Intramolecular Silicon-Assisted Cross-Coupling: Total Synthesis of (+)-Brasilenyne

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SUPPORTING INFORMATION

General Experimental

All reactions were performed in oven-dried (140 °C) or flame-dried glassware under an inert atmosphere of dry Ar or N₂. The following reaction solvents were distilled from the indicated drying agents: diethyl ether (Na, benzophenone), THF (Na, benzophenone), CH₂Cl₂ (P₂O₅), benzene (Na), toluene (Na), methanol (Mg(OMe)₂), triethylamine (CaH₂). *n*-Butyllithium solutions were titrated following the method of Gilman¹. Brine refers to a saturated aqueous solution of NaCl. Grignard solutions were titrated using 2,2'-phenanthroline as an indicator.² Kugelrohr distillations were performed on a Büchi GKR-50 Kugelrohr; boiling points (bp) corresponding to uncorrected air-bath temperatures (ABT). All reaction temperatures correspond to internal temperatures measured by Teflon-coated thermocouples unless otherwise noted.

¹H NMR spectra and ¹³C NMR spectra were recorded on a Varian Unity 400 (400 MHz, ¹H; 100 MHz, ¹³C), Unity 500 (500 MHz, ¹H; 126 MHz, ¹³C). Spectra are referenced to residual chloroform (7.26 ppm, ¹H; 77.0 ppm, ¹³C) and residual acetone (2.04 ppm, ¹H; 29.8 ppm, ¹³C). Chemical shifts are reported in ppm (); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. Mass spectroscopy was performed by the University of Illinois Mass Spectrometer Center. Electron impact (EI) spectra were performed on a Finnigan-MAT CH-5 spectrometer. Data are reported in the form of *m/z* (intensity relative to base peak = 100). Infrared spectra (IR) were recorded on a Mattson Galaxy 5020 spectrophotometer. Peaks are reported in cm⁻¹ with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Optical rotations were measured on Jasco DIP-360 polarimeter and were reported as follows: concentration (*c* = g/100 mL), solvent. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

Analytical thin-layer chromatography was performed on Merck silica or aluminum oxide, basic gel plates with QF-254 indicator. Visualization was accomplished with UV light and/or

Iodide. Diethyl ether was of reagent grade and used as received; other solvents for chromatography and filtration were technical grade and distilled from the indicated drying agents: hexane and pentane (CaCl_2); CH_2Cl_2 (CaCl_2); ethyl acetate (K_2CO_3). Column chromatography was performed using EM Science 230-400-mesh silica gel or Aldrich 150-mesh aluminum oxide, activated, basic, Brockmann I.

Analytical capillary gas chromatography (GC) was performed using the following gas chromatography fitted with a flame ionization detector (H_2 carrier gas, 1 mL/min): Hewlett Packard 5890 Series II. The following column was used: HP-5 50-m cross-linked 5%-Phenyl methyl silicone gum phase or Ultra-2 50-m cross-linked 5%-Phenyl methyl silicone gum phase. The detector temperature was 300 °C. Retention times (t_R) and integrated ratios were obtained from Hewlett Packard 3393A integrators.

All commercial reagents were purified by distillation or recrystallization prior to use. A 1.0 M solution of tetrabutylammonium fluoride in THF was prepared from solid tetrabutylammonium fluoride trihydrate ($\text{TBAF} \cdot 3\text{H}_2\text{O}$, Fluka) and distilled THF in a volumetric flask and was stored in a Schlenk bottle. -Allylpalladium chloride dimer [allylPdCl] $_2$ (APC) was purchased from ACROS and was recrystallized from benzene prior to use.

Scheme 1. Total Synthesis of (+)-Brasilenyne

Experimental Procedures

Preparation of 2-[(4*S*)-2-Ethyl-5-oxo-1,3-dioxolan-4-yl]acetic acid (**13**)

In a three-neck, 250 mL flask was placed L-(*S*)-malic acid (6.7 g, 50 mmol, purchased from Aldrich, 99% ee/CSP-GLC) and propanal (3.97 mL, 55 mmol, 1.1 equiv) in Et₂O (100 mL) under N₂ at –30 °C. BF₃·Et₂O (19.0 mL, 150 mmol, 3.0 equiv) was then added dropwise over 30 min. After complete addition of BF₃·Et₂O, the mixture was allowed to warm to 0 °C and was stirred for 1.5 h. The mixture was then poured into H₂O (100 mL) and was separated. The aqueous layer was extracted with Et₂O (2 x 100 mL). The combined organic layers were washed with brine (2 x 100 mL), then was dried (Na₂SO₄), and filtered. The ethereal solvent was removed by rotary evaporation and was then dried *in vacuo* to afford 7.4 g (85%) of crude **13** (*cis:trans* = 81:19), which was directly subjected to next reaction without further purification. (This reaction can be run on a 200 mmol scale in 84% yield.)

Analytical Data for **13** (*cis:trans* = 81:19):

¹H NMR: (500 MHz, CDCl₃)

(*cis*-isomer) 11.0 (br s, 1 H, HO), 5.52 (td, *J* = 4.5, 1.0, 1 H, HC(2)), 4.62 (ddd, *J* = 7.0, 4.0, 1.0, 1 H, HC(4)), 3.02 (dd, *J* = 17.5, 4.0, 1 H, HC(1'')), 2.84 (dd, *J* = 17.5, 7.0, 1 H, HC(1')), 1.88-1.78 (m, 2 H, H₂C(1')), 0.99 (t, *J* = 7.5, 3 H, H₃C(2'))

(*trans*-isomer) 11.0 (br s, 1 H, HO), 5.68 (td, *J* = 5.0, 1.5, 1 H, HC(2)), 4.65 (ddd, *J* = 5.5, 4.0, 1.5, 1 H, HC(4)), 2.96 (dd, *J* = 17.5, 4.0, 1 H, HC(1'')), 2.91 (dd, *J* = 17.5, 6.0, 1 H, HC(1')), 1.88-1.78 (m, 2 H, H₂C(1')), 0.98 (t, *J* = 7.5, 3 H, H₃C(2'))

¹³C NMR: (126 MHz, CDCl₃)

(*cis*-isomer) 175.2 (C(2')), 172.2 (C(5)), 105.6 (C(2)), 71.1 (C(4)), 35.3 (C(1')), 26.8 (C(1')), 6.7 (C(2'))

(*trans*-isomer) 175.5 (C(2')), 172.1 (C(5)), 106.8 (C(2)), 70.1 (C(4)), 35.5 (C(1')), 26.9 (C(1')), 6.7 (C(2'))

Preparation of 2-[(4S)-2-Ethyl-5-oxo-1,3-dioxolan-4-yl]ethanol (**14**)

In a three-neck, 250 mL flask was placed **13** (7.4 g, 42.5 mmol) in THF (40 mL) under N₂ at 0 °C. BH₃·THF (0.55 in THF, 85 mL, 46.75 mmol, 1.1 equiv) was then added dropwise with gentle bubbling was observed. After complete addition of BH₃·THF, the mixture was stirred at 0 °C for 3 h. MeOH (40 mL) was then added dropwise at 0 °C. After complete addition of MeOH, the mixture was directly concentrated. The residue was dissolved in CH₂Cl₂ (50 mL)/H₂O (50 mL) and was separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were dried (Na₂SO₄), and filtered. The solvent was removed by rotary evaporation and was then dried *in vacuo* to afford 5.6 g (82%) of crude **14** (*cis:trans* = 83:17), which was directly subjected to next reaction without further purification. (This reaction can be run on a 168 mmol scale in 82% yield.)

Analytical Data for **14** (*cis:trans* = 83:17):

¹H NMR: (500 MHz, CDCl₃)

(*cis*-isomer) 5.51 (td, *J* = 4.5, 1.0, 1 H, HC(2)), 4.45 (ddd, *J* = 7.0, 4.5, 1.0, 1 H, HC(4)), 3.89-3.80 (m, 2 H, H₂C(2'')), 2.19 (dtd, *J* = 14.5, 7.5, 5.0, 1 H, HC(1'')), 2.04 (ddt, *J* = 14.5, 7.0, 5.0, 1 H, HC(1')), 1.87 (qd, *J* = 7.5, 4.5, 2 H, H₂C(1')), 1.85 (br s, 1 H, HO), 1.02 (t, *J* = 7.5, 3 H, H₃C(2'))

(*trans*-isomer) 5.67 (td, *J* = 5.0, 1.0, 1 H, HC(2)), 4.55 (ddd, *J* = 7.0, 5.0, 1.0, 1 H, HC(4)), 3.89-3.80 (m, 2 H, H₂C(1)), 2.05-2.00 (m, 2 H, H₂C(1'')), 1.83 (qd, *J* = 7.5, 4.5, 2 H, H₂C(1')), 1.85 (br s, 1 H, HO), 1.00 (t, *J* = 7.5, 3 H, H₃C(2'))

¹³C NMR: (126 MHz, CDCl₃)

(*cis*-isomer) 173.8 (C(5)), 105.3 (C(2)), 79.2 (C(4)), 58.6 (C(2'')), 33.3 (C(1'')), 26.9 (C(1')), 6.7 (C(2'))

(*trans*-isomer) 174.0 (C(5)), 106.1 (C(2)), 71.7 (C(4)), 58.4 (C(2'')), 33.0 (C(1'')), 27.8 (C(1')), 6.8 (C(2'))

Preparation of *t*-Butyldimethyl-{2-[(4*S*)-2-ethyl-5-oxo-1,3-dioxolan-4-yl]ethoxy}-dimethylsilane (6**)**

In a three-neck, 100 mL flask was placed *t*-butylchlorodimethylsilane (7.91 g, 52.5 mmol, 1.5 equiv) in CH₂Cl₂ (20 mL) under N₂ at room temperature. Pyridine (8.48 mL, 105 mmol, 3.0 equiv) was then added dropwise. The mixture was stirred for 10 min and a solution of **14** (5.6 g, 35.0 mmol) in CH₂Cl₂ (15 mL) was added dropwise. The mixture was stirred for 4 h whereupon a white suspension was obtained. The mixture was poured into H₂O (35 mL) and the aqueous layer was extracted with CH₂Cl₂ (3 x 35 mL). The combined organic layers were dried (Na₂SO₄), and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 1/0 to 19/1) followed by Kugelrohr distillation to afford 8.15 g (85%) of **6** (*cis:trans* = 83:17) as a colorless liquid. (This reaction can be run on a 138 mmol scale in 83% yield.)

Analytical Data for **6** (*cis:trans* = 84:16):

bp: 110-115 °C (0.1 mmHg, ABT)

¹H NMR: (500 MHz, CDCl₃)

(*cis*-isomer) 5.48 (td, *J* = 4.5, 1.0, 1 H, HC(2)), 4.42 (ddd, *J* = 8.5, 4.5, 1.0, 1 H, HC(4)), 3.83 (dt, *J* = 10.5, 5.0, 1 H, HC(2'')), 3.74 (ddd, *J* = 10.5, 8.0, 5.0, 1 H, HC(2'')), 2.11 (dddd, *J* = 14.0, 8.0, 5.5, 4.0, 1 H, HC(1'')), 1.92-1.78 (m, 3 H, HC(1''), H₂C(1')), 1.00 (t, *J* = 7.5, 3 H, H₃C(2')), 0.88 (s, 9 H, 3 x H₃C(5'')), 0.05 (s, 6 H, 2 x H₃C(3''))

(*trans*-isomer) 5.62 (td, *J* = 4.5, 1.0, 1 H, HC(2)), 4.51 (ddd, *J* = 6.0, 5.0, 1.0, 1 H, HC(4)), 3.84-3.80 (m, 1 H, HC(2'')), 3.75-3.71 (m, 1 H, HC(2'')), 2.00-1.95 (m, 2 H, H₂C(1'')), 1.90-1.78 (m, 2 H, H₂C(1')), 0.99 (t, *J* = 7.5, 3 H, H₃C(2')), 0.87 (s, 9 H, 3 x H₃C(5'')), 0.05 (s, 6 H, 2 x H₃C(3''))

¹³C NMR: (126 MHz, CDCl₃)

(*cis*-isomer) 173.8 (C(5)), 105.0 (C(2)), 71.6 (C(4)), 58.2 (C(2'')), 33.9 (C(1'')), 27.0 (C(1')), 25.8 (3 x C(5'')), 18.2 (C(4'')), 6.7 (C(2'')), -5.5 (C(3'')), -5.6 (C(3''))

(*trans*-isomer) 173.9 (C(5)), 105.9 (C(2)), 70.8 (C(4)), 58.1 (C(2'')), 33.4 (C(1'')), 27.8 (C(1')), 25.8 (3 x C(5'')), 18.2 (C(4'')), 6.8 (C(2')), -5.56 (C(3'')), -5.63 (C(3''))

IR: (NaCl)

2954 (s), 2931 (s), 2885 (s), 1803 (s), 1739 (m), 1467 (m), 1409 (m), 1255 (s), 1199 (s), 1106 (s), 1008 ("m), 954 (s), 838 (s), 777 (s)

MS: (EI, 70 eV)

275 (59, M⁺ + 1), 274 (M⁺, 1), 259 (18), 245 (10), 217 (100), 173 (8), 131 (72), 115 (19), 101 (10)

TLC: R_f 0.30 (silica gel, hexane/EtOAc, 19/1, PMA)

Analysis: C₁₃H₂₆O₄Si (274.44)

Calculated: C, 56.90; H, 9.55%

Found: C, 56.84; H, 9.71%

Preparation of (3*S*)-{[(1*S*)-1-Ethyl-3-trimethylsilylpropynyl]oxy}tetrahydrofuran-2-one (**5**)

In a three-neck, 250 mL flask was placed **6** (5.48 g, 20.0 mmol, 1.5 equiv) and bis(trimethylsilyl)acetylene (6.8 g, 40.0 mmol, 2.0 equiv) in CH₂Cl₂ (100 mL) under N₂ at -72 °C. A freshly distilled TiCl₄ (3.07 mL, 28.0 mmol, 1.4 equiv) was then added in one portion. The resulting yellow solution was stirred at -72 °C for 3 h and MeOH (40 mL) was added. The mixture was allowed to warm to room temperature and was stirred for 30 min. The mixture was then directly concentrated and the residue was dissolved in CH₂Cl₂ (50 mL)/H₂O (50 mL). The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were dried (Na₂SO₄), and filtered. After removal of solvent, the residue was dissolved in benzene (50 mL). *p*-Toulenesulfonic acid monohydrate (38 mg, 0.02 mmol, 0.01 equiv) was then added and the mixture was heated to reflux for 1 h in a Dean-Stark apparatus. After cooling, the solvent was removed by rotary evaporation to give a crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 9/1) followed by Kugelrohr distillation to afford 4.13 g (86%) of **5** as a white solid. (This reaction can be run on a 40.0 mmol scale in 83% yield.)

Analytical Data for 5:

bp: 105-110 °C (0.3 mmHg, ABT)

¹H NMR: (500 MHz, CDCl₃)

4.62 (t, *J* = 7.0, 1 H, HC(3')), 4.48 (ddd, *J* = 8.0, 1 H, HC(3)), 4.39 (td, *J* = 9.0, 4.0, 1 H, HC(5)), 4.24 (ddd, *J* = 9.0, 8.5, 6.5, 1 H, HC(5)), 2.55 (dddd, *J* = 13.0, 8.0, 7.0, 4.0, 1 H, HC(4)), 2.29 (dq, *J* = 13.0, 8.5, 1 H, HC(4)), 1.80-1.66 (m, 2 H, H₂C(4')), 0.99 (t, *J* = 7.5, 3 H, H₃C(5')), 0.17 (s, 9 H, 3 x H₃C(6'))

¹³C NMR: (126 MHz, CDCl₃)

175.4 (C(2)), 103.7 (C(1')), 91.4 (C(2')), 70.98, 70.95, 65.4 (C(5)), 30.1 (C(4)), 28.7 (C(4')), 9.4 (C(5')), -0.2 (3 x C(6'))

IR: (NaCl)

2966 (s), 2894 (m), 2173 (m), 1764 (s), 1450 (m), 1384 (m), 1294 (m), 1249 (s), 1216 (s), 1180 (s), 1128 (s), 1105 (s), 1022 (s), 968 (s), 881 (m), 842 (s), 761 (s)

MS: (EI, 70 eV)

240 (1, M⁺), 225 (8), 211 (18), 183 (6), 158 (30), 155 (58), 139 (16), 131 (25), 123 (26), 109 (35), 97 (100), 86 (66), 73 (24)

Opt. Rot.: [α]_D²⁴ -138.6 (*c* = 1.08, CHCl₃)TLC: *R*_f 0.15 (silica gel, hexane/EtOAc, 19/1, PMA)Analysis: C₁₂H₂₀O₃Si (240.38)

Calculated: C, 59.96; H, 8.39%

Found: C, 59.72; H, 8.39%

Preparation of (3*S*)-{[(1*S*)-1-Ethyl-3-iodopropynyl]oxy}tetrahydrofuran-2-one (7)

In a three-neck, 100 mL flask was placed **5** (2.4 g, 10.0 mmol, 1.5 equiv) in DMF (20 mL) under N₂ at room temperature. *N*-Iodosuccinimide (2.7 g, 12.0 mmol, 1.2 equiv) and AgNO₃ (170 mg, 1.0 mmol, 0.1 equiv) was then added sequentially. The mixture was stirred at room temperature for 10 min and Et₂O (50 mL) was added. The mixture was washed with saturated aqueous NH₄Cl solution (2 x 25 mL). The aqueous layer was extracted with Et₂O (25 mL). The combined organic layers were washed with brine (30 mL), then were dried (Na₂SO₄),

and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 4/1) to afford 2.8 g (95%) of **7** as a pale yellow oil. (This reaction can be run on a 40.0 mmol scale in 93% yield.)

Analytical Data for **7:**

¹H NMR: (500 MHz, CDCl₃)

4.80 (t, *J* = 7.5, 1 H, HC(3')), 4.46 (t, *J* = 8.0, 1 H, HC(3)), 4.39 (td, *J* = 8.5, 4.0, 1 H, HC(5)), 4.24 (td, *J* = 8.5, 7.0, 1 H, HC(5)), 2.59-2.53 (m, 1 H, HC(4)), 2.28 (dq, *J* = 13.5, 8.5, 1 H, HC(4)), 1.79-1.69 (m, 2 H, H₂C(4')), 0.99 (t, *J* = 7.5, 3 H, H₃C(5'))

¹³C NMR: (100 MHz, CDCl₃)

175.3 (C(2)), 92.9 (C(2')), 71.7, 71.0, 65.4 (C(5)), 29.9 (C(4)), 28.9 (C(4')), 9.4 (C(5')), 9.4 (C(1'))

IR: (NaCl)

2971 (s), 2937 (s), 2877 (s), 2179 (m), 1776 (s), 1461 (s), 1382 (s), 1326 (s), 1220 (s), 1180 (s), 1130 (s), 1006 (s), 948 (s), 889 (m), 808 (m), 715 (m)

MS: (EI, 70 eV)

295 (21, M⁺ + 1), 265 (10), 237 (3), 209 (4), 193 (48), 167 (41), 143 (11), 103 (100), 85 (37), 83 (45), 66 (53)

Opt. Rot.: [α]_D²⁴ -122.7 (*c* = 1.17, CHCl₃)

TLC: *R*_f 0.21 (silica gel, hexane/EtOAc, 4/1, PMA)

Analysis: C₉H₁₁O₃I (294.09)

Calculated: C, 36.76; H, 3.77, I, 43.15%

Found: C, 36.50; H, 3.69, I, 42.88%

Preparation of (3*S*)-{[(1*S*,2*Z*)-1-Ethyl-3-iodo-2-propenyl]oxy}tetrahydrofuran-2-one (8**)**

In a three-neck, 50 mL flask was placed **7** (3.53 g, 12 mmol) and potassium azodicarboxylate (KO₂CN=NCO₂K) (3.49 g, 18 mmol, 1.5 equiv) in THF (12 mL)/*i*-PrOH (12 mL) under N₂ at room temperature. Acetic acid (1.97 mL, 36 mmol, 3.0 equiv) was then added slowly by syringe pump over 1 h. After complete addition of acetic acid, the mixture was stirred

for 1 h and additional potassium azodicarboxylate (3.49 g, 18 mmol, 1.5 equiv). Again, acetic acid (1.97 mL, 36 mmol, 3.0 equiv) was then added slowly by syringe pump over 1 h. After complete addition of acetic acid, the mixture was stirred for 1 h and additional potassium azodicarboxylate (1.16 g, 6 mmol, 0.5 equiv) and acetic acid (0.68 mL, 12 mmol, 1.0 equiv) were added sequentially by a procedure described above. The mixture was then poured into a 250 mL beaker together with Et₂O (20 mL) and aqueous HCl solution (3.0 M, 20 mL). The aqueous layer was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine (2 x 20 mL), then was dried (Na₂SO₄), and filtered. After removal of solvent, the residue was treated with pyridine (5 mL) and the mixture was stirred at room temperature for 12 h to remove the small amount of over reduction product. The mixture was dissolved in CH₂Cl₂ (20 mL) which was washed with aqueous HCl solution (3.0 M, 2 x 20 mL). The combined aqueous layers were extracted with CH₂Cl₂ (2 x 20 mL). The combined organic layers were dried (Na₂SO₄), and filtered. The solvent was removed by rotary evaporation to give a crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 4/1) followed by Kugelrohr distillation to afford 2.84 g (80%) of **8** as a pale yellow oil. (This reaction can be run on a 40.0 mmol scale in 78% yield.)

Analytical Data for **8**:

bp: 155-160 °C (0.3 mmHg, ABT)

¹H NMR: (500 MHz, CDCl₃)

6.54 (dd, *J* = 8.0, 1.0, 1 H, HC(1')), 6.13 (t, *J* = 8.0, 1 H, HC(2')), 4.58 (q, *J* = 7.0, 1 H, HC(3')), 4.37 (td, *J* = 9.0, 3.5, 1 H, HC(5)), 4.19 (td, *J* = 9.0, 6.5, 1 H, HC(5)), 4.15 (t, *J* = 8.0, 1 H, HC(3)), 2.45 (dddd, *J* = 13.0, 8.0, 6.5, 3.5, 1 H, HC(4)), 2.21 (dq, *J* = 13.0, 9.0, 1 H, HC(4)), 1.72 (d quint, *J* = 14.5, 7.5, 1 H, HC(4')), 1.57 (d quint, *J* = 14.5, 7.5, 1 H, HC(4')), 0.97 (t, *J* = 7.5, 3 H, H₃C(5'))

¹³C NMR: (126 MHz, CDCl₃)

175.2 (C(2)), 141.0 (C(2')), 85.2 (C(1')), 82.8 (C(3')), 71.4 (C(3)), 65.0 (C(5)), 30.3 (C(4)), 27.4 (C(4')), 9.3 (C(5'))

IR: (NaCl)

3068 (m), 2967 (m), 2933 (m), 2879 (m), 1779 (s), 1608 (m), 1461 (m), 1382 (m), 1332 (m), 1274 (m), 1220 (m), 1176 (s), 1130 (s), 1024 (s), 948 (m), 709 (m)

MS: (EI, 70 eV)

297 (54, M⁺ + 1), 267 (26), 239 (2), 195 (100), 169 (65), 153 (21), 103 (59), 86 (13), 68 (13)

Opt. Rot.: [α]_D²⁴ -16.3 (*c* = 1.06, CHCl₃)

TLC: *R*_f 0.17 (silica gel, hexane/EtOAc, 4/1, PMA)

<u>Analysis:</u>	C ₉ H ₁₃ O ₃ I	(296.11)		
Calculated:	C, 36.51;	H, 4.43,	I, 42.86%	
Found:	C, 36.34;	H, 4.17,	I, 42.58%	

Preparation of (2*S*)-*N*-Methoxy-*N*-methyl-2-[[*(1S,2Z)*-1-ethyl-3-iodo-2-propenyl]oxy]-4-hydroxybutanamide (15**)**

In a three-neck, 100 mL flask was placed *N,O*-dimethylhydroxylamine hydrochloride salt (1.76 g, 18.0 mmol, 2.0 equiv) in CH₂Cl₂ (10 mL) under N₂ at 0 °C. AlMe₃ (2.0 M in toluene, 9.0 mL, 18.0 mmol, 2.0 equiv) was then slowly added. The mixture was stirred at 0 °C for 30 min and was warmed to room temperature for 30 min. The clear solution was cooled to 0 °C and a solution of **8** (2.67 g, 9.0 mmol) in CH₂Cl₂ (10 mL) was slowly added. The mixture was allowed to warm to room temperature and was stirred for 1 h. The mixture was then cooled to 0 °C and was quenched by slowly addition of aqueous HCl solution (1.0 M, 18 mL); gentle bubbling was observed. The aqueous layers were extracted with CH₂Cl₂ (2 x 20 mL). The combined organic layers were dried (Na₂SO₄), and filtered. The solvent was removed by rotary evaporation to give a crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 4/1 to 3/7) to afford 2.99 g (93%) of **15** as a pale yellow oil. (This reaction can be run on a 40.0 mmol scale in 88% yield.)

Analytical Data for **15:**

¹H NMR: (500 MHz, CDCl₃)

6.51 (dd, *J* = 7.0, 1.0, 1 H, HC(1')), 6.14 (t, *J* = 8.0, 1 H, HC(2')), 4.49 (br dd, *J* = 7.2, 4.8, 1 H, HC(2)), 4.06 (dt, *J* = 8.0, 7.0, 1 H, HC(4)), 3.79-3.73 (m, 2 H, H₂C(4)), 3.72 (s, 3 H, H₃C(2')), 3.22 (s, 3 H, H₃C(1')), 2.38 (br s, 1 H, HO)), 1.98-1.87 (m, 2 H, H₂C(3)), 1.76 (d quint, *J* = 14.0, 7.5, 1 H, HC(4')), 1.58 (d quint, *J* = 14.5, 7.5, 1 H, HC(4')), 0.97 (t, *J* = 7.5, 3 H, H₃C(5'))

¹³C NMR: (126 MHz, CDCl₃)

172.8 (C(1)), 141.5 (C(2')), 84.9 (C(1')), 81.5 (C(3')), 72.6 (C(2)), 61.5 (C(2')), 60.0 (C(4)), 34.5 (C(3)), 32.4 (C(1')), 27.6 (C(4')), 9.1 (C(5'))

IR: (NaCl)

3436 (s), 2964 (m), 2935 (s), 2879 (s), 1735 (m), 1658 (s), 1461 (s), 1390 (s), 1330 (s), 1274 (s), 1180 (s), 1103 (s), 995 (s), 943 (m), 717 (s)

MS: (EI, 70 eV)

358 (27, $M^+ + 1$), 340 (11), 269 (7), 230 (13), 211 (12), 195 (100), 164 (49), 146 (38), 141 (35), 116 (14), 88 (10), 75 (33), 68 (61), 61 (45)

Opt. Rot.: $[\alpha]_D^{24} +67.5$ ($c = 1.08$, CHCl_3)

TLC: R_f 0.14 (silica gel, EtOAc/hexane, 7/3, PMA)

Analysis: $\text{C}_{11}\text{H}_{20}\text{O}_4\text{NI}$ (357.19)

Calculated: C, 36.99; H, 5.64, N, 3.92, I, 35.53%

Found: C, 36.84; H, 5.56, N, 3.86, I, 35.55%

Preparation of (2*S*)-*N*-Methoxy-*N*-methyl-2-([(1*S*,2*Z*)-1-ethyl-3-iodo-2-propenyl]oxy)-4-(4-methoxybenzyloxy)butanamide (9**)**

In a three-neck, 50 mL flask was placed **15** (7.14 g, 20 mmol) in CH_2Cl_2 (20 mL) under N_2 at room temperature. *p*-Methoxybenzyl chloride (4.7 g, 30 mmol, 1.5 equiv) and freshly prepared Ag_2O (2.78 g, 12 mmol, 0.6 equiv) was then added sequentially. The mixture was stirred for 6 h and additional *p*-methoxybenzyl chloride (4.7 g, 30 mmol, 1.5 equiv) and Ag_2O (2.78 g, 12 mmol, 0.6 equiv) was added sequentially. After 6 h stirring, additional *p*-methoxybenzyl chloride (3.13 g, 20 mmol, 1.0 equiv) and Ag_2O (2.78 g, 12 mmol, 0.6 equiv) was added again and the mixture was stirred for 12 h. The mixture was filtered through short column of Celite, which was then eluted with Et_2O (500 mL). The eluate was concentrated by rotary evaporation to give a crude product, which was purified by chromatography (silica gel, hexane/ Et_2O , 9/1 to 7/3, then hexane/ EtOAc , 1/1 to 3/7) to afford 7.82 g (82%) of **9** as a colorless oil and 0.57 g (8%) of **15**. (This reaction can be run on a 60 mmol scale in 80% yield.)

Analytical Data for 9:¹H NMR: (500 MHz, CDCl₃)

7.24 (dd, $J = 8.5, 1.5$, 2 H, 2 x HC(3'')), 6.86 (dd, $J = 8.5, 1.5$, 2 H, 2 x HC(4'')), 6.40 (dd, $J = 7.5, 1.0$, 1 H, HC(1')), 6.03 (t, $J = 8.0$, 1 H, HC(2')), 4.45 (d, $J = 12.0$, 1 H, HC(1'')), 4.43-4.41 (m, 1 H, HC(2)), 4.36 (d, $J = 12.0$, 1 H, HC(1'')), 4.02 (dt, $J = 8.0, 6.5$, 1 H, HC(3')), 3.79 (s, 3 H, H₃C(6'')), 3.68 (s, 3 H, H₃C(2'')), 3.63 (td, $J = 9.0, 5.0$, 1 H, HC(4)), 3.53 (ddd, $J = 9.5, 5.5, 4.5$, 1 H, HC(4)), 3.19 (s, 3 H, H₃C(1'')), 2.04-1.98 (m, 1 H, HC(3)), 1.88-1.82 (m, 1 H, HC(3)), 1.74 (d quint, $J = 14.0, 7.5$, 1 H, HC(4')), 1.58 (d quint, $J = 14.5, 7.5$, 1 H, HC(4')), 0.95 (t, $J = 7.5$, 3 H, H₃C(5'))

¹³C NMR: (126 MHz, CDCl₃)

173.4 (C(1)), 159.0 (C(5'')), 141.9 (C(2')), 130.5 (C(2'')), 129.0 (2 x C(3'')), 113.5 (2 x C(4'')), 84.0 (C(1')), 81.3 (C(3')), 72.2 (C(2)), 70.6 (C(1'')), 65.8 (C(4)), 61.3 (C(2'')), 55.1 (C(6'')), 32.5 (C(3), C(1'')), 27.4 (C(4')), 9.0 (C(5'))

IR: (NaCl)

2964 (s), 2935 (s), 2873 (s), 1735 (m), 1675 (s), 1612 (s), 1513 (s), 1461 (s), 1247 (s), 1174 (s), 1099 (s), 1035 (s), 997 (s), 821 (m), 715 (m)

MS: (FAB)

478 (20, M⁺ + 1), 448 (3), 352 (5), 284 (2), 195 (3), 146 (9), 121 (100)

Opt. Rot.: [α]_D²⁴ +80.7 ($c = 1.20$, CHCl₃)TLC: R_f 0.19 (silica gel, hexane/EtOAc, 3/2, PMA)Analysis: C₁₉H₂₈O₅Ni (477.34)

Calculated: C, 47.79; H, 5.91, N, 2.94, I, 26.59%

Found: C, 48.12; H, 5.90, N, 2.97, I, 26.79%

Preparation of (2S)-2-[[[(1S,2Z)-1-Ethyl-3-iodo-2-propenyl]oxy]-4-(4-methoxybenzyloxy)butanal (4)

In a three-neck, 100 mL flask was placed **9** (7.16 g, 15 mmol) in CH_2Cl_2 (30 mL) under N_2 at -73°C . A solution of DIBAL-H (1.0 M in hexane, 22.5 mL, 22.5 mmol, 1.5 equiv) was then slowly added. The mixture was stirred for 3 h at -73°C and acetone (5.0 mL) was added dropwise. The mixture was stirred for 1 h at -73°C . The mixture was then poured into a vigorously stirring mixture of CH_2Cl_2 (50 mL)/aqueous HCl solution (3.0 M, 50 mL) and was then separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), and filtered. The solvent was removed by rotary evaporation to give a crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 9/1 to 17/3) to afford 5.45 g (87%) of **4** as a pale yellow oil. (This reaction can be run on a 25.0 mmol scale in 88% yield.)

Analytical Data for 4:

^1H NMR: (500 MHz, CDCl_3)

9.70 (d, $J = 1.5$, 1 H, HC(1)), 7.23 (dd, $J = 8.5$, 2.0, 2 H, 2 x HC(3'')), 6.87 (dd, $J = 8.5$, 2.0, 2 H, 2 x HC(4'')), 6.44 (dd, $J = 8.0$, 1.0, 1 H, HC(1')), 6.01 (t, $J = 8.0$, 1 H, HC(2')), 4.41 (d, $J = 11.0$, 1 H, HC(1'')), 4.38 (d, $J = 11.0$, 1 H, HC(1'')), 4.13 (dt, $J = 8.0$, 6.0, 1 H, HC(3')), 3.96 (ddd, $J = 7.5$, 4.5, 1.5, 1 H, HC(2)), 3.80 (s, 3 H, $\text{H}_3\text{C}(6'')$), 3.57 (ddd, $J = 9.5$, 6.0, 5.0, 1 H, HC(4)), 3.52 (ddd, $J = 9.5$, 7.5, 6.0, 1 H, HC(4)), 1.98 (ddt, $J = 14.5$, 7.5, 5.0, 1 H, HC(3)), 1.86 (dddd, $J = 14.0$, 7.5, 6.0, 5.0, 1 H, HC(3)), 1.74 (d quint, $J = 14.5$, 7.5, 1 H, HC(4')), 1.59 (d quint, $J = 14.0$, 7.5, 1 H, HC(4')), 0.99 (t, $J = 7.5$, 3 H, $\text{H}_3\text{C}(5')$)

¹³C NMR: (126 MHz, CDCl₃)
 203.2 (C(1)), 159.1 (C(5'')), 140.8 (C(2')), 130.2 (C(2'')), 129.2 (2 x C(3'')), 113.7 (2 x C(4'')), 85.1 (C(1')), 82.2 (C(3')), 78.5 (C(2)), 75.2 (C(1'')), 64.9 (C(4)), 55.2 (C(6'')), 31.1 (C(3)), 27.5 (C(4')), 9.4 (C(5'))

IR: (NaCl)
 2962 (m), 2933 (m), 2873 (m), 1731 (s), 1612 (m), 1513 (s), 1461 (m), 1301 (m), 1247 (s), 1174 (m), 1101 (s), 1035 (s), 821 (m), 715 (m)

MS: (FD)
 418 (100, M⁺), 389 (1), 290 (7), 202 (1)

Opt. Rot.: [α]_D²⁴ +34.7 (*c* = 1.19, CHCl₃)

TLC: *R_f* 0.30 (silica gel, hexane/EtOAc, 4/1, PMA)

Analysis: C₁₇H₂₃O₄I (418.27)
 Calculated: C, 48.82; H, 5.54, I, 30.34%
 Found: C, 49.04; H, 5.60, I, 30.56%

Preparation of (4*R*,5*S*)-5-[(1*S*,2*Z*)-1-Ethyl-3-iodo-2-propenyl]oxy}-7-(4-methoxybenzyloxy)-1-hepten-4-ol (10)

In a three-neck, 100 mL flask was placed (+)-*B*-chlorodiisopinocampheylborane [(+)-DIP-Cl] (4.81 g, 15 mmol, 1.5 equiv, purchased from Aldrich) in Et₂O (15 mL) under N₂ at -73 °C. Allylmagnesium bromide (0.75 M in Et₂O, 20 mL, 15 mmol, 1.5 equiv) was then added dropwise. After complete addition of Grignard reagent, the mixture was allowed to warm to room temperature and was stirred for 1 h. The solvent was then removed *in vacuo*. The residue was extracted with pentane (20 mL) and was stirred vigorously for 30 min. The mixture was then filtered to a receiver flask by cannula under N₂. The white salt was washed with pentane (3 x 10 mL) and was then filtered. The filtrate was concentrated *in vacuo* to give corresponding allylborane reagent as a colorless oil. To the crude reagent was added Et₂O (30 mL) and was then cooled to -95 to -100 °C (EtOH/liquid nitrogen bath). A solution of **4** (4.18 g, 10 mmol) in

Et₂O (10 mL) was added along the surface of flask over 10 min under N₂. The flask was rinsed with Et₂O (5 mL) and was then added to the reaction flask. The mixture was stirred at –95 to –100 °C for 2 h and was concentrated *in vacuo* to afford crude product. To the crude product was added pentane (10 mL) and ethanolamine (1.81 mL, 30 mmol, 3.0 equiv) sequentially under N₂ at room temperature. The mixture was stirred for 12 h and was then filtered through a short column of Celite, which was eluted with pentane (300 mL). The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 17/3) to afford 4.10 g (89%) of **10** as a colorless oil. (This reaction can be run on a 20.0 mmol scale 85% yield.)

Analytical Data for **10:**

¹H NMR: (500 MHz, CDCl₃)

7.24 (dd, *J* = 9.0, 2.0, 2 H, 2 x HC(3'')), 6.88 (dd, *J* = 8.5, 2.0, 2 H, 2 x HC(4'')), 6.34 (d, *J* = 8.0, 1 H, HC(1')), 6.01 (t, *J* = 8.0, 1 H, HC(2')), 5.88 (ddt, *J* = 17.0, 10.0, 6.5, 1 H, HC(2)), 5.14 (dt, *J* = 17.0, 1.5, 1 H, HC(1)), 5.10 (dd, *J* = 10.0, 1.0, 1 H, HC(1)), 4.43 (d, *J* = 11.5, 1 H, HC(1'')), 4.39 (d, *J* = 11.5, 1 H, HC(1'')), 4.14 (dd, *J* = 8.0, 6.5, 1 H, HC(3')), 3.91-3.87 (m, 1 H, HC(4)), 3.80 (s, 3 H, H₃C(6'')), 3.57 (dt, *J* = 9.5, 5.5, 1 H, HC(7)), 3.52-3.46 (m, 2 H, HC(7), HC(5)), 2.51 (br s, 1 H, HO), 2.25 (t, *J* = 7.0, 2 H, H₂C(3)), 1.83-1.74 (m, 2 H, H₂C(6)), 1.64 (d quint, *J* = 14.0, 7.5, 1 H, HC(4')), 1.52 (d quint, *J* = 14.0, 7.5, 1 H, HC(4')), 0.95 (t, *J* = 7.5, 3 H, H₃C(5'))

¹³C NMR: (126 MHz, CDCl₃)

159.2 (C(5'')), 141.9 (C(2')), 135.1 (C(2)), 130.4 (C(2'')), 129.3 (2 x C(3'')), 117.3 (C(1)), 113.7 (2 x C(4'')), 83.8 (C(1')), 80.9 (C(3')), 76.5 (C(5)), 72.6 (C(1'')), 70.8 (C(4)), 66.2 (C(7)), 55.2 (C(6'')), 37.1 (C(3)), 29.0 (C(6)), 27.6 (C(4')), 9.5 (C(5'))

IR: (NaCl)

3467 (m), 3072 (m), 2962 (s), 2933 (s), 2873 (s), 1641 (m), 1612 (s), 1513 (s), 1461 (m), 1247 (s), 1174 (m), 1085 (s), 1035 (s), 916 (m), 821 (m), 713 (m)

MS: (FD)

460 (100, M⁺), 425 (2), 390 (1), 332 (16), 306 (3), 264 (3), 195 (2)

Opt. Rot.: [α]_D²⁴ +58.0 (*c* = 1.21, CHCl₃)

TLC: *R_f* 0.15 (silica gel, hexane/EtOAc, 4/1, PMA)

Analysis: C₂₀H₂₉O₄I (460.37)

Calculated: C, 52.18; H, 6.35%

Found: C, 52.52; H, 6.37%

Preparation of Dimethyl-{(4*R*,5*S*)-5-[[*(1*S*,2*Z*)-1-ethyl-3-iodo-2-propenyl]oxy}-7-(4-methoxybenzyloxy)-1-hepten-4-oxy}vinylsilane (16**)***

In a three-neck, 50 mL flask was placed **10** (2.3 g, 5.0 mmol) in CH₂Cl₂ (10 mL) under N₂ atmosphere at 0 °C. Et₃N (1.04 mL, 7.5 mmol, 1.5 equiv) and dimethylvinylchlorosilane (0.83 mL, 6.0 mmol, 1.2 equiv) was then added sequentially. The white suspension was allowed to warm to room temperature and was stirred for 30 min. The mixture was poured into ice water (10 mL) and the aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL). The combined organic layers were dried (Na₂SO₄), and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1) followed by Kugelrohr distillation to afford 2.48 g (91%) of **16** as a colorless oil. (This reaction can be run on a 20.0 mmol scale 90% yield.)

Analytical Data for **16**:

bp: 210-215 °C (0.05 mmHg, ABT)

¹H NMR: (500 MHz, CDCl₃)

7.25 (dd, *J* = 9.0, 2.0, 2 H, 2 x HC(3'')), 6.87 (dd, *J* = 8.5, 2.0, 2 H, 2 x HC(4'')), 6.32 (dd, *J* = 7.5, 1.0, 1 H, HC(1')), 6.18 (dd, *J* = 20.5, 15.0, 1 H, HC(1''')), 6.00 (t, *J* = 8.0, 1 H, HC(2')), 5.99 (dd, *J* = 15.0, 4.0, 1 H, H_bC(2'')), 5.83 (ddt, *J* = 17.0, 10.0, 7.0, 1 H, HC(6)), 5.76 (dd, *J* = 20.5, 4.0, 1 H, H_aC(2'')), 5.08-5.03 (m, 2 H, H₂C(7)), 4.43 (d, *J* = 11.5, 1 H, HC(1'')), 4.39 (d, *J* = 11.0, 1 H, HC(1'')), 4.20 (q, *J* = 7.5, 1 H, HC(3')), 3.86 (ddd, *J* = 7.5, 5.0, 2.5, 1 H, HC(4)), 3.80 (s, 3 H, H₃C(6'')), 3.52 (dd, *J* = 6.5, 2.0, 1 H, HC(1)), 3.50 (dd, *J* = 6.5, 4.5, 1 H, HC(1)), 3.44 (ddd, *J* = 7.5, 4.0, 2.5, 1 H, HC(3)), 2.29-2.16 (m, 2 H, H₂C(5)), 1.77-1.64 (m, 3 H, H₂C(2), HC(4')), 1.53 (d quint, *J* = 15.0, 7.5, 1 H, HC(4')), 0.93 (t, *J* = 7.5, 3 H, H₃C(5')), 0.21 (s, 3 H, H₃C(3'')), 0.20 (s, 3 H, H₃C(4''))

¹³C NMR: (126 MHz, CDCl₃)
 159.0 (C(5'')), 142.4 (C(2'')), 138.3 (C(1''')), 135.7 (C(6)), 132.8 (C(2''')), 130.7 (C(2'')), 129.2 (2 x C(3'')), 116.7 (C(7)), 113.6 (2 x C(4'')), 83.4 (C(1')), 81.1 (C(3')), 76.6 (C(3)), 73.8 (C(4)), 72.4 (C(1'')), 66.8 (C(1)), 55.2 (C(6'')), 38.2 (C(5)), 30.2 (C(2)), 27.7 (C(4')), 9.3 (C(5')), -1.1 (C(3''')), -1.4 (C(4'''))

IR: (NaCl)
 2962 (s), 2875 (m), 1612 (m), 1513 (m), 1463 (m), 1249 (s), 1097 (s), 1037 (s), 914 (m), 833 (s), 784 (s), 701 (m)

MS: (FD)
 544 (100, M⁺), 454 (1), 416 (9), 348 (1), 290 (1), 224 (2), 195 (2), 155 (10), 121 (9)

Opt. Rot.: [α]_D²⁴ +39.9 (*c* = 1.12, CHCl₃)

TLC: *R_f* 0.29 (silica gel, hexane/EtOAc, 9/1, PMA)

Analysis: C₂₄H₃₇O₄SiI (544.55)
 Calculated: C, 52.94; H, 6.85, I, 23.30%
 Found: C, 53.33; H, 7.00, I, 23.37%

Preparation of (6*R*)-2,2-Dimethyl-6-((1*S*)-1-(((1*S*,2*Z*)-1-ethyl-3-iodo-2-propenyl)oxy)-3-(4-methoxybenzyloxy)propan-1-yl)-1-oxa-2-silacyclohex-3-ene (3)

In a flame-dried, 25 ml flask was placed freshly distilled benzene (15 mL), which was then moved into a dry box. To this flask was added **16** (816 mg, 1.5 mmol) and Schrock's catalyst³ (57.4 mg, 0.075 mmol, 0.05 equiv) sequentially. The yellow-brown solution was stirred at room temperature for 1 h in the dry box. The solvent was removed by rotary evaporation to give a brown residue, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 9/1) to afford 713 mg (92%) of **3** as a pale yellow oil. (This reaction can be run on a 5.0 mmol scale 92% yield.)

Analytical Data for 3:¹H NMR: (500 MHz, CDCl₃)

7.26 (dd, $J = 9.0, 2.0$, 2 H, 2 x HC(3'')), 6.88 (dd, $J = 9.0, 2.0$, 2 H, 2 x HC(4'')), 6.80 (ddd, $J = 14.0, 6.0, 2.0$, 1 H, HC(6)), 6.32 (dd, $J = 7.5, 0.5$, 1 H, HC(1')), 6.03 (t, $J = 7.5$, 1 H, HC(2')), 5.75 (dd, $J = 14.0, 2.5$, 1 H, HC(7)), 4.42 (s, 2 H, H₂C(1'')), 4.30 (dt, $J = 8.0, 6.5$, 1 H, HC(3')), 4.03 (dt, $J = 11.5, 3.5$, 1 H, HC(4)), 3.80 (s, 3 H, H₃C(6'')), 3.53 (t, $J = 6.5$, 2 H, H₂C(1)), 3.49 (dt, $J = 8.0, 4.0$, 1 H, HC(3)), 2.30 (ddt, $J = 17.5, 11.0, 2.5$, 1 H, HC(5)), 2.11 (ddd, $J = 17.5, 6.5, 2.0$, 1 H, HC(5)), 1.81-1.74 (m, 2 H, H₂C(2)), 1.65 (d quint, $J = 14.5, 7.5$, 1 H, HC(4')), 1.51 (d quint, $J = 14.0, 7.5$, 1 H, HC(4')), 0.96 (t, $J = 7.5$, 3 H, H₃C(5')), 0.18 (s, 3 H, H₃C(8)), 0.17 (s, 3 H, H₃C(9))

¹³C NMR: (126 MHz, CDCl₃)

159.1 (C(5'')), 147.1 (C(6)), 142.4 (C(2')), 130.6 (C(2'')), 129.2 (2 x C(3'')), 127.1 (C(7)), 113.7 (2 x C(4'')), 83.2 (C(1')), 81.7 (C(3')), 76.9 (C(3)), 72.7 (C(4)), 72.5 (C(1'')), 66.7 (C(1)), 55.2 (C(6'')), 31.7 (C(5)), 30.6 (C(2)), 27.7 (C(4')), 9.7 (C(5')), -0.4 (C(8)), -0.7 (C(9))

IR: (NaCl)

2960 (s), 2933 (s), 2858 (s), 1612 (s), 1587 (s), 1513 (s), 1463 (m), 1355 (m), 1249 (s), 1091 (s), 1037 (s), 956 (s), 906 (m), 840 (s), 788 (s), 713 (m)

MS: (EI, 70 eV)

517 (3, M⁺ + 1), 379 (5), 321 (5), 303 (2), 215 (5), 195 (3), 185 (30), 127 (20), 121 (100), 68 (4)

Opt. Rot.: [α]_D²⁴ +45.1 ($c = 1.02$, CHCl₃)TLC: R_f 0.25 (silica gel, hexane/EtOAc, 9/1, PMA)Analysis: C₂₂H₃₃O₄SiI (516.60)

Calculated: C, 51.16; H, 6.44, I, 24.57%

Found: C, 51.21; H, 6.56, I, 24.30%

Preparation of (2*S*,8*R*,9*S*)-2-Ethyl-8-hydroxy-9-[2-(4-methoxybenzyloxy)ethyl]-1-oxa-3*Z*,5*Z*-cyclononadiene (2)

In a three-neck, 50 mL flask was placed TBAF•3H₂O (9.47 g, 30.0 mmol, 10.0 equiv) in THF (30 mL) under N₂ at room temperature. -Allylpalladium chloride dimer (APC) (82.4 mg, 0.225 mmol, 0.075 equiv, purchased from ACROS) was added. A solution of **3** (1.55 g, 3.0 mmol) in THF (10 mL) was then added by syringe pump for 60 h. After complete addition of **3**, the mixture was stirred for 1 h and was then concentrated. The residue was filtered through a short silica gel column, which was eluted with Et₂O (600 mL). The solvent was removed by rotary evaporation to give a brown residue, which was purified by chromatography (silica gel, hexane/EtOAc, 9/1 to 4/1) to afford 607 mg (61%) of **2** as a colorless oil.

Analytical Data for **2:**

¹H NMR: (500 MHz, CDCl₃)

7.23 (dd, *J* = 8.5, 2.0, 2 H, 2 x HC(5')), 6.87 (dd, *J* = 8.5, 2.0, 2 H, 2 x HC(6')), 6.16 (ddd, *J* = 11.0, 3.0, 1.5, 1 H, HC(7)), 5.93 (d, *J* = 11.0, 1 H, HC(6)), 5.87-5.82 (m, 1 H, HC(5)), 5.49 (ddd, *J* = 11.5, 6.0, 2.0, 1 H, HC(8)), 4.48 (d, *J* = 11.5, 1 H, HC(3')), 4.41 (d, *J* = 11.5, 1 H, HC(3')), 4.04 (dt, *J* = 7.0, 6.5, 1 H, HC(9)), 3.88 (dt, *J* = 8.0, 4.0, 1 H, HC(2)), 3.80-3.76 (m, 1 H, HC(2')), 3.79 (s, 3 H, H₃C(8')), 3.68-3.55 (br s, 1 H, HO), 3.57 (td, *J* = 8.5, 2.0, 1 H, HC(3)), 3.54 (ddd, *J* = 9.0, 6.0, 3.0, 1 H, HC(2')), 2.61 (dt, *J* = 13.0, 9.0, 1 H, HC(4)), 2.30 (dd, *J* = 13.0, 7.0, 1 H, HC(4)), 2.10 (ddt, *J* = 15.5, 9.0, 3.5, 1 H, HC(1')), 1.83 (dddd, *J* = 15.5, 6.0, 4.5, 3.0, 1 H, HC(1')), 1.60 (d quint, *J* = 14.5, 7.5, 1 H, HC(10)), 1.47 (d quint, *J* = 14.5, 7.5, 1 H, HC(10)), 0.85 (t, *J* = 7.5, 3 H, H₃C(11))

¹³C NMR: (126 MHz, CDCl₃)

159.3 (C(7')), 134.1 (C(8)), 133.0 (C(7)), 130.6 (C(5)), 129.7 (C(4')), 129.4 (2 x C(5')), 127.1 (C(6)), 113.8 (2 x C(6')), 78.8 (C(2)), 75.0 (C(9)), 73.0 (C(3')), 70.6 (C(3)), 66.0 (C(2')), 55.2 (C(8')), 36.9 (C(4)), 33.8 (C(1')), 29.1 (C(10)), 10.2 (C(11))

IR: (NaCl)

3419 (s), 3004 (s), 2960 (s), 2931 (s), 2873 (s), 1612 (s), 1513 (s), 1463 (s), 1363 (m), 1301 (s), 1247 (s), 1174 (s), 1064 (s), 1039 (s), 821 (m), 754 (s)

MS: (FD)332 (100, M⁺), 166 (1), 121 (2)Opt. Rot.: [α]_D²⁴ +162.7 (*c* = 0.9, CHCl₃)TLC: *R_f* 0.18 (silica gel, hexane/EtOAc, 7/3, PMA)Analysis: C₂₀H₂₈O₄ (332.44)

Calculated: C, 72.26; H, 8.49%

Found: C, 71.99; H, 8.35%

Preparation of (2*S*,8*R*,9*S*)-8-(*t*-Butyldimethylsilyloxy)-2-ethyl-9-[2-(4-methoxybenzyloxy)ethyl]-1-oxa-3*Z*,5*Z*-cyclononadiene (17**)**

In a three-neck, 50 mL flask was placed **2** (1.99 g, 6.0 mmol) in CH₂Cl₂ (12 mL) under N₂ at 0 °C. Pyridine (1.45 mL, 18 mmol, 3.0 equiv) and 4-dimethylaminopyridine (73.2 mg, 0.6 mmol, 0.1 equiv) was added sequentially. To the mixture was then added TBSOTf (2.07 mL, 9.0 mmol, 1.5 equiv) dropwise. The mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was poured into H₂O (12 mL) and the aqueous layer was extracted with CH₂Cl₂ (3 x 12 mL). The combined organic layers were dried (Na₂SO₄) and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 49/1 to 19/1) to afford 2.36 g (88%) of **17** as a colorless oil.

Analytical Data for 17:

bp: 195-200 °C (0.3 mmHg, ABT)

¹H NMR: (500 MHz, CDCl₃)

7.28 (dd, $J = 8.5, 2.0$, 2 H, 2 x HC(5')), 6.89 (dd, $J = 8.5, 2.0$, 2 H, 2 x HC(6')), 6.00 (dd, $J = 11.0, 1.0$, 1 H, HC(7)), 5.88-5.82 (m, 2 H, HC(5), HC(6)), 5.51 (dd, $J = 11.5, 7.5$, 1 H, HC(8)), 4.47 (d, $J = 11.5$, 1 H, HC(3')), 4.43 (d, $J = 11.5$, 1 H, HC(3')), 4.06 (td, $J = 8.0, 4.5$, 1 H, HC(9)), 3.83 (td, $J = 8.5, 3.0$, 1 H, HC(2)), 3.82 (s, 3 H, H₃C(8')), 3.73 (ddd, $J = 8.5, 6.5, 2.0$, 1 H, HC(3)), 3.63 (td, $J = 9.0, 5.0$, 1 H, HC(2')), 3.58 (td, $J = 9.0, 7.0$, 1 H, HC(2')), 2.95 (ddd, $J = 15.5, 8.5, 7.0$, 1 H, HC(4)), 2.20-2.16 (m, 1 H, HC(4)), 2.04 (dddd, $J = 13.5, 10.0, 7.0, 3.0$, 1 H, HC(1')), 1.84 (dtd, $J = 13.5, 8.5, 5.0$, 1 H, HC(1')), 1.68-1.60 (m, 1 H, HC(10)), 1.50 (d quint, $J = 15.0, 7.5$, 1 H, HC(10)), 0.91 (s, 9 H, 3 x H₃C(4'')), 0.83 (t, $J = 7.5$, 3 H, H₃C(11)), 0.12 (s, 3 H, H₃C(1'')), 0.09 (s, 3 H, H₃C(2''))

¹³C NMR: (126 MHz, CDCl₃)

159.1 (C(7')), 133.9 (C(8)), 130.8 (C(4')), 130.40 (C(5)), 130.37 (C(7)), 129.2 (2 x C(5')), 127.1 (C(6)), 113.7 (2 x C(6')), 81.8 (C(2)), 73.1 (C(3)), 73.0 (C(9)), 72.5 (C(3')), 67.3 (C(2')), 55.2 (C(8')), 36.8 (C(4)), 33.3 (C(1')), 29.4 (C(10)), 25.8 (3 x C(4'')), 17.9 (C(3'')), 9.6 (C(11)), -4.2 (C(1'')), -4.8 (C(2''))

IR: (NaCl)

3004 (m), 2956 (s), 2931 (s), 2858 (s), 1614 (m), 1513 (s), 1463 (m), 1361 (m), 1301 (m), 1249 (s), 1172 (m), 1085 (s), 1039 (s), 1006 (m), 943 (m), 836 (s), 775 (s)

MS: (FD)

446 (100, M⁺), 389 (3), 332 (6), 215 (2), 121 (3)

Opt. Rot.: [α]_D²⁴ +74.9 ($c = 1.155$, CHCl₃)

TLC: R_f 0.29 (silica gel, hexane/EtOAc, 9/1, PMA)

Analysis: C₂₆H₄₂O₄Si (446.71)

Calculated: C, 69.91; H, 9.48%

Found: C, 69.85; H, 9.50%

Preparation of (2*S*,8*R*,9*S*)-8-(*t*-Butyldimethylsilyloxy)-2-ethyl-9-(2-hydroxyethyl)-1-oxa-3*Z*,5*Z*-cyclononadiene (18**)**

In a three-neck, 100 mL flask was placed **17** (2.23 g, 5.0 mmol) in CH₂Cl₂ (47.5 mL) and H₂O (2.5 mL) at room temperature. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (1.7 g, 7.5 mmol, 1.5 equiv) was then added in one portion. The dark green solution was stirred for 30 min with brown suspension was observed. The mixture was poured into a saturated NaHCO₃ solution (50 mL). The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were dried (Na₂SO₄) and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/Et₂O, 9/1, then hexane/EtOAc, 17/3) to afford 1.37 g (84%) of **18** as a colorless oil.

Analytical Data for **18:**

¹H NMR: (500 MHz, CDCl₃)

6.05 (dd, *J* = 11.0, 2.5, 1 H, HC(7)), 5.86 (dd, *J* = 11.0, 2.5, 1 H, HC(6)), 5.78 (dt, *J* = 11.5, 8.0, 1 H, HC(5)), 5.45 (dd, *J* = 11.5, 8.0, 1 H, HC(8)), 4.09 (td, *J* = 8.0, 6.0, 1 H, HC(9)), 3.95 (td, *J* = 8.0, 3.0, 1 H, HC(2)), 3.79 (ddd, *J* = 12.0, 7.0, 4.5, 1 H, HC(2')), 3.72 (ddd, *J* = 12.0, 6.5, 5.5, 1 H, HC(2')), 3.68 (td, *J* = 7.5, 1.5, 1 H, HC(3)), 2.73 (ddd, *J* = 14.0, 9.5, 7.5, 1 H, HC(4)), 2.66 (br s, 1 H, HO), 2.22 (dd, *J* = 14.0, 7.5, 1 H, HC(4)), 1.90 (dddd, *J* = 14.5, 6.5, 5.0, 3.5, 1 H, HC(1')), 1.79 (dddd, *J* = 14.5, 8.0, 6.5, 5.0, 1 H, HC(1')), 1.73-1.65 (m, 1 H, HC(10)), 1.52 (d quint, *J* = 13.5, 7.5, 1 H, HC(10)), 0.86 (s, 9 H, 3 x H₃C(4')), 0.83 (t, *J* = 7.5, 3 H, H₃C(11)), 0.09 (s, 3 H, H₃C(1')), 0.06 (s, 3 H, H₃C(2'))

¹³C NMR: (126 MHz, CDCl₃)

133.1 (C(8)), 131.8 (C(7)), 129.7 (C(5)), 127.5 (C(6)), 83.1 (C(2)), 74.0 (C(9)), 72.6 (C(3)), 61.4 (C(2')), 38.0 (C(4)), 34.7 (C(1')), 29.2 (C(10)), 25.8 (3 x C(4')), 17.9 (C(3')), 9.8 (C(11)), -4.4 (C(1')), -4.9 (C(2'))

IR: (NaCl)

3436 (m), 3006 (m), 2956 (s), 2931 (s), 2885 (s), 2858 (s), 1436 (m), 1361 (m), 1255 (s), 1081 (s), 943 (m), 836 (s), 775 (s)

MS: (FD)326 (100, M⁺), 267 (15), 222 (2), 116 (1)Opt. Rot.: [α]_D²⁴ +103.4 (*c* = 1.075, CHCl₃)TLC: *R*_f 0.17 (silica gel, hexane/EtOAc, 4/1, PMA)Analysis: C₁₈H₃₄O₃Si (326.56)

Calculated: C, 66.21; H, 10.49%

Found: C, 66.21; H, 10.40%

Preparation of (2*S*,8*R*,9*S*)-8-(*t*-Butyldimethylsilyloxy)-2-ethyl-9-(2-oxoethyl)-1-oxa-3*Z*,5*Z*-cyclononadiene (11)

In a three-neck, 50 mL flask was placed **18** (1.14 g, 3.5 mmol) in CH₂Cl₂ (15 mL) at room temperature. Dess-Martin periodinane (1.93 g, 4.55 mmol, 1.3 equiv) was then added in one portion. The mixture was stirred for 2 h and was then filtered through a short silica gel column, which was eluted with hexane/EtOAc (1/1, 250 mL). The filtrate was concentrated by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1) to afford 941 mg (83%) of **11** as a colorless oil.

Analytical Data for **11**:¹H NMR: (500 MHz, CDCl₃)

9.73 (t, *J* = 2.5, 1 H, HC(2')), 6.10 (ddd, *J* = 11.0, 3.0, 1.0, 1 H, HC(7)), 5.89 (dd, *J* = 11.0, 3.0, 1 H, HC(6)), 5.78 (dt, *J* = 11.0, 8.5, 1 H, HC(5)), 5.48 (ddd, *J* = 11.0, 7.5, 1.0, 1 H, HC(8)), 4.33 (td, *J* = 7.5, 5.5, 1 H, HC(2)), 4.05 (q, *J* = 7.0, 1 H, HC(9)), 3.76 (td, *J* = 7.5, 1.5, 1 H, HC(3)), 2.73 (dt, *J* = 13.5, 8.5, 1 H, HC(4)), 2.69 (ddd, *J* = 16.5, 5.5, 2.0, 1 H, HC(1')), 2.56 (ddd, *J* = 16.0, 7.0, 3.0, 1 H, HC(1')), 2.22 (dd, *J* = 13.5, 7.5, 1 H, HC(4)), 1.59 (d quint, *J* = 14.5, 7.5, 1 H, HC(10)), 1.48 (d quint, *J* = 14.5, 7.5, 1 H, HC(10)), 0.85 (s, 9 H, 3 x H₃C(4')), 0.82 (t, *J* = 7.5, 3 H, H₃C(11)), 0.09 (s, 3 H, H₃C(1')), 0.04 (s, 3 H, H₃C(2'))

¹³C NMR: (126 MHz, CDCl₃)
 201.6 (C(2')), 133.4 (C(8)), 132.3 (C(7)), 129.4 (C(5)), 127.7 (C(6)), 78.3 (C(2)),
 74.3 (C(9)), 72.8 (C(3)), 48.1 (C(1')), 37.9 (C(4)), 28.8 (C(10)), 25.7 (3 x C(4')),
 17.8 (C(3')), 9.7 (C(11)), -4.5 (C(1'')), -4.8 (C(2''))

IR: (NaCl)
 3006 (m), 2956 (s), 2931 (s), 2885 (s), 2858 (s), 2721 (m), 1727 (s), 1463 (m),
 1407 (m), 1361 (m), 1257 (s), 1085 (s), 941 (m), 838 (s), 777 (s)

MS: (FD)
 324 (46, M⁺), 311 (3), 299 (11), 283 (83), 271 (16), 267 (31), 211 (3), 199 (2),
 183 (5), 162 (5), 128 (3)

Opt. Rot.: [α]_D²⁴ +113.5 (*c* = 1.055, CHCl₃)

TLC: *R_f* 0.36 (silica gel, hexane/EtOAc, 9/1, PMA)

Analysis: C₁₈H₃₂O₃Si (324.54)
 Calculated: C, 66.62; H, 9.95%
 Found: C, 65.90; H, 9.96%

Preparation of (2*S*,8*R*,9*S*)-8-(*t*-Butyldimethylsilyloxy)-2-ethyl-9-[(2*Z*)-5-(triisopropylsilyl)pent-2-en-4-ynyl]-1-oxa-3*Z*,5*Z*-cyclononadiene (19)

In a three-neck, 25 mL flask was placed 1,3-bis(triisopropylsilyl)propyne (1.06 g, 3.0 mmol, 1.5 equiv) in THF (10 mL) under N₂ at -20 °C. *n*-BuLi (1.6 M in hexane, 1.88 mL, 3.0 mmol, 1.5 equiv) was then added dropwise. The yellow solution was stirred for 30 min at -20 °C and was then cooled to -74 °C. A solution of **11** (648 mg, 2.0 mmol) in THF (5 mL) was added dropwise. The mixture was stirred for 2 h at -74 °C and was then slowly warmed to room temperature over 6 h. The reaction was quenched by adding a saturated NH₄Cl solution (10 mL) and was then separated. The aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel,

hexane/EtOAc, 1/0 to 49/1) to afford 833 mg (83%) of **19** as a colorless oil with a 6/1 (*Z/E*) mixtures. Pure *Z*-isomer can be obtained by radial chromatography (silica gel), which was eluted with hexane. The fraction 1 and 2 refer to *E*- and *Z*-isomer, respectively.

Analytical Data for **19**:

¹H NMR: (500 MHz, CDCl₃)

6.07 (ddd, *J* = 11.0, 7.0, 6.0, 1 H, HC(2')), 5.99 (dd, *J* = 11.5, 2.0, 1 H, HC(7)), 5.87-5.80 (m, 2 H, HC(5), HC(6)), 5.59 (dt, *J* = 11.0, 2.0, 1 H, HC(3')), 5.53 (dd, *J* = 11.5, 7.0, 1 H, HC(8)), 4.03 (td, *J* = 7.0, 5.5, 1 H, HC(9)), 3.89 (td, *J* = 7.5, 4.5, 1 H, HC(2)), 3.78 (ddd, *J* = 8.5, 7.0, 2.0, 1 H, HC(3)), 2.91 (ddd, *J* = 14.0, 8.5, 7.0, 1 H, HC(4)), 2.72 (dtd, *J* = 16.5, 7.5, 1.5, 1 H, HC(1')), 2.66 (dddd, *J* = 16.5, 6.0, 4.5, 2.5, 1 H, HC(1')), 2.17 (ddd, *J* = 12.5, 6.0, 1.0, 1 H, HC(4)), 1.66 (dq, *J* = 15.0, 7.5, 5.0, 1 H, HC(10)), 1.50 (d quint, *J* = 15.5, 7.5, 1 H, HC(10)), 1.10-1.08 (br m, 21 H, 3 x HC(6'), 6 x H₃C(7')), 0.88 (s, 9 H, 3 x H₃C(4')), 0.80 (t, *J* = 7.5, 3 H, H₃C(11)), 0.10 (s, 3 H, H₃C(1')), 0.06 (s, 3 H, H₃C(2'))

¹³C NMR: (126 MHz, CDCl₃)

142.6 (C(2')), 134.1 (C(8)), 130.5 (C(7)), 130.3 (C(5)), 127.1 (C(6)), 110.5 (C(3')), 104.1 (C(4')), 95.4 (C(5')), 83.4 (C(2)), 73.1 (C(9)), 72.7 (C(3)), 37.0 (C(4)), 34.4 (C(1')), 29.1 (C(10)), 25.8 (3 x C(4')), 18.6 (6 x C(7')), 17.9 (C(3')), 11.3 (3 x C(6')), 9.7 (C(11)), -4.3 (C(1')), -4.8 (C(2'))

IR: (NaCl)

3006 (m), 2942 (s), 2863 (s), 2146 (m), 1737 (w), 1637 (w), 1463 (s), 1388 (m), 1255 (m), 1085 (s), 1043 (m), 1004 (m), 883 (m), 836 (s), 775 (s), 744 (m)

MS: (FD)

502 (100, M⁺), 445 (11)

Opt. Rot.: [α]_D²⁴ +92.1 (*c* = 1.015, CHCl₃)

TLC: *R*_f 0.17 (silica gel, hexane/EtOAc, 49/1, PMA)

Analysis: C₃₀H₅₄O₂Si₂ (502.93)

Calculated: C, 71.65; H, 10.82%

Found: C, 71.43; H, 10.84%

Preparation of (2*S*,8*R*,9*S*)-2-Ethyl-8-hydroxy-9-[(2*Z*)-pent-2-en-4-ynyl]-1-oxa-3*Z*,5*Z*-cyclononadiene (12**)**

In a three-neck, 50 mL flask was placed **19** (753 mg, 1.5 mmol) in THF (20 mL) under N₂ at 0 °C. A TBAF solution (1.0 M in THF, 6.0 mL, 6.0 mmol, 4.0 equiv) was then added dropwise. The mixture was stirred 1.5 h at 0 °C and was then directly filtered through a short silica gel column, which was eluted with Et₂O (500 mL). The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 9/1 to 17/3) to afford 324 mg (93%) of **12** as a white solid. Compound **12** can be further recrystallized as needles from pentane at –30 °C.

Analytical Data for **12:**

mp: 49-50 °C (pentane)

¹H NMR: (500 MHz, CDCl₃)

6.23 (dddd, *J* = 11.0, 9.0, 6.0, 1.0, 1 H, HC(2')), 6.12 (ddd, *J* = 11.5, 2.5, 1.5, 1 H, HC(7)), 5.92 (ddd, *J* = 11.0, 1.5, 1.0, 1 H, HC(6)), 5.80 (ddd, *J* = 10.5, 9.5, 7.0, 1 H, HC(5)), 5.58 (d, *J* = 11.0, 1 H, HC(3')), 5.55 (dd, *J* = 11.5, 6.0, 1 H, HC(8)), 4.07 (q, *J* = 7.0, 1 H, HC(9)), 3.87 (dt, *J* = 8.5, 5.0, 1 H, HC(2)), 3.60 (tdd, *J* = 8.5, 5.0, 2.5, 1 H, HC(3)), 3.14 (d, *J* = 2.0, 1 H, HC(5')), 2.90-2.84 (m, 1 H, HC(1')), 2.70 (dt, *J* = 13.0, 9.5, 1 H, HC(4)), 2.58 (dtd, *J* = 15.0, 5.3, 1.5, 1 H, HC(1')), 2.28 (ddd, *J* = 13.0, 7.0, 1.0, 1 H, HC(4)), 2.10 (br s, 1 H, HO), 1.70 (d quint, *J* = 15.0, 7.5, 1 H, HC(10)), 1.55 (d quint, *J* = 15.5, 7.5, 1 H, HC(10)), 0.89 (t, *J* = 7.5, 3 H, H₃C(11'))

¹³C NMR: (126 MHz, CDCl₃)

142.5 (C(2')), 134.1 (C(8)), 132.6 (C(7)), 130.0 (C(5)), 127.4 (C(6)), 109.8 (C(3')), 82.2 (C(5')), 80.5 (C(4')), 79.7 (C(2)), 74.9 (C(9)), 70.3 (C(3)), 36.5 (C(4)), 34.5 (C(1')), 28.9 (C(10)), 10.1 (C(11))

IR: (NaCl)

3411 (s, OH), 3298 (s, -CC-H), 3006 (s), 2964 (s), 2931 (s), 2877 (s), 2096 (w), 1279 (w), 1619 (w), 1440 (s), 1378 (m), 1353 (m), 1240 (m), 1122 (s), 1062 (s), 917 (m), 892 (m), 858 (m), 752 (s)

MS: (EI, 70 eV)

233 (7, $M^{+}+1$), 232 (3, M^{+}), 215 (9), 203 (11), 187 (5), 185 (4), 167 (17), 149 (23), 131 (18), 121 (21), 107 (100), 95 (44), 79 (26), 67 (18)

Opt. Rot.: $[\alpha]_D^{24} +382.5$ ($c = 1.03$, CHCl_3)

TLC: R_f 0.14 (silica gel, hexane/EtOAc, 4/1, PMA)

Analysis: $\text{C}_{15}\text{H}_{20}\text{O}_2$ (232.33)

Calculated: C, 77.55; H, 8.68%

Found: C, 77.84; H, 8.72%

Preparation of (2*S*,8*S*,9*S*)-8-Chloro-2-ethyl-9-[(2*Z*)-pent-2-en-4-ynyl]-1-oxa-3*Z*,5*Z*-cyclononadiene [(+)-Brasilenyne (1**)]**

In a three-neck, 25 mL flask was placed **12** (232 mg, 1.0 mmol) in toluene (10 mL) under argon at room temperature. CCl_4 (0.48 mL, 5.0 mmol, 5.0 equiv) and (*n*-Oct) $_3\text{P}$ (4.46 mL, 10.0 mmol, 10.0 equiv) was then added sequentially. The mixture was stirred for 30 min at room temperature and was then warmed to 60–65 °C for 12 h. After cooling, a saturated aqueous Na_2SO_3 solution (10 mL) was then added and was vigorously stirred for 1 h. The mixture was separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and filtered. The solvent was removed by rotary evaporation to give crude product, which was purified by chromatography (silica gel, hexane/ Et_2O , 1/0 to 49/1) followed by recrystallization from pentane at –70 °C to afford 230 mg (92%, three crops) of **1** as a white solid.⁴

Analytical Data for 1:mp: 37-38 °C (pentane); lit. 36-37 °C¹H NMR: (500 MHz, CDCl₃)

6.23 (ddd, $J = 11.0, 2.5, 1.5$, 1 H, HC(7)), 6.07 (br d, $J = 11.5$, 1 H, HC(6)), 6.04 (dddd, $J = 11.0, 8.0, 7.0, 1.0$, 1 H, HC(2')), 5.81 (dtd, $J = 11.0, 7.5, 1.0$, 1 H, HC(5)), 5.55 (ddd, $J = 11.0, 7.0, 1.0$, 1 H, HC(8)), 5.54 (dd, $J = 11.0, 1.0$, 1 H, HC(3')), 4.29 (q, $J = 7.0$, 1 H, HC(9)), 4.08 (br d, $J = 8.0$, 1 H, HC(3)), 3.90 (ddd, $J = 8.0, 6.5, 1.0$, 1 H, HC(2)), 3.13 (d, $J = 2.0$, 1 H, HC(5')), 2.72 (dtd, $J = 14.0, 8.0, 1.0$, 1 H, HC(1')), 2.67 (dtd, $J = 13.5, 7.5, 1.0$, 1 H, HC(4)), 2.61 (dddd, $J = 14.0, 7.0, 6.5, 1.0$, 1 H, HC(1')), 2.48 (dd, $J = 13.5, 8.0$, 1 H, HC(4)), 1.72 (d quint, $J = 14.5, 7.5$, 1 H, HC(10)), 1.53 (d quint, $J = 14.5, 7.5$, 1 H, HC(10)), 0.91 (t, $J = 7.5$, 3 H, H₃C(11))

¹³C NMR: (126 MHz, CDCl₃)

141.39 (C(2')), 134.34 (C(8)), 133.52 (C(7)), 129.65 (C(6)), 128.74 (C(5)), 110.56 (C(3')), 82.17 (C(5')), 80.20 (C(4')), 75.65 (C(2)), 75.54 (C(9)), 63.00 (C(3)), 36.41 (C(1')), 35.98 (C(4)), 28.61 (C(10)), 10.08 (C(11))

IR: (NaCl)

3294 (s), 3008 (m), 2964 (s), 2933 (s), 2875 (m), 2096 (w), 1729 (w), 1623 (w), 1461 (m), 1434 (m), 1378 (m), 1351 (m), 1297 (m), 1224 (m), 1120 (s), 1087 (s), 1045 (m), 991 (m), 894 (w), 755 (m)

MS: (EI, 70 eV)

251 (3, M⁺+1), 250 (2, M⁺), 221 (12, M⁺-Et), 215 (24, M⁺-Cl), 197 (11), 185 (20), 167 (18), 149 (25), 131 (37), 121 (41), 107 (100), 91 (40), 79 (51), 65 (26)

Opt. Rot.: [α]_D²⁴ +228.0 ($c = 1.08$, CHCl₃); lit. [α]_D²¹ +216 ($c = 0.017$, CHCl₃)TLC: R_f 0.14 (silica gel, hexane/EtOAc, 4/1, PMA)**Preparation of Dicobalt complex (20)**

In a three-neck, 25 mL flask was placed **5** (240 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) under N_2 at 0 °C. A solution of $\text{Co}_2(\text{CO})_8$ (684 mg, 2.0 mmol, 2.0 equiv) in CH_2Cl_2 (10 mL) was then

added. The mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was directly concentrated to give crude product, which was purified by chromatography (silica gel, hexane/EtOAc, 19/1 to 9/1) to afford 500 mg (95%) of **20** as a red brown solid. (Sublimation of **20** at 65-68 °C (0.1 mmHg) for overnight gave deep red crystals, which were suitable for X-ray determination.)

Analytical Data for **20**:

mp: 68-69 °C (sublimation, 0.1 mmHg)

¹H NMR: (500 MHz, CDCl₃)

5.03 (dd, $J = 7.0, 5.5$, 1 H, HC(3')), 4.47 (dt, $J = 9.0, 7.0$, 1 H, HC(5)), 4.42 (dd, $J = 7.0, 5.5$, 1 H, HC(3)), 4.32 (td, $J = 7.5, 5.5$, 1 H, HC(5)), 2.51 (dq, $J = 14.0, 7.0$, 1 H, HC(4)), 2.32 (dq, $J = 13.0, 5.5$, 1 H, HC(4)), 1.81-1.75 (m, 2 H, H₂C(4')), 1.08 (t, $J = 7.5$, 3 H, H₃C(5')), 0.32 (s, 9 H, 3 x H₃C(7'))

¹³C NMR: (126 MHz, CDCl₃)

200.3 (6 x C(6')), 175.0 (C(2)), 110.2 (C(2')), 80.3 (C(3')), 78.8 (C(1')), 72.2 (C(3)), 66.1 (C(5)), 32.7 (C(4)), 30.0 (C(4')), 10.7 (C(5')), 1.0 (C(7'))

IR: (CHCl₃)

2967 (s), 2881 (s), 2480 (s), 2086 (s), 2051 (s), 2005 (s), 1770 (s), 1562 (s), 1454 (s), 1380 (s), 1247 (s), 1180 (s), 1099 (s), 1031 (s), 946 (s), 835 (s), 755 (s)

MS: (FAB)

498 (4, M⁺-CO), 470 (100, M⁺-2 x CO), 442 (38), 425 (80), 414 (58), 397 (65), 386 (50), 358 (48), 316 (22), 270 (30), 241 (18), 197 (22), 155 (40), 119 (80)

TLC: R_f 0.19 (silica gel, hexane/EtOAc, 9/1, PMA)

Analysis: C₁₈H₂₀O₉Co₂Si (526.31)

Calculated: C, 41.08; H, 3.83%

Found: C, 41.00; H, 3.64%

Table 1. ¹H NMR Data of Natural and Synthetic (+)-Brasilenyne (**1**)

Assignment (literature)	Natural 1 Solvent: CDCl ₃ (220 MHz) Ref. peak: TMS	Synthetic 1 Solvent: CDCl ₃ (500 MHz) Ref. peak: CHCl ₃ (7.26 ppm)	Assignment (synthetic)
HC(7)	6.24 (ddd, <i>J</i> = 10.0, 2.0, 1.0)	6.23 (ddd, <i>J</i> = 11.0, 2.5, 1.5)	HC(7)
HC(3')	~ 6.0 (dd, <i>J</i> = 11.0, 2.0)	6.07 (br d, <i>J</i> = 11.5)	HC(6)
HC(5)	~ 6.09 (m)	6.04 (dddd, <i>J</i> = 11.0, 8.0, 7.0, 1.0)	HC(2')
HC(2')	5.82 (dt, <i>J</i> = 11.0, 8.0)	5.81 (dtd, <i>J</i> = 11.0, 7.5, 1.0)	HC(5)
HC(8)	~ 5.55 (dd, <i>J</i> = 10.0, 8.0)	5.55 (ddd, <i>J</i> = 11.0, 7.0, 1.0)	HC(8)
HC(6)	~ 5.55 (dd, <i>J</i> = 11.0, 2.0)	5.54 (dd, <i>J</i> = 11.0, 1.0)	HC(3')
HC(9)	4.29 (dtd, <i>J</i> = 8.0, 7.0, 1.0)	4.29 (q, <i>J</i> = 7.0)	HC(9)
HC(2)	4.09 (ddd, <i>J</i> = 8.0, 3.0, 1.0)	4.08 (br d, <i>J</i> = 8.0)	HC(3)
HC(3)	3.91 (td, <i>J</i> = 7.0, 1.0)	3.90 (ddd, <i>J</i> = 8.5, 6.5, 1.0)	HC(2)
HC(5')	3.14 (d, <i>J</i> = 2.0)	3.13 (d, <i>J</i> = 2.0)	HC(5')
HC(4)	~ 2.7 (m)	2.72 (dtd, <i>J</i> = 14.0, 8.0, 1.0)	HC(1')
HC(4)	~2.7 (m)	2.67 (dtd, <i>J</i> = 13.5, 7.5, 1.0)	HC(4)
HC(1')	~ 2.60 (dt, <i>J</i> = 14.0, 8.0, 8.0)	2.61 (dddd, <i>J</i> = 14.0, 7.0, 6.5, 1.0)	HC(1')
HC(1')	2.50 (ddd, <i>J</i> = 14.0, 8.0, 3.0)	2.48 (dd, <i>J</i> = 13.5, 8.0)	HC(4)
HC(10)	1.73 (dq, <i>J</i> = 14.0, 7.0)	1.72 (d quint, <i>J</i> = 14.5, 7.5)	HC(10)
HC(10)	1.55 (dq, <i>J</i> = 14.0, 7.0)	1.53 (d quint, <i>J</i> = 14.5, 7.5)	HC(10)
HC(11)	0.91 (t, <i>J</i> = 7.0)	0.91 (t, <i>J</i> = 7.5)	HC(11)

Table 2. ^{13}C NMR Data of Natural and Synthetic (+)-Brasilenyne (**1**)

Natural 1 Solvent: CCl_4 (220 MHz) Ref. peak: TMS	Synthetic 1 Solvent: CDCl_3 (500 MHz) Ref. peak: CDCl_3 (77.0 ppm)	Assignment (synthetic 1)	^{13}C
141.2	141.39	HC(2')	+0.19
134.2	134.34	HC(8)	+0.14
133.3	133.52	HC(7)	+0.22
129.5	129.65	HC(6)	+0.15
128.6	128.74	HC(5)	+0.14
110.4	110.56	HC(3')	+0.16
82.0	82.17	HC(5')	+0.17
80.1	80.20	HC(4')	+0.10
76.0	75.65	HC(2)	-0.35
75.6	75.54	HC(9)	-0.06
62.9	63.00	HC(3)	+0.10
36.3	36.41	HC(1')	+0.11
35.9	35.98	HC(4)	+0.08
28.5	28.61	HC(10)	+0.11
9.94	10.08	HC(11)	+0.14

References

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- (3) The Schrock's molybdenum complex is commercially available (Strem) and can be prepared according to the reported procedure with consistent purity and reactivity, see: (1) Fox, H. H.; Yap, K. B.; Robbins, J.; Cai, S.; Schrock, R. R. *Inorg. Chem.* **1992**, *31*, 2287. (b) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875. (c) Oskam, J. H.; Fox, H. H.; Yap, K. B.; McConville, D. H.; O'Dell, R.; Lichtenstein, B. J.; Schrock, R. R. *J. Organomet. Chem.* **1993**, *459*, 185. (d) Fox, H. H.; Lee, J.-K.; Park, L. Y.; Schrock, R. R. *Organometallics* **1993**, *12*, 759.
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exp1 s2pul

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 solvent CDC13 d1
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 data/ui500nb/yang/~ dof 0
 YSM-VII-100-1-UI500- nnn
 0-brasilenyne.fid dnm c
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 sfrq 500.075 dseq
 tn H1 dres 1.0
 at 4.096 homo n
 np 65536 DEC2
 sw 8000.0 dfrq2 0
 fb 4000 dnm2
 bs 16 dpwr2 1
 tpr 55 dof2 0
 pw 7.3 dnm2 n
 d1 0 dnm2 c
 tof 0 dmf2 200
 nt 8 dseq2
 ct 8 dres2 1.0
 alock n homo2 n
 gain not used PROCESSING
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 il n wfile
 in n proc ft
 dp y fn not used
 bs nn math f
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 wp 5750.7 wexp
 vs 73 wbs
 sc 0 wnt
 wc 250
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 is 1114.13
 xfl 5143.2
 xfp 3630.5
 th 1
 ins 1.000
 ai cdc ph

synthetic
 (+)-brasilenyne 1

expl s2pul

SAMPLE DEC. & VT
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 solvent CDC13 dn H1
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 -VII-100-1-500-bra- dm YYY
 silenene.fid dnm w
 ACQUISITION dmf 12099

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 at 1.086 homo n
 np 65536 DEC2
 sw 30165.9 dfrq2 0
 fb 16600 dnm
 bs 16 dpwr2 1
 ss 1 dof2 0
 tpwr 55 dnm2 n
 pw 5.3 dnm2 c
 dl 1.000 dmf2 10000
 tof 1884.7 dseq2
 nt 160 dres2 1.0
 ct 160 homo2 n
 alock n
 gain not used lb PROCESSING
 gain 1.00

il n proc ft
 in n fn not used
 dp y math f
 hs nn

DISPLAY weir
 sp -1257.4 wexp
 wp 27642.5 wbs
 vs 56 wnt
 sc 0
 wc 250
 hzmm 110.57
 is 500.00
 rfl 10968.3
 rfp 9675.0
 th 11
 ins 100.000

VII-100-1-(+)-brasilenyne

Peak Report
 File: c:\first\data\mp
 Title: VII-100-1-(+)-brasilenyne
 Filter: None

cm-1	%T	cm-1	%T
3293.84	32.1291	3008.42	44.4936
2964.07	30.8750	2933.21	28.9139
2875.36	43.7401	2096.25	71.5146
1729.84	68.5818	1623.77	68.8236
1461.78	56.1036	1434.78	48.4299
1378.86	58.3744	1351.86	54.2410
1297.86	59.2564	1224.58	59.2800
1199.51	59.8911	1120.44	18.2005
1087.66	32.3923	1045.23	51.3054
991.23	54.7827	894.81	66.1621
755.96	34.1721

synthetic
 (+)-brasilenyne 1

transmittance

Wavenumbers