A Highly Convergent Approach toward (–)-Brevenal

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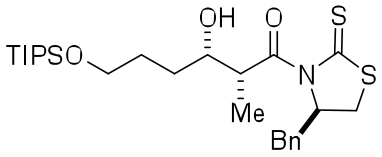
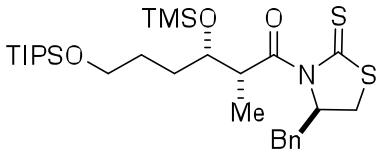
Supporting Information

Methods and Materials: Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer and values reported in cm^{-1}. Proton and carbon nuclear magnetic resonance (^1H and ^{13}C NMR) spectra were recorded on the Bruker 400 (^1H at 400 MHz; ^{13}C at 100 MHz). Optical rotations were determined using a Jasco P1010 polarimeter. Thin layer chromatography (TLC) was conducted on silica gel F254 TLC plates purchased from Scientific Adsorbents, Inc. Flash column chromatography was carried out using silica gel (32 to 63 μm) purchased from Scientific Adsorbents, Inc. The second generation Grubbs' precatalyst is defined as [Ru=CHPh$(Cl)_2(PCy_3)$(DHIMes)]. Diethyl ether (Et_2O), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and toluene were dried by being passed through a column of neutral alumina under nitrogen immediately prior to use. Alkylamines were distilled from calcium hydride immediately prior to use. All other reagents and solvents were used as received from the manufacturer, unless otherwise specified. All air and water sensitive reactions were performed in flasks flame dried under positive flow argon and conducted under an argon atmosphere.

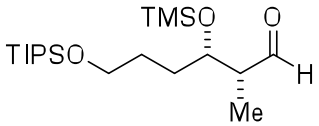


Aldol adduct 17: To a dry 1L round-bottom flask, under argon, was added *N*-acetylthiazolidinethione **15** (17.4g, 65.5 mmol) in 360 mL CH_2Cl_2. The solution was cooled to 0 °C and titanium tetrachloride (neat, 7.50 mL, 68.6 mmol) was added dropwise. The thick suspension was stirred for 5 min upon which (–)-sparteine was added (15.0 mL, 65.5 mmol). The dark red solution was stirred for 20 min at 0 °C, then cooled to -78 °C upon which *N*-methyl-2-pyrrolidinone (6.3 mL, 65.5 mmol) was added. The mixture was stirred 10 min at -78 °C and aldehyde **16** (neat, 17.6 g, 72.0 mmol) was added dropwise. The reaction mixture was stirred 1 h at -78 °C then warmed to 0 °C for 1 h upon which the reaction was quenched with half-saturated ammonium chloride. The

layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $NaSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (10% EtOAc/Hex to 25% EtOAc/Hex) to provide the product (34.0 g, 93%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (m, 21H), 1.27 (d, 3H, J = 6.8 Hz), 1.64 (m, 4H), 2.89 (d, 1H, J = 11.6 Hz), 3.05 (m, 1H), 3.25 (dd, 1H, J = 3.2 Hz, 12.8 Hz), 3.37 (m, 2H), 3.74 (m, 2H), 3.98 (m, 1H), 3.52 (m, 1H), 5.33 (m, 1H), 7.23 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 11.9, 18.0, 29.5, 31.8, 32.1, 36.7, 43.9, 63.5, 69.1, 72.4, 127.2, 128.9, 129.5, 136.5, 177.9, 201.2. IR (film): 3413, 3087, 3063, 3030, 2942, 2865, 2727, 1955, 1883, 1813, 1697, 1604, 1584, 1496, 1456, 1341, 1292, 1261, 1191, 1164 cm^{-1}. ESI-MS: $C_{26}H_{43}NO_3S_2Si$ [M+Na] calc.532.3, found 532.3, [2M+Na] calc. 1041.5, found 1041.5. $[\alpha]^{21}_D$ = -15.0° (c = 1.10, CH_2Cl_2).

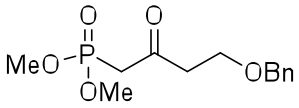


Protected aldol adduct: To a dry 500 mL round-bottom flask, under argon, was added aldol adduct **17** (33.0 g, 64.7 mmol) in 129 mL CH_2Cl_2. The solution was cooled to 0 °C upon which triethylamine (12.0 mL, 84.1 mmol) was added, followed by distilled trimethylsilyl chloride (9.9 mL, 77.7 mmol). 4-dimethylaminopyridine (0.396 g, 3.24 mmol) was added and the reaction mixture was stirred for 2 h at 0 °C. The reaction was quenched with saturated sodium bicarbonate and extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (100% Hex to 5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product (34.8 g, 92%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.12 (s, 9H), 1.06 (s, 21H), 1.24 (d, J = 6.8 Hz, 3H), 1.57 (m, 4H), 2.89 (d, 11.6 Hz), 3.08 (m, 1H), 3.33 (m, 2H), 3.69 (m, 2H), 3.99 (m, 1H), 4.56 (quintet, 1H, J = 6.4 Hz), 5.17 (septet, 1H, J = 3.6 Hz), 7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.44, 12.0, 12.8, 18.1, 29.2, 31.4, 32.2, 36.5, 44.8, 63.3, 69.6, 74.7, 127.2, 128.9, 129.5, 136.7, 177.0, 200.9. IR (film): 3028, 2943, 2892, 2865, 2725, 1699, 1496, 1456, 1363, 1341, 1292, 1252, 1191, 1164, 1104 cm^{-1}. ESI-MS: $C_{29}H_{51}NO_3S_2Si_2$ [M+Na] calc. 604.3, found 604.3. $[\alpha]^{21}_D$ = +183.8° (c = 0.7, CH_2Cl_2).

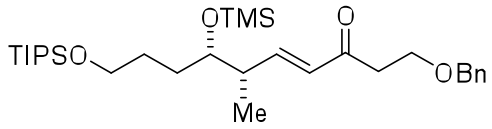


Aldehyde 11: To a dry 1L round-bottom flask equipped with an addition funnel, under argon, was added the protected aldol adduct (25.1 g, 43.1 mmol) in 287 mL CH_2Cl_2. The yellow solution was cooled to -78 °C, upon which DIBAL (1 M in hexanes) was added dropwise until the reaction mixture became colorless (~86 mL, 86.2 mmol).

The reaction mixture was immediately quenched with saturated potassium sodium tartrate, warmed to room temperature, and vigorously stirred for 1 h. 20 mL Et_2O was added and the reaction mixture was stirred 5 min, then extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a pale yellow oil (13.1 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 9H), 1.04 (m, 24H), 1.52 (m, 4H), 2.42 (m, 1H), 3.67 (m, 2H), 4.11 (m, 1H), 9.71 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.31, 7.79, 11.9, 18.0, 29.4, 31.2, 51.5, 63.0, 71.9, 204.9. IR (film): 2944, 2893, 2867, 2713, 1728, 1463, 1383, 1252, 1200, 1104 cm^{-1}. ESI-MS: $C_{19}H_{42}O_3Si_2$ [M+Na] calc. 397.2, found 397.2. $[\alpha]^{20}_D$ = -28.9° (c = 1.75, CH_2Cl_2).

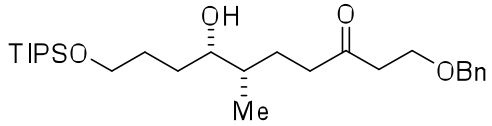


β-Ketophosphonate 12: To a dry 2L round-bottom flask equipped with an addition funnel, under argon, was added dimethyl methylphosphonate (43 mL, 400 mmol) in 332 mL THF. The solution was cooled to -78 °C and *n*-BuLi (1.6 M, 247 mL, 395 mmol) was added dropwise. The white suspension was stirred 1h at -78 °C upon which methyl β-benzyloxypropionate (19.5 g, 100 mmol) was added in 168 mL THF. The reaction mixture was stirred 1 h -78 °C at which point it was quenched with saturated ammonium chloride and warmed to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (85% EtOAc/Hex to 100% EtOAc) to provide the product as a colorless oil (20.3 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.77 (t, 2H, J = 6.0 Hz), 3.02 (d, 2H, J_{HP} = 22.4 Hz), 3.62 (m, 8H), 4.37 (s, 2H), 7.19 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.8, 42.1, 43.9, 52.9, 64.8, 73.0, 127.6, 128.3, 138.0, 200.3. IR (film): 3474, 3062, 3030, 2956, 2909, 2856, 1715, 1496, 1455, 1397, 1368, 1259, 1185 cm^{-1}. ESI-MS: $C_{13}H_{19}O_5P$ [M+Na] calc. 309.1, found 309.1, [M+Cs] calc. 419.0, found 419.0, [2M+Na] calc. 595.2, found 595.2. $[\alpha]^{20}_D$ = +0.89° (c = 1.25, CH_2Cl_2).



Enone 10: To a dry 2L round-bottom flask, under argon, was added β-ketophosphonate **12** (18.2 g, 63.6 mmol) in 114 mL THF. To the solution was added anhydrous barium hydroxide (6.53 g, 38.1 mmol) and the mixture was stirred 30 min at room temperature. Aldehyde **11** (17.0 g, 45.4 mmol) was added in 126 mL of 40:1 THF:H_2O, followed by an additional 154 mL of 40:1 THF:H_2O. The reaction mixture

was stirred 1 h at room temperature and was then diluted with EtOAc and filtered over celite. The solution was washed with saturated sodium bicarbonate and the aqueous layer was extracted with EtOAc (4x). The combined organic layers were dried over Na_2SO_4, filtered, and then concentrated under reduced pressure. The crude product was purified via flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a colorless oil (21.9 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.12 (s, 9H), 1.06 (m, 24H), 1.34-1.65 (bands, 4H), 2.45 (m, 1H), 2.89 (t, 2H, J = 6.4 Hz), 3.66 (m, 3H), 3.80 (t, 2H, J = 6.4 Hz), 4.53 (s, 2H), 6.11 (d, 1H, J = 16.4 Hz), 6.87 (dd, 1H, J = 7.6 Hz, 16.0 Hz), 7.39 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.48, 12.0, 14.7, 18.0, 29.2, 30.6, 40.0, 42.6, 63.3, 65.5, 73.2, 75.5, 127.6, 127.7, 128.4, 130.2, 138.2, 150.4, 198.5. IR (film): 3031, 2944, 2892, 2866, 2729, 2360, 1697, 1673, 1628, 1496, 1463, 1366, 1251, 1201, 1102 cm^{-1}. ESI-MS: $C_{30}H_{54}O_4Si_2$ [M+Na] calc. 557.4, found 557.4, [2M+Na] calc. 1091.8, found 1091.8. $[\alpha]^{21}_D$ = -29.9° (c = 0.90, CH_2Cl_2).

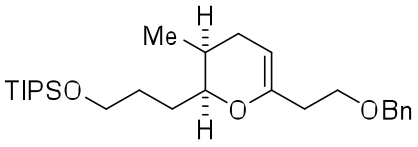


Hydroxyketone 18:

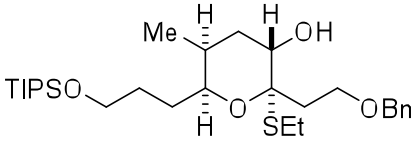
i) To a dry 2L round-bottom flask, under argon, was added CuI (1.56 g, 8.18 mmol) in 400 mL THF. The solution was cooled to -50 °C and MeLi (1.6 M, 5.1 mL, 8.18 mmol) was added dropwise. The yellow suspension was stirred 5 min upon which freshly distilled HMPA (82 mL, 470 mmol) was added, followed by DIBAL (1 M, 106 mL, 106 mmol). The mixture was stirred 30 min at -50 °C, at which point enone **10** (21.9 g, 40.9 mmol) was added in 200 mL THF. The reaction mixture was stirred 1 h at -50 °C. The dry ice bath was removed and 100 mL 1N HCl was added. The mixture was diluted with Et_2O and allowed to stir for 5 min. The layers were separated and the organic layer was washed with 1 N HCl (2x) then with H_2O (2x). The combined organic layers were dried over $MgSO_4$, filtered, and then concentrated under reduced pressure. The crude product (a mixture of the TMS-protected ketone and TMS-deprotected ketone) was passed through a silica plug (10% EtOAc/Hex to 50% EtOAc/Hex) then taken on to the next step.

ii) To a dry 1 L round-bottom flask, under argon, was added the mixture of TMS-protected ketone and TMS-deprotected ketone (21.3 g) in 400 mL anhydrous MeOH. Ammonium fluoride (29.0 g, 793 mmol, 20 equiv.) was added and the reaction mixture was stirred 2 h at room temperature. The reaction was quenched with saturated sodium bicarbonate and diluted with Et_2O. The layers were separated and the organic layer was washed with brine. The combined aqueous layers were extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% Hex to 20% EtOAc/Hex to 50%EtOAc/Hex) to provide the product as a pale yellow oil (17.1 g, 90% over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (m, 3H), 1.08 (m, 21H), 1.38-1.88 (bands, 8H), 2.10 (m, 1H), 2.51 (m, 1H), 2.73 (m, 1H), 3.49-3.78 (bands, 4H), 4.10 (m, 1H), 4.53 (m, 3H), 7.29 (m, 5H). ^{13}C NMR (100

MHz, $CDCl_3$): δ 10.9, 11.9, 12.0, 14.0, 18.0, 26.5, 26.6, 29.3, 29.6, 29.9, 30.1, 31.4, 38.1, 40.3, 41.5, 42.8, 63.5, 63.7, 65.4, 66.6, 71.0, 73.2, 73.4, 74.1, 96.0, 127.7, 128.4, 137.7, 209.8. IR (film): 3481, 2942, 2892, 2866, 2359, 1715, 1456, 1386, 1246, 1101 cm^{-1}. ESI-MS: $C_{27}H_{48}O_4Si$ [M+Na] calc. 487.3, found 487.3, [2M+Na] calc. 951.6, found 951.6. $[\alpha]^{21}_D$ = +1.56° (c = 2.20, CH_2Cl_2).



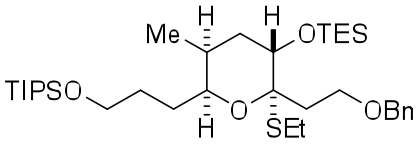
Enol ether 9: To a dry 100 mL round-bottom flask, under argon, was added activated 4 Å powdered molecular sieves (30 mL), hydroxyketone **18** (1.59 g, 3.42 mmol), and 34 mL toluene. CSA (0.556 g, 0.7 mmol) was added and the reaction mixture was allowed to stir 2.5 h at room temperature. The reaction was quenched with triethylamine, filtered to remove the molecular sieves, and washed with saturated sodium bicarbonate. The layers were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (94:5:1 Hex:EtOAc:Et_3N) to provide the product as a colorless oil (1.45 g, 95%). The product was immediately carried on to the next step due to its instability. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (d, J = 2 Hz, 3H), 1.09 (m, 21H), 1.49-1.73 (bands, 5H), 1.92 (m, 1H), 2.22 (m, 1H), 2.35 (t, 2H, J = 6.4 Hz), 3.61 (t, 2H, J = 6.8 Hz), 3.67-3.82 (bands, 3H), 4.49 (s, 1H), 4.54 (s, 2H), 7.30 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 13.5, 18.0, 27.0, 28.5, 29.3, 29.5, 34.8, 63.3, 68.1, 72.8, 78.0, 95.0, 127.4, 127.6, 128.3, 138.6, 150.1. IR (film): 2942, 2924, 2892, 2865, 1678, 1462, 1383, 1246, 1207, 1170, 1101 cm^{-1}. ESI-MS: $C_{27}H_{46}O_3Si$ [M+Na] calc. 469.3, found 469.3. $[\alpha]^{21}_D$ = -23.9° (c = 2.25, CH_2Cl_2).



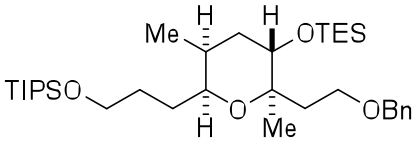
Thioacetal 19: To a dry 500 mL round-bottom flask, under argon, was added enol ether **9** (1.43 g, 3.20 mmol) in 32 mL CH_2Cl_2. The solution was cooled to -78 °C upon which freshly prepared "acetone-free" DMDO[1] (90 mL, 4.48 mmol) was added. TLC showed complete consumption of starting material. The dry ice bath was removed and the solvents were removed via an argon purge. 32 mL CH_2Cl_2 was added and the solution was cooled to 0 °C. Ethanethiol (12 mL, 160 mmol) was added, followed by $Zn(OTf)_2$ (0.116 g, 0.320 mmol). The reaction mixture was stirred 45 min at 0 °C, at which point the reaction was quenched with triethylamine. Excess ethanethiol was removed under an argon purge and the remaining solvent was removed under reduced pressure. The crude

[1] Crimmins, M. T.; McDougall, P. J.; Ellis, J. M. *Org. Lett.* **2006**, *8*, 4079.

product was purified via flash column chromatography (94:5:1 Hex:EtOAc:Et_3N) to provide the product as a colorless oil (1.39 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (d, J = 2 Hz, 3H), 1.07 (m, 21H), 1.23 (t, 4H, J = 7.6 Hz), 1.45-1.70 (bands, 5H), 1.90 (m, 1H), 2.05 (m, 3H), 2.32 (m, 2H), 3.63-3.81 (bands, 3H), 4.09 (m, 2H), 4.61 (m, 3H), 7.33 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.0, 12.8, 14.6, 18.0, 18.8, 28.8, 29.9, 31.9, 35.1, 41.1, 63.3, 67.5, 69.1, 72.1, 73.5, 94.0, 128.0, 128.1, 128.6, 136.9. IR (film): 3413, 3090, 3063, 3032, 2958, 2941, 2892, 2866, 1731, 1455, 1386, 1258, 1210 cm^{-1}. ESI-MS: $C_{29}H_{52}O_4SSi$ [M+Na] calc. 547.3, found 547.3, [2M+Na] calc. 1071.6, found 1071.6. $[\alpha]^{21}_D$ = -55.4° (c = 0.30, CH_2Cl_2).

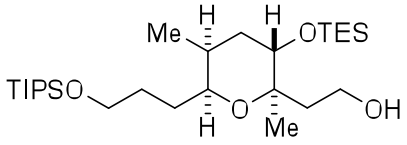


Protected thioacetal: To a dry 250 mL round-bottom flask equipped with an addition funnel, under argon, was added alcohol **19** (1.08 g, 2.06 mmol) in 21 mL THF. The solution was cooled to -78 °C and triethylsilyl chloride (2.1 mL, 12.3 mmol) was added. KHMDS (0.5 M, 25 mL, 12.6 mmol) was added dropwise. The reaction mixture was stirred 15 min at -78 °C upon which it was quenched with saturated sodium bicarbonate and warmed to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% Hex to 5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a cloudy light yellow oil (1.27 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.56 (q, J = 8.0 Hz, 6H), 0.94 (t, 12H, J = 8.0 Hz), 1.09 (m, 21H), 1.23 (m, 7H), 1.39-1.65 (bands, 7H), 1.86 (brs, 2H), 2.20 (m, 2H), 2.38 (m, 4H), 3.72 (m, 4H), 3.96 (m, 1H), 4.04 (dd, 1H, J = 1.2 Hz, 11.6 Hz), 4.52 (m, 2H), 7.30 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.18, 6.91, 12.0, 12.8, 14.7, 18.0, 19.6, 28.8, 29.9, 32.1, 37.0, 39.3, 63.4, 66.7, 68.3, 72.1, 73.1, 92.1, 127.5, 127.8, 128.3, 138.6. IR (film): 3088, 3064, 3031, 2943, 2867, 2729, 2239, 1944, 1804, 1496, 1462, 1414, 1382, 1362, 1290, 1260, 1242, 1207, 1107 cm^{-1}. ESI-MS: $C_{35}H_{66}O_4SSi_2$ [M+Na] calc. 661.4, found 661.4. $[\alpha]^{20}_D$ = -0.51° (c = 0.60, CH_2Cl_2).

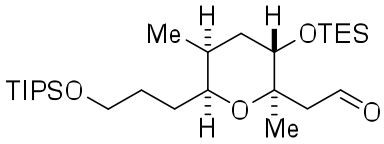


Protected pyran 20: To a dry 1 L round-bottom flask, under argon, was added the thioacetal (4.36 g, 6.82 mmol) in 68 mL CH_2Cl_2. The solution was cooled to -78 °C and *m*-CPBA (purified by washing with pH 7.5 buffer, 6.12 g, 35.5 mmol) was added. The reaction mixture was stirred 2 h at -78 °C. The dry ice bath was replaced with an ice water bath and 3 portions of $AlMe_3$ (8 mL per aliquot, 28.0 mmol per aliquot) were added

at 30 min intervals at 0 °C. 30 min after the last aliquot was added, an additional 3.7 mL $AlMe_3$ (13.0 mmol) was added. After stirring 30 min at 0 °C, the reaction was quenched slowly by dropwise addition of saturated potassium sodium tartrate. The mixture was stirred vigorously overnight at which point it was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $MgSO_4$, filtered, the concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 5% EtOAc/Hex) to provide the product as a cloudy pale yellow oil (3.62 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (q, 6H, J = 7.6 Hz), 0.95 (t, 12H, J = 8.0 Hz), 1.08 (m, 21H), 1.12 (s, 3H), 1.22-1.60 (bands, 5H), 1.80 (m, 3H), 2.01 (m, 1H), 3.54 (m, 1H), 3.68 (m, 5H), 4.51 (apparent s, 2H), 7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 1.03, 5.21, 6.95, 12.0, 12.5, 15.1, 18.1, 29.2, 29.8, 32.9, 36.6, 40.4, 63.5, 66.4, 69.5, 71.0, 73.0, 76.4, 127.4, 127.7, 128.3, 138.8. IR (film): 3030, 2943, 2867, 1732, 1462, 1414, 1382, 1241, 1102 cm^{-1}. ESI-MS: $C_{34}H_{64}O_4Si_2$ [M+Na] calc. 615.4, found 615.4. $[\alpha]^{20}_D$ = -5.42° (c = 1.00, CH_2Cl_2).

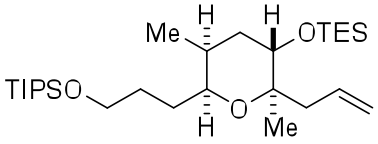


Hydroxypyran 21: To a dry 500 mL round-bottom flask, under argon, was added benzyl ether **20** (3.61 g, 6.09 mmol) in 61 mL THF. The solution was cooled to 0 °C and 61 mL 0.5 M Na/naphthalide (prepared by adding 1.04 g Na to a solution of 6.35 g naphthalene in 90 mL THF in a dry 250 mL round-bottom flask, under argon, cooled to 0 °C and sonicating 2 h). TLC showed immediate consumption of starting material. The reaction was quenched with water and the layers were separated. The aqueous layer was extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a colorless oil (2.61 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.56 (m, 6H), 0.95 (m, 12H), 1.05 (m, 21H), 1.20 (s, 3H), 1.49-1.65 (bands, 5H), 1.81 (m, 4H), 3.66 (m, 4H), 3.82 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.14, 6.86, 12.0, 12.4, 15.3, 18.0, 29.2, 29.5, 32.5, 36.3, 41.1, 59.6, 63.2, 68.3, 71.7, 80.1, 128.3. IR (film): 3523, 2943, 2888, 2868, 1731, 1463, 1415, 1383, 1240, 1102 cm^{-1}. ESI-MS: $C_{27}H_{58}O_4Si_2$ [M+Na] calc. 525.3, found 525.3, [M+K] calc. 541.3, found 541.3, [2M+Na] calc. 1027.7, found 1027.7, [2M+K] calc. 1043.6, found 1043.6. $[\alpha]^{20}_D$ = -7.43° (c = 0.80, CH_2Cl_2).

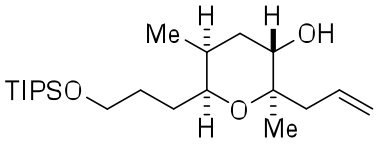


Aldehyde: To a dry 250 mL round-bottom flask equipped with an addition funnel, under argon, was added oxalyl chloride (2 M in CH_2Cl_2, 3.9 mL, 7.78 mmol) and 17 mL

CH_2Cl_2. The solution was cooled to -78 °C and anhydrous DMSO (0.74 mL, 10.4 mmol) in 17 mL CH_2Cl_2 was added dropwise. The mixture was stirred 15 min at -78 °C upon which the alcohol (2.61 g, 5.19 mmol) in 18 mL CH_2Cl_2 was added dropwise. The reaction was stirred 30 min at -78 °C then triethylamine (neat, 3.6 mL, 26.0 mmol) was added dropwise. The mixture was stirred 30 min at -78 °C then 30 min at 0 °C upon which it was transferred to a separatory funnel and washed with 60 mL each of H_2O, 1 N HCl, saturated sodium bicarbonate, then brine. Each wash was back-extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was passed through a short silica plug with 100% CH_2Cl_2, concentrated under reduced pressure, and then immediately subjected to the next reaction (2.56 g, 98%, yellow oil).

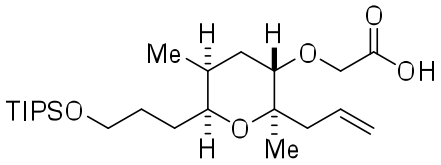


TES protected olefin 22: To a dry 200 mL round-bottom flask, under argon, was added methylenetriphenylphosphine bromide (7.29 g, 20.4 mmol) in 30 mL THF. The mixture was cooled to 0 °C and potassium *tert*-butoxide (1 M in THF, 15 mL, 15.3 mmol) was added. The bright yellow mixture was stirred 30 min at 0 °C upon which the aldehyde (2.56 g, 5.11 mmol) was added in 21 mL THF. The reaction was stirred 30 min at 0 °C then quenched with water. The layers were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 5% EtOAc/Hex) to provide the product as a colorless oil (2.31 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.58 (m, 6H), 0.96 (m, 12H), 1.07 (m, 24H), 1.23-1.55 (bands, 3H), 1.61 (m, 2H), 1.78 (m, 2H), 2.23 (m, 1H), 2.32 (m, 1H), 3.56 (m, 1H), 3.67 (m, 3H), 5.04 (m, 2H), 5.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.28, 6.93, 12.0, 12.5, 15.1, 18.0, 29.2, 29.8, 32.9, 36.9, 45.2, 63.5, 68.7, 71.1, 116.6, 134.9. IR (film): 3074, 2942, 2892, 2867, 2730, 1824, 1730, 1640, 1463, 1414, 1382, 1240, 1103 cm^{-1}. ESI-MS: $C_{28}H_{58}O_3Si_2$ [M+H] calc. 499.4, found 499.4, [M+Na] calc. 521.4, found 521.4. $[\alpha]^{20}_D$ = -5.17° (c = 1.05, CH_2Cl_2).

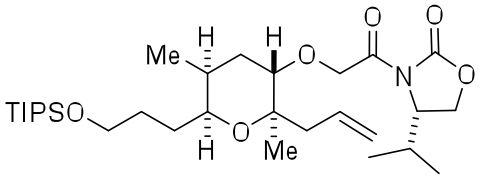


Hydroxypyran 23: To a 250 mL round-bottom flask was added the silyl ether (2.31 g, 4.63 mmol) in 46 mL 5:1 THF:H_2O. A solution of CSA in EtOH (0.1 M, 9 mL, 0.926 mmol) was added and the reaction mixture was stirred 3 h at room temperature. The reaction was quenched with saturated sodium bicarbonate and the layers were separated. The aqueous layer was extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% Hexanes to 10%

EtOAc/Hex to 25% EtOAc/Hex) to provide the product as a very pale yellow oil (1.38 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (d, 3H, J = 7.2 Hz), 1.05 (m, 21H), 1.11 (s, 3H), 1.20-1.53 (bands, 3H), 1.64-1.85 (bands, 5H), 2.30 (m, 2H), 3.55 (m, 1H), 3.67 (m, 3H), 5.07 (m, 2H), 5.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.3, 15.0, 18.0, 29.1, 29.7, 32.9, 36.1, 45.8, 63.4, 68.1, 71.3, 76.6, 117.2, 134.8. IR (film): 3371, 3074, 2942, 2892, 2866, 1640, 1464, 1383, 1246, 1220 cm^{-1}. ESI-MS: $C_{22}H_{44}O_3Si$ [M+Na] calc. 407.3, found 407.3. $[\alpha]^{20}_D$ = -19.2° (c = 0.85, CH_2Cl_2).



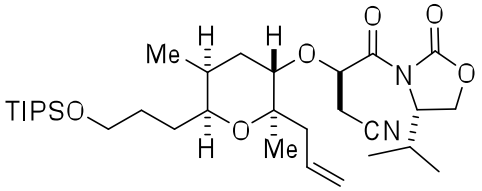
Glycolic acid: To a dry 25 mL round-bottom flask, under argon, was added NaH (60% in mineral oil, 0.324 g, 8.10 mmol). The mineral oil was removed by washing with pentane. 1 mL THF was added and the mixture was cooled to 0 °C upon which a solution of bromoacetic acid (0.450 g, 3.24 mmol) in 1 mL THF dropwise. The mixture was stirred 10 min at 0 °C then 30 min at room temperature, and then cooled back to 0 °C. Alcohol **23** (1.04 g, 2.70 mmol) was added in 2 mL THF and the reaction mixture was warmed to room temperature. 1.4 mL DMF was added and the reaction was stirred 3 days at room temperature then quenched with saturated ammonium chloride. The layers were separated and the aqueous layer was acidified with 1 N HCl to pH = 1 then was extracted with Et_2O (3x). The combined aqueous layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% Hexanes to 15% EtOAc/Hex to 85% EtOAc/Hex) to provide the product as a light yellow oil (0.865 g, 72%, 84% brsm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (d, 3H, J = 7.2 Hz), 1.06 (m, 21H), 1.16 (s, 3H), 1.32-1.55 (bands, 3H), 1.60-1.87 (bands, 5H), 2.35 (dddd, 2H, J = 7.2 Hz, 14.0 Hz), 3.49 (dd, 1H, J = 5.2 Hz, 12.0 Hz), 3.60 (m, 1H), 3.69 (m, 2H), 4.10 (m, 2H), 5.04 (apparent s, 1H), 5.08 (m, 1H), 5.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.3, 16.0, 18.0, 29.0, 29.6, 32.3, 32.5, 45.2, 63.4, 66.3, 71.3, 76.1, 77.4, 117.1, 134.6, 175.2. IR (film): 3079, 2942, 2892, 2866, 1733, 1640, 1464, 1383, 1245, 1129 cm^{-1}. ESI-MS: $C_{24}H_{46}O_5Si$ [M+Na] calc. 465.3, found 465.3. $[\alpha]^{20}_D$ = -17.5° (c = 0.85, CH_2Cl_2).



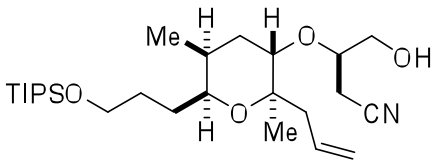
Glycolate 8: To a dry 100 mL round-bottom flask, under argon, was added the glycolic acid (0.601 g, 1.36 mmol) in 10 mL THF. The solution was cooled to -78 °C and triethylamine (0.21 mL, 1.50 mmol) was added followed by dropwise addition of freshly distilled pivaloyl chloride (0.18 mL, 1.50 mmol). The mixture was warmed to 0 °C for 1 h then cooled back to -78 °C.

In a separate, dry 25 mL round-bottom flask, under argon, was added the oxazolidinone (0.211 g, 1.63 mmol) in 4.5 mL THF. The solution was cooled to -78 °C and *n*-BuLi (1.6 M, 0.98 mL, 1.56 mmol) was added dropwise. The mixture was stirred 1 h at -78 °C.

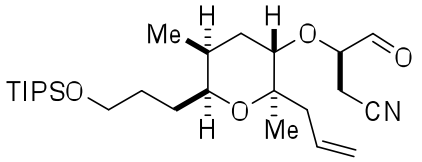
The lithiated oxazolidinone was added to the mixed anhydride at -78 °C. The reaction was stirred 1 h at -78 °C then 45 min at 0 °C upon which it was quenched with saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (10% EtOAc/Hex to 25% EtOAc/Hex) to provide the product as a colorless oil (0.637 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (m, 9H), 1.01 (m, 21H), 1.06-1.21 (m, 5H), 1.32-1.53 (m, 3H), 1.58 (m, 1H), 1.65-1.87 (m, 3H), 2.33 (m, 3H), 3.38 (m, 1H), 3.54 (m, 1H), 3.64 (m, 2H), 4.03 (m, 1H), 4.21 (m, 1H), 4.30 (dd, 1H, J = 2.3 Hz, 8.4 Hz), 4.39 (m, 1H), 4.60 (m, 2H), 4.98 (s, 1H), 5.01 (m, 1H), 5.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.9, 12.3, 14.5, 16.0, 17.8, 18.0, 28.1, 29.1, 29.7, 32.4, 32.6, 45.3, 58.1, 63.4, 68.9, 71.2, 76.2, 76.7, 117.0, 134.8, 154.0, 170.2. IR (film): 2966, 2942, 2896, 2866, 1785, 1722, 1639, 1464, 1389, 1302, 1257, 1210, 1100 cm^{-1}. ESI-MS: $C_{30}H_{55}NO_6Si$ [M+Na] calc. 576.4, found 576.4, [2M+Na] calc. 1129.8, found 1129.8. $[\alpha]^{20}_D$ = +19.7° (c = 0.90, CH_2Cl_2).



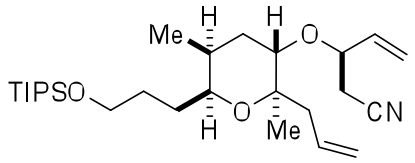
Nitrile: To a dry 100 mL round-bottom flask, under argon, was added NaHMDS (0.83 M, 2.3 mL, 1.89 mmol) in 4 mL THF. The solution was cooled to -78 °C and glycolate **8** (0.697 g, 1.26 mmol) in 9 mL THF was added dropwise. The mixture was stirred 30 min at -78 °C upon which bromoacetonitrile was added (0.35 mL, 5.04 mmol) dropwise. The reaction was stirred 1 h at -78 °C then quenched with saturated ammonium chloride and warmed to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (10% EtOAc/Hex to 15% EtOAc/Hex) to provide the product as a colorless oil (0.389 g, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (m, 6H), 0.95 (d, 3H, J = 6.8 Hz), 1.06 (m, 21H), 1.16 (s, 3H), 1.41 (m, 3H), 1.65 (m, 2H), 1.85 (m, 3H), 2,77 (m, 2H), 3.44 (dd, 1H, J = 4.8 Hz, 11.6 Hz), 3.57-3.75 (m, 3H), 4.32 (dd, 1H, J = 7.6 Hz, 10.4 Hz), 4.42 (m, 1H), 4.51 (m, 1H), 5.01 (m, 1H), 5.05 (s, 1H), 5.41 (m, 1H), 5.97 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.2, 14.8, 16.0, 17.8, 18.0, 23.0, 28.3, 29.0, 29.7, 32.1, 32.5, 44.8, 58.6, 63.4, 64.3, 69.6, 71.3, 75.6, 75.8, 116.8, 135.0, 153.8, 169.5. IR (film): 2962, 2942, 2896, 2866, 2252, 1781, 1720, 1464, 1389, 1248, 1207, 1105 cm^{-1}. ESI-MS: $C_{32}H_{56}N_2O_6Si$ [M+Na] calc. 615.4, found 615.4, [M+Cs] calc. 725.3, found 725.3. $[\alpha]^{20}_D$ = +37.0° (c = 0.30, CH_2Cl_2).



Alcohol 25: To a 50 mL round-bottom flask was added the oxazolidinone (0.386 g, 0.651 mmol) in 7 mL 3:1 THF:H_2O. Sodium borohydride (0.037 g, 0.977 mmol) was added and the reaction was stirred 1 h at room temperature. The reaction was quenched with saturated sodium potassium tartrate and stirred 30 min at room temperature. The layers were separated and the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (15% EtOAc/Hex to 30% EtOAc/Hex) to provide the product as a colorless oil (0.266 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (d, 3H, J = 6.8 Hz), 1.06 (m, 21H), 1.13 (s, 3H), 1.32-1.55 (m, 3H), 1.62 (m, 1H), 1.72 (brs, 1H), 1.85 (m, 4H), 2.31 (m, 2H), 2.58 (m, 2H), 3.52 (m, 1H), 3.68 (m, 6H), 5.05 (s, 1H), 5.10 (m, 1H), 6.01 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.4, 16.3, 18.0, 21.3, 29.0, 29.6, 32.5, 33.0, 45.3, 62.9, 63.4, 71.3, 72.8, 74.3, 75.8, 117.0,117.6, 134.8. IR (film): 3464, 3074, 2942, 2893, 2866, 2253, 1725, 1639, 1464, 1384, 1245, 1223, 1100 cm^{-1}. ESI-MS: $C_{26}H_{49}NO_4Si$ [M+Na] calc. 490.3, found 490.3. $[\alpha]^{19}_D$ = -10.5° (c = 1.10, CH_2Cl_2).



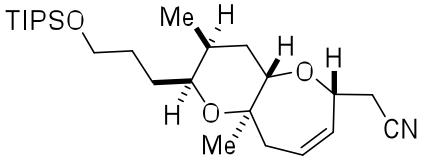
Aldehyde: To a dry 250 mL round-bottom flask equipped with an addition funnel, under argon, was added oxalyl chloride (2 M in CH_2Cl_2, 0.43 mL, 0.854 mmol) and 2 mL CH_2Cl_2. The solution was cooled to -78 °C and anhydrous DMSO (0.08mL, 1.14 mmol) in 2 mL CH_2Cl_2 was added dropwise. The mixture was stirred 15 min at -78 °C upon which alcohol **25** (0.266 g, 0.569 mmol) in 2 mL CH_2Cl_2 was added dropwise. The reaction was stirred 30 min at -78 °C then triethylamine (neat, 0.40 mL, 2.85 mmol) was added dropwise. The mixture was stirred 30 min at -78 °C then 30 min at 0 °C upon which it was transferred to a separatory funnel and washed with 20 mL each of H_2O, 1 N HCl, saturated sodium bicarbonate, then brine. Each wash was back-extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was passed through a short silica plug with 100% CH_2Cl_2, concentrated under reduced pressure, and then immediately subjected to the next reaction (0.251 g, 95%, yellow oil).



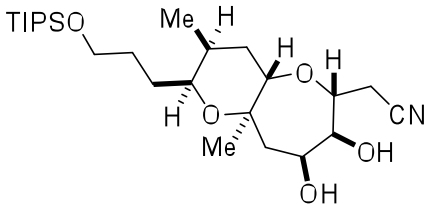
Diene 7:

Preparation of salt-free methylenetriphenylphosphorane: To a dry 50 mL round-bottom flask, under argon, was added 0.193 g 60% NaH, which was washed with pentane to remove the mineral oil, in 11 mL THF. To the solution was added 2.0 g methylenetriphenylphosphine bromide and the mixture was stirred overnight at room temperature, filtered, and then concentrated under reduced pressure. The ylide was store under argon until used.

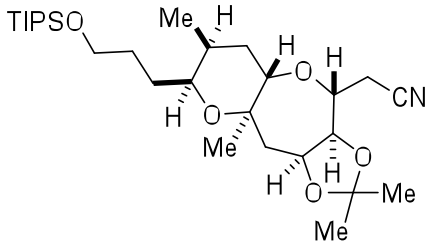
Preparation of diene **7**: To a dry 50 mL round-bottom flask, under argon, was added the ylide (0.208 g, 0.754 mmol) in 11 mL THF. The mixture was cooled to 0 °C and the aldehyde (0.251 g, 0.539 mmol) was added in 5 mL THF. The reaction was stirred 1 h at 0 °C the quenched with half-saturated sodium bicarbonate. The layers were separated and the aqueous layer was extracted with EtOAc (3x) (brine was used to break up any emulsion that may have formed). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Due to the instability of the product, the crude product was passed through a short silica plug (98:1:1 Hex:EtOAc:Et_3N to 95:4:1 Hex:EtOAc:Et_3N) to give the pure product (0.176 g, 70%), then taken on immediately to the next step.



Bicycle 26: To a dry 100 mL round-bottom flask, under argon, was added diene **7** (0.176 g, 0.379 mmol) in 38 mL degassed CH_2Cl_2. To this solution was added Grubb's 2nd generation catalyst (0.016 g, 0.0190 mmol). The reaction mixture was stirred 3 h at room temperature, upon which it was opened to air and allowed to stir overnight at room temperature. The mixture was then concentrated under reduced pressure and the crude product was purified via flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to give the purified product (0.136 g, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (d, 3H, J = 6.8 Hz), 1.05 (m, 21H), 1.19 (s, 3H), 1.36-1.43 (m, 2H), 1.46-1.53 (m, 1H), 1.57-1.64 (m, 1H), 1.69-1.88 (bands, 3H), 2.32 (m, 2H), 2.59 (m, 2H), 3.45-3.77 (bands, 4H), 4.31 (m, 1H), 5.51-5.56 (m, 1H), 5.84 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.3, 15.9, 18.0, 25.3, 29.0, 29.6, 32.8, 34.8, 43.9, 63.3, 71.3, 74.3, 75.0, 80.5, 117.5, 130.1, 130.5. IR (film): 2958, 2940, 2888, 2866, 1728, 1463, 1383, 1276, 1102 cm^{-1}. ESI-MS: $C_{25}H_{45}NO_3Si$ [M+Na] calc. 458.3, found 458.3. $[\alpha]^{19}_D$ = -41.0° (c = 0.05, CH_2Cl_2).

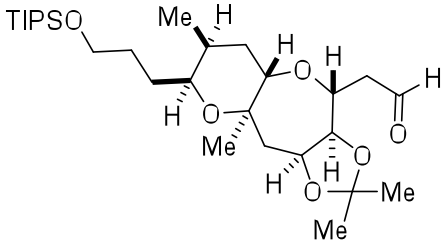


Diol: To a 100 mL round-bottom flask was added olefin **26** (0.132 g, 0.303 mmol) in 5 mL 4:1 acetone:H_2O. *N*-Methylmorpholine-*N*-oxide (0.089 g, 0.758 mmol) was added followed by osmium tetroxide (0.0151 mmol of a 20 mg/mL solution in water). The reaction was stirred overnight at room temperature upon which it was quenched with sodium sulfite (0.100 mg) and stirred 30 min at room temperature. EtOAc was added and the layers were separated. The aqueous layer was extracted with EtOAc (5x) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (50% EtOAc/Hex to 85% EtOAc/Hex) to provide the product as a colorless oil (0.137 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (d, 3H, J = 7.2 Hz), 1.06 (m, 21H), 1.23 (s, 3H), 1.37-1.44 (m, 2H), 1.45-1.53 (m, 1H), 1.58-1.68 (m, 2H), 1.68-1.80 (m, 3H), 1.85 (m, 1H), 2.21 (m, 2H), 2.61 (dd, 1H, J = 5.2 Hz, 16.8 Hz), 2.65 (dd, 1H, J = 5.2 Hz, 16.8 Hz), 2.77 (m, 1H), 3.68 (m, 4H), 3.91 (m, 2H), 4.15 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.4, 16.4, 18.0, 23.9, 29.0, 29.5, 32.3, 33.8, 44.9, 63.4, 68.8, 70.9, 74.3, 76.0, 77.5, 117.7. IR (film): 3425, 2942, 2896, 2866, 1726, 1463, 1384, 1247, 1103 cm^{-1}. ESI-MS: $C_{25}H_{47}NO_5Si$ [M+H] calc. 470.3, found 470.3, [M+Na] calc. 492.3, found 492.3, [M+Cs] calc. 602.2, found 602.2. $[\alpha]^{19}_D$ = -6.19° (c = 0.75, CH_2Cl_2).

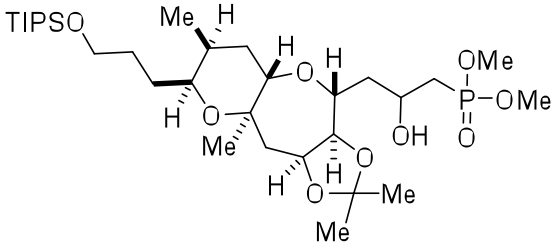


Acetonide 6: To a dry 25 mL round-bottom flask, under argon, was added the diol (0.089 g, 0.189 mmol) and 3.3 mL 10:1 CH_2Cl_2:2-methoxypropene. PPTS (0.019 g, 0.0758 mmol) was added and the mixture was stirred 45 min at room temperature. The reaction was quenched with saturated sodium bicarbonate and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic layers were dried over Na_2SO_4. filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a pale yellow oil (0.074 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (d, 3H, J = 6.8 Hz), 1.05 (m, 21H), 1.14 (s, 3H), 1.32 (s, 3H), 1.41 (s, 3H), 1.43 (m, 2H), 1.50 (m, 2H), 1.57-1.92 (bands, 5H), 2.29 (m, 1H), 2.48 (dd, 1H, J = 8.0 Hz, 16.8 Hz), 2.76 (m, 1H), 3.45 (m, 1H), 3.67 (m, 4H), 3.92 (m, 1H), 4.50

(m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.5, 14.4, 18.0, 22.9, 24.2, 27.3, 28.9, 29.6, 32.6, 33.5, 44.0, 63.4, 70.8, 73.6, 74.1, 76.6, 79.1, 83.4, 108.8, 117.8.

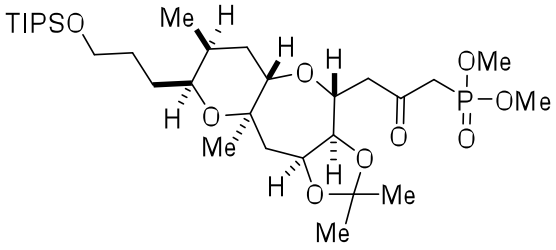


Aldehyde: To a dry 25 mL round-bottom flask, under argon, was added nitrile **6** (0.032 g, 0.0598 mmol) and 2 mL toluene. The solution was cooled to -78 °C and DIBAL (1 M, 0.12 mL, 0.120 mmol) was added dropwise. The reaction mixture was stirred 1 h at -78 °C and then quenched with saturated sodium potassium tartrate. The mixture was stirred vigorously at room temperature for 1 h. The layers were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a pale yellow oil (0.030 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (d, 3H, J = 7.2 Hz), 1.05 (m, 21H), 1.14 (s, 3H), 1.33 (s, 3H), 1.40 (s, 5H), 1.42-1.76 (bands, 7H), 1.86 (m, 1H), 1.94 (m, 1H), 2.28 (m, 1H), 2.58 (m, 1H), 2.78 (m, 1H), 3.47 (m, 1H), 3.68 (m, 4H), 3.94 (m, 2H), 4.50 (m, 1H), 9.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.5, 14.3, 18.0, 24.3, 27.3, 29.0, 32.7, 33.8, 44.2, 47.7, 63.4, 70.8, 73.8, 74.3, 76.2, 79.7, 83.0, 108.4, 200.6.

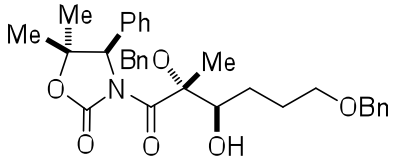


β-hydroxyphosphonate: To a dry 23 mL round-bottom flask, under argon, was added dimethyl methylphosphonate (0.05 mL, 0.468 mmol) in 1 mL THF. The solution was cooled to -78 °C and *n*-BuLi (1.6 M, 0.29 mL, 0.463 mmol) was added dropwise. The white suspension was stirred 1h at -78 °C upon which the aldehyde (0.024 g, 0.0468 mmol) was added in 2 mL THF. The reaction mixture was stirred 1 h -78 °C at which point it was quenched with saturated ammonium chloride and warmed to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% EtOAc to 1% MeOH/EtOAc) to provide the product as a pale

yellow oil (0.027 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (d, 3H, J = 7.2 Hz), 1.06 (m, 21H), 1.13 (s, 3H), 1.32 (s, 3H), 1.41 (m, 5H), 1.46-2.08 (bands, 12H), 2.24 (m, 1H), 3.43 (m, 1H), 3.60-3.72 (bands, 5H), 3.77 (m, 5H), 3.87 (m, 1H), 3.92 (m, 1H), 4.28 (m, 1H), 4.47 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.6, 14.3, 18.0, 24.3, 27.4, 28.9, 29.6, 32.7, 33.9, 34.0, 44.3, 63.4, 70.7, 73.8, 74.1, 74.3, 79.8, 80.2, 81.1, 83.2, 108.2. IR (film): 3380, 2942, 2896, 2866, 1729, 1463, 1382, 1264, 1171 cm^{-1}. ESI-MS: $C_{31}H_{61}O_9PSi$ [M+H] calc. 637.4 , found 637.4, [M+Na] calc. 659.4, found 659.4, [M+Cs] calc. 769.3, found 769.3. $[\alpha]^{19}_{D}$ = +15.0° (c = 0.07, CH_2Cl_2).

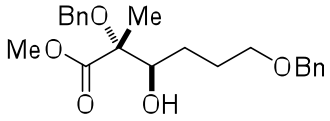


β-ketophosphonate 4: To a 50 mL round-bottom flask was added the β-hydroxyphosphonate (0.035 g, 0.0550 mmol) in 4 mL CH_2Cl_2 (wet). Sodium bicarbonate (0.046 g, 0.550 mmol) was added followed by Dess-Martin periodinane (0.059 g, 0.138 mmol). The reaction mixture was stirred 30 min at room temperature and then quenched with saturated 5:1 $Na_2S_2O_3$:$NaHCO_3$ and stirred 30 min at room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered, and then concentrated under reduced pressure. The crude product was purified via flash column chromatography (100% EtOAc to 1% MeOH/EtOAc) to provide the product as a colorless oil (0.033 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (d, 3H, J = 6.8 Hz), 1.05 (m, 21H), 1.10 (s, 3H), 1.30 (s, 3H), 1.37 (s, 3H), 1.40-1.70 (bands, 6H), 1.83 (m, 1H), 1.91 (m, 2H), 2.23 (dd, 1H, J = 6.4 Hz, 13.2 Hz), 2.75 (m, 1H), 2.92 (m, 1H), 3.14 (m, 2H), 3.44 (m, 1H), 3.65 (bands, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 3.89 (m, 2H), 4.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.6, 14.3, 18.0, 24.3, 27.2, 28.9, 29.6, 32.6, 33.6, 41.8, 43.1, 44.1, 47.8, 53.0, 53.1, 63.4, 70.8, 73.8, 74.3, 77.1, 79.4, 82.8, 108.4, 200.2. IR (film): 2942, 2892, 2866, 1719, 1463, 1383, 1263, 1212, 1170, 1100 cm^{-1}. ESI-MS: $C_{31}H_{59}O_9PSi$ [M+Na] calc. 657.3, found 657.3, [M+Cs] calc. 767.3, found 767.3. $[\alpha]^{20}_{D}$ = 13.4 ° (c = 0.11, CH_2Cl_2).



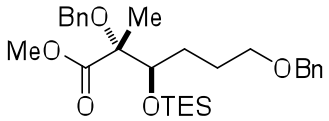
(R)-3-((2R,3R)-2,6-bis(benzyloxy)-3-hydroxy-2-methylhexanoyl)-5,5-dimethyl-4-phenyloxazolidin-2-one 29: To a dry 250 mL round bottom flask under argon

equipped with magnetic stir bar was added freshly distilled diisopropyl amine (3 mL, 21.2 mmol) followed by THF (68 mL). Resulting clear and colorless solution was cooled to –78 °C in a dry ice and acetone bath. *n*-BuLi (9.7 mL, 13.1 mmol) was added dropwise and the cold reaction was stirred for 20 min at –78 °C. (R)-5,5-dimethyl-4-phenyloxazolidin-2-one (3.57 g, 10.1 mmol) dissolved in THF (24 mL) added dropwise by syringe to the freshly prepared LDA to afford a pale yellow solution that was stirred for 30 min at –78 °C. Freshly prepared $Ti(O\textit{i}Pr)_3Cl$ (35 mL of a 1M solution in THF, 35 mmol) was added dropwise by syringe to give rise to a dark red/brown solution that was stirred at –40 °C for 1 h. After cooling the reaction mixture to –78 °C, 4-(benzyloxy)butanal (4.7 g, 26.4 mmol) was added dropwise to the reaction system as a solution in THF (24 mL). The reaction was stirred for 2 hrs at – 40 °C. After the reaction appeared complete by thin layer chromatography it was quenched while still cold by the addition of saturated NH_4Cl (10 mL) and celite. After warming to room temperature, the resulting suspension was filtered through a fritted funnel using ethyl acetate to rinse and concentrated. Purification by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 4.63 g (86%) of **29** as an off-white solid. R_f = 0.34 (30/70 ethyl acetate/hexanes); IR (film) 3442, 2937, 2863, 1781, 1697, 1647, 1497, 1455, 1320, 1270, 1101, 738, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.29 (m, 13H); 7.19-7.18 (m, 2H); 5.18 (s, 1H); 4.56-4.50 (m, 5H); 3.53-3.51 (m, 2H); 3.3 (bs, 1H); 1.92-1.88 (m, 1H); 1.77-1.66 (m, 2H); 1.73 (s, 3H); 1.55-1.50 (m, 1H); 1.52 (s, 3H); 0.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 151.8, 138.5, 138.3, 136.3, 128.9, 128.6, 128.4, 128.3, 127.7, 127.5, 127.4, 127.4, 85.9, 82.2, 73.5, 72.9, 70.2, 69.1, 66.7, 28.9, 28.6, 26.5, 23.7, 16.9; $[\alpha]_D^{23.8°C}$ = -45 (c = 0.81, CH_2Cl_2) HRMS (electrospray): Mass calculated for $C_{32}H_{37}NO_6$ $[M+H]^+$: 532.2699. Found 532.2705.

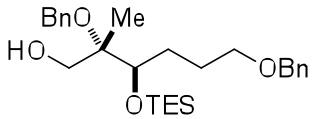


(2R,3R)-methyl 2,6-bis(benzyloxy)-3-hydroxy-2-methylhexanoate: To a flame dried 25 mL round bottom flask under argon equipped with stir bar was added **29** (1 g, 1.88 mmol) and CH_2Cl_2 (10 mL). The resulting clear and colorless solution was cooled to – 30 °C in a dry ice and methanol bath. To a separate flame dried 25 mL conical flask was added potassium methoxide (143 mg, 2.07 mmol) in a glove box. Removed from box and put under a positive pressure of argon. Anhydrous methanol (5 mL) was added and the resulting suspension was mixed until all of the potassium methoxide was dissolved. The resulting methoxide solution was added dropwise by syringe to the cold reaction flask containing the imide to afford a pale yellow solution. The reaction was allowed to slowly warm to 0 °C over 30 min. Care was taken to ensure the reaction did not exceed 0 °C since retro-aldol and other undesired side reactions occurred at higher temperatures. Once the reaction had reached 0 °C it appeared complete by analysis with thin layer chromatography. While still cold, the reaction was poured into a separatory funnel containing water and CH_2Cl_2. The layers were separated and the aqueous layer was extracted two additional times with CH_2Cl_2. The combined organic were dried over

Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-50% ethyl acetate/hexanes afforded 661 mg (94%) of the methyl ester as a clear and colorless oil. R_f = 0.29 (30/70 ethyl acetate/hexanes); IR (film) 3441, 2950, 2862, 1738, 1454, 1266, 1125 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.29 (m, 10H); 4.57 (d, J = 10.5 Hz, 1H); 4.54 (s, 2H); 4.53 (d, J = 10.5 Hz, 1H); 3.87-3.84 (dd, J = 10.0, 5.0 Hz, 1H); 3.81 (s, 3H); 3.55 (t, J = 6.0 Hz, 2H); 2.91 (d, J = 6.0 Hz, 1H); 1.93-1.90 (m, 1H); 1.80-1.73 (m, 2H); 1.57 (s, 3H); 1.55-1.50 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 138.4, 138.3, 128.4, 128.3, 127.7, 127.6, 127.5, 83.1, 75.8, 72.9, 70.2, 67.0, 52.2, 28.2, 26.6, 17.2; $[\alpha]_D^{23.8°C}$ = +7.1 (c = 1.6, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{22}H_{28}O_5$ $[M+H]^+$: 373.2015. Found 337.2026.

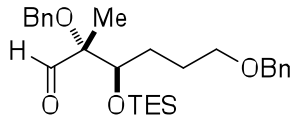


(2R,3R)-methyl 2,6-bis(benzyloxy)-2-methyl-3-(triethylsilyloxy)hexanoate 30: To a flame dried 10 mL round bottom flask under argon equipped with a magnetic stir bar was added the methyl ester (660 mg, 1.77 mmol) and CH_2Cl_2 (1.5 mL). The resulting clear and colorless solution was cooled to 0 °C and freshly distilled 2,6-lutidine was added dropwise by syringe (1 mL, 8.85 mmol). Last, triethysilyl triflate (TESOTf, 0.8 mL, 3.54 mmol) was added to the reaction flask. After 30 min the reaction appeared complete by thin layer chromatography. Saturated $NaHCO_3$ was added while the reaction was still cold. The layers were separated and the aqueous layer was extracted two additional times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10% ethyl acetate/hexanes as eluent afforded 757 mg (87%) of **30** as a pale yellow oil. R_f = 0.82 (30/70 ethyl acetate/hexanes); IR (film) 2952, 2875, 1740, 1455, 1126, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.28 (m, 10 H); 4.54 (d, J = 11.3 Hz, 1H); 4.51 (s, 2H); 4.32 (d, J = 11.3 Hz, 1H); 4.10 (dd, J = 7.7, 2.8 Hz, 1H); 3.76 (s, 3H); 3.49 (t, J = 6.3 Hz, 2H); 1.85-1.83 (m, 2H); 1.68-1.67 (m, 1H); 1.52-1.50 (m, 1H); 1.48 (s, 3H); 0.95 (t, J = 7.9 Hz, 9H); 0.59 (q, J – 7.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 138.7, 138.5, 128.3, 128.2, 127.6, 127.5, 127.4, 127.3, 84.0, 76.4, 72.7, 70.5, 66.7, 51.8, 29.2, 26.9, 14.7, 6.6, 5.4; $[\alpha]_D^{23.8°C}$ = +1.7 (c = 0.57, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{28}H_{42}O_5Si$ $[M+H]^+$: 487.2880. Found 487.2878.

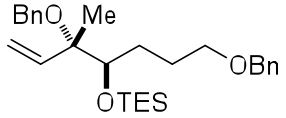


(2S,3R)-2,6-bis(benzyloxy)-2-methyl-3-(triethylsilyloxy)hexan-1-ol: To a dry 100 mL round bottom flask equipped with a magnetic stir bar under argon was added the methyl ester (2.85 g, 5.86 mmol) followed by CH_2Cl_2 (60 mL). The resulting clear and colorless solution was cooled to -78 °C in a dry ice and acetone bath. DIBAL (12 mL,

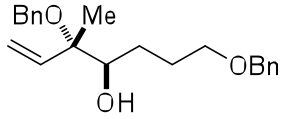
1M in hexanes, 12 mmol) was added dropwise by syringe to the cold reaction solution. After 1.5 hrs the reaction appeared complete by analysis with thin layer chromatography. Saturated Rochelle's salt solution was added while the reaction was still cold. After warming to 23 °C, the reaction mixture was stirred for 1 h. The layers were then separated and the aqueous layer was extracted two additional times with CH_2Cl_2. The combined organics were dried over Na_2SO_4, filitered and concentrated. Purification by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 2.66 g (99%) of a clear and colorless oil that was mixture of the aldehyde and alcohol. The mixture was used in the next reaction without further purification. Alcohol: R_f = 0.79 (30/70 ethyl acetate/hexanes); IR (film) 3460, 2954, 2875, 1454, 1114, 734 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.28 (m, 10H); 4.59-4.54 (m, 4H); 3.95-3.83 (dd, J = 8.8, 2.7 Hz, 1H); 3.76-3.71 (m, 2H); 3.54-3.50 (m, 2H); 2.75, (t, J = 5.5 Hz, 1H); 1.89-1.83 (m, 2H); 1.68 (m, 1H); 1.56-1.54 (m, 1H); 1.15 (s, 3H); 0.97 (t, J = 11.1 Hz, 9H); 0.64 (q, J = 7.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 138.6, 128.4, 127.6, 127.6, 127.5, 127.4, 79.7, 72.8, 70.5, 64.1, 29.4, 27.3, 15.9, 7.0, 5.3; $[\alpha]_D^{23.8°C}$ = +5.9 (c = 1.64, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{28}H_{42}O_3Si$ $[M+Na]^+$: 477.2801. Found 477.2801.



(2R,3R)-2,6-bis(benzyloxy)-2-methyl-3-(triethylsilyloxy)hexanal 31: To a dry 100 mL round bottom flask equipped with magnetic stir bar under argon was added oxalyl chloride (3.77 mL, 7.54 mmol) followed by CH_2Cl_2 (15 mL). Resulting clear and colorless solution was cooled to -78 °C in a dry ice and acetone bath. DMSO (0.989 mL, 13.9 mmol) was carefully added dropwise to the cold reaction mixture then the reaction was stirred for 10 min - bubbling was observed. The alcohol/aldehyde mixture (2.66 g, ~ 5.80 mmol) from the previous step was added dropwise to the reaction flask as a solution in CH_2Cl_2 (15 mL). The reaction was stirred from 30 min at -78 °C. Freshly distilled triethylamine (4.04 mL, 29.0 mmol) was added dropwise by syringe and the reaction was allowed to warm to 23 °C over 45 min. At this time the reaction appeared complete by thin layer chromatography. Water was added to the reaction and the layers were separated. The organic layers were washed with 1M HCl then saturated $NaHCO_3$ followed by brine. After drying over Na_2SO_4, the organic layers were filtered and concentrated. Purification by flash column chromatography on silica gel with 5% ethyl acetate/hexanes afforded 2.59 g (98% over 2 steps) of **31** as a pale yellow oil. R_f = 0.88 (30/70 ethyl acetate/hexanes); IR (film) 2954, 2875, 1737, 1455, 1119, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.64 (s, 1H); 7.38-7.29 (m, 10H); 4.57 (d, J = 11.3 Hz, 1H); 4.52 (s, 2H); 4.38 (d, J = 11.3 Hz, 1H); 3.99-3.96 (dd, J = 8.3, 3.7 Hz, 1H); 3.48 (t, J = 5.1 Hz, 2H); 1.80-1.75 (m, 2H); 1.65-1.60 (m, 1H); 1.52-1.51, (m, 1H); 1.34 (s, 3H); 0.93 (t, J = 7.8 Hz, 9H); 0.60 (q, J = 7.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.0, 138.6, 138.3, 128.4, 128.3, 127.6, 127.6, 127.5, 127.5, 84.7, 75.6, 72.8, 70.3, 66.5, 29.4, 26.6, 12.7, 6.9, 5.3; $[\alpha]_D^{23.8°C}$ = +23.5 (c = 0.37, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{22}H_{40}O_4Si$ $[M+Na]^+$: 479.2594. Found 470.2593.

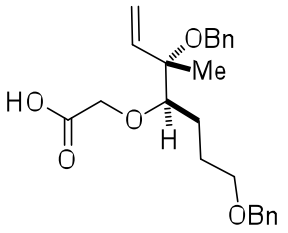


((3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-yloxy)triethylsilane: To a dry 100 mL round bottom flask equipped with magnetic stir bar under argon was added methyltriphenylphoshonium bromide (5 g, 14.2 mmol) then THF (25 mL). A 1M solution of potassium tertbutoxide in THF (10 mL, 10 mmol) was added to generate a yellow suspension that was stirred at room temperature for 30 min. After cooling the suspension to 0 °C a solution of the aldehyde (1.3 g, 2.85 mmol) in THF (25 mL) was added dropwise by syringe. The resulting reaction mixture was stirred for 1 h at 0 °C. The reaction appeared complete by thin layer chromatography. Saturated NH_4Cl was added and the reaction was extracted three times with ether. The combined organics were dried over $MgSO_4$, filtered and concentrated. Purification by flash column chromatography on silica gel with 5-10% ethyl acetate/hexanes afforded 1.27 g (98%) of the olefin as a pale yellow oil. IR (film) 2962, 2874, 1455, 1113, 1007, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.27 (m, 10H); 5.96 (dd, J = 17.8, 10.9 Hz, 1H); 5.35 (m, 1H); 5.34 (m, 1H); 5.25 (dd, J = 17, 1 Hz, 1H); 4.52 (s, 2H); 4.41 (d, J = 11.7 Hz, 1H); 4.38 (d, J = 11.7 Hz, 1H); 3.65 (dd, J = 9.3, 2.6 Hz, 1H); 3.50-3.47 (m, 2H); 1.90-1,70 (m, 2H); 1.65-1.55 (m, 1H); 1.45-1.35 (m, 1H); 1.28 (s, 3H); 0.93 (t, J = 8.0 Hz, 9H); 0.58 (q, J = 8.0 Hz, 6H);^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 139.9, 138.7, 128.3, 128.1, 127.6, 127.4, 127.3, 126.9, 116.8, 81.1, 78.9, 72.7, 70.6, 64.6, 29.1, 27.0, 16.4, 7.1, 5.4; $[\alpha]_D^{23.8°C}$ = +5.7 (c = 0.45, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{28}H_{42}O_3Si$ $[M+Na]^+$: 477.2801. Found 477.2801.

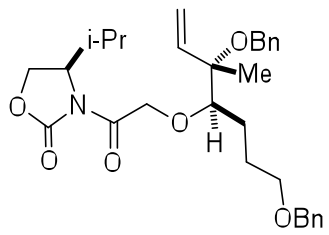


(3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-ol 32: To a dry 50 mL equipped with stir bar under argon was added the TES ether (486 mg, 1.07 mmol) followed by THF (10 mL). TBAF was added dropwise and the reaction was stirred for 45 min. Thin layer chromatography indicated that the reaction was complete at this time. Saturated NH_4Cl was added then the reaction was extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-20% ethyl acetate/hexanes afforded 317 mg (87%) of **32** as a clear and colorless oil. R_f = 0.59 (30/70 ethyl acetate/hexanes); IR (film) 3433, 2859, 1643, 1454, 1091 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.29 (m, 10); 6.00 (dd, J = 17.8, 11.0 Hz, 1H); 5.42 (d, J = 10.9 Hz, 1H); 5.32 (d, J = 17.8 Hz, 1H); 4.54 (s, 2H); 4.43 (s, 2H); 3.59-3.51 (m, 3H); 2.80 (d, J = 0.01 Hz, 1H); 1.93, (m, 1H); 1.74-1.71 (m, 2H); 1.41-1.38 (m, 1H); 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 138.9, 138.6, 128.4, 127.7, 127.5, 127.3, 117.9, 80.9, 77.4, 72.8, 70.3, 64.7, 27.8, 26.8, 17.4; $[\alpha]_D^{23.8°C}$ = +4.40 (c = 0.45, CH_2Cl_2);

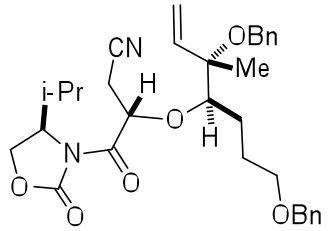
HRMS (electrospray): Mass calculated for $C_{28}H_{42}O_3Si$ $[M+H]^+$: 341.2117. Found 341.2121.



2-((3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-yloxy)acetic acid: To a flame dried 10 mL round bottom flask equipped with stir bar under argon was added NaH (60% in mineral oil, 640 mg, 16.0 mmol). The NaH was washed three times with pentanes then dried using a positive pressure of argon. THF (3 mL) added to afford a white suspension that was cooled to 0 °C. Recrystallized bromoacetic acid (892 mg, 6.40 mmol) dissolved in THF (2 mL) was added carefully dropwise by syringe to the NaH suspension as a solution – bubbling was observed. This suspension was stirred for 10 min at 0 °C and 30 min at 23 °C. After cooling back to 0 °C, the alcohol (1.82 g, 5.35 mmol) dissolved in DMF (2 mL) was added dropwise by syringe. The reaction was allowed to attain room temperature and was stirred for 3 days. At this time, analysis of the reaction by thin layer chromatography indicated that it was nearly complete. The reaction was diluted with ethyl acetate and 1M HCl was added carefully. The layers were then separated and the aqueous layer was extracted three times with ethyl acetate. The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-50% ethyl acetate/hexanes with 2 drops acetic acid per/100 mL eluent afforded 1.82 g (87%) of the acid as a clear and colorless oil. R_f = 0.30 (50/50 ethyl acetate/hexanes, rather streaky); IR (film) 3435, 2927, 2869, 1731, 1643, 1367, 1119 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.25 (bs, 1H); 7.39-7.29 (m, 10H); 6.07 (dd, J = 17.8, 11.0 Hz, 1H); 5.5 (d, J = 11.0 Hz, 1H); 5. 36 (d, J = 17.8 Hz, 1H); 4. 52 (s, 2H); 4.50 (d, J = 11.4 Hz, 1H); 4.48 (d, J = 11.4 Hz, 1H); 4. 35 (d, J = 17 Hz, 1H); 4.08 (d, J = 17.0 Hz, 1H); 3.52-3.44 (m, 3H); 1.80 (m, 1H); 1.70 (m, 2H); 1.55 (m, 1H); 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 138.2, 137.4, 136.9, 128.5, 128.2, 128.0, 127.7, 127.7, 119.3, 89.1, 82.3, 73.0, 70.6, 69.9, 65.5, 28.6, 26.6, 18.1; $[\alpha]_D^{25.0°C}$ = -8.09 (c = 0.44, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{24}H_{30}O_5$ $[M+Na]^+$: 421.1991. Found 421.2005.

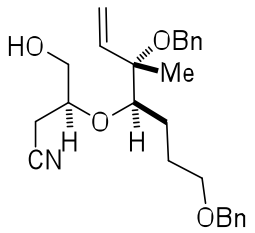


(R)-3-(2-((3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-yloxy)acetyl)-4-isopropyloxazolidin-2-one 34: To a dry 250 mL round bottom flask equipped with stir bar under argon was added the acid (765 mg, 1.92 mmol) then THF (22 mL). Freshly distilled triethylamine (0.294 mL, 2.11 mmol) was added and the resulting clear and colorless solution was cooled to -78 °C. Freshly distilled pivaloyl chloride (0.260 mL, 2.11 mmol) was added and stirring at -78 °C was continued for 30 min. The reaction was warmed to 0 °C and stirred for 1 h, a white precipitate formed during this time. To a separate dry 100 mL round bottom flask was added the oxazolidinone derived from R-valinol (372 mg, 2.88 mmol) and THF (22 mL) and the resulting solution was cooled to -78 °C. *n*-BuLi (2.6 mL, 2.49 mmol) was added dropwise by syringe and the cold reaction was stirred for 40 min to afford a very viscous solution. The freshly prepared mixed anhydride was cooled back to -78 °C and the lithiated oxazolidnone was added dropwise by cannula. If necessary, extra THF and warming of the lithiated oxazolidinone to 0 °C helped to transfer the viscous solution. The resulting white suspension was stirred for 1 h at -78 °C, 1 h at 0 °C then 1 h at 23 °C. At this time the reaction appeared complete by thin layer chromatography. Diluted with water and extracted three times with ether. The combined organics were washed with saturated $NaHCO_3$ and brine. Finally, the ether layers were dried over $MgSO_4$, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 888 mg (91%) of **34** as clear and colorless oil. R_f = 0.44 (30/70 ethyl acetate/hexanes); IR (film) 3035, 2962, 2927, 2868, 1780, 1720, 1389, 1255, 1209, 1138 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H); 6.40 (dd, J = 17.9, 10.9 Hz, 1H); 5.43 (dd, J = 11.0, 1.0 Hz, 1H); 5.28 (dd, J = 17.9, 1.0 Hz, 1H); 5.13 (d, J = 18.0 Hz, 1H); 4.79 (d, J = 17.9 Hz, 1H); 4.53 (d, J = 2.5 Hz, 1H); 4.49 (d, J = 2.5 Hz, 1H); 4.38 (d, J = 11.8 Hz, 1H); 4.29 (d, J = 11.8 Hz, 1H); 4.03 (m, 1H); 3.95 (m, 1H); 3.73 (t, J = 8.7 Hz, 1H); 3.53-3.49 (m, 3H); 2.34 (m, 1H); 1.95 (m, 1H); 1.80-1.65 (m, 2H); 1.45-1.35 (m, 1H); 1.31 (s, 3H); 0.84 (d, J = 7.0 Hz, 3H); 0.77 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 153.8, 139.8, 139.1, 138.6, 128.4, 128.2, 127.7, 127.5, 126.9, 126.7, 117.7, 88.6, 82.4, 74.0, 72.8, 70.2, 63.9, 63.8, 57.9, 27.8, 27.4, 26.7, 17.8, 17.2, 14.4; $[\alpha]_D^{25.5°C}$ = -19.5 (c = 0.44, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{30}H_{39}NO_6$ $[M+H]^+$: 510.2856 Found 510.2849.



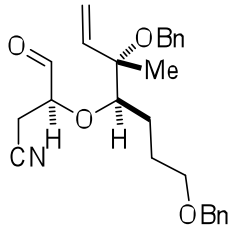
Alkylated Glycolimide: ***NaHMDS:*** To a flame dried 1 L round bottom with stir bar under argon was added NaH (21 g, 525 mmol). Wash three times with pentanes. Toluene (260 mL) added then freshly distilled HMDS (105 mL, 500 mmol). Fitted with telfon sleeve and condenser (otherwise condenser will get stuck to rbf), heat to reflux and stir overnight. Cool to room temperature and let settle. Filter through celite using an air free filter and schlenk technique to afford a clear and colorless solution. Titrate (see

below) with anhydrous sec-butanol in THF using (E)-N-(biphenyl-4-ylmethylene)-1-phenylmethanamine as indicator; it should be around 1 M. Dilute to 0.7 M with THF, it is important to use some THF otherwise the NaHMDS will start to crash out of the toluene. Store in a desiccator in the dark for up to one month. Titration: To a dry 10 mL rbf with stir bar add 1 mL of THF, 90 uL of sec-butanol, and a spatula tip of indicator. Add NaHMDS (about 1 mL) until solution changes from clear and colorless to dark blue. Calculate molarity. ***Glycolate alkylation:*** To a flame dried 50 mL round bottom flask with magnetic stir bar under argon was added NaHMDS (2 mL, 1.38 mmol) followed by THF (8 mL). Resulting clear and colorless solution was cooled to -78 °C. Glycolimide **34** (439 mg, 0.861 mmol) as a solution in THF (8 mL) was added dropwise by syringe to the cold reaction. Stirred for 45 min to afford a pale yellow solution. Last, bromoacetonitrile (0.240 mL, 3.44 mmol) was added dropwise by syringe. Immediately the reaction turned dark brown/red and was stirred for 1 h at -78 °C. Analysis by thin layer chromatography showed little change and it was later determined that the starting glycolimide and product co-spot. While still cold the reaction was quenched by the addition of saturated NH_4Cl and that it was allowed to warm to room temperature. After diluting with ethyl acetate the layers were separated and the aqueous layer was extracted two additional times with ethyl acetate. The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-25% ethyl acetate/hexanes afforded 300 mg (63%) of the alkylated product as a single diastereomer and 60 mg (13%) of a 1:1 mixture of diastereomers were isolated as clear and colorless oils. R_f = 0.59 (30/70 ethyl acetate/hexanes); IR 2964, 2929, 2871, 1775, 1390, 1207, 1120, 737 (film) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.26 (m, 10H); 6.45 (dd, J = 18.0, 10.8 Hz, 1H); 5.66 (at, J = 2.8 Hz, 1H); 5.45 (d, J = 10.8 Hz, 1H); 5.24 (d, J = 17.6 Hz, 1H); 4.53 (s, 2H); 4.35 (d, J = 13. 2 Hz, 1H); 4.16 (d, J = 13.2 Hz, 1H); 3.83 (m, 1H); 3.77-3.71 (m, 2H); 3.68 (m, 1H); 3.59 (m, 1H); 2.89 (m, 1H); 2.76-2.73 (m, 2H); 2.25 (m, 1H); 2.05 (m, 1H); 1.85 (m, 1H); 1.60 (m, 1H); 1.45 (m, 1H); 1.23 (s, 3H); 0.78 (d, J = 7.2 Hz, 3H); 0.72 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 153.5, 139.7, 138.6, 137.6, 128.6, 128.4, 127.8, 127.5, 127.1, 125.5, 118.4, 116.6, 90.0, 83.2, 77.5, 72.8, 70.0, 63.5, 63.2, 58.0, 27.9, 27.7, 26.7, 23.3, 17.7, 17.2, 14.5; $[\alpha]_D^{23.7°C}$ = -33.6 (c = 1.69, CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{32}H_{40}N_2O_6$ $[M+Na]^+$, 571.2784. Found 571.2798.

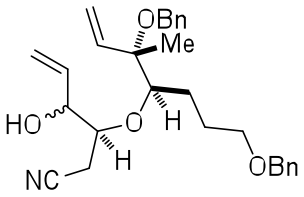


(S)-3-((3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-yloxy)-4-hydroxybutanenitrile 35: To a 10 mL round bottom flask equipped with stir bar under argon containing the alkylated glycolimide (120 mg, 0.200 mmol) was added THF (0.3 mL) and water (0.1mL). $NaBH_4$ (15 mg, 0.400 mmol) added and the resulting bright pink solution was stirred at room temperature until complete by analysis with thin layer

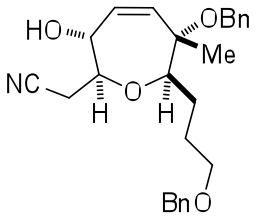
chromatography, approx. 2 h. In some cases additional $NaBH_4$ was required to drive reaction to completion. Saturated Rochelle's salt solution was added and reaction was stirred overnight. After 15 h, reaction was extracted three times with ethyl acetate. The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-40% ethyl acetate/hexanes afforded 71 mg (84%) of **35** as a clear and colorless oil. R_f = 0.29 (30/70 ethyl acetate/hexanes); IR (film) 3444, 2928, 2863, 1454, 1415, 1363, 1100, 737, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.29 (m, 10H); 6.10 (dd, J = 17.8, 11.0 Hz, 1H); 5.48 (d, J = 11.0 Hz, 1H); 5.32 (d, J = 17.9 Hz, 1H); 4.52 (s, 2H); 4.38 (s, 2H); 3.87 (m, 1H); 3.72 (m, 1H); 3.62 (m, 1H); 3.53 (m, 1H); 3.48 (m, 1H): 3.35 (m, 1H); 3.11 (m, 1H); 2.58-2.53 (m, 2H); 1.87 (m, 1H); 1.69 (m, 2H); 1.65 (m, 1H); 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.2, 138.0, 128.5, 128.4, 128.1, 127.9, 127.6, 118.6, 117.9, 84.2, 82.1, 75.9, 73.0, 70.3, 65.1, 62.6, 28.9, 26.7, 20.8, 17.8; $[\alpha]_D^{23.7°C}$ = -0.83 (c = 4.12 , CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{26}H_{33}NO_4$ $[M+Cs]^+$, 556.1464. Found 556.1491.



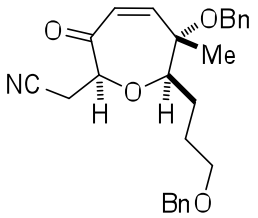
Aldehyde 36: To a dry 25 mL round bottom flask equipped with magnetic stir bar under argon was added oxalyl chloride (0.184 mL, 3.69 mmol) followed by CH_2Cl_2 (1.8 mL). Resulting clear and colorless solution was cooled to -78 °C in a dry ice and acetone bath. DMSO (0.048 mL, 6.82 mmol) was carefully added dropwise to the cold reaction mixture and the reaction was stirred for 10 min - bubbling was observed. The alcohol **35** (120 mg, 2.84 mmol) was added dropwise to the reaction flask as a solution in CH_2Cl_2 (3.3 mL). The reaction was stirred for 30 min at -78 °C. Freshly distilled triethylamine (0.200 mL, 14.2 mmol) was added dropwise by syringe and the reaction was kept at -78 °C for 45 min. It is very important to keep the reaction at -78 °C after the addition of triethylamine to avoid decomposition. The reaction was then warmed to 0 °C and stirred for 15 min. At this time the reaction appeared complete by thin layer chromatography. Water was added to the cold reaction and the layers were separated. The organic layers were washed with 1M HCl then saturated $NaHCO_3$ followed by brine. After drying over Na_2SO_4, the organic layers were filtered and concentrated. Purification by flash column chromatography on silica gel with 10-25% ethyl acetate/hexanes afforded 105 mg (88%) of **36** as a clear and colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H); 7.37-7.22 (m, 10H); 6.16 (dd, J = 17.8, 11.0 Hz, 1H); 5.51 (d, J = 11.0 Hz, 1H); 5.35 (d, J = 17.8 Hz, 1H); 4.52 (s, 2H); 4.44 (m, 1H); 4.37 (d, J = 11.1 Hz, 1H); 4.31 (d, J = 11.1 Hz, 1H); 3.70 (m, 1H); 3.58 (m, 1H); 3.51 (m, 1H); 2.67 (dd, J = 16.9, 4.2 Hz, 1H); 2.45 (dd, J = 16.9, 7.2 Hz, 1H); 1.95 (m, 1H); 1.80 (m, 1H); 1.65 (m, 1H); 1.50 (m, 1H); 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 138.5, 137.6, 128.5, 127.9, 127.8, 127.7, 127.6, 118.9, 117.2, 89.2, 82.9, 81.5, 72.9, 70.1, 64.9, 28.1, 26.7, 19.9, 17.9.



(3S,4R)-3-((3S,4R)-3,7-bis(benzyloxy)-3-methylhept-1-en-4-yloxy)-4-hydroxyhex-5-enenitrile 37: ***Divinyl Zinc:*** *Fusing $ZnCl_2$:* $ZnCl_2$ was added to a dry, pre-tarred 25 mL round bottom flask and put under vacuum. Heated with Bunsen burner until melted and black and bubbling stopped. Allowed to cool to room temperature. This fusing of $ZnCl_2$ was repeated three times. After fusing, the $ZnCl_2$ is whitish gray solid that must be re-weighed to account for loss of water. The fused $ZnCl_2$ (2 g, 14.8 mmol) was diluted with THF (9 mL) and sonicated for 1 h until it dissolved to afford a gray solution. *Vinyl Magnesium Bromide*: To a dry 100 mL 3-necked round bottom flask under argon equipped with stir bar and fitted with cold finger and addition funnel was added magnesium (0.660 g, 27.2 mmol). The entire apparatus was flame-dried. After cooling to room temperature THF (13 mL) was added and a crystal of iodine to afford an orange mixture. THF (4.4 mL) was added to the addition funnel followed by vinyl bromide (2.2 mL, 31.2 mmol). The vinyl bromide solution was carefully added dropwise to the 3-necked round bottom to initiate the reaction. Upon initiation of the Grignard reaction the mixture turns colorless then quickly changes to orange then eventually dark brown. The remaining vinyl bromide solution is then added dropwise so as to keep a gentle reflux. After the addition is complete the reaction mixture is stirred for 30 min, at this time nearly of the magnesium has been consumed. *Divinyl Zinc:* The freshly fused $ZnCl_2$ solution is carefully added by cannula to the freshly prepared vinyl Grignard to give rise to a ~ 1M solution of divinyl zinc in THF that is a charcoal colored mixture – it eventually will become a gray solution with a white precipitate. Typically it was used immediately but can be stored overnight under argon. ***Addition of Divinyl Zinc to 36***: To a dry 25 mL round bottom flask equipped with stir bar under argon was added the aldehyde **36** (59 mg, 0.140 mmol) and toluene (3 mL). The resulting solution was cooled to -78 °C in a dry ice and acetone bath. Freshly prepared divinyl zinc (0.750 mL, 0.750 mmol) was added dropwise by syringe to the cold reaction. After stirring 1 h at -78 C the reaction was warmed to room temperature. Analysis by thin layer chromatography showed the reaction was complete at this time. Water was carefully added and the reaction was extracted three times with ethyl acetate. The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel using 5-20% ethyl acetate/hexanes as eluent afforded 49 mg (78%) of **37** as an inseparable 5:1 mixture of diastereomers. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (m, 10H); 6.11 (dd, J = 17.6, 10.8 Hz, 1H); 5.49 (m, 1H); 5.46 (d, J = 11.2 Hz, 1H); 5.32 (d, J = 17.8 Hz, 1H); 5.15 (m, 2H); 4.52 (s, 2H); 4.38 (m, 1H); 4.37 (s, 2H); 3.95 (m, 1H); 3.69 (m, 1H); 3.49 (m, 2H); 3.35 (m, 1H); 2.56 (dd, J = 16.8, 4.0 Hz, 1H); 2.35 (m, 1H); 1.73 (m, 2H); 1.58 (m, 1H); 1.33 (s, 3H).

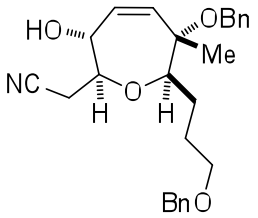


2-((2S,3R,6S,7R)-6-(benzyloxy)-7-(3-(benzyloxy)propyl)-3-hydroxy-6-methyl-2,3,6,7-tetrahydrooxepin-2-yl)acetonitrile 39: To a dry 100 mL round bottom flask equipped with stir bar under argon was added the diene (400 mg, 0.890 mmol) then CH_2Cl_2. The resulting clear and colorless solution was degassed by heated to 40 °C and bubbling argon through it. After cooling to room temperature, Grubbs 2nd generation catalyst was added (36 mg, 0.0424 mmol). Heated to 40 C. After 1 h the reaction appeared complete by analysis with thin layer chromatography. Cooled to room temperature, opened to air and stirred overnight. After concentrating, the reaction was purified by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 59 mg (16%) of **39** as a single diastereomer and 223 mg (59%) of a mixture of diastereomers. Major diastereomer: R_f = 0.26 (30/70 ethyl acetate/hexanes); IR (film) 3445, 2927, 1654, 1454, 1110, 1064, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.29 (m, 10H); 5.88 (d, J = 13.4, 1H); 5.65 (d, J = 13.3, 1H); 4.53 (s, 2H); 4.47 (m, 2H); 4.20 (m, 1H); 3.86 (d, J = 10.5 Hz, 1H); 3.86 (d, J = 10.5 Hz, 1H); 3.60 (m, 2H); 3.55 (m, 1H); 2.87 (d, J = 16.5 Hz, 1H); 2.64 (dd, J = 16.5, 7.5 Hz, 1H); 2.1 (m, 1H); 1.95 (m, 1H); 1.80 (m, 2H); 1.50 (m, 1H); 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 137.9, 131.9, 128.4, 128.3, 127.7, 127.5, 127.4, 127.3, 85.2, 81.1, 81.0, 72.8, 72.6, 70.2, 65.4, 26.6, 26.4, 22.7, 20.0; $[\alpha]_D^{23.7°C}$ = 7.0 (c = 0.150 , CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{26}H_{31}NO_4$ $[M+Na]^+$, 444.2151. Found 444.2137.

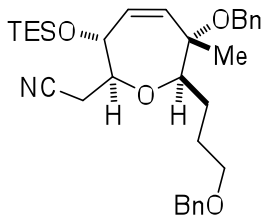


2-((2S,6S,7R)-6-(benzyloxy)-7-(3-(benzyloxy)propyl)-6-methyl-3-oxo-2,3,6,7-tetrahydrooxepin-2-yl)acetonitrile: To a dry 25 mL round bottom flask equipped with magnetic stir bar under argon was added oxalyl chloride (0.463 mL, 0.925 mmol) followed by CH_2Cl_2 (2 mL). Resulting clear and colorless solution was cooled to -78 °C in a dry ice and acetone bath. DMSO (0.121 mL, 1.71 mmol) was carefully added dropwise to the cold reaction mixture and the reaction was stirred for 10 min - bubbling was observed. The alcohol **15** (300 mg, 0.712 mmol) was added dropwise to the reaction flask as a solution in CH_2Cl_2 (2 mL). The reaction was stirred for 30 min at -78 °C. Freshly distilled triethylamine (0.500 mL, 3.56 mmol) was added dropwise by syringe and the reaction was kept at -78 °C for 45 min. It is very important to keep the reaction

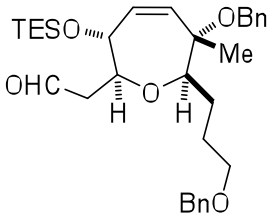
at -78 °C after the addition of triethylamine to avoid decomposition. The reaction was then warmed to 0 °C and stirred for 15 min. At this time the reaction appeared complete by thin layer chromatography. Water was added to the cold reaction and the layers were separated. The organic layers were washed with 1M HCl then saturated $NaHCO_3$ followed by brine. After drying over Na_2SO_4, the organic layers were filtered and concentrated. Purification by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 220 mg (73%) of the enone as a clear and colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H); 6.59 (d, J = 13.2 Hz, 1H); 6.09 (d, J = 10.4 Hz, 1H); 4.52 (s, 2H); 4.37 (s, 2H); 4.02 (m, 1H); 3.61 (m, 1H); 3.53 (m, 1H); 2.90 (dd, J = 16.8, 3.6 Hz, 1H); 2.67 (dd, J = 16.8, 7.6 Hz, 1H); 1.96 (m, 2H); 1.75 (m, 2H); 1.43 (s, 3H).



2-((2S,3R,6S,7R)-6-(benzyloxy)-7-(3-(benzyloxy)propyl)-3-hydroxy-6-methyl-2,3,6,7-tetrahydrooxepin-2-yl)acetonitrile (16): To a dry 10 mL round bottom flask equipped with stir bar under argon was added the enone (220 mg, 0.524 mmol) then MeOH (5 mL). The resulting clear and colorless solution was cooled to -80 °C in a dry ice/ether bath. $YbCl_3$ $6H_2O$ (203 mg, 0.524 mmol) added and reaction stirred for 10 min until mostly dissolved. Last, NaBH4 added (22 mg, 0.917 mmol) and reaction stirred for 10 min. At this time, the reaction appeared complete by analysis with thin layer chromatography. 1M HCl then ether carefully added and the reaction was allowed to attain room temperature. Reaction was extracted three times with ether and the combined organics were dried over $MgSO_4$. After concentrating, the reaction was purified by flash column chromatography on silica gel with 10-30% ethyl acetate/hexanes afforded 115 mg (52%) of **39** as a single diastereomer and 78 mg (35%) of a mixture of diastereomers. Major diastereomer: R_f = 0.26 (30/70 ethyl acetate/hexanes); IR (film) 3445, 2927, 1654, 1454, 1110, 1064, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.29 (m, 10H); 5.88 (d, J = 13.4, 1H); 5.65 (d, J = 13.3, 1H); 4.53 (s, 2H); 4.47 (m, 2H); 4.20 (m, 1H); 3.86 (d, J = 10.5 Hz, 1H); 3.86 (d, J = 10.5 Hz, 1H); 3.60 (m, 2H); 3.55 (m, 1H); 2.87 (d, J = 16.5 Hz, 1H); 2.64 (dd, J = 16.5, 7.5 Hz, 1H); 2.1 (m, 1H); 1.95 (m, 1H); 1.80 (m, 2H); 1.50 (m, 1H); 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 137.9, 131.9, 128.4, 128.3, 127.7, 127.5, 127.4, 127.3, 85.2, 81.1, 81.0, 72.8, 72.6, 70.2, 65.4, 26.6, 26.4, 22.7, 20.0; $[\alpha]_D^{23.7°C}$ = 7.0 (c = 0.150 , CH_2Cl_2); HRMS (electrospray): Mass calculated for $C_{26}H_{31}NO_4$ $[M+Na]^+$, 444.2151. Found 444.2137.

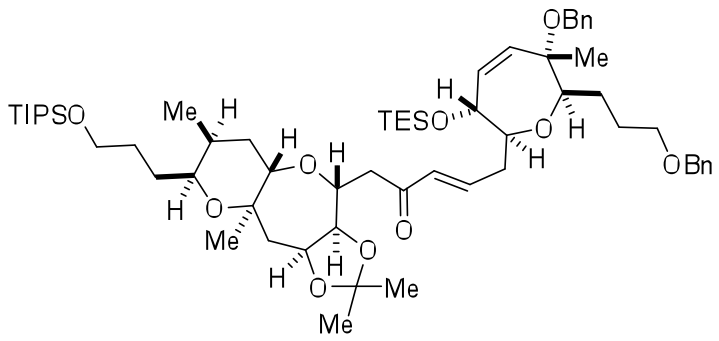


2-((2S,3R,6S,7R)-6-(benzyloxy)-7-(3-(benzyloxy)propyl)-6-methyl-3-(triethylsilyloxy)-2,3,6,7-tetrahydrooxepin-2-yl)acetonitrile: To a flame dried 10 mL round bottom flask under argon equipped with a magnetic stir bar was added alcohol **39** (64 mg, 0.152 mmol) and CH_2Cl_2 (1.5 mL). The resulting clear and colorless solution was cooled to 0 °C and freshly distilled 2,6-lutidine was added dropwise by syringe (0.084 mL, 0.760 mmol). Last, triethysilyl triflate (TESOTf, 0.069 mL, 0.304 mmol) was added to the reaction flask. After 30 min the reaction appeared complete by thin layer chromatography. Saturated $NaHCO_3$ was added while the reaction was still cold. The layers were separated and the aqueous layer was extracted two additional times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification by flash column chromatography on silica gel with 5% ethyl acetate/hexanes as eluent afforded 71 mg (88%) of the TES ether as a clear and colorless oil. 11 mg (99% total) of a mixture of diastereomers were also isolated. Major diastereomer: R_f = 0.70 (20/80 ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.26 (m, 10H); 5.83 (dd, J = 2.0, 13.2 Hz, 1H); 5.63 (dd, J = 2.0, 13.2 Hz, 1H); 4.52 (s, 2H); 4.51 (q, J = 11.6 Hz, 2H): 4.20 (m, 1H); 3.54 (m, 4H); 2.76 (m, 1H); 2.56 (dd, J = 2.0, 7.6, 1H); 2.10 (m, 1H); 1.90 (m, 1H); 1.75 (m, 1H); 1.55 (m, 1H); 1.28 (s, 3H); 1.00 (t, J = 8.0 Hz, 9H); 0.67 (q, J = 6.8 Hz, 6H).



2-((2S,3R,6S,7R)-6-(benzyloxy)-7-(3-(benzyloxy)propyl)-6-methyl-3-(triethylsilyloxy)-2,3,6,7-tetrahydrooxepin-2-yl)acetaldehyde 5: To a dry 10 mL round bottom flask containing the nitrile (20 mg, 0.0373 mmol) was added toluene (0.5 mL). Resulting clear and colorless solution was cooled to -78 °C. DIBAL (0.075 mL, 0.0746 mmol) added dropwise by syringe and reaction stirred for 1 h. Saturated Rochelle's salt solution was added and suspension warmed to room temperature and stirred for 1 h. Extracted three times with ether and combined organics dried over MgSO4, filtered and concentrated. Purification by flash column chromatography on silica gel with 10-20% ethyl acetate/hexanes afforded 20 mg (99%) of **5** as a clear and colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (d, J = 1.6 Hz, 1H); 7.34-7.28 (m, 10 H); 5.81 (dd, J = 13.2, 2.0 Hz, 1H); 5.68 (d, J = 13.2 Hz, 1H); 4.50 (s, 2H); 4.50 (q, J = 11.2 Hz, 2H); 4.17 (m, 1H); 4.01 (m, 1H); 3.90 (m, 1H); 3.50 (m, 2H); 2.80 (m, 1H); 2.55

(m, 1H); 1.83 (m, 2H); 1.5 (m, 1H); 1.4 (m, 1H); 1.26 (s, 3H); 0.96 (t, J = 8.0 Hz, 9H); 0.66 (q, J = 8.0 Hz, 6H).



Enone 3: To a dry 25 mL round-bottom flask, under argon, was added the β-ketophosphonate **4** (0.016 g, 0.0245 mmol) in 0.5 mL THF. To the solution was added anhydrous barium hydroxide (0.003 g, 0.0187 mmol) and the mixture was stirred 30 min at room temperature. Aldehyde **5** (0.012 g, 0.223 mmol) was added in 0.30 mL of 40:1 THF:H_2O, followed by an additional 0.33 mL of 40:1 THF:H_2O. The reaction mixture was stirred 1 h at room temperature and was then diluted with EtOAc and filtered over celite. The solution was washed with saturated sodium bicarbonate and the aqueous layer was extracted with EtOAc (4x). The combined organic layers were dried over Na_2SO_4, filtered, and then concentrated under reduced pressure. The crude product was purified via flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a colorless oil (0.021 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.67 (m, 6H), 1.00 (m, 12H), 1.08 (m, 21H), 1.13 (s, 3H), 1.27 (s, 4H), 1.33 (s, 3H), 1.39 (s, 3H), 1.41-2.00 (bands, 13H), 2.25 (m, 1H), 2.35 (m, 1H), 2.72-2.87 (bands, 3H), 3.57 (m, 4H), 3.68 (m, 3H), 3.86 (m, 1H), 3.94 (m, 1H), 4.01 (m, 1H), 4.14 (m, 1H), 4.41-4.53 (m, 5H), 5.65 (m, 2H), 6.21 (m, 1H), 6.95 (m, 1H), 7.30 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.10, 6.83, 12.1, 12.6, 14.3, 18.0, 19.5, 20.2, 24.4, 26.7, 27.4, 29.0, 32.7, 33.7, 37.0, 43.6, 44.3, 63.5, 65.3, 70.2, 70.8, 72.9, 73.4, 74.1, 74.3, 79.7, 81.1, 82.7, 83.7, 85.3, 108.3, 127.3, 127.4, 127.6, 128.3, 133.1, 133.5, 136.8, 138.7, 139.1, 144.6, 197.8. IR (film): 2957, 2939, 2869, 2363, 2340, 1730, 1679, 1463, 1384, 1271, 1103 cm^{-1}. ESI-MS: $C_{61}H_{98}O_{10}Si_2$ [M+H] calc. 1047.6, found 1047.6, [M+Na] calc. 1069.6, found 1069.6. $[\alpha]^{19}_D$ = +6.25° (c = 0.20, CH_2Cl_2).