Distal-Selective Hydroformylation using Scaffolding Catalysis

Candice L. Joe, Thomas P. Blaisdell, Allison F. Geoghan, Kian L. Tan

Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, MA, 02467

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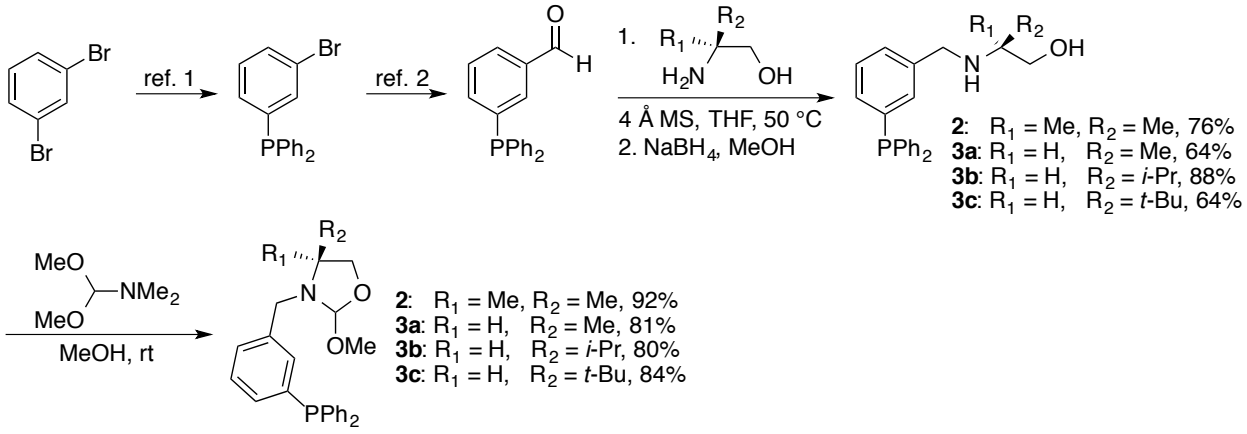
General Considerations

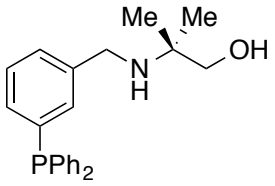
Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Lithium reagents were titrated against 2-pentanol using 1,10-phenanthroline as the indicator. Flash column chromatography was performed using Silicycle silica gel, SiliaFlash P60 (230-400 mesh) and ACS grade solvents as received from Fisher Scientific. All experiments were performed in oven or flame dried glassware under an atmosphere of nitrogen or argon using standard syringe and cannula techniques, except where otherwise noted. All reactions were run with dry, degassed solvents dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). ^{1}H, ^{13}C, ^{31}P, and ^{19}F NMR were performed on either Varian Gemini 400 MHz, Varian Unity Inova 500 MHz, Varian Gemini 500 MHz, or Varian 600 MHz spectrometers. Deuterated solvents were purchased from Cambridge Isotope Labs and stored over 3Å molecular sieves. C_6D_6 was degassed by three successive freeze-pump-thaw cycles and stored over 3Å molecular sieves in a dry box under a nitrogen atmosphere. All NMR chemical shifts are reported in ppm relative to residual solvent for ^{1}H and ^{13}C and external standard (neat H_3PO_4) for ^{31}P NMR. Coupling constants are reported in Hz. All IR spectra were gathered on a Bruker Alpha FT-IR equipped with a single crystal diamond ATR module and values are reported in cm^{-1}. HRMS and X-ray crystal structure data were generated in Boston College facilities. Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. An Agilent Technologies 7890A gas chromatography system equipped with a 7683B Series Injector was used to introduce samples into a J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness) or Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness). Detection was by FID and data was worked up with Agilent Technologies GC ChemStation software. Retention times are reported in minutes. Hydroformylation was performed in an Argonaut Technologies Endeavor® Catalyst Screening System using 1:1 H_2/CO supplied by Airgas, Inc.

Ligand Characterization

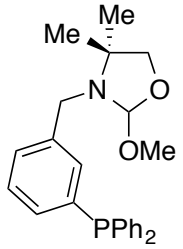
The following compounds were synthesized according to literature procedures and matched all reported spectroscopic data: (3-bromophenyl)diphenylphosphane, [1] 3-(diphenylphosphanyl)benzaldehyde, [2] bis(4-methoxyphenyl)phosphine oxide, [3] bis(4-(trifluoromethyl)phenyl)phosphine oxide.[4]



Ligand 2:

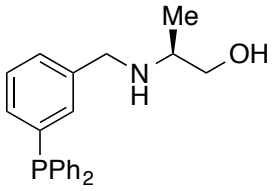


2-((3-(diphenylphosphanyl)benzyl)amino)-2-methylpropan-1-ol. To a 50-mL round-bottom flask containing 4 Å molecular sieves was added 3-(diphenylphosphanyl)benzaldehyde (500 mg, 1.72 mmol) and 2-amino-2-methylpropan-1-ol (250 mg, 2.97 mmol) in THF (9 mL). The solution was heated to 50 °C with vigorous stirring. After 6 hours, the molecular sieves were filtered off and the resulting solution was concentrated to a viscous residue, which was dissolved in anhydrous methanol (9 mL). The solution was cooled to 0 °C, sodium borohydride (195 mg, 5.15 mmol), and the reaction was allowed to warm to room temperature over 2 hours. The methanol was removed under reduced pressure. The residue was diluted with dichloromethane (20 mL) and the reaction was quenched by the addition of water (10 mL). The aqueous layer was extracted with an additional portion of dichloromethane (20 mL) and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (50% EtOAc/Hex containing 1% Et_3N) afforded the title compound as a colorless solid (469 mg, 76%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.28 – 7.35 (m, 12H), 7.26 – 7.27 (m, 1H), 7.13 – 7.16 (m, 1H), 3.63 (s, 2H), 3.30 (s, 2H), 1.10 (s, 6H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 141.2 (d, $J_{C\text{-}P}$ = 7.6 Hz), 137.6 (d, $J_{C\text{-}P}$ = 11.4 Hz), 137.4 (d, $J_{C\text{-}P}$ = 10.5 Hz), 133.9 (d $J_{C\text{-}P}$ = 20.0 Hz), 133.7 (d, $J_{C\text{-}P}$ = 23.8 Hz), 132.5 (d, $J_{C\text{-}P}$ = 16.2 Hz), 128.9, 128.8 (d, $J_{C\text{-}P}$ = 5.7 Hz), 128.7, 128.6 (d, $J_{C\text{-}P}$ = 6.7 Hz), 68.6, 54.2, 46.4, 24.4; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.4; **IR**: 2967, 1476, 1433, 1051, 742, 694, 467 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{23}H_{27}N_1O_1P_1$ $[M+H]^+$: 364.1830, found: 364.1837.

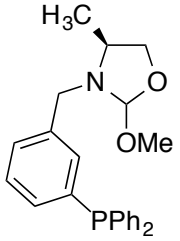


3-(3-(diphenylphosphanyl)benzyl)-2-methoxy-4,4-dimethyloxazolidine. *N,N*-dimethylformamide dimethylacetal (814 μL, 6.13 mmol) was added to a solution of 2-((3-(diphenylphosphanyl)benzyl)amino)-2-methylpropan-1-ol (446 mg, 1.23 mmol) in freshly distilled methanol (12 mL) and the reaction was stirred at room temperature for 3 hours. The volatiles were removed on high vacuum and the residue was re-dissolved in dry methanol (12 mL). After stirring for 2 hours at room temperature, the volatiles were removed under vacuum. The crude residue was brought into the glovebox and extracted with dry, degassed pentane (2 x 10 mL). Removal of the pentane under vacuum afforded the title compound as a colorless solid (457 mg, 92%). **^{1}H NMR** (C_6D_6, 500 MHz) δ 7.57 (d, 1H, J = 7.8 Hz), 7.43 (dt, 4H, J = 7.8, 1.5 Hz), 7.31 – 7.34 (m, 1H), 7.28 (d, 1H, J = 7.3 Hz), 7.03 – 7.12 (m, 7H), 5.16 (s, 1H), 3.65 (d, 1H, J = 4.9 Hz), 3.63 (d, 1H, J = 11.7 Hz), 3.51 (d, 1H, J = 7.3 Hz), 3.43 (d, 1H, J = 14.1 Hz), 3.01 (s, 3H), 0.90 (s, 3H), 0.82 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 140.2 (d, $J_{C\text{-}P}$ = 6.9 Hz), 137.5 (d, $J_{C\text{-}P}$ = 9.2 Hz), 137.0 (d, $J_{C\text{-}P}$ = 10.7 Hz), 134.2 (d, $J_{C\text{-}P}$ = 19.8 Hz), 133.9 (d, $J_{C\text{-}P}$ = 19.1 Hz), 133.3 (d, $J_{C\text{-}P}$ = 19.8 Hz), 129.4, 128.9, 128.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 128.6 (d, $J_{C\text{-}P}$ = 6.7 Hz), 128.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 112.2, 78.5, 59.5, 51.0, 47.1, 24.4, 22.9; **^{31}P NMR** (C_6D_6 , 202 MHz) δ – 5.4; **IR**: 2965, 2877, 1726, 1476, 1433, 1387, 1323, 1245, 1092, 1076, 1039, 940, 743, 695, 495 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{25}H_{29}N_1O_2P_1$ $[M+H]^+$: 406.1936, found: 406.1918.

Ligand 3a:

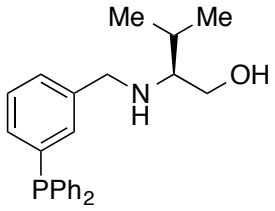


(*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)propan-1-ol. A mixture of 3-(diphenylphosphanyl)benzaldehyde (600 mg, 2.07 mmol), (*S*)-2-aminopropan-1-ol (202 mg, 2.69 mmol), and 4 Å molecular sieves in tetrahydrofuran (7 mL) was heated to 50 °C overnight. The molecular sieves were filtered off and the remaining solution was concentrated to a viscous residue. The crude material was dissolved in anhydrous methanol (7 mL) and sodium borohydride (235 mg, 6.21 mmol) was added at 0 °C. The reaction was allowed to warm to room temperature over 3 hours and was quenched by the addition of water (30 mL). The aqueous layer was extracted with dichloromethane (2 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified using silica gel chromatography (1% Et_3N/EtOAc) to afford the title compound as a colorless oil (456 mg, 64%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.28 – 7.35 (m, 12H), 7.27 – 7.26 (m, 1H), 7.15 – 7.18 (m, 1H), 3.82 (d, 1H, J = 13.2 Hz), 3.70 (d, 1H, J = 13.2 Hz), 3.54 – 3.57 (m, 1H), 3.22 (dd, 1H, J = 10.8, 6.9 Hz), 2.76 – 2.80 (m, 1H), 1.04 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 140.8 (d, $J_{C\text{-}P}$ = 7.6 Hz), 137.6 (d, $J_{C\text{-}P}$ = 11.5 Hz), 137.4 (d, $J_{C\text{-}P}$ = 10.7 Hz), 133.9 (d, $J_{C\text{-}P}$ = 19.8 Hz), 133.6 (d, $J_{C\text{-}P}$ = 22.9 Hz), 132.6 (d, $J_{C\text{-}P}$ = 16.8 Hz), 128.9, 128.8 (d, $J_{C\text{-}P}$ = 6.1 Hz), 128.7, 128.6 (d, $J_{C\text{-}P}$ = 6.7 Hz), 65.7, 53.9, 51.1, 17.4; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.4; **IR**: 3299, 2967, 2870, 1477, 1435, 1214, 1172, 1118m 1091, 1027, 998, 745, 726, 696, 541 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{22}H_{25}N_1O_1P_1$ $[M+H]^+$: 350.1674, found: 350.1685; **$[\alpha]_D^{20}$** = + 6.7 (c = 0.600, $CHCl_3$, l = 50 mm).

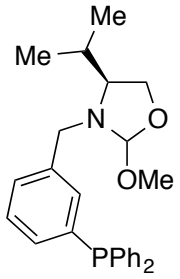


(4*S*)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxy-4-methyloxazolidine. To a solution of (*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)propan-1-ol (355 mg, 1.03 mmol) in freshly distilled methanol (15 mL) was added *N,N*-dimethylformamide dimethylacetal (684 μL, 5.15 mmol). The reaction was stirred vigorously at room temperature for 3 hours and the volatiles were removed under high vacuum. The residue was re-dissolved in dry methanol and the reaction was stirred for an additional 2 hours. The volatiles were removed under high vacuum and the crude residue was pumped into the glovebox. The residue as extracted with pentane (2 x 10 mL) and was concentrated under reduced pressure to afford the title compound as a viscous oil as a 1:1 mixture of diastereomers (325 mg, 81 %). **^{1}H NMR** (C_6D_6, 500 MHz) δ 7.64 (d, 0.5H, J = 8.3 Hz), 7.50 (d, 0.5H, J = 7.8 Hz), 7.41-7.44 (m, 4H), 7.30 – 7.34 (m, 1.5H), 7.20 (d, 0.5H, J = 7.8 Hz), 7.03 – 7.16 (m, 7H), 5.22 (s, 0.5H), 5.10 (s, 0.5H), 3.97 (t, 0.5H, J = 7.3 Hz), 3.75 (d, 0.5H, J = 13.2 Hz), 3.70 (dd, 0.5H, J = 7.6, 6.6 Hz), 3.59 (t, 1H, J = 13.7 Hz), 3.36 – 3.43 (s, 1.5H), 3.12 (s, 1.5H), 3.05 – 3.09 (m, 0.5H), 3.01 (s, 1.5H), 2.67 – 2.73 (m, 0.5H), 0.74 (d, 1.5H, J = 6.0 Hz), 0.70 (d, 1.5H, J = 6.0 Hz); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 139.3 (d, $J_{C\text{-}P}$ = 7.6 Hz), 138.7 (d, $J_{C\text{-}P}$ = 6.9 Hz), 137.1 – 137.6 (11 lines), 133.8 – 134.5 (8 lines), 132.7 (d, $J_{C\text{-}P}$ = 19.0 Hz), 132.5 (d, $J_{C\text{-}P}$ = 17.5 Hz), 128.9, 128l8 (d, $J_{C\text{-}P}$ = 1.5 Hz), 128.7 (d, $J_{C\text{-}P}$ = 6 .1 Hz), 128.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 113.5, 110.3, 72.8, 72.1, 56.8, 54.0, 53.3, 52.6, 50.8, 49.4, 17.3, 17.0; **^{31}P NMR** (C_6D_6, 202 MHz) δ – 5.4, – 5.5; **IR**: 2966, 2886, 1477, 1434, 1345, 1289, 1156, 1064, 744, 697, 495 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{24}H_{27}N_1O_2P_1$ $[M+H]^+$: 392.1779, found: 392.1782; **$[\alpha]_D^{20}$** = + 32.9 (c = 0.465, $CHCl_3$, l = 50 mm).

Ligand 3b:

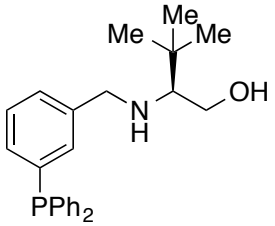


(*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)-3-methylbutan-1-ol. A solution of (*S*)-2-amino-3-methylbutan-1-ol (1.97 g, 19.1 mmol) and 3-(diphenylphosphanyl)benzaldehyde (3.69 g, 12.7 mmol) in DCM (100 mL) was stirred at room temperature for 3 hours. Triethylamine (2.7 mL, 19 mmol) and $NaBH(OAc)_3$ (5.38 g, 25.4 mmol) were added to the flask and the reaction as allowed to stir at room temperature overnight. The reaction was partitioned between water (70 mL) and DCM (150 mL). The organic layer was washed with an additional portion of water (70 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (1% Et_3N/EtOAc) to afford the title compound as a colorless oil (4.18 g, 88%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.27 – 7.35 (m, 13 H), 7.15 – 7.19 (m, 1H), 3.78 (d, 1H, J = 13.0 Hz), 3.71 (d, 1H, J = 13.5 Hz), 3.59 (dd, 1H, J = 10.5, 4.0 Hz), 3.33 (dd, 1H, J = 11.0, 4.0 Hz), 2.38 – 2.42 (m, 1H), 1.80 – 1.85 (m, 1H), 0.92 (d, 3H, J = 7.0 Hz), 0.87 (d, 3H, J = 7.0 Hz); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 140.9 (d, $J_{C\text{-}P}$ = 7.9 Hz), 137.7 (d, $J_{C\text{-}P}$ = 11.2 Hz), 137.4 (d, $J_{C\text{-}P}$ = 2.2 Hz), 137.3, 133.9 (d, $J_{C\text{-}P}$ = 19.1 Hz), 133.7 (d, $J_{C\text{-}P}$ = 21.3), 132.6 (d, $J_{C\text{-}P}$ = 16.8 Hz), 128.9 (d, $J_{C\text{-}P}$ = 11.2 Hz), 128.9 (d, $J_{C\text{-}P}$ = 5.6 Hz), 128.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 63.9, 60.6, 51.4, 29.0, 19.8, 18.6; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.4; **IR**: 3367, 2957, 2872, 1586, 1476, 1434, 1180, 1092, 1042, 998, 788, 744, 696, 497 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{24}H_{29}N_1O_1P_1$ $[M+H]^+$: 378.1987, found: 378.1975; **$[\alpha]_D^{20}$** = + 3.9 (c = 0.680, $CHCl_3$, l = 50 mm).

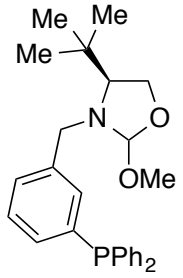


(4*S*)-3-(3-(diphenylphosphanyl)benzyl)-4-isopropyl-2-methoxyoxazolidine. To a stirring solution of (*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)-3-methylbutan-1-ol (1.23 g, 3.28 mmol) in freshly distilled methanol (32 mL) was added *N,N*-dimethylformamide dimethylacetal (2.2 mL 16 mmol). The reaction was stirred at room temperature for 2 hours and was concentrated under high vacuum. The residue was re-dissolved in methanol (32 mL), stirred at room temperature for 3 hours, and concentrated under high vacuum. The crude residue was brought in the glovebox and extracted with pentane (2 x 20 mL). The volatiles were removed under vacuum to afford the pure product as a colorless oil that exists as a 1:1 mixture of diastereomers (1.09 g, 80%). **^{1}H NMR** (C_6D_6, 500 MHz) δ 7.58 (d, 0.5H, J = 7.8 Hz), 7.47 (d, 0.5H, J = 7.8 Hz), 7.40-7.37 (m, 4H), 7.33-7.27 (m, 1.5H), 7.20 (d, 0.5H, J = 7.8 Hz), 7.09-6.99 (m, 7H), 5.15 (s, 0.5H), 5.04 (s, 0.5H), 3.86 (dd, 0.5H, J = 8.3, 7.8 Hz), 3.83 (d, 0.5H, J = 13.2 Hz), 3.69 (dd, 0.5H, J = 7.3, 7.8 Hz), 3.64 (dd, 0.5H, J = 7.8, 5.9 Hz), 3.63 (d, 0.5H, J = 10.0 Hz), 3.54 (dd, 1H, J = 14.7, 13.2 Hz), 3.40 (d, 0.5H, J = 14.2 Hz), 3.01 (s, 1.5H), 2.95 (s, 1.5H), 2.94 – 2.90 (m, 0.5H), 2.44 (app q, 0.5H, J = 7.3 Hz), 1.56-1.49 (m, 1H), 0.74 (d, 1.5H, J = 6.9 Hz), 0.65 (d, 1.5H, J = 3.4 Hz), 0.63 (d, 1.5H, J = 3.4 Hz), 0.57 (d, 1.5H, J = 6.9 Hz); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 139.6 (d, $J_{C\text{-}P}$ = 6.7 Hz), 139.2 (d, $J_{C\text{-}P}$ = 6.7 Hz), 137.2 – 137.5 (6 lines), 134.5 (d, $J_{C\text{-}P}$ = 9.5 Hz), 134.3 (d, $J_{C\text{-}P}$ =10.5 Hz), 133.9 (d, $J_{C\text{-}P}$ = 20.0 Hz), 132.9 (d, $J_{C\text{-}P}$ = 20.0 Hz), 132.6 (d, $J_{C\text{-}P}$ = 19.1 Hz), 129.6 (d, $J_{C\text{-}P}$ = 19.1 Hz), 128.9, 128.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 128.6 (d, $J_{C\text{-}P}$ = 13.4 Hz), 114.6, 110.6, 68.4, 67.5, 66.0, 63.6, 57.0, 52.9, 51.4, 50.1, 31.1, 28.6, 20.4, 19.6, 17.7, 15,5; **^{31}P NMR (**C_6D_6, 202 MHz) δ – 5.4, – 5.5; **IR**: 3069, 2929, 2279, 1884, 1817, 1585, 1364, 1155, 1057, 744, 697, 494 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{26}H_{31}N_1O_2P_1$ $[M+H]^+$: 420.2092, found: 420.2099; **$[\alpha]_D^{20}$** = + 34.7 (c = 0.480, $CHCl_3$, l = 50 mm).

Ligand 3c:

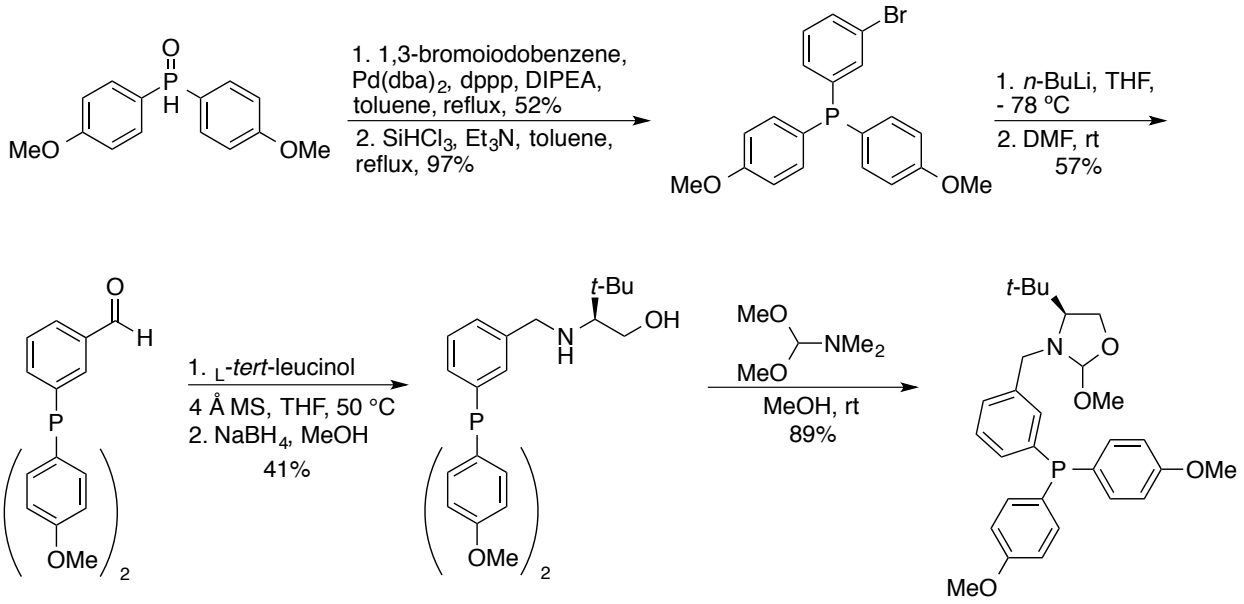


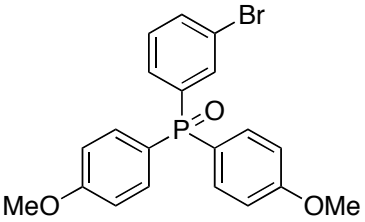
(*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol. A suspension of (*S*)-2-amino-3,3-dimethylbutan-1-ol (884 mg, 7.54 mmol), 3-(diphenylphosphanyl)benzaldehyde (1.46 g, 5.03 mmol) and activated 4 Å molecular sieves (1.00 g) in THF (18 mL) was heated to 50 °C with vigorous stirring overnight. After cooling to room temperature, the reaction was filtered and concentrated *in vacuo*. The oily residue was re-dissolved in dry methanol (18 mL), the solution cooled to 0°C, and $NaBH_4$ (382 mg, 10.1 mmol) was added portionwise. The reaction was allowed to warm to room temperature over 3 hours, after which time the methanol was removed under reduced pressure. The remaining residue as quenched by the addition of water (20 mL) and extracted with DCM (3 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue as purified by column chromatography (100 % EtOAc) to afford the title compound as a colorless oil (1.27 g, 64%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.28 – 7.34 (m, 13H), 7.17 – 7.18 (m, 1H), 3.83 (d, 1H, J = 13.2 Hz), 3.79 (d, 1H, J = 12.7 Hz), 3.60 (dd, 1H, J = 10.7, 4.9 Hz), 3.37 (dd, 1H, J = 10.7, 6.4 Hz), 2.30 – 2.32 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 140.9 (d, $J_{C\text{-}P}$ = 6.7 Hz), 137.8 (d, $J_{C\text{-}P}$ = 11.5 Hz), 137.3 (d, $J_{C\text{-}P}$ = 10.5 Hz), 133.9 (d, $J_{C\text{-}P}$ = 20.0 Hz), 133.7 (d, $J_{C\text{-}P}$ = 21.9 Hz), 132.7 (d, 18.1 Hz), 129.0, 128.9 (d, $J_{C\text{-}P}$ = 6.7 Hz), 128.8, 128.7 (d, $J_{C\text{-}P}$ = 7.6 Hz), 67.1, 60.2, 54.1, 34.6, 27.0; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.4; **IR**: 3338, 2952, 2867, 1476, 1434, 1413, 1091, 1043, 1026, 997, 788, 743, 695, 495 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{25}H_{31}N_1O_1P_1$ $[M+H]^+$: 392.2143, found: 394.2148; **$[\alpha]_D^{20}$** = − 0.87 (*c* = 0.655, $CHCl_3$, *l* = 50 mm).



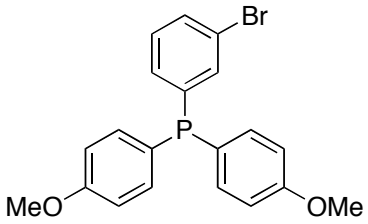
(4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine. *N,N*-dimethylformamide dimethylacetal (2.00 mL, 14.9 mmol) was added to (*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol (1.17 g, 2.99 mmol) in freshly distilled methanol (30 mL) and the reaction was stirred at room temperature for 3 hours. The volatiles were removed on high vacuum and the residue was re-dissolved in dry methanol (30 mL). After stirring for 2 hours at room temperature, the volatiles were removed under vacuum. The crude residue was brought into the glovebox and extracted with dry, degassed pentane (2 x 30 mL). Removal of the pentane under vacuum afforded the title compound as a pale yellow oil that exists as a 1:1 mixture of diastereomers (1.10 g, 84%). **^{1}H NMR** (C_6D_6, 500 MHz) δ 7.66 (d, 0.5H, J = 7.3 Hz), 7.59 (d, 0.5H, J = 7.3 Hz), 7.41 – 7.45 (m, 4H), 7.31 – 7.37 (m, 1H), 7.03 – 7.14 (m, 8H), 5.05 (s, 0.5H), 5.03 (s, 0.5H), 4.16 (d, 0.5H, J = 13.6 Hz), 3.90 – 3.93 (m, 0.5H), 3.82 (d, 0.5H, J = 13.7 Hz), 3.73 – 3.78 (m, 1H), 3.69 (dd, 0.5H, J = 8.3, 2.4 Hz), 3.61 (d, 1H, J = 6.9 Hz), 2.92 (s, 1.5H), 2.91 (s, 1.5H), 2.51 – 2.54 (m, 0.5H), 2.48 – 2.51 (m, 0.5H), 0.78 (s, 4.5H), 0.77 (s, 4.5H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 140.2 (d, $J_{C\text{-}P}$ = 6.1 Hz), 140.0 (d, $J_{C\text{-}P}$ = 6.1 Hz), 137.6 (d, $J_{C\text{-}P}$ =10.7 Hz), 137.4 (d, $J_{C\text{-}P}$ = 4.6 Hz), 137.3 (d, $J_{C\text{-}P}$ = 3.8 Hz), 137.1 (d, $J_{C\text{-}P}$ = 17.7 Hz), 133.6 – 134.3 (7 lines), 132.9 (d, $J_{C\text{-}P}$ = 21.4 Hz), 132.5 (d, $J_{C\text{-}P}$ = 22.1 Hz), 129.3, 128.9 (d, $J_{C\text{-}P}$ = 6.9 Hz), 128.8, 128.7 (d, $J_{C\text{-}P}$ = 6.9 Hz), 128.4 (d, $J_{C\text{-}P}$ = 7.0 Hz), 115.6, 110.5, 73.1, 68.5, 66.5, 65.4, 60.1, 53.0, 52.4, 52.3, 35.3, 33.8, 26.9, 26.4; **^{31}P NMR** (C_6D_6, 202 MHz) δ – 5.6; **IR**: 2953, 2898, 1477, 1437, 1393, 1360, 1198, 1141, 1085, 1065, 998, 946, 744, 696, 496 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{27}H_{33}N_1O_2P_1$ $[M+H]^+$: 434.2249, found: 434.2232; **$[\alpha]_D^{20}$** = + 25.2 (*c* = 0.495, $CHCl_3$, *l* = 50 mm).

Synthesis of Ligand 3d:

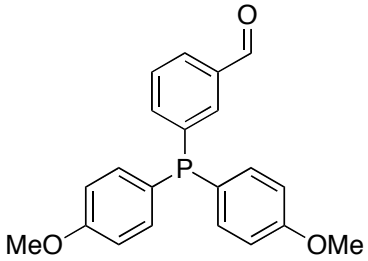




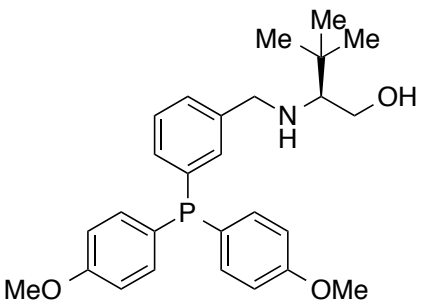
(3-bromophenyl)bis(4-methoxyphenyl)phosphine oxide. To a 100 mL, flame-dried, round-bottom flask in the glovebox was added $Pd(dba)_2$ (317 mg, 0.552 mmol) and 1,3-bis(diphenylphosphino)propane (228 mg, 0.552 mmol). The flask was fitted with a dry reflux condenser, and the apparatus was brought out of the glovebox and placed under argon. Toluene (22 mL), bis(4-methoxyphenyl)phosphine oxide (4.00 g, 15.3 mmol), 1-bromo-3-iodobenzene (2.35 mL, 18.4 mmol), and Hunig's base (3.37 mL, 19.3 mmol) were added to the flask successively. The reaction was heated to reflux overnight. After being cooled to room temperature, the crude mixture was partitioned between water (20 mL) and ethyl acetate (70 mL). The layers were separated and the aqueous layer was extracted with an additional portion of ethyl acetate (50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel chromatography (2% Et_3N/EtOAc) to afford an off white solid (3.31 g, 52%). **^{1}H NMR** ($(CD_3)_2CO$, 500 MHz) δ 7.81 (d, 1H, J = 11.7 Hz), 7.76 (d, 1H, J = 7.8 Hz), 7.65 (s, 1H), 7.61 (app dd, 4H, J = 11.3 Hz, 8.8 Hz), 7.46 – 7.50 (app dt, 1H, J = 7.8 Hz, 2.9 Hz), 7.09 (app dd, 4H, J = 8.8 Hz, 2.0 Hz), 3.87 (s, 6H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 162.8 (d, $J_{C\text{-}P}$ = 2.7 Hz), 136.5 (d, $J_{C\text{-}P}$ = 101 Hz), 134.8 (d, $J_{C\text{-}P}$ = 2.9 Hz), 134.4 (d, $J_{C\text{-}P}$ = 10.5 Hz), 133.7 (d, $J_{C\text{-}P}$ = 11.4 Hz), 130.6 (d, $J_{C\text{-}P}$ = 8.6 Hz), 130.2 (d, $J_{C\text{-}P}$ = 13.4 Hz), 123.4 (d, $J_{C\text{-}P}$ = 112 Hz), 123.2 (d, $J_{C\text{-}P}$ = 14.3 Hz), 114.3 (d, $J_{C\text{-}P}$ = 13.4 Hz), 55.5; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ + 27.5; **IR**: 1595, 1502, 1254, 1177, 1118, 802, 547 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{20}H_{19}Br_1O_3P_1$ $[M+H]^+$: 417.0255, found: 417.0249.



(3-bromophenyl)bis(4-methoxyphenyl)phosphine. To a solution of (3-bromophenyl)bis(4-methoxyphenyl)phosphine oxide (3.22 g, 7.72 mmol) in toluene (77 mL) was added triethylamine (5.90 mL, 42.5 mmol). The solution was cooled to 0 °C and trichlorosilane (3.90 mL, 38.6 mmol) was added slowly to the stirring solution. The flask was fitted with a reflux condenser and the solution was heated to reflux overnight. The reaction was cooled to 0 °C and quenched by the addition of 30% NaOH (40 mL). The aqueous layer was extracted with dichloromethane (2 x 50 mL) and the combined organic layers were washed with an additional portion of water (30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to yield an opaque oil that was used in the next step without purification (3.00 g, 97%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.41 – 7.43 (m, 1H), 7.34 (d, 1H, J = 6.5 Hz), 7.24 – 7.27 (m, 5H), 7.16 – 7.18 (m, 1H), 6.90 (d, 4H, J = 8.5 Hz), 3.81 (s, 6H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 160.6, 142.3 (d, $J_{C\text{-}P}$ = 15.3 Hz), 135.6 (d, $J_{C\text{-}P}$ = 21.9 Hz), 135.5 (d, $J_{C\text{-}P}$ = 19.1 Hz), 131.7 (d, $J_{C\text{-}P}$ = 19.1 Hz), 131.4, 130.1 (d, $J_{C\text{-}P}$ = 5.7 Hz), 127.6 (d, $J_{C\text{-}P}$ = 7.6 Hz), 123.2 (d, $J_{C\text{-}P}$ = 6.7 Hz), 114.6 (d, $J_{C\text{-}P}$ = 8.6 Hz), 55.4; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 7.8; **IR**: 1596, 1500, 1255, 1179, 1120, 829, 548 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{20}H_{19}Br_1O_2P_1$ $[M+H]^+$: 401.0306, found: 401.0291.

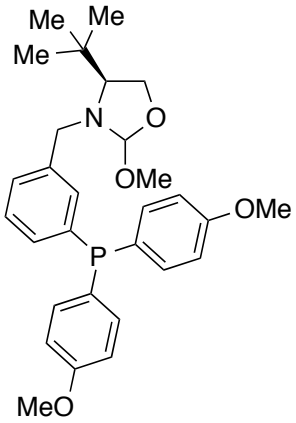


3-(bis(4-methoxyphenyl)phosphino)benzaldehyde. To a -78 °C solution of (3-bromophenyl)bis(4-methoxyphenyl)phosphine (3.23 g, 8.05 mmol) in THF (81 mL) was added *n*-BuLi (3.63 mL, 8.86 mmol, 2.44 M solution in hexane). After stirring at this temperature for 50 minutes, DMF (1.20 mL, 16.1 mmol) was added and the resulting solution was warmed to room temperature over 4 hours. The reaction was quenched by the addition of saturated ammonium chloride (60 mL) and extracted with ethyl acetate (150 mL). The organic layer was extracted with an additional portion of water (40 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the crude reaction mixture on silica gel (15% EtOAc/Hex) afforded the title compound as a colorless oil (1.53 g, 57%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 9.93 (s, 1H), 7.81 (d, 1H, J = 6.8 Hz), 7.74 (d, 1H, J = 6.8 Hz), 7.45 – 7.51 (m, 2H), 7.25 – 7.29 (m, 4H), 6.91 (d, 4H, J = 8.3 Hz), 3.82 (s, 6H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 192.4, 160.8, 141.1 (d, $J_{C\text{-}P}$ = 13.4 Hz), 138.9 (d, $J_{C\text{-}P}$ = 18.1 Hz), 136.5 (d, $J_{C\text{-}P}$ = 4.8 Hz), 135.6 (d, $J_{C\text{-}P}$ = 21.0 Hz), 134.8 (d, $J_{C\text{-}P}$ = 19.1 Hz), 129.2 (d, $J_{C\text{-}P}$ = 5.7 Hz), 129.0, 127.4 (d, $J_{C\text{-}P}$ = 7.6 Hz), 114.6 (d, $J_{C\text{-}P}$ = 8.6 Hz), 55.4; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 8.8; **IR**: 1698, 1594, 1498, 1287, 1250, 1178, 828 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{21}H_{20}O_3P_1$ $[M+H]^+$: 351.1150, found: 351.1146.



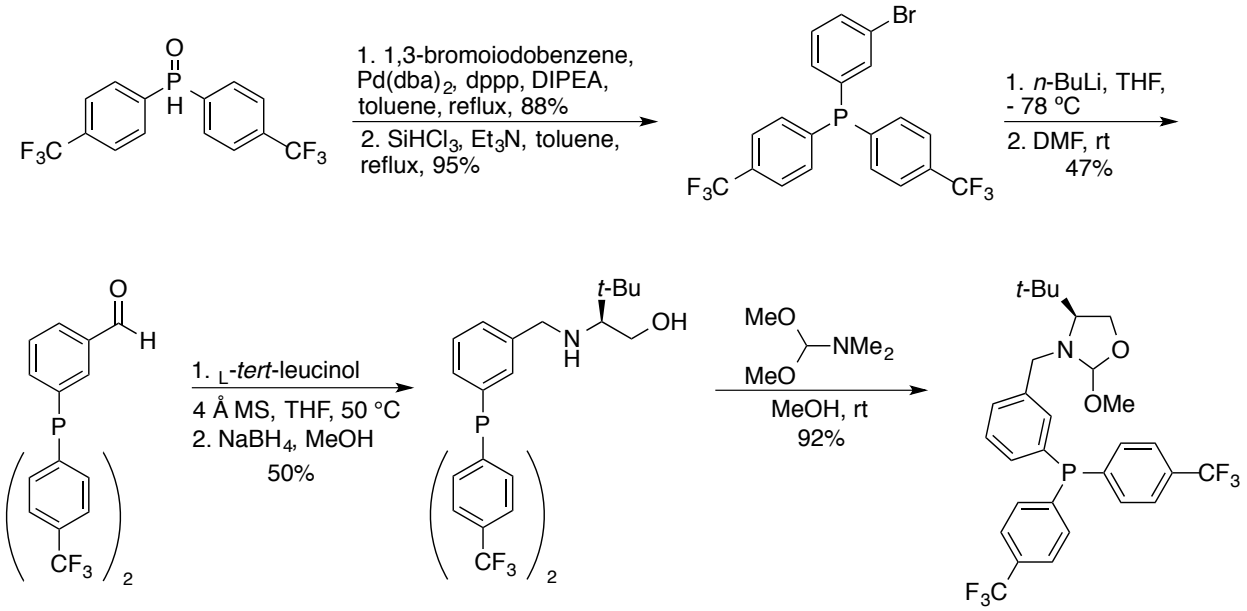
(*S*)-2-((3-(bis(4-methoxyphenyl)phosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol. A suspension of (*S*)-2-amino-3,3-dimethylbutan-1-ol (216 mg mg, 1.84 mmol), 3-(bis(4-methoxyphenyl)phosphino)benzaldehyde (322 mg, 0.920 mmol) and activated 4 Å molecular sieves (0.50 g) in THF (9 mL) was heated to 50 °C with vigorous stirring overnight. After cooling to room temperature, the reaction was filtered

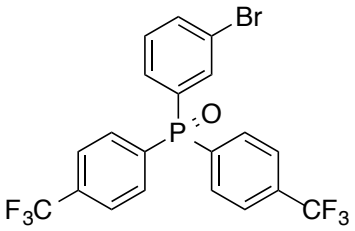
and concentrated *in vacuo*. The oily residue was re-dissolved in dry methanol (9 mL), the solution cooled to 0 °C, and $NaBH_4$ (104 mg, 2.76 mmol) was added portion-wise. The reaction was allowed to warm to room temperature over 3 hours and the methanol was removed under reduced pressure. The remaining residue as quenched by the addition of water (10 mL) and extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue as purified by column chromatography (1% Et_3N/EtOAc) to afford the title compound as a colorless oil (172 mg, 41%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.20 – 7.28 (m, 7H), 7.11 – 7.14 (m, 1H), 6.88 (d, 4H, J = 8.8 Hz), 3.83 (d, 1H, J = 13.1 Hz), 3.80 (s, 6H), 3.78 (d, 1H, J = 12.8 Hz), 3.60 (dd, 1H, J = 10.7, 4.9 Hz), 3.38 (dd, 1H, J = 10.7, 5.9 Hz), 2.30 – 2.32 (m, 1H), 0.91 (s, 9H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 160.5, 140.8 (d, $J_{C\text{-}P}$ = 6.9 Hz), 139.2 (3, $J_{C\text{-}P}$ = 11.6 Hz), 135.5 (d, $J_{C\text{-}P}$ = 20.8 Hz), 133.0 (d, $J_{C\text{-}P}$ = 20.8 Hz), 132.1 (d, $J_{C\text{-}P}$ = 17.3 Hz), 128.7 (d, $J_{C\text{-}P}$ = 5.8 Hz), 128.4, 128.3, 114.4 (d, $J_{C\text{-}P}$ = 6.9 Hz), 67.1, 60.2, 55.4, 54.1, 34.6, 27.5; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 8.6; **IR**: 3376, 2954, 2869, 1594, 1497, 1402, 1364, 1285, 1177, 1095, 1030, 827, 796, 531 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{27}H_{35}N_1O_3P_1$ $[M+H]^+$: 452.2355, found: 452.2373; **$[\alpha]_D^{20}$** = − 2.9 (c = 0.485, $CHCl_3$, l = 50 mm).



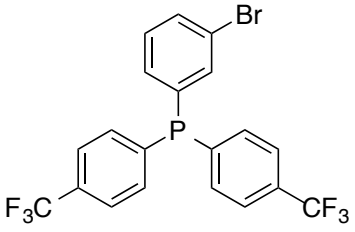
(4*S*)-3-(3-(bis(4-methoxyphenyl)phosphanyl)benzyl)-4-(*tert*-butyl)-2-methoxyoxazolidine. To a solution of (*S*)-2-((3-(bis(4-methoxyphenyl)phosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol (172 mg, 0.381 mmol) in freshly distilled methanol (5.5 mL) was added *N,N*-dimethylformamide dimethylacetal (254 μL, 1.91 mmol). The reaction was stirred vigorously at room temperature for 3 hours and the volatiles were removed under high vacuum. The residue was re-dissolved in dry methanol (5.5 mL) and the reaction was stirred for an additional 2 hours. The volatiles were removed under high vacuum and the crude residue was pumped into the glovebox. The residue as extracted with pentane (2 x 10 mL) and was concentrated under reduced pressure to afford the title compound as a viscous oil (167 mg, 89 %). **^{1}H NMR** (C_6D_6, 600 MHz) δ 7.70 (d, 0.6H, J = 7.3 Hz), 7.62 (d, 0.6H, J = 7.8 Hz), 7.37 – 7.47 (m, 5H), 7.12 – 7.20 (m, 1.8H), 6.73 – 6.76 (m, 4H), 5.10 (s, 0.6H), 5.08 (s, 0.4H), 4.22 (d, 0.4H, J = 13.7 Hz), 3.93 (t, 0.4H, J = 8.1 Hz), 3.87 (d, 0.4H, J = 13.7 Hz), 3.75 – 3.81 (m, 1.2H), 3.70 (dd, 0.4H, J = 8.3, 2.4 Hz), 3.65 (d, 1.2H, J = 5.4 Hz), 3.24 (s, 3.6H), 3.23 (s, 2.4H), 2.95 (s, 3H), 2.56 (dd, 0.4H, J = 7.8, 2.4 Hz), 2.52 (t, 0.6H, J = 8.3 Hz), 0.81 (s, 5.4H), 0.79 (s, 3.6H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 160.5, 139.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 139.8 (d, $J_{C\text{-}P}$ = 5.8 Hz), 138.8 (d, $J_{C\text{-}P}$ = 10.4 Hz), 138.5 (d, $J_{C\text{-}P}$ = 9.2 Hz), 135.5 (d, $J_{C\text{-}P}$ = 20.8 Hz), 135.4 (d, $J_{C\text{-}P}$ = 20.8 Hz), 135.1 (d, $J_{C\text{-}P}$ = 8.4 Hz), 133.6 (d, $J_{C\text{-}P}$ = 17.3 Hz), 133.1 (d, $J_{C\text{-}P}$ = 17.3 Hz), 132.2 (d, $J_{C\text{-}P}$ = 20.8 Hz), 131.8 (d, $J_{C\text{-}P}$ = 20.8 Hz), 128.5 – 128.8 (7 lines), 128.3 (d, $J_{C\text{-}P}$ = 8.1 Hz), 115.6, 114.4 (d, $J_{C\text{-}P}$ = 8.1 Hz), 110.5, 73.1, 68.5, 66.6, 65.4, 60.2, 55.4, 53.1, 52.4, 52.3, 35.3, 33.8, 26.8, 26.4; **^{31}P NMR** (C_6D_6, 202 MHz) δ – 8.7; **IR**: 2952, 2900, 1593, 1496, 1461, 1304, 1283, 1244, 1094, 1063, 1030, 826, 796, 530 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{29}H_{37}N_1O_4P_1$ $[M+H]^+$: 494.2460, found: 494.2445; **$[\alpha]_D^{20}$** = + 20.8 (c = 0.570, $CHCl_3$, l = 50 mm).

Synthesis of Ligand 3e:



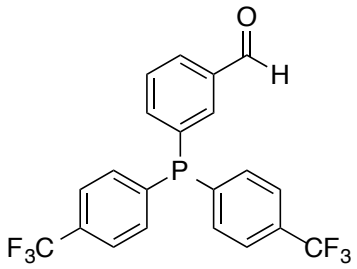


(3-bromophenyl)bis(4-(trifluoromethyl)phenyl)phosphine oxide. To a flame-dried, 25-mL, round-bottom flask in a dry box was added bis(4-(trifluoromethyl)phenyl)phosphine oxide (1.50 g, 4.44 mmol), bis(dibenzylideneacetone)palladium(0) (926 mg, 0.160 mmol), and 1,3-bis(diphenylphosphino)propane (660 mg, 0.160 mmol). The flask was brought out of the dry box and was placed under nitrogen. The flask was charged, successively, with toluene (5 mL), 3-bromo-1-iodobenzene (0.682 mL, 5.35 mmol), and *N,N*-diisopropylethylamine (1.01 mL, 5.62 mmol) and the reaction was heated to reflux overnight. The reaction was cooled to room temperature and was partitioned between water (20 mL) and DCM (40 mL). The aqueous layer was washed with an additional portion of DCM (40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel chromatography (20% EtOAc/Hex containing 1% Et_3N) to yield the title compound as colorless solid (1.91 g, 88%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.74 – 7.83 (m, 10H), 7.56 (dd, 1H, J = 12.0, 8.0 Hz), 7.39 (dt, 1H, J = 8.0, 3.5 Hz); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 136.1 (d, $J_{C\text{-}P}$ = 3.1 Hz), 135.7 (d, $J_{C\text{-}P}$ = 103.0 Hz), 134.7 (d, $J_{C\text{-}P}$ = 10.7 Hz), 134.6 (dq, $J_{C\text{-}P,F}$ = 32.8, 3.1 Hz), 133.7 (d, $J_{C\text{-}P}$ = 103.0 Hz), 132.7 (d, $J_{C\text{-}P}$ = 10.7 Hz), 130.8 (d, $J_{C\text{-}P}$ = 13.0 Hz), 130.6 (d, $J_{C\text{-}P}$ = 9.9 Hz), 126.0 – 126.1 (m), 123.9 (d, $J_{C\text{-}P}$ = 15.3 Hz), 123.6 (d, $J_{C\text{-}F}$ = 273 Hz); **^{19}F NMR** ($CDCl_3$, 470 MHz) δ – 63.8; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ + 25.3; **IR**: 3057, 1611, 1504, 1321, 1128, 1062, 836, 766, 685, 572 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{20}H_{13}Br_1F_6O_1P_1$ $[M+H]^+$: 492.9713, found: 492.9792.

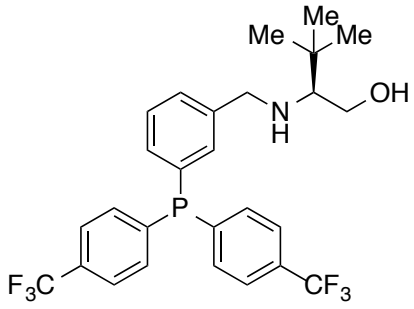


(3-bromophenyl)bis(4-(trifluoromethyl)phenyl)phosphane. To a flame-dried flask was added (3-bromophenyl)bis(4-(trifluoromethyl)phenyl)phosphine oxide (1.00 g, 2.03 mmol), Et_3N (1.57, 11.2 mmol), and toluene (20 mL). The solution was cooled to 0 °C and trichlorosilane was added dropwise. The flask was fitted with a reflux condenser and the reaction was heated to reflux overnight. The solution was cooled to room temperature,

quenched by the addition of 30% NaOH (30 mL), and further diluted with water (10 mL). The aqueous layer was extracted with DCM (3 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel chromatography (20% EtOAc/Hex) afforded the title compound as a colorless oil (932 mg, 95%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.63 (d, 4H, J = 8.0 Hz), 7.55 (d, 1H, J = 8.0 Hz), 7.45 (d, 1H, J = 7.5 Hz), 7.40 (t, 4H, J = 8.0 Hz), 7.21 – 7.22 (m, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 140.6 (d, $J_{C\text{-}P}$ = 13.7 Hz), 137.9 (d, $J_{C\text{-}P}$ =14.4 Hz), 136.3 (d, $J_{C\text{-}P}$ = 22.0 Hz), 133.8 (d, $J_{C\text{-}P}$ = 19.8 Hz), 133.0, 132.5 (d, $J_{C\text{-}P}$ = 19.5 Hz), 131.4 (q, $J_{C\text{-}P}$ = 33.0 Hz), 130.5 (d, $J_{C\text{-}P}$ = 6.8 Hz), 128.8 (d, $J_{C\text{-}P}$ = 24.8 Hz), 125.6 – 125.6 (m), 125.2 (q, $J_{C\text{-}F}$ = 272 Hz), 123.5 (d, $J_{C\text{-}P}$ = 8.4 Hz); **^{19}F NMR** ($CDCl_3$, 470 MHz) δ – 62.9; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.3; **IR**: 1606, 1396, 1166, 1106, 831, 781, 686 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{20}H_{13}Br_1F_6P_1$ $[M+H]^+$: 476.9842, found: 476.9842.

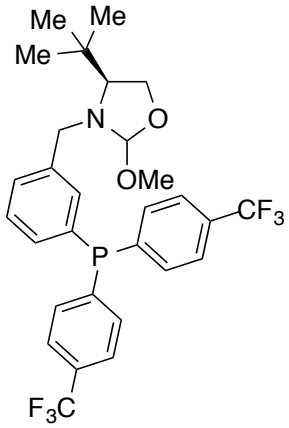


3-(bis(4-(trifluoromethyl)phenyl)phosphanyl)benzaldehyde. To a flame-dried, round-bottom flask was added (3-bromophenyl)-bis((4-trifluoromethyl)phenyl)phosphine (789 mg, 1.84 mmol) and THF (10 mL). The solution was cooled to – 78 °C, *n*-BuLi (0.884 mL, 2.21 mmol, 2.50 M solution in hexane) was added dropwise, and the reaction was stirred for 30 minutes at this temperature. *N,N*-dimethylformamide (0.226 mL, 23.0 mL) was added to the solution and the cold bath was removed. The reaction continued to stir at room temperature for 2 hours and was quenched by the addition of water (10 mL). The aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, a concentrated *in vacuo*. The crude reaction was purified by silica gel chromatography (10% EtOAc/Hex) to afford the title compound as a colorless oil (371 mg, 47%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 9.98 (s, 1H), 7.92 (d, 1H, J = 7.3 Hz), 7.86 (d, 1H, J = 7.8 Hz), 7.64 (d, 4H, J = 7.8 Hz), 7.53 – 7.58 (m, 2H), 7.41 (t, 4H, J = 7.6 Hz); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 191.8, 140.7 (d, $J_{C\text{-}P}$ = 14.3 Hz), 139.6 (d, $J_{C\text{-}P}$ = 19.1 Hz), 137.2 (d, $J_{C\text{-}P}$ = 14.3 Hz), 137.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 135.3 (d, $J_{C\text{-}P}$ = 22.9 Hz), 134.1 (d, $J_{C\text{-}P}$ = 20.2 Hz), 131.7 (q, $J_{C\text{-}F}$ = 32.4 Hz), 130.8, 129.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 125.7 – 125.9 (m), 124.0 (q, $J_{C\text{-}F}$ = 273 Hz); **^{19}F NMR** ($CDCl_3$, 470 MHz) δ – 62.9; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 6.1; **IR**: 3062, 2852, 2302, 1926, 1701, 1397, 1124, 1060, 1016, 794, 600 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{21}H_{14}F_6O_1P_1$ $[M+H]^+$: 427.0687, found: 427.0683.



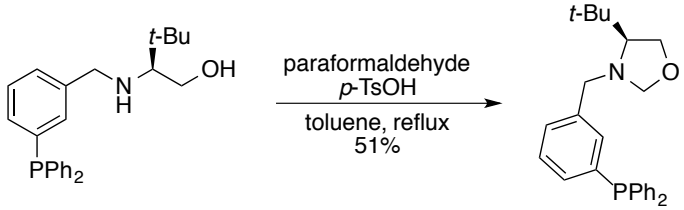
(*S*)-2-((3-(bis(4-(trifluoromethyl)phenyl)phosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol. A suspension of (*S*)-2-amino-3,3-dimethylbutan-1-ol (125 mg mg, 1.07 mmol), 3-(bis(4-(trifluoromethyl)phenyl)phosphanyl)benzaldehyde (350 mg, 0.821 mmol) and activated 4 Å molecular sieves (0.43 g) in THF (8 mL) was heated to 50 °C with vigorous stirring overnight. After cooling to room temperature, the reaction was filtered and concentrated *in vacuo*. The oily residue was re-dissolved in dry methanol (8 mL), the solution cooled to 0°C, and $NaBH_4$ (94 mg, 2.5 mmol) was added portionwise. The reaction was allowed to warm to room temperature over 3 hours and the methanol was removed under reduced pressure. The remaining residue as quenched by the addition of water (10 mL) and extracted with DCM (3 x 20 mL). The combined organic

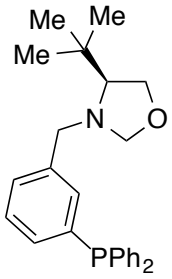
layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue as purified by column chromatography (1% Et_3N/EtOAc) to afford the title compound as a colorless oil (218 mg, 50%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.72 (s, 1H), 7.60 (d, 4H, J = 7.8 Hz), 7.35 – 7.41 (m, 5H), 7.31 (d 1H, J = 7.3 Hz), 7.19 (app t, 1H, J = 7.3 Hz), 3.88 (d, 1H, J = 13.2 Hz), 3.82 (d, 1H, J = 13.2 Hz), 3.61 – 3.64 (m, 1H), 3.37 – 3.40 (m, 1H), 2.32 (dd, 1H, J = 5.9, 4.9 Hz), 0.90 (s, 9H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 141.7 (d, $J_{C\text{-}P}$ = 9.3 Hz), 135.3 (d, $J_{C\text{-}P}$ = 10.4 Hz), 133.8 – 134.6 (6 lines), 133.0 (d, $J_{C\text{-}P}$ = 18.5 Hz), 131.3 (app quartet, $J_{C\text{-}F}$ = 32.4 Hz), 129.8, 129.4 (d, $J_{C\text{-}P}$ = 2.3 Hz), 124.2 (q, $J_{C\text{-}F}$ = 273 Hz), 67.4, 60.4, 54.1, 34.6, 27.5; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.6; **^{19}F NMR** ($CDCl_3$, 470 MHz) δ – 62.9; **IR**: 3415, 2958, 2870, 1477, 1396, 1323, 1127, 1107, 1060, 1016, 997, 832, 599 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{27}H_{29}F_6N_1O_1P_1$ $[M+H]^+$: 528.1891, found: 528.1874; **$[\alpha]_D^{20}$** = + 4.4 (c = 0.540, $CHCl_3$, l = 50 mm).



(4*S*)-3-(3-(bis(4-(trifluoromethyl)phenyl)phosphanyl)benzyl)-4-(*tert*-butyl)-2-methoxyoxazolidine. To a solution of (*S*)-2-((3-(bis(4-(trifluoromethyl)phenyl)phosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol (200 mg, 0.380 mmol) in freshly distilled methanol (6 mL) was added *N,N*-dimethylformamide dimethylacetal (256 μL, 1.90 mmol). The reaction was stirred vigorously at room temperature for 3 hours and the volatiles were removed under high vacuum. The residue was re-dissolved in dry methanol (6 mL) and the reaction was stirred for an additional 2 hours. The volatiles were removed under high vacuum and the crude residue was pumped into the glovebox. The residue as extracted with pentane (2 x 10 mL) and was concentrated under reduced pressure to afford the title compound as a viscous oil (198 mg, 92%). **^{1}H NMR** (C_6D_6, 500 MHz) δ 7.57 (d, 0.6H, J = 7.8 Hz), 7.53 (d, 0.4H, J = 7.8 Hz), 7.41 (d, 0.4H, J = 7.8 Hz), 7.07 – 7.28 (m, 10.6H), 4.98 (s, 0.4H), 4.96 (s, 0.6H), 4.19 (d, 0.4H, J = 13.7 Hz), 3.88 (t, 0.4H, J = 8.1 Hz), 3.85 (d, 0.4H, J = 13.7 Hz), 3.76 (t, 0.6H, J = 8.1 Hz), 3.64 – 3.70 (m, 1.6H), 3.58 (d, 0.6H, J = 15.2 Hz), 2.90 (s, 1.2H), 2.87 (s, 1.8H), 2.52 (dd, 0.4H, J = 7.8, 2.4 Hz), 2.46 (dd, 0.6H, J = 8.8, 7.8 Hz), 0.74 (s, 3.6H), 0.73 (s, 5.4H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 141.7 – 142.0 (5 lines), 141.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 140.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 135.1 (d, $J_{C\text{-}P}$ = 10.4 Hz), 134.8 (d, $J_{C\text{-}P}$ = 9.4 Hz), 133.7 – 134.2 (8 lines), 133.2 (d, $J_{C\text{-}P}$ = 24.3 Hz), 132.8 (d, $J_{C\text{-}P}$ = 24.3 Hz), 131.2 (q, $J_{C\text{-}F}$ = 32.4 Hz), 129.9, 129.8, 129.1 (d, $J_{C\text{-}P}$ = 9.3 Hz), 128.9 (d, $J_{C\text{-}P}$ = 8.1 Hz), 125.6, 124.2 (q, $J_{C\text{-}F}$ = 273 Hz), 115.9, 110.3, 73.3, 68.5, 66.4, 65.4, 60.0, 53.0, 52.4, 52.2, 35.3, 33.8, 26.8, 26.3; **^{31}P NMR** (C_6D_6, 202 MHz) δ – 5.8; **^{19}F NMR** ($CDCl_3$, 564 MHz) δ – 62.9 **IR**: 2956, 1606, 1477, 1396, 1320, 1164, 1124, 1106, 1059, 1016, 998, 831, 700, 599, 514 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{29}H_{31}F_6N_1O_2P_1$ $[M+H]^+$: 570.1997, found: 570.1985; **$[\alpha]_D^{20}$** = + 16.4 (c = 0.475, $CHCl_3$, l = 50 mm).

Synthesis of Ligand 4:

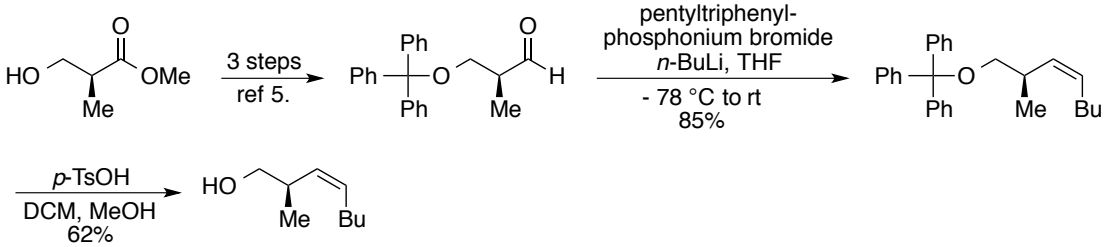


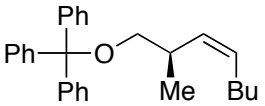


(*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)oxazolidine. To a stirring suspension of (*S*)-2-((3-(diphenylphosphanyl)benzyl)amino)-3,3-dimethylbutan-1-ol (383 mg, 0.979 mmol) and paraformaldehyde (44 mg, 1.5 mmol) in anhydrous toluene (25 mL) was added *p*-toluenesulfonic acid monohydrate (39 mg, 0.20 mmol). The solution was heated to reflux overnight with azeotropic removal of water. The reaction was cooled to room temperature and the volatiles were removed under reduced pressure. The remaining residue was diluted with chloroform (30 mL) and washed with saturated $NaHCO_3$ (15 mL). The aqueous layer was extracted with an additional portion of chloroform (30 mL), the combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (10% EtOAc/Hex) afforded the product as a colorless oil (203 mg, 51%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.27 – 7.36 (m, 13H), 7.19 (t, 1H, J = 7.5 Hz), 4.18 (d, 1H, J = 5.9 Hz), 4.00 (d, 1H, J = 6.4 Hz), 3.95 (t, 1H, J = 8.3 Hz), 3.79 (d, 1H, J = 13.7 Hz), 3.72 (d, 1H, J = 13.2 Hz), 3.50 (dd, 1H, J = 8.8, 7.3 Hz), 2.71 (t, 1H, J = 7.3 Hz), 0.82 (s, 9H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 140.8, 137.5 (d, $J_{C\text{-}P}$ = 10.4 Hz), 137.4 (d, $J_{C\text{-}P}$ = 9.3 Hz), 134.1 (d, $J_{C\text{-}P}$ = 25.4 Hz), 133.9 (d, $J_{C\text{-}P}$ = 18.5 Hz), 132.6 (d, $J_{C\text{-}P}$ = 19.7 Hz), 129.2 128.9, 128.7 (d, $J_{C\text{-}P}$ = 6.9 Hz), 128.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 87.2, 73.6, 66.7, 62.2, 34.6, 26.4; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ – 5.5; **IR**: 2953, 2867, 1477, 1434, 1392, 1157, 1068, 1013, 913, 743, 696, 495 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{26}H_{31}N_1O_1P_1$ $[M+H]^+$: 404.2143, found: 404.2131; **$[\alpha]_D^{20}$** = − 6.4 (c = 0.435, $CHCl_3$, l = 50 mm).

Substrate Syntheses and Characterization

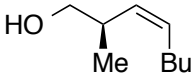
The following compounds were synthesized according to literature procedures and matched all reported spectroscopic data: (*S*)-2-methyl-3-(trityloxy)propanal, [5] 2-(((*R*)-4,4-dibromo-2-methylbut-3-en-1-yl)oxy)tetrahydro-2*H*-pyran, [6] methyl (*S*)-2-(hydroxymethyl)-3-methylbutanoate, [7] (*R*)-2-phenyloxirane, [8] (*R*)-2-(4-chlorophenyl)oxirane,[8] (*R*)-2-(4-bromophenyl)oxirane, [9] (*R*)-2-(4-methoxyphenyl)oxirane, [10] (*R*)-1-(3-(trifluoromethyl)phenyl)ethane-1,2-diol, [11] (*R*)-2-(3-(methoxy)phenyl)oxirane,[8] (*R*,*Z*)-non-3-ene-1,2-diol.[12]



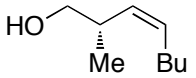


(*R*,*Z*)-(((2-methyloct-3-en-1-yl)oxy)methanetriyl)tribenzene. To a stirring suspension of (1-pentyl)triphenylphosphonium bromide (3.00 g, 7.26 mmol) in THF (30 mL) at – 78 °C was added *n*-butyllithium (2.2 mL, 2.4 M solution in hexane). The reaction was stirred at – 78 °C for 10 minutes and was then allowed to warm to 0 °C over 25 minutes. The bright orange solution was re-cooled to – 78 °C and (*S*)-2-methyl-3-(trityloxy)propanal (1.60 g, 4.84 mmol) was added as a solution in THF (5 mL). The reaction was quenched by the addition of water (20 mL), extracted with Et_2O (3 x 40

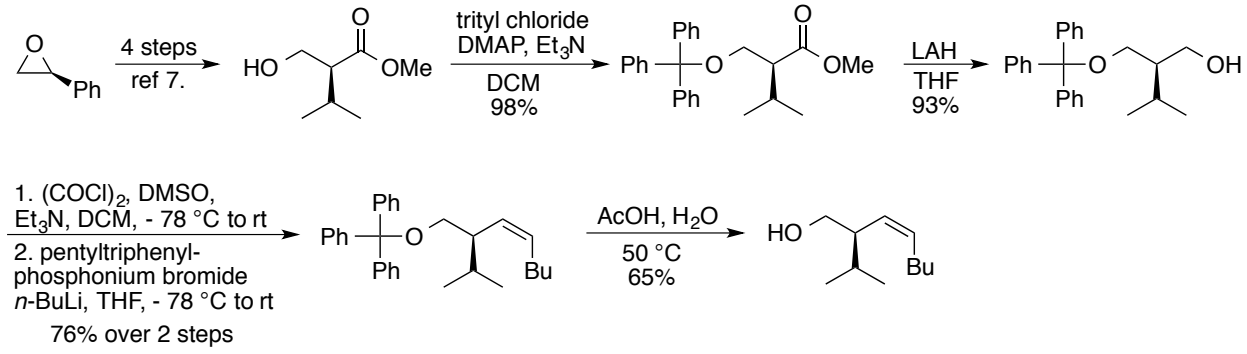
mL), and the combined organic phases were dried over $MgSO_4$. Filtration and removal of the solvent under reduced pressure afforded a yellow residue, which was subjected to silica gel chromatography (15% DCM/Hex) to afford the title compound as a colorless oil (1.58 g, 85%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 – 7.46 (m, 6H), 7.27 – 7.30 (m, 6H), 7.21 – 7.24 (m, 3H), 5.34 – 5.38 (m, 1H), 5.14 – 5.18 (m, 1H), 2.94 – 2.97 (m, 1H), 2.86 – 2.89 (m, 1H), 2.74 – 2.80 (m, 1H), 2.03 – 2.07 (m, 2H), 1.29 – 1.34 (m, 4H), 1.00 (d, 3H, *J* = 6.4 Hz), 0.90 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.7, 133.1, 130.3, 129.0, 127.9, 127.0, 86.4, 68.5, 33.0, 32.3, 27.5, 22.6, 18.4, 14.2; **IR** 2957, 2927, 2870, 1491, 1449, 1065, 1034, 774, 763, 705 cm^{-1}; **HRMS** (ESI$^+$) calcd. for $C_{28}H_{32}O_1Na_1$ $[M+Na]^+$: 407.2351, found: 407.2349; **$[\alpha]_D^{20}$** = − 39.4 (*c* = 0.420, $CHCl_3$, *l* = 50 mm).

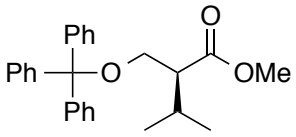


(*R*,*Z*)-2-methyloct-3-en-1-ol. In a round-bottom flask *p*-toluenesulfonic acid monohydrate (635 mg, 3.34 mmol) and (*R*,*Z*)-(((2-methyloct-3-en-1-yl)oxy)methanetriyl)tribenzene (3.21 g, 8.35 mmol) were stirred in dichloromethane (14 mL) and anhydrous methanol (10 mL) overnight. The volatiles were removed *in vacuo* and the residue was partitioned between saturated sodium bicarbonate (20 mL) and dichloromethane (40 mL). The aqueous layer was washed with an additional portion of dichloromethane (40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (15% EtOAc/Hex), affording a colorless oil (743 mg, 62%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.50 – 5.54 (m, 1H), 5.11 (dt, 1H, *J* = 11.2, 1.2 Hz), 3.48 (dd, 1H, *J* = 10.6, 5.9 Hz), 3.33 (dd, 1H, *J* = 10.6, 8.2 Hz), 2.68 – 2.73 (m, 1H), 2.02 – 2.12 (m, 2H), 1.42 (br s, 1H), 1.30 – 1.36 (m, 4H), 0.94 (d, 3H, *J* = 7.0 Hz), 0.89 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 132.7, 132.1, 67.9, 35.0, 32.3, 27.6, 22.6, 17.2, 14.2; **IR** 3330, 2956, 2927, 2972, 1456, 1378, 1068, 1002, 990, 713, 607 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{19}O_1$ $[M+H]^+$: 143.1436, found: 143.1430; **$[\alpha]_D^{20}$** = + 11.8 (*c* = 0.805, $CHCl_3$, *l* = 50 mm).



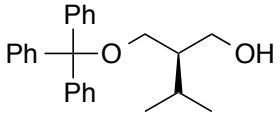
(*S*,*Z*)-2-methyloct-3-en-1-ol. Same experimental procedure followed as (*R*,*Z*)-2-methyloct-3-en-1-ol and all spectral and analytical data are identical except for the optical rotation **$[\alpha]_D^{20}$** = − 9.5 (*c* = 0.745, $CHCl_3$, *l* = 50 mm).



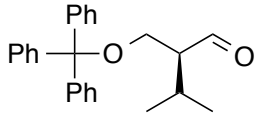


Methyl-(*S*)-3-methyl-2-((trityloxy)methyl)butanoate. Trityl chloride (3.00 g, 10.6 mmol), DMAP (74 mg, 0.59 mmol), methyl-(*S*)-2-(hydroxymethyl)-3-methylbutanoate (865 mg, 5.92 mmol), and dichlormethane (20 mL) were added to a round-bottom flask under nitrogen. Triethylamine (1.64 mL, 11.8 mmol) was added to the vigorously stirred solution

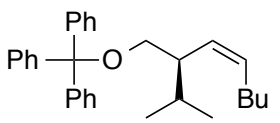
slowly and the reaction was stirred at room temperature overnight. The reaction was quenched by the addition of saturated NH_4Cl (30 mL) and extracted with dichloromethane (2 x 60 mL). The combined organics were washed with water (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reside was purified by silica gel chromatography (10% EtOAc/Hex) to afford the title compound as a viscous oil (2.25 g, 98%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.42 (m, 6H), 7.27 – 7.31 (m, 6H), 7.21 – 7.24 (m, 3H), 3.73 (s, 3H), 3.33 (t, 1H, J = 8.8 Hz), 3.25 (dd, 1H, J = 8.8, 5.4 Hz), 2.39 – 2.44 (m, 1H), 1.86 – 1.90 (m, 1H), 0.89 (t, 3H, J = 7.1 Hz), 0.83 (d, 3H, J = 6.5 Hz), 0.76 (d, 3H, J = 6.8 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.0, 144.2, 128.9, 127.9, 127.2, 86.8, 63.4, 53.5, 51.5, 28.1, 20.8, 20.7; **IR** 1961, 1736, 1491, 1448, 1221, 1195, 1079, 1033, 773, 763, 747, 633 cm^{-1}; **HRMS** (ESI^+) calcd. for $C_{26}H_{28}O_3Na_1$ $[M+Na]^+$: 411.1936, found: 411.1938; **$[\alpha]_D^{20}$** = + 14.3 (*c* = 0.355, $CHCl_3$, *l* = 50 mm).



(*R*)-3-methyl-2-((trityloxy)methyl)butan-1-ol. To a suspension of lithium aluminum hydride (210 mg, 5.52 mmol) in THF (12 mL) at 0 °C was added a solution of methyl-(*S*)-3-methyl-2-((trityloxy)methyl)butanoate (1.43 g, 3.58 mmol) in THF (6 mL). The reaction was allowed to warm to room temperature overnight. After cooling to 0 °C, the reaction was quenched by the slow, drop-wise addition of water (2.5 mL). Anhydrous $MgSO_4$ was added to the flask, and the slurry was filtered and concentrated under reduced pressure to afford the title compound as a viscous colorless oil (1.30 g, 98%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 – 7.45 (m, 6H), 7.29 – 7.33 (m, 6H), 7.23 – 7.26 (m, 3H), 3.72 – 3.76 (m, 1H), 3.65 – 3.70 (m, 1H), 3.38 (dd, 1H, J = 9.3, 3.9 Hz), 3.19 (dd, 1H, J = 9.3, 7.3 Hz), 2.42 (dd, 1H, J= 6.9, 4.9 Hz), 1.72 – 1.77 (m, 1H), 1.59 – 1.62 (m, 1H), 0.83 (d, 3H, J = 6.9 Hz), 0.76 (d, 3H, J = 6.8 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.0, 128.8, 128.1, 127.3, 87.5, 65.3, 64.7, 47.2, 26.9, 20.5; **IR** 3428, 2957, 2974, 1490, 1338, 1219, 1153, 1065, 1031 1002, 762, 745, 704, 648 cm^{-1}; **HRMS** (ESI^+) calcd. for $C_{25}H_{28}O_2Na_1$ $[M+Na]^+$: 383,1987, found: 383.1990; **$[\alpha]_D^{20}$** = + 23.1 (*c* = 0.170, $CHCl_3$, *l* = 50 mm).

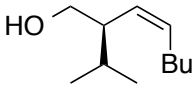


(*S*)-3-methyl-2-((trityloxy)methyl)butanal. To a solution of oxalyl chloride (1.10 mL, 12.5 mmol) in DCM (31 mL) at – 78 °C was added DMSO (2.20 mL, 31.3 mmol). After stirring at this temperature for 30 minutes a solution of (*R*)-3-methyl-2-((trityloxy)methyl)butan-1-ol (2.26 g, 6.27 mmol) in DCM (6 mL) was added drop-wise. The reaction mixture was stirred at – 78 °C for a further 45 minutes before Et_3N (3.50 mL, 25.0 mmol) was added drop-wise to the solution. After 15 minutes, the mixture was warmed to 0 °C and quenched by the addition of water (30 mL) then extracted with DCM (2 x 50 mL). The combined organic layers were washed with saturated $NaHCO_3$ (30 mL), brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a yellow oil that was used in the next reaction immediately without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.66 (d, 1H, J = 3.5 Hz), 7.36 – 7.39 (m, 6H), 7.24 – 7.26 (m, 6H), 7.20 – 7.22 (m, 3H), 3.35 (d, 2H, J = 6.0 Hz), 2.26 – 2.30 (m, 1H), 2.05 – 2.08 (m, 1H), 0.85 (d, 3H, J = 7.0 Hz), 0.77 (d, 3H, J = 6.5 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 205.0, 143.9, 128.8, 128.0, 127.3, 87.1, 61.2, 59.0, 26.2, 20.7, 20.2.

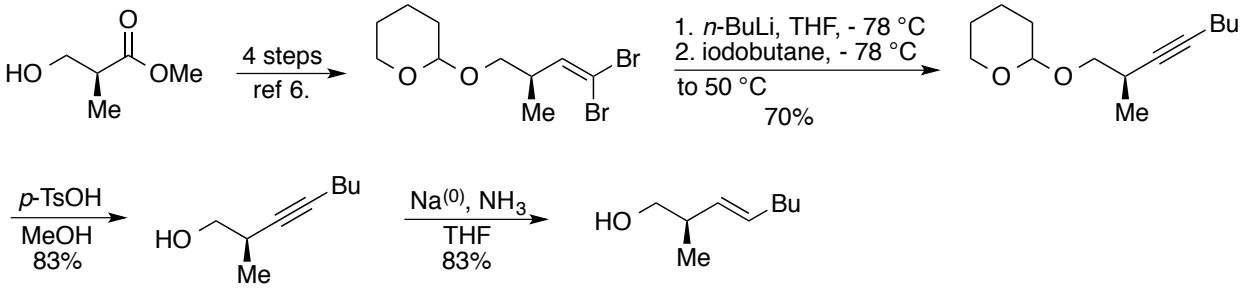


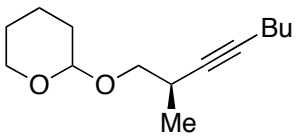
(*R*,*Z*)-(((2-isopropyloct-3-en-1-yl)oxy)methanetriyl)tribenzene. To a suspension of (1-pentyl)triphenylphosphonium bromide (3.12 g, 7.56 mmol) in THF (40 mL) at –78 °C was added *n*-butyllithium (3.00 mL,

6.93 mmol, 2.30 M in pentane). The bright solution was stirred at -78 °C for 15 minutes, warmed to 0 °C over 30 minutes, and re-cooled to –78 °C. (*S*)-3-methyl-2-((trityloxy)methyl)butanal (2.26 g, 6.30 mmol) was added as a solution in THF (6 mL) and the reaction was allowed to warm to room temperature overnight. The reaction was quenched by the addition of water (30 mL) and extracted with diethyl ether (2 x 60 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography (10% DCM/Hex) afforded the title compound as a colorless oil (1.98 g, 76%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 – 7.46 (m, 6H), 7.27 – 7.30 (m, 6H), 7.20 – 7.23 (m, 3H), 5.47 – 5.52 (m, 1H), 5.21 – 5.26 (m, 1H), 2.97 – 3.04 (m, 2H), 2.46 – 2.49 (m, 1H), 2.05 – 2.08 (m, 2H), 1.84 – 1.89 (m, 1H), 1.31 – 1.35 (m, 4H), 0.90 (t, 3H, *J* = 6.9 Hz), 0.77 (d, 3H, *J* = 6.9 Hz), 0.74 (d, 3H, *J* = 6.8 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.7, 131.9, 129.6, 129.0, 127.8, 127.0, 65.6, 44.1, 32.3, 29.0, 27.7, 22.7, 21.1, 18.8, 14.3; **IR** 2955, 2925, 2870, 1490, 1448, 1068, 1032, 898, 762, 744, 632 cm^{-1}; **HRMS** (ESI^+) calcd. for $C_{30}H_{36}O_1Na_1$ $[M+Na]^+$: 435.2664, found: 435.2659; **$[\alpha]_D^{20}$** = − 44.8 (*c* = 0.525, $CHCl_3$, *l* = 50 mm).



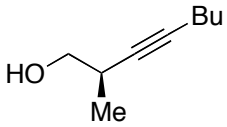
(*R*,*Z*)-2-isopropyloct-3-en-1-ol. A solution of glacial acetic acid (32 mL), water (3.5 mL), and (*R*,*Z*)-(((2-isopropyloct-3-en-1-yl)oxy)methanetriyl)tribenzene (1.98 g, 4.80 mmol) was heated to 50 °C for 5 hours. The reaction was cooled to room temperature and the volatiles removed under reduced pressure. Trityl alcohol was precipitated out by the addition of hexane and filtered off. The organic layer was concentrated *in vacuo* and the crude reside was subjected to column chromatography (7% EtOAc/Hex) to afford the title compound as a colorless oil (531 mg, 65%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.65 – 5.70 (m, 1H), 5.12 – 5.16 (m, 1H), 3.66 – 3.68 (m, 1H), 3.34 – 3.37 (m, 1H), 2.05 – 2.10 (m, 2H), 1.57 – 1.64 (m, 1H), 1.32 – 1.35 (m, 5H), 0.91 (d, 3H, *J* = 6.8 Hz), 0.89 – 0.91 (m, 3H), 0.86 (d, 3H, *J* = 6.8 Hz); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 134.9, 129.1, 64.9, 46.8, 32.2, 29.4, 27.8, 22.6, 21.0, 19.9, 14.2; **IR** 3331, 2956, 2927, 1465, 1214, 1060, 1034, 1013, 750, 668 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{23}O_1$ $[M+H]^+$: 171.1749, found: 171.1747; **$[\alpha]_D^{20}$** = − 3.3 (*c* = 0.470, $CHCl_3$, *l* = 50 mm).



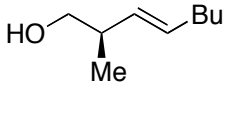


2-(((*R*)-2-methyloct-3-yn-1-yl)oxy)tetrahydro-2*H*-pyran. To a solution of 2-(((*R*)-4,4-dibromo-2-methylbut-3-en-1-yl)oxy)tetrahydro-2*H*-pyran (2.18 g, 6.64 mmol) in THF (50 mL) at – 78 °C was added *n*-BuLi (6.10 mL, 14.6 mmol, 2.40 M solution in hexane). The reaction was stirred at this temperature for 45 minutes and 1-iodobutane (3.80 mL, 33.3 mmol) was added. After warming the room temperature over 40 minutes, the reaction was heated to 55 °C for 3 hours. The reaction was cooled to room temperature, quenched by the addition of saturated

aqueous NH_4Cl (30 mL), diluted further with water (5 mL), and extracted with dichloromethane (2 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography (3% EtOAc/Hex) afforded the title compound as a colorless oil that exists as a 1:1 mixture of diastereomers (1.04 g, 70%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.65 (t, 0.5H, *J* = 3.4 Hz), 4.63 (t, 0.5H, *J* = 3.4 Hz), 3.84 – 3.91 (m, 1H), 3.73 (dd, 0.5H, *J* = 9.5, 6.1 Hz), 3.55 (dd, 0.5H, *J* = 9.5, 8.1 Hz), 3.50 – 3.51 (m, 1H), 3.45 (dd, 0.5H, *J* = 9.3, 6.4 Hz), 3.25 (dd, 0.5H, *J* = 9.5, 7.6 Hz), 2.66 – 2.70 (m, 1H), 2.14 (t, 2H, *J* = 6.9 Hz), 1.82 – 1.85 (m, 1H), 1.68 – 1.73 (m, 1H), 1.36 – 1.63 (m, 8H), 1.17 (d, 3H, *J* = 6.9 Hz), 0.89 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 99.1, 98.8, 82.3, 82.2, 81.3, 81.2, 72.1, 72.0, 62.4, 622, 31.4, 31.3, 30.8, 30.7, 27.0, 26.9, 25.7, 22.1, 19.6, 19.5, 18.6, 18.5, 18.4, 13.8; **IR** 2933, 2812, 1123, 1061, 1034, 973 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{25}O_2$ $[M+H]^+$: 225.1855, found: 225.1855.



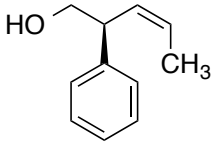
(*R*)-2-methyloct-3-yn-1-ol. To a round-bottom flask containing *p*-TsOH monohydrate (130 mg, 0.674 mmol) was added 2-(((*R*)-2-methyloct-3-yn-1-yl)oxy)tetrahydro-2*H*-pyran (1.51 g, 6.74 mmol) in anhydrous methanol (20 mL). The reaction was allowed to stir at room temperature until all starting material was consumed (approx. 3 hours). The solution was transferred to a separatory funnel, diluted with dichloromethane (40 mL) and washed with saturated aqueous $NaHCO_3$ (15 mL). The layers were separated and the aqueous layer was extracted with an additional portion of dichloromethane (30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Silica gel chromatography (15% EtOAc/Hex) afforded the title compound as a colorless oil (788 mg, 83%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.53 (dd, 1H, *J* = 10.3, 5.6 Hz), 3.44 (dd, 1H, *J* = 10.3, 7.1 Hz), 2.62 – 2.65 (m, 1H), 2.16 (dt, 2H, *J* = 7.3, 2.2 Hz), 1.81 (br s, 1H), 1.45 – 1.49 (m, 2H), 1.35 – 1.44 (m, 2H), 1.13 (d, 3H, *J* = 7.1 Hz), 0.90 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 82.9, 81.5, 67.3, 31.3, 29.8 22.1, 18.6, 17.5, 13.8; **IR** 3340, 2958, 2932, 2874, 1457, 1379, 1329, 1039, 1015 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{17}O_1$ $[M+H]^+$: 141.1279, found: 141.1281; **$[\alpha]_D^{20}$** = + 15.2 (*c* = 1.13, $CHCl_3$, *l* = 50 mm).



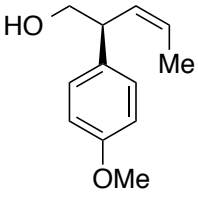
(*R*,*E*)-2-methyloct-3-en-1-ol. A flame-dried, three-neck, round-bottom flask fitted with a dry ice condenser was charged with ammonia (7.2 mL) at – 78 °C. Sodium metal (328 mg, 14.3 mmol) was added piece-wise at this temperature, upon which time the solution turned deep blue. The solution was allowed to stir while warming to – 35 °C over 20 minutes and (*R*)-2-methyloct-3-yn-1-ol (0.500 g, 3.57 mmol) was added drop-wise as a solution in THF (4 mL). The reaction was allowed to stir for 3 hours at – 30 °C and was quenched by the careful addition of solid NH_4Cl (approx 10 eq). The ammonia was allowed to evaporate and the reaction mixture was diluted with water (15 mL). Extraction with dichloromethane (2 x 30 mL), followed by drying over $MgSO_4$ and concentration *in vacuo* showed that trace amounts of starting material remained. The crude residue was re-subjected to the same reaction conditions and work-up procedure. Purification on a short plug of silica afforded the title compound as a colorless oil (419 mg, 83%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.50 – 5.55 (m, 1H), 5.22 – 5.26 (m, 1H), 3.44 – 3.48 (m, 1H), 3.32 – 3.36 (m, 1H), 2.27 – 2.32 (m, 1H), 2.00 – 2.02 (m, 2H), 1.44 (br s, 1H), 1.26 – 1.37 (m, 4H), 0.97 (d, 3H, *J* = 7.0 Hz), 0.88 (d, 3H, *J* = 7.0 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 132.7, 132.4, 67.5, 40.0, 32.5, 31.9, 22.4, 16.8, 14.1; **IR** 3340, 2957, 2924, 2972, 1457, 1378, 1034, 968 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{19}O_1$ $[M+H]^+$: 143.1436, found: 143.1433; **$[\alpha]_D^{20}$** = + 17.8 (*c* = 0.920, $CHCl_3$, *l* = 50 mm).

General Procedure for the Preparation of Aryl Substrates

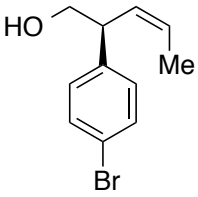
General Procedure A: To a suspension enantiopure aryloxirane (1 equiv) and CuCl(COD) (0.10 equiv) in THF (0.40 M) at – 78 °C was added (*Z*)-prop-1-en-1-ylmagnesium bromide (1.5 equiv, 1.0 M solution in THF). The reaction was allowed to warm to room temperature over 8 hours, quenched by the addition of water (15 mL), and extracted with EtOAc (2 x 40 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reside was subjected to silica gel chromatography (20% EtOAc/Hex) to afford the title compound.



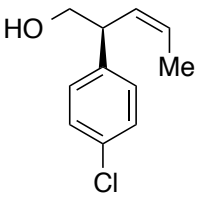
(*S*,*Z*)-2-phenylpent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-phenyloxirane (1.64 mL, 19.3 mmol) to afford the title compound as a colorless oil (1.43 g, 46%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 – 7.34 (m, 2H), 7.22 – 7.27 (m, 3H), 5.71 – 5.74 (m, 1H), 5.59 – 5.64 (m, 1H), 3.85 – 3.90 (m, 1H), 3.79 – 3.81 (m, 1H), 3.70 – 3.73 (m, 1H), 1.70 (dd, 3H, *J* = 6.5, 1.5 Hz), 1.47 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.8, 130.2, 129.0, 128.0, 127.6, 126.9, 67.2, 46.3, 13.5; **IR** 3560, 3026, 1493, 1452, 1050, 757, 714, 699, 668 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{13}$ $[M+H-H_2O]^+$: 145.1018, found: 145.1020; **$[\alpha]_D^{20}$** = + 164.0 (*c* = 0.440, $CHCl_3$, *l* = 50 mm).



(*S*,*Z*)-2-(4-methoxyphenyl)pent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-(4-methoxyphenyl)oxirane (795 mg, 5.29 mmol) to afford the title compound as a yellow oil (674 mg, 85%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 (d, 2H, *J* = 8.3 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 5.68 – 5.72 (m, 1H), 5.56 – 5.60 (m, 1H), 3.80 – 3.85 (m, 1H), 3.79 (s, 3H), 3.74 – 3.78 (m, 1H), 3.66 – 3.70 (m, 1H), 1.69 (dd, 3H, *J* = 6.8, 2.0 Hz), 1.45 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.6, 133.7, 130.5, 128.9, 127.3, 114.4, 67.3, 55.5, 45.4, 13.5; **IR** 3394, 3011, 2934, 2836, 1610, 1511, 1464, 1248, 1178, 1036, 828, 703 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{15}O_1$ $[M+H-H_2O]^+$: 175.1123, found: 175.1127; **$[\alpha]_D^{20}$** = + 156.5 (*c* = 0.450, $CHCl_3$, *l* = 50 mm).

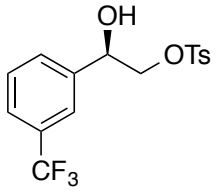


(*S*,*Z*)-2-(4-bromophenyl)pent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-(4-bromophenyl)oxirane (1.00 g, 5.02 mmol) to afford the title compound as a yellow oil (662 mg, 55%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, 2H, *J* = 8.3 Hz), 7.13 (d, 2H, *J* = 8.3 Hz), 5.70 – 5.75 (m, 1H), 5.54 – 5.58 (m, 1H), 3.81 – 3.84 (m, 1H), 3.76 – 3.79 (m, 1H), 3.70 (dd, 1H, *J* = 10.8, 7.3 Hz), 1.68 (d, 3H, *J* = 6.9 Hz), 1.47 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.9, 132.0, 129.7, 129.6, 128.1, 120.7, 67.0, 45.7, 13.5; **IR** 3362, 3016, 2930, 2874, 1487, 1377, 1214, 1072, 1052, 1010, 819, 785, 729, 668 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{12}Br_1$ $[M+H-H_2O]^+$: 223.0122, found: 223.0115; **$[\alpha]_D^{20}$** = + 133.4 (*c* = 0.710, $CHCl_3$, *l* = 50 mm).

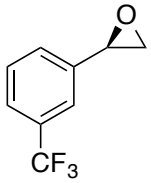


(*S*,*Z*)-2-(4-chlorophenyl)pent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-(4-chlorophenyl)oxirane (1.88 g, 12.2 mmol) to afford the title compound as a yellow oil (700 mg, 30%). **^{1}H NMR** (500 MHz,

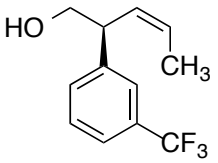
$CDCl_3$) δ 7.29 (d, 2H, J = 8.3 Hz), 7.18 (d, 2H, J = 8.3 Hz), 5.71 – 5.75 (m, 1H), 5.54 – 5.58 (m, 1H), 3.82 – 3.87 (m, 1H), 3.76 – 3.79 (m, 1H), 3.68 – 3.72 (m, 1H), 1.68 (d, 3H, J = 6.8 Hz), 1.48 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.4, 132.6, 129.7, 129.3, 129.0, 128.0, 67.1, 45.6, 13.5; **IR** 3362, 2932, 2875, 1491, 1092, 1048, 1014, 823, 735, 582 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{23}Cl_1$ $[M+H-H_2O]^+$: 179.0628, found: 179.0634; **$[\alpha]_D^{20}$** = + 166.1 (c = 0.870, $CHCl_3$, l = 50 mm).



(*R*)-2-hydroxy-2-(3-(trifluoromethyl)phenyl)ethyl 4-methylbenzenesulfonate. To a solution of (*R*)-1-(3-(trifluoromethyl)phenyl)ethane-1,2-diol (3.00 g, 13.8 mmol) in anhydrous pyridine (59 mL) at 0 °C was added *p*-toluenesulfonyl chloride (2.90 g, 15.2 mmol). The reaction was stirred under nitrogen overnight while warming to room temperature. The reaction was quenched by the addition of water (20 mL) and the aqueous layer was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reside was purified by silica gel chromatography (20% EtOAc/Hex) to afford the title compound as a yellow oil (2.32 g, 44%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, 2H, J = 8.3 Hz), 7.47 – 7.57 (m, 3H), 7.45 (d, 1H, J = 7.6 Hz), 7.32 (d, 2H, J = 8.3 Hz), 5.03 – 5.06 (m, 1H), 4.16 (dd, 1H, J = 10.8, 3.4 Hz), 4.04 (dd, 1H, J = 10.5, 8.1 Hz), 2.87 (br s, 1H), 2.43 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.2, 139.6, 132.6, 131.5 (q, J_{C-F} = 32.4 Hz), 130.2, 129.9, 129.4, 128.1, 125.5, 124.1 (q, J_{C-F} = 273 Hz), 123.3, 74.1, 71.6, 29.1; **^{19}F NMR** (470 MHz, $CDCl_3$) δ – 62.7; **IR** 3394, 3513, 1357, 1329, 1190, 1173, 1124, 1097, 1073, 974, 828, 811, 750, 703, 670, 662, 554 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{19}F_3N_1O_4S_1$ $[M+NH_4]^+$: 378.0987, found: 378.0979; **$[\alpha]_D^{20}$** = − 33.6 (c = 0.780, $CHCl_3$, l = 50 mm).

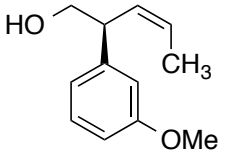


(*R*)-2-(3-(trifluoromethyl)phenyl)oxirane. A solution of (*R*)-2-hydroxy-2-(3-(trifluoromethyl)phenyl)ethyl 4-methylbenzenesulfonate (2.00 g, 5.39 mmol) in THF (9 mL) and 6 M aqueous NaOH (9 mL) was stirred vigorously at room temperature for 4 hours. The reaction was diluted with water (15 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford the pure epoxide as a colorless oil (1.00 g, 93%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 – 7.57 (m, 1H), 7.54 (s, 1H), 7.46 – 8.47 (m, 2H), 3.92 (dd, 1H, J = 3.9, 2.5 Hz), 3.18 (dd, 1H, J = 5.4, 4.4 Hz), 2.89 (dd, 1H, J = 5.6, 2.7 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.0, 131.3 (q, J_{C-F} = 32.4 Hz), 129.2, 129.0, 125.2, 124.1 (q, J_{C-F} = 273 Hz), 122.5, 52.0, 51.5; **^{19}F NMR** (470 MHz, $CDCl_3$) δ – 62.8; **IR** 2956, 2924, 2365, 2359, 1329, 1165, 1126, 1099, 1073, 1031, 803 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_8F_3O_1$ $[M+H]^+$: 189.0527, found: 189.0531; **$[\alpha]_D^{20}$** = − 3.4 (c = 0.860, $CHCl_3$, l = 50 mm).

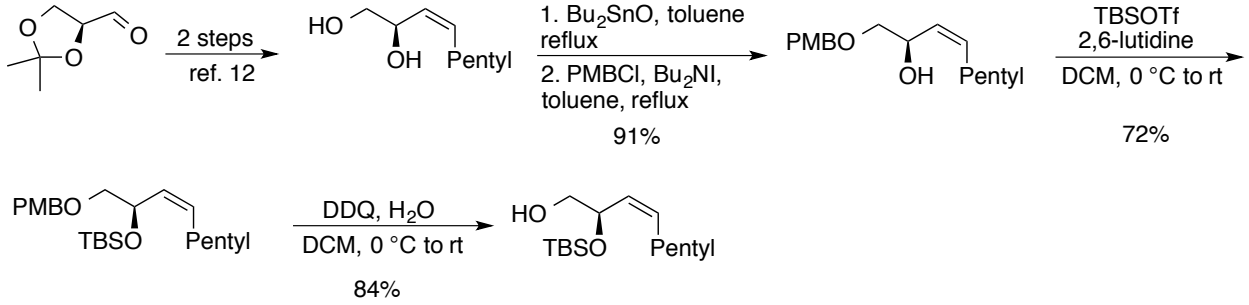


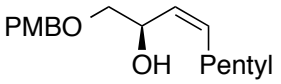
(*S*,*Z*)-2-(3-(trifluoromethyl)phenyl)pent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-(3-(trifluoromethyl)phenyl)oxirane (700 mg g, 3.72 mmol) to afford the title compound as a yellow oil (376 mg, 44%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 – 7.50 (m, 4H), 5.75 – 5.79 (m, 1H), 5.58 – 5.63 (m, 1H), 3.91 – 3.96 (m, 1H), 3.81 (dd, 1H, J = 10.9, 6.4 Hz), 3.75 (dd, 1H, J = 7.3, 3.4 Hz), 1.70 (d, 3H, J = 6.9 Hz), 1.51 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.9, 131.4, 131.2 (q, J_{C-F} = 31 Hz), 129.3, 129.2, 128.5, 124.7, 124.3 (q, J_{C-F} = 273 Hz), 123.8,

67.0, 46.0, 13.5; **^{19}F NMR** (470 MHz, $CDCl_3$) δ – 62.6; **IR** 3362, 1447, 1328, 1163, 1123, 1095, 802, 718, 702 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{12}F_3$ $[M+H-H_2O]^+$: 213.0891, found: 213.0892; **$[\alpha]_D^{20}$** = + 108.1 (*c* = 0.515, $CHCl_3$, *l* = 50 mm).

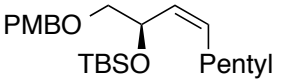


(*S*,*Z*)-2-(3-methoxyphenyl)pent-3-en-1-ol. Synthesized according to General Procedure A using (*R*)-2-(3-(methoxy)phenyl)oxirane (630 mg, 4.20 mmol) to afford the title compound as a yellow oil (270 mg, 34%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (t, 1H, *J* = 7.8 Hz), 6.86 (d, 1H, *J* = 7.8 Hz), 6.77 – 6.80 (m, 2H), 5.70 – 5.74 (m, 1H), 5.57 – 5.62 (m, 1H), 3.85 – 3.87 (m, 1H), 3.80 (s, 3H), 3.78 – 3.82 (m, 1H), 3.71 – 3.73 (m, 1H), 1.70 (d, 3H, *J* = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.1, 143.4, 130.1, 129.9, 127.7, 120.3, 114.0, 112.0, 67.1, 55.4, 46.3, 13.5; **IR** 3389, 2933, 2875, 1600, 1584, 1488, 1465, 1453, 1433, 1288, 1152, 1047, 778, 697 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{15}O_1$ $[M+H-H_2O]^+$: 175.1123, found: 173.1130; **$[\alpha]_D^{20}$** = + 207.6 (*c* = 0.375, $CHCl_3$, *l* = 50 mm).



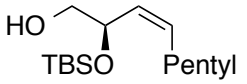


(*R*,*Z*)-1-((4-methoxybenzyl)oxy)non-3-en-2-ol. A round-bottom flask was charged with (*R*,*Z*)-non-3-ene-1,2-diol (200 mg, 1.26 mmol), dibutyltin oxide (430 mg, 1.71 mmol), and toluene (10 mL). The reaction was heated to reflux with azeotropic removal of water overnight. The reaction was cooled to room temperature and the Dean-Stark apparatus was removed. To the flask was added tetrabutylammonium iodide (650 mg, 1.76 mmol) and 4-methoxybenzyl chloride (276 mg, 1.76 mmol) and the reaction was heated to reflux for 4 hours. After cooling to room temperature, the reaction was quenched with water (10 mL) and extracted with DCM (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (12% EtOAc/Hex) afforded the title compound as a colorless oil (318 mg, 91%, contains 30% of an inseparable impurity). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J* = 9.3 Hz), 6.88 (d, 2H, *J* = 8.3 Hz), 5.54 – 5.56 (m, 1H), 5.34 – 5.35 (m, 1H), 4.63 – 4.65 (m, 1H), 4.50 (m, 2H), 3.81 (s, 3H), 3.42 (dd, 1H, *J* = 9.5, 3.8 Hz), 3.33 (dd, 1H, *J* = 9.8, 8.3 Hz), 2.37 (br s, 1H), 2.02 – 2.12 (m, 2H), 1.24 – 1.38 (m, 6H), 0.88 (t, 3H, *J* = 7.1 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.7, 134.6, 129.7, 129.6, 127.9, 114.1, 74.0, 73.2, 67.1, 55.5, 31.6, 29.5, 28.1, 22.7, 14.2; **IR** 3448, 3007, 2955, 2927, 2856, 1612, 1586, 1513, 1464, 1247, 1174, 1100, 1074, 1036, 821, 756 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{17}H_{30}N_1O_3$ $[M+NH_4]^+$: 296.2226, found: 296.2235; **$[\alpha]_D^{20}$** = − 36.8 (*c* = 0.445, $CHCl_3$, *l* = 50 mm).

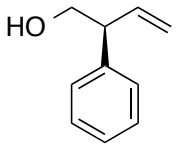


(*R*,*Z*)-*tert*-butyl((1-((4-methoxybenzyl)oxy)non-3-en-2-yl)oxy)dimethylsilane. To a 50-mL round-bottom flask was added (*R*,*Z*)-1-((4-methoxybenzyl)oxy)non-3-en-2-ol (318 mg, 1.14 mmol),

2,6-lutidine (0.33 mL, 2.9 mmol), and DCM (11 mL). The solution was cooled to 0 °C and TBSOTf (0.52 mL, 2.3 mmol) was added slowly over 3 minutes. The reaction was allowed to warm to room temperature over 90 minutes, quenched by the addition of saturated NH_4Cl (15 mL), and extracted with DCM (2 x 30 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (1% EtOAc/Hex) to afford the product as a colorless oil (301 mg, 67%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (app dd, 2H, *J* = 6.4, 2.0 Hz), 6.86 (app dd, 2H, *J* = 6.4, 2.0 Hz), 5.40 – 5.45 (m, 1H), 5.30 – 5.34 (m, 1H), 4.62 – 4.65 (m, 1H), 4.57 (d, 1H, *J* = 11.7 Hz), 4.50 (d, 1H, *J* = 11.7 Hz), 3.81 (s, 3H), 3.41 (dd, 1H, *J* = 10.0, 7.1 Hz), 3.33 (dd, 1H, *J* = 10.3, 4.9 Hz), 2.01 – 2.06 (m, 2H), 1.25 – 1.36 (m, 6H), 0.89 (s, 9H), 0.88 (t, 3H, *J* = 8.3 Hz), 0.070 (s, 3H), 0.056 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.2, 131.6, 131.0, 130.8, 129.3, 113.9, 75.0, 73.2, 68.9, 55.5, 31.8, 29.5, 28.2, 26.1, 22.7, 18.5, 14.2, -4.3, -4.4; **IR** 2955, 2928, 2855, 1513, 1463, 1248, 1172, 1120, 1091, 1039, 1006, 834, 776 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{23}H_{39}O_2Si_1$ $[M+H-H_2O]^+$: 375.2719, found: 375.2718; $[\alpha]_D^{20}$ = − 7.6 (*c* = 0.620, $CHCl_3$, *l* = 50 mm).



(*R*,*Z*)-2-((*tert*-butyldimethylsilyl)oxy)non-3-en-1-ol. . To a vigorously stirred solution of (*R*,*Z*)-*tert*-butyl((1-((4-methoxybenzyl)oxy)non-3-en-2-yl)oxy)dimethylsilane (150 mg, 0.38 mmol), DCM (6 mL), and water (1.5 mL) at 0 °C was added DDQ (106 mg). The reaction was allowed to warm to room temperature over 2 hours and was quenched by the addition of a 1:1:1 mixture of saturated aqueous sodium thiosulfate:saturated aqueous sodium bicarbonate:water (10 mL). The aqueous layer was extracted with DCM (2 x 30 mL) and the combined organic layers were dried over $MgSO_4$. Filtration, and removal of the solvent *in vacuo* afforded a crude residue which was purified by silica gel chromatography (10% EtOAc/Hex) to afford the title compound as a colorless oil (87 mg, 84%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.44 – 5.49 (m, 1H), 5.26 – 5.30 (m, 1H), 4.51 – 4.55 (m, 1H), 3.40 (dd, 2H, *J* = 7.1, 5.6 Hz), 1.98 – 2.08 (m, 3H), 1.25 – 1.38 (m, 6H), 089 (s, 9H), 0.88 (t, 3H, *J* = 8.3 Hz), 0.081 (s, 3H), 0.058 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 132.7, 129.9, 70.2, 66.9, 31.7, 29.5, 28.1, 26.0, 22.7, 18.3, 14.2, -4.0, -4.6; **IR** 3439, 2956, 2928, 2857, 1463, 1235, 1095, 1062, 1036, 1005, 835, 812 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{15}H_{31}O_1Si_1$ $[M+H-H_2O]^+$: 255.2144, found: 255.2140; $[\alpha]_D^{20}$ = + 4.0 (*c* = 0.315, $CHCl_3$, *l* = 50 mm).



(*S*)-2-phenylbut-3-en-1-ol. To a suspension of (*R*)-phenyloxirane (1.00 g, 8.32 mmol) and CuCl(COD) (172 mg, 0.84 mmol) in THF (12 mL) at – 78 °C was added vinylmagnesium bromide (10.0 mL, 10.0 mmol, 1.0 M solution in THF). The reaction as allowed to warm to room temperature over 8 hours. The reaction was quenched by the addition of saturated NH_4Cl (30 mL) and extracted with ethyl acetate (3 x 40 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10% EtOAc/Hex) to afford the title compound as a colorless oil (872 mg, 71%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.37 (m, 2H), 7.24 – 7.27 (m, 3H), 5.99 – 6.06 (m, 1H), 5.18 – 5.24 (m, 2H), 3.83 – 3.85 (m, 2H), 3.54 (q, 1H, *J* = 7.3 Hz), 1.53 (br s); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.8, 138.4, 129.0, 128.2, 127.2, 117.3, 66.3, 52.7; **IR** 3355, 3028, 2876, 1493, 1453, 1054, 1029, 994, 918, 756, 700, 680 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{11}$ $[M+H-H_2O]^+$: 131.0861, found: 131.0867; $[\alpha]_D^{20}$ = + 67.5 (*c* = 0.545, $CHCl_3$, *l* = 50 mm).

Hydroformylation Products

Table 2 – Substrate Table

General Hydroformylation Procedure. The Endeavor was charged with 500 μL of benzene per reaction well to fill the void volume between reactor wall and reaction tube, and oven dried glass reaction vials were placed into the wells. The Endeavor was sealed and purged with nitrogen (4×100 psi). The necessary injection(s) were made (see below). The Endeavor was purged with nitrogen (1×100 psi), stirring was started at 250 rpm, and the Endeavor was heated to and held at 55 ˚C for 10 minutes. Stirring was stopped, the Endeavor was charged with 400 psi H_2/CO, stirring was re-initiated at 700 rpm, and the Endeavor was maintained at constant reaction temperature of 55 °C and pressure of 400 psi H_2/CO for 15 h. The Endeavor was vented to ambient pressure and cooled to ambient temperature. The reaction vials were removed from the Endeavor, and the benzene was removed *in vacuo.* A solution of mesitylene in chloroform-*d* (100 μL, 0.5408 M) was added. The conversion of the reaction was determined by ^{1}H NMR in chloroform-*d* with respect to remaining starting material. The solvent was removed under reduced pressure. The crude hydroformylation mixture was added, as a solution in dichloromethane (3 mL), to a scintillation vial containing pyridinium chlorochromate (128.7 mg, 0.597 mmol), sodium acetate (16.0 mg, .195 mmol), and 4 Å molecular sieves. The reaction was stirred for 12 hours at room temperature and eluted through a short plug of silica gel (100% Et_2O). The regio- and diastereoselectivities were determined by either GC or ^{1}H NMR.

General Procedure A: In a dry box, (*R*,*Z*)-2-methyloct-3-en-1-ol (28.4 mg, 0.200 mmol), (4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine (8.7 mg, 0.020 mmol), a *p*-toluenesulfonic acid in benzene (351 μL, 2.0 x 10^{-4} mmol, 5.7 x 10^{-4} M solution) were mixed in C_6D_6 (0.8 mL) and allowed to equilibrate in a sealed NMR tube for 3 hours at 45 °C. (Note: the appearance of free MeOH can be monitored by ^{1}H NMR.) The solution was concentrated in the dry box to remove the generated MeOH, the residue was re-dissolved in C_6D_6, and was allowed to equilibrate for an additional 3 hours at 45 °C before being concentrated again in the dry box. The resulting mixture was dissolved in benzene (3.5 mL), mixed with 3% Rh(acac)$(CO)_2$ (1.5 mg, 0.006 mmol), and injected into the Endeavor, followed by 0.5 mL benzene to wash the injection port.

General Procedure B: Same as General Procedure A, except 20% (4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine (17.3 mg, 0.040 mmol) and 6% Rh(acac)$(CO)_2$ (3.1 mg, 0.012 mmol) were used.

General Procedure C: Same as General Procedure A, except 12% (4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine (10.4 mg, 0.024 mmol) and 4% Rh(acac)$(CO)_2$ (2.1 mg, 0.008 mmol) were used.

General Procedure D: Same as General Procedure A, except 5% (4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine (4.4 mg, 0.010 mmol) and 2% Rh(acac)$(CO)_2$ (1.1 mg, 0.004 mmol) were used.

Gas Chromatography Analysis Methods

GC Method A: J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness): 120 °C for 8 min, ramp 8 °C/min to 136 °C, 136 °C for 2 min, ramp 10 °C/min to a final temperature of 220 °C, 220 °C for 3 min.

GC Method B: J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness): 120 °C for 8 min, ramp 8 °C/min to 136 °C, 136 °C for 1 min, ramp 10 °C/min to a final temperature of 220 °C, 220 °C for 6 min.

GC Method C: Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness) 60 °C for 5 min, ramp 1 °C/min to 150 °C, 150 °C for 10 min, ramp 8 °C/min to a final temperature of 220 °C.

GC Method D: J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness): 140 °C for 6 min, ramp 40 °C/min to 220 °C, 220 °C for 5 min.

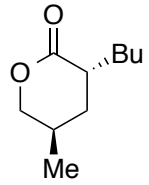
GC Method E: J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness): 140 °C for 3 min, ramp 8 °C/min to 220 °C, 220 °C for 10 min.

GC Method F: J&W Scientific column (HP-5, 30 m x 0.320 mm ID x 0.25 μm film thickness): 120 °C for 8 min, ramp 8 °C/min to 136 °C, 136 °C for 1 min, ramp 10 °C/min to a final temperature of 220 °C, 220 °C for 10 min

Table 2, Entry 1

(*R*,*Z*)-2-methyloct-3-en-1-ol was subjected to hydroformylation using General Procedure A. Achiral GC analysis using GC Method A afforded three peaks corresponding to each γ-lactone product (6.80 min and 7.93 min) and the combined δ-lactone products (8.47 min). The diastereoselectivity of the reaction was determined by ^{1}H NMR in CD_3OD. Silica gel chromatography (10% EtOAc/Hex) afforded the following compounds:

Major product:

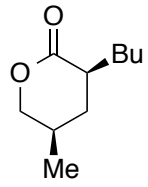


(3*R*,5*R*)-3-butyl-5-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless oil (27 mg, 78%). **GC Method A**: 8.47 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.20 (dd, 1H, J = 10.8, 4.9 Hz), 3.89 (t, 1H, J = 10.8 Hz), 2.46 – 2.51 (m, 1H), 2.12 – 2.17 (m, 1H), 1.84 – 1.88 (m, 1H), 1.69 – 1.72 (m, 2H), 1.42 – 1.45 (m, 1H), 1.33 – 1.37 (m, 4H), 1.00 (d, 3H, J = 6.9 Hz), 0.91 (t, 3H, J = 7.1 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.4, 73.2, 37.5, 32.7, 31.2, 29.3, 27.0, 22.8, 17.2, 14.2; **IR** 2957, 2931, 2872, 1740, 1459, 1380, 1341, 1103, 1047, 1007, 725 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{19}O_2$ $[M+H]^+$: 171.1380, found: 171.1384; **$[\alpha]_D^{20}$** = − 34.0 (c = 0.405, $CHCl_3$, l = 50 mm).

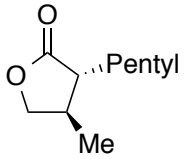
Proof of Absolute Stereochemistry:

The absolute stereochemistry was confirmed by 1D nOe experiements between the C(3) and C(5) hydrogen atoms. No nOe via a 1,3-diaxial interaction is observed between these groups. An nOe correlation is observed between the C(5)-H and the C(3)-butyl substituent; an nOe correlation is also observed between the C(3)-H and the C(5)-methyl substituent. See spectroscopic data for further details.

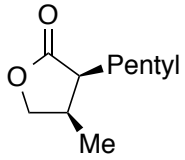
Minor Products:



(3*S*,5*R*)-3-butyl-5-methyltetrahydro-2*H*-pyran-2-one. **GC Method A**: 8.47 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.28 (dd, 1H, *J* = 11.3, 3.9 Hz), 3.83 – 3.90 (m, 1H), 2.39 – 2.43 (m, 1H), 2.03 – 2.12 (m, 1H), 1.86 – 1.92 (m, 1H), 1.67 – 1.71 (m, 1H), 1.44 – 1.51 (m, 2H), 1.23 – 1.33 (m, 4H), 0.97 (d, 3H, *J* = 6.4 Hz), 0.95 (t, 3H, *J* = 7.1 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.2, 74.8, 40.4, 34.4, 31.5, 29.0, 28.8, 22.8, 17.6, 14.2; **IR** 2978, 2931, 2973, 1734, 1459, 1213, 1155, 1109, 1045, 749, 750 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{19}O_2$ $[M+H]^+$: 171.1380, found: 171.1384; **$[\alpha]_D^{20}$** = + 3.4 (*c* = 0.260, $CHCl_3$, *l* = 50 mm).



***anti*-4-methyl-3-pentyldihydrofuran-2(3*H*)-one.** This compound has been synthesized previously in our laboratories and all spectroscopic data are in accordance.[13] **GC Method A**: 6.80 min.



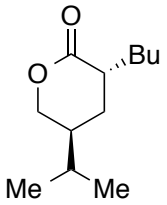
***syn*-4-methyl-3-pentyldihydrofuran-2(3*H*)-one**. This compound has been synthesized previously in our laboratories and all spectroscopic data are in accordance.[13] **GC Method A**: 7.93 min.

Table 2, Entry 2:

(*R*,*Z*)-2-isopropyloct-3-en-1-ol was subjected to hydroformylation using General Procedure B. Achiral GC analysis using GC Method B afforded three peaks corresponding to the γ-lactone product (12.19 min) and the combined δ-lactone products (13.68 min). The diastereoselectivity of the reaction was determined by chiral GC analysis using GC Method C to afford two signals,

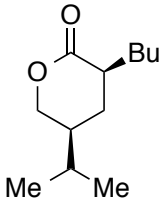
t_{minor} = 107.6 min, t_{major} = 107.9 min. Silica gel chromatography (10% EtOAc/Hex) afforded the following compounds:

Major Product:

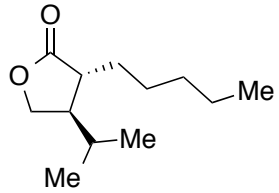


(3*R*,5*S*)-3-butyl-5-isopropyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless oil (22 mg, 57%). **GC Method B**: 13.68 min, **GC Method C**: 107.9 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.25 (dd, 1H, *J* = 11.7, 4.9 Hz), 3.98 – 4.02 (m, 1H), 2.39 – 2.41 (m, 1H), 1.81 – 1.85 (m, 2H), 1.74 – 1.79 (m, 1H), 1.56 – 1.61 (m, 2H), 1.30 – 1.40 (m, 4H), 0.94 (d, 3H, *J* = 6.9 Hz), 0.92 (d, 3H, *J* = 7.3 Hz), 0.90 (t, 3H, *J* = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.8, 70.2, 38.7, 37.6, 30.9, 29.9, 29.3, 28.5, 22.8, 20.2, 19.9, 14.1; **IR** 2957, 2932, 2873, 1746, 1467, 1390, 1370, 1245, 1165, 1151, 1114, 1071, 1031 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{23}O_2$ $[M+H]^+$: 199.1698, found: 199.1703; **$[\alpha]_D^{20}$** = − 58.6 (*c* = 0.480, $CHCl_3$, *l* = 50 mm).

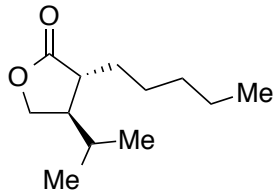
Minor Products:



(3*S*,5*S*)-3-butyl-5-isopropyltetrahydro-2*H*-pyran-2-one. Isolated with (3*R*,5*S*)-3-butyl-5-isopropyltetrahydro-2*H*-pyran-2-one in an 88:12 ratio. **GC Method B**: 13.7 min, **GC Method C**: 107.6 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.32 (ddd, 1H, *J* = 10.3, 5.1, 1.7 Hz), 4.04 (dd, 1H, *J* = 11.3, 9.0 Hz), 2.39 – 2.41 (m, 1H), 2.04 – 2.10 (m, 1H), 1.74 – 1.85 (m, 2H), 1.56 – 1.61 (m, 1H), 1.30 – 1.40 (m, 6H), 0.94 (d, 3H, *J* = 6.9 Hz), 0.92 (d, 3H, *J* = 7.3 Hz), 0.90 (t, 3H, *J* = 6.9 Hz).



(3*R*,4*R*)-4-isopropyl-3-pentyldihydrofuran-2(3*H*)-one. **GC Method B**: 12.15 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.29 – 4.32 (m, 1H), 3.95 – 3.98 (m, 1H), 2.32 (q, 1H, *J* = 6.5 Hz), 2.09 – 2.12 (m, 1H), 1.64 – 1.77 (m, 3H), 1.41 – 1.49 (m, 1H), 1.29 – 1.32 (m, 5H), 0.96 (d, 3H, *J* = 7.0 Hz), 0.91 (d, 3H, *J* = 7.1 Hz), 0.89 (t, 3H, *J* = 6.8 Hz); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.1, 69.5, 46.4, 43.2, 32.0, 30.8, 30.6, 26.5, 22.6, 20.3, 19.2, 14.2.

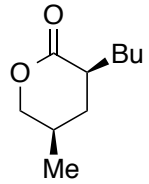


(3*R*,4*R*)-4-isopropyl-3-pentyldihydrofuran-2(3*H*)-one. Not observed or isolated in any hydroformylation reaction (reactions carried out with ligand **3c** and control reactions with PPh_3)

Table 2, Entry 3

(*R*,*E*)-2-methyloct-3-en-1-ol was subjected to hydroformylation using General Procedure A. Achiral GC analysis using GC Method A afforded three peaks corresponding to each γ-lactone product (6.80 min and 7.93 min) and the combined δ-lactone products (8.47 min). The diastereoselectivity of the reaction was determined by ^{1}H NMR in CD_3OD. Silica gel chromatography (10% EtOAc/Hex) afforded the following compounds:

Major Product:

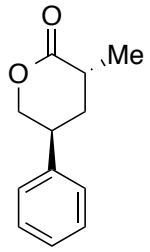


(3*S*,5*R*)-3-butyl-5-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless oil (18 mg, 52%). **GC Method A**: 8.47 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.28 (dd, 1H, *J* = 11.3, 3.9 Hz), 3.83 – 3.90 (m, 1H), 2.39 – 2.43 (m, 1H), 2.03 – 2.12 (m, 1H), 1.86 – 1.92 (m, 1H), 1.67 – 1.71 (m, 1H), 1.44 – 1.51 (m, 2H), 1.23 – 1.33 (m, 4H), 0.97 (d, 3H, *J* = 6.4 Hz), 0.95 (t, 3H, *J* = 7.1 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.2, 74.8, 40.4, 34.4, 31.5, 29.0, 28.8, 22.8, 17.6, 14.2; **IR** 2978, 2931, 2973, 1734, 1459, 1213, 1155, 1109, 1045, 749, 750 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{19}O_2$ $[M+H]^+$: 171.1380, found: 171.1384; **$[\alpha]_D^{20}$** = + 3.4 (*c* = 0.260, $CHCl_3$, *l* = 50 mm).

Table 2, Entry 4

(*S*,*Z*)-2-phenylpent-3-en-1-ol was subjected to hydroformylation using General Procedure C. Achiral GC analysis using GC Method D afforded three peaks corresponding to each γ-lactone product (7.67 min and 7.73 min) and the combined δ-lactone products (8.46 min). The diastereoselectivity of the reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (10% EtOAc/Hex) afforded the following compounds:

Major product:

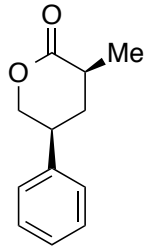


(3*R*,5*S*)-3-methyl-5-phenyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless semi-solid (25 mg, 66%). **GC Method D**: 8.46 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.38 (m, 2H), 7.25 – 7.30 (m, 3H), 4.33 – 4.41 (m, 2H), 3.28 – 3.32 (m, 1H), 2.82 – 2.86 (m, 1H), 2.28 – 2.34 (m, 1H), 1.95 – 2.02 (m, 1H), 1.31 (d, 3H, J = 6.8 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.4, 140.6, 129.2, 127.6, 127.4, 72.3, 38.5, 34.6, 33.1, 16.8; **IR** 2973, 2935, 1742, 1380, 1214, 1161, 1117, 1080, 1054, 1033, 755, 701, 668 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{15}O_2$ $[M+H]^+$: 191.1072, found: 191.1067; $[\alpha]_D^{20}$ = − 25.1(c = 0.255, $CHCl_3$, l = 50 mm).

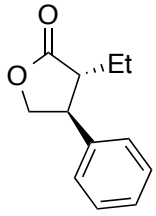
Proof of Absolute Stereochemistry:

The absolute stereochemistry was confirmed by 1D nOe experiements between the C(3) and C(5) hydrogen atoms. No nOe via a 1,3-diaxial interaction is observed between these groups. An nOe correlation is observed between the C(5)-H and the C(3)-methyl substituent; an nOe correlation is also observed between the C(3)-H and the C(5)-aryl substituent. See spectroscopic data for further details.

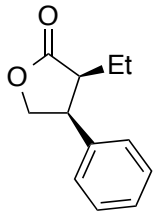
Minor Products:



(3*S*,5*S*)-3-methyl-5-phenyltetrahydro-2*H*-pyran-2-one. **GC Method D**: 8.46 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 – 7.36 (m, 2H), 7.27 – 7.30 (m, 1H), 7.23 – 7.25 (m, 2H), 4.48 – 4.50 (m, 1H), 4.26 (dd, 1H, J = 11.3, 10.3 Hz), 3.25 – 3.31 (m, 1H), 2.69 – 2.74 (m, 1H), 2.27 – 2.33 (m, 1H), 1.99 (q, 1H, J = 12.7 Hz), 1.36 (d, 3H, J = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.1, 140.3, 129.1, 127.6, 127.3, 74.5, 40.4, 36.2, 35.8, 16.9.



***anti*-3-ethyl-4-phenyldihydrofuran-2(3*H*)-one**. This compound has been synthesized previously in our laboratories and all spectroscopic data are in accordance.[13] **GC Method D**: 7.67 min.

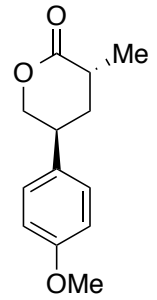


***syn*-3-ethyl-4-phenyldihydrofuran-2(3*H*)-one**. This compound has been synthesized previously in our laboratories and all spectroscopic data are in accordance.[13] **GC Method D**: 7.73 min.

Table 2, Entry 5

(*S*,*Z*)-2-(4-methoxyphenyl)pent-3-en-1-ol was subjected to hydroformylation using General Procedure C. Achiral GC analysis using GC Method B afforded two peaks corresponding to the combined γ-lactone products (18.16 min and 17.73 min) and the combined δ-lactone products (19.48 min). The diastereoselectivity of the reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:

Major product:

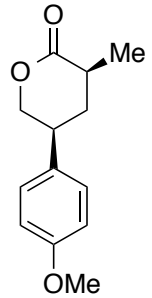


(3*R*,5*S*)-5-(4-methoxyphenyl)-3-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless solid (32 mg, 72%). **GC Method B**: 19.48 min; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 (d, 2H, J = 8.8 Hz), 6.88 (d, 2H, J = 8.8 Hz), 4.30 – 4.36 (m, 2H), 3.80 (s, 3H), 3.21 – 3.28 (m, 1H), 2.78 – 2.86 (m, 1H), 2.23 – 2.29 (m, 1H), 1.92 – 1.98 (m, 1H), 1.30 (d, 3H, J = 6.7 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.4, 159.0, 132.5, 128.4, 114.5, 72.5, 55.5, 37.6, 34.7, 33.0, 16.9; **IR** 2936, 1740, 1612, 130, 1278, 1248, 1214, 1161, 1084, 1055, 1033, 831, 750 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{17}O_3$ $[M+H]^+$: 221.1178, found: 221.1184; $\mathbf{[\alpha]_D^{20}}$ = − 16.2 (c = 0.420, $CHCl_3$, l = 50 mm).

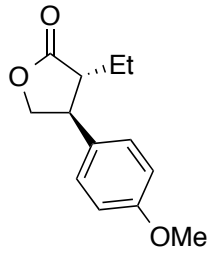
Proof of Absolute Stereochemistry:

The absolute stereochemistry was confirmed by 1D nOe experiements between the C(3) and C(5) hydrogen atoms. No nOe via a 1,3-diaxial interaction is observed between these groups. An nOe correlation is observed between the C(5)-H and the C(3)-methyl substituent; an nOe correlation is also observed between the C(3)-H and the C(5)-aryl substituent. See spectroscopic data for further details.

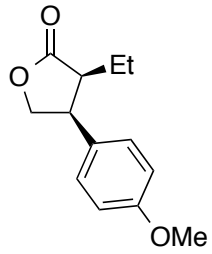
Minor Products:



(3*S*,5*S*)-5-(4-methoxyphenyl)-3-methyltetrahydro-2*H*-pyran-2-one. **GC Method B**: 19.48 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.10 (d, 2H, *J* = 8.8 Hz), 6.82 (d, 2H, *J* = 8.8 Hz), 4.45 (ddd, 1H, *J* = 13.2, 5.1, 2.2 Hz), 4.19 (t, 1H, *J* = 10.8 Hz), 3.80 (s, 3H), 3.20 – 3.26 (m, 1H), 2.66 – 2.71 (m, 1H), 2.23 – 2.29 (m, 1H), 1.84 (q, 1H, *J* = 12.7 Hz), 1.34 (d, 3H, *J* = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.1, 159.1, 132.2, 128.3, 114.4, 74.7, 55.5, 39.6, 36.2, 35.9, 17.3.



(3*R*,4*S*)-3-ethyl-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one. **GC Method B**: 17.73 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.18 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 4.49 – 4.52 (m, 1H), 4.06 – 4.09 (m, 1H), 3.81 (s, 3H), 3.34 – 3.42 (m, 1H), 2.61 – 2.66 (m, 1H), 1.77 – 1.83 (m, 1H), 1.67 – 1.73 (m, 1H), 0.94 (t, 3H, *J* = 7.6 Hz); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.4, 159.3, 130.4, 128.5, 114.7, 72.4, 55.5, 47.9, 46.6, 22.1, 11.2.

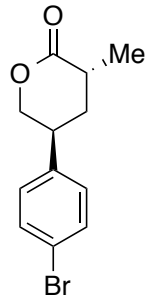


(3*S*,4*S*)-3-ethyl-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one. **GC Method B**: 18.16 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.08 (d, 2H, *J* = 8.8 Hz), 6.85 (d, 2H, *J* = 8.3 Hz), 4.55 (dd, 1H, *J* = 9.3, 5.9 Hz), 4.43 (dd, 1H, *J* = 9.3, 2.5 Hz), 3.80 (s, 3H), 3.65 – 3.69 (m, 1H), 2.67 – 2.72 (m, 1H), 1.61 – 1.66 (m, 1H), 1.07 – 1.12 (m, 1H), 0.90 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.9, 130.8, 128.9, 128.1, 114.5, 73.0, 55.5, 46.5, 44.2, 19.4, 12.3.

Table 2, Entry 6

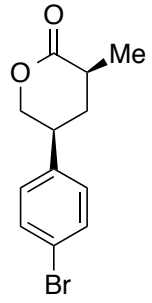
(*S*,*Z*)-2-(4-bromophenyl)pent-3-en-1-ol was subjected to hydroformylation using General Procedure C. The regioselectivity and diastereoselectivity of the hydroformylation reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:

Major product:

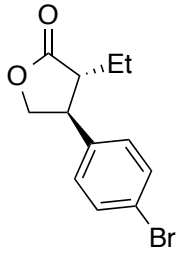


(3*R*,5*S*)-5-(4-bromophenyl)-3-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless solid (33 mg, 62%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 (d, 2H, *J* = 8.3 Hz), 7.12 (d, 2H, *J* = 8.3 Hz), 4.29 – 4.37 (m, 2H), 3.23 – 3.29 (m, 1H), 2.78 – 2.83 (m, 1H), 2.21 – 2.27 (m, 1H), 1.94 – 2.00 (m, 1H), 1.29 (d, 3H, *J* = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.0, 139.5, 132.3, 129.1, 121.5, 71.9, 38.0, 34.6, 33.0, 16.9; **IR** 2973, 2936, 1743, 1490, 1361, 1160, 1117, 1074, 1056, 1034, 1009, 821, 752 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{14}Br_1O_2$ $[M+H]^+$: 269.0177, found: 269.0187; **$[\alpha]_D^{20}$** = − 22.9 (*c* = 0.640, $CHCl_3$, *l* = 50 mm).

Minor products:

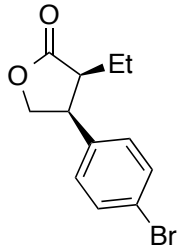


(3*S*,5*S*)-5-(4-bromophenyl)-3-methyltetrahydro-2*H*-pyran-2-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 (d, 2H, *J* = 8.8 Hz), 7.11 (d, 2H, *J* = 8.8 Hz), 4.46 – 4.49 (m, 1H), 4.22 (dd, 1H, *J* = 11.5, 9.5 Hz), 3.23 – 3.27 (m, 1H), 2.68 – 2.73 (m, 1H), 2.27 – 2.33 (m, 1H), 1.83 (q, 1H, *J* = 12.4 Hz), 1.35 (d, 3H, *J* = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.9, 139.5, 132.3, 129.0, 121.5, 73.9, 39.9, 36.0, 35.7, 17.1.



(3*R*,4*S*)-4-(4-bromophenyl)-3-ethyldihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, 2H, *J* = 8.3 Hz), 7.14 (d, 2H, *J* = 8.3 Hz), 4.52 (t, 1H, *J* = 8.8 Hz), 4.07 (t, 1H, *J* = 9.5 Hz), 3.37 – 3.43 (m, 1H), 2.62 – 2.66 (m, 1H), 1.78 – 1.84 (m, 1H), 1.67 – 1.72 (m, 1H), 0.93 (t,

3H, *J* = 7.6 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.8, 137.8, 132.5, 129.1, 121.9, 71.9, 47.9, 46.8, 22.2, 11.3.

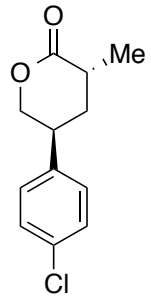


(3*S*,4*S*)-4-(4-bromophenyl)-3-ethyldihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, 2H, *J* = 8.8 Hz), 7.03 (d, 2H, *J* = 8.8 Hz), 4.55 (dd, 1H, *J* = 9.3, 6.4 Hz), 4.40 (dd, 1H, *J* = 9.3, 2.0 Hz), 3.65 – 3.69 (m, 1H), 2.73 (dt, 1H, *J* = 8.3, 5.4 Hz), 1.61 – 1.66 (m, 1H), 1.01 – 1.08 (m, 1H), 0.90 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.3, 137.9, 132.3, 129.5, 121.8, 72.5, 46.3, 44.5, 19.4, 12.3.

Table 2, Entry 7

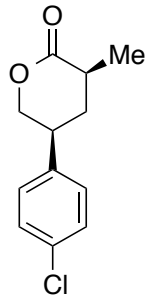
(*S*,*Z*)-2-(4-chlorophenyl)pent-3-en-1-ol was subjected to hydroformylation using General Procedure C. The regioselectivity and diastereoselectivity of the hydroformylation reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:

Major Product:



(3*R*,5*S*)-5-(4-chlorophenyl)-3-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless oil (30 mg, 68%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (d, 2H, *J* = 8.3 Hz), 7.19 (d, 2H, *J* = 8.3 Hz), 4.29 – 4.37 (m, 2H), 3.25 – 3.31 (m, 1H), 2.79 – 2.84 (m, 1H), 2.22 – 2.28 (m, 1H), 1.95 – 2.01 (m, 1H), 1.31 (d, 3H, *J* = 6.8 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.0, 139.0, 133.4, 129.3, 128.7, 71.9, 37.9, 34.5, 32.9, 16.8; **IR** 2973, 2936, 1743, 1493, 1413, 1236, 1161, 1117, 1090, 1057, 1034, 827 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{14}Cl_1O_2$ $[M+H]^+$: 225.0682, found: 221.0689; **$[\alpha]_D^{20}$** = − 22.4 (*c* = 0.500, $CHCl_3$, *l* = 50 mm).

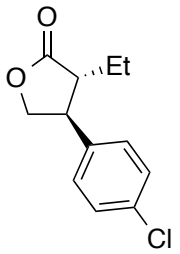
Minor Products:



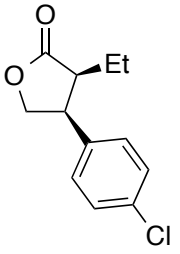
(3*S*,5*S*)-5-(4-chlorophenyl)-3-methyltetrahydro-2*H*-pyran-2-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 (dd, 2H, *J* = 6.4, 2.0 Hz), 7.16 (dd, 2H, *J* = 6.4, 2.0 Hz), 4.46 – 4.49 (m, 1H), 4.22 (dd, 1H, *J* = 11.3, 9.8 Hz), 3.23 – 3.29 (m, 1H), 2.67 – 2.73 (m, 1H), 2.27 – 2.32 (m, 1H), 1.82 (dd, 1H, *J* = 24.9, 12.7 Hz), 1.35 (d, 3H, *J* = 7.3 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.9, 138.9, 133.5, 129.3, 128.6, 74.0, 39.8, 36.0, 35.8, 17.2.

Proof of Absolute Stereochemistry:

The absolute stereochemistry was confirmed by 1D nOe experiements between the C(3) and C(5) hydrogen atoms. An nOe correlation is observed between these two hydrogen substituents. See spectroscopic data for further details.



(3*R*,4*S*)-4-(4-chlorophenyl)-3-ethyldihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (d, 2H, *J* = 8.3 Hz), 7.20 (d, 2H, *J* = 8.3 Hz), 4.52 (t, 1H, *J* = 8.6 Hz), 4.08 (t, 1H, *J* = 9.3 Hz), 3.39 – 3.45 (m, 1H), 2.62 – 2.66 (m, 1H), 1.78 – 1.84 (m, 1H), 1.67 – 1.73 (m, 1H), 0.94 (t, 3H, *J* = 7.6 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.9, 137.24 133.9, 129.6, 128.8, 72.0, 47.9, 46.8, 22.2, 11.3.

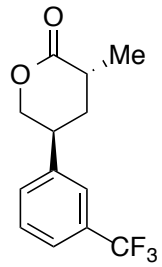


(3*S*,4*S*)-4-(4-chlorophenyl)-3-ethyldihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 (dd, 2H, *J* = 6.4, 2.0 Hz), 7.10 – 7.11 (m, 2H), 4.56 (dd, 1H, *J* = 9.3, 5.9 Hz), 4.42 (dd, 1H, *J* = 9.3, 2.0 Hz), 3.68 – 3.72 (m, 1H), 2.71 – 2.78 (m, 1H), 1.62 – 1.68 (m, 1H), 1.03 = 1.09 (m, 1H), 0.91 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 178.3, 137.4, 133.7, 129.3, 129.2, 72.6, 46.3, 44.4, 19.4, 12.3.

Table 2, Entry 8

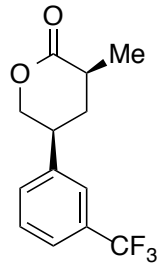
(*S*,*Z*)-2-(3-trifluoromethylphenyl)pent-3-en-1-ol was subjected to hydroformylation using General Procedure C. The regioselectivity and diastereoselectivity of the hydroformylation reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:

Major Product:

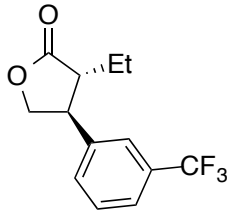


(3*R*,5*S*)-3-methyl-5-(3-(trifluoromethyl)phenyl)tetrahydro-2*H*-pyran-2-one. Isolated as a colorless oil (38 mg, 73%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, 1H, J = 7.8 Hz), 7.45 – 7.49 (m, 3H), 4.34 – 4.41 (m, 2H), 3.33 – 3.40 (m, 1H), 2.82 – 2.87 (m, 1H), 2.27 – 2.33 (m, 1H), 1.99 – 2.05 (m, 1H) 1.30 (d, 3H, J = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.9, 141.6, 131.5 (q, $J_{C\text{-}F}$ = 32 Hz), 130.9, 129.7, 124.5, 124.1, 124.0 (q, $J_{C\text{-}F}$ = 272 Hz), 71.7, 38.4, 34.5, 32.9, 16.8; **^{19}F NMR** (470 MHz, $CDCl_3$) δ − 62.7; **IR** 2977, 2939, 1745, 1382, 1162, 1121, 1059, 917, 805, 704, 664 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{14}F_3O_2$ $[M+H]^+$: 259.0946, found: 259.0946; **$[\alpha]_D^{20}$** = − 16.4 (c = 0.600, $CHCl_3$, l = 50 mm).

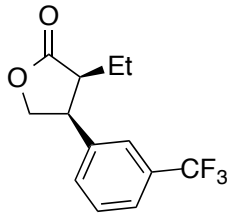
Minor Products:



(3*S*,5*S*)-3-methyl-5-(3-(trifluoromethyl)phenyl)tetrahydro-2*H*-pyran-2-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, 1H, J = 7.3 Hz), 7.46 – 7.50 (m, 3H), 4.51 (ddd, 1H, J = 13.7, 5.4, 2.2 Hz), 4.27 (dd, 1H, J = 11.3, 9.8 Hz), 3.33 – 3.38 (m, 1H), 2.70 – 2.75 (m, 1H), 2.32 – 2.36 (m, 1H), 1.85 (m, 1H), 1.36 (d, 3H, J = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.7, 141.5, 131.4, (q, $J_{C\text{-}F}$ = 32 Hz), 130.0, 129.7, 124.6, 124.2 (q $J_{C\text{-}F}$ = 273 Hz), 124.1, 73.3, 40.2, 36.0, 35.7, 17.1; **^{19}F NMR** (470 MHz, $CDCl_3$) δ − 62.7.



(3*R*,4*S*)-3-ethyl-4-(3-(trifluoromethyl)phenyl)dihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 (d, 1H, *J* = 7.8 Hz), 7.46 – 7.57 (m, 3H), 4.58 (t, 1H, *J* = 8.6 Hz), 4.13 (t, 1H, *J* = 9.5 Hz), 3.51 (app q, 1H, *J* = 9.6 Hz), 2.66 – 2.73 (m, 1H), 1.81 – 1.86 (m, 1H), 1.70 – 1.76 (m, 1H), 0.95 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.6, 129.9, 131.8 (q, $J_{C\text{-}F}$ = 32 Hz), 130.8, 130.0, 125.0, 124.4, 124.1 (q, $J_{C\text{-}F}$ = 272 Hz), 71.9, 47.9, 47.1, 22.3, 11.2; **^{19}F NMR** (470 MHz, $CDCl_3$) δ − 62.7.

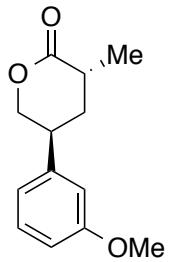


(3*S*,4*S*)-3-ethyl-4-(3-(trifluoromethyl)phenyl)dihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, 1H, *J* = 7.8 Hz), 7.48 (t, 1H, *J* = 7.8 Hz), 7.40 (s, 1H), 7.38 (d, 1H, *J* = 7.8 Hz), 4.60 (dd, 1H, *J* = 9.3, 6.4 Hz), 4.46 (dd, 1H, *J* = 9.5, 2.2 Hz), 3.78 – 3.81 (m, 1H), 2.76 – 2.81 (m, 1H), 1.62 – 1.66 (m, 1H), 1.00 – 1.06 (m, 1H), 0.93 (t, 3H, *J* = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.1, 139.9, 131.4 (q, $J_{C\text{-}F}$ = 32 Hz), 130.8, 129.8, 124.9, 124.8, 124.0 (q, $J_{C\text{-}F}$ = 273 Hz), 72.3, 46.3, 44.9, 19.5, 12.2; **^{19}F NMR** (470 MHz, $CDCl_3$) δ − 62.7.

Table 2, Entry 9

(*S*,*Z*)-2-(3-methoxyphenyl)pent-3-en-1-ol was subjected to hydroformylation using General Procedure C. Achiral GC analysis using GC Method E afforded three peaks corresponding to each γ-lactone product (10.36 min and 10.51 min) and the combined δ-lactone products (12.02 min). The diastereoselectivity of the reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:

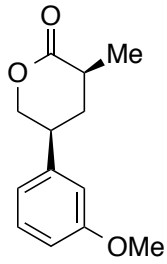
Major Product:



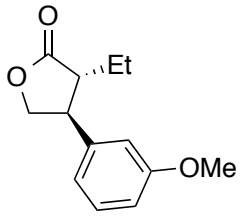
(3*R*,5*S*)-5-(3-methoxyphenyl)-3-methyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless solid (34 mg, 77%). **GC Method E**: 12.02 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.28 (m, 1H), 6.77 – 6.83 (m, 3H), 4.33 – 4.38 (m, 2H), 3.81 (s, 3H), 3.25 – 3.28 (m, 1H), 2.80 – 2.85 (m,

1H), 2.26 – 2.32 (m, 1H), 1.96 – 2.00 (m, 1H), 1.30 (d, 3H, J = 6.9 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.4, 160.2, 142.2, 132.2, 119.6, 113.7, 112.4, 72.2, 55.5, 38.5, 34.6, 33.0, 16.8; **IR** 2936, 1742, 1601, 1585, 1488, 1456, 1263, 1159, 1117, 1085, 1035, 781, 670 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{17}O_3$ $[M+H]^+$: 221.1178, found: 221.1172; **$[\alpha]_D^{20}$** = − 13.1 (c = 1.01, $CHCl_3$, l = 50 mm).

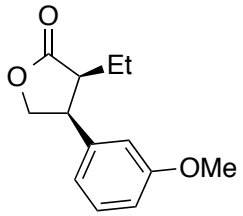
Minor Products:



(3*S*,5*S*)-5-(3-methoxyphenyl)-3-methyltetrahydro-2*H*-pyran-2-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27 – 7.30 (m, 1H), 6.77 – 6.83 (m, 3H), 4.49 (ddd, 1H, J = 11.3, 5.4, 2.5 Hz), 4.25 (dd, 1H, J = 11.3, 10.3 Hz), 3.80 (s, 3H), 3.22 – 3.27 (m, 1H), 2.67 – 2.73 (m, 1H), 2.27 – 2.32 (m, 1H), 1.83 – 1.91 (m, 1H), 1.35 (d, 3H, J = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.0, 160.2, 141.9, 130.2, 119.5, 113.5, 112.6, 74.4, 55.4, 40.4, 36.2, 35.8, 17.3.



(3*R*,4*S*)-3-ethyl-4-(3-methoxyphenyl)dihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (t, 1H, J = 7.3 Hz), 6.83 – 6.87 (m, 2H), 6.79 (s, 1H), 4.53 (t, 1H, J = 8.6 Hz), 4.12 (t, 1H, J = 9.3 Hz), 3.82 (s, 3H), 3.38 – 3.44 (m, 1H), 2.67 – 2.71 (m, 1H), 1.77 – 1.85 (m, 1H), 1.69 – 1.76 (m, 1H), 0.96 (t, 3H, J = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.3, 160.3, 140.4, 130.4, 119.7, 113.7, 112.8, 72.2, 55.5, 47.8, 47.3, 22.2, 11.2.

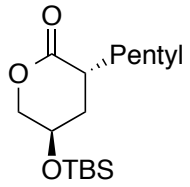


(3*S*,4*S*)-3-ethyl-4-(3-methoxyphenyl)dihydrofuran-2(3*H*)-one. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, 1H, J = 7.8 Hz), 6.82 (dd, 1H, J = 8.3, 2.4 Hz), 6.75 (d, 1H, J = 7.8 Hz), 6.69 (app t, 1H, J = 2.0 Hz), 4.55 (dd, 1H, J = 9.3, 5.9 Hz), 4.46 (dd, 1H, J = 9.3 2.5 Hz), 3.79 (s, 3H), 3.66 – 3.69 (m, 1H), 2.69 – 2.74 (m, 1H), 1.61 – 1.66 (m, 1H), 1.08 – 1.14 (m, 1H), 0.92 (t, 3H, J = 7.3 Hz); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.7, 160.1, 140.4, 130.2, 120.0, 113.9, 112.8, 72.7, 55.4, 46.4, 45.0, 22.8, 14.3.

Table 2, Entry 10

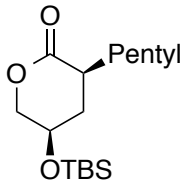
(*R*,*Z*)-2-((*tert*-butyldimethylsilyl)oxy)non-3-en-1-ol was subjected to hydroformylation using General Procedure C. Achiral GC analysis using GC Method F afforded four peaks corresponding to each γ-lactone product (18.26 min and 18.61 min) and each δ-lactone product (18.97 min and 19.13 min). Silica gel chromatography (10% EtOAc/Hex) afforded the following compounds:

Major Product:

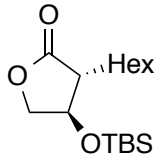


(*R*,*Z*)-2-((*tert*-butyldimethylsilyl)oxy)non-3-en-1-ol. Isolated as a colorless oil (30.9 mg, 51%). **GC Method F**: 18.97 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.27 (dd, 1H, *J* = 13.0, 5.1 Hz), 4.10 – 4.15 (m, 1H), 2.72 – 2.78 (m, 1H), 1.96 – 2.01 (m, 1H), 1.85 – 1.89 (m, 1H), 1.72 – 1.75 (m, 1H), 1.45 – 1.50 (m, 1H), 1.27 – 1.34 (m, 7H), 0.88 (s, 9H), 0.87 (t, 3H, *J* = 8.3 Hz), 0.076 (s, 3H), 0.072 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.2, 73.3, 64.1, 36.0, 33.9, 31.8, 30.9, 26.4, 25.9, 23.0, 18.2, 14.2, -4.7; **IR** 2954, 2929, 2858, 1737, 1464, 1255, 1213, 1102, 1059, 1026, 1007, 837, 807, 778 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{33}O_3Si_1$ $[M+H]^+$: 301.2199, found: 301.2199; $[\alpha]_D^{20} = -9.7$ (*c* = 775, $CHCl_3$, *l* = 50 mm).

Minor Products:

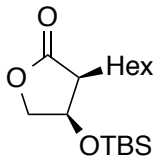


(3*S*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-3-pentyltetrahydro-2*H*-pyran-2-one. **GC Method F**: 19.13 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.21 (dd, 1H, *J* = 11.0, 2.7 Hz), 4.05 (dd, 1H, *J* = 11.0, 5.6 Hz), 2.34 – 2.39 (m, 1H), 2.24 – 2.29 (m, 1H), 1.85 – 1.90 (m, 1H), 1.54 – 1.60 (m, 2H), 1.29 – 1.33 (m, 7H), 0.88 (s, 9H), 0.87 (t, 3H, *J* = 8.3 Hz), 0.077 (s, 3H), 0.072 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.9, 72.9, 65.1, 38.2, 35.3, 31.9, 30.9, 26.6, 25.9, 22.7, 18.2, 14.2, -4.6.



(3*R*,4*R*)-4-((*tert*-butyldimethylsilyl)oxy)-3-hexyldihydrofuran-2(3*H*)-one. **GC Method F**: 18.26 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.32 – 3.45 (m, 1H), 4.24 – 4.27 (m, 1H), 3.95 – 3.98 (m, 1H), 2.43 – 2.46 (m, 1H), 1.69 – 1.73 (m, 1H), 1.47 – 1.56 (m, 1H), 1.42 – 1.48 (m, 2H),

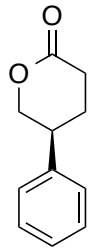
1.25 – 1.32 (m, 6H), 0.88 (s, 9H), 0.87 (t, 3H, J = 8.3 Hz), 0.082 (s, 3H), 0.066 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.8, 73.4, 73.3, 48.8, 31.8, 29.3, 28.4, 27.0, 25.8, 22.8, 18.0, 14.2, -4.4, -4.6.



(3*S*,4*R*)-4-((*tert*-butyldimethylsilyl)oxy)-3-hexyldihydrofuran-2(3*H*)-one. **GC Method F**: 18.61 min.; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.51 – 4.53 (m, 1H), 3.83 (dd, 1H, J = 11.3, 3.4 Hz), 3.67 (dd, 1H, J = 11.3, 2.9 Hz), 2.69 – 2.71 (m, 1H), 2.31 – 2.36 (m, 1H), 1.94 – 1.98 (m, 1H), 1.85 – 1.87 (m, 1H), 1.29 – 1.41 (m, 7H), 0.89 (s, 9H), 0.87 (t, 3H, J = 7.3 Hz), 0.077 (s, 3H), 0.062 (s, 3H).

Table 2, Entry 11

(*S*)-2-phenylbut-3-en-1-ol was subjected to hydroformylation using General Procedure D. The regioselectivity of the hydroformylation reaction was determined by ^{1}H NMR in $CDCl_3$. Silica gel chromatography (15% EtOAc/Hex) afforded the following compounds:



(*S*)-5-phenyltetrahydro-2*H*-pyran-2-one. Isolated as a colorless solid (28 mg, 80%). This compound has been synthesized previously in our laboratories (in racemic form) and all spectroscopic data are in accordance.[13] **$[\alpha]_D^{20}$** = + 25.1 (c = 0.520, $CHCl_3$, l = 50 mm).

Table 3 – Importance of Substrate Tether

The following compounds have been synthesized previously and are in accordance with reported NMR spectra: (*Z*)-4-phenylbut-2-en-1-ol,[14] 5-phenylpent-3-yn-1-ol,[15] (*Z*)-6-phenylhex-4-en-1-ol, [16] 3-hydroxy-2-(2-phenylethyl)propionic acid, [17] 3-benzyldihydrofuran-2(3*H*)-one, [18] 3-benzyltetrahydro-2*H*-pyran-2-ol,[19] 3-benzyltetrahydro-2*H*-pyran-2-one.[20]

General Procedure with Scaffolding Ligand: In a dry box, the appropriate alcohol substrate (0.200 mmol), (4*S*)-4-(*tert*-butyl)-3-(3-(diphenylphosphanyl)benzyl)-2-methoxyoxazolidine (8.7 mg, 0.020 mmol), a *p*-toluenesulfonic acid in benzene (351 μL, 2.0 x 10^{-4} mmol, 5.7 x 10^{-4} M solution) were mixed in C_6D_6 (0.8 mL) and allowed to equilibrate in a sealed NMR tube at 45 °C for 3 hours. (Note: the appearance of methanol can be monitored by ^{1}H NMR). The solution was concentrated in the dry box to remove the generated MeOH, the residue was redissolved in C_6D_6, and was allowed to equilibrate for an additional 4 hours at 45 °C before being concentrated again in the dry box. The appearance of free MeOH can be monitored by ^{1}H NMR. The resulting

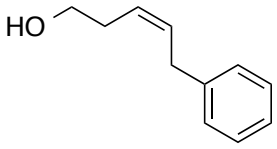
mixture was dissolved in benzene (3.5 mL), mixed with 3% $Rh(acac)(CO)_2$ (1.5 mg, 0.006 mmol), and injected into the Endeavor, followed by 0.5 mL benzene to wash the injection port.

General Procedure for Control reaction using PPh_3 as ligand: In a dry box, the appropriate alcohol substrate (0.200 mmol), triphenylphosphine (5.2 mg, 0.020 mmol), and $Rh(acac)(CO)_2$ (1.5 mg, 0.006 mmol) were mixed in benzene (3.5 mL). The resulting yellow solution was injected into the Endeavor, followed by 0.5 mL benzene to wash the injection port.

Table 3, Entry 1

Upon completion of the hydroformylation reaction, the benzene was removed *in vacuo* and internal standard (mesitylene in $CDCl_3$) was added to determine conversion, based on remaining starting material, by ^1H NMR. The mixture was concentrated on a rotary evaporator in a glass scintillation vial. To the vial was added a magnetic stir bar, acetonitrile (0.75 mL), water (0.75 mL), sodium phosphate (144 mg, 1.20 mmol), and 35% aqueous H_2O_2 (0.120 mL, 1.23 mmol). The reaction was cooled to 0 °C and a solution of sodium chlorite (tech. grade, 80%, 138 mg, 1.2 mmol) in water (0.75 mL), was added dropwise. The reaction was stirred and warmed to room temperature over 3 hours. The reaction as quenched by the addition of sodium sulfite (spatula tip) and 1M aqueous HCl (3 mL). The reaction was extracted with DCM (3 x 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reaction was analyzed by ^1H NMR in $CDCl_3$ to determine the regioselectivity of the reaction.

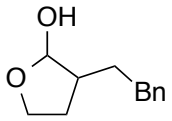
Table 3, Entry 2



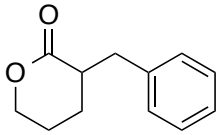
(*Z*)-5-phenylpent-3-en-1-ol. A round-bottom flask was charged with Lindlar's catalyst (330 mg) and purged with nitrogen. 5-phenylpent-3-yn-1-ol (660 mg, 4.11 mmol) in MeOH (12.5 mL) was added followed by quinoline (35 μL, 0.27 mmol). The flask was evacuated and refilled with H_2 four times, fitted with a H_2 balloon, and stirred at room temperature under H_2 for 2.5 h. The reaction was filtered through a plug of silica and concentrated. Column chromatography (20% EtOAc/Hex) yielded a light yellow oil (495 mg, 76%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28 – 8.31 (m, 2H), 7.18 – 7.21 (m, 3H), 5.74 – 5.79 (m, 1H), 5.51 – 5.56 (m, 1H), 3.71 (t, 2H, J = 6.6 Hz), 3.45 (d, 2H, J = 7.3 Hz), 2.44 – 2.48 (m, 2H), 1.44 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.9, 131.6, 128.7, 128.5, 126.4, 126.2, 62.5, 33.8, 31.0; **IR** 3337, 3025, 2939, 2883, 1602, 1495, 1453, 1400, 1047, 738, 679, 621, 562 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{15}O_1$ $[M+H-H_2O]^+$: 163.1123, found: 163.1128.

Upon completion of the hydroformylation reaction, the benzene was removed *in vacuo* and internal standard (mesitylene in $CDCl_3$) was added to determine conversion, based on remaining starting material, by ^1H NMR. The regioselectivity of the reaction was determined at this point by comparison of the lactol peaks in the crude ^1H NMR. The solvent was removed under reduced pressure. The crude hydroformylation mixture was added, as a solution in dichloromethane (3 mL), to a scintillation vial containing pyridinium chlorochromate (128.7 mg, 0.597 mmol), sodium acetate (16.0 mg, .195 mmol), and 4 Å molecular sieves. The reaction was stirred for 12 hours at room temperature, eluted through a short plug of silica gel (100% Et_2O), concentrated under reduced pressure, and subjected to silica gel chromatography (20% EtOAc/Hex). HPLC

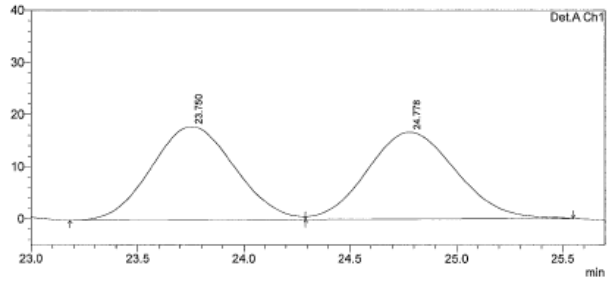
analysis of the δ-lactone was used to determine the enantioselectivity of the hydroformylation reaction.



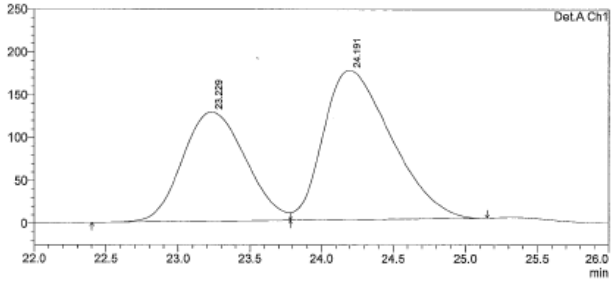
3-phenethyltetrahydrofuran-2-ol. Exists as a 1:1 mixture of diastereomers. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27 – 7.30 (m, 4H), 7.18 – 7.21 (m, 6H), 5.34 (t, 1H, J = 3.7 Hz), 5.22 (t, 1H, J = 2.4 Hz), 4.09 – 4.13 (m, 1H), 4.03 (dd, 1H, J = 15.7, 7.3 Hz), 3.93 – 3.97 (m, 1H), 3.82 (dd, 1H, J = 15.7, 7.3 Hz), 3.04 (d, 1H, J = 2.9 Hz), 2.83 (d, 1H, J = 2.9 Hz), 2.66 – 2.70 (m, 4H), 2.17 – 2.22 (m, 1H), 2.11 – 2.14 (m, 1H), 2.01 – 2.04 (m, 1H), 1.91 – 1.98 (m, 1H), 1.76 – 1.84 (m, 2H), 1.57 – 1.65 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.4, 142.0, 128.6, 128.5, 126.1, 126.0, 103.4, 98.4, 67.3, 67.1, 46.2, 44.0, 34.8, 34.4, 34.3, 30.7, 20.5, 29.1; **IR** 3394, 2930, 2858, 1496, 1454, 1118, 1029, 1012, 986, 908, 749, 699, 497 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{15}O_1$ $[M+H-H_2O]^+$: 175.1123, found: 175.1118.



3-benzyltetrahydro-2*H*-pyran-2-one. PCC oxidation and chromatography (15% EtOAc/Hex) afforded the title compound as a colorless oil). All spectroscopic data for this compound are in accordance with previously published reports.[20] **HPLC** (OD-H, 0.50 mL/min, 5% *i*-PrOH, 95% hexane, 220 nm) $t_{r(minor)}$ = 23.2 min and $t_{r(major)}$ = 24.2 min, 19% ee.



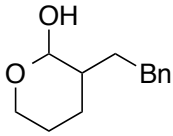
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.750	484698	17828	50.271	51.776
2	24.778	479468	16606	49.729	48.224
Total		964166	34434	100.000	100.000



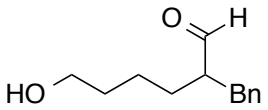
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.229	3879459	127157	40.391	42.204
2	24.191	5725203	174137	59.609	57.796
Total		9604663	301294	100.000	100.000

Table 3, Entry 3

Upon completion of the hydroformylation reaction, the benzene was removed *in vacuo* and internal standard (mesitylene in $CDCl_3$) was added to determine conversion, based on remaining starting material, by ^{1}H NMR. The regioselectivity of the reaction was determined at this point by comparison of the lactol and aldehyde peaks in the crude ^{1}H NMR.



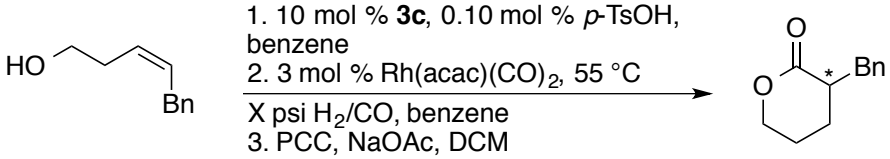
3-phenethyltetrahydro-2*H*-pyran-2-ol. Exists as a 1:1 mixture of diastereomers. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 – 7.29 (m, 4H), 7.18 – 7.21 (m, 6H), 5.11 (d, 1H, J = 2.5 Hz), 4.48 (d, 1H, J = 6.4 Hz), 3.97 – 4.02 (m, 2H), 3.55 – 3.58 (m, 1H), 3.47 – 3.50 (m, 1H), 2.60 – 2.73 (m, 4H), 1.99 – 2.03 (m, 2H), 1.67 – 1.76 (m, 2H), 1.45 – 1.61 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.6, 128.5, 125.9, 99.7, 94.0, 65.4, 60.0, 41.5, 39.4, 33.5, 33.2, 27.4, 25.5, 24.9, 23.8; **IR** 3387, 2933, 2855, 1496, 1454, 1273, 1130, 1072, 1027, 986, 903, 867, 577, 544 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{17}O_1$ $[M+H-H_2O]^+$: 189.1279, found: 189.1284.



2-benzyl-6-hydroxyhexanal. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.65 (d, 1H, J = 5.0 Hz), 7.25 – 7.30 (m, 2H), 7.15 – 7.22 (m, 3H), 3.61 (t, 2H, J = 6.4 Hz), 3.00 (dd, 1H, J = 14.1, 7.3 Hz), 2.74 (dd, 1H, J = 14.2, 6.8 Hz), 2.62 – 2.64 (m, 1H), 1.35 – 1.67 (m, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.7, 138.9, 129.1, 128.7, 126.6, 62.7, 53.6, 35.2, 32.8, 28.4, 23.4; **IR** 3027, 2935, 2861, 1703, 1454, 1406, 1210, 1170, 1072, 1053, 1030, 744, 699, 543 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{17}O_2$ $[M-H]^+$: 205.1229, found: 205.1227.

Optimization of Enantioselective Results

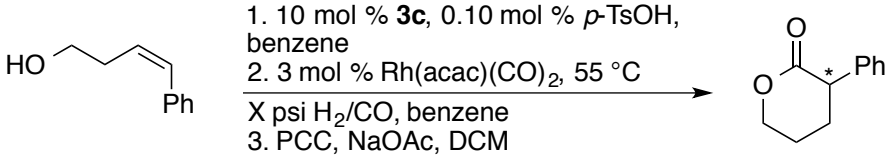
To further explore the asymmetric induction in the hydroformylation reaction, a pressure screen was carried out. While the running the reaction at lower pressures increases conversion, the regioselectivities are relatively unaffected by changes in pressure. Decreasing the pressure to 100 psi H_2/CO afforded full conversion of starting material and the distal lactone was isolated in 37% ee.



entry	X psi H_2/CO	% conversion[a]	rs (p:d)[b]	% ee[c]
1	100	Quant.	23:77	37
2	250	94%	29:71	20
3	400	84%	21:79	19

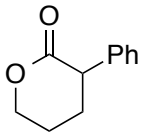
[a] Conversion based on remaining starting material after the hydroformylation reaction using mesitylene as an internal standard. [b] Regioselectivities (proximal:distal) determined by ^{1}H NMR prior to PCC oxidation by comparison of the lactol peaks. [c] Enantioselectivities determined by High Pressure Liquid Chromatography (HPLC).

A styrenyl-based substrate was also tested in enantioselective hydroformylation. Based on λ^3-coordination of the rhodium catalyst to the conjugated system, this substrate possesses an inherent preference to form the distal regioisomer. Employing PPh_3 as ligand under our optimal conditions (400 psi) affords the distal lactone selectively (25:75 rs, Entry 3). This inherent substrate selectivity is enhanced in the presence of ligand **3c** to (15:85 rs, Entry 3) in favor of the δ-lactone. Under these conditions, the δ-lactone is isolated in 19% ee (Entry 3). A pressure screen reveals that the regiochemical outcome is not strongly affected by the change in pressure, but slightly elevated conversions are observed at lower pressures. In contrast to the benzyl substrate where enantioselectivity and pressure exhibited an inverse relationship, the highest enenatioselectivity for the styrenyl substrate occurs at 400 psi.



entry	X psi H_2/CO	% conversion[a]	rs (p:d)[b]	% ee[c]
1	100	63%	18:82	12
2	250	65%	17:83	15
3	400	55% (33%)	15:85 (25:75)	19 (---)

[a] Conversion based on remaining starting material after the hydroformylation reaction using mesitylene as an internal standard. [b] Regioselectivities (proximal:distal) determined by ^{1}H NMR after PCC oxidation. [c] Enantioselectivities determined by High Pressure Liquid Chromatography (HPLC).



3-benzyltetrahydro-2*H*-pyran-2-one. PCC oxidation and chromatography (25% EtOAc/Hex) afforded the title compound as a colorless oil). All spectroscopic data for this compound are in accordance with previously published reports.[21] **HPLC** (OD-H, 1.0 mL/min, 8% *i*-PrOH, 92% hexane, 220 nm) $t_{r(minor)}$ = 25.2 min and $t_{r(major)}$ = 26.5 min, 19% ee.

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