

A General and Highly Selective Chelate-Controlled Intermolecular Oxidative Heck Reaction

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General Information: All commercially obtained reagents for the Heck arylation reaction were used as received: 1,4-benzoquinone and 2,6-dimethylbenzoquinone (Sigma-Aldrich); 5-bromoindole (Frontier Scientific Inc.); 4-methoxycarbonylphenylboronic acid, 2,5-difluorophenylboronic acid (Frontier Scientific Inc.); phenylboronic acid and 2-bromophenylboronic acid (Sigma-Aldrich); 1,2-Bis(phenylsulfinyl)ethane palladium(II) acetate "Catalyst **1**" (Sigma-Aldrich). Catalyst **1** was stored in a glove box under an argon atmosphere and weighed out in air prior to use. Solvents dioxane, tetrahydrofuran (THF), diethyl ether (Et₂O), and methylene chloride (CH₂Cl₂) were purified prior to use by passage through a bed of activated alumina (Glass Contour, Laguna Beach, California). Anhydrous N,N-dimethylformamide (DMF) (Sure Seal) was obtained from Sigma-Aldrich and used as received. All Heck arylation reactions were run under air with no precautions taken to exclude moisture. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV and potassium permanganate staining. Flash column chromatography was performed as described by Still using EM reagent silica gel 60 (230-240 mesh).¹ ¹H NMR spectra were recorded on a Varian Unity-400 (400 MHz) or Varian Unity-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, b = broad, ap = apparent; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C NMR spectra were recorded on a Varian Unity-400 (100 MHz) or Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.23 ppm). ¹⁹F NMR spectra were recorded on a Varian Unity-400 (376 MHz) or Varian-500 (470 MHz) spectrometer and are reported in ppm using a 1% C₆F₆/CDCl₃ standard referenced to -164.3 ppm. Regioselectivity of the Heck addition was determined by NMR analysis of the crude mixture. IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX and are reported in frequency of absorption (cm⁻¹). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Optical rotations were obtained using a JAS.CO DIP-370 digital polarimeter and a 3.5 x 100 mm cell.

General Procedure for Heck Arylation: To an 8 mL borosilicate vial were added sequentially: Catalyst **1** (10 mol%, 0.1 mmol), benzoquinone (2 equiv, 2 mmol), dioxane (0.33M, 3 mL), acetic acid (4 equiv, 4 mmol), olefin (1 equiv., 1 mmol), boronic acid (1.5 equiv., 1.5 mmol), and a stir bar. The vial was capped and stirred at room temperature with the reaction progress monitored by TLC or NMR aliquot (4hrs). The reaction mixture was diluted with H₂O and extracted with CH₂Cl₂ or hexane (2 times). The combined organics were dried over MgSO₄. The mixture was filtered and concentrated *in vacuo*. Purification by flash chromatography (EtOAc/hexanes mixtures) provided the pure product.

The only deviation from standard conditions have been increasing aryl boronic acids loadings for compounds **2**, **3**, **5**, and **14**. Increasing aryl boronic acids loading (from 1.5 to 2.0 equiv.) was found to improve internal:terminal product ratios due to further arylation of the minor terminal product to generate trisubstituted olefins. Increasing reaction times (from 4hrs to 24hrs) for compound **5**, **6**, **7**, **9**, and **10** (48h) was found to give better styrenyl:allylic ratios due to erosion of the minor allylic isomer.

Diene Formation Conditions: Following the General Procedure with 2 equiv. 2,6-dimethylbenzoquinone, 1.0 M dioxane, and reaction time of 48 hours. Drastically diminished yields are observed when benzoquinone is used, which was determined to be due to Diels-Alder reactions with the diene products and benzoquinone.

Reaction scheme showing the synthesis of *E*/*Z* allyl esters:

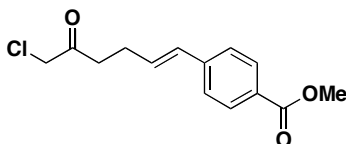
Starting materials: An allyl ester derivative (R-CH(X)-CH=CH₂, *n* = 1, 2, 1 equiv.) and a phenol derivative ((HO)₂B-Ar, 1.5 equiv.).

Reaction conditions:

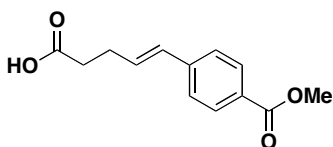
- Catalyst: Ph-S-Pd(OAc)_2 (10 mol%)
- Acid: AcOH (4 equiv.)
- Base: BQ (2 equiv.)
- Solvent: dioxane (0.33M)
- Temperature: rt
- Time: 4h

Product: An allyl ester derivative (R-CH(X)-CH=CH-Ar, *n* = 1, 2) with a ratio of **>20:1 *E*:*Z***.

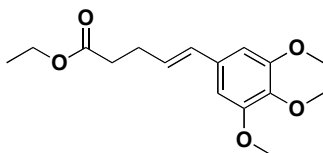
^aIsolated yield isomerically pure material (except **14**, **15**). Average 2 runs. ^b2.0 equiv. arylboronic acid. ^c13:1 styrene:diene, crude (SI). ^d45 °C, 1.2 equiv. arylboronic acid ^eReplacing $\text{Pb}(\text{OH})_2$ (1 atm), air (1 atm.), or H_2O_2 gave <10% yield (GC). ^f24h. ^g2.5 hours. ^h45°C, 48h. ⁱ $\text{Pb}(\text{OH})_2$ under identical conditions gave diminished styrene:allylic ratios of 1:4. ^jTHF (0.33 M).



(E)-methyl 4-(6-chloro-5-oxohex-1-enyl)benzoate (2): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), 1-chlorohex-5-en-2-one (1.0 mmol, 133.0 mg, 1 equiv.), 4-methoxycarbonylphenylboronic acid (2.0 mmol, 360.0 mg, 2.0 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with CH₂Cl₂ (50 mL) and rinsed with H₂O (50 mL). The aqueous layer was extracted with CH₂Cl₂ (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 15% ethyl acetate/hexanes then further purified via silica chromatography (125 mL SiO₂) with 100% methylene chloride as eluent to yield (E)-methyl 4-(6-chloro-5-oxohex-1-enyl)benzoate as a white solid. Run 1 (172.7 mg, 0.65 mmol, 65%, >20:1 *E*:*Z*, 16:1 int.:term., >20:1 int.:allyl, *13:1 styrenyl:diene); run 2 (166.6 mg, 0.62 mmol, 62%, >20:1 *E*:*Z*, 16:1 int.:term., >20:1 styrenyl:allyl, 13:1 styrenyl:diene). **Average Yield = 64%.** ¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 6.46 (d, *J* = 16 Hz, 1H), 6.32 (dt, *J* = 16, 6.4 Hz, 1H), 4.10 (s, 2H), 3.90 (s, 3H), 2.81 (t, 6.8 Hz, 2H), 2.56 (ap q, *J* = 6.8 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) 202.01, 167.12, 141.85, 131.16, 130.72, 130.12, 128.88, 126.13, 52.28, 48.40, 39.22, 27.06. IR (neat, cm⁻¹) 3011.79, 2991.84, 2947.42, 2910.79, 1725.83, 1716.12. HRMS (ESI) *m/z* calculated for C₁₄H₁₆O₃Cl [M+H]⁺: 267.0788, found 267.0795. *It is known the Pd(II) and benzoquinone can convert carbonyl compounds to α,β-unsaturated carbonyls.²



(E)-5-(4-(methoxycarbonyl)phenyl)pent-4-enoic acid (3): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), 4-pentenoic acid (1.0 mmol, 100.0 mg, 1 equiv.), 4-methoxycarbonylphenylboronic acid (2.0 mmol, 360.0 mg, 2.0 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with methylene chloride (50 mL) and rinsed with 10% aq. H₃PO₄ (50 mL). The aqueous layer was extracted with methylene chloride (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 20% acetone/hexanes as eluent to yield (E)-5-(4-(methoxycarbonyl)phenyl)pent-4-enoic acid as a white solid. Run 1 (184.9 mg, 0.79 mmol, 79%, >20:1 *E*:*Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (187.7 mg, 0.80 mmol, 80%, >20:1 *E*:*Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average Yield = 80%.** ¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 6.48 (d, *J* = 16 Hz, 1H), 6.34 (m, 1H), 3.90 (s, 3H), 2.56 (s, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 178.74, 167.18, 141.92, 131.12, 130.63, 130.12, 128.85, 126.16, 52.29, 33.62, 28.15. IR (neat, cm⁻¹) 3119.86, 3010.62, 2926.10, 1719.65, 1693.39. HRMS (ESI) *m/z* calculated for C₁₃H₁₄O₄Na [M+Na]⁺: 257.0790, found 257.0783. Spectra taken in d₆-DMSO matches reported assignments.³



(E)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (4): To a 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.1 mg, 10 mol%), benzoquinone (1 mmol, 108.0 mg, 2 equiv.), dioxane (1.5 mL, 0.33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), ethyl pent-4-enoate (0.5 mmol, 64.0 mg, 1 equiv.), 3,4,5-trimethoxyphenylboronic acid (0.75 mmol, 127.3 mg, 1.2 equiv.), and a stir bar sequentially under ambient conditions. The vial was capped and stirred at 45°C for 4 hours. The mixture was diluted with CH₂Cl₂ (50 mL) and rinsed with H₂O (50 mL). The aqueous layer was extracted with CH₂Cl₂ (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 20% ethyl acetate/hexanes as eluent to yield (E)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate as a white solid. Run 1 (111.5 mg, 0.38 mmol, 75%, >20:1 *E*:*Z*, 8:1 int.:term., >20:1 sty.:allyl.); run 2 (108.8, 0.37 mmol, 74%, >20:1 *E*:*Z*, 8:1 int.:term., >20:1 sty.:allyl.). Note: Could be purified to >20:1 int.:term. via column chromatography. **Average Yield = 75%.** ¹H NMR (400 MHz, CDCl₃) δ 6.55 (s, 2H), 6.35 (d, *J* = 15.6 Hz, 1H), 6.12 (dt, *J* = 15.6, 6.8 Hz, 1H), 4.14 (q, *J* = 6.8

Hz, 2H), 3.86 (s, 6H), 3.82 (s, 3H), 2.55-2.45 (m, 4H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.22, 153.48, 137.58, 133.40, 131.07, 128.29, 103.19, 61.16, 60.66, 56.25, 34.25, 28.42, 14.50. IR (neat, cm^{-1}) 2979.87, 2938.51, 2837.43, 1730.54. HRMS (ESI) m/z calculated for $\text{C}_{16}\text{H}_{23}\text{O}_5$ $[\text{M}+\text{H}]^+$: 295.1545, found 295.1537. A known compound however no spectral data is reported.⁴

Alternative Oxidants:

Oxygen:

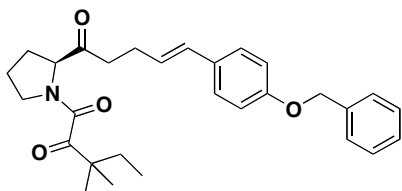
(*E*)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (4): To a 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.1 mg, 10 mol%), dioxane (1.5 mL, 0.33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), ethyl pent-4-enoate (0.5 mmol, 64.0 mg, 1 equiv.), 3,4,5-trimethoxyphenylboronic acid (0.75 mmol, 127.3 mg, 1.5 equiv.), an oxygen balloon, and a stir bar sequentially under ambient conditions. Nitrobenzene was added as an internal standard. The vial was capped and stirred at 45°C for 4 hours. GC analysis revealed a 11% conversion with a 5% yield of (*E*)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (response factor corrected).

Air:

Replacing the oxygen balloon with an air balloon in the above procedure yielded a 10% conversion with a 4% yield of (*E*)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (response factor corrected).

Hydrogen Peroxide:

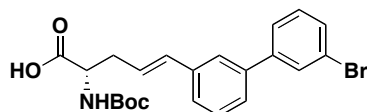
(*E*)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (4): To a 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.1 mg, 10 mol%), dioxane (1.5 mL, 0.33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), hydrogen peroxide (1.0 mmol, 68 μL , 2 equiv., 50% aq. solution), ethyl pent-4-enoate (0.5 mmol, 64.0 mg, 1 equiv.), 3,4,5-trimethoxyphenylboronic acid (0.75 mmol, 127.3 mg, 1.5 equiv.), and a stir bar sequentially under ambient conditions. Nitrobenzene was added as an internal standard. The vial was capped and stirred at 45°C for 4 hours. GC analysis revealed a 100% conversion with a 6% yield of (*E*)-ethyl 5-(3,4,5-trimethoxyphenyl)pent-4-enoate (response factor corrected).



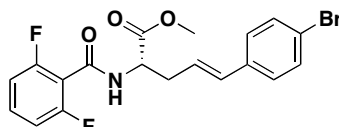
(*S,E*)-1-(2-(5-(4-(benzyloxy)phenyl)pent-4-enoyl)pyrrolidin-1-yl)-3,3-dimethylpentane-1,2-dione ((-)-5): To a 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.1 mg, 10 mol%), benzoquinone (1.0 mmol, 108.0 mg, 2 equiv.), dioxane (1.5 mL, 0.33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), (*S*)-3,3-dimethyl-1-(2-pent-4-enoylpyrrolidin-1-yl)pentane-1,2-dione (0.5 mmol, 139.5 mg, 1 equiv. derived from *N*-(*tert*-Butoxycarbonyl)-

L-proline *N'*-methoxy-*N'*-methylamide), 4-(benzyloxy)phenylboronic acid (1.0 mmol, 228.1 mg, 2.0 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 24 hours. The mixture was diluted with methylene chloride (50 mL) and rinsed with 5% K_2CO_3 (50 mL). The aqueous layer was extracted with methylene chloride (50 mL) and the combined organic layers were dried over MgSO_4 . After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 20 % ethyl acetate/petroleum ether as eluent to yield (*S,E*)-1-(2-(5-(4-(benzyloxy)phenyl)pent-4-enoyl)pyrrolidin-1-yl)-3,3-dimethylpentane-1,2-dione as a white solid. Run 1 (177.7 mg, 0.39 mmol, 77%, >20:1 *E*:*Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (175.4 mg, 0.38 mmol, 77%, >20:1 *E*:*Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average yield = 77%.** ^1H NMR (500 MHz, CDCl_3) δ 7.42 (d, $J = 7.0$ Hz, 2H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.25 (d, $J = 8.5$ Hz, 1H), 6.90 (d, $J = 8.5$ Hz, 2H), 6.36 (d, $J = 15.5$ Hz, 1H), 6.05 (dt, $J = 16.0, 7.0$ Hz, 1H), 5.05 (s, 2H), 4.61 (dd, $J = 9.0, 5.0$ Hz, 1H), 3.57 – 3.45 (m, 2H), 2.80 – 2.65 (m, 2H), 2.54 – 2.46 (m, 2H), 2.20 – 2.13 (m, 1H), 1.98 – 1.76 (m, 4H), 1.71 – 1.63 (m, 1H), 1.25 (s, 3H), 1.21 (s, 3H), 0.87 (t, $J = 7.0$ Hz, 3H), minor rotamer: 4.74 (dd, $J = 8.5, 5.0$ Hz, 1H), 3.67 – 3.64 (m, 2H), 2.33-2.26 (m, 1H), 1.29 (s, 3H), 1.14 (s, 3H), 0.80 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 207.04, 165.28, 158.20, 137.16, 130.69, 130.62, 130.43, 128.95(rotamer), 128.78, 128.16, 127.67, 127.33, 126.77, 126.54(rotamer), 115.34(rotamer), 115.05, 70.19, 66.01(rotamer), 64.21, 47.64, 47.20, 47.13(rotamer), 40.06, 39.40(rotamer), 33.11(rotamer), 32.50,

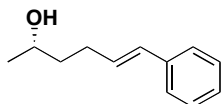
30.75(rotamer), 27.88, 26.81, 24.98, 24.23(rotamer), 24.00, 23.28, 22.28(rotamers), 9.17. IR (neat, cm^{-1}): 3030.11, 2964.43, 2923.88, 2879.91, 1721.50, 1699.12, 1634.63, 1606.08, 1508.52. HRMS (ES) m/z calculated for $\text{C}_{29}\text{H}_{36}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 462.2644, found 462.2649. $[\alpha]^{25}_{\text{D}} = -37.1$ ($c = 1.0$, CHCl_3). Spectral data matches reported assignments.⁵



(*S,E*)-2-(*tert*-butoxycarbonyl)-5-(3-[3-bromobenzene]phenyl)pent-4-enoic acid ((+)-6): To a 2 mL borosilicate vial was added catalyst **1** (0.022 mmol, 11.0 mg, 10 mol%), benzoquinone (0.44 mmol, 47.5 mg, 2 equiv.), dioxane (0.66 mL, .33 M), acetic acid (0.88 mmol, 52.8 mL, 4 equiv.), (*S*)-2-(*tert*-butoxycarbonyl)pent-4-enoic acid (0.22 mmol, 47.3 mg, 1 equiv., derived from L-allylglycine), 3-(3-bromobenzene)phenyl boronic acid (0.327 mmol, 90.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 24 hours. The mixture was diluted with ether (50 mL) and rinsed with 1 M H_3PO_4 (50 mL). The aqueous layer was extracted with ether (50 mL) and the combined organic layers were dried over MgSO_4 . After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 30% ethyl acetate/petroleum ether/1% acetic acid as eluent to yield (*S,E*)-2-(*tert*-butoxycarbonyl)-5-(3-[3-bromobenzene]phenyl)pent-4-enoic acid as a white solid. Run 1 (58.9 mg, 0.13 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (59.9, 0.13 mmol, 61%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average yield = 61%.** ^1H NMR (500 MHz, CHCl_3) δ 7.72 (s, 1H), 7.50-7.47 (m, 3H), 7.42-7.36 (m, 3H), 7.30 (t, $J = 8.0$ Hz, 1H), 6.55 (d, $J = 15.5$ Hz, 1H), 6.19 (dt, $J = 15.5$, 7.5 Hz, 1H), 5.05 (d, $J = 7.0$ Hz, 1H), 4.48 (m, 1H), 2.81-2.70 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, CHCl_3) δ 176.99, 155.78, 143.39, 140.30, 137.68, 134.15, 130.51 (2 C), 130.42, 129.34, 126.60, 126.04, 125.99, 125.42, 124.55, 123.13, 80.71, 53.29, 36.10, 28.54. IR (neat, cm^{-1}): 3426.17, 3115.84, 2975.37, 2530.59, 1713.05. HRMS (ESI) m/z calculated for $\text{C}_{22}\text{H}_{25}\text{NO}_4\text{Br}$ $[\text{M}+\text{H}]^+$: 446.0967, found 446.0969. $[\alpha]^{27}_{\text{D}} = +9.1^\circ$ ($c = 0.44$, CHCl_3). A known compound however no spectral data is reported.⁶

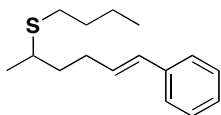


(*S,E*)-methyl 5-(4-bromophenyl)-2-(2,6-difluorobenzamido)pent-4-enoate ((+)-7): To a 2 mL borosilicate vial was added catalyst **1** (0.025 mmol, 12.5 mg, 10 mol%), benzoquinone (0.5 mmol, 54.0 mg, 2 equiv.), dioxane (0.75 mL, .33 M), acetic acid (1.0 mmol, 60.0 mg, 4 equiv.), (*S*)-methyl 2-(2,6-difluorobenzamido)pent-4-enoate (0.25 mmol, 67.3 mg, 1 equiv., derived from L-allylglycine), 4-bromophenylboronic acid (0.375 mmol, 74.6 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 24 hours. The mixture was diluted with ether (50 mL) and rinsed with H_2O (50 mL). The aqueous layer was extracted with ether (50 mL) and the combined organic layers were dried over MgSO_4 . After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 35% ethyl acetate/petroleum ether as eluent to yield (*S,E*)-methyl 5-(4-bromophenyl)-2-(2,6-difluorobenzamido)pent-4-enoate as a white solid. Run 1 (63.3 mg, 0.15 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (65.1 mg, 0.15 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average yield = 60%.** ^1H NMR (500 MHz, CDCl_3) δ 7.42 (d, $J = 8.5$ Hz, 2H), 7.38 (m, 1H), 7.20 (d, $J = 8.5$ Hz, 2H), 6.95 (t, $J = 8.0$ Hz, 2H), 6.61 (br d, $J = 7.0$ Hz, 1H), 6.45 (d, $J = 15.5$ Hz, 1H), 6.09 (dt, $J = 16.0$, 7.0 Hz, 1H), 5.00 (q, $J = 7.5$, 1H), 3.81 (s, 3H), 2.94 (m, 1H), 2.76 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 171.79, 160.27 (dd, J^1 ^{19}F - $^{13}\text{C} = 251.1$, 6.8 Hz, 1C), 160.06, 135.96, 133.59, 132.24 (t, J^3 ^{19}F - $^{13}\text{C} = 9.9$ Hz, 1C), 131.84, 128.04, 124.11, 121.55, 113.89 (t, J^2 ^{19}F - $^{13}\text{C} = 19.5$ Hz, 1C), 112.31 (d, J^2 ^{19}F - $^{13}\text{C} = 25.8$ Hz, 1C), 52.97, 52.65, 35.95. ^{19}F (376 MHz, CDCl_3) -112.36. IR (neat, cm^{-1}) 3336.51, 3272.50, 3081.23, 3060.90, 2967.34, 2924.14, 1743.88, 1676.48, 1514.27, 1223.17. HRMS (ESI) m/z calculated for $\text{C}_{19}\text{H}_{17}\text{NO}_3\text{F}_2\text{Br}$ $[\text{M}+\text{H}]^+$: 424.0360, found 424.0354. $[\alpha]^{27}_{\text{D}} = +44.2^\circ$ ($c = 0.44$, CHCl_3). A known compound however spectral data is not reported.⁷

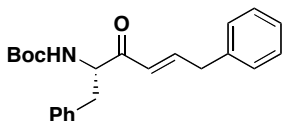


(*S,E*)-6-phenylhex-5-en-2-ol ((+)-8): To a 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.3 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3.0 mL, .33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), (*S*)-(+)-

2-hexenol (1.0 mmol, 100.0 mg, 1 equiv.), phenylboronic acid (1.5 mmol, 183.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 2.5 hours. The mixture was diluted with methylene chloride (50 mL) and rinsed with 3M NaOH (50 mL). The aqueous layer was extracted with methylene chloride (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 20 % ether:petroleum ether as eluent to yield (E)-6-phenylhex-5-en-2-ol as white solid. Run 1 (107.6 mg, 0.61 mmol, 61%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (105.8 mg, 0.60 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average yield = 61%** ¹H NMR (400 MHz, CDCl₃) δ 7.33 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.20 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.24 (dt, *J* = 15.6, 6.8 Hz, 1H), 3.88 (sex, *J* = 6.4 Hz, 1H), 2.40–2.24 (m, 2H), 1.70–1.57 (m, 2H), 1.39 (br s, 1H), 1.23 (d, *J* = 6.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 130.57, 130.52, 128.78, 127.23, 126.23 (2C), 67.93, 39.01, 29.66, 23.87. IR (neat, cm⁻¹): 3645.89–3151.87, 3079.26, 3057.15, 3023.31, 2963.55, 2926.95, 2871.97, 2853.80, 1648.31, 1596.93. HRMS (CI) *m/z* calculated for C₁₂H₁₇O [M+H]⁺: 177.1280, found 177.1277. [α]_D²⁵ = +12.4° (c = 1.0, CHCl₃). Spectral peaks are similar to reported peaks (spectrum reported in CCl₄).⁸

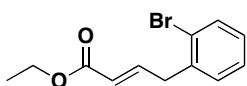


(E)-butyl (6-phenylhex-5-en-2-yl)sulfane (9): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3.0 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), butyl (hex-5-en-2-yl)sulfane (1.0 mmol, 170.0 mg, 1 equiv.), phenylboronic acid (1.5 mmol, 183.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 24 hours. The mixture was diluted with methylene chloride (50 mL) and rinsed with H₂O (50 mL). The aqueous layer was extracted with methylene chloride (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 5 % ether/petroleum ether as eluent to yield (E)-butyl (6-phenylhex-5-en-2-yl)sulfane as light yellow oil. Run 1 (138.0 mg, 0.56 mmol, 55%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.); run 2 (138.0 mg, 0.56 mmol, 56%, >20:1 *E:Z*, >20:1 int.:term., >20:1 sty.:allyl.). **Average yield = 56%**. ¹H NMR (500 MHz, CDCl₃) δ 7.34 (d, *J* = 8.5 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.20 (dt, *J* = 15.5, 7.0 Hz, 1H), 2.79 (sex., *J* = 7.0 Hz, 1H), 2.53 (t, *J* = 7.5 Hz, 2H), 2.35 (m, 2H), 1.73 (m, 1H), 1.64 (m, 1H), 1.56 (q, *J* = 8.0 Hz, 2H), 1.41 (m, 2H), 1.30 (d, *J* = 6.5 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 137.90, 130.50, 130.31, 128.71, 127.13, 126.13, 39.53, 36.69, 32.20, 30.66, 30.16, 22.39, 21.69, 13.96. IR (neat, cm⁻¹) 3059.47, 3023.77, 2956.85, 2926.52, 2870.53, 2858.22. HRMS (ESI) *m/z* calculated for C₁₆H₂₅S [M+H]⁺: 249.1677, found 249.1687.

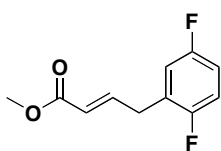


(S,E)-tert-butyl 3-oxo-1,6-diphenylhex-4-en-2-ylcarbamate ((+)-10): To an 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.0 mg, 10 mol%), benzoquinone (1.0 mmol, 108.0 mg, 2 equiv.), dioxane (1.5 mL, .33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), (S)-tert-butyl 3-oxo-1-phenylhex-5-en-2-ylcarbamate (0.5 mmol, 144.5 mg, 1 equiv., derived from *N*-Boc-L-phenylalanine), phenylboronic acid (0.75 mmol, 92.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at 45°C for 48 hours. The mixture was diluted with ether (50 mL) and rinsed with H₂O (50 mL). The aqueous layer was extracted with ether (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 20% ethyl acetate/petroleum ether as eluent to yield (S,E)-tert-butyl 3-oxo-1,6-diphenylhex-4-en-2-ylcarbamate as a clear solid. Run 1 (111.8 mg, 0.31 mmol, 61%, >20:1 *E:Z*, >20:1 int.:term., <1:20 sty.:allyl.); run 2 (113.3 mg, 0.31 mmol, 62%, >20:1 *E:Z*, >20:1 int.:term., <1:20 sty.:allyl.). **Average yield = 62%**. ¹H NMR (500 MHz, CDCl₃) δ 7.32 (t, *J* = 7.5, 2H), 7.27–7.20 (m, 4H), 7.10 (ap t, *J* = 6.5 Hz, 4H), 7.03 (dt, *J* = 15.5, 6.5 Hz, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 5.26 (d, *J* = 7.5 Hz, 1H), 4.79 (ap q, *J* = 6.5 Hz, 1H), 3.49 (d, *J* = 7.0 Hz, 2H), 3.07 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.98 (dd, *J* = 13.5, 6.0 Hz, 1H), 1.41 (s, 9H). ¹³C NMR (125 MHz, CDCl₃) δ 197.69, 155.32, 147.94, 137.41, 136.30, 129.68, 129.03, 128.97, 128.64, 128.15, 127.08, 127.02, 79.90, 58.57, 39.04, 38.70, 28.49. IR (neat, cm⁻¹) 3420.31, 3346.22, 3085.09, 3061.84, 3027.95, 2976.31, 2929.68, 1711.23, 1692.91. HRMS

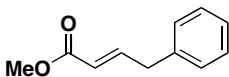
(ESI) m/z calculated for $C_{23}H_{28}NO_3$ $[M+H]^+$: 366.2069, found 366.2068. $[\alpha]_D^{27} = +51.3^\circ$ ($c = 1.0$, $CHCl_3$), -5.6° ($c = 1.0$, MeOH). Spectral data matches that of the reported compound.⁹



(*E*)-ethyl 4-(2-bromophenyl)but-2-enoate (11): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3.0 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), ethyl but-1-enoate (1.0 mmol, 114.0 mg, 1 equiv.), 2-bromobenzeneboronic acid (1.5 mmol, 300.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with Et_2O (50 mL) and rinsed with H_2O (50 mL). The aqueous layer was extracted with Et_2O (50 mL) and the combined organic layers were dried over $MgSO_4$. After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 15% diethyl ether/pentane as eluent to yield (*E*)-ethyl 4-(2-bromophenyl)but-2-enoate as a clear oil. Run 1 (131.8 mg, 0.49 mmol, 49%, >20:1 *E:Z*, >20:1 int.:term., 1:20 sty.:allyl); run 2 (134.5 mg, 0.50 mmol, 50%, >20:1 *E:Z*, >20:1 int.:term., 1:17 sty.:allyl); run 3 (137.2 mg, 0.51 mmol, 51%, >20:1 *E:Z*, >20:1 int.:term., 1:19 sty.:allyl). **Average Yield = 50%.** 1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, $J = 8$ Hz, 1H), 7.28 (m, 1H), 7.22 (d, $J = 7.5$ Hz, 1H), 7.15 (d, $J = 7.5$ Hz, 1H), 7.09 (dt, $J = 15.5, 7$ Hz, 1H), 5.79 (d, $J = 16$ Hz, 1H), 4.20 (q, $J = 7.5$ Hz, 2H), 3.68 (d, $J = 6.5$ Hz, 2H), 1.30 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.62, 145.64, 137.57, 133.21, 130.97, 128.70, 127.94, 124.81, 123.10, 60.56, 38.79, 14.45. IR (neat, cm^{-1}) 3055.85, 2979.23, 2935.80, 2903.09, 1717.18. HRMS (ESI) m/z calculated for $C_{12}H_{14}O_2Br$ $[M+H]^+$: 269.0177, found 269.0172. Spectral data matches that of the reported compound.¹⁰

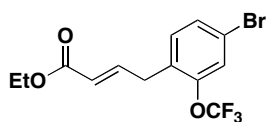


(*E*)-methyl 4-(2,5-difluorophenyl)but-2-enoate (12): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), methyl but-3-enoate (1.0 mmol, 100.0 mg, 1 equiv.), 2,5-difluorophenylboronic acid (1.5 mmol, 237.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with Et_2O (50 mL) and rinsed with H_2O (50 mL). The aqueous layer was extracted with Et_2O (50 mL) and the combined organic layers were dried over $MgSO_4$. After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 15% ether/pentane as eluent to yield (*E*)-methyl 4-(2,5-difluorophenyl)but-2-enoate as a clear oil. Run 1 (110.0 mg, 0.52 mmol, 52%, >20:1 *E:Z*, >20:1 int.:term., 1:17 sty.:allyl); run 2 (106.6 mg, 0.50 mmol, 50%, >20:1 *E:Z*, >20:1 int.:term., 1:17 sty.:allyl). **Average Yield = 51%.** 1H NMR (500 MHz, $CDCl_3$) δ 7.08–6.99 (m, 2H), 6.94–6.86 (m, 2H), 5.83 (d, $J = 15.5$ Hz, 1H), 3.74 (s, 3H), 3.53 (d, $J = 6$ Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.81, 145.13, 122.99, 117.41 (d, $J = 4.9$ Hz), 117.22 (d, $J = 4.9$ Hz), 116.78 (d, $J = 7.8$ Hz), 116.58 (d, $J = 8.8$ Hz), 115.22 (d, $J = 8.8$ Hz), 115.04 (d, $J = 8.8$ Hz), 51.79, 31.68. ^{19}F NMR (470 MHz, $CDCl_3$) δ -119.27, -124.52. IR (neat, cm^{-1}) 3036.60, 2995.61, 2953.20, 2851.99, 1724.78. HRMS (ESI) m/z calculated for $C_{11}H_{11}O_2F_2$ $[M+H]^+$: 213.0727, found 213.0723. Previously reported compound however no spectral data is reported.¹¹

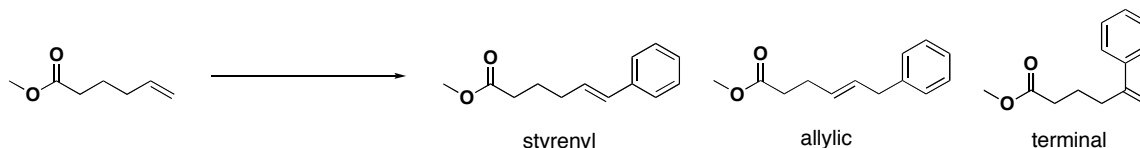


(*E*)-methyl 4-phenylbut-2-enoate and (*E*)-methyl 4-phenylbut-3-enoate (Manuscript Entry 11, Table 1, Footnote i): To an 8 mL borosilicate vial was added White Catalyst (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), methyl but-3-enoate (1.0 mmol, 102.0 mg, 1 equiv.), phenylboronic acid (1.5 mmol, 183.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with diethyl ether (50 mL) and rinsed with 5% K_2CO_3 (50 mL). The aqueous layer was extracted with diethyl ether (50 mL) and the combined organic layers were dried over $MgSO_4$. The crude product was purified via silica chromatography (125 mL SiO_2) with 10% diethyl ether/petroleum ether as eluent to yield (*E*)-methyl 4-phenylbut-2-enoate and (*E*)-methyl 4-phenylbut-3-enoate as a clear oil (125.0 mg, 0.71 mmol, 71%, >20:1 *E:Z*, 1:4 styrenyl: α,β -unsaturation).

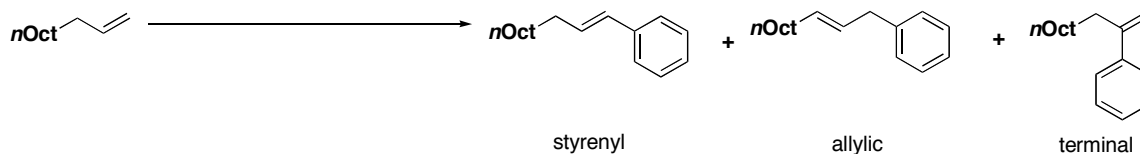
Silica gel chromatography was performed with liberal fraction collection. Crude product ratios are close to those of the purified material. ^1H NMR (500 MHz, CDCl_3) δ α,β -unsaturated: 7.12 (dt, $J = 15.5$, 6.0 Hz, 1H), 5.83 (d, $J = 15.0$ Hz, 1H), 3.73 (s, 3H), 3.54 (d, $J = 6.5$ Hz, 2H). Styrene: 6.51 (d, $J = 15.5$ Hz, 1H), 6.31 (dt, $J = 15.5$, 6.5 Hz, 1H), 3.27 (d, $J = 7.5$ Hz, 2H).



(E)-ethyl 4-(4-bromo-2-(trifluoromethoxy)phenyl)but-2-enoate (13): To a 4 mL borosilicate vial was added catalyst **1** (0.05 mmol, 25.0 mg, 10 mol%), benzoquinone (1.0 mmol, 108.0 mg, 2 equiv.), THF (1.5 mL, .33 M), acetic acid (2.0 mmol, 120.0 mg, 4 equiv.), ethyl but-3-enoate (0.5 mmol, 57.0 mg, 1 equiv.), 4-bromo-2-(trifluoromethoxy)phenylboronic acid (0.75 mmol, 213.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with ether (50 mL) and rinsed with H_2O (50 mL). The aqueous layer was extracted with ether (50 mL) and the combined organic layers were dried over MgSO_4 . After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 10% ether/petroleum ether as eluent to yield (E)-ethyl 4-(4-bromo-2-(trifluoromethoxy)phenyl)but-2-enoate as a yellow oil. Run 1 (159.1 mg, 0.3 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., <1:20 sty.:allyl.); run 2 (105.9 mg, 0.3 mmol, 60%, >20:1 *E:Z*, >20:1 int.:term., <1:20 sty.:allyl.). **Average yield = 60%.** ^1H NMR (500 MHz, CHCl_3) δ 7.42 (t, $J = 2.0$ Hz, 1H), 7.40 (dd, $J = 8.0$, 2.0 Hz, 1H), 7.12 (d, $J = 8.0$ Hz, 1H), 6.98 (dt, $J = 15.5$, 6.5 Hz, 1H), 5.78, (dt, $J = 15.5$, 1.5 Hz, 1H), 4.18 (q, $J = 7.0$ Hz, 2H), 3.52 (dd, $J = 6.5$, 1.5 Hz, 2H), 1.28 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 166.34, 144.67, 132.37, 130.50, 129.76, 124.30, 124.28, 123.55, 121.89, 121.06, 60.68, 32.18, 14.43. ^{19}F NMR (376 MHz, CDCl_3) δ -57.67. IR (neat, cm^{-1}) 3051.79, 2980.89, 2960.98, 2934.69, 2908.87, 2873.52, 1721.71, 1255.02, 1214.04, 1175.50. HRMS (ESI) m/z calculated for $\text{C}_{13}\text{H}_{13}\text{O}_3\text{F}_3\text{Br}$ $[\text{M}+\text{H}]^+$: 353.0000, found 353.0004. Previously reported compound.¹²



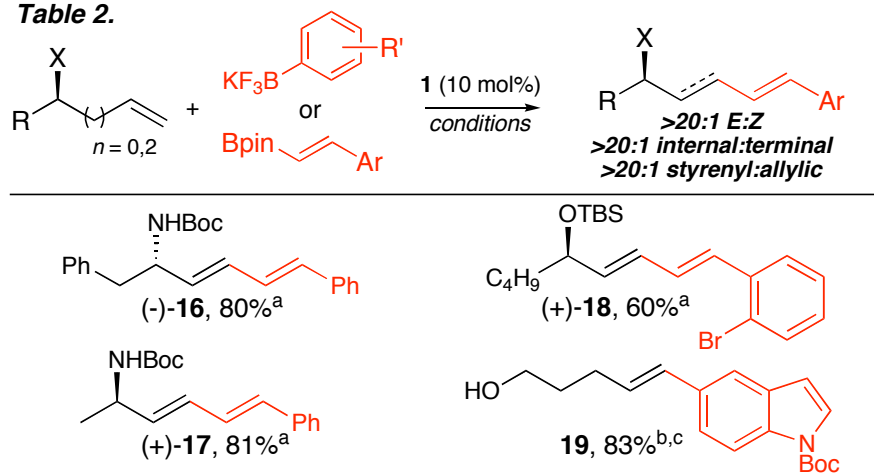
(E)-methyl 6-phenylhex-5-enoate (and other isomers, 14): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), methyl hex-5-enoate (1.0 mmol, 128.0 mg, 1 equiv.), phenylboronic acid (2.0 mmol, 244.0 mg, 2.0 equiv.) and a stir bar sequentially under ambient conditions. The vial as capped and stirred at room temperature for 24 hours. The mixture was diluted with diethyl ether (50 mL) and rinsed with 5% K_2CO_3 (50 mL). The crude product was purified via silica chromatography (125 mL SiO_2) with 5 % ether:petroleum ether as eluent to yield (E)-methyl 6-phenylhex-5-enoate and other isomers as clear oil. Silica gel chromatography was performed with liberal fraction collection. Crude product ratios match those of the purified material. *E:Z* selectivities were found to be >20:1 in all cases. Run 1 (124.4 mg, 0.61 mmol, 61%, internal:terminal 9:1, styrenyl:allylic 2:1); run 2 (120.4 mg, 0.59 mmol, 59%, internal:terminal 9:1, styrenyl:allylic 2:1). **Average yield = 60%.** ^1H NMR (500 MHz, CHCl_3) δ Styrenyl: 6.42 (d, $J = 16$ Hz, 1H), 6.20 (dt, $J = 16$, 6.5 Hz, 1H) Allylic: 5.68-5.62 (m, 1H), 5.56-5.50 (m, 1H) Terminal: 5.31 (d, $J = 1.5$ Hz), 5.09 (d, $J = 1.5$ Hz, 1H).



(E)-1-(undec-1-enyl)benzene (and other olefin isomers, 15): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL,

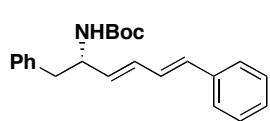
0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), 1-undecene (1.0 mmol, 154.0 mg, 1 equiv.), phenylboronic acid (1.5 mmol, 183.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial as capped and stirred at room temperature for 4 hours. The mixture was diluted with diethyl ether (50 mL) and rinsed with 5% K₂CO₃ (50 ml). The aqueous layer was extracted with diethyl ether (50 mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 100% petroleum ether as eluent to yield (*E*)-1-(undec-1-enyl)benzene and other olefin isomers as a clear oil. Silica gel chromatography was performed with liberal fraction collection. Crude product ratios match those of the purified material. *E*:*Z* selectivities were found to be >20:1 in all cases. Run 1 (0.154 g, 0.67 mmol, 67%, internal:terminal 8:1, styrenyl:allylic 1:1), run 2 (0.156 g, 0.68 mmol, 68%, internal:terminal 8:1, styrenyl:allylic 1:1). **Average yield = 68%**. ¹H NMR (400 MHz, CDCl₃) δ Styrenyl: 6.43 (d, *J* = 15.6 Hz, 1H), 6.28 (dt, *J* = 16, 6.8 Hz, 1H). Allylic: 5.66-5.52 (m, 2H), 3.38 (d, *J* = 6 Hz, 2H). Terminal: 5.31 (s, 1H), 5.10 (s, 1H), 2.55 (t, *J* = 6.8 Hz, 2H).

Table 2.



^a 2,6-dimethylbenzoquinone (2 equiv.), AcOH (4 equiv.), boronic ester (1.5 equiv.), dioxane (1.0 M), rt, 48h.

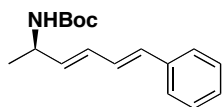
^b BQ (2 equiv.), AcOH (4 equiv.), ArBF₃K (1.5 equiv.), B(OH)₃ (2.0 equiv.), dioxane (0.33 M), rt, 4h. ^c Crude int.:term. = 16:1.



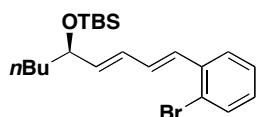
***tert*-butyl (*S*,3*E*,5*E*)-1,6-diphenylhexa-3,5-dien-2-ylcarbamate ((-)-**16**):** To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), 2,6-dimethylbenzoquinone (2.0 mmol, 272.0 mg, 2 equiv.), dioxane (1 mL, 1.0 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), (*S*)-*tert*-butyl 1-phenylbut-3-en-2-ylcarbamate (1.0 mmol, 248.0 mg, 1 equiv., derived from L-phenylalaninol),

(*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (1.5 mmol, 348.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 48 hours. The mixture was diluted with ethyl acetate (50 ml) and rinsed with H₂O (50 ml). The aqueous layer was extracted with ethyl acetate (50 ml) and the combined organic layers were thoroughly rinsed with 5% aq. K₂CO₃ and sat. aq. NaHSO₃ (Careful! Rapid Gas Evolution!) then dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 5% ethyl acetate/hexanes as eluent to yield *tert*-butyl (*S*,3*E*,5*E*)-1,6-diphenylhexa-3,5-dien-2-ylcarbamate as a white solid. Run 1 (283.5 mg, 0.81 mmol, 81%, >20:1 *E*:*Z*, >20:1 int.:term.); run 2 (277.9 mg, 0.75 mmol, 75%, >20:1 *E*:*Z*, >20:1 int.:term.). **Average Yield = 80%**. ¹H NMR (500 MHz, CDCl₃) δ 7.40 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 8 Hz, 4H), 7.23 (m, 4H), 6.75 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.29 (dd, *J* = 15, 10.5 Hz, 1H), 5.77 (m, 1H), 4.55 (br s, 2H), 2.91 (br s, 2H), 1.45 (s, 9H). ¹³C NMR (125 MHz, CDCl₃) 155.35, 137.55, 137.39, 133.95, 132.60, 130.86, 129.80, 128.81, 128.60, 128.43, 127.73, 126.73, 126.53, 79.69, 53.16, 41.98, 28.55. IR (neat, cm⁻¹) 3079.13, 3059.71, 3027.59, 2979.74, 2929.05, 1699.26. HRMS

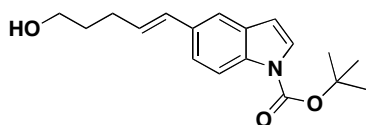
(ESI) m/z calculated for $C_{23}H_{28}O_2N$ $[M+H]^+$: 350.2120, found 350.2121. $[\alpha]_D^{27} = -21.3^\circ$ ($c = 1.0$, $CHCl_3$). Spectral data matches that of the reported compound.¹³



***tert*-butyl (*R*,*3E*,*5E*)-6-phenylhexa-3,5-dien-2-ylcarbamate ((+)-17):** To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), 2,6-dimethylbenzoquinone (2.0 mmol, 272.0 mg, 2 equiv.), dioxane (1 mL, 1.0 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), (*R*)-*tert*-butyl but-3-en-2-ylcarbamate (1.0 mmol, 172.0 mg, 1 equiv., derived from *R*-(-)-2-amino-1-propanol via tempo oxidation and wittig olefination), (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (1.5 mmol, 348.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 48 hours. The mixture was diluted with ethyl acetate (50 mL) and rinsed with H_2O (50 mL). The aqueous layer was extracted with ethyl acetate (50 mL) and the combined organic layers were thoroughly rinsed with 5% aq. K_2CO_3 and sat. aq. $NaHSO_3$ (Careful! Rapid Gas Evolution!) then dried over $MgSO_4$. After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 10% ethyl acetate/hexanes as eluent to yield *tert*-butyl (*R*,*3E*,*5E*)-6-phenylhexa-3,5-dien-2-ylcarbamate as a clear oil. Run 1 (223.3 mg, 0.82 mmol, 82%, >20:1 *E*:*Z*, >20:1 int.:term.); run 2 (216.5 mg, 0.79 mmol, 79%, >20:1 *E*:*Z*, >20:1 int.:term.). **Average Yield = 81%.** 1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 8$ Hz, 2H), 7.21 (t, $J = 7$ Hz, 1H), 6.74 (dd, $J = 15.5, 10.5$ Hz, 1H), 6.53 (d, $J = 15.5$ Hz, 1H), 6.31 (dd, $J = 15, 10.5$ Hz, 1H), 5.77 (dd, $J = 15, 5$ Hz, 1H), 4.50 (br s, 1H), 4.34 (br s, 1H), 1.46 (s, 9H), 1.26 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.30, 137.42, 136.11, 132.46, 129.82, 128.80, 128.55, 127.68, 126.51, 79.57, 47.78, 28.62, 21.23. IR (neat, cm^{-1}) 3374.93, 3361.91, 3021.85, 2976.24, 2928.38, 2973.63, 1687.12. HRMS (ESI) m/z calculated for $C_{17}H_{23}NO_2Na$ $[M+Na]^+$: 296.1626, found 296.1627. $[\alpha]_D^{27} = +70.4$ ($c = 1.0$, $CHCl_3$). Previously reported compound however no spectral data is given.¹⁴

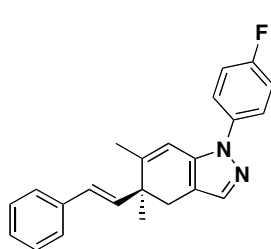
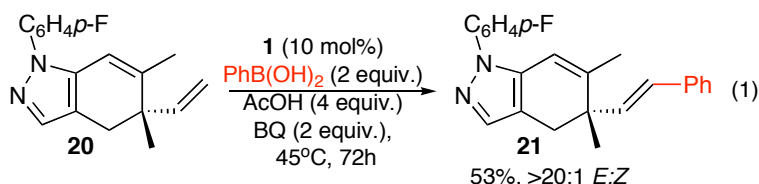


((*R*, 1*E*, 3*E*)-1-(2-bromophenyl)non-1,3-dien-5-yloxy)(*tert*-butyl)dimethylsilane ((+)-18): To a 2 mL borosilicate vial was added Catalyst **1** (0.025 mmol, 12.5 mg, 10 mol%), dimethylbenzoquinone (0.5 mmol, 68.0 mg, 2 equiv.), dioxane (0.25 mL, 1.0 M), acetic acid (1.0 mmol, 60.0 mg, 4 equiv.), (*R*)-*tert*-butyl(hept-1-en-3-yloxy)dimethylsilane (0.25 mmol, 57.0 mg, 1 equiv.), (*E*)-2-(2-bromostyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.375 mmol, 115.5 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 48 hours. The mixture was diluted with methylene chloride (50 mL) and rinsed with water (50 mL). The aqueous layer was extracted with methylene chloride (50 mL) and the combined organic layers were dried over $MgSO_4$. After concentration, the crude product was purified via silica chromatography (125 mL SiO_2) with 2 % ether:petroleum ether as eluent to yield ((*R*, 1*E*, 3*E*)-1-(2-bromophenyl)non-1,3-dien-5-yloxy)(*tert*-butyl)dimethylsilane as clear oil. Run 1 (122.1 mg, 0.30 mmol, 60%, >20:1 *E*:*Z*, >20:1 int.:term.); run 2 (120.0 mg, 0.29 mmol, 59%, >20:1 *E*:*Z*, >20:1 int.:term.). **Average yield = 60%** 1H NMR (400 MHz, $CHCl_3$) δ 7.55 (m, 2H), 7.26 (t, $J = 5.6$ Hz, 1H), 7.06 (dt, $J = 7.6, 1.6$ Hz, 1H), 6.86 (d, $J = 15.6$ Hz, 1H), 6.72 (dd, $J = 15.6, 10.8$ Hz, 1H), 6.35 (dd, $J = 15.2, 10.8$ Hz, 1H), 5.83 (dd, $J = 15.6, 6.8$ Hz, 1H), 4.19 (q, $J = 6.0$ Hz, 1H), 1.55 – 1.47 (m, 2H), 1.35 – 1.25 (m, 4H), 0.91 (s, 9H), 0.90 – 0.86 (m, 3H), 0.07 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.65, 137.22, 133.28, 131.60, 130.13, 129.37, 128.70, 127.60, 126.59, 123.96, 73.42, 38.27, 27.62, 26.13, 22.90, 18.50, 14.28, -4.05, -4.55. IR (neat, cm^{-1}): 3055.22, 3030.17, 2954.31, 2929.11, 2857.55. HRMS (EI) m/z calculated for $C_{21}H_{33}BrOSi$ $[M+H]^+$: 408.14841, found 408.14855. $[\alpha]_D^{27} = +6.9^\circ$ ($c = 0.42$, $CHCl_3$). Previously reported compound however no spectral data was given.¹⁵



(*E*)-*tert*-butyl 5-(5-hydroxypent-1-enyl)-1*H*-indole-1-carboxylate (19): To an 8 mL borosilicate vial was added Catalyst **1** (0.04 mmol, 20.9 mg, 10 mol%), benzoquinone (0.82 mmol, 89.0 mg, 2 equiv.), dioxane (1.2 mL, 0.33 M), acetic acid (1.65 mmol, 96.1 mg, 4 equiv.),

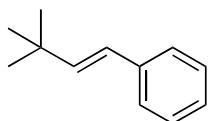
boric acid (0.82 mmol, 51.0 mg, 2 equiv.), 4-penten-1-ol (0.41 mmol, 35.0 mg, 1 equiv.), 1-(*tert*-butoxycarbonyl)-1*H*-indol-5-ylpotassium trifluoroborates (0.62 mmol, 200.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. The mixture was diluted with CH₂Cl₂ (50 ml) and rinsed with H₂O (50 ml). The aqueous layer was extracted with CH₂Cl₂ (50 ml) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 30% ethyl acetate/hexanes then further purified via silica chromatography (350 mL SiO₂) with 5% MeOH/CH₂Cl₂ as eluent to yield (*E*)-*tert*-butyl 5-(5-hydroxypent-1-enyl)-1*H*-indole-1-carboxylate as an oil. Run 1 (102.3 mg, 0.34 mmol, 82%, >20:1 *E*:*Z*, 16:1 int.:term., >20:1 int.:allyl.); run 2 (104.0 mg, 0.35 mmol, 84%, >20:1 *E*:*Z*, 16:1 int.:term., >20:1 int.:allyl.). **Average Yield = 83%.** ¹H NMR (500 MHz, CDCl₃) δ 8.06 (br d, *J* = 2.5 Hz, 1H), 7.57 (br d, *J* = 2.5 Hz, 1H), 7.51 (s, 1H), 7.35 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.54 (d, *J* = 3.5 Hz, 1H), 6.52 (d, *J* = 15 Hz, 1H), 6.24 (dt, *J* = 16, 6.5 Hz, 1H), 3.74 (t, *J* = 6 Hz, 2H), 2.35 (ap q, *J* = 7 Hz, 2H), 1.79 (ap p, *J* = 7 Hz, 2H), 1.68 (s, 9H), 1.40 (br s, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 149.91, 134.58, 132.64, 131.07, 130.82, 128.97, 126.48, 122.61, 118.55, 115.30, 107.57, 83.86, 62.71, 32.59, 29.60, 28.41. IR (neat, cm⁻¹) 3384.92, 3340.65, 3013.25, 2977.21, 2927.04, 2872.68, 1732.50. HRMS (ESI) *m/z* calculated for C₁₈H₂₄NO₃ [M+H]⁺: 302.1756, found 302.1753. Previously reported compound however no spectral data was given.¹⁶



(S,E)-1-(4-fluorophenyl)-5,6-dimethyl-5-styryl-4,5-dihydro-1*H*-indazole

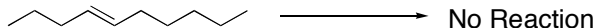
(21): To a 2 mL borosilicate vial was added Catalyst 1 (0.0099 mmol, 5.0 mg, 10 mol%), benzoquinone (0.18 mmol, 21.6 mg, 2 equiv.), dioxane (.3 mL, 0.33 M), acetic acid (0.4 mmol, 24.0 mg, 4 equiv.), (S)-1-(4-fluorophenyl)-5,6-dimethyl-5-vinyl-4,5-dihydro-1*H*-indazole (0.099 mmol, 26.5 mg, 1 equiv.), phenylboronic acid (0.2 mmol, 24.4 mg, 2 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at 45°C for 3 days. The mixture was diluted with methylene chloride (50 mL) and rinsed with 3M NaOH (50 mL). The aqueous layer was extracted with methylene chloride (50

mL) and the combined organic layers were dried over MgSO₄. After concentration, the crude product was purified via silica chromatography (125 mL SiO₂) with 15 % ether:petroleum ether as eluent to yield (S,E)-1-(4-fluorophenyl)-5,6-dimethyl-5-styryl-4,5-dihydro-1*H*-indazole as white solid. Run 1 (178.0 mg, 0.052 mmol, 52%, >20:1 *E*:*Z*); run 2 (187.0 mg, 0.054 mmol, 54%, >20:1 *E*:*Z*). **Average yield = 53%** ¹H NMR (500 MHz, CDCl₃) δ 7.50 (m, 2H), 7.44 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.20 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.33 (s, 1H), 6.24 (d, *J* = 16.0 Hz, 1H), 2.86 (d, *J* = 16.0 Hz, 1H), 2.73 (d, *J* = 16.0 Hz, 1H), 1.87 (d, *J* = 1.5 Hz, 3H), 1.35 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.66 (d, ¹J C-F = 245.1 Hz), 145.49, 138.01, 137.82, 137.55, 136.13, 135.28, 128.75, 127.53, 127.47, 126.46, 125.50 (d, ³J C-F = 8.3 Hz), 116.26 (d, ²J C-F = 22.8 Hz), 114.66, 112.30, 42.32, 34.30, 23.48, 20.87. ¹⁹F NMR (400 MHz, CDCl₃) δ -115.31. IR (neat, cm⁻¹): 3079.86, 3057.86, 3028.31, 2964.05, 2930.56, 2873.81, 2851.54, 2831.39, 1618.52, 1600.06. HRMS (ESI) *m/z* calculated for C₂₃H₂₂FN₂ [M+H]⁺: 345.1767, found 345.1776. [α]_D²⁵ = +95.0° (c = 0.38, CHCl₃, derived from 41.4% ee Hagemann's ester. See "Starting Material Synthesis for compound 21 on page S-15). Previously reported compound however no spectral data was given.¹⁷



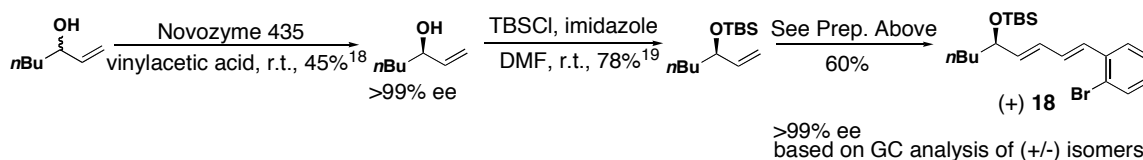
(E)-1-(3,3-dimethylbut-1-enyl)benzene (manuscript ref. 11): To a 40 mL borosilicate vial was added the following: catalyst 1 (0.1 mmol, 50.3 mg, 10 mol%), benzoquinone (2 mmol, 216.2 mg, 2 equiv.), 3,3-dimethyl-1-butene (1 mmol, 84.2 mg, 1 equiv.) in dioxane (3mL), acetic acid (4 mmol, 240 mg, 4 equiv.),

tributylphenyltin (1.5 mmol, 550.7 mg, 1.5 equiv.), and a stir bar. The mixture was stirred at room temperature for 4 hours. The mixture was diluted with 40 mL of sat. aq. NH_4Cl and extracted with hexanes (2 x 75 mL) and rinsed with 5% K_2CO_3 (1 x 75 mL). The organic layers were combined and dried over MgSO_4 . After concentration, the crude product was purified via silica gel chromatography (125 mL SiO_2) with 100% hexanes as eluent to yield (*E*)-1-(3,3-dimethylbut-1-enyl)benzene as a clear oil. Run 1 (0.097 g, 0.60 mmol, 60%, >20:1 *E:Z*); run 2 (0.096 g, 0.60 mmol, 60%, 20:1 *E:Z*). **Average yield = 60%.** ^1H NMR (400 MHz, CDCl_3) δ 7.39 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 6.34 (d, J = 16 Hz, 1H), 6.28 (d, J = 16 Hz, 1H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.0, 138.2, 128.7, 126.9, 126.2, 124.7, 33.6, 29.8. IR (neat, cm^{-1}) 3025.38, 2960.48, 2903.23, 2866.92. HRMS (CI) m/z calculated for $\text{C}_{12}\text{H}_{17}[\text{M}+\text{H}]^+$: 161.1330, found 161.1330.

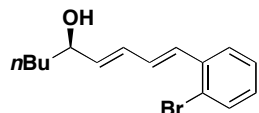


Internal Olefin (manuscript ref. 2c): To an 8 mL borosilicate vial was added catalyst **1** (0.1 mmol, 50.2 mg, 10 mol%), benzoquinone (2.0 mmol, 216.0 mg, 2 equiv.), dioxane (3 mL, 0.33 M), acetic acid (4.0 mmol, 240.0 mg, 4 equiv.), trans-4-decene (1.0 mmol, 140.0 mg, 1 equiv.), phenylboronic acid (1.5 mmol, 183.0 mg, 1.5 equiv.) and a stir bar sequentially under ambient conditions. The vial was capped and stirred at room temperature for 4 hours. Nitrobenzene was used as an internal standard. NMR analysis of the crude mixture shows no conversion of the starting material.

%EE DETERMINATION

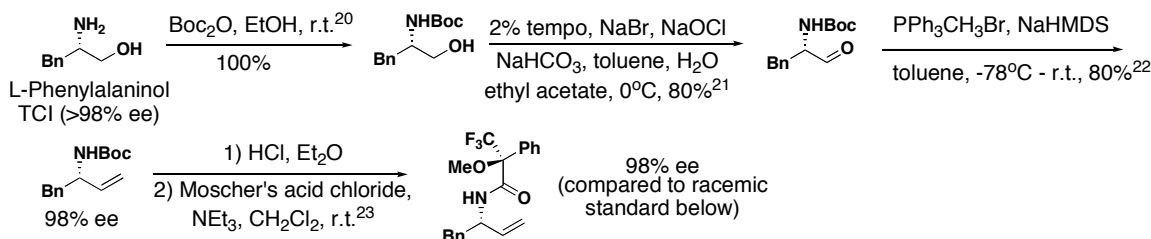


(*R*)-hept-1-en-3-yl acetate: Enantiopurity of the lipase resolved alcohol intermediate was determined by acetylation and chiral GC with a J&W Scientific Cyclodex-B, 30 meter, 0.25 mm diameter, 0.25 μm film column on a 5890 Hewlett Packard Series II GC, with a column flow rate 3.80 mL/min. Retention time of acetylated *R*-isomer was 8.187 min (*S*-isomer, 9.474 min) at an isothermal 65°C. Enantiopurity was determined to be >99%.

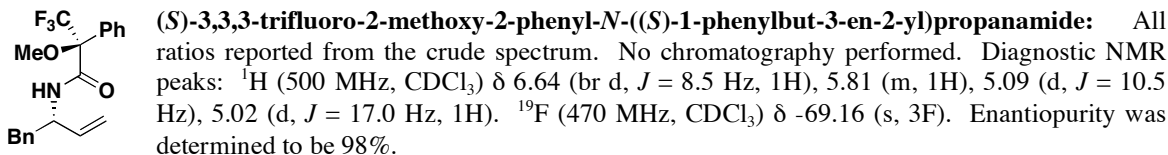
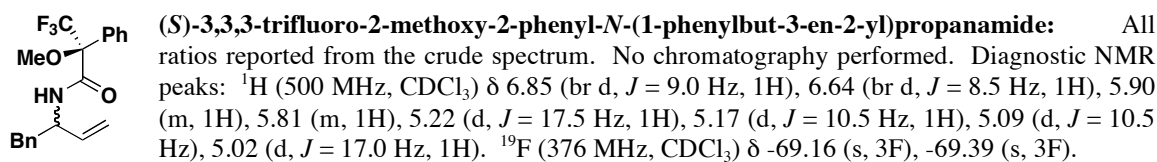
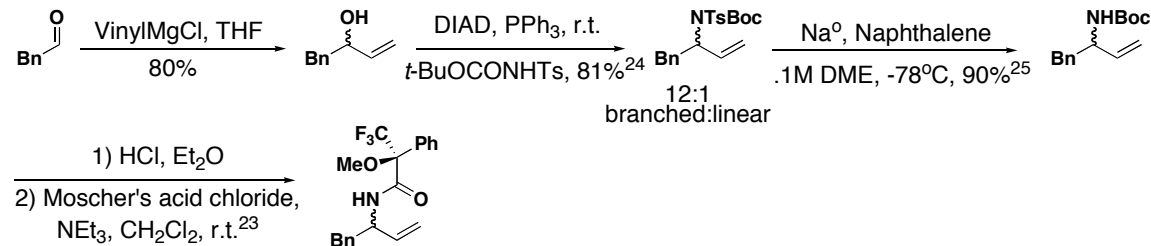


((*R*, 1*E*, 3*E*)-1-(2-bromophenyl)non-1,3-dien-5-yloxy)(*tert*-butyl)dimethylsilane: Enantiopurity of the product was determined by TBAF deprotection to the corresponding alcohol followed by HPLC analysis with a Daicel Chemical Industries, LTD chiral OD-H, 0.46 cm x 25 cm column. A flow rate of 1.0 mL/min and 45 psi with 4% *i*-PrOH/hexanes eluent gave the *R*-isomer at 15.109 min and the *S*-isomer at 26.766 min. Enantiopurity was determined to be >99%.

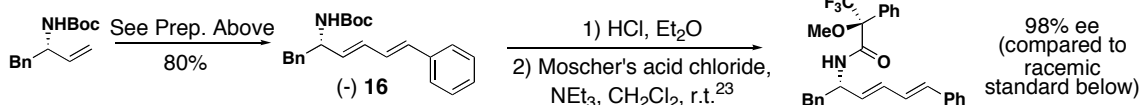
Chiral Starting Material



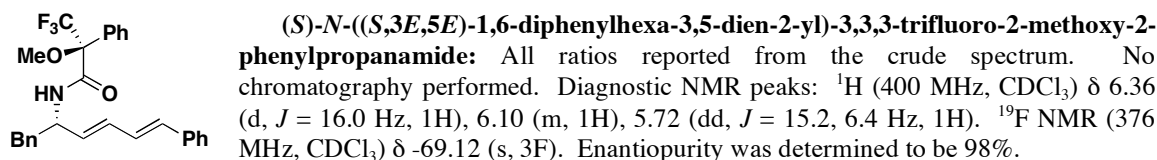
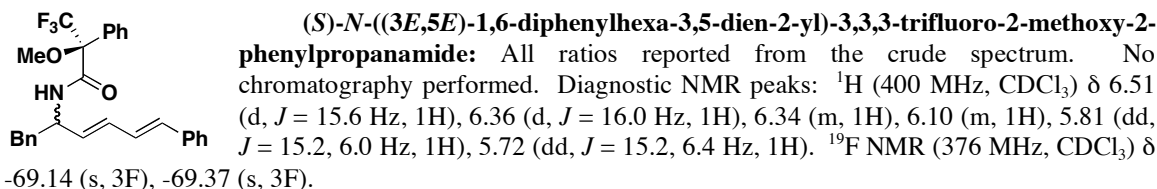
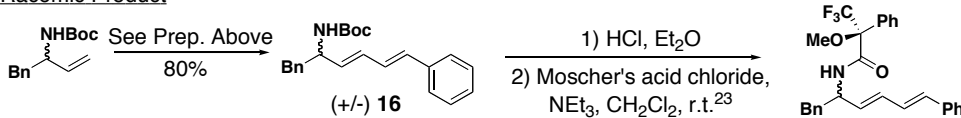
Racemic Starting Material

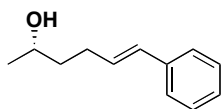


Chiral Product

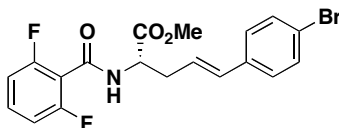


Racemic Product



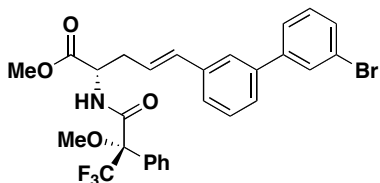
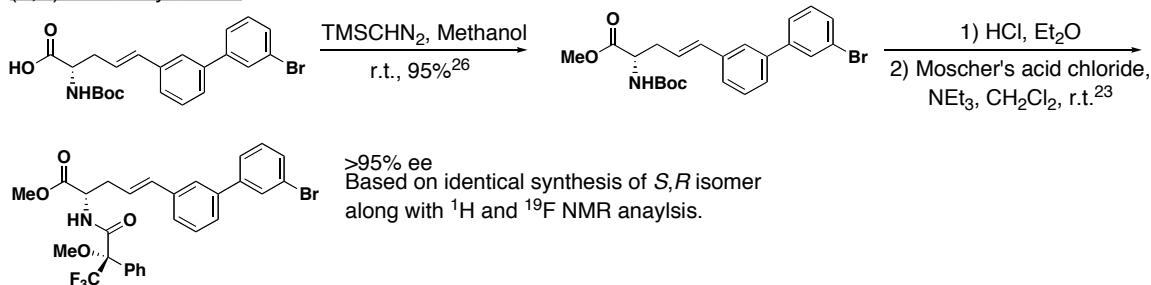


(*S,E*)-6-phenylhex-5-en-2-ol: Enantiopurity was determined by HPLC analysis with a Daicel Chemical Industries, LTD chiral OD-H, 0.46 cm x 25 cm column. A flow rate of 1.0 mL/min and 45 psi with 5% *i*-PrOH/hexanes eluent gave the *S*-isomer at 16.598 min and the *R*-isomer at 18.678 min. Enantiopurity was determined to be >99%.

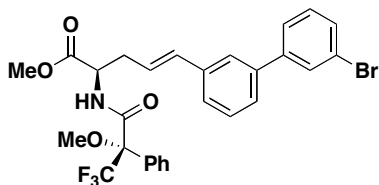


(*S,E*)-methyl 5-(4-bromophenyl)-2-(2,6-difluorobenzamido)pent-4-enoate: Enantiopurity was determined via Heck-arylation beginning from opposite enantiomers, followed by HPLC analysis with a Daicel Chemical Industries, LTD chiral OD-H, 0.46 cm x 25 cm column. A flow rate of 1.0 mL/min and 45 psi with 5.0% *i*-PrOH/hexanes eluent gave the *R*-isomer at 19.67 min and the *S*-isomer at 18.19 min. Enantiopurity was determined to be >99%.

(*S,S*)-Isomer Synthesis:



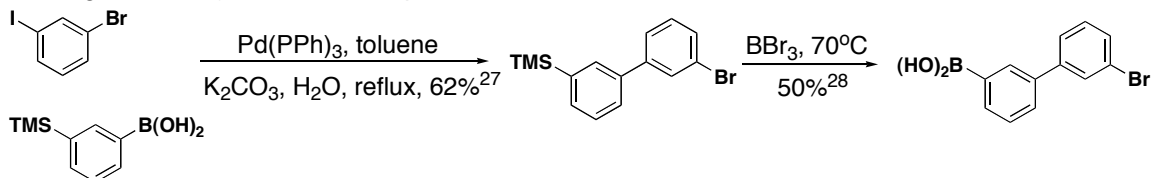
(*S,E*)-methyl 5-(phenyl-3-(bromo-3-phenyl))-2-((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanamido)pent-4-enoate: All ratios reported from the crude spectrum. No chromatography preformed. Diagnostic NMR peaks: ¹H (500 MHz, CDCl₃) δ 6.57 (d, *J* = 15.0 Hz, 1H), 6.15 (dt, *J* = 15.5, 7.5 Hz, 1H), 4.82 (ap q, *J* = 6.5 Hz, 1H). ¹⁹F NMR (470 MHz, CDCl₃) δ -69.36 (s, 3F). Enantiopurity was determined to be >95%.



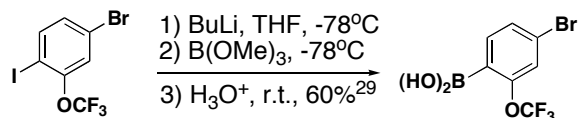
(*R,E*)-methyl 5-(phenyl-3-(bromo-3-phenyl))-2-((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanamido)pent-4-enoate: All ratios reported from the crude spectrum. No chromatography preformed. Diagnostic NMR peaks: ¹H (500 MHz, CDCl₃) δ 6.31 (d, *J* = 15.5 Hz, 1H), 6.01 (dt, *J* = 15.5, 7.5 Hz, 1H), 4.89 (m, 1H). ¹⁹F NMR (470 MHz, CDCl₃) δ -69.15 (s, 3F). Enantiopurity was determined to be >95%.

STARTING MATERIALS SYNTHESIS REFERENCES:

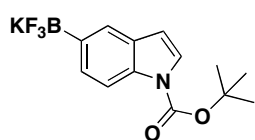
Starting Material Synthesis for Compound 6:



Starting Material Synthesis for Compound 13:

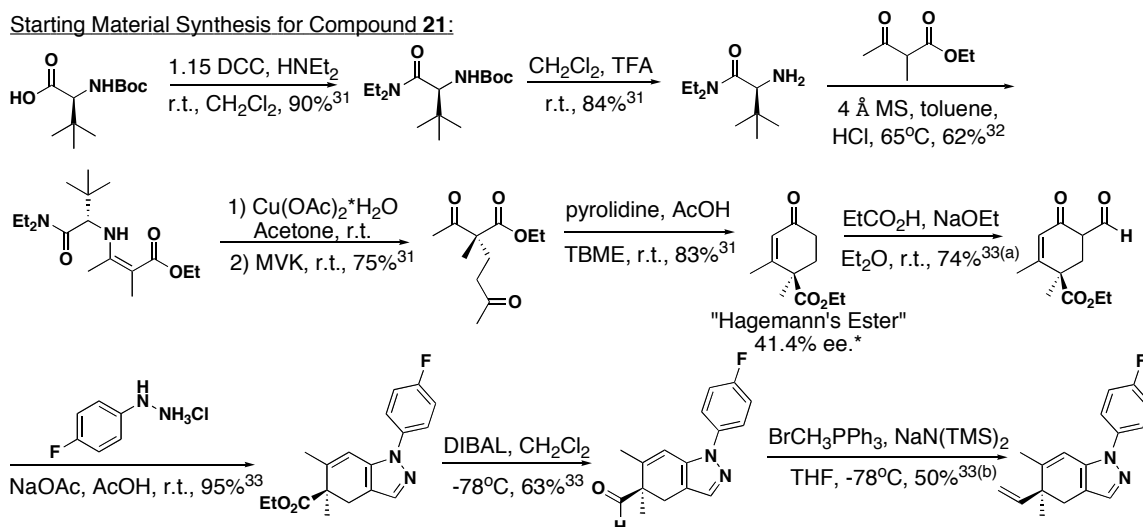


Starting Material Synthesis for Coupling Partner to Compound 19:



1-(tert-butoxycarbonyl)-1H-indol-5-ylpotassium trifluoroborate: A 50 mL round bottomed flask (RBF) was charged with a stir bar, *tert*-butyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole-1-carboxylate (0.805 g, 2.3 mmol), ether (4 mL), and methanol (7 mL). Aqueous 3M KF_2H (4.4 mL, 13.1 mmol) was added dropwise at room temperature. The mixture was stirred for 2 hours. The stir bar was removed and the solvents removed via rotary evaporation. Boiling acetone was added, and the hot solution was filtered. The filtrate was concentrated and dissolved in <20 mL of warm acetone. Petroleum ether (200 mL) was added to the mixture and the solution was undisturbed for 2 hours. The white precipitate was filtered off and rinsed with cold petroleum ether (50 mL) to award the title compound as a white solid (0.650 g, 2.0 mmol, 86%). ^1H NMR (500 MHz, d_6 -acetone) δ 7.92 (d, J = 8.0 Hz, 1H), 7.70 (s, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 4 Hz, 1H), 6.52 (d, J = 4 Hz, 1H), 1.68 (s, 9H). ^{19}F NMR (470 MHz, d_6 -acetone) δ -142.24. ^{13}C NMR (125 MHz, $(\text{CH}_3)_2\text{CO}$) δ 150.65, 135.13, 130.53, 129.30, 125.01, 124.81, 113.92, 108.59, 83.50, 28.30, (C *ipso* to B not observed). IR (neat, cm^{-1}): 3033.33, 2974.38, 2930.04, 1730.97, 992.97. HRMS (CI) m/z calculated for $\text{C}_{13}\text{H}_{14}\text{NO}_2\text{BF}_3\text{K}$ $[\text{M}+\text{H}]^+$: 284.1070, found 284.1071.³⁰

Starting Material Synthesis for Compound 21:



*Enantiomeric excess (%ee) was determined based off of optical rotation according to the equation $\%ee = (100 [\alpha]_{\text{obs}})/[\alpha]_{\text{lit. ref 31}}$, $\%ee = (100 [53.4]^{23}_{\text{D}})/[129]^{23}_{\text{D}} = 41.4\%$ ee.

Complete Manuscript Reference 8(a): Wu, Y. Q.; Wilkinson, D. E.; Limburg, D.; Li, J. H.; Sauer, H.; Ross, D.; Liang, S.; Spicer, D.; Valentine, H.; Fuller, M.; Guo, H.; Howorth, P.; Soni, R.; Chen, Y.; Steiner, J. P.; Hamilton, G. S. *J. Med. Chem.* **2002**, *45*, 3558.

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- ² Theissen, R. J. *J. Org. Chem.* **1971**, *36*, 752.
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