Exploiting Hidden Symmetry in Natural Products: Total Syntheses of Amphidinolides C and F

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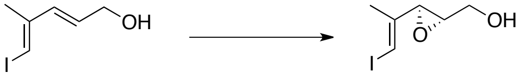
Electronic Supplementary Information: Experimental

General. Infrared spectra were recorded neat unless otherwise indicated and are reported in cm^{-1}. ^{1}H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. ^{13}C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent.

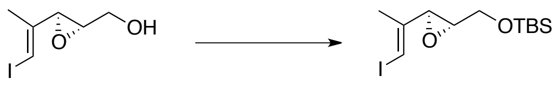
Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on EM Science Gedurian 230-400 mesh silica gel.

Air and/or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried in an oven at 120°C or by flame, then cooled under argon. Dry THF and CH_2Cl_2 were obtained via a solvent purification system. All other solvents and commercially available reagents were either purified via literature procedures or used without further purification.



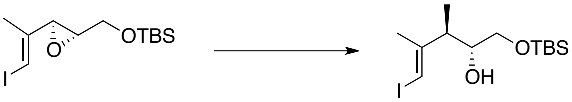
13 **SI-1**

Epoxide SI-1: To a stirred suspension of 4Å mol sieves (2.50 g) in dry CH_2Cl_2 (30.0 mL) at -35 °C was added $Ti(O\textit{i}\text{-}Pr)_4$ (563 mg, 0.59 mL, 1.97 mmol) followed by (+)-DET (605 mg, 0.50 mL, 2.96 mmol). The resulting mixture was stirred for 1 h and then TBHP (5.40 mL, 29.6 mmol, 5.5 M in decane) was added. After 1 h, a solution of allyl alcohol **13**[1] (2.21 g, 9.86 mmol) in CH_2Cl_2 (30.0 mL) was added dropwise over 45 min. After 16 h at -35 °C, the reaction was quenched with sat. aq. $NaHCO_3$ (20 mL) and diluted with Et_2O (50 mL). The resulting solution was passed through a celite pad and the aqueous layer was extracted with Et_2O (3 X 60 mL) and the combined organic layer was washed with H_2O and brine (50 mL each). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 15-20% EtOAc / hexanes, to give epoxide **SI-1** (2.06 g, 8.58 mmol, 87%) as white solid. Enatiomeric excess was determined by chiral HPLC {4.6 X 250 mm, Daicel AD column, 96:4 hexanes / *i*-PrOH, 0.5 mL min^{-1}, retention times 33.2 min (major) and 36.2 (minor)} to be 95% ee. Mp. 47-48 °C; $[\alpha]_D^{23}$ = -20.3 (*c* = 1.61, $CHCl_3$); IR: (neat) 3390, 3046, 2981, 2921, 2867, 1603, 1434, 1380, 1293, 1233, 1151, 1069, 1031, 999, 879, 786 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (s, 1H), 3.96 (d, *J* = 12.6 Hz, 1H), 3.67-3.73 (m, 1H), 3.55 (d, *J* = 2.0 Hz, 1H), 3.16 (dt *J* = 3.9, 2.9 Hz, 1H), 2.14 (s br, 1H), 1.75 (d, *J* = 0.88 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 80.1, 61.0, 58.2, 57.1, 19.0 ppm; HRMS (EI+) calcd. for $C_6H_9O_2I$ (M+) 239.9648, found 239.9639.



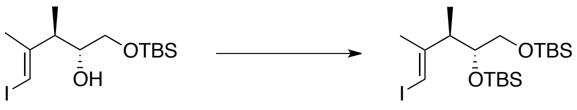
SI-1 **14**

TBS Ether 14: To a stirred solution of alcohol **SI-1** (1.95 g, 8.12 mmol) in DMF (12.0 mL) at 0 °C were added imidazole (967 mg, 14.2 mmol), TBS chloride (1.59 g, 10.5 mmol) and DMAP (245 mg, 2.03 mmol) sequentially. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and diluted with Et_2O (50 mL). The aqueous layer was extracted with Et_2O (2 X 50 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 4-8% EtOAc / hexanes, to give TBS ether **14** (2.85 g, 8.04 mmol, 99%) as colorless oil. $[\alpha]_D^{23}$ = -11.1 (c = 1.07, $CHCl_3$); IR: (neat) 2954, 2921, 2888, 2856, 1472, 1456, 1374, 1353, 1255, 1151, 1102, 1059, 1004, 960, 879, 824, 775, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.42 (s, 1H), 3.87 (dd, J = 12.0, 3.1 Hz, 1H), 3.74 (dd, J = 12.0, 4.2 Hz, 1H), 3.44 (d, J = 1.8, 1H), 3.07-3.09 (m, 1H), 1.76 (d, J = 1.0 Hz, 3H), 0.92 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 79.4, 62.6, 58.5, 57.4, 25.8, 19.1, 18.3, -5.3 ppm; HRMS (CI+) calcd. for $C_{12}H_{24}OSiI$ (M+H) 355.05906, found 355.05960.



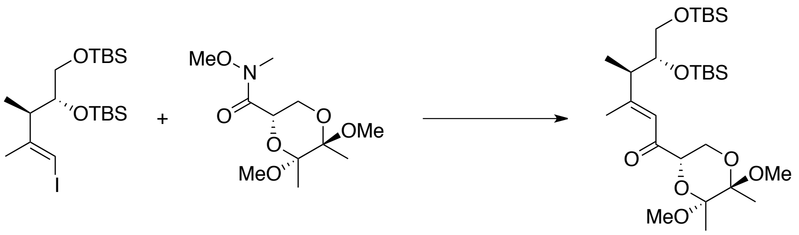
14 **SI-2**

Alcohol SI-2: To a stirred solution of epoxide **14** (1.53 g, 4.32 mmol) in CH_2Cl_2 (34.0 mL) at -90 °C was added Me_3Al (343 mg, 0.46 mL, 4.75 mmol). After 45 min, another portion of Me_3Al (343 mg, 0.46 mL, 4.75 mmol) was added. After another 1 h, the reaction mixture was quenched with sat. aq. Rochelle's salt (50 mL) and diluted with CH_2Cl_2 (50 mL). The resulting mixture was stirred vigorously at rt for 15 min to get two clear layers. The aqueous layer was extracted with CH_2Cl_2 (3 X 60 mL) and the combined organic layer was washed with brine (30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give alcohol **SI-2** {1.57 g, 4.24 mmol, 98% (10.2:1 dr)} as colorless oil. $[\alpha]_D^{23}$ = +9.4 (c = 1.00, $CHCl_3$); IR: (neat) 3564, 3466, 2954, 2927, 2856, 1472, 1456, 1255, 1113, 1091, 879, 835, 775, 672 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03 (s, 1H), 3.71 (dd, J = 9.5, 2.8 Hz, 1H), 3.53-3.60 (m, 1H), 3.48 (dd, J = 9.5, 6.5 Hz, 1H), 2.57 (dq, J = 7.3, 7.0 Hz, 1H), 2.36 (d, J = 3.9 Hz, 1H), 1.86 (d, J = 0.9 Hz, 3H), 1.03 (d, J = 7.0 Hz, 3H), 0.92 (s, 9H), 0.09 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 76.6, 73.2, 65.0, 45.9, 25.8, 20.8, 18.2, 15.6, -5.3, -5.4 ppm; HRMS (CI+) calcd. for $C_{13}H_{28}O_2ISi$ (M+H) 371.0904, found 371.0887.



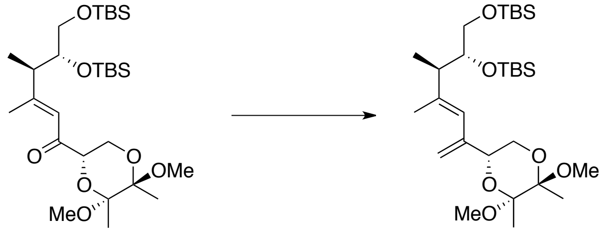
SI-2 **11**

TBS Ether 11: To a stirred solution of alcohol **SI-2** (644 mg, 1.73 mmol) in CH_2Cl_2 (11.0 mL) were added 2,6-lutidine (406 mg, 0.44 mL, 3.80 mmol) followed after 5 min by TBSOTf (921 mg, 0.80 mL, 3.47 mmol) at 0 °C. The reaction was allowed to warm up to rt. After 2 h, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and diluted with Et_2O (30 mL). The aqueous layer was extracted with Et_2O (2 X 30 mL) and the combined organic layer was washed with H_2O and brine (20 mL each). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 1% EtOAc / hexanes, to give TBS ether **11** (822 mg, 1.69 mmol, 98%) as colorless oil. $[\alpha]_D^{23}$ = +14.5 (*c* = 1.05, $CHCl_3$); IR: (neat) 2954, 2921, 2883, 2850, 1472, 1396, 1358, 1244, 1102, 1059, 950, 933, 841, 770, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 3.58 (dt, *J* = 6.8, 4.7 Hz, 1H), 3.48 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.39 (dd, *J* = 9.9, 7.0 Hz, 1H), 2.74 (qd, *J* = 7.1, 4.5 Hz, 1H), 1.83 (s, 3H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.07 (s, 6H), 0.05 (s, 6H) ppm; ^{13}C NMR (100 MHz, C_6D_6) δ 148.9, 77.6, 75.8, 65.4, 45.5, 25.9, 25.8, 22.2, 18.2, 18.0, 15.8, -4.3, -4.9, -5.4, -5.6 ppm; HRMS (CI+) calcd. for $C_{19}H_{42}O_2ISi_2$ (M+H) 485.1768, found 485.1777.



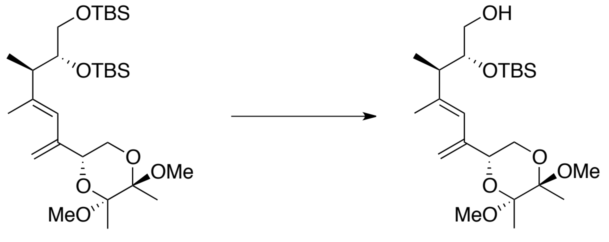
11 **15** **SI-3**

Enone SI-3: To a stirred solution of vinyl iodide **11** (400 mg, 0.826 mmol) in THF (6.5 mL) at -78 °C was added *n*-BuLi (0.30 mL, 0.757 mmol, 2.5 M in hexanes) dropwise. After 2 h at -78 °C, a solution of Weinreb amide **15**[2] (181 mg, 0.688 mmol) in THF (6.5 mL) was added dropwise over 15 min. After another 1.5 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-8% EtOAc / hexanes, to give enone **SI-3** (362 mg, 0.646 mmol, 94%) as colorless oil. $[\alpha]_D^{23}$ = -37.0 (*c* = 1.01, $CHCl_3$); IR: (neat) 2954, 2927, 2856, 1685, 1609, 1472, 1374, 1249, 1146, 1113, 1037, 835, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.55 (s, 1H), 4.23 (dd, *J* = 6.1, 4.4 Hz, 1H), 4.10 (dd, *J* = 11.2, 6.1 Hz, 1H), 3.90 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.69-3.73 (m, 1H), 3.50 (dd, *J* = 10.2, 5.1 Hz, 1H), 3.44 (dd, *J* = 10.2, 6.3 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 2.58 (qd, *J* = 7.1, 4.6 Hz, 1H), 2.23 (d, *J* = 0.96, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.14 (d, *J* = 7.1, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.074 (s, 3H), 0.070 (s, 3H), 0.045 (s, 3H), 0.042 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 197.2, 163.3, 121.1, 100.1, 99.2, 76.2, 75.1, 65.2, 58.9, 49.7, 48.3, 46.4, 25.9, 25.8, 19.4, 18.2, 18.0, 17.99, 17.93, 16.0, -4.2, -4.9, -5.34, -5.38 ppm; HRMS (ES+) calcd. for $C_{28}H_{56}O_7Si_2Na$ (M+Na) 583.3462, found 581.3470.



SI-3 **16**

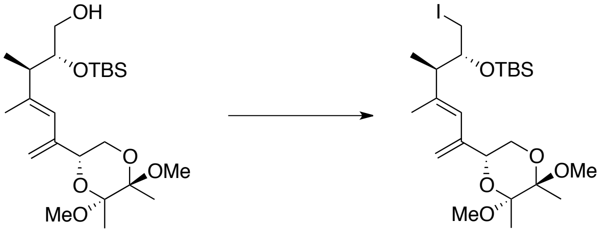
Diene 16: To a stirred solution of enone **SI-3** (225 mg, 0.401 mmol) in toluene (3.0 mL) in a sealed tube was added Petasis reagent[3] (0.92 mL, 1.20 mmol, 1.3 M in toluene) and heated to 80 °C in dark. After 4 h, the reaction was diluted with pentane (5.0 mL) and the precipitated solid was filtered off (rinse with 3 X 5 mL pentane). The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography over silica gel, eluting 3-4% EtOAc / hexanes, to give diene **16** (199 mg, 0.356 mmol, 89%) as colorless oil. $[\alpha]_D^{23}$ = -2.0 (*c* = 1.00, CHCl$_3$); IR: (neat) 2948, 2927, 2850, 1472, 1374, 1249, 1151, 1113, 1042, 830, 781 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.67 (s, 1H), 5.46 (s, 1H), 4.99 (s, 1H), 4.59 (dd, *J* = 11.3, 3.5 Hz, 1H), 3.81 (t, *J* = 11.1 Hz, 1H), 3.65-3.70 (m, 2H), 3.46 (d, *J* = 5.8 Hz, 2H), 3.41 (s, 3H), 3.36 (s, 3H), 2.46 (qd, *J* = 7.1, 4.2 Hz, 1H), 1.77 (d, *J* = 1.1, 3H), 1.44 (s, 3H), 1.39 (s, 3H), 1.08 (d, *J* = 7.1, 3H), 0.90 (s, 18H), 0.08 (s, 6H), 0.04 (s, 6H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.0, 142.1, 123.6, 114.3, 100.9, 100.1, 76.4, 73.7, 65.9, 65.5, 48.6, 48.3, 45.3, 25.99, 25.92, 18.3, 18.1, 17.9, 16.8, 16.0, -4.1, -4.8, -5.35, -5.39 ppm; HRMS (ES+) calcd. for $C_{29}H_{58}O_6Si_2Na$ (M+Na) 581.3670, found 581.3646.



16 **SI-4**

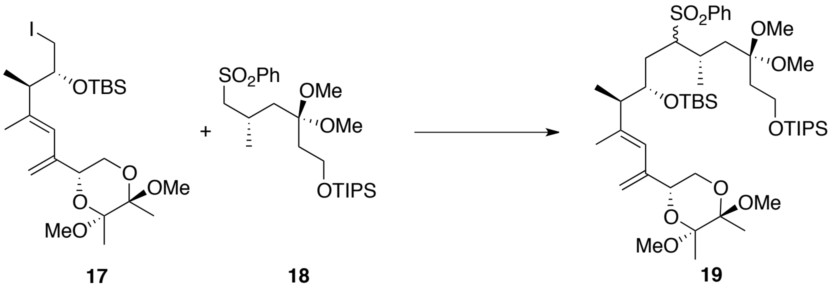
Alcohol SI-4: To a stirred solution of TBS ether **16** (156 mg, 0.279 mmol) in THF (3.0 mL) in a plastic bottle at 0 °C was added HF•Pyr. stock solution[4] (1.2 mL). After 30 min, the reaction was warmed to rt. After 6 h, the reaction was recooled to 0 °C and another portion of HF•Pyr. (0.60 mL) was added. After 20 min, the reaction was warmed to rt. After additional 2 h, the reaction was quenched with sat. aq. NaHCO$_3$ (5 mL) and the aqueous layer was extracted with EtOAc (3 X 30 mL). The dried (MgSO$_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-25% EtOAc /

hexanes, to give alcohol **SI-4** (113 mg, 0.254 mmol, 91%) as colorless oil. $[\alpha]_D^{23}$ = -26.0 (c = 1.01, $CHCl_3$); IR: (neat) 3490, 2953, 2929, 2883, 2855, 2832, 1470, 1462, 1372, 1252, 1147, 1116, 1042, 874, 835, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.74 (s, 1H), 5.44 (s, 1H), 5.01 (s, 1H), 4.59 (dd, J = 10.9, 3.7 Hz, 1H), 3.77-3.84 (m, 2H), 3.69 (dd, J = 10.8, 3.8 Hz, 1H), 3.50-3.59 (m, 2H), 3.40 (s, 3H), 3.36 (s, 3H), 2.49 (dq, J = 6.8, 6.7 Hz, 1H), 1.80 (t, J = 6.3, 1H), 1.78 (d, J = 1.2 Hz, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.08 (d, J = 7.0, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 141.9, 123.4, 115.2, 100.8, 100.0, 75.0, 73.8, 65.5, 64.2, 48.6, 48.3, 46.0, 25.8, 18.2, 18.1, 17.8, 16.6, 14.8, -4.4, -4.6 ppm; HRMS (ES+) calcd. for $C_{23}H_{44}O_6SiNa$ (M+Na) 467.2805, found 467.2802.

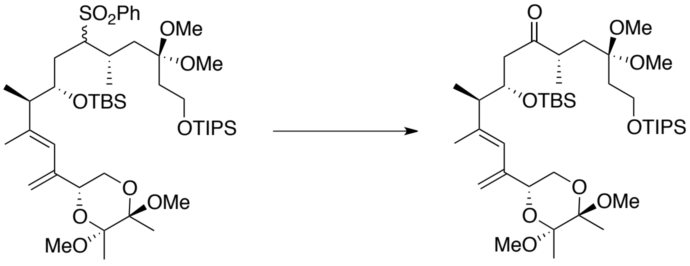


SI-4 **17**

Iodide 17: To a stirred solution of alcohol **SI-4** (85.1 mg, 0.191 mmol) in benzene (3.0 mL) at 0 °C were added imidazole (39.0 mg, 0.574 mmol), PPh_3 (126 mg, 0.478 mmol) and I_2 (97.3 mg, 0.382 mmol) sequentially. After 10 min, the reaction was warmed to rt. After 1 h, the reaction was quenched with sat. aq. $Na_2S_2O_3$ (5 mL) and the aqueous layer was extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-15% EtOAc / hexanes, to give iodide **17** (91.1 mg, 0.164 mmol, 86%) as colorless oil. $[\alpha]_D^{23}$ = +4.0 (c = 1.02, $CHCl_3$); IR: (neat) 2949, 2929, 2883, 2859, 2824, 1458, 1372, 1252, 1147, 1116, 1042, 835, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 (s, 1H), 5.48 (s, 1H), 5.03 (s, 1H), 4.61 (dd, J = 11.3, 3.4 Hz, 1H), 3.84 (dd, J = 11.2, 11.0 Hz, 1H), 3.70 (dd, J = 10.8, 3.7 Hz, 1H), 3.63 (dt, J = 6.5, 4.5 Hz, 1H), 3.42 (s, 3H), 3.37 (s, 3H), 3.18 (dd, J = 10.0, 4.2 Hz, 1H), 3.14 (dd, J = 10.0, 6.6 Hz, 1H), 2.59-2.66 (m, 1H), 1.79 (d, J = 1.1 Hz, 3H), 1.44 (s, 3H), 1.40 (s, 3H), 1.05 (d, J = 7.0, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 140.9, 124.3, 114.9, 100.9, 100.1, 74.6, 73.8, 65.8, 48.7, 48.3, 46.9, 25.8, 18.2, 18.0, 17.9, 16.5, 15.3, 11.4, -4.2, -4.7 ppm; HRMS (ES+) calcd. for $C_{23}H_{43}O_5ISiNa$ (M+Na) 577.1822, found 577.1810.

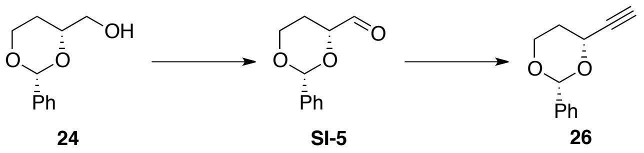


Coupled Sulfone 19: To a stirred solution of sulfone **18**^{2} (54.5 mg, 0.115 mmol) in THF (0.40 mL) at -78 °C was added LHMDS (104 μL, 104 μmol, 1M in THF). After 30 min, the reaction was warmed to 0 °C and treated with HMPA (100 μL) followed by a solution of iodide **17** (32.0 mg, 57.7 μmol) in THF (0.40 mL). After 1 h, the reaction was warmed to rt. After 6 h, the reaction was quenched with sat. aq. NH_4Cl (5 mL) at 0 °C and diluted with EtOAc (20 mL). The aqueous layer was extracted with EtOAc (3 X 20 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 10-25% EtOAc / hexanes, to sequentially give coupled sulfone **19** {44.5 mg, 49.4 μmol, 86%, (2-3:1 dr)} as colorless oil followed by recovered **18** (25.7 mg, 54.3 μmol). $[\alpha]_D^{23}$ = -21.5 (*c* = 1.00, $CHCl_3$); IR: (neat) 2945, 2890, 2863, 2832, 1462, 1439, 1372, 1299, 1252, 1143, 1112, 1084, 1042, 878, 835, 773, 734, 688 cm^{-1}; ^{1}H NMR {400 MHz, $CDCl_3$ (two diastereomers)} δ 7.87-7.91 (m, 2H (2 diastereomers)), 7.61-7.66 (m, 1H (2 diastereomers)), 7.52-7.59 (m, 2H (2 diastereomers)), 5.76 (s, 1H (1 diastereomer)), 5.61 (s, 1H (1 diastereomer)), 5.46 (s, 1H (2 diastereomers)), 5.00 (s, 1H (1 diastereomer)), 4.98 (s, 1H (1 diastereomer)), 4.55-4.61 (m, 1H (2 diastereomers)), 4.21 (td, *J* = 6.6, 2.9 Hz, 1H (1 diastereomer)), 4.08 (td, *J* = 8.8, 3.4 Hz, 1H (1 diastereomer)), 3.87-3.94 (m, 1H (1 diastereomer)), 3.78-3.84 (m, 1H (2 diastereomers)), 3.63-3.75 (m, 2H (2 diastereomers)), 3.52-3.56 (m, 1H (1 diastereomer)), 3.43 (s, 3H (1 diastereomer)), 3.40-3.42 (m, 1H, (1 diastereomer)), 3.41 (s, 3H, (1 diastereomer)), 3.37 (s, 3H, (1 diastereomer)), 3.36 (s, 3H, (1 diastereomer)), 3.19-3.21 (m, 1H (1 diastereomer)), 3.19 (s, 3H (1 diastereomer)), 3.16 (s, 3H (1 diastereomer)), 3.04 (s, 3H (1 diastereomer)), 2.98 (s, 3H (1 diastereomer)), 2.55 (q, *J* = 7.1 Hz, 1H (1 diastereomer)), 2.41 (qd, *J* = 7.0, 2.8 Hz, 1H (1 diastereomer)), 2.33 (qd, *J* = 6.9, 2.9 Hz, 1H (1 diastereomer)), 2.14-2.21 (m, 2H (2 diastereomers)), 1.97-2.07 (m, 1H (2 diastereomers)), 1.09-194 (m, 1H (2 diastereomers)), 1.82 (s, 3H (1 diastereomer)), 1.76 (s, 3H (1 diastereomer)), 1.58-1.74 (m, 2H (2 diastereomers)), 1.41-1.47 (m, 1H (2 diastereomers)), 1.46 (s, 3H (1 diastereomer)), 1.43 (s, 3H (1 diastereomer)), 1.40 (s, 3H (1 diastereomer)), 1.39 (s, 3H (1 diastereomer)), 1.30-1.37 (m, 1H (2 diastereomers)), 1.26 (d, *J* = 12.8 Hz, 3H (1 diastereomer)), 1.05-1.16 (m, 27 H (2 diastereomers)), 0.90 (s, 9H (1 diastereomer)), 0.89 (s, 9H (1 diastereomer)), 0.16 (s, 3H (1 diastereomer)), 0.12 (s, 3H (1 diastereomer)), 0.098 (s, 3H (1 diastereomer)), 0.090 (s, 3H (1 diastereomer)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 142.6, 141.7, 141.0, 139.9, 139.2, 133.3, 129.1, 129.0, 128.57, 128.51, 124.2, 123.3, 116.0, 115.2, 102.0, 101.8, 100.9, 100.1 (2 peaks), 73.9, 73.6, 72.2, 72.1, 65.8, 65.7, 65.4, 65.0, 59.3, 59.2, 48.7 (2 peaks), 48.34, 48.31, 47.96, 47.94, 47.8, 47.7, 47.6, 46.9, 46.2, 38.9, 36.9, 36.5, 34.0, 29.7, 29.4, 29.3, 28.3, 28.1, 27.4, 25.9, 25.8, 18.46, 18.43, 18.3, 18.1, 18.06, 18.04, 17.95, 17.91, 17.8, 16.4, 14.5, 12.0, 11.9, -4.1, -4.30, -4.38, -4.4 ppm; HRMS (ES+) calcd. for $C_{47}H_{86}O_{10}Si_2SNa$ (M+Na) 921.5378, found 921.5389.



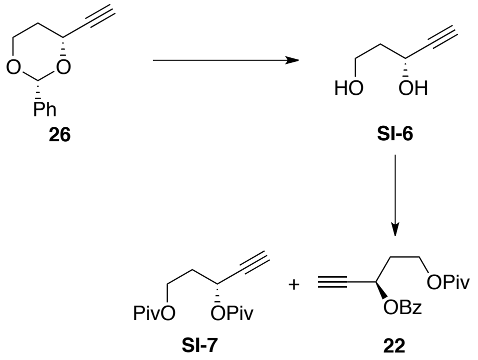
19 **12**

Ketone 12: To a stirred solution of diisopropylamine (7.0 μL, 47.8 μmol) in THF (0.30 mL) at -78 °C was added *n*-BuLi (20. 0 μL, 47.8 μmol, 2.5 M in hexanes). After 15 min, the reaction was warmed to 0 °C and stirred for 10 min. The reaction was re-cooled to -20 °C and treated with DMPU (106 mg, 0.10 mL, 0.827 mmol). A solution of sulfone **19** (21.5 mg, 23.9 μmol) in THF (0.30 mL) was added via cannula. After 15 min, neat TMSOOTMS (26.0 μL, 0.119 mmol) was added to the reaction in one portion. After additional 30 min, the reaction was slowly warmed to rt over 1 h and another portion of TMSOOTMS (13.0 μL, 59.7 μmol) was added. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (2 mL) and diluted with EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 X 10 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 5-25% EtOAc / hexanes with 2% Et_3N, to sequentially give ketone **12** {9.4 mg, 12.2 μmol, 51% (87% borsm)} as colorless oil followed by recovered sulfone **19** (8.9 mg, 9.9 μmol, 41%). $[\alpha]_D^{23}$ = -5.0 (*c* = 0.61, $CHCl_3$); IR: (neat) 2949, 2890, 2863, 2828, 1715, 1462, 1372, 1252, 1147, 1116, 1046, 878, 835, 777, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (s, 1H), 5.46 (s, 1H), 4.98 (s, 1H), 4.58 (dd, *J* = 11.4, 3.4 Hz, 1H), 4.27-4.30 (m, 1H), 3.80 (dd, *J* = 11.3, 10.9 Hz, 1H), 3.71 (td, *J* = 7.3, 3.0 Hz, 2H), 3.64 (dd, *J* = 10.8, 3.7 Hz, 1H), 3.41 (s, 3H), 3.35 (s, 3H), 3.14 (s, 3H), 3.08 (s, 3H), 2.58-2.69 (m, 3H), 2.43 (qd, *J* = 7.0, 3.5 Hz, 1H), 2.23 (dd, *J* = 14.5, 8.8 Hz, 1H), 1.92 (t, *J* = 7.4 Hz, 2H), 1.78 (d, *J* = 0.9 Hz, 3H), 1.40-1.45 (m, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 1.06-1.14 (m, 24H), 1.01 (d, *J* = 7.0, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.1, 142.8, 142.4, 123.8, 114.8, 101.5, 100.9, 100.1, 73.6, 70.1, 65.7, 59.3, 48.6, 48.3, 48.0, 47.9, 47.4, 46.7, 41.9, 36.7 (2 carbons), 25.8, 18.3, 18.2, 18.0 (2 carbons), 17.1, 14.7, 11.9, -4.5, -4.9 ppm; HRMS (ES+) calcd. for $C_{41}H_{80}O_9Si_2Na$ (M+Na) 795.5239, found 795.5221.



Alkyne 26: To a stirred solution of oxalyl chloride (8.88 g, 6.1 mL, 70.0 mmol) in CH_2Cl_2 (154.0 mL) at -78 °C was cannulated a solution of DMSO (11.43 g, 10.4 mL, 146.3 mmol) in CH_2Cl_2 (77.0 mL). After 15 min, a solution of alcohol **24**[5] (12.36 g, 63.6 mmol) in CH_2Cl_2 (77.0 mL) was cannulated to it. After 45 min, Et_3N (32.20 g, 44.7 mL, 318.2 mmol) was added. After 10 min, the cooling bath was removed and the reaction was quenched with H_2O (150 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 300 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* to give the crude aldehyde **SI-5**.

To a stirred solution of Ohira-Bestmann reagent **25**[6] (18.30 g, 95.4 mmol) in THF (320.0 mL) at -78 °C was added NaOMe (191.0 mL, 95.5 mmol, 0.5 M in THF) over 30 min. A solution of crude aldehyde **SI-5** in THF (160.0 mL) was cannulated to it and was slowly warmed to 0 °C over 2.5 h. The reaction was quenched with sat. aq. NH_4Cl (150 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 300 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give alkyne **26** (8.02 g, 42.6 mmol, 67%) as colorless oil. $[\alpha]_D^{23}$ = +29.0 (c = 1.02, $CHCl_3$); IR: (neat) 3287, 2967, 2931, 2857, 1455, 1399, 1303, 1119, 1097, 1007, 760 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.52-7.54 (m, 2H), 7.35-7.40 (m, 3H), 5.54 (s, 1H), 4.69 (dt, J = 11.5, 2.4 Hz, 1H), 4.30 (ddd, J = 11.7, 4.9, 1.3 Hz, 1H), 3.99 (td, J = 12.1, 2.5 Hz, 1H), 2.57 (d, J = 2.1 Hz, 1H), 2.27-2.33 (m, 1H), 1.80-1.83 (m, 1H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 137.8, 129.1, 128.3, 126.2, 101.6, 81.6, 73.8, 67.2, 66.6, 31.9 ppm; HRMS (EI+) calcd. for $C_{12}H_{12}O_2$ (M+) 188.08373, found 188.08406.

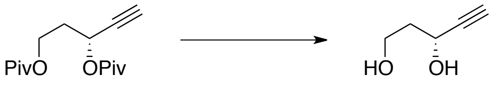


Benzoate 22: To a stirred solution of benzylidine acetal **26** (5.34 g, 28.3 mmol) in MeOH (108.0 mL) at rt was added p-TSA•H_2O (54.0 mg, 0.283 mmol). After 3 h, the reaction was quenched with Et_3N (425 mg, 0.60 mL, 4.20 mmol) and the solvent was removed *in vacuo* to give crude diol **SI-6**.

To a stirred solution of crude **SI-6** in CH_2Cl_2 / pyridine (81.0 mL, 2.5:1) at 0 °C was added pivaloyl chloride (3.76 g, 3.9 mL, 31.2 mmol). After 1.5 h, DMAP

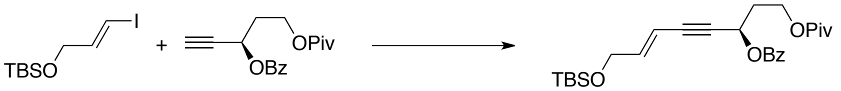
(343 mg, 2.83 mmol) followed by benzoyl chloride (4.98 g, 4.1 mL, 35.4 mmol) were added and the reaction was warmed to rt. After 2.5 h, the reaction was quenched with sat. aq. $NaHCO_3$ (75 mL) and the aqueous layer was extracted with Et_2O (3 X 200 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to sequentially give benzoate **22** (4.99 g, 17.3 mmol, 61%) as colorless oil followed by pivalate **SI-7** (1.45 g, 5.40 mmol, 19%). Benzoate **22**: $[\alpha]_D^{23}$ = +35.3 (*c* = 1.02, $CHCl_3$); IR: (neat) 3291, 3264, 2972, 2933, 2898, 2871, 1727, 1481, 1450, 1271, 1155, 1092, 1065, 1026, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06-8.09 (m, 2H), 7.59 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.44-7.48 (m, 2H), 5.74 (td, *J* = 6.7, 2.1 Hz, 1H), 4.30 (td, *J* = 6.3, 2.0 Hz, 2H), 2.55 (d, *J* = 2.1 Hz, 1H), 2.23-2.38 (m, 2H), 1.21 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 165.2, 133.3, 129.8, 129.5, 128.4, 80.3, 74.4, 61.3, 60.0, 38.7, 33.9, 27.1 ppm; HRMS (CI+) calcd. for $C_{17}H_{21}O_4$ (M+H) 289.1440, found 289.1434.

Pivalate **SI-7**: $[\alpha]_D^{23}$ = +49.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 3269, 2974, 2935, 2909, 2874, 1733, 1481, 1461, 1398, 1366, 1282, 1038, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 (td, *J* = 6.9, 2.1 Hz, 1H), 4.20 (td, *J* = 6.5, 1.4 Hz, 2H), 2.47 (d, *J* = 2.1 Hz, 1H) 2.10-2.22 (m, 2H), 1.23 (s, 9H), 1.21 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 177.0, 80.5, 73.8, 60.3, 59.9, 38.7, 33.7, 27.1, 26.9 ppm; HRMS (EI+) calcd. for $C_{15}H_{24}O_4$ (M+) 268.1674, found 268.1661.



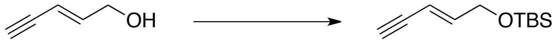
SI-7 **SI-6**

Diol SI-6: To a stirred solution of pivalate **SI-7** (2.02 g, 7.52 mmol) in MeOH (50.0 mL) at rt was added LiOH•H_2O (237 mg, 5.64 mmol). After 20 h, the reaction was quenched with Dowex-50W-X8 resin (7.1 g). After 15 min, the solid resin was removed by filtration. The filtrate was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 40-80% EtOAc / hexanes, to give diol **SI-6** (701 mg, 7.00 mmol, 93%) as colorless oil. $[\alpha]_D^{23}$ = +36.1 (*c* = 1.01, $CHCl_3$); IR: (neat) 3292, 2957, 2891, 2115, 1643, 1434, 1337, 1185, 1047, 965, 887 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.66-4.69 (m, 1H),4.02-4.06 (m, 1H), 3.88-3.91 (m,1H), 3.05 (d, *J* = 5.0 Hz, 1H), 2.54 (d, *J* = 2.1 Hz, 1H), 2.30 (br s, 1H), 2.04-2.08 (m, 1H), 1.95-1.99 (m, 1H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 84.1, 73.4, 61.5, 60.3, 38.6 ppm; HRMS (EI+) calcd. for $C_5H_8O_2$ (M+)100.0524, found 100.0523.



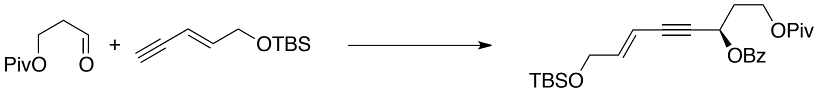
23 **22** **27**

Enyne 27: To a stirred solution of $PdCl_2(PPh_3)_2$ (995 mg, 1.41 mmol) in THF (163.0 mL) at rt was added CuI (810 mg, 4.25 mmol). A solution of alkyne **22** (8.17 g, 28.3 mmol) and vinyl iodide **23**[7] (9.30 g, 31.1 mmol) in THF (163.0 mL) was cannulated to it. Et_3N (43.0 g, 60.0 mL, 424.9 mmol) was added dropwise over 15 min. After 2.5 h, the reaction was quenched with sat. aq. NH_4Cl (150 mL) and the aqueous layer was extracted with Et_2O (3 X 300 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-15% EtOAc / hexanes, to give enyne **27** (10.11 g, 22.0 mmol, 78%) as colorless oil. $[\alpha]_D^{23}$ = +6.3 (*c* = 1.02, $CHCl_3$); IR: (neat) 2949, 2929, 2851, 1731, 1466, 1267, 1155, 1104, 952, 832, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07-8.10 (m, 2H), 7.59 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.44-7.48 (m, 2H), 6.27 (dt, *J* = 15.7, 4.0 Hz, 1H), 5.88 (dt, *J* = 1.5, 6.6 Hz, 1H), 5.80 (ddt, *J* = 15.7, 2.1, 1.9 Hz, 1H), 4.29 (t, *J* = 6.3 Hz, 2H), 4.23 (dd, *J* = 4.0, 2.1 Hz, 1H), 2.23-2.37 (m, 2H), 1.21 (s, 9H), 0.92 (s, 9H), 0.08 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 165.3, 143.9, 133.2, 129.8, 129.7, 128.4, 107.5, 85.4, 84.4, 62.7, 62.2, 60.3, 38.7, 34.2, 27.1, 25.8, 18.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{26}H_{38}O_5SiNa$ (M+Na) 481.2386, found 481.2398.



SI-8 **29**

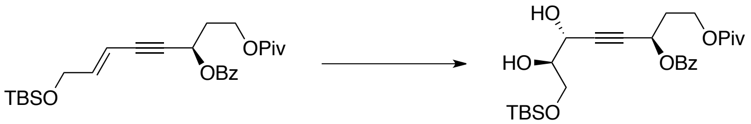
TBS Ether 29: To a stirred solution of alcohol **SI-8** (277 mg, 3.37 mmol) in DMF (5.0 mL) at 0 °C were sequentially added imidazole (459 mg, 6.74 mmol), TBS chloride (762 mg, 5.06 mmol) and DMAP (102 mg, 0.843 mmol) sequentially. After 1.5 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and the aqueous layer was extracted with Et_2O (2 X 50 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-10% Et_2O / pentane, to give TBS ether **29**[8] (604 mg, 3.07 mmol, 91%) as colorless oil. ^1H NMR (700 MHz, $CDCl_3$) δ 6.33 (dtd, *J* = 15.8, 4.1, 0.55 Hz, 1H), 5.78 (dq, *J* = 15.8, 2.2 Hz, 1H), 4.26 (ddd, *J* = 4.1, 2.2, 0.84 Hz, 1H), 2.89 (dq, *J* = 2.2, 0.77 Hz, 1H), 0.94 (s, 9H), 0.10 (s, 6H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 144.3, 107.6, 82.1, 77.3, 62.7, 25.8, 18.3, -5.3 ppm.



28 **29** **27**

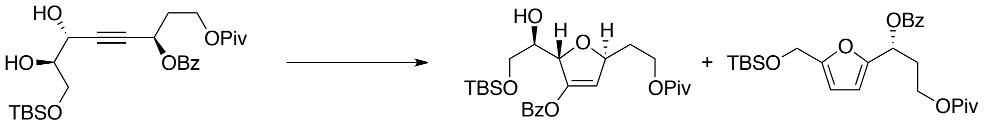
Propargyl Benzoate 27: To a stirred solution of (+)-*N*-methylephedrine (752 mg, 4.19 mmol) and $Zn(OTf)_2$ (1.45 g, 3.99 mmol) in toluene (3.4 mL) at rt was added Et_3N (0.59 mL, 424 mg, 4.19 mmol). After 2 h, alkyne **29** (824 mg, 4.19 mmol) was added in one portion. After 15 min, a solution of aldehyde **28**[9] (316 mg, 1.99 mmol) in toluene (4.9 mL) was added dropwise over 15 h via syringe pump. After another 5 h, CH_2Cl_2 (7.5 mL) was added and the reaction was cooled down to 0 °C. Then, benzoyl chloride (1.26 g, 1.1 mL, 8.99 mmol), Et_3N (908 mg, 1.3 mL, 8.99 mmol) and DMAP (121 mg, 0.998 mmol) were sequentially added to the reaction. After 2.5 h, the reaction was quenched with sat. aq. NH_4Cl (30 mL) and the aqueous layer was extracted with Et_2O (3 X 60 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-15% EtOAc / hexanes, to give propargyl benzoate **27** (321 mg, 0.699 mmol, 35%) as colorless oil.

Enantioselectivity (89.7% ee) was determined by conversion of the intermediate propargyl alcohol (12.3 mg, 0.035 mmol) into its corresponding (*R*)-MTPA ester (19.7 mg, 0.035 mmol, 99%) using (*S*)-MTPA-Cl (26.3 mg, 19.5 μL, 0.104 mmol) in CH_2Cl_2 (0.5 mL) at room temperature for 45 min. ^{19}F NMR (37.6 MHz, $CDCl_3$) -71.54 (94.85%), -71.66 (5.15%).



27 **21**

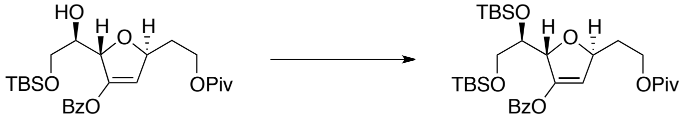
Diol 21: To a stirred solution of AD-mix-β (30.53 g) in *t*-BuOH/H_2O (660.0 mL, 1:1) at rt was added $MeSO_2NH_2$ (2.10 g, 22.0 mmol). After 15 min, the mixture was cooled down to 0 °C and transferred to a flask containing the enyne **27** (10.11 g, 22.0 mmol) at 0 °C. After 40 h, the reaction was quenched with solid Na_2SO_3 (35.0 g, 277.5 mmol) and the aqueous layer was extracted with EtOAc (4 X 400 mL). The combined organic layer was washed with brine (250 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-40% EtOAc / hexanes, to give diol **21** {9.44 g, 19.2 mmol, 87% (>20:1 dr)} as colorless oil. $[\alpha]_D^{23}$ = +17.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 3460, 2954, 2927, 2856, 1723, 1478, 1265, 1146, 1097, 841, 786, 715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.08 (m, 2H), 7.61 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 5.78 (td, *J* = 6.7, 1.3 Hz, 1H), 4.48 (td, *J* = 5.3, 1.4 Hz, 1H), 4.24-4.38 (m, 2H), 3.71-3.85 (m, 3H), 2.81-2.83 (m, 1H), 2.71 (d, *J* = 6.0 Hz, 1H), 2.23-2.38 (m, 1H), 1.22 (s, 9H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 165.2, 133.3, 129.8, 129.5, 128.4, 84.3, 82.7, 73.9, 63.6, 63.4, 61.5, 60.1, 38.7, 34.0, 27.1, 25.8, 18.2, -5.50, -5.54 ppm; HRMS (ES+) calcd. for $C_{26}H_{40}O_7SiNa$ (M+Na) 515.2441, found 515.2419.



21 **33** **35**

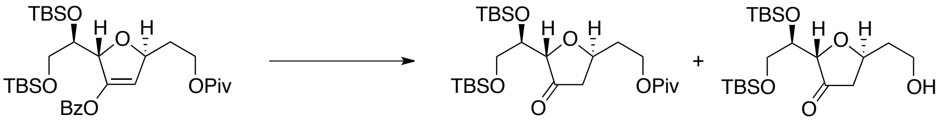
Dihydrofuran 33: To a stirred solution of diol **21** (5.30 g, 10.7 mmol) in dry C_6H_6 (105.0 mL) was added $AgBF_4$ (210 mg, 1.07 mmol) and heated to 80 °C in dark. After 1.45 h, the reaction was cooled down to rt and the solvent was reduced to 15 mL *in vacuo.* The residue was quickly passed through a short silica gel column, eluting with 10-20% EtOAc / hexanes, to sequentially give the furan **35** (762 mg, 1.60 mmol, 15 %) followed by dihydrofuran **33** (3.70 g, 7.51 mmol, 70%) as colorless oil. Dihydrofuran **33**: $[\alpha]_D^{23}$ = +10.5 (*c* = 1.02, $CHCl_3$); IR: (neat) 3513, 2956, 2925, 2855, 1750, 1727, 1260, 1158, 1112, 1084, 835, 777 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 2H), 7.64 (td, *J* = 7.4, 1.0 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 6.09 (t, *J* = 1.7 Hz, 1H), 4.97 (dt, *J* = 5.6, 1.9 Hz, 1H), 4.27 (dt, *J* = 11.1, 6.2 Hz, 1H), 4.21 (dt, *J* = 11.1, 6.5 Hz, 1H), 3.84 (td, *J* = 6.3, 2.0 Hz, 1H), 3.80 (dd, *J* = 9.8, 6.5 Hz, 1H), 3.75 (dd, *J* = 9.8, 6.1 Hz, 1H), 1.97-2.05 (m, 2H), 1.22 (s, 9H), 0.92 (s, 9H), 0.108 (s, 3H), 0.104 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.6, 163.4, 144.7, 133.9, 130.0, 128.74, 128.70, 112.5, 81.8, 80.6, 71.2, 63.9, 61.0, 38.7, 35.5, 27.2, 25.9, 18.3, -5.3; HRMS (ES+) calcd. for $C_{26}H_{40}O_7SiNa$ (M+Na) 515.2441, found 515.2409.

Furan **35**: $[\alpha]_D^{23}$ = +42.3 (*c* = 1.02, $CHCl_3$); IR (neat) 2957, 2932, 2857, 1727, 1452, 1264, 1153, 1097, 837, 778 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.57 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.44 (dd, *J* = 8.3, 7.4, Hz, 2H), 6.38 (d, *J* = 3.1 Hz, 1H), 6.22 (dd, *J* = 8.0, 6.3 Hz, 1H), 6.21 (d, *J* = 3.1 Hz, 1H), 4.65 (s, 2H), 4.21 (ddd, *J* = 11.2, 7.4, 5.7 Hz, 1H), 4.14 (dt, *J* = 11.2, 6.1 Hz, 1H), 2.48-2.53 (m, 1H), 2.39-2.44 (m, 1H), 1.21 (s, 9H), 0.90 (s, 9H), 0.088 (s, 3H), 0.084 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.3, 165.5, 154.7, 151.1, 133.0, 130.0, 129.7, 128.3, 109.8, 107.9, 66.3, 60.4, 58.2, 38.7, 31.8, 27.1, 25.8, 18.3, -5.24, -5.26 ppm; HRMS (ES+) calcd. for $C_{26}H_{38}O_6SiNa$ (M+Na) 497. 2335, found 497.2313.



33 **36**

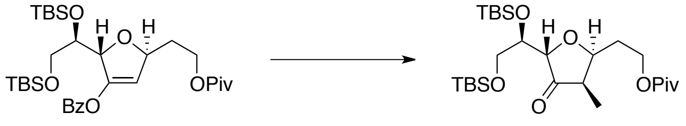
TBS Ether 36: To a stirred solution of alcohol **33** (3.70 g, 7.51 mmol) in CH_2Cl_2 (83.0 mL) at -78 °C were added 2,6-lutidine (3.21 g, 3.5 mL, 30.0 mmol) followed by TBSOTf (3.97 g, 3.5 mL, 15.0 mmol). After 3 h, the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL) and the aqueous layer was extracted with Et_2O (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give TBS ether **36** (3.87 g, 6.38 mmol, 85%) as colorless oil. $[\alpha]_D^{23}$ = +17.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 2956, 2925, 2886, 2855, 1750, 1731, 1466, 1260, 1155, 1088, 839, 777 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.08-8.09 (m, 2H), 7.63-7.66 (m, 1H), 7.50-7.52 (m, 2H), 6.11 (t, *J* = 1.5 Hz, 1H), 5.07-5.09 (m, 1H), 4.98 (dt, *J* = 5.7, 1.5 Hz, 1H), 4.20-4.27 (m, 2H), 3.85 (td, *J* = 6.6, 1.2 Hz, 1H), 3.78 (dd, *J* = 9.8, 7.5 Hz, 1H), 3.65 (dd, *J* = 9.7, 5.8 Hz, 1H), 1.97-2.04 (m, 2H), 1.22 (s, 9H), 0.94 (s, 9H), 0.84 (s, 9H), 0.114 (s, 3H), 0.112 (s, 3H), 0.05 (s, 3H), -0.03 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.6, 163.1, 144.9, 133.7, 129.9, 129.0, 128.6, 111.8, 81.8, 81.4, 72.9, 64.2, 61.1, 38.7, 35.5, 27.2, 26.0, 25.7, 18.4, 18.0, -4.1, -5.21, -5.24, -5.3 ppm; HRMS (ES+) calcd. for $C_{32}H_{55}O_7Si_2$ (M+H) 607.3486, found 607.3475.



36 **20** **SI-9**

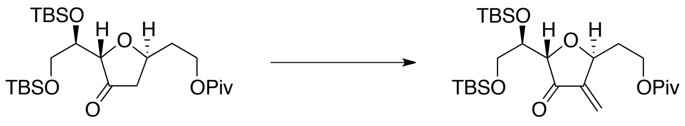
Ketone 20: To a stirred solution of enol-benzoate **36** (4.93 g, 8.12 mmol) in Et_2O (86.0 mL) at -78 °C was added MeLi•LiBr (7.4 mL, 16.2 mmol, 2.2 M in

Et_2O) dropwise. After 1.5 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and the aqueous layer was extracted with Et_2O (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to sequentially give ketone **20** (3.30 g, 6.57 mmol, 81%) followed by keto-ol **SI-9** (306 mg, 0.731 mmol, 9%) as colorless oils. Ketone **20**: $[\alpha]_D^{23}$ = -56.3 (*c* = 1.03, $CHCl_3$); IR: (neat) 2954, 2927, 2883, 2856, 1761, 1734, 1472, 1358, 1287, 1255, 1157, 1091, 835, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.64-4.71 (m, 1H), 4.25 (t, *J* = 6.3 Hz, 2H), 4.15 (br s, 1H), 4.03 (ddd, *J* = 8.9, 5.3, 1.7 Hz, 1H), 3.74 (t, *J* = 9.2 Hz, 1H), 3.55 (dd, *J* = 9.6, 5.3 Hz, 1H), 2.56 (dd, *J* = 18.0, 6.3 Hz, 1H), 2.25 (ddd, *J* = 18.0, 9.0, 1.0 Hz, 1H), 1.99-2.06 (m, 2H), 1.22 (s, 9H), 0.90 (s, 9H), 0.85 (s, 9H), 0.086 (s, 3H), 0.084 (s, 3H), 0.07 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.8, 178.4, 80.1, 74.9, 74.7, 63.0, 61.0, 43.6, 38.7, 35.5, 27.2, 25.9, 25.7, 18.3, 17.8, -4.4, -5.2, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{25}H_{51}O_6Si_2$ (M+H) 503.3224, found 503.3199.



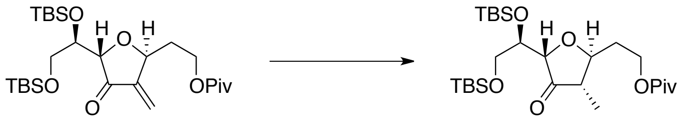
36 **38**

Ketone 38: To a stirred suspension of LiBr (104 mg, 1.19 mmol) in Et_2O (3.2 mL) at -78 °C was added MeLi (0.68 mL, 1.08 mmol, 1.6 M in Et_2O). A solution of enol-benzoate **36** (330 mg, 0.543 mmol) in Et_2O (5.0 mL, pre-cooled) was cannulated to it. After 3 h, DMPU (1.06 g, 1.0 mL, 8.27 mmol) was added followed by MeI (2.28 g, 1.0 mL, 16.0 mmol). After 2 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-6% EtOAc / hexanes, to give ketone **38** {206 mg, 0.398 mmol, 73% (5:1 dr)} as colorless oil. $[\alpha]_D^{23}$ = -87.1 (*c* = 1.00, $CHCl_3$); IR (neat) 2956, 2930, 2858, 1761, 1731, 1472, 1256, 1154, 1082, 836, 778 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) 4.68 (ddd, *J* = 10.2, 7.3, 3.7 Hz, 1H), 4.27-4.30 (m, 1H), 4.22-4.25 (m, 1H), 4.09 (d, *J* = 1.6 Hz, 1H), 4.02-4.05 (m, 1H), 3.73 (t, *J* = 9.2 Hz, 1H), 3.56 (dd, *J* = 9.5, 5.4 Hz, 1H), 2.55 (pen, *J* = 7.4 Hz, 1H), 1.81-1.85 (m, 1H), 1.72-1.77 (m, 1H), 1.22 (s, 9H), 1.09 (d, *J* = 7.4 Hz, 3H), 0.90 (s, 9H), 0.84 (s, 9H), 0.086 (s, 3H), 0.084 (s, 3H), 0.07 (s, 3H), 0.01 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 218.9, 178.5, 78.3, 76.7, 73.9, 63.0, 61.3, 45.6, 38.7, 29.9, 27.2, 25.9, 25.8, 18.3, 17.9, 9.6, -4.3, -5.2, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{26}H_{53}O_6Si_2$ (M+H) 517.3381, found 517.3388.



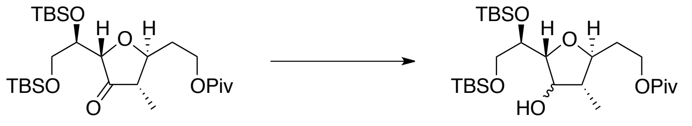
20 **39**

Enone 39: To a stirred solution of ketone **20** (1.91 g, 3.79 mmol) in THF (40.0 mL) at -78 °C was added LDA[10] (7.6 mL, 7.60 mmol, 1 M in THF / hexanes) and warmed to -50 °C over 15 min. After 35 min, DMPU (4.86 g, 4.6 mL, 37.9 mmol) was added followed by a solution of Eschenmoser's salt (3.51 g, 18.9 mmol) in THF (40.0 mL). The reaction was slowly warmed to -10 °C over 50 min and quenched with sat. aq. $NaHCO_3$ (30 mL) and the aqueous layer was extracted with Et_2O (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 4-10% EtOAc / hexanes, to give enone **39** (1.38 g, 2.68 mmol, 71%) as colorless oil. $[\alpha]_D^{23}$ = -117.6 (*c* = 1.00, $CHCl_3$); IR: (neat) 2953, 2929, 2883, 2855, 1731, 1645, 1474, 1256, 1158, 1112, 1084, 835, 781 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 6.12 (d, *J* = 2.8 Hz, 1H), 5.34 (d, *J* = 2.4 Hz, 1H), 5.08 (ddd, *J* = 8.6, 5.9, 2.8 Hz, 1H), 4.30-4.33 (m, 2H), 4.29 (d, *J* = 1.3 Hz, 2H), 4.06 (ddd, *J* = 9.0, 5.3, 1.5 Hz, 1H), 3.75 (dd, *J* = 9.4, 9.1 Hz, 1H), 3.54 (dd, *J* = 9.5, 5.2 Hz, 1H), 2.16-2.21 (m, 1H), 1.93-1.98 (m, 1H), 1.22 (s, 9H), 0.91 (s, 9H), 0.78 (s, 9H), 0.093 (s, 3H), 0.090 (s, 3H), 0.04 (s, 3H), -0.03 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 205.6, 178.5, 145.1, 116.8, 80.3, 74.9, 74.7, 63.0, 60.5, 38.7, 34.8, 27.2, 25.9, 25.6, 18.3, 17.8, -4.4, -5.3, -5.4, -5.5 ppm; HRMS (ES+) calcd. for $C_{26}H_{50}O_6Si_2Na$ (M+Na) 537.3044, found 537.3033.



39 **40**

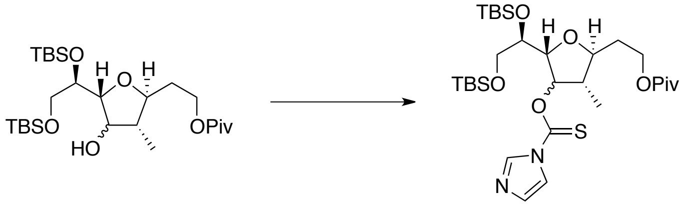
α-Methyl Ketone 40: To a stirred solution of enone **39** (1.28 g, 2.48 mmol) in toluene (45.0 mL) was added $(Ph_3P)_3RhCl$ (230 mg, 0.248 mmol) at rt and a hydrogen balloon was fitted to it. After 30 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 6-10% EtOAc / hexanes, to give α-methyl ketone **40** {1.14 g, 2.20 mmol, 89% (10:1 dr)} as colorless oil. $[\alpha]_D^{23}$ = -31.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 2959, 2932, 2878, 2856, 1761, 1728, 1462, 1287, 1255, 1151, 1118, 1069, 841, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.26-4.39 (m, 3H), 4.16 (ddd, *J* = 10.4, 8.6, 3.4 Hz, 1H), 4.07 (ddd, *J* = 9.4, 5.1, 1.6 Hz, 1H), 3.74 (t, *J* = 9.4 Hz, 1H), 3.54 (dd, *J* = 9.4, 5.1 Hz, 1H), 2.08-2.21(m, 2H), 1.93-2.02 (m, 1H), 1.22 (s, 9H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.85 (s, 9H), 0.089 (s, 3H), 0.086 (s, 3H), 0.07 (s, 3H), 0.009 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.0, 178.4, 81.3, 80.0, 74.3, 62.8, 60.9, 48.1, 38.7, 34.2, 27.2, 25.9, 25.8, 18.3, 17.7, 9.6, -4.5, -4.8, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{26}H_{53}O_6Si_2$ (M+H) 517.3381, found 517.3359.



40 **SI-10**

Alcohol SI-10: To a stirred solution of ketone **40** (1.10 g, 2.12 mmol) in MeOH (40.0 mL) at 40 °C was added $NaBH_4$ (81.0 mg, 2.12 mmol). After 1 h, another portion of $NaBH_4$ (40.5 mg, 1.06 mmol) was added. After additional 30 min, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and the aqueous layer was extracted with EtOAc (4 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give diastereomeric alcohol **SI-10** {1.01 g, 1.95 mmol, 92% (1.3:1 dr)} as colorless oil. Analytically pure samples of the individual diastereomers could be obtained via chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give sequentially the major diastereomer followed by the minor diastereomer. **SI-10** Major isomer: $[\alpha]_D^{23}$ = -44.2 (*c* = 1.03, $CHCl_3$); IR: (neat) 3493, 2948, 2921, 2856, 1728, 1472, 1391, 1363, 1287, 1282, 1255, 1157, 1097, 841, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.31 (ddd, *J* = 10.8, 7.2, 4.8 Hz, 1H), 4.17 (ddd, *J* = 10.8, 8.2, 6.4 Hz, 1H), 4.12-4.14 (m, 1H), 3.98 (ddd, *J* = 8.2, 8.1, 3.8 Hz, 1H), 3.88 (td, *J* = 9.7, 2.5 Hz, 1H), 3.73 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.56-3.65 (m, 3H), 1.88-1.97 (m, 2H), 1.64-1.72 (m, 1H), 1.21 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 1H), 0.93 (s, 9H), 0.90 (s, 9H), 0.137 (s, 3H), 0.134 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 86.9, 78.9, 74.5, 72.9, 65.9, 62.0, 44.9, 38.7, 33.6, 27.2, 25.8, 18.3, 9.7, -4.4, -4.9, -5.6 ppm; HRMS (ES+) calcd. for $C_{26}H_{55}O_6Si_2S$ (M+H) 519.3537, found 519.3512.

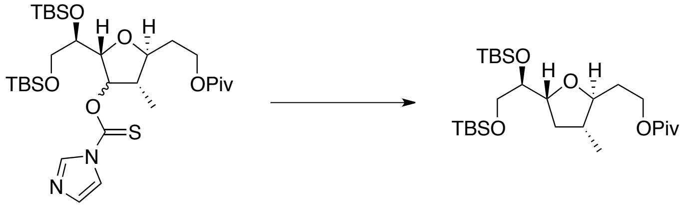
SI-10 Minor isomer: $[\alpha]_D^{23}$ = -28.9 (*c* = 1.05, $CHCl_3$); IR: (neat) 3504, 2954, 2921, 2883, 2856, 1734, 1712, 1456, 1282, 1255, 1167, 1075, 835, 781 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.26 (ddd, *J* = 10.8, 7.0, 4.8 Hz, 1H), 4.15 (ddd, *J* = 10.9, 8.4, 6.2 Hz, 1H), 3.68-3.74 (m, 3H), 3.60-3.66 (m, 4H), 1.87-1.96 (m, 2H), 1.76-1.81 (m, 1H), 1.21 (s, 9H), 1.09 (d, *J* = 6.6 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 85.4, 79.4, 78.6, 75.0, 65.8, 61.5, 46.1, 38.7, 33.6, 27.2, 25.87, 25.83, 18.29, 18.27, 13.9, -4.5, -4.7, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{26}H_{55}O_6Si_2S$ (M+H) 519.3537, found 519.3511.



SI-10 **SI-11**

Thioate SI-11: To a stirred solution of diastereomeric alcohol **SI-10** (1.01 g, 1.95 mmol) in toluene (24.0 mL) was added thiocarbonyldiimidazole (497 mg, 2.78 mmol) at rt and heated to 100 °C. After 24 h, the reaction cooled down to rt and the solvent was removed *in vacuo*. The residue was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 10-20% EtOAc / hexanes, to give diastereomeric thioate **SI-11** (1.12 g, 1.78 mmol, 91%) as colorless oil. Analytically pure samples of the individual diastereomers could be obtained via chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give sequentially the major diastereomer followed by the minor diastereomer. **SI-11** Major isomer: $[\alpha]_D^{23}$ = -18.5 (*c* = 1.00, $CHCl_3$); IR: (neat) 2954, 2927, 2883, 2856, 1761, 1734, 1472, 1358, 1287, 1255, 1157, 1091, 835, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.60 (s. 1H), 7.09 (s, 1H), 6.31 (dd, *J* = 3.4, 3.3 Hz, 1H), 4.29-4.35 (m, 1H), 4.19-4.25 (m, 2H), 3.79-3.88 (m, 2H), 3.59 (dd, *J* = 10.7, 2.4 Hz, 1H), 3.48 (dd, *J* = 10.7, 4.5 Hz, 1H), 2.29-2.38 (m, 1H), 1.93-2.01 (m, 1H), 1.74-1.83 (m, 1H), 1.22 (s, 9H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.84 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H), -0.01 (s, 3H), -0.02 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 178.3, 136.7, 131.2, 117.6, 85.8, 82.2, 79.9, 73.3, 65.9, 61.4, 45.5, 38.7, 33.3, 27.2, 25.9, 25.8, 18.4, 18.3, 10.5, -4.4, -4.6, -5.4 ppm; HRMS (ES+) calcd. for $C_{30}H_{57}O_6N_2Si_2S$ (M+H) 629.3476, found 629.3481.

SI-11 Minor isomer: $[\alpha]_D^{23}$ = -25.7 (*c* = 1.05, $CHCl_3$); IR: (neat) 2954, 2927, 2879, 2856, 1724, 1472, 1461, 1394, 1331, 1280, 1241, 1225, 1150, 1095, 989, 836, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.63 (s. 1H), 7.06 (t, *J* = 0.8 Hz, 1H), 5.96 (dd, *J* = 5.5, 3.9 Hz, 1H), 4.30 (dd, *J* = 11.3, 5.7 Hz, 1H), 4.26 (t, *J* = 3.3 Hz, 1H), 4.14-4.20 (m, 1H), 3.99-4.03 (m, 1H), 3.91 (td, *J* = 8.6, 3.3 Hz, 1H), 3.70 (dd, *J* = 9.7, 7.7 Hz, 1H), 3.61 (dd, *J* = 9.8, 5.0 Hz, 1H), 2.21-2.30 (m, 1H), 1.92-2.00 (m, 1H), 1.81-1.90 (m, 1H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.21 (s, 9H), 0.91 (s, 9H), 0.87 (s, 9H), 0.17 (s, 3H), 0.13 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.9, 178.4, 136.9, 130.9, 117.9, 90.7, 82.1, 81.9, 74.5, 63.9, 61.4, 46.7, 38.7, 33.2, 27.2, 25.9, 18.3, 18.0, 14.4, -4.1, -4.3, -5.33, -5.34 ppm; HRMS (ES+) calcd. for $C_{30}H_{57}O_6N_2Si_2S$ (M+H) 629.3476, found 629.3475.

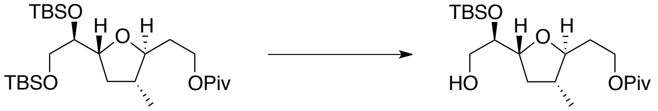


SI-11

41

Tetrahydrofuran 41: To a stirred solution of diastereomeric thioate **SI-11** (1.12 g, 1.78 mmol) in deoxygenated toluene (96.0 mL) at rt was added AIBN (29.3 mg, 0.178 mmol) and heated to 95 °C. Bu_3SnH (1.04 g, 0.96 mL, 3.56 mmol) was added dropwise over 45 min. After another 45 min, the reaction was cooled down to rt and the solvent was removed *in vacuo*. The residue was directly loaded onto the column and purified by flash chromatography over silica gel, eluting with 3-6% EtOAc / hexanes, to give tetrahydrofuran **41** (859 mg, 1.71

mmol, 96%) as colorless oil. $[\alpha]_D^{23}$ = -35.0 (*c* = 1.03, $CHCl_3$); IR: (neat) 2958, 2926, 2886, 2854, 1733, 1473, 1457, 1361, 1282, 1250, 1154, 1106, 1074, 938, 835, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.26 (ddd, *J* = 10.8, 7.1, 5.1 Hz, 1H), 4.14 (ddd, *J* = 10.8, 7.7, 6.6 Hz, 1H), 4.00-4.05 (m, 1H), 3.63-3.68 (m, 1H), 3.53-3.59 (m, 2H), 3.44 (td, *J* = 8.9, 2.9 Hz, 1H), 2.04 (dt, *J* = 12.0, 6.6 Hz, 1H), 1.80-1.94 (m, 2H), 1.64-1.73 (m, 1H), 1.52 (td, *J* = 11.6, 9.7 Hz, 1H), 1.20 (s, 9H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.908 (s, 9H), 0.904 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.068 (s, 3H), 0.063 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 81.6, 78.5, 75.7, 65.1, 62.1, 40.1, 38.6, 36.7, 33.1, 27.2, 25.9, 18.4, 18.2, 15.9, -4.3, -4.6, -5.3 ppm; HRMS (ES+) calcd. for $C_{26}H_{55}O_5Si_2$ (M+H) 503.3588, found 503.3586.



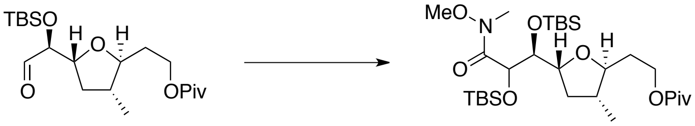
41 **SI-12**

Alcohol SI-12: To a stirred solution of TBS ether **41** (501 mg, 0.997 mmol) in THF (10.0 mL) at 0 °C was added a stock solution of HF•Pyr.[4] (5.5 mL) over 1 h. After 24 h, the reaction quenched with sat. aq. $NaHCO_3$ (30 mL) and the aqueous layer was extracted with EtOAc / Et_2O (2:1, 3 X 60 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give alcohol **SI-12** (322 mg, 0.828 mmol, 83%) as colorless oil. $[\alpha]_D^{23}$ = -31.3 (*c* = 1.04, $CHCl_3$); IR: (neat) 3494, 2957, 2930, 2882, 2855, 1730, 1477, 1461, 1284, 1252, 1153, 1102, 1055, 940, 838, 778 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.27 (ddd, *J* = 10.9, 7.1, 4.9 Hz, 1H), 4.14 (ddd, *J* = 10.9, 8.2, 6.3 Hz, 1H), 4.06 (dt, *J* = 9.7, 6.0 Hz, 1H), 3.65-3.69 (m, 2H), 3.53-3.57 (m, 1H), 3.48 (td, *J* = 6.3, 2.8 Hz, 1H), 2.37-2.39 (m, 1H), 2.09 (dt, *J* = 12.1, 6.5 Hz, 1H), 1.91-1.96 (m, 1H), 1.86-1.91 (m, 1H), 1.68-1.72 (m, 1H), 1.43 (td, *J* = 11.5, 10.1 Hz, 1H), 1.21 (s, 9H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 81.8, 79.8, 74.7, 64.2, 61.8, 39.9, 38.6, 36.8, 33.0, 27.1, 25.9, 18.2, 15.9, -4.4, -4.8 ppm; HRMS (ES+) calcd. for $C_{20}H_{40}O_5Si_2Na$ (M+Na) 411.2543, found 411.2542.

SI-12 **42**

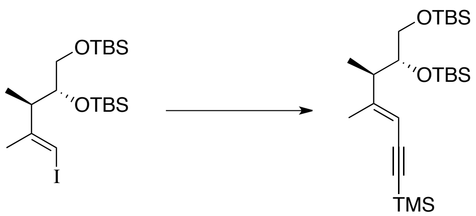
Aldehyde 42: To a stirred solution of oxalyl chloride (262 mg, 0.18 mL, 2.06 mmol) in CH_2Cl_2 (10.0 mL) at -78 °C was cannulated a solution of DMSO (341 mg, 0.31 mL, 4.31 mmol) in CH_2Cl_2 (2.7 mL). After 15 min, a solution of alcohol **SI-12** (670 mg, 1.72 mmol) in CH_2Cl_2 (6.0 mL and 2 X 0.75 mL wash) was cannulated to it. After 45 min, Et_3N (936 mg, 1.30 mL, 8.62 mmol) was added. After 20 min, the cooling bath was removed and the reaction was quenched with H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X

50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-20% EtOAc / hexanes, to give aldehyde **42** (650 mg, 1.67 mmol, 97%) as colorless oil. $[\alpha]_D^{23}$ = -72.6 (*c* = 1.04, $CHCl_3$); IR: (neat) 2953, 2925, 2859, 1731, 1478, 1454, 1283, 1252, 1155, 1112, 940, 839, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.69 (d, *J* = 1.4 Hz, 1H), 4.29 (ddd, *J* = 9.2, 6.6, 4.0 Hz, 1H), 4.23 (ddd, *J* = 10.9, 7.1, 5.2 Hz, 1H), 4.13 (ddd, *J* = 10.9, 7.8, 6.5 Hz, 1H), 3.95 (dd, *J* = 4.0, 1.4 Hz, 1H), 3.53 (td, *J* = 9.0, 3.0 Hz, 1H), 2.13 (dt, *J* = 12.1, 6.8 Hz, 1H), 1.83-1.96 (m, 2H), 1.59-1.73 (m, 2H), 1.20 (s, 9H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.95 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 203.8, 178.5, 82.6, 80.0, 78.5, 61.8, 39.7, 38.7, 36.1, 32.8, 27.2, 25.8, 18.3, 15.7, -4.6, -4.9 ppm; HRMS (CI+) calcd. for $C_{20}H_{39}O_5Si$ (M+H) 387.2567, found 387.2560.



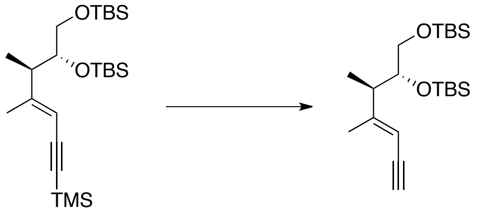
42 **10**

Weinreb Amide 10: To a stirred solution of aldehyde **42** (82.3 mg, 0.212 mmol) and $CH(CN)_2OTBS$[11] (125 mg, 0.636 mmol) in Et_2O (2.5 mL) at 0 °C was added NH(OMe)Me (0.43 mL, 0.851 mmol, 2 M in Et_2O) followed by DMAP (71.5 mg, 0.585 mmol). After 2 d, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give Weinreb amide **10** {81.5 mg, 0.168 mmol, 79% (2.5:1 dr)} as colorless oil. Major isomer: $[\alpha]_D^{23}$ = -10.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 2957, 2930, 2857, 1730, 1680, 1463, 1253, 1158, 1106, 1005, 836, 778 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.76 (br s, 1H), 4.26 (ddd, *J* = 11.0, 7.2, 4.9 Hz, 1H), 4.16-4.20 (m, 2H), 3.85 (br s, 1H), 3.75 (s, 3H), 3.47 (td, *J* = 9.1, 2.6 Hz, 1H), 3.19 (br s, 3H), 1.86-1.96 (m, 3H), 1.63-1.68 (m, 2H), 1.20 (s, 9H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 18H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.01 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.5, 173.2, 81.3, 77.8, 75.1, 69.2, 62.1, 61.6, 40.5, 38.6, 36.6, 33.4, 32.4, 27.2, 26.3, 25.8, 18.4, 18.3, 15.5, -4.1, -4.7, -5.0, -5.1 ppm; HRMS (ES+) calcd. for $C_{29}H_{60}NO_7Si_2$ (M+H) 590.3908, found 590.3921.



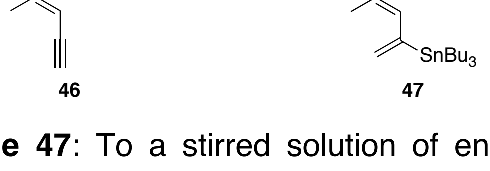
11 **SI-13**

TMS Enyne SI-13: To a stirred solution of $Pd(PPh_3)_4$ (116 mg, 0.100 mmol) and CuI (38.0 mg, 0.199 mmol) in diisopropylamine (6.5 mL) at 0 °C was cannulated a pre-cooled solution of vinyl iodide **11** (967 mg, 1.99 mmol) in diisopropylamine (2.6 mL). TMS acetylene **45** (299 mg, 0.43 mL, 2.99 mmol) was added immediately. After 20 min, the reaction was quenched with sat. aq. NH_4Cl (30 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-6% Et_2O / pentane, to give TMS enyne **SI-13** (890 mg, 1.95 mmol, 98%) as colorless oil. $[\alpha]_D^{23} = +27.5$ (c = 1.04, $CHCl_3$); IR: (neat) 2956, 2925, 2898, 2851, 2135, 1478, 1260, 1088, 832, 777 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.40 (br s, 1H), 3.64 (ddd, J = 6.7, 5.2, 4.2 Hz, 1H), 3.46 (dd, J = 10.0, 5.2 Hz, 1H), 3.42 (dd, J = 10.0, 6.8 Hz, 1H), 2.50 (qd, J = 7.0, 4.2 Hz, 1H), 1.94 (d, J = 1.1 Hz, 3H), 1.07 (d, J = 7.1 Hz, 3H), 0.91 (s, 9H), 0.90 (S, 9H), 0.21 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 155.4, 106.7, 103.8, 96.7, 76.3, 65.2, 44.0, 26.0, 25.9, 18.3, 18.2, 18.1, 15.8, 0.19, -4.1, -4.9, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{24}H_{51}O_2Si_3$ (M+H) 455.3197, found 455.3187.



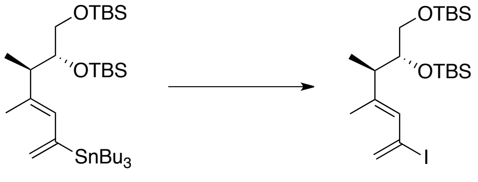
SI-13 **46**

Enyne 46: To a stirred solution of TMS enyne **SI-13** (718 mg, 1.57 mmol) in MeOH (8.0 mL) at rt was added finely powdered K_2CO_3 (165 mg, 1.19 mmol). After 2 h, the solvent was removed *in vacuo* and the residue was dissolved in Et_2O / H_2O (3:1, 100 mL). The aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 0-2% EtOAc / hexanes, to give enyne **46** (574 mg, 1.49 mmol, 95%) as colorless oil. $[\alpha]_D^{23} = +11.4$ (c = 1.01, $CHCl_3$); IR: (neat) 3312, 2952, 2925, 2885, 2857, 1474, 1466, 1387, 1356, 1253, 1119, 1099, 1063, 1012, 834, 810, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.37 (bs, 1H), 3.64 (dt, J = 6.5, 4.5 Hz, 1H), 3.48 (dd, J = 10.0, 5.1 Hz, 1H), 3.41 (dd, J = 10.0, 6.8 Hz, 1H), 3.05 (d, J = 2.0 Hz, 1H), 2.50-2.56 (m, 1H), 1.94 (d, J = 0.6 Hz, 3H), 1.08 (d, J = 7.1 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.077 (s, 3H), 0.070 (s, 3H), 0.059 (s, 3H), 0.056 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 105.5, 82.0, 79.7, 76.2, 65.2, 43.9, 25.9, 25.8, 18.2, 18.0, 15.8, -4.2, -4.9, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{21}H_{43}O_2Si_2$ (M+H) 383.2802, found 383.2819.



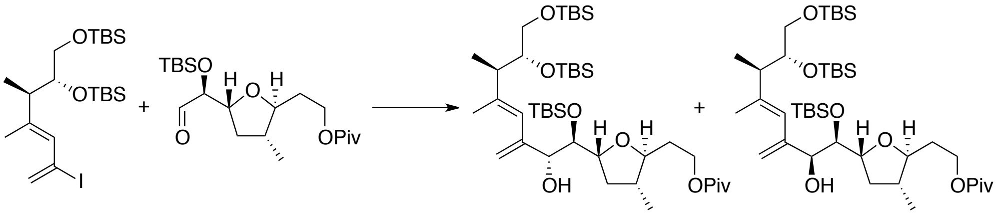
46 **47**

Dienyl Stannane 47: To a stirred solution of enyne **46** (889 mg, 2.32 mmol) in degassed THF (100.0 mL) at 0 °C was added $PdCl_2(PPh_3)_2$ (81.5 mg, 0.116 mmol) followed by Bu_3SnH (1.35 g, 1.45 mL, 4.64 mmol) over 2 min. After 25 min, the reaction was passed through a plug of silica gel eluting with hexanes (200 mL) buffered with 1% Et_3N. The solvent was removed *in vacuo* and the residue was purified by flash chromatography over silica gel, eluting with 0-6% Et_2O / pentane, to sequentially give dienyl stannane **47** {1.22 g, 1.81 mmol, 78% (89% borsm)} as colorless oil followed by recovered enyne **46** (98.3 mg, 0.257 mmol, 11%). $[\alpha]_D^{23}$ = +11.8 (c = 1.00, $CHCl_3$); IR: (neat) 2954, 2923, 2885, 2855, 1472, 1466, 1365, 1254, 1119, 1095, 1063, 1003, 956, 833, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.65 (dd, J = 3.5, 1.8 Hz, 1H), 5.32 (dd, J = 3.5, 1.2 Hz, 1H), 3.69 (td, J = 5.8, 3.8 Hz, 1H), 3.53 (dd, J = 10.0, 5.8 Hz, 1H), 3.47 (dd, J = 10.0, 5.8 Hz, 1H), 2.42 (qd, J = 7.2, 3.8 Hz, 1H), 1.71 (d, J = 1.1 Hz, 3H), 1.46-1.56 (m, 6H), 1.29-1.38 (m, 6H), 1.09 (d, J = 7.2 Hz, 3H), 0.90-0.95 (m, 33H), 0.098 (s, 3H), 0.094 (s, 3H), 0.06 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 135.2, 131.8, 126.6, 76.8, 65.6, 45.0, 29.0, 27.3, 26.0, 25.9, 18.3, 18.1, 16.0, 15.9, 13.6, 9.9, -4.1, -4.8, -5.3 ppm; HRMS (ES+) calcd. for $C_{33}H_{70}O_2Si_2SnNa$ (M+Na) 697.3834, found 697.3802.



47 **48**

Dienyl Iodide 48: To a stirred solution of dienyl stannane **47** (1.22 g, 1.81 mmol) in CH_2Cl_2 (86.0 mL) at 0 °C was cannulated a solution of I_2 (688 mg, 2.71 mmol) in CH_2Cl_2 (43.0 mL). After 20 min, the reaction was quenched with 10% aq. $Na_2S_2O_3$ (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 X 60 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-10% Et_2O / pentane, to give dienyl iodide **48** (871 mg, 1.70 mmol, 94%) as colorless oil. $[\alpha]_D^{23}$ = +7.5 (c = 1.01, $CHCl_3$); IR: (neat) 2954, 2927, 2883, 2855, 1603, 1472, 1254, 1123, 1095, 1063, 833, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 1H), 5.93 (s, 1H), 5.92 (t, J = 1.3 Hz, 1H), 3.68 (td, J = 5.8, 4.3 Hz, 1H), 3.42-3.49 (m, 2H), 2.43 (qd, J = 7.1, 4.3 Hz, 1H), 1.81 (d, J = 1.3 Hz, 3H), 1.08 (d, J = 7.1 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.08 (s, 3H), 0.079 (s, 3H), 0.071 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 131.1, 127.4, 104.0, 76.5, 65.2, 44.1, 26.0, 25.9, 18.3, 18.1, 16.2, 15.7, -4.1, -4.8, -5.2, -5.3 ppm; HRMS (ES+) calcd. for $C_{21}H_{44}IO_2Si_2$ (M+H) 511.1925, found 511.1914.

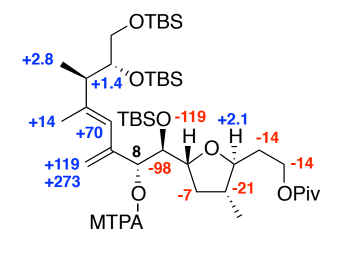


48 **42** **50** **51**

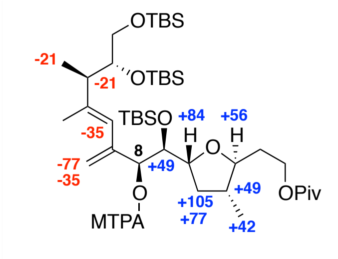
Alcohols 50 and **51**: To a stirred solution of dienyl iodide **48** (442 mg, 0.865 mmol) in THF (7.5 mL) at -78 °C was added *n*-BuLi (0.90 mL, 1.44 mmol, 2.5 M in hexanes). After 45 min, a solution of aldehyde **42** (279 mg, 0.721 mmol) in THF (7.5 mL, pre-cooled to -78 °C) was cannulated to it. After 1 h, the reaction was quenched with sat. aq. NH$_4$Cl (25 mL) and the aqueous layer was extracted with Et$_2$O (3 X 50 mL). The dried (MgSO$_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 4-10% EtOAc / hexanes, to sequentially give diastereomeric alcohols **50** and **51** {345 mg, 0.447 mmol, 62% (81% borsm; 3:1 dr)} as colorless oils followed by recovered aldehyde 4.3 (53.1 mg, 0.137 mmol, 19%). Major isomer **50**: $[\alpha]_D^{23}$ = +28.3 (*c* = 1.03, CHCl$_3$); IR: (neat) 3478, 2956, 2925, 2883, 2859, 1727, 1474, 1462, 1287, 1158, 1092, 835, 773 cm^{-1}; ^{1}H NMR (700 MHz, CDCl$_3$) δ 5.66 (s, 1H), 5.52 (s, 1H), 5.04 (s, 1H), 4.25-4.29 (m, 1H), 4.22 (br d, *J* = 5.88 Hz, 1H), 4.13-4.17 (m, 2H), 4.09 (d, *J* = 7.0 Hz, 1H), 3.67 (td, *J* = 6.0, 4.0 Hz, 1H), 3.61 (t, *J* = 2.8 Hz, 1H), 3.58 (td, *J* = 9.1, 2.8 Hz, 1H), 3.45-3.49 (m, 2H), 2.49 (qd, *J* = 7.1, 4.0 Hz, 1H), 1.98 (dt, *J* = 11.8, 6.8 Hz, 1H), 1.90-1.95 (m, 1H), 1.78 (s, 3H), 1.66-1.72 (m, 1H), 1.64 (td, *J* = 11.4, 9.5 Hz, 1H), 1.22 (s, 9H), 1.08 (d, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.95 (s, 9H), 0.914 (s, 9H), 0.910 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 178.5, 145.4, 141.5, 124.8, 113.8, 82.7, 78.1, 78.0, 76.6, 74.1, 65.4, 61.8, 45.3, 39.4, 38.7, 37.0, 32.8, 27.2, 26.0, 25.98, 25.94, 18.3, 18.2, 18.1, 16.3, 16.1, 15.6, -4.1, -4.3, 4.5, -4.8, -5.31, -5.37 ppm; HRMS (ES+) calcd. for C$_{41}$H$_{82}$O$_7$Si$_3$Na (M+Na) 793.5266, found 793.5294.

Minor isomer **51**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.65 (s, 1H), 5.34 (t, *J* = 1.6 Hz, 1H), 5.02 (s, 1H), 4.27(ddd, *J* = 10.8, 7.2, 4.9 Hz, 1H), 4.13 (ddd, *J* = 10.8, 8.0, 6.5 Hz, 1H), 4.04 (ddd, *J* = 9.8, 7.3, 6.0 Hz, 1H), 3.91 (d, *J* = 9.3 Hz, 1H), 3.69 (td, *J* = 5.7, 4.1 Hz, 1H), 3.57 (dd, *J* = 7.4, 1.3 Hz, 1H), 3.44-3.53 (m, 3H), 2.91 (d, *J* = 9.3 Hz, 1H), 2.46 (qd, *J* = 7.1, 4.0 Hz, 1H), 2.15 (dt, *J* = 11.9, 6.2 Hz, 1H), 1.87-1.96 (m, 2H), 1.82 (d, *J* = 1.2 Hz, 3H), 1.66-1.75 (m, 1H), 1.27-1.37 (m, 1H), 1.21 (s, 9H), 1.10 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 18H), 0.89 (s, 9H), 0.12 (s, 3H), 0.08 (s, 6H), 0.05 (s, 6H), 0.03 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 178.3, 145.8, 142.2, 123.7, 112.9, 81.6, 80.2, 76.0, 73.2, 65.5, 61.8, 45.3, 39.9, 38.6, 37.9, 33.2, 27.2, 26.06, 26.01, 25.9, 18.4, 18.3, 18.1, 17.6, 16.1, 16.0, -3.9, -4.1, -4.7, -4.8, -5.2, -5.3 ppm.

Mosher Ester Analysis[12] for the determination of C_8 Stereochemistry in Compounds 50 and 51.

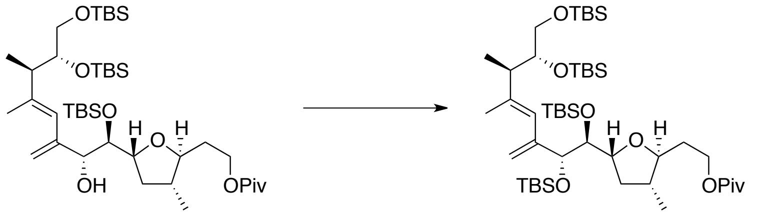


Mosher ester analysis
for major isomer **50**



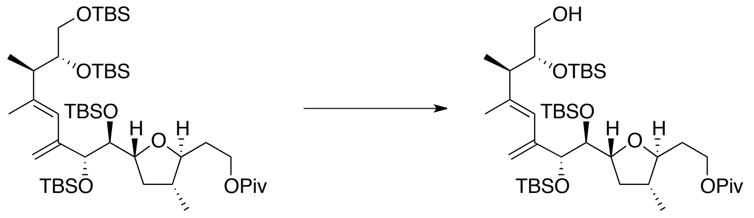
Mosher ester analysis
for minor isomer **51**

^1H NMR shift differencecs [(S)-MTPA-(R)-MTPA] reported in Hertz (CDCl3, 700 MHz).



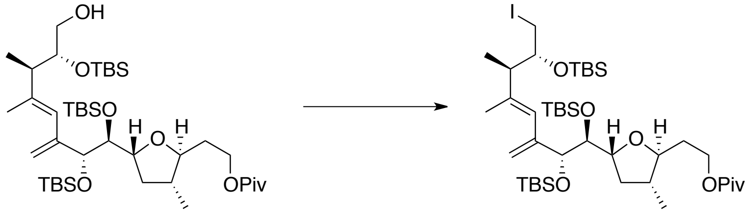
50 **SI-14**

TBS Ether SI-14: To a stirred solution of alcohol **50** (195 mg, 0.252 mmol) in CH_2Cl_2 (6.5 mL) at -78 °C were added 2,6-lutidine (103 mg, 118 µL, 1.01 mmol) followed by TBSOTf (133 mg, 117 µL, 0.505 mmol). After 3 h, the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL) and the aqueous layer was extracted with Et_2O (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-5% EtOAc / hexanes, to give TBS ether **SI-14** (195 mg, 0.220 mmol, 87%) as colorless oil. $[\alpha]_D^{23}$ = +34.6 (*c* = 1.04, $CHCl_3$); IR: (neat) 2956, 2925, 2883, 2859, 1731, 1470, 1462, 1256, 1158, 1100, 1081, 832, 773 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.66 (s, 1H), 5.33 (t, *J* = 2.0 Hz, 1H), 4.96 (s, 1H), 4.27 (ddd, *J* = 10.8, 7.2, 4.8 Hz, 1H), 4.11-4.15 (m, 2H), 3.97 (ddd, *J* = 9.8, 7.2, 6.2 Hz, 1H), 3.65-3.67 (m, 1H), 3.54 (dd, *J* = 7.3, 2.3 Hz, 1H), 3.43-3.47 (m, 2H), 3.31 (td, *J* = 9.2, 2.6 Hz, 1H), 2.51 (qd, *J* = 7.1, 4.0 Hz, 1H), 2.07 (dt, *J* = 12.3, 6.4 Hz, 1H), 1.87-1.92 (m, 1H), 1.76-1.83 (m, 1H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.64-1.69 (m, 1H), 1.21-1.27 (m, 1H), 1.20 (s, 9H), 1.09 (d, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.917 (s, 9H), 0.915 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.085 (s, 3H), 0.081 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H), 0.02 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 145.2, 140.9, 125.7, 114.3, 80.2, 79.5, 79.0, 78.5, 65.4, 62.1, 45.6, 40.3, 38.7, 37.9, 33.0, 27.2, 26.1, 26.0, 25.9, 18.43, 18.40, 18.3, 18.1, 16.06, 16.00, 15.9, -4.1, -4.2, -4.3, -4.7, -4.83, -4.85, -5.3, -5.4 ppm; HRMS (TOF+) calcd. for $C_{47}H_{96}O_7Si_4Na$ (M+Na) 907.6125, found 907.6106.



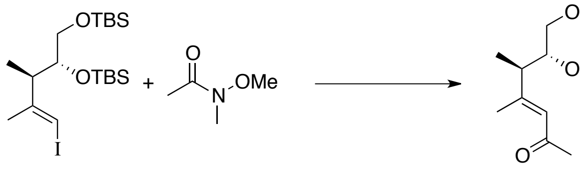
SI-14 **SI-15**

Alcohol SI-15: To a stirred solution of TBS ether **SI-14** (264 mg, 0.298 mmol) in THF (3.3 mL) at 0 °C was added a stock solution of HF•Pyr.[4] (1.2 mL). After 32 h, the reaction was quenched with sat. aq. $NaHCO_3$ (20 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 4 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 6-12% EtOAc / hexanes, to give alcohol **SI-15** (186 mg, 0.241 mmol, 81%) as colorless oil. $[\alpha]_D^{23}$ = +22.5 (*c* = 1.01, $CHCl_3$); IR: (neat) 3420, 2956, 2925, 2879, 2855, 1727, 1470, 1454, 1283, 1248, 1162, 1069, 839, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (s, 1H), 5.31 (t, *J* = 1.7 Hz, 1H), 4.97 (s, 1H), 4.26 (ddd, *J* = 10.8, 7.2, 4.8 Hz, 1H), 4.10-4.16 (m, 2H), 3.95 (ddd, *J* = 9.9, 7.0, 6.1 Hz, 1H), 3.78 (dt, *J* = 5.5, 4.8 Hz, 1H), 3.53-3.57 (m, 3H), 3.35 (td, *J* = 9.0, 2.8 Hz, 1H), 2.46-2.53 (m, 1H), 2.06 (dt, *J* = 12.1, 6.3 Hz, 1H), 1.85-1.93 (m, 1H), 1.80 (d, *J* = 1.1 Hz, 3H), 1.62-1.75 (m, 2H), 1.21-1.30 (m, 1H), 1.20 (s, 9H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.918 (s, 9H), 0.915 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 145.1, 140.6, 125.4, 114.8, 80.5, 79.4, 78.9, 78.6, 75.2, 64.4, 62.0, 46.4, 40.3, 38.6, 38.1, 33.1, 27.2, 26.1, 25.9, 25.8, 18.4, 18.3, 18.1, 16.0, 14.7, -4.2, -4.3, -4.6, -4.7 ppm; HRMS (ES+) calcd. for $C_{41}H_{82}O_7Si_3Na$ (M+Na) 793.5266, found 793.5232.



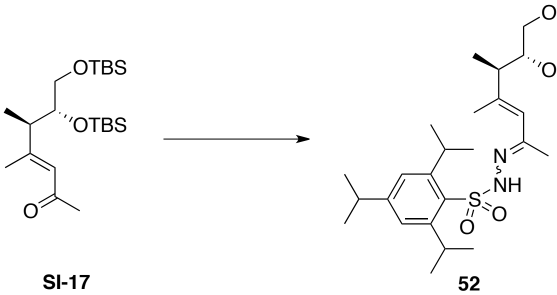
SI-15 **9**

Iodide 9: To a stirred solution of alcohol **SI-15** (186 mg, 0.241 mmol) in benzene (6.0 mL) at 5 °C were sequentially added imidazole (82.1 mg, 1.20 mmol), PPh_3 (190 mg, 0.723 mmol) and I_2 (153 mg, 0.602 mmol). After 10 min, the reaction was warmed to rt and wrapped with aluminum foil. After 1 h, the reaction was quenched with sat. aq. $Na_2S_2O_3$ (20 mL) and the aqueous layer was extracted with Et_2O (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-5% EtOAc / hexanes, to give iodide **9** (191 mg, 0.216 mmol, 90%) as colorless oil. $[\alpha]_D^{23}$ = +27.6 (*c* = 1.02, $CHCl_3$); IR: (neat) 2955, 2923, 2853, 1730, 1472, 1460, 1253, 1159, 1073, 1037, 834, 775 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.82 (s, 1H), 5.34 (dd, *J* = 2.1, 1.4 Hz, 1H), 4.99 (s, 1H), 4.27 (ddd, *J* = 10.8, 7.2, 4.8 Hz, 1H), 4.12-4.16 (m, 2H), 3.98 (ddd, *J* = 9.9, 6.8, 6.1 Hz, 1H), 3.69 (dt, *J* = 6.7, 4.4 Hz, 1H), 3.56 (dd, *J* = 6.9, 3.1 Hz, 1H), 3.37 (td, *J* = 9.1, 2.8 Hz, 1H), 3.18 (dd, *J* = 10.0, 4.3 Hz, 1H), 3.15 (dd, *J* = 10.0, 6.8 Hz, 1H), 2.67 (qd, *J* = 6.9, 4.7 Hz, 1H), 2.06 (dt, *J* = 12.2, 6.2 Hz, 1H), 1.88-1.92 (m, 1H), 1.80-1.85 (m, 1H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.65-1.70 (m, 1H), 1.27-1.32 (m, 1H), 1.21 (s, 9H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.93 (s, 9H), 0.92 (s, 18H), 0.14 (s, 3H), 0.108 (s, 3H), 0.106 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 145.0, 139.5, 126.3, 115.2, 80.5, 79.2, 78.6, 78.5, 74.9, 62.1, 47.1, 40.3, 38.7, 38.1, 33.2, 27.2, 26.2, 26.0, 25.8, 18.4, 18.3, 18.0, 16.1, 16.0, 15.0, 11.4, -4.0, -4.1, -4.2, -4.73, -4.75 ppm; HRMS (ES+) calcd. for $C_{41}H_{81}O_6Si_3INa$ (M+Na) 903.4283, found 903.4263.



11 **SI-16** **SI-17**

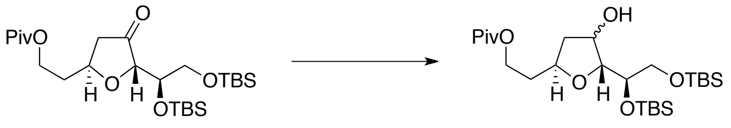
Enone SI-17: To a stirred solution of vinyl iodide **11** (407 mg, 0.839 mmol) in THF (7.0 mL) at -78 °C was *n*-BuLi (0.40 mL, 1.00 mmol, 2.5 M in hexanes). After 1.5 h, a solution of Weinreb amide **SI-16** (136 mg, 0.14 mL, 1.31 mmol) in THF (7.0 mL) was cannulated to it. After 1.5 h, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and the aqueous layer was extracted with Et_2O (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-6% EtOAc / hexanes, to give enone **SI-17** (289 mg, 0.721 mmol, 86%) as colorless oil. $[\alpha]_D^{23}$ = +17.0 (*c* = 1.03, $CHCl_3$); IR (neat) 2959, 2943, 2856, 1685, 1609, 1472, 1249, 1091, 835, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (br s, 1H), 3.68 (dt, *J* = 6.5, 4.9 Hz, 1H), 3.52 (dd, *J* = 10.1, 4.8 Hz, 1H), 3.45 (dd, *J* = 10.1, 6.6 Hz, 1H), 2.52 (qd, *J* = 7.1, 5.0 Hz, 1H), 2.18 (s, 3H), 2.15 (d, *J* = 1.2 Hz, 3H), 1.12 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 160.2, 125.2, 75.9, 65.2, 46.0, 31.9, 25.9, 25.8, 18.2, 18.0, 17.8, 15.8, -4.2, -4.9, -5.40, -5.44 ppm; HRMS (ES+) calcd. for $C_{21}H_{45}O_3Si_2$ (M+H) 401.2907, found 401.2907.



SI-17 **52**

Hydrazone 52: To a stirred solution of enone **SI-17** (206 mg, 0.514 mmol) in Et_2O (4.0 mL) at rt was added 2,4,6-triisopropyl benzenesulfonylhydrazide

(307 mg, 1.02 mmol). After 17 h, $MgSO_4$ (100 mg) was added to the reaction. The reaction was filtered through a celite plug and the plug was washed with Et_2O (20 mL). The solvent was removed *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-10% EtOAc / hexanes, to give hydrazone **52** {326 mg, 0.478 mmol, 93% (2:1 dr)} as colorless oil. *The major isomer was readily equilibrated to minor isomer and analytically pure major isomer was not obtained*. **52** Minor isomer: $[\alpha]_D^{23}$ = +15.5 (*c* = 1.00, $CHCl_3$); IR (neat) 3222, 2956, 2929, 2858, 1603, 1463, 1382, 1255, 1166, 1100, 835, 776 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.18 (s, 2H), 5.51 (s, 1H), 4.24 (sep, *J* = 6.8 Hz, 2H), 3.66 (ddd, *J* = 7.6, 5.1, 3.8 Hz, 1H), 3.54 (dd, *J* = 10.1, 5.1 Hz, 1H), 3.40 (dd, *J* = 10.1, 7.6 Hz, 1H), 2.92 (sep, *J* = 6.9 Hz, 1H), 2.61 (qd, *J* = 7.1, 3.8 Hz, 1H), 1.95 (s, 3H), 1.65 (d, *J* = 1.0 Hz, 3H), 1.27-1.29 (m, 18H), 1.15 (d, *J* = 7.1 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.099 (s, 3H), 0.095 (s, 3H), 0.079 (s, 3H), 0.078 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.9, 152.5, 151.3, 148.2, 131.6, 123.7, 118.5, 75.9, 64.9, 43.5, 34.1, 29.9, 25.9, 25.8, 24.8, 23.5, 18.2, 18.0, 17.9, 16.9, -4.2, -4.8, -5.33, -5.35 ppm; HRMS (ES+) calcd. for $C_{36}H_{69}O_4N_2SSi_2$ (M+H) 681.4517, found 681.4484.

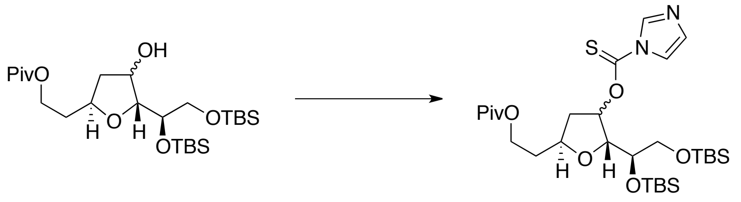


20 **SI-18**

Alcohol SI-18: To a stirred solution of ketone **20** (3.30 g, 6.57 mmol) in MeOH (83.0 mL) at rt was added $NaBH_4$ (249 mg, 6.57 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and the MeOH was removed *in vacuo*. EtOAc (150 mL) was added to the residue and the aqueous layer was extracted with EtOAc (3 X 150 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-20% EtOAc / hexanes, to give diastereomeric alcohol **SI-18** {3.17 g, 6.27 mmol, 95% (1.7: 1 dr)} as colorless oil. Analytically pure samples of the individual diastereomers could be obtained via chromatography over silica gel, eluting with 10-20% EtOAc / hexanes, to give sequentially the major diastereomer followed by the minor diastereomer. **SI-18** Major isomer: $[\alpha]_D^{23}$ = -30.8 (*c* = 1.00, $CHCl_3$); IR: (neat) 3490, 2960, 2929, 2855, 1731, 1470, 1287, 1260, 1158, 1092, 835, 781 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.40 (bs, 1H), 4.34-4.38 (m, 1H), 4.24 (ddd, *J* = 10.9, 6.2, 5.4 Hz, 1H), 4.16 (ddd, *J* = 10.9, 8.3, 6.1 Hz, 1H), 3.97 (ddd, *J* = 8.8, 8.3, 3.8 Hz, 1H), 3.70 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.58-3.65 (m, 2H), 2.15 (dd, *J* = 12.9, 5.2 Hz, 1H), 1.81-1.90 (m, 2H), 1.70 (ddt, *J* = 1.9, 4.6, 11.6 Hz, 1H), 1.21 (s, 9H), 0.93 (s, 9H), 0.90 (s, 9H), 0.139 (s, 6H), 0.133 (s, 3H), 0.11 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.5, 87.2, 74.0, 72.7, 65.8, 61.9, 41.2, 38.7, 35.0, 27.2, 25.8, 18.3, 18.2, -4.4, -4.9, -5.68, -5.69 ppm; HRMS (ES+) calcd. for $C_{25}H_{53}O_6Si_2$ (M+H) 505.3381, found 505.3394.

SI-18 Minor isomer: $[\alpha]_D^{23}$ = -28.7 (*c* = 1.01, $CHCl_3$); IR: (neat) 3490, 2960, 2925, 2859, 1734, 1715, 1474, 1256, 1155, 1092, 839, 777 cm^{-1}; ^1H NMR (700

MHz, $CDCl_3$) δ 4.24-4.28 (m, 1H), 4.19-4.22 (m, 1H), 4.10-4.17 (m, 2H), 3.68-3.70 (m, 3H), 3.64 (dd, *J* = 12.0, 5.9 Hz, 1H), 3.39 (m, 1H) 2.42 (ddd, *J* = 12.0, 7.0, 6.2 Hz, 1H), 1.93-1.97 (m, 1H), 1.87-1.92 (m, 1H), 1.72 (dt, *J* = 8.8, 12.1 Hz, 1H), 1.21 (s, 9H), 0.92 (s, 9H), 0.90 (s, 9H), 0.127 (s, 3H), 0.124 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.5, 86.1, 74.7, 74.1, 72.9, 65.5, 61.6, 40.4, 38.7, 35.4, 27.2, 25.8, 18.28, 18.24, -4.5, -4.7, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{25}H_{35}O_6Si_2$ (M+H) 505.3381, found 505.3394.

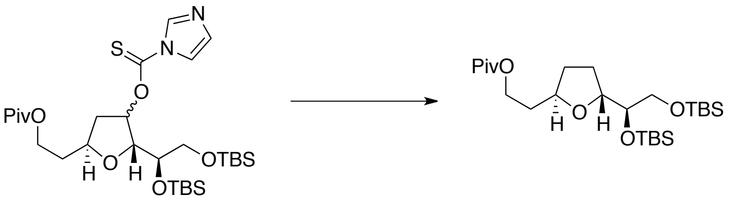


SI-18 **SI-19**

Thioate SI-19: To a stirred solution of diastereomeric alcohol **SI-18** (3.17 g, 6.27 mmol) in deoxygenated toluene (75.0 mL) at rt was added thiocarbonyl-diimidazole (3.36 g, 18.8 mmol) heated to 100 °C. After 20 h, the solvent was removed *in vacuo*. The residue was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 15-30% EtOAc / hexanes, to give diastereomeric thioate **SI-19** (3.82 g, 6.21 mmol, 99%) as colorless oil. Analytically pure samples of the individual diastereomers could be obtained via chromatography over silica gel, eluting with 15-30% EtOAc / hexanes, to give sequentially the major diastereomer followed by the minor diastereomer. **SI-19** Major isomer: $[\alpha]_D^{23}$ = -14.5 (*c* = 1.02, $CHCl_3$); IR: (neat) 2953, 2929, 2894, 2855, 1727, 1474, 1392, 1283, 1244, 1151, 1104, 832, 781 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.60 (s, 1H), 7.09 (dd, *J* = 1.6, 0.8 Hz, 1H), 5.97 (t, *J* = 3.3 Hz, 1H), 4.30-4.34 (m, 1H), 4.25 (ddd, *J* = 11.0, 6.3, 5.3 Hz, 1H), 4.19 (ddd, *J* = 11.0, 8.1, 6.2 Hz, 1H), 4.13 (dd, *J* = 7.8, 3.1 Hz, 1H), 3.95 (dt, *J* = 7.8, 4.5 Hz, 1H), 3.57-3.61 (m, 2H), 2.52 (ddd, *J* = 14.3, 6.2, 0.9 Hz, 1H), 2.06 (ddd, *J* = 14.3, 9.1, 4.6 Hz, 1H), 1.87-1.94 (m, 2H), 1.21 (s, 9H), 0.92 (s, 9H), 0.83 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), -0.02 (s, 3H), -0.04 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 182.6, 178.4, 136.6, 131.0, 117.7, 84.4, 82.2, 73.8, 72.6, 66.0, 61.5, 39.3, 38.7, 35.0, 27.2, 25.9, 25.8, 18.5, 18.3, -4.4, -4.6, -5.4, -5.5 ppm; HRMS (ES+) calcd. for $C_{29}H_{55}O_6N_2Si_2S$ (M+H) 615.3319, found 615.3309.

SI-19 Minor isomer: $[\alpha]_D^{23}$ = -21.4 (*c* = 1.04, $CHCl_3$); IR: (neat) 2956, 2929, 2883, 2855, 1727, 1470, 1396, 1337, 1287, 1244, 1228, 1158, 1088, 835, 773 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.64 (t, *J* = 1.4 Hz, 1H), 7.09 (dd, *J* = 1.6, 0.8 Hz, 1H), 6.00 (ddd, *J* = 7.3, 2.8, 2.1 Hz, 1H), 4.44 (t, *J* = 2.1 Hz, 1H), 4.38-4.42 (m, 1H), 4.23 (ddd, *J* = 11.1, 6.1, 5.6 Hz, 1H), 4.19 (ddd, *J* = 11.1, 8.1, 5.8 Hz, 1H), 3.93 (ddd, *J* = 7.7, 4.8, 2.8 Hz, 1H), 3.71 (dd, *J* = 9.8, 7.8 Hz, 1H), 3.58 (dd, *J* = 9.8, 4.9 Hz, 1H), 2.75 (dt, *J* = 14.0, 7.4 Hz, 1H), 1.96-2.01 (m, 1H), 1.89-1.94 (m, 2H), 1.21 (s, 9H), 0.90 (s, 18H), 0.15 (s, 3H), 0.13 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 183.5, 178.5, 136.9, 130.9, 117.8, 86.9, 83.2, 74.3, 63.5, 61.6, 38.7, 38.5, 35.4, 27.2, 25.9, 18.3, 17.9, -4.2, -

4.7, -5.32, -5.35 ppm; HRMS (ES+) calcd. for $C_{29}H_{55}O_6N_2Si_2S$ (M+H) 615.3319, found 615.3298.

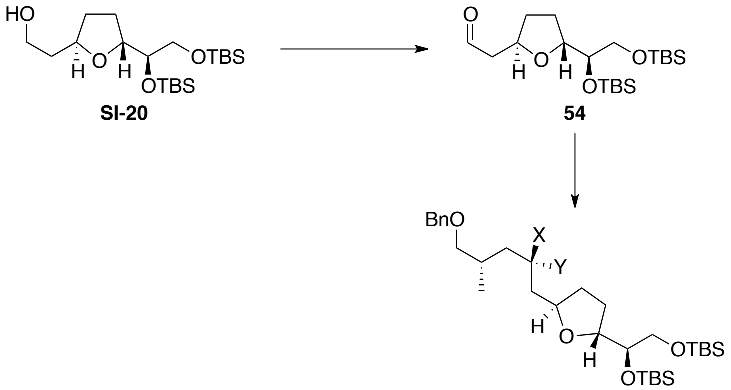


SI-19 **53**

Tetrahydrofuran 53: To a stirred solution of diastereomeric thioate **SI-19** (3.82 g, 6.21 mmol) in deoxygenated toluene (340.0 mL) at rt was added AIBN (102 mg, 0.621 mmol) and heated to 95 °C. Bu_3SnH (3.61 g, 3.4 mL, 12.4 mmol) was added dropwise over 45 min. After additional 1.5 h, the reaction was cooled down to rt and the solvent was removed *in vacuo*. The residue was directly loaded onto the column and purified by flash chromatography over silica gel, eluting with 3-6% EtOAc / hexanes, to give tetrahydrofuran **53** (2.76 g, 5.65 mmol, 91%) as colorless oil. $[\alpha]_D^{23}$ = -21.6 (*c* = 1.02, $CHCl_3$); IR: (neat) 2958, 2931, 2859, 1734, 1474, 1288, 1255, 1156, 1097, 836, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.12-4.22 (m, 2H), 3.98-4.10 (m, 2H), 3.67(dd, *J* = 11.6, 7.8 Hz, 1H), 3.55-3.59 (m, 2H), 2.02-2.09 (m, 1H), 1.74-1.98 (m, 4H), 1.51 (ddd, *J* = 18.2, 11.7, 8.6 Hz, 1H), 1.20 (s, 9H), 0.909 (s, 9H), 0.905 (s, 9H), 0.091 (s, 3H), 0.089 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.6, 78.9, 76.2, 75.8, 65.0, 62.1, 38.7, 34.8, 32.5, 27.5, 27.2, 26.0, 25.9, 18.4, 18.2, -4.2, -4.7, -5.3 ppm; HRMS (ES+) calcd. for $C_{25}H_{53}O_5Si_2$ (M+H) 489.3432, found 489.3418.

53 **SI-20**

Alcohol SI-20: To a stirred solution of pivalate **53** (1.51 g, 3.08 mmol) in Et_2O (58.0 mL) at 0 °C was added $LiAlH_4$ (235 mg, 6.17 mmol) in one portion. After 30 min, the reaction was quenched with dropwise addition of H_2O (3.0 mL) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 15-20% EtOAc/ hexanes, to give alcohol **SI-20** (1.20 g, 2.96 mmol, 96%) as colorless oil. $[\alpha]_D^{23}$ = -20.8 (*c* = 1.01, $CHCl_3$); IR: (neat) 3443, 2953, 2921, 2879, 2851, 1470, 1458, 1260, 1081, 1003, 835, 777cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.12-4.19 (m, 2H), 3.78-3.82 (m, 2H), 3.65 (dd, *J* = 11.2, 8.1 Hz, 1H), 3.54-3.59 (m, 2H), 3.01-3.04 (m, 1H), 2.02-2.09 (m, 1H), 1.92-2.00 (m, 1H), 1.68-1.87 (m, 3H), 1.58 (ddd, *J* = 18.2, 11.8, 8.6 Hz, 1H), 0.98 (t, *J* = 7.9 Hz, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.09 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 80.2, 79.3, 75.5, 64.8, 62.0, 37.0, 32.6, 27.2, 25.99, 25.90, 18.3, 18.1, -4.2, -4.7, -5.4 ppm; HRMS (ES+) calcd. for $C_{20}H_{45}O_4Si_2$ (M+H) 405.2856, found 405.2871.



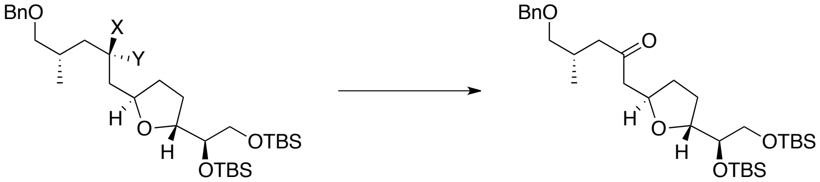
SI-20

54

56 X = H, Y = OH
57 X = OH, Y = H

Alcohols 56 and **57**: To a stirred solution of oxalyl chloride (453 mg, 0.31 mL, 3.56 mmol) in CH_2Cl_2 (21.5 mL) at -78 °C was cannulated a solution of DMSO (580 mg, 0.53 mL, 7.43 mmol) in CH_2Cl_2 (3.5 mL). After 10 min, a solution of alcohol **SI-20** (1.20 g, 2.96 mmol) in CH_2Cl_2 (6.0 mL) was cannulated to it. After 40 min, Et_3N (1. 50 g, 2.2 mL, 14.84 mmol) was added and the cooling bath was removed. After 15 min, the reaction was quenched with H_2O (40 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-20% EtOAc/ hexanes, to give aldehyde **54** (1.16 g, 2.88 mmol, 97%) as colorless oil.

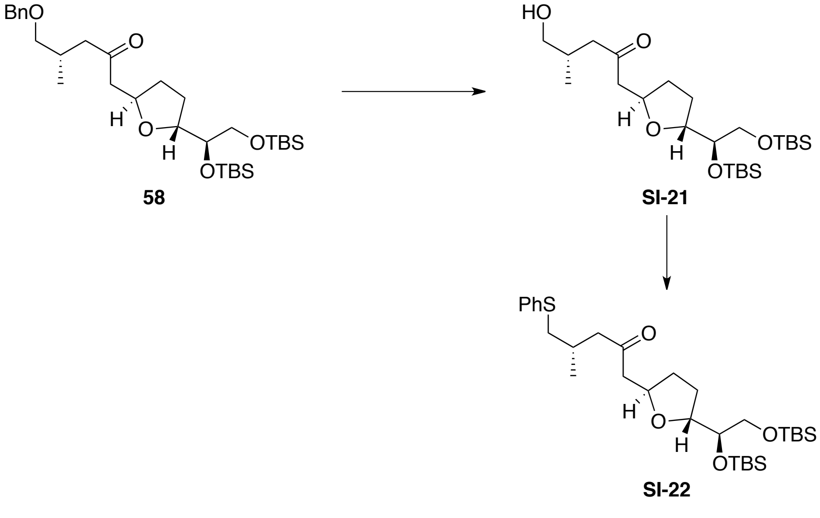
To a stirred solution of Iodide **55**[13] (860 mg, 2.96 mmol) in Et_2O (50.0 mL) at -78 °C was added *t*-BuLi (3.5 mL, 5.93 mmol, 1.7 M in pentane). After 10 min, the reaction was warmed to rt for 25 min and then cooled back down to -78 ºC. A solution of aldehyde **54** (995 mg, 2.47 mmol) in Et_2O (35.0 mL and 2 X 2.5 mL wash) was cannulated to it. After 30 min, the reaction was quenched with sat. aq. NH_4Cl (35 mL) and the aqueous layer was extracted with Et_2O (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give diastereomeric alcohols **56** and **57** {1.00 g, 1.78 mmol, 72% (91% borsm; 1.5:1 dr)} as colorless oil along with recovered aldehyde **54** (190 mg, 0.471 mmol, 19%). Major isomer **56**: $[\alpha]_D^{23}$ = -14.4 (*c* = 1.01, $CHCl_3$); IR: (neat) 3490, 2957, 2929, 2872, 2858, 1458, 1253, 1095, 835, 776, cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.35-7.36 (m, 4H), 7.28-7.30 (m, 1H), 4.53 (s, 2H), 4.13-4.17 (m, 2H), 3.93 (t, *J* = 9.0 Hz, 2H), 3.88 (s, 1H), 3.66 (dd, *J* = 11.7, 8.1 Hz, 1H), 3.56-3.58 (m, 2H), 3.39 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.31 (dd, *J* = 9.1, 6.5 Hz, 1H), 2.05-2.09 (m, 2H), 1.92-1.96 (m, 1H), 1.79-1.85 (m, 1H), 1.63-1.65 (m, 1H), 1.59 (ddd, *J* = 13.7, 9.0, 5.2 Hz, 1H), 1.48-1.56 (m, 2H), 1.25 (ddd, *J* = 13.7, 8.2, 3.7 Hz, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.914 (s, 9H), 0.910 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.073 (s, 3H), 0.070 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 138.7, 128.2, 127.5, 127.3, 80.0, 79.4, 76.4, 75.7, 72.8, 69.4, 65.0, 43.3, 42.1, 33.0, 30.2, 26.9, 25.98, 25.90, 18.3, 18.1, 17.3, -4.2, -4.7, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{31}H_{59}O_5Si_2$ (M+H) 567.3901, found 567.3882.



56 X = H, Y = OH
57 X = OH, Y = H

58

Ketone 58: To a stirred solution of diastereomeric alcohols **56** and **57** (747 mg, 1.31 mmol) in CH_2Cl_2 (26.0 mL) with 4Å mol. sieves (500 mg) were added NMO (463 mg, 3.95 mmol) followed by TPAP (46.3 mg, 0.131 mmol). After 30 min, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 10-15% EtOAc / hexanes, to give ketone **58** (708 mg, 1.25 mmol, 95%) as colorless oil. $[\alpha]_D^{23}$ = -12.6 (*c* = 1.03, $CHCl_3$); IR: (neat) 2954, 2929, 2856, 1713, 1471, 1361, 1253, 1096, 835, 777, 735 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.33-7.37 (m, 4H), 7.28-7.31 (m, 1H), 4.49 (s, 2H), 4.32 (ddd, *J* = 12.3, 8.6, 6.2 Hz, 1H), 4.08 (td, *J* = 7.4, 3.4 Hz, 1H), 3.66 (dd, *J* = 11.7, 7.9 Hz, 1H), 3.55-3.57 (m, 2H), 3.35 (dd, *J* = 9.2, 5.6 Hz, 1H), 3.28 (dd, *J* = 9.2, 6.8 Hz, 1H), 2.72 (dd, *J* = 15.5, 6.8 Hz, 1H), 2.62 (dd, *J* = 16.3, 5.4 Hz, 1H), 2.51 (dd, *J* = 15.5, 6.1 Hz, 1H), 2.38-2.42 (m, 1H), 2.34 (dd, *J* = 16.3, 7.6 Hz, 1H), 2.10-2.14 (m, 1H), 1.91-1.95 (m , 1H), 1.81-1.87 (m, 1H), 1.44-1.49 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.90 (s, 18H), 0.09 (s, 3H), 0.08 (s, 3H), 0.068 (s, 3H), 0.065 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 209.0, 138.5, 128.3, 127.59, 127.53, 78.9, 75.7, 75.5, 75.0, 72.9, 65.0, 49.3, 47.5, 32.5, 29.5, 27.4, 26.0, 25.9, 18.4, 18.2, 17.2, -4.2, -4.7, -5.32, -5.34 ppm; HRMS (ES+) calcd. for $C_{31}H_{56}O_5Si_2Na$ (M+Na) 587.3564, found 587.3553.



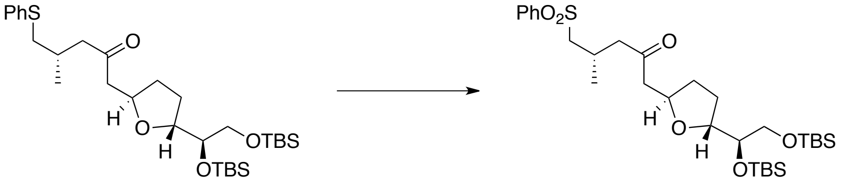
58

SI-21

SI-22

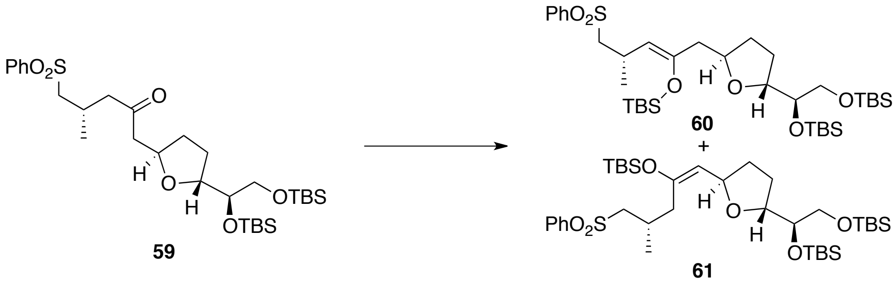
Sulfide SI-22: To a stirred solution of benzyl ether **58** (139 mg, 0.246 mmol) in *i*-PrOH (10.0 mL) was added Pd/C (105 mg, 10 mol% by weight). The flask was fitted with a H_2 balloon and purged with H_2. After 20 h, the reaction was passed through a small plug of celite and washed with EtOAc (20 mL). The solvent was removed *in vacuo* to give the crude alcohol **SI-21**.

To a stirred solution of crude alcohol **SI-21** (101 mg, 0.212 mmol) in THF (2.0 mL) at 0 °C was added Ph_2S_2 (93 mg, 0.425 mmol) followed by *n*-Bu_3P (112 µL, 0.446 mmol) and the reaction was warmed to rt. After 15 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give sulfide **SI-22** (96.2 mg, 0.169 mmol, 69%) as colorless oil. $[\alpha]_D^{23}$ = -22.8 (*c* = 1.00, $CHCl_3$); IR: (neat) 2954, 2928, 2884, 2856, 1712, 1471, 1360, 1253, 1088, 835, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.37 (m, 2H), 7.26-7.31 (m, 2H), 7.15-7.20 (m, 1H), 4.31 (tdd, *J* = 8.5, 6.9, 5.7 Hz, 1H), 4.08 (td, *J* = 7.4, 3.4 Hz, 1H), 3.66 (dd, *J* = 11.5, 8.0 Hz, 1H), 3.54-3.58 (m, 2H), 2.93 (dd, *J* = 13.0, 6.4 Hz, 1H), 2.84 (dd, *J* = 13.0, 6.7 Hz, 1H), 2.73 (dd, *J* = 17.0, 5.6 Hz, 1H), 2.65 (dd, *J* = 15.3, 7.0 Hz, 1H), 2.40-2.48 (m, 2H), 2.29-2.37 (m, 1H), 2.07-2.15 (m, 1H), 1.89-1.97 (m, 1H), 1.80- 1.87 (m, 1H), 1.42-1.51 (m, 1H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.907 (s, 9H), 0.905 (s, 9H), 0.089 (s, 3H), 0.081 (s, 3H), 0.065 (s, 3H), 0.061 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 208.6, 136.7, 129.0, 128.9, 125.8, 78.9, 75.7, 75.5, 64.9, 49.4, 49.0, 40.4, 32.5, 28.7, 27.3, 26.0, 25.9, 19.6, 18.4, 18.2, -4.2, -4.7, -5.33, -5.34 ppm; HRMS (ES+) calcd. for $C_{30}H_{55}O_4SSi_2$ (M+H) 567.3360, found 567.3348.



SI-22 **59**

Sulfone 59: To a stirred solution of sulfide **SI-22** (117 mg, 0.206 mmol) in CH_3CN (3.2 mL) at rt was added NMO (72.5 mg, 0.619 mmol) followed by TPAP (36.2 mg, 0.103 mmol). After 14 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 10-15% EtOAc / hexanes, to give sulfone **59** (104 mg, 0.173 mmol, 84%) as colorless oil. $[\alpha]_D^{23}$ = -21.3 (*c* = 1.01, $CHCl_3$); IR: (neat) 2955, 2929, 2884, 2856, 1712, 1471, 1306, 1253, 1149, 1086, 835, 777 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.92-7.94 (m, 2H), 7.67 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.58-7.60 (m, 2H), 4.29 (tdd, *J* =8.5, 7.6, 5.7 Hz, 1H), 4.08 (td, *J* = 7.4, 3.3 Hz, 1H), 3.63 (dd, *J* = 11.6, 8.1 Hz, 1H), 3.53-3.56 (m, 2H), 3.25 (dd, *J* = 14.2, 6.0 Hz, 1H), 3.01 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.77 (dd, *J* = 17.7, 5.7 Hz, 1H), 2.62 (dd, *J* = 15.2, 7.4 Hz, 1H), 2.61 (dd, *J* = 17.7, 6.7 Hz, 1H), 2.52-2.57 (m, 1H), 2.46 (dd, *J* = 15.2, 5.4 Hz, 1H), 2.08-2.12 (m, 1H), 1.91-1.96 (m, 1H), 1.81-1.87 (m, 1H), 1.44-1.50 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 18H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 207.7, 139.7, 133.6, 129.3, 127.9, 78.9, 75.7, 75.5, 64.9, 60.9, 49.3, 48.6, 32.5, 27.3, 26.0, 25.9, 24.6, 20.2, 18.4, 18.1, -4.2, -4.7, -5.3 ppm; HRMS (ES+) calcd. for $C_{30}H_{54}O_6SSi_2Na$ (M+Na) 621.3077, found 621.3065.



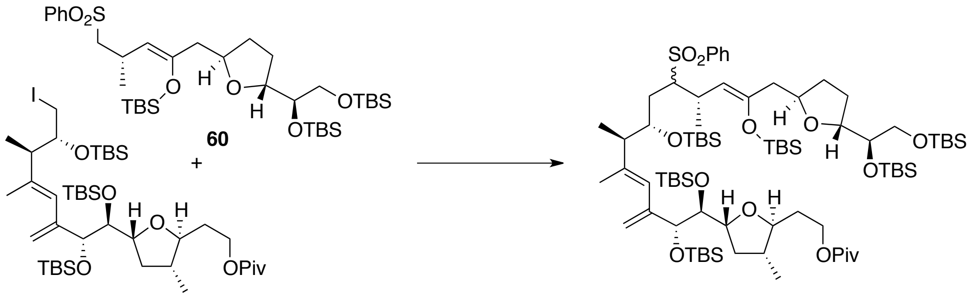
59

60

61

TBS Enol Ethers 60 and **61**: To a stirred solution of keto-sulfone **59** (104 mg, 0.173 mmol) in CH_2Cl_2 (2.5 mL) at -78 °C were added 2,6-lutidine (149 mg, 0.16 mL, 1.39 mmol) followed by TBSOTf (184 mg, 0.16 mL, 0.695 mmol). After 15 min, the reaction was warmed to 0 °C. After additional 4 h, by the time the reaction warmed to rt, was quenched with sat. aq. $NaHCO_3$ (15 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to sequentially give isomeric enol ethers **60** and **61** {145 mg, 0.164 mmol, 95% (2.5:1 rr)} as colorless oils. Major isomer **60**: $[\alpha]_D^{23}$ = +4.5 (*c* = 1.00, $CHCl_3$); IR: (neat) 2955, 2929, 2885, 2857, 1670, 1472, 1306, 1254, 1151, 1086, 1003, 836 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.91-7.93 (m, 2H), 7.64 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.54-7.57 (m, 2H), 4.28 (d, *J* = 8.7 Hz, 1H), 4.05 (td, *J* = 7.4, 3.4 Hz, 1H), 4.00 (ddd, *J* = 8.4, 6.2, 6.1 Hz, 1H), 3.65 (dd, *J* = 11.8, 8.0 Hz, 1H), 3.53-3.56 (m, 2H), 3.14-3.19 (m, 1H), 3.11 (dd, *J* = 14.0, 5.3 Hz, 1H), 3.00 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.28 (dd, *J* = 14.8, 6.0 Hz, 1H), 1.95-1.99 (m, 1H), 1.93 (dd, *J* = 14.7, 6.7 Hz, 1H), 1.88-1.92 (m, 1H), 1.76-1.82 (m, 1H), 1.41-1.46 (m, 1H), 1.15 (d, *J* = 6.7 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.057 (s, 3H), 0.054 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 148.3, 140.3, 133.3, 129.1, 127.9, 112.0, 79.0, 75.9, 65.0, 62.3, 42.4, 32.1, 27.2, 26.0, 25.9, 25.86, 25.80, 25.6, 20.6, 18.4, 18.2, 18.1, -3.7, -3.8, -4.2, -4.6, -5.32, -5.34 ppm; HRMS (ES+) calcd. for $C_{36}H_{69}O_6SSi_3$ (M+H) 713.4123, found 713.4148.

Minor isomer **61**: $[\alpha]_D^{23}$ = -9.9 (*c* = 1.17, $CHCl_3$); IR: (neat) 2955, 2929, 2885, 2857, 1671, 1472, 1318, 1307, 1255, 1144, 1087, 836 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.92-7.94 (m, 2H), 7.64 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.57-7.60 (m, 2H), 4.63 (td, *J* = 8.8, 5.7 Hz, 1H), 4.51 (d, *J* = 8.8 Hz, 1H), 4.07 (ddd, *J* = 8.1, 7.0, 3.0 Hz, 1H), 3.73 (dd, *J* = 12.4, 7.6 Hz, 1H), 3.59-3.62 (m, 2H), 3.29 (dd, *J* = 14.3, 3.3 Hz, 1H), 2.90 (dd, *J* = 14.3, 9.1 Hz, 1H), 2.18-2.25 (m, 1H), 1.99-2.05 (m, 2H), 1.85-1.94 (m, 3H), 1.44-1.50 (m, 1H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.85 (s, 9H), 0.10 (s, 6H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 149.1, 139.6, 133.5, 129.3, 127.9, 113.5, 79.2, 75.5, 73.9, 65.3, 61.1, 44.2, 33.5, 27.8, 26.4, 26.0, 25.7, 19.6, 18.4, 18.3, 18.1, -4.0, -4.1, -4.2, -4.7, -5.2 ppm; HRMS (ES+) calcd. for $C_{36}H_{69}O_6SSi_3$ (M+H) 713.4123, found 713.4094.



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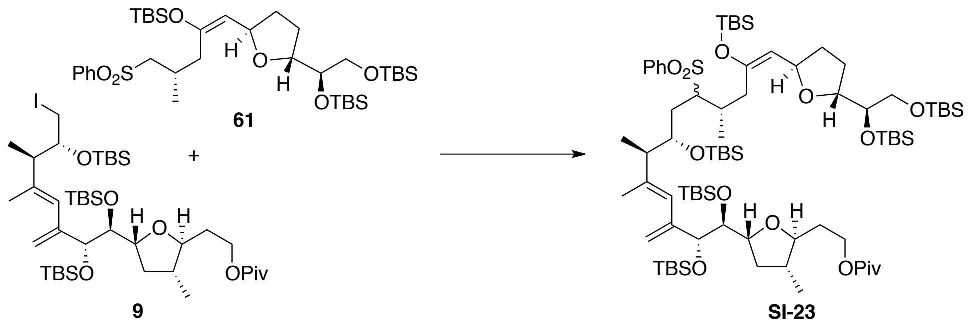
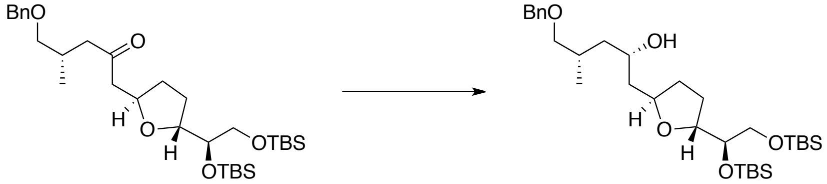
9

63

Coupled Sulfone 63: To a stirred solution of sulfone **60** (35.9 mg, 50.3 μmol) in THF (0.20 mL) at -78 °C was added LHMDS (111 μL, 0.111 mmol, 1M in THF). After 30 min, the reaction was warmed to 0 °C and HMPA (77.2 mg, 75 μL, 0.431 mmol) was added to it. A solution of iodide **9** (15.9 mg, 18.0 μmol) in THF (0.20 mL) was cannulated to it and the reaction was slowly warmed to rt over 2 h. After 6 h, the reaction was quenched with sat. aq. NH$_4$Cl (5.0 mL) and the aqueous layer was extracted with Et$_2$O (3 X 15 mL). The dried (MgSO$_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give coupled sulfone **63** (13.8 mg, 9.38 μmol, 52%) as colorless oil. $[\alpha]_D^{23}$ = -12.5 (*c* = 1.12, CHCl$_3$); IR: (neat) 2956, 2929, 2885, 2857, 1731, 1667, 1472, 1388, 1254, 1146, 1076, 836 cm^{-1}; ^{1}H NMR {700 MHz, CDCl$_3$ (two diastereomers)} δ 7.87-7.88 (m, 2H (1 diastereomer)), 7.83-7.84 (m, 2H (1 diastereomer)), 7.62 (tt, *J* = 7.4, 1.2 Hz, 1H (1 diastereomer)), 7.59 (tt, *J* = 7.4, 1.2 Hz, 1H (1 diastereomer)), 7.48-7.50 (m, 2H (2 diastereomers)), 5.78 (s, 1H (1 diastereomer)), 5.71 (s, 1H (1 diastereomer)), 5.36 (br s, 1H (1 diastereomer)), 5.33 (br s, 1H (1 diastereomer)), 5.03 (s, 1H (1 diastereomer)), 4.89 (s, 1H (1 diastereomer)), 4.61 (d, *J* = 9.2 Hz, 1H (1 diastereomer)), 4.25-4.29 (m, 2H (2 diastereomers)), 4.21 (d, *J* = 8.6 Hz, 1H (major)), 4.08-4.16 (m, 2H (2 diastereomers)), 3.65-3.68 (m, 1H (2 diastereomers)), 3.53-3.60 (m, 3H (2 diastereomers)), 3.37 (td, *J* = 9.1, 2.7 Hz, 1H (1 diastereomer)), 3.33 (td, *J* = 9.1, 2.7 Hz, 1H (1 diastereomer)), 3.19 (ddd, *J* = 8.0, 4.7, 2.8 Hz, 1H (1 diastereomer)), 3.12 (ddd, *J* = 8.5, 5.0, 1.5 Hz, 1H (1 diastereomer)), 2.99-3.03 (m, 1H (1 diastereomer)), 2.39-2.43 (m, 1H (2 diastereomers)), 2.36 (dd, *J* = 14.2, 4.2 Hz, 1H (1 diastereomer)), 2.23 (qd, *J* = 6.8, 3.2 Hz, 1H (1 diastereomer)), 2.11 (dt, *J* = 12.2, 6.4 Hz, 1H (1 diastereomer)), 2.07 (dt, *J* = 12.2, 6.1 Hz, 1H (1 diastereomer)), 1.94-1.99 (m ,1H (2 diastereomers)), 1.77-1.93 (m, 7H (2 diastereomers)), 1.86 (d, *J* = 0.9 Hz, 3H (1 diastereomer)), 1.75 (d, *J* = 1.0 Hz, 3H (1 diastereomer)), 1.66-1.73 (m, 2H (2 diastereomers)), 1.35-1.40 (m, 1H (2 diastereomers)), 1.23-1.28 (m, 1H (2 diastereomers)), 1.216 (s, 9H (1 diastereomer)), 1.213 (s, 9H (1 diastereomer)), 1.09 (d, *J* = 6.9 Hz, 3H (2 diastereomers)), 1.04 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.00 (d, *J* = 6.5 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 0.88-0.95 (m, 54H (2 diastereomers)), 0.05-0.19 (m, 36H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 178.4, 148.6, 148.2, 145.7, 145.5, 140.3, 139.8, 139.7, 138.6, 133.1, 129.3, 129.0, 128.8, 128.4, 125.8, 124.7, 114.8, 114.4, 110.1, 109.7, 80.5, 80.4, 79.6, 79.4, 79.3, 79.2, 79.1, 78.9, 78.8, 75.9, 72.3, 71.5, 65.7, 65.1, 64.7, 62.1, 48.5, 47.9, 42.9, 42.7, 40.3, 38.6, 38.2, 38.0, 34.6, 34.5, 33.17, 33.12, 31.9, 31.8, 30.7, 29.7, 29.3, 28.4, 27.4, 27.3, 27.2, 26.1, 26.03, 26.00, 25.9, 25.7, 20.1, 18.45, 18.41, 18.3, 18.2, 18.16, 18.11, 17.5, 17.4, 16.0, 15.9, 11.2, -3.51, -3.59, -3.7, -3.8, -3.9, -4.0, -4.24, -4.26, -4.30, -4.38, -4.60, -4.64, -4.67, -4.7, -5.3 ppm; HRMS (ES+) calcd. for $C_{77}H_{148}O_{12}Si_6SNa$ (M+Na) 1487.9205, found 1487.9250.



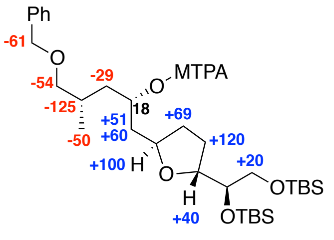
Coupled Sulfone SI-23: To a stirred solution of sulfone **61** (58.2 mg, 81.6 µmol) in THF (0.33 mL) at -78 °C was added LHMDS (180 µL, 0.180 mmol, 1M in THF). After 30 min, the reaction was warmed to 0 °C and HMPA (125 mg, 122 µL, 0.698 mmol) was added to it. A solution of iodide **9** (25.8 mg, 29.3 µmol) in THF (0.33 mL) was cannulated to it and the reaction was slowly warmed to rt over 2 h. After 7.5 h, the reaction was quenched with sat. aq. NH_4Cl (5.0 mL) and the aqueous layer was extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give coupled sulfone **SI-23** (19.3 mg, 13.1 µmol, 45%) as colorless oil. $[\alpha]_D^{23} = +0.5$ (c = 1.00, $CHCl_3$); IR: (neat) 2956, 2930, 2886, 2857, 1731, 1671, 1472, 1463, 1388, 1305, 1254, 1147, 1076, 836, 777 cm^{-1}, ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.87-7.89 (m, 2H (2 diastereomers)), 7.62-7.64 (m, 1H (2 diastereomers)), 7.54-7.58 (m, 2H (2 diastereomers)), 5.76 (s, 1H (1 diastereomer)), 5.74 (s, 1H (1 diastereomer)), 5.33 (br s, 1H (2 diastereomers)), 4.99 (s, 1H (1 diastereomer)), 4.88 (s, 1H (1 diastereomer)), 4.71 (td, J = 8.6, 5.8 Hz, 1H (1 diastereomer)), 4.62 (td, J = 8.6, 5.6 Hz, 1H (1 diastereomer)), 4.52 (d, J = 8.5 Hz, 1H (1 diastereomer)), 4.49 (d, J = 8.6 Hz, 1H (1 diastereomer)), 4.26-4.30 (m, 1H (2 diastereomers)), 4.12-4.16 (m, 2H (2 diastereomers)), 4.05-4.11 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 4.00 (dt, J = 9.7, 3.2 Hz, 1H (1 diastereomer)), 3.96 (ddd, J = 9.8, 7.5, 6.0 Hz, 1H (1 diastereomer)), 3.92 (ddd, J = 9.7, 7.8, 6.2 Hz, 1H (1 diastereomer)), 3.74 (dd, J = 9.2, 4.6 Hz, 1H (1 diastereomer)), 3.72 (dd, J = 9.5, 4.6 Hz, 1H (1 diastereomer)), 3.58-3.63 (m, 2H (2 diastereomers)), 3.55-3.57 (m, 1H (2 diastereomers)), 3.37 (td, J = 9.1, 2.7 Hz, 1H (1 diastereomer)), 3.32 (td, J = 9.1, 2.6 Hz, 1H (1 diastereomer)), 3.19 (dt, J = 8.0, 2.3 Hz, 1H (1 diastereomer)), 3.11-3.13 (m, 1H (1 diastereomer)), 2.59 (dd, J = 14.5, 3.2 Hz, 1H (1 diastereomer)), 2.40 (qd, J = 6.9, 3.1 Hz, 1H (1 diastereomer)), 2.28-2.35 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.99-2.12 (m, 4H (1H of 1 diastereomer and 3H of 2 diastereomers)), 1.82-1.95 (m, 4H (2 diastereomers)), 1.81 (d, *J* = 1.1 Hz, 3H (1 diastereomer)), 1.77 (d, *J* = 1.0 Hz, 3H (1 diastereomer)), 1.63-1.75 (m, 3H (2 diastereomers)), 1.45-1.54 (m, 1H (2 diastereomers)), 1.23-1.30 (m, 1H (2 diastereomers)), 1.216 (s, 9H (1 diastereomer)), 1.214 (s, 9H (1 diastereomer)), 1.05 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.03 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 0.96-1.00 (m, 6H (2 diastereomers)), 0.89-0.95 (m, 54H (2 diastereomers)), -0.05-0.18 (m, 36H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 150.3, 149.1, 145.4, 145.2, 140.6, 139.6, 139.5, 139.1, 133.4, 129.2, 128.5, 128.4, 126.4, 125.4, 115.1, 114.6, 113.6, 112.1, 80.4, 80.3, 79.67, 79.63, 79.3, 79.2, 79.1, 78.8, 75.7, 75.6, 74.1, 72.3, 65.2, 64.7, 64.4, 62.15, 62.10, 48.1, 47.0, 42.8, 40.3, 38.6, 38.2, 38.1, 38.0, 36.0, 34.6, 34.5, 33.6, 33.1, 33.0, 31.6, 30.9, 29.7, 29.5, 29.0, 28.6, 27.79, 27.73, 27.4, 27.2, 26.1, 26.05, 26.04, 26.01, 25.9, 25.8, 25.7, 25.2, 20.7, 18.4, 18.3, 18.2, 18.1, 18.09, 18.04, 17.9, 17.3, 17.0, 16.0, 15.9, 14.1, 13.6, 12.0, 11.4, -3.8, -3.91, -3.96, -4.1, -4.2, -4.30, -4.34, -4.4, -4.51, -4.58, -4.63, 4.66, -4.71, -4.73, -5.3 ppm; HRMS (ES+) calcd. for $C_{77}H_{149}O_{12}SSi_6$ (M+H) 1465.9385, found 1465.9435.



58 **56**

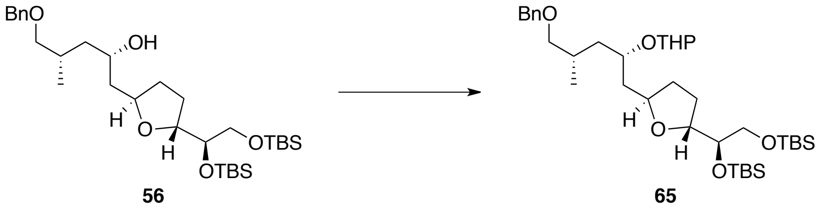
Alcohol 56: To a stirred solution of ketone **58** (708 mg, 1.25 mmol) in THF (100.0 mL) was added L-Selectride (3.8 mL, 3.80 mmol, 1 M in THF) and warmed to -30 °C over 1 h. After 5 h, the reaction was quenched with sat. aq. NH_4Cl (30 mL) and the aqueous layer was extracted with Et_2O (3 X 60 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give alcohol **56** {638 mg, 1.12 mmol, 90% (15:1 dr)} as colorless oil.

Mosher Ester Analysis[12] for determination of C_{18} Stereochemistry in Alcohol 56.

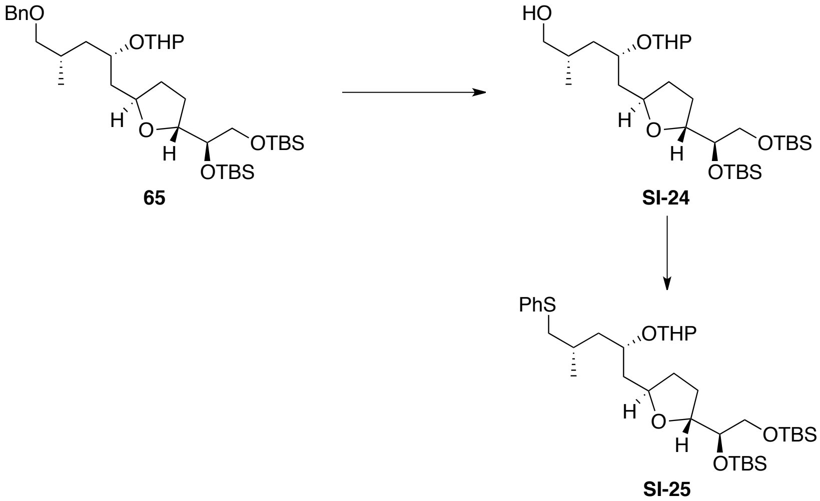


Mosher ester analysis
for major isomer **56**

^{1}H NMR shift differencecs [(S)-MTPA-(R)-MTPA] reported in Hertz (CDCl3, 700 MHz).

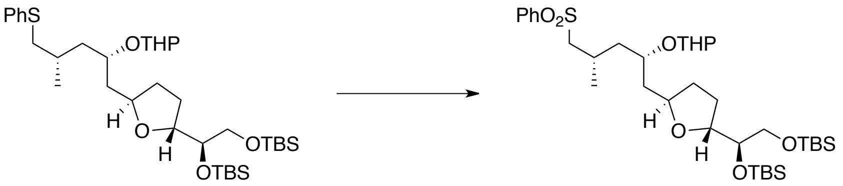


THP Ether 65: To a stirred solution of alcohol **56** (473 mg, 0.834 mmol) in CH_2Cl_2 (6.2 mL) were added dihydropyran (1.75 g, 1.9 mL, 20.8 mmol) followed by PPTS (6.1 mg, 24.2 µmol). After 15 h, the reaction was quenched with Et_3N (864 mg, 1.2 mL, 8.52 mmol) and was concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 4-10% EtOAc / hexanes, to give THP ether **65** (538 g, 0.826 mmol, 99%) as colorless oil. $[\alpha]_D^{23}$ = -17.8 (*c* = 1.00, $CHCl_3$); IR: (neat) 2952, 2929, 2856, 1471, 1462, 1360, 1253, 1094, 1077, 1024, 835, 776 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.34-7.37 (m, 4H (2 diastereomers)), 7.27-7.30 (m, 1H (2 diastereomers)), 4.61-4.65 (m, 1H (2 diastereomers)), 4.53 (s, 2H (1 diastereomer)), 4.52 (s, 2H (1 diastereomer)), 4.03-4.10 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.90-3.99 (m, 2H (2 diastereomers)), 3.85-3.89 (m, 1H (1 diastereomer)), 3.67-3.70 (m, 1H (2 diastereomers)), 3.55-3.59 (m, 2H (2 diastereomers)), 3.46-3.50 (m, 1H (2 diastereomers)), 3.39 (dd, *J* = 9.1, 5.7 Hz, 1H (1 diastereomer)), 3.37 (dd, *J* = 9.0, 5.4 Hz, 1H (1 diastereomer)), 3.27 (dd, *J* = 9.1, 7.0 Hz, 1H (1 diastereomer)), 3.24 (dd, *J* = 9.0, 7.2 Hz, 1H (1 diastereomer)), 2.10-2.17 (m, 1H (1 diastereomer)), 1.96-2.05 (m, 2H (2 diastereomers)), 1.89-1.94 (m, 1H (2 diastereomers)), 1.78-1.85 (m, 3H (2H of 2 diastereomers and 1H of 1 diastereomer)), 1.65-1.72 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.50-1.63 (m, 6H (1H of 1 diastereomer and 5H of 2 diastereomers)), 1.41-1.48 (m, 1H (2 diastereomers)), 1.32-1.37 (m, 1H (2 diastereomers)), 1.01 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.00 (d, *J* = 6.7 Hz, 3H (1 diastereomer)), 0.921 (s, 9H (1 diastereomer)), 0.920 (s, 9H (1 diastereomer)), 0.909 (s, 9H (1 diastereomer)), 0.908 (s, 9H (1 diastereomer)), 0.908 (s, 3H (2 diastereomers)), 0.905 (s, 3H (2 diastereomers)), 0.08 (s, 3H (2 diastereomers)), 0.07 (s, 3H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 138.9, 138.8, 128.3, 128.2, 127.56, 127.55, 127.4, 127.3, 99.3, 97.0, 78.66, 78.61, 76.5, 76.4, 76.36, 76.30, 76.1, 74.2, 72.9, 72.8, 72.2, 65.2, 65.1, 63.1, 63.0, 42.0, 40.7, 39.1, 38.3, 33.2, 32.8, 31.39, 31.35, 30.0, 29.9, 27.4, 27.3, 26.0, 25.9, 25.56, 25.52, 20.3, 20.2, 18.4, 18.2, 18.1, 17.5, 17.0, -4.2, -4.70, -4.72, -5.33, -5.36 ppm; HRMS (ES+) calcd. for $C_{36}H_{66}O_6Si_2Na$ (M+Na) 673.4296, found 673.4268.



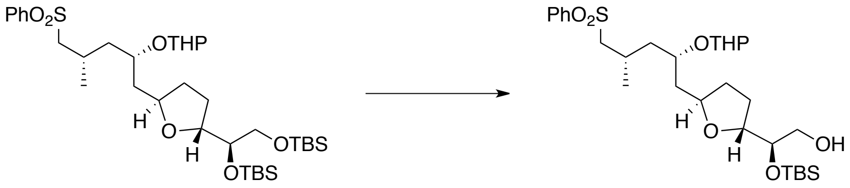
Sulfide SI-25: To a stirred solution of benzyl ether **65** (538 mg, 0.826 mmol) in *i*-PrOH (34.0 mL) was added Pd/C (354 mg, 10 mol% by weight). The flask was fitted with a H_2 balloon and purged with H_2. After 20 h, the reaction was passed through a plug of celite and the celite plug was washed with EtOAc (50 mL). The solvent was removed *in vacuo* to give crude alcohol **SI-24**.

To a stirred solution of crude alcohol **SI-24** in THF (5.5 mL) at 0 °C were added Ph_2S_2 (361 mg, 1.65 mmol) followed by *n*-Bu_3P (351 mg, 0.44 mL, 1.73 mmol) and the reaction was warmed to rt. After 15 h, the solvent was removed *in vacuo* and the residue was purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give sulfide **SI-25** (480 mg, 0.735 mmol, 89%) as colorless oil. $[\alpha]_D^{23}$ = -28.5 (c = 1.01, $CHCl_3$); IR: (neat) 2953, 2933, 2855, 1478, 1439, 1376, 1256, 1112, 1073, 1022, 835, 777 cm^{-1}; ^1H NMR {400 MHz, $CDCl_3$ (two diastereomers)} δ 7.33-7.37 (m, 2H (2 diastereomers)), 7.25-7.29 (m, 2H (2 diastereomers)), 7.13-7.18 (m, 1H (2 diastereomers)), 4.55-4.64 (m, 1H (2 diastereomers)), 4.03-4.10 (m, 1H (2 diastereomers)), 3.75-4.01 (m, 3H (2 diastereomers)), 3.66-3.71 (m, 1H (2 diastereomers)), 3.53-3.59 (m, 2H (2 diastereomers)), 3.40-3.48 (m, 1H (2 diastereomers)), 2.92-3.02 (m, 1H (2 diastereomers)), 2.73-2.81 (m, 1H (2 diastereomers)), 2.06-2.14 (m, 1H (1 diastereomer)), 1.96-2.05 (m, 1H (2 diastereomers)), 1.87-1.95 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.68-1.85 (m, 4H (2 diastereomers)), 1.55-1.67 (m, 2H (2 diastereomers)), 1.39-1.54 (m, 6H (2 diastereomers)), 1.08 (d, J = 7.0 Hz, 3H (1 diastereomer)), 1.07 (d, J = 7.1 Hz, 3H (1 diastereomer)), 0.91 (s, 18H (2 diastereomers)), 0.09 (s, 6H (2 diastereomers)), 0.075 (s, 3H (2 diastereomers)), 0.071 (s, 3H (2 diastereomers)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 137.2, 129.1, 129.0, 128.77, 128.71, 125.6, 125.6, 125.4, 99.6, 96.7, 78.6, 78.5, 77.2, 76.3, 76.2, 76.1, 76.0, 74.6, 72.1, 65.2, 65.1, 63.1, 62.8, 42.0, 41.9, 41.7, 41.0, 40.6, 33.2, 32.9, 31.3, 31.2, 29.53, 29.50, 27.37, 27.32, 26.0, 25.9, 25.5, 25.4, 20.2, 20.0, 19.5, 19.1, 18.4, 18.2, 18.1, -4.1, -4.70, -4.74, -5.34, -5.36 ppm; HRMS (ES+) calcd. for $C_{35}H_{64}O_5SSi_2Na$ (M+Na) 675.3911, found 675.3931.



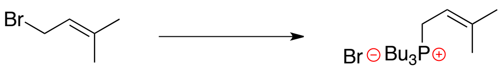
SI-25 **66**

Sulfone 66: To a stirred solution of sulfide **SI-25** (480 mg, 0.735 mmol) in freshly distilled CH_3CN (12.0 mL) at rt were sequentially added 4Å mol. sieves (450 mg), NMO (258 mg, 2.20 mmol) followed by TPAP (129 mg, 0.367 mmol). After 15 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give sulfone **66** (468 mg, 0.683 mmol, 93%) as colorless oil. $[\alpha]_D^{23}$ = -16.6 (*c* = 1.01, $CHCl_3$); IR: (neat) 2952, 2929, 2856, 1471, 1307, 1253, 1148, 1086, 1024, 835, 776 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-7.96 (m, 2H (2 diastereomers)), 7.64-7.68 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 4.56 (dd, *J* = 5.6, 2.7 Hz, 1H (1 diastereomer)), 4.53 (dd, *J* = 5.4, 2.8 Hz, 1H (1 diastereomer)), 4.05-4.09 (m, 1H (2 diastereomers)), 3.95 (ddd, *J* = 13.6, 9.0, 4.8 Hz, 1H (1 diastereomer)), 3.90 (ddd, *J* = 13.6, 9.1, 4.7 Hz, 1H (1 diastereomer)), 3.85-3.89 (m, 1H (2 diastereomers)), 3.75-3.80 (m, 1H (2 diastereomers)), 3.64-3.67 (m, 1H (2 diastereomers)), 3.52-3.56 (m, 2H (2 diastereomers)), 3.41-3.48 (m, 1H (2 diastereomers)), 3.30 (dd, *J* = 14.2, 4.5 Hz, 1H (1 diastereomer)), 3.18 (dd, *J* = 14.2, 4.2 Hz, 1H (1 diastereomer)), 2.97 (t, *J* = 8.4 Hz, 1H (1 diastereomer)), 2.95 (t, *J* = 8.4 Hz, 1H (1 diastereomer)), 2.32-2.37 (m, 1H (1 diastereomer)), 2.20-2.25 (m, 1H (1 diastereomer)), 1.94-2.00 (m, 2H (1H of 2 diastereomers and 1H of 1 diastereomer)), 1.88-1.93 (m, 1H (2 diastereomers)), 1.71-1.83 (m, 3H (2H of 2 diastereomers and 1H of 1 diastereomer)), 1.60-1.68 (m, 2H (1H of 1 diastereomers and 1H of 2 diastereomers)), 1.40-1.58 (m, 8H (1H of 1 diastereomer and 7H of 2 diastereomers)), 1.15 (d, *J* = 6.4 Hz, 3H (1 diastereomer)), 1.14 (d, *J* = 6.5 Hz, 3H (1 diastereomer)), 0.910 (s, 9H (1 diastereomer)), 0.908 (s, 9H (1 diastereomer)), 0.898 (s, 9H (1 diastereomer)), 0.896 (s, 9H (1 diastereomer)), 0.085 (s, 3H (2 diastereomers)), 0.081 (s, 3H (2 diastereomers)), 0.07 (s, 3H (2 diastereomers)), 0.06 (s, 3H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.09, 140.01, 133.5, 133.3, 129.2, 129.1, 128.0, 127.9, 100.0, 96.9, 78.49, 78.46, 76.1, 76.06, 76.02, 76.00, 74.8, 71.6, 65.1, 65.0, 63.2, 63.1, 63.0, 41.9, 41.8, 41.3, 40.3, 33.2, 32.9, 31.3, 31.2, 27.3, 27.2, 26.08, 26.04, 25.9, 25.48, 25.40, 20.3, 20.2, 20.0, 19.6, 18.47, 18.45, 18.1, -4.1, -4.70, -4.73, -5.3 ppm; HRMS (ES+) calcd. for $C_{35}H_{64}O_7SSi_2Na$ (M+Na) 707.3809, found 707.3815.



66 **SI-26**

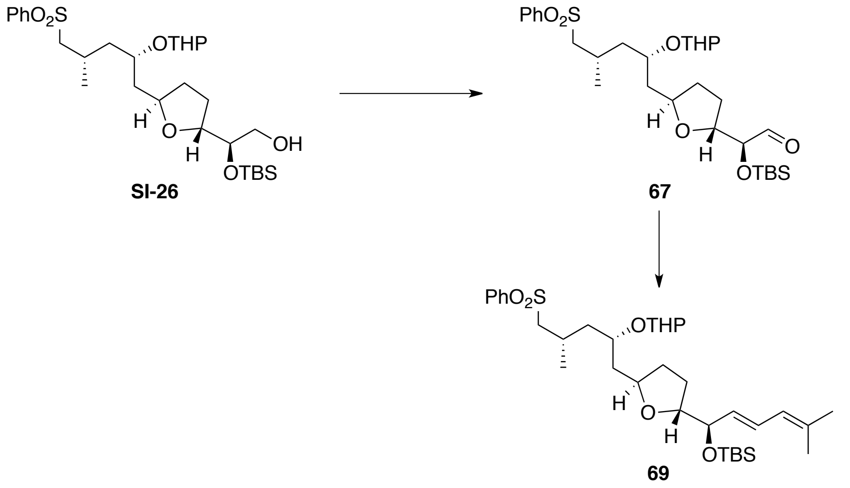
Alcohol SI-26: To a stirred solution of TBS ether **66** (311 mg, 0.454 mmol) in THF (4.4 mL) at 0 °C was added a stock solution of HF•Pyr.[4] (2.5 mL) over 3 h. After 24 h, the reaction quenched with sat. aq. $NaHCO_3$ (25 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-60% EtOAc / hexanes, to give alcohol **SI-26** (215 mg, 0.376 mmol, 83%) as colorless oil. $[\alpha]_D^{23}$ = -26.3 (c = 1.00, C_6H_6); IR: (neat) 3467, 2931, 2855, 1463, 1447, 1377, 1306, 1253, 1146, 1085, 1024, 836, 777 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-7.96 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 4.56 (dd, J = 5.3, 2.8 Hz, 1H (1 diastereomer)), 4.54 (dd, J = 5.4, 2.8 Hz, 1H (1 diastereomer)), 4.06-4.10 (m, 1H (2 diastereomers)), 4.01-4.05 (m, 1H (1 diastereomer)), 3.93-3.97 (m, 1H (1 diastereomers)), 3.84-3.89 (m, 1H (2 diastereomers)), 3.74-3.79 (m, 1H (2 diastereomers)), 3.65-3.70 (m, 2H (2 diastereomer)), 3.56-3.60 (m, 1H (2 diastereomers)), 3.42-3.49 (m, 1H (2 diastereomers)), 3.29 (dd, J = 14.2, 4.8 Hz, 1H (1 diastereomer)), 3.17 (dd, J = 14.2, 4.5 Hz, 1H (1 diastereomer)), 2.99 (dd, J = 9.9, 8.0 Hz, 1H (1 diastereomer)), 2.97 (dd, J = 9.9, 8.1 Hz, 1H (1 diastereomer)), 2.53 (t, J = 5.7 Hz, 1H (1 diastereomer)), 2.45 (t, J = 5.8 Hz, 1H (1 diastereomer)), 2.34-2.39 (m, 1H (1 diastereomer)), 2.22-2.29 (m, 1H (1 diastereomer)), 2.00-2.06 (m, 1H (2 diastereomers)), 1.90-1.99 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.72-1.80 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.61-1.71 (m, 2H (2 diastereomers)), 1.43-1.59 (m, 7H (2 diastereomers)), 1.14 (d, J = 6.6 Hz, 3H (1 diastereomer)), 1.12 (d, J = 6.7 Hz, 3H (1 diastereomer)), 0.92 (s, 9H (2 diastereomers)), 0.110-0.118 (m, 6H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.2, 140.1, 133.4, 133.3, 129.2, 129.1, 128.0, 127.9, 100.0, 96.8, 80.39, 80.32, 76.5, 76.2, 74.4, 74.3, 71.3, 64.6, 63.29, 63.23, 63.0, 62.9, 41.97, 41.90, 41.5, 40.2, 32.9, 32.5, 31.2, 27.5, 27.4, 26.0, 25.8, 25.4, 25.3, 20.26, 20.23, 20.1, 19.7, -4.5, -4.6 ppm; HRMS (ES+) calcd. for $C_{29}H_{50}O_7SSiNa$ (M+Na) 593.2944, found 593.2949.



SI-27 **68**

Phosphonium Bromide 68:To a stirred solution of allyl bromide **SI-27**[14] (1.68 g, 11.2 mmol) in Et_2O (45.0 mL) at 0 °C was added PBu_3 (5.74 g, 7.0 mL, 28.1 mmol). After 15 min, the reaction was warmed to rt. After 15 h, the reaction filtered through a sintered glass funnel and the residue was washed with hexanes

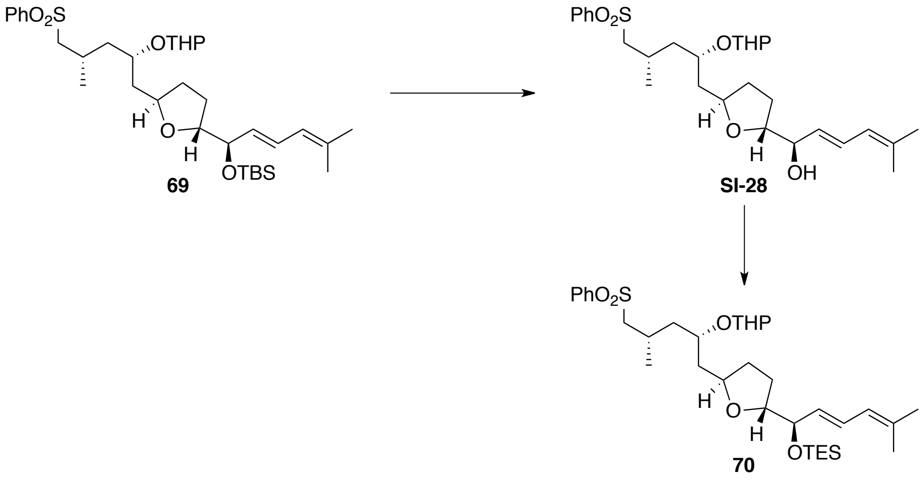
(75 mL) to give the phosphonium bromide **68**[15] (3.68 g, 10.4 mmol, 93%) as white needle-shaped solid. ^{1}H NMR (700 MHz, CDCl$_3$) δ 5.00-5.04 (m, 1H), 3.39 (dd, *J* = 15.2, 7.9 Hz, 2H), 2.40-2.44 (m, 6H), 1.77-1.78 (m, 6H), 1.47-1.57 (m, 12H), 0.95 (t, *J* = 7.1 Hz, 9H) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 141.88, 141.81, 109.09, 109.04, 25.9, 24.0, 23.9, 23.84, 23.82, 20.7, 20.4, 19.1, 19.0, 18.8, 13.4 ppm.



Diene 69: To a stirred solution of oxalyl chloride (55.1 mg, 39.0 µL, 0.441 mmol) in CH$_2$Cl$_2$ (2.2 mL) at -78 °C was cannulated a solution of DMSO (73.2 mg, 66.0 µL, 0.919 mmol) in CH$_2$Cl$_2$ (0.60 mL). After 15 min, a solution of alcohol **SI-26** (210 mg, 0.367 mmol) in CH$_2$Cl$_2$ (1.6 mL and 2 X 0.25 mL wash) was cannulated to it. After 45 min, Et$_3$N (188 mg, 0.26 mL, 1.84 mmol) was added. After 20 min, the cooling bath was removed and the reaction was quenched with H$_2$O (25 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 X 50 mL). The dried (MgSO$_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-40% EtOAc / hexanes, to give aldehyde **67** (201 mg, 0.353 mmol, 96%) as colorless oil.

To a stirred solution of tributyl phosphonium salt **68** (175 mg, 0.498 mmol) in THF (3.9 mL) at -45 °C was added *n*-BuLi (0.20 mL, 0.500 mmol, 2.5 M in hexane) and was warmed to rt over 45 min. After 2 h, the reaction was cooled back down to -78 °C and a solution of aldehyde **67** (189 mg, 0.332 mmol) in THF (3.9 mL) was cannulated to it. The reaction was slowly warmed to rt over 2.5 h. After another 3 h, the reaction was quenched with H$_2$O (8 drops) and the solvent was removed *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give diene **69** {197 mg, 0.317 mmol, 96% (11:1 *E:Z* inseparable mixture)} as colorless oil. $[\alpha]_D^{23}$ = +20.4 (*c* = 1.00, CHCl$_3$); IR: (neat) 2949, 2925, 2859, 1458, 1450, 1302, 1260, 1147, 1069, 1022, 835, 781 cm^{-1}; ^{1}H NMR {400 MHz, CDCl$_3$ (two diastereomers)} δ 7.92-7.96 (m, 2H (2 diastereomers)), 7.62-7.67 (m, 1H (2 diastereomers)), 7.54-7.59 (m, 2H (2 diastereomers)), 6.45 (dd, *J* = 15.1, 11.0 Hz, 1H (2 diastereomers of E isomer)), 6.20 (t, *J* = 11.4 Hz, 1H (2 diastereomers of Z isomer), 6.06 (dt, *J* =

11.5, 1.2 Hz, 1H (2 diastereomers of Z isomer)), 5.83 (d, *J* = 11.0 Hz, 1H (2 diastereomers of E isomer)), 5.53 (dd, *J* = 15.1, 5.7 Hz, 1H (1 diastereomer of E isomer)), 5.52 (dd, *J* = 15.1, 5.8 Hz, 1H (1 diastereomer of E isomer)), 5.30 (t, *J* = 10.1 Hz, 1H (2 diastereomers of Z isomer)), 4.53-4.56 (m, 1H (2 diastereomers)), 4.16 (t, *J* = 5.6 Hz, 1H (2 diastereomers)), 3.90-3.97 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.82-3.89 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.72-3.80 (m, 1H (2 diastereomer)), 3.40-3.48 (m, 1H (2 diastereomers)), 3.31 (dd, *J* = 14.2, 4.5 Hz, 1H (1 diastereomer)), 3.18 (dd, *J* = 14.1, 4.2 Hz, 1H (1 diastereomer)), 2.97 (dd, *J* = 14.2, 8.3 Hz, 1H (1 diastereomer)), 2.95 (dd, *J* = 14.2, 8.4 Hz, 1H (1 diastereomer)), 2.30-2.38 (m, 1H (1 diastereomer)), 2.19-2.27 (m, 1H (1 diastereomer)), 1.82-1.99 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.84-1.89 (m, 1H (2 diastereomers)), 1.78 (s, 3H (2 diastereomers)), 1.76 (s, 3H (2 diastereomers)), 1.71-1.76 (m, 1H (1 diastereomer)), 1.59-1.70 (m, 3H (2 diastereomers)), 1.38-1.58 (m, 7H (2 diastereomers)), 1.14 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.13 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.91 (s, 9H (2 diastereomers)), 0.07 (s, 3H (2 diastereomers)), 0.04 (s, 3H (2 diastereomers)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 140.1, 134.9, 134.8, 133.4, 133.3, 130.0, 129.9, 129.2, 129.1, 128.0, 127.9, 127.4, 127.3, 124.73, 124.71, 99.7, 97.0, 82.0, 81.9, 76.1, 76.0, 75.6, 74.5, 71.7, 63.29, 63.23, 63.1, 62.9, 42.0, 41.8, 41.4, 40.4, 32.9, 32.6, 31.3, 31.2, 27.1, 27.0, 26.1, 25.9, 25.8, 25.46, 25.40, 20.3, 20.2, 20.0, 19.7, 18.28, 18.26, -4.4, -4.6, -4.7 ppm; HRMS (ES+) calcd. for $C_{34}H_{56}O_6SSiNa$ (M+Na) 643.3465, found 643.3471.



Dienyl Sulfone 70: To a stirred solution of TBS ether **69** (187 mg, 0.301 mmol) in THF (3.0 mL) at 0 °C was added TBAF (0.90 mL, 0.900 mmol, 1 M in THF). The reaction was slowly warmed to rt over 3 h. After another 12 h, the reaction quenched with H_2O (15 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude alcohol **SI-28**.

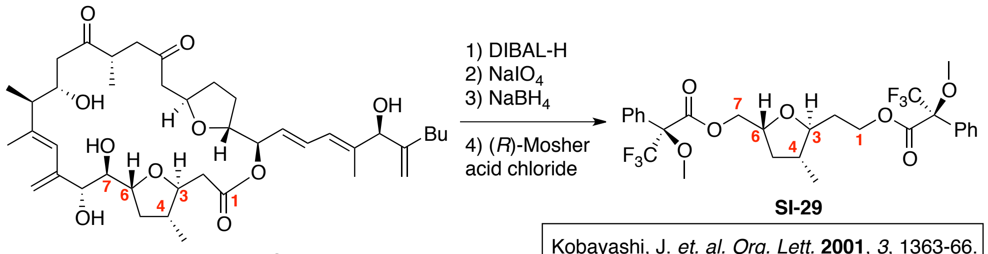
To a stirred solution of crude alcohol **SI-28** in CH_2Cl_2 (4.0 mL) at 0 °C were sequentially added Et_3N (244 mg, 0.34 mL, 2.40 mmol), DMAP (18.3 mg, 0.151 mmol) and TESCl (162 mg, 0.18 mL, 1.05 mmol). After 8 h, the reaction was quenched with half-saturated aq. NH_4Cl (15 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give dienyl sulfone **70** (177 mg, 0.285 mmol, 95%) as colorless oil. $[\alpha]_D^{23}$ = +10.4 (*c* = 1.00, $CHCl_3$); IR: (neat) 2951, 2915, 2875, 1446, 1378, 1306, 1148, 1075, 1023, 843, 740 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-7.96 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 6.43-6.47 (m, 1H (2 diastereomers of E isomer)), 6.22 (t, *J* = 11.4 Hz, 1H (2 diastereomers of Z isomer), 6.07-6.10 (m, 1H (2 diastereomers of Z isomer)), 5.83 (d, *J* = 11.0 Hz, 1H (2 diastereomers of E isomer)), 5.51-5.55 (m, 1H (2 diastereomers of E isomer)), 5.30 (t, *J* = 10.3 Hz, 1H (2 diastereomers of Z isomer)), 4.55 (dd, *J* = 5.5, 2.8 Hz, 1H (1 diastereomer)), 4.54 (dd, *J* = 5.5, 2.8 Hz, 1H (1 diastereomer)), 4.16 (t, *J* = 5.8 Hz, 1H (2 diastereomers)), 3.92-3.97 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.82-3.89 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.73-3.80 (m, 1H (2 diastereomer)), 3.42-3.48 (m, 1H (2 diastereomers)), 3.31 (dd, *J* = 14.2, 4.5 Hz, 1H (1 diastereomer)), 3.18 (dd, *J* = 14.2, 4.2 Hz, 1H (1 diastereomer)), 2.97 (dd, *J* = 14.2, 8.3 Hz, 1H (1 diastereomer)), 2.96 (dd, *J* = 14.2, 8.4 Hz, 1H (1 diastereomer)), 2.31-2.38 (m, 1H (1 diastereomer)), 2.20-2.26 (m, 1H (1 diastereomer)), 1.92-1.99 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.84-1.89 (m, 1H (2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.72-1.77 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.58-1.71 (m, 3H (2 diastereomers)), 1.38-1.55 (m, 7H (2 diastereomers)), 1.15 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.14 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.96 (t, *J* = 8.0 Hz, 9H (2 diastereomers)), 0.61 (q, *J* = 7.9 Hz, 6H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.2, 140.1, 135.0, 134.9, 133.4, 133.3, 130.0, 129.9, 129.2, 129.1, 128.0, 127.9, 127.5, 127.4, 124.74, 124.71, 99.7, 97.1, 82.0, 81.9, 76.1, 76.0, 75.6, 75.5, 74.5, 71.7, 63.3, 63.2, 63.1, 62.9, 42.1, 41.8, 41.4, 40.4, 32.9, 32.5, 31.3, 31.2, 27.2, 27.1, 26.1, 25.9, 25.47, 25.41, 20.3, 20.2, 20.0, 19.6, 18.2, 6.8, 5.0 ppm; HRMS (ES+) calcd. for $C_{34}H_{56}O_6SSiNa$ (M+Na) 643.3465, found 643.3464.

Proof of Stereochemistry at C_3, C_4, C_6, C_7, C_{12}, C_{13}, C_{20}, C_{23} and C_{24}:

While the relative and absolute configuration of amphidinolide C (**1**) was established by NMR studies, degradation technique and Mosher ester analysis,[16] the stereochemistry of amphidinolide F (**4**) was not unambiguously assigned.[17] The stereochemical assignment of amphidinolide F was based on analogy to amphidinolide C and the fact that both (**1** and **4**) were isolated from same microorganism. While these studies could tentatively assign the structure of **4**, it stipulated effort for unequivocal stereochemical assignment. This section describes our effort to confirm the stereochemistry in our synthetic intermediates.

Kobayashi and co-workers performed a degradation study on amphidinolide C (**1**).[16b] The naturally occurring amphidinolide C was degraded to the bis-Mosher ester **SI-29**. Our synthetic tetrahydrofuran **41** was converted to same bis-Mosher ester. The ^{1}H NMR spectrum of the naturally derived bis-Mosher ester was in excellent agreement with our synthetic bis-Mosher ester. This study explicitly confirmed the C_3, C_4 and C_6 stereochemistry in our southern tetrahydrofuran **41**. The C_6 and C_7 stereochemistry was generated via Sharpless asymmetric dihydroxylation in single step (see Scheme 4 in manuscript). Therefore, confirmation of C_6 configuration in turn proved the configuration at C_7. Since C_{20}, C_{23} and C_{24} stereochemistry in **53** came from the common intermediate **20**, proof of C_3, C_6 and C_7 configuration justified the stereochemistry at C_{20}, C_{23} and C_{24}. The C_{12}, C_{13} stereochemistry was confirmed by the degradation of intermediate **SI-2** to known alcohol **SI-30**[18] and by comparing the NMR data and specific rotation value.

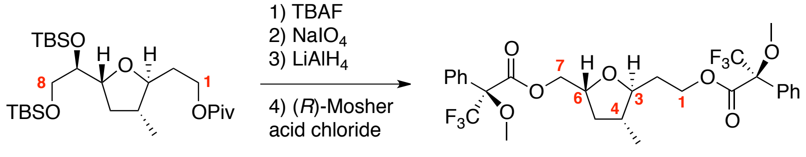
The C_{16} stereochemistry came from commercially available Roche's ester and as shown before, the C_8 configuration was confirmed by advanced Mosher's ester analysis. Thus, these studies clearly established all the stereochemistry present in assigned structure amphidinolide F (**4**). It should be mentioned that our several attempts to make crystalline derivatives from different intermediates were unsuccessful.



amphidinolide C (**1**)

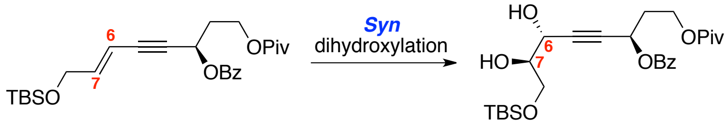
SI-29

Kobayashi, J. *et. al. Org. Lett.* **2001**, *3*, 1363-66.



41

SI-29



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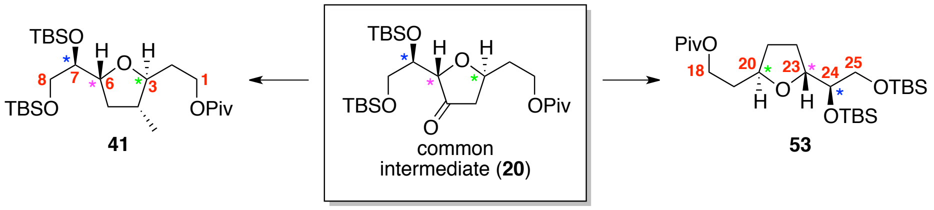
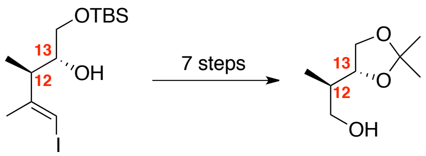

41

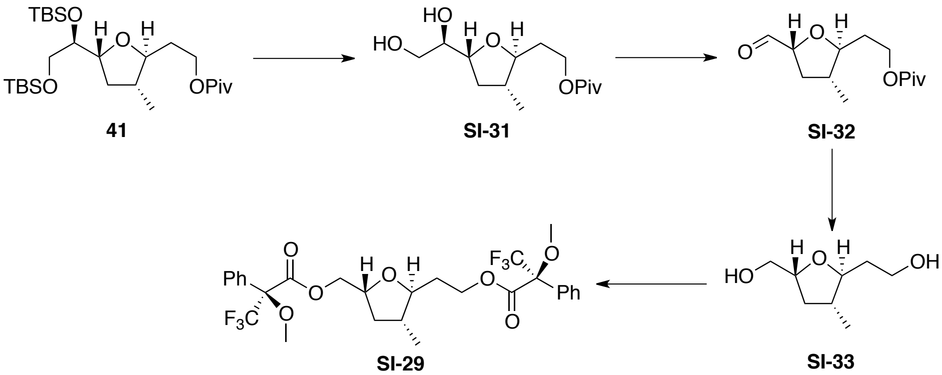
common intermediate (**20**)

53



SI-2

SI-30

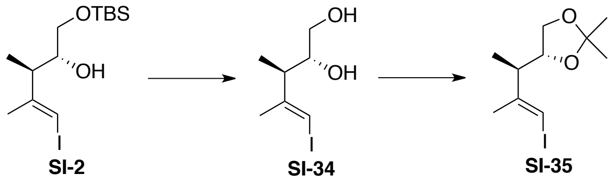


Bis-Mosher Ester SI-29: To a stirred solution of TBS ether **41** (63.4 mg, 0.126 mmol) in THF (1.4 mL) was added TBAF (0.50 mL, 0.500 mmol, 1 M in THF) at rt. After 6 h, the reaction was quenched with H_2O (7.5 mL). The aqueous layer was extracted with EtOAc (3 X 15 mL) and the combined organic layer was washed with H_2O and brine (10 mL each). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude diol **SI-31**.

To a stirred solution of crude diol **SI-31** in THF/H_2O (2.8 mL, 1:1) at 0 °C was added $NaIO_4$ (81.0 mg, 0.378 mmol). After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (5 mL) and sat. aq. $Na_2S_2O_3$ (5 mL). The aqueous layer was extracted with Et_2O (3 X 15 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* to give the crude aldehyde **SI-32**.

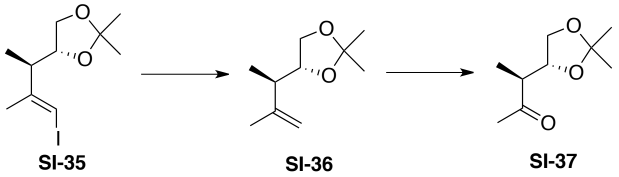
To a stirred solution of crude aldehyde **SI-32** in Et_2O (2.0 mL) at 0 °C was added $LiAlH_4$ (14.4 mg, 0.378 mmol) in one portion. After 30 min, the reaction was quenched with dropwise addition of H_2O (0.10 mL) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 50-100% EtOAc/ hexanes, to give diol **SI-33** (16.1 mg, 0.100 mmol, 79%) as colorless oil.

To a stirred solution of diol **SI-33** (6.6 mg, 41.2 mmol) in CH_2Cl_2 (0.75 mL) at rt was added DMAP (30.2 mg, 0.247 mmol) followed by (*R*)-(-)-Mosher acid chloride (31.2 mg, 23.0 mL, 0.123 mmol). After 1 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc/ hexanes, to give bis-Mosher ester **SI-29**[16b] (22.7 mg, 38.3 mmol, 93%) as colorless oil. ^1H NMR (700 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.68 (d, *J* = 7.7 Hz, 2H), 7.14-7.17 (m, 2H), 7.02-7.10 (m, 4H), 4.34 (ddd, *J* = 10.8, 7.8, 5.2 Hz, 1H), 4.22 (dt, *J* = 10.8, 7.4 Hz, 1H), 4.02 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.92 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.76-3.80 (m, 1H), 3.46 (d, *J* = 0.6 Hz, 3H), 3.40 (d, *J* = 0.7 Hz, 3H), 3.14 (td, *J* = 9.1, 2.6 Hz, 1H), 1.59 (dtd, *J* = 13.9, 7.6, 2.7 Hz, 1H), 1.47 (dt, *J* = 12.2, 6.8 Hz, 1H), 1.37-1.42 (m, 1H), 1.26-1.32 (m, 1H), 0.87 (ddd, *J* = 12.2, 10.9, 9.3 Hz, 1H), 0.52 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 166.28, 166.24, 132.7, 132.6, 129.5, 129.4, 128.3, 128.2, 127.99, 127.94, 126.4, 124.7, 123.1, 121.4, 85.1, 85.06, 85.00, 84.9, 84.8, 84.7, 84.6, 84.5, 81.4, 74.7, 67.3, 63.7, 54.99, 54.96, 39.6, 36.4, 32.5, 15.2 ppm.



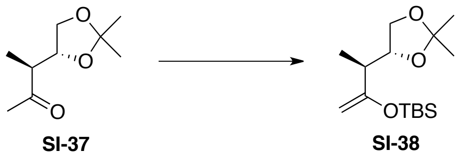
Acetonide SI-35: To a stirred solution of alcohol **SI-2** (996 mg, 2.69 mmol) in THF (30.0 mL) was added TBAF (5.4 mL, 5.40 mmol, 1 M in THF) at rt. After 1 h, the reaction was quenched with H_2O (15 mL). The aqueous layer was extracted with EtOAc (4 X 50 mL) and the combined organic layer was washed with H_2O and brine (20 mL each). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude diol **SI-34**.

To a stirred solution of crude diol **SI-34** in CH_2Cl_2 (24.0 mL) at rt were added dimethoxypropane (1.40 g, 1.65 mL, 13.4 mmol) followed by TsOH•H_2O (52.1 mg, 0.269 mmol). After 12 h, the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give acetonide **SI-35** (685 mg, 2.31 mmol, 86%) as colorless oil. $[\alpha]_D^{23}$ = +7.8 (*c* = 1.00, $CHCl_3$); IR: (neat) 2981, 2932, 2878, 1451, 1380, 1364, 1260, 1211, 1157, 1059, 862 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.04 (s, 1H), 4.00-4.07 (m, 2H), 3.60-3.65 (m, 1H), 2.53-2.60 (m, 1H), 1.87 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 109.2, 77.8, 76.9, 67.7, 46.6, 26.7, 25.5, 21.6, 15.3 ppm; HRMS (EI+) calcd. for $C_{10}H_{17}O_2I$ (M+) 296.02736, found 296.02680.

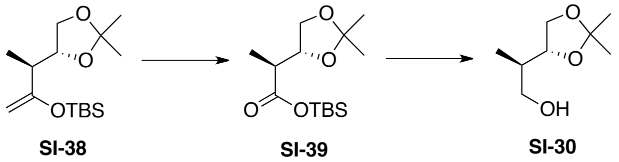


Methyl Ketone SI-37: To a stirred solution of vinyl iodide **SI-35** (764 mg, 2.58 mmol) in THF (16.0 mL) at -78 °C was added *n*-BuLi (1.2 mL, 3.00 mmol, 2.5 M in hexanes) dropwise. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give crude alkene **SI-36**.

To a stirred solution of crude alkene **SI-36** in CH_2Cl_2 (20.0 ml) at -78 °C was bubbled ozone gas until a pale blue color persisted. Argon gas was bubbled through until the solution became colorless and PPh_3 (2.03 g, 7.74 mmol) was added to it and the cooling bath was removed. After 3 h, the solvent was evaporated *in vacuo* and the crude mixture was loaded directly onto silica gel and was purified by flash chromatography, eluting with 20-25% Et_2O / pentane, to give ketone **SI-37** (302 mg, 1.75 mmol, 68%) as colorless oil. $[\alpha]_D^{23}$ = +5.6 (*c* = 1.10, $CHCl_3$); IR: (neat) 2986, 2932, 1712, 1456, 1369, 1249, 1211, 1151, 1053, 852 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21 (dt, *J* = 8.3, 6.5 Hz, 1H), 4.08 (dd, *J* = 8.3, 6.2 Hz, 1H), 3.65 (dd, *J* = 8.3, 6.8 Hz, 1H), 2.76 (dq, *J* = 7.6, 7.0 Hz, 1H), 2.23 (s, 3H), 1.42 (s, 3H), 1.34 (s, 3H), 1.05 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.6, 109.2, 76.9, 67.4, 50.3, 29.7, 26.6, 25.3, 12.3 ppm; HRMS (CI+) calcd. for $C_9H_{17}O_3$ (M+H) 173.1178, found 173.1162.



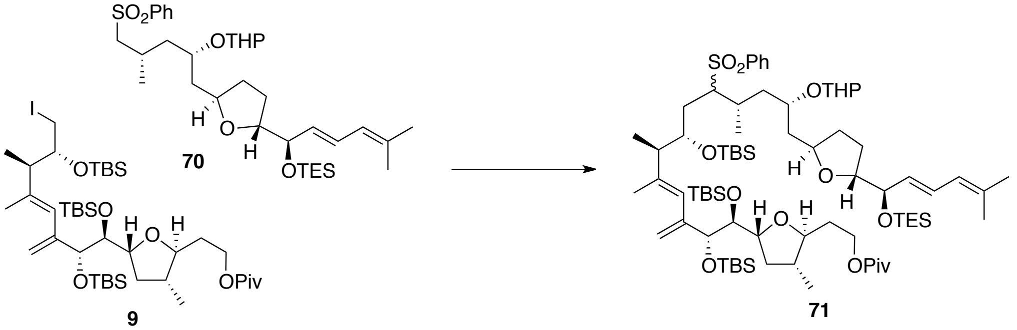
TBS Enol Ether SI-38: To a stirred solution of ketone **SI-37** (200 mg, 1.16 mmol) in CH_2Cl_2 (7.0 mL) at 0 °C were added 2,6-lutidine (498 mg, 0.54 mL, 4.64 mmol) followed by TBSOTf (614 mg, 0.53 mL, 2.32 mmol). After 1.5 h, the reaction was quenched with sat. aq. $NaHCO_3$ (5 mL) and diluted with Et_2O (20 mL) and H_2O (5 mL). The aqueous layer was extracted with Et_2O (2 X 30 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 3-5% EtOAc / hexanes, to give TBS enol-ether **SI-38** (315 mg, 1.10 mmol, 95%) as colorless oil. $[\alpha]_D^{23}$ = -12.8 (*c* = 1.03, $CHCl_3$); IR: (neat) 2986, 2959, 2932, 2850, 1630, 1478, 1363, 1255, 1064, 999, 841, 781cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21 (dd, *J* = 13.6, 7.2 Hz, 1H), 4.11 (d, *J* = 0.8 Hz, 1H), 4.07 (s, 1H), 3.97 (dd, *J* = 8.0, 6.2 Hz, 1H), 3.66 (t, *J* = 8.0 Hz, 1H), 2.41 (dq, *J* = 7.2, 6.9 Hz, 1H), 1.43 (s, 3H), 1.36 (s, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.95 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 108.6, 89.5, 77.1, 66.8, 43.4, 26.6, 25.7, 25.5, 18.1, 13.2, -4.6, -4.7 ppm; HRMS (CI+) calcd. for $C_{15}H_{31}O_3Si$ (M+H) 287.2043, found 287.2044.



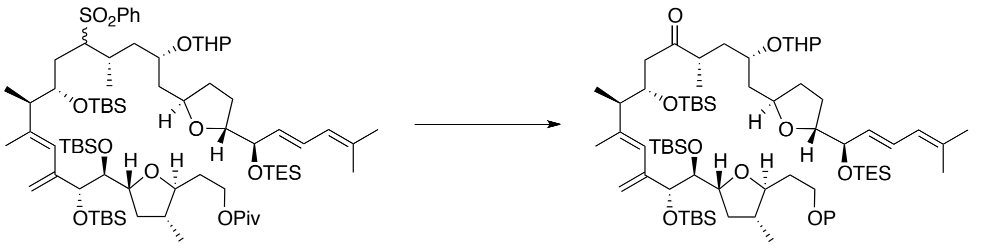
Alcohol SI-30: To a stirred solution of TBS enol-ether **SI-38** (141 mg, 0.492 mmol) in CH_2Cl_2 (10.0 ml) at -78 °C was bubbled ozone gas until a pale blue color persisted. Argon gas was bubbled until the solution became colorless and PPh_3 (386 mg, 1.47 mmol) was added to it and the cooling bath was removed. After 3 h at rt, the solvent was evaporated *in vacuo* to give crude **SI-39**.

The crude **SI-39** was re-dissolved in dry THF (2.0 mL). This solution was added dropwise to a mixture of $LiAlH_4$ (112 mg, 2.95 mmol) in dry THF (2 mL) at 0 °C over 15 min and stirred at that temperature for 3 h. The reaction was quenched with minimal amount of methanol (15 drops) and diluted with EtOAc (20 mL) and water (5 mL) and the aqueous layer was extracted with EtOAc (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 30-35% EtOAc / hexanes, to give known alcohol **SI-30**[18] (42 mg, 0.262 mmol, 53%) as colorless oil. $[\alpha]_D^{23}$ = -

10.9 (c = 1.04, C_6H_6), -18.7 (c = 0.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (dd, J = 8.0, 6.0 Hz, 1H), 3.96 (q, J = 7.6 Hz, 1H), 3.60-3.70 (m, 3H), 2.77 (dd, J = 8.0, 2.8 Hz, 1H), 1.87 (m, 1H), 1.44 (s, 3H), 1.39 (s, 3H), 0.85 (d, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, C_6D_6) δ 108.9, 79.9, 68.4, 66.5, 39.3, 26.5, 25.6, 12.7 ppm.



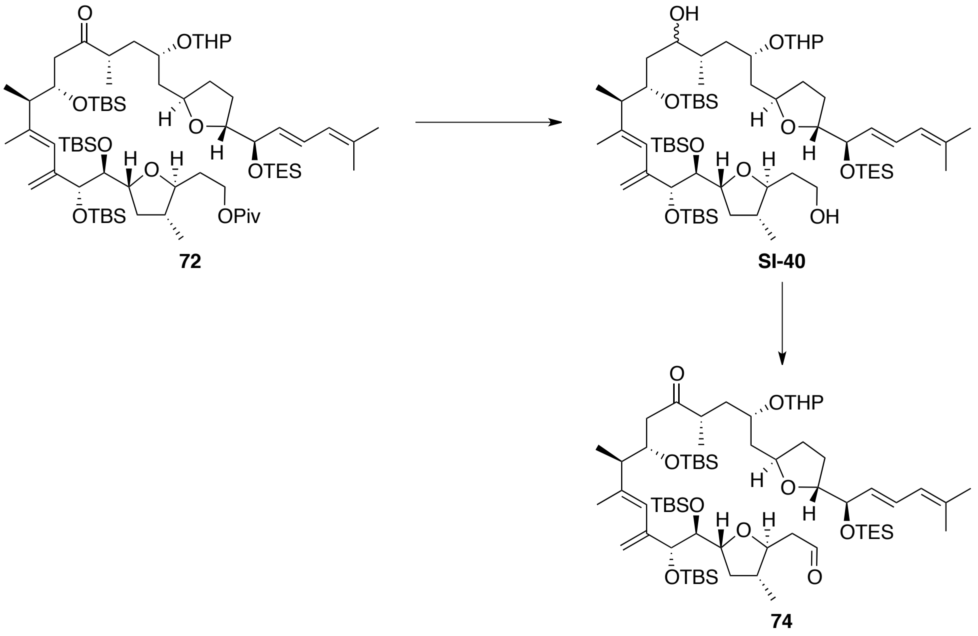
Coupled Sulfone 71: To a stirred solution of sulfone **70** (216 mg, 0.348 mmol) in THF (1.5 mL) at -78 °C was added LHMDS (0.35 mL, 0.350 mmol, 1 M in THF). After 15 min, the reaction was warmed to 0 °C. After 15 min, HMPA (361 mg, 0.35 mL, 2.01 mmol) was added. After another 25 min, a solution of iodide **9** (122 mg, 0.138 mmol) in THF (1.8 mL and 2 X 0.10 mL wash) was cannulated to it. The reaction was slowly warmed to rt over 2 h. After 16 h, the reaction was quenched with sat. aq. NH_4Cl (15 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-30% EtOAc / hexanes, to give diastereomeric coupled sulfone **71** (137.3 mg, 99.9 mmol, 72%) as colorless oil along with recovered sulfone **70** (108 mg, 0.174 mmol). $[\alpha]_D^{23}$ = -7.9 (c = 1.00, C_6H_6); IR: (neat) 2955, 2930, 2856, 1730, 1462, 1379, 1305, 1252, 1145, 1076, 1034, 835, 776 cm^{-1}; ^1H NMR {(700 MHz, $CDCl_3$ (four diastereomers)} δ 7.88-7.94 (m, 2H (4 diastereomers)), 7.60-7.65 (m, 1H (4 diastereomers)), 7.52-7.57 (m, 2H (4 diastereomers)), 6.44-6.49 (m, 1H (4 diastereomers)), 5.84 (d, J = 11.0 Hz, 1H (4 diastereomers)), 5.80 (s, 1H (1 diastereomer)), 5.78 (s, 1H (1 diastereomer)), 5.71 (s, 1H (2 diastereomers)), 5.52-5.55 (m, 1H (4 diastereomers)), 5.33 (s, 1H (2 diastereomers)), 5.31 (s, 1H (2 diastereomers)), 5.05 (s, 1H (1 diastereomer)), 5.00 (s, 1H (1 diastereomer)), 4.87 (s, 1H (1 diastereomer)), 4.86 (s, 1H (1 diastereomer)), 4.52 (dd, J = 5.6, 2.6 Hz, 1H (2 diastereomers)), 4.47 (dd, J = 5.7, 2.6 Hz, 1H (1 diastereomer)), 4.38 (dd, J = 5.6, 2.6 Hz, 1H (1 diastereomer)), 4.35 (dt, J = 9.6, 3.1 Hz, 1H (1 diastereomer)), 4.32 (dt, J = 10.3, 2.9 Hz, 1H (1 diastereomer)), 4.25-4.29 (m, 1H (4 diastereomers)), 4.10-4.16 (m, 4H (1H of 2 diastereomers and 3H of 4 diastereomers)), 3.95-3.99 (m, 1H (2 diastereomers)), 3.87-3.95 (m, 3H (4 diastereomers)), 3.81-3.86 (m, 1H (2 diastereomers)), 3.76-3.80 (m, 1H (1 diastereomer)), 3.65-3.71 (m, 1H (3 diastereomers)), 3.53-3.56 (m, 1H (4 diastereomers)), 3.46-3.49 (m, 1H (1 diastereomer)), 3.36-3.43 (m, 2H (1H of 1 diastereomer and 1H of 4 diastereomers)), 3.32 (td, J = 9.2, 2.6 Hz, 1H (2 diastereomers)), 3.20 (td, J = 9.0, 2.0 Hz, 1H (1 diastereomer)), 3.12-3.16 (m, 1H (3 diastereomers)), 2.37-2.41 (m, 2H (1H of 2 diastereomers and 1H of 4 diastereomers)), 2.16-2.21 (m, 1H (2 diastereomers)), 2.04-2.12 (m, 1H (4 diastereomers)), 1.95-2.03 (m, 2H (4 diastereomers)), 1.74-1.95 (m, 6H (4 diastereomers)), 1.88 (s, 3H (2 diastereomers)), 1.87 (s, 3H (2 diastereomers)), 1.78 (s, 3H (4 diastereomers)), 1.77 (s, 3H (4 diastereomers)), 1.58-1.73 (m, 6H (4 diastereomers)), 1.34-1.56 (m, 8H (4 diastereomers)), 1.16-1.32 (m, 16H (4 diastereomers)), 1.07-1.11 (m, 3H (4 diastereomers)), 0.86-1.00 (m, 36H (4 diastereomers)), 0.61 (q, J = 8.0 Hz, 6H (4 diastereomers)), 0.04-0.17 (m, 18H (4 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 145.5, 145.4, 140.5, 139.9, 139.69, 139.66, 139.1, 139.0, 135.1, 135.0, 133.3, 133.1, 130.0, 129.8, 129.09, 129.05, 129.03, 128.9, 128.3, 127.4, 127.3, 126.1, 124.8, 124.79, 124.72, 115.3, 125.2, 114.6, 100.6, 100.3, 97.3, 82.1, 81.9, 80.5, 80.4, 80.3, 79.6, 79.5, 79.4, 79.3, 79.2, 78.8, 78.6, 77.2, 77.0, 76.8, 76.3, 76.2, 75.67, 75.61, 74.7, 72.37, 72.33, 71.7, 71.4, 66.3, 65.78, 65.75, 63.6, 63.3, 63.2, 62.17, 62.11, 48.5, 48.3, 46.9, 41.6, 41.5, 40.37, 40.34, 40.0, 38.7, 38.1, 38.0, 36.6, 36.0, 35.2, 34.6, 33.1, 33.0, 32.9, 32.4, 31.5, 31.3, 31.2, 29.7, 29.2, 29.1, 28.9, 28.6, 27.5, 27.4, 27.3, 27.2, 26.7, 26.3, 26.1, 26.0, 25.97, 25.94, 25.4, 25.3, 24.7, 23.3, 20.8, 20.7, 20.6, 20.4, 20.3, 18.4, 18.38, 18.31, 18.2, 18.07, 18.02, 17.3, 17.0, 16.0, 15.9, 14.9, 11.9, 11.4, 6.9, 4.9, -3.8, -4.1, -4.20, -4.28, -4.3, -4.4, -4.5, -4.65, -4.69 ppm; HRMS (ES+) calcd. for $C_{75}H_{136}O_{12}SSi_4Na$ (M+Na) 1395.8727, found 1395.8761.



71

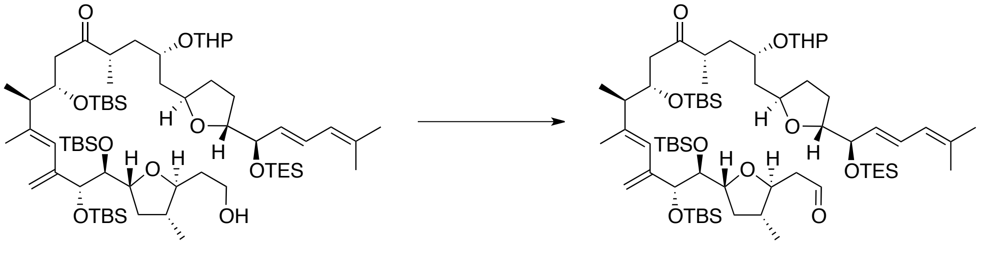
72 P = Piv
73 P = H

Ketone 72 and **Keto-ol 73**: To a stirred solution of sulfone **71** (113.6 mg, 82.6 μmol) in THF (1.4 mL) at -50 °C was added LDA[10] (0.21 mL, 0.210 mmol, 1 M in THF / hexanes). After 5 min, DMPU (794 mg, 0.75 mL, 6.17 mmol) was added and was slowly warmed to -25 °C over 30 min. The reaction was cooled back down to -50 °C and a solution of Davis' oxaziridine[19] (59.4 mg, 0.227 mmol) in THF (0.50 mL) was cannulated to it. The reaction was allowed to warm to -35 °C over 20 min and then quenched with sat. aq. NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 6-20% EtOAc / hexanes, to give ketone **72** (46.3 mg, 37.1 μmol, 45%) and keto-ol **73** (20.7 mg, 17.8 μmol, 22%) as colorless oil along with recovered sulfone **71** (30.4 mg, 22.1 μmol, 27%). Ketone **72**: $[\alpha]_D^{23}$ = +27.4 (c = 1.00, C_6H_6); IR: (neat) 2955, 2930, 2856, 1731, 1461, 1376, 1252, 1156, 1076, 1034, 835, 776 cm^{-1}; ^{1}H NMR {700 MHz, CDCl$_3$ (two diastereomers)} δ 6.47 (dd, *J* = 15.1, 11.0 Hz, 1H (2 diastereomers)), 5.84 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (2 diastereomers)), 5.52-5.56 (m, 1H (2 diastereomers)), 5.32 (s, 1H (2 diastereomers)), 4.96 (s, 1H (2 diastereomers)), 4.54-4.59 (m, 1H (2 diastereomers)), 4.36-4.40 (m, 1H (2 diastereomers)), 4.25-4.28 (m, 1H (2 diastereomers)), 4.16-4.19 (m, 1H (2 diastereomers)), 4.11-4.14 (m, 1H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 4.00 (ddd, *J* = 13.5, 8.1, 5.5 Hz, 1H (1 diastereomer)), 3.89-3.97 (m, 4H (1H of 1 diastereomer and 3H of 2 diastereomers)), 3.82-3.86 (m, 1H (1 diastereomer)), 3.71-3.75 (m, 1H (1 diastereomer)), 3.47-3.53 (m, 2H (2 diastereomers)), 3.33 (td, *J* = 9.1, 2.6 Hz, 1H (2 diastereomers)), 2.81 (qd, *J* = 6.9, 4.3 Hz, 1H (1 diastereomer)), 2.58-2.69 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.52 (dd, *J* = 12.1, 5.3 Hz, 1H (1 diastereomer)), 2.49 (dd, *J* = 12.1, 5.4 Hz, 1H (1 diastereomer)), 2.37-2.41 (m, 1H (2 diastereomers)), 2.04-2.09 (m, 1H (2 diastereomers)), 1.95-2.02 (m, 1H (2 diastereomers)), 1.84-1.92 (m, 4H (2 diastereomers)), 1.80-1.84 (m, 1H (1 diastereomer)), 1.82 (s, 3H (2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.78 (s, 3H (2 diastereomers)), 1.64-1.71 (m, 3H (2 diastereomers)), 1.49-1.56 (m, 5H (2 diastereomers)), 1.40-1.47 (m, 2H (2 diastereomers)), 1.22-1.28 (m, 1H (2 diastereomers)), 1.21 (s, 9H (2 diastereomers)), 1.08 (d, *J* = 7.0 Hz, 3H (2 diastereomers)), 1.06 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 1.04 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 0.98 (d, *J* = 6.4 Hz, 3H (2 diastereomers)), 0.97 (t, *J* = 7.9 Hz, 9H (2 diastereomers)), 0.915 (s, 9H (2 diastereomers)), 0.910 (s, 9H (2 diastereomers)), 0.89 (s, 9H (2 diastereomers)), 0.62 (q, *J* = 7.9 Hz, 6H (2 diastereomers)), 0.12 (s, 3H (2 diastereomers)), 0.08 (s, 3H (2 diastereomers)), 0.07 (s, 3H (2 diastereomers)), 0.047 (s, 3H (1 diastereomer)), 0.043 (s, 3H (1 diastereomer)), 0.03 (s, 3H (1 diastereomer)), 0.02 (s, 3H (1 diastereomer)), 0.015 (s, 3H (1 diastereomer)), 0.012 (s, 3H (1 diastereomer)) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 213.1, 212.5, 178.4, 145.2, 140.8, 135.0, 134.9, 130.0, 129.8, 127.5, 127.4, 125.46, 125.40, 124.75, 124.72, 114.9, 99.5, 97.9, 82.1, 82.0, 80.5, 79.4, 78.9, 78.6, 77.4, 76.28, 76.24, 75.58, 75.54, 74.1, 72.1, 70.49, 70.44, 63.8, 63.4, 62.0, 48.1, 48.0, 45.3, 43.3, 43.0, 41.8, 41.1, 40.3, 38.6, 38.1, 37.3, 36.8, 33.1, 32.9, 32.5, 31.4, 31.3, 29.7, 27.4, 27.28, 27.20, 26.1, 25.97, 25.92, 25.90, 25.4, 20.8, 20.4, 18.4, 18.3, 18.2, 17.9, 17.16, 17.10, 16.1, 16.0, 15.6, 13.97, 13.93, 6.8, 5.0, -4.23, -4.27, -4.43, -4.47, -4.77, -4.79, -4.8 ppm; HRMS (ES+) calcd. for C$_{69}$H$_{130}$O$_{11}$Si$_4$Na (M+Na) 1269.8588, found 1269.8671.



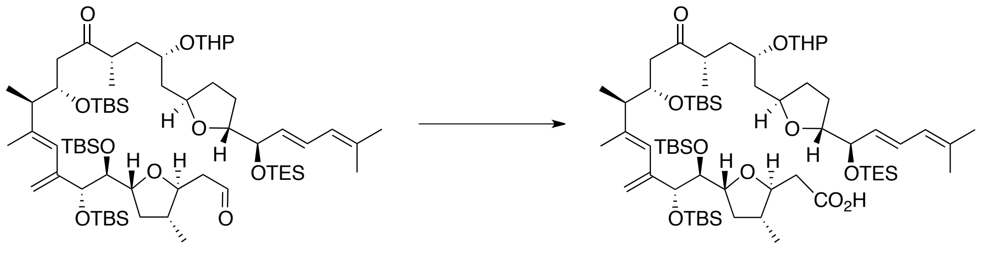
Aldehyde 74: To a stirred solution of pivalate **72** (37.0 mg, 29.6 µmol) in Et_2O (2.2 mL) at -20 °C was added $LiAlH_4$ (5.6 mg, 0.148 mmol) in one portion. After 25 min, the reaction was quenched with H_2O (5 drops) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 10 mL). The dried ($MgSO_4$) combined solution was concentrated *in vacuo* to give crude diol **SI-40**.

To a stirred solution of oxalyl chloride (18.6 mg, 13.0 µL, 0.148 mmol) in CH_2Cl_2 (0.80 mL) at -78 °C was cannulated a solution of DMSO (22.7 mg, 21.0 µL, 0.296 mmol) in CH_2Cl_2 (0.40 mL). After 15 min, a solution of crude diol **SI-40** in CH_2Cl_2 (0.95 mL and 2 X 0.10 mL wash) was cannulated to it. After 45 min, Et_3N (29.7 mg, 41.7 µL, 0.296 mmol) was added. After 10 min, the reaction was quenched with H_2O (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **74** (27.2 mg, 23.4 µmol, 79%) as colorless oil. $[\alpha]_D^{23} = +17.8$ (c = 0.45, C_6H_6); IR: (neat) 2953, 2928, 2855, 1728, 1641, 1461, 1377, 1252, 1075, 1033, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 9.82 (dd, J = 2.9, 2.3 Hz, 1H (2 diastereomers)), 6.47 (dd, J = 15.1, 11.0 Hz, 1H (2 diastereomers)), 5.84 (d, J = 11.0 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (2 diastereomers)), 5.54 (dt, J = 15.1, 6.6 Hz, 1H (2 diastereomers)), 5.32 (s, 1H (2 diastereomers)), 4.97 (s, 1H (2 diastereomers)), 4.54-4.59 (m, 1H (2 diastereomers)). 4.38-4.41 (m, 1H (2 diastereomers)), 4.17 (dd, J = 12.3, 6.1 Hz, 1H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 3.98-4.03 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.93-3.97 (m, 1H (2 diastereomers)), 3.88-3.92 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.83-3.86 (m, 1H (1 diastereomer)), 3.73-3.76 (m, 1H (1 diastereomer)), 3.73 (td, J = 8.9, 3.4 Hz, 1H (2 diastereomers)), 3.54 (ddd, J = 7.1, 4.3, 2.8 Hz, 1H (2 diastereomers)), 3.47-3.51 (m, 1H (2 diastereomers)), 2.82 (qd, J = 6.8, 4.2 Hz, 1H (1 diastereomer)), 2.68 (dd, J = 17.3, 6.7 Hz, 1H (1 diastereomer)), 2.60-2.64 (m, 1H (1 diastereomer)), 2.62 (dd, J = 17.4, 6.7 Hz, 1H (1 diastereomer)), 2.58 (dd, J = 3.3, 2.3 Hz, 1H (1 diastereomer)), 2.56 (dd, J = 3.3, 2.3 Hz, 1H (1 diastereomer)), 2.45-2.51 (m, 2H (2 diastereomers)), 2.38-2.42 (m, 1H (2 diastereomers)), 2.05-2.10 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.95-2.02 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.84-1.90 (m, 3H (2 diastereomers)), 1.83 (d, J = 1.0 Hz, 3H (2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.78 (s, 3H (2 diastereomers)), 1.66-1.72 (m, 2H (2 diastereomers)), 1.49-1.56 (m, 5H (2 diastereomers)), 1.39-1.47 (m, 2H (2 diastereomers)), 1.23-1.31 (m, 2H (2 diastereomers)), 1.09 (d, J = 7.0 Hz, 3H (2 diastereomers)), 1.06 (d, J = 6.9 Hz, 3H (1 diastereomer)), 1.04 (d, J = 6.9 Hz, 3H (1 diastereomer)), 1.02 (d, J = 6.4 Hz, 3H (2 diastereomers)), 0.97 (t, J = 7.9 Hz, 9H (2 diastereomers)), 0.91 (s, 9H (2 diastereomers)), 0.89 (s, 18H (2 diastereomers)), 0.62 (q, J = 7.9 Hz, 6H), 0.12 (s, 3H (1 diastereomer)), 0.08 (s, 3H (2 diastereomers)), 0.01-0.04 (m, 12H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) 212.5, 202.0, 145.1, 141.0, 135.0, 134.9, 130.0, 129.8, 127.5, 127.4, 125.1, 124.7, 115.0, 99.5, 97.9, 82.1, 82.0, 79.9, 79.4, 78.69, 78.65, 77.4, 76.2, 75.5, 74.2, 72.1, 70.3, 63.5, 48.0, 47.6, 45.1, 43.4, 43.0, 41.9, 41.1, 40.6, 37.6, 37.2, 36.8, 32.9, 32.5, 31.4, 31.3, 29.7, 27.4, 27.2, 26.1, 25.96, 25.90, 25.4, 20.8, 20.4, 18.4, 18.3, 18.2, 17.9, 17.3, 17.2, 16.0, 15.6, 15.5, 13.8, 6.9, 5.0, -4.1, -4.3, -4.4, -4.7, -4.8 ppm; HRMS (ES+) calcd. for $C_{64}H_{120}O_{10}Si_4Na$ (M+Na) 1183.7856, found 1183.7847.



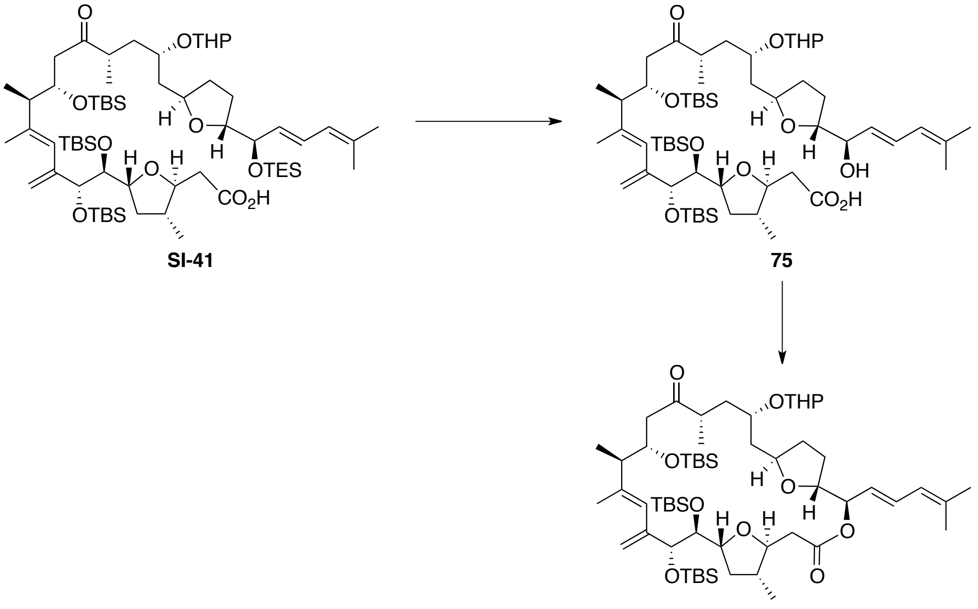
73 **74**

Aldehyde 74: To a stirred solution of oxalyl chloride (10.6 mg, 7.3 µL, 83.7 µmol) in CH_2Cl_2 (0.50 mL) at -78 °C was cannulated a solution of DMSO (13.1 mg, 11.9 µL, 0.167 mmol) in CH_2Cl_2 (0.25 mL). After 15 min, a solution of alcohol **73** (19.5 mg, 16.7 µmol) in CH_2Cl_2 (0.50 mL and 2 X 0.10 mL wash) was cannulated to it. After 45 min, Et_3N (16.9 mg, 23.4 µL, 0.167 mmol) was added. After 10 min, the reaction was quenched with H_2O (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **74** (16.5 mg, 14.2 µmol, 85%) as colorless oil.



74 SI-41

Carboxylic Acid SI-41: To a stirred solution of aldehyde **74** (27.2 mg, 23.4 µmol) in *t*-BuOH/H_2O (1:1, 2.3 mL) at 0 °C were sequentially added 2-methyl-2-butene (82.1 mg, 124 mL, 1.17 mmol), NaH_2PO_4•H_2O (32.3 mg, 0.234 mmol) and $NaClO_2$ (10.7 mg, 0.117 mmol). After 15 min, the reaction was warmed to rt. After another 2 h, the reaction was diluted with H_2O (7.5 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30 % EtOAc / hexanes, to give carboxylic acid **SI-41** (24.1 mg, 20.4 µmol, 87%) as light yellow oil. $[\alpha]_D^{23}$ = +14.3 (*c* = 1.00, $CHCl_3$); IR: (neat) 3376, 2953, 2927, 2855, 1713, 1654, 1461, 1377, 1252, 1076, 1034, 835 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 9.79 (br s, 1H (2 diastereomers)), 6.45-6.49 (m, 1H (2 diastereomers)), 5.84 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (1 diastereomer)), 5.58 (s, 1H (1 diastereomer)), 5.54 (ddd, *J* = 15.1, 10.6, 5.9 Hz, 1H (2 diastereomers)), 5.39 (s, 1H (1 diastereomer)), 5.35 (s, 1H (1 diastereomer)), 5.02 (s, 1H (1 diastereomer)), 5.00 (s, 1H (1 diastereomer)), 4.52-4.60 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 4.38 (td, *J* = 5.8, 3.6 Hz, 1H (1 diastereomer)), 4.11-4.19 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 4.10 (s, 1H (1 diastereomer)), 3.99-4.06 (m, 1H (2 diastereomers)), 3.93-3.98 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.86-3.92 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.72-3.76 (m, 1H (1 diastereomer)), 3.66 (ddd, *J* = 9.6, 6.9, 3.7 Hz, 1H (1 diastereomer)), 3.59 (dd, *J* = 7.0, 1.9 Hz, 1H (1 diastereomer)), 3.57 (dd, *J* = 6.6, 2.5 Hz, 1H (1 diastereomer)), 3.48-3.56 (m, 1H (2 diastereomers)), 2.88 (qd, *J* = 6.7, 3.5 Hz, 1H (1 diastereomer)), 2.69-2.75 (m, 1H (2 diastereomers)), 2.59-2.66 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.48 (dd, *J* = 15.9 Hz, 1H (2 diastereomers)), 2.37-2.46 (m, 2H (2 diastereomers)), 2.05-2.15 (m, 2H (2 diastereomers)), 1.91-2.03 (m, 3H (2 diastereomers)), 1.84-1.89 (m, 1H (2 diastereomers)), 1.85 (s, 3H (1 diastereomer)), 1.83 (s, 3H (1 diastereomer)), 1.79 (s, 3H (2 diastereomers)), 1.78 (s, 3H (2 diastereomers)), 1.65-1.73 (m, 3H (2 diastereomers)), 1.50-1.56 (m, 5H (2 diastereomers)), 1.42-1.48 (m, 2H (2 diastereomers)), 1.32-1.38 (m, 1H (2 diastereomers)), 1.11 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.10 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.05 (d, *J* = 6.9 Hz, 3H (2 diastereomers)), 1.03 (d, *J* = 6.4 Hz, 3H (2 diastereomers)), 0.97 (t, *J* = 7.9 Hz, 9H), 0.93 (s, 9H, (1 diastereomer)), 0.925 (s, 9H (1 diastereomer)), 0.922 (s, 9H (1 diastereomer)), 0.91 (s, 9H (1 diastereomer)), 0.899 (s, 9H (1 diastereomer)), 0.892 (s, 9H (1 diastereomer)), 0.62 (q, *J* = 7.9 Hz, 6H), 0.02-0.13 (m, 18H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.0, 212.5, 171.7, 144.9, 141.5, 141.3, 135.1, 134.9, 129.9, 129.8, 127.5, 127.4, 125.0, 124.7, 124.6, 124.4, 115.0, 114.4, 99.5, 98.5, 82.2, 82.0, 80.25, 80.20, 80.1, 79.1, 78.8, 78.0, 77.4, 76.3, 76.1, 75.6, 75.5, 74.1, 72.2, 70.4, 69.8, 64.6, 63.5, 47.9, 47.6, 45.2, 44.6, 43.4, 42.8, 41.8, 41.2, 39.8, 38.0, 37.7, 37.6, 37.5, 37.2, 36.8, 33.0, 32.5, 31.6, 31.3, 29.7, 27.4, 27.2, 26.0, 25.98, 25.95, 25.8, 25.4, 25.2, 21.2, 20.4, 18.3, 18.2, 17.9, 17.3, 17.1, 16.1, 15.6, 15.5, 15.1, 14.0, 13.3, 6.8, 5.0, -3.9, -4.3, -4.43, -4.48, -4.5, -4.6, -4.74, -4.77, -4.8 ppm; HRMS (ES+) calcd. for $C_{64}H_{120}O_{11}Si_4Na$ (M+Na) 1199.7805, found 1199.7843.



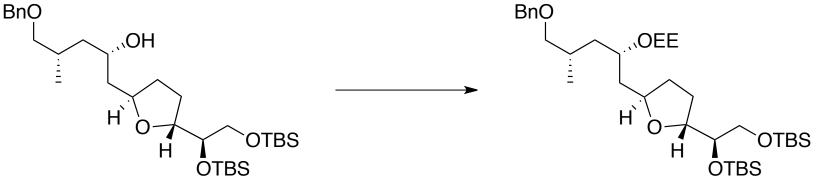
SI-41

75

77

Macrolactone 75: To a stirred solution of TES ether **SI-41** (20.9 mg, 17.7 µmol) in dry MeOH (1.7 mL) at 0 °C was added methanolic PPTS solution (34 µL).[20] After 15 min, the reaction was warmed to rt. After another 35 min, the reaction was quenched with sat. aq. $NaHCO_3$ (6.0 mL) and the aqueous layer was extracted with EtOAc (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude seco-acid **75**.

To a stirred solution of Shina anhydride **76**[21] (7.3 mg, 21.3 mmol) and DMAP (5.2 mg, 42.6 mmol) in DCE (12.0 mL) was slowly added a solution of crude seco-acid **75** in DCE (1.3 mL) over 24 h. After another 12 h, the solvent was removed *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give macrolactone **77** (12.9 mg, 12.3 µmol, 69%) as colorless oil. $[\alpha]_D^{23}$ = +3.1 (*c* = 0.71, $CHCl_3$); IR: (neat) 2953, 2927, 2855, 1740, 1710, 1553, 1462, 1385, 1252, 1076, 1034, 835 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (***Note:*** *NMR analysis indicated that compound* ***77*** *exists as a mixture of conformational isomers*)} δ 6.5 (dd, *J* = 14.8, 11.1 Hz, 1H (2 diastereomers)), 6.15 (s, 1H (1 diastereomer)), 6.13 (s, 1H (1 diastereomer)), 5.78 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.36-5.40 (m, 1H (2 diastereomers)), 4.95-5.03 (m, 2H (2 diastereomer)), 4.91 (s, 1H (2 diastereomers)), 4.59-4.62 (m, 1H (2 diastereomers)), 4.22 (s, 1H (1 diastereomer)), 4.20 (s, 1H (1 diastereomer)), 3.84-4.05 (br m, 6H (2 diastereomers)), 3.49-3.65 (br m, 3H (2 diastereomers)), 3.00 (dd, *J* = 18.4, 10.4 Hz, 1H (1 diastereomer)), 2.96 (dd, *J* = 18.2, 10.2 Hz, 1H (1 diastereomer)), 2.76 (br s, 1H (2 diastereomers)), 2.56 (br s, 1H (2 diastereomers)), 2.39-2.50 (m, 3H (2 diastereomers)), 2.28-2.33 (m, 1H (2 diastereomers)), 2.02-2.11 (br m, 3H (2 diastereomers)), 1.84-1.99 (m, 5H (2 diastereomers)), 1.78 (s, 6H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.68-1.76 (m, 3H (2 diastereomers)), 1.48-1.60 (m, 9H (2 diastereomers)), 1.22-1.31 (m, 2H (2 diastereomers)), 1.10 (br s, 3H (2 diastereomers)), 1.04 (t, *J* = 6.5 Hz, 3H (2 diastereomers)), 0.91 (s, 18H (2 diastereomers)), 0.86 (s, 9H (2 diastereomers)), -0.01-0.11 (m, 18H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 212.2, 211.7, 170.5, 170.4, 146.5, 146.4, 140.6, 137.5, 131.2, 128.9, 128.3, 128.1, 125.1, 125.0, 124.2, 114.4, 114.3, 101.1, 97.3, 81.8, 81.7, 80.0, 79.2, 79.0, 78.7, 78.2, 77.9, 75.7, 75.4, 75.3, 71.7, 64.1, 63.7, 56.0, 47.0, 46.3, 42.7, 42.2, 42.0, 41.8, 40.7, 39.9, 39.8, 38.6, 36.6, 34.8, 34.6, 34.5, 34.2, 32.7, 32.6, 31.9, 31.7, 31.5, 31.0, 30.3, 29.4, 28.9, 26.4, 26.9, 25.9, 25.8, 25.4, 25.3, 24.7, 22.7, 21.0, 20.7, 18.7, 18.5, 18.4, 17.9, 16.7, 16.4, 16.4, 15.3, 14.1, -4.1, -4.5, -4.6, -4.7, -4.8, -5.2. -5.3 ppm; HRMS (ES+) calcd. for $C_{58}H_{104}O_{10}Si_3Na$ (M+Na) 1067.6835, found 1067.6857.

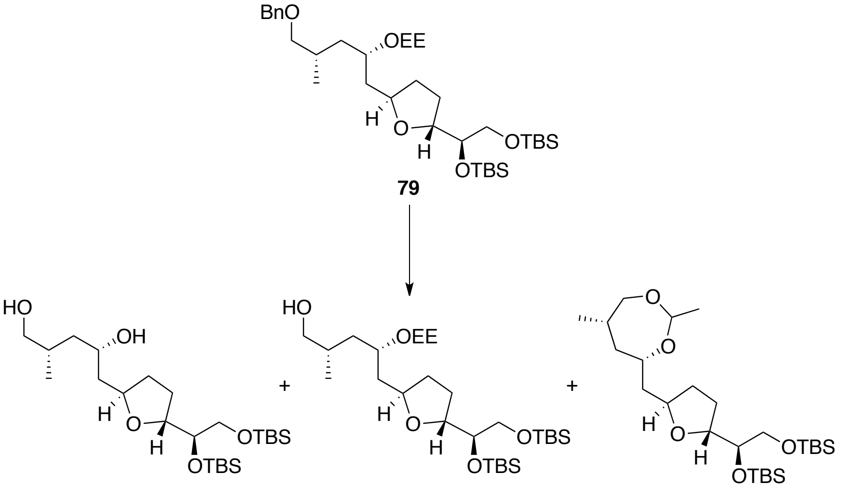


56

79

EE Ether 79: To a stirred solution of alcohol **56** (946 mg, 1.67 mmol) in CH_2Cl_2 (26.0 mL) were added ethyl vinyl ether (3.00 g, 4.0 mL, 41.7 mmol) followed by PPTS (1.5 mg, 41.7 μmol). After 14 h, the reaction was quenched with Et_3N (1.44 g, 2.0 mL, 14.2 mmol) and was concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 3-6% EtOAc / hexanes, to give EE ether **79** (1.00 g, 1.57 mmol, 94%) as colorless oil. $[\alpha]_D^{23}$ = -21.0 (*c* = 1.00, C_6H_6); IR: (neat) 2954, 2929, 2857, 1471, 1361, 1253, 1091, 960, 835, 777 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.35-7.36 (m, 4H (2 diastereomers)), 7.29-7.30 (m, 1H (1 diastereomer)), 4.72 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.68 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.52 (s, 2H (2 diastereomers)), 4.06-4.10 (m, 1H (2 diastereomers)), 3.94-4.01 (m, 1H (2 diastereomers)), 3.87 (ddd, *J* = 13.0, 8.1, 4.0 Hz, 1H (1 diastereomer)), 3.78 (ddd, *J* = 12.6, 8.4, 4.4 Hz, 1H (1 diastereomer)), 3.61-3.69 (m, 2H (2 diastereomers)), 3.54-3.58 (m , 2H (2 diastereomers)), 3.45-3.53 (m, 1H (2 diastereomers)), 3.35-3.38 (m, 1H (2 diastereomers)), 3.23-3.28 (m, 1H (2 diastereomers)), 2.08-2.13 (m, 1H (1 diastereomer)), 1.98-2.04 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.90-1.96 (m, 2H (2 diastereomers)), 1.77-1.85 (m, 1H (2 diastereomers)), 1.54-1.63 (m, 2H (2 diastereomers)), 1.42-1.48 (m, 1H (2 diastereomers)), 1.31-1.37 (m, 1H (2 diastereomers)), 1.30 (d, *J* =

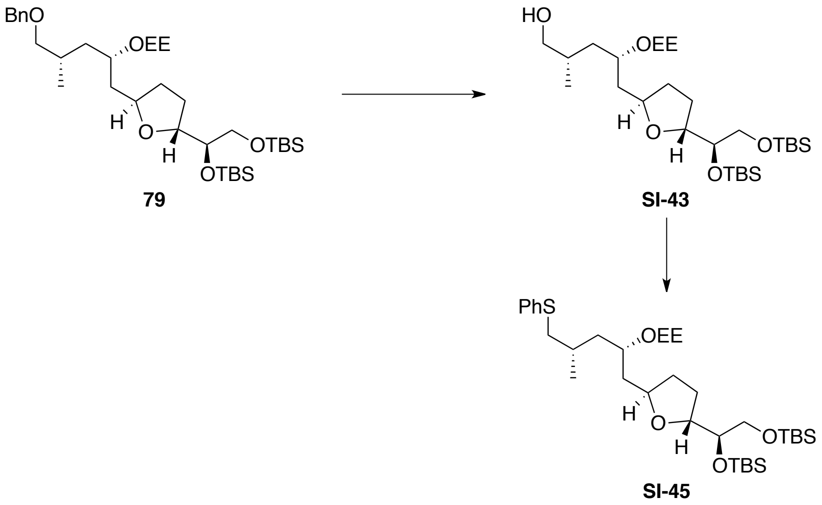
5.2 Hz, 3H (2 diastereomers)), 1.21 (t, J = 7.0 Hz, 3H (2 diastereomers)), 1.01 (d, J = 6.6 Hz, 3H (1 diastereomer)), 1.00 (d, J = 6.6 Hz, 3H (1 diastereomer)), 0.91 (s, 9H (2 diastereomers)), 0.90 (s, 9H (2 diastereomers)), 0.094 (s, 3H), 0.090 (s, 3H), 0.08 (s, 3H)), 0.07 (s, 3H)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 138.8, 138.7, 128.3, 128.2, 127.5, 127.4, 127.3, 99.6, 98.3, 78.6, 78.5, 76.4, 76.3, 76.2, 76.0, 72.9, 72.87, 72.84, 71.9, 65.1, 60.7, 60.5, 41.8, 41.2, 39.0, 38.6, 33.2, 32.9, 29.8, 29.7, 27.39, 27.36, 26.0, 25.9, 20.9, 20.7, 18.4, 18.1, 17.3, 17.0, 15.4, 15.3, -4.1, -4.2, -4.6, -4.7 ppm; HRMS (ES+) calcd. for $C_{35}H_{66}O_6Si_2Na$ (M+Na) 661.4296, found 661.4295.



79

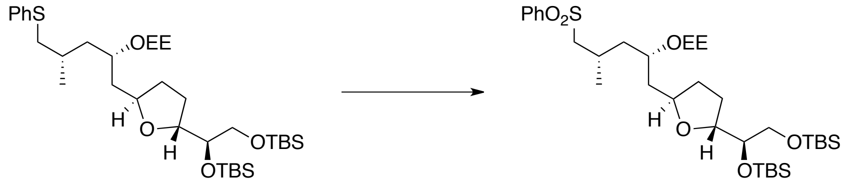
SI-42 **SI-43** **SI-44**

Pd/C-mediated Debenzylation: To a stirred solution of benzyl ether **79** (333 mg, 0.521 mmol) in *i*-PrOH (22.0 mL) was added Pd / C (225 mg, 10 mol% by weight). The flask was fitted with a H_2 balloon and purged with H_2. After 15 h, the reaction was passed through a plug of celite and the celite plug was washed with EtOAc (50 mL). The solvent was removed *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-50% EtOAc / hexanes, to sequentially give cyclic acetal **SI-44** (52.4 mg, 0.104 mmol, 20 %), alcohol **SI-43** (202 mg, 0.368 mmol, 71%) and diol **SI-42** (17.4 mg, 36.5 mmol, 7%) as colorless oils. (*The reaction is highly contingent upon the quality of Pd/C: up to 50% of cylic acetal* ***SI-44*** *was formed with different batches of Pd/C.*) Cyclic acetal **SI-44**: $[\alpha]_D^{23}$ = -18.7 (c = 1.00, $CHCl_3$); IR (neat) 2953, 2930, 2858, 1464, 1387, 1253, 1146, 1094, 835, 776 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 4.94 (q, J = 5.2 Hz, 1H), 4.08 (td, J = 7.5, 3.5 Hz, 1H), 4.00-4.04 (m, 1H), 3.78-3.82 (m, 1H), 3.67-3.70 (m, 1H), 3.55-3.62 (m, 3H), 3.46 (ddd, J = 11.8, 3.4, 1.6 Hz, 1H), 2.00-2.04 (m, 1H), 1.80-1.97 (m, 5H), 1.47-1.51 (m, 1H), 1.26 (d, J = 5.2 Hz, 3H), 1.18 (dt, J = 13.7, 11.2 Hz, 1H), 0.914 (s, 9H), 0.912 (s, 9H), 0.86 (d, J = 6.8 Hz, 3H), 0.09 (s, 6H), 0.078 (s, 3H), 0.074 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 98.4, 78.7, 76.5, 76.1, 74.9, 67.3, 65.1, 43.3, 42.3, 34.3, 32.5, 27.4, 26.0, 25.9, 20.5, 18.4, 18.2, 17.6, -4.1, -4.7, -5.33, -5.34 ppm; HRMS (ES+) calcd. for $C_{26}H_{54}O_5Si_2Na$ (M+Na) 525.3408, found 525.3388.



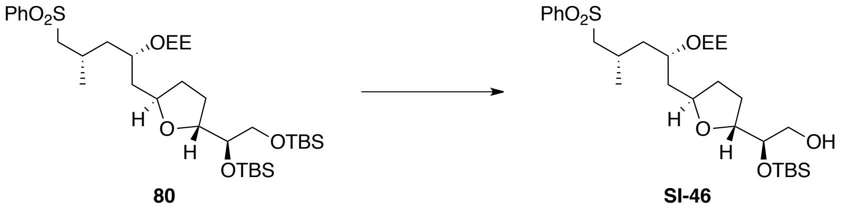
Sulfide SI-45: To a stirred solution of benzyl ether **79** (616 mg, 0.964 mmol) in THF (10.0 mL) at -78 °C was added freshly prepared LiDBB solution[22] (7.0 mL, 2.80 mmol, 0.4 M in THF) in one portion. After 10 min, the reaction was quenched with sat. aq. NH_4Cl (30 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 50 mL). The dried extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-40% EtOAc / hexanes, to give alcohol **SI-43** (506 mg, 0.922 mmol, 96%) as colorless oil.

To a stirred solution of alcohol **SI-43** (506 mg, 0.922 mmol) in THF (6.8 mL) at 0 °C were added Ph_2S_2 (426 mg, 1.95 mmol) followed by *n*-Bu_3P (413 mg, 0.52 mL, 2.04 mmol) and the reaction was warmed to rt. After 16 h, the solvent was removed *in vacuo* and the residue was purified by flash chromatography over silica gel, eluting with 5-10% EtOAc / hexanes, to give sulfide **SI-45** (576 mg, 0.898 mmol, 97%) as colorless oil. $[\alpha]_D^{23}$ = -36.9 (*c* = 1.03, C_6H_6); IR: (neat) 2955, 2929, 2857, 1472, 1376, 1253, 1091, 959, 835, 776, 736, 690 cm^{-1}; ^1H NMR {400 MHz, $CDCl_3$ (two diastereomers)} δ 7.33-7.36 (m, 2H (2 diastereomers)), 7.25-7.29 (m, 2H (2 diastereomers)), 7.13-7.18 (m, 1H (2 diastereomers)), 4.70 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.64 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.05-4.11 (m, 1H (2 diastereomers)), 3.92-4.01 (m, 1H (2 diastereomers)), 3.82-3.88 (m, 1H (1 diastereomer)), 3.72-3.79 (m, 1H (1 diastereomer)), 3.64-3.71 (m, 1H (2 diastereomers)), 3.50-3.62 (m, 3H (2 diastereomers)), 3.37-3.47 (m, 1H (1 diastereomer)), 2.93-2.99 (m, 1H (2 diastereomers)), 2.74-2.81 (m, 1H (2 diastereomers)), 1.87-2.10 (m, 3H (2 diastereomers)), 1.68-1.85 (m, 3H (2 diastereomers)), 1.51-1.58 (m, 1H (2 diastereomers)), 1.39-1.48 (m, 2H (2 diastereomers)), 1.27 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.23 (d, *J* = 5.2 Hz (1 diastereomer)), 1.19 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.14 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.08 (d, *J* = 6.5 Hz, 3H (1 diastereomer)), 1.07 (d, *J* = 6.5 Hz, 3H (1 diastereomer)), 0.91 (s, 18H (2 diastereomers)), 0.09 (s, 6H (2 diastereomers)), 0.073 (s, 3H (2 diastereomers)), 0.070 (s, 3H (2 diastereomers)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 129.1, 129.0, 128.79, 128.73, 125.6, 125.5, 99.8, 98.1, 78.6, 78.5, 77.2, 76.24, 76.20, 76.1, 73.1, 71.8, 65.0, 60.7, 60.3, 41.99, 41.91, 41.6, 41.3, 41.1, 33.2, 33.0, 29.3, 27.3, 26.0, 25.9, 20.8, 20.6, 19.3, 19.1, 18.4, 18.1, 15.3, -4.1, -4.2, -4.7, -5.3 ppm; HRMS (ES+) calcd. for $C_{34}H_{64}O_5SSi_2Na$ (M+Na) 663.3911, found 663.3882.

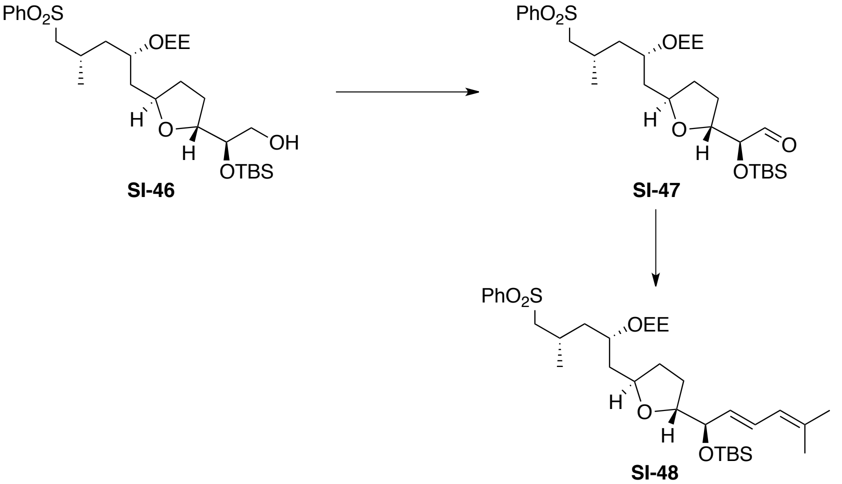


SI-45 **80**

Sulfone 80: To a stirred solution of sulfide **SI-45** (592 mg, 0.923 mmol) in CH_3CN (16.0 mL) at rt were added NMO (325 mg, 2.77 mmol) followed by TPAP (163 mg, 0.461 mmol). After 12 h, the reaction was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give sulfone **80** (574 mg, 0.852 mmol, 92%) as colorless oil. $[\alpha]_D^{23}$ = -27.8 (*c* = 1.00, C_6H_6); IR: (neat) 2955, 2929, 2856, 1471, 1446, 1377, 1307, 1253, 1147, 1086, 835, 776, 689 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-7.96 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.62 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.05-4.09 (m, 1H (2 diastereomers)), 3.88-3.94 (m, 1H (2 diastereomers)), 3.81-3.85 (m, 1H (1 diastereomer)), 3.69-3.72 (m, 1H (1 diastereomer)), 3.63-3.66 (m, 1H (2 diastereomers)), 3.59-3.63 (m, 1H (1 diastereomer)), 3.50-3.56 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 3.40-3.47 (m, 1H (2 diastereomers)), 3.23 (dd, *J* = 14.2, 4.7 Hz, 1H (1 diastereomer)), 3.17 (dd, *J* = 14.2, 4.3 Hz, 1H (1 diastereomer)), 2.97 (dd, *J* = 8.2, 5.5 Hz, 1H (1 diastereomer)), 2.95 (dd, *J* = 8.3, 5.7 Hz, 1H (1 diastereomer)), 2.32-2.37 (m, 1H (1 diastereomer)), 2.21-2.26 (m, 1H (1 diastereomer)), 1.96-2.01 (m, 1H (2 diastereomers)), 1.86-1.94 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.78-1.84 (m, 1H (2 diastereomers)), 1.72-1.76 (m, 1H (1 diastereomer)), 1.39-1.62 (m, 4H (2 diastereomers)), 1.23 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.21 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.19 (t, *J* = 7.1 Hz, 3H (1 diastereomer)), 1.17 (t, *J* = 7.1 Hz, 3H (1 diastereomer)), 1.148 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.145 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.909 (s, 9H (1 diastereomer)), 0.907 (s, 9H (1 diastereomer)), 0.89 (s, 9H (2 diastereomers)), 0.06-0.08 (m, 12H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 141.2, 141.0, 133.5, 133.3, 129.2, 129.1, 128.04, 128.0, 99.9, 97.9, 78.6, 78.5, 76.0, 75.9, 72.9, 71.1, 65.0, 63.26, 63.20, 60.7, 60.6, 41.8, 41.7, 41.5, 40.7, 33.2, 33.0, 27.3, 27.2, 26.0, 25.9, 25.86, 25.83, 20.7, 20.6, 19.8, 19.7, 18.4, 18.1, 15.4, 15.3, -4.20, -4.22, -4.6, -4.7, -5.3 ppm; HRMS (ES+) calcd. for $C_{34}H_{64}O_7SSi_2Na$ (M+Na) 695.3809, found 695.3818.



Alcohol SI-46: To a stirred solution of TBS ether **80** (574 mg, 0.852 mmol) in THF (8.0 mL) at 0 °C was added a stock solution of HF•Pyr.[4] (4.8 mL) over 30 min. After 24 h, the reaction quenched with sat. aq. $NaHCO_3$ (50 mL) and the aqueous layer was extracted with EtOAc / Et_2O (2:1, 3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-60% EtOAc / hexanes, to give alcohol **SI-46** (380 mg, 0.679 mmol, 80%) as colorless oil. $[\alpha]_D^{23}$ = -30.2 (*c* = 1.01, C_6H_6); IR: (neat) 3468, 2957, 2930, 2857, 1462, 1447, 1377, 1306, 1253, 1145, 1086, 1056, 836, 777, 689 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-7.95 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.63 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.06-4.10 (m, 1H (2 diastereomers)), 3.94-4.01 (m, 1H (2 diastereomers)), 3.80-3.83 (m, 1H (1 diastereomer)), 3.65-3.71 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 3.56-3.61 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.52 (ddd, *J* = 14.0, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.46 (ddd, *J* = 14.0, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.42 (ddd, *J* = 14.0, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.22 (dd, *J* = 14.2, 5.0 Hz, 1H (1 diastereomer)), 3.16 (dd, *J* = 14.2, 4.6 Hz, 1H (1 diastereomer)), 2.95-2.99 (m, 1H (2 diastereomers)), 2,45-2.47 (m, 1H (2 diastereomers)), 2.32-2.38 (m, 1H (1 diastereomer)), 2.21-2.28 (m, 1H (1 diastereomer)), 2.01-2.06 (m, 1H (2 diastereomers)), 1.88-1.97 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.72-1.79 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.61-1.69 (m, 1H (2 diastereomers)), 1.49-1.57 (m, 1H (2 diastereomers)), 1.42-1.48 (m, 2H (2 diastereomers)), 1.24 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.23 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.19 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.17 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.13 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.12 (d, *J* = 6.7 Hz, 3H (1 diastereomer)), 0.92 (s, 9H (2 diastereomers)), 0.112-0.117 (m, 6H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.1, 140.0, 133.5, 133.4, 129.2, 129.1, 128.0, 127.9, 99.9, 97.7, 80.4, 80.3, 76.3, 76.2, 74.47, 74.42, 72.8, 70.7, 64.6, 63.13, 63.10, 60.5, 60.3, 41.7, 41.5, 40.6, 32.9, 32.7, 27.5, 25.88, 25.81, 25.78, 20.59, 20.50, 20.0, 19.7, 18.1, 15.4, 15.3, -4.5, -4.6 ppm; HRMS (ES+) calcd. for $C_{28}H_{50}O_7SSiNa$ (M+Na) 581.2944, found 581.2930.

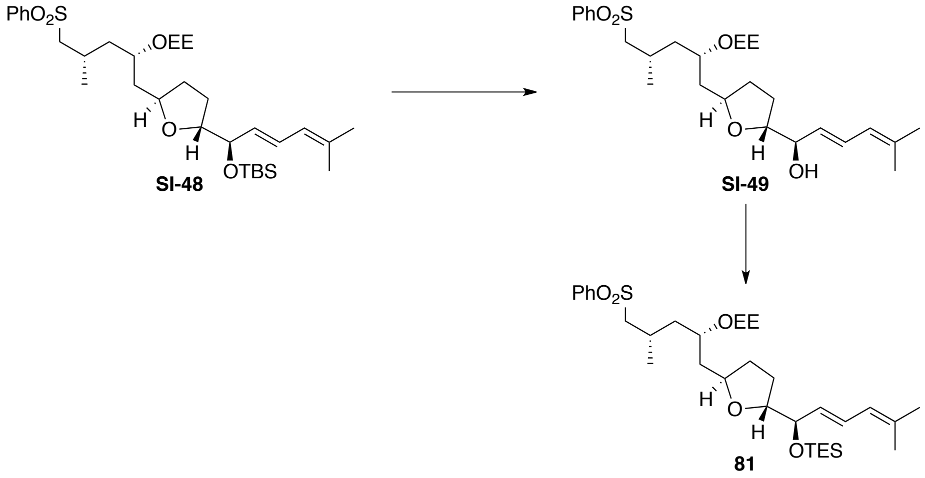


SI-46 **SI-47** **SI-48**

Diene SI-48: To a stirred solution of oxalyl chloride (103 mg, 72 µL, 0.814 mmol) in CH_2Cl_2 (4.2 mL) at -78 °C was cannulated a solution of DMSO (133 mg, 0.12 mL, 1.70 mmol) in CH_2Cl_2 (1.2 mL). After 15 min, a solution of alcohol **SI-46** (380 mg, 0.679 mmol) in CH_2Cl_2 (2.0 mL and 2 X 0.5 mL wash) was cannulated to it. After 45 min, Et_3N (346 mg, 0.48 mL, 3.39 mmol) was added. After 10 min, the cooling bath was removed and the reaction was quenched with H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 50 mL) and the dried ($MgSO_4$) extract was concentrated *in vacuo* and was quickly passed through a short plug of silica gel to give crude aldehyde **SI-47**.

To a stirred solution of tributyl phosphonium salt **68** (341 mg, 0.970 mmol) in THF (7.6 mL) at -45 °C was added *n*-BuLi (0.40 mL, 1.00 mmol, 2.5 M in hexane) and was warmed to rt over 45 min. After 2 h, the reaction was cooled back down to -78 °C and a solution of crude aldehyde **SI-47** in THF (7.6 mL) was cannulated to it. The reaction was slowly warmed to rt over 2.5 h. After another 3 h, the reaction was quenched with H_2O (15 drops) and the solvent was removed *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give diene **SI-48** {401 mg, 0.658 mmol, 97% (11:1 *E:Z*; inseparable mixture)} as colorless oil. $[\alpha]_D^{23}$ = +12.7 (*c* = 1.02, C_6H_6); IR: (neat) 2956, 2928, 2856, 1446, 1378, 1308, 1253, 1148, 1086, 959, 836, 776, 689 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-796 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 6.43-6.47 (m, 1H (2 diastereomers of E isomer)), 6.21 (t, *J* = 11.2 Hz, 1H of Z isomer), 6.06-6.09 (m, 1H of Z isomer)), 5.83 (d, *J* = 11.0 Hz, 1H (2 diastereomers of E isomer)), 5.53 (ddd, *J* = 14.1, 5.7, 3.1 Hz, 1H (2 diastereomers of E isomer)), 5.29 (q, *J* = 10.1 Hz, 1H of Z isomer), 4.67 (q, J = 5.2 Hz, 1H (1 diastereomer)), 4.63 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.46 (dd, *J* = 9.0, 5.2 Hz, 1H of Z isomer), 4.16 (t, *J* = 5.6 Hz, 1H (2 diastereomers)), 3.86-3.94 (m, 2H (2 diastereomers)), 3.79-3.83 (m, 1H (1 diastereomer)), 3.67-3.71 (m, 1H (1 diastereomer)), 3.60 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.53 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.41-3.47 (m, 1H (2 diastereomers)), 3.25 (dd, *J* = 14.2, 4.7 Hz, 1H (1 diastereomer)), 3.18 (dd, *J* =

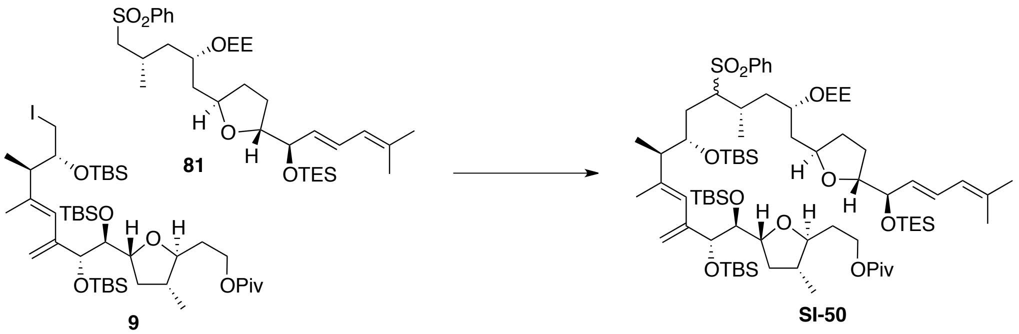
14.2, 4.4 Hz, 1H (1 diastereomer)), 2.95-2.99 (m, 1H (2 diastereomers)), 2.32-2.37 (m, 1H (1 diastereomer)), 2.21-2.26 (m, 1H (1 diastereomer)), 1.92-1.98 (m, 1H (2 diastereomers)), 1.84-1.91 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.67-1.75 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.57-1.66 (m, 1H (2 diastereomers)), 1.39-1.54 (m, 3H (2 diastereomers)), 1.24 (d, J = 5.2 Hz, 3H (1 diastereomer)), 1.22 (d, J = 5.2 Hz, 3H (1 diastereomer)), 1.19 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.18 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.154 (d, J = 6.6 Hz, 3H (1 diastereomer)), 1.152 (d, J = 6.6 Hz, 3H (1 diastereomer)), 0.921 (s, 9H (1 diastereomer)), 0.920 (s, 9H (1 diastereomer)) ppm, 0.05-0.08 (m, 6H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.2, 140.0, 135.04, 135.02, 133.5, 133.3, 129.97, 129.95, 129.2, 129.1, 128.0, 127.9, 127.45, 127.43, 124.7, 99.9, 98.0, 82.1, 82.0, 76.0, 75.7, 75.6, 72.8, 71.1, 63.19, 63.12, 60.6, 60.5, 41.8, 41.7, 41.6, 40.7, 32.9, 32.7, 27.24, 27.21, 25.9, 25.8, 20.7, 20.5, 20.0, 19.7, 18.2, 15.4, 15.3, -4.4, -4.6 ppm; HRMS (ES+) calcd. for $C_{33}H_{56}O_6SSiNa$ (M+Na) 631.3465, found 631.3459.



Dienyl Sulfone 81: To a stirred solution of TBS ether **SI-48** (401 mg, 0.658 mmol) in THF (6.7 mL) at rt was added TBAF (2.0 mL, 2.00 mmol, 1 M in THF). After 12 h, the reaction quenched with H_2O (25 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude alcohol **SI-49**.

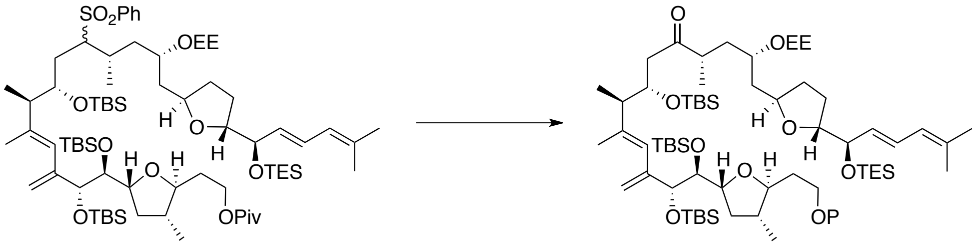
To a stirred solution of crude alcohol **SI-49** in CH_2Cl_2 (8.7 mL) at 0 °C were sequentially added Et_3N (523 mg, 0.73 mL, 5.17 mmol), DMAP (39.1 mg, 0.323 mmol) and TESCl (341 mg, 0.38 mL, 2.26 mmol). The reaction was slowly warmed to rt over 2 h. After another 3 h, the reaction was quenched with sat. aq. NH_4Cl (25 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give dienyl sulfone **81** (379 mg, 0.622 mmol, 95%) as colorless oil. $[\alpha]_D^{23}$ = +18.0 (c = 1.00, C_6H_6); IR: (neat) 2957, 2913, 2876, 1446, 1377, 1308, 1148, 1086, 1018, 959, 841, 741, 689 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-

796 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 6.42-6.46 (m, 1H (2 diastereomers of E isomer)), 6.21 (t, *J* = 11.3 Hz, 1H of Z isomer), 6.07-6.09 (m, 1H of Z isomer)), 5.82 (d, *J* = 11.0 Hz, 1H (2 diastereomers of E isomer)), 5.52 (ddd, *J* = 15.0, 6.1, 3.0 Hz, 1H (2 diastereomers of E isomer)), 5.29 (q, *J* = 10.2 Hz, 1H of Z isomer), 4.66 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.63 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.46-4.48 (m, 1H of Z isomer), 4.15 (t, *J* = 5.6 Hz, 1H (2 diastereomers)), 3.86-3.94 (m, 2H (2 diastereomers)), 3.78-3.82 (m, 1H (1 diastereomer)), 3.67-3.70 (m, 1H (1 diastereomer)), 3.60 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.53 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.41-3.47 (m, 1H (2 diastereomers)), 3.25 (dd, *J* = 14.2, 4.7 Hz, 1H (1 diastereomer)), 3.17 (dd, *J* = 14.2, 4.4 Hz, 1H (1 diastereomer)), 2.94-2.98 (m, 1H (2 diastereomers)), 2.31-2.36 (m, 1H (1 diastereomer)), 2.20-2.26 (m, 1H (1 diastereomer)), 1.92-1.98 (m, 1H (2 diastereomers)), 1.84-1.91 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.68-1.75 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.57-1.65 (m, 1H (2 diastereomers)), 1.38-1.53 (m, 3H (2 diastereomers)), 1.24 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.22 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.19 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.17 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.148 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.147 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.96 (t, *J* = 8.0 Hz, 9H (2 diastereomers)), 0.61 (q, *J* = 7.9 Hz, 6H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 140.2, 140.0, 135.13, 135.11, 133.5, 133.3, 129.96, 129.95, 129.2, 129.1, 128.0, 127.9, 127.54, 127.53, 124.6, 99.8, 98.0, 82.1, 82.0, 76.0, 75.68, 75.63, 72.8, 71.1, 63.17, 63.10, 60.6, 60.5, 41.9, 41.7, 41.6, 40.7, 32.9, 32.7, 27.32, 27.30, 25.9, 25.8, 20.6, 20.5, 19.9, 19.7, 18.2, 15.4, 15.3, 6.8, 5.0 ppm; HRMS (ES+) calcd. for $C_{33}H_{56}O_6SSiNa$ (M+Na) 631.3465, found 631.3466.



Coupled Sulfone SI-50: To a stirred solution of sulfone **81** (325 mg, 0.533 mmol) in THF (2.2 mL) at -60 °C was added LHMDS (0.54 mL, 0.540 mmol, 1 M in THF) and warmed to -10 °C over 1 h. HMPA (515 mg, 0.50 mL, 2.87 mmol) was added and the reaction was warmed to 0 °C over 15 min. The reaction was cooled back down to -10 °C and a solution of iodide **9** (188 mg, 0.213 mmol) in THF (2.0 mL and 2 X 0.35 mL wash) was cannulated to it and warmed to 0 °C. After 1.5 h, the cooling bath was removed. After another 1 h, the reaction was quenched with sat. aq. NH$_4$Cl (20 mL) and the aqueous layer was extracted with

Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give diastereomeric coupled sulfone **SI-50** (215 mg, 0.157 mmol, 74%) as colorless oil along with recovered sulfone **81** (191 mg, 0.313 mmol). $[\alpha]_D^{23}$ = -10.0 (*c* = 1.00, C_6H_6); IR (neat): 2956, 2935, 2886, 2862, 1730, 1467, 1382, 1304, 1252, 1148, 1081, 1007, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (four diastereomers)} δ 7.89-7.94 (m, 2H (4 diastereomers)), 7.60-7.65 (m, 1H (4 diastereomers)), 7.52-7.57 (m, 2H (4 diastereomers)), 6.43-6.48 (m, 1H (4 diastereomers)), 5.79 (m, 2H (1H of 2 diastereomers and 1H of 4 diastereomers)), 5.69 (s, 1H (1 diastereomer)), 5.68 (s, 1H (1 diastereomer)), 5.52 (dt, *J* = 15.1, 6.4 Hz, 1H (4 diastereomers)), 5.30-5.33 (m, 1H (4 diastereomers)), 5.05 (s, 1H (1 diastereomer)), 5.01 (s, 1H (1 diastereomer)), 4.88 (s, 1H (1 diastereomer)), 4.86 (s, 1H (2 diastereomers)), 4.66 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.61 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.59 (q, *J* = 5.1 Hz, 1H (1 diastereomer)), 4.49 (q, *J* = 5.1 Hz, 1H (1 diastereomer)), 4.36-4.39 (m, 1H (2 diastereomers)), 4.25-4.29 (m, 1H (4 diastereomers)), 4.07-4.16 (m, 4H (1H of 2 diastereomers and 3H of 4 diastereomers)), 3.96-4.00 (m, 1H (2 diastereomers)), 8.84-3.94 (m, 3H (1H of 2 diastereomers and 2H of 4 diastereomers)), 3.71-3.76 (m, 1H (1 diastereomer)), 3.65-3.69 (m, 1H (1 diastereomer)), 3.52-3.62 (m, 2H (1H of 2 diastereomers + 2H of 4 diastereomers)), 3.43-3.48 (m, 1H (2 diastereomers)), 3.36-3.42 (m, 2H (1H of 2 diastereomers and 1H of 4 diastereomers)), 3.27-3.35 (m, 1H of 2 diastereomers)), 3.10-3.21 (m, 1H (2 diastereomers)), 2.40-2.44 (m, 1H (2 diastereomers)), 2.31-2.34 (m, 1H (2 diastereomers)), 2.14-2.30 (m, 1H (4 diastereomers)), 2.00-2.12 (m, 2H (4 diastereomers)), 1.76-1.99 (m, 6H (4 diastereomers)), 1.90 (s, 3H (2 diastereomers)), 1.88 (s, 3H (2 diastereomers)), 1.79 (s, 3H (4 diastereomers)), 1.777 (s, 3H (2 diastereomers)), 1.771 (s, 3H (2 diastereomers)), 1.62-1.71 (m, 3H (4 diastereomers)), 1.36-1.46 (m, 2H (4 diastereomers)), 1.26-1.33 (m, 4H (4 diastereomers)), 1.19-1.23 (m, 13H (4 diastereomers)), 1.13-1.18 (m, 4H (4 diastereomers)), 1.06-1.10 (m, 3H (4 diastereomers)), 0.98-1.01 (m, 3H), 0.95-0.98 (m, 9H (4 diastereomers)), 0.85-0.93 (m, 27H (4 diastereomers)), 0.59-0.63 (m, 6H (4 diastereomers)), 0.03-0.18 (m, 18H (4 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 145.56, 145.50, 145.4, 140.5, 140.2, 140.1, 139.8, 139.6, 139.0, 138.8, 135.1, 135.0, 133.3, 133.2, 133.1, 129.99, 129.97, 129.92, 129.91, 129.2, 129.1, 129.09, 129.06, 128.98, 128.94, 128.3, 125.8, 125.7, 124.79, 124.74, 124.6, 115.33, 115.30, 114.6, 114.5, 100.0, 99.5, 97.8, 97.7, 82.2, 82.19, 82.11, 80.54, 80.50, 80.3, 79.6, 79.53, 79.51, 79.2, 78.8, 78.7, 78.6, 76.28, 76.23, 76.18, 76.10, 75.8, 75.79, 75.75, 75.6, 72.4, 72.3, 72.0, 71.4, 71.1, 70.8, 70.6, 66.3, 65.6, 65.5, 62.15, 62.10, 61.1, 60.78, 60.75, 48.5, 48.4, 47.3, 47.0, 42.4, 42.1, 41.7, 41.4, 40.35, 40.32, 39.6, 39.2, 38.6, 38.1, 38.0, 35.8, 35.2, 33.1, 33.0, 32.8, 32.68, 32.63, 31.9, 29.7, 29.4, 29.3, 29.2, 28.8, 28.78, 28.71, 28.6, 27.6, 27.59, 27.54, 27.4, 27.2, 26.1, 26.0, 25.97, 25.91, 20.9, 20.7, 20.6, 20.5, 18.4, 18.3, 18.2, 18.1, 18.0, 17.9, 17.5, 17.2, 16.0, 15.9, 15.5, 15.4, 15.2, 11.7, 11.3, 6.93, 6.91, 4.9, -3.8, -4.15, -4.18, -4.2, -4.3, -4.4, -4.5, -4.6, -4.7 ppm; HRMS (ES+) calcd. for $C_{74}H_{136}O_{12}SSi_4Na$ (M+Na) 1383.8727, found 1383.8776.

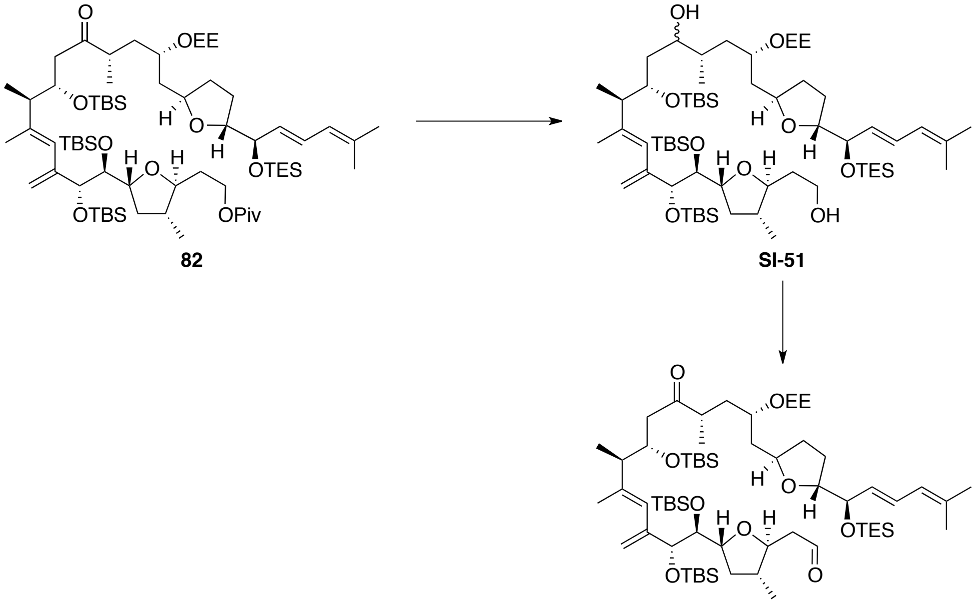


SI-50

82 P = Piv
83 P = H

Ketone 82 and **Alcohol 83**: To a stirred solution of sulfone **SI-50** (173.4 mg, 0.127 mmol) in THF (2.2 mL) at -50 °C was added LDA[10] (0.32 mL, 0.320 mmol, 1 M in THF / hexanes). After 5 min, DMPU (1.27 g, 1.2 mL, 9.88 mmol) was added and was slowly warmed to -25 °C over 20 min. The reaction was cooled back down to -50 °C and a solution of Davis' oxaziridine[19] (91.4 mg, 0.350 mmol) in THF (1.0 mL) was cannulated to it. The reaction was warmed to -35 °C over 20 min and then quenched with sat. aq. NH_4Cl (20 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 6-20% EtOAc / hexanes, to give the ketone **82** (66.0 mg, 53.4 µmol, 42%) and keto-ol **83** (33.6 mg, 29.2 µmol, 23%) as colorless oil along with the recovered sulfone **SI-50** (49.9 mg, 36.6 µmol, 29%). Ketone **82**: $[\alpha]_D^{23}$ = +30.0 (*c* = 1.03, C_6H_6); IR (neat): 2956, 2932, 2859, 1731, 1719, 1461, 1377, 1251, 1078, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 6.43-6.48 (m, 1H (2 diastereomers)), 5.83 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.59 (s, 1H (2 diastereomers)), 5.53 (ddd, *J* = 15.1, 6.0, 3.2 Hz, 1H (2 diastereomers)), 5.32 (s, 1H (2 diastereomers)), 4.96 (s, 1H (2 diastereomers)), 4.65-4.68 (m, 1H (2 diastereomers)), 4.35-4.37 (m, 1H (2 diastereomers)), 4.24-4.28 (m, 1H (2 diastereomers)), 4.10-4.16 (m, 2H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 3.89-3.97 (m, 3H (2 diastereomers)), 3.74-3.78 (m, 1H (1 diastereomer)), 3.57-3.67 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.45-3.53 (m, 2H (2 diastereomers)), 3.33 (dt, *J* = 9.2, 2.7 Hz, 1H (2 diastereomers)), 2.77 (qd, *J* = 7.4, 4.3 Hz , 1H (1 diastereomer)), 2.57-2.66 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.54 (dd, *J* = 5.6, 3.5 Hz, 1H (1 diastereomer)), 2.51 (dd, *J* = 5.6, 3.5 Hz, 1H (1 diastereomer)), 2.36-2.41 (m, 1H (2 diastereomers)), 2.03-2.07 (m, 1H (2 diastereomers)), 1.94-2.01 (m, 2H (2 diastereomers)), 1.80-1.91 (m, 3H (2 diastereomers)), 1.81 (s, 3H (2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.63-1.71 (m, 2H (2 diastereomers)), 1.48-1.52 (m, 1H (2 diastereomers)), 1.37-1.46 (m, 2H (2 diastereomers)), 1.26-1.30 (m, 4H (2 diastereomers)), 1.19-1.22 (m, 12H (2 diastereomers)), 1.08 (d, *J* = 7.0 Hz, 3H (2 diastereomers)), 1.05 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 1.04 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 0.98 (d, *J* = 6.4 Hz, 3H (2 diastereomers)), 0.97 (t, *J* = 7.9 Hz, 3H (2 diastereomers)), 0.907 (s, 9H (2 diastereomers)), 0.905 (s, 9H (1 diastereomer)), 0.904 (s, 9H (1 diastereomer)), 0.892 (s, 9H (1 diastereomer)), 0.890 (s, 9H (1 diastereomer)), 0.61 (q, *J* = 7.9 Hz, 6H (2 diastereomers)), 0.113 (s, 3H (1 diastereomer)), 0.111

(s, 3H (1 diastereomer)), 0.08 (s, 3H (2 diastereomers)), 0.06 (s, 3H (2 diastereomers)), 0.04 (s, 3H (1 diastereomer)), 0.03 (s, 3H (1 diastereomer)), 0.02 (s, 3H (2 diastereomers)), 0.007 (s, 3H (1 diastereomer)), 0.004 (s, 3H (1 diastereomer)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.1, 212.7, 178.4, 145.1, 140.93, 140.91, 135.16, 135.13, 129.87, 129.83, 127.4, 125.4, 124.6, 115.04, 115.00, 99.8, 98.8, 98.4, 82.19, 82.14, 80.45, 80.43, 79.4, 78.8, 78.5, 76.1, 76.0, 75.6, 72.5, 71.3, 70.47, 70.40, 62.1, 61.3, 61.1, 47.9, 47.8, 45.5, 45.4, 43.0, 42.8, 41.8, 41.2, 40.3, 38.6, 38.0, 37.0, 36.9, 33.1, 32.9, 32.7, 29.7, 27.4, 27.2, 26.1, 26.0, 25.97, 25.90, 20.8, 20.7, 18.4, 18.36, 18.30, 17.9, 17.1, 17.0, 16.1, 16.0, 15.7, 15.4, 15.3, 14.1, 14.0, 6.9, 4.9, -4.23, -4.26, -4.44, -4.46, -4.7, 4.8 ppm; HRMS (ES+) calcd. for $C_{68}H_{130}O_{11}Si_4Na$ (M+Na) 1257.8588, found 1257.8564.



82

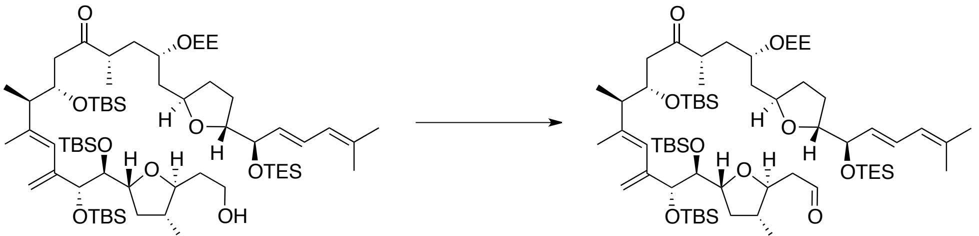
SI-51

84

Aldehyde 84: To a stirred solution of pivalate **82** (46.2 mg, 37.3 μmol) in Et_2O (2.7 mL) at -20 °C was added $LiAlH_4$ (3.6 mg, 93.4 μmol) in one portion. After 25 min, the reaction was quenched with H_2O (10 drops) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude diol **SI-51**.

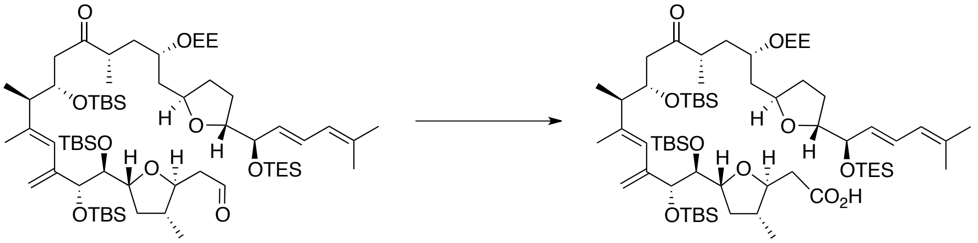
To a stirred solution of oxalyl chloride (23.7 mg, 16.5 μL, 0.187 mmol) in CH_2Cl_2 (1.0 mL) at -78 °C was cannulated a solution of DMSO (29.2 mg, 27 μL, 0.374 mmol) in CH_2Cl_2 (0.50 mL). After 20 min, a solution of crude diol **SI-51** in CH_2Cl_2 (1.2 mL and 2 X 0.25 mL wash) was cannulated to it. After 45 min, Et_3N (37.8 mg, 53 μL, 0.374 mmol) was added. After 10 min, the reaction was quenched with H_2O (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **84** (35.6 mg, 30.9 μmol, 83%) as colorless oil. $[\alpha]_D^{23}$ = +14.9 (*c* = 0.35, C_6H_6); IR: (neat) 2959, 2927, 2857, 1732, 1710, 1662, 1635, 1465, 1380, 1078, 835, 781 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 9.82 (dd, *J* =

2.9, 2.3 Hz, 1H (2 diastereomers)), 6.44-6.48 (m, 1H (2 diastereomers)), 5.83 (d, J = 11.0 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (2 diastereomers)), 5.53 (ddd, J = 15.1, 6.0, 3.2 Hz, 1H (2 diastereomers)), 5.32 (t, J = 1.7 Hz, 1H (2 diastereomers)), 4.97 (s, 1H (2 diastereomers)), 4.68 (q, J = 5.2 Hz, 1H (1 diastereomer)), 4.66 (q, J = 5.2 Hz, 1H (1 diastereomer)), 4.37-4.39 (m, 1H (2 diastereomers)), 4.16 (t, J = 5.9 Hz, 1H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 3.99-4.02 (m, 1H (2 diastereomers)), 3.89-3.97 (m, 1H (2 diastereomers)), 3.75-3.78 (m, 1H (1 diastereomer)), 3.73 (td, J = 3.5 Hz, 1H (2 diastereomers)), 3.58-3.67 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.54 (dt, J = 7.1, 2.5 Hz, 1H (2 diastereomers)), 3.45-3.52 (m, 1H (2 diastereomers)), 2.76-2.81 (m, 1H (1 diastereomer)), 2.59-2.68 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.57 (dd, J = 3.4, 2.3 Hz, 1H (1 diastereomer)), 2.55 (dd, J = 3.4, 2.3 Hz, 1H (1 diastereomer)), 2.47-2.52 (m, 2H (2 diastereomers)), 2.38-2.42 (m, 1H (2 diastereomers)), 2.06-2.10 (m, 1H (2 diastereomers)), 1.95-2.01 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.84-1.90 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.83 (s, 3H (2 diastereomers)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.65-1.72 (m, 1H (2 diastereomers)), 1.48-1.53 (m, 1H (2 diastereomers)), 1.38-1.46 (m, 2H (2 diastereomers)), 1.296 (d, J = 5.2 Hz, 3H (1 diastereomer)), 1.291 (d, J = 5.2 Hz, 3H (1 diastereomer)), 1.22 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.21 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.09 (d, J = 7.0 Hz, 3H (2 diastereomers)), 1.06 (d, J = 6.9 Hz, 3H (1 diastereomer)), 1.05 (d, J = 6.9 Hz, 3H (1 diastereomer)), 1.02 (d, J = 6.5 Hz, 3H (2 diastereomers)), 0.97 (t, J = 7.9 Hz, 3H (2 diastereomers)), 0.913 (s, 9H (1 diastereomer)), 0.912 (s, 9H (1 diastereomer)), 0.897 (s, 9H (2 diastereomers)), 0.896 (s, 9H (2 diastereomers)), 0.62 (q, J = 7.9 Hz, 6H (2 diastereomers)), 0.12 (s, 3H (1 diastereomer)), 0.11 (s, 3H (1 diastereomer)), 0.08 (s, 3H (2 diastereomers)), 0.04 (s, 6H (2 diastereomers)), 0.028 (s, 3H (2 diastereomers)), 0.025 (s, 3H (2 diastereomers)), 0.01 (s, 3H (1 diastereomer)), 0.007 (s, 3H (1 diastereomer)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.0, 212.6, 202.1, 145.0, 141.1, 141.0, 135.1, 135.0, 129.9, 129.8, 127.5, 127.4, 125.2, 124.6, 115.1, 115.0, 99.8, 98.4, 82.2, 82.1, 79.9, 79.8, 79.3, 78.66, 78.60, 76.1, 76.0, 75.6, 72.6, 71.3, 70.4, 70.3, 61.3, 61.1, 48.0, 47.9, 47.6, 45.4, 45.3, 43.1, 42.8, 41.8, 41.2, 40.6, 37.5, 37.1, 36.9, 32.9, 32.7, 29.7, 27.4, 26.1, 26.0, 25.95, 25.91, 25.89, 20.8, 20.7, 18.4, 18.3, 18.2, 17.9, 17.26, 17.24, 16.1, 15.7, 15.6, 15.4, 15.3, 14.0, 13.9, 6.9, 4.9, -4.1, -4.2, -4.45, -4.46, -4.7, -4.8 ppm; HRMS (ES+) calcd. for $C_{63}H_{120}O_{10}Si_4Na$ (M+Na) 1171.7856, found 1171.7769.



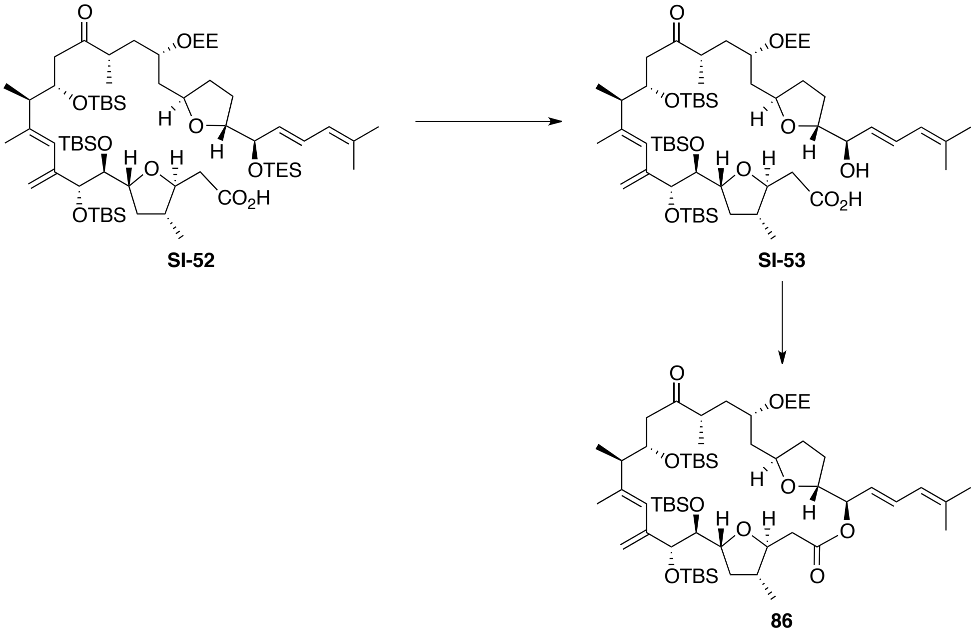
83 **84**

Aldehyde 84: To a stirred solution of oxalyl chloride (10.4 mg, 7.2 µL, 82.4 µmol) in CH_2Cl_2 (0.50 mL) at -78 °C was cannulated a solution of DMSO (12.9 mg, 11.8 µL, 0.165 mmol) in CH_2Cl_2 (0.25 mL). After 15 min, a solution of alcohol **83** (19.0 mg, 16.5 µmol) in CH_2Cl_2 (0.50 mL and 2 X 0.10 mL wash) was cannulated to it. After 45 min, Et_3N (16.7 mg, 24 µL, 0.165 mmol) was added. After 10 min, the reaction was quenched with H_2O (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **84** (15.8 mg, 13.7 µmol, 83%) as colorless oil.



84 **SI-52**

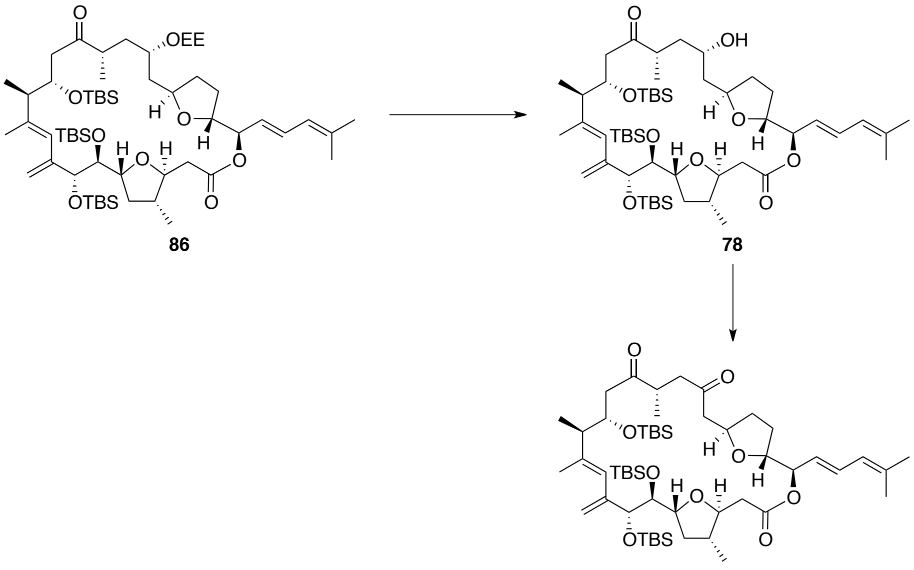
Carboxylic Acid SI-52: To a stirred solution of aldehyde **84** (35.6 mg, 30.9 µmol) in *t*-BuOH/H_2O (1:1, 3.0 mL) at 0 °C were sequentially added 2-methyl-2-butene (108 mg, 0.16 mL, 1.54 mmol), $NaH_2PO_4 \cdot H_2O$ (42.7 mg, 0.309 mmol) and $NaClO_2$ (14.1 mg, 0.154 mmol). After 15 min, the reaction was warmed to rt. After another 1.5 h, the reaction was diluted with H_2O (7.5 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30 % EtOAc / hexanes, to give carboxylic acid **SI-52** (30.7 mg, 26.3 µmol, 85%) as light yellow oil. $[\alpha]_D^{23} = +23.4$ ($c = 0.87$, C_6H_6); IR (neat): 3385, 2959, 2930, 2886, 2862, 1713, 1465, 1382, 1252, 1084, 1005, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 10.00 (bs, 1H (2 diastereomers)), 6.43-6.48 (m, 1H (2 diastereomers)), 5.83 (d, $J = 10.9$ Hz, 1H (2 diastereomers)), 5.60 (s, 1H (1 diastereomer)), 5.59 (s, 1H (1 diastereomer)), 5.53 (ddd, $J = 15.1, 6.0, 2.8$ Hz, 1H (2 diastereomers)), 5.36 (t, $J = 1.8$ Hz, 1H (1 diastereomer)), 5.35 (t, $J = 1.7$ Hz, 1H (1 diastereomer)), 5.00 (s, 1H (2 diastereomers)), 4.68 (q, $J = 5.2$ Hz, 1H (1 diastereomer)), 4.66 (q, $J = 5.2$ Hz, 1H (1 diastereomer)), 4.41-4.44 (m, 1H (1 diastereomer)), 4.36-4.38 (m, 1H (1 diastereomer)), 4.17 (t, $J = 5.4$ Hz, 1H (1 diastereomer)), 4.16 (t, $J = 5.3$ Hz, 1H (1 diastereomer)), 4.10-4.13 (m, 2H (2 diastereomers)), 3.89-3.98 (m, 2H (2 diastereomers)), 3.76-3.80 (m, 1H (1 diastereomer)), 3.61-3.68 (m, 2H (2 diastereomers)), 3.52-3.60 (m, 2H (2 diastereomers)), 3.46-3.50 (m, 1H (1 diastereomer)), 2.78-2.83 (m, 1H (1 diastereomer)), 2.58-2.70 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 2.39-2.54 (m, 3H (2 diastereomers)), 2.10-2.14 (m, 1H (2 diastereomers)), 1.94-2.01 (m, 2H (2 diastereomers)), 1.81-1.93 (m, 3H (2 diastereomers)), 1.83 (d, J = 1.0 Hz, 3H (1 diastereomer)), 1.82 (d, J = 1.0 Hz, 3H (1 diastereomer)), 1.79 (s, 3H (2 diastereomers)), 1.77 (s, 3H (2 diastereomers)), 1.66-1.73 (m, 1H (2 diastereomers)), 1.48-1.53 (m, 1H (2 diastereomers)), 1.36-1.47 (m, 2H (2 diastereomers)), 1.27-1.34 (m, 4H (2 diastereomers)), 1.22 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.21 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.104 (d, J = 7.0 Hz, 3H (1 diastereomer)), 1.102 (d, J = 7.0 Hz, 3H (1 diastereomer)), 1.05 (d, J = 6.9 Hz, 3H (2 diastereomers)), 1.03 (d, J = 6.5 Hz, 3H (1 diastereomer)), 1.01 (d, J = 6.5 Hz, 3H (1 diastereomer)), 0.97 (t, J = 7.9 Hz, 3H (2 diastereomers)), 0.89-0.92 (m, 27H (4 diastereomers)), 0.62 (q, J = 7.9 Hz, 6H (2 diastereomers)), 0.01-0.12 (m, 18H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.0, 212.6, 172.0, 144.9, 141.5, 141.4, 135.16, 135.10, 129.88, 129.82, 127.5, 125.1, 124.8, 124.6, 115.1, 114.7, 99.7, 98.5, 82.2, 82.1, 80.2, 80.16, 80.11, 78.9, 78.7, 78.0, 76.17, 76.12, 75.6, 75.5, 72.5, 71.2, 70.4, 70.2, 61.7, 61.1, 47.8, 47.7, 45.4, 45.1, 43.1, 42.7, 41.8, 41.2, 39.8, 37.9, 37.7, 37.58, 37.55, 37.1, 36.9, 32.9, 32.6, 29.7, 27.4, 26.09, 26.01, 25.9, 25.8, 20.8, 20.7, 18.3, 18.2, 17.9, 17.2, 17.1, 16.1, 15.69, 15.65, 15.5, 15.39, 15.34, 14.1, 13.8, 6.9, 4.9, -3.9, -4.40, -4.43, -4.47, -4.71, -4.74, -4.78 ppm; HRMS (ES+) calcd. for $C_{63}H_{120}O_{11}Si_4Na$ (M+Na) 1187.7805, found 1187.7740.



Macrolactone 86: To a stirred solution of carboxylic acid **SI-52** (30.7 mg, 26.3 μmol) in dry MeOH (2.5 mL) at 0 °C was added methanolic PPTS solution (50 μL).[20] After 15 min, the reaction was warmed to rt. After another 35 min, the reaction was quenched with sat. aq. $NaHCO_3$ (8 mL) and the aqueous layer was

extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude seco-acid **SI-53**.

To a stirred solution of crude seco-acid **SI-53** in THF (1.0 mL) at 0 °C were added Et_3N (4.7 mg, 6.6 µL, 46.7 µmol) followed by 2,4,6-trichlorobenzoylchloride **85** (7.6 mg, 4.9 µL, 31.1 µmol). After 45 min, the reaction was diluted with toluene (1.8 mL). In a separate flask, a solution of DMAP (5.7 mg, 46.7 µmol) in toluene (7.0 mL) was warmed to 70 °C and the solution of mixed acid anhydride was added dropwise over 6 h to it. After another 30 min, the reaction was cooled down to rt and was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give macrolactone **86** (17.7 mg, 17.1 µmol, 65%) as colorless oil. $[\alpha]_D^{23} = +2.0$ (*c* = 1.00, $CHCl_3$); IR: (neat) 2959, 2930, 2859, 1745, 1708, 1465, 1384, 1255, 1090, 837, 778 cm^{-1}; ^{1}H NMR {700 MHz, $CDCl_3$ (***Note:*** *NMR analysis indicated that compound **86** exists as a mixture of conformational isomers*)} δ 6.52-6.56 (m, 1H (2 diastereomers)), 6.17 (s, 1H (1 diastereomer)), 6.16 (s, 1H (1 diastereomer)), 5.78 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.35-5.38 (m, 1H (2 diastereomers)), 5.00 (s, 1H (1 diastereomer)), 4.98 (s, 1H (1 diastereomer)), 4.95 (t, *J* = 8.3 Hz, 1H (2 diastereomers)), 4.91 (s, 1H (1 diastereomer)), 4.70 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.20 (s, 1H (1 diastereomer)), 4.19 (s, 1H (1 diastereomer)), 3.96-4.05 (m, 2H (2 diastereomers)), 3.89-3.94 (m, 2H (2 diastereomers)), 3.54-3.76 (m, 4H (2 diastereomers)), 2.95-3.05 (m, 1H (2 diastereomers)), 2.71-2.75 (m, 1H (1 diastereomer)), 2.59-2.63 (m, 1H (1 diastereomer)), 2.45-2.51 (m, 2H (2 diastereomers)), 2.27-2.38 (m, 2H (2 diastereomers)), 2.11 (br s, 1H (2 diastereomers)), 2.04-2.07 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.91-1.99 (m, 2H (2 diastereomers)), 1.85-1.89 (m, 1H (1 diastereomer)), 1.70-1.81 (m, 10H (2 diastereomers)), 1.49-1.60 (m, 4H (2 diastereomers)), 1.28-1.34 (m, 5H (2 diastereomers)), 1.23 (t, *J* = 7.0 Hz, 3H (2 diastereomers)), 1.08-1.13 (m, 6H (2 diastereomers)), 1.03-1.05 (m, 3H (2 diastereomers)), 0.91 (s, 18H (2 diastereomers)), 0.85 (s, 9H (2 diastereomers)), 0.02-0.11 (m, 18H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 212.0, 211.6, 170.49, 170.45, 146.4, 146.3, 140.83, 140.80, 137.6, 137.5, 131.26, 131.22, 129.0, 125.05, 125.01, 124.2, 114.36, 114.33, 99.7, 97.8, 81.8, 80.0, 79.2, 79.1, 78.8, 78.20, 78.17, 77.7, 77.6, 75.5, 75.2, 71.7, 71.6, 70.2, 62.2, 61.7, 56.0, 47.2, 47.1, 46.2, 42.5, 41.8, 41.7, 40.78, 40.74, 39.88, 39.80, 38.79, 38.73, 34.7, 34.5, 32.7, 31.9, 30.3, 30.2, 29.4, 29.2, 29.0, 26.5, 26.1, 25.9, 25.8, 22.7, 21.2, 21.0, 18.7, 18.58, 18.52, 17.9, 16.6, 16.4, 16.3, 16.2, 16.0, 15.6, 15.2, 14.1, -3.9, -4.0, -4.4, -4.5, -4.6, -4.7, -4.8, -5.4, -5.5 ppm; HRMS (ES+) calcd. for $C_{57}H_{104}O_{10}Si_3Na$ (M+Na) 1055.6835, found 1055.6757.



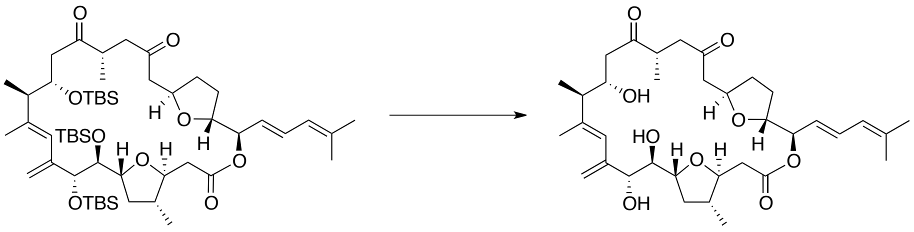
86

78

87

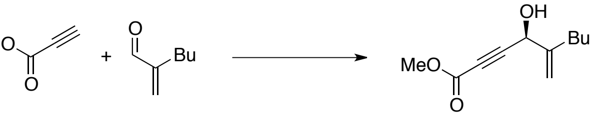
Diketone 87: The macrolactone **86** (6.8 mg, 6.57 µmol) in THF/AcOH/H_2O (0.78 mL, 4:4:1) was stirred at rt. After 20 h, the reaction was quenched with sat. aq. $NaHCO_3$ (5 mL) and the aqueous layer was extracted with EtOAc / Et_2O (2:1, 3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude alcohol **78**.

To a stirred solution of crude alcohol **78** in CH_2Cl_2 (1.0 mL) at 0 °C were added pyridine (10.4 mg, 10.7 µL, 0.131 mmol) followed by Dess-Martin Periodinane (16.7 mg, 39.5 µmol). After 15 min, the reaction was warmed to rt. After another 2.45 h, the reaction was quenched with sat. aq. $NaHCO_3$ (mL) and the aqueous layer was extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give diketone **87** (3.9 mg, 4.06 µmol, 62%) as colorless oil: $[\alpha]_D^{23}$ = +0.92 (*c* = 0.55, $CHCl_3$); IR: (neat) 2959, 2929, 2860, 1740, 1708, 1662, 1632, 1467, 1387, 1258, 1098, 1045, 838, 781 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (***Note:** NMR analysis indicated that compound **87** exists as a mixture of conformational isomers*)} δ 6.54 (dd, *J* = 15.2, 11.0 Hz, 1H), 6.01 (br s, 0.5H), 5.77 (br d, *J* = 11.0 Hz, 1H), 5.57-5.68 (br m, 0.2H), 5.36-5.47 (br m, 1.3H), 5.12 (br s, 1H), 5.05 (br s, 1H), 4.95 (br s, 1H), 4.42-4.61 (br m, 1H), 4.25 (br s, 1H), 3.91-4.06 (br m, 3H), 3.71 (br s, 0.7H), 3.55 (br s, 1.3H), 2.98 (br s 1H), 2.84-2.87 (br m, 1H), 2.73 (br s, 1H), 2.60 (dd, *J* = 14.3, 3.3 Hz, 1H), 2.43 (br s, 4H), 2.17 (br s, 1H), 2.00 (br s, 2H), 1.86-1.94 (m, 2H), 1.79 (br s, 3H), 1.78 (s, 3H), 1.77 (s, 3H)1.62-1.65 (m, 1H), 1.52-1.58 (m, 2H), 1.22-1.27 (m, 1H), 1.14 (br s, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.03 (br s, 3H), 0.90 (s, 27H), 0.03-0.09 (m, 18H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 211.0, 207.5, 170.5, 146.3, 140.7, 140.3, 137.87, 137.80, 131.6, 128.6, 124.7, 124.2, 114.7, 113.7, 81.4, 80.0, 79.5, 78.7, 75.2, 71.6, 50.4, 46.7, 46.3, 42.8, 41.1, 40.6, 39.8, 38.3, 36.6, 32.2, 28.5, 26.4, 26.06, 26.01, 25.8, 18.5, 18.4, 17.7, 16.5, 15.9, 15.6, -4.1, -4.6, -4.8; HRMS (ES+) calcd. for $C_{53}H_{94}O_9Si_3Na$ (M+Na) 981.6103, found 981.6069.



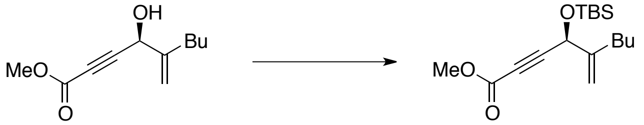
87 amphidinolide F (**4**)

Amphidinolide F (**4**)**:** To a solution of tri-TBS ether **87** (3.9 mg, 4.06 μmol) in CH_3CN (0.60 mL) at rt was added $Et_3N{\bullet}3HF$ (0.48 mL) followed by Et_3N (0.41 mL). After 7 d, the reaction was diluted with EtOAc (15 mL) and poured into sat. aq. solution of $NaHCO_3$ (7 mL) and the aqueous layer was extracted with EtOAc (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 1-5% MeOH / EtOAc, to give amphidinolide F (**4**) (1.4 mg, 2.27 μmol, 56%) as pale yellow amorphous solid. $[\alpha]_D^{23} = -49.0$ (c = 0.10, $CHCl_3$), {lit.[17] $[\alpha]_D^{30} = -57$ (c = 0.10, $CHCl_3$)}; ^1H NMR {700 MHz, $CDCl_3$ (***Note:*** *NMR data is concentration dependent, data reported below is for 1.4 mg of* ***4*** *in 0.18 mL of* $CDCl_3$*)*} δ 6.55 (dd, J = 14.9, 11.0 Hz, 1H), 6.02 (br s, 1H), 5.79 (br d, J = 11.0 Hz, 1H), 5.37 (dd, J = 15.0, 8.4 Hz, 1H), 5.22 (t, J = 8.2 Hz, 1H), 5.20 (d, J = 1.3 Hz, 1H), 4.98 (br s, 1H), 4.35-4.39 (m, 1H), 4.15 (br s, 1H), 4.11 (dd, J = 14.9, 7.3 Hz, 1H), 4.01 (br s, 1H), 3.97 (br t, J = 9.0 Hz, 1H), 3.85-3.88 (m, 1H), 3.84 (dt, J = 9.5, 2.6 Hz, 1H), 3.80 (br t, J = 7.8 Hz, 1H), 3.56 (br s, 2H), 3.13-3.18 (m, 1H), 3.08 (dd, J = 17.5, 8.9 Hz, 1H), 2.77 (dd, J = 15.2, 9.1 Hz, 1H), 2.74 (dd, J = 15.8, 8.4 Hz, 1H), 2.49-2.58 (m, 4H), 2.34-2.38 (m, 1H), 2.28-2.32 (m, 1H), 2.09-2.14 (m, 2H), 1.94-1.98 (m, 1H), 1.81-1.86 (m, 1H), 1.79 (s, 3H), 1.78 (s, 3H), 1.74 (d, J = 1.1 Hz, 3H), 1.47-1.54 (m, 2H), 1.36-1.40 (m, 1H), 1.12 (d, J = 7.2 Hz, 3H), 1.06 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.5 Hz, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.77, 207.77, 171.22, 144.45, 140.04, 138.29, 132.06, 124.52, 124.19, 124.04, 116.11, 81.45, 79.90, 78.94, 77.84, 76.51(2C), 75.01, 70.62, 49.38, 48.57, 46.03, 45.55, 42.79, 39.79, 38.70, 36.77, 31.98, 28.43, 26.08, 18.51, 16.24, 15.53, 15.40, 13.77; HRMS (ES+) calcd. for $C_{35}H_{53}O_9$ (M+H) 617.3690, found 617.3685.



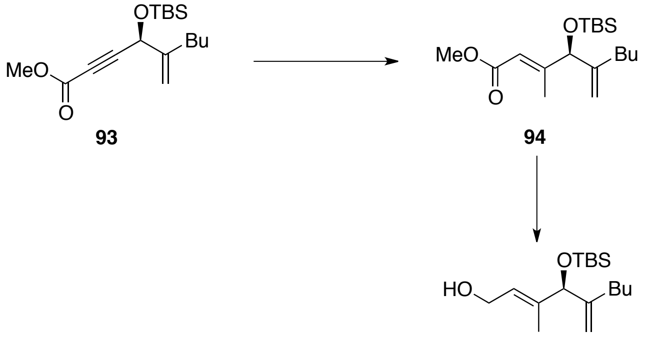
90 **89** **92**

Alcohol 92: To a stirred solution of Me_2Zn (14.3 mL, 17.1 mmol, 1.2 M in toluene) in toluene (29.5 mL) at rt was added methyl propiolate **90** (1.36 g, 1.45 mL, 16.2 mmol) and then was left without stirring. After 90 min, the reaction was cannulated to another flask containing the Trost prophenol ligand **91**[23] (62.9 mg, 0.098 mmol). After 10 min, aldehyde **89**[24] (650 g, 0.78 mL, 5.79 mmol) was added and the reaction was cooled down to 5 °C. After 24 h, the reaction was quenched by sat. aq. NH_4Cl (40 mL) and extracted with Et_2O (3 X 75 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give propargyl alcohol **92** (988 mg, 5.03 mmol, 87%) as colorless oil. Enatiomeric excess was determined by chiral HPLC {4.6 X 250 mm, Daicel AD column, 99:1 hexanes / *i*-PrOH*,* 0.7 mL min^{-1}, retention times 57.3 min (major) and 63.6 (minor)} to be 92%. $[\alpha]_D^{23}$ = +3.9 (*c* = 1.02, $CHCl_3$); IR (neat) 3428, 2963, 2932, 2868, 2239, 1721, 1439, 1254, 1033, 753 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.32 (s, 1H), 5.04 (s, 1H), 4.96 (d, *J* = 6.6 Hz, 1H), 3.81 (s, 3H), 2.17-2.25 (m, 2H), 2.11 (br d, *J* = 6.6 Hz, 1H), 1.48-1.53 (m, 2H), 1.38 (dq, *J* = 14.8, 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 153.7, 146.3, 112.6, 86.2, 77.1, 65.3, 52.9, 31.5, 29.8, 22.4, 13.9 ppm; HRMS (EI+) calcd. for $C_{11}H_{16}O_3$ (M+) 196.10995, found 196.10942.



92 **93**

TBS Ether 93: To a stirred solution of alcohol **92** (843 mg, 4.29 mmol) in CH_2Cl_2 (60.0 mL) at -78 °C was added 2,6-lutidine (2.77 g, 3.0 mL, 25.8 mmol) followed by TBSOTf (3.45 g, 3.0 mL, 12.9 mmol). After 2.5 h, the reaction was quenched by sat. aq. $NaHCO_3$ (40 mL) and extracted with CH_2Cl_2 (3 X 75 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-6% EtOAc / hexanes, to give TBS ether **93** (1.27 g, 4.09 mmol, 95%) as colorless oil. $[\alpha]_D^{23}$ = -29.6 (*c* = 1.03, $CHCl_3$); IR (neat) 2956, 2931, 2859, 2236, 1721, 1465, 1435, 1250, 1061, 838, 779 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.24 (s, 1H), 4.95 (s, 1H), 4.93 (s, 1H), 3.79 (s, 3H), 2.13-2.22 (m, 2H), 1.49 (dt, *J* = 14.6, 7.8 Hz, 2H), 1.37 (dq, *J* = 15.0, 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.93 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 153.9, 146.8, 111.4, 87.4, 76.2, 65.9, 52.7, 31.0, 29.8, 25.7, 22.4, 18.2, 13.9, -4.7, -5.1 ppm; HRMS (EI+) calcd. for $C_{17}H_{30}O_3Si$ (M+) 310.19643, found 310.19794.

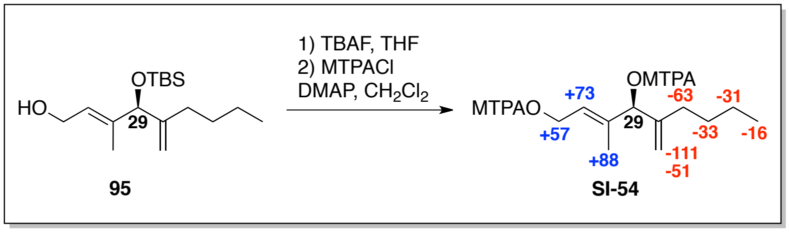


93 **94** **95**

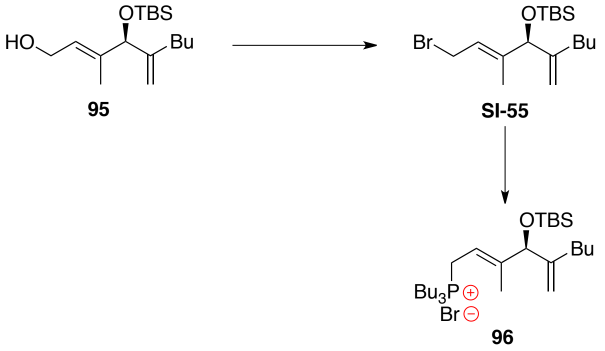
Alcohol 95: To a stirred suspension of CuI (1.01 g, 5.33 mmol) in THF (17.5 mL) at -40 °C was added methyl magnesium bromide (3.6 mL, 10.7 mmol, 3.0 M in Et_2O). After 15 min, the reaction was cooled down to -78 °C. A solution of ester **93** (552 mg, 1.77 mmol) in THF (4.5 ml) was cannulated to it over 15 min. After 3 h, the reaction was allowed to warm to 5 °C over 4 h. The reaction was quenched by half-saturated aq. NH_4Cl (100 mL) and extracted with Et_2O (3 X 45 mL) to give crude addition adduct **94**.

To a stirred solution of crude adduct **94** in Et_2O (32.0 mL) at -10 °C was added $LiAlH_4$ (133 mg, 3.50 mmol) in one portion. After 20 min, the reaction was quenched with dropwise addition of H_2O (2.0 mL) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give alcohol **95** (470 mg, 1.57 mmol, 89%) as colorless oil. $[\alpha]_D^{23}$ = -23.9 (*c* = 1.00, $CHCl_3$); IR (neat) 3319, 2956, 2929, 2858, 1468, 1252, 1073, 1006, 836, 775 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.70 (tt, *J* = 6.7, 1.2 Hz, 1H), 5.14 (br d, *J* = 0.7 Hz, 1H), 4.89 (br s, 1H), 4.41 (s, 1H), 4.23 (t, *J* = 5.6 Hz, 2H), 1.91-1.95 (m, 1H), 1.81-1.86 (m, 1H), 1.53 (s, 3H), 1.38-1.45 (m, 2H), 1.29-1.35 (m, 2H), 1.19 (t, *J* = 5.6 Hz, 1H), 0.92 (s, 9H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 149.3, 139.5, 124.7, 109.9, 80.4, 59.4, 30.7, 30.0, 25.8, 22.6, 18.3, 14.0, 11.5, -4.9, -5.0 ppm; HRMS (ES+) calcd. for $C_{17}H_{35}O_2Si$ (M+H) 299.2406, found 299.2398.

Mosher Ester Analysis[12] for determination of C_{29} Stereochemistry in Alcohol 95.

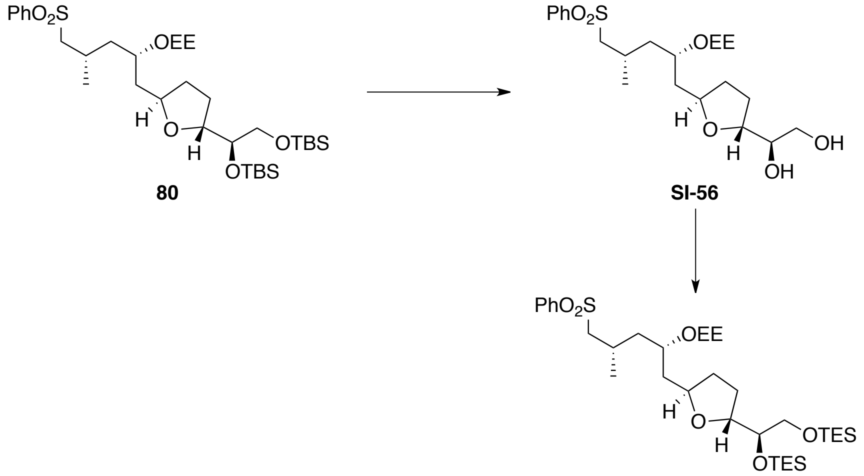


^1H NMR shift differencecs [(S)-MTPA-(R)-MTPA] reported in Hertz (CDCl3, 700 MHz).



Phosphonium Bromide 96: To a stirred solution of alcohol **95** (693 mg, 2.32 mmol) in CH_2Cl_2 (19.0 mL) at 0 °C was added PPh_3 (731 mg, 2.78 mmol) followed by CBr_4 (924 mg, 2.78 mmol). The reaction was allowed to warm to rt over 2.5 h. The reaction quickly passed through a small plug of silica gel, eluting with 2% EtOAc / hexanes, to give bromide **SI-55** as a colorless oil.

To a stirred solution of crude bromide **SI-55** (822 mg, 2.27 mmol) in Et_2O (18.0 mL) at 0 °C was added PBu_3 (1.14 g, 1.4 mL, 5.63 mmol). After 15 min, the reaction was warmed to rt. After 15 h, the reaction filtered through a sintered glass funnel and the residue was washed with hexanes (3 X 25 mL) to give phosphonium bromide **96** (1.20 g, 2.13 mmol, 92%) as white powdered solid. Mp. 52-54 ºC; $[\alpha]_D^{23}$ = +11.9 (*c* = 1.03, $CHCl_3$); IR (neat) 2956, 2929, 2860, 1464, 1251, 1096, 1075, 877, 836, 776 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.45-5.49 (m, 1H), 5.10 (s, 1H), 4.94 (br d, *J* = 1.4 Hz, 1H), 4.43 (d, *J* = 3.5 Hz, 1H), 3.54 (ddd, *J* = 15.5, 15.4, 8.1 Hz, 1H), 3.48 (ddd, *J* = 15.6, 15.5, 8.1 Hz, 1H), 2.46-2.51 (m, 6H), 1.91 (dt, *J* = 15.9, 7.9 Hz, 1H), 1.68-1.71 (m, 4H), 1.51-1.60 (m, 11H), 1.39-1.44 (m, 2H), 1.29-1.34 (m, 2H), 0.99 (t, *J* = 7.0 Hz, 9H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$, ^{31}P coupled) δ 148.5, 145.9, 145.9 (d, *J* = 10.6 Hz), 111.8, 109.1 (d, *J* = 8.8 Hz), 80.5, 29.6 (d, *J* = 38.7 Hz), 25.7, 24.1 (d, *J* = 15.8 Hz), 23.9 (d, *J* = 5.3 Hz), 22.7, 20.2 (d, *J* = 47.5 Hz), 19.1 (d, *J* = 47.5 Hz) 18.2, 14.0, 13.9, 13.5 -4.8, -5.1 ppm. HRMS (ES+) calcd. for $C_{29}H_{60}OPSi$(M-Br) 483.4151, found 483.4127.

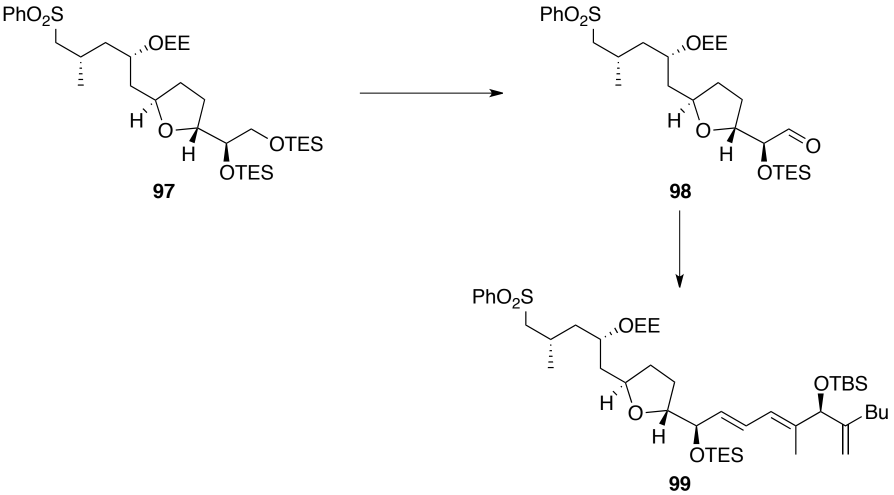


97

TES Ether 97: To a stirred solution of TBS ether **80** (348 mg, 0.517 mmol) in THF (6.6 mL) at 0 ºC was added TBAF (2.1 mL, 2.10 mmol, 1 M in THF) and allowed to warm to rt. After 12 h, the reaction quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude diol **SI-56**.

To a stirred solution of crude diol **SI-56** in CH_2Cl_2 (6.6 mL) at 0 ºC were sequentially added Et_3N (418 mg, 0.58 mL, 4.14 mmol), DMAP (31.3 mg, 0.258 mmol) and TESCl (278 mg, 0.31 mL, 1.81 mmol). After 12 h, the reaction was quenched with sat. aq. NH_4Cl (35 mL) and the aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give TES ether **97** (346 mg, 0.514 mmol, 99%) as colorless oil. $[\alpha]_D^{23}$

= -21.5 (*c* = 1.00, CHCl$_3$); IR (neat) 2954, 2916, 2876, 1462, 1447, 1377, 1309, 1238, 1147, 1086, 1008, 740 cm^{-1}; ^{1}H NMR {700 MHz, CDCl$_3$ (two diastereomers)} δ 7.93-7.96 (m, 2H (2 diastereomers)), 7.64-7.67 (m, 1H (2 diastereomers)), 7.56-7.59 (m, 2H (2 diastereomers)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.62 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.02-4.06 (m, 1H (2 diastereomers)), 3.90-3.96 (m, 1H (2 diastereomers)), 3.79-3.83 (m, 1H (1 diastereomer)), 3.67-3.71 (m, 1H (1 diastereomer)), 3.60-3.65 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.51-3.59 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 3.40-3.47 (m, 1H (2 diastereomers)), 3.23 (dd, *J* = 14.2, 4.7 Hz, 1H (1 diastereomer)), 3.17 (dd, *J* = 14.2, 4.3 Hz, 1H (1 diastereomer)), 2.97 (dd, *J* = 8.2, 5.7 Hz, 1H (1 diastereomer)), 2.95 (dd, *J* = 8.5, 5.9 Hz, 1H (1 diastereomer)), 2.31-2.38 (m, 1H (1 diastereomer)), 2.21-2.26 (m, 1H (1 diastereomer)), 1.97-2.02 (m, 1H (2 diastereomers)), 1.87-1.94 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.78-1.84 (m, 1H (2 diastereomers)), 1.73-1.77 (m, 1H (1 diastereomer)), 1.59-1.63 (m, 1H (1 diastereomer)), 1.54-1.58 (m, 1H (1 diastereomer)), 1.39-1.52 (m, 3H (2 diastereomers)), 1.24 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.21 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.19 (t, *J* = 7.1 Hz, 3H (1 diastereomer)), 1.17 (t, *J* = 7.1 Hz, 3H (1 diastereomer)), 1.148 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.144 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.97 (t, *J* = 8.0 Hz, 18H (1 diastereomer)), 0.96 (t, *J* = 8.0 Hz, 18H (1 diastereomer)), 0.59-0.64 (m, 12H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, CDCl$_3$) δ 140.1, 140.0, 133.5, 133.4, 129.2, 129.1, 128.0, 127.9, 99.9, 98.0, 78.6, 78.5, 76.1, 76.0, 72.9, 71.2, 64.7, 63.2, 63.1, 60.7, 60.5, 41.8, 41.7, 41.5, 40.8, 33.1, 32.9, 27.4, 25.8, 20.7, 20.5, 19.8, 19.6, 15.4, 15.3, 6.9, 6.8, 5.1, 4.3 ppm; HRMS (ES+) calcd. for C$_{34}$H$_{64}$O$_7$SSi$_2$Na (M+Na) 695.3809, found 695.3795.



97

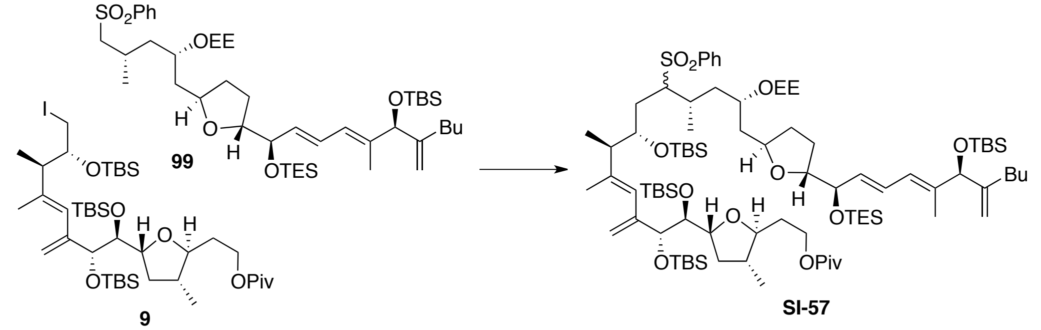
98

99

Trienyl Sulfone 99: To a stirred solution of oxalyl chloride (139 mg, 95.5 μL, 1.09 mmol) in CH$_2$Cl$_2$ (3.0 mL) at -78 ºC was cannulated a solution of DMSO (177 mg, 0.16 mL, 2.18 mmol) in CH$_2$Cl$_2$ (0.6 mL). The reaction was warmed to -50 ºC over 20 min. A solution of alcohol TES ether **97** (294 mg, 0.437 mmol) in

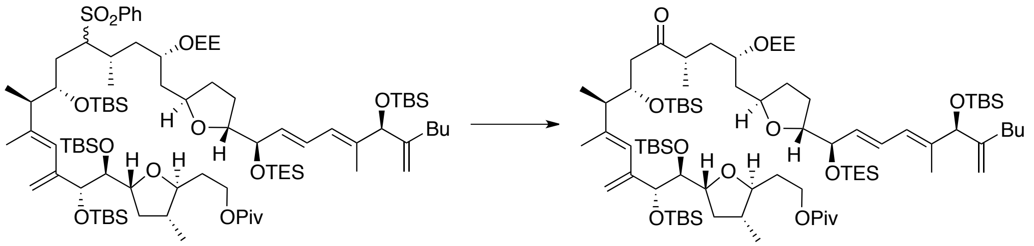
CH_2Cl_2 (2.0 mL and 2 X 0.5 mL wash) was cannulated to it. After 1 h, Et_3N (447 mg, 0.62 mL, 4.37 mmol) was added. After 10 min, the cooling bath was removed and the reaction was quenched with H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 20-40% EtOAc / hexanes, to give aldehyde **98** (177 mg, 0.318 mmol, 73%) as colorless oil.

To a stirred solution of tributyl phosphonium salt **96** (392 mg, 0.695 mmol) in THF (3.7 mL) at -78 °C was added *n*-BuLi (0.28 mL, 0.700 mmol, 2.5 M in hexane) and was warmed to -60 °C. After 1.5 h, the reaction was cooled back down to -78 °C and a solution of aldehyde **98** (177 mg, 0.318 mmol) in THF (3.7 mL and 2 X 0.20 mL wash) was cannulated to it. After 2 h, the reaction was slowly warmed to -5 °C over 2.5 h and then quenched with H_2O (30 mL). The aqueous layer was extracted with Et_2O (3 X 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes, to give trienyl sulfone **99** {251 mg, 0.305 mmol, 96% (10:1 *E:Z*, inseparable mixture)} as colorless oil. $[\alpha]_D^{23}$ = -6.0 (*c* = 1.00, $CHCl_3$); IR: (neat) 2955, 2930, 2875, 1462, 1446, 1377, 1307, 1250, 1148, 1086, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 7.93-796 (m, 2H (2 diastereomers)), 7.64-7.68 (m, 1H (2 diastereomers)), 7.56-7.60 (m, 2H (2 diastereomers)), 6.46 (ddd, *J* = 11.0, 3.3, 1.2 Hz, 1H (1 diastereomer of E isomer)), 6.44 (ddd, *J* = 11.0, 3.3, 1.2 Hz, 1H (1 diastereomer of E isomer)), 6.34 (d, *J* = 11.6 Hz, 2 diastereomers of Z isomer)), isomer)), 6.22-6.26 (m, 1H (2 diastereomers of Z isomer)), 6.06 (d, *J* = 11.0 Hz, 1H (2 diastereomers of E isomer)), 5.66 (dd, *J* = 6.3, 3.9 Hz, 1H (1 diastereomer of E isomer)), 5.64 (dd, *J* = 6.3, 3.9 Hz, 1H (1 diastereomer of E isomer)), 5.38-5.42 (m, 1H (2 diastereomers of Z isomer)), 5.13 (s, 1H (2 diastereomers of E isomer)), 4.89 (s, 1H (2 diastereomers of Z isomer)), 4.87 (s, 1H (2 diastereomers of E isomer)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.63 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.44 (s, 1H (2 diastereomers of Z isomer)), 4.41 (s, 1H (2 diastereomers of E isomer)), 4.14 (t, *J* = 5.8 Hz, 1H (2 diastereomers)), 3.89-3.97 (m, 2H (2 diastereomers)), 3.79-3.83 (m, 1H (1 diastereomer)), 3.67-3.71 (m, 1H (1 diastereomer)), 3.60 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.53 (ddd, *J* = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 3.41-3.48 (m, 1H (2 diastereomers)), 3.25 (dd, *J* = 14.2, 4.7 Hz, 1H (1 diastereomer)), 3.18 (dd, *J* = 14.2, 4.3 Hz, 1H (1 diastereomer)), 2.98 (dd, *J* = 8.1, 6.2 Hz, 1H (1 diastereomer)), 2.96 (dd, *J* = 8.3, 6.4 Hz, 1H (1 diastereomer)), 2.32-2.37 (m, 1H (1 diastereomer)), 2.21-2.26 (m, 1H (1 diastereomer)), 1.94-2.00 (m, 1H (2 diastereomers)), 1.86-1.92 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.74-1.84 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 1.68-1.73 (m, 1H (2 diastereomers)), 1.62-1.67 (m, 1H (2 diastereomers)), 1.59 (d, *J* = 1.0 Hz, 3H (2 diastereomers)), 1.47-1.53 (m, 1H (2 diastereomers)), 1.36-1.46 (m, 4H (2 diastereomers)), 1.27-1.34 (m, 2H (2 diastereomers)), 1.24 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.22 (d, *J* = 5.2 Hz, 3H (1 diastereomer)), 1.20 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.18 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.156 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 1.152 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.960 (t, *J* = 8.0 Hz, 9H (1 diastereomers)), 0.958 (t, *J* = 8.0 Hz, 9H (1 diastereomers)), 0.91 (s, 9H (2 diastereomers)), 0.88-0.92 (m, 3H ((2 diastereomers)), 0.58-0.62 (m, 6H ((2 diastereomers)); ^{13}C NMR (176 MHz, $CDCl_3$) δ 149.6, 140.1, 139.9, 138.56, 138.52, 133.5, 133.4, 132.2, 132.1, 129.2, 129.1, 128.0, 127.9, 127.25, 127.21, 125.2, 109.6, 99.9, 98.0, 82.05, 82.01, 80.6, 76.1, 76.0, 75.8, 72.8, 71.1, 63.1, 63.0, 60.7, 60.5, 41.9, 41.7, 41.6, 40.8, 32.9, 32.6, 30.9, 30.0, 27.4, 25.8, 22.5, 20.6, 20.5, 20.0, 19.7, 18.3, 15.4, 15.3, 14.0, 11.9, 6.9, 4.9, -5.01, -5.04; HRMS (ES+) calcd. for $C_{45}H_{80}O_7SSi_2Na$ (M+Na) 843.5061, found 843.5055.



Coupled Sulfone SI-57: To a stirred solution of sulfone **99** (297 mg, 0.361 mmol) in THF (1.4 mL) at -60 ºC was added LHMDS (0.37 mL, 0.370 mmol, 1 M in THF) and warmed to -10 ºC over 1 h. HMPA (361 mg, 0.35 mL, 2.00 mmol) was added and the reaction was warmed to 0 ºC over 15 min. The reaction was cooled back down to -10 ºC and a solution of iodide **9** (122 mg, 0.138 mmol) in THF (1.5 mL and 2 X 0.15 mL wash) was cannulated to it and warmed to 0 ºC. After 2.5 h, the cooling bath was removed. After another 30 min, the reaction was quenched with sat. aq. NH_4Cl (20 mL) and the aqueous layer was extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give diastereomeric coupled sulfone **SI-57** (183 mg, 0.116 mmol, 84%) along with recovered sulfone **99** (170 mg, 0.207 mmol) as colorless oils. $[\alpha]_D^{23}$ = -3.6 (*c* = 1.00, $CHCl_3$); IR: (neat) 2956, 2928, 2856, 1731, 1462, 1378, 1306, 1251, 1146, 1076, 835 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (four diastereomers)} δ 7.89-7.94 (m, 2H (4 diastereomers)), 7.60-7.65 (m, 1H (4 diastereomers)), 7.52-7.58 (m, 2H (4 diastereomers)), 6.43-6.48 (m, 1H (4 diastereomers)), 6.07 (d, *J* = 10.5 Hz, 1H (2 diastereomers)), 6.06 (d, *J* = 10.8 Hz, 1H (2 diastereomers)), 5.81 (s, 1H (1 diastereomer)), 5.79 (s, 1H (1 diastereomer)), 5.68 (s, 1H (1 diastereomer)), 5.67 (s, 1H (1 diastereomer)), 5.64 (dd, *J* = 15.1, 6.5 Hz, 1H (4 diastereomers)), 5.32 (s, 1H (2 diastereomers)), 5.31 (s, 1H (2 diastereomers)), 5.13 (s, 1H (4 diastereomers)), 5.06 (s, 1H (1 diastereomer)), 5.01 (s, 1H (1 diastereomer)), 4.87 (s, 2H (1H of 2 diastereomers and 1H of 4 diastereomers)), 4.66 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.62 (q, *J*

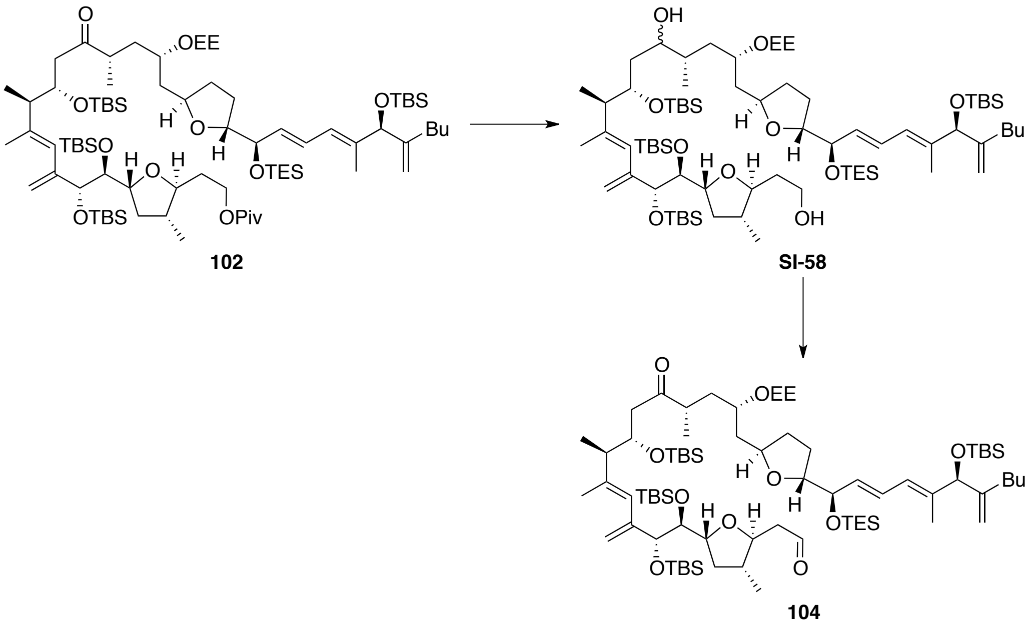
= 5.2 Hz, 1H (1 diastereomer)), 4.59 (q, *J* = 5.1 Hz, 1H (1 diastereomer)), 4.49 (q, *J* = 5.1 Hz, 1H (1 diastereomer)), 4.417 (s, 1H (2 diastereomers)), 4.410 (s, 1H (2 diastereomers)), 4.36-4.38 (m, 1H (2 diastereomers)), 4.25-4.29 (m, 1H (4 diastereomers)), 4.06-4.16 (m, 4H (1H of 2 diastereomers and 3H of 4 diastereomers)), 3.96-4.00 (m, 1H (2 diastereomers)), 3.87-3.96 (m, 3H (1H of 2 diastereomers and 2H of 4 diastereomers)), 3.72-3.77 (m, 1H (1 diastereomer)), 3.65-3.69 (m, 1H (1 diastereomer)), 3.52-3.63 (m, 2H (1H of 2 diastereomers and 1H of 4 diastereomers)), 3.44-3.49 (m, 1H (2 diastereomers)), 3.36-3.42 (m, 1H (4 diastereomers)), 3.28-3.35 (m, 1H of 2 diastereomers)), 3.10-3.20 (m, 1H (4 diastereomers)), 2.40-2.44 (m, 1H (2 diastereomers)), 2.30-2.33 (m, 1H (2 diastereomers)), 2.20-2.25 (m, 1H (2 diastereomers)), 2.13-2.18 (m, 1H (2 diastereomers)), 2.05-2.12 (m, 1H (4 diastereomers)), 1.98-2.04 (m, 1H (2 diastereomers)), 1.86-1.97 (m, 7H (1H of 2 diastereomers and 6H of 4 diastereomers)), 1.78-1.85 (m, 4H (4 diastereomers)), 1.72-1.77 (m, 1H (4 diastereomers)), 1.62-1.71 (m, 4H (4 diastereomers)), 1.60 (s, 3H (2 diastereomers)), 1.59 (s, 3H (2 diastereomers)), 1.49-1.56 (m, 1H (4 diastereomers)), 1.34-1.48 (m, 5H (4 diastereomers)), 1.26-1.33 (m, 6H (4 diastereomers)), 1.20-1.24 (m, 1H (4 diastereomers)), 1.21 (s, 9H (2 diastereomers)), 1.20 (s, 9H (2 diastereomers)), 1.15-1.19 (m, 3H (1H of 4 diastereomers and 3H of 2 diastereomers)), 1.13 (d, *J* = 5.1 Hz, 3H (2 diastereomers)), 1.06-1.10 (m, 3H (4 diastereomers)), 0.98-1.01 (m, 3H (4 diastereomers)), 0.95 (t, *J* = 7.9 Hz, 9H (4 diastereomers)), 0.87-0.93 (m, 39H (4 diastereomers)), 0.59-0.63 (m, 6H (4 diastereomers)), 0.01-0.17 (m, 24H (4 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 149.6, 145.58, 145.50, 145.4, 140.5, 140.2, 140.1, 139.89, 139.83, 139.7, 138.9, 138.7, 138.57, 138.54, 133.37, 133.31, 133.1, 132.3, 132.2, 129.2, 129.1, 129.09, 129.00, 128.9, 128.3, 127.1, 125.8, 125.7, 125.26, 125.22, 125.1, 124.7, 115.3, 114.6, 114.4, 109.5, 100.0, 99.5, 97.8, 97.7, 82.19, 82.12, 80.6, 80.5, 80.3, 79.6, 79.4, 79.2, 78.8, 78.6, 76.4, 76.3, 76.2, 76.18, 76.15, 72.3, 72.1, 71.3, 71.1, 70.8, 70.6, 66.3, 65.59, 65.53, 62.17, 62.11, 61.3, 61.2, 60.8, 60.7, 48.4, 47.3, 47.0, 42.5, 42.2, 41.8, 41.5, 41.3, 40.8, 40.37, 40.33, 39.6, 38.7, 38.1, 38.0, 36.6, 36.0, 35.8, 35.1, 34.6, 34.5, 33.7, 33.1, 33.0, 32.8, 32.6, 32.5, 31.6, 30.93, 30.90, 30.0, 29.7, 29.3, 29.0, 28.8, 28.77, 28.72, 28.6, 28.4, 27.8, 27.7, 27.2, 25.3, 24.7, 23.8, 23.3, 22.7, 22.5, 20.9, 20.79, 20.74, 20.6, 20.5, 18.8, 18.4, 18.37, 18.34, 18.28, 18.23, 18.0, 17.9, 16.0, 15.9, 15.5, 15.4, 15.3, 14.1, 14.0, 11.9, 11.4, 11.3, 6.94, 6.91, 5.0, -3.8, -4.1, -4.2, -4.3, -4.4, -4.5, -4.65, -4.69, -5.01, -5.05 ppm; HRMS (ES+) calcd. for $C_{86}H_{160}O_{13}SSi_5Na$ (M+Na) 1596.0324, found 1596.0127.



SI-57

102 P = Piv
103 P = H

Ketone 102 and **Keto-ol 103**: To a stirred solution of sulfone **SI-57** (171.6 mg, 0.109 mmol) in THF (1.9 mL) at -50 ºC was added LDA[10] (0.27 mL, 0.270 mmol, 1 M in THF / hexanes). After 5 min, DMPU (1.06 g, 1.0 mL, 8.23 mmol) was added and slowly warmed to -35 ºC over 15 min. The reaction was cooled back down to -50 ºC and a solution of Davis' oxaziridine[19] (78.3 mg, 0.299 mmol) in THF (0.85 mL) was cannulated to it. The reaction was warmed to -35 ºC over 15 min and then quenched with sat. aq. NH_4Cl (25 mL). The aqueous layer was extracted with Et_2O (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 6-20% EtOAc / hexanes, to give ketone **102** (92.5 mg, 63.8 µmol, 59%) and keto-ol **103** (24.2 mg, 17.7 µmol, 16%) as colorless oil along with recovered sulfone **SI-57** (39.6 mg, 25.1 µmol, 23%). $[\alpha]_D^{23}$ = +17.0 (*c* = 1.00, C_6H_6); IR: (neat) 2956, 2929, 2856, 1731, 1725, 1462, 1376, 1251, 1155, 1076, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 6.48 (ddd, *J* = 11.0, 4.5, 1.1 Hz, 1H (1 diastereomer)), 6.45 (ddd, *J* = 11.0, 4.5, 1.1 Hz, 1H (1 diastereomer)), 6.06 (d, *J* = 10.9 Hz, 1H (2 diastereomers)), 5.66 (dd, *J* = 6.1, 4.4 Hz, 1H (1 diastereomer)), 5.64 (dd, *J* = 6.2, 4.4 Hz, 1H (1 diastereomer)), 5.59 (s, 1H (2 diastereomers)), 5.53 (ddd, *J* = 15.1, 6.0, 3.2 Hz, 1H (2 diastereomers)), 5.32 (s, 1H (2 diastereomers)), 5.14 (s, 1H (2 diastereomers)), 4.96 (s, 1H (2 diastereomers)), 4.87 (s, 1H (2 diastereomers)), 4.68 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.66 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.41 (s, 1H (2 diastereomers)), 4.35-4.38 (m, 1H (2 diastereomers)), 4.25-4.28 (m, 1H (2 diastereomers)), 4.10-4.15 (m, 2H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 3.91-4.01 (m, 3H (2 diastereomers)), 3.74-3.78 (m, 1H (1 diastereomer)), 3.58-3.67 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.46-3.53 (m, 2H (2 diastereomers)), 3.33 (dt, *J* = 9.1, 2.7 Hz, 1H (2 diastereomers)), 2.78 (qd, *J* = 6.9, 4.4 Hz , 1H (1 diastereomer)), 2.62-2.67 (m, 1H (1H of 1 diastereomer and 1H of 1 diastereomer)), 2.57-2.66 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.59 (dd, *J* = 17.5, 6.3 Hz, 1H (1 diastereomer)), 2.54 (dd, *J* = 5.7, 2.6 Hz, 1H (1 diastereomer)), 2.52 (dd, *J* = 5.7, 2.6 Hz, 1H (1 diastereomer)), 2.37-2.41 (m, 1H (2 diastereomers)), 2.04-2.08 (m, 1H (2 diastereomers)), 1.96-2.03 (m, 1H (2 diastereomers)), 1.87-1.92 (m, 3H (2 diastereomers)), 1.78-1.86 (m, 3H (2 diastereomers)), 1.82 (s, 3H (2 diastereomers)), 1.64-1.74 (m, 3H (2 diastereomers)), 1.60 (s, 3H (2 diastereomers)), 1.48-1.52 (m, 1H (2 diastereomers)), 1.36-1.46 (m, 4H (2 diastereomers)), 1.26-1.33 (m, 6H (2 diastereomers)), 1.20-1.23 (m, 12H (2 diastereomers)), 1.08 (d, *J* = 7.0 Hz, 3H (2 diastereomers)), 1.06 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.05 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 0.98 (d, $J = 6.4$ Hz, 3H (2 diastereomers)), 0.96 (t, $J = 7.9$ Hz, 3H (2 diastereomers)), 0.89-0.92 (m, 39H (2 diastereomers)), 0.62 (q, $J = 7.9$ Hz, 6H (1 diastereomers)), 0.61 (q, $J = 7.9$ Hz, 6H (1 diastereomers)), 0.116 (s, 3H (1 diastereomer)), 0.114 (s, 3H (1 diastereomer)), 0.08 (s, 3H (2 diastereomers)), 0.06 (s, 3H (2 diastereomers)), 0.046 (s, 3H (2 diastereomers)), 0.043 (s, 3H (1 diastereomer)), 0.041 (s, 3H (1 diastereomer)), 0.026 (s, 3H (2 diastereomers)), 0.022 (s, 3H (2 diastereomers)), 0.009 (s, 3H (1 diastereomer)), 0.007 (s, 3H (1 diastereomer)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) 213.1, 212.7, 178.4, 149.6, 145.1, 140.93, 140.90, 138.5, 138.4, 132.18, 132.11, 127.24, 127.20, 125.4, 125.2, 115.05, 115.00, 109.5, 99.8, 98.5, 82.1, 80.7, 80.46, 80.43, 79.4, 78.8, 78.5, 76.2, 76.1, 75.9, 75.8, 72.6, 71.3, 70.48, 70.40, 62.1, 61.4, 61.1, 47.96, 47.92, 45.6, 45.4, 43.1, 42.8, 41.8, 41.3, 40.3, 38.7, 38.0, 37.1, 37.0, 33.1, 32.9, 32.6, 30.9, 30.1, 27.6, 27.2, 26.1, 25.98, 25.90, 25.8, 22.5, 20.8, 20.7, 18.4, 18.37, 18.34, 18.0, 17.1, 16.2, 16.0, 15.8, 15.4, 15.3, 14.1, 14.0, 11.9, 6.9, 4.9, -4.2, -4.44. -4.44, -4.77, -4.79, -4.8, -5.00, -5.05 ppm; HRMS (ES+) calcd. for $C_{80}H_{154}O_{12}Si_5Na$ (M+Na) 1470.0184, found 1470.0157.



102

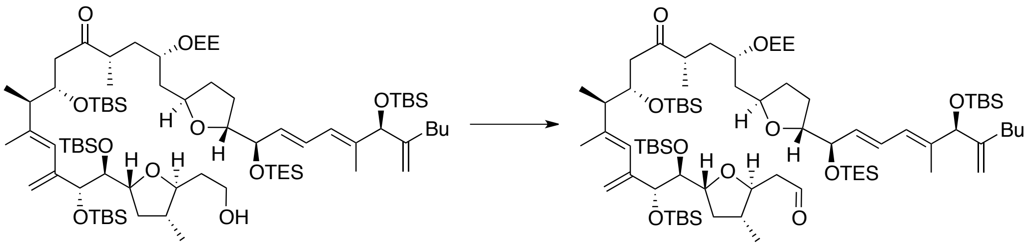
SI-58

104

Aldehyde 104: To a stirred solution of pivalate **102** (84.7 mg, 58.4 µmol) in Et_2O (4.2 mL) at -20 °C was added $LiAlH_4$ (5.6 mg, 0.146 mmol) in one portion. After 25 min, the reaction was quenched with H_2O (15 drops) and the organic layer was decanted. The solid formed was washed with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude diol **SI-58**.

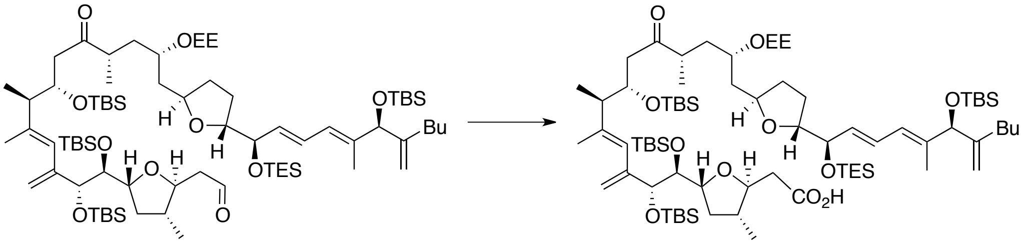
To a stirred solution of oxalyl chloride (45.1 mg, 31 µL, 0.351 mmol) in CH_2Cl_2 (1.5 mL) at -78 °C was cannulated a solution of DMSO (55.0 mg, 50 µL, 0.701 mmol) in CH_2Cl_2 (0.75 mL). After 20 min, a solution of crude diol **SI-58** in CH_2Cl_2 (2.0 mL and 2 X 0.40 mL wash) was cannulated to it. After 45 min, Et_3N (71.0 mg, 99 µL, 0.701 mmol) was added. After 10 min, the reaction was quenched with H_2O (15 mL) and the aqueous layer was extracted with CH_2Cl_2 (3

X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **104** (51.5 mg, 37.8 µmol, 65%) as colorless oil. $[\alpha]_D^{23}$ = +17.3 (*c* = 0.48, C_6H_6); IR: (neat) 2956, 2929, 2857, 1713, 1462, 1377, 1251, 1076, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 9.82 (dd, *J* = 2.9, 2.3 Hz, 1H (2 diastereomers)), 6.48 (ddd, *J* = 11.0, 4.5, 1.2 Hz, 1H (1 diastereomer)), 6.46 (ddd, *J* = 11.0, 4.5, 1.2 Hz, 1H (1 diastereomer)), 6.06 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.65 (ddd, *J* = 15.1, 6.1, 4.3 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (2 diastereomers)), 5.33 (t, *J* = 1.7 Hz, 1H (2 diastereomers)), 5.14 (s, 1H (2 diastereomers)), 4.97 (s, 1H (2 diastereomers)), 4.87 (s, 1H (2 diastereomers)), 4.68 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.42 (s, 1H (2 diastereomers)), 4.37-4.39 (m, 1H (2 diastereomers)), 4.14 (dt, *J* = 5.7, 5.5 Hz, 1H (2 diastereomers)), 4.08 (s, 1H (2 diastereomers)), 3.98-4.02 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.92-3.96 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.75-3.79 (m, 1H (1 diastereomer)), 3.73 (td, *J* = 8.9, 3.5 Hz, 1H (1 diastereomer)), 3.58-3.66 (m, 2H (2 diastereomers)), 3.54 (dt, *J* = 6.9, 2.5 Hz, 1H (2 diastereomers)), 3.46-3.50 (m, 1H (2 diastereomers)), 2.76-2.81 (m, 1H (1 diastereomer)), 2.59-2.68 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 2.57 (dd, *J* = 3.4, 2.3 Hz, 1H (1 diastereomer)), 2.55 (dd, *J* = 3.4, 2.3 Hz, 1H (1 diastereomer)), 2.47-2.53 (m, 2H (2 diastereomers)), 2.38-2.42 (m, 1H (2 diastereomers)), 2.06-2.10 (m, 1H (2 diastereomers)), 1.96-2.05 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.86-1.93 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.81-1.86 (m, 2H (2 diastereomers)), 1.83 (s, 3H (2 diastereomers)), 1.67-1.73 (m, 1H (2 diastereomers)), 1.60 (d, *J* = 0.9 Hz, 3H (1 diastereomer)), 1.37-1.52 (m, 6H (2 diastereomers)), 1.27-1.32 (m, 5H (2 diastereomer)), 1.22 (t, *J* = 6.9 Hz, 3H (1 diastereomer)), 1.21 (t, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.09 (d, *J* = 7.0 Hz, 3H (2 diastereomers)), 1.06 (d, *J* = 7.0 Hz, 3H (1 diastereomer)), 1.05 (d, *J* = 6.9 Hz, 3H (1 diastereomer)), 1.02 (d, *J* = 6.5 Hz, 3H (2 diastereomers)), 0.97 (t, *J* = 7.9 Hz, 9H (1 diastereomer)), 0.96 (t, *J* = 7.9 Hz, 9H (1 diastereomer)), 0.89-0.92 (m, 39H (2 diastereomers)), 0.622 (q, *J* = 7.9 Hz, 6H (1 diastereomer)), 0.620 (q, *J* = 7.9 Hz, 6H (1 diastereomer)), 0.008-0.12 (m, 24H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.0, 212.6, 202.2, 202.1, 149.6, 145.0, 141.1, 141.0, 138.5, 138.4, 132.2, 132.1, 127.24, 127.20, 125.2, 115.1, 115.0, 109.5, 99.8, 98.5, 82.1, 80.7, 79.8, 79.4, 78.66, 78.60, 76.2, 76.1, 75.9, 75.8, 72.6, 71.3, 70.4, 70.3, 61.4, 61.1, 48.0, 47.9, 47.6, 45.4, 45.3, 43.1, 42.8, 41.9, 41.3, 40.6, 37.6, 37.2, 37.0, 32.9, 32.6, 30.9, 30.1, 29.7, 27.6, 26.17, 26.11, 25.96, 25.91, 25.90, 25.8, 22.5, 20.8, 20.7, 18.4, 18.35, 18.33, 18.0, 17.2, 15.6, 15.4, 15.3, 14.0, 11.8, 6.8, 5.0, -4.1, -4.3, -4.46, -4.47, -4.7, -4.8 , -5.02, -5.06 ppm; HRMS (ES+) calcd. for $C_{75}H_{144}O_{11}Si_5Na$ (M+Na) 1383.9453, found 1183.9542.



103 **104**

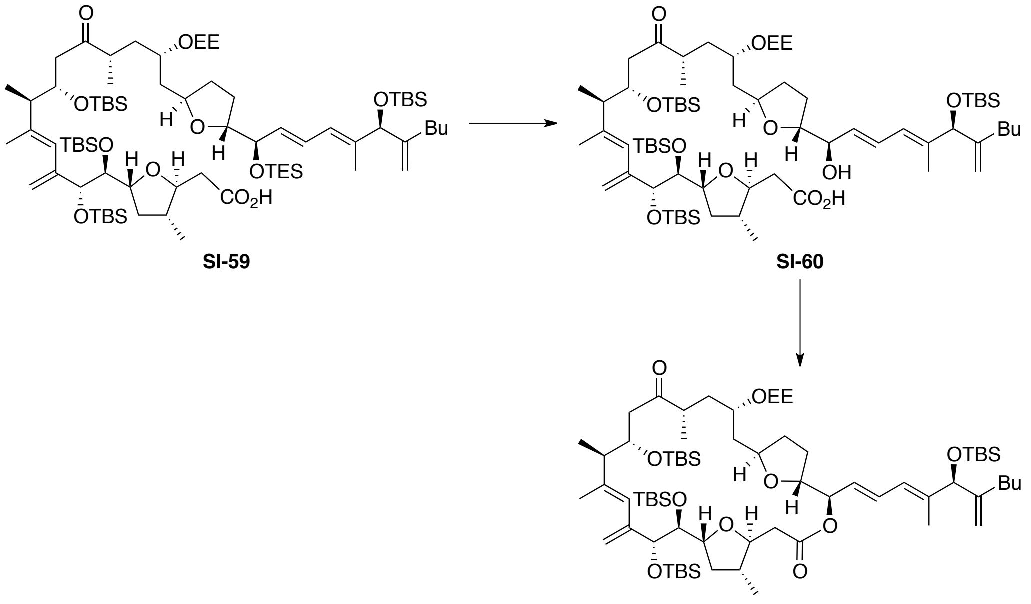
Aldehyde 104: To a stirred solution of oxalyl chloride (10.6 mg, 7.3 µL, 83.5 µmol) in CH_2Cl_2 (0.50 mL) at -78 °C was cannulated a solution of DMSO (13.1 mg, 11.9 µL, 0.167 mmol) in CH_2Cl_2 (0.20 mL). After 15 min, a solution of alcohol **103** (24.2 mg, 16.7 µmol) in CH_2Cl_2 (0.50 mL and 2 X 0.15 mL wash) was cannulated to it. After 45 min, Et_3N (16.7 mg, 24 µL, 0.167 mmol) was added. After 10 min, the reaction was quenched with H_2O (7.5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give aldehyde **104** (19.7 mg, 14.4 µmol, 82%) as colorless oil.



104 **SI-59**

Carboxylic Acid SI-59: To a stirred solution of aldehyde **104** (45.2 mg, 33.1 µmol) in *t*-BuOH/H_2O (1:1, 3.5 mL) at 0 °C were sequentially added 2-methyl-2-butene (113 mg, 0.17 mL, 1.65 mmol), $NaH_2PO_4{\bullet}H_2O$ (45.8 mg, 0.331 mmol) and $NaClO_2$ (15.1 mg, 0.165 mmol). After 15 min, the reaction was warmed to rt. After another 2 h, the reaction was diluted with H_2O (10 mL) and the aqueous layer was extracted with EtOAc / Et_2O (1:1, 3 X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 10-30 % EtOAc / hexanes, to give carboxylic acid **SI-59** (43.5 mg, 31.5 µmol, 95%) as light yellow oil. $[\alpha]_D^{23}$ = +16.8 (*c* = 1.00, C_6H_6); IR (neat): 3351, 2956, 2929, 2857, 1714, 1471, 1462, 1377, 1251, 1077, 835, 776 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (two diastereomers)} δ 10.07 (br s, 1H (2 diastereomers)), 6.48 (ddd, *J* = 11.0, 5.5, 1.2 Hz, 1H (1 diastereomer)), 6.46 (ddd, *J* = 11.0, 5.4, 1.2 Hz, 1H (1 diastereomer)), 6.06 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.65 (ddd, *J* = 15.1, 6.2, 3.6 Hz, 1H (2 diastereomers)), 5.60 (s, 1H (1 diastereomer)), 5.59 (s, 1H (1 diastereomer)), 5.36 (s, 1H (1 diastereomer)), 5.35 (s, 1H (1 diastereomer)), 5.14 (s, 1H (2 diastereomers)), 5.00 (s, 1H (2 diastereomers)), 4.87 (s, 1H (2 diastereomers)), 4.68 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.67 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.41-4.45 (m, 1H (1 diastereomer)), 4.42 (s, 1H (2 diastereomers)), 4.38 (td, *J* = 6.0, 3.6

Hz, 1H (1 diastereomer)), 4.10-4.16 (m, 3H (2 diastereomers)), 3.98-4.02 (m, 1H (1 diastereomer)), 3.93-3.97 (m, 2H (1H of 1 diastereomer and 1H of 2 diastereomers)), 3.76-3.80 (m, 1H (1 diastereomer)), 3.53-3.68 (m, 4H (2 diastereomers)), 3.48 (ddd, J = 14.1, 9.2, 7.0 Hz, 1H (1 diastereomer)), 2.78-2.83 (m, 1H (1 diastereomer)), 2.59-2.70 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 2.38-2.54 (m, 3H (2 diastereomers)), 2.12 (td, J = 12.2, 6.0 Hz, 1H (2 diastereomers)), 1.97-2.03 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.87-1.94 (m, 3H (1H of 1 diastereomer and 2H of 2 diastereomers)), 1.81-1.86 (m, 2H (2 diastereomers)), 1.83 (d, J = 0.9 Hz, 3H (1 diastereomer)), 1.82 (d, J = 0.9 Hz, 3H (1 diastereomer)), 1.67-1.73 (m, 1H (2 diastereomers)), 1.60 (d, J = 0.8 Hz, 3H (2 diastereomers)), 1.38-1.52 (m, 6H (2 diastereomers)), 1.27-1.34 (m, 5H (2 diastereomers)), 1.23 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.21 (t, J = 7.0 Hz, 3H (1 diastereomer)), 1.104 (d, J = 7.0 Hz, 3H (1 diastereomer)), 1.102 (d, J = 7.0 Hz, 3H (1 diastereomer)), 1.06 (d, J = 6.9 Hz, 3H (2 diastereomers)), 1.03 (d, J = 6.5 Hz, 3H (1 diastereomer)), 1.01 (d, J = 6.5 Hz, 3H (1 diastereomer)), 0.97 (t, J = 7.9 Hz, 9H (1 diastereomers)), 0.96 (t, J = 7.9 Hz, 9H (2 diastereomers)), 0.89-0.92 (m, 39H (2 diastereomers)), 0.62 (q, J = 7.9 Hz, 6H (1 diastereomer)), 0.61 (q, J = 7.9 Hz, 6H (1 diastereomer)), 0.02-0.12 (m, 24H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.0, 212.6, 172.2, 149.65, 149.62, 144.9, 141.5, 141.4, 138.6, 138.5, 132.18, 132.10, 127.27, 127.23, 125.2, 125.1, 124.8, 115.1, 114.8, 109.5, 99.7, 98.5, 82.1, 80.7, 80.1, 78.9, 78.7, 78.0, 76.3, 76.2, 75.9, 75.8, 72.6, 71.2, 70.4, 70.2, 61.7, 61.1, 47.8, 47.7, 45.4, 45.2, 43.1, 42.8, 41.8, 41.3, 39.9, 37.9, 37.8, 37.6, 37.5, 37.1, 37.0, 32.9, 32.6, 30.9, 30.1, 29.7, 27.5, 26.1, 25.95, 25.90, 25.8, 22.5, 20.8, 20.7, 18.36, 18.33, 18.30, 18.0, 17.2, 17.1, 16.2, 15.7, 15.6, 15.5, 15.4, 15.3, 14.1, 14.0, 13.8, 11.8, 6.8, 5.0, -3.9, -4.40, -4.43, -4.48, -4.72, -4.74, -4.78, -5.01, -5.05 ppm.



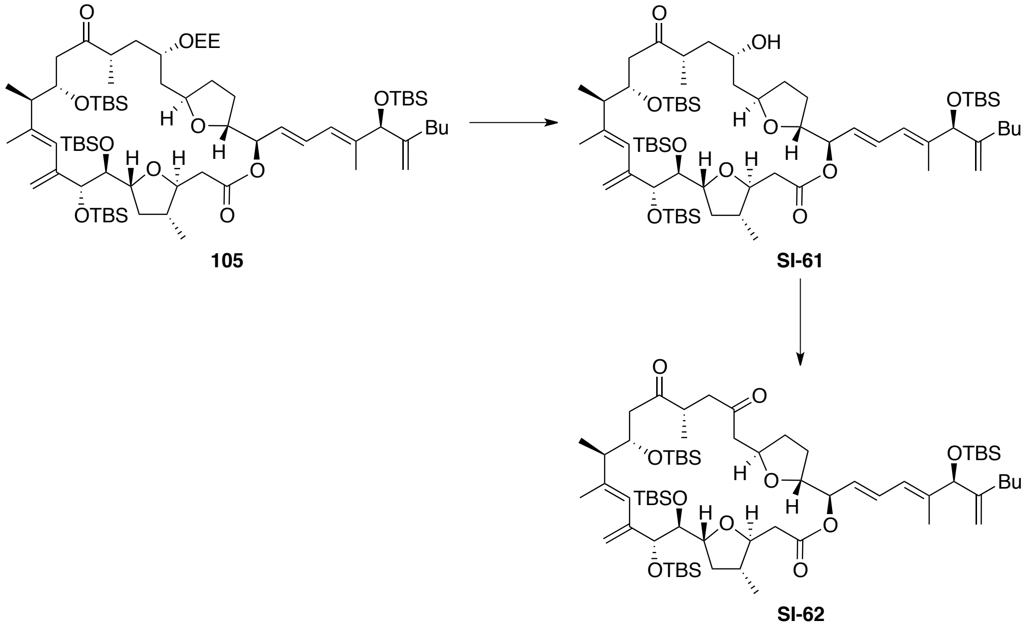
SI-59

SI-60

105

Macrolactone 105: To a stirred solution of carboxylic acid **SI-59** (43.5 mg, 31.5 µmol) in dry MeOH (3.0 mL) at 0 °C was added methanolic PPTS solution 35 µL.[25] After 10 min, the reaction was warmed to rt. After another 30 min, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and the aqueous layer was extracted with EtOAc (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude seco-acid **SI-60**.

To a stirred solution of crude seco-acid **SI-60** in THF (1.2 mL) at 0 °C were added Et_3N (5.7 mg, 7.9 µL, 56.8 µmol) followed by 2,4,6-trichlorobenzoylchloride **85** (9.2 mg, 5.9 µL, 37.8 µmol). After 45 min, the reaction was diluted with toluene (2.2 mL). In a separate flask, a solution of DMAP (6.9 mg, 56.8 µmol) in toluene (8.5 mL) was warmed to 70 °C and the solution of mixed acid anhydride was added dropwise over 6 h to it. After another 30 min, the reaction was cooled down to rt and was directly loaded onto column and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give macrolactone **105** (24.8 mg, 19.9 µmol, 63%) as colorless oil. $[\alpha]_D^{23}$ = +1.8 (*c* = 1.00, $CHCl_3$); IR: (neat) 2958, 2929, 2856, 1743, 1708, 1463, 1380, 1255, 1089, 835, 777 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (***Note:*** *NMR analysis indicated that compound **105** exists as a mixture of conformational isomers*)} 6.53 (ddd, *J* = 11.0, 4.1, 0.7 Hz, 1H (1 diastereomer)), 6.51 (ddd, *J* = 11.0, 4.1, 0.7 Hz, 1H (1 diastereomer)), 6.17 (br s, 1H (1 diastereomer)), 6.16 (br s, 1H (1 diastereomer)), 6.04 (d, *J* = 11.0 Hz, 1H (2 diastereomers)), 5.50 (dd, *J* = 15.1, 7.2 Hz, 1H (2 diastereomers)), 5.10 (s, 1H (2 diastereomers)), 5.01 (br s, 1H (2 diastereomers)), 4.99 (br s, 1H (2 diastereomers)), 4.92 (br s, 1H (1 diastereomer)), 4.91 (br s, 1H (1 diastereomer)), 4.87 (s, 1H (2 diastereomers)), 4.71 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.68 (q, *J* = 5.2 Hz, 1H (1 diastereomer)), 4.40 (s, 1H (2 diastereomers)), 4.21 (d, *J* = 9.3 Hz, 1H (2 diastereomers)), 4.00-4.06 (m, 2H (2 diastereomers)), 3.91-3.96 (m, 2H (2 diastereomers)), 3.68-3.75 (br m, 1H (2 diastereomers)), 3.60-3.65 (br m, 1H (2 diastereomers)), 3.56 (br s, 1H (1 diastereomer)), 3.55 (br s, 1H (1 diastereomer)), 3.48 (ddd, *J* = 14.1, 9.1, 7.0 Hz, 1H (1 diastereomer)), 2.95-3.02 (m, 1H (2 diastereomers)), 2.71-2.75 (br m, 1H (1 diastereomer)), 2.59-2.63 (br m, 1H (1 diastereomer)), 2.52 (dd, *J* = 14.4, 7.4 Hz, 1H (2 diastereomers)), 2.45-2.49 (m, 1H (2 diastereomers)), 2.28-2.41 (br m, 2H (2 diastereomers)), 2.12 (br s, 1H (2 diastereomers)), 2.06 (td, *J* = 11.7, 6.0 Hz, 1H (2 diastereomers)), 1.96-2.01 (m, 1H (2 diastereomer)), 1.87-1.95 (m, 3H (2 diastereomers)), 1.72-1.81 (m, 6H (2 diastereomers)), 1.62-1.65 (m, 1H (2 diastereomers)), 1.61 (s, 3H (2 diastereomers)), 1.51-1.58 (m, 4H (2 diastereomers)), 1.37-1.42 (m, 2H (2 diastereomers)), 1.27-1.34 (m, 7H (2 diastereomers)), 1.20-1.25 (m, 2H (2 diastereomers)), 1.08-1.14 (m, 4H (2 diastereomers)), 1.05 (br s, 3H (1 diastereomer)), 0.99 (d, *J* = 6.6 Hz, 3H (1 diastereomer)), 0.86-0.92 (m, 39H (2 diastereomers)), -0.01-0.12 (m, 24H (2 diastereomers)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 211.9, 211.5, 170.44, 170.41, 149.5, 146.4, 146.3, 140.85, 140.81, 140.4, 140.3, 130.2, 130.1, 128.9, 127.2, 124.2, 114.4, 110.0, 99.8, 97.8, 81.8, 80.6, 80.0, 79.2, 79.1, 78.8, 77.89, 77.84, 77.7, 77.6, 75.5, 75.3, 71.9, 71.7, 71.6, 70.2, 62.1, 61.6, 47.1, 46.3, 42.5, 41.8, 40.8, 40.7, 39.8, 39.7, 38.78, 38.70, 36.1, 34.8, 34.68, 34.63, 34.5, 32.7, 31.6, 30.5, 30.0, 29.0, 26.4, 26.0, 25.87, 25.83, 25.3, 22.6, 22.5, 21.1, 20.9, 20.7, 18.77, 18.72, 18.5, 18.3, 17.9, 16.6, 16.4, 16.3, 16.2, 16.0, 15.6, 15.2, 14.1, 14.0, 12.4, 11.4, -3.9, -4.0, -4.5, -4.60, -4.65, -4.7, -4.8, -5.0, -5.3, -5.4 ppm; HRMS (ES+) calcd. for $C_{69}H_{128}O_{11}Si_4Na$ (M+Na) 1267.8431, found 1267.8395.



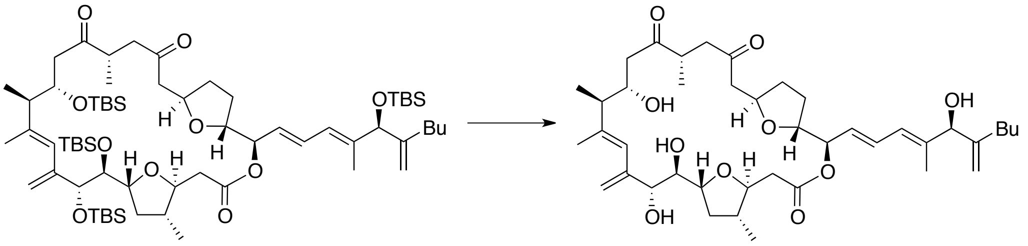
105

SI-61

SI-62

Diketone SI-62: The macrolactone **105** (17.8 mg, 14.2 μmol) in THF/AcOH/H_2O (1.5 mL, 4:4:1) was stirred at rt. After 22 h, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and the aqueous layer was extracted with EtOAc / Et_2O (2:1, 3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give crude alcohol **SI-61**.

To a stirred solution of crude alcohol **SI-61** in CH_2Cl_2 (1.2 mL) at 0 °C were added pyridine (7.1 mg, 6.9 µL, 85.2 µmol) followed by Dess-Martin Periodinane (18.1 mg, 42.6 µmol). After 15 min, the reaction was warmed to rt. After another 3 h, the reaction was quenched with sat. aq. $NaHCO_3$ (7.5 mL) and the aqueous layer was extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 5-15% EtOAc / hexanes, to give diketone **SI-62** (9.8 mg, 8.36 µmol, 59%) as colorless oil: $[\alpha]_D^{23}$ = +1.7 (*c* = 0.45, $CHCl_3$); IR: (neat) 2956, 2930, 2858, 1738, 1709, 1660, 1632, 1465, 1388, 1257, 1099, 1045, 837, 780 cm^{-1}; ^1H NMR {700 MHz, $CDCl_3$ (***Note:*** *NMR analysis indicated that compound **SI-62** exists as a mixture of conformational isomers*)} δ 6.53 (dd, *J* = 15.2, 11.0 Hz, 1H), 6.04 (d, *J* = 11.0 Hz, 1H), 6.01 (br s, 1H), 5.51 (br s, 1H), 5.13 (br s, 1H), 5.11 (d, *J* = 0.8 Hz, 1H), 4.96 (br s, 1H), 4.87 (d, *J* = 1.0 Hz, 1H), 4.51 (br s, 1H), 4.40 (s, 1H), 4.21-4.30 (m, 1H), 4.04-4.12 (br m, 1H), 3.96 (br s, 1H), 3.91 (br s, 1H), 3.72 (br s, 1H), 3.55 (br s, 1H), 3.00 (br s 1H), 2.86 (br d, *J* = 17.8 Hz, 1H), 2.71 (br s, 1H), 2.60 (dd, *J* = 14.2, 3.5 Hz, 1H), 2.46 (br s, 2H), 2.41 (br s, 2H), 2.18 (br s, 1H), 1.99-2.05 (m, 2H), 1.88-1.94 (m, 3H), 1.74-1.81 (m, 3H), 1.49-1.69 (m, 4H), 1.61 (s, 3H), 1.37-1.42 (m, 2H), 1.28-1.34 (m, 3H), 1.16 (br s, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.03 (br s, 3H), 0.89-0.92 (m, 39H), 0.02-0.10 (m, 24H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 210.9, 207.5, 170.5, 149.5, 146.2, 140.7, 140.4, 130.7, 128.5, 126.9, 124.1, 114.8, 110.0, 81.5, 80.6, 80.0, 79.6, 78.8, 75.3, 71.5, 50.4, 46.8, 46.2, 42.9, 41.1, 40.6, 39.8, 38.4, 36.6, 32.2, 30.5, 30.0, 28.5, 26.3, 26.0, 25.87, 25.83, 22.5, 18.6, 18.4, 18.3, 17.9, 17.6, 16.6, 15.8, 15.6, 14.0, 12.4, -4.1, -4.6, -4.8, -5.0 ppm; HRMS (ES+) calcd. for $C_{65}H_{119}O_{10}Si_4$ (M+H) 1171.7880, found 1171.7856.



SI-62

amphidinolide C (**1**)

Amphidinolide C (**1**)**:** To a solution of tetra-TBS ether **SI-62** (8.2 mg, 6.99 µmol) in CH_3CN (1.3 mL) at rt was added $Et_3N{\bullet}3HF$ (1.1 mL) followed by Et_3N (0.90 mL). After 6 d, the reaction was diluted with EtOAc (15 mL) and poured into sat. aq. solution of $NaHCO_3$ (10 mL) and the aqueous layer was extracted with EtOAc (4 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by flash chromatography over silica gel, eluting with 2-6% MeOH / EtOAc, to give amphidinolide C (**1**) (2.1 mg, 2.27 µmol, 42%) as white amorphous solid. $[\alpha]_D^{23}$ = -98.5 (*c* = 0.21, $CHCl_3$), {lit.[16] $[\alpha]_D^{26}$ = -106 (*c* = 1.0, $CHCl_3$)}; ^1H NMR (700 MHz, C_6D_6) δ 6.74 (dd, *J* = 15.1, 11.0 Hz, 1H), 6.228 (br s, 1H), 6.226 (br d, *J* = 11.0 Hz, 1H), 5.68 (dd, *J* = 15.1, 8.1 Hz, 1H), 5.44 (t, *J* = 7.4 Hz, 1H), 5.22 (br s, 1H), 5.15 (br d, *J* = 1.1 Hz, 1H), 4.97 (br s, 1H), 4.92 (br s, 1H), 4.32 (br s, 1H), 4.31 (d, *J* = 4.6 Hz, 1H), 4.22-4.26 (m, 1H), 4.06 (dt, *J* = 8.6, 5.8 Hz, 1H), 4.04 (td, *J* = 8.5, 2.6 Hz, 1H), 3.98 (q, *J* = 7.0 Hz, 1H), 3.82 (td, *J* = 9.1, 2.6 Hz, 1H), 3.60 (br s, 1H), 3.55 (t, *J* = 5.0 Hz, 1H), 3.43 (br t, *J* = 7.8 Hz, 1H), 3.02-3.07 (m, 1H), 2.98 (dd, *J* = 17.8, 8.3 Hz, 1H), 2.70 (dd, *J* = 15.9, 8.8 Hz, 1H), 2.56 (dd, *J* = 15.5, 9.5 Hz, 1H), 2.36-2.41 (m, 2H), 2.34 (dd, *J* = 15.5, 2.7 Hz, 1H), 2.21-2.25 (m, 1H), 2.11 (dd, *J* = 17.8, 4.7 Hz, 1H), 2.07 (dd, *J* = 14.5, 4.0 Hz, 1H), 2H), 1.94 (dt, *J* = 15.4, 7.9 Hz, 1H), 1.78-1.85 (m, 1H), 1.75 (d, *J* = 1.2 Hz, 3H), 1.67-1.71 (m, 1H), 1.64 (d, *J* = 1.0 Hz, 3H), 1.51-1.55 (m, 1H), 1.44-1.49 (m, 1H), 1.34-1.37 (m, 4H), 1.17-1.21 (m, 2H), 1.07 (ddd, *J* = 18.0, 12.1, 8.8 Hz, 1H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.83 (7, *J* = 7.3 Hz, 3H), 0.67 (d, *J* = 6.1 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 213.3, 207.4, 171.0, 149.3, 146.0, 140.9, 140.7, 131.1, 125.5, 125.1, 115.2, 110.4, 81.8, 80.0, 79.9, 79.1, 77.9, 77.2, 76.4, 75.7, 71.1, 49.2, 48.7, 46.4, 45.8, 42.3, 40.2, 39.2, 37.0, 32.3, 31.7, 30.4, 28.2, 22.8, 16.2, 15.8, 15.4, 15.3, 14.2, 12.6 ppm; HRMS (ES+) calcd. for $C_{41}H_{62}O_{10}Na$(M+Na) 737.4241, found 737.4229.

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10. **Preparation of LDA Solution:** To a solution of diisopropylamine (0.14 mL / mmol) in THF (0.46 mL / mmol) at -78 °C was added *n*-BuLi (0.40 mL / mmol, 2.5

M in hexanes). After 5 min, the white slurry was warmed to -10 °C and stirred for an additional 15 min.

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20. **Preparation of PPTS Solution:** The stock solution was prepared by mixing PPTS (20.0 mg) in dry MeOH (3.0 mL).

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25. **Preparation of PPTS Solution:** The stock solution was prepared by mixing PPTS (36.7 mg) in dry MeOH (3.0 mL).