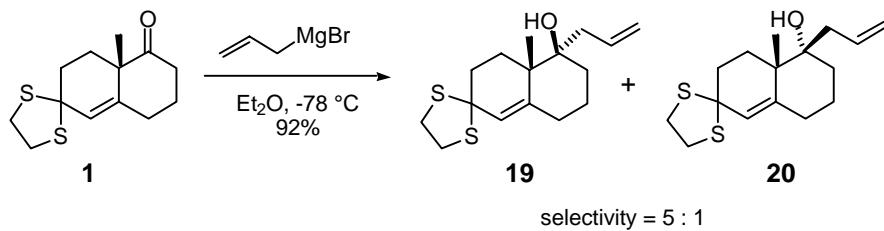


Transannular Macrocyclization Via Intramolecular *B*-Alkyl Suzuki Reaction
Sherry R. Chemler and Samuel J. Danishefsky*

Supporting Information

General. All commercial materials were used without further purification unless otherwise noted. THF, diethyl ether and methylene chloride used as reaction solvents were obtained from a dry solvent system (alumina) and used without further drying. All reactions were performed under a positive pressure of dry N₂ except the Suzuki reactions, which were performed under a dry Ar atmosphere. Solvents used in the Suzuki reactions were degassed by blowing Ar through them for ca. 10 min. ¹H and ¹³C NMR spectra were recorded in CDCl₃ at 400 MHz and 100 MHz, respectively. Analytical thin-layer chromatography was performed on E. Merck silica gel (40-63 μ m) or Sigma H-type gel (10-40 μ m).

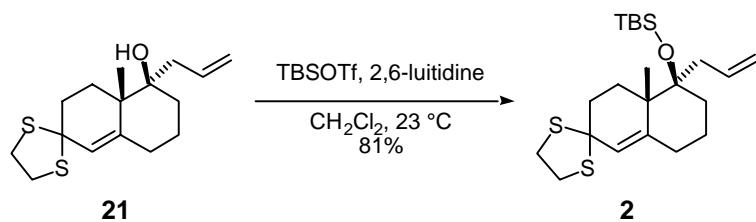


Procedure for alcohol **19:** A solution of ketone **1**¹ (4.0 g, 15.7 mmol) in Et₂O (70 mL) and THF (70 mL) was treated at -78 °C with allylmagnesium bromide (28 mL of a 1 M solution in Et₂O, 1.8 equiv). The reaction was stirred at -78 °C for 4 h, then was allowed to warm to 0 °C over 2 h and was quenched with sat. aqueous NH₄Cl. The mixture was extracted with Et₂O (2 x 100 mL), the combined organic layers were dried with MgSO₄, filtered and concentrated *in vacuo*. Pure diastereomeric alcohols **19** and **20**

were obtained by chromatography on SiO_2 (10 - 30% $\text{Et}_2\text{O}/\text{hexane}$ gradient) where the minor alcohol **20**, (0.72 g, 15% yield, white solid) eluted first, followed by the major alcohol **19** (3.58 g, 77% yield, colorless oil).

Data for major alcohol **19**: ^1H NMR (400 MHz, CDCl_3) δ 5.85 (m, 1 H), 5.64 (s, 1 H), 5.13-5.09 (m, 2 H), 3.39-3.35 (m, 3 H), 3.26 (m, 1 H), 2.37 (dd, J = 14.2, 6.7 Hz, 1 H), 2.27 (dd, J = 14.3, 7.9 Hz, 1 H), 2.30-2.10 (m, 4 H), 2.00 (dd, J = 14.5, 5.0 Hz, 1 H), 1.70 (ddd, J = 13.3, 13.3, 4.3 Hz, 1 H), 1.65-1.51 (m, 3 H), 1.42-1.28 (m, 2 H), 1.19 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.1, 134.3, 127.3, 118.2, 76.4, 65.4, 42.8, 39.9, 39.6, 39.2, 38.3, 32.0, 30.6, 29.4, 21.9, 20.8; IR (neat) ν 3479.1, 2938.5, 1638.7, 1437.2, 1019.4 cm⁻¹; HRMS (CI, NH_3) calcd for $[\text{C}_{16}\text{H}_{24}\text{OS}_2]^+$ 296.1268, found 296.1255 $[\text{M}]^+$.

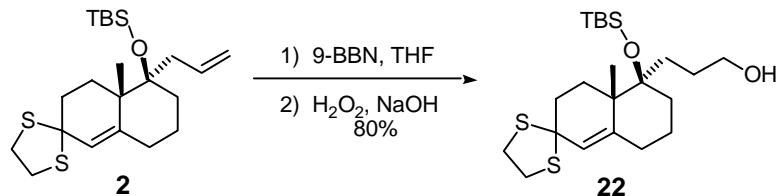
Data for minor alcohol **20**: mp = 113.7-115 °C. ^1H NMR (400 MHz, CDCl_3) δ 5.92 (m, 1 H), 5.76 (d, J = 1.4 Hz, 1 H), 5.14-5.06 (m, 2 H), 3.45-3.30 (m, 3 H), 3.23 (m, 1 H), 2.40 (ddd, J = 13.6, 11.1, 3.4 Hz, 1 H), 2.37 (d, J = 13.8 Hz, 1 H), 2.28-2.07 (m, 4 H), 2.00 (m, 1 H), 1.68-1.43 (m, 6 H), 1.14 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.2, 134.5, 129.2, 118.2, 75.7, 65.0, 42.7, 39.9, 39.7, 39.5, 37.8, 31.4, 31.2, 30.0, 21.8, 21.6; IR (neat) ν 3553.2, 2933.3, 1638.5, 1435.1 cm⁻¹; HRMS (CI, NH_3) calcd for $[\text{C}_{16}\text{H}_{24}\text{OS}_2]^+$ 296.1268, found 296.1282 $[\text{M}]^+$.



Procedure for silyl ether **2**: A solution of alcohol **21** (3.58 g, 12.0 mmol) in CH_2Cl_2 (25 mL) was treated with a solution of TBSOTf (6.1 mL, 26.6 mmol, 2.2 equiv) and 2,6-luitidine (6.2 mL, 53.1 mmol, 4.4 equiv) in CH_2Cl_2 (25 mL). The reaction mixture was stirred 48 h at 23 °C, then was quenched with sat. aqueous NaHCO_3 (25

mL). The layers were separated and the organic layer was dried with MgSO_4 , filtered and concentrated *in vacuo*. Purification of the crude oil by chromatography on SiO_2 (5-15% Et_2O /hexane eluent) afforded 4.93 g (81% yield) of silyl ether **2** as a white solid.

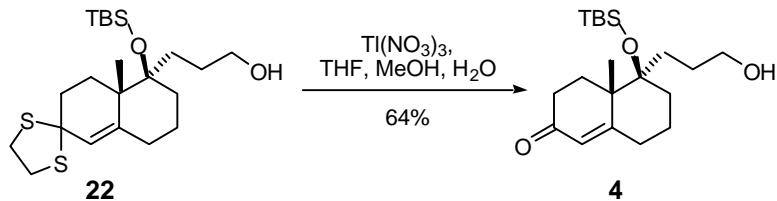
Data for ether **2**: mp = 75.5-76.5 °C. ^1H NMR (400 MHz, CDCl_3) δ 5.87 (m, 1 H), 5.60 (s, 1 H), 5.08-5.04 (m, 2 H), 3.39-3.34 (m, 3 H), 3.25 (m, 1 H), 2.47 (dd, J = 14.6, 4.9 Hz, 1 H), 2.28-2.08 (m, 5 H), 1.96 (dd, J = 14.4, 4.8 Hz, 1 H), 1.82 (ddd, J = 12.9, 12.9, 3.8 Hz, 1 H), 1.73 (d, J = 12.8 Hz, 1 H), 1.59-1.51 (m, 2 H), 1.34 (tt, J = 13.6, 4.6 Hz, 1 H), 1.15 (s, 3 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.8, 135.0, 126.9, 117.2, 80.5, 65.6, 44.1, 40.9, 39.8, 39.6, 38.4, 32.0, 30.5, 29.8, 26.0, 22.0, 21.7, 18.7, -1.0, -1.3; IR (neat) ν 2953.5, 2923.9, 2854.7, 1632.0, 1468.9, 1434.3, 1256.5, 1083.6 cm⁻¹; HRMS (DCI, NH_3) calcd for $[\text{C}_{22}\text{H}_{38}\text{OS}_2\text{Si}]^+$ 410.2133, found 410.2126 $[\text{M}]^+$.



Procedure for alcohol **22**: Olefin **2** (3.00g, 7.61 mmol) in THF (15 mL) was treated with solid 9-BBN dimer (1.3 g, 10.65 mmol, 1.4 equiv) at 23 °C and was stirred 1 h. This solution was then treated with a mixture of H_2O_2 (3 mL) and 2 M NaOH (8 mL) at 0 °C, and the reaction was warmed to 23 °C and stirred 1.5 h. The mixture was extracted with Et_2O (2 x 50 mL) and the combined organic layers were washed with H_2O (10 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude oil was chromatographed on SiO_2 (10-30% EtOAc /hexane gradient), affording 2.62 g (80% yield) of alcohol **22** as a white foam.

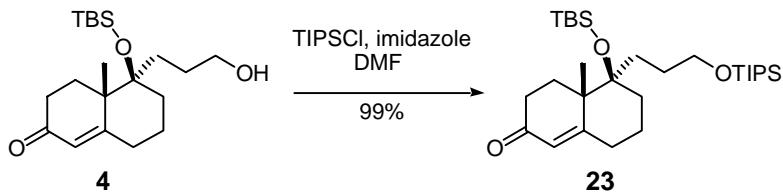
Data for alcohol **22**: ^1H NMR (400 MHz, CDCl_3) δ 5.57 (s, 1 H), 3.69-3.57 (m, 2 H), 3.40-3.30 (m, 3 H), 3.22 (m, 1 H), 2.29-2.08 (m, 4 H), 1.94 (dd, J = 14.4, 4.7 Hz, 1

H), 1.84 (ddd, $J = 13.4, 9.3, 4.4$ Hz, 1 H), 1.79-1.42 (m, 8 H), 1.28 (m, 1 H), 1.14 (s, 3 H), 0.86 (s, 9 H), 0.11 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.9, 126.9, 80.3, 65.5, 63.6, 44.4, 39.7, 39.5, 38.3, 32.0, 31.7, 30.6, 29.7, 27.2, 26.0, 22.4, 21.7, 18.7, -1.2, -1.4; IR (neat) 3348.7, 2933.7, 2854.7, 1641.8, 1468.9, 1434.3, 1251.5, 1118.2, 1088.5, 1058.9 cm⁻¹; HRMS (DCI, NH_3) calcd for $[\text{C}_{22}\text{H}_{40}\text{O}_2\text{S}_2\text{Si}]^+$ 428.2239, found 428.2223 [M]⁺.



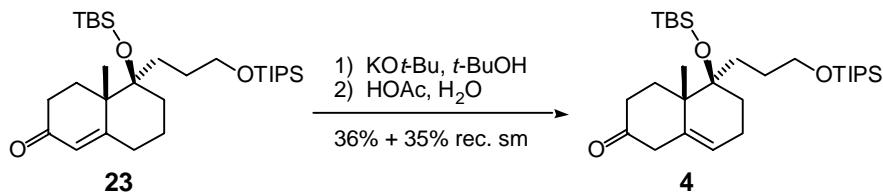
Procedure for ketone **4**:³ A solution of dithioketal **22** (3.80 g, 8.86 mmol) in a 2:2:1 THF/MeOH/H₂O solvent mixture was treated with a solution of Tl(No₃)₃ in MeOH (50 mL). After being stirred 10 min, the reaction was diluted with H₂O (30 mL) and extracted with Et₂O (2 x 100 mL). The organic layer was dried with MgSO₄, filtered and concentrated *in vacuo*. Purification of the crude oil by chromatography on SiO₂ (10-40% EtOAc/hexane gradient) yielded 2.00 g (64%) of ketone as clear, yellow crystals.

Data for ketone **4**: mp = 115-118 °C. ^1H NMR (400 MHz, CDCl_3) δ 5.77 (d, $J = 1.8$ Hz, 1 H), 3.67-3.56 (m, 2 H), 2.43-2.24 (m, 5 H), 1.96 (ddd, $J = 17.4, 13.5, 4.0$ Hz, 1 H), 1.89-1.70 (m, 3 H), 1.70-1.35 (m, 6 H), 1.30 (s, 3 H), 0.88 (s, 9 H), 0.15 (s, 3 H), 0.14 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.5, 169.5, 125.8, 80.2, 63.3, 46.2, 34.6, 32.7, 31.4, 31.0, 27.7, 26.8, 26.0, 21.6, 20.4, 18.7, -1.2, -1.3; IR (neat) ν 3426.1, 2955.3, 2859.0, 1669.9, 1252.6, 1054.7, 835.3 cm⁻¹; HRMS (DCI, NH_3) calcd for $[\text{C}_{20}\text{H}_{37}\text{O}_3\text{Si}]^+$ 353.2512, found 353.2496 [M + H]⁺.



Procedure for silyl ether **23:** A solution of alcohol **4** (2.00 g, 5.68 mmol) in DMF (10 mL) was treated with imidazole (0.54 g, 7.95 mmol, 1.4 equiv) and TIPSCl (1.46 g, 6.82 mmol, 1.2 equiv) and was stirred for 3 h at 23 °C. The reaction was quenched with H₂O (10 mL) and extracted with Et₂O (2 x 50 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated *in vacuo*. Pure ether **23** (2.88 g, 99% yield) was obtained after chromatography of the crude oil on SiO₂ (5-10% EtO₂/hexane gradient).

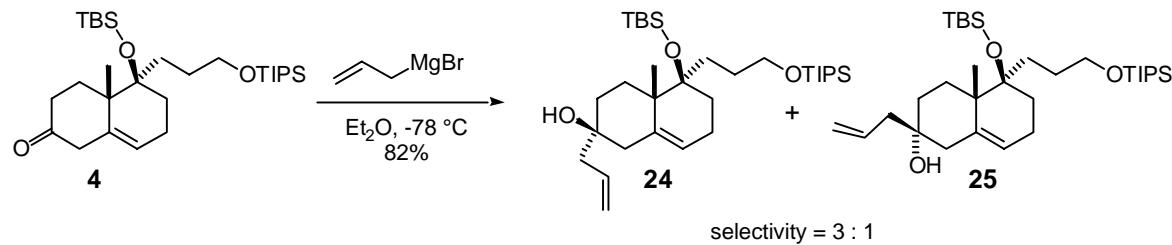
Data for **23:** ¹H NMR (400 MHz, CDCl₃) δ 5.76 (d, J = 1.8 Hz, 1 H), 3.69-3.60 (m, 2 H), 2.49-2.35 (m, 3 H), 2.30 (ddd, J = 12.8, 12.8, 6.0 Hz, 1 H), 2.21 (dd, J = 15.4, 4.8 Hz, 1 H), 1.94 (ddd, J = 13.3, 13.3, 4.0 Hz, 1 H), 1.88-1.35 (m, 7 H), 1.29 (s, 3 H), 1.10-1.00 (m, 22 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 199.4, 169.6, 125.7, 80.2, 63.6, 46.2, 34.6, 32.9, 31.4, 31.1, 27.7, 27.2, 26.0, 21.5, 20.4, 18.7, 18.0, 17.7, 12.3, 11.9, -1.3, -1.4; IR (neat) ν 2944.6, 2859.0, 1675.2, 1616.4, 1461.2, 1252.6, 1108.2 cm⁻¹; HRMS (DCI, NH₃) calcd for [C₂₉H₅₇O₃Si₂]⁺ 509.3846, found 509.3854 [M + H]⁺.



Procedure for ketone **4:**² Ketone **23** (2.88 g, 5.67 mmol) in *t*-BuOH (10 mL) was treated at 15 °C with KO*t*-Bu (5.10 g, 45.4 mmol), added in three portions. This mixture was stirred 45 min, when was quenched by the rapid addition of a 10% AcOH solution in

H_2O . This mixture was extracted with Et_2O (2 x 30 mL) and the combined organic extracts were dried over MgSO_4 , filtered and concentrated *in vacuo*. Purification of the crude reaction mixture by chromatography on SiO_2 (10-30% Et_2O /hexane gradient) afforded starting enone **23** (1.00 g, 35%, eluting first) and 1.04 g (36%) of the desired de-conjugated ketone **4**.

Data for ketone **4**: ^1H NMR (400 MHz, CDCl_3) δ 5.28 (s, 1 H), 3.72-3.60 (m, 2 H), 3.18 (dq, J = 17.5, 2.4 Hz, 1 H), 2.89 (d, J = 17.5 Hz, 1 H), 2.41 (ddd, J = 11.4, 8.2, 3.0 Hz, 1 H), 2.30 (ddd, J = 14.0, 8.7, 5.2 Hz, 1 H), 2.17 (ddd, J = 13.1, 8.5, 5.0 Hz, 1 H), 2.06-1.95 (m, 3 H), 1.79 (m, 1 H), 1.70 (m, 1 H), 1.66-1.52 (m, 4 H), 1.24 (s, 3 H), 1.10-1.00 (m, 21 H), 0.89 (s, 9 H), 0.16 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 211.2, 137.2, 121.9, 79.3, 63.8, 47.4, 43.3, 38.6, 31.5, 28.5, 28.2, 27.8, 26.1, 26.0, 24.5, 24.3, 18.7, 18.0, 12.0, -1.0, -1.3; IR (neat) 2944.6, 2859.0, 1723.4, 1664.5, 1461.2, 1252.6, 1102.8, 1054.7 cm^{-1} ; ESIMS calcd for $[\text{C}_{29}\text{H}_{56}\text{O}_3\text{Si}_2\text{Na}]^+$ 531.4, found 531.1 [$\text{M} + \text{Na}]^+$.

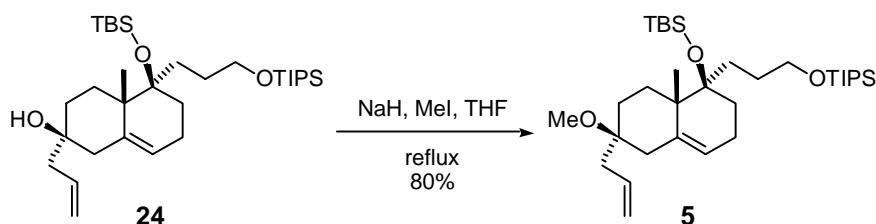


Procedure for alcohol **24**: A solution of ketone **4** (1.10 g, 2.16 mmol) in Et_2O (20 mL) at -78 °C was treated with $\text{Al}(\text{Et}_2\text{O})_3\text{MgBr}$ (3.3 mL of a 1 M solution in Et_2O , 1.5 equiv). The reaction was allowed to warm to -10 °C over 16 h, then was quenched with sat. NH_4Cl (aq) (20 mL) and extracted with Et_2O (2 x 50 mL). The combined organic extracts were dried over MgSO_4 , filtered and concentrated *in vacuo*. Purification of the crude reaction mixture on SiO_2 (10-30% Et_2O /hexane eluent) afforded the minor alcohol

25 (eluting first, 0.245 g, 21% yield) followed by the major alcohol **24** (0.72 g, 61% yield).

Data for major alcohol **24**: ^1H NMR (400 MHz, CDCl_3) δ 5.83 (m, 1 H), 5.21 (s, 1 H), 5.18-5.08 (m, 2 H), 3.76 (m, 1 H), 3.68 (m, 1 H), 2.38 (dq, J = 13.7, 2.2 Hz, 1 H), 2.19-2.06 (m, 3 H), 2.00-1.85 (m, 3 H), 1.78-1.51 (m, 9 H), 1.45 (m, 1 H), 1.18 (s, 3 H), 1.10-0.87 (m, 21 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.1, 133.4, 121.3, 119.1, 79.3, 72.5, 64.0, 45.1, 43.6, 41.2, 33.8, 31.9, 28.7, 28.0, 27.4, 26.1, 24.3, 22.3, 18.8, 18.0, 12.0, -0.9, -1.3; IR (neat) 3383.3, 2944.6, 2859.0, 1461.2, 1247.2, 1102.8, 1054.7 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{32}\text{H}_{62}\text{O}_3\text{Si}_2]^+$ 550.4237, found 550.4249 $[\text{M}]^+$.

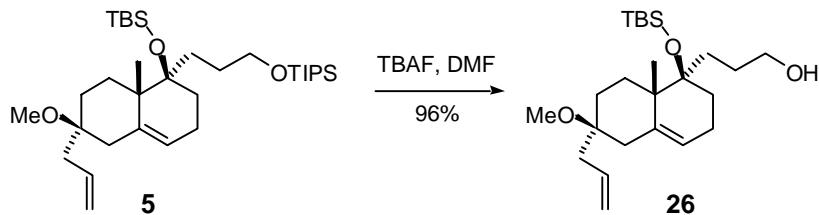
Data for minor alcohol **25**: ^1H NMR (400 MHz, CDCl_3) δ 5.89 (m, 1 H), 5.28 (s, 1 H), 5.14-5.07 (m, 2 H), 3.70-3.62 (m, 2 H), 2.36 (dq, J = 14.8, 2.5 Hz, 1 H), 2.21 (d, J = 7.4 Hz, 2 H), 2.04-1.85 (m, 5 H), 1.79-1.50 (m, 7 H), 1.38 (dt, J = 13.3, 3.1 Hz, 1 H), 1.26 (m, 1 H), 1.11 (s, 3 H), 1.10-1.02 (m, 21 H), 0.87 (s, 9 H), 0.14 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 139.2, 133.8, 122.3, 118.3, 79.3, 71.5, 64.2, 47.4, 43.9, 43.7, 32.8, 32.0, 31.6, 30.3, 28.9, 28.2, 26.1, 24.3, 21.0, 18.8, 18.0, 11.7, -1.0, -1.3; IR (neat) 3597.3, 3468.9, 2955.3, 2859.0, 1461.2, 1252.6, 1102.8, 1060.0 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{32}\text{H}_{62}\text{O}_3\text{Si}_2]^+$ 550.4237, found 550.4225 $[\text{M}]^+$.



Procedure for methyl ether **5**:³ A solution of NaH (0.156 g, 6.5 mmol, 5 equiv) in THF (4 mL) was treated with a solution of alcohol **24** (0.713 g, 1.30 mmol) in THF (4 mL) followed by MeI (4.4 mL, 52 mmol, 40 equiv) at 23 °C. After being stirred for 10

min, the solution was refluxed for 2 h, then was cooled to 23 °C and quenched with sat. aqueous NH₄Cl (5 mL). The resulting mixture was extracted with Et₂O (2 x 20 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Ether **5** (0.589 g, 80% yield) was obtained pure as a colorless oil by chromatography of the crude reaction mixture on SiO₂ (5-10% Et₂O/hexane eluent).

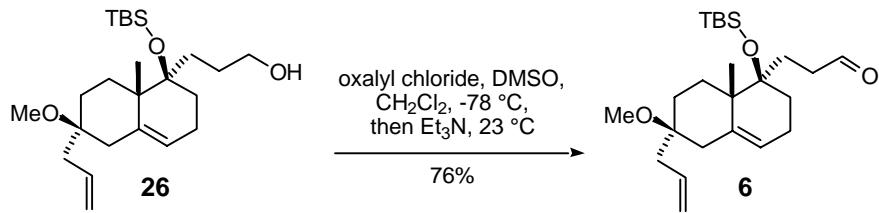
Data for ether **5**: ¹H NMR (400 MHz, CDCl₃) δ 5.78 (m, 1 H), 5.20 (d, J = 1.9 Hz, 1 H), 5.09-5.04 (m, 2 H), 3.75 (m, 1 H), 3.66 (m, 1 H), 3.54 (s, 3 H), 2.32 (dq, J = 13.6, 2.3 Hz, 1 H), 2.24-2.12 (m, 3 H), 2.00-1.87 (m, 3 H), 1.74-1.55 (m, 8 H), 1.43 (m, 1 H), 1.24 (s, 3 H), 1.10-1.00 (m, 21 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.09 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 139.9, 133.7, 121.3, 117.2, 79.4, 76.7, 64.0, 48.4, 43.8, 41.4, 36.0, 31.9, 30.1, 28.7, 28.0, 27.0, 26.1, 24.3, 22.3, 18.8, 18.0, 12.0, -0.90, -1.30; IR (neat) 2943.1, 2857.5, 1460.5, 1251.8, 1102.0, 1069.9 cm⁻¹; HRMS (DCM/NBA) calcd for [C₃₃H₆₃O₃Si₂]⁺ 563.4316, found 563.4289 [M - H]⁺.



Procedure for alcohol **26**: Silyl ether **5** (0.589 g, 1.04 mmol) in DMF (5 mL) was treated at 23 °C with TBAF (2.1 mL of a 1 M solution in THF). After being stirred for 0.5 h, the reaction mixture was diluted with H₂O (10 mL) and extracted with Et₂O (2 x 30 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO₂ (10-30% EtOAc/hexane eluent) afforded 0.408 g (96% yield) of alcohol **26** as a colorless oil.

Data for alcohol **26**: ¹H NMR (400 MHz, CDCl₃) δ 5.79 (m, 1 H), 5.20 (d, J = 2.1 Hz, 1 H), 5.04 (m, 2 H), 3.64-3.61 (m, 2 H), 3.22 (s, 3 H), 2.32 (dq, J = 13.6, 2.1 Hz, 1

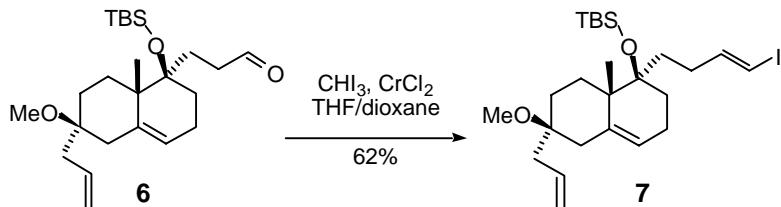
H), 2.24-2.12 (m, 3 H), 2.03-1.88 (m, 3 H), 1.79-1.39 (m, 10 H), 1.15 (s, 3 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.0, 133.7, 121.2, 117.3, 79.2, 63.8, 48.4, 43.8, 41.3, 36.1, 31.7, 30.0, 29.0, 27.9, 27.1, 26.1, 24.3, 22.3, 18.8, 17.7, -0.9, -1.3; IR (neat) 3392.5, 2953.8, 2857.5, 1637.0, 1471.1, 1251.8, 1064.6 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{24}\text{H}_{45}\text{O}_3\text{Si}]^+$ 409.3138, found 409.3132 $[\text{M} + \text{H}]^+$.



Procedure for aldehyde **6:** A solution of DMSO (0.21 mL, 2.99 mmol, 3 equiv) in CH_2Cl_2 (2 mL) at -78°C was treated with oxalyl chloride (1.1 mL of a 2 M solution in CH_2Cl_2 , 2.25 mmol, 2.25 equiv). After 15 min, a solution of alcohol **26** (0.408 g, 0.998 mmol) in CH_2Cl_2 (2 mL) was cannulated into the reaction mixture and the resulting solution was stirred for 15 min, then treated with Et_3N (0.63 mL, 4.49 mmol, 4.5 equiv) and warmed to 23°C . After being stirred for 1 h, the reaction was quenched with sat. aqueous NaHCO_3 and extracted with Et_2O (2 x 20 mL). The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude oil was chromatographed on SiO_2 (5-15% Et_2O /hexane gradient), affording 0.307 g (76%) of aldehyde **6** as a colorless oil.

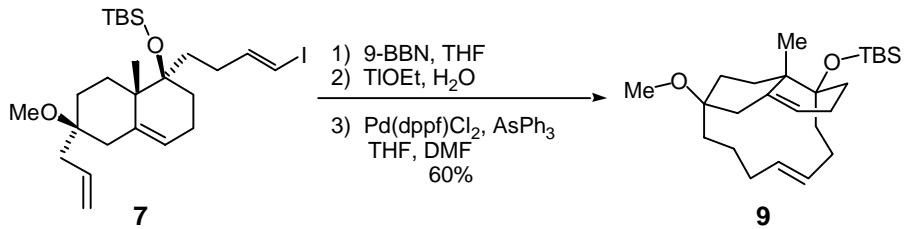
Data for aldehyde **6:** ^1H NMR (400 MHz, CDCl_3) δ 9.81 (d, $J = 2.9$ Hz, 1 H), 5.77 (m, 1 H), 5.21 (s, 1 H), 5.09-5.00 (m, 2 H), 3.20 (s, 3 H), 2.62 (dddd, $J = 17.1, 11.6, 4.3, 1.0$ Hz, 1 H), 2.50 (dddd, $J = 16.8, 11.5, 5.2, 1.9$ Hz, 1 H), 2.32 (dq, $J = 13.7, 2.3$ Hz, 1 H), 2.25-2.12 (m, 3 H), 2.05-1.87 (m, 4 H), 1.80-1.50 (m, 5 H), 1.45 (m, 1 H), 1.16 (s, 3 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.4, 140.0, 133.5, 121.0, 117.4, 78.7, 76.6, 48.5, 44.0, 41.3, 40.0, 36.1, 30.0, 29.5, 27.3, 26.1,

24.2, 22.2, 18.8, -0.90, -1.30; IR (neat) 2928.7, 1727.2, 1471.6, 1255.4, 1073.5 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{24}\text{H}_{43}\text{O}_3\text{Si}]^+$ 407.2981, found 407.2997 $[\text{M} + \text{H}]^+$.



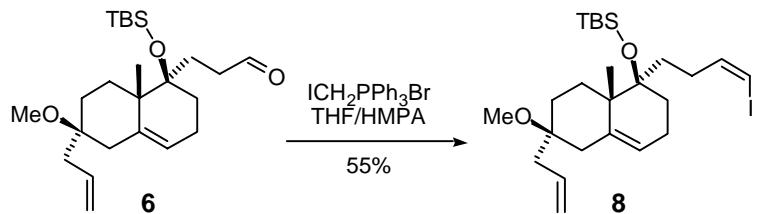
Procedure for vinyl iodide **7**:⁴ A solution of CrCl_2 (0.644 g, 5.24 mmol, 10 equiv) in THF (1.3 mL) was treated at 23 °C with a solution of aldehyde **6** (0.213 g, 0.524 mmol) and iodoform (0.619 g, 1.57 mmol, 3 equiv) in dioxane (9 mL). After being stirred 20 h, the reaction was quenched with H_2O (10 mL) and the resulting mixture was extracted with Et_2O (2 x 25 mL). The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. Purification of the crude oil by chromatography on SiO_2 (5-15% Et_2O /hexane gradient) afforded 0.173 g (62% yield) of vinyl iodide **7** as an 11:1 mixture of *E*:*Z* vinyl iodide isomers **7** and **8**.

Data for vinyl iodide **7**: ^1H NMR (400 MHz, CDCl_3) δ 6.53 (dt, $J = 14.3, 7.2$ Hz, 1 H), 6.01 (dt, $J = 14.3, 1.3$ Hz, 1 H), 5.80 (m, 1 H), 5.21 (d, $J = 3.7$ Hz, 1 H), 5.12-5.01 (m, 2 H), 3.24 (s, 3 H), 2.32 (dq, $J = 13.8, 2.1$ Hz, 1 H), 2.28-1.88 (m, 8 H), 1.79-1.40 (m, 7 H), 1.15 (s, 3 H), 0.87 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.8, 140.0, 139.9, 133.6, 121.0, 117.4, 79.0, 74.3, 48.4, 43.8, 41.3, 36.2, 34.3, 31.6, 30.0, 28.9, 27.2, 26.1, 24.3, 22.2, 18.8, -0.90, -1.30; IR (neat) 2938.5, 2889.3, 1466.7, 1250.4, 1068.6 cm^{-1} ; HRMS (DCM/NBA) calcd for $[\text{C}_{25}\text{H}_{42}\text{IO}_2\text{Si}]^+$ 529.2001, found 529.2022 $[\text{M} - \text{H}]^+$.



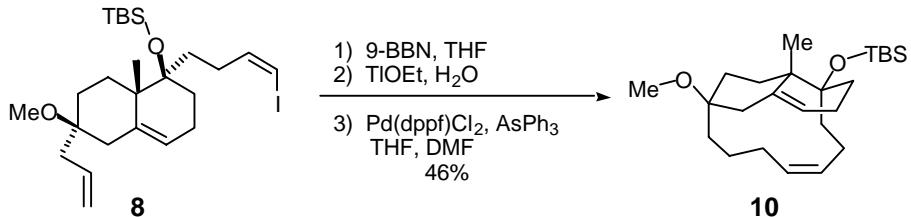
Procedure for macrocycle **9**: A solution of vinyl iodide **7** (0.050 g, 0.094 mmol) in THF (0.5 mL) was treated with 9-BBN (0.2 mL of a 0.72 M solution in THF, 0.143 mmol, 1.5 equiv) at 23 °C. After being stirred for 1.5 h, the reaction was quenched with H₂O (0.010 mL, 0.56 mmol, 6 equiv) and then treated with TIOEt (0.020 mL, 0.282 mmol, 3 equiv). This mixture was then diluted with THF (4 mL) and the resulting solution was added dropwise over 3 h (syringe-pump addition) to a solution of Pd(dppf)Cl₂ (0.015 g, 0.019 mmol, 0.2 equiv) and AsPh₃ (0.006 g, 0.019 mmol, 0.2 equiv) in THF (28 mL) and DMF (3 mL) under an Ar atmosphere. This mixture was stirred an additional 12 h, then was diluted with pH 7.2 phosphate buffer (6 mL) and treated with 30% H₂O₂ (2 mL). After being stirred for 0.5 h, the reaction was extracted with a 1:1 Et₂O/hexane solution (2 x 50 mL) and the combined organic layers were washed with H₂O (10 mL) and dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO₂ (5-15% Et₂O/hexane gradient) afforded 23 mg (60%) of intramolecular Suzuki adduct **9** as a colorless oil.

Data for macrocycle **9**: ¹H NMR (400 MHz, CDCl₃) δ 5.19 (ddd, J = 14.8, 11.9, 2.5 Hz, 1 H), 5.07-4.98 (m, 2 H), 3.20 (s, 3 H), 2.37-2.25 (m, 3 H), 2.19-2.02 (m, 5 H), 1.99-1.81 (m, 3 H), 1.72 (dq, J = 13.2, 3.7 Hz, 1 H), 1.63-1.52 (m, 2 H), 1.46-1.30 (m, 5 H), 1.14 (s, 3 H), 1.14 (m, 1 H), 0.92 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 141.9, 137.1, 130.4, 119.6, 80.6, 78.1, 77.2, 48.6, 43.5, 42.8, 37.7, 35.9, 32.0, 28.7, 27.3, 26.9, 26.2, 25.0, 24.5, 23.8, 20.5, 18.8, -1.60, -2.40; IR (neat) 2926.2, 1470.5, 1251.5, 1095.8, 1066.6 cm⁻¹; HRMS (DCI, NH₃) calcd for [C₂₅H₄₄O₂Si]⁺ 404.3110, found 404.3100 [M]⁺.



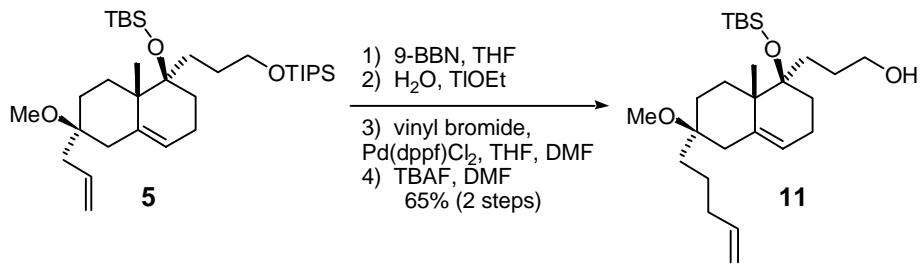
Procedure for vinyl iodide **8**: Iodomethyl triphenylphosphonium bromide⁵ (0.547 g, 1.03 mmol, 3.0 equiv) in THF (3.4 mL) was treated with NaHMDS (0.83 mL of a 1.0 M solution in THF, 0.826 mmol, 2.4 equiv) at 23 °C, stirred for 5 min, then was cooled to -78 °C and treated with HMPA. Aldehyde **6** (0.140 g, 0.344 mmol) in 0.5 mL THF was transferred via cannula to this reaction mixture and the resulting mixture was stirred at -78 °C for 2 h. The reaction was warmed to 23 °C and quenched with sat. aqueous NH₄Cl (5 mL). The resulting mixture was extracted with Et₂O (2 x 20 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Purification of the crude oil by chromatography on SiO₂ (5-15% Et₂O/hexane gradient) afforded vinyl iodide **8** (0.101 g, 55% yield) as a 13:1 mixture of *Z* : *E* vinyl iodide isomers **8** and **7**. A side product corresponding most closely to the terminal alkyne (0.044 g) was also isolated.

Data for vinyl iodide **8**: ^1H NMR (400 MHz, CDCl_3) δ 6.22-6.15 (m, 2 H), 5.80 (m, 1 H), 5.22 (s, 1 H), 5.10-5.00 (m, 2 H), 3.20 (s, 3 H), 2.34-1.93 (m, 9 H), 1.76-1.55 (m, 6 H), 1.45 (m, 1 H), 1.17 (s, 3 H), 0.90 (s, 9 H), 0.21 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.5, 139.9, 133.7, 121.2, 117.3, 82.2, 79.1, 76.7, 48.5, 43.8, 41.3, 36.1, 33.5, 30.4, 30.0, 28.9, 27.1, 26.2, 24.5, 22.3, 18.8, -0.70, -1.20; IR (neat) 2953.8, 2932.4, 1471.1, 1251.8, 1069.9, 834.5, 770.3 cm^{-1} ; HRMS (FAB, DCM/NBA) calcd for $[\text{C}_{25}\text{H}_{42}\text{IO}_2\text{Si}]^+$ 529.2001, found 529.1992 $[\text{M} - \text{H}]^+$.



Procedure for macrocycle **10:** Vinyl iodide **8** (0.099 g, 0.187 mmol), neat, was treated with 0.5 mL of a 0.57 M solution of 9-BBN in THF (0.28 mmol, 1.5 equiv) at 23 °C. After being stirred 1.5 h, the reaction was quenched by addition of H₂O (0.020 mL, 0.935 mmol, 5 equiv) and was then treated with TIOEt (0.040 mL, 0.561 mmol, 3 equiv) followed by dilution of the mixture with THF (4 mL). The resulting solution was added dropwise over 3 h (syringe-pump addition) to a solution of Pd(dppf)Cl₂ (0.0305 g, 0.0374 mmol, 0.2 equiv) and AsPh₃ (0.012 g, 0.038 mmol, 0.2 equiv) in THF (55 mL) and DMF (5 mL) under an Ar atmosphere. This mixture was stirred an additional 12 h, then was diluted with pH 7.2 phosphate buffer (12 mL) and treated with 30% H₂O₂ (4 mL). After being stirred for 0.5 h, the reaction was extracted with a 1:1 Et₂O/hexane solution (2 x 100 mL) and the combined organic layers were washed with H₂O (20 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO₂ (5-15% Et₂O/hexane gradient) afforded 35 mg (46%) of intramolecular Suzuki adduct **10** as a colorless oil.

Data for macrocycle **10:** ¹H NMR (400 MHz, CDCl₃) δ 5.66 (ddd, J = 11.2, 11.2, 4.5 Hz, 1 H), 5.17 (ddd, J = 11.5, 11.5, 5.2 Hz, 1 H), 5.09 (d, J = 2.3 Hz, 1 H), 3.18 (s, 3 H), 2.72 (m, 1 H), 2.40-2.25 (m, 3 H), 2.20-2.01 (m, 4 H), 2.01-1.80 (m, 4 H), 1.80-1.65 (m, 2 H), 1.60-1.30 (m, 6 H), 1.11 (s, 3 H), 0.90 (s, 9 H), 0.15 (s, 3 H), 0.10 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 141.7, 132.8, 127.8, 120.8, 79.1, 78.7, 77.2, 48.5, 44.1, 42.2, 38.5, 34.7, 29.5, 29.3, 27.8, 26.2, 25.6, 24.1, 23.1, 20.5, 18.8, -1.5, -2.3; IR (neat) 2951.9, 2932.3, 1462.5, 1251.9, 1070.8 cm⁻¹; HRMS (DEI) calcd for [C₂₅H₄₄O₂Si]⁺ 404.3110, found 4404.3098 [M]⁺.

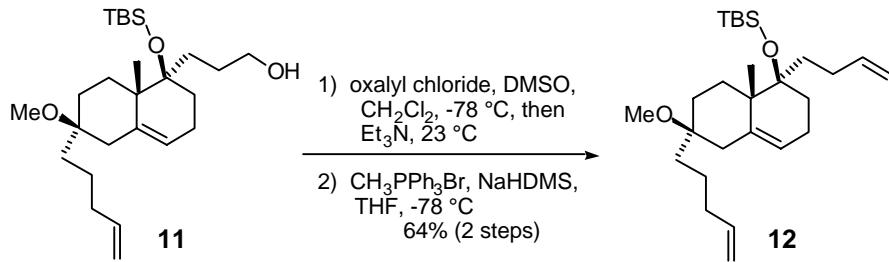


Procedure for alcohol **11**: A solution of olefin **5** (0.165 g, 0.292 mmol) in THF (0.6 mL) was treated with solid 9-BBN dimer (0.054 g, 0.440 mmol w/r to monomer, 1.5 equiv) at 23 °C. After being stirred 2 h, the reaction was quenched by the addition of H₂O (0.030 mL, 1.46 mmol, 5 equiv) and then was treated with TlOEt (0.062 mL, 0.876 mmol, 3 equiv). This mixture was transferred via cannula to a solution of vinyl bromide (1.5 mL of a 1 M THF solution, 1.46 mmol, 5 equiv), Pd(dppf)Cl₂ (0.048 g, 0.058 mmol, 0.2 equiv) and AsPh₃ (0.018 g, 0.058 mmol, 0.2 equiv) in THF (1 mL) and DMF (0.5 mL) under an Ar atmosphere. After 2 h, the reaction was quenched by the addition of 3 mL of pH 7.2 phosphate buffer and 1 mL 30% H₂O₂. After 0.5 h, the mixture was extracted with a solution of 1:1 Et₂O/hexane (2 x 20 mL), the combined organic layers were washed with H₂O (10 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude reaction mixture on SiO₂ (5-15% Et₂O/hexanes gradient) afforded 0.233 g of the desired product, contaminated with AsPh₃.

This mixture was dissolved in DMF (1 mL) and treated with TBAF (1 mL of a 1 M solution in THF). After 0.5 h, the reaction mixture was diluted with H₂O (5 mL) and extracted with Et₂O (2 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO₂ (10-30% EtOAc/hexane) afforded 0.084 g (65% over two steps) of alcohol **11**.

Data for alcohol **11**: ^1H NMR (400 MHz, CDCl_3) δ 5.72 (m, 1 H), 5.19 (d, J = 2.1 Hz, 1 H), 5.04-4.93 (m, 2 H), 3.64-3.62 (m, 2 H), 3.17 (s, 3 H), 2.31 (dd, J = 13.6, 2.1 Hz, 1 H), 2.13 (dd, J = 13.6, 2.3 Hz, 1 H), 2.03-1.92 (m, 5 H), 1.80-1.20 (m, 14 H), 1.16 (s, 3 H), 0.88 (s, 9 H), 0.13 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.3,

138.9, 120.8, 114.5, 79.2, 76.9, 63.9, 48.3, 43.9, 41.7, 33.9, 31.6, 30.5, 30.1, 29.0, 28.0, 27.4, 26.1, 24.3, 22.4, 21.2, 18.8, -0.90, -1.30; IR (neat) 3372.2, 2959.1, 2861.3, 1463.1, 1256.5, 1060.8 cm⁻¹; ESIMS calcd for [C₂₆H₄₈O₃SiNa]⁺ 459.3, found 458.9 [M + Na]⁺.

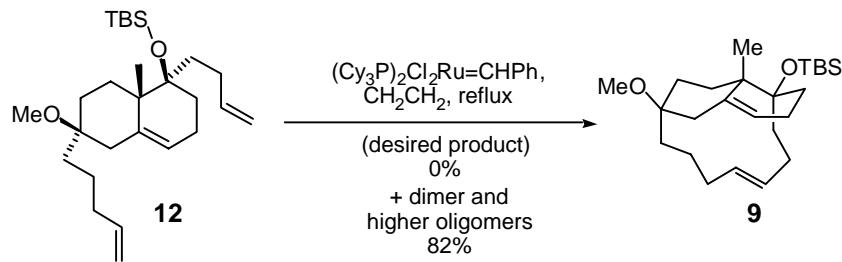


Procedure for olefin **12**: A solution of DMSO (0.040 mL, 0.57 mmol, 3 equiv) in CH₂Cl₂ (0.5 mL) at -78 °C was treated with oxalyl chloride (0.21 mL of a 2 M solution in CH₂Cl₂, 0.428 mmol, 2.25 equiv). After 15 min, this solution was treated with a solution of alcohol **11** in CH₂Cl₂ (0.5 mL), stirred an additional 0.5 h, then was treated with Et₃N and warmed to 23 °C. After 1 h, the reaction mixture was quenched with sat. aqueous NaHCO₃ (5 mL) and extracted with Et₂O (20 mL). The organic layer was washed with sat. aqueous NaHSO₄ (5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting aldehyde was used crude in the next reaction after drying *in vacuo* (ca. 0.05 mm Hg) for 2 h.

A suspension of methyl triphenylphosphonium bromide (0.081 g, 0.228 mmol, 1.2 equiv) in THF (0.5 mL) was treated with NaHMDS (0.22 mL of a 1 M solution in THF, 0.219 mmol, 1.15 equiv) at 0 °C. After 5 min, the mixture was cooled to -78 °C and was treated with a solution of the freshly prepared aldehyde in THF (0.5 mL). This mixture was stirred at -78 °C for 1 h, warmed to 0 °C for 15 min, then was quenched with sat. aqueous NH₄Cl (10 mL) and extracted with Et₂O (2 x 20 mL). The combined organic

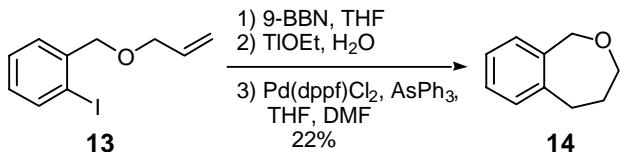
layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO_2 (5-20% Et_2O /hexane gradient) afforded 0.53 g (64% over 2 steps) of olefin **12**.

Data for olefin **12**: ^1H NMR (400 MHz, CDCl_3) δ 5.89-5.73 (m, 2 H), 5.19 (d, J = 2.2 Hz, 1 H), 5.05-4.93 (m, 4 H), 3.17 (s, 3 H), 2.33-1.88 (m, 9 H), 1.74-1.51 (m, 6 H), 1.49-1.28 (m, 5 H), 1.16 (s, 3 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.3, 139.5, 138.8, 120.9, 114.6, 114.0, 79.3, 76.7, 48.3, 43.9, 41.7, 34.9, 33.9, 30.4, 30.1, 29.0, 28.9, 27.3, 26.1, 24.3, 22.4, 21.3, 18.8, -1.0, -1.3; IR (neat) ν 3075.8, 2928.2, 2854.4, 1641.9, 1473.2, 1257.1, 1072.6 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{27}\text{H}_{48}\text{O}_2\text{Si}]^+$ 432.3424, found 432.3420 $[\text{M}]^+$.



Procedure for attempted ring closing metathesis (RCM) of **12**: A solution of olefin **12** (0.0486 g, 0.112 mmol) in CH_2Cl_2 (0.002 M) was treated with the Grubbs' catalyst⁶ $(\text{Cy}_3\text{P})_2\text{Cl}_2\text{Ru=CHPh}$ (0.006 g, 0.007 mmol, 0.06 equiv) and was refluxed under Ar for 2 h. An additional 0.008 g of catalyst was added to the reaction mixture and refluxing was continued for 46 h. The solution was cooled to 23 °C and the solvent removed *in vacuo*. Chromatography of the crude oil yielded 0.0216 g of a solid white material which, by ^1H NMR analysis, contained several (3-4) compounds in roughly equivalent amounts which resembled macrocycle **9**. However, mass spectroscopy of this mixture led to the identification of one of these compounds as a dimeric species (ESIMS

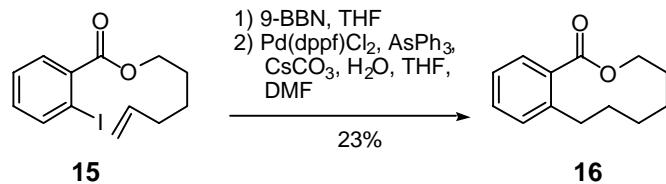
calc for $[C_{50}H_{89}O_4Si_2Na]^+$ 831.6, found 831.5 [dimer + Na] $^+$). A later eluting mixture of compounds (0.0154 g) was also obtained, also somewhat resembling by 1H NMR analysis, macrocycle **9**. The combined mass of these isolated products accounts for 84% of the material.



Procedure for ether **14**: Aryl iodide **13**⁷ (0.102 g, 0.397 mmol) in THF (0.8 mL) at 23 °C was treated with solid 9-BBN dimer (0.073 g, 0.595 mmol w/r monomer, 1.5 equiv) and the resulting mixture was stirred for 1 h. This mixture was then diluted with THF (4 mL) and treated with H₂O (0.021 mL, 1.19 mmol, 3 equiv) and then TIOEt (0.084 mL, 1.19 mmol, 3 equiv). This solution was added dropwise over 4 h (syringe pump) to a solution of Pd(dppf)Cl₂ (0.065 g, 0.079 mmol, 0.2 equiv) and AsPh₃ (0.024 g, 0.079 mmol, 0.2 equiv) in THF (120 mL) and DMF (12 mL) under an Ar atmosphere. After 9 h, the reaction mixture was treated with pH 7.2 phosphate buffer (10 mL) and 30% H₂O₂ (3 mL) and stirred at 23 °C for 1 h. This mixture was extracted with hexanes (2 x 30 mL) and the combined organic layers were washed with H₂O (10 mL), dried over MgSO₄, filtered and concentrated *in vacuo* (avoiding high vacuum as the product is volatile). Chromatography on SiO₂ (2-5% Et₂O/hexane gradient) afforded 0.013 g (22%) of cyclic ether **14**.

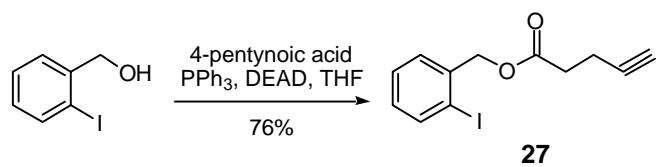
Data for ether **14** (the 1H NMR spectrum of this compound compares favorably to the spectrum of this compound taken in CHClF₂)⁸: 1H NMR (400 MHz, CDCl₃) δ 7.22-7.13 (m, 4 H), 4.67 (s, 2 H), 4.06 (t, J = 5.1 Hz, 2 H), 3.01 (t, J = 5.7 Hz, 2 H), 1.85 (m, 2 H); ^{13}C NMR (100 MHz, CDCl₃) δ 142.7, 140.0, 129.1, 128.5, 127.8, 126.1, 75.7, 75.0,

35.5, 30.3; IR (neat) ν 2933.8, 2843.6, 1725.4, 1459.9, 1094.1, 753.4 cm⁻¹; HRMS (DEI) calcd for [C₁₀H₁₃O]⁺ 148.0888, found 148.0884 [M]⁺.



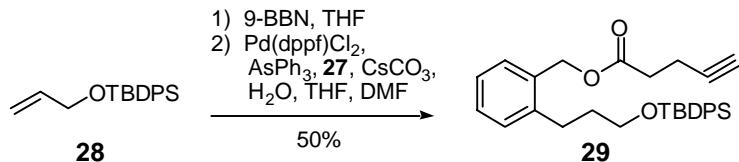
Procedure for lactone **16**: Aryl iodide **15**⁹ (0.083 g, 0.261 mmol) in THF (1.3 mL) at 23 °C was treated with solid 9-BBN dimer (0.073 g, 0.595 mmol w/r monomer, 2.3 equiv) and the resulting mixture was stirred for 2 h. This solution was added dropwise over 2.5 h to a solution of Pd(dppf)Cl₂ (0.042 g, 0.052 mmol, 0.2 equiv) and AsPh₃ (0.016 g, 0.052 mmol, 0.2 equiv) in THF (34 mL) and DMF (17 mL) under an Ar atmosphere. After 16 h, the reaction mixture was diluted with H₂O (20 mL) and extracted with a 1:1 Et₂O/hexane solvent mixture. The combined organic layers were washed with H₂O (10 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography on SiO₂ (2-10% Et₂O/hexane gradient) afforded 0.012 g (23%) of lactone **16**.

Data for lactone **16**: ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, J = 7.6, 1.3 Hz, 1 H), 7.37 (ddd, J = 7.4, 7.4, 1.4 Hz, 1 H), 7.26 (dd, J = 7.6, 1.1 Hz, 1 H), 7.22 (d, J = 7.7 Hz, 1 H), 4.44 (t, J = 5.4 Hz, 2 H), 2.86 (t, J = 7.5 Hz, 2 H), 1.83-1.72 (m, 4 H), 1.71-1.64 (m, 2 H), 1.53-1.47 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 169.0, 144.1, 131.6, 130.8, 130.4, 126.0, 65.9, 32.3, 29.0, 27.6, 26.1, 22.4; IR (neat) ν 2931.5, 1714.5, 1281.5 cm⁻¹; HRMS (EI) calcd for [C₁₃H₁₆O₂]⁺ 204.1150, found 204.1150 [M]⁺.



Procedure for ester **27**: A solution of 2-iodobenzyl alcohol (5.75 g, 24.6 mmol, 1.1 equiv) and 4-pentynoic acid (2.19 g, 22.3 mmol) in THF (20 mL) at 23 °C was treated with PPh₃ (8.2 g, 31.2 mmol, 1.4 equiv) and diethyl azodicarboxylate (4.6 mL, 29.0 mmol, 1.3 mmol). After 1 h, the reaction was diluted with sat. aqueous NaHCO₃ and the resulting mixture was extracted with Et₂O (2 x 50 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude residue on SiO₂ (5-15% Et₂O/hexane) afforded 5.9 g (76%) of ester **27**.

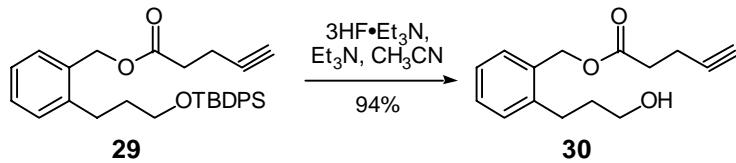
Data for ester **27**: ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, J = 7.9 Hz, 1 H), 7.40-7.33 (m, 2 H), 7.03 (td, J = 7.8, 1.9 Hz, 1 H), 5.17 (s, 2 H), 2.68-2.64 (m, 2 H), 2.58-2.50 (m, 2 H), 1.99 (t, J = 2.5 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.3, 139.5, 138.1, 129.9, 129.5, 128.3, 98.3, 82.3, 70.2, 69.2, 33.3, 14.3; IR (neat) ν 3296.2, 3060.8, 2921.7, 1738.6, 1160.9 cm^{-1} ; HRMS (DEI) calcd for $[\text{C}_{12}\text{H}_{11}\text{O}_2\text{I}]^+$ 313.9806, found 313.9807 $[\text{M}]^+$.



Procedure for silyl ether **29**: A solution of olefin **28** (0.5 g, 1.69 mmol, 1.2 equiv) in THF (3 mL) was treated at 23 °C with solid 9-BBN dimer (0.292 g, 2.39 mmol, 1.7 equiv). After 1.5 h, the borane solution was transferred via cannula to a mixture of aryl iodide **27** (0.441 g, 1.41 mmol), Pd(dppf)Cl₂ (0.106 g, 0.13 mmol, 0.09 equiv), AsPh₃ (0.086 g, 0.281 mmol, 0.2 equiv), and CsCO₃ (1.38 g, 4.22 mmol, 3 equiv) in a solvent mixture of THF (6 mL), DMF (3 mL) and H₂O (0.6 mL). After being stirred 1 h, the mixture was diluted with H₂O (10 mL) and extracted with a 1:1 Et₂O/hexane solution (2 x 30 mL). The combined organic layers were washed with H₂O (10 mL) and dried over

MgSO_4 , filtered and concentrated *in vacuo*. Silyl ether **29** (0.344 g, 50% yield) was isolated from the crude oil by chromatography on SiO_2 (5-15% Et_2O /hexane gradient).

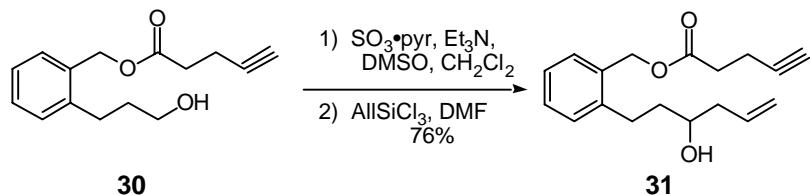
Data for silyl ether **29**: ^1H NMR (400 MHz, CDCl_3) δ 7.71-7.69 (m, 4 H), 7.46-7.28 (m, 7 H), 7.26-7.20 (m, 3 H), 5.19 (s, 2 H), 3.74 (t, J = 6.1 Hz, 2 H), 2.79 (dd, J = 9.9, 7.8 Hz, 2 H), 2.59-2.55 (m, 2 H), 2.52-2.48 (m, 2 H), 1.95 (t, J = 2.4 Hz, 1 H), 1.85 (m, 2 H), 1.09 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.5, 141.2, 135.6, 133.9, 133.3, 129.8, 129.6, 129.5, 128.7, 127.6, 126.1, 82.4, 69.1, 64.5, 63.2, 33.9, 33.3, 28.7, 26.9, 19.2, 14.3; IR (neat) ν 3296.7, 3067.1, 2931.5, 2858.5, 1740.6, 1427.6, 1161.5, 1109.4 cm⁻¹; ESIMS calcd for $[\text{C}_{31}\text{H}_{36}\text{O}_3\text{SiNa}]^+$ 507.2, found 507.2 $[\text{M} + \text{Na}]^+$.



Procedure for alcohol **30**: Silyl ether **29** (0.34 g, 0.70 mmol) in CH_3CN (2 mL) was treated with Et_3N (0.6 mL, 4.2 mmol, 6 equiv) and 3HF• Et_3N (0.34 mL, 2.1 mmol, 3 equiv) at 23 °C. After being stirred for 5 h, the reaction was quenched with H_2O (10 mL) and extracted with Et_2O (2 x 20 mL). The combined organic layers were washed with sat. aqueous NaHCO_3 (10 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude oil was chromatographed on SiO_2 (10-30% EtOAc /hexanes gradient), affording 0.163 g (94% yield) of alcohol **30** as a colorless oil.

Data for alcohol **30**: ^1H NMR (400 MHz, CDCl_3) δ 7.36-7.19 (m, 4 H), 5.21 (s, 2 H), 3.69 (t, J = 6.2 Hz, 2 H), 2.77 (dd, J = 9.5, 7.7 Hz, 2 H), 2.62-2.58 (m, 2 H), 2.54-2.49 (m, 2 H), 1.98 (t, J = 2.4 Hz, 1 H), 1.91-1.84 (m, 2 H), 1.64 (bs, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.6, 140.8, 133.3, 129.9, 129.5, 128.8, 126.2, 82.4, 69.1, 64.5, 62.1, 33.9, 33.3, 28.5, 14.3; IR (neat) ν 3416.3, 3296.0, 3025.3, 2935.0, 2874.9, 2122.9,

1730.6, 1384.6, 1159.0, 1058.8 cm⁻¹; ESIMS calcd for $[C_{15}H_{18}O_3Na]^+$ 269.1, found 268.6 $[M + Na]^+$.

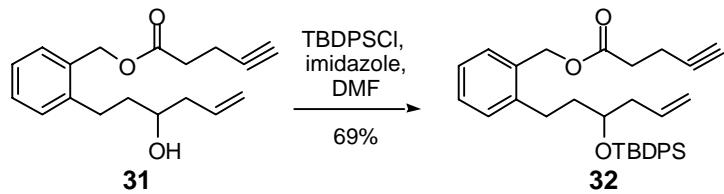


Procedure for alcohol **31**:¹⁰ Alcohol **30** (0.147 g, 0.598 mmol) in CH₂Cl₂ (4 mL) and DMSO (1 mL) was treated at 23 °C with Et₃N (0.430 mL, 3.11 mmol, 5.2 equiv) followed by SO₃•py (0.381 g, 2.39 mmol, 4 equiv). After being stirred 12 h, the reaction mixture was diluted with NaHCO₃ (5 mL) and extracted with Et₂O (2 x 20 mL). The combined organic layers were washed with sat. aqueous NaHSO₄ (5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The crude aldehyde was dried *in vacuo* (ca. 0.1 mm Hg) for 2 h.

Data for the aldehyde intermediate: ^1H NMR (400 MHz, CDCl_3) δ 9.84 (s, 1 H), 7.37-7.21 (m, 4 H), 5.20 (s, 2 H), 3.01 (t, J = 7.4 Hz, 2 H), 2.80 (t, J = 7.8 Hz, 2 H), 2.59 (m, 2 H), 2.54-2.50 (m, 2 H), 1.97 (t, J = 2.4 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 201.0, 171.5, 139.5, 133.3, 130.3, 129.3, 129.1, 126.7, 82.3, 69.2, 64.6, 44.9, 33.3, 24.5, 14.3; IR (neat) ν 3284.8, 2922.5, 1726.8, 1154.0 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{15}\text{H}_{20}\text{NO}_3]^+$ 262.1443, found 262.1447 $[\text{M} + \text{NH}_4]^+$.

The freshly prepared aldehyde was dissolved in DMF (2 mL) and was treated at 23 °C with allyltrichlorosilane (0.260 mL, 1.79 mmol, 3 equiv).¹¹ After 3 h, the reaction was quenched with sat. aqueous NaHCO₃ (5 mL) and extracted with Et₂O (2 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography on SiO₂ (10-30% Et₂O/hexane gradient) afforded 0.130 g (76%) of alcohol **31** as a colorless oil.

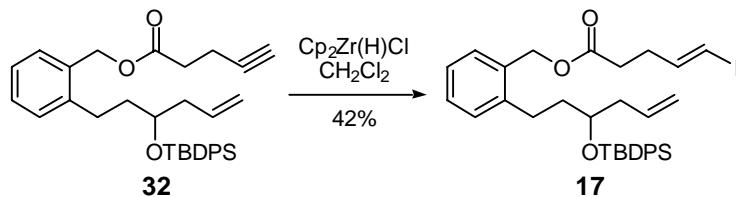
Data for alcohol **31**: ^1H NMR (400 MHz, CDCl_3) δ 7.36-7.19 (m, 4 H), 5.83 (m, 1 H), 5.25-5.13 (m, 4 H), 3.61 (m, 1 H), 2.88 (ddd, J = 14.0, 9.9, 5.6 Hz, 1 H), 2.73 (ddd, J = 13.9, 9.7, 6.9 Hz, 1 H), 2.62-2.58 (m, 2 H), 2.54-2.49 (m, 2 H), 2.31 (m, 1 H), 2.20 (dt, J = 15.3, 7.8 Hz, 1 H), 1.98 (t, J = 2.4 Hz, 1 H), 1.89 (bs, 1 H), 1.83-1.68 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 141.6, 134.9, 133.7, 130.4, 130.0, 129.2, 126.6, 118.8, 82.8, 70.3, 69.6, 65.0, 42.6, 38.6, 33.8, 28.9, 14.8; IR (neat) ν 3461.1, 3294.6, 2922.5, 1736.6, 1163.8 cm^{-1} ; HRMS (DEI) calcd for $[\text{C}_{18}\text{H}_{23}\text{O}_3]^+$ 287.1647, found 287.1645 $[\text{M} + \text{H}]^+$.



Procedure for **32**: A solution of alcohol **31** (0.150 g, 0.524 mmol) in DMF (1 mL) was treated at 23 °C with imidazole (0.050 g, 0.734 mmol, 1.4 equiv) and TBDPSCl (0.164 mL, 0.629 mmol, 1.2 equiv). After being stirred for 16 h, the reaction mixture was diluted with H_2O (5 mL) and extracted with Et_2O (2 x 20 mL). The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. Chromatography on SiO_2 (5-10% Et_2O /hexane gradient) afforded 0.191 g (69%) of silyl ether **32** as a colorless oil.

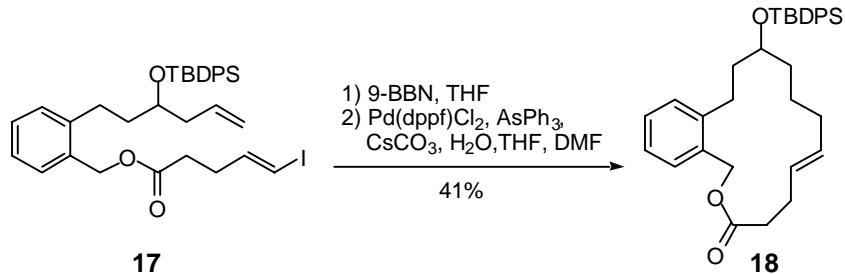
Data for silyl ether **32**: ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.70 (m, 4 H), 7.47-7.37 (m, 6 H), 7.31 (dd, J = 7.4, 1.0 Hz, 1 H), 7.25-7.15 (m, 2 H), 7.05 (d, J = 7.5 Hz, 1 H), 5.76 (m, 1 H), 5.11 (s, 2 H), 5.08-4.96 (m, 2 H), 3.90 (m, 1 H), 2.70 (ddd, J = 11.2, 7.9, 5.5 Hz, 1 H), 2.59-2.47 (m, 5 H), 2.35-2.24 (m, 2 H), 1.96 (t, J = 2.4 Hz, 1 H), 1.78-1.66 (m, 2 H), 1.10 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.4, 135.9, 135.9, 134.5, 134.3, 134.2, 133.2, 129.8, 129.6, 129.6, 129.3, 128.7, 127.6, 127.5, 126.0, 117.2, 82.4, 72.5, 69.1, 64.4, 41.1, 37.5, 33.3, 28.0, 27.1, 19.4, 14.3; IR (neat) ν 3301.8, 3066.6,

2933.6, 2862.0, 1740.6, 1428.6, 1157.6, 1111.6 cm⁻¹; HRMS (DCI, NH₃) calcd for [C₃₄H₄₄NO₃Si]⁺ 542.3090, found 542.3103 [M + NH₄]⁺.



Procedure for vinyl iodide **17**:¹² A solution of alkyne **32** (0.205 g, 0.390 mmol) in CH₂Cl₂ (2 mL) at 23 °C was treated with Cp₂Zr(H)Cl. After 50 min, the reaction mixture was treated with 0.6 mL of a solution of I₂ (0.1 g, 0.390 mmol) in 1 mL of THF (addition of iodine was ceased after the red color of I₂ persisted in the solution). This solution was stirred 10 min, then diluted with H₂O (5 mL) and extracted with Et₂O (2 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography on SiO₂ (5-15% Et₂O/hexane gradient) afforded 0.165 g of a 2:1 mixture of vinyl iodide **17** and the starting alkyne **32**. Separation of this mixture by HPLC afforded 0.107 g (42%) of the pure **17**.

Data for vinyl iodide **17**: ^1H NMR (400 MHz, CDCl_3) δ 7.72-7.69 (m, 4 H), 7.46-7.36 (m, 6 H), 7.28 (dd, J = 7.4, 1.3 Hz, 1 H), 7.21 (m, 2 H), 7.04 (dd, J = 7.5, 0.7 Hz, 1 H), 6.49 (dt, J = 14.4, 6.6 Hz, 1 H), 6.07 (d, J = 14.4 Hz, 1 H), 5.75 (m, 1 H), 5.08 (s, 1 H), 5.05-4.95 (m, 2 H), 3.90 (m, 1 H), 2.69 (ddd, J = 13.8, 11.5, 5.8 Hz, 1 H), 2.55 (ddd, J = 14.0, 10.9, 6.0 Hz, 1 H), 2.41-2.20 (m, 6 H), 1.77-1.64 (m, 2 H), 1.09 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 144.0, 141.5, 135.9, 135.9, 134.5, 134.3, 133.2, 129.8, 129.6, 129.6, 129.4, 128.7, 127.6, 127.5, 126.1, 117.2, 72.5, 64.3, 41.1, 37.5, 32.8, 31.1, 27.9, 27.1, 19.4; IR (neat) ν 3070.0, 2930.2, 2856.5, 1737.1, 1427.5, 1176.5, 1111.2 cm^{-1} ; HRMS (DCM/NBA) calcd for $[\text{C}_{34}\text{H}_{42}\text{O}_3\text{ISi}]^+$ 653.1950, found 653.1954 $[\text{M} + \text{H}]^+$.



Procedure for macrocycle **18**: A solution of vinyl iodide **17** (0.106 g, 0.162 mmol) in THF (0.8 mL) was treated with solid 9-BBN dimer (0.030 g, 0.244 mmol w/r to monomer, 1.5 equiv) at 23 °C. After being stirred for 1.5 h, the solution was added dropwise over 1 h to a solution of Pd(dppf)Cl₂ (0.027 g, 0.032 mmol, 0.2 equiv), AsPh₃ (0.010 g, 0.032 mmol, 0.2 equiv) in THF (26 mL) and DMF (13 mL) under an Ar atmosphere. This mixture was stirred an additional 3 h, then was diluted with H₂O (20 mL) and extracted with a 1:1 mixture of Et₂O/hexane (2 x 40 mL). The combined organic layers were washed with H₂O (10 mL) and dried over MgSO₄, filtered and concentrated *in vacuo*. Chromatography of the crude oil on SiO₂ (5-15% Et₂O/hexane gradient) afforded 35 mg (41%) of macrocycle **18** as a colorless oil.

Data for macrocycle **18**: ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.70 (m, 4 H), 7.47-7.37 (m, 6 H), 7.25-7.14 (m, 3 H), 6.92 (d, J = 7.3 Hz, 1 H), 5.39 (dt, J = 15.1, 7.3 Hz, 1 H), 5.28 (m, 1 H), 5.10 (A of ABq, J = 11.7 Hz, 1 H), 4.96 (B of ABq, J = 11.7 Hz, 1 H), 3.81 (m, 1 H), 2.55 (ddd, J = 15.4, 11.7, 5.1 Hz, 1 H), 2.44-2.28 (m, 5 H), 1.95 (m, 1 H), 1.81-1.70 (m, 3 H), 1.57-1.39 (m, 4 H), 1.09 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.2, 142.0, 135.9, 134.7, 134.4, 132.8, 131.9, 131.2, 129.5, 129.5, 129.3, 128.3, 127.5, 127.5, 125.9, 71.8, 65.5, 36.4, 34.1, 33.3, 30.7, 27.5, 27.1, 26.7, 23.2, 19.4; IR (neat) 2968.1, 2928.8, 1732.6, 1619.1, 1599.5, 1476.6, 1205.4, 1179.9, 1031.0 cm^{-1} ; HRMS (DCI, NH_3) calcd for $[\text{C}_{34}\text{H}_{43}\text{O}_3\text{Si}]^+$ 527.2981, found 527.2963 $[\text{M} + \text{H}]^+$.

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