Allene-alkyne cross-coupling for stereoselective synthesis of substituted 1,4-dienes and cross-conjugated trienes

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SUPPORTING INFORMATION:

General. All reactions were conducted in flame-dried glassware under nitrogen using anhydrous solvents. Toluene and tetrahydrofuran were distilled from sodium/benzophenone ketyl before using. Diethyl ether was used after passing through an activated alumina column. $Ti(O\textit{i}Pr)_4$ was used after distillation of the commercially available reagent. $ClTi(O\textit{i}Pr)_3$ was purchased as a 1M solution in hexanes from Aldrich® and was used without further analysis or purification. All other commercially available reagents were used as received.

^1H NMR data were recorded at 500 MHz or 400 MHz using a Bruker AM-500, Bruker Avance DPX-500 or Bruker AM-400 instrument. ^1H NMR chemical shifts are reported relative to residual $CHCl_3$ (7.26 ppm). ^{13}C NMR data were recorded at 126 MHz or 100 MHz using a Bruker AM-500, Bruker Avance DPX-500 or Bruker AM-400 instrument. ^{13}C chemical shifts are reported relative to the central line of $CDCl_3$ (77.00 ppm). Infrared spectra were recorded using a Midac Spectrometer M-series. Low resolution mass spectrometry (LRMS) was performed on a Waters Micromass® ZQ™ instrument using electrospray ionization (EI). High resolution mass spectrometry (HRMS) was performed on a 9.4T Bruker Qe FT-ICR instrument using EI. 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.

All allenes are known compounds prepared according to the published procedures:

Allene 12. Molander, G. A.; Cormier, E. P.; *J. Org. Chem.* **2005**, *7*, 2622 - 2626.

Allene 16. Djahanbini, D.; Cazes, B.; Gore, J. *Tetrahedron* **1987**, *43*, 3441-3452.

Allene 18. Hormuth, S.; Reissig, H. *J. Org. Chem*. **1994**, *59*, 67-73.

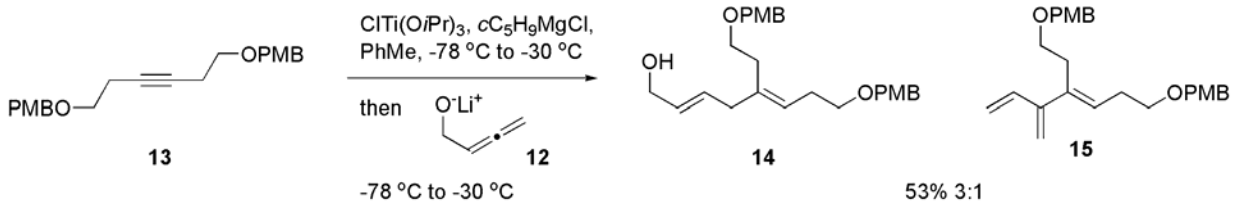
Allene 26. Xu, D.; Lu, Z.; Li, Z.; Ma, S.; *Tetrahedron* **2004**, *60*, 11879-11887.

Allene 29. Ma, S.; Jiao, N.; Zhao, S.; Hou, H. *J. Org. Chem.* **2002**, *67*, 2837-2847.

Allenes 34, 36. Imada, Y.; Nishida, M.; Kutsuwa, K.; Murahashi, S.; Naota, T. *Org. Lett.* **2005**, *7*, 5837-5839.

Allene 38. Murakami, M.; Kadowaki, S.; Matsuda, T. *Org. Lett.* **2005**, *7*, 3953-3956.

Allene 49. Kang, S-K.; Kim, S-G.; Cho, D-G. *Tetrahedron: Asymmetry* **1992**, *3*, 1509-1510.

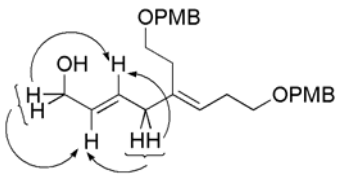


Synthesis of 1,4-Diene 14 and Triene 15. To a –78 °C solution of alkyne **13**[1] (266 mg, 0.75 mmol) in 5.0 mL of PhMe was added 1.50 mL of $ClTi(OiPr)_3$ (1.0M in hexanes, 1.50 mmol) and 1.53 mL of cC_5H_9MgCl (1.96M in Et_2O, 3.00 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **12** (105 mg, 1.50 mmol) in 1.0 mL PhMe was added 610 μL of *n*BuLi (2.45M in hexanes, 1.50 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to –30 °C over 1.5 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was

warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography (10 % EtOAc/hexanes, then 50 % EtOAc/hexanes) of the crude material (**14**:**15** = 3:1 by ^{1}H NMR) provided 128 mg (40 %) of diene **14** and 40 mg (13%) of triene **15** as clear, colorless oils.

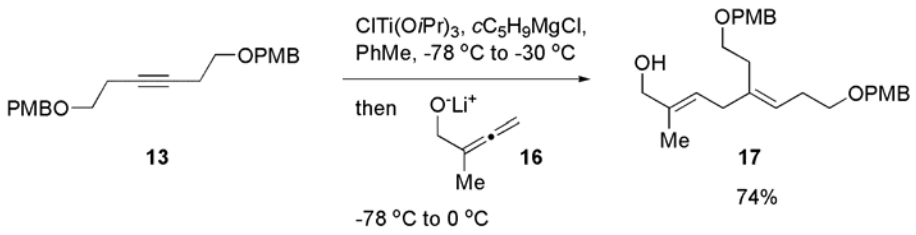
(2*E*,5*Z*)-8-(4-methoxybenzyloxy)-5-(2-(4-methoxybenzyloxy)ethyl)octa-2,5-dien-1-ol, 14. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.23 (m, 4H), 6.88-6.86 (m, 4H), 5.64-5-63 (m, 2H), 5.26 (t, *J* = 7.3 Hz, 1H), 4.42 (s, 2H), 4.41 (s, 2H), 4.09 (br s, 2H), 3.80 (s, 3H), 3.80 (s, 3H), 3.44 (t, *J* = 7.3, 2H), 3.42 (t, *J* = 6.9 Hz, 2H), 2.75 (br s, 2H), 2.37-2.32 (m, 4H), 1.25 (t, *J* = 6.0, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 136.2, 130.9, 130.6, 130.5, 129.2, 129.1, 123.9, 113.7, 72.4, 69.7, 68.4, 63.6, 55.2, 40.3, 30.8, 28.6; IR (thin film, NaCl) 3426, 2934, 2858, 1613, 1513, 1464, 1361, 1248, 1173, 1093, 1035, 820 cm^{-1}; HRMS (EI, K) calcd for $C_{26}H_{34}O_5K$, 465.2043 *m/z* (M + K); observed, 465.2020 $(M + K)^+$ *m/z*.

Observed nOe enhancements for structure determination:



(3*E*)-1-(4-methoxybenzyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-5-vinyl-3,5-hexadiene, 15. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.23 (m, 4H), 6.88-6.85 (m, 4H), 6.37 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.51 (t, *J* = 6.9 Hz, 1H), 5.24 (d, *J* = 17.3 Hz, 1H), 5.10 (d, *J* = 10.4 Hz, H), 5.06 (s, 1H), 4.97 (s, 1H), 4.43 (s, 2H), 4.39 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.47 (t, *J* = 7.3 Hz, 2H), 3.42 (t, *J* = 7.3 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 2.46 (dt, *J* = 13.9, 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.09, 159.05, 149.2, 137.8, 136.7, 130.63, 130.57, 129.2, 129.1, 127.4, 116.2, 114.2, 113.72, 113.69, 72.50, 72.48, 69.5, 68.7, 55.2, 30.1,

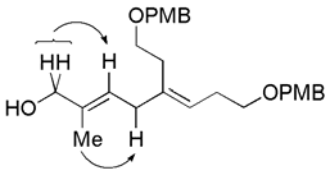
28.9; IR (thin film, NaCl) 2935, 2857, 1613, 1586, 1513, 1464, 1361, 1302, 1249, 1173, 1097, 1035, 821 cm^{-1}; HRMS (EI, H) calcd for $C_{26}H_{33}O_4$, 409.2380 *m/z* (M + H); observed, 409.2370 $(M + H)^+$ *m/z*.

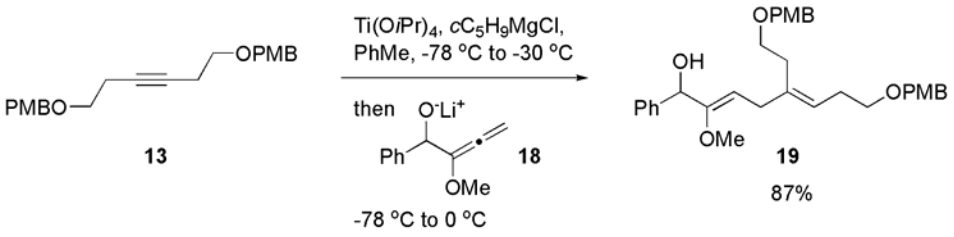


Synthesis of 1,4-Diene 17. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 850 µL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.85 mmol) and 860 µL of cC_5H_9MgCl (1.96M in Et_2O, 1.69 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **16**[2] (69 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 µL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (20 % EtOAc/hexanes, then 50 % EtOAc/hexanes) provided 127 mg (74 %) of diene **17** as a clear, colorless oil. A small portion was further purified by HPLC [EtOAc/hexanes: gradient from 35 % to 55 % (0-20 min, 25 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] to obtain a sample for analytical characterization.

(2*E*,5*Z*)-8-(4-methoxybenzyloxy)-5-(2-(4-methoxybenzyloxy)ethyl)-2-methylocta-2,5-dien-1-ol, 17. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.23 (m, 4H), 6.89-6.85 (m, 4H), 5.42-5.37 (m, 1H), 5.24 (t, *J* = 7.1 Hz, 1H), 4.42 (s, 2H), 4.41 (s, 2H), 4.00 (d, *J* = 5.8 Hz, 2H), 3.80 (s, 3H), 3.80 (s, 3H), 3.46-3.39 (m, 4H), 2.75 (d, *J* = 7.3 Hz, 2H), 2.34 (dt, *J* = 14.7, 7.6 Hz, 2H), 2.33 (t, *J* = 7.3 Hz, 2H), 1.64 (s, 3H), 1.34 (t, *J* = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 136.6, 136.0, 130.6, 130.5, 129.21, 129.16, 123.8, 123.1, 113.7, 77.2, 72.5, 69.8, 68.8, 68.6, 55.2, 35.7, 31.1, 28.6, 13.6; IR (thin film, NaCl) 3433, 2907, 2857, 1613, 1513, 1464, 1360, 1302, 1173, 1093, 1035, 802 cm^{-1}; HRMS (EI, H) calcd for $C_{27}H_{37}O_5$, 441.2642 *m/z* (M + H); observed, 463.2634 $(M + H)^+$ *m/z*.

Observed nOe enhancements for structure determination:



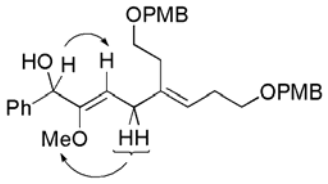


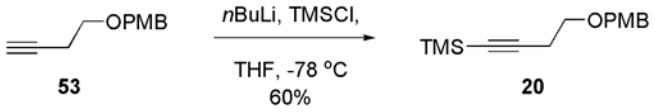
Synthesis of 1,4-Diene 19. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 μL of Ti(O*i*Pr)$_4$ (0.84 mmol) and 860 μL of *c*C_5H_9MgCl (1.96M in Et_2O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **18** (33 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 μL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was

stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly from –78 °C to –30 °C over 1 hr, then from –30 °C to 0 °C over 1 hr, then at 0 °C for 1 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography (20 % EtOAc/hexanes, then 50 % EtOAc/hexanes) of the crude material provided 180 mg (87 %) of diene **19** as a clear, colorless oil. A small portion was further purified by HPLC [EtOAc/hexanes: gradient from 30 % to 45 % (0-10 min, 25 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] to obtain a sample for analytical characterization.

(2*Z*,5*Z*)-8-(4-methoxybenzyloxy)-5-(2-(4-methoxybenzyloxy)ethyl)-2-methoxy-1-phenylocta-2,5-dien-1-ol, 19. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.35-7.32 (m, 2H), 7.30-7.22 (m, 5H), 6.89-6.84 (m, 4H), 5.27 (t, *J* = 7.3 Hz, 1H), 5.20 (d, *J* = 4.7 Hz, 1H), 4.93 (t, *J* = 7.6 Hz, 1H), 4.42 (s, 2H), 4.40 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.51 (s, 3H), 3.46 (t, *J* = 7.3 Hz, 2H), 3.41 (t, *J* = 6.9 Hz, 2H), 2.85 (d, *J* = 7.3 Hz, 2H), 2.38-2.32 (m, 4H), 2.27 (d, *J* = 4.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.14, 159.12, 156.9, 141.5, 136.8, 130.7, 130.6, 129.2, 129.1, 128.3, 127.7, 126.6, 123.1, 113.8, 113.7, 111.1, 77.2, 74.0, 72.49, 72.46, 69.8, 68.6, 59.7, 55.3, 33.0, 31.2, 28.6; IR (thin film, NaCl) 3423, 2936, 2847, 1613, 1513, 1454, 1360, 1302, 1248, 1174, 1091, 1035, 820, 703 cm^{-1}; HRMS (EI, Na) calcd for $C_{33}H_{40}O_6Na$, 555.2825 *m/z* (M + Na); observed, 555.2730 $(M + Na)^+$ *m/z*.

Observed nOe enhancements for structure determination:

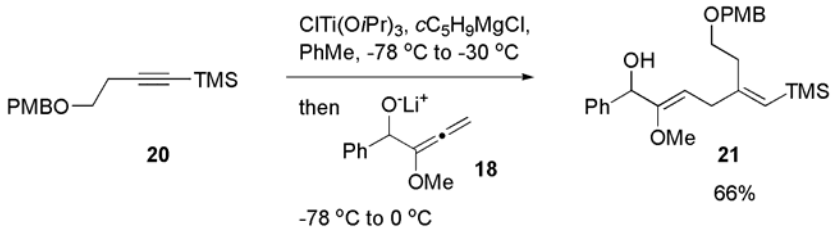




53 20

Synthesis of Alkyne 20. To alkyne **53** (328 mg, 1.72 mmol) in 14 mL of THF was added 1.1 mL of *n*BuLi (2.45M in hexanes, 2.58 mmol) dropwise at –78 °C. The reaction was stirred for 30 min at –78 °C, then 435 μL of TMSCl was added and the reaction was stirred overnight warming to room temperature. The resulting mixture was quenched with water and extracted with Et_2O (3 x 5 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 10 mL) and brine (1 x 10 mL) and dried over anhydrous Na_2SO_4. Purification of the crude material by flash column chromatography (5 % EtOAc/hexanes) provided 270 mg (60 %) of **20** as a clear, pale yellow oil.

(4-(4-methoxybenzyloxy)but-1-ynyl)trimethylsilane, 20. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 6.89-6.87 (m, 2H), 4.49, (s, 2H), 3.81 (s, 2H), 3.57 (t, *J* = 7.3 Hz, 2H), 2.53 (t, *J* = 7.3 Hz, 2H), 0.15 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3, 130.3, 129.2, 113.8, 103.8, 85.7, 72.6, 68.1, 55.3, 21.3, 0.1; IR (thin film, NaCl) 2958, 2178, 1616, 1457, 1249, 1100, 1037, 842, 760 cm^{-1}; LRMS (EI, Na) calcd for $C_{15}H_{22}O_2SiNa$, 285.14 *m/z* (M + Na); observed, 285.2 $(M + Na)^+$ *m/z*.

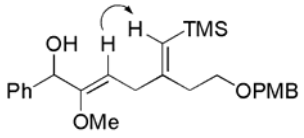


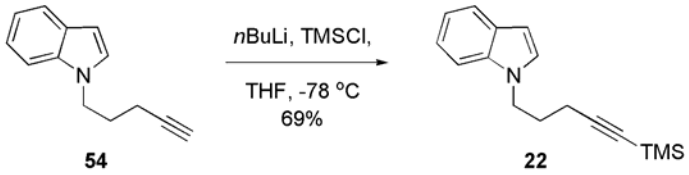
Synthesis of 1,4-Diene 21. To a –78 °C solution of alkyne **20** (116 mg, 0.44 mmol) in 2.9 mL of PhMe was added 660 μL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.84 mmol) and 680 μL of cC_5H_9MgCl (1.96M in Et_2O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned black while warming slowly to –30 °C over 1 hr. The reaction

mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **18** (54 mg, 0.31 mmol) in 1.0 mL PhMe was added 130 μL of *n*BuLi (2.45M in hexanes, 0.31 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (10 % EtOAc/hexanes, then 20 % EtOAc/hexanes) provided 90 mg (66 %) of diene **21** as a clear, colorless oil in a 4:1 mixture of regioisomers. Attempts at further purification using HPLC [EtOAc/hexanes: gradient from 16 % to 35 % (0-10 min, 25 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] were unsuccessful; analytical characterization of **21** was carried out on a 5:1 mixture of regioisomers.

(2*Z*,5*Z*)-7-(4-methoxybenzyloxy)-2-methoxy-1-phenyl-5-((trimethylsilyl)methylene)hept-2-en-1-ol, 21. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.22 (m, 6H), 6.88-6.85 (m, 3H), 5.33 (s, 1H), 5.23 (d, *J* = 5.0 Hz, 1H), 4.98 (t, *J* = 8.2 Hz, 1H), 4.42 (s, 2H), 3.80 (s, 3H), 3.50 (t, *J* = 7.6 Hz, 2H), 3.50 (s, 3H), 2.92 (d, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.6 Hz, 2H), 2.22 (d, *J* = 4.7 Hz, 1H), 0.08 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 157.0, 154.3, 141.5, 130.6, 129.2, 128.4, 127.8, 126.6, 126.2, 113.7, 110.8, 74.1, 72.6, 69.3, 59.7, 55.3, 36.6, 35.1, 0.3; IR (thin film, NaCl) 3433, 2952, 2835, 1616, 1513, 1457, 1248, 1088, 1036, 838 cm^{-1}; HRMS (EI, K) calcd for $C_{26}H_{36}O_4SiK$, 479.2014 *m/z* (M + K); observed, 479.1999 $(M + K)^+$ *m/z*.

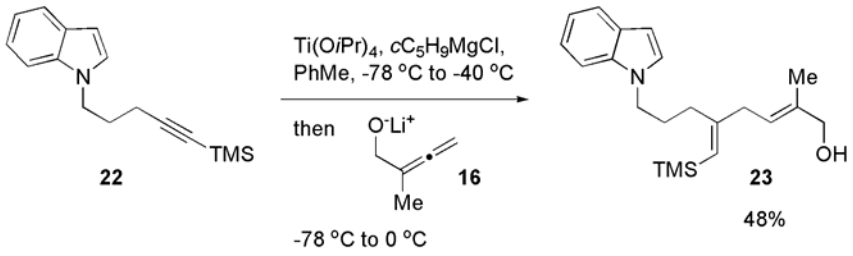
Observed nOe enhancements for structure determination:





Synthesis of Alkyne 22. To alkyne **54**[3] (74 mg, 0.4 mmol) in 2.0 mL of THF was added 240 μL of *n*BuLi (2.5M in hexanes, 0.6 mmol) dropwise at –78 °C. The reaction was warmed to 0 °C over 2 hr, then 91 μL of TMSCl was added and the reaction was stirred at 0 °C for 1 hr. Removal of the solvent in vacuo and purification of the crude material by flash column chromatography (5 % EtOAc/hexanes) provided 70 mg (69 %) of **22** as a clear, colorless oil.

1-(5-(trimethylsilyl)pent-4-ynyl)-1H-indole, 22. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.14-7.11 (m, 2H), 6.52 (d, *J* = 3.2 Hz, 1H), 4.29 (t, *J* = 6.9 Hz, 2H), 2.22 (t, *J* = 6.6 Hz, 2H), 2.04 (dt, *J* = 13.6, 6.9 Hz, 2H), 0.20 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.9, 128.6, 127.9, 121.4, 120.9, 119.3, 109.3, 105.7, 101.2, 86.1, 44.6, 28.8, 17.2, 0.1; IR (thin film, NaCl) 3056, 2959, 2175, 1512, 1464, 1316, 1249, 1169, 1025, 842, 761, 740, 639 cm^{-1}; LRMS (EI, H) calcd for $C_{16}H_{22}NSi$, 256.14 *m/z* (M + H); observed, 256.0 $(M + H)^+$ *m/z*.

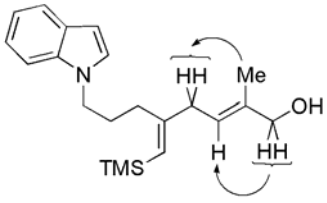


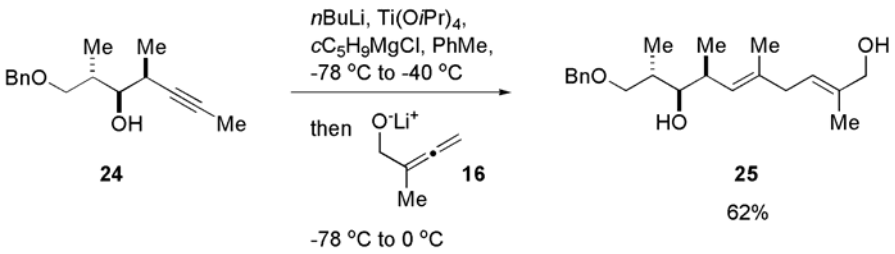
Synthesis of 1,4-Diene 23. To a solution of alkyne **22** (60 mg, 0.23 mmol) in 1.6 mL of PhMe was added 105 μL of $Ti(OiPr)_4$. After cooling to –78 °C, 390 μL of cC_5H_9MgCl (1.85M in Et_2O, 0.72 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned black while warming slowly to –40 °C over 1 hr. The reaction mixture was stirred at –40 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **16** (14 mg, 0.16 mmol) in 0.5 mL PhMe was added 68 μL of *n*BuLi (2.5M in hexanes, 0.17 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 10 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 20 mL), brine (1 x 20 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent in vacuo gave a crude oil as a 4:1 mixture of regioisomers by ^1H NMR. Flash column chromatography (10 % EtOAc/hexanes, then 20 % EtOAc/hexanes) provided 26 mg (48 %) of diene **23** as a clear, colorless oil. Further purification of a small sample using HPLC [EtOAc/hexanes: gradient from 13 % to 28 % (0-10 min, 25 mL/min), 28 % to 40 % (10-15 min, 25 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample for characterization.

(2*E*,5*E*)-8-(1H-indol-1-yl)-2-methyl-5-((trimethylsilyl)methylene)oct-2-en-1-ol, 23. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.20 (dt, *J* = 6.9, 1.3 Hz, 1H), 7.11-7.08 (m, 2H), 6.49 (dd, *J* = 3.2, 0.6 Hz, 1H), 5.33 (tq, *J* = 7.3, 1.3 Hz, 1H), 5.22 (app t, *J* = 1.3 Hz, 1H), 4.13 (t, *J* = 6.9 Hz, 2H), 3.95 (d, *J* = 6.9 Hz, 2H), 2.76 (d, *J* = 6.9 Hz, 2H), 2.14-2.11 (m, 2H), 1.96-1.90 (m, 2H), 1.55 (s, 1H), 1.54 (s, 3H), 0.01 (s, 9H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8, 136.1, 135.7, 128.4, 127.4, 125.1, 123.0, 121.2, 120.8, 119.0, 109.0, 100.9, 68.5, 46.2, 37.0, 33.3, 29.5, 13.3, 0.0; IR (thin film, NaCl) 3374, 2951, 1612, 1512, 1464, 1316, 1247, 1174, 1014, 838, 739 cm^{-1}.

Observed nOe enhancements for structure determination:



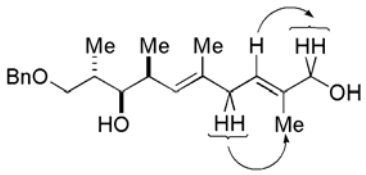


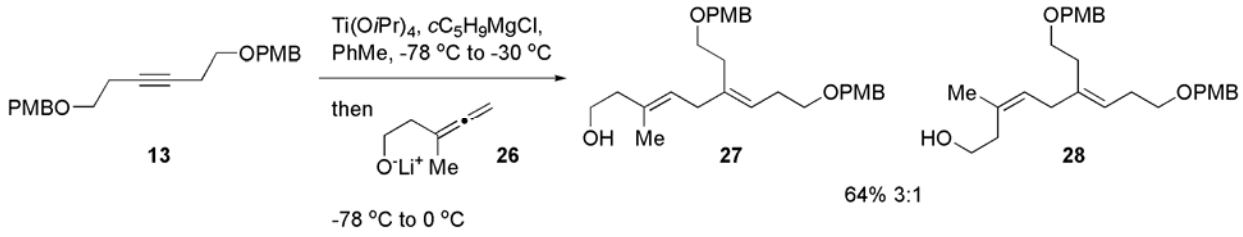
Synthesis of 1,4-Diene 25. To a –78 °C solution of alkyne **24**[4] (40 mg, 0.23 mmol) in 1.2 mL of PhMe was added 64 μL of *n*Buli (2.5M in hexanes, 0.16 mmol). After stirring for 10 min at –78 °C, 70 μL of $Ti(OiPr)_4$ and 260 μL of cC_5H_9MgCl (1.85M in Et_2O, 0.48 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned black while warming slowly to –40 °C over 1 hr. The reaction mixture was stirred at –40 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **16** (9 mg, 0.11 mmol) in 0.5 mL PhMe was added 44 μL of *n*BuLi (2.5M in hexanes, 0.11 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 10 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 20 mL), brine (1 x 20 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography (20 % EtOAc/hexanes) provided 23 mg

(62 %) of diene **25** as a clear, colorless oil. A small sample was further purified using HPLC [EtOAc/hexanes: gradient from 16 % to 35 % (0-10 min, 25 mL/min) on a Microsorb (Si 80-199-C5 F310195) column] to obtain an analytically pure sample for characterization.

(2*E*,5*E*,7*S*,8*R*,9*S*)-10-(benzyloxy)-2,5,7,9-tetramethyldeca-2,5-diene-1,8-diol, 25. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.40 (dt, *J* = 7.2, 1.3 Hz, 1H), 5.10 (dd, *J* = 9.5, 1.3 Hz, 1H), 4.52 (A of AB, *J* = 12.0 Hz, 1H), 4.48 (B of AB, *J* = 12.0 Hz, 1H), 4.02 (d, *J* = 5.7 Hz, 2H), 3.60 (dd, *J* = 9.1, 4.4 Hz, 1H), 3.45 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.30 (dd, *J* = 11.7, 5.7 Hz, 1H), 3.10 (d, *J* = 5.7 Hz, 1H), 2.69 (d, *J* = 7.3 Hz, 2H), 2.50-2.43 (m, 1H), 1.93-1.85 (m, 1H), 1.67 (s, 3H), 1.54 (s, 3H), 1.27 (br s, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.8, 135.9, 132.9, 128.6, 128.4, 127.8, 127.7, 124.2, 80.1, 74.4, 73.6, 37.9, 36.1, 35.8, 16.3, 15.4, 14.9, 13.7; IR (thin film, NaCl) 3415, 2963, 2915, 2864, 1653, 1455, 1357, 1076, 1013, 736, 698 cm^{-1}; HRMS (EI, Na) calcd for $C_{21}H_{32}O_3Na$, 355.2249 *m/z* (M + Na); observed, 355.2239 $(M + Na)^+$ *m/z*.

Observed nOe enhancements for structure determination:





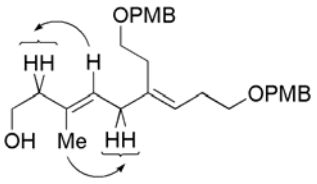
Synthesis of 1,4-Diene 27. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 μL of Ti(O*i*Pr)$_4$ (0.85 mmol) and 860 μL of *c*C_5H_9MgCl

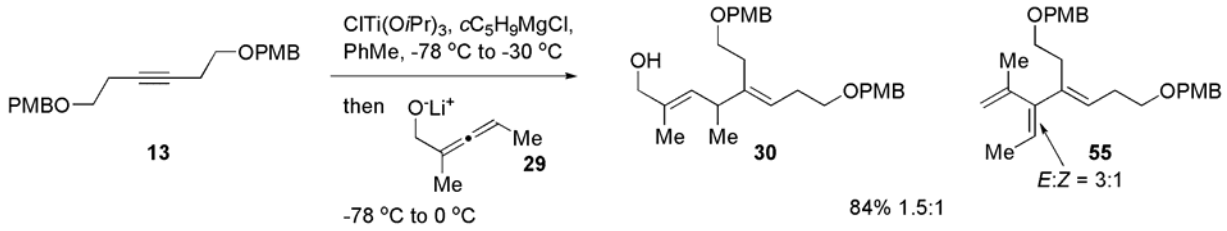
(1.96M in Et_2O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **26** (38 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 μL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography (15 % EtOAc/hexanes, then 40 % EtOAc/hexanes) of the crude material provided 113 mg (64 %) of diene **27** as a clear, colorless oil in a 3:1 (*E*:*Z*) mixture of olefin isomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 35 % to 50 % (0-15 min, 25 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **27.**

(3*E*,6*Z*)-9-(4-methoxybenzyloxy)-6-(2-(4-methoxybenzyloxy)ethyl)-3-methylnona-3,6-dien-1-ol, 27. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.23 (m, 4H), 6.89-6.85 (m, 4H), 5.25-5.21 (m, 2H), 4.42 (s, 2H), 4.41 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.65 (dt, *J* = 12.3, 6.3 Hz, 2H), 3.44 (t, *J* = 7.6 Hz, 2H), 3.41 (t, *J* = 6.9 Hz, 2H), 2.74 (d, *J* = 7.3 Hz, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.33 (dt, *J* = 15.4, 7.6 Hz, 2H), 2.25 (t, *J* = 6.0 Hz, 2H), 1.61 (s, 3H), 1.37 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 136.8, 132.6, 130.64, 130.56, 129.19, 129.16, 125.7, 123.0, 113.7, 72.5, 69.8, 68.6, 60.2, 55.2, 42.7, 36.2, 31.1, 28.6, 15.7; IR (thin film,

NaCl) 3439, 2857, 1613, 1513, 1464, 1302, 1248, 1173, 1093, 1036, 820 cm^{-1}; HRMS (EI, H) calcd for $C_{28}H_{39}O_5$, 455.2792 *m/z* (M + H); observed, 455.2785 $(M + H)^+$ *m/z*.

Observed nOe enhancements for structure determination:



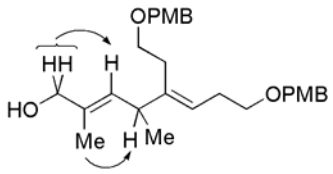


Synthesis of 1,4-Diene 30 and Triene 55. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 850 µL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.85 mmol) and 860 µL of cC_5H_9MgCl (1.96M in Et_2O, 1.69 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **29** (39 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 µL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to –30 °C over 1 hr, then at –30 °C for 1 hr, then from –30 °C to 0 °C over 1 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography (5 % EtOAc/hexanes, then 10 % EtOAc/hexanes, then 50 %

EtOAc/hexanes) of the crude material (**30**:**55** = 1.5:1 by ^{1}H NMR) provided 91 mg (51 %) of diene **30** and 57 mg (33 %) of triene **55** as clear, colorless oils. Triene **55** was isolated as a 3:1 mixture of olefin isomers, favoring *E*-isomer **55** (shown) over *Z*-isomer **55a**. Separation of the triene olefin isomers using HPLC [EtOAc/hexanes: gradient from 10 % to 15 % (0-10 min, 29 mL/min); then 15 % to 30 % (10-15 min, 29 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided analytically pure samples of **55** and **55a**.

(2*E*,5*E*)-8-(4-methoxybenzyloxy)-5-(2-(4-methoxybenzyloxy)ethyl)-2,4-dimethylocta-2,5-dien-1-ol, 30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.23 (m, 4H), 6.88-6.86 (m, 4H), 5.28 (t, *J* = 6.9 Hz, 1H), 5.21 (d, *J* = 9.5 Hz, 1H), 4.42 (s, 2H), 4.40 (s, 2H), 3.95 (d, *J* = 5.7 Hz, 2H), 3.80 (s, 3H), 3.79, (s, 3H), 3.41 (dt, *J* = 14.8, 7.3 Hz, 4H), 3.03 (dq, *J* = 8.8, 6.9 Hz, 1H), 2.42-2.26 (m, 4H), 1.64 (s, 3H), 1.36 (t, *J* = 6.0 Hz, 1H), 0.95 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 141.1, 134.0, 130.7, 130.63, 130.57, 129.18, 129.15, 121.4, 113.7, 72.45, 72.41, 69.9, 69.1, 68.8, 55.2, 38.7, 30.4, 28.6, 19.8, 13.8; IR (thin film, NaCl) 3429, 2958, 2859, 1613, 1513, 1463, 1361, 1302, 1248, 1173, 1093, 1035, 820 cm^{-1}; HRMS (EI, H) calcd for $C_{28}H_{39}O_5$, 455.2792 *m/z* (M + H); observed, 455.2788 $(M + H)^+$ *m/z*.

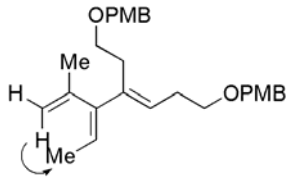
Observed nOe enhancements for structure determination:



(3*E*,5*E*)-1-(4-methoxybenzyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-5-(2-propenyl)-3,5-heptadiene, 55. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.24 (m, 4H), 6.88-6.86 (m, 4H), 5.53 (t, *J* = 6.8 Hz, 1H), 5.51 (t, *J* = 7.1 Hz, 1H), 5.13-5.11 (m, 1H), 4.66-4.65 (m, 1H), 4.42 (s, 2H), 4.41 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.44 (t, *J* = 7.1 Hz, 2H), 3.42 (t, *J* =

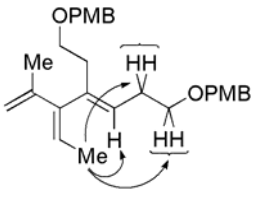
8.1 Hz, 2H), 2.57 (t, *J* = 8.1 Hz, 2H), 2.43 (dt, *J* = 14.1, 7.1 Hz, 2H), 1.72 (s, 3H), 1.68 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.0, 145.4, 143.0, 136.5, 130.7, 130.6, 129.2, 129.1, 125.7, 119.2, 115.2, 113.7, 77.0, 72.4, 69.7, 69.0, 55.2, 29.1, 28.6, 22.9, 14.9; IR (thin film, NaCl) 2935, 2854, 1613, 1513, 1257, 1361, 1302, 1248, 1173, 1093, 1036, 820 cm^{-1}; LRMS (EI, Na) calcd for $C_{28}H_{36}O_4Na$, 459.26 *m/z* (M + Na); observed, 459.3 $(M + Na)^+$ *m/z*.

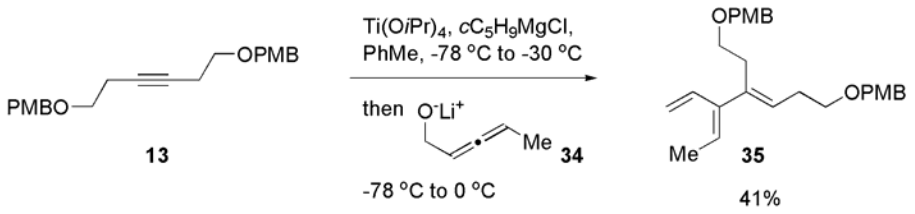
Observed nOe enhancements for structure determination:



(3E,5Z)-1-(4-methoxybenzyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-5-(2-propenyl)-3,5-heptadiene, 55a. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.21 (m, 4H), 6.88-6.84 (m, 4H), 5.65 (q, *J* = 6.9 Hz, 1H), 5.24 (t, *J* = 7.3 Hz, 1H), 4.86 (s, 2H), 4.41 (s, 2H), 4.35 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.49 (t, *J* = 3.5 Hz, 2H), 3.38 (t, *J* = 7.3 Hz, 2H), 2.49 (dt, *J* = 14.2, 6.9 Hz, 2H), 1.86 (s, 3H), 1.66 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.11, 159.07, 145.2, 143.0, 135.2, 130.78, 130.75, 129.2, 127.9, 122.3, 113.75, 113.71, 77.2, 72.52, 72.46, 69.9, 68.7, 55.3, 31.3, 28.8, 20.7, 15.3; IR (thin film, NaCl) 2954, 2854, 1614, 1514, 1457, 1302, 1248, 1173, 1098, 1036, 821 cm^{-1}; LRMS (EI, Na) calcd for $C_{28}H_{36}O_4Na$, 459.26 *m/z* (M + Na); observed, 459.3 $(M + Na)^+$ *m/z*.

Observed nOe enhancements for structure determination:



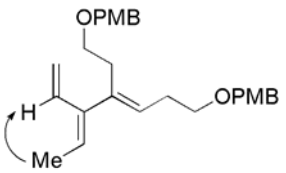


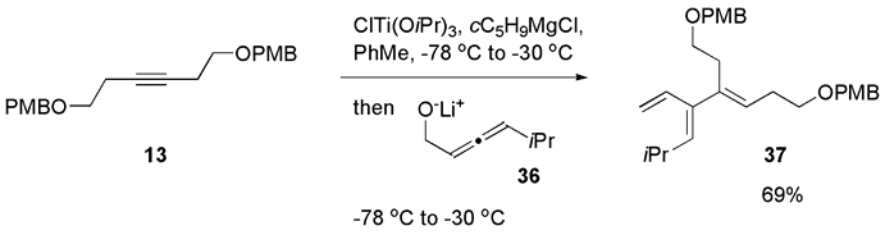
Synthesis of Triene 35. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 μL of Ti(O*i*Pr)$_4$ (0.85 mmol) and 860 μL of *c*C$_5$H$_9$MgCl (1.96M in Et$_2$O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **34**[5] (33 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 μL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH$_4$Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. NaHCO$_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na$_2$SO$_4$. Flash column chromatography (15 % EtOAc/hexanes, then 40 % EtOAc/hexanes) of the crude material provided 146 mg of a clear, colorless oil. Further purification by HPLC [EtOAc/hexanes: gradient from 8 % to 15 % (0-15 min, 30 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided 45 mg (41 %)[6] of analytically pure triene **35.**

(3*E*,5*E*)-1-(4-methoxybenzyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-5-vinyl-3,5-heptadiene, 35. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.26-7.22 (m, 4H), 6.88-6.85 (m, 4H), 6.55 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.43 (q, *J* = 6.9 Hz, 1H), 5.37 (t, *J* = 7.3 Hz, 1H), 5.16 (d, *J* = 10.7 Hz, 1H), 5.10 (dd, *J* = 17.8, 1.6 Hz, 1H), 4.42 (s, 2H), 4.37 (s, 2H), 3.80 (s, 3H), 3.79 (s,

3H), 3.46 (t, *J* = 6.9 Hz, 2H), 3.37 (t, *J* = 7.3 Hz, 2H), 2.52 (t, *J* = 7.6 Hz, 2H), 2.42 (dt, *J* = 14.5, 6.9 Hz, 2H), 1.73 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 159.0, 141.9, 138.7, 132.3, 130.7, 130.6, 129.18, 129.15, 126.6, 124.5, 116.4, 113.71, 113.67, 72.5, 72.4, 69.8, 68.8, 55.2, 30.3, 28.8, 13.6; IR (thin film, NaCl) 2854, 1653, 1614, 1513, 1457, 1302, 1248, 1173, 1096, 1036 cm^{-1}; HRMS (EI, H) calcd for $C_{27}H_{35}O_4$, 423.2530 *m/z* (M + H); observed, 423.2528 $(M + H)^+$ *m/z*.

Observed nOe enhancements for structure determination:



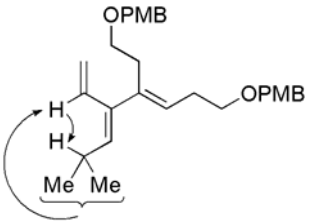


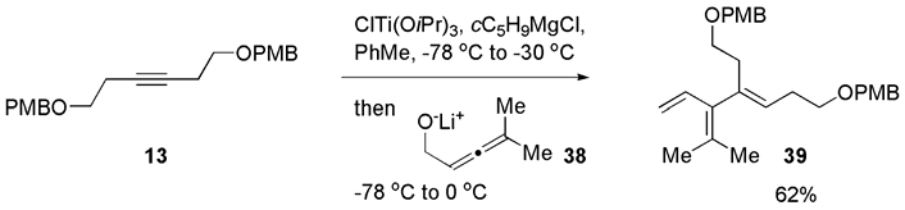
Synthesis of Triene 37. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 850 µL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.85 mmol) and 860 µL of cC_5H_9MgCl (1.96M in Et_2O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **36** (44 mg, 0.39 mmol) in 1.0 mL PhMe was added 160 µL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to –30 °C over 1 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat.

$NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes, then 7.5 % EtOAc/hexanes) provided 121 mg (69 %) of triene **37** as a clear, colorless oil.

(3*E*,5*E*)-1-(4-methoxybenzyloxy)-4-(2-methoxybenzyloxy)ethyl)-5-vinyl-7-methyl-3,5-octadiene, 37. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.21 (m, 4H), 6.88-6.83 (m, 4H), 6.53 (dd, *J* = 17.4, 10.6 Hz, 1H), 5.36 (t, *J* = 7.3 Hz, 1H), 5.15 (d, *J* = 10.1 Hz, 1H), 5.13-5.06 (m, 2H), 4.42 (s, 2H), 4.37 (s, 2H), 3.78 (s, 3H), 3.78 (s, 3H), 3.46 (t, *J* = 7.1 Hz, 2H), 3.36 (t, *J* = 7.3 Hz, 2H), 2.74-2.65 (m, 1H), 2.51 (t, *J* = 7.6 Hz, 2H), 2.42 (dt, *J* = 14.1, 7.3 Hz, 2H), 0.95 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.0, 138.7, 138.5, 138.1, 132.6, 130.7, 130.6, 129.2, 129.1, 126.6, 116.4, 113.69, 113.65, 72.44, 72.39, 69.7, 68.7, 55.21, 55.20, 30.2, 28.8, 26.9, 23.1; IR (thin film, NaCl) 2957, 2864, 1613, 1513, 1464, 1360, 1302, 1248, 1173, 1097, 1037, 820 cm^{-1}; HRMS (EI, K) calcd for $C_{29}H_{38}O_4K$, 489.2402 *m/z* (M + K); observed, 489.2385 $(M + K)^+$ *m/z*.

Observed nOe enhancements for structure determination:

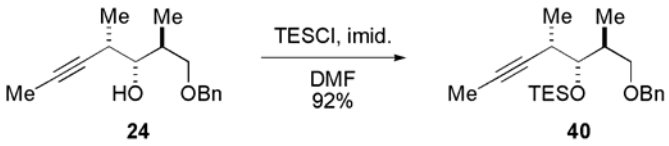




Synthesis of Triene 39. To a –78 °C solution of alkyne **13** (200 mg, 0.56 mmol) in 3.7 mL of PhMe was added 840 μL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.84 mmol) and 860 μL of cC_5H_9MgCl (1.96M in Et_2O, 1.68 mmol) dropwise via a gas-tight syringe. The resulting

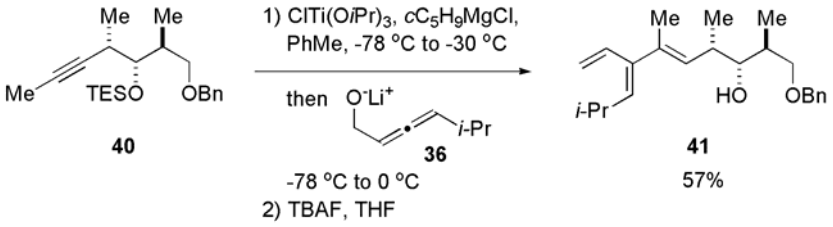
clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **38** (33 mg, 0.34 mmol) in 1.0 mL PhMe was added 160 μL of *n*BuLi (2.45M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes, then 10 % EtOAc/hexanes) provided 91 mg (69 %) of triene **39** as a clear, colorless oil.

(3*E*)-1-(4-methoxybenzyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-5-vinyl-6,6'-dimethyl-3,5-hexadiene, 39. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.22 (m, 4H), 6.87-6.84 (m, 4H), 6.70 (dd, *J* = 17.0, 10.7 Hz, 1H), 5.19 (t, *J* = 7.3 Hz, 1H), 5.00-4.95 (m, 2H), 4.41 (s, 2H), 4.35 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.49 (t, *J* = 7.3 Hz, 2H), 3.38 (t, *J* = 7.3 Hz, 2H), 2.50-2.46 (m, 4H), 1.81 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.11, 159.07, 136.7, 135.9, 134.1, 131.8, 130.81, 130.77, 128.13, 113.8, 77.2, 72.52, 72.46, 69.9, 68.8, 55.3, 31.6, 28.8, 22.9, 19.6; IR (thin film, NaCl) 2906, 2853, 1613, 1513, 1464, 1361, 1302, 1248, 1173, 1096, 1036, 820 cm^{-1}; HRMS (EI, Na) calcd for $C_{28}H_{36}O_4Na$, 459.2614 *m/z* (M + Na); observed, 459.2506 $(M + Na)^+$ *m/z*.



Synthesis of Alkyne 40. To alkyne **24** (3.00 g, 12.2 mmol) in 47 mL of DMF was added 1.66 mg of imidazole (24.4 mmol) followed by 3.51 mL of TESCl (20.7 mmol) at room temperature. The reaction was stirred overnight at room temperature and quenched with water (200 mL). After extraction with EtOAc (3 x 75 mL), the combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 100 mL) and brine (1 x 100 mL) and dried over anhydrous Na_2SO_4. Purification of the crude material by flash column chromatography (5 % EtOAc/hexanes) provided 4.03 g (92 %) of **40** as a clear, colorless oil.

(2*S*,3*R*,4*S*)-1-(benzyloxy)-2,4-dimethyl-3-triethylsilanyloxy-5-heptyne, 40. $[\alpha]_{589}^{20}$ +16.9 ^{o} (*c* 3.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.18 (m, 4H), 7.15-7.11 (m, 1H), 4.37 (A of AB, *J* = 12.3 Hz, 1H), 4.37 (B of AB, *J* = 13.2 Hz, 1H), 3.54 (dd, *J* = 9.4, 4.7 Hz, 1H), 3.47 (dd, *J* = 6.3, 4.7 Hz, 1H), 3.23 (dd, *J* = 9.1, 7.6 Hz, 1H), 2.48-2.42 (m, 1H), 2.07-1.99 (m, 1H), 1.62 (d, *J* = 2.2 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.83 (t, *J* = 7.9 Hz, 9H), 0.51 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 128.2, 127.5, 127.3, 82.6, 78.1, 76.8, 72.9, 72.5, 38.0, 30.0, 16.9, 14.9, 7.0, 5.3, 3.5; IR (thin film, NaCl) 2956, 2916, 2876, 1454, 1377, 1239, 1101, 1009, 808, 736, 697 cm^{-1}; LRMS (EI, Na) calcd for $C_{26}H_{36}O_2SiNa$, 383.25 *m/z* (M + Na); observed, 383.3 $(M + Na)^+$ *m/z*.



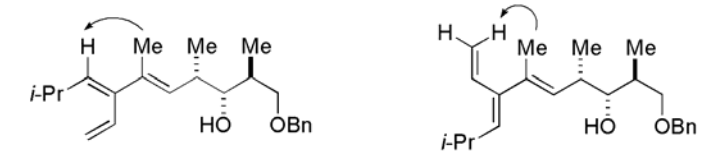
Synthesis of Triene 41. To a –78 ^{o}C solution of alkyne **40** (33 mg, 0.09 mmol) in 910 μL of PhMe was added 180 μL of $ClTi(OiPr)_3$ (1.0M in hexanes, 0.18 mmol) and 190 μL of cC_5H_9MgCl (1.96M in Et_2O, 0.36 mmol) dropwise via a gas-tight syringe. The resulting

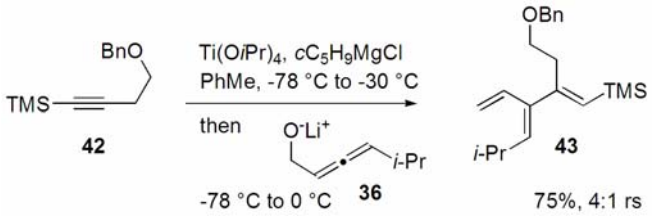
clear, yellow solution turned dark reddish brown while warming slowly to –30 °C over 1 hr. The reaction mixture was stirred at –30 °C for 1 hr and then cooled to –78 °C. To a separate –78 °C solution of allene **36** (9 mg, 0.08 mmol) in 0.5 mL PhMe was added 30 μL of *n*BuLi (2.45M in hexanes, 0.08 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 min, removed from the cold bath and added to the –78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 2 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 5 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 10 mL), brine (1 x 10 mL) and dried over anhydrous Na_2SO_4. After concentration *in vacuo*, the crude mixture was diluted in THF (800 μL) and treated with TBAF (80 μL, 1M in THF, 0.08 mmol). The reaction mixture was stirred for 2 hr at room temperature and concentrated *in vacuo*. Flash column chromatography (15 % EtOAc/hexanes) provided 15 mg (57 %) of triene **41** as a clear, colorless oil in a 3:1 mixture of regioisomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 10 % to 20 % (0-10 min, 28 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **41.**

(2*S*,3*R*,4*S*,5*E*,7*E*)-1-(benzyloxy)-2,4,6,9-tetramethyl-3-hydroxy-7-vinyl-5,7-decadiene, 41. $[\alpha]_{589}^{20}$ –5.6 ° (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 6.48 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.24 (dd, *J* = 9.8, 1.3 Hz, 1H), 5.18 (d, *J* = 9.5 Hz, 1H), 5.14 (ddd, *J* = 11.0, 2.2, 1.3 Hz, 1H), 5.03 (dd, *J* = 17.3, 2.2 Hz, 1H), 4.53 (A of AB, *J* = 12.0 Hz, 1H), 4.48 (B of AB, *J* = 12.0 Hz, 1H), 3.65 (dd, *J* = 9.1, 4.1 Hz, 1H), 3.46 (dd, *J* = 9.1, 5.0 Hz, 1H), 3.32 (dd, *J* = 12.3, 6.3 Hz, 1H), 3.05 (d, *J* = 6.3 Hz, 1H), 2.73-2.66 (m, 1H), 2.57-2.49 (m, 1H), 1.94-1.87 (m, 1H), 1.67 (d, *J* = 1.3 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 1.04

(d, J = 6.6 Hz, 3H), 0.97 (d, J = 6.6 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6, 137.8, 136.6, 134.7, 132.9, 132.0, 128.4, 127.8, 127.7, 113.4, 80.0, 74.0, 73.6, 36.9, 35.8, 27.0, 23.2, 16.2, 15.8, 15.2 cm^{-1}; IR (thin film, NaCl) 3498, 2960, 2929, 2867, 1653, 1455, 1362, 1078, 989, 910, 736, 698 cm^{-1}; HRMS (EI, H) calcd for $C_{23}H_{35}O_2$, 343.2632 *m/z* (M + H); observed, 343.2625 $(M + H)^+$ *m/z*.

Observed nOe enhancements for structure determination:



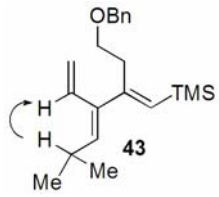


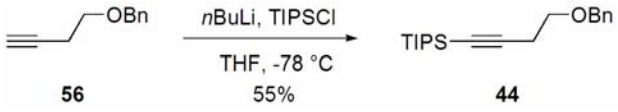
Synthesis of Triene 43. To a −78 °C solution of alkyne **42** (129 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 µL of Ti(O*i*Pr)$_4$ and 727 µL of *c*C_5H_9MgCl (2.31M in Et_2O, 1.69 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark brown while warming slowly to −30 °C over 1 hr. The reaction mixture was stirred at −30 °C for 1 hr and then cooled to −78 °C. To a separate −78 °C solution of allene **36** (33 mg, 0.39 mmol) in 1.0 mL PhMe was added 156 µL of *n*BuLi (2.5M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 minutes, removed from the cold bath and added to the −78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The

combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes then 10 % EtOAc/hexanes) provided 75 % of triene **43** as a clear, colorless oil in a 4:1 mixture of regioisomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 3 % to 4.5 % (0-10 min, 20 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **43**.

((1*E*,3*E*)-2-(2-(benzyloxy)ethyl)-5-methyl-1-trimethylsilyl-3-vinyl-1,3-hexadiene, 43. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.12 (m, 5H), 6.39 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.29 (s, 1H), 5.08-4.95 (m, 3H), 4.33 (s, 2H), 3.29 (t, *J* = 7.9 Hz, 2H), 2.61-2.54 (m, 1H), 2.50 (t, *J* = 7.6 Hz, 2H), 1.40 (s, 6H), 0.00 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 154.2, 140.1, 137.1, 132.2, 130.3, 128.0, 127.3, 127.2, 116.4, 72.6, 69.4, 40.3, 35.1, 26.7, 22.8, 0.0: IR (thin film, NaCl) 2955, 1605, 1454, 1361, 1248, 1010, 838, 734, 697 cm^{-1}; LRMS (EI, Na) calcd for $C_{21}H_{32}OSiNa$, 351.21 *m/z* (M + Na); observed, 351.2 (M + Na)$^+$ *m/z*.

Observed nOe enhancements for structure determination:

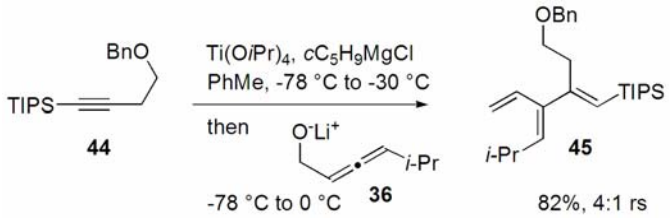




Synthesis of Alkyne 44. To alkyne **56**[7] (2.24 g, 14.0 mmol) in 30 mL of THF was added 8.4 mL of *n*BuLi (2.5 M in hexanes, 21.0 mmol) dropwise at -78 °C. The reaction was stirred for 1 hr at -78 °C, then 6.0 mL of TIPSCl was added and the reaction was stirred overnight warming to room temperature. The resulting mixture was quenched with water and

extracted with Et_2O (3 x 20 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 20 mL) and brine (1 x 10 mL) and dried over anhydrous Na_2SO_4. Purification of the crude material by flash column chromatography (10 % EtOAc/hexanes) provided 2.41 g (55%) of **44** as a clear, yellow oil.

(4-(benzyloxy)but-1-ynyl)triisopropylsilane, 44. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.20 (m, 5H), 4.483 (s, 2H), 3.56 (t, *J* = 6.9 Hz, 2H), 2.51 (t, *J* = 6.94 Hz, 2H), 1.03-0.92 (m, 15H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 138.2, 128.4, 127,6, 105.3, 81.5, 72.97, 68.9, 21.4, 18.6, 11.2; IR (thin film, NaCl) 2943, 2865, 2175, 1613, 1513, 1464, 1248, 1068, 1039, 883, 821, 678 cm^{-1}; LRMS (EI, Na) calcd for $C_{19}H_{30}OSiNa$, 325.3 *m/z* (M + Na); observed, 325.9 $(M + Na)^+$ *m/z*.

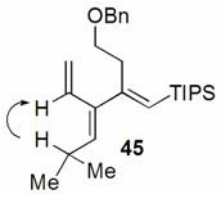


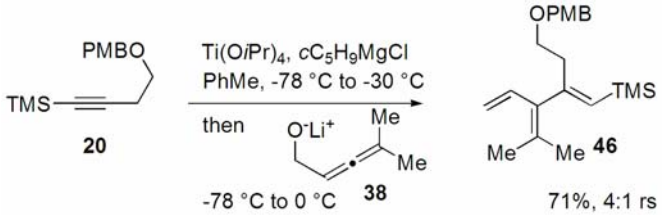
Synthesis of Triene 45. To a −78 °C solution of alkyne **44** (177 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 µL of $Ti(OiPr)_4$ and 731 µL of cC_5H_9MgCl (2.31 M in Et_2O, 1.69 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark brown while warming slowly to −30 °C over 1 hr. The reaction mixture was stirred at −30 °C for 1 hr and then cooled to −78 °C. To a separate −78 °C solution of allene **36** (39 mg, 0.34 mmol) in 1.0 mL PhMe was added 136 µL of *n*BuLi (2.5M in hexanes, 0.34 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 minutes, removed from the cold bath and added to the −78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The

combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes then 10 % EtOAc/hexanes) provided 82 % of triene **45** as a clear, colorless oil in a 4:1 mixture of regioisomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 4 % to 4.5 % (0-10 min, 20 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **45**.

((1*E*,3*E*)-2-(2-(benzyloxy)ethyl)-5-methyl-1-triisopropylsilyl-3-vinyl-1,3-hexadiene, 45. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.24 (m, 2H), 7.19-7.18 (m, 3H), 6.51 (dd, *J* = 17.3, 10.1 Hz, 1H), 5.22 (s, 1H), 5.11-5.06 (m, 3H), 4.37 (s, 2H) 3.35 (t, *J* = 7.9 Hz, 2H), 2.67-2.60 (m, 1H), 2.55 (t, *J* = 7.9 Hz, 2H), 1.48 (s, 6H), 1.12 (m, 3H), 0.99 (d, *J* = 6.6 Hz, 12H), 0.90 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 155.8, 140.9, 138.6, 132.2, 128.2, 127.5, 127.4, 125.5, 116.4, 72.8, 69.3, 36.6, 26.7, 23.0, 19.0, 12.3; IR (thin film, NaCl) 2958, 2865, 1598, 1463, 1361, 1100, 911, 882 cm^{-1}; LRMS (EI, H) calcd for $C_{27}H_{45}OSi$, 413.3161 *m/z* (M + H); observed, 413.2979 $(M + H)^+$ *m/z*.

Observed nOe enhancements for structure determination:

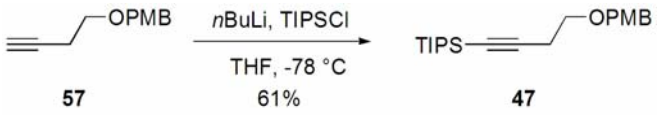




Synthesis of Triene 46. To a −78 °C solution of alkyne **20** (146 mg, 0.56 mmol) in 3.7 mL of PhMe was added 250 µL of $Ti(OiPr)_4$ and 727 µL of cC_5H_9MgCl (2.04M in Et_2O,

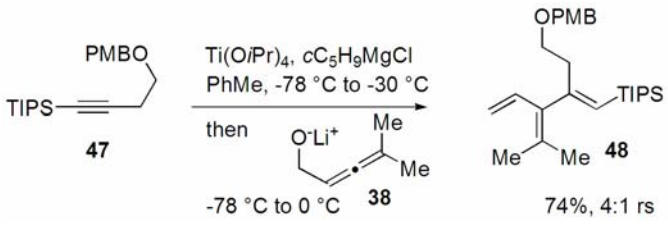
1.69 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark brown while warming slowly to −30 °C over 1 hr. The reaction mixture was stirred at −30 °C for 1 hr and then cooled to −78 °C. To a separate −78 °C solution of allene **38** (33 mg, 0.34 mmol) in 1.0 mL PhMe was added 156 µL of *n*BuLi (2.51M in hexanes, 0.34 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 minutes, removed from the cold bath and added to the −78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes then 10 % EtOAc/hexanes) provided 71 % of triene **46** as a clear, colorless oil in a 4:1 mixture of regioisomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 4 % to 4.5 % (0-10 min, 20 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **46**.

(*E*)-2-(2-(4-methoxybenzyloxy)ethyl)-4-methyl-1-trimethylsilyl-3-vinyl-1,3-pentadiene, 46. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13-7.10 (m, 2H), 6.75-6.72 (m, 2H), 6.39 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.29 (s, 1H), 5.08-4.95 (m, 2H), 4.26 (s, 2H), 3.67 (s, 3H), 3.26 (t, *J* = 7.9 Hz, 2H), 2.49 (t, *J* = 7.9 Hz, 2H), 1.40 (s, 6H), 0.00 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 158.8, 154.2, 140.1, 137.1, 132.2, 130.5, 130.2, 128.9, 116.4, 113.5, 72.3, 69.1, 55.0, 35.2, 26.7, 22.9, 0.0; IR (thin film, NaCl) 2955, 1605, 1454, 1361, 1248, 1010, 838, 734, 697 cm^{-1}; LRMS (EI, Na) calcd for $C_{21}H_{32}O_2SiNa$ 367.2 *m/z* (M + Na); observed, 367.6 (M + Na)$^+$ *m/z*.



Synthesis of Alkyne 47. To alkyne **57** (2.69 g, 14.0 mmol) in 30 mL of THF was added 8.4 mL of *n*BuLi (2.5 M in hexanes, 21.0 mmol) dropwise at -78 °C. The reaction was stirred for 1 hr at -78 °C, then 6.0 mL of TIPSCl was added and the reaction was stirred overnight warming to room temperature. The resulting mixture was quenched with water and extracted with Et_2O (3 x 20 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 20 mL) and brine (1x 10 mL) and dried over anhydrous Na_2SO_4. Purification of the crude material by flash column chromatography (10 % EtOAc/hexanes) provided 2.98 g (61%) of **47** as a clear, yellow oil.

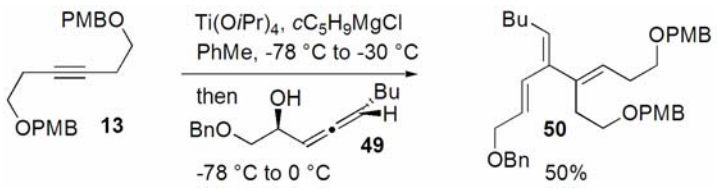
(4-(4-methoxybenzyloxy)but-1-ynyl)triisopropylsilane, 47. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.12 (m, 5H), 6.39 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.29 (s, 1H), 5.08-4.95 (m, 3H), 4.33 (s, 2H), 3.29 (t, *J* = 7.9 Hz, 2H), 2.61-2.54 (m, 1H), 2.50 (t, *J* = 7.6 Hz, 2H), 1.40 (s, 6H), 0.00 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 154.2, 140.1, 137.1, 132.2, 130.3, 128.0, 127.3, 127.2, 116.4, 72.6, 69.4, 40.3, 35.1, 26.7, 22.8, 0.0; IR (thin film, NaCl) 2943, 2865, 2175, 1613, 1513, 1238, 1096, 1039, 883, 821, 678 cm^{-1}; LRMS (EI, Na) calcd for $C_{20}H_{32}O_2SiNa$, 355.3 *m/z* (M + Na); observed, 355.7 $(M + Na)^+$ *m/z*.



Synthesis of Triene 48. To a −78 °C solution of alkyne **47** (110 mg, 0.34 mmol) in 3.7 mL of PhMe was added 152 µL of Ti(O*i*Pr)$_4$ and 442 µL of *c*C_5H_9MgCl (2.31 M in Et_2O, 1.02 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark brown while warming slowly to −30 °C over 1 hr. The reaction mixture was stirred at −30 °C

for 1 hr and then cooled to −78 °C. To a separate −78 °C solution of allene **38** (24 mg, 0.24 mmol) in 1.0 mL PhMe was added 96 μL of *n*BuLi (2.51M in hexanes, 0.39 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 minutes, removed from the cold bath and added to the −78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes then 10 % EtOAc/hexanes) provided 74 % of triene **48** as a clear, colorless oil in a 4:1 mixture of regioisomers. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 4 % to 4.5 % (0-10 min, 20 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **48**.

(*E*)-2-(2-(4-methoxybenzyloxy)ethyl)-4-methyl-1-triisopropylsilyl-3-vinyl-1,3-pentadiene, 48. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16-7.14 (d, 2H), 6.79-6.78 (d, 2H), 6.51 (dd, *J* = 17.0, 9.8 Hz, 1H), 5.21 (s, 1H), 5.08-5.01 (m, 2H), 4.30 (s, 2H), 3.73 (s, 3H), 3.32 (t, *J* = 7.9 Hz, 2H), 2.53 (t, *J* = 7.9 Hz, 2H), 1.46 (s, 6H), 1.10-1.06 (m, 3H), 0.99 (d, *J* = 6.9 Hz, 12H), 0.90 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.5, 156.3, 141.4, 137.5, 132.6, 131.2, 129.6, 125.8, 116.8, 114.1, 72.9, 69.4, 55.6, 37.032, 27.2, 23.5, 19.4, 12.8; IR (thin film, NaCl) 2957, 2864, 1513, 1463, 1248, 1097 cm^{-1}; LRMS (EI, Na) calcd for $C_{27}H_{44}O_2SiNa$, 451.30 *m/z* (M + Na); observed, 451.3 $(M + Na)^+$ *m/z*.

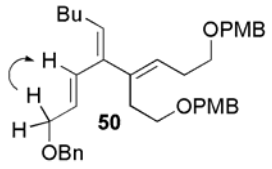


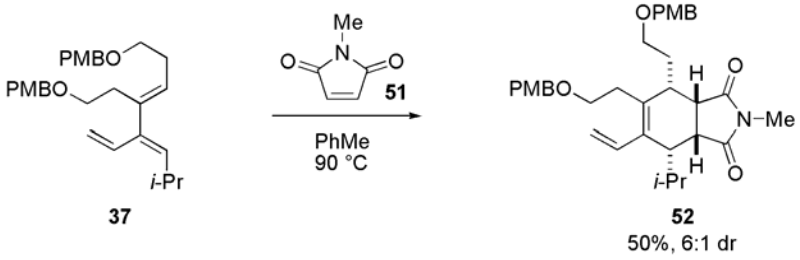
Synthesis of Triene 50. To a −78 °C solution of alkyne **13** (75 mg, 0.23 mmol) in 2.0 mL of PhMe was added 102 μL of Ti(O*i*Pr)$_4$ and 336 μL of *c*C_5H_9MgCl (2.04 M in Et_2O, 0.686 mmol) dropwise via a gas-tight syringe. The resulting clear, yellow solution turned dark brown while warming slowly to −30 °C over 1 hr. The reaction mixture was stirred at −30 °C for 1 hr and then cooled to −78 °C. To a separate −78 °C solution of allene **49** (30 mg, 0.16 mmol) in 1.0 mL PhMe was added 64 μL of *n*BuLi (2.5M in hexanes, 0.16 mmol) dropwise via gas-tight syringe. The resulting solution was stirred for 15 minutes, removed from the cold bath and added to the −78 °C titanium solution dropwise via cannula. After warming slowly to 0 °C over 2 hr, the reaction was quenched with 5 mL of sat. NH_4Cl solution. The mixture was warmed to room temperature before extracting with EtOAc (3 x 15 mL). The combined organic layer was washed with sat. $NaHCO_3$ solution (1 x 30 mL), brine (1 x 30 mL) and dried over anhydrous Na_2SO_4. Flash column chromatography of the crude material (5 % EtOAc/hexanes then 10 % EtOAc/hexanes) provided 50 % of triene **50** as a clear, colorless oil. Separation of the isomers by HPLC [EtOAc/hexanes: gradient from 4 % to 4.5 % (0-10 min, 20 mL/min) on a Microsorb (Si 80-120-C5 H410119) column] provided an analytically pure sample of **50**.

((3*E*,5*E*)-5-(3-benzyloxypropylidene)-1-(4-methoxybenxyloxy)-4-(2-(4-methoxybenzyloxy)ethyl)-3,5-decadiene, 50. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.18 (m, 5H), 7.151 (d, *J* = 8.2 Hz, 4H), 6.784 (d, *J* = 8.8 Hz, 4H), 6.51 (dd, *J* = 10.7, 6.9 Hz, 1H), 5.22-5.21 (m, 1H), 5.11-5.06 (m, 2H), 4.30 (s, 6H), 4.05 (d, *J* = 6.9 Hz, 2H), 3.73 (s, 6H), 3.32 (t, *J* = 7.6 Hz, 4H), 2.53 (t, *J* = 7.6 Hz, 4H), 1.97 (bs, H_2O), 1.00 (m, 6H), 0.90 (m, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 159.0, 155.9, 141.0, 137.1, 137.0, 132.2, 130.7, 129.1, 129.0, 125.4, 116.4, 113.7, 113.6, 72.5, 72.4, 69.0, 36.6, 30.9, 26.7, 23.1, 19.0, 12.3; IR (thin film,

NaCl) 2960, 2861, 1525, 1460, 1234, 1098 cm^{-1}; LRMS (EI, Na) calcd for $C_{38}H_{48}O_5Na$, 607.3 *m/z* (M + Na); observed, 607.9 $(M + Na)^+$ *m/z*.

Observed nOe enhancements for structure determination:



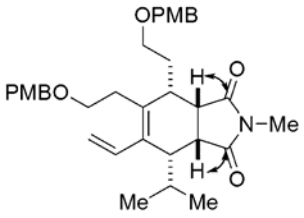


Synthesis of Cycloadduct 52. A solution of triene **37** (0.032 g, 0.071 mmol), and N-methylmaleimide (**51**) (0.034 g, 0.312 mmol) in toluene (700 μL) were heated at 90 °C for 24 hr. The reaction was then concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (20 %-25 % EtOAc/hexanes) to yield carbocycle **52** as a viscous, colorless oil (20 mg, 50 %, 6:1 dr). The major diastereomer was separated by HPLC [EtOAc/hexanes: 17 %-22 % (0-30 min, 10 mL/min), on a Microsorb (Si 80-120-C5 H410119) column] to yield analytically pure **52**.

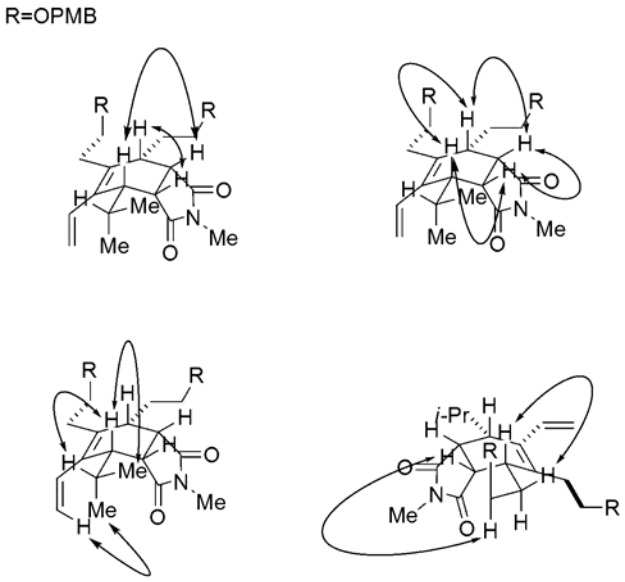
(3a*R*,4*S*,7*R*,7a*S*)-4-isopropyl-6,7-bis(2-(4-methoxybenzyloxy)ethyl)-2-methyl-5-vinyl-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione, 52. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.89-6.84 (m, 4H), 6.25 (dd, *J* = 17.7, 11.4 Hz, 1H), 5.16 (dd, *J* = 11.7, 1.9 Hz, 1H), 4.87 (dd, *J* = 17.7, 1.6 Hz, 1H), 4.51-4.32 (m, 4H), 3.80 (s, 3H), 3.78 (s, 3H), 3.76-3.67 (m, 2H), 3.22-3.10 (m, 3H), 2.95 (dd, *J* = 8.5, 6.3 Hz, 1H), 2.76 (s, 3H), 2.67-2.60 (m, 1H), 2.51-2.53 (m, 4H), 2.17-2.08 (m, 1H), 1.91-1.81 (m, 1H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3,

178.2, 159.2, 159.1, 138.3, 134.7, 133.7, 130.5, 130.4, 129.4, 129.2, 117.9, 113.8, 113.7, 72.5, 72.4, 68.9, 67.6, 55.4, 55.3, 42.6, 42.4, 36.3, 29.6, 27.5, 25.8, 24.3, 23.6, 21.7; IR (thin film, NaCl) 2957, 2865, 1696, 1612, 1513, 1433, 1301, 1248, 1089 cm^{-1}; LRMS (EI, Na) calcd for $C_{34}H_{43}NO_6Na$, 584.31 *m/z* (M + Na); observed 584.4 $(M + Na)^+$ *m/z*.

Observed HMBC correlations for structure determination:



Observed nOe enhancements for structure determination:



References:

[1] Ryan, J.; Micalizio, G. C. *J. Am. Chem. Soc*. **2006**, *128*, 2764-2765.
[2] Allene **16** was used as a 3:1 mixture (minor component: 2-pentyn-1-ol). Reaction yield was based on the calculated amount of allene **16** present.
[3] Grotjahn, D. B.; Vollhardt, K. P. C. *J. Am. Chem. Soc*. **1986**, *108*, 2091-2093.
[4] Bahadoor, A. B.; Micalizio, G. C. *J. A. Chem. Soc.*, **2005**, *127*, 3694-3695.
[5] Allene **34** was used as a 2:1 mixture (minor component: trans-2-penten-1-ol). Reaction yield was based on the calculated amount of allene **34** present.
[6] Yield reported post preparative HPLC due to difficulty in removing triene **35** from the coupled product derived from union of alkyne **13** with trans-2-penten-1-ol.
[7] Razon, P.; N'Zoutani, M.-A.; Dhulut, S.; Bezzenine-Lafollée, P.; Ardisson, J.; *Synthesis* **2005**, *1*, 109-121.