Supporting Information for

Enantioselective ProPhenol-Catalyzed Addition of 1,3-Diynes to Aldehydes to Generate Synthetically Versatile Building Blocks and Diyne Natural Products

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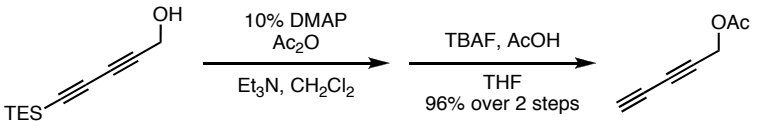
General Information. Glassware was oven-dried for at least 8 h at 115 ^{o}C or flame-dried under vacuum immediately prior to use. All reactions were performed under an inert atmosphere (N_2 or Ar) unless otherwise noted. Microwave vials (2-5 mL, 16 mm OD x 83 mm) were obtained from Chemglass. TLC analysis of reaction mixtures was performed using EMD silica gel 60 F_{254} plates (0.25 mm). Chromatography was carried out on Silicycle silica gel (230-400 mesh). All nuclear magnetic resonance (NMR) spectra were obtained at ambient temperature using Inova-300, Mercury-400, or Unity-500 Varian spectrometers. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) relative to residual protiated solvent. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration). ^{13}C NMR chemical shifts (δ) are reported in ppm relative to the carbon resonance of the deuterated solvent. Melting points (uncorrected) were measured with a Thomas Hoover Capillary Melting Point Apparatus. Infrared (IR) spectra were recorded as a thin film on NaCl plates with a Thermo Scientific Nicolet IR100 FTIR. Enantiomeric excesses were determined by chiral HPLC analysis on a Thermo Separation Products Spectra Series P-100 equipped with a spectrophotometric detector (230 or 254 nm). Optical rotations were obtained using a Jasco DIP-1000 digital polarimeter with a sodium 589 nm filter.

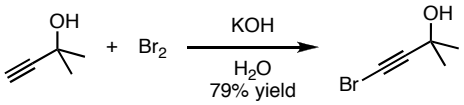
Materials. Reagents that were purchased from commercial suppliers were checked for purity and used without further purification unless otherwise noted. If possible, aldehydes used in the asymmetric alkynylation were distilled under nitrogen immediately prior to use. Toluene, tetrahydrofuran and methylene chloride were dried and purified by passing through a column of activated alumina under nitrogen pressure. Dichloroethane was distilled from CaH_2 under nitrogen. The ProPhenol ligands were obtained from Sigma-Aldrich. Dimethylzinc solution (1.2 M in toluene) was purchased from Acros and stored in a Schlenk flask under argon.

Experimental.



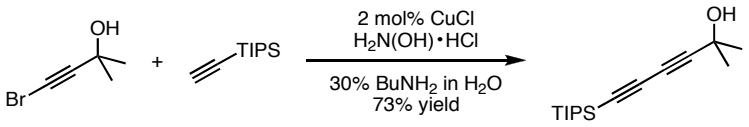
Penta-2,4-diynyl ethanoate (2b). The primary alcohol 5-(triethylsilyl)penta-2,4-diyn-1-ol[1] (1 g, 5.14 mmol, 1 equiv) and DMAP (63 mg, 0.51 mmol, 0.1 equiv) were added to an oven-dried flask equipped with a stir bar, then dissolved in CH_2Cl_2 (12 mL). The reaction mixture was cooled to 0 ^oC, then Et_3N (0.79 mL, 5.66 mmol, 1.1 equiv) was added, followed by the dropwise addition of acetic anhydride (0.54 mL, 5.66 mmol, 1.1 equiv). After stirring for 30 min, the reaction was diluted with aqueous saturated $NaHCO_3$ (15 mL). The biphasic mixture was extracted with Et_2O (3 x 15 mL), then the combined organic layers were dried over $MgSO_4$, filtered and concentrated on a rotary evaporator.

The resulting orange oil ($\mathbf{R}_f$ = 0.38 in 90:10 hexanes:EtOAc) was dissolved in THF (12 mL) and then cooled to 0 ^oC. Acetic acid (0.32 mL, 5.66 mmol, 1.1 equiv) was added to the mixture, followed by TBAF (6.17 mL, 6.17 mmol, 1.2 equiv, 1 M solution in THF). After stirring for 1 h, the reaction mixture was quenched with water (15 mL). Following extraction with Et_2O (3 x 15 mL), the organic layer was washed with aqueous saturated K_2CO_3 (15 mL) and then dried over $MgSO_4$. After filtration and concentration, the crude material was purified by column chromatography (90:10 hexanes:EtOAc) to afford the title compound as a yellow oil (604 mg, 96% yield over 2 steps). The diyne was measured to have a density of 1.02 g/mL. $\mathbf{R}_f$ = 0.26 (90:10 hexanes:EtOAc). ^{1}H NMR spectrum agrees with literature report:[2] **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.71 (d, J = 1.2 Hz, 2H), 2.20 (t, J = 1.2 Hz, 1H), 2.10 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 170.0, 70.7, 70.2, 68.8, 67.2, 52.1, 20.7.

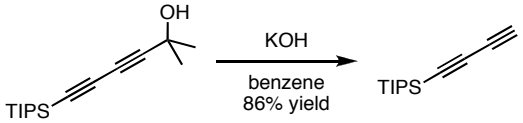


4-Bromo-2-methyl-3-butyn-2-ol.[1] Potassium hydroxide pellets (30 g, 0.537 mol, 5.2 equiv) were added to a round-bottom flask with a stirbar and then dissolved in water (200 mL). The resulting solution was cooled in an ice bath. Bromine (4 mL, 0.0762 mol, 0.75 equiv) was then added dropwise to the vigorously stirred solution. After 15 min, 2-methyl-3-butyn-2-ol (10 mL,

0.103 mol, 1 equiv) was added slowly with an addition funnel. The reaction solution was stirred in the ice bath for 30 min, then warmed to room temperature. The aqueous solution was extracted with Et_2O (5 x 50 mL). The combined etheral phase was dried over $MgSO_4$, filtered and concentrated. The crude material was purified by column chromatography (90:10 pet ether:EtOAc) to afford the product as a yellow oil (10 g, 79% yield). ^{1}H NMR spectrum agrees with literature report: **^{1}H NMR** ($CDCl_3$, 400 MHz): 2.06 (s, 1H), 1.52 (s, 6H).[1]

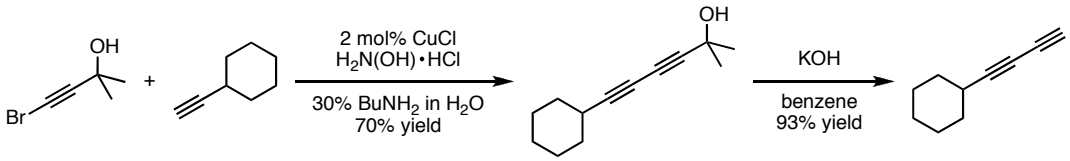


2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol.[3] CuCl (63 mg, 0.640 mmol, 0.02 equiv) was added to a solution of 30% butylamine in water (89 mL). The solution immediately turned blue, but the color was quenched by the addition of a spatula tip's worth of hydroxylamine hydrochloride. After triisopropylsilylacetylene (7.0 g, 38.4 mmol, 1.2 equiv) was added, the reaction mixture was immediately cooled in an ice bath. The bromoalkyne (5.21 g, 32.0 mmol, 1 equiv) was added in a single portion as a solution in ether (~5 mL). The reaction was stirred vigorously at 0 ^{o}C. Approximately every 2 minutes a spatula tip's worth $H_2N(OH)$•HCl was added, or as the solution developed a green color. After 15 min, a reddish-orange color developed and the reaction was complete by TLC. The aqueous mixture was extracted with Et_2O (4 x 50 mL); the combined organic phases were washed with brine (100 mL), then dried over $MgSO_4$. The crude oil was purified by column chromatography (92:8 pet ether:EtOAc) to afford a yellow oil (6.19 g, 73% yield), which solidified on standing. ^{1}H NMR spectrum agrees with literature report: **^{1}H NMR** ($CDCl_3$, 400 MHz): 1.98 (br s, 1H), 1.54 (s, 6H), 1.08 (s, 21H).[3]



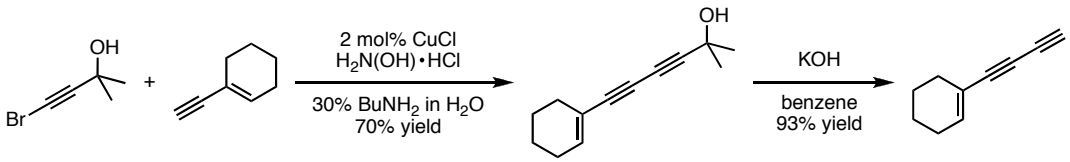
4-Triisopropylsilyl-1,3-butadiyne (4).[4] A round-bottom flask was charged with diynol (2.0 g, 7.56 mmol, 1 equiv) and dissolved in benzene (380 mL). To the stirred solution was added powdered KOH (933 mg, 16.6 mmol, 2.2 equiv). The reaction was then heated to reflux under an N_2 atmosphere. After 4 h, the reaction was cooled to room temperature and concentrated in vacuo. The crude orange oil was filtered through a pad of silica gel (~200 mL) eluting with

petroleum ether (400 mL). Upon removal of solvent, a pale yellow oil was obtained (1.34 g, 86% yield). The diyne was measured to have a density of 0.835 g/mL. Note that although the oil quickly turned a reddish-orange color, the diyne was stable for months in the freezer. NMR spectral data agrees with literature report:[4] **^{1}H NMR** ($CDCl_3$, 400 MHz): 2.07 (s, 1H), 1.09 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 89.1, 82.1, 68.7, 65.6, 18.6, 11.3.



Buta-1,3-diynylcyclohexane. Cyclohexylacetylene (1.29 mL, 10.0 mmol, 1.2 equiv) was cross-coupled with 4-bromo-2-methyl-3-butyn-2-ol (1.36 g, 8.34 mmol, 1 equiv) as previously described. The intermediate 6-cyclohexyl-2-methylhexa-3,5-diyn-2-ol was isolated by column chromatography (88:12 hexanes:EtOAc) as a white solid (1.12 g, 70% yield). $\mathbf{R}_f$ = 0.37 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 2.48-2.44 (m, 1H), 1.90 (s, 1H), 1.80-1.75 (m, 2H), 1.72-1.64 (m, 2H), 1.53 (s, 6H), 1.49-1.43 (m, 3H), 1.32-1.28 (m, 3H).

6-Cyclohexyl-2-methylhexa-3,5-diyn-2-ol (1.12 g, 5.87 mmol, 1 equiv) was treated with powdered KOH (726 mg, 12.9 mmol, 2.2 equiv) in benzene (292 mL) as previously described. After 3 h at reflux, the reaction solution was filtered through a pad of SiO_2 (~200 mL), eluting with 90:10 pet ether:Et_2O (300 mL) to afford the title compound as an orange oil (723 mg, 93% yield). The density of the diyne was measured to be 0.892 g/mL. $\mathbf{R}_f$ = 0.66 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 2.46-2.42 (m, 1H), 2.00 (s, 1H), 1.81-1.78 (m, 2H), 1.73-1.67 (m, 2H), 1.52-1.44 (m, 3H), 1.34-1.25 (m, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 82.3, 68.6, 65.1, 64.6, 32.0, 29.3, 25.7, 24.7.

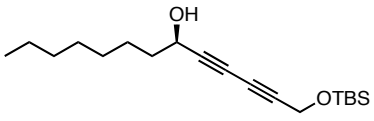


1-(Buta-1,3-diynyl)cyclohex-1-ene. 1-Ethynylcyclohexene (333 μL, 2.83 mmol, 1.2 equiv) was cross-coupled with 4-bromo-2-methyl-3-butyn-2-ol (385 mg, 2.36 mmol, 1 equiv) as previously described. The intermediate 6-cyclohexenyl-2-methylhexa-3,5-diyn-2-ol was isolated by column chromatography (85:15 hexanes:EtOAc) as a white solid (318 mg, 71% yield). $\mathbf{R}_f$ = 0.26 (90:10

hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 6.28-6.26 (m, 1H), 2.12-2.09 (m, 4H), 1.94 (s, 1H), 1.64-1.53 (m, 10H).

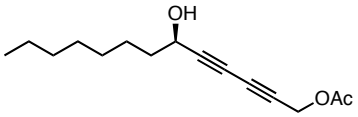
6-Cyclohexenyl-2-methylhexa-3,5-diyn-2-ol (315 mg, 1.67 mmol, 1 equiv) was treated with powdered KOH (207 mg, 3.68 mmol, 2.2 equiv) in benzene (83 mL) as previously described. After 3 h at reflux, the reaction solution was filtered through a pad of SiO_2 (~100 mL), eluting with 95:5 pet ether:EtOAc (200 mL) to afford the title compound as a pale yellow oil (207 mg, 95% yield), which turned orange on standing. The density of the diyne was measured to be 0.915 g/mL. $\mathbf{R}_f$ = 0.62 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 300 MHz): 6.24-6.21 (m, 1H), 2.27 (s, 1H), 2.04-2.00 (m, 4H), 1.57-1.45 (m, 4H). **^{13}C NMR** ($CDCl_3$, 75 MHz): 139.9, 128.4, 119.2, 71.1, 70.3, 68.5, 28.5, 25.9, 22.1, 21.3.

Typical procedure for asymmetric diyne addition into α,β-unsaturated aldehydes. A flame-dried microwave vial equipped with a stir bar was charged with triphenylphosphine oxide (8.7 mg, 0.031 mmol, 0.2 equiv), ProPhenol ligand **1** (10 mg, 0.016 mmol, 0.1 equiv) and toluene (1.0 mL) under argon. The TIPS diyne **4** (77 μL, 0.31 mmol, 2 equiv) was added via syringe, followed by dimethylzinc (261 μL, 0.31 mmol, 2 equiv, 1.2 M in toluene). The alkynyl zinc solution was stirred at room temperature for 30 minutes, then the reaction solution was cooled to 0 °C and the appropriate aldehyde was added (0.16 mmol, 1 equiv). The reaction was left to proceed under argon at 4 °C. After 24 h, the reaction solution was quenched with aqueous, saturated NH_4Cl (2 mL) and stirred vigorously for 10 min. The toluene phase was separated and the aqueous phase was extracted with Et_2O (4 x 2 mL). The combined organic fractions were dried over sodium sulfate, filtered and concentrated on a rotary evaporator. The crude product was then purified by flash column chromatography on silica gel.

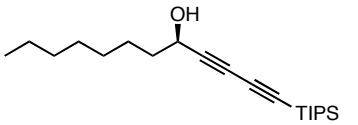


1-(*tert*-Butyldimethylsilyloxy)trideca-2,4-diyn-6-ol (3a). Optimal results were obtained when 3 equiv of diyne **2a** and Me_2Zn were used. Purification by column chromatography (92:8 hexanes:EtOAc) furnished the title compound as a yellow oil (76% yield). $\mathbf{R}_f$ = 0.30 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.42 (dd, J = 6.8 Hz, 1H), 4.38 (s, 2H), 1.90 (br s, 1H), 1.74-1.68 (m, 2H), 1.45-1.42 (m, 2H), 1.28 (m, 8H), 0.90 (s, 9H), 0.88 (t, J = 7.2 Hz, 3H), 0.12 (s, 6H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 80.1, 78.4, 69.3,

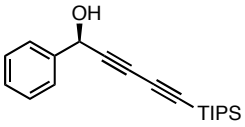
69.1, 63.1, 52.3, 37.7, 32.0, 29.4, 26.0, 25.2, 22.9, 18.5, 14.3, -5.0. **HPLC:** Chiralpak IB Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r major 10.7, minor 11.8 min (65% ee). **IR:** 3350, 2929, 2858, 2158, 1464, 1364, 1256, 1091, 837, 780 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{19}H_{34}O_2NaSi]^+$ 345.2226, found 345.2235. $[\alpha]_D^{23}$ = -3.1 (c 0.60, CH_2Cl_2).



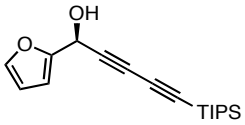
6-Hydroxytrideca-2,4-diynyl ethanoate (3b). Optimal results were obtained when 3 equiv of diyne **2b** and Me_2Zn were used. Purification by column chromatography (82:18 hexanes:EtOAc) furnished the title compound as a yellow oil (73% yield). R_f = 0.25 (80:20 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.74 (d, *J* = 0.8 Hz, 2H), 4.42 (t, *J* = 6.8 Hz, 1H), 2.10 (s, 3H), 1.91 (br s, 1H), 1.74-1.68 (m, 2H), 1.43 (m, 2H), 1.29 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 170.2, 80.9, 73.3, 70.6, 68.7, 62.9, 52.4, 37.5, 31.8, 29.2, 25.1, 22.7, 20.7, 14.2. **HPLC:** Chiralpak IB Column, 92:8 heptane:EtOAc, flow rate 1.0 mL/min, T_r major 30.0, minor 33.4 min (82% ee). **IR:** 3417, 2928, 2857, 2360, 2257, 1752, 1432, 1378, 1223, 1029 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{15}H_{22}O_3Na]^+$ 273.1467, found 273.1460. $[\alpha]_D^{25}$ = -5.8 (c 0.65, CH_2Cl_2).



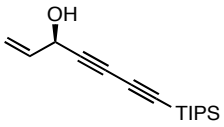
1-(Triisopropylsilyl)dodeca-1,3-diyn-5-ol (5). Optimal results were obtained when 3 equiv of diyne **4** and Me_2Zn were used. Purification by column chromatography (92:8 hexanes:Et_2O) furnished the title compound as an orange oil (63% yield). R_f = 0.14 (95:5 hexanes:Et_2O). **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.41 (m, 1H), 1.94 (d, *J* = 5.2 Hz, 1H), 1.75-1.69 (m, 2H), 1.48-1.43 (m, 2H), 1.29 (m, 8H), 1.08 (s, 21H), 0.88 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 88.9, 84.8, 77.6, 70.2, 63.0, 37.5, 31.8, 29.2, 29.2, 25.1, 22.7, 18.6, 14.2, 11.3. **HPLC:** Chiralpak IB Column, 99:1 heptane:EtOAc, flow rate 1.0 mL/min, T_r major 16.3, minor 18.5 min (79% ee). **IR:** 3307, 2942, 2866, 2221, 2103, 1463, 1383, 883 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{21}H_{38}ONaSi]^+$ 357.2590, found 357.2584. $[\alpha]_D^{25}$ = -7.0 (c 0.84, CH_2Cl_2).



1-Phenyl-5-(triisopropylsilyl)penta-2,4-diyn-1-ol (6a). Purification by column chromatography (95:5 hexanes:EtOAc) afforded the title compound as an orange oil (84% yield). $\mathbf{R}_f$ = 0.29 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 7.53-7.51 (m, 2H), 7.42-7.35 (m, 3H), 5.53 (d, J = 6.0 Hz, 1H), 2.22 (d, J = 6.0 Hz, 1H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 80.9, 80.2, 80.2, 80.1, 77.8, 77.6, 77.0, 76.8, 76.4, 73.6, 73.1. **HPLC:** Chiralpak AD Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 12.9, major 15.1 min (87% ee). **IR:** 3325, 3065, 3033, 2944, 2891, 2866, 2221, 2104, 1602, 1494, 1461, 1385, 1241, 997, 883, 856 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{20}H_{28}ONaSi$]$^+$ 335.1807, found 335.1801.

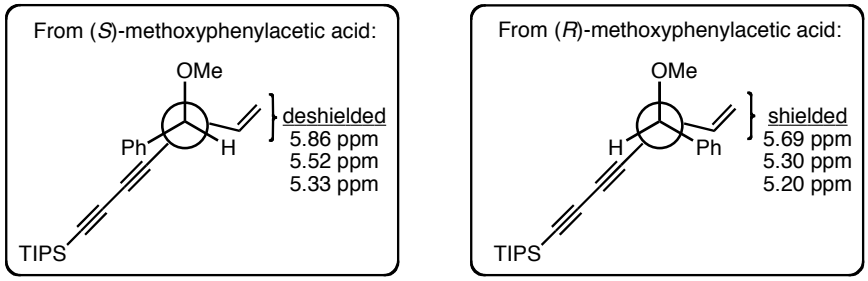


2-Furyl-5-(triisopropylsilyl)penta-2,4-diyn-1-ol (6b). Purification by column chromatography (92:8 hexanes:EtOAc) afforded the title compound as a yellow oil, which solidified upon standing (95% yield, mp 50-53 ^{o}C). $\mathbf{R}_f$ = 0.21 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.42 (m, 1H), 6.48 (br d, 1H), 6.37 (m, 1H), 5.53 (d, J = 7.2 Hz, 1H), 2.31 (d, J = 7.2 Hz, 1H), 1.09 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 151.8, 143.4, 110.6, 108.4, 88.6, 86.3, 73.1, 71.2, 58.7, 18.6, 11.3. **HPLC:** Chiralpak AD Column, 98:2 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 8.2, major 9.4 min (98% ee). **IR:** 3272, 2945, 2891, 2866, 2360, 2103, 1462, 1384, 1141, 1012, 997, 885, 838, 679 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{18}H_{26}O_2NaSi$]$^+$ 325.1600, found 325.1610. **$[\alpha]_D^{23}$** = 1.68 (c 0.85, CH_2Cl_2).

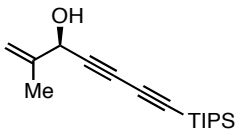


(*R*)-(–)-7-(Triisopropylsilyl)hepta-1-en-4,6-diyn-3-ol (6c). Optimal results were obtained when 3 equiv of diyne **4** and Me_2Zn were used. Purification by column chromatography (96:4 hexanes:EtOAc) afforded the title compound as a yellow oil (89% yield). $\mathbf{R}_f$ = 0.19 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 300 MHz): 6.01-5.90 (m, 1H), 5.48 (m, 1H), 5.27 (m, 1H), 4.94 (m, 1H), 1.91 (d, J = 6.6 Hz, 1H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 135.9, 117.5, 88.7, 85.8, 74.8, 71.6, 63.7, 18.6, 11.3. **IR:** 3322, 2944, 2892, 2866, 2105,

1463, 1017, 995, 922, 883, 826 cm^{-1}. **HRMS** (TOF ES^+) calcd for [M + Na^+, $C_{16}H_{26}ONaSi]^+$ 285.1651, found 285.1639. The enantiomeric excess was determined by derivitization of the product to the *O*-methylmandelate ester (86% ee). $\mathbf{[\alpha]_D^{24}}$ = -36.1 (c 0.4, CH_2Cl_2). The reaction performed with 10 mol% (*R*,*R*)-ProPhenol afforded *ent*-**6c** in 87% ee and 98% yield; $\mathbf{[\alpha]_D^{23}}$ = 34.7 (c 0.48, CH_2Cl_2).

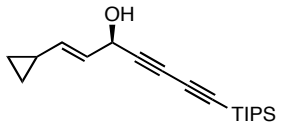


The absolute configuration of *ent*-**6c** was determined to be the (*S*)-enantiomer using the *O*-methylmandelate ester method.[5] A flame-dried one-dram vial equipped with a stir bar was charged with diynol **6c** (12 mg, 0.046 mmol, 1 equiv), (*R*)-α-methoxyphenylacetic acid (15 mg, 0.091 mmol, 2 equiv) and DMAP (1 mg, 0.0082 mmol, 0.18 equiv) was dissolved in anhydrous CH_2Cl_2 (1.2 mL). The reaction mixture was cooled to 0 °C, then EDCI (26 mg, 0.14 mmol, 3 equiv) was added in a single portion. After stirring for 30 min at room temperature, the solution was filtered through a pipet plug of SiO_2 (~1 mL) and eluted with 15% Et_2O in hexanes. Removal of solvent afforded the desired *O*-methylmandelate ester derivative as a colorless oil (>18 mg, >99% yield). $\mathbf{R_f}$ = 0.30 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 7.43 (m, 2H), 7.36 (m, 3H), 5.98 (d, *J* = 5.5 Hz, 1H), 5.69 (m, 1H), 5.30 (dm, *J* = 17.5 Hz, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.81 (s, 1H), 3.43 (s, 3H), 1.08 (s, 21H). The (*S*)-*O*-methylmandelate ester was prepared in a similar fashion. $\mathbf{R_f}$ = 0.24 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.45 (m, 2H), 7.40-7.34 (m, 3H), 5.96 (dt, *J* = 6.0, 1.2 Hz, 1H), 5.86 (m, 1H), 5.52 (ddd, *J* = 16.8, 1.2, 0.5 Hz, 1H), 5.33 (ddd, *J* = 10.0, 1.2, 0.9 Hz, 1H), 4.81 (s, 1H), 3.43 (s, 3H), 1.07 (s, 21H).

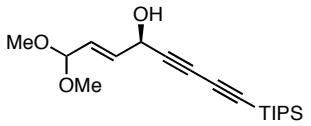


2-Methyl-7-(triisopropylsilyl)hepta-1-en-4,6-diyn-3-ol (6d). Purification by column chromatography (95:5 hexanes:EtOAc) furnished the title compound as an orange oil (94% yield). $\mathbf{R_f}$ = 0.19 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.18

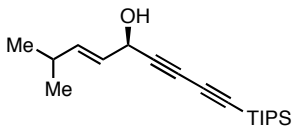
(m, 1H), 4.96 (m, 1H), 4.85 (d, *J* = 6.4 Hz, 1H), 2.04 (d, *J* = 6.4 Hz, 1H), 1.87 (s, 3H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 143.1, 113.3, 88.8, 85.4, 75.2, 71.2, 66.7, 18.6, 18.2, 11.3. **HPLC:** Chiralcel OD-H Column, 99:1 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r minor 10.7, major 12.1 min (87% ee). **IR:** 3307, 2945, 2891, 2867, 2360, 2104, 1462, 1384, 1236, 1015, 882, 678 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{17}H_{28}ONaSi]^+$ 299.1807, found 299.1811. **$[\alpha]_D^{24}$** = -18.0 (c 0.80, CH_2Cl_2).



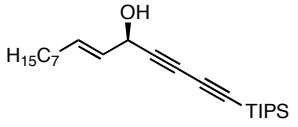
(*E*)-1-Cyclopropyl-7-(triisopropylsilyl)hepta-1-en-4,6-diyn-3-ol (6e). Purification by column chromatography (92:8 hexanes:EtOAc) afforded the title compound as a pale orange oil, which solidified upon standing (97% yield, mp 38 °C). **R_f** = 0.21 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.65 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.37 (dd, *J* = 15.2, 9.2 Hz, 1H), 4.86 (dd, *J* = 6.4, 6.0 Hz, 1H), 2.06 (d, *J* = 6.0 Hz, 1H), 1.45-1.38 (m, 1H), 1.07 (s, 21H), 0.75 (m, 2H), 0.43 (m, 2H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 139.0, 125.4, 88.9, 85.4, 75.6, 71.1, 63.3, 18.6, 13.5, 11.3, 7.1. **HPLC:** Chiralpak AD Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 11.6, major 13.2 min (97% ee). **IR:** 3325, 2944, 2891, 2866, 2361, 2103, 1665, 1462, 996, 960, 882 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{19}H_{30}ONaSi]^+$ 325.1964, found 325.1975. **$[\alpha]_D^{24}$** = -81.3 (c 1.10, CH_2Cl_2).



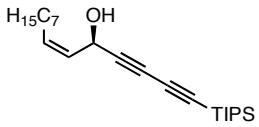
(*E*)-1,1-Dimethoxy-8-(triisopropylsilyl)octa-2-en-5,7-diyn-4-ol (6f). Purification by column chromatography (80:20 hexanes:EtOAc) furnished the title compound as an orange oil (91% yield). **R_f** = 0.34 (80:20 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 6.00-5.85 (m, 2H), 4.98 (dd, *J* = 6.8, 5.6 Hz, 1H), 4.84 (d, *J* = 4.4 Hz, 1H), 3.33 (s, 6H), 2.13 (d, *J* = 6.8 Hz, 1H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 132.4, 129.4, 101.7, 88.6, 86.0, 74.5, 71.7, 62.5, 52.9, 18.6, 11.3. **HPLC:** Chiralpak IA Column, 95:5 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 6.5, major 7.2 min (95% ee). **IR:** 3400, 2944, 2866, 2220, 2103, 1676, 1463, 1367, 1132, 1057, 971 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{19}H_{32}O_3NaSi]^+$ 359.2018, found 359.2015. **$[\alpha]_D^{24}$** = -19.1 (c 1.15, CH_2Cl_2).



(*E*)-8-Methyl-1-(triisopropylsilyl)nona-6-en-1,3-diyn-5-ol (6g). Purification by column chromatography (97:3 hexanes:EtOAc) afforded the title compound as an orange oil (89% yield). $\mathbf{R}_f$ = 0.20 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 5.88-5.83 (m, 1H), 5.55-5.50 (m, 1H), 4.88 (dd, *J* = 6.0, 7.0 Hz, 1H), 2.33 (m, 1H), 1.93 (d, *J* = 6.0 Hz, 1H), 1.08 (s, 21H), 1.02 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 142.0, 125.3, 89.1, 85.6, 75.9, 71.4, 63.8, 30.8, 22.2, 18.8, 11.5. **HPLC:** Chiralpak AD Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 10.2, major 11.5 min (96% ee). **IR:** 3308, 2959, 2867, 2103, 1463, 996, 968, 883, 678 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{19}H_{32}ONaSi]^+$ 327.2120, found 327.2122.

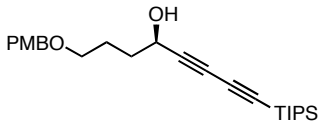


(*E*)-1-(Triisopropylsilyl)tetradeca-6-en-1,3-diyn-5-ol (6h). Purification by column chromatography (92:8 hexanes:EtOAc) furnished the title compound as an orange oil (93% yield). $\mathbf{R}_f$ = 0.28 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 5.89 (m, 1H), 5.57 (m, 1H), 4.88 (dd, *J* = 4.8, 6.0 Hz, 1H), 2.06 (dt, *J* = 5.6, 5.6 Hz, 2H), 1.93 (d, *J* = 4.8 Hz, 1H), 1.39 (m, 2H), 1.27 (m, 8H), 1.08 (s, 21H), 0.88 (t, *J* = 5.6 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 135.5, 128.0, 89.0, 85.6, 75.9, 71.4, 63.7, 32.3, 32.1, 29.4, 29.4, 29.0, 22.9, 18.8, 14.4, 11.5. **HPLC:** Chiralpak IA Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 9.4, major 10.7 min (97% ee). **IR:** 3434, 2927, 2866, 2361, 2103, 1641, 1463, 996, 965, 883 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{23}H_{40}ONaSi]^+$ 383.2746, found 383.2747. **$[\alpha]_D^{23}$** = -47.5 (c 1.45, CH_2Cl_2).

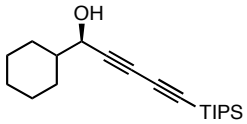


(*Z*)-1-(Triisopropylsilyl)tetradeca-6-en-1,3-diyn-5-ol (6i). Optimal results were obtained when 3 equiv of diyne **4** and Me_2Zn were used. Purification by column chromatography (95:5 hexanes:EtOAc) furnished the title compound as an orange oil (95% yield). $\mathbf{R}_f$ = 0.32 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.64-5.50 (m, 2H), 5.20 (m, 1H), 2.13-2.08 (m, 2H), 1.90 (d, *J* = 5.2 Hz, 1H), 1.32 (m, 2H), 1.27 (br m, 10H),

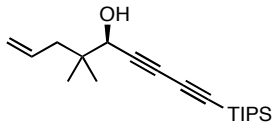
1.07 (s, 21H), 0.88 (t, J = 6.8 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 134.8, 127.9, 89.1, 85.6, 76.4, 70.4, 58.8, 32.0, 29.5, 29.4, 29.3, 27.9, 22.9, 18.7, 14.3, 11.4. **HPLC:** Chiralpak AD Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r major 9.8, minor 10.8 min (63% ee). **IR:** 3306, 2927, 2866, 2102, 1463, 1383, 1304, 1242, 996, 883, 846, 678 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{23}H_{40}ONaSi]^+$ 383.2746, found 383.2744. **$[\alpha]_D^{25}$** = 130.9 (c 1.78, CH_2Cl_2).



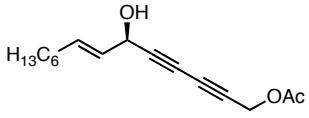
1-(4-Methoxybenzyloxy)-8-(triisopropylsilyl)octa-5,7-diyn-4-ol (6j). Optimal results were obtained when the reaction was performed with 3 equiv each of Me_2Zn and diyne **4**. Purification by column chromatography (85:15 hexanes:EtOAc) furnished the title compound as a pale yellow oil (69% yield). **R_f** = 0.32 (75:25 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.26 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 4.49-4.45 (m, 3H), 3.80 (s, 3H), 3.51-3.47 (m, 3H), 3.19 (d, J = 6.0 Hz, 1H), 1.87-1.84 (m, 3H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 159.5, 130.1, 129.7, 114.1, 89.2, 84.7, 77.7, 73.0, 70.3, 69.9, 62.7, 55.5, 35.3, 25.6, 18.8, 11.4. **HPLC:** Chiralpak IB Column, 95:5 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r major 8.8, minor 10.0 min (80% ee). **IR:** 3399, 2944, 2865, 2361, 2219, 2101, 1725, 1613, 1513, 1463, 1248, 1037, 883 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{25}H_{38}O_3NaSi]^+$ 437.2488, found 437.2468. **$[\alpha]_D^{25}$** = 18.4 (c 0.82, CH_2Cl_2).



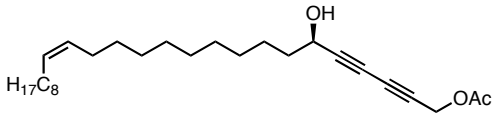
1-Cyclohexyl-5-(triisopropylsilyl)penta-2,4-diyn-1-ol (6k). Optimal results were obtained when 3 equiv of diyne **4** and Me_2Zn were employed. Purification by column chromatography (95:5 hexanes:EtOAc) afforded the title compound as an orange oil, which then solidified upon standing (72% yield, mp 46-48 ^{o}C). **R_f** = 0.23 (95:5 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.21 (m, 1H), 1.87-1.84 (m, 3H), 1.79-1.76 (m, 2H), 1.69-1.54 (m, 2H), 1.27-1.11 (m, 4H), 1.08 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 89.0, 84.6, 76.7, 71.0, 67.7, 44.2, 28.5, 28.3, 26.3, 25.9, 25.8, 18.6, 11.3. **HPLC:** Chiralpak AD Column, 99:1 heptane:^{i}PrOH, flow rate 1.0 mL/min, T_r minor 8.2, major 8.9 min (67% ee). **IR:** 3410, 2928, 2865, 2360, 2101, 1647, 1462, 1015, 883, 812 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na$^+$, $C_{20}H_{34}ONaSi]^+$ 341.2277, found 341.2272. **$[\alpha]^{26}_D$** = -10.2 (c 0.65, CH_2Cl_2).



6,6-Dimethyl-1-(triisopropylsilyl)nona-8-en-1,3-diyn-5-ol (6l). Optimal results were obtained when 3 equiv of diyne **4** and Me_2Zn were used. Purification by column chromatography (95:5 hexanes:EtOAc) furnished the title compound as an orange oil (90% yield). $\mathbf{R}_f$ = 0.39 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.88-5.78 (m, 1H), 5.13-5.07 (m, 2H), 4.15 (d, *J* = 6.0 Hz, 1H), 2.21-2.08 (m, 2H), 1.89 (d, *J* = 6.0 Hz, 1H), 1.08 (s, 21H), 0.99 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 134.6, 118.1, 89.0, 84.5, 76.2, 71.6, 70.8, 42.8, 39.3, 22.8, 22.7, 18.6, 11.3. **HPLC:** Chiralcel OD-H Column, 99:1 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r minor 11.8, major 14.6 min (83% ee). **IR:** 3369, 3076, 2944, 2867, 2219, 2104, 1640, 1464, 1028, 997, 883 cm^{-1}. **HRMS** (TOF ES$^+$) calcd for [M + Na^+, $C_{20}H_{34}ONaSi]^+$ 341.2277, found 341.2281.



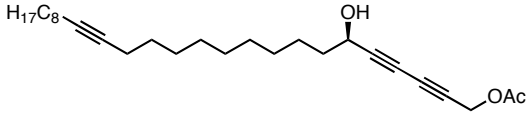
(*E*)-6-Hydroxytetradeca-7-en-2,4-diynyl ethanoate (7a). Purification by column chromatography (85:15 hexanes:EtOAc) furnished the title compound as a pale yellow oil (93% yield). $\mathbf{R}_f$ = 0.29 (80:20 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.87 (dtd, *J* = 1.2, 6.8, 15.2 Hz, 1H), 5.55 (tdd, *J* = 1.4, 6.4, 15.2 Hz, 1H), 4.87 (d, *J* = 6.4 Hz, 1H), 4.73 (d, *J* = 0.8 Hz, 2H), 2.18 (br s, 1H), 2.09 (s, 3H), 2.04 (dt, *J* = 6.8, 7.2 Hz, 2H), 1.42-1.25 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 170.2, 135.3, 127.6, 79.1, 73.7, 70.6, 69.6, 63.3, 52.4, 32.0, 31.7, 28.9, 28.8, 22.6, 20.7, 14.1. **HPLC:** Chiralpak IB Column, 90:10 heptane:EtOAc, flow rate 1.0 mL/min, T_r major 22.0, minor 28.7 min (97% ee). **IR:** 3417, 2928, 2856, 1752, 1432, 1378, 1222, 1029, 968 cm^{-1}. **$[\alpha]_D^{24}$** = -60.8 (c 1.35, CH_2Cl_2).



(*Z*)-6-Hydroxypentacosa-16-en-2,4-diynyl ethanoate (7b). A flame-dried microwave tube with a stir bar was charged with triphenylphosphine oxide (17.4 mg, 0.063 mmol, 0.4 equiv), (*S*,*S*)-ProPhenol ligand **1** (20 mg, 0.031 mmol, 0.2 equiv) and toluene (1.0 mL) under argon. Diyne **2b** (56 μL, 0.47 mmol, 3

equiv) was added, followed by Me_2Zn (391 μL, 0.47 mmol, 3 equiv, 1.2 M in toluene). The alkynyl zinc solution was stirred for 30 minutes, then the reaction solution was cooled to 0 °C and the known aldehyde[6] was added (55 μL, 0.16 mmol, 1 equiv). The reaction solution was stirred under argon at 4 °C for 32 h, then quenched with aqueous, saturated NH_4Cl (2 mL). The toluene phase was separated and the aqueous phase was extracted with Et_2O (4 x 2 mL). The combined organic fractions were dried over sodium sulfate, filtered and concentrated on a rotary evaporator.

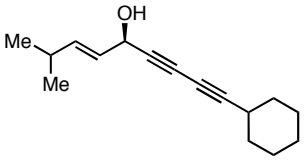
Purification by column chromatography (88:12 hexanes:EtOAc) furnished the title compound as a pale yellow oil (56 mg, 85% yield). $\mathbf{R_f}$ = 0.21 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.34 (m, 2H), 4.73 (d, *J* = 0.8 Hz, 2H), 4.41 (dt , *J* = 6.0, 6.4 Hz, 1H), 2.04-1.98 (m, 5H), 1.74-1.68 (m, 2H), 1.41 (m, 2H), 1.26 (m, 24H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 170.2, 130.0, 129.9, 80.9, 73.2, 70.6, 68.7, 62.8, 52.4, 37.5, 32.0, 29.8, 29.6, 29.5, 29.4, 29.3, 29.2, 27.3, 25.1, 22.8, 20.7, 14.2. **HPLC:** Chiralcel OJ-H Column, 96:4 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r major 10.6, minor 11.7 min (88% ee). **IR:** 3429, 3004, 2926, 2854, 2361, 2258, 2160, 1753, 1464, 1378, 1221, 1029 cm^{-1}. **HRMS** (TOF ES^+) calcd for $[M + Na^+, C_{27}H_{44}O_3Na]^+$ 439.3188, found 439.3174. $\mathbf{[\alpha]_D^{23}}$ = -4.2 (c 1.05, CH_2Cl_2).



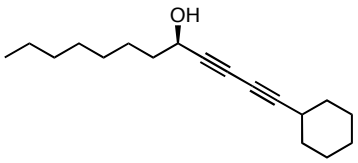
6-Hydroxypentacosa-2,4,16-triynyl ethanoate (7c). A flame-dried microwave vial equipped with a stir bar was charged with triphenylphosphine oxide (17.4 mg, 0.063 mmol, 0.4 equiv), (*S*,*S*)-ProPhenol ligand **1** (20 mg, 0.031 mmol, 0.2 equiv) and toluene (1.0 mL) under argon. Diyne **2b** (56 μL, 0.47 mmol, 3 equiv) was added, followed by Me_2Zn (391 μL, 0.47 mmol, 3 equiv, 1.2 M in toluene). The alkynyl zinc solution was stirred for 30 minutes, then the reaction solution was cooled to 0 °C and the known aldehyde[6] was added (53 μL, 0.16 mmol, 1 equiv). The reaction solution was stirred under argon at 4 °C for 32 h, then quenched with aqueous, saturated NH_4Cl (2 mL). The toluene phase was separated and the aqueous phase was extracted with Et_2O (4 x 2 mL). The combined organic fractions were dried over sodium sulfate, filtered and concentrated on a rotary evaporator.

Purification by column chromatography (82:18 hexanes:EtOAc) furnished the title compound as a yellow oil, which solidified upon standing (58 mg, 90% yield). $\mathbf{R_f}$ = 0.26 (90:10

hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.73 (d, *J* = 0.8 Hz, 2H), 4.41 (dt, *J* = 5.2, 6.0 Hz, 1H), 2.14-2.10 (m, 4H), 2.09 (s, 3H), 2.00 (br s, 1H), 1.73-1.67 (m, 2H), 1.49-1.26 (m, 26H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 170.2, 80.9, 80.3, 80.2, 73.2, 70.6, 68.7, 62.8, 52.4, 37.5, 31.9, 29.5 (br), 29.3, 29.3, 29.2 (br), 29.2, 28.9, 28.9 (br), 25.1, 22.7, 20.7, 18.8, 14.2. **HPLC:** Chiralcel OJ-H Column, 96:4 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r major 20.7, minor 24.6 min (87% ee). **IR:** 3438, 2928, 2855, 1752, 1463, 1377, 1221, 1029 cm^{-1}. **$[\alpha]_D^{23}$** = -5.8 (c 0.57, CH_2Cl_2).

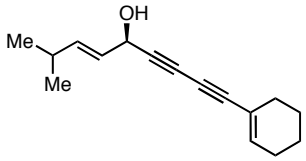


(*E*)-1-Cyclohexyl-8-methylnona-6-en-1,3-diyn-5-ol (7d). Optimal results were obtained when 3 equiv of diyne and Me_2Zn were used. Purification by column chromatography (90:10 hexanes:EtOAc) furnished the title compound as a pale yellow oil (98% yield). **R_f** = 0.18 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.83 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.51 (dd, *J* = 15.2, 6.4 Hz, 1H), 4.86 (dd, *J* = 4.0, 6.4 Hz, 1H), 2.49-2.44 (m, 1H), 2.35-2.27 (m, 1H), 2.02 (br d, *J* = 5.6 Hz, 1H), 1.80-1.67 (m, 4H), 1.51-1.42 (m, 3H), 1.32-1.18 (m, 3H), 1.00 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 141.4, 125.5, 86.0, 75.3, 70.9, 64.4, 63.5, 32.1, 30.6, 29.5, 25.7, 24.7, 22.0. **HPLC:** Chiralpak AD-H Column, 98:2 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r minor 10.2, major 11.2 min (91% ee). **$[\alpha]_D^{24}$** = -65.6 (c 0.29, CH_2Cl_2).

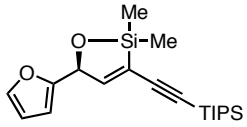


1-Cyclohexyldodeca-1,3-diyn-5-ol (7e). Optimal results were obtained when 3 equiv of diyne and Me_2Zn were used. Purification by column chromatography (88:12 hexanes:EtOAc) furnished the title compound as a pale yellow oil (77% yield). **R_f** = 0.19 (90:10 hexanes:Et_2O). **^{1}H NMR** ($CDCl_3$, 500 MHz): 4.40 (dt, *J* = 5.5, 6.5 Hz, 1H), 2.47 (br m, 1H), 1.85-1.78 (m, 3H), 1.71- 1.67 (m, 4H), 1.50-1.40 (m, 5H), 1.31-1.26 (br m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 85.7, 70.1, 64.5, 63.2, 46.0, 37.9, 32.3, 32.0, 29.7, 29.5, 29.4, 25.9, 25.3, 24.9, 22.9, 14.4. **HPLC:** Chiralcel OD-H Column, 98:2

heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r major 27.3, minor 29.7 min (73% ee). $[\alpha]_D^{24}$ = -7.5 (c 0.63, CH_2Cl_2).

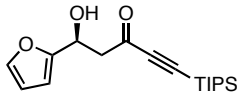


(*E*)-1-Cyclohexenyl-8-methylnona-6-en-1,3-diyn-5-ol (7f). Optimal results were obtained when 3 equiv of diyne and Me_2Zn were used. Purification by column chromatography (88:12 hexanes:EtOAc) furnished the title compound as an orange oil (>99% yield). R_f = 0.22 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 6.27 (m, 1H), 5.85 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.52 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.91 (dd, *J* = 6.0, 5.5 Hz, 1H), 2.34-2.30 (m, 1H), 2.12-2.09 (m, 4H), 2.05 (d, *J* = 6.0 Hz, 1H), 1.64-1.55 (m, 4H), 1.05 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 141.5, 139.2, 125.4, 119.5, 81.2, 80.6, 70.8, 70.7, 63.6, 30.6, 28.6, 25.9, 22.1, 22.0, 21.3. **HPLC:** Chiralcel OD-H Column, 99.5:0.5 heptane:^{i}PrOH, flow rate 0.8 mL/min, T_r minor 22.7, major 25.1 min (88% ee). $[\alpha]_D^{23}$ = -77.5 (c 0.75, CH_2Cl_2).

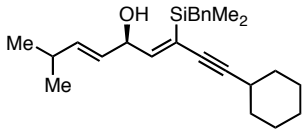


5-(Furan-2-yl)-2,2-dimethyl-3-((triisopropylsilyl)ethynyl)-2,5-dihydro-1,2-oxasilole (8). This hydrosilylation protocol is a modification of a literature report by Trost and Ball.[7] Furyl diynol **6b** (45 mg, 0.15 mmol, 1 equiv) was weighed into a flame-dried one-dram vial and dissolved in anhydrous CH_2Cl_2 (0.30 mL, 0.5 M relative to diyne), then cooled to 0 ^{o}C and put under an argon atmosphere. Ethoxydimethylsilane (31 μL, 0.22 mmol, 1.5 equiv) was syringed into the solution, followed by the addition of $[Cp^*Ru(MeCN)_3][PF_6]$ (3.8 mg, 0.0074 mmol, 0.05 equiv). The reaction mixture was stirred at room temperature for 75 min, after which the solution was diluted with hexanes (0.5 mL). Removal of the ruthenium catalyst was effected by filtration of the solution through a plug of Florisil (~2 mL), eluting with 6:1 hexanes:Et_2O (10 mL). The yellow solution was concentrated on a rotary evaporator to furnish an orange oil. Note that cyclic siloxane **8** decomposes on silica gel. The crude siloxane was directly carried through to the Tamao-Fleming oxidation without further purification. R_f = 0.35 (85:15 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 300 MHz): 7.39 (dd, *J* = 0.9, 0.9 Hz, 1H), 6.96

(d, J = 1.8 Hz, 1H), 6.32 (dd, J = 3.0, 2.1 Hz, 1H), 6.24 (d, J = 2.7 Hz), 5.77 (d, J = 1.8 Hz), 1.09 (s, 21H), 0.37 (s, 6H).

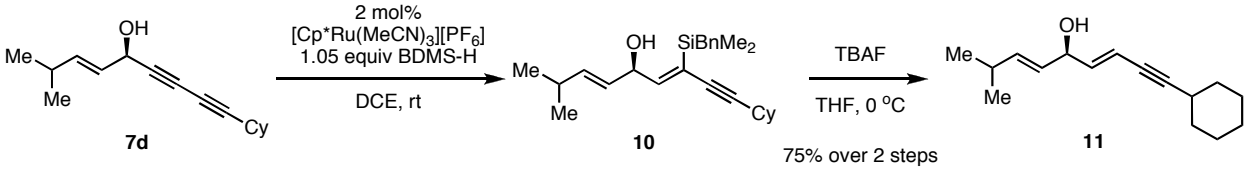


5-(Furan-2-yl)-5-hydroxy-1-(triisopropylsilyl)pent-1-yn-3-one (9). The Tamao-Fleming oxidation procedure is a modification of a literature report.[8] Crude cyclic siloxane **8** from the hydrosilylation was dissolved in anhydrous DMF (2.0 mL). Activated 4Å MS powder (84 mg) was added to the reaction solution, then cooled to 0 ^{o}C. KHF_2 (23 mg, 0.30 mmol, 2 equiv) and purified mCPBA (64 mg, 0.37 mmol, 2.5 equiv) were added sequentially. The heterogeneous reaction mixture was stirred at 0 ^{o}C. After 1 h, the solution was diluted with H_2O (10 mL) and then extracted with EtOAc (4 x 5 mL). The combined organics were washed with water (2 x 5 mL) and then brine (10 mL), then dried over Na_2SO_4. Purification by column chromatography (88:12 hexanes:EtOAc) furnished the title compound as an orange oil (33 mg, 70% yield). $\mathbf{R_f}$ = 0.18 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.38 (dd, J = 1.6, 0.8 Hz, 1H), 6.33 (dd, J = 3.2, 1.6 Hz, 1H), 6.29 (dd, J = 3.2, 0.8 Hz, 1H), 5.28 (m, 1H), 3.26-3.19 (m, 1H), 3.12-3.07 (m, 1H), 2.90 (br d, J = 4.8 Hz, 1H), 1.10 (s, 21H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 185.5, 154.4, 142.4, 110.4, 106.7, 103.8, 97.8, 63.6, 50.6, 18.5, 11.0. **IR:** 3435, 2945, 2892, 2867, 2147, 1676, 1505, 1463, 1385, 1219, 1109, 1071, 1012, 882, 736, 679 cm^{-1}. $\mathbf{[\alpha]_D^{26}}$ = -6.3 (c 0.22, CH_2Cl_2).



(3*Z*,6*E*)-3-(Benzyldimethylsilyl)-1-cyclohexyl-8-methylnona-3,6-dien-1-yn-5-ol (10). Diynol **7d** (70 mg, 0.30 mmol, 1 equiv) was added to a flame-dried one-dram vial equipped with a stirbar. Under an argon atmosphere, the oil was dissolved in anhydrous dichloroethane (0.61 mL, 0.5 M relative to diynol) and then cooled to 0 ^{o}C. Benzyldimethylsilane (51 μL, 0.32 mmol, 1.05 equiv) was syringed into the reaction mixture, followed by the addition of $[Cp^*Ru(MeCN)_3][PF_6]$ (3.1 mg, 0.0061 mmol, 0.02 equiv) in a single portion. The reaction was stirred at room temperature for 15 min, then diluted with hexanes (1 mL). The solution was filtered through a plug of SiO_2 (~2 mL) and eluted with 4:1 hexanes:Et_2O solution (15 mL). Following removal of the solvent, the crude oil was purifed by

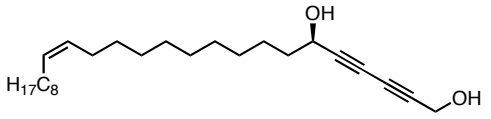
column chromatography (90:10 hexanes:EtOAc). The title compound was isolated as a yellow oil (107 mg, 92% yield). $\mathbf{R}_f$ = 0.31 (90:10 hexanes:EtOAc). **^{1}H NMR** ($CDCl_3$, 500 MHz): 7.25-7.22 (m, 2H), 7.11-7.05 (m, 3H), 6.41 (d, *J* = 9.5 Hz, 1H), 5.59 (ddd, *J* = 16.0, 7.0, 1.5 Hz, 1H), 5.32 (ddd, *J* = 16.0, 6.0, 1.5 Hz, 1H), 4.52 (dd, *J* = 9.5, 6.0 Hz, 1H), 2.52 (m, 1H), 2.33-2.24 (m, 3H), 1.84-1.81 (m, 2H), 1.72-1.70 (m, 2H), 1.53-1.48 (m, 3H), 1.35-1.26 (m, 3H), 0.96 (dd, *J* = 7.0, 1.5 Hz, 6H), 0.23 (app d, 6H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 151.9, 139.8, 139.6, 128.4, 128.3, 127.2, 124.6, 124.4, 98.2, 91.1, 82.6, 71.6, 45.6, 33.0, 30.9, 30.0, 26.0, 25.9, 25.1, 22.2, 22.1, -1.5, -1.6.



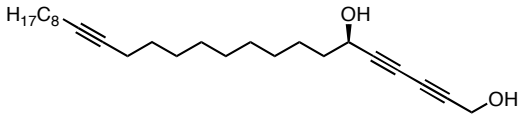
(3*E*,6*E*)-1-Cyclohexyl-8-methylnona-3,6-dien-1-yn-5-ol (11). Diynol **7d** (33 mg, 0.14 mmol, 1 equiv) was added to a flame-dried one-dram vial equipped with a stirbar. Under an argon atmosphere, the oil was dissolved in freshly distilled DCE (0.29 mL, 0.5 M relative to diynol) and then cooled to 0 °C. Benzyldimethylsilane (24 μL, 0.15 mmol, 1.05 equiv) was syringed into the reaction mixture, followed by the addition of $[Cp^*Ru(MeCN)_3][PF_6]$ (1.4 mg, 0.0029 mmol, 0.02 equiv) in a single portion. The reaction was stirred at room temperature for 15 min, then diluted with hexanes (0.5 mL). The solution was filtered through a plug of SiO_2 (~1 mL) and eluted with 4:1 hexanes:Et_2O solution (8 mL). Removal of solvent afforded vinylsilane **10** which was carried on without further purification. $\mathbf{R}_f$ = 0.45 (88:12 pet ether:EtOAc).

Crude vinylsilane **10** was dissolved in anhydrous THF (0.71 mL), then cooled to 0 °C. To the stirred solution was added TBAF (214 μL, 0.21 mmol, 1.5 equiv, 1.0 M in THF freshly prepared from the TBAF hydrate solid). The reaction mixture was stirred at 0 °C for 20 min, then diluted with 1 mL of water. The mixture was extracted with Et_2O (4 x 1 mL), and then the combined organics were washed with brine (2 mL), dried over $MgSO_4$, filtered and concentrated on a rotary evaporator. Crude material was purified by column chromatography (gradient from 92:8 to 90:10 hexanes:EtOAc) to afford the title compound as a pale yellow oil (25 mg, 75% yield over 2 steps). $\mathbf{R}_f$ = 0.38 (88:12 pet ether:EtOAc). **^{1}H NMR** ($CDCl_3$, 400 MHz): 6.05 (ddd, *J* = 15.6, 6.0, 0.8 Hz, 1H), 5.73-5.64 (m, 2H), 5.40 (ddd, *J* = 15.6, 6.4, 1.2 Hz, 1H), 4.59 (dd, *J* = 6.0, 6.4 Hz, 1H), 2.47 (br m, 1H), 2.31-2.26 (m, 1H), 1.82-1.79 (m, 2H), 1.71-1.68 (m, 2H), 1.61

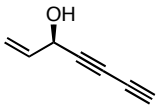
(br s, 1H), 1.52-1.39 (m, 3H), 1.29-1.23 (m, 3H), 0.98 (d, J = 6.8 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 142.5, 140.2, 127.3, 110.7, 95.7, 78.2, 73.2, 32.6, 30.7, 29.7, 25.8, 24.9, 22.1. **$[\alpha]_D^{23}$** = -43.3 (c 0.28, CH_2Cl_2).



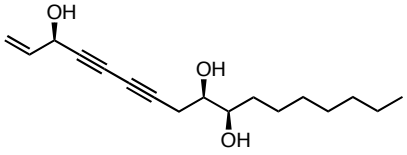
(*R*)-Strongylodiol A (12). Diynol **7b** (24 mg, 0.058 mmol) was dissolved in methanol (1.2 mL) in a one-dram vial. Anhydrous potassium carbonate (24 mg, 0.17 mmol, 3 equiv) was then added. The reaction mixture was stirred vigorously at room temperature for 1 h, then diluted with 2 mL of water. Following extraction with EtOAc (4 x 2 mL), the combined organic phase was dried over sodium sulfate, filtered and concentrated. The title compound was recovered as a white residue (21 mg, 99% yield). **R_f** = 0.24 (75:25 hexanes:EtOAc). NMR spectral data agrees with the isolation[9] and synthetic[6] reports. **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.35 (m, 2H), 4.43 (br m, 1H), 4.35 (d, J = 4.4 Hz, 2H), 2.04-1.99 (m, 4H), 1.85 (br m, 1H), 1.77-1.67 (m, 2H), 1.59 (br s, 1H), 1.46-1.42 (m, 2H), 1.27 (br m, 26H), 0.88 (t, J = 7.2 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 130.0, 129.5, 80.6, 69.9, 68.9, 63.0, 51.6, 37.6, 32.0, 29.9, 29.6, 29.6, 29.4, 29.3, 29.2, 27.3, 25.1, 22.8, 22.1, 14.2. **$[\alpha]_D^{25}$** = -4.5 (c 2.15, $CHCl_3$).



(*R*)-Strongylodiol B (13). Diynol **7c** (30 mg, 0.072 mmol) was dissolved in methanol (1.6 mL) in a one-dram vial. Anhydrous potassium carbonate (30 mg, 0.22 mmol, 3 equiv) was then added. The reaction mixture was stirred vigorously at room temperature for 1 h, then diluted with 1 mL of water. Following extraction with EtOAc (3 x 2 mL), the combined organic phase was dried over sodium sulfate, filtered and concentrated. The title compound was recovered as a white solid (27 mg, 99% yield). **R_f** = 0.20 (75:25 hexanes:EtOAc). NMR spectral data agree with the isolation[9] and synthetic[6] reports. **^{1}H NMR** ($CDCl_3$, 400 MHz): 4.42 (t, J = 6.8 Hz, 1H), 4.34 (br s, 2H), 2.13 (m, 4H), 2.00 (br s, 1H), 1.87 (br s, 1H), 1.76-1.66 (m, 2H), 1.50-1.25 (m, 26H), 0.87 (t, J = 6.8 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 80.8, 80.5, 80.4, 77.7, 70.0, 69.1, 63.1, 51.7, 37.7, 32.1, 29.7 (br), 29.5 (br), 29.4 (br), 29.4, 29.3, 29.1, 29.0, 25.2, 22.9, 19.0, 14.4. **$[\alpha]_D^{23}$** = -6.2 (c 2.1, $CHCl_3$).



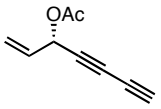
Hepta-1-en-4,6-diyn-3-ol (15).[10] Silyldiynol **6c** (37 mg, 0.14 mmol, 1 equiv) was brought up in THF (0.6 mL) and cooled to 0 °C. Acetic acid (10 μL, 0.17 mmol, 1.2 equiv), then TBAF (170 μL, 0.17 mmol, 1.2 equiv, 1.0 M in THF) were added to the reaction mixture. After stirring for 20 min, the solution was diluted with water (1 mL). The mixture was extracted with Et_2O (3 x 1 mL), then the combined organics were washed with brine and dried over Na_2SO_4. After filtration and concentration, the crude material was purified by column chromatography (88:12 hexanes:EtOAc). The title compound was isolated as a yellow oil (15 mg, >99% yield). Care was taken during the isolation as the desired product is volatile. $\mathbf{R}_f$ = 0.15 (90:10 hexanes:EtOAc). NMR spectral data are consistent with a previous report:[10] **^{1}H NMR** ($CDCl_3$, 500 MHz): 5.99-5.91 (m, 1H), 5.51-5.46 (m, 1H), 5.30-5.26 (m, 1H), 4.93 (dd, *J* = 5.6, 6.0 Hz, 1H), 2.23 (d, *J* = 0.9 Hz, 1H), 2.03 (br d, *J* = 6.8 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 135.6, 117.6, 74.7, 70.5, 69.1, 67.3, 63.4. $[\alpha]_D^{24}$ = -31.6 (c 0.75, CH_2Cl_2).



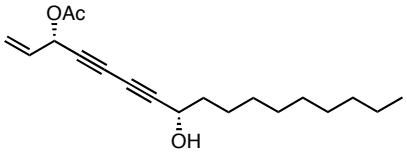
(3*R*,9*R*,10*R*)-Panaxytriol (14). Diynol **15** (6.1 mg, 0.057 mmol, 1 equiv) was added to a flame-dried one-dram vial equipped with a stir bar, then dissolved in anhydrous THF (0.19 mL) and cooled to -78 °C. Butyllithium (47 μL, 0.12 mmol, 2.05 equiv, 2.51 M in hexanes) was slowly added via syringe to the cooled solution. After 1 h, BF_3•Et_2O (15 μL, 0.12 mmol, 2.1 equiv) was added to the pale yellow slurry and stirred for 10 min. A solution of epoxide **16** (15.5 mg, 0.063 mmol, 1.1 equiv) in THF (0.2 mL) was then added to the reaction mixture. The reaction solution was warmed slowly to -40 °C over the course of 3 h, at which point diynol **15** was quantitatively consumed. TBAF (115 μL, 0.11 mmol, 2 equiv, 1.0 M in THF) was added and stirred at room temperature for 20 min. The THF solution was diluted with water (2 mL), and extracted with EtOAc (3 x 2 mL). The combined organic phase was dried over Na_2SO_4, filtered and concentrated on a rotary evaporator.

Purification by column chromatography (60:40 pet ether:EtOAc) furnished the title compound as a yellow oil (11 mg, 70% yield). $\mathbf{R}_f$ = 0.37 (75:25 hexanes:EtOAc). NMR spectral

data is consistent with literature reports:[10,11] **^{1}H NMR** ($CDCl_3$, 500 MHz): 6.00-5.94 (m, 1H), 5.52-5.48 (m, 1H), 5.30-5.37 (m, 1H), 4.95 (dd, *J* = 5.5, 7.5 Hz, 1H), 3.69-3.60 (m, 2H), 2.65-2.57 (m, 2H), 2.34 (d, *J* = 7.0 Hz, 1H), 1.98 (d, *J* = 5.0 Hz, 1H), 1.94 (d, *J* = 6.0 Hz, 1H), 1.55-1.27 (m, 12H), 0.91 (t, *J* = 7.5 Hz, 3H). **$[\alpha]_D^{23}$** = -13.1 (c 0.25, $CHCl_3$).



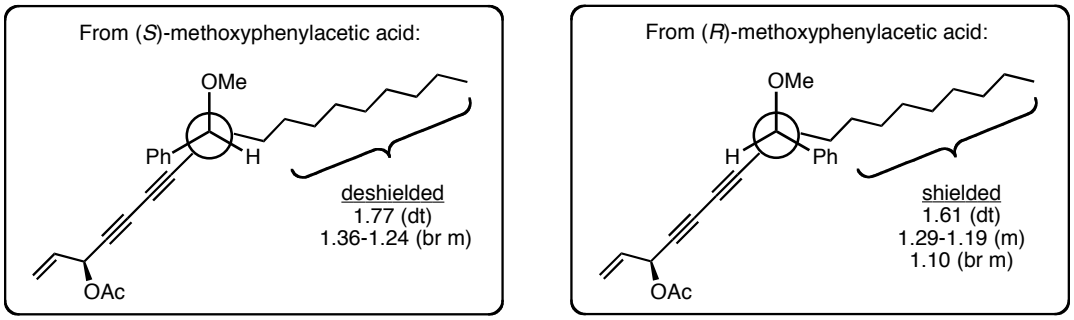
Hepta-1-en-4,6-diyn-3-yl ethanoate (18).[10] A flame-dried one-dram vial equipped with a stir bar was charged with diyne *ent*-**6c** (64 mg, 0.24 mmol, 1 equiv) and DMAP (3 mg, 0.024 mmol, 0.1 equiv), then dissolved in anhydrous CH_2Cl_2 (1.2 mL) under nitrogen. The reaction solution was cooled to 0 ^oC. Triethylamine (37 μL, 0.27 mmol, 1.1 equiv) was added, followed by acetic anhydride (25 μL, 0.27 mmol, 1.1 equiv). The reaction mixture was stirred for 2 h at 4 ^oC, then quenched with aqueous saturated $NaHCO_3$ (2 mL). Following extraction with Et_2O (3 x 2 mL), the combined organics were dried over Na_2SO_4, filtered and concentrated. The crude yellow oil (**R_f** = 0.45 in 90:10 hexanes:EtOAc) was then dissolved in THF (1.2 mL) and cooled to 0 ^oC. Acetic acid (15 μL, 0.27 mmol, 1.1 equiv), then TBAF (293 μL, 0.29 mmol, 1.2 equiv, 1.0 M in THF) were added to the reaction mixture. After 20 min, the solution was diluted with water (2 mL). The mixture was extracted with Et_2O (3 x 2 mL); the organics were washed with brine, then dried over Na_2SO_4. After filtration and concentration, the crude material was purified by column chromatography (90:10 hexanes:Et_2O). The title compound was isolated as an orange oil (26 mg, 71% yield). **R_f** = 0.34 (90:10 hexanes:EtOAc). NMR spectral data are consistent with a previous report:[10] **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.94-5.82 (m, 2H), 5.58-5.52 (m, 1H), 5.38-5.34 (m, 1H), 2.23 (d, *J* = 1.2 Hz, 1H), 2.10 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): 169.7, 132.0, 120.1, 71.5, 71.2, 69.5, 67.3, 64.4, 21.1.



(3*S*,8*S*)-8-Hydroxyheptadeca-1-ene-4,6-diyn-3-yl ethanoate (17). A flame-dried microwave tube with a stir bar was charged with triphenylphosphine oxide (6.7 mg, 0.024 mmol, 0.4 equiv), (*R*,*R*)-ProPhenol ligand **1** (7.7 mg, 0.012 mmol, 0.2 equiv) and toluene (0.4 mL) under argon. The diyne **18** (25 mg, 0.17 mmol, 2.8

equiv) was added via syringe, followed by Me_2Zn (151 μL, 0.18 mmol, 3 equiv, 1.2 M in toluene). After stirring the alkynyl zinc solution at rt for 20 minutes, it was cooled to 0 °C and freshly distilled decyl aldehyde (11 μL, 0.060 mmol, 1 equiv) was added. The reaction mixture was stirred under argon at 4 °C for 28 h, then quenched with aqueous, saturated NH_4Cl (1 mL). The toluene phase was separated and the aqueous phase was extracted with Et_2O (3 x 1 mL). The combined organic fractions were dried over Na_2SO_4, filtered and concentrated on a rotary evaporator.

Purification of the crude material by column chromatography (85:15 hexanes:Et_2O) furnished the title compound as a yellow oil (12 mg, 67% yield). $\mathbf{R}_f$ = 0.34 (80:20 hexanes:EtOAc). Compound characterization data is consistent with the isolation report.[12] **^{1}H NMR** ($CDCl_3$, 500 MHz): 5.91 (m, 1H), 5.89-5.84 (m, 1H), 5.55 (d, *J* = 16.5 Hz, 1H), 5.35 (d, *J* = 10 Hz, 1H), 4.42 (dt, *J* = 5.5, 6.0 Hz, 1H), 2.11 (s, 3H), 1.85 (d, *J* = 5.0 Hz, 1H), 1.75-1.66 (m, 2H), 1.45-1.41 (m, 2H), 1.30-1.26 (m, 12H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): 169.6, 132.0, 119.8, 81.4, 74.4, 70.9, 68.7, 64.5, 62.9, 37.5, 32.0, 29.6, 29.5, 29.4, 29.3, 25.1, 22.8, 21.0, 14.2. $\mathbf{[\alpha]_D^{23}}$ = -24.3 (c 1.02, 0.75% ethanol in $CHCl_3$).



The absolute stereochemistry of the second diyne addition was determined by the *O*-methoxymandelate ester method[5] to give the (*S*)-enantiomer. (*S*)-*O*-methylmandelate ester ($\mathbf{R}_f$ = 0.27 in 90:10 hexanes:EtOAc) was prepared in quantitative yield as previously described; **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.44-7.42 (m, 2H), 7.40-7.34 (m, 3H), 5.91-5.81 (m, 2H), 5.56-5.51 (m, 1H), 5.43 (t, *J* = 6.4 Hz, 1H), 5.37-5.33 (m, 1H), 4.78 (s, 1H), 3.43 (s, 3H), 2.10 (s, 3H), 1.77 (dt, *J* = 7.2, 6.8 Hz, 2H), 1.36-1.24 (br m, 14H), 0.88 (t, *J* = 7.2 Hz, 3H). (*R*)-*O*-methylmandelate ester ($\mathbf{R}_f$ = 0.24 in 90:10 hexanes:EtOAc) was also isolated in quantitative yield; **^{1}H NMR** ($CDCl_3$, 400 MHz): 7.43-7.41 (m, 2H), 7.38-7.33 (m, 3H), 5.92-5.82 (m, 2H), 5.57-5.52 (m, 1H), 5.42 (t, *J* = 6.4 Hz, 1H), 5.37-5.34 (m, 1H), 4.77 (s, 1H), 3.42 (s, 3H), 2.11 (s, 3H), 1.61 (dt, *J* = 7.2, 6.4 Hz, 2H), 1.29-1.19 (m, 8H), 1.10 (br m, 6H), 0.88 (t, *J* = 7.2 Hz, 3H).

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