Proline-Based *N*-Oxides as Readily Available and Modular Chiral Catalysts. Enantioselective Reactions of Allyltrichlorosilane with Aldehydes

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General Information. Infrared (IR) spectra were recorded on a Perkin Elmer 781 spectrophotometer, ν_{max} in cm^{-1} . The absorptions are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR were recorded on a Varian GN-400 (400 MHz). Chemical shifts are reported in ppm with the solvent reference as the internal standard (CHCl_3 : δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hex = hextet, hep = heptet, o = octet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian GN-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm with the solvent reference as the internal standard (CHCl_3 : δ 77.2 ppm). Melting points were taken with a Laboratory Devices Melt-Temp and are uncorrected. Enantiomeric ratios were determined by chiral HPLC or chiral GLC. Analytical liquid chromatography was performed on a Shimadzu chromatograph with a Chiracel OD (4.6 mm x 250 mm) or a Chiracel AS (4.6 mm x 250 mm) chiral column by Chiral Technologies. Analytical gas liquid chromatography (GLC) was performed on a Hewlett Packard 6890 with an Alpha Dex 120 (30 m x 0.25 mm x 0.25 μm film thickness), a Beta Dex 120 (30 m x 0.25 mm x 0.25 μm film thickness) or a Gamma Dex 120 (30 m x 0.25 mm x 0.25 μm film thickness) column by Supelco. Optical rotations were measured on a Rudolph Research Analytical Autopol IV Automatic Polarimeter. Elemental analysis (Anal) were performed by Robertson Microlit Laboratories, Inc., Madison, NJ, and are reported in percent abundance.

All reactions were conducted in oven (135 °C) or flame-dried glassware under an inert atmosphere of dry nitrogen. 1,2-Dichloroethane was purchased from Acros and distilled from CaH_2 before use. Diethyl ether and hexanes were purchased from Fisher and distilled from CaH_2 under nitrogen. Methanol, isopropanol, tetrahydrofuran and methylene chloride were purchased from Fisher and used without purification. 3-Chloroperbenzoic acid (*m*-CPBA) (75%) was purchased from Aldrich and used without purification. Dimethylformamide (DMF) was purchased from Fisher and was purged with nitrogen for 2 h and stored over 3 Å molecular sieves. All amino acids and protected amino acids, *O*-benzotriazole-*N,N,N',N'*-tetramethyluronium-hexafluorophosphate (HBTU), *O*-benzotriazole-*N,N,N',N'*-tetramethyl uronium-tetrafluoroborate (TBTU), and 1-hydroxybenzotriazole hydrate (HOBt) were purchased from Advanced ChemTech and used without purification. Palladium on carbon (10% dry) was purchased from Acros and used as received. All other amines for amide couplings (for ligand synthesis) were purchased from Lancaster and used without purification. All ketones (for ligand synthesis) were purchased from Aldrich and used without purification. All aldehydes were purchased from Aldrich and were either distilled (liquids) or sublimed (solids) before use. Allyltrichlorosilane was purchased from Lancaster and distilled under nitrogen before use. (*Z*) and (*E*) crotyltrichlorosilanes were synthesized according to literature procedure.¹

¹) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron*, **1997**, 53, 3513-3526.

Representative procedure for the synthesis of Proline Based N-Oxide Ligands.

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-benzyl)-2-pyrrolidine carboxamide (**3**).

Step 1:² To a dry 250 mL flask, *L*-proline (17.3 g, 0.150 mol) and potassium hydroxide (25.4 g, 0.450 mol) were dissolved in isopropanol (100 mL) and heated to 40 °C. Benzyl chloride (18.9 mL, 0.16 mol) was added over three hours via syringe pump. The reaction was stirred for an additional 6 h (nine hours total), at which time the reaction was allowed to cool to room temperature. Concentrated HCl was added to reach a pH of 4-5. Chloroform (40 mL) was added and the reaction was allowed to stir at room temperature for 12 h. The reaction was filtered to remove the white precipitate. The precipitate was washed with chloroform (3 x 20 mL). The solvent was removed from the combined organic layers to yield a yellow solid, which was washed with acetone (4 x 50 mL). The solid was dried over P₂O₅ to yield the unpurified benzylated acid (29.2 g, 95% unpurified yield).

Step 2: A portion of the unpurified benzylated acid (1.0 g, 5.0 mmol) was dissolved in DMF (25 mL) and THF (10 mL). To this solution was added benzylamine (586 μL, 5.00 mmol), potassium carbonate (2.10 g, 15.0 mmol), and HBTU (1.9 g, 5.0 mmol). The reaction was allowed to stir for 3 h, after which time water (50 mL) was added. The crude mixture was extracted with ethyl acetate (2 x 50 mL). The organic layer was washed with 1% aqueous sodium carbonate (5 x 50 mL) and brine (1 x 25 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield the unpurified amide (1.1 g, 76% unpurified yield).

Step 3:³ The unpurified benzyl amide (1.1 g, 3.7 mmol) was dissolved in methylene chloride (50 mL). Potassium carbonate (1.0 g, 7.5 mmol) was added and the reaction cooled to -78 °C. *m*-CPBA (0.86 g of 75% pure, net 0.65 g, 3.7 mmol) was then added, and the reaction was allowed to stir at -78 °C for 3 h. At this time, the reaction was allowed to warm to room temperature. After stirring for 2 h at room temperature, methylene chloride (50 mL) was added to dilute the reaction and celite (500 mg) was added to aid filtration. The reaction was filtered, and methylene chloride was removed under reduced pressure. The resulting oil was diluted with methylene chloride/hexanes from which pure **3** was crystallized as an off-white solid (735 mg, 45% yield over 3 steps). M.P. 119-120 °C. IR (neat, thin film): 2957 (br), 1673 (s), 1542 (s), 1499 (w), 1350 (w), 748 (m), 698 (s) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.64 (1H, br), 7.42-7.39 (5H, m), 7.36-7.25 (4H, m), 7.24 (1H, tt, *J* = 6.0, 2.8 Hz), 4.49-4.45 (4 H, m), 3.66 (1H, dd, *J* = 11.2, 7.6 Hz), 3.32 (1 H, p, *J* = 10.8 Hz), 3.25 (1H, tt, *J* = 8.4, 2.4 Hz), 2.52 – 2.32 (3 H, m), 1.88-1.80 (1H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 167.8, 138.6, 132.2, 130.0, 129.8, 128.9, 127.6, 127.2, 72.4, 71.0, 66.7, 42.9, 27.6, 20.1. Anal Calcd for C₁₉H₂₂N₂O₂: C, 73.52; H, 7.14; N, 9.03. Found C, 73.28; H, 7.41; N, 9.32. Optical Rotation: [α]_D²⁵ -43° (c 1.0, CHCl₃).

² Adapted from Belokon', Y. N.; Tararov, V. I.; Maleev, V. I.; Savel'eva, T. F.; Ryzhov, M. G. *Tetrahedron: Asymmetry*, **1998**, 9, 4249-4252.

³ O'Neil, I. A.; Potter, A. J. *Chem. Commun.* **1998**, 1487-1488 and references cited therein.

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-1-butyl)-2-pyrrolidinecarboxamide (3a). The same general procedure (modified for scale) as **3** was followed, only substituting *n*-butylamine (618 μ L, 6.00 mmol) for benzylamine in step 2. Unpurified **3a** was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3a** (729 mg, 51%

yield, 3 steps) as a pale yellow solid. M.P. 64-65 °C. IR (neat, thin film): 2958 (m), 2927 (m), 2864 (w), 1660 (s), 1560 (s), 1454 (m), 748 (w), 705 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.04 (1H, br), 7.43 (5H, br), 4.51 (1H, d, *J* = 12.8 Hz), 4.46 (1H, d, *J* = 12.8 Hz), 3.63 (1H, t, *J* = 8.0 Hz), 3.37-3.24 (4H, m), 2.48-2.30 (3H, m), 1.87-1.79 (1H, m), 1.58-1.51 (2H, m), 1.40 (2H, h, *J* = 7.2 Hz), 0.94 (3H, t, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 167.7, 132.3, 130.1, 129.9, 129.0, 72.4, 71.0, 66.7, 38.7, 31.9, 27.6, 20.7, 20.1, 14.1. Anal Calcd for C₁₆H₂₄N₂O₂: C, 69.53; H, 8.75; N, 10.14. Found C, 69.30; H, 8.77; N, 10.03. Optical Rotation: $[\alpha]^{25}_{\text{D}}$ -15° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-1-methylethyl)-2-pyrrolidinecarboxamide (3b). The same general procedure as **3** was followed, only substituting isopropylamine (415 μ L, 5.00 mmol) for benzylamine in step 2. Unpurified product **3b** was purified by silica gel chromatography (97:3

CH₂Cl₂:MeOH) to yield pure **3b** (465 mg, 34% yield, 3 steps) as an off-white solid. M.P. 129-130 °C. IR (neat, thin film): 2955 (br), 1665 (s), 1551 (s), 1457 (w), 1369 (w), 841 (w), 752 (m), 715 (m), 664 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 10.99 (1H, d, *J* = 7.2 Hz), 7.42 (5H, br), 4.60 (1H, d, *J* = 13.2 Hz), 4.45 (1H, d, *J* = 13.2 Hz), 4.08 (1H, o, *J* = 6.8 Hz), 3.58 (1H, dd, *J* = 10.8, 7.6 Hz), 3.32 (1H, q, *J* = 9.6 Hz), 3.24 (1H, dt, *J* = 8.4, 1.6 Hz), 2.46-2.29 (3H, m), 1.86-1.79 (1H, m), 1.22 (3H, d, *J* = 6.4 Hz), 1.16 (3H, d, *J* = 6.8 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 166.8, 132.3, 130.0, 129.9, 129.0, 72.2, 70.9, 66.6, 41.0, 27.5, 23.2, 22.8, 20.1. Anal Calcd for C₁₅H₂₂N₂O₂: C, 68.67; H, 8.45; N, 10.68. Found C, 68.40; H, 8.80; N, 10.48. Optical Rotation: $[\alpha]^{25}_{\text{D}}$ -14° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(1,1-dimethylethyl))-2-pyrrolidinecarboxamide (3c). The same general procedure (modified for scale) as **3** was followed, only substituting *t*-butylamine (661 μ L, 6.00 mmol) for benzylamine in step 2. Unpurified **3c** was purified by silica gel

chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3c** (632 mg, 45% yield, 3 steps) as a white solid. M.P. 92-94 °C. IR (neat, thin film): 2958 (br), 1666 (s), 1566 (s), 1454 (w), 1378 (w), 1229 (m), 755 (w), 711 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.01 (1H, s), 7.42 (5H, br), 4.47 (2H, s), 3.45 (1H, t, *J* = 8.0 Hz), 3.30 (1H, dd, *J* = 19.6, 10.4 Hz), 3.22 (1H, dt, *J* = 8.4, 1.6 Hz), 2.45-2.28 (3H, m), 1.84-1.76 (1H, m), 1.39 (9H, s). ¹³C NMR (CDCl₃, 100 MHz): δ 166.5, 132.3, 130.1, 129.8, 129.0, 72.6, 70.8, 66.4, 50.8, 29.1, 27.4, 20.0. Anal Calcd for C₁₆H₂₄N₂O₂: C, 69.53; H, 8.75; N, 10.14. Found C, 69.27; H, 9.00; N, 10.25. Optical Rotation: $[\alpha]^{25}_{\text{D}}$ -8.8° (c 0.5, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-benzhydryl)-2-pyrrolidinecarboxamide (3d). The same general procedure (modified for scale) as **3** was followed, only substituting aminodiphenylmethane (840 μ L, 5.0 mmol) for benzylamine in step 2. Unpurified **3d** was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3d** (1.12 g, 57% yield, 3 steps) as a white solid. M.P.

122-124 °C. IR (neat, thin film): 3062 (w), 3031 (w), 2949 (w), 1671 (s), 1533 (m), 1495 (m), 1451 (w), 752 (m), 702 (s), 551 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 12.62 (1H, d, *J* = 8.8 Hz), 7.43-

7.21 (15H, m), 6.32 (1H, d, $J = 8.8$ Hz), 4.46 (1H, d, $J = 13.6$ Hz), 4.33 (1H, d, $J = 13.6$ Hz), 3.66 (1H, dd, $J = 11.6, 8.4$ Hz), 3.34 (1H, q, $J = 10.0$ Hz), 3.23 (1H, dt, $J = 8.8, 2.4$ Hz), 2.56-2.32 (3H, m), 1.90-1.81 (1H, m). ^{13}C NMR (CDCl_3 , 100 MHz): δ 166.9, 142.5, 142.0, 132.2, 130.0, 129.8, 128.9, 128.8, 128.6, 127.4, 127.3, 127.1, 127.0, 72.6, 70.7, 66.4, 56.7, 27.4, 20.2. Anal Calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_2$: C, 77.69; H, 6.78; N, 7.25. Found C, 77.47; H, 6.99; N, 7.06. Optical Rotation: $[\alpha]_{\text{D}}^{25} -63^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-phenyl)-2-pyrrolidinecarboxamide (3e).

The same general procedure (modified for scale) as **3** was followed, only substituting aniline (570 μL , 5.00 mmol) for benzylamine in step 2.

Unpurified **3e** was purified by silica gel chromatography (97:3 CH_2Cl_2 :MeOH) to yield pure **3e** (738 mg, 48% yield, 3 steps) as an off white solid. M.P. 152-153 $^\circ\text{C}$. IR (neat, thin film): 2955 (br), 1671 (s), 1596 (m), 1558 (s), 1501 (w), 1445 (m), 1325 (w), 759 (m), 702 (m), 532 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 13.75 (1H, s), 7.63 (2H, dd, $J = 7.6, 1.2$ Hz), 7.48-7.45 (2H, m), 7.41-7.38 (3H, m), 7.32 (2H, t, $J = 7.6$ Hz), 7.09 (1H, tt, $J = 7.6, 1.2$ Hz), 4.56 (1H, d, $J = 13.2$ Hz), 4.52 (1H, d, $J = 13.2$ Hz), 3.70 (1H, dd, $J = 11.2, 7.6$ Hz), 3.41-3.36 (2H, m), 2.60-2.37 (3H, m), 1.96-1.84 (1H, m). ^{13}C NMR (CDCl_3 , 100 MHz): δ 165.6, 138.1, 132.3, 130.0, 129.8, 129.0, 128.9, 124.1, 120.3, 72.6, 71.3, 66.9, 27.6, 20.3. Anal Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2$: C, 72.95; H, 6.80; N, 9.45. Found C, 72.79; H, 7.04; N, 9.44. Optical Rotation: $[\alpha]_{\text{D}}^{25} -75^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(R)-1,2,2-trimethyl-propyl)-2-pyrrolidinecarboxamide (3f).

The same general procedure (modified for scale) as **3** was followed, only substituting (*R*)-3,3-dimethyl-2-butylamine (652 μL , 5.00 mmol) for benzylamine in step 2. Unpurified

3f was purified by silica gel chromatography (97:3 CH_2Cl_2 :MeOH) to yield pure **3f** (875 mg, 56% yield, 3 steps) as a sticky white solid. M.P. 178-180 $^\circ\text{C}$. IR (neat, thin film): 2970 (s), 2870 (m), 1666 (s), 1549 (s), 1455 (m), 1369 (m), 1133 (w), 754 (m), 698 (m), 661 (m), 493 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 11.40 (1H, d, $J = 7.2$ Hz), 7.45-7.41 (5H, m), 4.52 (1H, d, $J = 12.8$ Hz), 4.41 (1H, d, $J = 12.8$ Hz), 3.86 (1H, dq, $J = 9.2, 6.8$ Hz), 3.59 (1H, t, $J = 8.4$ Hz), 3.33 (1H, dd, $J = 20.4, 9.6$ Hz), 3.23 (1H, $J = 8.4, 2.0$ Hz), 2.51-2.30 (3H, m), 1.87-1.78 (1H, m), 1.14 (3H, d, $J = 6.8$ Hz), 0.95 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 166.8, 132.3, 130.2, 129.9, 72.7, 70.9, 66.5, 53.0, 34.6, 27.7, 26.7, 20.1, 16.6. Anal Calcd for $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_2$: C, 71.02; H, 9.27; N, 9.20. Found C, 70.77; H, 9.34; N, 8.90. Optical Rotation: $[\alpha]_{\text{D}}^{25} -25^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(S)-1,2,2-trimethyl-propyl)-2-pyrrolidinecarboxamide (3g).

The same general procedure (modified for scale) as **3** was followed, only substituting (*S*)-3,3-dimethyl-2-butylamine (652 μL , 5.00 mmol) for benzylamine in step 2. Unpurified **3g** was

purified by silica gel chromatography (97:3 CH_2Cl_2 :MeOH) to yield pure **3g** (890 mg, 59% yield, 3 steps) as a white solid. M.P. 137-138 $^\circ\text{C}$. IR (neat, thin film): 2964 (s), 2864 (w), 1666 (s), 1549 (m), 1511 (m), 1449 (w), 1362 (w), 1213 (w), 1133 (w), 748 (m), 704 (m) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 11.36 (1H, d, $J = 8.0$ Hz), 7.45-7.42 (5H, m), 4.59 (1H, d, $J = 12.8$ Hz), 4.47 (1H, d, $J = 12.8$ Hz), 3.91 (1H, ddd, $J = 13.6, 9.2, 6.8$ Hz), 3.61 (1H, dd, $J = 11.2, 7.6$ Hz), 3.30 (1H, q, $J = 10.0$ Hz), 3.17 (1H, dt, $J = 8.4, 1.6$ Hz), 2.48-2.30 (3H, m), 1.86-1.78 (1H, m), 1.13 (3H, d, $J = 6.4$ Hz), 1.02 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 167.0, 132.2, 130.2, 129.8, 129.0, 72.5, 70.8,

66.1, 53.3, 34.3, 27.6, 27.0, 20.1, 16.3. Anal Calcd for C₁₈H₂₈N₂O₂: C, 71.02; H, 9.27; N, 9.20. Found C, 70.80; H, 9.46; N, 9.10. Optical Rotation: $[\alpha]^{25}_{\text{D}} +15^{\circ}$ (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(R)-phenylglycine-methyl-ester)-2-pyrrolidinecarboxamide (3h). The same general procedure as **3** was followed, only substituting (*R*)-phenylglycine methyl ester (0.98 g, 5.0 mmol) for benzylamine in step 2. Unpurified product **3h** was purified by

silica gel chromatography (98:2 CH₂Cl₂:MeOH) to yield pure **3h** (784 mg, 42% yield, 3 steps) as a white solid. M.P. 134-135 °C. IR (neat, thin film): 2961 (w), 1747 (s), 1678 (s), 1532 (m), 1457 (w), 1338 (w), 1269 (w), 1206 (m), 1174 (w), 1017 (w), 759 (m), 721 (m), 589 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 12.56 (1H, d, *J* = 6.8 Hz), 7.48 (2H, d, *J* = 7.2 Hz), 7.39-7.28 (8H, m), 5.51 (1H, d, *J* = 7.2 Hz), 4.43 (1H, d, *J* = 12.8 Hz), 3.71 (3H, s), 3.62 (1H, dd, *J* = 10.8, 7.6 Hz), 3.39-3.26 (2H, m), 2.68-2.58 (1H, m), 2.51-2.34 (2H, m), 1.92-1.82 (1H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 170.7, 167.7, 136.4, 132.2, 129.9, 129.8, 129.0, 128.9, 128.4, 127.5, 72.3, 70.9, 67.0, 56.8, 52.8, 27.5, 20.2. Anal Calcd for C₂₁H₂₄N₂O₄: C, 68.46; H, 6.57; N, 7.60. Found C, 68.27; H, 6.90; N, 7.47. Optical Rotation: $[\alpha]^{25}_{\text{D}} -128^{\circ}$ (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(S)-phenylglycine-methyl-ester)-2-pyrrolidinecarboxamide (3i). The same general procedure (modified for scale) as **3** was followed, only substituting (*S*)-phenylglycine methyl ester (0.98 g, 5.0 mmol) for benzylamine in step 2. Unpurified product **3i** was

purified by silica gel chromatography (98:2 CH₂Cl₂:MeOH) to yield pure **3i** (492 mg, 26% yield, 3 steps) as a white solid. M.P. 159-161 °C. IR (neat, thin film): 2949 (m), 1747 (s), 1671 (s), 1533 (m), 1464 (w), 1331 (w), 1212 (m), 1168 (w), 752 (m), 702 (m), 589 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 12.77 (1H, d, *J* = 7.2 Hz), 7.52-7.30 (10 H, m), 5.56 (1H, d, *J* = 7.2 Hz), 4.95 (1H, d, *J* = 12.8 Hz), 4.73 (1H, d, *J* = 12.8 Hz), 3.74 (3H, s), 3.63 (1H, dd, 11.2, 8.0 Hz), 3.37 (1H, q, *J* = 9.6 Hz), 3.26 (1H, dt, *J* = 8.0, 1.6 Hz), 2.46-2.25 (3H, m), 1.86-1.80 (1H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 171.5, 168.1, 135.6, 132.5, 130.4, 129.8, 129.2, 129.0, 128.6, 127.6, 71.9, 70.5, 65.8, 57.1, 52.9, 27.0, 20.3. Anal Calcd for C₂₁H₂₄N₂O₄: C, 68.46; H, 6.57; N, 7.60. Found C, 68.08; H, 6.92; N, 7.43. Optical Rotation: $[\alpha]^{25}_{\text{D}} +64^{\circ}$ (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-R-phenylalanine-methyl-ester)-2-pyrrolidinecarboxamide (3j). The same general procedure (modified for scale) as **3** was followed, only substituting (*R*)-phenylalanine methyl ester (733 mg, 3.40 mmol) for benzylamine in step 2. Unpurified **3j** was purified by silica gel chromatography (99.5:0.5

CH₂Cl₂:MeOH) to yield pure **3j** (992 mg, 52% yield, 3 steps) as a white solid. M.P. 136-137 °C. IR (neat, thin film): 2951 (br), 1740 (s), 1666 (s), 1536 (s), 1493 (w), 1455 (m), 1369 (w), 1220 (m), 754 (m), 704 (s) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.89 (1H, d, *J* = 7.6 Hz), 7.41-7.33 (5H, m), 7.27 (2H, t, *J* = 8.0 Hz), 7.15-7.11 (3H, m), 4.89 (1H, ddd, *J* = 10.4, 7.6, 4.4 Hz), 4.17 (1H, d, *J* = 13.2 Hz), 3.91 (1H, d, *J* = 13.2 Hz), 3.76 (3H, s), 3.45-3.34 (2H, m), 3.25-3.13 (2H, m), 3.02 (1H, dd, *J* = 13.6, 10.4 Hz), 2.52-2.21 (3H, m), 1.82-1.74 (1H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 171.7, 168.0, 137.1, 132.2, 130.1, 128.7, 129.3, 128.8, 128.7, 127.0, 72.0, 70.3, 66.2, 53.4, 52.6, 37.9, 27.2, 20.1. Anal Calcd for C₂₂H₂₆N₂O₄: C, 69.09; H, 6.85; N, 7.32. Found C, 68.90; H, 6.86; N, 7.24. Optical Rotation: $[\alpha]^{25}_{\text{D}} -1.0^{\circ}$ (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-S-phenylalanine-ethyl-ester)-2-pyrrolidinecarboxamide (3k). The same general procedure (modified for scale) as **3** was followed, only substituting (*S*)-phenylalanine ethyl ester (783 mg, 3.40 mmol) for benzylamine in step 2. Unpurified **3k** was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3k** (728 mg, 51% yield, 3 steps) as a yellow oil which solidified upon standing. M.P. 46-47 °C. IR (neat, thin film): 2964 (br), 1741 (s), 1666 (s), 1536 (m), 1499 (w), 1220 (m), 1189 (m), 1027 (w), 748 (m), 698 (s) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 12.15 (1H, d, *J* = 8.0 Hz), 7.40-7.35 (5H, m), 7.30-7.24 (4H, m), 7.20 (1H, tt, *J* = 7.2, 2.0 Hz), 4.81 (1H, dq, *J* = 8.8, 4.8 Hz), 4.62 (1H, d, *J* = 13.2 Hz), 4.57 (1H, d, *J* = 13.2 Hz), 4.19 (1H, d, *J* = 7.2 Hz), 4.16 (1H, d, *J* = 7.2 Hz), 3.49 (1H, dd, *J* = 11.2, 8.0 Hz), 3.31-3.16 (3H, m), 3.07 (1H, dd, *J* = 14.0, 9.2 Hz), 2.35-2.11 (3H, m), 1.80-1.77 (1H, m), 1.21 (3H, t, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 171.3, 167.9, 136.5, 132.1, 130.2, 129.4, 129.2, 128.6, 128.3, 126.7, 72.1, 69.9, 65.6, 61.3, 53.4, 37.8, 26.8, 19.9, 14.3. Anal Calcd for C₂₃H₂₈N₂O₄: C, 69.67; H, 7.12; N, 7.07. Found C, 69.46; H, 7.39; N, 6.98. Optical Rotation: [α]_D²⁵ -27° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(R)-1-phenyl-ethyl)-2-pyrrolidinecarboxamide (3l). The same general procedure as **3** was followed, only substituting (*R*)-1-phenylethylamine (620 μL, 5.0 mmol) for benzylamine in step 2. Unpurified **3l** was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3l** (895 mg, 54% yield, 3 steps) as a white solid. M.P. 138-139 °C. IR (neat, thin film): 2964 (br), 1666 (s), 1547 (s), 1497 (w), 1441 (w), 755 (m), 698 (s) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.83 (1H, d, *J* = 8.0 Hz), 7.49-6.42 (5H, m), 7.36-7.30 (4H, m), 7.23 (1H, tt, *J* = 6.8, 2.0 Hz), 5.12 (1H, p, *J* = 6.8 Hz), 4.51 (1H, d, *J* = 13.2 Hz), 4.50 (1H, d, *J* = 13.2 Hz), 3.62 (1H, dd, *J* = 10.8, 8.0 Hz), 3.35 (1H, q, *J* = 9.6 Hz), 3.26 (1H, dt, *J* = 10.8, 8.4 Hz), 2.45-2.26 (3H, m), 1.86-1.79 (1H, m), 1.51 (3H, d, *J* = 6.8 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 166.8, 143.8, 132.4, 130.2, 129.9, 129.0, 128.7, 127.0, 126.1, 72.5, 71.1, 66.9, 48.7, 27.6, 23.7, 20.1. Anal Calcd for C₂₀H₂₄N₂O₂: C, 74.04; H, 7.46; N, 8.64. Found C, 73.81; H, 7.69; N, 8.64. Optical Rotation: [α]_D²⁵ +9.4° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-benzyl)-(N-(S)-1-phenylethyl)-2-pyrrolidine carboxamide (3m). The same general procedure (modified for scale) as **3** was followed, only substituting (*S*)-1-phenylethylamine (620 μL, 5.0 mmol) for benzylamine in step 2. Unpurified **3m** was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3m** (596 mg, 36% yield, 3 steps) as an off-white solid. M.P. 123-124 °C. IR (neat, thin film): 2967 (br), 1672 (s), 1540 (s), 1497 (w), 1459 (w), 770 (m), 708 (m), 501 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.88 (1H, d, *J* = 8.0 Hz), 7.45 (2H, dd, *J* = 8.4, 1.6 Hz), 7.40-7.31 (5H, m), 7.27-7.21 (3H, m), 5.17 (1H, p, *J* = 6.8 Hz), 4.41 (1H, d, *J* = 12.8 Hz), 4.29 (1H, d, *J* = 12.8 Hz), 5.54 (1H, dd, *J* = 11.6, 8.0 Hz), 3.30 (1H, q, *J* = 10.0 Hz), 3.21 (1H, dt, *J* = 8.4, 2.4 Hz), 2.55-2.31 (3H, m), 1.92-1.81 (1H, m), 1.52 (3H, d, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 166.8, 144.1, 132.2, 130.0, 129.8, 129.0, 128.7, 127.1, 126.3, 72.3, 70.8, 66.4, 48.8, 27.4, 23.2, 20.2. Anal Calcd for C₂₀H₂₄N₂O₂: C, 74.04; H, 7.46; N, 8.64. Found C, 74.07; H, 7.60; N, 8.51. Optical Rotation: [α]_D²⁵ -84° (c 1.0, CHCl₃).

(1S,2S)-(1-Oxido)-(1-methyl)-(N-(R)-1-phenylethyl)-2-pyrrolidinecarboxamide (3n). (*S*)-*N*-Methylproline⁴ (0.65 g, 5.0 mmol), (*R*)-1-phenylethylamine (0.64 mL, 5.0 mmol), and K₂CO₃ (1.0 g, 7.5 mmol) were added to DMF (20 mL) and THF (15 mL) and were stirred for 30 minutes to

dissolve the acid. HBTU (2.1 g, 5.5 mmol) was added and the reaction was allowed to stir for 2 h after which time water (50 mL) was added. The reaction was extracted with ethyl acetate (2 x 50 mL). The organic layer was washed with 1% aqueous sodium carbonate (5 x 50 mL) and brine (1 x 25 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield unpurified amide (0.96 g, 83% unpurified yield).

The unpurified amide (0.96 g, 4.1 mmol) was dissolved in methylene chloride (60 mL). Potassium carbonate (1.1 g, 8.3 mmol) was then added and the reaction was cooled to -78 °C. *m*-CPBA (0.95 g of 75% pure, net 0.71 g, 4.1 mmol) was then added, and the reaction was allowed to stir at -78 °C for 3 h. At this time, the reaction was allowed to warm to room temperature. After stirring for 2 h at room temperature, methylene chloride (50 mL) was added to dilute the reaction and celite (500 mg) was added to aid filtration. The reaction was then filtered, and the methylene chloride was removed under reduced pressure. The resulting oil was purified by silica gel chromatography (94:6 CH₂Cl₂:MeOH) to yield pure **3n** as a off white solid (688 mg, 56% yield over 2 steps from *N*-methylproline). M.P. 101-103 °C. IR (neat, thin film): 2962 (br), 1671 (s), 1545 (s), 1495 (w), 1445 (m), 1212 (w), 866 (w), 765 (m), 696 (m), 513 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.71 (1H, d, *J* = 7.6 Hz), 7.38-7.19 (5H, m), 5.12 (1H, p, *J* = 6.8 Hz), 3.68 (1H, t, *J* = 8.4 Hz), 3.59 (1H, tt, *J* = 8.4, 2.0 Hz), 3.46 (1H, q, *J* = 9.6 Hz), 3.33 (3H, s), 2.50-2.35 (3H, m), 2.06-1.95 (1H, m), 1.51 (3H, d, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 166.3, 143.6, 128.7, 127.1, 126.0, 76.1, 71.6, 55.5, 48.7, 28.2, 23.5, 20.7. Anal Calcd for C₁₄H₂₀N₂O₂: C, 67.71; H, 8.12; N, 11.28. Found C, 67.56; H, 8.09; N, 11.12. Optical Rotation: [α]_D²⁵ +35° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-methylethyl)-(N-(R)-1-phenylethyl)-2-pyrrolidinecarboxamide (3o).

Step 1: Palladium on Carbon (10% by wt., dry, 0.12 g) was added to a dry 100 mL flask and flushed with N₂. Methanol (20 mL) was then slowly added. To this suspension was charged (*S*)-proline (1.2 g, 10 mmol) and acetone (3.7 mL, 50 mmol). The flask was charged with H₂ and was kept under a balloon of H₂ for 16 h. At this time the reaction was purged with N₂ and filtered through celite. Removal of the methanol under reduced pressure led to the unpurified acid (1.5 g, 96% unpurified yield).

Step 2: The unpurified acid (1.5 g, 50 mmol) was dissolved in DMF (40 mL) and THF (30 mL). (*R*)-Phenylethylamine (1.2 mL, 9.6 mmol) and K₂CO₃ (2.0 g, 14 mmol) were added and the mixture was allowed to stir for 30 minutes to dissolve the acid. TBTU (3.4 g, 11 mmol) was then added and the reaction was allowed to stir for 2 h after which time water (50 mL) was added. The reaction was extracted with ethyl acetate (2 x 50 mL). The organic layer was washed with 1% aqueous sodium carbonate (5 x 50 mL) and brine (1 x 25 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield 1.99 g of unpurified amide (79% unpurified yield).

Step 3: The unpurified amide (1.5 g, 5.8 mmol) was then dissolved in methylene chloride (80 mL). Potassium carbonate (1.60 g, 11.5 mmol) was then added and the reaction was cooled to -78 °C. *m*-CPBA (1.3 g of 75% pure, net 0.99 g, 5.8

⁴ Synthesized from (*S*)-proline and formaldehyde, see Aurelio, L.; Box, J. S.; Brownlee, R. T. C.; Hughes, A. B.; Sleebs, M. M. *J. Org. Chem.* **2003**, *68*, 2652-2667.

mmol) was then added, and the reaction was allowed to stir at -78 °C for 3 h. At this time, the reaction was allowed to warm to room temperature. After stirring for 2 h at room temperature, methylene chloride (50 mL) was added to dilute the reaction and celite (500 mg) was added to aid filtration. The reaction was then filtered, and the methylene chloride was removed under reduced pressure. The resulting oil was purified by silica gel chromatography (96:4 CH₂Cl₂:MeOH) to yield pure **3o** as an off white solid (1.1 g, 52% yield over 3 steps). M.P. 113-114 °C. IR (neat, thin film): 2970 (br), 1660 (s), 1547 (s), 1491 (w), 1441 (w), 1372 (w), 761 (w), 698 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.77 (1H, d, *J* = 7.6 Hz), 7.37-7.20 (5H, m), 5.09 (1H, p, *J* = 6.8 Hz), 3.65 (1H, t, *J* = 8.8 Hz), 3.53 (1H, p, *J* = 6.4 Hz), 3.42-3.37 (1H, m), 3.23 (1H, dd, *J* = 19.2, 8.8 Hz), 2.46-2.33 (3H, m), 1.95-1.87 (1H, m), 1.464 (3H, d, *J* = 6.8 Hz), 1.457 (3H, d, *J* = 6.8 Hz), 3.39 (3H, d, *J* = 6.4 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 167.9, 143.0, 128.6, 126.9, 126.0, 73.3, 68.5, 66.6, 48.6, 29.3, 29.3, 23.2, 20.5, 18.3. Anal Calcd for C₁₆H₂₄N₂O₂: C, 69.53; H, 8.75; N, 10.14. Found C, 69.58; H, 8.81; N, 9.98. Optical Rotation: [α]_D²⁵ +1.8° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-ethylpropyl)-(N-(R)-1-phenylethyl)-2-pyrrolidine-carboxamide (3p). **3p** was synthesized in the same manner as **3o** (adjusted for scale) but with 3-pentanone (6.3 mL, 60 mmol) instead of acetone in step 1. Unpurified **3p** was purified by silica gel chromatography (98:2 CH₂Cl₂:MeOH) to yield pure **3p** as a white solid (1.4 g, 53% yield). M.P.

110-111 °C. IR (neat, thin film): 2970 (br), 2877 (w), 1660 (s), 1542 (s), 1493 (m), 1449 (m), 1374 (w), 1213 (w), 1126 (w), 1021 (w), 878 (w), 760 (w), 704 (m), 524 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.95 (1H, d, *J* = 8.0 Hz), 7.31-7.19 (5H, m), 5.12 (1H, dq, *J* = 6.8, 1.2 Hz), 3.74 (1H, t, *J* = 8.0 Hz), 3.39-3.25 (2H, m), 3.05 (1H, ddd, *J* = 12.0, 7.2, 3.6 Hz), 2.44-2.29 (4H, m), 1.94-1.84 (2H, m), 1.74-1.61 (2H, m), 1.47 (3H, d, *J* = 6.8 Hz), 1.080 (3H, t, *J* = 8.0 Hz), 1.075 (3H, t, *J* = 7.6). ¹³C NMR (CDCl₃, 100 MHz): δ 167.6, 143.8, 128.6, 127.0, 126.0, 79.7, 72.6, 65.3, 48.5, 28.5, 23.5, 23.4, 23.3, 20.5, 12.8, 12.6. Anal Calcd for C₁₈H₂₈N₂O₂: C, 71.02; H, 9.27; N, 9.20. Found C, 70.87; H, 9.41; N, 9.27. Optical Rotation: [α]_D²⁵ +8.2° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cyclopentyl)-(N-(R)-1-phenylethyl)-2-pyrrolidine-carboxamide (3q).

Step 1: Palladium on Carbon (10% by wt., dry, 0.23 g) was added to a dry 100 mL flask and flushed with N₂. Methanol (40 mL) was then slowly added. To this suspension was charged (*S*)-proline (2.3 g, 20 mmol) and cyclopentanone (2.0 mL, 22 mmol). The reaction was placed under an atmosphere H₂ (balloon) for 16 h. At this time the reaction was purged with N₂ and filtered through celite. Removal of the methanol under reduced pressure led to a pale yellow solid which was collected and washed with diethyl ether (3 x 25 mL) to yield the unpurified acid (2.6 g, 71% unpurified yield) as an off white solid.

Step 2: The unpurified acid (1.5 g, 8.0 mmol) was then dissolved in DMF (40 mL) and THF (30 mL). (*R*)-1-Phenylethylamine (1.0 mL, 8.0 mmol) and K₂CO₃ (1.7 g, 12 mmol) were then added and the mixture was allowed to stir for 30 minutes to dissolve the acid. TBTU (3.1 g, 9.6 mmol) and HOBT (1.5 g, 9.6 mmol) were then added and the reaction was allowed to stir for 2 h after which time water (50 mL) was added. The reaction was extracted with ethyl acetate (2 x 50 mL). The organic layer was washed with 1% aqueous sodium carbonate (5 x 50 mL) and with brine (1 x 25 mL), dried over

anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield unpurified amide (0.76 g, 33% unpurified yield).

Step 3: The unpurified amide (0.76 g, 2.6 mmol) was then dissolved in methylene chloride (40 mL). Potassium carbonate (0.73 g, 5.3 mmol) was then added and the reaction was cooled to -78 °C. *m*-CPBA (0.61 g of 75% pure, net 0.46 g, 2.6 mmol) was then added, and the reaction was allowed to stir at -78 °C for 3 h. At this time, the reaction was allowed to warm to room temperature. After stirring for 2 h at room temperature, methylene chloride (50 mL) was added to dilute the reaction and celite (500 mg) was added to aid filtration. The reaction was then filtered, and the methylene chloride was removed under reduced pressure. The resulting oil was purified by silica gel chromatography (97:3 CH₂Cl₂:MeOH) to yield pure **3q** as a white solid (514 mg, 15% yield over 3 steps). M.P. 86-88 °C. IR (neat, thin film): 2962 (m), 2867 (w), 1665 (s), 1539 (s), 1495 (w), 1445 (w), 872 (w), 771 (w), 702 (m), 545 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.67 (1H, d, *J* = 7.6 Hz), 7.31-7.20 (5H, m), 5.08 (1H, p, *J* = 7.2 Hz), 3.61-3.55 (2H, m), 3.44 (1H, t, *J* = 10.4 Hz), 3.30 (1H, q, *J* = 9.6 Hz), 2.40-2.35 (3H, m), 2.22-2.14 (3H, m), 1.91-1.82 (3H, m), 1.67-1.57 (3H, m), 1.48 (3H, d, *J* = 6.8 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 167.8, 143.8, 128.5, 126.8, 125.9, 78.3, 75.4, 69.4, 48.5, 29.4, 27.3, 27.1, 24.3, 23.6, 23.0, 20.7. Anal Calcd for C₁₈H₂₆N₂O₂: C, 71.49; H, 8.67; N, 9.26. Found C, 71.25; H, 8.80; N, 9.12. Optical Rotation: [α]_D²⁵ -5.4° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1-phenylethyl)-2-pyrrolidine-carboxamide (3r).

Step 1: Palladium on Carbon (10% by wt., dry, 0.50 g) was added to a dry 500 mL flask and flushed with N₂. Methanol (200 mL) was then slowly added. To this suspension was charged (*S*)-proline (11.5 g, 100 mmol) and cyclohexanone (11.4 mL, 110 mmol). The reaction flask was purged with H₂ and was kept under a balloon of H₂ for 16 h. At this time the reaction was purged with N₂ and filtered through celite. Removal of the methanol under reduced pressure led to a pale yellow solid which was collected and washed with diethyl ether (3 x 75 mL) to yield the unpurified acid (17.4 g, 88% unpurified yield) as an off white solid.

Step 2: The unpurified acid (1.55 g, 7.90 mmol) was dissolved in DMF (16 mL) and THF (12 mL). (*R*)-1-Phenylethylamine (1.0 mL, 7.9 mmol) and K₂CO₃ (1.63 g, 11.8 mmol) were then added and the mixture was allowed to stir for 30 minutes to dissolve the acid. TBTU (2.8 g, 8.6 mmol) and HOBt (1.32 g, 8.60 mmol) were then added and the reaction was allowed to stir for 2 h after which time water (30 mL) was added. The reaction was extracted with ethyl acetate (3 x 40 mL). The organic layer was washed with 1% aqueous sodium carbonate (5 x 30 mL) and with brine (1 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield unpurified amide (2.12 g, 90 % unpurified yield).

Step 3: The unpurified amide (2.12 g, 7.10 mmol) was then dissolved in methylene chloride (50 mL). Potassium carbonate (2.00 g, 14.1 mmol) was then added and the reaction was cooled to -78 °C. *m*-CPBA (1.60 g of 75% pure, net 1.22 g, 7.10 mmol) was then added, and the reaction was allowed to stir at -78 °C for 2 h. At this time, the reaction was allowed to warm to room temperature. After stirring for 2 h at room temperature, methylene chloride (50 mL) was added to dilute the reaction and celite (2 g) was added to aid filtration. The reaction was then filtered, and the methylene chloride was removed under reduced pressure. The resulting solid was

collected and stirred with diethyl ether (50 mL) for 5 minutes. The resulting solids were collected and washed with diethyl ether (3x 50 mL) to yield pure **3r** as a white powder (1.67 g, 60% yield over 3 steps). Crystals suitable for X-ray analysis were grown from CH₂Cl₂/hexanes. M.P. 121-122 °C. IR (neat, thin film): 2943 (br), 2861 (m), 1665 (s), 1552 (s), 1501 (w), 1451 (m), 866 (w), 759 (m), 702 (m), 526 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.81 (1H, d, *J* = 6.8 Hz), 7.31-7.19 (5H, m), 5.10 (1H, p, *J* = 7.2 Hz), 3.65 (1H, br), 3.42 (1H, dd, *J* = 6.0, 4.8 Hz), 3.29 (1H, dd, *J* = 10.8, 8.8 Hz), 3.14 (1H, tt, *J* = 12.0, 3.6 Hz), 2.40-2.37 (4H, m), 2.14 (1H, d, *J* = 12.0 Hz), 1.93-1.90 (3H, m), 1.71-1.58 (3H, m), 1.48 (3H, d, *J* = 6.8 Hz), 1.35-1.12 (3H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 168.0, 143.8, 128.5, 126.8, 125.9, 77.5, 76.3, 72.7, 66.6, 48.5, 28.7, 27.9, 25.7, 25.6, 25.3, 23.1, 20.4. Anal Calcd for C₁₉H₂₈N₂O₂: C, 72.12; H, 8.92; N, 8.88. Found C, 71.93; H, 9.20; N, 8.88. Optical Rotation: [α]_D²⁵ -1.3° (c 3.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-tetrahydro-pyran-4-yl)-(N-(R)-1-phenylethyl)-2-pyrrolidinecarboxamide (3s). The procedure for **3q** was followed, only tetrahydro-pyran-4-one (0.99 g, 5.0 mmol) was substituted for cyclopentanone in step 1. Unpurified **3s** was purified by silica gel chromatography (95:5 CH₂Cl₂:MeOH) to yield pure **3s** as a white solid (580 mg, 66% yield over 3 steps).

M.P. 135-137 °C. IR (neat, thin film): 2964 (br), 2852 (br), 1666 (s), 1549 (s), 1499 (w), 1462 (w), 1257(w), 1164 (w), 1095 (w), 1027 (w), 990 (w), 878 (2), 773 (w), 711 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.60 (1H, d, *J* = 8.0 Hz), 7.31-7.21 (5H, m), 5.08 (1H, p, *J* = 6.8 Hz), 4.13-4.10 (2H, m), 3.64 (1H, t, *J* = 8.8 Hz), 3.45-3.24 (6H, m), 2.42-2.36 (3H, m), 2.24 (1H, d, *J* = 12.0 Hz), 2.16-1.91 (5 H, m), 1.49 (1H, t, *J* = 6.4 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 167.6, 143.7, 128.7, 127.0, 126.0, 73.2, 73.1, 67.1, 66.6, 66.5, 48.7, 28.7, 28.2, 28.1, 23.2, 20.4. Anal Calcd for C₁₈H₂₆N₂O₃: C, 67.90; H, 8.23; N, 8.80. Found C, 68.02; H, 8.43; N, 8.79. Optical Rotation: [α]_D²⁵ +5.8° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cycloheptyl)-(N-(R)-1-phenylethyl)-2-pyrrolidinecarboxamide (3t). The procedure for **3q** was followed, only cycloheptanone (2.60 mL, 22.0 mmol) was substituted for cyclopentanone in step 1. Unpurified **3t** was recrystallized from CH₂Cl₂/hexanes to yield pure **3t** (894 mg, 25% yield for 3 steps) as an off white solid.

M.P. 105-107 °C. IR (neat, thin film): 2924 (m), 2855 (w), 1671 (s), 1539 (s), 1451 (m), 759 (w), 656 (m), 532 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.94 (1H, d, *J* = 7.6 Hz), 7.32-7.21 (5H, m), 5.13 (1H, p, *J* = 7.6 Hz), 3.75 (1H, dd, *J* = 11.2, 8.0 Hz), 3.55 (1H, tt, *J* = 8.8, 3.6 Hz), 3.41-3.25 (2H, m), 2.51-2.30 (4H, m), 2.11-2.06 (1H, m), 1.90-1.52 (10 H, m), 1.49 (3H, d, *J* = 7.2 Hz), 1.43-1.32 (1H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 167.6, 143.8, 128.6, 126.9, 126.0, 77.6, 72.3, 64.8, 48.5, 29.7, 28.8, 28.6, 28.4, 27.9, 25.9, 25.1, 23.5, 20.5. Anal Calcd for C₂₀H₃₀N₂O₂: C, 72.69; H, 9.15; N, 8.48. Found C, 72.90; H, 9.15; N, 8.24. Optical Rotation: [α]_D²⁵ -5.0° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cyclooctyl)-(N-(R)-1-phenylethyl)-2-pyrrolidinecarboxamide (3u). The procedure for **3q** was followed, only cyclooctanone (2.80 g, 22.0 mmol) was substituted for cyclopentanone in step 1. Unpurified **3u** was recrystallized from CH₂Cl₂/hexanes to yield pure **3u** (897 mg, 21% yield for 3 steps) as a white solid.

M.P. 117-119 °C. IR (neat, thin film): 2924 (m), 2861 (w), 1659 (s), 1545 (m), 1495 (w), 1457 (w), 904 (w), 771 (w), 702 (m), 513 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.88 (1H, d, *J* = 8.0 Hz), 7.33-7.20 (5H, m), 5.12 (1H, p, *J* = 7.6 Hz), 3.75 (1H, dd, *J* = 11.2, 7.6 Hz), 3.44-3.27 (3H, m), 2.56-2.20 (6H, m),

1.91-1.56 (12H, m), 1.49 (3H, d, $J = 6.8$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 167.7, 143.8, 128.6, 127.0, 126.0, 76.3, 72.5, 64.9, 48.6, 29.0, 28.8, 28.5, 27.0, 26.5, 26.4, 26.2, 25.8, 23.5, 20.5. Anal Calcd for $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_2$: C, 73.22; H, 9.36; N, 8.13. Found C, 72.97; H, 9.42; N, 8.42. Optical Rotation: $[\alpha]^{25}_{\text{D}} -2.2^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1,2,2-trimethyl-propyl)-2-pyrrolidinecarboxamide (3v). The procedure (modified for scale) for **3r** was followed, only (*R*)-3,3-dimethyl-2-butylamine (1.30 mL, 10.0 mmol) was substituted for (*R*)-1-phenylethylamine in step 2. Unpurified

3v was recrystallized from CH_2Cl_2 /Hexanes to yield pure **3v** as an off-white solid (1.01 g, 50% yield over 3 steps). M.P. 178-180 $^\circ\text{C}$. IR (neat, thin film): 2955 (s), 2861 (m), 1659 (s), 1558 (m), 1451 (w), 1363 (w), 1136 (w), 891 (w), 746 (w), 664 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 11.35 (1H, d, $J = 7.6$ Hz), 3.77 (1H, dq, $J = 9.6, 6.8$ Hz), 3.61 (1H, t, $J = 9.2$ Hz), 3.40 (1H, tt, $J = 8.4, 3.2$ Hz), 3.26 (1H, q, $J = 9.6$ Hz), 3.07 (1H, tt, $J = 11.6, 3.6$ Hz), 2.46-2.31 (4H, m), 2.09 (1H, dt, $J = 12.0, 2.8$ Hz), 1.92-1.86 (3H, m), 1.68-1.50 (3H, m), 1.31-1.11 (3H, m), 1.06 (3H, d, $J = 6.6$ Hz), 0.90 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.0, 76.3, 72.9, 66.7, 52.7, 34.6, 29.0, 27.9, 27.8, 26.6, 25.7, 25.6, 25.3, 20.4, 15.8. Anal. Calcd for $\text{C}_{17}\text{H}_{32}\text{N}_2\text{O}_3$: C, 68.88; H, 10.88; N, 9.45. Found C, 68.68; H, 11.09; N, 9.38. Optical Rotation: $[\alpha]^{25}_{\text{D}} -49^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1-cyclohexyl-ethyl)-2-pyrrolidinecarboxamide (3w). The procedure for **3r** was followed, only (*R*)-1-cyclohexylethylamine (0.73 mL, 5.0 mmol) was substituted for (*R*)-1-phenylethylamine, with adjustments for scale, in step 2.

Unpurified **3w** purified by silica gel chromatography (95:5 CH_2Cl_2 :MeOH) to yield pure **3w** as pale yellow solid (0.81 g, 44% yield over 3 steps). M.P. 149-151 $^\circ\text{C}$. IR (neat, thin film): 2924 (s), 2855 (m), 1671 (s), 1546 (m), 1451 (m), 904 (w), 866 (w), 759 (w), 671 (w), 526 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 11.15 (1H, d, $J = 8.0$ Hz), 3.80 (1H, ddq, $J = 13.2, 9.6, 6.8$ Hz), 3.61 (1H, t, $J = 8.8$ Hz), 3.40 (1H, t, $J = 8.4$ Hz), 3.27 (1H, q, $J = 9.6$ Hz), 3.09 (1H, t, $J = 12.0$ Hz), 2.48-2.33 (4H, m), 2.11 (1H, d, $J = 8.0$ Hz), 1.91-1.87 (2H, m), 1.79-1.50 (8H, m), 1.36-0.93 (10H, m), 1.12 (3H, d, $J = 6.4$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.1, 76.2, 72.8, 66.5, 49.1, 43.3, 29.8, 29.1, 29.0, 27.9, 27.8, 26.7, 26.5, 26.5, 25.7, 25.6, 25.3, 20.3, 18.0. Anal Calcd for $\text{C}_{19}\text{H}_{34}\text{N}_2\text{O}_3$: C, 70.76; H, 10.63; N, 8.69. Found C, 70.69; H, 10.90; N, 8.40. Optical Rotation: $[\alpha]^{25}_{\text{D}} -38^\circ$ (c 1.0, CHCl_3).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1-(1,2,3,4-tetrahydronaphthyl))-2-pyrrolidinecarboxamide (3x). The procedure for **3r** was followed, only (*R*)-1,2,3,4-tetrahydro-1-naphthylamine (0.74 mL, 5.0 mmol) was substituted for (*R*)-1-Phenylethylamine, with adjustments for scale, in step 2. Unpurified **3x** was recrystallized from

CH_2Cl_2 to yield pure **3x** as an off-white solid (1.12 g, 58% yield over 3 steps). M.P. 172-174 $^\circ\text{C}$. IR (neat, thin film): 2936 (m), 2855 (w), 1659 (s), 1539 (s), 1489 (w), 1451 (m), 1338 (w), 872 (w), 752 (m), 664 (w), 532 (m) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 11.56 (1H, d, $J = 8.8$ Hz), 7.30-7.27 (2H, m), 7.19-7.08 (2H, m), 5.25-5.19 (1H, m), 3.75 (1H, t, $J = 9.6$ Hz), 3.42 (1H, dt, $J = 11.2, 2.8$ Hz), 3.32 (1H, q, $J = 10.0$ Hz), 3.16 (1H, tt, $J = 11.2, 3.2$ Hz), 2.89-2.76 (2H, m), 2.56-2.38 (4H, m), 2.19-2.11 (2H, m), 1.99-1.79 (6H, m), 1.72-1.57 (3H, m), 1.38-1.15 (3H, m). ^{13}C NMR (CD_3OD , 100 MHz): δ 169.2, 137.5, 136.6, 129.3, 128.3, 127.5, 126.3, 76.6, 73.5, 66.7, 47.7, 31.2, 29.4, 28.9,

28.3, 27.9, 25.8, 25.7, 25.5, 20.7, 20.2. Anal Calcd for C₂₁H₃₀N₂O₃: C, 73.65; H, 8.83; N, 8.18. Found C, 73.80; H, 9.05; N, 7.93. Optical Rotation: $[\alpha]^{25}_D$ -21° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1-(4-methoxy-phenyl-ethyl))-2-pyrrolidinecarboxamide (3y). The procedure for **3r** was followed, only (*R*)-1-(4-methoxyphenyl)ethylamine (364

mg, 2.5 mmol) was substituted for (*R*)-1-Phenylethylamine in step 2. Unpurified **3y** was collected and triturated with diethyl ether (20 mL). The solid was then collected and washed with diethyl ether (3 x 20 mL) to yield **3y** as an off-white solid (594 mg, 61% yield over 3 steps). M.P. 71-73 °C. IR (neat, thin film): 2933 (br), 2858 (m), 1660 (s), 1611 (w), 1542 (m), 117 (s), 1449 (w), 1294 (w), 1250 (s), 1182 (m), 1027 (w), 835 (m), 748 (w), 531 (w) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.71 (1H, d, *J* = 7.6 Hz), 7.23 (2H, d, *J* = 8.4 Hz), 6.83 (2H, d, *J* = 8.8 Hz), 5.04 (1H, p, *J* = 7.2 Hz), 3.77 (3H, s), 3.63 (1H, t, *J* = 8.8 Hz), 3.40 (1H, dt, *J* = 6.0, 1.6 Hz), 3.26 (1H, dt, *J* = 10.4, 8.8 Hz), 3.13 (1H, tt, *J* = 12.0, 3.2 Hz), 2.41-2.33 (4H, m), 2.13 (1H, d, *J* = 12.4 Hz), 1.92-1.86 (3H, m), 1.71-1.57 (3H, m), 1.45 (3H, d, *J* = 6.8 Hz), 1.38-1.10 (3H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 167.9, 158.5, 136.2, 127.1, 114.0, 76.4, 72.9, 66.7, 55.5, 48.0, 28.8, 25.8, 25.7, 25.4, 23.1, 20.5. Anal Calcd for C₂₀H₃₀N₂O₃: C, 69.33; H, 8.73; N, 8.09. Found C, 69.21; H, 9.00; N, 8.12. Optical Rotation: $[\alpha]^{25}_D$ +7.8° (c 1.0, CHCl₃).

(1R,2S)-(1-Oxido)-(1-cyclohexyl)-(N-(R)-1-(4-chloro-phenyl-ethyl))-2-pyrrolidinecarboxamide (3z). The procedure for **3r** was followed, only (*R*)-1-(4-Chlorophenyl)ethylamine (0.34 mL,

2.5 mmol) was substituted for (*R*)-1-Phenylethylamine, with adjustments for scale, in step 2. Unpurified **3z** was collected and washed with diethyl ether (3 x 20 mL) to yield **3z** as an off-white solid (371 mg, 37% yield over 3 steps). M.P. 91-93 °C. IR (neat, thin film): 2939 (br), 2864 (w), 1666 (s), 1542 (s), 1493 (m), 1449 (w), 1344 (w), 1095 (w), 1015 (w), 829 (m), 754 (w), 543 (m) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 11.89 (1H, d, *J* = 7.2 Hz), 7.26 (2H, d, *J* = 2.0 Hz), 7.26 (2H, d, *J* = 2.0 Hz), 5.06 (1H, p, *J* = 7.2 Hz), 3.65 (1H, t, *J* = 9.6 Hz), 3.43 (1H, dt, *J* = 8.0, 2.4 Hz), 3.32-3.25 (1H, m), 3.14 (1H, tt, *J* = 12.0, 4.0 Hz), 2.43-2.33 (4H, m), 2.14 (1H, d, *J* = 12.0 Hz), 1.94-1.91 (3H, m), 1.69-1.58 (3H, m), 1.46 (3H, d, *J* = 7.2 Hz), 1.36-1.15 (3H, m). ¹³C NMR (CDCl₃, 100 MHz): δ 168.2, 142.6, 132.6, 128.7, 127.5, 76.5, 72.8, 66.8, 48.0, 28.9, 27.9, 25.8, 25.7, 25.4, 23.1, 20.5. Anal Calcd for C₁₉H₂₇ClN₂O₂: C, 65.04; H, 7.76; N, 7.98. Found C, 64.83; H, 7.94; N, 7.93. Optical Rotation: $[\alpha]^{25}_D$ +7.8° (c 1.0, CHCl₃).

Representative procedure for the Catalytic Asymmetric Allylation of Aldehydes with Allyltrichlorosilane and Proline Based N-Oxide Ligand. In a N₂ atmosphere glovebox, ligand **3r** was weighed out to a dry round-bottomed flask and dissolved in 1,2-dichloroethane (DCE). The aldehyde was added and the reaction was allowed to stir for 5 minutes. Allyltrichlorosilane was then added drop wise. The reaction was sealed with a septum and Teflon tape and taken out of glovebox. The reaction was allowed to stir for 24 hours at room temperature (23 °C). To quench, the reaction was cooled to 0 °C in an ice bath and diisopropylethylamine (DIPEA, 5 equiv. with respect to the aldehyde) was added.⁵ 3 M NaOH (aq) was then added and the reaction was vigorously stirred for 2 h. The reaction was extracted with diethyl ether (3 x), and the combined organic layers were washed with 10% citric acid (1 x), brine (1 x), dried over anhydrous Na₂SO₄

⁵ The addition of DIPEA during workup was found to facilitate the hydrolysis of the O-Si bond. In addition, for electron-rich substrates (such as entry 5, Table 4), epimerization of the product was found when the reaction was quenched under acidic conditions.

and concentrated. The products were purified by silica gel chromatography. The purified products were analyzed for enantioenrichment by chiral HPLC (Chiralcel OD or AS), or GLC (Supelco Alpha, Beta, or Gamma Dex 120).

(R)-1-Phenyl-3-buten-3-ol (Entry 1, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and benzaldehyde (102 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (217 μ L, 1.5 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (85:15 hexanes:diethyl ether) to yield a pale yellow oil (128 mg, 86% yield, 87% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.38-7.27 (5H, m), 5.82 (1H, ddt, J = 17.2, 10.0, 7.2 Hz), 5.17 (1H, dd, J = 17.2, 1.2 Hz), 5.15 (1H, dd, J = 10.4, 1.2 Hz), 4.74 (1H, dt, J = 6.4, 2.4 Hz), 2.58-2.6 (2H, m), 2.06 (1H, d, J = 2.8 Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.9, 134.5, 128.5, 127.6, 125.9, 118.5, 73.5, 44.1. Optical Rotation: $[\alpha]_D^{25} +62^\circ$ (c 1.0, CHCl_3).⁶

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 99:1 hexanes:isopropanol, 0.8 mL/min, λ = 220 nm.); chromatograms are illustrated below for a 87% ee sample:

⁶ Corresponds to (*R*) enantiomer. See (a) Malkov, A. V.; Orsini, M.; Pernazza, D.; Muir, K. W.; Langer, V.; Meghani, P.; Kocovsky, P. *Org. Lett.* **2002**, *4*, 1047-1049. ^1H and ^{13}C NMR data are consistent with known product. See (b) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, *123*, 9488-9489.

(R)-1-(2-Bromophenyl)-3-buten-1-ol (Entry 2, Table 4). The general procedure was followed with ligand **3r** (63 mg, 0.20 mmol), and *o*-bromobenzaldehyde (234 μ L, 2.00 mmol) in DCE (4.0 mL, 0.5 M in substrate).

Allyltrichlorosilane (362 μ L, 2.50 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (95:5 hexanes:diethyl ether) to yield a white solid (368 mg, 81% yield, 82% ee). M.P. 45-46 °C. IR (neat, thin film): 3383 (br), 3075 (w), 2980 (w), 2911 (w), 1640 (w), 1564 (w), 1470 (m), 1438 (m), 1199 (w), 1023 (m), 916 (m), 872 (w), 759 (s), 614 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 7.56 (1H, dd, J = 7.6, 1.6 Hz), 7.52 (1H, dd, J = 8.0, 1.2 Hz), 7.34 (1H, dt, J = 7.2, 0.8 Hz), 7.13 (1H, dt, J = 7.6, 2.0 Hz), 5.88 (1H, dddd, J = 16.8, 10.0, 7.6, 6.4 Hz), 5.20 (1H, d, J = 17.2 Hz), 5.18 (1H, d, J = 10.0 Hz), 5.11 (1H, dt, J = 7.6, 3.6 Hz), 2.67-2.61 (1H, m), 2.36 (1H, dt, J = 14.0, 8.0 Hz), 2.22 (1H, d, J = 3.6 Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 142.7, 134.3, 132.7, 128.9, 127.7, 127.4, 121.9, 118.8, 72.0, 42.4. Anal Calcd for $\text{C}_{10}\text{H}_{11}\text{BrO}$: C, 52.89; H, 4.88. Found C, 52.73; H, 4.86. Optical Rotation: $[\alpha]_D^{25} +77^\circ$ (c 1.0, CHCl_3).⁷

Optical purity is established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 130 °C for 20 min, 0.5 °C/ minute to 150 °C, 15 psi); chromatograms are illustrated below for an 82% ee sample:

⁷ Assigned (*R*) by analogy.

(*R*)-1-(4-Chlorophenyl)-3-buten-1-ol (Entry 3, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and *p*-chlorobenzaldehyde (141 mg, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (217 μ L, 1.50 mmol) was then added. The reaction was

sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (85:15 hexanes:diethyl ether) to yield a pale yellow oil (155 mg, 85% yield, 84% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.34-7.28 (4H, m), 5.79 (1H, dddd, $J = 17.6, 9.6, 8.0, 6.4$ Hz), 5.17 (1H, d, $J = 17.6$ Hz), 5.16 (1H, d, $J = 10.6$ Hz), 4.73 (1H, ddd, $J = 8.0, 4.8, 3.2$ Hz), 2.55-2.41 (2H, m), 2.03 (1H, d, $J = 2.8$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 142.3, 134.0, 133.2, 128.6, 127.3, 119.0, 72.8, 44.2. Optical Rotation: $[\alpha]_D^{25} +62^\circ$ (c 1.0, CHCl_3).⁸

Optical purity is established by chiral GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 100 $^\circ\text{C}$ for 10 min, 1 $^\circ\text{C}/\text{minute}$ to 180 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below for an 85% ee sample:

⁸ Corresponds to (*R*) enantiomer. ^1H NMR data is consistent with published spectrum. See Ref. 6^a. ^{13}C NMR is consistent with product.

(R)-1-(3-Nitrophenyl)-3-buten-1-ol (Entry 4, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and *m*-nitrobenzaldehyde (151 mg, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.30 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (75:25 hexanes:diethyl ether) to yield a yellow oil (146 mg, 76% yield, 72% ee). IR (neat, thin film): 3427 (br), 3081 (w), 2911 (w), 1646 (w), 1533 (s), 1350 (s), 1199 (w), 1054 (m), 992 (w), 922 (w), 809 (m), 740 (m), 689 (m) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 8.24 (1H, s), 8.13 (1H, d, $J = 8.0$ Hz), 7.70 (1H, d, $J = 7.6$ Hz), 7.52 (1H, t, $J = 7.6$ Hz), 5.79 (1H, dddd, $J = 17.2$, 10.8, 8.0, 6.8 Hz), 5.20 (1H, d, $J = 9.6$ Hz), 5.19 (1H, d, $J = 17.6$ Hz), 4.88-4.84 (1H, m), 2.61-2.43 (2H, m), 2.27 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 148.4, 146.0, 133.3, 132.0, 129.4, 122.6, 121.0, 119.8, 72.3, 44.2. Anal Calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_3$: C, 62.17; H, 5.74; N, 7.25. Found C, 62.00; H, 5.79; N, 7.19. Optical Rotation: $[\alpha]_D^{25} +47^\circ$ (c 1.0, CHCl_3).⁹

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 99.5:0.5 hexanes:isopropanol, 0.50 mL/min, $\lambda = 210$ nm.); chromatograms are illustrated below for a 72% ee sample:

⁹ Assigned (*R*) by analogy.

(*R*)-1-(4-Methoxyphenyl)-3-buten-1-ol (Entry 5, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and *p*-anisaldehyde (122 μ L, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate).

Allyltrichlorosilane (217 μ L, 1.50 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (85:15 hexanes:diethyl ether) to yield a pale yellow oil (154 mg, 85% yield, 87% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.28 (2H, dt, J = 8.4, 2.4 Hz), 6.89 (2H, dt, J = 8.0, 2.0 Hz), 5.78 (1H, ddt, J = 17.6, 10.4, 7.2 Hz), 5.16 (1H, dd, J = 17.6, 1.6 Hz), 5.13 (1H, dd, J = 10.4, 1.6 Hz), 4.69 (1H, dt, J = 6.4, 2.0 Hz), 3.81 (3H, s), 2.50 (2H, t, J = 6.4 Hz), 1.98 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 159.1, 136.1, 134.7, 127.2, 118.3, 113.9, 73.2, 55.5, 44.1. Optical Rotation: $[\alpha]_D^{25} +57^\circ$ (c 1.0, CHCl_3).¹⁰

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 98:2 hexanes:isopropanol, 1.0 mL/min, λ = 220 nm.); chromatograms are illustrated below for an 88% ee sample:

¹⁰ Corresponds to (*R*) enantiomer. See Ref. 6^a. ^1H and ^{13}C NMR data are consistent with known product. See Ref. 6^b.

(R)-1-(3,4-Dimethoxyphenyl)-3-buten-1-ol (Entry 6, Table 4). The general procedure was followed with ligand **3r** (47 mg, 0.15 mmol), and 3,4-dimethoxybenzaldehyde (166 mg, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.30 mmol) was then added.

The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (70:30 hexanes:diethyl ether) to yield a white solid (151 mg, 73% yield, 92% ee). M.P. 94-95 $^{\circ}$ C. ^1H NMR (CDCl_3 , 400 MHz): δ 6.93 (1H, d, J = 2.0 Hz), 6.88 (1H, dd, J = 8.4, 2.0 Hz), 6.83 (1H, d, J = 8.4 Hz), 5.81 (1H, ddt, J = 17.7, 10.4, 7.6 Hz), 5.17 (1H, dd, J = 17.2, 2.0 Hz), 5.14 (1H, dd, J = 9.6, 2.0 Hz), 4.68 (1H, t, J = 6.8 Hz), 3.89 (3H, s), 3.87 (3H, s), 2.50 (2H, t, J = 7.2 Hz), 2.03 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 149.2, 148.6, 136.8, 134.7, 118.5, 118.3, 111.2, 109.3, 73.5, 56.3, 56.2, 44.2. Optical Rotation: $[\alpha]_D^{25} +30^{\circ}$ (c 1.0, C_6H_6).¹¹

Optical purity is established by chiral HPLC analysis (Chiralcel AS (4.6 mm x 250 mm), 99.5:0.5 hexanes:isopropanol, 0.75 mL/min, λ = 220 nm.); chromatograms are illustrated below for a 92% ee sample:

¹¹ Corresponds to (*R*) enantiomer. ^1H and ^{13}C NMR data are consistent with published. See Shimada, T.; Kina, A.; Hayashi, T. *J. Org. Chem.* **2003**, 68, 6329-6337.

(R)-1-(1-Naphthyl)-3-buten-1-ol (Entry 7, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and 1-naphthaldehyde (156 mg, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.30 mmol) was then added. The reaction was sealed and allowed to react

for 24 h. After workup, the product was purified by silica gel chromatography (95:5 hexanes:diethyl ether) to yield a yellow oil (176 mg, 89% yield, 79% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 8.09 (1H, d, J = 8.0 Hz), 7.89 (1H, d, J = 8.4 Hz), 7.79 (1H, d, J = 8.0 Hz), 7.68 (1H, d, J = 6.8 Hz), 7.55-7.47 (3H, m), 5.94 (1H, ddt, J = 17.2, 10.0, 6.8 Hz), 5.55 (1H, dd, J = 8.4, 4.0 Hz), 5.23 (1H, d, J = 17.2 Hz), 5.20 (1H, d, J = 10.8 Hz), 2.81-2.75 (1H, m), 2.66-2.58 (1H, m). ^{13}C NMR (CDCl_3 , 100 MHz): δ 139.5, 134.8, 133.9, 130.4, 129.0, 128.1, 126.1, 125.6, 125.5, 123.0, 122.9, 118.5, 70.2, 43.2. Optical Rotation: $[\alpha]_D^{25} +84^\circ$ (c 1.0, CHCl_3).¹²

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 90:10 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm.); chromatograms are illustrated below for a 79% ee sample:

¹² Corresponds to (*R*) enantiomer. See Ref. 6^a. ^1H and ^{13}C NMR data are consistent with known product.

(R)-1-(2-Naphthyl)-3-buten-1-ol (Entry 8, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and 2-naphthaldehyde (156 mg, 1.00 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyl-trichlorosilane (181 μ L, 1.30 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (95:5 hexanes:diethyl ether) to yield a white solid (177 mg, 89% yield, 83% ee). M.P. 34-35 $^{\circ}$ C. ^1H NMR (CDCl_3 , 400 MHz): δ 7.86-7.82 (4H, m), 7.50-7.45 (3H, m), 5.84 (1H, ddt, J = 17.2, 10.4, 7.2 Hz), 5.20 (1H, d, J = 18.0 Hz), 5.16 (1H, d, J = 10.4 Hz), 4.95 (1H, dd, J = 7.2, 4.8 Hz), 2.68-2.55 (2H, m), 2.11 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 141.3, 134.4, 133.4, 133.1, 128.3, 128.1, 127.8, 126.2, 126.0, 124.6, 124.1, 118.7, 73.6, 44.1. Optical Rotation: $[\alpha]_D^{25} +58^{\circ}$ (c 1.0, CHCl_3).¹³

Optical purity is established by chiral HPLC analysis (Chiralcel AS (4.6 mm x 250 mm), 99:1 hexanes:isopropanol, 0.50 mL/min, λ = 254 nm.); chromatograms are illustrated below for an 83% ee sample:

¹³ Corresponds to (R) enantiomer. See Ref. 6^a. ^1H and ^{13}C NMR data are consistent with known product. See Ref. 6^b.

(*R*)-1-(2-Furyl)-3-buten-1-ol (Entry 9, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and 2-furaldehyde (83 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.30 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (90:10 hexanes:diethyl ether) to yield a yellow oil (81 mg, 59% yield, 71% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.38 (1H, dd, $J = 2.0, 0.8$ Hz), 6.33 (1H, dd, $J = 3.6, 2.0$ Hz), 6.23 (1H, dd, $J = 3.6, 2.0$ Hz), 5.81 (1H, ddt, $J = 17.2, 10.0, 6.8$ Hz), 5.19 (1H, d, $J = 17.2$ Hz), 5.15 (1H, d, $J = 10.0$ Hz), 4.75 (1H, br), 2.69-2.57 (2H, m), 2.05 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 156.1, 142.0, 133.8, 118.7, 110.3, 106.2, 67.2, 40.4. Optical Rotation: $[\alpha]_D^{25} +10^\circ$ (c 1.0, EtOH).¹⁴

Optical purity is established by chiral HPLC analysis (Chiralcel AS (4.6 mm x 250 mm), 99.5:0.5 hexanes:isopropanol, 0.50 mL/min, $\lambda = 220$ nm.); chromatograms are illustrated below for a 72% ee sample:

¹⁴ Corresponds to (*R*) enantiomer. See Ref. 6^a. ^1H and ^{13}C NMR data are consistent with published. See Racherla, U. S.; Liao, Y.; Brown, H. C. *J. Org. Chem.* **1992**, *57*, 6614-6617.

(*R*)-1-(1-Furyl)-3-buten-1-ol (Entry 10, Table 4). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and 3-furaldehyde (87 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.30 mmol) was then added. The reaction was sealed and allowed to react for 24 h.

After workup, the product was purified by silica gel chromatography (90:10 hexanes:diethyl ether) to yield a yellow oil (88 mg, 64% yield, 82% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.39 (2H, br), 6.41 (1H, s), 5.82 (1H, ddt, J = 16.8, 10.4, 6.8 Hz), 5.17 (1H, d, J = 16.8 Hz), 5.15 (1H, d, J = 10.4 Hz), 4.72 (1H, br), 2.57-2.45 (2H, m), 1.95 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 139.1, 134.2, 128.6, 118.7, 108.7, 66.4, 42.8. Optical Rotation: $[\alpha]^{25}_{\text{D}}$ +11° (c 1.0, EtOH).¹⁵

Optical purity is established by chiral HPLC analysis (Chiralcel AS (4.6 mm x 250 mm), 99:1 hexanes:isopropanol, 0.50 mL/min, λ = 220 nm.); chromatograms are illustrated below for an 82% ee sample:

¹⁵ Corresponds to (*R*) enantiomer. ^1H and ^{13}C NMR data are consistent with published data.

(1E,3R)-1-Phenyl-1,5-hexadiene-3-ol (R=H, eq 1). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and *trans*-cinnamaldehyde (126 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.3 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (90:10 hexanes:diethyl ether) to yield a yellow oil (137 mg, 79% yield, 71% ee). ^1H NMR (CDCl_3 , 400 MHz): δ 7.38 (2H, d, J = 7.6 Hz), 7.32 (1H, t, J = 8.0 Hz), 7.24 (1H, t, J = 7.2 Hz), 6.61 (1H, d, J = 16.0 Hz), 6.25 (1H, dd, J = 16.0, 6.4 Hz), 5.86 (1H, ddt, J = 17.6, 10.0, 7.2 Hz), 5.19 (1H, d, J = 17.6 Hz), 5.17 (1H, d, J = 10.0 Hz), 4.36 (1H, br), 2.48-2.35 (2H, m), 1.88 (1H, br). ^{13}C NMR (CDCl_3 , 100 MHz): δ 136.7, 134.1, 131.6, 130.4, 128.6, 127.7, 126.6, 118.6, 71.9, 42.3. Optical Rotation: $[\alpha]_D^{25} +23^\circ$ (c 1.0, CHCl_3).¹⁶

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 90:10 hexanes:isopropanol, 0.75 mL/min, λ = 220 nm.); chromatograms are illustrated below for a 71% ee sample:

¹⁶ Corresponds to (*R*) enantiomer, See Ref. 6^a. ^1H and ^{13}C NMR data are consistent with published.

(1E,3R)-1-Methyl-1-phenyl-1,5-hexadiene-3-ol (R=Me, eq 1). The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol), and α -methyl-*trans*-cinnamaldehyde (142 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). Allyltrichlorosilane (181 μ L, 1.3 mmol) was then added. The

reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (96:4 hexanes:diethyl ether) to yield a yellow oil (117 mg, 62% yield, 76% ee). IR (neat, thin film): 3364 (br), 3075 (w), 3024 (w), 2980 (w), 2917 (w), 1639 (w), 1489 (w), 1445 (m), 998 (m), 916 (m), 752 (m), 712 (s), 513 (w) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 7.40-7.30 (4H, m), 7.27 (t, 1H, $J = 7.2$ Hz), 6.58 (1H, s), 5.89 (1H, ddt, $J = 17.6, 10.0, 7.2$ Hz), 5.24 (1H, d, $J = 17.6$ Hz), 5.20 (1H, d, $J = 10.0$ Hz), 4.28 (1H, br), 2.55-2.41 (2H, m), 1.94 (3H, s), 1.89 (1H, d, 2.8 Hz). ^{13}C NMR (CDCl_3 , 100 MHz): δ 139.6, 137.6, 134.6, 129.1, 128.2, 126.5, 125.8, 118.1, 76.8, 40.4, 14.0. Anal Calcd for $\text{C}_{13}\text{H}_{16}\text{O}$: C, 82.94; H, 8.57. Found C, 82.64; H, 8.72. Optical Rotation: $[\alpha]_D^{25} +2.6^\circ$ (c 1.0, CHCl_3).¹⁷

Optical purity is established by chiral GLC analysis (Supelco Alpha Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 120 $^\circ\text{C}$ isothermal, 15 psi); chromatograms are illustrated below for a 76% ee sample:

¹⁷ Assigned (*R*) by analogy.

(1*R*,2*R*)-2-Methyl-1-phenyl-3-buten-1-ol (6).¹⁸ The general procedure was followed with ligand **3r** (32 mg, 0.10 mmol) and benzaldehyde (53 μ L, 1.0 mmol) in DCE (1.0 mL, 0.5 M in substrate). (*E*)-Crotylsilane (4:96 *Z:E*) **4** (118 μ L, 0.750 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (96:4 hexanes:diethyl ether) to yield a yellow oil (63 mg, 78% yield, 82% ee). ¹H NMR (CDCl₃, 400 MHz): δ 7.36-7.28 (5H, m), 5.82 (1H, ddd, *J* = 17.6, 10.0, 8.4 Hz), 5.21 (1H, d, *J* = 17.2 Hz), 5.20 (1H, d, *J* = 10.4 Hz), 4.36 (1H, dd, *J* = 8.0, 2.8 Hz), 2.49 (1H, hex, 7.2 Hz), 2.15 (1H, d, 2.8 Hz), 0.87 (3H, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 142.5, 140.7, 128.3, 127.7, 116.9, 78.1, 16.9. Optical Rotation: $[\alpha]_D^{25} +97^\circ$ (c 1.0, CHCl₃).

Optical purity is established by chiral HPLC analysis (Chiralcel OD (4.6 mm x 250 mm), 95:5 hexanes:isopropanol, 0.5 mL/min, λ = 220 nm.); chromatograms are illustrated below for an 82% ee sample:

¹⁸ Rotation, ¹H, and ¹³C NMR data are consistent with known product. See Ref. 6^b.

(1R,2S)-2-Methyl-1-phenyl-3-buten-1-ol (7).¹⁹ The general procedure was followed with ligand **3r** (63 mg, 0.20 mmol), and benzaldehyde (102 μ L, 1.0 mmol) in DCE (2.0 mL, 0.5 M in substrate). (*Z*)-Crotylsilane (97:3 *Z:E*) **5** (233 μ L, 1.5 mmol) was then added. The reaction was sealed and allowed to react for 24 h. After workup, the product was purified by silica gel chromatography (95:5 hexanes:diethyl ether) to yield a yellow oil (117 mg, 72% yield, 76% ee). ¹H NMR (CDCl₃, 400 MHz): δ 7.36-7.25 (5H, m), 5.77 (1H, ddd, *J* = 17.2, 9.6, 6.8 Hz), 5.08 (1H, m), 5.04 (1H, m), 4.62 (1H, d, *J* = 4.4 Hz), 2.63-2.55 (1H, m), 1.97 (1H, br), 1.02 (3H, d, *J* = 6.4 Hz). ¹³C NMR (CDCl₃, 100 MHz): δ 142.6, 140.0, 128.2, 127.4, 126.6, 115.6, 77.5, 44.9, 14.4. Optical Rotation: $[\alpha]^{25}_D$ +21° (c 1.0, CHCl₃).

Optical purity is established by chiral GLC analysis (Supelco Gamma Dex 120 (30 m x 0.15 mm x 0.25 μ m film thickness), 90 °C 120 min, 0.5 °C/ min to 130 °C, 15 psi); chromatograms are illustrated below for a 79% ee sample:

¹⁹ Rotation, ¹H, and ¹³C NMR data are consistent with known product. See Ref. 6^b.