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.

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 trimethylsilane and referenced internally to the residually protonated solvent. $^{13}$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 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°C or by a bunsen flame, then cooled under argon. Solvents and commercial reagents were purified in accord with Perrin and Armarego$^1$ or used without further purification.

![Adduct 36](image)

**Adduct 36**: To a stirred solution of **12** (4.8 g, 10 mmol) in CH$_2$Cl$_2$ (50 mL) was added Et$_3$N (3.4 mL, 24 mmol). The solution was cooled to −78°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°C for 2 h. Aldehyde **35**$^2$ (1.6 g, 12 mmol) was added dropwise to the enolate solution. The reaction mixture was stirred at −78°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. H$_2$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 CH$_2$Cl$_2$ (200 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 x 150 mL). The dried (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: [α]$_D^{23} + 10.2^\circ$ (c 0.4, CHCl$_3$); IR (neat) 3348, 2930, 2846, 1730, 1705, 1654, 1562, 1448, 1149, 833; $^1$H NMR (400 MHz, CDCl$_3$) δ 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); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 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$^+$) calcd. for C$_31$H$_{37}$O$_5$BrNO$_3$S (M+H) 614.1575, found 614.1571.

![TBS Silyl Ether 37](image)

**TBS Silyl Ether 37**: To a stirred solution of **36** (5.65 g, 9.2 mmol) in CH$_2$Cl$_2$ (25 mL) at 0°C were sequentially added Et$_3$N (3.2 mL, 23 mmol) and TBSOTf (3.65 g, 13.8 mmol). The mixture was stirred at 0°C for 3 h and quenched with sat. aq. NH$_4$Cl (50 mL). The aqueous solution was extracted with CH$_2$Cl$_2$ (4 x 100 mL). The dried (MgSO$_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 40% EtOAc / hexanes, to give product **36** (4.13 g, 62%) as colorless oil: [α]$_D^{23} + 23.5^\circ$ (c 1.1, CHCl$_3$); IR (neat) 2930, 2846, 1730, 1705, 1654, 1562, 1448, 1149, 833; $^1$H NMR (400 MHz, CDCl$_3$) δ 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); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 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\textsuperscript{+}) calcd. for \(\text{C}_{27}\text{H}_{49}\text{BrNO}_{2}\text{Si}(\text{M}-\text{H})\) 726.2284, found 726.2296.

**Alcohol 13:** To a stirred solution of 37 (3.47 g, 4.76 mmol) in \(\text{CH}_{2}\text{Cl}_{2}\) at \(-78^\circ\text{C}\) was added DIBAL-H (11.4 mL, 11.4 mmol, 1M in \(\text{CH}_{2}\text{Cl}_{2}\)). The solution was stirred at \(-78^\circ\text{C}\) for 1 h and allowed to warm to 0\(^\circ\text{C}\) 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\(_2\text{O}\) (3 x 100 mL). The dried (MgSO\(_4\)) 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: \([\alpha]_D^{23} = 21.6^\circ\) (c 0.25, CHCl\(_3\)); IR (neat) 3348, 2960, 2930, 2854, 1650, 1417, 1384, 771; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 5.87 (m, 1 H), 5.61 (d, \(J = 1.5\) Hz, 1 H), 4.00 (dd, \(J = 11.1, 3.9\) Hz, 1 H), 3.48 (dd, \(J = 7.6, 3.9\) Hz, 1 H), 2.00 - 2.07 (m, 1 H), 0.96 (d, \(J = 7.2\) Hz, 3 H), 0.91 (s, 3 H), 0.11 (s, 3 H), 0.08 (s, 3 H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 136.5, 118.2, 81.5, 53.8, 26.6, 26.1, 18.6, 15.5, -4.1, -4.7; HRMS (FAB\textsuperscript{+}) calcd. for \(\text{C}_{21}\text{H}_{26}\text{BrO}_{2}\text{Si}(\text{M}+\text{H})\) 309.0885, found 309.0883.

**Iodide 38:** To a solution of triphenylphosphine (115 mg, 0.44 mmol) in \(\text{CH}_2\text{Cl}_2\) at 0\(^\circ\text{C}\) 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 \(\text{CH}_2\text{Cl}_2\) (1 mL) was added via cannula. The mixture was stirred at 0 \(^\circ\text{C}\) for 10 min, then warmed to room temperature. After 12 h, the mixture was quenched by saturated Na\(_2\)S\(_2\)O\(_5\) (1.5 mL), diluted with water (2 mL). The aqueous solution was extracted with \(\text{CH}_2\text{Cl}_2\) (3 x 5 mL). The dried (MgSO\(_4\)) 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: \([\alpha]_D^{23} = 11.3^\circ\) (c 0.61, CHCl\(_3\)); IR (neat) 2952, 2922, 2854, 1629, 1416, 1246, 1082, 842, 774; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.37 (m, 1 H), 1.70 - 1.74 (m, 1 H), 0.92 (d, \(J = 6.4\) Hz, 3 H), 0.17 (s, 3 H), 0.13 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 136.9, 119.4, 80.6, 38.4, 26.2, 18.6, 17.8, 15.5, -4.1, -4.3; HRMS (FAB\textsuperscript{+}) calcd. for \(\text{C}_{15}\text{H}_{25}\text{BrI}(\text{M}+\text{H})\) 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 disopropylamine (1.64 mL, 11.70 mmol) in THF (8.0 mL) at \(-78^\circ\text{C}\). The resulting suspension was warmed to 0\(^\circ\text{C}\) briefly and then was cooled to \(-78^\circ\text{C}\). 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 \(-78^\circ\text{C}\) for 1 h, at 0\(^\circ\text{C}\) for 15 min and room temperature for 5 min. The mixture was cooled to 0\(^\circ\text{C}\) 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\(^\circ\text{C}\), the reaction was quenched by addition of sat. aq. NH\(_4\)Cl (50 mL) and the resulting mixture was extracted with EtOAc (4 x 100 mL). The dried (MgSO\(_4\)) 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\textsuperscript{+}) calcd. for \(\text{C}_{25}\text{H}_{43}\text{BrNO}_{2}\text{Si}(\text{M}+\text{H})\) 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 disopropylamine (0.57 mL, 4.06 mmol) in THF (4.0 mL) at −78 °C. The resulting solution was stirred at −78 °C for 10 min, then warmed to 0 °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 °C for 15 min and then was warmed to room temperature. After 15 min, the suspension was cooled to 0 °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 °C. The mixture was stirred for 30 min at 0 °C and extracted with EtO (4 x 50 mL). The dried (MgSO₄) 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: [α]D⁺²³ – 34.6° (c 0.41, CHCl₃); IR (neat) 3340, 2964, 2926, 2850, 1709, 1452, 1254, 1031, 964, 842, 774; ¹H NMR (400 MHz, CDCl₃) δ 9.51 (d, J = 8.1 Hz, 3 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, 3 H), 0.86 (d, J = 8.1 Hz, 3 H), 0.04 (d, J = 6.3 Hz, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 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⁺) calcd For C₁₅H₂₈Br₂O₂Si (M+H) 351.1354, found 351.1339.

Aldehyde 41: To a stirred solution of 40 (31.4 mg, 0.089 mmol) in CH₂Cl₂ (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: [α]D⁻²³ – 49.5° (c 0.19, CHCl₃); IR (neat) 3340, 2960, 2934, 2854, 1717, 1465, 1246, 1086, 837, 770; ¹H NMR (300 MHz, CDCl₃) δ 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, 3 H), 0.86 (d, J = 8.1 Hz, 3 H), 0.04 (d, J = 6.3 Hz, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 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⁺) calcd For C₁₅H₂₈Br₂O₂Si (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 °C was added n-BuLi (65 µL, 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 °C for 10 min, and allowed to warm to room temperature. The solution was quenched with sat. aq. NH₄Cl (1 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The dried (MgSO₄) 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 CH₂Cl₂ (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: [α]D⁻²³ – 33.3° (c 0.12, CHCl₃); IR (neat) 2964, 2926, 2850, 1709, 1452, 1254, 1031, 964, 842, 774; ¹H NMR (300 MHz, CDCl₃) δ 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); \(^{13}\)C NMR (75 MHz, 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\(^+\)) calcd For C\(_{20}\)H\(_{41}\)^{79}BrO\(_3\)PSi (M+H) 499.1644, found 499.1637.

Bisspiroketal 16 and 17: To a stirred solution of ketone 15\(^3\) (7.5 mg, 0.0093 mmol) in THF (0.8 mL) and H\(_2\)O (0.2 mL) was added PPTS (2.36 mg, 0.0093 mmol). After 18 h, the reaction was quenched with solid 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 provide sequentially transoidal 17\(^5\) (2.22 mg, 36 %) followed by cisoidal 16\(^\alpha\) (2.44 mg, 40 %).

Bisspiroketal 16 and 18: To a stirred solution of ketone 15\(^3\) (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 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 C\(_{14}\)-epi transoidal 18 (8.8 mg, 40%), transoidal 17 (1.5 mg, 7%) and cisoidal 16\(^\alpha\) (7.0 mg, 32%) and as colorless oil. 18: [\(\alpha\)]\(_D\) –36.5° (c 0.23, CHCl\(_3\)); IR (neat) 2931, 2857, 1456, 1110, 976, 700; \(^1\)H NMR (400 MHz, 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); \(^{13}\)C NMR (100 MHz, 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\(^+\)) calcd. For C\(_{41}\)H\(_{73}\)O\(_3\)Si (M+H) 652.3584, found 652.3568.

Diazooester 19: To a stirred solution of 17 (11.5 mg, 0.017 mmol) in THF (0.5 mL) at \(-78^\circ\)C was added LiDBB (1 mL, 0.22 mmol). After 5 min, the solution was quenched with sat. aq. NH\(_4\)Cl (0.5 mL) and allowed warm to room temperature. The mixture was extracted with Et\(_2\)O (4 x 1 mL) and dried by MgSO\(_4\). The dried extract (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 CH\(_2\)Cl\(_2\) (1.0 mL) at 0°C were sequentially added dimethylaniline (17.5 µL, 0.138 mmol) and crude glyoxylic acid chloride \(p\)-
toluenesulfonyl hydrazone$^4$ (0.138 mmol). The mixture was stirred for 15 min prior to addition of Et$_3$N (38.4 µL, 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$_2$Cl$_2$ solution was washed with saturated aqueous citric acid (3 x 1 mL) and dried over Na$_2$SO$_4$. 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: $[^\alpha]_D^{25}$ = -57.3$^\circ$ (c 0.15, CHCl$_3$); IR (neat) 2964, 2929, 2863, 2110, 1697, 1110, 972, 702 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 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$^+$) calc'd. for C$_{36}$H$_{47}$N$_2$O$_6$Si (M+H) 631.3203, found 631.3192.

Diazoster 18: To a stirred solution of 18 (11.6 mg, 0.017 mmol) in THF (0.5 mL) at $-78^\circ$C was added LiDBB (1 mL, 0.22 mmol). After 5 min, the solution was quenched with sat. aq. NH$_4$Cl (0.5 mL) and allowed warm to room temperature. The mixture was extracted with Et$_3$O (4 x 1 mL) and dried by MgSO$_4$. The dried extract (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 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$_2$Cl$_2$ (1.0 mL) at 0°C were sequentially added dimethylaniline (37.2 µL, 0.29 mmol) and crude glyoxylic acid chloride p-toluenesulfonyl hydrazone$^4$ (0.58 mmol). The mixture was stirred for 15 min prior to addition of Et$_3$N (81.0 µL, 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$_2$Cl$_2$ solution was washed with saturated aqueous citric acid (3 x 1 mL) and dried over Na$_2$SO$_4$. 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: $[^\alpha]_D^{25}$ = -59.1$^\circ$ (c 0.23, CHCl$_3$); IR (neat) 2964, 2934, 2850, 2332, 2105, 1696, 1094, 968, 694; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 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$^+$) calc'd. for C$_{36}$H$_{47}$N$_2$O$_6$Si (M+H) 631.3203, found 631.3220.

Lactone 21: The diazoester 19 (26.8 mg, 0.042 mmol) was dissolved in dry CH$_2$Cl$_2$ (0.42 mL), and the solution was added dropwise (syringe pump), under Ar, over a period of 30 min to a solution of Rh$_2$[(4S-MPPI)Me]$_2$ (0.58 mg, 0.42 µmol) in dry CH$_2$Cl$_2$ (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: [α]D25
– 50° (c, 0.10, CHCl3); IR (neat) 2960, 2926, 2850, 2336, 1785, 1107, 972, 698 cm–1; 1H NMR (300 MHz, CDCl3) δ 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); 13C NMR (300 MHz, CDCl3) δ 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); 13C NMR (100 MHz, CDCl3) δ 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, 19.6, 15.7; HRMS (FAB+) calcd. for C35H47O6Si (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) 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. NH4Cl (100 mL) and extracted with EtOAc / Et2O (1 : 1) (4 x 100 mL). The dried (MgSO4) 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) 3389, 2913, 1867, 1452, 1364, 1107, 1010, 741, 698 cm–1; HRMS (FAB+) calcd. for C10H15O2 (M+H) 167.1072, found 167.1076.

Ester 47: To a solution of oxalyl chloride (6.56 mL, 0.075 mol) in CH2Cl2 (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 CH2Cl2 (20 mL) was added via cannula. After, 15 min, Et3N (47.52 mL, 0.34 mol) was added dropwise and stirred at –50°C for 10 min. The solution was allowed to warm to room temperature within 1 h and quenched with water (100 mL). The aqueous solution was extracted with CH2Cl2 (3 x 100 mL). The dried (MgSO4) 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 CH2Cl2 (80 mL) was added Ph3P=CHCO2Me (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; 1H NMR (400 MHz, CDCl3) δ 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); 13C NMR (100 MHz, CDCl3) δ 167.2, 146.3, 138.4, 128.8, 128.1, 122.9, 73.4, 68.6, 51.8, 33.0; HRMS (FAB+) calcd. for C13H17O3 (M+H) 221.1177, found 221.1184.

Alcohol 48: To a solution of ester 47 (8.59 g, 39 mmol) in CH2Cl2 (228 mL) at –78°C was added DIBAL–H (93 mL, 93 mmol, 1.0 M in CH2Cl2). 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 (MgSO4) extract was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20 – 50% EtOAc / hexanes, to give known product 475 (6.05, 81%) as a colorless oil: IR (neat) 3389, 2913, 1867, 1452, 1364, 1107, 1010, 741, 698; 1H NMR (400 MHz, CDCl3) δ 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); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 138.7, 131.4, 129.5, 128.8, 128.1, 128.0, 73.3, 70.0, 63.9, 33.0; HRMS (FAB$^+$) calcd. for C$_{12}$H$_{14}$O$_2$ (M-H) 191.1072, found 191.1070.

**Ether 49:** To a solution of alcohol 48 (3.08 g, 16.04 mmol) in CH$_2$Cl$_2$ at 0°C was added Et$_3$N (3.35 mL, 24.06 mmol) and MsCl (1.49 mL, 19.24 mmol). After 30 min, the solution was quenched with sat. aq. NH$_4$Cl (30 mL) and extracted with EtOAc (3 x 50 mL). The dried (MgSO$_4$) extract was concentrated in vacuo and purified by chromatography over silica gel, eluting with 30 - 50% EtOAc / hexanes, to give 49 (3.02 g, 78%) as a colorless oil: IR (neat) 3031, 2858, 1452, 1360, 1149; $^1$H NMR (300 MHz, CDCl$_3$) δ 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); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 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 NaI (8.33 g, 55.92 mmol). After 1 h, the solution was quenched with sat. aq. NH$_4$Cl (50 mL) and extracted with EtOAc (3 x 50 mL). The dried (MgSO$_4$) extract was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10 - 40% EtOAc / hexanes, to give iodide 50 (2.64 g, 78%) as a colorless oil: IR (neat) 3032, 2863, 1355, 1183, 1098, 934, 736, 690; $^1$H NMR (300 MHz, CDCl$_3$) δ 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); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 138.8, 131.8, 130.1, 128.9, 128.1, 73.4, 69.6, 33.0, 6.9; HRMS (FAB$^+$) calcd. for C$_{12}$H$_{14}$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°C was added a solution of 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. NH$_4$Cl (10 mL) and allowed warm to room temperature. The solution was extracted with EtOAc (3 x 50 mL). The dried (MgSO$_4$) extract was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10 – 40% EtOAc / hexanes, to give product 24 (1.69 g, 92%) as a colorless oil: [α]$_D$$_{25}^{23}$ +10.8° (c 0.6, CHCl$_3$); IR (neat) 2930, 2850, 1776, 1696, 1376, 1208, 1098, 698; $^1$H NMR (300 MHz, CDCl$_3$) δ 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); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 177.0, 153.5, 135.8, 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 (FAB$^+$) calcd. for C$_{23}$H$_{29}$O$_3$N (M+) 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 H$_2$O (6.4 mL) at 0°C were sequentially added solid NaHCO$_3$ (517 mg, 6.15 mmol) and AD mix β* (1.81 g). The
mixture was warmed to room temperature. After 18 h, the reaction was quenched with solid Na₂S₂O₃ until effervescence ceased. After an additional 10 min, the reaction was diluted with saturated aqueous NaCl (50 mL) and extracted with EtOAc (4 x 100 mL). The dried (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10 – 50% EtOAc / hexanes, to give product 25 (187 mg, 55%, 4 : 1 d.r.) as a colorless oil: [α]D²³ + 20.0° (c 0.1, CHCl₃); IR (neat) 3448, 2930, 2858, 1764, 1440, 1195. 1166, 1103, 1018, 732, 694; ¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.34 (m, 5 H), 4.53 – 4.59 (m, 2 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 (FAB⁺) calcd. for C₁₂H₂₀O₄ (M+) 264.1362, found 264.1369.

Mosher Ester Analysis of Lactone 25. Calculated by difference in ppm [(S)-Mosher Ester – (R)-Mosher ester, CDCl₃, 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. NH₄Cl (5 mL), diluted with sat. aq. NaCl (5 mL) and extracted with EtOAc (3 x 50 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified chromatography over silica gel, eluting with 10 – 40% EtOAc / hexanes, to give product 51 (400 mg, 88%) as a colorless oil: [α]D²³ + 12.6° (c 0.15, CHCl₃); IR (neat) 2943, 2871, 1772, 1456, 1128, 1107, 871, 673 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 (FAB⁺) calced. for C₂₃H₄₂O₃Si (M+) 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°C were sequentially added MeOH (48.5 µL) and LiBH₄ (0.72 mL, 1.43 mmol, 2.0 M in THF). After 4 h, the reaction was quenched with sat. aq. NH₄Cl (20 mL) and extracted with Et₂O (4 x 50 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified chromatography over silica gel, eluting with 20 – 50% EtOAc / hexanes, to give diol 52 (429 mg, 99%) as a colorless oil: [α]D²³ + 10.0° (c 0.84, CHCl₃); IR (neat) 3338, 2947, 2867, 1452, 1364, 1094, 875, 732, 677; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 (FAB⁺) calced. for C₂₃H₄₂O₃Si (M+) 452.3087, found 452.3089.
Pivolyalted Alcohol 53: To a stirred solution of 52 (342 mg, 0.80 mmol) in CH₂Cl₂ (2.68 mL) at −78°C were sequentially added DMAP (9.8 mg), Et₃N (101 mg, 1.0 mmol) and PivCl (115.7 mg, 0.96 mmol). The solution was allowed to warm to −30°C over a period of 2 h. The mixture was then recooled to −78°C and an additional portion of PivCl (57.8 mg, 0.48 mmol) and Et₃N (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. NH₄Cl (15 mL) and extracted with Et₂O (4 x 50 mL). The dried (MgSO₄) 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: [α]D²³ + 5.6° (c 0.17, CHCl₃); IR (neat) 3465, 2938, 2863, 1726, 1461, 1288, 1166, 1094, 884, 728, 677; ¹H NMR (400 MHz, CDCl₃) δ 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 = 6.8 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₂₉H₃₂O₂Si (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°C was added NaN₃ (35.6 mg, 0.89 mmol, 60% in mineral oil). After 10 min, the reaction was warmed to −10°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. NH₄Cl (5 mL), diluted with sat. aq. NaCl (50 mL) and extracted with EtOAc (4 x 50 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified chromatography over silica gel, eluting with 2 - 20% EtOAc / Hexanes, to 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. NH₄Cl (5 mL) and extracted with Et₂O (3 x 50 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified chromatography over silica gel, eluting with EtOAc / hexanes: CH₂Cl₂ : 1 : 6.7 : 6.7, to give product 55 (64 mg, 24%) as a colorless oil over two steps: [α]D²³ + 4.5° (c 0.38, CHCl₃); IR (neat) 3494, 2960, 2934, 2875, 1726, 1452, 1162, 1086, 732, 690; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₂₇H₃₉O₃ (M+H) 443.2797, found 443.2797.

TES Ether 55: To a stirred solution of 55 (64 mg, 0.14 mmol) in CH₂Cl₂ (0.72 mL) at 0°C were sequentially added DMAP (1.7 mg), Et₃N (21.2 mg, 0.21 mmol), and TESCl (25.62 mg, 0.17 mmol). After 45 min, the reaction was quenched with sat. aq. NH₄Cl (1 mL) and extracted with Et₂O (4 x 10 mL). The
dried (MgSO₄) 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: [α]D²⁵ + 27.8° (c 0.28, CHCl₃); IR (neat) 2960, 2880, 1722, 1448, 1275, 1162, 1098, 1002, 737; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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⁺) calcd. for C₃₅H₇₅O₅Si (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 H₂O (5.05 µL) and LiBH₄ (0.14 mL, 0.28 mmol, 2.0 M in THF). The reaction was warmed to r.t. and sat. aq. NH₄Cl (7.47 µL) was added dropwise. An additional portion of LiBH₄ (70 µL, 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. NH₄Cl (5 mL) and extracted with Et₂O (4 x 10 mL). The dried (MgSO₄) 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: [α]D²⁵ + 30.0° (c 0.15, CHCl₃); IR (neat) 3397, 2955, 2880, 1452, 1094, 1040, 997, 728; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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⁺) calcd. for C₃₅H₇₅O₃Si (M+H) 473.3087, found 473.3091.

**Aldehyde 26**: To a stirred solution of 57 (28 mg, 0.059 mmol) in CH₂Cl₂ (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 µmol) 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: [α]D²⁵ + 21.0° (c 0.14, CHCl₃); IR (neat) 2947, 2875, 1722, 1448, 1094, 1006, 736, 694; ¹H NMR (400 MHz, CDCl₃) δ 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, 1H), 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); ¹³C NMR (100 MHz, CDCl₃) δ 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⁺) calcd. for C₃₅H₇₃O₃Si (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°C was added LDA (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. NH₄Cl (2 mL) and extracted with Et₂O (4 X 30 mL). The dried (MgSO₄) 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 CH₂Cl₂ (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: ¹H NMR (300 MHz, CDCl₃) δ 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); ¹³C NMR (75 MHz, CDCl₃) δ 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°C was added Na₂HPO₄ (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/H₂O (2.64 mL, 4 : 1) was added PPTS (13.2 mg, 0.052 mmol). After 15 h, the solution was quenched with solid NaHCO₃ (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: [α]D²³  = −60.7° (c 0.14, CHCl₃); IR (neat) 2926, 2854, 1452, 1233, 1082, 1103, 972, 698; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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.
Lactone 22: To a stirred solution of 29 (5.0 mg, 0.0063 mmol) in THF (0.5 mL) at −78°C was added LiDBB (1 mL, 0.22 mmol). The green color solution was stirred at −78°C for 5 min, and quenched by sat. aq. NH₄Cl (0.5 mL) and extracted with Et₂O (4 x 1 mL). The dried extract (MgSO₄) was filtered through a small plug of silica gel and 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 / CH₂CN (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% EtOAc / hexanes, filtered through a small plug of silica gel (10 mg) and concentrated in vacuo to give ketone 22 (2.8 mg, 78%) as a colorless oil: δ (CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 (ESI) calcd. for C₃₀H₄₇O₆Si (M-H) 785.4237, found 785.4221.

Lactol 61: To a stirred solution of lactone 30 (1.8 mg, 0.003 mmol) in CH₂Cl₂ (0.2 mL) at −78°C was added DIBAL-H (0.05 mL, 0.05 mmol, 1.0 M in CH₂Cl₂). 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 CH₂Cl₂ (5 x 1 mL). The dried extract (MgSO₄) was filtered through a small plug of silica gel and 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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 (ESI) calcd. for C₃₀H₄₇O₆Si (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°C was added KHMDS (74.0 µL, 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°C for 10 min and allowed warm to room temperature for 15 h. The solution was quenched with five drops of sat. aq. NH₄Cl and purified by chromatography over silica gel, eluting with 2 – 20% EtOAc / hexanes, to give product 32 (4.0 mg, 45%) as a colorless oil: [α]₀°₂₃ – 66.7° (c 0.06, CHCl₃); IR (neat) 2955, 2926, 2854, 2328, 1701, 1452, 1242, 1107, 1082, 972, 893, 698; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₅₂H₇₅BrO₇Si₂ (M) 948.4391, found 948.4397.

**Alcohol 31:** To a solution of 32 (1.4 mg, 0.00147 mmol) in THF (20 µL) at room temperature was added TBAF (29 µL, 0.029 mmol, 1.0 M in THF). After 30 min, the solution was quenched with five drops of sat. aq. NH₄Cl. 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: [α]₀°₂₃ – 55.0° (c 0.06, CHCl₃); IR (neat) 3389, 2951, 2922, 2854, 2332, 1701, 1658, 1557, 1456, 1027, 976, 800, 694; ¹H NMR (400 MHz, CD₂OD) δ 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); ¹³C NMR (100 MHz, CD₂OD) δ 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 C₂₉H₄₂⁷⁷BrO₇ (M- Me) 581.2113, found 581.2127.
**Acid 34:** To a solution of 33 (1.7 mg, 0.0028 mmol) in CH₂Cl₂ (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/H₂O (0.2 mL, 1:1) was added NaClO₂ (1.52 mg, 0.0168 mmol), NaH₂PO₄·H₂O (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. Na₂S₂O₃ (0.2 mL) and purified through pipette of silica gel to give product 34 (0.7 mg, 60%) as a colorless oil: [α]D 23 −32.5° (c 0.04, MeOH); IR (neat) 3275, 2917, 2850, 1671, 1566, 1435, 1313, 1237, 1082, 867, 837; ¹H NMR (400 MHz, 0.5% CD₃COOD in CD₃OD) δ 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 C₃₀H₄₂⁸⁸BrO₇ (M-OH) 595.2093, found 595.2108.
References

(6) AD mix $\beta^* = (\text{DHQD})_2\text{PHAL}$ (100 mg), $\text{K}_2\text{OsO}_2\cdot 2\text{H}_2\text{O}$ (14.2 mg), $\text{K}_2\text{CO}_3$ (478 mg), $\text{K}_3\text{Fe(CN)}_6$ (1.22 g).
(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.