Conversion of Allylic Alcohols to Stereodefined Trisubstituted Alkenes: A Complementary Process to the Claisen Rearrangement

Justin K. Belardi and Glenn C. Micalizio*

Department of Chemistry, Yale University, New Haven, CT 06520-8107

E-mail: glenn.micalizio@yale.edu

SUPPORTING INFORMATION:

General. All reactions were conducted in flame-dried glassware under nitrogen using anhydrous solvents. Tetrahydrofuran, diethyl ether, and dimethylformamide were used after passing through activated alumina columns. Vinyltrimethylsilane and chlorovinyldimethylsilane were distilled prior to use. All other commercially available reagents were used as received.

^{1}H NMR data were recorded at 500 MHz or 400 MHz using a Bruker AM-500, Bruker Avance DPX-500 or Bruker AM-400 instrument. ^{1}H NMR chemical shifts are reported relative to residual $CHCl_3$ (7.26 ppm). ^{13}C NMR data were recorded at 126 MHz using a Bruker AM-500 or Bruker Avance DPX-500 instrument. ^{13}C chemical shifts are reported relative to the central line of $CDCl_3$ (77.0 ppm). Infrared spectra were recorded using a Thermo Electron Nicolet 6700 FT-IR Spectrometer. Low resolution mass spectrometry was performed on an Agilent Technologies 6890 Network GC System with a 5973 Network Mass Selective Detector. Optical rotations were measured on Perkin Elmer Model 341 polarimeter using a 1 mL capacity micro cell with a 10 cm path length. Chromatographic purifications were performed using 60Å, 35-75μm particle size silica gel from Silicycle. All compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise. Semi-preparative and analytical HPLC normal phase separations were performed using an HPLC system composed of two Dynamax SD-1 pumps, a Rheodyne injector and a Dynamax UV-1 absorbance detector.

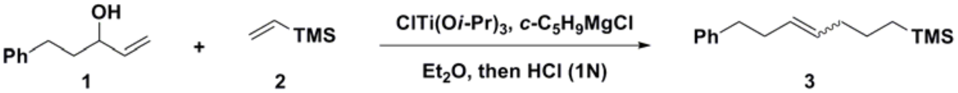
General procedure for reductive cross-coupling reactions between allylic alcohols and vinyltrimethylsilane: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol (0.34 equiv) in THF (0.5M). The solution was cooled to –78 °C and *n*-BuLi (2.5M in hexanes, 0.4 equiv) was added dropwise over 2 min. This solution was rapidly warmed to 0 °C and stirred at that temperature for 15 min. After recooling to –78 °C, vinyltrimethylsilane (1.0 eq) was added as a 0.1M solution in diethylether. To this solution was added $ClTi(Oi\text{-}Pr)_3$ (1.0 M in hexanes; 1.0 equiv), and *c*-C_5H_9MgCl (2.0M in diethyl ether; 2.0 equiv). The resulting yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (~ 3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity. Finally, the crude material was purified by flash column chromatography on silica gel to provide coupled product.

Note: It has been observed that warming the combined reaction mixture to 0 °C rapidly typically results in an increase in the amount of regioisomeric impurities derived from alkylation at the internal carbon of the allylic alcohol in upwards of 32%.

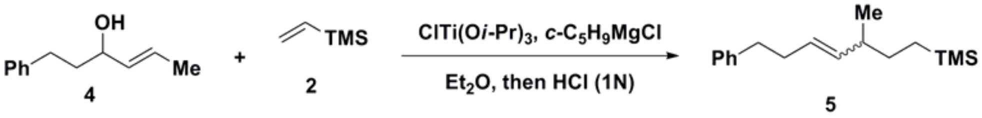
General procedure for reductive cross-coupling reactions between allylic alcohols and chlorodimethylvinylsilane: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon at –78 °C was added chlorodimethylvinylsilane (1.0 equiv; as a 0.1M solution in diethylether), $ClTi(Oi\text{-}Pr)_3$ (1.0 equiv, 1.0 M in hexanes) and *c*-C_5H_9MgCl (2.0 equiv; 2.0M in diethyl ether). The solution was allowed to rapidly warm to –50 °C, then maintained at this temperature for 2 h before cooling –78 °C. During this time the solution turned from a bright yellow color to dark brown.

To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol (0.34 equiv) in THF (0.5M). The solution was cooled to –78 °C and *n*-BuLi (0.4 equiv, 2.5M in hexanes) was added dropwise over 2 min. This solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred to the preformed dark brown mixture via cannula.

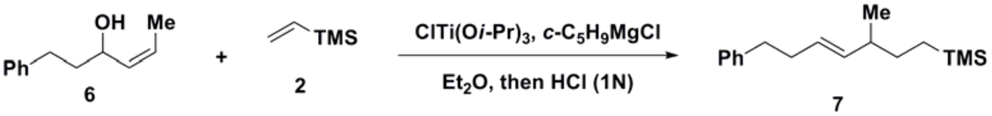
The combined solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl and stirred rapidly for 20 min at rt. The mixture was quenched with 1N HCl (~ 3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity. The crude material was then purified by flash column chromatography on silica gel to provide pure product.



Synthesis of 1-trimethylsilyl-7-phenyl-4-heptene, 3: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **1** (100 mg, 0.62 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (290 µL, 2.5M in hexanes, 0.72 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min, then cooled to –78 °C. Ether (18 mL), vinyltrimethylsilane **2** (280 µL, 1.8 mmol), $ClTi(Oi\text{-}Pr)_3$ (1.8 mL, 1.0 M in hexanes, 1.8 mmol), and $c\text{-}C_5H_9MgCl$ (1.8 mL, 2.0M in diethyl ether; 3.6 mmol) were then added sequentially to the cold solution. This solution was then slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material indicated that the product was formed as a 1:1 mixture of *(E)* and *(Z)* olefin isomers. The crude material was then purified by flash column chromatography on silica gel to provide product **3** (100 mg, 0.41 mmol) in 66% yield as a mixture of olefin isomers.



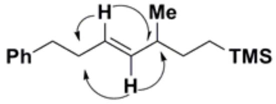
Synthesis of 1-trimethylsilyl-7-phenyl-3-methyl-4-heptene, 5: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **4** (100 mg, 0.57 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (267 µL, 2.5M in hexanes, 0.67 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min, then cooled to –78 °C. Ether (16 mL), vinyltrimethylsilane **2** (258 µL, 1.7 mmol), ClTi(O*i*-Pr)$_3$ (1.7 mL, 1.0 M in hexanes, 1.7 mmol), and *c*-C$_5$H$_9$MgCl (1.7 mL, 2.0M in diethyl ether; 3.4 mmol) were then added sequentially to the cold solution. This solution was then slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (5 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material indicated that the product was formed as a 1:1 mixture of *(E)* and *(Z)* olefin isomers. The crude material was then purified by flash column chromatography on silica gel to provide product **5** (86 mg, 0.33 mmol) in 58% yield as a mixture of olefin isomers.

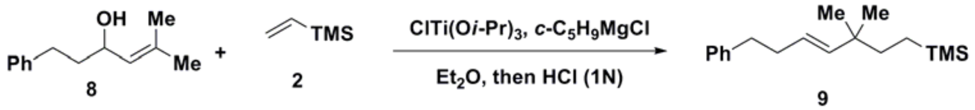


Synthesis of (*E*)-1-trimethylsilyl-7-phenyl-3-methyl-4-heptene, 7: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **6** (100 mg, 0.57 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (267 μL, 2.5M in hexanes, 0.67 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min, then cooled to –78 °C. Ether (16 mL), vinyltrimethylsilane **2** (258 μL, 1.7 mmol), ClTi(O*i*-Pr)$_3$ (1.7 mL, 1.0 M in hexanes, 1.7 mmol), and *c*-C$_5$H$_9$MgCl (1.7 mL, 2.0M in diethyl ether; 3.4 mmol) were then added sequentially to the cold solution. This solution was then slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity *(E:Z* = 9:1). Purification of this material by flash column chromatography on silica gel then delivered **7** (95 mg, 0.33 mmol) in 64% yield as a 9:1 mixture of olefin isomers.

Data for (*E*)-1-trimethylsilyl-7-phenyl-3-methyl-4-heptene, 7: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.15 (m, 5H), 5.44-5.32 (m, 1H), 5.26 (dd, *J* = 15.4, 7.6 Hz, 1H), 2.72-2.64 (m, 2H), 2.36-2.28 (m, 2H), 2.00-1.92 (m, 1H), 1.28-1.16 (m, 2H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.48-0.34 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.1, 136.4, 128.5, 128.2, 127.7, 125.6, 39.7, 36.2, 34.4, 31.2, 20.3, 14.0, -1.7; IR (thin film, NaCl) 3064, 2953, 2912, 2870, 1605, 1496, 1453, 1247, 967, 863, 834, 746, 697 cm^{-1}; LRMS (EI, $M^{+\cdot}$), calcd for $C_{17}H_{28}Si$, 260.20 *m/z* $(M)^+$; observed, 260.2 $(M)^+$ *m/z*.

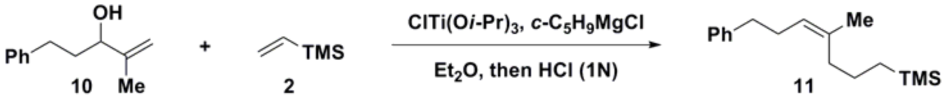
nOe's for (*E*)-1-trimethylsilyl-7-phenyl-3-methyl-4-heptene, 7:





Synthesis of (*E*)-(1-trimethylsilyl-3,3-dimethyl-7-phenyl-4-heptene, 9: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **8** (100 mg, 0.53 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (246 µL, 2.5M in hexanes, 0.62 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min and cooled to –78 °C. Ether (16 mL), vinyltrimethylsilane **2** (239 µL, 1.5 mmol), $ClTi(Oi\text{-}Pr)_3$ (1.5 mL, 1.0 M in hexanes, 1.5 mmol), and *c*-C_5H_9MgCl (1.5 mL, 2.0M in diethyl ether; 3.0 mmol) were then added sequentially to the cold solution. The yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude product was taken to determine selectivity (*E:Z* ≥ 20:1). Finally, this material was purified by flash column chromatography on silica gel eluting with hexanes to provide product **9** (101 mg, 0.37 mmol) in 69% yield.

Data for (*E*)-1-trimethylsilyl-3,3-dimethyl-7-phenyl-4-heptene, 9: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.16 (m, 5H), 5.34-5.30 (m, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 2.36-2.30 (m, 2H), 1.21-1.16 (m, 2H), 0.92 (s, 6H), 0.35-0.30 (m, 2H), -0.03 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 140.9, 128.5, 128.2, 125.6, 125.3, 37.0, 36.4, 36.4, 34.6, 26.8, 10.6, -1.8; IR (thin film, NaCl) 3027, 2954, 1454, 1381, 1248, 1184, 1031, 973, 863, 835, 746, 698 cm^{-1}; LRMS (EI, M$^{+\cdot}$); calcd for $C_{18}H_{30}Si$, 274.21 *m/z* (M)$^+$; observed, 274.3 (M)$^+$ *m/z*.

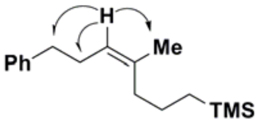


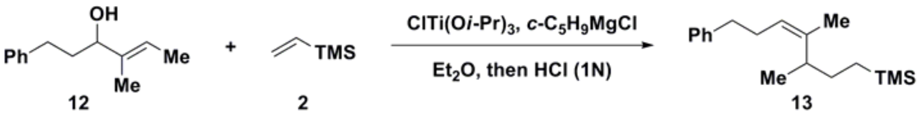
Synthesis for (*Z*)-1-trimethylsilyl-4-methyl-7-phenyl-4-heptene, 11: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **10** (100 mg, 0.57 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (268 µL, 2.5M in hexanes, 0.67 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min and cooled to –78 °C. Ether (17 mL), vinyltrimethylsilane **2** (263 µL, 1.7 mmol), $ClTi(O\textit{i}\text{-}Pr)_3$ (1.7 mL, 1.0 M in hexanes, 1.7 mmol), and *c*-C_5H_9MgCl (1.7 mL, 2.0M in diethyl ether; 3.4 mmol) were then added sequentially to the cold solution.

The resulting yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity ($Z{:}E \geq 20{:}1$). This material was then purified by flash column chromatography on silica gel eluting with hexanes to provide product **11** (74 mg, 0.28 mmol) in 50% yield. The product was further purified by HPLC (eluting in hexanes) to furnish a sample of **11** suitable for characterization**.**

Data for (*Z*)-1-trimethylsilyl-4-methyl-7-phenyl-4-heptene, 11: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.16 (m, 5H), 5.20 (t, *J* = 7.2 Hz, 1H), 2.63 (t, *J* = 7.8 Hz, 2H), 2.31 (app q, *J* = 7.2 Hz, 2H), 2.01 (t, *J* = 7.6 Hz, 2H), 1.67 (d, *J* = 0.9 Hz, 3H), 1.39-1.30 (m, 2H), 0.49-0.42 (m, 2H), -0.02 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 136.1, 128.4, 128.2, 125.7, 124.4, 36.5, 35.6, 30.0, 23.4, 22.3, 16.6, -1.7; IR (thin film, NaCl) 3027, 2953, 2924, 2858, 1496, 1453, 1248, 836, 746, 697 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{17}H_{28}Si$, 260.20 *m/z* $(M)^+$; observed, 260.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-1-trimethylsilyl-4-methyl-7-phenyl-4-heptene, 11:



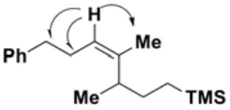


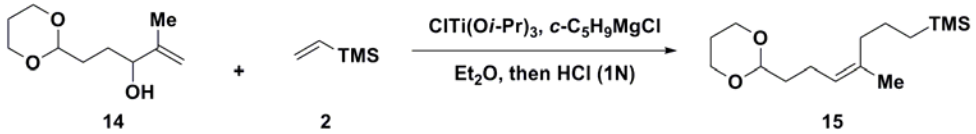
Synthesis of (*Z*)-1-trimethylsilyl-3,4-dimethyl-7-phenyl-4-heptene, 13: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **12** (100 mg, 0.52 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (246 µL, 2.5M in hexanes, 0.62 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C, stirred for 15 min and cooled to –78 °C. Ether (15 mL), vinyltrimethylsilane **2** (239 µL, 1.5 mmol), ClTi(O*i*-Pr)$_3$ (1.5 mL, 1.0 M in hexanes, 1.5 mmol), and *c*-C$_5$H$_9$MgCl (1.5 mL, 2.0M in diethyl ether; 3.0 mmol) were then added sequentially to the cold solution. The resulting yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, the mixture was quenched with 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity (*Z:E* $\geq$ 20:1). Finally, this material was purified by flash column chromatography on silica gel eluting with hexanes to provide product **13** (93 mg, 0.34 mmol) in 65% yield. The product was further purified by HPLC (eluting in hexanes) to furnish a sample of **13** suitable for characterization**.**

Data for (*Z*)-1-trimethylsilyl-3,4-dimethyl-7-phenyl-4-heptene, 13: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.30-7.15 (m, 5H), 5.21 (t, *J* = 7.0 Hz, 1H), 2.63 (t, *J* = 7.9 Hz, 2H), 2.50 (dq, *J* = 13.9, 6.9 Hz, 1H), 2.40-2.28 (m, 2H), 1.53 (s, 3H), 1.24 (app. q, *J* = 8.2 Hz, 2H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.38-0.29 (m, 2H), -0.04 (s, 9H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 142.4, 139.7, 128.4, 128.2, 125.7, 124.7, 37.2, 36.6, 29.4, 28.8, 19.0, 17.9, 14.6, -1.8; IR (thin film, NaCl)

3027, 2955, 2920, 2856, 1453, 1377, 1247, 862, 833, 697 cm^{-1}; LRMS (EI, M$^{+\cdot}$); calcd for $C_{18}H_{30}Si$, 274.21 *m/z* (M)$^+$; observed, 274.2 (M)$^+$ *m/z*.

nOe's for (*Z*)-1-trimethylsilyl-3,4-dimethyl-7-phenyl-4-heptene, 13:

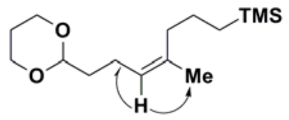


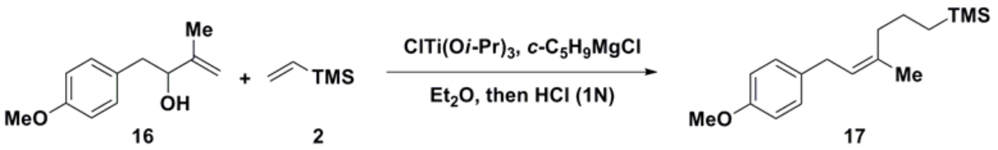


Synthesis of (*Z*)-(7-(1,3-dioxan-2-yl)-4-methyl-1-trimethylsilyl-4-heptene, 15: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **14** (100 mg, 0.54 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (253 µL, 2.5M in hexanes, 0.63 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min at this temperature before cooling to –78 °C. Ether (16 mL), vinyltrimethylsilane **2** (244 µL, 1.7 mmol), $ClTi(Oi\text{-}Pr)_3$ (1.6 mL, 1.0 M in hexanes, 1.6 mmol), and *c*-C_5H_9MgCl (1.6 mL, 2.0M in diethyl ether; 3.2 mmol) were then added sequentially to the cooled solution. The resulting yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added and the resulting solution was stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity (*Z:E* $\geq$ 20:1). The crude material was then purified by flash column chromatography on silica gel (10% ethyl acetate-hexanes) to provide product **15** (90 mg, 0.33 mmol) in 62% yield.

Data for (*Z*)-(7-(1,3-dioxan-2-yl)-4-methyl-1-trimethylsilyl-4-heptene, 15: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.10 (t, *J* = 7.6 Hz, 1H), 4.49 (t, *J* = 5.0 Hz, 1H), 4.09 (dd, *J* = 11.7, 5.0 Hz, 2H), 3.74 (td, *J* = 12.3, 1.9 Hz, 2H), 2.13-2.00 (m, 5H), 1.65 (s, 3H), 1.65-1.55 (m, 2H), 1.40-1.30 (m, 3H), 0.49-0.43 (m, 2H), -0.03 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 124.3, 101.9, 66.9, 35.4, 25.9, 23.3, 22.3, 22.3, 16.5, -1.7; IR (thin film, NaCl) 2953, 2850, 1403, 1377, 1148, 1087, 1048, 1005, 942, 837, 692 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{15}H_{30}O_2Si$, 270.20 *m/z* $(M)^+$; observed, 270.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-(7-(1,3-dioxan-2-yl)-4-methyl-1-trimethylsilyl-4-heptene, 15:

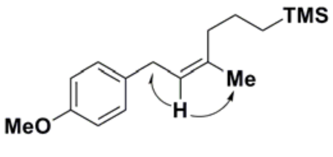


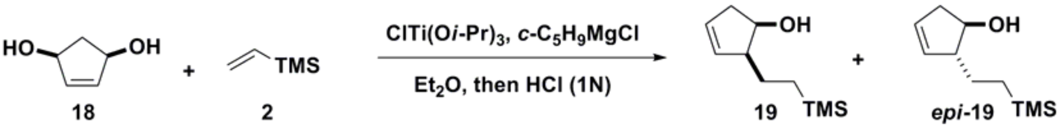


Synthesis of (*Z*)-6-(4'-methoxyphenyl)-4-methyl-1-trimethylsilyl-4-hexene, 17: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **16** (100 mg, 0.52 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (243 μL, 2.5M in hexanes, 0.61 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min, after which time it was cooled to –78 °C. Ether (15 mL), vinyltrimethylsilane **2** (236 μL, 1.5 mmol), $ClTi(O\textit{i}\text{-}Pr)_3$ (1.5 mL, 1.0 M in hexanes, 1.5 mmol), and *c*-C_5H_9MgCl (1.5 mL, 2.0 M in diethyl ether; 3.0 mmol) were then added sequentially to the cooled solution. The yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity *(Z:E* ≥ 20:1). Finally, purification of this material by flash column chromatography on silica gel (2 % ethyl acetate-hexanes) afforded product **17** (102 mg, 0.37 mmol) in 71 % yield. The product was further purified by HPLC (2 % ethyl acetate/hexanes) to provide a sample of **17** suitable for characterization.

Data for (*Z*)-6-(4'-methoxyphenyl)-4-methyl-1-trimethylsilyl-4-hexene, 17: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.09 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 5.31 (td, *J* = 7.3, 1.3 Hz, 1H), 3.78 (s, 3H), 3.29 (d, *J* = 7.6 Hz, 2H), 2.14 (t, *J* = 7.6 Hz, 2H), 1.71 (d, *J* = 1.3 Hz, 3H), 1.45-1.38 (m, 2H), 0.52-0.48 (m, 2H), -0.02 (s, 9H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 157.7, 136.2, 134.0, 129.2, 124.1, 113.8, 55.3, 35.6, 33.2, 23.4, 22.4, 16.7, -1.7; IR (thin film, NaCl) 2954, 1612, 1511, 1457, 1246, 1174, 1039, 836 cm^{-1}; LRMS (EI, M$^{+\cdot}$); calcd for $C_{17}H_{28}OSi$, 276.19 *m/z* (M)$^+$; observed, 276.1 (M)$^+$ *m/z*.

nOe's for (*Z*)-6-(4'-methoxyphenyl)-4-methyl-1-trimethylsilyl-4-hexene, 17:

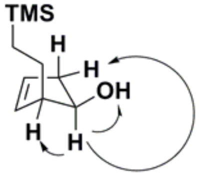




Synthesis of *cis*-2-(1'-trimethylsilyl-eth-2'-yl)-cyclopent-3-en-1-ol, 19: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added diol **18** (100 mg, 1.0 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (938 μL, 2.5M in hexanes, 2.4 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred at this temperature for 15 min (turned into a white slurry). The mixture was then cooled to –78 °C and diluted with diethylether (30 mL). Then vinyltrimethylsilane **2** (453 μL, 2.9 mmol), ClTi(O*i*-Pr)$_3$ (2.9 mL, 1.0 M in hexanes, 2.9 mmol), and *c*-C$_5$H$_9$MgCl (2.9 mL, 2.0M in diethyl ether; 5.8 mmol) were added sequentially to the cold solution. This yellow solution was slowly warmed to 0 °C over 2 h, during which time it became a thick brown mixture. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and stirring was continued for an additional 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (10% ethyl acetate-hexanes) to provide products **19** and ***epi*-19** (117 mg, 0.64 mmol) in 64% yield as a 5:1 mixture of diastereomers. Further purification on silica gel (5% ethyl acetate-hexanes) provided pure diastereomers **19** and ***epi*-19** for characterization.

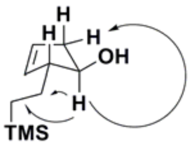
Data for *cis*-2-(1'-trimethylsilyl-eth-2'-yl)-cyclopent-3-en-1-ol, 19: ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.77-5.66 (m, 2H), 4.40-4.35 (m, 1H), 2.64-2.57 (m, 1H), 2.55-2.48 (m, 1H), 2.34-2.28 (m, 1H), 1.60-1.54 (m, 1H), 1.46-1.38 (m, 2H), 0.61-0.58 (m, 2H), -0.01 (s, 9H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 133.3, 127.9, 73.1, 53.4, 42.2, 21.9, 15.2, -1.8; IR (thin film, NaCl) 3354, 3057, 2952, 1411, 1248, 1176, 1075, 1016, 835, 758, 690 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{10}H_{20}OSi$, 184.13 *m/z* $(M)^+$; observed, 184.2 $(M)^+$ *m/z*.

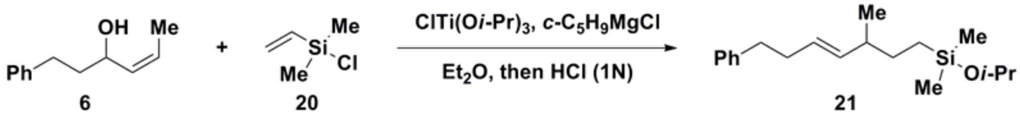
nOe's for *cis*-2-(1'-trimethylsilyl-eth-2'-yl)-cyclopent-3-en-1-ol, 19:



Data for *trans*-2-(1'-trimethylsilyl-eth-2'-yl)-cyclopent-3-en-1-ol, *epi*-19: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72-5.65 (m, 2H), 4.12-4.07 (m, 1H), 2.74-2.67 (m, 1H), 2.49-2.44 (m, 1H), 2.28-2.21 (m, 1H), 1.55 (d, *J* = 5.7 Hz, 1H), 1.40-1.25 (m, 2H), 0.60-0.48 (m, 2H), -0.03 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.1, 127.7, 77.2, 58.3, 41.9, 27.3, 14.4, -1.8; IR (thin film, NaCl) 3336, 3054, 2951, 1419, 1248, 1181, 1066, 951, 863, 688 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{10}H_{20}OSi$, 184.13 *m/z* $(M)^+$; observed, 184.2 $(M)^+$ *m/z*.

nOe's for *trans*-2-(1'-trimethylsilyl-eth-2'-yl)-cyclopent-3-en-1-ol, *epi*-19:





Synthesis of (*E*)-isopropoxydimethyl(3-methyl-7-phenylhept-4-enyl)silane, 21: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (17 mL) and chlorodimethylvinylsilane **20** (230 μL, 1.7 mmol). The solution was cooled to –78 °C and $ClTi(Oi\text{-}Pr)_3$ (1.7 mL, 1.0 M in hexanes, 1.7 mmol) and *c*-C_5H_9MgCl (1.7 mL, 2.0

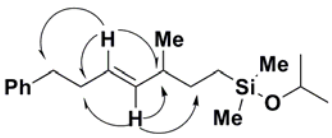
M in diethyl ether, 3.4 mmol) were added sequentially. The solution was rapidly warmed to –50 °C and stirred at this temperature for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

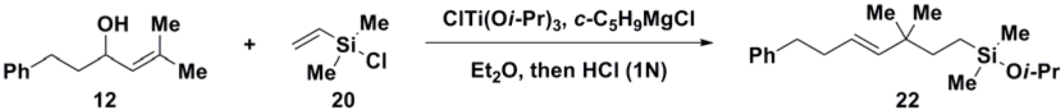
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **6** (100 mg, 0.57 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (267 μL, 2.5M in hexanes, 0.67 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture.

The combined brown solution was slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity (*E:Z* = 10:1). The crude material was then purified by flash column chromatography on silica gel to provide product **21** (91 mg, 0.52 mmol) in 53% yield as a 10:1 mixture of olefin isomers. The product was characterized as this mixture.

Data for (*E*)-isopropoxydimethyl(3-methyl-7-phenylhept-4-enyl)silane, 21: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.14 (m, 5H), 5.40 (dt, *J* = 15.1, 6.6 Hz, 1H), 5.26 (dd, *J* = 15.1, 7.7 Hz, 1H), 3.96 (septuplet, *J* = 6.3 Hz, 1H), 2.67 (t, *J* = 7.7 Hz, 2H), 2.31 (q, *J* = 7.8 Hz, 2H), 1.97 (m, 1H), 1.32-1.18 (m, 2H), 1.15 (d, *J* = 6.0 Hz, 6H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.58-0.42 (m, 2H), 0.08 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 136.8, 128.5, 128.2, 127.9, 125.6, 64.7, 39.6, 36.2, 34.4, 30.5, 25.8, 20.3, 14.2, -1.6; IR (thin film, NaCl) 3028, 2969, 2924, 1454, 1367, 1249, 1173, 1127, 1028, 879, 839, 778, 698 cm^{-1}; LRMS (EI, M$^{+\cdot}$); calcd for $C_{19}H_{32}OSi$, 304.22 *m/z* (M)$^+$; observed, 304.3 (M)$^+$ *m/z*.

nOe's for (*E*)-isopropoxydimethyl(3-methyl-7-phenylhept-4-enyl)silane, 21:





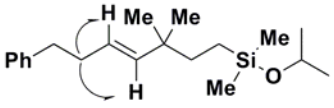
Synthesis of (*E*)-(3,3-dimethyl-7-phenylhept-4-enyl)(isopropoxy)dimethylsilane, 22: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (15 mL) and chlorodimethylvinylsilane **20** (213 μL, 1.5 mmol), then cooled to –78 °C. $ClTi(Oi\text{-}Pr)_3$ (1.5 mL, 1.0 M in hexanes, 1.5 mmol) and *c*-C_5H_9MgCl (1.5 mL, 2.0 M in diethyl ether, 3.0 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The temperature was maintained at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

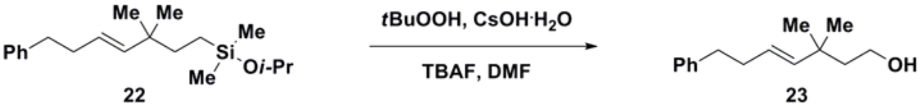
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **12** (100 mg, 0.52 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (246 μL, 2.5M in hexanes, 0.62 mmol) was added dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the previously prepared dark brown mixture.

The combined solution was slowly warmed to 0 °C over 2 h, then stirred at 0 °C for 30 min. To this mixture was added 1N HCl (3 mL) and stirred rapidly for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the NMR of the crude material was taken to determine selectivity (*E:Z* ≥ 20:1). The crude material was then purified by flash column chromatography on silica gel to provide product **22** (125 mg, 0.39 mmol) in 75% yield. The product was further purified by HPLC (eluting in hexanes) to furnish a sample of **22** suitable for characterization**.**

Data for (*E*)-(3,3-dimethyl-7-phenylhept-4-enyl)(isopropoxy)dimethylsilane, 22: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.14 (m, 5H), 5.33-5.30 (m, 2H), 3.96 (septuplet, *J* = 6.0 Hz, 1H), 2.67 (t, *J* = 7.8 Hz, 2H), 2.34-2.28 (m, 2H), 1.25-1.19 (m, 2H), 1.15 (d, *J* = 6.0 Hz, 6H), 0.92 (s, 6H), 0.45-0.40 (m, 2H), 0.07 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 140.6, 128.5, 128.2, 125.6, 125.4, 64.7, 36.4, 36.4, 36.2, 34.7, 26.7, 25.8, 10.9, -1.7; IR (thin film, NaCl) 3028, 2969, 2923, 1496, 1453, 1381, 1366, 1250, 1173, 1128, 1028, 974, 841, 698 cm^{-1}; LRMS (EI, M$^{+\cdot}$); calcd for $C_{20}H_{34}OSi$, 318.24 *m/z* (M)$^+$; observed, 318.1 (M)$^+$ *m/z*.

nOe's for (*E*)-(3,3-dimethyl-7-phenylhept-4-enyl)(isopropoxy)dimethylsilane, 22:



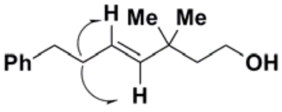


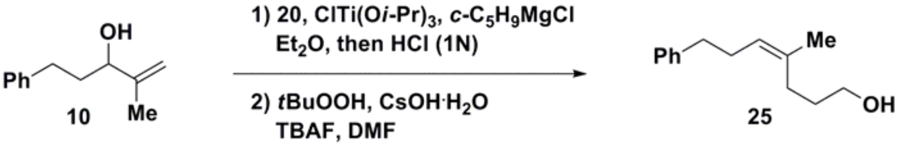
Synthesis of (*E*)-3,3-dimethyl-7-phenylhept-4-en-1-ol, 23: To a cooled (0 °C) solution of *t*BuOOH (711 mL, ~5.5 M in decane, 3.9 mmol) in DMF (2.0 mL) was added CsOH•H_2O (562 mg, 3.3 mmol). The mixture was warmed to rt, and a solution of isopropoxysilane **22** (89mg, 0.28 mmol) in DMF (0.8 mL) was added dropwise by syringe. After 10 min, TBAF

(1.4 mL, 1.0 M in THF, 1.4 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (15 mL) and ether (15 mL). The aqueous layer was extracted with ether and the combined organic layer was then washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (20% ethyl acetate-hexanes) to provide product **23** (54 mg, 0.25 mmol) in 88% yield. The product was further purified by HPLC (20% ethyl acetate/hexanes) to furnish a sample of **23** suitable for characterization.

Data for (*E*)-3,3-dimethyl-7-phenylhept-4-en-1-ol, 23: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.14 (m, 5H), 5.44-5.33 (m, 2H), 3.56 (dt, *J* = 7.3, 5.7 Hz, 2H), 2.67 (t, *J* = 8.5, 6.3 Hz, 2H), 2.32 (dt *J* = 8.5, 6.3 Hz, 2H), 1.56 (t, *J* = 7.0 Hz, 2H), 1.17 (t, *J* = 5.4 Hz, 1H), 0.99 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.9, 140.6, 128.5, 128.2, 125.7, 125.7, 60.3, 45.5, 36.1, 34.9, 34.5, 27.7; IR (thin film, NaCl) 3350, 3026, 2958, 2928, 1453, 1362, 1024, 973, 698 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{15}H_{22}O$, 218.17 *m/z* $(M)^+$; observed, 218.0 $(M)^+$ *m/z*.

nOe's for (*E*)-3,3-dimethyl-7-phenylhept-4-en-1-ol, 23:





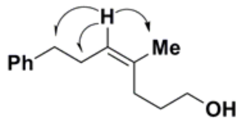
Synthesis of (*Z*)-4-methyl-7-phenylhept-4-en-1-ol, 25: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (15 mL) and chlorodimethylvinylsilane **20** (231 μL, 1.7 mmol), then cooled to –78 °C. ClTi(O*i*-Pr)$_3$ (1.7 mL, 1.0 M in hexanes, 1.7 mmol) and *c*-C$_5$H$_9$MgCl (1.7 mL, 2.0 M in diethyl ether, 3.4 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

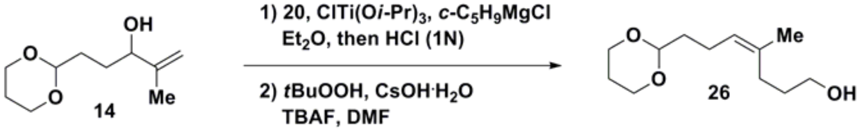
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **10** (100 mg, 0.57 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (267 μL, 2.5M in hexanes, 0.67 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (4.2 mL, ~5.5 M in decane, 23 mmol) in DMF (15 mL) was added CsOH•H$_2$O (3.3 g, 20 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (8.4 mL, 1.0 M in THF, 8.4 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (20% ethyl acetate-hexanes) to provide product **25** (67 mg, 0.33 mmol) in 58% yield (2 steps). The product was further purified by HPLC (20% ethyl acetate/hexanes) to furnish a sample of **25** suitable for characterization.

Data for (*Z*)-4-methyl-7-phenylhept-4-en-1-ol, 25: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.16 (m, 5H), 5.22 (t, *J* = 7.0 Hz, 1H), 3.60-3.54 (m, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.32 (app q, *J* = 7.2 Hz, 2H), 2.06 (t, *J* = 7.3 Hz, 2H), 1.70 (d, *J* = 1.3 Hz, 3H), 1.60-1.54 (m, 2H), 1.24 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 135.4, 128.5, 128.2, 125.7, 124.9, 62.8, 36.3, 30.8, 29.9, 28.0, 23.3; IR (thin film, NaCl) 3367, 2933, 1496, 1453, 1059, 698 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{14}H_{20}O$, 204.15 *m/z* $(M)^+$; observed, 204.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-4-methyl-7-phenylhept-4-en-1-ol, 25:





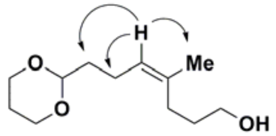
Synthesis of (*Z*)-7-(1,3-dioxan-2-yl)-4-methylhept-4-en-1-ol, 26: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (8 mL) and chlorodimethylvinylsilane **20** (109 μL, 0.79 mmol), then cooled to –78 °C. $ClTi(Oi\text{-}Pr)_3$ (790 μL, 1.0 M in hexanes, 0.79 mmol) and $c\text{-}C_5H_9MgCl$ (790 μL, 2.0 M in diethyl ether, 1.6 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

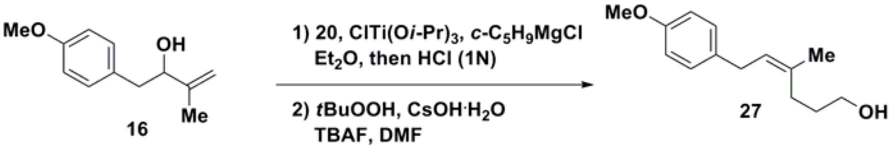
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **14** (50 mg, 0.27 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (126 μL, 2.5M in hexanes, 0.32 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (2.0 mL, ~5.5 M in decane, 11 mmol) in DMF (8 mL) was added $CsOH{\bullet}H_2O$ (1.5 g, 9.5 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (4.0 mL, 1.0 M in THF, 4.0 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (30% ethyl acetate-hexanes) to provide product **26** (29 mg, 0.14 mmol) in 51% yield (2 steps) (*Z*:*E* ≥ 20:1).

Data for (*Z*)-7-(1,3-dioxan-2-yl)-4-methylhept-4-en-1-ol, 26: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14 (t, *J* = 7.4 Hz, 1H), 4.50 (t, *J* = 5.3 Hz, 1H), 4.10 (dd, *J* = 10.8, 5.0 Hz, 2H), 3.75 (td, *J* = 12.4, 2.5 Hz, 2H), 3.61 (app q, *J* = 6.0 Hz, 2H), 2.14-2.02 (m, 5H), 1.70-1.58 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.2, 124.9, 101.8, 66.9, 62.4, 35.4, 30.6, 27.7, 25.8, 23.3, 22.3; IR (thin film, NaCl) 3435, 2960, 2856, 1658, 1642, 1436, 1404, 1378, 1242, 1146, 1132, 1082, 1047, 997, 926, 892, 854 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{12}H_{22}O_3$, 214.16 *m/z* $(M)^+$; observed, 214.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-7-(1,3-dioxan-2-yl)-4-methylhept-4-en-1-ol, 26:





Synthesis of (*Z*)-6-(4-methoxyphenyl)-4-methylhex-4-en-1-ol, 27: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (8 mL) and chlorodimethylvinylsilane **20** (106 μL, 0.76 mmol), then cooled to –78 °C. $ClTi(O\textit{i}\text{-}Pr)_3$ (760 μL, 1.0 M in hexanes, 0.76 mmol) and *c*-C_5H_9MgCl (760 μL, 2.0 M in diethyl ether, 1.5 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C.

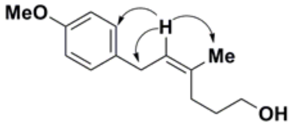
The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

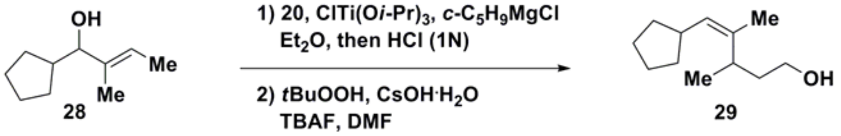
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **16** (44 mg, 0.23 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (122 µL, 2.5M in hexanes, 0.30 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (2.0 mL, ~5.5 M in decane, 11 mmol) in DMF (8 mL) was added CsOH•H_2O (1.5 g, 9.5 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (4.0 mL, 1.0 M in THF, 4.0 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (20% ethyl acetate-hexanes) to provide product **27** (29 mg, 0.13 mmol) in 58% yield (2 steps) ($Z:E \geq 20:1$). Product **27** decomposes slowly upon exposure to air to an inseparable product hypothesized to come from benzylic oxidation followed by allylic transposition. Therefore, product **27** is characterized with this as a small impurity.

Data for (*Z*)-6-(4-methoxyphenyl)-4-methylhex-4-en-1-ol, 27: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 5.35 (t, *J* = 7.5 Hz, 1H), 3.78 (s, 3H), 3.65 (br t, *J* = 5.6 Hz, 2H), 3.31 (d, *J* = 7.2 Hz, 2H), 2.21 (t, *J* = 7.2 Hz, 2H), 1.75 (s, 3H), 1.73-1.67 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 135.5, 133.7, 129.1, 124.6, 113.8, 62.8, 55.2, 33.0, 30.8, 28.0, 23.3; IR (thin film, NaCl) 3425, 1658, 1641, 1632, 1540, 1512, 1362, 1246, 1175, 1035 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{14}H_{20}O_2$, 220.15 *m/z* $(M)^+$; observed, 220.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-6-(4-methoxyphenyl)-4-methylhex-4-en-1-ol, 27:





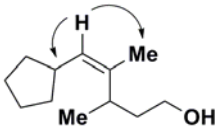
Synthesis of (*Z*)-5-cyclopentyl-3,4-dimethylpent-4-en-1-ol, 29: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (9.5 mL) and chlorodimethylvinylsilane **20** (132 μL, 0.95 mmol), then cooled to –78 °C. $ClTi(Oi\text{-}Pr)_3$ (950 μL, 1.0 M in hexanes, 0.95 mmol) and *c*-C_5H_9MgCl (950 μL, 2.0 M in diethyl ether, 1.9 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

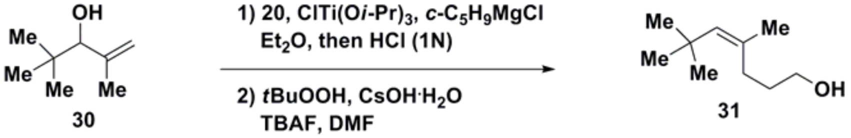
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **28** (50 mg, 0.32 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (152 µL, 2.5M in hexanes, 0.38 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (2.4 mL, ~5.5 M in decane, 13 mmol) in DMF (9 mL) was added CsOH•H_2O (1.9 g, 9.5 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (4.7 mL, 1.0 M in THF, 4.7 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (15% ethyl acetate-hexanes) to provide product **29** (40 mg, 0.22 mmol) in 69% yield (2 steps) (*Z*:*E* ≥ 20:1).

Data for (*Z*)-5-cyclopentyl-3,4-dimethylpent-4-en-1-ol, 29: ^1H NMR (500 MHz, $CDCl_3$) δ 5.07 (dd, *J* = 9.5, 1.3 Hz, 1H), 3.64-3.53 (m, 2H), 2.88-2.80 (m, 1H), 2.72-2.63 (m, 1H), 1.78-1.50 (m, 8H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.36 (t, *J* = 5.7 Hz, 1H), 1.22-1.12 (m, 2H), 0.99 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2, 131.7, 62.0, 38.2, 37.4, 34.2, 34.0, 31.3, 25.3, 19.7, 17.9; IR (thin film, NaCl) 3354, 2956, 2869, 1451, 1374, 1047, 995, 848 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{12}H_{22}O$, 182.17 *m/z* $(M)^+$; observed, 182.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-5-cyclopentyl-3,4-dimethylpent-4-en-1-ol, 29:





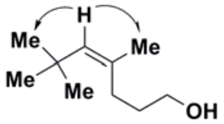
Synthesis of (*Z*)-4,6,6-trimethylhept-4-en-1-ol, 31: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (11 mL) and chlorodimethylvinylsilane **20** (158 μL, 1.1 mmol), then cooled to –78 °C. $ClTi(O\textit{i}\text{-}Pr)_3$ (1.1 mL, 1.0 M in hexanes, 1.1 mmol) and *c*-C_5H_9MgCl (1.1 mL, 2.0 M in diethyl ether, 2.2 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

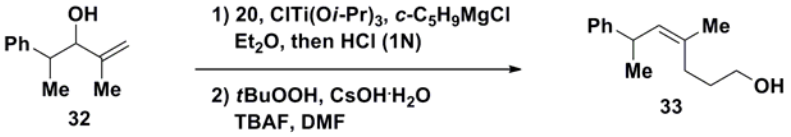
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **30** (50 mg, 0.39 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (184 μL, 2.5M in hexanes, 0.46 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (2.5 mL, ~5.5 M in decane, 14 mmol) in DMF (10 mL) was added $CsOH{\bullet}H_2O$ (2.3 g, 13 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (5.7 mL, 1.0 M in THF, 5.7 mmol) was added, the mixture was heated to 70 °C, and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (15% ethyl acetate-hexanes) to provide product **31** (31 mg, 0.22 mmol) in 56% yield (2 steps) ($Z{:}E \geq 20{:}1$).

Data for (*Z*)-4,6,6-trimethylhept-4-en-1-ol, 31: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19 (s, 1H), 3.69-3.64 (m, 2H), 2.23-2.18 (m, 2H), 1.72-1.66 (m, 2H), 1.67 (d, J = 1.6 Hz, 3H), 1.39 (t, J = 5.3 Hz, 1H), 1.09 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 133.9, 63.3, 32.2, 31.5, 31.4, 28.8, 24.9; IR (thin film, NaCl) 3355, 2957, 1709, 1656, 1463, 1395, 1362, 1200, 1175, 1065, 907, 831, 735, 590 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{10}H_{20}O$, 156.15 *m/z* $(M)^+$; observed, 156.1 $(M)^+$ *m/z*.

nOe's for (*Z*)-4,6,6-trimethylhept-4-en-1-ol, 31:





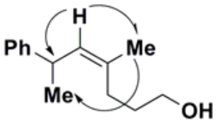
Synthesis of (*Z*)-4-methyl-6-phenylhept-4-en-1-ol, 33: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (8 mL) and chlorodimethylvinylsilane **20** (115 μL, 0.8 mmol), then cooled to –78 °C. ClTi(O*i*-Pr)$_3$ (830 μL, 1.0 M in hexanes, 0.8 mmol) and *c*-C$_5$H$_9$MgCl (830 μL, 2.0 M in diethyl ether, 1.6 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

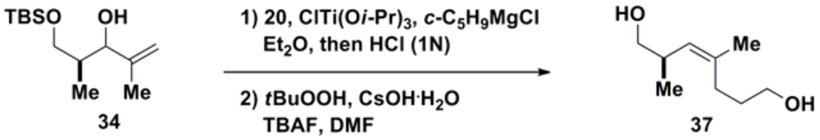
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **32** (4:1 mixture of diastereomers, 50 mg, 0.28 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (132 μL, 2.5M in hexanes, 0.33 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (2.0 mL, ~5.5 M in decane, 11 mmol) in DMF (8 mL) was added CsOH•H_2O (1.7 g, 10 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (4.1 mL, 1.0 M in THF, 4.1 mmol) was added, and the mixture was warmed to 70 °C and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (25% ethyl acetate-hexanes) to provide product **33** (37 mg, 0.18 mmol) in 64% yield (2 steps) (*Z:E* ≥ 20:1).

Data for (*Z*)-4-methyl-6-phenylhept-4-en-1-ol, 33: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.15 (m, 5H), 5.34 (d, *J* = 9.1 Hz, 1H), 3.74-3.66 (m, 1H), 3.58 (app q, *J* = 6.3 Hz, 2H), 2.18 (t, *J* = 7.7 Hz, 2H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.70-1.57 (m, 2H), 1.31 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 133.7, 131.2, 128.4, 126.8, 125.8, 62.7, 37.8, 30.8, 28.2, 23.3, 22.9; IR (thin film, NaCl) 3328, 3025, 2960, 2867, 1652, 1493, 1450, 1375, 1046, 1015, 759, 698 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_{14}H_{20}O$, 204.15 *m/z* $(M)^+$; observed, 204.2 $(M)^+$ *m/z*.

nOe's for (*Z*)-4-methyl-6-phenylhept-4-en-1-ol, 33:





Synthesis of (*R*,*Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (6 mL) and chlorodimethylvinylsilane **20** (83 μL, 0.6 mmol), then cooled to –78 °C. ClTi(O*i*-Pr)$_3$ (600 μL, 1.0 M in hexanes, 0.6 mmol) and *c*-C_5H_9MgCl (600 μL, 2.0 M in diethyl ether, 1.2 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

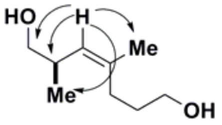
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **34** (1.5:1 mixture of diastereomers, 50 mg, 0.20 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (96 μL, 2.5M in hexanes, 0.24 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

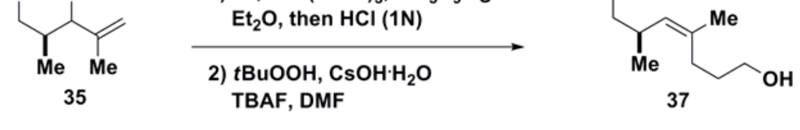
To a cooled (0 °C) solution of *t*BuOOH (1.7 mL, ~5.5 M in decane, 9.5 mmol) in DMF (7 mL) was added $CsOH{\bullet}H_2O$ (1.4 g, 8.2 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (3.4 mL, 1.0 M in THF, 3.4 mmol) was added, and the mixture was warmed to 70

°C and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (60% ethyl acetate-hexanes) to provide product **37** (21 mg, 0.13 mmol) in 66% yield (2 steps) ($Z{:}E \geq 20{:}1$).

Data for (*R*,*Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37: $[\alpha]_{589}^{20}$ +21.6 ° (c = 0.36, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.94 (d, J = 9.8 Hz, 1H), 3.62 (t, J = 5.9 Hz, 2H), 3.51 (dd, J = 10.4, 5.4 Hz, 1H), 3.30 (dd, J = 10.0, 8.8 Hz, 1H), 2.73-2.64 (m, 1H), 2.29 (ddd, J = 13.6, 8.2, 8.2 Hz, 1H), 2.09 (ddd, J = 13.6, 6.6, 6.6 Hz, 1H), 2.00-1.50 (br s, 2H), 1.73 (d, J = 1.6 Hz, 3H), 1.70-1.64 (m, 2H), 0.90 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.8, 128.9, 68.0, 61.9, 35.1, 30.4, 28.0, 23.3, 17.3; IR (thin film, NaCl) 3348, 2931, 2869, 1722, 1452, 1377, 1275, 1035, 846 cm^{-1}; LRMS (EI, $M^{+\cdot}$); calcd for $C_9H_{18}O_2$, 158.13 *m/z* $(M)^+$; observed, 158.2 $(M)^+$ *m/z*.

nOe's for (*R*,*Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37:





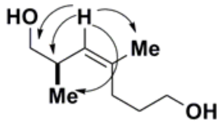
Synthesis of (*R*,*Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (6 mL) and chlorodimethylvinylsilane **20** (55 μL, 0.4 mmol), then cooled to –78 °C. $ClTi(Oi\text{-}Pr)_3$ (400 μL, 1.0 M in hexanes, 0.4 mmol) and $c\text{-}C_5H_9MgCl$ (400 μL, 2.0 M in diethyl ether, 0.8 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C. The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

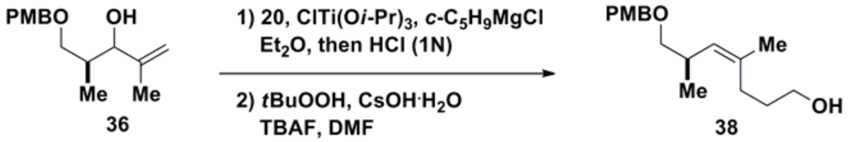
To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **35** (1.2:1 mixture of diastereomers, 50 mg, 0.13 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (64 μL, 2.5M in hexanes, 0.15 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (1.0 mL, ~5.5 M in decane, 5.6 mmol) in DMF (7 mL) was added $CsOH \bullet H_2O$ (800 mg, 4.8 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (2.0 mL, 1.0 M in THF, 2.0 mmol) was added, and the mixture was warmed to 70 °C and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (60% ethyl acetate-hexanes) to provide product **37** (12 mg, 0.08 mmol) in 61% yield (2 steps) (Z:E $\geq$ 20:1).

Data for (*R,Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37: $[\alpha]_{589}^{20}$ +21.6 ^{o} (c = 0.36, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.94 (d, J = 9.8 Hz, 1H), 3.62 (t, J = 5.9 Hz, 2H), 3.51 (dd, J = 10.4, 5.4 Hz, 1H), 3.30 (dd, J = 10.0, 8.8 Hz, 1H), 2.73-2.64 (m, 1H), 2.29 (ddd, J = 13.6, 8.2, 8.2 Hz, 1H), 2.09 (ddd, J = 13.6, 6.6, 6.6 Hz, 1H), 2.00-1.50 (br s, 2H), 1.73 (d, J = 1.6 Hz, 3H), 1.70-1.64 (m, 2H), 0.90 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.8, 128.9, 68.0, 61.9, 35.1, 30.4, 28.0, 23.3, 17.3; IR (thin film, NaCl) 3348, 2931, 2869, 1722, 1452, 1377, 1275, 1035, 846 cm^{-1}; LRMS (EI, $M^{+\cdot}$); LRMS (EI, $M^{+\cdot}$); calcd for $C_9H_{18}O_2$, 158.13 *m/z* $(M)^+$; observed, 158.2 $(M)^+$ *m/z*.

nOe's for (*R,Z*)-2,4-dimethylhept-3-ene-1,7-diol, 37:





Synthesis of (*R,Z*)-7-(4-methoxybenzyloxy)-4,6-dimethylhept-4-en-1-ol, 38: To a flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added ether (6 mL) and chlorodimethylvinylsilane **20** (81 µL, 0.59 mmol), then cooled to –78 °C. $ClTi(O\textit{i}\text{-}Pr)_3$ (590 µL, 1.0 M in hexanes, 0.59 mmol) and $c\text{-}C_5H_9MgCl$ (590 µL, 2.0 M in diethyl ether, 1.2 mmol) were then added sequentially, and the solution was allowed to rapidly warm to –50 °C.

The solution was stirred at –50 °C for 2 h before cooling back to –78 °C (during this time the solution turned from a bright yellow color to dark brown).

To a separate flame-dried flask equipped with a magnetic stir-bar and flushed with argon was added the allylic alcohol **36** (1.5:1 mixture of diastereomers, 50 mg, 0.20 mmol) in THF (1.0 mL). The solution was cooled to –78 °C, and *n*-BuLi (94 µL, 2.5M in hexanes, 0.23 mmol) was added slowly dropwise over 2 min. The solution was rapidly warmed to 0 °C and stirred for 15 min before being transferred via cannula to the dark brown mixture. The solution was then slowly warmed to 0 °C over 2 h. After stirring at 0 °C for 30 min, 1N HCl (3 mL) was added, and the mixture was rapidly stirred for 20 min at rt. This solution was filtered through a pad of silica gel to remove water and titanium salts and the silica gel was subsequently rinsed with 150 ml of EtOAc. After concentration *in vacuo*, the crude product was used in the following reaction without purification.

To a cooled (0 °C) solution of *t*BuOOH (1.5 mL, ~5.5 M in decane, 8.2 mmol) in DMF (6 mL) was added CsOH•H_2O (1.2 g, 7.0 mmol). After the mixture was warmed to rt, a solution of crude isopropoxysilane in DMF (1.0 mL) was added dropwise by syringe. After 10 min, TBAF (2.9 mL, 1.0 M in THF, 2.9 mmol) was added, and the mixture was warmed to 70 °C and stirred at that temperature for 4h. The mixture was cooled to rt, and $Na_2S_2O_3$ was added. The mixture was then partitioned between water (45 mL) and ether (45 mL). The aqueous layer was extracted with ether (3 x 20 mL) and the combined organic layer was washed with $NaHCO_3$ (aq., sat) and brine, before being dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude material was purified by flash column chromatography on silica gel (25% ethyl acetate-hexanes) to provide product **38** (34 mg, 0.12 mmol) in 61% yield (2 steps) as a 1.2:1 mixture of olefin isomers.