Suplementary Material
Novel Synthesis of the C1-C15 Polyether Domain of the Thyrsyferol and Venustatriol Natural Products.

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General methods. Unless otherwise noted, all reactions were carried out under nitrogen or argon atmosphere using oven dried glassware and standard gas tight syringe, cannula and septa techniques. THF was distilled over Na/benzophenone under nitrogen. CH_2Cl_2, CH_3CN, CH_3NO_2 and NEt_3 were distilled from CaH_2. DMSO was distilled from CaH_2 under vacuum. Flash chromatography was performed using Baker Flash silica gel 60 (40 μm) and the solvents indicated. Analytical TLC was performed using 0.25 mm or 0.5 mm EM silica gel F_{254} plates that were analyzed by fluorescence upon 254 nm irradiation or by staining with anisaldehyde reagent (450 mL of 95% EtOH, 25 mL of conc H_2SO_4, 15 mL acetic acid and 25 mL anisaldehyde). Optical rotations were obtained using a JASCO DIP-370 digital polarimeter. IR spectra were obtained using a Perkin-Elmer 683 infrarred spetrophotometer and IR data are reported in cm^{-1}. NMR spectra were obtained using the INOVA 500 and 300 MHz Varian instruments. High resolution mass spetrometric data was performed by the University of Minnesota Mass Spectrometry Laboratory.

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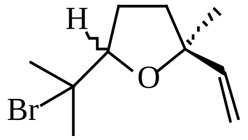

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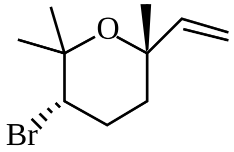

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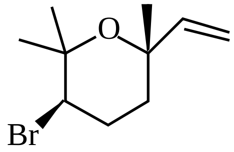
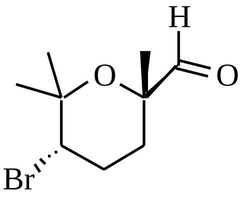


11

Tetrahydrobromofurans (9) and tetrahydrobromopyrans (10 and 11). To a stirred 0 ℃ solution of (3*S*)-(+)-linalool (0.80 g, 5.2 mmol) in CH_3NO_2 (70 mL) was added TBCO (2.36 g, 5.76 mol) in the dark. After 5 h the reaction mixture was poured into 1 M aqueous NaOH solution and stirred for 10 min. The organic phase was separated and washed with additional 1 M NaOH solution (70 mL). The combined aqueous phases were extracted with ether (3 x 100 mL). The combined organic phases were washed with saturated aqueous NaCl (50 mL), dried over $MgSO_4$, filtered, and concentrated. Purification by MPLC (silica, hexanes) gave the two tetrahydrofurans (**9a**:**9b**, 1.6:1, 0.20 g, 0.87 mmol, 17%) and a mixture of the two tetrahydropyrans (**10:11**, 1.6:1, 0.74 g, 3.2 mmol, 62%). **9a** R_f 0.11 (hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (3H, s), 1.70 (3H, s), 1.73 (3H, s), 1.72-2.12 (4H, m), 3.99 (1H, dd, *J*=6.9 Hz), 4.98 (1H, dd, *J*=2, 10.8 Hz), 5.21 (1H, dd, *J*=2, 17.4 Hz), 5.97 (1H, dd, *J*=10.8, 17.4 Hz). **9b** R_f 0.11 (hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.32 (3H, s), 1.71 (3H, s), 1.72 (3H, s), 1.70-2.08 (4H, m), 3.90 (1H, dd, *J*=6, 7.3 Hz), 4.98 (1H, dd, *J*=2, 10.5 Hz), 5.16 (1H, dd, *J*=2, 17 Hz), 1094, 1032; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.15 (3H, s), 1.33 (3H, s), 1.64 (1H, ddd, *J*=4, 14, 14 Hz), 2.05-2.16 (1H, m), 2.11-2.16 (2H, m), 2.24 (1H, dddd, *J*=4, 13, 13, 13 Hz), 3.95 (1H, dd, *J*=4, 12 Hz), 4.99-5.09 (2H, m), 5.98 (1H, dd, *J*=11, 18 Hz); HRMS (CI) calcd for $C_{10}H_{18}OBr$ $[M+H]^+$ 233.0537 found 233.0531, calcd for $C_{10}H_{21}OBrN$ $[M+NH_4]^+$ 250.0802 found 250.0832. **11** R_f 0.11 (hexanes); IR (neat) 2956, 2919, 2815, 1462, 1377, 1260, 1094, 1032; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.29 (3H, s), 1.38 (3H, s), 1.40 (3H, s), 2.08 (1H, ddd, *J*=4, 7.5, 13 Hz), 1.82 (1H, ddd, J=4, 7.5, 14 Hz), 1.92 (1H, dddd, *J*=4, 7, 9, 9 Hz), 2.08 (1H, ddd, *J*=4, 7.5, 13 Hz), 2.28 (1H, dddd, *J*=4, 4, 9, 9 Hz), 4.99-5.09 (2H, m), 5.92 (1H, dd, *J*=11, 18 Hz); HRMS (CI) calcd for $C_{10}H_{18}OBr$ $[M+H]^+$ 233.0537 found 233.0531, calcd for $C_{10}H_{21}OBrN$ $[M+NH_4]^+$ 250.0802 found 250.0832.



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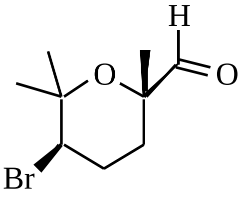
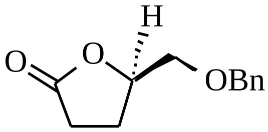


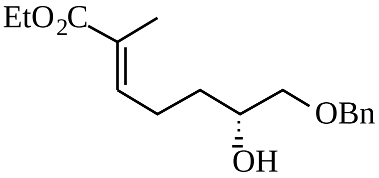
6

Aldehydes (**12** and **6**). To a stirred rt solution of the mixture of **10** and **11** (0.14 g, 0.60 mmol) in THF (1.7 mL) was added a solution of NMO (0.10 g, 0.90 mmol) in H_2O (0.4 mL) and OsO_4 (200 μL of a 0.15 M solution in H_2O, 0.03 mmol). After the solution was stirred at rt for 24 h, it was cooled to 0 °C and $NaIO_4$ (0.19 g, 0.90 mmol) and H_2O (0.45 mL) were added. The mixture was allowed to warm to rt and after 4 h was diluted with H_2O (20 mL) and extracted with ether (3 x 10 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by MPLC to obtain a mixture of **12** (69 mg, 0.29 mmol, 49%) and **6** (43 mg, 0.18 mmol, 31%). **12** R_f 0.51 (hexanes-ethyl acetate, 8:2, v/v); IR (neat) 2980, 2960, 1730, 1450, 1380, 1260, 1000; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.07 (3H, s), 1.28 (3H, s), 1.39 (3H, s), 1.40 (3H, s), 1.43-1.51 (1H, m), 1.95-2.08 (2H, m), 2.28-2.32 (1H, m). **6** R_f 0.43 (hexanes-ethyl acetate, 8:2, v/v); $[\alpha]_D$=+17.95° (c 0.44, $CHCl_3$); IR (neat) 2980, 2960, 1730, 1450, 1380, 1260, 1000; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.23 (3H, s), 1.30 (3H, s), 1.43 (3H, s), 1.87-1.92 (1H, m), 2.00-2.09 (2H, m), 2.14-2.20 (1H, m), 4.13 (1H, dd, *J*=2.2, 3 Hz), 9.55 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.85, 24.45, 26.29, 26.55, 30.91, 58.27, 204.51; HRMS (CI) calcd for $C_9H_{19}O_2BrN$ $[M+NH_4]^+$ 252.0593, found 252.0598.



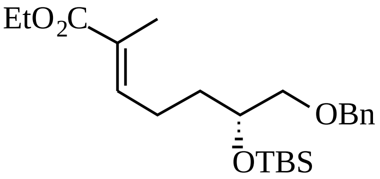
14

Lactone (14). To a solution of **13** (1.69 g, 14.50 mmol) in CH_2Cl_2:pentane (2:1, 21 mL) was added benzyl-2,2,2-trichloroacetimidate (3.24 mL, 17.4 mmol). The resulting solution was cooled to 0 °C and trifluoromethanesulfonic acid (0.26 mL, 2.9 mmol) was added dropwise. After 30 min, the reaction mixture was filtered through celite and the filtrate was washed with saturated aqueous $NaHCO_3$ (25 mL), and saturated aqueous NaCl (25 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. Flash chromatography (silica, hexanes-ethyl acetate, 7:3, v/v) gave **14** (1.89 g, 9.13 mmol, 63%). R_f 0.33 (hexanes-ethyl acetate, 7:3, v/v); $[\alpha]_D$=-13° (c 1.7, $CHCl_3$); IR (neat) 3100-2800, 1780, 1450, 1190, 1120; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.12-2.37 (2H, m), 2.44-2.70 (2H, m), 3.59 (1H, dd, *J*=4.2, 10.8 Hz), 3.69 (1H, dd, *J*=3.6, 10.6 Hz), 4.58 (2H, AB, *J*=12.3), 4.66-4.71 (1H, m) 7.27-7.37 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.22, 28.51, 71.63, 73.66, 79.09, 127.72, 127.932, 128.47, 137.72, 177.47; HRMS (CI) calcd for $C_{12}H_{15}O_3$ $[M+H]^+$ 207.1017, found 207.1014.



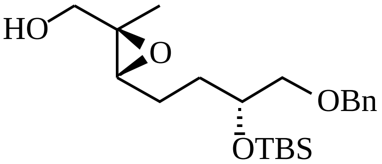
15

Hydroxyester (15). To a -78 °C solution of **14** (1.87 g, 9.09 mmol) in toluene (37 mL) was added DIBAL (9.98 mL of a 1 M solution in toluene, 9.98 mmol) and the resulting solution was stirred for 1 h, then MeOH (2.8 mL) was added carefully. After warming to rt, the reaction mixture was diluted with ethyl acetate (100 mL) and washed with saturated Na/K tartrate (25 mL) and saturated aqueous NaCl (25 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude lactol was dissolved in benzene (50 mL) and to this solution was added carbethoxyethylenetriphenylphosphorane (3.94 g, 10.8 mmol). After the reaction mixture was heated to reflux for 2 h, the solvent was removed under vaccuum. Flash chromatography (silica, hexanes-ethyl acetate, 75:25, v/v) gave **15** as a colorless oil (2.04 g, 6.99 mmol, 77%). R_f 0.5 (hexanes-ethyl acetate, 7:3, v/v); $[\alpha]_D$=-1.4° (c 2.26, $CHCl_3$); IR (neat) 3450, 3000-2850, 1700, 1450, 1360, 1260, 1130, 1090; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28 (3H, t, *J*=7.2 Hz), 1.52-1.62 (2H, m), 1.83 (3H, s), 2.26-2.35 (2H, m), 3.34 (1H, dd, *J*=7.5, 9.2 Hz), 3.50 (1H, dd, *J*=3, 9.3 Hz), 3.78-3.85 (1H, m), 4.18 (2H, q, *J*=7.2 Hz), 4.55 (2H, s), 6.74 (1H, ddd, *J*=1.2, 7.5, 7.5 Hz), 7.29-7.36 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.37, 14.30, 24.70, 31.85, 60.46, 69.72, 73.39, 74.40, 76.64, 127.76, 127.85, 128.37, 128.42, 128.48, 137.84, 141.33, 168.18; HRMS (CI) calcd for $C_{17}H_{28}NO_4$ $[M+NH_4]^+$ 310.2011, found 310.2030.



16

Silyl ether (16). To a solution of **16** (1.44 g, 4.95 mmol) in DMF (3 mL) at 0 °C was added imidazole (0.87 g, 13 mmol) and TBSCl (1.49 g, 9.90 mmol) and the resulting mixture was stirred at rt for 3 h. The reaction mixture was diluted with ether (50 mL) and washed with H_2O (20 mL) and saturated aqueous NaCl (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Flash chromatography (silica, hexanes-ethyl acetate, 95:5 v/v) gave **16** (1.90 g, 4.70 mmol, 95%). R_f 0.27 (hexanes-ethyl acetate, 95:5, v/v); $[\alpha]_D$=+14° (c 2.11, $CHCl_3$); IR (neat) 2960-2850, 1710, 1460, 1450, 1360, 1250, 1120, 1090; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (3H, s), 0.06 (3H, s), 0.89 (9H, s), 1.29 (3H, t, *J*=6.9 Hz), 1.55-1.80 (2H, m), 1.82 (3H, s), 2.10-2.35 (2H, m), 3.36 (1H, dd, *J*=6, 9.5 Hz), 3.42 (1H, dd, *J*=5.4, 9.5 Hz), 3.81-3.90 (1H, m), 4.18 (2H, q, *J*=6.9 Hz), 4.52 (2H, s), 6.77 (1H, ddd, *J*=1.5, 7, 7 Hz), 7.26-7.37 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ -4.80, -4.33, 12.33, 14.31, 18.15, 24.41, 25.87, 33.44, 60.39, 70.88, 71.20, 73.35, 74.33, 74.65, 127.50, 127.58, 127.63, 127.84, 128.34, 138.27, 138.27, 142.04, 168.22; HRMS (CI) calcd for $C_{23}H_{39}O_4Si$ $[M+H]^+$ 407.2607 found 407.2615.

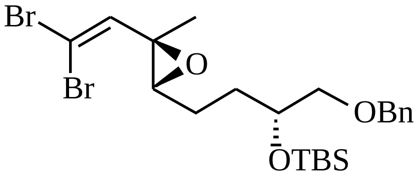


17

Epoxide (17). To a solution of **16** (1.69 g, 4.16 mmol) in CH_2Cl_2 at -78 °C was added DIBAL (9.15 mL of a 1 M solution in CH_2Cl_2) and the resulting solution was stirred for 30 min. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with saturated aqueous Na/K tartrate (25 mL) and saturated aqueous NaCl (25 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Flash chromatography (silica, hexanes-ethyl acetate, 8:2, v/v) gave the allylic alcohol (1.09 g, 2.99 mmol, 72%). R_f 0.27 (hexanes-ethyl acetate, 8:2, v/v); $[\alpha]_D$=+13.4° (c 0.59, $CHCl_3$); IR (neat) 3400, 3000-2860, 1450, 1370, 1250, 1100, 1000; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (3H, s), 0.07 (3H, s), 0.89 (9H, s), 1.45-1.67 (2H, m), 1.66 (3H, s), 3.37 (1H, dd, *J*=5.4, 9.7 Hz), 3.42 (1H, dd, *J*=5.4, 9.6 Hz), 3.820-3.89 (1H, m), 3.97 (2H, d, *J*=6.3 Hz), 4.53 (2H, s), 5.42 (1H, ddd, J=1.2, 7.8, 7.8 Hz), 7.34 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ -4.75, -4.30, 13.65, 18.18, 23.44, 25.90, 34.51, 68.95, 71.16, 73.33, 74.60, 126.13, 127.53, 127.61, 128.33, 134.84, 138.39; HRMS (CI) calcd for $C_{21}H_{37}NO_3Si$ $[M+NH_4]^+$ 382.2767, found 382.2765, calcd for $C_{21}H_{38}NO_2Si$ $[M-H_2O+NH_4]^+$ 364.2662, found 364.2659, calcd for $C_{21}H_{35}O_2Si$ $[M-OH]^+$ 347.2397, found 347.2420.

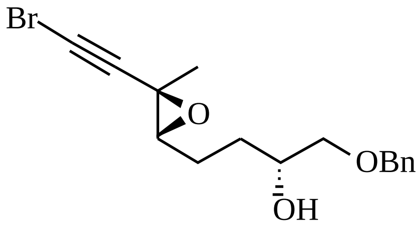
A mixture of powdered activated 4 Å molecular sieves (0.20 g) and CH_2Cl_2 (4 mL) was cooled to 0 °C. (-)-D-diethyl tartrate (40 mg, 0.19 mmol) and titanium isopropoxide (39 mg, 0.14 mmol) were added sequentially. After the mixture was cooled to -20 °C, *tert*-butylhydroperoxide (0.82 mL of a 5 M solution in decane, 4.1 mmol,) was added dropwise in 10 min, and the resulting mixture was stirred for 30 min.

over 10 min. Stirring was mantained at ca. -23 °C for 5 h. Then the reaction mixture was warmed to 0 °C, H_2O (0.78 mL) was added, and the mixture was stirred for 30 min. A 30% aqueous solution of NaOH saturated with NaCl (170 μL) was added and the mixture was stirred vigorously or 15 min. The aqueous phase was extracted with additional CH_2Cl_2 (2 x 8 mL), and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under vacuum. Flash chromatography (silica, hexanes-ethyl acetate, 77:23, v/v) gave **17** (0.90 g, 2.4 mmol, 86%), >98% ee by NMR of MTPA ester. R_f 0.38 (hexanes-ethyl acetate, 7:3, v/v); $[\alpha]_D$=+17° (c 1.33, $CHCl_3$); IR (neat) 3440, 2960-2860, 1460, 1450, 1300, 1320, 1250, 1110, 1070, 1030; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.05 (3H, s), 0.06 (3H, s), 0.89 (9H, s), 1.28 (3H, s), 1.55-1.72 (5H, m), 3.05 (1H, dd, *J*=5.7 Hz), 3.37 (1H, dd, *J*=5.7, 9.6 Hz), 3.44 (1H, dd, *J*=5.4, 9.6 Hz), 3.58 (1H, dd, *J*=8.7, 12 Hz), 3.66 (1H, dd, *J*=4.5, 12 Hz), 3.86-3.94 (1H, m), 4.53 (2H, s), 7.34 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ -4.78, -4.37, 14.16, 18.14, 23.83, 25.86, 31.21, 60.02, 60.97, 65.35, 70.83, 73.35, 74.19, 127.58, 127.63, 128.35, 138.26; HRMS (CI) calcd for $C_{21}H_{35}O_3Si$ $[M-OH]^+$ 363.2346, found 363.2348, calcd for $C_{21}H_{37}O_4Si$ $[M+H]^+$ 381.2451, found 381.2473, calcd for $C_{21}H_{40}NO_4Si$ $[M+NH_4]^+$ 398.2716, found 398.2731.



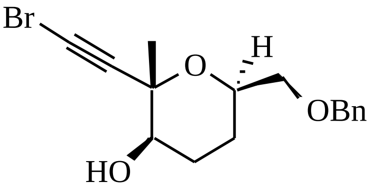
18

Dibromoalkene (18). To a solution of the epoxy alcohol **17** (0.26 g, 0.69 mmol) in CH_2Cl_2:DMSO (5:1, 6.5 mL) at 0 °C was added triethylamine (0.57 mL, 4.1 mmol) and SO_3.pyridine (0.33 g, 2.1 mmol). After the resulting solution was stirred at 0 °C for 4 h, it was diluted with ethyl acetate (20 mL) and washed with H_2O (5 mL), saturated aqueous NH_4Cl (5 mL), and saturated aqueous NaCl (5 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude aldehyde was filtered through a pad of silica gel with hexanes-ethyl acetate (95:5, v/v) and the eluant was concentrated to yield the corresponding aldehyde (0.24 g, 0.63 mmol, 92%). To a mixture of CBr_4 (0.44 g, 1.3 mmol) in CH_2Cl_2 (8 mL) at 0 °C under Ar was added a solution of PPh_3 (0.69 g, 2.6 mmol) in CH_2Cl_2 (1.2 mL). After 20 min the mixture was cooled to -78 °C and NEt_3 (0.67 mmol, 93 μL) was added. A solution of the aldehyde (0.24 g, 0.63 mmol) in CH_2Cl_2 (2 mL) was added via syringe over 3 min. After 45 min, hexanes (22 mL) was added and after stirring for 30 min the crude mixture was filtered. The filtrate was concentrated and the residue was purified by flash chromatography (silica, hexanes-ethyl acetate, 97:33, v/v) to give **18** (0.30 g, 0.58 mmol, 91%). R_f 0.40 (hexanes-ethyl acetate, 95:5, v/v); $[\alpha]_D$=-24.4° (c 1.57, $CHCl_3$); IR (neat) 2954-2856, 1599, 1458, 1376, 1254, 1112, 1078; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.05 (3H, s), 0.06 (3H, s), 0.88 (9H, s), 1.39 (3H, s), 1.60-1.89 (4H, m), 3.01 (1H, dd, *J*=6 Hz), 3.36 (1H, dd, *J*=6, 9.6 Hz), 3.43 (1H, dd, *J*=5.4, 9.6 Hz), 3.85-3.93 (1H, m), 4.53 (2H, AB, *J*=12.3 Hz), 6.73 (1H, s), 7.33 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ -4.76, -4.35, 16.03, 18.13, 24.225, 25.86, 31.11, 61.23, 64.29, 70.79, 73.33, 74.129, 91.70, 127.60, 127.63, 128.36, 138.29, 139.34; HRMS (CI) calcd for $C_{22}H_{36}Br_2O_3Si$ $[M+H]^+$ 533.0714, found 533.0701, calcd for $C_{22}H_{39}Br_2NO_3Si$ $[M+NH_4]^+$ 550.0979, found 550.0971.



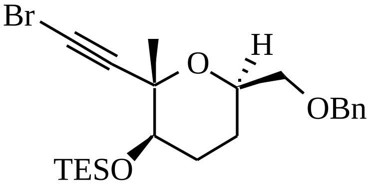
19

Alkyne (19). To a 0 °C solution of **18** (0.19, 0.36 mmol) in THF (1.8 mL) was added dropwise TBAF (1.46 mL of a 1 M solution in THF). The mixture was allowed to warm to rt and stir for 9 h. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with saturated aqueous NH_4Cl (10 mL) and saturated aqueous NaCl (10 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (hexanes-ethyl acetate, 65:35, v/v) to give **19** (0.11 g, 0.32 mmol, 88%) as a colorless oil. R_f 0.32 (hexanes-ethyl acetate, 7:3, v/v); $[\alpha]_D$=-13.6° (c 0.66, $CHCl_3$); IR (neat) 3445, 3000-2891, 2208, 1603, 1453, 1381, 1365, 1305, 1244, 1099, 1074, 1028; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.50 (3H, s), 1.63-1.66 (4H, m), 2.46 (1H, d, *J*=3 Hz), 3.16 (1H, dd, *J*=6 Hz), 3.36 (1H, dd, *J*=7.5, 9.3 Hz), 3.52 (1H, dd, *J*=3, 9.3 Hz), 3.82-3.91 (1H, m), 4.56 (2H, s), 7.35 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.12, 24.03, 29.40, 42.72, 51.86, 64.08, 69.54, 73.42, 74.30, 80.76, 127.80, 127.90, 128.52, 137.81; HRMS (CI) calcd for $C_{16}H_{18}BrO_3$ $[M-OH]^+$ 321.0486, found 321.0485, calcd for $C_{16}H_{20}BrO_3$ $[M+H]^+$ 339.0591, found 339.0572, calcd for $C_{16}H_{23}BrNO_3$ $[M+NH_4]^+$ 356.0856, found 356.0852.



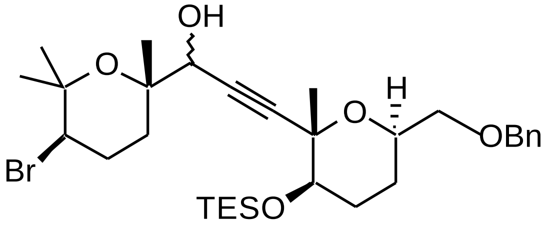
20

Tetrahydropyran (20). To a stirred -78 °C solution of **19** (0.10 g, 0.29 mmol) in CH_2Cl_2 (8.5 mL) under Ar was added a borontrifluoride etherate (286 μl of a 0.1 M solution in CH_2Cl_2) dropwise. After 30 min the mixture was warmed to -10 °C. After the reaction mixture was stirred at -10 °C for 6 h, it was diluted with H_2O (30 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (silica, hexanes-ethyl acetate, 8:2, v/v) gave **20** (89 mg, 0.26 mmol, 91%). R_f 0.32 (hexanes-ethyl acetate, 7:3, v/v); $[\alpha]_D$=-6.28°(c 0.29, $CHCl_3$); IR (neat) 3436, 3030-2867, 2203, 1496, 1452, 1367, 1262, 1202, 1124, 1094, 1071; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.52 (3H, s), 1.48-1.64 (2H, m), 1.86 (1H, ddd, *J*=2.5, 6.7, 14 Hz), 1.95 (1H, d, *J*=10 Hz), 2.21 (1H, dddd, *J*=2.5, 5.2, 14, 14 Hz), 3.45 (1H, dd, *J*=4.5, 10 Hz), 3.54 (1H, dd, *J*=5, 10 Hz), 3.58-3.62 (1H, m), 4.59 (2H, AB, *J*=12.5 Hz), 7.35-7.36 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.18, 25.29, 27.21, 47.61, 69.80, 72.57, 73.57, 73.05, 73.43, 74.35, 80.20, 127.65, 127.76, 128.39, 138.23; HRMS (CI) calcd for $C_{16}H_{18}BrO_3$ $[M-OH]^+$ 321.0486, found 321.0459, calcd for $C_{16}H_{20}BrO_3$ $[M+H]^+$ 339.0591, found 339.0548, calcd for $C_{16}H_{23}BrNO_3$ $[M+NH_4]^+$ 356.0856, found 356.0859.



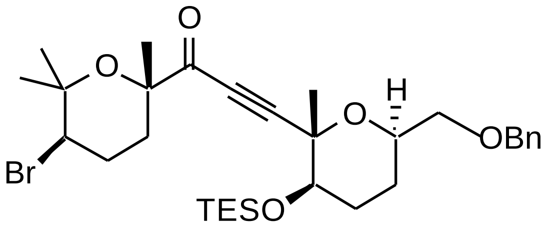
7

Alkynyl bromide (7). To a solution of **20** (67 mg, 0.19 mmol) in DMF (0.5 mL) at 0 °C was added imidazole (93 mg, 1.4 mmol) and TESCl (0.11 mL, 0.68 mmol) and the resulting mixture was stirred at rt for 6 h. The reaction mixture was diluted with ether (15 mL) and washed with H_2O (5 mL) and saturated aqueous NaCl (5 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Flash chromatography (silica, hexanes-ethyl acetate, 95:5 v/v) gave **7** (73 mg, 0.16 mmol, 85%). R_f 0.26 (hexanes-ethyl acetate, 98:2, v/v) $[\alpha]_D$=-19.8° (c 0.45, $CHCl_3$); IR (neat) 3402, 2952, 2879, 2360, 1639, 1454, 1370, 1259, 1206, 1110, 1076, 1022; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.64 (6H, q, *J*=8 Hz), 0.97 (9H, t, *J*=8 Hz), 1.67-1.76 (2H, m), 2.10-2.21 (2H, m), 3.42 (1H, dd, *J*=5.4, 10 Hz), 3.57 (1H, dd, *J*=5.4, 10 Hz), 4.02-4.13 (1H, m), 4.59 (2H, AB, *J*=12.3 Hz), 7.34-7.36 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.89, 6.91, 21.79, 25.68, 28.39, 46.43, 70.22, 72.59, 73.37, 73.43, 74.52, 81.05, 127.52, 127.83, 128.32, 138.47; HRMS (CI) calcd for $C_{22}H_{34}O_3SiBr$ $[M+H]^+$ 453.1452, found 453.1476, calcd for $C_{22}H_{37}NO_3SiBr$ $[M+NH_4]^+$ 470.1717, found 470.1726.



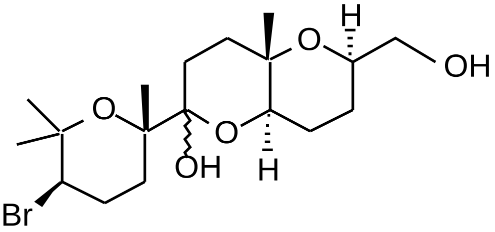
21

Propargylic alcohols (21). To a rt mixture of $CrCl_2$ (32 mg, 0.26 mmol) in DMF (0.68 mL) was added dropwise a solution of the aldehyde **6** (24 mg, 0.10 mmol) and alkynyl bromide **7** (59 mg, 0.13 mmol) in DMF (0.4 mL) in a glove box under nitrogen. The reaction mixture was stirred at rt for 20 h. Ethyl acetate (3 mL) and saturated aqueous NH_4Cl (3 mL) were added, and the mixture was stirred for 20 min. The aqueous phase was washed with ethyl acetate (2 x 2 mL). The combined organic phases were washed with saturated aqueous NaCl (2 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (silica, hexanes-ethyl acetate, 8:2, v/v) gave a mixture of the two propargylic alcohols **21** (40 mg, 66 μmol, 66%). R_f 0.29 (hexanes-ethyl acetate, 85:15, v/v); IR (neat) 3400, 2951, 2878, 1454, 1376, 1208, 1122, 1074, 1020; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.62 (6H, q, *J*=8 Hz), 0.97 (9H, t, *J*=8 Hz), 1.35 (3H, s), 1.366 (3H, s), 1.45 (3H, s), 1.46 (3H, s), 1.57-1.73 (4H, m), 2.03 (1H, ddd, *J*=4.5, 13.7, 13.7 Hz), 2.11-2.19 (2H, m), 2.25 (1H, dddd, *J*=4, 13, 13.3, 13.3 Hz), 2.75 (1H, d, *J*=3 Hz) 3.41 (1H, dd, *J*=5, 10 Hz), 3.57 (1H, dd, *J*=5, 10 Hz), 3.63 (1H, dd, *J*=2.5 Hz), 3.85 (1H, dd, *J*=4, 12.7 Hz), 4.04-4.08 (1H, m), 4.14 (1H, d, *J*=3 Hz), 4.54-4.56 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.90, 6.92, 21.84, 23.01, 23.06, 25.86, 27.77, 28.58, 30.72, 30.92, 57.27, 69.89, 70.29, 72.65, 73.23, 73.47, 76.39, 76.62, 84.06, 86.65, 127.49, 127.71, 128.29, 138.56; HRMS (CI) calcd for $C_{31}H_{53}NO_5BrSi$ $[M+NH_4]^+$ 626.2863, found 626.2873.



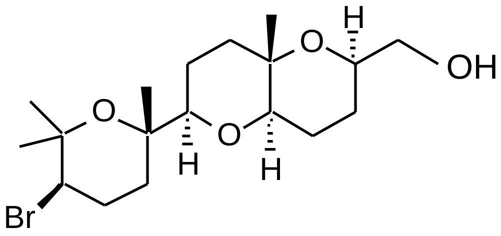
22

Ynone (22). To a stirred rt mixture of the mixture of propargylic alcohols **21** (28 mg, 46 μmol) in hexanes (1.5 mL) was added activated MnO_2 (80 mg, 0.91 mmol). After stirring for 7 h, the reaction mixture was filtered through celite with CH_2Cl_2. The filtrate was concentrated and the residue was purified by flash chromatography (silica, hexanes: ethyl acetate, 97:3, v/v) to give the ynone **22** (25 mg, 41 μmol, 89%). R_f 0.37 (hexanes-ethyl acetate, 9:1, v/v); $[\alpha]_D$=+4.4° (c 0.46, $CHCl_3$); IR (neat) 2964, 2360, 2210, 1679, 1450, 1410, 1261, 1091, 1022; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.63 (6H, q, *J*=8 Hz), 0.98 (9H, t, *J*=8 Hz), 1.36 (3H, s), 1.41 (3H, s), 1.42 (3H, s), 1.53 (3H, s), 1.72 (2H, m), 1.89-1.95 (1H, m), 2.01-2.07 (1H, m), 2.09-2.28 (4H, m), 3.44 (1H, dd, *J*=5, 10 Hz), 3.39 (1H, dd, *J*=5, 10 Hz), 3.72 (1H, dd, *J*=2.5 Hz), 4.22 (1H, dd, *J*=3, 5 Hz), 4.13-4.15 (1H, m), 4.59 (2H, AB, *J*=12.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.89, 6.89, 21.61, 23.71, 25.17, 26.09, 26.67, 27.00, 28.91, 30.40, 58.49, 69.80, 73.81, 75.48, 79.13, 84.44, 127.47, 127.69, 128.29, 128.50; HRMS (CI) calcd for $C_{31}H_{51}O_5BrSiN$ $[M+NH_4]^+$ 624.2707, found 624.2713.



23

Hemiketal (23). A mixture of **22** (14 mg, 23 μmol) and 20% $Pd(OH)_2$ on carbon (7.2 mg) in MeOH (2 mL) was stirred vigorously under 1 atm of H_2 for 2 h. The mixture was filtered through celite with ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography (silica, ethyl acetate) to give **23** (9.1 mg, 23 μmol, 98%). R_f 0.26 (ethyl acetate); $[\alpha]_D$=-12.5° (c 0.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.20 (3H, s), 1.33 (3H, s), 1.30-1.40 (1H, m), 1.38 (3H, s), 1.45 (3H, s), 1.45-1.61 (2H, m), 1.74-1.96 (4H, m), 2.05-2.19 (3H, m), 2.67-2.83 (2H, m), 3.45 (1H, dd *J*=2 Hz), 3.48-3.57 (2H, m), 3.59-3.64 (1H, m), 4.01 (1H, dd, *J*=4.5, 8.5 Hz); HRMS (CI) calcd for $C_{18}H_{30}O_4Br$ [M-OH]+ 389.1320, found 389.1296, calcd for $C_{18}H_{32}O_5Br$ $[M+H]^+$ 407.1425, found 407.1441, calcd for $C_{18}H_{35}O_5NBr$ $[M+NH_4]^+$ 424.1690, found 424.1708.



5

Tricycle (5). To a stirred 0 °C solution of **23** (2.5 mg, 6.1 μmol) in CH_3CN (1.25 mL) under Ar was added $HSiEt_3$ (9.8 μL, 61 μmol) and TMSOTf (3.3 μL, 18 μmol). After the reaction mixture was stirred for 1 h it was diluted with saturated aqueous $NaHCO_3$ (2 mL) and extracted with ethyl acetate (3 x 2 mL). The organic phase was washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (silica, hexanes-ethyl acetate, 7:3, v/v) to give **5** (2.3 mg, 5.8 μmol, 95%). R_f 0.28 (hexanes-ethyl acetate, 6:4, v/v); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.21 (3H, s), 1.22 (3H, s), 1.28 (3H, s), 1.41 (3H, s), 1.42-1.59 (4H, m), 1.73-1.88 (6H, m), 1.99 (1H, bs), 2.12 (1H, dddd, *J*=4, 4, 8.5, 8.5 Hz), 2.25 (1H, dddd, *J*=4, 13, 13, 13 Hz), 3.47 (1H, dd, *J*=5.5, 11.2 Hz), 3.52 (1H, d, *J*=5.5 Hz), 3.89 (1H, dd, *J*=4, 13 Hz), 3.93-3.98 (1H, m); HRMS (CI) calcd for $C_{18}H_{32}O_4Br$ $[M+H]^+$ 391.1471, found 391.1484, calcd for $C_{18}H_{35}O_4NBr$ $[M+NH_4]^+$ 408.1741, found 408.1724.