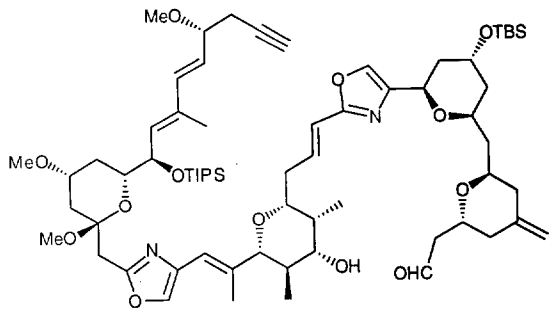
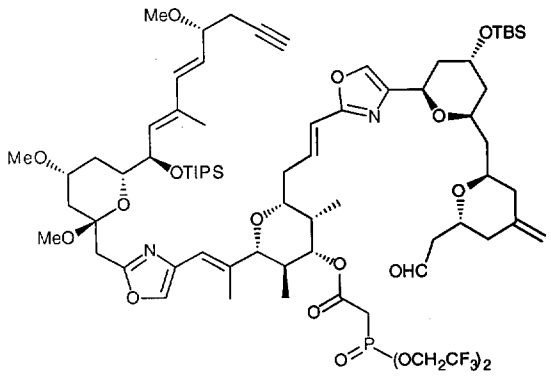
2.30 (dd, J = 13.2, 4.6 Hz, 1 H), 2.22 (m, 2 H), 2.12 (s, 3 H), 2.12 (m, 1 H), 2.01 (m, 3 H), 1.90 (m, 2 H), 1.81 (s, 3 H), 1.76 (m, 1 H), 1.63 (d, J = 11.4 Hz, 1 H), 1.59 (m, 1 H), 1.49 (m, 3 H), 1.26 (m, 21 H), 1.12 (d, J = 6.8 Hz, 3 H), 1.07 (s, 9 H), 1.02 (d, J = 6.4 Hz, 3 H), 0.14 (s, 6 H); ^{13}C NMR (125 MHz, , C_6D_6) δ 199.5, 161.2, 159.6, 150.4, 149.8, 144.3, 141.6, 14.5, 138.6, 138.2, 137.1, 136.1, 135.8, 134.4, 134.0, 133.2, 131.8, 131.0, 130.1, 120.1, 119.0, 118.8, 112.4, 112.3, 110.8, 100.5, 89.4, 83.3, 81.0, 807, 77.5, 74.4, 73.8, 72.3, 70.3, 69.9, 69.5, 69.3, 68.5, 67.4, 65.3, 56.3, 55.8, 55.7, 55.2, 47.9, 47.7, 40.1, 39.7, 39.5, 39.4, 39.3, 39.1, 36.6, 35.9, 33.8, 31.9, 26.1, 22.9, 18.3, 18.2, 14.3, 13.9, 13.7, 12.8, 6.0, -4.8, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 1353.8139 [$(M+H)^+$; calcd for $C_{76}H_{117}O_{15}N_2Si_2$: 1353.7993].



(+)-116

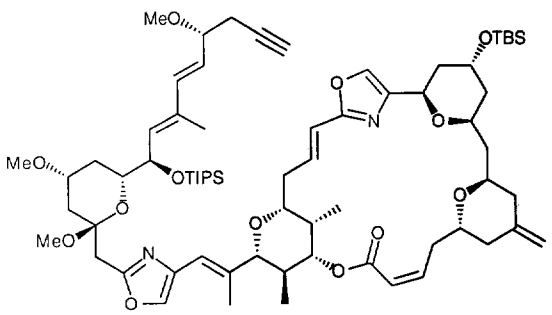
To a solution of dimethoxybenzylether-aldehyde (9.1 mg, 0.0067 mmol) in methylene chloride (2 mL) and pH = 7 Buffer (0.20 mL) was added DDQ (3.4 mg, 2.2 equiv). The reaction mixture was stirred for 50 min and poured into saturated $NaHCO_3$ (10 mL). The aqueous solution was extracted with methylene chloride (3 x 10 mL); the combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:2 then 1:1) as eluant, gave (+)-**116** (7.8 mg, 98% yield): $[\alpha]_D^{20}$ +23.3 (*c* 0.30, $CHCl_3$); IR (neat) 3441 (w), 2936 (s), 2338 (w), 1726 (s), 1090 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 9.60 (dd, J = 2.9, 1.8 Hz, 1 H), 7.46 (s, 1 H), 7.21 (s, 1 H), 6.82 (ddd, J = 15.8, 8.3, 6.3 Hz, 1 H), 6.42 (d, J = 16.0 Hz, 1 H), 6.38 (s, 1 H), 6.38 (d, J = 15.8 Hz, 1 H), 5.71 (dd, J = 15.7 Hz, 1 H), 5.63 (d, J = 8.9 Hz, 1 H), 5.25 (d, J = 11.1 Hz, 1 H), 4.82 (dd, J = 8.9, 6.1 Hz, 1 H), 4.78 (s, 1 H), 4.74 (s, 1 H), 4.27 (m, 1 H), 4.14 (m, 1 H), 4.11 (m, 2 H), 3.84 (ddd, J = 12.0, 6.1, 1.9 Hz, 1 H), 3.77 (m, 1 H), 3.71 (m, 1 H),

3.47 (s, 3 H), 3.40 (d, J = 14.8 Hz, 1 H), 3.34 (d, J = 10.1 Hz, 1 H), 3.28 (dt, J = 7.0, 7.0, 1.5 Hz, 1 H), 3.16 (s, 3 H), 3.15 (s, 3 H), 3.07 (m, 1 H), 3.01 (d, J = 14.8 Hz, 1 H), 2.64 (ddd, J = 12.6, 4.5, 1.4 Hz, 1 H), 2.54 (dd, J = 5.7, 2.7 Hz, 1 H), 2.51 (dd, J = 5.6, 2.6 Hz, 1 H), 2.44 (m, 1 H), 2.43 (m, 2 H), 2.37 (dd, J = 6.9, 2.7 Hz, 1 H), 2.30 (dd, J = 13.2, 4.5 Hz,1 H), 2.23 (m, 2 H), 2.13 (m, 2 H), 2.11 (s, 3 H), 2.00 (m,1 H), 1.98 (m, 1 H). 1.93, m, 1 H), 1.82 (s, 3 H), 1.75 (m, 1 H), 1.72 (m, 1 H), 1.66 (m, 2 H), 1.60 (m, 1 H), 1.56 (m, 1 H), 1.49 (dt, J = 11.2, 11.2, 2.3 Hz, 1 H), 1.40 (q, J = 11.6 Hz, 1 H), 1.13 (m, 21 H), 0.98 (s, 9 H), 0.85 (d, J = 6.8 Hz, 3 H), 0.75 (d, J = 6.5 Hz, 3 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, C_6D_6) δ 199.5, 161.2, 159.5, 144.6, 141.7, 138.9, 138.3, 137.2, 136.5 135.6, 134.5, 134.1, 133.3, 130.7, 119.0, 118.7, 110.8, 100.5, 89.2, 81.0, 80.7, 77.7, 76.5, 74.4, 73.8, 72.3, 70.3, 69.5, 69.3, 68.4, 67.4, 65.4, 56.3, 55.3, 47.9, 47.7, 40.1, 39.8, 39.7, 39.5, 39.4, 39.3, 39.1, 38.4, 36.3, 36.0, 34.7, 32.7, 26.2, 18.3, 14.3, 13.7, 13.5, 12.8, 5.6, -4.8, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 1225.7159 [$(M+Na)^+$; calcd for $C_{67}H_{105}O_{13}N_2Si_2Na$: 1225.7131].



To a solution of alcohol (+)-**116** (4.0 mg, 0.0033 mmol) in methylene chloride (1 mL) was added acid **85** (12 mg, 12 equiv) in methylene chloride (1 mL), EDCI·MeI (10 mg, 10 equiv) and HOBT (catalytic amount). The reaction mixture was stirred for 30 min and added directly to silica gel. Flash chromatography, using EtOAc-hexanes (1:1) as eluant, gave the seco-macrocyle (4.2 mg, 86% yield): $[\alpha]_D^{20}$ +17.0 (*c* 0.30, $CHCl_3$); IR (neat) 2971 (s), 2853, (s), 2359 (w), 1731 (s), 1729 (s), 1260 (s), 1090 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 9.60 (dd, J = 2.9, 1.6 Hz, 1 H), 7.43 (s, 1 H), 7.20 (s, 1 H), 6.81 (ddd, J = 14.7, 8.2, 6.4 Hz, 1 H), 6.42 (s, J = 16.0 Hz, 1 H), 6.36 (d, J = 15.8 Hz, 1 H), 6.33 (s, 1 H), 5.71 (dd, J =

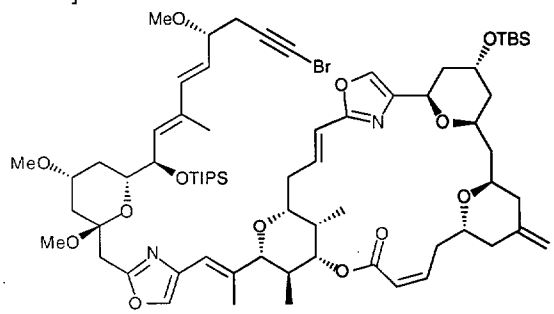
15.6, 7.4 Hz, 1 H), 5.63 (d, J = 8.8 Hz, 1 H), 5.23 (d, J = 10.5 Hz, 1 H), 4.82 (m, 2 H), 4.77 (s, 1 H), 4.74 (s, 1 H), 4.27 (m, 1 H), 4.10 (m, 7 H), 3.84 (ddd, J = 14.0, 6.1, 1.9 Hz, 1 H), 3.78 (m, 1 H), 3.73 (q, J = 6.5 Hz, 1 H), 3.47 (s, 3 H), 3.40 (d, J = 14.9 Hz, 1 H), 3.37 (d, J = 11.7 Hz, 1 H), 3.30 (dt, J = 5.9, 5.9, 1.9 Hz, 1 H), 3.17 (s, 3 H), 3.15 (s, 3 H), 3.02 (d, J = 14.8 Hz, 1 H), 2.66 (d, J = 21.3 Hz, 2 H), 2.63 (m,1 H), 2.54 (dd, J = 5.7, 2.7 Hz, 1 H), 2.50 (dd, J = 5.5, 2.7 Hz, 1 H), 2.45 (dd, J = 8.2, 2.9 Hz, 1 H), 2.41 (m, 2 H), 2.39 (m, 1 H), 2.32 (dd, J = 13.3, 4.5 Hz, 1 H), 2.23 (m, 2 H), 2.13 (s, 3 H), 2.10 (m, 1 H), 2.01 (m, 4 H), 1.93 (m, 2 H), 1.82 (s, 3 H), 1.78 (m, 2 H), 1.64 (m, 1 H), 1.58 (t, J = 6.0 Hz, 1 H), 1.56 (t, J = 6.0 Hz, 1 H), 1.46 (dt, J = 11.2, 11.2, 2.5 Hz, 1 H), 1.41 (q, J = 11.6 Hz, 1 H), 1.24 (m, 21 H), 1.07 (s, 9 H), 0.99 (d, J = 7.2 Hz, 3 H), 0.81 (d, J = 6.5 Hz, 3 H), 0.15 (s, 6 H) ; ^{13}C NMR (125 MHz, C_6D_6) δ 199.5, 161.0, 159.7, 144.6, 141.7, 139.6, 138.8, 137.2, 135.8, 134.5, 134.2, 133.3, 119.3, 119.2, 110.8, 100.5, 88.8, 80.9, 80.8, 80.7, 77.1, 74.4, 73.8, 72.3, 70.3, 69.5, 69.3, 68.6, 67.4, 65.4, 62.4, 62.2, 56.3, 55.3, 47.9, 47.7, 40.1, 39.7, 39.5, 39.4, 39.3, 39.1, 36.2, 36.0, 34.5, 33.4, 32.7, 32.5, 26.1, 18.3, 18.2, 14.1, 13.7, 13.3, 12.8, 6.2, -4.8, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 1511.6891 [$(M+Na)^+$; calcd for $C_{73}H_{111}O_{17}N_2Si_2F_6PNa$ 1511.6891].



(+)-117

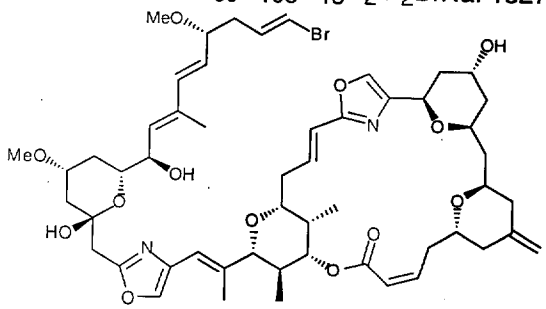
To a solution of toluene (6 mL) was added 18-crown-6 (100 mg, 56 equiv) and K_2CO_3 (12 mg, 12 equiv) and the reaction mixture was stirred for 4 h. The aldehyde (10.8 mg, 0.0073 mmol) in toluene (4 mL) was added *via* cannula. The reaction mixture was stirred for 1 h, poured into brine (10 mL), and extracted with EtOAc (3 x 10 ml). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification *via* preparative TLC using Et_2O-hexanes (4:1) gave major *Z*-isomer (+)-**117** (6.7 mg,

77 %, 4:1 dr): $[\alpha]_D^{20}$ +3.0 (*c* 0.3, neat); IR ($CHCl_3$) 2934 (s), 2864 (s), 2364 (w), 1720 (s), 1092 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.15 (s, 1 H), 6.94 (s, 1 H), 6.89 (ddd, *J*=16.1, 9.2, 7.3 Hz, 1 H), 6.35 (s, 1 H), 6.28 (d, *J* = 15.7 Hz, 1 H), 6.18 (d, *J* = 15.9 Hz, 1 H), 5.78 (dd, *J* = 11.2, 2.4 Hz, 1 H), 5.62 (dd, *J* = 15.7, 7.4 Hz, 1 H), 5.54 (d, *J* = 8.9 Hz, 1 H), 5.45 (dt, *J* = 10.6, 3.1, 3.1 Hz, 1 H), 5.17 (br s, 1 H), 4.94 (d, *J* = 11.4 Hz, 1 H), 4.73 (m, 2 H), 4.61 (dd, *J* = 11.2, 4.4 Hz, 1 H), 4.48 (m, 1 H), 4.23 (dt, *J* = 10.3, 3.1, 3.1 Hz, 1 H), 4.06 (m, 1 H), 4.02 (m, 1 H), 3.95 (m, 1 H), 3.75 (ddd, *J* = 11.9, 5.9, 1.9 Hz, 1 H), 3.69 (m, 1 H), 3.62 (q, *J* = 6.3 Hz, 1 H), 3.43 (d, *J* = 10.1 Hz, 1 H), 3.39 (s, 3 H), 3.31 (d, *J* = 14.7 Hz, 1 H), 3.08 (s, 3 H), 3.06 (s, 3 H), 3.03 (br d, *J* = 11.8 Hz, 1 H), 2.93 (d, *J* = 14.8 Hz, 1 H), 2.64 (m, 1 H), 2.55 (dd, *J* = 12.7, 4.8 Hz, 1 H), 2.45 (dd, *J* = 5.6, 3.0 Hz, 1 H), 2.42 (m, 3 H), 2.32 (dd, *J* = 7.1, 2.6 Hz, 1 H), 2.28 (dd, *J* = 6.7, 2.6 Hz, 1 H), 2.15 (m, 1 H), 2.09 (s, 3 H), 2.07 (m, 1 H), 1.98 (m, 1 H), 1.81 (t, *J* =2.6 Hz, 1 H), 1.73 (s, 3 H), 1.65 (m, 5 H), 1.47 (dd, *J* = 13.0, 4.8 Hz, 1 H), 1.34 (m, 4 H), 1.15 (m, 21 H), 1.03 (d, *J* = 7.1 Hz, 3 H), 0.92 (s, 9 H), 0.75 (d, *J* = 6.7 Hz, 3 H), 0.01 (s, 3 H), -0.02 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 168.4, 161.4, 159.7, 145.2, 143.5, 142.6, 139.7, 138.7, 138.0, 137.3, 135.4, 134.9, 134.2, 134.1, 121.1, 119.8, 119.1, 110.1, 100.5, 89.7, 81.0, 80.7, 79.9, 78.4, 74.4, 73.8, 73.4, 72.3, 70.3, 69.6, 68.9, 67.3, 65.6, 56.3, 55.2, 48.2, 42.3, 40.4, 40.3, 39.9, 37.8, 36.2, 36.2, 34.8, 32.9, 32.9, 32.3, 31.0, 26.2, 26.1, 18.4, 18.3, 14.3, 13.8, 13.4, 12.9, 6.3, -4.8, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 1249.6988 [$(M+Na)^+$; calcd for $C_{69}H_{106}O_{13}N_2Si_2Na$: 1249.7131].



To a solution of alkyne (+)-**117** (7.8 mg, 6.35 x 10^{-3} mmol) in acetone (2.5 mL) was added silver nitrate (1 mg) and *N*-bromosuccinimide (4 mg, 4 equiv). The reaction mixture was stirred for 1 h, poured into saturated $NaHCO_3$ (5 mL) and saturated sodium thiosulfate (5 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash

chromatography, using EtOAc-hexanes (1:2) as eluant, gave the alkynyl bromide (7.8 mg, 95% yield) as an oil: $[\alpha]_D^{20}$ +5.0 (*c* 0.20, methylene chloride); IR (neat) 2929 (s), 2859 (s), 1719 (s), 1187 (s), 1098 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.35 (s, 1 H), 6.95 (s, 1 H), 6.89 (ddd, *J* = 16.4, 12.0, 9.3 Hz, 1 H), 6.35 (s, 1 H), 6.22 (d, *J* = 15.8 Hz, 1 H), 6.19 (d, *J* = 16.0 Hz, 1 H), 5.78 (dd, *J* = 11.2, 2.9 Hz, 1 H), 5.54 (m, 2 H), 5.45 (dt, *J* = 10.7, 10.7, 2.7 Hz, 1 H), 5.17 (s, 1 H), 4.94 (d, *J* = 11.1, Hz, 1 H), 4.74 (s, 1 H), 4.73 (m, 1 H), 4.61 (dd, *J* = 11.1, 4.3 Hz, 1 H), 4.38 (m, 1 H), 4.23 (m, 1 H), 4.08 (m, 1 H), 4.02 (m, 1 H), 3.94 (m, 1 H), 3.75 (ddd, *J* = 12.1, 7.8, 1.8 Hz, 1 H), 3.68 (m, 1 H), 3.53 (dd, *J* = 13.2, 6.6 Hz, 1 H), 3.43 (d, *J* = 10.1 Hz, 1 H), 3.39 (s, 3 H), 3.32 (d, *J* = 14.8 Hz, 1 H), 3.07 (s, 3 H), 3.03 (s, 3 H), 2.93 (d, *J* = 14.8 Hz, 1 H), 2.66 (m, 1 H),2.55 (dd, *J* = 13.2 Hz, 1 H), 2.38 (m, 5 H), 2.24 (dd, *J* = 16.6, 6.8 Hz, 1 H), 2.15 (m, 1 H), 2.08 (s, 3 H), 2.07 (m, 1 H), 1.98 (m, 1 H), 1.70 (s, 3 H), 1.64 (m, 5 H), 1.48 (d, *J* = 13.4 Hz, 1 H), 1.33 (m, 5 H), 1.16 (m, 21 H), 1.03 (d, *J* = 6.9 Hz, 3 H), 0.92 (s, 9 H), 0.76 (d, *J* = 6.5 Hz, 4 H), 0.09 (s, 3 H), -0.01 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 165.1, 161.1, 159.4, 144.9, 143.2, 142.3, 138.7, 137.6, 137.1, 136.1, 134.1, 133.9, 133.2, 133.1, 120.8, 119.6, 118.8, 109.8, 100.2, 89.4, 80.2, 79.6, 78.2, 77.1, 74.1, 73.1, 72.0, 69.3, 68.6, 67.1, 65.3, 56.0, 55.0, 47.7, 47.6, 41.8, 39.9, 39.8, 39.7, 39.3, 37.3, 35.7, 35.7, 34.3, 32.5, 31.8, 30.5, 29.9, 26.9, 25.7, 18.0, 17.9, 13.9, 13.4, 13.1, 12.7, 6.0, -5.1, -5.1; high resolution mass spectrum (CI, NH_3) *m/z* 1327.6178 [$(M+Na)^+$; calcd for $C_{69}H_{105}O_{13}N_2Si_2BrNa$: 1327.6236].

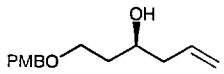


(+)-1

To a solution of the alkynyl bromide (3.2 mg, 2.45 x 10^{-3} mmol) in THF (2.5 mL) was added $Cl_2Pd(PPh_3)_2$ (0.02 equiv), and tributyltin hydride (3 x 10 μL). The reaction mixture was stirred for 30 min, poured into saturated $NaHCO_3$, extracted with methylene chloride (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The product was filtered through a plug of silica, using hexanes-EtOAc (10:1 then

3:1) as eluent, and concentrated. The vinylstannane was dissolved in acetonitrile (2 mL) and *N*-bromosuccinimide (2 mg) was added at 0 °C. The reaction mixture was stirred for 30 min poured into saturated $NaHCO_3$ (5 mL) and saturated sodium thiosulfate (5 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The product was filtered through a plug of silica, using EtOAc-hexanes (1:1) as eluant, and concentrated *in vacuo*. Protected phorboxazole A was stirred in THF (1.8 mL) and 6% HCl (0.72 mL). The reaction mixture was stirred for 80 h, poured into saturated $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc as eluant, gave (+)-**1** (1.5 mg, 60% yield, 3 steps) as a 4:1 mixture. The mixture was separated using a reverse phase Zorbax C_{18} column, eluting with CH_3CN/water (55/45) to give (0.45 mg) (+)-**1**: $[\alpha]_D^{20}$ +48 (*c* 0.12, $CHCl_3$); ^1H, COSY, ROSY consistent with natural phorboxazole A; high resolution mass spectrum (CI, NH_3) *m/z* 1045.3972 [$(M+Na)^+$; calcd for $C_{53}H_{71}O_{13}N_2BrNa$: 1045.4037].

Compounds Not On the Linear Sequence



To a solution of (–)-β-methoxy isocampheylborane (9.64 g, 1.1 equiv) in Et_2O (60 mL) at 0° C was added allyl magnesium bromide (29.1 mL, 1.0 M in Et_2O, 1.05 equiv). The reaction mixture was stirred for 1 h, filtered under argon, rinsed with Et_2O (100 mL), and cooled to –98 °C. Aldehyde **18** (5.34 g, 27.7 mmol) in Et_2O (100 mL) was then added *via* cannula over 1 h. The reaction was stirred for 1 h, followed by addition of 3N NaOH (10 mL) and 30% HOOH (5 mL), then heated at reflux for 2 h. The reaction mixture was poured into water (200 mL), extracted with Et_2O (2 x 200 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4 then 1:2) as eluant, gave the corresponding homoallylic alcohol (5.66 g, 91% yield) as an oil: $[\alpha]_D^{20}$ =1.0 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3500 (w), 2960 (s), 1610 (s), 1250 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 6.7, 1.9 Hz, 1 H), 6.85 (dd, *J* = 6.6, 2.1 Hz, 1 H), 5.8 (m, 1 H), 5.09 (dd, *J* = 9.8, 1.5 Hz, 1 H), 5.07 (dd, *J* = 6.9, 1.4 Hz, 1 H), 4.43 (s, 2 H), 3.83 (m, 1 H), 3.78 (s, 3 H), 3.66 (ddd, *J* = 9.4, 5.5, 3.9 Hz, 1 H), 3.59 (ddd, *J* = 9.4, 7.1, 5.6 Hz, 1 H), 2.83 (s, 1 H), 2.23 (m, 2 H), 1.72 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 134.9, 130.1, 129.3, 117.5, 113.9,

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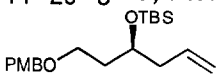
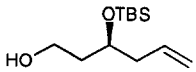
73.0, 70.4, 68.6, 55.3, 41.9, 35.9; high resolution mass spectrum (CI, NH_3) *m/z* 236.1417 [$(M+H)^+$; calcd for $C_{14}H_{21}O_3$: 236.1412], Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.27; H, 8.68.

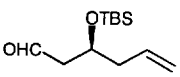


(+)-19

Silyl Ether (+)-19: To a solution of the primary alcohol (5.13 g, 22.8 mmol) in DMF (57 mL, 0.4 M) was added imidazole (3.88 g, 2.5 equiv) and *t*-butyldimethylsilylchloride (4.13 g, 1.2 equiv). After stirring for 3 h, the reaction mixture was poured into water (100 mL), and extracted with Et_2O (100 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:20) as eluant, gave (+)-**19** (7.67 g, 96% yield) as an oil: $[\alpha]_D^{20}$ 14.5 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3010 (s), 2860 (s), 1250(s). 835 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 9.5, 2.9 Hz, 2 H), 6.86 (dd, *J* = 9.5, 2.8 Hz, 2 H), 5.78 (m, 1 H), 5.02 (dd, *J* = 5.1, 1.4 Hz, 1 H), 4.99 (dd, *J* = 7.4, 1.2 Hz, 1 H), 4.42 (d, *J* = 11.5 Hz, 1 H), 4.37 (d, *J* = 11.5 Hz, 1 H), 3.86 (m, 1 H), 3.79 (s, 3 H), 3.50 (dt, *J* = 6.9, 1.0, 1.0 Hz, 2 H), 2.21 (m, 2 H), 1.75 (m, 1 H), 1.67 (m, 1 H), 0.87 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 135.0, 130.7, 129.3, 116.9, 113.8, 72.6, 69.0, 66.8, 55.3, 42.3, 36.7, 25.9, 18.1, -4.3, -4.7; high resolution mass spectrum (CI, NH_3) *m/z* 349.2199 [$(M+H)^+$; calcd for $C_{20}H_{39}O_3Si$: 349.2199], Anal. Calcd for $C_{20}H_{34}O_3Si$: C, 68.52; H, 9.78. Found: C, 68.91; H, 10.01.



To a solution of *p*-methoxybenzyl ether (+)-**19** (7.49 g, 21.4 mmol) in methylene chloride (100 mL) was added pH = 7 buffer (7 mL) and DDQ (5.34 g, 1.1 equiv). After 30 min, the reaction mixture was poured into saturated $NaHCO_3$ (100 mL), and extracted with methylene chloride. The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:10) as eluant, gave the primary alcohol (4.62 g, 94% yield) as an oil: $[\alpha]_D^{20}$ +15.2 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3500 (w), 2960 (s), 1260 (s), 1070 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.74 (dddd, *J* = 14.6, 12.3, 8.6, 4.5 Hz, 1 H), 5.05 (m, 2 H), 3.95 (ddd, *J* = 12.7, 8.4, 3.8 Hz, 1 H), 3.80 (ddd, *J* = 10.8, 5.6, 5.6 Hz, 1 H), 3.70 (ddd, *J* = 10.8, 5.6, 5.6 Hz, 1 H), 2.28 (m, 2 H), 2.20 (bs, 1 H), 1.79 (dddd, *J* = 14.6, 12.3, 8.6, 4.5 Hz, 1 H), 1.65 (dddd, *J* = 14.1, 10.4, 5.9, 4.8 Hz, 1 H), 0.88 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5, 117.3, 71.2, 60.2, 41.7, 37.7, 25.8, 17.9, -4.4, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 231.1786 [$(M+H)^+$; calcd for $C_{12}H_{27}O_2Si$: 231.1780], Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.23; H, 11.66.



(+)-20

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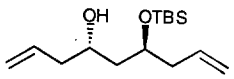
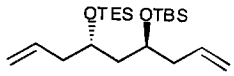
Aldehyde (+)-20: To a solution of the primary alcohol (4.53 g, 19.7 mmol) in methylene chloride (69 mL) was added PCC (5.39 g, 1.27 equiv). After stirring for 2 h, the reaction mixture was filtered through celite (500 g) and concentrated *in vacuo*. Flash chromatography, using Et_2O-pentane (1:20) as eluant, gave (+)-**20** (3.51 g, 78% yield) as an oil: $[\alpha]_D^{20}$ +11.1 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2940 (s), 1730 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.78 (dd, *J* = 2.4, 2.3 Hz, 1 H), 5.75 (m, 1 H), 5.07 (m, 2 H), 4.24 (m, 1 H), 2.51 (ddd, *J* = 6.6, 4.4, 2.3 Hz, 1 H), 2.28 (m, 1 H), 0.85 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 133.8, 118.1, 67.8, 50.4, 42.3, 25.7, 18.0, -4.4, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 229.1618 [$(M+H)^+$; calcd for $C_{12}H_{25}O_2Si$: 229.1623].



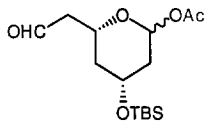
To a solution of (–)-β-methoxyisocampheylborane (5.33 g, 1.1 equiv) in Et_2O (100 mL) was added allyl magnesium bromide (16 mL, 1.0 M in Et_2O, 1.05 equiv); the reaction mixture was stirred for 1 h and cooled to –78° C. Aldehyde (+)-**20** (3.50 g, 15.3 mmol) in Et_2O (50 mL) was added *via* cannula, and the reaction was stirred for 1h. Following addition of 3N NaOH (10 mL) and hydrogen peroxide (5 mL), the reaction was heated at reflux for 2 h. The reaction mixture was poured into brine (50 mL), extracted with EtOAc (3 x 50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave the corresponding homoallylic alcohol (4.06 g, 98% yield, 10 to 1 de) as an oil: $[\alpha]_D^{20}$ +14.4 (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 3490 (w), 2940 (s), 1075 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.79 (m, 2 H), 5.08 (m, 4 H), 4.01 (m, 2 H), 3.05 (d, *J* = 2.3 Hz, 1 H), 2.31 (m, 2 H), 2.20 (m, 2 H), 0.90 (s, 9 H), 0.80 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.9, 134.6, 117.4, 70.9, 67.5, 42.4, 41.3, 41.1, 25.8, 25.6, 18.0, -4.5, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 271.2088 [$(M+H)^+$; calcd for $C_{15}H_{31}O_2Si$: 271.2093].



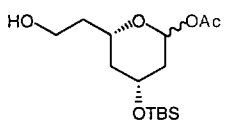
(+)-**21**

Silyl Ether (+)-21: To a -78 °C solution of the secondary alcohol (528 mg, 1.95 mmol) and 2,6-lutidine (0.447 mL, 2.5 equiv) in methylene chloride (19 mL) was added TESOTf (0.672 mL, 1.2 equiv). The reaction was stirred for 1 h, then poured into saturated $NaHCO_3$ (25 mL), and extracted with methylene chloride (3 x 25 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:99) as eluant, gave (+)-**21** (750 mg, 100% yield) as an oil: $[\alpha]_D^{20}$ +17.9 (*c* $CHCl_3$, 1.17); IR ($CHCl_3$) 2960 (s), 1070 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.79 (m, 2 H), 5.04 (m, 4 H), 3.80 (m, 2 H), 2.22 (m, 4 H), 1.59 (m, 2 H), 0.94 (t, *J* = 8.0 Hz, 9 H), 0.86 (s, 9 H), 0.58 (qt, *J* = 15.8, 8.0 Hz, 6 H), 0.04 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.0, 135.0, 116.9, 116.8, 69.8, 69.7, 44.8, 42.5, 42.4, 25.9, 18.1, 6.9, 5.3, -4.0, -4.3; high resolution mass spectrum (CI, NH_3) *m/z* 385.2963

[$(M+H)^+$; calcd for $C_{21}H_{45}O_2Si_2$: 385.2958]. Anal. Calcd for $C_{21}H_{44}O_2Si_2$: C, 65.56; H, 11.53. Found: C, 65.82; H, 11.71.

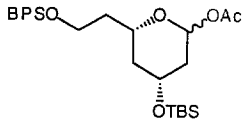


Aldehyde 22. Through a -78 °C solution of alkene (+)-**21** (2.13 g, 5.52 mmol) in methylene chloride (37 mL) was bubbled ozone until a faint blue color persisted. PPh_3 (2.90 g, 2 equiv) was then added and the reaction mixture was stirred overnight then concentrated *in vacuo*. The resultant bisaldehyde was then stirred in THF (110 mL), acetic acid (50 mL), and water (30 mL). After 8 h, the reaction was neutralized with saturated $NaHCO_3$, poured into brine (100 mL), and extracted with EtOAc (3 x 100 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The product was dissolved in methylene chloride (40 mL) followed by the addition of pyridine (4.04 mL, 50 mmol) and acetic anhydride (3.4 mL, 33 mmol). The reaction mixture was stirred for 12 h, poured into saturated $NaHCO_3$ (50 mL), extracted with methylene chloride (3 x 50 mL). The organics were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4) as eluant, gave a mixture (2:1, equatorial:axial) of acetate isomers (956 mg, 57% 3-step yield) as a colorless oil: IR ($CHCl_3$) 3020 (s), 1750 (s), 1735 (s), 1120 (s) cm^{-1}; major isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, J = 1.8 Hz, 1 H), 5.62 (dd, J = 10.2, 2.2 Hz,1 H), 3.97 (m, 1 H), 3.86 (m, 1 H), 2.70 (ddd, J = 16.9, 7.2, 2.1 Hz, 1 H), 2.64 (m, 1 H), 2.07 (s, 3 H), 2.04 (m, 1 H), 1.94 (m, 1 H), 1.5 (m, 1 H), 1.37 (m, 1 H), 0.86 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 169.1, 92.3, 68.2, 66.7, 48.8, 40.3, 39.8, 25.7, 21.1, -4.6, -4.6; minor isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 9.72 (t, J = 1.7 Hz, 1 H), 6.18 (d, J = 2.6 Hz, 1 H), 4.33 (m, 1 H), 4.08 (m, 1 H), 2.66 (m, 1 H), 2.52 (m, 1 H), 2.07 (s, 3 H), 1.97 (m, 1 H), 1.64 (m, 1 H), 1.50 (m, 1 H), 1.37 (m, 1 H), 0.86 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.0, 169.8, 92.7, 65.8, 63.7, 49.0, 40.7, 38.3, 25.7, 21.1, -4.6, -4.6; high resolution mass spectrum (CI, NH_3) *m/z* 334.2055 [$(M+NH_4)^+$; calcd for $C_{15}H_{32}O_5NSi$: 334.2049]. Anal. Calcd for $C_{15}H_{28}O_5Si$: C, 56.93; H, 8.91. Found: C, 57.15; H, 9.24.

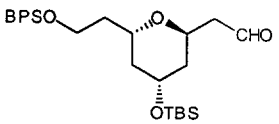


To a -10 °C solution of aldehyde **22** (1.343 g, 4.23 mmol) in ethanol (70 mL) was added $NaBH_4$ (160 mg, 1 equiv). The reaction was stirred for 10 min and quenched with saturated aqueous NH_4Cl (20 mL), poured into brine (30 mL), and extracted with methylene chloride (3 x 30 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:2) as eluant, gave the corresponding primary alcohols (1.30 g, 96% yield) as an oil: IR ($CHCl_3$) 3540 (w), 2960 (s). 1750 (s), 1045 (s) cm^{-1}; major isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 5.54 (dd, J = 10.2,

2.2 Hz, 1 H), 3.86 (m, 1 H), 3.75 (m, 2 H), 3.68 (m, 1 H), 2.16 (bs, 1 H), 2.07 (s, 3 H), 2.02 (m, 1 H), 1.78 (m, 2 H), 1.65 (m, 1 H), 1.48 (m, 1 H), 1.35 (m, 1 H), 0.86 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 92.6, 72.0, 66.9, 60.2, 40.7, 39.9, 37.4, 25.7, 21.1, -4.6, -4.6; minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (d, J = 2.6 Hz, 1 H), 4.06 (m, 1 H), 4.02 (m, 1 H), 3.75 (m, 2 H), 2.16 (bs, 1 H), 2.05 (s, 3 H), 1.97 (m, 1 H), 1.93 (m, 1 H), 1.79 (m, 2 H), 1.65 (m, 1 H), 1.48 (m, 1 H), 0.86 (s, 9 H), 0.04 (s, 6 H); high resolution mass spectrum (CI, NH_3) *m/z* 336.1212 [$(M+NH_4)^+$; calcd for $C_{15}H_{34}O_5NSi$: 336.1205]. Anal. Calcd for $C_{15}H_{30}O_5Si$: C, 56.51; H, 9.49. Found: C, 56.16; H, 9.79.

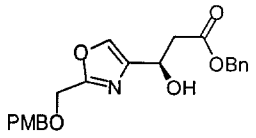


To a solution of the primary alcohol (3.78g, 11.8 mmol), imidazole (1.6 g, 2 equiv) and BPS-Cl (4.25 g, 1.3 equiv) in DMF (49 mL) was added DMAP (289 mg, 0.2 equiv). The reaction was stirred 2 h and was then poured into saturated $NaHCO_3$ (30 mL), and extracted with Et_2O (3 x 40 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave the primary BPS ether (5.90 g, 90% yield) as a colorless oil: IR ($CHCl_3$) 3020 (s), 2960 (s), 1745 (s), 1110 (s) cm^{-1}; major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.37 (m, 6 H), 5.61 (dd, J = 10.1, 2.2 Hz, 1 H), 3.85 (m, 2 H), 3.78 (m, 1 H), 3.67 (m, 1 H), 2.09 (s, 3 H), 2.05 (m, 1 H), 1.82 (m, 1 H), 1.74 (m, 1 H), 1.52 (m, 1 H), 1.33 (m, 2 H), 1.03 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 135.5, 133.9, 129.6, 127.6, 92.8, 70.2, 67.1, 60.0, 40.7, 40.3, 38.3, 26.8, 25.8, 21.2, 19.2, -4.5, -4.6; minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.37 (m, 6 H), 6.24 (d, J = 2.4 Hz, 1 H), 4.11 (m, 1 H), 4.08 (m, 1 H), 3.78 (m, 1 H), 3.67 (m, 1 H), 2.00 (s, 3 H), 1.97 (m, 2 H), 1.67 (m, 1 H), 1.46 (m, 1 H), 1.33 (m, 2 H), 1.03(s, 9 H), 0.87 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 135.6, 133.8, 129.6, 127.6, 93.2, 67.4, 64.3, 59.8, 41.3, 38.8, 38.6, 26.8, 25.8, 21.2, 19.2, -4.5, -4.6; high resolution mass spectrum (CI, NH_3) *m/z* 579.2918 [$(M+Na)^+$; calcd for $C_{31}H_{48}O_5Si_2Na$: 579.2938].



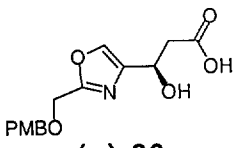
Aldehyde (–)-24: To a 0 °C solution of the acetal (3.4 g, 6.11 mmol) and enol ether **23** (1.45 g, 1.5 equiv) in methylene chloride (20 mL) was added $ZnCl_2$ (11.9 mL, 1.0 M in Et_2O, 2 equiv). The reaction was stirred for 5 min, quenched with saturated $NaHCO_3$ (25 mL), and extracted with methylene chloride (3 x 25 mL). The organics were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:12) as eluant, gave (–)-**24** (2.35 g, 72% yield) as a colorless oil: $[\alpha]_D^{20}$ -22.1 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2930 (s), 1725 (s), 1110 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (dd, J = 2.7, 2.2 Hz,

1 H), 7.63 (m, 4 H), 7.35 (m, 6 H), 4.47 (m, 1 H), 4.00 (m, 1 H), 3.95 (m, 1 H), 3.74 (m, 1 H), 3.68 (m, 1 H), 2.62 (ddd, J = 15.9, 8.6, 2.8 Hz, 1 H), 2.37 (ddd, J = 15.9, 5.3, 2.0 Hz, 1 H), 2.10 (m, 1 H), 1.86 (ddd, J = 13.3, 8.2, 4.2 Hz, 1 H), 1.61 (m, 2 H), 1.38 (ddd, J =13.5, 8.0, 6.8 Hz, 1 H), 1.03 (s, 9 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 135.6, 133.9, 129.6, 127.6, 67.6, 64.8, 64.1, 60.8, 47.6, 38.7, 38.4, 37.4, 26.9, 25.8, 19.2, 18.0, -4.8, -4.8; high resolution mass spectrum (CI, NH_3) *m/z* 558.3417 [$(M+NH_4)^+$; calcd for $C_{31}H_{52}O_4NSi_2$: 558.3435]. Anal. Calcd for $C_{31}H_{48}O_4Si_2$: C, 68.84; H, 8.94. Found: C, 68.90; H, 9.14.



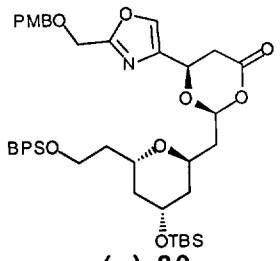
(+)-**28**

Carriera Adduct (+)-28: To a solution of the Carriera *R*-(+)-binapthylimino alcohol (71.1 mg, 0.044 equiv) in toluene (24 mL) was added freshly distilled $Ti(O\textit{i}\text{-}Pr)_4$ (18.2 μL, 0.02 equiv), and the resulting orange solution was stirred for 1 h at rt. To this was added a solution of dry di-*tert*-butyl salicylic acid (31 mg, 0.04 equiv) in toluene (2 mL) *via* cannula, and stiring was continued for 1 h. The solution was cooled to –40 °C. Trimethylsilyl chloride (78 μL, 0.2 equiv) and triethylamine (430 μL, 1 equiv) were added, followed by the addition of a solution of aldehyde **25** (762 mg, 3.082 mmol) in toluene (15 mL) *via* cannula. After stirring for 20 min at –40 °C, silyl ketene acetal **26** (1.5 mL, 2 equiv) was added, and the solution was allowed to slowly warm to 0 °C over 5 hours, then to rt. The reaction mixture was poured into brine (50 mL) and EtOAc (50 mL). The aqueous layer was extracted with EtOAc (2 x 30 mL); the collected organics were dried over Na_2SO_4, and concentrated *in vacuo*. This aldol product was dissolved in THF (10 mL), and a solution of TBAF in THF (1 M, 5 mL, 5.0 mmol) was added. After stirring for 15 min, the reaction mixture was poured into saturated NH_4Cl (50 mL) and EtOAc (50 mL). The aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organics were washed with 5% $NaHCO_3$ solution (100 mL), then brine (100 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (2:3 then 3:2) as eluant, gave (+)-**28** (1.01 g, 83% yield) as a pale yellow solid: $[\alpha]_D^{20}$ = +13.6 (c 1.0, $CHCl_3$; IR ($CHCl_3$) 3550 (br), 3000 (m), 2955 (w), 2935 (w), 1725 (s), 1610 (m), 1510 (s), 1245 (s), 1220 (m), 1170 (s) 1075 (m), 1030 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1 H), 7.33 (m, 5 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 5.16 (d, J = 12.4 Hz, 1 H), 5.13 (d, J = 12.4 Hz, 1 H), 5.11 (dd, J = 3.9, 8.2, 1 H), 4.52 (s, 2 H), 4.50 (s, 2 H), 3.78 (s, 3 H), 3.39 (br s, 1 H), 2.94 (dd, J = 16.4, 3.9, 1 H), 2.85 (dd, J = 16.6, 8.5, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 161.2, 159.5, 142.3, 135.5, 135.4, 129.4, 129.1, 128.6, 128.4, 128.2, 113.9, 72.6, 66.6, 64.1, 63.4, 55.3, 40.6; high resolution mass spectrum (ESI) *m/z* 398.1608 [$(M+H)^+$]; calcd for $C_{22}H_{24}NO_6$: 398.1603]. Anal. Calcd for $C_{22}H_{24}NO_6$: C, 66.49; H, 5.83; N 3.52. Found: C, 66.90; H, 5.90; N, 3.45.



(+)-29

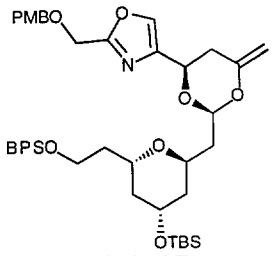
Acid alcohol (+)-29: To a solution of benzyl ester (+)-**28** (1.29 g, 3.24 mmol) in MeOH (32 mL) was added an aqueous 1M LiOH solution (32 mL, 10 equiv). After stirring for 20 min at rt, a 1N HCl solution (50 mL) was slowly added, followed by EtOAc (75 mL). The aqueous layer was extracted with EtOAc (3 x 25mL). The organic layers were combined, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. Flash chromatography, using acetic acid-EtOAc (1:200 then 1:100) as eluant, gave (+)-**29** (930 mg, 93% yield) as an off-white solid: $[\alpha]_D^{20}$ = +19.4 (c 0.975, $CHCl_3$); IR ($CHCl_3$) 3300 (br), 3000 (s), 2960 (m), 2940 (m), 2910 (w), 2860 (w), 1710 (s), 1610 (m), 1510 (m), 1410 (w), 1300 (w), 1245 (s), 1075 (s), 1030 (s), 800 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 1 Hz, 1 H), 7.25 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 5.10 (m, 1 H), 4.52 (s, 4 H), 3.79 (s, 3 H), 2.91 (dd, *J* = 16.5, 4.1 Hz, 1 H), 2.83 (dd, *J* = 16.5, 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 161.6, 159.5, 142.0, 135.5, 129.7, 129.0, 113.9, 72.8, 63.6, 63.3, 55.3, 40.3; high resolution mass spectrum (ESI) *m/z* 308.3138 [$(M+H)^+$]; calcd for $C_{15}H_{18}NO_6$: 308.3136].



(–)-30

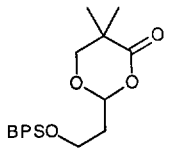
Dioxanone (–)-30: To a solution of carboxylic acid (+)-**29** (39 mg, 1.3 equiv) in methylene chloride (0.127 mL) was added HMDS (0.032 mL, 1.5 equiv) and the reaction mixture was stirred for 12 h. The solvent was removed under high vacuum and the flask was charged with aldehyde **(–)-30** (52 mg, 0.096 mmol), methylene chloride (0.25 mL) and 2,6 *di-t*-butyl-4-methyl pyridine (3.9 mg). The reaction was cooled to -78 °C. TMS-OTf (0.0046 mL, 0.3 equiv) was added and the reaction was warmed to rt. The reaction was stirred for 18 h, quenched with triethylamine (0.100 mL), poured into saturated $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4) as eluant, gave major isomer (–)-**30** (48 mg, 61% yield) as an oil: $[\alpha]_D^{20}$ -16.1 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3020 (s), 1745 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.45 (s, 1 H), 7.36 (m, 6 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 6.86 (dd, *J* = 6.6, 1.7 Hz, 1 H), 5.45 (dd, *J* = 7.9, 2.6 Hz, 1 H), 4.67 (dd, *J* = 9.7, 5.2 Hz, 1 H), 4.53 (s, 2 H), 4.51 (s, 2 H), 4.29 (m, 1 H), 3.97 (m, 2 H), 3.81 (m, 1 H), 3.79 (s, 3 H), 3.72 (m, 1 H), 2.91 (dd, *J* = 17.6, 9.7 Hz, 1 H), 2.70 (dd, *J* = 17.7, 5.3 Hz, 1 H), 2.20 (m, 1 H), 2.14 (m, 1 H), 1.82 (m, 2 H), 1.72 (m, 1 H), 1.62 (m,

2 H), 1.37 (m, 1 H), 1.02 (s, 9 H), 0.86 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ166.5, 161.7, 159.5, 138.9, 136.4, 135.5, 134.2, 133.8, 129.6, 127.7, 113.9, 100.5, 72.8, 68.9, 66.5, 64.9, 64.5, 63.4, 60.6, 55.3, 39.8, 39.0, 38.4, 37.6, 34.7, 26.9, 26.8, 19.2, 18.1, -4.8, -4.8; high resolution mass spectrum (ES, NH_3) m/z 830.4125[$(M+H)^+$; calcd for $C_{46}H_{64}O_9NSi_2$: 830.4120]. Anal. Calcd for $C_{46}H_{63}NO_9Si_2$: C, 66.19; H, 7.94; N, 1.43. Found: C, 66.10; H, 7.93; N, 1.43.



(–)-17

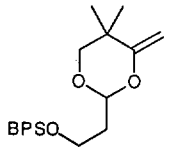
Enol Ether (–)-17: To a solution of dioxanone (–)-**30** (17 mg, 0.021 mmol) was added dimethyltitanocene (0.5 mL, 0.5 M in THF, 12 equiv). The reaction mixture was heated to 65 °C for 12 h. The reaction mixture was placed directly onto basic alumina (activated 10 % water). Flash chromatography, using EtOAc-hexanes-triethylamine (10:70:1) as eluant, gave (–)-**17** (14 mg, 82% yield) as a yellow oil: $[\alpha]_D^{20}$ -39.2 (*c* 0.5, C_6H_6); IR (CCl_4) 3020 (w), 2950 (s), 1660 (w), 1250 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (m, 4 H), 7.27 (m, 7 H), 7.18 (m, 2 H), 6.76 (dd, *J* = 7.9, 5.2 Hz, 2 H), 5.02 (dd, *J* = 7.5, 2.7 Hz, 1 H), 4.61 (d, *J* = 0.9 Hz, 1 H), 4.57 (dd, *J* = 11.4, 2.9 Hz, 1 H), 4.47 (m, 1 H), 4.37 (s, 2 H), 4.32 (s, 2 H), 4.10 (d, *J* = 1.3 Hz, 1 H), 3.98 (m, 2 H), 3.89 (m, 2 H), 3.29 (s, 3 H), 2.64 (dd, *J* = 13.7, 11.7 Hz, 1 H), 2.37 (m, 1 H), 2.26 (ddd, *J* =12.6, 9.8, 3.1 Hz, 1 H), 2.20 (m, 1 H), 1.94 (ddd, *J* = 13.9, 7.5, 4.6 Hz, 1 H), 1.77 (m, 2 H), 1.62 (m, 2 H), 1.35 (m, 1 H), 1.19 (s, 9 H), 0.95 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 159.9, 156.2, 141.7, 136.0, 135.9, 133.9, 133.8, 129.9, 129.8, 114.1, 100.6, 93.9, 72.4, 72.4, 66.6, 65.6, 63.5, 61.2, 54.7, 40.2, 39.5, 38.9, 38.5, 34.4, 27.2, 26.0, 19.5, 18.2, -4.5, -4.6.



33

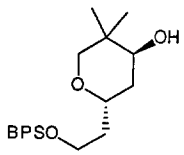
Dioxanone 33: To a solution of 3-hydroxypivalic acid **32** (1.43 g, 12.2 mmol) in methylene chloride (12.2 mL) was added HMDS (1.96 g, 1.2 equiv) and the reaction mixture was stirred for 12 h. The solvent was evaporated under high vacuum and the flask was charged with the aldehyde (5.71 g, 1.5 equiv), methylene chloride (37 mL). The reaction mixture was cooled to -78 °C. TMSOTf (0.221 mL, 0.1 equiv) was added and the reaction was stirred for 2 h. The reaction was quenched with Et_3N (1 mL), poured into saturated $NaHCO_3$ (40 mL), and extracted with methylene chloride (3 x 40 mL). The combined extracts

were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave **33** (4.77 g, 95% yield) as a colorless oil: IR ($CHCl_3$) 3010 (s), 1735 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (m, 4 H), 7.38 (m, 6 H), 5.49 (dd, *J* = 5.7, 5.0 Hz, 1 H), 3.83 (m, 2 H), 3.74 (d, *J* = 11.4 Hz, 1 H), 3.62 (d, *J* = 11.1 Hz, 1 H), 2.03 (m, 2 H), 1.34 (s, 3 H), 1.18 (s, 3 H), 1.03 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 135.5, 133.6, 133.5, 129.7, 129.7, 127.7, 127.7, 102.7, 75.2, 58.6, 39.7, 38.0, 26.8, 26.9, 26.6, 21.4, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 413.2128 [$(M+H)^+$; calcd for $C_{24}H_{33}O_4Si$: 413.2148].



35

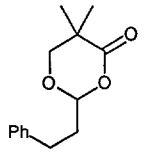
Enol Ether 35: To dioxanone **33** (1.06 g, 2.57 mmol) was added dimethyltitanocene (10 mL, 0.5 M toluene, 2 equiv) and the reaction mixture was heated to 65 °C. The reaction mixture was stirred for 12 h and placed directly onto basic alumina (activated 10 % water). Flash chromatography, using triethylamine-hexanes (1:100) as eluant, provided **35** (2.60 g, 52% yield) as a yellow oil: IR ($CHCl_3$) 3020 (s), 1650 (w), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.76 (m, 4 H), 7.22 (m, 6 H), 4.96 (dd, *J* = 2.4, 2.3 Hz, 1 H), 4.20 (s, 1 H), 3.93 (m, 2 H), 3.35 (d, *J* = 10.6 Hz, 1 H), 3.26 (d, *J* = 10.7 Hz, 1 H), 2.14 (m, 2 H), 1.27 (s, 3 H), 1.16 (s, 9 H), 0.69 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 166.5, 136.0, 134.2, 129.9, 128.5, 113.2, 101.7, 91.1, 77.0, 59.7, 46.0, 38.4, 35.2, 27.1, 26.4, 22.0, 19.5; high resolution mass spectrum (CI, NH_3) *m/z* 411.2343 [$(M+H)^+$; calcd for $C_{25}H_{35}O_3Si$: 411.2355].



38

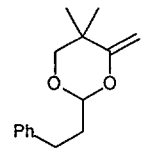
Alcohol 38: To a -78 °C solution of enol ether **35** (91 mg, 0.220 mmol) in toluene (2.2 mL) was added triisobutylaluminum (0.440 mL, 1.0 M in toluene, 2 equiv). The reaction mixture was warmed to rt and after 1 h triisobutylaluminum (0.22 mL, 1 equiv) was added. The reaction mixture stirred 1 h and was poured into saturated $NaHCO_3$ (20 mL), and extracted with EtOAc (2 x 20mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave **38** (62 mg, 77% yield, 6:1 dr) as an oil: IR ($CHCl_3$) 3650 (w), 2950 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.37 (m, 6 H), 3.82 (ddd, *J* = 10.2, 7.9, 5.3 Hz, 1 H), 3.74 (ddd, *J* =10.4, 5.7, 5.5 Hz, 1 H), 3.52 (m, 1 H), 3.43 (d, *J* = 11.5 Hz, 1 H), 3.03 (d, *J* = 11.6 Hz, 1 H), 1.77 (m, 1 H), 1.67 (m,

2 H), 1.35 (m, 2 H), 1.04 (s, 9 H), 0.93 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 134.0, 129.5, 127.6, 77.0, 75.4, 73.9, 60.2, 38.8, 37.0, 36.0, 26.9, 23.0, 19.2, 16.8; high resolution mass spectrum (CI, NH_3) *m/z* 413.2508 [$(M+H)^+$; calcd for $C_{25}H_{37}O_3Si$: 413.2512].



34

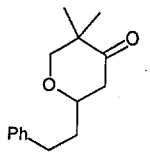
Dioxanone 34: To a solution of acid **32** (1.397 g, 13.7 mmol) in methylene chloride (13.7 mL) was added HMDS (2.43 g, 1.1 equiv). The reaction mixture was stirred for 12 h and the solvent was removed *in vacuo*. Dihydrocinnamaldehyde (2.76 g, 1.5 equiv) was added and the reactants were dissolved in methylene chloride (40 mL). The reaction mixture was cooled to -78 °C and TMS-OTf (304 mg, 0.1 equiv) was added. The reaction stirred for 2 h, quenched with saturated $NaHCO_3$ (40 mL), and extracted with methylene chloride (2 x 40 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave **34** (3.18 g, 99% yield) as an oil: IR ($CHCl_3$) 3015 (s), 2975 (s), 1740 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (m, 2 H), 7.19 (m, 3 H), 5.27 (t, *J* = 4.9 Hz, 1 H), 3.79 (d, *J* = 11.4 Hz, 2 H), 3.65 (d, *J* = 11.3 Hz, 2 H), 2.79 (dd, *J* = 9.2, 6.8 Hz, 2 H), 2.10 (m, 2 H), 1.39 (s, 3 H), 1.18 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ174.3, 140.7, 128.5, 128.4, 126.2, 104.0, 75.1, 39.7, 36.4, 29.0, 26.6, 21.3; high resolution mass spectrum (CI, NH_3) m/z 235.1341 [$(M+H)^+$; calcd for $C_{14}H_{18}O_3$: 235.1334]. Anal. Calcd for $C_{14}H_{18}O_3$, C, 71.77; H, 7.74. Found: C, 71.93; H, 7.79.



36

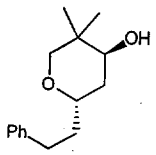
Enol Ether 36: To a solution of dioxanone **34** (583 mg, 2.49 mmol) was added dimethyl titanocene (0.5 M in toluene, 9.96 mL, 2 equiv) and the reaction mixture was heated to 65 °C for 12 h. Hexanes (10 mL) was added and the solids were filtered and the reaction mixture was concentrated *in vacuo*. Flash chromatography on basic alumina, using triethylamine-hexanes (1:100) as eluant, gave **36** (520 mg, 88% yield) as a yellow oil: IR (CHCl3) 2975 (s), 1650 (s) cm-1; 1H NMR (500 MHz, $CDCl_3$) δ 7.05 (m, 5 H), 4.58 (s, 1 H), 4.53 (t, *J* = 4.9 Hz, 1 H), 4.18 (s, 1 H), 3.35 (d, *J* = 10.7 Hz, 1 H), 3.16 (d, *J* = 10.7 Hz, 1 H), 2.80 (m, 2 H), 2.08 (m, 2 H), 1.30 (s, 3 H), 0.69 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 141.9, 128.8, 128.3,

127.8, 103.0, 90.9, 76.9, 36.8, 35.1, 30.1, 26.4, 22.0; high resolution mass spectrum (CI, NH_3) *m/z* 233.1535[$(M+H)^+$; calcd for $C_{15}H_{21}O_2$: 233.1542].



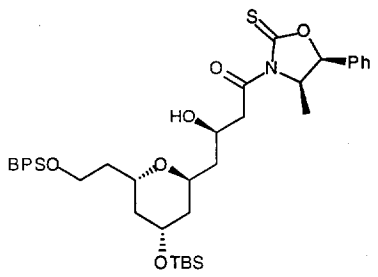
39

Ketone 39: To a -78 °C solution of enol ether **36** (18 mg, 0.076 mmol) in methylene chloride (1.5 mL) was added dimethylaluminum chloride (0.076 mL, 1.0 M in hexanes, 1 equiv). The reaction mixture was stirred at -78 °C for 5 min, warmed to rt for 5 min, quenched with Et_3N (0.5 mL), poured into saturated $NaHCO_3$ (10 mL), extracted with methylene chloride (3 x 10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave **39** (17 mg, 95% yield) as an oil: IR ($CHCl_3$) 3020 (s), 1720 (s), 1175 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (m, 1 H), 7.17 (m, 3 H), 3.76 (d, *J* = 11.5 Hz, 1 H), 3.55 (dddd, *J* =12.2, 8.2, 7.5, 4.2 Hz, 1 H), 3.36 (d, *J* = 11.5 Hz, 1 H), 2.78 (ddd, *J* = 9.5, 9.2, 5.1 Hz, 1 H), 2.71 (ddd, *J* = 9.2, 7.1, 2.1 Hz, 1 H), 2.52 (dd, *J* = 11.5, 14.7 Hz, 1 H), 2.25 (dd, *J* = 14.6, 2.8 Hz, 1 H), 1.25 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.5, 141.4, 128.4, 128.4, 126.0, 78.0, 77.4, 46.3, 44.6, 37.8, 31.4, 24.3, 19.1; high resolution mass spectrum (CI, NH_3) *m/z* 233.1545 [$(M+H)^+$; calcd for $C_{15}H_{21}O_2$: 233.1541].



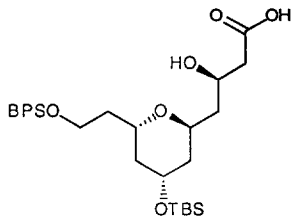
40

Alcohol 40: To a -78 °C solution of enol ether **36** (93 mg, 0.394 mmol) in toluene (3.94 mL) was added triisobutylaluminum (0.787 mL, 1.0 M in toluene, 2 equiv). The reaction mixture was slowly warmed to rt over 1 h and triisobutylaluminum (0.394 mL, 1 equiv) was added. After 1 h, the reaction was poured into saturated $NaHCO_3$ (20 mL), and extracted with EtOAc (3 x 20 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave **40** (60 mg, 75%, 6:1 dr) as an oil: IR ($CHCl_3$) 3610 (w), 3470 (w), 2950 (s), 1075 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (m, 2 H), 7.17 (m, 3 H), 3.49 (d, *J* =11.5 Hz, 1 H), 3.40 (dd, *J* = 6.2, 2.4 Hz, 1 H), 3.27 (m, 1 H), 3.05 (d, *J* = 11.5 Hz, 1 H), 2.73 (m, 1 H), 2.67 (m, 2 H), 1.41 (m, 2 H), 0.96 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 128.5, 128.3, 125.8, 77.3, 76.3, 75.3, 37.6, 36.9, 36.1, 31.7, 23.0, 16.8; high resolution mass spectrum (CI, NH_3) *m/z* 234.1625 [$(M+H)^+$; calcd for $C_{15}H_{22}O_2$: 234.1620]. Anal. Calcd for $C_{15}H_{22}O_2$, C, 76.88; H, 9.46. Found: C, 77.26; H, 9.85.



(+)-46

Amide (+)-46: To a solution of tin (II) triflate (353 mg, 2.3 equiv) in methylene chloride (4 mL) at –50 °C was added *N*-ethylpiperidine (0.124 mL, 2.4 equiv) and thiazolidinone **(–)-45** (133 mg, 1.5 equiv). The reaction mixture was stirred for 4 h, then cooled to –78 °C. The aldehyde **(–)-24** (200 mg, 0.37 mmol) in methylene chloride (2 mL) was then added *via* cannula. The reaction mixture was stirred for 1 h, quenched with pH = 7 buffer (5 mL), filtered through celite, poured into saturated $NaHCO_3$ (25 mL). And extracted with methylene chloride (3 x 25 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo.* Flash chromatography, using EtOAc-hexanes (1:4) as eluant, gave **(+)-46** (191 mg, 67% yield, 4:1 dr): $[\alpha]_D^{20}$ +7.8 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3450 (w), 2960 (s), 1700 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.38 (m, 11 H), 5.71 (d, *J* = 7.1 Hz, 1 H), 4.97 (dq, *J* = 6.8, 6.7 Hz, 1 H), 4.35 (m, 1 H), 4.23 (m, 1 H), 4.03 (m, 2 H), 3.78 (m, 1 H), 3.70 (m, 1 H), 3.60 (d, *J* = 1.7 Hz, 1 H), ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.1, 172.4, 135.6, 135.9, 133.9, 132.4, 129.5, 128.9, 128.7, 127.6, 125.9, 83.4, 68.7, 67.5, 64.9, 60.8, 59.0, 44.7, 39.5, 39.4, 38.6, 37.6, 26.9, 25.8, 19.2, 18.0, 14.2, -4.7; high resolution mass spectrum (CI, NH_3) *m/z* 776.3873 [$(M+H)^+$; calcd for $C_{43}H_{62}O_6NSSi_2$: 776.3836].



To a solution of amide (+)-**46** (741 mg, 0.955 mmol) in THF (7 mL) at 0 °C was added lithium hydroxide (2.86 mL, 1 M, 3 equiv) and hydrogen peroxide (1.29 mL, 30 %). The reaction mixture was stirred for 5 min, poured into saturated sodium thiosulfate (25 mL), acidified to pH 2.5 (HCl), and extracted with EtOAc (3 x 25 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo.* Flash chromatography, using acetic acid-EtOAc-hexanes (1:25:75) as eluant, gave the corresponding β-hydroxy acid (571 mg, 100% yield) as a oil: $[\alpha]_D^{20}$ 18.3 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3450 (w), 2940 (s), 1710 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.38 (m, 6 H), 4.15 (m, 1 H), 4.10 (m, 1 H), 4.03 (m, 2 H), 3.71 (m, 2 H), 2.50 (dd, *J* = 15.9, 4.3 Hz, 1 H), 2.43 (dd, *J* = 15.9, 7.3 Hz, 1 H), 2.23 (m, 1 H),

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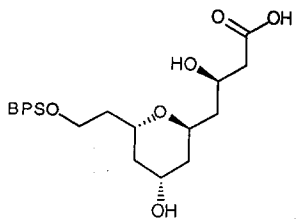
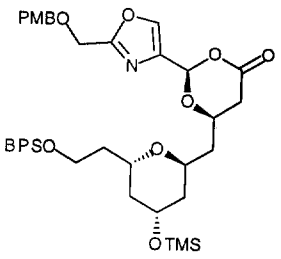
1.86 (ddd, J = 13.2, 4.7, 4.5 Hz, 1 H), 1.76 (m, 2 H), 1.55 (m, 2 H), 1.44 (m, 2 H), 1.03 (s, 9 H), 0.86 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 135.6, 133.9, 133.8, 129.7, 127.7, 68.4, 68.1, 64.5, 61.0, 41.1, 39.8, 39.5, 623.3202 [$(M+Na)^+$; calcd for $C_{33}H_{52}O_6Na$: 623.3200].



(–)-47

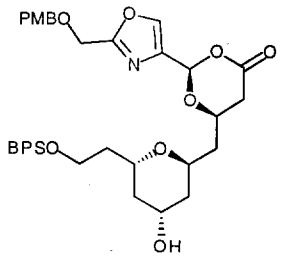
Diol (–)-47: To a solution of the silyl ether (109 mg, 0.182 mmol) in acetonitrile (3.3 mL) and *t*-butanol (0.33 mL) at 0 °C was added 25 % fluorosilisic acid (0.035 mL). The reaction mixture was stirred for 4 h, poured into pH = 2.5 HCl (20 mL), and extracted with EtOAc (3 x 20 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using acetic acid-EtOAc (1:100) as eluant, gave (–)-**47** (66 mg, 75% yield) as an oil: $[\alpha]_D^{20}$ -21.5 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3600 (w), 3450 (w), 2950 (s), 1715 (s), 1110 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.39 (m, 6 H), 4.23 (m, 1 H), 4.15 (m, 1 H), 4.01 (m, 2 H), 3.73 (m, 2 H), 2.50 (m, 2 H), 2.07 (s, 1 H), 1.79 (m, 1 H), 1.71 (ddd, J = 13.1, 4.7, 4.2 Hz, 1 H), 1.62 (m, 1 H), 1.49 (ddd, J = 14.4, 3.2, 3.2 Hz, 1 H), 1.37 (ddd, J = 13.2, 7.9, 7.9 Hz, 1 H), 1.03 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2, 135.6, 135.6, 133.7, 133.6, 129.7, 127.7, 69.7, 67.9, 67.4, 66.6, 64.660.6, 41.1, 38.7, 38.5, 38.4, 37.6, 26.9, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 509.2343 [$(M+Na)^+$; calcd for $C_{27}H_{38}O_6SiNa$: 509.2335].



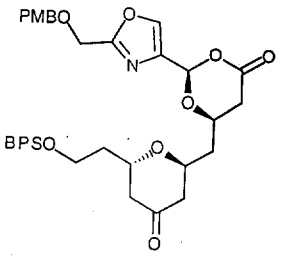
(–)-48

Dioxanone (–)-48: To a solution of diol acid (–)-**47** (76 mg, 0.157 mmol) in methylene chloride (0.157 mL) was added HMDS (31 mg, 0.17 mmol, 1.1 equiv) and stirred for 18 h. The solvent was removed *in vacuo* and the reaction mixture was dissolved in methylene chloride (1.88 mL) and aldehyde **25** (116 mg, 3 equiv) was added . The reaction mixture was cooled to –78 °C and trimethyltrifluoromethanesulfonate (0.031 mL, 1.0 M, 0.2 equiv) was added. The reaction was warmed to –20 °C and stirred for ca. 40 h, then quenched with pyridine (0.5 mL), and poured into saturated $NaHCO_3$. The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:2) as

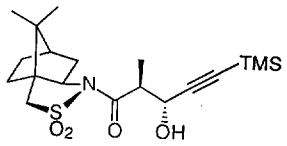
eluant, gave (–)-**48** (74 mg, 65% yield) as an oil: $[\alpha]_D^{20}$ -20.3 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2960 (s), 1750 (s), 1250 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1 H), 7.63 (m, 4 H), 7.38 (m, 6 H), 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 6.6 Hz, 2 H), 5.99 (s, 1 H), 4.55 (s, 2 H), 4.54 (s, 2 H), 4.11 (m, 2 H), 3.95 (m, 2 H), 3.85 (m, 1 H), 3.79 (s, 2 H), 3.71 (m, 2 H), 2.77 (dd, *J* = 17.7, 4.4 Hz, 1 H), 2.55 (dd, *J* = 17.8, 10.8 Hz, 1 H), 2.39 (ddd, *J* = 15.8, 11.1, 4.8 Hz, 1 H), 1.84 (m, 2 H), 1.71 (m, 1 H), 1.62 (m, 1 H), 1.51 (m, 1 H), 1.26 (m, 2 H), 1.02 (s, 9 H), 0.09 (s, 9 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 131.8, 159.6, 137.8, 137.0, 135.6, 135.5, 134.0, 133.7, 129.7, 129.1, 127.8, 127.7, 114.0, 96.7, 72.7, 72.3, 66.5, 66.2, 64.7, 63.4, 6.6, 60.2, 55.3, 40.2, 39.7, 38.3, 37.9, 35.7, 26.9, 19.2, 0.2; high resolution mass spectrum (CI, NH_3) *m/z* 788.3657 [$(M+H)^+$; calcd for $C_{43}H_{58}O_9N\,Si_2$: 788.3650].



To a solution of silyl ether (–)-**48** (65 mg, 0.083 mmol) in THF (1.6 mL) at 0 °C was added pyridine (0.65 mL, 1 equiv) and hydrogen fluoride pyridine complex (0.008 mL, 1 equiv). The reaction mixture was stirred for 2 h, poured into saturated $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (3:1) as eluant, gave the corresponding alcohol (36 mg, 68% yield): $[\alpha]_D^{20}$ -26.7 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3450 (w), 2910 (s), 1750 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1 H), 7.62 (m, 4 H), 7.38 (m, 6 H), 7.25 (d, *J* = 9.1 Hz, 2 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 6.01 (s, 1 H), 4.54 (s, 2 H), 4.52 (s, 2 H), 4.13 (m, 2 H), 3.98 (m, 1 H), 3.82 (m, 1 H), 3.78 (s, 3 H), 3.72 (m, 2 H), 2.79 (dd, *J* = 17.7, 4.4 Hz, 1 H), 2.57 (dd, *J* = 17.8, 10.8 Hz, 1 H), 2.34 (dddd, *J* = 14.4, 10.7, 9.4, 5.0 Hz, 1 H), 1.88 (m, 1 H), 1.77 (m, 3 H), 1.62 (m, 1 H), 1.57 (m, 1 H), 1.28 (m, 1 H), 1.03 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 161.8, 159.5, 137.8, 136.9, 135.5, 135.4, 133.8, 133.6, 129.7, 129.7, 129.0, 127.8, 113.9, 96.7, 72.8, 72.3, 66.4, 66.3, 64.3, 63.4, 60.5, 55.3, 39.9, 38.2, 38.0, 37.6, 35.6, 26.9, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 738.3066 [$(M+Na)^+$; calcd for $C_{40}H_{49}O_9NSiNa$: 738.3074].



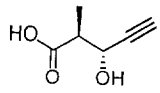
To a solution of the secondary alcohol (26 mg, 0.0363 mmol) in methylene chloride (1.0 mL) was added pyridine (0.030 mL) and Dess-Martin periodinane (31 mg, 2 equiv). The reaction mixture was stirred for 2 h, poured into saturated $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:1 then 3:1) as eluant, gave the correponding ketone (20 mg, 77% yield) as an oil: $[\alpha]_D^{20}$ -10.6 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2950, (s), 1750 (s), 1715 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1 H), 7.62 (m, 4 H), 7.39 (m, 6 H), 7.25 (d, *J* = 8.8 Hz, 2 H), 6.86 (dd, *J* = 6.7, 2.1 Hz, 2 H), 6.08 (s, 1 H), 4.53 (s, 2 H), 4.52 (s, 2 H), 4.39 (m, 1 H), 4.15 (m, 2 H), 3.78 (s, 3 H), 3.75 (ddd, *J* = 10.4, 8.0, 1.9 Hz, 1 H), 3.67 (ddd, *J* = 12.0, 11.0, 5.6 Hz, 1 H), 2.71 (dd, *J* = 17.7, 4.5 Hz, 1 H), 2.57 (dd, *J* = 17.7, 10.7 Hz, 1 H), 2.55 (m, 1 H), 2.31 (m, 2 H), 2.12 (ddd, *J* = 14.4, 8.4, 6.1 Hz, 1 H), 1.82 (m, 1 H), 1.69 (m, 2 H), 1.02 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 165.8, 161.8, 159.5, 137.8, 136.8, 135.5, 133.5, 133.4, 129.8, 129.8, 129.7, 129.7, 127.8, 113.9, 96.7, 72.7, 71.6, 69.6, 67.7, 63.3, 59.9, 55.3, 46.5, 46.5, 39.8, 36.7, 35.9, 26.8,, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 736.2953 [$(M+Na)^+$; calcd for $C_{40}H_{47}O_9NSiNa$: 736.2917].



(–)-**59**

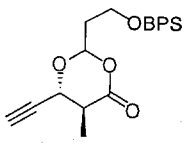
Sultam (–)-59. To a solution of Et_3B (1.0 M in hexane, 41.4 mL, 2.5 equiv) was slowly added trifluoromethanesulfonic acid (3.65 mL, 2.5 equiv); the resultant yellow-orange solution was stirred for 20 min further, then cooled to -15 °C. A solution of sultam (–)-**56** (4.5 g, 16.6 mmol) in methylene chloride (50 mL) was added *via* cannula, followed by a solution of Hunig's base (7.5 mL, 2.6 equiv) in methylene chloride (25 mL). The resultant clear yellow solution was stirred for 30 min at -10 °C then cooled to -78 °C. In another flask, a solution of $TiCl_4$ (1.0 M in methylene chloride, 50 mL, 3 equiv) at -78 °C was treated with aldehyde **57** (6.0 mL, 2 equiv) dropwise. The boron enolate solution was added *via* cannula into this solution over 10 min. The reaction mixture was stirred for 2 h, warmed to 0 °C, and quenched with saturated NH_4Cl (200 mL) and water (100 mL). The aqueous layer was extracted with methylene chloride (4 x 50 mL), and the organic solution was washed with brine (200 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4 then 3:7) as eluant, provided

(–)-**59** as a yellow foam, (5.54 g, 84%): $[\alpha]_D^{20}$ = -15.1 (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 3600 (m, br), 3015 (m), 2965 (m), 2400 (m), 1690 (m), 1455 (w), 1390 (m), 1335 (s), 1265 (m), 1250 (s), 1205 (s), 1165 (m), 1135 (s), 1065 (m), 1040 (m), 845 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.41 (t, *J* = 8.6 Hz, 1H), 3.88 (dd, *J* = 7.8, 4.9 Hz, 1 H), 3.51 (d, *J* = 13.8 Hz, 1 H), 3.46 (d, *J* = 13.8 Hz, 1 H), 3.34 (m, 1 H), 2.60 (d, *J* = 9.2 Hz, 1 H), 2.17 (m, 1 H), 2.05 (dd, *J* = 13.8, 7.8 Hz, 1 H), 1.88 (m, 3 H), 1.36 (m, 2 H), 1.27 (d, *J* = 6.7 Hz, 3 H), 1.17 (s, 3 H), 0.95 (s, 3 H), 0.14 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 104.2, 91.1, 66.5, 65.5, 53.2, 48.4, 47.8, 46.5, 44.7, 38.4, 32.9, 26.4, 21.0, 10.9, 14.0, -0.2 ; high resolution mass spectrum (CI) *m/z* 420.1645 [$(M+Na)^+$; calcd for $C_{19}H_{31}NO_4SSiNa$: 420.1641].



(+)-**61**

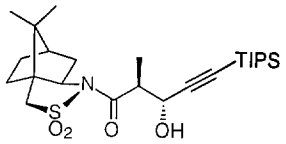
Hydroxyacid (+)-61: To a 0 °C solution of aldol (–)-**59** (5.89 g, 14.8 mmol) in THF-water (3:1, 150 mL) was added 30% HOOH (8.4 mL, 5 equiv) and 1 N LiOH (18.5 mL, 1.25 equiv). The resultant solution was stirred for 1.5 h at 0 °C and then quenched with saturated Na_2SO_3 (35 mL) and 10% NH_4Cl (ca. 25 mL) until pH = 10. The aqueous layer was extracted with methylene chloride (3 x 100 mL); the organic extracts were set aside. The aqueous layer was acidified to pH = 2 with 10 % HCl (35 mL) and extracted with EtOAc (3 x 100 mL). Each set of organic extractions were independently dried over $MgSO_4$, and concentrated *in vacuo*. The methylene chloride extractions afforded 2.91 g (91%) of the Oppolzer auxiliary (–)-**63**. The methylene chloride extractions provided (+)-**61** (1.67 g, 88% yield) as a clear oil: $[\alpha]_D^{20}$ = +20.1 (*c* 1.86, $CHCl_3$); IR ($CHCl_3$) 3310 (s), 3100 (v br), 3020 (s), 3010 (s), 2890 (m), 2400 (w), 2110 (w), 1715 (s), 1460 (m), 1340 (m), 1315 (m), 1295 (m), 1205 (s), 1135 (s), 1025 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 (dd, *J* = 7.7, 2.2 Hz, 1 H), 2.77 (m, 1 H), 2.51 (d, *J* = 2.2 Hz, 1 H), 1.31 (d, *J* = 7.2 Hz, 3 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.7, 81.9, 74.6, 63.9, 46.1, 13.6; high resolution mass spectrum (ESI) *m/z* 146.0817 [$(M+NH_4)^+$; calcd for $C_6H_{12}O_3N$: 146.0821].



64

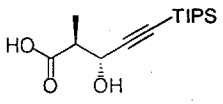
Dioxanone 64. To a 0 °C solution of hydroxyacid (+)-**61** (2.15 g, 16.8 mmol) in methylene chloride (7 mL) was added HMDS (3.78 mL, 1.1 equiv). The resultant mixture was stirred overnight and concentrated *in vacuo*. To the *bis*-TMS compound was added 2,6-*di*-*t*-butyl-4-methylpyridine (180 mg, 0.05 equiv), aldehyde **49** (8.44 g, 1.6 equiv), and methylene chloride. The resulting solution was cooled to -78 °C, and trimethylsilyltriflate (440 μL, 0.17 equiv) was added. The resultant solution was stirred at -78 °C

overnight, treated with pyridine (1.6 mL), warmed to rt, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, provided **64** (4.88 g, 69% yield) as a clear oil that solidified on standing. Recrystallization from hexane afforded analytically pure white needles: $[\alpha]_D^{20}$ = +1.1 (*c* 0.71, $CHCl_3$); mp= 89.5-92 °C; IR ($CHCl_3$) 3310 (s), 3075 (m), 3015 (s), 2965 (s), 2940 (s), 2895 (s), 2860 (s), 2130 (w), 1750 (s), 1590 (w), 1460 (m), 1430 (s), 1385 (m), 1360 (s), 1325 (s), 1290 (m), 1205 (s), 1110 (s), 975 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64-7.60 (m, 4 H), 7.42-7.35 (m, 6 H) 5.51 (t, *J* = 5.6 Hz, 1 H), 4.21 (dd, *J* = 7.1, 2.2 Hz, 1 H), 3.85 (t, *J* = 5.8 Hz, 2 H), 2.77 (dq, *J* = 11.0, 7.3 Hz, 1 H), 2.64 (d, *J* = 2.2, 1 H) 2.10-2.00 (m, 2 H), 1.36 (d, *J* = 7.2 Hz, 3 H), 1.04 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 135.5, 133.4, 129.4, 127.7, 101.3, 79.0, 75.9, 71.0, 58.4, 41.9, 37.9, 26.8, 19.2, 12.0; high resolution mass spectrum (CI) *m/z* 440.2240 $[(M+NH_4)^+$; calcd for $C_{25}H_{34}NO_4Si$: 440.2257].



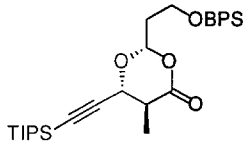
(–)-60

Oppolzer Aldol (–)-60: To a solution of Et_3B (1.0 M in hexane, 25.0 mL, 2.5 equiv) was slowly added trifluoromethanesulfonic acid (2.21 mL, 2.5 equiv). The resultant yellow-orange solution was stirred for 20 min further, then cooled to -10 °C. A solution of sultam (–)-**56** (2.71 g, 10.0 mmol) in methylene chloride (20 mL) was added *via* cannula, followed by addition of a solution of Hunig's base (4.72 mL, 2.7 equiv) in methylene chloride (10 mL). The resultant clear yellow solution was stirred for 15 min at -10 °C then cooled to -78 °C. In another flask, a solution of $TiCl_4$ (1.0 M in methylene chloride, 50 mL, 5 equiv) was treated with a solution of aldehyde **58** (4.2 g, 2 equiv) in methylene chloride (10 mL), added dropwise at –78 °C. The boron enolate solution was added rapidly *via* cannula into this solution. The reaction mixture was stirred for 6 h, quenched with saturated NH_4Cl (100 mL) and water (100 mL), and warmed to rt. The aqueous layer was extracted with methylene chloride (3 x 50 mL); the combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9 then 3:7) as eluant, provided (–)-**60** as a thick yellow oil, (4.40 g, 88%): $[\alpha]_D^{20}$ = -23.3 (*c* 0.54, $CHCl_3$); IR ($CHCl_3$) 3590 (br), 3020 (w), 2970 (s), 2955 (s), 2875 (s), 2125 (w), 1695 (m), 1465 (m), 1390 (m), 1335 (s), 1270 (s), 1210 (s), 1135 (s), 1070 (m), 1000 (m), 910 (s), 720 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.48 (d, *J* = 8.8 Hz, 1 H), 3.87 (dd, *J* = 7.8, 4.9 Hz, 1 H), 3.50 (d, *J* = 13.8 Hz, 1 H), 3.42 (d, *J* = 13.8, 1 H), 3.30 (dq, *J* = 8.73, 6.7 Hz, 1 H), 2.40 (br s, 1 H), 2.15 (m, 1 H0, 2.03 (m, 1 H), 1.78 (m, 3 H), 1.34 (m, 2 H), 1.27 (d, *J* = 6.7 Hz, 3 H), 1.15 (s, 3 H), 1.04 (s, 21 H), 0.94 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 106.1, 87.7, 66.7, 65.5, 53.2, 48.4, 47.7, 47.2, 44.6, 38.3, 32.9, 26.4, 20.8, 19.9, 18.5, 13.6, 11.1; high resolution mass spectrum (ESI) *m/z* 464.2653 $[(M-H)^+$; calcd for $C_{25}H_{43}NO_3SSi$: 464.2654].



(+)-62

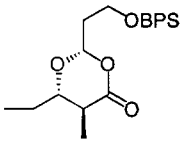
Hydroxyacid (+)-62: To a 0 °C solution of aldol (–)-**60** (4.34 g, 9.02 mmol) in THF-water (3:1, 90 mL) was added 1 N LiOH (11.0 mL, 1.2 equiv). The reaction mixture was heated to 55 °C for 4 h, cooled to rt, and quenched with 5% NH_4Cl (50 mL) and a few drops of 1 N HCl until pH = 10. The aqueous layer was extracted with methylene chloride (2 x 50 mL); the organic layer was washed with 10% ammonium hydroxide and set aside. The aqueous layer was acidified to pH = 2 with conc. HCl (35 mL) and extracted with EtOAc (2 x 100 mL). Each set of organic extractions were independently dried over $MgSO_4$, and concentrated *in vacuo*. The methylene chloride extractions afforded 2.72 g of the Oppolzer auxiliary (–)-**63**. The methylene chloride extractions provided (+)-**62** (2.10 g, 82% yield) as a clear oil: $[\alpha]_D^{20}$ = +13.7 (*c* 0.38, $CHCl_3$); IR ($CHCl_3$) 3200 (v br), 3020 (m), 2955 (s), 2900 (m), 2875 (s), 2400 (w), 2160 (w), 1710 (s), 1460 (m), 1385 (m), 1200 (m), 1020 (m), 990 (m), 880 (m), 660 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 (d, *J* = 7.4 Hz, 1 H), 2.76 (m, 1 H), 2.08 (s, 1 H), 1.33 (d, *J* = 7.23 Hz, 3 H), 1.04 (s, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 105.6, 87.6, 64.6, 46.5, 18.5, 13.7, 11.1; high resolution mass spectrum (ESI) *m/z* 285.1877 [$(M+H)^+$; calcd for $C_{15}H_{29}O_3Si$: 285.1886].



65

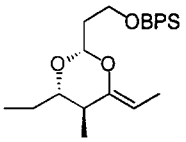
Dioxanone 65: A solution of hydroxyacid (+)-**62** (2.00 g, 7.03 mmol) in methylene chloride (7 mL) was treated with HMDS (1.75 mL, 1.1 equiv). The resultant mixture was stirred overnight at rt and concentrated *in vacuo*. To the *bis*-TMS compound was added 2,6-*di*-*t*-butyl-4-methylpyridine (71 mg, 0.05 equiv), aldehyde **49** (3.58 g, 1.6 equiv), and methylene chloride (26 mL). The resulting solution was cooled to -78 °C, and trimethylsilyltriflate (275 μL, 0.22 equiv) was added. The resultant solution was stirred at -78 °C overnight, treated with pyridine (0.5 mL), warmed to rt, and concentrated *in vacuo*. Flash chromatography using silica-water (10:1), and EtOAc-hexanes (1:19 then 1:10) as eluant, provided (–)-**65** (3.00 g, 75% yield, 2.2:1 *cis*:*trans*) as a clear oil: IR ($CHCl_3$) 2950 (s), 2895 (m), 2870 (s), 1745 (s), 1590 (w), 1460 (m), 1430 (m), 1385 (w), 1360 (m), 1325 (w), 1210 (m), 1110 (s), 975 (m), 700 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (m, 4 H), 7.38 (m, 6 H), 5.88, 5.50 (diastereomers, t, *J* = 5.4 Hz, t, *J* = 5.4 Hz, 1 H), 4.42, 4.24 (diastereomers, d, *J* = 7.3 Hz, d, *J* = 11.0 Hz, 1 H), 3.85 (m, 2 H), 2.82, 2.75 (diastereomers, m, m, 1 H), 2.05 (m, 2 H), 1.37, 1.35 (diastereomers, d, *J* = 7.3 Hz, d, *J* = 7.0 Hz, 3 H), 1.08 (s, 9 H), 1.04 (s, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 135.5, 133.5, 133.5, 129.8, 129.7, 129.7, 129.6, 127.7, 127.7, 127.6, 102.3, 101.3, 96.1, 89.7, 71.7, 68.7, 58.6, 58.5, 42.5, 41.7, 37.8, 37.4, 26.9, 26.8, 19.2,

19.1, 18.5, 14.0, 12.1, 11.1, 11.0; high resolution mass spectrum (CI) *m/z* 579.3308 [$(M+H)^+$; calcd for $C_{34}H_{51}O_4Si_2$: 579.3326].



(–)-**67**

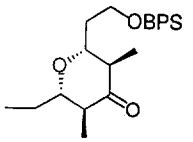
Dioxanone Alkane (–)-67. To a solution of alkyne (+)-**64** (102.2 mg, 0.242 mmol) in EtOH-methylene chloride (2:1, 3 mL) was added a spatula tip of 10% palladium on carbon. The reaction mixture was blanketed in H_2, stirred overnight at rt, and concentrated *in vacuo,* providing (–)-**67** (102 mg, 99% yield) as a clear oil: $[\alpha]_D^{20}$ = -4.9 (*c* 1.68, $CHCl_3$); IR ($CHCl_3$) 2965 (s), 2930 (s), 2880 (m), 2855 (s), 1735 (s), 1590 (w), 1460 (m), 1425 (m), 1380 (m), 1350 (m), 1210 (s), 1105 (s), 975 (s), 690 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63-7.58 (m, 4 H), 7.41-7.31 (m, 6 H), 5.54 (t *J* = 5.5 Hz, 1 H), 3.85 (t, *J* = 6.0 Hz, 2 H), 3.42 (ddd, *J* = 10.9, 8.3, 3.0 Hz, 1 H), 2.43 (dq, *J* = 10.3, 7.3 Hz,1 H), 2.12 - 1.95 (m, 2 H), 1.79-1.73 (m, 1 H), 1.52-1.47 (m, 1 H), 1.24 (d, *J* = 7.3 Hz, 3 H), 1.04 (s, 9 H), 0.99 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 135.5, 133.6, 129.7, 127.7, 101.0, 81.8, 58.7, 40.9, 38.0, 26.8, 26.6, 19.2, 12.7, 9.3; high resolution mass spectrum (CI) *m/z* 425.2131 [$(M-H)^+$; calcd for $C_{25}H_{34}O_4Si$: 425.2148].



(–)-**68**

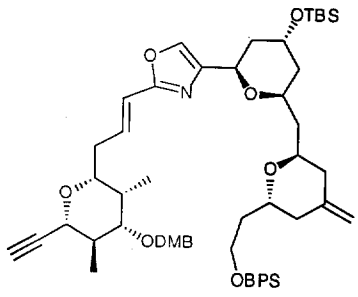
Enol ether (–)-68: To a 0 °C solution of $TiCl_4$ (1.0 M in methylene chloride, 4 mL, 17 equiv) was added THF (10 mL). To the yellow solution was added TMEDA (1.2 mL, 34 equiv) and the mixture was stirred for 10 min at rt. Zinc dust (590 mg, 39 equiv) and $PbCl_2$ (13 mg, 0.2 equiv) were then added through a solid addition funnel. The color of the suspension turned from brownish yellow to dark greenish blue. After 30 min, a solution of dioxanone (–)-**67** (99.2 mg, 0.233 mmol) and CH_3CHBr_2 (200 μL, 9.5 equiv) in THF (2 mL) was added to the mixture. After 1 h, the reaction was cooled to 0 °C and quenched with saturated K_2CO_3 (1.3 mL). After stirring at 0 °C for another 15 min, the mixture was poured into Et_2O (15 mL), filtered through basic Al_2O_3 with 10% water, using Et_2O-Et_3N (200:1, 100 mL) as an eluent, and concentrated *in vacuo.* Flash chromatography, using EtOAc-hexanes (1:50, silylated silica gel) provided (–)-**68** as a clear oil, (48 mg, 47%): $[\alpha]_D^{20}$ = -52.6 (*c* 0.39, C_6H_6); IR ($CHCl_3$) 3070 (w), 2965 (s), 2940 (s), 2880 (s), 2860 (s), 1685 (w), 1460 (m), 1425 (m), 1190 (m), 1105 (s), 990 (m), 700 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.77-7.72 (m, 4 H), 7.22-7.18 (m, 6 H), 4.96 (t, *J* = 5.2 Hz, 1 H), 4.64 (dq, *J* = 6.8, 1.8 Hz, 1 H), 3.99-3.93 (m, 2H), 3.04 (ddd, *J* = 10.6, 8.1, 2.8 Hz, 1 H), 2.22-2.17 (m, 3 H), 1.70 (dd, *J* = 6.7, 2.0 Hz, 3 H), 1.58-1.52

(m, 1 H), 1.39-1.32 (m, 1 H), 1.17 (s, 9 H), 0.93 (t, J = 7.4 Hz, 3 H), 0.70, (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ154.3, 135.6, 134.0, 129.5, 101.4, 99.8, 82.9, 59.7, 37.9, 36.6, 25.9, 24.9, 18.5, 11.8, 9.9, 9.4; high resolution mass spectrum (ESI) *m/z* 437.2513 [(M-H)$^+$; calcd for $C_{27}H_{37}O_3Si$: 437.2512].



(+)-69

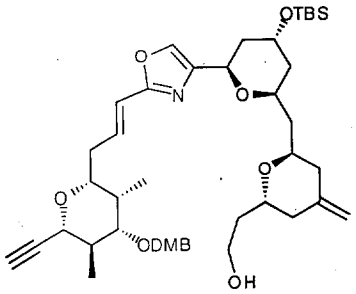
Pyranone (+)-69: A solution of enol ether (–)-68 (57 mg, 0.130 mmol) in methylene chloride (2.6 mL) was cooled to -78 °C and treated with Me_2AlCl (1.0 M in hexane, 130 μL, 1 equiv). The resultant solution was stirred for 10 min, placed in a -10 °C bath, stirred for 1 h, treated with triethylamine (1 mL) and saturated $NaHCO_3$ (10 mL), diluting with methylene chloride (20 mL). The aqueous layer was extracted with methylene chloride (2 x 10 mL), and the organic solution was washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:19 then 1:10) as eluant, provided (+)-69 (32.8 mg, 91% yield) as a clear oil: $[\alpha]_D^{20}$ = +7.7 (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 3070 (w), 2965 (s), 2935 (s), 2880 (s), 2855 (s), 1705 (s), 1455 (m), 1430 (w), 1380 (w), 1340 (w), 1205 (w), 1100 (s), 690 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.40 (m, 6 H), 3.90 (m, 1 H), 3.89 (m, 1 H), 3.39 (ddd, J = 10.5, 9.4, 2.23 Hz, 1 H), 3.06 (ddd, J = 10.6, 8.3, 2.7 Hz, 1 H), 2.31 (m, 2 H), 1.98 (m, 1 H), 1.71 (m, 2 H), 1.47 (m, 1 H), 1.02 (s, 9 H), 0.97 (d, J = 8.7 Hz, 3 H), 0.95 (d, J = 8.7 Hz, 3 H), 0.92 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 135.5, 134.0, 129.6, 127.6, 83.6, 79.5, 60.1, 50.0, 49.7, 37.2, 27.0, 26.9, 19.2, 9.5, 9.4; high resolution mass spectrum (CI) *m/z* 439.2671 [(M+H)$^+$; calcd for $C_{27}H_{39}O_3Si$: 439.2668].



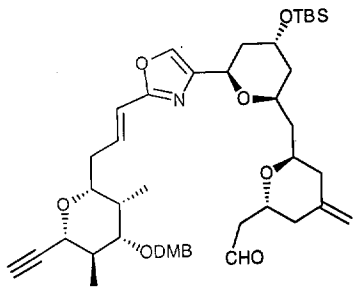
(+)-83

Alkene (+)-83: To a 0 °C solution of phosphonium salt (–)-12 (76 mg, 0.0821 mmol) in DMF (4 mL) was added lithium hexamethyldisilazane (0.182 mL, 1.16 equiv, 0.5 M THF). The reaction mixture was stirred for 30 min and charged with aldehyde (+)-11 (33 mg, 1.16 equiv) in DMF (1 mL) *via* cannula at –10 °C. After 30 min, the reaction mixture was poured into water (20 mL) and extracted with Et_2O (3 x 20 mL). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using

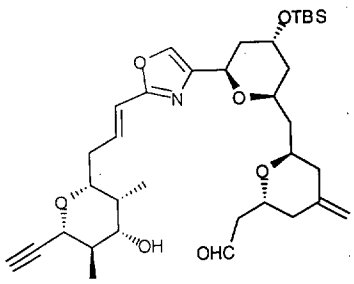
EtOAc-hexanes (1:4) as eluant, gave (+)-**83** (73 mg, 87% yield) as an oil: $[\alpha]_D^{20}$ +14.7 (*c* 0.59, $CHCl_3$); IR ($CHCl_3$) 2950 (s), 1220 (s), 750 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.36 (m, 6 H), 6.88 (d, *J* = 1.6 Hz, 1 H), 6.85 (dd, *J* = 8.1, 1.6 Hz, 1 H), 6.62 (ddd, *J* = 15.6, 8.3, 6.3 Hz, 1 H), 6.34 (d, *J* = 16.1 Hz, 1 H), 4.82 (dd, *J* = 11.3, 1.9 Hz, 1 H), 4.69 (s, 2 H), 4.55 (d, *J* = 11.3, 1 H), 4.25 (d, *J* = 11.3 Hz, 1 H), 4.23 (m,1 H), 3.99 (m, 3 H), 3.85 (s, 3 H), 3.85 (s, 3 H), 3.72 (m, 3 H), 3.43 (dt, *J* = 7.0, 1.7 Hz, 1 H), 3.09 (dd, *J* = 10.5, 4.6 Hz, 1 H), 2.61 (m, 1 H), 2.45 (d, *J* = 1.9 Hz, 1 H), 2.09 (m, 1 H), 2.01 (dd, *J* = 13.2, 5.9 Hz, 1 H), 1.94 (dd, *J* = 13.2, 6.9 Hz, 1 H), 1.83 (m, 4 H), 1.61 (m, 6 H), 1.06 (d, *J* = 6.5 Hz, 3 H), 1.02 (s, 9 H), 0.96 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 149.1, 148.7, 143.4, 142.3, 135.6, 135.0, 134.2, 134.0, 133.9, 130.9, 129.5, 127.6, 120.2, 119.0, 111.2, 111.1, 110.1, 82.4, 81.7, 78.3, 73.4, 73.0, 69.9, 69.1, 68.9, 67.5, 64.8, 60.7, 56.0, 55.8, 39.6, 39.3, 39.3, 39.0, 38.3, 36.8, 36.6, 36.1, 33.8, 26.9, 25.8, 19.2, 18.1, 13.9, 5.6, -4.8, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 1040.5508 [$(M+Na)^+$; calcd for $C_{60}H_{83}O_9N\ Si_2\ Na$: 1040.5504].



To a solution of silyl ether (+)-**83** (9.4 mg, 0.0092 mmol) in THF (2.5 mL) at –20°C was added 18-crown-6 (49 mg, 20 equiv) and KOH (25 mg, 48 equiv). The reaction mixture was warmed to rt over 3 h, poured into saturated NH_4Cl (10 mL), and extracted with methylene chloride (2 x 10 mL). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:1) as eluant, gave the corresponding primary alcohol (6 mg, 85% yield): $[\alpha]_D^{20}$ +16.8 (*c* 0.60, $CHCl_3$); IR ($CHCl_3$) 3500 (w), 3000 (s). 2390 (w), 1210 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1 H), 6.86 (m, 3 H), 6.65 (ddd, *J* = 16.0, 8.4, 6.3 Hz, 1 H), 6.36 (d, *J* = 16.1 Hz, 1 H), 4.84 (dd, *J* = 10.6, 3.4 Hz, 1 H), 4.75 (s, 1 H), 4.72 (s, 1 H), 4.57 (d, *J* = 11.3 Hz, 1 H), 4.27 (d, *J* = 11.2 Hz, 1 H), 4.26 (m, 1 H), 4.09 (m, 1 H), 4.04 (m, 1 H), 3.98 (m, 1 H), 3.88 (s, 6 H), 3.73 (m, 3 H), 3.45 (ddd, *J* = 6.9, 6.9, 1.6 Hz, 1 H), 3.11 (dd, *J* = 10.5, 4.6 Hz, 1 H), 2.63 (m, 1 H), 2.47 (d, *J* = 2.1 Hz, 1 H). 2.39 (m, 2 H), 2.29 (dd, *J* = 13.1, 3.8 Hz, 1 H), 2.11 (m, 1 H), 2.02 (m, 2 H), 1.97 (m, 1 H), 1.85 (m, 4 H), 1.60 (m, 4 H), 1.08 (d, *J* = 6.5 Hz, 3 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.91 (s, 6 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 149.1, 148.7, 142.9, 141.8, 135.4, 134.4, 130.9, 120.2, 118.8, 111.2, 111.1, 110.4, 82.4, 81.7, 78.3, 76.4, 73.4, 73.0, 70.6, 69.9, 69.9, 67.2, 64.8, 60.2, 56.0, 55.8, 40.1, 39.2, 39.2, 38.8, 37.9, 36.8, 36.3, 36.2, 36.1, 33.8, 25.9, 18.1, 13.9, 5.6, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 802.4319 [$(M+Na)^+$; calcd for $C_{44}H_{65}O_9N\ Si\ Na$: 802.4326].



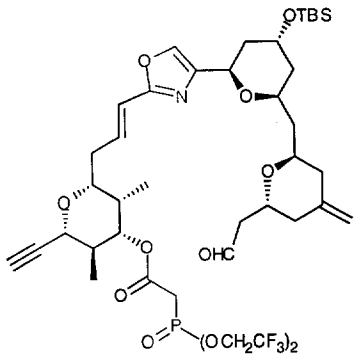
To a solution of the primary alcohol (7.5 mg, 0.0096 mmol) in DMSO (2 mL) was added triethylamine (0.022 mL, 17 equiv) and sulfur trioxide·pyridine complex (15 mg, 10 equiv). The reaction mixture was stirred for 2 h, poured into water (10 mL), and extracted with EtOAc (2 x 10 mL). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:2) as eluant, gave the corresponding aldehyde (7.2 mg, 96% yield): $[\alpha]_D^{20}$ +20.8 (*c* 0.36, $CHCl_3$); IR ($CHCl_3$) 2930 (s), 1725 (s), 1260 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.75 (m, 1 H), 7.46 (s, 1 H), 6.84 (m, 3 H), 6.67 (m, 1 H), 6.36 (d, *J* = 16.1 Hz, 1 H), 4.85 (dd, *J* = 8.2, 5.8 Hz, 1 H), 4.79 (s, 1 H), 4.77 (s, 1 H), 4.56 (d, *J* = 10.7, 1 H), 4.35 (m, 1 H), 4.27 (d, *J* = 11.2 Hz, 1 H), 4.27 (m, 1 H), 4.03 (m, 2 H), 3.87 (s, 6 H), 3.72 (dd, *J* = 10.7, 2.1 Hz, 1 H), 3.45 (ddd, *J* = 7.0, 7.0, 1.8 Hz, 1 H), 3.11 (dd, *J* = 10.5, 4.6 Hz, 1 H), 2.65 (dd, *J* = 7.7, 2.6 Hz, 1 H), 2.62 (dd, *J* = 7.6, 2.6 Hz, 1 H), 2.49 (dd, *J* = 5.6, 1.9 Hz, 1 H), 2.47 (d, *J* = 2.1 Hz, 1 H), 2.46 (m, 1 H), 2.40 (m, 3 H), 2.11 (m, 1 H), 2.04 (m, 3 H), 1.88 (m, 3 H), 1.49 (m, 2 H), 1.07 (d, *J* = 6.5 Hz, 3 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.91 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 160.9, 149.1, 148.7, 143.2, 140.9, 135.1, 134.3, 130.9, 120.2, 118.9, 111.2, 111.1, 82.4, 81.7, 78.3, 73.4, 73.1, 69.9, 69.7, 69.1, 67.4, 67.3, 64.7, 56.0, 55.8, 47.8, 39.7, 39.0, 39.0, 38.9, 38.2, 36.9, 36.1, 33.8, 25.8, 18.1, 13.9, 5.6, -4.8, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 778.4339 [$(M+H)^+$; calcd for $C_{44}H_{66}O_9NSiNa$:778.4350].



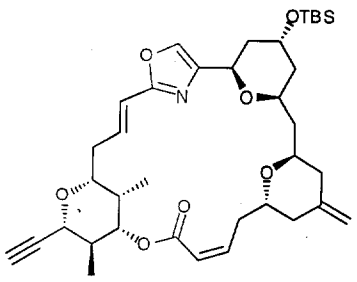
(+)-84

Alcohol (+)-84: To a solution of the dimethoxybenzyl ether (15.5 mg, 0.02 mmol) in methylene chloride (3 mL) was added pH = 7 buffer (0.3 mL) and DDQ (10.5 mg, 2.3 equiv). The reaction mixture was stirred for 40 min, poured into saturated $NaHCO_3$ (10 mL), and extracted with methylene chloride (3 x 10 mL). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography,

using EtOAc-hexanes (1:2 then 2:3) as eluant, gave (+)-**84** (11.6 mg, 93% yield): $[\alpha]_D^{20}$ +20.9 (*c* 0.57, $CHCl_3$); IR ($CHCl_3$) 3300 (w), 2950 (s), 1725 (s), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 2.2 Hz, 1 H), 7.44 (s, 1 H), 6.63 (ddd, *J* = 15.9, 8.2, 6.4 Hz, 1 H), 6.34 (d, *J* = 16.0 Hz, 1 H), 4.83 (dd, *J* = 9.6, 4.2 Hz, 1 H), 4.78 (s, 1 H), 4.77 (s, 1 H), 4.34 (m, 1 H), 4.26 (m, 1 H), 4.02 (m, 2 H), 3.72 (dd, *J* = 10.6, 2.1 Hz, 1 H), 3.48 (ddd, *J* = 11.9, 11.9, 8.7 Hz, 1 H), 3.39 (dd, *J* = 10.5, 4.8 Hz, 1 H), 2.62 (m, 2 H), 2.46 (m, 2 H), 2.36 (m, 3 H), 2.03 (m, 3 H), 1.92 (m, 1 H), 1.82 (m, 3 H), 1.63 (m, 1 H), 1.49 (m, 2 H), 1.09 (d, *J* = 6.5 Hz, 3 H), 0.96 (d, *J* = 6.9 Hz, 1 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 160.8, 143.2, 141.0, 135.1, 134.2, 118.9, 111.2, 81.5, 78.6, 76.1, 73.5, 72.8, 69.7, 69.1, 67.4, 67.3, 64.7, 47.8, 39.7, 39.0, 38.9, 38.2, 38.1, 38.0, 35.9, 25.8, 18.1, 13.5, 5.4, -4.8, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 628.3646 [$(M+H)^+$; calcd for $C_{35}H_{54}O_7NSi$: 628.3669].

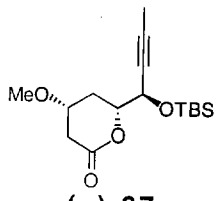


To a solution of alcohol (+)-**84** (11 mg, 0.0175 mmol) in methylene chloride (2 mL) was added acid **85** (26 mg) in methylene chloride (1 mL), EDCI·MeI (26 mg, 5 equiv) and HOBT (1 mg). The reaction mixture was stirred for 20 min and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:1) as eluant, gave the phosphonate aldehyde (11.1 mg, 70% yield) as an oil: $[\alpha]_D^{20}$ +7.0 (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 2910 (s), 1725 (s), 1260 (s), 1180 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.78 (t, *J* = 2.2 Hz, 1 H), 7.44 (s, 1 H), 6.60 (ddd, *J* = 16.0, 8.2, 6.4 Hz, 1 H), 6.34 (d, *J* = 16.1 Hz, 1 H), 4.84 (dd, *J* = 8.8, 5.2 Hz, 1 H), 4.76 (s, 1 H), 4.75 (s, 1 H), 4.70 (dd, *J* = 11.1, 4.8 Hz, 1 H), 4.45 (m, 4 H), 4.26 (m, 1 H), 4.12 (m, 1 H), 3.81 (dd, *J* = 10.6, 2.2 Hz, 1 H), 3.78 (m, 1 H), 3.56 (m, 1 H), 3.49 (m, 1 H), 3.20 (d, *J* = 21.4 Hz, 2 H), 2.62 (dd, *J* = 7.6, 2.3 Hz, 1 H), 2.59 (dd, *J* = 7.6, 2.6 Hz, 1 H), 2.51 (d, *J* = 2.1 Hz, 1 H), 2.50 (dd, *J* = 4.8, 2.1 Hz, 1 H), 2.32 (m, 1 H), 2.25 (d, *J* = 12.4 Hz, 1 H), 2.10 (m, 1 H), 1.98 (m, 6 H), 1.84 (m, 2 H), 1.62 (m, 1 H), 1.53 (m, 2 H), 1.02 (d, *J* = 8.5 Hz, 3 H), 0.97 (d, *J* = 6.9 Hz, 3 H), 0.90 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 163.9, 160.7, 143.6, 143.2, 134.4, 134.3, 119.2, 103.4, 80.8, 79.9, 78.2, 75.4, 74.0, 73.5, 72.7, 68.9, 67.4, 64.8, 62.8, 62.8, 62.5, 62.5, 62.3, 49.7, 42.4, 40.5, 40.3, 39.0, 38.1, 35.7, 35.6, 35.3, 29.7, 25.8, 17.7, 13.3, 5.9, -4.8, -4.9; high resolution mass spectrum (CI, NH_3) *m/z* 914.3534 [$(M+H)^+$; calcd for $C_{40}H_{59}O_{11}NSiF_6P$: 914.3499].



(+)-86

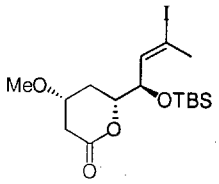
Macrocycle (+)-86: To a solution of 18-crown-6 (75 mg, excess) in toluene (5 mL) was added potassium carbonate (20 mg, excess) and stirred for 3 h. The reaction mixture was cooled to –40 °C; the phosphonate aldehyde (10 mg, 0.0109 mmol) in toluene (2 mL) was then added *via* cannula. The reaction mixture was warmed to –10 °C, stirred for 3 h, poured into water (10 mL), and extracted with Et_2O (2 x 10 mL). The combined extracts were dried over $MgSO_4$, and concentrated *in vacuo*. Purification *via* flash chromatography, using EtOAc/hexanes (1:3) as eluant, gave (+)-**86** (5.2 mg, 76% yield, 4:1, Z :E): $[\alpha]_D^{20}$ +11.3 (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 2980 (s), 1720 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 1 H), 6.64 (m, 1 H), 6.28 (d, *J* = 15.8 Hz, 1 H), 5.91 (m, 2 H), 4.97 (s, 1 H), 4.71 (dd, *J* = 7.0, 6.8 Hz, 1 H), 4.60 (s, 1 H), 4.42 (dd, *J* = 11.1, 4.3 Hz, 1 H), 4.28 (m, 1 H), 4.14 (m, 1 H), 4.04 (m, 1 H), 3.95 (m, 1 H), 3.84 (d, *J* = 8.5 Hz, 1 H), 3.46 (m, 2 H), 2.70 (d, *J* = 12.0 Hz, 1 H), 2.58 (m, 1 H), 2.52 (s, 1 H), 2.40 (m, 2 H), 2.31 (m, 2 H), 2.05 (m, 3 H), 1.83 (m, 3 H), 1.40 (m, 2 H), 1.00 (d *J* = 6.5 Hz, 3 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 0.62 (s, 3 H), 0.60 (s, 3 H); high resolution mass spectrum (CI, NH_3) *m/z* 652.3680 [$(M+H)^+$; calcd for $C_{37}H_{54}O_7NSi$: 652.3669].



(–)-97

TBS Lactone (–)-97. To a solution of (–)-**112** (77.1 mg, 0.389 mmol) in DMF (800 μL) was added imidazole (110 mg, 4 equiv) and TBSCl (120 mg, 2 equiv). After 2.5 h, the reaction mixture was quenched with 5 % $NaHCO_3$ and diluted with Et_2O (30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL). The collected organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4 then 1:2) as eluant, afforded (–)-**97** (112 mg, 92 % yield) as a clear oil; $[\alpha]_D^{23}$ -14.9 (*c* 0.69, $CHCl_3$); IR ($CHCl_3$) 2920 (m), 2840 (s), 2215 (w), 1735 (s), 1455 (m), 1385 (m), 1240 (s), 1100 (s), 830 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.55 (dq, *J* = 5.2, 2.1 Hz, 1H), 4.15 (ddd, *J* = 11.5, 5.3, 3.7 Hz, 1H), 3.76-3.70 (m, 1 H), 3.36 (s, 3 H), 2.90 (ddd, *J* = 17.2, 5.7, 1.2 Hz, 1 H), 2.47-2.43 (m, 1 H), 2.47 (dd, *J* = 17.1, 8.3 Hz, 1 H), 1.82 (d, *J* = 2.0 Hz, 3 H), 1.75 (ddd, *J* = 13.6, 11.6, 10.0 Hz, 1 H), 0.89 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 83.5, 79.0, 76.5, 72.4, 65.5, 56.2,

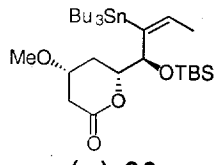
37.1, 29.9, 26.0, 18.4, 3.8, -4.5, -4.8; high resolution mass spectrum *m/z* 313.1832 [(M+H)$^+$; calcd for $C_{16}H_{29}O_4Si$: 313.1835].



(–)-13

Vinyl iodide (–)-13. To a solution of (–)-**97** (7.7 mg, 0.0246 mmol) in benzene (2 mL) was added $PdCl_2(PPh_3)_2$, followed by the slow dropwise addition of Bu_3SnH (50 μL) until TLC indicated consumption of starting material. The reaction mixture was concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:19 then 3:17) as eluant, afforded stannanes **98/99**, which were used without further purification.

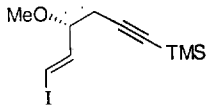
To a solution of the stannanes in methylene chloride at 0 °C was added a solution of I_2 in methylene chloride dropwise until a light purple color persisted. After 5 min, saturated Na_2SO_3 (5 mL), saturated $NaHCO_3$ (5 mL), and methylene chloride (10 mL) were added. After stirring for 5 min, the aqueous layer was extracted with methylene chloride (2 x 20 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography, using E_{tOAc}-hexanes (1:4 then 3:7) as eluant, aff$_{or}$ded (–)-13 (7.8 mg, 72% over 2 steps) and (–)-99 (3.0 mg, 20%). (–)-13: [_] EQ \o(23,D) -18.9 (c 0.35, CHCl3); IR (CHCl3) 2940 (s), 2915 (s), 2840 (s), 1735 (s), 1635 (w), 1460 (m), 1375 (m), 1355 (m), 1250 (s), 1100 (s), ^{835} (s) ^{c}m-1; 1H NMR (500 MHz, $CDCl_3$) δ 6.17 (dq, *J* = 8.9, 1.4 Hz, 1 H), 4.45 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.11 (ddd, *J* = 11.9, 4.7, 3.3 Hz, 1H), 3.72-3.67 (m, 1 H), 3.35 (s, 3 H), 2.87 (ddd, *J* = 17.2, 5.8, 1.3 Hz, 1 H), 2.46 (d, *J* = 1.3 Hz, 3 H), 2.44 (dd, *J* = 17.2, 8.1 Hz, 1 H), 2.32-2.25 (m, 1 H), 1.55 (ddd, *J* = 13.3, 11.9, 9.6 Hz, 1 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 139.2, 98.6, 79.1, 72.3, 71.0, 56.0, 36.7, 29.7, 28.9, 25.7, 18.2, -4.6, -4.9; high resolution mass spectrum *m/z* 441.0950 [(M+H)$^+$; calcd for $C_{16}H_{30}O_4ISi$: 441.0958].



(–)-99

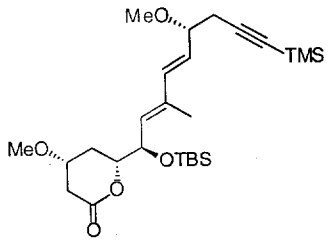
(–)-99: $[\alpha]_D^{23}$ -2.8 (*c* 0.18, $CHCl_3$); IR ($CHCl_3$) 2940 (s), 2920 (s), 2820 (s), 1730 (s), 1455 (m), 1370 (m), 1350 (m), 1240 (s), 1090 (s), 830 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73 (q, *J* = 6.9 Hz, 1 H), 4.74 (d, *J* = 7.5 Hz, 1H), 3.90 (ddd, *J* = 14.9, 7.4, 2.8 Hz, 1H), 3.65-3.58 (m, 1 H), 3.31 (s, 3 H), 2.82 (dd, *J* = 17.1, 5.8 Hz, 1 H),, 2.46 (dd, *J* = 17.2, 7.5 Hz, 1 H), 2.17-2.12 (m, 1 H), 1.75 (d, *J* = 6.7 Hz, 3 H), 1.48-1.41 (m, 7 H), 1.35-1.25 (m, 6 H), 0.94-0.84 (m, 15 H), 0.88 (s, 9 H), 0.13 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 169.6, 145.3, 136.7, 80.8, 74.5, 72.6, 56.0, 36.6, 30.9, 29.1, 27.5, 26.0, 18.3, 16.0, 13.7, 10.9, -4.3, -4.4. high resolution mass spectrum (ESI) *m/z* 627.2885 [$(M+Na)^+$; calcd for $C_{28}H_{56}NaO_4SiSn$: 627.2868].



(–)-123

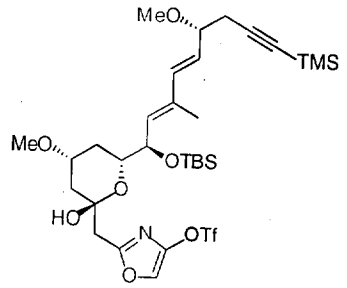
Vinyl iodide (–)-123. To a solution of (–)-**14** (8.6 mg, 0.0188 mmol) in methylene chloride (500 μL) was added a solution of I_2 in methylene chloride (5 mL). When a purple color persisted, $NaSO_3$ (10 mL), $NaHCO_3$ (10 mL), and methylene chloride (20 mL) were added. The aqueous solution was extracted with methylene chloride (3 x 15 mL); the combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (3:97) as eluant, gave (–)-**123** (5.6 mg, 97%) as a clear oil. $[\alpha]_D^{23}$ -34.3 (*c* 0.54, $CHCl_3$); IR ($CHCl_3$) 2940 (m), 2905 (m), 2800 (m), 2160 (m), 1600 (m), 1460 (w), 1345 (m), 1240 (s), 1100 (s), 930 (m), 835 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.48 (dd, *J* = 14.5, 7.1 Hz, 1 H), 6.40 (d, *J* = 14.6 Hz, 1 H), 3.71 (ddd, *J* = 7.3, 7.3, 5.6 Hz, 1 H), 3.32 (s, 3 H), 2.52 (dd, *J* = 16.8, 5.6 Hz, 1 H), 2.39 (dd, *J* = 16.8, 7.5 Hz, 1 H), 0.15 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 102.1, 87.5, 82.3, 79.0, 57.0, 26.1, 0.1; high resolution mass spectrum *m/z* 307.0004 [$(M-H)^+$; calcd for $C_{10}H_{16}OSiI$: 307.0002].



(–)-102

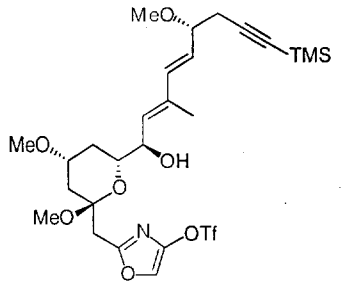
Diene (–)-102: To a solution of stannane (–)-**14** (162 mg, 1.4 equiv) and iodide (–)-**13** (110 mg, 0.250 mmol) in DMF (2.0 mL) was added $Ph_2PO_2NBu_4$ (115 mg, 1 equiv). This solution was degassed with 6 cycles of evacuation/backfilling with argon. $Pd_2(dba)_3$•$CHCl_3$ (8 mg, 0.03 equiv) was added, followed by 6 more degassing cycles. After 3.5 h, EtOH was added (20 mL), and the reaction mixture was filtered through Celite. After concentration, the reaction mixture was dissolved in Et_2O (20 mL), filtered through Celite, washed with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (3:17 then 1:3) as eluant, to afford (–)-**102** (114.1 mg, 92 %) as a clear oil: $[\alpha]_D^{23}$ -18.1 (*c* 0.54, $CHCl_3$); IR ($CHCl_3$) 2940 (s), 2920 (s), 2840 (s), 2160 (m), 1730 (s), 1445 (m), 1335 (m), 1250 (s), 1090 (s), 835 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (d, *J* = 15.7 Hz, 1 H), 5.59 (dd, *J* = 15.6, 7.6 Hz, 1 H), 5.45 (d, *J* = 8.0 Hz, 1 H), 4.61 (dd, *J* = 8.0, 4.9 Hz, 1H), 4.13 (ddd, *J* = 12.0, 4.8, 3.2 Hz, 1H), 3.76 (ddd, *J* = 7.4, 7.4, 7.4 Hz, 1H), 3.69-3.65 (m, 1 H), 3.33 (s, 3 H), 3.29 (s, 3 H), 2.86 (ddd, *J* = 17.2,

5.8, 1.4 Hz, 1 H), 2.57 (dd, J = 16.7, 5.2 Hz, 1 H), 2.42 (dd, J = 17.2, 8.1 Hz, 1 H), 2.41 (dd, J = 16.7, 7.3 Hz, 1 H), 2.28-2.22 (m, 1 H), 1.81 (d, J = 1.0 Hz, 3 H), 1.58-1.52 (m, 1 H), 0.86 (s, 9 H), 0.11 (s, 9 H), 0.06 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 136.8, 135.5, 130.3, 128.6, 103.2, 86.7, 80.6, 80.1, 72.4, 70.4, 56.7, 56.0, 36.7, 30.1, 27.0, 25.8, 18.1, 13.4, 0.1, -4.4, -4.8. high resolution mass spectrum *m/z* 517.2792 [(M+Na)$^+$; calcd for $C_{26}H_{46}NaO_5Si_2$: 517.2782].

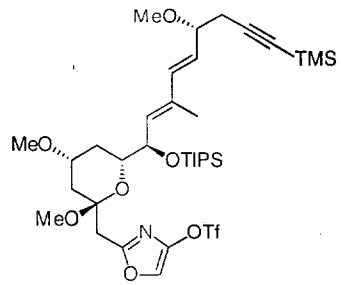


(+)-111

Oxazole Adduct (+)-111: Lactone (–)-**102** (23.9 mg, 0.0483 mmol) and oxazole **15b** (150 mg, 10 equiv) were dissolved in benzene and concentrated *in vacuo*, then redissolved in THF, and cooled to –78 °C. With good stirring, *i*-PrMgCl (2.0 M in THF, 121 μL, 5 equiv) was added dropwise. The solution was warmed to –20 °C over 30 min and stirred at that temperature for 3.5 h. The reaction was quenched with 5% $NaHCO_3$ solution (40 mL) and diluted with Et_2O (50 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL); the collected organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:4) as eluant, gave recovered (–)-**102** (5.2 mg, 22%) as well as (+)-**111** (24.4 mg, 70%) as a clear oil: $[\alpha]_D^{23}$ +11.1 (*c* 0.61, $CHCl_3$); IR ($CHCl_3$) 3500 (br, w), 2910 (m), 2410 (w), 2150 (w), 1590 (m), 1430 (s), 1230 (s), 1130 (s), 1080 (s), 840 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (s, 1H), 6.21 (d, J = 15.7 Hz, 1 H), 5.48 (dd, J = 15.7, 7.7 Hz, 1 H), 5.32 (d, J = 9.0 Hz, 1 H), 4.36 (dd, J = 9.0, 5.6 Hz, 1H), 3.93 (d, J = 2.2 Hz, 1 H), 3.81 (ddd, J = 12.3, 6.0, 2.2 Hz, 1H), 3.77 (dddd, J = 11.1, 11.1, 4.7, 4.4 Hz, 1H), 3.71-3.67 (m, 1 H), 3.34 (s, 3 H), 3.31 (s, 3 H), 3.08 (d, J = 15.2 Hz, 1H), 3.04 (d, J = 15.2 Hz, 1H), 2.58 (dd, J = 16.7, 5.5 Hz, 1 H), 2.42 (dd, J = 16.7, 7.2 Hz, 1 H), 2.28 (ddd, J = 6.1, 4.5, 1.6 Hz, 1 H), 2.08-2.04 (m, 1 H), 1.64 (d, J = 1.1 Hz, 3 H), 1.31-1.26 (m, 1 H), 1.08 (app q, J = 11.5 Hz, 1 H), 0.80 (s, 9 H), 0.11 (s, 9 H), -0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 144.6, 137.4, 134.2, 132.2, 127.5, 126.6, 118.6 (q), 103.3, 96.6, 86.6, 80.7, 73.5, 73.2, 71.1, 56.6, 55.6, 40.9, 40.1, 31.9, 26.9, 25.8, 18.1, 13.1, 0.1, -4.6, -5.0. high resolution mass spectrum *m/z* 748.2580 [(M+Na)$^+$; calcd for $C_{31}H_{50}F_3NNaO_9SSi_2$: 748.2580].



To a solution of adduct (+)-**111** (38.7 mg, 0.0533 mmol) in MeOH (7 mL) was added *p*-TSA (6 mg, 0.6 equiv). After stirring overnight, 5% $NaHCO_3$ (40 mL) and Et_2O (50 mL) were added. The aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (2 x 30 mL) dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (2:3) as eluant, gave the deprotected methyl ketal (23.7 mg, 71%) as a clear oil: $[\alpha]_D^{23}$ -46.3 (*c* 0.40, $CHCl_3$); IR ($CHCl_3$) 3550 (br), 2920 (m), 2420 (w), 2150 (w), 1590 (s), 1425 (s), 1230 (s), 1130 (s), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 6.25 (d, *J* = 15.8 Hz, 1 H), 5.64 (dd, *J* = 15.7, 7.2 Hz, 1 H), 5.44 (d, *J* = 8.9 Hz, 1 H), 4.37 (dd, *J* = 7.7, 7.7 Hz, 1H), 3.78 (dd, *J* = 6.9, 6.9 Hz, 1 H), 3.61-3.58 (m, 1 H), 3.48 (ddd, *J* = 12.0, 7.0, 2.1 Hz, 1H), 3.30 (s, 3 H), 3.29 (s, 6 H), 3.24 (d, *J* = 14.9 Hz, 1 H), 3.07 (d, *J* = 14.9 Hz, 1H), 2.54 (dd, *J* = 16.8, 5.8 Hz, 1 H), 2.49 (br s, 1 H), 2.40 (dd, *J* = 16.8, 6.8 Hz, 1 H), 2.20 (ddd, *J* = 12.7, 4.6, 1.6 Hz, 1 H), 1.95-1.90 (m, 1 H), 1.83 (d, *J* = 1.1 Hz, 3 H), 1.38 (dd, *J* = 12.7, 11.1 Hz, 1 H), 1.11 (app q, *J* = 12.0 Hz, 1 H), 0.12 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 145.0, 137.6, 136.4, 129.5, 128.9, 127.0, 118.6 (q), 103.1, 99.8, 86.7, 80.4, 73.4, 72.8, 71.1, 56.8, 55.7, 48.2, 39.2, 36.0, 32.7, 27.1, 13.4, 0.1; high resolution mass spectrum *m/z* 648.1881 [$(M+Na)^+$; calcd for $C_{26}H_{38}F_3NNaO_9SSi$: 648.1886].



(–)-10

Final Side Chain (–)-10. To a 0 °C solution of the hemiketal (19.0 mg, 0.0304 mmol) in methylene chloride (2 mL) was added a solution of lutidine (42 μL, 12 equiv) and TIPSOTf (41 μL, 5 equiv) in methylene chloride (1 mL) *via* cannula. After 3 h, the reaction was quenched with 5% $NaHCO_3$ (50 mL) and Et_2O (50 mL), and the aqueous layer was extracted with Et_2O (3 x 30 mL). The organic layers were washed with brine (40 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexanes (1:9) as eluant, gave (–)-**10** (21.3 mg, 90%) as a clear oil: $[\alpha]_D^{23}$ -39.6 (*c* 1.12, $CHCl_3$); IR

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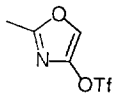
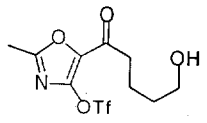
($CHCl_3$) 2950 (s), 2850 (s), 2150 (m), 1720 (w), 1585 (m), 1430 (s), 1230 (s), 1130 (s), 1080 (s), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 6.22 (d, J = 15.7 Hz, 1 H), 5.56 (dd, J = 15.7, 7.5 Hz, 1 H), 5.40 (d, J = 8.9 Hz, 1 H), 4.60 (dd, J = 8.9, 6.1 Hz, 1H), 3.76 (app q, J = 5.9 Hz, 1 H), 3.59-3.51 (m, 2 H), 3.30 (s, 3 H), 3.29 (s, 3 H), 3.28 (s, 3 H), 3.21 (d, J = 14.9 Hz, 1H), 2.96 (d, J = 14.9 Hz, 1H), 2.57 (dd, J = 16.8, 5.7 Hz, 1 H), 2.42 (dd, J = 16.8, 7.1 Hz, 1 H), 2.17 (ddd, J = 12.7, 4.6, 1.6 Hz, 1 H), 2.00 (ddd, J = 12.1, 4.2, 2.2 Hz, 1 H), 1.76 (d, J = 0.9 Hz, 3 H), 1.34 (dd, J = 12.6, 11.1 Hz, 1 H), 1.04-1.01 (m, 22 H), 0.06 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 144.8, 137.0, 134.3, 132.7, 127.8, 126.9, 118.5 (q), 103.3, 99.7, 86.5, 80.6, 74.1, 73.3, 71.6, 56.6, 55.5, 47.9, 39.2, 36.0, 31.9, 27.0, 18.0, 13.6, 12.4, 0.1; high resolution mass spectrum *m/z* 804.3232 [$(M+Na)^+$; calcd for $C_{35}H_{58}F_3NNaO_9SSi_2$: 804.3221].



15a

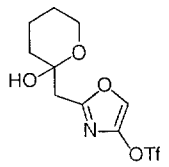
Oxazole Triflate 15a. To a well-stirred, foil-covered suspension of silver isocyanate (420 mg, 2.80 mmol) in Et_2O (10 mL) was added acetyl chloride (220 μL, 1.1 equiv). After 3.5 h, the yellow suspension was filtered through a frit under argon. An alcohol-free diazomethane solution was added dropwise until a yellow color persisted, at which point argon was blown in until clear and the solution was concentrated *in vacuo*. The solution was redissolved in THF (10 mL), cooled to –78 °C, and charged with Et_3N (1.17 mL, 3 equiv) and trifluoroacetic anhydride (565 μL, 1.2 equiv). The solution was warmed to rt over 45 min, poured into Et_2O (40 mL), filtered though Celite, and concentrated *in vacuo*. Flash chromatography, using hexanes:Et_2O:methylene chloride (2:1:1) as eluant, gave **15a** (309 mg, 48 %) as a clear oil: IR ($CHCl_3$) 3175 (w), 3130 (w), 1590 (s), 1420 (s), 1325 (s), 1270 (s), 1230 (s), 1130 (s), 850 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1 H), 2.45 (s, 3 H); ^{13}C NMR (125 MHz, CDCl3) δ 160.2, 144.8, 126.3, 118.6 (q, J = 321 Hz), 14.3; high resolution mass spectrum m/z 231.9895 [(M+H)+; calcd for $C_5H_5F_3NO_4S$: 231.9891].



109

Triflate Adduct 109. To a –78 °C solution of oxazole **15a** (42.8 mg, 1.5 equiv) in THF (2 mL) was added *t*-BuLi (1.7 M in pentane, 109 μL, 1.5 equiv). After 5 min, a –78 °C solution of δ-valerolactone (12.6 mg, 0.126 mmol) in THF (1 mL) was added. The reaction was quenched after 40 min with 5 % $NaHCO_3$ (30 mL), diluted with Et_2O (30 mL), and extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using

EtOAc-hexanes (1:1), gave **109** (24.6 mg, 59%) as a clear oil: IR (neat) 3442 (br), 2943 (m), 1731 (m), 1694 (m), 1599 (m), 1434 (m), 1336 (m) cm^{-1}; ^1H NMR (500 MHz, CDCl3) δ 4.31 (t, J = 5.5 Hz, 2 H), 3.64 (t, J = 6.3 Hz, 2 H), 2.83 (t, J = 7.2 Hz, 2 H), 2.53 (s, 3 H), 1.82-1.73 (m, 2 H), 1.65-1.57 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.8, 161.6, 145.5, 136.8, 118.6, 62.2, 39.2, 31.8, 19.4, 14.8; high resolution mass spectrum *m/z* 354.0227 [$(M+Na)^+$; calcd for $C_{10}H_{12}F_3NNaO_6S$: 354.0235].



110

Triflate Adduct 110. Oxazole **15b** (60.0 mg, 3 equiv) was dissolved in methylene chloride (5 mL) and Et_3N (1 drop) and concentrated *in vacuo*. δ-Valerolactone (6.5 μL, 0.065 mmol) was added to the oxazole, which was then redissolved in THF (1.4 mL), and cooled to –78 °C. With good stirring, *i*-PrMgCl (1.9 M in THF, 65 μL, 2 equiv) was added dropwise. After 30 min, the reaction was quenched with 5% $NaHCO_3$ solution (20 mL) and diluted with Et_2O (20 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL); the collected organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Flash chromatography, using EtOAc-hexane (1:1) as eluant, gave **110** (14.1 mg, 66%) as a clear oil: IR (neat) 3417 (br), 2948 (m), 1728 (m), 1595 (m), 1434 (s), 1226 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 1H), 3.96-3.88 (m, 2 H), 3.67 (d, J = 2.3 Hz, 1 H), 3.59-3.51 (m, 2 H), 3.06 (d, J = 15.2 Hz, 1H), 2.98 (d, J = 15.2 Hz, 1H), 2.57 (t, J = 9 Hz, 1 H), 1.9-1.5 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 144.6, 126.7, 94.7, 61.6, 41.0, 34.2, 24.9, 19.7, 18.6. high resolution mass spectrum *m/z* 354.0250 [$(M+Na)^+$; calcd for $C_{10}H_{12}F_3NNaO_6S$: 354.0235].