Stereoselective Syntheses of the C(1)-C(9) Fragment of Amphidinolide C

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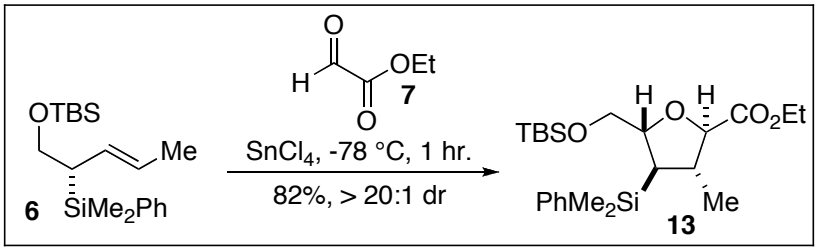
General Methods: All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, diethyl ether, and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated otherwise, all reactions were conducted under an atmosphere of nitrogen using flame-dried or oven-dried (140 °C) glassware. Triethylamine and diisopropylethylamine were dried by distillation over calcium hydride. Four Å molecular sieves were activated under high vacuum with heat (180 °C) for 12 h and re-activated by thorough flame drying immediately prior to use.

Physical Properties and Spectroscopic Measurements: ^{1}H NMR spectra were recorded on commercial instruments at 400 MHz or 500 MHz. ^{13}C NMR spectra were recorded at 100 MHz or 125 MHz. The proton signal for residual non-deuterated solvent (δ 7.27 for $CHCl_3$) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the δ 77.2 resonance of $CDCl_3$. Infrared (IR) spectra were recorded as films on a commerical FTIR instrument. Optical rotations were measured on a commercial polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Melting points were determined on a hot stage melting point apparatus and are uncorrected. Mass spectra were recorded at the University of Michigan, The Scripps Research Institute (La Jolla), or the University of Florida.

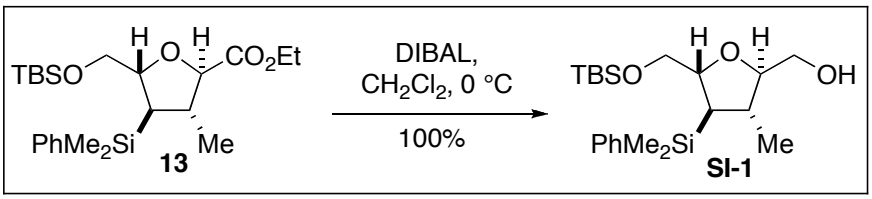
Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid) or potassium permanganate solution. Column chromatography was performed using Kieselgel 60 (230-400 mesh) silica gel.

HPLC purifications were performed using an HPLC system composed of two Varian Prostar 210 pumps connected to normal phase column. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using a Varian Prostar UV and a Varian RI detector.

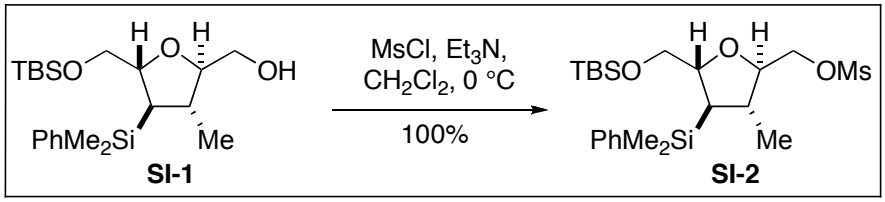


(2R,3S,4R,5S)-5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4-(dimethyl-phenyl-silanyl)-3-methyl-tetrahydro-furan-2 -carboxylic acid ethyl ester (13): To a mixture of crotylsilane **6**[1] (0.500 g, 1.5 mmol, 1.0 equiv.) and ethyl glyoxylate **7** (0.750 mL, 40% solution in toluene, *ca* 3.00 mmol, 2.0 equiv.) in dichloromethane (10 mL) at –78 °C was added tin (IV) chloride as a 1 M solution in dichloromethane (1.5 mL, 1.0 equiv.). The

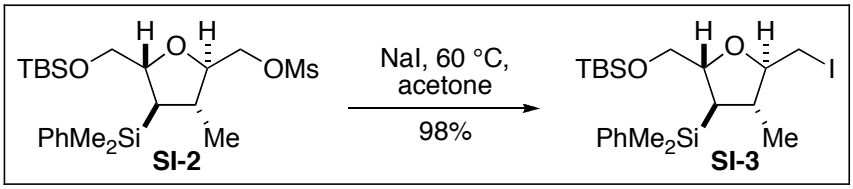
resulting solution was stirred for 45 min, quenched by slow addition of triethylamine (5 mL), and allowed to warm to room temperature. Ethyl acetate, hexanes, and 6 N HCl were added (*caution!*) and the mixture was vigorously stirred for 2 min. The layers were separated and the organic layer was washed with sodium bicarbonate (until the aqueous layer has pH > 7) and dried over sodium sulfate. Concentration of the solution *in vacuo* and purification of the crude product by chromatography on SiO_2 afforded tetrahydrofuran **13** (543 mg, 1.23 mmol, 82%) as a yellow oil. $[\alpha]_D^{27.0}$ = +4.9 (*c* 3.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2H), 7.39-7.33 (m, 3H), 4.18 (m, 3H), 3.93 (d, *J* = 8.0 Hz, 1H), 3.70 (dd, *J* = 2.5, 12.0 Hz, 1H), 3.22 (dd, *J* = 3.5, 11.5 Hz, 1H), 2.22 (m, 1H), 1.46 (dd, *J* = 9.5, 10.5 Hz, 1H), 1.26 (td, *J* = 1.0, 7.0 Hz, 3H), 1.07 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.36 (s, 3H), 0.35 (s, 3H), 0.01 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 137.2, 133.7, 129.3, 127.9, 84.0, 83.9, 64.8, 60.6, 43.0, 34.2, 25.9, 18.5, 18.3, 14.2, -3.8, -4.3, -5.3, -5.5; IR (thin film, NaCl) 2955, 2927, 2855, 1750, 1734, 1471, 1462, 1427, 1377, 1251, 1187, 1113, 938, 836, 776, 733, 700 cm^{-1}; HRMS (ESI) *m/z* for $C_{23}H_{40}O_4Si_2$ $(M+Na)^+$ calcd 459.2363, observed 459.2361.



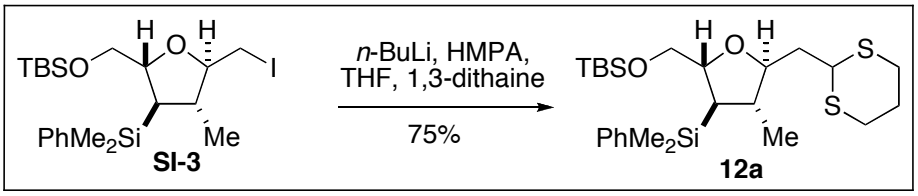
(2R,3S,4R,5S)-[5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4-(dimethyl-phenyl-silanyl)-3-methyl-tetrahydro-furan-2-yl]-methanol (SI-1): To a solution of ethyl ester **13** (1.03 g, 2.31 mmol, 1.0 equiv.) in dry THF (30 mL) at 0 °C was added DIBAL as a 1M solution in dichloromethane (5.78 mL, 2.50 equiv.). The resulting solution was stirred for 2.5 h, quenched by slow addition of saturated aq. sodium potassium tartrate solution (50 mL), and stirred for an additional 6 h. The organic layer was washed with saturated sodium bicarbonate, dried over sodium sulfate, and concentrated *in vacuo* to afford alcohol **SI-1** as a pale yellow oil (1.01g, 2.31 mmol, 100%) of sufficient purity for use in subsequent manipulations. $[\alpha]_D^{27.0}$ = –13.0 (*c* 2.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.38-7.34 (m, 3H), 4.01 (ddd, *J* = 3.0, 5.5, 8.0 Hz, 1H), 3.75 (app d, *J* = 9.0 Hz, 1H), 3.52 (ABX, *J* = 3.0, 11.5 Hz, 1H), 3.49 (ABX, *J* = 4.5, 15.0 Hz, 1H), 3.47 (m, 1H), 3.31 (ABX, *J* = 3.5, 14.5 Hz, 1H), 2.05-1.98 (m, 2H), 0.89 (s, 9H), 0.37 (s, 3H), 0.36 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.5, 133.7, 129.2, 127.9, 86.0, 82.3, 66.3, 62.4, 37.4, 34.8, 26.0, 18.4, 17.3, -3.9, -4.2, -5.3, -5.3; IR (thin film, NaCl) 3448, 3068, 2953, 2927, 2855, 1471, 1462, 1427, 1382, 1360, 1250, 1112, 918, 776 cm^{-1}; HRMS (ESI) *m/z* for $C_{21}H_{38}O_3Si_2$ $(M+Na)^+$ calcd 417.2257, observed 417.2254.



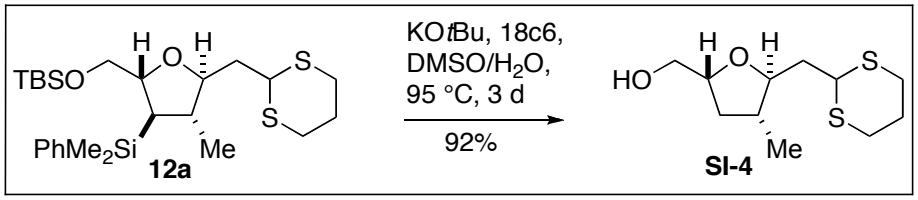
(2R,3S,4R,5S)-Methanesulfonic acid 5-(*tert*-butyl-dimethyl-silanyloxymethyl)-4-(dimethyl-phenyl-silanyl)-3-methyl-tetrahydro-furan-2-ylmethyl ester (SI-2): To a solution of alcohol **SI-1** (1.41g, 3.57 mmol, 1.0 equiv.), triethylamine (1.50 mL, 10.7 mmol, 3.0 equiv.), and DMAP (10 mg) in dichloromethane (50 mL) at 0 °C was added methanesulfonyl chloride (0.350 mL, 4.46 mmol, 1.25 equiv.). The solution was stirred for 45 min and quenched via the addition of saturated sodium bicarbonate. The resulting organic layer was dried over sodium sulfate, filtered, and concentrated to a residue under reduced pressure, and purified by chromatography on SiO_2 to afford mesylate **SI-2** (1.72g, 3.58 mol, 100%) as a clear oil. $[\alpha]_D^{27.0}$ = –8.8 (*c* 6.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.40-7.35 (m, 3H), 4.32 (dd, *J* = 2.5, 11.5 Hz, 1H), 4.13 (dd, *J* = 5.5, 11.5 Hz, 1H), 4.00 (ddd, *J* = 2.5, 4.0, 7.0 Hz, 1H), 3.65 (ddd, *J* = 3.0, 6.0, 8.5 Hz, 1H), 3.56 (dd, *J* = 2.5, 11.0 Hz, 1H), 3.27 (dd, *J* = 5.0, 11.0 Hz, 1H), 3.00 (s, 3H), 1.94 (m, 1H), 1.30 (dd, *J* = 8.5, 10.5 Hz, 1H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.37 (s, 3H), 0.37 (s, 3H), 0.01 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.3, 134.0, 129.7, 128.2, 83.6, 82.7, 70.4, 66.2, 38.9, 38.0, 34.7, 26.2, 18.6, 17.6, -3.6, -3.9, -5.0, -5.1; IR (thin film, NaCl) 2955, 2929, 2857, 2885, 1472, 1463, 1428, 1359, 1252, 1176, 1113, 1133, 1050, 982, 957, 899, 842, 813, 776, 735, 701 cm^{-1}; HRMS (ESI) *m/z* for $C_{22}H_{40}O_5SSi_2$ $(M+Na)^+$ calcd 495.2033, observed 495.2036.



(2S,3R,4S,5R)-2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-(dimethyl-phenyl-silanyl)-5-iodomethyl-4-methyl-tetrahydro-furan (SI-3): A solution of mesylate **SI-2** (0.500g, 1.05 mmol, 1.0 equiv.) and sodium iodide (1.27g, 8.42 mmol, 8.0 equiv.) in acetone (10 mL) was placed in a 75 °C oil bath for 48 h. The acetone was removed under reduced pressure, and the resulting solid was suspended in ethyl acetate/hexanes and washed successively with sodium sulfite, saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over sodium sulfate, the solvents were removed under reduced pressure, and the resulting oil was purified by chromatography on SiO_2 to afford iodide **SI-3** (0.521 g, 1.03 mmol, 98%) as a clear oil. $[\alpha]_D^{27.0}$ = –9.0 (*c* 2.84, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.51 (m, 2H), 7.38-7.36 (m, 3H), 4.06 (m, 1H), 3.62 (dd, *J* = 2.0, 11.0 Hz, 1H), 3.38 (dd, *J* = 4.0, 11.0 Hz, 1H), 3.26-3.22 (m, 2H), 3.15 (dd, *J* = 5.0, 11.0 Hz, 1H), 1.88 (m, 1H), 1.44 (dd, *J* = 8.5, 11.0 Hz, 1H), 0.90 (s, 9H), 0.90 (d, *J* = 6.0 Hz, 3H), 0.38 (s, 3H), 0.37 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 133.7, 129.2, 127.9, 84.1, 82.0, 65.8, 43.2, 34.7, 26.0, 18.3, 17.7, 9.7, -3.8, -4.1, -5.2, -5.4; IR (thin film, NaCl) 2926, 2854, 1471, 1427, 1250, 1112, 1050, 938, 834, 775 cm^{-1}; HRMS (ESI) *m/z* for $C_{21}H_{37}IO_2Si_2$ $(M+Na)^+$ calcd 527.1275, observed 527.1273.

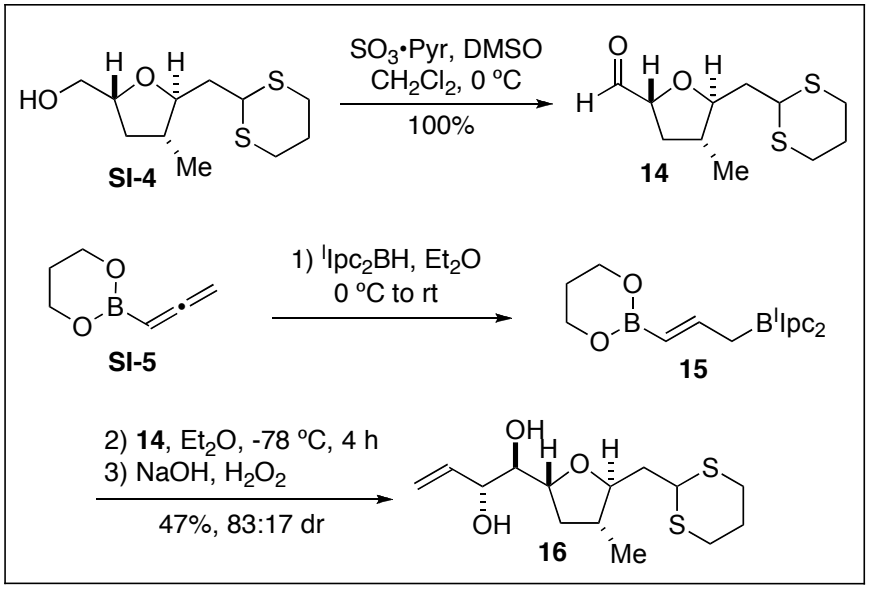


(2S,3R,4S,5R)-2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-(dimethyl-phenyl-silanyl)-5-[1,3]dithian-2-ylmethyl-4-methyl-tetrahydro-furan (12a): To a solution of 1,3-dithiane (1.04 g, 8.66 mmol, 3.0 equiv.) in THF/HMPA (12 mL/3 mL) at –20 °C was added *n*-BuLi as a 1.55M solution in hexanes (5.59 mL, 8.66 mmol, 3.0 equiv.). The resultant orange solution was stirred for 1 h, and then primary iodide **SI-3** (1.46 g, 2.89 mmmol, 1.0 equiv.) was added slowly via cannula (2 mL THF, 1 mL wash). The solution was stirred for 2 h, quenched via slow addition of saturated ammonium chloride, and diluted with diethyl ether. The resulting organic phase was washed four times with small portions of saturated sodium chloride, dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 to afford **12a** (1.08 g, 2.17 mmol, 75%) as a pale yellow oil. $[\alpha]_D^{27.0}$ = –14.7 (*c* 2.52, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.38-7.33 (m, 3H), 4.23 (dd, *J* = 3.5, 7.5 Hz, 1H), 4.00 (m, 1H), 3.63 (td, *J* = 2.0, 10.0 Hz, 1H), 3.50 (dd, *J* = 2.5, 11.0 Hz, 1H), 3.32 (dd, *J* = 5.0, 11.0 Hz, 1H), 2.93-2.77 (m, 4H), 2.13-2.08 (m, 1H), 1.91-1.82 (m, 2H), 1.74-1.71 (m, 1H), 1.68-1.61 (m, 1H), 1.16 (dd, *J* = 11.0, 14.0 Hz, 1H), 0.90 (s, 9H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.34 (s, 3H), 0.34 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 133.8, 129.2, 127.8, 81.6, 81.3, 66.4, 44.7, 42.8, 39.8, 35.0, 30.6, 29.9, 26.1, 26.0, 18.4, 17.1, -3.9, -4.0, -5.3, -5.3; IR (thin film, NaCl) 3067, 2952, 2926, 2899, 2854, 1471, 1461, 1426, 1379, 1359, 1274, 1250, 1129, 1112, 1055, 1065, 896 cm^{-1}; HRMS (ESI) *m/z* for $C_{25}H_{44}O_2S_2Si_2$ $(M+Na)^+$ calcd 519.2219, observed 519.2222.



(2R,4R,5S)-(5-[1,3]Dithian-2-ylmethyl-4-methyl-tetrahydro-furan-2-yl)-methanol (SI-4): To a flame dried pressure tube was added **12a** (0.170 g, 0.341 mmol, 1.0 equiv.), potassium *tert*-butoxide (150 mg), DMSO (2.85 mL), 18-crown-6 (0.090 g, 0.34 mmol, 1.0 equiv.) deionized water (150 μL), and TBAF as a 1.0M solution in tetrahydrofuran (1.2 mL, 1.2 mmol, 3.5 equiv.). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and set to stir at 95 °C for 24 h. The resulting dark brown solution was diluted with ethyl acetate/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated potassium bicarbonate, and brine. The organic layer was dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 to afford **SI-4** (78 mg, 0.315 mmol, 92%) as a pale yellow oil. $[\alpha]_D^{27.0}$ –29.1 (*c* 2.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.29 (dd, *J* = 4.5, 10.5, 1H), 4.11 (m, 1H), 3.73 (dt, *J* = 3.0, 9.5 Hz, 1H), 3.68 (ABX, *J* = 3.5, 11.5 Hz, 1H), 3.51

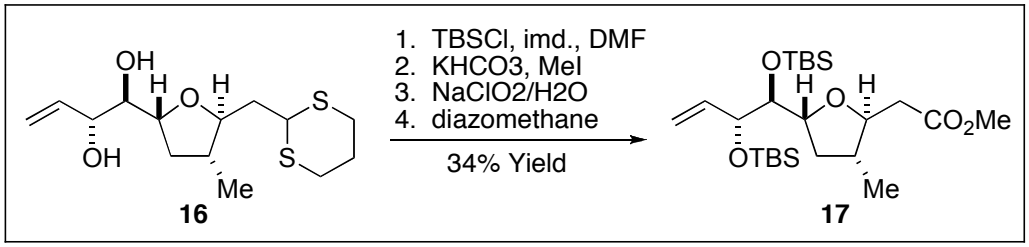
(ABX, J = 6.0, 11.5 Hz, 1H), 2.97-2.80 (m, 4H), 2.16-2.07 (m, 2H), 1.96-1.83 (m, 4H), 1.39 (m, 1H), 1.05 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.2, 78.5, 64.9, 44.5, 40.1, 40.1, 36.3, 30.5, 30.0, 25.9, 16.3; IR (thin film, NaCl) 3431, 2952, 1457, 1422, 1378, 1275, 1243, 1188, 1114, 1046, 909, 868, 800, 763 cm^{-1}; HRMS (ESI) *m/z* for $C_{11}H_{20}O_2S_2$ $[M+Na]^+$ calcd 271.0802, observed 271.0795.



(1R,2R,2'R,4'R,5'S)-1-(5'-[1,3]Dithian-2-ylmethyl-4'-methyl-tetrahydro-furan-2'-yl)-but-3-ene-1,2-diol (16): A solution of **SI-4** (80 mg, 0.323 mmol, 1.0 equiv.) in dichloromethane (4 mL) was cooled to 0 ºC. DMSO (230 μL, 3.23 mmol, 10 equiv.) and *i*Pr$_2$NEt (284 μL, 1.62 mmol, 5.0 equiv.) were added and the mixture was stirred for 5 min. SO_3•Pyr (154 mg, 0.968 mmol, 3.0 equiv.) was then added in one portion followed by 1 h of stirring at 0 ºC. The mixture was then diluted with dichloromethane, quenched with saturated aqueous sodium bicarbonate, and warmed to room temperature. The aqueous layer was separated and extracted with dichloromethane twice. The combined organic layers were then dried over sodium sulfate, concentrated to a residue **14** (80 mg, 0.325 mmol, 100%) which was used without further purification.

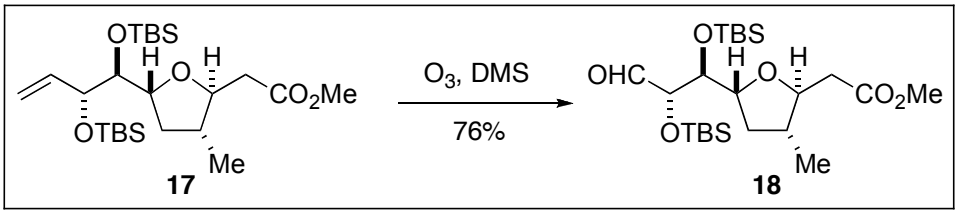
In a glove box $^{l}Ipc_2BH$[2] (231 mg, 0.813 mmol, 2.5 equiv.) was weighed into a round bottom flask. (Note: The borane was crushed with a glass rod prior to use in order to achieve efficient hydroboration.) The flask was capped with a rubber septum, removed from the glove box, and cooled to 0 ºC. Et_2O (2 mL) was added, followed by addition of neat allenylborane **SI-5**[3] (100 μL, 0.813 mmol, 2.5 equiv.). The mixture was stirred at 0 ºC for 2 h and then cooled to -78 ºC. A solution of aldehyde **14** (80 mg, 0.325 mmol, 1.0 equiv.) in Et_2O (1.5 mL, plus 0.5 mL rinse) was added dropwise by syringe followed by 4 h of stirring at -78 ºC. The dry ice bath was removed, and of 2M aq. NaOH (0.5 mL) was added followed by placement of an ice bath to maintain the mixture at 0 ºC. Additional 2M aq. NaOH (0.5 mL) and 30% H_2O_2 (1 mL) was added and the mixture was stirred at 0 ºC for 2 h, followed by dilution with ethyl acetate and saturated aqueous sodium bicarbonate. The aqueous layer was separated and extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 to afford **16** (47 mg, 0.155

mmol, 47%, ~83:17 dr) as a colorless oil. $[\alpha]_D^{27.0}$ = -38 (*c* 4.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94 (ddd, *J* = 4.5, 10.5, 16 Hz, 1H), 5.39 (ddd, *J* = 1.0, 1.5, 16.0 Hz, 1H), 5.24 (ddd, *J* = 1.0, 1.5, 10.5 Hz, 1H), 4.27 (bs, 1H), 4.22 (dd, *J* = 5.0, 8.5 Hz, 1H), 4.14 (ddd, *J* = 3.0, 6.0, 9.5 Hz, 1H), 3.70 (td, *J* = 2.0, 9.5 Hz, 1H), 3.48 (bs, 1H), 3.26 (bs, 1H), 2.95-2.80 (m, 4H), 2.12 (m, 1H), 2.01 (m, 1H), 1.95 (m, 1H), 1.90-1.80 (m, 3H), 1.73 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 116.3, 83.1, 78.2, 77.5, 73.9, 45.7, 40.2, 40.1, 36.9, 30.8, 30.6, 26.1, 16.1; IR (thin film, NaCl) 3442, 2955, 2929, 1457, 1422, 1380, 1276, 1244, 1193, 1114, 1003, 910, 758, 667 cm^{-1}; HRMS (ESI) *m/z* for $C_{14}H_{24}O_3S_2$ $(M+Na)^+$ calcd 327.1065, observed 327.1062.

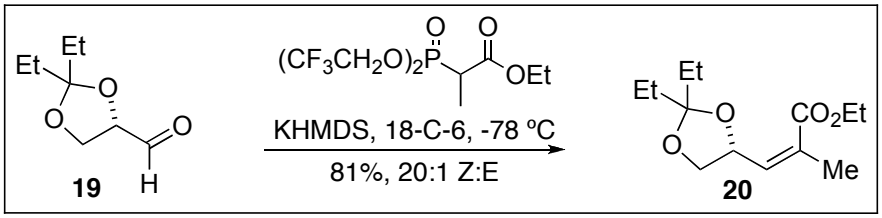


(2S,3R,4R,1'S,2'R)-{5-[1,2-Bis-(*tert*-butyl-dimethyl-silanyloxy)-but-3-enyl]-3-methyl-tetrahydro-furan-2-yl}-acetic acid methyl ester (17): To a solution of diol **16** (0.045 g, 0.149 mmol) in N,N-dimethylformamide (0.500 mL) was added imidazole (0.105 g, 1.5 mmol, 10 equiv.) and *t*-butyldimethylsilylchloride (0.115 g, 0.75 mmol, 5 equiv.). The resulting solution was stirred overnight at room temperature, diluted with diethyl ether, and washed with saturated sodium bicarbonate. The resulting organic layer was dried over sodium sulfate, taken to a residue (55 mg, 70% yield first step) and dissolved in acetonitrile (1 mL). To the solution was added methyl iodide (0.100 mL, 1.5 mmol, 10 equiv.), water (0.250 mL), and sodium bicarbonate (0.150 g, 1.5 mmol, 10 equiv.). The resulting solution was stirred for 24 h, diluted with diethyl ether, and washed with brine. The organic layer was dried over sodium sulfate and the solvents removed under reduced pressure to afford the corresponding crude aldehyde (34 mg, 77% yield second step) as a yellow oil. The aldehyde was dissolved in *t*-BuOH (2 mL) and 2-methyl-2-butene (0.750 mL) and treated with 0.500 mL aliquots of a stock solution prepared by the dissolution of $NaClO_2$ (0.375 g) and NaH_2PO_4 (0.375 g) in water (2.5 mL). After the addition of two aliquots of the oxidant solution, the reaction was quenched with 1.0 *N* HCl and extracted thrice with ethyl acetate. The organic layers were dried over sodium sulfate and solvents removed under reduced pressure. The crude acid is dissolved in benzene (1.0 mL) and methanol (0.300 mL) and trimethylsilyldiazomethane is added as a 2.0 M solution in hexanes (0.050 mL, 0.1 mmol, *ca* 1.25 equiv.). After 15 min the solvents are removed under reduced pressure and the residue purified by chromatography on SiO_2 to afford first **17** (12 mg, 0.025 mmol, 34%) as a pale yellow oil in addition to a mixture of mono-desilylated byproducts (8 mg, 0.022 mmol, 30%) which could be readily converted to **17** upon treatment with imd/TBSCl. Characterization data for **17**: $[\alpha]_D^{27.0}$ = –15.4 (*c* 0.76, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (ddd, *J* = 7.0, 10.0, 16.0 Hz, 1H), 5.11 (d, *J* = 16.0 Hz, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 4.05 (dt, *J* = 1.0, 7.0 Hz, 1H), 3.87 (m, 1H), 3.80 (m, 1H), 3.68 (s, 3H), 3.52 (dd, *J* = 3.0, 7.0 Hz, 1H), 2.51 (ABX, *J* = 4.0, 15.0, 1H), 2.44 (ABX, *J* = 8.5, 15.0 Hz, 1H), 2.03 (m, 1H), 1.85 (m, 1H), 1.33 (app q, *J* = 12.0, 1H),

1.03 (d, J = 6.5 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 138.9, 115.8, 81.2, 80.3, 79.8, 76.5, 51.8, 40.5, 39.6, 37.8, 26.3, 26.2, 18.7, 18.6, 16.2, -4.1, -4.1, -4.3, -4.4; IR (thin film, NaCl) 2955, 2929, 2887, 1857, 1746, 1472, 1462, 1436, 1253, 1199, 1141, 1076, 1040, 1024, 1005, 923, 869, 834, 814, 777, 669 cm^{-1}; HRMS (ESI) m/z for $C_{24}H_{48}O_5Si_2$ $(M+Na)^+$ calcd 495.2938, observed 495.2930.

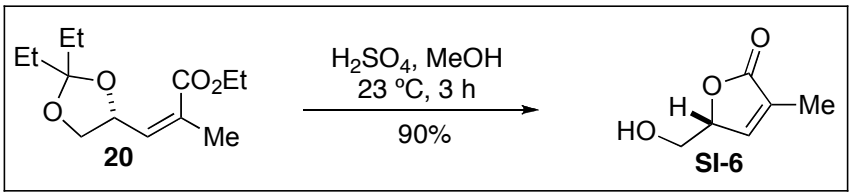


(2S,3R,5R,1'S,2'S)-{5-[1,2-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-oxo-propyl]-3-methyl-tetrahydro-furan-2-yl}-acetic acid methyl ester (18): To a solution of **17** (8.2 mg, 0.017 mmol) in dichloromethane (1 mL) at –78 °C was bubbled ozone until the solution obtained a blue hue (*ca* 30 sec). To the solution was added dimethylsulfide (1 mL) and the resulting mixture was warmed to room temperature overnight. The solvents were removed under reduced pressure and the resulting residue was purified by chromatography on SiO_2 to afford aldehyde **18** (6.2 mg, 0.013 mmol, 76%) as a colorless oil: $[\alpha]_D^{27.0}$ = –8.6 (*c* 0.56, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (d, J = 1.0 Hz, 1H), 4.09 (dt, J = 6.0, 11.0 Hz, 1H), 4.02 (dd, J = 1.5, 2.0 Hz, 1H), 3.91-3.85 (m, 2H), 3.69 (s, 3H), 2.54 (ABX, J = 3.5, 15.0 Hz, 1H), 2.41 (ABX, J = 9.5, 15.0 Hz, 1H), 2.07 (m, 1H), 1.91 (m, 1H), 1.60 (m, 1H), 1.04 (d, J = 7.0 Hz, 3H), 0.93 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 171.9, 81.4, 80.8, 79.0, 78.6, 51.6, 40.1, 39.2, 26.9, 25.9, 25.8, 18.3, 18.2, 15.5, -4.8, -4.8, -4.8, -4.9; IR (thin film, NaCl) 2954, 2929, 2887, 2858, 1741, 1472, 1437, 1388, 1361, 1254, 1200, 1105, 1039, 1006, 836, 780 cm^{-1}; HRMS (ESI) m/z for $C_{23}H_{46}O_6Si_2$ $(M+Na)^+$ calcd 497.2731, observed 497.2738.

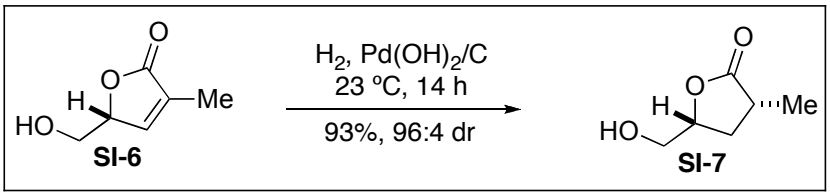


(Z)-3-((R)-2,2-Diethyl-[1,3]dioxolan-4-yl)-2-methyl-acrylic acid ethyl ester (20). 18-Crown-6 (54.4 g, 206 mmol, 5.0 equiv.) and ethyl 2-[bis(2,2,2-trifluoroethyl)phosphono] propionate[4] (13.7 g, 41.2 mmol, 1.0 equiv.) were together concentrated from benzene, dissolved in 300 mL THF, and cooled to -78 ºC. The flask was equipped with an addition funnel that was charged with potassium hexamethyldisilazide (8.18 g, 41.2 mmol, 1 equiv.) dissolved in 150 mL THF. This solution was added slowly dropwise over 1 h while maintaining the reaction temperature below -65 ºC as monitored with a thermocouple. Upon completion of the addition, the

reaction was stirred an additional 15 min to allow the temperature to return to -78 ºC. A solution of glyceraldehyde isopentylidene ketal **19** (6.52 g, 41.2 mmol, 1.0 equiv.; first evaporated from benzene) in 50 mL THF was then added rapidly dropwise over 10 min, and the resulting mixture was stirred at -78 ºC for 6 h. After the reaction was diluted with diethyl ether and quenched with saturated aqueous ammonium chloride, the biphasic mixture was warmed to room temperature. The aqueous phase was separated and extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated *in vacuo*, and purified by chromatography on SiO_2 (5 – 10% EtOAc:Hexanes) to afford **20** as a colorless oil (8.11 g, 33.5 mmol, 81%, >95:5 Z:E). Analytically pure samples of the Z olefin could be collected during column chromatography. $[\alpha]_D^{25.0} = -54.6$ (*c* 2.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.07 (dq, *J* = 6.9, 1.5 Hz, 1H), 5.26 (m, 1H), 4.32 (dd, *J* = 8.0, 6.7 Hz, 1H), 4.20 (qd, *J* = 7.2, 0.9 Hz, 2H), 3.54 (dd, *J* = 7.8, 7.8, 1H), 1.94 (dd, *J* = 1.5, 1.0 Hz, 3H), 1.69 (q, *J* = 7.4 Hz, 2H), 1.65 (q, *J* = 7.4 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 141.7, 129.6, 113.4, 74.2, 68.8, 60.6, 29.7, 29.5, 20.0, 14.2, 8.2, 8.0; IR (film) 2977, 2941, 2882, 1715, 1652, 1464, 1371, 1342, 1311, 1272, 1229, 1198, 1173, 1150, 1077, 1059, 1027, 1012 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{13}H_{22}O_4$ $[M+Na]^+$ calcd 265.1416, found 265.1411.

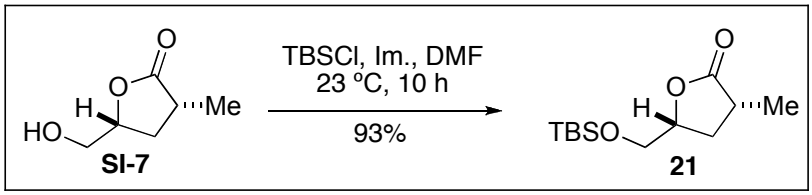


(R)-5-Hydroxymethyl-3-methyl-5*H*-furan-2-one (SI-6). Ketal **20** (7.65 g, 31.6 mmol, 1 equiv.) was dissolved in MeOH (75 mL) and concentrated H_2SO_4 (~ 50 μL) was added. The mixture was stirred for 3 h, after which it was concentrated *in vacuo* and purified by chromatography on SiO_2 (50 – 100% EtOAc:Hexanes) to afford **SI-6** as a colorless oil (3.64 g, 28.4 mmol, 90%). $[\alpha]_D^{25.5} = +41.6$ (*c* 2.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06 (app. quin., *J* = 1.6 Hz, 1H), 5.00 (m, 1H), 3.94 (ddd, *J* = 11.9, 6.6, 3.7 Hz, 1H), 3.71 (dt, *J* = 11.9, 5.8 Hz, 1H), 2.77 (bs, 1H), 1.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.3, 145.7, 131.5, 81.9, 62.8, 10.7; IR (film) 3444, 3087, 2929, 2878, 1732, 1659, 1533, 1448, 1384, 1343, 1276, 1206, 1072 cm^{-1}; HRMS (APCI-TOF) *m/z* for $C_6H_8O_3$ $[M+H]^+$ calcd 129.0552, found 129.0546.

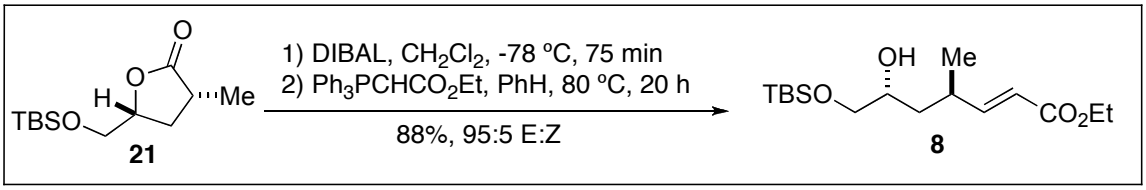


(3R,5R)-5-Hydroxymethyl-3-methyl-dihydro-furan-2-one (SI-7). Pearlman's catalyst (250 mg) was added to a solution of **SI-6** (499 mg, 3.89 mmol, 1.0 eq) in THF (20 mL). The flask was equipped with a 3-way joint attached to a nitrogen/vacuum

manifold and a hydrogen balloon. The flask was evacuated and backfilled three times with nitrogen and 3 times with hydrogen, then left to stir 14 h under an atmosphere of hydrogen. The suspension was then filtered through a pad of celite, rinsed with ethyl acetate, concentrated, and purified by chromatography on SiO_2 (50 – 100% EtOAc:Hexanes) to afford **SI-7** as a colorless oil (473 mg, 3.63 mmol, 93%, 96:4 dr). $[\alpha]_D^{24.5}$ = -35.2 (*c* 2.30, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.50 (dddd, *J* = 10.2, 6.1, 5.0, 2.8 Hz, 1H), 3.92 (ddd, *J* = 12.5, 6.1, 2.8), 3.63 (ddd, *J* = 12.5, 6.6, 5.0 Hz, 1H), 2.76 (ddq, *J* = 11.8, 9.0, 7.1 Hz, 1H), 2.39 (ddd, *J* = 12.5, 9.0, 6.1 Hz, 1H), 2.22 (dd, *J* = 6.6, 6.1 Hz, 1H), 1.80 (ddd, *J* = 12.5, 11.8, 10.2 Hz, 1H), 1.30 (d, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 179.7, 78.8, 63.9, 35.8, 31.9, 15.3; IR (film) 3429, 2976, 2937, 2879, 1761, 1647, 1456, 1379, 1359, 1322, 1292, 1199, 1174, 1100, 1068, 1030 cm^{-1}; HRMS (APCI-TOF) *m/z* for $C_6H_{10}O_3$ $[M+H]^+$ calcd 131.0708, found 131.0703.



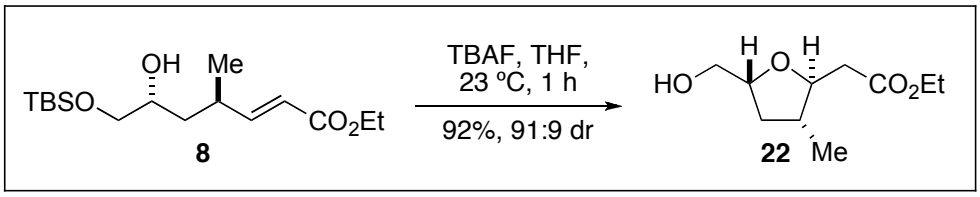
(3R,5R)-5-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-methyl-dihydro-furan-2-one (21). Imidazole (1.25 g, 18.2 mmol, 5.0 equiv.) was added to a solution of **SI-7** (473 mg, 3.63 mmol, 1.0 eq) in DMF (22 mL), followed by *tert*-butyldimethylsilyl chloride (845 mg, 5.44 mmol, 1.5 equiv.) in one portion. The mixture was stirred for 10 h at room temperature then cooled to 0 ºC. The reaction was diluted with ethyl acetate and quenched with water, then the aqueous phase was separated and extracted with ethyl acetate. The combined organic layers were washed with brine, dried with Na_2SO_4, concentrated, and purified by chromatography on SiO_2 (2 – 10% EtOAc:Hexanes) to afford **21** (826 mg, 3.38 mmol, 93%) as a colorless oil. $[\alpha]_D^{24.5}$ = -9.0 (*c* 2.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.43 (ddt, *J* = 9.8, 6.3, 3.8 Hz, 1H), 3.84 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.71 (dd, *J* = 11.4, 4.1, 1H), 2.69 (ddq, *J* = 11.4, 9.2, 7.1, 1H), 2.38 (ddd, *J* = 12.6, 9.2, 6.3, 1H), 1.81 (ddd, *J* = 12.6, 11.4, 9.7, 1H), 1.29 (d, *J* = 7.1 Hz, 3H)), 0.90 (s, 9H), 0.084 (s, 3H), 0.077 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 179.5, 78.3, 64.0, 35.4, 32.0, 25.8, 18.3, 15.4, -5.4, -5.4; IR (film) 2955, 2931, 2884, 2858, 1776, 1472, 1462, 1388, 1361, 1323, 1255, 1201, 1171, 1128, 1066, 1034, 1007 cm^{-1}; HRMS (APCI-TOF) *m/z* for $C_{12}H_{24}O_3Si$ $[M+H]^+$ calcd 245.1573, found 245.1568.



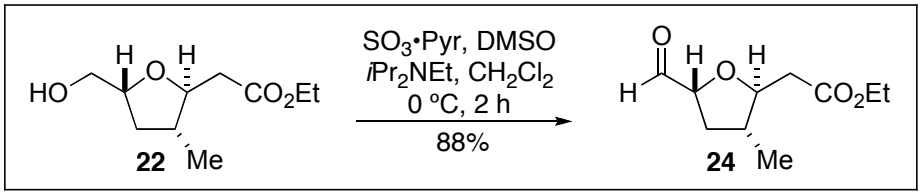
(E)-(4R,6R)-7-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-4-methyl-hept-2-enoic acid ethyl ester (8). A solution of **21** (2.29 g, 9.37 mmol, 1.0 equiv.) in dichloromethane (50 mL) was cooled to -78 ºC. A 1.0 M solution of DIBAL in dichloromethane (10.3 mL, 10.3 mmol, 1.1 equiv.) was then added slowly dropwise over

45 min, after which the mixture was stirred at -78 ºC an additional 30 min. After the reaction was quenched with MeOH (2 mL), the flask was removed from the cold bath. Saturated aqueous sodium potassium tartrate and ethyl acetate were then added and the suspension was stirred vigorously for 1 h while warming to room temperature. The aqueous layer was separated and extracted with ethyl acetate twice. The combined organic layers were washed with water then brine, dried over sodium sulfate, concentrated, and used in the next step without further purification.

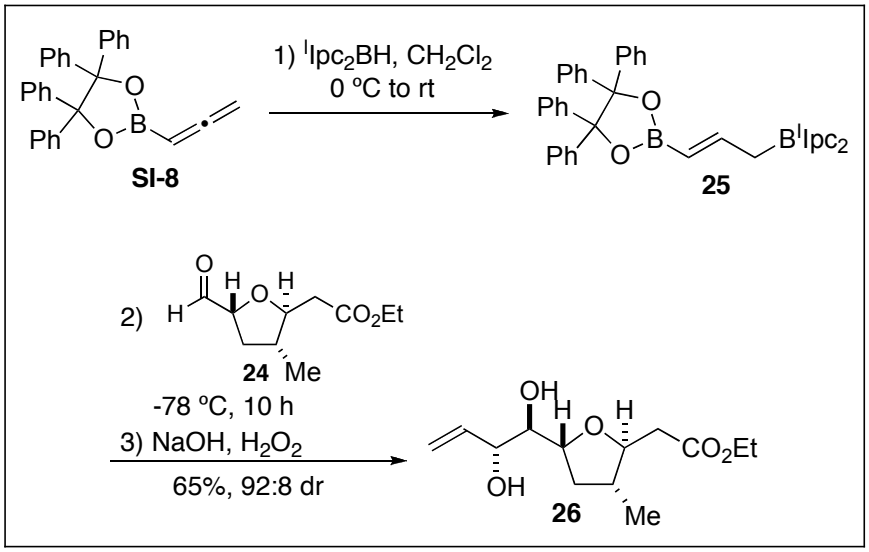
The crude product was dissolved in benzene (50 mL) and (carbethoxymethylene)triphenylphosphorane (4.25 g, 12.2 mmol, 1.3 equiv.) was added. The flask was equipped with a reflux condenser and stirred at 80 ºC for 20 h. After cooling to room temperature, the mixture was concentrated *in vacuo* and purified by chromatography on SiO_2 (5 – 10 – 20% EtOAc:Hexanes) to give **8** (2.610 g, 8.25 mmol, 88% over 2 steps, 95:5 E:Z) as a colorless oil. Analytically pure samples of the E olefin could be collected during column chromatography. $[\alpha]_D^{24.7}$ = -22.5 (*c* 2.40, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.94 (dd, *J* = 15.7, 7.5 Hz, 1H), 5.80 (dd, *J* = 15.7, 1.3 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.72 (m, 1H), 3.62 (dd, *J* = 9.9, 3.4, 1H), 3.39 (dd, *J* = 9.9, 7.2 Hz, 1H), 2.58 (m, 1H), 2.38 (d, *J* = 3.3 Hz, 1H), 1.59 (ddd, *J* = 13.8, 8.8, 5.9 Hz, 1H), 1.32 (ddd, *J* = 13.7, 8.4, 4.3 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) 166.9, 154.3, 119.5, 69.3, 67.3, 60.2, 38.7, 32.8, 25.9, 18.7, 18.3, 14.3, -5.3, -5.4; IR (film) 3489, 2956, 2930, 2858, 1778, 1720, 1651, 1471, 1463, 1389, 1368, 1256, 1208, 1179, 1097, 1038, 1005 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{16}H_{32}O_4Si$ $[M+H]^+$ calcd 317.2143, found 317.2141.



((2S,3R,5R)-5-Hydroxymethyl-3-methyl-tetrahydro-furan-2-yl)-acetic acid ethyl ester (22). A solution of **8** (2.84 g, 8.97 mmol, 1.0 equiv.) in THF (80 mL) was cooled to 0 ºC and a freshly prepared 1.0 M solution of tetrabutylammonium fluoride trihydrate in THF (10.8 mL, 10.8 mmol, 1.2 equiv.) was added in one portion. After 5 min, the mixture was warmed to room temperature and stirred for 1 h. Upon completion, the crude product was concentrated *in vacuo* and purified by chromatography on SiO_2 (20 – 50% EtOAc:Hexanes) to afford **22** (1.67 g, 8.26 mmol, 92%, 91:9 dr) as a colorless oil. Analytically pure samples of the *trans* diastereomer could be collected during column chromatography. $[\alpha]_D^{24.3}$ = -44.9 (*c* 3.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.17 (q, *J* = 7.1 Hz, 2H), 4.12 (m, 1H), 3.87 (ddd, *J* = 8.7, 7.9, 4.3 Hz, 1H), 3. 67 (dd, *J* = 11.8, 2.9 Hz, 1H), 3.50 (dd, *J* = 11.7, 5.7 Hz, 1H), 2.55 (dd, *J* = 15.2, 4.3 Hz, 1H), 2.48 (dd, *J* = 15.2, 7.9 Hz, 1H), 2.10 (ddd, *J* = 12.0, 7.2, 6.2 Hz, 1H), 2.00 (m, 1H), 1.44 (ddd, *J* = 12.0, 10.4, 9.4 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 171.5, 81.5, 78.8, 64.8, 60.5, 39.1, 39.3, 36.3, 16.3, 14.2; IR (film) 3454, 2961, 2932, 2874, 1733, 1457, 1382, 1369, 1328, 1277, 1252, 1195, 1168, 1145, 1115, 1085, 1037 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{10}H_{18}O_4$ $[M+H]^+$ calcd 203.1278, found 203.1279.

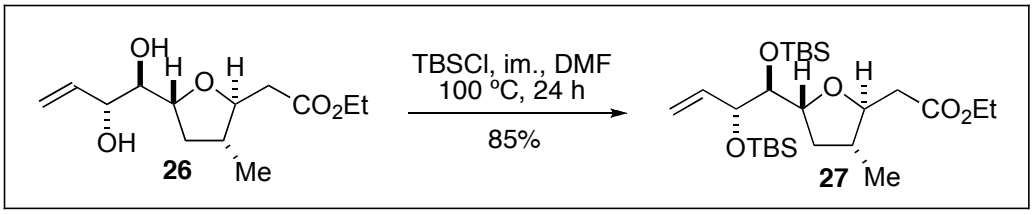


((2S,3R,5R)-5-Formyl-3-methyl-tetrahydro-furan-2-yl)-acetic acid ethyl ester (24). A solution of **22** (500 mg, 2.47 mmol, 1.0 equiv.) in dichloromethane (25 mL) was cooled to 0 ºC. DMSO (880 µL, 12.4 mmol, 5.0 equiv.) and *i*Pr_2NEt (3.0 mL, 17.3 mmol, 7.0 equiv.) were added and the mixture was stirred for 5 min. SO_3•Pyr (1.21 g, 7.42 mmol, 3.0 equiv.) was then added in one portion followed by 2 h of stirring at 0 ºC. The mixture was then diluted with dichloromethane, quenched with saturated aqueous sodium bicarbonate, and warmed to room temperature. The aqueous layer was separated and extracted with dichloromethane twice. The combined organic layers were then dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 (40 – 50% EtOAc:Hexanes) to afford **24** (435 mg, 2.17 mmol, 88%) as a colorless oil. $[\alpha]_D^{23.6}$ = -1.5 (*c* 1.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.68 (d, *J* = 2.1 Hz, 1H), 4.32 (ddd, *J* = 8.4, 8.0, 2.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.98 (td, *J* = 8.0, 4.5 Hz, 1H), 2.60 (dd, *J* = 15.2, 4.5 Hz, 1H), 2.53 (dd, *J* = 15.2, 7.7 Hz, 1H), 2.38 (dt, *J* = 12.7, 7.6 Hz, 1H), 2.05 (m, 1H), 1.63 (ddd, *J* = 12.7, 9.5, 8.5 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 202.8, 170.9, 83.1, 81.9, 60.7, 39.0, 39.0, 35.8, 16.2, 14.2; IR (film) 2964, 2932, 2876, 1735, 1458, 1383, 1369, 1327, 1276, 1254, 1198, 1167, 1106, 1039 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{10}H_{16}O_4$ $[M+H]^+$ calcd 201.1121, found 201.1122.



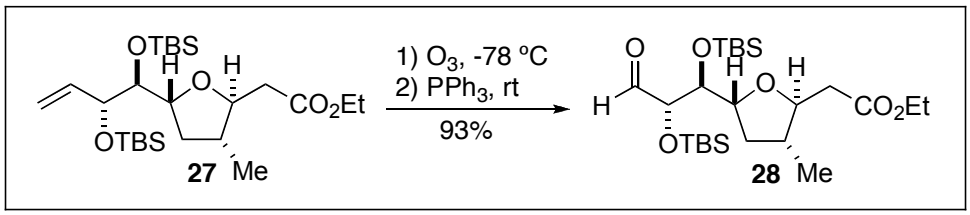
[(2S,3R,5R)-5-((1R,2R)-1,2-Dihydroxy-but-3-enyl)-3-methyl-tetrahydro-furan-2-yl]-acetic acid ethyl ester (26). In a glove box $^{l}Ipc_2BH$[2] (693 mg, 2.42 mmol, 1.2 equiv.) was weighed into a round bottom flask. (Note: The borane was crushed with a glass rod prior to use in order to achieve efficient hydroboration.) The flask was

capped with a rubber septum, removed from the glove box, and cooled to 0 ºC. Dichloromethane (7.5 mL) was added, followed by rapid dropwise addition of a solution of allenylborane **SI-8**[3] (1.00 g, 2.42 mmol, 1.2 equiv.) in dichloromethane (6 mL, plus 1.5 mL rinse) by cannula. The mixture was stirred at 0 ºC for 2 h after which dissolution was still incomplete, so the ice bath was removed to allow the mixture to warm to room temperature for 30 min. When the solid borane was no longer visible, the solution was cooled to -78 ºC over 10 min. A solution of aldehyde **24** (403 mg, 2.01 mmol, 1.0 equiv.) in dichloromethane (4 mL, plus 1 mL rinse) was added dropwise by syringe followed by 10 h of stirring at -78 ºC. The dry ice bath was removed, and of 2M aq. NaOH (1 mL) was added followed by placement of an ice to maintain the mixture at 0 ºC. Additional 2M aq. NaOH (2 mL) and 50% H_2O_2 (1 mL) was added and the mixture was allowed to warm to room temperature overnight (10 h), followed by dilution with ethyl acetate and saturated aqueous sodium bicarbonate. The aqueous layer was separated and extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 (25 – 50% EtOAc:Hexanes) to afford **26** (337 mg, 1.30 mmol, 65%, 92:8 dr) as a colorless oil. $[\alpha]_D^{23.4}$ = -44.3 (*c* 2.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.91 (ddd, *J* = 17.3, 10.4, 6.9 Hz, 1H), 5.11 (ddd, *J* = 17.3, 1.9, 1.2 Hz, 1H), 5.09 (ddd, *J* = 10.4, 1.9, 1.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.06 (ddt, *J* = 6.9, 2.7, 1.1 Hz, 1H), 3.87 (ddd, *J* = 10.1, 7.0, 5.8 Hz, 1H), 3.81 (ddd, *J* = 9.1, 8.1, 4.2 Hz, 1H), 3.52 (dd, *J* = 7.0, 2.7 Hz, 1H), 2.50 (dd, *J* = 14.7, 4.3 Hz, 1H), 2.42 (dd, *J* = 14.7, 8.1 Hz, 1H), 2.03 (m, 1H), 1.90 (ddp, *J* = 11.1, 9.1, 6.6 Hz, 1H), 1.35 (ddd, *J* = 11.8, 11.2, 10.1 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 171.6, 138.8, 115.5, 81.0, 80.1, 79.5, 76.1, 60.2, 40.3, 39.7, 37.6, 26.1, 26.0, 18.5, 18.4, 16.0, 14.2, -4.3, -4.3, -4.5, -4.6; IR (film) 3076, 2956, 2929, 2887, 2857, 1740, 1472, 1462, 1388, 1361, 1325, 1274, 1252, 1195, 1141, 1076, 1040, 1005 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{25}H_{50}O_5Si_2$ $[M+H]^+$ calcd 487.3269, found 487.3267.



{(2S,3R,5R)-5-[(1S,2R)-1,2-Bis-(*tert*-butyl-dimethyl-silanyloxy)-but-3-enyl]-3-methyl-tetrahydro-furan-2-yl}-acetic acid ethyl ester (27). Imidazole (240 mg, 3.53 mmol, 6.0 equiv.) was added to a solution of **26** (150 mg, 0.60 mmol, 1.0 eq) in DMF (6 mL), followed by *tert*-butyldimethylsilyl chloride (450 mg, 2.99 mmol, 5.0 equiv.) in one portion. The flask was equipped with a reflux condenser. The mixture was then heated to 100 ºC, stirred for 24 h, cooled to 0 ºC, diluted with ethyl acetate, and quenched with water. The aqueous layer was separated and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated, and purified by chromatography on SiO_2 (2% EtOAc:Hexanes) to afford **27** (249 mg, 0.51 mmol, 85%) as a colorless oil. $[\alpha]_D^{23.6}$ = -11.8 (*c* 2.60, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400

MHz) δ 5.91 (ddd, *J* = 17.3, 10.4, 6.9 Hz, 1H), 5.11 (ddd, *J* = 17.3, 1.9, 1.2 Hz, 1H), 5.09 (ddd, *J* = 10.4, 1.9, 1.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.06 (ddt, *J* = 6.9, 2.7, 1.1 Hz, 1H), 3.87 (ddd, *J* = 10.1, 7.0, 5.8 Hz, 1H), 3.81 (ddd, *J* = 9.1, 8.1, 4.2 Hz, 1H), 3.52 (dd, *J* = 7.0, 2.7 Hz, 1H), 2.50 (dd, *J* = 14.7, 4.3 Hz, 1H), 2.42 (dd, *J* = 14.7, 8.1 Hz, 1H), 2.03 (m, 1H), 1.90 (ddp, *J* = 11.1, 9.1, 6.6 Hz, 1H), 1.35 (ddd, *J* = 11.8, 11.2, 10.1 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 171.6, 138.8, 115.5, 81.0, 80.1, 79.5, 76.3, 60.4, 40.3, 39.7, 37.6, 26.1, 26.0, 18.5, 18.4, 16.0, 14.2, -4.3, -4.3, -4.5, -4.6; IR (film) 3076, 2956, 2929, 2887, 2857, 1740, 1472, 1462, 1388, 1361, 1325, 1274, 1252, 1195, 1141, 1076, 1040, 1005 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{25}H_{50}O_5Si_2$ $[M+H]^+$ calcd 487.3269, found 487.3267.



{(2S,3R,5R)-5-[(1S,2S)-1,2-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-oxo-propyl]-3-methyl-tetrahydro-furan-2-yl}-acetic acid ethyl ester (28). To a solution of **27** (130 mg, 0.267 mmol, 1.0 equiv.) in dichloromethane (1.8 mL) and MeOH (0.6 mL) was added $NaHCO_3$ (25 mg) and Sudan III dye (~2 mg). The bright red solution was cooled to -78 ºC and stirred vigorously while O_2 was bubbled in by pipette for 1 min. The ozone generator was then turned on, and O_3 was bubbled in for 6 min until the red color disappeared. N_2 was then bubbled through by a different pipette to remove traces of O_3, followed by addition of triphenylphosphine (79 mg, 0.300 mmol, 1.1 equiv.) in one portion. The mixture was allowed to warm slowly to room temperature while stirring for 12 h. After concentrating *in vacuo*, the crude mixture was purified by chromatography on SiO_2 (0 – 5% EtOAc:Hexanes) to afford **28** (121 mg, 0.248 mmol, 93%) as a colorless oil. $[\alpha]_D^{23.1}$ = -5.4 (*c* 2.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.61 (d, *J* = 1.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.09 (dt, *J* = 10.1, 6.3 Hz, 1H), 4.03 (dd, *J* = 2.0, 1.3 Hz, 1H), 3.89 (dd, *J* = 6.5, 2.0 Hz, 1H), 3.87 (m, 1H), 2.52 (dd, *J* = 14.8, 3.6 Hz, 1H), 2.39 (dd, *J* = 14.8, 8.8 Hz, 1H), 2.07 (dt, *J* = 12.3, 6.4 Hz, 1H), 1.91 (ddp, *J* = 11.2, 9.4, 6.6 Hz, 1H), 1.60 (td, *J* = 11.7, 10.1 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.93 (s, 9H), 0.88 (s, 9H), 0.10, (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 203.0, 171.4, 81.5, 80.9, 79.0, 78.6, 60.5, 40.1, 39.5, 36.9, 25.9, 25.8, 18.3, 18.2, 15.6, 14.1, -4.7, -4.8, -4.8, -4.9; IR (film) 2930, 2910, 2886, 2857, 1734, 1472, 1463, 1388, 1362, 1325, 1253, 1196, 1104, 1039, 1006 cm^{-1}; HRMS (ESI-TOF) *m/z* for $C_{24}H_{48}O_6Si_2$ $[M+H]^+$ calcd 489.3062, found 487.3062.

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