(+)-Rimocidin Synthetic Studies. Construction of an Advanced C(1-18) Polyol Fragment.

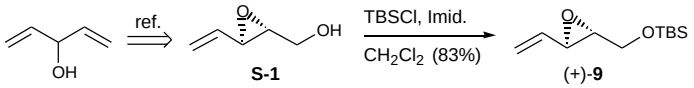
Supporting Information

Amos B. Smith, III,* Suresh M. Pitram, and Michael J. Fuertes

Department of Chemistry, Monell Chemical Senses Center and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA 19104

Materials and Methods. Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethy ether and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. Hexamethylphosphoramide (HMPA) was freshly distilled from calcium hydride under vacuum and stored over 4 Å molecular sieves under Ar. *n*-Butyllithium was purchased from Acros. *t*-Butyl-lithium was purchased from Aldrich. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040-0.062 mm) supplied by Silicycle and Sorbent technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were reported on a Jasco Model FT/IR-480 Plus spectrometer. Proton NMR spectra were recorded on a Bruker AM-500 spectrometer. Carbon-13 NMR spectra were recorded on a Bruker AM-500 spectrometer. Chemical shifts are reported relative to either chloroform (δ 7.26) or benzene (δ 7.15) for ^{1}H NMR and either chloroform (δ 77.0) or benzene (δ 128.0) for ^{13}C NMR. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center.

Vinyl epoxides (+)- and (-)-9 were prepared accordingly.



For preparation of compound **S-1** see the following reference: Romero, A.; Wong, C. H. *J. Org. Chem.* **2000**, *65*, 8264-8268.

Vinyl Epoxide (+)-9: A solution of the alcohol (2.8 g, 28 mmol) in dry DMF (30 mL) was cooled to 0 °C. Imidazole (2.9 g, 42 mmol) was added followed by portionwise addition of TBSCl (5.6 g, 37 mmol). The solution was warmed to room temperature, stirred for 2 h and diluted with ethyl acetate (200 mL) and sat. aqueous NH_4Cl (30 mL). The organic layer was separated and washed with H_2O (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo* to give a

yellow oil. Purification via flash chromatography (hexanes/ethyl acetate, 95:5) yielded (+)-**9** (5.1 g, 24 mmol, 85% yield). $[\alpha]_D^{23}$ +16.5 (c = 1.15, $CHCl_3$); IR (film) 3061, 2948, 2849, 1590, 1472, 1425, 1114, 823, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 5.60 (ddd, *J* = 7.5, 10.3, 17.3 Hz, 1 H), 5.49 (ddd, *J* = 0.5, 1.4, 17.2 Hz, 1 H), 5.28 (dd, *J* = 1.4, 10.1 Hz, 1 H), 3.86 (dd, *J* = 3.2, 12.0 Hz, 1 H), 3.72 (dd, *J* = 4.5, 12.0 Hz, 1 H), 3.26 (dd, *J* = 2.1, 7.5, 1 H), 3.01-2.98 (m, 1 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 119.3, 63.0, 60.3, 56.1, 25.9, 18.2, -5.3, -5.3; high resolution mass spectrum (CI) *m/z* 214.1377 [M^+; calcd for $C_{11}H_{22}O_2Si$: 214.1389].

Vinyl Epoxide (-)-9: $[\alpha]_D^{23}$ -19.0 (c = 0.86, $CHCl_3$); ^1H and ^{13}C NMR are identical to (+)-**9**.

Dithianes (+)-6 and (+)-11: A solution of 1,3-dithiane (1.38 g, 11.5 mmol) and HMPA (4.0 mL, 23.0 mmol) in THF (40 mL) was cooled to -78 ºC. *n*-BuLi (1.6 M in hexanes, 7.80 mL, 12.5 mmol) was added dropwise via syringe, and the reaction mixture allowed to warm to -25 ºC while stirring for 1 h. The mixture was re-cooled to -78 ºC and a solution of the vinyl epoxide (+)-**9** (2.00 g, 9.3 mmol) in THF (10 mL) was added dropwise via cannula. The mixture was warmed to ambient temperature over 1 h. After stirring an additional 2 h the reaction was quenched with saturated aqueous NH_4Cl (20 mL) and then diluted with Et_2O (150 mL). The layers were separated, the aqueous phase extracted with Et_2O (3 x 50 mL), and the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 9:1) provided both (+)-**6** (2.3 g, 6.8 mmol, 73% yield) and (+)-**11** (0.47 g, 1.4 mmol, 15% yield) as colorless oils. (+)-**6**: $[\alpha]_D^{23}$ +21.5 (c = 1.2, $CHCl_3$); IR (film) 3465, 2930, 2895, 2857, 1471, 1427, 1276, 1113, 998, 920, 824, 741, 701, 614 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.87 (dt, *J* = 10.0, 17.1 Hz, 1 H), 5.25 (dd, *J* = 1.8, 10.2 Hz, 1 H), 5.15 (dd, *J* = 1.8, 17.1 Hz, 1 H), 4.32 (d, *J* = 7.9 Hz, 1 H), 4.10 (ddd, *J* = 3.4, 6.0, 6.0 Hz, 1 H), 3.56 (d, *J* = 6.0 Hz, 2 H), 2.94-2.82 (m, 4 H), 2.47-2.43 (m, 1 H), 2.13-2.08 (m, 1 H), 1.91-1.83 (m, 1 H), 0.90 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.9, 119.5, 70.6, 65.4, 51.1, 49.4, 30.7, 30.6, 26.0, 25.9, 18.3, -5.3, -5.4; high

resolution mass spectrum (ES+) *m/z* 357.1349 [(M+Na)$^+$; calcd for $C_{15}H_{30}O_2S_2SiNa$: 357.1354];. (+)-**11:** $[\alpha]_D^{23}$ +19.7 (c = 0.9, $CHCl_3$); IR (film) 3485, 2929, 2895, 1471, 1427, 1276, 1114, 1000, 920, 824, 741, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 (dt, *J* = 17.1, 10.0 Hz, 1 H), 5.21 (dd, *J* = 10.1, 1.7 Hz, 1 H), 5.11 (dd, *J* = 17.1, 1.7 Hz, 1 H), 4.25 (d, *J* = 7.6 Hz, 1 H), 4.19-4.15 (m, 1 H), 3.65 (d, *J* = 1.6, 1 H), 3.64 (s, 1 H), 2.91-2.80 (m, 4 H), 2.52-2.48 (m, 1 H), 2.34 (d, *J* = 3.7 Hz, 1 H), 2.11-2.08 (m, 1 H), 1.91-1.81 (m, 1 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.7, 119.7, 70.7, 65.9, 51.0, 49.4, 30.7, 30.5, 26.8, 26.0, 18.3, -4.4, -4.7; high resolution mass spectrum (ES+) *m/z* 357.1358 [(M+Na)$^+$; calcd for $C_{15}H_{30}O_2S_2SiNa$: 357.1354.

Epoxide (+)-12: $[\alpha]_D^{23}$ +17.8 (c = 0.90, $CHCl_3$); IR (film) 2931, 2898, 1635, 1422, 1276, 1245, 1064, 994, 910, 883, 727 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (dt, *J* = 10.0, 17.1 Hz, 1 H), 5.29 (dd, *J* = 1.7, 10.2 Hz, 1 H), 5.20 (dd, *J* = 1.5, 17.1 Hz, 1 H), 4.30 (d, *J* = 6.9 Hz, 1 H), 4.09 (ddd, *J* = 4.6, 6.0, 9.3 Hz, 1 H), 3.63 (dd, *J* = 1.4, 4.7 Hz, 1 H), 2.95-2.82 (m, 4 H), 2.49-2.46 (m, 1 H), 2.14-2.09 (m, 2 H), 1.91-1.83 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.9, 118.8, 70.9, 64.7, 51.6, 49.5, 30.7, 30.6, 25.9; high resolution mass spectrum (CI) *m/z* 220.0584 [M$^+$; calcd for $C_9H_{14}OS_2$: 220.0592].

Dithianes (+)-14 and (+)-15: A solution of 2-TIPS-1,3-dithiane (3.2 g, 11.5 mmol) and HMPA (4.0 mL, 23.0 mmol) in THF (40 mL) was cooled to -78 ºC. *t*-BuLi (1.7 M in pentane, 0.52 mmol) was added dropwise via syringe, and the reaction mixture allowed to warm to -25 ºC while stirring for 1 h. The mixture was re-cooled to -78 ºC and a solution of the vinyl epoxide (+)-**9** (2.00 g, 9.3 mmol) in THF (10 mL) was added dropwise via cannula. The mixture was warmed to ambient temperature over 1 h. After stirring an additional 2 h the reaction was quenched with saturated aqueous NH_4Cl (20 mL) and then diluted with Et_2O (150 mL). The layers were separated, the aqueous phase extracted with Et_2O (3 x 5 mL), and the combined organic layers dried over

$MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate 9:1) provided both (+)-**14** (3.3 g, 6.7 mmol, 72% yield) and (+)-**15** (0.69 g, 1.4 mmol, 15% yield) as colorless oils. (+)-**14:** $[\alpha]_D^{23}$ +18.5(c = 1.5 $CHCl_3$); IR (film) 3415, 2930, 2864, 1437, 1428, 1113, 882, 823, 740, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.14 (ddd, *J* = 6.4, 7.6, 15.5 Hz, 1 H), 5.59 (dd, *J* = 6.5, 15.5 Hz, 1 H), 4.19-4.16 (m, 1 H), 3.65 (dd, *J* = 3.6, 10.0 Hz, 1 H), 3.45 (dd, *J* = 8.1, 10.0 Hz, 1 H), 3.22-3.06 (m, 4 H), 2.56 (d, *J* = 3.0 Hz, 1 H), 2.42-2.37 (m, 2 H), 2.06-2.02 (m, 1 H), 1.98-1.93 (m, 1 H), 1.48 (hept, *J* = 7.6 Hz, 3 H), 1.22 (d, *J* = 7.5 Hz, 18 H), 0.91 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.0, 129.7, 72.8, 67.0, 42.9, 40.3, 25.9, 24.6, 24.5, 20.0, 17.7, 12.1, -5.3, -5.4; high resolution mass spectrum (ES+) *m/z* 513.2680 [$(M+Na)^+$; calcd for $C_{24}H_{50}O_2S_2SiNa$: 513.2688]; (+)-**15:** $[\alpha]_D^{23}$ +19.9 (c = 1.2, $CHCl_3$); IR (film) 3442, 2930, 2865, 1472, 1427, 1113, 998, 882, 823, 740, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.99 (dddd, *J* = 1.0, 7.0, 7.2, 15.3 Hz, 1 H), 5.56 (ddt, *J* = 1.2, 6.6, 15.5 Hz, 1 H), 4.23 (dd, *J* = 6.0, 11.5 Hz, 1 H), 3.53-3.45 (m, 2 H), 3.18 (dddd, *J* = 1.2, 6.8, 15.5, 30.0 Hz, 1 H), 3.15 (ddd, *J* = 7.3, 15.5, 30.0 Hz, 1 H), 3.09-3.02 (m, 2 H), 2.40-2.36 (m, 2 H), 2.05-2.02 (m, 1 H), 2.01-1.91 (m, 1 H), 1.45 (hept, *J* = 7.6 Hz, 3 H), 1.22 (d, *J* = 7.5 Hz, 18 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.4, 130.9, 74.0, 66.8, 42.3, 40.3, 25.8, 24.5, 24.3, 20.0, 18.1, 14.2, 12.1, -4.3, -4.8; high resolution mass spectrum (ES+) *m/z* 513.2685 [$(M+Na)^+$; calcd for $C_{24}H_{50}O_2S_2SiNa$: 513.2688].

Dithiane (+)-7: $[\alpha]_D^{23}$ +17.0 (c = 0.80, $CHCl_3$); IR (film) 2984, 2933, 2897, 1422, 1369, 1213, 1155, 1050, 969, 863 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 7.0, 7.6, 15.3 Hz, 1 H), 5.57 (ddt, *J* = 1.2, 7.6, 15.3 Hz, 1 H), 4.49 (dd, *J* = 7.4, 14.0 Hz, 1 H), 4.07 (dd, *J* = 6.2, 8.1 Hz, 1 H), 4.05 (d, *J* = 7.3 Hz, 1 H), 3.58 (t, *J* = 7.9 Hz, 1 H), 2.89-2.79 (m, 4 H), 2.50 (ddd, *J* = 1.2, 14.6, 21.9 Hz, 1 H), 2.50 (ddd, *J* = 1.2, 7.0, 21.9 Hz, 1 H), 2.13-2.07 (m, 1 H), 1.88-1.80 (m, 1 H), 1.41 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.9, 129.9, 109.2, 76.7, 69.4, 46.9, 38.2,

30.4, 30.3, 26.7, 25.8, 25.7; high resolution mass spectrum (CI) *m/z* 260.0892 [M^+; calcd for $C_{12}H_{20}O_2S_2$: 260.0905].

Dithiane (+)-16: $[\alpha]_D^{23}$ +14.2 (c = 1.0, $CHCl_3$); IR (film) 2983, 2935, 1456, 1422, 1378, 1368, 1214, 1154, 1059, 861 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.09-4.03 (m, 1 H), 4.05 (d, *J* = 7.2 Hz, 1 H), 4.03 (dd, *J* = 6.2, 7.4 Hz, 1 H), 3.51 (t, *J* = 7.4 Hz, 1 H), 2.90-2.80 (m, 4 H), 2.14-2.09 (m, 1 H), 1.90-1.83 (m, 1 H), 1.79 (dd, *J* = 7.3, 14.5 Hz, 2 H), 1.67-1.60 (m, 2 H), 1.57-1.50 (m, 2 H), 1.40 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.7, 75.6, 69.4, 47.4, 35.4, 33.1, 30.4, 27.0, 26.0, 25.7, 22.9; high resolution mass spectrum (CI) *m/z* 262.1064 [M^+; calcd for $C_{12}H_{22}O_2S_2$: 262.1061].

Dithianes (+)-18 and (+)-19: A solution of 2-Ph-1,3-dithiane (1.16 g, 5.91 mmol) and HMPA (3.0 mL, 17.2 mmol) in THF (20 mL) was cooled to -78 ºC. *n*-BuLi (1.6 M in hexanes, 4.0 mL, 6.4 mmol) was added dropwise via syringe, and the reaction mixture allowed to warm to -25 ºC while stirring for 1 h. The mixture was re-cooled to -78 ºC and a solution of vinyl epoxide (+)-**9** (1.01 g, 4.71 mmol) in THF (5 mL) was added dropwise via cannula. The mixture was warmed to ambient temperature over 1 h. After stirring an additional 2 h the reaction was quenched with saturated aqueous NH_4Cl (20 mL) and then diluted with Et_2O (100 mL). The layers were separated, the aqueous phase extracted with Et_2O (3 x 25 mL), and the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 9:1) provided both (+)-**18** (1.57 g, 3.82 mmol, 81% yield) and (+)-**19** (0.15 g, 0.38 mmol, 8% yield) as colorless oils. (+)-**18:** $[\alpha]_D^{23}$ +13.5 (c = 1.2, $CHCl_3$); IR (film) 3500, 2953, 2928, 2902, 2856, 1472, 1442, 1422, 1257, 1116, 1088, 918, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 1.2, 8.4 Hz, 2 H), 7.39 (dd, *J* = 7.3, 8.1 Hz, 2 H), 7.27 (dd, *J* = 1.1, 7.4 Hz, 1 H), 6.02 (dt, *J* = 10.1, 17.1 Hz, 1 H), 5.23 (dd, *J* = 2.0, 10.2 Hz, 1 H), 4.98 (dd, *J* = 2.1, 17.1 Hz, 1 H), 4.06 (app t, *J* = 6.7 Hz, 1 H), 3.36 (dd, *J* = 6.7, 9.7 Hz, 1 H), 3.28 (dd, *J* = 6.9, 9.8 Hz, 1 H), 2.77-2.60 (m, 5 H), 1.96 (br s,

1 H), 1.93-1.89 (m, 2 H), 0.84 (s, 9 H), -0.03 (s, 3 H), -0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 132.1, 129.8, 128.6, 127.1, 120.4, 70.0, 64.7, 62.7, 58.4, 27.6, 27.5, 25.8, 24.9, 18.1, -5.4, -5.5; high resolution mass spectrum (ES+) *m/z* 433.1673 [$(M+Na)^+$; calcd for $C_{21}H_{34}O_2S_2SiNa$: 433.1667]; (+)-**19:** $[\alpha]_D^{23}$ +15.0 (c = 1.1 $CHCl_3$); IR (film) 3476, 2946, 2876, 1471, 1440, 1420, 1257, 1117, 1090, 922, 821 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 1.2, 8.1 Hz, 2 H), 7.40 (dd, *J* = 7.4, 8.2 Hz, 2 H), 7.28 (dt, *J* = 1.2, 7.3 Hz, 1 H), 6.04 (dt, *J* = 10.2, 17.3 Hz, 1 H), 5.25 (dd, *J* = 1.8, 10.1 Hz, 1 H), 5.10 (dd, *J* = 1.9, 17.1 Hz, 1 H), 4.24 (m, 1 H), 3.19-3.16 (m, 2 H), 2.79-2.61 (m, 5 H), 1.93-1.88 (m, 2 H), 0.87 (s, 9 H), -0.05 (s, 3 H), -0.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 133.0, 129.7, 128.4, 126.8, 119.9, 72.3, 65.5, 63.1, 59.0, 27.6, 27.5, 25.7, 25.0, 18.3, -4.3, -4.7; high resolution mass spectrum (ES+) *m/z* 433.1658 [$(M+Na)^+$; calcd for $C_{21}H_{34}O_2S_2SiNa$: 433.1667].

Epoxide (+)-**20:** $[\alpha]_D^{23}$ +13.3 (c = 1.3, $CHCl_3$); IR (film) 2990, 2905, 1482, 1442, 1422, 1279, 1034, 990, 923, 904, 833 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 1.2, 8.5 Hz, 2 H), 7.41 (dd, *J* = 7.4, 8.1 Hz, 2 H), 7.30 (dt, *J* = 1.2, 7.3 Hz, 1 H), 5.36 (ddd, *J* = 8.8, 10.3, 17.1 Hz, 1 H), 5.23 (dd, *J* = 1.6, 10.3 Hz, 1 H), 5.13 (dt, *J* = 1.1, 17.0 Hz, 1 H), 3.05 (ddd, *J* = 2.7, 3.9, 9.7 Hz, 1 H), 2.77-2.60 (m, 5 H), 2.31-2.28 (m, 2 H), 1.95-1.87 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 132.1, 129.8, 128.4, 127.0, 120.3, 62.5, 53.3, 48.8, 47.2, 27.6, 27.5, 24.9; high resolution mass spectrum (CI) *m/z* 278.0798 [M^+; calcd for $C_{15}H_{18}OS_2$: 278.0799].

Bis-dithiane (-)-21: A solution of dithiane (+)-**16** (408 mg, 1.55 mmol) and HMPA (0.80 mL, 4.60 mmol) in THF (8 mL) under Ar was cooled to -78 ºC. *n*-BuLi (2.5 M in hexanes, 0.68 mL, 1.70 mmol) was added dropwise via syringe, and the reaction mixture was stirred at -78 ºC for 0.5 h. A solution of epoxide (+)-**20** (440 mg, 1.58 mmol) in anhydrous THF (4 mL) was added dropwise via cannula. The mixture was warmed to ambient temperature over 1 h. After stirring an additional 1 h the reaction was quenched with saturated aqueous NH_4Cl (2 mL) and then diluted

with ethyl acetate (15 mL). The layers were separated, the aqueous phase extracted with ethyl acetate (3 x 5 mL), and the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 9:1→4:1) provided (+)-**21**(540 mg, 1.01 mmol, 65% yield) as a colorless oil: $[\alpha]_D^{23}$ -28.9 (c = 0.9, $CHCl_3$); IR (film) 3489, 2950, 2864, 1472, 1440, 1421, 1257, 1117, 1087, 920, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 1.2, 8.5 Hz, 2 H), 7.32 (app t, *J* = 7.7 Hz, 2 H), 7.23 (dd, *J* = 1.1, 7.2 Hz, 1 H), 6.00 (ddd, *J* = 9.0, 10.3, 17.2 Hz, 1 H), 5.35 (dd, *J* = 1.5, 17.2 Hz, 1 H), 5.19 (dd, *J* = 1.5, 10.2 Hz, 1 H), 4.12-3.99 (m, 3 H), 3.50 (t, *J* = 7.2 Hz, 1 H), 3.44 (dd, *J* = 5.9, 11.7 Hz, 1 H), 3.26 (dd, *J* = 7.8, 11.7 Hz, 1 H), 3.25-3.19 (m, 2 H), 2.61-2.56 (m, 2 H), 2.52-2.39 (m, 3 H), 2.35 (ddd, *J* = 7.3, 12.6, 14.5 Hz, 1 H), 2.12 (dd, *J* = 6.0, 8.8 Hz, 1 H), 2.09-2.04 (m, 1 H), 1.98-1.90 (m, 2 H), 1.84-1.60 (m, 5 H), 1.53-1.44 (m, 2 H), 1.39 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 137.2, 129.9, 128.5, 127.2, 116.0, 108.6, 75.8, 69.4, 62.5, 42.9, 40.2, 35.5, 33.4, 32.1, 31.9, 30.3, 30.1, 28.3, 27.4, 27.0, 25.7, 25.0, 20.6; high resolution mass spectrum (ES+) *m/z* 563.1776 [$(M+Na)^+$; calcd for $C_{27}H_{40}O_3S_4Na$: 563.1758].

Epoxide (-)-22: $[\alpha]_D^{23}$ -12.0 (c = 0.8, benzene); IR (film) 2856, 1472, 1442, 1422, 1257, 1116, 1088, 918, 837, 740, 701 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.49 (dd, *J* = 1.3, 8.1 Hz, 2 H), 7.18 (dd, *J* = 7.5, 8.1 Hz, 2 H), 7.05 (dt, *J* = 1.2, 7.4 Hz, 1 H), 3.40 (dd, *J* = 5.7, 10.9, 1 H), 3.18 (dd, *J* = 8.2, 10.9 Hz, 1 H), 3.07-3.01 (m, 2 H), 2.57-2.44 (m, 5 H), 2.28 (dd, *J* = 3.8, 5.3 Hz, 1 H), 2.17-2.12 (m, 2 H), 2.07-2.01 (m, 3 H), 1.97-1.87 (m, 3 H), 1.80-1.71 (m, 3 H), 1.59-1.45 (m, 3 H), 1.42-1.38 (m, 1 H), 1.30-1.23 (m, 2 H), 1.13 (t, *J* = 7.4 Hz, 3 H), 0.96 (s, 9 H), -.0.05 (s, 3 H), -0.06 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.1, 131.0, 128.4, 127.0, 63.8, 51.5, 46.2, 43.2, 40.0, 35.4, 33.3, 32.6, 32.3, 31.3, 31.2, 28.9, 27.5, 26.2, 26.1, 25.2, 23.1, 21.4, 18.4, 14.4, -5.3, -5.3; high resolution mass spectrum (ES+) *m/z* 621.2354 [$(M+Na)^+$; calcd for $C_{30}H_{50}O_2S_4SiNa$: 621.2361].

Dithiane (-)-**23:** $[\alpha]_D^{23}$ -18.5 (c = 1.1, $CHCl_3$); IR (film) 2928, 2885, 1467, 1251, 941, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dt, *J* = 10.0, 17.2 Hz, 1 H), 5.23 (dd, *J* = 2.1, 10.2 Hz, 1 H), 5.13 (dd, *J* = 2.0, 17.2 Hz, 1 H), 4.29 (ddd, *J* = 2.0, 5.4, 7.7 Hz, 1 H), 4.25 (d, *J* = 10.7 Hz, 1 H), 3.47 (dd, *J* = 5.5, 9.8 Hz, 1 H), 3.42 (dd, *J* = 8.0, 9.7 Hz, 1 H), 2.88-2.77 (m, 4 H), 2.63-2.58 (m, 1 H), 2.12-2.07 (m, 1 H), 1.95-1.84 (m, 1 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.12 (s, 3 H), 0.09 (s, 3 H), 0.05 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 119.0, 71.2, 64.9, 50.9, 47.9, 30.3, 30.0, 26.1, 26.0, 25.9, 18.2, 18.1, -3.8, -4.0, -5.3, -5.4; high resolution mass spectrum (ES+) *m/z* 471.2207 [$(M+Na)^+$; calcd for $C_{21}H_{44}O_2S_4Si_2Na$: 471.2219].

Dithiane (-)-**24:** $[\alpha]_D^{23}$ -30.4 (c = 0.9, $CHCl_3$); IR (film) 3474, 2953, 2928, 2856, 1471, 1257, 1105, 837, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5 H), 5.94 (dt, *J* = 10.0, 17.2 Hz, 1 H), 5.30 (dd, *J* = 2.3, 10.2 Hz, 1 H), 5.14 (dd, *J* = 2.3, 17.2 Hz, 1 H), 4.57 (d, *J* = 2.4 Hz, 2 H), 4.47 (dd, *J* = 4.6, 9.8 Hz, 1 H), 4.44-4.42 (m, 1 H), 3.48-3.41 (m, 3 H), 3.33 (t, *J* = 9.5 Hz, 1 H), 3.21 (d, *J* = 9.8 Hz, 1 H), 3.19 (br s, 1 H), 3.02-2.96 (m, 1 H), 2.93-2.88 (m, 1 H), 2.72-2.65 (m, 2 H), 2.26 (dd, *J* = 2.1, 15.8 Hz, 1 H), 2.03 (dd, *J* = 8.5, 15.8 Hz, 1 H), 2.00-1.95 (m, 1 H), 1.92-1.87 (m, 1 H), 0.91 (s, 9 H), 0.83 (s, 9 H), 0.06 (s, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.0, 128.2, 127.7, 127.4, 119.5, 74.4, 73.2, 72.1, 67.5, 64.4, 55.9, 49.5, 40.3, 25.9, 25.9, 25.8, 25.4, 24.3, 18.2, 18.0, -3.5, -3.9, -5.4, -5.5; high resolution mass spectrum (ES+) *m/z* 635.3044 [$(M+Na)^+$; calcd for $C_{31}H_{56}O_4S_2Si_2Na$: 635.3056].

Acetonide (-)-**25:** $[\alpha]_D^{23}$ -29.7 (c = 1.2 $CHCl_3$); IR (film) 2968, 2940, 2881, 1605, 1463, 1355, 1172, 1080, 922 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5 H), 5.63 (ddd, *J* =7.1, 10.0, 17.3 Hz, 1 H), 5.11 (dd, *J* = 2.4, 10.3 Hz, 1 H), 5.03 (dd, *J* = 2.4, 17.3 Hz, 1 H), 4.56 (dd, *J* = 12.3, 32.7 Hz, 2 H), 4.10 (app t, *J* = 7.2 Hz, 1 H), 4.06-4.02 (m, 1 H), 3.92-3.88 (m, 1 H), 3.45 (ddd, *J* = 5.9, 9.9, 21.9 Hz, 2 H), 3.36 (dd, *J* = 5.0, 10.0 Hz, 2 H), 2.22 (t, *J* = 9.7 Hz, 1 H), 1.53-1.49 (m, 1 H), 1.47 (s, 3 H), 1.40 (s, 3 H), 1.04 (app q, *J* = 13.1 Hz, 1 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.09 (s,

3 H), 0.08 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.1, 128.2, 127.7, 127.4, 120.1, 100.4, 76.4, 71.2, 67.6, 65.0, 64.5, 63.3, 44.3, 36.9, 27.8, 27.7, 23.5, 23.4, 14.3, 13.6, -4.0, -3.8, -3,4, -3.4; high resolution mass spectrum (ES+) *m/z* 587.3557 [$(M+Na)^+$; calcd for $C_{31}H_{56}O_5Si_2Na$: 587.3564].

Epoxide (-)-**5:** $[\alpha]_D^{23}$ -20.1 (c = 0.5 $CHCl_3$); IR (film) 3050, 2953, 2913, 2875, 1602, 1457, 1413, 1156, 1124, 1097, 1065, 1008, 962, 854, 817, 744 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5 H), 5.72 (dt, *J* = 10.0, 17.2 Hz, 1 H), 5.19 (dd, *J* = 1.5, 17.2 Hz, 1 H), 5.13 (dd, *J* = 1.5, 17.2 Hz, 1 H), 4.56 (dd, *J* = 12.2, 26.3 Hz, 2 H), 4.10-4.03 (m, 2 H), 3.98-3.96 (m, 1 H), 3.62-3.56 (m, 2 H), 3.50 (dd, *J* = 5.7, 10.0 Hz, 1 H), 3.37 (dd, *J* = 4.8, 10.0 Hz, 1 H), 2.20 (m, 1 H), 1.54 (dt, *J* = 2.4, 13.1 Hz, 1 H), 1.47 (s, 3 H), 1.42 (s, 3 H), 1.26 (dd, *J* = 11.8, 12.9 Hz, 1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.0, 128.2, 127.7, 127.4, 119.5, 100.4, 74.4, 73.8, 65.4, 63.6, 51.5, 47.8, 44.0, 36.8, 26.5, 26.4; high resolution mass spectrum (ES+) *m/z* 341.1733 [$(M+Na)^+$; calcd for $C_{19}H_{26}O_4Na$: 341.1729].

Tris-dithiane (-)-26: A solution of 2-TBS-1,3-dithiane (26.0 mg, 0.11 mmol) in Et_2O (1.0 mL) was cooled to -78 ºC. t-BuLi (1.7 M in pentanes, 70 µL, 0.12 mmol) was added dropwise via syringe, and the reaction mixture was allowed to warm to -45 ºC while stirring for 1 h. The mixture was re-cooled to -78 ºC and a solution of epoxide (-)-**5** (60.0 mg, 0.10 mmol) in Et_2O (0.50 mL) was added dropwise via cannula. The mixture was warmed to -25 ºC over 1 h, re-cooled to -78 ºC, and treated dropwise with a solution of epoxide (-)-**22** (64.0 mg, 0.20 mmol) and HMPA (50 µL, 0.29 mmol) in Et_2O (0.50 mL) via cannula. The reaction mixture was warmed to ambient temperature over 3 h, quenched with saturated aqueous NH_4Cl (1 mL), and diluted with EtOAc (5 mL). The layers were separated, the aqueous phase was extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 9:1→4:1→2:1) provided (+)-**26** (64.4 mg, 0.56 mmol,

56%) as a pale yellow oil: $[\alpha]_D^{23}$ -10.8 (c = 0.6, benzene); IR (film) 3500, 2920, 1460, 1420, 1380, 1355, 1250, 1220, 1160, 1100, 910, 740 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.50 (dd, *J* = 1.3, 8.3 Hz, 2 H), 7.30-7.24 (m, 2 H), 7.19-7.05 (m, 6 H), 5.82 (dt, *J* = 10.0, 17.2 Hz, 1 H), 5.07 (dd, *J* = 1.5, 17.2 Hz, 1 H), 4.98 (dd, *J* = 1.5, 17.2 Hz, 1 H), 4.38 (app t, *J* = 3.2 Hz, 2 H), 4.30-4.28 (m, 1 H), 4.11-4.05 (m, 1 H), 3.99-3.94 (m, 1 H), 3.50-3.47 (m, 1 H), 3.41 (dd, *J* = 5.8, 10.9 Hz, 1 H), 3.30 (ddd, *J* = 3.6, 4.9, 8.6 Hz, 1 H), 3.20 (dd, *J* = 8.2, 10.9 Hz, 1 H), 3.10-3.02 (m, 1 H), 2.65-2.11 (m, 11 H), 1.99-1.93 (m, 1 H), 1.82-1.13 (m, 24 H), 1.49 (s, 3 H), 1.34 (s, 3 H), 1.15 (t, *J* = 7.4 Hz, 3 H), 0.96 (s, 9 H), 0.91 (s, 9 H), -0.04 (s, 3 H), -0.05 (s, 6 H), -0.06 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.1, 139.1, 134.2, 134.2, 131.1, 130.8, 129.7, 127.0, 126.9, 119.4, 99.0, 74.2, 73.5, 69.2, 67.9, 63.8, 63.2, 55.0, 54.9, 43.5, 40.5, 38.2, 36.4, 35.4, 33.2, 32.3, 31.4, 31.2, 31.1, 31.0, 30.5, 30.4, 30.2, 29.8, 29.4, 29.0, 27.5, 26.3, 26.1, 25.2, 23.1, 22.9, 21.3, 19.7, 18.4, 14.5, 14.4, -3.4, -3.5, -3.8, -3.9; high resolution mass spectrum (ES+) *m/z* 1173.5130 [$(M+Na)^+$; calcd for $C_{59}H_{98}O_6S_6S\ i_2Na$: 1173.5124].

Phenyl Ketone (+)-**28:** $[\alpha]_D^{23}$ +8.8 (c = 0.4, $CHCl_3$); IR (film) 2956, 2855, 1717, 1677, 1595, 1575, 1451, 1360, 1210, 1175, 1120, 1084, 992; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00-7.93 (m, 2 H), 7.60-7.56 (m, 2 H), 7.55-7.24 (m, 6 H), 5.66 (dt, *J* = 10.3, 17.1 Hz, 1 H), 5.15 (dd, *J* = 1.3, 10.2 Hz, 1 H), 5.03 (dd, *J* = 1.3, 17.0 Hz, 1 H), 4.51 (s, 2 H), 4.15-3.98 (m, 1 H), 3.66-3.51 (m, 3 H), 3.48-3.42 (m, 2 H), 3.43-3.23 (m, 4 H), 3.15 (s, 3 H), 2.83-2.71 (m, 2 H), 2.68-2.44 (m, 3 H), 1.90-1.64 (m, 4, H), 1.52-1.12 (m, 10 H), 1.13 (t, *J* = 7.4 Hz, 3 H) 0.85 (s, 9 H), 0.83 (s, 9 H), 0.80 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 6 H), 0.03 (s, 9 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.6, 203.4, 137.9, 136.3, 134.0, 133.3, 128.7, 128.5, 128.4, 128.2, 127.7, 119.3, 93.4, 76.0, 75.4, 73.4, 68.7, 67.2, 65.0, 63.4, 62.3, 55.6, 49.6, 49.3, 46.7, 46.2, 43.6, 43.3, 32.6, 34.2, 25.4, 25.3, 24.8, 18.5, 18.2, 18.0, 18.3, 17.6, 16.1, 12.3, -1.2, -3.4, -3.5, -3.8, -4.3, -4.4, -4.8; high resolution mass spectrum (ES+) *m/z* 1091.6643 [$(M+Na)^+$; calcd for $C_{59}H_{104}O_9Si_4Na$: 1091.6655].