Methyl (3*R*)-3-(*tert*-butyldiphenylsilyloxy)-butyrate (5a). A solution of methyl (*R*)-3-hydroxy-butyrate (**5**, 1.9 g, 16.0 mmol) in 20 mL of anhydrous CH_2Cl_2 at 0 °C was treated with imidazole (2.2 g, 32.0 mmol) in one portion. After 10 min, *tert*-butyldiphenyl-chlorosilane was added dropwise and the resulting exothermic reaction was allowed to warm to 25 °C for 4 h. The reaction mixture was diluted with Et_2O (200 mL), and washed successively with 5% aqueous NH_4Cl (100 mL) and saturated aqueous NaCl (100 mL). The organic layer was dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash chromatography (SiO_2, 6 x 12 cm, 0–5% EtOAc/hexanes gradient) to provide **5a** (5.6 g, 97%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69 (m, 4H), 7.41 (m, 6H), 4.31 (m, 1H), 3.60 (s, 3H), 2.57 (dd, *J* = 7.1, 14.6 Hz, 1H), 2.40 (dd, *J* = 5.7, 14.6 Hz, 1H), 1.12 (d, *J* = 6.1 Hz, 3H), 1.03 (s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 171.8, 135.8, 135.8, 134.2, 133.8, 129.6, 129.5, 127.5, 127.5, 66.8, 51.4, 44.4, 26.8, 23.6, 19.1; IR (film) ν_{max} 2953, 2858, 1742, 1428, 1378, 1303 1194, 1111 cm^{-1}; ESIMS *m*/*z* 379 (M + Na^+, $C_{21}H_{28}O_3Si$ requires 379). (–)-(3*R*)-**5a**: $[\alpha]^{25}_D$ –5.1 (*c* 0.67, CH_2Cl_2).

(3*R*)-3-(*tert*-Butyldiphenylsilyloxy)-butan-1-al (6). A solution of **5a** (5.6 g, 15.7 mmol) in 100 mL of anhydrous toluene at –78 °C was treated dropwise with DIBAL-H (17.3 mL, 17.3 mmol). After 10 min, the reaction was treated successively with MeOH

(1.0 mL) and saturated aqueous NH_4Cl (10.0 mL). The resulting mixture was stirred 1 h at 25 °C followed by addition of Et_2O (200 mL) and after 1 h further stirring addition of $MgSO_4$ (3 g). The resulting suspension was filtered through celite and concentrated under reduced pressure to provide **6** (5.0 g, 92%) which was carried on crude as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.77 (t, 1H), 7.69 (m, 4H), 7.44 (m, 6H), 4.34 (m, 1H), 2.50 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 202.0, 135.8, 135.8, 134.0, 133.5, 129.8, 129.7, 127.7, 127.5, 65.6, 52.7, 26.8, 23.8, 19.1; IR (film) ν_{max} 2962, 2858, 1728, 1427, 1111, 1024 cm^{-1}; ESIMS *m/z* 349 (M + Na^+, $C_{20}H_{26}O_2Si$ requires 349).

Ethyl (5*R*)-5-(*tert*-butyldiphenylsilyloxy)-hex-2-enoate (7). To a stirred suspension of LiCl (0.78 g, 18.4 mmol), triethylphosphonoacetate (3.65 mL, 18.4 mmol) and diisopropylethylamine (2.67 mL, 15.3 mmol) in 80 mL of anhydrous CH_3CN at 25 °C was added a solution of **6** (5.0 g, 15.3 mmol) in anhydrous CH_3CN. After 12 h, the reaction mixture was diluted with Et_2O (200 mL), and washed successively with H_2O (200 mL) and saturated aqueous NaCl (200 mL). The organic layer was dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (SiO_2, 6 x 12 cm, 4% EtOAc/hexanes) provided **7** (5.8 g, 95%) as a colorless oil: δ 7.70 (m, 4H), 7.43 (m, 6H), 6.94 (dt, *J* = 15.3, 7.5 Hz, 1H), 5.78 (d, *J* = 15.3 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.98

(m, 1H), 2.33 (m, 2H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 7.5 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 166.4, 145.5, 135.8, 135.8, 134.3, 133.9, 129.6, 129.6, 127.6, 127.5, 123.4, 68.5, 60.1, 42.1, 26.9, 23.2, 19.2, 14.2; IR (film) ν_{max} 2964, 1722, 1654, 1427, 1265, 1176, 1111 cm^{-1}; ESIMS *m*/*z* 419 ($M + Na^+$, $C_{24}H_{32}O_3Si$ requires 419). (+)-(5*R*)-**7**: $[\alpha]^{25}_D$ +31 (*c* 0.71, CH_2Cl_2).

(5*R*)-5-(*tert*-Butyldiphenylsilyloxy)-hex-2-en-1-ol (8). A solution of **7** (5.6 g, 14.1 mmol) in 100 mL of anhydrous CH_2Cl_2 at –20 °C was treated dropwise with DIBAL-H (30.0 mL, 30.0 mmol). After 2 h, the reaction was warmed to 0 °C for 1 h and then for 2 h at 25 °C. The reaction was then treated with saturated aqueous NH_4Cl (10.0 mL) and stirred 1 h at 25 °C. The resulting mixture was then diluted with Et_2O (200 mL) and stirred 1 h at 25 °C followed by addition of $MgSO_4$ (3 g). The resulting suspension was filtered through celite and concentrated under reduced pressure. Flash chromatography (SiO_2, 6 x 12 cm, 0–30% EtOAc/hexanes) provided **8** (4.8 g, 96%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 (m, 4H), 7.42 (m, 6H), 5.57 (m, 2H), 4.01 (d, *J* = 4.1 Hz, 2H), 3.90 (m, 1H), 2.18 (m, 2H), 1.09 (d, *J* = 6.0 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 500 MHz) δ135.8, 135.8, 134.7, 134.6, 131.3, 129.4, 129.3, 127.5, 127.4, 69.2, 63.6, 42.2, 26.9, 23.2, 19.2; IR (film) ν 3333, 2857, 1428, 1111, 997

cm^{-1}; ESIMS *m*/*z* 377 ($M + Na^+$, $C_{22}H_{30}O_2Si$ requires 377). (+)-(5*R*)-**8**: $[\alpha]^{25}_D$ +20 (*c* 0.71, CH_2Cl_2).

(2*R*, 3*R*, 5*R*)-5-(*tert*-Butyldiphenylsilyl)-2,3-(oxiranyl)-hexan-1-ol (9). To a suspension of flame dried 5Å molecular sieves in 20 mL of anhydrous CH_2Cl_2 at –30 °C was added in sequential fashion: (D)-(–)-diethyl tartrate (116 μL, 0.67 mmol), $Ti(OiPr)_4$ (168 μL, 0.56 mmol) and *tert*-butylhydroperoxide (2.5 mL, 3.4 M solution, 8.5 mmol). The reaction mixture was stirred at –30 °C for 30 min before the addition of **8** (2.0 g, 5.6 mmol) in anhydrous CH_2Cl_2 (3.0 mL). The reaction was then stored in a –30 °C freezer for 12 h without the need for stirring. The reaction was then warmed to –20 °C and quenched by the addition of 10% NaOH/saturated aqueous NaCl (2.0 mL). Upon further warming to –10 °C, the reaction was diluted with Et_2O (50 mL), treated with $MgSO_4$ (2.0 g) and celite (500 mg) and stirred an addition 15 min. The reaction was allowed to stand and settle for 1 h before filtration through celite using Et_2O. Concentration of the solvents under reduced pressure, followed by flash chromatography (SiO_2, 6 x 8 cm, 30% EtOAc/hexanes) afforded **9** (1.9 g, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71 (m, 4H), 7.43 (m, 6H), 4.07 (m, 1H), 3.85 (ddd, *J* = 12.6, 5.7, 2.6 Hz, 1H), 3.55 (ddd, *J* = 12.6, 7.2, 4.5 Hz, 1H), 3.08 (dt, *J* =5.9, 2.3 Hz, 1H), 2.84 (m, 1H), 1.81 (m, 2H), 1.74 (dt, *J* = 13.9, 5.8 Hz, 1H), 1.17 (d, *J* = 6.2 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR

($CDCl_3$, 400 MHz) δ 135.8, 135.8, 134.3, 134.0, 129.6, 129.6, 127.6, 127.5, 67.4, 61.6, 58.1, 52.9, 41.1, 26.9, 23.2, 19.1; IR (film) 3446, 2931, 2857, 1472, 1427, 1111 cm^{-1}; ESIMS *m*/*z* 393 (M + Na^+, $C_{22}H_{30}O_3Si$ requires 393). (+)-(2*R*, 3*R*, 5*R*)-**9**: $[\alpha]^{25}_D$ +23 (*c* 0.8, CH_2Cl_2).

(2*R* , 3*R* , 5*R*)-5-(*tert*-Butyldiphenylsilyl)-2,3-(oxiranyl)-hexan-1-al (9a). A solution of **9** (1.8 g, 4.9 mmol) and Et_3N (3.4 mL, 24 mmol) in 50 mL of 4:1 CH_2Cl_2/DMSO at 0 °C was treated with SO_3•pyridine (2.9 g, 17 mmol) and stirred 30 min at 25 °C. The reaction was diluted with EtOAc (200 mL), washed sequentially with H_2O (3 x 50 mL), saturated aqueous $NaHCO_3$ (50 mL), and saturated aqueous NaCl (50 mL) and dried ($MgSO_4$). Evaporation of the solvents under reduced pressure directly provided pure **9a** (1.6 g, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.96 (d, *J* = 6.3 Hz, 1H), 7.68 (m, 4H), 7.45 (m, 6H), 4.09 (m, 1H), 3.39 (dt, *J* = 6.6, 1.9 Hz, 1H), 3.06 (dd, *J* = 6.3, 1.9 Hz, 1H), 1.75 (m, 2H), 1.19 (d, *J* = 6.2 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR ($CDCl_3$, 500 MHz) δ 198.2, 135.8, 135.7, 134.0, 133.7, 129.8, 129.7, 127.7, 127.6, 67.2, 58.6, 53.9, 40.6, 26.9, 23.2, 19.1; IR (film) 2931, 1733, 1472, 1111 cm^{-1}; ESIMS *m*/*z* 391 (M + Na^+, $C_{22}H_{28}O_3Si$ requires 391). (–)-(2*R*, 3*R*, 5*R*)-**9a**: $[\alpha]^{25}_D$ –15 (*c* 0.54, CH_2Cl_2).

(3*R* , 4*R*, 6*R*)-6-(*tert*-Butyldiphenylsilyl)-3,4-(oxiranyl)-hept-1-ene (10). Methyltriphenylphosphonium bromide (1.93 g, 5.42 mmol) and a stir bar were added to a flask and thoroughly flame dried. Anhydrous THF (30 mL) was added via cannula under Ar and the resulting suspension was cooled to 0 °C prior to the addition of NaHMDS (5.13 mL, 5.13 mmol, 1.0 M in THF) in dropwise fashion. The resulting gold suspension was warmed to 25 °C for 30 min and then recooled to –10 °C prior to the addition of **9a** (1.05 g, 2.85 mmol) in anhydrous THF (5.0 mL). The reaction was complete within 10 min, and was quenched by the addition of saturated aqueous NH_4Cl (50 mL). The mixture was then extracted with Et_2O (100 mL), washed sequentially with H_2O (50 mL) and saturated aqueous NaCl (50 mL) and dried ($MgSO_4$). Removal of the solvents under reduced pressure followed by flash chromatography (SiO_2, 6 x 6 cm, 5% EtOAc/hexanes) provided **10** (0.85 g, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69 (m, 4H), 7.45 (m, 6H), 5.58 (ddd, *J* = 17.3, 9.9, 7.4 Hz, 1H), 5.45 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.28 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.09 (m, 1H), 3.06 (dd, *J* = 7.4, 2.1 Hz, 1H), 3.00 (dt, *J* = 5.8, 2.1 Hz, 1H), 1.82 (dt, *J* = 13.9, 5.8 Hz, 1H), 1.66 (dt, 3.9, 5.8 Hz, 1H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 135.8, 135.8, 134.4, 134.0, 129.6, 129.5, 127.6, 127.5, 119.1, 67.5, 58.5, 57.3, 41.5, 26.9, 23.2, 19.2; IR (film) 2963, 2857, 1472, 1379, 1111 cm^{-1}; ESIMS *m*/*z* 389 ($M + Na^+$, $C_{23}H_{30}O_2Si$ requires 389). (+)-(3*R*, 4*R*, 6*R*)-**10**: $[\alpha]^{25}_D$ +15 (*c* 0.67, CH_2Cl_2).

(3*R*, 4*R*, 6*R*)-6-(Hydroxy)-3,4-(oxiranyl)-hept-1-ene (3). To a solution of **10** (0.78 g, 2.13 mmol) in 20 mL of anhydrous THF at 25 °C was treated with *n*Bu_4NF (2.55 mL, 1.0 M solution in THF, 2.55 mmol) and stirred 4 h. The reaction was concentrated under reduced pressure, and directly loaded onto the column. Flash chromatography (SiO_2, 3 x 8 cm, 0–50% EtOAc/hexanes gradient) provided **3** (0.243 g, 89%) as a colorless and volatile oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.36 (ddd, *J* = 17.0, 7.2, 3.0 Hz, 1H), 5.26 (dd, *J* = 17.0, 1.8 Hz, 1H), 5.07 (dd, *J* = 9.8, 1.8 Hz), 3.87 (m, 1H), 2.92 (dd, *J* = 7.2, 2.2 Hz, 1H), 2.77 (m, 1H), 2.0 (br s, 1H), 1.64 (dt, *J* = 14.2, 4.4 Hz, 1H), 1.39 (dt, *J* = 14.2, 7.6 Hz, 1H), 1.08 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 135.2, 119.6, 66.4, 58.3, 58.2, 40.8, 23.4; IR (film) 3403, 2966, 1428, 1113 cm^{-1}; ESIMS *m*/*z* 151 ($M + Na^+$, $C_7H_{12}O_2$ requires 151). (+)-(3*R*, 4*R*, 6*R*)-**3**: $[\alpha]^{25}_D$ +18 (*c* 0.38, CH_2Cl_2).

(*E*,*E*)-2-(1,3-Pentadien-1-yl)-1,3-dithiane (4). To a stirred solution of 1,3 propanedithiol (**11**, 5.0 mL, 50.0 mmol), $MgClO_4$ (0.6 g, 2.5 mmol) and H_2SO_4 (20 μL) in anhydrous $CHCl_3$ (80 mL) at –10 °C was added hexadienal (5.5 mL, 50.0 mmol) in anhydrous $CHCl_3$ (20 mL) in dropwise fashion via cannula. The reaction stirred at 25 °C for 2 h before being poured into cold 10% KOH (100 mL) followed by stirring for 15 min. The organic layer was separated, washed sequentially with 10% KOH (50 mL), H_2O

(50 mL), dried ($MgSO_4$) and filtered through celite. Concentration under reduced pressure was followed by flash chromatography (SiO_2, 6 x 12 cm, 4% EtOAc/hexanes) to provide **4** (6.4 g, 67%) as a slightly yellow oil (9:1 *E*:*Z*): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.33 (dd, *J* = 15.1, 10.4 Hz, 1H), 6.01 (ddd, *J* = 15.1, 10.4, 1.3 Hz, 1H) 5.74 (dq, *J* = 15.1, 6.6 Hz, 1H), 5.59 (dd, *J* = 15.1, 7.8 Hz, 1H), 4.64 (d, *J* = 7.8 Hz, 1H), 2.85 (m, 4H), 2.07 (m, 1H), 1.83 (m, 1H), 1.74 (d, *J* = 6.6 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 134.2, 131.9, 130.7, 126.9, 47.9, 30.7, 25.6, 18.6; IR (film) ν_{max} 3018, 2899, 1421, 1274, 986 cm^{-1}; ESIMS *m*/*z* 209 (M + Na^+, $C_9H_{14}S_2$ requires 209). *Z* isomer: ^{1}H NMR δ 6.67 (dd, *J* = 15.1, 11.0 Hz, 1H), 4.70 (d, 7.8 Hz, 1H).

2-(Chloromethyl)-4,6-dimethoxy-benzaldehyde (13). $POCl_3$ (11.1 mL, 119.0 mmol) was dropped slowly via cannula into anhydrous DMF (17.0 mL) at 0 °C, and the resulting solution was stirred at 25 °C for 20 min. A solution of 3,5-dimethoxy-benzylalcohol (**12**, 5.0 g, 29.0 mmol) in anhydrous DMF (3.0 mL) was added slowly and the reaction was warmed to 75 °C for 2 h. The reaction was allowed to cool to 25 °C and poured into ice water (250 mL). The mixture was neutralized with 2N NaOH to pH = 7 and stirred 1.5 h at 25 °C. The resulting precipitate was filtered, washed thoroughly with H_2O (5 x 50 mL) and dried under vacuum to give pure **13** (6.0 g, 93%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.46 (s, 1H), 6.75 (d, *J* = 2.1 Hz, 1H), 6.44 (d, *J* = 2.1 Hz, 1H), 5.10 (s,

2H), 3.91 (s, 3H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 189.9, 165.2, 165.0, 142.3, 115.9, 107.5, 97.6, 56.0, 55.6, 44.8; IR (film) ν_{max} 2980, 2884, 1670, 1597, 1327, 1204, 1150 cm^{-1}; ESIMS *m*/*z* 237 ($M + Na^+$, $C_{10}H_{11}O_3Cl$ requires 237).

2-(Chloromethyl)-4,6-dimethoxy-benzoic acid (2). Aldehyde **13** (0.75 g, 3.4 mmol) and sulfamic acid (1.13 g, 11.7 mmol) in 21 mL H_2O:THF:DMSO (20:10:1) at 0 °C was treated with $NaClO_2$ (1.25 g, 11.0 mmol) in 3 mL H_2O. The reaction was stirred 20 min at 0 °C. The reaction was diluted with EtOAc (100 mL), washed with saturated aqueous NH_4Cl (2 x 50 mL) and saturated aqueous NaCl, and dried (Na_2SO_4). Evaportation of the solvents gave a 7:1 mixture of **2**:chloro-**2**. This material was carried onto the next step crude as only the desired acid **2** proceeded to esterify. For **2**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.84 (d, *J* = 2.2 Hz, 1H), 6.52 (d, *J* = 2.2 Hz, 1H), 5.02 (s, 2H), 3.99 (s, 3H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 167.1, 163.0, 159.8, 142.9, 110.8, 108.4, 98.7, 56.8, 55.7, 45.2; IR (film) ν_{max} 3000 (br), 2896, 1691, 1333, 1288 cm^{-1}; ESIMS *m*/*z* 253 ($M + Na^+$, $C_{10}H_{11}O_4Cl$ requires 253).

Benzoic ester (14). To a suspension of **2** (0.53 g, 2.3 mmol) in 10 mL of anhydrous CH_2Cl_2 and catalytic DMF (10 μL) at 0 °C was added oxalyl chloride (1.13 mL, 2.0 M solution in CH_2Cl_2, 2.3 mmol). The suspension became a gold solution over 1

h stirring at 25 °C. The reaction was then recooled to 0 °C, and treated sequentially with Et_3N (0.73 mL, 5.2 mmol) and **3** (0.225 g, 1.75 mmol) in anhydrous CH_2Cl_2 (3 mL), and DMAP (catalytic). The reaction was allowed to stir 12 h at 25 °C. The reaction was then diluted with CH_2Cl_2 (50 mL), washed saturated aqueous NH_4Cl (50 mL) and dried ($MgSO_4$). Evaportation of the solvents under reduced pressure followed by flash chromatography (SiO_2, 3 x 6 cm, 0–30% EtOAc/hexanes gradient) yielded **14** (0.47 g, 80%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.53 (d, *J* = 2.2 Hz, 1H), 6.43 (d, *J* = 2.2 Hz, 1H), 5.56 (ddd, *J* = 17.3, 10.2, 6.2 Hz, 1H), 5.46 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.36 (m, 1H), 5.26 (dd, *J* = 10.2, 1.6 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.15 (dd, *J* = 7.3, 2.0 Hz, 1H), 3.04 (dt, *J* = 5.7, 2.0 Hz, 1H), 2.01 (dt, *J* = 14.4, 6.3 Hz, 1H), 1.89 (dt, *J* = 14.4, 6.3 Hz, 1H), 1.42 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 166.9, 162.1, 159.0, 138.1, 135.8, 119.7, 116.5, 106.7, 99.3, 70.1, 58.5, 57.4, 56.4, 56.0, 44.0, 38.5, 20.3; IR (film) ν_{max} 2978, 1717, 1615, 1456, 1338, 1270, 1164, 1100, 1046 cm^{-1}; ESIMS *m*/*z* 363 (M + Na^+, $C_{17}H_{21}O_5Cl$ requires 363). (–)-(*R*, *R*, *R*)-**14**: $[\alpha]^{25}_D$ –7.6 (*c* 0.45, CH_2Cl_2).

Dithiane adduct (16). The dithiane **4** (0.100 g, 0.54 mmol) was charged to a flame dried flask equipped with a stir bar under Ar pressure. Anhydrous THF (4.0 mL) was added via cannula and the resulting solution was cooled to –30 °C. *n*BuLi (0.22 mL,

2.5 M solution in hexanes, 0.54 mmol) was added dropwise and the resulting dark green reaction was stirred at –30 °C for 1 h. The solution was cooled to –78 °C and was cannulated *into* a solution of **14** (0.092 mg, 0.27 mmol) in anhydrous THF (4.0 mL) at –78 °C. The resulting purple reaction was stirred 90 min at –78 °C before it was stored overnight in a –78 °C freezer. The reaction was then quenched by the addition of 1 N HCl (5 mL). The mixture was extracted with CH_2Cl_2 (15 mL) and dried (Na_2SO_4). Evaporation of the solvents under reduced pressure followed by flash chromatography (SiO_2, 3 x 6 cm, 20% EtOAc/hexanes) afforded a 4:1 mixture of α (**15**):γ (**15a**) alkylation products. This mixture was easily separated by HPLC (Dynamax 60 Å, SiO_2, 25 x 100 mm, 20 mL/min, 12% EtOAc/hexanes, 50 mg injections) to afford pure **15** (80 mg, 60%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.54 (d, *J* = 2.2 Hz, 1H), 6.36 (d, *J* = 2.2 Hz, 1H), 6.31 (dd, *J* = 14.5, 4.0 Hz, 1H), 6.14 (ddd, *J* = 15.0, 10.7, 1.4 Hz, 1H), 5.71 (dq, *J* = 13.6, 6.7 Hz, 1H), 5.59 (ddd, *J* = 17.4, 10.2, 7.3 Hz, 1H), 5.52 (d, *J* = 5.5 Hz, 1H), 5.46 (dd, *J* = 17.4, 1.4 Hz, 1H), 5.31 (m, 1H), 5.26 (dd, *J* = 10.1, 1.5 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.27 (s, 2H), 3.15 (dd, *J* = 7.3, 2.0 Hz, 1H), 3.07 (dt, *J* = 5.7, 2.0 Hz, 1H), 2.88 (m, 2H), 2.64 (m, 2H), 2.03 (dt, *J* = 14.4, 6.3 Hz, 1H), 1.98 (m, 1H), 1.87 (dt, *J* = 14.4, 6.3 Hz, 1H), 1.85 (m, 1H) 1.77 (d, *J* = 6.7 Hz, 3H), 1.44 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 167.0, 160.3, 158.0, 135.5, 135.3, 134.3, 132.9, 130.6, 130.2, 119.2, 118.0, 108.1, 97.8, 69.3, 58.2, 57.0, 55.7, 55.3, 55.1, 45.0, 38.0, 27.3, 25.0, 19.8,

18.2; IR (film) ν_{max} 2936, 1716, 1605, 1455, 1276, 1161, 1095 cm^{-1}; ESIMS *m*/*z* 513 (M + Na^+, $C_{26}H_{34}O_5S_2$ requires 513). (–)-(*R*, *R*, *R*)-**15**: $[\alpha]^{25}_D$ –5.5 (*c* 1.0, CH_2Cl_2).

γ-adduct (15a): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.33 (s, 2H), 5.51 (ddd, *J* = 17.3, 10.2, 6.2 Hz, 1H), 5.81 (dd, *J* = 9.5, 3.1 Hz, 1H), 5.58 (ddd, *J* = 17.2, 9.5, 7.1 Hz, 1H), 5.47 (d, *J* = 17.0, 1H), 5.35 (m, 4H), 3.81 (s, 3H), 3.76 (s, 3H), 3.61 (m, 1H), 3.15 (dd, *J* = 7.2, 2.0 Hz, 1H), 3.05 (m, 1H), 2.82–2.61 (m, 6H), 2.08 (m, 2H), 2.04 (m, 1H), 1.89 (m, 1H), 1.62 (d, *J* = 5.6 Hz, 3H), 1.44 (dd, *J* = 6.3, 3.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ; ESIMS *m*/*z* 513 (M + Na^+, $C_{26}H_{34}O_5S_2$ requires 513).

14-membered macrolide (17). A solution of **15** (30 mg, 61 μmol) in 30 mL anhydrous CH_2Cl_2 under Ar was treated with Ru-catalyst **16** (5 mg, 6.1 μmol) and heated to 45 °C for 5 h. The reaction was concentrated and loaded directly onto a column and flash chromatography (SiO_2, 2 x 5 cm, 0–40% EtOAc/hexanes gradient) provided pure macrocycle **17** (15.0 mg, 55%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.17 (d, *J* = 2.0 Hz, 1H), 6.70 (dd, *J* = 15.7, 8.8 Hz, 1H), 6.34 (d, *J* = 2.0 Hz, 1H), 6.02 (dd, *J* = 9.9, 9.8 Hz, 1H), 5.94 (d, *J* = 15.6 Hz, 1H), 5.39 (m, 2H), 3.77 (s, 3H), 3.73 (s, 3H), 3.75 (d, *J* = 15.6, 1H), 3.46 (m, 1H), 3.45 (d, *J* = 15.6 Hz, 1H), 3.05 (m, 3H), 2.88 (m, 2H), 2.34 (dt, *J* = 14.5, 3.3 Hz, 1H), 2.06 (m, 1H), 1.97 (m, 1H), 1.70 (m, 1H), 1.55 (d, *J* = 6.6 Hz,

3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 167.6, 160.8, 157.6, 136.7, 135.6, 130.5, 129.3, 128.5, 118.3, 106.3, 97.1, 69.3, 56.5, 55.8, 55.7, 55.4, 53.0, 40.5, 37.1, 27.9, 27.2, 24.3, 18.8; IR (film) ν_{max} 2937, 1717, 1603, 1456, 1277, 1161 cm^{-1}; ESIMS *m*/*z* 471 ($M + Na^+$, $C_{23}H_{28}O_5S_2$ requires 471). (–)-(*R, R, R*)-**17**: $[\alpha]^{25}_D$ –74 (*c* 0.65, CH_2Cl_2).

Macrolide ketone (18). A solution of **17** (12.5 mg, 27.9 μmol) in 5.0 mL of anhydrous CH_2Cl_2 was treated with *m*CPBA (6.5 mg, 28.0 μmol, 75%) in one portion and stirred 5 min. The reaction was diluted with CH_2Cl_2 (20 mL), washed with 5% aqueous $NaHCO_3$ (2 x 15 mL) and dried ($MgSO_4$). The solvents were removed under reduced pressure and the crude monosulfoxide was dissolved in 5.4 mL of THF:H_2O:Ac_2O:Et_3N (10:1:3:4) and heated to 60 °C for 12 h. The reaction was concentrated under reduced pressure and flash chromatography (SiO_2, 2 x 5 cm, 0–50% EtOAc/hexanes) provided the desired ketone **18** (7.0 mg, 70%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (dd, *J* = 15.8, 11.4 Hz, 1H), 6.36 (s, 1H), 6.36 (s, 1H), 6.24 (dd, *J* = 11.2, 11.1 Hz, 1H), 6.02 (d, *J* = 16.0 Hz, 1H), 5.82 (dd, *J* = 10.5, 4.4 Hz, 1H), 5.36 (m, 1H), 3.96 (d, *J* = 13.8 Hz, 1H), 3.86 (d, *J* = 13.8 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.57 (m, 1H), 3.10 (m, 1H), 2.45 (dt, *J* = 15.1, 4.0 Hz, 1H), 1.73 (ddd, *J* = 15.1, 7.4, 3.0 Hz, 1H), 1.55 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 198.3, 167.1, 161.8, 158.8, 140.4, 136.9, 134.7, 131.7, 130.2, 116.1, 103.7, 98.0, 69.7, 55.9, 55.8, 55.5, 54.9, 42.5, 37.0, 18.9; IR (film)

ν_{max} 2938, 1661, 1604, 1203, 1162 cm^{-1}; ESIMS *m*/*z* 381 ($M + Na^+$, $C_{20}H_{22}O_6$ requires 381). (–)-(*R, R, R*)-**18**: $[\alpha]^{25}_D$ –130 (*c* 0.20, CH_2Cl_2).

Chlorinated macrolide (19). A solution of **18** (2.1 mg, 5.9 μmol) in 1 mL of acetone was added to a solution of $Ca(OCl)_2$ (1.5 mg, 7.1 μmol) in 10:1 H_2O:acetic acid (1.1 mL) at 0 °C and stirred 30 min. The reaction was diluted with CH_2Cl_2 (10 mL), washed with 5% aqueous $NaHCO_3$ (10 mL), and dried ($MgSO_4$). The solvents were removed under reduced pressure, and the crude was purified via flash chromatography (SiO_2, 1 x 4 cm, 50% EtOAc/hexanes) to provide **19** as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (dd, *J* = 16.0, 10.1 Hz, 1H), 6.55 (s, 1H), 6.15 (t, *J* = 10.2 Hz, 1H), 6.10 (d, *J* = 16.1 Hz, 1H), 5.73 (dd, *J* = 11.0, 4.5 Hz, 1H), 5.39 (m, 1H), 3.98 (d, *J* = 16.1 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 3.78 (d, *J* = 16.0 Hz, 1H), 3.44 (m, 1H), 3.05 (m, 1H), 2.44 (dt, *J* = 14.6, 3.5 Hz, 1H), 1.64 (m, 1H), 1.55 (d, *J* = 6.5 Hz, 3H); ESIMS *m*/*z* 381 ($M + H^+$, $C_{20}H_{21}ClO_6$ requires 393). (+)-(*R, R, R*)-**19**: $[\alpha]^{25}_D$ –55 (*c* 0.1, $CHCl_3$).