PHORBOXAZOLE SYNTHETIC STUDIES. 1. CONSTRUCTION OF A C(3-19) SUBTARGET EXPLOITING AN EXTENSION OF THE PETASIS-FERRIER REARRANGEMENT.

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Experimental Section

Materials and Methods. All reactions were carried out under argon with dry, freshly distilled solvents, vacuum-flamed glassware, and magnetic stirring, unless otherwise stated. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone; benzene and toluene were distilled from sodium, and dichloromethane (CH_2Cl_2) from calcium hydride. Triethylamine and pyridine were distilled from calcium hydride and stored over KOH.

All reactions were monitored by thin layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Flash chromatography was performed with the indicated solvents and E. Merck silica gel 60 (particle size 0.040-0.063 mm). Yields refer to chromatographically and spectroscopically pure compounds, except as otherwise indicated.

All melting points were obtained on a Thomas-Hoover apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrophotometer. Proton and carbon NMR spectra were recorded on a Bruker AM-500 spectrometer. Chemical shifts are reported in δ values relative to tetramethylsilane. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter in the solvent indicated. High resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Center on either a VG Micromass 70/70H or VG ZAB-E spectrometer. Microanalyses were performed by the University of Pennsylvania elemental analysis center.

(+)-**11:** Obtained as a colorless 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].

12: Obtained 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.

(–)-**8:** Obtained 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}; ^1H 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.

(+)-**7:** To a solution of *R*-(+)-NOBIN (71.1 mg, 0.136 mmol) in toluene (24 mL) was added freshly distilled $Ti(OiPr)_4$ (18.2 μL, 0.0617 mmol), and the resulting orange solution was stirred for 1 h at room temperature. To this was added a solution of dry di-*tert*-butyl salicylic acid (31 mg, 0.123 mmol) in toluene (2 mL) via cannula, and stirring was continued for 1 h. The solution was cooled to -40°C. Trimethylsilyl chloride (78 μL, 0.617 mmol) and triethylamine (430 μL, 3.082 mmol) were added, followed by the addition of a solution of aldehyde **9** (762mg, 3.082 mmol) in toluene (15 mL) via cannula. After stirring for 20 minutes at -40 °C, silyl ketene acetal **14** (1.50 mL, 6.00 mmol) was added, and the solution was allowed to slowly warm to 0°C over 5 h, then to room temperature. The reaction mixture was poured into brine (50 mL) and EtOAc (50 mL). The aqueous layer was extracted EtOAc (2 x 30 mL); the collected organics were dried over Na_2SO_4, and concentrated in vacuo. This crude aldol product was dissolved in THF (10 mL), and a solution of tetrabutylammonium fluoride (1.0 M in THF, 5 mL, 5.0 mmol) was added, stirring for 15 minutes. The reaction mixture was poured into saturated ammonium chloride (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), washed with brine (100 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification via flash chromatography (40-60% ethyl acetate/hexane) gave (+)-**7** (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}; ^1H NMR (500 MHz, CDCl3) δ 7.55 (s, 1H), 7.35-7.29 (m, 5H), 7.25 (d, *J* = 8.6Hz, 2H), 6.86 (d, *J* = 8.6Hz, 2H), 5.16 (d, *J* = 12.4Hz, 1H), 5.13 (d, *J* = 12.4Hz, 1H), 5.11 (dd, *J*= 8.2, 3.9, 1H), 4.52 (s, 2H), 4.50 (s, 2H), 3.78 (s, 3H), 3.39 (br s, 1H), 2.94 (dd, *J* = 16.4, 3.9, 1H), 2.85 (dd, *J* = 16.6, 8.5, 1H); ^{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 $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found C, 66.90; H, 5.90; N, 3.45.

(–)-**16:** Obtained as a colorless 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, $CDCl_3$) δ 166.5, 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.

(–)-**6:** Obtained 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; high resolution mass spectrum (ES, NH_3) *m/z* 850.4208 [$(M+Na)^+$; calcd for $C_{47}H_{65}O_8NSi_2Na$: 850.4146].

5,5-dimethyl-2-(2-phenyl)ethyl-1,3-dioxan-4-one: To a solution of 2,2-dimethyl-3-hydroxy-propanoic acid (1.397 g, 13.7 mmol) in CH_2Cl_2 (13.7 mL) was added HMDS (2.43 g, 15 mmol). The reaction mixture was stirred for 12 h and solvent evaporated. Dihydrocinnamaldehyde

(2.76 g, 20.6 mmol) was added and the reactants dissolved in CH_2Cl_2 (40 mL). The reaction mixture was cooled to -78 °C, TMS-OTf (304 mg, 1.37 mmol) was added, and the reaction stirred for 2 h. The reaction was quenched with saturated $NaHCO_3$ (40 mL), extracted with CH_2Cl_2 (2 x 40 mL), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography (hexanes/ethyl acetate 9:1) gave the title compound (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, $CDCl_3$) δ 174.3, 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.

17: To a solution of 5,5-dimethyl-2-(2-phenyl)ethyl-1,3-dioxan-4-one (583 mg, 2.49 mmol) was added dimethyl titanocene (0.5 M in toluene, 9.96 mL, 4.98 mmol) 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. Purification via flash chromatography (basic alumina, hexanes 1% Et_3N) gave **17** (520 mg, 88% yield) as a yellow oil: IR ($CHCl_3$) 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, 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].

18 (X = OH, H): To a solution of enol ether **17** (93 mg, 0.394 mmol) in toluene (3.94 mL) at -78 °C was added triisobutylaluminum (0.787 mL, 1.0 M solution toluene, 0.788 mmol). The reaction mixture was slowly warmed to ambient temperature over 1 h and triisobutylaluminum (0.394 mL) was added. After 1 h, the reaction was poured into saturated aqueous $NaHCO_3$ (20

mL), extracted with ethyl acetate (3 x 20 mL), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography (hexanes/ethyl acetate 9:1) gave minor isomer trans-**18** (10 mg, 10% yield) and major isomer cis-**18** (60 mg, 75%) 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 C15H22O2, C, 76.88; H, 9.46. Found: C, 77.26; H, 9.85.

18 (X = O): To a solution of enol ether **17** (18 mg, 0.076 mmol) in CH_2Cl_2 (1.5 mL) at -78 °C was added dimethylaluminum chloride (1.0 M in hexanes, 76 μL, 0.076 mmol). The reaction mixture was stirred at -78 °C for 5 min, warmed to ambient temperature for 5 min, quenched with triethylamine (0.5 mL), poured into saturated aqueous $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 x 10ml), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography (hexanes/ethyl acetate 9:1) gave **18** (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].

(–)-**21:** To a solution of *R*-Binol (780 mg, 2.72 mmol), powdered 4A molecular sieves (5.24 g), and titanium tetraisopropoxide (386 mg, 1.36 mmol) in diethyl ether (40 mL) was added trifluoroacetic acid (6.5 mg, 0.057 mmol). The reaction mixture was heated at reflux for 1 h, cooled to ambient temperature and aldehyde **20** (3.87g, 13.6 mmol) in diethyl ether (14 mL) was added

via cannula. The reaction mixture was cooled to -78 °C followed by addition of 1-methoxy-3-(trimethylsilyl)oxy-1,3-butadiene (2.80g, 16.3 mmol). The reaction was warmed to -20 °C (45 h), followed by addition of saturated aqueous $NaHCO_3$ (10 mL) and the reaction mixture was filtered through Celite. The organic phase was washed with saturated aqueous $NaHCO_3$ (25 mL), dried over $MgSO_4$, filtered, and concentrated. The crude product was dissolved in CH_2Cl_2 (200 mL) and trifluoroacetic acid (0.68 mL) was added at 0 °C and stirred for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (50 mL), extracted with CH_2Cl_2 (3 x 25 mL), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography (hexanes/ethyl acetate 6:4) gave (–)-**21** (3.29 g, 63% yield, 88% ee) as a colorless oil: $[\alpha]_D^{20}$ -35.8˚ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980 (s) 1670 (s) 1595 (w) 1280 (s) 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4 H), 7.3 (m, 6 H), 7.26 (d, *J*= 6.0 Hz, 1 H). 5.37 (dd, *J*= 6.0, 1.0 Hz, 1H), 4.66 (m, 1 H), 3.85 (ddd, *J*= 13.0, 10.5, 8.2 Hz, 1 H), 3.78 (ddd, *J*= 10.7, 5.5, 5.3 Hz, 1 H), 2.46 (m, 2 H), 2.00 (m, 1 H), 1.88 (m, 1 H), 1.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 163.0, 135.5, 133.5, 129.8, 127.7, 107.1, 59.2, 41.9, 37.2, 29.8, 19.1; high resolution mass spectrum (CI, NH_3) *m/z* 381.1888 [$(M+H)^+$; calcd for $C_{23}H_{29}O_3Si$: 381.1885].

(–)-**22:** Obtained as a yellow oil; $[\alpha]_D^{20}$ -26.0˚ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2950 (s), 2860 (s), 1725 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.65 (t, *J* = 2.3 Hz, 1 H) 7.64 (m, 4 H), 7.38 (m, 6 H), 4.77 (s, 2 H), 4.20 (m, 1 H), 4.04 (m, 1 H), 3.74 (ddd, *J*= 10.3, 7.7, 5.9 Hz, 1 H), 3.67 (ddd, *J*= 10.4, 6.3, 5.5 Hz, 1 H), 2.61 (ddd, *J*= 16.2, 7.8, 2.6 Hz, 1 H) 2.44 (ddd, *J*= 16.2, 5.5, 1.9 Hz, 1 H), 2.36 (m, 2 H), 2.01 (m, 2 H), 1.88 (ddd, *J*= 14.0, 11.3, 8.4 Hz, 1 H), 1.65 (ddd, *J*= 14.0, 7.8, 6.4 Hz, 1 H) 1.03 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 141.1, 135.6, 133.9, 129.6, 127.6, 111.2, 69.7, 67.2, 60.4, 47.6, 39.6, 39.2, 35.6, 26.9, 19.2; high resolution mass spectrum (CI, NH_3) *m/z* 423.2339 [$(M+H)^+$; calcd for $C_{26}H_{35}O_3Si$: 423.2355].

(–)-**24:** Obtained as a colorless oil: $[\alpha]_D^{20}$ -25.7˚ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3450 (w), 2950 (s), 1740 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.37 (m, 6 H), 4.77 (s, 1 H),

4.71 (s, 1 H), 4.21 (m, 1 H), 4.05 (m, 1 H), 3.80 (m, 1 H), 3.73 (ddd, *J*= 13.6, 10.5, 4.6 Hz, 1 H), 3.65 (ddd, *J*= 12.0, 10.6, 6.2 Hz, 1 H), 2.48 (m, 2 H), 2.41 (dd, *J*= 13.3, 5.4 Hz 1 H), 2.22 (dd, *J*= 13.2, 3.4 Hz, 1 H), 1.89 (m, 1 H), 1.76 (dt, *J*= 14.4, 9.8 Hz, 1 H), 1.67 (m, 1 H), 1.54 (dt, *J*=14.4, 2.9 Hz, 1 H) 1.04 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 140.8, 135.6, 133.8, 133.6, 129.7, 127.7, 111.0, 71.7, 70.5, 67.8, 60.5, 41.3, 40.5, 35.5, 34.5, 26.9, 19.2; high resolution mass spectrum (ES, NH_3) *m/z* 505.2401 [$(M+Na)^+$; calcd for $C_{28}H_{38}O_5SiNa$: 505.2386].

(–)-**25:** To a solution of (–)-**24** (260 mg, 0.54 mmol) in CH_2Cl_2 (0.622 mL) was added HMDS (0.152 mL, 0.65 mmol) and the reaction mixture stirred for 12 h. Solvent and excess reagent were removed on high vacuum and the flask charged with aldehyde **9** (375 mg, 1.51 mmol), CH_2Cl_2 (7.55ml) and cooled to -78 °C. The TMS-OTf (20 μL, 0.108 mmol) was added and reaction mixture warmed to -25 °C for 65 h followed by addition of triethylamine (0.30 mL). The reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 mL), extracted with CH_2Cl_2 (3 x 25 mL), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography using silylated silica gel (elution gradient, ethyl ether/hexanes 6:4 to ethyl ether to ethyl acetate/hexanes 1:1 with 1% acetic acid) gave recovered aldehyde **9** (190 mg), recovered acid (–)-**24** (75 mg, 28.5 %) and dioxanone (–)-**25** as a separable 15 to 1 mixture (271 mg, 71% yield, 99% BORSM) as a colorless oil: $[\alpha]_D^{20}$ -27.0˚ (*c* 1.0, THF); IR (CCl_4) 2910 (s), 1760 (s), 1110 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.78 (m, 4H), 7.40 (s, 1 H), 7.29 (m, 6 H), 7.17 (m, 2 H), 6.75 (dd, *J* = 6.6, 2.0 Hz, 2 H), 5.90 (s, 1 H), 4.68 (s, 2 H), 4.33 (s, 2 H), 4.28 (s, 2 H), 3.92 (m, 1 H), 3.77 (m, 2 H), 3.69 (m, 1 H), 3.55 (m, 1 H) 3.31 (s, 3 H), 2.34 (dd, J= 17.6, 4.8 Hz, 1 H), 2.22 (dd, J= 17.6, 10.4 Hz, 1 H), 2.16 (dd, J= 13.1, 4.3 Hz, 1 H), 2.02 (dd, J= 13.2, 4.2 Hz, 1 H), 1.95 (ddd, J=14.3, 9.0, 5.4 Hz, 1 H), 1.8 (m, 2 H), 1.71 (dd, J= 13.2, 6.6 Hz, 1 H), 1.59 (m, 1 H), 1.17 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 165.4. 161.9, 159.9, 142.0, 138.4, 137.5, 135.9, 134.2, 134.1, 130.1, 129.8, 129.8, 128.5, 128.5, 114.2, 110.6, 97.0, 72.4, 72.1, 69.2, 67.5, 63.3, 61.0, 54.8, 39.7, 39.6, 39.1, 36.3, 36.2, 27.1, 19.4; high resolution mass spectrum (CI, NH_3) *m/z* 712.3302 [$(M+H)^+$; calcd for $C_{41}H_{50}O_8NSi$: 712.3306].

(–)-**26:** To a solution of dioxanone (–)-**25** (157 mg, 0.221 mmol) was added freshly prepared dimethyl titanocene (2.20 mL, 0.5 M THF, 1.11 mmol) and the reaction mixture heated at 65 °C for 16 h. The reaction mixture was placed directly onto basic alumina (activated 10% by weight H_2O). Purification via flash chromatography (ethyl ether/hexanes 1:3 with 1% Et_3N) gave (–)-**26** (20 mg, 74% yield) as a yellow oil: $[\alpha]_D^{20}$ -11.4˚ (*c* 1.0, THF); IR (CCl_4) 2920 (s)1665 (w), 1610 (w), 1190 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.81 (m, 4 H), 7.58 (S, 1 H), 7.28 (m, 6 H), 7.17 (m, 2 H), 6.75 (dd, *J* = 6.6, 2.0 Hz, 2 H), 5.76 (s, 1 H), 4.72 (d, J= 1.7 Hz, 1 H), 4.7 (s, 1 H), 4.7 (s, 1 H), 4.34 (s 2 H), 4.31 (s, 2 H), 3.95 (m, 1 H), 3.81 (m, 4 H), 3.31 (s, 3 H), 2.20 (m, 4 H), 2.06 (dd, J= 13.8, 2.7 Hz, 1 H), 1.85 (m, 3 H), 1.60 (m, 1 H), 1.42 (m, 1 H), 1.19 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 161.4, 159.8, 156.6, 142.4, 139.8, 137.4, 136.0, 134.2, 130.0, 129.0, 128.2, 114.1, 110.4, 97.5, 94.1, 74.2, 72.2, 69.0, 67.9, 63.4, 61.1, 54.7, 40.0, 39.7, 39.2, 36.9, 34.9, 30.5, 27.1, 19.4; high resolution mass spectrum (CI, NH_3) *m/z* 710.3508 [$(M+H)^+$; calcd for $C_{42}H_{52}O_7NSi$: 710.3513].

(–)-**27:** To a solution of enol ether (–)-**26** (20 mg, 0.028 mmol) in CH_2Cl_2 (0.535 mL) at -78 °C was added dimethyl aluminum chloride (1.0M hexanes, 28 μL, 0.033 mmol). After 5 min the reaction mixture was warmed to ambient temperature with a water bath (1 min), quenched with saturated aqueous $NaHCO_3$ (5 mL), extracted with CH_2Cl_2 (3 x 10 mL), dried ($MgSO_4$), filtered and concentrated. Purification via flash chromatography (hexanes, ethyl acetate 2:1) gave (–)-**27** (17.8 mg, 89% yield) as an oil: $[\alpha]_D^{20}$ -15.0˚ (*c* 0.23, $CHCl_3$); IR ($CHCl_3$) 2940 (s), 1720 (s), 1105 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.49 (s, 1 H), 7.38 (m, 6 H), 7.25 (m, 2 H), 6.87 (dd, *J*= 6.6, 2.1 Hz, 2 H), 4.72 (s, 2 H), 4.52 (s, 2 H), 4.51 (s, 2 H), 4.5 (m, 1 H), 4.00 (m, 1 H), 3.92 (m, 1 H), 3.82 (m, 1 H), 3.79 (s, 3 H), 3.74 (m, 1 H), 3.67 (m, 1 H), 2.69 (dd, *J*=14.4, 11.8 Hz, 1 H) 2.58 (dt, *J*= 14.3, 2.6 Hz, 1 H), 2.49 (ddd, *J*= 14.5, 2.3, 2.1 Hz, 1 H), 2.33 (m, 3 H), 2.16 (m, 1 H), 2.02 (m, 2 H), 1.78 (m, 1 H), 1.65 (m, 2 H), 1.04 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6, 161.3, 159.5, 141.7, 140.4, 135.9, 135.5, 133.9, 129.7, 129.6, 129.2, 127.7, 113.9, 110.5,

74.3, 72.3, 72.8, 71.7, 69.0, 68.2, 63.5, 60.5, 55.3, 47.2, 46.3, 39.6, 39.5, 39.4, 36.4, 26.9, 19.2; high resolution mass spectrum (ES, NH_3) *m/z* 732.3359[$(M+Na)^+$; calcd for $C_{42}H_{51}O_7NSiNa$: 732.3333].

(–)-**28:** Obtained as a colorless oil: $[\alpha]_D^{20}$ -11.3° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2940 (s), 1500 (w), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.48 (s, 1 H), 7.37 (m, 6 H), 7.26 (d, *J*= 8.6 Hz, 2 H), 6.86 (dd, *J*= 6.7, 2.1 Hz, 2 H), 4.84 (dd, *J*= 11.5, 1.8 Hz, 1 H), 4.70 (s, 2 H), 4.52 (s, 2 H), 4.51 (s, 2 H), 4.24 (m, 1 H), 3.99 (m, 3 H), 3.78 (s, 3 H), 3.71 (ddd, *J*=12.9, 9.3, 6.1 Hz, 1 H), 3.67 (ddd, *J*= 12.0, 10.3, 6.1 Hz, 1 H), 2.34 (dd, *J*= 13.2, 4.5 Hz, 1 H), 2.29 (dd, *J*= 13.2, 4.1 Hz, 1 H), 2.02 (dd, *J*= 13.2, 5.8 Hz, 1 H), 1.95 (dd, *J*=13.2, 6.9 Hz, 1 H), 1.88 (m, 2 H), 1.78 (m, 2 H), 1.65 (m, 2H), 1.02 (s, 9 H), 0.90 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 159.5, 142.7, 142.3, 135.6, 134.0, 133.9, 129.7, 129.5, 129.2, 127.6, 113.9, 110.1, 72.6, 69.1, 68.8, 67.5, 64.7, 63.7, 60.7, 55.3, 39.7, 39.6, 39.3, 39.2, 39.0, 38.3, 36.6, 26.9, 25.8, 19.2, 18.1, -4.8, -4.9 ; high resolution mass spectrum (ES, NH_3) *m/z* 848.4363 [$(M+Na)^+$; calcd for $C_{48}H_{67}O_7NSi_2Na$: 848.4354].

(–)-**5:** Obtained as a colorless oil: $[\alpha]_D^{20}$ -7.2° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 2940 (s) 1460 (w), 1100 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.50 (s, 1 H), 7.37 (m, 6 H), 4.79 (d, *J* = 11.2 Hz, 1 H), 4.71 (m, 2 H), 4.26 (m, 3 H), 4.00 (m, 2 H), 3.93 (m, 1 H), 3.75 (ddd, J=13.0, 10.3, 7.0 Hz, 1 H), 3.67 (ddd, J= 12.0, 10.4, 6.0 Hz, 1 H), 2.60 (m, 6 H), 2.32 (m, 2 H), 2.02 (dd, J=13.2, 5.8 Hz, 1 H), 1.96 (dd, J= 13.2, 6.8 Hz, 1 H), 1.84 (m, 3 H), 1.65 (m, 6 H), 1.53 (m, 11 H), 1.44 (m, 2 H), 1.02 (s, 9 H), 0.96 (s, 9 H), 0.93 (m, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 144.1, 142.2, 136.4, 135.5, 133.9, 133.9, 129.6, 129.5, 127.6, 110.1, 69.3, 69.1, 68.7, 67.5, 64.7, 64.5, 60.7, 60.6, 39.5, 39.3, 39.3, 39.0, 38.6, 36.5, 28.0, 27.5, 26.9, 25.8, 24.3, 24.2, 23.9, 23.8, 23.8. 23.7, 23.6, 23.6. 21.2, 19.8, 18.0, 13.6, 13.4, -4.8, -4.9; high resolution mass spectrum (ES, NH_3) *m/z* 890.5711 [$(M-I)^+$; calcd for $C_{52}H_{85}O_5NSi_2P$: 890.5703].