

# Synthesis of the ABCD and ABCDE Ring Systems of Azaspiracid.

**Xiao-Ti Zhou and Rich G. Carter\***

*Department of Chemistry, Oregon State University, Corvallis, OR 97331.*

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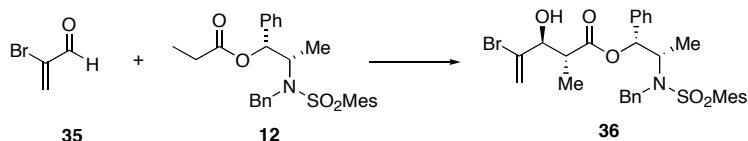
**Electronic Supplementary Information: Experimental**

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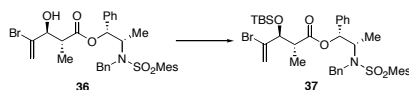
**General.** Infrared spectra were recorded neat unless otherwise indicated and are reported in  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR spectra were recorded in deuterated solvents and are reported in ppm relative to trimethylsilane and referenced internally to the residually protonated solvent.  $^{13}\text{C}$  NMR spectra were recorded in deuterated solvents and are reported in ppm relative to trimethylsilane and referenced internally to the residually protonated solvent. Optical rotations were recorded using a sodium lamp at 589 nm in  $\text{CHCl}_3$ .

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  $120^\circ\text{C}$  or by a bunsen flame, then cooled under argon. Solvents and commercial reagents were purified in accord with Perrin and Armarego<sup>1</sup> or used without further purification.

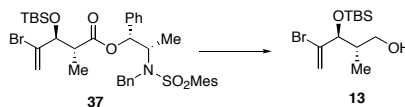


**Adduct 36:** To a stirred solution of **12** (4.8 g, 10 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was added  $\text{Et}_3\text{N}$  (3.4 mL, 24 mmol). The solution was cooled to  $-78^\circ\text{C}$  and a solution of dicyclohexylboron triflate (22 mL, 22 mmol, 1.0 M in hexanes) was added dropwise over 20 min. The resulting solution was stirred at  $-78^\circ\text{C}$  for 2 h. Aldehyde **35**<sup>2</sup> (1.6 g, 12 mmol) was added dropwise to the enolate solution. The reaction mixture was stirred at  $-78^\circ\text{C}$  for 1 h and was allowed to warm to room temperature over 1 h, then quenched by addition of pH 7 buffer solution (40 mL). The mixture was diluted with MeOH (200 mL) and 30% aq.  $\text{H}_2\text{O}_2$  (20 mL) was added carefully. The whole mixture was stirred vigorously overnight and then concentrated. The residue was partitioned between water (100 mL) and  $\text{CH}_2\text{Cl}_2$  (200 mL). The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (2 x 150 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20 - 40% EtOAc / hexanes, to give product **36** (5.65 g, 92%) as colorless oil:  $[\alpha]_D^{23} + 10.2^\circ$  (*c* 0.4,  $\text{CHCl}_3$ ); IR (neat) 3348, 2972, 2930, 1730, 1452, 1309, 1145, 753;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 – 7.40 (m, 8 H), 6.88 – 6.91 (m, 4 H), 5.96 (d,  $J = 1.6$  Hz, 1 H), 5.86 (d,  $J = 4.0$  Hz, 1 H), 5.68 (d,  $J = 1.6$  Hz, 1 H), 4.82 (d,  $J = 16.4$  Hz, 1 H), 4.61 (d,  $J = 16.4$  Hz, 1 H), 4.12 – 4.22 (m, 2 H), 3.19 (d,  $J = 6.4$  Hz, 1 H), 2.92 – 2.98 (m, 1 H), 2.54 (s, 6 H), 2.32 (s, 3 H), 1.21 (d,  $J = 7.2$  Hz, 3 H), 1.13 (d,  $J = 7.2$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.3, 143.0, 140.6, 138.9, 138.4, 134.3, 133.8, 132.5, 128.8, 128.7, 128.4, 128.0, 127.8, 127.5, 126.5, 126.2, 120.3, 79.1, 78.2, 57.2, 48.7, 43.9, 23.3, 21.3, 14.7, 13.7; HRMS (FAB<sup>+</sup>) calcd. for  $\text{C}_{31}\text{H}_{37}^{79}\text{BrNO}_5\text{S}$  (M+H) 614.1575, found 614.1571.

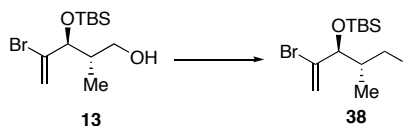


**TBS Silyl Ether 37:** To a stirred solution of **36** (5.65 g, 9.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (25 mL) at  $0^\circ\text{C}$  were sequentially added  $\text{Et}_3\text{N}$  (3.2 mL, 23 mmol) and TBSOTf (3.65 g, 13.8 mmol). The mixture was stirred at  $0^\circ\text{C}$  for 3 h and quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (50 mL). The aqueous solution was extracted with  $\text{CH}_2\text{Cl}_2$  (4 x 100 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 40% EtOAc / hexanes, to give product **37** (4.13 g, 62%) as colorless oil:  $[\alpha]_D^{23} + 23.5^\circ$  (*c* 1.1,  $\text{CHCl}_3$ ); IR (neat) 2930, 2846, 1730, 1705, 1654, 1562, 1448, 1149, 833;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (d,  $J = 6.8$  Hz, 2 H), 7.10 – 7.34 (m, 6 H), 6.93 (s, 2 H), 6.72 (d,  $J = 7.2$  Hz, 2 H), 5.81 (d,  $J = 1.6$  Hz, 1 H), 5.71 (d,  $J = 5.2$  Hz, 1 H), 5.62 (d,  $J = 1.6$  Hz, 1 H), 4.94 (d,  $J = 16.4$  Hz, 1 H), 4.41 (d,  $J = 16.4$  Hz, 1 H), 4.25 (d,  $J = 8.8$  Hz, 1 H), 4.03 – 4.06 (m, 1 H), 2.83 – 2.87 (m, 1 H), 2.47 (s, 6 H), 2.31 (s, 3 H), 1.16 (d,  $J = 6.8$  Hz, 3 H), 0.91 (d,  $J = 8.8$  Hz, 3 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  173.2, 142.8, 140.9, 139.0, 138.6, 136.2, 132.6, 128.9, 128.8, 128.7, 128.3,

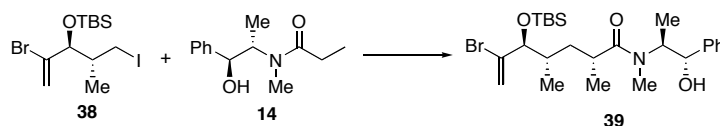
127.8, 126.6, 120.1, 78.9, 78.5, 57.1, 48.7, 45.7, 26.2, 25.9, 23.3, 21.3, 18.6, 15.0, 14.3, -4.3, -4.5; HRMS (FAB<sup>+</sup>) calcd. for C<sub>37</sub>H<sub>49</sub><sup>79</sup>BrNO<sub>3</sub>Si (M-H) 726.2284, found 726.2296.



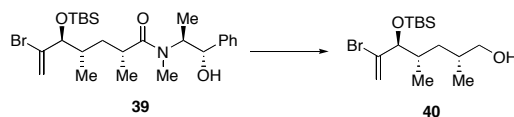
**Alcohol 13:** To a stirred solution of **37** (3.47 g, 4.76 mmol) in CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added DIBAL-H (11.4 mL, 11.4 mmol, 1M in CH<sub>2</sub>Cl<sub>2</sub>). The solution was stirred at -78 °C for 1 h and allowed to warm to 0 °C and quenched by addition of 10% aq. sodium tartrate (10 mL). The solution was stirred at room temperature for 3 h and extracted with Et<sub>2</sub>O (3 x 100 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 40% EtOAc / hexanes, to give product **13** (1.27 g, 86%) as colorless oil: [α]<sub>D</sub><sup>23</sup> - 21.6° (c 0.25, CHCl<sub>3</sub>); IR (neat) 3348, 2960, 2930, 2854, 1250, 1073, 833, 770; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.87 (m, 1 H), 5.61 (d, *J* = 1.5 Hz, 1 H), 4.03 (d, *J* = 6.3 Hz, 1 H), 3.75 (dd, *J* = 11.1, 3.9 Hz, 1 H), 3.60 (dd, *J* = 11.1, 3.9 Hz, 1 H), 2.30 (br, OH), 2.03 - 2.07 (m, 1 H), 0.96 (d, *J* = 7.2 Hz, 3 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 136.5, 118.2, 81.5, 65.1, 38.6, 26.1, 18.4, 14.5, -4.1, -4.7; HRMS (FAB<sup>+</sup>) calcd. for C<sub>12</sub>H<sub>26</sub><sup>79</sup>BrO<sub>2</sub>Si (M+H) 309.0885, found 309.0883.



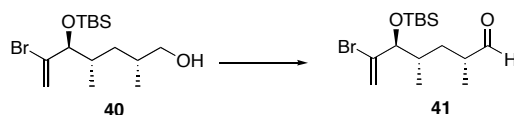
**Iodide 38:** To a solution of triphenylphosphine (115 mg, 0.44 mmol) in CH<sub>2</sub>Cl<sub>2</sub> at 0 °C were sequentially added imidazole (81.7 mg, 1.2 mmol) and iodine (111.6 mg, 0.44 mmol). After 10 min, a solution of alcohol **13** (124 mg, 0.40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was added *via* cannula. The mixture was stirred at 0 °C for 10 min, then warmed to room temperature. After 12 h, the mixture was quenched by saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (1.5 mL), diluted with water (2 mL). The aqueous solution was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 5 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5 - 20% EtOAc / hexanes, to give product **38** (148 mg, 88%) as colorless oil: [α]<sub>D</sub><sup>23</sup> - 11.3° (c 0.61, CHCl<sub>3</sub>); IR (neat) 2952, 2922, 2854, 1629, 1461, 1246, 1082, 842, 774; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.87 (d, *J* = 1.2 Hz, 1 H), 5.63 (d, *J* = 1.2 Hz, 1H), 3.83 (d, *J* = 7.6 Hz, 1 H), 3.48 (dd, *J* = 9.6, 5.2 Hz, 1 H), 3.39 (dd, *J* = 9.6, 5.2 Hz, 1 H), 1.65 - 1.68 (m, 1 H), 0.94 (s, 9 H), 0.92 (d, *J* = 6.4 Hz, 3 H), 0.17 (s, 3 H), 0.13 (s, 3 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 136.9, 119.4, 80.6, 38.4, 26.2, 18.6, 17.8, 15.5, -4.1, -4.3; HRMS (FAB<sup>+</sup>) calcd. for C<sub>12</sub>H<sub>25</sub><sup>79</sup>BrIOSi (M+H) 418.9902, found 418.9875.



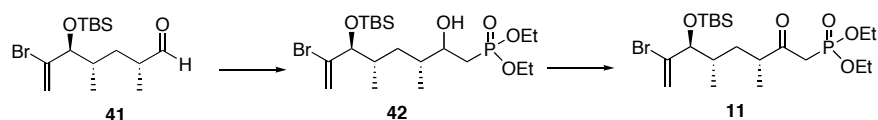
**Amide 39:** A solution of *n*-BuLi (4.35 mL, 10.88 mmol, 2.5 M in hexanes) was added *via* cannula to a suspension of lithium chloride (1.46 g, 34.54 mmol) and diisopropylamine (1.64 mL, 11.70 mmol) in THF (8.0 mL) at -78 °C. The resulting suspension was warmed to 0 °C briefly and then was cooled to -78 °C. An ice-cooled solution of amide **14** (1.20 g, 5.44 mmol) in THF (5 mL) was added *via* cannula. The mixture was stirred at -78 °C for 1 h, at 0 °C for 15 min and room temperature for 5 min. The mixture was cooled to 0 °C and iodide **38** (1.14 g, 2.72 mmol) in THF (2 mL) was added to the reaction *via* cannula. After 18 h at 0 °C, the reaction was quenched by addition of sat. aq. NH<sub>4</sub>Cl (50 mL) and the resulting mixture was extracted with EtOAc (4 x 100 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 50% EtOAc / hexanes, to give product **39** (1.28 g, 92%) as colorless oil: HRMS (FAB<sup>+</sup>) calcd. for C<sub>25</sub>H<sub>43</sub><sup>79</sup>BrNO<sub>3</sub>Si (M+H) 512.2195, found 512.2176.



**Alcohol 40:** A solution of *n*-BuLi (1.51 mL, 3.77 mmol, 2.5 M in hexanes) was added to a solution of diisopropylamine (0.57 mL, 4.06 mmol) in THF (4.0 mL) at  $-78^{\circ}\text{C}$ . The resulting solution was stirred at  $-78^{\circ}\text{C}$  for 10 min, then warmed to  $0^{\circ}\text{C}$  and held at this temperature for 10 min. Borane-ammonia complex (90%, 119.6 mg, 3.87 mmol) was added in one portion and the suspension was stirred at  $0^{\circ}\text{C}$  for 15 min and then was warmed to room temperature. After 15 min, the suspension was cooled to  $0^{\circ}\text{C}$ . A solution of amide **39** (496 mg, 0.96 mmol) in THF (1.5 mL) was added *via* cannula. The reaction was warmed to room temperature and held that temperature for 2 h and then quenched by addition of 3 N HCl (3 mL) at  $0^{\circ}\text{C}$ . The mixture was stirred for 30 min at  $0^{\circ}\text{C}$  and extracted with  $\text{Et}_2\text{O}$  (4 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 50% EtOAc / hexanes, to give product **40** (283 mg, 84%) as colorless oil:  $[\alpha]_{\text{D}}^{23} - 34.6^{\circ}$  (*c* 0.41,  $\text{CHCl}_3$ ); IR (neat) 3340, 2951, 2922, 2854, 1625, 1465, 1250, 1077, 837, 770;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.86 (s, 1 H), 5.60 (d,  $J = 1.2$  Hz, 1 H), 3.85 (d,  $J = 5.6$  Hz, 1 H), 3.52 – 3.60 (m, 1 H), 3.41 (m, 1 H), 1.90 – 1.95 (m, 1 H), 1.69 – 1.75 (m, 2 H), 1.55 – 1.62 (m, 1 H), 1.44 (br, 1 H), 1.00 (d,  $J = 6.8$  Hz, 3 H), 0.94 (s, 9 H), 0.92 (d,  $J = 7.2$  Hz, 3 H), 0.10 (s, 3 H), 0.07 (s, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  136.9, 117.8, 81.6, 67.9, 34.9, 34.8, 33.7, 26.2, 19.0, 18.6, 17.9, -4.1, -4.6; HRMS (FAB<sup>+</sup>) calcd For  $\text{C}_{15}\text{H}_{31}^{79}\text{BrO}_2\text{Si}$  (M+H) 351.1354, found 351.1339.



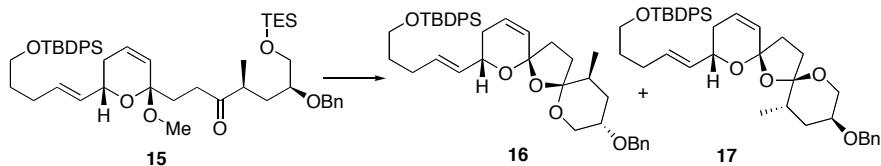
**Aldehyde 41:** To a stirred solution of **40** (31.4 mg, 0.089 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL) with powdered 4 Å mol. sieves (50 mg) were sequentially added NMO (13.5 mg, 0.116 mmol) and TPAP (1.57 mg, 0.0045 mmol) at room temperature. After 30 min, the reaction was diluted with 25% EtOAc / hexanes (5 mL), filtered through a small plug of silica gel (25% EtOAc / hexanes rinse) and concentrated *in vacuo* to give aldehyde **41** (25.0 mg, 81%) as colorless oil:  $[\alpha]_{\text{D}}^{23} - 49.5^{\circ}$  (*c* 0.19,  $\text{CHCl}_3$ ); IR (neat) 2960, 2934, 2854, 1717, 1465, 1246, 1086, 837, 770;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  9.51 (d,  $J = 3.0$  Hz, 1 H), 5.85 – 5.86 (m, 1 H), 5.58 – 5.59 (m, 1 H), 3.86 (d,  $J = 4.8$  Hz, 1 H), 2.38 – 2.44 (m, 1 H), 1.92 – 2.12 (m, 2 H), 1.11 – 1.15 (m, 1 H), 1.08 (d,  $J = 6.9$  Hz, 3 H), 0.91 (s, 9 H), 0.86 (d,  $J = 8.1$  Hz, 3 H), 0.04 (d,  $J = 6.3$  Hz, 6 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  205.8, 136.3, 117.9, 81.3, 44.6, 34.7, 32.4, 26.2, 18.6, 17.5, 15.2, -4.1, -4.7; HRMS (FAB<sup>+</sup>) calcd For  $\text{C}_{15}\text{H}_{28}^{79}\text{BrO}_2\text{Si}$  (M-H) 347.1041, found 347.1034.



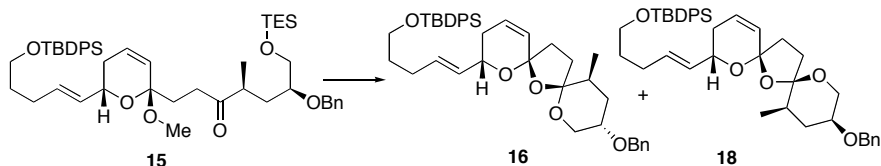
**Phosphonate 11:** To a solution of diethyl methylphosphonate (27.0 mg, 0.178 mmol) in THF (1.48 mL) at  $-78^{\circ}\text{C}$  was added *n*-BuLi (65  $\mu\text{L}$ , 0.16 mmol). After 10 min, a solution of aldehyde **41** (51.7 mg, 0.148 mmol) in THF (0.2 mL) was added. The solution was stirred at  $-78^{\circ}\text{C}$  for 10 min, and allowed to warm to room temperature. The solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (1 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 5 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 50% EtOAc / hexanes, to give adduct **42** (56 mg, 76%) as colorless oil.

To a solution of adduct **42** (17.1 mg, 0.034 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.68 mL) at room temperature was added PDC (25.6 mg, 0.068 mmol) and 4 Å mol. sieves (100 mg). The solution was stirred at room temperature overnight. The solution was diluted with 50% EtOAc, filtered through a small plug of silica gel. The filtrate was concentrated *in vacuo* to give **11** (14.6 mg, 86%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 33.3^{\circ}$  (*c* 0.12,  $\text{CHCl}_3$ ); IR (neat) 2964, 2926, 2850, 1709, 1452, 1254, 1031, 964, 842, 774;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.86 (s, 1 H), 5.59 (d,  $J = 1.5$  Hz, 1 H), 4.09 – 4.18 (m, 4 H), 3.85 (d,  $J = 4.8$  Hz, 1 H), 2.96 –

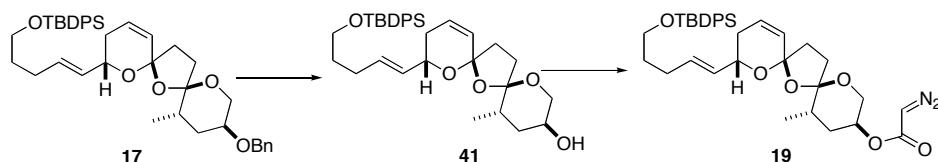
3.22 (m, 2 H), 2.81 – 2.88 (m, 1 H), 1.93 – 2.02 (m, 1 H), 1.84 (m, 1H), 1.32 (t,  $J = 6.9$  Hz, 6 H), 1.12 (d,  $J = 7.2$  Hz, 3 H), 0.95 – 1.03 (m, 1 H), 0.91 (s, 9 H), 0.89 (d,  $J = 6.0$  Hz, 3 H), 0.05 (s, 3 H), 0.03 (s, 3 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  206.0, 205.9, 136.2, 117.8, 81.2, 62.9, 62.8, 45.6, 41.4, 39.7, 34.8, 34.2, 26.2, 18.6, 18.0, 17.5, 16.8, 16.7, -4.1, -4.7; HRMS (FAB<sup>+</sup>) calcd For  $\text{C}_{20}\text{H}_{41}^{79}\text{BrO}_5\text{PSi}$  (M+H) 499.1644, found 499.1637.



**Bispiroketal 16 and 17:** To a stirred solution of ketone **15**<sup>3</sup> (7.5 mg, 0.0093 mmol) in THF (0.8 mL) and  $\text{H}_2\text{O}$  (0.2 mL) was added PPTS (2.36 mg, 0.0093 mmol). After 18 h, the reaction was quenched with solid  $\text{NaHCO}_3$  (10 mg). After 5 min, the solution was diluted with 30% EtOAc / hexanes, filtered through a small plug of silica gel (30% EtOAc / hexanes rinse) and concentrated *in vacuo*. The crude oil was purified by chromatography over silica gel, eluting with 5 – 50% EtOAc / hexanes, to give sequentially transoidal **17**<sup>3</sup> (2.22 mg, 36 %) followed by cisoidal **16**<sup>3</sup> (2.44 mg, 40 %).



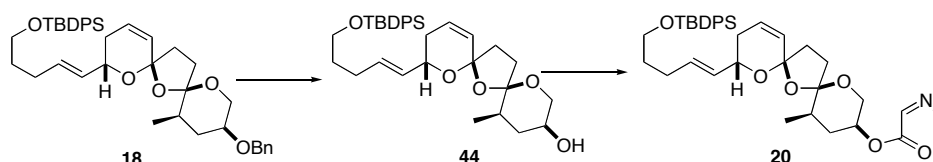
**Bispiroketal 16 and 18:** To a stirred solution of ketone **15**<sup>3</sup> (25.6 mg, 0.032 mmol) in hexanes (4 mL) was added CSA (37.1 mg, 0.16 mmol). After 18 h, the reaction was quenched with solid  $\text{NaHCO}_3$  (200 mg). After 5 min, the solution was diluted with 30% EtOAc / hexanes, filtered through a small plug of silica gel (30% EtOAc / hexanes rinse) and concentrated *in vacuo*. The crude oil was purified by chromatography over silica gel, eluting with 5 – 50% EtOAc / hexanes, to provide sequentially  $\text{C}_{14}$ -*epi* transoidal **18** (8.8 mg, 40%), transoidal **17** (1.5 mg, 7%) and cisoidal **16**<sup>3</sup> (7.0 mg, 32%) and as colorless oil. **18**:  $[\alpha]_{\text{D}}^{23} -36.5^\circ$  ( $c$  0.23,  $\text{CHCl}_3$ ); IR (neat) 2931, 2857, 1456, 1110, 976, 700;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (dd,  $J = 8.0, 1.6$  Hz, 4 H), 7.31 – 7.44 (m, 11 H), 5.94 – 5.98 (m, 1 H), 5.63 – 5.68 (m, 2 H), 5.50 (dd,  $J = 15.6, 6.0$  Hz, 1 H), 4.60 (d,  $J = 11.6$  Hz, 1 H), 4.53 (d,  $J = 11.6$  Hz, 1 H), 4.35 – 4.40 (m, 1H), 3.69 – 3.73 (m, 1 H), 3.65 (t,  $J = 6.4$  Hz, 2 H), 3.63 (m, 1 H), 3.52 – 3.58 (m, 1 H), 2.29 – 2.35 (m, 1 H), 1.55 – 2.17 (m, 12 H), 1.05 (s, 9 H), 0.91 (d,  $J = 6.4$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  139.0, 135.7, 134.2, 132.2, 130.5, 129.8, 129.7, 128.5, 128.0, 127.8, 127.7, 108.5, 104.8, 73.2, 70.7, 69.1, 68.2, 63.4, 60.6, 36.3, 35.3, 33.1, 32.2, 31.8, 30.2, 29.9, 28.8, 27.0, 25.8, 22.8, 21.2, 19.4, 17.0, 14.3; HRMS (FAB<sup>+</sup>) calcd. for  $\text{C}_{41}\text{H}_{52}\text{O}_5\text{Si}$  (M+) 652.3584, found 652.3568.



**Diazoester 19:** To a stirred solution of **17** (11.5 mg, 0.017 mmol) in THF (0.5 mL) at  $-78^\circ\text{C}$  was added LiDBB (1 mL, 0.22 mmol). After 5 min, the solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (0.5 mL) and allowed warm to room temperature. The mixture was extracted with  $\text{Et}_2\text{O}$  (4 x 1 mL) and dried by  $\text{MgSO}_4$ . The dried extract ( $\text{MgSO}_4$ ) was filtered through a small plug of silica gel (10 – 50% EtOAc / hexanes), the filtrate was concentrated *in vacuo* to give the unstable alcohol **41** and used in the next step without further purification.

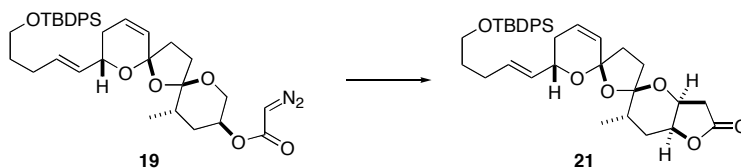
To a stirred solution of crude alcohol **41** (0.0138 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (1.0 mL) at  $0^\circ\text{C}$  were sequentially added dimethylaniline (17.5  $\mu\text{L}$ , 0.138 mmol) and crude glyoxylic acid chloride *p*-

toluenesulfonyl hydrazone<sup>4</sup> (0.138 mmol). The mixture was stirred for 15 min prior to addition of Et<sub>3</sub>N (38.4  $\mu$ L, 0.276 mmol). The resulting dark orange solution was stirred for 10 min at 0°C and then 20 min at room temperature. The CH<sub>2</sub>Cl<sub>2</sub> solution was washed with saturated aqueous citric acid (3 x 1 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. The extract was concentrated in *vacuo* and purified by chromatography over silica gel, eluting with 5 – 20% EtOAc / hexanes, to give diazoester **19** (6.6 mg, 60% two steps) as a colorless oil:  $[\alpha]_D^{23} -57.3^\circ$  (*c* 0.15, CHCl<sub>3</sub>); IR (neat) 2964, 2929, 2863, 2110, 1697, 1110, 972, 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.67 (dd, *J* = 7.5, 1.8 Hz, 4 H), 7.26 – 7.43 (m, 6 H), 5.95 – 6.01 (m, 1 H), 5.62 – 5.69 (m, 2 H), 5.50 (dd, *J* = 15.3, 6.0 Hz, 1 H), 5.02 – 5.05 (m, 1 H), 4.72 (br, 1 H), 4.36 – 4.39 (m, 1 H), 3.80 (dd, *J* = 11.4, 8.1 Hz, 1 H), 3.72 (dd, *J* = 11.4, 4.2 Hz, 1 H), 3.67 (t, *J* = 6.3 Hz, 2 H), 1.63 – 2.19 (m, 13 H), 1.06 (s, 9 H), <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  166.6, 135.9, 134.4, 132.5, 130.7, 130.1, 129.9, 129.6, 128.6, 128.0, 109.4, 104.9, 69.4, 66.5, 64.0, 63.6, 46.7, 36.6, 36.4, 33.3, 32.3, 31.4, 30.5, 30.1, 29.0, 27.2, 19.6, 16.3, 14.6; HRMS (FAB<sup>+</sup>) calcd. for C<sub>36</sub>H<sub>47</sub>N<sub>2</sub>O<sub>6</sub>Si (M+H) 631.3203, found 631.3192.



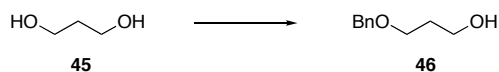
**Diazoester 18:** To a stirred solution of **18** (11.6 mg, 0.017 mmol) in THF (0.5 mL) at -78°C was added LiDBB (1 mL, 0.22 mmol). After 5 min, the solution was quenched with sat. aq. NH<sub>4</sub>Cl (0.5 mL) and allowed warm to room temperature. The mixture was extracted with Et<sub>2</sub>O (4 x 1 mL) and dried by MgSO<sub>4</sub>. The dried extract (MgSO<sub>4</sub>) was filtered through a small plug of silica gel (10 – 50% EtOAc / Hexanes), the filtrate was concentrated in *vacuo* to give the unstable alcohol **44** and used next step without further purification.

To a stirred solution of crude alcohol **44** (33.0 mg, 0.058 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) at 0°C were sequentially added dimethylaniline (37.2  $\mu$ L, 0.29 mmol) and crude glyoxylic acid chloride *p*-toluenesulfonyl hydrazone<sup>4</sup> (0.58 mmol). The mixture was stirred for 15 min prior to addition of Et<sub>3</sub>N (81.0  $\mu$ L, 0.58 mmol). The resulting dark orange solution was stirred for 10 min at 0°C and then 20 min at room temperature. The CH<sub>2</sub>Cl<sub>2</sub> solution was washed with saturated aqueous citric acid (3 x 1 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. The extract was concentrated in *vacuo* and purified by chromatography over silica gel, eluting with 5 – 20% EtOAc / hexanes, to give diazoester **20** (29.3 mg, 65% two steps) as a colorless oil:  $[\alpha]_D^{23} -59.1^\circ$  (*c* 0.23, CHCl<sub>3</sub>); IR (neat) 2964, 2934, 2850, 2332, 2105, 1696, 1094, 968, 694; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.67 (dd, *J* = 7.5, 1.8 Hz, 4 H), 7.34 – 7.44 (m, 6 H), 5.96 – 6.01 (m, 1 H), 5.62 – 5.68 (m, 2 H), 5.49 (dd, *J* = 15.3, 6.0 Hz, 1 H), 4.86 – 4.92 (m, 1 H), 4.68 (s, 1 H), 4.33 – 4.40 (m, 1 H), 3.59 – 3.72 (m, 2 H), 3.64 (t, *J* = 6.0 Hz, 2 H), 1.59 – 2.36 (m, 13 H), 1.04 (s, 9 H), 0.89 (d, *J* = 6.3 Hz, 3 H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  166.4, 135.9, 134.4, 132.5, 130.6, 129.9, 128.6, 128.0, 125.4, 108.5, 105.2, 69.3, 69.0, 63.5, 62.2, 46.6, 36.5, 35.3, 34.6, 33.2, 32.3, 30.4, 29.0, 27.4, 27.2, 21.9, 19.6, 17.0; HRMS (FAB<sup>+</sup>) calcd. for C<sub>36</sub>H<sub>47</sub>N<sub>2</sub>O<sub>6</sub>Si (M+H) 631.3203, found 631.3220.

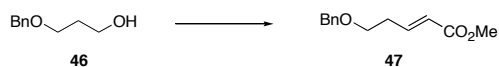


**Lactone 21:** The diazoester **19** (26.8 mg, 0.042 mmol) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (0.42 mL), and the solution was added dropwise (syringe pump), under Ar, over a period of 30 min to a solution of Rh<sub>2</sub>[(4*S*-MPPIM)<sub>4</sub>] (0.58 mg, 0.42  $\mu$ mol) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.42 mL) heated at 42°C (oil bath). After an additional 30 min, the reaction was cooled to room temperature. The cooled reaction mixture was concentrated and filtered through a short pipette of silica gel (1:2; hexanes:EtOAc). The filtrate was concentrated in *vacuo* and purified by chromatography over silica gel, eluting with 5 – 50% EtOAc /

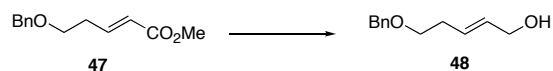
hexanes, to give lactone **21** (3.0 mg, 12%) as a colorless oil:  $[\alpha]_D^{23} - 50^\circ$  (*c*, 0.10, CHCl<sub>3</sub>); IR (neat) 2960, 2926, 2850, 2336, 1785, 1107, 972, 698 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.65 (dd, *J* = 7.5, 1.5 Hz, 4 H), 7.34 – 7.44 (m, 6 H), 5.98 – 6.03 (m, 1 H), 5.61 – 5.71 (m, 2 H), 5.47 (dd, *J* = 15.6, 6.3 Hz, 1 H), 4.31 – 4.41 (m, 3 H), 3.64 (t, *J* = 6.0 Hz, 2 H), 2.68 – 2.69 (m, 2 H), 1.59 – 2.32 (m, 13 H), 1.04 (s, 9 H), 0.90 (d, *J* = 6.9 Hz, 3 H); <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.84 – 7.87 (m, 4 H), 7.31 – 7.33 (m, 6 H), 5.59 – 5.88 (m, 4 H), 4.52 – 4.57 (m, 1 H), 3.71 (t, *J* = 6.3 Hz, 2 H), 3.46 – 3.48 (m, 2 H), 2.47 (d, *J* = 17.1 Hz, 1 H), 2.29 – 2.35 (m, 1 H), 1.98 (dd, *J* = 17.1, 4.2 Hz, 1 H), 1.63 – 2.21 (m, 12 H), 1.26 (s, 9 H), 0.87 (d, *J* = 6.9 Hz, 3 H); <sup>13</sup>C NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  174.6, 136.1, 134.5, 131.5, 130.1, 128.8, 111.1, 104.7, 75.8, 71.9, 69.5, 63.5, 38.7, 36.3, 32.8, 32.6, 30.8, 30.4, 29.1, 27.2, 24.3, 19.6, 15.7; HRMS (FAB<sup>+</sup>) calcd. for C<sub>36</sub>H<sub>47</sub>O<sub>6</sub>Si (M+H) 603.3141, found 603.3150.



**Alcohol 46:** To a stirred solution of 1,3-propanediol (**45**) (15.46 mL, 0.214 mol) in THF (130 mL) at 0°C were sequentially added BnBr (8.49 mL, 71.5 mmol), 20% tetra-*n*-butylammonium iodide (5.28 g, 14.3 mmol) and NaH (3.0 g, 75 mmol, 60% dispersion in mineral oil). After 15 min, the solution allowed warm to room temperature overnight. The solution was quenched with sat. aq. NH<sub>4</sub>Cl (100 mL) and extracted with EtOAc / Et<sub>2</sub>O (1 : 1) (4 x 100 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20 – 50% EtOAc / hexanes, to give product **46** (10.75 g, 91%) as a colorless oil: IR (neat) 3381, 2934, 2871, 1444, 1094, 1073, 736, 694; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.28 – 7.37 (m, 5 H), 4.51 (s, 2 H), 3.70 – 3.76 (m, 2 H), 3.63 (t, *J* = 6.0 Hz, 2 H), 2.97 (t, *J* = 5.4 Hz, 1 H), 1.81 – 1.89 (2 H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  138.6, 128.9, 128.1, 73.6, 69.3, 61.5, 32.7; HRMS (FAB<sup>+</sup>) calcd. for C<sub>10</sub>H<sub>15</sub>O<sub>2</sub> (M+H) 167.1072, found 167.1076.

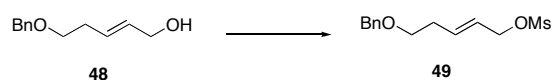


**Ester 47:** To a solution of oxalyl chloride (6.56 mL, 0.075 mol) in CH<sub>2</sub>Cl<sub>2</sub> (170 mL) was cooled to – 50°C, DMSO (10.67 mL, 0.15 mol) was added carefully dropwise. After 5 min, a solution of alcohol **46** (11.35 g, 0.068 mol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added *via* cannula. After, 15 min, Et<sub>3</sub>N (47.52 mL, 0.34 mol) was added dropwise and stirred at –50°C for 10 min. The solution was allowed warm to room temperature within 1 h and quenched with water (100 mL). The aqueous solution was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 100 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* to give crude aldehyde (8.97 g, 80%). To the solution of this crude aldehyde (8.97 g, 0.054 mol) in CH<sub>2</sub>Cl<sub>2</sub> (80 mL) was added Ph<sub>3</sub>P=CHCO<sub>2</sub>Me (21.92 g, 0.066 mol). After overnight, the solution was diluted with 20% EtOAc / hexanes (50 mL), filtered through a small plug of silica gel (20% EtOAc / hexanes rinse), concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 – 50% EtOAc / hexanes, to give product **47** (11.28 g, 95%) as a colorless oil: IR (neat) 3031, 2951, 2863, 1722, 1654, 1431, 1267, 1170, 1103, 1035, 976, 732, 694; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.29 – 7.40 (m, 5 H), 6.99 – 7.06 (m, 1 H), 5.92 – 5.96 (m, 1 H), 4.55 (s, 2 H), 3.76 (s, 3 H), 3.62 (t, *J* = 6.4 Hz, 2 H), 2.52 – 2.57 (m, 2 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  167.2, 146.3, 138.4, 128.8, 128.1, 122.9, 73.4, 68.6, 51.8, 33.0; HRMS (FAB<sup>+</sup>) calcd. for C<sub>13</sub>H<sub>17</sub>O<sub>3</sub> (M+H) 221.1177, found 221.1184.



**Alcohol 48:** To a solution of ester **47** (8.59 g, 39 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (228 mL) at – 78°C was added DIBAL-H (93 mL, 93 mmol, 1.0 M in CH<sub>2</sub>Cl<sub>2</sub>). After 1 h, the solution was allowed warm to 0°C and quenched with 10% aq. sodium tartrate solution (200 mL). The mixture was stirred at room temperature for 3 h and extracted with EtOAc (4 x 100 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20 – 50% EtOAc / hexanes, to give known product **47**<sup>5</sup> (6.05, 81%) as a colorless oil: IR (neat) 3389, 2913, 1867, 1452, 1364, 1107, 1010, 741, 698; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.30 – 7.38 (m, 5 H), 5.73 – 5.75 (m, 2 H), 4.55 (s, 2 H), 4.10 (br, 2 H), 3.55 (t, *J* =

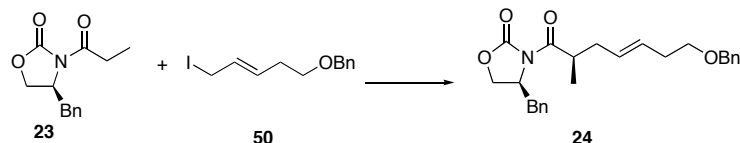
6.8 Hz, 2 H), 2.38 – 2.43 (m, 2 H), 1.91 (br, 1 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  138.7, 131.4, 129.5, 128.8, 128.1, 128.0, 73.3, 70.0, 63.9, 33.0; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{12}\text{H}_{15}\text{O}_2$  (M-H) 191.1072, found 191.1070.



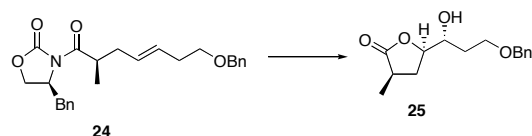
**Ether 49:** To a solution of alcohol **48** (3.08 g, 16.04 mmol) in  $\text{CH}_2\text{Cl}_2$  at  $0^\circ\text{C}$  was added  $\text{Et}_3\text{N}$  (3.35 mL, 24.06 mmol) and  $\text{MsCl}$  (1.49 mL, 19.24 mmol). After 30 min, the solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (30 mL) and extracted with  $\text{Et}_2\text{O}$  (3 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 30 - 50%  $\text{EtOAc}$  / hexanes, to give **49** (3.02 g, 70%) as a colorless oil: IR (neat) 3032, 2863, 1355, 1183, 1098, 934, 736, 698;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 – 7.35 (m, 5 H), 5.90 – 5.97 (m, 1 H), 5.64 – 5.74 (m, 1 H), 4.67 (dd,  $J = 6.6, 0.6$  Hz, 2 H), 4.51 (s, 2 H), 3.54 (t,  $J = 6.3$  Hz, 2 H), 2.93 (s, 3 H), 2.40 – 2.44 (m, 2 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  138.6, 136.4, 128.8, 128.1, 124.4, 73.3, 71.1, 69.3, 38.6, 33.0.



**Iodide 50:** To a solution of ether **49** (3.02 g, 11.18 mmol) in DMF (22.36 mL) at room temperature was added  $\text{NaI}$  (8.33 g, 55.92 mmol). After 1 h, the solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (50 mL) and extracted with  $\text{Et}_2\text{O}$  (3 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 40%  $\text{EtOAc}$  / hexanes, to give iodide **50** (2.64 g, 78%) as a colorless oil: IR (neat) 3031, 2858, 1452, 1360, 1149, 1103, 964, 732, 690;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 – 7.38 (m, 5 H), 5.72 – 5.86 (m, 2 H), 4.53 (s, 2 H), 3.88 – 3.94 (m, 2 H), 3.50 – 3.57 (m, 2 H), 2.34 – 2.41 (m, 2 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  138.8, 131.8, 130.1, 128.9, 128.1, 73.4, 69.6, 33.0, 6.9; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{12}\text{H}_{14}\text{IO}$  (M-H) 301.0089, found 301.0090.



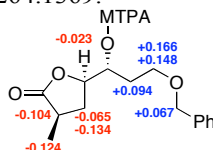
**Adduct 24:** To a stirred solution of oxazolidinone **23** (1.05 g, 4.5 mmol) in THF (9.0 mL) at  $-78^\circ\text{C}$  was added a solution of  $\text{NaHMDS}$  (4.76 mL, 4.76 mmol, 1.0 M in THF). After an additional 20 min, allyl iodide **50** (3.42 g, 11.26 mmol) was added *via* cannula. After 1 h, the mixture was quenched with saturated aqueous sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) and allowed warm to room temperature. The solution was extracted with  $\text{EtOAc}$  (3 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 – 40%  $\text{EtOAc}$  / hexanes, to give product **24** (1.69 g, 92%) as a colorless oil:  $[\alpha]_D^{23} + 10.8^\circ$  ( $c$  0.6,  $\text{CHCl}_3$ ); IR (neat) 2930, 2850, 1776, 1696, 1376, 1208, 1098, 698;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.18 – 7.37 (m, 10 H), 5.51 – 5.54 (m, 2 H), 4.63 – 4.70 (m, 1 H), 4.48 (s, 2 H), 4.10 – 4.20 (m, 2 H), 3.77 – 3.84 (m, 1 H), 3.47 (t,  $J = 6.9$  Hz, 2 H), 3.26 (dd,  $J = 13.2, 3.3$  Hz, 1 H), 2.62 – 2.70 (m, 1 H), 2.43 – 2.50 (m, 1 H), 2.29 – 2.36 (m, 2 H), 2.16 – 2.22 (m, 1 H), 1.16 (d,  $J = 6.9$  Hz, 3 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  177.0, 153.5, 138.8, 135.7, 129.9, 129.8, 129.3, 129.0, 128.7, 128.0, 127.9, 127.7, 73.2, 70.3, 66.4, 55.7, 38.5, 37.9, 37.3, 33.4, 16.7; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{25}\text{H}_{29}\text{O}_4\text{N}$  (M<sup>+</sup>) 407.2097, found 407.2103.



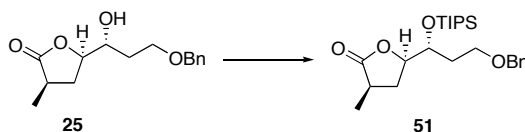
**Lactone 25:** To a stirred solution of **24** (522 mg, 1.28 mmol) in *t*-BuOH (6.4 mL) and  $\text{H}_2\text{O}$  (6.4 mL) at  $0^\circ\text{C}$  were sequentially added solid  $\text{NaHCO}_3$  (517 mg, 6.15 mmol) and AD mix  $\beta^*6$  (1.81 g). The



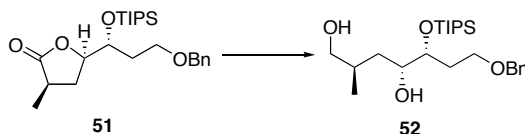
mixture was warmed to room temperature. After 18 h, the reaction was quenched with solid  $\text{Na}_2\text{S}_2\text{O}_3$  until effervescence ceased. After an additional 10 min, the reaction was diluted with saturated aqueous  $\text{NaCl}$  (50 mL) and extracted with  $\text{EtOAc}$  (4 x 100 mL). The dried ( $\text{MgSO}_4$ ) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 – 50%  $\text{EtOAc}$  / hexanes, to give product **25** (187 mg, 55%, 4 : 1 d.r.) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 20.0^\circ$  ( $c$  0.1,  $\text{CHCl}_3$ ); IR (neat) 3448, 2930, 2858, 1764, 1440, 1195, 1166, 1103, 1018, 926, 732, 694;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 – 7.34 (m, 5 H), 4.53 – 4.59 (m, 2 H), 4.31 – 4.36 (m, 1 H), 3.83 – 3.88 (m, 1 H), 3.68 – 3.79 (m, 2 H), 2.75 (d,  $J = 4.4$  Hz, OH), 2.69 – 2.74 (m, 1 H), 2.36 – 2.43 (m, 1 H), 1.78 – 1.91 (m, 3 H), 1.31 (d,  $J = 7.2$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.6, 138.3, 128.9, 128.2, 128.1, 81.2, 73.7, 71.7, 67.8, 35.9, 32.9, 32.7, 15.5; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{15}\text{H}_{20}\text{O}_4$  ( $\text{M}^+$ ) 264.1362, found 264.1369.



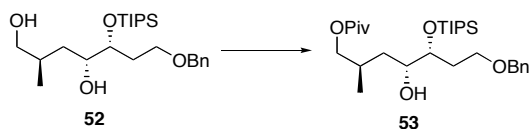
Mosher Ester Analysis<sup>7</sup> of Lactone **25**. Calculated by difference in ppm [(*S*)-Mosher Ester – (*R*)-Mosher ester,  $\text{CDCl}_3$ , 400 MHz NMR].



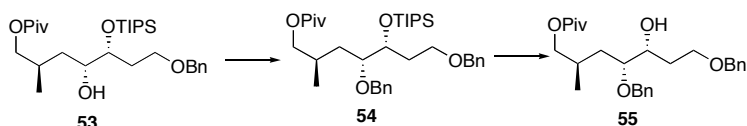
**TIPS Ester 25:** To a solution of lactone **25** (286 mg, 1.08 mmol) in DMF were sequentially added 10% DMAP (13.1 mg), TIPSOTf (398 mg, 1.30 mmol) and imidazole (110 mg, 1.62 mmol). The mixture was stirred at room temperature for 18 h, quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (5 mL), diluted with sat. aq.  $\text{NaCl}$  (5 mL) and extracted with  $\text{EtOAc}$  (3 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 10 – 40%  $\text{EtOAc}$  / hexanes, give product **51** (400 mg, 88%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 12.6^\circ$  ( $c$  0.15,  $\text{CHCl}_3$ ); IR (neat) 2943, 2871, 1772, 1456, 1128, 1107, 871, 673  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.37 (m, 5 H), 4.51 (d,  $J = 12.0$  Hz, 1 H), 4.45 (d,  $J = 12.0$  Hz, 1 H), 4.31 – 4.38 (m, 1 H), 4.01 – 4.07 (m, 1 H), 3.57 – 3.66 (m, 2 H), 2.58 – 2.67 (m, 1 H), 2.30 – 2.39 (m, 1 H), 1.78 – 1.95 (m, 2 H), 1.62 – 1.73 (m, 1 H), 1.24 (d,  $J = 7.2$  Hz, 3 H), 1.05 – 1.10 (m, 21 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 138.7, 128.7, 128.1, 128.0, 80.9, 73.4, 71.8, 66.3, 36.0, 33.5, 33.1, 18.6, 15.4, 13.1; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{24}\text{H}_{41}\text{O}_4\text{Si}$  ( $\text{M}+\text{H}$ ) 421.2774, found 421.2769.



**Diol 52:** To a stirred solution of **51** (430 mg, 1.02 mmol) in THF (3.4 mL) at  $0^\circ\text{C}$  were sequentially added MeOH (48.5  $\mu\text{L}$ ) and  $\text{LiBH}_4$  (0.72 mL, 1.43 mmol, 2.0 M in THF). After 4 h, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (20 mL) and extracted with  $\text{Et}_2\text{O}$  (4 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 20 – 50%  $\text{EtOAc}$  / hexanes, give diol **52** (429 mg, 99%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} + 10.0^\circ$  ( $c$  0.84,  $\text{CHCl}_3$ ); IR (neat) 3338, 2947, 2867, 1452, 1364, 1094, 875, 732, 677;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 – 7.35 (m, 5 H), 4.52 (d,  $J = 12.0$  Hz, 1 H), 4.48 (d,  $J = 12.0$  Hz, 1 H), 3.89 – 3.93 (m, 1 H), 3.51 – 3.64 (m, 7 H), 2.00 – 2.05 (m, 1 H), 1.78 – 1.85 (m, 2 H), 1.52 – 1.57 (m, 1 H), 1.37 – 1.45 (m, 1 H), 1.06 – 1.07 (m, 21 H), 0.89 (d,  $J = 7.2$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  138.2, 128.8, 128.1, 74.6, 73.5, 73.1, 69.4, 67.1, 39.2, 35.4, 34.1, 18.6, 18.5, 13.0; HRMS ( $\text{FAB}^+$ ) calcd. for  $\text{C}_{24}\text{H}_{45}\text{O}_4\text{Si}$  ( $\text{M}+\text{H}$ ) 425.3087, found 425.3089.

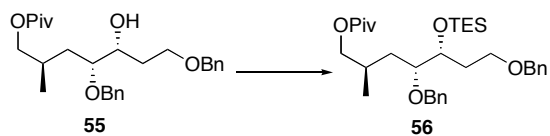


**Pivolated Alcohol 53:** To a stirred solution of **52** (342 mg, 0.80 mmol) in  $\text{CH}_2\text{Cl}_2$  (2.68 mL) at  $-78^\circ\text{C}$  were sequentially added DMAP (9.8 mg),  $\text{Et}_3\text{N}$  (101 mg, 1.0 mmol) and PivCl (115.7 mg, 0.96 mmol). The solution was allowed to warm to  $-30^\circ\text{C}$  over a period of 2 h. The mixture was then recooled to  $-78^\circ\text{C}$  and an additional portion of PivCl (57.8 mg, 0.48 mmol) and  $\text{Et}_3\text{N}$  (50.5 mg, 0.5 mmol) were added to the mixture. The reaction was allowed to warm to room temperature over a period of 45 min. The solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (15 mL) and extracted with  $\text{Et}_2\text{O}$  (4 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 5 – 50% EtOAc / hexanes, to give product **53** (333 mg, 82%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} + 5.8^\circ$  ( $c$  0.17,  $\text{CHCl}_3$ ); IR (neat) 3465, 2938, 2863, 1726, 1461, 1288, 1166, 1094, 884, 728, 677;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.36 (m, 5 H), 4.52 (d,  $J = 12.0$  Hz, 1 H), 4.47 (d,  $J = 12.0$  Hz, 1 H), 3.88 – 3.98 (m, 3 H), 3.61 (d,  $J = 10.8$  Hz, 1 H), 3.55 (t,  $J = 6.0$  Hz, 2 H), 2.59 (br, OH), 1.99 – 2.10 (m, 2 H), 1.79 – 1.87 (m, 1 H), 1.57 – 1.64 (m, 1 H), 1.20 (s, 9 H), 1.07 – 1.08 (s, 21 H), 0.95 (d,  $J = 6.8$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.0, 138.4, 128.8, 128.1, 74.5, 73.5, 70.9, 70.3, 67.1, 39.2, 37.5, 34.4, 29.9, 27.6, 18.6, 18.5, 16.7, 13.1; HRMS (FAB $^+$ ) calcd. for  $\text{C}_{29}\text{H}_{53}\text{O}_5\text{Si}$  (M+H) 509.3662, found 509.3663.



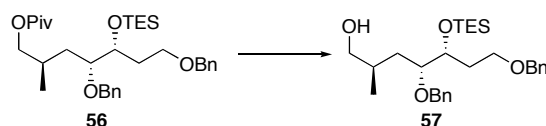
**Alcohol 55:** To a stirred solution of **53** (302 mg, 0.59 mmol) in DMF (1.48 mL) and BnBr (3.05 g, 17.83 mmol) at  $-50^\circ\text{C}$  was added NaH (35.6 mg, 0.89 mmol, 60% in mineral oil). After 10 min, the reaction was warmed to  $-10^\circ\text{C}$  over a period of 50 min. After an additional 1 h, the reaction was further warmed to room temperature. After 30 min, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (5 mL), diluted with sat. aq. NaCl (50 mL) and extracted with EtOAc (4 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 2 - 20% EtOAc / Hexanes, give benzyl ether product **54** (211 mg, 82%) as a colorless oil. The benzyl ether contained with an amount of impurities (50%) resulting from protecting group migration during the benzylation, which were removed after desilylation.

To the mixture solution of benzyl ether **54** in THF (0.5 mL) was added TBAF (1.13 mL, 1.13 mmol, 1.0 M in THF) *via* syringe. After 1 h, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (5 mL) and extracted with  $\text{Et}_2\text{O}$  (3 x 50 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with EtOAc : hexanes :  $\text{CH}_2\text{Cl}_2 = 1 : 6.7 : 6.7$ , to give product **55** (64 mg, 24%) as a colorless oil over two steps:  $[\alpha]_{\text{D}}^{23} + 4.5^\circ$  ( $c$  0.38,  $\text{CHCl}_3$ ); IR (neat) 3494, 2960, 2934, 2875, 1726, 1452, 1162, 1086, 732, 690;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 – 7.38 (m, 10 H), 4.63 (s, 2 H), 4.55 (s, 2 H), 3.88 – 3.99 (m, 3 H), 3.73 – 3.78 (m, 1 H), 3.65 – 3.68 (m, 1 H), 3.49 – 3.55 (m, 1 H), 2.88 (d,  $J = 4.0$  Hz, OH), 2.01 – 2.06 (m, 1 H), 1.81 – 1.86 (m, 2 H), 1.65 – 1.72 (m, 1 H), 1.43 – 1.49 (m, 1 H), 1.23 (s, 9 H), 0.96 (d,  $J = 6.8$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  178.9, 138.8, 138.4, 128.9, 128.8, 128.2, 128.1, 79.9, 73.7, 73.0, 72.2, 69.8, 69.3, 39.2, 34.3, 32.9, 29.9, 27.6, 17.2; HRMS (FAB $^+$ ) calcd. for  $\text{C}_{27}\text{H}_{39}\text{O}_5$  (M+H) 443.2797, found 443.2797.

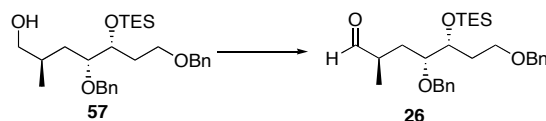


**TES Ether 55:** To a stirred solution of **55** (64 mg, 0.14 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.72 mL) at  $0^\circ\text{C}$  were sequentially added DMAP (1.7 mg),  $\text{Et}_3\text{N}$  (21.2 mg, 0.21 mmol), and TESCl (25.62 mg, 0.17 mmol). After 45 min, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (1 mL) and extracted with  $\text{Et}_2\text{O}$  (4 x 10 mL). The

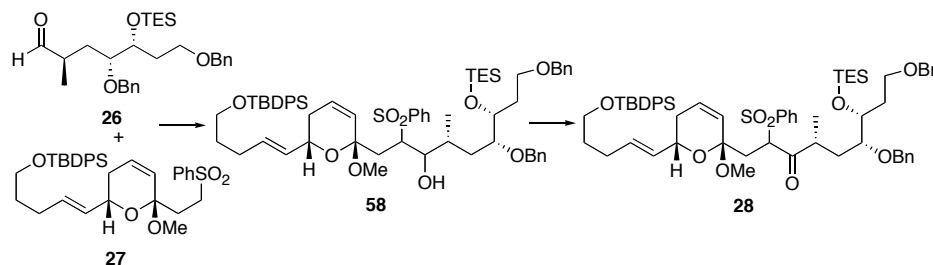
dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 5 – 20% EtOAc / hexanes, to give product **56** (77.2 mg, 99%) as a colorless oil:  $[\alpha]_D^{23} + 27.8^\circ$  (*c* 0.28, CHCl<sub>3</sub>); IR (neat) 2960, 2880, 1722, 1448, 1275, 1162, 1098, 1002, 737; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.29 – 7.38 (m, 10 H), 4.66 (d, *J* = 11.6 Hz, 1 H), 4.53 (s, 2 H), 4.51 (d, *J* = 11.6 Hz, 1 H), 4.14 – 4.18 (m, 1 H), 4.00 (dd, *J* = 10.8, 5.6 Hz, 1 H), 3.92 (dd, *J* = 10.8, 5.6 Hz, 1 H), 3.58 – 3.62 (m, 2 H), 3.47 – 3.51 (m, 1 H), 2.03 – 2.09 (m, 2 H), 1.43 – 1.66 (m, 3 H), 1.23 (s, 9 H), 0.98 (t, *J* = 8.0 Hz, 9 H), 0.90 (d, *J* = 6.8 Hz, 3 H), 0.61 (q, *J* = 8.0 Hz, 6 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  179.0, 139.1, 128.7, 128.3, 128.0, 127.8, 79.5, 73.2, 72.3, 70.2, 68.6, 67.7, 39.3, 32.4, 31.7, 29.9, 27.7, 16.7, 7.4, 5.4; HRMS (FAB<sup>+</sup>) calcd. for C<sub>33</sub>H<sub>53</sub>O<sub>5</sub>Si (M+H) 557.3662, found 557.3664.



**Alcohol 55:** To a stirred solution of **56** (77.2 mg, 0.13 mmol) in THF (0.68 mL) at 0°C were added H<sub>2</sub>O (5.05  $\mu$ L) and LiBH<sub>4</sub> (0.14 mL, 0.28 mmol, 2.0 M in THF). The reaction was warmed to r.t. and sat. aq. NH<sub>4</sub>Cl (7.47  $\mu$ L) was added dropwise. An additional portion of LiBH<sub>4</sub> (70  $\mu$ L, 0.14 mmol, 2.0 M in THF) was added during the course of the reaction. After 3 h, the reaction was quenched with sat. aq. NH<sub>4</sub>Cl (5 mL) and extracted with Et<sub>2</sub>O (4 x 10 mL). The dried (MgSO<sub>4</sub>) extract was concentrated *in vacuo* and purified chromatography over silica gel, eluting with 10 – 40% EtOAc / hexanes, to give product **57** (58.5 mg, 89%) as a colorless oil:  $[\alpha]_D^{23} + 30.0^\circ$  (*c* 0.15, CHCl<sub>3</sub>); IR (neat) 3397, 2955, 2880, 1452, 1094, 1040, 997, 728; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.29 – 7.38 (m, 10 H), 4.69 (d, *J* = 11.2 Hz, 1 H), 4.53 (s, 2 H), 4.50 (d, *J* = 11.2 Hz, 1 H), 4.20 – 4.24 (m, 1 H), 3.45 – 3.62 (m, 5 H), 2.30 (br, OH), 2.02 – 2.10 (m, 1 H), 1.77 – 1.83 (m, 1 H), 1.60 – 1.66 (m, 2 H), 1.44 – 1.50 (m, 1 H), 0.98 (t, *J* = 8.0 Hz, 9 H), 0.92 (d, *J* = 6.8 Hz, 3 H), 0.61 (q, *J* = 8.0 Hz, 6 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  139.1, 138.4, 128.8, 128.7, 128.5, 128.2, 127.9, 127.8, 81.0, 73.1, 72.3, 69.0, 68.0, 67.5, 34.3, 32.8, 31.4, 17.8, 7.3, 5.4; HRMS (FAB<sup>+</sup>) calcd. for C<sub>28</sub>H<sub>45</sub>O<sub>4</sub>Si (M+H) 473.3087, found 473.3091.

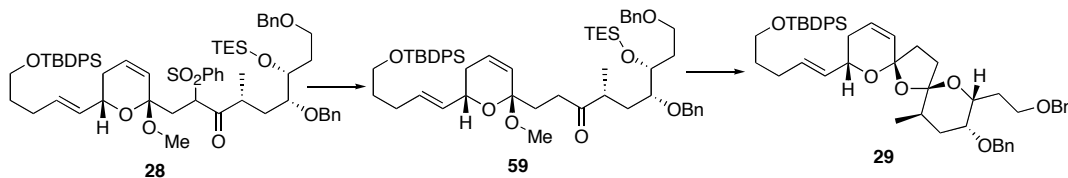


**Aldehyde 26:** To a stirred solution of **57** (28 mg, 0.059 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) with powdered 4 Å mol. sieves (70 mg) were sequentially added NMO (8.98 mg, 0.076 mmol) and TPAP (1.04 mg, 2.95  $\mu$ mol) at room temperature. After 30 min, the reaction was diluted with 25% EtOAc / hexanes (5 mL), filtered through a small plug of silica gel (25% EtOAc / hexanes rinse) and concentrated *in vacuo* to give **26** (26.6 mg, 95%) as a colorless oil:  $[\alpha]_D^{23} + 21.0^\circ$  (*c* 0.14, CHCl<sub>3</sub>); IR (neat) 2947, 2875, 1722, 1448, 1094, 1006, 736, 694; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.56 (d, *J* = 2.4 Hz, 1 H), 7.29 – 7.38 (m, 10 H), 4.59 (d, *J* = 11.2 Hz, 1 H), 4.53 (s, 2 H), 4.43 (d, *J* = 11.2 Hz, 1 H), 4.15 – 4.18 (m, 1 H), 3.57 – 3.62 (m, 2 H), 3.43 – 3.47 (m, 1 H), 2.46 – 2.49 (m, 1 H), 2.06 – 2.15 (m, 1 H), 1.86 – 1.90 (m, 1 H), 1.62 – 1.69 (m, 2 H), 1.05 (d, *J* = 7.2 Hz, 3 H), 0.97 (t, *J* = 7.6 Hz, 9 H), 0.59 (q, *J* = 7.6 Hz, 6 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  205.4, 139.0, 138.5, 128.8, 128.7, 128.5, 128.1, 127.9, 127.8, 80.0, 73.1, 72.3, 68.2, 67.4, 44.7, 31.5, 30.7, 14.0, 7.3, 5.3; HRMS (FAB<sup>+</sup>) calcd. for C<sub>28</sub>H<sub>43</sub>O<sub>4</sub>Si (M+H) 471.2930, found 471.2929.



**Ketone Sulfone 28:** To a stirred solution of **27** (128 mg, 0.212 mmol) in THF (1.41 mL) at  $-78^{\circ}\text{C}$  was added LDA<sup>8</sup> (0.22 mL, 0.22 mmol, 1.0 M in THF) dropwise. After 25 min, a solution of the aldehyde **26** (86.1 mg, 0.183 mmol) in precooled THF (0.2 mL) was added *via* cannula to the sulfone solution. After 25 min, the reaction was removed from the cooling bath. The solution was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (2 mL) and extracted with  $\text{Et}_2\text{O}$  (4 X 30 mL). The dried ( $\text{MgSO}_4$ ) extract was concentrated *in vacuo* to give crude hydroxy sulfone **58**. The crude hydroxy sulfone **58** was used next step immediately.

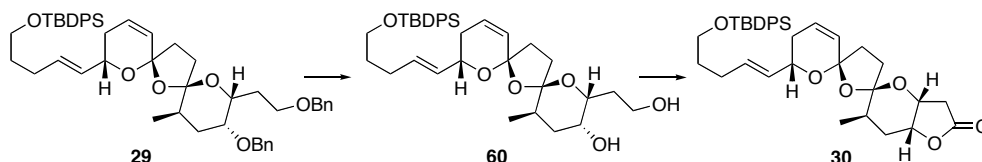
To a stirred solution of crude hydroxy sulfone **58** (0.183 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.61 mL) were sequentially added powdered 4 Å mol. sieves (30 mg), TPAP (96 mg, 0.27 mmol) and NMO (32 mg, 0.27 mmol). After 4 h, the reaction was diluted with 25 % EtOAc / hexanes, filtered through a small plug of silica gel and concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 – 40% EtOAc / hexanes, to give ketone sulfone **28** (114 mg, 66% over two steps) as a colorless oil:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 – 7.79 (m, 25 H), 5.83 – 5.89 (m, 1 H), 5.41 – 5.59 (m, 2 H), 5.27 – 5.35 (m, 1 H), 4.66 – 4.72 (m, 1 H), 4.62 (d,  $J = 9.3$  Hz, 1 H), 4.51 (d,  $J = 10.8$  Hz, 1 H), 4.46 (d,  $J = 10.8$  Hz, 1 H), 4.38 (d,  $J = 9.3$  Hz, 1 H), 4.08 – 4.19 (m, 2 H), 3.54 – 3.68 (m, 4 H), 3.42 – 3.44 (m, 1 H), 3.23 – 3.40 (m, 1 H of a diastereomer), 3.10 (s, 3 H of a diastereomer), 3.07 (s, 3 H of a diastereomer), 3.0 – 3.10 (m, 1 H of a diastereomer), 2.65 (dd,  $J = 13.6, 10.4$  Hz, 1 H of a diastereomer), 2.31 (dd,  $J = 13.6, 10.4$ , 1 H of a diastereomer), 1.47 – 2.22 (m, 13 H), 1.06 (s, 9 H of a diastereomer), 1.05 (s, 9 H of a diastereomer), 0.94 (t,  $J = 8.1$  Hz, 9 H), 0.56 (q,  $J = 7.8$  Hz, 6 H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  205.6, 205.4, 139.1, 136.0, 134.4, 132.6, 130.6, 130.0, 129.8, 128.8, 128.7, 128.6, 128.4, 128.0, 97.7, 96.8, 79.4, 78.8, 73.1, 72.2, 69.8, 69.7, 69.2, 68.4, 68.1, 67.5, 63.7, 49.2, 44.3, 35.2, 32.3, 31.8, 30.6, 29.0, 27.3, 19.6, 15.5, 14.9, 7.4, 5.4.



**Spirocycle 29:** To a stirred solution of **28** (61.0 mg, 0.064 mmol) in THF (1.0 mL) and MeOH (3.8 mL) at  $-10^{\circ}\text{C}$  was added  $\text{Na}_2\text{HPO}_4$  (61.0 mg, 0.011 mmol). After 5 min, 5% Na / Hg amalgam (469 mg, 0.99 mmol, 5% in Hg) was added. After 1 h, the reaction was diluted with 20% EtOAc / hexanes, filtered through a small plug of silica gel and concentrated *in vacuo* to give crude ketone **59** (42.4 mg, 82%) which was used next step without further purification.

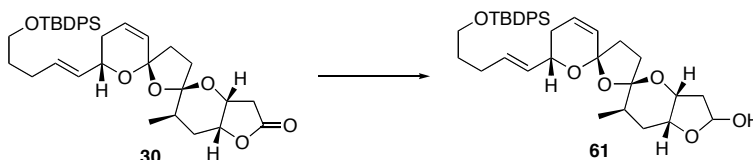
To a stirred solution of ketone **59** (42.4 mg, 0.052 mmol) in THF/ $\text{H}_2\text{O}$  (2.64 mL, 4 : 1) was added PPTS (13.2 mg, 0.052 mmol). After 15 h, the solution was quenched with solid  $\text{NaHCO}_3$  (25 mg). After 5 min, the solution was diluted with 40% EtOAc / hexanes, filtered through a small plug of silica gel and concentrated *in vacuo*. The crude oil was purified by chromatography over silica gel, eluting with 2 – 20% EtOAc / hexanes, to give **29** (20.4 mg, 50%) as a colorless oil:  $[\alpha]_D^{23} - 60.7^{\circ}$  ( $c$  0.14,  $\text{CHCl}_3$ ); IR (neat) 2926, 2854, 1452, 1233, 1082, 1103, 972, 698;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67 (dd,  $J = 7.6, 1.6$  Hz, 4 H), 7.28 – 7.44 (m, 16 H), 5.83 – 5.86 (m, 1 H), 5.62 – 5.69 (m, 1 H), 5.47 – 5.54 (m, 2 H), 4.67 (d,  $J = 12.4$  Hz, 1 H), 4.50 (d,  $J = 12.0$  Hz, 1 H), 4.45 (d,  $J = 12.0$  Hz, 1 H), 4.42 (d,  $J = 12.4$  Hz, 1 H), 4.33 – 4.36 (m, 1 H), 4.02 (dd,  $J = 9.6, 2.4$  Hz, 1 H), 3.65 (t,  $J = 6.4$  Hz, 2 H), 3.49 – 3.58 (m, 2 H), 3.29 (s, 1 H), 2.27 – 2.33 (m, 1 H), 1.56 – 2.17 (m, 14 H), 1.05 (s, 9 H), 0.87 (d,  $J = 6.8$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  139.1, 138.9, 135.9, 134.4, 132.4, 130.8, 130.3, 129.9, 128.7, 128.6, 128.4, 128.1, 128.0, 127.9,

127.8, 109.7, 104.7, 74.1, 73.3, 71.0, 69.2, 68.9, 67.6, 63.6, 36.7, 33.4, 32.5, 32.4, 32.2, 30.4, 30.2, 30.1, 29.1, 27.2, 19.6, 16.7; HRMS (FAB<sup>+</sup>) calcd. for C<sub>50</sub>H<sub>61</sub>O<sub>6</sub>Si (M-H) 785.4237, found 785.4221.

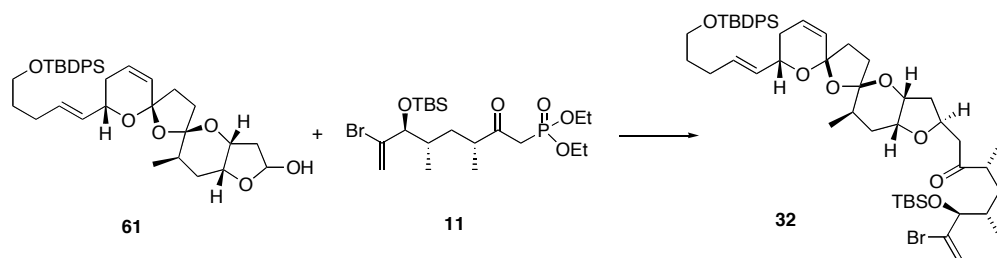


**Lactone 22:** To a stirred solution of **29** (5.0 mg, 0.0063 mmol) in THF (0.5 mL) at  $-78^{\circ}\text{C}$  was added LiDBB (1 mL, 0.22 mmol). The green color solution was stirred at  $-78^{\circ}\text{C}$  for 5 min, and quenched by sat. aq.  $\text{NH}_4\text{Cl}$  (0.5 mL) and extracted with  $\text{Et}_2\text{O}$  (4 x 1 mL). The dried extract ( $\text{MgSO}_4$ ) was filtered through a small plug of silica gel (10 – 50%  $\text{EtOAc}$  / Hexanes), the filtrate was concentrated in *vacuo* to give diol **60** (3.6 mg, 94%) and used next step without further purification.

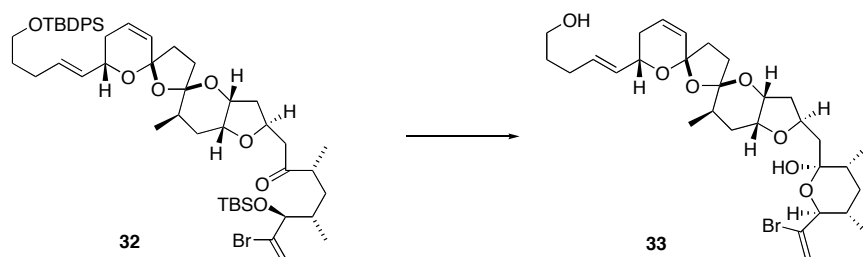
To a stirred solution of crude diol **60** (3.6 mg, 0.0059 mmol) in *t*-BuOH /  $\text{CH}_3\text{CN}$  (0.2 mL, 1:1) were sequentially added 4 Å mol. sieves (10 mg), NMO (1.73 mg, 0.0147 mmol) and 5% TPAP (0.1 mg). After overnight, the solution was diluted with 50%  $\text{EtOAc}$  / hexanes, filtered through a small plug of silica gel and concentrated in *vacuo*. The crude oil was purified by chromatography over silica gel, eluting with 5 – 33%  $\text{EtOAc}$  / hexanes, to give ketone **22** (2.8 mg, 78%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 53.6^{\circ}$  (*c* 0.11,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (dd,  $J = 7.6, 1.2$  Hz, 4 H), 7.36 – 7.44 (m, 6 H), 5.98 – 6.03 (m, 1 H), 5.63 – 5.71 (m, 2 H), 5.49 (dd,  $J = 15.6, 6.0$  Hz, 1 H), 4.45 (dd,  $J = 4.4, 2.4$  Hz, 1 H), 4.36 – 4.38 (m, 1 H), 4.30 – 4.34 (m, 1 H), 3.65 (t,  $J = 6.4$  Hz, 2 H), 2.69 (dd,  $J = 17.2, 4.4$  Hz, 1 H), 2.52 (d,  $J = 17.4$  Hz, 1 H), 2.31 – 2.39 (m, 1 H), 1.56 – 2.18 (m, 12 H), 1.05 (s, 9 H), 0.87 (d,  $J = 6.4$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.8, 135.9, 134.4, 132.6, 130.4, 129.9, 129.1, 129.0, 127.9, 109.2, 105.2, 78.2, 76.9, 69.3, 68.3, 63.5, 38.9, 36.4, 33.1, 32.3, 30.4, 30.1, 29.2, 29.0, 27.2, 19.6, 16.2; HRMS (FAB<sup>+</sup>) calcd. for C<sub>36</sub>H<sub>47</sub>O<sub>6</sub>Si (M+H) 603.3141, found 603.3150.



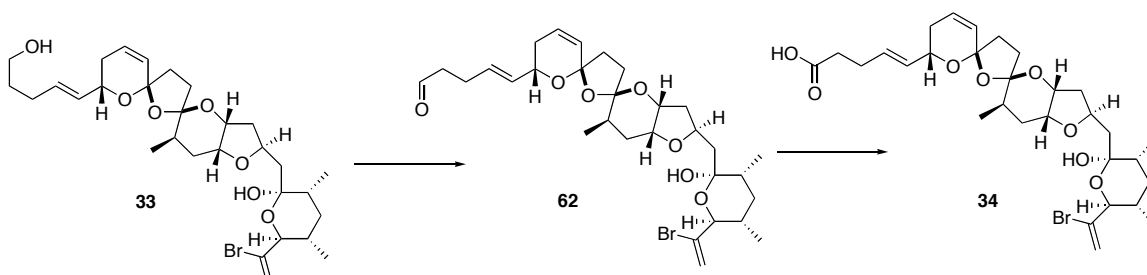
**Lactol 61:** To a stirred solution of lactone **30** (1.8 mg, 0.003 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.2 mL) at  $-78^{\circ}\text{C}$  was added DIBAL-H (0.05 mL, 0.05 mmol, 1.0 M in  $\text{CH}_2\text{Cl}_2$ ). After 20 min, the solution was quenched with 10% aq. sodium tartrate (0.1 mL) and allowed warm to room temperature. The mixture was stirred at room temperature for 1 h and extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 1 mL). The dried extract ( $\text{MgSO}_4$ ) was concentrated in *vacuo* to give crude product **61** (1.4 mg, 78%) as colorless oil: IR (neat) 3402, 2926, 2850, 1456, 1237, 1107, 972, 821, 694;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (dd,  $J = 8.0, 1.6$  Hz, 4 H), 7.39 – 7.47 (m, 6 H), 6.00 – 6.03 (m, 1 H), 5.68 – 5.70 (m, 2 H), 5.52 (dd,  $J = 15.2, 6.0$  Hz, 1 H of a diastereomer), 5.37 (dd,  $J = 15.2, 6.0$  Hz, 1 H of a diastereomer), 4.36 – 4.39 (m, 1 H), 4.31 (br, 1 H), 4.16 (br, 1 H of a diastereomer), 4.08 – 4.12 (m, 1 H of a diastereomer), 3.92 (br, 1 H of a diastereomer), 3.68 (t,  $J = 6.0$  Hz, 2 H), 2.69 (br, 1 H of a diastereomer), 1.64 – 2.50 (m, 15 H), 1.07 (s, 9 H), 0.92 (d,  $J = 6.4$  Hz, 3 H of a diastereomer), 0.88 (d,  $J = 6.4$  Hz, 3 H of a diastereomer);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  136.0, 134.4, 132.7, 130.5, 129.9, 129.5, 129.0, 128.0, 109.7, 105.2, 99.5, 99.0, 75.7, 72.1, 71.2, 69.4, 69.2, 63.6, 43.0, 42.0, 36.5, 33.7, 32.4, 31.6, 30.5, 30.1, 29.9, 29.1, 27.3, 19.7, 16.4; HRMS (FAB<sup>+</sup>) calcd. for C<sub>36</sub>H<sub>47</sub>O<sub>6</sub>Si (M-H) 603.3141, found 603.3166.



**Adduct 30:** To a solution of phosphonate **11** (18.5 mg, 0.037 mmol) in THF (0.36 mL) at  $-78^{\circ}\text{C}$  was added KHMDS (74.0  $\mu\text{L}$ , 0.037 mmol, 0.5 M in toluene). After 10 min, a solution of lactol **61** (5.6 mg, 0.00927 mmol) in THF (0.1 mL) was added *via* cannula. The solution was stirred at  $-78^{\circ}\text{C}$  for 10 min and allowed warm to room temperature for 15 h. The solution was quenched with five drops of sat. aq.  $\text{NH}_4\text{Cl}$  and purified by chromatography over silica gel, eluting with 2 – 20% EtOAc / hexanes, give product **32** (4.0 mg, 45%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 66.7^{\circ}$  ( $c$  0.06,  $\text{CHCl}_3$ ); IR (neat) 2955, 2926, 2854, 2328, 1701, 1452, 1242, 1107, 1082, 972, 837, 698;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66 (dd,  $J = 8.0, 1.6$  Hz, 4 H), 7.36 – 7.44 (m, 6 H), 5.97 – 6.00 (m, 1 H), 5.86 (s, 1 H), 5.61 – 5.69 (m, 2 H), 5.59 (s, 1 H), 5.49 (dd,  $J = 15.6, 6.0$  Hz, 1 H), 4.59 – 4.63 (m, 1 H), 4.33 – 4.36 (m, 1 H), 4.22 (br, 1 H), 3.88 (br, 1 H), 3.85 (d,  $J = 4.8$  Hz, 1 H), 3.65 (t,  $J = 6.4$  Hz, 2 H), 2.84 (dd,  $J = 16.8, 6.0$  Hz, 1 H), 2.56 – 2.65 (m, 1 H), 2.55 (dd,  $J = 16.8, 6.0$  Hz, 1 H), 2.30 – 2.36 (m, 1 H), 1.62 – 2.20 (m, 17 H), 1.10 (d,  $J = 6.8$  Hz, 3 H), 1.04 (s, 9 H), 0.92 (s, 9 H), 0.89 (d,  $J = 6.8$  Hz, 3 H), 0.84 (d,  $J = 6.4$  Hz, 3 H), 0.06 (d,  $J = 10.4$  Hz, 6 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.1, 136.1, 135.7, 134.2, 132.3, 130.5, 129.7, 128.3, 127.8, 117.6, 109.6, 104.6, 81.1, 76.1, 74.8, 72.2, 68.9, 63.3, 46.3, 45.4, 40.7, 36.4, 34.6, 34.2, 33.1, 32.2, 31.6, 30.3, 29.9, 29.5, 28.8, 27.0, 26.0, 19.4, 18.4, 17.9, 17.2, 16.3, -4.3, -4.8; HRMS (FAB $^+$ ) calcd. for  $\text{C}_{52}\text{H}_{77}^{79}\text{BrO}_7\text{Si}_2$  (M) 948.4391, found 948.4397.



**Alcohol 31:** To a solution of **32** (1.4 mg, 0.00147 mmol) in THF (20  $\mu\text{L}$ ) at room temperature was added TBAF (29  $\mu\text{L}$ , 0.029 mmol, 1.0 M in THF). After 30 min, the solution was quenched with five drops of sat. aq.  $\text{NH}_4\text{Cl}$ . The mixture was purified by chromatography over silica gel, eluting with 2 – 50% EtOAc / hexanes, to give product **33** (0.5 mg, 57%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 55.0^{\circ}$  ( $c$  0.06,  $\text{CHCl}_3$ ); IR (neat) 3389, 2951, 2922, 2854, 2332, 1701, 1658, 1557, 1456, 1027, 976, 800, 694;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  5.95 – 5.98 (m, 1 H), 5.85 (s, 1 H), 5.63 – 5.73 (m, 2 H), 5.57 (s, 1 H), 5.49 (dd,  $J = 15.6, 6.4$  Hz, 1 H), 4.59 (s, 1 H), 4.40 – 4.46 (m, 1 H), 4.33 – 4.35 (m, 1 H), 4.20 (br, 1 H), 3.93 (d,  $J = 10.0$  Hz, 1 H), 3.86 (br, 1 H), 3.53 (t,  $J = 6.4$  Hz, 2 H), 2.31 – 2.34 (m, 1 H), 1.37 – 2.20 (m, 21 H), 0.91 (d,  $J = 6.8$  Hz, 3 H), 0.87 (d,  $J = 6.4$  Hz, 3 H), 0.76 (d,  $J = 6.4$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  136.2, 132.8, 131.9, 130.6, 129.2, 120.5, 110.8, 106.0, 99.9, 81.6, 77.0, 73.7, 70.5, 62.3, 54.9, 46.3, 42.4, 37.3, 36.6, 35.0, 33.9, 33.2, 32.7, 31.5, 30.8, 30.6, 29.7, 23.9, 17.6, 17.4; HRMS (FAB $^+$ ) calcd. for  $\text{C}_{29}\text{H}_{42}^{79}\text{BrO}_7$  (M-Me) 581.2113, found 581.2127.



**Acid 34:** To a solution of **33** (1.7 mg, 0.0028 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.2 mL) was added TPAP (1.0 mg, 0.0028 mmol). After 10 min, the solution was diluted with 20% EtOAc / hexanes and filtered through a small plug of silica gel. The filtrate was concentrated in *vacuo* to give crude aldehyde **62** (1.15 mg, 68%) and used next step without further purification.

To a stirred solution of aldehyde **62** (1.15 mg, 0.0019 mmol) in *t*-BuOH /  $\text{H}_2\text{O}$  (0.2 mL, 1:1) was added  $\text{NaClO}_2$  (1.52 mg, 0.0168 mmol),  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$  (2.32 mg, 0.00168 mmol) and 2-methyl-2-butene (1.2 mg, 0.0168 mmol). After 10 min, the solution was quenched with sat. aq.  $\text{Na}_2\text{S}_2\text{O}_3$  (0.2 mL) and purified through pipette of silica gel to give product **34** (0.7 mg, 60%) as a colorless oil:  $[\alpha]_{\text{D}}^{23} - 32.5^\circ$  (*c* 0.04, MeOH); IR (neat) 3275, 2917, 2850, 1671, 1566, 1435, 1313, 1237, 1082, 867, 837;  $^1\text{H}$  NMR (400 MHz, 0.5%  $\text{CD}_3\text{COOD}$  in  $\text{CD}_3\text{OD}$ )  $\delta$  5.94 – 5.97 (m, 1 H), 5.85 (s, 1 H), 5.62 – 5.74 (m, 2 H), 5.56 (s, 1 H), 5.52 (dd,  $J = 15.6, 6.0$  Hz, 1 H), 4.39 – 4.44 (m, 1 H), 4.32 – 4.34 (m, 1 H), 4.19 (br, 1 H), 3.92 (d,  $J = 10.0$  Hz, 1 H), 3.85 (br, 1 H), 1.39 – 2.33 (m, 24 H), 0.91 (d,  $J = 6.8$  Hz, 3 H), 0.86 (d,  $J = 6.4$  Hz, 3 H), 0.75 (d,  $J = 6.4$  Hz, 3 H); HRMS (FAB $^+$ ) calcd. for  $\text{C}_{30}\text{H}_{42}^{81}\text{BrO}_7$  (M-OH) 595.2093, found 595.2108.

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- (6) AD mix  $\beta^*$  = (DHQD)<sub>2</sub>PHAL (100 mg), K<sub>2</sub>OsO<sub>2</sub>·2H<sub>2</sub>O (14.2 mg), K<sub>2</sub>CO<sub>3</sub> (478 mg), K<sub>3</sub>Fe(CN)<sub>6</sub> (1.22 g).
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- (8) The 1.0 M LDA solution was prepared fresh immediately prior to use: To a stirred solution of *N,N*-diisopropylamine (404 mg, 560  $\mu$ L, 4.0 mmol) in THF (1.84 mL) at -78°C was added *n*-BuLi (1.6 mL, 4.0 mmol, 2.5 M in hexanes) dropwise. After 5 min, the white suspension was warmed to -10°C. After 30 min, the solution was employed in the relevant reaction.