

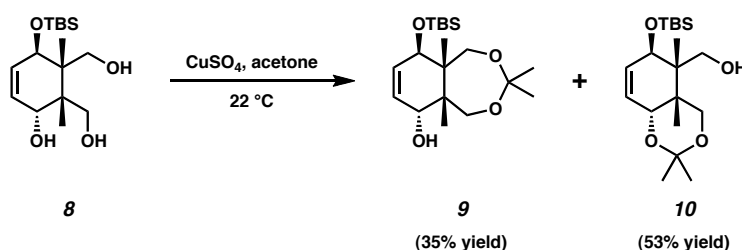


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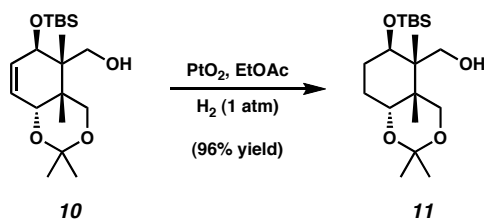
## Supplementary Material for: Unexpected Decarbonylation during an Acid-Mediated Cyclization to Access the Carbocyclic Core of Zoanthenol.

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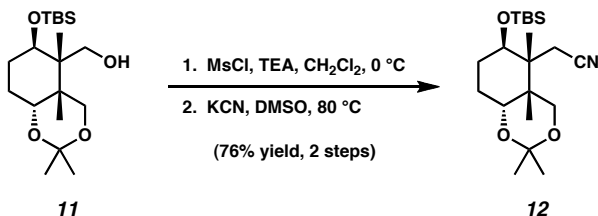
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**1,3-Dioxepane 9 and Acetone 10.** To a solution of triol **8** (3.75 g, 11.9 mmol, 1.00 equiv) in acetone (120 mL) was added anhydrous  $\text{CuSO}_4$  (9.46 g, 59.3 mmol, 5.00 equiv), and the reaction mixture was stirred for 40 min. An additional portion of  $\text{CuSO}_4$  (1.89 g, 11.9 mmol, 1.00 equiv) was added to the reaction mixture, and after an additional 3 h of stirring, a final portion of  $\text{CuSO}_4$  (1.00 g, 6.27 mmol, 0.53 equiv) was added. After 30 min, the reaction mixture was filtered, concentrated, and purified by flash chromatography on silica gel (5 to 15% EtOAc in hexanes) to give 1,3-dioxepane **9** (1.48 g, 35% yield) as a waxy solid:  $R_f$  0.66 (35% EtOAc in hexanes);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.57 (dt,  $J = 2.1, 10.2$  Hz, 1H), 5.49 (dt,  $J = 2.1, 10.2$  Hz, 1H), 4.99 (s, 1H), 4.23 (app. q,  $J = 2.4$  Hz, 1H), 3.73 (d,  $J = 12.3$  Hz, 1H), 3.58 (d,  $J = 12.6$  Hz, 1H), 3.56 (d,  $J = 12.6$  Hz, 1H), 3.19 (d,  $J = 12.6$  Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 0.90 (s, 9H), 0.71 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  131.7, 129.2, 101.8, 73.5, 68.1, 63.8, 63.0, 46.9, 46.3, 26.5, 25.7, 25.4, 18.8, 18.7, 11.7, -3.7, -4.5; IR (Neat film NaCl) 3446, 2983, 2954, 2858, 1472, 1372, 1253, 1221, 1085, 1070, 1044, 835, 775  $\text{cm}^{-1}$ ; HRMS (FAB+)  $[\text{M}-\text{H}_2+\text{H}]^+$  calc'd for  $[\text{C}_{19}\text{H}_{35}\text{SiO}_4]^+$ :  $m/z$  355.2305, found 355.2317 and acetone **10** (2.25 g, 53% yield) as an oil:  $R_f$  0.76 (35% EtOAc in hexanes);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.93 (dd,  $J = 4.4, 9.6$  Hz, 1H), 5.69 (dd,  $J = 4.8, 9.9$  Hz, 1H), 4.12

(d,  $J = 4.5$  Hz, 1H), 4.01 (d,  $J = 12.9$  Hz, 1H), 3.91 (s, 1H), 3.76 (d,  $J = 10.2$  Hz, 1H), 3.64 (d,  $J = 10.2$  Hz, 1H), 3.56 (d,  $J = 12.9$  Hz, 1H), 1.49 (s, 3H), 1.43 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  133.5, 124.4, 98.6, 71.7, 70.9, 68.9, 65.2, 43.8, 35.1, 28.4, 25.7, 20.9, 20.0 (bs), 17.9, 15.3, -4.1, -5.1; IR (Neat film NaCl) 3451, 2955, 2931, 2886, 2858, 1379, 1256, 1104, 1056, 836, 775  $\text{cm}^{-1}$ ; HRMS (FAB+)  $[\text{M}+\text{H}]^+$   $m/z$  calc'd for  $[\text{C}_{19}\text{H}_{36}\text{SiO}_4+\text{H}]^+$ : 357.2461, found 357.2478.



**Alcohol 10.** To a solution of acetone **10** (5.64 g, 15.8 mmol, 1.00 equiv) in EtOAc (198 mL) was added  $\text{PtO}_2$  (108 mg, 0.475 mmol, 0.03 equiv), and the reaction mixture was sparged with a stream of  $\text{H}_2$  gas for 4 h. The reaction mixture was concentrated ( $\sim 10$  mL), filtered through a plug of silica gel, and concentrated to give hydrogenated alcohol **11** (5.47 g, 96% yield) as an oil:  $R_f$  0.76 (35% EtOAc in hexanes);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.43 (dd,  $J = 5.5, 12.0$  Hz, 1H), 3.98 (dd,  $J = 5.0, 10.3$  Hz, 1H), 3.88 (d,  $J = 13.0$  Hz, 1H), 3.79 (app. t,  $J = 3.0$  Hz, 1H), 3.45 (s, 1H), 3.32 (d,  $J = 12.0$  Hz, 1H), 3.04 (app. t,  $J = 11.0$  Hz, 1H), 2.12 (app. tt,  $J = 3.8, 14.3$  Hz, 1H), 1.86 (app. tt,  $J = 3.0, 14.0$  Hz, 1H), 1.48 (s, 3H), 1.47–1.37 (m, 1H), 1.42 (s, 3H), 0.97 (s, 3H), 0.93 (s, 3H), 0.90 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  98.5, 75.0, 74.4, 69.5, 66.8, 43.5, 35.0, 29.5, 25.9, 25.1, 21.9, 20.2, 18.8, 18.0, 17.2, -4.6, -5.0; IR (Neat film NaCl) 3497, 2953, 2936, 2883, 2858, 1472, 1379, 1257, 1196, 1083, 1060, 1034, 1005, 866, 834, 774  $\text{cm}^{-1}$ ; HRMS (FAB+)  $[\text{M}+\text{H}]^+$   $m/z$  calc'd for  $[\text{C}_{19}\text{H}_{38}\text{SiO}_4+\text{H}]^+$ : 359.2618, found 359.2632.

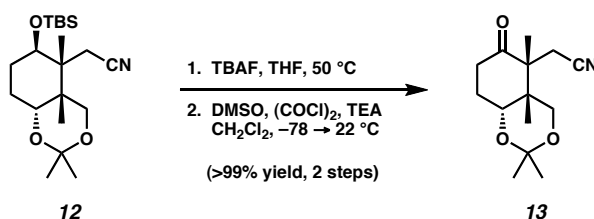


**Nitrile 12.** To a cooled ( $0$   $^\circ\text{C}$ ) solution of alcohol **11** (880 mg, 2.45 mmol, 1.00) and TEA (1.02 mL, 7.36 mmol, 3.00 equiv) in  $\text{CH}_2\text{Cl}_2$  (25 mL) was added methanesulfonyl chloride (228  $\mu\text{L}$ , 2.95 mmol, 1.20 equiv) in a dropwise manner. After 30

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min at 0 °C, the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL), ice cold H<sub>2</sub>O (50 mL), and brine (25 mL), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 35 mL). The combined organics were washed with brine (30 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated to a waxy solid that was used in the next step immediately.

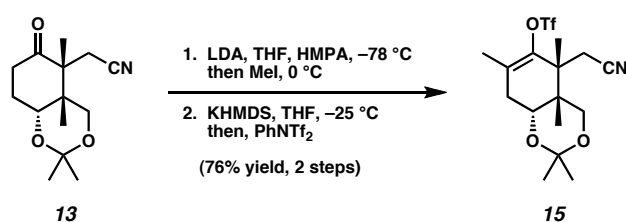
The above residue was dissolved in DMSO (25 mL) and treated with KCN (400 mg, 6.14 mmol, 2.50 equiv) at 80 °C for 4 h. The reaction mixture was cooled to ambient temperature, diluted with EtOAc (50 mL) and H<sub>2</sub>O (150 mL), and extracted with EtOAc (7 x 40 mL). The combined organics were washed with brine (30 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated, and purified by flash chromatography on silica gel (2.5 to 10% EtOAc in hexanes) to provide nitrile **12** (682 mg, 76% yield) as a solid : *R<sub>f</sub>* 0.42 (20% EtOAc in hexanes); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 4.07 (d, *J* = 8.7 Hz, 1H), 3.83 (d, *J* = 8.4 Hz, 1H), 3.70–3.60 (m, 2H), 3.49 (d, *J* = 8.1 Hz, 1H), 3.46 (d, *J* = 8.7 Hz, 1H), 2.18–2.04 (m, 1H), 1.74–1.45 (m, 3H), 1.55 (s, 6H), 1.14 (s, 3H), 0.90 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 121.7, 78.8, 76.1, 74.8, 71.0, 70.1, 50.8, 48.8, 28.8 (2C), 27.6 (2C), 25.8, 22.6, 18.0, 9.5, -3.9, -5.0; IR (Neat film NaCl) 2956, 2934, 2882, 2860, 1460, 1254, 1183, 1080, 1047, 916, 868, 835, 772 cm<sup>-1</sup>; HRMS (FAB+) [M-H<sub>2</sub>+H]<sup>+</sup> *m/z* calc'd for [C<sub>20</sub>H<sub>36</sub>NO<sub>3</sub>Si]<sup>+</sup>: 366.2464, found 366.2459.



**Ketone 13.** To a solution of nitrile **12** (889.8 mg, 2.421 mmol, 1.00 equiv) in THF (14.5 mL) was added a 1.0 M solution of TBAF (7.26 μL, 7.262 mmol, 3.00 equiv) in THF, and the reaction mixture was heated to 50 °C for 12 h. The reaction mixture was cooled to ambient temperature, quenched with sat. NH<sub>4</sub>Cl aq. (75 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> (125 mL). The aqueous layer was further extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 20 mL), dried over MgSO<sub>4</sub>, and concentrated into an oil, which was used without further purification.

A solution of DMSO (1.37 mL, 19.4 mmol, 8.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was cooled to -78 °C and oxalyl chloride (1.48 mL, 16.9 mmol, 7.00 equiv) was added in a dropwise manner. After 30 min at -78 °C, a solution of the crude alcohol generated above in CH<sub>2</sub>Cl<sub>2</sub> (10 mL, + 2 x 2 mL rinse) was added in a dropwise manner down the wall of the flask. After 1.5 h at -78 °C, TEA 6.75 mL, 48.4 mmol, 20.0 equiv) was added and the reaction mixture was allowed to warm slowly to ambient temperature, diluted with half-saturated NH<sub>4</sub>Cl (100 mL), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 x 50 mL). The combined organics were washed with saturated NaHCO<sub>3</sub> (75 mL), dried (MgSO<sub>4</sub>), concentrated to an oil, and purified by flash

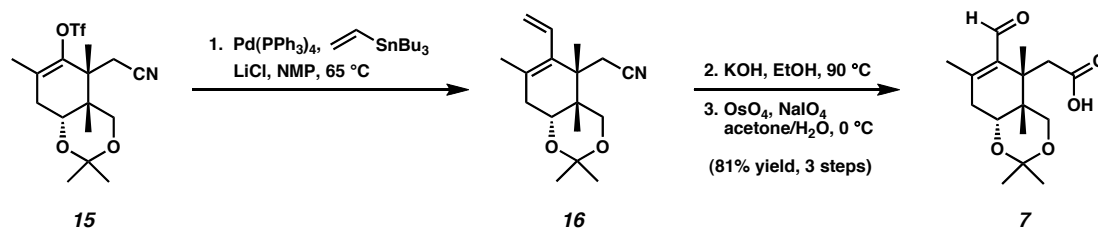
chromatography on silica gel (20 to 35% EtOAc in hexanes) to provide ketone **13** (617 mg, 2.45 mmol, > 99% yield, 2 steps) as an oil:  $R_f$  0.49 (50% EtOAc in hexanes);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  4.53 (d,  $J = 8.7$  Hz, 1H), 4.01 (dd,  $J = 4.4, 10.7$  Hz, 1H), 3.95 (d,  $J = 9.3$  Hz, 1H), 3.50 (d,  $J = 9.3$  Hz, 1H), 3.41 (d,  $J = 8.1$  Hz, 1H), 2.68–2.41 (m, 2H), 2.41–2.24 (m, 1H), 2.10–1.90 (m, 1H), 1.61 (s, 6H), 1.23 (s, 3H), 1.14 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  210.6, 121.3, 77.5, 75.0, 74.1, 70.7, 58.0, 50.4, 35.6, 28.6, 27.7, 27.5, 21.4, 16.7; IR (Neat film NaCl) 2983, 2881, 2254, 1714, 1387, 1373, 1171, 1052, 907, 729, 651  $\text{cm}^{-1}$ ; HRMS (EI)  $[\text{M}]^+$   $m/z$  calc'd for  $[\text{C}_{14}\text{H}_{21}\text{NO}_3]^+$ : 251.1521, found 251.1518.



**Triflate 15.** A solution of LDA in THF was prepared by dropwise addition of 2.50 M *n*-BuLi solution in hexanes (580  $\mu\text{L}$ , 1.45 mmol, 1.05 equiv) to diisopropylamine (252  $\mu\text{L}$ , 1.79 mmol, 1.30 equiv) in THF (15.0 mL) at 0  $^\circ\text{C}$ , followed by stirring for 30 min. Upon cooling the solution to  $-78\text{ }^\circ\text{C}$ , a solution of ketone **13** (347 mg, 1.38 mmol, 1.00 equiv) in THF (15.0 mL) was added in a dropwise manner, and the reaction mixture was stirred at  $-78\text{ }^\circ\text{C}$  for 2 h. HMPA (552  $\mu\text{L}$ , 3.18 mmol, 2.30 equiv) was added and the reaction mixture was brought to 0  $^\circ\text{C}$  for 1 h. After cooling again to  $-78\text{ }^\circ\text{C}$ , the solution containing the enolate was added to a solution of MeI (258  $\mu\text{L}$ , 4.14 mmol, 3.00 equiv) in THF (4.00 mL) at  $-30\text{ }^\circ\text{C}$  in a dropwise manner over 25 min. After 6 h at  $-25\text{ }^\circ\text{C}$ , the reaction mixture was quenched with  $\text{H}_2\text{O}$  (30 mL) and  $\text{CH}_2\text{Cl}_2$  (30 mL), and extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 30 mL). The combined organics were washed, dried ( $\text{MgSO}_4$ ), and concentrated to an oil, which was purified by flash chromatography on silica gel (10 to 25% EtOAc in hexanes) to give to an inseparable mixture of diastereomeric methyl ketones (286 mg, 78% yield).

To a cooled ( $-25\text{ }^\circ\text{C}$ ) solution of KHMDS (300 mg, 1.50 mmol, 1.40 equiv) in THF (17 mL) was added the above mixture of methyl ketones (286 mg, 1.07 mmol, 1.00 equiv) in THF (15 mL) in a dropwise manner over 10 min. After 2.5 h at  $-25\text{ }^\circ\text{C}$ ,  $\text{PhNTf}_2$  (614 mg, 1.72 mmol, 1.60 equiv) in THF (10.7 mL) was added, and the reaction maintained for an additional 30 min at  $-25\text{ }^\circ\text{C}$ . The reaction mixture was quenched into half-saturated  $\text{NaHCO}_3$  (100 mL) and extracted with EtOAc (4 x 70 mL). The combined organics were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to an oil, which was purified by flash chromatography on silica gel (15 to 25%  $\text{Et}_2\text{O}$  in hexanes) to provide triflate **15** (420 mg, 98% yield, 76% yield for 2 steps) as an oil:  $R_f$  0.41 (50%  $\text{Et}_2\text{O}$  in hexanes);  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  4.16 (d,  $J = 8.7$  Hz, 1H), 3.95 (d,  $J = 9.3$  Hz, 1H),

3.52 (dd,  $J = 6.2, 8.6$  Hz, 1H), 3.46 (d,  $J = 9.0$  Hz, 1H), 3.36 (d,  $J = 9.0$  Hz, 1H), 2.17 (dd,  $J = 6.0, 18.0$  Hz, 1H), 1.95 (dd,  $J = 8.1, 18.0$  Hz, 1H), 1.50 (s, 3H), 1.01 (s, 3H), 0.97 (s, 3H), 0.90 (s, 3H), 0.88 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  145.7, 125.1, 121.5, 119.5 (app. d,  $J_{\text{C-F}} = 296$  Hz), 75.2, 74.7, 74.3, 71.0, 51.2, 50.4, 36.1, 28.2, 27.4, 21.6, 18.1, 16.4; IR (Neat film NaCl) 2988, 2942, 2884, 1403, 1211, 1141, 1053, 990, 874  $\text{cm}^{-1}$ ; HRMS (EI)  $[\text{M}]^+$   $m/z$  calc'd for  $[\text{C}_{16}\text{H}_{22}\text{NO}_3\text{F}_3\text{S}]^+$ : 397.1171, found 397.1179.

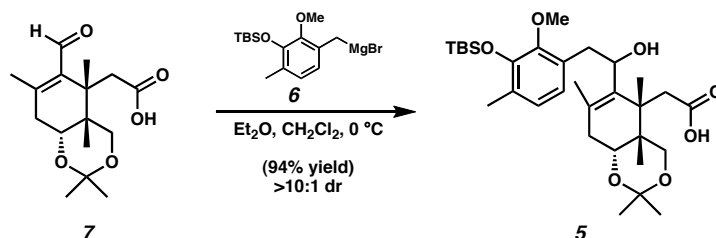


**Enal 7.** To a solution of triflate **15** (1.41 g, 3.54 mmol, 1.00 equiv),  $\text{Pd}(\text{PPh}_3)_4$  (307 mg, 0.266 mmol, 0.075 equiv), and LiCl (450 mg, 10.6 mmol, 3.00 equiv) in NMP (59 mL) was added tributyl(vinyl)stannane (1.55 mL, 5.31 equiv, 1.50 equiv), and the mixture was heated to 65 °C for 0.5 h. The reaction mixture was cooled to ambient temperature, quenched with  $\text{H}_2\text{O}$  (300 mL) and  $\text{Et}_2\text{O}$  (200 mL), and extracted with  $\text{Et}_2\text{O}$  (4 x 125 mL). The combined organics were washed with brine (170 mL), dried ( $\text{MgSO}_4$ ), and concentrated to an oil, which was purified by flash chromatography on silica gel (2.5 to 10% EtOAc in hexanes) to provide the intermediate diene **16** (1.04 g, quantitative yield) as a viscous oil containing a small amount of solvent.

To a stirred solution of nitrile **16** (370.3 mg, 1.35 mmol, 1 equiv) in EtOH (26.9 mL, 0.05 M) was added KOH aq. (26.9 mL, 5 wt% in  $\text{H}_2\text{O}$ , 0.05 M). The reaction was then heated to 80 °C for 44 hours. The reaction was then cooled to ambient temperature and the EtOH was removed by rotary evaporation. The resulting aqueous solution was diluted with 60 mL  $\text{CH}_2\text{Cl}_2$ , 26.9 mL HCl (2M), and further extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 40 mL). The organic layers were dried over  $\text{MgSO}_4$  and concentrated to an oil (406.7 mg, 1.38 mmol, > 99% yield), which was carried on to the next step without further purification.

To a solution of the carboxylic acid intermediate (133.2 mg, 0.4525 mmol, 1 equiv) in acetone (5.7 mL, 0.08 M) and water (5.7 mL, 0.08 M) at 0 °C was added  $\text{OsO}_4$  (11.5 mg, 45.25  $\mu\text{mol}$ , 0.1 M) and  $\text{NaIO}_4$  (241.7 mg, 1.13 mmol, 2.5 equiv). The reaction mixture was stirred at 0 °C for 1 h then diluted with  $\text{H}_2\text{O}$  (25 mL), EtOAc (25 mL), further extracted with EtOAc (3 x 15 mL), dried over  $\text{MgSO}_4$ , and concentrated to an oil. Purification by flash chromatography (30% to 60% acetone/hexanes, with 3 drops AcOH per 100 mL eluent during the last half of the column) afforded enal **7** (111.5 mg, 0.3762 mmol, 83% yield) as a white amorphous solid.  $R_f$  0.28 (40% EtOAc in hexanes);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  10.14 (s, 1H), 4.06 (d,  $J = 9.0$  Hz, 1H), 4.01 (d,  $J = 9.0$  Hz, 1H), 3.89 (d,  $J = 9.0$  Hz, 1H), 3.88 (t,  $J = 3.7$  Hz, 1H), 3.76 (d,  $J = 9.3$  Hz,

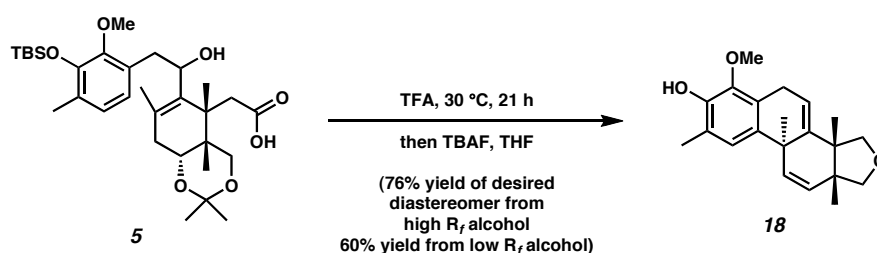
1H), 2.63 (comp. m, 1H), 2.27 (dd,  $J = 19.3, 4.0$  Hz, 1 H), 2.18 (s, 3H), 1.53 (s, 3H), 1.46 (s, 3H), 1.26 (s, 3H), 1.01 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  190.6, 175.9, 150.1, 138.5, 80.9, 78.2, 76.2, 74.2, 47.4, 45.2, 38.1, 26.8, 23.0, 21.7, 19.3, 18.2; IR (Neat film NaCl) 3600–2500, 2981, 2939, 2882, 1731, 1668, 1385, 1175, 1154, 1049, 918  $\text{cm}^{-1}$ ; MS (FAB+)  $[\text{M}+\text{H}]^+$   $m/z$  calc'd for  $[\text{C}_{16}\text{H}_{24}\text{O}_5+\text{H}]^+$ : 297.1702, found 297.1697.



**Allylic alcohol 5.** A flame-dried two-neck round bottom flask equipped with a reflux condenser and septum was charged with magnesium turnings (1.03 g, 42.4 mmol, 32.4 equiv) and  $\text{Et}_2\text{O}$  (12 mL) under an  $\text{N}_2$  atmosphere and heated to reflux. To this mixture was added 1,2-dibromoethane (150  $\mu\text{L}$ , 1.74 mmol, 1.33 equiv) in a dropwise manner [Caution: gas evolution!]. When gas evolution ceased, a solution of benzylic bromide (677 mg, 1.96 mmol, 1.50 equiv) in  $\text{Et}_2\text{O}$  (7.0 mL) was added in a dropwise manner over 30 min and heating was continued for an additional 30 min. The Grignard reagent (**6**) was then cooled to 0  $^\circ\text{C}$  and 3 equivalents were added dropwise to a cooled (0  $^\circ\text{C}$ ) solution of enal **5** (100 mg, 0.337 mmol, 1.00 equiv) in  $\text{Et}_2\text{O}$  (3.8 mL) and  $\text{CH}_2\text{Cl}_2$  (7.4 mL) (1:2 ratio, 0.03 M overall). After 15 min at 0  $^\circ\text{C}$ , the reaction was quenched with  $\text{H}_2\text{O}$  (5 mL) and 2 M citric acid (2.0 mL) and allowed to come to ambient temperature. The mixture was diluted with  $\text{H}_2\text{O}$  (30 mL) and  $\text{Et}_2\text{O}$  (30 mL), and extracted with  $\text{Et}_2\text{O}$  (50 mL then 3 x 10 mL). The combined organics were washed with brine (30 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated to an oil. Purification by flash chromatography on silica gel (15 to 65%  $\text{EtOAc}$  in hexanes with 3 drops  $\text{AcOH}$  per 100 mL eluent for last half of column) provided allylic alcohol **5** (178.3 mg, 0.3168 mmol, 94% yield, > 10:1 dr) as a partially separated mixture of two diastereomers **5a** and **5b**.

**High  $R_f$  diastereomer 5a:**  $R_f$  0.72 (50% acetone in hexanes);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.86 (d,  $J = 7.8$  Hz, 1 H), 6.72 (d,  $J = 7.8$  Hz, 1H), 4.56 (d,  $J = 9.3$  Hz, 1H), 4.04 (d,  $J = 8.5$  Hz, 1H), 3.89 (app. t,  $J = 8.8$  Hz, 2H), 3.81 (t,  $J = 4.2$  Hz, 1H), 3.78 (d,  $J = 8.8$  Hz, 1H), 3.72 (s, 3H), 3.09 (dd,  $J = 13.9, 10.5$  Hz, 1 H), 2.79 (dd,  $J = 13.9, 2.4$  Hz, 1H), 2.41 (dd,  $J = 18.1, 3.9$  Hz, 1H), 2.21 (s, 3H), 2.05 (dd,  $J = 18.1, 4.2$  Hz, 1H), 1.52 (s, 3H), 1.03 (s, 9H), 1.01 (s, 3H), 0.19 (s, 3H), 0.17 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  176.5, 149.4, 147.3, 135.9, 130.4, 129.8, 126.4, 123.2, 78.0, 76.4, 75.0, 73.6, 60.0, 47.3, 39.2, 36.7, 26.7, 26.0, 23.1, 20.6, 18.6, 17.0, -4.0, -4.1; IR (Neat film NaCl) 3426, 2956, 2932, 2859, 1731, 1464, 1419, 1286, 1253, 1178, 1074, 1046, 918, 840, 782, 733  $\text{cm}^{-1}$ ; MS (FAB+)  $[\text{M}+\text{H}-\text{H}_2]^+$  calc'd for  $[\text{C}_{31}\text{H}_{49}\text{O}_7\text{Si}]^+$ :  $m/z$  561.3248, found 561.3253.

**Low  $R_f$  diastereomer 5b:**  $R_f$  0.61 (50% acetone in hexanes);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.86 (d,  $J = 7.8$  Hz, 1H), 6.74 (d,  $J = 7.8$  Hz, 1H), 4.27 (dd,  $J = 10.3, 2.7$  Hz, 1H), 4.14 (d,  $J = 8.3$  Hz, 1H), 3.98 (d,  $J = 9.8$  Hz, 1H), 3.81 (app. t,  $J = 5.9$  Hz, 1H), 3.74 (d,  $J = 8.3$  Hz, 1H), 3.71 (d,  $J = 8.8$  Hz, 1H), 3.70 (s, 3H), 3.14 (dd,  $J = 13.9, 10.3$  Hz, 1H), 2.81 (dd,  $J = 13.9, 2.7$  Hz, 1H), 2.38 (dd,  $J = 18.1, 4.9$  Hz, 1H), 2.21 (s, 3H), 2.13 (dd,  $J = 17.8, 6.1$  Hz, 1H), 1.98 (s, 3H), 1.52 (s, 6H), 1.18 (s, 3H), 1.06 (s, 3H), 1.03 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  176.0, 149.5, 147.3, 136.0, 130.4, 129.7, 126.3, 123.2, 78.1, 76.1, 74.1, 73.7, 60.0, 49.9, 47.1, 38.1, 37.4, 26.0, 25.8, 23.7, 21.1, 20.7, 19.9, 18.6, 17.0, -4.0, -4.1; IR (Neat film NaCl) 3600–2500, 2930, 2859, 1722, 1464, 1419, 1286, 1253, 1178, 1074, 1045, 918, 840, 734  $\text{cm}^{-1}$ ; MS (FAB+)  $[\text{M}+\text{H}-\text{H}_2]^+$   $m/z$  calc'd for  $[\text{C}_{31}\text{H}_{49}\text{O}_7\text{Si}]^+$ : 561.3248, found 561.3225.



**Tetracycle 18 from 5a.** A solution of allylic alcohol **5a** (30 mg, 0.053 mmol, 1.0 equiv) in TFA (3 mL, 10 mg/mL) was warmed to 30 °C and stirred for 21 h (reaction times as low as 30 min provide similar results) before cooling to ambient temperature. TFA was removed by rotary evaporation, diluted with benzene and concentrated to an oil (3x) then redissolved in THF (2 mL, 0.025 M). A solution of TBAF (54  $\mu\text{L}$ , 0.106 mmol, 2.0 equiv) in THF (2.0 M) was added, and the reaction mixture was stirred for 3 h, quenched with  $\text{H}_2\text{O}$  (20 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 20 mL), dried over  $\text{MgSO}_4$ , and purified by flash chromatography (10 to 20% EtOAc in hexanes) to provide tetracycle **18** (13.3 mg, 0.041 mmol, 76% yield) as a yellow solid.

**Tetracycle 18 from 5b.** A solution of allylic alcohol **5b** (30 mg, 0.053 mmol, 1.0 equiv) in TFA (3 mL, 10 mg/mL) was warmed to 30 °C and stirred for 21 h (reaction times as low as 30 min provide similar results) before cooling to ambient temperature. TFA was removed by rotary evaporation, diluted with benzene and concentrated to an oil (3x) then redissolved in THF (2 mL, 0.025 M). A solution of TBAF (54  $\mu\text{L}$ , 0.106 mmol, 2.0 equiv) in THF (2.0 M) was added, and the reaction mixture was stirred for 3 h, quenched with  $\text{H}_2\text{O}$  (20 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (5 x 20 mL), dried over  $\text{MgSO}_4$ , and purified by flash chromatography (10 to 20% EtOAc in hexanes) to provide tetracycle **18** (10.4 mg, 0.032 mmol, 60% yield) as a yellow solid. Crystals suitable for X-ray analysis were obtained by crystallization from  $\text{Et}_2\text{O}$ /heptanes at ambient temperature: mp 150–153 °C ( $\text{Et}_2\text{O}$ /heptane);  $R_f$  0.39 (30% acetone in hexanes);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.86 (s, 1H), 6.18 (d,  $J = 10.3$  Hz, 1H), 6.14 (d,  $J = 6.4$  Hz, 1H), 5.69 (d,  $J = 10.3$  Hz, 1H), 5.54 (s, 1H), 4.33 (d,  $J = 7.6$  Hz, 1H), 3.86 (s,

2H), 3.63 (dd,  $J = 19.9, 7.0$  Hz, 3.49 (d,  $J = 7.3$  Hz, 1H), 3.16 (d,  $J = 19.6$  Hz, 1H), 2.24 (s, 3H), 1.26 (s, 3H), 1.20 (s, 3H), 0.76 (s, 3H) ;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  144.3, 143.4, 143.1 138.8, 134.1, 131.4, 125.8, 123.9, 121.8, 120.7, 80.1, 78.1, 77.2, 60.9, 48.7, 46.6, 39.0, 28.9, 25.0, 20.6, 17.1, 15.8; IR (Neat film NaCl) 3368, 2961, 2925, 1871, 1485, 1462, 1421, 1320, 1211, 1070, 907, 733  $\text{cm}^{-1}$ ; MS (FAB+)  $[\text{M}+\text{H}-\text{H}_2]^+$   $m/z$  calc'd for  $[\text{C}_{21}\text{H}_{25}\text{O}_3]^+$ : 325.1799, found 325.1804.