Total Synthesis of Maoecrystal V: Early-Stage C–H Functionalization and Lactone Formation by Radical Cyclization

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Supplementary Information

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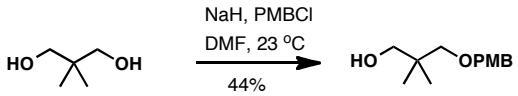
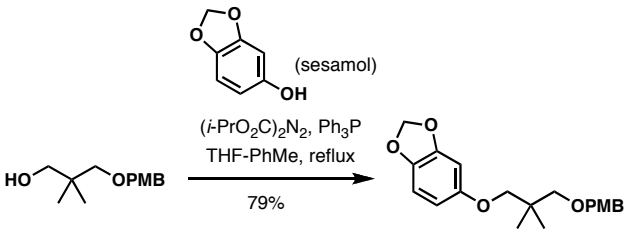
Synthesis

General Information. All reactions were carried out under an inert atmosphere of dry argon in oven or flame-dried glassware, unless the reaction procedure states otherwise. Tetrahydrofuran (THF) and ether (diethyl ether) were distilled from sodium-benzophenone in a continuous still under an atmosphere of argon. Dichloromethane, di-*iso*-propylamine and triethylamine were distilled from calcium hydride in a continuous still under and atmosphere of argon. Reaction temperatures were controlled by IKA ETS-D4 fuzzy thermo couples. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with Silica Gel 60 F_{254} (EMD no. 5715-7) and visualized using combinations of UV, anisaldehyde, ceric ammonium molybdate (CAM), potassium permanganate, and iodine staining. Flash column chromatography was preformed using 40-63 μm silica gel (Merck, Geduran, no. 11567-1) as the stationary phase. Proton magnetic resonance spectra were recorded at 400, 500, and 600 MHz on Varian Unity Inova. Carbon magnetic resonance spectra were recorded at 400 MHz, 500 MHz, and 600 MHz on Varian Unity Inova, and Varian Unity Inova spectrometers. All Chemical shifts were reported in δ units relative to tetramethylsilane. High Resolution mass spectral data were obtained by the Mass Spectrometry laboratory at the University of California, Santa Barbara.



6

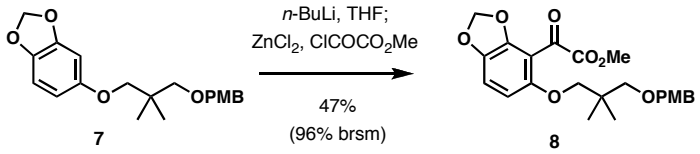
Alcohol 6. Sodium hydride (60% dispersion in mineral oil, 8.00 g, 0.20 mol) was added portion-wise to a solution of 2,2-dimethyl-1,3-propanediol (20.8 g, 0.20 mol) in DMF (400 mL) at 23 °C. The resulting mixture was stirred for 1 h, then *p*-methoxybenzyl chloride (31.3 g, 0.20 mol) was added. After stirring for additional 14 h, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and extracted with diethyl ether. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (10-20% ethyl acetate in hexanes) to afford the alcohol **6** (19.9 g, 88.8 mmol, 44%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.24 (d, J=8.6 Hz, 2H), 6.88 (d, J=8.6 Hz, 2H), 4.44 (s, 2H), 3.81 (s, 3H), 3.44 (d, J=5.9 Hz, 2H), 3.29 (s, 2H), 2.61 (t, J=5.9 Hz, 1H), 0.92 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm): 159.2, 130.2, 129.1, 113.8, 79.2, 73.2, 71.9, 55.2, 36.2, 21.9. HRMS-EI (*m/z*): M^+ calcd for $C_{13}H_{20}O_3$, 224.1412; found, 224.1419.



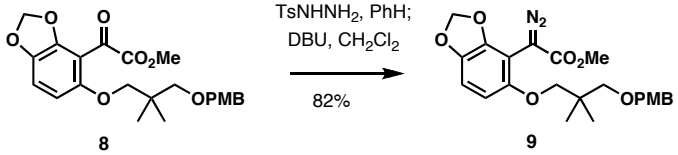
6 7

Ether 7. Diisopropyl azodicarboxylate (9.10 g, 45.0 mmol) was added to a solution of sesamol (8.29 g, 60.0 mmol), alcohol **6** (9.10 g, 30.0 mmol) and Ph_3P (11.8 g, 45.0 mmol) in THF (120 mL) and toluene (10 mL) at 0 °C. The resulting mixture was then heated at reflux for 18 h. After cooling to room temperature, the mixture was filtered through a short silica gel column. The filtrate was concentrated and the residue was purified by column

chromatography on silica gel (5-10% ethyl acetate in hexanes) to afford the ether **7** (8.15 g, 23.7 mmol, 79%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.21 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 6.69 (d, J=8.5 Hz, 1H), 6.48 (d, J=2.5 Hz, 1H), 6.32 (dd, J1=2.5 Hz, J2=8.5 Hz, 1H), 5.90 (s, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.67 (s, 2H), 3.29 (s, 2H), 1.01 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 158.9, 155.1, 148.1, 141.3, 130.9, 128.9, 113.6, 107.8, 105.7, 101.0, 98.1, 75.6, 74.5, 72.8, 55.2, 36.1, 22.2. HRMS-EI (*m/z*): M^+ calcd for $C_{20}H_{24}O_5$, 344.1624; found, 344.1632.



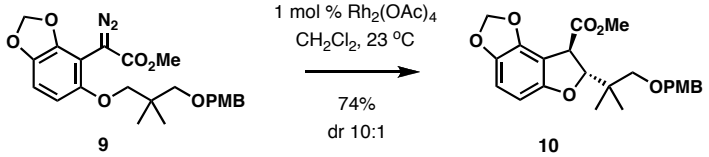
α-Ketone ester 8. *n*-Butyllithium (13.2 mL, 2.37 M in hexanes, 31.4 mmol) was added dropwise to a solution of **7** (9.00 g, 26.1 mmol) in THF (100 mL) at 0 °C and the resulting solution was stirred at room temperature for 2 h. A solution of zinc chloride (20.9 mL, 1.25 M in THF, 26.1 mmol) was added to the above solution at -78 °C. After stirring for 20 min at the same temperature, methyl chlorooxoacetate (4.8 mL, 52.2 mmol) was added and the reaction mixture was allowed to stir at 23 °C for 6.5 h. The reaction mixture then was quenched with water and extracted with 50% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (5-20% ethyl acetate in hexanes) to deliver the product **8** (5.23 g, 12.2 mmol, 47%) along with starting material **7** (4.59 g, 13.3 mmol, 51%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.20 (d, J=8.7 Hz, 2H), 6.86 (d, J=8.4 Hz, 1H), 6.83 (d, J=8.7 Hz, 2H), 6.36 (d, J=8.4 Hz, 1H), 6.05 (s, 2H), 4.41 (s, 2H), 3.87 (s, 3H), 3.80 (s, 3H), 3.74 (s, 2H), 3.24 (s, 2H), 0.98 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 183.8, 163.7, 159.0, 154.1, 149.2, 142.4, 130.6, 129.0, 113.6, 112.6, 109.1, 103.6, 102.7, 75.6, 75.2, 72.8, 55.2, 52.7, 36.1, 22.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{23}H_{26}O_8Na$, 453.1525; found, 453.1532.



α-Diazoester 9. A mixture of **8** (4.76 g, 11.1 mmol) and $TsNHNH_2$ (2.06 g, 11.1 mmol) in benzene (60 mL) was heated at reflux for 2 h, during which water was collected in a Dean-Stark apparatus. After cooling, the solvent was removed by rotary evaporator and the residue was directly submitted to next step without purification.

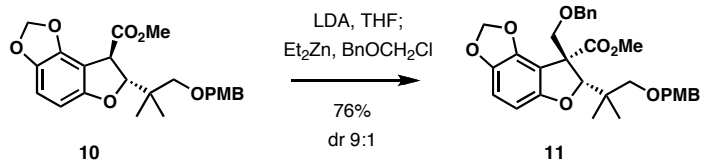
DBU (5.0 mL, 33.3 mmol) was added to the above crude hydrazone solution in CH_2Cl_2 (56 mL) at 23 °C. The reaction mixture was stirred for 10 h before water was added and the mixture was extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated, and the residue was purified by column chromatography on silica gel (10-20% ethyl acetate in hexanes) to afford the diazo substrate **9** (4.01 g, 9.06 mmol, 82%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.19 (d, J=8.7 Hz, 2H), 6.82 (d, J=8.7 Hz, 2H), 6.72 (d, J=8.5 Hz, 1H), 6.32 (d, J=8.5 Hz, 1H), 5.97 (s, 2H), 4.41 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.71 (s, 2H), 3.29 (s, 2H), 1.01 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm): 159.0, 152.0, 146.9, 141.8, 130.8, 128.9, 113.6, 107.9, 103.2, 101.6, 97.5, 75.7, 74.8,

72.9, 55.2, 52.1, 36.1, 22.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{23}H_{26}N_2O_7Na$, 465.1638; found, 465.1638.



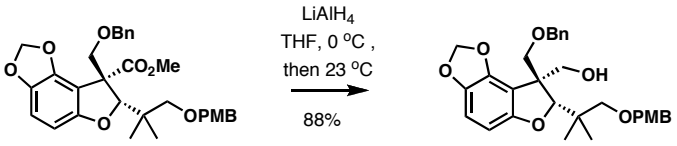
9 10

Dihydrobenzofuran 10. The freshly prepared diazoester **9** (0.522 g, 1.18 mmol) was dissolved in CH_2Cl_2 (29 mL). Molecular sieves (4Å, 5.22 g) were added. Rhodium(II) acetate (5.2 mg, 11.8 μmol) was added and the reaction mixture was stirred at 23 °C for 10 h. The reaction mixture was filtered through a short pad of Celite and concentrated. The residue was purified by column chromatography on silica gel (15-20% ethyl acetate in hexanes) to afford **10** (0.361 g, 0.873 mmol, 74%, dr = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.19 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.61 (d, J=8.3 Hz, 1H), 6.21 (d, J=8.3 Hz, 1H), 5.93 (d, J=1.3 Hz, 1H), 5.86 (d, J=1.3 Hz, 1H), 4.99 (d, J=7.1 Hz, 1H), 4.39 (d, J=11.8 Hz, 1H), 4.38 (d, J=7.1 Hz, 1H), 4.32 (d, J=11.8 Hz, 1H), 3.80 (s, 3H), 3.72 (s, 3H), 3.31 (d, J=9.1 Hz, 1H), 3.27 (d, J=9.1 Hz, 1H), 0.98 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 172.1, 159.0, 156.4, 143.5, 141.9, 130.5, 128.8, 113.6, 107.8, 107.4, 101.5, 99.8, 91.0, 75.9, 72.8, 55.2, 52.5, 46.7, 38.8, 20.5, 20.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{23}H_{26}O_7Na$, 437.1576; found, 437.1576.



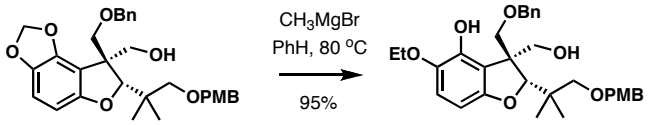
10 11

Ester 11. A solution of *n*-BuLi (3.8 mL, 2.08 M in hexanes, 7.82 mmol) was added dropwise to a solution of *i*-Pr_2NH (1.2 mL, 8.34 mmol) in THF (16 mL) at -78 °C. After stirring at the same temperature for 20 min, a solution of **10** (2.16 g, 5.21 mmol) in THF (20 mL) was added. After stirring for further 20 min, $ZnEt_2$ (0.8 mL, 1.0 M in heptane, 5.0 mmol) was added and the solution was stirred for 10 min at -78 °C. Then dry DMPU (8.0 mL) was added and followed by BOMCl (Sigma-Aldrich, Inc., ~60% purity, 2.4 mL, 10.4 mmol). The mixture was then stirred at 0 °C for 0.5 h and 23 °C for 1 h. The reaction was quenched carefully with a saturated aqueous NH_4Cl solution at 0 °C, and extracted with 50% ethyl acetate in hexanes. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to afford ester **11** (2.12 g, 3.97 mmol, 76%, dr = 9:1). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.29-7.23 (m, 5H), 7.22-7.18 (m, 2H), 6.85 (d, J=8.7 Hz, 2H), 6.64 (d, J=8.2 Hz, 1H), 6.24 (d, J=8.2 Hz, 1H), 5.88 (d, J=1.4 Hz, 1H), 5.81 (d, J=1.4 Hz, 1H), 4.95 (s, 1H), 4.52 (s, 2H), 4.46 (s, 2H), 4.12 (d, J=9.6 Hz, 1H), 3.85 (d, J=9.6 Hz, 1H), 3.79 (s, 3H), 3.64 (s, 3H), 3.41 (d, J=8.9 Hz, 1H), 3.22 (d, J=8.9 Hz, 1H), 1.00 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 171.7, 159.0, 155.8, 143.0, 142.0, 138.1, 130.8, 128.9, 128.1, 127.5, 127.4, 113.6, 111.9, 107.5, 101.3, 100.0, 90.0, 77.2, 73.2, 72.8, 70.9, 57.8, 55.2, 52.3, 38.8, 20.3, 20.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{31}H_{34}O_8Na$, 557.2151; found, 557.2152.



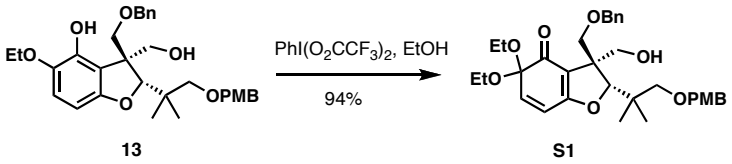
11 **12**

Alcohol 12. Lithium aluminum hydride (0.364 g, 9.58 mmol) was added to a solution of **11** (2.56 g, 4.79 mmol) in THF (48 mL) at 0 °C. The mixture was allowed to warm to 23 °C and stirred for 2 h. The reaction was carefully quenched by adding 0.36 mL of water at 0 °C. After stirring for 5 min at 0 °C, 0.36 mL of aqueous NaOH (15% w/w) solution was added and the mixture was stirred for 5 min. Water (1.08 mL) was added and the mixture was stirred for additional 5 min. The white solid was filtered off, the filtrate was concentrated and the residue was purified by column chromatography on silica gel (25% of ethyl acetate in hexanes) to afford **12** (2.13 g, 4.20 mmol, 88%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.34–7.24 (m, 5H), 7.21 (d, J=8.7 Hz, 2H), 6.85 (d, J=8.7 Hz, 2H), 6.60 (d, J=8.2 Hz, 1H), 6.22 (d, J=8.2 Hz, 1H), 5.88 (d, J=1.4 Hz, 1H), 5.84 (d, J=1.4 Hz, 1H), 4.65 (s, 1H), 4.57 (d, J=12.3 Hz, 1H), 4.54 (d, J=12.3 Hz, 1H), 4.38 (d, J=11.7 Hz, 1H), 4.34 (d, J=11.7 Hz, 1H), 4.02 (dd, J1=7.1 Hz, J2=11.4 Hz, 1H), 3.93 (dd, J1=6.0 Hz, J2=11.4 Hz, 1H), 3.89 (d, J=9.4 Hz, 1H), 3.83 (d, J=9.4 Hz, 1H), 3.80 (s, 3H), 3.34 (d, J=9.1 Hz, 1H), 3.29 (d, J=9.1 Hz, 1H), 3.01 (*virt.* t, J=6.5 Hz, 1H), 1.11 (s, 3H), 1.05 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 159.1, 155.0, 143.0, 141.7, 138.2, 130.2, 129.1, 128.3, 127.6, 127.5, 113.7, 113.4, 107.3, 101.0, 100.4, 91.0, 77.1, 73.4, 72.9, 71.7, 63.0, 56.1, 55.2, 39.2, 22.5, 22.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{30}H_{34}O_7Na$, 529.2202; found, 529.2202.



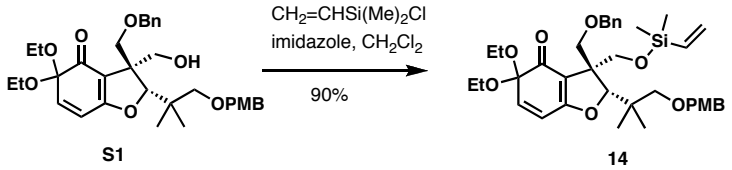
12 **13**

Alcohol 13. Methylmagnesium bromide (6.9 mL, 3.0 M in Et_2O, 20.7 mmol) was added dropwise to a solution of **12** (2.10 g, 4.15 mmol) in benzene (41 mL) at room temperature. The reaction flask was sealed and heated to 80 °C for 6 h. After cooling, the reaction was acidified by careful addition of 1 M HCl at 0 °C. The mixture was extracted with 50% ethyl acetate in hexanes and the combined organic layer was washed with brine, dried over Na_2SO_4. After concentration, the residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to afford **13** (2.05 g, 3.92 mmol, 95%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 8.64 (brs, 1H), 7.39–7.28 (m, 5H), 7.21 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.69 (d, J=8.5 Hz, 1H), 6.22 (d, J=8.5 Hz, 1H), 4.68 (d, J=12.1 Hz, 1H), 4.61 (d, J=12.1 Hz, 1H), 4.36 (s, 2H), 4.26 (s, 1H), 4.01 (q, J=7.0 Hz, 2H), 3.98 (d, J=9.1 Hz, 2H), 3.94 (d, J=11.8 Hz, 1H), 3.89 (d, J=11.8 Hz, 1H), 3.80 (s, 3H), 3.72 (d, J=9.1 Hz, 1H), 3.36 (d, J=9.1 Hz, 1H), 3.31 (d, J=9.1 Hz, 1H), 2.85 (brs, 1H), 1.41 (t, J=7.0 Hz, 3H), 1.10 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 159.1, 153.8, 143.8, 141.6, 136.7, 130.2, 129.1, 128.7, 128.2, 128.0, 116.4, 114.6, 113.7, 99.3, 90.6, 77.0, 73.9, 72.8, 72.0, 65.5, 60.4, 56.6, 55.2, 39.0, 22.7, 22.2, 15.1. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{31}H_{38}O_7Na$, 545.2515; found, 545.2516.



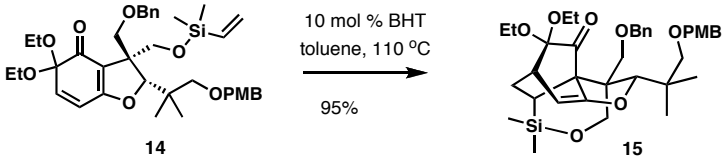
13 **S1**

***Ortho*-quinone S1.** Iodobenzene bis(trifluoroacetate) (1.83 g, 4.25 mmol) was added to a mixture of the substrate **13** (2.02 g, 3.87 mmol) and $NaHCO_3$ (0.780 g, 9.29 mmol) in EtOH (39 ml) at 23 °C. The mixture was stirred for 20 min. Then the solvent was removed by evaporation and the residue was purified by column chromatography on silica gel (20–25% ethyl acetate in hexanes) to afford the quinone **S1** (2.05 g, 3.62 mmol, 94%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.31–7.27 (m, 4H), 7.27–7.23 (m, 1H), 7.22 (d, J=8.7 Hz, 2H), 6.84 (d, J=8.7 Hz, 2H), 6.53 (d, J=10.1 Hz, 1H), 6.33 (d, J=10.1 Hz, 1H), 5.11 (s, 1H), 4.84 (brs, 1H), 4.56 (d, J=12.2 Hz, 1H), 4.50 (d, J=12.2 Hz, 1H), 4.42 (s, 2H), 4.05 (d, J=10.7 Hz, 1H), 4.00 (d, J=10.7 Hz, 1H), 3.79 (s, 3H), 3.75 (d, J=9.2 Hz, 1H), 3.70–3.53 (m, 5H), 3.34 (d, J=9.0 Hz, 1H), 3.13 (d, J=9.0 Hz, 1H), 1.21 (t, J=7.0 Hz, 3H), 1.14 (t, J=7.0 Hz, 3H), 1.05 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 191.4, 171.5, 159.1, 143.7, 138.4, 130.4, 129.0, 128.2, 127.4, 127.3, 118.8, 114.8, 113.6, 95.2, 93.3, 77.2, 73.2, 72.9, 70.8, 62.4, 58.59, 58.58, 55.9, 55.2, 39.6, 21.7, 21.6, 15.5, 15.4. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{33}H_{42}O_8Na$, 589.2777; found, 589.2778.



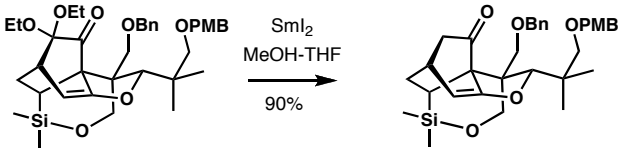
S1 **14**

Vinylsilane 14. Chlorodimethylvinylsilane (0.985 mL, 7.13 mmol) was added to a solution of the substrate **S1** (2.02 g, 3.56 mmol) and imidazole (0.970 g, 14.2 mmol) in CH_2Cl_2 (36 mL) at 23 °C. The reaction mixture was stirred for 5 h before quenched with water, and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes) delivering the product **14** (2.09 g, 3.20 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.28–7.20 (m, 7H), 6.81 (d, J=8.7 Hz, 2H), 6.41 (d, J=10.2 Hz, 1H), 6.27 (d, J=10.2 Hz, 1H), 6.06 (dd, J1=14.9 Hz, J2=19.8 Hz, 1H), 5.99 (dd, J1=4.4 Hz, J2=14.9 Hz, 1H), 5.73 (dd, J1=4.4 Hz, J2=19.8, 1H), 5.05 (s, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.46–4.40 (m, 3H), 4.09 (d, J=9.3 Hz, 1H), 3.85 (d, J=10.9 Hz, 1H), 3.78 (s, 3H), 3.72 (d, J = 10.9 Hz, 1H), 3.68–3.59 (m, 3H), 3.53 (dq, J1=7.1 Hz, J2=9.3 Hz, 1H), 3.47 (dq, J1=7.1 Hz, J2=9.3 Hz, 1H), 3.40 (d, J=8.8 Hz, 1H), 3.38 (d, J=8.8 Hz, 1H), 1.20 (t, J=7.1 Hz, 3H), 1.15 (s, 3H), 1.11 (s, 3H), 1.06 (t, J=7.1 Hz, 3H), 0.134 (s, 3H), 0.128 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 189.6, 169.0, 158.9, 142.4, 138.7, 136.9, 133.4, 130.9, 128.7, 128.1, 127.4, 127.2, 119.4, 113.6, 112.8, 93.0, 92.8, 77.5, 73.2, 72.7, 70.3, 60.9, 58.5, 58.3, 55.3, 55.2, 38.8, 21.4, 20.6, 15.6, 15.3, –2.4. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{37}H_{50}O_8SiNa$, 673.3173; found, 673.3181.



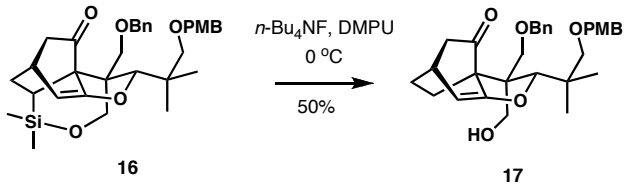
14 15

Enol ether 15. A solution of the substrate **14** (2.05 g, 3.15 mmol), 2,6-di-tertbutyl-4-methylphenol (69.4 mg, 0.315 mmol) in toluene (63 mL) was heated at 110 °C for 24 h. After cooling, the solvent was removed by evaporation and the residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes) to afford the title compound **15** (1.95 g, 3.00 mmol, 95%) as a single isomer. ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.33-7.27 (m, 4H), 7.23 (t, J=6.9 Hz, 1H), 7.19 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 5.26 (d, J=7.1 Hz, 1H), 4.50 (d, J=11.6 Hz, 1H), 4.47 (d, J=11.6 Hz, 1H), 4.41 (*virt.* t, J=11.2 Hz, 1H), 4.34 (d, J=12.0 Hz, 1H), 4.14 (d, J=12.1 Hz, 1H), 4.10 (s, 1H), 3.89 (d, J=8.9 Hz, 1H), 3.85 (d, J=12.0 Hz, 1H), 3.80 (s, 3H), 3.69-3.57 (m, 3H), 3.48 (dq, J1=7.5 Hz, J2=9.5 Hz, 1H), 3.22 (d, J=8.9 Hz, 1H), 3.11 (d, J=8.9 Hz, 1H), 3.06-3.02 (m, 1H), 2.08 (ddd, J1=3.8 Hz, J2=10.3 Hz, J3=11.6 Hz, 1H), 1.57 (*virt.* t, J=9.6 Hz, 1H), 1.34 (ddd, J1=2.0 Hz, J2=9.3 Hz, J3=11.4 Hz, 1H), 1.18 (t, J=7.1 Hz, 3H), 1.06 (t, J=7.1 Hz, 3H), 1.00 (s, 6H), 0.15 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 196.9, 158.9, 153.2, 138.9, 130.7, 128.9, 128.0, 127.4, 127.1, 113.7, 98.6, 96.1, 89.9, 77.3, 73.2, 72.6, 72.3, 65.3, 61.9, 58.2, 57.3, 55.2, 52.3, 38.1, 36.9, 25.2, 22.5, 21.2, 17.6, 15.5, 15.3, -1.1, -3.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{37}H_{50}O_8SiNa$, 673.3173; found, 673.3176.



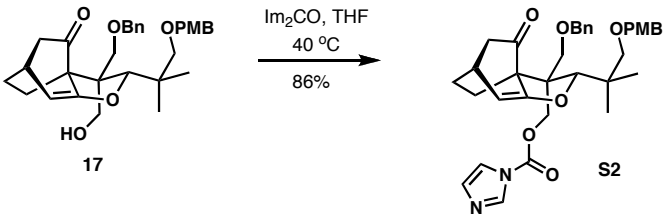
15 16

Ketone 16. A solution of SmI_2 (47 mL, 0.1 M in THF, 4.70 mmol) was added to a solution of the substrate **15** (0.615 g, 0.945 mmol) in THF (9 mL) and MeOH (0.9 mL). After stirring at 23 °C for 2 h, the reaction mixture was diluted with hexanes, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with 10% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes) to deliver the product **16** (0.477 g, 0.848 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.33-7.28 (m, 4H), 7.26-7.22 (m, 1H), 7.20 (d, J=8.7 Hz, 2H), 6.86 (d, J=8.7 Hz, 2H), 5.27 (d, J=7.0 Hz, 1H), 4.52 (d, J=11.7 Hz, 1H), 4.46 (d, J=11.7 Hz, 1H), 4.40 (d, J=12.0 Hz, 1H), 4.39 (d, J=9.0 Hz, 1H), 4.35 (d, J=12.0 Hz, 1H), 4.18 (d, J=12.1 Hz, 1H), 4.01 (s, 1H), 3.88 (d, J=9.0 Hz, 1H), 3.86 (d, J=12.1 Hz, 1H), 3.80 (s, 3H), 3.25 (d, J=8.9 Hz, 1H), 3.15 (d, J=8.9 Hz, 1H), 2.96-2.92 (m, 1H), 2.14 (dd, J1=1.9 Hz, J2=17.4 Hz, 1H), 2.10-2.00 (m, 1H), 1.87 (ddd, J1=3.6 Hz, J2=10.5 Hz, J3=11.5 Hz, 1H), 1.57-1.51 (m, 1H), 1.42 (dd, J1=8.2 Hz, J2=10.2 Hz, 1H), 1.02 (s, 6H), 0.15 (s, 3H), 0.07 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 205.7, 159.0, 154.1, 139.1, 130.7, 128.9, 128.1, 127.4, 127.1, 113.7, 100.0, 90.3, 77.5, 73.1, 72.7, 71.7, 65.1, 62.0, 55.2, 52.6, 41.9, 38.1, 30.1, 29.3, 22.5, 21.2, 18.0, -1.1, -3.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{33}H_{42}O_6SiNa$, 585.2648; found, 585.2654.



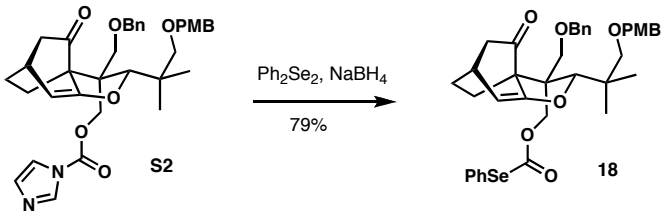
16 17

Alcohol 17. A solution of *n*-Bu_4NF (3.8 mL, 1.0 M in THF, 3.80 mmol) was added to a solution of the substrate **16** (0.430 g, 0.764 mmol) in DMPU (20 mL) at 0 °C. After stirring at the same temperature for 1 h, the reaction mixture was diluted with hexanes, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with 10% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (pre-neutralized with 1% NEt_3 in hexanes, eluent: 10% ethyl acetate in hexanes) to deliver the product **17** (0.195 g, 0.385 mmol, 50%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.34–7.29 (m, 2H), 7.28–7.24 (m, 3H), 7.21 (d, J=8.7 Hz, 1H), 6.86 (d, J =8.7 Hz, 1H), 5.26 (d, J=7.0 Hz, 1H), 4.53 (d, J=11.7 Hz, 1H), 4.46 (d, J=8.8 Hz, 1H), 4.41 (d, J=11.8 Hz, 1H), 4.40 (d, J=11.7 Hz, 1H), 4.38 (d, J=11.8 Hz, 1H), 4.14 (s, 1H), 4.02 (dd, J1=6.2 Hz, J2=11.4 Hz, 1H), 3.85 (dd, J1=5.2 Hz, J2=11.4 Hz, 1H), 3.80 (s, 3H), 3.72 (d, J=8.8 Hz, 1H), 3.27 (d, J=9.0 Hz, 1H), 3.21 (d, J=9.0 Hz, 1H), 3.09 (brs, 1H), 2.91–2.86 (m, 1H), 2.28 (ddd, J1=3.6 Hz, J2=11.9 Hz, J3=13.1 Hz, 1H), 2.16–2.05 (m, 1H), 1.97 (ddd, J1=5.6 Hz, J2=10.0 Hz, J3=13.3 Hz, 1H), 1.82–1.74 (m, 1H), 1.72–1.64 (m, 1H), 1.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 210.1, 159.0, 155.9, 138.3, 130.3, 129.0, 128.3, 127.40, 127.36, 113.7, 97.8, 91.3, 77.3, 73.2, 72.8, 71.8, 63.9, 61.7, 55.2, 53.5, 43.3, 38.7, 30.2, 27.8, 24.2, 22.4, 22.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{31}H_{38}O_6Na$, 529.2566; found, 529.2570.

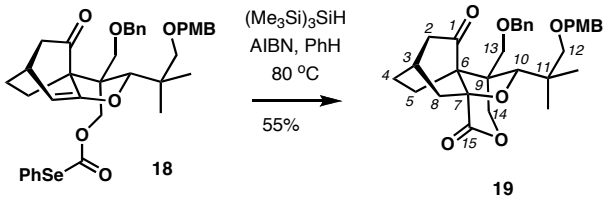


17 S2

Ester S2. A solution of the substrate **17** (0.140 g, 0.270 mmol) and carbonyldiimidazole (0.439 g, 2.70 mmol) in THF (13.5 mL) was heated at 40 °C for 2 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (pre-neutralized with 1% NEt_3 in hexanes, eluent: 30% ethyl acetate in hexanes) to deliver the product **S2** (0.140 g, 0.233 mmol, 86%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 8.09 (s, 1H), 7.39 (s, 1H), 7.31–7.26 (m, 2H), 7.25–7.21 (m, 3H), 7.19 (d, J=8.6 Hz, 2H), 7.04 (s, 1H), 6.85 (d, J=8.6 Hz, 2H), 5.34 (d, J=7.0 Hz, 1H), 4.74 (d, J=11.3 Hz, 1H), 4.64 (d, J=9.0 Hz, 1H), 4.60 (d, J=11.3 Hz, 1H), 4.49 (d, J=11.7 Hz, 1H), 4.40 (d, J=11.7 Hz, 1H), 4.38–4.25 (m, 3H), 3.80 (s, 3H), 3.56 (d, J=9.0 Hz, 1H), 3.26 (d, J=9.1 Hz, 1H), 3.13 (d, J=9.1 Hz, 1H), 2.93–2.88 (m, 1H), 2.18–2.07 (m, 2H), 1.94–1.83 (m, 2H), 1.82–1.75 (m, 1H), 1.59–1.49 (m, 1H), 1.00 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ 207.8, 159.1, 148.2, 138.2, 137.3, 130.7, 130.3, 129.0, 128.3, 127.52, 127.48, 117.2, 113.7, 98.3, 90.4, 77.0, 73.2, 72.8, 69.5, 67.9, 60.9, 55.2, 51.9, 42.8, 38.8, 30.0, 27.7, 23.3, 22.6, 21.7. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{35}H_{40}O_7N_2Na$, 623.2733; found, 623.2732.

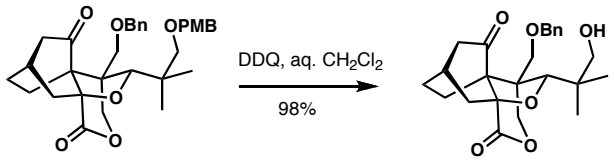


Selenocarbonate 18. Sodium borohydride (44.3 mg, 1.17 mmol) was added to a solution of PhSeSePh (0.364 g, 1.17 mmol) in DMF (11.7 mL) at 23 °C. After stirring for 10 min, the resulting solution was transferred via cannula to a flask containing the substrate **S2** (0.140 g, 0.233 mmol). After stirring for 3 h, the reaction mixture was diluted with 10% ethyl acetate in hexanes, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with 10% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (pre-neutralized with 1% NEt_3 in hexanes, eluent: 10% ethyl acetate in hexanes) to deliver the product **18** (0.127 g, 0.184 mmol, 79%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.61–7.57 (m, 2H), 7.42–7.30 (m, 5H), 7.29–7.25 (m, 3H), 7.20 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 5.24 (d, J=7.0 Hz, 1H), 4.68 (d, J=11.3 Hz, 1H), 4.52 (d, J = 11.7 Hz, 1H), 4.50 (d, J=8.9 Hz, 1H), 4.45 (d, J=11.3 Hz, 1H), 4.42–4.34 (m, 3H), 4.23 (s, 1H), 3.80 (s, 3H), 3.65 (d, J=8.9 Hz, 1H), 3.27 (d, J=8.9 Hz, 1H), 3.15 (d, J=8.9 Hz, 1H), 2.90–2.83 (m, 1H), 2.16–2.02 (m, 2H), 1.88–1.72 (m, 3H), 1.64–1.57 (m, 1H), 1.00 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 207.7, 166.8, 159.0, 155.5, 138.6, 135.8, 130.6, 129.2, 129.1, 128.9, 128.2, 127.3, 127.2, 125.8, 113.7, 97.7, 90.4, 77.4, 73.0, 72.7, 69.7, 67.4, 60.9, 55.2, 52.1, 43.1, 38.7, 29.9, 27.7, 23.3, 22.2, 21.5. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{38}H_{42}O_7{}^{76}SeNa$, 709.2020; found, 709.2015.



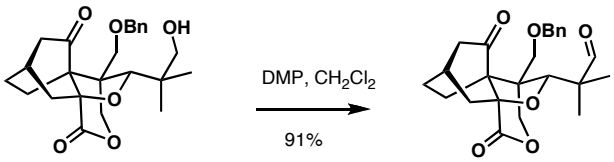
Lactone 19. A solution of AIBN (13.7 mg, 83.4 μmol) and tris(trimethylsilyl)silane (0.103 mL, 0.334 mmol) in benzene (5 mL) was added to a solution of the substrate **18** (0.115 g, 0.167 mmol) in benzene (2 mL) via a syringe pump over a period of 12 h at 80 °C. The resulting reaction mixture was stirred for additional 12 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (pre-neutralized with 1% NEt_3 in hexanes, eluent: 10–20% ethyl acetate in hexanes) to deliver the product **19** (49.0 mg, 91.7 μmol, 55%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.33 (t, J=7.3 Hz, 2H, CH_2*Ph*), 7.28 (d, J=7.3 Hz, 1H, CH_2*Ph*), 7.23–7.18 (m, 4H, CH_2*Ph*, $CH_2C_6H_4$OMe), 6.87 (d, J=8.6 Hz, 2H, $CH_2C_6H_4$OMe), 4.60 (d, J=11.9 Hz, 1H, *H*H-*14*), 4.57 (d, J=9.3 Hz, 1H, *H*H-*13*), 4.49 (dd, J1=1.1 Hz, J2=11.9 Hz, 1H, H*H*-*14*), 4.45 (d, J=11.8 Hz, 1H, C*H*HPh), 4.38–4.30 (m, 4H, CH*H*Ph, C*H*$_2$C$_6$H$_4$OMe, H-*10*), 3.81 (s, 3H, $CH_2C_6H_4O$*Me*), 3.49 (d, J=9.3 Hz, 1H, H*H*-*13*), 3.17 (d, J=9.2 Hz, 1H, *H*H-*12*), 3.07 (d, J=9.2 Hz, 1H, H*H*-*12*), 3.01 (ddd, J1=2.8 Hz, J2=4.3 Hz, J3=14.4 Hz, 1H, *H*H-*8*), 2.42–2.31 (m, 2H, H-*2*), 2.31–2.26 (m, 1H, H-*3*), 2.03–1.96 (m, 2H, H-*5*), 1.72–1.66 (m, 1H, *H*H-*4*), 1.64–1.53 (m, 2H, H*H*-*4*, H*H*-*8*), 0.98 (s, 3H, C*Me*Me), 0.95 (s, 3H, CMe*Me*). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm): 210.6 (C-*1*), 170.0 (C-*15*), 159.0 (*Ar*), 138.0 (*Ar*), 130.5 (*Ar*), 129.0 (*Ar*), 128.4 (*Ar*), 127.6 (*Ar*), 127.4 (*Ar*), 113.7 (*Ar*), 86.6 (C-*10*), 82.7 (C-*7*), 77.0 (C-*12*), 73.4 (*C*H_2Ph), 72.7 (C*H*$_2$C$_6$H$_4$OMe), 69.6 (C-*14*),

68.8 (C-*13*), 56.4 (C-*6*), 55.2 ($CH_2C_6H_4OMe$), 48.0 (C-*9*), 44.7 (C-*2*), 38.8 (C-*11*), 33.6 (C-*8*), 27.1 (C-*3*), 22.7 (C*Me*Me), 22.4 (C-*4*), 20.5 (CMe*Me*), 19.6 (C-*5*). HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{32}H_{38}O_7Na$, 557.2515; found, 557.2505.



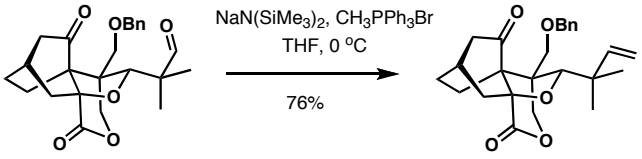
19 **S3**

Alcohol S3. DDQ (21.2 mg, 93.5 μmol) was added to a solution of the substrate **19** (25.0 mg, 46.8 μmol) in CH_2Cl_2 (2 mL) and H_2O (0.2 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic phase was sequentially washed with a saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (30% ethyl acetate in hexanes) to deliver the product **S3** (19.7 mg, 45.8 μmol, 98%). ^1H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.34 (t, J=7.2 Hz, 2H), 7.29 (t, J=7.2 Hz, 1H), 7.23 (d, J=7.2 Hz, 2H), 4.57 (d, J=12.1 Hz, 1H), 4.51 (dd, J1=1.1 Hz, J2=12.1 Hz, 1H), 4.470 (d, J=11.6 Hz, 1H), 4.467 (d, J=9.5 Hz, 1H), 4.39 (d, J=11.6 Hz, 1H), 4.34 (d, J=1.1 Hz, 1H), 3.63 (d, J=9.5 Hz, 1H), 3.38-3.31 (m, 2H), 3.04 (ddd, J1=2.8 Hz, J2=4.3 Hz, J3=14.5 Hz, 1H), 2.43-2.33 (m, 2H), 2.32-2.28 (m, 1H), 2.06-1.93 (m, 3H), 1.74-1.67 (m, 1H), 1.65-1.58 (m, 2H), 1.01 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$); δ(ppm): 210.5, 169.5, 137.7, 128.4, 127.8, 127.5, 87.9, 83.0, 73.5, 72.7, 69.5, 68.9, 56.4, 48.2, 44.7, 39.0, 33.5, 27.1, 22.6, 20.4, 20.1, 19.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{24}H_{30}O_6Na$, 437.1940; found, 437.1927.



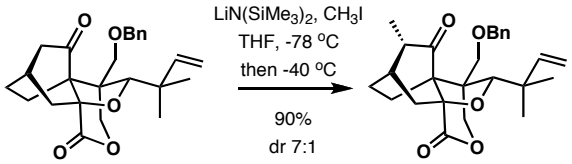
S3 **S4**

Aldehyde S4. Sodium bicarbonate (0.104 g, 1.24 mmol) and Dess-Martin periodinane (0.132 g, 0.311 mmol) were added sequentially to a solution of alcohol **S3** (82.0 mg, 0.198 mmol) in CH_2Cl_2 (10 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution, and extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to deliver the product **S4** (74.1 mg, 0.180 mmol, 91%). ^1H NMR (600 MHz, $CDCl_3$); δ (ppm): 9.61 (s, 1H), 7.34 (*virt.* t, J=7.2 Hz, 2H), 7.29 (t, J=7.3 Hz, 1H), 7.21 (d, J=7.1 Hz, 2H), 4.46-4.41 (m, 4H), 4.37 (d, J=11.7 Hz, 1H), 4.22 (d, J=12.3 Hz, 1H), 3.51 (d, J=9.4 Hz, 1H), 3.04 (ddd, J1=2.4 Hz, J2=4.3 Hz, J3=14.5 Hz, 1H), 2.44-2.34 (m, 2H), 2.33-2.30 (m, 1H), 2.03-1.94 (m, 2H), 1.75-1.67 (m, 1H), 1.66-1.56 (m, 2H), 1.19 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm): 210.4, 203.9, 169.0, 137.5, 128.4, 127.8, 127.5, 88.6, 83.2, 73.6, 68.9, 68.5, 56.5, 48.7, 48.2, 44.7, 33.1, 27.0, 22.4, 22.2, 19.4, 18.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{24}H_{28}O_6Na$, 435.1784; found, 435.1769.



S4 20

Alkene 20. A solution of $NaN(SiMe_3)_2$ (0.3 mL, 0.6 M in toluene, 0.180 mmol) was added to a suspension of CH_3PPh_3Br (70.1 mg, 0.196 mmol) in THF (2 mL) at 0 °C. After stirring at the same temperature for 15 min, the resulting reaction mixture was transferred to a solution of aldehyde **S4** (18.4 mg, 44.6 μmol) in THF (1 mL) at 0 °C. After stirring for 0.5 h, the reaction was quenched with a saturated aqueous NH_4Cl solution and extracted with 20% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to deliver the product **20** (14.0 mg, 34.1 μmol, 76%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.33 (t, J=7.3 Hz, 2H), 7.28 (t, J=7.3 Hz, 1H), 7.21 (d, J=7.3 Hz, 1H), 5.96 (dd, J1=10.8 Hz, J2=17.6 Hz, 1H), 5.07 (dd, J1=0.9 Hz, J2=17.6 Hz, 1H), 5.04 (d, J=10.8 Hz, 1H), 4.509 (d, J=9.3 Hz, 1H), 4.507 (d, J=11.7 Hz, 1H), 4.46 (d, J=11.7 Hz, 1H), 4.37 (dd, J1=1.5 Hz, J2=11.7 Hz, 1H), 4.36 (d, J=11.7 Hz, 1H), 4.14 (d, J=1.5 Hz, 1H), 3.44 (d, J=9.3 Hz, 1H), 3.05 (ddd, J1=2.6 Hz, J2=4.5 Hz, J3=14.4 Hz, 1H), 2.43–2.32 (m, 2H), 2.31–2.27 (m, 1H), 2.03–1.92 (m, 2H), 1.72–1.64 (m, 1H), 1.63–1.56 (m, 2H), 1.08 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm): 210.8, 169.8, 142.8, 137.9, 128.4, 127.6, 127.4, 112.2, 89.4, 82.8, 73.5, 69.2, 68.5, 56.3, 48.2, 44.7, 40.2, 33.5, 27.1, 26.3, 24.7, 22.6, 19.6. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{25}H_{30}O_5Na$, 433.1991; found, 433.1983.



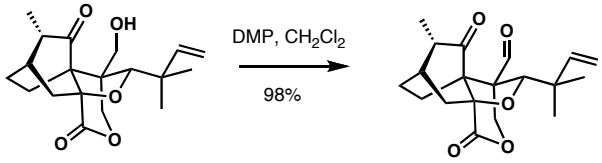
20 21

Alkene 21. A solution of $LiN(SiMe_3)_2$ (0.350 mL, 1.0 M in toluene, 0.350 mmol) was added to a solution of the substrate **20** (47.0 mg, 0.114 mmol) in THF (10 mL) at –78 °C. After stirring at that temperature for 15 min, iodomethane (30 μL, 0.482 mmol) was added. The reaction mixture was stirred at –78 °C for 1 h, then at –40 °C for 4 h. The reaction was quenched with a saturated aqueous NH_4Cl solution and extracted with 20% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to deliver the product **21** as an inseparable mixture of diastereomers (43.7 mg, 0.103 mmol, 90%, dr = 7:1). **Major isomer:** ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.35–7.27 (m, 3H), 7.21 (d, J=6.7 Hz, 2H), 5.96 (dd, J1=10.8 Hz, J2=17.6 Hz, 1H), 5.07 (dd, J1=1.2 Hz, J2=17.6 Hz, 1H), 5.04 (dd, J1=1.2 Hz, J2=10.8 Hz, 1H), 4.52 (d, J=9.2 Hz, 1H), 4.50 (d, J=11.7 Hz, 1H), 4.43 (d, J=11.5 Hz, 1H), 4.38–4.34 (m, 2H), 4.08 (d, J=1.2 Hz, 1H), 3.45 (d, J=9.2 Hz, 1H), 3.10 (dd, J1=4.7 Hz, J2=14.4 Hz, 1H), 2.33–2.27 (m, 1H), 2.08–2.04 (m, 1H), 2.03–1.85 (m, 2H), 1.84–1.76 (m, 1H), 1.65–1.59 (m, 1H), 1.53–1.47 (m, 1H), 1.21 (d, J=7.6 Hz, 3H), 1.07 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 213.8, 170.0, 142.8, 137.9, 128.3, 127.7, 127.6, 112.2, 89.3, 82.4, 73.5, 69.4, 68.5, 56.8, 48.5, 48.3,

40.2, 35.0, 32.3, 26.3, 24.7, 19.4, 18.3, 15.5. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{32}O_5Na$, 447.2147; found, 447.2138.

21 **S5**

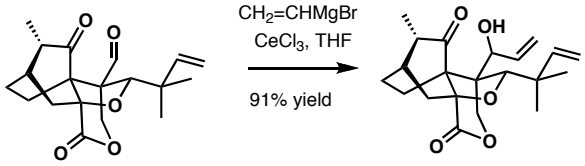
Alcohol S5. DDQ (0.112 g, 0.495 mmol) was added to a solution of the substrate **21** as a mixture of diastereomers (21.0 mg, 49.5 μmol, dr = 7:1) in CH_2Cl_2 (2 mL) and H_2O (0.2 mL). The flask was sealed and heated at 50 °C for 11.5 h. After cooling, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic phase was sequentially washed with a saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (30% ethyl acetate in hexanes) to deliver the product **S5** as a single diastereomer (13.3 mg, 39.8 μmol, 80%), together with recovered starting material **21** as a mixture of the diastereomers (2.6 mg, 6.12 μmol, dr = 10:1, 12%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.03 (dd, J1=10.8 Hz, J2=17.6 Hz, 1H), 5.10 (dd, J1=1.0 Hz, J2=17.6 Hz, 1H), 5.06 (dd, J1=1.0 Hz, J2=10.8 Hz, 1H), 4.51 (d, J=11.8 Hz, 1H), 4.09 (d, J=1.5 Hz, 1H), 4.01 (dd, J1=1.5 Hz, J2=11.8 Hz, 1H), 3.95 (dd, J1=8.3 Hz, J2=12.1 Hz, 1H), 3.58 (dd, J1=4.6 Hz, J2=12.1 Hz, 1H), 3.30 (dd, J1=4.6 Hz, J2=8.3 Hz, 1H), 3.14 (dd, J1=4.6 Hz, J2=14.6 Hz, 1H), 2.40-2.34 (m, 1H), 2.13-2.09 (m, 1H), 1.98-1.85 (m, 2H), 1.74 (ddd, J1=7.9 Hz, J2=10.9 Hz, J3=14.8 Hz, 1H), 1.67 (*virt.* dt, J1=1.8 Hz, J2=14.6 Hz, 1H), 1.60-1.56 (m, 1 H), 1.23 (d, J=7.5 Hz, 3H), 1.09 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 217.7, 169.7, 143.0, 112.3, 87.7, 82.1, 67.8, 61.2, 58.1, 48.9, 48.7, 40.4, 35.1, 32.7, 25.7, 25.0, 19.3, 18.2, 15.5. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{26}O_5Na$, 357.1678; found, 357.1669.



S5 **S6**

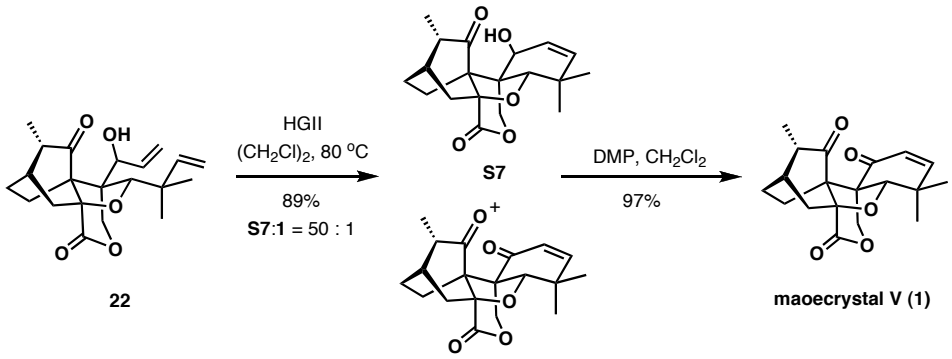
Aldehyde S6. Sodium bicarbonate (6.8 mg, 80.7 μmmol) and Dess-Martin periodinane (11.4 mg, 26.9 μmol) were added sequentially to a solution of alcohol **S5** (3.0 mg, 8.97 μmol) in CH_2Cl_2 (0.450 mL) at 23 °C. After stirring for 2 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution, extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to deliver the product **S6** (2.9 mg, 8.72 μmol, 98%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 10.23 (s, 1H), 5.99 (dd, J1=10.8 Hz, J2=17.4 Hz, 1H), 5.14 (d, J=17.4 Hz, 1H), 5.12 (d, J=10.8 Hz, 1H), 4.59 (d, J=12.1 Hz, 1H), 4.56 (d, J=1.3 Hz, 1H), 4.49 (dd, J1=1.3 Hz, J2=12.1 Hz, 1H), 3.07 (dd, J1=4.4 Hz, J2=14.8 Hz, 1H), 2.42 (q, J=7.4 Hz, 1H), 2.16-2.12 (m, 1H), 2.04-1.97 (m, 1H), 1.95-1.88 (m, 1H), 1.81 (*virt.* dt, J=2.0 Hz, J2=14.8 Hz, 1H), 1.66 (ddd, J1=7.4 Hz, J2=11.0 Hz, J3=14.5 Hz, 1H), 1.61-1.57 (m, 1H), 1.19 (d, J=7.4 Hz, 3H), 1.14 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$); δ (ppm):

213.8, 198.3, 168.6, 141.6, 113.6, 87.8, 83.0, 67.0, 65.7, 55.8, 47.8, 40.3, 34.7, 33.0, 26.3, 24.5, 18.4, 18.2, 14.9. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{24}O_5Na$, 355.1521; found, 355.1522.



S6 **22**

Allylic alohol 22. A suspension of dry $CeCl_3$ (65.1 mg, 0.264 mmol)[1] in THF (1 mL) was stirred at 23 °C for 2 h. Vinylmagnesium bromide (0.3 mL, 0.88 M in THF, 0.264 mmol) was added to the above suspension at -78 °C. After stirring at the same temperature for 1 h, a solution of the substrate **S6** (10.0 mg, 30.1 μmol) in THF (2 mL) was added. After stirring for further 1 h at -78 °C, the reaction mixture was diluted with hexanes, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with 50% ethyl acetate in hexanes. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to deliver the product **22** as a single isomer with unknown configuration (9.9 mg, 27.5 μmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.21 (dd, J1=10.8 Hz, J2=17.6 Hz, 1H), 5.75-5.66 (m, 2H), 5.22 (d, J=17.0 Hz, 1H), 5.18-5.11 (m, 2H), 5.08 (dd, J1=1.3 Hz, J2=10.8 Hz, 1H), 4.63 (d, J=11.8 Hz, 1H), 4.46 (d, J=1.9 Hz, 1H), 4.07 (dd, J1=1.9 Hz, J2=11.8 Hz, 1H), 3.83 (dd, J1=6.7 Hz, J2=11.9 Hz, 1H), 3.15 (dd, J1=4.7 Hz, J2=14.4 Hz, 1H), 2.42-2.35 (m, 1H), 2.13-2.08 (m, 1H), 1.90-1.80 (m, 2H), 1.79-1.71 (m, 1H), 1.63-1.58 (m, 1H), 1.55-1.49 (m, 1H), 1.23 (d, J=7.5 Hz, 3H), 1.21 (s, 3H), 1.14 (s, 3H). .^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 218.3, 169.2, 143.4, 137.0, 116.7, 111.9, 86.0, 82.4, 71.9, 67.7, 58.8, 51.3, 48.5, 40.9, 35.2, 32.1, 25.9, 24.9, 19.6, 18.3, 15.7. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{21}H_{28}O_5Na$, 383.1834; found, 383.1836.



22 **1** **maoecrystal V (1)**

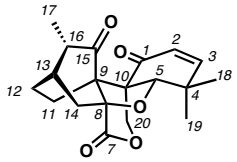
Cyclohexenol S7. A solution of Hoveyda-Grubbs second generation catalyst (2.9 mg, 4.63 μmol) in degassed $ClCH_2CH_2Cl$ (1 mL) was added to substrate **22** (8.4 mg, 23.3 μmol). The flask was sealed, and the mixture was heated at 80 °C for 2 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to deliver a mixture of **S7** and **1** (6.9 mg, 20.8 μmol, **S7:1** = 50:1). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.07 (brs, 1H), 5.48 (dd, J1=2.3 Hz, J2=10.2 Hz,

[1] Prepared as in : Zakarian, A.; Batch, A.; Holton, R. A. *J. Am. Chem. Soc.* **2003**, 125, 7822–7824.

1H), 5.41 (dd, J1=1.5 Hz, J2=10.2 Hz, 1H), 4.67 (d, J=12.6 Hz, 1H), 4.52 (dd, J1=1.6 Hz, J2=12.6 Hz, 1H), 4.11 (d, J=1.6 Hz, 1H), 3.23 (dd, J1=4.8 Hz, J2=14.4 Hz, 1H), 2.36–2.29 (m, 1H), 2.16–2.08 (m, 2H), 1.96–1.89 (m, 1H), 1.88–1.79 (m, 1H), 1.74–1.60 (m, 3H), 1.24 (d, J = 7.5 Hz, 3H), 1.11 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 216.1, 169.9, 136.5, 128.0, 86.5, 84.1, 67.2, 67.1, 53.7, 49.3, 47.5, 36.6, 35.0, 32.5, 31.3, 20.1, 19.2, 18.2, 15.8. LRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{24}O_5Na$, 355.2; found 355.1.

Maoecrystal V. Sodium bicarbonate (18.5 mg, 0.220 mmmol) and Dess-Martin periodinane (23.4 mg, 55.2 μmol) were added sequentially to a solution of the above mixture (6.1 mg, 18.4 μmol) in CH_2Cl_2 (1 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution, extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated and the residue was purified by preparative thin-layer chromatography (20% ethyl acetate in hexanes) to deliver maoecrystal V (5.9 mg, 3.03 μmol, 97%). ^{1}H NMR (600 MHz, **$CDCl_3$**); δ (ppm): 6.66 (d, J=10.2 Hz, 1H), 5.96 (d, J=10.2 Hz, 1H), 4.63 (d, J=12.2 Hz, 1H), 4.43 (d, J=1.2 Hz, 1H), 4.13 (dd, J1=1.2 Hz, J2=12.2 Hz, 1H), 3.19 (dd, J1=4.7 Hz, J2=14.6 Hz, 1H), 2.37–2.29 (m, 1H), 2.18–2.03 (m, 3H), 2.01–1.94 (m, 1H), 1.72–1.67 (m, 1H), 1.67–1.61 (m, 1H), 1.30 (s, 3H), 1.26 (d, J=7.4 Hz, 3H), 1.23 (s, 4H). ^{13}C NMR (201 MHz, **$CDCl_3$**); δ (ppm): 211.5, 194.8, 169.1, 156.7, 127.0, 84.9, 84.1, 69.2, 56.6, 51.9, 48.3, 38.3, 34.5, 32.6, 30.6, 18.54, 18.52, 18.0, 15.1. ^{1}H NMR (600 MHz, **d_5-pyridine**); δ (ppm): 6.54 (d, J=10.1 Hz, 1H), 5.99 (d, J=10.1 Hz, 1H), 4.73 (d, J=12.4 Hz, 1H), 4.66 (s, 1H), 4.32 (d, J=12.4 Hz, 1H), 3.28 (dd, J1=4.7 Hz, J2=14.4 Hz, 1H), 2.31 (q, J=7.4 Hz, 1H), 2.20–2.09 (m, 2H), 1.91–1.84 (m, 1H), 1.77 (d, J=14.4 Hz, 1H), 1.76–1.70 (m, 2H), 1.52–1.44 (m, 1H), 1.22 (s, 3H), 1.09 (d, J=7.4 Hz, 3H), 1.06 (s, 3H). ^{13}C NMR (201 MHz, **d_5-pyridine**); δ (ppm): 211.8, 194.8, 169.5, 156.7, 127.3, 85.5, 84.7, 69.5, 57.0, 52.4, 48.4, 38.3, 34.9, 32.9, 30.5, 18.7, 18.4, 18.3, 15.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{22}O_5Na$, 353.1365; found, 353.1360.

Table 1. Comparison of ^{1}H NMR Data of Synthetic and Reported Maoecrystal V (d_5-Pyridine)

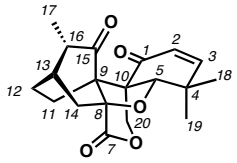


1

position	synthetic **1** (600 MHz)	reported for natural **1** (400 MHz)[2]
2	6.54 (d, J=10.1 Hz, 1H)	6.54 (d, J=10.3 Hz, 1H)
3	5.99 (d, J=10.1 Hz, 1H)	5.99 (d, J=10.3 Hz, 1H)
20a	4.73 (d, J=12.4 Hz, 1H)	4.73 (d, J=12.3 Hz, 1H)
5β	4.66 (s, 1H)	4.66 (s, 1H)
20b	4.32 (d, J=12.4 Hz, 1H)	4.32 (d, J=12.3 Hz, 1H)
14β	3.28 (dd, J=4.7,14.4 Hz, 1H)	3.28 (dd, J=4.8,14.1 Hz, 1H)
16α	2.31 (q, J=7.4 Hz, 1H)	2.31 (m, 1H)
11	2.20-2.09 (m, 2H)	2.14 (m, 2H)
13α	1.91-1.84 (m, 1H)	1.88 (m, 1H)
14α	1.77 (d, J=14.4 Hz, 1H)	1.77 (d, J=14.1 Hz, 1H)
12β	1.76-1.70 (m, 2H)	1.73 (m, 2H)
12α	1.52-1.44 (m, 1H)	1.48 (m, 1H)
19	1.22 (s, 3H)	1.21 (s, 3H)
17	1.09 (d, J=7.4 Hz, 3H)	1.09 (d, J=7.3 Hz, 3H)
18	1.06 (s, 3H)	1.04 (s, 3H)

[2] Li, S. H.; Niu, X. M.; Shen, Y. H.; Zhang, H. J.; Sun, H. D.; Li, M. L.; Tian, Q. E.; Lu, Y.; Cao, P.; Zhang, Q. T. *Org. Lett.* **2004**, *6*, 4327–4330.

Table 2. Comparison of ^{13}C NMR Data of Synthetic and Reported Maoecrystal V (d_5-Pyridine)



1

position	synthetic **1** (201 MHz)	reported for natural **1** (100 MHz)[2]
15	211.8	211.7
1	194.8	194.8
7	169.5	169.5
3	156.7	156.7
2	127.3	127.2
5	85.5	85.5
8	84.7	84.6
20	69.5	69.5
9	57.0	56.9
10	52.4	52.4
16	48.4	48.3
4	38.3	38.3
14	34.9	34.9
13	32.9	32.9
18	30.5	30.4
11	18.7	18.7
19	18.4	18.4
12	18.3	18.2
17	15.0	15.0

[2] Li, S. H.; Niu, X. M.; Shen, Y. H.; Zhang, H. J.; Sun, H. D.; Li, M. L.; Tian, Q. E.; Lu, Y.; Cao, P.; Zhang, Q. T. *Org. Lett.* **2004**, *6*, 4327–4330.