Supporting Information I

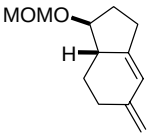
Tandem Cyclization of Alkynes via Rhodium Alkynyl and Alkenylidene Catalysis

Jung Min Joo, Yu Yuan and Chulbom Lee*
Department of Chemistry, Princeton University
Princeton, New Jersey 08544

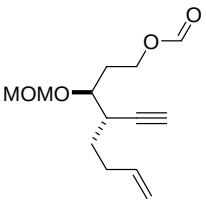
Part I. Rhodium-Catalyzed Tandem Cyclization
Part II. Preparation of Substrates

General Information: Unless otherwise noted, all reactions were conducted as described under an argon atmosphere using anhydrous solvents (either distilled or passed through an activated alumina column or activated molecular sieves column). Commercially available reagents were used without further purification. Thin layer chromatography (TLC) was performed using EM Science silica gel 60 F254 plates and visualized by using UV light (254 nm) and/or anisaldehyde, cerium sulfate or potassium permanganate stains. Flash column chromatography was performed on EM Science silica gel 60 (40-63 μm) using the indicated solvent system. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on a Varian Mercury 300 MHz or Varian Inova 400, 500, 600 MHz spectrometers. Chemical shifts in ^{1}H NMR spectra were reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm). Data for ^{1}H NMR are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant in Hertz (Hz) and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift in ppm from the central peak of $CDCl_3$ (77.0 ppm). FT-IR spectra were obtained on a Perkin-Elmer Paragon 500 and reported in frequency of the absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from the Princeton University Mass Spectrometry Facility and the Scripps Center for Mass Spectrometry.

Part I. Rhodium-Catalyzed Tandem Cyclization

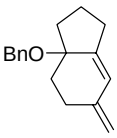


3-Methoxymethoxy-6-methylene-2,3,3a,4,5,6-hexahydro-1*H*-indene (2, Table 1, entry 6). To a flame dried one dram glass vial equipped with a screw-cap and a Teflon septum were added $[Rh(COD)Cl]_2$ (3.1 mg, 0.0063 mmol), $P(4\text{-F-}C_6H_4)_3$ (7.9 mg, 0.025 mmol) and DMF (0.50 mL). This mixture was stirred for 5 min before enyne **1a** (68 mg, 0.21 mmol) in DMF (0.50 mL) was added via syringe at 25 °C. The syringe was washed with DMF (2×0.50 mL). After addition of Et_3N (58 μL, 0.42 mmol), the resulting solution was moved to a pre-heated sand bath (85 °C). After stirring for 14 h, the reaction mixture was cooled to room temperature and loaded directly onto a silica gel column. Purification by flash column chromatography (hexanes:ether = 12:1) yielded **2** (33 mg, 85%) as a colorless oil. R_f 0.60 (hexanes:EtOAc = 8:1); IR (film) 2935, 2360, 1151, 1114, 1040, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.98 (s, 1H), 4.74 (d, *J* = 6.7 Hz, 1H), 4.74 (s, 1H), 4.72 (s, 1H), 4.70 (d, *J* = 6.7 Hz, 1H), 3.60 (td, *J* = 8.9, 6.9 Hz, 1H), 3.41 (s, 3H), 2.60-2.52 (m, 1H), 2.52-2.45 (m, 1H), 2.45-2.35 (m, 1H), 2.34-2.20 (m, 3H), 2.18-2.10 (m, 1H), 1.72-1.62 (m, 1H), 1.30-1.21 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 143.6, 123.1, 108.6, 95.8, 83.2, 55.2, 47.2, 30.2, 30.3, 27.6, 27.2; HRMS (EI) calcd for $C_{12}H_{18}O_2$ $[M]^+$ 194.1307, found 194.1296.

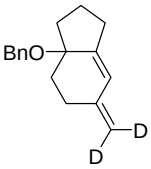


Formic acid 4-ethynyl-3-methoxymethoxy-oct-7-enyl ester (Table 1, entry 1). To a flame dried one dram glass vial equipped with a screw-cap and a Teflon septum were added $[Rh(COD)Cl]_2$ (2.9 mg, 0.0059 mmol), $P(4\text{-F-}C_6H_4)_3$ (7.5 mg, 0.024 mmol) and DMF (0.50 mL). This mixture was stirred for 5 min before enyne **1a** (64 mg, 0.21 mmol) in DMF (0.50 mL) was added via syringe at 25 °C. The syringe was washed with DMF (2×0.50 mL). The resulting solution was moved to a pre-heated sand bath (85 °C). After being stirred for 6 h, the reaction mixture was cooled to room temperature and loaded directly onto a silica gel column. Purification by flash column chromatography yielded the unreacted enyne **1a** (41 mg, 64%) and the formate (9 mg, 19%) as a colorless oil. R_f 0.31 (hexanes:EtOAc = 8:1); IR (film) 3287, 2926, 1726, 1175, 1035, 917, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 5.81 (ddt, *J* = 17.1,

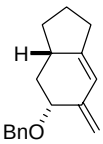
10.1, 7.0 Hz, 1H), 5.07 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.01 (d, *J* = 9.5 Hz, 1H), 4.74 (d, *J* = 7.0 Hz, 1H), 4.67 (d, *J* = 7.0 Hz, 1H), 4.40-4.28 (m, 2H), 3.65 (ddd, *J* = 9.2, 5.2, 3.0 Hz, 1H), 3.41 (s, 3H), 2.78 (ddd, *J* = 10.1, 4.9, 2.4 Hz, 1H), 2.40-2.30 (m, 1H), 2.20-2.10 (m, 1H), 2.14 (d, *J* = 2.4 Hz, 1H), 2.10-2.03 (m, 1H), 2.03-1.94 (m, 1H), 1.60-1.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 137.5, 115.5, 96.4, 83.8, 76.2, 71.5, 60.7, 56.0, 36.0, 31.5, 30.4, 29.7; HRMS (ESI-TOF) calcd for $C_{13}H_{20}NaO_4$ $[M+Na]^+$ 263.1259, found 263.1253.



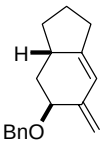
3a-Benzyloxy-6-methylene-2,3,3a,4,5,6-hexahydro-1*H*-indene (4a, Table 2, entry 1). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.0 mg, 0.0061 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (7.8 mg, 0.025 mmol), Et_3N (58 μL, 0.41 mmol) and enyne **3a** (76 mg, 0.21 mmol) were reacted in DMF (2.1 mL, 0.10 M) for 11 h to give **4a** (36 mg, 73%) as a colorless oil after purification by flash column chromatography. R_f 0.40 (hexanes:EtOAc = 20:1); IR (film) 2940, 2858, 1254, 1194, 1068, 734, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.23 (m, 5H), 6.10 (s, 1H), 4.84 (s, 1H), 4.83 (s, 1H), 4.43 (s, 2H), 2.72-2.60 (m, 2H), 2.45-2.35 (m, 2H), 2.35-2.27 (m, 2H), 1.98-1.87 (m, 1H), 1.79-1.69 (m, 1H), 1.42-1.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 143.3, 139.4, 128.3, 127.6, 127.2, 125.1, 110.4, 80.9, 65.2, 36.1, 30.9, 29.6, 26.3, 21.7; MS m/z (GC/MS): 240.2 (M^+), 149, 132.



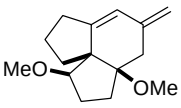
3a-Benzyloxy-6-dideuteriomethylene-2,3,3a,4,5,6-hexahydro-1*H*-indene (4b, Table 2, entry 1). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.0 mg, 0.0061 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (7.6 mg, 0.024 mmol), Et_3N (63 μL, 0.45 mmol) and enyne **3b** (84 mg, 0.23 mmol) were reacted in DMF (2.3 mL, 0.10 M) for 11 h to give **4b** (41 mg, 75%) as a colorless oil after purification by flash column chromatography. IR (film) 2942, 2857, 1453, 1194, 1069, 925, 734, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.23 (m, 5H), 6.10 (s, 1H), 4.83 (s, 0.2H), 4.81 (s, 0.2H), 4.43 (s, 2H), 2.72-2.60 (m, 2H), 2.43-2.35 (m, 2H), 2.35-2.27 (m, 2H), 1.98-1.87 (m, 1H), 1.79-1.69 (m, 1H), 1.42-1.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 143.1, 139.4, 128.3, 127.6, 127.2, 125.1, 80.9, 65.2, 36.1, 30.9, 29.6, 26.2, 21.7 (The methylene carbon peak, 110.4, is absent.); HRMS (EI) calcd for $C_{17}H_{19}D_2O$ $[M+H]^+$ 243.1716, found 243.1711.



5-Benzyloxy-6-methylene-2,3,3a,4,5,6-hexahydro-1*H*-indene (6, Table 2, entry 2). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.0 mg, 0.0061 mmol), P(4-F-C_6H_4)$_3$ (7.6 mg, 0.024 mmol), Et_3N (58 μL, 0.42 mmol) and enyne **5** (77 mg, 0.21 mmol) were reacted in DMF (2.1 mL, 0.10 M) for 11 h to give **6** (28 mg, 55%) as a colorless oil after purification by flash column chromatography. R_f 0.74 (hexanes:EtOAc = 8:1); IR (film) 2950, 2860, 1588, 1452, 1112, 1070, 886, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.22 (m, 5H), 5.98 (s, 1H), 5.21 (s, 1H), 4.84 (s, 1H), 4.76 (d, *J* = 12.2 Hz, 1H), 4.65 (d, *J* = 11.9 Hz, 1H), 4.14 (d, *J* = 11.6 Hz, 1H), 2.45-2.33 (m, 3H), 2.27 (dt, *J* = 18.0, 8.9 Hz, 1H), 1.97 (dt, *J* = 11.9, 6.5 Hz, 1H), 1.84-1.76 (m, 1H), 1.67-1.57 (m, 1H), 1.34-1.24 (m, 1H), 1.23-1.13 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 145.0, 138.9, 128.3, 127.5, 127.4, 120.6, 107.1, 76.8, 70.7, 41.9, 34.9, 33.2, 29.8, 24.1; HRMS (EI) calcd for $C_{17}H_{20}O$ $[M]^+$ 240.1514, found 240.1500.

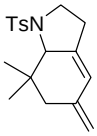


5-Benzyloxy-6-methylene-2,3,3a,4,5,6-hexahydro-1*H*-indene (8, Table 2, entry 3). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.0 mg, 0.0061 mmol), P(4-F-C_6H_4)$_3$ (7.6 mg, 0.024 mmol), Et_3N (59 μL, 0.43 mmol) and enyne **7** (79 mg, 0.21 mmol) were reacted in DMF (2.1 mL, 0.10 M) for 11 h to give **8** (29 mg, 57%) as a colorless oil after purification by flash column chromatography. R_f 0.79 (hexanes:EtOAc = 8:1); IR (film) 2938, 2863, 1588, 1453, 1091, 1068, 895, 829, 734, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.22 (m, 5H), 5.94 (s, 1H), 4.96 (s, 1H), 4.83 (s, 1H), 4.65 (d, *J* = 12.5 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 4.05 (s, 1H), 2.72-2.62 (m, 1H), 2.50 (dd, *J* = 17.2, 10.3 Hz, 1H), 2.37 (dt, *J* = 13.1, 3.4 Hz, 1H), 2.29 (dt, *J* = 17.7, 9.2 Hz, 1H), 1.99 (dt, *J* = 11.6, 6.7 Hz, 1H), 1.84-1.76 (m, 1H), 1.70-1.58 (m, 1H), 1.34-1.25 (m, 1H), 1.15-1.05 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 141.8, 139.1, 128.2, 127.6, 127.2, 118.7, 112.5, 76.2, 69.0, 36.7, 35.0, 33.1, 30.3, 23.7; HRMS (ESI-TOF) calcd for $C_{17}H_{21}O$ $[M+H]^+$ 241.1592, found 241.1592.

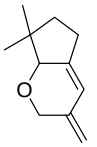


1,3a-Dimethoxy-5-methylene-2,3,3a,4,5,7,8,9-octahydro-1*H*-cyclopenta[*d*]indene (10, Table 2, entry 4). Following the procedure for **2**, the reaction of enyne **9** (72 mg, 0.20 mmol) with

$[Rh(COD)Cl]_2$ (3.0 mg, 6.0 μmol), P(4-F-C_6H_4)$_3$ (7.6 mg, 24 μmol) and Et_3N (56 μL, 0.40 mmol) in DMF (2.0 mL, 0.10 M) at 85 °C for 2 h afforded diene **10** (34 mg, 72%) as a colorless oil. IR (film) 2937, 2824, 1462, 1199, 1089, 882 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.04 (s, 1H), 4.85 (s, 1H), 4.78 (s, 1H), 3.68 (t, *J* = 7.9 Hz, 1H), 3.28 (s, 3H), 3.21 (s, 3H), 2.69 (d, *J* = 16.5 Hz, 1H), 2.53 (m, 1H), 2.35 (m, 1H), 2.28 (d, *J* = 16.5 Hz, 1H), 2.06 (m, 1H), 1.96 (m, 1H), 1.86 (m, 3H), 1.72 (m, 1H), 1.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 141.6, 119.9, 110.5, 89.7, 81.6, 58.0, 57.7, 50.2, 35.3, 32.2, 31.8, 26.5, 24.6, 22.6; HRMS (EI) calcd for $C_{15}H_{22}O_2$ $[M]^+$ 234.1620, found 234.1603.

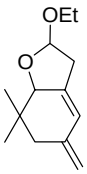


7,7-Dimethyl-5-methylene-1-(toluene-4-sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (12, Table 2, entry 5). Following the procedure for **2**, the reaction of enyne **11** (89 mg, 0.20 mmol) with $[Rh(COD)Cl]_2$ (3.0 mg, 6.0 μmol), P(4-F-C_6H_4)$_3$ (7.6 mg, 24 μmol) and Et_3N (56 μL, 0.40 mmol) in DMF (2.0 mL, 0.10 M) at 85 °C for 12 h afforded diene **12** (49 mg, 78%) as a pale white solid. MP 135–136 °C; IR (film) 2962, 2927, 1598, 1463, 1347, 1161 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 5.98 (s, 1H), 4.81 (s, 2H), 4.08 (s, 1H), 3.73 (dd, *J* = 12.5, 8.0 Hz, 1H), 3.00 (td, *J* = 11.8, 5.1 Hz, 1H), 2.43 (s, 3H), 2.34 (d, *J* = 15.6 Hz, 1H), 2.12 (d, *J* = 15.9 Hz, 1H), 2.01 (dd, *J* = 14.0, 4.9 Hz, 1H), 1.63 (m, 1H), 1.26 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 141.4, 140.7, 136.2, 130.0, 127.9, 124.1, 112.3, 68.3, 49.5, 44.3, 36.5, 31.7, 29.6, 21.7, 19.0; HRMS (EI) calcd for $C_{18}H_{23}O_2NS$ $[M]^+$ 317.1450, found 317.1452.

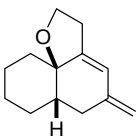


7,7-Dimethyl-3-methylene-2,3,5,6,7,7a-hexahydro-cyclopenta[*b*]pyran (14, Table 2, entry 6). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.0 mg, 0.0061 mmol), P(4-F-C_6H_4)$_3$ (7.8 mg, 0.025 mmol), Et_3N (57 μL, 0.41 mmol) and enyne **13** (60 mg, 0.21 mmol) were reacted in DMF (2.1 mL, 0.10 M) for 4 h to give **14** (15 mg, 45%) as a colorless oil after purification by flash column chromatography. R_f 0.41 (hexanes:EtOAc = 20:1); IR (film) 2956, 2866, 1461, 1109, 1087, 882 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.09 (s, 1H), 4.72 (s, 2H), 4.43 (d, *J* = 13.4 Hz, 1H), 4.27 (d, *J* = 13.7 Hz, 1H), 3.90 (s, 1H), 2.37 (t, *J* = 7.6 Hz, 2H), 1.56 (t, *J* = 7.6 Hz, 2H), 1.17 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 140.0, 120.6, 106.3, 85.7, 69.4, 40.3, 35.8, 26.5, 25.0, 19.8; HRMS (ESI-TOF) calcd for $C_{19}H_{26}NaO_5S$ $[M+H]^+$ 389,1399, found

389.1397.

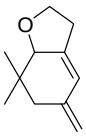


2-Ethoxy-7,7-dimethyl-5-methylene-2,3,5,6,7,7a-hexahydro-benzofuran (16, Table 2, entry 7). Following the procedure for **2**, $[Rh(COD)Cl]_2$ (3.1 mg, 0.0063 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (8.0 mg, 0.025 mmol), Et_3N (35 μL, 0.25 mmol) and enyne **15** (71 mg, 0.21 mmol, dr = 1.2:1) were reacted in DMF (2.1 mL, 0.10 M) for 11 h. Purification by flash chromatography provided two diastereomeric dienes (the less polar isomer, 15 mg, 34%; the more polar isomer, 13 mg, 30%) both as colorless oils. The less polar diastereomer: R_f 0.75 (hexanes:EtOAc = 8:1); IR (film) 2974, 2927, 1117, 1046, 1027, 964, 893 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.26-5.22 (dd, *J* = 5.5, 1.8 Hz, 1H), 4.78 (s, 1H), 4.77 (s, 1H), 4.25 (s, 1H), 3.81 (dq, *J* = 9.5, 7.0 Hz, 1H), 3.51 (dq, *J* = 9.5, 7.0 Hz, 1H), 2.73 (dd, *J* = 17.7, 5.2 Hz, 1H), 2.59 (d, *J* = 17.4 Hz, 1H), 2.21 (d, *J* = 15.3 Hz, 1H), 2.05 (d, *J* = 15.3 Hz, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.12 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 140.2, 121.5, 110.7, 102.6, 82.8, 62.9, 43.6, 37.8, 34.0, 28.3, 17.9, 15.3; HRMS (EI) calcd for $C_{13}H_{20}O_2$ $[M]^+$ 208.1463, found 208.1463. The more polar diastereomer: R_f 0.63 (hexanes:EtOAc = 8:1); IR (film) 2976, 2926, 1118, 1044, 1024, 953, 892 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.04 (s, 1H), 5.14 (d, *J* = 5.5 Hz, 1H), 4.81 (s, 1H), 4.79 (s, 1H), 4.25 (s, 1H), 3.79 (dq, *J* = 9.5, 7.0 Hz, 1H), 3.41 (dq, *J* = 9.5, 7.0 Hz, 1H), 2.79c (d, *J* = 15.3 Hz, 1H), 2.48 (d, *J* = 15.6 Hz, 1H), 2.19 (d, *J* = 15.0 Hz, 1H), 2.07 (d, *J* = 15.0 Hz, 1H), 1.16 (t, *J* = 7.0 Hz, 3H), 1.11 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 139.1, 122.5, 111.1, 101.7, 85.8, 62.3, 43.4, 38.6, 34.7, 28.6, 18.3, 14.9.

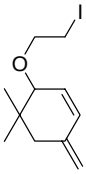


5-Methylene-3,5,6,6a,7,8,9,10-octahydro-2*H*-1-oxa-cyclopenta[*d*]naphthalene (18, Table 2, entry 8). Following the procedure for **2**, the reaction of enyne **17** (64 mg, 0.20 mmol) with $[Rh(COD)Cl]_2$ (3.0 mg, 6.0 μmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (7.6 mg, 24 μmol) and Et_3N (56 μL, 0.40 mmol) in DMF (2.0 mL, 0.10 M) at 85 °C for 3 h afforded diene **18** (37 mg, 97%) as a colorless oil. IR (film) 2929, 2558, 1608, 1448, 1062, 1021 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.92 (s, 1H), 4.80 (s, 1H), 4.78 (s, 1H), 3.99 (ddd, *J* = 9.1, 8.5, 4.9 Hz, 1H), 3.87 (td, *J* = 8.3, 7.0 Hz, 1H), 2.77 (m, 1H), 2.63 (m, 1H), 2.52 (ddd, *J* = 15.0, 7.4, 4.6 Hz, 1H), 2.17 (dd, *J* = 15.8, 4.5 Hz, 1H), 1.90 (m, 1H), 1.77 (m, 1H), 1.60 (m, 1H), 1.51 (m, 4H), 1.42 (m, 2H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 147.4, 143.6, 121.4, 109.9, 80.5, 64.2, 38.9, 32.5, 30.2, 29.3, 27.6, 21.6, 20.4; HRMS (EI) calcd for $C_{13}H_{18}O$ $[M]^+$ 190.1358, found 190.1361.

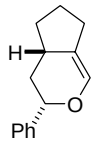


7,7-Dimethyl-5-methylene-2,3,5,6,7,7a-hexahydro-benzofuran (20, Table 2, entry 9). To a flame dried one dram glass vial equipped with a screw-cap and a Teflon septum were added $[Rh(ethylene)_2Cl]_2$ (2.2 mg, 0.0057 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (7.1 mg, 0.023 mmol) and DMF (0.50 mL). This mixture was stirred for 5 min before enyne **19** (55 mg, 0.19 mmol) in DMF (0.50 mL) was added via syringe at 25 °C. The syringe was washed with DMF (2×0.50 mL). After addition of Et_3N (52 μL, 0.38 mmol), the resulting solution was stirred at room temperature for 5 h. The reaction mixture was loaded directly onto a silica gel column and purified by flash column chromatography (hexanes:ether = 12:1) to yield **20** (25 mg, 81%) as a colorless oil. R_f 0.33 (hexanes:EtOAc = 20:1); IR (film) 2964, 2867, 1470, 1063, 893 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H), 4.79 (s, 1H), 4.77 (s, 1H), 3.97 (s, 1H), 3.89 (t, *J* = 7.2 Hz,, 2H), 2.70-2.62 (m, 1H), 2.55-2.46 (m, 1H), 2.20 (d, *J* = 15.0 Hz, 1H), 2.05 (d, *J* = 15.3 Hz, 1H), 1.11 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 141.8, 121.4, 110.7, 84.9, 66.9, 43.4, 34.7, 31.1, 28.4, 17.9; HRMS (EI) calcd for $C_{11}H_{16}O$ $[M]^+$ 164.1201, found 164.1192.

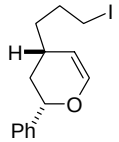


3-(2-Iodo-ethoxy)-4,4-dimethyl-6-methylene-cyclohexene (21, Table 2, entry 10). To a flame dried one dram glass vial equipped with a screw-cap and a Teflon septum were added $[Rh(ethylene)_2Cl]_2$ (2.5 mg, 0.0064 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (8.1 mg, 0.026 mmol) and THF (0.50 mL). This mixture was stirred for 5 min before enyne **19** (62 mg, 0.21 mmol) in THF (0.50 mL) was added via syringe at 25 °C. The syringe was washed with THF (2×0.50 mL). After addition of Et_3N (59 μL, 0.42 mmol), the resulting solution was stirred for 2 days. The reaction mixture was loaded directly onto a silica gel column and purified by flash column chromatography (hexanes:ether = 12:1) to yield **21** (40 mg, 65%) as a colorless oil. R_f 0.42 (hexanes:EtOAc = 20:1); IR (film) 2964, 2927, 2869, 1470, 1112, 1084, 897 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.13 (d, *J* = 10.0 Hz, 1H), 5.69 (d, *J* = 10.0 Hz, 1H), 4.86 (s, 1H), 4.81 (s, 1H), 3.86 (dt, *J* = 10.8, 6.8 Hz, 1H), 3.68 (dt, *J* = 10.8, 6.8 Hz, 1H), 3.57 (s, 1H), 3.26-3.20 (m, 2H), 2.17 (d, *J* = 14.4 Hz, 1H), 2.08 (d, *J* = 14.3 Hz, 1H), 0.96 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6,

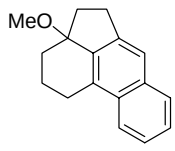
130.7, 128.2, 113.5, 82.2, 70.9, 42.5, 35.3, 27.2, 21.3, 3.6; MS m/z (GC/MS): 292 (M^+), 277.



3-Phenyl-3,4,4a,5,6,7-hexahydro-cyclopenta[*c*]pyran (24, eq 1). To a flame dried one dram glass vial equipped with a screw-cap and a Teflon septum were added $[Rh(COD)Cl]_2$ (2.9 mg, 0.0059 mmol), P(4-F-$C_6H_4)_3$ (7.5 mg, 0.024 mmol) and DMF (0.50 mL). This mixture was stirred for 5 min before enyne **22** (64 mg, 0.20 mmol) in DMF (0.50 mL) was added via syringe at 25 °C. The syringe was washed with DMF (2×0.50 mL). After addition of Et_3N (55 μL, 0.39 mmol), the resulting solution was moved to a pre-heated sand bath (85 ^oC). After being stirred for 1 h, the reaction mixture was cooled to room temperature and loaded directly onto a silica gel column. Purification by flash column chromatography (hexanes:ether = 12:1) yielded **24** (20 mg, 52%) and **25** (10 mg, 15%) both as colorless oils. Characterization of enol ether **24**: R_f 0.33 (hexanes:EtOAc = 20:1); IR (film) 2950, 2854, 1678, 1135, 1117, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.25 (m, 5H), 6.44 (s, 1H), 4.79 (d, *J* = 11.6 Hz, 1H), 2.61-2.52 (m, 1H), 2.35 (t, *J* = 15.1 Hz, 1H), 2.29-2.20 (m, 2H), 2.00 (dt, *J* = 11.9, 7.0 Hz, 1H), 1.84-1.76 (m, 1H), 1.70-1.62 (m, 1H), 1.50-1.42 (m, 1H), 1.10 (qd, *J* = 10.7, 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 136.3, 128.4, 127.6, 126.1, 118.6, 76.9, 38.1, 36.9, 33.1, 26.1, 24.5; HRMS (EI) calcd for $C_{14}H_{16}O$ $[M]^+$ 200.1201, found 200.1196.



4-(3-Iodo-propyl)-2-phenyl-3,4-dihydro-2*H*-pyran (25, eq 1). R_f 0.51 (hexanes:EtOAc = 8:1); IR (film) 2915, 2851, 1644, 1240, 1056, 759, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.24 (m, 5H), 6.48 (d, *J* = 6.0 Hz, 1H), 4.83 (d, *J* = 11.2 Hz, 1H), 4.63 (d, *J* = 6.0 Hz, 1H), 3.16 (t, *J* = 7.2 Hz, 2H), 2.53-2.41 (m, 1H), 2.10-2.00 (m, 1H), 1.87 (dt, *J* = 14.4, 7.2 Hz, 2H), 1.50-1.36 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 141.6, 128.5, 127.8, 125.9, 105.1, 77.5, 37.9, 36.8, 31.5, 30.7, 6.7; HRMS (EI) calcd for $C_{14}H_{17}IO$ $[M]^+$ 328.0324, found 328.0322.

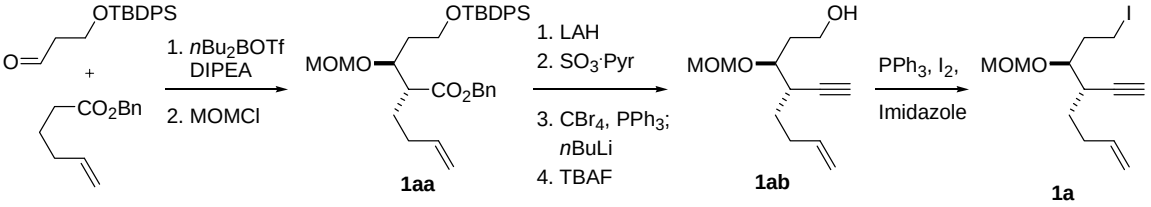


3a-Methoxy-1,2,3,3a,4,5-hexahydro-acephenanthrylene (28, eq 2). Following the procedure for **2**, the reaction of enyne **26** (12.0 mg, 33.0 μmol) with $[Rh(COD)Cl]_2$ (0.8 mg, 1.6 μmol),

P(4-F-C_6H_4)$_3$ (2.1 mg, 6.6 μmol) and Et_3N (8.4 μL, 60 μmol) in DMF at 100 °C for 1 h afforded **28** (6.5 mg, 83%) as a colorless oil. IR (film) 2932, 1457, 1324, 1284, 1197, 1081 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.84 (m, 1H), 7.72 (m, 1H), 7.41 (s, 1H), 7.36 (m, 2H), 3.21 (m, 1H), 3.04 (m, 1H), 3.03 (s, 3H), 2.61 (m, 2H), 2.39 (dd, *J* = 13.1, 6.7 Hz, 1H), 2.29 (m, 2H), 1.74 (m, 1H), 1.47 (ddd, *J* = 13.1, 11.0, 7.5 Hz, 1H), 1.15 (td, *J* = 13.8, 2.8 Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.0, 141.3, 135.6, 131.2, 129.2, 127.9, 125.9, 125.4, 124.0, 121.4, 81.6, 51.1, 36.7, 31.0, 30.5, 24.1, 19.2; HRMS (EI) calcd for $C_{17}H_{18}O$ [M]$^+$ 238.1358, found 238.1349.

Part II. Preparation of Substrates

Preparation of Iodoenyne 1a



To a solution of benzyl hex-5-enoate (1.20 g, 5.00 mmol) in dry CH_2Cl_2 (10 mL) at –78 °C were added *n*-Bu_2BOTf (1.0 M in CH_2Cl_2, 7.64 mL, 7.64 mmol) and *i*Pr_2NEt (1.53 mL, 8.78 mmol).[1] After 2 h, a solution of 3-(*tert*-butyl-diphenyl-silanyloxy)propionaldehyde (2.00 g, 6.40 mmol) in CH_2Cl_2 (5 mL) was added dropwise at –78 °C. The resultant mixture was stirred at –78 °C for 1 h and at 0 °C for 1 h, at which point a solution of pH 7 phosphate buffer (10 mL) in MeOH (20 mL) was added. After 5 min, 30% H_2O_2 (12 mL) in MeOH (24 mL) was added, and the stirring was continued at room temperature for 12 h. Extractive work-up followed by chromatography afforded a mixture of the aldol products as a colorless oil (2.42 g, 80%). The syn/anti ratio was determined to be 91:9 on the basis of a NMR analysis. R_f 0.48 (hexanes:EtOAc = 4:1); IR (film) 3501, 3071, 2931, 2858, 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.66 (m, 5H), 7.48-7.33 (m, 10H), 5.79 (ddt, *J* = 17.1, 10.4, 6.7 Hz, 1H), 5.16 (s, 2H), 5.01 (dd, *J* = 17.4, 1.2 Hz, 1H), 4.98 (d, *J* = 10.4 Hz, 1H), 4.12-4.06 (m, 1H), 3.91-3.85 (m, 1H), 3.85-3.78 (m, 1H), 3.55 (d, *J* = 3.4 Hz, 1H), 2.61 (dd, *J* = 14.0, 6.7 Hz, 1H), 2.11 (dt, *J* = 14.3, 7.3 Hz, 1H), 2.03 (dt, *J* = 14.0, 7.3 Hz, 1H), 1.87 (d, *J* = 7.3 Hz, 1H), 1.84 (d, *J* = 7.3 Hz, 1H), 1.79-1.70 (m, 1H), 1.68-1.60 (m, 1H), 1.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 137.7, 135.8, 135.5, 134.8, 132.9, 132.8, 129.8, 128.5, 128.2, 127.8, 115.2, 72.0, 66.2, 63.0, 51.2, 35.8, 31.6, 27.2, 26.8, 26.5, 19.0; HRMS (EI) calcd for $C_{28}H_{31}O_4Si$ [M-C_4H_9]$^+$ 459.1992, found 459.1980.

[1] Abiko, A.; Liu, J.-F. *J. Org. Chem.* **1996**, *61*, 2590.

To a solution of the alcohol (5.72 g, 11.1 mmol) in CH_2Cl_2 (20 mL) were added DIPEA (7.71 mL, 44.3 mmol) and chloromethyl methyl ether (3.36 mL, 44.3 mmol) at 25 °C. After 48 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (30 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×40 mL). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 12:1) provided **1aa** (5.66 g, 91%) as a colorless oil. R_f 0.73 (hexanes:EtOAc = 4:1); IR (film) 3071, 2932, 2858, 1736, 1472, 1154, 1111, 739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74-7.66 (m, 5H), 7.48-7.33 (m, 10H), 5.84-5.73 (m, 1H), 5.17 (s, 2H), 5.02 (d, *J* = 17.1 Hz, 1H), 4.99 (d, *J* = 9.5 Hz, 1H), 4.64 (d, *J* = 3.7 Hz, 2H), 4.15-4.06 (m, 1H), 3.85-3.75 (m, 2H), 3.32 (d, *J* = 4.0 Hz, 3H), 2.80 (dd, *J* = 9.8, 4.9 Hz, 1H), 2.18-2.09 (m, 1H), 2.09-1.98 (m, 1H), 1.84-1.74 (m, 3H), 1.67-1.58 (m, 1H), 1.09 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 137.6, 135.9, 135.5, 133.7, 129.6, 128.4, 128.2, 128.1, 127.6, 115.3, 96.4, 75.7, 66.2, 60.1, 55.8, 49.0, 34.8, 31.8, 27.1, 26.8, 19.1; HRMS (EI) calcd for $C_{30}H_{35}O_5Si$ $[M-C_4H_9]^+$ 503.2254, found 503.2258.

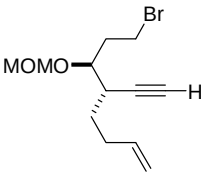
To a suspension of LAH (402 mg, 10.6 mmol) in ether (15 mL) at 0 °C was added dropwise a solution of **1aa** (5.66 g, 10.1 mmol) in ether (20 mL). After stirring for 45 min, the reaction was carefully quenched stepwise with H_2O (0.4 mL), aqueous NaOH (1 N, 0.4 mL), then H_2O (1.2 mL) at 0 °C, after which it was stirred at room temperature for 30 min. The resultant mixture was filtered through Celite, washed with ether, and concentrated under reduced pressure. The crude alcohol thus obtained was dissolved in DMSO-CH_2Cl_2 (1:1, 40 mL) and treated with Et_3N (8.18 mL, 58.7 mmol) and SO_3·pyridine complex (4.67 g, 29.4 mmol) at 0 °C. After 1 h, the reaction mixture was poured into saturated aqueous NH_4Cl (30 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 8:1) provided the aldehyde (4.00 g, 74%) as a colorless oil. R_f 0.68 (hexanes:EtOAc = 4:1).

To a solution of PPh_3 (13.5 g, 51.5 mmol) in CH_2Cl_2 (50 mL) was added CBr_4 (8.50 g, 25.7 mmol) at 0 °C. After 15 min, the aldehyde (3.90 g, 8.6 mmol) in CH_2Cl_2 (30 mL) was added dropwise at 0 °C over 5 min. The resulting mixture was stirred at 0 °C for 10 min and poured into saturated aqueous $NaHCO_3$ (50 mL). After extraction with CH_2Cl_2 (3×50 mL), the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated to give the dibromide. To a solution of the crude dibromide in THF (50 mL) was added dropwise *n*-BuLi (1.6 M in hexanes, 10.7 mL, 17.2 mmol) at –78 °C. After stirring at –78 °C for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (40 mL). After extraction with ether (2×50

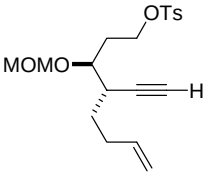
mL), the combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 8:1) provided the alkyne (2.72 g, 70%) as a colorless oil. R_f 0.61 (hexanes:EtOAc = 7:1).

The alkyne (120 mg, 0.266 mmol) in THF (7 mL) was treated with TBAF (1.0 M in THF, 0.399 mL, 0.399 mmol) at room temperature for 3 h. The resulting mixture was poured into saturated aqueous NH_4Cl (10 mL) and extracted with ether (3×15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 2:1) to give alcohol **1ab** (51.0 mg, 90%) as a pale yellow oil. R_f 0.10 (hexanes:EtOAc = 4:1); IR (film) 3419, 3298, 2947, 1641, 1034, 916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddt, *J* = 17.2, 10.4, 7.2 Hz, 1H), 5.07 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.00 (d, *J* = 9.2 Hz, 1H), 4.77 (d, *J* = 6.8 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 3.80-3.72 (m, 3H), 3.44 (s, 3H), 2.80-2.70 (m, 1H), 2.40-2.26 (m, 2H), 2.22-2.10 (m, 1H), 2.13 (d, *J* = 2.8 Hz, 1H), 2.00-1.84 (m, 2H), 1.58-1.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 115.2, 96.6, 84.0, 77.6, 71.2, 59.1, 55.9, 36.0, 33.7, 31.3, 30.0; HRMS (ESI-TOF) calcd for $C_{12}H_{20}NaO_3$ $[M+Na]^+$ 235.1310, found 235.1297.

To a solution of alcohol **1ab** (0.152 g, 0.720 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.282 g, 1.07 mmol), imidazole (0.146 g, 2.14 mmol) and I_2 (0.273 g, 1.07 mmol). After being stirred for 1 h, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (15 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes:ether = 12:1) provided iodide **1a** (0.210 g, 91%) as a colorless oil. R_f 0.61 (hexanes:EtOAc = 8:1); IR (film) 3295, 2930, 1738, 1243, 1036, 917 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.77 (ddt, *J* = 16.8, 9.9, 7.0 Hz, 1H), 5.04 (dd, *J* = 16.8, 1.5 Hz, 1H), 4.97 (d, *J* = 9.5 Hz, 1H), 4.72 (d, *J* = 7.0 Hz, 1H), 4.70 (d, *J* = 7.0 Hz, 1H), 3.58 (ddd, *J* = 9.2, 4.8, 2.6 Hz, 1H), 3.40 (s, 3H), 3.37-3.32 (m, 1H), 3.27-3.22 (m, 1H), 2.80-2.74 (m, 1H), 2.31 (td, *J* = 13.2, 5.9 Hz, 1H), 2.26-2.20 (m, 1H), 2.16-2.08 (m, 1H), 2.10 (d, *J* = 2.6 Hz, 1H), 2.07-2.00 (m, 1H), 1.54-1.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 115.5, 96.6, 83.9, 79.3, 71.3, 56.0, 35.5, 35.3, 31.4, 30.4, 2.8; HRMS (ESI-TOF) calcd for $C_{12}H_{19}INaO_2$ $[M+Na]^+$ 345.0327, found 345.0325.

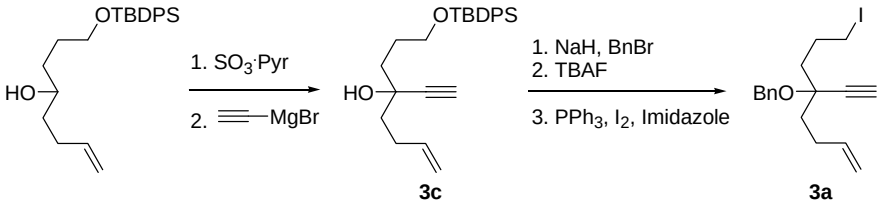


8-Bromo-5-ethynyl-6-methoxymethoxy-oct-1-ene (1b, Table 1, entry 11). To a solution of **1ab** (90.0 mg, 0.424 mmol) in CH_2Cl_2 (4 mL) at 0 °C were added pyridine (102 μL, 1.27 mmol), PPh_3 (156 mg, 0.594 mmol) and CBr_4 (211 mg, 0.636 mmol). After stirring at room temperature for 2 h, the solvent was removed and the resulting residue was purified by flash chromatography (hexanes:EtOAc = 7:1) to afford bromide **1b** (106 mg, 91%) as a colorless oil. R_f 0.64 (hexanes:EtOAc = 8:1); IR (film) 3295, 2930, 1442, 1142, 1100, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.02 (dd, *J* = 16.8, 1.5 Hz, 1H), 4.96 (d, *J* = 10.2 Hz, 1H), 4.69 (dd, *J* = 12.4, 7.2 Hz, 2H), 3.67 (ddd, *J* = 9.2, 4.8, 2.8 Hz, 1H), 3.57-3.46 (m, 2H), 3.38 (s, 3H), 2.80-2.73 (m, 1H), 2.34-2.20 (m, 2H), 2.16-1.96 (m, 3H), 1.52-1.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 115.5, 96.6, 83.9, 77.4, 71.3, 56.0, 35.7, 34.4, 31.5, 30.4, 30.2.



Toluene-4-sulfonic acid 4-ethynyl-3-methoxymethoxy-oct-7-enyl ester (1c, Table 1, entry 12). To a solution of alcohol **1ab** (100 mg, 0.471 mmol) and pyridine (1 mL) at 0 °C was added TsCl (99.0 mg, 0.518 mmol). After stirring at room temperature for 14 h, the mixture was diluted with ether (10 mL) and poured into saturated aqueous $NaHCO_3$ (10 mL) at 0 °C. After the organic phase was separated, the aqueous phase was further extracted with ether (2×15 mL). The combined organic extracts were washed with 2 N HCl (3×20 mL) and water (20 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 5:1) provided tosylate **1c** (126 mg, 73%) as a colorless oil. R_f 0.48 (hexanes:EtOAc = 4:1); IR (film) 3285, 2924, 1360, 1177, 1036, 917, 816, 664, 554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 5.74 (ddt, *J* = 17.1, 10.1, 6.8 Hz, 1H), 5.22 (dd, *J* = 18.5, 1.6 Hz, 1H), 4.97 (d, *J* = 11.3 Hz, 1H), 4.59 (d, *J* = 7.1 Hz, 1H), 4.54 (d, *J* = 7.1 Hz, 1H), 4.21-4.14 (m, 2H), 3.58-3.50 (m, 1H), 3.30 (s, 3H), 2.78-2.68 (m, 1H), 2.42 (s, 3H), 2.35-2.20 (m, 1H), 2.16-2.04 (m, 1H), 2.07 (d, *J* = 2.4 Hz, 1H), 1.99-1.88 (m, 2H), 1.48-1.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 137.3, 132.9, 129.8, 127.8, 115.4, 96.5, 83.5, 75.8, 71.4, 67.2, 55.8, 35.9, 31.4, 30.6, 30.2, 21.5; HRMS (ESI-TOF) calcd for $C_{19}H_{26}NaO_5S$ $[M+Na]^+$ 389,1399, found 389.1397.

Preparation of Iodoenyne 3a



To a solution of 1-(*tert*-butyl-diphenyl-silyloxy)-oct-7-en-4-ol[2] (2.84 g, 7.42 mmol) and Et_3N (4.14 mL, 29.7 mmol) in DMSO-CH_2Cl_2 (1:1, 20 mL) was added SO_3·pyridine complex (2.36 g, 14.9 mmol) at 0 °C. After the solution was stirred at 0 °C for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (30 mL). After extraction with CH_2Cl_2 (3×40 mL), the combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 7:1) provided the ketone (2.63 g, 93%) as a colorless oil. R_f 0.73 (hexanes:EtOAc = 4/1).

To a solution of the ketone (2.63 g, 6.91 mmol) in THF (20 mL) at 0 °C was added ethynyl magnesium bromide (0.5 M in THF, 41.4 mL, 20.7 mmol). After stirring at room temperature for 1 h, the resulting solution was poured into saturated aqueous NH_4Cl (70 mL). After extraction with ether (2×70 mL), the combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 4:1) provided tertiary alcohol **3c** (2.58 g, 92%) as a colorless oil. R_f 0.36 (hexanes:EtOAc = 8:1); IR (film) 3392, 3305, 2932, 2858, 1428, 1112, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71-7.65 (m, 4H), 7.47-7.35 (m, 6H), 5.88 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 5.08 (ddd, *J* = 17.1, 3.6, 1.6 Hz, 1H), 4.98 (ddt, *J* = 10.3, 2.0, 1.2 Hz, 1H), 3.79-3.71 (m, 2H), 2.46 (s, 1H), 2.40-2.28 (m, 2H), 1.96-1.68 (m, 6H), 1.56 (br s, 1H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 135.6, 135.6, 133.5, 133.4, 129.7, 127.7, 114.7, 86.5, 72.6, 70.5, 64.3, 41.2, 39.3, 28.7, 27.5, 26.8, 19.1; HRMS (EI) calcd for $C_{22}H_{25}O_2Si$ $[M\text{-}C_4H_9]^+$ 349.1624, found 349.1611.

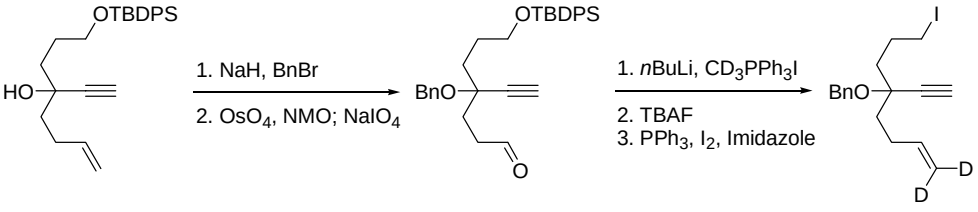
To a suspension of NaH (0.233 g, 60% dispersion in oil, 5.83 mmol) in DMF (10 mL) at 0 °C was added a solution of **3c** (1.58 g, 3.89 mmol) in DMF (5 mL). The solution was stirred for 20 min at the same temperature, and tetrabutylammonium iodide (144 mg, 0.389 mmol) and benzyl bromide (0.693 mL, 5.83 mmol) were added. After removing the cold bath, the resulting mixture was stirred for 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (30 mL) and then diluted with ether (40 mL). After extraction with ether (3×40 mL), the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated

[2] Yuasa, Y.; Ando, J.; Shibuya, S. *J. Chem. Soc. Perkin Trans. 1* **1996**, 793.

to give the benzyl ether. The crude benzyl ether in THF (30 mL) was treated with TBAF (1.0 M in THF, 5.83 mL, 5.83 mmol) at room temperature for 1 h. The reaction mixture was poured into saturated aqueous NH_4Cl (30 mL) and extracted with ether (3×30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 1:1) afforded the alcohol (0.810 g, 81%) as a colorless oil. R_f 0.22 (hexanes:EtOAc = 4:1); IR (film) 3359, 3295, 2952, 2871, 1454, 1058, 914, 736, 697, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.22 (m, 5H), 5.83 (ddt, *J* = 17.2, 10.4, 6.4 Hz, 1H), 5.04 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.96 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.62 (d, *J* = 11.2 Hz, 1H), 4.58 (d, *J* = 10.8 Hz, 1H), 3.60 (t, *J* = 6.0 Hz, 2H), 2.54 (s, 1H), 2.32-2.17 (m, 2H), 2.14 (br s, 1H), 1.88-1.79 (m, 4H), 1.79-1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.0, 128.2, 127.6, 127.4, 114.6, 83.9, 76.2, 75.0, 66.1, 62.5, 37.6, 35.0, 28.2, 27.2; HRMS (ESI-TOF) calcd for $C_{17}H_{23}O_2$ $[M+H]^+$ 259.1698, found 259.1695.

To a solution of the alcohol (0.194 g, 0.75 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.335 g, 1.28 mmol), imidazole (0.174 g, 2.55 mmol) and I_2 (0.324 g, 1.28 mmol). After being stirred for 1 h, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (15 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 15:1) provided iodide **3a** (0.230 g, 83%) as a colorless oil. R_f 0.42 (hexanes:EtOAc = 20:1); IR (film) 3290, 2949, 2863, 1453, 1060, 912, 733, 696, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.24 (m, 5H), 5.91-5.80 (m, 1H), 5.07 (d, *J* = 17.1 Hz, 1H), 4.99 (d, *J* = 10.4 Hz, 1H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.61 (d, *J* = 11.0 Hz, 1H), 3.28-3.17 (m, 2H), 2.57 (s, 1H), 2.34-2.19 (m, 2H), 2.14-1.99 (m, 2H), 1.94-1.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.0, 128.3, 127.6, 127.4, 114.7, 83.8, 75.7, 75.2, 66.2, 39.5, 37.7, 28.2, 28.2, 6.9; HRMS (ESI-TOF) calcd for $C_{17}H_{22}IO$ $[M+H]^+$ 369.0715, found 369.0708.

Preparation of Iodoenyne 3b



3c **3d** **3b**

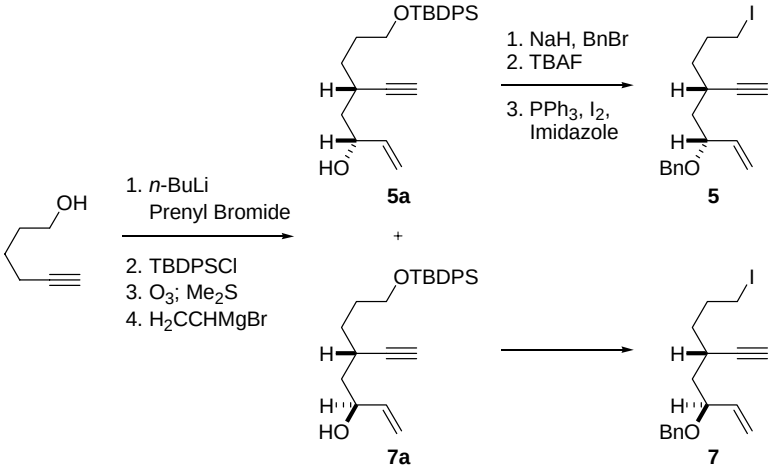
To a suspension of NaH (0.160 g, 60% dispersion in oil, 4.00 mmol) in DMF (10 mL) at 0 °C was added a DMF solution (5 mL) of **3c** (1.10 g, 2.71 mmol). The solution was stirred for 10 min at the same temperature, and benzyl bromide (0.600 mL, 5.04 mmol) was added. After removing the cold bath, the resulting mixture was stirred for 1 h. Then the reaction was quenched by

addition of saturated aqueous NH_4Cl (5 mL) and diluted with ether (10 mL). After extraction with ether (3×20 mL), the combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated to give the benzyl ether. To a CH_2Cl_2 solution (10 mL) of the crude benzyl ether were added NMO (48% aqueous solution, 1.08 mL, 5.00 mmol) and OsO_4 (4% aqueous solution, 0.12 mL, 0.019 mmol) sequentially at room temperature. The resulting solution was stirred for 3 h before the reaction was quenched by saturated aqueous Na_2SO_3 (10 mL). The organic layer was washed by water (3×20 mL), and the combined aqueous layers were extracted by CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated to afford the crude diol as a light yellow oil. To a MeOH solution (10 mL) of the above diol at 0 °C was added aqueous $NaIO_4$ (1.07 g, 5.00 mmol). This suspension was stirred at the same temperature for 30 min, and the reaction was quenched by saturated aqueous Na_2SO_3 (10 mL). The resulting mixture was diluted by CH_2Cl_2 (10 mL) and water (10 mL), and the aqueous layer was extracted by CH_2Cl_2 (4×20 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under vacuum. Purification of the residue by flash chromatography (hexanes:EtOAc = 10:1) afforded the aldehyde **3d** (0.883 g, 83% for 3 steps) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, *J* = 1.5 Hz, 1H), 7.69 (m, 4H), 7.44-7.29 (m, 11H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.55 (d, *J* = 11.3 Hz, 1H), 3.71 (m, 2H), 2.71 (m, 2H), 2.56 (s, 1H), 2.10 (m, 2H), 1.91 (m, 2H), 1.75 (m, 2H), 1.08 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 138.8, 135.8, 134.1, 129.8, 128.5, 127.9, 127.8, 127.7, 83.7, 75.9, 75.6, 66.4, 63.9, 39.5, 35.1, 31.6, 27.3, 27.1, 19.4.

To a suspension of CD_3PPh_3I (611 mg, 1.50 mmol, purchased from Aldrich, 95 atom % D) in THF (5 mL) at –78 °C, *n*–BuLi (2.5 M in hexanes, 0.60 mL, 1.50 mmol) was added. The resulting yellow solution was stirred for 10 min, and aldehyde **3d** (393 mg, 1.00 mmol) in THF (4 mL) was added. The reaction mixture was maintained at –78 °C for another 10 min before it was warmed to room temperature for 1 h. After TLC indicated the complete consumption of the starting material, the reaction was quenched by addition of acetone (1 mL) and water (5 mL) at 0 °C. After extraction with CH_2Cl_2 (3×10 mL), the combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated to give the deuterated alkene. The crude alkene in THF (5 mL) was treated with TBAF (1.0 M in THF, 2.00 mL, 2.00 mmol) at room temperature for 2 h. The solvent was removed *in vacuo*, and the residue was purified by flash chromatography (hexanes:EtOAc = 10:1 to 4:1 to 2:1) to give the alcohol (143 mg, 55% for 2 steps) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 5.87 (m, 1H), 5.06 (dd, *J* = 17.2, 1.6 Hz, 0.2 H), 4.98 (dd, *J* = 10.4, 1.6 Hz, 0.2 H), 4.66 (d, *J* = 11.0 Hz, 1H), 4.63 (d, *J* = 11.0 Hz, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 2.58 (s, 1H), 2.27 (m, 2H), 2.07 (br s, 1H), 1.89 (m, 4H), 1.80 (m, 2H).

To a solution of PPh_3 (262 mg, 1.00 mmol) in CH_2Cl_2 (4 mL) were added imidazole (85.0 mg, 1.25 mmol) and iodine (279 mg, 1.10 mmol) at room temperature. A solution of the alcohol (140 mg, 0.538 mmol) in CH_2Cl_2 (2 mL) was added to the resulting suspension via cannula. After being stirred at room temperature for 30 min, the reaction mixture was diluted by EtOAc (20 mL) and sequentially washed with saturated aqueous $Na_2S_2O_3$ (5 mL), saturated aqueous $NaHCO_3$ (15 mL), and brine (15 mL), and dried over Na_2SO_4. The solvent was removed *in vacuo*, and the residue was purified by column chromatography (petroleum ether:ether = 10:1) to afford iodide **3b** (199 mg, 100%) as a colorless oil. ^{1}H NMR spectroscopic data indicated 86% incorporation of deuterium. IR (film) 3291, 2950, 2862, 1453, 1062, 904, 733, 696, 665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.24 (m, 5H), 5.91-5.83 (m, 1H), 5.07 (d, *J* = 17.1 Hz, 0.2H), 4.99 (d, *J* = 10.1 Hz, 0.2H), 4.66 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 11.0 Hz, 1H), 3.28-3.17 (m, 2H), 2.58 (s, 1H), 2.34-2.19 (m, 2H), 2.14-2.00 (m, 2H), 1.94-1.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 137.8, 128.3, 127.6, 127.4, 83.8, 75.7, 75.2, 66.2, 39.5, 37.7, 28.1, 28.2, 6.9 (The methylene carbon, 114.7, is absent.); HRMS (ESI-TOF) calcd for $C_{17}H_{20}D_2IO$ $[M+H]^+$ 371.0839, found 371.0832.

Preparation of Iodoenyne 5



Following a reported procedure,[3] *n*-butyllithium (2.5 M in hexanes, 14 mL, 35 mmol) was added slowly over 10 min to a solution of hex-5-yn-1-ol (0.98 g, 10 mmol) in THF (50 mL) at room temperature. The resulting yellow solution was stirred at 25 °C for 10 min and then cooled to 0 °C. 1-Bromo-3-methyl-2-butene (1.3 mL, 10 mmol) was added slowly over 10 min, and the solution became greenish. The resulting mixture was stirred at room temperature for 3 h and then heated to 40 °C for 1 h. Ether (50 mL) and water (50 mL) were added, and the separated aqueous

[3] Hollingworth, G. J.; Pattenden, G.; Schulz, D. J. *Aust. J. Chem.* **1995**, *48*, 381.

phase was then extracted with ether (2×50 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 5:1) provided the alcohol (0.90 g, 54%) as a colorless oil. R_f 0.35 (hexanes:EtOAc = 1:1); IR (film) 3345, 3306, 2930, 2869, 1452, 1056, 631 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.25-5.17 (m, 1H), 3.68 (td, *J* = 6.2, 2.0 Hz, 2H), 2.41-2.32 (m, 1H), 2.19 (t, *J* = 6.5 Hz, 2H), 2.06 (d, *J* = 2.4 Hz, 1H), 1.85-1.75 (m, 1H), 1.72 (s, 3H), 1.72-1.62 (m, 1H), 1.62 (s, 3H), 1.61-1.43 (m, 2H), 1.31 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.5, 121.3, 87.6, 69.4, 62.5, 33.4, 31.7, 30.4, 25.7, 17.9; HRMS (EI) calcd for $C_{11}H_{18}O$ $[M]^+$ 166.1358, found 166.1361.

To a solution of the alcohol (1.60 g, 9.62 mmol) in DMF (20 mL) at room temperature were added imidazole (1.05 g, 15.4 mmol) and TBDPSCl (3.00 mL, 11.5 mmol). After 30 min, the mixture was quenched with saturated aqueous NH_4Cl (40 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2×40 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated to give the TBDPS ether. Through a rapidly stirred solution of the crude TBDPS ether in CH_2Cl_2 (20 mL) was bubbled ozone at –78 °C, until the reaction was complete as judged by TLC (ca. 30 min). The reaction mixture was treated with dimethyl sulfide (2.0 mL) and then allowed to warm to 20 °C over 1 h. The solution was diluted with CH_2Cl_2 (30 mL), washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 6:1) provided the aldehyde (1.83 g, 47%) as a colorless oil. R_f 0.69 (hexanes:EtOAc = 4:1); IR (film) 3291, 3071, 2932, 2858, 1727, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.75-7.69 (m, 4H), 7.48-7.39 (m, 6H), 3.75 (t, *J* = 6.1 Hz, 2H), 2.96-2.88 (m, 1H), 2.63 (ddd, *J* = 16.8, 7.9, 1.8 Hz, 1H), 2.54 (ddd, *J* = 16.8, 6.1, 1.8 Hz, 1H), 2.14 (d, *J* = 2.4 Hz, 1H), 1.88-1.79 (m, 1H), 1.78-1.64 (m, 2H), 1.64-1.56 (m, 1H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.5, 135.5, 133.8, 129.5, 127.6, 85.4, 70.6, 63.2, 48.3, 31.0, 29.8, 26.8, 25.4, 19.1; HRMS (ESI-TOF) calcd for $C_{24}H_{31}O_2Si$ $[M+H]^+$ 379.2093, found 379.2089.

To a solution of the aldehyde (4.3 g, 11 mmol) in THF (20 mL) at 0 °C was added vinyl magnesium bromide (1.0 M in THF, 23 mL, 23 mmol). After stirring at room temperature for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (30 mL). After extraction with ether (2×50 mL), the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 8:1) gave two diastereomeric alcohols (**5a**: 1.0 g, 22% and **7a**: 1.3 g, 28%) both as colorless oils. **5a**: R_f 0.45 (hexanes:EtOAc = 4:1); IR (film) 3379, 3306, 2932, 2858,

1428, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75-7.70 (m, 4H), 7.48-7.39 (m, 6H), 5.95 (ddd, *J* = 17.1, 10.4, 5.8 Hz, 1H), 5.32 (d, *J* = 17.4 Hz, 1H), 5.15 (d, *J* = 10.4 Hz, 1H), 4.47 (d, *J* = 3.4 Hz, 1H), 3.74 (t, *J* = 6.3 Hz, 2H), 2.76-2.68 (m, 1H), 2.14 (d, *J* = 2.1 Hz, 1H), 2.03 (d, *J* = 3.4 Hz, 1H), 1.90-1.80 (m, 1H), 1.78-1.69 (m, 1H), 1.69-1.54 (m, 4H), 1.10 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 135.5, 133.9, 129.5, 127.6, 114.2, 87.0, 70.7, 70.3, 63.6, 42.1, 31.5, 30.1, 27.7, 26.8, 19.2; HRMS (ESI-TOF) calcd for $C_{26}H_{35}O_2Si$ $[M+H]^+$ 407.2406, found 407.2404. **7a**: R_f 0.40 (hexanes:EtOAc = 4:1); IR (film) 3357, 3306, 2931, 2858, 1428, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74-7.69 (m, 4H), 7.48-7.39 (m, 6H), 5.87 (ddd, *J* = 17.1, 10.4, 6.7 Hz, 1H), 5.33 (d, *J* = 17.4 Hz, 1H), 5.17 (d, *J* = 10.4 Hz, 1H), 4.37 (q, *J* = 6.7 Hz, 1H), 3.73 (t, *J* = 6.0 Hz, 2H), 2.50-2.42 (m, 1H), 2.19 (s, 1H), 2.14 (d, *J* = 2.4 Hz, 1H), 1.88-1.78 (m, 2H), 1.76-1.54 (m, 4H), 1.10 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 135.5, 133.9, 129.5, 127.5, 115.5, 87.1, 71.9, 70.3, 63.5, 42.0, 31.3, 29.8, 28.1, 26.8, 19.2; HRMS (ESI-TOF) calcd for $C_{26}H_{35}O_2Si$ $[M+H]^+$ 407.2406, found 407.2414.

To a suspension of NaH (89 mg, 60% dispersion in oil, 2.2 mmol) in DMF (5 mL) at 0 °C was added a solution of **5a** (0.60 g, 1.5 mmol) in DMF (10 mL). After stirring at the same temperature for 20 min, TBAI (55 mg, 0.15 mmol) and benzyl bromide (0.26 mL, 2.2 mmol) were added. The cold bath was removed and the stirring was continued for 2 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (30 mL) and then diluted with ether (40 mL). After extraction with ether (3×30 mL), the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated to give the benzyl ether. The crude benzyl ether thus obtained was dissolved in THF (10 mL) and treated with TBAF (1.0 M in THF, 3.0 mL, 3.0 mmol) at room temperature. After 4 h, the reaction mixture was diluted with ether (20 mL), poured into saturated aqueous NH_4Cl (20 mL), and extracted with ether (3×30 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 1:1) furnished the alcohol (0.32 g, 84%) as a colorless oil. R_f 0.15 (hexanes:EtOAc = 4:1); IR (film) 3373, 3298, 2942, 2866, 1454, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H), 5.79 (ddd, *J* = 17.2, 10.4, 7.6 Hz, 1H), 5.29 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.24 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.16-4.07 (m, 1H), 3.68 (t, *J* = 6.6 Hz, 2H), 2.82-2.72 (m, 1H), 2.06 (s, 1H), 1.85-1.76 (m, 1H), 1.76-1.64 (m, 2H), 1.62-1.45 (m, 3H), 1.41-1.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.5, 128.3, 127.9, 127.5, 116.9, 86.9, 78.5, 70.8, 70.0, 62.6, 41.3, 31.3, 30.3, 27.8; HRMS (EI) calcd for $C_{17}H_{22}O_2$ $[M]^+$ 258.1620, found 258.1614.

To a solution of the alcohol (0.140 g, 0.54 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.256 g, 0.98 mmol), imidazole (0.133 g, 1.95 mmol) and I_2 (0.248 g, 0.98 mmol). After being stirred

for 1 h, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (10 mL). After extraction with ether (2×15 mL), the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 15:1) provided iodide **5** (0.159 g, 80%) as a colorless oil. R_f 0.67 (hexanes:EtOAc = 8:1); IR (film) 3297, 2941, 2862, 1454, 1109, 1068, 928, 736, 698, 638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.20 (m, 5H), 5.75 (ddd, *J* = 17.6, 10.4, 7.6 Hz, 1H), 5.27 (d, *J* = 17.6 Hz, 1H), 5.22 (d, *J* = 10.4 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.35 (d, *J* = 11.6 Hz, 1H), 4.07 (ddd, *J* = 10.4, 7.6, 2.8 Hz, 1H), 3.22-3.12 (m, 2H), 2.79-2.70 (m, 1H), 2.10-1.98 (m, 1H), 2.03 (d, *J* = 2.4 Hz, 1H), 1.98-1.86 (m, 1H), 1.67 (ddd, *J* = 13.6, 10.4, 4.4 Hz, 1H), 1.61-1.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.4, 128.3, 127.9, 127.5, 117.0, 86.4, 78.4, 70.7, 70.3, 41.2, 35.8, 31.1, 27.2, 6.5; HRMS (ESI-TOF) calcd for $C_{17}H_{22}IO$ $[M+H]^+$ 369.0715, found 369.0719.

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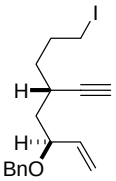

7

To a suspension of NaH (120 mg, 60% dispersion in oil, 3.0 mmol) in DMF (3 mL) at 0 °C was added a solution of the alcohol **7a** (0.80 g, 2.0 mmol) in THF (9 mL) and DMF (3 mL). After 20 min, TBAI (73 mg, 0.20 mmol) and benzyl bromide (0.35 mL, 3.0 mmol) were added. The cold bath was removed, and the solution was stirred for 12 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (30 mL) and then diluted with ether (40 mL). After extraction with ether (3×40 mL), the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 8:1) to give the benzyl ether (0.88 g, 90%) as a colorless oil.

The benzyl ether (0.88 g, 1.8 mmol) dissolved in THF (10 mL) was treated with TBAF (1.0 M in THF, 2.7 mL, 2.7 mmol) at room temperature. After 2 h, the reaction mixture was diluted with ether (20 mL) and quenched with saturated aqueous NH_4Cl (20 mL). After the organic layer was separated, the aqueous phase was further extracted with ether (3×30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 1:1) gave the alcohol (0.40 g, 89%) as a colorless oil. R_f 0.11 (hexanes:EtOAc = 4:1); IR (film) 3381, 3300, 2943, 2867, 1454, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H), 5.68 (ddd, *J* = 17.2, 10.0, 8.4 Hz, 1H), 5.28 (dd, *J* = 17.2, 1.6 Hz,

1H), 5.26 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 3.96 (dd, *J* = 14.4, 7.6 Hz, 1H), 3.56 (t, *J* = 6.4 Hz,, 2H), 2.44-2.36 (m, 1H), 2.03 (d, *J* = 2.4 Hz, 1H), 1.92 (dd, *J* = 13.2, 6.4 Hz, 1H), 1.90 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.78-1.68 (m, 1H), 1.62-1.52 (m, 2H), 1.52-1.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.1, 128.3, 127.8, 127.4, 118.3, 87.0, 78.6, 70.0, 69.8, 62.4, 40.2, 30.7, 30.1, 27.5; HRMS (EI) calcd for $C_{17}H_{22}O_2$ $[M]^+$ 258.1620, found 258.1617.

To a solution of the alcohol (0.150 g, 0.58 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.274 g, 1.05 mmol), imidazole (0.142 g, 2.09 mmol) and I_2 (0.265 g, 1.05 mmol). After being stirred for 1 h, the resulting mixture was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (10 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 15:1) provided iodide **7** (0.180 g, 84%) as a colorless oil. R_f 0.64 (hexanes:EtOAc = 8:1); IR (film) 3297, 2923, 2857, 1454, 1092, 1069, 930, 736, 698, 639 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H), 5.70 (ddd, *J* = 17.6, 10.4, 8.0 Hz, 1H), 5.29 (d, *J* = 17.6 Hz, 1H), 5.28 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.34 (d, *J* = 12.0 Hz, 1H), 3.95 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.20-3.08 (m, 2H), 2.52-2.39 (m, 1H), 2.10-1.81 (m, 3H), 2.04 (d, *J* = 2.4 Hz, 1H), 1.64-1.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.1, 128.3, 127.8, 127.5, 118.4, 86.6, 78.5, 70.1, 69.7, 40.2, 35.2, 31.0, 26.9, 6.4; HRMS (ESI-TOF) calcd for $C_{17}H_{22}IO$ $[M+H]^+$ 369.0715, found 369.0714.

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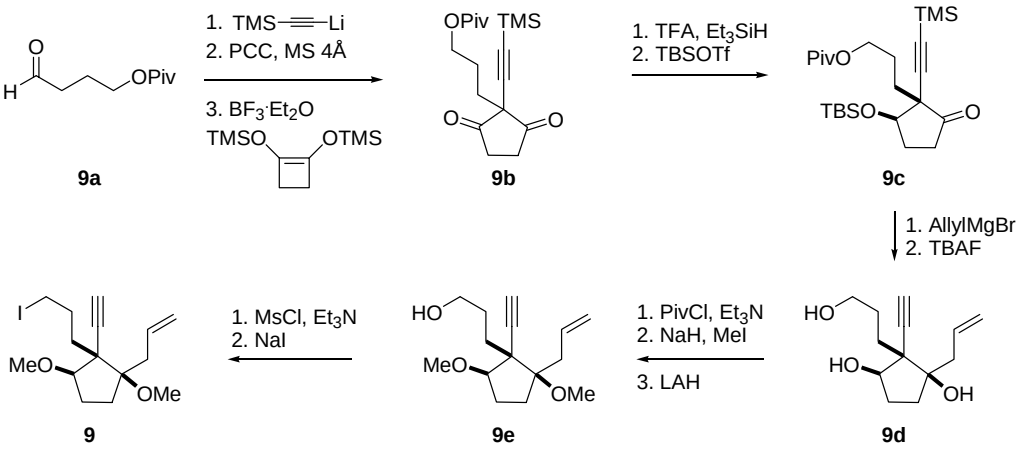


To a solution of trimethylsilylacetylene (2.10 mL, 15.0 mmol) in THF (20 mL) was added *n*-BuLi (2.5 M in hexanes, 6.00 mL, 15.0 mmol) at –78 °C. The mixture was stirred at –78 °C for

10 min followed by addition of a THF (10 mL) solution of aldehyde **9a**[4] (2.58 g, 15.0 mmol). After being allowed to warm to 0 °C over 1 h, the reaction was quenched with saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (2×30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to afford the crude alcohol as a colorless oil.

To a solution of the above alcohol (811 mg, 3.00 mmol) in CH_2Cl_2 (20 mL) was added a ground mixture of PCC (1.29 g, 6.00 mmol) and MS 4Å (1.0 g) at 0 °C. The resulting dark brown suspension was stirred at room temperature for 5 h, and the solids were removed by filtering through a silica gel pad. The filtrate was concentrated and purified by column chromatography (hexanes:EtOAc = 10:1) to afford the alkynone (800 mg, 99%) as a colorless oil.

Following a reported procedure,[5] the alkynone obtained above (805 mg, 3.00 mmol) was reacted with 1,2-bis(trimethylsilyloxy)cyclobutene (1.04 g, 4.50 mmol) in CH_2Cl_2 (30 mL) in the presence of $BF_3{\cdot}OEt_2$ (0.600 mL, 4.50 mmol) at –78 °C. Then the reaction mixture was warmed to room temperature, H_2O (1.00 mL, 5.56 mmol) and $BF_3{\cdot}OEt_2$ (4.00 mL, 31.6 mmol) were added. This mixture was stirred for another 1.5 h before filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 10:1 to 4:1) to afford **9b** (530 mg, 53%) as a white solid. IR (film) 2963, 2175, 1730, 1449, 1284, 1251 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.05 (t, J = 6.1 Hz, 2H), 3.06 (dd, J = 19.0, 6.8 Hz, 2H), 2.74 (dd, J = 18.6, 6.4 Hz, 2H), 1.85 (m, 2H), 1.78 (m, 2H), 1.20 (s, 9H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.4, 178.6, 97.4, 92.8, 63.8, 56.4, 39.0, 35.2, 30.0, 27.4, 24.1, -0.1; HRMS (ESI-TOF) calcd for $C_{18}H_{29}O_4Si$ $[M+H]^+$ 337.1835, found 337.1825.

Triethylsilane (0.270 mL, 1.74 mmol) was added to a solution of **9b** in TFA (12 mL) at –10 ºC.[5] After being stirred at this temperature for 10 h, the reaction mixture was poured into cold saturated aqueous $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Purification by column chromatography (hexanes:EtOAc = 10:1 to 4:1) afforded the alcohol (503 mg, 94%) as a colorless oil.

To a mixture of the alcohol obtained above (500 mg, 1.48 mmol) and Et_3N (0.230 mL, 1.64 mmol) in THF (10 mL) was added TBSOTf (0.390 mL, 1.64 mmol) at 0 ºC. The resulting solution was stirred at 0 °C for 30 min, poured into saturated aqueous $NaHCO_3$ (30 mL), and extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were dried over $MgSO_4$, filtered,

[4] Camara, F.; Angarita, J.; Mootoo, D. R. *J. Org. Chem.* **2005,** *70*, 6870.
[5] Thornton, P. D.; Burnell, D. J. *Org. Lett.* **2006,** *8*, 3195.

and concentrated. Purification by column chromatography (hexanes:EtOAc = 25:1 to 10:1) afforded **9c** (605 mg, 90%) as a colorless oil. IR (film) 2957, 2931, 2859, 1756, 1730, 1285 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.34 (dd, *J* = 3.6, 2.2 Hz, 1H), 4.11 (m, 1H), 4.05 (m, 1H), 2.41 (m, 3H), 1.94 (m, 2H), 1.70 (m, 3H), 1.20 (s, 9H), 0.86 (s, 9H), 0.14 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.7, 178.8, 103.0, 91.1, 77.1, 64.8, 55.6, 38.9, 33.5, 29.0, 27.4, 26.0, 25.9, 24.4, 18.2, 0.1, -4.3, -4.7; HRMS (ESI-TOF) calcd for $C_{24}H_{45}O_4Si_2$ $[M+H]^+$ 453.2851, found 453.2851.

To a solution of **9c** (335 mg, 0.740 mmol) in THF (10 mL) was added dropwise allyl magnesium bromide (1.0 M in ether, 5.00 mL, 5.00 mmol) at –78 °C. The resulting mixture was stirred at –78 °C for 2 h and then at 0 °C for 2 h, followed by addition of saturated aqueous NH_4Cl (10 mL) and extraction with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford the diol as a colorless oil.

To a solution of the crude diol in THF (4 mL) was added TBAF (1.0 M in THF, 4.00 mL, 4.00 mmol) at 0 ºC. The mixture was then warmed to room temperature, stirred for 2 h and concentrated. Purification by column chromatography (hexanes:EtOAc = 2:1 to 1:1 to 1:2) afforded **9d** (153 mg, 92% for 2 steps) as a colorless oil. IR (film) 3299, 2943, 2874, 1431, 1036, 1007 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.94 (m, 1H), 5.14 (m, 2H), 4.79 (d, *J* = 6.1 Hz, 1H), 4.25 (br s, 1H), 4.04 (s, 1H), 3.93 (br s, 1H), 3.83 (dt, *J* = 11.0, 4.6 Hz, 1H), 3.59 (td, *J* = 9.8, 3.7 Hz, 1H), 2.57 (dd, *J* = 14.1, 7.4 Hz, 1H), 2.38 (dd, *J* = 14.4, 7.4 Hz, 1H), 2.34 (m, 1H), 2.20 (s, 1H), 2.10 (m, 2H), 1.90 (m, 2H), 1.81 (m, 1H), 1.71 (m, 1H), 1.44 (ddd, *J* = 13.1, 11.9, 5.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 118.4, 86.0, 85.8, 79.5, 73.6, 62.8, 53.9, 40.9, 36.0, 30.9, 28.5, 24.4; HRMS (ESI-TOF) calcd for $C_{13}H_{20}O_3Na$ $[M+Na]^+$ 247.1305, found 247.1300.

To a mixture of alcohol **9d** (365 mg, 1.65 mmol) and Et_3N (0.280 mL, 2.00 mmol) in CH_2Cl_2 (10 mL) was added trimethylacetyl chloride (0.220 mL, 1.80 mmol) at 0 °C. The resulting solution was stirred at room temperature for 3 h and then was quenched by addition of saturated aqueous $NaHCO_3$ (15 mL). The aqueous layer was extracted with CH_2Cl_2 (3×15 mL), and the combined organic layers were dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (hexanes:EtOAc = 4:1) to afford the diol (305 mg, 60%) as a colorless oil.

To a solution of the above diol (99.0 mg, 0.320 mmol) in THF (5 mL) was added NaH (60% dispersion in mineral oil, 40.0 mg, 1.00 mmol) at 0 ºC. The resulting suspension was stirred at this temperature for 10 min, after which methyl iodide (0.120 mL, 2.00 mmol) was added. After

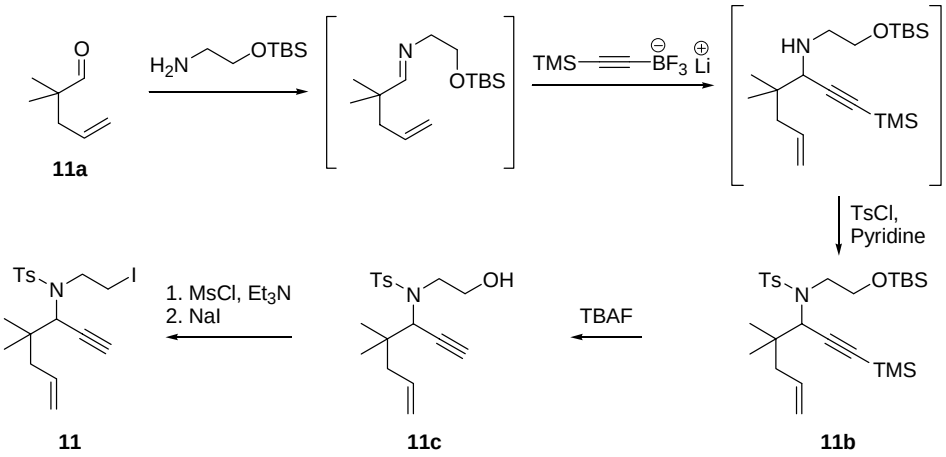
being stirred for another 2 h, the reaction was quenched by addition of saturated aqueous NH_4Cl (5 mL). After extraction with CH_2Cl_2 (3×10 mL), the combined organic layers were dried over $MgSO_4$ and concentrated to afford the dimethyl ether as a colorless oil.

To a solution of the above crude dimethyl ether in ether (5 mL) was added LAH (38.0 mg, 1.00 mmol) at 0 ºC. After stirring the resulting suspension at this temperature for 30 min, the reaction was quenched by addition of 1 N NaOH (1 mL) followed by addition of anhydrous $MgSO_4$. After vigorous stirring for 15 min, the solid was removed by filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 4:1 to 2:1) to afford **9e** (80 mg, 99% for 2 steps) as a colorless oil. IR (film) 3424, 3301, 2940, 1453, 1079, 913 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.89 (m, 1H), 5.10 (m, 2H), 3.81 (dd, *J* = 7.6, 4.9 Hz, 1H), 3.65 (dd, *J* = 9.2, 6.4 Hz, 2H), 3.32 (s, 3H), 3.27 (s, 3H), 2.85 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.44 (dd, *J* = 14.0, 6.7 Hz, 1H), 2.31 (s, 1H), 2.07 (m, 1H), 1.92 (m, 3H), 1.80 (m, 2H), 1.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 117.6, 88.9, 87.8, 87.0, 73.8, 63.6, 57.9, 53.2, 50.9, 38.1, 30.9, 29.6, 27.5, 24.3; HRMS (EI) calcd for $C_{15}H_{24}O_3$ $[M]^+$ 252.1725, found 252.1713.

To a mixture of alcohol **9e** (80.0 mg, 0.320 mmol) and Et_3N (0.140 mL, 1.00 mmol) in CH_2Cl_2 (5 mL) was added MsCl (70.0 μL, 1.00 mmol) at –30 °C. The resulting solution was stirred at –30 °C for 10 min and quenched by addition of saturated aqueous $NaHCO_3$ (10 mL). After extraction with CH_2Cl_2 (3×5 mL), the combined organic layers were dried over $MgSO_4$ and concentrated to afford the crude mesylate as a colorless oil.

To a solution of the above crude mesylate in acetone (5 mL) was added NaI (150 mg, 1.00 mmol) at room temperature. The reaction mixture was stirred for 12 h, and acetone was evaporated. The resulting yellow solid was dissolved in water (10 mL) and extracted with EtOAc (2×10 mL). The combined organic layers were washed with saturated aqueous $Na_2S_2O_3$ (15 mL) and brine (15 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 15:1 to 10:1) afforded **9** (115 mg, 88%) as a colorless oil. IR (film) 3291, 2936, 1456, 1176, 1080, 914 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.89 (m, 1H), 5.12 (m, 2H), 3.77 (dd, *J* = 7.6, 5.2 Hz, 1H), 3.33 (s, 3H), 3.29 (s, 3H), 3.25 (m, 1H), 3.18 (m, 1H), 2.85 (dd, *J* = 15.3, 7.0 Hz, 1H), 2.44 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.33 (s, 1H), 2.17 (m, 1H), 2.07 (m, 2H), 1.93 (ddd, *J* = 14.4, 10.4, 4.6 Hz, 1H), 1.80 (m, 2H), 1.64 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 117.7, 88.8, 87.6, 86.9, 74.0, 58.0, 52.8, 50.9, 38.1, 30.9, 30.9, 29.9, 27.5, 8.0; HRMS (ESI-TOF) calcd for $C_{15}H_{23}IO_2Na$ $[M+Na]^+$ 385.0635, found 385.0635.

Preparation of Iodoenyne 11



To a solution of aldehyde **11a**[6] (560 mg, 5.00 mmol) and *tert*-butyldimethylsilyl oxyethylamine[7] (912 mg, 5.20 mmol) in CH_2Cl_2 (10 mL) was added $MgSO_4$ (3.0 g) at room temperature. The resulting suspension was stirred at room temperature for 12 h and then the solid was removed by filtering through a sintered glass funnel. The filtrate was concentrated and the crude light yellow imine was used immediately for the next step.

Following a reported procedure,[8] *n*-BuLi (2.5 M in hexanes, 4.00 mL, 10.0 mmol) was added to a solution of trimethylsilylacetylene (1.40 mL, 10.0 mmol) in THF (10 mL) at –78 °C. After being stirred for 30 min, $BF_3{\cdot}OEt_2$ (1.27 mL, 10.0 mmol) was added and the resulting solution was stirred for another 10 min. Then a solution of the above imine in THF (5 mL) was added to the reaction mixture and stirred at –78 °C for 1 h. After being stirred at room temperature for another 1 h, the reaction was quenched by addition of 1 N NaOH (10 mL) and extracted with ether (3×15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated to afford the amine as a pale yellow oil.

To a pyridine solution of the amine obtained above (half weight of the crude product) were added DMAP (24.2 mg 0.200 mmol) and TsCl (381 mg, 2.00 mmol) at room temperature. This solution was heated to 40 °C for 4 h and diluted by EtOAc (50 mL). The organic layer was washed with 2 N HCl (3×30 mL), saturated aqueous $NaHCO_3$ (2×30 mL) and brine (30 mL), dried over Na_2SO_4, and concentrated. Purification by column chromatography (hexanes:EtOAc = 10:1 to 6:1) afforded **11b** (522 mg, 40% for 3 steps) as a colorless oil. IR (film) 2958, 2930, 2858, 1471, 1347, 1257 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 7.9 Hz,

[6] Yang, J.; Long, Y. O.; Paquette, L. A. *J. Am. Chem. Soc.* **2003,** *125*, 1567.
[7] Parsons, A. F.; Pettifer, R. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 651.
[8] Wada, M.; Sakurai, Y.; Akiba, K. *Tetrahedron Lett.* **1984,** *25*, 1083.

2H), 5.87 (m, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 5.08 (d, *J* =17.0 Hz, 1H), 4.41 (s, 1H), 4.14 (m, 1H), 3.91 (m, 1H), 3.09 (ddd, *J* = 15.3, 10.1, 5.8 Hz, 1H), 2.96 (ddd, *J* = 15.0, 7.7, 5.2 Hz, 1H), 2.43 (s, 3H), 2.22 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.09 (dd, *J* = 13.4, 6.7 Hz, 1H), 1.04 (s, 3H), 1.00 (s, 3H), 0.91 (s, 9H), 0.10 (s, 6H), -0.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 134.6, 134.4, 129.6, 128.4, 118.2, 100.0, 92.5, 63.4, 61.2, 49.1, 44.4, 39.2, 26.2, 24.2, 23.1, 21.7, 18.5, -0.2, -5.0, -5.0; HRMS (ESI-TOF) calcd for $C_{27}H_{48}NO_3SSi_2$ $[M+H]^+$ 522.2888, found 522.2890.

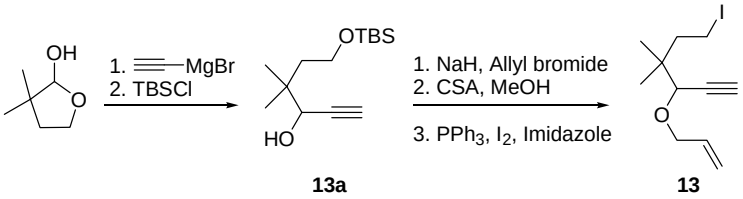
To a solution of **11b** (530 mg 1.02 mmol) in THF (4 mL) was added TBAF (1.0 M in THF, 4.00 mL, 4.00 mmol) at 0 ºC. The resulting mixture was warmed to room temperature and stirred for 2 h. After evaporation of the solvent, the residue was purified by flash chromatography (hexanes:EtOAc = 2:1 to 1:1) to afford **11c** (339 mg, 99%) as a colorless oil. IR (film) 3445, 3295, 2973, 1340, 1162, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.86 (m, 1H), 5.14 (d, *J* = 12.3 Hz, 1H), 5.11 (d, *J* =16.4 Hz, 1H), 4.57 (d, *J* = 2.4 Hz, 1H), 4.01 (m, 1H), 3.90 (m, 1H), 3.36 (ddd, *J* = 16.9, 6.5, 5.5 Hz, 1H), 3.03 (ddd, *J* = 15.8, 6.4, 4.5 Hz, 1H), 2.94 (br s, 1H), 2.44 (s, 3H), 2.24 (dd, *J* = 13.4, 7.9 Hz, 1H), 2.14 (d, *J* = 2.5 Hz, 1H), 2.11 (dd, *J* = 13.8, 7.1 Hz, 1H), 1.06 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 134.2, 134.1, 129.8, 128.3, 118.6, 78.1, 76.1, 62.9, 60.8, 50.0, 44.3, 39.4, 24.2, 23.2, 21.8; HRMS (ESI-TOF) calcd for $C_{18}H_{25}NO_3SNa$ $[M+Na]^+$ 358.1447, found 358.1456.

To a solution of alcohol **11c** (100 mg, 0.300 mmol) and Et_3N (0.140 mL, 1.00 mmol) in CH_2Cl_2 (5 mL) was added MsCl (70.0 μL, 1.00 mmol) at –30 °C. The resulting solution was stirred at –30 °C for 10 min and quenched by addition of saturated aqueous $NaHCO_3$ (10 mL). After extraction with CH_2Cl_2 (3×10 mL), the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford the mesylate as a colorless oil.

To a solution of the above crude mesylate in acetone (10 mL) was added NaI (150 mg, 1.00 mmol) at room temperature. The reaction mixture was heated to 50 °C and stirred for 36 h, then acetone was evaporated under reduced pressure. The resulting yellow solid was dissolved in water (10 mL) and extracted with EtOAc (2×10 mL). The combined organic layers were sequentially washed with saturated aqueous $Na_2S_2O_3$ (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 15:1 to 10:1) afforded iodide **11** (125 mg, 94%) as a colorless oil. IR (film) 3292, 2974, 1344, 1160, 1107, 1089 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 5.87 (m, 1H), 5.13 (m, 2H), 4.46 (d, *J* = 2.4 Hz, 1H), 3.77 (m, 1H), 3.32 (m, 3H), 2.45 (s, 3H), 2.24 (dd, *J* =13.7, 8.2 Hz, 1H), 2.11 (d, *J* = 2.4 Hz, 1H), 2.09 (dd, *J* = 13.7, 6.7 Hz, 1H), 1.05 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 134.4, 134.0, 129.9, 128.3,

118.8, 78.0, 76.1, 60.3, 50.4, 44.3, 39.0, 24.0, 23.1, 21.8, 3.9; HRMS (EI) calcd for $C_{17}H_{21}O_2NSI$ $[M\text{-}CH_3]^+$ 430.0332, found 430.0324.

Preparation of Iodoenyne 13



13a **13**

To a solution of 2,2-dimethyl-4-butanal[9] (3.93 g, 33.8 mmol) in THF (50 mL) at 0 °C was added ethynyl magnesium bromide (0.5 M in THF, 135 mL, 67.7 mmol). After stirring at room temperature for 30 min, the resulting solution was poured into saturated aqueous NH_4Cl (100 mL). After extraction with ether (2×100 mL), the combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 1:1) provided the diol (4.73 g, 98%) as a colorless oil. R_f 0.30 (hexanes:EtOAc = 1:1).

To a solution of the diol (4.73 g, 33.3 mmol) in CH_2Cl_2 (50 mL) at room temperature were added imidazole (2.94 g, 43.2 mmol) and TBSCl (5.51 g, 36.6 mmol). After being stirred for 1 h, the mixture was poured into saturated aqueous NH_4Cl (50 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×30 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 8:1) provided **13a** (7.69 g, 90%) as a colorless oil. R_f 0.79 (hexanes:EtOAc = 1:1); IR (film) 3376, 3312, 1471, 1256, 1089, 837 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (d, *J* = 7.9 Hz, 1H), 4.05 (dd, *J* = 7.9, 2.2 Hz, 1H), 3.71 (t, *J* = 5.6 Hz, 2H), 2.40 (dd, *J* = 2.2, 1.6 Hz, 1H), 1.98-1.86 (m, 1H), 1.38 (dt, *J* = 15.1, 4.2 Hz, 1H), 1.03 (s, 6H), 0.91 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 83.8, 73.2, 69.9, 59.7, 41.1, 38.1, 25.8, 25.2, 23.8, 18.2, -5.5, -5.6; HRMS (EI) calcd for $C_{10}H_{19}O_2Si$ $[M\text{-}C_4H_9]^+$ 199.1154, found 199.1150.

To a suspension of NaH (281 mg, 60% dispersion in oil, 7.02 mmol) in THF (10 mL) at 0 °C was added a solution of **13a** (1.50 g, 5.85 mmol) in THF (5 mL). The mixture was stirred at the same temperature for 20 min, and then allyl bromide (0.658 mL, 7.60 mmol) was added. The cold bath was removed, and the solution was stirred for 3 h. The reaction was quenched by addition of

[9] Johnston, D.; McCusker, C. F.; Muir, K.; Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 681.

saturated aqueous NH_4Cl (15 mL) and diluted with ether (10 mL). The organic layer was separated, and the aqueous layer was further extracted with ether (2×15 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc = 10:1) provided the allyl ether (1.50 g, 87%) as a colorless oil. R_f 0.70 (hexanes:EtOAc = 8:1).

Camphorsulfonic acid (118 mg, 0.505 mmol) was added to a solution of the allyl ether (1.50 g, 5.05 mmol) in MeOH (15 mL) at room temperature. After 1 h, Et_3N (2 mL) was added and the solvent was evaporated to give a residue. Purification by flash chromatography (hexanes:EtOAc = 3:1) afforded the primary alcohol (845 mg, 92%) as a colorless oil. R_f 0.08 (hexanes:EtOAc = 8:1); IR (film) 3373, 3294, 2966, 2869, 1724, 1464, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85-5.72 (m, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 4.24-4.16 (m, 1H), 3.83 (dd, *J* = 12.8, 6.4 Hz, 1H), 3.67 (d, *J* = 3.2 Hz, 1H), 3.62-3.50 (m, 2H), 2.87 (br s, 1H), 2.37 (d, *J* = 3.2 Hz, 1H), 1.77-1.64 (m, 1H), 1.54-1.44 (m, 1H), 0.93 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 117.4, 80.7, 76.7, 75.1, 70.0, 58.8, 41.0, 37.2, 24.3, 23.7; HRMS (EI) calcd for $C_{11}H_{17}O_2$ $[M-H]^+$ 181.1229, found 181.1228.

To a solution of the alcohol (0.140 g, 0.77 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.302 g, 1.15 mmol), imidazole (0.157 g, 2.30 mmol) and I_2 (0.292 g, 1.15 mmol). After stirring for 40 min, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (15 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:dichloromethane = 20:1) provided the iodide **13** (0.180 g, 80%) as a colorless oil. R_f 0.50 (hexanes:EtOAc = 20:1); IR (film) 3295, 2964, 2869, 1471, 1074, 928, 631 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.94-5.86 (m, 1H), 5.32 (d, *J* = 17.4 Hz, 1H), 5.22 (d, *J* = 10.4 Hz, 1H), 4.30 (dd, *J* = 12.8, 4.0 Hz, 1H), 3.93 (dd, *J* = 12.8, 6.4 Hz, 1H), 3.75 (s, 1H), 3.22 (t, *J* = 8.9 Hz, 2H), 2.47 (s, 1H), 2.22-2.13 (m, 1H), 2.13-2.05 (m, 1H), 1.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 117.4, 80.8, 75.9, 75.2, 70.0, 44.0, 40.5, 23.0, 22.9, 1.1; HRMS (EI) calcd for $C_{10}H_{14}IO$ $[M-CH_3]^+$ 277.0089, found 277.0084.

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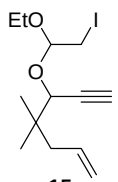
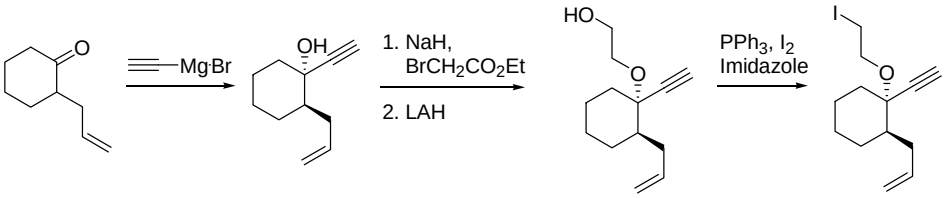


15

Following a reported procedure,[10] a mixture of 4,4-dimethyl-hept-6-en-1-yn-3-ol[11] (140 mg, 1.01 mmol) and ethyl vinyl ether (97.4 μL, 1.01 mmol) in CH_2Cl_2 (5 mL) was added to a suspension of *N*-iodosuccinimide (341 mg, 1.52 mmol) in CH_2Cl_2 (5 mL) at 0 °C over 5 min. After stirring at room temperature for 2 h, water (5 mL) was added, and the stirring was continued for an additional 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2×15 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:ether = 10:1) provided the iodide **15** (0.271 g, 80%) as a colorless oil. R_f 0.80 (hexanes:EtOAc = 8:1); IR (film) 3301, 2976, 2931, 2876, 1639, 1114, 1040, 1019, 917, 631 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90-5.78 (m, 1H), 5.14-5.05 (m, 2H), 4.88 (t, *J* = 5.2 Hz, 0.5H), 4.81 (dd, *J* = 6.5, 4.0 Hz, 0.5H), 4.11 (d, *J* = 1.8 Hz, 0.5H), 3.89 (d, *J* = 1.8 Hz, 0.5H), 3.88-3.80 (m, 0.5H), 3.73-3.60 (m, 1.5H), 3.34-3.20 (m, 2H), 2.49 (s, 1H), 2.24-2.16 (m, 2H), 1.30-1.22 (m, 3H), 1.06-0.98 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.6, 134.5, 117.9, 117.7, 101.2, 99.2, 81.5, 80.6, 75.6, 75.1, 74.3, 73.4, 62.9, 62.4, 42.7, 38.5, 38.1, 23.0, 22.7, 15.3, 14.9, 6.0, 5.4; HRMS (ESI-TOF) calcd for $C_{13}H_{21}INaO_2$ $[M+Na]^+$ 359.0484, found 359.0488.

Preparation of Iodoenyne 17



17a **17b** **17c** **17**

To a solution of ketone **17a**[12] (1.38 g, 10.0 mmol) in THF (10 mL) was added ethynyl magnesium bromide (0.5 M in THF, 40.0 mL, 20.0 mmol) at –78 °C. After being allowed to warm to 0 °C over 2 h, the reaction was quenched with saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (3×50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (hexanes:ether = 30:1 to 15:1 to 10:1) afforded alcohol **17b** (722 mg, 44%) and its diastereomer (690 mg, 42%) both as colorless oils (the stereochemistry was assigned based on the spectroscopic comparison with a prenyl analogue)[13]. IR (film) 3407, 3305, 2934, 2858, 1447, 1058 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.85 (m, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), 2.61 (m, 1H), 2.51 (s, 1H),

[10] Yanada, R.; Koh, Y.; Nishimori, N.; Matsumura, A.; Obika, S.; Mitsuya, H.; Fujii, N.; Takemoto, Y. *J. Org. Chem.* **2004**, *69*, 2417.
[11] Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255.
[12] Ihara, M.; Taniguchi, T.; Makita, K.; Takano, M.; Ohnishi, M.; Taniguchi, N.; Fukumoto, K.; Kabuto, C. *J. Am. Chem. Soc.* **1993,** *115*, 8107.
[13] Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002,** *124*, 5025.

2.49 (s, 1H), 1.98 (m, 2H), 1.68 (m, 3H), 1.52 (m, 3H), 1.16 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 116.5, 85.2, 74.5, 73.1, 47.5, 41.0, 36.0, 29.5, 25.5, 24.0; HRMS (EI) calcd for $C_{11}H_{15}O$ $[M-H]^+$ 163.1123, found 163.1130.

To a solution of alcohol **17b** (328 mg, 2.00 mmol) in DMF (5 mL) was added NaH (135 mg, 60% dispersion in mineral oil, 3.38 mmol) at 0 °C. The suspension was stirred for 20 min, and TBAI (83.0 mg, 0.225 mmol) and ethyl bromoacetate (0.750 mL, 6.76 mmol) were added. The cold bath was removed, and the reaction mixture was stirred for 8 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (10 mL) and diluted with ether (20 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford the crude ester as a light yellow oil.

To a solution of the above ester in ether (10 mL) was added LAH (152 mg, 4.00 mmol) at 0 ºC. After stirring the resulting suspension at this temperature for 30 min, the reaction was quenched by addition of 1 N NaOH solution (4.0 mL) followed by addition of anhydrous $MgSO_4$. After vigorous stirring for 15 min, the solid was removed by filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 4:1) to afford **17c** (140 mg, 30% for 2 steps, 67% brsm) as a colorless oil. IR (film) 3412, 3304, 2933, 2560, 1446, 1095 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.01 (m, 2H), 3.78 (ddd, *J* = 9.5, 4.9, 3.0 Hz, 1H), 3.74 (m, 2H), 3.64 (ddd, *J* = 8.8, 5.2, 3.0 Hz, 1H), 2.66 (m, 1H), 2.53 (s, 1H), 2.18 (dtd, *J* = 12.2, 5.8, 1.2 Hz, 1H), 2.00 (t, *J* = 6.1 Hz, 1H), 1.91 (dt, *J* = 14.1, 9.5 Hz, 1H), 1.78 (m, 1H), 1.73 (m, 1H), 1.67 (m, 1H), 1.55 (m, 2H), 1.35 (td, *J* = 12.5, 3.7 Hz, 1H), 1.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 115.6, 82.5, 78.2, 76.6, 64.5, 62.5, 46.5, 36.8, 35.5, 28.8, 25.3, 23.6; HRMS (EI) calcd for $C_{13}H_{19}O_2$ $[M-H]^+$ 207.1385, found 207.1381.

To a solution of PPh_3 (262 mg, 1.00 mmol) in CH_2Cl_2 (2.0 mL) were added imidazole (85.0 mg, 1.25 mmol) and iodine (279 mg, 1.10 mmol) at room temperature. A solution of alcohol **17e** (140 mg, 0.672 mmol) in CH_2Cl_2 (5 mL) was added to the resulting suspension via cannula. After being stirred for 30 min, the resulting solution was diluted by EtOAc (20 mL) and sequentially washed with saturated aqueous $Na_2S_2O_3$ (5 mL), saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL), and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by column chromatography (petroleum ether:ether = 20:1 to 15:1) to afford iodide **17** (185 mg, 86%) as a colorless oil. IR (film) 3297, 2933, 2857, 1445, 1101, 1069 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (m, 1H), 5.01 (m, 2H), 3.91 (ddd, *J* = 14.0, 7.3, 6.4 Hz, 1H), 3.79 (ddd, *J* = 13.7, 7.3, 6.4 Hz, 1H), 3.26 (m, 2H), 2.74 (m, 1H), 2.53 (s, 1H), 2.13 (m, 1H), 1.87 (m, 1H), 1.80 (m,

1H), 1.71 (m, 1H), 1.65 (m, 1H), 1.51 (m, 2H), 1.37 (td, *J* = 12.8, 3.7 Hz, 1H), 1.94 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 115.9, 82.4, 78.3, 76.7, 64.7, 46.5, 37.2, 35.1, 28.5, 25.2, 23.6, 4.5; HRMS (EI) calcd for $C_{13}H_{19}IO$ $[M]^+$ 318.0481, found 318.0478.

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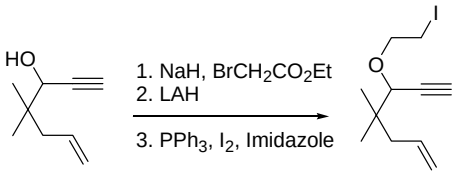

19

To a suspension of NaH (217 mg, 60% dispersion in oil, 5.43 mmol) in THF (3 mL) at 0 °C was added a solution of 4,4-dimethyl-hept-6-en-1-yn-3-ol[11] (500 mg, 3.62 mmol) in THF (9 mL) and DMF (3 mL). The solution was stirred at the same temperature for 20 min, and TBAI (134 mg, 0.362 mmol) and ethyl bromoacetate (1.20 mL, 10.9 mmol) were added. After removing the cold bath, the resulting mixture was stirred for 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (10 mL) and then diluted with ether (10 mL). After extraction with ether (2×20 mL), the combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated to give the crude ester. To a suspension of LAH (434 mg, 10.9 mmol) in ether (5 mL) at 0 °C was added dropwise a solution of the crude ester in ether (10 mL). After stirring at 0 °C for 1 h, the reaction was carefully quenched stepwise with H_2O (0.43 mL), aqueous NaOH (1 N, 0.43 mL), then H_2O (1.29 mL) at 0 °C, after which it was stirred at room temperature for 30 min. The reaction mixture was filtered through Celite, washed with ether, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 5:1) to give the alcohol (440 mg, 67%) as a colorless oil. R_f 0.26 (hexanes:EtOAc = 4:1); IR (film) 3400, 3305, 2964, 2873, 1640, 1110, 916 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82-5.72 (m, 1H), 5.02 (d, *J* = 11.3 Hz, 1H), 5.01 (d, *J* = 16.2 Hz, 1H), 3.85-3.79 (m, 1H), 3.76-3.65 (m, 3H), 3.45-3.38 (m, 1H), 2.42 (d, *J* = 0.6 Hz, 1H), 2.31 (br s, 1H), 2.14 (dd, *J* = 13.1, 7.6 Hz, 1H), 2.08 (dd, *J* = 13.1, 7.6 Hz, 1H), 0.96 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.6, 117.5, 81.2, 77.3, 74.9, 70.7, 61.6, 42.8, 38.2, 23.0, 22.6.

To a solution of the alcohol (0.231 g, 1.27 mmol) in THF (7 mL) at 0 °C were added Ph_3P (0.499 g, 1.90 mmol), imidazole (0.259 g, 3.80 mmol) and I_2 (0.483 g, 1.90 mmol). After being stirred for 30 min, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (15 mL). After extraction with ether (2×15 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:ether = 15:1) provided iodide **17** (0.329 g, 89%) as a colorless oil.

R_f 0.53 (hexanes:EtOAc = 20:1); IR (film) 3303, 2964, 2873, 1639, 1076, 917, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90-5.78 (m, 1H), 5.10 (d, *J* = 16.8 Hz, 1H), 5.09 (d, *J* = 10.1 Hz, 1H), 4.05 (dt, *J* = 10.4, 7.0 Hz, 1H), 3.78 (d, *J* = 1.8 Hz, 1H), 3.63 (dt, *J* = 10.4, 7.0 Hz, 1H), 3.35-3.26 (m, 2H), 2.47 (d, *J* = 1.8 Hz, 1H), 2.23 (dd, *J* = 13.5, 7.6 Hz, 1H), 2.15 (dd, *J* = 13.5, 7.6 Hz, 1H), 1.03 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 117.7, 81.1, 76.9, 75.1, 69.9, 42.8, 38.3, 23.0, 22.7, 2.9; HRMS (EI) calcd for $C_{10}H_{14}IO$ $[M\text{-}CH_3]^+$ 277.0089, found 277.0074.

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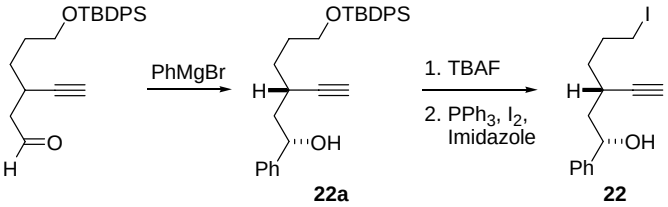

22a **22**

To a solution of the aldehyde (1.68 g, 4.44 mmol) in THF (10 mL) at 0 °C was added phenyl magnesium bromide (1.8 M in THF, 4.93 mL, 8.88 mmol). After stirring at room temperature for 30 min, the reaction was quenched with saturated aqueous NH_4Cl (20 mL). After extraction with ether (2×30 mL), the combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 8:1) to yield **22a** (1.22 g, 60%) and its diastereomeric alcohol (0.680 g, 34%) both as colorless oils. Alcohol **22a**: 0.45 (hexanes:EtOAc = 4:1); IR (film) 3381, 3305, 2931, 2858, 1428, 1112, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.60 (m, 5H), 7.42-7.20 (m, 10H), 4.89 (t, *J* = 6.8 Hz, 1H), 3.63 (t, *J* = 5.6 Hz, 2H), 2.33 (br s, 1H), 2.27-2.18 (m, 1H), 2.15 (s, 1H), 2.06-1.96 (m, 1H), 1.82-1.67 (m, 2H), 1.66-1.46 (m, 3H), 1.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 135.5, 133.9, 129.5, 128.5, 127.7, 127.6, 126.0, 87.2, 73.3, 70.7, 63.5, 44.1, 31.3, 29.8, 28.5, 26.8, 19.2; HRMS (EI) calcd for $C_{30}H_{36}O_2Si$ $[M]^+$ 456.2485, found 456.2469.

To a solution of **22a** (0.62 g, 1.4 mmol) in THF (8 mL) was added TBAF (1.0 M in THF, 2.0 mL, 2.0 mmol) at room temperature. After 5 h, the reaction mixture was diluted with ether (20 mL) and quenched with saturated aqueous NH_4Cl (20 mL). The aqueous phase was extracted with ether (3×30 mL), dried over Na_2SO_4, filtered, and concentrated. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 1:2) to give the diol (0.27 g, 92%) as a colorless oil. R_f 0.25 (hexanes:EtOAc = 1:1); IR (film) 3338, 3294, 2943, 2877, 1454, 1060, 1021, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H), 4.89 (t, *J* = 7.0 Hz, 1H), 3.58 (t, *J* = 6.0 Hz, 2H), 2.36 (br s, 1H), 2.26-2.17 (m, 1H), 2.14 (d, *J* = 2.4 Hz, 1H), 2.06-1.96 (m,

1H), 1.80-1.66 (m, 2H), 1.62-1.40 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 128.5, 127.8, 126.0, 87.0, 73.1, 70.7, 62.4, 44.1, 31.0, 30.0, 28.4; HRMS (EI) calcd for $C_{14}H_{18}O_2$ $[M]^+$ 218.1307, found 218.1305.

To a solution of the alcohol (0.150 g, 0.69 mmol) in THF (5 mL) at 0 °C were added Ph_3P (0.234 g, 0.89 mmol), imidazole (0.122 g, 1.79 mmol) and I_2 (0.227 g, 0.89 mmol). After being stirred for 3 min, the resulting solution was diluted with ether (10 mL) and washed with saturated aqueous $Na_2S_2O_3$ (15 mL). After extraction with ether (2×20 mL), the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (hexanes:EtOAc = 5:1) provided iodide **22** (0.159 g, 71%) as a colorless oil. R_f 0.29 (hexanes:EtOAc = 4:1); IR (film) 3372, 3293, 2941, 1453, 1219, 1027, 701, 635 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.25 (m, 5H), 4.89 (t, *J* = 6.9 Hz, 1H), 3.30-3.19 (m, 2H), 2.30-2.19 (m, 2H), 2.17 (d, *J* = 2.1 Hz, 1H), 2.06-1.96 (m, 2H), 1.91-1.81 (m, 1H), 1.77 (dt, *J* = 12.5, 7.0 Hz, 1H), 1.63-1.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 128.6, 127.9, 126.0, 86.5, 73.0, 71.1, 43.9, 35.5, 30.8, 27.8, 6.4; HRMS (EI) calcd for $C_{14}H_{17}IO$ $[M]^+$ 328.0324, found 328.0317.

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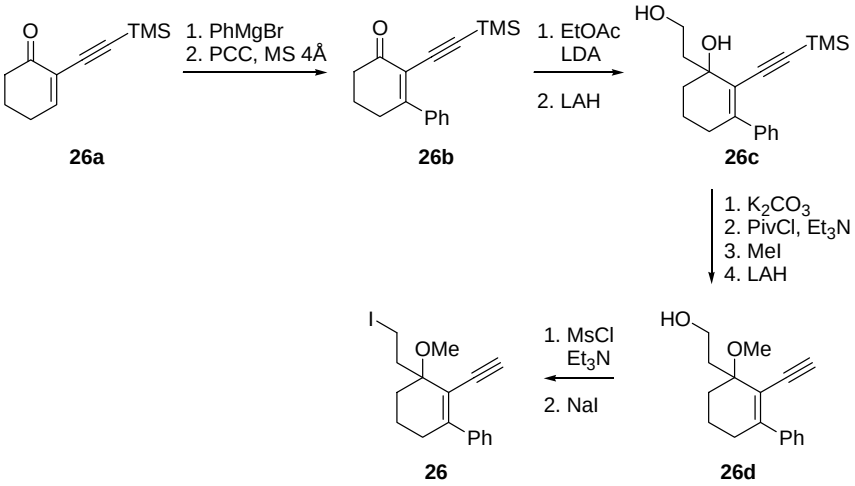

26a **26b** **26c** **26** **26d**

To a solution of **26a**[14] (600 mg, 3.12 mmol) in THF (10 mL) at –78 °C was added phenyl magnesium bromide (1.0 M in THF, 5.00 mL, 5.00 mmol). After being allowed to warm to 0 °C over 2 h, the reaction was quenched by addition of saturated aqueous NH_4Cl (15 mL). After extraction with EtOAc (2×25 mL), the combined organic layers were dried over Na_2SO_4 and concentrated to afford the crude alcohol as a colorless oil.

[14] Yao, T. L.; Zhang, X. X.; Larock, R. C. *J. Org. Chem.* **2005,** *70*, 7679.

To a solution of the above alcohol in CH_2Cl_2 (20 mL) was added a ground mixture of PCC (1.07 g, 5.00 mmol) and MS 4Å (1.0 g) at 0 °C. The resulting dark brown suspension was stirred at room temperature for 4 h, and the solids were removed by filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 10:1 to 4:1) to afford enone **26b** (606 mg, 72%) as a colorless oil. IR (film) 1677, 1359, 1246, 1113, 903, 843 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.40 (m, 3H), 2.81 (t, *J* = 5.8 Hz, 2H), 2.56 (t, *J* = 6.7 Hz, 2H), 2.12 (m, 2H), 0.10 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 165.1, 139.8, 129.6, 128.1, 128.0, 121.4, 101.7, 99.6, 37.7, 32.3, 22.3, -0.1; HRMS (EI) calcd for $C_{17}H_{20}OSi$ $[M]^+$ 268.1283, found 268.1280.

To a solution of diisopropylamine (0.700 mL, 5.00 mmol) in THF (10 mL) was added *n*-BuLi (2.5 M in hexanes, 2.00 mL, 5.00 mmol) at –78 °C. The resulting solution was warmed to 0 °C briefly and then cooled to –78 °C followed by addition of a solution of EtOAc (0.480 mL, 5.00 mmol) in THF (5 mL) via cannula. The reaction mixture was stirred at –78 °C for 30 min and a solution of enone **26b** (386 mg, 1.44 mmol) in THF (5 mL) was then added via cannula. After being stirred at –78 °C for 3 min, the reaction was quenched by addition of saturated aqueous NH_4Cl (20 mL, Direct trapping of the lithium alkoxide with MeOTf at –78 °C provided the desired product in 5% yield. Rising temperature to –60 °C, the retro-aldol reaction took place to give the starting enone **26b**). After extraction with EtOAc (3×25 mL), the combined organic layers were dried over Na_2SO_4 and concentrated to afford the crude alcohol as a colorless oil.

To a solution of the above alcohol in ether (20 mL) was added LAH (116 mg, 3.00 mmol) at 0 ºC. After stirring the resulting suspension at this temperature for 30 min, the reaction was quenched by addition of 1 N NaOH solution (3.0 mL) followed by addition of anhydrous $MgSO_4$. After vigorous stirring for 15 min, the solid was removed by filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 4:1 to 2:1) to afford diol **26c** (417 mg, 92% for 2 setps) as a colorless oil. IR (film) 3363, 2953, 2138, 1249, 1070, 841 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.31 (m, 3H), 4.02 (ddd, *J* = 11.3, 9.2, 4.0 Hz, 1H), 3.89 (dt, *J* = 10.9, 4.8 Hz, 1H), 2.52 (m, 1H), 2.40 (m, 2H), 1.93 (m, 2H), 1.86 (m, 2H), 1.75 (m, 1H), 0.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 141.7, 128.1, 127.9, 123.5, 102.8, 100.2, 72.5, 60.6, 59.8, 41.9, 33.6, 31.8, 19.1, -0.1; HRMS (EI) calcd for $C_{19}H_{24}OSi$ $[M\text{-}H_2O]^+$ 296.1596, found 296.1591.

To a solution of **26c** (54.0 mg, 0.170 mmol) in MeOH (5 mL) was added solid K_2CO_3 (27.6 mg, 0.200 mmol) at 0 °C. The resulting solution was stirred at room temperature for 3 h and then was

filtered through a silica gel pad. The filtrate was concentrated *in vacuo* to afford the crude terminal alkyne as a colorless oil.

To a mixture of the alkyne and Et_3N (0.140 mL, 1.00 mmol) in CH_2Cl_2 (5 mL) was added trimethylacetyl chloride (0.120 mL, 1.00 mmol) at 0 °C. The resulting solution was stirred at room temperature for 3 h and then was quenched by addition of saturated aqueous $NaHCO_3$ (10 mL). After extraction with CH_2Cl_2 (3×15 mL), the combined organic layers were dried over $MgSO_4$ and concentrated to afford the crude ester as a colorless oil.

To a solution of the above pivaloate ester in THF (5 mL) was added NaH (60% dispersion in mineral oil, 40.0 mg, 1.00 mmol) at 0 ºC. The resulting suspension was stirred at this temperature for 10 min, after which methyl iodide (0.120 mL, 2.00 mmol) was added. After being stirred for another 2 h, the reaction was quenched by addition of saturated aqueous NH_4Cl (5 mL). After extraction with CH_2Cl_2 (2×10 mL), the combined organic layers were dried over $MgSO_4$ and concentrated to afford the crude methyl ether as a colorless oil.

To a solution of the above crude methyl ether in ether (10 mL) was added LAH (38.0 mg, 1.00 mmol) at 0 ºC. After stirring the resulting suspension at this temperature for 30 min, the reaction was quenched by addition of 1 N NaOH solution (1.0 mL) followed by addition of anhydrous $MgSO_4$. After vigorous stirring for 15 min, the solid was removed by filtering through a silica gel pad. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 4:1 to 2:1) to afford **26d** (31 mg, 71% for 4 steps) as a colorless oil. IR (film) 3423, 3284, 2939, 1442, 1071, 758 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29-7.41 (m, 5H), 3.95 (td, *J* = 11.3, 3.4 Hz, 1H), 3.82 (m, 1H), 3.35 (s, 3H), 3.07 (br s, 1H), 2.88 (s, 1H), 2.44 (m, 3H), 2.07 (td, *J* = 11.8, 2.4 Hz, 1H), 1.94 (m, 1H), 1.85 (m, 2H), 1.74 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 141.9, 128.1, 128.0, 120.8, 81.5, 81.4, 79.1, 59.5, 50.7, 40.4, 32.1, 28.6, 20.0; HRMS (ESI-TOF) calcd for $C_{17}H_{20}O_2Na$ $[M+Na]^+$ 279.1355, found 279.1351.

To alcohol **26d** (11.0 mg, 43.0 μmol) and Et_3N (70.0 μL, 0.500 mmol) in CH_2Cl_2 (3.0 mL) was added MsCl (19.4 μL, 0.250 mmol) at –30 °C. After stirring for 10 min, the mixture was diluted with CH_2Cl_2 (5 mL) and poured into saturated aqueous $NaHCO_3$ (5 mL). After extraction with CH_2Cl_2 (3×5 mL), the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford the crude mesylate as a colorless oil.

To a solution of the above crude mesylate in acetone (5 mL) was added NaI (75.0 mg, 0.500

mmol) at room temperature. The resulting suspension was stirred for 36 h and concentrated. The yellow solid was dissolved in water (10 mL) and extracted with EtOAc (3×10 mL). The combined organic layers were sequentially washed with saturated aqueous $Na_2S_2O_3$ (5 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (hexanes:EtOAc = 15:1 to 10:1) to afford iodide **26** (12 mg, 81%) as a colorless oil. IR (film) 3285, 2938, 2870, 1442, 1182, 1072 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29-7.40 (m, 5H), 3.33 (s, 3H), 3.31 (m, 1H), 3.26 (m, 1H), 2.90 (s, 1H), 2.63 (td, *J* = 13.1, 5.2 Hz, 1H), 2.44 (m, 3H), 1.98 (m, 1H), 1.92 (m, 1H), 1.78 (m, 1H), 1.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 141.9, 128.2, 128.0, 127.9, 119.9, 81.8, 81.5, 78.1, 50.9, 44.3, 32.2, 28.9, 19.5, -0.2; HRMS (EI) calcd for $C_{17}H_{19}IO$ $[M]^+$ 366.0481, found 366.0463.