Supporting Information

Diastereoselective Additions of Chiral Vinylzinc Reagents to α -Chiral Aldehydes

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Experimental Procedures and ^1H NMR spectra for all compounds

Experimental Section

General Methods. All reactions were performed under an atmosphere of argon or nitrogen in flamed dried glassware. All reagents were used as purchased without further purification. Ether and toluene were dried by passing through activated alumina under argon gas. Proton and carbon magnetic resonance spectra were recorded on Varian Unity spectrometers at 300 and 500 MHz for proton and 75 and 125 MHz for carbon. Chemical shifts (δ) are reported in ppm referenced to CHCl_3 at 7.26 for proton and CDCl_3 at 77.00 for carbon. Peak multiplicities are abbreviated singlet (s); doublet (d); triplet (t); quartet (q); multiplet (m). Coupling constants are reported in hertz (Hz). Infrared spectra were recorded on a Nicolet 410 instrument using NaCl plates and the values are reported in cm^{-1} . Optical rotations were measured on a Perkin-Elmer 343 polarimeter with a sodium lamp (589 nm, D line) using a 1 dm, 1 mL quartz sample cell. Flash chromatography was performed on silica gel using Biotage Flash 12+ and Flash 40+ columns. Analytical thin layer chromatography (TLC) was run on Merck silica gel 60 F254 precoated plates (250 μm thickness).

(E, 5R/S 6R, 7R, 8R, 9R)-9,11-Di(t-Butyldimethylsiloxy)-6,8,9-trimethyl-7-(p-methoxybenzyloxy)-3-undecen-5-ol (3). **A. Addition of the Vinylolithium Reagent 2a:** To a solution of vinyl iodide **5** (0.091 g, 0.202 mmol) in Et_2O (2 mL) at -78°C was added $t\text{-BuLi}$ (0.245 mL, 1.7 M in pentanes, 0.415 mmol). The reaction mixture was warmed to 0°C for 1 h and then recooled to -78°C . Aldehyde **1** (0.042 g, 0.078 mmol) was then added dropwise in a small amount of Et_2O . After stirring at -78°C for 1 h the mixture was allowed to slowly warm to room temperature overnight. The reaction was quenched by the addition of aqueous NH_4Cl . The aqueous layer was extracted with Et_2O and the combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 2.5% EtOAc /hexanes) to afford the two diastereomeric alcohols **3** as a light yellow oil (0.042 g, 63%; 1:1 mixture of diastereomers): ^1H NMR (CDCl_3): High R_f (**anti isomer**): δ 7.67 (m, 4H), 7.41 (m, 6H), 7.22 (d, $J = 8.6$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 5.19 (d, $J = 8.5$ Hz, 1H), 4.67 (d, $J = 2.1$ Hz, 2H), 4.23 (m, 2H), 3.93 (m, 1H), 3.82 (s, 3H), 3.74 (t, $J = 7.3$ Hz, 2H), 3.62 (t, $J = 7.7$ Hz, 2H), 2.28 (t, $J = 7.1$ Hz, 2H), 1.62-1.84 (m, 4H), 1.59, (s, 3H), 1.06 (s, 9H), 0.92 (s, 9H), 0.86 (s, 9H), 0.78 (d, $J = \text{Hz}$, 3H), 0.74 (d, $J = \text{Hz}$, 3H), 0.07-0.11 (m, 12H); Low R_f (**syn isomer**): δ 7.68 (m, 4H), 7.41 (m, 6H), 7.25 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.32 (d, $J = 8.8$ Hz, 1H), 4.31-4.58 (m, 4H), 4.18 (t, $J = 5.1$ Hz, 1H), 4.10 (d, $J = 9.1$ Hz, 1H), 3.97 (d, $J = 7.5$ Hz, 1H), 3.78 (s, 3H), 3.74 (t, $J = 7.7$

Hz, 2H), 3.62 (t, $J = 7.7$ Hz, 2H), 2.28 (m, 2H), 1.62-1.84 (m, 3H), 1.65 (s, 3H), 1.06 (s, 9H), 0.98 (d, $J =$ Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.78 (d, $J =$ Hz, 3H), 0.07-0.11 (m, 12H).

B. Addition of the Vinyl Grignard Reagent 2b: To a solution of vinyl iodide **5** (0.127 g, 0.281 mmol) in Et₂O (3 mL) at -78 °C was added t-BuLi (0.34 mL, 1.70 M in pentane, 0.57 mmol) rapidly. The mixture was stirred for 1 h and then MgBr₂ (0.059 g, 0.320 mmol) was added in one portion. The mixture was warmed to 0 °C for 1 h and then recooled to -78 °C. Aldehyde **1** (0.101 g, 0.188 mmol) was then added dropwise in a small amount of Et₂O. After stirring at -78 °C for 1 h the mixture was allowed to slowly warm to room temperature overnight. The reaction was quenched by the addition of NH₄Cl (aq.). The aqueous layer was extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 2.5% EtOAc/hexanes) to afford alcohol **3** (0.103 g, 63%; 75 : 25 mixture of anti and syn isomers) as a colorless oil.

C.Addition of the Vinylaluminum Reagent 2c: To a magnetically stirred solution of zirconocene dichloride (0.015 g, 0.05 mmol) in CH₂Cl₂ (1 mL) at -20 °C was added trimethylaluminum (2M in hexanes, 0.230 mL, 0.46 mmol) dropwise. After 10 min water (5 μ L, 0.28 mmol) was added dropwise. **Caution: Exothermic reaction!** After an additional 10 min, 1-(t-butyldiphenylsiloxy)-3-butyne (0.046 g, 0.15 mmol) in CH₂Cl₂ (0.50 mL) was added slowly. The reaction mixture was warmed to rt and stirred for 1 h. The mixture was cooled to -78 °C and aldehyde **1** (0.042 g, 0.08 mmol) in ether (1 mL) was added dropwise. After stirring at -78 °C for 1 h the mixture was allowed to slowly warm to room temperature overnight. The reaction was quenched by the addition of tartaric acid (aq.). The resulting biphasic mixture was filtered through Celite and extracted with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 2.5% EtOAc/hexanes) to afford alcohol **3** (0.043 g, 63%; 75:25 mixture of anti and syn isomers) as a colorless oil.

(E) 1-(t- Butyldiphenylsiloxy)-4-iodo-3-methyl-3-butene (5). To a solution of vinyl iodide **15** (1.51 g, 7.12 mmol) in DMF (5 mL) at 0 °C was added imidazole (0.603 g, 8.86 mmol) followed by TBDPSCl (2.0 mL, 7.7 mmol). The reaction mixture was allowed to warm to rt for 3 h and then was quenched by the addition of aqueous NaHCO₃. The aqueous layer was extracted with pentanes and the combined organic extracts were washed with water, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed (2.5% EtOAc-hexanes) to afford vinyl iodide **5** as a light yellow oil (3.11 g, 97%): ¹H NMR (CDCl₃): δ 7.68 (m, 4H), 7.40 (m, 6H), 5.90 (s, 1H), 3.72 (m, 2H), 2.43 (t, $J = 5.0$ Hz, 2H), 1.77 (s, 3H), 1.06 (s, 9H).

(E) 1-(*t*-Butyldimethylsiloxy)-4-iodo-3-methyl-3-butene (6). To a solution of vinyl iodide **15** (4.48 g, 21.13 mmol) in DMF (15 mL) at 0 °C was added imidazole (2.16 g, 31.69 mmol) followed by TBSCl (3.49 g, 23.24 mmol). The mixture was allowed to warm to rt for 1 h and then was quenched by the addition of aqueous NaHCO₃. The aqueous layer was extracted with pentanes and then the combined organic extracts were washed with water, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes) to afford vinyl iodide **6** as a clear oil (6.68 g, 97%): *R*_f 0.25 (hexanes); IR (film) 2942, 2855, 1466 cm⁻¹; ¹H NMR (CDCl₃): δ 6.02 (q, *J* = 1.2 Hz, 1H), 3.68 (t, *J* = 6.6 Hz, 2H), 2.41 (td, *J* = 0.9, 6.3 Hz, 2H), 1.89 (d, *J* = 0.9 Hz, 3H), 0.88 (s, 9H), 0.035 (s, 6H); ¹³C NMR (CDCl₃): δ 144.97, 76.37, 61.23, 42.54, 25.84, 24.21, 18.16, -5.37.

(2S,3R,4E) 1,7-Bis-(*tert*-butyldimethylsilyloxy)-2,5-dimethyl-4-hepten-3-ol (10a). The standard procedure (see **11a**) for vinyl iodide lithiation was employed with vinyl iodide **6** (0.298 g, 0.915 mmol), aldehyde **9a** (0.074 g, 0.366 mmol), *t*-BuLi (1.7M pentane, 1.2 mL, 2.04 mmol), ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol), and the lithium alkoxide of (1*R*, 2*S*)-*N*-methylephedrine (0.17 M, 5.88 mL, 1.00 mmol) affording alcohol **10a** (0.103 g, 70% yield, 92 : 8 mixture of anti and syn diastereomers) as a clear oil: *R*_f 0.7 (15% EtOAc : hexanes); [α]_D²⁰ +22.0 (c 1.2 CHCl₃); IR (film) 3432 (br), 2951, 1474 cm⁻¹; ¹H NMR (CDCl₃): δ 5.21 (dd, *J* = 1.5 Hz, 9 Hz, 1H), 4.29 (t, *J* = 8.5 Hz, 1H), 3.79 (m, 2H), 3.70 (t, *J* = 7.5 Hz, 2H), 3.61 (m, 1H), 2.62 (m, 2H), 1.70 (d, *J* = 1.5 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.76 (d, *J* = 7 Hz, 3H), 0.09 (s, 6H), 0.05 (s, 6H); ¹³C NMR (CDCl₃): δ 135.71, 128.38, 73.33, 68.36, 62.20, 43.00, 40.53, 29.69, 25.94, 25.81, 17.15, 13.11, -5.31, -5.57, -5.64.

(*S*)-*O*-Methyl Mandelic Ester of 10a. Alcohol **10a** (0.012 g, 0.030 mmol) was taken up in 1 mL of CH₂Cl₂. (*S*)-*O*-Methyl mandelic acid (0.010 g, 0.060 mmol), DCC (0.013 g, 0.063 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.005 g, 0.009 mmol, 30%) as a clear oil: ¹H NMR (CDCl₃): δ 7.31-7.42 (m, 5H), 5.51 (m, 1H), 4.93 (dd, *J* = 1.0 Hz, 9.5 Hz, 1H), 4.72 (s, 1H), 3.55 (m, 2H), 3.45 (m, 1H), 3.42 (s, 3H), 3.38 (m, 1H), 2.14 (t, *J* = 7 Hz, 2H), 1.90 (m, 1H), 1.67 (d, *J* = 1.5 Hz, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.02 (s, 6H), -0.02 (d, *J* = 9 Hz, 6H).

(*R*)-*O*-Methyl Mandelic Ester of 10a. Alcohol **10a** (0.012 g, 0.030 mmol) was taken up in 1 mL of CH₂Cl₂. (*R*)-*O*-Methyl mandelic acid (0.010 g, 0.060 mmol), DCC (0.013 g, 0.063 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.012 g, 0.022 mmol, 73%) as a clear oil: ¹H NMR (CDCl₃): δ 7.32-7.45 (m, 5H), 5.50 (m, 1H), 5.10 (dd, *J* = 1.0 Hz, 8.5 Hz, 1H), 4.69 (s, 1H), 3.66 (t, *J* = 6.5 Hz, 2H), 3.38 (s, 3H), 3.25 (m, 1H), 3.11 (m, 1H), 2.22 (m, 2H), 1.76 (m, 1H), 1.75 (d, *J* = 1.0 Hz, 3H), 0.89 (s, 9H), 0.82 (s, 9H), 0.71 (d, *J* = 7.0 Hz, 3H), 0.04 (s, 6H), -0.10 (d, *J* = 12 Hz, 6H).

(*E*, 2*S*, 3*S*)-1,7-Bis-(tert-butyldimethylsilyloxy)-2,5-dimethyl-4-hepten-3-ol (11a**). A. Standard**

Procedure for Lithiation/Transmetalation of Vinyl Iodide 6: To a magnetically stirred solution of vinyl iodide **6** (0.298 g, 0.914 mmol) in Et₂O (2 mL) at -78 °C was added *t*-BuLi (1.7M in pentane, 1.2 mL, 2.04 mmol). The mixture was stirred for 15 min and then a solution of ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol, prepared by dissolving 5 g of commercial ZnBr₂ in 25 mL of Et₂O with sonication) was added dropwise by syringe. The mixture was warmed to 0 °C and stirred for 1 h. Then a solution of the lithium alkoxide of (1*S*, 2*R*)-*N*-methylephedrine (0.20M in toluene, 5.0 mL, 1.00 mmol) was added dropwise. The resulting mixture was stirred for 1 h at 0 °C before aldehyde **9a** (0.076 g, 0.376 mmol) in toluene (1 mL) was added dropwise. The reaction mixture was stirred for 1 h and then was quenched by the addition of NH₄Cl. The aqueous layer was extracted with ether and the combined extracts were washed with Na₂S₂O₃, brine, dried over MgSO₄, concentrated under vacuum and chromatographed on silica gel (hexanes to 2.5% EtOAc-hexanes) to afford alcohol **11a** as a light yellow oil (0.106 g, 70%, 92 : 8 mixture of syn and anti diastereomers): *R*_f 0.70 (15% EtOAc : Hexanes); [α]_D²⁰ +3.9 (c 0.35 CHCl₃); IR (film) 3484 (br), 2925, 1466 cm⁻¹; ¹H NMR (CDCl₃): δ 5.30 (d, *J* = 9 Hz, 1H), 4.48 (dd, *J* = 3.3 Hz, 8.7 Hz, 1H), 3.668 (m, 4H), 2.24 (m, 2H), 1.88 (m, 1H), 1.68 (d, *J* = 1.2 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.83 (d, *J* = 7.5 Hz, 3H), 0.08 (s, 6H), 0.05 (s, 6H).

B. Without *N*-Methylephedrine: The above procedure was employed with vinyl iodide **6** (0.300 g, 0.920 mmol), aldehyde **9a** (0.073 g, 0.361 mmol), *t*-BuLi (1.7M pentane, 1.2 mL, 2.04 mmol), and ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol) affording alcohol **11a** (0.108 g, 74% yield, 55 : 45 mixture of syn and anti

diastereomers **11a** and **10a**) as a clear oil. All analytical data was consistent with the N-methylephedrine-directed addition products

(E, 2S, 3R)-1-Benzyloxy-7-(tert-butyldimethylsilyloxy)-2,5-dimethyl-4-hepten-3-ol (10b). **A. With (1R, 2S)-N-Methylephedrine** The standard procedure for lithiation was employed with vinyl iodide **6** (0.150 g, 0.459 mmol) aldehyde **9b** (0.033 g, 0.185 mmol), t-BuLi (1.7M pentane, 0.60 mL, 1.02 mmol), ZnBr₂ (0.89M in Et₂O, 0.55 mL, 0.49 mmol), and the lithium alkoxide of (1R, 2S)-N-methylephedrine (0.17 M, 2.95 mL, 0.50 mmol) affording alcohol **10b** (0.048 g, 68% yield, 95 : 5 mixture of anti and syn diastereomers) as a clear oil: R_f 0.45 (15% EtOAc : hexanes); [α]_D²⁰ +21.0 (c 0.83 CHCl₃); IR (film) 3458 (br), 2916 cm⁻¹; ¹H NMR (CDCl₃): δ 7.26-7.37 (m, 5H), 5.20 (d, J = 9.5 Hz, 1H), 4.54 (s, 2H), 4.30 (t, J = 8 Hz, 1H), 3.69 (m, 2H), 3.60 (q, J = 4.5 Hz, 1H), 3.49 (t, J = 8.5 Hz, 1H), 2.24 (m, 2H), 1.90 (m, 1H), 1.70 (s, 3H), 0.89 (s, 9H), 0.82 (d, J = 7 Hz, H); ¹³C NMR (CDCl₃): δ 137.84, 136.07, 128.42, 128.01, 127.70, 127.63, 75.01, 73.38, 72.67, 62.08, 42.97, 39.18, 25.73, 18.30, 17.13, 13.35, -5.31.

B. Without N-Methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.149 g, 0.456 mmol), aldehyde **9b** (0.036 g, 0.202 mmol), and ZnBr₂ (0.89M in Et₂O, 0.55 mL, 0.49 mmol) affording alcohol **10b** (0.059 g, 77% yield, 75 : 25 mixture of anti and syn diastereomers) as a clear oil. All analytical data was consistent with the N-methylephedrine-directed cases

C. With (1S, 2R)-N-methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.151 g, 0.464 mmol), aldehyde **9b** (0.035 g, 0.196 mmol), t-BuLi (1.7M pentane, 0.60 mL, 1.02 mmol), ZnBr₂ (0.89M in Et₂O, 0.55 mL, 0.49 mmol), and the lithium alkoxide of (1S, 2R)-N-methylephedrine (0.20 M, 2.50 mL, 0.50 mmol) affording alcohol **10b** (0.052 g, 70% yield, 75:25 mixture of anti and syn diastereomers) as a clear oil: R_f 0.45 (15% EtOAc : hexanes); ¹H NMR (CDCl₃) (**Boldface resonances for 11b**): δ 7.26-7.37 (m, 5H), **5.24 (d, J = 9.5 Hz, 1H)**, 5.20 (d, J = 9.5 Hz, 1H), 4.54 (s, 2H), **4.50 (s, 2H)**, 4.30 (t, J = 8 Hz, 1H), 3.69 (m, 2H), 3.60 (q, J = 4.5 Hz, 1H), 3.49 (t, J = 8.5 Hz, 1H), 2.24 (m, 2H), **2.10 (m, 1H)**, 1.90 (m, 1H), 1.70 (s, 3H), **1.67 (s, 3H)**, 0.89 (s, 9H), 0.82 (d, J = 7 Hz, H)

(S)-O-Methyl Mandelic Ester of 10b. Alcohol **10b** (0.014 g, 0.036 mmol) was taken up in 1 mL of CH₂Cl₂. (S)-O-Methyl mandelic acid (0.012 g, 0.072 mmol), DCC (0.015 g, 0.072 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the

mandelic ester (0.013 g, 0.025 mmol, 68%) as a clear oil: ^1H NMR (CDCl_3): δ 7.25-7.47 (m, 10H), 5.54 (m, 1H), 4.95 (d, J = 9 Hz, 1H), 4.36 (s, 2H), 3.55 (m, 2H), 3.49 (m, 2H), 3.40 (s, 3H), 3.30 (m, 1H), 3.22 (m, 1H), 2.14 (t, J = 7 Hz, 2H), 1.67 (d, J = 1 Hz, 3H), 0.89 (d, J = 7 Hz, 3H), 0.85 (s, 9H), 0.02 (s, 6H).

(*R*)-*O*-Methyl Mandelic Ester of 10b. Alcohol **10b** (0.014 g, 0.036 mmol) was taken up in 1 mL of CH_2Cl_2 . (*R*)-*O*-Methyl mandelic acid (0.012 g, 0.072 mmol), DCC (0.015 g, 0.072 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et_2O -hexanes) to afford the mandelic ester (0.015 g, 0.028 mmol, 79%) as a clear oil: ^1H NMR (CDCl_3): δ 7.21-7.44 (m, 10H), 5.52 (m, 1H), 5.12 (dd, J = 1.5 Hz, 9.5 Hz, 1H), 4.69 (s, 1H), 4.16 (s, 2H), 3.66 (t, J = 8.0 Hz, 2H), 3.37 (s, 3H), 3.07 (m, 1H), 2.96 (m, 1H), 2.23 (m, 2H), 1.92 (m, 1H), 1.75 (d, J = 1.5 Hz, 3H), 0.89 (s, 9H), 0.76 (d, J = 6.5 Hz, 3H), 0.04 (s, 6H).

(*E*, 2*S*, 3*R*)-2,7-Bis-(tert-Butyldimethylsilyloxy)-5-methyl-4-hepten-3-ol (13a). A. With (1*R*, 2*S*)-*N*-methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.298 g, 0.915 mmol), aldehyde **12a** (0.076 g, 0.376 mmol), *t*-BuLi (1.7M pentane, 1.2 mL, 2.04 mmol), ZnBr_2 (0.89M in Et_2O , 1.10 mL, 1.00 mmol), and the lithium alkoxide of (1*R*, 2*S*)-*N*-methylephedrine (0.20 M, 5.00 mL, 1.00 mmol) affording alcohol **13a** (0.118 g, 75% yield, 95 : 5 mixture of anti and syn diastereomers) as a clear oil: R_f 0.70 (7:1 hexanes: EtOAc); $[\alpha]_D^{20}$ +7.6 (c 1.15 CHCl_3); IR (film) 3441 (br), 2916 cm^{-1} ; ^1H NMR (CDCl_3): δ 5.19 (dd, J = 8.2 Hz, 1.5 Hz, 1H), 4.28 (dd, J = 8.5 Hz, 3.5 Hz, 1H), 3.80 (m, 1H), 3.70 (t, J = 7.5 Hz, 2H), 2.24 (m, 2H), 1.69 (d, J = 1.5 Hz, 3H), 1.07 (d, J = 3.5 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.08 (s, 6H) 0.04 (s, 6H); ^{13}C NMR (CDCl_3): δ 136.77, 125.02, 72.28, 71.22, 62.01, 42.97, 25.92, 25.80, 18.04, 17.48, 17.21, -4.52, -4.83, -5.38.

B. Without *N*-methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.299 g, 0.917 mmol), aldehyde **12a** (0.070 g, 0.372 mmol), and ZnBr_2 (0.89M in Et_2O , 1.10 mL, 1.00 mmol) affording alcohol **13a** (0.116 g, 80% yield, 65:35 mixture of anti and syn diastereomers) as a clear oil. All analytical data was consistent with the *N*-methylephedrine directed cases.

(*E*, 2*S*, 3*S*)-2,7-Bis-(*tert*-Butyldimethylsilyloxy)-5-methyl-4-hepten-3-ol (14a**).** The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.304 g, 0.932 mmol), aldehyde **12a** (0.069 g, 0.364 mmol), *t*-BuLi (1.7M in pentane, 1.2 mL, 2.04 mmol), ZnBr₂ (0.89M in Et₂O, 1.13 mL, 1.01 mmol), and the lithium alkoxide of (1*S*, 2*R*)-*N*-methylephedrine (0.20 M, 5.00 mL, 1.00 mmol) affording alcohol **14a** (0.103 g, 72% yield, 95 : 5 mixture of syn and anti diastereomers) as a clear oil: *R*_f 0.70 (7:1 hexanes:EtOAc); [α]_D²⁰ +25.8 (c 1.27 CHCl₃); IR (film) 3423 (br), 2925 cm⁻¹; ¹H NMR (CDCl₃): δ 5.13 (dd, *J* = 9 Hz, 1.2 Hz, 1H), 4.04 (t, *J* = 7.8 Hz, 1H), 3.69 (t, *J* = 6.9 Hz, 2H), 3.60 (m, 1H), 2.23 (m, 2H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.08 (d, *J* = 6 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.09 (s, 6H), 0.04 (s, 6H); ¹³C NMR (CDCl₃): δ 138.00, 125.50, 73.03, 72.75, 61.99, 42.98, 25.90, 25.80, 18.27, 18.01, 17.47, -4.19, -4.86, -5.35.

(*R*)-*O*-Methyl Mandelic Ester of **14a.** Alcohol **14a** (0.01 g, 0.026 mmol) was taken up in 1 mL of CH₂Cl₂. (*R*)-*O*-Methyl mandelic acid (0.009 g, 0.054 mmol), DCC (0.011 g, 0.053 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.008 g, 0.015 mmol, 57%) as a clear oil: ¹H NMR (CDCl₃): δ 7.28-7.46 (m, 5H), 5.40 (q, *J* = 5.1 Hz, 1H), 4.81 (dd, *J* = 1.2 Hz, 9.5 Hz, 1H), 4.73 (s, 1H), 3.76 (m, 1H), 3.61 (m, 1H), 3.48 (m, 2H), 3.42 (s, 3H), 2.09 (t, *J* = 7.2 Hz, 2H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.06 (d, *J* = 5.7 Hz), 0.89 (s, 9H), 0.87 (s, 9H), 0.08 (s, 6H), 0.02 (s, 6H).

(*S*)-*O*-Methyl Mandelic Ester of **14a.** Alcohol **14a** (0.010 g, 0.026 mmol) was taken up in 1 mL of CH₂Cl₂. (*S*)-*O*-Methyl mandelic acid (0.009 g, 0.054 mmol), DCC (0.011 g, 0.053 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.009 g, 0.017 mmol, 64%) as a clear oil: ¹H NMR (CDCl₃): δ 7.31-7.46 (m, 5H), 5.40 (q, *J* = 4.8 Hz, 1H), 5.19 (d, *J* = 1.2 Hz, 9.6 Hz, 1H), 4.73 (s, 1H), 3.75 (m, 1H), 3.66 (t, *J* = 7.0 Hz, 2H), 3.38 (s, 3H), 2.23 (t, *J* = 6.9 Hz, 2H), 1.74 (d, *J* = 1.2 Hz, 3H), 0.89 (s, 9H), 0.84 (d, *J* = 6.6 Hz), 0.83 (s, 9H), 0.05 (s, 6H), -0.04 (d, *J* = 13.2 Hz, 6H).

(E, 2S, 3S)-2-Benzyloxy-7-(tert-Butyldimethylsilyloxy)-5-methyl-4-hepten-3-ol (14b). **A. With (1R, 2S)-N-methylephedrine:** The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.298 g, 0.915 mmol), aldehyde **12b** (0.062 g, 0.378 mmol), t-BuLi (1.7M pentane, 1.2 mL, 2.04 mmol), ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol), and the lithium alkoxide of (1R, 2S)-N-methylephedrine (0.20 M, 5.00 mL, 1.00 mmol) affording alcohol **14b** (0.98 g, 72% yield, 85:15 mixture of syn and anti diastereomers) as a clear oil: R_f 0.50 (15% EtOAc : hexanes); ¹H NMR (CDCl₃) (**Boldface resonances for 13b**): δ 7.28-7.44 (m, 5H), **5.24 (d, J = 9.2 Hz, 1H)**, 5.16 (d, J = 9.2 Hz, 1H), 4.57 (dd, J = 66.3 Hz, 11.4 Hz, 2H), 4.22 (t, J = 8.4 Hz, 1H), **3.90 (m, 1H)**, 3.70 (t, J = 6.9 Hz, 2H), **3.48 (m, 1H)**, 3.40 (m, 1H), 2.25 (m, 2H), 1.74 (d, J = 1.5 Hz, 3H), **1.66 (d, J = 1.5 Hz, 3H)**, 1.14 (d, J = 3.9 Hz, 3H), 0.89 (s, 9H), 0.051 (s, 6H)

B. With (1S, 2R)-N-methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.304 g, 0.932 mmol), aldehyde **12b** (0.059 g, 0.360 mmol), t-BuLi (1.7M pentane, 1.2 mL, 2.04 mmol), ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol), and the lithium alkoxide of (1S, 2R)-N-methylephedrine (0.20 M, 5.00 mL, 1.00 mmol) affording alcohol **14b** (0.100 g, 76% yield, 95 : 5 mixture of syn and anti diastereomers) as a clear oil: R_f 0.50 (15% EtOAc : hexanes); [α]_D²⁰ +31.7 (c 1.97 CHCl₃); IR (film) 3466 (br), 2925 cm⁻¹; ¹H NMR (CDCl₃): δ 7.28-7.44 (m, 5H), 5.16 (d, J = 9.2 Hz, 1H), 4.57 (dd, J = 66.3 Hz, 11.4 Hz, 2H), 4.22 (t, J = 8.4 Hz, 1H), 3.70 (t, J = 6.9 Hz, 2H), 3.40 (m, 1H), 2.25 (m, 2H), 1.74 (d, J = 1.5 Hz, 3H), 1.14 (d, J = 3.9 Hz, 3H), 0.89 (s, 9H), 0.051 (s, 6H); ¹³C NMR (CDCl₃): δ 138.56, 138.18, 128.42, 127.76, 125.01, 79.16, 72.06, 71.13, 61.89, 42.95, 25.88, 18.25, 17.44, 15.34, -5.36.

C. Without N-methylephedrine: The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **6** (0.302 g, 0.925 mmol), ZnBr₂ (0.89M in Et₂O, 1.10 mL, 0.979 mmol) and aldehyde **12b** (0.60 g, 0.365 mmol), affording alcohol **14b** (0.110 g, 82% yield, 95 : 5 mixture of syn and anti diastereomers) as a clear oil. All analytical data was consistent with the N-methylephedrine directed cases.

(R)-O-Methyl Mandelic Ester of 14b. Alcohol **14b** (0.017 g, 0.046 mmol) was taken up in 1 mL of CH₂Cl₂. (R)-O-Methyl mandelic acid (0.016 g, 0.092 mmol), DCC (0.019 g, 0.092 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.017g, 0.033 mmol, 71%) as a clear oil: ¹H NMR (CDCl₃): δ 7.26-7.41 (m, 10H), 5.58 (m,

1H), 5.00 (d, J = 9.5 Hz, 1H), 4.73 (s, 1H), 4.54 (dd, J = 12 Hz, 48.5 Hz, 2H), 3.61 (m, 1H), 3.55 (m, 2H), 3.40 (s, 3H), 2.14 (t, J = 7 Hz, 2H), 1.66 (d, J = 1 Hz, 3H), 1.11 (d, J = 6.5 Hz), 0.86 (s, 9H), 0.02 (s, 6H).

(S)-O-Methyl Mandelic Ester of 14b. Alcohol **14b** (0.017 g, 0.046 mmol) was taken up in 1 mL of CH₂Cl₂. (S)-O-Methyl mandelic acid (0.016 g, 0.092 mmol), DCC (0.019 g, 0.092 mmol), and DMAP (a few crystals) were added and the mixture was stirred for 45 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (hexanes to 10% Et₂O-hexanes) to afford the mandelic ester (0.019g, 0.038 mmol, 83%) as a clear oil: ¹H NMR (CDCl₃): δ 7.13-7.45 (m, 10H), 5.59 (m, 1H), 5.17 (d, J = 9.5 Hz, 1H), 4.75 (s, 1H), 4.27 (dd, J = 12 Hz, 48 Hz, 2H), 3.66 (m, 2H), 3.47 (m, 1H), 3.38 (s, 3H), 2.23 (t, J = 7 Hz, 2H), 1.76 (d, J = 1.5 Hz, 3H), 0.93 (d, J = 6.5 Hz), 0.88 (s, 9H), 0.04 (s, 6H).

(E)-4-Iodo-3-methyl-3-buten-1-ol (15). To a magnetically stirred solution of zirconocene dichloride (1.7 g, 5.9 mmol) in CH₂Cl₂ (100 mL) at -20 °C was added trimethylaluminium (2M in hexanes, 41 mL, 82 mmol) dropwise. After 10 min, water (740 uL, 41.1 mmol) was added dropwise. **Caution: Exothermic reaction!** After an additional 10 min, 3-buten-1-ol (2 mL, 26.4 mmol) (pretreated with trimethyl aluminium (2M in hexanes, 4 mL, 8 mmol) in CH₂Cl₂ (20 mL) at 0 °C) was added slowly. The reaction mixture was allowed to warm to rt and was stirred for 2.5 h. The mixture was then cooled to -20 °C and I₂ (8.06 g, 31.8mmol) in ether (60 mL) was added dropwise. The mixture was allowed to warm to rt and was stirred for 2 h. The reaction was quenched by the careful addition of water. The resulting biphasic mixture was filtered through Celite, washed with Na₂S₂O₃ and brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was chromatographed on silica gel (20% ether-hexanes) to afford vinyl iodide **15** as a light yellow oil (4.48 g, 80%): R_f 0.25 (15% EtOAc-hexanes); IR (film) 3344 (br), 2925 cm⁻¹; ¹H NMR (CDCl₃): δ 6.02 (q, J = 1.2 Hz, 1H), 3.72 (q, J = 6 Hz, 2H), 2.48 (td, J = 1.2, 6.3 Hz, 2H), 1.89 (d, J = 1.2 Hz, 3H); ¹³C NMR (CDCl₃): δ 144.79, 77.65, 60.21, 42.56, 23.99.

(2E, 5E) 6-Iodo-5-methyl-2,5-hexadienoic Acid Methyl Ester (17). To a solution of vinyl iodide **15** (2.21 g, 10.41 mmol) in CH₂Cl₂ (95 mL) at room temperature was added solid NaHCO₃ (8.74 g, 104.01 mmol) followed by Dess-Martin Periodinane (5.31 g, 12.52 mmol). The mixture was stirred for 4 h at room temperature and then was cooled to 0 °C. Methyl (triphenylphosphoranylidene)acetate (6.96 g, 20.81 mmol) was added and the mixture was allowed to warm to room temperature for 3 h. The reaction was

quenched by the addition of equal volumes of aqueous NaHCO₃ and aqueous Na₂S₂O₃. The aqueous layer was extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (2.5% to 10% EtOAc/hexanes) to afford ester **17** as a colorless oil (2.13 g, 77%): R_f 0.47 (15% EtOAc-hexanes); IR (film) 2933, 1728, 1649 cm⁻¹; ¹H NMR (CDCl₃): δ 6.90 (m, 1H), 6.07 (s, 1H), 5.82 (d, J = 9.6 Hz, 1H), 3.79 (s, 3H), 3.09 (d, J = 6.3 Hz, 2H), 1.85 (s, 3H); ¹³C NMR (CDCl₃): δ 165.68, 143.97, 143.18, 122.24, 77.00, 50.84, 40.92, 23.33.

(2E, 5E)-6-Iodo-5-methyl-2,5-hexadien-1-ol (18). To a solution of ester **17** (1.85 g, 6.97 mmol) in CH₂Cl₂ (70 mL) at -78 °C was added DIBAL-H (18 mL, 1M in hexanes, 18 mmol) dropwise. After addition was complete, the mixture was stirred for 30 min at -78 °C and then was warmed to rt for 30 min. The reaction was quenched by the addition of sat. Rochelle's salts (30 mL) and the biphasic mixture was stirred for two hours or until the two layers became clear. The aqueous layer was extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 10% EtOAc/hexanes) to afford alcohol **18** as a colorless oil (1.52 g, 92%): R_f 0.26 (15% EtOAc-hexanes); IR (film) 3327, 2908 cm⁻¹; ¹H NMR (CDCl₃): δ 5.95 (s, 1H), 5.67 (m, 2H), 4.12 (d, J = 4.5 Hz, 2H), 2.92 (d, J = 2.8 Hz, 2H), 1.83 (s, 3H); ¹³C NMR (CDCl₃): δ 146.01, 131.52, 128.26, 75.98, 62.98, 41.89, 23.88.

(2E, 5E)-1-(t-Butyldiphenylsiloxy)-6-iodo-5-methyl-2,5-hexadiene (19). To a solution of alcohol **18** (1.66 g, 6.97 mmol) in DMF (20 mL) at 0 °C was added imidazole (0.62 g, mmol) followed by TBDPSCl (2.3 mL). The mixture was allowed to warm to rt for 3 h and then was quenched by the addition of aqueous NaHCO₃. The aqueous layer was extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes) to afford vinyl iodide **19** as a light yellow oil (3.22 g, 97%): R_f 0.25 (hexanes); ¹H NMR (CDCl₃): δ 7.68 (m, 4H), 7.42 (m, 6H), 5.90 (s, 1H), 5.62 (m, 2H), 4.12 (d, J = 2.7 Hz, 2H), 2.90 (d, J = 5.0 Hz, 2H), 1.82 (s, 3H), 1.06 (s, 9H).

(7*R*/S, 8 *R*, 9 *R*, 10 *R*, 11 *R*)-11,13-Di-(*t*-butyldimethylsilyloxy)-1-(*t*-butyldiphenylsilyloxy)-9-(*p*-methoxybenzyloxy)-5,8,10-trimethyltrideca-2,5-dien-7-ol (21). **A. Vinylolithium Addition:** To a solution of vinyl iodide **20** (0.150 g, 0.315 mmol) in Et₂O (3 mL) at –78 °C was added *t*-BuLi (0.38 mL, 1.70 M in pentane, 0.64 mmol) rapidly. The mixture was stirred for 1 h and then aldehyde **1** (0.100 g, 0.188 mmol) was added dropwise in a small amount of Et₂O. After stirring at –78 °C for 1 h the reaction mixture was allowed to slowly warm to room temperature overnight. The reaction was quenched by the addition of NH₄Cl (aq.). The aqueous layer was extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 2.5% EtOAc/hexanes) to afford a 1:1 mixture of syn and anti diastereomeric alcohols as a colorless oil (0.105 g, 63%): ¹H NMR (CDCl₃): High R_f (**anti isomer**): δ 7.67 (m, 4H), 7.41 (m, 6H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.62 (m, 2H), 5.20 (d, *J* = 8.5 Hz, 1H), 4.67 (d, *J* = 2.1 Hz, 2H), 4.26 (m, 4H), 4.20 (d, *J* = 5.1 Hz, 1H), 3.93 (d, *J* = 5.3 Hz, 1H), 3.82 (s, 3H), 3.62 (t, *J* = 7.7 Hz, 2H), 2.68 (t, *J* = 7.1 Hz, 2H), 1.62-1.84 (m, 4H), 1.59, (s, 3H), 1.06 (s, 9H), 0.92 (s, 9H), 0.86 (s, 9H), 0.78 (d, *J* = Hz, 3H), 0.74 (d, *J* = Hz, 3H), 0.07-0.11 (m, 12H); Low R_f (**syn isomer**): δ 7.68 (m, 4H), 7.39 (m, 6H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.62 (m, 2H), 5.24 (d, *J* = 8.3 Hz, 1H), 4.42-4.64 (m, 3H), 4.18 (m, 3H), 3.81 (s, 3H), 3.62 (m, 4H), 2.69 (t, *J* = 5.4 Hz, 2H), 1.62-1.84 (m, 4H), 1.65 (s, 3H), 1.06 (s, 9H), 1.03 (d, *J* = Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.80 (d, *J* = Hz, 3H), 0.07-0.11 (m, 12H).

B. Vinyl Grignard Reagent Addition: To a solution of vinyl iodide **20** (0.134 g, 0.282 mmol) in Et₂O (3 mL) at –78 °C was added *t*-BuLi (0.34 mL, 1.70 M in pentane, 0.57 mmol) rapidly. The mixture was stirred for 1 h and then MgBr₂ (0.059 g, 0.320 mmol) was added in one portion. The mixture was warmed to 0 °C for 1 h and then recooled to –78 °C. Aldehyde **1** (0.101 g, 0.188 mmol) was then added dropwise in a small amount of Et₂O. After stirring at –78 °C for 1 h the reaction mixture was allowed to slowly warm to room temperature overnight. The reaction was quenched by the addition of NH₄Cl (aq.). The aqueous layer was extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexanes to 2.5% EtOAc/hexanes) to afford the two diastereomeric alcohols **21** as a colorless oil (0.105 g, 63%; 75:25 mixture of anti and syn diastereomers). All analytical data matched that of the product of part A.

C. Vinylzinc Addition. The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **20** (0.113 g, 0.237 mmol), aldehyde **1** (0.050 g, 0.093 mmol), and ZnBr₂ (0.89M in Et₂O, 0.300 mL, 0.267 mmol) affording alcohol **21** (0.057 g, 68% yield, 80:20 mixture of anti and syn diastereomers) as a clear oil. All analytical data matched that of the product of part A.

D. Vinylzinc Addition in the Presence of (1*R*, 2*S*) *N*-Methylephedrine. The standard procedure for vinyl iodide lithiation was employed with vinyl iodide **20** (0.110 g, 0.231 mmol), aldehyde **1** (0.048 g, 0.089 mmol), ZnBr₂ (0.89M in Et₂O, 0.290 mL, 0.258 mmol), and the lithium alkoxide of (1*R*, 2*S*)-*N*-methylephedrine (0.20 M, 1.4 mL, 0.280 mmol) affording alcohol **21** (0.058 g, 73% yield, 92 : 8 mixture of anti and syn diastereomers) as a clear oil.

COC(=O)[C@H](c1ccccc1)O[C@@H](C=C(C)CC/C=C\CCCC)C[C@H](R)[C@@H](TBSO)CCOTBSO

R = PMB
ODPS

Chemical structure of compound 10, a substituted cyclohexane derivative. The structure shows a cyclohexane ring with various substituents. The substituents are: TBSO, TBSO, TBSO, TBSO, TBSO, and TBSO. The R group is defined as PMB (p-methoxybenzyl).

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