Gold(I)-Catalyzed Enantioselective Hydroamination of *N*-Allenyl Carbamates

Zhibin Zhang, Christopher F. Bender, and Ross A. Widenhoefer

Duke University

French Family Science Center

Durham, NC 27708–0346

rwidenho@chem.duke.edu

Experimental procedures, spectroscopic, and analytical data for new compounds and scans of chiral
HPLC traces and NMR spectra of pyrrolidine products and new compounds (90 pages).

Experimental

General Methods. Reactions were performed under a nitrogen atmosphere utilizing standard Shlenk and drybox techniques unless specified otherwise. NMR were obtained on Varian spectrometers operating at 300, 400 or 500 MHz for ^1H NMR and 75, 101 or 126 MHz for ^{13}C NMR in CDCl_3 at 25 °C or 55 °C and are noted accordingly. IR spectra were obtained on a Nicolet Avatar 360-FT IR spectrometer. Gas chromatography was performed on a HP 5890 gas chromatograph equipped with a 15 m or 25 m polydimethylsiloxane capillary column and FID detector. Chiral HPLC was performed on a Hewlett-Packard 1090 series II chromatograph equipped with a 25 cm Chiralpak AD-H column. Column chromatography was performed employing 230-400 mesh silica gel (Silicycle). Catalytic reactions were performed in sealed glass tubes under an atmosphere of dry nitrogen unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). Thin layer chromatography (TLC) was performed on silica gel 60 F₂₅₄ (EMD Chemicals Inc.). Room temperature is 23 °C.

All solvents were purchased from Aldrich or Acros in anhydrous form and used as received. All reagents were purchased from major suppliers and used as received. An authentic sample of (*S*)-benzyl 2-vinylpyrrolidine-1-carboxylate [98% ee, (*S*)-**15**] was prepared from (*S*)-benzyl 2-formylpyrrolidine-1-carboxylate via the method of Takeuchi.^{S1} (*S*)-Benzyl 2-formylpyrrolidine-1-carboxylate was prepared from commercially available Z-L-prolinol (Aldrich) employing the method of Seijas.^{S2} 2,2-Diphenyl-4,5-hexadienenitrile (**S1**),^{S3} 1-acetoxy-2,3-nonadiene (**S2**),^{S3} benzyl (2,2-diphenyl-4,5-hexadienyl)carbamate (**2a**),^{S3} 1-prop-2-ynyl-cyclohexanecarbonitrile (**S3**),^{S4} 4-methyl-2,3-pentadien-1-ol (**S4**),^{S5} AgNTf₂,^{S6} AgBARF,^{S7} [(*S*)-**1**]Au₂Cl₂^{S3} and Au[P(*t*-Bu)₂*o*-biphenyl]Cl (**S5**)^{S8} were prepared by previously reported methods.

***N*-Allenyl Carbamates**

Methyl (2,2-diphenyl-4,5-hexadienyl)carbamate (2d). A solution of DIBAL-H (1 M in toluene, 20.0 mL, 20.0 mmol) was added to a solution of **S1** (3.26 g, 13.3 mmol) in ether (100 mL) at –42 °C over 30 min and stirred for 3 h. To the resulting solution, NaBH₄ (1.52 g, 40.2 mmol) was added in one portion followed by slow addition of EtOH (100 mL) over 30 min. The reaction mixture was stirred vigorously for 3 h at 0 °C, diluted with ether (75 mL), and washed with saturated aqueous potassium carbonate (2 × 75 mL). The layers were separated and the organic fraction was extracted with 1 M HCl (3 × 75 mL). The combined acidic extracts were made basic (pH ≥ 13) with 15% NaOH (75 mL) and extracted with CH₂Cl₂ (3 × 75 mL). The combined organic extracts were dried (MgSO₄) and concentrated to give 2,2-diphenyl-4,5-hexadienylamine (**S6**, 2.44 g) as a pale yellow oil that was 91% pure by GC analysis. A solution of crude **S6** in chloroform (28 mL) was treated with HBF₄·OEt₂ (1.36 mL, 9.99 mmol) at 0 °C and stirred for 1 h. The resulting white solid was collected by filtration and triturated with cold chloroform (5 mL) to yield **S6**·HBF₄ (2.80 g, 63% from **S1**) that was used in subsequent steps without further purification.

Triethylamine (0.53 mL, 3.8 mmol) and methyl chloroformate (245 µL, 1.87 mmol) were added sequentially to a suspension of **S6**·HBF₄ (508 mg, 1.51 mmol) in CH₂Cl₂ at 0 °C (15 mL). The reaction mixture was warmed to room temperature overnight with stirring. Ether (30 mL) was added and the resulting suspension was washed with water (2 × 20 mL) and brine (20 mL), dried (MgSO₄), and concentrated. The oily residue was chromatographed (SiO₂; CH₂Cl₂) to give **2d** as a white solid (0.38 g, 83%). TLC (CH₂Cl₂): *R_f* = 0.41. ¹H NMR (55 °C, 300 MHz): δ 7.18-7.33 (m, 10 H), 4.75 (quintet, *J* = 7.1 Hz, 1 H), 4.49-4.53 (m, 2 H), 4.24 (br s, 1 H), 3.95 (d, *J* = 6.0 Hz, 2 H), 3.61 (s, 3 H), 2.85 (td, *J* = 2.2, 7.8 Hz, 2 H). ¹³C{¹H} NMR (55 °C, 75 MHz): δ 210.2, 157.0, 145.1, 128.5, 128.3, 126.7, 85.3,

73.9, 52.2, 50.9, 48.2, 37.5. IR (neat, cm^{-1}): 2953, 1695, 1446, 1379, 1199, 698. HRMS calcd (found) for $\text{C}_{20}\text{H}_{21}\text{NO}_2$ (M^+): 307.1572 (307.1569).

2,2,2-Trichloroethyl (2,2-diphenyl-4,5-hexadienyl)carbamate (2b) and **9H-fluoren-9-ylmethyl (2,2-diphenyl-4,5-hexadienyl)carbamate (2c)** were synthesized from **S7**· HBF_4 using a procedure similar to that used to synthesize **2d**.

For 2b: Colorless oil, 83%. TLC (EtOAc–hexanes = 1:10): R_f = 0.33. ^1H NMR (55 °C, 300 MHz): δ 7.18–7.34 (m, 10 H), 4.73 (quintet, J = 7.1 Hz, 1 H), 4.67 (s, 3 H), 4.01 (d, J = 6.0 Hz, 2 H), 2.83–2.89 (m, 2 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 126 MHz): δ 210.3, 154.7, 144.9, 128.6, 128.3, 126.9, 95.9, 85.3, 74.8, 74.1, 51.0, 48.4, 37.6. IR (neat, cm^{-1}): 2883, 1718, 1407, 1351, 1113, 697. HRMS calcd (found) for $\text{C}_{21}\text{H}_{20}\text{Cl}_3\text{NO}_2$ (M^+): 423.0560 (423.0556).

For 2c:^{S3} White solid, 73%. TLC (EtOAc–hexanes = 1:6): R_f = 0.20. ^1H NMR (55 °C, 500 MHz): δ 7.76 (d, J = 7.7 Hz, 2 H), 7.20–7.53 (m, 16 H), 4.78 (br s, 1 H), 4.49–4.51 (m, 2 H), 4.31–4.37 (m, 3 H), 4.18 (t, J = 7.3 Hz, 1 H), 3.98 (br s, 2 H), 2.84 (d, J = 7.3 Hz, 2 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 126 MHz): δ 210.2, 156.4, 145.1, 144.3, 141.6, 128.5, 128.3, 127.8, 127.2, 126.8, 125.2, 120.1, 85.4, 74.0, 67.0, 51.1, 48.3, 47.6, 37.6.

N-(2,2-Diphenyl-4,5-hexadienyl)-acetamide (2e) was prepared from reaction of **S6**· HBF_4 with AcCl employing a synthesis similar to that used to synthesize **2d**.

For 2e: White solid. TLC (ether– CH_2Cl_2 = 1:5): R_f = 0.41. ^1H NMR (55 °C, 400 MHz): δ 7.19–7.34 (m, 10 H), 4.96 (br s, 1 H), 4.75 (septet, J = 7.0 Hz, 1 H), 4.50 (td, J = 2.6, 6.7 Hz, 2 H), 4.01 (d, J = 5.8 Hz, 2 H), 2.83 (td, J = 2.6, 7.7 Hz, 2 H), 1.83 (s, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 210.2, 169.8, 145.2, 128.5, 128.3, 126.8, 85.3, 73.9, 50.9, 46.5, 37.9, 23.4. IR (neat, cm^{-1}): 3288, 1952, 1640, 1541, 853, 695. HRMS calcd (found) for $\text{C}_{20}\text{H}_{21}\text{NO}$ (M^+): 291.1623 (291.1623).

Benzyl (6-methyl-2,2-diphenyl-4,5-heptadienyl)carbamate (4). Methanesulfonylchloride (0.95 mL, 12.3 mmol) was added dropwise to a solution of **S4** (1.01 g, 10.3 mmol), DMAP (128 mg, 1.05 mmol), and Et₃N (2.15 mL, 15.3 mmol) in CH₂Cl₂ (40 mL) at 0 °C. The resulting suspension was stirred for 1 h, treated with water (20 mL), and extracted with CH₂Cl₂ (3 × 20 mL). The combined organic extracts were washed with 1 M HCl (20 mL), saturated aqueous sodium bicarbonate (20 mL), and brine (20 mL), dried (MgSO₄), and concentrated to give methyl 4-methyl-2,3-pentadien-1-sulfonate (**S7**) as a yellow oil that was used in the subsequent step without further purification.

A solution of diphenylacetonitrile (1.61 g, 8.33 mmol) in DMF (12 mL) was added dropwise to a suspension of NaH (95%, 285 mg, 11.3 mmol) in THF (25 mL) at 0 °C. The resulting mixture was stirred vigorously for 1 h, treated sequentially with a solution of crude **S7** (all material obtained in previous step) in DMF (12 mL) and a single portion of NaI (1.51 g, 10.0 mmol), and warmed to room temperature overnight with stirring. The resulting mixture was treated with water (50 mL) and extracted with ether (3 × 30 mL). The combined organic extracts were dried (MgSO₄), concentrated, and the resulting residue was chromatographed (SiO₂; EtOAc–hexanes = 1:19) to give 6-methyl-2,2-diphenyl-4,5-heptadienenitrile **S8** as a colorless, viscous oil (1.58 g, 43%). Compound **4** was synthesized from **S8** in 34% yield as a viscous, colorless oil employing a synthesis similar to that used to synthesize **10** from **S9**.

For S8: TLC (EtOAc–hexanes = 1:12): *R_f* = 0.19. ¹H NMR (25 °C, 300 MHz): δ 7.26-7.42 (m, 10 H), 4.89-4.98 (m, 1 H), 3.05 (d, *J* = 7.0 Hz, 2 H), 1.53 (d, *J* = 2.9 Hz, 6 H). ¹³C{¹H} NMR (25 °C, 75 MHz): δ 204.5, 140.0, 128.9, 127.9, 127.3, 122.3, 96.7, 83.2, 52.1, 40.5, 20.2. IR (neat, cm⁻¹): 2910, 2856, 1493, 1446, 753, 695. HRMS calcd (found) for C₂₀H₁₉N (M⁺): 273.1517 (273.1519).

For 4: TLC (EtOAc–hexanes = 1:6): *R_f* = 0.32. ¹H NMR (55 °C, 400 MHz): δ 7.19-7.35 (m, 15 H), 5.04 (s, 2 H), 4.64 (br s, 1 H), 4.39 (br s, 1 H), 3.99 (d, *J* = 5.8 Hz, 2 H), 2.81 (d, *J* = 7.5 Hz, 2

H), 1.52 (d, $J = 2.7$ Hz, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 203.9, 156.5, 145.3, 136.9, 128.6, 128.4, 128.3, 128.2, 126.6, 94.7, 84.2, 66.9, 50.9, 48.4, 38.4, 20.3. IR (neat, cm^{-1}): 3433, 2909, 1719, 1506, 1220, 696. HRMS calcd (found) for $\text{C}_{28}\text{H}_{29}\text{NO}_2$ (M^+): 411.2198, (411.2191).

Benzyl (6-ethyl-2,2-diphenyl-4,5-octadienyl)carbamate (5). HOTs· H_2O (10 mg, 0.053 mmol) was added to a solution of 3-ethyl-1-pentyn-3-ol (4.42 g, 39.4 mmol) and 3,4-dihydro-2*H*-pyran (5.05 g, 60.0 mmol) in CH_2Cl_2 at 0 °C, the resulting solution was stirred for 2 h, diluted with Et_2O (10 mL), quenched with saturated NaHCO_3 (25 mL), and extracted with ether (50 mL) and CH_2Cl_2 (50 mL). The combined organic extracts were dried (MgSO_4), concentrated, and the resulting oily residue was distilled under reduced pressure (50 °C, 500 mTorr) to give 2-(1,1-diethyl-2-propynyloxy)-tetrahydropyran (**S10**) as a colorless oil (6.85 g, 89 %).

A solution of *n*-BuLi (2.5 M in toluene, 16.5 mL, 41.3 mmol) was added over 30 min to a solution of **S10** (6.1 g, 31 mmol) in THF (91 mL) at -78 °C. The resulting mixture was warmed to 0 °C and HMPA (6.6 mL) was added followed by paraformaldehyde (1.86 g, 62.0 mmol). The reaction mixture was slowly warmed to room temperature and stirred vigorously for 4 h. The mixture was cooled to 0 °C and quenched with saturated aqueous NH_4Cl , the organic fraction dried (MgSO_4) and concentrated. The resulting residue was chromatographed (SiO_2 ; EtOAc–hexanes = 1:10 $\rightarrow$ 1:1) to yield 4-ethyl-4-(tetrahydropyran-2-yloxy)-2-hexyn-1-ol (**S11**) as a colorless oil (6.02 g, 86%).

A solution of **S11** (5.97 g, 26.4 mmol) in ether (25 mL) was added to a stirred suspension of LiAlH_4 (2.51 g, 66.1 mmol) in ether (80 mL) at 0 °C and warmed to room temperature overnight. The reaction mixture was cooled to 0 °C and quenched by successive addition of water (3.7 mL), 15 % NaOH [(w/w), 3.7 mL] and water (3.7 mL). The resulting white suspension was filtered through Celite, eluted with ether, and concentrated. The resulting residue was distilled under reduced pressure (39 °C at

500 mTorr) to yield 4-ethyl-2,3-hexadien-1-ol (**S12**) as a colorless oil (2.88 g, 86 %). Compound **5** was synthesized from **S12** employing a procedure similar to that used to synthesize **4** from **S4**.

For S10: TLC (EtOAc–hexanes = 1:5): R_f = 0.57. ^1H NMR (25 °C, 400 MHz): δ 5.02 (dd, J = 3.6, 5.2 Hz, 1 H), 3.86–3.92 (m, 1 H), 3.42–3.47 (m, 1 H), 2.41 (s, 1 H), 1.43–1.84 (m, 10 H), 0.92 (t, J = 7.6 Hz, 3 H), 0.91 (t, J = 7.6 Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 96.0, 84.5, 78.4, 74.2, 63.4, 32.7, 32.0, 32.0, 25.6, 20.5, 8.7, 8.4. IR (neat, cm^{-1}): 3303, 2941, 1118, 1026, 989, 626. HRMS calcd (found) for $\text{C}_{12}\text{H}_{20}\text{O}_2$ (M^+): 196.1463 (196.1465).

For S11: TLC (EtOAc–hexanes = 1:1): R_f = 0.53. ^1H NMR (25 °C, 400 MHz): δ 5.05 (t, J = 4.0 Hz, 1 H), 4.24 (d, J = 6.0 Hz, 2 H), 3.88–3.93 (m, 1 H), 3.45–2.50 (m, 1 H), 3.12 (t, J = 6.0 Hz, 1 H), 1.45–1.83 (m, 10 H), 0.92 (t, J = 7.6 Hz, 3 H), 0.90 (t, J = 7.2 Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 95.5, 85.8, 85.1, 78.4, 63.1, 50.9, 32.7, 32.1, 32.0, 25.6, 20.1, 8.9, 8.5. IR (neat, cm^{-1}): 3414, 2940, 2874, 1453, 1023, 988. HRMS calcd (found) for $\text{C}_{13}\text{H}_{22}\text{O}_3$ (M^+): 226.1569 (226.1572).

For S12: TLC (EtOAc–hexanes = 1:5): R_f = 0.31. ^1H NMR (25 °C, 400 MHz): δ 5.37 (quintet-t, J = 2.8, 6.0 Hz, 1 H), 4.04 (d, J = 5.6 Hz, 2 H), 1.95 (dq, J = 3.2, 7.2 Hz, 4 H), 1.62 (br s, 1 H), 0.97 (t, J = 7.6 Hz, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 199.2, 111.9, 94.2, 61.3, 25.7, 12.5. IR (neat, cm^{-1}): 3322, 2965, 2878, 1961, 1455, 1009. HRMS calcd (found) for $\text{C}_8\text{H}_{14}\text{O}$ (M^+): 126.1045 (126.1045).

For 6-ethyl-2,2-diphenyl-4,5-octadienenitrile (S13): TLC (EtOAc–hexanes = 1:5): R_f = 0.58. Colorless oil. ^1H NMR (25 °C, 400 MHz): δ 7.24–7.41 (m, 10 H), 5.09 (quintet of triplets, J = 2.8, 7.2 Hz, 1 H), 3.09 (d, J = 7.2 Hz, 2 H), 1.78–1.93 (m, 4 H), 0.88 (t, J = 7.6 Hz, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 202.7, 140.2, 129.0, 128.0, 127.4, 122.4, 109.1, 86.9, 52.1, 41.0, 25.5, 12.4. IR (neat, cm^{-1}): 2965, 2929, 1493, 1448, 753, 695. HRMS calcd (found) for $\text{C}_{22}\text{H}_{23}\text{N}$ (M^+): 301.1830 (301.1834).

For 5: Colorless oil. TLC (EtOAc–hexanes = 1:5): R_f = 0.49. ^1H NMR (55 °C, 400 MHz): δ 7.18-7.35 (m, 15 H), 5.03 (s, 2 H), 4.82 (br s, 1 H), 4.42 (br s, 1 H), 4.01 (d, J = 6.0 Hz, 2 H), 2.86 (d, J = 7.6 Hz, 2 H), 1.78-1.93 (m, 4 H), 0.90 (t, J = 7.2 Hz, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 202.1, 156.4, 145.3, 136.7, 128.7, 128.4, 128.3, 126.6, 107.5, 87.8, 66.8, 50.6, 48.3, 38.9, 25.5, 12.5. IR (neat, cm^{-1}): 3434, 2963, 1721, 1505, 1220, 753. HRMS calcd (found) for $\text{C}_{30}\text{H}_{33}\text{NO}_2$ (M^+): 439.2511 (439.2509).

Benzyl (5-cyclohexylidene-2,2-diphenyl-4-pentenyl)-carbamate (6). Carbamate **6** was synthesized from 1-ethynyl-1-cyclohexanol employing a protocol similar to that used to synthesize **5**.

For 2-(1-ethynylcyclohexyloxy)-tetrahydropyran (S14): Colorless oil. TLC (EtOAc–hexanes = 1:9): R_f = 0.45. ^1H NMR (25 °C, 400 MHz): δ 5.12 (dd, J = 3.4, 5.1 Hz, 1 H), 3.93-3.98 (m, 1 H), 3.47-3.53 (m, 1 H), 2.48 (s, 1 H), 2.00-2.04 (m, 1 H), 1.79-1.91 (m, 2 H), 1.46-1.74 (m, 12 H), 1.20-1.29 (m, 1 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 95.8, 85.5, 74.9, 73.9, 63.6, 38.8, 38.5, 32.2, 25.5, 25.4, 23.1, 23.1, 20.6. IR (neat, cm^{-1}): 3299, 2934, 2857, 1447, 1026, 988. HRMS calcd (found) for $\text{C}_{10}\text{H}_{20}\text{O}_2$ (M^+): 208.1463 (208.1463).

For 3-[1-(tetrahydro-2-pyranyloxy)-cyclohexyl]-2-propyn-1-ol (S15): Colorless oil. TLC (EtOAc–hexanes = 1:4): R_f = 0.21. **S15** underwent minor decomposition (~10%) prior to the ^{13}C NMR being obtained. ^1H NMR (25 °C, 400 MHz): δ 5.11-5.13 (m, 1 H), 4.29 (s, 2 H), 3.92-3.97 (m, 1 H), 3.47-3.53 (m, 1 H), 2.65 (br s, 1 H), 1.96-1.99 (m, 1 H), 1.81-1.84 (m, 2 H), 1.45-1.72 (m, 12 H), 1.22-1.28 (m, 1 H). IR (neat, cm^{-1}): 3414, 2934, 2857, 1445, 1022, 988. HRMS calcd (found) for $\text{C}_{14}\text{H}_{22}\text{O}_3$ (M^+): 238.1569 (238.1570).

For 3-cyclohexylidene-prop-2-en-1-ol (S16): Colorless oil that contained traces of ether and CH_2Cl_2 (~9% by ^1H NMR analysis). TLC (ether- CH_2Cl_2 = 1:19): R_f = 0.47. ^1H NMR (25 °C, 400

MHz): δ 5.15-5.19 (m), 4.03 (d, J = 5.6 Hz, 2 H), 2.10 (dt, J = 2.1, 6.2 Hz, 4 H), 1.45-1.59 (m, 6 H), 1.41 (br s, 1 H).

For 5-cyclohexylidene-2,2-diphenyl-4-pentenitrile (S17): Colorless oil, 70%. TLC (EtOAc–hexanes = 1:25): R_f = 0.23. ^1H NMR (25 °C, 400 MHz): δ 7.22-7.39 (m, 10 H), 4.91 (tt, J = 2.1, 7.0 Hz, 1 H), 3.02 (d, J = 7.0 Hz, 2 H), 1.90-1.94 (m, 4 H), 1.41-1.49 (m, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 201.2, 140.0, 128.8, 127.9, 127.2, 122.2, 103.5, 83.0, 52.2, 40.8, 31.1, 27.2, 26.1. IR (neat, cm^{-1}): 2925, 2851, 1965, 1493, 1442, 695. HRMS calcd (found) for $\text{C}_{23}\text{H}_{23}\text{N}$ (M^+): 313.1830 (313.1832).

For 6: Colorless oil. TLC (EtOAc–hexanes = 1:9): R_f = 0.22. ^1H NMR (25 °C, 400 MHz): δ 7.18-7.35 (m, 15 H), 5.04 (s, 2 H), 4.65 (br s, 1 H), 4.41 (br s, 1 H), 3.99 (d, J = 5.8 Hz, 2 H), 2.82 (d, J = 7.7 Hz, 2 H), 1.92-1.94 (m, 4 H), 1.48-1.50 (m, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 200.6, 156.5, 145.4, 136.9, 128.6, 128.4, 128.3, 128.2, 128.2, 126.6, 102.0, 84.0, 66.9, 50.9, 48.4, 38.9, 31.4, 27.6, 26.3. IR (neat, cm^{-1}): 3357, 2925, 2851, 1720, 1505, 1221. HRMS calcd (found) for $\text{C}_{31}\text{H}_{33}\text{NO}_2$ (M^+): 451.2511 (451.2503).

Benzyl (2,2-diphenyl-4,5-undecadienyl)carbamate (10). A solution of diphenylacetonitrile (964 mg, 4.99 mmol) in THF (3 mL) was added dropwise to a solution of LDA (6.0 mmol) in THF (50 mL) at -78 °C. The resulting solution was stirred for 1 h and treated sequentially with a solution of **S3** (1.12 g, 6.15 mmol) in THF (3 mL) and a suspension of $\text{Pd}(\text{OAc})_2$ (56 mg, 0.25 mmol) and PPh_3 (196 mg, 0.75 mmol) in THF (3 mL) at -78 °C. The resulting suspension was warmed to room temperature overnight with stirring, treated with water (50 mL), and extracted with ether (3×25 mL). The combined organic extracts were washed with brine (25 mL), dried (MgSO_4), and concentrated. The resulting residue was chromatographed (SiO_2 ; EtOAc–hexanes = 1:30) to yield 2,2-diphenyl-5,6-

undecadienenitrile (**S9**, 660 mg, 42%) as a colorless oil that was ~95% pure by ^1H NMR analysis and that was used in subsequent steps without further purification.

A solution of DIBAL-H (1 M in toluene, 1.90 mL, 1.90 mmol) was added to a solution of **S9** (404 mg, 1.28 mmol) in ether (10 mL) at -42°C over 30 min and stirred for 3 h. To the resulting solution, NaBH_4 (147 mg, 3.89 mmol) was added in one portion followed by the slow addition of EtOH (10 mL) over 30 min. The reaction mixture was stirred vigorously for 3 h at 0°C , treated with saturated aqueous potassium carbonate (5 mL) and ether (10 mL) and the resulting layers were separated. The organic fraction was washed with water (2×10 mL) and brine (10 mL), dried (MgSO_4), and concentrated to give crude 2,2-diphenyl-5,6-dodecadienylamine (**S18**) as a viscous oil that was used in the subsequent steps without further purification.

Benzyl chloroformate (220 μL , 1.55 mmol) was added to a suspension of crude **S18** and NaHCO_3 (166 mg, 1.98 mmol) in EtOH/water [2/1 (v/v), 7.5 mL] at 0°C and stirred vigorously at room temperature for 1 h. Water (5 mL) was added and the resulting mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO_4), and concentrated. The resulting residue was chromatographed (SiO_2 ; EtOAc–hexanes = 1:12) to give **10** (0.23 g, 39% from **S9**) as a colorless, viscous oil.

For S9: TLC (EtOAc–hexanes = 1:30): R_f = 0.17. ^1H NMR (25°C , 300 MHz): δ 7.26-7.41 (m, 10 H), 4.98-5.10 (m, 2 H), 3.06-3.10 (m, 2 H), 1.81-1.86 (m, 2 H), 1.26-1.34 (m, 6 H), 0.88 (t, J = 7.0 Hz, 3 H).

For 10: TLC (EtOAc–hexanes = 1:12): R_f = 0.19. ^1H NMR (55°C , 400 MHz): δ 7.18-7.33 (m, 15 H), 5.04 (s, 2 H), 4.90-4.94 (m, 1 H), 4.74 (br s, 1 H), 4.37 (br s, 1 H), 4.03 (dd, J = 6.2, 13.0 Hz, 1 H), 3.94 (dd, J = 5.6, 13.3 Hz, 1 H), 2.78-2.89 (m, 2 H), 1.80-1.86 (m, 2 H), 1.22-1.33 (m, 6 H), 0.89 (t, J = 7.0 Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55°C , 101 MHz): δ 205.9, 156.4, 145.2, 136.9, 128.7, 128.4,

128.4, 128.3, 128.3, 128.2, 126.7, 126.7, 90.6, 86.0, 66.9, 50.9, 48.4, 38.3, 31.5, 29.2, 28.8, 22.6. IR (neat, cm^{-1}): 2925, 2856, 1721, 1506, 1220, 696. HRMS calcd (found) for $\text{C}_{31}\text{H}_{35}\text{NO}_2$ (M^+): 453.2668 (453.2670).

Benzyl (1-buta-2,3-dienylcyclohexylmethyl)carbamate (12). Compound **12** was prepared from 1-(2,3-butadienyl)cyclohexanecarbonitrile (**S19**) employing a synthesis similar to that used to synthesize **10** from **S9**. Compound **S19** was synthesized from **S3** employing a procedure analogous to that used to convert **S20** to **S21**.

For S19: TLC (EtOAc–hexanes = 1:5): R_f = 0.57. ^1H NMR (25 °C, 400 MHz): δ 5.13 (tt, J = 6.8, 8.0 Hz, 1 H), 4.70 (td, J = 2.4, 6.4 Hz, 2 H), 2.20 (td, J = 2.4, 8.0 Hz, 2 H), 1.93-1.98 (m, 2 H), 1.52-1.74 (m, 5 H), 1.22 (dt, J = 3.2, 13.2 Hz, 2 H), 1.09-1.17 (m, 1 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz): δ 210.4, 123.2, 84.2, 75.1, 39.9, 39.5, 35.4, 25.4, 23.1. IR (neat, cm^{-1}): 2933, 2858, 2230, 1956, 1448, 845. HRMS calcd (found) for $\text{C}_{11}\text{H}_{15}\text{N}$ (M^+): 161.1204 (161.1205).

For 12: TLC (EtOAc–hexanes = 1:9): R_f = 0.13. ^1H NMR (55 °C, 400 MHz): δ 7.29-7.36 (m, 5 H), 5.11 (s, 2 H), 5.06 (br septet, J = 7.0 Hz, 1 H), 4.72 (br s, 1 H), 4.62-4.64 (m, 2 H), 3.16 (d, J = 6.3 Hz, 2 H), 2.01 (d, J = 8.2 Hz, 2 H), 1.31-1.53 (m, 10 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 209.8, 156.9, 137.0, 128.7, 128.3, 128.2, 85.4, 73.9, 66.9, 47.6, 37.6, 35.7, 33.4, 26.3, 21.6. IR (neat, cm^{-1}): 2923, 2854, 1700, 1408, 1352, 1110. HRMS calcd (found) for $\text{C}_{19}\text{H}_{25}\text{NO}_2$ (M^+): 299.1885 (299.1889).

Benzyl 4,5-hexadienylcarbamate (13): 4-Pentynenitrile (**S22**, 5.04 g, 63.7 mmol) was added dropwise to a suspension of LiAlH_4 (4.83 g, 127 mmol) in ether (175 mL) at 0 °C. The resulting suspension was stirred at room temperature for 1 h, cooled to 0 °C, and quenched by successive addition of water (6.8 mL), 15% NaOH (6.8 mL) and water (6.8 mL). The resulting suspension was warmed to room temperature, filtered through a pad of Celite, and eluted with ether (100 mL). The resulting

solution of 5-pentynylamine (**S23**) was concentrated to ~10 mL and used in the subsequent step without further purification.

A solution of crude **S23** (all material obtained in previous step), Boc₂O (14.5 g, 66.5 mmol), and Et₃N (22 mL, 157 mmol) in CH₂Cl₂ (235 mL) was generated at 0 °C and warmed to room temperature overnight. The reaction mixture was washed with water (2 × 100 mL), 1 M HCl (2 × 100 mL), and brine (100 mL), dried (MgSO₄), and concentrated. The resulting oily residue was chromatographed (SiO₂; CH₂Cl₂) to yield *t*-butyl 4-pentynylcarbamate (**S20**) as a colorless oil (5.03 g, 43% from **S22**).

A solution of **S20** (3.66 g, 20.0 mmol), CuBr (1.17 g, 8.16 mmol), *i*-Pr₂NH (5.7 mL, 40 mmol), paraformaldehyde (1.20 g, 40.0 mmol) in dioxane (105 mL) was refluxed (oil bath temperature 108 °C) for 2 d. The resulting suspension was concentrated to ~10 mL, diluted with ether (300 mL), filtered through a pad of Celite, and eluted with ether (100 mL). The resulting brown solution was concentrated and chromatographed (SiO₂; EtOAc–hexanes = 1:19) to give *t*-butyl 4,5-hexadienylcarbamate (**S21**) as a colorless oil (1.78 g, 45%).

HBF₄·OEt₂ (510 µL, 3.75 mmol) was added to a solution of **S21** (592 mg, 3.00 mmol) in CH₂Cl₂ (30 mL) at 0 °C. The resulting mixture was stirred at room temperature for 2 h, treated sequentially with Et₃N (1.10 mL, 7.83 mmol) and benzyl chloroformate (470 µL, 3.31 mmol) at 0 °C, and warmed to room temperature overnight. The resulting mixture was diluted with CH₂Cl₂ (30 mL), washed with water (15 mL), 1 M HCl (15 mL), sat. NaHCO₃ (15 mL), and brine, dried (MgSO₄), and concentrated. The resulting residue was chromatographed (SiO₂; Et₂O–CH₂Cl₂ = 1:40) to give **13** as a colorless oil (0.41 g, 60 %).

For S20:^{S9} TLC (CH₂Cl₂): *R*_f = 0.35. ¹H NMR (55 °C, 300 MHz): δ 4.64 (br s, 1 H), 3.22 (dt, *J* = 6.2, 6.5 Hz, 2 H), 2.23 (dt, *J* = 2.7, 7.0 Hz, 2 H), 1.96 (t, *J* = 2.6 Hz, 1 H), 1.71 (quintet, *J* = 7.0 Hz, 2 H), 1.43 (s, 9 H). ¹³C{¹H} NMR (55 °C, 75 MHz): δ 156.1, 83.6, 79.3, 69.1, 39.7, 28.7, 28.5, 16.0.

For S21: TLC (Et₂O–CH₂Cl₂ = 1:19): R_f = 0.53. ¹H NMR (55 °C, 500 MHz): δ 5.09 (septet, J = 6.7 Hz, 1 H), 4.67 (td, J = 3.2, 6.7 Hz, 2 H), 4.53 (br s, 1 H), 3.15 (br q, J = 6.9 Hz, 2 H), 2.00-2.05 (m, 2 H), 1.60 (septet, J = 7.3 Hz, 2 H), 1.44 (s, 9 H). ¹³C{¹H} NMR (55 °C, 126 MHz): δ 208.7, 156.1, 89.3, 79.2, 75.3, 40.1, 29.4, 28.6, 25.6. IR (neat, cm⁻¹): 3346, 2975, 1689, 1516, 1250, 1167. HRMS calcd (found) for C₁₁H₁₉NO₂ (M⁺): 197.1416 (197.1418).

For 13: TLC (Et₂O–CH₂Cl₂ = 1:40): R_f = 0.46. ¹H NMR (55 °C, 400 MHz): δ 7.28-7.36 (m, 5 H), 5.11 (s, 2 H), 5.10 (septet, J = 6.7 Hz, 1 H), 4.72 (br s, 1 H), 4.68 (td, J = 3.2, 6.7 Hz, 2 H), 3.24 (q, J = 6.7 Hz, 2 H), 2.01-2.08 (m, 2 H), 1.65 (septet, J = 7.2 Hz, 2 H). ¹³C{¹H} NMR (55 °C, 101 MHz): δ 208.9, 156.6, 137.0, 128.7, 128.2, 89.2, 75.3, 66.8, 40.8, 29.4, 25.5. IR (neat, cm⁻¹): 3330, 2937, 1695, 1526, 1246, 1134. HRMS calcd (found) for C₁₄H₁₇NO₂ (M⁺): 231.1259 (231.1256).

Pyrrolidines

Optimization of Au(I)-Catalyzed Protocol:

Optimization studies for the Au-catalyzed enantioselective conversion of **2a** to **3a** are depicted in Tables S1-S3.

Table S1. [(*S*)-1]Au₂Cl₂/silver-catalyzed enantioselective hydroamination of **2a** ([**2a**]_{initial} = 0.15 M) as a function of toluene/dioxane and AgOTs/AgOTf.

AgX	solvent	time (h)	T (°C)	conversion (%)	ee (%)
AgOTs	toluene	72	rt	53	—
AgOTs	dioxane	72	rt	45	—
AgOTf	toluene	2	rt	100	58
AgOTf	dioxane	2	rt	100	54
AgOTf	toluene	18	−20	100	70

Table S2. [(*S*)-1]Au₂Cl₂/silver-catalyzed enantioselective hydroamination of **2a** ([**2a**]_{initial} = 0.15 M) as a function of silver salts.

AgX	time (h)	conversion (%)	ee (%)
AgOTs	160 h	100	58
AgOTf	2 h	100	58
AgNTf ₂	1 h	100	43
AgBF ₄	144 h	75	51
BARF	48 h	95	7
AgPF ₆	4 h	100	65
AgAsF ₆	10 min	100	65
AgSbF ₆	1 h	100	58
AgClO ₄	10 min	100	66
AgOBz	60 h	0	—
Ag ₂ CO ₃	42 h	0	—
AgCO ₂ CF ₃	42 h	0	—
AgNO ₃	42 h	0	—
AgOCN	42 h	0	—
AgAsF ₆ ^a	13.5 h	100	73
AgClO ₄ ^a	13.5 h	94	76

^aReaction performed at −20 °C.

Table S3. [(*S*)-**1**] Au_2Cl_2 / AgClO_4 -catalyzed enantioselective hydroamination of **2a** ($[\mathbf{2a}]_{\text{initial}} = 0.15 \text{ M}$) as a function of solvent.

solvent	time	conversion (%)	ee (%)
<i>m</i> -xylene	5 min	90	67
	10 min	100	
<i>o</i> -xylene	5 min	97	66
	10 min	100	
chlorobenzene	5 min	72	61
	30 min	97	
mestylene	30 min	63	66
	2.5 h	95	
MeOH	12 h	28	—
	24 h	28	
CH_2Cl_2	5 min	51	42
	1 h	100	
CCl_4	5 min	8	62
	20.5 h	97	
acetone	5 min	41	50
	3 h	100	
THF	5 min	37	62
	22 h	72	
$\text{CHCl}_2\text{CHCl}_2$	5 min	70	34
	1 h	100	
toluene ^a	24 h	100	80
<i>m</i> -xylene ^a	24 h	100	81

^aReaction performed at -40°C .

Benzyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (3a). A mixture of [(*S*)-**1**] Au_2Cl_2 (12.1 mg, 7.5×10^{-3} mmol) and AgClO_4 (3.1 mg, 15×10^{-3} mmol) in *m*-xylene (0.4 mL) was stirred at room temperature for 5 min, cooled to -50°C , and treated with a solution of **2a** (115 mg, 0.30 mmol) in *m*-xylene (0.6 mL). The resulting suspension was stirred at -40°C for 24 h. Column chromatography of

the reaction mixture (hexanes–EtOAc = 40:1 → 20:1) gave **3a** (111 mg, 97%) as a colorless oil.^{S3} The enantiomeric purity of **3a** was determined by chiral HPLC analysis (Figure S1). TLC (EtOAc–hexanes = 1:4): R_f = 0.34. ¹H NMR (25 °C, 300 MHz, 1:1 mixture of rotomers): δ 7.22-7.46 (m, 15 H), 5.77-5.91 (m, 1 H), 5.06-5.39 (m, 4 H), [4.83 (dd, J = 2.0, 15.2 Hz), 4.67 (dd, J = 2.0, 15.2 Hz), 1:1, 1 H], 4.14-4.27 (m, 1 H), [3.77 (d, J = 15.6 Hz), 3.76 (d, J = 15.6), 1:1, 1 H], 2.86-2.93 (m, 1 H), [2.52 (dd, J = 13.2, 16.8 Hz), 2.47 (dd, J = 12.8, 16.8 Hz), 1:1, 1 H]. ¹³C{¹H} NMR (25 °C, 75 MHz, 1:1 mixture of rotomers): δ 155.6, 154.8, 145.5, 144.8, 139.3, 138.6, 137.1, 137.0, 128.8, 128.7, 128.4, 128.3, 128.2, 127.8, 127.6, 126.9, 126.7, 126.6, 126.5.

All remaining enantioselective hydroamination reactions were performed in an analogous manner. Chiral HPLC analyses for enantiomerically enriched and racemic pyrrolidines are depicted in Figures S1 – S11. Samples of racemic pyrrolidines were prepared via cyclization of the corresponding *N*-allenyl carboxamide derivatives catalyzed by a 1:1 mixture of Au[P(*t*-Bu)₂(*o*-biphenyl)]Cl and AgOTf employing a published procedure.^{S3}

2,2,2-Trichloroethyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (3b). White solid. TLC (EtOAc–hexanes = 1:10): R_f = 0.19. ¹H NMR (25 °C, 500 MHz, 1.3:1 mixture of rotomers): δ 7.17-7.31 (m, 10 H), [5.85 (dd, J = 7.3, 10.2 Hz), 5.80 (dd, J = 7.3, 10.1 Hz), 1:1.3, 1 H], 5.18-5.25 (m, 1 H), [5.14 (d, J = 10.1 Hz), 5.09 (d, J = 10.1 Hz), 1:1.3, 1 H], [4.97 (d, J = 11.6 Hz), 4.88 (d, J = 11.9 Hz), 1:1.3, 1 H], [4.78 (d, J = 11.7 Hz), 4.72 (d, J = 11.3 Hz), 1.3:1, 1 H], 4.62-4.65 (m, 1 H), 4.22-4.27 (m, 1 H), [3.85 (d, J = 11.3 Hz), 3.76 (d, J = 11.4 Hz), 1:1.3, 1 H], [2.94 (dd, J = 2.0, 6.9 Hz), 2.92 (dd, J = 2.1, 6.9 Hz), 1:1.3, 1 H], 2.45-2.53 (m, 1 H). ¹³C{¹H} NMR (25 °C, 126 MHz, 1.3:1 mixture of rotomers): δ 154.0, 152.7, 145.2, 145.2, 144.4, 138.3, 137.8, 128.9, 128.8, 128.7, 126.9, 126.8, 126.8, 126.7, 126.6, 126.6, 116.4, 116.2, 96.0, 95.7, 74.9, 74.7, 59.8, 59.6, 56.5, 56.2, 53.1, 52.9, 45.5, 44.6. IR

(neat, cm^{-1}): 2883, 1718, 1407, 1351, 1113, 697. HRMS calcd (found) for $\text{C}_{21}\text{H}_{20}^{35}\text{Cl}_3\text{NO}_2$ (M^+): 423.0560 (423.0565).

9H-Fluoren-9-ylmethyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (3c).^{S3} Colorless oil. TLC (EtOAc–hexanes = 1:6): R_f = 0.23. ^1H NMR (25 °C, 300 MHz, 1:1 mixture of rotomers): δ 7.18–7.83 (m, 18 H), [5.81 (ddd, J = 7.3, 10.0, 17.3), 5.72 (ddd, J = 7.3, 10.2, 17.2), 1:1, 1 H], [5.24 (d, J = 16.9 Hz), 5.15 (d, J = 10.2), 1:1, 1 H], [4.97 (d, J = 18.5 Hz), 4.95 (d, J = 8.9 Hz), 1:1, 1 H], 4.78 (d, J = 11.5 Hz, 0.5 H), 4.04–4.56 (m, 4.5 H), [3.77 (d, J = 11.3 Hz), (d, J = 11.5 Hz), 1:1, 1 H], 2.85–2.91 (m, 1 H), [2.49 (dd, J = 9.5, 12.4 Hz), 2.44 (dd, J = 9.6, 12.8 Hz), 1:1, 1 H]. $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 75 MHz, 1:1 mixture of rotomers): δ 155.7, 154.6, 145.5, 145.4, 144.9, 144.8, 144.3, 144.2, 144.1, 141.5, 141.5, 141.4, 139.0, 138.5, 128.8, 128.7, 127.8, 127.6, 127.2, 127.2, 127.1, 127.0, 126.9, 126.7, 126.6, 126.6, 126.5, 126.5, 125.2, 125.1, 125.0, 120.1, 120.0, 115.8, 115.2, 67.2, 59.5, 59.1, 56.3, 56.2, 53.0, 52.7, 47.5, 47.4, 45.8, 44.7.

Methyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (3d). Colorless oil. TLC (CH_2Cl_2): R_f = 0.24. ^1H NMR (25 °C, 500 MHz, 1:1 mixture of rotomers): δ 7.17–7.31 (m, 10 H), 5.71–5.81 (m, 1 H), [5.21 (d, J = 17.1 Hz), 5.09 (d, J = 16.2 Hz), 1:1, 1 H], [5.11 (d, J = 8.4 Hz), 5.03 (d, J = 10.2 Hz), 1:1, 1 H], [4.73 (d, J = 11.6 Hz), 4.54 (d, J = 11.1 Hz), 1:1, 1 H], [4.18 (td, J = 7.4, 8.0 Hz), 4.05 (td, J = 7.2, 8.4 Hz), 1:1, 1 H], [3.76 (s), 3.67 (s), 1:1, 3 H], 3.70–3.74 (m, 1 H), 2.82–2.87 (m, 1 H), 2.40–2.49 (m, 1 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 126 MHz, 1:1 mixture of rotomers): δ 156.2, 155.4, 145.6, 145.5, 145.1, 144.9, 139.3, 138.7, 128.8, 128.7, 126.9, 126.7, 126.6, 126.5, 115.8, 114.9, 59.6, 59.0, 56.3, 56.2, 53.0, 52.7, 52.5, 45.7, 44.7. IR (neat, cm^{-1}): 2953, 1695, 1446, 1379, 1199, 698. HRMS calcd (found) for $\text{C}_{20}\text{H}_{21}\text{NO}_2$ (M^+): 307.1572 (307.1577).

1-Acetyl-4,4-diphenyl-2-vinylpyrrolidine (3e). White solid. TLC (ether– CH_2Cl_2 = 1:8): R_f = 0.28. ^1H NMR (25 °C, 400 MHz, 1:4 mixture of rotomers): δ 7.15–7.32 (m, 10 H), [5.79 (ddd, J = 6.8,

10.4, 17.1 Hz), 5.75 (ddd, $J = 7.7, 9.9, 17.4$ Hz), 1:4, 1 H], 5.06-5.19 (m, 2 H), [5.01 (dd, $J = 2.4, 12.3$ Hz), 4.33 (dd, $J = 1.9, 10.8$ Hz), 4:1, 1 H], [4.42-4.47 (m), 4.04-4.10 (m), 1:4, 1 H], [3.97 (d, $J = 10.8$ Hz), 3.61 (d, $J = 12.3$ Hz), 1:4, 1 H], [2.93 (dd, $J = 6.8, 12.6$ Hz), 2.93 (dd, $J = 6.7, 12.5$ Hz), 1:4, 1 H], [2.54 (dd, $J = 9.2, 12.6$ Hz), 2.40 (dd, $J = 9.2, 12.8$ Hz), 4:1, 1 H], [2.13 (s), 1.97 (s), 1:4, 3 H]. $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz, 1:4 mixture of rotomers): δ 170.8, 169.0, 145.4, 145.3, 144.9, 144.7, 139.2, 138.4, 128.8, 128.8, 128.7, 128.7, 126.9, 126.8, 126.8, 126.8, 126.7, 126.6, 126.5, 126.4, 116.3, 115.0, 60.3, 56.6, 58.2, 55.1, 53.3, 51.9, 46.5, 44.1, 23.3, 22.4. IR (neat, cm^{-1}): 3054, 1629, 1425, 1196, 945, 698. HRMS calcd (found) for $\text{C}_{20}\text{H}_{21}\text{NO}$ (M^+): 291.1623 (291.1624).

Benzyl 2-(2-methylpropenyl)-4,4-diphenylpyrrolidine-1-carboxylate (7). Colorless oil. TLC (EtOAc–hexanes = 1:6): $R_f = 0.22$. ^1H NMR (25 °C, 400 MHz, 1.5:1 mixture of rotomers): δ 7.17-7.41 (m, 15 H), [5.33 (d, $J = 12.6$ Hz), 5.20 (d, $J = 12.5$ Hz), 1:1.5, 1 H], 5.03-5.11 (m, 2 H), [4.77 (d, $J = 11.6$ Hz), 4.63 (d, $J = 11.3$ Hz), 1.5:1, 1 H], [4.43 (dt, $J = 7.5, 8.4$ Hz), 4.31 (dt, $J = 6.8, 9.1$ Hz), 1:1.5, 1 H], [3.71 (d, $J = 11.6$ Hz), 3.69 (d, $J = 11.6$ Hz), 1:1.5, 1 H], 2.77-2.85 (m, 1 H), [2.39 (dd, $J = 9.7, 12.5$ Hz), 2.34 (dd, $J = 9.7, 12.5$ Hz, 1 H), 1.5:1, 1 H], [1.73 (s), 1.64 (s), 1:1.5, 3 H], [1.71 (s), 1.40 (s), 1:1.5, 3 H]. $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz, 1:1.5 mixture of rotomers): δ 155.4, 154.6, 145.8, 145.1, 137.2, 137.0, 134.0, 133.3, 128.7, 128.6, 128.4, 128.1, 127.8, 127.7, 126.9, 126.6, 126.6, 126.5, 126.4, 125.8, 66.9, 66.8, 56.0, 55.1, 54.6, 53.0, 52.6, 45.6, 44.9, 26.0, 25.7, 18.2, 17.9. IR (neat, cm^{-1}): 3029, 2924, 1696, 1410, 1098, 696. HRMS calcd (found) for $\text{C}_{28}\text{H}_{29}\text{NO}_2$ (M^+): 411.2198 (411.2196).

Benzyl 2-(2-ethyl-1-butenyl)-4,4-diphenylpyrrolidine-1-carboxylate (8). Colorless oil. TLC (EtOAc–hexanes = 1:5): $R_f = 0.43$. ^1H NMR (25 °C, 400 MHz, 1.8:1 mixture of rotomers): δ 7.17-7.39 (m, 15 H), [5.30 (d, $J = 12.4$ Hz), 5.18 (d, $J = 12.8$ Hz), 1:1.8, 1 H], 4.99-5.07 (m, 2 H), [4.74 (dd, $J = 1.6, 11.6$ Hz), 4.59 (d, $J = 11.6$ Hz), 1.8:1, 1 H], [4.50 (dt, $J = 7.6, 8.4$ Hz), 4.38 (dt, $J = 6.8, 8.8$ Hz), 1:1.8, 1 H], [3.76 (d, $J = 9.2$ Hz), 3.73 (d, $J = 11.6$ Hz), 1:1.8, 1 H], 2.77-2.86 (m, 1 H), [2.40 (dd, $J =$

9.6, 12.4 Hz), 2.34 (dd, $J = 9.6, 12.8$ Hz), 1.8:1, 1 H], [2.18-2.27 (m), 1.70-1.79 (m), 1:1.8, 1 H], 1.89-2.06 (m, 3 H), [1.00 (t, $J = 7.6$ Hz, 3 H), 0.91 (t, $J = 7.2$ Hz, 3 H), 1:1.8, 3 H], [0.97 (t, $J = 7.6$ Hz), 0.82 (t, $J = 7.6$ Hz), 1:1.8, 3 H]. $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz, 1.8:1 mixture of rotomers): δ 155.5, 154.6, 145.9, 145.2, 144.7, 143.6, 137.3, 137.1, 128.8, 128.7, 128.4, 128.2, 127.8, 127.0, 126.7, 126.6, 126.6, 126.5, 124.8, 124.0, 66.9, 66.8, 56.1, 54.8, 54.3, 53.2, 52.7, 46.2, 45.5, 29.0, 28.9, 23.9, 23.6, 13.7, 13.5, 12.7, 12.5. IR (neat, cm^{-1}): 2963, 1875, 1697, 1409, 1099, 696. HRMS calcd (found) for $\text{C}_{30}\text{H}_{33}\text{NO}_2$ (M^+): 439.2511 (439.251).

Benzyl 2-cyclohexylidenemethyl-4,4-diphenylpyrrolidine-1-carboxylate (9). Colorless oil. TLC (EtOAc-hexanes = 1:6): $R_f = 0.35$. ^1H NMR (25 °C, 400 MHz, 1.8:1 mixture of rotomers): δ 7.19-7.42 (m, 15 H), 5.34 (d, $J = 12.3$ Hz, 0.4 H), 5.05-5.21 (m, 2.6 H), [4.79 (d, $J = 11.6$ Hz), 4.64 (d, $J = 11.4$ Hz), 1.8:1, 1 H], [4.51 (dt, $J = 7.3, 8.9$ Hz), 4.40 (dt, $J = 6.8, 9.1$ Hz), 1:1.8, 1 H], [3.73 (d, $J = 12.1$ Hz), 3.70 (d, $J = 11.6$ Hz), 1:1.8, 1 H], 2.77-2.85 (m, 1 H), [2.42 (dd, $J = 9.9, 12.5$), 2.37 (dd, $J = 9.9, 12.5$ Hz), 1.8:1, 1 H], 1.88-2.22 (m, 4 H), 1.35-1.70 (m, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 155.4, 154.5, 145.8, 145.1, 141.8, 140.6, 137.2, 137.2, 128.7, 128.6, 128.4, 128.1, 127.7, 127.7, 126.9, 126.6, 126.4, 123.5, 122.7, 66.8, 66.7, 56.1, 54.3, 53.7, 53.1, 52.7, 46.2, 45.4, 37.1, 36.9, 29.4, 29.0, 28.6, 28.3, 27.9, 27.5, 26.8, 26.8. IR (neat, cm^{-1}): 2926, 1695, 1410, 1098, 731, 696. HRMS calcd (found) for $\text{C}_{31}\text{H}_{33}\text{NO}_2$ (M^+): 451.2511 (451.2513).

(E)-Benzyl 2-hept-1-enyl-4,4-diphenylpyrrolidine-1-carboxylate (11). Colorless oil. TLC (CH_2Cl_2 -hexanes = 3:1): $R_f = 0.51$. ^1H NMR (25 °C, 400 MHz, 1.4:1 mixture of rotomers): δ 7.14-7.39 (m, 15 H), 5.62 (td, $J = 6.4, 15.2$ Hz, 1 H), 5.29-5.49 (m, 2 H), 5.02-5.11 (m, 2.6 H), [4.73 (d, $J = 11.6$ Hz), 4.57 (d, $J = 11.6$ Hz), 1.4:1, 1 H], [4.13 (dt, $J = 7.6, 8.4$), 4.06 (dt, $J = 7.2, 8.8$ Hz), 1:1.4, 1 H], [3.69 (d, $J = 11.6$ Hz), 3.67 (d, $J = 11.2$ Hz), 1:1.4, 1 H], [2.81 (dd, $J = 1.6, 6.8$ Hz), 2.78 (dd, $J = 1.6, 6.8$), 1:1.4, 1 H], [2.43 (dd, $J = 10.0, 12.4$ Hz), 2.38 (dd, $J = 9.2, 12.4$ Hz), 1.4:1, 1 H], 1.88-2.03 (m,

2 H), 1.21-1.34 (m, 6 H), 0.84-0.86 (m, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (25 °C, 101 MHz, 1.4:1 mixture of rotomers): δ 155.7, 154.8, 145.7, 145.0, 137.3, 137.1, 132.8, 132.4, 130.8, 130.0, 128.8, 128.7, 128.4, 128.3, 128.2, 127.8, 127.7, 127.0, 126.7, 126.7, 126.6, 126.5, 66.9, 59.0, 58.7, 56.3, 53.1, 52.7, 46.2, 45.1, 32.3, 32.2, 31.6, 29.0, 28.9, 22.7, 14.3. IR (neat, cm^{-1}): 2924, 1698, 1409, 1351, 1103, 696. HRMS calcd (found) for $\text{C}_{31}\text{H}_{35}\text{NO}_2$ (M^+): 453.2668 (453.2677).

Benzyl 3-vinyl-2-aza-spiro[4.5]decane-2-carboxylate (14). Colorless oil. TLC (EtOAc–hexanes = 1:5): R_f = 0.47. ^1H NMR (55 °C, 400 MHz): δ 7.26-7.35 (m, 5 H), 5.81 (ddd, J = 6.8, 10.1, 17.1 Hz, 1 H), 5.02-5.17 (m, 4 H), 4.34 (dd, J = 7.0, 14.4 Hz, 1 H), 3.59 (d, J = 10.0 Hz, 1 H), 3.09 (d, J = 10.9 Hz, 1 H), 2.02 (dd, J = 8.0, 12.6 Hz, 1 H), 1.34-1.53 (m, 10 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 155.5, 140.0, 137.4, 128.5, 127.9, 114.2, 66.8, 59.2, 57.4, 44.7, 41.7, 36.7, 35.4, 26.3, 23.9, 23.2. IR (neat, cm^{-1}): 2923, 2854, 1700, 1408, 1352, 1110. HRMS calcd (found) for $\text{C}_{19}\text{H}_{25}\text{NO}_2$ (M^+): 299.1885 (299.1889).

For (S)-15:^{S1} Colorless oil. TLC (ether– CH_2Cl_2 = 1:40): R_f = 0.31. ^1H NMR (55 °C, 400 MHz): δ 7.26-7.32 (m, 5 H), 5.78 (ddd, J = 5.5, 10.1, 17.1 Hz, 1 H), 5.05-5.17 (m, 4 H), 4.40 (br t, J = 7.2 Hz, 1 H), 3.49 (d, J = 7.2 Hz, 1 H), 3.47 (d, J = 6.2 Hz, 1 H), 1.71-2.07 (m, 4 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (55 °C, 101 MHz): δ 155.1, 138.5, 137.4, 128.5, 127.9, 114.3, 66.8, 59.4, 46.7, 31.8, 23.1.

Comparison of absolute stereochemistry of **3a** and **8** :

Enantiomerically enriched samples of **3a** and **8** were converted to benzyl 4,4-diphenylpyrrolidine-2-methylcarboxylate carbamate (**16**) via a two step process of oxidation^{S10} and esterification. Both samples displayed the same absolute configuration.

A solution of **3a** (36.0 mg, 9.3×10^{-2} mmol, 58 % ee) in *t*-BuOH (0.9 mL) was added to a solution of NaIO_4 (187 mg, 0.874 mmol), KMnO_4 (30.4 mg, 0.192 mmol), K_2CO_3 (17.1 mg, 0.124

mmol), and *t*-BuOH (0.9 mL) in water (3.6 mL) at room temperature and the resulting suspension stirred vigorously for 2 h. Ethylene glycol (0.03 mL, 0.5 mmol) was added and the mixture stirred for an additional 2 h. 1 M HCl (1 mL) was added to the resultant brown suspension and the aqueous mixture was extracted with EtOAc (5 × 3 mL). The combined organic extracts were washed with brine (5 mL), dried (MgSO₄), and concentrated to yield crude benzyl 4,4-diphenylproline carbamate (**S24**) a colorless oil that was used in the subsequent step without further purification.

Potassium carbonate (14.7 mg, 0.106 mmol) was added to a solution of **S24** (all material obtained in previous step) in DMF (1 mL) at 0 °C and stirred for 10 min. Methyl iodide (11.8 μL, 0.190 mmol) was added to the resulting suspension and the reaction mixture was warmed to room temperature and stirred for 3 h. The resulting suspension was diluted with EtOAc (20 mL) and washed with water (2 × 5 mL) and brine (5 mL), dried (MgSO₄), and concentrated. The resulting residue was chromatographed (SiO₂; EtOAc–hexanes = 1:3) to give **16** as a colorless oil (18.3 mg, 47 %, 57% ee). TLC (EtOAc–hexanes = 1:3): *R_f* = 0.33. ¹H NMR (25 °C, 400 MHz, 1.2:1 mixture of rotomers): δ 7.17-7.39 (m, 15 H), [5.28 (d, *J* = 12.3 Hz), 5.19 (d, *J* = 12.3 Hz), 1:1.2, 1 H], [5.14 (d, *J* = 12.5 Hz), 5.06 (d, *J* = 12.5 Hz), 1:1.2, 1 H], [4.69 (d, *J* = 10.8 Hz), 4.56 (d, *J* = 11.1 Hz), 1.2:1, 1 H], [4.26 (dd, *J* = 7.3, 9.4 Hz), 4.21 (dd, *J* = 7.3, 9.6 Hz), 1:1.2, 1 H], 3.90 (d, *J* = 11.3 Hz, 1 H), [1.37 (s), 3.51 (s), 1:1.2, 3 H], 2.96-3.02 (m, 1 H), 2.65-2.73 (m, 1 H). ¹³C{¹H} NMR (25 °C, 75 MHz, 1.2:1 mixture of rotomers): δ 172.9, 172.7, 154.7, 154.3, 144.5, 144.2, 144.1, 136.8, 136.5, 128.9, 128.9, 128.7, 128.5, 128.3, 128.2, 127.9, 127.0, 162.9, 126.5, 67.5, 67.4, 58.6, 58.3, 56.2, 53.8, 53.1, 52.5, 52.2, 42.7, 41.8. IR (neat, cm⁻¹): 2953, 2360, 1748, 1707, 1417, 1197. HRMS calcd (found) for C₂₆H₂₆NO₄ (MH⁺): 416.1862 (416.1863).

A racemic sample of **16** was prepared from racemic **3a** employing a similar procedure. Compound **8** (84% ee) was converted to **16** (84% ee) in 20% yield employing a preparation similar to

that used to synthesize **16** from **3a**. Chiral HPLC analyses for the enantiomerically enriched and racemic samples of **16** are depicted in Figure S12.

Figure S1. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **3a**. The enantiomers eluted at 15.9 and 17.6 min (hexanes-isopropanol = 75:25 @ 0.5 mL/min).

Figure S2. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **3b**. The enantiomers eluted at 12.2 and 13.4 min (hexanes-isopropanol = 90:10 @ 0.5 mL/min).

Figure S3. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **3c**. The enantiomers eluted at 17.0 and 18.4 min (hexanes-isopropanol = 75:25 @ 0.5 mL/min).

Figure S4. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **3d**. The enantiomers eluted at 13.5 and 14.9 min (hexanes-isopropanol = 90:10 @ 0.5 mL/min).

Figure S5. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **3e**. The enantiomers eluted at 17.4 and 19.8 min (hexanes-isopropanol = 90:10 @ 0.5 mL/min).

Figure S6. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **7**. The enantiomers eluted at 21.8 and 25.6 min (hexanes-isopropanol = 90:10 @ 0.5 mL/min).

Figure S7. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **8**. The enantiomers eluted at 12.0 and 14.9 min (hexanes-isopropanol = 75:25 @ 0.5 mL/min).

Figure S8. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **9**. The enantiomers eluted at 13.4 and 19.6 min (hexanes-isopropanol = 75:25 @ 0.5 mL/min).

Figure S9. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **11**. The enantiomers eluted at 41 and 44.5 min (hexanes-isopropanol = 95:5 @ 0.5 mL/min).

Figure S10. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) **14**. The enantiomers eluted at 46.2 and 49.3 min (hexanes-isopropanol = 99:1 @ 0.5 mL/min).

Figure S11. HPLC trace for racemic (left trace) and enantiomerically enriched (center trace) (*S*)-**15** generated from enantioselective hydroamination of **13** and an authentic sample of (*S*)-**15** (right trace).

The enantiomers eluted at 14.5 and 15.9 min (hexanes-isopropanol = 95:5 @ 0.5 mL/min).

Figure S12. HPLC trace for racemic (left trace) **16** and enantiomerically enriched (center trace) **16** obtained by oxidation/esterification of **3a** and enantiomerically enriched (right trace) **16** obtained by oxidation/esterification of **8**. The enantiomers eluted at 25.4 and 29.9 min (hexanes-isopropanol = 75:25 @ 0.5 mL/min).

Figure S13. ^1H NMR spectra of **2d**.

Figure S14. ^{13}C NMR spectrum of **2d**.

Figure S15. ^1H NMR spectra of **2b**.

Figure S16. ^{13}C NMR spectrum of **2b**.

Figure S17. ^1H NMR spectra of **2e**.

Figure S18. ^{13}C NMR spectrum of **2e**.

Figure S19. ^1H NMR spectra of **S8**.

Figure S20. ^{13}C NMR spectrum of **S8**.

Figure S21. ^1H NMR spectra of **4**.

Figure S22. ^{13}C NMR spectrum of **4**.

Figure S23. ^1H NMR spectra of **S10**.

Figure S24. ^{13}C NMR spectrum of **S10**.

Figure S25. ^1H NMR spectra of **S11**.

Figure S26. ^{13}C NMR spectrum of **S11**.

Figure S27. ^1H NMR spectra of **S12**.

Figure S28. ^{13}C NMR spectrum of **S12**.

Figure S29. ^1H NMR spectra of **S13**.

Figure S30. ^{13}C NMR spectrum of **S13**.

Figure S31. ^1H NMR spectra of **5**.

Figure S32. ^{13}C NMR spectrum of **5**.

Figure S33. ^1H NMR spectra of **S14**.

Figure S34. ^{13}C NMR spectrum of **S14**.

Figure S35. ^1H NMR spectra of **S15**.

Figure S36. ^1H NMR spectra of **S17**.

Figure S37. ^{13}C NMR spectrum of **S17**.

Figure S38. ^1H NMR spectra of **6**.

Figure S39. ^{13}C NMR spectrum of **6**.

Figure S40. ^1H NMR spectra of **10**.

Figure S41. ^{13}C NMR spectrum of **10**.

Figure S42. ^1H NMR spectra of **S19**.

Figure S43. ^{13}C NMR spectrum of **S19**.

Figure S44. ^1H NMR spectra of **12**.

Figure S45. ^{13}C NMR spectrum of **12**.

Figure S46. ^1H NMR spectra of **S21**.

Figure S47. ^{13}C NMR spectrum of **S21**.

Figure S48. ^1H NMR spectra of **13**.

Figure S49. ^{13}C NMR spectrum of **13**.

Figure S50. ^1H NMR spectra of **3a**.

Figure S51. ^{13}C NMR spectrum of **3a**.

Figure S52. ^1H NMR spectra of **3b**.

Figure S53. ^{13}C NMR spectrum of **3b**.

Figure S54. ^1H NMR spectra of **3c**.

Figure S55. ^{13}C NMR spectrum of **3c**.

Figure S56. ^1H NMR spectra of **3d**.

Figure S57. ^{13}C NMR spectrum of **3d**.

Figure S58. ^1H NMR spectra of **3e**.

Figure 59. ^{13}C NMR spectrum of **3e**.

Figure S60. ^1H NMR spectra of **7**.

Figure S61. ^{13}C NMR spectrum of 7.

Figure S62. ^1H NMR spectra of **8**.

Figure S63. ^{13}C NMR spectrum of **8**.

Figure S64. ^1H NMR spectra of **9**.

Figure S65. ^{13}C NMR spectrum of **9**.

Figure S66. ^1H NMR spectra of **11**.

Figure S67. ^{13}C NMR spectrum of **11**.

Figure S68. ^1H NMR spectra of **14**.

Figure S69. ^{13}C NMR spectrum of **14**.

Figure S70. ^1H NMR spectra of (*S*)-15.

Figure S71. ^{13}C NMR spectrum of (*S*)-15.

Figure S72. ^1H NMR spectra of **16**.

Figure S73. ^{13}C NMR spectra of **16**.

References

- S1) Takeuchi, Y.; Yamada, A.; Suzuki, T.; Koizumi, T. *Tetrahedron* **1996**, *52*, 225.
- S2) Seijas, J. A.; Vázquez-Tato, M. P.; Castedo, L.; Estévez, R. J.; Ónega, M. G.; Ruíz, M. *Tetrahedron* **1992**, *48*, 1637.
- S3) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066.
- S4) Chang, S.; Lee, M.; Jung, D. Y.; Yoo, E. J.; Cho, S. H.; Han, S. K. *J. Am. Chem. Soc.* **2006**, *128*, 12366.
- S5) Murakami, M.; Kadowaki, S.; Matsuda, T. *Org. Lett.* **2005**, *7*, 3953.
- S6) Vij, A.; Zheng, Y. Y.; Kirchmeier, R. L.; Shreeve, J. M. *Inorg. Chem.* **1994**, *33*, 3281.
- S7) Miller, K. J.; Kitagawa, T. T.; Abu-Omar, M. M. *Organometallics* **2001**, *20*, 4403.
- S8) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178.
- S9) McDonald, F. E.; Chatterjee, A. K. *Tet. Lett.* **1997**, *38*, 7687.
- S10) Method analogous to that of: Expósito, A.; Fernández-Suárez, M.; Iglesias, T.; Muñoz, L.; Riguera, R. *J. Org. Chem.* **2001**, *66*, 4206.