*)-2,5-bis(5-phenylbiphenyl-3-yl)pyrrolidine and 0.3 mmol (0.6 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in pentane with 1% triethylamine) to give the product as a white solid (143 mg, 68%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.84 (t, *J* = 1.5 Hz, 2H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.73-7.70 (m, 9H), 7.56-7.49 (m, 13H), 7.44-7.40 (m, 4H), 7.33-7.28 (m, 3H), 7.22-7.19 (m, 1H), 7.12-7.11 (m, 2H), 7.08 (d, *J* = 9.0 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.09 (d, *J* = 9.0 Hz, 1H), 5.38 (d, *J* = 7.0 Hz, 2H), 2.63-2.54 (m, 2H), 1.85-1.78 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): 149.3 (d, *J* = 10.0 Hz), 149.0, 147.4 (d, *J* = 4.0 Hz), 141.9, 141.1, 132.6, 132.3, 131.2, 130.3, 129.9, 128.9, 128.2, 128.1, 128.0, 127.5, 127.3, 127.0, 125.9, 125.5, 124.7, 124.6, 124.1, 124.0, 121.9, 121.8, 121.1, 62.7 (d, *J* = 13.5 Hz), 33.1; ^{31}P NMR (162 MHz, $CDCl_3$): 146.2-146.0 (m); IR (neat): 3056, 3032, 2966, 2938, 1594, 1498, 1460, 1433, 1325, 1229, 1202, 1111, 1068, 946, 877, 820, 798, 756, 696; $[\alpha]_{24}^{D}$ = –37.2 (*c* 0.39, CH_2Cl_2); HRMS (ESI) *m/z* 864.2993 ($C_{60}H_{44}NNaO_2P$ [M+Na$^+$] requires 864.3007).

***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(4-biphenyl)pyrrolidine) phosphoramidite (L43):**

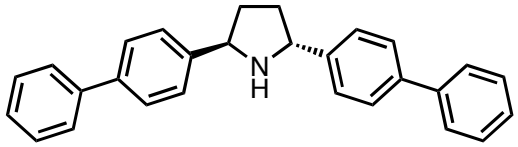


(*R*)-*tert*-butyl 2-(biphenyl-4-yl)pyrrolidine-1-carboxylate (10f): The reaction was performed with 3.32 g (14.25 mmol) of 4-bromobiphenyl and 2.93 g (17.1 mmol) of *N*-Boc pyrrolidine. Purified by flash chromatography on silica gel (90% dichloromethane in petroleum ether) to give the product as a white solid (3.80 g, 82%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.61-7.52 (m, 4H), 7.43 (t, *J* = 7.0 Hz, 2H), 7.33 (t, *J* = 6.8 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.99 (br s, 0.36H), 4.80 (br s, 0.64H), 3.65-3.54 (m, 2H), 2.35-2.32

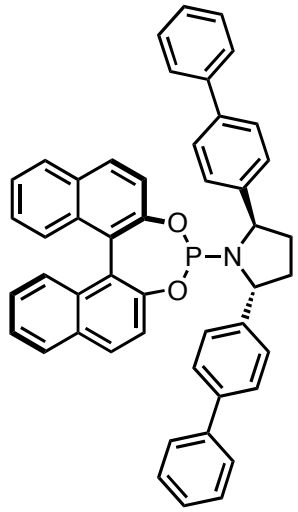
(m, 1H), 1.97-1.83 (m, 3H), 1.47 (s, 3H), 1.20 (s, 6H); Chiral HPLC: Chiralcel® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 12.11 (major), 14.05 (minor).



(2*R*,5*R*)-*tert*-butyl 2,5-di(biphenyl-4-yl)pyrrolidine-1-carboxylate (11f): The reaction was performed with 1.11 g (4.75 mmol) of 4-bromobiphenyl and 1.84 g (5.7 mmol) of (*R*)-*tert*-butyl 2-(biphenyl-4-yl)pyrrolidine-1-carboxylate. Purified by flash chromatography on silica gel (10% ethyl acetate in petroleum ether), followed by crystallization from dichloromethane:pentane to give the product as a white solid (526 mg, 23%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.64-7.56 (m, 8H), 7.47-7.41 (m, 4H), 7.37-7.30 (m, 6H), 5.39 (d, *J* = 7.6 Hz, 1H), 5.21 (d, *J* = 7.2 Hz, 1H), 2.60-2.46 (m, 2H), 1.86-1.77 (m, 2H), 1.17 (s, 9H).

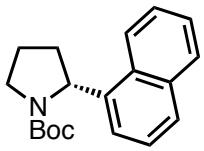


(2*R*,5*R*)-2,5-di(biphenyl-4-yl)pyrrolidine (12f): The reaction was performed with 404 mg (0.85 mmol) of (2*R*,5*R*)-*tert*-butyl 2,5-di(biphenyl-4-yl)pyrrolidine-1-carboxylate. Obtained the product as an off-white solid (315 mg, 99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.62-7.57 (m, 8H), 7.52-7.49 (m, 4H), 7.46-7.42 (m, 4H), 7.37-7.32 (m, 2H), 4.63 (t, *J* = 7.0 Hz, 2H), 2.51-2.43 (m, 2H), 2.03-1.93 (m, 2H).

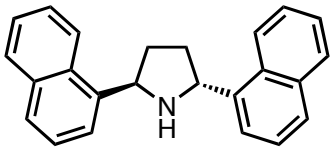


***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(4-biphenyl)pyrrolidine) phosphoramidite (L43):** The reaction was performed with 300 mg (0.8 mmol) of (2*R*,5*R*)-2,5-di(biphenyl-4-yl)pyrrolidine and 0.96 mmol (1.92 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in pentane with 1% triethylamine) to give the product as a white solid (455 mg, 82%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85-7.81 (m, 2H), 7.72-7.68 (m, 5H), 7.63 (d, *J* = 8.0 Hz, 4H), 7.53-7.49 (m, 4H), 7.42-7.38 (m, 6H), 7.34-7.11 (m, 8H), 6.12 (d, *J* = 8.8 Hz, 1H), 5.19 (d, *J* = 6.8 Hz, 1H), 2.51-2.40 (m, 2H), 1.78-1.69 (m, 2H); ^{31}P NMR (162 MHz, $CDCl_3$): 145.7; ^{13}C-NMR (100 MHz, $CDCl_3$): 149.5 (d, *J* = 9.8 Hz), 149.0, 145.0 (d, *J* = 4.6 Hz), 141.0, 139.9, 132.7, 132.2, 131.3, 130.2, 130.0, 128.9, 128.5, 128.2, 127.9, 127.3, 127.1, 127.0, 125.9, 125.4, 124.6, 124.1, 124.0, 124.0, 122.1, 121.9, 120.9, 62.2 (d, *J* = 12.9 Hz), 33.3; IR (neat): 3055, 3028, 2971, 2944, 2891, 1950, 1912, 1619, 1591, 1509, 1485, 1462, 1328, 1231, 1215, 1163, 1104, 1069, 1007, 947, 821, 763, 750, 696; $[\alpha]_{24}^{D}$ = 34.5 (*c* 2.46, $CHCl_3$); HRMS (ESI): calculated for $C_{48}H_{36}NNaO_2P$ $[M+Na]^+$: 712.2381, found 712.2385.

***O,O′-(R)*-(1,1′-dinaphthyl-2,2′-diyl)-*N*-((*R,R*)-2,5-di(1-naphthyl)pyrrolidine) phosphoramidite (L44):**

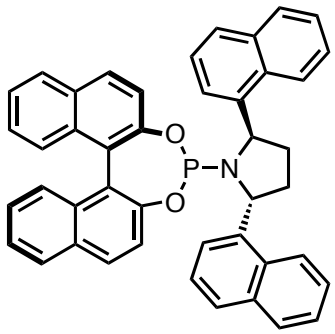


(*R*)-*tert*-butyl 2-(naphthalen-1-yl)pyrrolidine-1-carboxylate (10g): The reaction was performed with 1.98 g (14.25 mmol) of 1-bromonaphthalene and 2.93 g (17.1 mmol) of *N*-Boc pyrrolidine. Purified by flash chromatography on silica gel (90% dichloromethane in petroleum ether) to give the product as a white solid (3.52 g, 83%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.00 (d, *J* = 8.0 Hz, 1H), 7.89-7.83 (m, 1H), 7.75-7.72 (m, 1H), 7.52-7.39 (m, 3H), 7.26-7.24 (m, 1H), 5.77-5.75 (m, 0.37H), 5.61-5.60 (m, 0.63H), 3.79-3.58 (m, 2H), 2.49-2.41 (m, 1H), 1.92-1.89 (m, 3H), 1.48 (s, 3H), 1.10 (s, 6H); Chiral HPLC: Chiralcel® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 230 nm, t_R = 11.25 (major), 15.73 (minor).

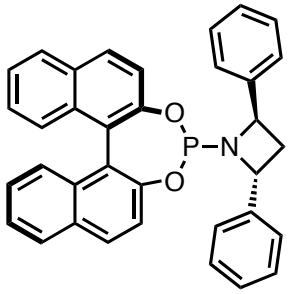


(2*R*,5*R*)-2,5-di(naphthalen-1-yl)pyrrolidine (12g): The preparation was performed in two steps. Starting with 661 μL (4.75 mmol) of 1-bromonaphthalene and 1.70g (5.7 mmol) of (*R*)-*tert*-butyl 2-

(naphthalen-1-yl)pyrrolidine-1-carboxylate (**10g**) the arylation under dilute conditions gave 500 mg of a yellow solid (**11g**) after chromatography consisting of the desired disubstituted *N*-Boc pyrrolidine and impurities. Further purification proved difficult. This material was deprotected under the conditions given in the general procedure. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to provide the desired pyrrolidine as a white solid (152 mg, 10% for 2 steps). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.24 (d, *J* = 8.8 Hz, 2H), 7.90-7.83 (m, 4H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.56-7.47 (m, 6H), 5.40 (t, *J* = 5.6 Hz, 2H), 2.67-2.56 (m, 2H), 2.17 (br s, 1H), 2.09-2.01 (m, 2H).

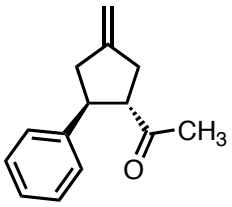


***O,O'-(R)*-(1,1'-dinaphthyl-2,2'-diyl)-*N*-((*R,R*)-2,5-di(1-naphthyl)pyrrolidine) phosphoramidite (L44):** The reaction was performed with 65 mg (0.2 mmol) of (2*R*,5*R*)-2,5-di(naphthalen-1-yl)pyrrolidine and 0.24 mmol (0.48 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on silica gel (25% dichloromethane in pentane with 1% triethylamine) to give the product as a white solid (77 mg, 60%). ^{1}H-NMR (400 MHz, $CDCl_3$): 8.07 (d, *J* = 6.8 Hz, 2H), 7.96-7.91 (m, 4H), 7.86-7.81 (m, 4H), 7.73-7.70 (m, 2H), 7.50-7.46 (m, 2H), 7.35-7.15 (m, 7H), 7.12-7.05 (m, 3H), 6.26 (d, *J* = 8.8 Hz, 1H), 6.03 (d, *J* = 6.8 Hz, 2H), 5.43 (dd, *J* = 8.8, 0.8 Hz, 1H), 2.63-2.52 (m, 2H), 1.84-1.76 (m, 2H); ^{31}P NMR (162 MHz, $CDCl_3$): 146.7; ^{13}C-NMR (100 MHz, $CDCl_3$): 149.0 (d, *J* = 10.6 Hz), 148.9, 141.3, 133.9, 132.6 (d, *J* = 1.5 Hz, 131.9 (d, *J* = 1.5 Hz), 131.3, 130.7, 130.1, 129.7, 128.7, 128.2, 127.8, 127.6, 127.0, 126.7, 126.0, 125.8, 125.6, 125.2, 125.1, 124.6, 124.5, 124.1 (d, *J* = 4.6 Hz), 123.8, 122.9, 121.9, 121.4, 120.8, 58.9, 32.2; IR (neat): 3051, 2925, 2853, 1592, 1510, 1463, 1325, 1265, 1230, 1200, 1156, 1114, 1091, 1069, 947, 821, 799, 778, 749; $[\alpha]_{24}^{D}$ = –279.0 (c 0.15, CH_2Cl_2); HRMS (ESI) *m/z* 638.2234 ($C_{44}H_{33}NO_2P$ [M+H$^+$] requires 638.2249).

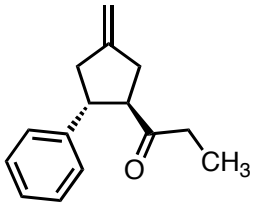


O,O′-(R)-(1,1′-dinaphthyl-2,2′-diyl)-N-((R,R)-2,5-diphenylazetidine) phosphoramidite (L45): The reaction was performed with 314 mg (1.5 mmol) of (2*R*,4*R*)-2,4-diphenylazetidine[12,13] and 1.8 mmol (3.6 mL of a 0.5M solution) of BINOL chlorophosphite. Purified by flash chromatography on deactivated alumina (15% dichloromethane in hexanes with 1% triethylamine) to give the product as a white solid (572 mg, 73%). Use of alumina was critical as extensive decomposition was observed on silica gel. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.87 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.39-7.37 (m, 4H), 7.36-7.24 (m, 10H), 7.20-7.07 (m, 4H), 6.39 (d, *J* = 9.2 Hz, 1H), 5.41 (td, *J* = 7.4, 2.0 Hz, 2H), 2.75 (td, *J* = 7.2, 2.0 Hz, 2H); ^{31}P NMR (162 MHz, $CDCl_3$): 149.6; ^{13}C-NMR (100 MHz, $CDCl_3$): 149.4, 149.3, 149.2, 132.7 (d, *J* = 1.6 Hz), 132.1 (d, *J* = 1.5 Hz), 131.3, 130.1, 130.0, 129.1, 128.6, 128.2, 128.1, 127.7, 127.3, 127.1, 126.8, 125.8, 125.3, 124.6, 124.0, 123.9, 121.9 (d, *J* = 1.5 Hz), 121.4, 121.1 (d, *J* = 2.3 Hz), 62.5 (d, *J* = 12.9 Hz), 39.1 (d, *J* = 9.1 Hz); IR (neat): 3061, 3030, 3006, 2959, 2921, 1619, 1591, 1508, 1462, 1328, 1230, 1212, 1069, 948, 820, 750, 697; $[\alpha]_{23}^{D}$ = –171.2 (c 2.44, $CHCl_3$); HRMS (ESI): calculated for $C_{35}H_{26}NNaO_2P$ $[M+Na]^+$: 546.1599, found 546.1599.

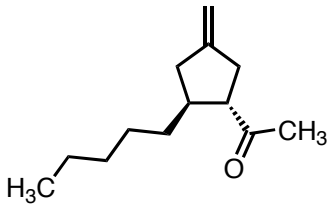
Typical Procedure for Synthesis of Methylenecyclopentanes via [3+2] Trimethylenemethane Cycloaddition Reactions with Electron Deficient Olefins. A flask containing $Pd(dba)_2$ (2.2 mg, 0.00375 mmol, 0.05 eq) and ligand (0.0075 mmol, 0.10 eq) was evacuated and purged with argon. Toluene (0.2 ml) was added and the mixture stirred for 2 minutes at room temperature. A solution of olefin (0.075 mmol, 1.0 eq) in toluene (0.3 ml) was added via cannula. 3-acetoxy–2–trimethylsilylmethyl–1-propene (25 μL, 0.12 mmol, 1.6 eq) was added and the solution was stirred at the stated temperature for 4 hours, monitored by GC for complete consumption of the olefin. The mixture was loaded directly onto a silica gel column and purified by flash chromatography on silica gel (ethyl acetate in pentane) to afford the desired product. For compounds that were obtained in multiple reactions, the conditions used are specified.



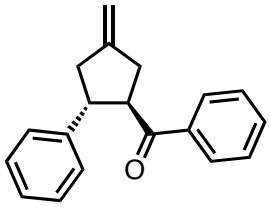
1-((1*S*,2*S*)-4-methylene-2-phenylcyclopentyl)ethanone[2] **(8a):** The reaction was performed with 43.9 mg (0.3 mmol) of benzylidene acetone, 8.6 mg (0.015 mmol) $Pd(dba)_2$, 19.1 mg (0.03 mmol) ligand **L38**, and 100 μL (0.48 mmol) donor **1**. Purified by flash chromatography on silica gel (10% ethyl acetate in pentane) to give the product as a clear oil (54.5 mg, 91%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.33-7.20 (m, 5H), 4.93 (br s, 2H), 3.32 (dq, *J* = 9.0, 2.0 Hz, 1H), 3.17 (dq, *J* = 8.8, 2.4 Hz, 1H), 2.88-2.50 (m, 4H), 1.95 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 209.8, 148.8, 143.0, 128.6, 127.2, 126.7, 106.5, 59.6, 48.8, 41.8, 36.3, 30.3; IR (neat): 3070, 2917, 1707, 1655, 1493, 1428, 1357, 1172, 877; $[\alpha]_D$ = 91.2 (c 0.69, $CHCl_3$, rotation taken on sample with 82% ee); Chiral GC: CycloSil-B column, 140 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.2 flow rate, t_R = 33.20 (major), 35.65 (minor).



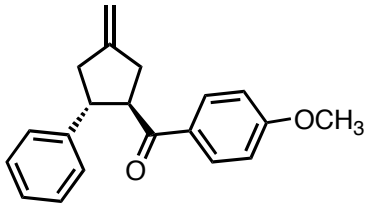
1-((1*R*,2*R*)-4-methylene-2-phenylcyclopentyl)propan-1-one (8b): The reaction was performed with 48.1 mg (0.3 mmol) of (*E*)-phenyl-penten-3-one and 16.1 mg (0.03 mmol) ligand **(*S*,*S*,*S*)-L27.** Purified by flash chromatography on silica gel to give the product as a clear oil (46.3 mg, 72%). R_f = 0.50 (20% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 4.92 (br s, 2H), 3.33 (dq, *J* = 2.4, 9.2 Hz, 1H), 3.16 (dq, *J* = 2.0, 9.2 Hz, 1H), 2.87-2.51 (m, 4H), 2.32-2.24 (m, 1H), 2.13-2.05 (m, 1H), 0.90 (t, *J* = 5.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 210.8, 149.6, 106.0, 58.3, 42.5, 38.9, 36.3, 34.8, 32.0, 29.3, 27.8, 22.6, 14.0; IR (neat): 3063, 2968, 2940, 1709, 1654, 1493, 1374, 1115, 1018; $[\alpha]_D$ = -100.6 (c 0.78, $CHCl_3$, rotation taken on sample with 83% ee); HRMS (EI): calculated for $C_{15}H_{18}O$: 214.1358, found 214.1354; Chiral GC: CycloSil-B column, 140 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.2 flow rate, t_R = 52.98 (minor), 55.78 (major).



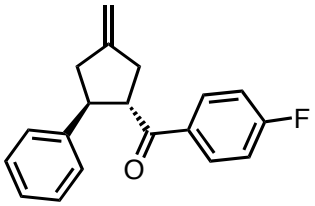
1-((1*S*,2*S*)-4-methylene-2-pentylcyclopentyl)ethanone (8c): The reaction was performed with 21.0 mg (0.15 mmol) of (*E*)-non-3-en-2-one, 4.3 mg (0.0075 mmol) $Pd(dba)_2$, 9.6 mg (0.015 mmol) ligand **L38** and 50 μL (0.24 mmol) donor **1**. Purified by flash chromatography on silica gel (4% ethyl acetate in pentane) to give the product as a clear oil (23.2 mg, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.86-4.83 (m, 2H), 2.64-2.55 (m, 3H), 2.48-2.43 (m, 1H), 2.22-2.16 (m, 4H), 2.00-1.93 (m, 1H), 1.46-1.41 (m, 1H), 1.32-1.20 (m, 7H), 0.89-0.86 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 210.8, 149.6, 106.1, 58.3, 42.5, 38.9, 36.4, 34.8, 31.9, 29.3, 27.8, 22.6, 14.0; IR (neat): 2927, 2859, 1711, 1456, 1360, 1165; $[\alpha]_{24}^{D}$ = 68.6 (c 0.57, $CHCl_3$, rotation taken on sample with 95% ee); HRMS (EI): calculated for $C_{13}H_{22}O$: 194.1671, found 194.1669; Chiral GC: CycloSil-B column, 110 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.2 flow rate, t_R = 42.67 (major), 43.79 (minor).



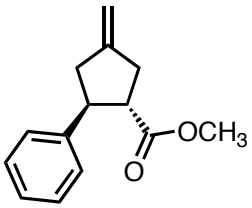
((1*R*,2*R*)-4-methylene-2-phenylcyclopentyl)(phenyl)methanone[2] (8d): The reaction was performed with 62.5 mg (0.30 mmol) of (*E*)-chalcone and 16.1 mg (0.03 mmol) ligand **(*S*,*S*,*S*)-L27.** Purified by flash chromatography on silica gel to give the product as a clear oil (65 mg, 83%). R_f = 0.70 (50% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.84-7.82 (m, 2H), 7.50-7.48 (m, 1H), 7.40-7.37 (m, 2H), 7.28-7.23 (m, 4H), 7.22-7.13 (m, 1H), 4.98 (s, 1H), 4.94 (s, 1H), 3.97 (q, *J* = 9.2 Hz, 1H), 3.73 (dq, *J* = 9.4, 1.2 Hz, 1H), 2.97-2.88 (m, 2H), 2.71-2.62 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 201.2, 149.3, 143.4, 133.0, 128.5, 128.3, 127.3, 126.5, 106.5, 54.2, 47.9, 40.8, 38.4; IR (neat): 3061, 2926, 1680, 1597, 1493, 1448, 1233; $[\alpha]_D$ = -70.6 (c 0.57, $CHCl_3$, rotation taken on sample with 80% ee); Chiral HPLC: Chiralcel® AD column, 10% isopropanol in heptane, 0.5 mL/min, λ = 254 nm, t_R = 11.18 (minor), 12.80 (major).



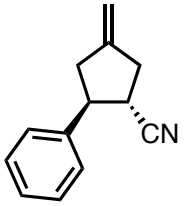
(4-methoxyphenyl)((1*R*,2*R*)-4-methylene-2-phenylcyclopentyl)methanone (8e): The reaction was performed with 71.5 mg (0.30 mmol) of (*E*)-4'-methoxychalcone and 16.1 mg (0.03 mmol) ligand **(*S*,*S*,*S*)-L27**. Purified by flash chromatography on silica gel to give the product as a clear oil (64 mg, 73%). R_f = 0.64 (50% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.83-7.79 (m, 2H), 7.27-7.21 (m, 4H), 7.16-7.12 (m, 1H), 6.86-6.82 (m, 2H), 4.97 (s, 1H), 4.93 (s, 1H), 3.96-3.89 (m, 1H), 3.81 (s, 3H), 3.74-3.67 (m, 1H), 2.96-2.85 (m, 2H), 2.70-2.62 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 199.6, 163.3, 149.4, 143.4, 130.6, 129.8, 128.4, 127.2, 126.4, 113.6, 106.3, 55.4, 53.7, 47.9, 40.9, 38.4; IR (neat): 3073, 2940, 2836, 1670, 1600, 1260, 1171, 1030; $[\alpha]_D$ = -58.28 (*c* = 0.47, $CHCl_3$, rotation taken on sample with 72% ee); HRMS (EI): calculated for $C_{20}H_{20}O_2$: 292.1463, found 292.1476; Chiral HPLC: Chiralcel® AD column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 11.24 (minor), 13.07 (major).



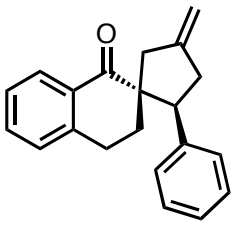
(4-fluorophenyl)((1*S*,2*S*)-4-methylene-2-phenylcyclopentyl)methanone (8f): The reaction was performed with 17.0 mg (0.075 mmol) of (*E*)-4'fluorochalcone, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (15.0 mg, 71%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.84-7.82 (m, 2H), 7.54-7.50 (m, 1H), 7.42-7.38 (m, 2H), 7.23-7.20 (m, 2H), 6.94-6.90 (m, 2H), 4.99-4.97 (m, 1H), 4.95-4.93 (m, 1H), 3.95-3.88 (m, 1H), 3.74-3.67 (m, 1H), 2.95-2.89 (m, 2H), 2.69-2.57 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 201.0, 148.9, 136.7, 133.1, 128.7, 128.6, 128.5, 128.3, 115.3, 115.2, 106.7, 54.3, 47.1, 41.0, 38.4; IR (neat): 3063, 2945, 1677, 1597, 1510, 1448, 1222, 1159, 1015; $[\alpha]_{23}^{D}$ = 88.0 (c 0.38, $CHCl_3$, rotation taken on sample with 92% ee); EA: calculated for $C_{19}H_{17}FO$: C: 81.40, H: 6.11, found C: 81.24, H: 6.31; Chiral HPLC: Chiralcel® AD column, 2% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 8.68 (major), 10.62 (minor).



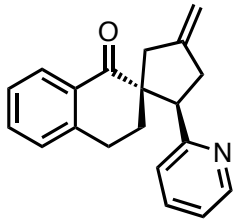
(1*S*,2*S*)-methyl 4-methylene-2-phenylcyclopentanecarboxylate[2] **(8g):** The reaction was performed with 24.3 mg (0.15 mmol) of methyl cinnamate, 4.3 mg (0.0075 mmol) $Pd(dba)_2$, 9.6 mg (0.015 mmol) ligand **L38**, and 50 μL (0.24 mmol) donor **1**. Purified by flash chromatography on silica gel (8% ethyl acetate in pentane) to give the product as a clear oil (31.4 mg, 97%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.32-7.19 (m, 5H), 4.94 (br s, 2H), 3.59 (s, 3H), 3.48-3.02 (m, 1H), 3.00-2.94 (m, 1H), 2.88-2.80 (m, 2H), 2.72-2.67 (m, 1H), 2.56-2.49 (m, 1H); Chiral GC: CycloSil-B column, 140 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.5 flow rate, t_R = 30.12 (major), 31.13 (minor).



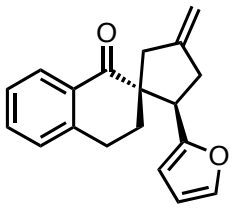
(1*S*,2*S*)-4-methylene-2-phenylcyclopentanecarbonitrile (8h): The reaction was performed with 19.4 mg (0.15 mmol) of cinnamonitrile, 4.3 mg (0.0075 mmol) $Pd(dba)_2$, 9.6 mg (0.015 mmol) ligand **L38**, and 50 μL (0.24 mmol) donor **1**. Purified by flash chromatography on silica gel (8% ethyl acetate in pentane) to give the product as a white solid (26.9 mg, 98%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38-7.34 (m, 2H), 7.31-7.26 (m, 3H), 5.04-5.00 (m, 2H), 3.43-3.35 (m, 1H), 3.01-2.94 (m, 1H), 2.91-2.84 (m, 2H), 2.80-2.73 (m, 1H), 2.62-2.54 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 145.8, 139.8, 128.8, 127.5, 126.9, 122.2, 108.3, 50.0, 39.6, 37.3, 36.4; IR (neat): 3071, 3032, 2917, 2241, 1654, 1456, 1429, 1260, 1228, 1144, 1076; mp: 86.0-88.0 °C; $[\alpha]_D$ = 113.4 (c 0.34, $CHCl_3$, rotation taken on sample with 95% ee); EA: calculated for $C_{13}H_{13}N$: C: 85.21, H: 7.15, N: 7.64, found C: 85.10, H: 7.31, N: 7.82; Chiral GC: CycloSil-B column, 140 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.5 flow rate, t_R = 46.73 (major), 48.74 (minor).



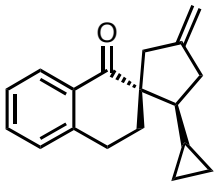
(1*R*,2*S*)-4-methylene-2-phenyl-3',4'-dihydro-1'*H*-spiro[cyclopentane-1,2'-naphthalen]-1'-one (8i): The reaction was performed with 19.4 mg (0.083 mmol) of benzylidene tetralone, 2.3 mg (0.004 mmol) $Pd(dba)_2$, 5.4 mg (0.01 mmol) diphenylpyrrolidine ligand **(*S,S,S*)-L27**, and 27 μL (0.13 mmol) donor **1**. Purified by flash chromatography on silica gel to give the product as a clear oil (22.5 mg, 94%). R_f = 0.65 (10% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 8.05 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.44-7.39 (m, 1H), 7.28-7.13 (m, 7H), 5.03 (br s, 1H), 4.98 (br s, 1H), 4.23 (m, 1H), 2.97-2.74 (m, 5H), 2.61-2.56 (m, 1H), 1.74-1.70 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 200.8, 148.5, 143.3, 140.7, 133.2, 132.2, 128.7, 128.5, 128.1, 128.0, 126.6, 126.4, 107.3, 56.5, 49.0, 41.8, 36.3, 27.5, 25.7; IR (neat): 3065, 2926, 1678, 1600, 1453, 1229; $[\alpha]_D$ = -91.9 (c 0.40, $CHCl_3$); HRMS (EI): calculated for $C_{21}H_{20}O$: 288.1514, found 288.1514; Chiral HPLC: Chiralcel® OD column, 1% isopropanol in heptane, 0.8 mL/min, λ = 254 nm, t_R = 9.27 (minor), 9.82 (major).



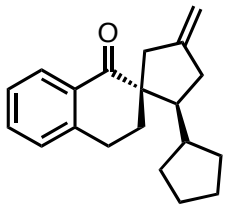
(1*R*,2*R*)-4-methylene-2-(pyridin-2-yl)-3',4'-dihydro-1'*H*-spiro[cyclopentane-1,2'-naphthalen]-1'-one (8j): The reaction was performed with 70.6 mg (0.30 mmol) of 2-pyrilidine tetralone, 8.6 mg (0.015 mmol) $Pd(dba)_2$, 24.2 mg (0.045 mmol) diphenylpyrrolidine ligand **(*S,S,S*)-L27**, and 100 μL (0.483 mmol) donor **1**. Purified by flash chromatography on silica gel to give the product as a clear oil (75.5 mg, 87%). R_f = 0.30 (30% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 8.51 (br s, 1H), 8.44-8.42 (m, 1H), 8.06-8.04 (m, 1H), 7.58-7.54 (m, 1H), 7.46-7.42 (m, 1H), 7.32-7.26 (m, 1H), 7.19-7.16 (m, 2H), 5.05 (br s, 1H), 5.01 (br s, 1H), 4.25 (t, *J* = 8.4 Hz, 1H), 3.01-2.78 (m, 4H), 2.60-2.56 (m, 1H), 1.82-1.77 (m, 1H), 1.72-1.61 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 200.2, 150.1, 148.0, 147.5, 143.1, 136.3, 136.0, 133.4, 131.9, 128.6, 128.0, 126.7, 123.1, 108.0, 56.4, 46.6, 41.4, 35.7, 27.2, 25.6; IR (neat): 3066, 2931, 1673, 1599, 1425, 1225, 1026; $[\alpha]_D$ = -88.6 (c 0.52, $CHCl_3$); HRMS (EI): calculated for $C_{20}H_{19}NO$: 289.1467, found 289.1467; Chiral HPLC: Chiralcel® AD column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 9.29 (minor), 11.31 (major).



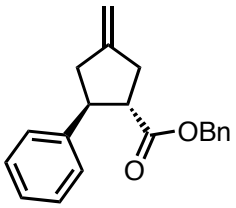
(1*R*,2*R*)-2-(furan-2-yl)-4-methylene-3',4'-dihydro-1'*H*-spiro[cyclopentane-1,2'-naphthalen]-1'-one (8k): The reaction was performed with 67.3 mg (0.30 mmol) of 2-furylidine tetralone, 8.6 mg (0.015 mmol) $Pd(dba)_2$, 24.2 mg (0.045 mmol) diphenylpyrrolidine ligand **(*S*,*S*,*S*)-L27**, and 100 μL (0.483 mmol) donor **1**. Purified by flash chromatography on silica gel to give the product as a clear oil (49.9 mg, 60%). R_f = 0.62 (5% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 8.08 (d, *J* = 6.8 Hz, 1H), 7.45-7.43 (m, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.26-7.24 (m, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.24 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.05 (d, *J* = 3.2 Hz, 1H), 5.00 (br s, 1H), 4.96 (br s, 1H), 4.21 (t, *J* = 9.2 Hz, 1H), 3.01-2.68 (m, 5H), 2.57-2.52 (m, 1H), 1.81-1.63 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 200.3, 155.2, 147.9, 143.4, 141.3, 133.2, 132.0, 128.5, 128.0, 126.6, 109.9, 107.6, 106.6, 56.2, 43.3, 41.5, 34.5, 27.5, 25.7; IR (neat): 2927, 1678, 1600, 1453, 1226; $[\alpha]_D$ = -71.6 (c 0.66, $CHCl_3$); HRMS (EI): calculated for $C_{19}H_{18}O_2$: 278.1307, found 278.1308; Chiral HPLC: Chiralcel® OD column, 1% isopropanol in heptane, 0.5 mL/min, λ = 230 nm, t_R = 19.07 (minor), 20.12 (major).



(1*R*,2*S*)-2-cyclopropyl-4-methylene-3',4'-dihydro-1'*H*-spiro[cyclopentane-1,2'-naphthalen]-1'-one (8l): The reaction was performed with 59.5 mg (0.30 mmol) of cyclopropylidene tetralone, 8.6 mg (0.015 mmol) $Pd(dba)_2$, 24.2 mg (0.045 mmol) diphenylpyrrolidine ligand **(*S*,*S*,*S*)-L27**, and 100 μL (0.483 mmol) donor **1**. Purified by flash chromatography on silica gel to give the product as a clear oil (52.9 mg, 70%). R_f = 0.74 (5% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 8.03 (d, *J* = 6.8 Hz, 1H), 7.48-7.45 (m, 1H), 7.32-7.18 (m, 2H), 4.88-4.86 (m, 2H), 3.06-2.95 (m, 2H), 2.70-2.59 (m, 2H), 2.42-2.21 (m, 4H), 2.01-1.96 (m, 1H), 0.61-0.58 (m, 1H), 0.46-0.40 (m, 1H), 0.28-0.25 (m, 1H), 0.18-0.15 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 201.8, 149.1, 143.5, 133.1, 132.5, 128.5, 127.8, 126.5, 106.8, 55.2, 49.4, 42.2, 36.7, 26.9, 25.9, 11.6, 3.9, 3.6; IR (neat): 3073, 2928, 1678, 1601, 1454, 1224; $[\alpha]_D$ = -64.1 (c 0.45, $CHCl_3$); HRMS (EI): calculated for $C_{18}H_{20}O$: 252.1514, found 252.1508; Chiral HPLC: Chiralcel® AD column, 0.5% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 8.78 (minor), 9.90 (major).

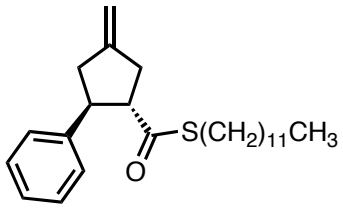


(1*R*,2*S*)-2-cyclopentyl-4-methylene-3',4'-dihydrospiro[cyclopentane-1,2'-naphthalen]-1'-one (8m): The reaction was performed with 67.9 mg (0.30 mmol) of cyclopentylidene tetralone, 8.6 mg (0.015 mmol) $Pd(dba)_2$, 24.2 mg (0.045 mmol) diphenylpyrrolidine ligand **(*S,S,S*)-L27**, and 100 μL (0.483 mmol) donor **1**. Purified by flash chromatography on silica gel to give the product as a clear oil (44.3 mg, 53%). R_f = 0.62 (10% ethyl acetate/petroleum ether); ^{1}H-NMR (400 MHz, $CDCl_3$): 8.03 (d, *J* = 6.8 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.33-7.18 (m, 2H), 4.88 (br s, 2H), 3.03-2.99 (m, 1H), 2.90-2.82 (m, 2H), 2.79-2.65 (m, 2H), 2.37-2.33 (m, 1H), 2.14-2.06 (m, 2H), 1.83-1.01 (m, 10H); ^{13}C-NMR (100 MHz, $CDCl_3$): 201.8, 149.4, 143.3, 133.1, 128.4, 127.9, 126.6, 106.7, 54.7, 50.3, 43.3, 42.5, 36.6, 32.2, 31.4, 25.6, 25.0, 24.9, 24.4; IR (neat): 3069, 2946, 2866, 1676, 1600, 1454, 1230; $[\alpha]_D$ = -33.4 (c 0.45, $CHCl_3$); HRMS (EI): calculated for $C_{20}H_{24}O$: 280.1827, found 280.1835; Chiral HPLC: Chiralcel® AD column, 0.5% isopropanol in heptane, 1.0 mL/min, λ = 230 nm, t_R = 7.37 (minor), 9.43 (major).

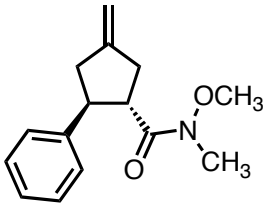


(1*S*,2*S*)-benzyl 4-methylene-2-phenylcyclopentanecarboxylate (8n): The reaction was performed with 17.9 mg (0.075 mmol) of benzyl cinnamate, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (4% ethyl acetate in pentane) to give the product as a clear oil (15.3 mg, 70%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.30-7.27 (m, 5H), 7.24-7.20 (m, 3H), 7.11-7.08 (m, 2H), 5.05 (d, *J* = 12.5 Hz, 1H), 5.00 (d, *J* = 12.5 Hz, 1H), 4.95-4.93 (m, 2H), 3.45-3.39 (m, 1H), 3.07-3.01 (m, 1H), 2.87-2.81 (m, 2H), 2.76-2.69 (m, 1H), 2.56-2.49 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 174.4, 148.5, 142.2, 135.8, 128.5, 128.4, 128.0, 127.8, 127.2, 126.7, 106.7, 66.1, 51.7, 49.4, 41.3, 37.2; IR (neat): 3065, 3031, 2951, 2849, 1949, 1871, 1792, 1657, 1603, 1496, 1455, 1432, 1386, 1352, 1261, 1172, 1158, 1009, 881, 751; $[\alpha]_{24}^{D}$ = 72.9 (c 0.32, $CHCl_3$); HRMS (ESI): calculated for $C_{20}H_{20}NaO_2$: 315.1361, found 315.1367. Enantiomeric excess was determined by

conversion to the to the corresponding methyl ester **8g** using Otera's catalyst (6 mol% catalyst, 60 equiv CH_3OH, 0.1M $PhCH_3$, 15h, 12% conversion) and chiral GC.

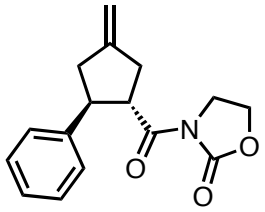


(1*S*,2*S*)-*S*-dodecyl 4-methylene-2-phenylcyclopentanecarbothioate (8o): The reaction was performed with 24.9 mg (0.075 mmol) of (*E*)-*S*-dodecyl 3-phenylprop-2-enethioate, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (3% ethyl acetate in pentane) to give the product as a clear oil (29.0 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.31-7.26 (m, 2H), 7.24-7.18 (m, 3H), 4.95-4.92 (m, 2H), 3.48 (dt, J = 10.0, 8.0 Hz, 1H), 3.20 (dt, J = 10.0, 8.0 Hz, 1H), 2.89-2.77 (m, 4H), 2.75-2.67 (m, 1H), 2.56-2.49 (m, 1H), 1.50-1.43 (m, 2H), 1.32-1.22 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 201.0, 148.4, 142.3, 128.5, 127.2, 126.7, 106.6, 60.6, 49.3, 41.3, 37.9, 31.9, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 28.8, 28.7, 22.7, 14.1; IR(neat): 3066, 3029, 2924, 2853, 1685, 1603, 1493, 1456, 1431, 1375, 1346, 1262, 1163, 1058, 1028, 881, 819, 754, 698; $[\alpha]_{25}^{D}$ = 97.9 (c 0.62, $CHCl_3$); HRMS (ESI): calculated for $C_{25}H_{38}NaOS$ $[M+Na]^+$: 409.2541, found 409.2544; Chiral HPLC: Chiralcel® OJ column, 0.3% isopropanol in heptane, 1.0 mL/min, λ = 220 nm, t_R = 5.54 (minor), 6.47 (major).

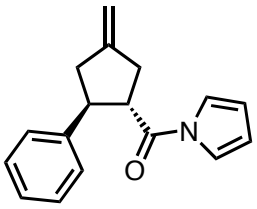


(1*S*,2*S*)-*N*-methoxy-*N*-methyl-4-methylene-2-phenylcyclopentanecarboxamide (8p): The reaction was performed with 14.3 mg (0.075 mmol) of *N*-methoxy-*N*-methylcinnamamide, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (20% ethyl acetate in pentane) to give the product as a clear oil (9.3 mg, 50%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.30-7.26 (m, 4H), 7.20-7.17 (m, 1H), 4.94 (s, 1H), 4.93 (s, 1H), 3.59-3.53 (s, 1H), 3.42-3.37 (m, 1H), 3.33 (s, 3H), 3.10 (s, 1H), 2.88 (dd, J = 17.0, 7.2 Hz, 1H), 2.77 (dd, J = 16.0, 8.0, Hz, 1H), 2.66-2.57 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): 175.1, 149.5, 143.0, 128.4, 127.3, 126.5, 106.2, 61.3, 48.6, 48.4, 40.5, 37.9, 32.1; IR (neat): 3065, 3029, 2961, 2937, 2852, 1950, 1876, 1804, 1660,

1603, 1494, 1456, 1430, 1387, 1315, 1176, 1098, 1008, 879, 759, 700; $[\alpha]_{25}^{D}$ = 70.9 (c 0.59, $CHCl_3$); HRMS (ESI): calculated for $C_{15}H_{19}NNaO_2$ $[M+Na]^+$: 268.1313, found 268.1314; Chiral GC: CycloSil-B column, 140 °C isothermal, 50:1 split ratio, 15.0 split flow, 1.2 flow rate, t_R = 109.00 (major), 112.63 (minor).

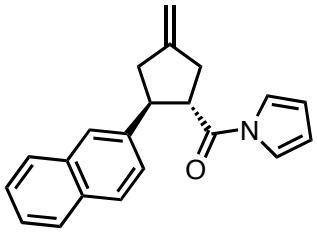


3-((1*S*,2*S*)-4-methylene-2-phenylcyclopentanecarbonyl)oxazolidin-2-one (8q): The reaction was performed with 16.3 mg (0.075 mmol) of 3-cinnamoyloxazolidin-2-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (dichloromethane:pentane 5/1) to give the product as a clear oil (19.0 mg, 94%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.30-7.27 (m, 4H), 7.23-7.18 (m, 1H), 4.95-4.94 (m, 1H), 4.92-4.91 (m, 1H), 4.37-4.22 (m, 3H), 3.98-3.85 (m, 2H), 3.67-3.60 (m, 1H), 3.08-3.02 (m, 1H), 2.88-2.81 (m, 1H), 2.62-2.47 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 174.4, 153.0, 148.3, 142.2, 128.4, 127.5, 126.6, 106.7, 61.8, 49.9, 48.3, 42.6, 41.2, 37.5; IR (neat): 3065, 3029, 2956, 2922, 2851, 1778, 1695, 1602, 1494, 1478, 1455, 1432, 1387, 1361, 1288, 1247, 1223, 1109, 1043, 972, 883, 758, 702; $[\alpha]_{23}^{D}$ = 70.0 (*c* 0.44, $CHCl_3$); HRMS (ESI): calculated for $C_{16}H_{17}NNaO_3$ $[M+Na]^+$: 294.1106, found 294.1103; Chiral HPLC: Chiralcel® OD column, 10% isopropanol in heptane, 1.0 mL/min, λ = 220 nm, t_R = 17.50 (minor), 24.75 (major).

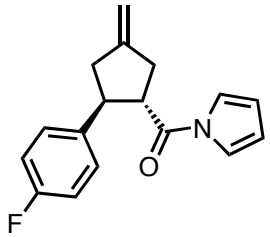


((1*S*,2*S*)-4-methylene-2-phenylcyclopentyl)(1*H*-pyrrol-1-yl)methanone (8v): The reaction was performed with 14.8 mg (0.075 mmol) of (*E*)-3-phenyl-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (15.1 mg, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.28-7.25 (m, 4H), 7.21-7.18 (m, 3H), 6.21 (t, *J* = 2.4 Hz, 2H), 5.01-5.00 (m, 1H), 4.99-4.96 (m, 1H), 3.77-3.70 (m, 1H), 3.59-3.52 (m, 1H), 2.98-2.92 (m, 2H), 2.85-2.77 (m, 1H), 2.71-2.63 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.8, 148.2, 142.3, 128.7, 127.2, 126.9,

119.0, 113.1, 107.1, 51.3, 48.5, 40.5, 38.4; IR (neat): 3149, 3074, 3030, 2950, 1709, 1655, 1493, 1467, 1409, 1292, 1117, 1074, 885; $[\alpha]_{23}^{D}$ = 86.5 (*c* 0.35, $CHCl_3$); HRMS (EI) *m*/*z* 251.1303 ($C_{17}H_{17}NO$ requires 251.1310); Chiral GC: CycloSil-B column, 150°C isothermal, 50:1 split ratio, 15.0 split flow, 1.5 flow rate, t_R = 140.63 (major), 142.04 (minor).

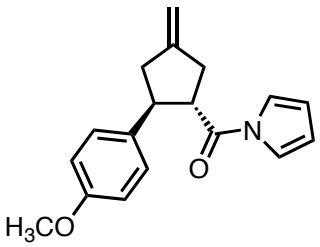


((1*S*,2*S*)-4-methylene-2-(naphthalen-2-yl)cyclopentyl)(1*H*-pyrrol-1-yl)methanone (8w): The reaction was performed with 18.5 mg (0.075 mmol) of (*E*)-3-(naphthalen-2-yl)-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (20.9 mg, 92%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.78-7.74 (m, 3H), 7.71-7.70 (m, 1H), 7.46-7.40 (m, 3H), 7.20 (br s, 2H), 6.18 (dd, *J* = 2.8, 2.4 Hz, 2H), 5.05-5.03 (m, 1H), 5.02-4.99 (m, 1H), 3.95-3.88(m, 1H), 3.71-3.64 (m, 1H), 3.05-2.96 (m, 2H), 2.89-2.73 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.8, 148.2, 139.6, 133.4, 132.4, 128.4, 127.7, 127.5, 126.1, 125.9, 125.6, 125.3, 119.0, 113.2, 107.2, 51.2, 48.5, 40.6, 38.6; IR (neat): 3148, 3106, 3055, 3023, 2982, 2950, 2924, 2843, 1710, 1656, 1601, 1508, 1467, 1410, 1367, 1291, 1250, 1116, 1074, 743; $[\alpha]_{22}^{D}$ = 63.5 (*c* 0.52, $CHCl_3$); HRMS (ESI): calculated for $C_{21}H_{19}NNaO$ $[M+Na]^+$: 324.1364, found 324.1374; Chiral HPLC: Chiralpak® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 230 nm, t_R = 14.22 (major), 15.37 (minor).

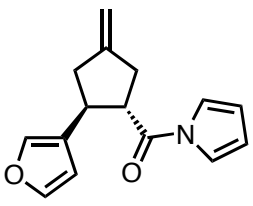


((1*S*,2*S*)-2-(4-fluorophenyl)-4-methylenecyclopentyl)(1*H*-pyrrol-1-yl)methanone (8x): The reaction was performed with 16.1 mg (0.075 mmol) of (*E*)-3-(4-fluorophenyl)-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (26.6 mg, 99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.28-7.20 (m, 4H), 6.97-6.93 (m, 2H), 6.22 (t, *J* =

2.4 Hz, 2H), 5.02-5.00 (m, 1H), 4.99-4.96 (m, 1H), 3.75-3.68 (m, 1H), 3.53-3.46 (m, 1H), 2.97-2.90 (m, 2H), 2.83-2.74 (m, 1H), 2.66-2.57 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.6, 161.7 (d, J = 243.5 Hz), 147.8, 137.8 (d, J = 3.8 Hz), 128.6 (d, J = 8.3 Hz), 119.0, 115.4 (d, J = 21.3 Hz), 113.3, 107.3, 51.5, 47.7, 40.6, 38.4; IR (neat): 3149, 3107, 3073, 2923, 2850, 1887, 1708, 1657, 1604, 1510, 1467, 1409, 1373, 1341, 1291, 1259, 1226, 1160, 1116, 1074, 887, 836, 743; $[\alpha]_{26}^{D}$ = 89.0 (c 0.54, $CHCl_3$); HRMS (ESI): calculated for $C_{17}H_{16}FNNaO$ $[M+Na]^+$: 292.1114, found 292.1121; Chiral HPLC: Chiralpak® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 220 nm, t_R = 10.98 (major), 12.09 (minor).

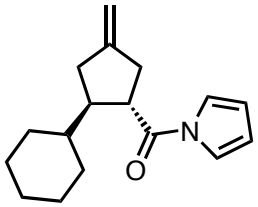


((1*S*,2*S*)-2-(4-methoxyphenyl)-4-methylenecyclopentyl)(1*H*-pyrrol-1-yl)methanone (8y): The reaction was performed with 17.0 mg (0.075 mmol) of (*E*)-3-(4-methoxyphenyl)-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (8% ethyl acetate in pentane) to give the product as a clear oil (27.3 mg, 97%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.20-7.15 (m, 4H), 6.80 (dt, J = 8.4, 2.0 Hz, 2H), 6.21 (t, J = 2.4 Hz, 2H), 5.00-4.98 (m, 1H), 4.97-4.95 (m, 1H), 3.75 (s, 3H), 3.71-3.64 (m, 1H), 3.53-3.46 (m, 1H), 2.95-2.88 (m, 2H), 2.83-2.78 (m, 1H), 2.66-2.57 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.9, 158.4, 148.3, 134.2, 128.1, 119.0, 114.0, 113.1, 107.0, 55.2, 51.5, 47.8, 40.6, 38.4; IR (neat): 3147, 2931, 2835, 1704, 1656, 1611, 1511, 1464, 1371, 1287, 1245, 1179, 1114, 1073, 1032, 885, 829, 741; $[\alpha]_{25}^{D}$ = 84.1 (c 0.58, $CHCl_3$); HRMS (ESI): calculated for $C_{18}H_{19}NNaO_2$ $[M+Na]^+$: 304.1313, found 304.1312; Chiral HPLC: Chiralpak® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 220 nm, t_R = 15.61 (major), 18.07 (minor).



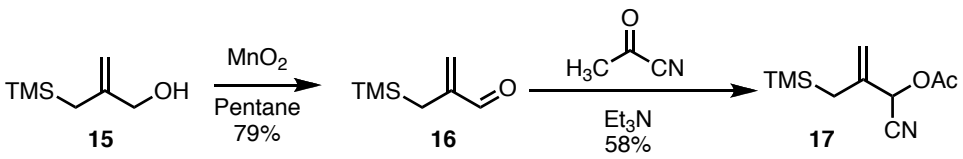
((1*S*,2*S*)-2-(furan-3-yl)-4-methylenecyclopentyl)(1*H*-pyrrol-1-yl)methanone (8z): The reaction was performed with 14.0 mg (0.075 mmol) of (*E*)-3-(furan-3-yl)-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg

(0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (24.0 mg, 99%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.33 (t, J = 1.6 Hz, 1H), 7.28-7.24 (m, 3H), 6.29-6.26 (m, 3H), 5.01-4.99 (m, 1H), 4.96-4.95 (m, 1H), 3.67-3.60 (m, 1H), 3.40 (q, J = 9.2 Hz, 1H), 2.92-2.86 (m, 2H), 2.80-2.72 (m, 1H), 2.58-2.50 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.9, 147.8, 143.3, 138.8, 126.1, 119.1, 113.3, 109.2, 107.2, 50.8, 39.3, 39.1, 38.1; IR (neat): 3147, 3107, 3074, 2951, 2922, 2848, 1708, 1655, 1500, 1466, 1409, 1369, 1291, 1250, 1116, 1073, 1024, 937, 874, 787; $[\alpha]_{25}^{D}$ = 95.7 (c 0.55, $CHCl_3$); HRMS (ESI): calculated for $C_{15}H_{15}NNaO_2$ $[M+Na]^+$: 264.1000, found 264.1010; Chiral HPLC: Chiralpak® AD column, 1% isopropanol in heptane, 1.0 mL/min, λ = 220 nm, t_R = 10.32 (minor), 11.38 (major).

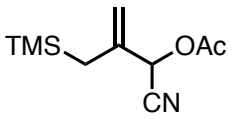


((1*S*,2*R*)-2-cyclohexyl-4-methylenecyclopentyl)(1*H*-pyrrol-1-yl)methanone (8ab): The reaction was performed with 15.2 mg (0.075 mmol) of (*E*)-3-cyclohexyl-1-(1*H*-pyrrol-1-yl)prop-2-en-1-one, 2.2 mg (0.00375 mmol) $Pd(dba)_2$, 4.8 mg (0.0075 mmol) ligand **L38**, and 25 μL (0.12 mmol) donor **1**. Purified by flash chromatography on silica gel (5% ethyl acetate in pentane) to give the product as a clear oil (25.7 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36 (br s, 2H), 6.32 (t, J = 2.4 Hz, 2H), 4.88 (s, 1H), 4.84 (s, 1H), 3.23 (q, J = 9.2 Hz, 1H), 2.81-2.75 (m, 1H), 2.69-2.63 (m, 1H), 2.59-2.46 (m, 2H), 2.21-2.13 (m, 1H), 1.72-0.84 (m, 11H); ^{13}C-NMR (100 MHz, $CDCl_3$): 173.2, 149.0, 119.1, 113.2, 106.3, 48.3, 46.7, 42.1, 39.3, 36.5, 31.9, 30.6, 26.4, 26.3, 26.3; IR (neat): 3149, 3074, 2925, 2851, 1715, 1659, 1467, 1449, 1409, 1377, 1320, 1292, 1261, 1119, 1073, 937, 880, 744; $[\alpha]_{25}^{D}$ = 76.4 (c 0.56, $CHCl_3$); HRMS (ESI): calculated for $C_{17}H_{23}NNaO$ $[M+Na]^+$: 280.1677, found 280.1680; Chiral HPLC: Chiralcel® OD-H column, 0.1% isopropanol in heptane, 0.8 mL/min, λ = 220 nm, t_R = 9.06 (major), 10.02 (minor).

Synthesis of 1-cyano-2-((trimethylsilyl)methyl)allyl acetate (17):

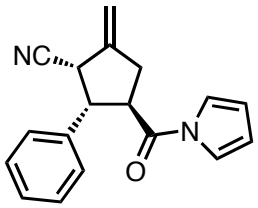


To a solution of 2-((trimethylsilyl)methyl)prop-2-en-1-ol **15** (3.0 g, 20.8 mmol) in pentane (75 ml) was added MnO_2 (30.0 g, 10 eq by weight). The suspension was stirred vigorously for 12 hours, filtered through celite, and concentrated by rotovap to give the aldehyde **16** as a clear, pale yellow volatile liquid (2.30 g, 78%). The 2-((trimethylsilyl)methyl)acrylaldehyde (2.30 g, 16.2 mmol) was combined with triethylamine (226 μL, 1.62 mmol) and the mixture cooled to 0 °C. Pyruvonitrile (1.72 mL, 24.3 mmol) was added to the mixture dropwise over 30 minutes. A slow rate of addition was very important as it directly affected the purity of the product obtained. The slurry was stirred at 23 °C for 5 minutes and loaded directly onto a silica gel column. The product was purified by flash chromatography (5% → 10% diethyl ether in hexanes) to give the donor **17** as a clear liquid (2.0 g, 58%).

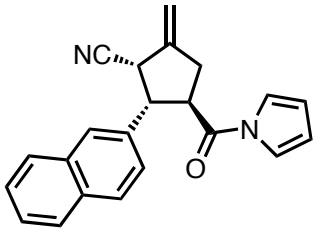


1-cyano-2-((trimethylsilyl)methyl)allyl acetate[14] (17): ^{1}H-NMR (500 MHz, $CDCl_3$) 5.70 (s, 1H), 5.30 (d, J = 1.2 Hz, 1H), 5.00 (d, J = 0.7 Hz, 1H), 2.17 (s, 3H), 1.64 (dd, J = 2.7, 1.0 Hz, 3H), 0.06 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$) 168.8, 137.6, 115.6, 114.9, 64.5, 22.3, 20.4, -1.4; IR (neat): 2956, 2899, 1758, 1642, 1422, 1372, 1250, 1213, 1164, 1047, 1024, 944, 907, 849, 771, 696.

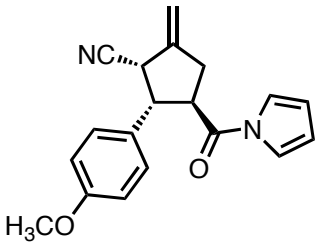
General Procedure for Synthesis of Substituted Methylenecyclopentanes via [3+2] Cycloaddition Reactions of α,β-Unsaturated Acylpyrroles with Nitrile TMM Donor. A flask containing $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.05 eq), 2-naphthyl pyrrolidine phosphoramidite **L38** (6.4 mg, 0.01 mmol, 0.10 eq), and acylpyrrole (0.1 mmol, 1.0 eq) was evacuated and purged with argon. Toluene (0.5 ml) was added and the mixture stirred for 5 minutes at room temperature. Nitrile TMM donor **17** (35 μL, 0.15 mmol, 1.5 eq) was added and the solution was stirred at the stated temperature for 2-4 hours. The mixture was loaded directly onto a silica gel column and purified by flash chromatography on silica gel (ethyl acetate in hexanes) to afford the desired product. All materials were obtained diastereomerically pure.



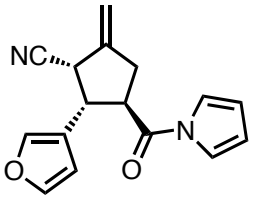
(1*S*,2*R*,3*R*)-5-methylene-2-phenyl-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23a): The reaction was performed with 14.8 mg (0.075 mmol) of acylpyrrole and 28 μL (0.12 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (20% ethyl acetate in hexanes) to give the product as a clear oil (18.0 mg, 87%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38-7.26 (m, 7H), 6.31 (dd, J = 2.8, 2.0 Hz, 2H), 5.44-5.42 (m, 1H), 5.32 (q, J = 2.0 Hz, 1H), 4.09-4.07 (m, 1H), 4.01-3.98 (m, 1H), 3.92-3.86 (m, 1H), 3.17-3.09 (m, 1H), 2.95-2.87 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.8, 143.3, 137.7, 129.0, 128.2, 127.8, 119.1, 118.0, 113.9, 112.2, 50.1, 47.6, 41.2, 35.6; IR (neat): 3147, 3032, 2925, 2853, 2242, 1711, 1664, 1604, 1469, 1411, 1285, 1122, 1076, 912; $[\alpha]_{25}^{D}$ = 12.0 (c 0.95, $CHCl_3$); HRMS (ESI): calculated for $C_{18}H_{16}N_2NaO$ $[M+Na]^+$: 299.1160, found 299.1168; Chiral HPLC: Chiralpak® IC column, 10% isopropanol in heptane, 1.0 mL/min, λ = 240 nm, t_R = 15.52 (major), 29.11 (minor).



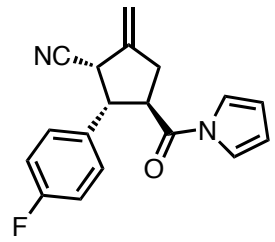
(1*S*,2*R*,3*R*)-5-methylene-2-(naphthalen-2-yl)-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23b): The reaction was performed with 18.5 mg (0.075 mmol) of acylpyrrole and 28 μL (0.12 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) to give the product as a white solid (20.6 mg, 84%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.86-7.79 (m, 3H), 7.73 (d, J = 1.6 Hz, 1H), 7.50-7.45 (m, 2H), 7.41 (dd, J = 8.8, 2.0 Hz, 1H), 7.30-7.25 (m, 2H), 6.30 (dd, J = 2.8, 2.0 Hz, 2H), 5.47-5.45 (m, 1H), 5.36-5.34 (m, 1H), 4.19-4.13 (m, 2H), 4.02-3.97 (m, 1H), 3.22-3.15 (m, 1H), 2.99-2.92 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.8, 143.4, 135.1, 133.2, 133.0, 128.9, 128.0, 127.7, 126.9, 126.5, 126.3, 125.4, 119.1, 118.0, 114.0, 112.3, 50.2, 47.7, 41.2, 35.7; IR (neat): 3147, 3057, 2925, 2853, 2239, 1708, 1663, 1601, 1469, 1411, 1362, 1322, 1286, 1122, 1075, 907; $[\alpha]_{25}^{D}$ = 11.5 (c 0.54, $CHCl_3$); HRMS (ESI): calculated for $C_{22}H_{18}N_2NaO$ $[M+Na]^+$: 349.1317, found 349.1316; Chiral HPLC: Chiralpak® IA column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 10.59 (minor), 16.08 (major).



(1*S*,2*R*,3*R*)-2-(4-methoxyphenyl)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23c): The reaction was performed with 17.0 mg (0.075 mmol) of acylpyrrole and 28 μL (0.12 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (20% ethyl acetate in hexanes) to give the product as a clear oil (18.4 mg, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.29-7.24 (m, 2H), 7.21 (dt, *J* = 8.8, 2.7 Hz, 2H), 6.88 (dt, *J* = 6.8, 2.4 Hz, 2H), 6.31 (dd, *J* = 2.8, 2.0 Hz, 2H), 5.41 (q, *J* = 2.0 Hz, 1H), 5.30 (q, *J* = 2.0 Hz, 1H), 4.05-4.01 (m, 1H), 3.96-3.92 (m, 1H), 3.87-3.82 (m, 1H), 3.79 (s, 3H), 3.14-3.06 (m, 1H), 2.94-2.86 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.9, 159.3, 143.4, 129.7, 128.9, 119.1, 118.2, 114.3, 113.9, 112.1, 55.2, 49.5, 47.8, 41.4, 35.5; IR (neat): 3147, 2931, 2838, 2242, 1710, 1612, 1515, 1469, 1286, 1251, 1182, 1121, 1033, 910; $[\alpha]_{25}^{D}$ = -1.4 (c 1.28, $CHCl_3$); HRMS (ESI): calculated for $C_{19}H_{18}N_2NaO_2$ $[M+Na]^+$: 329.1266, found 329.1273; Chiral HPLC: Chiralpak® IA column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 10.99 (minor), 17.18 (major).

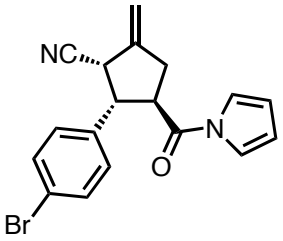


(1*S*,2*R*,3*R*)-2-(furan-3-yl)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23d): The reaction was performed with 14.0 mg (0.075 mmol) of acylpyrrole and 28 μL (0.12 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (20% ethyl acetate in hexanes) to give the product as a clear oil (19.6 mg, 98%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.43-7.40 (m, 2H), 7.31-7.26 (m, 2H), 6.43-6.42 (m, 1H), 6.33 (dd, *J* = 2.8, 2.4 Hz, 2H), 5.43 (q, *J* = 2.0 Hz, 1H), 5.29 (q, *J* = 2.0 Hz, 1H), 4.02-3.99 (m, 1H), 3.93-3.89 (m, 1H), 3.74-3.68 (m, 1H), 3.11-3.03 (m, 1H), 2.90-2.83 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.7, 143.8, 143.0, 140.0, 120.0, 119.1, 118.2, 114.0, 112.4, 109.5, 47.9, 41.5, 40.7, 35.1; IR (neat): 3146, 2925, 2243, 1710, 1606, 1503, 1469, 1411, 1369, 1286, 1122, 1076, 1024, 907, 875; $[\alpha]_{24}^{D}$ = 6.9 (c 0.86, $CHCl_3$); HRMS (ESI): calculated for $C_{16}H_{14}N_2NaO_2$ $[M+Na]^+$: 289.0953, found 289.0948; Chiral HPLC: Chiralpak® IA column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 9.63 (minor), 14.92 (major).



(1*S*,2*R*,3*R*)-2-(4-fluorophenyl)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile

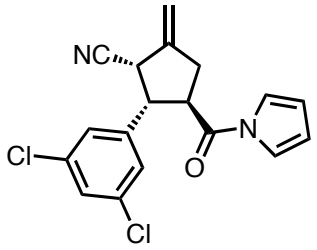
(23e): The reaction was performed with 16.1 mg (0.075 mmol) of acylpyrrole and 28 μL (0.12 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (20% ethyl acetate in hexanes) to give the product as a clear oil (21.1 mg, 96%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.29-7.24 (m, 4H), 7.05 (dt, *J* = 8.8, 2.0 Hz, 2H), 6.32 (t, *J* = 2.4 Hz, 2H), 5.43 (q, *J* = 2.0 Hz, 1H), 5.32 (q, *J* = 2.0 Hz, 1H), 4.07-4.04 (m, 1H), 4.01-3.97 (m, 1H), 3.87-3.81 (m, 1H), 3.16-3.08 (m, 1H), 2.93-2.86 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.5, 162.4 (d, *J* = 246 Hz), 143.0, 133.4 (d, *J* = 3.7 Hz), 129.5 (d, *J* = 8.2 Hz), 119.1, 117.9, 116.0 (d, *J* = 21.5 Hz), 114.0, 112.5, 49.3, 47.7, 41.2, 35.6; IR (neat): 3147, 2925, 2242, 1710, 1606, 1512, 1469, 1410, 1285, 1229, 1162, 1122, 1076, 909; $[\alpha]_{25}^{D}$ = 11.5 (c 1.28, $CHCl_3$); HRMS (ESI): calculated for $C_{18}H_{15}FN_2NaO$ $[M+Na]^+$: 317.1066, found 317.1056; Chiral HPLC: Chiralpak® IA column, 10% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 9.66 (minor), 14.73 (major).



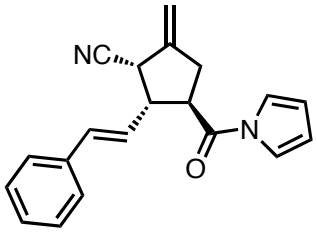
(1*S*,2*R*,3*R*)-2-(4-bromophenyl)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile

(23f): The reaction was performed with 27.6 mg (0.1 mmol) of acylpyrrole and 35 μL (0.15 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) to give the product as a white solid (35.5 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.49 (dd, *J* = 8.8, 2.4 Hz, 2H), 7.30-7.22 (m, 2H), 7.19-7.15 (m, 2H), 6.32 (dd, *J* = 2.8, 2.4 Hz, 2H), 5.44-5.42 (m, 1H), 5.33-5.31 (m, 1H), 4.07-4.05 (m, 1H), 3.99-3.95 (m, 1H), 3.86-3.81 (m, 1H), 3.15-3.08 (m, 1H), 2.93-2.85 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.4, 142.9, 136.6, 132.2, 129.5, 122.3, 119.1, 117.8, 114.1, 112.6, 49.4, 47.5, 41.0, 35.6; IR (neat): 2961, 2916, 2849, 2243, 1704, 1665, 1467, 1261, 1070, 901, 800; $[\alpha]_{26}^{D}$ = 3.9 (c 0.41, $CHCl_3$); HRMS (ESI): calculated for $C_{18}H_{15}BrN_2NaO$ $[M+Na]^+$: 377.0265, found 377.0255; Chiral HPLC:

Chiralpak® IA column, 5% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 16.25 (minor), 29.06 (major).

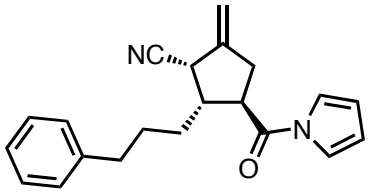


(1*S*,2*R*,3*R*)-2-(3,5-dichlorophenyl)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23g): The reaction was performed with 26.6 mg (0.1 mmol) of acylpyrrole and 35 μL (0.15 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) to give the product as an oily solid (31.0 mg, 90%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.33 (t, *J* = 2.0 Hz, 1H), 7.30-7.22 (br s, 2H), 7.18 (dd, *J* = 2.0, 0.8 Hz, 2H), 6.35 (dd, *J* = 2.4, 2.0 Hz, 2H), 5.47-5.45 (m, 1H), 5.35 (q, *J* = 2.0 Hz, 1H), 4.09-4.05 (m, 1H), 3.98 (dd, *J* = 8.0, 6.4 Hz, 1H), 3.85-3.79 (m, 1H), 3.20-3.12 (m, 1H), 2.90-2.83 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 170.1, 142.3, 141.0, 135.6, 128.6, 126.4, 119.1, 117.4, 114.3, 113.1, 49.0, 47.3, 41.0, 35.7; IR (neat): 3148, 3080, 3017, 2927, 2854, 2243, 1709, 1589, 1567, 1469, 1435, 1370, 1335, 1287, 1121, 1075, 918, 860, 799, 745, 707; $[\alpha]_{24}^{D}$ = 13.6 (c 0.39, $CHCl_3$); HRMS (ESI): calculated for $C_{18}H_{14}Cl_2N_2NaO_2$ $[M+Na]^+$: 367.0381, found 367.0385; Chiral HPLC: Chiralpak® IA column, 5% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 11.08 (minor), 13.27 (major).

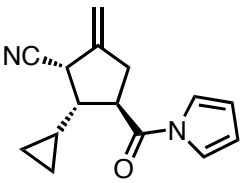


(1*S*,2*R*,3*R*)-5-methylene-3-(1*H*-pyrrole-1-carbonyl)-2-styrylcyclopentanecarbonitrile (23h): The reaction was performed with 22.3 mg (0.1 mmol) of acylpyrrole and 35 μL (0.15 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) to give the product as a white solid (19.0 mg, 63%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.37-7.35 (m, 2H), 7.32-7.28 (m, 4H), 7.26-7.23 (m, 1H), 6.63 (d, *J* = 15.5 Hz, 1H), 6.32 (dd, *J* = 2.5, 2.0 Hz, 2H), 6.20 (dd, *J* = 15.5, 9.5 Hz, 1H), 5.42 (q, *J* = 2.0 Hz, 1H), 5.28 (q, *J* = 2.0 Hz, 1H), 3.91-3.88 (m, 1H), 3.65-3.60 (m, 1H), 3.57-3.52 (m, 1H), 3.04-2.98 (m, 1H), 2.87-2.81 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): 170.5, 142.7, 135.9, 134.8, 128.6, 128.2, 126.6, 124.8, 119.1, 118.1, 114.0, 112.7; 48.6, 47.5, 40.2, 35.2; IR (neat): 3148, 3082, 3027, 2924, 2852,

2240, 1710, 1665, 1600, 1469, 1410, 1317, 1286, 1122, 1074, 967, 909, 749, 694; HRMS (ESI): calculated for $C_{20}H_{18}N_2NaO$ $[M+Na]^+$: 325.1317, found 325.1312; Chiral HPLC: Chiralpak® IA column, 20% isopropanol in heptane, 1.0 mL/min, $\lambda = 254$ nm, $t_R = 6.44$ (minor), 14.46 (major).



(1*S*,2*R*,3*R*)-5-methylene-2-(3-phenylpropyl)-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23i): The reaction was performed with 23.9 mg (0.1 mmol) of acylpyrrole and 35 μL (0.15 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) to give the product as a clear oil (26.0 mg, 82%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.34-7.25 (m, 4H), 7.19-7.14 (m, 3H), 6.35 (t, $J = 2.5$ Hz, 2H), 5.35 (q, $J = 2.5$ Hz, 1H), 5.20 (q, $J = 2.0$ Hz, 1H), 3.77 (d, $J = 7.5$ Hz, 1H), 3.36 (q, $J = 8.5$ Hz, 1H), 2.95-2.90 (m, 1H), 2.78-2.73 (m, 1H), 2.70-2.67 (m, 1H), 2.66-2.61 (m, 2H), 1.77-1.56 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): 171.1, 142.9, 141.5, 128.4, 128.3, 125.9, 119.1, 118.2, 113.9, 112.6, 46.8, 45.0, 38.9, 36.0, 35.7, 30.5, 29.7; IR (neat): 3402, 3148, 3107, 3084, 3062, 3026, 2928, 2858, 2238, 1950, 1876, 1711, 1664, 1602, 1544, 1494, 1468, 1411, 1374, 1320, 1284, 1121, 1073, 1029, 954, 908, 815, 745, 700; $[\alpha]_{25}^{D} =$ -22.8 (c 1.00, $CHCl_3$); HRMS (ESI): calculated for $C_{21}H_{22}N_2NaO$ $[M+Na]^+$: 341.1630, found 341.1628; Chiral HPLC: Chiralpak® IA column, 5% isopropanol in heptane, 1.0 mL/min, $\lambda = 254$ nm, $t_R = 8.35$ (minor), 10.74 (major).



(1*S*,2*R*,3*R*)-2-cyclopropyl-5-methylene-3-(1*H*-pyrrole-1-carbonyl)cyclopentanecarbonitrile (23j): The reaction was performed with 16.1 mg (0.1 mmol) of acylpyrrole and 35 μL (0.15 mmol) of nitrile TMM donor **17**. Purified by flash chromatography on silica gel (15% ethyl acetate in hexanes) to give the product as a clear oil (20.2 mg, 84%). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.37-7.33 (br s, 2H), 6.35 (t, $J = 2.5$ Hz, 2H), 5.40 (q, $J = 2.0$ Hz, 1H), 5.24 (q, $J = 2.0$ Hz, 1H), 3.86-3.84 (m, 1H), 3.63-3.59 (m, 1H), 2.95-2.92 (m, 1H), 2.82-2.74 (m, 1H), 1.95 (ddd, $J = 13.0, 9.0, 7.5$ Hz, 1H), 0.95-0.89 (m, 1H), 0.78-0.71 (m, 1H), 0.52-0.46 (m, 1H), 0.38-0.32 (m, 1H), 0.27-0.21 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): 171.6, 143.2, 119.1,

118.6, 113.8, 112.2, 51.1, 47.4, 39.7, 35.5, 12.5, 5.2, 3.7; IR (neat): 3148, 3082, 3002, 2961, 2851, 2241, 1706, 1664, 1544, 1466, 1409, 1365, 1283, 1260, 1112, 1073, 1021, 902, 802, 743; $[\alpha]_{24}^{D}$ = -22.3 (c 0.35, $CHCl_3$); HRMS (ESI): calculated for $C_{15}H_{16}N_2NaO$ $[M+Na]^+$: 263.1160, found 263.1164; Chiral HPLC: Chiralpak® IA column, 2% isopropanol in heptane, 1.0 mL/min, λ = 254 nm, t_R = 12.10 (minor), 13.88 (major).

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