Design and Stereoselective Preparation of a New Class of Chiral Olefin Metathesis Catalysts and Application to Enantioselective Synthesis of Quebrachamine. Catalyst Development Inspired by Natural Product Synthesis

Elizabeth S. Sattely,[#] Simon J. Meek,[#] Steven J. Malcolmson,[#]
Richard R. Schrock,[+] and Amir H. Hoveyda[#,*]

[#]*Department of Chemistry, Merkert Chemistry Center, Boston College*
Chestnut Hill, Massachusetts 02467

[+]*Department of Chemistry, Massachusetts Institute of Technology*
Cambridge, Massachusetts 02139

SUPPORTING INFORMATION: PART A

General: All reactions were carried out in oven- (135 °C) or flame-dried glassware under an inert atmosphere of dry N_2 unless otherwise stated. Alcohols **35**, **A**, **B, C, H**, and **K**, and substrate **2** were dried by azeotropic distillation with C_6H_6 prior to use in reactions with Mo-based reagents (the numbering of compounds refers to those in the body of the text; other compounds are abbreviated by letters). Infrared (IR) spectra were recorded on a Nicolet 210 spectrometer or on a Bruker FTIR Alpha (ATR Mode) spectrometer, υ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), or weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuteration as the internal reference ($CDCl_3$: δ 7.26, C_6D_6: δ 7.16). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, br = broad, m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.16). Enantiomer ratios were determined by HPLC (Chiral Technologies Chiralpak columns (4.6 mm x 250 mm)) in comparison with authentic racemic materials. High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Boston College Mass Spectrometry Laboratory or at the University of Illinois Mass Spectrometry Laboratory. Elemental analysis was performed at Midwest Microlab, LLC (Indianapolis, IN). Optical rotation values were recorded on a Rudolph Research Analytical Autopol IV polarimeter. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected.

Solvents: Solvents were purged with argon and purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: diethyl ether (Aldrich) and dichloromethane (Doe & Ingalls) were passed through activated alumina columns; benzene

(Aldrich), toluene (Doe & Ingalls), and pentane[1] (J T. Baker) were passed successively through activated Cu and alumina columns. Tetrahydrofuran (Aldrich) was distilled from sodium benzophenone ketyl. Methanol (Doe & Ingalls) and ethanol (Doe & Ingalls) were distilled from magnesium methoxide and magnesium ethoxide, respectively. Acetonitrile (Acros) was used as received. Petroleum ether (Doe & Ingalls) was used as received.

Metal-based Complexes: Mo-based bis(alkoxide) complexes **19** and **24**-**30** were prepared according to published procedures.[2] Mo-bis(pyrrolide) complexes **33a** and **33b** were prepared according to published procedures.[3] Mo-monoalkoxide-monopyrrolide complex *rac*-**32** was prepared according to published procedures.[4] Mo complexes were handled under an inert atmosphere in a dry box. Ru-based complexes **10**[5] and **18**[6] were obtained from Materia, Inc. and purified by silica gel column chromatography and recrystallization prior to use. Ru-based complexes **16**[7] and **17**[8] were prepared according to published procedures. Ru-based complexes **15**[9] and **23a**[10] were purchased from Materia and used as received. Ru-based complexes **20**[11] and **21**[12] were prepared according to published procedures. Synthesis of Ru-based complex **22** is unpublished. Ru-based complex **23b** was generated in situ from **23a** according to the published procedure.[10] Ru-based complexes were handled under an inert atmosphere in a dry box for comparison purposes.

REAGENTS:

Acetic acid (glacial) was purchased from Fisher and used as received.

2-Acetylbutyrolactone was purchased from Aldrich and used as received.

Allyl chloroformate was purchased from Aldrich and distilled from $CaCl_2$ prior to use.

***d_6*-Benzene** was purchased from Cambridge Isotope Laboratories and distilled from Na into activated 4 Å molecular sieves prior to use.

---

(1) *n*-Pentane was allowed to stir over concentrated H_2SO_4 for three days, washed with water, followed by a saturated aqueous solution of $NaHCO_3$, dried over $MgSO_4$, and filtered before use in the solvent purification system.

(2) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592–4633 and references cited therein.

(3) (a) Hock, A. S.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 16373–16375. (b) Singh, R.; Czekelius, C.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *Organometallics* **2007**, *26*, 2528–2539.

(4) Singh, R.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2007**, *129*, 12654–12655.

(5) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

(6) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953-956.

(7) Wakamatsu, H.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2403–2405.

(8) Grela, K.; Harutyunyan, S.; Michrowska, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 4038–4040.

(9) Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589–1592.

(10) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225–3228.

(11) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502–12508.

(12) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.

(*R*)-1,1'-binaphthyl-2,2'-diol ((*R*)-binol) was purchased from Kankyo Kakagu Center, Co. and used as received.

***tert*-Butyldimethylsilyl trifluoromethanesulfonate** was purchased from Aldrich or Oakwood and distilled prior to use.

***n*-Butyl lithium** (15% in hexanes) was purchased from Strem and titrated with *s*-butanol (1,10-phenanthroline as indicator) prior to use.

d_1-Chloroform was purchased from Cambridge Isotope Laboratories and distilled from CaH_2 into activated 4 Å molecular sieves prior to use with Mo complexes.

Chloromethyl methyl ether was purchased from Aldrich and used as received.

2-Chloropropane was purchased from Aldrich and distilled from CaH_2 prior to use.

Concentrated aqueous NH_4OH (Assay, as NH_3, w/w 28.9%) was purchased from Fisher and used as received.

Dimethylsulfoxide was purchased from Aldrich and distilled from CaH_2 prior to use.

Ethylene (99.99%) was purchased from AGA Gas, Inc. and used as received.

***N*,*O*-Dimethylhydroxylamine hydrochloride** was purchased from Aldrich and used as received.

***N*-Fluorobenzenesulfonimide** was purchased from Aldrich and used as received.

Hydrogen chloride (4.0 M in dioxane) was purchased from Aldrich and used as received.

Hydrogen gas was purchased from Airgas and used as received.

Iodine was purchased from Aldrich and used as received.

Lithium aluminum hydride was purchased from Aldrich and used as received.

Oxalyl chloride was purchased from Aldrich and distilled neat prior to use.

pH 7 buffer was generated by dissolving 1.20 g of sodium dihydrogen phosphate and 0.885 g disodium hydrogen phosphate in 1 L of deionized water.

Platinum(IV) oxide was purchased from Aldrich and used as received.

Potassium carbonate was purchased from Fisher and used as received.

Potassium hydroxide was purchased from Fisher and used as received.

Rhodium(II) acetate dimer (99%) was purchased from Strem and used as received.

Sodium azide was purchased from Aldrich and used as received.

Sodium bisulfite was purchased from Fisher and used as received.

Sodium cyanoborohydride was purchased from Aldrich and purified in the following way before use: $NaCNBH_3$ was dissolved in minimal THF and filtered; the mother liquor was then diluted with CH_2Cl_2 (4x the volume of THF) causing $NaCNBH_3$ to precipitate. The white solid was collected and dried in vacuo.

Sodium hydroxide was purchased from Fisher and used as received.

Sodium hydride (60% dispersion in mineral oil) was purchased from Strem and used as received.

Tetrakis(triphenylphosphine) palladium was purchased from Strem and used as received.

Trimethylsilylacetylene was purchased from TCI America and distilled from CaH_2 prior to use.

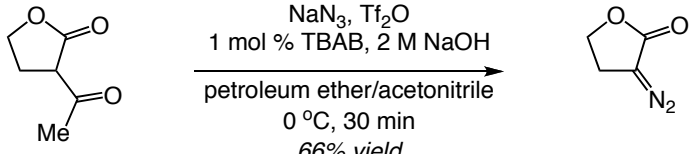
Tetrabutylammonium bromide was purchased from Aldrich and recrystallized in the following way prior to use: benzene (5 mL/g) at 80 ºC by adding hot hexanes (15 mL/g) and allowing to cool.

Triethylamine was purchased from Aldrich and distilled from CaH_2 prior to use.

Trifluoromethanesulfonyl anhydride was purchased from Aldrich and distilled from P_2O_5 prior to use.

Tryptamine was purchased from Aldrich and recrystallized from benzene prior to use.

Synthesis of Triene 2

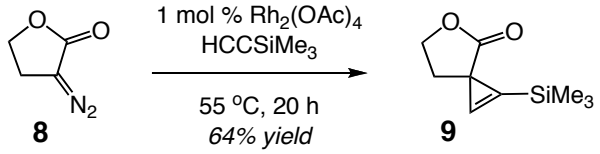


7 **8**

3-Diazodihydrofuran-2(3*H*)-one (8). The following is a simple modification of a procedure reported by Swain *et al*.[13] Sodium azide (4.83 g, 74.3 mmol, 4 equiv), sodium hydroxide (155 mL of 2 M in water, 310 mmol), tetrabutylammonium bromide (60.0 mg, 0.190 mmol, 0.01 equiv), and petroleum ether (80 mL) were combined in a 500-mL round-bottom flask with magnetic stir bar open to the air and allowed to cool to 0 °C. With vigorous magnetic stirring, Tf_2O (6.20 mL, 37.1 mmol, 2 equiv) was added dropwise from a syringe. After 10 min, a solution of 2-acetyl-butyrolactone **7** (2.00 mL, 18.6 mmol) in 70 mL of acetonitrile was poured into the vessel through a funnel, followed by an additional 10 mL of acetonitrile to complete the transfer. The initially colorless reaction mixture immediately turned yellow. After allowing to stir for 30 min at 0 °C, the mixture was diluted with ice water (50 mL) and chilled EtOAc (50 mL) and transferred to a separatory funnel. After phase separation and removal of the organic fraction, the aqueous layer was washed with 2 additional portions of cold EtOAc (100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The resulting orange-brown oily residue was loaded onto a short column of silica gel (4" long, 2" wide), and the product was quickly eluted with 1:1 petroleum ether:EtOAc. The progress of the chromatography was monitored visually, and the yellow-colored fractions were concentrated to afford 1.37 g (12.2 mmol, 66% yield) of product as a bright yellow crystalline solid. Though usually taken directly into the Rh-catalyzed cyclopropenation reaction, this

(13) Brown, R. C. D.; Bataille, C. J. R.; Bruton, G.; Hinks, J. D.; Swain, N. A. *J. Org. Chem.* **2001**, *66*, 6719-6728.

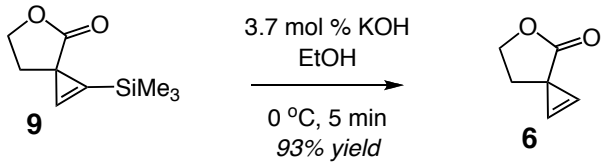
material could be stored as a crystalline solid for weeks at 4 °C with no detectable signs of decomposition. m.p. = 35-36 °C. IR (neat): 2989 (w), 2120 (s), 2100 (s), 1732 (s), 1460 (w), 1385 (s), 1246 (m), 1078 (m), 1018 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.40 (2H, t, *J* = 7.7 Hz), 3.37 (2H, t, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 65.4, 49.5, 23.2. HRMS (EI$^+$) $[M]^+$ calcd for $C_4H_4N_2O_2$: 112.0273, found: 112.0273.



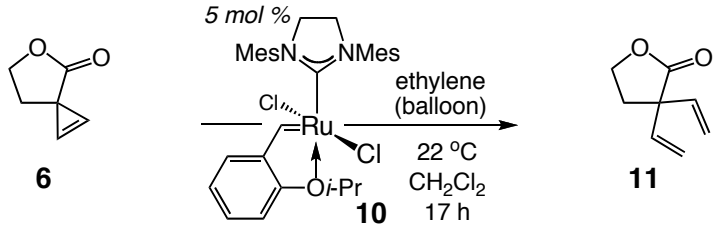
8 **9**

1-(Trimethylsilyl)-5-oxaspiro[2.4]hept-1-en-4-one (9). Rhodium(II) acetate dimer (54.0 mg, 0.122 mmol, 1 mol %) was placed in a 100-mL round-bottom flask, containing an oversized magnetic stir bar and suspended in 40 mL of trimethylsilylacetylene. The flask was equipped with a reflux condenser, submerged in an oil bath, and allowed to stir vigorously at 55 °C, at which point a gentle reflux began and some of the catalyst dissolved, giving the mixture a light green color. With gentle stirring in a separate flask, diazobutanolide **8** (1.37 g, 12.2 mmol) was dissolved in 20 mL of trimethylsilylacetylene, and the resulting bright yellow solution was taken up in a 20 mL gas-tight syringe fitted with a 12" needle. With a syringe pump, this solution was then added through the condenser *directly to the stream of refluxing solvent at the neck of the flask* over a 20 h period. Dropwise addition of the starting material from the headspace above the reaction mixture leads to comparatively higher and less constant concentrations (low dilution), resulting in increased side production of the olefinic dimer corresponding to **8**. Following the addition, small amounts of a fine white precipitate[14] were present and the mixture was allowed to cool to 22 °C. The reflux condenser was exchanged for a short path distillation head, connected to a cold trap (–78 °C), and the solvent was recovered for later reuse by simple stirring of the mixture under reduced pressure (~20 torr). Concentration affords a green, oil-solid residue that was redissolved in 10 mL of $CHCl_3$ and adsorbed onto silica gel by rotary evaporation. The resulting silica powder containing the product was poured onto the top of a silica gel column (5" long, 3" wide), packed in 3:1 petroleum ether:EtOAc with subsequent elution. The use of $KMnO_4$ stain for TLC visualization allows detection of a minor impurity just above the desired product. Concentration of the major fractions afforded 1.42 g (7.79 mmol, 64% yield) of product as a colorless oil, which could be solidified to an off-white solid upon cooling the neat sample to –78 °C under vacuum. m.p. = 38-39 °C. IR (neat): 3107 (w), 2960 (m), 2905 (m), 1766 (s), 1708 (s), 1454 (w), 1373 (m), 1252 (s), 1211 (s), 1172 (s), 1023 (s), 954 (w), 846 (s), 759 (m), 726 (w), 708 (w), 632 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (1H, t, *J* = 1.3 Hz), 4.42 (2H, dt, *J* = 8.1, 6.2 Hz), 2.16 (1H, dddd, *J* = 13.1, 8.5, 7.3, 1.2 Hz), 1.99 (1H, dddd, *J* = 14.7, 8.1, 7.0, 1.4 Hz), 0.25 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.3, 117.1, 115.1, 65.3, 30.5, 24.1, –1.3; HRMS (ES$^+$) $[M+Na]^+$ calcd for $C_9H_{14}O_2SiNa$: 205.0661, found: 205.0665.

(14) Presumably corresponding to undesired carbene dimerization.

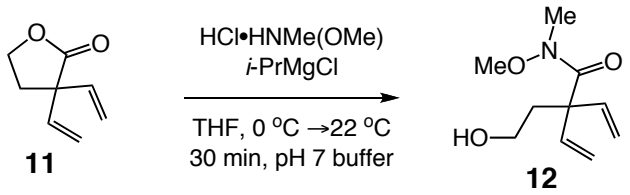


5-Oxaspiro[2.4]hept-1-en-4-one (6). Cyclopropene **9** (1.22 g, 6.69 mmol) was dissolved in 33 mL of anhydrous EtOH in a 50-mL round-bottom flask with magnetic stir bar and the solution was allowed to cool to 0 °C. A 0.25 M solution of KOH in anhydrous EtOH was freshly prepared in another vessel and then added (1.00 mL, 0.250 mmol, 0.037 equiv) dropwise, at which point the initially colorless solution turned light yellow in color. TLC analysis after 4 min showed the complete absence of starting material, and the solution was neutralized by the dropwise addition of 1.0 mL of aqueous HCl (0.25 M). If the reaction is stirred for longer than 5 min, *lactone opening* (from KOEt generated *in situ*) to the corresponding hydroxyester becomes prominent. The reaction mixture was diluted with EtOAc (10 mL) and poured into a separatory funnel containing 100 mL of water. The mixture was then washed three times with 100 mL portions of EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to provide 685 mg of product as a light bronze oil (6.22 mmol, 93% yield). Though not analytically pure, this material could be routinely taken into the Ru-catalyzed ring-opening metathesis reaction without complication. m.p. = 50-52 °C. IR (neat): 3152 (m), 3108 (s), 2919 (s), 2873 (m), 1766 (s), 1652 (s), 1484 (w), 1455 (m), 1377 (s), 1217 (s), 1182 (s), 1043 (m), 1021 (s), 959 (m), 872 (w), 808 (w), 719 (m), 634 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (2H, dt, J = 1.2, 0.4 Hz), 4.45 (2H, dt, J = 7.7, 0.5 Hz), 2.16 (2H, ttd, J = 7.7, 1.2, 0.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.5, 105.9, 65.4, 29.8, 23.7; HRMS (ES$^+$) $[M+H]^+$ Calcd for $C_6H_7O_2$: 111.0446, found: 111.0449.



3,3-Divinyldihydrofuran-2(3*H*)-one (11). Cyclopropene **6** (469 mg, 4.26 mmol) was transferred to a 100-mL round-bottom flask with magnetic stir bar with benzene, which was subsequently evaporated in vacuo to remove any adventitious water (azeotropic distillation). The oil was then dissolved in 43 mL of CH_2Cl_2. An ethylene (99.99% anhydrous) balloon, fitted with a stainless steel needle, and an exit needle were used to bubble the gas gently through the light yellow solution for 5 min. Recyclable ruthenium catalyst **10** (80.0 mg, 0.128 mmol, 3 mol %) was then added as a solid, causing the solution to turn dark green in color. The reaction was allowed to stir for 12 h at 22 °C under positive ethylene pressure from the balloon, at which time

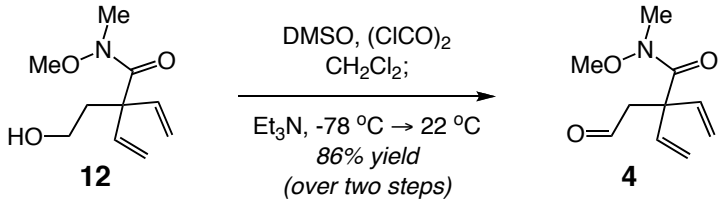
the solution was brown in color and translucent, and TLC analysis confirmed that starting material was still present. Thus, a second portion of the Ru catalyst (53.0 mg, 0.846, 2 mol %) was added and the solution allowed to stir under ethylene for an additioal 12 h. After complete consumption of **6**, the reaction mixture was reduced to half of its volume by rotary evaporation, and the product mixture was adsorbed onto silica gel with further concentration. Purification was achieved by silica gel column chromatography (8:2:1 petroleum ether:CH_2Cl_2:EtOAc). The product (412 mg, 2.98 mmol, 70% yield) was contaminated with trace (<5%) amounts of the material resulting from cross metathesis of 2-isopropoxystyrene with one of the vinyl alkenes. This heavier impurity along with any residual Ru impurities were easily removed by Kugelrohr distillation under vacuum with gentle heating (80 °C) to afford **11** as an analytically pure colorless oil. IR (neat): 3088 (w), 2984 (w), 2914 (w), 1770 (s), 1634 (w), 1484 (w), 1454 (w), 1413 (w), 1372 (m), 1172 (s), 1084 (w), 1027 (s), 997 (m), 928 (m), 844 (w), 754 (w), 714 (w), 662 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.88 (2H, dd, *J* = 17.4, 10.5 Hz), 5.30 (2H, d, *J* = 10.3 Hz), 5.23 (2H, d, *J* = 17.7 Hz), 4.28 (2H, t, *J* = 6.7 Hz), 2.38 (2H, t, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 136.6, 116.9, 65.5, 53.2, 33.8; HRMS (ES^+) $[M+Na]^+$ Calcd for $C_8H_{10}O_2Na$ (M+Na): 161.0578, found: 161.0581.



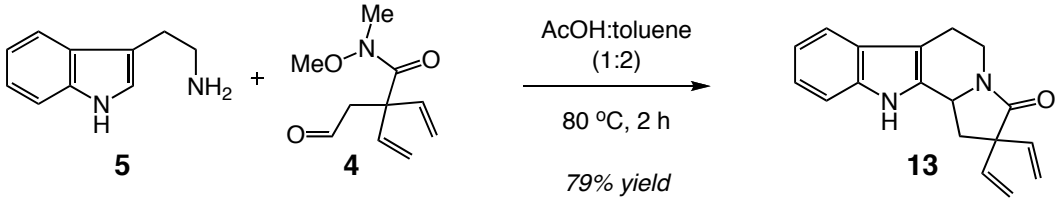
2-(2-Hydroxyethyl)-*N*-methoxy-*N*-methyl-2-vinylbut-3-enamide (12). A 100-mL round-bottom flask with magnetic stir bar was charged with **11** (612 mg, 4.43 mmol), THF (44 mL), and MeNHOMe•HCl (562 mg, 5.76 mmol, 1.3 equiv) and the resulting heterogeneous mixture was allowed to cool to 0 °C. *i*-Propylmagnesium chloride (6.22 mL, 1.85 M in THF, 11.5 mmol, 2.6 equiv, freshly prepared from Mg turnings and 2-chloropropane) was added dropwise to the reaction mixture over 5 min by syringe. The ice bath was removed and the mixture was allowed to warm to ambient temperature, during which time the solid dissolved to form a light yellow, homogeneous solution. After 25 min, no starting material remained according to TLC analysis. The solution was allowed to cool to 0 °C and the mixture quenched by the dropwise addition of pH 7 phosphate buffer (5 mL). The mixture was transferred to a separatory funnel and diluted further with 100 mL of pH 7 phosphate buffer. The mixture was washed three times with 100 mL portions of CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated to a light yellow oil that proved to be >98% pure as judged by ^{1}H NMR spectroscopy[15] (883 mg, 4.43 mmol, >98% yield). This material, sensitive to both acid and base, must be used directly since it undergoes cyclization to regenerate starting material upon storage. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12 (2H, dd, *J* = 17.6, 10.6 Hz), 5.24 (2H, d, *J* = 10.8 Hz), 5.10

(15) $CDCl_3$ for ^{1}H NMR analysis was passed through a plug of basic alumina just prior to use.

(2H, d, *J* = 17.7 Hz), 3.69 (2H, dd, *J* = 11.5, 5.7 Hz), 3.58 (3H, s), 3.17 (3H, s), 2.13 (2H, t, *J* = 6.14 Hz).

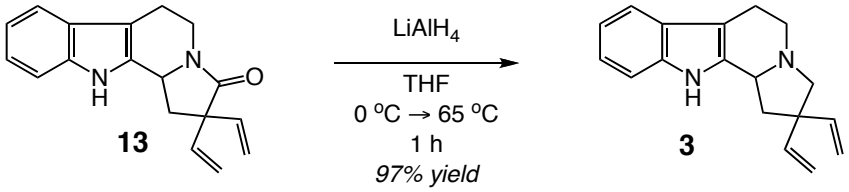


***N*-Methoxy-*N*-methyl-2-(2-oxoethyl)-2-vinylbut-3-enamide (4).** In a 100-mL round-bottom flask, DMSO (0.723 mL, 10.2 mmol, 2.3 equiv) was dissolved in 8 mL of CH_2Cl_2, and the resulting colorless solution was allowed to cool to –78 °C. Oxalyl chloride (8.86 mL, 1.0 M in CH_2Cl_2, 8.86 mmol, 2 equiv) was added down the wall of the flask (for precooling). Vigorous gas evolution was observed as the reaction mixture was allowed to stir for 5 min, and 1 mL of CH_2Cl_2 was used to rinse any residual oxalyl chloride off the inner wall of the flask. In a separate vessel, a solution of **12** (4.43 mmol) in CH_2Cl_2 (25 mL) was allowed to cool to –78 °C. The solution of **12** was then transferred to the reaction mixture through a cannula over 10 min causing cloudiness. After allowing to stir for 30 min at –78 °C, Et_3N (4.57 mL, 32.8 mmol, 7.4 equiv) was added from a syringe, at which point the reaction mixture again became homogeneous. The cooling bath was removed and the solution was allowed to *slowly* warm to 22 °C over 2 h. Precipitation was again observed at –30 °C and at –15 °C the mixture turned light pink in color. Once at 22 °C, 50 mL of pH 7 phosphate buffer was added; the solution was transferred to a separatory funnel, and the organic layer collected. The aqueous layer was washed with two additional 50 mL portions of CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to a red oil. Purification by silica gel column chromatography (1:1 petroleum ether:EtOAc, column 5" long, 3" wide) afforded 747 mg (3.79 mmol, 86% yield) of aldehyde **4** as a light yellow oil. IR (neat): 2949 (w), 1720 (s), 1650 (s), 1378 (m), 1777 (w), 998 (m), 928 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.67 (1H, t, *J* = 2.0 Hz), 6.22 (2H, dd, *J* = 17.7, 10.8 Hz), 5.29 (2H, d, *J* = 10.7 Hz), 5.14 (2H, d, *J* = 17.7 Hz), 3.60 (3H, s), 3.18 (3H, s), 2.85 (2H, d, *J* = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 173.2, 138.6, 115.7, 60.6, 53.3, 51.26, 34.1; HRMS (ES$^+$) $[M+Na]^+$ Calcd for $C_{10}H_{15}NO_3Na$: 220.0950, found: 220.0943.



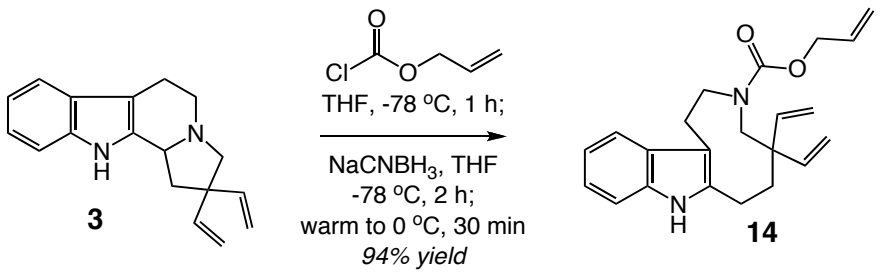
2,2-Divinyl-5,6,11,11b-tetrahydro-1*H*-indolizino[8,7-*b*]indol-3(2*H*)-one (13). A 250-mL round-bottom flask with magnetic stir bar was charged with aldehyde **4** (743 mg, 3.77 mmol), toluene (94 mL), tryptamine (913 mg, 5.70 mmol, 1.5 equiv), and glacial acetic acid (47 mL). The flask was equipped with a reflux condenser and the solution was allowed to warm to 80 °C

for 1 h, at which time an aliquot taken for ^{1}H NMR spectroscopy confirmed the absence of starting material. The reaction was allowed to cool to 22 °C and concentrated on a rotary evaporator. The resulting brown oily residue was redissolved in 10 mL of $CHCl_3$ and adsorbed onto silica gel under reduced pressure. The sample was then loaded onto a silica gel column (4.5" long, 3" wide) and the product was eluted with 1.5:1 petroleum ether:EtOAc. Though the product is UV active, PMA stain was useful for the visualization of close-running impurities. After concentration of the fractions containing product, the resulting material was flashed again on the same size column, this time with 8:1 CH_2Cl_2:EtOAc as eluant. This latter operation removes a minor UV active impurity that co-spots with **13** in the first solvent system yet runs behind it in the second. Concentration resulted in spontaneous precipitation of the product as a powdery white solid (831 mg, 2.99 mmol, 79% yield). m.p. = 155-156 °C. IR (neat): 3283 (br), 2858 (w), 1675 (s), 1438 (m), 1311 (w), 1012 (w), 930 (m), 740 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (1H, br s), 7.50 (1H, d, *J* = 7.7 Hz), 7.36 (1H, dt, *J* = 8.0, 1.1 Hz), 7.20 (1H, td, *J* = 8.2, 1.3 Hz), 7.14 (1H, br td, *J* = 7.8, 1.1 Hz), 6.07 (1H, dd, *J* = 17.5, 10.6 Hz), 5.90 (1H, dd, *J* = 17.5, 10.5 Hz), 5.31 (1H, dd, *J* = 4.3, 0.6 Hz), 5.27 (1H, dd, *J* = 2.8, 0.6 Hz), 5.22 (1H, dd, *J* = 10.6, 0.9 Hz), 5.14 (1H, dd, *J* = 17.5, 0.9 Hz), 4.86 (1H, ddt, *J* = 9.6, 6.1, 1.8 Hz), 4.56 (1H, ddd, *J* = 13.0, 4.5, 2.6 Hz), 3.07 (1H, ddd, *J* = 13.0, 8.9, 7.4 Hz), 2.87 (1H, dd, *J* = 4.6, 2.2 Hz), 2.85 (1H, br dd, *J* = 3.7, 2.0 Hz), 2.67 (1H, dd, *J* = 12.1, 6.1 Hz), 2.09 (1H, dd, *J* = 12.1, 9.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 139.0, 137.2, 136.5, 132.8, 127.0, 122.4, 120.0, 118.6, 116.2, 115.8, 111.2, 108.3, 56.1, 51.2, 37.9, 37.8, 21.3; HRMS (ES$^+$) $[M+Na]^+$ Calcd for $C_{18}H_{18}N_2ONa$: 301.1317, found: 301.1326.



2,2-Divinyl-2,3,5,6,11,11b-hexahydro-1*H*-indolizino[8,7-*b*]indole (3). Lithium aluminum hydride (401 mg, 10.6 mmol, 5 equiv) was weighed into a 100-mL round-bottom flask with a magnetic stir in an N_2-filled dry-box. The sample was removed from the box, suspended in 10 mL of THF, and allowed to cool to 0 °C. A solution of **13** (589 mg, 2.12 mmol) in THF (25 mL) was then transferred to the reaction mixture slowly through a cannula. Tetrahydrofuran (7 mL) was used to rinse the flask containing **13**. The flask was fitted with a condenser and the mixture was heated at reflux for 1 h, a point at which no starting material remained as judged by TLC analysis. The mixture was allowed to cool to –15 °C and quenched by the careful addition of saturated aqueous sodium potassium tartrate (5 mL). The contents of the flask were then transferred to a 250-mL Erlenmeyer with magnetic stir bar, diluted further with 50 mL of saturated aqueous sodium potassium tartrate, and allowed to stir vigorously for 1 h to dissolve all lithium salts. The biphasic mixture was then transferred to a separatory funnel and the organic layer collected. The aqueous layer was washed with 50 mL portions of CH_2Cl_2 (3x). The

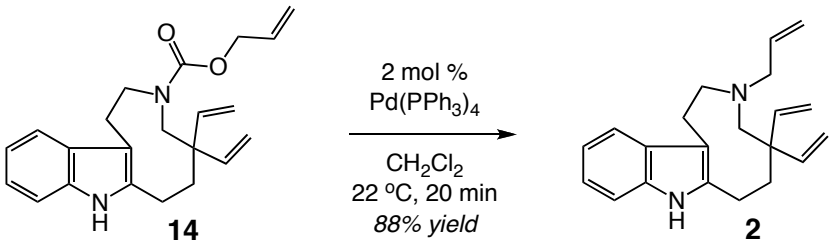
combined organic layers were washed with saturated aqueous NaCl (150 mL), dried over Na_2SO_4, and filtered. Solvent removal directly afforded the product in pure form as white crystalline solid (543 mg, 2.05 mmol, 97% yield). m.p. = 146-148 °C. IR (neat): 3406 (m), 3070 (m), 2931 (m), 1644 (w), 1450 (m), 1331 (w), 1010 (w), 918 (s), 740 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (1H, br s), 7.51 (1H, br d, *J* = 8.0 Hz), 7.32 (1H, br d, *J* = 7.4 Hz), 7.16 (1H, td, *J* = 8.4, 1.3 Hz), 7.11 (1H, td, *J* = 8.3, 1.2 Hz) 6.09 (1H, dd, *J* = 17.4, 10.7 Hz), 5.79 (1H, dd, *J* = 17.2, 10.7 Hz), 5.24 (1H, dd, *J* = 4.9, 1.0 Hz), 5.20 (1H, dd, *J* = 11.7, 1.0 Hz), 4.98 (1H, dd, *J* = 7.7, 1.2 Hz), 4.94 (1H, br s), 4.46 (1H, ddt, *J* = 8.0, 6.3, 1.9 Hz), 3.30 (1H, ddd, *J* = 13.4, 5.1, 2.0 Hz), 3.11 (1H, ddd, *J* = 13.4, 11.0, 4.4 Hz), 3.01 (1H, d, *J* = 8.9 Hz), 2.92 (1H, d, *J* = 7.9 Hz), 2.91 (1H, dddd, *J* = 15.6, 11.0, 5.1, 2.1 Hz), 2.63 (1H, ddt, *J* = 15.4, 4.1, 1.9 Hz), 2.51 (1H, ddd, *J* = 12.7, 7.9, 0.8 Hz), 1.89 (1H, dd, *J* = 12.7, 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 143.2, 136.2, 136.1, 127.5, 121.6, 119.6, 118.3, 113.4, 113.3, 110.8, 107.8, 60.1, 55.3, 50.6, 46.1, 41.7, 17.4; HRMS (ES$^+$) $[M+H]^+$ Calcd for $C_{18}H_{21}N_2$: 265.1705, found: 265.1713.



Allyl 5,5-divinyl-1,2,4,5,6,7-hexahydroazonino[5,4-*b*]indole-3(8*H*)-carboxylate (14). A flame-dried 250 mL round-bottom flask with stir bar was charged with tertiary amine **3** (543 mg, 2.05 mmol) and THF (100 mL) and allowed to cool to –78 °C. Allyl chloroformate (2.18 mL, 20.5 mmol, 10 equiv) was added dropwise from a syringe and the reaction mixture was allowed to stir for 1 h, during which time a cloudy white precipitate was observed. A colorless solution of $NaCNBH_3$ (902 mg, 14.4 mmol, 7 equiv) in THF (30 mL) was added through a cannula down the wall of the flask for precooling. Tetrahydrofuran (5 mL) was used to rinse the flask containing the reducing agent, which was similarly transferred, and then 2 mL of THF served to completely wash the inner walls of the reaction flask. The mixture was allowed to stir for 2 h at –78 °C and allowed to warm to 0 °C. TLC analysis showed that no starting material remained after 30 min. After transferring the mixture to a separatory funnel containing 100 mL of 1 M NaOH, the organic layer collected, and the aqueous layer was washed with two 100 mL portions of EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to a cloudy oil. Purification was achieved by passage through a short silica column (4" long, 2" wide) in 3:1 petroleum ether:EtOAc. Concentration of product fractions afforded 674 mg (1.92 mmol, 94% yield) of **14** as a white solid.[16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (1H, br s), 7.45 (1H, br d, *J* = 7.4 Hz), 7.28 (1H, br d, *J* = 7.9 Hz), 7.12 (1H, td, *J* = 7.1, 1.4 Hz), 7.08 (1H, td, *J* = 7.1, 1.2 Hz), 5.89 (1H, ddd, *J* = 22.5, 10.9, 5.5 Hz), 5.71 (2H, dd, *J* = 17.6, 11.0 Hz), 5.27 (1H, dd, *J*

(16) Due to the unstable nature of **14**, only ^{1}H NMR characterization data was obtained.

= 17.2, 1.4 Hz), 5.19 (1H, dd, *J* = 10.4, 1.4 Hz), 4.96 (2H, dd, *J* = 10.9, 1.0 Hz), 4.88 (1H, dd, *J* = 17.6, 1.0 Hz), 4.53 (2H, dt, *J* = 5.6, 1.4 Hz), 3.69 (2H, br t, *J* = 4.7 Hz), 3.44 (2H, s), 3.14 (2H, t, *J* = 5.2 Hz), 2.94 (2H, t, *J* = 6.5 Hz), 2.17 (2H, t, *J* = 6.6 Hz).

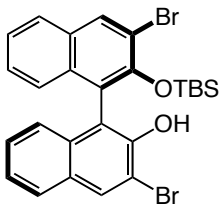


3-Allyl-5,5-divinyl-1,2,3,4,5,6,7,8-octahydroazonino[5,4-*b*]indole (2). A solution of allylcarbamate **14** (674 mg, 1.92 mmol) in CH_2Cl_2 (7.7 mL) was added in a 50-mL round-bottom flask with magnetic stir bar. Tetrakis(triphenylphosphine)palladium(0) (44.4 mg, 0.0384 mmol, 2 mol %) was weighed and added directly to the solution as a solid, causing the solution to turn bright yellow and initiating the process of gas (CO_2) evolution (handling and addition of the catalyst was done in an N_2-filled dry-box). The solution was allowed to stir for 20 min at 22 °C, a point at which TLC analysis indicated that the reaction was complete. Silica gel was then added to consume the volume of solvent present in the reaction, and the product was adsorbed onto the silica by careful concentration. After loading the sample onto a column of silica gel (4" long, 2" wide) and eluting with 8:1 petroleum ether:Et_2O washed with 2% v/v concentrated aqueous NH_4OH, the product was isolated in pure form as colorless, thick, glassy oil (515 mg, 1.68 mmol, 88% yield). IR (neat): 3403 (s), 3080 (w), 2931 (m), 2800 (m), 1637 (w), 1464 (w), 1339 (w), 1003 (m), 916 (s), 742 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (1H, br s), 7.45 (1H, br d, *J* = 7.3 Hz), 7.28 (1H, ddd, *J* = 7.5, 1.6, 0.7 Hz), 7.10 (1H, td, *J* = 7.1, 1.5 Hz), 7.06 (1H, td, *J* = 6.9, 1.3 Hz) 5.77 (2H, dd, *J* = 17.8, 10.8 Hz), 5.61 (1H, dddd, *J* = 16.3, 10.4, 5.8, 5.8 Hz), 5.05 (2H, dd, *J* = 10.8, 1.3 Hz), 4.94 (2H, dd, *J* = 17.8, 1.3 Hz), 4.90-4.88 (1H, m), 4.86 (1H, dddd, *J* = 12.5, 2.2, 1.5, 1.5 Hz), 3.06 (2H, dt, *J* = 5.9, 1.5 Hz), 2.97 (2H, dd, *J* = 4.9, 4.9 Hz), 2.78 (2H, dd, *J* = 5.7, 5.7 Hz), 2.64-2.61 (4H, m) 2.19 (2H, dd, *J* = 7.0, 3.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.0, 137.3, 136.1, 135.1, 129.0, 120.7, 119.1, 117.7, 116.0, 113.1, 110.3, 109.8, 61.2, 57.0, 53.5, 48.3, 32.4, 24.2, 22.3; HRMS (ES^+) $[M+H]^+$ Calcd for $C_{22}H_{27}N_2$: 307.2174, found: 307.2167.

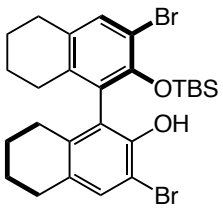
Synthesis of Chiral Phenol Ligands

All ligands were prepared from enantiomerically pure (*R*)-binol. Chiral phenols **35**, **A** and **B** were prepared according to known procedures.[17]

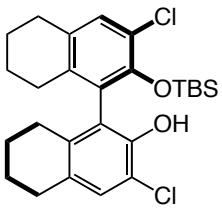
(17) Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature*; doi:10.1038/nature07594



35

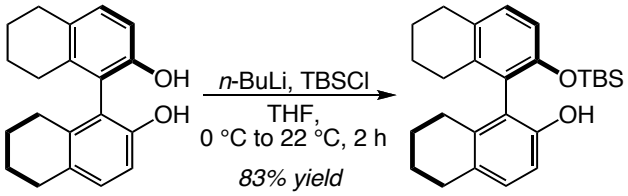


A



B

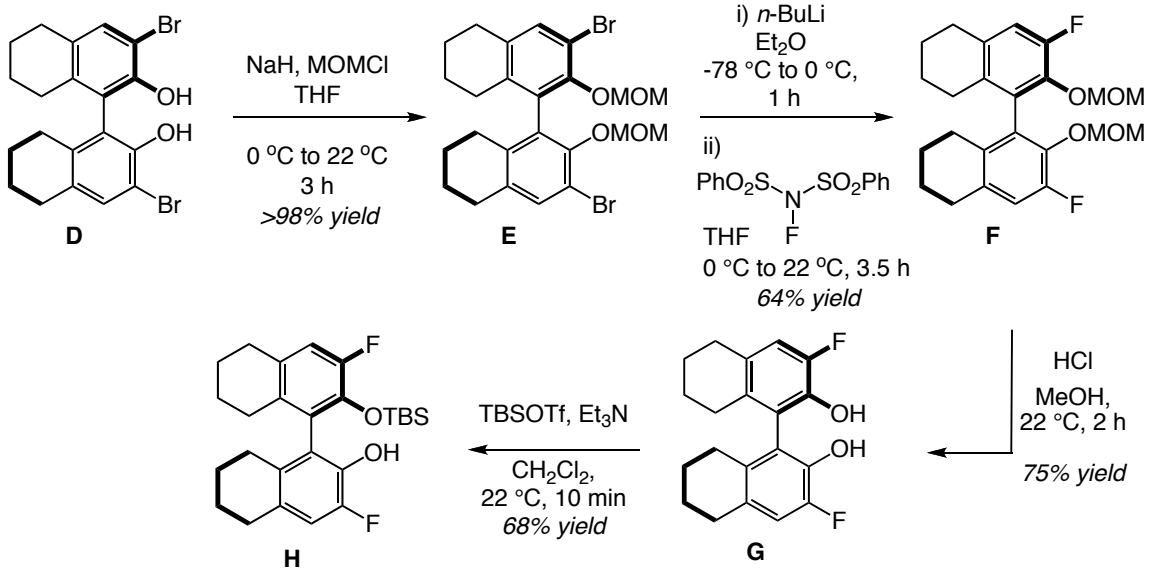
(*R*)-5,5',6,6',7,7',8,8'-Octahydro-3,3'-1,1'-binaphthyl-2,2'-diol and (*R*)-5,5',6,6',7,7',8,8'-octahydro-3,3'-dibromo-1,1'-binaphthyl-2,2'-diol (**D**) were synthesized according to previously reported procedures.[18]



C

(*R*)-2'-(*tert*-Butyldimethylsilyloxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2-ol (C). A 50-mL round-bottom flask with magnetic stir bar was charged with (*R*)-5,5',6,6',7,7',8,8'-octahydro-3,3'-1,1'-binaphthyl-2,2'-diol (1.00 g, 3.40 mmol) and THF (5.8 mL), and the mixture was allowed to cool to 0 °C (ice bath) while stirring. *n*-Butyllithium (2.32 mL, 1.50 M in hexanes, 3.50 mmol) was added dropwise by syringe, causing a white precipitate to form. After 15 min, a solution of TBSCl (522 mg, 3.50 mmol) in THF (5.5 mL) was added to the mixture by cannula and the mixture was allowed to warm to 22 °C. After 2 h, the mixture became clear and colorless and the reaction was quenched through addition of a saturated aqueous solution of $NaHCO_3$ (20 mL). The layers were partitioned and the aqueous layer washed with EtOAc (3 x 20 mL). The combined organic layers were washed with a saturated aqueous solution of NaCl (75 mL), dried over $MgSO_4$, filtered, and concentrated. The resulting yellow oil was purified by silica gel chromatography (15:1 petroleum ether:Et_2O) to yield **C** (1.16 g, 2.80 mmol, 83.0% yield) as a colorless, viscous oil. IR (neat) 3539 (w), 3510 (w), 3446 (br), 2928 (s), 2883 (m), 2857 (s), 1591 (m), 1472 (s), 1390 (w), 1361 (w), 1329 (w), 1285 (s), 1255 (s), 1213 (w), 1188 (m), 1174 (m), 1156 (m), 1074 (w), 1061 (w), 1006 (m), 980 (m), 967 (m), 939 (w), 870 (w), 854 (s), 836 (s), 809 (m), 779 (m), 692 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *d* 7.03 (1H, d, *J* = 8.0 Hz), 6.96 (1H, d, *J* = 8.4 Hz), 6.75 (1H, d, *J* = 8.0 Hz), 6.73 (1H, d, *J* = 8.0 Hz), 4.44 (1H, s), 2.82-2.68 (4H, m), 2.43-2.33 (2H, m), 2.28-2.10 (2H, m), 1.81-1.62 (8H, m), 0.68 (9H, s), 0.14 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) *d* 151.5, 150.3, 138.2, 136.3, 130.8, 130.2, 129.2, 129.1, 125.0, 123.3, 116.7, 112.2, 29.5, 29.5, 27.4, 27.4, 25.2, 23.4, 23.3, 23.2, 23.1, 17.8, –4.1, –4.8; HRMS (ESI^+) $[M+H]^+$ calcd for $C_{26}H_{37}O_2Si$: 409.2563, found: 409.2551; $[\alpha]_D^{20}$ +60.5 (*c* = 1.33, $CHCl_3$).

(18) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930–1946.



(*R*)-3,3'-Difluoro-2'-(*tert*-butyldimethylsilyloxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2-ol (H). A 25-mL round-bottom flask with magnetic stir bar was charged with NaH (60% dispersion in mineral oil, 354 mg, 8.80 mmol) and THF (5 mL). The resulting suspension was allowed to cool to 0 °C (ice bath) while stirring. A solution of diol **D** (1.00 g, 2.20 mmol) in THF (4.5 mL) was added to the NaH mixture by cannula; the vial containing the diol was rinsed with THF (0.6 mL), which was similarly transferred to the mixture. After 1 h, chloromethyl methyl ether (370 μL, 4.90 mmol) was added dropwise by syringe, and the solution was allowed to warm to 22 °C. After 3 h, the reaction was quenched by the addition of H_2O (10 mL). The layers were partitioned and the aqueous layer washed with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The resulting yellow oil was purified by flash silica gel column chromatography (15:1 petroleum ether:Et_2O) to afford **E** (1.19 g, 2.20 mmol, >98% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (2H, br s), 4.93 (2H, d, J_{AB} = 6.0 Hz), 4.84 (2H, d, J_{AB} = 6.0 Hz), 2.85 (6H, s), 2.79-2.72 (4H, m), 2.40 (2H, ddd, J = 17.2, 6.4, 6.4 Hz), 2.11 (2H, ddd, J = 17.2, 6.0, 6.0 Hz), 1.78-1.62 (8H, m).

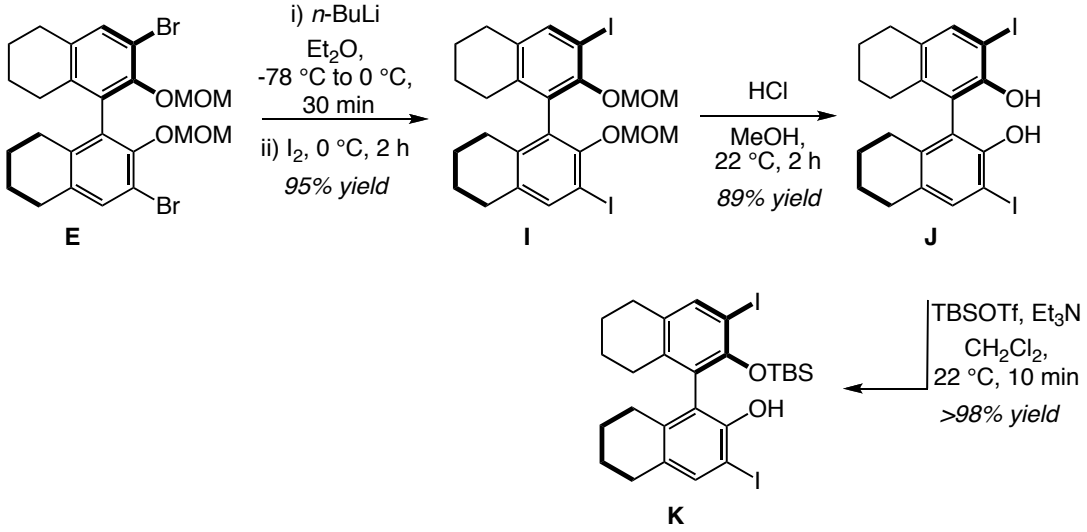
A 100-mL round-bottom flask with magnetic stir bar was charged with bis(methoxymethyl ether) **E** (1.96 g, 3.60 mmol) and Et_2O (16 mL). The mixture was allowed to cool to –78 °C (dry ice/acetone bath), after which *n*-butyl lithium (6.90 mL, 1.57 M in hexanes, 10.9 mmol) was added dropwise by syringe. The resulting mixture was allowed to warm to 0 °C (ice bath) and stir for 1 h, over which time a white precipitate formed. A solution of *N*-fluorobenzenesulfonimide (3.43 g, 10.9 mmol) in THF (15 mL) was added to the mixture by cannula; the vial containing *N*-fluorobenzenesulfonimide was rinsed with THF (1 mL), which was similarly transferred. The mixture was allowed to warm to 22 °C. Precipitates formed over the course of the reaction. After 3.5 h, the reaction was quenched by addition of H_2O (40 mL) and the precipitates dissolved completely. The biphasic mixture was washed with Et_2O (3 x 50

mL). The combined organic layers were washed with a saturated aqueous solution of NaCl (100 mL), dried over $MgSO_4$, filtered, and concentrated. The resulting yellow oil was purified by flash silica gel column chromatography (dry load method, 20:1 petroleum ether:Et_2O) to furnish **F** as viscous yellow oil (971 mg (ca.), 2.30 mmol, 64% yield; contaminated with ~5% **E**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84 (2H, d, J_{HCCF} = 11.6 Hz), 4.98 (2H, dd, J_{AB} = 6.0, J_{HF} = 0.8 Hz), 4.83 (2H, d, J_{AB} = 6.0 Hz), 3.05 (6H, s), 2.78-2.72 (4H, m), 2.35 (2H, ddd, J = 16.8, 7.2, 7.2 Hz), 2.11 (2H, ddd, J = 16.8, 6.8, 6.8 Hz), 1.78-1.62 (8H, m).

Under an atmosphere of air, a 25-mL round-bottom flask with magnetic stir bar was charged with bis(methoxymethyl ether) **F** (971 mg, 2.30 mmol; contaminated with ~5% **E**) and MeOH (7 mL). Hydrogen chloride (1.20 mL, 4.00 M in dioxane, 4.60 mmol) was added dropwise by syringe and the mixture was allowed to stir. After 40 min, the mixture was diluted with H_2O (10 mL) and was subsequently washed with EtOAc (3 x 20 mL). The combined organic layers were washed with a saturated aqueous solution of NaCl (2 x 60 mL), dried over $MgSO_4$, filtered, and concentrated. The resulting yellow oil was purified by silica gel column chromatography (gravity elution, 9:1 CH_2Cl_2:petroleum ether to 100% CH_2Cl_2) to afford diol **G** (567 mg, 1.70 mmol, 75% yield) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (2H, d, J_{HCCF} = 10.8 Hz), 4.65 (2H, d, J_{HF} = 3.2 Hz), 2.74 (4H, dd, J = 5.6, 5.6 Hz), 2.29 (2H, ddd, J = 16.8, 6.8, 6.8 Hz), 2.09 (2H, ddd, J = 16.8, 6.4, 6.4 Hz), 1.78-1.60 (8H, m).

A 50-mL round-bottom flask containing a magnetic stir bar was charged with diol **G** (242 mg, 0.751 mmol), CH_2Cl_2 (15 mL), and Et_3N (136 μL, 0.976 mmol). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (224 μL, 0.976 mmol) was added by syringe in one portion and the mixture was allowed to stir for 10 min. At this time, the mixture was diluted with a saturated aqueous solution of $NaHCO_3$ (15 mL) and the layers were partitioned. The aqueous layer was washed with CH_2Cl_2 (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to furnish a viscous yellow oil, which was subsequently purified by flash silica gel column chromatography (15:1 petroleum ether: Et_2O) to deliver **H** (228 mg, 0.513 mmol, 68% yield) as white solid. m.p. = 104–106 °C; IR (neat): 3589 (w), 3538 (w), 2928 (s), 2884 (m), 2857 (s), 1608 (w), 1586 (w), 1471 (s), 1436 (m), 1342 (m), 1315 (s), 1283 (m), 1254 (s), 1227 (s), 1196 (m), 1175 (m), 1104 (m), 1072 (w), 1013 (w), 970 (s), 940 (s), 904 (m), 865 (s), 839 (s), 826 (s), 813 (s), 783 (w), 736 (w), 684 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85 (1H, d, J_{HCCF} = 11.6 Hz), 6.80 (1H, d, J_{HCCF} = 11.2 Hz), 4.59 (1H, d, J_{HF} = 2.8 Hz), 2.80-2.63 (4H, m), 2.39-2.25 (2H, m), 2.18-2.01 (2H, m), 1.83-1.54 (8H, m), 0.65 (9H, s), 0.12 (3H, d, J_{HF} = 3.2 Hz), -0.30 (3H, d, J_{HF} = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$)[19]: δ 153.1, 150.7, 150.6, 148.2, 138.7, 138.6, 138.6, 138.4, 132.3, 132.2, 131.7, 131.7, 131.0, 131.0, 129.7, 129.6, 127.4, 125.0, 116.5, 116.3, 115.1, 114.9, 29.5, 29.5, 26.9, 26.8, 25.3, 23.2, 23.1, 23.0, 22.9, 18.1, -4.4, -4.5, -5.0, -5.0; HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{26}H_{35}F_2O_2Si$: 445.2374, found: 445.2383; $[\alpha]_D^{20}$ +60.8 (c = 0.914, $CHCl_3$).

(19) Ten of the 12 aromatic carbons, as well as the two methyl groups of the TBS ether, appear as doublets due to splitting from ^{19}F; however, because of the proximity of peaks in the spectrum, the doublets and their coupling constants could not be assigned with certainty. Therefore, all peaks are reported as individual singlets.



(*R*)-3,3'-Diiodo-2'-(*tert*-butyldimethylsilyloxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2-ol (K). A 50-mL round bottom flask with magnetic stir bar was charged with bis(methoxymethyl ether) **E** (562 mg, 1.04 mmol) and Et_2O (21 mL). The mixture was allowed to cool to –78 °C (dry ice/acetone bath), after which *n*-butyl lithium (2.24 mL, 1.39 M in hexanes, 3.12 mmol) was added dropwise by syringe. The resulting mixture was allowed to warm to 0 °C (ice bath) and stir for 30 min, over which time a white precipitate formed. A solution of iodine (924 mg, 3.64 mmol) in Et_2O (4 mL) was added to the mixture by cannula; the vial containing iodine was rinsed with Et_2O (1 mL), which was similarly transferred. After 2 h, the reaction was quenched by the addition of a saturated aqueous solution of $Na_2S_2O_3$ (10 mL); the biphasic mixture was allowed to stir until the orange color of iodine had disappeared. The layers were then partitioned and the aqueous layer washed with EtOAc (3 x 5 mL). The combined organic layers were washed with a saturated aqueous solution of NaCl (50 mL), dried over $MgSO_4$, filtered, and concentrated. The resulting brown oil was purified by flash silica gel column chromatography (30:1 petroleum ether:Et_2O) to deliver **I** (625 mg, 0.985 mmol, 95% yield) as colorless foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, s), 4.87 (2H, d, J_{AB} = 6.0 Hz), 4.83 (2H, d, J_{AB} = 6.0 Hz), 2.83 (6H, s), 2.78-2.70 (4H, m), 2.40 (2H, ddd, J = 17.6, 6.4, 6.4 Hz), 2.11 (2H, ddd, J = 17.2, 6.0, 6.0 Hz), 1.76-1.60 (8H, m).

A 50-mL round-bottom flask with magnetic stir bar was charged with bis(methoxymethyl ether) **I** (625 mg, 0.985 mmol) and MeOH (5 mL). Hydrogen chloride (490 μL, 4.0 M in dioxane, 2.0 mmol) was added dropwise by syringe and the mixture was allowed to stir. After 2 h, the mixture was diluted with H_2O (20 mL) and the desired product precipitated from solution. The mixture was filtered and the solid dried *in vacuo* to afford diol **J** (478 mg, 0.875 mmol, 89% yield) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (2H, s), 4.96 (2H, s), 2.73 (4H, dd, J = 5.6, 5.6 Hz), 2.27 (2H, ddd, J = 17.2, 6.4, 6.4 Hz), 2.09 (2H, ddd, J = 17.2, 6.0, 6.0 Hz), 1.77-1.58 (8H, m).

Protection of diol **J** as the *tert*-butyldimethylsilyl ether was accomplished through the procedure used in the synthesis of alcohol **G**. The resulting yellow foam was purified by flash silica gel column chromatography (15:1 petroleum ether: Et_2O) to provide **K** (572 mg, 0.866 mmol, >98% yield) as white solid. m.p. = 66-74 °C; IR (neat): 3522 (w), 3489 (w), 2925 (m), 2854 (m), 1570 (w), 1438 (s), 1420 (m), 1390 (m), 1356 (w), 1339 (w), 1313 (m), 1251 (s), 1214 (m), 1177 (m), 1156 (m), 1074 (m), 1016 (m), 979 (m), 966 (m), 944 (w), 911 (w), 860 (m), 836 (s), 780 (s), 728 (m), 697 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (1H, s), 7.44 (1H, s), 5.04 (1H, s), 2.78-2.66 (4H, m), 2.45-2.30 (2H, m), 2.05-1.92 (2H, m), 1.78-1.53 (8H, m), 0.89 (9H, s), 0.14 (3H, s), -0.36 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): 150.9, 149.7, 141.0, 138.2, 138.0, 137.8, 133.6, 132.3, 126.8, 124.0, 87.8, 81.4, 29.2, 29.1, 27.3, 27.0, 26.6, 23.1, 23.0, 22.9, 22.8, 18.7, -1.6, -3.5; HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{26}H_{35}I_2O_2Si$: 661.0496, found: 661.0468; $[\alpha]_D^{20}$ +22.1 (c = 0.830, $CHCl_3$).

Stereoselective *in situ*-Generation of Monoalkoxide Complexes

General Procedure: A 4-mL vial with magnetic stir bar was charged with **33b** (5.4 mg, 9.1 μmol), **35** (5.1 mg, 9.1 μmol), and C_6D_6 (500 μL) in an N_2-filled glovebox. The vial was tightly capped and the mixture was allowed to stir for 1 h, after which it was transferred to a screw-cap NMR tube by pipet. The NMR tube was tightly capped and sealed with Teflon tape. For *in situ*-generated complexes, only the diagnostic signals of the α-carbon of the *syn*-alkylidenes are reported. ^{1}H NMR (400 MHz, C_6D_6): δ 12.92 (1H, s), 11.58 (1H, s); d.r. = 1:7 (entry 2, Table 1).[20] NMR data are summarized in Table 1.

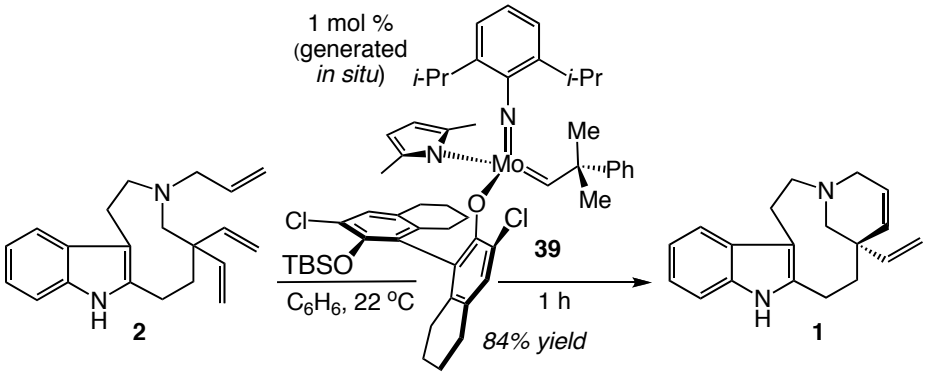
(20) The diastereomeric ratio (dr) was measured by 400 MHz ^{1}H NMR analysis and reflects the ratio of *syn*-alkylidene isomers. In certain cases, *anti*-alkylidene isomers can also be detected, usually representing <5% of the mixture.

Table 1. Diastereoselective Substitution to Furnish Stereogenic-at-Mo Complexes

entry	Complex	Chemical Shift (ppm)	dr[a]
1	**36a**	12.38, 11.73	1:19
2	**36b**	12.92, 11.58	1:7
3	**37a**	12.86, 12.84	>20:1
4	**37b**	12.90, 12.42	1:7
5	**38**	12.35, 12.25	1:2.5
6	**39**	12.62[c], 12.30	1:6
7	**40**	13.06, 12.54	1:5
8	**41**[b]	12.70, 12.47	1:3

[a] The diastereomeric ratio (dr) was measured by 400 MHz ^{1}H NMR analysis and reflects the ratio of *syn*-alkylidene isomers. In certain cases, *anti*-alkylidene isomers can also be detected, usually representing <5% of the mixture. [b] Formed at 60 °C for 2 h. [c] doublet J_{HCMoF} = 4.4 Hz

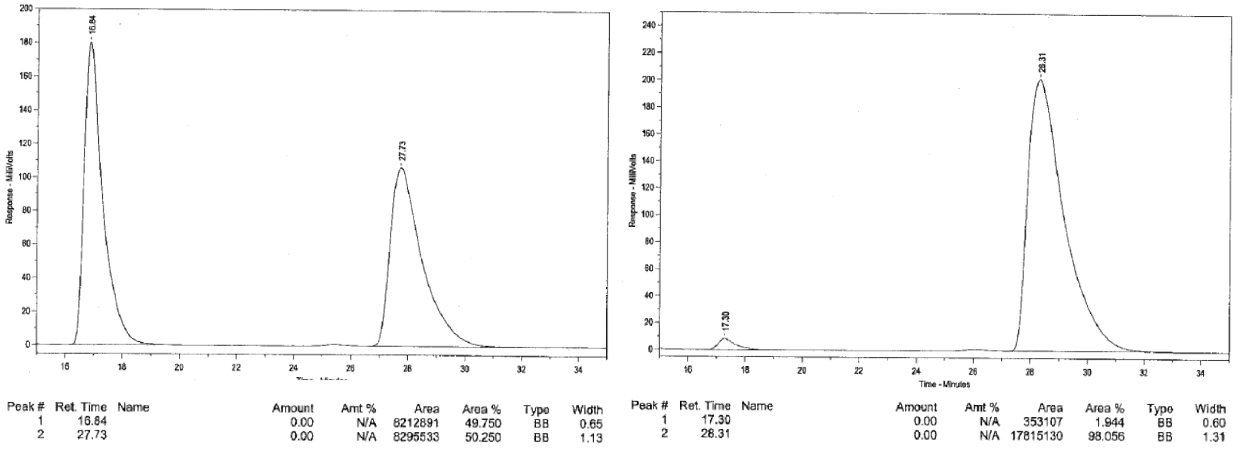
Representative Procedure for *in situ*-Generation of Catalyst 37b: In an N_2-filled glovebox, a 4-mL vial containing a magnetic stir bar was charged with **33b** (10.0 mg, 16.9 μmol), **A** (9.40 mg, 16.9 μmol), and C_6H_6 (845 μL, 0.02 M); the mixture became brilliantly orange. The vial was capped and the solution was allowed to stir for 1 h at 22 °C. The catalyst solution was transferred to the reaction mixture by a syringe (dried at 65 °C under vacuum).



General Procedure for Catalytic Enantioselective Olefin Metathesis with *in situ*-Generated Catalyst.

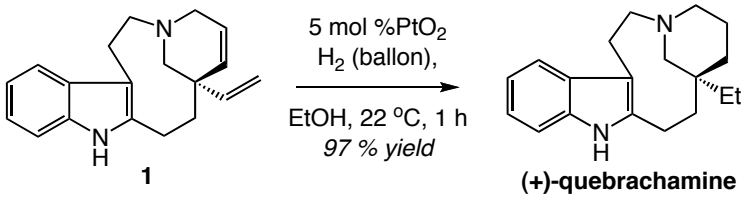
Tetradehydro-(+)-quebrachamine (1). In an N_2-filled glovebox, a 4-mL vial equipped with a magnetic stir bar was charged with triene **2** (10.1 mg, 0.0330 mmol) and C_6H_6 (50 μL). The solution was treated with 1 mol % of *in situ*-generated chiral complex **39** (16.5 μL, 0.02 M, 0.331 μmol; final substrate concentration = 0.5 M) and allowed to stir for 1 h. The reaction was then quenched by exposure to air and concentrated *in vacuo* (% conversion determined by 400 MHz ^{1}H NMR analysis). The resulting brown oil was purified by silica gel chromatography (8:1 petroleum ether:Et_2O washed with 2% v/v concentrated aqueous NH_4OH) to afford **1** (7.70 mg,

0.0277 mmol, 84% yield) as a colorless oil. IR (Neat): 3400 (s), 3023 (w), 2912 (s), 2846 (m), 2783 (m), 2727 (m), 1632 (m), 1462 (s), 1435 (m), 1333 (m), 1299 (m), 1164 (m), 999 (m), 911 (m), 740 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (1H, br s), 7.51–7.47 (1H, m), 7.31–7.28 (1H, m), 7.13–7.05 (2H, m), 5.90 (1H, ddd, J = 9.9, 4.8, 1.5 Hz), 5.61 (1H, dd, J_{ABX} = 17.5, 10.5 Hz), 5.44 (1H, ddd, J = 9.9, 4.0, 2.0 Hz), 4.92 (1H, dd, J = 6.8, 1.3 Hz), 4.88 (1H, s), 3.73 (1H, ddd, J_{ABX} = 14.2, 10.5, 1.5 Hz), 3.32–3.25 (1H, m), 3.13-3.07 (1H, m), 2.88–2.82 (1H, m), 2.80–2.64 (4H, m), 2.42-2.33 (2H, m), 2.01-1.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8, 139.3, 135.5, 132.2, 128.9, 127.5, 120.9, 119.0, 118.0, 112.0, 110.1, 110.1, 59.3, 54.1, 52.0, 43.6, 40.1, 25.5, 23.0; HRMS (ESI^+) $[M+H]^+$ calcd for $C_{19}H_{23}N_2$: 279.1861, found: 279.1854; $[\alpha]_D^{20}$ +99.2 (c = 0.513, $CHCl_3$) for a sample of 96% ee. (98:2 er). The enantiomeric purity of **1** (96% ee; 98:2 er) was determined by HPLC analysis (Chiralpak OD, 95:5 hexanes:*i*-PrOH, 1.0 mL/min, 254 nm) in comparison with authentic racemic material. The absolute stereochemistry was determined through subsequent catalytic hydrogenation to obtain (+)-quebrachamine (see below).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	16.84		0.00	N/A	8212891	49.750	BB	0.65
2	27.73		0.00	N/A	8295533	50.250	BB	1.13

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	17.30		0.00	N/A	353107	1.944	BB	0.60
2	28.31		0.00	N/A	17815130	98.056	BB	1.31



(+)-Quebrachamine. A 4-mL vial containing a magnetic stir bar was charged with diene **2** (5.40 mg, 19.4 μmol) and 5 mol % PtO_2 (0.220 mg, 194 μL, 0.1 M heterogeneous dispersion in EtOH). A septum was used to cap the vial and the stirring suspension was treated with 1 atm H_2, administered through a balloon. After a brief purge to ensure exchange of the atmosphere with H_2, the mixture was allowed to stir for 1 h. At this time, the mixture was pushed through a plug of silica gel and eluted with CH_2Cl_2 washed with 2% v/v concentrated aqueous NH_4OH (10 mL). Removal of the volatiles furnished a colorless oil that was purified by flash silica gel column chromatography (CH_2Cl_2 washed with 2% v/v concentrated aqueous NH_4OH) to afford (+)-quebrachamine (5.30 mg, 18.8 μmol, 97.0% yield) as a white solid. m.p. = 143–144 °C [Lit.[21]

147–149 ºC]; IR (Neat): 3403 (s), 2957 (m), 2921 (s), 2850 (s), 2784 (m), 2730 (m), 1462 (s), 1440 (m), 1348 (w), 1131 (w), 741 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (1H, br s), 7.49-7.47 (1H, m), 7.29-7.26 (1H, m), 7.09 (1H, td, J = 7.2, 1.6 Hz), 7.06 (1H, td, J = 7.2, 1.6 Hz), 3.25 (1H, bs d, J = 11.6 Hz), 2.94 (1H, ddd, J_{ABX} = 14.8, 11.6, 4.8 Hz), 2.84 (1H, ddd, J_{ABX} = 14.8, 4.4, 2.8 Hz), 2.74 (1H, ddd, J_{ABX} = 15.6, 10.4, 2.0 Hz), 2.67 (1H, ddd, J_{ABX} = 15.2, 7.2, 2.0 Hz), 2.48-2.43 (1H, m), 2.41 (1H, dd, J = 4.4, 2.8 Hz), 2.33 (1H, td, J = 11.6, 4.4 Hz), 2.25 (1H, td, J = 11.6, 2.8 Hz), 1.92 (1H, ddd, J = 14.0, 6.8, 2.0 Hz), 1.65-1.53 (2H, m), 1.50 (1H, d, J = 11.6 Hz), 1.33-1.08 (5H, m), 0.85 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 135.0, 129.1, 120.3, 118.8, 117.5, 110.1, 108.9, 56.9, 55.2, 53.4, 37.3, 34.9, 33.6, 32.2, 22.8, 22.6, 22.1, 7.9; HRMS (ESI^+) $[M+H]^+$ calcd for $C_{19}H_{27}N_2$: 283.2174, found: 283.2183; $[\alpha]_D^{20}$ +103 (c = 0.353, $CHCl_3$) for a sample of 96% ee (98:2 er) [Lit.[21] $[\alpha]_D^{20}$ +117 (c = 0.180, $CHCl_3$)].

(21) (a) Walls, F.; Collera, O.; Sandoval, A. L. *Tetrahedron* **1958**, *2*, 173-182. (b) Node, M.; Nagasawa, H.; Fuji, K. *J. Am. Chem. Soc.* **1987**, *109*, 7901–7903. (c) Temme, O.; Taj, S-A.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 6007–6015.